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SYNTHESIS AND SPECTRAL PROPERTIES OF (+)-2,2,4,4,6-PENTAMETHYL-3-AZABICYCLO[3,3,1] NONAN-7-ONE-3-OXYL.

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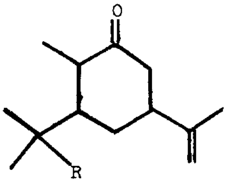
Interest has been expressed recently in the theoretical implications of the e.p.r.[1-4] and c.d.[5,6] spectral characteristics of stable, bicyclic nitroxide radicals. In this connection we wish to report the synthesis of the optically-active nitroxide (6) which exhibits certain spectral properties of current interest.

Following the general scheme of nitroxide radical synthesis which we have described recently,[7] Michael addition of 2-nitropropane anion to (+)-carvone yielded a diastereoisomeric mixture of adducts (1) which could be partially separated by chromatographic techniques. Reduction of this mixture with zinc and ammonium chloride and oxidation of the resultant hydroxylamines with silver oxide gave the corresponding nitroso compounds (2). Reaction of these with iodine in chloroform solution resulted in the formation of the iodo-nitroxide (3),[8 †] m.p. 124-127°(decomp.), $[\alpha]_D^{25}$ = -28°(hexane), $\underline{a}_N(CCl_4)$ = 15.2 Oe, $\underline{g}$ = 2.0071, together with some unreacted nitroso material. Hydrogenation of (3) over Lindlar catalyst gave the corresponding hydroxylamine (4), τ ($CDCl_3$) = 8.79 (6H,s), 8.78 (3H,d, J = 7Hz), 8.68 (3H,s), 6.72 and 6.32 (2H, ABq, J = 10Hz) and 4.88 (1H,b, exchangeable) which could be reoxidised to (3). Reduction of (3) over Pd-C yielded the hydroxylamine (5), τ ($CDCl_3$) = 8.80 (12H,s), 8.78 (3H,d, J = 7Hz) and 5.37 (1H,b, exchangeable) which was oxidised to the parent nitroxide (6),[†] m.p. 106.5-108.5°,

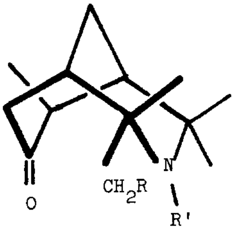
[†] Both these compounds analysed correctly by high-resolution mass spectrometry.

$[\alpha]_D^{25}$ = +32.1° (hexane), $\underline{a}_N(CCl_4)$ = 15.3 Oe, $\underline{g}$ = 2.0070.



(1) R = NO_2

(2) R = NO



(3) R = I, R' = $\dot{O}$

(4) R = I, R' = OH

(5) R = H, R' = OH

(6) R = H, R' = $\dot{O}$

The high-resolution e.p.r. spectrum of a degassed solution of (6) displays further hyperfine couplings in the form of a triplet, $\underline{a}_H$ = 0.99 Oe and a doublet, $\underline{a}_H$ = 0.52 Oe. As a result of preliminary deuteration studies the larger coupling is ascribed to the two bridgehead protons and the smaller coupling to one of the bridge protons. The magnitude of the coupling to the bridgehead protons would suggest that the N-O bond adopts a predominantly axial (*i.e.* *endo*) configuration thus permitting a W-plan arrangement[9] between the orbital containing the unpaired electron and the protons at C-1 and C-5. The proton at C-9 responsible for the smaller coupling cannot be assigned with certainty at the present time, but by analogy with previous work[10,11] the most likely contender is the proton *anti* with respect to the nitroxide function.

The c.d. spectrum of (3) (MeOH) exhibits a positive maximum at 296 nm (Δε = + 1.72) corresponding to the carbonyl n → π* transition and a small negative maximum for the nitroxide n → π* transition at 476 nm (Δε = -0.05). On the other hand, the c.d. spectrum of (6) (MeOH) shows a positive maximum at 295 nm (Δε = +1.56*)

* Using a corollary of the Kronig-Kramers theorem the molecular amplitude *a*, is calculated to be +62.8 which is very similar in magnitude to the extrapolated[12] (67) and theoretical[13] (71) values for optically-active 2-axial methylcyclohexanone.

but no maximum for the nitroxide group. This latter observation is probably the result of the high degree of symmetry in the vicinity of the nitroxide chromophore. Consonant with all the spectral characteristics is the fact that (6) has a dipole moment of 5.2D in benzene solution at 25° which would suggest a chair-chair conformation for this compound, either with an axial-type N-O bond or a slight distortion of the piperidinoxyl ring[14]. Confirmatory evidence in favour of a C-6 axial methyl group in (4) and (6) is provided by the benzene-induced upfield shift of the methyl doublet by 0.36 and 0.26 ppm respectively.

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