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MASS SPECTROMETRY OF ONIUM COMPOUNDS—XII

RADICAL FORMATION IN THE EVAPORATION OF THE CINNOLINIUM CATION*

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Abstract—The mass spectra of the methiodides of cinnoline and 4-methylcinnoline have the highest mass peak at the mass of the cation. The respective appearance potentials were 6·5 eV and 6·2 eV compared to 9·15 eV, and 9·00 eV for the tertiary cinnolines. The very low appearance potentials for the cations have been interpreted as due to ionization of free radicals corresponding to the respective cations rather than as a fragmentation process from an adduct between the cation and anion. The free radicals are formed in a pyrolytic process. Further support for radical formation was found in the appearance potentials of a dihydrocinnoline, the value being 7·6 eV.

Dihydrocinnolines were available by polarographic reduction of the corresponding cinnolinium cations.

Cyclic voltammetry studies of the methiodides show that the 4-Me group strongly affects the chemical reactions following the charge transfer process.

THE main pyrolytic process before evaporation of N-quaternary salts in the mass spectrometer have been stated to be dealkylations and Hofmann eliminations.[2] We have recently reported on dealkylations and transalkylations,[3–5] on the possibility for valence isomerism in the evaporation process of betaines[5–8] as well as direct evaporation in the betaine form.[4, 8] In a recent paper the existence of the cation of 2,4-dimethylcinnolinium iodide in the gas phase was reported.[9] No clear distinction seems to have been made between pyrolytic reactions and electron impact induced

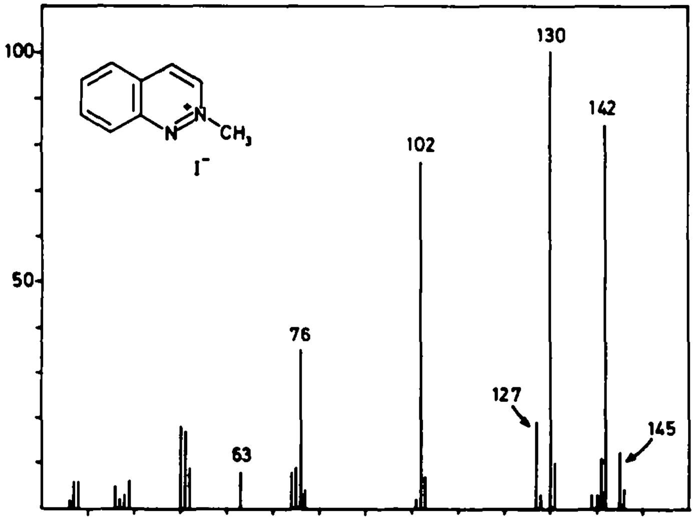


FIG 1

processes. The cation as such cannot evaporate and a prior process to the evaporation must have taken place. We therefore decided that a closer examination of suitable N-quaternary cations would be necessary. For this purpose the methiodide and the trideuteriomethiodide of cinnoline and 4-methylcinnoline were used.

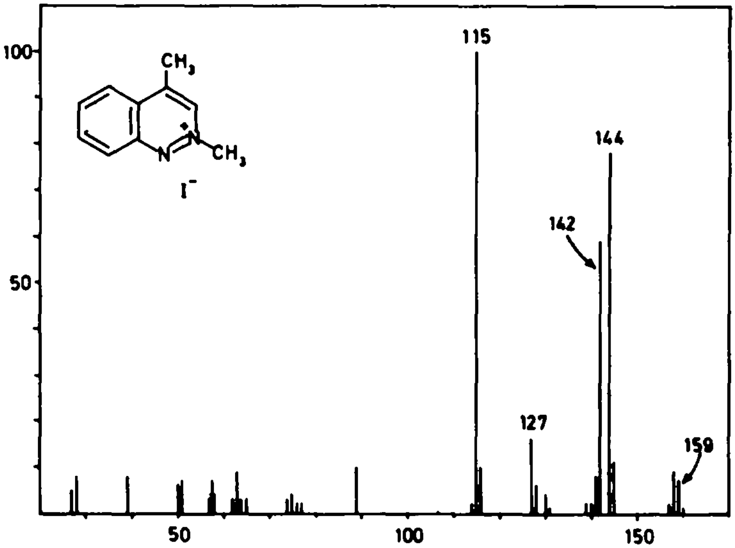
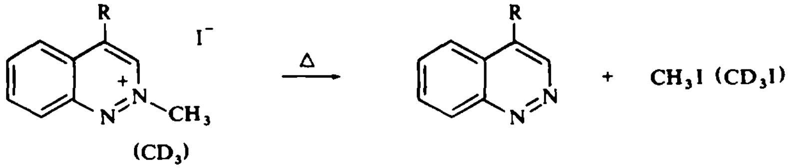


FIG 2

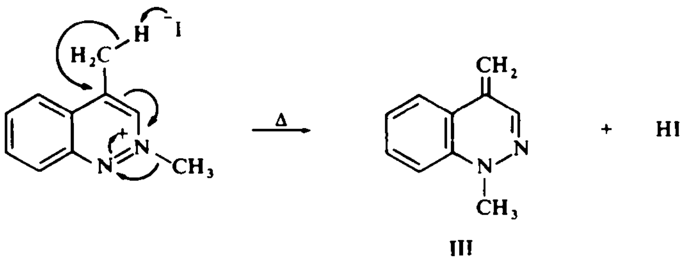
After some dispute on the site of quaternization of these compounds it is now agreed that this occurs on N(2) rather than on N(1).[10] The main pyrolytic pathway in the source of the mass spectrometer is N-demethylation with formation of the parent cinnoline derivative (*m/e* 130 and *m/e* 144) and methyl iodide (*m/e* 142) (Figs 1 and 2).



Ia: R = H
Ib: R = CH_3

IIa: R = H
IIb: R = CH_3

Besides dealkylation the 4-Me derivative (Ib) and its deuterated analogue show loss of hydrogen iodide in contrast to the 4-desmethyl derivative (Ia). The proton lost therefore comes from the strongly activated 4-Me group. In the formation of an anhydro base in this system it is thought that the most likely structure (III) arises through synchronous proton abstraction and migration of the Me group from N(2) to N(1).

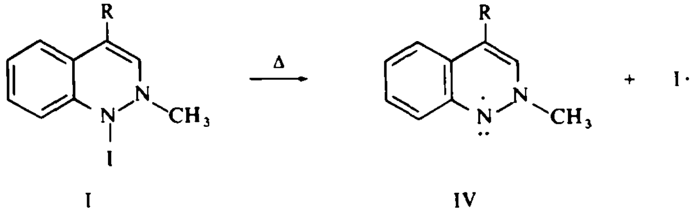


Scheme 1

The most interesting feature of the spectra, however, is the appearance of peaks with the elemental composition corresponding to the two cations at m/e 145 and m/e 159 respectively. (Figs 1 and 2). Gaseous species with the highest mass number corresponding to the cation have also been reported in the case of triphenylcyclopropenium bromide but was considered a fragment from the unstable adduct between the cation and anion.[11] During this work a similar observation was reported for some pyrylium salts.[12] Alternative explanations, however, may be formation of charge transfer complexes between anion and cation, which may dissociate into free radicals during or immediately after evaporation. Another possibility is ion pair formation upon electron impact of the complex in gas phase. We have tried to distinguish between these possibilities by using the metastable refocusing technique[13] and the appearance potential of the ions in question. The usefulness of the latter in discussing the structure of the neutral species formed on pyrolysis of N-quaternary compounds has been proved in the case of the anilinium oxides[14] and pyridinium oxides.[15]

Addition of the anion to the cinnolinium cation can take place on either N(1) or C(3). In the former case a relatively weak N-halogen bond is formed, and in the latter case rupture of the common double bond destroys the benzene aromaticity. No peak corresponding to the mass of the adduct was detected either with iodide or chloride anions nor were any metastable transitions from such species to m/e 145 or m/e 159 found. The ionization potentials of the species with mass to charge ratio corresponding to the respective cations, however, were found to be extremely low *viz* 6·5 eV for the N-methylcinnolinium cation (m/e 145) and 6·2 eV for the 4-Me homologue (m/e 159). These values should be compared with the values 9·15 eV and 9·00 eV for cinnoline and 4-methylcinnoline respectively. A possible adduct between the cation and anion would be expected to have relatively low ionization potential since such a structure would resemble an aromatic hydrazine derivative. To elucidate this possibility the cinnolinium iodides were reduced to the 1,2-dihydro derivatives by polarography. The IP value for 1,2-dihydro-2-methylcinnoline was found to be 7·6 eV as compared with 7·64 eV for phenylhydrazine. The latter value was determined by photoionization,[16] however, and is expected to be somewhat lower than the electron impact value. The appearance potential for the $|M-I|$ fragment from the adduct should be at least equal to or higher than the ionization potential of the adduct. Assuming that exchange of a hydrogen with halogen in the 1,2-dihydrocinnoline (V) does not reduce the ionization potential by as much as one unit the low IP value is best explained by ionization of a free radical or possibly by an ion pair formation from the adduct.

The presence of a cinnoline radical in the gas phase could be the result of a homolytic cleavage of the N—X bond in the adduct. The cleavage can occur either in the gas phase or in solid state prior to evaporation and the final result is a redox process (Scheme 2).



SCHEME 2

The free radicals formed are volatile,[17] and if formed in the solid state must be assumed to evaporate immediately. But free radicals are also very reactive species and could well dimerize or give a hydro derivative. No dimer was detected but species of low abundance were present at one mass unit higher than the mass of the cation. High resolution showed this to be a mixture of the isotope peak from the cation species and a peak with the elemental composition of the 1,2-dihydro derivative. It has been shown that a radical in gas phase may pick up a hydrogen radical from water absorbed on the walls of the ion source,[18] but only a smaller fraction of the radicals picks up a deuterium radical in such experiments.* Due to the low abundance of the reduced species as well as low deuterium incorporation on simultaneous introduction of deuterium oxide these experiments were inconclusive.

The ionization potential of a free radical is in most cases considerably lower than the value for the corresponding all covalently bonded parent molecule. Thus the difference between the ionization potentials of some stable free radicals and their hydro derivatives have been found to be more than 1 eV.[19] Very low IP values have also been reported for radicals from hydrazine[20] and certain hydrazine derivatives.[21] Such compounds bear some resemblance to the 1,2-dihydrocinnoline radical.

The recorded ionization potential for the desmethyl derivative (IVa) agrees well with the calculated value of 6·5 eV which was arrived at by a semi-empirical MO calculation using the unrestricted Hartree-Fock method.[22] This method has successfully been applied to other free radicals.[23]

The presence of iodine radicals are obscured by the large amount of methyl iodide present which fragments by loss of a Me group to *m/e* 127. In some cases, however, small amounts of molecular iodine were found at *m/e* 254, which indicates dimerization of iodine radicals.

It is thus seen that both the experimental data and the theoretical calculation strongly indicate the presence of cinnoline radicals in the gas phase.

Fragmentation of the 1,2-*dihydro derivatives.* Preparative polarographic reduction of the cinnolinium iodides (I) in N HCl gave the corresponding 1,4-dihydro salts (VI). The compounds were thermally dissociated in the mass spectrometer into hydrogen halide and the 1,2-dihydro base (V).

The most important fragmentation pathways of the latter are expected to be

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* Unpublished work.

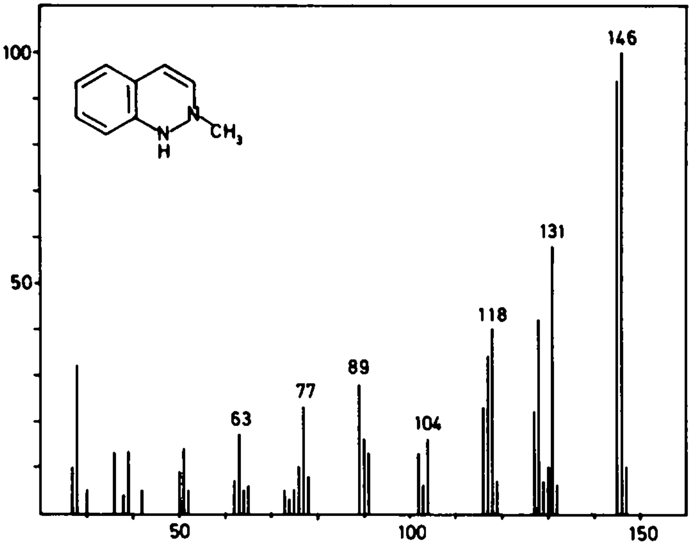


Fig 3

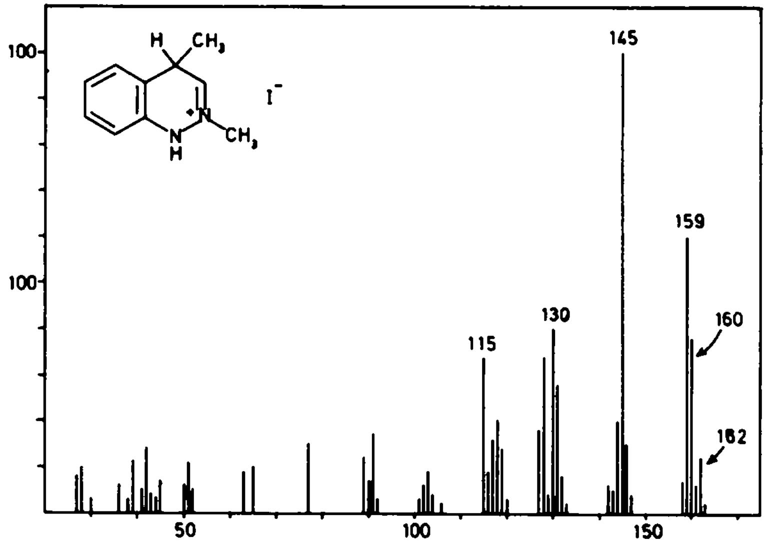
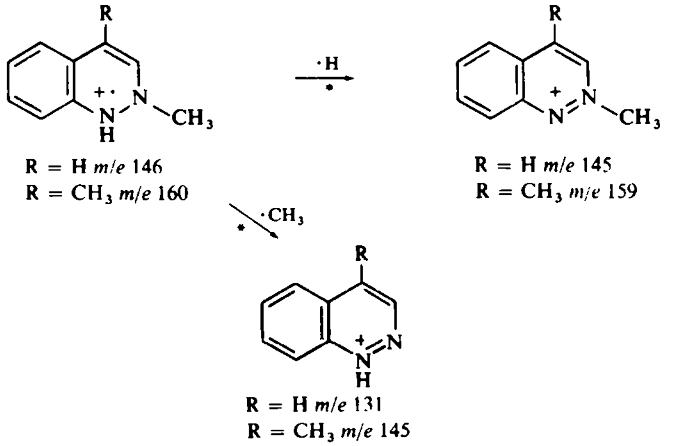


Fig 4

α-cleavage with respect to nitrogen. Thus the most intense fragment peaks in the spectra (Figs 3 and 4) are due to loss of hydrogen and a Me group respectively. The N(2)-trideuteriomethyl derivatives (V) showed loss of $\cdot CD_3$, but no loss of deuterium. On simultaneous introduction of deuterium oxide into the instrument the molecular ion was largely shifted one mass unit higher, and with loss of deuterium as an important process. The fragmentation processes are consistent with the above results and are given in Scheme 3 below.



SCHEME 3

On gradual increase of the evaporation temperature the spectra became more complex. Disproportionation of the 1,2-dihydro compound seemed to take place since a peak appeared two mass units higher than that corresponding to the molecular ion of the 1,2-dihydro derivative. The ionized species are the N-quaternary cinnolinium salts (I) which decompose in the usual manner to give prominent peaks of *m/e* 144 and *m/e* 130 corresponding to the tertiary cinnolines (II) and methyl iodide (*m/e* 142) (Fig 4).

Since the dihydro tertiary amine is present in the solid state together with the N-quaternary analogue, generated in the redox process, N-alkylation-dealkylation processes are possible. Thus the mass spectrum shows two new high mass unit peaks. One is fourteen mass units above the 1,2-dihydro derivative (V), the other of low intensity is fourteen units above the tetrahydro derivative. After about 15 minutes the 1,2-dihydro derivative had almost disappeared and the spectrum was now dominated by the fragmentations of the tetrahydro and the quaternary compounds. Disproportionation of 1,2-dihydro aromatics are not unexpected on physical-chemical grounds and have also previously been reported such as in the mass spectra of dihydroquinoxaline derivatives.[24]

Cyclic voltammetry. The polarographic behaviour of cinnolines has been described.[25] The first step in the polarographic reduction of cinnoline and its 4-Me analogue in N HCl was shown to be the formation of 1,4-dihydro derivatives. The product from the first two electron reduction of corresponding N(2) quaternary salts has been formulated as 1,2-dihydro derivatives, but no product was isolated.[25] In acid solution the reduced species are best formulated as 1,4-dihydro derivatives since the corresponding hydrazines are known to be unstable.[26]

For our mass spectrometry studies we required dihydro derivatives of the N(2)-quaternary compounds Ia and Ib. Prior to preparative polarographic reduction a closer examination of the systems by means of cyclic voltammetry was undertaken. At a cyclic scan rate of 0·2 V/s compound Ib in N HCl showed two cathodic waves at − 0·365 V and − 0·790 V and an anodic wave at − 0·335 V (Fig 5). The desmethyl compound (Ia) had three cathodic waves at −0·337 V, −0·800 V and at −0·910 V, but no anodic wave (Fig 6). Since the Me derivative (Ib) showed an anodic wave a separate study of the first cathodic process was carried out by selecting the switching voltage between the two cathodic peak voltages. The peak potentials for the cathodic and anodic waves were found to be independent of the scan rates from 0·2 V/s to the 17 mV/s, the minimum rate studied. The corresponding currents, however, showed great variations. The anodic peak current (i_a) was very low at the lowest scan rate, but was increased to nearly the same value as the cathodic peak current (i_c) at high scan rate (Fig 7). Fig 8 shows a diagram of the ratio i_a/i_c as a function of the scan rate (v). The behaviour corresponds to a charge transfer followed by an irreversible chemical reaction.[27] The difference between the anodic and cathodic peak potentials is about 32 mV which is close to the value for a two electron transfer process in a perfectly reversible process.[27] Benzo[*c*]cinnoline is reduced to the corresponding hydrazine in a polarographically nearly reversible process.[25] The first step in the polarographic reduction of Ib is therefore a reversible formation of the 1,2-dihydro derivative Vb which undergoes irreversible protonation to the cyclic hydrazone VIb. The irreversibility of the process Vb → VIb was verified by NMR which showed that no H(4) exchange by deuterium had taken place when VIb was kept in TFA/D_2O solution overnight.

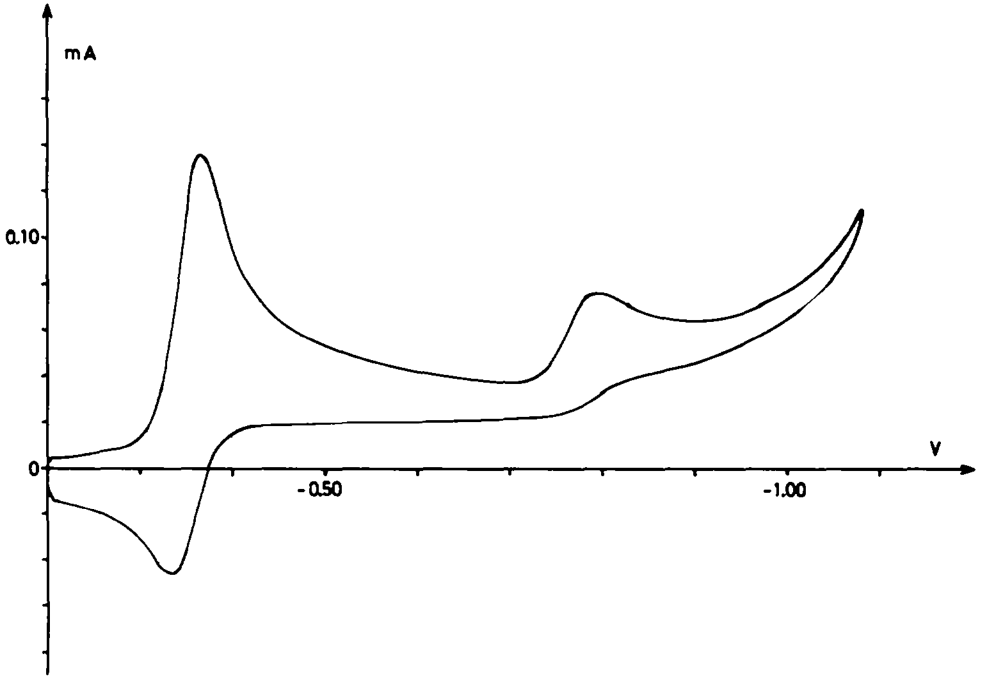


FIG 5. Cyclic voltammogram of 2,4-dimethylcinnolinium iodide (Ib) in N HCl. Scan rate 0·2 V/s. Switching potential − 1·1 V.

Polarographic reduction of phenylhydrazones leads to cleavage of the N—N bond with formation of an aldimine which may be reduced further. The corresponding product from a cinnoline undergoes ring closure to an indole (IX).[25] At sufficiently

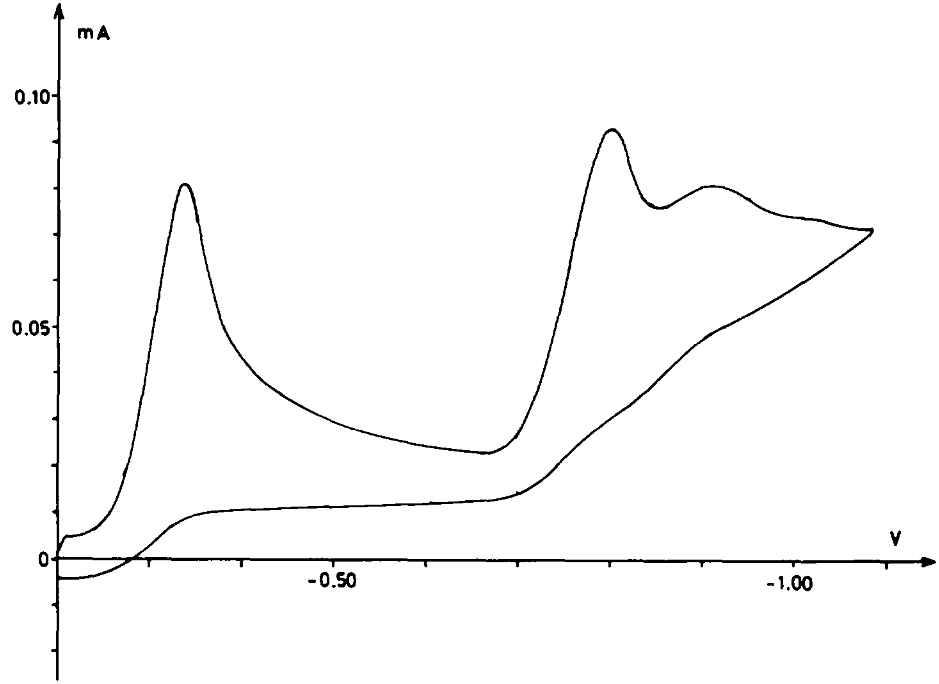


FIG 6. Cyclic voltammogram of 2-methylcinnolinium iodide (Ia) in N HCl. Scan rate 0·2 V/s. Switching potential − 1·1 V.

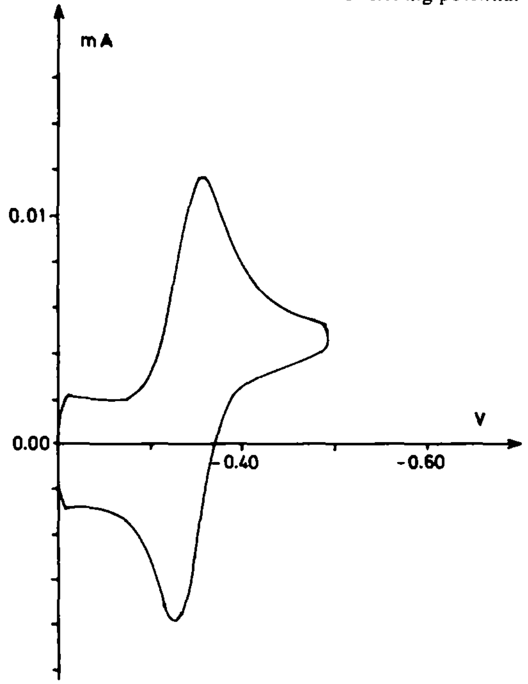


FIG 7. Cyclic voltammogram of 2,4-dimethylcinnolinium iodide (Ib). Scan rate 0·2 V/s. Switching potential − 0·5V.

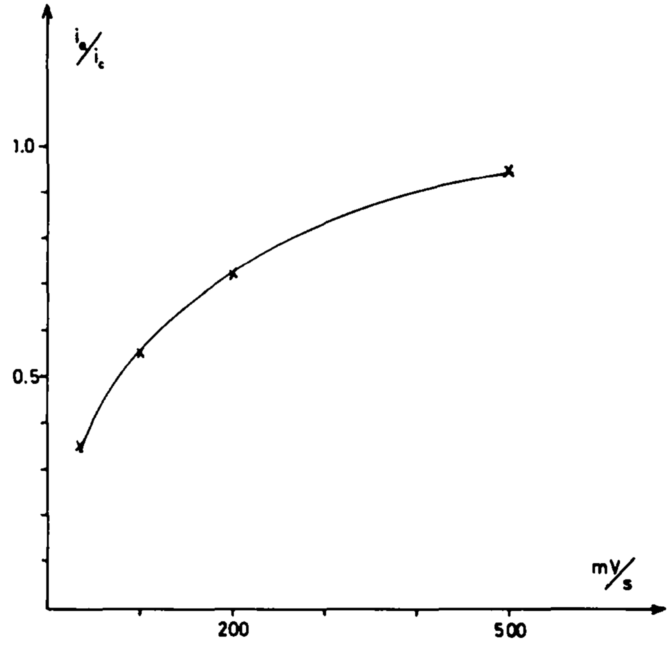


FIG 8. Diagram of the ratio of the anodic (i_a) and cathodic (i_c) peak currents versus scan rate for Ib in N HCl. Switching potential − 0·5 V.

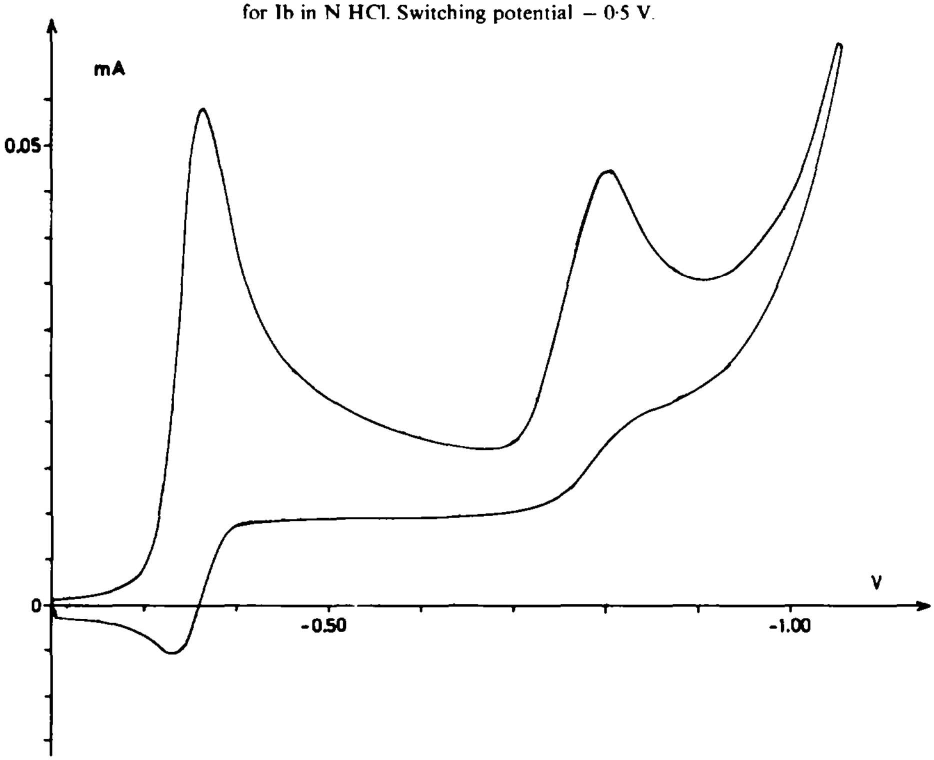
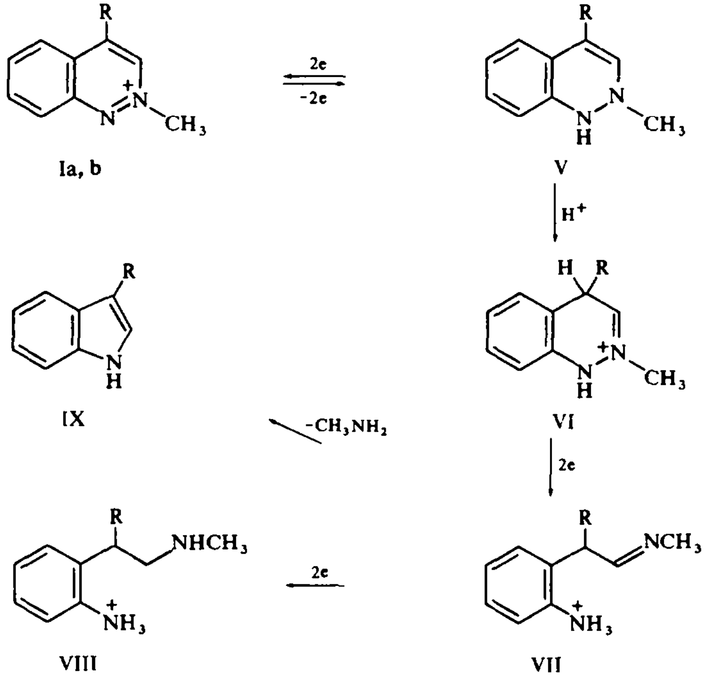


FIG 9. Cyclic voltammogram of 2-methylcinnolinium iodide (I_a) in N HCl. Scan rate 33 mV/s. Switching potential − 1·1 V.

negative voltage the second cathodic wave appears. At higher scan rates the peak potential is at slightly less negative value. The peak current is low at high scan rates, but increases with decrease in scan rate and is nearly the same as the first cathodic peak current at a scan rate of 17 mV/s. Simultaneously the anodic peak current decreases and is almost absent at the slowest scan rate. Fig 9 shows the cyclic diagram at 33 mV/s scan rate. The discussed reaction pathways are given below: (Scheme 4).



SCHEME 4

The lack of a third cathodic wave in case of Ib must be ascribed to rapid formation of skatole (IXb). The latter has been isolated after a four electron reduction of Ib.[25]

The 2-methylcinnolinium iodide (Ia) showed a somewhat different behaviour. The first cathodic wave was slowly displaced from − 0·333 V at a scan rate of 0·2 V/s to − 0·305 V at a scan rate of 17 mV/s. No anodic wave was found even at the highest scan rate. By sufficiently negative switching potential two new cathodic waves appeared rather closely together. Reduction in the scan rate to 17 mV/s displaced the second peak voltage to −0·75 V. The corresponding peak current was relatively independent of the scan rate in contrast to what was found for compound Ib. The third cathodic wave was greatly reduced at the lower scan rates and was almost absent at 17 mV/s. The lack of anodic wave and the insensitivity of the peak current versus the scan rate for the second wave is interpreted as being due to a very rapid formation of VIa. Thus the concentration of the 1,2-dihydro derivative (Va) at any time during the reduction process is very low. This interpretation agrees with the observation that the second cathodic wave is independent of the scan rate. The third cathodic wave may be due to further reduction of the imine (VIIa). The indole formation (IX) must take place at a lower rate than in the case of the 4-Me derivative.

From the above findings it follows that the 4-methyl group strongly affects the chemical reactions following the charge transfer processes.

EXPERIMENTAL

The NMR spectra were recorded on a Varian A-60A instrument, and the mass spectra were recorded on an AEI 902 mass spectrometer. All compounds were introduced by the heated direct insertion probe except for the tertiary cinnolines which were introduced through the heated inlet system. The source temp was kept at 225° and the electron energy and trap current at 70 eV and 100 μA respectively. The minimum sample temperature to give useful ion current is given in the Table below.

	Ia	Ib	VIa	VIb
°C	170	170	110	110

High resolution measurements were performed with a resolving power of 15000. The technique of obtaining ionization efficiency curves is described elsewhere.[14] During these experiments the trap current was kept at 20 μA and the repeller electrode was at cage potential. Xenon was used as a reference gas. The ionization potentials were determined by the semilog plot method.[28] The results are the average of three determinations and the accuracy is considered to be within 0·1 eV for the tertiary cinnolines. For the cations (radicals) and the 1,2-dihydro derivative the accuracy is much less and is estimated to be within 0·2 eV. Cyclic voltammetry and coulometry experiments were performed with a versatile solid state instrument constructed mainly from the design of Goolsby and Sawyer.[29] A Mosely 7030 AM X-Y recorder and a Honeywell Electronic 194 strip-chart recorder were used in conjunction with the instrument. A three-electrode assembly was used for all measurements. The working electrode for the cyclic voltammetry experiments was a Metrohm E410 hanging mercury drop, and for the controlled potential reductions a mercury pool was used. The reference electrode was an aqueous Ag/AgCl and a platinum coil served as auxiliary electrode. These electrodes were isolated in glass tubes with fine-porosity fitted-glass discs. The shield tubes were filled with N HCl as in the sample soln. The soln was stirred with a magnetic stirrer and a Teflon-covered stirring bar. Oxygen-free N_2 was bubbled through the soln for 10 min before and also during the electrolysis.

The tertiary cinnolines were purified by recrystallization from light petroleum (60–80°). The methiodides of the cinnolines have been prepared by refluxing the tertiary compounds with MeI in MeOH.[10, 30, 31] We found that a better procedure was to dissolve an equivalent amount of the cinnoline and MeI in acetone and leave the soln in the dark overnight at room temp. The methiodide which had crystallized from the soln, 78% of Ia and 87% of Ib, was recrystallized from n-propanol. 2-Methylcinnolinium iodide (Ia), orange red crystals, m.p. 171–172° (dec.) (Lit. 168°)[31] 2,4-Dimethylcinnolinium iodide (Ib), orange yellow crystals, m.p. 212·0–212·5° (dec) (Lit. 201–203 [10] and 207° [30]).

The preparative reduction of Ia and Ib was carried out at a controlled potential of – 0·4 V. Two electrons were consumed.

The NMR spectrum of VIb in TFA/D_2O had the 4-Me group as a doublet at 8·45 τ (J = 7 cs). The N(2) Me group was at 5·87 τ. In the parent quaternary compound (Ib) the respective Me group protons appeared as singlets at 6·90 τ and 5·02 τ. The 4-methine proton in VIb showed up as an octet at 7·0 τ, while the 3-proton and the benzene protons were grouped in a multiplet at 2·3–4·0 τ. The chemical shifts for the latter protons are about 2 τ units higher than in Ib. These NMR data are in full agreement with structure VI for the reduced product. Similar results were obtained for VIa.

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