Synthesis of Nitronyl Alcohols and Their Benzoate Esters

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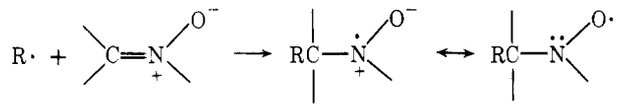
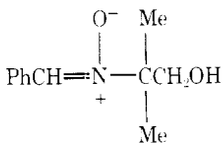
The synthesis of six new nitronyl alcohols is reported: $PhCH{=}N^{+}(O^{-})C(CH_3)_2(CH_2)_mOH$, in which m = 1, 2, and 3; and $PhCH{=}N^{+}(O^{-})C(CH_3)_n(CH_2OH)_p$, in which $n + p = 3$ and $0 \leq n \leq 3$ and $0 \leq p \leq 3$. All are produced by condensation of benzaldehyde and the appropriately substituted hydroxylamine derived from the nitro alcohol of the corresponding structure. The synthesis of the benzoates of the nitronyl alcohols starting from the benzoates of the corresponding nitro alcohols is also described.

The addition of radicals to nitrones produces nitroxides.[2]

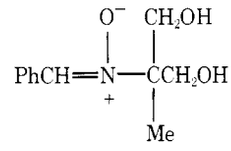


This reaction seems to be fairly general for radicals with the unpaired electron centered on carbon (carbon-centered radicals[3]) and also for oxygen-centered radicals.[4] Because the ESR spectrum of the nitroxides produced should be in principle unique for each radical trapped, the addition reaction is useful in detecting low concentrations of reactive free radicals which cannot be detected directly by ESR methods. This technique has been named spin trapping.[3,5] The potential applications and limitations of this method are under investigation in these laboratories.

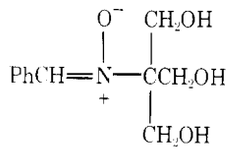
It is obvious that a water-soluble nitrone would be desirable for free-radical studies in aqueous solution. The extensively studied α-phenyl-*tert*-butylnitrone (PBN) dissolves very slowly in water up to about 0.1 M. One would expect improved water solubility with retention of stability on spin trapping when the *tert*-butyl methyl hydrogens are replaced by hydroxy groups (I–III). The synthesis of these compounds as well



I

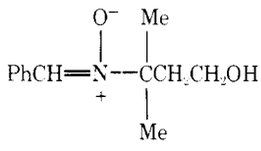


II

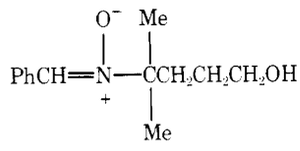


III

as their benzoate esters is described in this paper. Also, the preparation of two phenylnitrones with an extended methylene chain will be given (IV and V).

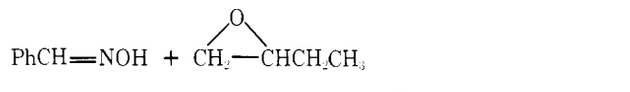


IV

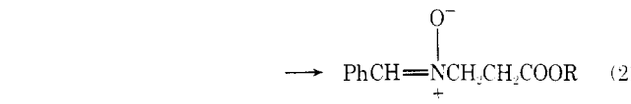


V

Apparently these *N*-*tert*-alkylnitronyl alcohols have not been previously prepared, although a few other nitronyl alcohols and esters have been reported. The following reactions were used to prepare the nitronyl alcohols reported in the literature.[6-8]



(1)



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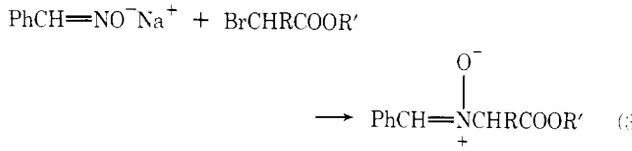
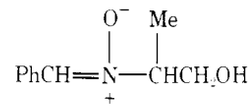


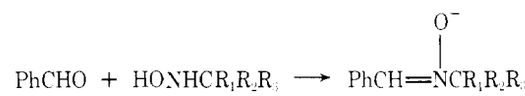
(3)

The synthesis of VI is also included here.



VI

General Approach to the Synthesis of Nitronyl Alcohols. The nitronyl alcohols reported here were synthesized by the condensation of benzaldehyde with the appropriately substituted hydroxylamine. The substituted hydroxylamine



is obtained from the zinc/ammonium chloride reduction of the appropriate nitro alcohol. The nitro alcohols needed for the synthesis of I, II, and III were prepared from formaldehyde and the appropriate nitroalkane. However, they can also be obtained commercially. The nitro alcohols for IV and V were prepared by special methods. In every case the nitronyl alcohol benzoate ester was made by the condensation of benzaldehyde with the hydroxylamine of the nitro alcohol benzoate ester.

Synthesis. α-Phenyl-*N*-(1-hydroxy-2-methyl-2-propyl)nitrone (I). Since this compound bears a close resemblance to PBN, the name "hydroxy PBN" or HOPBN will be used. HOPBN can be prepared from formaldehyde, 2-nitropropane, and benzaldehyde in good yield. The assignment of structure is based on NMR, IR, and UV spectroscopy. In $CDCl_3$ the following assignments are made: multiplet at δ

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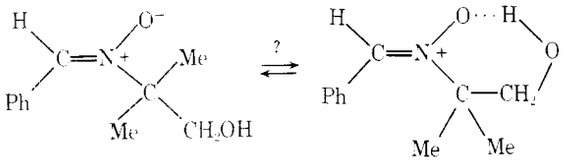
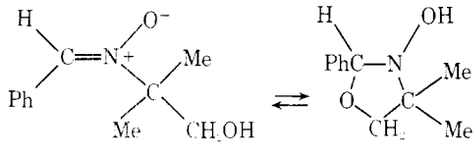
8.23 due to the ortho protons of the phenyl group, multiplet at δ 7.40 due to the meta, para, and vinyl protons, broad singlet at δ 4.45 due to the hydroxy proton, singlet at δ 3.73 due to the methylene protons, and singlet at δ 1.55 due to the protons of the two methyl groups. Integration is consistent with this assignment. The spectrum in the region of the phenyl group is identical with that of PBN and frequently has diagnostic value for identifying the presence of N-substituted phenylnitrones, particularly in polar solvents like D_2O or Me_2SO-d_6.[9] In polar solvents the ortho protons are strongly deshielded, appearing at δ 8.4, whereas the meta and para protons appear at δ 7.1–7.4. This separation frequently allows resolution of the vinyl proton singlet at δ 7.4–7.8. In KBr absorptions due to the OH and C=N stretch are found at 3180 and 1591 cm^{-1}, respectively. The ultraviolet spectrum of HOPBN is identical with that of PBN: λ_{max} 298 (ethanol), 305 (hexane) nm (ϵ_{max} ca. 15 000). The two broad, moderately intense absorptions have been reported to be characteristic of N-alkylated phenylnitrones.[10]

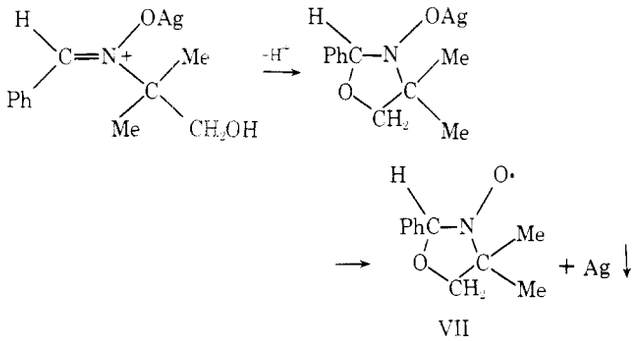
The question as to the possibility of intramolecular H bonding in this compound is under investigation.



HOPBN is a stable white crystalline solid completely soluble in water. No evidence for the cyclic hydroxylamine isomer has been found. Thus, although aliphatic hydroxylamines



react instantly with alcoholic silver nitrate at room temperature upon mixing to yield a dark gray, silver precipitate, pure samples of HOPBN (or PBN) do not produce precipitates in the presence of silver ions. However, when followed by ESR spectroscopy, a small amount of nitroxide is observed upon mixing HOPBN with alcoholic silver nitrate at room temperature. This signal increases with time. The same result is obtained with lead tetraacetate. Further studies of this reaction are under way. The Lewis acid centers probably facilitate cyclization by coordination with the nitronyl oxygen. The structural assignment of VII is based on the synthesis of the amine precursor.[11]



VII

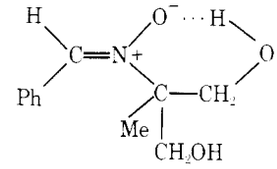
The benzoate ester of I was prepared by reducing the benzoate ester of 2-methyl-2-nitropropanol to the hydroxylamine followed by condensation with benzaldehyde. This method appears to be quite general for the preparation of nitronyl benzoates. Attempts to synthesize the benzoate ester of I directly from HOPBN were unsuccessful.

$$NO_2CMe_2CH_2OH \xrightarrow{BzCl} NO_2CMe_2CH_2OBz \xrightarrow{Zn}$$

$$HONHCMe_2CH_2OBz \xrightarrow{PhCHO} PhCHN(O)CMe_2CH_2OBz$$

The acetate ester of 2-methyl-2-nitropropanol did not survive the Zn/NH_4Cl reduction. Hydrolysis occurred, producing I upon reaction with benzaldehyde.

α-Phenyl-*N*-(1,3-dihydroxy-2-methyl-2-propyl)nitrone (II). The name "dihydroxy PBN" or $(HO)_2$PBN will be used for this compound. $(HO)_2$PBN was prepared from nitroethane, formaldehyde, and benzaldehyde in relatively poor overall yield. This compound is a white low-melting hygroscopic solid. The structural assignment is based on NMR spectroscopy. In D_2O the vinyl proton peak falls between the ortho and meta/para multiplets. The peaks for the methyl and hydroxy protons are singlets with the correct relative areas. Of interest is the fact that the diastereotopic methylene protons appear as two triplets with different chemical shifts. The possibility of intramolecular H bonding of one hydroxymethylene group is under investigation.



II

The dibenzoate ester of II was prepared from the dibenzoate ester of 2-methyl-2-nitro-1,3-propanediol.

α-Phenyl-*N*-(2-hydroxymethyl-1,3-dihydroxy-2-propyl)nitrone (III). $(HO)_3$PBN was prepared from nitromethane, formaldehyde, and benzaldehyde in moderately low yield. The compound is a white crystalline solid. The structural assignment is based on NMR, IR, and UV spectroscopy and elemental analysis (see Experimental Section). The NMR spectrum of $(HO)_3$PBN differs from that of $(HO)_2$PBN in that both the hydroxy and methylene protons appear as singlets in this case. No evidence for a difference in chemical shift for one methylene group as compared to the other two is available at this time.

The tribenzoate ester of III was prepared from the tribenzoate ester of 2-hydroxymethyl-2-nitro-1,3-propanediol.

α-Phenyl-*N*-(4-hydroxy-2-methyl-2-butyl)nitrone (IV). Since this compound still bears a close resemblance to PBN, except that instead of a *tert*-butyl group a *tert*-pentyl group is attached to the nitrogen atom of the nitrone, the term "hydroxy PPN" or HOPPN will be used to designate ω-hydroxy-α-phenyl-*N*-(*tert*-pentyl)nitrone. The synthesis of HOPPN was accomplished by condensation of benzaldehyde with the substituted hydroxylamine obtained from reduction of 3-nitro-3-methylbutanol. The latter was made from the hydrolysis of 3-methyl-3-nitrobutyl acetate produced in the peracid oxygenation of 5-methyl-5-nitro-2-hexanone. A 13% overall yield was obtained.

$$NO_2CHMe_2 \xrightarrow{CH_2=CHCOCH_3} NO_2CMe_2CH_2CH_2COCH_3$$

$$\xrightarrow{CF_3COOOH} NO_2CMe_2CH_2CH_2OCOCH_3$$

$$\xrightarrow{NaOH} NO_2CMe_2CH_2CH_2OH \xrightarrow[NH_4Cl]{Zn} HONHCMe_2CH_2CH_2OH$$

$$\xrightarrow{PhCHO} PhCH{=}\overset{+}{N}(O^-)CMe_2CH_2CH_2OH$$

α-Phenyl-*N*-(5-hydroxy-2-methyl-2-pentyl)nitrone (V). Since the hydroxyalkyl group in this compound is *tert*-hexyl, the term "hydroxy PHN" or HOPHN will be used to designate ω-hydroxy-α-phenyl-*N*-(*tert*-hexyl)nitrone. The synthesis of HOPHN was accomplished by condensation of benzaldehyde with the substituted hydroxylamine obtained from the reduction of 4-nitro-4-methylpentanol. The latter was made by reduction of 4-nitro-4-methylpentanal with sodium cyanoborohydride. A 15% overall yield was obtained. Structure assignment was by NMR spectroscopy.

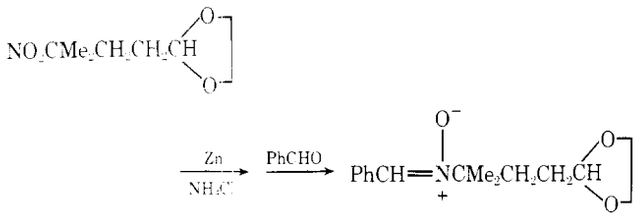
$$NO_2CHMe_2 \xrightarrow{CH_2=CHCHO} NO_2CMe_2CH_2CH_2CHO$$

$$\xrightarrow{NaCNBH_3} NO_2CMe_2CH_2CH_2CH_2OH$$

$$\xrightarrow[NH_4Cl]{Zn} HONHCMe_2CH_2CH_2CH_2OH$$

$$\xrightarrow{PhCHO} PhCH{=}\overset{+}{N}(O^-)CMe_2CH_2CH_2CH_2OH$$

An attempt was made to obtain the nitrone by protecting the aldehydic function from the zinc/NH_4Cl reduction of the nitro group. Although the expected protected phenylnitrone was obtained, hydrolysis destroyed the nitrone function. This method was not successful in producing HOPHN. The assignment of structure was based on NMR spectroscopy.



α-Phenyl-*N*-(1-hydroxy-2-propyl)nitrone (VI). The condensation of benzaldehyde with the hydroxylamine ob-

$$PhCHO + HONHCHMeCH_2OH \longrightarrow PhCH{=}\overset{+}{N}(O^-)CHMeCH_2OH$$

VI

tained from 2-nitropropanol produced VI in 55% overall yield. Structural assignment was based on NMR spectroscopy.

Experimental Section

Synthesis of α-Phenyl-*N*-(1-hydroxy-2-methyl-2-propyl)-nitrone (I). To a cooled flask containing 2-methyl-2-nitropropanol (5.95 g, 0.05 mol) in 150 mL of ethanol was added ammonium chloride (3.25 g, 0.061 mol) in 50 mL of distilled water. Fine zinc powder (13 g, 0.2 mol) was added over a period of 15 min with stirring and continued cooling (<30 °C). After stirring for 4 h the zinc salts were filtered off and washed with hot 95% ethanol (2 × 100 mL) and hot chloroform (2 × 100 mL). The light green filtrate (the blue color comes from the nitroso function) was concentrated to 50 mL by rotoevaporation and extracted with chloroform (4 × 100 mL). The combined extracts were concentrated to 100 mL and used in the next step.

Benzaldehyde (5.25 g, 0.05 mol) was added to the above chloroform solution, and the mixture was gently refluxed for 3.5 h. After cooling, drying over anhydrous $MgSO_4$, and concentrating by rotoevaporation, a solid paste was recovered which after two recrystallizations from cold CCl_4 yielded a fine white powder (5.2 g, 55% yield overall): mp 75–76 °C; NMR ($CDCl_3$) δ 8.23 (m, 2 H, C_6H_5 ortho), 7.40 (m, 4 H, C_6H_5 2 meta and 1 para, 1 vinyl), 4.45 (s, broad, 1 H, CH_2OH), 3.73 (s, 2 H, CH_2OH), 1.55 (s, 6 H, $2CH_3$); IR (KBr) 3180 (OH), 1591 (C=N) cm^{-1}; UV λ_{max} 298 (EtOH), 305 (hexane) nm (ϵ_{max} ca. 15 000). Anal. Calcd for $C_{11}H_{15}NO_2$: C, 68.37; H, 7.82; N, 7.25. Found: C, 68.22; H, 7.88; N, 7.34

Synthesis of α-Phenyl-*N*-(1,3-dihydroxy-2-methyl-2-propyl)nitrone (II). Reduction of 2-methyl-2-nitro-1,3-propanediol to the hydroxylamine derivative and condensation with benzaldehyde were accomplished on a 0.05-mol scale by the procedure used for the preparation of I. Two recrystallizations from cold benzene yielded low-melting white crystals (1.6 g, 15.3% yield overall): mp 52–55 °C (hygroscopic); NMR (D_2O) δ 8.18 (m, 2 H, C_6H_5 ortho), 7.38 (m, 4 H, C_6H_5 2 meta and 1 para, 1 vinyl), 4.10 (s, broad, 2 H, $2CH_2OH$), 3.98 (m, 4 H, $2CH_2OH$), 1.41 (s, 3 H, CH_3); IR (film) 3280 (OH), 1588 (C=N) cm^{-1}; UV (EtOH) λ_{max} 296 nm. An analytically pure sample suitable for elemental analysis could not be prepared.

Synthesis of α-Phenyl-*N*-(2-hydroxymethyl-1,3-dihydroxy-2-propyl)nitrone (III). Reduction of 2-hydroxymethyl-2-nitro-1,3-propanediol to the hydroxylamine derivative and condensation with benzaldehyde by the method used for I gave white powdery crystals after four recrystallizations from methanol/petroleum ether (2.48 g, 22% overall yield): mp 89–91 °C; NMR (D_2O) δ 7.70 (m, 2 H, C_6H_5 ortho), 7.20 (s, 1 H, vinyl), 7.0 (m, 3 H, C_6H_5 meta and 1 para), 4.45 (s, 6 H, $3CH_2OH$); IR (KBr) 3380–3190 (broad OH), 1590 (C=N) cm^{-1}; UV (EtOH) λ_{max} 298 nm (ϵ_{max} ca. 15 000). Anal. Calcd for $C_{11}H_{15}NO_4$: C, 58.66; H, 6.71; N, 6.22. Found: C, 58.49; H, 6.60; N, 6.15.

Synthesis of α-Phenyl-*N*-(4-hydroxy-2-methyl-2-butyl)nitrone (IV). To a solution of trifluoroperacetic acid (32.5 g, 0.25 mol) in methylene chloride prepared from trifluoroacetic anhydride and 90% hydrogen peroxide by the method of Emmons and Pagano[12] was added 5-methyl-5-nitro-2-hexanone (prepared from the Michael addition of 2-nitropropane to vinyl methyl ketone) dropwise with cooling over a period of 1 h. The mixture was allowed to stand overnight and was then poured into 500 mL of water. The organic layer separated and was extracted with 10% $NaHCO_3$ (2 × 100 mL) and saturated NaCl (100 mL). Rotoevaporation yielded a white sweet-smelling slurry, which from NMR spectroscopy was estimated to contain 66% of 3-methyl-3-nitrobutyl acetate. The mixture was refluxed in methanolic KOH for 2 days. The dark tarry mixture was filtered through glass wool, concentrated to 100 mL under vacuum, and extracted with ether (5 × 100 mL). The ether extract was concentrated to 100 mL, filtered through glass wool, and rotoevaporated to yield a dark brown oil. This was heated to boiling in 50% H_2O/EtOH and treated with charcoal (Norit). After filtering and concentrating to 50 mL on the rotoevaporator, extraction with chloroform yielded 3-methyl-3-nitrobutanol (4.25 g, 12.8% yield) as a pale yellow oil: NMR ($CDCl_3$) δ 4.50 (s, broad, 1 H, OH), 3.70 (t, J = 6 Hz, 2 H, CH_2OH), 2.23 (t, J = 6 Hz, OCH_2CH_2), 1.65 (s, 6 H, $2CH_3$); IR (neat) 3350 (OH), 1551 (NO_2) cm^{-1}.

Reduction to the hydroxylamine was accomplished by the standard procedure used in the preparation of I.

The resulting chloroform solution of the hydroxylamine derivative was gently refluxed with benzaldehyde (3.40 g, 0.32 mol) for 3 h. Rotoevaporation yielded a green oil, and TLC on silica gel indicated the presence of two components. The mixture was separated on a 11 × 1 in silica gel (60–200 mesh) column using ethyl acetate/chloroform (50:50) as elutant. The nitronyl alcohol was collected within the 250–330-mL fraction of elutant (flow rate, 1 cm^3/min). Rotoevaporation followed by vacuum desiccation yielded the nitronyl alcohol as a clear viscous oil (0.85 g, 12.9%): NMR ($CDCl_3$) δ 8.18 (m, 2 H, C_6H_5 ortho), 7.48 (s, 1 H, vinyl), 7.23 (m, 3 H, C_6H_5 2 meta and 1 para), 4.55 (s, broad, 1 H, OH), 3.47 (t, J = 5 Hz, 2 H, CH_2OH), 2.29 (t, J = 5 Hz, 2 H, CH_2CH_2O), 1.61 (s, 6 H, $2CH_3$); IR (neat) 3350 (OH), 1584 (C=N) cm^{-1}; UV (EtOH) λ_{max} 298 nm (ϵ_{max} ca. 15 000).

Synthesis of α-Phenyl-*N*-(5-hydroxy-2-methyl-2-pentyl)-nitrone (V). In a well-ventilated hood freshly prepared 4-methyl-4-nitropentanal (5.3 g, 0.064 mol) from 2-nitropropane and acrolein was added to cooled 50% aqueous methanol (100 mL) at pH 4 (H_2SO_4). This was followed by the addition of sodium cyanoborohydride (4.04 g, 0.065 mol) in small portions over 30 min with periodic additions of H_2SO_4 to maintain pH 4. After stirring for 4 h at room temperature, the deep brown liquid was diluted with 250 mL of H_2O and extracted with chloroform (4 × 100 mL). A pale yellow oil (8.0 g, 84%) was isolated by rotoevaporation: NMR ($CDCl_3$) δ 4.25 (s, broad, 1 H, OH), 3.65 (t, J = 5 Hz, 2 H, CH_2OH), 1.90 (m, 2 H, CH_2), 1.61 (s, 6 H, $2CH_3$), 1.50 (m, 2 H, CH_2); IR (neat) 3345 (OH) and 1550 (NO_2) cm^{-1}, with no trace of carbonyl absorption.

Reduction to the hydroxylamine derivative was accomplished by the procedure used in the preparation of I. The resulting green oil was eluted through a 10 × 1 in silica gel (200 mesh) column using 25% ethyl acetate in chloroform. The nitronyl alcohol was collected in the fraction between 300 to 380 mL of elutant (flow rate, 1 mL/min). Evaporation of the solvent followed by 24 h of vacuum desiccation yielded the nitrone as a colorless jelly (2.05 g, 14.53% overall): NMR (CCl_4) δ 8.20 (m, 2 H, C_6H_5 ortho), 7.38 (s, 1 H, vinyl), 7.25 (m, 3 H, C_6H_5 2 meta and 1 para), 3.65 (s, broad, 1 H, OH), 3.40 (t, J = 4 Hz,

2 H, CH_2OH), 1.80 (m, 2 H, CH_2), 1.45 (s, 6 H, $2CH_3$), 1.35 (m, 2 H, CH_2); IR (neat) 3350 (OH), 1585 (C=N) cm^{-1}; UV (EtOH) λ_{max} 298 nm (ϵ_{max} ca. 15 000).

Synthesis of the Ethylene Glycol Acetal of V. A mixture of 4-methyl-4-nitropentanal (25 g, 0.17 mol), ethylene glycol (10.78 g, 0.18 mol), and 0.5 g of *p*-toluenesulfonic acid in 50 mL of benzene was vigorously refluxed under a Dean-Stark trap for 3 h. The solution was cooled, diluted to 150 mL with benzene, extracted with saturated $NaHSO_3$ (2 × 50 mL) and saturated NaCl, and rotoevaporated, and the oil recovered was distilled under vacuum (120 °C at 6 mm). The dioxolane was isolated as a colorless liquid (25.3 g, 78.8%): IR 1546 (NO_2) cm^{-1}, with no carbonyl absorption.

Reduction to the hydroxylamine and condensation with benzaldehyde were on a 0.1-mol scale following the procedure used in the preparation of I. The crude nitrone was isolated as a green oil, which solidified upon refrigeration. Recrystallization from hexane/petroleum ether yielded pure white crystals (19.9 g, 76%): mp 64–65 °C; NMR ($CDCl_3$) δ 8.25 (m, 2 H, C_6H_5 ortho), 7.45 (s, 1 H, vinyl), 7.30 (m, 3 H, C_6H_5 2 meta and 1 para), 4.84 (t, J = 4 Hz, 1 H, methine), 3.85 (m, 4 H, acetal), 2.0 (m, 2 H, CH_2), 1.65 (m, 2 H, CH_2), 1.60 (s, 6 H, $2CH_3$); IR (KBr) 1585 (C=N) cm^{-1}. Anal. Calcd for $C_{15}H_{21}NO_3$: C, 68.50; H, 8.03; N, 5.32. Found: C, 68.48; H, 8.01; N, 5.29.

Synthesis of the Benzoate Ester of Nitrone I. Pyridine (3.9 g, 0.05 mol) was added to 2-methyl-2-nitropropanol (5.95 g, 0.05 mol) and benzoyl chloride (7.0 g, 0.05 mol) in 50 mL of dry benzene. After refluxing vigorously for 1 h the solution was cooled and extracted with 1 N HCl (2 × 100 mL), 1 N KOH (2 × 100 mL), and 50 mL of saturated NaCl. Rotoevaporation yielded the benzoate as a sweet-smelling yellow oil (9.8 g, 95%): IR (neat) 1728 (C=O), 1549 (NO_2) cm^{-1}.

Reduction to the hydroxylamine derivative and condensation with benzaldehyde were accomplished by following the procedure used for I. The crude nitronyl ester was recrystallized from cold benzene to yield white crystals (7.12 g, 48% overall): mp 95–96 °C; NMR ($CDCl_3$) δ 8.32 (m, 2 H, C_6H_5 ortho, nitrone), 7.90 (m, 2 H, C_6H_5 ortho, ester), 7.60 (s, 1 H, vinyl), 7.40 (m, 6 H, $2C_6H_5$ 4 meta and 2 para), 4.69 (s, 2 H, CH_2O), 1.75 (s, 6 H, $2CH_3$); IR (KBr) 1732 (C=O), 1684 (C=N) cm^{-1}. Anal. Calcd for $C_{18}N_{19}NO_3$: C, 72.71; H, 6.44; N, 4.71. Found: C, 72.59; H, 6.44; N, 4.80.

Synthesis of the Dibenzoate Ester of Nitrone II. Pyridine (7.8 g, 0.10 mol) was added to 60 mL of dry benzene containing 2-methyl-2-nitro-1,3-propanediol (6.75 g, 0.05 mol) and 2 equiv of benzoyl chloride (14.5 g, 0.10 mol). The turbid solution was refluxed for 6 h, cooled, diluted with 100 mL of benzene, and extracted with 1 N HCl (2 × 100 mL), 1 N KOH (2 × 100 mL), and 100 mL of saturated NaCl. Rotoevaporation yielded a crude solid which recrystallized from ethyl acetate/petroleum ether to yield white crystals of the dibenzoate (13.2 g, 84.9%): mp 85–86 °C; NMR ($CDCl_3$) δ 8.23 (m, 4 H, $2C_6H_5$ ortho), 7.65 (m, 6 H, $2C_6H_5$ 4 meta and 2 para), 4.97 (s, 4 H, $2CH_2O$), 1.90 (s, 3 H, CH_3); IR (KBr) 1732 (intense 2C=O), 1547 (NO_2) cm^{-1}.

Reduction to the hydroxylamine derivative and condensation with benzaldehyde were accomplished by the procedure used in the preparation of I. From 10.5 g of the nitro alcohol was obtained 12.6 g (89.5%) of nitronyl ester as fine white crystals: mp 154–155 °C (ethyl acetate); NMR ($CDCl_3$) δ 8.30 (m, 2 H, C_6H_5 ortho, nitrone), 7.95 (m, 4 H, $2C_6H_5$ ortho, ester), 7.63 (s, 1 H, vinyl), 7.40 (m, 6 H, $3C_6H_5$ 2 meta and 2 para), 4.88 (m, 4 H, $2CH_2O$), 1.85 (s, 3 H, CH_3); IR (KBr) 1730 (intense C=O), 1588 (C=N) cm^{-1}. Anal. Calcd for $C_{25}H_{23}NO_5$: C, 71.93; H, 5.55; N, 3.35. Found: C, 71.88; H, 5.60; N, 3.32.

Synthesis of the Tribenzoate Ester of Nitrone III. A solution of commercial 2-hydroxymethyl-2-nitro-1,3-propanediol (3.0 g, 0.02 mol) in 50 mL of dry benzene was added to 3 equiv of benzoyl chloride (8.43 g, 0.06 mol) in dry pyridine (4.68 g, 0.06 mol). The mixture was refluxed for 3 h, cooled, washed with 100 mL of water, and extracted with 1 N HCl (2 × 50 mL), 1 N KOH (2 × 50 mL), and saturated NaCl solution. Rotoevaporation yielded a crude yellow solid which after two recrystallizations from ethyl acetate/pentane gave the tribenzoate as white crystals (2.34 g, 25%): mp 110–111 °C; NMR ($CDCl_3$) δ 8.10 (m, 6 H, $3C_6H_5$ ortho), 7.60 (m, 9 H, $3C_6H_5$ 6 meta and 3 para), 5.08 (s, 6 H, $3CH_2O$); IR (KBr) 1739 (very intense C=O), 1550 (NO_2) cm^{-1}.

Reduction to the hydroxylamine derivative was by the procedure used for I except that dioxane/water was used instead of ethanol/water. The condensation with benzaldehyde gave a white solid (1.60 g, 61%) which was recrystallized twice from ethyl acetate/pentane to yield the nitronyl ester as fine white crystals: mp 123–124 °C; NMR ($CDCl_3$) δ 8.26 (m, 2 H, C_6H_5 ortho, nitrone), 7.80 (m, 6 H, $3C_6H_5$ ortho, ester), 7.65 (s, 1 H, vinyl), 7.30 (m, 12 H, $4C_6H_5$ 8 meta and 4 para), 5.08 (s, 6 H, $3CH_2O$); IR (KBr) 1733 (intense C=O), 1593 (C=N) cm^{-1}. Anal. Calcd for $C_{31}H_{27}NO_7$: C, 70.84; H, 5.18; N, 2.67. Found: C, 70.78; H, 5.12; N, 2.61.

Synthesis of α-Phenyl-*N*-(1-hydroxy-2-propyl)nitrone (VI). This nitronyl alcohol was prepared by the same procedure used for I by starting with commercial 2-nitropropanol (5.25 g, 0.05 mol). Two recrystallizations of the crude product from ethyl acetate/petroleum ether gave pure white crystals (4.94 g, 55% overall): mp 139–140 °C; NMR ($CDCl_3$) δ 8.18 (m, 2 H, C_6H_5 ortho), 7.33 (m, 4 H, C_6H_5 2 meta and 1 para, 1 vinyl), 3.90 (m, 4 H, CH_2OH, methyne, CH_2OH), 1.31 (d, J = 10 Hz, 3 H, CH_3); IR (KBr) 3280 (OH), 1595 (C=N) cm^{-1}; UV (EtOH) λ_{max} 298 nm (ϵ_{max} ca. 15 000). Anal. Calcd for $C_{10}H_{13}NO_2$: C, 67.02; H, 7.31; N, 7.82. Found: C, 66.96; H, 7.36; N, 7.75.

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Registry No.—I, 55277-95-7; I benzoate, 63829-80-1; II, 65102-43-4; II dibenzoate, 65102-44-5; III, 65102-45-6; III tribenzoate, 65138-31-0; IV, 65102-46-7; V, 65102-47-8; V ethylene glycol acetal, 65102-48-9; VI, 63829-45-8; 2-methyl-2-nitropropanol, 76-39-1; 2-methyl-2-nitro-1,3-propanediol, 77-49-6; 2-hydroxymethyl-2-nitro-1,3-propanediol, 126-11-4; 5-methyl-5-nitro-2-hexanone, 4604-49-3; 3-methyl-3-nitrobutyl acetate, 65102-49-0; 3-methyl-3-nitrobutanol, 65102-50-3; 4-methyl-4-nitropentanal, 57620-49-2; ethylene glycol, 107-21-1; benzoyl chloride, 98-88-4; 2-nitropropanol, 2902-96-7; *p*-formaldehyde, 30525-89-4; 2-nitropropane, 79-46-9; nitroethane, 79-24-3; nitromethane, 75-52-5; benzaldehyde, 100-52-7; 2-hydroxyamino-2-methylpropanol, 4706-13-2; 2-hydroxyamino-2-methyl-1,3-propanediol, 24395-58-2; 2-hydroxyamino-2-hydroxymethyl-1,3-propanediol, 65102-51-4; 3-hydroxyamino-3-methylbutanol, 65102-52-5; 4-hydroxyamino-4-methylpentanol, 65102-53-6; 2-hydroxyaminopropanol, 39796-64-0; 2-methyl-2-nitropropyl benzoate, 65102-54-7; 2-hydroxyamino-2-methylpropyl benzoate, 63829-78-7; 2-methyl-2-nitro-1,3-propanediol dibenzoate, 65102-55-8; 2-hydroxyamino-2-methyl-1,3-propanediol dibenzoate, 65102-56-9; 2-hydroxymethyl-2-nitro-1,3-propanediol tribenzoate, 65102-57-0; 2-hydroxyamino-2-hydroxymethyl-1,3-propanediol tribenzoate, 65102-58-1.

Supplementary Material Available: Syntheses of 2-methyl-2-nitropropanol, 2-methyl-2-nitro-1,3-propanediol, and 2-hydroxymethyl-2-nitro-1,3-propanediol (1 page). Ordering information is given on any current masthead page.

References and Notes

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