STUDIES OF NOVEL DIAZANAPHTHOQUINONES
AND
ION-RESPONSIVE FLUORESCENT QUINOXALINE DERIVATIVES

Thesis Submitted for the Degree

of

Doctor of Philosophy

by

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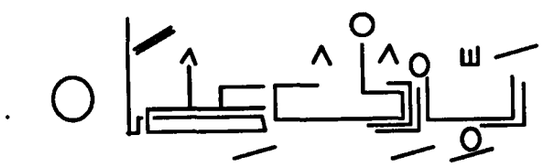

(Rabbi zid-nee ilmaa)

O my Lord, increase me in knowledge.

(Al-Quran, 20: 115)

Dedicated
to
my

Abba Je (Late) *Mian Rafiq Ahmad*
and
Ammi Je *Naziran Begum*

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Last but not least, I would like to thank my elder sister and brother and their families in London, who tolerated me and my continuous talk about my thesis towards the end of this work.

ABSTRACT

The work reported is divided into two parts: firstly a section dealing with the preparation of some novel diazanaphthoquinones and their reactions, especially the Diels-Alder reaction, and secondly an account of some quinoxaline derivatives and their fluorescence properties.

Quinoxaline quinones containing electron-donating groups at both the 2- and 3-position have shown a difference in their stability and their behaviour in the Diels-Alder reaction compared to the stability and the reactions of quinoxaline quinone. Symmetrical dienes in the Diels-Alder reaction yielded the initial addition products, which were resistant to oxidation, whereas unsymmetrical dienes produced fully aromatized products. Crown ether derivatives of 5,8-dimethoxyquinoxaline and the corresponding quinoxaline quinones were prepared.

An improved method for the preparation of a fluorescent derivatising reagent is described. This compound was then used to prepare ion-responsive fluoroionophores containing monoazacrown ethers of different cavity sizes. The complexation of these fluoroionophores, in dichloromethane, was achieved by using perchlorates of alkali and alkaline earth metals. A strong correlation between the size of the metal ion and the cavity size of the crown ether was seen in the fluorescence quantum yields of the complex, and a fluoroionophore containing a diazacrown ether gave particularly noteworthy results. A bathochromic shift with a strong hyperchromic effect was the most important feature caused by complexation with metal ions for these fluoroionophores.

Fluorescent open chain ethers (podands) were also prepared and their complexation with metal ions was studied. A strong bathochromic shift and a hypochromic effect was observed especially in their excitation spectra.

A further novel fluorescent derivatising reagent was prepared by extending the conjugated system. This gave the expected improved results upon the preparation of the derivatives including fluoroionophores having crown ethers of different cavity sizes. However, the changes in fluorescence did not correlate with the relationship between the sizes of the metals ion and the cavity of the crown ether. Nevertheless, a large bathochromic shift was observed on complexation with metal ions.

CONTENTS

CHAPTER 1

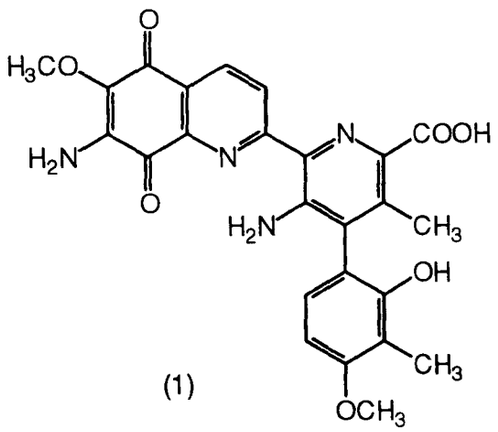
STUDIES OF SOME NOVEL DIAZANAPHTHOQUINONES

INTRODUCTION

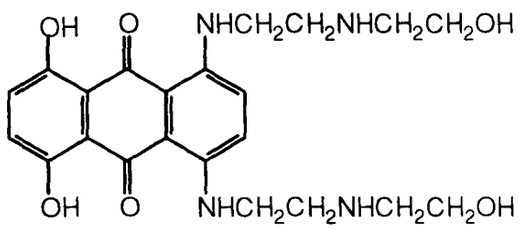
1. HETEROCYCLIC QUINONES

The quinone moiety is found commonly in nature. Compounds containing the quinone nucleus play an important role in numerous biological processes due to their participation in reduction-oxidation processes.[1] Some heterocyclic quinones have chemotherapeutic value as antitumour, antibacterial and antifungal agents.[2]

Streptonigrin (1) is a heterocyclic quinone which exhibits pronounced antitumour activity[3] and these effects have been proved to be due to the 7-amino-5,8-quinolinedione moiety.[4] In order to investigate the role of the heterocyclic nucleus in the antitumour activity, a comparative study of structural analogues of benzoquinolinediones,[5] quinazolinediones,[6] acridine-1,4-diones,[7] benzimidazole-4,7-dione[8] and quinoxaline-5,8-diones[9] has been made by different workers. Among other substituents, the presence of



(1)



(2)

the aziridinyl group on the quinazoline-5,8-dione[6,10] nucleus or the [(dialkylamino)alkyl]amino side chain at the 1-position on isoquinoline,[11] or both substituents in the same molecule[12] displays a relatively high antitumour activity.

Mitoxantrone (2) and related anthraquinones are of special interest in cancer chemotherapy. This compound has been shown to intercalate[13] and, on the basis of a theoretical model[14] for intercalation, it was predicted that the azaanthraquinone analogues of (2) would be very effective intercalants. The study of such compounds as potential antitumour agents is thus of considerable interest.[15]

1.1 Methods of Preparation

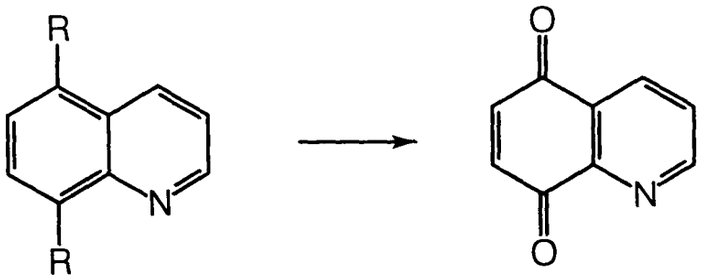
Heterocyclic quinones have been prepared by using one of the following general methods:-

(i) the oxidation of the heteroaromatic compounds, and

(ii) cyclisation or addition reactions

1.1.1 Oxidation of the Heteroaromatic Compound

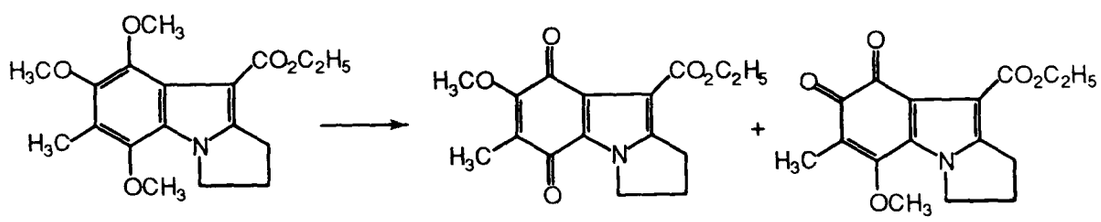
Various strong oxidising agents such as dichromates,[16] nitric acid[17] or nitrous acid[18] have been used for the preparation of *o*- and *p*-quinones. Dichromates have been found effective for the oxidation of *o*-dimethoxy and *p*-dimethoxy compounds whereas nitric acid oxidises the 5,8-dihydroxy- (3) and 5,8-diamino-quinoline (4) to *p*-quinones (5).[17]



(3) R = OH
(4) R = NH_2

(5)

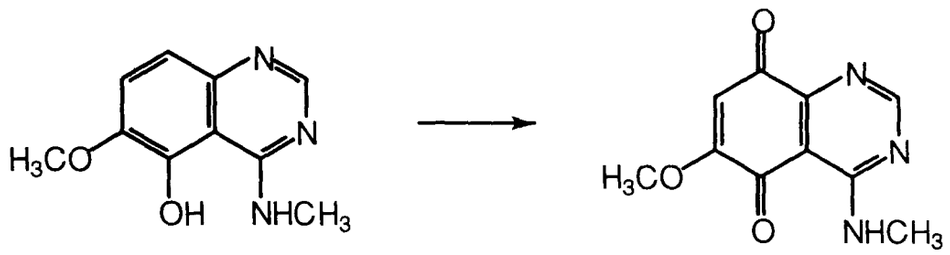
Nitrous acid has been used to obtain the mitosene derivative (7) by the oxidative demethylation of 4,5,7-trimethoxyindole derivative (6).[18] A small quantity of *o*-quinone derivative (8) is also formed. The possible disadvantage of using a strongly acidic



(6) (7) (8)

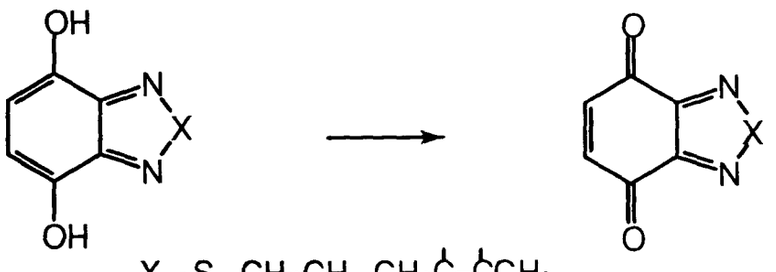
oxidising agent is the formation of byproducts, such as nitro derivatives when nitric acid[19] is used and oxidative coupling reaction products when dichromates[20] are employed. This is due to the electron-releasing properties of hydroxy, amino and alkoxy groups.

Mild oxidising agents, which allow the survival of other oxidation sensitive structural features while permitting demethylation, include Fremy's salt,[20] silver oxide[21] and ceric ammonium nitrate.[22]



(9) (10)

Fremy's salt (dipotassium nitrosodisulphonate, $O\text{-}N(SO_3K)_2$ is a particularly effective reagent for the oxidation of aromatic rings containing only one alkoxy, hydroxy or amino group.[20] For instance, 7-hydroxyindoles and 4-aminoindoles are converted into the corresponding 4,7-quinones.[23] Similarly, 4-methylamino-5-hydroxy-6-methoxyquinazoline (9) give the *p*-quinone, 4-methylamino-6-methoxy-5,8-quinoazolinedione (10).[24] The second oxygen of the *p*-quinone is shown to come from the oxygen labelled Fremy's salt via a free radical mechanism.[25] The inconvenient procedure and the lack of stability of the reagent are its major disadvantages.[20]

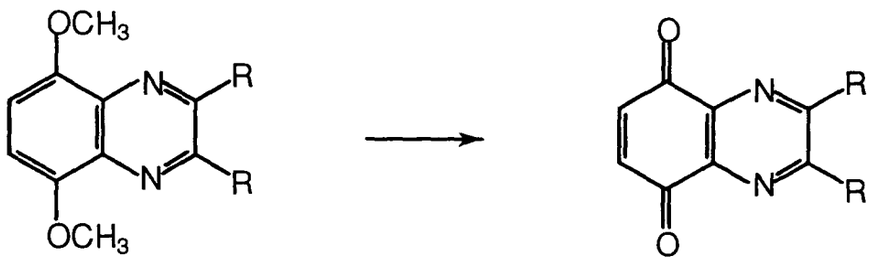


X = S, -CH=CH-, $CH_3\overset{\overset{|}{C}}{=}\overset{\overset{|}{C}}{C}CH_3$

(11) (12)

Silver(1) oxide has been used to convert 1,4-dihydroxy compounds (11) into *p*-quinones (12).[21,26] Rapoport *et al.*[27] used nitric acid and silver(I) oxide as a combination of reagents causing ether splitting and oxidation in a one-pot process. The suggested mechanism for the formation of the *p*-quinone involves the cleavage of the aryl-oxygen bond.[28]

Cerium(IV) ammonium nitrate (CAN) is cheaper, and is a multi-electron oxidant,[29] which has been used extensively for the fast and convenient preparation of quinones from dihydroxy[30,31] and dimethoxy compounds.[32,33,34] For instance, 5,8-dimethoxyquinoxalines (13) were oxidatively demethylated with CAN in aqueous acetonitrile to afford the corresponding 5,8-quinoxalinedione (14) in 49-70% yield.[35] Acetic acid has also been used instead of acetonitrile in order to overcome the solubility problems associated with some substrates.[36]

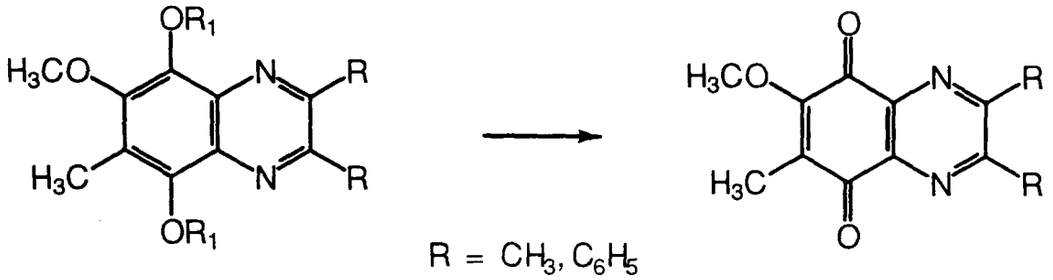


R = H, CH_3, C_6H_5

(13) (14)

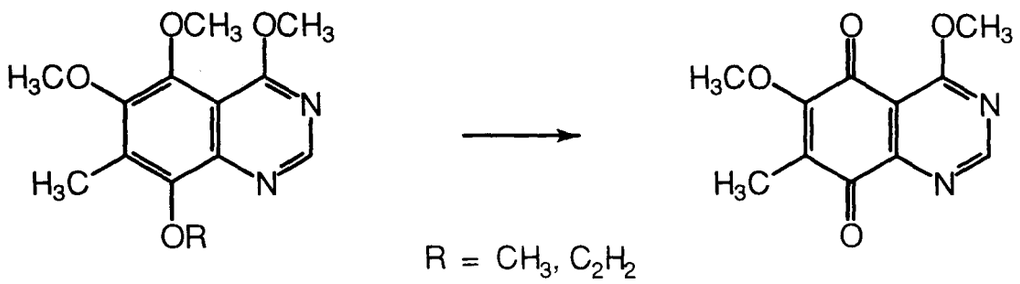
Recently, Kitahara *et al.*[37] reported the facile formation of *p*-quinones (16) and (18) from (15) and (17), respectively in 68-75% yield. A possible complicating factor is the formation of a nitro-derivative on an unsubstituted position rather than, or in addition to, quinone formation.[38] The mechanism of oxidation involves the cerium (IV) ion with aryl-oxygen bond cleavage.[32,34,39]

Ferric chloride, in the presence of hydrochloric acid and manganese dioxide, has also been used for the preparation of different substituted quinones (22)-(24) from the corresponding substituted quinoxalines (19)-(21). The latter were obtained by the reaction of 1,2-bis-(2-pyridyl)ethane-1,2-dione with suitably substituted benzene-1,2-diamines.[40]



R = CH_3, C_6H_5
R_1 = CH_3, C_2H_5

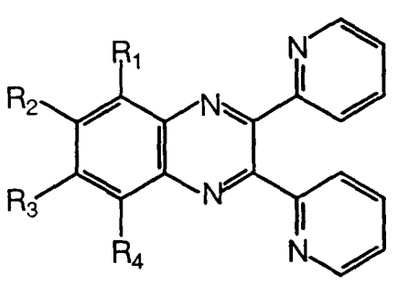
(15) (16)



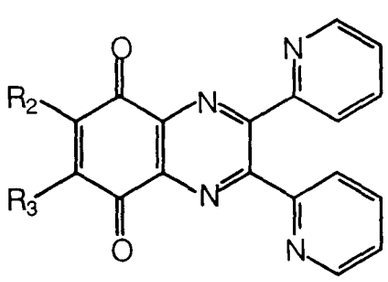
R = CH_3, C_2H_2

(17) (18)

Other oxidising agents such as lead tetraacetate,[41] benzoyl-*tert*-butyl nitroxide,[42] sodium metaperiodate,[43] and nitronium tetrafluoroborate[44] have also proved effective reagents for the preparation of heterocyclic quinones.



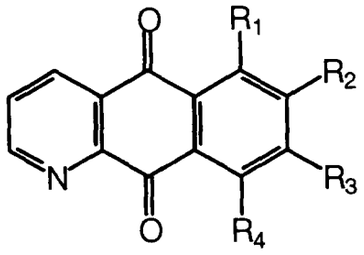
(19) $R_1 = R_2 = H$; $R_3 = CH_3$; $R_4 = NH_2$
(20) $R_1 = R_2 = H$; $R_3 = OCH_3$; $R_4 = NH_2$
(21) $R_1 = R_4 = NH_2$; $R_2 = R_3 = CH_3$



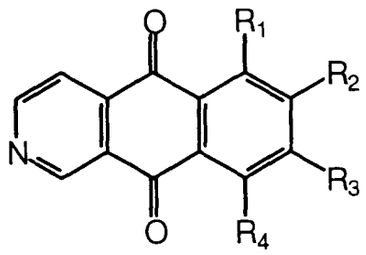
(22) $R_3 = CH_3$; $R_2 = H$
(23) $R_3 = OCH_3$; $R_2 = H$
(24) $R_2 = R_3 = CH_3$

1.1.2 Cyclisation or Addition Reactions

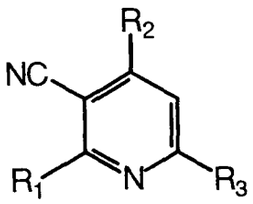
The main application of these methods have been in the formation of more extended heterocyclic quinones.[38] The approach has been used in the synthesis of benzoquinoline-, isoquinoline-, quinoxaline-, thiophene- and indole-quinones. For instance, dihydroxy-1- and 2-azaanthraquinones (25) and (26) have been obtained by the action of quinolinic anhydride or cinchomeronic anhydride on 1,4-dimethoxybenzene under Friedel-Crafts conditions.[45]



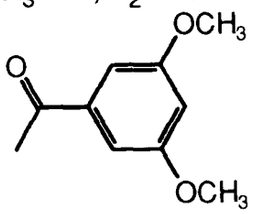
(25) $R_1 = R_4 = OH; R_2 = R_3 = H$
(27) $R_1 = R_3 = OCH_3; R_2 = R_4 = H$



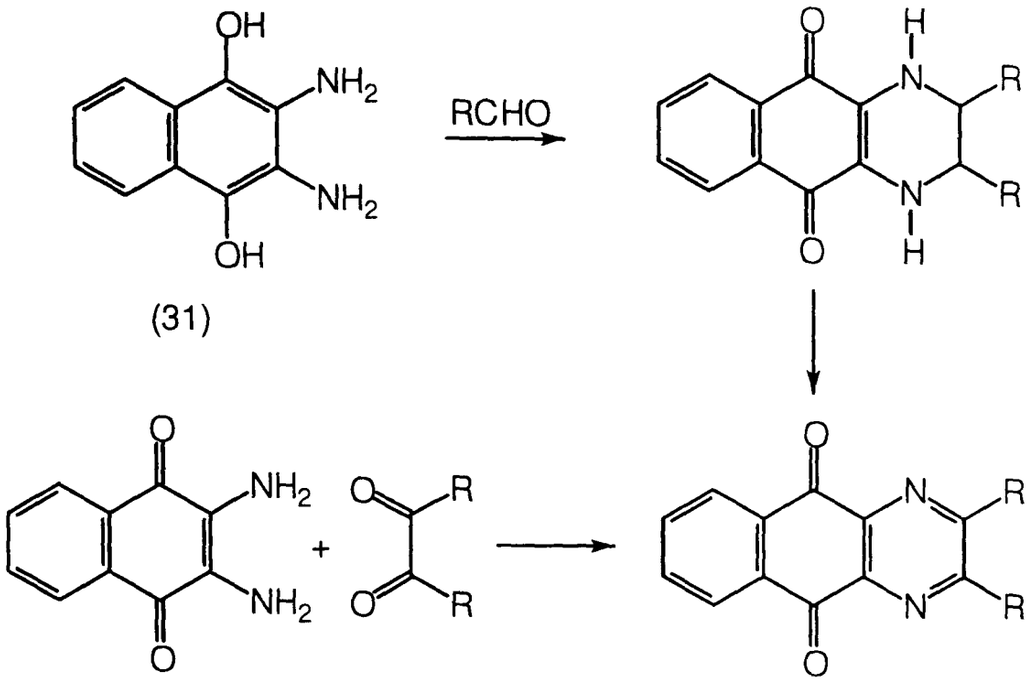
(26) $R_1 = R_4 = OH; R_2 = R_3 = H$
(28) $R_2 = R_4 = OCH_3; R_1 = R_3 = H$



(29) $R_2 = R_3 = H; R_1 = X$
(30) $R_1 = R_3 = H; R_2 = X$

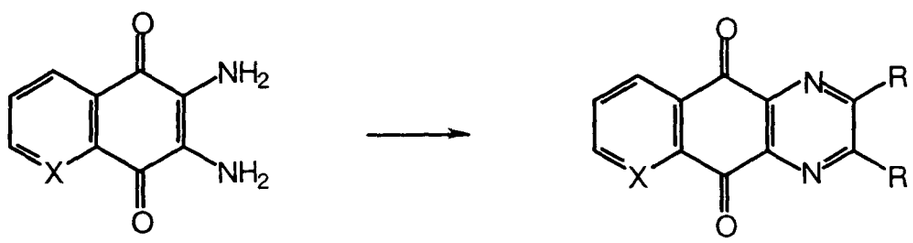
Where X = 

Similarly, dimethoxy-1- and -2-azaanthraquinone (27) and (28) have been obtained by the cyclisation of the cyano-compounds (29) and (30).[45] Substituted benzoquinoxaline quinone (33) has been prepared by the condensation of (31) with aromatic aldehydes and subsequent oxidation of the product.[46] Compound (33) was also prepared by the condensation of 1,2-diamino-1,4-naphthalenedione with benzil[46] (Scheme 1).



Scheme 1

Renault *et al.* have obtained different substituted benzo- and pyridino-quinoxaline quinones, (35) and (36), by the condensation of (32) and 6,7-diaminoquinoline quinone (34), respectively, with different α,β-diketones[47] (Scheme 2).

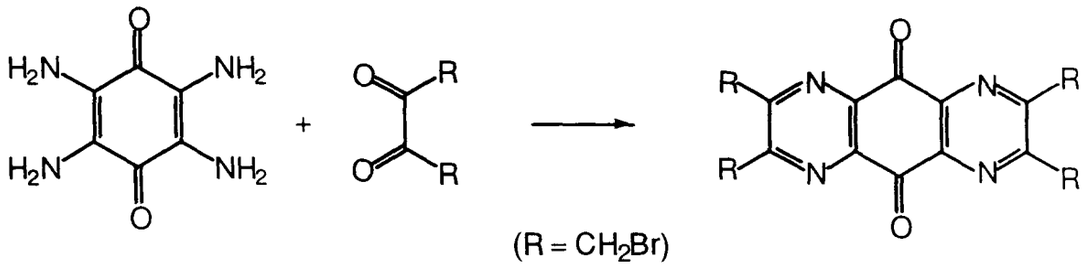


(32) X = CH
(34) X = N

(35) X = CH
(36) X = N

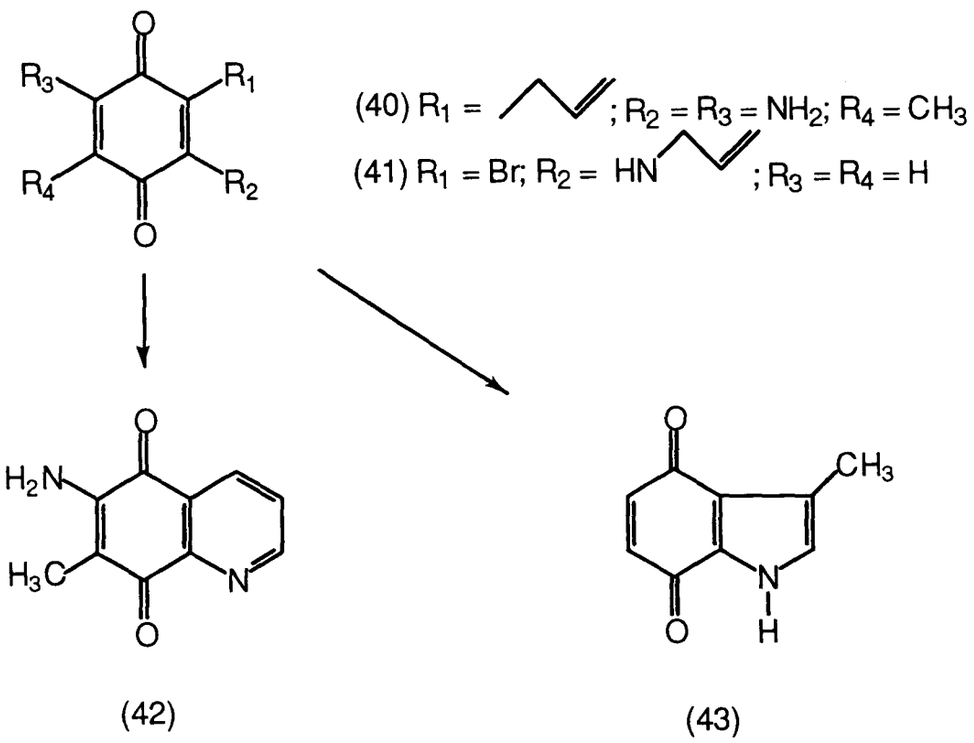
Scheme 2

The same workers obtained the5,10-pyrazino[2,3-g]quinoxalinedione (39) by the condensation of 2,3,5,6-tetraaminobenzoquinone (37) with 1,4-dibromobutanedione (38).[47]



(37) (38) (39)

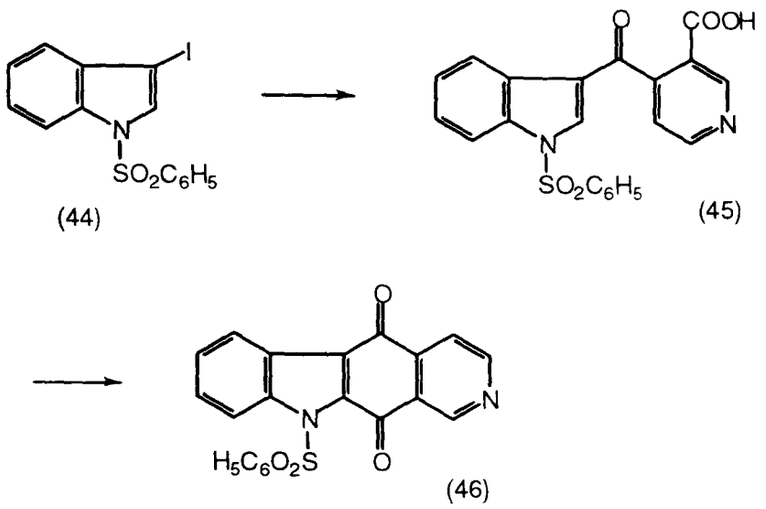
The quinoline quinone (42)[48] and indole-quinone (43)[49] have been obtained by cyclisation of suitably substituted benzoquinones (40) and (41) by using chloranil[48] and



(42) (43)

Scheme 3

$Pd(OAc)_2$ in triethylamine[49], respectively (Scheme 3). Saulnier and Gribble[50] have used the 3-iodoindole (44) to obtain the 3-lithio product, and subsequent reaction of this with cinchomeronic anhydride gave the 4-pyridylketone (45), which on esterification and then cyclisation gave quinone (46).

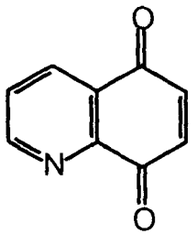


1.2 Reactions of Heterocyclic Quinones

1.2.1 Substitution Reactions

There are very few examples in the literature of comparisons of the reactivity of heterocyclic quinones, therefore, quantitative data showing the effect of the presence of a particular heteroatom and of its position relative to the quinonoid nucleus are not available. However, it is clear that for most of the general reactions of heterocyclic quinones, i.e. electrophilic substitution, nucleophilic substitution and cycloaddition reactions, the nature and position of the hetero atom has a significant effect on the products of a reaction and on the reaction path.[51] For instance, it has been shown that both in quinazoline-5,8-dione(50) and quinoline-5,8-dione (47), electrophilic substitution and nucleophilic substitution take place at the 7- and 6-position,[52,53,54] respectively. On the other hand, in the case of 5,8-isoquinolinedione (48) electrophilic and nucleophilic attack preferably occur at the 6- and 7-position, respectively. Whereas in 5,8-quinoxalinedione (49), being a symmetrical quinone, the 6- and 7-positions are equivalent for these reactions.

The overall reactivity of these mono- and diaza-heterocyclic quinones (47)-(50) can be explained on the basis of the contributing structures (51)-(54) respectively. The inductive effect of the nitrogen atom and resonance effect of the pyridino[54] and pyrimidino[6] group are responsible for the electron deficiency at the 8-position in



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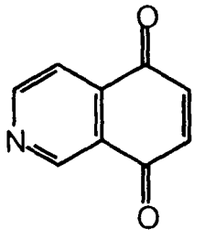

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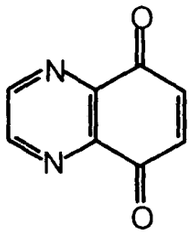

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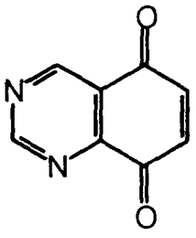

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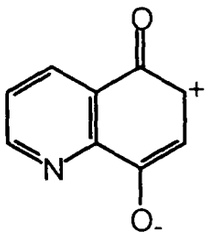

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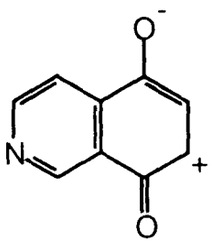

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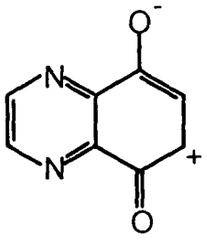

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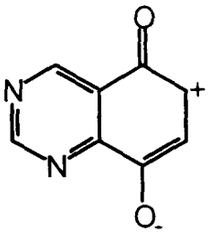
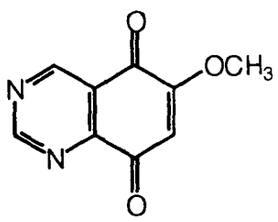
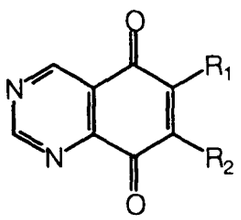


(54)

structrues (51) and (54), which result in nucleophilic attack at the 6-position. Similarly, there are equal chances for the nucleophilic attack at 6- and 7-position in structure (53). In the case of contributing structure (52) for 5,8-isoquinolinedione (48), the carbonyl group which is a 4-substituent on the pyridine ring, shows greater electron deficiency compared to a carbonyl group which is a 3-substituent. Hence nucleophilic attack takes place at the 7-position.[54]



(55)



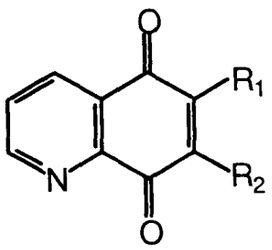
(56) R_1 = —N⟨ ⟩; R_2=H

(57) $R_1 = R_2$ = —N△

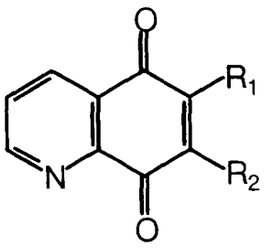
(58) R_1 = OCH_3; R_2 = Br

(59) R_1 = —N△; R_2 = H

The reaction of the separate reagents, piperidine in methanol, aziridine, or bromine with 6-methoxy-5,8-quinazolinedione (55) gave (56), 6,7-bisaziridinyl-5,8-quinazolinedione (57), and 7-bromo-6-methoxy-5,8-quinazolinedione (58) in 85%, 59% and 80% yield, respectively. 6-Aziridinyl-5,8-quinazolinedione (59) was shown to be the intermediate in the formation of compound (57).[6,24] Similarly, 6-toluidinyl-5,8-quinolinedione (62) was obtained either exclusively or as a major product along with only a small quantity of 7-toluidinyl-5,8-quinolinedione (63) from the reaction of toluidine with 6- or 7-substituted quinolinedione (60)-(61) or 5,8-quinolinedione (47).[55]

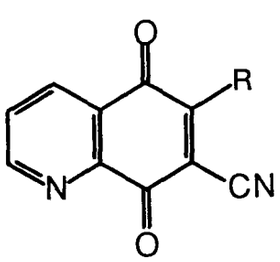


(60) $R_1 = Cl; R_2 = H$
(61) $R_1 = H; R_2 = Cl$

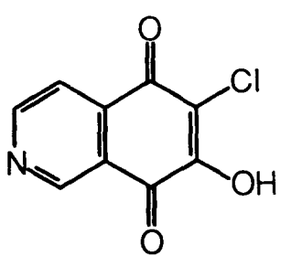


(62) $R_1 = NHC_6H_4(p\text{-}CH_3); R_2 = H$
(63) $R_1 = H; R_2 = NHC_6H_4(p\text{-}CH_3)$

Treatment of 6,7-dicyano-5,8-quinolinedione (64) with water gave the expected 6-hydroxy-7-cyano-5,8-quinolinedione (65).[54] In the replacement reaction of a chloro group by hydroxide ion from 6,7-dichloro-5,8-isoquinolinedione, greater selectivity was observed[54] compared to that found with the 6,7-dichloroquinoline-5,8-dione derivative of (47), and 7-hydroxy-6-chloro-5,8-isoquinolinedione (66) was obtained in 87% yield.



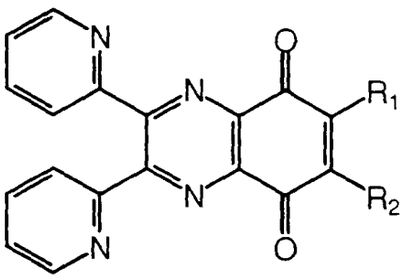
(64) R = CN
(65) R = OH



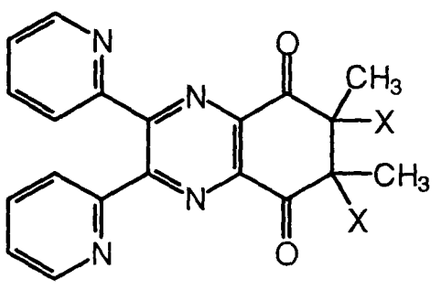
(66)

6,7-Bis(1-aziridinyl)-2,3-bis(2-pyridyl)-5,8-quinoxalinedione (68),[40] together with a small quantity of mono-substituted compound (69), has been obtained by the reaction of aziridine with 6-methoxy-2,3-bis(2-pyridyl)-5,8-quinoxalinedione (67). The methyl substituted quinone (70) gave the 7-bromo derivative (71) in the presence of bromine.

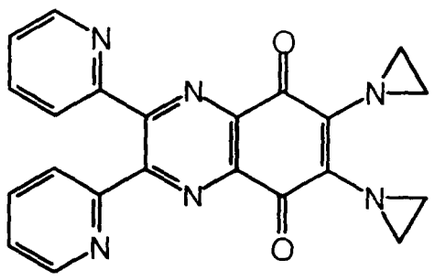
On the other hand, compound (72) was obtained only by using N-bromosuccinimide under UV irradiation as the brominating agent.[40] The same brominating agent and sulphuryl chloride produced the addition compounds (74) and (75), respectively, on reaction with the 6,7-dimethylquinone (73).[40]



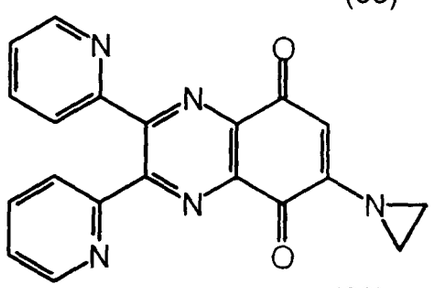
(67) $R_1 = H; R_2 = OCH_3$
(70) $R_1 = H; R_2 = CH_3$
(71) $R_1 = Br; R_2 = CH_3$
(72) $R_1 = Br; R_2 = OCH_3$
(73) $R_1 = R_2 = CH_3$



(74) = Cl
(75) = Br



(68)



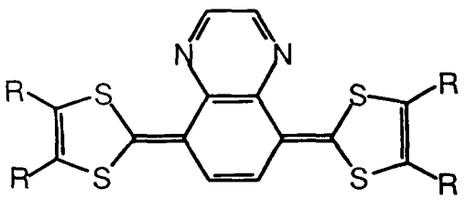
(69)

1.2.2 Reaction at the Carbonyl Group

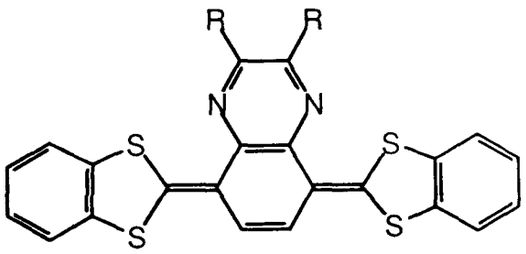
A series of compounds (76)[56] and (77),[57] having highly electron donating properties, and which were used in the preparation of conductive, charge-transfer complexes, has been prepared quantitatively by a retro-Diels-Alder reaction of cyclopentadiene-quinoxalinequinone adduct. The adducts were synthesised by Wittig-

Horner reaction of the corresponding phosphorus reagent.[58]

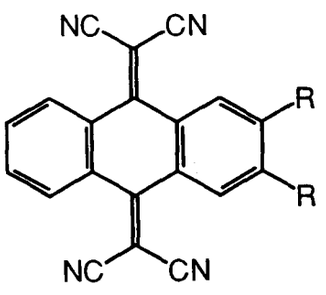
On the other hand, tetracyanoquinodimethanes (78) and (79) have been prepared by the same workers[59] using a titanium tetrachloride catalyst to cause condensation of



(76) R = H, CH_3, R,R = $S(CH_2CH_2)S$

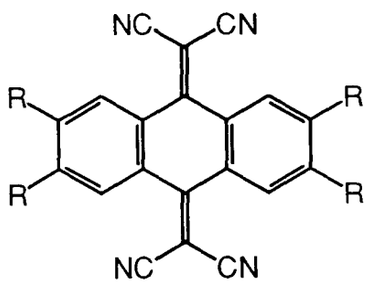


(77) R = H, CH_3, C_6H_5



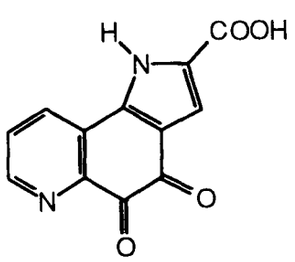
(78)

R = H, CH_3, C_6H_5

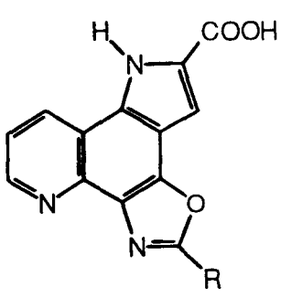


(79)

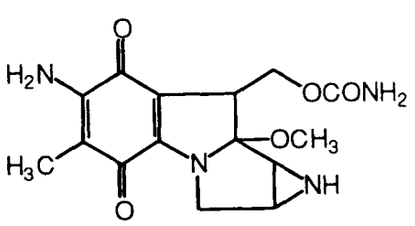
the corresponding azaanthraquinones with malononitrile. Similarly, 7,9-didecarboxymethoxatin (80), having an *o*-quinonoid structure, has been converted into oxazoles (81) and (82) by the reaction with benzylamine and glycine,[60] respectively.



(80)

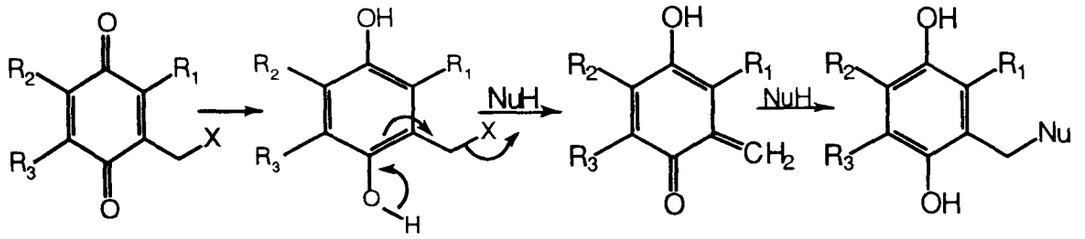


(81) R = C_6H_5
(82) R = H



(83)

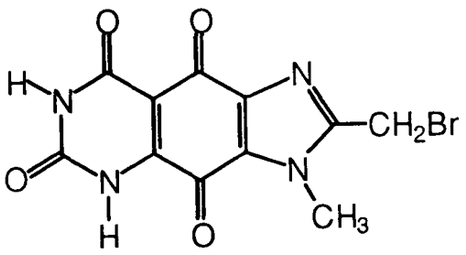
One of the most common reactions of heterocyclic quinones is their reduction. An especially interesting example is bioreductive activation,[61] as this is thought to occur in the mechanism of alkylation by mitomycin C (83).[62] In a simple example, the principle of bioreductive activation and subsequent alkylation has been illustrated by the conversion of (84) through to (85)[63] (Scheme 4).



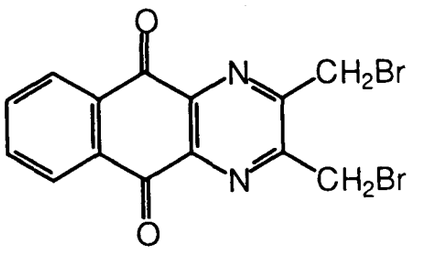
(84) (85)

Scheme 4

The idea of bioreductive alkylation in hypoxic cells has been used in the design of several antitumour agents including the bromomethyl derivative of imidazo[4,5-g]quinazoline-4,5,7,9-tetraone (86)[64] and the bis(bromomethyl) derivative of 5,10-benzo[g]quinoxalinedione (87).[65]



(86)

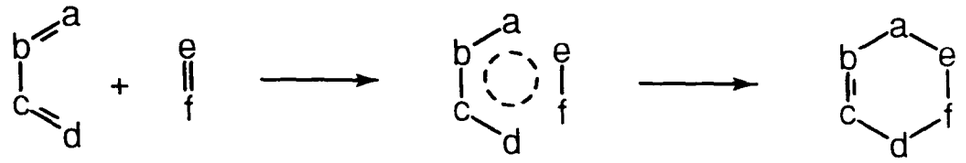


(87)

1.2.3 Diels-Alder Reactions

The Diels-Alder reaction (Otto Diels and Kurt Alder; Nobel Prize, 1950) is one of the most fundamental and useful reactions in organic synthesis.[66] It is a (4+2)π electron cycloaddition[67] in which a conjugated diene (88),[68] which may be a heterodiene[69] or a heterocyclic diene,[70] undergoes a stereospecific addition via a six membered cyclic transition state (90) with another component, called a dienophile (89)[71].

The reaction product is called the adduct (91). Although the majority of (4n+2)πe cycloadditions are concerted,[72] there are a few cases where zwitterionic[73] or radical intermediates are so stabilised that a stepwise reaction becomes a viable alternative.[73] This particularly applies when a heterodiene[69] or a heterodienophile[71] is a reactant. The



(88) (89) (90) (91)

isolation of a zwitterionic intermediate and the demonstration of solvent effects are the major pieces of evidence in favour of a stepwise mechanism.[73] The Diels-Alder reaction is found to be promoted by electron-donating substituents in the dienes because this raises the energy level of the HOMO in the diene and by electron-withdrawing substituents in the dienophile which lowers the energy level of the LUMO of dienophile (Fig 1a). Overall, this enhances the interaction between the reactants.

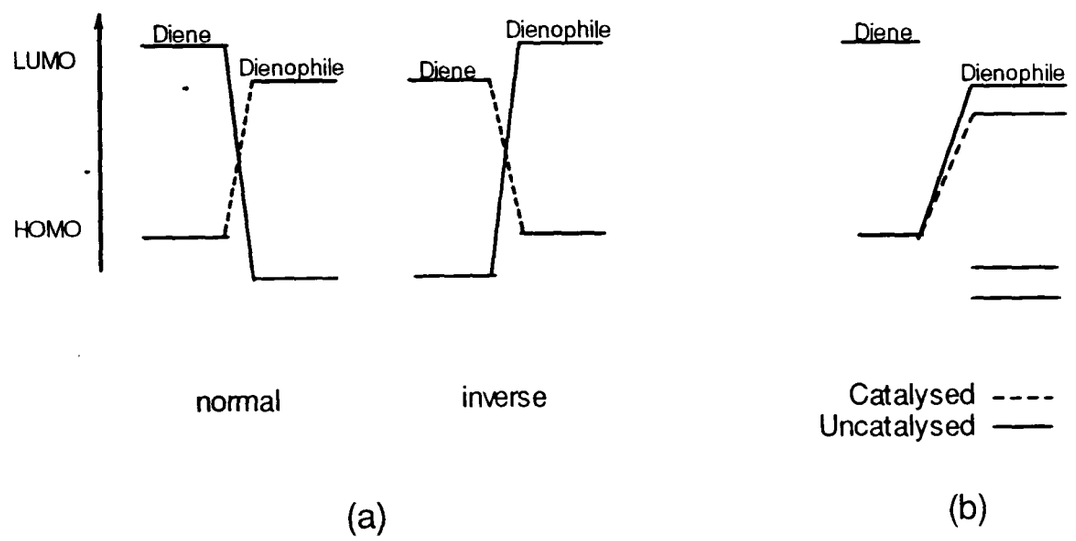
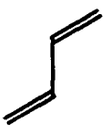


Fig. 1 Frontier Molecular Orbital diagram (a) normal and inverse electron demand (b) effect of the Lewis acid in Diels-Alder reactions.

Substituents, or the presence of a hetero atom in the diene or dienophile, appear not to effect the symmetry of the orbitals involved.

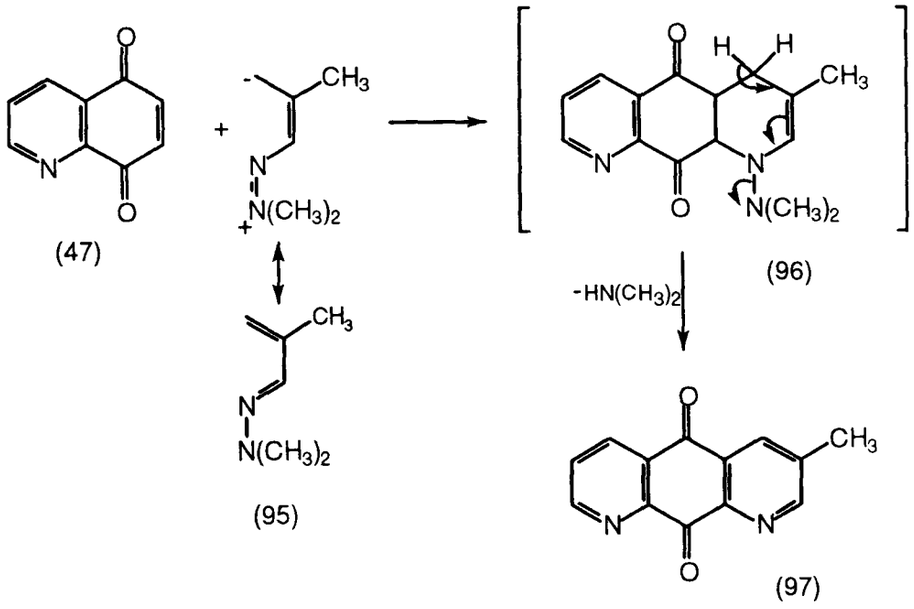
The dienes must react in the cisoid conformation (92) rather than a transoid conformation (93).[68] The rate of the reaction may be accelerated by Lewis acid,

(92)



(93)

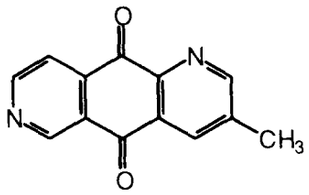
pressure, ultrasound, radical cations or by solvents.[74,75] These effects can be explained on the basis of a Frontier Molecular Orbital (FMO) diagram (as shown in Fig 1), where the effect of Lewis acid catalysis is to lower the dienophile LUMO energy, bringing it closer in energy to that of the diene HOMO (Fig 1b).[76,77] The great advantage of the Diels-Alder reaction in organic synthesis lies in its high regioselectivity[78] (only one orientation predominates), stereoselectivity[79] (one diastereoisomer predominates), and that it is an addition process and therefore a "clean" reaction. The (4n+2)πe cycloaddition reactions are symmetry allowed thermochemically and symmetry forbidden photochemically.



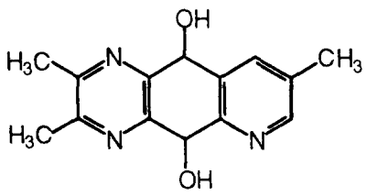
Scheme 5

Monoazanaphthoquinones (47) and (48) and diazanaphthoquinone (94) gave diazaanthraquinones (97)-(98) and triazaanthraquinone (100)[54] respectively, in a highly

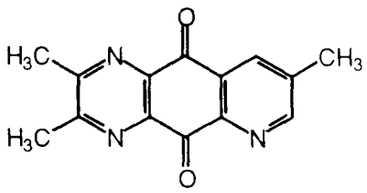
regiospecific cycloaddition[80] with 1-(dimethylamino)-3-methyl-1-azabuta-1,3-diene (methacrolein N,N-dimethylhydrazone)[52] (95), after the elimination of dimethylamine from the initial 1:1 cycloadduct (96) and subsequent oxidation (Scheme 5). For instance, quinoline-5,8-dione (47) gave only one product; 3-methyl-1,8-diazaanthraquinone (97) in 75% yield.



(98)

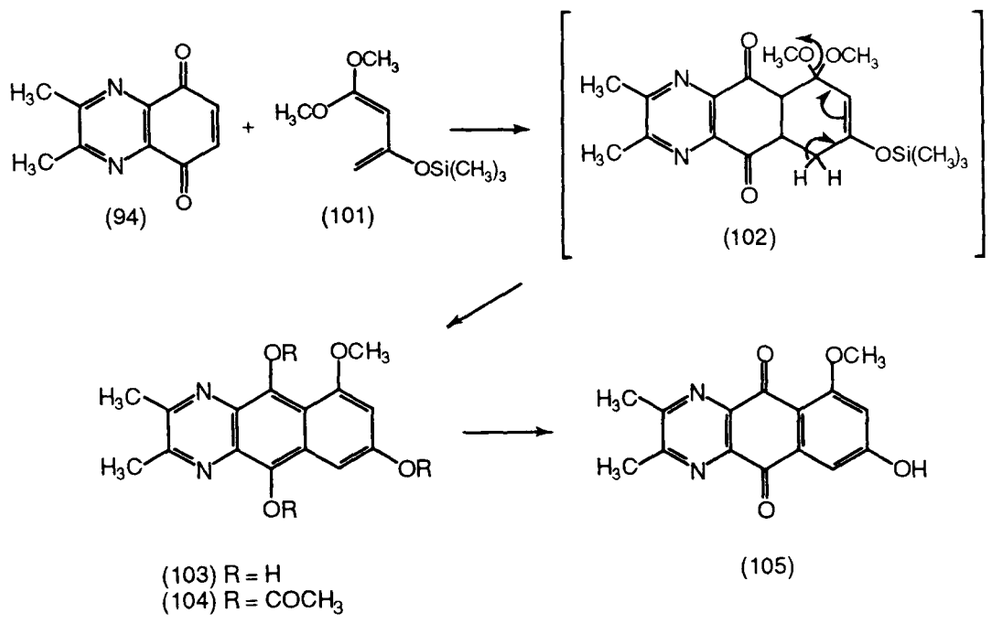


(99)



(100)

Similarly cycloaddition of (95) with isoquinoline-5,8-dione (48) produced 3-methyl-1,6-diazaanthraquinone (98). But in the case of 2,3-dimethylquinoxaline-5,8-dione (94), the first isolated product after the reaction with (95) was the 9,10-dihydroxytriazaanthracene (99). The quinol (99) was oxidised to 2,3,7-trimethyl-



(94) (101) (102)

(103) R = H
(104) R = $COCH_3$

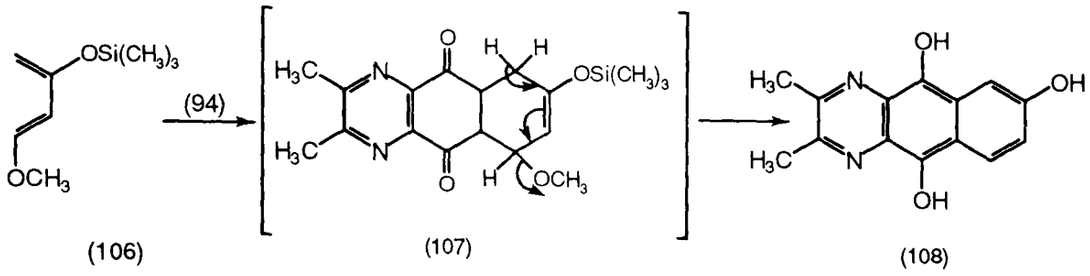
(105)

Scheme 6

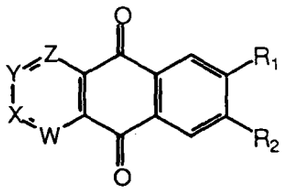
1,4,5-triazaanthraquinone (100).[54] The initial 1:1 cycloadduct corresponding to (96) has not been isolated. Similarly the quinone (94) (Scheme 6) gave the trihydroxy compound (103) on cycloaddition with 1,1-dimethoxy-3-trimethylsilyloxy-1,3-butadiene (101)[81] and acetylation of (103) afforded the corresponding acetate (104). Oxidation of

the trihydroxy compound (103) gave the quinone (105)[82] (Scheme 6).

2,3-Dimethyl-5,8-quinolinedione (94) has been shown to behave similarly towards the reaction with *trans*-1-methoxy-3-trimethylsilyoxy-1,3-butadiene (106)[83] to produce the trihydroxy compound (108) as initial cycloadduct through an unstable intermediate (107). This quinonol (108) was oxidised to the quinone (109) with silver oxide. Whereas, 5,8-quinolinedione (47) and 5,8-isoquinolinedione (48) gave directly the oxidised products[82] (110) and (111) (Scheme 7).



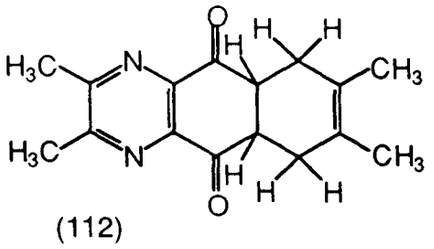
(106) (107) (108)



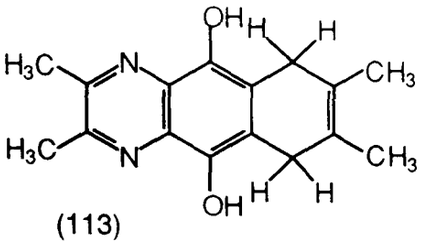
(109) Z = W = N; Y = X = CCH_3 ; R_1 = OH; R_2 = H
(110) W = N; X = Y = Z = CH; R_1 = OH; R_2 = H
(111) X = N; W = Y = Z = CH; R_2 = OH; R_1 = H

Scheme 7

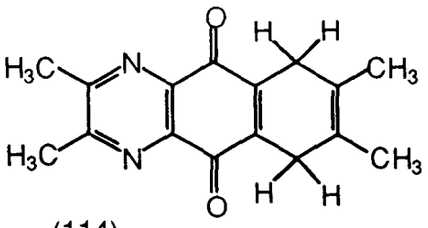
Similarly, the reaction of quinone (94) with 2,3-dimethyl-1,3-butadiene gave, after prolonged reaction at elevated temperature, the tautomeric form of the initial cycloadduct, 6,9-dihydro-2,3,7,8-tetramethylbenzo[g]quinoxaline-5,10-diol (113),[82] whereas Joulie and coworkers[84] obtained the initial cycloadduct 5a,6,9,9a-tetrahydro-2,3,7,8-tetramethylbenzo[g]quinoxaline-5,10-dione (112) in addition to the diol (113) after a shorter reaction time. The diketone (112) was converted completely to the latter product (113) by treatment with 40% aqueous hydrochloric acid. Compound (113) was converted to 6,9-dihydro-2,3,7.8-tetramethylbenzo[g]quinoxaline-5,8-dione (114) by oxidation with silver oxide in 1,2-dimethoxyethane. The cycloadducts (115) and (116) have been characterised as reaction products from the reaction of 5,8-quinolinedione (47) with 2,3-dimethyl-1,3-butadiene in refluxing ethanol for 45 min[85] and 24 h,[82] respectively.



(112)



(113)



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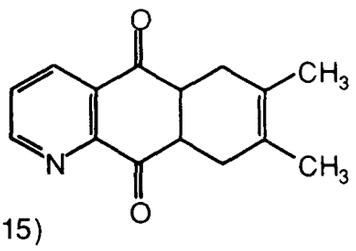
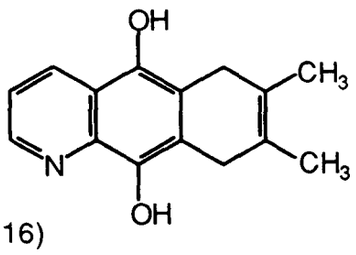
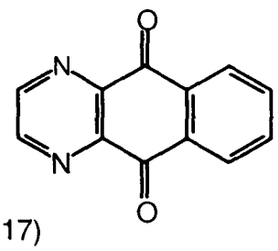


(115)

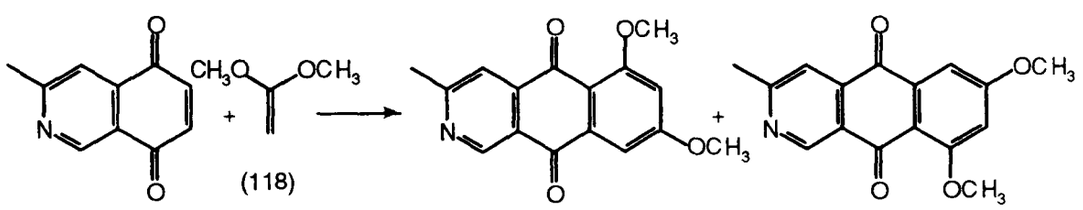


(116)



(117)

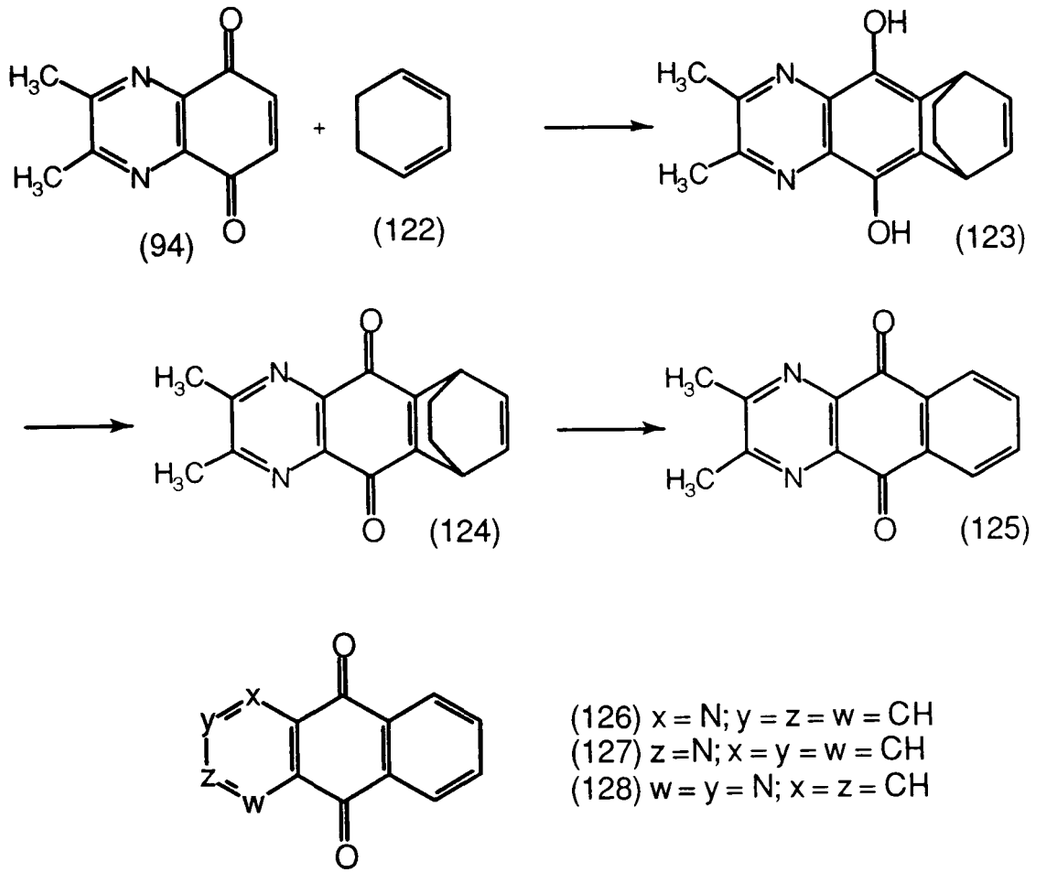
The reaction of quinoxaline-5,8-dione (49) with 1-acetoxy-1,3-butadiene produced the fully aromatized compound; benzo[g]quinoxaline-9,10-dione (117) directly, presumably by the elimination of acetic acid from the initial 1:1 cycloproduct followed by the oxidative aromatization.[82] An interesting reaction is the addition of 1,1-dimethoxyethylene (118) to 3-methylisoquinoline-5,8-dione (119) which gave a mixture of (120) to (121) in a ratio of 7:1[85] (Scheme 8).



(119) (118) (120) (121)

Scheme 8

The cycloaddition of 2,3-dimethyl-5,8-quinoxalinedione (94) with cyclohexadiene (122), a cyclic diene, has been investigated, and a highly regioselective reaction gave the 1:1 cycloadduct (123), which, on tautomerism and ready oxidation with silver (II) oxide, gave (124). The thermal elimination of ethylene from this bridged ring



Scheme 9

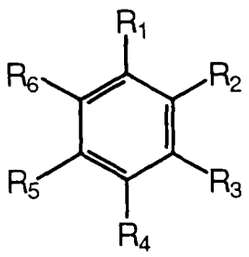
system gave the quinone (125)[82] (Scheme 9). The cycloaddition of 1,3-cyclohexadiene (122) with other heterocyclic quinones, (47), (48) and (49) also yielded the aza- and diazaanthraquinones (126)-(128), respectively, in a similar way[82] (Scheme 9).

DISCUSSION

2 DIMETHOXYQUINOXALINES AND QUINOXALINE QUINONE CHEMISTRY

2.1 PREPARATION OF DIMETHOXYQUINOXALINES

The preparation of 2,3-diamino-1,4-dimethoxybenzene (134) in large quantity is difficult, which is unfortunate because this compound is potentially useful for the synthesis of several heterocyclic quinones. The nitration of 1,4-dimethoxybenzene (129) always gives a mixture of 2,3-dinitro-1,4-dimethoxybenzene (131) and 2,5-dinitro-1,4-dimethoxybenzene (132).[86] The first (131) is always obtained as the major product (80 % yield),[53,86,87] but the separation and then purification of this compound is difficult.

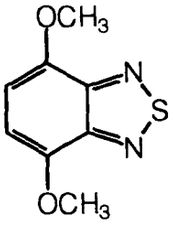


(129) $R_2 = R_3 = R_5 = R_6 = H$; $R_1 = R_4 = OCH_3$
(130) $R_1 = R_4 = R_5 = R_6 = H$; $R_2 = R_3 = OCH_3$
(131) $R_2 = R_3 = NO_2$; $R_5 = R_6 = H$; $R_1 = R_4 = OCH_3$
(132) $R_2 = R_5 = NO_2$; $R_3 = R_6 = H$; $R_1 = R_4 = OCH_3$
(133) $R_2 = R_3 = OCH_3$; $R_5 = R_6 = NO_2$; $R_1 = R_4 = H$
(134) $R_2 = R_3 = NH_2$; $R_5 = R_6 = H$; $R_1 = R_4 = OCH_3$
(135) $R_2 = R_3 = OCH_3$; $R_5 = R_6 = NH_2$; $R_1 = R_4 = H$

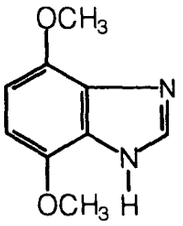
1,2-Dimethoxybenzene[88] (130) on nitration yields 1,2-dinitro-4,5-dimethoxybenzene[88] (133), which is then reduced to 1,2-diamino-4,5-dimethoxybenzene (135) by hydrogenation with palladium on charcoal (10 %).[88]

In the present work, the mixture of dinitro-1,4-dimethoxybenzenes was reduced[53] and then the mixture of diamino-1,4-dimethoxybenzenes, containing mainly (134), was used directly for the preparation of several *p*-dimethoxy-substituted heterocycles, as described in literature[53,86,87] for the preparation of 2,3-dimethyl-5,8-dimethoxyquinoxaline[89] (94), 4,7-dimethoxy-2,1,3-benzothiadiazole (136), 4,7-

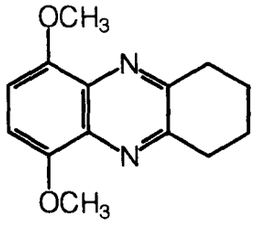
dimethoxybenzimidazole (137), and 1,2,3,4-tetrahydro-5,8-dimethoxyphenazine(138). Thus 5,8-dimethoxyquinoxaline (13, R = H), 2,3-dimethyl-5,8-dimethoxyquinoxaline (94), 2,3-diphenyl-5,8-dimethoxyquinoxaline (139), ethyl 2-hydroxy-5,8-



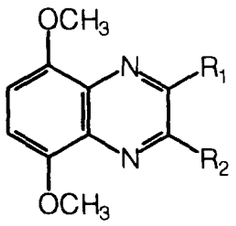
(136)



(137)

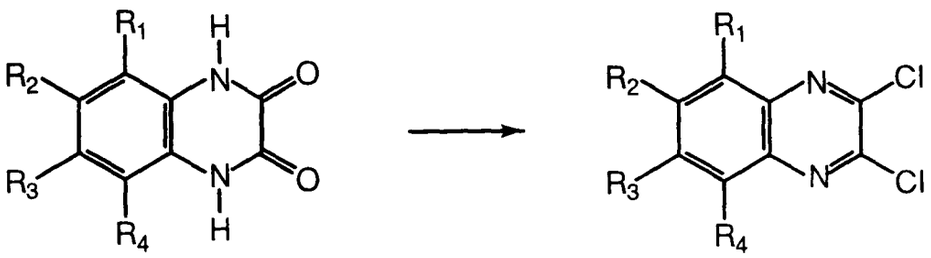


(138)



(139) $R_1 = R_2 = C_6H_5$
(140) $R_1 = OH$; $R_2 = CO_2C_2H_5$
(141) $R_1 = R_2 = CH_2Br$

dimethoxyquinoxaline-3-carboxylate (140), 2,3-bis(bromomethyl)-5,8-dimethoxyquinoxaline (141) and 1,4-dihydro-2,3-dioxo-5,8-dimethoxyquinoxaline (142) were obtained by refluxing the reduction reaction mixture containing diamino-1,4-dimethoxybenzene, in the presence of acid, with glyoxal bisulphite compound, butane-2,3-dione, benzil, ethyl ketomalonate, 1,4-dibromobutane-2,3-dione and diethyl oxalate, respectively. 1,4-Dihydro-2,3-dioxo-6,7-dimethoxyquinoxaline (143) was also prepared in a similar way, by the condensation of the diamino compound (135) with diethyl oxalate (Scheme 10). All these dimethoxy compounds are known and the melting points and other data were similar to those given in literature.[87,89]

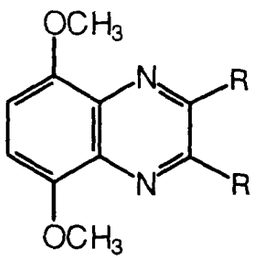


(142) $R_1 = R_4 = OCH_3$; $R_2 = R_3 = H$
(143) $R_1 = R_4 = H$; $R_2 = R_3 = OCH_3$

(144) $R_1 = R_4 = OCH_3$; $R_2 = R_3 = H$
(145) $R_1 = R_4 = H$; $R_2 = R_3 = OCH_3$

Scheme 10

1,4-Dihydro-2,3-dioxo-5,8-dimethoxyquinoxaline (142) and its isomer (143) were then chlorinated using phosphoryl chloride in N,N-dimethylaniline to obtain the 2,3-dichlorodimethoxyquinoxalines[89] (144) and (145), respectively (Scheme 10). Quinoxaline (144) was expected to be a useful precursor for some novel 2,3-disubstituted-5,8-dimethoxyquinoxaline by nucleophilic substitution and 2,3,5,8-tetramethoxyquinoxaline (146), 2,3-diethoxy-5,8-dimethoxyquinoxaline (147) and 2,3-bis(thioethyl)-5,8-dimethoxyquinoxaline (148) were made by treating the sodium salt of the respective alcohol or thiol with 2,3-dichloro-5,8-dimethoxyquinoxaline (144) in the corresponding alcohol except in case of (148) where ethanol was used.



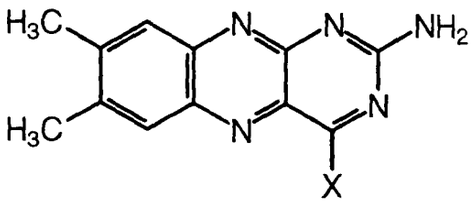
(146) R = OCH_3
(147) R = OC_2H_5
(148) R = SC_2H_5

The ^1H NMR spectrum of the tetramethoxy compound (146) showed a singlet at 3.97 ppm due to the 5- and 8-methoxyl groups, whereas, the methoxyl groups at 2- and 3-position produced a singlet down field at 4.18 ppm. The mass spectrum showed a base peak for the molecular ion at 250 daltons, which was in agreement with molecular formula $C_{12}H_{14}N_2O_4$. A peak at 235 daltons was probably due to the loss of one methyl group from the molecular ion. The melting points and other data for compounds (147) and (148) were similar to those in literature.[89]

2.1.1 1,4-Dihydroxy- and 1,4-diamino-5,8-dimethoxypyridazino[4,5-*b*]quinoxaline

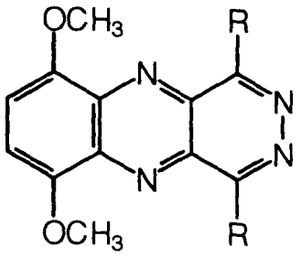
Heterocyclic quinones possessing (a) aminoalkyl substituents and (b) the phthalazine quinones have been proved to be active against tumours.[12,54,82] Apart from this, the compounds (153) and (156) are also of interest due to their structural resemblance to (149); an derivative of benzopteridine.[90] Benzopteridine can act as an antagonist of both riboflavin and folic acid[90,91] as well as a blood platelet antiaggregation agent.[92] Hence, it was decided to prepare a quinoxaline quinone having these two features in the same molecule.

The well known ability of the esters of *o*-dicarboxylic acids[93,94] and *o*-dinitriles to form 1,4-dihydroxypyridazine and 1,4-diaminopyridazine rings, respectively, by their reactions with hydrazine hydrate was used in the synthesis of compounds (150) and



(X = OH or NH_2)

(149)

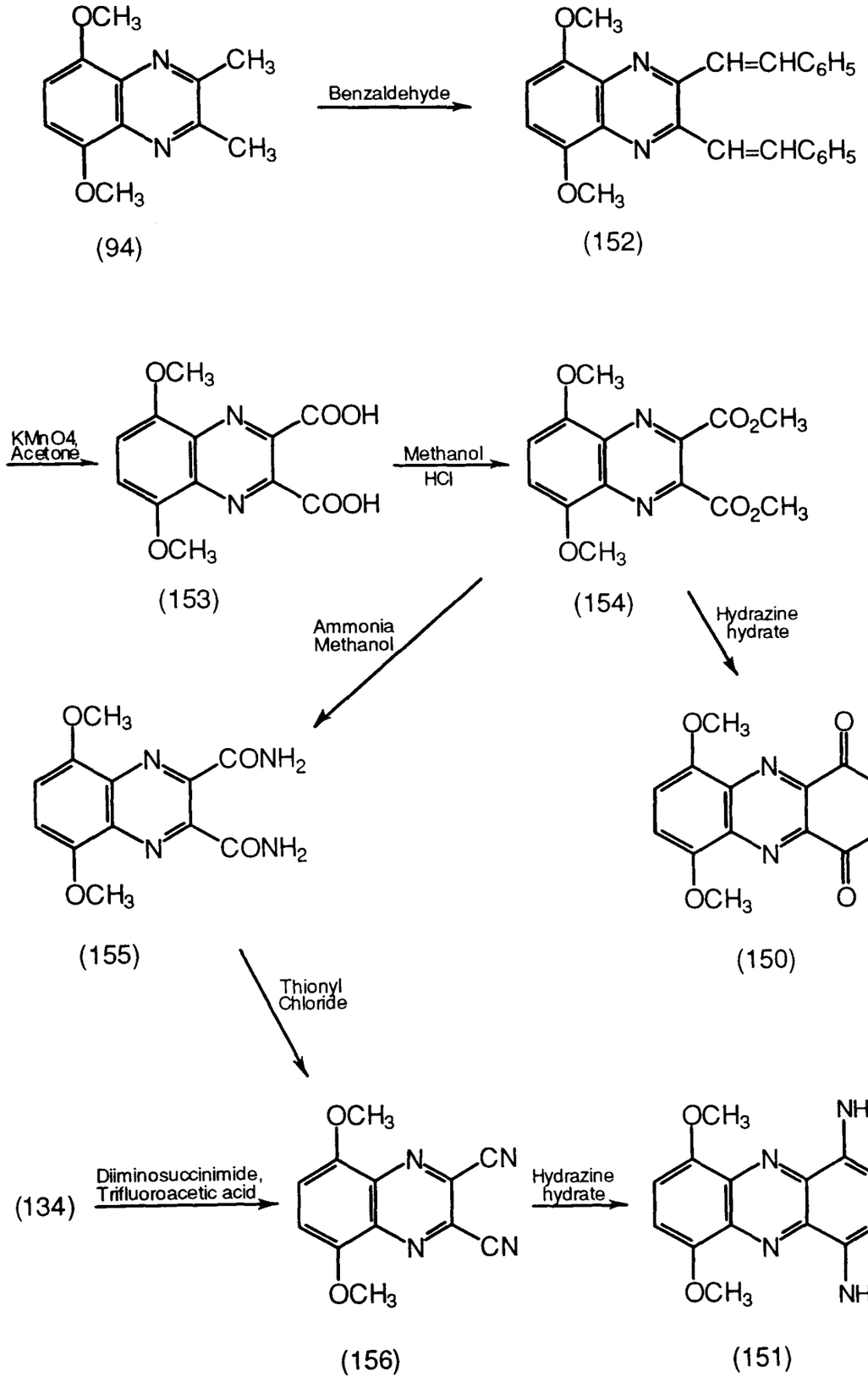


(150) R = OH
(151) R = NH_2

(151). The starting material was 5,8-dimethoxyquinoxaline-2,3-dicarboxylic acid (153), obtained in a series of reactions similar to those described[93] for the preparation of quinoxaline-2,3-dicarboxylic acid (Scheme 11). The 2,3-distyryl compound (152) was obtained by the reaction of (11) with benzaldehyde in presence of boric acid. The ^1H NMR spectrum of (152) showed the presence of two doublets at 7.69 and 7.89 ppm, with a coupling constant J = 15.8 Hz, which were assigned to the α- and β-vinylic hydrogen atoms, respectively. The coupling constant indicated *trans* stereochemistry. The mass spectrum of (152) produced the expected molecular ion peak at 394 daltons. The other important peaks at 379 and 365 daltons, were probably due to the loss of one and two methyl groups from the molecule, respectively.

The distyryl compound (152) was oxidised by potassium permanganate in acetone to produce the dicarboxylic acid (153), which was subsequently converted into its methyl ester (154) by treatment with methanol saturated with dry hydrogen chloride. The IR spectrum of the ester showed a strong absorption at 1730 cm^{-1} due to the carbonyl group and the four methyl groups produced a singlet at 4.03 ppm in the ^1H NMR spectrum. The mass spectrum of (154) showed a molecular ion peak at 306 daltons, in agreement with the molecular formula, and a base peak at 188 daltons due to the loss of two methyl carboxyl groups.

Compound (150) was synthesised from the dimethyl ester (154) by the action of and hydrazine hydrate (Scheme 11). The reaction product (150) had an IR spectrum


OCH3
CH3
CH3
OCH3
Benzaldehyde
CH=CHC6H5
CH=CHC6H5
(94)
(152)
KMnO4
Acetone
COOH
COOH
(153)
Methanol
HCl
CO2CH3
CO2CH3
(154)
Ammonia
Methanol
Hydrazine
hydrate
CONH2
CONH2
(155)
NH
NH
O
O
(150)
Thionyl
Chloride
(134)
Diiminosuccinimide,
Trifluoroacetic acid
CN
CN
(156)
Hydrazine
hydrate
NH2
NH2
(151)

Scheme 11

which showed two peaks at 3490 and 3385 cm^{-1}, attributed to the N-H of amido group, and a strong absorption at 1665 cm^{-1} due to the carbonyl group. The N-H of (155) produced two singlets at 7.95 and 7.67 ppm, in the ^1H NMR spectrum, which were exchanged with D_2O. The mass spectrum showed the expected molecular ion peak at 274 daltons and peaks at 259 and 245 daltons were probably due to the loss of one and two methyl groups, respectively.

5,8-Dimethoxyquinoxaline-2,3-dicarboxamide (155) was obtained by dissolving the ester (154) in methanol and then saturating the solution with dry ammonia. The dinitrile (156) was obtained from 5,8-dimethoxy-2,3-dicarboxamide (155) by dehydration of the diamide (155) with thionyl chloride in dimethylformamide in 46 % yield (Scheme 11). The IR spectrum of (156) showed a strong absorption at 2260 cm^{-1} due to cyano group and the ^1H NMR spectrum showed a singlet at 4.09 ppm due to methoxyl groups. The mass spectrum of (156) had a molecular ion peak at 240 daltons and two peaks at 225 and 211 daltons probably due to the loss of one and two methyl groups. 1 , 4 - Diamino-5,8-dimethoxypyridazino[4,5-b]quinoxaline (151) was obtained by the reaction of the dinitrile (156) with hydrazine hydrate in methanol at room temperature (Scheme 11). The IR spectrum of (151) showed two peaks at 3425 and 3320 cm^{-1} attributable to amino groups. The two strong peaks at 1690 and 1670 cm^{-1} were tentatively assigned to imino hydrogens present in the tautomeric system. The N-H groups produced two exchangeable singlets at 7.95 and 7.65 ppm in the ^1H NMR spectrum. The mass spectrum of (151) showed a molecular ion peak at 272 daltons, in agreement with the molecular formula $C_{12}H_{12}N_6O_2$, and a peak at 255 daltons was probably due to the loss of NH_3 from the molecule. Several attempts were made to alkylate the amino groups of (156) using N,N-dimethylaminopropyl chloride, but unfortunately intractable mixtures were obtained.

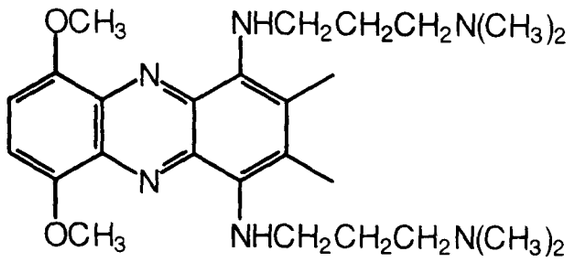
2.1.1.1 An Improved Method for the Preparation of 2,3-Dicyano-5,8-dimethoxyquinoxaline (156)

A successful attempt was made to improve the yield (77 %) of (155) by use of a shorter reaction sequence, i.e. treatment of the solid mixture of diaminodimethoxy

compound (134) with diiminosuccinonitrile in trifluoroacetic acid. The diiminosuccinonitrile was prepared by the reaction diaminomaleonitrile with dichlorodicyanobenzoquinone in acetonitrile.[95]

2.1.2 Reaction of 5,8-Dimethoxyquinoxaline-2,3-bis-(methylenepyridinium) dibromide (157) with Butan-2,3-dione

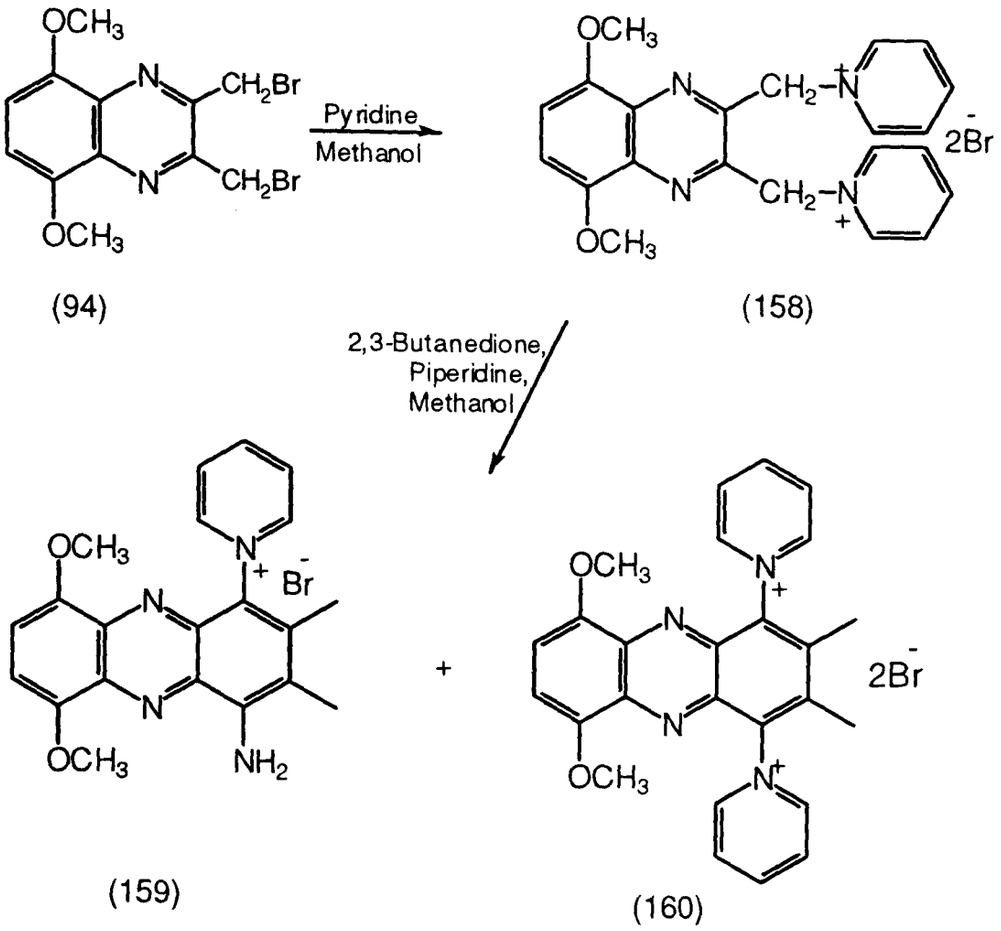
After failures in the attempted alkylation of the amino group of (151) using a variety of methods, an attempt was made to develop an entirely different route (Scheme 12) for the preparation of an N-alkylated product (157).[96]



(157)

The bromomethyl product (141) was treated with pyridine to obtain the dipyridinium bromide salt (158) . The ^{1}H NMR spectrum of (158) showed a singlet at 6.64 ppm due to the methylene hydrogen atoms. The 2- and 6-hydrogens of the pyridinium group produced a doublet at 9.27 ppm with a coupling constant of 5.3 Hz and the 4-, 3-, and 5-hydrogens gave rise to two pairs of double doublets which appeared as two triplets at 8.77 and 8.29 ppm, respectively. The mass spectrum showed the expected peak at 424 daltons, in agreement with molecular formula $C_{26}H_{24}N_4O_2Br_2$.

The dipyridinium salt (158) has two active methylene groups and this compound was condensed with 2,3-butanedione in the presence of a catalytic quantity of piperidine.[96] A mixture of two products was obtained (Scheme 12). These were separated by column chromatography. The first eluted component was the major product and was characterised as 1-amino-2,3-dimethyl-5,8-dimethoxy-9,10-diazaanthracene-4-pyridinium bromide (159). The IR spectrum of (159) showed two peaks at 3400 and 3300 cm^{-1} due to the amino group. The proton signals in the ^{1}H



Scheme 12

NMR spectrum of (159) showed the un symmetrical nature of the molecule. Thus, the 2- and 3-methyl groups produced two singlets at 2.23 and 2.31 ppm, and the methoxyl groups gave signals at 3.85 and 4.11 ppm due to the 5- and 8-methoxy groups, respectively. The integration also indicated the presence of only one pyridinium group, which gave rise to a signal as a doublet at 9.11 ppm (J = 7.8 Hz) and two pairs of double doublets which appeared as two triplets[97] at 8.89 and 8.35 ppm due to the 2'-, 4'- and 3'-protons, respectively. The E.I. mass spectrum had no molecular ion peak at 361 daltons, but a base peak at 358 (M^+-3H) daltons might be due to the reaction inside the ionisation chamber. The elemental analysis and FAB accurate mass data on a peak at 361 daltons was in agreement with the structure (159).

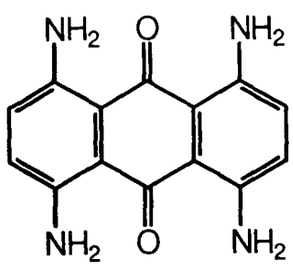
The second component was characterised as 2,3-dimethyl-5,8-dimethoxy-9,10-diazaanthracene-1,4-bis-pyridinium dibromide (160). The ^{1}H NMR spectrum indicated the symmetrical nature of the molecule: the two methyl and two methoxy groups

produced singlets at 2.46 and 3.98 ppm, respectively. The integration of the peaks showed the presence of pyridinium groups equal in number to the methyl and methoxyl groups. The pyridinium rings produced a doublet at 9.16 ppm, with a coupling constant J = 5.5 Hz, and two pairs of double doublets which appeared as two triplets at 9.10 and 8.54 ppm due to 2'-, 4'- and 3'-protons.

The possible explanation for the formation of (159) might be the ring opening of the pyridinium group in the presence of a base.[98,99,100] The initial product during the reaction of (141) with biacetyl was probably (159) which, on reaction with a nucleophile, e.g. methanol or piperidine, at one of the highly activated pyridinium groups, caused the ring cleavage (Scheme 13). The driving force for the reaction might be the delocalisation of the resultant negative charge on the 9,10-diazaanthracene and especially on the pyridinium group.[98] This might also be the reason for the cleavage of only one pyridinium group.

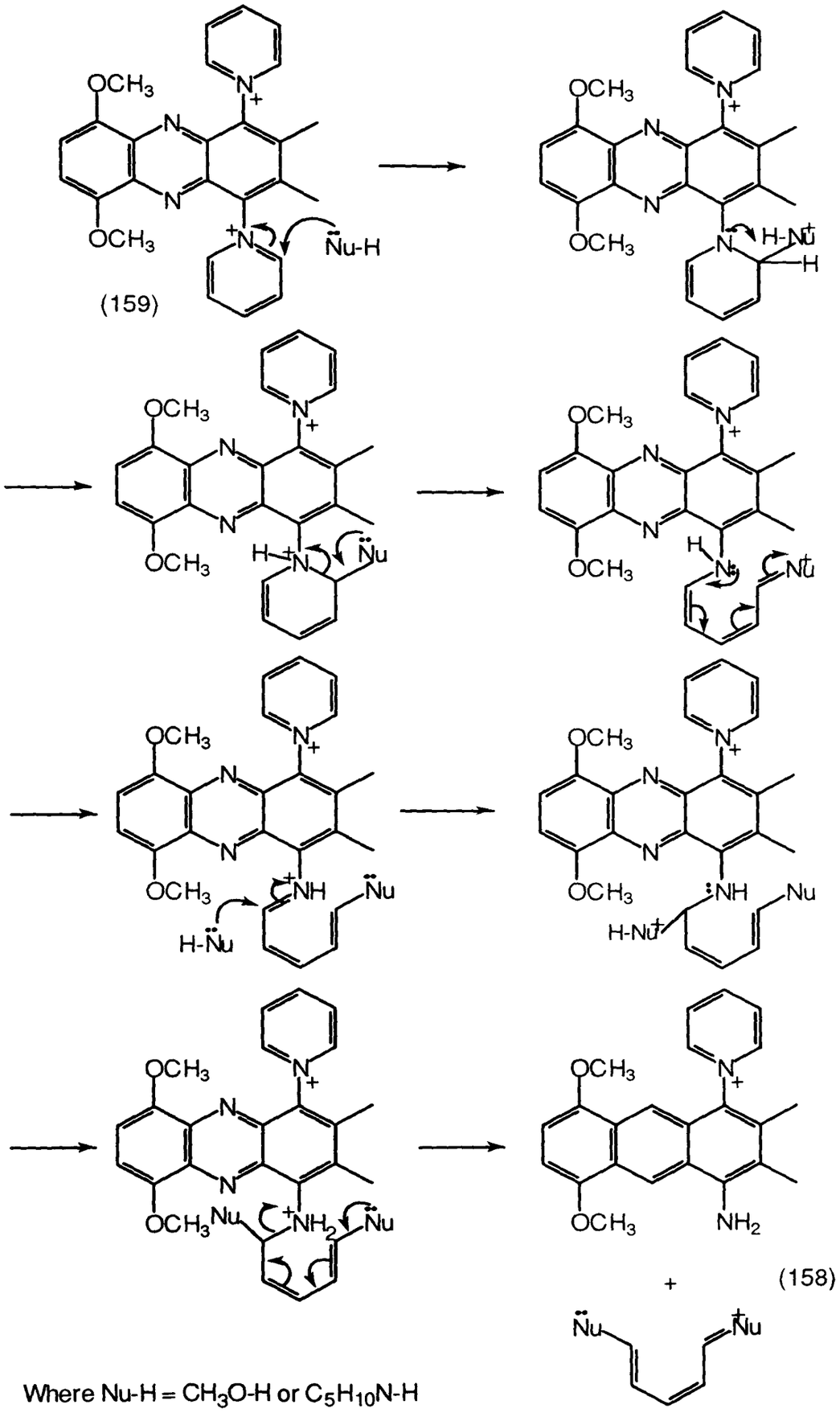
2.1.3 Reaction of 2,3-Dichloro-5,8-(6,7-)dimethoxyquinoxaline (144) with Thiourea

Polyheterocyclic compounds are of current interest as functional materials for electronic, opto-electronic and photonic devices.[101] The heterocycles have been used as charge-generation materials for organic photoconductors and as electron donating molecules for organic superconductors. Some of the dye chromophores such as



(161)

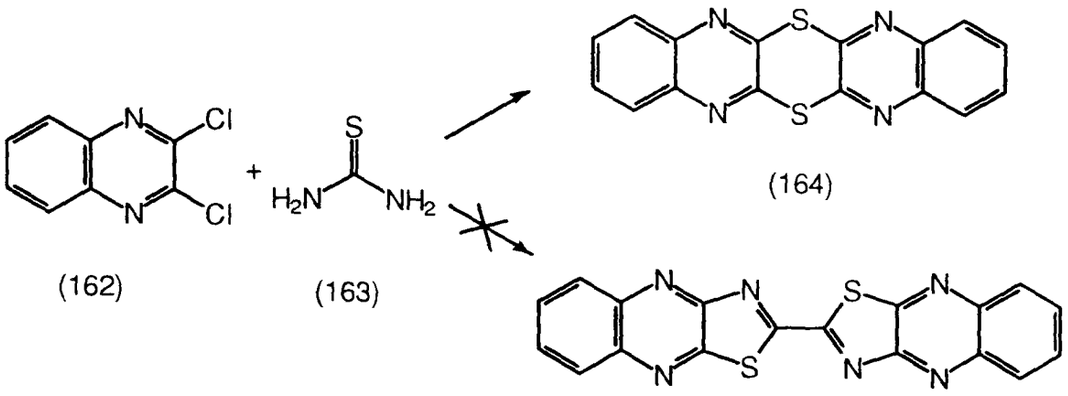
tetraaminoanthraquinone (161) act as electron donating molecules in intermolecular charge transfer (ICT) complexes having high electrical conductivity.[102] Recently, Matsuota *et al.*[103] have reported an interesting reaction between 2,3-dichloroquinoxaline



Where Nu-H = CH_3O-H or $C_5H_{10}N$-H

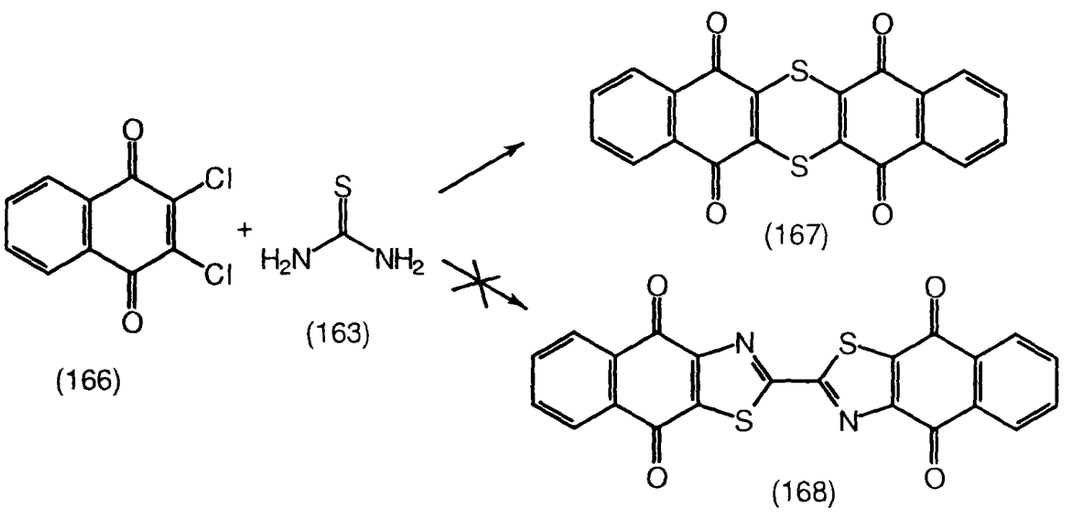
Scheme 13

(162) and thiourea (163) to produce an electron donating molecule (164); this structure is a correction of an earlier formula (165).[104]



(162) (163) (164) (165)

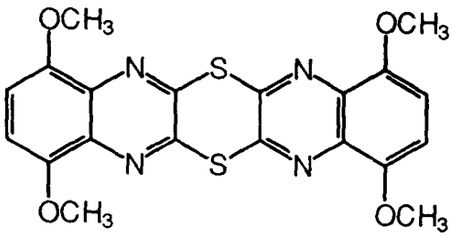
The same workers,[105] also reported the synthesis and characterisation of the tetraone (167) by the reaction of 2,3-dichloronaphthoquinone (166) with thiourea; again the earlier bisthiazole structure (168) is incorrect.[106]



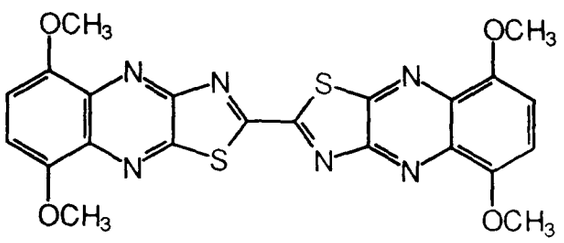
(166) (163) (167) (168)

In the presentwork, a successful attempt was made to synthesise other electron donating molecules (169) and (175) similar to (164) by using the dichlorodimethoxyquinoxalines (144) and (145), respectively, by following Masuoka's procedure. An attempt was also made to isolate and then characterise the expected intermediate (171), which was of interest for structural assignment as well as for gaining

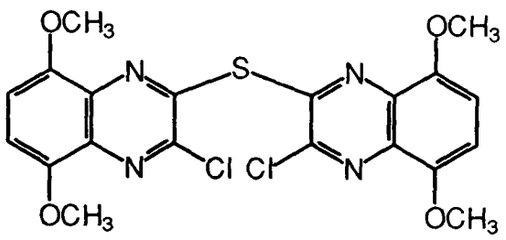
an understanding of the mechanism for the formation of (169) and (173). When dichlorodimethoxyquinoxaline was treated with thiourea (equimolar quantities) in dimethylformamide in the presence of triethylamine, a mixture of two products was obtained: compound (169) was separated by filtration directly from the cold reaction mixture due to its high insolubility in several organic solvents. The second, more soluble compound (171), was separated from the filtrate by the addition of water followed by solvent extraction.



(169)



(170)



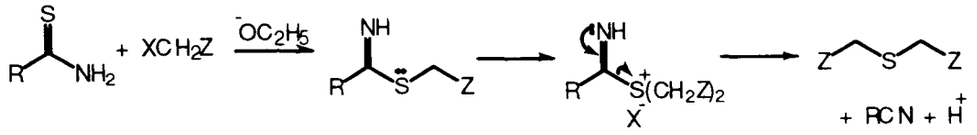
(171)

Compound (169) was characterised as 1,4,8,11-tetramethoxydibenzo[b,i]-6,13-dithia-5,7,12,14-tetrazaanthracene, not the possible (170). The ^{1}H NMR spectrum in deuterated trifluoroacetic acid, indicated a symmetrical structure (169) and showed two singlets at 4.14 and 7.38 ppm due to hydrogens of the four methoxyl groups and four aromatic hydrogens, respectively. The mass spectrum of (169) showed the molecular ion peak at 440 daltons which was in agreement with molecular formula $C_{20}H_{16}N_4O_4S_2$, but not with molecular formula $C_{22}H_{12}N_6O_4S_2$, corresponding to the structure (170).

The soluble component (171) from the above mentioned reaction, was characterised as bis(2-chloro-5,8-dimethoxyquinoxalin-3-yl)sulphide. The ^{1}H NMR spectrum of (171) indicated its unsymmetrical structure by the appearance of two singlets at 3.76 and 4.01 ppm for two different sets of two methoxyl groups. The mass spectrum of (171) confirmed the presence of the two chlorine atoms by the presence of three molecular ion peaks at 482, 480 and 478 daltons due to ^{37}Cl and ^{35}Cl isotopes.

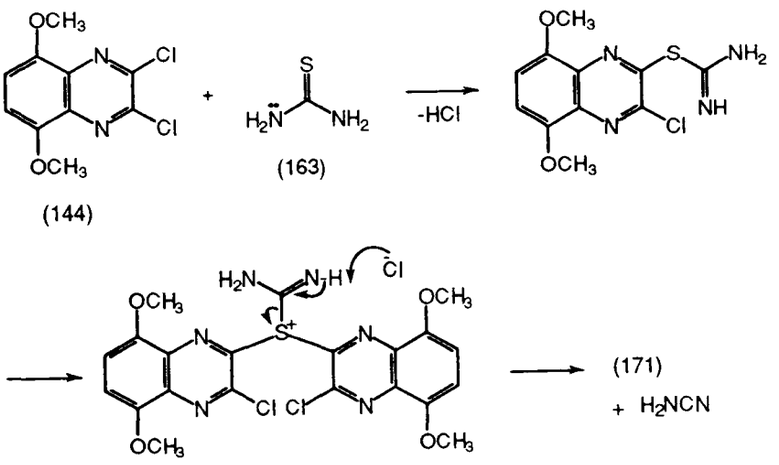
respectively, in a ratio of 1:2:3, which was in agreement with molecular formula $C_{20}H_{16}N_4O_4Cl_2S$. Fragment ion peaks at 447, 445 and 443 and 415 and 413 daltons were probably due to the loss of chlorine and then two methyl groups from the molecular ion. The cyclic disulfide (169) was obtained exclusively by using an excess of thiourea (163).

The reaction between (144) and thiourea seems to be initiated by the nucleophilic attack of sulfur at the 2- or 3-position of (144) as reported in the literature[105,107] for the reaction of α-halogenated compounds with thioacetamides (Scheme 14), which suggests



Scheme 14

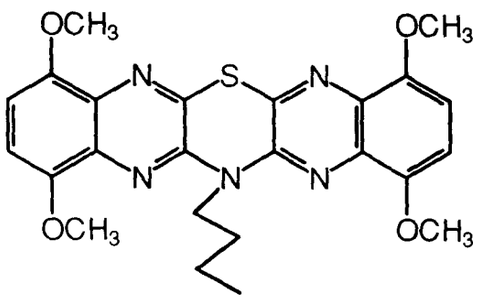
that the reaction proceeds by the cleavage of the thiouronium salt. The cyclic sulphide (171) is a likely intermediate in the formation of (169). This is additional evidence in favour of the formation of (169), instead of (170). A possible reaction pathway is given (Scheme 15).



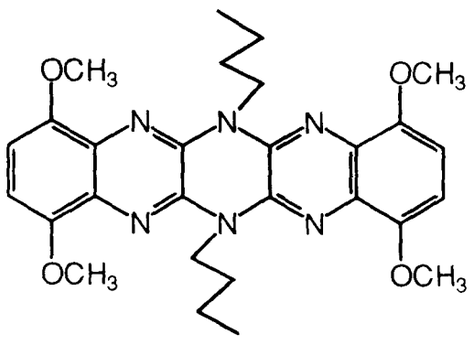
Scheme 15

An attempt was made to utilise (171)) in the synthesis of (172) by treatment with n-butylamine. However, an unexpected compound, 6,13-dibutyl-6,13-dihydro-1,4,8,11-

tetramethoxy-5,6,7,12,13,14-hexaazapentacene (173), was obtained as the only product. The ^1H NMR spectrum indicated a symmetrical structure having four aromatic hydrogens and four methoxy groups which gave rise to two singlets at 6.73 and 3.95 ppm, respectively. The 2- and 3-methylene hydrogens of the n-butyl group gave rise to two heptets at 1.83 and 1.50 ppm, whereas the 1-methylene and terminal methyl



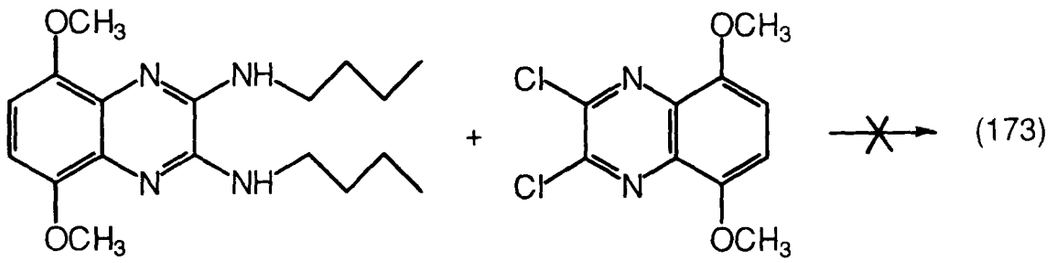
(172)



(173)

produced a quartet and a triplet at 4.47 and 1.03 ppm, respectively. The mass spectrum of (173) showed a molecular ion peak at 518 daltons which was in agreement with a molecular formula $C_{28}H_{34}N_6O_4$, but not with a molecular formula $C_{24}H_{25}N_5O_4S$ corresponding to structure (172)). The elemental analysis of (173) confirmed the absence of sulfur and was in agreement with the molecular formula given. Thus the product of the reaction appeared to be (173).

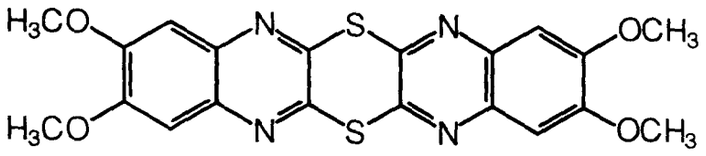
Compound (174) was treated with dichloroquinoxaline (144) under the same conditions, in order to obtain (173) by a different route but the starting material was



(174) (144)

recovered even after boiling under reflux for 24 hours. The failure of the reaction was probably due to the large steric hindrance caused by the n-butyl group, which prevented the attack of amine on the 2- or 3-position of (144).

In a similar way, 2,3,9,10-tetramethoxy-6,13-dihydro-5,7,12,14-tetraza-6,13-dithiapentacene (175)); a structural isomer of (169) was obtained as a single product by the reaction of (145) with an excess of thiourea (163) The formation of the product was preceded by a clear colour change of the reaction mixture from dark brown to light



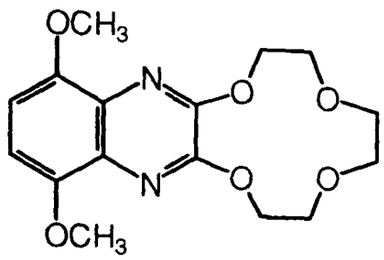
(175)

yellow. The ^{1}H NMR spectrum of (175) was obtained in deuterated trifluoroacetic acid and here the four aromatic hydrogen atoms produced a singlet at 7.65 ppm; a relatively low field compared to the resonance of the aromatic hydrogens of (169). This is probably due to the smaller distance from the protons to the nitrogen atom. The methoxyl groups gave rise to a singlet at 4.24 ppm. The mass spectrum of (175) showed a molecular ion peak at 440 daltons, while the two peaks at 425 and 410 daltons were probably due to the loss of one and two methyl groups from the molecular ion, respectively.

2.1.4 Crown Ethers Containing a Dimethoxyquinoxaline Moiety

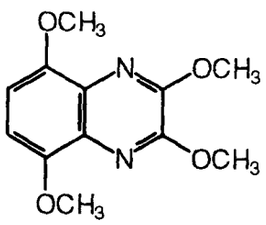
Multihetero-macrocycles which contain pyridino,[108,109] pyrazino,[110] pyrimidino[111] and other heterocyclic subunits[112] have been reported in the literature due to their biological and medicinal interest. From a survey of the literature, the inclusion of the *o*- and *p*-dimethoxyquinoxaline, and the corresponding quinoxaline quinones, within the "crown-ether" framework has not been reported. In the present work, an effort was made to synthesis this new type of macrocyclic system.

Firstly, an attempt was made to prepare the crown ether (176) from 1,4-dihydro-2,3-dioxo-5,8-dimethoxyquinoxalinedione (142) by using triethyleneglycol ditosylate in anhydrous tetrahydrofuran containing caesium fluoride[113] or the dibromo derivative of triethyleneglycol in dry dimethylformamide containing sodium hydride,[114] but the compound (176) was not obtained and (142) was recovered. To find out the possible

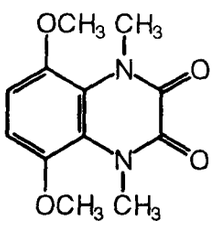


(176)

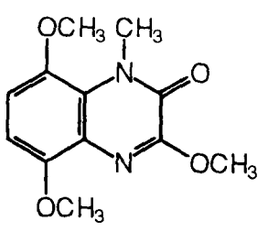
reason, the literature for the methylation of (142) was surveyed. Oguchi[89] reported the methylation using sodium hydroxide and dimethylsulphate and obtained only 1,4-dimethyl-2,3-dioxo-1,2,3,4-tetrahydroquinoxaline (177) in 65 % yield. Unfortunately, no spectral data was given but the melting point (180°C) and elemental analysis (Found: N, 10.58. Calculated N, 11.20%) were given. In the present work, (142) was methylated using Oguchi's reaction conditions and the melting point of the crude product was found to be 180-181°C, but by column chromatography two compounds, (178) (m.p. 202-203°C) and (179) (m.p. 176-177°C), instead of (177), were obtained. The first eluted product was characterised as 2,5,8-trimethoxy-4-methyl-2(1H)-oxo-quinoxaline (178).



(146)



(177)



(178)

(179)

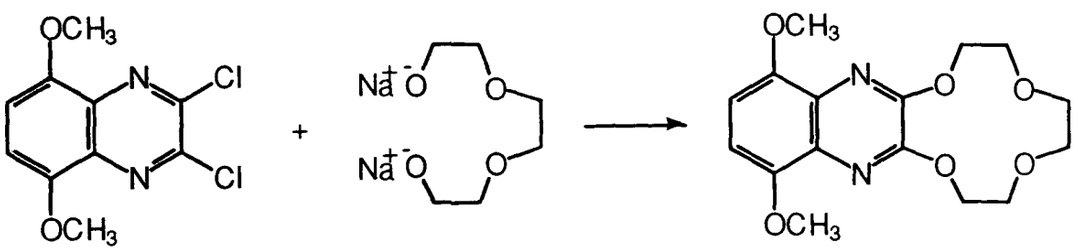
A strong absorption at 1670 cm^{-1} in the IR spectrum of (178) was due to the carbonyl group and there was no characteristic peak for the hydroxyl group. The ^1H NMR spectrum of (178) showed the presence of an unsymmetrical compound rather than symmetrical compounds (177) or (146). Two singlets at 3.82 and 4.10 ppm were attributable to N-methyl and O-methyl groups, respectively, while the two methoxyl groups at the 5- and 8-position produced two singlets at 3.92 and 3.95 ppm, respectively. Further evidence for the unsymmetrical nature of (178) was the appearance of two

doublets at 6.80 and 6.73 ppm attributable to hydrogen atoms at the 7- and 6-position, respectively. The mass spectrum of (178) showed a molecular ion peak at 250 daltons, which agreed with the molecular formula $C_{12}H_{14}N_2O_4$.

The second eluted product was characterised as 2-hydroxy-4-methyl-5,8-dimethoxy-3(4H)-quinoxalinone (179). The IR spectrum of (179) showed a strong absorption at 3600-3500 cm^{-1} due the hydroxyl group. Its ^1H NMR spectrum showed a peak at 8.91 ppm, exchanged with D_2O, which was assigned to hydroxyl group. Two methoxyl groups and one N-methyl gave rise to three singlets at 3.88, 3.85 and 3.82 ppm, respectively. The mass spectrum of (179) showed a molecular ion peak as a base peak at 236 daltons, in agreement with molecular formula $C_{11}H_{12}N_2O_4$.

The results of the methylation of 1,4-dihydro-5,8-dimethoxyquinoxaline-2,3-dione (142) indicated that this alkylation technique is likely to produce a mixture of products instead of a single product. Hence, another route was sought for the preparation of (176).

2,3-Dichloro-5,8-dimethoxyquinoxaline (144) reacts very easily with 2 equivalents of sodium alkoxide to give disubstituted products.[89,115,116] Hence, an attempt was made to prepare (176) by treating (144) with an equimolar quantity of the disodium salt of triethylene glycol (182) (generated by treating triethylene glycol with sodium metal, in refluxing anhydrous tetrahydrofuran) using a high dilution technique.

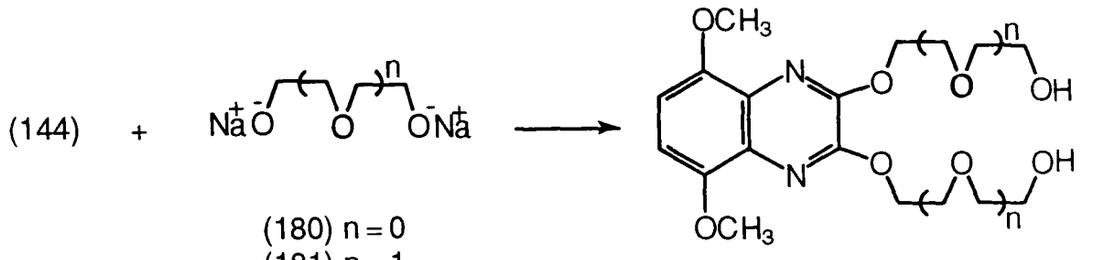


(144) (182) (176)

The ^1H NMR spectrum of the 12-crown-4 in the product showed a broad singlet at 5.02 ppm attributable to the 5- and 12-methylene hydrogen atoms of (176), while a broad singlet at 4.30 was due to 8- and 9-methylene hydrogens. The hydrogen atoms of the 5'- and 8'-methoxyl group overlapped with the 6- and 11- methylene hydrogens

to produce a broad singlet at 4.20 ppm, and the aromatic quinoxyl hydrogens gave rise to a singlet at 7.38 ppm. The mass spectrum of (176) showed a molecular ion peak at 336 daltons, in agreement with the molecular formula $C_{16}H_{20}N_2O_6$.

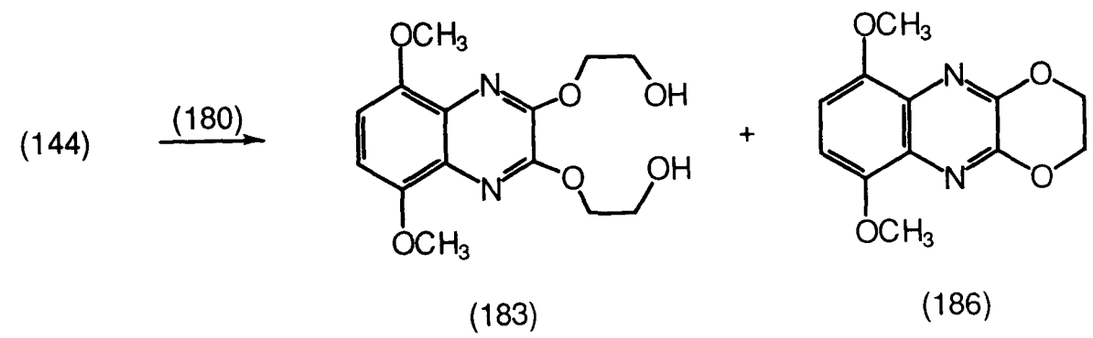
The formation of the 12-crown-4 (176) encouraged to prepare different crown ethers containing the dimethoxyquinoxaline moiety. Hence, as a first stage, dihydroxycompounds (183), (184) and (185) were prepared by treatment of (144) with the disodium salt of ethylene glycol (180), diethylene glycol (181) and triethylene glycol (182), respectively (Scheme 16).



Schceme 16

The reaction of 2,3-dichloro-5,8-dimethoxyquinoxaline (144) with the disodium ethylene glycolate (180) (1:2 molar eq), generated from ethylene glycol and sodium metal, in refluxing anhydrous tetrahydrofuran, gave two compounds (183) and (186)

Compound (183) was identified as 2,3-bis(2-hydroxyethoxy)-5,8-dimethoxyquinoxaline. The IR spectrum of (183) a broad peak at 3350 cm^{-1} due to the

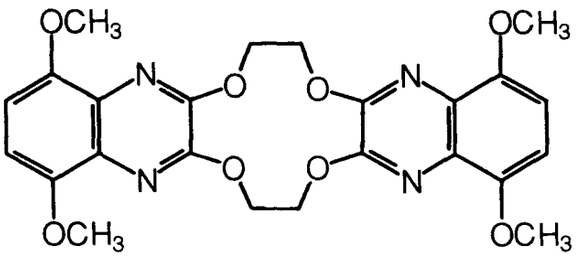


hydroxyl groups. The α-methylene hydrogens appeared as a broad triplet at 4.52 ppm in the ^1H NMR spectrum, whereas the β-methylene hydrogens produced a broad triplet

at 3.84 ppm, which overlapped with the singlet due to the 5- and 8-methoxy groups at 3.88 ppm. The hydrogen atom of hydroxyl group gave rise to a sharp triplet at 4.80 ppm which was exchanged with D_2O. The down field shift of the α-methylene hydrogens is associated with imidate characteristics within the molecule.[111]

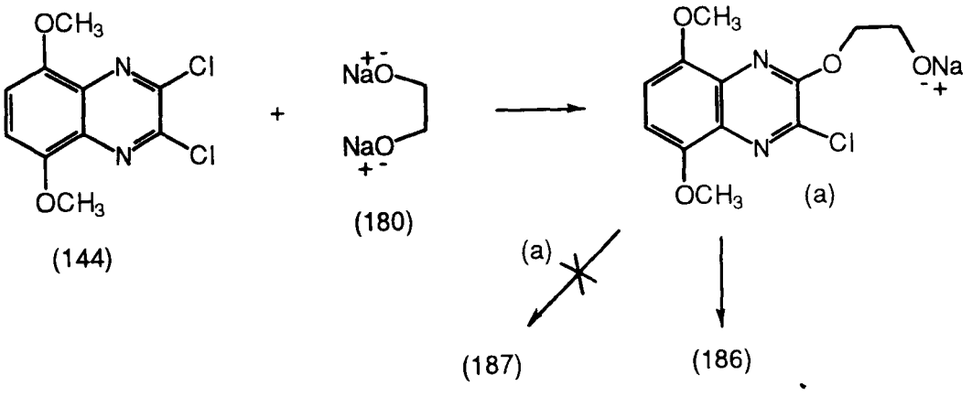
$$-N{=}CH{-}O{-}CH_2- \qquad -N^{-}{-}CH{=}O^{+}{-}CH_2-$$

The mass spectrum of (183) showed a molecular ion peak at 310 daltons which was in agreement with its molecular formula, while the peaks at 222, 207 and 193 daltons were probably due to the loss of two ethylene oxide, two ethylene oxide and one methyl group, and two ethylene oxide and two methyl groups, respectively.



(187)

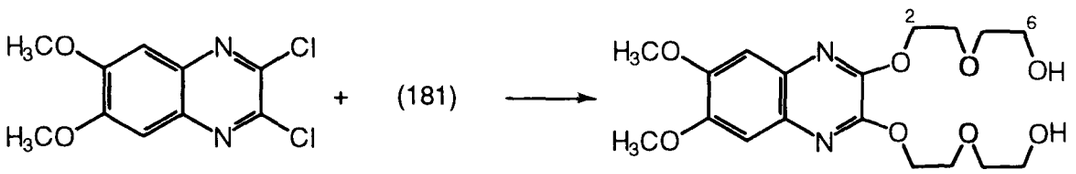
The compound (187) is, in some respects, very similar to compound (186). Unfortunately, all the three peaks expected in the ^1H NMR spectra for the compounds (186) and (187) are the same. The major evidence in favour of structure of (186), is the appearance of a base peak for molecular ion in its mass spectrum, at 248 daltons, as expected for the molecular formula, $C_{12}H_{12}N_2O_4$. The product (186) is formed by an intramolecular cyclisation reaction (Scheme 17).



Scheme 17

The chemical evidence for the structure of (186) was obtained by the reaction of (183) with sodium hydride in dimethylformamide alone, or with the addition separately of sodium iodide or triethylene glycolyl ditosylate. The reaction product in each case was (186) which can only be explained on the basis of the formation of the six-membered ring system. An interesting feature of the above reactions is that the yield of (186) was very poor (11 %) in the direct reaction of compound (144) with disodium salt of ethylene glycol (80), but the reaction of (183) gave compound (186) in good yield (60-70 %). In this connection, it is interesting that 2,3-bis(2'-hydroxyethoxy)-5,8-dimethoxyquinoxaline (183) was obtained exclusively and in high yield (80-85 %) when an excess of the disodium salt of ethylene glycol(1:4 molar equivalents) was used in the reaction with (144).

Similarly, the dihydroxy compounds (184) and (188) were obtained as the only product, when an excess of disodium diethylene glycolate (181) was treated separately with the dichloro compounds (144) (Scheme 16) and (145), respectively.

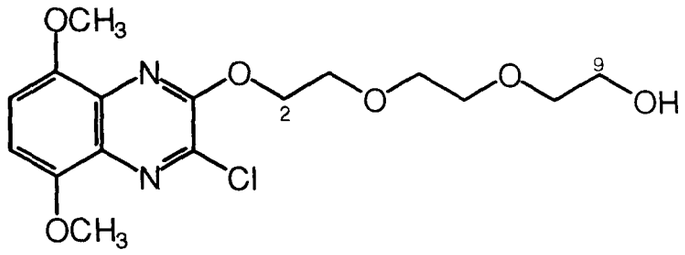


(145) (188)

The structures of (184) and (188) were confirmed by their IR spectrum where a broad peak at 3400 cm^{-1} attributable to the hydroxy group was clear. This group produced a singlet at 3.48 and 3.53 ppm, respectively, in their ^1H NMR spectra. A singlet at 3.85 and 3.96 ppm in the ^1H NMR spectra of (184) and (188), respectively, was attributable to the 5- and 8-methoxyl groups and 6'-methylene hydrogens. The 3-' and 5'-methylene hydrogen atoms of (184) produced a triplet at 3.52 ppm, whereas the 2'- methylene hydrogen atoms gave rise to a triplet at 4.62 ppm. The 2'-methylene hydrogen atoms in (188) produced a triplet at the same position (4.62 ppm) as for (184). The mass spectrum of (184) and (188) showed a molecular ion peak at 398 daltons, in agreement with the molecular formula $C_{18}H_{26}N_2O_8$.

Compound (144) (1 mole) was treated with an excess of disodium triethylene glycolate (5 mole) (generated from triethylene glycol (182) and sodium metal) in

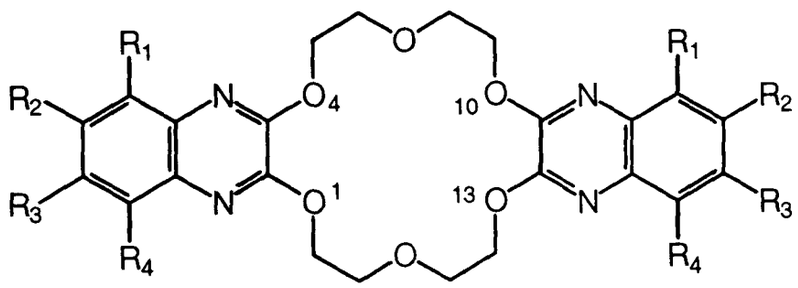
refluxing anhydrous tetrahydrofuran to produce (185), but a mixture of (185) and (189) was obtained even after 12 h. The IR spectrum of the dihydroxy compound (185) showed a peak at 3300 cm^{-1} due to the hydroxyl group. The aromatic hydrogens 6-H and 7-H, produced a singlet at 6.81 ppm, which showed the symmetrical nature of (185). The mass spectrum of (185) showed a molecular ion peak at 486 daltons.



(189)

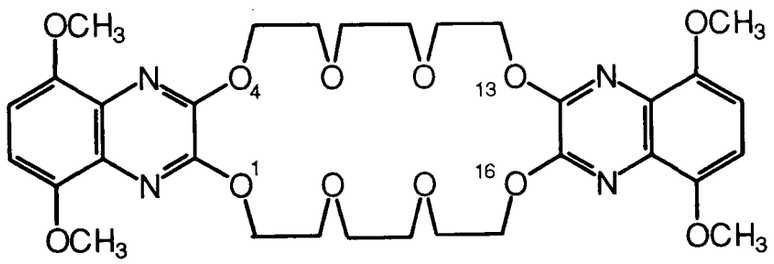
The formation of (189) was probably due to the steric crowding of the long 3-substituent which protects the 2-position from nucleophilic attack by disodium triethylene glycolate. The IR spectrum of (189) showed a strong absorption at 3390 cm^{-1} due to the hydroxyl group. Its ^{1}H NMR spectrum indicated the unsymmetrical nature of (189) by showing two doublets at 6.31 and 6.86 ppm with an ortho coupling constant J = 8.7 Hz. These peaks were assigned for 6-H and 7-H, respectively. The mass spectrum of (189) showed two peaks for molecular ions at 274 and 272 for ^{37}Cl and ^{35}Cl, which confirmed the presence of one chlorine atom in the molecule (189).

2,3,11,12-Bis(5',8'-dimethoxyquinoxalinyl)-1,4,7,10,13,16-hexaoxacyclooctadeca-2,11-diene (190) and 2,3,11,12-bis(6',7'-dimethoxyquinoxyl)-1,4,7,10,13,16-



(190) $R_1 = R_4 = OCH_3$; $R_2 = R_3 = H$
(191) $R_1 = R_4 = H$; $R_2 = R_3 = OCH_3$

hexaoxacyclooctadeca-2,11-diene (191) were obtained by treating the dihydroxy compounds (184) and (188) with the 2,3-dichlorodimethoxyquinoxalines (144) and (145), respectively. Both products (190) and (191) were solid, the former compound (190) was very insoluble in all organic solvents except trifluoroacetic acid. This solvent was used as the solvent for ^{1}H NMR spectroscopy in which the α-methylene hydrogen atoms of (190) produced a broad singlet at 5.07 ppm, whereas the β-methylene hydrogens gave rise to a peak at 4.32 ppm. The aromatic hydrogens produced a singlet at 7.19 ppm. Compound (191) was soluble in $CDCl_3$, and its ^{1}H NMR spectrum showed the α-methylene hydrogen atoms as a triplet at 4.61 ppm, whereas the β-methylene hydrogens of (191) gave rise to a triplet at 3.97 ppm. The aromatic hydrogens in (190) and (191) produced a singlet at 7.19 and 7.07 ppm, respectively. The mass spectrum of (190) and (191) showed the expected a molecular ion peak at 584 daltons.



(192)

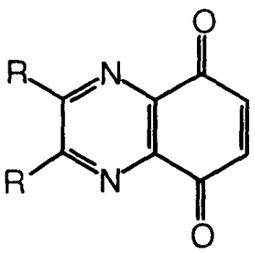
2,3,14,15-Bis(5',8'-dimethoxyquinoxalinyl)-1,4,7,10,13,16,19,22-octaoxacyclotetradodeca-2,14-diene (192) was obtained by treating the diol (185) with the dichloro compound (144) using a high dilution technique. The ^{1}H NMR spectrum of (192) showed a triplet at 4.67 ppm (assigned for the α-methylene hydrogens) and the aromatic hydrogens produced a singlet at 6.79 ppm. Four methoxyl groups and the β-methylene hydrogens gave rise to a multiplet centred at 3.95 ppm, and the γ-methylene hydrogens produced a triplet at 3.70 ppm. The mass spectrum of (192) showed the expected molecular ion peak.

2.2 PREPARATION OF DIAZANAPHTHOQUINONES

2.2.1 Preparation of 2,3-Disubstituted Quinoxaline-5,8-diones

The formation of quinones from dimethoxy compounds has usually been achieved by using the relatively long route[21,87,117] of demethylation with anhydrous aluminium chloride to obtain the dihydroxy compounds and subsequent oxidation of the diols using one of several available oxidising agents.

In the present work, attempts were made to obtain the different heterocyclic quinones in a single step from the *p*-dimethoxy compounds by using ceric ammonium nitrate as the oxidising agent.[118,119] The known quinones, (49), (94) and (193),



(49) R = H
(94) R = CH_3
(193) R = C_6H_5

were made by this oxidation of the respective *p*-dimethoxy compounds, and had similar melting points, and other data, to that given in the literature of these compounds.[118]

The novel heterocyclic quinones, made by the oxidation of the *p*-dimethoxy compounds include:-

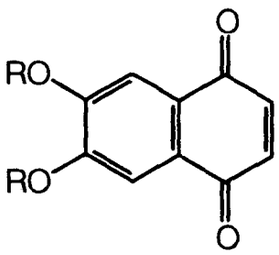
(a) quinoxaline quinones containing electron-donating groups at the 2- and 3-position

(b) quinoxaline quinones containing electron-withdrawing groups at the 2- and 3-position, and

(c) quinoxaline quinones containing crown ethers.

2.2.1.1 Quinoxaline Quinones Containing Electron-Donating Groups

Quinoxaline quinones containing electron-donating groups (194), (195) and (196) were prepared by the oxidation of the corresponding 2,3-disubstituted-*p*-dimethoxyquinoxalines (146), (147) and (148), respectively. The IR spectra of (194)-

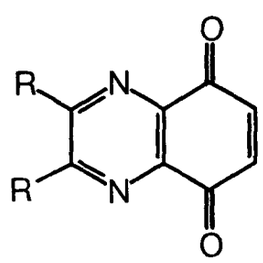


(194) R = OCH_3
(195) R = OC_2H_5
(196) R = SC_2H_5

(196) showed a strong absorption in the range of 1690-1670 cm^{-1}, due to the carbonyl groups. The ^1H NMR spectra showed the absence of 5- and 8-methoxy group whereas the hydrogen atoms at 6- and 7-position produced a singlet at 6.95 - 6.90 ppm. The mass spectrum of (194) showed a base peak for molecular ion at 220 daltons in agreement with the molecular formula $C_{10}H_8N_2O_4$. Two fragments at 205 and 190 daltons were probably due to the loss of one and two methyl group from the molecular ion, respectively. The mass spectrum of (195) showed a molecular ion peak at 248 daltons, in agreement with the molecular formula $C_{12}H_{12}N_2O_4$. Two peaks at 219 and 192 daltons were probably due to the loss of one ethyl group and then two molecules of CO from the molecular ion, respectively. The mass spectrum of (196) showed the expected molecular ion peak at 280 daltons and a peak at 251 daltons, probably due to the loss of one ethyl group from the molecular ion.

2.2.1.1 Quinoxaline Quinones Containing Electron-Withdrawing Groups

Quinoxaline quinones containing electron-withdrawing groups (197) and (198) were prepared by the oxidation of (154) and (156), respectively. The IR spectrum of



(197) R = CO_2CH_3
(198) R = CN

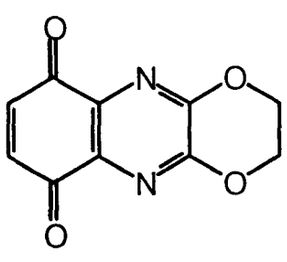
(197) showed two strong absorptions at 1750 and 1690 cm^{-1} due to the carbonyl groups of the ester and quinone, respectively. The IR spectrum of (198) showed a strong

absorption at 1700 cm^{-1} due to the carbonyl group, whereas a peak at 2260 cm^{-1} was due to the cyano group. The ^1H NMR spectra of (197) and (198) showed a singlet at 7.29 and 7.28 ppm, respectively, assigned for the hydrogen atoms of the quinonoid ring.

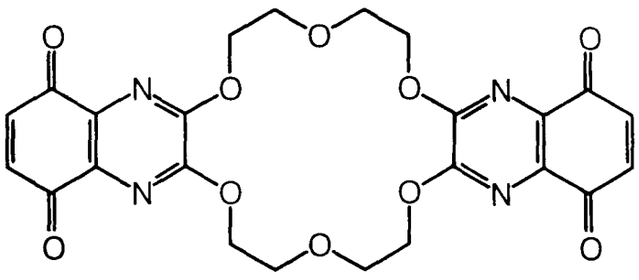
The appearance of 6-H and 7-H of both (194), (195) and (196) at relatively high field (6.95-6.90 ppm) compared to the quinone hydrogens (7.28-7.29 ppm) in (197) and (198), was probably due to the strong electron-donating effect of the alkoxy and thioalkyl groups, because hydrogen atoms at the same position in the simple quinoxaline-5,8-dione (49) produced a singlet at 7.24 ppm,[54,118] which is very close to the values for the same hydrogens in quinoxaline quinones (197) and (198) containing electron-withdrawing groups.

2.2.1.3 Quinoxaline Quinones Containing A Crown Ether

2,3-Dihydro-1,4-dioxa-9,10-diazaanthracene-5,8-dione (199) was obtained by the oxidation of (186) in the presence of ceric ammonium nitrate. A sharp peak at 1680 cm^{-1} in the IR spectrum of the product (199) was attributed to the carbonyl group. The molecular ion peak in the mass spectrum of the compound (199) was at 218 daltons, which was in agreement with the molecular formula $C_{10}H_6N_2O_2$.



(199)



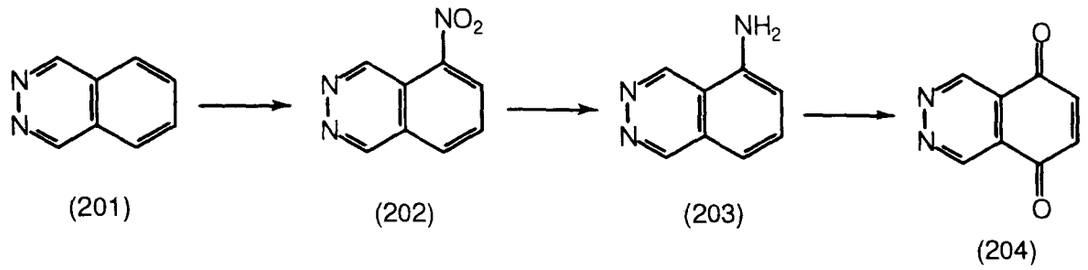
(200)

Oxidation of the tetramethoxy heterocycle (190) with ceric ammonium nitrate gave the multiheteromacrocyclic diquinone; 2,3,11,12-bis(5',8'-oxoquinoxalinyl)-1,4,7,10,13,16-hexaoxacyclooctadeca-2,11-diene (200). The IR spectrum showed a strong absorption at 1675 cm^{-1} attributable to carbonyl groups. The singlet for the 5'- and 8'-methoxyl groups seen in the ^1H NMR spectrum of (190), did not appear in the ^1H NMR spectrum of (200), but the quinone hydrogen atoms produced a singlet at 7.05 ppm. The mass spectrum of (200) showed the expected molecular ion peak at 524

daltons.

2.2.2 Phthalazine-5,8-dione (204)

Phthalazine-5,8-dione (204) was obtained by using the following reaction sequence (Scheme 18). 5-Nitrophthalazine (202) was obtained (54 %) by a small

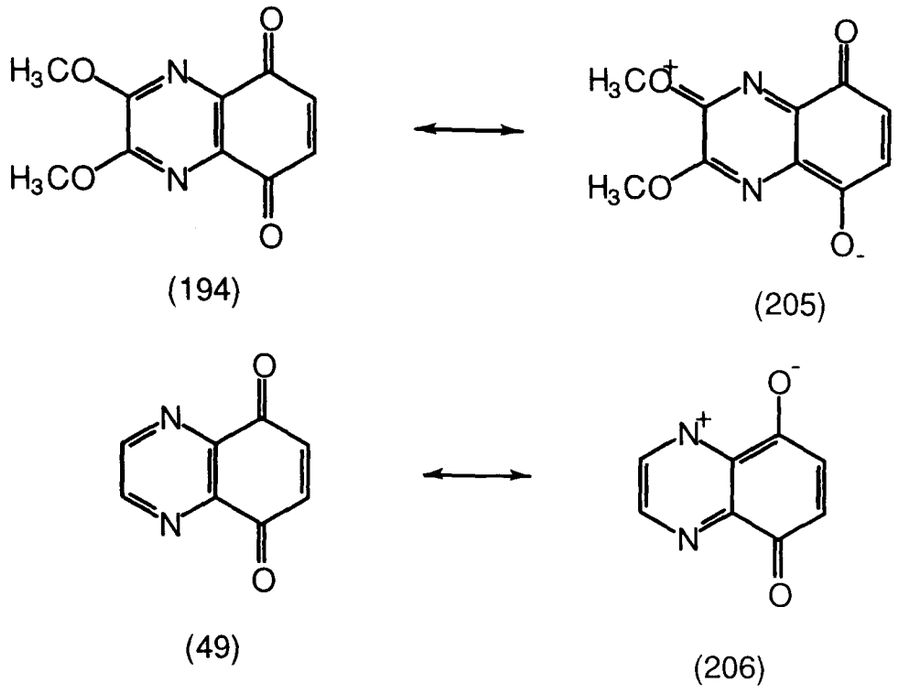


(201) (202) (203) (204)

Scheme 18

modification of a known method[120] for the nitration of phthalazine (201). The modification was to decrease the reaction time from 12 h to 9 h, using a larger quantity of potassium nitrate (8.5 g) for each 3.0 g of phthalazine, and a very careful dropwise addition of 10 M sodium hydroxide solution for the basification of the reaction mixture. The reduction of the 5-nitro compound (202) to the corresponding 5-amino compound (203) was carried out by using sodium dithionite[54] but the yield was low (20-22 %). An unsuccessful attempt was made to increase the yield by using catalytic hydrogenation over palladium charcoal at room temperature. On the other hand, the reduction with $Ti(III)Cl_3$ gave the 5-amino compound[121] in about 42 % yield. The oxidation of the aminophthalazine (203) to phthalazine-5,8-dione (204) was achieved by using potassium dichromate and conc. sulphuric acid following the method employed for the formation of naphthaquinone from 5-aminonaphthalene.[122] It was seen by t.l.c that, at the time of preparation, phthalazine-5,8-dione (204) was pure but, with the passage of time, the quinone decomposed and remained at the base line. This change takes place in the solid as well as in solution. To avoid this problem, the quinone must be prepared immediately prior to its use and special care must be taken to protect the quinone from light.

The stability of the quinones prepared in this work varied. The 2,3-disubstituted quinoxaline quinones containing electron donating groups, (194), (195), (196) and also (193), were found to be more stable at room temperature in the crystalline form or in



(194) (205)

(49) (206)

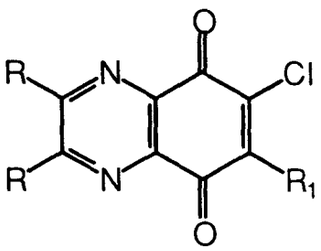
solution than the unsubstituted diazanaphthaquinone (49) and (204). The substituted quinoxalinequinones (197) and (198) were more stable than (49) and (204); this might be due the extensive conjugation to the carboxylate and cyano group, respectively. The probable reason for the stability of quinones (194), (195), (196) and (193) was thought to be presence of the significant contributing structures, e.g., (205). In case of quinones (49), (197), (198) and (204), this stability factor was not present and the positive charge was on the divalent nitrogen atom, e.g. (206).

2.3 OXIDATIVE CHLORINATION OF *p*-DIMETHOXYQUINOXALINES

The oxidation of tetramethoxy compound (146) was done using conc. hydrochloric acid and conc. nitric acid and gave 6,7-dichloro-2,3-dimethoxyquinoxaline-5,8-dione (208) as a single product in 56 % yield. A much higher yield than that obtained (1.1 %) when 2,3-dichloro-quinoxaline-5,8-dione (207),[54] was obtained by the oxidation of 5,8-dimethoxyquinoxaline (13). The difference was probably due to the electron-donating effect of the groups at the 2- and 3-position. The IR spectrum of (208) showed a strong absorption at 1720 cm^{-1} due to the carbonyl groups. The methoxyl groups at the 2- and 3-positions produced a singlet at 4.21 ppm in its ^1H NMR specrum. The presence of the two chlorine atoms was confirmed by the appearance of

three molecular ion peaks at 292, 290 and 288 daltons, due to the isotopes of chlorine.

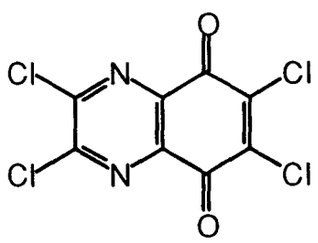
2,3-Diethoxy-5,8-dimethoxyquinoxaline (147), on oxidative chlorination with the same reagent, gave rise to a mixture of two products: dichloro (209) and monochloro derivative (210). Compound (209) showed a peak at 1700 cm^{-1} due to the carbonyl groups, whereas the monochloro compound (210) showed two peaks at 1700 and 1680 cm^{-1}. The presence of only one chloro group in (210) was also seen in its ^1H NMR



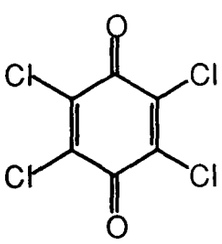
(207) R = H; R_1 = Cl
(208) R = OCH_3; R_1 = Cl
(209) R = OC_2H_5; R_1 = Cl
(210) R = OC_2H_5; R_1 = H

spectrum where 7-H produced a singlet at 7.13 ppm. Moreover, the mass spectrum of (210) showed two peaks at 284 and 282 daltons in agreement with molecular formula $C_{12}H_{11}N_2O_4Cl$.

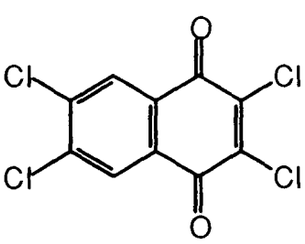
The oxidative chlorination of 2,3-dichloro-5,8-dimethoxyquinoxaline (144) produced a very interesting tetrachloro compound (211) which could be named as "chloroquinoxanil" parallel to the high potential oxidants, chloranil[123] (212) and its benzo analogue (213). 2,3,6,7-Tetrachloroquinoxaline quinone (211) contains not only the



(211)



(212)



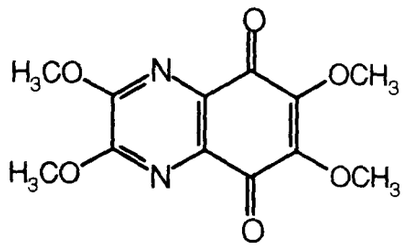
(213)

quinone group but also a basic group (nitrogen) as a part of the ring. The IR spectrum of (211) showed a strong absorption at 1705 cm^{-1} due to the carbonyl groups and the mass spectrum showed five peaks (304,302,300,298 and 296 daltons) due to the presence of four chlorine atoms.

2.4 REACTIONS OF DIAZANAPHTHOQUINONES

2.4.1 Reaction of 2,3,6,7-Tetrachloroquinoxaline-5,8-dione (211) with Sodium Methoxide

Compound (211) was treated with sodium methoxide at room temperature, and a tetramethoxy compound (214) was obtained. Its IR spectrum showed a strong

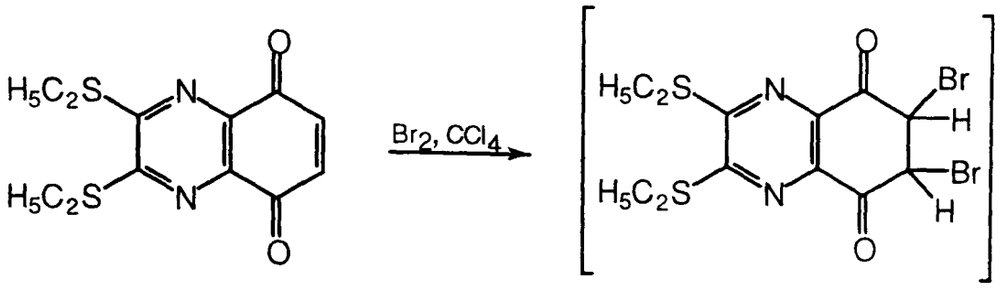


(214)

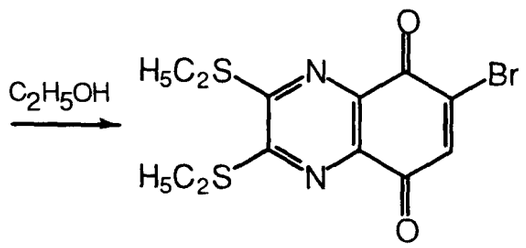
absorption at 1680 cm^{-1} due to the carbonyl groups. The methoxyl groups at 6- and 7-position produced a singlet at 4.08 ppm in the ^1H NMR spectrum, whereas the 2- and 3-methoxyl groups gave rise to a down field singlet at 4.19 ppm due to the neighbouring pyrazine ring.[111] The mass spectrum of (214) showed a molecular ion peak at 280 daltons and four fragment ion peaks at 265, 250 , 235 and 220 daltons, probably due to the loss of one, two, three and four methyl groups, respectively, from the molecular ion.

2.4.2 Reaction of 2,3-Bis(ethylthio)-5,8-dimethoxyquinoxaline (196) with Bromine

2,3-Bis(ethylthio)-5,8-dimethoxyquinoxaline (196), on reaction with bromine in carbon tetrachloride produced a non-separable mixture of two products; one of them might be the unstable adduct of bromine and (196), because two hydrogens of the adduct were seen as a singlet at 5.44 ppm in the ^1H NMR of this mixture. The reaction mixture were then refluxed in ethanol to obtain the monobromoquinone (215) (Scheme 19). Its IR spectrum showed two peaks at 1700 and 1685 cm^{-1}, indicating the unsymmetrical nature of the molecule. The presence of one bromine atom in (215) was also



(196)



(215)

Scheme 19

shown in its ^{1}H NMR spectrum where 7-H produced a singlet at 7.08 ppm and the mass spectrum which showed the molecular ion as two peaks at 360 and 358 daltons for Br^{81} and ^{79}Br.

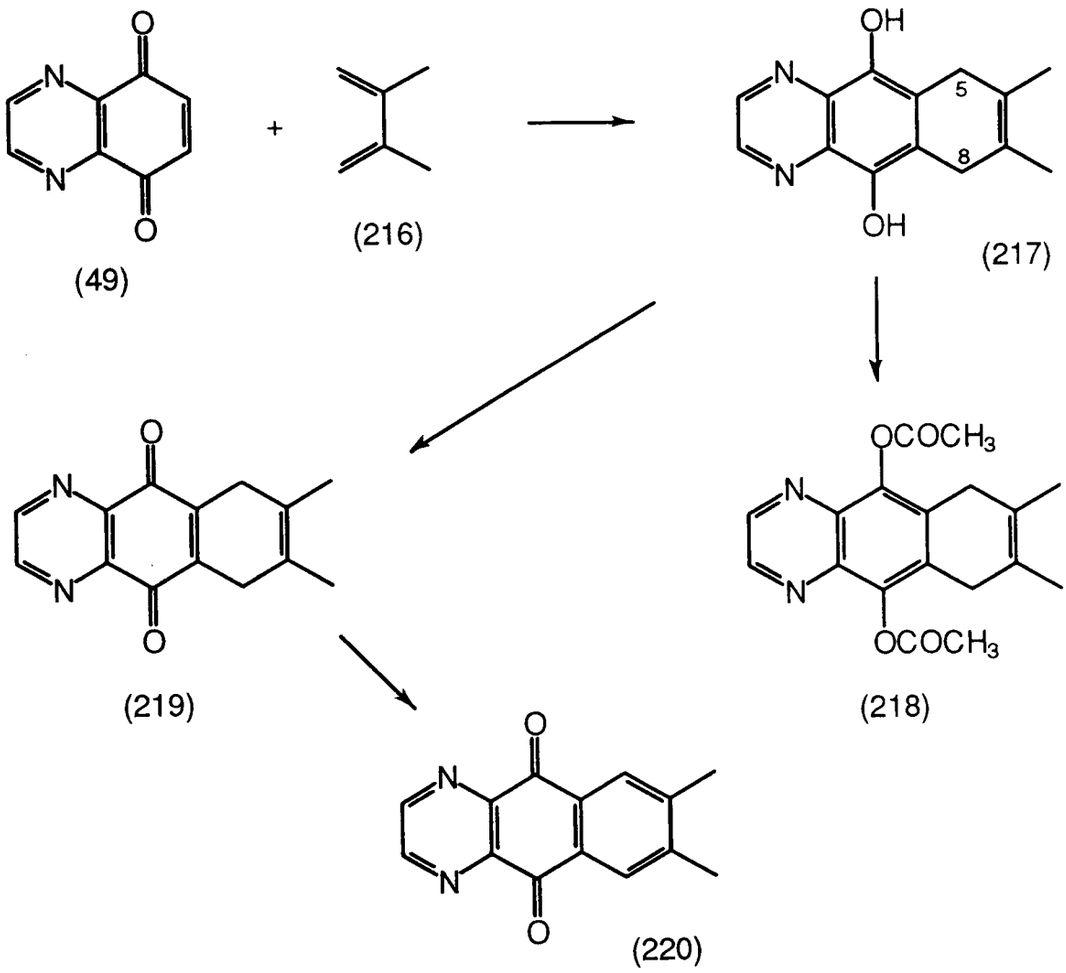
2.5 THE DIELS-ALDER REACTIONS

2.5.1 Reaction of Quinoxaline Quinone (49) with 2,3-Dimethyl-1,3-butadiene (216)

The Diels-Alder reaction of 2,3-dimethyl-1,3-butadiene (216) with different quinones (49), (194), (195) and (196) was attempted by using a known method[53,84] for the reaction of the diene with either quinoline-5,8-dione[53] (47) or 2,3-dimethylquinoxaline-5,8-dione (94).[84]

Quinoxaline-5,8-dione (49) gave a similar result (Scheme 20) to those reported for the reaction of (47) and (94) with the diene (216) in refluxing absolute ethanol for 16 h. The cycloaddition product (217) was obtained as its dihydroxy tautomer, 5,8-dihydro-6,7-dimethyl-9,10-dihydroxy-1,4-diazaanthracene (Scheme 20). The IR

spectrum of (217) plainly showed a peak at 3380 cm^{-1} due to the hydroxyl group. The absence of any absorption band in the range of 1650-1750 cm^{-1} excluded the possible presence of its keto isomer. The ^1H NMR spectrum showed a singlet at 3.34 ppm due to the 5- and 8-methylene hydrogen atoms, and the protons of the hydroxyl groups produced a singlet at 9.27 ppm, exchanged with D_2O. The mass spectrum of (217) showed a molecular ion peak at 242 which was in agreement with the molecular formula, but the base peak was at 227, probably formed by the loss of one methyl group from the molecular ion.



Scheme 20

The structure of the dihydroxy product (217) was confirmed by acetylating the hydroxy group to produce 5,8-dihydro-6,7-dimethyl-9,10-diacetoxy-1,4-diazaanthracene(218) (Scheme 20). A sharp peak at 1755 cm^{-1} in its IR spectrum was attributable to the acetoxy carbonyl group. The ^1H NMR spectrum showed one singlet

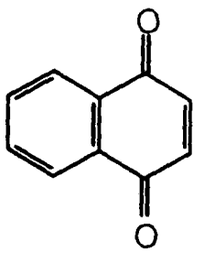
at 2.49 ppm due to the acetoxy group, whereas the methyl groups at the 6- and 7-positions produced a singlet at 1.80 ppm. The methylene hydrogens gave rise to a singlet at 3.37 ppm. The mass spectrum showed a molecular ion peak at 326 daltons in agreement with the molecular formula $C_{18}H_{18}N_2O_4$.

Treatment of (217) with silver(II) oxide produced a smooth oxidation to give 5,8-dihydro-6,7-dimethyl-1,4-diazaanthacene-9,10-dione (219) which had a sharp peak in its IR spectrum at 1680 cm^{-1} due to the carbonyl group. In its ^1H NMR spectrum, the methylene hydrogens 5- and 8-H produced a singlet at 3.47 ppm, whereas the 6- and 7-methyl groups gave rise to a peak at 1.79 ppm. The mass spectrum of (219) showed a molecular ion peak at 240 daltons, which was in agreement with molecular formula $C_{14}H_{12}N_2O_4$ but a more intense peak at 238 was probably due to the loss of two hydrogen atoms to produce a fully aromatic system. A very intense peak at 210 daltons was probably due to the loss of two methyl groups from the molecular ion.

The partially reduced aromatic system (219) was further oxidised to the fully aromatic system by passing air through the boiling solution to obtain 6,7-dimethyl-1,4-diazaanthracene-9,10-dione (220). This fully oxidised cycloaddition product showed a strong absorption at 1685 cm^{-1} in its IR spectrum attributable to the carbonyl group. Hydrogen atoms on the benzene ring gave rise to a singlet at 8.13 ppm in the NMR spectrum and the two methyl groups at the 6- and 7-positions produced a singlet at 2.47 ppm. The mass spectrum showed a base peak for the molecular ion at 238 daltons, while two peaks at 223 and 210 daltons were probably due to the loss of one methyl group and one CO molecule from the molecular ion.

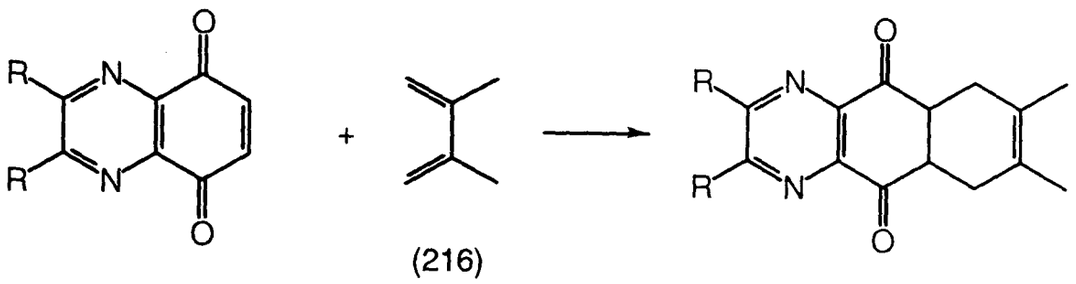
2.5.2 Reaction of Diazanaphthoquinones (194)-(196) with 2,3-Dimethyl-1,3-butadiene (216)

Joullie et al.[53] and afterwards Warren[21] reported separately that in Diels-Alder reactions, quinoxaline quinone (49) possesses dienophilicity greater than that of 1,4-naphthoquinone (221). It may be assumed that, due to the presence of the electron donating groups at the 2- and 3-positions, the dienophilicity of the substituted quinoxaline quinones (194), (195) and (196) would be reduced compared to the dienophilicity of the unsubstituted quinoxaline quinone. The appearance of a singlet due



(221)

to 6-H and 7-H in case of (194), (195) and (196), at relatively high field (6.95 - 6.90 ppm) compared to the position of singlets (7.28 and 7.29 ppm) in quinoxaline quinone (197)-(198) containing electron-withdrawing substituents and also for quinoxaline-5,8-dione (49) (7.24 ppm), is an indicator of the reduced dienophilicity of (194), (195) and (196). Hence, the initial cycloaddition products (222), (223) and (224) (Scheme 21)



(194) R = OCH_3
(195) R = OC_2H_5
(196) R = SC_2H_5

(216)

(222) R = OCH_3
(223) R = OC_2H_5
(224) R = SC_2H_5

Scheme 21

formed in the reaction of the 2,3-substituted quinones (194), (195) and (196) with diene (216) were of a different type from the initial cycloaddition products obtained by the reaction of quinoline-5,8-dione (47) and 2,3-dimethylquinoxaline-5,8-dione (94) and diene (216) or the reaction between quinoxaline-5,8-dione (49) and (216) (Scheme 21). In the case of the production of (222), the reaction was completed in 2 h instead of 16-24 h required for the reaction of quinones (47) and (94) with diene (216).[82,84] In the preparation of (223), after a 2 h reflux of the reaction mixture an inseparable mixture of products was obtained. However, the reaction went to completion and gave a clean

product when the reaction mixture was stirred overnight.

In a similar reaction (224) was the only product when the reaction mixture of quinone (196) and diene (216) was stirred, but three days were required for the reaction to go to completion (scheme 21). An attempt was made to reduce this reaction time by changing the solvent from ethanol to a mild polar solvent, dichloromethane. Surprisingly when the quinones (194)-(196) were stirred at room temperature, the time taken for the completion of the reaction was 5-8 h.

The IR spectra of (222), (223) and (224) showed a strong absorption in the range of 1705-1695 cm^{-1} due to 9- and 10-carbonyl groups. In their ^{1}H NMR spectra, the methyl groups at 6- and 7-positions produced a singlet in the range of 1.63-1.61 ppm. The allylic 5- and 8-methylene hydrogens gave rise to a triplet in the range of 2.33-2.31 ppm.[84] The bridgehead hydrogen atoms, 8a-H and 10a-H produced a complex multiplet (broad double doublet) at lower field (in the range of 3.41-3.33 ppm) due to the presence of carbonyl group at an adjacent position. The mass spectrum of the (222) showed a molecular ion peak at 302 daltons which was in agreement with molecular formula $C_{16}H_{18}N_2O_4$. A base peak at 287 daltons was probably due to the loss of one methyl group from the molecular ion. The mass spectra of (223) and (224) showed the base peak for the molecular ions at 330 and 362 daltons, in agreement with their molecular formulae.

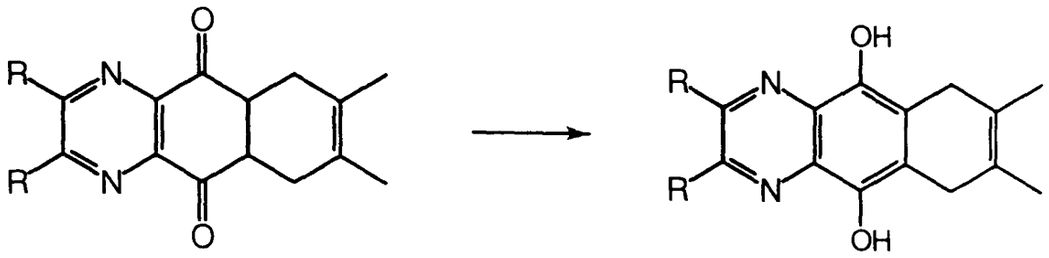
An attempt was made to establish the structure of compounds (222), (223) and (224) by the use of ^{13}C NMR spectroscopy. The spectrum of compound (223) showed the bridgehead carbon atoms, i.e. 8a-C and 10a-C as a doublet (J = 132 Hz) at 47.1 ppm, which confirmed the presence of single hydrogen atom on each of these carbon atoms. The 5- and 8-carbon atoms produced a triplet at 30.7 ppm due to the presence of two hydrogen atoms on each carbon atom.

An attempt was made to oxidise the tetrahydro-aromatic quinone (222) by using silver(II) oxide but after even 24 h stirring, the compound (222) was recovered.

2.5.2.1 Enolisation of the Cycloadducts (222)-(224)

2,3-Disubstituted-6,7-dimethyl-5,5a,8,8a-tetrahydro-1,4-diazaanthracene-9,10-dione (222)-(224) were enolised by the action of conc. hydrochloric acid (90%)[82,84] and the coloured 2,3-disubstituted-5,8-dihydro-6,7-dimethyl-9,10-dihydroxy-1,4-

diazaanthracenes (225)-(227) were obtained in all the cases directly from the reaction mixtures (Scheme 22).



(222) R = OCH_3
(223) R = OC_2H_5
(224) R = SC_2H_5

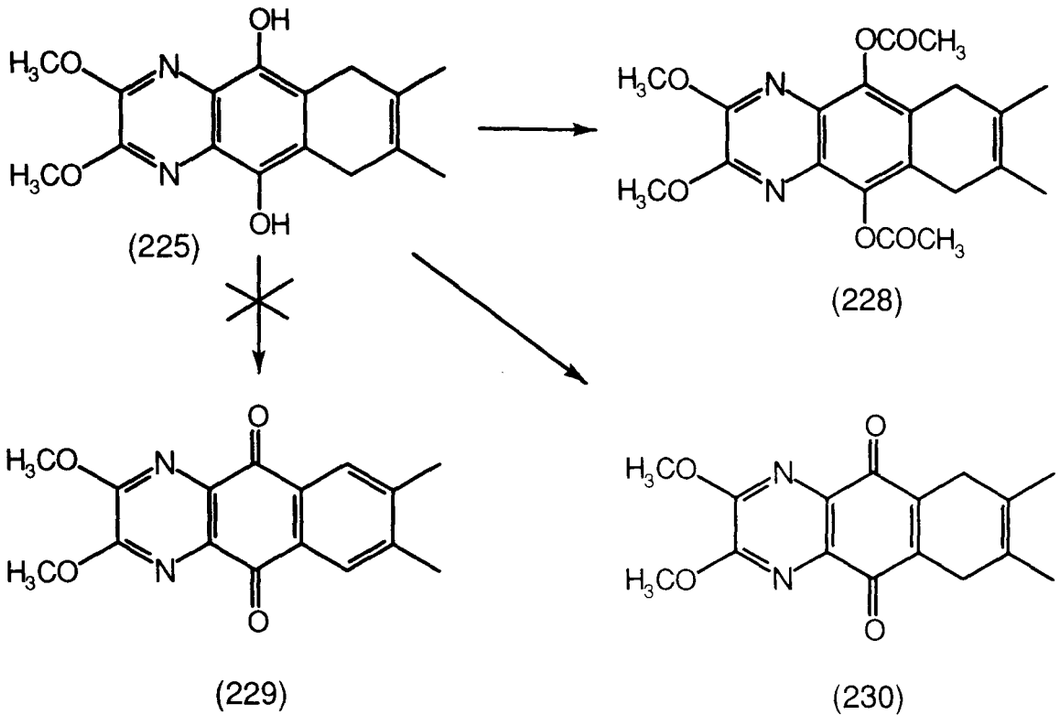
(225) R = OCH_3
(226) R = OC_2H_5
(227) R = SC_2H_5

Scheme 22

The structure of the compounds (225)-(227) was confirmed by the presence in the IR spectrum of a broad peak in the range of 3440-3460 cm^{-1}, attributable to hydroxyl group. The proton of the hydroxyl group appeared in the ^1H NMR spectrum as a singlet between 6.39-6.71 ppm, and a broad triplet in the range of 3.42-3.36 ppm (attributed to the 8a-H and 10a-H in the initial cycloaddition addition) was not present in the spectra of (225)-(227). The methylene hydrogen atoms in (225)-(227) appeared as singlets at 3.40, 3.38 and 3.56 ppm, respectively, instead of a weak doublet for the methylene hydrogen in the range of 2.52-2.23 ppm in the initial cycloaddition product (222)-(224). The mass spectra of (225)-(227) showed the expected molecular ion peaks at 302, 330 and 362 daltons. In the case of (225), the base peak at 287 daltons was probably due to loss of one methyl group from the molecular ion.

The structure of 2,3-dimethoxy-5,8-dihydro-6,7-dimethyl-9,10-dihydroxy-1,4-diazaanthracene (225) was confirmed by the acetylation of hydroxyl groups to produce 2,3-dimethoxy-5,8-dihydro-6,7-dimethyl-9,10-acetoxy-1,4-diazaanthracene (228) (Scheme 23). A sharp peak at 1760 cm^{-1} in the IR spectrum of (228) was attributable to the carbonyl group. The methylene hydrogens in (228) gave rise to a singlet at 3.29 ppm in the ^1H NMR spectrum. The mass spectrum showed a molecular ion peak at 386 daltons, in agreement with the molecular formula $C_{20}H_{22}N_2O_6$, while the peaks at 371, 329 and 302 daltons, were probably due to the loss of one methyl, one methyl with one

molecule of ketene, and two molecules of ketene, respectively, from the molecular ion.



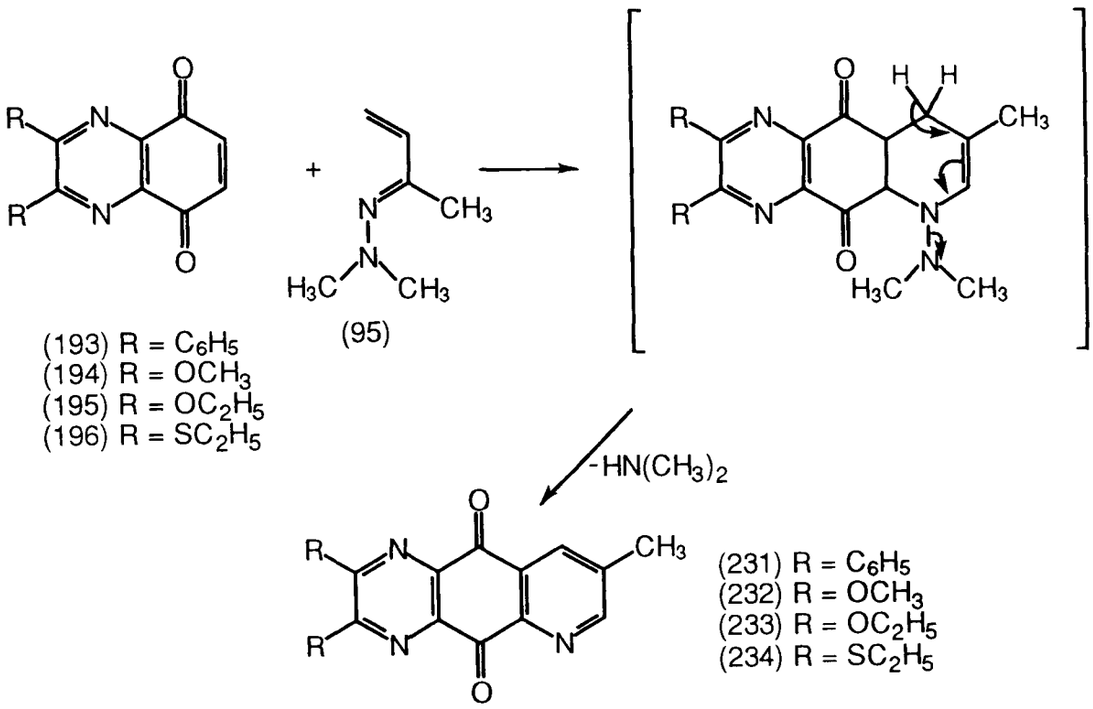
Scheme 23

An attempt was made to convert the quinol (225) to quinone (229) by the treatment of (225) with silver(II) oxide in dimethoxyethane at room temperature. However, this procedure gave (230), but not the expected (229). 2,3-Dimethoxy-6,7-dimethyl-5,8-dihydro-1,4-diazanthracene-9,10-dione (230) had a sharp peak at 1680 cm^{-1} in its IR spectrum, attributable to the carbonyl group. The methylene hydrogens, 5-H and 8-H produced a singlet at 3.15 ppm in ^1H NMR spectrum. The mass spectrum of (230) showed the molecular ion peak at 300 daltons, in agreement with its molecular formula, whereas the two peaks at 285 and 270 daltons were probably due to the loss of one and two methyl groups from the molecular ion, respectively.

2.5.3 Reaction of Diazanaphthoquinone (193)-(196) and (204) with N,N-Dimethylamino-1-aza-1,3-butadiene (95)

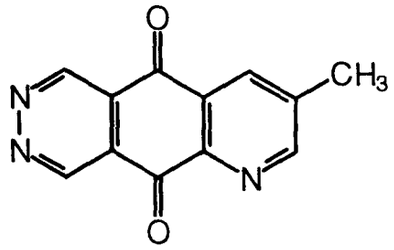
N,N-Dimethylamino-1-aza-1,3-butadiene (95) was prepared from methacrolein by a known method[124] and treated separately with the different 2,3-disubstituted-quinoxaline-5,8-diones (193-196) and phthalazine-5,8-dione (204) in anhydrous benzene[82] at room temperature and in each case, an unstable primary adduct was obtained along

with either 2,3,7-trisubstituted-1,4,5-triazaanthracene-9,10-dione (231)-(234) (Scheme 24) or 7-methyl-2,3,5-triazaanthracene-9,10-dione (235). When the reaction mixture was refluxed for 1-2 h in absolute ethanol (rather than benzene), the fully aromatized compounds (231)-(235) were obtained as single products in 61-93 % yield. The structure of the cycloaddition products, 7-methyl-2,3-diphenyl-1,3,5-triazaanthracene-9,10-dione (231) 7-methyl-2,3-dimethoxy-1,3,5-triazaanthracene-9,10-dione (232), 7-methyl-2,3-diethoxy-1,3,5-triazaanthracene-9,10-dione (233)-methyl-2,3-bis(ethylthio)



Scheme 24

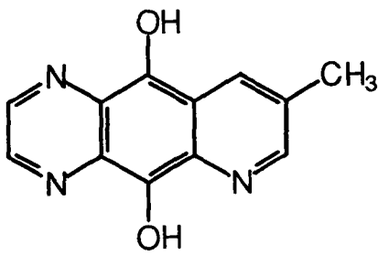
-1,3,5-triazaanthracene-9,10-dione (234), and 7-methyl-2,3,5-triazaanthracene-9,10-dione (235) was confirmed by the presence of two sharp peaks in the range of 1700-1695 cm^{-1} and 1685-1680 cm^{-1} in the IR spectrum, attributable to 9- and 10-carbonyl groups in their IR spectra, except for (235), which showed only one peak at 1700 cm^{-1}. In the ^1H NMR spectra of (231)-(235), the 7-methyl group produced a singlet in the range of 2.54-2.62 ppm, whereas the hydrogens at the 6- and 8-position gave rise two doublets: one between 8.30-8.48 ppm with a meta coupling constant J = 2.4-2.8 Hz and the second at 8.99-8.84 ppm with meta coupling constant J = 2.3-2.9 Hz, respectively.



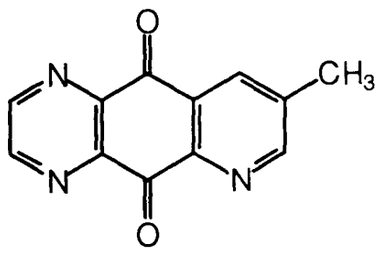
(235)

The mass spectra of (231)-(235) showed the molecular ion peaks at 377, 285, 313, 345, and 225 daltons, respectively, in agreement with their molecular formulae (all of these values are odd numbers, showing the presence of an odd number of nitrogen atoms). In the case of (232) and (233), two peaks at 270 and 298 daltons, respectively, were probably due to loss of one methyl group from the molecular ions. The two peaks at 316 and 288 daltons, in the mass spectrum of (234) were probably due to M^+-C_2H_5 and M^+-(C_2H_5 + $1C_2H_4$), respectively. The mass spectrum of (231) showed a fragment peak at 218 daltons probably due to the loss of two phenyl groups from the molecular ion.

Quinoxaline-5,8-dione (49) was treated with N,N-dimethylamino-1-aza-1,3-butadiene (95) but, instead of a single product (237), a mixture of a non-separable products (236) and (237) was obtained. The presence of the hydroxyl group in (236) and the



(236)

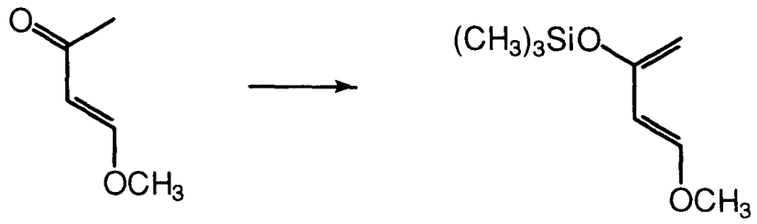


(237)

carbonyl group in (237) was confirmed by the presence of a broad peak at 3440 cm^{-1} and a relatively small peak at 1675 cm^{-1}, respectively, in the IR spectrum of the crude mixture.

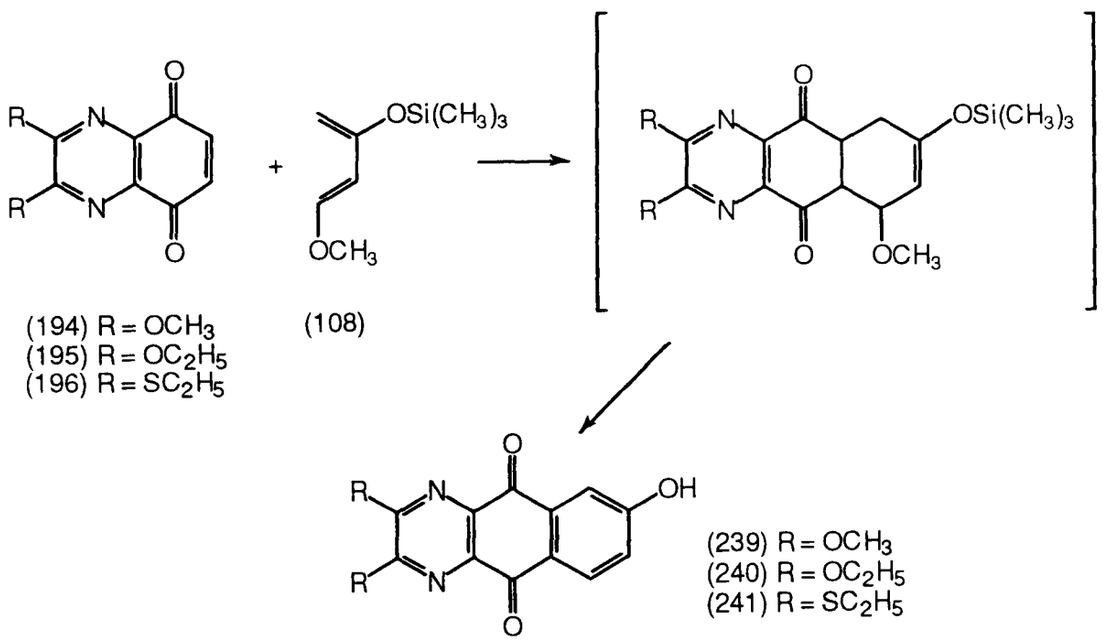
2.5.4 Reaction of Diazanaphthoquinones (194)-(196) with *trans*-1-Methoxy-3-(trimethylsilyl)oxy-1,3-butadiene (108)

trans-1-Methoxy-3-(trimethylsilyl)oxy-1,3-butadiene (108) was obtained by a known method.[125] treating trans-4-methoxybutene-2-one (238) with trimethylsilyl chloride in the presence of triethylamine and anhydrous zinc chloride.



(238) (108)

The diene (108) underwent a ready cycloaddition on separate reaction with the different 2,3-disubstituted-quinoxaline-5,8-diones (194)-(196) (Scheme 25) in chloroform at room temperature. A coloured solid product was obtained directly from the reaction



Scheme 25

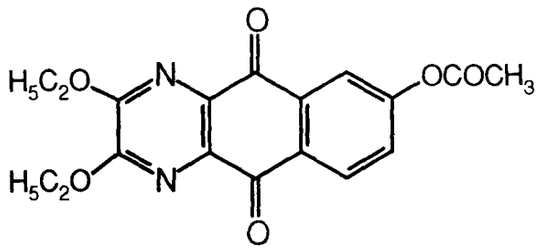
mixture in each case and the products were found to be the aromatic compounds; 6-hydroxy-2,3-dimethoxy-1,4-diazaanthracene-9,10-dione (239), 6-hydroxy-2,3-diethoxy-

1,4-diazaanthracene-9,10-dione (240) and 6-hydroxy-2,3-bis(thioethyl)-1,4-diazaanthracene-9,10-dione (241), respectively (Scheme 25).

The products (239)-(241) were characterised by their IR spectra each of which showed a broad peak in the range of 3250-3190 cm^{-1} attributable to the 6- hydroxy group and, in addition, two sharp peaks in the range of 1690-1685 cm^{-1} and 1665-1655 cm^{-1} due to the 9- and 10-carbonyl group, respectively. The ^1H NMR spectra showed a doublet in the range of 8.06-8.02 ppm with a *meta* coupling constant J = 2.4-2.9 Hz and at 7.48-7.45 ppm another doublet with *ortho* coupling constant J = 8.3-8.8 Hz due to 5-H and 8-H, respectively, whereas a double doublet in the range of 7.26-7.20 ppm (J = 8.3,2.4 Hz) was attributable to hydrogen atom at the 7-position.

The mass spectra of (239)-(231) showed molecular ion peaks at 286, 314 and 346 daltons, respectively, which were in agreement with their molecular formulae. Two peaks at 271 and 299 daltons in the mass spectra of (239) and (240), respectively, were probably due to the loss of one methyl group from molecular ion, whereas two peaks at 286 and 258 daltons in the mass spectrum of (240) were probably due to the loss of one and two molecules of ethylene, respectively, from the molecular ion.

Further confirmation of the structure (240) was achieved by acetylation to produce 6-acetoxy-2,3-diethoxy-1,4-diazaanthracene-9,10-dione (242).



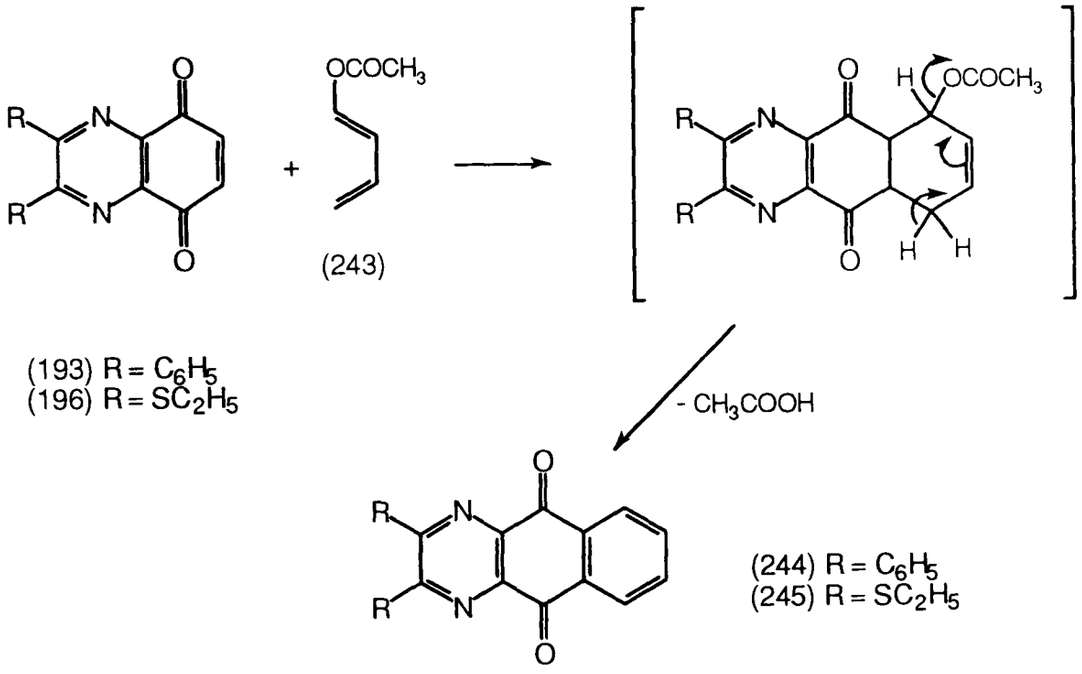
(242)

The IR spectrum (242) showed the presence of three carbonyl groups (peaks at 1765, 1690 and 1650 cm^{-1}) and the disappearance of the peak due to the hydroxyl group. The ^1H NMR spectrum of (242) showed in addition to other signals, a singlet at 2.41 ppm due to methyl of the 6-acetoxyl group. The mass spectrum of (242) showed a molecular ion peak at 356 daltons. A peak at 314 daltons was probably due to the loss of a ketene molecule from the molecular ion.

2.5.5 Reaction of Diazanaphthoquinones (193),(196) and (204) with 1-Acetoxy-1,3-butadiene (243)

The reactions of 1-acetoxy-1,3-butadiene (243) with 2,3-disubstituted quinoxaline quinones (193), (196) and phthalazine quinone (204) were also studied. The reactions occured with the elimination of a molecule of acetic acid from the initial 1:1 cyclo-adduct, and then oxidative aromatisation to yield the fully aromatic products (244)-(246). Potts et al.[82] has also reported the similar behaviour of this diene (243) on reaction with quinoxaline quinone (49).

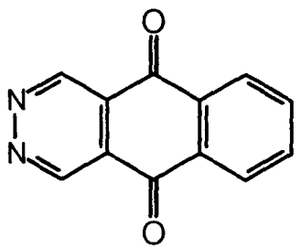
Quinones (193) and (196) produced a non-separable mixture of two components in their reactions with the diene (243) in benzene,[82] In each case this was probably due to the presence of the aromatic compound (244) and (245), respectively, along with the intermediate adduct. The mixtures were then refluxed separately in ethanol for 1h to obtain the single fully aromatised product (244) and (245) (Scheme 26).



Scheme 26

The IR spectra of compounds (244) and (245) showed a strong absorption at 1700 and 1695 cm^{-1}, respectively, due to the carbonyl groups. The ^1H NMR spectra of

these compounds also showed the symmetrical nature of the molecules, which was only due to the elimination of the acetic acid from the intermediate adducts. 5-H and 8-H in (244) and (245) produced a double doublet at 8.54 ppm (J = 5.9,3.4 Hz) and 8.27 ppm (J = 5.9,3.8 Hz), respectively, whereas, 6-H and 7-H also gave rise to two double doublet separately at 7.90 ppm (J = 5.9,3.4 Hz) and 7.77 ppm (J = 5.9,3.2 Hz), respectively. The mass spectra of (244) and (245) showed the expected molecular ion peaks, and were in agreement with molecular formulae $C_{24}H_{14}N_2O_2$ and $C_{16}H_{14}N_2O_2S_2$, respectively.



(246)

Phthalazine-5,8-dione (204) produced a fully aromatic product (246) directly, on reaction with diene (243) in benzene. The IR spectrum of (246) showed a strong absorption at 1735 cm^{-1}. A singlet at 9.86 ppm in the ^1H NMR spectrum of (246) was due to the 1- and 4-H, and 5-H, 8-H and H6-, 7-H gave rise to two double doublets at 8.23 ppm (J = 6.1, 3.7 Hz) and 8.01 ppm (J = 5.9,3.7 Hz), respectively. The mass spectrum of (246) showed a molecular ion peak as a base peak at 212 daltons in agreement with molecular formula $C_{12}H_6N_2O_2$.

GENERAL EXPERIMENTAL TECHNIQUES

All melting points were determined using an Electrothermal Digital apparatus and are uncorrected.

Infrared spectra were recorded using a Perkin-Elmer 1420 ratio recording spectrometer in the range of 600-4000 cm^{-1} and calibrated against a polystyrene film. The spectra were recorded as potassium bromide discs.

Proton nuclear magnetic resonance spectroscopy was carried out using a Varian CFT-20 (80 MHz) or a Jeol JNM-FX200 (200 MHz) Spectrometer and the spectra were recorded for solutions in deuterated solvent relative to tetramethylsilane (internal standard). Resonances are reported as ppm for the chemical shift from tetramethylsilane at 0 ppm.

Low resonance electron impact mass spectra were recorded using a MS902 AEI mass spectrometer. The accurate mass determinations and fast atom bombardment (FAB) spectrum were provided by the SERC Mass Spectrometry Service Centre, University College of Swansea.

Micro-analytical determinations were carried out by Medac Ltd. using a Control Equipment Corporation Model 240 XA (static combustion system) and a Carlo Erba 1106 (dynamic combustion system).

Thin layer chromatography (t.l.c) was carried out on commercial silica gel plates [Camlab, 0.25 mm with fluorescent indicator UV_{254}]. Column chromatography was carried out on Kieselgel 60 (230-400 mesh ASTM). Columns were generally packed dry and developed under light positive pressure.

Solvents were redistilled before use.

EXPERIMENTAL

Dimethoxyquinoxalines

2,3- and 2,5-Dinitro-1,4-dimethoxybenzene (131)

Nitric acid (18 cm^3, sp.gravity 1.42) was added to a solution of 1,4-dimethoxybenzene (129) (13.8 g) in a glacial acetic acid (35 cm^3). After the reaction subsided, more conc. nitric acid (18 cm^3) was added. The reaction mixture was heated for 5 min at 80-90°C and then diluted with water (300 cm^3). A mixture of 2,3- and 2,5-dinitro-1,4-dimethoxybenzene was filtered off and crystallised from glacial acetic acid (16.72 g, 72 %), m.p. 158-160° C (lit.,[87] m.p. 155-160° C).

4,5-Dinitroveratrole (133)

To a well stirred solution of veratrole (130) (120 g) in acetic acid (362 cm^3), cooled at 0-5° C in an ice-bath, was added conc. nitric acid (170 cm^3, sp. gravity 1.42) over a 15 min period of time, keeping the temperature below 40° C by the appropriate rate of addition of the acid. Stirring was continued for a further 30 min, then again conc. nitric acid (531 cm^3) was added over a period of 15 min, and stirring was continued for a further 1.5 h. The reaction mixture, which contained solid 4,5-dinitroveratrole (133), was then poured into a large volume of cold water (300 cm^3). The precipitated nitro compound was filtered off, washed with water until free from acid, and recrystallised from ethyl acetate (174 g, 88 %). m.p. 129-130° C (lit.,[88] m.p. 131° C).

A mixture of 2,3- and 2,5-diamino-1,4-dimethoxybenzene (134)

A mixture of 2,3- and 2,5-dinitro-1,4-dimethoxybenzene (132) (5.0 g) in absolute ethanol (75 cm^3) was hydrogenated over palladium charcoal (10 %, 300 mg) for 2 h at 50 lb/in^2 in a Parr hydrogenator. The brown solution (134), containing a mixture of 2,3- and 2,5-diamino-1,4-dimethoxybenzene was filtered immediately and was used as a source of the mixture of diamines in further reactions.

A fresh solution of the mixed diamino compound (134) was prepared using these quantities in each of the subsequent preparations.

1,2-Dimethoxy-4,5-diaminobenzene monohydrochloride (135)

A solution of 4,5-dinitroveratrole (133) (3.0 g) in absolute ethanol (100 cm^3) was hydrogenated over palladium charcoal (10 %, 0.5 g) for 4 h at 60 lb/in^2 at room temperature in a Parr hydrogenator. The catalyst was filtered off, the filtrate concentrated to 20 cm^3, and conc. hydrochloric acid (5 cm^3) added. The resultant precipitate was separated by filtration, washed with dichloromethane and crystallised from ethanol to give bright purple 4,5-diaminoveratrole monohydrochloride (135) (1.95 g, 73 %). m.p. 237-239° C(decomp) (lit.,[88] m.p. 240° C).

5,8-Dimethoxyquinoxaline (13)

The solution obtained in the preparation of the mixture (134) was evaporated *in vacuo* to obtain a deep violet residue which was immediately added to a warm saturated solution of glyoxal sodium sulphite adduct (6 g) in water (50 cm^3). The reaction mixture was stirred and heated at 70° C for 45 min, and filtered to remove the black residue. The filtrate was basified with sodium hydroxide pellets and filtered again to obtain a clear blood red, solution, which was extracted with dichloromethane (3 x 100 cm^3). The extract was then washed with water, dried over anhydrous magnesium sulphate and percolated through a column of neutral alumina. The bright yellow eluent was concentrated to afford greenish yellow crystals of 5,8-dimethoxyquinoxaline (13) (3.1 g), m.p. 146-147° C (lit.,[86] m.p. 147-148° C).

2,3-Dimethyl-5,8-dimethoxyquinoxaline (94)

The solution (134) was diluted with water (75 cm^3) and treated with butane-1,2-dione (6 cm^3). The red solution was stirred for 5 min and poured into ice-water (150 cm^3) to yield yellow crystals of 2,3-dimethyl-5,8-dimethoxyquinoxaline (94) (3.8 g, 84 %) which were recrystallised from petroleum ether (60-80°C) (3.6 g), m.p. 170-171°C (lit.,[87] m.p. 170° C).

2,3-Diphenyl-5,8-dimethoxyquinoxaline (139)

Benzil (2.5 g) in hot glacial acetic acid (15 cm^3) was added to the boiling solution (134) and heating was continued for 20 min with stirring. The solution was cooled to room temperature, and the solid filtered off to give yellow 2,3-diphenyl-5,8-

dimethoxyquinoxaline (139) which was washed with water and finally with acetone (3.14 g), m.p. 226-227° C (lit.,[89] m.p. 227° C).

Ethyl 2-hydroxy-5,8-dimethoxyquinoxaline-3-carboxylate (140)

Ethyl ketomalonate (2 g) was added to a solution (134) and refluxed for 1 h. On cooling the reaction mixture, bright yellow crystals of ethyl 2-hydroxy-5,8-dimethoxyquinoxaline-3-carboxylate (140) were filtered off and recrystallised from hot ethanol (2.11 g), m.p. 242-243° C (lit.,[125] m.p. 243° C).

2,3-Bis(bromomethyl)-5,8-dimethoxyquinoxaline (141)

The solvent from the solution (134) was evaporated *in vacuo* and the residue was dissolved in carbon tetrachloride (100 cm^3). To this solution, 1,4-dibromo-2,3-butanedione (2 g) was added, refluxed the reaction mixture for 4h, and then cooled. The resulting brown solid was filtered off and recrytallised from benzene to yield 2,3-Bis(bromomethyl)-5,8-dimethoxyquinoxaline (141) (3.2 g), m.p. 168-169° C; IR(KBr) ν_{max} 2960, 2840, 1605, 1560, 1480, 1300, 1265, 1130, 1040, 1010, 940, 800 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.31 (s, 2H, 6- and 7-H), 4.85 (s, 4H, 2- and 3-$\underline{CH_2}Br$), 4.01 (s, 6H, 2- and 3-OCH_3); MS, m/z(r.i.) 378(38, M^+ for ^{81}Br), 376(82, M^+ for ^{81}Br and ^{79}Br) 374(35, M^+ for ^{79}Br), 297(48), 295(40), 282(33), 281(21), 220(29), 205(31), 202(11), 195(28), 187(12), 172(11). (Found: C, 38.23; H, 3.01; N, 7.62; S, 42.87; Br, 28.67. $C_{12}H_{12}N_2O_2Br_2$ requires C, 38.33; H, 3.22; N, 7.45; Br, 42.50 %).

1,4-Dihydro-2,3-dioxo-5,8-dimethoxyquinoxaline (142)

Diethyl oxalate (40 g) in glacial acetic acid (25 cm^3) was added to the solution (134) and refluxed with stirring for 3 h. After cooling the reaction mixture, the resultant crystals were separated by filtration, washed thoroughly with water, and finally with acetone, to give bright light green 1,4-dihydro-2,3-oxo-5,8-dimethoxyquinoxaline (142). The compound was purified by repeated dissolution in alkali (sodium hydroxide; 2M) and then reprecipitation with acetic acid, (3.8 g), m.p. 324-327° C (lit.,[89] m.p. 325-329° C).

1,4-Dihydro-2,3-dioxo-6,7-dimethoxyquinoxaline (143)

Above described procedure was followed using 1,2-diamino-4,5-

dimethoxybenzene (135) (5 g, 26 mmol) and diethyl oxalate (40 g) in glacial acetic acid (25 cm^3) to give 1,4-dihydro-2,3-dioxo-6,7-dimethoxyquinoxaline (143) (4.6 g, 85 %), m.p. 344-345° C (lit.,[126] m.p. 345-346° C).

General Method for the Preparation of 2,3-Dichloro-5,8- and 6,7-dimethoxyquinoxaline (144) and (145), respectively.

the appropriate 1,4-Dihydro-2,3-dioxo-dimethoxyquinoxaline (1 g, 4.5 mmol) was heated under reflux with phosphoryl chloride (10 cm^3) and N,N-dimethylaniline (5 cm^3) for 3.5 h. The cooled reaction mixture was slowly poured into stirred ice-water (200 cm^3) and extracted with dichloromethane (3 x 100 cm^3). The extract was then washed with water, dried over anhydrous sodium sulphate, evaporated *in vacuo*, and the greenish yellow residue was percolated through a neutral alumina column to yield yellow crystals of 2,3-dichloro-5,8-dimethoxyquinoxaline (144) (0.98 g, 84 %), m.p. 215-216°C (lit[89]., m.p. 215° C) or light green crystals of 2,3-dichloro-6,7-dimethoxyquinoxaline (145) (0.89 g, 76 %), m.p. 177-178° C (lit.,[126] m.p. 178° C).

2,3,5,8-Tetramethoxyquinoxaline (146)

A solution of 2,3-dichloro-5,8-dimethoxyquinoxaline (144) (2.58 g, 10 mmol) in methanol (25 cm^3) was added to a freshly prepared solution of sodium methoxide [prepared by adding sodium hydride (0.920 g, 40 mmol) to methanol (50 cm^3)]. The reaction mixture was refluxed for 3 h and then poured into ice-water (100 cm^3). The resulting precipitate was filtered off, washed with water, and crystallised from methanol to give 2,3,5,8-tetramethoxyquinoxaline (146) (2.2 g, 87 %), m.p. 174-175° C; IR(KBr) ν_{max} 2920, 1600, 1505, 1470, 1400, 1325, 1225, 1110, 1005, 840 cm^{-1}; ^1H NMR (80 MHz, $CDCl_3$) 6.82 (s, 2H, 6-H and 7-H), 4.18 (s, 6H, 2- and 3-OCH_3), 3.97 (s, 6H, 5- and 8-OCH_3); MS, m/z(r.i.) 251(12), 250 (100, M^+), 235(96), 220(41), 206(240 192(23). (Found: C, 57.52; H, 5.61; N, 11.18. $C_{12}H_{14}N_2O_4$ requires C, 57.60; H, 5.60; N, 11.20 %).

2,3-Diethoxy-5,8-dimethoxyquinoxaline (147)

The procedure described above was followed, using ethanol in place of methanol to obtain 2,3-diethoxy-5,8-dimethoxyquinoxaline (147) (2.3 g, 82 %), m.p. 179-179°C

(lit.,[89] m.p. 179-180° C).

2,3-Bis(ethylthio)-5,8-dimethoxyquinoxaline (148)

To a solution of 2,3-dichloro-5,8-dimethoxyquinoxaline (144) (2.58 g, 10 mmol) in ethanol (50 cm^3), was added sodium salt of ethanethiol (3.36 g, 40 mmol). The reaction mixture was refluxed for 2 h and then poured into ice-water (100 cm^3). The resulting yellow precipitate was filtered off and crystallised from ethanol to yield 2,3-bis(ethylthio)-5,8-dimethoxyquinoxaline (148) (2.91 g, 94 %), m.p. 221-222° C (lit.,[89] m.p. 222°C).

1,4-Disubstituted-5,8-dimethoxypyridazino(4,5-*b*)quinoxalines

1,4-Dihydroxy- and 1,4-diamino-5,8-dimethoxypyridazino[4,5-b]quinoxaline were prepared by using a method in literature.[93]

2,3-Distyryl-5,8-dimethoxyquinoxaline (152)

A mixture of 2,3-dimethyl-5,8-dimethoxyquinoxaline (94) (12.5 g, 58 mmol), benzaldehyde (70 cm^3), and boric acid, was heated at 200-215°C for 45 min with the removal of liberated water by distillation. The melt was poured into ethanol, and the mixture was refluxed for 30 min. After cooling the mixture more ethanol (100 cm^3) was added, the resulting solid was filtered off, and recrystallised from hot ethanol to yield 2,3-distyryl-5,8-dimethoxyquinoxaline (152) as long yellow needles (15.8 g, 70 %), m.p. 177-178° C; IR(KBr) ν_{max} 3040, 2920, 1610, 1595, 1480, 1445, 1335, 1255, 1160, 1125, 950, 800, 740 cm^{-1}; ^1H NMR (80 MHz, $CDCl_3$) δ 7.89 (d, 2H, J = 15.7 Hz, β-vinyl-H), 7.69 (d, 2H, J = 15.9 Hz, α-vinyl-H), 7.65-7.30 (m, 10H, 2- and 3-Ph-H), 6.90 (s, 2H, 6- and 7-H), 4.05 (s, 6H, 5- and 8-OCH_3); MS, m/z(r.i.) 396(6), 395(27), 394(100, M^+), 379(29, M^+-1CH_3), 365(20), 317(14, M^+-1C_6H_5), 314(12), 291(14), 115(11), 76(14). (Found: C, 79.01; H, 5.57; N, 6.94. $C_{26}H_{22}N_2O_2$ requires C, 79.18; H, 5.58; N, 7.10 %).

5,8-Dimethoxy-2,3-dicarboxylic acid (153)

To a solution of 2,3-distyryl-5,8-dimethoxyquinoxaline (151) (10.6 g, 27 mmol) in acetone (600 cm^3), finely divided potassium permanganate (36 g) was added in small portions, and the stirring was continued for 2 h in an ice-bath. The mixture was filtered off, and the residue was washed with hot water until the filtrate gave no turbidity or

precipitation on acidification. After cooling, the filtrate was acidified with conc. hydrochloric acid to pH 1-2, the resulting yellow precipitate was filtered off, and washed with ether to remove benzoic acid. The solid was crystallised from hot water to produce long orange needles of 5,8-dimethoxy-2,3-dicarboxylic acid (153) (4.3 g, 58 %), m.p. 197-198° C (lit,.[127] 186° C (decomp); IR(KBr) ν_{max} 3390 (OH), 2940, 1740 (C=O), 1620, 1600, 1530, 1490, 1445, 1380, 1320, 1275, 1235, 1180, 1135, 1035, 825, 800, 715 cm^{-1}; ^1H NMR (80 MHz, d_6-DMSO) δ 7.33 (s,2H, 6- and 7-H), 3.96 (s, 6H, 5- and 8-OCH_3); MS, m/z(r.i.) 279(14), 278(94, M^+), 263(24, M^+-1CH_3), 249(24), 234(46, M^+-1CO_2), 175(98), 159(100), 147(23), 132(40), 104(36), 76(43), 44(50).

Dimethyl 5,8-dimethoxyquinoxaline-2,3-dicarboxylate (154)

Dry hydrogen chloride was passed in the course of 5 min into methanol (50 cm^3). The dicarboxylic acid (152) (2.1 g, 7.5 mmol) was then added, and the reaction mixture was heated under reflux for 3 h. After cooling the mixture to room temperature, the resulting yellow precipitate was filtered off, washed thoroughly with water, and recrystallised from a mixture of methanol and dichloromethane to give yellow dimethyl 5,8-dimethoxyquinoxaline-2,3-dicarboxylate (154), (1.8 g, 78 %), m.p. 221-223° C; IR(KBr) ν_{max} 3020, 2940, 2845, 1730 (C=O), 1610, 1545, 1490, 1465, 1390, 1300, 1270, 1250, 1180, 1120, 1055, 980, 850, 830, 815, 800, 715, 665 cm^{-1}; ^1H NMR (80 MHz, $CDCl_3$) δ 7.11 (s, 2H, 6- and 7-H), 4.03 (s, 12H, 2-,3-CO_2CH_3 and 5-,8-OCH_3); MS, m/z(r.i.) 307(7), 306(41, M^+), 245(19), 216(14), 188(100, M^+-2CO_2CH_3), 173(16, M^+-2CO_2CH_3 and 1CH_3), 132(16), 104(21), 76(15), 45(10). (Found: C, 55.18; H, 4.62; N, 9.18. $C_{14}H_{14}N_2O_6$ requires C, 54.90; H, 4.61; N, 9.15 %).

1,4-Dihydroxy-5,8-dimethoxypyridazineo[4,5-*b*]quinoxaline (150)

To a solution of dimethyl 5,8-dimethoxyquinoxaline-2,3-dicarboxylate (154) (0.15 g, 0.5 mmol) in methanol, was added hydrazine hydrate (2 cm^3) dropwise and stirring was continued for 2h. The reaction mixture was cooled, and the resulting golden yellow precipitate of the salt of (153) and hydrazine was filtered off. The salt was dissolved in water, acidified with dil. hydrochloric acid, the resulting orange precipitate filtered off, washed with water, and crystallised from dimethylformamide to yield reddish brown

1,4-dihydroxy-5,8-dimethoxypyridazino[4,5-*b*]quinoxaline (150) (0.081 g, 61 %), m.p. > 325 °C; IR(KBr) ν_{max} 3490 (H_2O), 3385 (NH), 2940, 2860, 1665 (C=O), 1590, 1530, 1465, 1390, 1270, 1150, 1055, 960, 845(, 815,730 cm^{-1}; ^1H NMR (200 MHz, d6-DMSO) δ 11.6 (bs, 2H, 1- and 4-OH, exchanged with D_2O), 7.39 (s, 2H, 6- and 7-H), 4.02 (s, 6H, 5- and 8-OCH3); MS, m/z(r.i.) 276(20), 275(30), 274(100, M^+), 259(86, M^+-1CH_3), 245(59), 104(10), 43(19). (Found: C, 51.73; H, 3.63; N, 19.96. $C_{12}H_{10}N_4O_4.1/2H_2O$ requires C, 51.70; H, 3.59; N, 20.10 %).

5,8-Dimethoxyquinoxaline-2,3-dicarboxamide (155)

Dry ammonia was passed for 4 h into a suspension of dimethyl 5,8-dimethoxyquinoxaline-2,3-dicarboxylate (154) (1.5 g, 5 mmol) in methanol (200 cm^3). The yellow suspension disappeared during the reaction and another yellow precipitate appeared. This was filtered off and recrystallised from hot water to yield bright yellow 5,8-dimethoxyquinoxaline-2,3-dicarboxamide (155) (1.16 g, 86 %), m.p. 179-180° C; IR(KBr) ν_{max} 3425,3320 (NH_2), 2940, 2840, 1690 (C=O), 1670 (C=O), 1595, 1490, 1380, 1320, 1265, 1190, 1130, 1100, 1025, 970, 820, 740 cm^{-1}; ^1H NMR (80 MHz, d_6-DMSO) δ 7.95 (s, 2H, 2- and 3-CO$\underline{NH_2}$), 7.67 (s, 2H, 2- and 3-CO$\underline{NH_2}$), 7.30 (s, 2H, 6- and 7-H), 3.97 (s, 6H, 5- and 8-OCH_3); MS, m/z(r.i.) 276(8, M^+), 259(16, M^+-1NH_3), 230(11), 175(100), 147(10), 91(14), 43(32). (Found: C, 52.07; H, 4.32; N, 20.10. $C_{12}H_{12}N_4O_6$ requires C, 52.18; H, 4.34; N 20.28 %).

2,3-Dicyano-5,8-dimethoxyquinoxaline (156)

Method (a): A suspension of 5,8-dimethoxyquinoxaline-2,3-dicarboxamide (155) (1.5 g, 5.4 mmol), dimethylformamide (25 cm^3), and thionyl chloride (3.5 cm^3), was refluxed for 1 h under dry conditions, and then poured over ice. The resulting aqueous mixture was neutralised with sodium bicarbonate, and was extracted with ether. The ether layer was dried (anhydrous calcium chloride) and the solvent was evaporated *in vacuo* and residue was crystallised from a mixture of methanol and dichloromethane (7:3) to yield red 2,3-dicyano-5,8-dimethoxyquinoxaline (156) (0.6 g, 46 %), m.p. 281-282° C; IR(KBr) ν_{max} 3450 (H_2O), 2900, 2880, 2260 (CN), 1605, 1520, 1500, 1450, 1370, 1320, 1285, 1160, 1120, 1070, 960, 850, 740, 710, 650 cm^{-1}; ^1H NMR (80 MHz, $CDCl_3$) δ 7.30 (s, 2H, 6- and 7-H), 4.09 (s, 6H, 5- and 8-OCH_3); MS, m/z(r.i.) 241(14), 240(87,

M^+), 225(100, $1CH_3$), 211(50), 97(16), 169(14), 26(5). (Found: C, 58.99; H, 3.35: N, 23.05. $C_{12}H_8N_4O_2.1/4H_2O$ requires C, 58.89; H, 3.27; N, 22.90 %).

Method (b): A powdered mixture of diiminosuccinonitrile[95] (3.0 g) and a mixture of 2,3-diamino- and 2,5-diamino-1,4-dimethoxybenzenemonohydrogen chloride (3.2 g) [(prepared by the addition of conc. hydrochloric acid (5 cm^3) to the mixture of 2,3- and 2,5-diamino-1,4-dimethoxybenzene (134) followed by the evaporation of the solvent to dryness)] was added over 15 min to trifluoroacetic acid (60 cm^3) while the temperature was maintained at 20°C, with occasional ice-bath cooling. The reaction mixture was stirred overnight at room temperature and then poured on to ice-cold water (200 cm^3). The resulting precipitate was filtered off, washed thoroughly with water, finally with cold methanol, and crystallised from a mixture of methanol and dichloromethane (7:3) to yield bright red 2,3-dicyano-5,8-dimethoxyquinoxaline (155) (1.88 g, 77 %), m.p. 281-282° C.

1,4-Diamino-5,8-dimethoxypyridazino[4,5-*b*]quinoxaline (151)

Hydrazine hydrate (3 cm^3) was added, with stirring, to a solution of 2,3-dicyano-5,8-dimethoxyquinoxaline (155) (0.5 g, 2.1 mmol) in methanol (100 cm^3) at room temperature. The reaction mixture was stirred for 24 h. The resulting precipitate was filtered off, washed with water, and recrystallised from aqueous dimethylformamide to give bright purple 1,4-diamino-5,8-dimethoxypyridazino[4,5-*b*]quinoxaline (151) (0.38 g, 67 %), m.p. > 325° C; IR(KBr) ν_{max} 3340 (H_2O), 3300, 3180 (NH_2), 1620, 1510, 1490, 1385, 1270, 1155, 1105, 1060, 965, 805, 730 cm^{-1}; ^1H NMR (80 MHz, d_6-DMSO) δ 7.33 (s, 2H, 6- and 7-H), 6.14 (bs, 4H, 1- and 4-NH_2 exchanged with D_2O), 4.02 (s, 6H, 5- and 8-OCH_3); MS, m/z(r.i.) 273(14), 272(82, M^+), 257(10, M^+-$1CH_3$), 242(11, M_+-$2CH_3$), 213(22), 121(100), 78(14). (Found: C, 49.98; H, 4.76; N, 28.69. $C_{12}H_{12}N_6O_2.H_2O$ rquires C, 49.65; H, 4.82; N, 28.96 %).

5,8-Dimethoxyquinoxaline-2,3-bis-(methylenepyridinium) dibromide (157)

2,3-Bis(bromomethyl)-5,8-dimethoxyquinoxaline (141) (2 g, 5.5 mmol) was added to dry pyridine (40 cm^3) and stirred for 30 min at room temperature. The resulting yellow solid was filtered off, washed with acetone, and recrystallised from

methanol to yield 5,8-dimethoxyquinoxaline-2,3-bis-(methylenepyridinium) dibromide (157) (1.57 g, 79 %), m.p. > 350° C; IR(KBr) ν_{max} 3400 (H_20), 3040, 2940, 1630, 1600, 1495, 1365, 1325, 1270, 1145, 1070, 835, 725, 710 cm^{-1}; ^1H NMR (80 MHz, d_6-DMSO) δ 9.27 (d, 4H, J = 5.3 Hz, 2- and 3-py-$H_{2,6}$), 8.77 (t, 2H, 2, 3-py-H_4), 8.29 (t, 4H, 2- and 3-py-$H_{3,5}$), 7.13 (s, 2H, 6- and 7-H), 6.64 (s, 4H, 2- and 3-CH_2), 3.69 (s, 6H, 5- and 8-OCH_3); MS, m/z(r.i.) 376(2), 374(4, M^+-2Br), 295(8), 295(8), 216(4, M^+-2Br and 2py), 201(7), 187(7), 96(21), 79(100), 52(68). (Found: C, 47.73; H, 4.56; N, 10.11; Br, 30.34. $C_{22}H_{22}N_4O_2Br_2.H_2O$ requires C, 47.82; H, 4.34; N, 10.14; Br, 28.98 %).

Reaction of 5,8-Dimethoxyquinoxaline-2,3-bis-(methylenepyridinium) dibromide (157) with Butane-2,3-dione

Piperidine (1 cm^3) was added to a solution of 5,8-dimethoxyquinoxaline-2,3-methylenepyridinium dibromide (157) (1 g, 2.7 mmol) and butan-2,3-dione (0.241 g, 2.8 mmol) in methanol (50 cm^3), and refluxed for 1 h. The reaction mixture was then poured into ethyl acetate (100 cm^3) and the resulting precipitate filtered off and washed with chloroform. This crude mixture of two components was separated by column chromatography [(methanol and chloroform (1:1)]. The first eluted component was characterised as 1-amino-2,3-dimethyl-5,8-dimethoxy-9,10-diazaanthracene-4-pyridinium bromide (158) (0.95 g, 59 %), m.p. 271° C (decomp); IR(KBr) ν_{max} 3400, 3300 (NH_2), 2920, 2840, 1620, 1590, 1530, 1480, 1465, 1440, 1395, 1325, 1265, 1160, 1105, 1085, 810, 730, 690, 620 cm^{-1}; ^1H NMR (200 MHz, CD_3OD) δ 9.11 [(d, 2H, J = 7.9 Hz, 4-py(2-H and 6-H)], 8.89 [(t, 1H, 4-py(4-H)], 8.35 [(t, 2H, 4-py(3-H and 5-H)], 7.09 (s, 2H, and 7-OCH_3), 4.11 (s, 3H, 5-OCH_3), 3.85 (s, 3H, 8-OCH_3), 2.31 (s, 3H, 3-CH_3), 2.23 (s, 3H, 2-CH_3); MS, m/z(r.i.) 362(9, M^++1H), 360(8, M^+-1H), 359(26, M^+-2H), 358(100, M^+-3H), 344(40), 343(47), 329(43), 328(51), 314(32), 313(12), 298(68), 283(44), 268(86), 79(15). (Found: c, 55.33; H, 4.86; N, 11.95; Br, 18.01. $C_{21}H_{21}N_4O_2Br.3/4H_2O$ requires C, 55.44; H, 4.62; N, 12.32; Br, 17.60 %) [Acc. mass; Found: 361.1685 (M^+-Br). $C_{21}H_{21}N_4O_2$ requires 361.1664)].

The second component was characterised as 2,3-Dimethyl-5,8-dimethoxy-9,10-diazaanthracene-1,4-bis-pyridinium dibromide (159) (0.724 g, 34 %), m.p. 150-153° C(decomp); IR(KBr) ν_{max} 3440 (H_20), 3150, 2940, 2840, 1620, 1600, 1480, 1470, 1390, 1330, 1270, 1180, 1165, 1105, 1040, 975, 935, 840, 775, 680 cm^{-1}; ^1H NMR (200 MHz,

D_2O) δ 9.16 [(d, 4H, *J* = 5.5 Hz, 1- and 4-py(2-H and 6-H)], 9.10 [(t, 2H, 1- and 4-py(4-H)], 8.54 [(t, 4H, 1- and 4-py(3-H and 5-H)], 7.40 (s, 2H, 6- and 7-H), 3.98 (s, 6H, 5- and 8-OCH_3), 2.46 (s, 6H, 2- and 3-CH_3); MS, m/z(r.i.) 424(2, M^+-2Br), 410(6), 396(6), 343(15), 329(34), 315(84), 240(9), 95(88), 79(100). (Found: C, 50.23; H, 4.35; N, 8.99; Br, 25.29. $C_{26}H_{24}N_4O_2Br_2.2H_2O$ requires C, 50.32; H, 4.51; H, 9.03; Br, 25.48 %).

Reactions of 2,3-Dichloro-5,8-Dimethoxyquinoxaline with Thiourea

2,3-Dichloro-5,8-dimethoxyquinoxaline (145) (2.27 g, 8.8 mmol) and thiourea (0.688 g, 8.8 mmol) was dissolved in dimethylformamide (30 cm^3), and triethylamine (1.8 g) was added with stirring. The reaction mixture was refluxed for 5 h. The yellow product precipitated out during the reaction. After cooling the reaction mixture, the product was collected by filtration, and washed firstly with water, and then methanol. The solid was recrystallised from formaldehyde to yield bright yellow needles. This compound was characterised as 1,4,8,11-tetramethoxy-6,13-dihydro-5,7,12,14-tetraza-6,13-dithiapentacene (169) (1.01 g, 52 %), m.p. > 360° C; IR(KBr) ν_{max} 2940, 2820, 1600, 1540, 1490, 1300, 1265, 1175, 1160, 1130, 960, 815, 805 cm^{-1}; ^1H NMR (200 MHz, d-TFA) δ 7.38 (s, 4H, 6-, 6'-, 7-, and 7'-H), 4.14 (s, 12H, 5-, 5'-, 8-, and 8'-OCH_3); MS, m/z(r.i.) 440(13, M^+), 425(5, M^+-CH_3), 227(9), 149(15), 86(6), 57(13), 43(27), 32(16). (Found: C, 54.47; H, 3.92; N, 12.39; S, 14.44. $C_{20}H_{16}N_4O_4S_2$ requires C, 54.53; H, 3.66; N, 12.72; S, 14.54 %).

Bis(2-chloro-5,8-dimethoxyquinoxalin-3-yl)sulphide (171)

Water (50 cm^3) was added to the initial filtrate from the above reactionto produce a yellow precipitate. The solid was collected and crystallised from a mixture of ethyl acetate and dichloromethane (3:1). The yellow bis(2-chloro-5,8-dimethoxyquinoxalin-3-yl)sulphide (171) (0.946 g, 45 %), had m.p. 221-222° C; IR(KBr) ν_{max} 2940, 2840, 1605, 1510, 1490, 1370, 1300, 1265, 1180, 1160, 1110, 995, 920, 835, 820, 800, 730 cm^{-1}; ^1H NMR (80 MHz, $CDCl_3$) δ 7.21 (s, 4H, 6-,6'-,7- and 7'-H), 4.01 (s, 6H, 8-, 8-' or 5-, 5'-OCH_3), 3.76 (s, 6H, 5-, 5-' or 8-, 8'-OCH_3); MS, m/z(r.i.) 482(2), 480 (3, M^+ for ^{37}Cl) and 478(5, M^+ for ^{35}Cl), 447 (12), 445(42), 443(100), 415(11), 413(15), 383(13), 225(4), 223(9). (Found: C, 49.99; H, 3.36; N, 11.41; S, 6.67; Cl, 14.46. $C_{20}H_{16}N_4O_4SCl_2$ requires C, 50.12; H, 3.36; N, 11.69; S, 6.69; Cl, 14.79 %).

6,13-Dibutyl-6,13-dihydro-1,4,8,11-tetramethoxy-5,6,7,12,13,14-hexaazapentacene (173)

The dichloro compound (171) (0.526 g, 1.1 mmol), and n-butylamine (0.321 g, 4.4 mmol), were dissolved in anhydrous tetrahydrofuran (50 cm^3) containing anhydrous potassium carbonate (1.0 g) and refluxed for 6 h. After the completion of the reaction, the solvent was evaporated *in vacuo,* and the residue was dissolved in water. The product was extracted with dichloromethane (3 x 100 cm^3), the dichloromethane layer was dried (anhydrous sodium sulphate) and purified by t.l.c. [petroleum ether (b.p.40-60° C) and ethyl acetate (2:1)] to give the hexaazapentacene (171) (0.381 g, 67 %), m.p. 301-302° C; IR(KBr) $_{max}$ 2950,2890, 1620, 1500, 1420, 1380, 1320, 1275, 1225, 1190, 1110, 1035, 800 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 6.73 (s, 4H, 2-, 3-, 9- and 10-H), 4.47 (t, 4H, 6- and 13-N$\underline{CH_2}CH_2CH_2CH_3$), 3.95 (s, 12H, 1-, 4-, 8- and 11-OCH_3), 1.83 (hept, 4H, 6- and 13-$NCH_2\underline{CH_2}CH_2CH_3$), 1.62 (hept, 6- and 13-$NCH_2CH_2\underline{CH_2}CH_3$), 1.03 (t, 6H, 6- and 13-$NCH_2CH_2CH_2\underline{CH_3}$). MS, m/z(r.i.) 519(32), 518(91, M^+), 462(43, M^+-1CH_3), 447(42, M^+-2CH_3), 433(15), 405(22), 475(13), 149(22), 91(26), 57(18), 43(25). (Found: C, 63.58; H, 6.48; N, 15.89. $C_{28}H_{34}N_6O_4.1/2H_2O$ requires C, 63.57; H, 6.64; N, 15.93 %).

2,3,9,10-Tetramethoxy-6,13-dihydro-5,7,12,14-tetraza-6,13-dithiapentacene (175)

2,3-Dichloro-6,7-dimethoxyquinoxaline (145) (2.27 g, 8.8 mmol) and thiourea (0.668 g, 8.8 mmol) were dissolved in dimethylformamide (30 cm^3), and triethylamine (1.8 g) was added with stirring . The reaction mixture was refluxed for 4 h when a colour change from dark brown to bright yellow occured. The yellow crystalline solid was filtered off, washed with water and then ethanol, and recrystallised from dimethylformamide to give yellow 2,3,9,10-tetramethoxy-6,13-dihydro-5,7,12,14-tetraza-6,13-dithiapentacene (175) (1.32 g, 68%), m.p. > 360° C; IR(KBr) ν_{max} 3010, 2940, 1610, 1500, 1465, 1415, 1350, 1260, 1150, 1130, 1050, 1025, 1005, 880, 845, 830 cm^{-1}; ^1H NMR (200 MHz, d-TFA) δ 7.65 (s, 4H, 5-, 5'-, 8- and 8'-H) 4.24 (s, 12H, 6-,6'-,7- and 7'-OCH_3); MS, m/z(r.i.) 440(100, M^+), 425(5, M^+-1CH_3), 410(33, M^+-2CH_3), 408(8, M^+-1S), 387(5), 365(4), 83(3), 43(4), 32(11). (Found: C, 53.82; H, 3.86; N, 12.41; S, 14.31. $C_{20}H_{16}N_4O_4S_2.1/4H2O$ requires C, 53.99; H, 3,59; N, 12.59; S, 14.39 %).

Dimethoxyquinoxalines having Crown Ether Substituents

2,3-(5',8'-Dimethoxyquinoxalinyl)-1,4,7,10-tetraoxacyclododeca-2-ene (176):

To a solution of 2,3-dichloro-5,8-dimethoxyquinoxaline (144) (0.258 g, 1.0 mmol) in anhydrous tetrahydrofuran (100 cm^3), a solution of the disodium salt of triethylene glycol [(prepared by treating triethylene glycol (0.15 g, 1.1 mmol) with sodium metal (0.05 g, 2.2 mmol)] was added dropwise during 30 min, and stirring was continued for 12 h at 40-45° C. The resulting solid was filtered off, washed with water, and finally with acetone. For further purification the solid was dissolved in a minimum quantity of trichloroacetic acid, and the compound was reprecipitated by diluting the mixture with water. The colourless solid was filtered off, and washed thoroughly with water to yield 2,3-(5',8'-dimethoxyquinoxalyl)-1,4,7,10-tetraoxacyclododeca-2-ene (176) (0.151 g, 45 %), m.p. 158-159° C; IR(KBr) ν_{max} 2920, 2840, 1610, 1580, 1475, 1325, 1250, 1225, 1140, 1090, 1000, 950 800, 790 cm^{-1}; ^1H NMR (200 MHz, d-TFA) δ 7.38 (s, 2H, 6'- and 7'-H) 5.01 (bs, 4H, 5- and 12-CH_2), 4.30 (s, 4H, 8- and 9-CH_2), 4.19 (s, 10H, 6-,11-CH_2 and 5'-,8'-OCH_3); MS, m/z(r.i.) 337(18), 336(100, M^+), 321(41, M^+-1CH_3), 307(25), 276(12), 220(48), 207(23), 192(15). (Found: C, 53.96; H, 5.80; N, 7.78. $C_{16}H_{20}N_2O_6.1H_2O$ requires C, 54.23; H, 5.64; N, 7.90 %).

Methylation of 1,4-Dihydro-5,8-dimethoxyquinoxaline-2,3-dione (142)[89]

1,4-Dihydro-2,3-dioxo-5,8-dimethoxyquinoxaline-2,3-dione (142) (0.250 g, 1.2 mmol) was dissolved in aqueous sodium hydroxide (2M, 30 cm^3) and then dimethyl sulphate (6.0 cm^3) was added. The reaction mixture was stirred for 2h at room temperature, then diluted with water (100 cm^3), and extracted with chloroform (3 x 100 cm^3). The extract was dried (anhydrous sodium sulphate), and the solvent removed *in vacuo*. The crude mixture was separated by t.l.c [(ethyl acetate/dichloromethane (4:1)]. The component of higher R_f was crystallised from ethyl acetate to yield 2,5,8-trimethoxy-4-methyl-3(4H)-quinoxalinone (178) (0.037 g, 13 %), m.p. 176-177° C; IR(KBr) ν_{max} 2965, 1670 (C=O), 1630, 1500, 1460, 1325, 1250, 1160, 1100, 1050, 980, 810 cm^{-1}; ^1H NMR (80 MHz, $CDCl_3$) δ 6.80 (d, 1H, J = 8.8 Hz, 8-H), 6.73 (d, 1H, J = 9.0 Hz, 7-H), 4.10 (s, 2H, 2-OCH_3), 3.95 (s, 3H, 8-OCH_3), 3.92 (s, 3H, 5-OCH_3), 3.83 (s, 3H, N-CH_3); MS, m/z(r.i.) 250(24; M^+), 234(14), 222(68), 208(25), 207(100),

192(47), 164(22), 149(19). (Found: C; 57.39; H, 5.52; N, 11.14. $C_{12}H_{14}N_2O_4$ requires C, 57.59; H, 5.64; N, 11.19 %). The compound obtained from the lower component, was crystallised from ethyl acetate as colourless needles of 2-hydroxy-4-methyl-5,8-dimethoxy-3(4H)-quinoxalinone (179) (0.127 g, 48 %), m.p. 202-203° C; IR(KBr) ν_{max} 3600, 3500(OH), 3100, 3080, 2920, 1700 (C=O), 1680 (C=O), 1525, 1455, 1390, 1260, 1100, 1040, 985, 845 cm^{-1}; ^1H NMR (80 MHz, $CDCl_3$) δ 8.91 (bs, 1H, 2-OH exchanged with D_2O), 6.64 (s, 2H, 6- and 7-H), 3.88 (s, 3H, 8-OCH_3), 3.85 (s, 3H, 5-OCH_3), 3.82 (s, 3H, N-CH_3); MS, m/z(r.i.) 237(14), 236(100, M^+), 221(28), 207(5), 193(68), 178(17), 165(12), 150(17). (Found: C, 55.87; H, 5.13; N, 11.77. $C_{11}H_{12}N_2O_4$ requires C, 55.93; H, 5.12; N, 11.86 %).

2,3-Bis(2'-hydroxyethoxy)-5,8-dimethoxyquinoxaline (183)

To a solution of compound (144) (2.58 g, 10 mmol) in dry tetrahydrofuran (30 cm^3), a freshly prepared solution of disodium salt of 1,2-ethanediol [(prepared by treating sodium metal (1 g, 44 mm) with 1,2-ethanediol (2.5 g, 40 mmol)] in dry tetrahydrofuran (20 cm^3) was added and refluxed for 4h. A solid separated out during the reflux, and was filtered off, thoroughly washed with water, and crystallised from hot methanol to give 2,3-bis(2'-hydroxyethoxy)-5,8-dimethoxyquinoxaline (183) (2.51 g, 81 %), m.p. 222-223° C; IR(KBr) ν_{max} 3350 (OH), 2915, 2825, 1620, 1595, 1500, 1450, 1365, 1320, 1250, 1105, 1030, 920, 810 cm^{-1}; ^1H NMR (200 MHz, d_6-DMSO) δ 6.95 (s, 2H, 6- and 7-H), 4.80 (t, 2H, 2- and 3-$OCH_2CH_2\underline{OH}$ exchanged with D_2O), 4.50 (t, 4H, 2- and 3-O$\underline{CH_2}CH_2OH$), 3.88 (s, 6H, 5- and 8-OCH_3), 3.77 (q, 4H, 2- and 3-$OCH_2\underline{CH_2}OH$); MS, m/z(r.i.) 310(12, M^+), 222(35), 207(12), 193(7), 174(14), 57(34), 45(31), 44(47). (Found: C, 53.82; H, 5.92; N, 8.92. $C_{14}H_{18}N_2O_6$ requires C, 54.19; H, 5.85; N, 9.03 %).

2,3-Dihydro-1,4-dioxa-5,8-dimethoxy-9,10-diazaanthracene (186)

2,3-Bis(2'-hydroxyethoxy)-5,8-dimethoxyquinoxaline (183) (0.31 g, 1 mmol) was dissolved in dry dimethylsulfoxide (20 cm^3) followed by the addition of sodium hydride (0.05 g, 2.2 mmol). The reaction mixture was stirred at room temperature for 4 h under nitrogen, then diluted with water (100 cm^3), and extracted with dichloromethane. The combined extracts were washed several times with water, dried (anhydrous sodium

sulphate) and, after evaporation of the solvent in vacuo, the residue was crystallised from ethyl acetate to yield yellow needles of 2,3-dihydro-1,4-dioxa-5,8-dimethoxy-9,10-diazaanthracene (186) (0.146 g, 59 %), m.p. 176-177° C; IR(KBr)ν_{max} 2920, 2825, 1620, 1505, 1465, 1345, 1260, 1190, 1080, 920, 810 cm^{-1}; ^1H NMR (80 MHz, $CDCl_3$) δ 6.82 (s, 2H, 6- and 7-H), 4.55 (s, 4H, 2- and 3-CH_2), 3.95 (s, 6H, 5- and 8-OCH_3); MS, m/z(r.i.) 249(16), 248(100; M^+), 233(64, M^+-CH_3), 219(43), 207(21), 192(8), 164(13). (Found: C, 57.98; H, 5.04; N, 11.28. $C_{12}H_{12}N_2O_4$ requires C, 58.06; H, 4.87; N, 11.28 %).

General Method for the Preparation of 2,3-Bis(6'-hydroxy-1',4'-dioxahexyl)5,8-dimethoxyquinoxaline (184) and 2,3-bis(6'-hydroxy-1',4'-dioxahexyl)-6,7-dimethoxyquinoxaline (188)

A solution of the 2,3-dichlorodimethoxyquinoxaline (2.58 g, 10 mmol) in dry tetrahydrofuran (30 cm^3) was added to a solution of the disodium salt of diethylene glycol in tetrahydrofuran (10 cm^3) [(prepared by treating diethylene glycol (4.15 g, 40 mmol) with sodium metal (1 g, 44 mmol)]. The stirred reaction mixture was refluxed for 5h. The extent of the reaction was indicated by a change in colour of the reaction mixture from pale yellow to very light yellow, and was checked by t.l.c. After reduction of the volume of tetrahydrofuran to 5 cm^3 by evaporation, the reaction mixture was diluted with water (100 cm^3) and then extracted with dichloromethane (3 x 100 cm^3). The combined extract was washed thoroughly with water, dried (anhydrous sodium sulphate), evaporated *in vacuo,* and the residue crystallised from a mixture of ethyl acetate and dichloromethane (3:2).

2,3-Bis(6'-hydroxy-1',4'-dioxahexyl)-5,8-dimethoxyquinoxaline (184): colourless needles (2.62 g, 66 %), m.p. 145-146° C; IR(KBr) ν_{max} 3400 (OH), 2930, 2840, 1620, 1600, 1530, 1450, 1365, 1345, 1260, 1240, 1155, 1100, 1010, 950, 900, 815, 805 cm^{-1}; ^1H NMR (80 MHz, d_6-DMSO) δ 6.92 (s, 2H, 6- and 7-H), 4.56 (t, 4H, 2- and 3-$O\underline{CH_2}CH_2OCH_2CH_2OH$), 3.85 (bs, 10H, 5- and 8-OCH_3 and 2- and 3-$OCH_2CH_2OCH_2\underline{CH_2}OH$), 3.52 (s, 8H, 2- and 3-$OCH_2\underline{CH_2}O\underline{CH_2}CH_2OH$), 3.48 (s, 2H, 2- and 3-$OCH_2CH_2OCH_2\underline{CH_2}OH$ exchanged with D_2O); MS, m/z(r.i.) 399(8), 398(38, M^+), 310(7), 249(13), 222(82), 207(70), 193(31), 59(39), 57(24), 45(100), 44(22). (Found: C, 54.19; H, 6.72; N, 7.04. $C_{18}H_{26}N_2O_8$ requires C, 54.26; H, 6.58; N, 7.03 %).

2,3-Bis(6'-hydroxy-1',4'-dioxahexyl)-6,7-dimethoxyquinoxaline (188) gave colourless crystals (2.81 g, 71 %), m.p. 101-102° C; IR(KBr) ν_{max} 3470,3400 (OH), 2920, 2860, 1610, 1575, 1460, 1325, 1250, 1225, 1130, 1040, 900, 845 cm^{-1}; ^1H NMR (80 MHz, $CDCl_3$) δ 7.09 (s, 2H, 5- and 8-H), 4.62 (t, 4H, 2- and 3-O$\underline{CH_2}CH_2OCH_2CH_2OH$), 3.96 (bs, 6H, 6- and 7-OCH_3) 3.91 (t, 4H, 2- and 3-$OCH_2CH_2OCH_2\underline{CH_2}OH$), 3.70 (s, 8H, 2- and 3-$OCH_2\underline{CH_2}O\underline{CH_2}CH_2OH$), 3.52 (s, 2H, 2- and 3-$OCH_2CH_2OCH_2CH_2\underline{OH}$ exchanged with D_2O); MS, m/z(r.i.) 399(8), 398(33, M^+), 310(10), 249(10), 240 (15), 222(100), 207(31), 193(14), 57(7), 45(58), 44(12). (Found: C, 54.08; H, 6.51; N, 6.95. $C_{18}H_{26}N_2O_8$ requires C, 54.26; H, 6.58; N, 7.03 %).

2,3-Bis(9'-hydroxy-1',4',7'-trioxanonanyl)-5,8-dimethoxyquinoxaline (185) and 2-Chloro-3-(9'-hydroxy-1',4'-7'trioxanonanyl)-5,8-dimethoxyquinoxaline (189)

A solution of 2,3-dichloro-5,8-dimethoxyquinoxaline (144) (1.29 g, 5 mmol) in dry tetrahydrofuran (30 cm^3) was added to a solution of the disodium salt of triethylene glycol in tetrahydrofuran (10 cm^3) [(prepared by treating triethylene glycol (2.65 g, 25 mmol) with sodium metal (0.5 g, 22 mmol)]. The stirred reaction mixture was refluxed for 12 h. After reducing the volume of tetrahydrofuran to 5 cm^3 by evaporation, the reaction mixture was diluted with water (100 cm^3) and then extracted with dichloromethane (3 x 100 cm^3). The combined extract was washed thoroughly with water, dried (anhydrous sodium sulphate), the solvent evaporated *in vacuo* and the resulting crude mixture of two components was separated by preparative t.l.c [ethyl acetate, petroleum ether 40-60° C (1:1)]. The compound having the higher R_f value was crystallised from the same solvent and characterised as 2-chloro-3-(9'-hydroxy-1',4'-7'trioxanonanyl)-5,8-dimethoxyquinoxaline (189) (1.13 g, 61 %), m.p. 163-165° C; IR(KBr) ν_{max} 3390 (OH), 3010, 2940, 2830, 1610, 1600, 1495, 1445, 1350, 1265, 1110, 930, 850, 760, 700 cm^{-1}; ^1H NMR (80 MHz, $CDCl_3$) δ 6.93 (d, 1H, J = 8.7 Hz, 6-H), 6.86 (d, 1H, J = 8.7 Hz, 7H), 4.75 (t, 2H, 2'-CH_2-), 3.98 (s, 3H, 8-OCH_3), 3.96 (s, 3H, 5-OCH_3). 3.95 (t, 2H, 9'-CH_2-), 3.79-3.60 (m, 8H, 3',5',6' and 8'-CH_2-), 3.53 (bs, 1H, 9'-OH exchanged with D_2O); MS, m/z(r.i.) 374,372 (11,33, M_+ for ^{37}Cl and ^{35}Cl), 269,267(5,16 for ^{37}Cl and ^{35}Cl), 242,240(25, 74 for ^{37}Cl and ^{35}Cl), 227,225 (23,68 for ^{37}Cl and ^{35}Cl), 213,211(13,38, for ^{37}Cl and ^{35}Cl), 189(16), 133(11), 45(100). (Found: C, 51.46; H, 5.72; N, 7.58; Cl, 9.57. $C_{16}H_{21}N_2O_6Cl$ requires C, 51.55; H, 5.68; N, 7.51; Cl,

9.51 %). The second component was crystallised from a mixture of ethyl acetate and dichloromethane (4:1) to give 2,3-bis(9'-hydroxy-1',4'-7'trioxanonanyl)-5,8-dimethoxyquinoxaline (185) as a waxy solid (0.925 g, 38 %), m.p. 89-90° C; IR(KBr) ν_{max} 3520, 3300 (OH), 3000, 2940,2840, 1615, 1595,1500, 1475, 1450, 1350, 1330, 1275, 1245, 1215, 1115, 1080, 1005, 950, 895, 815, 755, 710, 650 cm^{-1}; ^1H NMR (80 MHz, $CDCl_3$) δ 6.81 (s, 2H, 6- and 7-H), 4.74 (t, 4H, 2- and 3-$OCH_2CH_2OCH_2CH_2OCH_2CH_2OH$), 3.94 (s, 6H, 5- and 8-OCH_3), 3.98-3.45 (m, 20H, 2- and 3-$OCH_2CH_2OCH_2CH_2OCH_2CH_2OH$); MS, m/z(r.i.) 487(3), 486(8, M^+), 442(3), 354(20), 31(98), 249(21), 222(100), 207(65), 193(24), 179(18), 45(75). (Found: C, 53.06; H, 6.95; N, 5.77. $C_{22}H_{34}N_2O_{10}1/2H_2O$ requires C, 53.33; H, 7.07; N, 5.65 %).

General Method for the Preparation of Crown Ethers Containing Two Dimethoxyquinoxaline Groups (190)-(192)

To a solution of dihydroxy compound (184),(188) or (185) (1 mmol) in dry tetrahydrofuran (75 cm^3), sodium hydride (1.2 mmol) was added, and the reaction mixture was stirred for 15 min at room temperature. Then a solution of 2,3-dichloro-5,8-dimethoxyquinoxaline (144) (1 mmol) in the same solvent (10 cm^3) was added dropwise during 1h. The stirring was continued, and the reaction mixture was refluxed for 6 h. After cooling the mixture, the resulting white solid was filtered off, washed with water, and crystallised from dichloromethane to give colourless crystals.

2,3,11,12-Bis(5',8'-dimethoxyquinoxalyl)-1,4,7,10,13,16-hexaoxacyclooctadeca-2,11-diene (190) (0.421 g, 72%), m.p. 321-322° C; IR(KBr) ν_{max} 2930, 2840, 1615, 1590, 1475, 1325, 1250, 1140, 1035, 940, 910, 800 cm^{-1}; ^1H NMR (200 MHz, d-TFA) δ 7.19 (s, 4H, 6'-, 6''-, 7'- and 7''-H), 5.07 (bs, 8H, 5-, 9-, 14- and 18-CH_2-), 4.32 (bs, 8H, 6-, 8-, 15- and 17-CH_2-), 4.15 (s, 12H, 5'-, 5''-, 8'- and 8''-OCH_3); MS, m/z(r.i.) 584(18, M^+), 351(7), 308(8), 303(10), 291(13), 278(12), 174(22), 97(52), 85(42), 57(85), 44(27), 43(47). (Found: C, 56.73; H, 5.38; N, 9.31. $C_{28}H_{32}N_4O_{10}.1/2H_2O$ requires C, 56.66; H, 5.56; N, 9.44 %).

2,3,11,12-Bis(6',7'-dimethoxyquinoxalyl)-1,4,7,10,13,16-hexaoxacyclooctadeca-2,11-diene (191) was obtained as colourless crystals (0.391 g, 67 %), m.p. > 330° C; IR(KBr) ν_{max} 2930, 2840, 1615, 1590, 1475, 1325, 1250, 1140, 1035, 940, 910, 800 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.07 (s, 4H, 5'-, 5''-, 8'- and 8''-H), 4.61 (t, 8H, 5-,

9-, 14- and 18-CH_2-), 3.97 (bs, 8H, 6-, 8-, 15- and 17-CH_2-), 3.95 (s, 12H, 6'-, 6''-, 7'- and 7''-OCH_3); MS, m/z(r.i.) 584(12; M^+), 570(11), 542(7), 368(6), 306(8), 291(21)), 277(15), 264(20), 263(30), 249(20), 248(14), 222(40), 207(22), 173(12), 149 (19), 137(14), 97(56), 91(63), 45(10). (Found: C, 56.88; H, 5.62; N, 9.28. $C_{28}H_{32}N_4O_{10}.1/2H_2O$ requires C, 56.66; H, 5.56; N, 9.44 %).

2,3,14,15-Bis(5',8'-dimethoxyquinoxalyl)-1,4,7,10,13,16,19,22-octaoxacyclotetradecadeca-2,14-diene (192) (0.215 g, 32%), m.p. 218-219° C; IR(KBr) ν_{max} 2940, 2830, 1610, 1595, 1490, 1365, 1260, 1130, 1010, 960, 810 cm^{-1}; ^1H NMR (200 MHz, CDCl3) δ 6.79 (s, 4H, 6'-, 6''-, 7'-, 7''-H) 4.67 (t, 8H, 5-, 12-, 17-, 24-CH_2-) 3.95 (m, 20H, 5'-, 5''-, 8'- & 8''-OCH_3 and 6-, 11-, 18-, 23-CH_2-) 3.77 (t, 8H 8-, 9-, 20-, 21-CH_2-); MS, m/z(r.t.) 672(10, M^+), 628(100, M^+-1C_2H_4O), 458(20), 457(73), 325(45), 326(53), 310(77), 296(38), 267(12), 249(49), 222(46), 207(30), 193(18), 45(18), 44(22). (Acc. mass; Found: 672.2640. $C_{32}H_{40}N_4O_{12}$ requires 672.2642).

DIAZANAPHTHOQUINONES

General Method for preparation of Quinoxaline-5,8-diones by the Oxidation of 5,8-Dimethoxyquinoxalines:

A stirred solution/suspension of 5,8-dimethoxyquinoxaline (1 mmol) in a mixture of acetonitrile and water (20 cm^3, 4:1 v/v) was treated with ceric ammonium nitrate (4 mmol) in an ice-bath. The stirring was continued for 12-25 min, and the mixture was diluted with water (50 cm^3). The quinone was extracted with dichloromethane (3 x 50 cm^3), and the extract washed repeatedly with water. The combined extract was dried (anhydrous sodium sulphate), the solid removed, the solvent evaporated *in vacuo,* and the residue crystallised from an appropriate solvent.

Quinoxaline-5,8-dione (49) was crystallised from ethyl acetate as a dark brown quinone (49) (0.083 g, 52 %), m.p. 172-173° C (lit.,[118] m.p. 172° C).

2,3-Dimethylquinoxaline-5,8-dione (94) was obtained from ethyl acetate as a brown dione (94) (0.156 g, 71 %), m.p. 205-206° C (lit.,[118] m.p. 206-207° C).

2,3-Diphenylquinoxaline-5,8-dione (193) was crystallised from methanol to give the dark yellow crystal, (0.290 g, 93 %), m.p. 226-227° C (lit.,[118] m.p. 227 °C).

2,3-dimethoxyquinoxaline-5,8-dione (194) was crystallised from a mixture of ethyl acetate and dichloromethane (9:1) to yield yellow crystals, (0.207 g, 97 %), m.p. 224-225° C; IR(KBr) ν_{max} 2910, 1670 (C=O), 1605, 1550, 1495, 1405, 1305, 1250,1110, 1040, 970, 860, 820 cm^{-1}; ^1H NMR (80 MHz, $CDCl_3$) δ 6.93 (s, 2H, 6- and 7-H), 4.21 (s, 6H, 2- and 3-OCH_3); MS, m/z(r.i.) 220(100, M^+), 205(7, M^+-CH_3), 191(50), 190(15, M^+-$2CH_3$), 175(85), 162(47), 149(18), 134(31), 124(15), 54(58), 43(10). (Found: C, 54.49; H, 3.62; N, 12.53. $C_{10}H_8N_2O_4$ requires C, 54.54; H, 3.63; N; 12.72 %).

2,3-Diethoxyquinoxaline-5,8-dione (195) was crystallised from ethyl acetate and dichloromethane mixture (9:1) to produce bright yellow crystals (0.223 g, 90 %), m.p. 171° C; IR(KBr) ν_{max} 2920, 1680 (C=O), 1610, 1555, 1495, 1465, 1300, 1250, 1040, 860 cm^{-1}; ^1H NMR (80 MHz, $CDCl_3$) δ 6.90 (s, 2H, 6- and 7-H), 4.66 (q, 4H, 2- and 3-O$\underline{CH_2}CH_3$), 1.49 (t, 6H, 2- and 3-$OCH_2\underline{CH_3}$); MS, m/z(r.i.) 249(4), 248(13, M^+), 221(26), 192(33), 177(18), 149(13), 136(15), 108(11), 57(24), 43(47). (Found: C, 57.89; H, 4.66; N, 10.98. $C_{12}H_{12}N_2O_4$ requires C, 58.06; H, 4.83; N, 11.29 %).

2,3-Bis(ethylthio)quinoxaline-5,8-dione (196) was crystallised from a mixture of ethanol and chloroform (9:1) to give the bright yellow dione (196) (0.26 g, 93 %) , m.p. 198°C; IR(KBr) ν_{max} 2950, 2890(H-Aliph), 1690, 1615(C=O), 1500, 1350, 1235, 1160, 1110, 1075, 940, 860 cm^{-1}; ^1H NMR (80 MHz, $CDCl_3$), δ 6.95 (s, 2H, 6-H and 7-H), 3.41(q, 4H, 2- and 3-O$\underline{CH_2}CH_3$), 1.46 (t, 6H, 2-and 3- $OCH_2\underline{CH_3}$); MS, m/z(r.i.) 281(5), 280(30, M^+), 251(100, M^+-C_2H_5), 225(16), 218(6), 149(22) 136(17), 45(130, 44(12), 43(36). (Found: C, 51.06; H, 4.24; N, 9.88; S, 22.57. $C_{12}H_{12}N_2O_2S_2$ requires C, 51.41; H, 4.31; N, 9.99 S, 22.85 %).

2,3-Bis(methoxycarbonyl)quinoxaline-5,8-dione (197) was crystallised from a mixture of methanol and dichloromethane (4:1) to give colourless crystals, (0.182 g, 66 %), m.p. 189-190° C; IR(KBr) ν_{max} 3040, 2965, 1750 (C=O, ester), 1690(C=O), 1605, 1545,1450, 1365, 1295, 1240, 1160, 1115, 1080, 1010, 955, 880, 840, 820, 800 cm^{-1}; ^1H NMR (80 MHz, $CDCl_3$) δ 7.29 (s, 2H, 6- and 7-H), 4.05 (s, 6H, 2- and 3-$COOCH_3$), MS, m/z(r.i.)

278(28), 276(6, M^+), 261(39), 246(100), 220(25), 160(80), 132(20), 78(20), 59(31). (Found: C, 51.99; H, 2.94; N, 10.05. $C_{12}H_8N_2O_6$ requires C, 52.18; H, 2.92; N, 10.14 %).

2,3-Dicyanoquinoxaline-5,8-dione (198) was crystallised from the same solvent mixture as above to produce colourless crystals, (0.145 g, 69 %), m.p. 216-217° C; IR(KBr)ν_{max} 2940, 2880, 2060(CN), 1700(C=O), 1620, 1540, 1370, 1325, 1200, 1160, 1085, 1000, 860, 695, 615 cm^{-1}; ^1H NMR (80 MHz, $CDCl_3$) δ 7.28 (s, 2H, 6- and 7-H); MS, m/z(r.i.) 212(33), 210(74, M^+), 184(25), 182(36, M^+-CO)), 156(18), 149(38). (Found: C, 57.15; H, 0.77; N, 26.74. $C_{10}H_2N_4O_2$ requires C, 57.15 ; H, 0.96; N, 26.66 %).

2,3-Dihydro-1,4-dioxa-9,10-diazaanthracene-5,8-dione (199) was crystallised from ethyl acetate to produce yellow crystals, (0.091 g, 86 %), IR(KBr) ν_{max} 2940, 1680 (C=O), 1615, 1565, 1460, 1390, 1300, 1265, 1060, 940, 870 cm^{-1}; ^1H NMR (80 MHz, $CDCl_3$) δ 7.01 (s, 2H, 6- and 7-H), 4.63 (s, 4H, 2- and 3-CH_2); MS, m/z(r.i.) 219(82), 218(100; M^+), 192(92), 161(21), 134(58). (Found: C, 54.73; H, 2.78; N, 12.62. $C_{10}H_6N_2O_4$ requires C, 55.05; H, 2.77; N, 12.84 %).

2,3,11,12-bis(5',8'-dioxoquinoxalinyl)-1,4,7,10,13,16-hexaoxacyclooctadeca-2,11-diene (200)

To a stirred suspension of (190) (0.524 g) in acetonitrile-water (30 cm^3, 4:1) was added a solution of ceric ammonium nitrate (2 .0 g) in water to give a clear solution. After few min, a yellow precipitate formed. The stirring was continued for 20 min to complete the reaction. The yellow solid was then filtered off , washed with water, and recrystallised from a mixture of ethyl acetate and dichloromethane (3:2), to yield yellow 2,3,11,12-bis(5',8'-dioxoquinoxalyl)-1,4,7,10,13,16-hexaoxacyclooctadeca-2,11-diene (200) (0.487 g, 93 %), m.p. > 330° C(decomp); IR(KBr) ν_{max} 2920, 2840, 1675 (C=O), 1610, 1565, 1485, 1310, 1250, 1135, 1040, 940, 860 cm^{-1}; ^1H NMR (200 MHz, d-TFA) δ 7.05 (s, 4H, 6'-, 6''-, 7'- and 7''-H), 4.94 (bs, 8H, 5-, 9-, 14- and 18-methylene hydrogens); MS m/z(r.i.) 528(4), 526(16), 524(37, M^+), 484 (15), 278(100), 246(14),

219(23), 218(60), 190(36), 175(43), 45(37), 43(49). (Found: C, 52.22; H, 3.75; N, 10.27. $C_{24}H_{20}N_4O_{10}.1.5H_2O$ requires C, 52.26; H, 4.17; N, 10.16 %).

Phthalazine-5,8-dione

5-Nitrophthalazine (202)

A solution of phthalazine (201) (2.6 g, 20 mmol) in conc. sulphuric acid (25 cm^3) was heated at 90° C with potassium nitrate (7.5 g, 75 mmol) for 10 h, and poured into crushed ice. The mixture was neutralised by careful dropwise addition of aqueous sodium hydroxide (10 M). The yellow 5-nitrophthalazine (202) was separated by filtration. The filtrate was again treated with a few drops of sodium hydroxide solution, and more nitrophthalazine was obtained by filtration. The crude product was recrystallised from ethanol (1.89 g, 54 %), m.p. 187-188° C (lit.,[54] 188-189° C).

5-Aminophthalazine (203)

A freshly prepared solution of sodium dithionite (17.4 g) in water (40 cm^3) was quickly added to a boiling solution of 5-nitrophthalazine (202) (3.5 g, 20 mmol) in tetrahydrofuran-methanol (200 cm^3, 1:2), and boiling under reflux was continued for 20 min. The reaction mixture was then diluted with water (300 cm^3), evaporated *in vacuo* to remove organic solvents, extracted with ethyl acetate (3 x 200 cm^3) and then continuously extracted with ethyl acetate for 48 h. The organic extracts were combined, washed with water, and evaporated *in vacuo*. The residue (0.638 g, 22 %) was crystallised from methanol to give 5-aminophthalazine (203), m.p. 221-222° C (lit.,[54] 223-224° C).

Phthalazine-5,8-dione (204)

5-Aminophthalazine (203) (1 g, 7mmol) in water (25 cm^3) was reacted with sulphuric acid (6 M, 1 cm^3) and cooled to 5° C. After the addition of ice (66 g), the mixture was stirred whilst an ice-cold solution of sulphuric acid (6 M, 40 cm^3) in aqueous potassium dichromate (1 M, 56 cm^3) was added rapidly and the stirring was continued in an ice-bath for 1 h. The mixture was extracted with chloroform, the extract washed with dil. sulphuric acid (0.5 M), and potassium dichromate solution (1 M), and finally with saturated sodium chloride solution. The solvent was removed *in vacuo* and

the residue was crystallised from methanol to yield brownish-red phthalazine-5,8-dione, (0.424 g, 42 %), m.p. 167-171° C (decomp) [(lit.,[128] m.p. 173° C (decomp)].

Oxidative Chlorination of *p*-Dimethoxyquinoxalines.

General method

2,3-Disubstituted-6,7-dichloroquinoxaline-5,8-diones (208)-(211) were prepared by the method described in the literature for the preparation of 6,7-dichloroquinoxaline-5,8-dione.[54]

To a stirred suspension of the 2,3-disubstituted-5,8-dimethoxyquinoxaline (10 mmol) in conc. hydrochloric acid (10 cm^3), was added conc. nitric acid (2.0 cm^3) dropwise over a period of 0.5 h. The stirring was continued for 1h, and the reaction mixture was then poured over chipped ice (100 g). The resulting solid was filtered off, washed thoroughly with water and recrystallised from methanol.

The following compounds were prepared by this procedure:-

2,3-Dimethoxy-6,7-dichloroquinoxaline-5,8-dione (208) (0.181 g, 69%), m.p. >300° C(sublimed); IR(KBr) ν_{max} 3010, 1720 (C=O), 1610, 1545, 1515, 1465, 1400, 1365, 1260, 1130, 1010, 845 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 4.21 (s, 6-H, 2- and 3-OCH_3); MS, m/z(r.i.) 292, 290, 288 (32, 100 ,95; M^+ for ^{37}Cl and ^{35}Cl), 277, 275, 273 (33, 53, 4, M-1CH_3 for ^{37}Cl and ^{35}Cl), 262, 260, 258 (13, 22, 11, M^+-2CH_3 for ^{37}Cl and ^{35}Cl), 247, 245, 243 (14, 46, 67, M^+-CO for ^{37}Cl and ^{35}Cl). (Acc. mass, Found: 287.9705 and 289.9675. $C_{10}H_6N_2O_4Cl_2$ requires 287.9704 and 289.9673 for ^{35}Cl and ^{37}Cl, respectively).

The oxidative chlorination of 2,3-diethoxy-5,8-dimethoxyquinoxaline (147) produced a mixture of two components, which was separated by column chromatography [(petroleum ether 40-60° C and ethyl acetate (4:1)]. The component of lower R_f value on t.l.c was characterised as 2,3-diethoxy-6,7-dichloroquinoxaline-5,8-dione (209) (0.151 g, 48 %), m.p. 146-147° C; IR(KBr) ν_{max} 2920, 2840, 1700 (C=O), 1595, 1665, 1495, 1400, 1350, 1300, 1095, 1015, 875 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 4.66 (q, 4H, 2- and 3-OCH_2CH_3), 1.50 (t, 6H, 2- and 3-OCH_2CH_3); MS, m/z(r.i.) 320, 318, 316 (12, 47, 56, M^+ for ^{37}Cl and ^{35}Cl), 292, 290, 288 (10, 42, 58, M^+-CO), 264, 262, 260 (18, 82, 100, M^+-2CO), 236, 234, 232 (7, 26, 35, M^+-2CO and C_2H_4). (Found: C, 45.48; H, 2.98; N, 8.69; Cl, 21.91. $C_{12}H_{10}N_2O_4Cl_2$ requires C, 45.56; H, 3.16; N, 8.86; Cl, 22.15 %).

The component of higher R_f value (upper spot on t.l.c) was characterised as 6-chloro-2,3-diethoxyquinoxaline-5,8-dione (210) (0.031 g, 11 %), m.p. 97-98° C; IR(KBr) ν_{max} 2940, 2850, 1700 (C=O), 1680 (C=O), 1605, 1560, 1480, 1300, 1255, 1050, 1020 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.13 (s, 1H, 6-H), 4.66 (q, 4H, 2- and 3-O$\underline{CH_2}CH_3$), 1.49 (t, 6H, 2- and 3- O$CH_2\underline{CH_3}$); MS, m/z(r.i.) 284, 282(15,19, M^+ for ^{37}Cl and ^{35}Cl), 256, 254(12, 28, M^+-CO), 228, 226(27, 46, M^+-2CO), 200, 198(8, 14, M^+-2CO and C_2H_4), 172, 170(5, 12, M^+-2CO and $2C_2H_4$). (Found: C, 50.88; H, 3.61; N, 10.02; Cl, 12.29. $C_{12}H_{11}N_2O_4Cl$ requires C, 51.06; H, 3.90; N, 9.92; Cl, 12.58 %).

2,3,6,7-Tetrachloroquinoxaline-5,8-dione (211) (0.227 g, 77 %), m.p. 302-305° C(sublim); IR(KBr) ν_{max} 2920, 1705 (C=O), 1600, 1520, 1415, 1380, 1330, 980, 865, 735 cm^{-1}; ^1H NMR (80 MHz, d_6-DMSO) δ No proton; MS, m/z(r.i.) 304, 302, 300, 298, 296(2,10,20,23,9, M^+ for ^{37}Cl and ^{35}Cl), 274, 272, 270, 268(3,9,16,14, M^+-CO), 246, 244, 242, 240(2,5,10,8, M^+-2CO). (Found: C, 32.29; N, 9.21; Cl, 47.41. $C_8Cl_4N_2O_2$ requires C, 32.25; N, 9.40; Cl, 47.60 %).

Reactions of Diazanaphthoquinones

Reaction of Sodium Methoxide with 2,3,6,7-Tetrachloroquinoxaline-5,8-dione (211):

2,3,6,7-Dichloroquinoxaline-5,8-dione (211) (0.296 g, 1 mmol) was dissolved in methanol (30 cm^3) and sodium methoxide was added. The reaction mixture was stirred for 1h at room temperature. The resulting solid was filtered off, and crystallised from a mixture methanol and dichloromethane to yield bright orange 2,3,6,7-tetramethoxyquinoxaline-5,8-dione (214) (O.229 g, 82 %), m.p. 239-240° C; IR(KBr) ν_{max} 2915, 1680, 1665 (C=O), 1620, 1555, 1545, 1400, 1320, 1250, 1130, 1080, 970, 820 cm^{-1}; ^1H NMR (80 MHz, $CDCl_3$) δ 4.19 (s, 6H, 2- and 3-OCH_3), 4.08 (s, 6H, 6- and 7-OCH_3); MS, m/z(r.i.) 282(18), 280(92, M^+), 265(90, M^+-CH_3), 250(74, M^+-$2CH_3$), 235(100, M^+-$3CH_3$), 220(30, M^+-$4CH_3$), 209(55), 192(40), 166(80). (Found: C, 51.42; H, 4.28; N, 10.00. $C_{12}H_{12}N_2O_6$ requires C, 51.39; H, 4.27; N, 9.96 %).

Reaction of 2,3-bis(ethylthio)quinoxaline-5,8-dione (196) with Bromine

2,3-Bis(ethylthio)quinoxaline-5,8-dione (196) (0.5 g, 1.8 mmol) was dissolved in carbon tetrachloride (25 cm^3), followed by dropwise addition of bromine (3 cm^3), and

stirred for a further 0.5 h. The solvent was then evaporated *in vacuo*, the residue dissolved in ethanol and refluxed for 1 h. After completion of the reaction (monitored by t.l.c), the solvent was evaporated *in vacuo*, and the residue crystallised from a mixture of ethyl acetate and dichloromethane (2:1) to produce 6-bromo-2,3-bis(ethylthio)-quinoxaline-5,8-dione (215), m.p. 166-168° C; IR(KBr) ν_{max} 2960, 2840, 1700 (C=O), 1685 (C=O), 1605, 1560, 1480, 1300, 1265, 1130, 1040, 1010, 940, 800 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.08 (s, 1H, 6-H), 3.89 (q, 4H, 2- and 3-S$\underline{CH_2}CH_3$), 1.32 (t, 6H, 2- and 3- $SCH_2\underline{CH_3}$); MS, m/z(r.i.) 360(35, M^+ for ^{81}Br), 358, (38, M^+ for Br^{79}), 332(12, M^+-CO), 300(28, M^+-CO), 304(27, M^+-2CO), 302(37, M^+-2CO), 275(6, M^+-2CO and C_2H_5), 273(8, M^+-2CO and C_2H_5). (Found: C, 40.30; H, 3.11; N, 7.62; S, 17.87; Br, 28.67. $C_{12}H_{11}N_2O_2S_2Br$ requires C, 40.12; H, 3.09; N, 7.80; S, 17.82; Br, 28.46 %).

Reactions of Diazanaphthoquinones (49) with 2,3-Dimethyl-1,3-butadiene (216)

5,8-Dihydro-6,7-dimethyl-9,10-dihydroxy-1,4-diazaanthracene (217)

Quinoxaline-5,8-dione (49) (0.160 g, 1.0 mmol), and 2,3-dimethyl-1,3-butadiene (0.165 g, 1.1 mmol), in absolute ethanol (20 cm^3), were heated under reflux for 16 h. After cooling the mixture, the red solid was filtered off and recrystallised from ethanol to give 5,8-dihydro-6,7-dimethyl-9,10-dihydroxy-1,4-diazaanthracene (217) (0.241 g, 89 %), m.p. 248-249° C; IR(KBr) ν_{max} 3380 (OH), 2910, 2840, 1580, 1490, 1380, 1275, 1100, 1030, 925, 830 cm^{-1}; ^1H NMR (200 MHz, d_6-DMSO) δ 9.27 (s, 2H, 9- and 10-OH exchanged with D_2O), 8.71 (s, 2H, 2- and 3-H), 3.34 (s, 4H, 5- and 8-CH_2), 1.78 (s, 6H, 6- and 7-CH_3); MS, m/z(r.i.) 242(89, M^+), 240(13, M^+-2H), 238(5, M^+-4H), 227(100, M^+-CH_3), 212(15, M^+-2CH_3), 199(13), 180(12), 149(140, 117(15), 77(13). (Found: C, 69.21; H, 5.64; N, 11.55. $C_{14}H_{14}N_2O_2$ requires C, 69.41; H, 5.82; N, 11.56 %).

5,8-Dihydro-6,7-dimethyl-9,10-diacetoxy-1,4-diazaanthracene (218)

5,8-Dihydro-6,7-dimethyl-9,10-dihydroxy-1,4-diazaanthracene (217) (0.150 g, 0.6 mmol) was treated with acetic anhydride (5 cm^3) and pyridine (1 cm^3), warmed to 40-50° C for 3 h, and then poured into ice-water (30 cm^3). The solid was filtered off and crystallised from ethyl acetate as colourless 5,8-dihydro-6,7-dimethyl-9,10-acetoxy-1,4-diazaanthracene (218) 0.121 g, 60 %), m.p. 251-252° C; IR(KBr) ν_{max} 2910, 2820,

1755 (C=O), 1610, 1505, 1475, 1360, 1200, 1110, 1040, 860 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 8.69 (s, 2H, 2- and 3-H), 3.37 (s, 4H, 5- and 8-CH_2), 2.49 (s, 6H, 9- and 10-OOC$\underline{CH_3}$), 1.80 (s, 6H, 6- and 7-CH_3); ^{13}C NMR (200 MHz, $CDCl_3$) δ 169.0 (s, 9- and 10-O$\underline{C}OCH_3$), 144.4 (s, C-2 and C-3), 140.9 (s, C-9 and C-10), 135.0 (s, C-1a and C-4a), 130.3 (s, C-5a and C-8a), 121.9 (s, C-6 and C-7), 31.3 (t, C-5 and C-8), 20.6 (q, 9- and 10-OCO$\underline{C}H_3$), 18.6 (q, 6- and 7-$\underline{C}H_3$); MS, m/z(r.i.) 326(12, M^+), 284(11, M^+-CH_2=C=O), 242(100, M^+-2CH_2=C=O), 227(41), 212(13), 198(20), 149(24). (Found: C, 60.27; H, 5.55; N, 8.54. $C_{18}H_{18}N_2O_4$ requires C, 66.25; H, 5.56; N, 8.58 %).

5,8-Dihydro-6,7-dimethyl-1,4-diazaanthracene-9,10-dione (219)

A mixture 5,8-dihydro-6,7-dimethyl-9.10-dihydroxy-1,4-diazaanthracene (41) (0.150 g, 0.6 mmol), and silver(II)oxide (0.160 g) in 1,2-dimethoxyethane (20 cm^3), was stirred for 4h at room temperature in the dark. The solid was filtered off and washed repeatedly with hot chloroform. The filtrate and combined washings were evaporated *in vacuo,* and the residue crystallised from a mixture of ethanol and dichloromethane (8:1) to produce bright yellow needles of 5,8-dihydro-6,7-dimethyl-1,4-diazaanthracene-9,10-dione (219) (0.108 g, 73 %), m.p. 243-244° C; IR(KBr) ν_{max} 2920, 1680 (C=O), 1595, 1420, 1385, 1300, 1190, 960 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 9.00 (s, 2H, 2- and 3-H), 3.47(s, 4H, 5- and 8-CH_2), 1.79 (s, 6H, 6- and 7-CH_3); MS, m/z(r.i.) 240(16, M^+), 239(13, M^+-1H), 238(59, M^+-2H), 225(7,M^+-1CH_3), 223(9), 210(51, M^+-2CH_3), 182(12), 132(33), 104(18),77(30), 69(30). (Found: C, 69.87; H,4.91; N, 11.55. $C_{14}H_{12}N_2O_2$ requires C, 70.00; H, 5.00; N, 11.55 %).

6,7-Dimethyl-1,4-diazaanthracene-9,10-dione (220)

5,8-Dihydro-6,7-dimethyl-1,4-diazaanthracene (219) (0.050 g, 0.2 mmol) was dissolved in dichloromethane (20 cm^3), and air was passed through the refluxing solution for 4h. The solvent was evaporated, and the residue was crystallised from a mixture of ethanol and dichloromethane (4:1) to yield light brown 6,7-dimethyl-1,4-diazaanthracene-9,10-dione (220) (0.032 g, 66 %), m.p. 277-278° C; IR(KBr) ν_{max} 2905, 1685 (C=O), 1600, 1525, 1445, 1320, 1195, 1060, 960, 870 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 9.02 (s, 2H, 2- and 3-H), 8.13 (s, 2H, 5- and 8-H), 2.47 (s, 6H, 6- and 7-CH_3); MS, m/z(r.i.) 239(13), 238(100, M^+), 223(41, M^+-CH_3), 210(75, M^+-CO), 182(17, M^+-2CO), 149(5),

132(48), 77(24). (Found: C, 70.57; H, 4.18; N, 11.62. $C_{14}H_{10}N_2O_2$ requires C, 70.58; H, 4.23; N, 11.76 %).

Reaction of Diazanaphthoquinones (194)-(196) with 2,3-Dimethyl-1,3-butadiene (216)

General method: A mixture of the 2,3-disubstituted quinoxaline-5,8-dione (2 mmol) and 2,3-dimethyl-1,3-butadiene (2.2 mmol) in dichloromethane (30 cm^3), was stirred at room temperature for 5-8 h. A precipitate slowly separated out, and was filtered off. The solid was crystallised from a mixture of ethyl acetate and dichloromethane (1:4).

The following compounds were obtained by this method:-

3-Dimethoxy-6,7-dimethyl-5,8,8a,10a-tetrahydro-1,4-diazaanthracene-9,10-dione (222) (0.556 g, 92 %), m.p. 286-287° C; IR(KBr) ν_{max} 2920, 2860, 1695 (C=O), 1510, 1310, 1280, 1245, 1120, 1050, 960, 940, 810 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 4.21 (s, 6H, 2- and 3-OCH_3), 3.39 (t, 2H, 8a- and 10a-H), 2.37 (m, 4H, 5- and 8-CH_2), 1.63 (s, 6H, 6- and 7-CH_3); MS, m/z(r.i.) 303(18), 302(93, M^+), 287(100, M^+-1CH_3), 272(14, M^+-2CH_3), 257(13), 242(5), 228(13), 198(31), 181(9), 43(17). (Found: C, 63.79; H, 5.85; N, 9.07. $C_{16}H_{18}N_2O_4$ requires C, 63.57; H, 6.00; N, 9.27 %).

2,3-Diethoxy-6,7-dimethyl-5,8,8a,10a-tetrahydro-1,4-diazaanthracene-9,10-dione(223) (0.586 g, 89 %), m.p. 194-195° C; IR(KBr)ν_{max} 3000, 2920, 2840, 1705 (C=O), 1565, 1500, 1470, 1350, 1295, 1255, 1140, 1110, 1053, 910, 840 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 4.63 (q,4H, 2- and 3-O$\underline{CH_2}CH_3$) 3.32 (t, 2H, 8a- and 10a-H), 2.30 (m, 4H, 5- and 8-CH_2), 1.61 (s, 6H, 6- and 7-CH_3), 1.47 (t, 6H, 2- and 3-$OCH_2\underline{CH_3}$); ^{13}C NMR (200 MHz, $CDCl_3$) δ 195.6 (s, C-9 and C-10), 152.8 (s, C-2 and C-3), 138.2 (s, C-4a and C-9a), 123.9 (s, C-6 and C-7), 64.4 (t, 2- and 3-O$\underline{C}H_2CH_3$), 47.1 (d, J = 132 Hz, C-8a and C-10a), 30.7 (t, C-5 and C-8), 18.8 (q, 6- and 7-$\underline{C}H_3$), 14.1 (q, 2- and 3-$OCH_2\underline{C}H_3$); MS, m/z(r.i.) 331(19), 330(100, M^+), 315(29, M^+-CH_3), 305(25), 287(25, M^+-CH_3 and 1C_2H_4), 273(94, M^+-2C_2H_4), 255(55), 241(12), 227(20), 188(12), 167(32). (Found: C, 65.27; H, 6.64; N, 8.39. $C_{18}H_{22}N_2O_4$ requires C, 65.44; H, 6.71; N, 8.48 %).

2,3-Bis(ethylthio)-6,7-dimethyl-5,8,8a,10a-tetrahydro-1,4-diazaanthracene-9,10-dione (224) (0.622 g, 86 %), m.p. 159-160° C; IR(KBr) ν_{max} 2920, 2890, 1705 (C=O), 1485,

1320, 1225, 1195, 1130, 1090, 1020, 910, 830, 780 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 3.51-3.24 (m, 6H, 8a-H, 10a-H,2- and-3-S$\underline{CH_2}CH_3$), 2.31 (m, 4H, 5- and 8-CH_2), 1.63 (s, 6H, 6- and 7-CH_3), 1.48 (t, 6H, 2- and 3-$SCH_2\underline{CH_3}$); MS, m/z(r.i.) 364(13), 363(25), 362(100, M^+), 347(32, M^+-CH_3), 333(72, M^+-C_2H_5), 329(30), 300(21), 289(11), 198(13), 83(13), 57(20), 43(20), 32(17). (Found : C, 59.38; H, 5.88; N, 7.89; S, 17.42. $C_{18}H_{22}N_2O_2S_2$ requires C, 59.66; H, 6.07; N, 7.73; S, 17.67 %).

Enolisation of 2,3-disubstituted-6,7-dimethyl-5,8,8a,10a-tetrahydro-1,4-diazaanthracene-9,10-diones (222)-(224)

General method: A solution of the 2,3-disubstituted 6,7-dimethyl-5,8,8a,10a-tetrahydro-1,4-diazaanthracene-9,10- dione (222)-(224) (1.0 mmol) in 90 % aqueous hydrochloric acid (10 cm^3) was stirred for 3-4 h at 80-90° C. After the completion of the reaction (monitored by t.l.c), the reaction mixture was diluted with water (50 cm^3), the resulting solid was filtered off, washed thoroughly with water and crystallised from ethanol to yield the 2,3-disubstituted-5,8-dihydro-6,7-dimethyl-9,10-dihydroxy-1,4-diazaanthacenes (225)-(227).

The following compounds were obtained by this procedure:-

2,3-Dimethoxy-5,8-dihydro-6,7-dimethyl-9,10-dihydroxy-1,4-diazaanthracene (225) as yellow micro crystals (0.274g, 91 %), m.p. 254-255° C(decomp); IR(KBr) ν_{max} 3460 (OH), 2930, 2840 (H-Aliph) 1600, 1530, 1490, 1420, 1370, 1295, 1120, 980, 805 cm^{-1}; ^1H NMR (80 MHz, $CDCl_3$) δ 6.39 (s, 2H, 9- and 10-OH exchanged with D_2O), 4.12 (s, 6H, 2- and 3-OCH_3), 3.40 (s, 4H, 5- and 8-CH_2), 1.82 (s, 6H, 6-and 7-CH_3); MS, m/z(r.i.) 302(37, M^+), 287(46), 272(10), 198(19), 149(11), 579(30), 43(29). (Found: C, 62.61; H, 5.79; N, 9.02. $C_{16}H_{18}N_2O_4.1/2H_2O$ requires C, 62.64; H, 5.87; N, 9.13 %).

2,3-Diethoxy-5,8-dihydro-6,7-dimethyl-9,10-dihydroxy-1,4-diazaanthracene (226) as light green micro crystals, (0.293 g, 89 %), m.p. 193-195° C; IR(KBr) ν_{max} 3490(OH), 2940, 2835 (H-Aliph), 1620, 5140, 1585, 1370, 1290, 1110, 985, 810 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 6.87 (s, 2H, 9- and 10-OH exchanged with D_2O), 4.57 (q, 4H, 2- and 3-$\underline{CH_2}CH_3$), 3.38 (s, 4H, 5- and 8-CH_2), 1.82(s, 6H, 6- and 7-CH_3), 1.50 (t, 6H, 2- and 3-$CH_2\underline{CH_3}$); MS, m/z(r.i.) 331(20), 330(100, M^+), 315(40), 301(12), 273(77), 255(40), 241(18), 167(35). (Found: C, 64.74; H, 6.61; N, 8.35. $C_{18}H_{22}N_2O_4.1/4H_2O$

requires C, 64.57; H, 6.87; N, 8.37 %).

2,3-Bis(ethylthio)-5,8-dihydro-6,7-dimethyl-9,10-dihydroxy-1,4-diazaanthracene (227) as yellowish brown micro crystals,(0.336 g, 93 %), m.p. 147-148° C; IR(KBr) ν_{max} 3450 (OH), 2910, 2820 (H-Aliph), 1615, 1550, 1480, 1365, 1295, 1100, 980, 825 cm^{-1}; ^1H NMR (80 MHz, $CDCl_3$) δ 6.71(s, 2H, 9- and 10-OH exchanged with D_2O), 3.56 (s, 4H, 5- and 8-CH_2), 3.38 (q, 4H, 2- and 3-S$\underline{CH_2}CH_3$), 1.79 (s, 6H, 6- and 7-CH_3), 1.46 (t, 6H, 2- and 3-$SCH_2\underline{CH_3}$); MS, m/z(r.i.) 363(10), 362(100, M^+), 347(35), 333(9), 305(16), 277(81), 259(32), 245(21), 167(19), 43(31). (Found: C, 59.49; H, 5.82; N, 7.60. $C_{18}H_{22}N_2O_2S_2$ requires C, 59.64; H, 6.12; N, 7.73 %).

2,3-Dimethoxy-5,8-dihydro-6,7-dimethyl-9,10-diacetoxy-1,4-diazaanthracene (228):

2,3-Dimethoxy-5,8-dihydro-6,7-dimethyl-9,10-dihydroxy-1,4-diazaanthracene (225) (0.1 g, 0.33 mmol) was dissolved in acetic anhydride (5 cm^3) followed by the addition of 3 drops of pyridine. The reaction mixture was stirred for 3h at 40-50° C and then poured into ice-water (30 cm^3). The resulting solid was filtered off, washed with water, and crystallised from ethyl acetate as light yellow needles of 2,3-dimethoxy-5,8-dihydro-6,7-dimethyl-9,10-diacetoxy-1,4-diazaanthracene (228) (0.088 g, 69 %), m.p. 238-239° C; IR(KBr) ν_{max} 2920, 2840, 1685 (C=O), 1600, 1540, 1430, 1320, 1255, 1120, 1040, 940, 810 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 4.05 (s, 6H, 2- and 3-OCH_3), 3.29 (s, 4H, 5- and 8-CH_2), 2.43 (s, 6H, 9- and 10-$OOCCH_3$), 1.78 (s, 6H, 6- and 7-CH_3); MS, m/z(r.i.) 386(13, M^+), 371(8), 329(11), 302(100, M^+-$2CH_2$=C=O), 300(18), 287(83), 285(32), 271(12), 249(15), 220(24), 207(13), 198(9), 170(19). (Found: C, 60.47; H, 5.38; N, 6.99. $C_{20}H_{22}N_2O_6.1/2H_2O$ requires C, 60.75; H, 5.56; N, 7.08 %).

2,3-Dimethoxy-5,8-dihydro-6,7-dimethyl-1,4-diazaanthracene-9,10-dione (230)

Compound (225) (0.302 g, 1.0 mmol) in 1,2-dimethoxyethane (10 cm^3) was stirred with silver(I) oxide (0.350 g) at room temperature in the dark, for 5h. The reaction product was filtered off, the residue was washed with hot chloroform and the solvent was evaporated. The resulting solid was crystallised from a mixture of ethanol and dichloromethane (9:1) to afford red 2,3-dimethoxy-5,8-dihydro-6,7-dimethyl-1,4-diazaanthracene-9,10-dione (230) (0.117 g, 39 %), m.p. 157-158° C; IR(KBr) ν_{max} 2930,

2840, 1680 (C=O), 1565, 1530, 1410, 1330, 1226, 1110, 930, 860 cm^{-1}; ^1H NMR (80 MHz, $CDCl_3$) δ 4.20 (s, 6H, 2- and 3-OCH_3), 3.15 (s, 4H, 5- and 8-CH_2), 1.76 (s, 6H, 6- and 7-CH_3); MS, m/z(r.i.) 301(6), 300(11; M^+), 285(39, M^+-CH_3), 270(5, M^+-$2CH_3$), 257(10), 218(11), 198(13). (Found: C, 63.89; H, 5.29; N, 9.21. calculated for $C_{16}H_{16}N_2O_4$ C, 64.00; H, 5.33; N, 9.33 %).

Reactions of Diazanaphthoquinones (193)-(196) and (204) with N,N-Dimethyl-1-azabutadiene (95)

N,N-Dimethyl-1-azabutadiene (methacrolein hydrazine)[124] (95): N,N-Dimethyl hydrazine (5.0 g) was dissolved in ice-cold water (25 cm^3). Methacrolein (6.0 g) was added dropwise wise to this solution during 25 min, with stirring, and then treated with solid potassium hydroxide (10 g). The upper organic layer was separated and was distilled to yield N,N-dimethyl-1-azabutadiene (6.6 g, 69 %) b.p. 56-60°C/29 mm Hg (lit.,[124] b.p. 56°C/29 mm Hg).

General Method: A mixture of a 2,3-disubstituted quinoxaline-5,8-dione (1.0 mmol) and N,N-dimethyl-1-azabutadiene[124] (2.0 mmol) in anhydrous benzene (20 cm^3) was stirred at room temperature for 4-5 h. A coloured precipitate slowly separated out, and then the benzene was evaporated under reduced pressure. The residue was dissolved in 95 % ethanol (20 cm^3) and heated on a steam-bath for 2-3 h. After evaporation of the solvent, the residue was recrystallised from ethanol to yield the 2,3-disubstituted triazaanthraquinones.

The following compounds were obtained by this procedure:-

2,3-Diphenyl-7-methyl-1,4,5-triazaanthracene-9,10-dione (231) as yellow crystals (0.229 g, 61 %), m.p. 294-295° C; IR(KBr) ν_{max} 3090, 3015 (H-Aryl), 2925, 1700 (C=O), 1680 (C=O), 1600, 1520, 1450, 1320, 1240, 1095, 920, 780 cm^{-1}; ^1H NMR (80 MHz, $CDCl_3$) δ 8.95 (d, 1H, J = 1.7 Hz, 8-H), 8.46 (d, 1H, J = 2.5 Hz, 6-H), 7.61 (m, 4H, 2- and 3-Ph-H), 7.34 (m, 2- and 3-Ph-H), 2.60 (s, 3H, 7-CH_3); MS, m/z(r.i.) 378(33), 377(100, M^+), 218(25), 203(13), 175(34), 149(16), 77(21). (Found: C, 76.28; H, 4.02; N, 10.98. $C_{24}H_{15}N_3O_2$ requires C, 76.39; H, 3.97; N, 11.14 %).

2,3- Dimethoxy-7-methyl-1,4,5-triazaanthracene-9,10-dione (232) as brown needles, (0.259 g, 91 %) m.p. 216-217° C IR(KBr) ν_{max} 2940, 2830, 1695 (C=O), 1680 (C=O), 1600, 1560, 1495, 1310, 1250, 1050, 985, 800 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 8.93

(d,1H, J = 2.9 Hz, 8-H), 8.40 (d, 1H, J = 2.4 Hz, 6-H), 4.31 (s, 3H, 3-OCH_3), 4.29 (s, 3H, 2-OCH_3), 2.57 (s, 3H, 7-CH_3); MS, m/z(r.i.) 286(23), 285(100, M^+), 284(20), 270(5), 263(60), 256(27), 249(29), 248(76), 240(36). (Found: C, 58.75; H, 3.83; N, 14.55. $C_{14}H_{11}N_3O_4$ requires C, 58.95; H, 3.89; N, 14.73 %).

2,3-Diethoxy-7-methyl-1,4,5-triazaanthracene-9,10-dione (233) as light yellow crystals, (0.275 g, 88 %), m.p. 206-207° C; IR(KBr) ν_{max} 2930, 1700 (C=O), 1685 (C=O), 1600, 1560, 1470, 1405, 1310, 1255, 1105, 1025, 910, 895 cm^{-1}; ^1H NMR (80 MHz, $CDCl_3$) δ 8.84 (d, 1H, J = 2.1 Hz, 8-H), 8.32 (d, 1H, J = 2.8 Hz, 6-H), 4.74 (q, 2H, 3-O$\underline{CH_2}CH_3$), 4.72 (q, 2H, 2-O$\underline{CH_2}CH_3$), 2.54 (s, 3H, 7-CH_3), 1.52 (t, 6H, 2- and 3-$OCH_2\underline{CH_3}$); MS, m/z(r.i.) 313(33; M^+), 298(9, M^+-1CH_3), 285(58), 270(11), 257(71), 229(72), 201(28) 173(22), 118(64). (Found: C, 61.23; H, 4.78; N, 13.41. $C_{16}H_{15}N_3O_4$ requires C, 61.34; H, 4.83; N, 13.41 %).

2,3-bis(ethylthio)-7-methyl-1,4,5-triazaanthracene-9,10-dione (234) as green needles, (0.32 g, 93 %) m.p. 227-228° C; IR(KBr) ν_{max} 2935, 2840, 1700 (C=O), 1680 (C=O), 1600, 1520, 1490, 1345, 1250, 1165, 1010, 930, 810, 750 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 8.94 (d, 1H, J = 2.5 Hz, 8-H), 8.39 (d, 1H, J = 2.5 Hz, 6-H), 3.49 (q, 4H, 2- and 3-O$\underline{CH_2}CH_3$), 2.58 (s, 3H, 7-CH_3), 1.49 (t, 4H, 2- and 3-$OCH_2\underline{CH_3}$); MS, m/z(r.i.) 347(21), 345(8, M^+), 320(6), 316(100), 288(31), 258(10), 173(20). (Found: C, 55.35; H, 4.31; N, 12.07; S, 18.32. $C_{16}H_{15}N_3O_2S_2$ requires C, 55.63; H, 4.38; N, 12.16; S, 18.56 %).

7-Methyl-2,3,5-triazaanthracene-9,10-dione (235) was obtained, using same procedure as described above, by treating phthalazine-5,8-dione (204) with N,N-dimethyl-1-azabutadiene, as long brown needles (0.207 g, 92 %), m.p. 214-215° C; IR(KBr) ν_{max} 2930, 1700 (C=O), 1600, 1450, 1325, 1280, 1035, 955, 735 cm^{-1}; ^1H NMR (80 MHz, $CDCl_3$) δ 10.00 (d, 1H, J = 1.0 Hz, 4-H), 9.93 (d, 1H, J = 1.0 MHz, 4-H), 8.98 (d, 1H, J = 2.4 Hz, 8-H), 8.38 (d, 1H, J = 2.3 Hz, 6-H), 2.62 (s, 3H, 7-CH_3); MS, m/z(r.i.) 225(10, M^+), 165(15), 149(68), 125(10), 97(30), 71(72). (Found: C, 63.89; H, 2.95; N, 18.56. $C_{12}H_7N_3O_2$ requires C, 64.00; H, 3.13; N, 18.66 %).

Reaction of Diazanaphthoquinones (194)-(196) with *trans*-1-Methoxy-3-trimethylsilyloxy-1,3-butadiene (108)

trans-1-methoxy-3-trimethylsilyloxy-1,3-butadiene (108)

A mixture of anhydrous powdered zinc chloride (0.1 g) in dry triethylamine (5.75 g, 50 mmol) was stirred for 1h at room temperature, under nitrogen, until the salt was suspended in the amine, then a solution of trans-1-methoxy-3-trimethylsilyloxy-1,3-butadiene (2.5 g, 25 mmol) in anhydrous benzene (20 cm^3) was added to this suspension, followed by the addition of trimethylchlorosilane (5.4 g, 50 mmol). An exothermic reaction was noted and, after 30 min, the temperature was raised to 40° C, and stirring was continued overnight. After cooling, the reaction mixture, it was diluted with anhydrous ether (200 cm^3), and the solid filtered off. The filtrate and combined washings were concentrated in vacuo to give a brown oil which was distilled to obtain *trans*-1-methoxy-3-trimethylsilyloxy-1,3-butadiene (108) (0.85 g, 21 %), b.p. 53-56°C/5 mm of Hg (lit.,[83] b.p. 54-55°C/5 mm of Hg).

General Method: 2,3-Disubstituted-quinoxaline-5,8-dione (0.5 mmol) and *trans*-1-methoxy-3-trimethylsilyloxy-1,3-butadiene (1.0 mmol) were added to chloroform (25 cm^3) and stirred at room temperature for 5-6 h under nitrogen. The solid was filtered off, washed with chloroform and recrystallised from ethanol, to obtain 2,3-disubstituted-6-hydroxy-1,4-diazaanthracene-9,10-diones (239)-(241).

The following compounds were obtained by this procedure:-

2,3-Dimethoxy-6-hydroxy-1,4-diazaanthracene-9,10-dione (239) as orange needles (0.070 g, 49 %), m.p. 287-289° C; IR(KBr) ν_{max} 3230 (OH), 2920, 1685 (C=O), 1665 (C=O), 1606, 1570, 1500, 1460, 1415, 1320, 1265, 1090, 980 cm^{-1}; ^1H NMR (200 MHz, d_6-DMSO) δ 8.02 (d, 1H, *J* = 8.8 Hz, 8-H), 7.45 (d, 1H, *J* = 2.9 Hz, 5-H), 7.20 (dd, 1H, *J* = 8.3,2.4 Hz, 7-H), 4.11 (s, 3H, 2-OCH_3), 4.10 (s, 3H, 3-OCH_3); MS, m/z(r.i.) 288(3), 287(19), 286(100, M^+), 271(8, M^+-CH_3), 257(25, M^+-$2CH_3$), 239(19), 207(12), 192(14). (Found: C, 57.15; H, 3.40; N, 9.42. $C_{14}H_{10}N_2O_5.1/2H_2O$ requires C, 56.95; H, 3.38; N, 9.49 %).

2,3-Diethoxy-6-hydroxy-1,4-diazaanthracene-9,10-dione (240) as yellow needles (0.068 g, 43 %), m.p. 285-286° C; IR(KBr) ν_{max} 3250 (OH), 2925, 1690 (C=O), 1660

(C=O), 1600, 1565, 1500, 1470, 1320, 1260, 1020, 900, 810 cm^{-1}; ^1H NMR (200 MHz, d_6-DMSO) δ 8.02 (d, 1H, *J* = 8.3 Hz, 8-H), 7.45 (d, 1H, *J* = 2.4 Hz, 5-H), 7.20 (dd,1H, *J* = 8.3,2.4 Hz, 7-H), 4.58 (q, 2H, 2-O$\underline{CH_2}CH_3$), 4.57 (q, 2H, 3-O$\underline{CH_2}CH_3$), 1.42 (t, 6H, 2- and 3-OCH$_2\underline{CH_3}$); MS, m/z(r.i.) 315(15), 314(72, M^+), 299(41, M^+-CH_3), 286(100, M^+-C_2H_4), 258(93, M^+-$2C_2H_4$), 243(34), 230(68), 214(23), 186(14), 174(12), 149(5), 57(21), 45(10), 44(11), 43(20). (Found: C, 60.51; H, 4.55; N, 8.57. $C_{16}H_{14}N_2O_5.1/4H_2O$ requires C, 60.28; H, 4.39; N, 8.79 %).

2,3-Bis(ethylthio)-6-hydroxy-1,4-diazaanthracene-9,10-dione (241) as yellow needles (0.088 g, 51 %), m.p. 303-304° C; IR(KBr) ν_{max} 3195 (OH), 2940, 2870, 1685 (C=O), 1655 (C=O), 1600, 1570, 1520, 1485, 1350, 1270, 1160, 1120, 1020, 925,850, 725 cm^{-1}; ^1H NMR (200 MHz, d_6-DMSO) δ 8.06 (d, 1H, *J* = 8.8 Hz, 8-H), 7.48 (d, 1H, *J* = 2.9 Hz, 5-H), 7.23 (dd, 1H, *J* = 8.3,2.4 Hz, 7-H), 3.38 (q, 2H, 2-OCH$_2$CH$_3$), 3.37 (q, 2H, 3-O$\underline{CH_2}CH_3$), 1.40 (t, 6H, 2- and 3-OCH$_2\underline{CH_3}$); MS, m/z(r.i.) 346(9, M^+), 317(100, M^+-C_2H_5), 289(12; M^+-$2C_2H_4$), 284(47), 130(14), 121(15), 44(32), 43(16). (Found: C, 55.10; H, 3.98; N, 7.83; S, 17.84. $C_{16}H_{14}N_2O_3S_3.1/4H_2O$ requires C, 54.77; H, 3.99; N, 7.98; S, 18.25 %).

2,3-Diethoxy-6-acetoxy-1,4-diazaanthracene-9,10-dione (242)

2,3-Diethoxy-6-hydroxy-1,4-diazaanthracene-9,10-dione (240) (0.118 g, 0.37 mmol) was dissolved in acetic anhydride (5.0 cm^3), followed by the addition of 3 drops of pyridine. The reaction mixture was stirred for 2h at 40-50° C, and then poured into ice-water (30 cm^3). The resulting solid was filtered off, washed with water, and crystallised from ethanol to yield 2,3-diethoxy-6-acetoxy-1,4-diazaanthracene-9,10-dione (242) as light brown micro crystals (0.084 g, 71 %), m.p. 193-194° C; IR(KBr) ν_{max} 2920, 2845, 1765 (C=O, ester), 1690 (C=O), 1650 (C=O), 1605, 1565, 1500, 1465, 1310, 1260, 1110, 925, 830, 800 cm^{-1}; ^1H NMR (80 MHz, d_6-DMSO) δ 8.01 (d, 1H, *J* = 8.0 Hz, 8-H), 7.45 (d, 1H, *J* = 2.3 Hz, 5-H), 7.20 (dd, 1H, *J* = 8.4,2.4 Hz, 7-H), 4.58 (q, 4H, 2- and 3-O$\underline{CH_2}CH_3$), 2.41 (s, 3H, 6-OOCCH$_3$), 1.42 (t, 6H, 2- and 3-OCH$_3$); MS, m/z(r.i.) 356(11, M^+), 314(68, M^+-CH_2=C=O), 286(76, M^+-CH_2=C=O and C_2H_4), 258(71, M^+-CH_2=C=O and $2C_2H_4$), 242(14), 230(27). (Found: C, 60.39; H, 4.19; N, 7.71. $C_{18}H_{16}N_2O_6$ requires C, 60.67; H, 4.49; N, 7.86 %).

Reaction of Diazaanaphthoquinones (193), (196) and (204) 1-Acetoxy-1,3-butadiene (243).

General Method: A mixture of diazanaphthoquinone (0.3 mmol), 1-acetoxy-1,3-butadiene (0.32 mmol) and anhydrous benzene (20 cm^3) was refluxed for 2 h. After evaporation of the solvent *in vacuo*, the residue was dissolved in ethanol and refluxed for 2-4 h. On the completion of the reaction (monitored by t.l.c), the solvent was evaporated *in vacuo* and the residue was crystallised from ethanol.

The following compounds were obtained by this procedure:-

2,3-Diphenyl-1,4-diazaanthracene-9,10-dione (244), (0.056 g, 52 %), m.p. 228-229° C; IR(KBr) ν_{max} 3080, 3010 (H-Aryl), 2935, 1700 (C=O), 1600, 1530, 1450, 1345, 1240, 1140, 1080, 940, 760 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 8.54 (dd, 2H, *J* = 5.9, 3.4 Hz, 5- and 8-H), 7.90 (dd, 2H, *J* = 5.9, 3.4 Hz, 6- and 7-H), 7.69-7.61 (m, 4H, *o*-ph-H), 7.46-7.31 (m, 6H, *m*- and *p*-Ph-H); MS, m/z(r.i.) 363(11), 362(100, M^+), 334(42), 285(21), 257(15), 229(13), 196(15), 149(9). (Found: C, 77.79; H, 3.92; N, 7.43. $C_{24}H_{14}N_2O_2.1/2H_2O$ requires C, 77.62; H, 4.04; N, 7.54 %).

2,3-Bis(ethylthio)-1,4-diazaanthracene-9,10-dione (245), (0.048 g, 49 %), m.p. 189-190° C; IR(KBr) ν_{max} 2940, 2890, 1695 (C=O), 1600, 1495, 1465, 1350, 1270, 1240, 1170, 1015, 975, 800, 725 cm_{-1}; ^1H NMR (80 MHz, $CDCl_3$) δ 8.27 (dd, 2H, *J* = 5.9, 3.8 Hz, 5- and 8-H), 7.77 (dd, 2H, *J* = 5.9, 3.2 Hz, 6- and 7-H), 3.47 (q, 4H, 2- and 3-$O\underline{CH_2}CH_3$), 1.48 (t, 6H, 2- and 3-$OCH_2\underline{CH_3}$); MS, m/z(r.i.) 330 (8, M^+), 301(100, M^+-C_2H_5), 268 (52), 186 (13), 114 (20). (Found: C, 56.47; H, 4.26; N, 8.24; S, 18.52. $C_{16}H_{14}N_2O_2S_2.1/2H_2O$ requires C, 56.63; H, 4.42; N, 8.25; S, 18.87 %).

2,3-Diazaanthracene-9,10-dione (246)

A mixture of phthalazine-5,8-dione (204) (0.08 g, 0.5 mmol), 1-acetoxy-1,3-butadiene (0.1 g) and benzene (25 cm^3), was allowed to stand for 12h at room temperature, and then the solvent evaporated *in vacuo*. The residue was recrystallised from a mixture of ethyl acetate and petroleum spirit (b.p.40-60° C) (3:2) to give light brown 2,3-diazaanthracene-9,10-dione (52) (0.019 g, 18 %), m.p. 231-232°C; IR(KBr) ν_{max} 2910, 1735 (C=O), 1450, 1320, 1235, 1180, 1095, 1020, 930 cm^{-1}; ^1H NMR (200 MHz, d_6 DMSO) δ 9.86 (s, 2H, 1- and 4-H), 8.23 (dd, 2H, *J* = 6.1, 3.7 Hz 5- and 8-

H), 8.01 (dd, 2H, J = 5.5, 3.7 Hz, 6- and 7-H); MS, m/z(r.i.) 212 (4), 211 (14), 210 (100; M^+), 183 (6, M^+-HCN), 155 (15, M-HCN and CO), 149 (31), 130 (28), 127 (48), 98 (41). (Found: C, 68.55; H, 2.79; N; 13.19. $C_{12}H_6N_2O_2$ requires C, 68.57; H, 2.85; N, 13.33 %).

CHAPTER 2

STUDIES OF SOME NOVEL ION-RESPONSIVE FLUORESCENT DERIVATIVES OF QUINOXALINE

INTRODUCTION

4 LUMINESCENCE

Luminescence is one of the oldest and most established phenomena used in chemical analysis where emission of light is involved.[129] Brewster noted the red emission from chlorophyll in 1833, and later Stokes described the mechanism of the absorption processes[130] in 1852. Stokes also introduced the term "fluoresence" after the mineral fluorspar (Latin fluo = to flow + spar = a rock) which exhibits a bluish white fluorescence.

4.1 Types of Luminescence

The various types of luminescence can be classified according to the means by which energy is supplied to excite the luminescent molecule.[131] Chemiluminescence is produced by energy from chemical reactions , bioluminescence is due to energy released by living organisms, triboluminescence (greek tribo = to rub) is produced by the release of energy when certain crystals such as sugar are broken, i.e., by physical or chemical processes, cathode-luminescence is produced from exposure to cathode rays, and thermoluminescence occurs at temperature corresponding to red heat. Photoluminescence is caused by the excitation of molecules by absorption of photons of electromagnetic radiation. There are two forms of photoluminescence, i.e. phosphorescence and fluorescence. If the release of electromagnetic energy is by the movement of an electron from the excited triplet state to the ground state, the process is called phosphorescence, whereas fluorescence is due to the release of energy when an electron moves from an excited state to the ground state.

4.2 FLUORESCENCE

The process by which fluorescence is produced can be divided[132] into:

(1) absorption of light and

(2) emission of light

4.2.1 Absorption of light

Molecules have two kinds of molecular orbitals: (i) bonding molecular orbital,

which are orbitals of lower energy than atomic orbitals, e.g. sigma (σ) or pi (π) orbitals, and (ii) antibonding molecular orbital, which are orbitals of higher energy than atomic orbitals, e.g. σ^* or π^* orbitals (Fig 2). The non-bonding electrons associated with O, N and S atoms for instance occupy n orbitals, whose energy is much higher than the corresponding σ- and π-orbitals.[133] The absorption of a photon of suitable energy by a molecule may result in the promotion of an electron to an n-π^*, π-π^* state etc, in the order of increasing energy shown in Fig 2.

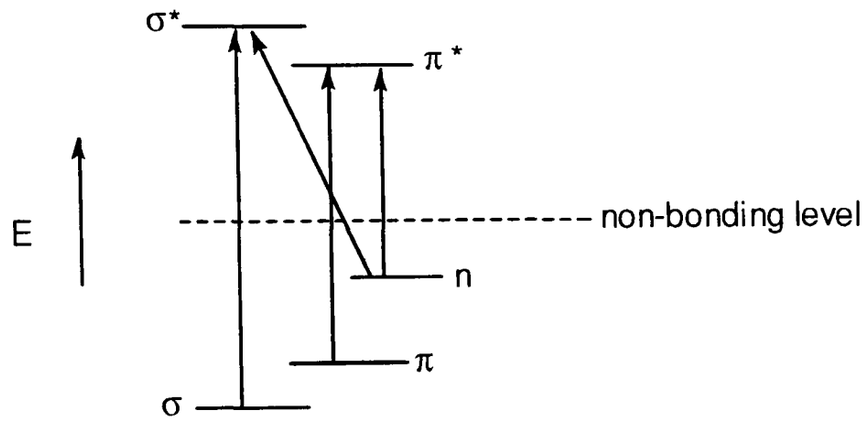


Fig. 2 n-π^* Electronic excitation of formaldehyde

When a molecule absorbs radiation, its energy increases by an amount equal to the energy of the photon[134] as expressed in eq (1)

$$E = h\nu = hc/\lambda \qquad \ldots\ldots (1)$$

Where h is the Plank's constant, ν and λ are the frequency and the wavelength of the radiation, respectively, and c is the velocity of the light. The light absorbance characteristic of any molecule, in solution, can be determined by using the Beer-Lambert law. This law states that absorption by the solution will be proportion to its molecular concentration, provided the solvent itself does not have any absorption in that region of the spectrum.[135] This law is expressed as

Absorption or extinction or optical density = $\log_{10} I_o/I = \varepsilon cl$

Where I_o = Intensity of incident light

I = Intensity of transmitted light

ε = Absorption coefficient

c = Molar concentration of the solute

l = Path length of the light in the solution

If 'c' is expressed in gram moles per litre and 'l' in cm, then the absorption coefficient becomes a molar extinction coefficient. The absorption intensity is usually expressed in terms of ε and the majority of the applications in spectrophotometry are based on the above-mentioned equation.

After the absorption of energy, the molecule relaxes to the lowest vibrational level of the first excited state by radiationless routes. These are called internal conversion or vibrational relaxation. The molecules remain in the excited state for 10^{-8} - 10^{-7} sec.[131,136]

4.2.1.1 Physical Properties of the Excited Molecules

The reactivity of excited molecules often differs considerably from that of the molecules in the ground state.

In the excited state many bonds are longer than in the ground state, e.g. the C-C bond lengths of ethylene and benzene in their ground states are 0.134 and 0.140 nm, respectively, but in their excited state they are 0.169 and 0.144 nm, respectively. This effect is greatest in molecules which have electron donor and acceptor substituents suitably sited in the same molecule.[137] The increase in bond length is accompanied by a decrease in bond energy; most bonds are weaker in the excited states. The higher the energy of the excited state the weaker the bonds and the greater is the polarisability or electrical deformability of the molecule.[137] In general, the charge distribution is quite different in the excited states from the ground states and this is reflected in the dipole moments.[138] For example, the charge distributions of *p*-aminobenzaldehyde in three of its electronic states;[139] i.e. ground state, n-π* state and π-π* or charge-transfer (CT) state are shown in Fig 3.

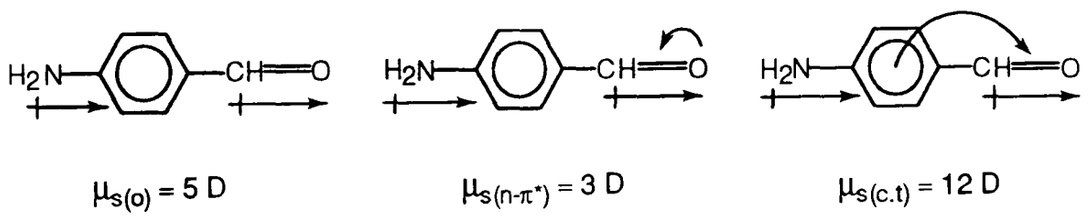


Fig. 3 Dipole moment of 4-aminobenzaldehyde in various electronic states.

Kottis *et al.*[138] investigated the compound, 7-amino-3-methyl-1,4-benzoxazin-2-one (247), which contains an electron donor (amino group) and electron acceptor group (carbonyl group or nitrogen atom of the benzoxazinone), and showed a large intramolecular charge separation between the donor and the acceptor in the excited state (Fig 4).

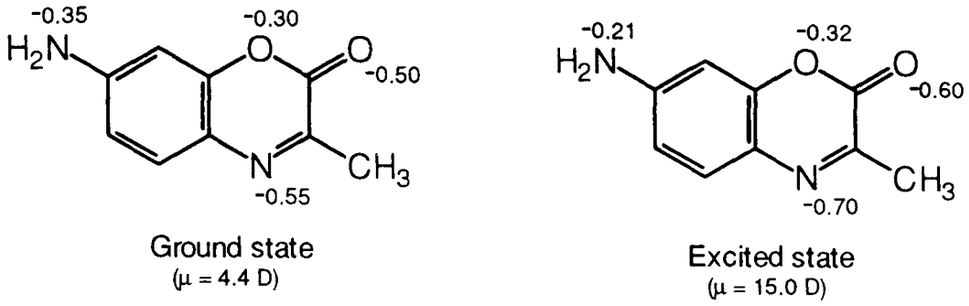
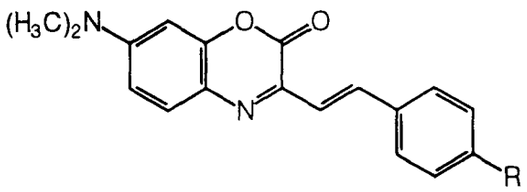


Fig. 4 Electronic charge calculations of aminobenzoxazinone (247) in the ground and electronic states.

More recently, Valeur *et al.*[140] investigated the aminobenzoxazinone (248) derivatives which exhibit very different properties according to the nature of R , but the common feature is the presence of electron donor (amino group) and electron acceptor (carbonyl group and heterocyclic nitrogen atom of the oxazinone) moieties which leads to an intramolecular charge transfer upon excitation that results in a large increase of the dipole moment (Fig 5).



R = -$N(CH_3)_2$	$\mu_{(g)}$ = 1.1 D	$\mu_{(ex)}$ = 2.4 D
R = -CHO	$\mu_{(g)}$ = 8.7 D	$\mu_{(ex)}$ = 20.5 D

Fig. 5 Dipole moment of styrylaminobenzoxazinone (248) in the ground and excited states.

4.2.2 Emission of Light

An excited molecule loses its energy mainly by two types of processes

(1) radiative processes, and

(2) non-radiative processes

4.2.2.1 Radiative Processes

According to Jablonski[141] and Kasha,[142] most absorbing molecules have two excited electronic states S1 (Singlet state containing paired electrons) and T1 (Triplet state having unpaired electrons) (Fig 6). When this excited molecule reverts back to its

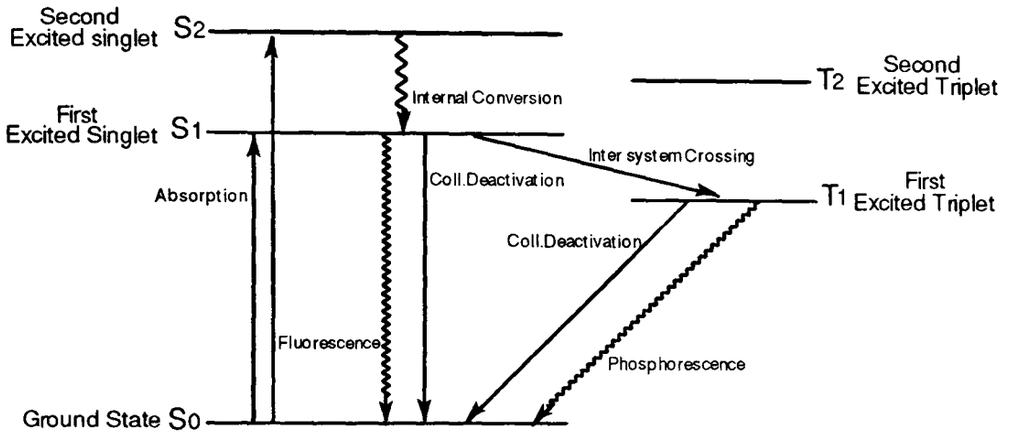


Fig. 6 A simple Jablonski diagram showing some of the radiative and non-radiative processes.

ground state, an emission of radiation takes place. This emission process is known as luminescence and it may consists of either a direct transition of the electrons from the first excited state S1 to the ground state S0 in a very short time (of the order of 10^{-9} sec), or the transmission of the electron from level S1 to an intermediate lower energy triplet state T1, before light is emitted in the transition T1 to S0 in a longer time (10^{-3} sec). The former process is known as fluorescence, and the latter, phosphorescence. According to Stokes' law,[131] the emitted light or fluorescent light always has greater wavelength than the exciting light. This difference in absorbed and emitted wavelength is caused by relaxation of the excited molecule by internal conversion, i.e. a loss of energy not available for emission.

4.2.2.1.1 Types of Fluorescence

The fluorescence normally observed in solution is called Stokes fluorescence.[131] If thermal energy is added to an excited state, emission may occur at shorter wavelength than the excitation wavelength. This is anti-Stokes fluorescence,[131] which is often observed in dilute gases at higher temperatures. Resonance fluorescence[131] is the reemission of photons possessing the same energy as the absorbed photons. It is the basis of atomic fluorescence used for the assay of many elements but is never observed in solution because of solvent interactions.

Certain chemical systems show a long-lived emission, known as delayed fluorescence, which corresponds spectrally with the normal fluorescence spectrum of a molecule.[143] This can occur in two separate ways, either by thermal depopulation of T_1 to S_1 states, or by triplet annihilation. The former process is known as E-type delayed fluorescence which was first observed in eosin. The latter is P-type delayed fluorescence, and is observed mainly in dye molecules having extended conjugation. It does not normally occur in monocyclic aromatic molecules because the singlet-triplet energy gap is relatively large. P-Type delayed fluorescence is observed for many hydrocarbons in fluid solution, concentrated rigid solution, and in the crystal phase.[143]

4.2.2.1.2 Quantum Yield of Fluorescence

The quantum yield or quantum efficiency of any fluorescent molecule can be defined as the total energy emitted per quantum of energy absorbed,[144] i.e.

$$\text{Quantum Yield } (\Phi) = \frac{\text{number of quanta emitted}}{\text{number of quanta absorbed}}$$

The higher the value of Φ up to a maximum of 1, the greater the fluorescence efficiency of the compound. Fluorescence spectrometers are used for the measurement of Φ. Quantum yields have also been measured by photoacoustic spectroscopy[145] and by calorimetric measurements.[146]

The quantum yield of an unknown compound can be determined by measuring the fluorescence of a dilute solution of the compound, and of a standard such as quinine sulphate, whose quantum yield is known [Φ =0.59 in 0.1 M $HClO_4$].[147] Other standard

compounds such as 9,10-diphenylanthracene,[146] Rhodamine B and fluorescein,[148] can also be used.

The relative quantum efficiency can be calculated by using the following relationship.[149]

$$\Phi 2 = \Phi 1 \times \frac{F2}{F1} \times \frac{A1}{A2}$$

$\Phi 1$ = Quantum yield of the standard
$\Phi 2$ = Quantum yield of the sample
F1 = Area under emission curve for standard
F2 = Area under emission curve for sample
A1 = Absorbance of the standard
A2 = Absorbance of the sample

Quantum yields were measured by Weber and Teale[148] by using glycogen solutions as standard, and a comparison was then made with the fluorescence from a solution with the same absorbance or the excitation light.[148] Two different instruments, a UV-absorption spectrometer, and a fluorescence spectrometer, are normally used for the measurements of absorbance and fluorescence spectra, respectively. An attempt was made by Shore and Pardee[150] to eliminate the errors associated with the two types of spectrometer in the determination of quantum yield. They reported a method using a Beckman spectrophotometer to measure both the absorption and fluorescence spectrum. Moreover, William and Winfield[151] measured quantum yields by using a computer controlled luminescence spectrometer and, after a little modification, used the same instrument for the measurements of absorbance and fluorescence.

4.2.2.2 Non-Radiative Processes

Radiationless processes occur between isoenergetic vibrational levels of different electronic states. A radiationless transition taking place between the excited state of one molecule and the ground state of another molecule, gives rise to a photochemical transformation.[134] If the electronic state participating in the radiationless transition are different states of the molecule, then the transition is a photophysical process,[152] e.g. internal conversion or intersystem crossing. Internal conversion is a radiationless

transition between isoenergetic states of the same multiplicity, e.g. S_2 to S_1 or T_2 to T_1. Intersystem crossing is a radiationless process between states of different multiplicity, e.g., S_1 to T_1 or T_1 to S_1. The intersystem crossing S_1 to T_1 is competitive with fluorescence and reduces the fluorescence quantum yield.

4.2.3 CHARACTERISTICS OF A FLUORESCENT COMPOUND

A fluorescence process tends to be favoured if a compound has the following characteristics.[153,154]

1- A longest wavelength absorption in the UV or visible region of the spectrum, because absorption of higher energy (shorter wavelength radiation) may result in predissociation.

2- The excited singlet state should be relatively stable to a deactivation process; it should have a half life of about 10^{-8} sec.

3- The excited singlet S_1 and triplet T_1 should be well separated in energy to avoid intersystem crossing.

4- The molecule should not contain any structural feature or functional group which enhances the rate of radiationless transfer, e.g. paramagnetic species or the presence of an atom of high atomic number which enhances the rate of intersystem crossing.

4.2.4 ENVIRONMENTAL EFFECTS ON FLUORESCENCE

4.2.4.1 Effect of Solvent

The presence of a solvent produces alteration in both the absorption and emission wavelength. If the solvent change produces a shift in the emission wavelength only, then the occurrence of interaction between solvent and solute in the excited state is indicated,[155] as seen in the case of indole.[156]

Generally, heterocyclic compounds tend to be more fluorescent in polar solvents, while some are only fluorescent in acid. Under both these conditions the lone pair of electrons is used in hydrogen bonding and the longest absorption wavelength becomes π-π^* instead of n-π^*.[157] Thus acridine is virtually non-fluorescent in hexane or benzene, but moderately so in water or moist alcohol. The fluorescence of acridine in hexane can

be greatly intensified if trichloroacetic acid is added.[158]

4.2.4.2 Effect of Temperature

Large variations in temperature cause pronounced changes in the absorption and emission spectra. A low temperature results in greater resolution and fine structure, while broadening of lines and consequent loss of fine structure occurs at high temperature. Fluorescence intensity tends to decrease with increasing temperature because of the increased conversion rate of electronic into vibrational energy.[159] Slight temperature changes are probably unimportant since fluorescence intensity seldom falls by more than 1% for a 1° C rise in temperature.[160] However, a few compounds are known, e.g. *p*-anisidine[160] and tryptophan,[136] where intensity may vary up to 5 % for a 1°C temperature change.

4.2.4.3 Effect of Concentration

At low concentration, the fluorescence can be increased feasibly down to 10^{-5} µg/ml, and a linearity extends up to 100 µg/ml or higher.[161] In this range of concentrations, the energy available for excitation is uniformly distributed through the solution, and it is possible to measure fluorescence from the surface of the solution at a glancing angle just as with crystals.

At higher concentration, molecules may combine together as aggregates or dimers in the excited state, known as excimers[162](a word derived from excited dimer), which affects the observed fluorescence, e.g. pyrene in dilute solutions (2×10^{-4} M) shows a violet fluorescence (at 384 nm) due to the monomer, but at higher concentration (2×10^{-3} M), the violet fluorescence decreases.[163] Similar effects have been shown, e.g., for 1,1-diethyl-2,2-pyridocyanine iodide[164] and chlorophyll.[165]

4.2.4.4 Effect of pH

The strengths of aromatic acids and bases are functions of electron distribution in the aromatic ring, and hence a molecule will show a change in acidity or basicity in the excited state.[166]

The Bronsted acidity difference between the ground state and lowest excited singlet state of organic molecules is large, commonly ranging from 4 to 9 pK units.

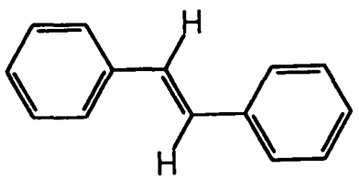
Some compounds like benzenethiol and aromatic amines become much stronger acids on excitation, whereas nitrogen and sulfur heterocycles, carboxylic acids, aldehydes and ketones, become much more basic,[167] e.g. the pka values of 2-naphthol,[168] and the quinolinium ion,[169] on excitation change from 9.5 and 5.1, to 3.1 and 10.5, respectively. Thus when ionisable compounds are investigated in dissociating media, the changes in fluorescence run parallel with the changes in absorption caused by varying pH. For instance, the fluorescence of β-naphthylamine[170] extends into visible region, due to its resonance structures, but in sufficiently strong acid, the emitted light is limited to the ultraviolet region similar to that of naphthalene. Phenol[171] develops a long wavelength band in the presence of alkali due to the resonance structures of the phenolate ion. The fluorescence of some purines and pyrimidines also depends on the acidity or alkalinity of medium.[172]

4.2.5 STRUCTURAL EFFECTS ON FLUORESCENCE

The structural requirements for fluorescence in an organic compound have three main factors, namely sufficient conjugation, geometry (or planarity), and substituent effects.

4.2.5.1 Conjugation

An extended, conjugated system, of double bonds in a molecule is usually essential for fluorescence, making the molecule capable of absorbing light at lower frequency or higher wavelength. Hence 1,4-diphenyl-1,3-butadiene fluoresces strongly (λ_{abs} = 350 nm, 80 Kcal/mole), but in simple 1,3-butadiene, predissociation is favoured due to the absorption of light of low wavelength (λ = 210 nm) or high energy (140 Kcal/mole).[173] Similarly, *trans*-stilbene (249), which contains one more double bond than biphenyl (250), is considerably more fluorescent. Conjugation enhances the mobility of the π-electrons and, as a result, shifts the absorption and therefore the



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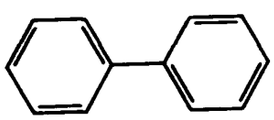
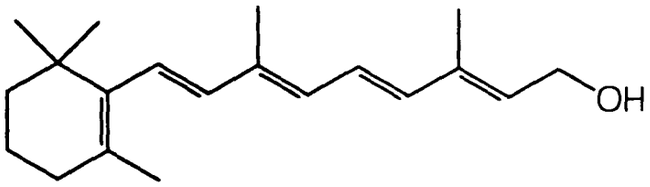


(250)

emission wavelength, towards the red end of the spectrum, e.g. the quantum yield of benzene, naphthalene, anthracene and tetracene are 0.11, 0.29, 0.46, and 0.52, respectively, with λ_{em} 278, 321, 400 and 480 nm, respectively. Similarly, heterocyclic compounds containing a nitrogen atom are much less fluorescent than their parent hydrocarbon, but the effect of increase in the conjugation is the same. For instance, the fluorescence of the acridine is greater than quinoline, which is greater than pyridine.[174]

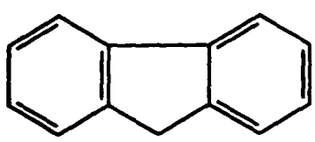


(251)

Molecules containing a cyclic conjugated system are likely to fluorescence more strongly than the double bonds in a chain arrangement. For instance, the quantum efficiency of naphthlene is at least five times that of vitamin A (251).[175]

4.2.5.2 Geometry or Planarity

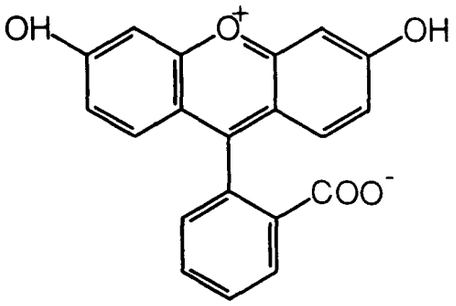
Planarity in the molecule is an essential condition for conjugation. Deviation from planarity inhibits the free mobility of π-electrons, and results in the loss of fluorescence. For instance, sterically crowded *cis*-stilbene is less than 1% as fluorescent as its planar *trans*-isomer.[176] Molecular rigidity sometimes increases the extent of planarity in a system, and so increases the fluorescence efficiency,[177] e.g. fluorene (252)



(252)

(Φ = 0.54) has higher quantum efficiency than biphenyl (250) (Φ = 0.23). Similarly, fluorescein (253) and phenolphthalein (254) contain the same degree of conjugation but

due to rigidity in the fluorescein molecule (253), it is highly fluorescent while phenolphthalein (254) shows little fluorescence.[178]



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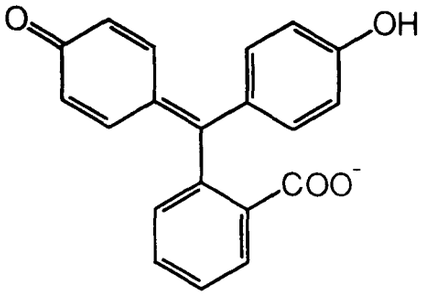


(254)

4.2.5.3 Effect of Substitution

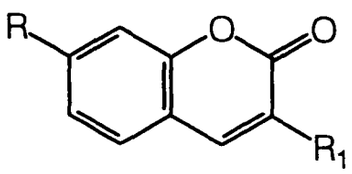
Substituents which enhance the π-electron mobility normally increase the fluorescence. Thus, in general, electron donating substituents,[154] e.g. -OH, $-OCH_3$, $-NH_2$, $-NHCH_3$, $-N(CH_3)_2$ and in unusual cases electron withdrawing substituent,[179] e.g. -CN tend to enhance the fluorescence, whilst the majority of electron withdrawing substituents,[180] i.e. CO, $-NO_2$, $-SO_3H$ and -COOH, are likely to diminish or eliminate the fluorescence. Halogens, e.g. Br or I, usually quench the fluorescence[181] due to the large magnetic field associated with them, which facilitates the inter-system crossing process.[154]

The fluorescence of heterocyclic compounds is particularly sensitive to the effect of the substituents,[182] e.g. 5- and 8-hydroxyquinoline are much more fluorescent than quinoline, but 3- or 6-hydroxyquinoline show even greater fluorescence being 200 fold more fluorescent than the parent compound. In the case of indoles, 4-hydroxyindoles are non-fluorescent but 5- and 6-hydroxy derivatives are fluorescent.[182]

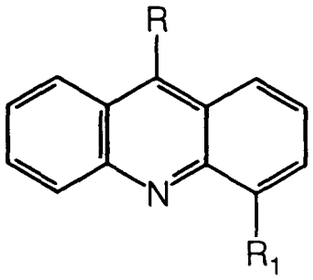
4.2.5.4 Donor-Acceptor Type[183] Systems

The result of disubstitution and polysubstition is more difficult to predict since the overall effect on the mobility of π-electrons produced by the different substituents has to be considered. For instance, *p*-hydroxyaniline has about the same fluorescence intensity as aniline but the *p*-substitution of aniline with a weakly electron-withdrawing group such as -COOH or SO_3H produces a far more intensely fluorescent compound.[184]

In such a donor-acceptor type of system, the electronic excitation is mostly accompanied by an internal charge transfer (ICT) in the direction of acceptor substituents, which increases the dipole moment of the molecule. This donor-acceptor type of system is the classification into which the majority of organic fluorescent molecules fall, e.g. 7-hydroxycoumarin[185] (255) and 9-aminoacridine[186] (257) are intensely fluorescent, 3-

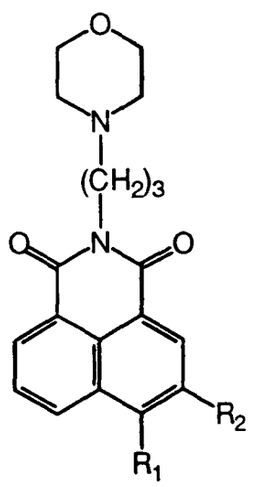


(255) R = OH; R_1 = H
(256) R = H; R_1 = OH



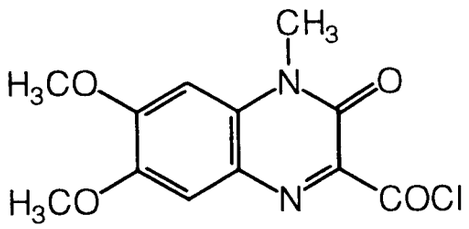
(257) R = NH_2; R_1 = H
(258) R = H; R_1 = NH_2

hydroxycoumarin (256) is only weakly fluorescent, and 4-aminoacridine (258) is not fluorescent. The most probable explanation is the more effective donation of the lone pair of electrons on the exocyclic heteroatom of the donor substituent in (256) and (257) to the electron acceptors (C=O and -N=, respectively). This kind of resonance is not present for the substituents at the 3- and 4-positions in (257) and (258) respectively. A similar situation is present in the case of N-substituted 1,8-naphthalimides, where the compound containing a 4-amino group (259) is more fluorescent than the compound containing a 3-amino group (260).[187]



(259) R_1 = NH_2; R_2 = H
(260) R_2 = NH_2; R_1 = H

There are many fluorescent derivatisation reagents, mostly containing the donor-acceptor system, of use for the detection of amines, alcohols, thiols, and carboxylic acids. The reagents include 4-chloroformyl-7-methoxycoumarins,[188] 4-dimethylamino-1-naphthoylnitrile,[189] 2-dansylethyl-chloroformate,[190] 7-{(chlorocarbonyl)methoxy}-4-methylcoumarin,[191] 4-diazomethyl-7-methoxycoumarin,[192] 7-methoxycoumarin-3- and -4-carbonyl azides,[193] 2-(4-isocyanatophenyl)-6-methylbenzothiazole[194] and naphthyl-isocyanate.[195] Generally these reagents do not permit the determination of alcohol at the femtomole level per injection volume in HPLC, except 7-methoxycoumarin-3-carbonylazide. Recently, Nakamura *et al.* described 3,4-dihydro-6,7-dimethoxy-4-methyl-3(4H)-oxoquinoxaline-2-carbonyl chloride (261) as a highly sensitive fluorescence derivatisation reagent for alcohols[196] and amines[197] in HPLC.



(261)

4.2.6 Chromoionophore and Fluoroionophore

The first crown compound, made by Pederson[198] (Dupont, Delaware, USA; Nobel Prize 1987.) in 0.4% yield, was a cyclic hexa-ether, dibenzo-18-crown-6.[199] Pederson gave the name "crown compound" because according to him "cations could be crowned and decrowned without physical change to either, just as the heads of royalty."[199] These potentially exolipophilic compounds selectively complex alkali and alkaline earth metal ions in their endopolarophilic cavity.[200] Hence, crown ethers can also be termed as ionophores.[201]

The combination of a chromogenic group and an ionophore in a molecule produces a chromoionophore which, on complexation displays spectral changes in its absorption spectrum. However, a compound which shows a spectral change in its emission spectrum or a change in its fluoresence quantum efficiency upon complexation with metal ions is referred to as a fluoroionophore.[201] Spectral changes can be defined

as bathochromic shifts, i.e. changes to longer wavelength (lower energy) or hypsochromic shifts, i.e. changes to shorter wavelength (higher energy). An increase in the intensity of a band is called a hyperchromic effect. Usually, a change in the absortion spectrum is followed by changes in the emission spectrum.[135]

Chromoionophore and fluoroionophores can be divided in to two categories, on the basis of the distance/space between the ionophore and the chromophore or fluorophore, i.e.

(1) Chromo- and fluoro-ionophore with spacer, and

(2) Chromo- and fluoro-ionophore without spacer

4.2.6.1 Chromo- and Fluoro-ionophore with Spacer

These are proximal, non-adjacent systems, which arise from the fluorophore-spacer-ionophore (receptor) format with one, two or three carbon atoms in the spacer chain (Fig 7). In this kind of system, a strong long range interaction develops in the

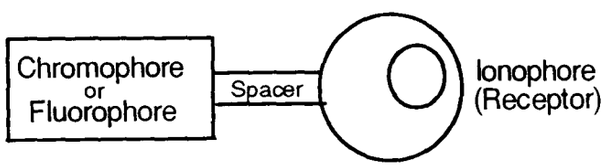


Fig. 7 Diagrammatic representation of the fluoroionophores with spacer.

form of an electron transfer from the ion free receptor to the fluorophore on photoexcitation of the molecule. The photoinduced electron transfer (PET) process[202,203]

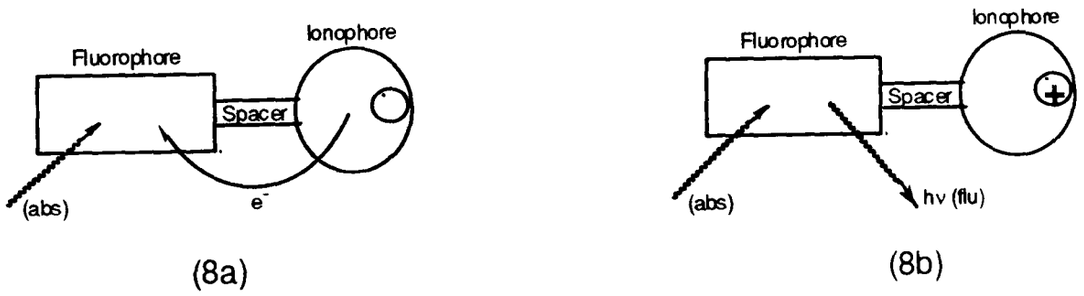


Fig 8 A diagrammatic representation of photoinduced-electron transfer process in fluoroionophores with a spacer (a) before and (b) after the complexation of the ionophore with metal ions.

is responsible for switching off the fluorescence[204] (Fig 8a). A suppression of the PET process by complexation with alkali or alkaline earth metal ions means that fluorescence can again become the dominant decay channel of the excited fluorophore (Fig 8a). This effect can be explained in terms of frontier orbital energy diagrams (Fig 9a and 9b for

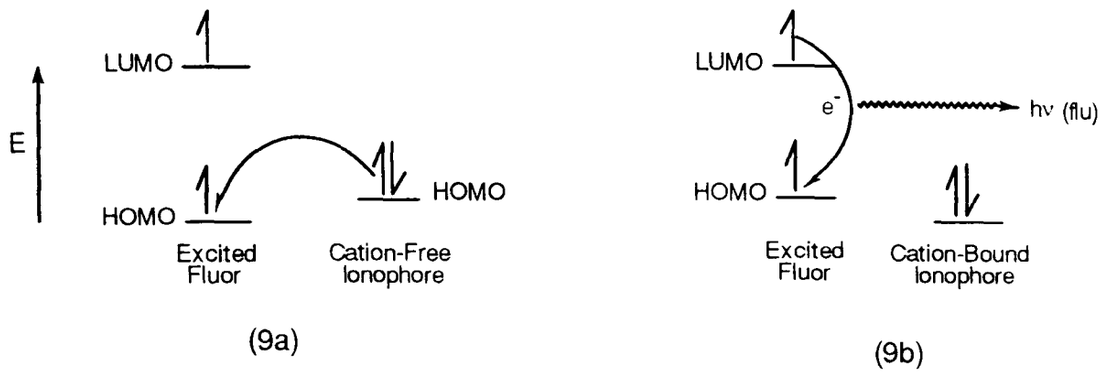
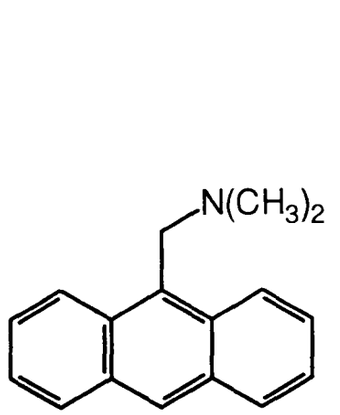


Fig. 9 Frontier orbital diagram of fluoroionophores with a spacer (a) before and (b) after the complexation of the ionophore with metal ions.

the processes in Fig 8a and 8b respectively). Examples of similar systems are (262) where an amine is separated from the common fluoroionphore anthracene by a methylene group. Here the amino group acts as a receptor for protons.[205] Similarly, in (263) the dimethylaniline group acts as receptor.[206] The fluorescence is enhanced by protonation of the non-bonded electrons of the nitrogen atom.[206]



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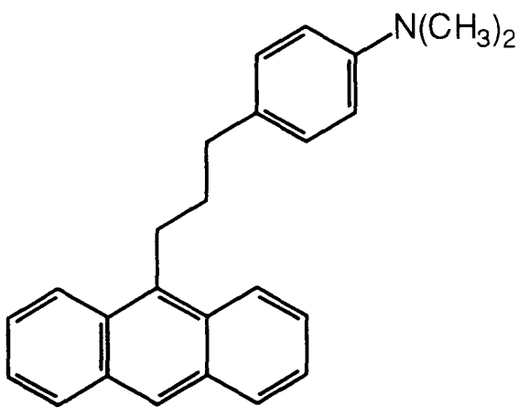
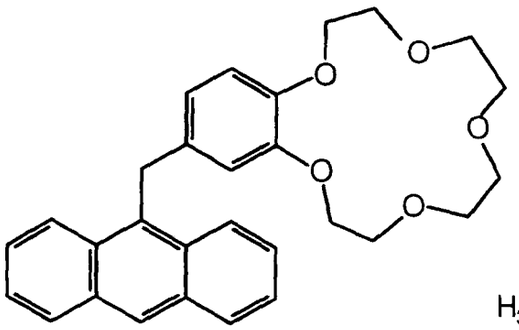
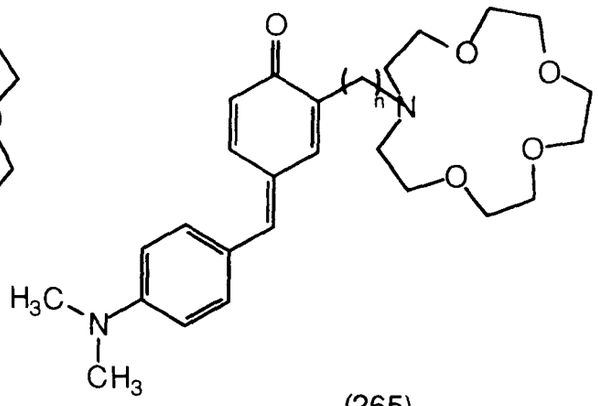


(263)

The chain length of the spacer sometimes has a marked effect on the fluorescence enhancement.[207,208] The replacement of the amino or dimethyl aniline receptor by a crown ether also favours the PET process, e.g. compound (264) shows a 47 fold enhancement of the fluorescence in the presence of K^+ ion.[209] Similarly,



(264)



(265)

compound (265) displays large bathochromic shift and strong hyperchromic effect in its absorption spectra upon complexation with an alkali and alkaline earth metal ion in decreasing order of $Mg^{++} > Ca^{++} > Ba^{++} > Li^{+} > Na^{+} > K^{+}$ for n = 5 and nearly the same bathochromic shift but relatively weak hyperchromic effect for n = 6.[210]

4.2.6.2 Chromo- and Fluoro-ionophores without Spacer

The systems where the ionophore (receptor) is directly attached to the fluorophore, without any methylene spacer in between, (Fig 10) are integral systems

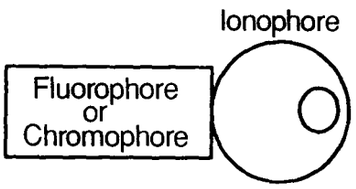
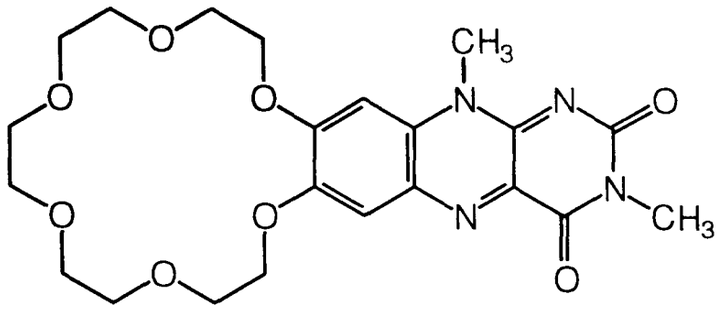


Fig. 10 A diagrammatic representation of the fluoroionophore without spacer.

which form the majority of known indicators for protons and other ions.[211] Optical excitation leads to internal charge transfer (ICT)[212] in these fluorophores, and ion binding to a site on a chromophore or fluorophore itself will naturally modulate these changes, and hence the absorption, and emission band wavelengths.

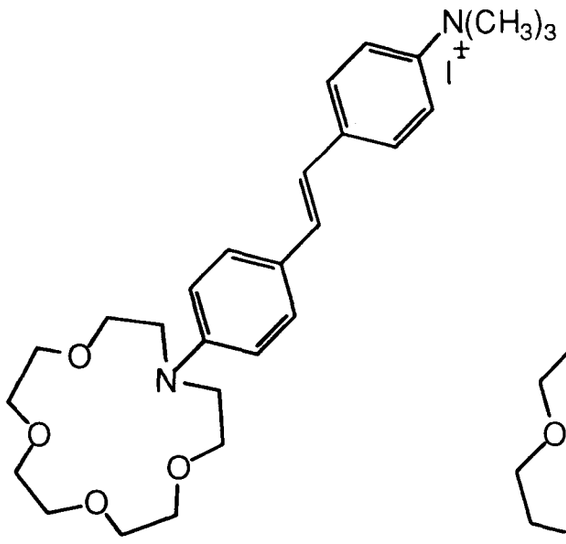
Chromoionophores and fluoroionophores, where the oxygen or nitrogen atom of the ionophore is attached near the donor part of the molecule, or is the electron donating group of the donor unit, usually display a hypsochromic shift in their absorption and emission spectra, and usually produce quenching of fluorescence upon complexation

with metal ions.[213,214] For example, (266) has a crown ether attached to the umiflavin-

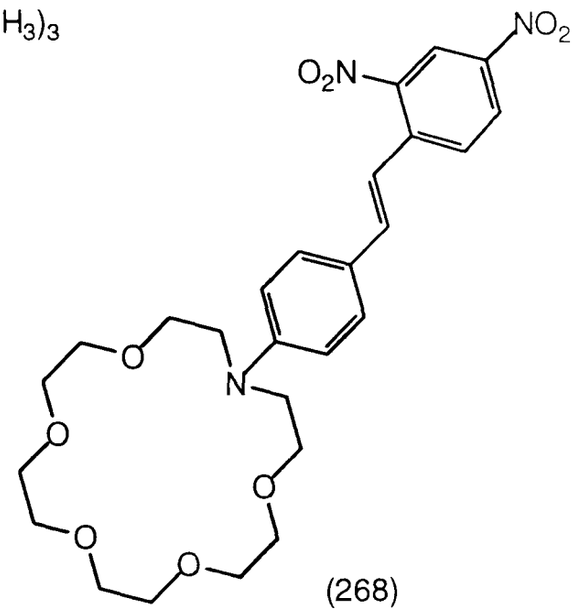


(266)

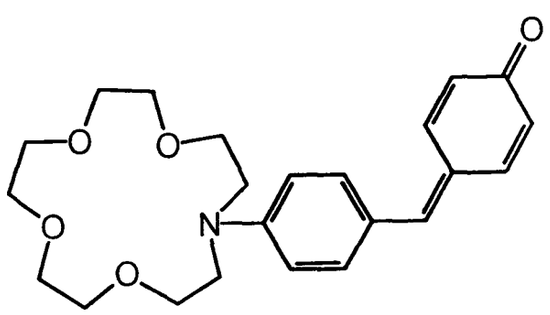
nucleus, and displays a hypsochromic shift in its absorption and emission spectra with



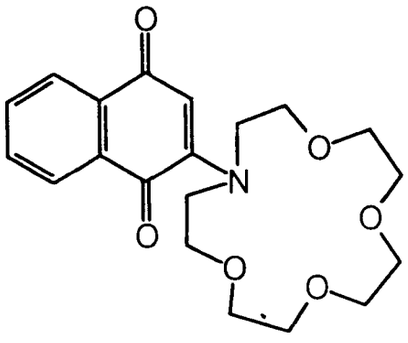
(267)



(268)

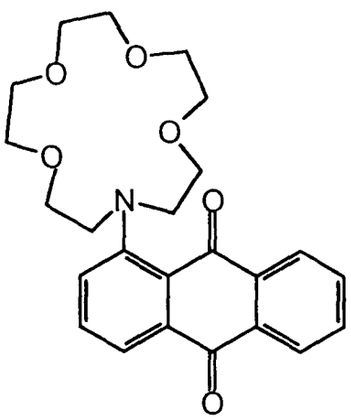


(269)

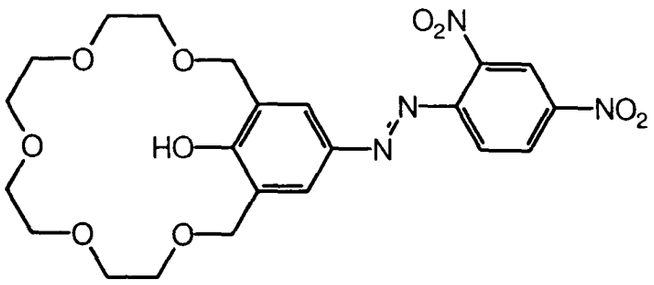


(270)

a decrease in fluorescence intensity upon complexation with alkali metal ions.[215] Similar results have been seen with compounds (267)-(273): most of them exhibit hypsochromic shift and hypochromic effect upon complexation with alkali and alkaline earth metals,[216-220] e.g. the yellowish orange (λ_{max} = 467 nm) stilbene dye (268) shifts to yellow (λ_{max} = 370 nm) on complexation with K^+ and Ca^{++} ion, but in the presence of Ba^{++} ion, the solution appears nearly colourless. A characteristic blue shift (λ_{max} = 583 nm to λ_{max} = 485 nm) with a hypochromic effect, is observed in quinone imine (269) when Ca^{++} salts are added.[216]



(271)

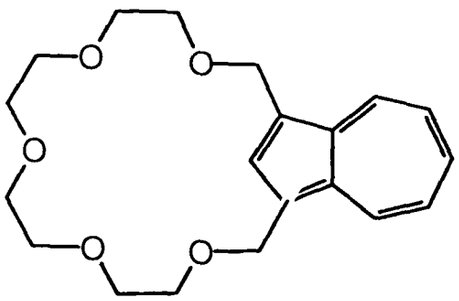


(272)

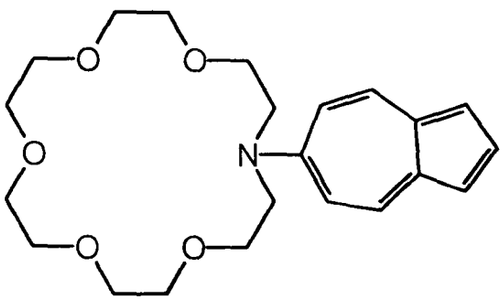
A chloroform-pyridine solution of (acidic) dinitrophenylazophenyl crown ether (272) (n = 1) produces a maximum hypsochromic shift on the addition of Li^+ ion.[218] The visible absorption (λ_{max} = 618 nm) band of the azulene derivative (273) is shifted hypsochromically with Ca^{++} (λ_{max} = 610nm) and Ba^{++} (λ_{max} = 612 nm).[219] In azulene, the five membered ring is negatively polarised, but during excitation a reversal of the dipole direction occurs, producing a partial positive charge on the smaller ring.[221]

The electronic excitation of the above kind of chromo- and fluoro-ionophore is usually accompanied by a charge density shift in the direction of the acceptor substituent of the chromophore or fluorophore respectively, i.e. an increase of dipole moment takes place.[222] It is likely that the nitrogen and oxygen atoms of ionophores of the above discussed fluoro- and chromo-ionophores (267)-(273) become positively polarised upon complexation, and hence the excited states are more strongly destabilised by cations than the ground state, therefore hypsochromic shifts result.[223] The bathochromic shift of the

most important[201] but rare class of chromoionophore and fluoroionophore which have the ionophore attached near the acceptor part of the chromophore and fluoroionophore respectively, can be explained on the basis of internal charge transfer (PET)[224] process. Here, the nitrogen or oxygen atom of the ionophore, being positively charged on complexation in the ground states, has to be considered as a part of the electron acceptor. Thus, the ground state is destabilised, and the excited state is stablised, causing bathochromic band shifts. For example the azulenyl crown ether[225] (274), where the cycloheptatriene ring act as acceptor on excitation,[226] is particularly sensitive and selective for Ba^{++} ions. Complexation of these ions causes a bathochromic shift with colour change from yellowish orange (λ_{max} = 477 nm) to purple-red (λ_{max} = 560 nm).



(273)

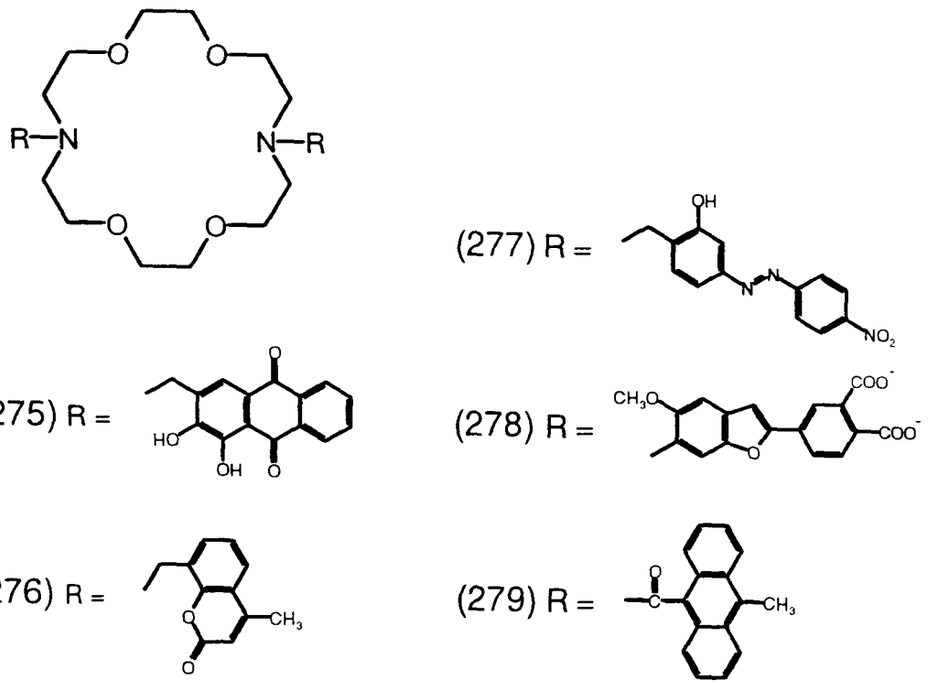


(274)

Compound (265) contains an ionophore attached to the electron acceptor part of the molecule and displays a very strong bathochromic shift and hyperchromic effect upon complexation with alkali and alkaline earth metals.[210]

Chromogenic or fluorogenic derivatives of diaza-18-crown-6 have been prepared by different workers (275-279).[227-230] Most of them have a common feature: the attachment of the nitrogen atom of the ionophore to the donor site of the chromophore or fluorophore. This is the cause of the hypsochromic shift in their absorption spectra, upon complexation with a metal ion, and this complexation also produces a hypsochromic shift, and hyperchromic effect, in the fluoresence spectrum for compounds (275)[227] and (276).[228]

The compounds (275) and (276) bind Ca^{++} ion selectively with detection limits of 1 x 10^{-5} and 5 x 10^{-6} M, respectively. A side arm containing an ionic group which



can form a six-membered chelate ring is usually flexible enough to interact effectivly with the crown ether bound metal ion[228,231] (Fig 11).

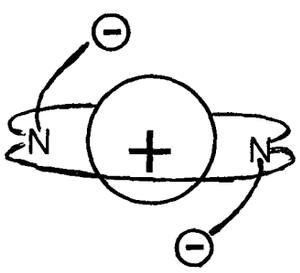


Fig. 11 Diagram showing the role of the side arms in complexation of the fluoroionophore by metal ions.

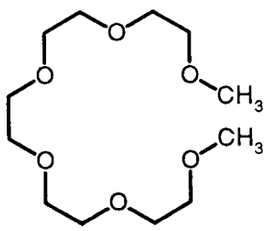
Compound (278) binds K^+ ion selectively with a hypsochromic and hyperchromic change in the absorption (λ_{max} = 394 nm to λ_{max} = 377 nm), and emission (λ_{max} = 518 nm to λ_{max} = 494 nm) spectra. The quantum yield of the fluorescence changes from Φ_f = 0.0075 for the ion-free ligand to Φ_f = 0.12 for the K^+ ion bound ligand, whereas in

the anthracenoyl derivative (279) of the diaza-18-crown-6[230], a 3-6 % fluorescence quenching has been seen upon complexation with alkali or alkaline earth metal ions.

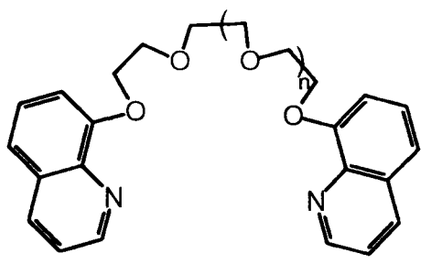
4.2.7 PODANDS

Podands are open chain crown ethers and have been known for a long time, for example, as polyethylene glycol,[232] and are represented here by the particular case of pentaethylene glycol (280) dimethyl ether. The podands have an ability to form complexes with alkali and alkaline earth metals.[232,233]

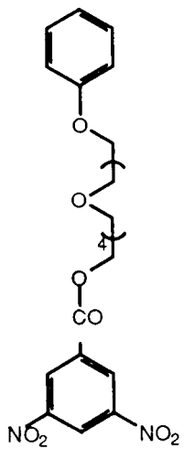
The podands which terminates in a quinoline group (281) (n = 2, trade name Kryptofix-5) is one of the most widely used podands[234] and this binds Na^+ very selectively.[235] Long chain intramolecular donor acceptor podands like (282) exhibit a



(280)

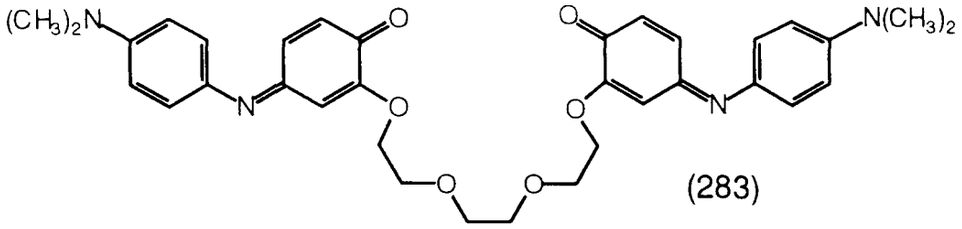


(281)

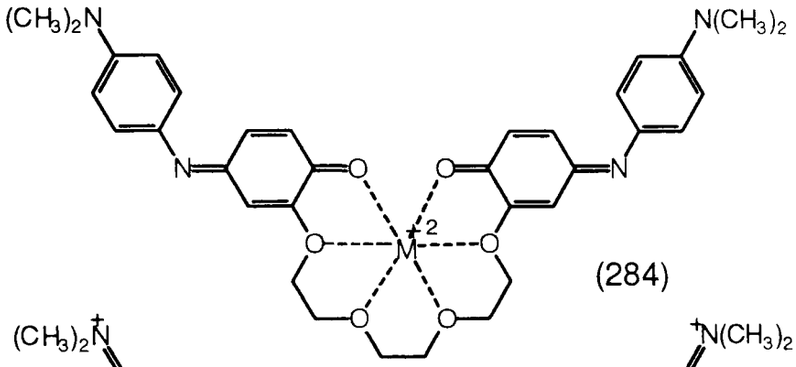


(282)

considerable increase in their absorption of UV lights and a bathochromic shift on the addition of metal ions.[236] Compound (283), with a long polyether chain attached to the acceptor part of the chromophore, displays a large hyperchromic effect and bathochromic shift (λ_{max} = 572 nm to λ_{max} = 669 nm) upon complexation with Ca^{++} ion. This is explained on the basis of the resonance structures (284) and (285)[237] for the complex.



(283)



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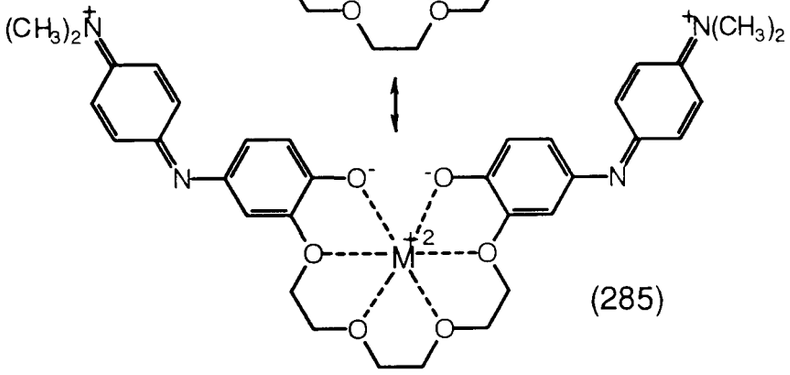
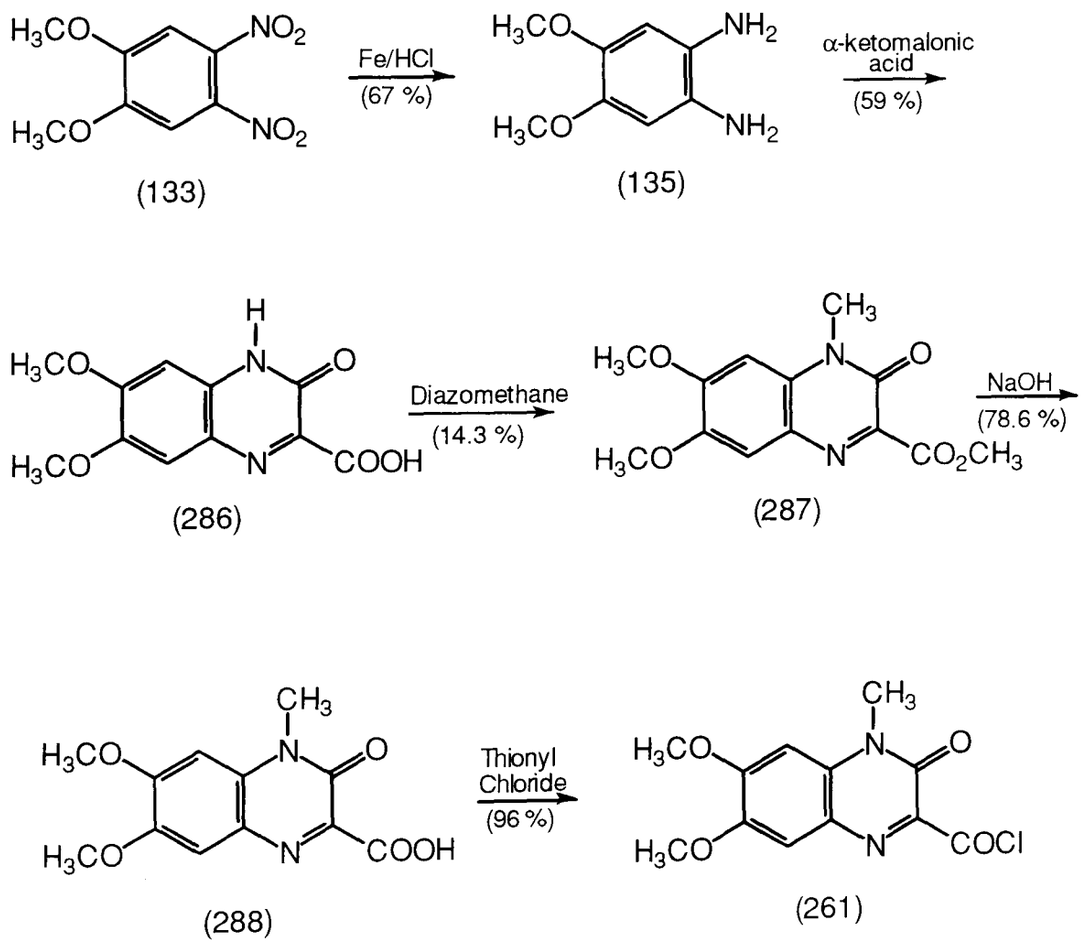


(285)

DISCUSSION

5 Preparation of 6,7-Dimethoxy-4-methyl-3(4H)-quinoxalinone-2-carbonyl Chloride (261)

Fluorescence detection is the basis of some of the most sensitive methods used in biopharmaceutical analysis. Several fluorescence labelling reagents[192-196,238-241] have been developed for compounds containing hydroxyl or amino groups. Recently, Iwata *et al.*[196] have reported a new derivatisation reagent; 6,7-dimethoxy-4-methyl-3(4H)-quinoxalinone-carbonyl chloride (261) for the detection of alcohols and amines in the low f mole range by HPLC.[196,197] The preparation of the reagent (Scheme 27) required the nitration of 1,2-dimethoxybenzene (130) using conc. nitric acid[238] to give



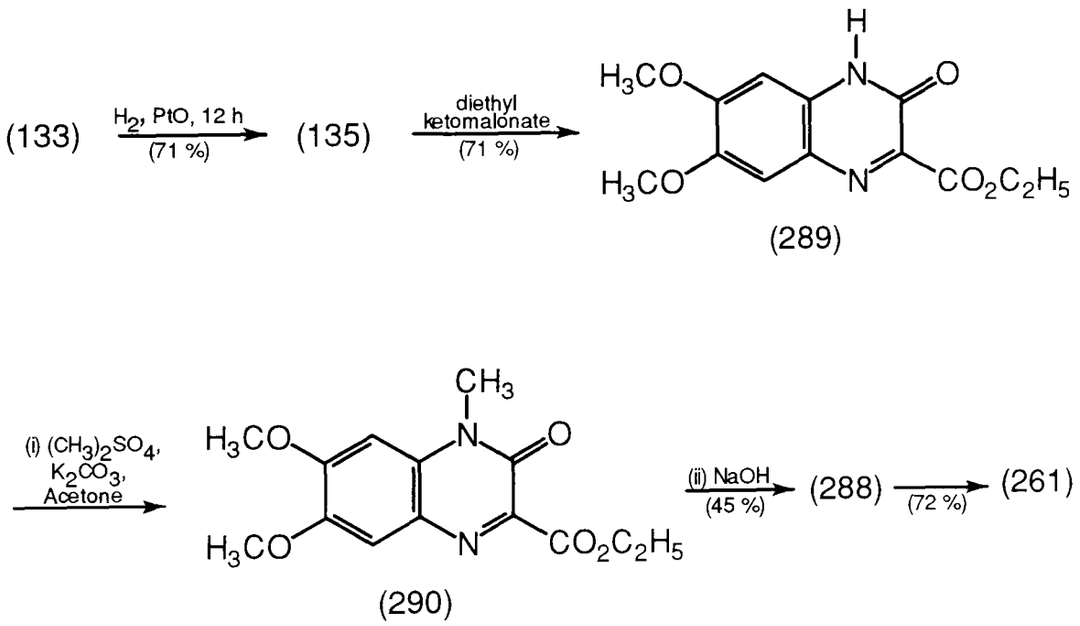
Scheme 27

1,2-dinitro-3,4-dimethoxybenzene (133) and then the reduction of the nitro groups to 1,2-diamino-3,4-dimethoxybenzene (135) by iron and hydrochloric acid.[239] The diamino compound (135), as a hydrochloride salt, itself a fluorogenic reagent for aldehydes and

α-carbonyl compounds,[242-245] was converted to 6,7-dimethoxy-3(4H)-quinoxalinone-2-carboxylic acid (286) by condensation with α-ketomalonic acid.[196] A crucial step was the methylation of (286) with diazomethane[246] to yield methyl 6,7-dimethoxy-4-methyl-3(4H)-quinoxalinone-2-carboxylate (287) but this was achieved in only 14.3 % yield.

The ester (287) was hydrolysed in alkali to the corresponding acid (288) in 78.6 % yield. Compound (288) was then treated with thionyl chloride to obtain the reagent, 6,7-dimethoxy-4-methyl-3(4H)-quinoxalinone-2-carbonyl chloride (261) in quantitative yield. The overall yield for this synthesis (Scheme 27) was 4 %.

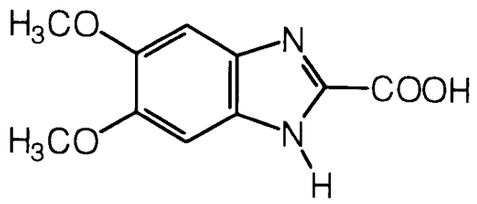
At the time the work reported in this thesis was being done, another group published their work[247] on an improved preparation of (261) (Scheme 28) and added



Scheme 28

evidence in support of the structure (261). These workers used different reagents and a different sequences of reactions (Scheme 28). They pointed out that:

(a) the condensation of (135) and α-ketomalonic acid gave a byproduct, stated to be (291), though the only quoted evidence for the structure was a mass spectrum.



(291)

(b) There is a question whether N-methylation or O-methylation of quinoxaline 2-carboxylic acid (286) has occurred in the original synthetic route (Scheme 27).

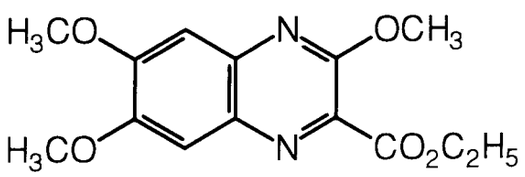
According to Dave *et al.*[247] the determination of whether N-or O-methylation has occurred, cannot be answered unambiguously from IR, UV or ^{1}H NMR spectra. However, Dave *et al.*[247] stated that the compound (290) was the N-methyl compound on the basis of evidence from nOe experiments. The modifications made by them in the synthetic route were:-

(a) In step 2, hydrogen and platinum oxide was used as the reducing system.

(b) In step 3, diethyl ketomalonate was employed, instead of α-ketomalonic acid,in order to avoid the formation of (291).

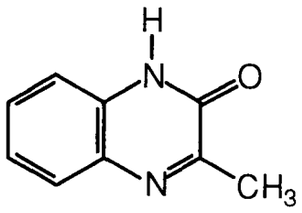
(c) In step 4, methylation was accomplished by reaction with dimethyl sulphate in acetone in the presence of anhydrous potassium carbonate to obtain only (290) in 45 % yield.

In the work reported in this thesis, palladium on charcoal (10 %) was found to be a convenient catalyst for the preparation of (135) by hydrogenation and this method was preferred to the dissolving metal procedure,[239] or the use of an easily poisoned platinum catalyst.[247] Methylation of (289) with an ethereal solution of diazomethane[249] gave a mixture of two isomers; (290) and (292) which were separated by column



(292)

chromatography in 45 and 47 % yield, respectively. However, when dimethyl sulphate in acetone and anhydrous potassium carbonate was used, the reaction was not completed after 8 h when the reaction mixture was kept at 40°C, as described for a similar reaction



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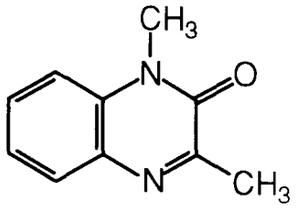
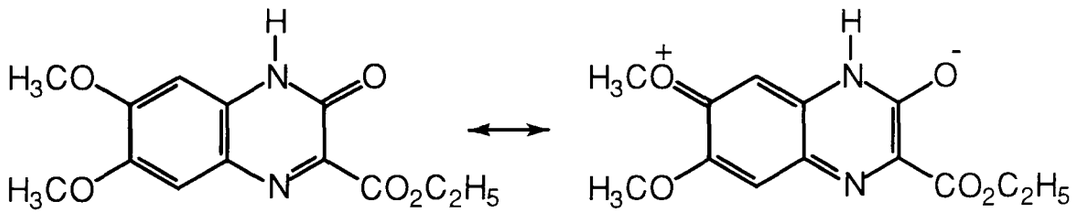


(294)

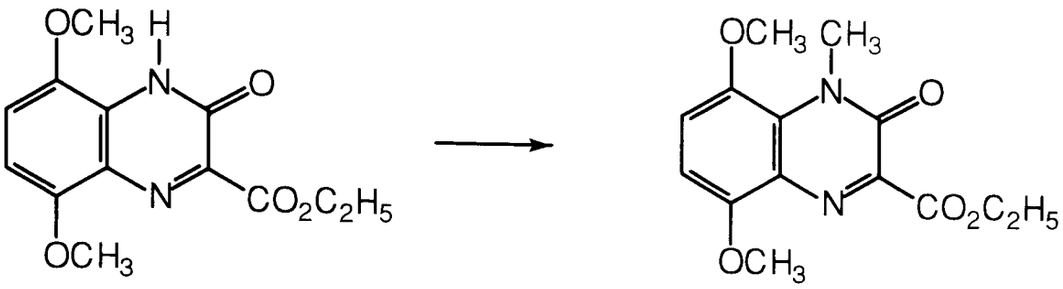
by Cheeseman,[248] who methylated (293) to obtain the N-methylated product (294). In the work reported here, compound (292) was obtained together with starting material and (290). When the reaction mixture was refluxed for 1h instead of being kept at 40° C for 8 h, the products were (290) and (292) in 39 and 11 % isolated yield, respectively. The formation of (292) can be explained on the basis of contributing structure (295) of (289), methoxyl groups at the 6- and 7-positions seen to enhance the nucleophilicity of



(289) (295)

the oxygen atom of amide group. Hence, methylation takes place at both the nitrogen and oxygen atoms. This effect is not present in compound (293).

The methylation of (140), an isomer of (289), with dimethyl sulphate in acetone in the presence of anhydrous potassium carbonate, surprisingly gave only one methylated product (296). This different behaviour of (140) from (289) is due to different electronic effects on the lactam system by the 5,8- and 6,7-dimethoxyl groups, respectively. The fluorescence quantum yield for these two compounds is direct evidence of these effects, because (296) is not fluorescent while (290) is highly fluorescent (Table 2).



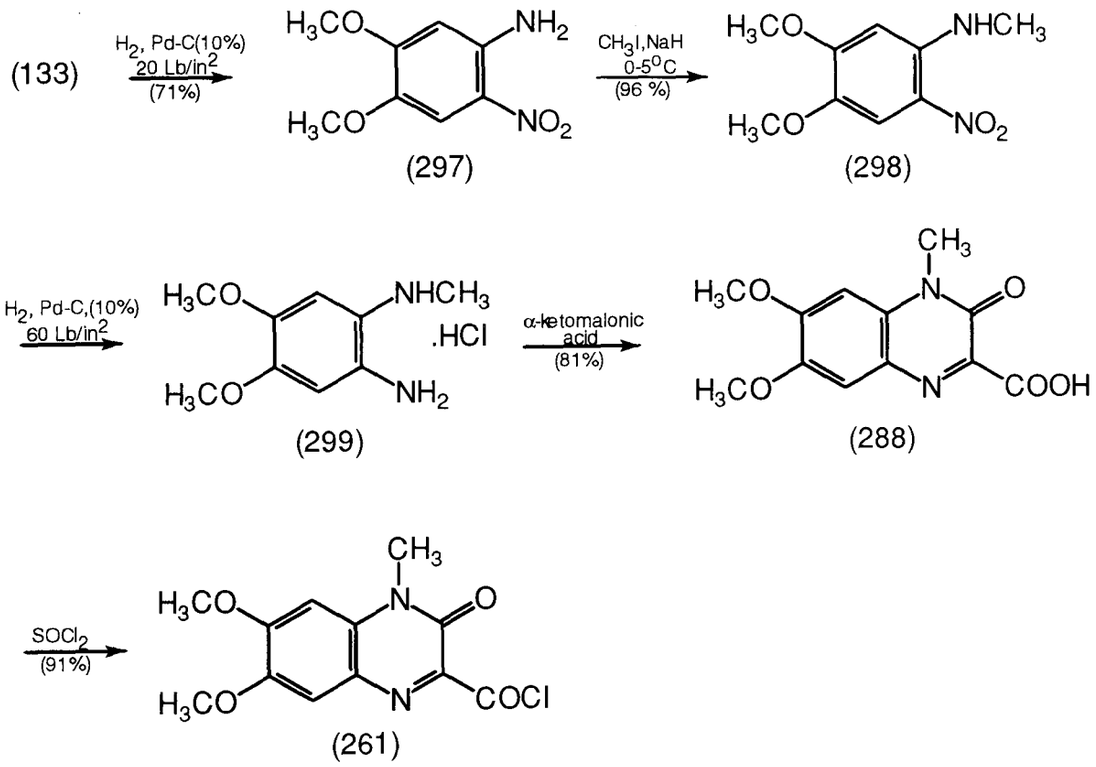
(140) (296)

5.1 Characterisation of the Methylated Products of Ethyl 6,7-dimethoxy-3(4H)-quinoxalinone-2-carboxylate (289)

An attempt was made to characterise both of the isomers (290) and (292). The melting points and physical appearance showed clear differences (Table 1). The IR spectrum of (290), indicated the presence of two carbonyl groups by two sharp peaks at 1730 (C=O; ester) and 1650 cm^{-1} (C=O; amide), whereas only one peak at 1720 cm^{-1} attributable to a CO stretching vibration was seen in the IR spectrum of (292) (Table 1) and this must be assigned to the ester group. Thus, the amide group is absent from (292). In the ^1H NMR spectrum, the hydrogen atoms at the 5- and 8-positions in (290) produced two singlets at 7.38 and 6.67 ppm, respectively, in agreement with the literature.[247] However, the 5- and 8-hydrogen atoms in (292), gave two singlets at 7.35 and 7.15 ppm, respectively, which indicated the presence of an entirely different substituent in the neighbourhood of 5-H in (292). Moreover, the appearance of a singlet at 4.11 ppm and the absence of the singlet at 3.71 ppm in ^1H NMR spectrum of (290) also indicated that the methyl group was now attached to that electronegative atom whose lone pair of electron must be in a more extensive conjugated system[247,250] (Table 2). The mass spectra showed nearly the same mode of fragmentation of the respective molecular ions, the only differences were in the lower mass fragment ions. The UV spectra showed absorption bands at 396 and 361 nm for (290) and (292), respectively (Table 2). The red shift in case of (290) indicated that the electronic distribution in this donor-acceptor system is very different from that of (292).[251] The fluorescence spectra showed a higher fluorescence quantum yield for (290) compared to (292) (Table 2) and this is strong evidence in favour of structure (292).

5.1.1 An Improved Method for the Preparation of 6,7-Dimethoxy-4-methyl-3(4H)-oxoquinoxaline-2-carbonyl Chloride (261)

It was thought that the probable reason for the low overall yield obtained in both routes to (261) (Scheme 27 and 28) was that the methylation was performed after the condensation step. Hence, in this work, the methylation was done before the condensation step (Scheme 29). 5-Amino-4-nitroveratrole (297) was prepared from (133)



Scheme 29

by use of a palladium on charcoal catalyst and hydrogen at 15-20 lb/in^2 at room temperature, following a literature method,[252] with some small modifications (Scheme 29). Other attempts to cause reduction of only one of the nitro groups included (i) transfer hydrogenation with cyclohexene and palladium on charcoal (10 %),[253] and (ii) hydrogenation under atmospheric pressure in acetic acid.[252] In the first method of transfer hydrogenation a large amount of catalyst was required (e.g. 0.760 g of palladium charcoal (10 %) was used for 0.288 g of the dinitro compound) and the second method gave an intractable mixture.

An attempt was made to obtain the mono-N-methylated product (298) by the reaction of succinimide and formaldehyde, followed by the hydrolysis,[254] but a mixture

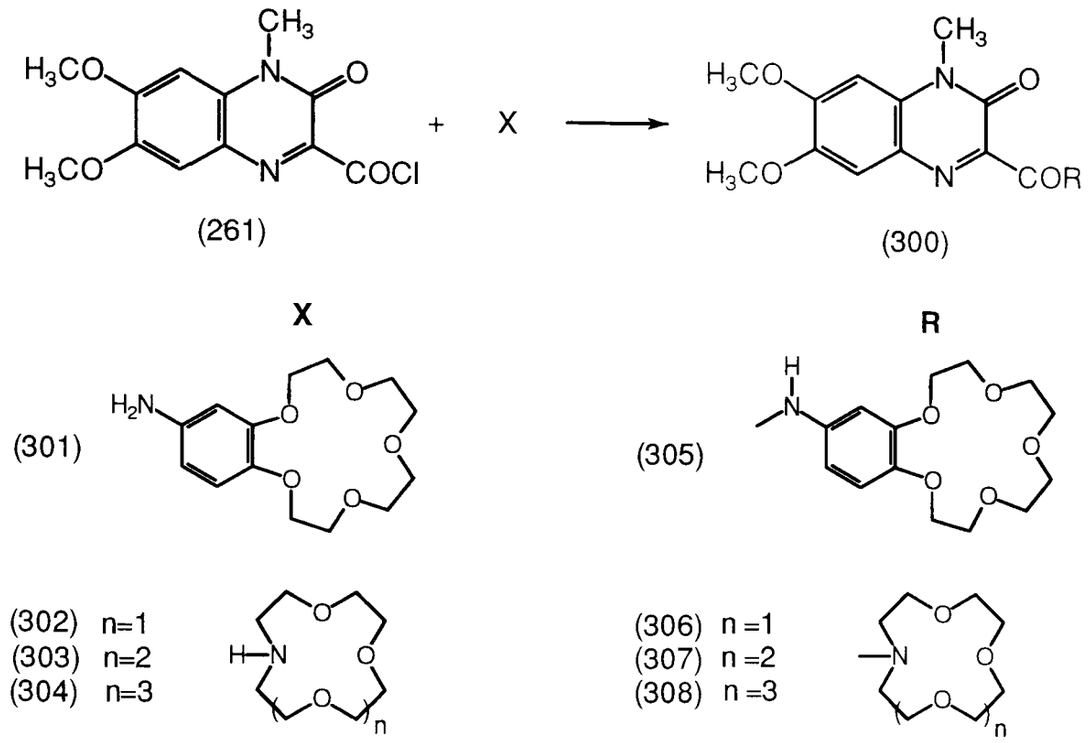
of starting material and the desired product (298) was obtained. The reaction of dimethyl sulphate in acetone in the presence of anhydrous potassium carbonate[248] on (297) gave a mixture of starting material and (298) in a 1:1 ratio (approximately) after boiling the mixture for 24 h. When methyl iodide in dimethylformamide in the presence of sodium hydride was used at room temperature, only the N,N-dimethyl derivative was obtained as a single product. However, the same reagents but with the temperature carefully controlled to 0-5° C, gave an excellent yield (96 %) of only the monomethylated compound (298). The product was characterised by its ^{1}H NMR spectrum, where the methyl group gave a doublet at 3.03 ppm due to adjacent N-H group which itself produced a broad singlet at 8.47 ppm and was exchanged with D_2O. The mass spectrum and the elemental analysis of (298) indicated the molecular formula $C_9H_{12}N_2O_4$. The reduction of the nitro group in (298) to the amino compound (298) was achieved by using hydrogen at a pressure of 60 lb/in^2 in the presence of palladium on charcoal (10 %) at room temperature. The IR spectrum of (299) showed a number of peaks in the range of 3410-3100 cm^{-1} due to NH and NH_2 groups, which produced two broad singlets in ^{1}H NMR spectrum, at 6.98 and 3.72 ppm, respectively, exchanged with D_2O. The aromatic hydrogens 6-H and 3-H gave rise to two singlets separately at 6.79 and 6.77 ppm. The mass spectrum of (298) showed a molecular ion peak at 182 daltons (loss of HCl), in agreement with the molecular formula $C_9H_{14}N_2O_2$. Two peaks at 167 and 152 daltons were probably due to the loss of one and two methyl groups, respectively.

Compound (299) was condensed with 2-ketomalonic acid to form (288) in 81 % yield and finally converted to acid chloride[196] (261) in 91 % yield.

5.1.2 Preparation of the Derivatives of 6,7-Dimethoxy-4-methyl-3(4H)-quinoxalinone-2-carbonyl Chloride

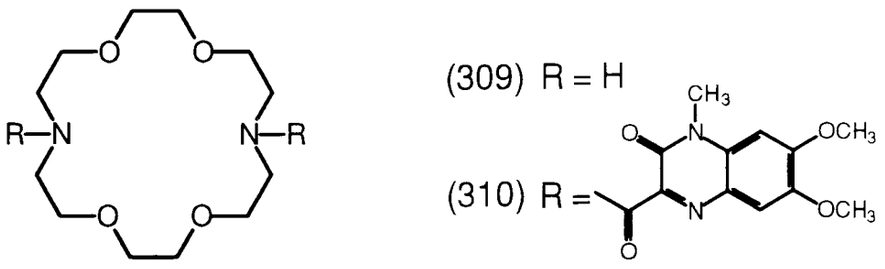
The high fluorescence quantum efficiency of some of the reported derivatives of (261)[196,197] encouraged to prepare some derivatives of the fluoroionophore (300) and podand types because of their potential importance as analytical and biological probes.[247] For this purpose, crown ethers having different cavity sizes, i.e. 4'-amino-15-crown-5 (301), 1-aza-12-crown-4 (302), 1-aza-15-crown-5 (303) and 1-aza-18-crown-6 (304) were used for the preparation of fluoroionophores (305)-(308) (Scheme 30), and, 4,13-diaza-18-crown-6 (309) was used for the preparation of fluoroionophore (310). The podands

(311), (312) and (313) were prepared by using 1,8-diamino-3,6-dioxaoctane, 2,3-bis(2'-hydroxyethoxy)-5,8-dimethoxyquinoxaline (183) and 2,3-bis(6'-hydroxy-1',4'-dioxahexyl)-5,8-dimethoxyquinoxaline (184).

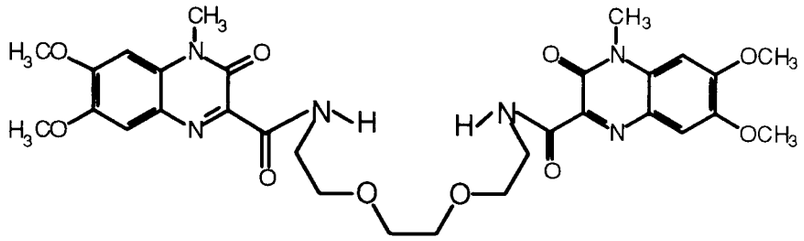


Scheme 30

Commercially available 4'-nitrobenzo-15-crown-5 was catalytically reduced[255] to obtained the corresponding amino compound (301). The appropriate amide or ester link between the fluorophore and the remainder of the molecule was achieved by treating the appropriate amine or alcohol with sodium hydride to obtained the salt in benzene and this was then refluxed with the acid chloride (261) for 4-6 h. Compounds (306)-(308) and (310) were purified by t.l.c but (305) was obtained in a pure state after column

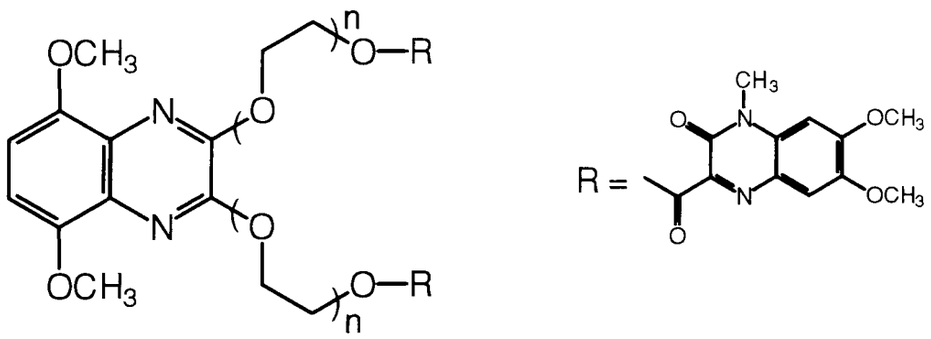


chromatography. Compounds (312) and (313) could not be purified by either column or thin layer chromatography due to their rapid hydrolysis on silica gel. Hence, they were purified by repeated crystallisation. All the derivatives (306)-(308) and (310)-(313) were stable in the solid form for at least one year and as solutions in methanol or dichloromethane for at least one month when stored at room temperature.



(311)

The IR spectra of (305)-(308) and (310) showed two strong absorptions in the range of 2940-2900 and 2890-2840 cm^{-1} due to aliphatic C-H stretching vibrations and two strong absorptions in the range of 1675-1640 and 1640-1615 cm^{-1} due to the two amide functions. Compound (305) showed only one absorption for the carbonyl group at 1675 cm^{-1} which might be due to overlapping of the two absorption bands. The N-H stretching of (305) was at 3440 cm^{-1}. The IR spectra of podands (312) and (313)



(312) n = 1
(313) n = 2

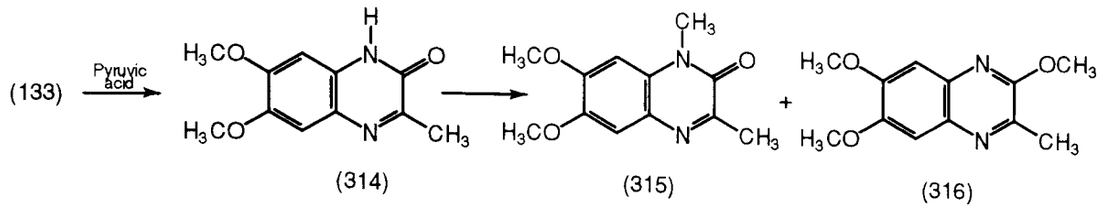
showed a strong absorption in the range of 1735-1730 and 1655-1650 cm^{-1} due to the carbonyl groups of ester and amide, respectively, whereas two amide carbonyl functions

in (311) gave rise to peaks at 1675 and 1640 cm^{-1}. The N-H stretching frequency of this compound was at 3290 cm^{-1}. The ^1H NMR spectra of all these derivatives (305)-(308) and (310) showed a similar pattern of signals for the protons in 6,7-dimethoxy 4-methyl-3(4H)-quinoxalinone group. The aromatic hydrogens at the 5- and 8-positions gave rise to two singlets in the range of 7.17-7.25 and 6.59-6.69 ppm, respectively, due to the different nature of nitrogen atoms in the heterocycle.[247] The three proton singlet at lowest field (3.9-4.0 ppm) was due to the 6-OCH_3 group, because the lone pair of electrons on the oxygen atom can be delocalised to the lactam carbonyl group whereas the electrons of the 7-OCH_3 group can not be so delocalised. Thus, the singlet due to 7-OCH_3 appeared at higher field (3.9-4.0 ppm) in the spectra of (306)-(308) and (310)-(313), with the one exception (311) where the 7-OCH_3 signal appeared at 3.75 ppm. The protons of the N-methyl group produced a singlet in the range of 3.81-3.83 ppm in the spectra of compounds (305)-(308) whereas in group (310)-(313), the singlet due to the N-methyl was at 3.65-3.69 ppm. The portion of the glycol units in compound (305)-(308) and (310) gave rise to a multiplet in the range of 3.89-3.45 ppm. The methylene group bonded to the ester in (312) and (313) produced a triplet at 4.96 and 4.73 ppm, respectively, whereas the α-methylene hydrogens of the ethoxy group, attached to 5,8-dimethoxyquinoxalinyl group gave rise to a triplet at 4.87 and 4.60 ppm, respectively. The ^1H NMR spectrum of (306) produced two triplets at 4.17 and 3.91 due to 5''-, 15''- and 6''-, 14''-methylene hydrogen atoms, and the remaining methylene group gave rise to a singlet at 3.76 ppm.

The mass spectra of all the compounds showed the molecular ion peaks, which were in agreement with their respective molecular formulae. However, a common feature of the mass spectra of all of these compounds (305)-(308) and (310)-(313) was the presence of a fragment at 247 and 219 daltons, probably due to the fragment, 6,7-dimethoxy-4-methyl-3(4H)-quinoxalinone-2-carbonyl and then loss of one molecule of carbon monoxide from this fragment.

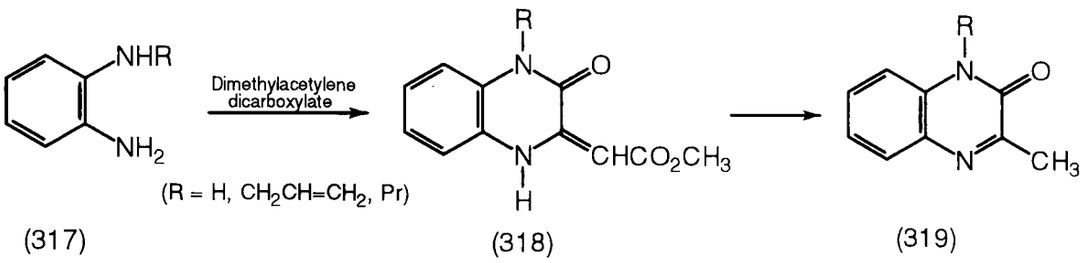
5.2 6,7-Dimethoxy-1,3-dimethyl-2(1H)-oxoquinoxaline (315)

Iwata *et al.*[245] have described the preparation of compound (315) by the reaction of (133) with pyruvic acid (Scheme 31) followed by methylation. However, the route



Scheme 31

is complicated by the formation of an isomer (316) in the methylation of (314) and this resulted in a low yield of (315). Suschitzky *et al.*[256] have described the preparation of a similar compound from the N-substituted derivative (317) of *o*-phenylenediamine and dimethyl acetylenedicarboxylate to give an intermediate (318) which was then hydrolysed to (319) in good yield (Scheme 32).

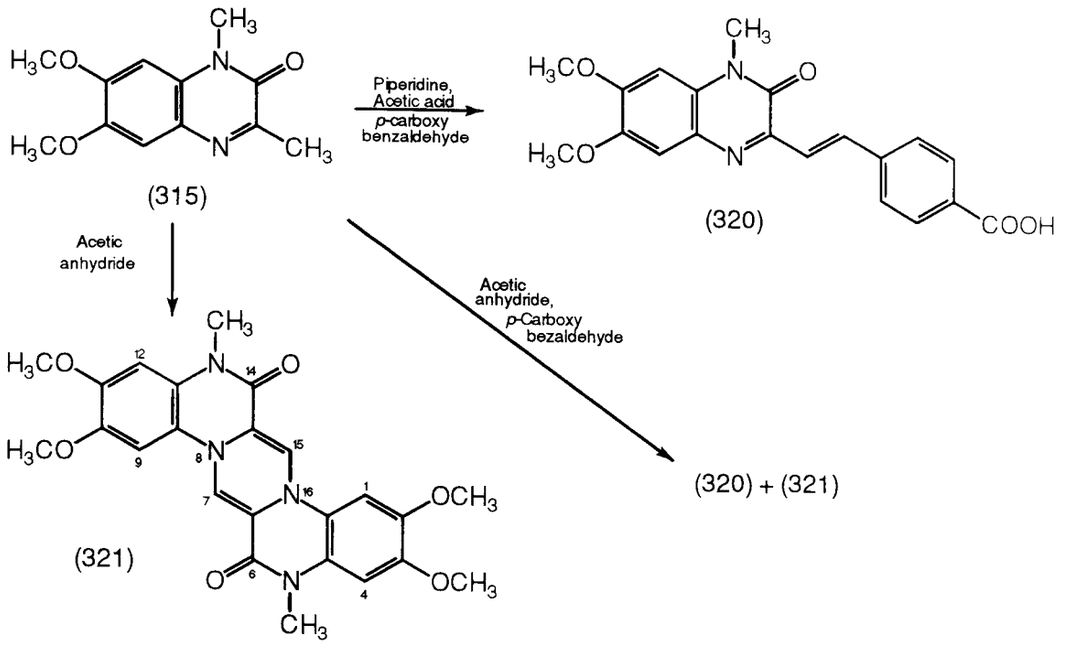


Scheme 32

In the work reported here, a successful attempt was made to increase the yield of (315) by the reaction of (299) with pyruvic acid. All the spectral data for the product was in agreement with that given for (315).[245]

5.3 Preparation of 6,7-Dimethoxy-4-methyl-2-(4'-carboxyphenylvinyl)-3(4H)-quinoxalinone (320)

A highly fluorescent compound (320) was prepared by the condensation of 6,7-dimethoxy-1,3-dimethyl-2(1H)-oxoquinoxaline (315) with *p*-carboxybenzaldehyde in the presence of acetic anhydride[257] (Scheme 33). A mixture of two products resulted: a yellow soluble compound (320), and an insoluble red compound(321). After dilution of the reaction mixture with water and neutralisation of the mixture, the red precipitate (321) was filtered off, and compound (320) was extracted from the yellow filtrate with dichloromethane. Subsequently, better routes to both compounds were found.



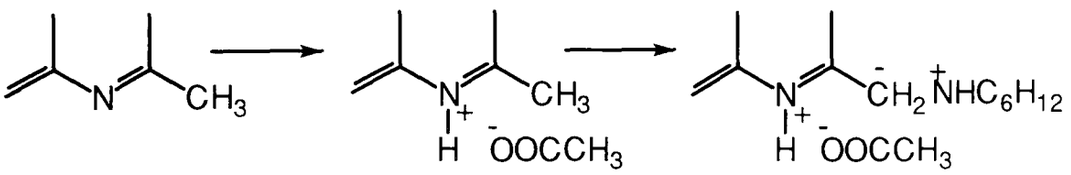
Scheme 33

The IR spectrum of (320) had peaks at 3440 and 1715 cm^{-1} due to the hydroxyl and carbonyl group, respectively, and a peak at 1645 cm^{-1} attributable to the amide carbonyl group. The ^1H NMR spectrum indicated the presence of only the *trans*-isomer[257] because the olefinic protons appeared as doublets (J = 16.2 Hz) at 7.98 and 7.70 ppm assigned to the α- and β-vinyl hydrogens, respectively. The large steric hindrance was thought to be the possible reason for the absence of *cis*-isomer. The *ortho* hydrogens of the phenyl group gave rise to doublets (J = 8.3 Hz) at 7.96 and 7.77 for the 3'-, 5'-H and 2'-, 6'-H, respectively. The hydrogen atom at the 8-position produced a low field singlet at 7.31 ppm due to the effect of the neighbouring nitrogen atom which is electron-withdrawing, whereas the 5-H gave rise to a singlet at 7.01 ppm due to the effect of neighbouring electron donating N-methyl group.[247] Two singlets at 3.97 and 3.87 were attributed to the 6- and 7-OCH_3, respectively. The probable reason for the relatively down field appearance of the singlet for 6-OCH_3 is the extensive delocalisation of the lone pair of electrons on the oxygen atom, an effect which is not possible for the methoxyl group at the 7-position.[258] The singlet at 3.70 ppm was attributed to the N-methyl group. The mass spectrum of the compound (320) showed a molecular ion peak at 366 daltons which agreed with the molecular formula $C_{20}H_{18}N_2O_5$. Loss of one methyl group gave a peak at 351 daltons, and the two peaks

at 322 and 219 daltons were probably due to the sequential loss of a carbon dioxide molecule and styryl group from the compound (320), respectively.

A successful attempt was made to improve the yield of compound (320) by using comparatively mild reaction conditions.[259] Toluene was used as solvent and the reaction mixture boiled in the presence of catalytic quantities of piperidine and acetic acid in a flask fitted with a Dean and Stark apparatus. The role[259] of the expected catalyst, piperidinium acetate, may be explained on the basis of:-

(i) The initial quaternisation of the heterocyclic compound which facilitated the abstraction of proton from α-methyl group by piperidine (Scheme 34).



Scheme 34

(ii) Fig (12) where the catalyst facilitates the removal of a water molecule to form a carbon-carbon double bond.

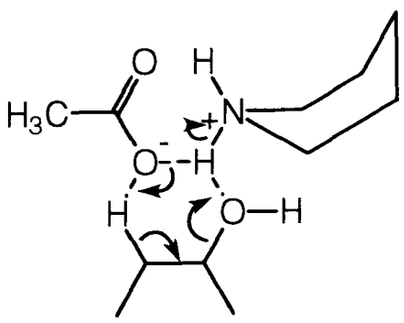


Fig. 12 Role of piperidiniun acetate in the removal of a water molecule.

Compound (320) was now obtained as a yellow solid directly from the reaction mixture (74% after crystallisation).

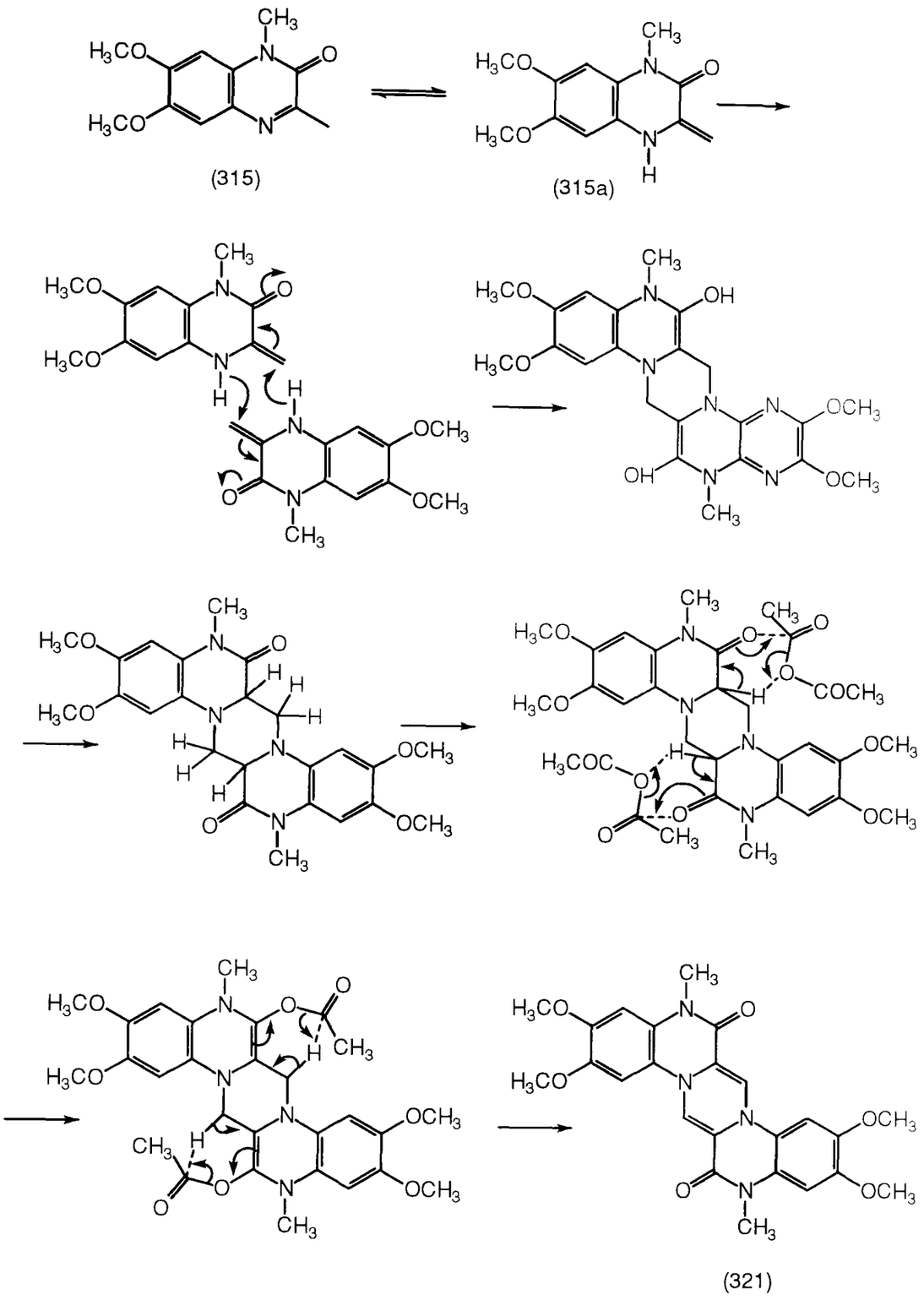
The formation of the highly insoluble non-fluorescent red compound (321) in the first preparation of (320) under acidic conditions was thought to be due to an intermolecular reaction of (315) in presence of acetic anhydride. This idea was

supported when the reaction was done under the same conditions but in the absence of *p*-carboxybenzaldehyde. Under these conditions, compound (321) was the only product. The red product (321) was sparingly soluble in the usual organic solvents and was eventually purified by dissolving it in trifluoroacetic acid with the production of an intensely blue solution, followed by the dilution of this solution with water to precipitate the compound (321) as a red powder (56%).

Compound (321) was characterised by its ^{1}H NMR spectrum which contained only singlet peaks, and did not show the peaks due to the styryl group. A singlet at 9.30 ppm can be assigned for 7- and 15-H because these are electron deficient positions due to the enone system. Two singlets at 7.51 and 7.30 ppm were assigned to the 1-, 9- and 4- and 12-H respectively. Two methoxy groups at 3- and 11-position gave rise a singlet at 4.31 ppm, whereas a singlet at 3.19 ppm was assigned 2- and 10-OCH_3, while the N-methyl protons produced a singlet at 4.16 ppm. The IR spectrum showed peaks at 3420, 1650 and 1630 cm^{-1} which were attributed to the stretching frequencies of the hydroxyl group of water of crystallisation, carbonyl (amide) function and C=N bond, respectively. The E.I mass spectrum had a base peak at 466 daltons due to M^++2 ion. A peak at 233 daltons, which half of the (466; M^++2), was also the supporting evidence for the symmetrical structure of (321). The FAB (NOBA) spectrum for (321) showed the presence of an M+H peak at 465 daltons, and an accurate mass measurement on this peak gave 465.17740, and the calculated value for $C_{24}H_{25}N_4O_6$ is 465.17439.

Compound (315) may exist in its tautomeric form (315a), because in nitrogen containing compounds, the hydrogen atom of an α-methyl group is quite acidic, hence, in the formation of (321), it is supposed that two molecules of (315a) react intermolecularly in a Michael type addition reaction to produce an enol which can easily tautomerise to its keto form, which has acidic α-hydrogen atoms due to the presence of the adjacent carbonyl function and an electronegative nitrogen atom (Scheme 35).

This compound reacts with acetic anhydride through a six-membered transition state to give a diacetoxy product with the loss of two molecules of acetic acid. Then, the acetyl group is eliminated with the acidic β-hydrogen in an intramolecular reaction through a six-membered transition state to give the α,β-unsaturated carbonyl as well as α,β-unsaturated tertiary amine system, but with the loss of two molecules of



Scheme 35

acetaldehyde. The driving force for the removal of acetaldehyde is probably

(i) the formation of a six-membered transition state,

(ii) the formation of α,β-unsaturated conjugated system

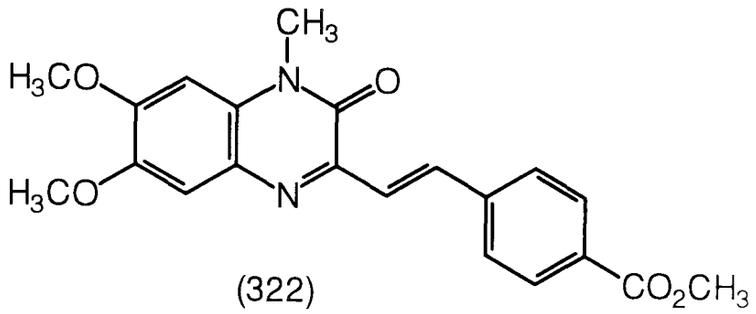
(iii) the acidic nature of the β-hydrogen in the acetoxy intermediate,

(iv) the loss of steric hindrance due to the removal of a molecule of acetaldehyde.

(v) the formation of a conjugated system.

5.4 Preparation of 6,7-Dimethoxy-4-methyl-2-(4'-methoxycarbonylphenylvinyl)-3(4H)-quinoxalinone (322)

The acid (320) was converted to its methyl ester (322) by treatment with dimethyl sulphate and anhydrous potassium carbonate in acetone.



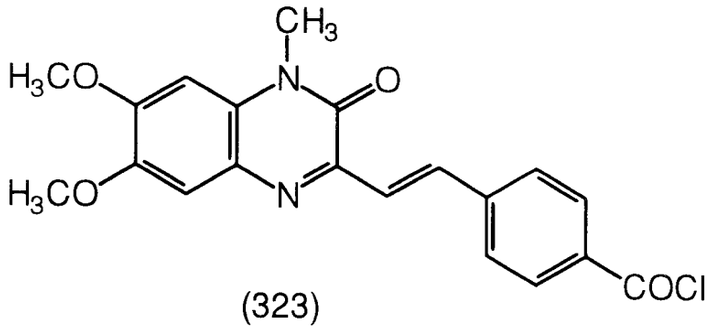
(322)

The ^{1}H NMR spectrum of the ester (322) showed a singlet at 3.90 ppm due to the methyl ester function, in addition to the other expected peaks. The IR spectrum showed two peaks at 1710 and 1650 cm^{-1} attributable to the carbonyl groups of ester and amide functions, respectively. The mass spectrum of (322) showed the molecular peak at 380 daltons which agreed with the molecular formula. Two peaks at 365 and 321 daltons were probably due to the loss of one methyl and one methoxycarbonyl, respectively.

5.5 6,7-Dimethoxy-4-methyl-2-vinylphenyl-3(4H)-quinoxalinone-4'-carbonyl Chloride (323)

There are various examples of fluorescent derivatising agents in the literature.[192-197,238-241] Compound (320) proved to have excellent fluorescence properties when compared to several other reagents including (261). The latter gave blue fluorescence only under UV light, with λ_{exc} = 401 nm and λ_{em} = 473 nm in acetonitrile, hence it was thought that (323) (λ_{exc} = 437 nm and λ_{em} = 503 nm) might be a useful derivatising agent for amines and alcohols. For this purpose, (320) was converted into its acid

chloride (323), by reaction with thionyl chloride for only 20 min to give yellow crystals of (323).

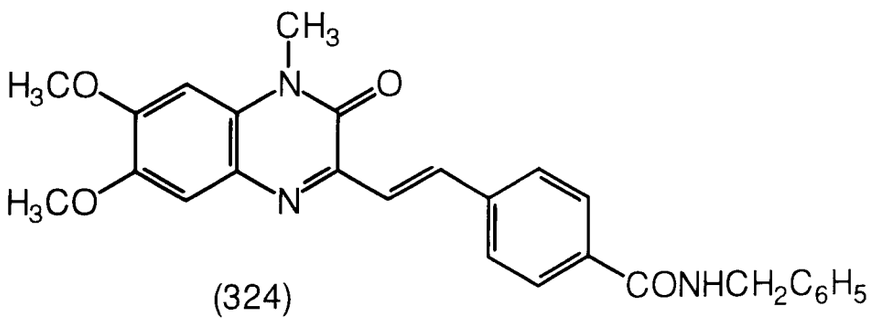


(323)

The structure of (323) was determined from its spectra. The IR spectrum showed strong absorptions at 1740 and 1655 cm^{-1} due to the carbonyl group of the acid chloride and amide group, respectively. The ^{1}H NMR spectral data also confirmed the structure of (323). The mass spectrum showed the presence of the molecular ions at 386 and 384 daltons in the relative abundance ratio of 1:3 due to the ^{37}Cl and ^{35}Cl isotopes, respectively. Moreover, a peak at 379 daltons was probably due to the loss of a methyl group. The elemental analysis also indicated the presence of chlorine and the data was in agreement with the molecular formula $C_{22}H_{17}N_{24}O_4Cl$.

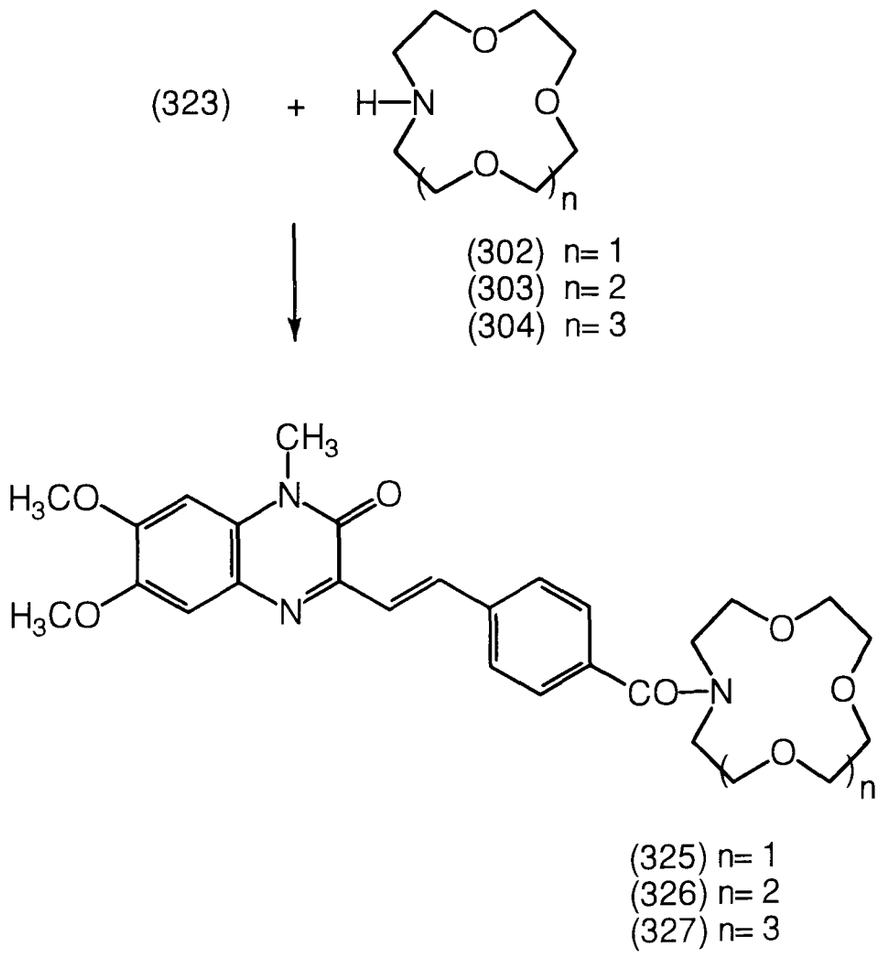
5.5.1 Preparation of Derivatives of 6,7-Dimethoxy-4-methyl-2-vinylphenyl-3(4H)-quinoxalinone-4'-carbonyl Chloride (323)

Further confirmation of the structure of (323) and evidence of its utility as a fluorescence derivatising agent was obtained by the preparation of its derivatives (324)-(327) with benzylamine and monoazacrown ethers separately.



(324)

The structure of compound (324) was confirmed firstly by the presence of peaks at 3300, 1655 and 1635 cm^{-1} attributable to the stretching frequencies of the N-H bond and C=O bonds of the two amide groups respectively. The N-H and methylene groups were coupled and appeared as a triplet at 6.42 ppm and doublet at 4.66 ppm, respectively. The phenyl ring of benzylamine gave a multiplet (7.38-7.29 ppm). The positions of the rest of the peaks were consistent with those obtained from related compounds containing the styryl group. The mass spectrum of this amido derivative (324) showed a molecular ion peak at 455 daltons, which indicated the formula $C_{27}H_{25}N_3O_4$.



Scheme 36

The highly fluorescent nature of compounds (320) and (323) encouraged to investigate their utility as fluorescent chelating agents or fluoroionophores. A series of monoazacrown ethers having different ring sizes (12-crown-4) (302), (15-crown-5) (303) and (18-crown-6) (304), were used to obtain the respective fluoroionophores (325)-(327)

by reaction with (323) in acetonitrile (Scheme 36). In all the cases, the solvent was evaporated *in vacuo,* and the resulting compounds (325)-(327) were separated on preparative t.l.c plates, using a mixture of ethyl acetate and petroleum ether (b.p. 40-60° C) in a ratio of 4:1 to remove the hydrolysed acid (320), and then crystallised from a mixture of methanol and dichloromethane (8:1) to give 61-68 % yield.

Compounds (325)-(327) were characterised by their spectroscopic data and the elemetal analysis which showed the peaks for carbonyl (C=O) of the amide groups in the range of 1655- 1645 cm^{-1}. In the ^1H NMR spectra the methylene protons of the crown ether produced multiplets in the range of 3.80-3.56 ppm. Two doublets (J = 16-16.4 Hz) which appeared at 8.00 and 7.72 ppm were due to the α- and β-vinyl hydrogen atoms, respectively. The 3'-, 5'- and 2'-, 6'-hydrogen atoms of the phenyl group gave rise to two doublets (J = 8.8-8.3 and 8.3-7.8 Hz) in the range of 7.70- 7.65 and 7.42-7.32 ppm, respectively, while the 5- and 8- hydrogens produced singlets at 7.33-7.27 and 6.71-6.66 ppm, respectively. The 6- and 7-OCH_3 group protons gave singlets in the range of 4.04-4.00 and 3.99-3.95, respectively, whereas the singlets in the range of 3.76-3.75 was attributable to the N-methyl group. The elemental analysis and mass spectra were in agreement with the expected molecular formulae $C_{28}H_{33}N_3O_7$, $C_{30}H_{37}N_3O_8$ and $C_{32}H_{41}N_3O_9$ for (325), (326) and (327), respectively.

DISCUSSION

6 FLUORESCENCE

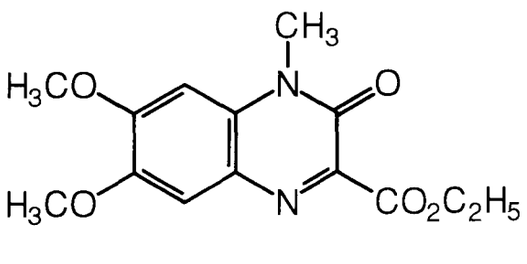
Fluorescence spectroscopy is widely used in various fields of chemistry, biology and medicine in particular due to the high sensitivity and selectivity of the method. Also there is considerable interest in fluorescence techniques for trace metal detection, and for the recognition and measurement of metal components in various systems, especially in biological materials.[261,262] The introduction of metal chelating groups into the structure of fluorescent dyes is designed to produce derivatives that undergo changes in fluorescence intensity or wavelength upon formation of the complexes, thus producing a metal ion detection and quantitative analysis.

More recently, fluoroionophores consisting of fluorophores linked to a crown ether, i.e. ionophores able to complex ions, offered a new powerful tool of investigation because a large change in the photophysical properties may be observed upon metal ion binding.[209,215]

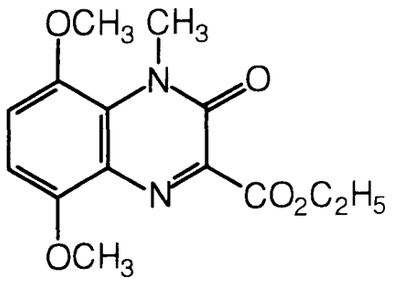
Application of these compounds to the recognition and measurement of metal cations in solution at low concentration have been reported.[209,214,263]

6.1 Fluorescence of 6,7-Dimethoxy-4-methyl-3(4H)-quinoxalinone-2-carboxylic acid and its Derivatives

The high value of the quantum efficiency (Φ_f) of (290) (Φ_f = 0.38 and 0.42 in dichloromethane and methanol, respectively) led to think that the isomer (296) might



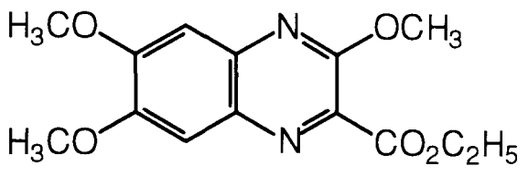
(290)



(296)

also be equally fluorescent. Hence, (296) was prepared by the methylation of (140) but surprisingly it was not fluorescent. The high value of Φ_f (Table 2) for (290) may be

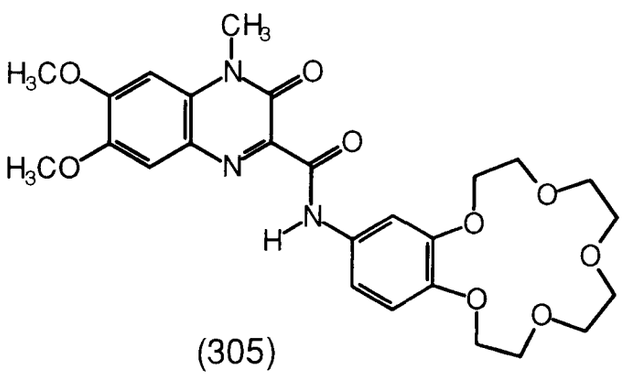
explained as due to the totally different charge distribution[264] caused by the *p*-dimethoxy groups in (296) compared to that caused by the *o*-dimethoxy groups in (290). This seems to be the only likely significant difference between (290) and (296). Further evidence for the role of electron distribution in fluorescence came from a study of the O-methylated isomer (292) (Φ_f = 0.9) of compound (290). The low fluorescence quantum efficiency for (292) may be caused by the lack of stabilisation of the first excited[265] state by the 3-CO group which does occur for the N-methylated isomer (290).



(292)

The highly fluorescent nature of (290) encouraged to use this reagent for the preparation of some fluoroionophores and podands and to study their complexation with alkali and alkaline earth metal ions.

Firstly, aminobenzo-18-crown-6 (301) was used to prepare (305) by treating the crown compound (301) with (261), but the product (305) was not fluorescent. Iwata et al.[196] have found the similar results when phenol was treated with (261) to give an ester.



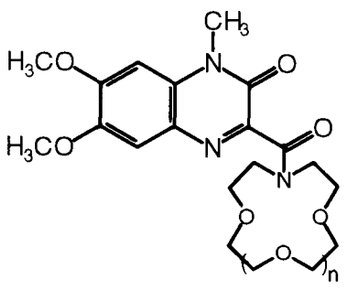
(305)

However, here the presence of the phenyl group might be responsible for the lack of visible emitted light. It was thought that presence of the N-H group might be responsible for the non-fluorescent nature of (305). However, when benzylamine was

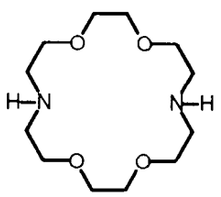
treated with the acid chloride (261), the resulting amide was highly fluorescent (Φ_f = 0.29). Hence, the presence of the N-H group was not the cause of the non-fluorescent nature of (305).

6.1.1 Fluorescence of the Derivatives of the 6,7-Dimethoxy-4-methyl-3(4H)-quinoxalinone-2-carboxylic Acid Containing a Crown Ether Unit

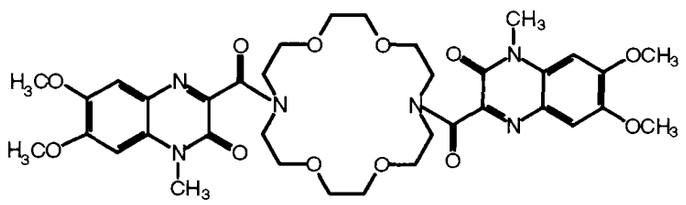
Azacrown ethers having different cavity sizes, i.e. 12-crown-4 (302), 15-crown-5 (303) and 18-crown-6 (304) were used to prepare the fluoroionophores (306)-(308). Diaza-18-crown-6 (309) was used to prepare the fluoroionophores (310) containing two fluorophores.



(306) n = 1
(307) n = 2
(308) n = 3



(309)



(310)

The fluorescence quantum yields of the compounds (306)-(308) and (310) were measured separately in solution using solvents of different polarity, i.e. dichloromethane and methanol. The latter is also capable of hydrogen bond formation (Table 3)

In the cases of fluoroionophores (306)-(308) containing monoazacrown ether, the fluorescence quantum yield in methanol was in the range of 0.19-0.25, whereas in dichloromethane it was lower, in the range of 0.07-0.08 (Table 2). In methanol, due to higher polar nature and tendency to form hydrogen bonds, the π-π^* transitions becomes stablised (lower in energy) in the excited state compared to the ground state stabilisation,

hence the compound emits at longer wavelength (λ_{em} = 469 nm). On the other hand, dichloromethane has relatively low polarity and is unable to provide the stabilisation of π-π^* excited state, so the compound in solution emits light at relatively lower wavelength (λ_{em} = 454 nm) with low quantum efficiency (Table 3). A change in cavity size makes no remarkable differences in the fluorescence quantum yield when the compound are in dichloromethane. However, a slight tendency to increasing Φ_f values with increasing cavity size was seen in methanol (Table 3)

The low quantum yield of (306)-(308) compared to the parent (288) and (292), might be explained on the basis of quenching due to an intramolecular interaction[263] in (306)-(308), which is not possible in the parent compound.

The fluorescence quantum yield of fluoroionophore (310), containing two fluorophores attached at the two nitrogen atoms of diaza-18-crown-6 (309) was measured in methanol (Φ_f = 0.21) and dichloromethane (Φ_f = 0.11) (Table 3). The low

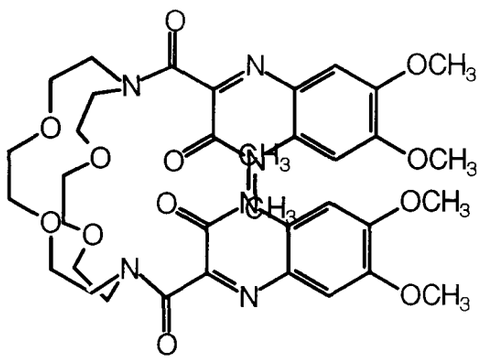
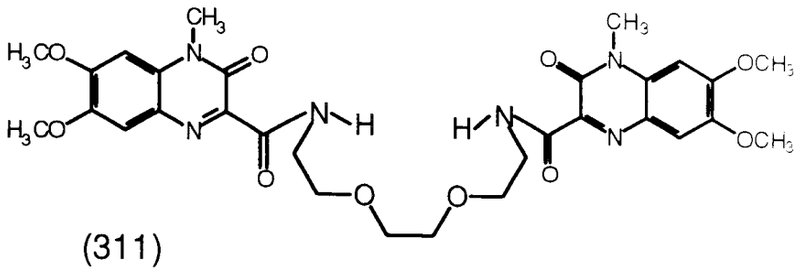


Fig. 13 A simple representation of the crowded structure of the diaza crown ether (310)

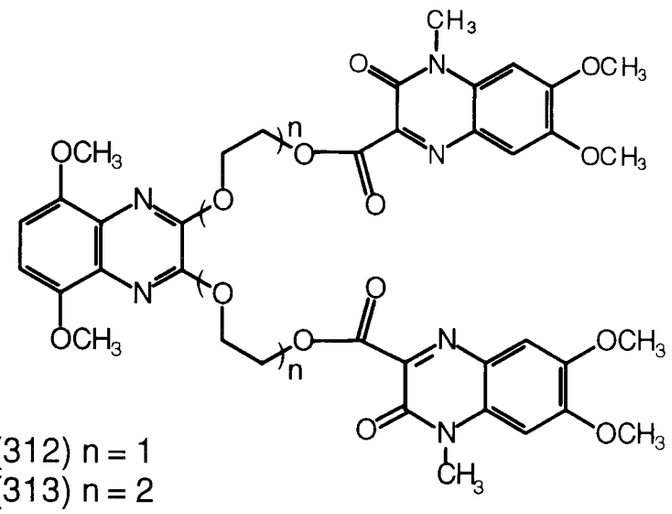
quantum yield of (310) in dichloromethane might be due to the self quenching of the two dimethoxyquinoxaline moieties, because they come close enough together (Fig 13), as shown for a nearly similar fluoroionophore reported in literature.[263]

6.1.2 Fluorescence of the Podands

The podands (open chain polyethers) are not frequently reported in the literature, and examples were prepared having fluorophores attached at ends of the chains (311)-(313).



(311)



(312) n = 1
(313) n = 2

The podand (311) was not fluorescent in methanol but it was slightly fluorescent (Φ_f = 0.09) in dichloromethane (Table 4). The non-fluorescence in methanol may be due to:-

(i) The formation of helical structure (Fig. 14 a), as in proteins, where there are intramolecular hydrogen bonds.

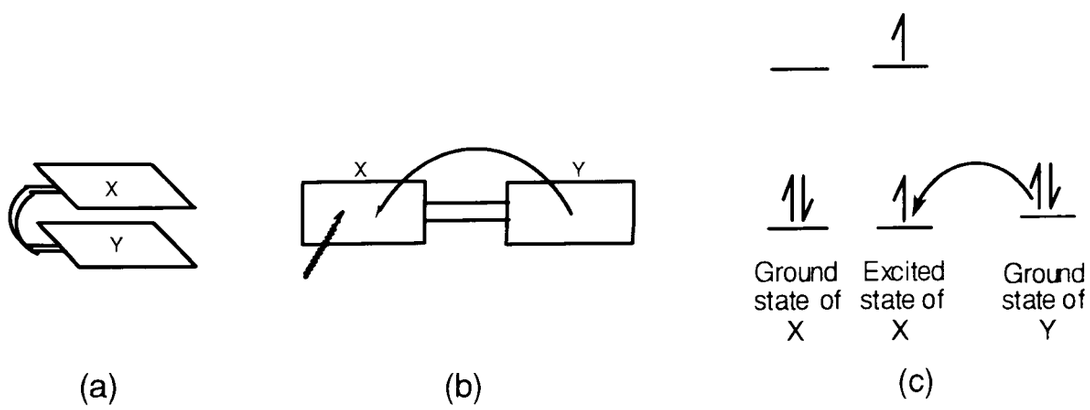


Fig 14 (a) A helical structure of the podand (311). (b) and (c) showing the photoinduced-electron transfer (PET) process in (311).

(ii) The formation of an exciplex,[266,267] where one electron from one fluorophore (Y) moves to the resultant partially filled orbital of the second fluorophore (X) by excitation of its electron from the ground state to its excited state; photoinduced-electron transfer (PET)[209] (Fig. 14b and c). Hence, the excited state loses its energy in a non-radiative way.

(iii) Some indirect indication for the presence of a helical type structure (Fig. 14a) was found in the observation of that (310), where two fluorophores are far away from each other, is fluorescent. In this compound, the PET process is not possible and energy is lost in a radiative way.

The podands (312) and (313) produced an entirely different result from that seen with (311) (Table 4). Here, the fluorescence quantum yields of both podands were found to be much higher (Φ_f = 0.36) in methanolic solution than in dichloromethane solution (Φ_f = 0.09). The explanation may be due to the difference in functional groups, i.e. ester and amide, there being less chance of intramolecular hydrogen bonding in the former case than the later and, therefore, perhaps less chance of a helical structure in the former case. However, in dichloromethane it may be due to lower polarity of the medium, the molecule prefering to be in a 'crowded structure' which results in the quenching of the fluorescence.[263,266,267]

6.1.3 Complexation of the Derivatives of 6,7-Dimethoxy-4-methyl-3(4H)-quinoxalinone-2-carboxylic Acid Containing a Crown Ether Unit

The complexation study of the fluoroionophores (306)-(308) and (310) was carried out in the dichloromethane, using perchlorates of Li^+, Na^+, K^+, Mg^{++}, Ca^{++} and Ba^{++} ions. The spectral data for the complexation of fluoroionophores (306)-(308) and (310) showed that the maximum fluorescence quantum yield was obtained on complexation with only those alkali and alkaline earth metals whose ionic size corresponded to the cavity size of the ionophores[268] (Table 5). Hence, Li^+, Na^+ and K^+ ions gave maximum fluorescence quantum yields when the cavity size fitted the ionic radius, e.g., Li^+ in (306) gave Φ_f = 0.24 whereas Na^+, K^+, Mg^{++}, Ca^{++} and Ba^{++} produced the Φ_f values 0.17, 0.10, 0.13, 0.13 and 0.14, respectively. Similar results were obtained for (307) and (308), where the maximum quantum yield was for Na^+ (Φ_f = 0.26) and for K^+ (0.33), respectively (Table 5 and 6).

A marked bathochromic shift in the excitation wavelength (3-13 nm) as well as in fluorescence emission wavelength (2-19 nm) was observed on complexation of (306), whereas fluoroionophores (307) and (308) showed this shift to a lesser extent both in excitation (1-5 nm) and emission (0-3) maxima in their spectra (Table 5).

A large hyperchromic effect was observed in the excitation as well as emission maxima of all these fluoroionophores (306)-(308) on complexation with all these alkali and alkaline earth metals [Fig. (16)-(19)].

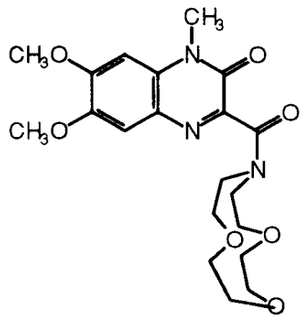
On complexation with metal ions, the nitrogen atom of the ionophores becomes slightly positively charged, which in turn creates an increased positive charge at the carbon atom of the carbonyl group. This increased electron deficiency of the 'acceptor part' of the molecule is responsible for the extra electron pull from the donor part of the molecule, thus the dipole moment of the whole molecule is increased. This effect is responsible for the extra stabilisation, i.e. lowering of the energy level of the excited state. Hence, fluoroionophores (306)-(308) absorb and emitt their energy at relatively longer wavelength.[201,210]

The higher fluorescence quantum yield of the complexed fluoroionophores (306)-(308) with metal ions as compared to the quantum yields of the respective free ligands (Table 5) was due to nearly complete destruction of the intramolecular interaction between the ionophore and the fluorophore of the free ligands, which was thought to be responsible for the quenching of the fluorescence[263] (Table 5).

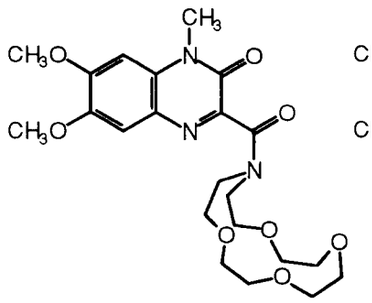
Now the question arises, if there is not any internal quenching of the fluorescence, and moreover, the metal ions are selective for the cavity sizes[268,269] of the ionophores, e.g. Li^+ for 12-crown-4 (302), Na^+ for 15-crown-5 (303) and K^+ for 18-crown-6 (304), why is the fluorescence quantum yield not found to be the same for all these fluoroionophores (306)-(308) on complexation with metal ions? This may be explained by the consideration of the structure of the whole molecule, which suggests that the fluorescence of the complexed fluoroionophores (306)-(308) were mainly controlled by the direct interactions between the bound cation and oxygen atom of the carbonyl groups of the fluorophore.[263]

Stick models of (306)-(308) show that oxygen atom of both carbonyl, amido and exocyclic carbonyl groups, on rotation through C-N bond interacts with the metal ions and thus helps to maintain the ion in the cavity of ionophore.[263]

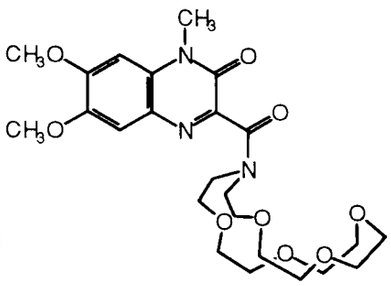
A stick model of (306) shows that the small size of aza-12-crown-4 (302) prevents the oxygen atom of the exocyclic carbonyl group from giving its additional support for the complexation, because this carbonyl group is approximately at a right angle to the 'plane' through the ionophore. Hence, only one carbonyl group (amido) helps to maintain the metal ion in the cavity of the ionophore.



(306)

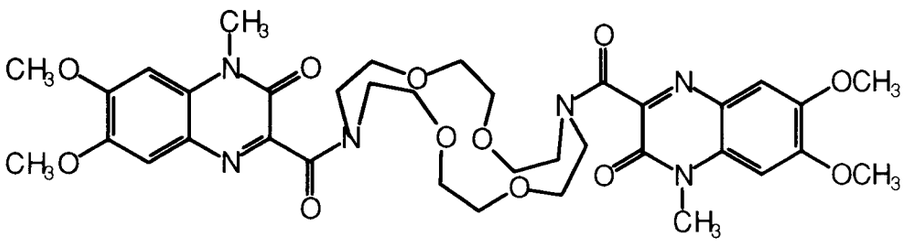


(307)



(308)

On the other hand, in fluoroionophore (308), the oxygen atoms of both carbonyl groups are in a position to prevent the rapid movement of the metal ion from the cavity, because here, the axis of the exocyclic carbonyl group is approximately parallel to the cavity of the aza-18-crown-6 (according to the stick model).



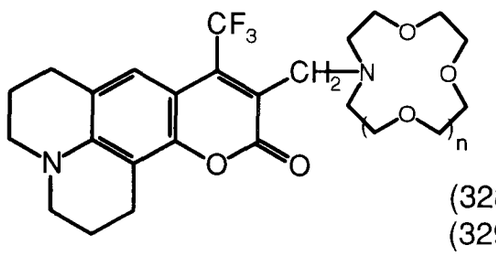
(310)

The maximum quantum yield of complexed (310) occurs with K^+ ion. The ion fits well in the cavity of diaza-18-crown-6 (305) (Table 6). It may be that, in this case, the oxygen atoms of two carbonyl groups on each side (upper and lower) of the diaza-18-crown-6 help the metal ion to remain in the cavity.[263,270]

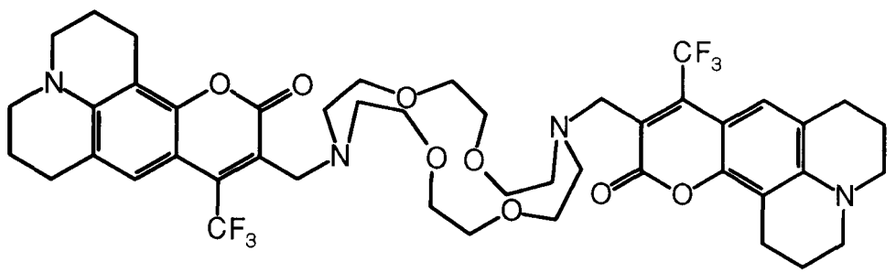
The self quenching of the free ligand (310) due to the interaction of the two dimethoxyquinoxalinone moieties are partially or completely suppressed when the cation fits best into the crown cavity, because the preferred confirmation is likely to be

extended in this case, whereas, it is folded when the cation is smaller than the crown cavity[263] (Table 6).

Recently, Valeur *et al.*[263] reported their work on the effect of cation-binding on the photophysical properties of a coumarin linked to monoaza and diaza-crown ethers (328)-(330). They used a fluorophore in which the donor part is rigid, and where the nitrogen atom can delocalise its pair of electrons up to the acceptor part of the molecule.



(328) n =1
(329) n =2



(330)

This was made more electron deficient by introducing a trifluoromethyl group at the 4-position. It is interesting to compare their results with those reported here, because the differences between the series (306)-(308) & (310) and (328)-(330) are relatively small, i.e. the presence of the nitrogen atom instead of trifluoromethyl group and an extra carbonyl group in place of methylene group, which increases the electron withdrawing character of the acceptor part of the dimethoxyquinoxalinone fluoroionophore. The reported fluorescence quantum yield of (328) and (329) was 0.08, and 0.15 in acetonitrile and these compounds gave the maximum fluorescence quantum yield (Φ_f = 0.17 and 0.19, respectively) on complexation with Na^+. This compares with the quantum yield of Φ_f = 0.24 and 0.26 on complexation of (306) and (308), with Li^+ and Na^+, respectively. The parallel compound (330) had a surprising low fluorescence

quantumn yield (Φ_f = 0.016) which was enhanced to Φ_f = 0.10 on complexation with Ba^{++}, whereas the fluorescence quantum yield of (310) was 0.09 in dichloromethane, and gave the excellent result (Φ_f = 0.41) on complexation with K^+.

Valeur *et al.*[263] explained the increase of fluorescence quantum yield on complexation, on the basis of the involvement of the oxygen atom of the carbonyl group which helps to stabilise the cations in the cavity (Fig 10), but in case of (306)-(308) and (310) the involvement of the oxygen atom of both carbonyl groups is possible. This may be the explanation for the higher fluorescence quantum yields of (306)-(308) and (310) compared to those of (328)-(329) and (330).

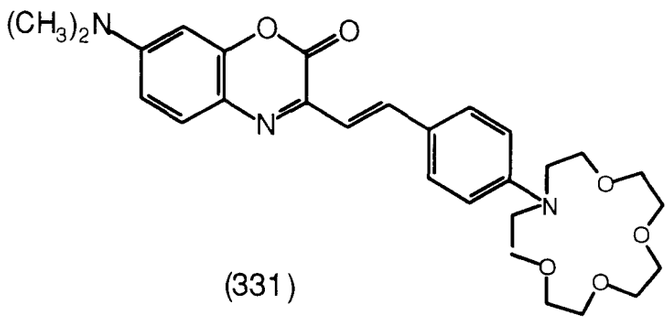
6.1.4 Complexation of the Podands

The complexation of podands (312) and (313) with alkali and alkaline earth metals, produced entirely different results [Fig. (20)-(21)] from the fluoroionophores (306)-(308). A strong bathochromic shift with a hypochromic effect was seen in the complexation of (312) with metal ions except for Na^+ and K^+ ions which produced a hyperchromic effect in the excitation spectra (Table 7). Similarly in the emission spectra, a hyperchromic effect was observed only on complexation with Na^+ and K^+, whereas other metals produced a hyperchromic effect with a slight shift in all cases. The quantum yield was lower than for the free ligand on complexation with metal ions except Na^+ and K^+ (Table 7).

The complexation of Li^+, Na^+, K^+, Mg^{++}, Ca^{++} and Ba^{++} ions with (313) produced a hypochromic effect in all cases, with a bathochromic shift in their excitation spectra, but the magnitude of this red shift was lower (λ_{exc} = 409 nm for Ba^{++}) than that found in when the podand was (312) (λ_{exc} = 430 nm for Ba^{++}). This might be due to high charge density and the size of Ba^{++} ion, which allows the ion to be relatively strongly 'fixed' into the open cavity of (312) but not readily accepted and held in (313). The emission spectra on complexation of (313) produced the same results (Table 7).

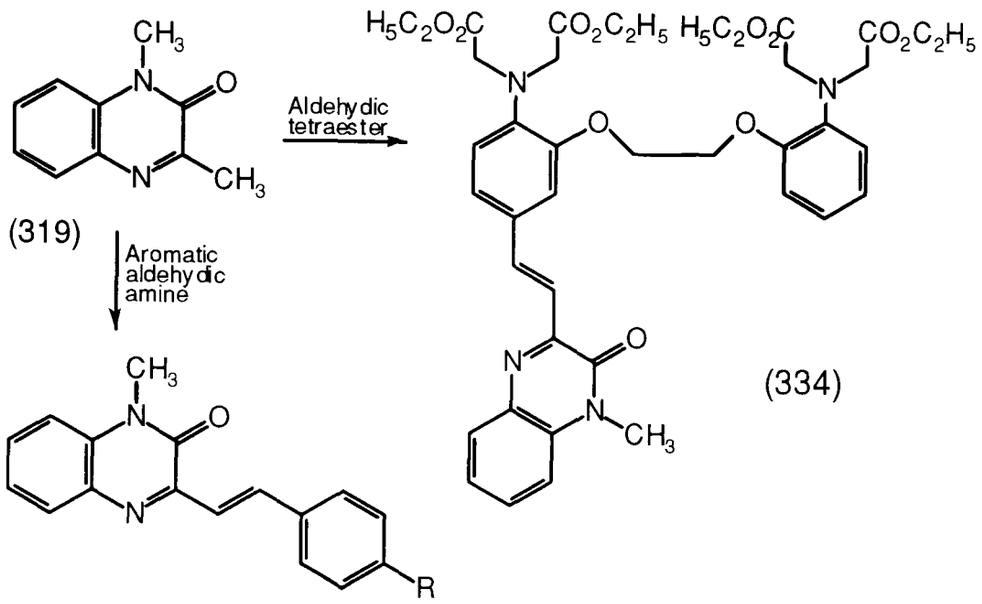
6.2 Fluorescence of the Derivatives of the 6,7-Dimethoxy-4-methyl-2-(4'-carboxyphenylvinyl)-3(4H)-quinoxalinone

Valeur *et al.*[271] also synthesised, and studied, the photophysical properties of some styryl derivatives[140] including crowned styryl derivative (331) of benzoxinones.[271]



(331)

More recently, Cazaux *et al.*[272,273] used the 1,3-dimethylquinoxalinone (319, R = CH_3) to synthesise and characterise the photophysical properties of the styryl derivatives (332) and (333) and the tetraester (334).



(319)

(334)

(332) R = $N(CH_3)_2$

(333) R = CH_3

The excellent fluorescent properties of (306)-(308) and (310) [Fig. (16)-(19)] encouraged to synthesise the styryl derivative of dimethoxy1,3-dimethylquinoxalinone (315) by the condensation of *p*-carboxybenzaldehyde to give (320).

A comparison of the UV spectrum of the acids (288) and (320) showed a bathochromic shift, i.e. λ_{abs} = 412 and 434 nm, respectively (Table 8). The latter compound showed similar fluorescence quantum yields in both solvents; methanol (Φ_f = 0.33) and dichloromethane (Φ_f = 0.34) (Table 8) but a relatively low quantum yield

was observed for (288) in methanol (Φ_f = 0.15) compared to dichloromethane (Φ_f = 0.39) (Table 2).

Similarly a bathochromic shift was observed in the emission spectrum for (320) when compared with that for (288) both in methanol (λem = 503 and 469 nm) and dichloromethane (λ_{em} = 507 and 476 nm) (Table 8 and 2).

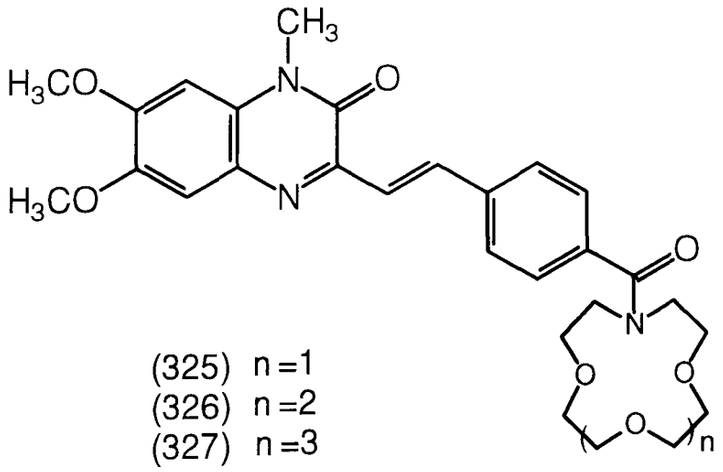
The solution of (320) and its methyl ester (322) produced greenish yellow fluorescence as seen in day light or under UV light, whereas, the solution of (288) was colourless in daylight but produced a bluish fluorescence under UV.

The photophysical properties of (320) and (322) encouraged to make derivatives. Hence, the styryl acid (320) was converted into its acid halide (323), which was found to be more stable than (261) both in the solid state and in solution at room temperature.

The benzyl derivative (324) of the acid chloride (323) produced similar results to those of (320) and (322) (Table 8).

6.2.1 Fluorescence of the Derivatives of the 6,7-Dimethoxy-4-methyl-2-(4'-carboxyphenylvinyl)-3(4H)-quinoxalinone Containing a Crown Ether Unit

The fluoroionophores (325)-(327) were prepared by treating the acid chloride (323) with monoaza crown ethers of different cavity sizes, i.e. aza-12-crown-4 (302), aza-15-crown-5 (303) and aza-18-crown-6 (304).

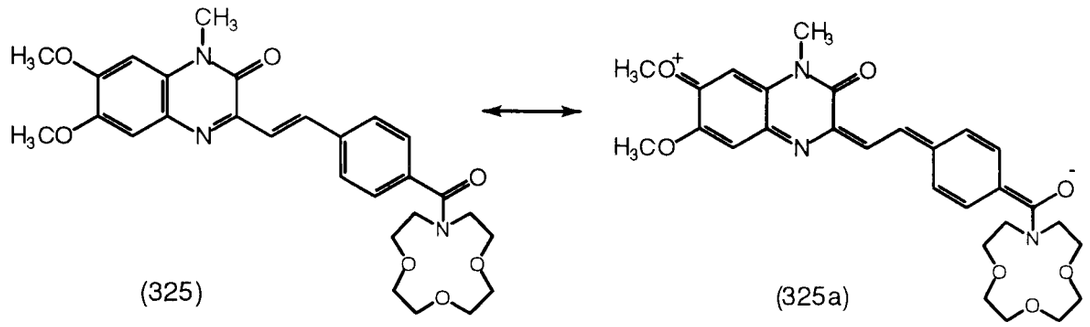


(325) n=1
(326) n=2
(327) n=3

The UV absorption spectra of (325)-(327) showed a bathochromic shift in the absorption maxima, i.e. λ_{abs} = 423, 423 and 424 nm in methanol and 427, 427 and 428 nm in dichloromethane, respectively (Table 9), when compared to the absorption

maxima observed for (306)-(308), i.e. λ_{abs} = 380, 380, and 381 nm in methanol and 378, 379, and 379 nm in dichloromethane, respectively (Table 10). Similarly a large bathochromic shift was observed in the fluorescence emission spectra of (325)-(327) when compared to (306)-(308) (Table 10).

The fluorescence quantum yields were surprisingly high (Φ_f = 0.30-0.34) in methanol and (Φ_f = 0.34-0.38) in dichloromethane for crowned styryl derivatives (325)-(327) as compared with those of crowned non-styryl derivatives (306)-(308) (Table 10),



(325) (325a)

which is probably due to the more extensive delocalisation (325a) of the electron pair of the methoxyl oxygen atom through the phenyl group to the carbonyl of amide group.

6.2.2 Complexation of the Derivatives of the 6,7-Dimethoxy-4-methyl-2-(4'-carboxyphenylvinyl)-3(4H)-quinoxalinone Containing a Crown Ether Unit

The complexation of the fluoroionophores (325)-(327) was done in dichloromethane. A bathochromic shift with a hyperchromic effect was observed in both the excitation and emission spectra on complexation of (325)-(327) with Li^+, Na^+, K^+, Mg^{++}, Ca^{++} and Ba^{++} ions (Table 11).

The marked difference between the fluorescence quantum yields of the free ligands and the complexed ligands which was seen for (306)-(308)(Table 5) was not seen for (325)-(327) (Table 11) [Fig. (22)-(23)]. The large distance between the nitrogen atom of the ionophore unit and the dimethoxyl group might be responsible for this difference in behaviour. On complexation with metal ion a partial positive charge is created at the amide nitrogen atom,[201] and this may be in a position to affect the electronic distribution in the fluorophore of (306)-(308) but, due to the extended

conjugation, and long distance, may not be able to affect the electronic distribution of the fluorophore of (325)-(327) (Fig. 15). This idea is strengthened by the observation of the poor correlation between the ionic size and the cavity size on the one hand and fluorescence quantum yield (Table 12) on the other for (325)-(327), whereas the correlation is strong for the complexes of (306)-(308) (Table 6).

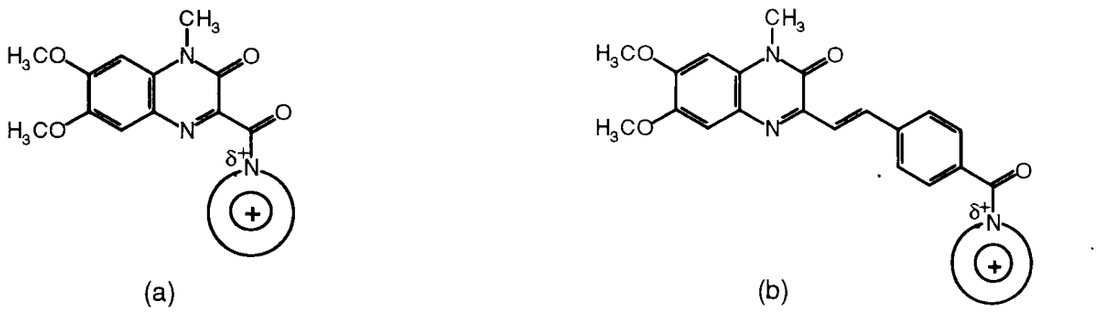


Fig. 15 Metal ion complexation of the fluoroionophores (a) without styryl group and (b) containing a styryl group.

Consideration of compounds having the same crown ether, but from the styryl and non-styryl quinoxaline acid series, showed that the fluorescence quantum yield decreased on complexation of (325) with metal ions in the order $Ca^{++}>K^{+}>Mg^{++}>Na^{+}>Li^{+}>Ba^{++}$, whereas in (306) the order was $Li^{+}>Na^{+}>Ba^{++}>Mg^{++}>Ca^{++}>K^{+}$. Again for (326), the order was $Ca^{++}>Na^{+}>Mg^{++}>Li^{+}>K^{+}>Ba^{++}$, but for (307) the ranking was $Na^{+}>Ca^{++}>Ba^{++}>Mg^{++}>Li^{+}>K^{+}$. The fluorescence quantum yields of (327) on complexation with Li^{+}, Na^{+}, K^{+} or Mg^{++} were approximately same (Φ_f = 0.38), but were higher with Ca^{++} (Φ_f =0.43) and lower with Ba^{++} (Φ_f =0.33). This showed that in the series of fluoroionophores containing a styryl group (325)-(327), the metal ion with high charge density, e.g. Ca^{++} causes a major affect on the photophysical properties.

A change (bathochromic shift) in the fluorescence emission maxima was seen (1-15 nm) on complexation of (325)-(327), whereas this effect was low (0-3 nm) in their excitation maxima. Valeur[271] has reported a hypsochromic shift on complexation of (331) with alkali and alkaline earth metals , whereas, a bathochromic shift was observed on complexation of (325)-(327) in this work. The latter is the more desirable effect in photophysical studies of fluoroionophores.[201] Moreover, it was possible to use the fluoroionophores (306)-(308) and (310) or (325)-(327) to detect a lower concentration

of alkali and alkaline earth metal ions than has been reported for the use of (331). The concentration range of the metal ions (Table 5) for the complexation to produce maximum fluorescence quantum yield was 5 x 10^{-7} to 10^{-4} M in 7.5 x 10^{-7} M solution of fluoroionophores (306)-(308) and (310), whereas, it was 5 x 10-5 to 10^{-3} M in 4.5 x 10^{-7} M solution of fluoroionophores (325)-(327) (Table 11). The concentration range of the metal ions for the complexation to produce maximum fluorescence quantum was reported to be 10^{-4} to 2 x 10^{-2} M in 1.5 x 10^{-6} M solution of the (331).[271]

6.3 Effect of the acid

A study of the effect of the addition of hydrochloric acid on UV absorption spectrum of (326) in dichloromethane showed a marked red shift from λ_{abs} = 427, 337 nm to λ_{abs} = 510, 406 nm with an obvious change in the colour (green to orange-red) of the solution (Fig. 24). But surprisingly, this effect was not observed on changing the solvent from dichloromethane to methanol (Fig. 25). A possible explanation was that protonation of the solvent occured in the latter case rather than the protonation of the compound, whereas, in dichloromethane, (326) was the only species available for protonation. This change in colour and the red shift in the UV absorption spectrum was not seen in either solvent for (307). This difference in behaviour of (307) and (326) might be due to the extended conjugated system in (326). Hence, it appeared that the compounds containing conjugated system, were acid sensitive in non-hydroxylic solvents.

GENERAL EXPERIMENTAL TECHNIQUES

Synthesis

All melting points were determined using an Electrothermal Digital apparatus and are uncorrected.

Infrared spectra were recorded using a Perkin-Elmer 1420 ratio recording spectrometer in the range of 600-4000 cm^{-1} and calibrated against a polystyrene film. The spectra were recorded as potassium bromide discs.

Proton nuclear magnetic resonance spectroscopy was carried out using a Varian CFT-20 (80 MHz) or a Jeol JNM-FX200 (200 MHz)and the spectra were recorded for solutions in deuterated solvent relative to tetramethylsilane (internal standard). Resonances are reported as ppm for the chemical shift from tetramethylsilane at 0 ppm.

Low resonance electron impact mass spectra were recorded using a MS902 AEI mass spectrometer. The accurate mass determinations and fast atom bombardment (FAB) spectrum were provided by the SERC Mass Spectrometry Service Centre, University College of Swansea.

Micro-analytical determinations were carried out by Medac Ltd. on a Control Equipment Corporation Model 240 XA (static combustion system) and a Carlo Erba 1106 (dynamic combustion system).

Thin layer chromatography (t.l.c) was carried out on commercial silica gel plates [Camlab, 0.25 mm with fluorescent indicator UV_{254}]. Column chromatography was carried out on Kieselgel 60 (230-400 mesh ASTM). Columns were generally packed dry and developed under light positive pressure.

Solvents were redistilled before use.

Optical Measurements

UV spectra were recorded in the range 200-600 nm using a Perkin-Elmer Lambda 9 UV/VIS/NIR spectrophotometer in quartz cells using dichloromethane or methanol (HPLC grade) as solvent.

Excitation and fluorescence emission spectra were obtained at room temperature (25^0 C) using a LS 50B Luminescence spectrometer. Fluorescence emission spectra were recorded with 10 nm excitation and emission bandwidth for all solutions with optical densities in the range of 0.01 - 0.012 A at the excitation wavelength in silica cells (10 mm pathlength). Fluorescence quantum yields were calculated by comparison of the integral of the emission spectrum with the corresponding integral for quinine sulphate in perchloric acid (0.1 M) of equal absorbance, i.e. with optical density 0.01 A. The standard solution was taken to have a quantum yield of 0.59. The solutions of the metal ions were prepared by dissolving the metal perchlorate (AnalaR grade) in a few drops of methanol and diluting to a known volume with dichloromethane. These solutions were used immediately.

EXPERIMENTAL

Preparation of 6,7-Dimethoxy-4-methyl-3(4H)-quinoxalinone-2-Carbonyl Chloride (261)

Preparation of ethyl 6,7-dimethoxy-3(4H)-quinoxalinone-2-carboxylate (289)

A mixture of 1,2-diamino-4,5-dimethoxybenzene monohydrochloride (135) (1.0 g, 4.9 mmol), ethyl 2-ketomalonate (1.0 g, 5.75 mmol) and absolute ethanol (50 cm^3), was heated for 2 h in a boiling water-bath. The reaction mixture was cooled in an ice-bath, the solid filtered off, and the crude product was crystallised from ethanol to gave ethyl 6,7-dimethyl-3(4H)-quinoxalinone-2-carboxylate (289) (0.938 g, 69 %), m.p. 248-250° C (lit.,[247] m.p. 249-250° C).

Methylation of ethyl 6,7-dimethoxy-3(4H)-quinoxalinone-2-carboxylate (289)

Preparation of diazomethane

N-Methyl-N-nitrosotoluene-*p*-sulphonamide (2.14 g) in ether (30 cm^3) was cooled in an ice-bath, and a cold solution of potassium hydroxide (0.4 g in 10 cm^3 of 96 % ethanol) was added. After 5 min, the ethereal diazomethane solution was distilled off (b.p. 40-45° C) and collected.

Methylation of (289) using diazomethane

A stirred cold solution of (289) (0.5 g) in dry methanol (100 cm^3) was treated with ethereal diazomethane solution (20 cm^3) in small portions. The reaction was monitored by t.l.c and after the completion of the reaction, the solvent was removed, and the crude mixture was separated by column chromatography [(ethyl acetate/petroleum spirit (b.p. 40-60° C) (1:1)]. The first compound eluted, was recrystallised from ethyl acetate-dichloromethane (9:1) as ethyl 3,6,7-trimethoxyquinoxaline-2-carboxylate (292) (0.245 g, 47 %) m.p. 131-132° C; IR(KBr) ν_{max} 3100, 3010 (H-aryl), 2990, 2850 (H-aliph), 1720 (C=O), 1630 (C=O), 1560, 1500, 1430, 1370, 1340, 1230, 1165, 1100, 1020, 920, 845, 810, 760, 685, 610 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 7.37 (s, 1H, 8-H), 7.15 (s, 1H, 5-H), 4.48 (q, 2H, 2-COO$\underline{CH_2}CH_3$), 4.11 (s, 3H, 3-OCH_3), 4.03(s, 3H, 6-OCH_3), 3.98 (s, 3H, 7-OCH_3), 1.44 (t, 3H, 2-COOCH$_2\underline{CH_3}$); MS, m/z(r.i.) 294(2),

293(16), 292(100, M^+), 277(M^+-CH_3), 247(17, M^+-C_2H_5), 220(36), 219(46; M^+-$COOC_2H_5$), 205(11), 204(17), 190(62), 189(55), 149(4). (Found: C, 57.64; H, 5.54; N,9.60. $C_{14}H_{16}N_2O_5$ requires C, 57.53; H, 5.52; N, 9.58 %). The second compound eluted from the column chromatography was crystallised from methanol-dichloromethane (4:1) as bright yellow ethyl 6,7-dimethoxy-4-methyl-3(4H)-quinoxalinone-2-carboxylate (290) (0.234 g, 45 %), m.p. 258-260° C (lit.,[247] m.p.259-260° C); IR(KBr)ν_{max} 3090, 3010 (H-aryl), 2960, 2840 (H-aliph), 1730 (C=O, ester), 1650 (C=O, amide), 1620 (C=N), 1585 (C=C), 1520, 1465, 1400, 1340, 1290, 1235, 1175 (C-N), 1135 (C-O), 1090, 1010, 920, 860, 750, 660 cm^{-1}; ^1H NMR (80 MHz, $CDCl_3$) δ 7.34 (s, 1H, 8-H), 6.64 (s, 1H, 5-H), 4.47(q, 2 H, 2-COO$\underline{CH_2}CH_3$), 4.02 (s, 1H, 6-OCH_3), 3.92 (s, 3H, 7-OCH_3), 3.71(s, 3H, N-CH_3), 1.43 (t, 3H, 2-COOCH$_2\underline{CH_3}$); MS, m/z(r.i.) 294(3), 293(15), 292 (100, M^+), 277(11, M^+-CH_3), 247(15, M^+-OC_2H_5), 220(45), 219(13; M^+-$COOC_2H_5$), 190(11), 189(7), 177(14), 149(7), 57(3), 41(3). (Found: C, 57.48; H, 5.52; N, 9.60. $C_{14}H_{16}N_2O_5$ requires C, 57.53; H, 5.53; N, 9.58 %).

Methylation of (289) using dimethyl sulphate

A mixture of (289) (0.1 g, 0.36 mmol), anhydrous potassium carbonate (1.0 g) and acetone (50 cm^3) was stirred for 15 min, then dimethyl sulphate (2.0 cm^3) was added dropwise, and the reaction mixture maintained at 40°C for 4 h, followed by boiling under reflux for 0.5 h. The reaction mixture was poured into water, the resultant precipitate filtered off, and the two component mixture was separated on preparative t.l.c plates(20 x 20 cm^3) [ethyl acetate/petroleum spirit (b.p. 40-60° C) (4:1)]. The first component eluted (0.012 g, 11%), was characterised (m.p. 130-131° C) as ethyl 3,6,7-trimethoxyquinoxaline-2-carboxylate (292) and the second component (0.041 g, 39 %) m.p. 259-260° C (lit.,[247] m.p. 259-260° C) as ethyl 6,7-dimethoxy-4-methyl-3(4H)-quinoxalinone-2-carboxylate (290).

Methylation of ethyl 5,8-dimethoxy-3(4H)-quinoxalinone-2-carboxylate (140)

Compound (140) (0.5 g, 1.8 mmol) was methylated with dimethyl sulphate using the same method as described above. The resulting crude precipitate was crystallised from ethanol to give yellow ethyl 5,8-dimethoxy-4-methyl-3(4H)-quinoxalinone-2-carboxylate (296) (0.330 g, 63 %) m.p. 168-169°C (lit.,[125] m.p. 168-169° C); IR(KBr)

ν_{max} 3105, 3010 (H-aryl), 2960,2835 (H-aliph), 1750 (C=O, ester), 1650 (C=O, amide), 1605, 1590, 1500, 1465, 1415, 1335, 1285, 1245, 1175, 1100, 1060, 1030, 960, 815, 770, 730, 660, 640 cm^{-1}; ^1H NMR (80 MHz, $CDCl_3$) δ 7.06 (d, 1H, 6-H), 6.67 (d, 1H, 7-H), 4.43 (q, 2H,2-$COO\underline{CH_2}CH_3$), 3.94 (s, 6H, 5- and 8-OCH_3), 3.84 (s, 3H, N-CH_3), 1.40 (t, 3H, 2-$COOCH_2\underline{CH_3}$); MS, m/z(r.i.) 293 (2), 292(7, M^+), 278(100, M^+-CH_3), 263(47), 247(31), 235(58), 231(12), 218(45), 190(19). (Found: C, 57.08; H, 5.43; N, 9.44. $C_{14}H_{16}N_2O_5$ requires C, 57.53; H, 5.52; N, 9.58 %).

6,7-Dimethoxy-4-methyl-3(4H)-quinoxalinone-2-carboxylic acid (288)

The ester (290) (0.5 g, 1.71 mmol) was dissolved in sodium hydroxide solution (3M, 100 cm^3) and stirred for 70 min. After neutralising the reaction mixture with dil. hydrochloric acid, the compound was extracted with dichloromethane (100 cm^3) and washed with water. The combined extract was dried (anhydrous sodium sulphate), the solid filtered off, the solvent evaporated, and the residue crystallised from ethanol to yield yellow 6,7-dimethoxy-4-methyl-3(4H)-quinoxalinone-2-carboxylic acid (288) (0.336 g, 81 %) m.p. 233-234° C (lit.,[247] m.p. 234-236° C).

An Improved Method for the Preparation of 6,7-Dimethoxy-4-methyl-3(4H)-quinoxalinone-2-carbonyl Chloride (261)

4-Amino-5-nitroveratrole (297)

A mixture of 4,5-dinitroveratrole (133) (5.0 g, 22 mmol), palladium charcoal (10 %) (0.5 g), and ethanol (150 cm^3) was shaken under a hydrogen atmosphere at 15-20 lb/in^2 at room temperature for 6 h in a Parr hydrogenator (at 80-90 strokes/min). The mixture was allowed to stand under hydrogen overnight (without shaking), and then the resulting orange-red precipitate was dissolved by additon of acetone (50 cm^3). The catalyst was filtered off, and the filtrate was reduced in volume *in vacuo*. The 4-amino-5-nitroveratrole (297) which separated out was filtered off, and crystallised from ethanol (3.1 g, 71 %) m.p. 170-171° C (lit.,[273] m.p. 171° C).

N-Methyl-2-nitro-4,5-dimethoxyaniline (298)

Sodium hydride (0.26 g, 11.3 mmol) was added to a solution of 4-amino-5-nitroveratrole (297) (2.11 g, 11 mmol) in dry dimethylformamide (40 cm^3) at 0-5°C and the mixture stirred for 10 min before methyl iodide (3.0 cm^3) was added dropwise at the same temperature (0-5°C) during 30 min. Sodium hydride (0.05 g) was added along with methyl iodide (0.5 cm^3) in cases of incomplete reaction. The stirring was continued for 1 h each at ice-bath, and then at room temperature. The reaction mixture was diluted with water (100 cm^3), and cooled. The resulting precipitate was filtered off, washed twice with water, and crystallised from ethanol to yield yellow N-methyl-2-nitro-4,5-dimethoxyaniline (298) (2.16 g, 96 %) m.p. 145-146° C; IR(KBr) ν_{max} 3590, 3390 (N-H), 2950, 2840, 1650, 1590, 1440, 1410, 1365, 1250, 1220, 1060, 995, 890, 860, 830, 790, 755 cm^{-1}; ^1H NMR (80 MHz, $CDCl_3$) δ 8.47 (bs, 1H, N-H disappeared on addition of D_2O), 7.57 (s, 1H, 3-H), 6.12(s, 1H, 6-H), 3.95 (s, 3H, 5-OCH_3), 3.84 (s, 3H, 4-OCH_3), 3.03(d, 3H, N-CH_3 changed into a multiplet on addition of D_2O); MS, m/z(r.i.) 213(11), 212(100, M^+), 198(42), 197(67, M^+-CH_3), 183(30), 150(23), 136(13), 108(31), 66(12). (Found: C, 51.09; H, 5.61; N, 12.98. $C_9H_{12}N_2O_4$ requires C, 50.94; H, 5.66; N, 13.20%).

2-(N-Methylamino)-4,5-dimethoxyaniline monohydrochloride (299)

N-Methyl-2-nitro-4,5-dimethoxyaniline (298) (2.16 g, 10.1 mmol), palladium on charcoal (10 %) (0.5 g) was shaken under an atmosphere of hydrogen at 60 lb/in^2 at room temperature for 4 h. The catalyst was filtered off, the filtrate concentrated to 20 cm^3, and conc. hydrochloric acid (5 cm^3) added. The resulting greyish purple precipitate was filtered off, washed with dichloromethane and crystallised from ethanol to give 2-methylamino-4,5-dimethoxyaniline monohydrochloride (299) (1.87 g, 84 %) m.p. 207-209° C (decomp); IR(KBr) ν_{max} 3410 (NH), 3240,3160 (NH_2), 3000, 2940, 2920, 1600, 1580, 1440,1380, 1150, 1050, 850, 770 cm^{-1}; ^1H NMR (200 MHz, d_6-DMSO) δ 6.98 (bs, 1H, NH, exchanged with D_2O), 6.79 (s,1H, 6-H), 6.77(s, 1H, 3-H), 3.74 (s, 6H, 4- and 5-OCH_3), 3.71 (bs, 2H, NH_2 exchanged with D_2O), 2.57 (s, 3H, N-CH_3); MS, m/z(r.i.) 182 (69, M^+), 167(100, M^+-1CH_3) 152(35, M^+-2CH_3), 124(79, M^+-2CH_3 and N_2). (Found: C, 45.65; H, 6.28; N, 11.59, Cl, 14.48. $C_9H_{15}N_2O_2Cl.H_2O$ requires C, 45.76; H, 6.35; N, 11.83; Cl, 14.83 %)

6,7-Dimethoxy-4-methyl-3(4H)-quinoxalinone-2-carboxylic acid (288)

A solution of 2-methylamino-4,5-dimethoxyaniline monohydrochloride (299) (2.95 g, 13.5 mmol) and 2-ketomalonic acid (1.65 g, 14 mmol) in hydrochloric acid (0.5 M, 100 cm^3) was heated for 2 h in a boiling water-bath. The mixture was basified with sodium hydroxide solution (0.5 M), extracted with dichloromethane (3 x 100 cm^3), the extracts washed with water, dried (anhydrous sodium sulphate), and the solid collected. The solvent was evaporated *in vacuo,* and the residue crystallised from a mixture of methanol and dichloromethane (1:1) to give yellow 6,7-dimethoxy-4-methyl-3(4H)-quinoxalinone-2-carboxylic acid (288) (2.89 g, 81 %). m.p. 233-235° C (lit.,[247] m.p. 234-235° C).

6,7-Dimethoxy-4-methyl-3(4H)-quinoxalinone-2-carbonyl chloride (261)

A solution of 6,7-dimethoxy-4-methyl-3(4H)-quinoxalinone-2-carboxylic acid (288) (1.0 g, 3.8 mmol) in freshly distilled thionyl chloride (20 cm^3) was refluxed for 1 h, and cooled. The precipitate formed on addition of petroleum spirit (b.p. 40-60° C) (50 cm^3), was crystallised from a mixture of benzene and petroleum spirit (b.p. 40-60° C) (9:1) to give orange 6,7-dimethoxy-4-methyl-3(4H)-quinoxalinone-2-carbonyl chloride (261) (0.972 g, 91 %) m.p. 258-261° C (decomp) (lit.,[196] m.p. 261° C).

2,3-(4'-Aminobenzo)-1,4,7,10,13-pentaoxacyclodeca-2-ene[255] (301)

A solution of 2,3-(4'-nitrobenzo)-1,4,7,10,13-pentaoxacyclopentadecane-2-ene (0.5 g, 1.6 mmol) in freshly distilled dimethylformamide (30 cm^3) was shaken for 1 h at room temperature in a Parr hydrogenator, under an atmosphere of hydrogen at a pressure of 25-35 lb/in^2 in the presence of palladium on charcoal (10 %) (0.2 g). After the completion of the reaction, the catalyst was filtered off, and the bulk of solvent was removed by vacuum distillation. Water (50 cm^3) was added, the mixture extracted with chloroform, dried (anhydrous sodium sulphate), and the solvent distilled off. A brown oil remained which solidified upon standing. The solid was dissolved in hot iso-propyl alcohol, and the solution cooled to -10° C to obtain 2,3-(4'-aminobenzo)-1,4,7,10,13-pentaoxacyclodeca-2-ene (301) (0.366 g, 81 %) m.p. 72-73° C (lit.,[255] m.p. 73-74° C).

General Method for the Preparation of the Derivatives of 6,7-Dimethoxy-4-methyl-3(4H)-quinoxalinone-2-Carbonyl Chloride

A mixture of the appropriate amine (0.5 mmol) and sodium hydride (0.52 mmol) in dry benzene (30 cm^3) was stirred for 15 min followed by the addition of the acid chloride (261) (0.51 mmol). The reaction mixture was refluxed for 3-6 h, then washed thoroughly with dil. hydrochloric acid (0.1 M), and finally with distilled water. The dried solution was evaporated *in vacuo* to yield the crude product.

In this way, the following compounds were obtained:-

N-(6,7-Dimethoxy-3-methyl-3(4H)-quinoxalinone-2-carbonyl)-4-aminobenzo-15-crown-5 (305).

The crude product was purified by column chromatography[(ethyl acetate/dichloromethane (20:1)] followed by crystallisation [ethyl acetate/dichloromethane (7:3)] to give the amide (305) (0.169 g, 64 %), m.p. 181-182° C; IR(KBr) ν_{max} 3440 (N-H), 2910, 2850, 1675 (C=O), 1595, 1545, 1500, 1440, 1390, 1230, 1120, 1000, 930, 850 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.66 (d, 1H, *J* = 2.5 Hz, 6'-Ph-H), 7.63 (s, 1H, 8-H), 7.20 (dd, 1H, *J* = 8.8, 2.4 Hz, 5'-Ph-H), 6.87 (d, 1H, *J* = 8.3 Hz, 3'-Ph-H), 6.73 (s, 1H, 5-H), 4.73 (s, 1H, N-H exchanged with D_2O), 4.17 (t, 4H, 5''-,15''-methylene hydrogens), 4.07 (s, 3H, 6-OCH_3), 3.98 (s, 3H, 7-OCH_3), 3.91 (t, 4H, 6''- and 14''-methylene hydrogens), 3.84 (s, 3H, N-CH_3), 3.76 (s, 8H, 8''-, 9''-, 11''- and 12''-methylene hydrogens); MS, m/z(r.i.) 531(9), 530(27), 529(100, M^+), 309(11), 283(21), 247(17), 234(6), 220(13), 219(11), 206(13), 177(43), 15(22), 45(15), 44(9), 43(26). (Found: C, 57.65; H, 5.87; N, 7.62. $C_{26}H_{31}N_3O_9.1/2H_2O$ requires C, 57.99; H, 5.76; N; 7.80 %).

2'-(1,4,7-trioxa-10-azacyclododecan-10-ylcarbonyl)-6'-,7'-dimethoxy-4'-methylquinoxaline-3'(4'H)-one (306)

The crude product was purified by preparative t.l.c [ethyl acetate/dichloromethane (9:1)], followed by crystallisation of the solid from a mixture of ethyl acetate/dichloromethane (4:1) to yield the light yellow amide (306) (0.173 g, 82%) m.p. 124-125° C; IR(KBr) ν_{max} 2920, 2875 (H-aliph), 1655 (C=O), 1635 (C=O), 1590, 1550,

1515, 1460, 1390, 1365, 1300, 1270, 1240, 1130, 1030, 990, 915, 860, 820, 750, 635 cm^{-1}; ^1H NMR (80 MHz, $CDCl_3$) δ 7.24 (s, 1H, 8-H), 6.66 (s, 1H, 5-H), 4.00 (s, 3H, 6-OCH_3), 3.91 (s, 3H, 7-OCH_3), 3.83 (s, 3H, N-CH_3), 3.86-3.49 (m, 16H, methylene hydrogens); MS, m/z(r.i.) 422(9), 421(35, M^+), 284(9), 247(34), 219(28), 191(27), 149(15), 97(51), 83(51), 57(100), 43(49), 41(34). (Found: C, 56.85; H, 6.43; N, 9.91. $C_{20}H_{27}N_3O_7$ requires C, 57.00; H, 6.46; N, 9.97 %).

2'-(1,4,7,10-Tetraoxa-13-azacyclopentadecane-13-ylcarbonyl)-6'-7'-dimethoxy-4'-methylquinoxalin-3'(4'H)-one (307)

The crude product was purified by t.l.c [ethyl acetate/methanol (9:1)] and the solid was crystallised from ethyl acetate/methanol (7:3) to give the yellow amide (307) (0.161 g, 69 %) m.p. 174-175° C; IR(KBr) ν_{max} 3000, 2910, 2840 (H-aliph), 1650 (C=O), 1635 (C=O), 1590, 1545, 1505, 1465, 1390, 1260, 1240, 1125, 1085, 1010, 930, 865, 820, 750, 670, 630 cm^{-1}; ^1H NMR (80 MHz, $CDCl_3$) δ 7.25 (s,1H, 8-H), 6.66 (s, 1H, 5-H), 4.01 (s, 3H, 6-OCH_3), 3.91 (s, 3H, 7-OCH_3), 3.81 (s, 3H, N-CH_3), 3.68-3.51(m, 20H, methylene hydrogens); MS, m/z(r.i.) 467(8), 466(33), 465(100, M^+), 450(3, M^+-CH_3), 435(4), 247(10), 219(4), 57(3), 45(25), 44(21). (Found: 56.66; H, 6.72; N, 8.93. $C_{22}H_{31}N_3O_8$ requires C, 56.76; H, 6.71; N, 9.03 %).

2'-(1,4,7,10,13-Pentaoxa-16-azacyclootadecane-16-ylcarbonyl)-6'-7'-dimethoxy-4'-methylquinoxalin-3'(4'H)-one (308)

The crude product was purified by t.l.c [ethyl acetate/methanol (9:1)] and crystallised from a mixture of ethyl acetate and dichloromethane (7:3) to give the yellow amide (308) (0.160 g, 63 %) m.p. 151-152° C; IR(KBr) ν_{max} 2940, 2860 (H-Aliph), 1640 (C=O), 1615 (C=O), 1585, 1545, 1510, 1465, 1390, 1265, 1140, 1090, 1035, 1015, 940, 870, 830, 750, 670, 640 cm^{-1}; ^1H NMR (80 MHz, $CDCl_3$) δ 7.25 (s, 1H, 8-H), 6.66 (s,1H, 5-H), 4.00 (s, 3H, 6-OCH_3), 3.91 (s, 3H, 7-OCH_3), 3.83 (s, 3H, N-CH_3), 3.74-3.45(m, 24H, methylene hydrogens); MS, m/z(r.i.) 511(70), 509(100, M^+), 333(6), 276(30), 262(54), 247(48), 235(55), 234(41), 220(20), 219(50), 191(36), 149(12), 114(24), 100(45), 86(42), 72(41), 57(65), 56(71), 45(79), 44(20), 41(30). (Found: C, 56.43; H, 6.99; N, 8.14. $C_{24}H_{35}N_3O_9$ requires C, 56.57; H6.92: N, 8.25 %).

General Method for the Preparation of Diamides (310) and (311)

A mixture of the appropriate amine (0.5 mmol) and sodium hydride (1.22 mmol) in dry benzene (30 cm^3) was stirred for 15 min followed by the addition of acid chloride (261) (1.1 mmol). The reaction mixture was refluxed for 3-6 h, then washed thoroughly with dil. hydrochloric acid (0.1 M), finally with distilled water. The dried solution was evaporated *in vacuo* to yield the crude product.

In this way the following compounds were obtained:-

N,N'-Bis[6'-7'-dimethoxy-4'-methyl-3'(4'H)-oxoquinoxal-2'-ylcarbonyl]-1,4,10,13-tetraoxa-7,16-diazacycloctadecane (310)

The crude product was purified by t.l.c [ethyl acetate/methanol (4:1)] followed by crystallisation from ethyl acetate/dichloromethane (9:1) to produce the light yellow diamide (310) (0.298 g, 79 %), m.p. 153-154° C; IR(KBr) ν_{max} 3460(H_2O), 2940, 2890 (H-aliph), 1660 (C=O), 1640 (C=O), 1590, 1550, 1510, 1465, 1390, 1265, 1240, 1120, 1085, 860, 820, 750, 635 cm^{-1}; ^1H NMR (80 MHz, $CDCl_3$) δ 7.26 (s, 2H, 8- and 8'-H), 6.67 (s, 2H, 5-and 5'-H), 4.02 (s, 6H, 6- and 6'-OCH_3), 3.92 (s, 6H, 7- and 7'-OCH_3), 3.69 (s, 6H, 4- and 4'-NCH_3), 3.89-3.49 (m, 24H, methylene hydrogens); MS, m/z(r.i.) 754(13, M^+), 57(4), 44(20), 43(27), 31(18). (Found: C, 55.96; H, 6.15; N, 10.76. $C_{36}H_{46}N_6O_{12}.1H_2O$ requires C, 55.95; H, 6.21; N, 10.88 %).

N,N'-Bis[6'-,7'-dimethoxy-4'-methyl-3'(4'H)-oxoquinoxal-2'-ylcarbonyl]-1,8-diamino-3,6-dioxaoctane (311)

The crude product was crystallised from methanol/dichloromethane (1:1) to obtain the bright yellow diamide (311) (0.205 g, 64 %) m.p. 240-241° C; IR(KBr) ν_{max} 3290 (N-H), 2950, 2890 (H-aliph), 1675 (C=O), 1640 (C=O), 1610, 1555, 1475, 1430, 1405, 1340, 1250, 1210, 1170, 1020, 870, 830, 815, 660 cm^{-1}; ^1H NMR (80 MHz, $CDCl_3$) δ 10.08(s, 2H, NH exchanged with D_2O), 7.10 (s, 2H, 8- and 8'-H), 6.59 (s, 2H, 5- and 5'-H), 4.01 (s, 6H,6- and 6'-OCH_3), 3.81 (s, 3H, 7- and 7'-OCH_3), 3.79-3.75 (m, 12H, methylene hydrogens), 3.68 (s, 6H, 4- and 4'-NCH_3); MS, (r.i.) 641(2), 640(42, M^+) 490(19), 420(53), 278(32), 264(33), 247(54), 234(36), 220(100), 205(36), 191(23), 149(32), 79(12), 44(56), 43(20). (Found: C, 55.98; H, 5.55; N, 12.82. $C_{30}H_{36}N_6O_{16}$ requires C, 56.24; H, 5.66; N, 13.12 %).

General Method for the Preparation of Diesters (312) and (313)

A mixture of the appropriate dihydroxy compound (0.5 mmol) and sodium hydride (1.2 mmol) in dry benzene (30 cm^3) was stirred for 15 min followed by the addition of acid chloride (261) (1.1 mmol). The reaction mixture was refluxed for 3-6 h, then washed thoroughly with distilled water. The dried solution was evaporated *in vacuo*, and the residue was crystallised from a mixture of methanol and dichloromethane (4:1) to yield the product.

In this way, the following compounds were obtained:-

5,8-Dimethoxy-2,3-bis[2-(6',7'-dimethoxy-4'-methylquinoxalin-3'(4'H)-oxo-2'-carbonyloxy)ethoxy]quinoxaline (312) (0.284 g, 71 %) m.p. 226-227° C; IR(KBr) ν_{max} 3450 (H_2O), 2950, 2830 (H-aliph), 1735 (C=O), 1655 (C=O), 1615, 1685, 1540, 1510, 1470, 1450, 1390, 1325, 1275, 1245, 1140, 1085, 1000, 850, 825, 800 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.24 (s, 2H, 8- and 8'-H), 6.77 (s, 2H, 6- and 7-H), 6.62 (s, 2H, 5- and 5'-H), 4.96 (t, 4H, β- and β'-CH_2), 4.87(t, 4H, α- and α'-CH_2), 4.03 (s, 6H, 6- and 6'-OCH_3), 3.93 (s, 6H, 5- and 8-OCH_3), 3.92 (s, 6H, 7- and 7'-OCH_3), 3.69 (s, 6H, N- and N'-CH_3); MS, m/z(r.i.) 524(5), 466(7), 450(6), 438(22), 287(12), 278(100), 264(53), 234(13), 220(84), 219(51), 207(15), 192(12), 149(19), 79(10), 44(81), 43(9). (Found: C, 55.40; H, 4.85; N, 10.11. $C_{38}H_{38}N_6O_{14}.1H_2O$ requires C, 55.60; H, 4.87; N, 10.24 %).

5,8-Dimethoxy-2,3-bis[6-(6',7'-dimethoxy-4'-methylquinoxaline-3'(4'H)-oxo-2'-carbonyloxy)-1,4-dioxahexyl]quinoxaline (313) (0.343 g, 77 %) m.p. 177-179° C ; IR(KBr) ν_{max} 2960,2840 (H-Aliph), 1730 (C=O), 1650 (C=O), 1615, 1585, 1520, 1470, 1400, 1340, 1235, 1130, 1090, 1015, 860, 810, 650 cm^{-1}; ^1H NMR (200) MHz, $CDCl_3$) δ 7.31 (s, 2H, 8- and 8'-H), 6.77 (s, 2H, 6- and 7-H), 6.63 (s, 2H, 5- and 5'-H), 4.73 (t, 4H, δ- and δ'-CH_2), 4.59 (t, 4H, α- and α'-CH_2), 4.03 (s, 6H, 6- and 6'-OCH_3), 4.02-3.97 (m, 8H, β-, β'-, γ- and γ'-CH_2), 3.99 (s, 3H, 5- and 8-OCH_3, 3.92(s, 6H, 7- and 7'-OCH_3), 3.69 (s, 6H, N-CH_3 and N'-CH_3); MS, m/z(r.i.) 890(30, M^+), 334(7), 308(6), 278(55), 263(17), 247 (15), 220(100), 205 (47), 177(20), 149(30), 95(45). (Found: C, 56.42; H, 5.28; N, 9.10. $C_{42}H_{46}N_6O_{16}$ requires C, 56.63; H, 5.20; N, 9.43 %).

Preparation of 6,7-Dimethoxy-1,3-dimethyl-2(1H)-oxoquinoxaline (315)

A solution of 2-methylamino-4,5-dimethoxyaniline monohydrochloride (299) (0.530 g, 2.5 mmol), pyruvic acid (0.220 g, 2.5 mmol) and hydrochloric acid (0.5 M, 30 cm^3) was heated for 3 h in a boiling water-bath. The reaction was monitored by t.l.c which showed that the starting material was still present, hence more pyruvic acid (0.110 g, 1.0 mmol) was and heating was continued for 1 h. After basification of the mixture with aqueous sodium hydroxide (0.5 M), the compound was extracted with dichloromethane (3 x 100 cm^3), the extract dried (anhydrous sodium sulphate), the solid filtered off, and the filtrate evaporated *in vacuo*. The residue was crystallised from a mixture of ethyl acetate and dichloromethane (4:1) to yield 6,7-dimethoxy-1,3-dimethyl-2(1H)-oxoquinoxaline (315) (0.416g, 73 %) m.p. 169-170° C (lit.,[245] m.p. 170-171° C).

Preparation of 6,7-dimethoxy-4-methyl-2-(4'-carboxyphenylvinyl)-3(4H)-quinoxalinone (320)

A mixture of 1,2-dihydro-6,7-dimethoxy-1,3-dimethyl-2-oxoquinoxaline (315) (0.5 g; 2.13 mmol), 4-carboxybenzaldehyde (0.330 g; 2.20 mmol) and acetic anhydride (30 cm^3) was heated under reflux for 3 h. The reaction mixture developed a yellow fluorescence, and a red precipitate was formed. The mixture was cooled, the solid filtered off, and the filtrate was diluted with water (100 cm^3). The liquid was made neutral by addition of sodium carbonate solution, extracted with dichloromethane (3 x 100 cm^3), and the extract dried over anhydrous sodium sulphate. The solvent was evaporated *in vacuo*, and the resulting yellow solid was purified by repeated dissolution in sodium hydroxide solution (1 M) and precipitation by the addition of dil. hydrochloric acid. Finally, the solid was crystallised from a mixture of methanol and dichloromethane (4:1) to yield orange 6,7-dimethoxy-4-methyl-2-(4'-carboxyphenylvinyl)-3(4H)-quinoxalinone (320), (0.117 g, 42 %), m.p. 301-302° C; IR (KBr) ν_{max} 3480 (OH), 3060, 3020 (H-aryl), 2940, 2830 (H-aliph), 1715, 1645 (C=O), 1580 (C=C), 1520, 1470, 1430, 1395, 1325, 1275, 1170 (C-N), 1020, 850, 825, 800, 765 cm^{-1}; ^1H NMR (200 MHz, d_6-DMSO) δ 8.00(d, 1H, J = 16.2 Hz, α-vinyl-H) 7.96 (d, 2H, J = 8.3 Hz, 3'- and 5'-H), 7.77 (d, 2H, J = 8.3 Hz, 2'- and 6'-H), 7.70 (d, 1H, J = 16.2 Hz, β-vinyl-H), 7.32 (s, 1H, 8-H), 7.01 (s, 1H, 5-H), 3.97 (s, 1H, 6-OCH_3), 3.87 (s, 3H, 7-OCH_3), 3.70 (s, 3H, N-CH_3); MS, m/z(r.i), 367(24), 366(100, M^+), 365(29),

351(37, M^+-1CH_3), 337(16), 322(6, M^+-CO_2), 321(14), 284(29), 278(21), 234(62), 219(29; M^+- 4-carboxystyryl), 207(15), 191(20), 163(22), 149(73). (Found: C, 65.33; H, 5.23; N, 7.50. $C_{20}H_{18}N_2O_5$ requires C, 65.57; H, 4.95; N, 7.65 %).

2,3,10,11-Tetramethoxy-5,13-dimethylpyrazino[1,2-a;4,5-a']diquinoxaline-6,14(5H,13H)-dione(321)

The red solid compound (321) was purified by dissolving it in trifluoroacetic acid to produce an intensely blue solution. Dilution of the solution with water gave a precipitate of the red solid which was then filtered off, washed with water, methanol and finally with acetone to give the bright red micro crystals of 2,3,10,11-tetramethoxy-5,13-dimethylpyrazino[1,2-a;4,5-a']diquinoxaline-6,14(5H,13H)-dione (321) (0.155 g; 47 %), m.p. >350° C; IR (KBr) ν_{max} 3420 (H_2O), 3080 (H-aryl), 2940, 2830 (H-aliph), 1650 (C=O), 1630 (C=N), 1590 (C=C), 1530, 1515, 1480, 1460, 1430, 1400, 1360, 1330, 1285, 1245, 1220, 1180 (C-O), 1165 (C-N), 1030, 990, 945, 850, 830, 800, 790, 690 cm^{-1}; ^1H NMR (200 MHz, d-TFA) δ 9.30 (s, 2H, 7- and 15-H), 7.51 (s, 2H, 1- and 9-H) 7.30 (s, 2H, 4- and 12H), 4.30 (s, 6H, 3- and 11-OCH_3), 4.19 (s, 6H, 2- and 10-OCH_3), 4.16 (s, 6H, 5- and 13-NCH_3); MS, m/z (r.i) 468(4), 467(35), 466(100, M^++2), 452(11), 451(33), 440(11), 380(19), 365(14), 234(15), 233(19), 219(4), 205(4), 163(5), 69(8), 57(10). (Found: C, 60.79; H, 5.14; N, 11.70. $C_{24}H_{24}N_4O_6.1/2H_2O$ requires C, 60.88; H, 5.28; N, 11.83 %) [FAB (NOBA): 465 (M+1), Found: 465.1774. $C_{24}H_{24}N_4O_6$ requires 465.1743)].

An improved method for the preparation of (321)

A mixture of 1,2-dihydro-6,7-dimethoxy-1,3-dimethyl-2-oxoquinoxaline (315) (0.1 g; 0.421 mmol) and acetic anhydride (20 cm^3) was refluxed with stirring for 3 h. A red solid was precipitated out which was filtered off and purified as before to obtain 2,3,10,11-tetramethoxy-5,13-dimethylpyrazino[1,2-a; 4,5-a']diquinoxaline-6,14(5H,13H)-dione (321) (0.055 g, 56 %),

An improved method for the preparation of 6,7-dimethoxy-4-methyl-2-(4'-carboxyphenylvinyl)-3(4H)-quinoxalinone (320)

Glacial acetic acid (0.8 cm^3) and piperidine (1.0 cm^3) were added to a solution

of 1,2-dihydro-6,7-dimethoxy-1,3-dimethyl-2-oxoquinoxaline (315) (0.5 g, 2.13 mmol) and 4-carboxybenzaldehyde (0.330 g; 2.20 mmol) in dry toluene (50 cm^3), and the mixture boiled in a flask fitted with a Dean and Stark apparatus for 24 h. The yellow solid was filtered off, washed with a small amount of ice-cold water, and crystallised from a mixture of methanol and dichloromethane (4:1) to obtain orange 6,7-dimethoxy-4-methyl-2-(4'-carboxyphenylvinyl)-3(4H)-quinoxalinone (320)(0.578 g; 74 %),m.p.301-302° C; the spectral data was the same as described above.

Preparation of 6,7-dimethoxy-4-methyl-2-(4'-methoxycarbonylphenylvinyl)-3(4H)-quinoxalinone (322)

6,7-Dimethoxy-4-methyl-2-(4'-carboxyphenylvinyl)-3(4H)-quinoxalinone (320) (0.274 g, 0.75 mmol) in dry acetone (50 cm^3) was added to anhydrous potassium carbonate (1.0 g) and stirred for 15 min. Then dimethyl sulphate (2.0 cm^3) was added dropwise, and the reaction mixture was refluxed and stirred for 1.5 h. The mixture was poured into cold water (150 cm^3), the precipitate filtered off, and crystallised from methanol to yield yellow 6,7-dimethoxy-4-methyl-2-(4'-methoxycarbonylphenylvinyl)-3(4H)-quinoxalinone (322) (0.253 g, 89 %), m.p. 232-233° C; IR(KBr) ν_{max} 3060, 3010 (H-aryl), 2940,2860 (H-aliph), 1710 (C=O, ester), 1650 (C=O, amide), 1605, 1575, 1515, 1450, 1390, 1270, 1170 (C-N), 1115 (C=O), 1020, 875 cm^{-1}; ^1H NMR (60 MHz, $CDCl_3$) δ 8.05 (d, 1H, J = 16.2 Hz, α-vinyl-H), 8.00 (d, 2H, J = 8.7 Hz, 3' and 5'-H), 7.71 (d, 1H, J = 16.2 Hz, β-vinyl-H) 7.75 (d, 2H, J = 8.6 Hz, 2'- and 6'-H), 7.28 (s,1H, 8-H), 6.67 (s, 1H, 5-H), 4.01 (s, 3H, 6-OCH_3), 3.96 (s,3H, 7-OCH_3), 3.90 (s, 3H, CO_2CH_3), 3.73 (s, 3H, 4-NCH_3); MS, m/z(r.i.) 382(5), 381(22), 380(100, M^+), 365(21, M^+-CH_3), 321(7, M^+-CO_2), 175(11), 57(8). (Found: C, 66.08; H, 5.38; N, 7.24. $C_{21}H_{20}N_2O_5$ requires C, 66.31; H, 5.30; N, 7.36 %).

Preparation of 3,4-dihydro-6,7-dimethoxy-4-methyl-2-vinylphenyl-3(4H)-quinoxalinone-4'-carbonyl Chloride (323)

6,7-Dimethoxy-4-methyl-2-(4'-carboxyphenylvinyl)-3(4H)-quinoxalinone (320) (0.549 g, 1.5 mmol) was added to freshly distilled thionyl chloride (20 cm^3) and refluxed for 20 min. The reaction mixture was then poured into light petroleum-ether (b.p. 40-60°C) (100 cm^3) to give a yellow brown precipitate which was filtered off, and

crystallised from a mixture of benzene and petroleum-ether (b.p. 40-60° C) (1:1) to give yellow microcrystals of 6,7-dimethoxy-4-methyl-2-vinylphenyl-3(4H)-quinoxalinone-4'-carbonyl chloride (323) (0.534 g, 93 %), m.p. 278-280° C; IR (KBr) ν_{max} 2930, 2850 (H-aryl), 1740 (C=O), 1655 (C=O), 1620 (C=N), 1600 (C=C), 1520, 1465, 1395, 1320, 1280, 1220, 1175 (C-N), 1030, 880, 850, 650 cm^{-1}; ^1H NMR (200 MHz, d_6-DMSO) δ 8.00 (d, 1H, *J* = 16.1 Hz, α-vinyl-H), 7.97 (d, 2H, *J* = 8.3 Hz, 3'- and 5'-H), 7.78 (d, 2H, *J* = 8.3 Hz, 2'- and 6'-H), 7.70 (d, 1H, *J* = 16.1 Hz, β-vinyl-H), 7.39 (s, 1H, 8-H), 7.01 (s, 1H, 5-H), 3.79 (s, 3H, 6-OCH_3), 3.87 (s, 3H, 7-OCH_3), 3.71 (s, 3H, 4-NCH_3): MS, m/z (r.i.) 386, 384 (36, 13; M^+ for ^{37}Cl and ^{35}Cl), 369(9, M^+-CH_3), 349(7, M^+-^{35}Cl). (Found: C, 62.16; H, 4.30; N, 7.17; Cl, 8.93. $C_{20}H_{17}N_2O_4Cl$ requires C, 62.42; H, 4.45; N, 7.28; Cl, 9.21 %).

General Method for the Preparation of the Derivatives of 3,4-Dihydro-6,7-dimethoxy-4-methyl-2-vinylphenyl-3(4H)-quinoxalinone-4'-carbonyl Chloride

A mixture of the appropriate amine (0.25 mmol) and sodium hydride (0.26 mmol) in dry benzene (30 cm^3) was stirred for 15 min followed by the addition of 6,7-dimethoxy-4-methyl-2-vinylphenyl-3(4H)-quinoxalinone-4'-carbonyl chloride (323) (0..26 mmol). The reaction mixture was refluxed for 3-5 h, then washed thoroughly with dil. hydrochloric acid (0.1 M), finally with distilled water. The dried solution was evaporated *in vacuo* to yield the crude product.

In this way, the compounds following were obtained:-

6,7-Dimethoxy-4-methyl-2-[4'-(N-benzylcarboxamido)]phenylvinyl-3(4H)-quinoxalinone (324): (0.95 g, 81 %), m.p. 255-256° C; IR(KBr) ν_{max} 3300 (N-H), 3060, 3020 (H-aryl), 2940, 2830 (H-aliph), 1655 (C=O), 1635 (C=O), 1585, 1525, 1475, 1460, 1395, 1275, 1240, 1170 (C-N), 1100 (C=O), 1030, 980, 815, 705 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 8.04 (d, 1H, *J* = 16.4 Hz, α-vinyl-H), 7.81 (d, 2H, *J* = 8.6 Hz, 3'- and 5'-H), 7.76 (d, 1H, *J* = 16.5 Hz, β-vinyl-H), 7.72 (d,2H, *J* = 8.6 Hz, 2'- and 6'-H), 7.33 (m, 5H, Ph-H), 7.32 (S, 1H, 8-H) 6.70 (s, 1H, 5-H), 6.42 (t, 1H, N-H disappeared with D_2O), 4.66 (d, 2H, *J* = 5.5 Hz, -CH_2-), 4.04 (S 3H, 6-OCH_3), 3.98 (s, 3H, 7-OCH_3), 3.75 (s, 3H, N-CH_3); MS, m/z(r.i.): 457(11), 456(30), 455(100, M^+), 440(15, M^+-1CH_3), 426(7), 381(10), 248(12), 239(13), 192(11), 149(7), 91(41), 57(36). (Found: C, 70.22; H, 5.41; N, 9.21. $C_{27}H_{25}N_3O_4.1/4H_2O$ requires C, 70.51; H, 5.44; N, 9.14 %).

(2-[*p*-(1,4,7-Trioxa-10-azacyclododecan-10-ylcarbonyl)phenylvinyl]-6,7-dimethoxy-4-methylquinoxalin-3(4H)-one (325) (0.92 g, 68 %), m.p. 214-215° C; IR(KBr) ν_{max} 3060, 3010 (H-aryl), 2940, 2880 (H-aliph), 1655 (C=O), 1630 (C=O), 1595, 1520, 1465, 1365, 1270, 1240, 1125 (C=O), 1020, 850, 810, 760, 630 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 8.3 (d, 1H, *J*= 16.2 Hz, α-vinyl-H), 7.74 (d, 1H, *J*= 16.2 Hz, β-vinyl-H), 7.67 (d, 2H, *J*= 8.3 Hz, 3'- and 5'-H), 7.54 (d, 2H, *J*= 7.8 Hz, 2'- and 6'-H), 7.33 (s, 1H, 8-H), 6.70 (s, 1H, 5-H), 4.04 (s, 3H, 6-OCH_3), 3.99 (s, 3H, 7-OCH_3), 3.79-3.56 (m, 16H, methylene hydrogens), 3.76 (s, 3H, N-CH_3); MS, m/z(r.i.) 524(12), 523(27, M^+), 278(18), 234(9), 220(15), 176(9), 149(20), 97(32), 57(100), 45(44), 44(41), 43(61). (Found: C, 63.03; H, 6.41; N, 7.78. $C_{28}H_{33}N_3O_7.1/2H_2O$ requires C, 63.15; H, 6.39; N, 7.89 %).

2-[*p*-(1,4,7,10-Tetraoxa-13-azacyclopentadecan-13-ylcarbonyl)phenylvinyl]-6,7-dimethoxy-4-methylquinoxalin-3(4H)-one (326) (0.09 g, 61 %), m.p. 194-195° C; IR(KBr) ν_{max} 3470 (H_2O), 3070, 3010 (H-aryl), 2950, 2880 (H-aliph), 1645(C=O), 1585, 1515, 1465, 1420, 1390, 1330, 1275, 1240, 1130 (C-O), 1090, 1020, 985, 950, 850, 820, 760 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) 8.01 (d, 1H, *J* = 16.3 Hz, α-vinyl-H),7.65 (d, 1H, *J* = 16.1 Hz, β-vinyl-H) 7.62 (d, 2H, *J* = 8.3 Hz, 3'- and 5'-H), 7.37 (d, 2H, *J* = 8.2 Hz, 2'- and 6'-H), 7.27 (s, 1H, 8-H), 6.66 (s, 1H, 5-H), 4.00 (s, 3H, 6-OCH_3), 3.95 (s, 3H, 7-OCH_3), 3.77 (s, 3H, 4-NCH_3), 3.75-3.54 (m, 20H, methylene hydrogens); MS, m/z(r.i.) 568(46), 567(100, M^+), 552(4, M^+-1CH_3), 539(8), 435(9), 339(15), 149(3), 133(11), 56(11), 45(13), 44(8), 43(8). (Found: 61.78; H, 6.58; N, 6.93. $C_{30}H_{37}N_3O_8.H_2O$ requires C, 61.53; H, 6.66; N, 7.17 %).

2-[*p*-(1,4,7,10,13-Pentaoxa-16-azacyloctadecan-16-ylcarbonyl)phenylvinyl]-6,7-dimethoxy-4-methylquinoxalin-3(4H)-one (327) (0.101 g, 63 %), m.p. 169-170° C; IR(KBr) ν_{max} 3430 (H_2O), 3060 (H-aryl), 2920, 2865, (H-aliph), 1655 (C=O), 1625 (C=O), 1590, 1520, 1470, 1430, 1390, 1360, 1270, 1160, 1120 (C=O), 1020, 950, 830, 810, 750 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 8.03 (d, 1H, *J* = 16.6 Hz, α-vinyl-H), 7.74 (d, 1H, *J* = 16.1 Hz, β-vinyl-H), 7.67 (d, 2H, *J* = 8.8 Hz, 3'- and 5'-H), 7.43 (d, 2H, *J* = 8.3 Hz, 2'- and 6'-H), 7.33 (s, 1H, 8-H), 6.71 (s, 1H, 5-H), 4.04 (s, 3H, 6-OCH_3), 3.99 (s, 3H, 7-OCH_3), 3.76 (s, 3H, N-CH_3), 3.80-3.58 (m, 24H, methylene hydrogens); MS, m/z(r.i.) 613(33), 612(46), 611(96, M^+), 563(12), 510(16), 509(53), 380(10), 349(30),

247(6), 234(20), 220(10), 149(11), 85(10), 57(35), 45(41), 44(36), 43 (42). (Found: C, 61.74; H, 6.76; N, 6.72. $C_{32}H_{41}N_3O_9.1/2H_2O$ requires C, 61.93; H, 6.77; N, 6.77 %).

Table 1. Comparison of the Spectral Data for the Different Isomers of Dimethoxyquinoxalinone

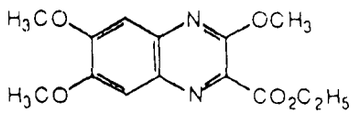
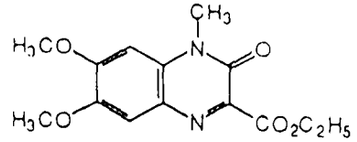
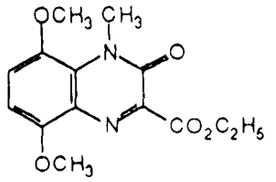
Comp.	m.p. (C°)	IR (cm^{-1})	^1H NMR 8-H (s)	5-H (s)	2-$CO_2C_2H_5$ (q)	2-$CO_2C_2H_5$ (t)	3-OCH_3 (s)	6-OCH_3 (s)	7-OCH_3 (s)	N-CH_3 (s)
 (292)	131-132	1720 (C=O)	7.37	7.15	4.47	1.44	4.11	4.03	3.98	
 (290)	159-160	1730 (C=O, ester) 1650 (C=O, amide)	7.34	6.77	4.47	1.43		4.02	3.92	3.71
 (296)	168-169	1750 (C=O, ester) 1650 (C=O, amide)	6-H (d) 7.06	7-H (d) 6.67	4.43	1.40		5- and 8-OCH3 (s) 3.94		3.84

Table 2. Spectral Data of 6,7-Dimethoxy-4-methyl-3(4H)-oxoquinoxaline-2-carboxylic acid and its Derivatives (where M=methanol and C=dichloromethane).

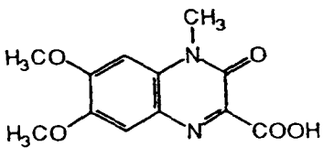
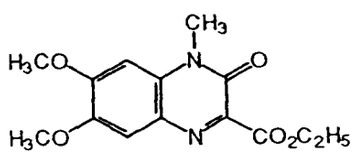
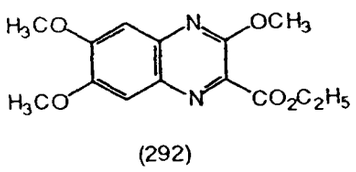
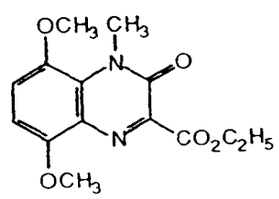
Compound	Solvent	UV λ_{abs} (nm)	Absorb.	log ε	Fluorescence λ_{em} (nm)	Int.	Φ_f
 (288)	M	399	0.543	4.15	469	149	0.15
		245	0.949				
	C	412	0.673	4.25	476	376	0.39
		326	0.350		476	284	0.20
		249	0.830				
 (290)	M	396	0.746	4.33	500	250	0.42
		318	0.433	4.10	500	300	0.33
		244	1.264				
	C	395	0.463	4.13	481	327	0.38
		311	0.278	3.91	481	254	0.34
		246	0.832				
 (292)	M	362	0.696	4.30	443	110	0.12
		246	1.246		443	135	0.10
	C	363	0.663	4.28	435	51	0.08
		246	1.012				
 (296)	M	333	0.506	4.17	Not Flu.		
		280	0.908				

Table 3. Spectral Data of the Fluoroionophores without the Styryl Group (306)-(308) and (310), (where M=methanol and C=dichloromethane).

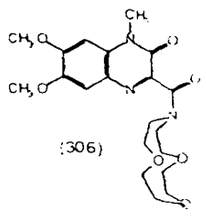
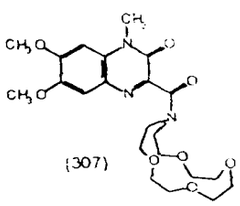
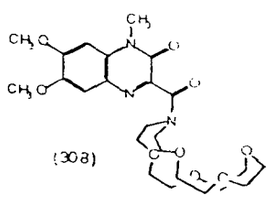
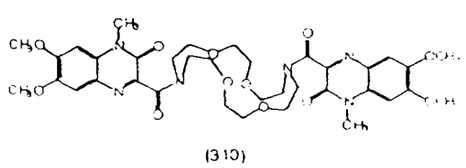
Compound	Solvent	UV λ_{abs} (nm)	Absorb.	log ε	Fluorescence λ_{em} (nm)	Int.	Φ_f
 (306)	M	380	0.439	4.26	469	219	0.19
		301	0.183	3.88	469	157	0.15
		243	0.695	4.46			
	C	378	0.417	4.24	455	65	0.07
		300	0.184	3.89			
		244	0.655	4.44			
 (307)	M	380	0.416	4.28	469	187	0.21
		304	0.174	3.90	469	202	0.20
		242	0.658	4.48			
	C	380	0.490	4.35	453	84	0.08
		302	0.193	3.95	453	43	0.04
		244	0.765	4.55			
 (308)	M	381	0.417	4.32	469	240	0.25
		305	0.160	3.91	469	153	0.16
		243	0.633	4.50	469	181	0.20
	C	379	0.423	4.33	453	92	0.08
		303	0.166	3.92	453	45	0.04
		244	0.661	4.52			
 (310)	M	381	0.378	4.45	470	171	0.21
		305	0.156	4.07	470	134	0.14
		242	0.561	4.62			
	C	380	0.484	4.38	451	122	0.11
		303	0.199	4.11	451	118	0.10
		244	0.759	4.60			

Table 4. Spectral Data of the Podands (311)-(313) (where M=methanol and C=dichloromethane).

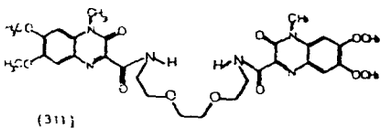
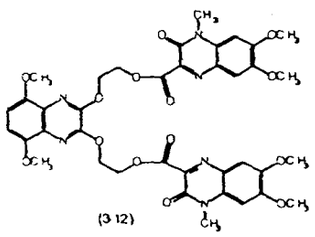
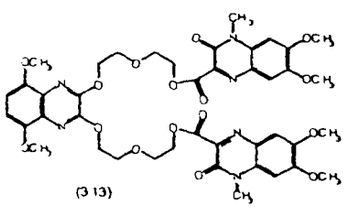
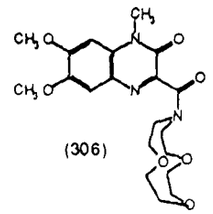
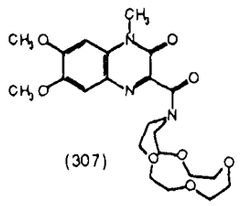
Compound	Solvent	UV λ_{abs} (nm)	Absorb.	loge	Fluorescence λ_{em} (nm)	Int.	Φ_f
 (311)	M	402	0.669	4.63	Not Fluorescent		
		316	0.426	4.43			
		247	0.952	4.78			
	C	409	0.418	4.42	476	86	0.09
		321	0.283	4.25	476	48	0.05
		247	0.582	4.57			
 (312)	M	398	0.406	4.51	500	341	0.36
		317	0.298	4.38	500	244	0.23
		248	0.840	4.83			
	C	400	0.308	4.39	485	187	0.10
		314	0.225	4.26	485	69	0.06
		262	0.656	4.72			
 (313)	M	397	0.387	4.53	500	340	0.36
		317	0.273	4.38	500	207	0.21
		248	0.786	4.84			
	C	398	0.296	4.42	484	97	0.09
		313	0.228	4.30	484	61	0.05
		249	0.639	4.75			

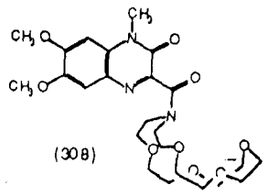
Table 5. Spectral Data of the Fluoroionophores (306)-(308) and (310) containing the 6,7-Dimethoxy-4-methyl-3(4H)-oxoquinoxaline-2-carbonyl group and their Complexes with Alkali and Alkaline Earth Metals in Dichloromethane.



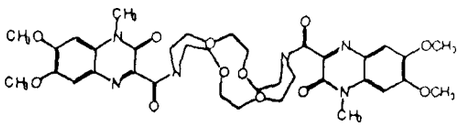
(306)



(307)



(308)



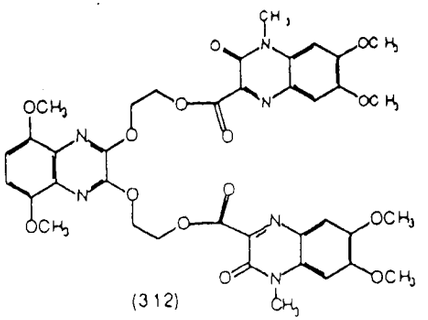
(310)

Metal ions	λ_{exc} (nm)	Conc. (M)	λ_{em} (nm)	Φ_f	λ_{exc} (nm)	Conc. (M)	λ_{em} (nm)	Φ_f	λ_{exc} (nm)	Conc. (M)	λ_{em} (nm)	Φ_f	λ_{exc} (nm)	Conc. (M)	λ_{em} (nm)	Φ_f
0	385	7.5×10^{-7}	454	0.06	385	7.5×10^{-7}	457	0.07	386	7.5×10^{-7}	455	0.07	386	4.5×10^{-7}	454	0.09
Li^+	392	5×10^{-5}	459	0.24	388	5×10^{-6}	457	0.18	387	5×10^{-5}	456	0.24	388	2×10^{-6}	455	0.25
Na^+	389	5×10^{-6}	456	0.17	388	5×10^{-5}	457	0.26	388	1×10^{-5}	458	0.31	389	1×10^{-4}	454	0.40
K^+	387	1×10^{-5}	456	0.10	390	5×10^{-5}	457	0.24	387	5×10^{-5}	458	0.33	389	5×10^{-5}	455	0.41
Mg^{++}	390	1×10^{-5}	467	0.13	390	1×10^{-5}	457	0.19	387	3×10^{-6}	457	0.26	390	1×10^{-6}	456	0.17
Ca^{++}	396	1×10^{-4}	473	0.13	388	1×10^{-5}	457	0.23	387	1×10^{-5}	456	0.27	390	1×10^{-5}	456	0.36
Ba^{++}	398	1×10^{-4}	464	0.14	390	5×10^{-5}	458	0.20	388	2×10^{-6}	457	0.25	389	5×10^{-6}	454	0.34

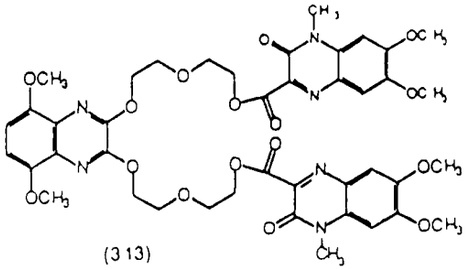
Table 6. Fluorescence Quantum Yields of the Fluoroionophores (306)-(308) & (310) and their Complexes with Alkali and Alkaline Earth Metals.

Compound		Free Ligand	Complexes Li^+	Na^+	K^+	Mg^{++}	Ca^{++}	Ba^{++}	Cavity size (Å)
		Ionic Diameter (Å)	1.36	1.94	2.66	1.32	1.98	2.68	
(306)	Φ_f	0.06	0.24	0.17	0.10	0.13	0.13	0.14	1.2-1.5
(307)	Φ_f	0.07	0.18	0.26	0.13	0.18	0.23	0.19	1.7-2.2
(308)	Φ_f	0.07	0.24	0.30	0.33	0.26	0.27	0.25	2.6-3.3
(310)	Φ_f	0.11	0.25	0.39	0.41	0.17	0.36	0.33	2.6-3.2

Table 7. Spectral Data of the Podands (312)-(313) and their Complexes with Alkali and Alkaline Earth Metals in Dichloromethane.



(312)



(313)

Metal ions	λ_{exc} (nm)	Conc. (M)	λ_{em} (nm)	Φ_f	λ_{exc} (nm)	Conc. (M)	λ_{em} (nm)	Φ_f
0	397	7.5×10^{-7}	485	0.07	400	7.5×10^{-7}	485	0.06
Li^+	424	2×10^{-6}	488	0.03	411	2×10^{-6}	487	0.03
Na^+	407	1×10^{-5}	487	0.09	412	2×10^{-6}	486	0.04
K^+	403	1×10^{-5}	486	0.11	402	3×10^{-5}	485	0.06
Mg^{++}	403	5×10^{-6}	488	0.02	425	2×10^{-6}	488	0.05
Ca^{++}	408	5×10^{-5}	487	0.06	428	3×10^{-6}	488	0.04
Ba^{++}	430	5×10^{-5}	487	0.05	409	1×10^{-6}	485	0.03

Table 8. Spectral Data of 6,7-Dimethoxy-4-methyl-(4'-carboxyphenylvinyl)-3(4H)-oxoquinoxaline and its Derivatives (where M=methanol, A=acetonitrile and C=dichloromethane).

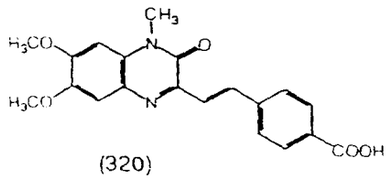
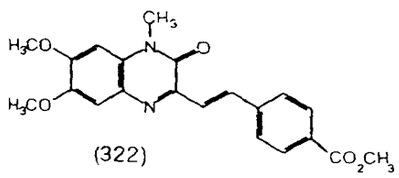
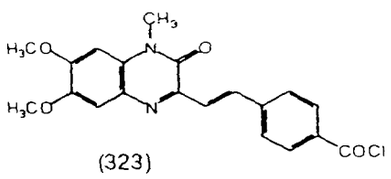
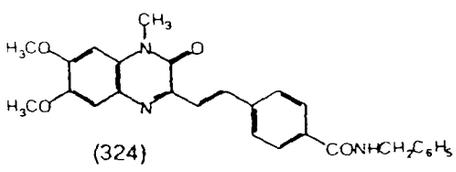
Compound	Solvent	UV λ_{abs} (nm)	Absorb.	log ε	Fluorescence λ_{em} (nm)	Int.	Φ_f
 (320)	M	424	0.518	4.27	504	285	0.33
		339	0.305	4.04	503	262	0.35
	C	434	0.895	4.51	507	313	0.34
		339	0.542	4.29	507	367	0.41
		282	0.450	4.21	507	188	0.19
		243	0.552	4.30			
 (322)	M	428	0.706	4.42	514	436	0.40
		339	0.407	4.18	313	452	0.35
		291	0.345	4.11	254	471	0.28
		241	0.481	4.26			
	C	433	0.985	4.57	503	329	0.39
		339	0.598	4.35	503	255	0.28
		282	0.465	4.26	503	230	0.24
		242	0.636	4.38			
 (323)	A	437	0.722	4.40	503	300	0.33
		340	0.472	4.25	503	241	0.26
		275	0.738	4.47	503	88	0.09
 (324)	M	426	0.959	4.64	510	285	0.32
		337	0.545	4.39	510	249	0.27
		290	0.463	4.32	510	243	0.26
	C	431	0.657	4.47	500	328	0.35
		338	0.378	4.23	500	266	0.28
		281	0.317	4.16	500	245	0.25
		245	0.403	4.26			

Table 9. Spectral Data of the Fluoroionophores containing the Styryl Group(326)-(328) (where M=methanol and C=dichloromethane).

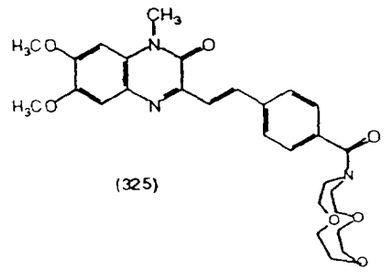
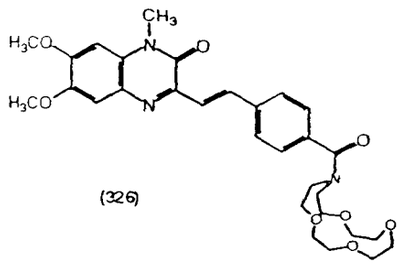
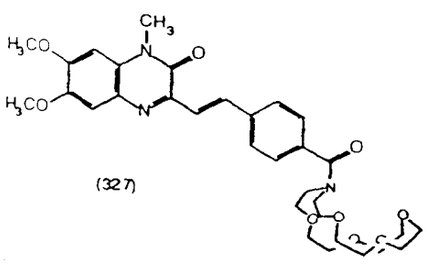
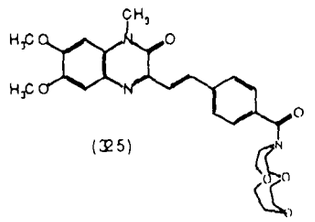
Compound	Solvent	UV λ_{abs} (nm)	Absorb.	log ε	Fluorescence λ_{em} (nm)	Int.	Φ_f
 (325)	M	423	0.592	4.49	505	295	0.34
		336	0.316	4.21	505	249	0.27
	C	427	0.501	4.46	490	347	0.36
		338	0.306	4.20	490	259	0.26
		279	0.253	4.12	490	269	0.26
 (326)	M	423	0.723	4.61	506	283	0.32
		337	0.400	4.35	506	244	0.26
		279	0.343	4.48	506	230	0.24
		241	0.587	4.52			
	C	427	0.616	4.54	491	313	0.34
		338	0.345	4.29	491	238	0.24
		279	0.277	4.19	491	267	0.26
		243	0.451	4.40			
 (327)	M	424	0.640	4.59	505	270	0.30
		336	0.334	4.31	505	237	0.25
		250	0.524	4.50	505	324	0.35
	C	428	0.472	4.46	491	325	0.23
		337	0.258	4.19	491	229	0.14
		279	0.231	4.15	491	145	

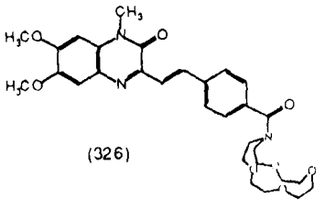
Table 10. Comparison of the Spectral Data between the Fluoroionophores without the Styryl Group (306)-(308) and Fluoroionophores with the Styryl Group (325)-(327) (where M=methanol and C=dichloromethane).

Compounds	Solvent	λ_{exc} (nm)	λ_{em} (nm)	Φ_f
(306)	M	380	469	0.19
	C	378	454	0.07
(325)	M	423	505	0.34
	C	427	490	0.36
(307)	M	380	469	0.21
	C	379	453	0.08
(326)	M	423	506	0.32
	C	427	491	0.34
(308)	M	381	469	0.25
	C	379	453	0.08
(327)	M	424	505	0.30
	C	428	491	0.35

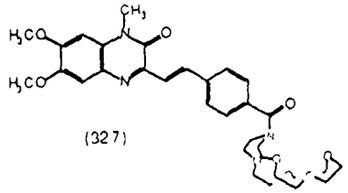
Table 11. Spectral Data of the Derivatives of 4-Carboxystyryldimethoxyquinoxalinone containing a Crown Ether and their Complexes with Alkali and Alkaline Earth Metals in Dichloromethane.



(325)



(326)



(327)

Metal ions	λ_{exc} (nm)	Conc. (M)	λ_{em} (nm)	Φ_f	λ_{exc} (nm)	Conc. (M)	λ_{em} (nm)	Φ_f	λ_{exc} (nm)	Conc. (M)	λ_{em} (nm)	Φ_f
0	431	4.5×10^{-7}	488	0.31	431	4.5×10^{-7}	490	0.31	431	4.5×10^{-7}	491	0.31
Li^+	431	1×10^{-3}	495	0.34	434	5×10^{-4}	502	0.40	433	1×10^{-4}	502	0.38
Na^+	432	1×10^{-3}	498	0.35	432	1×10^{-3}	502	0.41	432	5×10^{-4}	500	0.38
K^+	431	5×10^{-5}	491	0.36	433	1×10^{-4}	503	0.39	433	2×10^{-4}	499	0.38
Mg^{++}	431	1×10^{-3}	493	0.36	431	5×10^{-4}	493	0.40	432	1×10^{-4}	499	0.38
Ca^{++}	431	5×10^{-4}	497	0.37	434	5×10^{-3}	505	0.41	434	5×10^{-4}	500	0.43
Ba^{++}	431	5×10^{-5}	491	0.32	432	2×10^{-3}	501	0.37	433	5×10^{-4}	500	0.33

Table 12. Fluorescence Quantum Yields of the Fluoroionophores (325)-(327) and their Complexes with Alkali and Alkaline Earth Metals.

Compound		Free Ligand	Ionic Diameter (Å)	Complexes Li^+ 1.36	Na^+ 1.94	K^+ 2.66	Mg^{++} 1.32	Ca^{++} 1.98	Ba^{++} 2.68	Cavity size (Å)
(325)	Φ_f	0.313		0.338	0.358	0.368	0.359	0.376	0.325	1.2-1.5
(326)	Φ_f	0.309		0.403	0.415	0.396	0.408	0.419	0.373	1.7-2.2
(327)	Φ_f	0.310		0.380	0.387	0.385	0.383	0.429	0.330	2.6-3.3

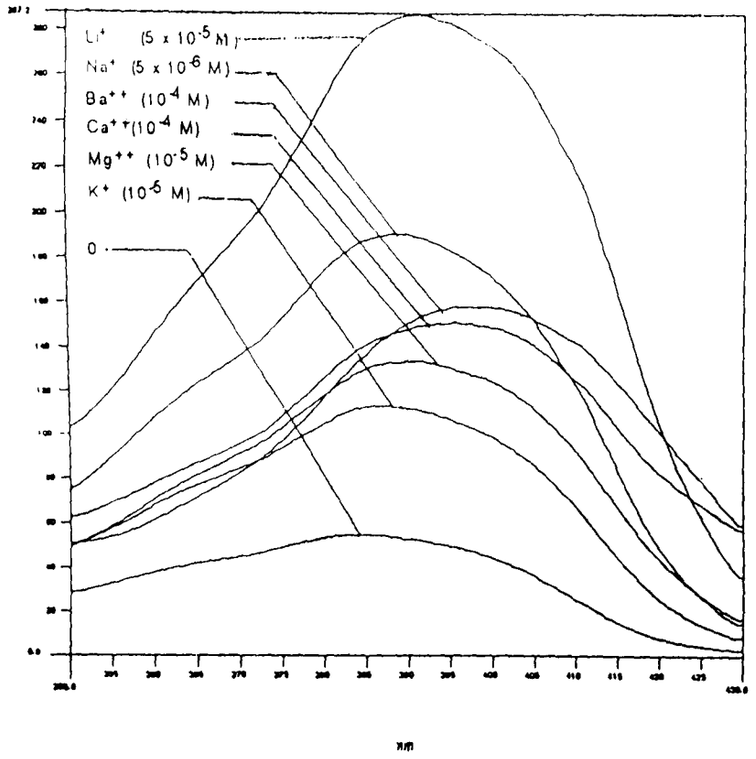


Fig. 16a Excitation spectrum of (306) in dichloromethane (7.5 x 10^{-7} M) before and after the addition of the alkali and alkaline earth metals perchlorates, at room temperature.

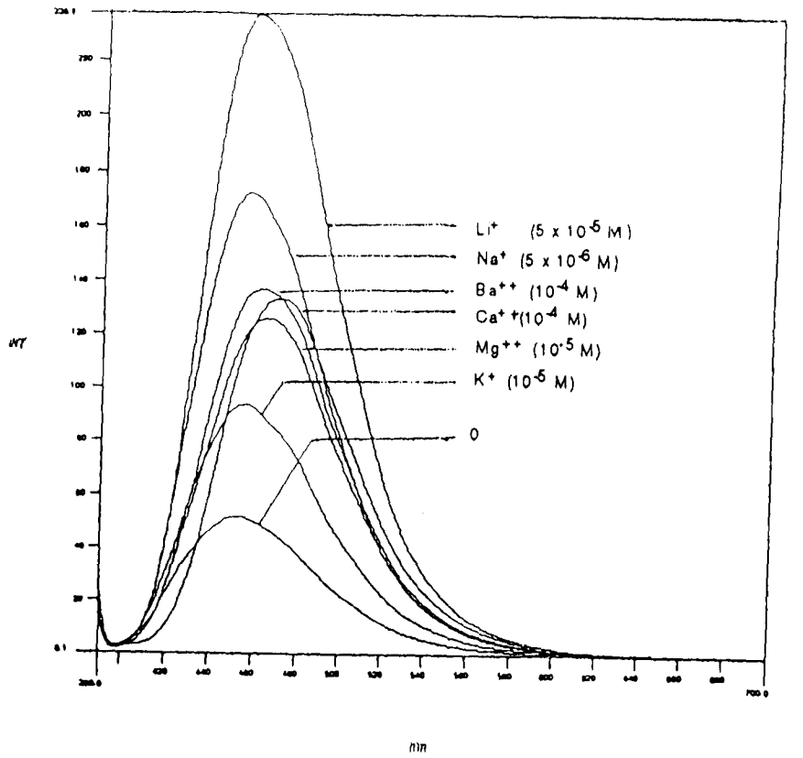


Fig. 16b Fluorescence spectra of (306) in dichloromethane (7.5x10^{-7}) before and after the addition of alkali and alkaline earth metals perchlorates, at room temperature (at $\lambda_{(exc)}$ = 378 nm).

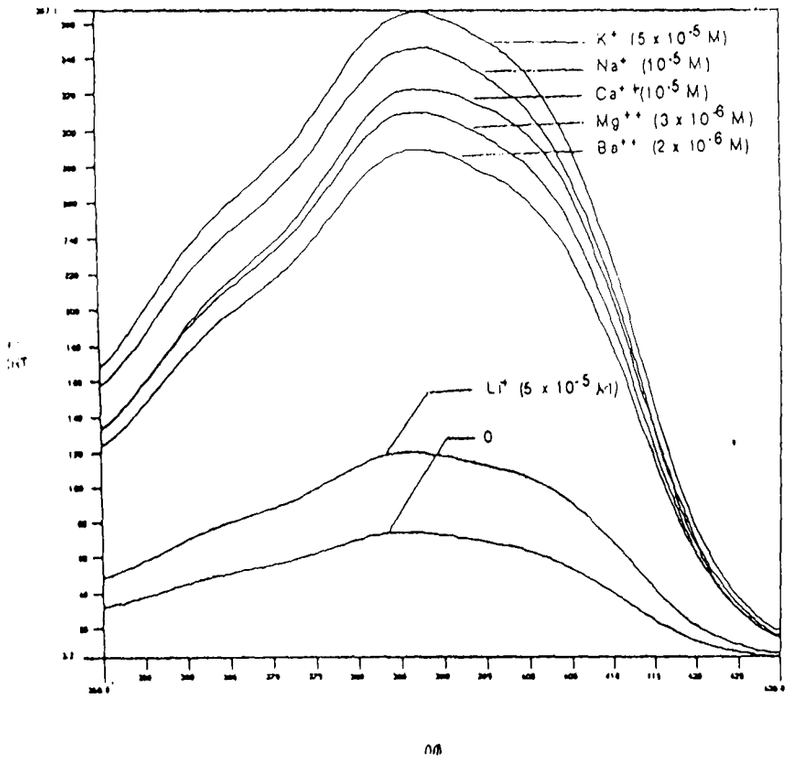


Fig. 17a Excitation spectrum of (308) in dichloromethane (7.5×10^{-7} M) before and after the addition of the alkali and alkaline earth metals perchlorates, at room temperature.

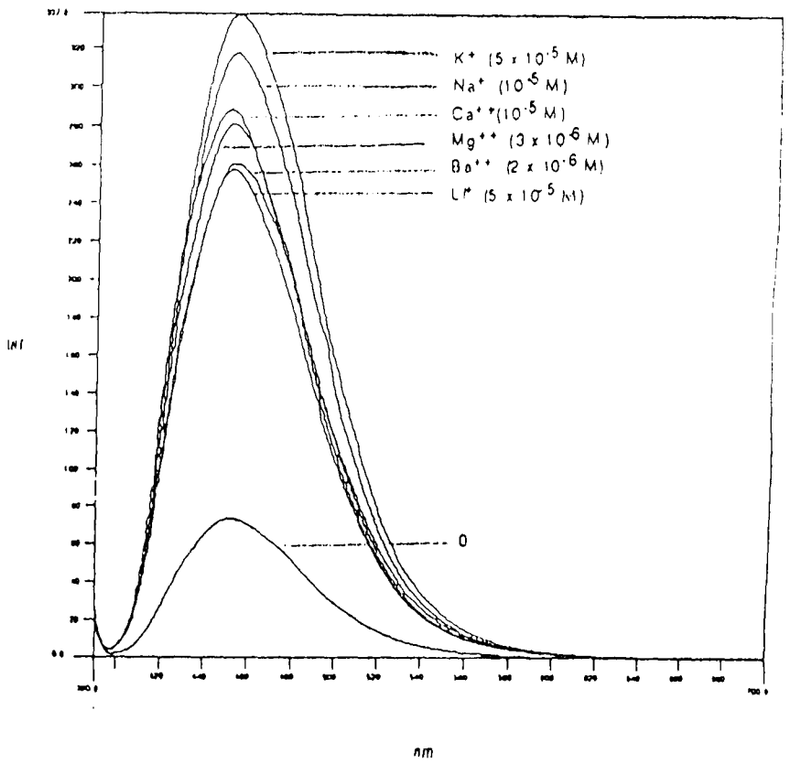


Fig. 17b Fluorescence spectra of (308) in dichloromethane (7.5×10^{-7}) before and after the addition of alkali and alkaline earth metals perchlorates, at room temperature (at $\lambda_{(exc)}$ = 379 nm).

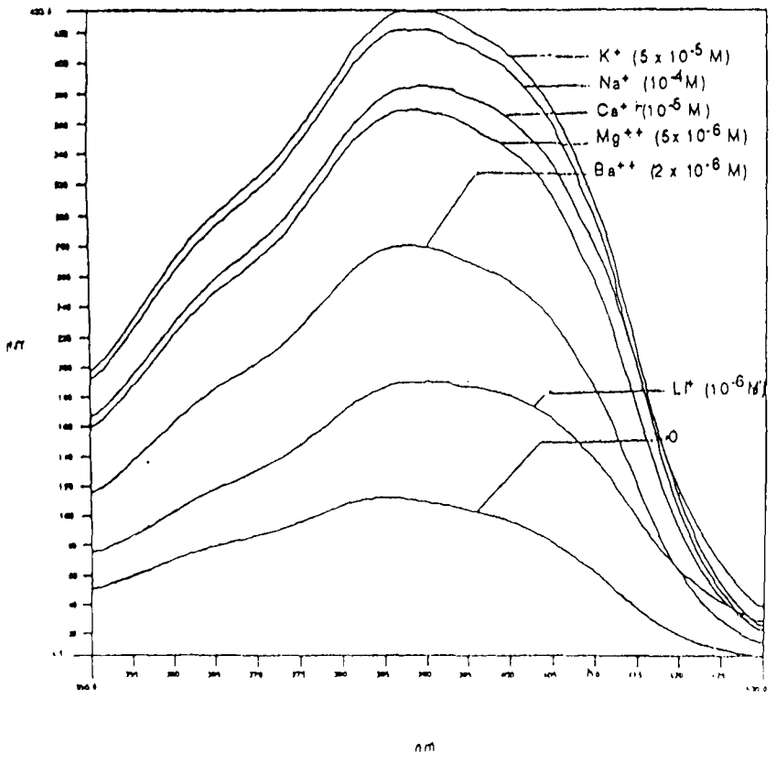


Fig. 18a Excitation spectrum of (310) in dichloromethane (4.5×10^{-7} M) before and after the addition of the alkali and alkaline earth metals perchlorates, at room temperature.

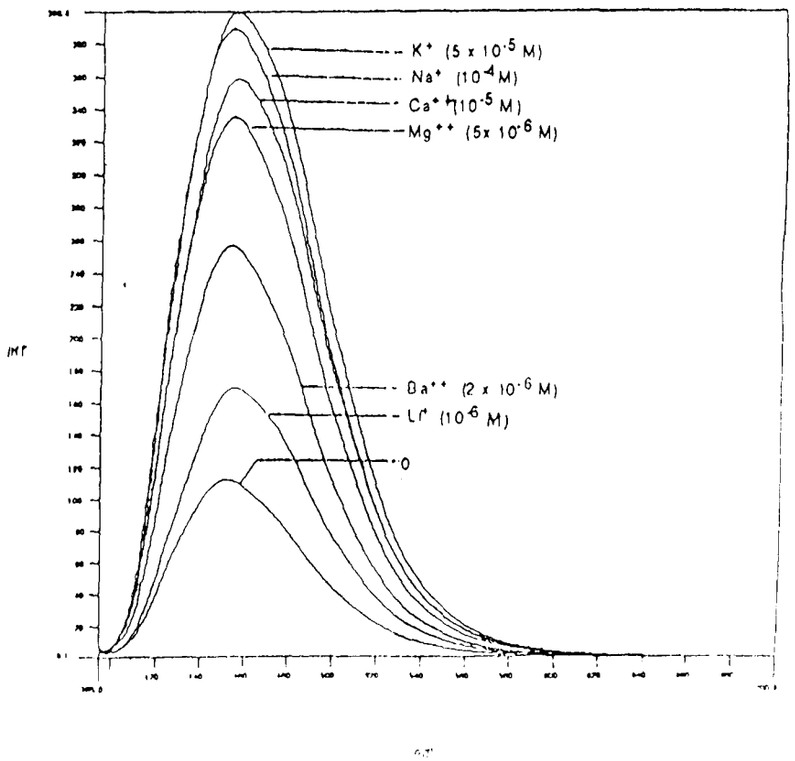


Fig. 18b Fluorescence spectra of (310) in dichloromethane (4.5×10^{-7}) before and and after the addition of alkali and alkaline earth metals perchlorates, at room temperature (at $\lambda_{(exc)}$ = 380 nm).

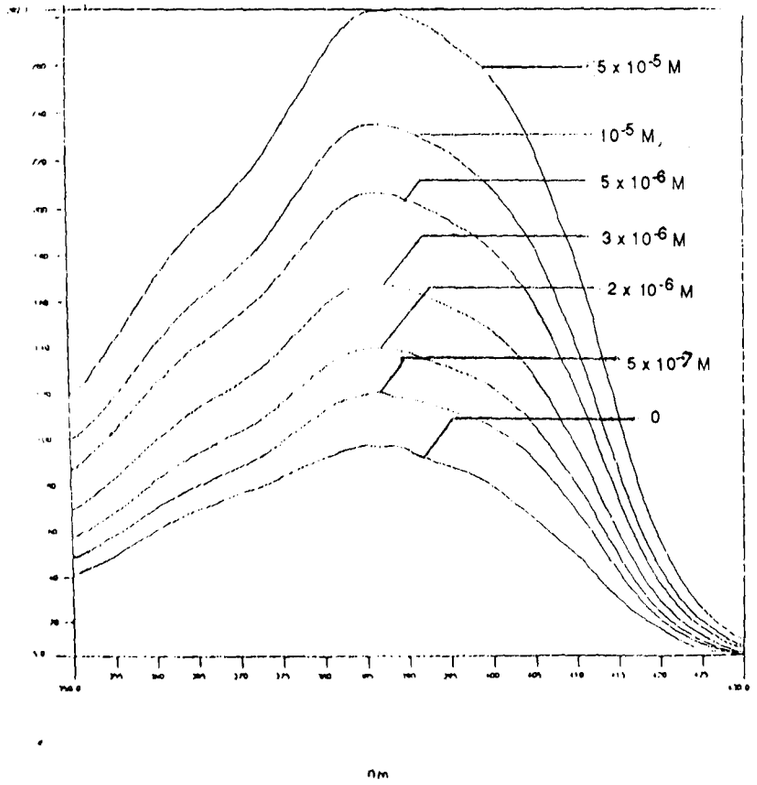


Fig. 19a Effect of the addition of potassium perchlorate upon the excitation spectrum of (310) in dichloromethane (4.5 x 10^{-7} M) at room temperature.

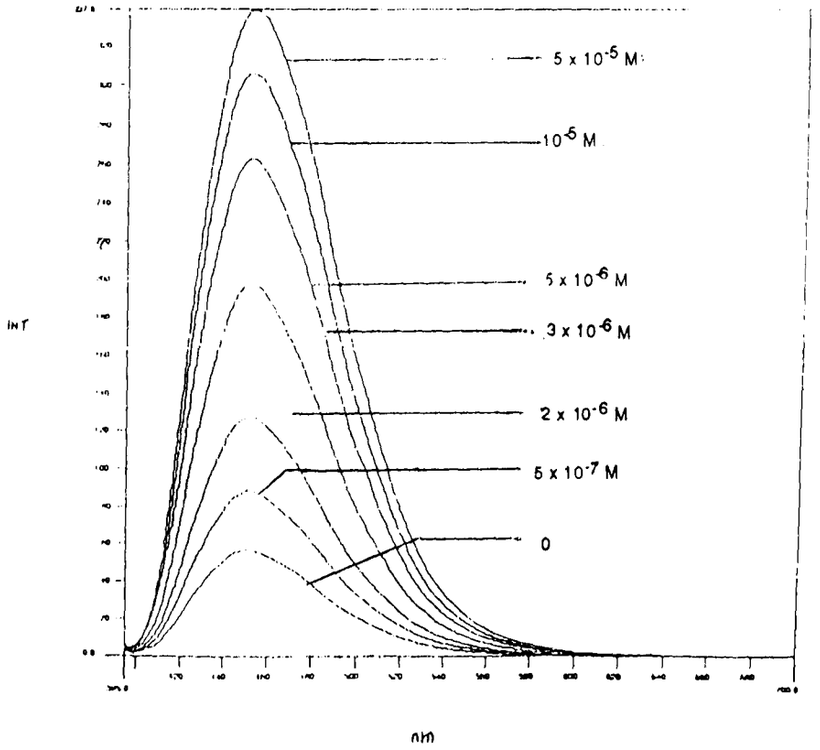


Fig. 19b Effect of the addition of potassium perchlorate upon the fluorescence spectrum of (310) in dichloromethane (4.5 x 10^{-7} M) at room temperature (at λ_{exc} = 380 nm).

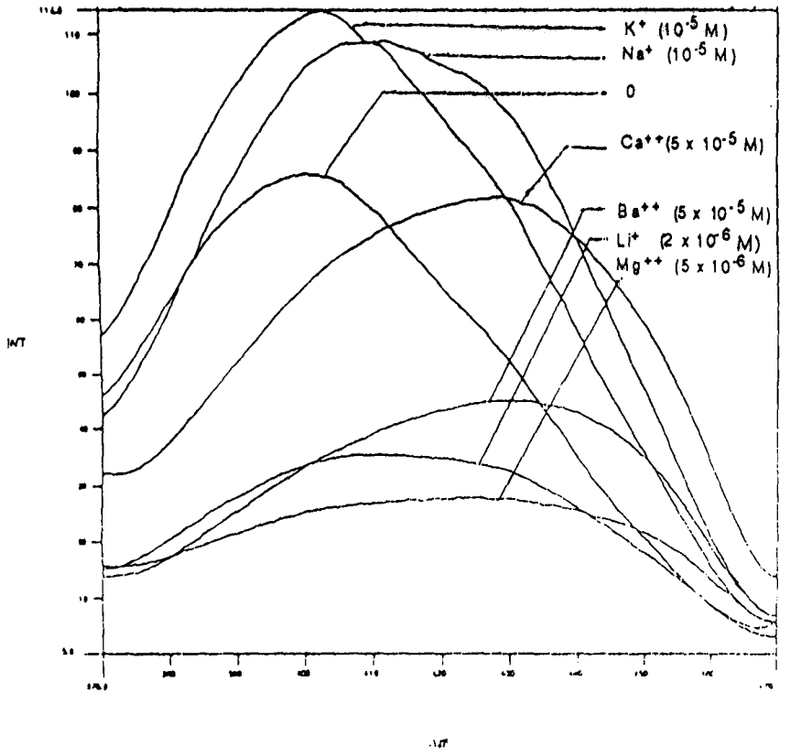


Fig. 20a Excitation spectrum of (312) in dichloromethane (7.5×10^{-7} M) before and after the addition of the alkali and alkaline earth metals perchlorates, at room temperature.

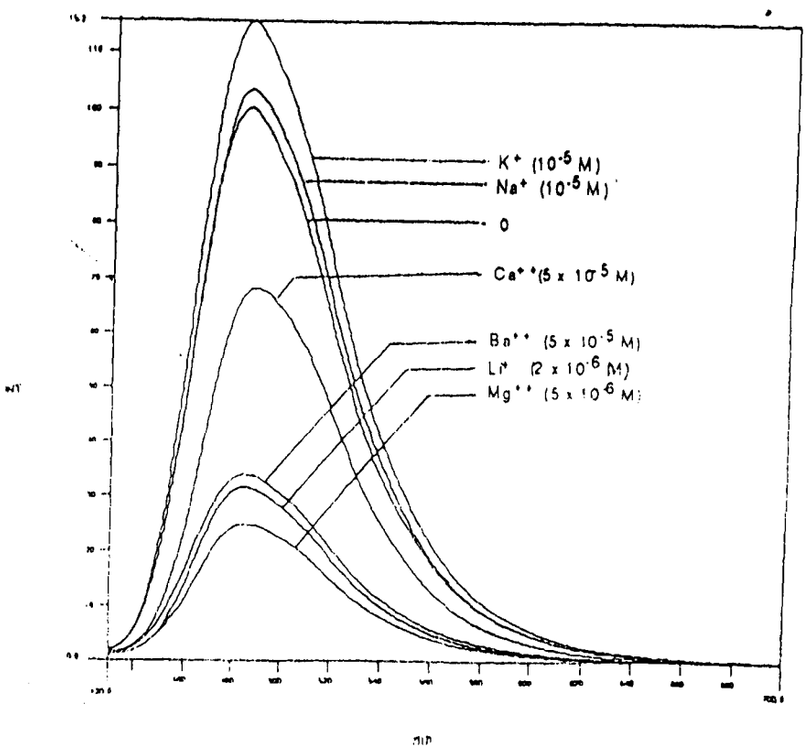


Fig. 20b Fluorescence spectra of (312) in dichloromethane (7.5×10^{-7}) before and and after the addition of alkali and alkaline earth metals perchlorates, at room temperature (at $\lambda_{(exc)}$ = 400 nm).

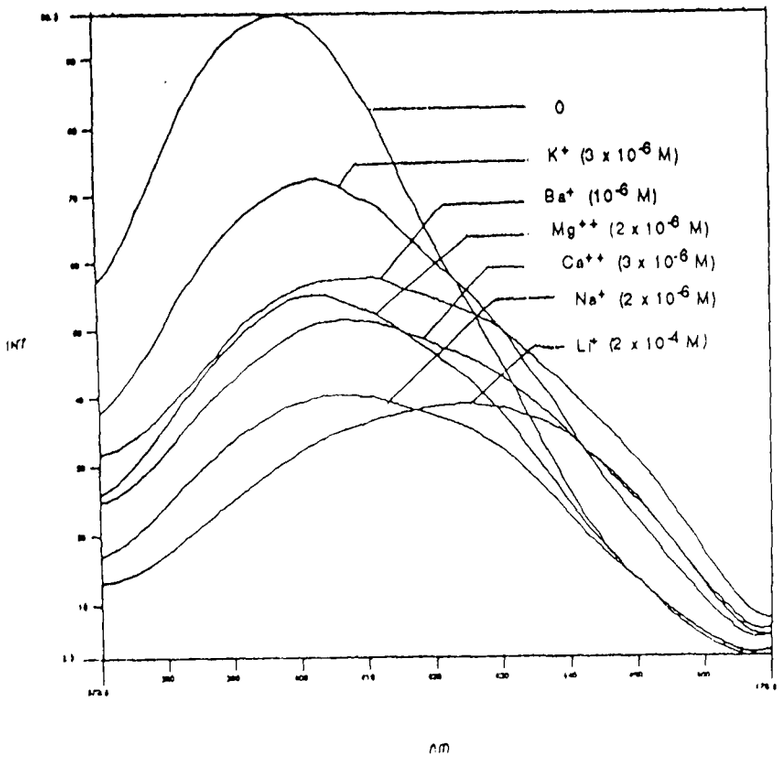


Fig. 21a Excitation spectrum of (313) in dichloromethane (7.5×10^{-7} M) before and after the addition of the alkali and alkaline earth metals perchlorates, at room temperature.

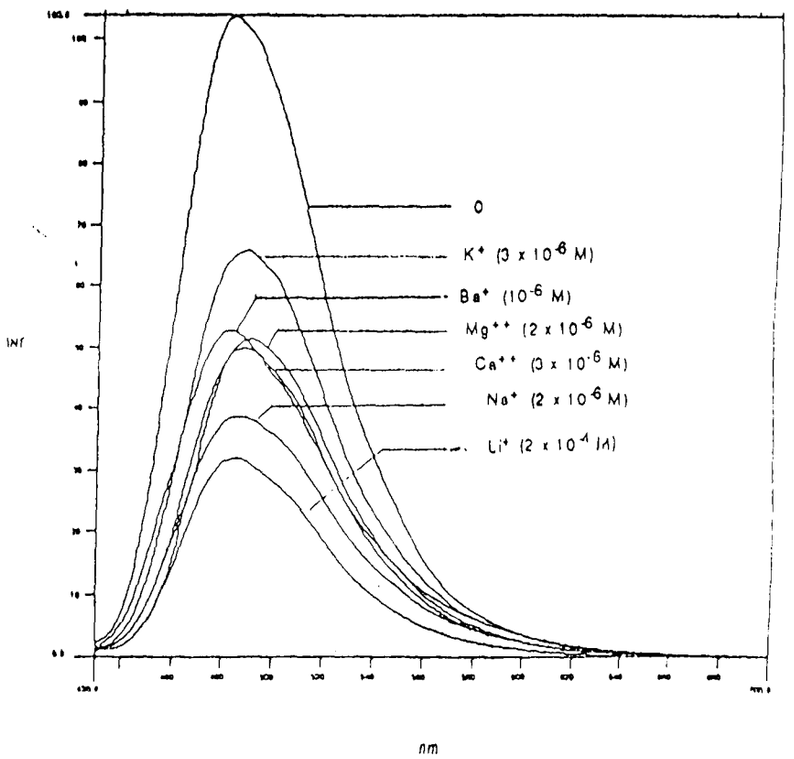


Fig. 21b Fluorescence spectra of (313) in dichloromethane (7.5×10^{-7}) before and and after the addition of alkali and alkaline earth meatals perchlorates, at room temperature (at $\lambda_{(exc)}$ = 398 nm).

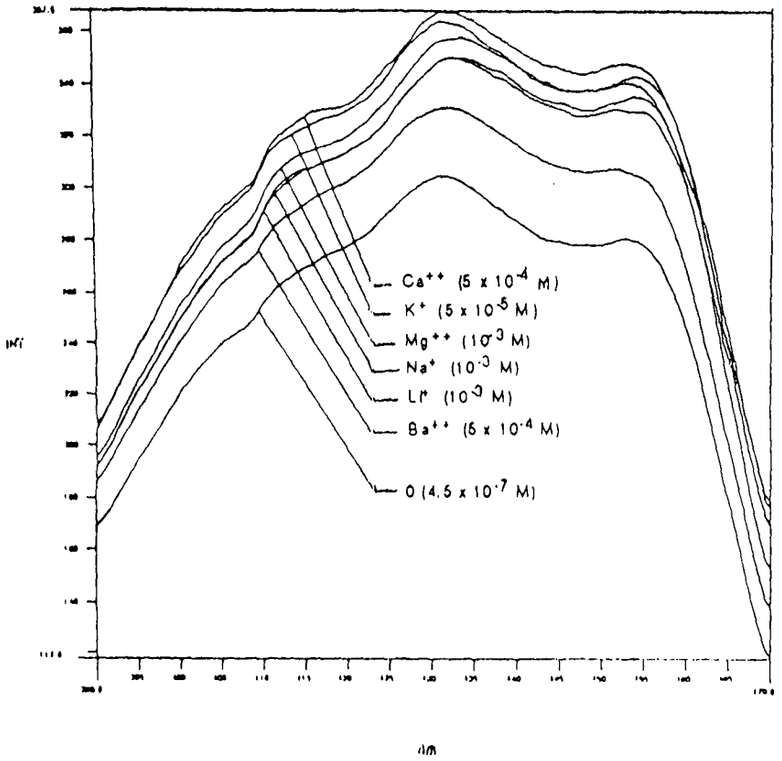


Fig. 22a Excitation spectrum of (325) in dichloromethane (4.5×10^{-7} M) before and after the addition of the alkali and alkaline earth metals perchlorates, at room temperature.

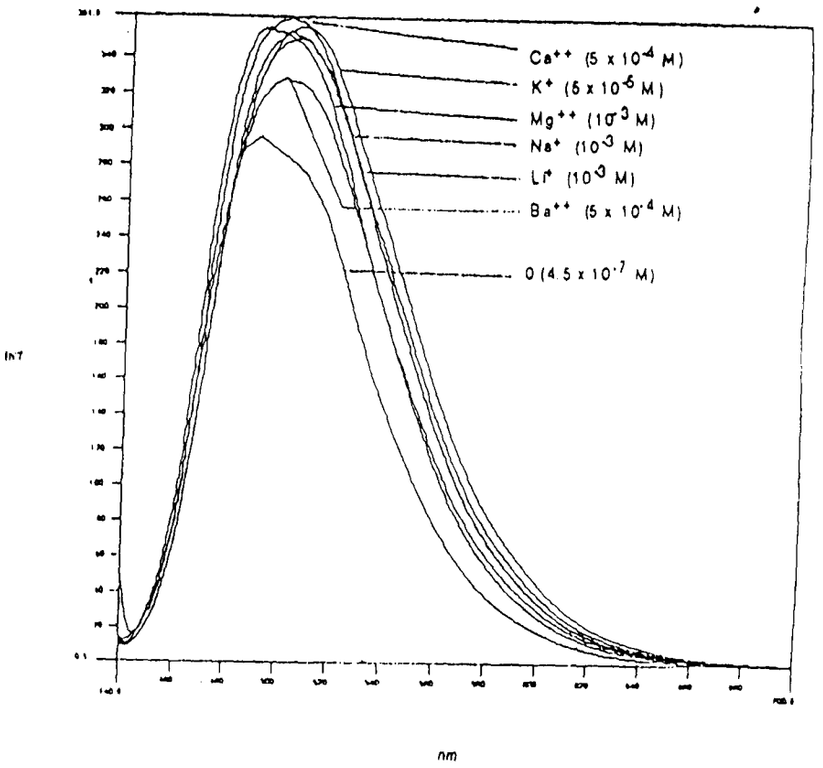


Fig. 22b Fluorescence spectra of (325) in dichloromethane (4.5×10^{-7}) before and after the addition of alkali and alkaline earth metals perchlorates, at room temperature (at $\lambda_{(exc)}$ = 428 nm).

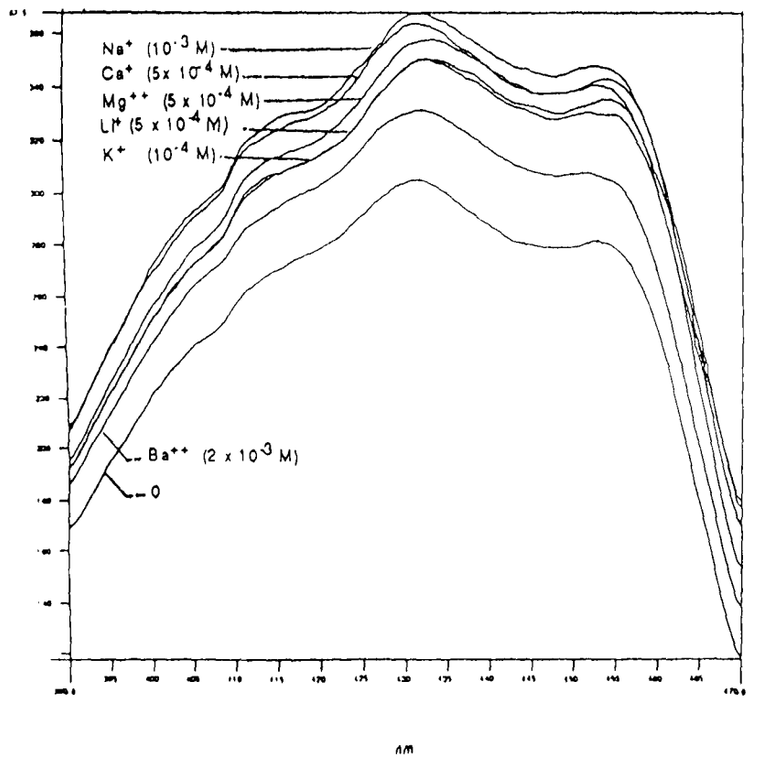


Fig 23a Excitation spectrum of (326) in dichloromethane (4.5 x 10^{-7} M) before and after the addition of the alkali and alkaline earth metals perchlorates, at room temperature.

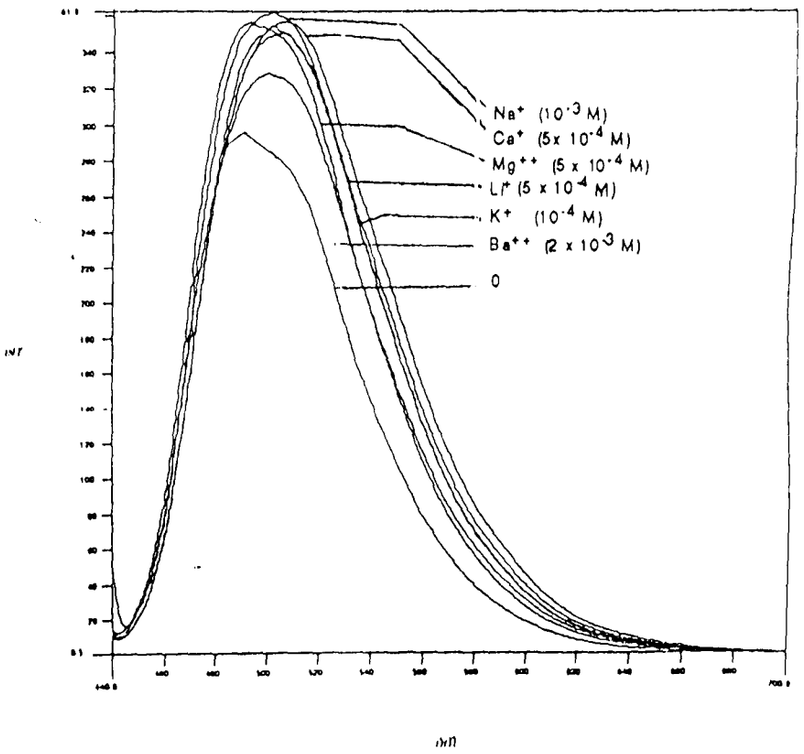


Fig 23b Fluorescence spectra of (326) in dichloromethane (4.5×10^{-7}) before and after the addition of alkali and alkaline earth meatals perchlorates, at room temperature (at $\lambda_{(exc)}$ = 428 nm).

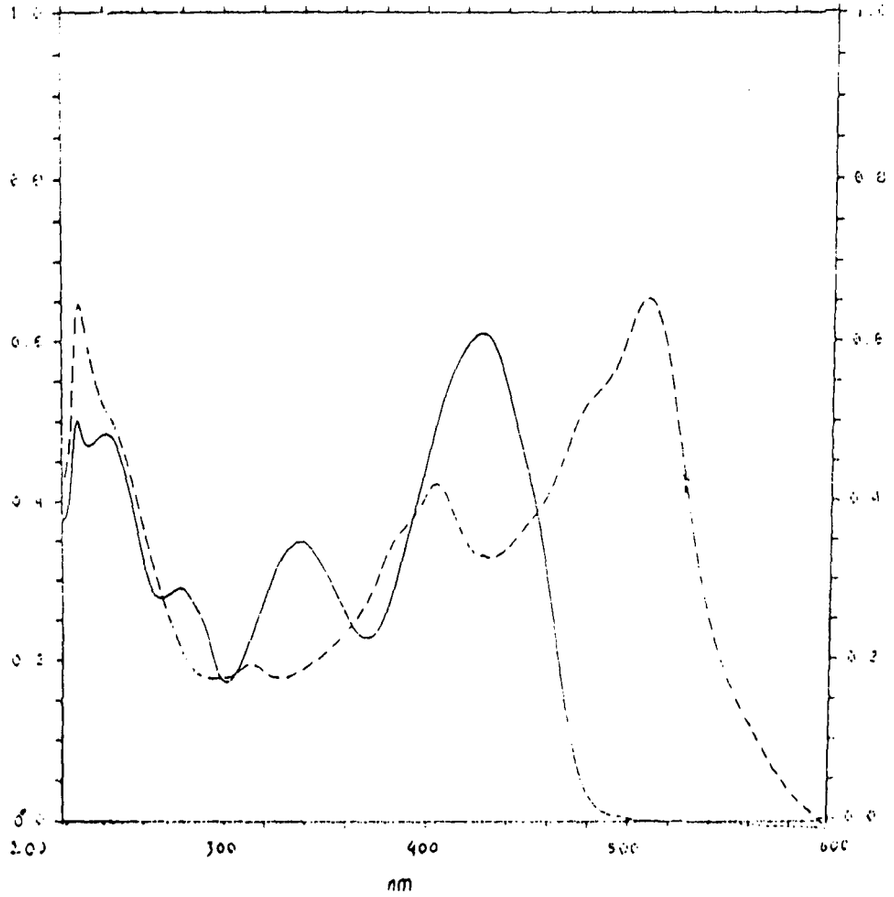


Fig. 24 Effect of the addition of hydrochloric acid upon UV absorption spectrum of (326) in dichloromethane at room temperature; --- without acid, ... in presence of acid.

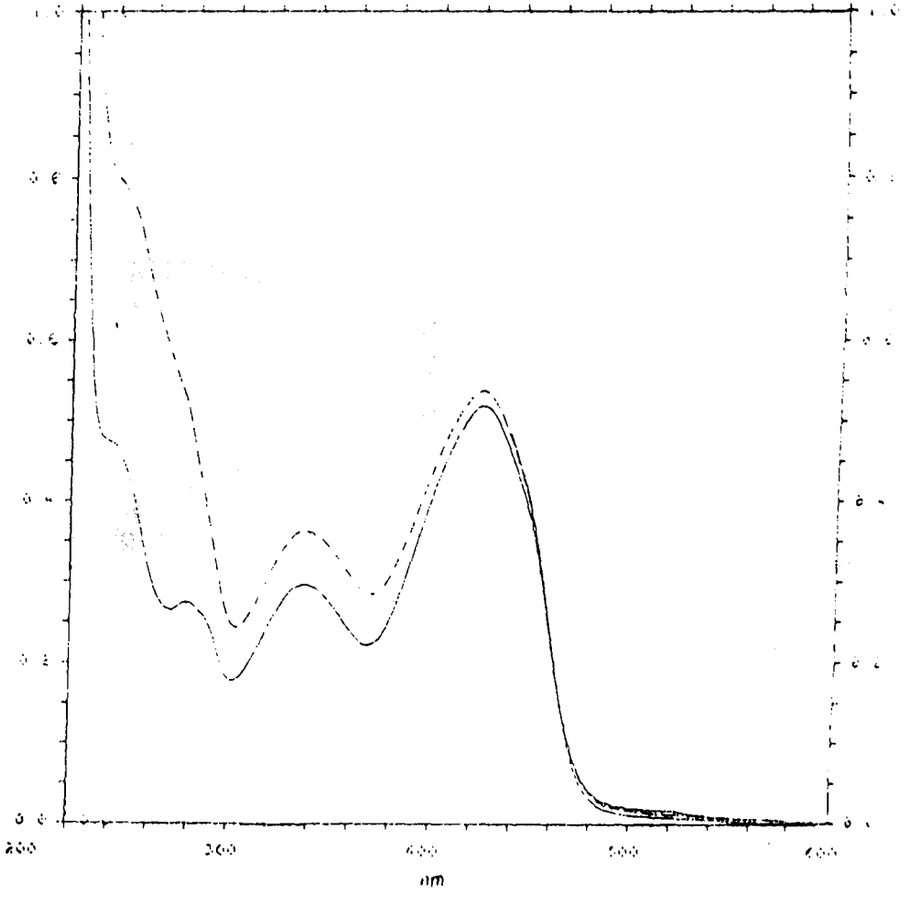


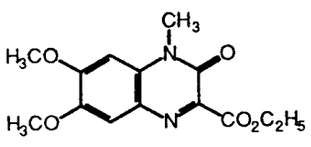
Fig. 25 Effect of the addition of hydrochloric acid upon UV absorption spectrum of (326) in methanol at room temperature; (---) without acid, (....) in presence of acid.

Conclusion

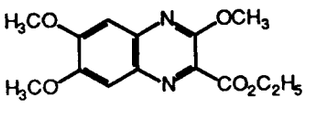
The study of certain diazanaphthoquinones has shown that the quinoxaline quinones carrying electron-donating groups at both the 2- and 3-positions have different properties from quinoxaline quinone, quinoxaline quinones carrying electron-withdrawing groups in the 2- and 3-positions, and phthalazine quinone. For instance, the quinones having electron-donating substituents can be stored at room temperature for at least one year whereas the other quinones are less stable. The behaviour of the quinones in the Diels-Alder reaction is also different. Thus, the first group of quinones react with symmetrical dienes to produce addition products which are resistant to oxidation and to enolisation except under relatively vigorous acidic conditions. However, an unsymmetrical diene gives the fully aromatic product directly.

The study of fluorescent derivatives of quinoxaline, especially the ion-responsive fluorescent derivatives, produced the following conclusions:

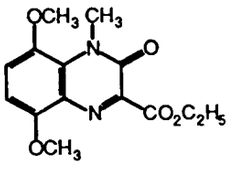
(1) The fluorophores having a powerful 'donor-accepter' system, i.e. a lone pair of electrons at the 'donor' capable of moving to the 'acceptor' part of the molecule, always have a comparatively high fluorescence quantum yield. (several examples can be given but, for instance, (290) is more fluorescent than (292).



(290)



(292)



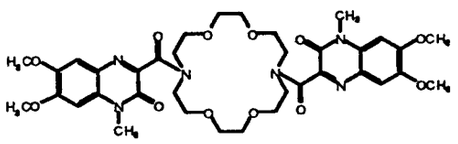
(296)

(2) The movement of the electron pair must be readily promoted, as seen in (290) compared to its isomer (296). This factor also affects the wavelength of the light absorbed (Table 2).

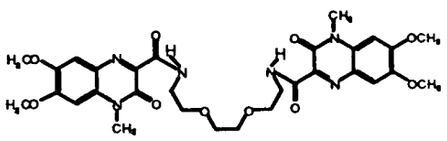
(3) The fluoroionophores (without spacer) having a crown ether directly attached to the 'acceptor' part of the fluorophore, give a higher fluorescence quantum yield and a red shift in excitation and emission spectra on complexation with alkali and alkaline earth metal ions.

(4) When the fluorophore is separated from a crown ether by a chain, the compound, e.g. (329) or (330), may adopt a structure in which the groups on the fluorophore assist in the complexation of the metal ion in the cavity of the ionophore. The compound, e.g. (308) or (310), having a suitable group in the chain may partcipitate in aiding the complexation. These effects produce an increased fluorescence quantum yield upon complexation.

(5) For fluoroionophores having two fluorophores, e.g. (310), the distance between the fluorophores is a significant feature. The excellent results obtained upon complexation of (310) (Fig. 19) are due to this factor approaching optimum value. Moreover, the non-fluorescent nature of the podands (311) is in line with this idea (Table 3 and 4).



(310)



(311)

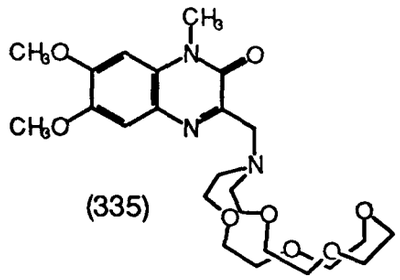
(6) An extension of the conjugated system in the fluorophore results in a red shift in its absorption and emission spectra (Table 3 and 8).

(7) Fluoroionophores having a conjugated system, e.g. (326), are acid sensitive in non-hydroxylic solvents.

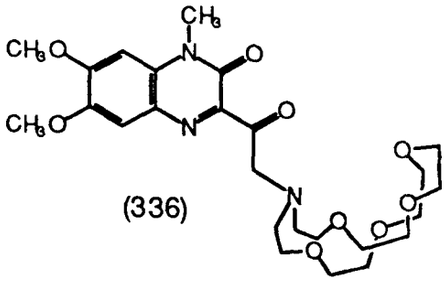
Some Suggestions for the Further Work

With the above conclusion in mind, further work on the following kind of fluoroionophores might be undertaken in order to obtain an ideal system, i.e. a high quantum yield with a large Stokes' shift.

(i) The preparation of series of the compounds similar to (306)-(310), but with a methylene group instead of exocyclic carbonyl group, e.g. (335), or in addition to the exocyclic group, e.g. (336).

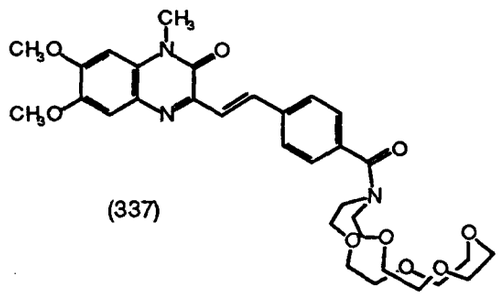


(335)

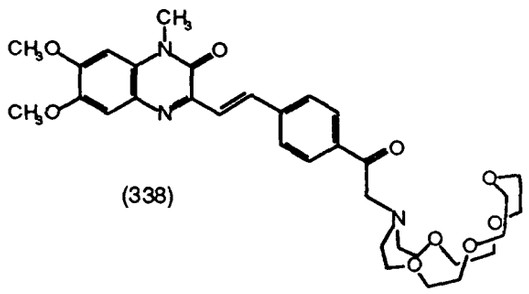


(336)

(ii) A series of the compounds similar to (325)-(327), but with a methylene group instead of exocyclic carbonyl group, e.g. (337) or in addition to the exocyclic group , e.g. (338).

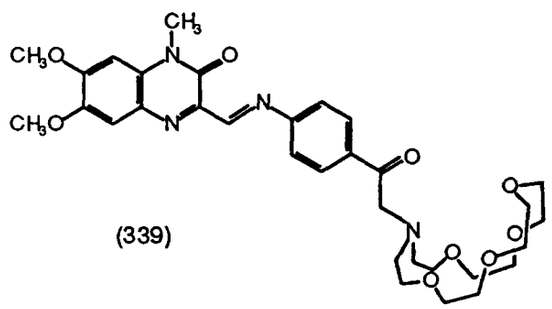


(337)

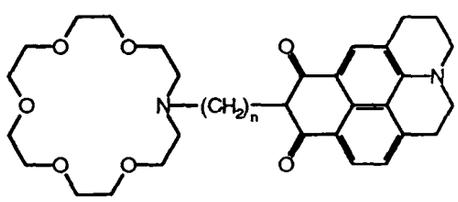


(338)

(iii) Compounds, having the same pattern as in (325)-(327) but with C=N instead of C=C between the quinoxaline and phenyl group, i.e. (339) which would increase the electron accepting power of the 'acceptor' in the molecule.



(339)



(340)

(iv) A study on the effect of the spacer length, i.e. CH_2, CH_2CH_2, and $CH_2CH_2CH_2$ between the fluorophore and ionophore in compound (340). In the absence of metal ion, the crown ether would remain in close proximity to the fluoroionophore but on complexation it would be at a distance from the fluoroionophore.

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Appendix

Novel compounds Prepared:-

Chapter 1

2,3-Bis(bromomethyl)-5,8-dimethoxyquinoxaline (141)

2,3,5,8-Tetramethoxyquinoxaline (146)

2,3-Distyryl-5,8-dimethoxyquinoxaline (152)

Dimethyl 5,8-dimethoxyquinoxaline-2,3-dicarboxylate (154)

1,4-Dihydroxy-5,8-dimethoxypyridazine[4,5-b]quinoxaline (150)

5,8-Dimethoxyquinoxaline-2,3-dicarboxamide (155)

2,3-Dicyano-5,8-dimethoxyquinoxaline (156)

1,4-Diamino-5,8-dimethoxypyridazino[4,5-b]quinoxaline (151)

5,8-Dimethoxyquinoxaline-2,3-bis-(methylenepyridinium) dibromide (157)

1-Amino-2,3-dimethyl-5,8-dimethoxy-9,10-diazaanthracene-4-pyridinium bromide(158)

2,3-Dimethyl-5,8-dimethoxy-9,10-diazaanthracene-1,4-bis-pyridinium dibromide (159)

1,4,8,11-Tetramethoxy-6,13-dihydro-5,7,12,14-tetraza-6,13-dithiapentacene (169)

Bis(2-chloro-5,8-dimethoxyquinoxal-3-yl)sulphide (171)

6,13-Dibutyl-6,13-dihydro-1,4,8,11-tetramethoxy-5,6,7,12,13,14-hexazapentacene (173)

2,3,9,10-Tetramethoxy-6,13-dihydro-5,7,12,14-tetraza-6,13-dithiapentacene (175)

2,3-(5',8'-Dimethoxyquinoxalyl)-1,4,7,10-tetraoxacyclododeca-2-ene (176)

2,5,8-Trimethoxy-4-methyl-3(4H)-quinoxalinone (178)

2-Hydroxy-4-methyl-3(4H)-oxo-5,8-dimethoxyquinoxaline (179)

2,3-Bis(2'-hydroxyethoxy)-5,8-dimethoxyquinoxaline (183)

2,3-Dihydro-1,4-dioxa-5,8-dimethoxy-9,10-diazaanthracene (186)

2,3-Bis(6'-hydroxy-1',4'-dioxahexyl)-5,8-dimethoxyquinoxaline (184)

2,3-Bis(9'-hydroxy-1',4',7'-trioxanonanyl)-5,8-dimethoxyquinoxaline (185)

2,3,11,12-Bis(5',8'-dimethoxyquinoxalyl)-1,4,7,10,13,16-hexaoxacyclooctadeca-2,11-diene (190)

2,3,11,12-Bis(6',7'-dimethoxyquinoxalyl)-1,4,7,10,13,16-hexaoxacyclooctadeca-2,11-diene (191)

2,3,14,15-Bis(5',8'-dimethoxyquinoxalyl)-1,4,7,10,13,16,19,22-

octaoxacyclotetradecadeca-2,14-diene (192)

2,3-Dimethoxyquinoxaline-5,8-dione (194)

2,3-Diethoxyquinoxaline-5,8-dione (195)

2,3-Bis(ethylthio)quinoxaline-5,8-dione (196)

2,3-Di(methoxycarbonyl)quinoxaline-5,8-dione (197)

2,3-Dicyanoquinoxaline-5,8-dione (198)

2,3-Dihydro-1,4-dioxa-9,10-diazaanthracene-5,8-dione (199)

2,3,11,12-Bis(5',8'-dioxoquinoxalyl)-1,4,7,10,13,16-hexaoxacyclooctadeca-2,11-diene (200)

2,3-Dimethoxy-6,7-dichloroquinoxaline-5,8-dione (208)

2,3-Diethoxy-6,7-dichloroquinoxaline-5,8-dione (209)

6-Chloro-2,3-diethoxyquinoxaline-5,8-dione (210)

2,3,6,7-Tetrachloroquinoxaline5,8-dione (211)

2,3,6,7-Tetramethoxyquinoxaline-5,8-dione (214)

6-Bromo-2,3-bis(ethylthio)-quinoxaline-5,8-dione (215)

5,8-Dihydro-6,7-dimethyl-9,10-dihydroxy-1,4-diazaanthracene (217)

5,8-Dihydro-6,7-dimethyl-9,10-diacetoxy-1,4-diazaanthracene (218)

5,8-Dihydro-6,7-dimethyl-1,4-diazaanthracene-9,10-dione (219)

6,7-Dimethyl-1,4-diazaanthracene-9,10-dione (220)

3-Dimethoxy-6,7-dimethyl-5,8,8a,10a-tetrahydro-1,4-diazaanthracene-9,10-dione (222)

2,3-Diethoxy-6,7-dimethyl-5,8,8a,10a-tetrahydro-1,4-diazaanthracene-9,10-dione (223)

2,3-Bis(ethylthio)-6,7-dimethyl-5,8,8a,10a-tetrahydro-1,4-diazaanthracene-9,10-dione (224)

2,3-Dimethoxy-5,8-dihydro-6,7-dimethyl-9,10-dihydroxy-1,4-diazaanthracene (225)

2,3-Diethoxy-5,8-dihydro-6,7-dimethyl-9,10-dihydroxy-1,4-diazaanthracene (226)

2,3-Bis(ethylthio)-5,8-dihydro-6,7-dimethyl-9,10-dihydroxy-1,4-diazaanthracene (227)

2,3-Dimethoxy-5,8-dihydro-6,7-dimethyl-9,10-diacetoxy-1,4-diazaanthracene (228)

2,3-Dimethoxy-5,8-dihydro-6,7-dimethyl-1,4-diazaanthacene-9,10-dione (230)

2,3-Diphenyl-7-methyl-1,4,5-triazaanthracene-9,10-dione (231)

2,3-Dimethoxy-7-methyl-1,4,5-triazaanthracene-9,10-dione (232)

2,3-Diethoxy-7-methyl-1,4,5-triazaanhtracene-9,10-dione (233)

2,3-Dis(ethylthio)-7-methyl-1,4,5-triazaanthracene-9,10-dione (234)

7-Methyl-2,3,5-triazaanthracene-9,10-dione (235)

2,3-Dimethoxy-6-hydroxy-1,4-diazaanthracene-9,10-dione (239)

2,3-Diethoxy-6-hydroxy-1,4-diazaanthracene-9,10-dione (240)

2,3-Bis(ethylthio)-6-hydroxy-1,4-diazaanthracene-9,10-dione (241)

2,3-Diethoxy-6-acetoxy-1,4-diazaanthracene-9,10-dione (242)

2,3-Diphenyl-1,4-diazaanthracene-9,10-dione (244)

2,3-Bis(ethylthio)-1,4-diazaanthracene-9,10-dione (245)

2,3-Diazaanthracene-9,10-dione (246)

Chapter 2

Ethyl 3,6,7-trimethoxyquinoxaline-2-carboxylate (292)

N-Methyl-2-nitro-4,5-dimethoxyaniline (298)

2-(N-Methylamino)-4,5-dimethoxyaniline monohydrochloride (299)

N-(6,7-Dimethoxy-3-methyl-3(4H)-quinoxalinone-2-carbonyl)-4-aminobenzo-15-crown-5 (305)

2'-(1,4,7-Trioxa-10-azacyclododecane-13-ylcarbonyl)-6'-,7'-dimethoxy-4'-methylquinoxaline-3'(4'H)-one (306)

2'-(1,4,7,10-Tetraoxa-13-azacyclopentadecane-13-ylcarbonyl)-6'-7'-dimethoxy-4'-methylquinoxaline-3'(4'H)-one (307)

2'-(1,4,7,10,13-Pentaoxa-16-azacyclootadecane-16-ylcarbonyl)-6'-7'-dimethoxy-4'-methylquinoxaline-3'(4'H)-one (308)

N,N'-Bis(6'-7'-dimethoxy-4'-methyl-3'(4'H)-oxoquinoxal-2'-ylcarbonyl)-1,4,7,10-tetraoxa-7,16-diazacycloctadecane (310)

2'-(1,4,7-Trioxa-10-azacyclododecane-13-ylcarbonyl)-6'-,7'-dimethoxy-4'-methylquinoxaline-3'(4'H)-one (306)

N,N'-bis(6'-,7'-dimethoxy-4'-methyl-3'(4'H)-oxoquinoxal-2'-ylcarbonyl)-1,8-diamino-3,6-dioxaoctane (311)

5,8-Dimethoxy-2,3-bis[2-(6',7'-dimethoxy-4'-methylquinoxaline-3'(4'H)-one-2'-carbonyloxy)ethoxy]quinoxaline (312)

5,8-Dimethoxy-2,3-bis[6-(6',7'-dimethoxy-4'-methylquinoxaline-3'(4'H)-oxo-2'-carbonyloxy)-1,4-dioxahexyl]quinoxaline (313)

6,7-Dimethoxy-4-methyl-2-(4'-carboxyphenylvinyl)-3(4H)-quinoxaline (320)

2,3,10,11-Tetramethoxy-5,13-dimethylpyrazino[1,2-a;4,5-a']diquinoxaline-6,14(5H,13H)-dione (321)

6,7-Dimethoxy-4-methyl-2-(4'-methoxycarbonylphenylvinyl)-3(4H)-quinoxalinone (322)

6,7-Dimethoxy-4-methyl-2-vinylphenyl-3(4H)-quinoxalinone-4'-carbonyl chloride (323)

6,7-Dimethoxy-4-methyl-2-{4'-(N-benzylcarboxamide]}phenylvinyl-3(4H)-quinoxalinone (324)

(2-[-*p*-(1,4,7-Trioxa-13-azacyclododecan-13-ylcarbonyl)phenylvinyl]-6,7-dimethoxy-4-methylquinoxalin-3(4H)-one (325)

2-[-*p*-(1,4,7,10-Tetraoxa-13-azacyclopetadecan-13-ylcarbonyl)phenylvinyl]-6,7-dimethoxy-4-methylquinoxalin-3(4H)-one (326)

2-[-*p*-(1,4,7,10,13-Pentaoxa-13-azacyloctadecan-13-ylcarbonyl)phenylvinyl]-6,7-dimethoxy-4-methylquinoxalin-3(4H)-one (327)