

THE CHEMISTRY OF THE ACRIDIZINIUM ION

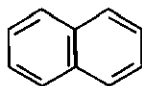
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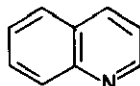
This paper reviews the various methods for the preparation of the acridizinium ion. One of the most successful method involved the use of cyclic acetal 2-(1,3-dioxolan-2-yl)pyridine (9), since the resulting intermediate obtained on treatment with benzyl bromide or substituted benzyl bromides are well suited for cyclisation in hot polyphosphoric acid. Acridizinium benzologs have also been prepared by replacement of the benzyl halides by naphthyl or phenanthrylmethyl halides or the pyridine carboxaldehyde by isoquinoline 1- or 3-carboxaldehydes. The properties, such as, oxidation, reduction, reaction with bases and electrophilic reagents are all discussed in detail.

The occurrence of aromatic compounds formally related to the classical aromatic hydrocarbons by the replacement of a CH by N has long been recognised. The structural relationship of quinoline (2) to naphthalene (1) was understood nearly hundred years ago¹, while the relationship of isoquinoline² was recognised a few years later.

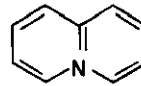
The quinolizinium ion (3) represents the nitrogen analog of naphthalene in which the



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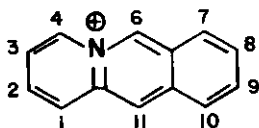
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nitrogen atom occurs at a bridgehead position. In contrast to quinoline and isoquinoline, the other two simple nitrogen analogs of naphthalene, the chemistry of the quinolizinium ion has been little studied and knowledge regarding this ion has been gained almost entirely from investigations of alkaloids containing this nucleus as part of a fairly complex structure. Among the

alkaloids the quinolizinium nucleus probably occurs most widely as its dihydro derivative. For example, the dibenzoquinolizinium ion is the parent structure for the various berberine alkaloids³⁻⁶, palmatin⁷, columbamine⁸, jatrorrhizine⁹, copliline¹⁰, worenine¹¹, dehydrocorydaline and dehydropthalic trifoline^{12,13}.

Despite the continuing attention devoted to simple aromatic systems, the first synthesis of the quinolizinium ion (3) was not announced until 1954^{14,15}, and this date may be regarded as the beginning of the systematic study of the quinolizinium ion and its benzologs¹⁶.

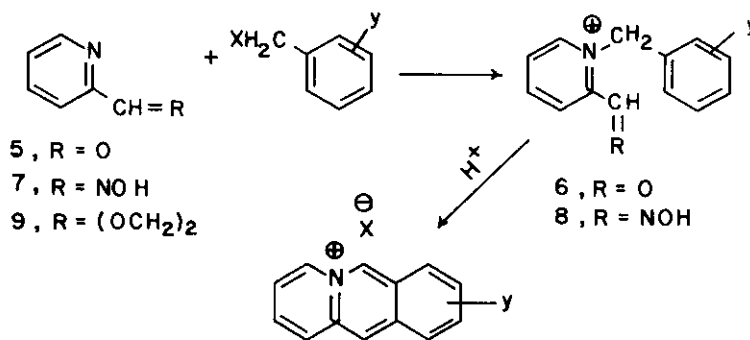
As regards the nomenclature, the tricyclic system is described as benzolog of quinolizinium ion or azonialog¹⁷ of anthracene and has also been given the trivial name "Acridizinium Ion". The chemical abstract numbering for the system is given below (4)¹⁸.



In the azonia arene nomenclature, the numbering is that of the parent hydrocarbon (4, a-azoniaanthracene)¹⁹.

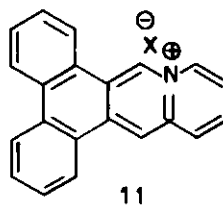
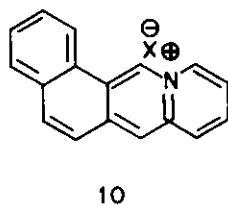
SYNTHESES

The first method for the preparation of the acridizinium ion involved the reaction between commercially available benzyl bromide or a substituted benzyl bromide and pyridine-2-aldehyde (5). The crude salt (6) thus obtained cyclised in boiling hydrobromic acid to afford benzo(b)-quinolizinium derivatives^{16,20}. Due to the unstable nature of the aldehyde, a more stable derivative picolinic aldoxime (7) offered the advantages of greater stability and ease of quarterisation and in addition the intermediate salt 8 was more easily purified and cyclised more rapidly than the aldehyde salt 6²¹. To overcome the resulting low yields in such cyclisations, a number of derivatives related to the oxime (7) were examined²². Use of semicarbazone (5, R=NNHCONH₂), thiosemicarbazone (5, R=NNHCSNH₂) and phenylhydrazone (5, R=NNHC₆H₅) did not produce any better results. The best results were obtained by condensing cyclic acetal, 2(1,3-dioxalan-2-yl)-pyridine (9) with benzyl halides particularly those containing a deactivating substituent²³. Hydrobromic acid as cyclising agent gave the highest yield as compared to polyphosphoric acid, hydrogen fluoride or sulphuric acid.



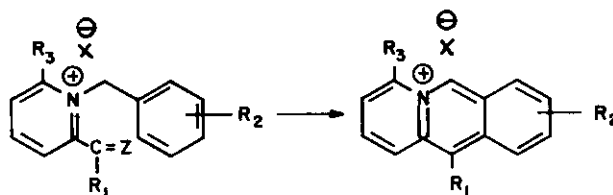
The results are summarized in Table I.

Substituting 1-bromomethylnaphthalene or 9-bromophenanthrene for benzyl halide in 6, benz-(h)acridizinium bromide (10) and dibenz(h,j)acridizinium bromide (11) were obtained in good yields²⁴.



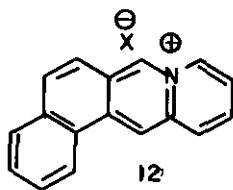
On the other hand, 2-bromomethylnaphthalene with pyridine-2-aldehyde afforded a salt, which on cyclisation was believed to have yielded benz[j]acridizinium bromide (12), the structure of

TABLE I

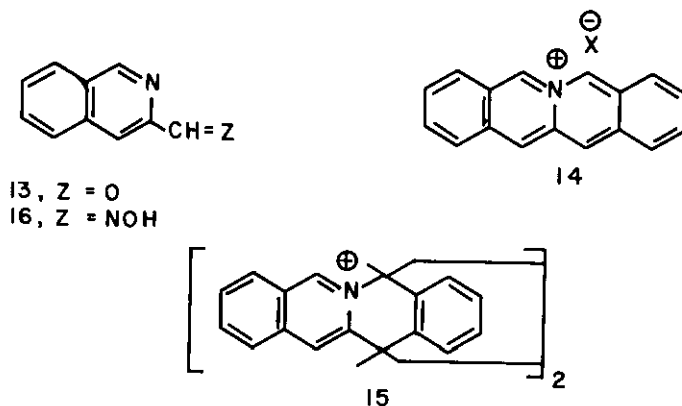


R ₁	R ₂	R ₃	Z	Cyclising agent	Yield %	Ref.
H	H	H	NOH	HBr	89	21
H	H	H	O	HBr	60	21
H	H	H	(OCH ₂) ₂	HBr	95	22
H	H	H	(OCH ₂) ₂	HF	65	22
H	H	H	(OCH ₂) ₂	H ₂ SO ₄	40	22
H	H	H	(OCH ₂) ₂	PPA	77	22
H	9-CH ₃	H	NOH	HBr	92.5	21
H	9-CH ₃	H	O	HBr	55	16,21
CH ₃	H	H	NOH	HBr	21	21
CH ₃	H	H	O	HBr	0.3	21
CH ₃	H	H	(OCH ₂) ₂	PPA	35	22
CH ₃	9-CH ₃	H	NOH	HBr	40	21
CH ₃	8-OH	H	NOH	HBr	99	21
H	H	CH ₃	(OCH ₂) ₂	HBr	9	22
H	11-CH ₃	H	O	HF	3	25
H	7-CH ₃	H	O	HBr	45.7	16
H	H	H	NNHCONH ₂	HBr	47	22
H	7-C ₆ H ₅	H	NOH	HBr	89	50
H	9-C ₆ H ₅	H	NOH	HBr	71	50
H	9-Iso-propyl	H	(OCH ₂) ₂	HBr	51	82
H	Benzo(h)		NOH	HBr	85	21
H	Benzo(h)		O	HBr	52	21

which was deduced from its ultraviolet spectrum²⁴.

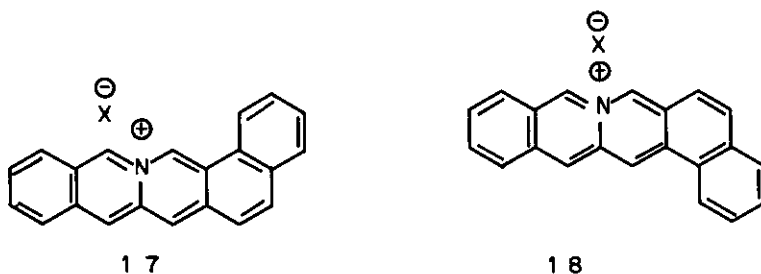


Substituting isoquiniline-3-carboxyaldehyde (13) for picoline aldoxime in 6 followed by cyclisation did not yield the expected product 14, but instead afforded a dimer (15). However, use of its oxime (16) afforded the corresponding benz(b)acridizinium salt (14) in 23% yield ²⁵.

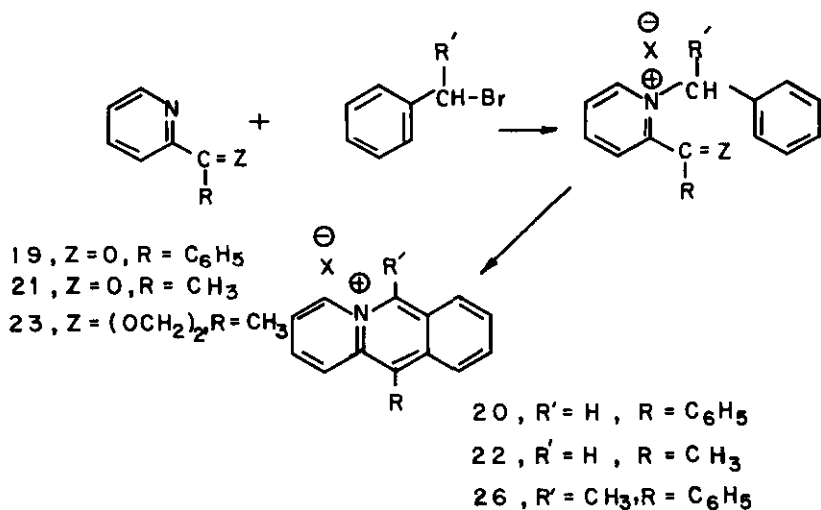


The formation of the dimer (15) was attributed to the low reactivity of the quaternary salt, which required longer refluxing time for cyclisation as compared to the oxime, which required about 10 minutes.

In a similar reaction, dibenz[b,h]- and dibenz[b,j]acridizinium bromides (17 and 18) were prepared from the corresponding salts prepared from 1-bromomethyl or 2-bromomethylnaphthalene and isoquinoline carboxyaldehyde in 43 and 66% yields, respectively ²⁶.

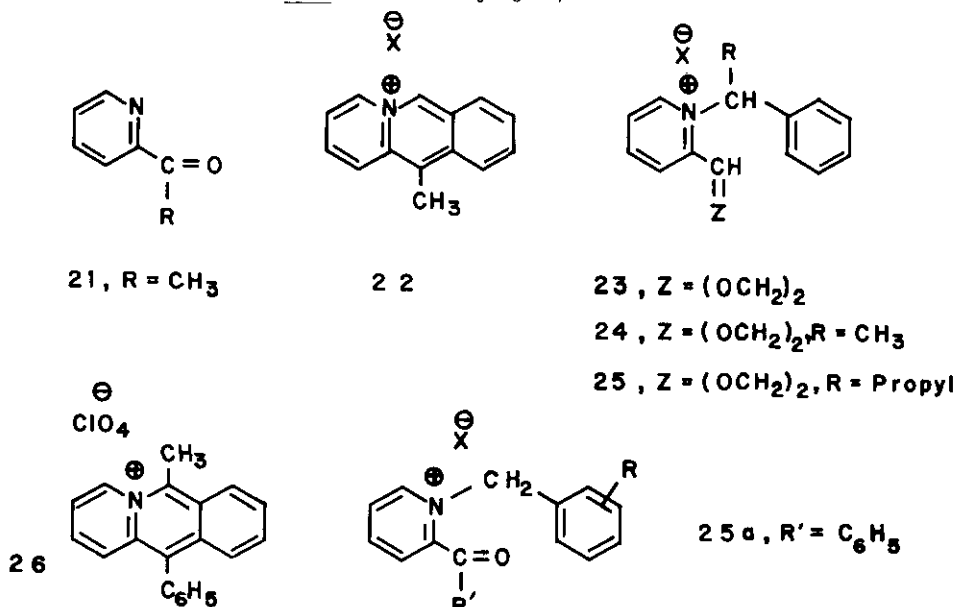


An alkyl or aryl group may be introduced into the meso positions of the acridizinium ion, generally with better success in the 11-position than in the 6-position. Quaternisation of a variety of benzyl halides with 2-benzoyl pyridine (19) followed by cyclisation with hydrogen fluoride afforded 11-phenylacridizinium ion (20) in 89.5% yield ²⁷.



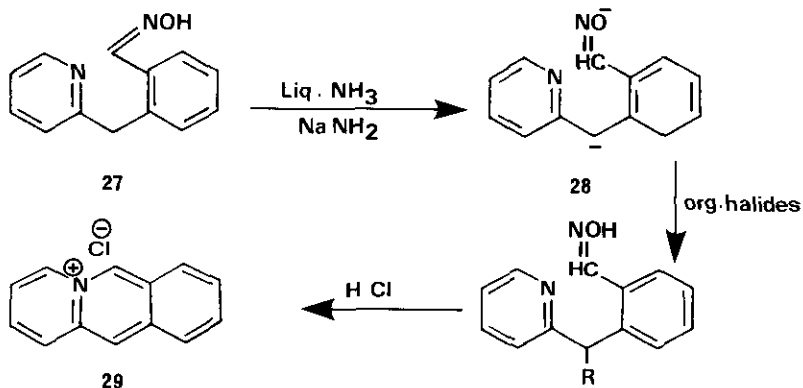
Under comparable conditions, 2-acetylpyridine (21) afforded a poor yield of 22 (3%), but use of cyclic ketal (23) improved the yield to 35%²⁷. In a similar manner, 6-methyl and 6-propyl acrididinium salts were prepared from the quaternary salts (24 and 25) using hydrobromic acid as the cyclising agent²⁸.

Of the five benzoyl pyridinium salts (25a) studied, the quaternary salt derived from *p*-methoxybenzyl bromide failed to cyclise under the usual conditions, probably because the positions available are unactivated and *meta* to a methoxyl group.

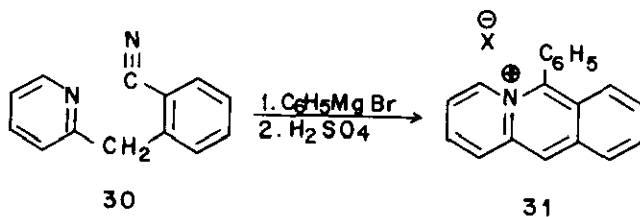


Quaternisation of 2-benzoylpyridine with 1-phenylethyl bromide followed by cyclisation of the crude salt gave a low yield (8%) of 6-methyl-11-phenylacridizinium perchlorate (26) ²⁷.

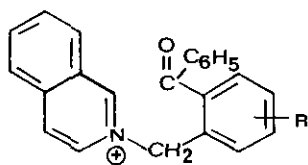
11-Alkyl substituted acridizinium compounds were also prepared from 2-(*o*-hydroxyimino-methyl)benzylpyridine (27) via the dianion (28). Addition of organic halides followed by cyclisation with boiling hydrochloric acid afforded 29 ²⁹.



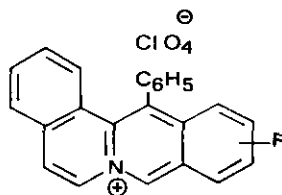
The 6-phenylacridizinium ion has been obtained by a route which is of theoretical interest only ³⁰. *o*-(2-Pyridylmethyl)benzonitrile (30) was treated with an excess of phenylmagnesium bromide, and after suitable hydrolysis to the crude ketone, was cyclised in concentrated sulphuric acid to yield 31.



Extension of this procedure lead to the synthesis of benzacridizinium derivatives with a substituent in the central nucleus. Cyclisation of the quaternary salt (32) with polyphosphoric acid afforded 7-phenylbenz(h)acridizinium perchlorate (33) in 90% yield. Only a single highly activated 1-benzoyl-2-benzylisoquinolinium salt (34) was found to cyclise in liquid hydrogen fluoride ³¹.



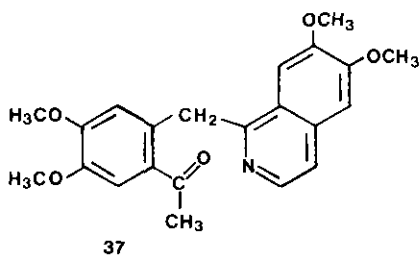
34, R=H



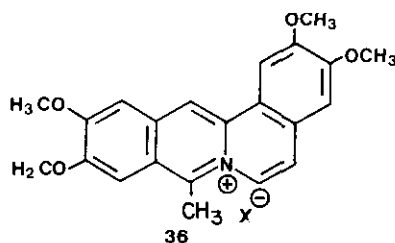
35, R=10-OCH₃

With a methoxy group at para position to the expected ring closure, cyclisation was greatly facilitated and in fact a 91% yield of the 10-methoxy-13-phenylbenzacridizinium perchlorate (35) was obtained.

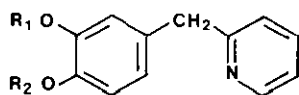
Coralyn (36) was prepared via acetopapaverine (37) by the acetyltive cyclisation of papaverine^{32,33}. This suggested that 2-(3,4-dialkoxybenzyl)pyridine might be made to undergo a similar acyulative cyclisation. Thus cyclisation of alkoxybenzylpyridine derivatives (38) at 100° in sulphuric acid in the presence of an appropriate anhydride afforded the corresponding



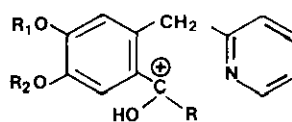
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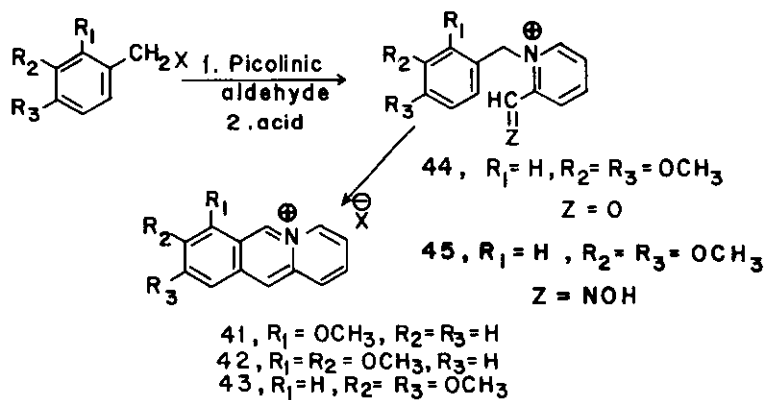
quinolizinium derivatives³⁴. This type of synthesis can be regarded not only as the prototype of the Woodward synthesis³⁵⁻³⁸ of quinolizinium derivatives, but also a further example

of aromatic cyclodehydration³⁹, one involving electrophilic attack on aromatic nitrogen rather than the usual carbon via the conjugate acid (39). The results are summarised in Table II.



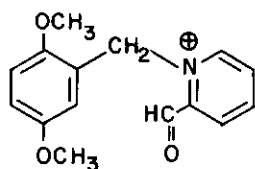
R ₁	R ₂	R ₃	R ₄	R ₅	R ₆	Cyclising agent	Yield %	Ref.
H	H	H	H	H	C ₆ H ₅	HF	77	26
H	H	OCH ₃	H	H	C ₆ H ₅	HF	41	26
H	CH ₃	H	H	H	C ₆ H ₅	HF	34	26
H	H	H	CH ₃	H	C ₆ H ₅	HF	53	26
H	H	H	H	CH ₃	CH ₃	HF	8.6	26
H	OCH ₃	OCH ₃	H	CH ₃	H	H ₂ SO ₄ /acetic anhydride	31	34
H	OC ₂ H ₅	OC ₂ H ₅	H	CH ₃	H	H ₂ SO ₄ /propionic anhydride	74	34
H	—(CH ₂ O) ₂ —	H	H	CH ₃	H	H ₂ SO ₄ /acetic anhydride	25	34
H	H	H	H	CH ₃	H	HBr	11	28
H	H	H	H	H	C ₆ H ₅	HBr	71	28
—(CH ₂ O) ₂ —	H	H	H	H	H	HCl	31	40
H	—(CH ₂ O) ₂ —	H	H	H	H	HCl	42	40
OCH ₃	OCH ₃	H	H	H	H	HCl	75	46

Extension of the same general method to the synthesis of alkoxy derivatives of the acridizinium ion leads to the preparation of 8-methoxy, 7,8- and 8,9-dimethoxyacridizinium salts (41,42,43)⁴⁰. Hydrochloric acid was found to bring about the cyclisation in good yields and without any ether cleavage, as was the case when hydrobromic acid was used as the cyclising agent.

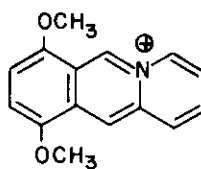


Contrary to Bradshers findings ⁴⁰, Watthey and coworkers ⁴¹ have reported that cyclisation of the pyridinium salt 44 or 45 with concentrated hydrochloric acid at 100° did not only give an impure product but also led to the ether cleavage. However, they succeeded in cyclising the quaternary salt with hydrobromic acid at 75° over a period of 5 minutes. Their results are in agreement to those of Kupchan, et al. ⁴².

Bradsher and Barker ⁴³ have reported their failure in the isolation of any pure product from the cyclisation of the quaternary salt 46 and instead, have isolated a mixture of 47 and one molecule of hydroxylamine hydrobromide.

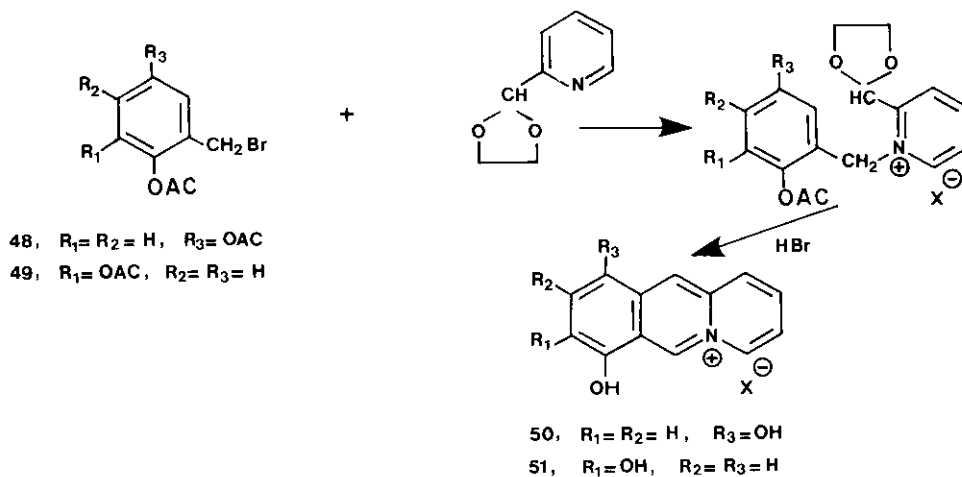


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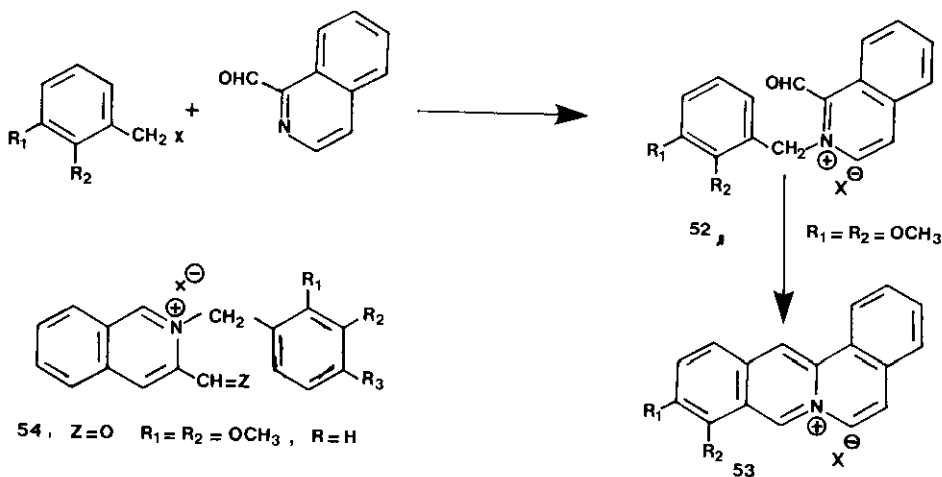


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Fields and co-workers ⁴⁴ have converted bromomethylhydroquinone diacetates (48 and 49) into the corresponding hydroxyacridizinium derivatives (50 and 51) by cyclisation of the pyridinium salts in boiling hydrobromic acid or with a 15-32% hydrogen bromide-acetic acid mixture.



Condensation of 1-isoquinoline aldehyde with alkoxybenzyl halides followed by cyclisation of the crude salt (52) with hydrochloric acid resulted in the formation of an expected benz [a]acrididinium chloride (53) in 52% yield⁴⁵. It was also observed that even 2-benzyl-3-formyl-isoquinolinium salt (54) could be cyclised, if the benzyl group contains substituents, which



sufficiently enhance the rate of cyclisation. Thus alkoxybenzologs of 54(Z=0), on heating with hydrochloric acid for 5-15 minutes afforded the corresponding alkoxybenz[*b*]acridizinium salts ²⁶. The salt (53) might be regarded as the parent substance of all the photoberberine alkaloid and could be referred as a dehydroprotoberberinium salt. By the use of alkoxybenzyl halides, several alkoxybenzyl[*b*]acridizinium salts were synthesised. The results are summarised in Table III.

The dehydroberberinium salt (55) was prepared from the quaternary salt obtained from 6,7-methylenedioxyisoquinoline-1-aldehyde (56) and substituted benzyl halides. Cyclisation of the quaternary salt with hydrochloric acid afforded dehydroberberinium chloride (55) in 30% yield. Use of the corresponding oxime in the formation of the quaternary salt followed by cyclisation with polyphosphoric acid increased the yield to 67% ⁴⁶.

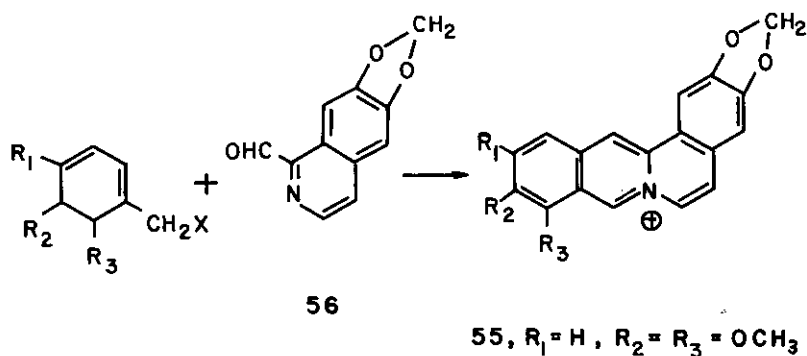
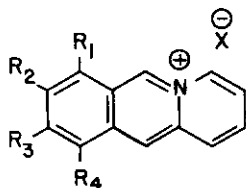


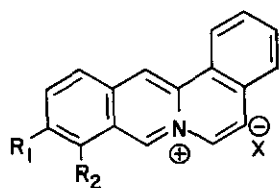
TABLE III



R ₁	R ₂	R ₃	R ₄	Cyclising agent	Yield %	Ref.
H	OCH ₃	H	H	HCl	44	62
H	OH	H	H	HBr	37	40
OCH ₃	OCH ₃	H	H	HBr	75	40
O — CH ₂ — O		H	H	HCl	42	40
H	O — CH ₂ — O	H	H	HCl	31	40
H	OCH ₃	OCH ₃	CH ₃	HBr	62	41
OCH ₃	H	H	OCH ₃	HBr	72	41



R ₁	R ₂	R ₃	Cyclising agent	Yield	Ref.
H	OCH ₃	H	HBr	76	26
OCH ₃	OCH ₃	H	HCl	29	26
H	OCH ₃	OCH ₃	HCl	74	26
H	O — CH ₂ — O —		HCl	39	26

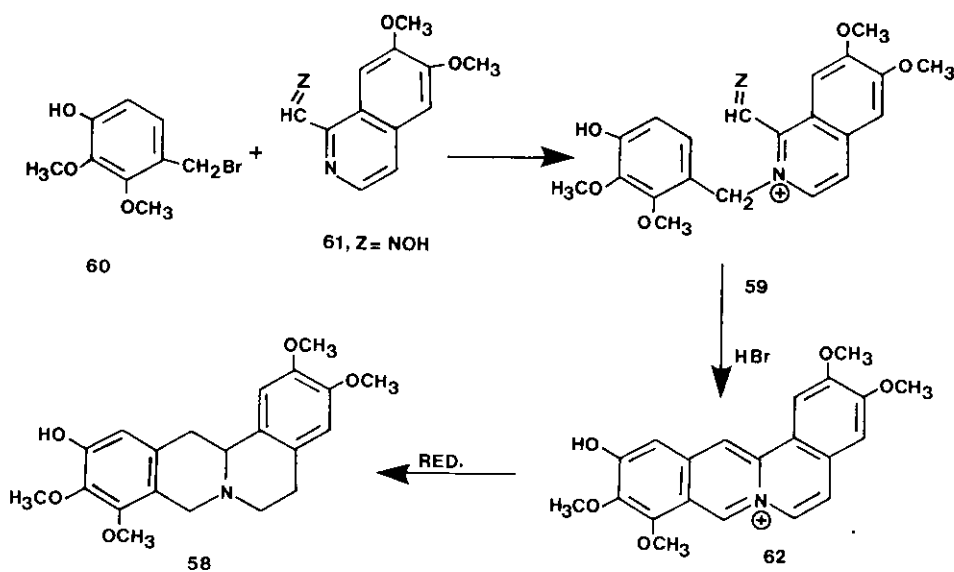


R ₁	R ₂	Cyclising agent	Yield %	Ref.
H	H	HCl	52	45
OCH ₃	H	HCl	78	45
OCH ₃	OCH ₃	HCl	53 ^a	45
O — CH ₂ — O		HCl	66 ^b	45

a = yield reported is that of the perchlorate.

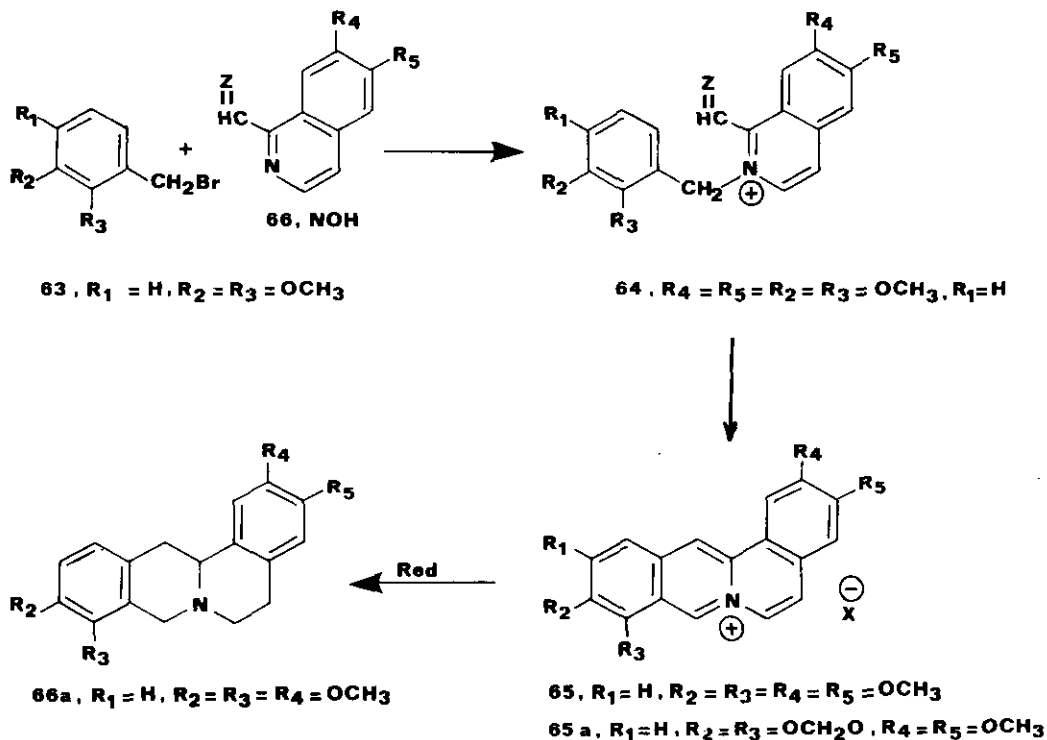
b = crystallised from the cyclisation mixture as the chloride.

Extension of this procedure led Bradsher and his co-workers⁴⁷ to the establishment of the structure of an alkaloid, stepharotine (58). Hydrobromic acid cyclisation of the quaternary salt (59) prepared from 2,3-dimethoxy-4-hydroxybenzyl bromide (60) and 6,7-dimethoxyisoquinoline-1-carboxylidoxime (61) afforded 11-hydroxy-2,3,9,10-tetramethoxybenz[*a*]acridizinium bromide (62), which on reduction over Adams catalyst gave (±) 11-hydroxy-2,3,9,10-tetramethoxy-5,6,13a-tetrahydro-8-dibenzo[*a,g*]quinolizine (58).



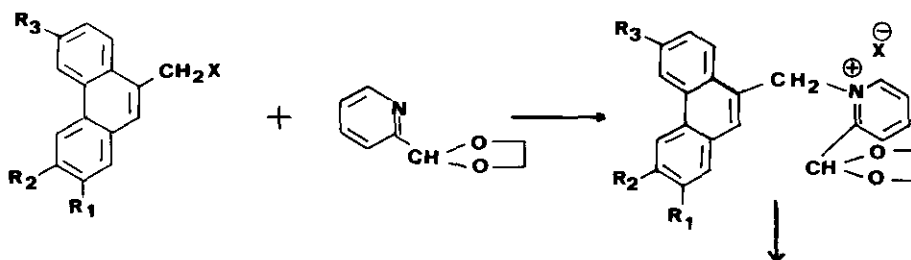
Quaternisation of the same aldehyde (61, z=0) with 2,3-dimethoxybenzyl bromide (63) in acetonitrile followed by cyclisation of the crude salt (64) with boiling hydrochloric acid resulted in the formation of the dehydropalmatine and was isolated as bromide (65) in 30% yield⁴⁸. The yield was raised to 80% by using the oxime 66 in the presence of dimethyl formamide for quaternisation followed by cyclisation. Reduction of 65 over Adams catalyst yielded (±)-tetrahydropalmatine (66^a) as hydrobromide. In a similar reaction dehydropiber-

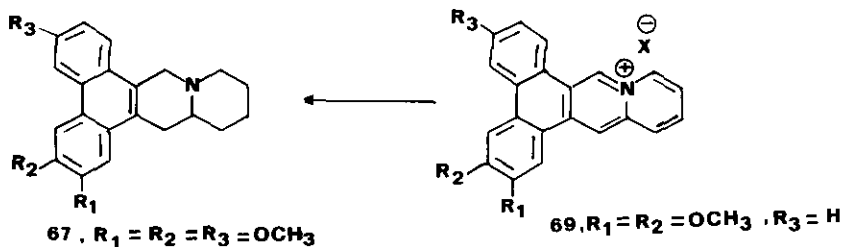
berinium chloride (65a) and other derivatives were prepared. The results are summarised in Table IV.



Synthesis of some of the analogs of cryptopleurine (67) was carried out by quaternisation of 2,3-dimethoxy-9-bromomethylphenanthrene (68) with 2-(1,3-dioxolan-2-yl)pyridine followed by cyclisation of the crude salt with hydrobromic acid. The resulting product, 2,3-dimethoxydibenzo[h,j]acridizinium bromide (69) was isolated in quantitative yield.^{49,50}

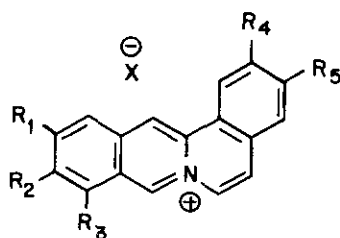
In a similar reaction 6-methoxy and 2,3,6-trimethoxydibenzo[h,j]acridizinium salts were prepared and isolated as perchlorates.





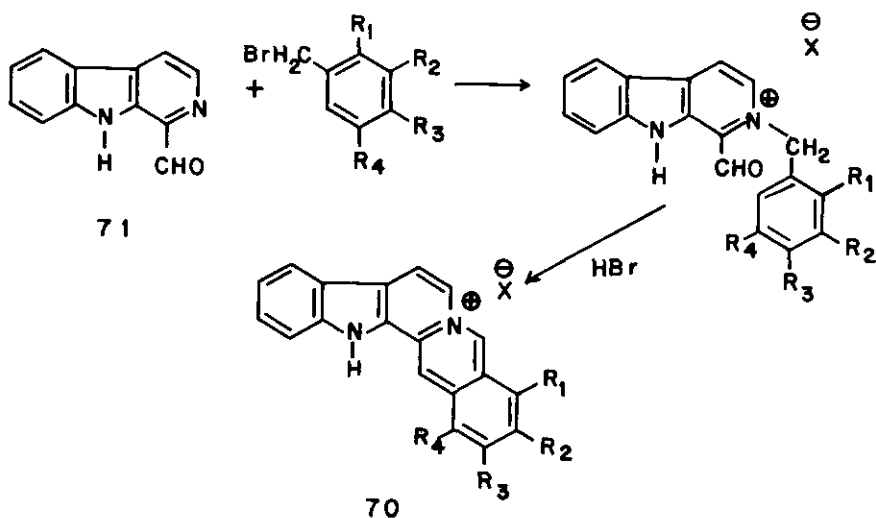
Bradsher and Umans⁵¹ synthesised indolo(2,3-a)acridizinium bromide (70) which is considered as the parent system of the yohimbine, reserpine and alstoniline alkaloids. This was carried out by quaternisation of the pyridoindole carboxyaldehyde (71) with benzyl bromide in dimethyl formamide followed by cyclisation of the crude salt with polyphosphoric acid at 120⁰ for 24 hours. Its structure was further confirmed by synthesising its 8,9-methyl derivative from

TABLE IV



R ₁	R ₂	R ₃	R ₄	R ₅	Z	Cyclising agent	Yield %	Ref.
H	OCH ₃	OCH ₃	O — CH ₂ — O	O	O	HCl	30	46
H	OCH ₃	OCH ₃	O — CH ₂ — O	O	NOH	HCl	67	46
O — CH ₂ — O	H	H	O — CH ₂ — O	O	O	HCl	66	46
H	OCH ₃	OCH ₃	OCH ₃	OCH ₃	O	HCl	30	47
H	OCH ₃	OCH ₃	OCH ₃	OCH ₃	NOH	HCl	80	47
O — CH ₂ — O	H	H	H	H	NOH	HCl	100	47
H	O — CH ₂ — O	O	O — CH ₂ — O	O	NOH	HCl	85	47
OCH ₃	OCH ₃	H	O — CH ₂ — O	O	NOH	HCl	-	46 ^a

a = as perchlorate.



1-methyl-2-(3-isoquinolyl)-indole and bromoacetone⁵². The results are summarised in Table 5.

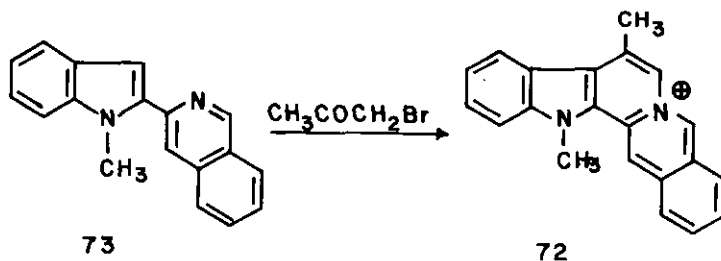
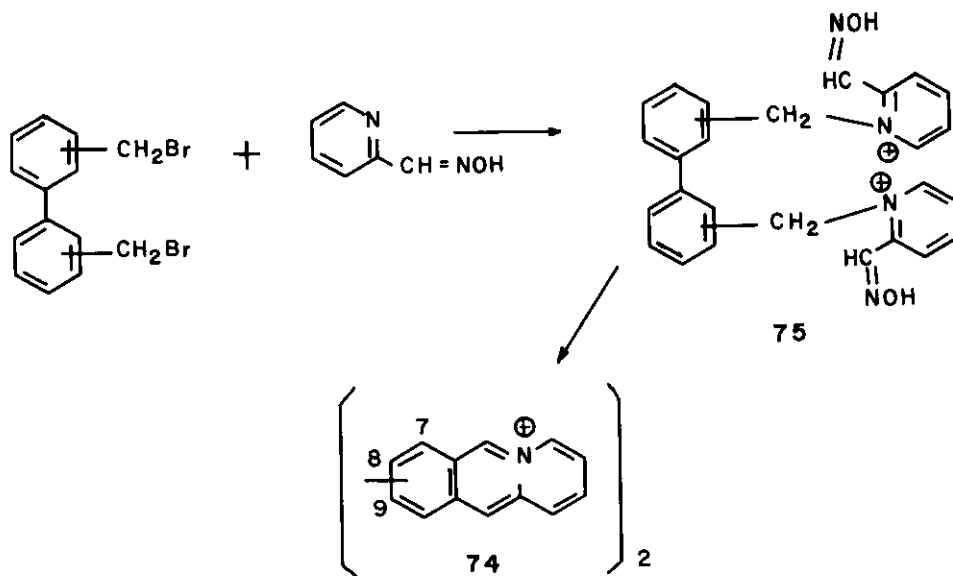


TABLE V

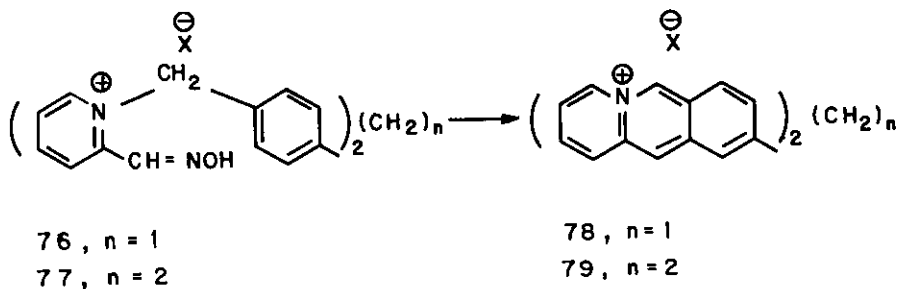
R_1	R_2	R_3	Cyclising agent	yield %	Ref.
H	H	H	PPA	72	50
OCH ₃	H	H	HCl	80	50
H	OCH ₃	OCH ₃	HCl	81	50

The interest in the pharmacology of bis-quaternary nitrogen system with regard to their application as hypotensive, ganglionic and neuromuscular blocking agents^{54,55} suggested the

possibility of synthesising some bis-acridizinium compounds (74). Cyclisation of the quaternary salt (75) with boiling hydrobromic acid resulted in the formation of 7,7'-bis(acridizinium bromide). Similarly 8,8'-bis and 9,9'-bis(acridizinium bromides) were prepared in good yields ⁵⁶.

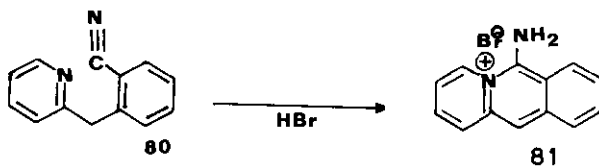


From 4,4'-bis(bromomethyl)diphenylmethane and 4,4'-bis(bromomethyl)biphenyl via the quaternary salts 76 and 77, 9,9'-methylenebis(acridizinium bromide) (78) and 9,9'-ethylenebis(acridizinium bromide) (79) were obtained in reasonable yields.

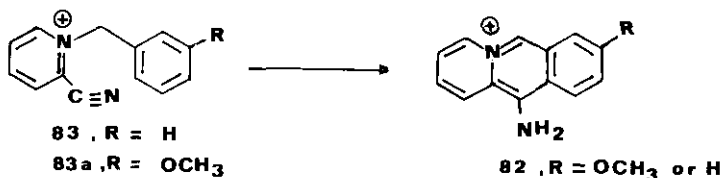


Aminoacridizinium Salts.

The first report of the successful preparation of 6-aminoacridizinium bromide was that of Bradsher and Sherer ⁵⁷, who found that cyclisation of 9-(2-pyridylmethyl)benzotrile (80) with hydrobromic acid yielded 6-aminoacridizinium bromide (81). This synthesis suggested that 11-aminoacridizinium derivatives (82) might be obtained by acid catalysed cyclisation of 1-benzyl-2-cyanopyridinium salts (83 and 83a). The best results were obtained by using concentrated sulphuric acid at 100° for cyclisation. Use of hydrogen chloride resulted in the cleavage of the

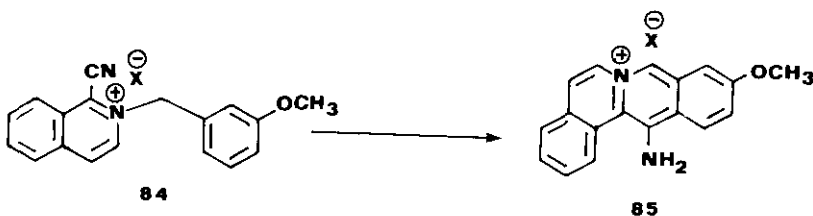


quaternary salt (82) yielding 2-picolinamide hydrochloride. Introduction of a methoxyl group para

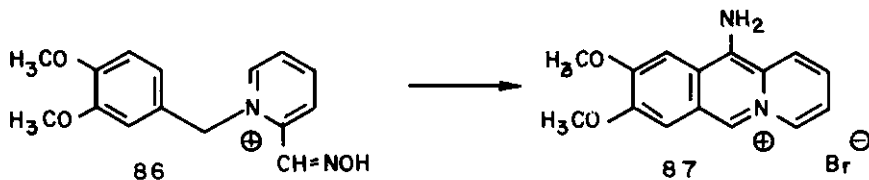


to the position of expected cyclisation (83) resulted in an improved yield (70%). The method however, failed to yield the benzologs of 83 from the cyclisation of 1- α - or 1- β -naphthyl-2-cyanopyridinium salts⁵⁸.

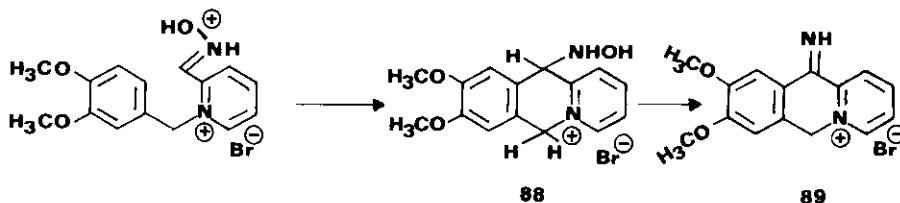
In a similar reaction cyclisation of the quaternary salt (84, X=BF₄) prepared from 1-cyanoisoquinoline and *m*-methoxybenzyl bromide with 100% phosphoric acid at 130° afforded 10-methoxy-13-aminobenz(a)acridinium tetrafluoroborate (85) in 88% yield⁵⁸.



Watthey et al⁴¹ in contradicting the results of Bradsher and co-workers²¹ have reported that the cyclisation of 86 by hydrobromic acid did not afford the corresponding benz(b)quinolizinium bromide but gave a product which was shown to have the structure corresponding to 8,9-dimethoxy-11-aminoacridizinium bromide (87).



The proposed mechanism suggested the protonation of the oxime followed by cyclisation to yield an intermediate (88), which then dehydrates to the imine (89) a tautomer of 87. Such transformations are also involved in Semmler-Wolf aromatizations^{59,60} in general and presumably in the acid promoted conversion of 3,5-dimethylcyclohexanone oxime to 3,5-xylamine⁶¹.



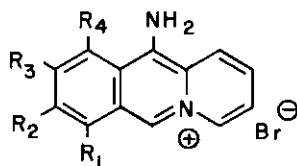
It was concluded that those substances which cyclise to give only the amino derivatives have a methoxy group para to the site of the cyclisation flanked by a methoxy group and a hydrogen atom, and those which gave little or no amino compound react more slowly enabling oxime hydrolysis to occur. The results are summarised in Table VI.

Quinones

Bradsher and Barker⁶² have reported that the reaction of 2-bromomethyl-1,4-dimethoxynaphthalene (90) with picolinaldoxime (92) afforded a 99% yield of the quaternary salt (91), which on cyclisation followed by ether cleavage and oxidation resulted in the formation of a monoxime (93). This monoxime on boiling for 48 hours with a mixture of glacial acetic acid and 48% hydrobromic acid afforded 6a-azonianaphthacene quinone (94) in low yield.

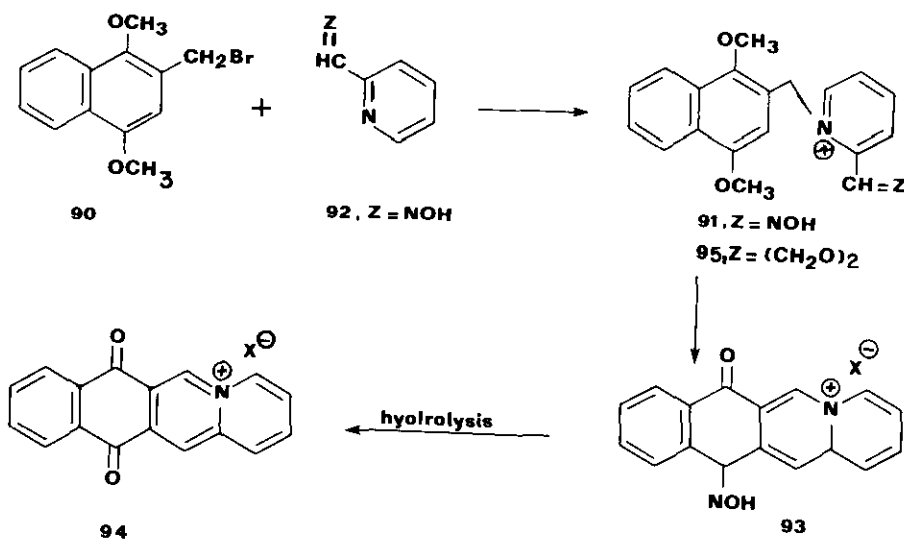
Use of 2-(1,3-dioxalan-2-yl)pyridine instead of the oxime gave the quaternary salt (95)

TABLE VI

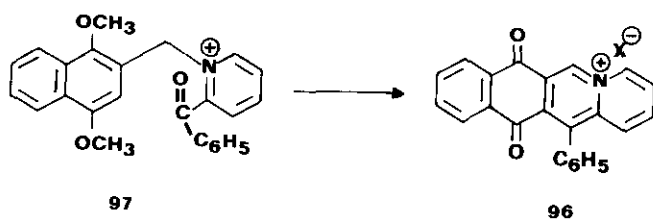


R ₁	R ₂	R ₃	R ₄	Cyclising agent	Yield %	Ref.
OCH ₃	OCH ₃	H	H	HBr	66	41
H	OCH ₃	OCH ₃	OCH ₃	HBr	70	41
OCH ₃	OCH ₃	OCH ₃	H	H ₂ SO ₄	35	58
H	H	OCH ₃	H	H ₂ SO ₄	70	58

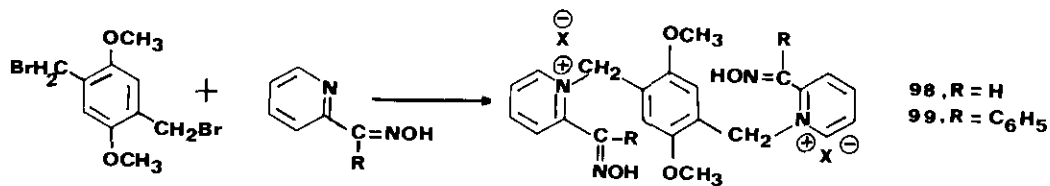
which cyclised to yield 93 directly in an overall yield of 63%. Its 11-phenyl derivative (96)

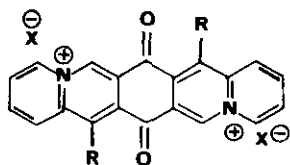


was synthesised from the quaternary salt (97) in an overall yield of 74%. Similarly the diquar-



ternary salts (98,99) were cyclised on heating for 24 hours at 100° in 48% hydrobromic acid in the presence of air to yield 100 and 101 in 71 and 50% yield respectively⁴³.



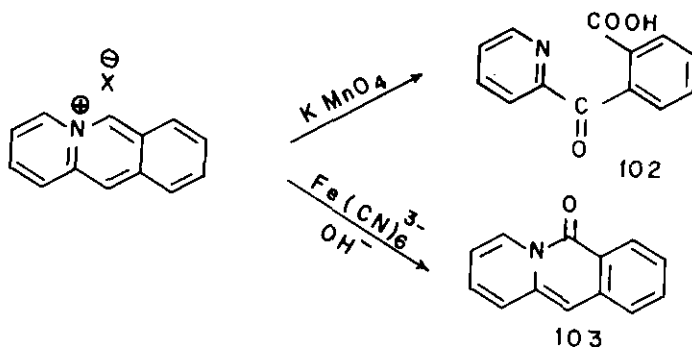


100, R = H
 101, R = C₆H₅

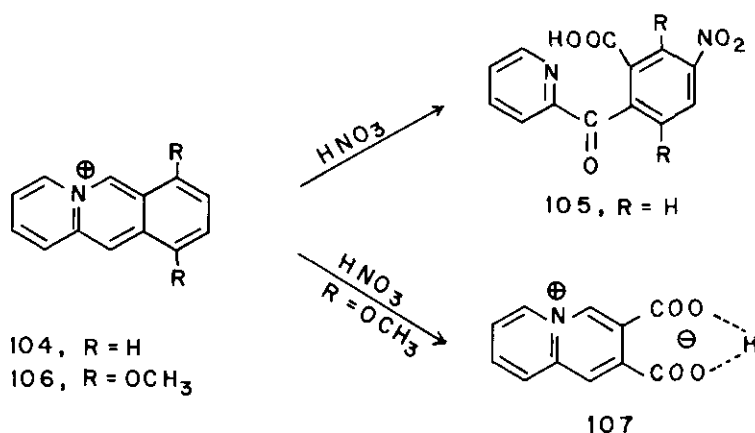
Reactions

Acridinium salts are yellow, giving a fluorescent solutions in water or polar solvents and such solutions have an ultraviolet absorption spectrum reminiscent of that of anthracene¹⁶, except for a general shift to longer wave lengths and an intensified absorption at longer wave lengths. Acridinium salts appear to be stable provided they are shielded from light.

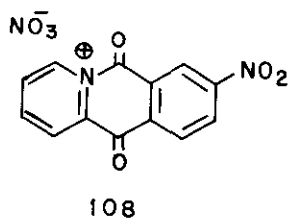
Oxidation of the acridinium ion can occur in several ways. With permanganate 2-(2-carboxybenzoyl)pyridine (102) and not phthalic acid as reported earlier¹⁶ was isolated in 30% yield⁶³. On the other hand, alkaline ferricyanide gave a 9% yield of 6H-benzo[b]quinoline-6-one (103)⁶⁴.



Heating acridinium bromide (104) with 12M nitric acid at 100° for 3 hours resulted in the formation of 2-(2-carboxy-4-nitrobenzoyl)pyridine (105), while a similar oxidation carried out on 7,10-dimethoxyacridinium ion (106) afforded the betaine (107) of 2,3-dicarboxyquinolinium hydroxide⁶⁵. The oxidation of 104 may be considered to be similar to that of the attack of nitric acid on anthracene to yield anthraquinone. The intermediate acylammonium salt (108) would be expected to hydrolyse rapidly to the keto acid (104, R=H). Later work⁶³, however, had shown that treatment of the acridinium ion with a mixture of nitric acid and



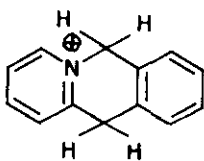
sulphuric acid at -5° resulted in the formation of a mononitroacridizinium salt which on oxida-



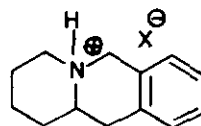
tion with concentrated nitric acid at 100° afforded 2-(2-carboxynitrobenzoyl)pyridine (109), which on decarboxylation, yielded 2-(2-nitrobenzoyl)pyridine, confirming that the original nitration product was the 10-nitro derivative (110). It was concluded that oxidation must precede nitration or else the product would be 110 and therefore 102 cannot be an intermediate as it has been recovered unchanged when subjected to the conditions of the oxidative nitration.



The reduction of the acridizinium nucleus can be made to occur stepwise. With a palladium catalyst, the reduction may be interrupted after the addition of one mole of hydrogen, affording 6,11-dihydroacridizinium ion (111). With a substituent at 6- and 11-positions, reduction over a palladium catalyst likewise afforded a 6,11-dihydro derivative. With a platinum catalyst both rings common to the nitrogen atom are reduced, affording benzo[b]octahydroquinolizinium salt

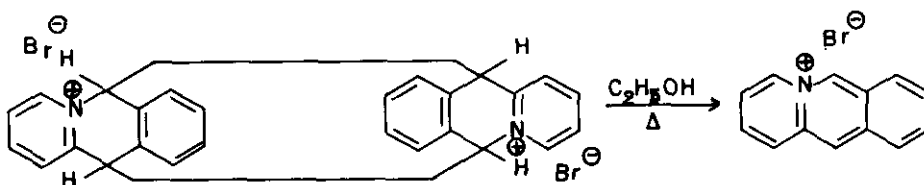


111



112

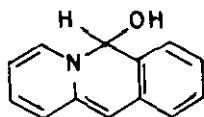
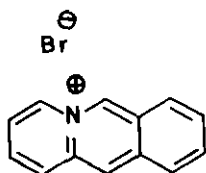
(112) ¹⁶. The same compound (112) was obtained, when sodium borohydride was used as a reducing agent ⁶⁷. The acrididinium ion was found to be more sensitive to light than is anthracene, but like it, is believed to undergo photodimerisation through the meso positions ⁶⁸. The photodimer (113) when refluxed for 24 hours with 48% hydrobromic acid remained unchanged, but refluxing it in 95% ethanol solution for 18 hours afforded acrididinium bromide in 82% yield.



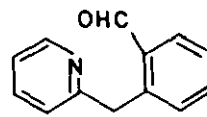
113

Action of Bases

The acrididinium ion is quite stable in acid solution but is sensitive to attack by bases. It has been reported ^{57,38,69} that addition of base to an aqueous solution of acrididinium ion leads to the precipitation of a red or brown powder, which could not be recrystallised and was shown to be a mixture of the pseudo base (114) and the aldehyde (115). The structure of 115 was established by the formation of an oxime or a semicarbazone, which on refluxing for



114

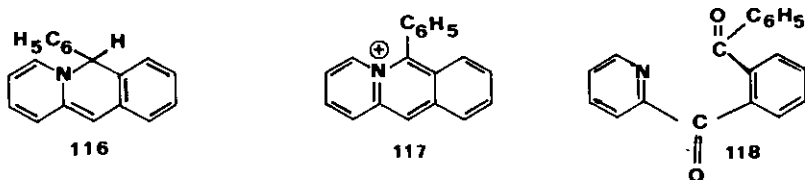


115

1 hour in hydrobromic acid, was converted to acrididinium bromide in 91% yield.

It has also been reported ⁵⁷ that acrididinium bromide on treatment with phenylmagnesium bromide resulted in the formation of a dihydro base (116), which on refluxing with ethanolic

picric acid yielded the picrate of the base 116 and not the picrate of the aromatic quaternary salt (117) as reported earlier⁶⁹. The structure of 117 was further established by the oxidation of 116 to 118 and by an independent synthesis of the diketone, 2-(2-picolinyl)benzophenone.

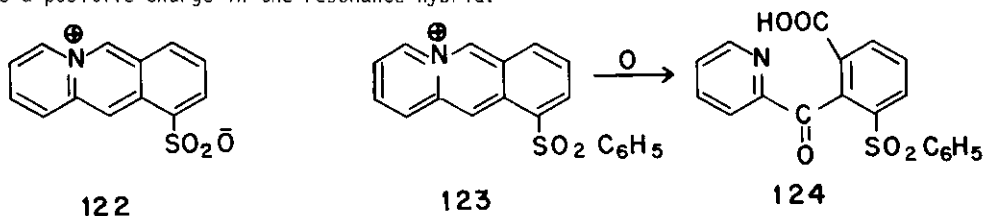


Condensation of phenylacetonitrile with acridizinium bromide in the presence of base^{57,70} resulted in the formation of 2-(2-(α -cyanostyryl)benzyl)pyridine (120) and not 121 as was reported earlier. This seems possible only, if one assumes that the formylbenzylpyridine (115) was an intermediate in the condensation reaction.



Sulphonation

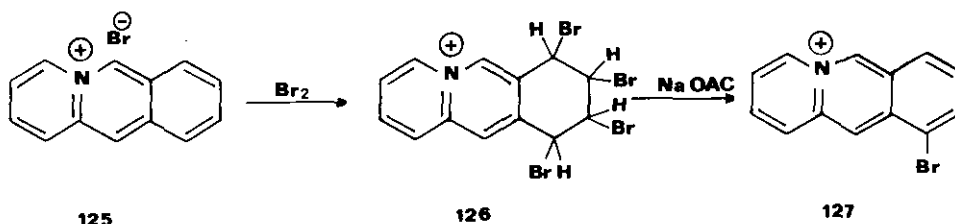
Fozard and Jones^{70,71} have demonstrated that in the presence of an activating group, the quinolizinium ion does appear to undergo electrophilic substitution. When acridizinium bromide was dissolved in 20% fuming sulphuric acid, a sulphobetaine (122) was obtained in 82% yield⁷². Oxidation with nitric acid of its phenyl sulphone derivative (123) gave a keto acid (124), the structure of which was established by an independent synthesis showing thereby, that sulphonation has occurred at the 10-position⁷². The formation of 122 was rationalised on the basis that the 10-position is an α rather than a β position, and unlike the position 7 is not a position which bears a positive charge in the resonance hybrid.



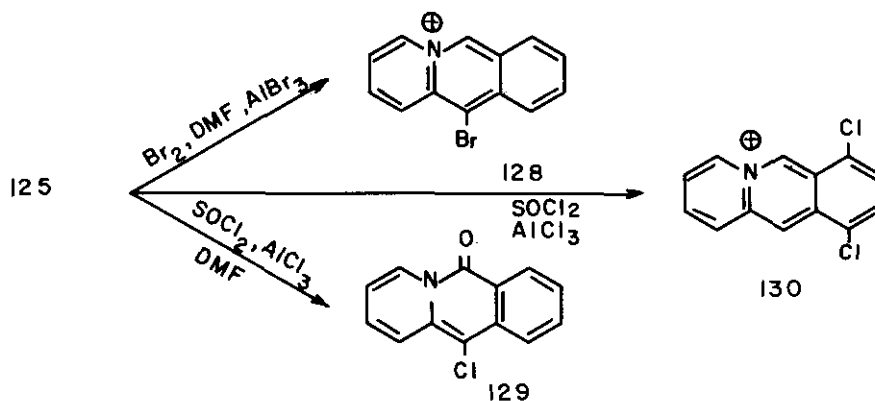
Halogenation

The mechanism of halogenation of the acridizinium ion appears less clear. Addition of

bromine to the acridizinium ion (125) in the absence of the solvent resulted in the formation of an addition compound (126) in which bromine was supposed to have added to the 7,8,9 and 10 positions ⁷³. This is in agreement to the addition of bromine to the terminal ring of 9,10-dichloroanthracene ⁷⁴. The new cation 126 reverts back to the

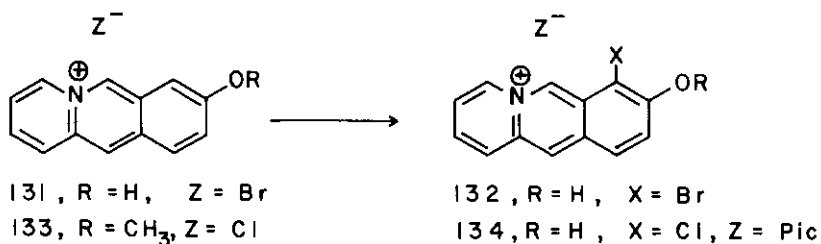


acridizinium ion on heating, and on treatment with sodium acetate afforded 10-bromoacridizinium ion (127). Bromination in the presence of aluminium bromide and dimethylformamide yielded the 11-bromo derivative (128), while from the chlorination with sulphuryl chloride, 11-chloro-6 H-benzo[b]quinolizine-6-one (129) was isolated.



It appears most likely that, under the experimental conditions, the acridizinium nucleus like that of anthracene ⁷⁵ was chlorinated in the meso positions affording the 6,11-dichloroacridizinium cation, which then undergoes nucleophilic attack by water at the active 6-position, yielding the chlorobenzoquinolizine-6-one (129). Halogenation by sulphuryl chloride in the absence of dimethylformamide afforded 7,10-dichloroacridizinium ion (130), the structure of which was established by an independent synthesis. Halogenation of the acridizinium ion containing an activating substituent was shown to yield a mono derivative. Thus bromination of 8-hydroxyacridizinium bromide (131) in acetic acid afforded 7-bromo-8-hydroxyacridizinium bromide (132). Using sulphuryl chloride in dimethylformamide, 8-methoxyacridizinium chloride

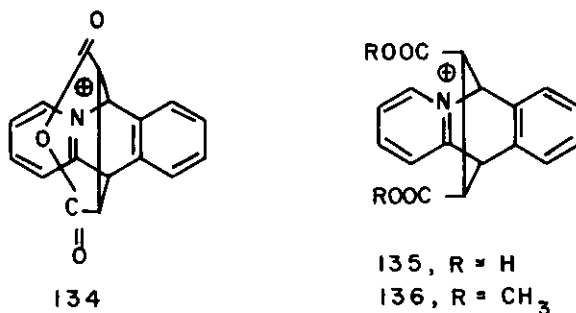
(133) gave the corresponding 7-chloro derivative in 60% yield ⁷⁶ .



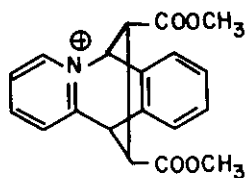
Transannular Addition of Dienophiles

The observation that acridizinium bromide undergoes photodimerisation ⁶⁸ suggested that it might also resemble anthracene ⁷⁷⁻⁷⁹ , in functioning as the diene component in the Diels-Alder reaction. In fact it had been shown that acridizinium ion adds up substituted ethylenes across the meso positions of the nucleus. The first example involved the addition of the common dienophiles, maleic anhydride, maleate and fumarate esters ⁸⁰ . Later work with the cycloaddition reactions included, acrylonitrile, ketene acetals ⁸¹ arylmaleimides ⁹¹ and norbornene derivatives ⁹² . The results are summarised in Table VII. All these reactions are unique example of Diels-Alder reaction in which the "diene" component bore a positive charge.

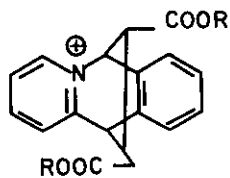
Addition of maleic anhydride to acridizinium bromide in acetic acid afforded an adduct (134) which on hydrolysis with perchloric acid followed by esterification of the hydrolysed product (135) resulted in the formation of cis dimethyl ester (136) . The anti configuration with respect to the benzene ring, since the infrared and nmr spectra



showed proximity of one of the carbomethoxy groups to the quaternary nitrogen atom ⁸² . With methyl maleate, an adduct 137 was isolated in 43% yield and was designated syn configuration. In this reaction a rearranged product (138) was also obtained in 13% yield. It is most likely



137

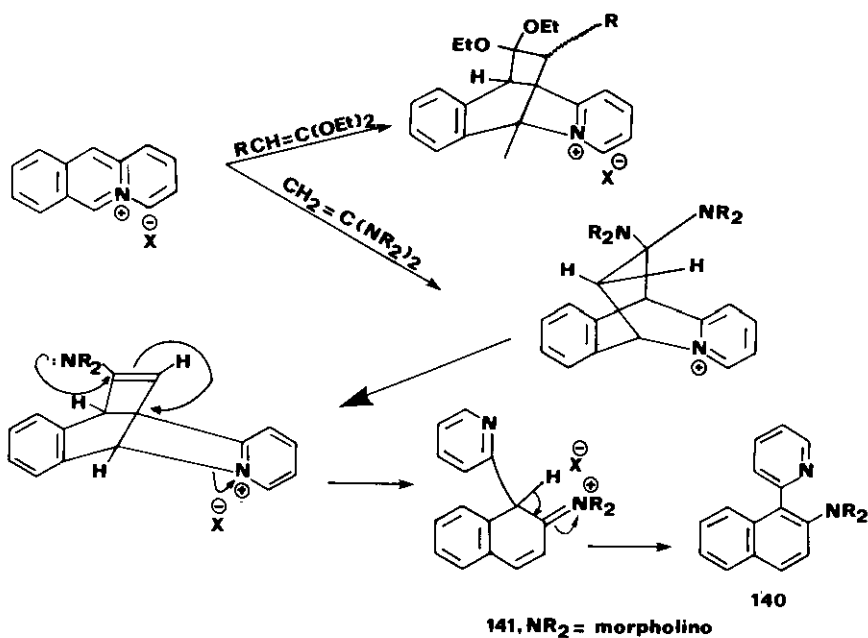


138, R = CH₃

139, R = C₂H₅

that the addition of maleate esters took place as a two step reaction and the carbonium ion first formed rotates through 180° before cyclisation. It was also shown that the release of hydrogen bromide during the reaction has no bearing on the course of the reaction⁸⁴. Diethyl maleate, on the other hand gave almost exclusively a trans product (139) identical with that obtained when diethyl fumarate was used as the ethylenic reactant. The increased rate of addition of fumarate was attributed to the steric rather than electronic effect, otherwise the order of reactivity should be reversed in going from a classical to an inverse electron demand type of 1,4-cyclo-addition.

Fields, Regan and Dignan⁸¹ have reported that ketene acetals react rapidly and stereoselectively by Diels-Alder addition with a variety of types of azoniapolycyclic aromatic compounds (Table VII). Without exception the cycloaddition gave the positional isomers with the alkoxy

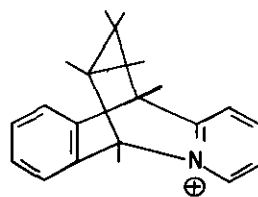


groups nonadjacent to the quaternary nitrogen as a mixture, where possible, of two geometrical forms in which the R group resides either syn or anti to the quaternary nitrogen.

It was also shown that the reaction of 1,1-dimorpholino ethylene with the acridizinium bromide gave 2-morpholino-1-(2-pyridyl)naphthalene (140) probably resulting from an elimination reaction involving enamine (141) as an intermediate⁸¹. When the ketene acetal adducts (142) were subjected to acid hydrolysis, cleavage occurred with the formation of 9,10-dihydro-12-oxo-4a-azonia-9,10-ethanoanthracenes (143) as an intermediate product and depending on the nature of the R group at C-11, 143 proved to be more or less labile to acidic as well as basic reagents.

Table VII

Adducts of Acridizinium Ion and Dienophiles



Dienophile	Reaction solvent	Conditions		Yield %	Ref.
		Temp.	Hr.		
CH ₂ =CH ₂	A	70	18	93	81
CH ₂ =CHC ₂ H ₅	A	70	66	66	81
CH ₂ =CHCH=CH ₂	A	70	18	93	81
CH ₂ =CHCH ₂ OH	B	100	18	77	81
CH ₂ =CHCN	D	70	48	68	81
CH ₂ =CHC ₆ H ₅	B	100	2.5	93	81
CH ₂ =C(CH ₃) ₂ =CH ₂	B	100	1.5	66	81
CH ₂ C(OEt) ₂	C	25	0.1	92	81
BrCH=C(OEt) ₂	C	70	2	100	81
CH ₃ CH=C(OEt) ₂	C	25	0.1	93	81
C ₆ H ₅ CH=C(OEt) ₂	C	70	0.1	100	81
C ₆ H ₅ CH=CHN(Et) ₂	C	25	0.1	91	81
Cyclopentadiene	D	25	1.5	94	81
Cyclopentene	D	60	96	76	81
Maleic anhydride	E	100	13	87	80
Diethyl malate	E	95	48	65	80

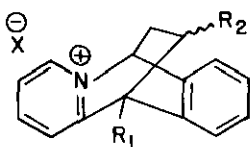
Table VII continued.....

Diethyl fumerate	E	105	10	54	80
Dimethyl maleate	E	100	72	60	82
Dimethyl fumerate	E	100	24	96	82

Reaction media: A = methanol in autoclave; B = nitromethane ;

C = acetonitrile; D = acetonitrile-methanol(3:1 by volume); E =acetic acid

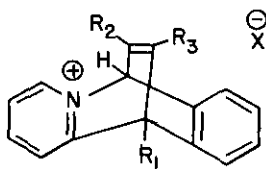
B. Addition of Vinyl derivatives to Acridizinium Bromide salts.



Vinyl derivative	R ₁	R ₂	Temp. Hr.	Time	Method	Yield	Ref.
OEt	H	OEt	20	72	A	91	86
OEt	Ph	OEt	20	72	A	33	86
OBu	H	OBu	82	12	B	64	86
OAc	H	OAc	65	72	A	89	86
N-carbazy]	H	N-carbazy]	20	15	B	68	86
1-pyrr.	H	1-pyrrolidin- 2-one	20	12	B	50	86

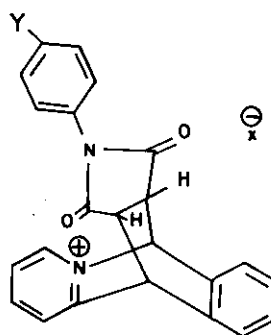
A = Fluoroborate salts were prepared by adding fluoroboric acid to the known bromide; B = addition of fluoroboric acid instead of perchloric acid in the isolation of the cation from polyphosphoric acid cyclisation mixtures.

C. Products of the Reaction of Some Acridizinium Fluoroborates with Derivatives of Acetylene at 135-140°



R ₁	R ₂	R ₃	Time Hr.	yield %	Ref.
Me	H	Ph	0.75	62	86
Ph	H	Ph	0.75	50	86
Me	COOCH ₃	COOCH ₃	0.10	93	86
Ph	COOCH ₃	COOCH ₃	0.175	30	86
Me	Ph	Ph	40	85	86
Ph	Ph	Ph	239	40	86

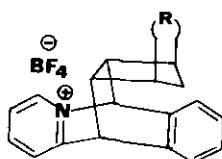
D. Cycloaddition products of Acridizinium Salts with N-Arylmaleimides



X	Y	Method	Yield %	Ref.
ClO ₄	H	A	95	91
Br	H	A	90	91
Br	H	B	75	91
ClO ₄	Me	B	70	91
Br	Me	B	70	91
ClO ₄	Cl	A	90	91
Br	Cl	A	90	91
Br	Cl	B	75	91
ClO ₄	OMe	A	90	91
Br	OMe	A	90	91
Br	OMe	B	90	91
ClO ₄	N(Me) ₃	A	60	91

A = Acridizinium salt was heated in acetic acid suspension at 100° with an excess of maleimide, the time being about 20 hours for perchlorate and 2 hours for bromides
 B = The molten reactants were heated at 160-170° for 15 min.

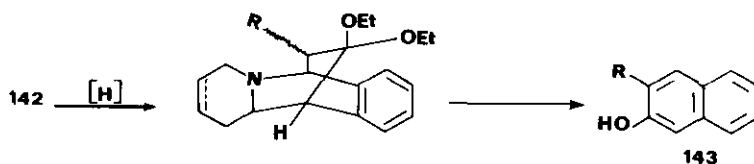
E. Addition of endo 5,6-substituted Norbornenes to Acridizinium Fluoroborates



Substituent ring R	Time	Temp.	Configuration syn: anti	Yield	Ref.
None	24	82 ^a	60:40	82	92
(CH ₂) ₃	48	82 ^a	85:15	42	92
CONHCO	72	82 ^a	100:0	62	92
CON(CH ₃)CO	120	82 ^a	100:0	99	92
COOCO	96	120 ^p	100:0	25	92
CH ₂ OCH ₂	24	82 ^a	100:0	53	92
CH ₂ NH ₂ ⁺ CH ₂	96	120 ^p	70:30	22	92

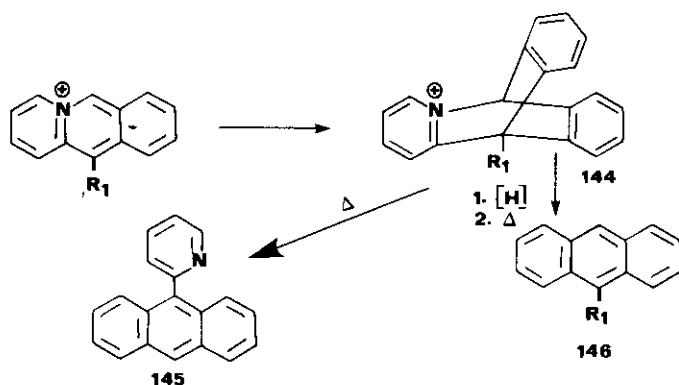
a = Refluxing acetonitrile ; p = Sealed tube.

More significant applications of the reaction products of the acridizinium ion with alkenes have been made by Field et al.¹⁰⁰⁻¹⁰³ According to the authors if the cycloadduct 142 is reduced, the product when hydrolysed and heated loses unidentified amine products affording the nitrogen free naphthol (143).

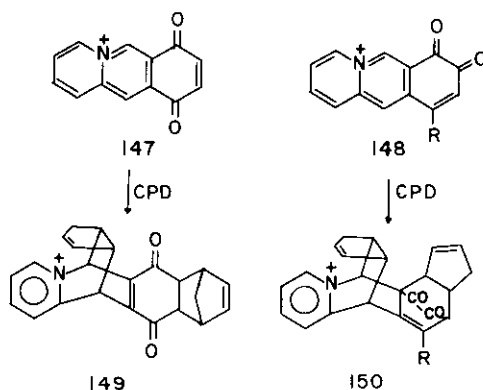


Another important observation by Field et al.¹⁰² was that the acridizinium ion (29) will undergo cycloaddition with benzyne, affording azoniatriptycene (144) in good yield. The presence of a phenyl group at position II (29, R₁=Ph) did not interfere with the cycloaddition nor did a variety of substituents on ring C. Field et al.¹⁰² have further shown that thermolysis of the adduct (144) afforded 9-(2-pyridyl)anthracene derivatives (145), while the second involves thermolysis of the reduction product of (144) affording anthracene derivatives (146) in excellent

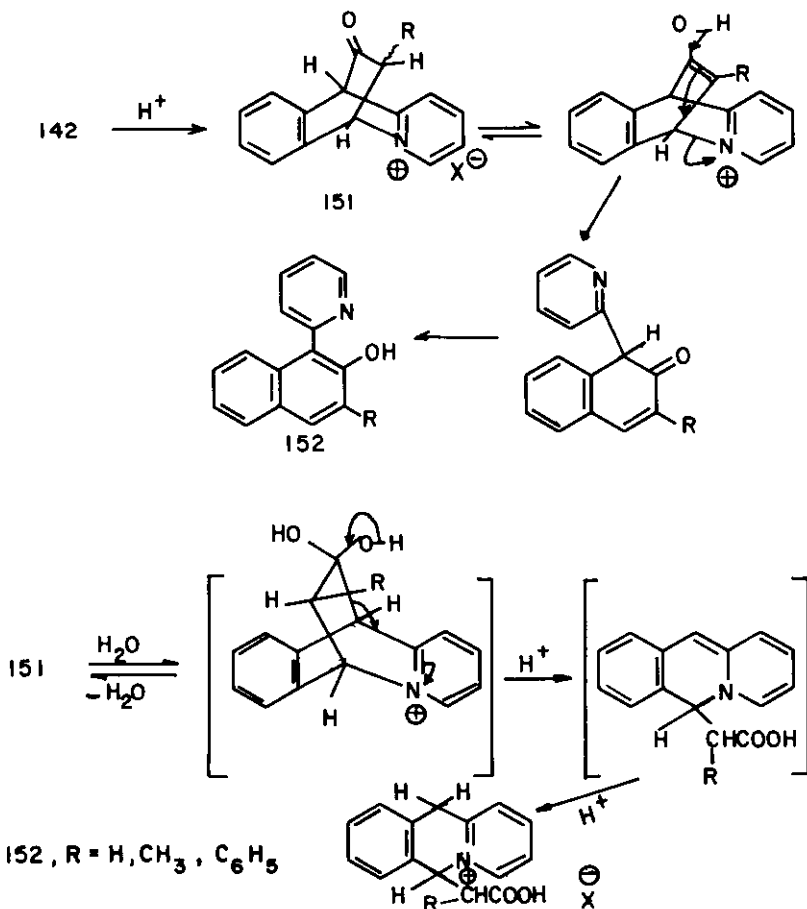
yield 103.



Field and Miller¹⁰⁴ have shown that cycloaddition occurred across the meso position of quinone derivatives (147) and (148) with excess cyclopentadiene but in both instances there was a second addition involving the quinone ring yielding what were believed to be 149 and 150 respectively.



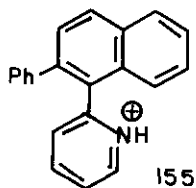
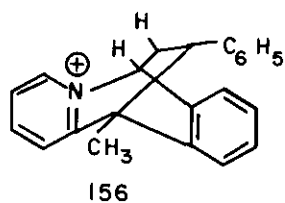
Bradsher and Day⁸⁵ have reported that in the cycloaddition of alkyl vinyl ethers and cyclopentadiene to the acridinium ion, extreme stereoselectivity was observed. The product (153 and 154) obtained were shown to have syn configuration with respect to the phenylene ring⁸⁶. These results are in agreement to those observed with the cycloaddition reactions of 2,3-dimethylisoquinolinium ion⁸⁷⁻⁸⁹. The results were distinctly different types of fragmentation to yield 1-(2-pyridyl)2-naphthols (151) and/or 9,10-(carboxymethyl)-4a-azoniaanthracene salts (152), the latter being the major product⁸⁴.



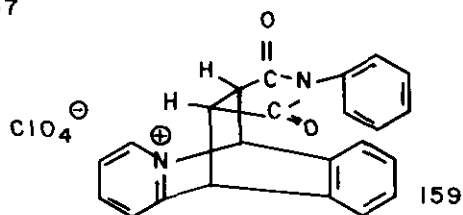
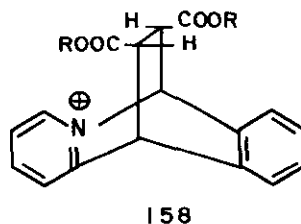
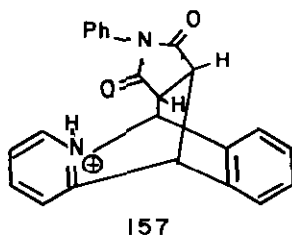
Contraary to the results obtained by Field et al.⁸¹, Bradsher and Burnham⁸⁶ have reported



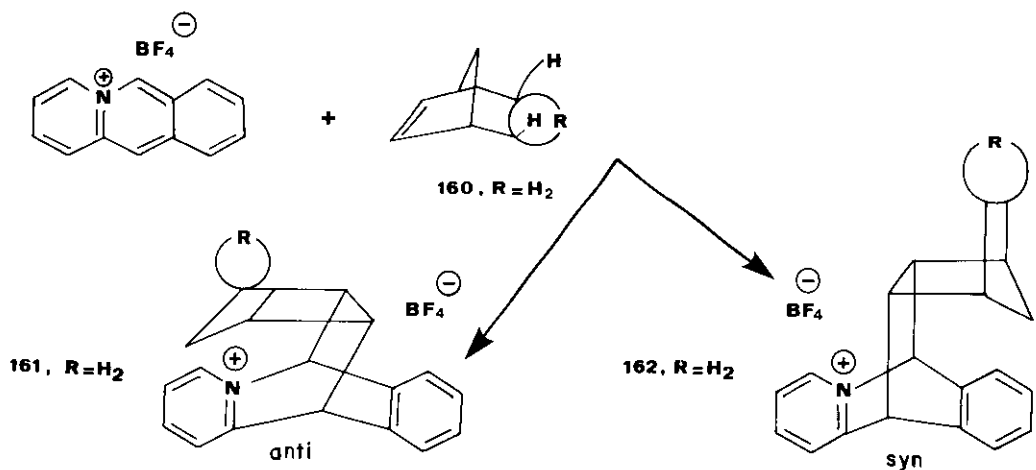
that the cycloaddition of less electron deficient acetylene derivatives could be made to succeed at higher temperatures. Although with phenyl acetylene, acridizinium ion yielded a rearranged product (155) similar to the one reported by Fields et al.⁸⁶ in the cycloaddition of dimorpholinoethylene, but 11-methylacridizinium ion afforded the normal adduct (156) without any rearrangement thus demonstrating, that phenyl acetylene adds to 11-methylacridizinium ion with the same regio-specificity⁹⁰ as does styrene.



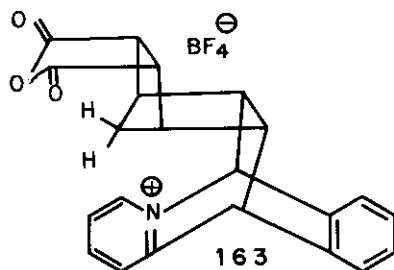
To find out any possible alteration in the stereochemistry of the cycloaddition of N-aryl-maleimides to the acridizinium ion by changing the polarity of the N-aryl group. Bradsher and Harvan⁹¹ have observed that cycloaddition occurs stereospecifically anti with regard to the benzenoid nucleus. The maleimide adduct (157) on heating with 48% hydrobromic acid yielded a trans-diacid (158) whereas pyrolysis afforded the derivative of N-aryl-1-(2-pyridyl)naphthalene-2,3-dicarboximide (159).



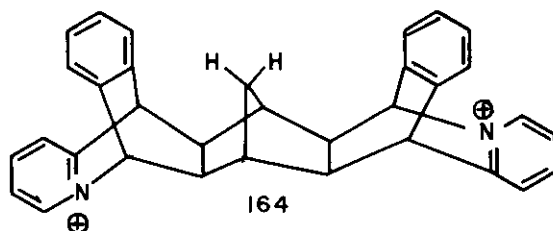
Addition of the acridizinium ion to norbornene (160) gave an exo addition product (161) and (162). Norbornene derivatives which had an endo ring attached at position 5 and 6 gave predominantly syn addition with respect to benzenoid ring, the highest yields were obtained, when hetero atom was in the ring. This stereoselectivity has been attributed to the attraction of the unshared electrons available on the central atom of the endo ring to the positive charge of the acridizinium nitrogen. Norbornene-exo-5,6-dicarboxylic anhydride on the other hand gave a



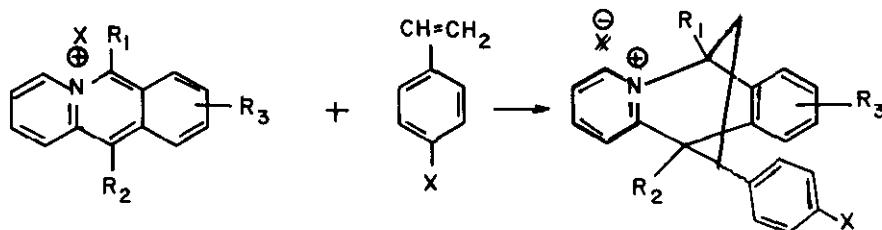
mixture from which a pure anti adduct (163) was isolated in an overall yield of 15%.



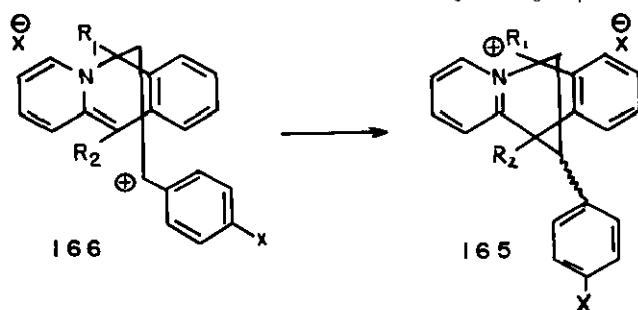
Addition of two moles of acridizinium ion to norbornadiene afforded the syn, syn diadduct (164) in 15% yield⁹².



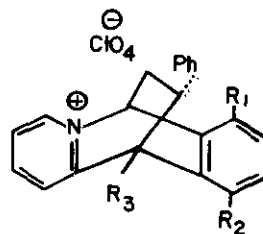
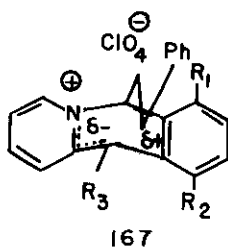
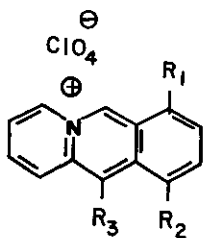
The classical paper of Sauer and Wiest⁹³ concerning the existence of Diels-Alder reactions with inverse electron demand first made it possible to understand, how a cation could function as a "diene". Acridizinium ion does not undergo cycloaddition with the electron deficient tetracyanoethylene but does react with the electron rich styrene. Synthetic⁸¹ and kinetic⁸³ evidence has shown beyond doubt that the ion functions as the electron deficient species. Rates of addition of para substituted styrene to the acridizinium ion follows the inverse electron demand pattern, p-nitrostyrene being slowest and p-methoxystyrene being fastest in the series.



The formation of an adduct (165) was rationalised by suggesting the formation of a benzylic carbonium ion (166) as an intermediate which could then cyclise by attack of the electrons at position 11, suggesting further that the reaction occurs through a regiospecific reaction ⁸³.



With a substituent at position 9 in the acrididinium ion where by resonance effects could not be readily transmitted to position 6, while steric effects would be minimized, the rate of addition of styrene was shown to be accelerated by electron withdrawing substituents and the rates afforded a significant Hammett plot ⁹⁴. It was also explained that the 9-substituents affected the cycloaddition rate by altering the availability of the positive charge at position 6 of the acrididinium ion. On the other hand, acrylonitrile was shown to be somewhat less responsive to polar influences than styrene, but reacted by the same mechanism involving an electrophilic attack upon the alkene by the positively charged 6-position of the acrididinium nucleus. The introduction of a methyl group at 6-position of the acrididinium ion was shown to slow the reaction significantly. On the other hand introduction of a methyl group at position II produced over a 13 fold increase in the rate of cycloaddition with styrene ⁸⁴. This must be due to the fact that the methyl at position II is under strain as the result of peri interaction with adjacent hydrogens and that this strain is relieved when the methyl group moves out of plane during cycloaddition (167) ⁸⁹. For further proof of this explanation rate of cycloaddition with 7,10,11-trimethylacrididinium ion was studied and it was found that the rate of cycloaddition with styrene ⁹⁶ was more than ten times that of the 11-methyl derivative and this result was taken as a direct evidence of steric acceleration ⁹⁷ rather than electronic in origin ⁹⁸. Similar results were obtained with anthracene derivatives ⁹⁹, where the introduction of methyl groups into both of the meso positions of anthra-



- a, $R_1 = R_2 = R_3 = H$
 b, $R_1 = R_2 = H, R_3 = Me$
 c, $R_1 = R_2 = R_3 = Me$

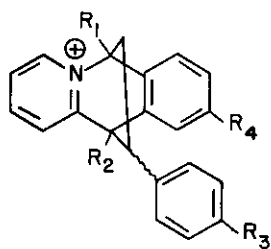
cene resulted in a 218-fold acceleration of the rate of cycloaddition with maleic anhydride, while methoxyl groups at the same positions resulted in decrease in rate. It has also been clarified that the decrease in rate is not due to the impaired coplanarity but more likely due to the greater effective size of the methyl group, which is actually more responsible for the rapid rate of cycloaddition for 9,10-dimethylantracene. The rates of cycloaddition of various dienophiles are given in Table VIII.

The presence of a methyl group at position II of the acridinium ion causes an enhancement in the rate of cycloaddition, but similar enhancement in the rate at the other meso position is not seen, which has now been attributed to the electron deficiency, which is responsible for an entropy effect large enough to overwhelm any steric acceleration expected from the relief of a peri strain¹⁰⁴. Arrhenius activation energy measurements have further shown, that the energy of activation for the formation of the styrene cycloadduct from 6-methylacridinium ion was actually lower by 1.1 K cal/mol than that for the similar reaction of the acridinium ion. Similarly large negative entropy activation (-37.6 eu) for a methyl group at position 6 in comparison with a less important entropy factor (-34.7 eu) for a methyl group at position II supports the evidence concerning the importance of position 6 in the rate determining step of cycloaddition of acridinium salts.

As regards the mechanism of cationic polar cycloaddition spectroscopic evidence has indicated that the acridinium ion form charge transfer complexes with donor molecules. Analysis of the second order rate constant for the cycloaddition of N-vinylcarbazole with the acridinium ion has also shown a decrease in the rate constant with increased concentration of N-vinylcarbazole. These data have been interpreted as evidence of a charge transfer complex in the reaction mixture. The differences in the energies of activation for reaction via the regiosomeric and stereomeric transition states must in most cases arise from differences in the polar influences lying along the reaction pathway which must include the initial frontier orbital interaction¹⁰⁵.

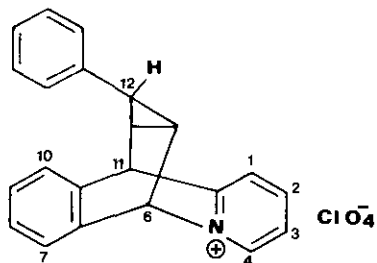
TABLE VIII

Rate of Cycloaddition of Styrene to Acridizinium Perchlorate

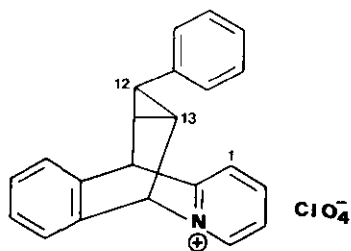


R ₁	R ₂	R ₃	R ₄	Rate K, min ⁻¹ × 10 ⁻³	Ref.
H	H	OCH ₃	H	18 ± 1	83
CH ₃	H	OCH ₃	H	5.7 ± 0.2	83
H	CH ₃	OCH ₃	H	180 ± 10	83
CH ₃	CH ₃	OCH ₃	H	93 ± 6	83
H	H	CH ₃	H	8.1 ± 0.2	83
CH ₃	H	CH ₃	H	3.2 ± 0.2	83
H	CH ₃	CH ₃	H	94 ± 2	83
CH ₃	CH ₃	CH ₃	H	57 ± 4	83
H	H	H	H	5.0 ± 0.1	83
CH ₃	H	H	H	2.5 ± 0.2	83
H	CH ₃	H	H	68 ± 3	83
CH ₃	CH ₃	H	H	43 ± 1	83
H	H	NO ₂	H	2.3 ± 0.3	83
CH ₃	H	NO ₂	H	1.8 ± 0.3	83
H	CH ₃	NO ₂	H	36 ± 5	83
CH ₃	CH ₃	NO ₂	H	30 ± 2	83
H	H	H	Me	2.0 ± 0.1	94
H	H	H	CH(Me) ₂	2.8 ± 0.1	94
H	H	H	H	5.0 ± 0.2	94
H	H	H	F	5.4 ± 0.2	94
H	H	H	I	10.6 ± 0.6	94
H	H	H	Cl	10.1 ± 0.5	94
H	H	H	Br	11.2 ± 0.8	94
H	H	H	COOH	18.1 ± 0.7	94
H	H	H	COOMe	24.7 ± 1.0	94
H	H	H	NO ₂	105 ± 0.5	94

NMR studies of a large number of adducts obtained from the acridizinium ion, Field et al ⁸¹ concluded that both syn and anti addition products has occurred in every case. However separation of syn and anti addition products had never been achieved. Bradsher and Westermann ¹⁰⁶ were the first to achieve such separation in case of styrene adduct (168 and 169) by fractional crystallisation using I-butanol as a solvent.



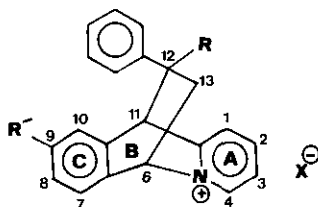
168. Syn isomer, m.p. 245-47°



169, anti isomer, m.p. 203-204°

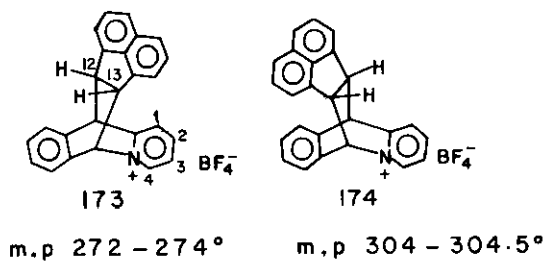
Syn isomer (168) which was least soluble was found to be the major one. NMR studies of these two isomers showed the signals for two aromatic protons at an unusually high field δ 6.5-6.8. These shielded aromatic protons were attributed to the phenyl group at position 12 atop the bridge and results from the two ortho hydrogens sweeping through the π cloud of the phenylene or the pyridinium ring. Another signal useful for distinguishing stereoisomers was the C-4 signal which occurs downfield and is easily identified and measured. In the anti isomer (162), C-12 phenyl group is positioned correctly to shield the 13-b proton and this shielding edge of the phenyl group is directed towards the pyridinium ring. This contribution is significant in that the C-4 hydrogen in the anti isomer is centered at δ 9.20, whereas the corresponding syn absorbance occurs at δ 9.7. Some of these differences in the NMR spectra have been used in identifying the syn and anti adducts in case of p-methoxystyreneacridizinium adducts on the basis of their ABMX patterns, making it possible to assign to the anti isomer the methoxy signal occurring at the lower field. On a similar basis an adduct obtained from p-methylstyrene and the acridizinium ion revealed that the methyl group at lower field was that of the anti isomer, whereas in an adduct of α -methylstyrene and acridizinium ion, the C-12 methyl group was positioned above the pyridinium ring (170). Its signal appeared at a lower field than that of a stereoisomer in which the methyl group was over a phenylene ring. Integration of the signals showed that 64% of the methylstyrene adduct had the phenyl

170 R = H; R' = Me
171 R' = Me; R = H



group in the syn position (170).

With an adduct of styrene and 9-methylacridizinium ion, two distinct methyl resonances were observed. The higher intensity one was identified due to the syn isomer (172) as this isomer can produce the maximum shielding. With the syn isomer, this shielding is magnified when the aryl group is constrained in a rigid configuration as in case of acenaphthalene adduct (173 and 174) in which case C-4 proton signal for the anti isomer (173) appeared at τ 8.35 compared to the high



melting syn isomer (174) with the value for the C-4 proton at τ 9.13.

These differences in NMR spectra have been utilised in determining the isomeric composition of about 25 unseparated mixtures.

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