favors the radicals, decay is second order. In view of the complexities of the reaction, the precise meaning of the measured decay rate constants is uncertain.

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Studies of Stable Free Radicals. X.[1] Nitronyl Nitroxide Monoradicals and Biradicals as Possible Small Molecule Spin Labels

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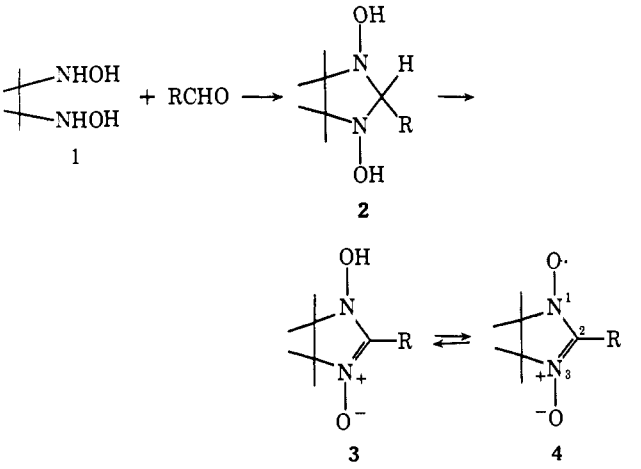
Abstract: The preparation, chemistry, and spectra of nitronyl nitroxides, a versatile new class of stable radicals, are described. The compounds are readily prepared from most aldehydes. Their esr spectra may have use in determining the extent of α substitution of the aldehyde where only small amounts of the aldehyde are available. Reaction of α-haloalkyl nitronyl nitroxides with amines proceeds readily, and the esr spectra of the resulting amino radicals may serve to distinguish between primary and secondary amines. Both conjugated and unconjugated biradicals have been prepared. The zero-field splitting data suggest that the conjugated biradicals exist in several possible planar conformations.

Stable free radicals that can undergo reactions at sites of high spin density are useful in the spin labeling of small molecules. By the attachment of such a radical to a host molecule spin density is distributed to the host. The electron spin resonance spectrum can then yield information concerning the site of attachment. Utilization of this technique has primarily been confined to spin labeling with semidiones.[4] Spin trapping experiments with nitroso compounds or nitrones in which reaction of a reactive radical yields a nitroxide is also a form of spin labeling, although these experiments are generally designed to give esr information about the reactive radical rather than the diamagnetic trap.[5]

In the course of studies to develop spin-labeling techniques for small molecules, a new class of stable radicals called nitronyl nitroxides was discovered.[6] These compounds can be readily prepared from many aldehydes by simple test tube reactions and their esr spectra yield direct information concerning the substitution of the aldehyde. In this and subsequent papers, the chemistry of nitronyl nitroxides will be discussed together with spectral data which can yield structural information concerning the starting aldehyde.

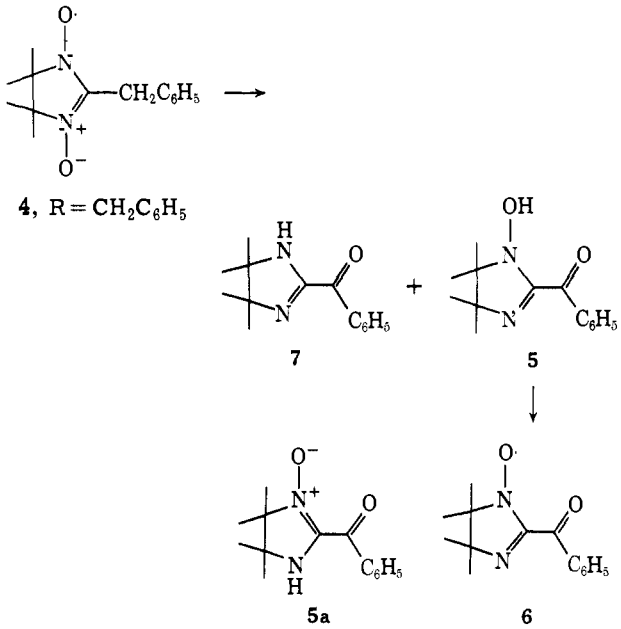
Aliphatic Nitronyl Nitroxides. Aliphatic aldehydes react rapidly with 2,3-dimethyl-2,3-bis(hydroxylamino)-butane (**1**). Although it is usually possible to isolate an anhydro adduct **2**, direct treatment of the reaction mixture with sodium periodate or lead dioxide gives an instantaneous color due to the formation of a nitronyl nitroxide **4**. Nitronyl nitroxides derived from saturated aldehydes are generally red whereas unsaturated aldehydes yield violet or blue radicals depending on whether the solvent is polar or nonpolar. When desired, the initial dihydro adducts **2** can be obtained as stable diamagnetic white solids. If sodium periodate or lead dioxide is added in limited amount to these compounds it is possible to obtain the highly air-sensitive intermediates **3**. Catalytic hydrogenation of the nitronyl nitroxides regenerates **3**, though rapid catalytic reoxidation occurs if the catalyst is not completely separated. The radicals when isolated are quite stable and in most cases can be stored at 0° for months without decomposition.



α hydrogens of 2-alkyl groups on nitronyl nitroxides are weakly acidic. Deuterium exchange of the 2-methyl hydrogens of **4**, R = CH_3, in alkaline deuterium oxide occurs without loss of the esr signal. Strong bases such as potassium *tert*-butoxide in DMSO cause

(1) For paper IX, see E. F. Ullman, L. Call, and J. H. Osiecki, *J. Org. Chem.*, 35, 3623 (1970).
(2) Synvar Postdoctoral Fellow, 1967–1969.
(3) Synvar Postdoctoral Fellow, 1967–1968.
(4) G. A. Russell, E. T. Strom, E. R. Talaty, K. Y. Chang, R. D. Stephans, and M. C. Young, *Rec. Chem. Progr.*, 27, 3 (1966).
(5) E. G. Jansen, *Accounts Chem. Res.*, 4, 31 (1971).
(6) For preliminary communications describing portions of this work, see J. H. Osiecki and E. F. Ullman, *J. Amer. Chem. Soc.*, **90**, 1078 (1968); D. G. B. Boocock, R. Darcy, and E. F. Ullman, *ibid.*, **90**, 5945 (1968).

rapid loss of both the color and the esr signal, possibly as a result of oxidation of the radical anion by unionized nitronyl nitroxide.[7] Alkyl nitronyl nitroxides bearing α hydrogens which are allylic also undergo exchange but are less stable. The benzyl derivative **4** ($R = CH_2C_6H_5$) failed to crystallize and was completely converted to diamagnetic products on standing at room temperature for several days or on boiling for 1 hr in benzene. The major product, obtained in 23% yield, was the imidazoline **5** ($\nu_{C=O}$ 1675 cm^{-1}), the structure of which was partially demonstrated by lead dioxide



4, $R = CH_2C_6H_5$

7 **5** **5a** **6**

oxidation to give a stable yellow radical **6**. The new radical displayed an esr spectrum characteristic of other imino nitroxides having seven lines in the ratio 1:1:2:1:2:1:1 due to two nonequivalent nitrogens.[1] Distinction between **5** and its tautomer **5a** was deduced from the similarity of the carbonyl absorption and ultraviolet spectra of **5** and **7**, a second minor product of the reaction. Although the mechanism of decomposition has not been studied, the phenyl substituent in **4**, $R = CH_2C_6H_5$, apparently decreases the stability of the radical by facilitating α-hydrogen abstraction.

Deliberate attempts to abstract α hydrogens with halogens, hypohalites, or *N*-bromosuccinimide from 2-alkyl nitronyl nitroxides yielded complex mixtures. α-Haloalkyl nitronyl nitroxides could, however, be formed directly from α-halo aldehydes and **1** in the usual fashion. The halomethyl derivatives **4**, $R = CH_2Cl$, CH_2Br, and CH_2I, are very reactive toward nucleophiles with increasing reactivity in the order Cl < Br < I. The thermal stability of these compounds follows the inverse order, and **4**, $R = CH_2I$, could only be prepared by treatment of one of the other halides with potassium iodide. The halides reacted with water, alcohols, and amines to give the corresponding α-substituted 2-methylnitronyl nitroxides. While few of the thus-formed aminomethyl derivatives were sufficiently stable to isolate due to the increased lability of the α hydrogens, the highly hindered dibenzylamine **4**, $R = CH_2N(CH_2C_6H_5)_2$, and the *p*-toluenesulfonamide and phthalimide derivatives of **4**, $R = CH_2NH_2$, were isolable.

Condensation of the bishydroxylamine **1** with unsaturated aldehydes proceeded normally. Cinnamaldehyde, phenylpropargaldehyde, crotonaldehyde, and acrolein each yielded the corresponding nitronyl nitroxide although **4**, $R = CH{=}CH_2$, from acrolein proved to be unstable. The phenylethynyl derivative **4**, $R = C{\equiv}CC_6H_5$, could also be prepared by bromination of **4**, $R = CH{=}CHC_6H_5$, to give **4**, $R = CHBrCHBrC_6H_5$, followed by sodium methoxide dehydrobromination.

Reaction of the bishydroxylamine **1** with glutaraldehyde or succinaldehyde in aqueous solutions yielded the corresponding anhydro adducts **8**, $n = 2, 3$, which on oxidation with sodium periodate gave the red biradicals **9**, $n = 2, 3$. A similar experiment using malondialdehyde gave a very low yield of **8**, $n = 1$, which failed on oxidation to give a stable radical. The failure to form **9**, $n = 1$, is presumably related to the instability of alkyl nitronyl nitroxides with allylic α hydrogens. The dimethylene biradical **9**, $n = 2$, could be oxidized by the use of sodium hypochlorite with formation of the green ethylene biradical **11**. This reaction probably proceeds through the radical cation **10** which would then be expected to lose a proton and be further oxidized (Scheme I). Chlorine and bromine readily added to **11** to give the halo biradicals **12**, but dehydrohalogenation of **12** to give an acetylenic biradical was not successful. Treatment of **12**, X = Br, with a variety of bases invariably caused reductive debromination to give back **11**. Although potassium *tert*-butoxide appeared to effect dehydrochlorination of **12**, X = Cl, the several blue-gray biradicals that were formed were unstable. Treatment of the biradical **11** with nitrous acid[1] led to the sequential removal of two oxygen atoms to give the imino nitroxides **13** and **14**. Interestingly, deoxygenation of **9**, $n = 2$, under the same conditions yielded a bisimino nitroxide **15**, which gave the ethylenic biradical **13** on longer treatment under the same conditions.

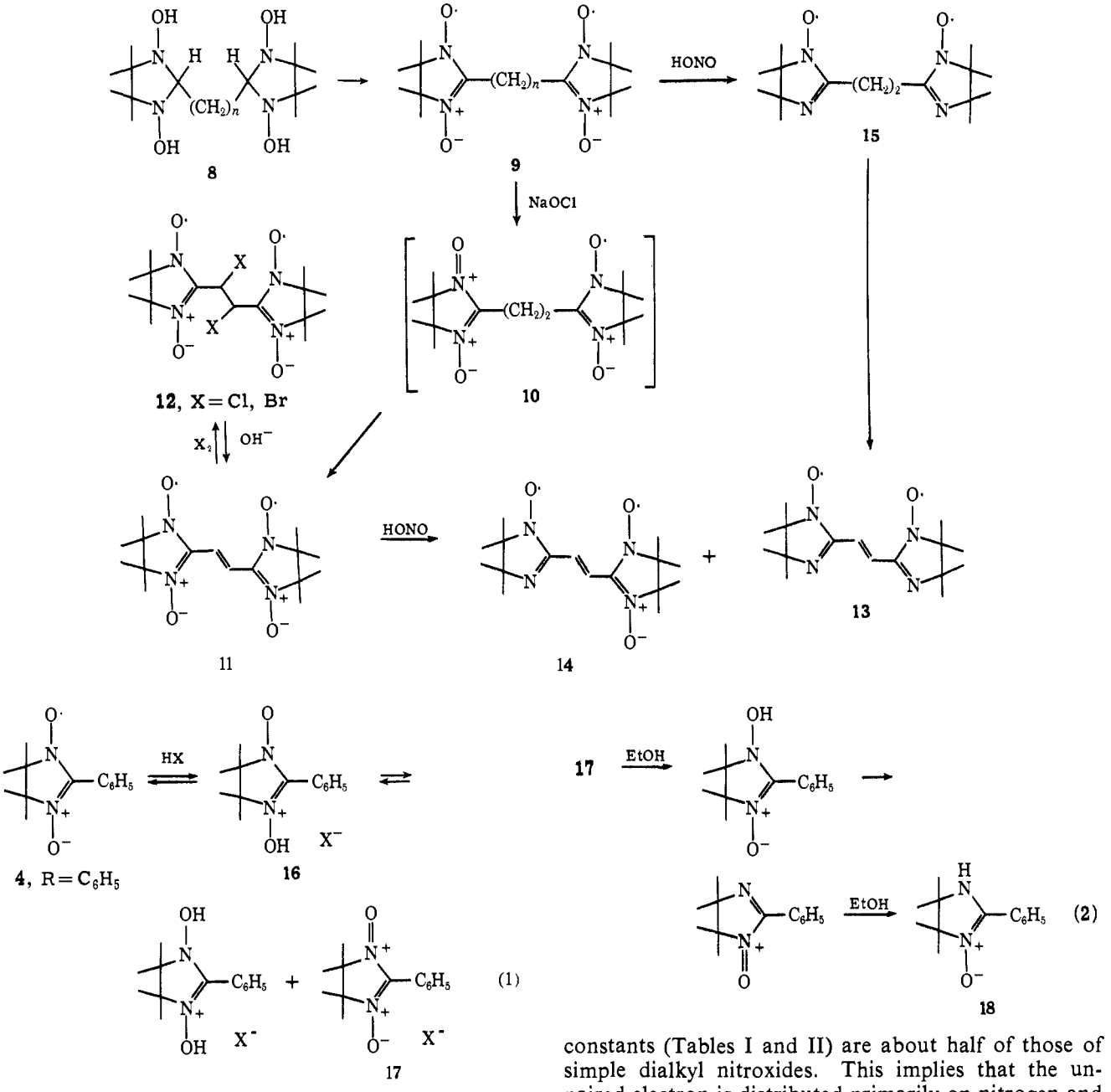
Aryl Nitronyl Nitroxides. The reaction of aryl aldehydes with the bishydroxylamine **1** proceeded more slowly than did alkyl aldehydes. The colorless dihydro adducts **2** oxidized readily *via* **3** to yield crystalline indefinitely stable blue nitronyl nitroxides **4**, R = Ar. Aromatic dialdehydes similarly combined with the bishydroxylamine **1** to give, after oxidation, the corresponding bisnitronyl nitroxides.

The aryl derivative **4**, $R = C_6H_5$, could be subjected to boiling water or alkali without decomposition. However, treatment with aqueous 1 *N* hydrochloric acid led to diminution of the esr signal with formation of an orange color. Stronger acid caused a further decrease in the signal which could be fully restored by neutralization with base. These changes suggest the disproportionation process 1 which was supported by the observation of an esr spectrum of **16** (a_H = 4.7 G, $a_{N(1)}$ = 5.7 G, and $a_{N(2)}$ = 4.5 G) when **4**, $R = C_6H_5$, was treated with trifluoroacetic acid in benzene. In this solvent hydrogen bonding within tight ion pairs may inhibit disproportionation.

The disproportionation product **17**, X = Cl, could be prepared independently from **4**, $R = C_6H_5$, by treatment of a carbon tetrachloride solution with chlorine

(7) Transient formation of an anion under these conditions has been demonstrated by C-benzylation of **4** ($R = CH_2C_6H_5$): unpublished observation by D. G. B. Boocock.

Scheme I



gas. This cation was diamagnetic and displayed a single methyl peak at δ 1.83 in the nmr (SO_2Cl_2 solvent). The cation **17** was an exceptionally powerful oxidizing agent as exemplified by the instability of its bromide salt. Thus evaporation of a carbon tetrachloride solution of **4**, R = C_6H_5, and bromine led initially to the orange bromide **17**, X = Br, which gradually lost bromine with re-formation of the nitronyl nitroxide. The cation **17** was gradually reduced to **4**, R = C_6H_5, in most solvents except halocarbons and acetonitrile and it reacted with aqueous alkali to give hydrogen peroxide. In ethanol, **17** was converted to the known amidine oxide **18**.[1] A probable course for the formation of **18** is given in eq 2 in which ethanol serves as a hydride donor.

Esr Spectra of Monoradicals. The esr spectra of nitronyl nitroxides show 5 major lines in the ratio 1:2:3:2:1 expected for coupling with two identical nitrogens (Figure 1). The nitrogen hyperfine coupling constants (Tables I and II) are about half of those of simple dialkyl nitroxides. This implies that the unpaired electron is distributed primarily on nitrogen and oxygen and is consistent with HMO calculations that suggest that the highest filled singly occupied orbital is antisymmetric with the C_2 carbon lying in the nodal plane. Like other nitroxides, coupling to nitrogen is solvent dependent. Polar and protonic solvents tend to stabilize dipolar resonance forms that contribute to increased spin distribution to nitrogen. Conversely, electron-withdrawing substituents in the 2 position destabilize resonance forms with high positive charge on nitrogen and thus decrease the nitrogen coupling (Table II).

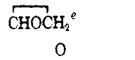
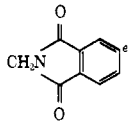
The esr spectra of the nitronyl nitroxides show weak coupling with the twelve methyl hydrogens of ~0.2 G which is often unresolved but is manifest by line widths of ~1.0 G. Of particular interest is the coupling to the α hydrogens of the substituents at C_2. The ease of forming nitronyl nitroxides from virtually any aldehyde permits the multiplicity of this coupling to be used to determine by simple test tube reactions the degree of α

Table I. Melting Point, Yield, and Esr Data for Aryl and Alkyl Nitronyl Nitroxides (4)

R	Mp, °C[a]	Yield, %[b]	a_N,[c] H_2O	a_N,[c] C_6H_6	$a_{\alpha\text{-H}}$,[c,d] C_6H_6	g, H_2O[k]
p-$C_6H_4NO_2$	175–176[e]	24	8.06	7.38		2.00629
C_6H_5	85[f]	74	8.18	7.43		2.00627
p-C_6H_4OH	134–135[f]	19	8.29	7.53		2.00624
p-$C_6H_4N(CH_3)_2$	151–154[f,g]	11	8.28	7.57		2.00623
CH_3	92–93[g]		8.25	7.4	3.3	2.00627
CH_2CH_3	68–69[g]	63	8.21	7.42	2.0	2.00621
$CH(CH_3)_2$	99–100[g]	68	8.21	7.40	*h*	
$C(CH_3)_3$	133–134[i]	47	8.18	7.44		
$CH_2CH(CH_3)_2$	53–54[f,g]	55	8.20	7.44	1.99	
$CH_2C_6H_5$	Oil[j]	35		7.41	1.8	

[a] Satisfactory analytical analysis (<0.3% error) for all solid compounds. [b] Overall yield of pure radical from RCHO and bishydroxylamine **1** (not optimized). [c] Coupling constants in gauss. [d] Usually about 0.05 G smaller in water. [e] From benzene. [f] From ether. [g] From petroleum ether. [h] Unresolved. [i] Sublimed *in vacuo*. [j] Chromatographed on silica gel. [k] ±0.00005.

Table II. Melting Point, Yield, and Esr Data for Alkenyl and α-Substituted Alkyl Nitronyl Nitroxides (4)

R	Mp, °C	Yield, %[a]	a_N,[b] H_2O	a_N,[b] C_6H_6	$a_{\alpha\text{-H}}$,[b] C_6H_6	a_X,[b] C_6H_6
$CH{=}CH_2$	Oil[c]	<5		7.65[d]	1.5[d]	1.5[d]
$CH{=}CHCH_3$[e]	57[f]	36	8.30	7.6	1.5	1.25 (β-H)
$CH{=}CHC_6H_5$[e]	126–127[g]	23	8.26	7.5	1.4	1.4 (β-H)
$C{\equiv}CC_6H_5$[e]	125–126[c]	11	8.12	7.25		
CH_2OH[e]	65–68[c]	31		7.45	2.34	
	60–62[f]	50	8.13	7.31	1.0[g]	
	131–132[h]		8.05	7.40	2.65	0.0 (α-N)
CH_2NHTs[e]	105–107[h]			7.35	2.4	0.0 (α-N)
CH_2Cl[e]	73–75[i]	37	8.20	7.2	1.5	1.5 (Cl)
CH_2Br[e]	93–94[i]	28	8.0	7.0[j]	1.5[j]	7.0 (Br)[j]
CH_2I[k]	60[c]			7[l]	*l,m*	15 (I)[l,n]
$CH(OC_2H_5)_2$[e]	52–53[c]	7	7.86	7.3	*m*	
CF_3[e]	70–74[c,o]	5	7.7	6.9		3.5 (F)

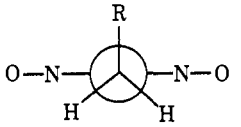
[a] Overall yield of pure radical from RCHO and bishydroxylamine **1** (not optimized). See Experimental Section for yields of alternative methods of preparation. [b] Coupling constants in gauss. [c] Purified by chromatography on silica gel. [d] Spectrum in $CHCl_3$. [e] Satisfactory elemental analysis (<0.3% error) and confirmation by mass spectrometry. [f] From petroleum ether. [g] Spectrum in water; unresolved in benzene. [h] From ether. [i] From hexane. [j] Spectrum in hexane. [k] Empirical formula determined by mass spectrometry. [l] Spectrum in ether. [m] Unresolved. [n] Only two iodine lines resolved, ref 10. [o] Sublimed.

substitution of even trace quantities of aldehydes. Thus while nitronyl nitroxides from α-trisubstituted aldehydes give simple five-line esr patterns, α-disubstituted aldehydes produce five very poorly resolved doublets and α-monosubstituted aldehydes give five 1:2:1 triplets or, in certain cases where the β substituent is asymmetric, 1:1:1:1 quartets (Figure 1).

The magnitude of the α-hydrogen hyperfine coupling is, as expected, dependent on the degree of α substitution (Table I). The coupling $a_{\alpha\text{-H}}$ is expected to vary with the dihedral angle, θ, between the p orbital at C_2 and the C_α–H bond according to eq 3.[8] For **4**,

$$a_{\alpha\text{-H}} = \langle B_1 + B_2 \cos^2 \theta \rangle \rho \qquad (3)$$

R = CH_3, $a_{\alpha\text{-H}} = -3.5$ G[9] and, since the methyl group can rotate freely, $\cos^2\theta$ takes on an average value of 0.5. Taking the constants $B_1 = 4$ G and $B_2 = 50$ G,[8b] the spin density ρ at C_2 is estimated as −0.12. The smaller coupling of the α-methylene derivatives implies restricted rotation about the C_2–C_α bond in which the methylene group assumes the average conformation given in **19**. Methine substituents have even smaller,



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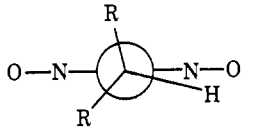

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often incompletely resolved, α-hydrogen coupling which suggests an average conformation close to that of **20**. In a subsequent paper the use of these conformational effects for spin labeling will be more fully described.

The coupling constants for other α substituents were less predictable. The halides **4**, R = CH_2Cl, CH_2Br, and CH_2I, all display strong halogen coupling (Figure 2). This occurs despite the fact that bromine and iodine coupling in other free radicals is often absent due to rapid nuclear relaxation associated with the large halogen nuclear quadrupole moments. In the present examples all the expected lines due to chlorine and bromine were observed, although only two of the six iodine lines were resolved.[10] Nuclear quadrupole relaxation effects were particularly apparent in **4**, R = CH_2I, where strong line broadening necessitated the use of low viscosity solvents for determination of the coupling data. The magnitude of the bromine and iodine

(8) (a) E. W. Stone and A. H. Maki, *J. Chem. Phys.*, 37, 1326 (1962); (b) P. B. Ayscough, "Electron Spin Resonance in Chemistry," Methuen & Co., London, England, 1967, p 77.

(9) Studies of other α-alkyl nitronyl nitroxides by nmr have demonstrated that $a_{\alpha\text{-H}}$ is negative, see ref 12.

(10) *Cf.* E. F. Ullman and L. Call, *J. Amer. Chem. Soc.*, **92**, 7210 (1970).

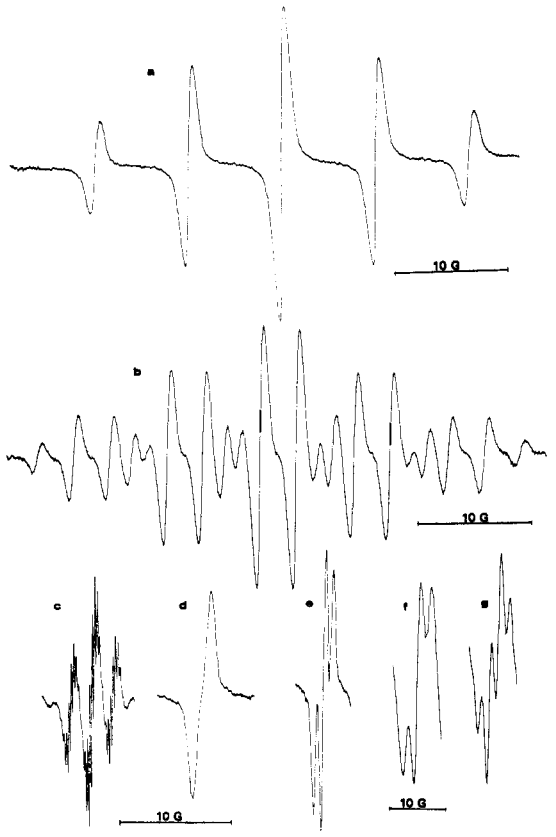


Figure 1. Esr spectra of nitronyl nitroxides **4** in water: a, R = C_6H_5; b, R = CH_3. Low-field fifth of esr spectra of nitronyl nitroxides **4**: c, R = $CH_2C_6H_5$ (benzene); d, R = $CH(CH_3)_2$ (benzene); e, R = $CH{=}CHC_6H_5$ (benzene); f, R = $CH_2NHCH_2C_6H_5$ (chloroform); g, R = $CH_2N(CH_2C_6H_5)_2$ (chloroform).

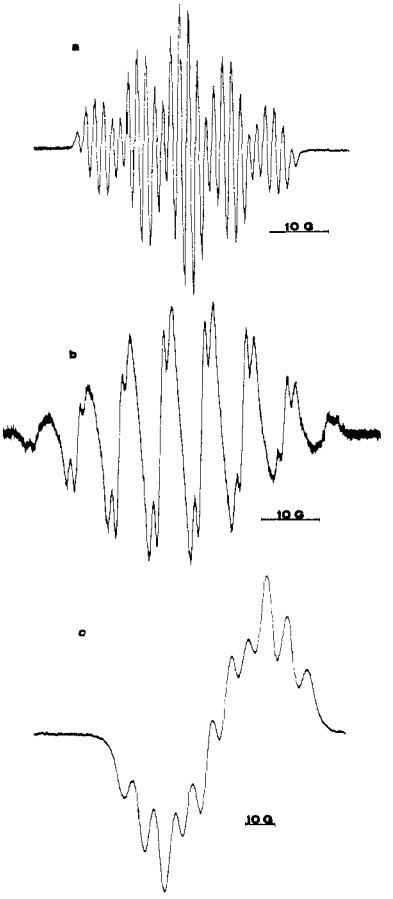
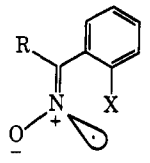


Figure 2. Esr spectra of nitronyl nitroxide **4**: a, R = CH_2Cl (benzene); b, R = CH_2Br (hexane); c, R = CH_2I (ether).

coupling constants was unexpectedly large (Table II). The only examples of such high halogen couplings in organic compounds appear to be the iminoxyl radicals **21**.[11] In **21**, X = halogen, exceptionally large coupling with X is observed because of through-space interaction with the singly occupied σ orbitals on nitrogen.



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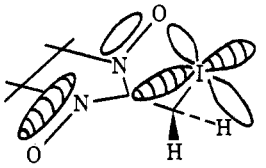

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The abnormal optical spectra (see below) of **4**, R = CH_2–halogen, suggest that through-space interaction may also occur in the nitronyl nitroxides. Bromine and iodine are held above the plane of the nitronyl nitroxide ring so as to permit good overlap of a halogen d orbital with the antisymmetric singly occupied π orbital. We suggest that direct d–π overlap (*cf.* **22**) may account both for the high halogen coupling constants and the abnormal optical spectra.

Coupling in the aminomethyl nitronyl nitroxides proved to be unexpectedly complex (Figure 1). The tertiary amino radicals had each of the five major ring-nitrogen lines split into quartets. The line spacing within each quartet was approximately even but the inner and outer lines varied in relative intensity with many derivatives having approximately 1:4:4:1 ratios at room temperature (Table III). Although the spectra were not greatly changed at higher temperatures, low-temperature or higher viscosity solvents caused changes in relative line intensities. By contrast, the secondary

Table III. α-Hydrogen Hyperfine Splitting in the Esr Spectra of α-Aminomethylnitronyl Nitroxides **4** in Chloroform at 25°

R	No. of resolved lines	Gauss $a_{\alpha\text{-H}(1)}$	Gauss $a_{\alpha\text{-H}(2)}$	Approx rel line intensities
CH_2NH_2	3	2.0	2.0	2:5:2
CH_2NHCH_3	3	2.6	2.6	2:7:2
$CH_2NHCH_2C_6H_5$[a]	3	2.05	2.05	2:5:2[b]
$CH_2NHC(CH_3)_3$	3	~1.5	~2.2	2:5:2[c]
$CH_2NHCH(CH_3)COOH$	3	1.9	1.9	1:5:1
$CH_2NHCH(CH_3)COOC_2H_5$	3	~1.9	~2.6	1:3:1[c]
$CH_2N(CH_3)_2$	4	1.6	3.5	2:7:7:2
$CH_2N(C_2H_5)_2$	4	1.2	2.4	3:2:2:3[d]
	4	1.8	3.6	1:4:4:1[e]
$CH_2N(CH_2C_6H_5)_2$	4	1.55	3.25	2:7:7:2
$CH_2N(CH_3)C_6H_5$	4	1.7	3.5	1:3:3:1
$CH_2N(CH_3)CH_2C_6H_5$	4	1.5	3.0	2:7:7:2
$CH_2N(CH_3)CH_2COOC_2H_5$[f]	4	1.8	3.2	1:5:5:1

[a] Spectrum in ether. [b] Center line broadened at −110°. [c] Center line nearly resolved into two lines. [d] Inner lines much weaker in tetralin. [e] Outer lines much weaker in tetralin. [f] Spectrum in water.

(11) B. C. Gilbert and R. O. C. Norman, *J. Chem. Soc. B*, 722 (1966); 123 (1968).

Table IV. Magnetic Susceptibility and Solution Esr Data for Nitronyl and Imino Nitroxide Biradicals

Biradical[a]		Esr in 2-CH_3-THF at 25°[b] Lines resolved	$a_{N(1)}$[b]	$a_{N(2)}$[b]	a_H[b]	$\chi_m \times 10^3$[c]	% triplet[c] at 36°
9, $n = 3$	B⌒⌒⌒B	0				2.39	75
9, $n = 2$	B⌒⌒B	13			2 (?)[d]	2.30[e]	69[e]
15	B′⌒⌒B′	17	9.2 (1)	4.0 (1)	2.0 (2)		
11	B⌒=⌒B	0				1.50	47
14	B′⌒=⌒B	15				2.00	63
13	B′⌒=⌒B′	7	8 (1)	4 (1)		2.16	68
23	*m*-B–C_6H_4–B	9	3.8 (2)	3.8 (2)		2.39	75
24	*m*-B′–C_6H_4–B′	7	8 (1)	4 (1)			
25	*p*-B–C_6H_4–B	9	3.7 (2)	3.7 (2)		2.39	75
26	*p*-B′–C_6H_4–B′	11					

[a] B = nitronyl nitroxide and B′ = imino nitroxide groups substituted at the 2 positions. [b] Hyperfine coupling constants in ga ss. Numbers in parentheses give the number of nuclei producing the indicated coupling. [c] Susceptibilities measured in CH_2Cl_2 at 36° by the nmr method of D. F. Evans, ref 18, except where otherwise indicated. The fraction of molecules in the triplet state was estimated from the calculated theoretical molar susceptibility of triplets at 36° of 3.19×10^{-3}. [d] Minimum spacing of resolved lines; spectrum not fully interpreted. [e] Susceptibility in $CDCl_3$ at 24° from ref 13.

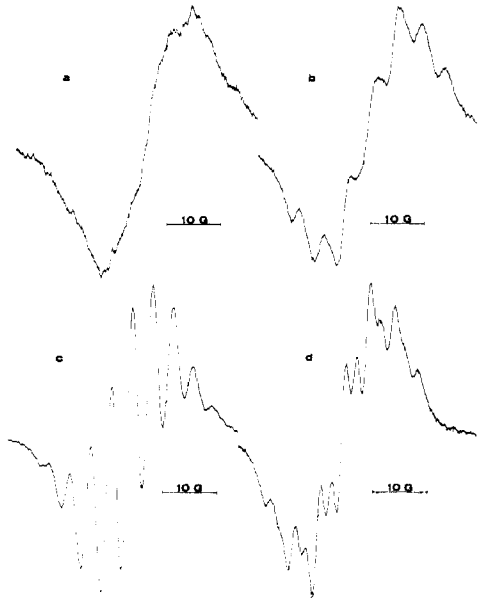

Figure 3. Room temperature esr spectra of biradicals in 2-methyltetrahydrofuran: a, **11**; b, **13** (similar to **24**); c, **25** (similar to **23**); d, **26** (see Table IV for structures).

amino radicals had each ring-nitrogen line split into approximately 1:2:1 triplets. In two examples the inner line was broadened and appeared to be partially resolved into two lines. Lowering the temperature increased broadening of the inner lines without improving the resolution.

The hyperfine coupling patterns observed in the tertiary aminomethyl radicals are similar to those reported previously for **4**, R = $CH_2CH(CH_3)C_6H_5$.[12] This compound appears to have at least two unequally populated conformations that interconvert rapidly relative to $a_{\alpha\text{-H}}$ at room temperature. In each conformation the twist angles θ (*cf.* eq 3) for the two α hydrogens are different. Each conformation can therefore give rise to four α-hydrogen lines. Under conditions of rapid equilibration, the positions of these sets of lines are averaged, thus giving four new lines. On decreasing the equilibration rate by increasing the viscosity or lowering the temperature, averaging is incomplete and line broadening occurs.

The similarity of the esr patterns of the aminomethylnitronyl nitroxides to **4**, R = $CH_2CH(CH_3)C_6H_5$, suggests that coupling to the α-nitrogen atoms is unimportant in these compounds. The differences in the spectra of the secondary and tertiary amines reflect different conformational preferences between the two groups of compounds. Although detailed interpretations of these spectra have not been made, the differences in the spectra of the two classes of amines suggest an attractive spin-labeling technique for distinguishing between primary and secondary amines. Aminonitronyl nitroxides can be prepared with a few milligrams of the unknown amine, potassium iodide, and **4**, R = CH_2Cl, in a test tube reaction and the colored radicals are easily isolated by tlc for esr studies.

Esr Spectra of Biradicals. Magnetic susceptibility and solution esr data for the biradicals are given in Table IV. The room temperature esr spectra of the 2- and 3-carbon bridged biradicals (**9**, **11**, **13–15**) were very poorly resolved due to large electron–electron dipolar interactions (Figure 3). The coupling constants, where discernible, were similar to those of the related monoradicals. If J, the electron–electron exchange interaction, were greater than the hyperfine coupling a, the coupling constants would be expected to be half those of the related monoradicals, and coupling to all four nitrogens would be observed.[13] Thus it appears that $J < a$. However, the magnetic susceptibilities of these compounds, with the exception of **9**, $n = 3$, suggest that the triplet levels are populated less than the statistically expected 75%; *i.e.*, the compounds appear to be ground-state singlets with thermally accessible triplet states.[13] Since J is a measure of the singlet–triplet separation, the magnetic susceptibility data imply that $J \approx RT$.

These conclusions are in apparent disagreement because $a \ll RT$. A possible explanation is that there

(12) R. W. Kreilick, J. Becher, and E. F. Ullman, *J. Amer. Chem. Soc.*, **91**, 5121 (1969).

(13) For a discussion of the interpretation of the room temperature esr spectra and magnetic susceptibility of biradicals, see P. W. Kopf, R. Kreilick, D. G. B. Boocock, and E. F. Ullman, *ibid.*, **92**, 4531 (1970).

are two or more biradical conformations present. In the ethylene biradicals **11**, **13**, and **14**, the preferred geometry is probably planar. The predominance of this conformation would account for the large exchange interaction suggested by the magnetic susceptibility data, and expected dipolar interactions in this conformation would prevent resolution of the room temperature esr spectrum. On the other hand, a small fraction of molecules having a less stable twisted geometry might be expected to behave as biradicals with $J < a$. These molecules would show less dipolar line broadening and would give esr hyperfine patterns superimposed, as observed in **13** and **14**, on the broad lines of the planar form.[14]

The room temperature esr spectra of the aromatic biradicals were better resolved although significant dipolar broadening also was present (Figure 3). Both the *m*- and *p*-bisnitronyl nitroxides, **23** and **25**, displayed nine-line patterns characteristic of coupling to four equivalent nitrogens. The nitrogen coupling was roughly half that of the phenyl monoradical **4**, R = C_6H_5. This is the expected pattern[13] if $J > a_N$. On the other hand, the *m*-bisimino nitroxide **24** showed the typical seven-line pattern of the 2-phenylimino nitroxide,[1] **6** (C_6H_5 in place of COC_6H_5), suggesting $J < a_N$, while the para derivative **26** had a complex pattern where J and a_N appear to be of similar magnitude. Apparently, therefore, the bisnitronyl nitroxides have larger exchange interactions than the bisimino nitroxides and the para biradicals **25** and **26** have larger exchange interactions than their meta isomers **23** and **24**. Although the latter conclusion seems intuitively reasonable, the former does not. Nitronyl nitroxides have an orbital node at C_2 which should reduce orbital overlap with the aromatic ring relative to the nonsymmetrical imino nitroxides. The apparent smaller exchange interactions of the imino nitroxides might therefore reflect geometrical effects similar to those proposed for the ethylene biradicals **11**, **13**, and **14**.

Zero-Field Splitting of Biradicals. The zero-field splitting parameters of the biradicals are given in Table V. All the compounds studied displayed a half-field line near $g = 4$. The dimethylene and trimethylene bisnitronyl nitroxides **9** showed the expected six lines near $g = 2$ typical of biradical spectra in frozen glasses.[13,15] However, in the spectra of the other biradicals, the $\pm(D + 3E)/2$ lines were usually poorly resolved and E values could not be assigned with certainty. Moreover the bisimino nitroxide **13** displayed two additional pairs of weak lines and **14** displayed one additional pair. The number of additional pairs of lines corresponds in each case to the theoretical number of additional conformers expected if the radicals assume all possible planar conformations. Similarly, the *m*-bisimino nitroxide **24** had two additional pairs of very weak lines and **27** had one additional pair. The number of additional pairs again corresponds to the expected number of additional conformers. The para isomers gave more complex spectra due to partial resolution of nitrogen hyperfine coupling and only $\pm D$ lines could be unambiguously assigned. The spectrum of the *p*-bisimino nitroxide **26** appeared to have two pairs of $\pm D$ lines consistent with the expected number of conformers although the assignment for the inner pair is not certain.

Table V. Zero-Field Splitting Parameters in Gauss for Nitronyl and Imino Nitroxide Biradicals in 2-Methyltetrahydrofuran Glass at −180°.

	Biradical[a]	Found D	Found E[b]	Calcd D	Calcd E	Conformation[c]
11		170	10	120	9	
14		122	4	115	6	Syn
		152 (w)		121	10	Anti
13		93	3	103	5	Syn,syn
		152 (w)		131	6	Syn,anti
		121 (w)		118	9	Anti,anti
23	*m*-B–C_6H_4–B	89	1	111	4	
27	*m*-B′–C_6H_4–B	128 (w)		133	4	Syn
		67	0	81	4	Anti
24	*m*-B′–C_6H_4–B′	183 (w)		164	3	Syn,syn
		90		91	4	Syn,anti
		52	3	68	2	Anti,anti
25	*p*-B–C_6H_4–B	63		55	2	
26	*p*-B′–C_6H_4–B′	57		58	1	Syn
		48 (?)	0 (?)	53	1	Anti

[a] B = nitronyl nitroxide and B′ = imino nitroxide groups substituted at the 2 positions. [b] E values estimated from $\pm(D - 3E)/2$ line by assuming that the line arises from the conformation with the smallest observed D value. [c] Syn and anti designations refer to the orientations of the imino nitroxide oxygens. These are taken relative to the α hydrogens in the ethylene biradicals **11**, **13**, and **14** and relative to the meta substituent in the meta biradicals **23**, **24**, and **27**. Only planar conformations are given.

The zero-field coupling parameter D is a measure of the average electron–electron separation projected along the principal molecular axis. In order to calculate D values for the various conformers it was assumed that the zero-field splitting lines of all the conjugated biradicals arise from planar conformations and that the ethylene biradicals have the trans configuration. In order to simplify the calculation, the nitronyl nitroxides were assumed to have their electron density concentrated at two points midway along each nitrogen–oxygen bond and imino nitroxides were assumed to have two-thirds of their electron density midway along the nitrogen–oxygen bond and one-third at the imino-nitrogen nucleus. These values are based on the known ~1:2 ratio of the coupling of the imino nitrogen and the nitroxide nitrogen of aryl imino nitroxide monoradicals.[1]

Calculations of D values were made for all possible planar conformations and are compared with the observed values in Table V. Despite the simplifying assumptions there appears to be good qualitative agreement. Alternative assumptions requiring nonplanar geometries or cis-olefin configurations are inadequate to account for the observed spectra. Interestingly, the largest singlet–triplet splitting, as determined from magnetic susceptibility measurements (compound **11**), is associated with the largest error in the D-value calculations. The large splitting suggests that it may be incorrect to assume for this compound that negligible unpaired electron density is localized on the ethylene carbons.

(14) Alternative explanations based on polymerization of the biradicals are not consistent with the absence of concentration dependence of the biradical spectra. Although monoradical impurities cannot be rigorously excluded, they are considered unlikely because of the similarity of the spectra of biradical samples purified in different ways.

(15) E. Wasserman, L. C. Snyder, and W. A. Yager, *J. Chem. Phys.*, 41, 1763 (1964).

Table VI. Ultraviolet Absorption Maxima of Nitronyl Nitroxides 4 in Hexane

R	λ_{max}, mμ (ε) (l. mol^{-1} cm^{-1})				
CH_3		307 (16,400)	318 (23,000)	535 (1800)	563 (1800)
CH_2CH_3		310 (14,500)	322 (21,900)	537 (1600)	567 (1660)
$CH(CH_3)_2$		310 (12,100)	321 (18,000)	537 (1200)	565 (1200)
$C(CH_3)_3$[a]		313 (15,300)	325 (23,300)	546 (1380)	579 (1330)
CH_2Cl			337 (18,200)	550 (500)	
CH_2Br	250 (4,100)		346 (16,200)		570 (400)
$CHBrCHBrC_6H_5$	254 (6,240)		346 (12,600)	548 (390)	576 (420)
CH_2I	282 (5,900)		364 (8,900)		590 (300)
$CH{=}CHCH_3$	233 (7,060)	347 (11,000)	363 (18,200)	604 (390)	660 (420)
	263 (8,840)				
C_6H_5[b]	238 (8,640)	346 (9,300)	362 (17,700)	587 (407)	637 (450)
	266 (12,850)				

[a] Spectrum in cyclohexane. [b] Additional shorter wavelength peaks at 232 mμ (ε 7520) and 212 (10,700).

Table VII. Melting Points and Yields of 1,3-Dihydroxy-4,4,5,5-tetramethylimidazolidines 2

R	Mp, °C[a]	Yield, %	R	Mp, °C[a]	Yield, %
p-$C_6H_4NO_2$	161–163[b,c]	34	$-CH{=}CHC_6H_5$	185–186[b,e]	52
$-C_6H_5$	168–169[b,d]	74	$-C{\equiv}CC_6H_5$	110–111[b,c]	21
p-C_6H_4OH	198–200 (d)[d,e]	47	$-CH_2OH$	124–125[g]	62
p-$C_6H_4N(CH_3)_2$	168–169[f]	17	$-CHCH_2O$	148[g]	55
$-CH_2C_6H_5$	106–108[b,e]	38	$-CH_2Br$	123–124[f]	69
$-CH_2CH_2-$	212–216[d,g]	77	$-CH(OC_2H_5)_2$	147–148[d,g]	11
$-CH{=}CHCH_3$	158–159[c,h]	46			

[a] Satisfactory elemental analysis (<0.3% error) for all compounds. [b] From ether. [c] From petroleum ether. [d] From benzene. [e] From methanol. [f] Chromatographed on silica gel. [g] From ethyl acetate. [h] From tetrahydrofuran.

Optical Spectra. The electronic absorption of the nitronyl nitroxides is characterized by two pairs of peaks (Table VI). The long wavelength pair is of low intensity and is shifted to shorter wavelengths in more polar solvents. This behavior is characteristic of $n \rightarrow \pi^*$ transitions. Two such transitions are expected due to weak splitting of the energy levels of the two oxygen n orbitals. The short wavelength pair is more intense and also shows hypsochromic shifts in more polar solvents. These presumably are $\pi \rightarrow \pi^*$ transitions. Although increased α substitution produces a small bathochromic shift of both pairs of peaks, α substitution by halogens, particularly bromine and iodine, produces dramatic shifts and also results in the appearance of a new short wavelength transition. Most probably these shifts are due to perturbation by halogen of the singly occupied nitronyl nitroxide π orbital. Thus the halogen d orbital and the antisymmetric p orbital have like symmetries and should overlap well in the molecular geometry indicated in **22**. The new bands in the spectra of the bromo and iodo derivatives most probably are charge-transfer bands.

The infrared spectra of the nitronyl nitroxides are noteworthy in that two characteristic bands are always present. One of these appears at 1130–1145 cm^{-1} and has not been assigned. The other is the N–O stretching frequency which is at 1350–1375 cm^{-1} and is not significantly different than that of unconjugated nitroxides (1345 cm^{-1} for di-*tert*-butyl nitroxide).[16]

Experimental Section

The esr spectra were recorded using a Varian E3 spectrometer operating at 9.5 GHZ. Estimation of g values was carried out using Fremy's salt (g = 2.00550 ± 0.00005) as reference.[17] The nmr spectra were determined on a Varian T60 nmr spectrometer. Magnetic susceptibilities were determined by the nmr concentric tube technique of Evans[18] using methylene dichloride as solvent.

1,3-Dihydroxy-4,4,5,5-tetramethylimidazolidines 2. Representative procedures are given below for the formation of the anhydro adducts **2** of aldehydes with 2,3-bis(hydroxylamino)-2,3-dimethylbutane[19] (**1**). In most preparations roughly equivalent amounts of the reactants or a slight excess of the aldehyde were employed. Suspensions of the reactants in benzene or solutions in methanol at 0–80° were both employed successfully. Reaction periods of 15–60 min were used for aliphatic aldehydes and 6–30 hr for aromatic aldehydes. Physical properties and yields of **2** are given in Table VII.

1,3-Dihydroxy-2-phenyl-4,4,5,5-tetramethylimidazolidine (2, R = C_6H_5). A solution of 2,3-bis(hydroxylamino)-2,3-dimethylbutane, 4.44 g (0.3 mol), and 3.5 g (0.33 mol) of benzaldehyde in 150 ml of methanol was stirred at room temperature for 24 hr. Removal of the precipitate and concentration of the mother liquors to obtain a second crop yielded 5.25 g (74%) of the anhydro adduct which could be used directly in the preparation of the nitronyl nitroxide. A sample recrystallized from benzene–ether had mp 168–169°; ν_{max}^{KBr} 3260 cm^{-1} (OH); nmr (DMSO) δ 1.03 (s, 2-CH_3), 1.07 (s, 2-CH_3), 4.51 (s, CH), 7.20–7.55 (m, 5-ArH), 7.71 (2-OH).

1,3-Dihydroxy-2-(1-propenyl)-4,4,5,5-tetramethylimidazolidine (2, R = $CH{=}CHCH_3$). To 3 g of 2,3-bis(hydroxylamino)-2,3-dimethylbutane suspended in 80 ml of dry benzene containing 10 g of Linde, Type 3A, molecular sieve at 7° was slowly added 20 ml of crotonaldehyde while stirring vigorously under nitrogen. The reaction mixture was stirred for 85 min after which 40 ml of petroleum ether was added to precipitate the adduct. After 1 hr the reaction mixture was filtered and the solid mixed with the molecular sieve was taken up in dry tetrahydrofuran, filtered, and concentrated *in vacuo*. Upon addition of petroleum ether and cooling, 1.85 g (46%) of the product was obtained: mp 158–159°; ν_{max}^{KBr} 3230 cm^{-1} (OH); nmr (DMSO) δ 0.98 (s, 4-CH_3), 1.07 (d, J = 2 cps, 1-CH_3), 3.94 (t, J = 2 cps, CH), 5.50 (m, CH=CH), 7.52 (2-OH).

2-Bromomethyl-1,3-dihydroxy-4,4,5,5-tetramethylimidazolidine (2, R = CH_2Br). A mixture of 19 g of bromoacetaldehyde diethyl acetal (0.1 mol) and 9 g of anhydrous oxalic acid (0.1 mol) was

(16) A. K. Hoffmann and A. Henderson, *J. Amer. Chem. Soc.*, 83, 4671 (1961).
(17) Varian Associates, "EPR at Work Series," No. 28.
(18) D. F. Evans, *J. Chem. Soc.*, 2003 (1959).
(19) Prepared according to the method of M. Lamchen and T. W. Mittag, *J. Chem. Soc. C*, 2300 (1966). Commercially available as the sulfate from Eastman Kodak Co.

heated slowly to 130° over 30 min. The bath temperature was raised slowly to 150°, and 6 ml of distillate boiling in the range 75–85° was collected. After drying over sodium sulfate the distillate was redistilled to give 5.8 g, bp 90–115°, of crude bromoacetaldehyde. To 2 ml of this product was added 10 ml of benzene, and 1.0 g of 2,3-bis(hydroxylamino)-2,3-dimethylbutane. After stirring for 30 min at room temperature the mixture was filtered, and the precipitate recrystallized from benzene. This crude product was further purified by chromatography on silica with ether to give 630 mg (35%): mp 123–124° dec; ν_{max}^{KBr} 1320 cm^{-1} (OH); nmr ($CDCl_3$) δ 1.08 (s, 2-CH_3), 1.13 (s, 2-CH_3), 3.58 (d, J = 5 cps, CH_2), 4.19 (t, J = 5 cps, CH), 5.25 (2-OH).

4,4,5,5-Tetramethylimidazoline 3-Oxide 1-Oxyls (4). 1,3-Dihydroxy-4,4,5,5-tetramethylimidazolidines **2** were oxidized to nitronyl nitroxides **4** with lead dioxide or manganese dioxide in benzene or ether at room temperature. An excess of oxidant was usually used. The reaction time was dependent on the amount of oxidant, varying from 10 min to 3 hr. Alternatively, sodium periodate in cold water was employed. Since overoxidation led to reduced yields, a limited amount of oxidant was used in this procedure. Overoxidation could also be controlled by carrying out the reaction in the presence of an immiscible solvent such as chloroform in which the product was soluble. Isolation of the radicals often involved column or tlc chromatography. Because of the photosensitivity of these compounds it was found essential to protect them from light during isolation. Tables I and II give physical properties and overall yields of the radicals.

2-Phenyl-4,4,5,5-tetramethylimidazoline 3-Oxide 1-Oxyl (4, R = C_6H_5). A solution of 1.45 g of 1,3-dihydroxy-2-phenyl-4,4,5,5-tetramethylimidazolidine in 250 ml of benzene was stirred with 20 g of lead dioxide for 45 min at room temperature. Filtration and evaporation of the solvent yielded the crystalline dark blue radical in quantitative yield. It could be recrystallized from ether: mp 85°; $\nu_{max}^{CHCl_3}$ 1140, 1371 cm^{-1}; λ_{max}^{EtOH} 238 mμ (ε 9400), 263 (12,200), 360 (13,300), 588 (685) (Tables I and VI).

1,4-Bis(4′,4′,5′,5′-tetramethylimidazoline-2′-yl)benzene Bis-1′,1′′-oxide Bis-3′,3′′-oxyl (25). To 1.48 g of 2,3-bis(hydroxylamino)-2,3-dimethylbutane suspended in 70 ml of dry benzene was added 0.67 g of terephthalaldehyde. After boiling for 6 hr the solvent was evaporated *in vacuo* and the residue was taken up in 220 ml of methanol–chloroform (1:10). This solution was stirred with a solution of 1 g of sodium periodate in 20 ml of water at 7–10° for 3 min. The organic layer was immediately separated, washed with water, dried, and evaporated *in vacuo*. The residue was chromatographed on silica gel with chloroform to give 0.21 g (5.5%) of the above deep blue biradical: mp 231–232° dec; $\nu_{max}^{CHCl_3}$ 1130, 1165, 1350, 1385 cm^{-1}; λ_{max}^{EtOH} 590 mμ (ε 650), 378 (11,350), 362 (12,200), 327 (sh, 12,400), 302 (17,850), 280 (16,500), 224 (11,600).

Anal. Calcd for $C_{20}H_{28}N_4O_4$: C, 61.83; H, 7.27; N, 14.42. Found: C, 61.65; H, 7.36; N, 14.21.

Chromatography also yielded 56 mg of a second blue radical which was identified as **4-(4′,4′,5′,5′-tetramethylimidazoline-2′-yl)-benzaldehyde 3′-oxide 1′-oxyl (4, R = *p*-C_6H_4CHO)**: mp 145–147°; *m/e* 261 (M^+); esr (C_6H_6) $a_{N(1)} = a_{N(3)}$ = 7.4 G; $\nu_{max}^{CHCl_3}$ 1165, 1360, 1385, 1700 cm^{-1}; λ_{max}^{EtOH} 585 mμ (ε 420), 380 (7600), 364 (7050), 298 (15,350), 238 (11,600).

Anal. Calcd for $C_{14}H_{17}N_2O_3$: C, 64.35; H, 6.56; N, 10.72. Found: C, 64.07; H, 6.60; N, 10.62.

1,3-Bis(4′,4′,5′,5′-tetramethylimidazoline-2′-yl)benzene Bis-1′,1′′-oxide Bis-3′,3′′-oxyl (23). A mixture of 1.34 g of isophthaldehyde, 300 ml of benzene, and 12 g of 2,3-bis(hydroxylamino)-2,3-dimethylbutane was heated at 65–75° for 10 hr. The solvent was removed *in vacuo* and the residue chromatographed on silica gel with ether as solvent to give 2.1 g of a bisanhydro adduct. To a suspension of this compound in 400 ml of water at 10–15° was added a slight excess of sodium periodate, and the reaction mixture was stirred vigorously for 5–10 min. After a rapid chloroform extraction and evaporation of the solvent *in vacuo*, the blue residue was chromatographed on silica gel with ether to give 0.55 g (14%) of the dark blue biradical which was recrystallized from ether–petroleum ether: mp 214–215°; $\nu_{max}^{CHCl_3}$ 1135, 1165, 1355, 1370 cm^{-1}; *m/e* 388 (M^+); λ_{max}^{EtOH} 580 mμ (ε 1140), 360 (19,300), 350 (17,250), 265 (25,100), 255 (24,400), 215 (30,200).

Anal. Calcd for $C_{20}H_{28}N_4O_4$: C, 61.83; H, 7.27; N, 14.42. Found: C, 61.73; H, 7.28; N, 14.22.

1,3-Bis(4′,4,′5′,5′-tetramethylimidazoline-2′-yl)benzene Bis-3′,3′′-oxyl (24). A yellow-orange fraction obtained from the chromatogram in the previous experiment was purified by preparative tlc (silica gel, ether). The compound crystallized from acetone–petroleum ether: mp 142–143°; $\nu_{max}^{CHCl_3}$ 1135, 1370, 1375 cm^{-1}; λ_{max}^{EtOH} 498 mμ (sh, ε 363), 467 (sh, 750), 437 (970), 425 (945), 300 (sh, 6550), 285 (7280), 215 (41,200); *m/e* 356 (M^+).

Anal. Calcd for $C_{20}H_{28}N_4O_2$: C, 67.38; H, 7.92; N, 15.72. Found: C, 67.13; H, 7.87; N, 15.63.

1,3-Bis(4′,4′,5′,5′-tetramethylimidazoline-2′-yl)benzene 1′-Oxide Bis-3′,3′′-oxyl (27). A third chromatographic fraction from the previous experiment was purified by preparative tlc. After extraction from the plate with ether and removal of the solvent *in vacuo* a solid greyish-blue compound was obtained. The material recrystallized from ether–petroleum ether but was found to be unstable on standing; *m/e* 372 (M^+). For esr and magnetic susceptibility studies the compound was chromatographed just prior to use.

2-Hydroxymethyl-4,4,5,5-tetramethylimidazoline 3-Oxide 1-Oxyl (4, R = CH_2OH). To a suspension of 50 mg (0.26 mmol) of 1,3-dihydroxy-2-hydroxymethyl-4,4,5,5-tetramethylimidazolidine in 100 ml of ether was added 2.0 g of manganese dioxide with stirring. After 10 min the ether was decanted off and evaporated *in vacuo*. The residue was chromatographed on silica gel with ether. The residue obtained from evaporation of the main red fraction was triturated with petroleum ether to give 25 mg (50%) of the radical, mp 65–68° (Table II).

2-Isopropyl-4,4,5,5-tetramethylimidazoline 3-Oxide 1-Oxyl [4, R = $CH(CH_3)_2$]. A suspension of 150 mg of 2,3-bis(hydroxylamino)-2,3-dimethylbutane and 0.45 ml of isobutyraldehyde in 10 ml of benzene was boiled for 30 min and then evaporated to dryness *in vacuo*. The residue was dissolved in 30 ml of ether and stirred for 3 min with 2 g of lead dioxide. After filtration, the deep red solution was evaporated and the residue chromatographed on silica with ether. The product, 135 mg (68%), was recrystallized from petroleum ether, mp 99–100° (Table I).

3-Diethoxymethyl-4,4,5,5-tetramethylimidazoline 3-Oxide 1-Oxyl [4, R = $CH(OC_2H_5)_2$]. To 100 mg (0.38 mmol) of 1,3-dihydroxy-2-diethoxymethyl-4,4,5,5-tetramethylimidazolidine dissolved in 50 ml of ether was added ~5 g of lead dioxide and the mixture was shaken for 10 min. The lead dioxide was then allowed to settle and the ether decanted off and filtered. The filtrate was concentrated *in vacuo* and chromatographed on silica gel with ether. The resulting red oil crystallized on addition of little petroleum ether: yield 65 mg (65%); mp 52–53°; λ_{max}^{EtOH} 310 mμ (ε 15,000), 322 (21,900), 530 (1000) (Table II).

Thermal Decomposition of 2-Benzyl-4,4,5,5-tetramethylimidazoline 3-Oxide 1-Oxyl (4, R = $CH_2C_6H_5$). A solution of 1 g of the radical in 10 ml of benzene was boiled for 1 hr under an atmosphere of nitrogen. The resulting yellow solution was diluted with 50 ml of ether and chromatographed on silica with the same solvent. Fractional crystallization from chloroform–hexane of the fastest moving band gave 230 mg of 2-benzoyl-3-hydroxy-4,4,5,5-tetramethylimidazoline (**5**): mp 187–188°; λ_{max}^{EtOH} 253 mμ (ε 13,200), 410 (170); $\nu_{max}^{CHCl_3}$ 1600, 1676, 3520 cm^{-1}; nmr (DMSO) δ 1.13 (s, 4-CH_3), 7.7–8.0 (5-ArH), 8.9 (broad s, OH); *m/e* 246 (M^+).

Anal. Calcd for $C_{14}H_{18}N_2O_2$: C, 68.27, H, 7.37; N, 11.37. Found: C, 68.17; H, 7.16; N, 11.34.

Rechromatography of the mother liquors yielded, after recrystallization from petroleum ether, 90 mg of 2-benzoyl-4,4,5,5-tetramethylimidazoline (**7**): mp 75–76°; λ_{max}^{EtOH} 256 mμ (ε 9900), tailing to 420 mμ; $\nu_{max}^{CHCl_3}$ 1600, 1660, 3370 cm^{-1}; nmr ($CDCl_3$) δ 1.21 (s, 4-CH_3), 5.22 (broad s, NH), 7.5–8.4 (5-ArH); *m/e* 230 (M^+).

Anal. Calcd for $C_{14}H_{18}N_2O$: C, 73.01; H, 7.88; N, 12.17. Found: C, 73.02; H, 7.77; N, 12.16.

2-Benzoyl-4,4,5,5-tetramethylimidazoline 1-Oxyl (6). A mixture of 10 mg of 2-benzoyl-3-hydroxy-4,4,5,5-tetramethylimidazoline (**5**), 15 ml of ether, and 200 mg of lead dioxide was stirred for 5 min. After filtration and evaporation, the residue was chromatographed on silica with ether. The dark orange product (8 mg) was recrystallized from ether–petroleum ether at room temperature by concentrating the solution *in vacuo*: mp 74–75°; $\lambda_{max}^{C_6H_{14}}$ 252 mμ (ε 16,700), 317 (1400), long wavelength tail; $\nu_{max}^{CCl_4}$ 1368, 1600, 1638 cm^{-1}; esr (C_6H_6) $a_{N(1)}$ = 8.5 G, $a_{N(3)}$ = 4.2 G; *m/e* 245 (M^+).

2-Benzyl-3-hydroxy-4,4,5,5-tetramethylimidazoline 1-Oxide (3, R = $CH_2C_6H_5$). A mixture of 1 g of 2-benzyl-1,3-dihydroxy-4,4,5,5-tetramethylimidazolidine (**2**, R = CH_2Ph) and 3.5 g of lead dioxide (3.5 g) in 25 ml of benzene was stirred until the solution was a permanent pink color. Evaporation of the solvent *in vacuo* and recrystallization of the residue from chloroform–hexane gave 600 mg (59%) of the colorless product: mp 110° dec; λ_{max}^{EtOH} 272 mμ (ε 6100); $\nu_{max}^{CHCl_3}$ 1375, 3200 cm^{-1} (broad); *m/e* 248 (M^+).

Anal. Calcd for $C_{14}H_{20}N_2O_2$: C, 67.61; H, 8.12; N, 11.28. Found: C, 67.63; H, 8.18; N, 10.96.

1,3-Dioxy-2-phenyl-4,4,5,5-tetramethylimidazolinium Chloride (17). A solution of 70 mg of 2-phenyl-4,4,5,5-tetramethylimidazoline 3-oxide 1-oxyl (**4**, R = C_6H_5) in 10 ml of dry carbon tetrachloride was treated with a slow stream of dry chlorine gas until the blue color was completely discharged. The orange-red precipitate was filtered off under nitrogen to give 75 mg (93%) of the salt: mp 146–147° dec; nmr (SO_2Cl_2) δ 1.83 (s, 4-CH_3), 7.66 (m, 5-ArH); $\lambda_{max}^{CH_3CN}$ 311 mμ (ε 17,400), 445 (2580).

3-Hydroxy-2-phenyl-4,4,5,5-tetramethylimidazoline 1-Oxide (3, R = C_6H_5). A solution of 0.117 g of 2-phenyl-4,4,5,5-tetramethylimidazoline 3-oxide 1-oxyl (**4**, R = C_6H_5) in 7 ml of methanol was hydrogenated (22°, 760 mm) with platinum oxide as catalyst. The theoretical volume of hydrogen was taken up within 4 min and the solution became colorless. The solution was filtered under nitrogen and the solvent removed *in vacuo* to give 0.10 g (95%) of the white crystalline product: mp 122–123°; λ_{max}^{EtOH} 239 mμ (ε 11,500), 317 (6000); *m/e* 233 (M − 1).

Anal. Calcd for $C_{13}H_{18}N_2O_2$: C, 66.67; H, 7.74; N, 11.96. Found: C, 66.74; H, 7.72; N, 12.09.

2-Phenyl-4,4,5,5-tetramethylimidazoline 3-Oxide (18). 1,3-Dioxy-2-phenyl-4,4,5,5-tetramethylimidazolinium chloride (**17**), prepared from 200 mg of the phenyl nitronyl nitroxide (**4**, R = C_6H_5), was warmed on a steam bath in 5 ml of dry ethanol. The solvent was then removed *in vacuo* and the residue dissolved in water. After adjusting to pH 8, the solution was repeatedly extracted with chloroform. Evaporation of the extracts yielded 112 mg (60%) of the product, mp 188–189°, which was identical with an authentic sample.[1]

2-Iodomethyl-4,4,5,5-tetramethylimidazoline 3-Oxide 1-Oxyl (4, R = CH_2I). A solution of 100 mg of 2-chloromethyl-4,4,5,5-tetramethylimidazoline 3-oxide 1-oxyl (**4**, R = CH_2Cl) in 20 ml of a saturated solution of potassium iodide in acetone was allowed to stand for 5 min at room temperature. After evaporation of the solvent *in vacuo*, the residue was extracted with ether and the extracts were chromatographed on silica. Great care to protect against exposure to light was required because of the high photosensitivity of this compound. The dark blue crystalline product, after washing with hexane, weighed 60 mg (41%): mp 60°; $\nu_{max}^{CCl_4}$ 1135, 1375 cm^{-1}; *m/e* 297 (M$^+$) (Tables II and VI).

N-Substituted 2-Aminomethyl-4,4,5,5-tetramethylimidazoline 3-Oxide 1-Oxyls. The aminonitronyl nitroxides were prepared by warming solutions of ~5 mg of 2-chloromethyl-4,4,5,5-tetramethylimidazoline 3-oxide 1-oxyl (**4**, R = CH_2Cl) and ~0.1 g of amine in ~0.5 ml of acetonitrile at ~60° for 15–30 min in the presence of a few crystals of potassium iodide. The solutions were diluted with chloroform, washed with water, and applied to silica tlc plates. After partial elution with 50% methanol–ether the plates were allowed to dry and then eluted with petroleum ether–ether. The red spots were scraped from the plates and the scrapings extracted with chloroform or ether for esr measurements (Table III).

2-Dibenzylaminomethyl-4,4,5,5-tetramethylimidazoline 3-Oxide 1-Oxyl [4, R = $CH_2N(CH_2C_6H_5)_2$]. A solution of 50 mg of 2-chloromethyl-4,4,5,5-tetramethylimidazoline 3-oxide 1-oxyl **4** (R = CH_2Cl) and 0.2 ml of dibenzylamine in 5 ml of acetonitrile was stirred with a few crystals of potassium iodide for 3 hr at 60°. The mixture was then diluted with 10 ml of chloroform, washed with water, dried over sodium carbonate, and evaporated *in vacuo*. The residue was chromatographed on silica with ether. The red product was crystallized from ether to give 35 mg (39%) of the amino radical: mp 114–116°; λ_{max}^{EtOH} 312 mμ (ε 12,700, sh), 322 (16,900), 530 (1200), 560 (1100, sh); $\nu_{max}^{CCl_4}$ 1160 and 1370 cm^{-1} (Table II).

2-(*p*-Toluenesulfonamidomethyl)-4,4,5,5-tetramethylimidazoline 3-Oxide 1-Oxyl (4, R = $CH_2NHSO_2C_6H_4CH_3$). Dry ammonia was bubbled for 30 min into a solution of 50 mg of 2-chloromethyl-4,4,5,5-tetramethylimidazoline 3-oxide 1-oxyl (**4**, R = CH_2Cl) in 10 ml of acetonitrile containing a few crystals of potassium iodide. The solution was then diluted with chloroform and sequentially washed with water, dried over sodium carbonate, and evaporated *in vacuo*. The red aminomethyl-4,4,5,5-tetramethylimidazoline 3-oxide 1-oxyl (**4**, R = CH_2NH_2) (30 mg) obtained by chromatography on silica with methanol–chloroform was an unstable oil. On warming this compound on a steam bath with 10 ml of chloroform, 75 mg of *p*-toluenesulfonyl chloride and 1 drop of pyridine the *p*-toluenesulfonamide was formed. Evaporation of the solvent and chromatography of the residue on silica gel with ether followed by crystallization from ether gave 23 mg (28%) of the red product: mp 105–107°; λ_{max}^{EtOH} 217 mμ (ε 42,800), 237 (10,100), 307 (sh, 14,600), 316 (18,500), 523 (1300), 550 (sh, 1200); *m/e* 340 (M$^+$) (Table II).

Phthalimidomethyl-4,4,5,5-tetramethylimidazoline 3-Oxide 1-Oxyl [4, R = $CH_2N(CO)_2C_6H_4$]. A suspension of 200 mg of potassium phthalimide and 50 mg of potassium iodide in a solution of 70 mg of 2-chloromethyl-4,4,5,5-tetramethylimidazoline 3-oxide 1-oxyl in 20 ml of acetonitrile was stirred for 2 hr on a steam bath. After dilution with chloroform and extraction with water the reaction mixture was chromatographed on silica with ether. Crystallization of the red product from ether gave 60 mg (56%): mp 131–132°; λ_{max}^{EtOH} 237 mμ (ε 9900, sh), 307 (14,100), 317 (18,900), 523 (1400), 550 (1300, sh); $\nu_{max}^{CCl_4}$ 1180, 1375, 1730, 1780 cm^{-1}; *m/e* 316 (M$^+$) (Table II).

2-(2′-Phenyl-1′,2′-dibromoethyl)-4,4,5,5-tetramethylimidazoline 3-Oxide 1-Oxyl (4, R = $CHBrCHBrC_6H_5$). A solution of 0.80 g of bromine in 10 ml of carbon tetrachloride was added dropwise to a stirred solution of 0.50 g of 2-(β-styryl)-4,4,5,5-tetramethylimidazoline 3-oxide 1-oxyl (**4**, R = $CH{=}CHC_6H_5$) in 150 ml of carbon tetrachloride at 0°. After the addition the mixture was stirred at room temperature for 3 hr followed by evaporation *in vacuo* and chromatography on silica gel with ether. Crystallization of the product from ether yielded 0.70 g (82%) of dark purple crystals: mp 143–144°; $\nu_{max}^{CHCl_3}$ 1135, 1370 cm^{-1}; esr (C_6H_{14}) $a_{N(1)} = a_{N(3)} = 7.5$ G, $a_{Br} = 4.5$ G, $a_{\alpha\text{-}CH} < 0.7$ G; *m/e* 417, 419, 421 (M$^+$) (Table VI).

Anal. Calcd for $C_{15}H_{19}N_2O_2Br_2$: C, 42.98; H, 4.57; N, 6.69; Br, 38.13. Found: C, 43.20; H, 4.53; N, 6.83; Br, 38.34.

2-Phenylethynyl-4,4,5,5-tetramethylimidazoline 3-Oxide 1-Oxyl (4, R = $C{\equiv}CC_6H_5$). A mixture of 0.21 g of the above dibromonitronyl nitroxide and 0.10 g of sodium methoxide in 30 ml of tetrahydrofuran was stirred at room temperature for 1.5 hr. The solvent was removed *in vacuo* and the residue chromatographed on silica gel with ether. The major fraction yielded 56 mg (44%) of a dark blue solid: mp 125–126° dec; $\nu_{max}^{CHCl_3}$ 1132, 1165, 1370, 2205 cm^{-1}; λ_{max}^{EtOH} 643 mμ (ε 296), 603 (296), 365 (11,900), 357 (10,650) (sh), 310 (21,000), 292 (22,000), 236 (9330), 219 (12,300), 214 (11,900) (Table II).

1,2-Bis(4′,4′,5′,5′-tetramethylimidazoline-2′-yl)ethylene Bis-3′,3′′-oxide Bis-1′,1′′-oxyl (11). To 600 ml of ice-cold 6% aqueous sodium hypochlorite solution was added 5 g (14.7 mmol) of finely powdered 1,2-bis(4′,4′,5′,5′-tetramethylimidazoline-2′-yl)ethane 3′,3″-oxide 1′,1″-oxyl (**9**, *n* = 2). The mixture was maintained at 30–35° with stirring for 7 hr and extracted twice with the minimum amount of chloroform. The combined extracts were washed with water and chromatographed on silica gel with chloroform. The column was extruded and the dark green fraction extracted with chloroform–acetone. Removal of solvent and washing with petroleum ether yielded 2.9 g (58%) of olive green crystals which after recrystallization from chloroform–petroleum ether had mp 200° dec; ν_{max}^{KBr} 1135, 1160, 1375 cm^{-1}; λ_{max}^{EtOH} 233 mμ (ε 12,500), 264 (7650) 335 (sh, 23,000), 350 (28,250), 395 (10,100), 570 (320); *m/e* 338 (M$^+$).

Anal. Calcd for $C_{16}H_{26}N_4O_4$: C, 56.78; H, 7.74; N, 16.56. Found: C, 57.08; H, 7.77; N, 16.61.

Deoxygenation of 1,2-Bis(4′,4′,5′,5′-tetramethylimidazoline-2′-yl)-ethane Bis-3′,3′′-oxide Bis-1′,1′′-oxyl (9, *n* = 2). To a solution of 50 mg of 1,2-bis(4′,4′,5′,5′-tetramethylimidazoline-2′-yl)ethane bis-3′,3′′-oxide bis-1′,1′′-oxyl (**9**, *n* = 2) in 5 ml of dimethylformamide was added 450 mg of sodium nitrite and 10 drops of concentrated hydrochloric acid. The solution was warmed at 35° until it turned orange brown and then poured into 50 ml of water. The resulting solution was neutralized with 2 *N* NaOH and then shaken for 5 min with 5 g of lead dioxide. After filtering, the solution was extracted with chloroform and the extracts were chromatographed on silica gel with ether. Evaporation of the faster moving red-brown fraction gave 17.5% of 1,2-bis(4′,4′,5′,5′-tetramethylimidazoline-2′-yl)ethylene bis-1′,1′′-oxyl (**13**): mp 140–143°; ν_{max}^{KBr} 1140, 1365, 1380 cm^{-1}; λ_{max}^{EtOH} 252 mμ (ε 17,300), 354 (6800) with tailing to 630 mμ; *m/e* 306 (M$^+$.

Anal. Calcd for $C_{16}H_{26}N_4O_2$: C, 62.72; H, 8.55; N, 18.29. Found: C, 62.80; H, 8.61; N, 18.38.

Evaporation of a slower moving orange-brown band gave 14 mg (31%) of 1,2-bis(4′,4′,5′,5′-tetramethylimidazoline-2′-yl)ethane bis-1′,1′′-oxyl (**15**): mp 95–98°; ν_{max}^{KBr} 1140, 1365, 1375 cm^{-1}; λ_{max}^{EtOH} 632 mμ (ε 14,680), 380 (1690); *m/e* 308 (M$^+$).

Anal. Calcd for $C_{16}H_{26}N_4O_2$: C, 62.30; H, 9.15; N, 18.17. Found: C, 62.44; H, 9.05; N, 18.22.

Deoxygenation of 1,2-Bis(4′,4′,5′,5′-tetramethylimidazoline-2′-yl)ethylene Bis-3′,3′′-oxide Bis-1′,1′′-oxyl (11). To a solution of 200 mg (0.59 mmol) of **11** in 80 ml of dimethylformamide was added 20 ml of water followed by 200 mg of sodium nitrite and 10 drops of glacial acetic acid. The mixture was stirred at 70–80° for 3 hr

and then poured into water and extracted with chloroform. The combined extracts were sequentially washed with water, dried (magnesium sulfate), filtered, and evaporated to dryness *in vacuo*. The residue was chromatographed on silica gel using ether. The faster moving red-brown fraction yielded 45 mg (25%) of **13** identical with that obtained in the previous experiment. The next fraction was green and on evaporation yielded 44 mg (23%) of the imino nitroxide nitronyl nitroxide biradical **14**: mp 170° dec; ν_{max}^{KBr} 1140, 1380 cm^{-1}; λ_{max}^{EtOH} 238 mμ (ε 11,500), 298 (15,950), 350 (8500), 380 (8300); *m/e* 322 (M$^+$).

Anal. Calcd for $C_{16}H_{26}N_4O_3$: C, 59.60; H, 8.13; N, 17.38. Found: C, 59.39; H, 8.10; H, 17.30.

In addition to the above products 35 mg (17%) of the starting biradical was recovered from a slow-moving fraction.

1,2-Bis(4′,4′,5′,5′-tetramethylimidazoline-2′-yl)-1,2-dichloroethane Bis-3′,3′′-oxide 1′,1′′-Oxyl (12, X = Cl). To a solution of the ethylene bisnitronyl nitroxide **11** (500 mg, 1.48 mmol) in 50 ml of chloroform was added all at once 1.5 ml of chloroform saturated with chlorine gas and the mixture left to stand for 30 min. The chloroform was removed *in vacuo* and the residue extracted with methanol followed by petroleum ether and dried to yield 450 mg (74.5%) of the title compound: decomposes at 202–203° (rapid heating); ν_{max}^{KBr} 1135, 1380 cm^{-1}; *m/e* 408, 410, 412 (M$^+$). The absence of strong oxidizing properties and the presence of a strong esr signal in this product require that the chlorines be covalently bound.

1,2-Bis(4′,4′,5′,5′-tetramethylimidazoline-2′-yl)-1,2-dibromoethane Bis-3′,3′′-oxide Bis-1′,1′′-oxyl (12, X = Br). The preceding procedure was repeated using 200 mg of the biradical **11** and 470 mg of bromine. The highly insoluble product precipitated from the reaction mixture and was purified by extracting with methanol to yield 228 mg (77%) of the title compound: *m/e* 496, 498, 500 (M$^+$), 418, 416 (M − HBr); decomposes ~202°. On treatment with sodium methoxide in tetrahydrofuran this product is converted in poor yield to the starting biradical **11**.

1,4-Bis(4′,4′,5′,5-tetramethylimidazoline-2′-yl)benzene Bis-1′,1′′-oxyl (26). A few milligrams of the *p*-bisnitronyl nitroxide **25** in 1 ml of chloroform was shaken with 1 ml of water containing several crystals of sodium nitrite and 1 drop of acetic acid. The color changed rapidly to dark brown and the chloroform layer was dried and evaporated. Separation by tlc on silica gel using ether gave an orange brown solid: mp 230–233° dec; *m/e* 356 (M$^+$).

Calculations. Zero-field splitting parameters *X*, *Y*, and *Z* expressed in gauss along the major molecular axes of the biradicals were evaluated from the expression $\mu_0 r^{-3}(3\cos^2\theta - 1)$ where μ_0 is 0.927×10^{-26} erg/G, *r* is the distance between the two unpaired electrons in centimeters, and θ is the angle between the electron–electron axis and the molecular axis.[20] *D* and *E* values were derived from the relationships[21] $D = 3Z/2$ and $E = (X - Y)/2$. Each unpaired electron was assumed to be distributed over two points as described in the text. Distances and angles were estimated using Dreiding models. The principal molecular axes of the benzene biradicals **23–27** were taken through the 1 and 3 positions of the benzene ring in the meta derivatives and through the 1 and 4 positions in the para derivatives. The principal axes of the ethylene biradicals **11**, **13**, and **14** were defined by a line passing through a point midway along a nitrogen–oxygen bond of one ring and through a like point having a syn relationship in the second ring. In the two **13** conformations where the oxygens are not syn related, the line passed through a syn related nitogen atom of the second ring.

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Kinetics of the Reaction of Methyllithium with 2,4-Dimethyl-4′-methylmercaptobenzophenone[1a]

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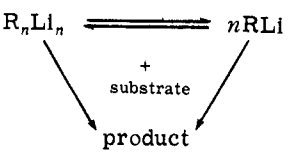
Abstract: The rate of the addition of halide-free methyllithium to the carbonyl group of 2,4-dimethyl-4′-methylmercaptobenzophenone has been found to be one-fourth order in alkyllithium and first order with respect to ketone in diethyl ether solvent at 25.0° with a rate constant of 200 ± 7 (l./mol)$^{1/4}$ sec^{-1}. Addition of lithium bromide or lithium iodide depresses the rate level but does not change the kinetic order in this system. The data are accommodated by a reaction mechanism involving predominant reaction through monomeric methyllithium which is in equilibrium with tetrameric methyllithium.

The tendency of lithium reagents to form specific aggregates[2] such as the tetrameric methyllithium[3] (Me_4Li_4) in diethyl ether necessitates assessing the relative reactivities toward a particular substrate of the aggregate compared to less associated species such as the monomer which might be present in low concentration.



Recently,[4] it has been found that the ethylenation of isopropyl-, *sec*-butyl-, and *tert*-butyllithium at −24.8°

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