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CONFIGURATIONAL ASSIGNMENT OF α-PHENYL-α,N-DIMETHYLNITRONES BY A LANTHANIDE SHIFT REAGENT IN PROTON MAGNETIC RESONANCE SPECTROSCOPY

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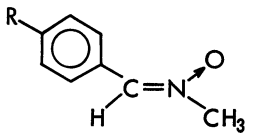
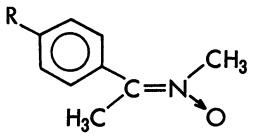
The ketonitrones, α-phenyl- and α-p-tolyl-α,N-dimethylnitrones (IIa and IIb, respectively), have been determined to be E isomers by application of a paramagnetic lanthanide shift reagent and benzene-induced solvent shifts in PMR spectroscopy.

The presence of geometrical isomers of nitrones is well known.[1] The preparation of aldonitrones by usual methods[2] is known to give solely one isomer, the configuration of which, as illustrated by structure I, has already been confirmed by X-ray analysis of a crystal of α-p-chloro-phenyl-N-methylnitrone (Ic),[3] and by the dipole-moment of the p-nitro derivative (Id).[4] On the other hand, the ketonitrones α-phenyl- and α-p-tolyl-α,N-dimethylnitrones (IIa and IIb, respectively) have been assumed to have the anti methyl configuration (E isomer)[5] from the fact that their reaction behaviour against tosyl chloride[6] is analogous to that of α-picoline N-oxide.[7] Abnormally low intensity of the absorption maxima in the UV spectra[4] and the large downfield shift of the N-methyl signals in the PMR spectra[8] are compatible with this tentative configuration of II. However, confirmatory evidence for the configuration of II has not so far been reported.



(Ia: R = H)
(Ib: R = CH_3)
(Ic: R = Cl)
(Id: R = NO_2)



(IIa: R = H)
(IIb: R = CH_3)

Our interest was focused on the application of the paramagnetic shift reagent tris(dipivalomethanato)europium (III), $Eu(DPM)_3$, in PMR spectroscopy[9] to assign the configuration of these ketonitrones (IIa and IIb), which were prepared by the method previously described[6] and were identified by their elemental analyses and their UV, IR, and PMR spectra. The PMR spectra of IIa and IIb, and of Ia and Ib (for comparison) were measured with a Varian A-60A spectrometer using TMS as an internal standard in $CDCl_3$ (about 0.1 mole/l) at various concentrations of $Eu(DPM)_3$ at 39°, and also in CCl_4 and C_6D_6 to infinite dilutions.

Table 1 shows the paramagnetic shift values (S-value), represented as the slopes of straight lines obtained by plotting the shift values induced by $Eu(DPM)_3$ for various proton signals against the molar ratio of $Eu(DPM)_3$ to

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Table 1. PMR spectral data on the nitrones[a]

Compound		N-CH_3	α-H	α-CH_3	ortho-H	meta-H	para-H	para-CH_3
Ia	δ_{CDCl_3}	3.83	7.32	—				—
	S-value (obsd)	+13.8	+9.04	—	+8.76	+0.44	+0.37	—
	S-value (calcd)[c]	+12.2	+9.59	—			+0.40	—
	δ_{CCl_4}	3.80 (3.80)[b]	7.23 (7.28)[b]	—	(8.17)[b]	(7.37)[b]		—
	$\Delta\delta(C_6D_6 - CCl_4)$	-0.75 (-0.73)[b]	-0.72 (-0.73)[b]	—	(+0.17)[b]	(-0.20)[b]		—
Ib	δ_{CDCl_3}	3.83	7.28	—	8.09	7.20	—	2.37
	S-value (obsd)	+12.8	+8.08	—	+7.94	+0.15	—	-0.16
	S-value (calcd)[c]	+11.5	+8.87	—			—	-0.16
	δ_{CCl_4}	3.78 (3.77)[b]	7.20 (7.23)[b]	—	8.02 (8.05)[b]	7.14 (7.17)[b]	—	2.37 (2.38)[b]
	$\Delta\delta(C_6D_6 - CCl_4)$	-0.69 (-0.67)[b]	-0.69 (-0.63)[b]	—	+0.21 (+0.27)[b]	-0.14 (-0.10)[b]	—	-0.32 (-0.32)[b]
IIa	δ_{CDCl_3}	3.66	—	2.44				—
	S-value (obsd)	+10.2	—	+6.22	+3.17	+1.36	+1.23	—
	S-value (calcd)[c]	+10.2	—	+6.24			+1.23	—
	δ_{CCl_4}	3.55	—	2.31				—
	$\Delta\delta(C_6D_6 - CCl_4)$	-0.13	—	+0.00				—
IIb	δ_{CDCl_3}	3.65	—	2.42	7.16	7.23	—	2.39
	S-value (obsd)	+9.52	—	+5.83	+2.76	+1.10	—	+0.67
	S-value (calcd)[c]	+9.50	—	+5.86			—	+0.67
	δ_{CCl_4}	3.53	—	2.28	7.15	7.15	—	2.38
	$\Delta\delta(C_6D_6 - CCl_4)$	-0.23	—	+0.05	-0.39	-0.47	—	-0.37

[a] δ_{CDCl_3}: chemical shift in ppm downfield from TMS at about 0.1 mole/l in $CDCl_3$.
δ_{CCl_4}: chemical shift in ppm downfield from TMS at infinite dilution in CCl_4.
$\Delta\delta(C_6D_6 - CCl_4)$: benzene-induced solvent shift in ppm (plus sign denotes a downfield shift).
[b] Taken from Ref. 22b. [c] See the text.

nitrone. In II, the configuration of the N-methyl with respect to the benzene ring can apparently be assigned as syn from the fact that the para-methyl proton signal in IIb was shifted downfield (+0.67 ppm), whereas that in Ib was shifted upfield (-0.16 ppm). The latter should be noted as an example of upfield shift by $Eu(DPM)_3$.[10]

To confirm this assignment, we calculated the shift values, using the McConnell-Robertson equation for the pseudocontact shift,[11] $S_i = K(3\cos^2\theta_i - 1)/r_i^3$, where r_i is the distance between the metal atom and the ith proton and θ_i is the angle between this vector and the principal axis of anisotropy in each complex, on the assumptions that the contact term contribution to the paramagnetic shift is negligible (i.e., the pseudocontact interaction is operative),[12] and that the principal axis of the nitrone-$Eu(DPM)_3$ complex is at the metal-ligand (Eu—O) bond.[16] Initially, a set of values for $(3\cos^2\theta_i - 1)/r_i^3$ was obtained for the protons, except o- and m-H, by substitution of

r_i and θ_i values obtained from Dreiding models with arbitrary orientation of the europium atom in each complex. Calculation was reiterated until K, obtained from the observed S-values and the calculated values of $(3\cos^2\theta_i - 1)/r_i^3$, became as constant as possible for each complex. When the best-fit calculated S-values were reached, the molecular geometries of the Ia, Ib, IIa, and IIb complexes with $Eu(DPM)_3$ became as follows: the distances between the oxygen and the europium atom were 3.2 Å, 3.4 Å, 2.5 Å, and 2.6 Å; the Eu-O-N angles were 119°, 117°, 142°, and 132°;[18] the angles of deviation from the N→O bond axis towards the N-methyl group were 29°, 29°, 0°, and 0°; and K-values were 1330 (±14%), 1308 (±11%), 832 (±1%), and 821 (±1%), respectively. The large difference in the O-Eu distances between I and II and the angle deviation seen in I must be due to steric interaction between the benzene ring and the N→O group. Consequently, it was confirmed that in II the configuration of the N→O group with respect to the benzene ring is anti, while in I it is syn.

Table 1 also lists the benzene-induced solvent shifts,[22] $\Delta\delta(C_6D_6 - CCl_4)$, obtained at infinite dilution for the nitrones examined. The benzene-induced shift values are qualitatively consistent with the configurations of I and II; i.e., it is reasonable that downfield shifts were observed for the o-H signal in I and for the α-Me signal in II if a proton at the oxygen-side of a plane perpendicular to N→O and passing through the N atom suffers a downfield shift and one on the opposite side an upfield shift, analogously to the prediction by the benzene-induced shift rule for a C=O group.[22a] That the p-Me and m-H signals in I were shifted upfield, is also ascribable to the steric effect of the benzene ring.

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