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Non-equivalence of Methylene Protons in Some Nitroxide Radicals of the Type XYZC—CH_2—N(O·)-*tert*-Butyl and XYN—CH_2—N(O·)-*tert*-Butyl

CARL LAGERCRANTZ and MORIO SETAKA*

Department of Medical Physics, University of Göteborg, S-400 33 Göteborg 33, Sweden

A number of nitroxide radicals of the type XYZC$-CH_2-$N(O·)-*tert*-butyl and one of the type XYN$-CH_2-$N(O·)-*tert*-butyl were found to exhibit ESR spectra with unequal splittings of the methylene protons together with temperature-dependent line width alternations. The origin of the non-equivalence and the line width alternations was shown to be connected with the presence of unsymmetrically related conformers produced by a steric hindrance combined with an unsymmetric center in position β to the nitrogen atom of the nitroxide group.

In connection with ESR studies on the trapping of short-lived free radicals by the nitroxide method,[1] it was observed that some acyclic nitroxides of the type XYZC$-CH_2-$N(O·)-*tert*-butyl and one of the type XYN$-CH_2-$N(O·)-*tert*-butyl gave rise to spectra exhibiting unequal splittings of the methylene protons.

In this paper it is shown that the non-equivalence of the methylene protons originates from the presence of unsymmetrically related conformers produced by a steric hindrance combined with an unsymmetric center in position β to the nitrogen atom of the nitroxide group. Non-equivalence of β-methylene** protons connected with the presence of a chiral atom has been observed for nitronyl nitroxide radicals,[3] nitroxide radicals,[4] and some nitro radicals.[5]

RESULTS

Primary short-lived radicals $R-CH_2\cdot$ (I) were produced in water or a slightly alkaline aqueous solution by the abstraction of a hydrogen atom from methyl groups of the parent compounds $R-CH_3$ (II) by photochemically generated OH radicals. The nitroxides (III) were subsequently formed in the reaction of the primary radicals with *tert*-nitrosobutane, eqn. 1.

$$\underset{\text{II}}{R-CH_3} \xrightarrow{\cdot OH} \underset{\text{I}}{R-CH_2\cdot}$$

$$\underset{\text{I}}{R-CH_2\cdot} + \textit{tert}\text{-nitrosobutane} \longrightarrow \underset{\text{III}}{R-CH_2-N(O\cdot)\text{-}\textit{tert}\text{-butyl}} \qquad (1)$$

The experimental details have been described elsewhere.[1]

5,5-Dimethylhydantoin, 5-methylhydantoin, isopropyl alcohol, 2-hydroxy-2-methylpropanoic acid, and *N*,*N*-dimethylformamide were found to give rise to the nitroxides *1*–*5*, which exhibit unequal β-methylene proton splittings, whereas *tert*-butyl alcohol and 2,2-dimethylpropanoic acid gave rise to the structurally similar nitroxides *6* and *7* which exhibited equivalent β-methylene proton splittings above room temperature.

The ESR spectra of the nitroxides *1*–*5* consisted of 3 × 4 lines indicating an interaction with the ^{14}N nucleus and two non-equivalent

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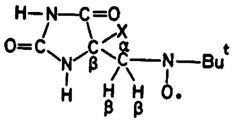
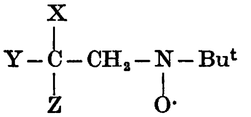
* On leave from the Faculty of Pharmaceutical Sciences, University of Tokoy, Bunkyo-ku, Tokyo.

** The notation used for the atoms concerned is in conformity with the nomenclature used for radicals, *e.g.* by Briere *et al.*[2]



1, 2

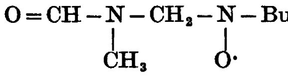
1 X = CH_3; *2* X = H



$Y-\overset{X}{\underset{Z}{C}}-CH_2-\underset{O\cdot}{N}-Bu^t$

3, 4, 6, 7

3 $X=CH_3$, $Y=OH$, $Z=H$; *4* $X=CH_3$, $Y=OH$, $Z=COO^-$; *6* $X=CH_3$, $Y=CH_3$, $Z=OH$; *7* $X=CH_3$, $Y=CH_3$, $Z=COO^-$.



$O=CH-\underset{CH_3}{N}-CH_2-\underset{O\cdot}{N}-Bu^t$

5

protons, evidently those of the methylene group. The nitroxides *3* and *5* gave rise to further splittings, nitroxide *3* to a doublet caused by the hydrogen atom on the β-carbon atom, nitroxide *5* to a triplet by interaction with the ^{14}N nucleus of the amide group. The proton splittings of the nitroxides *1*, *3*, and *4* varied somewhat with the temperature in an inversed way, so that the large one decreased and the small one increased when the temperature was raised (Table 1). The spectra obtained with nitroxides *3*, *4* and *5* are shown in Figs. 1, 2, and 3, respectively.

Line width alternations were observed with the nitroxides with the unequal β-proton splittings. The two inner lines of the 1:1:1:1 quartet caused by the two non-equivalent methylene

Table 1. Nitroxide radicals of the type $R-CH_2-N(O^\cdot)$-*tert*-butyl formed by trapping of the radicals $R-\dot{C}H_2$ produced in the reaction between photochemically generated OH radicals and a methyl group of the parent compounds. Scavenger: *tert*-nitrosobutane. Splitting constants in gauss. Solvent: H_2O.

Parent compound	Nitroxide radical	Temp. °C	a_N	$a_{H(2)}$	$a_{H(1)}$	$a_{H(2)}+a_{H(1)}$	$a_X^{a,b}$
5,5-Dimethylhydantoin	*1*	+3	15.8	20.3	3.68	24.0	
»	*1*	+20	15.9	20.0	4.08	24.1	
»	*1*	+46	15.8	19.3	4.52	23.8	
»	*1*	+84	15.9	18.4	5.38	23.8	
»	*1*	+98	15.8	17.9	5.55	23.5	
5-Methylhydantoin	*2*	+20	16.1	26.0	0.72	26.7	
Isopropyl alcohol	*3*	−8	16.0	14.2	9.3	23.5	0.73
»	*3*	+25	16.3	13.3	8.9	22.2	0.74
»	*3*	+35	16.3	12.9	9.3	22.2	0.75
»	*3*	+49	16.4	12.6	9.8	22.4	0.76
»	*3*	+61	16.3	12.4	9.9	22.3	0.75
2-Hydroxy-2-methylpropanoic acid	*4*	−19	16.3	19.7	7.6	27.3	
»	*4*	−1.5	16.3	18.9	8.9	27.8	
»	*4*	+19	16.3	17.4	10.3	27.7	
»	*4*	+50	16.4	16.4	11.3	27.6	
»	*4*	+95	16.5	15.0	12.7	27.2	
N,*N*-Dimethylformamide	*5*	−16	15.4	10.3	9.3	19.6	2.35
»	*5*	0	15.4	10.1	9.1	19.2	2.35
»	*5*	+16	15.3	10.1	9.1	19.2	2.38
»	*5*	+35	15.4	10.0	8.9	18.9	2.43
»	*5*	+50	15.4	9.90	8.9	18.8	2.48
tert-Butyl alcohol	*6*	−25	16.3	11.0	11.0		
»	*6*	0	16.3	10.9	10.9		
»	*6*	+23	16.3	11.1	11.1		
»	*6*	+51	16.4	11.2	11.2		
»	*6*	+84	16.3	11.1	11.2		
2,2-Dimethylpropanoic acid	*7*	−20	15.8	21.6	5.82	27.42	
»	*7*	−9	16.2	22.0	5.60	27.60	
»	*7*	−1	16.1	13.5	13.5		
»	*7*	+23	16.3	13.5	13.5		
»	*7*	+72	16.3	13.0	13.0		

[a] Radical *3*. Doublet splitting from the proton on the β-carbon atom. [b] Radical *5*. Triplet splitting from the nitrogen atom of the amide group.

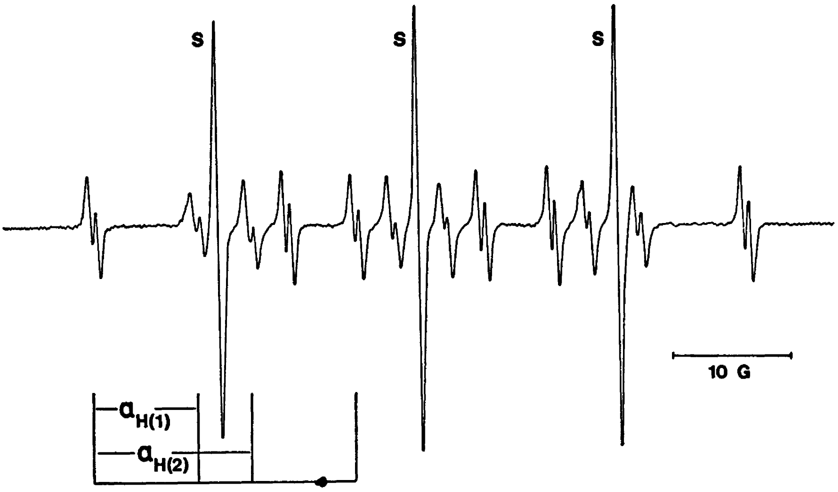


Fig. 1. ESR spectrum of the nitroxide radical *3* derived from isopropyl alcohol at +25 °C. Solvent: H_2O. S: symmetrical nitroxide radicals derived from the scavenger.

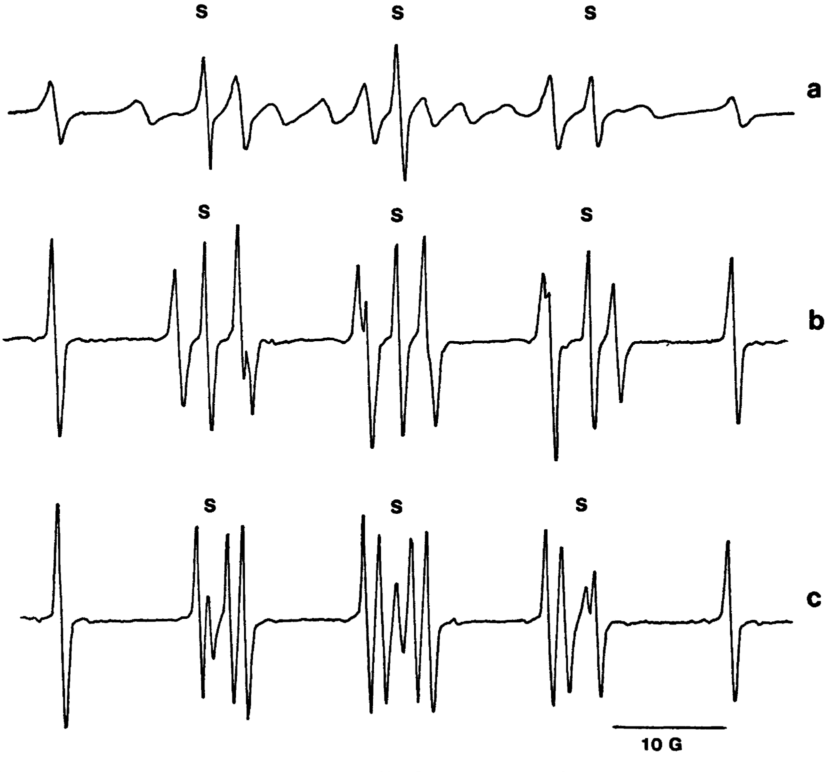


Fig. 2. ESR spectrum of the nitroxide radical *4* derived from 2-hydroxy-2-methylpropanoic acid. Solvent: H_2O + a small amount of alkali. S: symmetrical nitroxide radicals derived from the scavenger. *a* at −19 °C, *b* at +29 °C, and *c* at +83 °C.

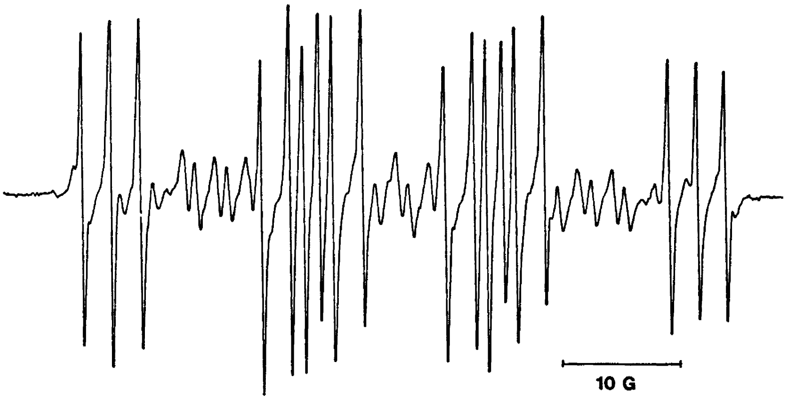


Fig. 3. ESR spectrum of the nitroxide radical *5* derived from *N*,*N*-dimethylformamide, at +35 °C. Solvent: H_2O.

protons broadened upon decreasing the temperature, but sharpened when the temperature was increased, so that all 12 lines became of equal height, as seen from the spectra in Fig. 2 obtained at different temperatures with nitroxide *4*, derived from 2-hydroxy-2-methylpropanoic acid. However, the spectra obtained with nitroxide *5* (Fig. 3) exhibited still very pronounced line width alternations, with broadening of the inner lines of the methylene quartets, even at the highest accessible temperature (+50 °C). The basic 12-line structure of the spectra was preserved for the nitroxides *1*–*5* in the entire experimentally accessible range of temperature, *i.e.* from −20 °C to about +90 °C.

Nitroxide *6* gave rise to 3×3 (1:2:1)-line spectra, indicating equivalence of the methylene protons. The center line of the 1:2:1 triplet became broadened already below +50 °C. Nitroxide *7* exhibited 3×3 (1:2:1)-line spectra above room temperature. Below room temperature, the center line of the 1:2:1 triplets broadened and below −10 °C there was a change into a 3×4 (1:1:1:1)-line spectrum, indicating nonequivalence of the methylene protons.

DISCUSSION

Most acyclic nitroxides of the type $R-CH_2-N(O\cdot)-R'$ hitherto described in the literature give rise to ESR spectra with equivalent methylene protons at room temperature. Many such nitroxides show line width alternations at lower temperatures due to the presence of a steric hindrance which introduces two symmetrically related conformers (A and B in Fig. 4).[6,7] This case was actually observed with nitroxide *6* below +50 °C. At even lower temperatures the rate of jumping between the conformers A and B became slow enough to allow the spectrometer to record a superposition spectrum of the individual conformers, the spectra of which are identical. The center line of the methylene triplets is now resolved into two separate lines, and the spectrum consists of 12 lines of equal intensity. Such an interpretation is evidently valid also for the spectra obtained with nitroxide *7* below −10 °C.

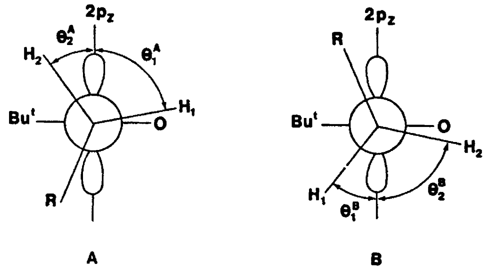


Fig. 4. Steric arrangement around the bond axis between the nitrogen atom of the nitroxide group and the α-carbon atom. The conformers A and B are symmetrically related, so that $\theta_1^A = \theta_2^B$ and $\theta_2^A = \theta_1^B$. The arrangement on the nitrogen atom was made planar.

The results obtained with the nitroxides *1*–*5* cannot be explained by the mechanism outlined.

If this mechanism had been valid, the 12-line spectra would have exhibited a broadening of the inner lines of the methylene 1:1:1:1 quartet upon increasing the temperature, not a broadening upon decreasing the temperature which was actually observed. Furthermore, the 12-line spectra would have been changed into 9-line spectra with 1:2:1 methylene triplets in the high temperature range, a finding which was not observed for any of the nitroxides *1–5*.

The nitroxides *1–4* with unequal β-proton splittings all have a center of chirality in position β to the nitrogen atom of the nitroxide group, whereas no such center is present in the nitroxides *6* and *7* which show equivalent β-protons at high temperature. A hindered rotation around the bond axis between the α-carbon atom and the chiral β-atom introduces two conformers which are mutually unsymmetrical due to a steric interaction between the oxygen atom or the *tert*-butyl group on the nitrogen atom and the non-identical substituent groups XYZ on the chiral β-atom. The origin of the unsymmetrically related conformers in the case of radical *5* is less easily explained. The nitrogen atom of the amide group is evidently involved but it is not clear if the unsymmetry originates from the nitrogen atom as a chiral center, or indirectly from the steric behaviour of one of the substituent groups, possibly the COH group.

The mutually unsymmetrical conformers, A and B in Fig. 5, infer that the dihedral angles are related by the inequalities $\theta_1{}^A \neq \theta_2{}^B$ and $\theta_2{}^A \neq \theta_1{}^B$. Considering the splitting constant of a β-proton of nitroxides to be proportional to the cosine square of the dihedral angle concerned,[8] the non-equivalence of the β-protons is produced as follows. As a result of the unsymmetry conformers A and B will be represented by individual ESR spectra with non-identical splitting constants, as shown for one of the three methylene splittings in Fig. 6a and b. At low temperature, when the rate of jumping between conformations A and B is slow, the spectrometer will resolve all eight lines of the actual superposition spectrum of the two conformers (Fig. 6c). When the temperature is raised and the rate of interconversion increases past the limit of slow exchange, the lines coalescence in pairs into a 4-line spectrum, which gradually sharpens towards the situation shown in Fig. 6d.

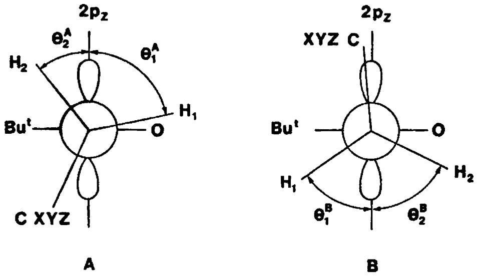


Fig. 5. Steric arrangement around the bond axis between the nitrogen atom of the nitroxide group and the α-carbon atom. The conformers A and B are unsymmetrically related, so that $\theta_1{}^A \neq \theta_2{}^B$ and $\theta_2{}^A \neq \theta_1{}^B$. The arrangement on the nitrogen atom was made planar.

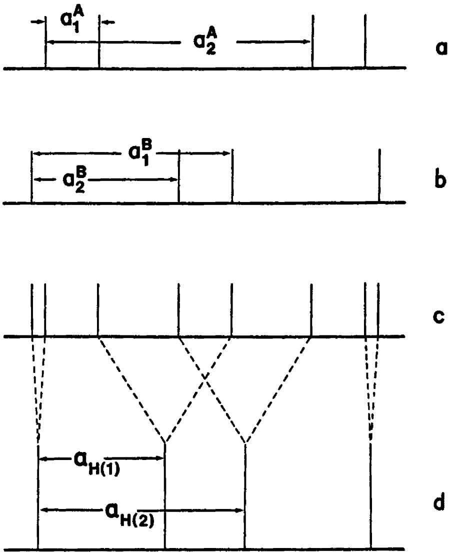


Fig. 6. Schematic ESR spectra of one of the three methylene splittings for nitroxides with the unsymmetrically related conformers A and B.
a and *b*: individual spectra corresponding to conformers A and B. *c*: actual spectrum at low jumping rate, *d*: at high rate.

This mechanism explains the origin of the four-line splittings produced by the methylene protons as observed with nitroxides *1–5*. Evidently the rate of interconversion between different conformations exceeds the limit of slow exchange in the whole range of the experimentally accessible temperatures. The broadening of the inner lines as compared with the outer ones of the methylene quartet observed at low temperatures originates from the coalescence of pairs of lines in conformations A and B far more widely separated than the corresponding pairs of the wings. The continuous variation of $a_{(H1)}$ and $a_{(H2)}$ so that the sum $a_{H(1)}+a_{H(2)}$ remains constant as seen from Table 1, is believed to be connected with an unequal population of the two conformations A and B. The position of the inner lines of the methylene quartets formed by coalescence (see Fig. 6d) is a weighted mean of the positions of the parent lines in conformations A and B. An increase in the temperature will therefore move the inner lines towards the line position of the conformation, whose population was increased by the rise in temperature.

The interpretation made for the origin of the unequal β-methylene splittings of the nitroxides *1*–*5* is in some details similar to that proposed by Gilbert *et al.*[5] for the nitro radicals mentioned above, and seem to satisfactorily explain our findings.

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