EPR STUDY OF NITROXYL RADICALS OF SUBSTITUTED 5-ANILINOTRIAZOLES, 5-ANILINOTETRAZOLES, AND 2-ANILINOBENZIMIDAZOLES

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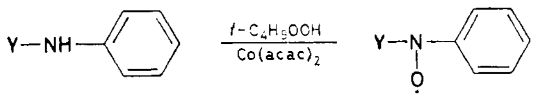
Dedicated to Professor Alexander Tkáč on the occasion of his 70th birthday.

Substituted 5-anilinotriazoles *V*, 5-anilinotetrazoles *VI* and 2-anilinobenzimidazoles *VII* were oxidized by $RO_2^{\bullet}$ radicals to the corresponding nitroxyls *VIII*–*X* in a non-polar medium. The nitroxyls were characterized by the distribution of spin density into both benzene and N-heterocyclic rings. The influence of substituents at various positions on the values of a_N^{NO} splitting constant was evaluated. The EPR spectral parameters of nitroxyls *VIII*–*X* were compared with those for the diphenylnitroxyl radical *IV*.

The EPR study of reactions of $RO_2^{\bullet}$ radicals with secondary amines *I* containing N-heterocyclic rings Y in combination with a benzene ring[1-3] showed the primary radical products of oxidation to be nitroxyl radicals *II* (Scheme 1).

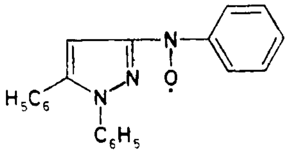


(*A*)

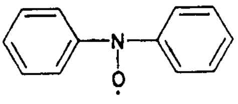
I *II*

SCHEME 1

This procedure was applied for preparation of a series of new nitroxyl radical types with pyrazole[1,2], benzimidazole[2], indole[2], and phthalimide rings[3]. Very stable nitroxyl radicals were obtained by oxidation of substituted 3-anilino-1,5-diphenylpyrazoles by the $Co(acac)_2$–tert-C_4H_9OOH system in benzene solution[1]. Comparison of splitting constant values of protons of benzene ring and the a_N^{NO} value of nitroxyl *III* with analogous data for the diphenylnitroxyl radical *IV* (ref.[4]) indicated an enhancement of spin density in the benzene ring of radical *III*. This phenomenon was associated with decrease of the density at the exocyclic nitrogen atom (a_H values in *ortho* and *para* positions of the nitroxyl *III* are by 20% in average higher and the a_N^{NO} values by 10% lower than those of the nitroxyl *IV*).



III



IV

This paper presents experimental results of an EPR study of oxidation of secondary amines *I* containing 5-membered N-heterocyclic systems with 3 or 4 nitrogen atoms and fused N-heterocyclic rings related to benzimidazole.

EXPERIMENTAL

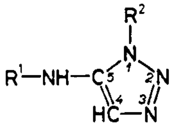
Substituted 5-anilinotriazoles *V*, 5-anilinotetrazoles *VI*, and 2-anilinobenzimidazoles *VII* were oxidized with the $Co(acac)_2$–tert-C_4H_9OOH system in benzene or dichloromethane at room temperature according to procedure published in our previous paper[3]. Compounds *V*–*VII* were synthesized according to refs[5–9].

TABLE I

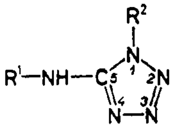
ESR parameters (a, mT) for nitroxyl radicals *VIII* in benzene and dichloromethane

Radical	a_{NO}^N	a_H^o	a_H^m	a_H^p	a_H^{CH}		a_N		$a_H^{R^2}$	Solvent
VIIIa	0·945	0·250	0·084	0·250	0·067	0·045;	0·162	—	—	benzene
VIIIb	0·935	0·227	0·084	0·227	0·141	0·018;	0·080;	0·137	0·027	benzene
	0·960	0·233	0·086	0·233	0·142	0·022;	0·081;	0·145	0·030	CH_2Cl_2
VIIIc	0·935	0·219	0·087	0·219	0·126	0·031;	0·094;	0·138	0·038	benzene
VIIId	0·915	0·226[a] 0·232[a]	0·081[a] 0·085[a]	0·241	0·118	0·015;	0·075;	0·148	—	benzene
	0·937	0·227	0·081	0·241	0·085	0·035;	0·089;	0·140	—	CH_2Cl_2
VIIIe	0·937	0·229[a] 0·239[a]	0·081[a] 0·083[a]	0·262	0·118	0·015;	0·072;	0·148	—	benzene[b]
	0·960	0·230[a] 0·238[a]	0·085	0·262	0·130	0·019;	0·080;	0·145	—	CH_2Cl_2
VIIIf	0·960[c]	—	—	—	—	—	—	—	—	benzene

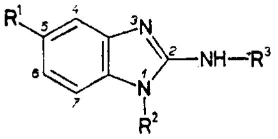
[a] Splitting from one hydrogen atom; [b] in benzene–dichloromethane (volume ratio 5 : 1); [c] further splittings unresolved.



V	R^1	R^2
a	C_6H_5	t-C_4H_9
b	C_6H_5	$CH(CH_3)_2$
c	C_6H_5	$CH_2CH(CH_3)_2$
d	C_6H_5	C_6H_5
e	4-$CH_3C_6H_4$	4-$CH_3C_6H_4$
f	4-$CH_3OC_6H_4$	4-$CH_3OC_6H_4$



VI	R^1	R^2
a	C_6H_5	$CH(CH_3)_2$
b	C_6H_5	C_6H_5
c	4-$CH_3C_6H_4$	4-$CH_3C_6H_4$

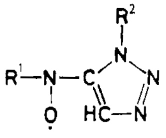


VII	R^1	R^2	R^3
a	H	H	C_6H_5
b	H	H	4-$CH_3OC_6H_5$
c	NO_2	H	C_6H_5
d	NO_2	H	4-$CH_3OC_6H_5$
e	H	CH_3	C_6H_5
f	H	CH_3	4-$CH_3OC_6H_5$
g	H	C_6H_5	C_6H_5
h	H	C_6H_5	4-$CH_3OC_6H_5$

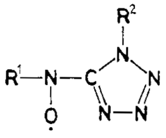
The EPR spectra were recorded with a Bruker ER 200 D spectrometer combined with an Aspect 2000 computer. Samples were bubbled with argon prior to measurement to obtain well resolved spectra.

RESULTS AND DISCUSSION

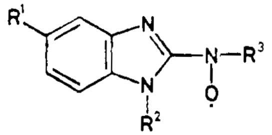
Nitroxyls *VIII*–*X* were the only radical products identified during oxidation of compounds *V*–*VII* by the above-mentioned procedure in accordance with the Scheme 1. The EPR spectral parameters of radicals *VIII*–*X* are summarized in Tables I–IV, the experimental and simulated spectra of radical *IXb* are shown in Fig. 1; the g-factor for all radicals under investigation is in the 2·0061–2·0065 interval.



VIII



IX



X

Comparison of splitting constants of nitroxyls *VIII* with those of *IX* evidenced that replacement of the -CH= group in position 4 of the triazole ring for a nitrogen atom resulted in a more efficient delocalization of the spin density into the N-heterocyclic ring, this being characteristic of an enhanced aromaticity of the tetrazole ring with respect to the triazole system. This fact was reflected in lower a_N^{NO} values for

TABLE II

ESR parameters (a, mT) for nitroxyl radicals *IX* and *XI* in benzene

Radical	a_N^{NO}	a_H^o	a_H^m	a_H^p	a_N				$a_H^{R^2}$
IXa	0·895	0·212	0·078	0·212	0·020;	0·060;	0·116;	0·122	0·060
IXb	0·855	0·210	0·076	0·210	0·025;	0·061;	0·104;	0·127	—
IXc	0·865	0·210	0·076	0·235	0·025;	0·061;	0·104;	0·127	—
XI	0·995	—	—	—	0·036;	0·078;	0·120;	0·165	—

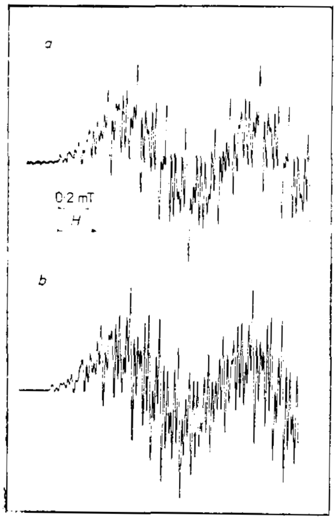


FIG. 1

Experimental (*a*) and simulated (*b*) ESR spectra of radical *IXb* in benzene (only one half of the complete spectrum width is shown) radicals *IX* in comparison with those for *VIII* (decrease by 0·04–0·05 mT). A concurrent decrease of splitting constants in ***ortho*** and ***para*** positions of the benzene ring (cf. nitroxyls ***VIIIb***, ***VIIId***, ***VIIIe*** and ***IXa–IXc***, respectively, in benzene) was observed with compounds having the same substituent in position 1 of the N-heterocyclic ring.

Influence of the substituents nature in position 1 of the triazole ring on the a_N^{NO} value can be mapped from the EPR parameters of radicals *VIIIa – VIIId*. Substitution by benzene ring increased the possibility to delocalize the spin density within the N-heterocyclic moiety of the radical; consequently, decrease of the a_N^{NO} values takes place when passing from alkyl to phenyl substituted nitroxyls. This tendency remained preserved even with nitroxyls *IX*.

None of the radicals of types *VIII* or *IX* revealed splitting from protons of the benzene ring in position 1. Alkyl substituted nitroxyls showed β-splitting with protons of the isopropyl (*VIIIb, IXa*), or isobutyl (*VIIIc*) groups. The EPR study of pyridyl radicals disclosed[10] the a_H^β values of isopropyl and ethyl groups bonded to the endocyclic nitrogen atom to be lower than the a_N value of this atom (for $CH(CH_3)_2$ a_N: $a_H^\beta \sim 4$, for CH_2CH_3 a_N: $a_H^\beta \sim 2$). Bearing this fact in mind we

TABLE III

Splitting constant a_N^{NO} of nitroxyl radicals *X* in benzene

Radical	a_N^{NO}, mT	Radical	a_N^{NO}, mT
Xa	0·896	*Xe*	0·920
Xb	0·910	*Xf*	0·940
Xc	0·875	*Xg*	0·869
Xd	0·895	*Xh*	0·895

TABLE IV

ESR parameters (*a*, mT) for radicals *Xe*, *Xg*, and *XIII* in benzene

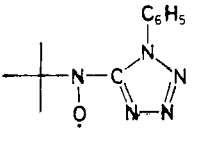
Radical	a_N^{NO}	a_N^1	a_N^2	a_H^4	a_H^5	a_H^6	a_H^7	a_H^1	$a_H^{o,p}$	a_H^m
Xe	0·920	0·050	0·180	0·180	0·050	0·108	0·050	—	0·200	0·078
Xg	0·869	—	0·186	0·154	0·050	0·079	—	—	0·202	0·074
XIII[a]	1·020	0·085	0·210	0·115	—	0·070	—	0·075[b]	—	—

[a] Taken from ref.[13]; [b] splitting from CH_3 protons.

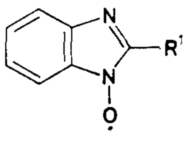
presume that the value consistent with the given facts has to be ascribed to nitrogen atom in position 1, i.e. the low values a_N 0·015–0·045 mT for radical *VIII* and 0·020–0·061 mT for radical *IX* are not those for the nitrogen atom in position 1 of the N-heterocyclic ring. More precise assignment of splitting constants a_N can be achieved on the basis of quantum-chemical calculations, or by experiments with ^{15}N-labelled compounds *V* and *VI*.

Replacement of the phenyl group at the exocyclic nitrogen atom of compound *VI* for a tert-butyl one resulted in a significant rise of the a_N^{NO} splitting constant of the nitroxyl *XI* (Table II) as a consequence of lowered conjugation; this is in line with the tendency observed when proceeding from diarylnitroxyls to alkylarylnitroxyls[4,11].

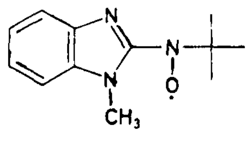
Due to low resolution of the EPR spectra of majority of nitroxyls *X* stemming from 2-anilinobenzimidazoles *VII* only values for basic nitrogen splitting a_N^{NO} (Table III) could be determined. The high-resolution EPR spectra enabling us to determine the splitting constants for all benzene and benzimidazole ring atoms were obtained with nitroxyls Xe and *Xg* (Table IV). The experimental a_N^{NO} values in the 0·87 to 0·94 mT range can unambiguously be assigned to the exocyclic nitrogen atom of radicals *Xa*–*Xd*, because splitting from the endocyclic nitrogen atom in position 1 would be substantially lower. This follows from comparing our data for radicals *X* with those reported for nitroxyls *XII* (a_N^{NO} for radical *XII* is within 0·47 and 0·53 mT (ref.[12]) in relation to the substituent R^1). Introduction of CH_3O group into *para* position of the benzene ring (radicals *Xb*, *Xd*, *Xf*, *Xh*) resulted in an increase of the a_N^{NO} value by 0·01–0·03 mT against radicals without substitution (*Xa*, *Xc*, *Xe*, *Xg*). The presence of NO_2 group in position 5 of the benzimidazole ring (*Xc*, *Xd*) led to a decrease of this value by 0·02 mT when contrasted with radicals *Xa*, *Xb*. These observations are in line with electron-donating and electron-accepting properties of the substituents given and their influence on the a_N^{NO} value for splitting of nitroxyl radicals. Influence of NO_2 group is not as significant under the given structural conditions of radicals *Xc* and *Xd* as when bonded to *para* position of the benzene ring[3]. Influence of R^2 substituents on the a_N^{NO} value follows from comparison of values for nitroxyls *Xa*, *Xe* and *Xg*. Substitution with an alkyl group (*Xe*) increases, whereas substitution with the phenyl group (*Xg*) decreases the a_N^{NO} value. This experimental fact evidenced the tendency also observed with radicals *VIII* and *IX*. The a_N^{NO} splitting constant for nitroxyl *Xe* is by 0·1 mT lower



XI



XII



XIII

than that for tert-butyl substituted radical *XIII* prepared by Aurich and coworkers[13] (Table IV). These findings indicated, similarly as with radicals *IXb* and *XI*, the delocalization effect of the phenyl ring.

Considering the EPR data of nitroxyl radicals *VIII*–*X* one can say that the unpaired electron is delocalized both in benzene and N-heterocyclic rings like with nitroxyls from 3-anilinopyrazoles[1]. Concurrently, a decrease of the a_N^{NO} value was observed on comparison with the diphenylnitroxyl radical, which was accompanied by an increase of splitting constants with benzene ring protons. Regarding the fact that substituents at the exocyclic nitrogen atom do not considerably influence the spin density at the oxygen atom of the nitroxyl[14] one can assume the spin density rise at the benzene ring to take place due to its decrease at the nitrogen atom of the nitroxyl. Extension of conjugation to the N-heterocyclic moiety of the radical by an aryl substitution at N^1 nitrogen resulted in a further decrease of the a_N^{NO} splitting constant value.

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