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AMINE-INDOLE RADICAL CATIONS

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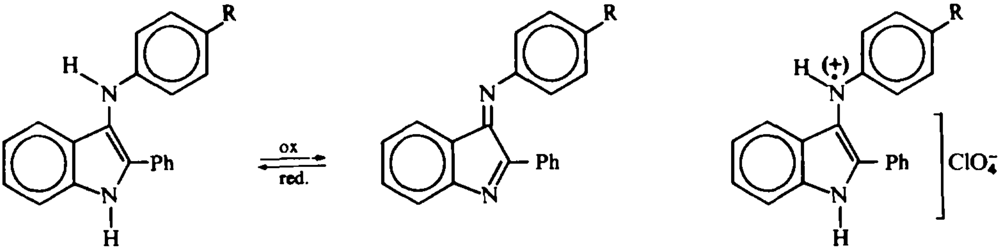
Abstract—2-Phenyl-3-phenyl-amine indole radical cations have been synthesized and isolated as perchloric acid salts. They are considered to be the protonated forms of semiquinone radicals intermediate in a redox process between 3-amine-indoles and 3-imine-indoles. ESR spectra are reported.

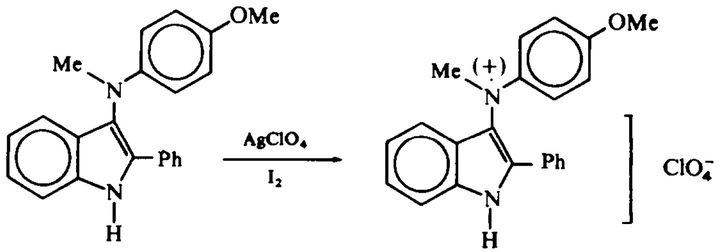
In a previous investigation it was demonstrated[1,2] that the amine-indoles I are easily oxidized to the corresponding imine-indoles II using different hydrogen acceptors, namely *p*-benzoquinone, nitroso-compounds, diethyl-azo-dicarboxilate and benzoyl-peroxide.



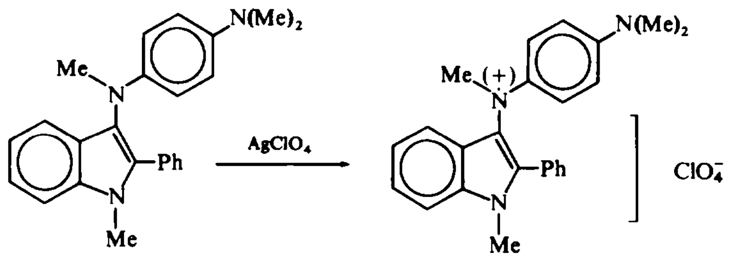
I II III

R = H, Hal, Me, OMe, $N(Me)_2$

It was also shown that it is possible to reduce imine-indoles to the corresponding amines using hydrogen donors like hydrazo-benzene, phenyl-hydrazine or molecular hydrogen.[3] Polarographic reduction studies clearly show that a two step reversible redox process, involving a semiquinone radical intermediate, is operating here.[4] In this work we show that it is possible to isolate the semiquinones intermediate between I and II in their protonated forms, as the perchlorates of the radical cations. Treatment of the amino-indoles I [R = OMe, $N(Me)_2$] with one equivalent of $AgClO_4$ in acetone or MeCN solution leads to the isolation of black green compounds whose elemental analysis corresponds to the amine–cation radical perchlorates III. The radical character was checked by ESR measurements and the ESR spectra will be discussed later. Analogous treatment of amine-indoles I with R = H, Me, Hal did not lead to the isolation of the corresponding radical-cations, owing to their low stability: as a matter of fact when solutions of I (R = H, Me, Hal) in different solvents (including acetone and MeCN) are oxidized, ESR signals corresponding to unstable radicals, of the same nature as the ones described above, appear. This fact is not surprising for the effect of the electrons releasing OMe or $N(Me)_2$ groups in the *para* position leads to a rise in the radical stability. On the other hand, it is known that only the di-*p*-anisyl[5] and the di-*p*-dimethyl-amine-phenyl-amine[6] radical cations were synthesized; the di-*p*-tolyl-amine radical cation[6] rapidly decomposes in solution. Recently it was possible to study other diarylamine radical cations using a flow technique,[7] owing to their extremely low stability. Some N-methylated derivatives being necessary for the ESR assignments, the previously unknown compounds IV and V were synthesized and transformed into the corresponding cation radicals VI and VII by oxidation with $AgClO_4$ and I_2 or $AgClO_4$.



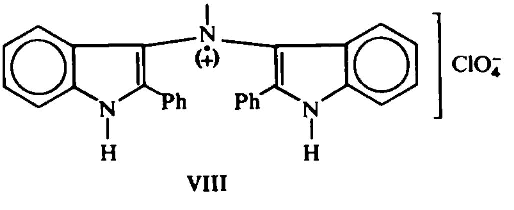
IV VI



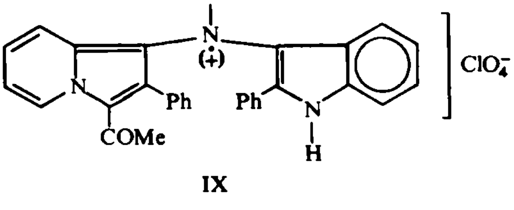
V VII

Both VI and VII were obtained by *in situ* oxidation of the appropriate amine and VI was also isolated and characterized as the perchlorate salt of the radical cation. The difficulty in synthesizing considerable amounts of V explains why we did not characterize radical VII which shows, in any case, the same stability as radical VI when dissolved in an appropriate solvent.

During this work two other amine-cation radicals of a different kind were synthesized by $AgClO_4$ oxidation of the appropriate amine. Steric and mesomeric effect can account for the great stability of radical VIII and IX.



VIII



IX

All radicals show typical absorption maxima in the visible region; solvent seems to strongly influence the radical stability: qualitative observations on the radical spectra show that they are stable within a period of 24 hours in MeCN or 1.2-dichloro-ethane solution, generally unstable or poorly stable in the other solvents.

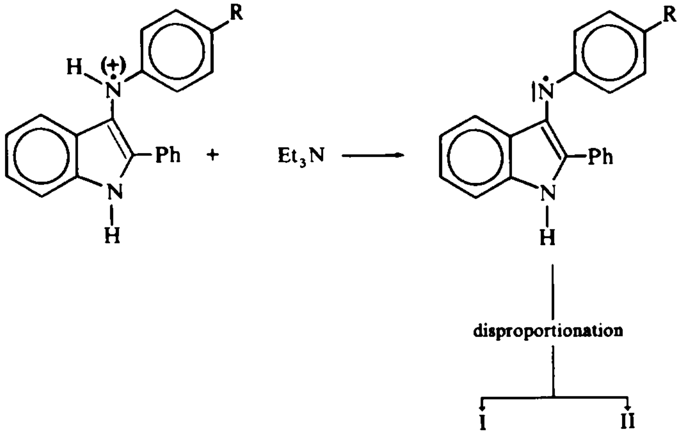
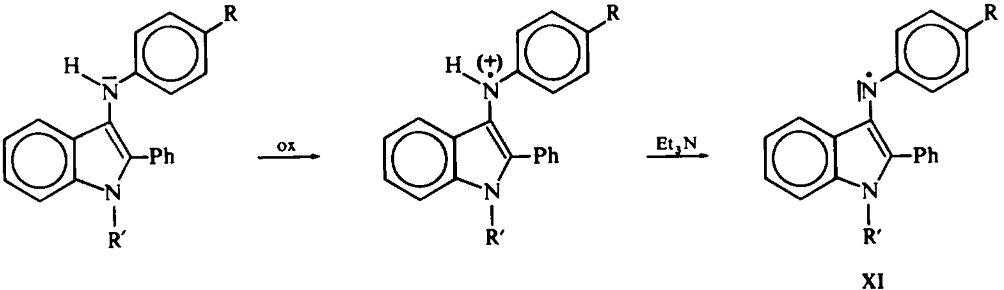


Table 1 summarizes experimental and spectroscopic characteristics of radical cations; Table 2 shows the same data concerning the amines that were synthesized in this work.

An attempt was made to obtain the unprotonated form of the semiquinone radical by adding variable amounts of Et_3N to a MeCN or $C_2H_4Cl_2$ solution of the cation radical, but it failed since the neutral radical that is probably formed, immediately disproportionates, leading to the amine and the imine that can be seen in the reaction mixture. Unfortunately we were not able to prepare the amine X that is likely to be a source of radical XI which cannot disproportionate. The higher basicity of the amino NH group with respect to the indolic NH does not permit the preferential alkilation of the indolic nitrogen.



X

XI

ESR measurements.

Amine cation radical III (R = OMe) dissolved in degassed MeCN shows an ESR spectrum (Fig 1) characterized by 4 lines of relative intensity 1 :2 :2 :1 attributed to the

Table 1

Radicals	Yields based on starting amine	UV and visible spectra in $C_2H_4Cl_2$ mμ (log ε)	m.p. (solvents)*	Analysis %
III: *p*-OMe	75%	265 (5·18) 408 (3·74) 463 (3·56)s 607 (3·64)	100 dec. (CH_2Cl_2/ether)	Found: C. 60·90; H. 4·40; N. 7·27 Calc: 60·97 4·38 6·77
III: *p*-N(Me)$_2$	42%	253 (4·33) 300 (4·23) 440 (3·77) 703 (4·67)	191 dec. (MeCN/ether)	Found: C. 61·74; H. 4·89; N. 10·14 Calc: 61·90 4·96 9·84
VI	82%	259 (4·34) 292 (4·25) 350 (8·86)s 425 (3·84) 750 (3·66)	165 (CH_2Cl_2/ether)	Found: C. 62·05; H. 5·25; N. 6·44 Calc: 61·76 4·71 6·55
VIII	70%	295 (4·52) 360 (4·13) 652 (4·42)	240 dec. (MeCN/ether)	Found: C. 67·62; H. 4·27; N. 8·28 Calc: 67·41 4·27 8·42
IX	43%	278 (4·09) 318 (3·93) 685 (4·27)	>340 (MeCN/ether)	Found: C. 66·86; H. 4·21; N. 7·98 Calc: 66·60 4·28 7·77

* Crystallization was performed dissolving the radical in the first solvent at room temp. then adding the second solvent. Heating of the solutions causes immediate decomposition of the radical.

TABLE 2

Amine	m.p. (solvents)	Yields	Analysis %	UV and visible spectra in EtOH 95%	IR spectra in Nujol —NH (cm^{-1})
di-indolyl-*	204 ether/light petroleum	80%			3430–3390
indolyl-indolizyl-	250 benzene/light petroleum	70%	Found: C. 81·90; H. 5·32; N. 10·12 Calc: 81·61 5·25 9·52	237 (4·62) 307 (4·35)s 474 (4·06)	3220b
IV	177 benzene/light petroleum	65%	Found: C. 80·42; H. 6·14; N. 8·53 Calc: 80·45 6·23 8·73	247 (4·57) 308 (4·42)	
V	138 ligroin	10%	Found: C. 80·61; H. 7·01; N. 12·35 Calc: 81·10 7·09 11·82	251 (4·49) 308 (4·42)	3400

* J. Schmitt. M. Langlois and C. Perren. *Bull. Soc. Chim. France* 1234 (1969)

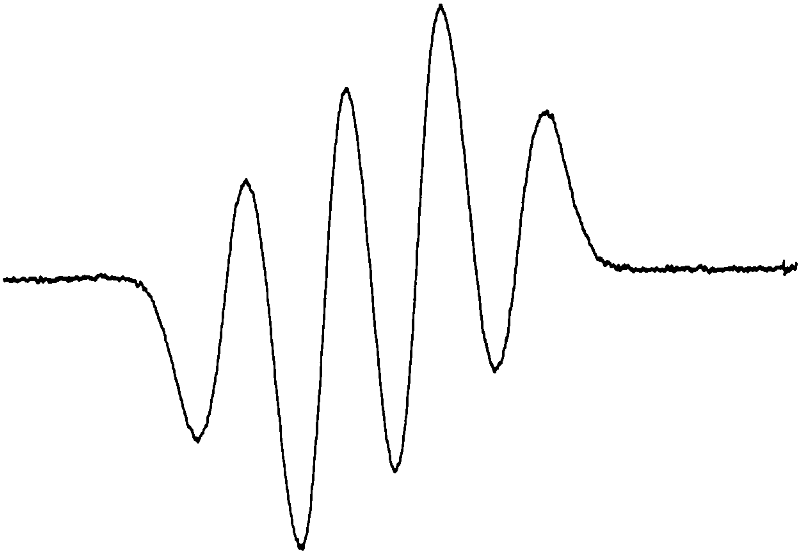


Fig 1. Electron spin resonance first derivative spectrum of radical III (R = OMe).

coupling of the unpaired electron with one nitrogen and one hydrogen nucleus of the amino-group ($a^{H}_{NH} = a^{N}_{NH} = 7$ gauss). The same signal shows a solution of the amine (I; R = OMe) in degassed MeCN when traces of $AgClO_4$ were added: in both cases the signal remained unchanged within a time of 24 hr. Identical spectra were obtained when $AgClO_4$ (or $AgClO_4 + I_2$) was added to solutions of amines (I: R = H, Me, Hal) in degassed MeCN. The low stability of such radicals does not permit an exact evaluation of the coupling constants that are undoubtedly in the range of seven gauss ($a^{H}_{NH} = a^{N}_{NH}$). The same spectra show radicals VIII ($a^{H}_{NH} = a^{N}_{NH} = 7$ gauss) and IX ($a^{H}_{NH} = a^{N}_{NH} = 6{\cdot}6$ gauss). The question whether indolic or amino NH groups are responsible for the absorption lines in the ESR spectra was resolved by the observation that radical VI shows a six-line spectrum of relative intensities 1:4:7:7:4:1 (Fig 2)

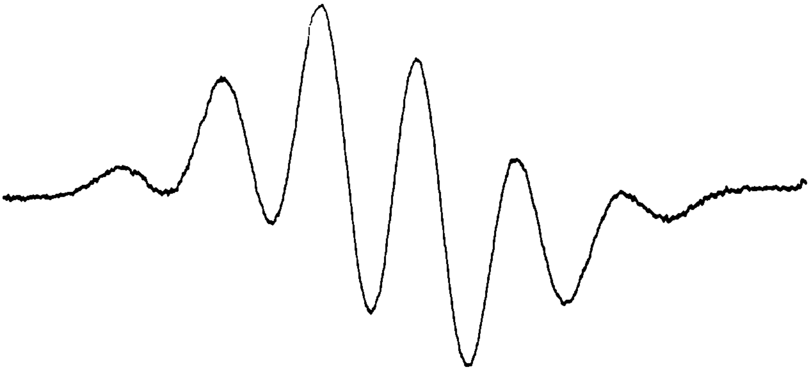


Fig 2. Electron spin resonance first derivative spectrum of radical VI.

attributed to the coupling of the unpaired electron with one nitrogen and three hydrogen nuclei ($a^{N}_{NMe} = a^{H}_{NMe} = 8{\cdot}5$ gauss). The intensity ratio 1:1 in both N to H or N to H_{Me} in amino or methylamino groups is a well known characteristic.[8]

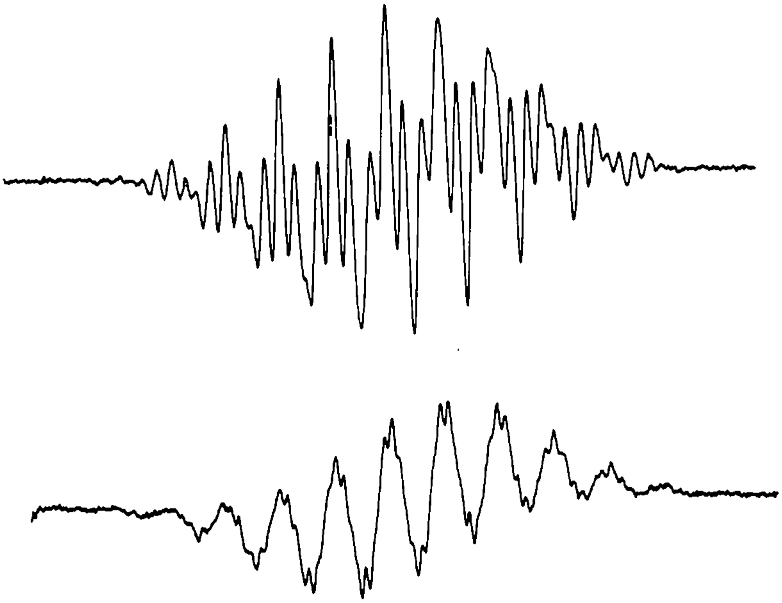


FIG 3. Top, ESR first derivative spectrum attributed to radical III [R = $N(Me)_2$]; bottom, ESR first derivative spectrum attributed to radical VII.

A deviation from the pattern shown by other radicals in the series is that of cation radical III [R = $N(Me)_2$] (Fig 3). Owing to the bad resolution of the spectrum an evaluation of all the splitting constants appears to be an unreasonable task and, on the other hand, this is not the aim of the authors; however, a fundamental pattern of nine groups of lines which can be attributed to the coupling of one nitrogen and six hydrogen nuclei ($a^{N}_{N(Me)_2} = a^{H}_{N(Me)_2} = 6{\cdot}7$ gauss) appears to be a reasonable, rough interpretation of this spectrum. The same pattern characterizes radical VII (Fig 3) leading to the idea that in these two radicals the highest spin density resides on the *p*-dimethylamino group, which is reasonable if one considers the higher basicity of this group with respect to the indolic or the amino NH groups.[9]

EXPERIMENTAL

Amine-radical cations. To a stirred solution of 1 mM of the appropriate amine[2] in acetone or MeCN, 1 mM of $AgClO_4$ dissolved in the same solvent was added drop by drop, at room temp. The colourless solution of the amine turned to a deep green colour while a silver mirror was formed. After ten min the filtered solution was evaporated to dryness and the solid residue crystallized. In the particular case of 2-phenyl-3-(N-methyl-N-*p*-anisyl-) amine-indole (IV) the oxidation was performed using 1 mM of $AgClO_4$ and 0·5 mM of I_2 as oxidizing agents.

Amine-indoles—Bis-indolyl-amine. 1·08 g of 2-phenyl-3-(2′-phenyl-3′-indolyl-)-3-H-indole[10] dissolved in 180 ml of C_6H_6 were hydrogenated at a pressure of 2 atm and a temp of 20–25° on 0·2 g of Pt/C 5% as catalyst. After two hr the catalyst was filtered and the solution evaporated to dryness and crystallized as described.

2-Phenyl-3-(2'-phenyl-3'-acetyl-1'-indolizyl)-amine-indole. 1·1 g of the corresponding imine[11] were dissolved in 130 ml of C_6H_6 and hydrogenated as previously described. The catalyst was filtered and the solution concd until a white precipitate separated.

2-Phenyl-3-(N-p-anisyl-)amine-indole (IV). 1·6 g of 2-phenyl-3-(*p*-anisyl-)amine-indole[2] were dissolved in 50 ml of MeOH. After addition of 2 ml of MeI the solution was heated at 140° for 3 hr in a 500 ml autoclave under N_2 pressure (7 atm). After cooling, the solution was concentrated and 1 g of IV separated.

1-Methyl-2-phenyl-3-(N-methyl-N-p-dimethylamine-phenyl-)-amine-indole (V). The reaction was performed as previously described using 3·27 g of the appropriate imine,[2] 6·8 g of MeI and heating for 5 hr at 140° and 13 atm. After cooling, 26 ml of 33% NH_3 was added, and the resulting solution heated for an additional 6 hr at 200° and 25 atm. The solution was cooled, diluted with water (200 ml) and extracted with $CHCl_3$ (2 × 50 ml). The resulting solution was dried and evaporated to dryness. The residue dissolved in light petroleum–EtOAc 9:1 was purified using an Al_2O_3 chromatographic column.

Spectra UV and visible spectra were recorded using a Beckman DK 2A spectrophotometer, ESR spectra were recorded on a VARIAN E-4 ESR spectrometer, using solvents dried by conventional methods.

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