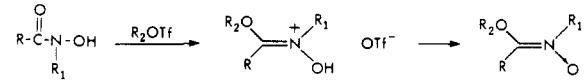
α-Heteroatom-Substituted Nitrones. Synthesis and Reactions of Acyclic α-Alkoxynitrones[1a]

James A. Warshaw, David E. Gallis,[1b] Bruce J. Acken, Orestes J. Gonzalez, and DeLanson R. Crist*

Department of Chemistry, Georgetown University, Washington, D.C. 20057

Received March 16, 1987

A general method was developed for the synthesis of acyclic α-alkoxynitrones (imidate *N*-oxides), a relatively new class of compounds. Regioselective alkylation of hydroxamic acids under neutral conditions with alkyl trifluoromethanesulfonates (triflates) gave nitrone hydrotriflates, and deprotonation by one of three methods gave the rather unstable nitrones in overall yields from 4 to 85%. A wide range of substitution was possible, with R = H, Me, or Ar, R_1 = Me or *t*-Bu, and R_2 = Me or Et. The reactivity of these nitrones toward examples



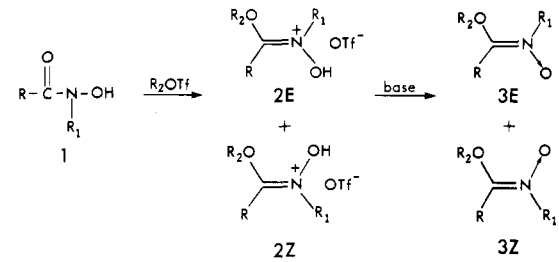
of various classes of reagents was investigated. Nitrone **3e** (R = H, R_1 = *t*-Bu, R_2 = Me), the most reactive one studied, gave the following results: (1) with nucleophiles (aniline, *n*-butylamine, thiophenol, *n*-butyl mercaptan, and potassium cyanide), substitution of the α-OMe group produced new nitrones with amino, thio, and cyano groups in the α position; (2) with a reducing agent ($NaBH_4$), *N-tert*-butylnitrone was formed; (3) with an oxidizing agent (*m*-chloroperbenzoic acid), oxidation and cleavage gave methyl formate and 2-methyl-2-nitrosopropane monomer and dimer; (4) with an electrophilic acylating agent (*p*-nitrobenzoyl chloride), methyl *p*-nitrobenzoate, *N,O*-bis(*p*-nitrobenzoyl)-*N-tert*-butylhydroxylamine, and *N-tert*-butyl-*O*-(*p*-nitrobenzoyl)hydroxylamine were produced. In parallel with the similar reactivity of aldo- and ketonitrones to ketones, the present α-alkoxynitrones undergo reactions analogous to those of esters with nucleophilic-type reagents.

Nitrones have been known for many years,[2] but interest in their chemistry has grown considerably recently, mostly due to their increasing use as synthons in cycloaddition reactions[3] and natural product synthesis[4] and as radical spin traps.[5]

Nitrones with α-heteroatom substitution, however, have remained a little-studied class of compounds. In particular, only a few nonheterocyclic α-alkoxynitrones (or imidate *N*-oxides) have been reported, notably cyclic nitrones[6] which undergo reactions with organometallic reagents[6b] and are useful as spin labels.[6]

Recently, Ashburn and Coates reported the first synthesis of an acyclic α-alkoxynitrone, α-ethoxy-α-phenyl-*N*-methylnitrone, prepared by condensation of benzamide acetal with *N*-methylhydroxylamine hydrochloride.[7] We had previously identified two *N-tert*-butyl examples (R = H, Ph) from the ring opening[8a] of 3-methoxyoxaziridines.[8b] The only known reactions of these compounds are cycloaddition[7] with acetylenedicarboxylate and phenyl isocyanate and a "transesterification" reaction[8a] with alcohol.

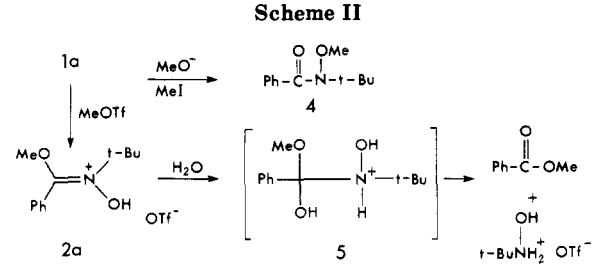
Scheme I



1a: R = Ph; R_1 = *t*-Bu
b: R = *p*-$MeOC_6H_4$; R_1 = *t*-Bu
c: R = *p*-$NO_2C_6H_4$; R^1 = *t*-Bu
d: R = Me; R^1 = *t*-Bu
e: R = H; R_1 = *t*-Bu
f: R = Ph; R_1 = Me

2, 3a: R = Ph; R_1 = *t*-Bu; R_2 = Me
b: R = *p*-$MeOC_6H_4$; R_1 = *t*-Bu; R_2 = Me
c: R = *p*-$NO_2C_6H_4$; R_1 = *t*-Bu; R_2 = Me
d: R = CH_3; R_1 = *t*-Bu; R_2 = Me
e: R = H; R_1 = *t*-Bu; R_2 = Me
f: R = Ph; R_1 = Me; R_2 = Me
g: R = Ph; R_1 = *t*-Bu; R_2 = Et
h: R = Ph; R_1 = Me; R_2 = Et

Scheme II



(1) (a) Taken, in part, from the Ph.D. Dissertation of J. A. Warshaw, Georgetown University, 1987. (b) Present address: Environmental Resources Management, Inc., Exton, PA 19341.

(2) (a) Smith, L. I. *Chem. Rev.* **1938**, 193-285. (b) Hamer, J.; Macaluso, A. *Chem. Rev.* **1964**, *19*, 473-495. (c) Delpierre, G. R.; Lamchen, M. *Q. Rev.* **1965**, 329-349. (d) Breuer, E. In *The Chemistry of Amino, Nitroso and Nitro Compounds and Their Derivatives*; Patai, S., Ed.; Wiley: Chichester, West Sussex, 1982; Part I, pp 459-564. (e) Stamm, H. In *Methodicum Chimicum*; Korte, F., Ed.; Academic: New York, 1975; Vol. 6, pp 329-401.

(3) (a) Black, D. S. C.; Crozier, R. F.; Davis, V. C. *Synthesis* **1975**, 205-221. (b) Tufariello, J. J. In *1,3-Dipolar Cycloaddition Chemistry*; Padwa, A., Ed.; Wiley: New York, 1984; Vol. 2, pp 83-168. (c) Padwa, A. *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 123-136. (d) Oppolzer, W. *Angew. Chem., Int. Ed. Engl.* **1977**, *16*, 10-23. (e) Balasubramanian, N. *Org. Prep. Proc. Int.* **1985**, *17*, 23-47.

(4) Tufariello, J. J. *Acc. Chem. Res.* **1979**, *12*, 396-403.

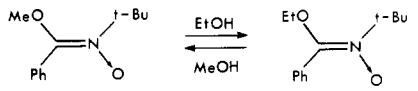
(5) Janzen, E. G. *Acc. Chem. Res.* **1971**, *4*, 31-40.

(6) (a) Keana, J. F. W.; Lee, T. D. *J. Am. Chem. Soc.* **1975**, *97*, 1273-1274. (b) Lee, T. D.; Keana, J. F. W. *J. Org. Chem.* **1976**, *41*, 3237-3241.

(7) Ashburn, S. P.; Coates, R. M. *J. Org. Chem.* **1985**, *50*, 3076-3081.

(8) (a) Gonzalez, O. J. Ph.D. Dissertation, Georgetown University, 1981. (b) Gonzalez, O. J.; Gallis, D. E.; Crist, D. R. *J. Org. Chem.* **1986**, *51*, 3266-3270. See ref 37 of the present work for the first synthesis of this type of oxaziridine.

0022-3263/89/1954-1736$01.50/0



We now report a new synthesis of acyclic α-alkoxynitrones and exploratory reactions with examples of other main classes of reagents: amines, mercaptans, and cyanide as nucleophiles, *p*-nitrobenzoyl chloride as an electrophile, *m*-chloroperbenzoic acid (MCPBA) as an oxidizing agent, sodium borohydride as a reducing agent, and phenylmagnesium bromide as an organometallic reagent. In addition to providing insight into the reactivity of the nitrone–α-alkoxy combination, several new α-heteroatom-substituted nitrones were discovered.

Results and Discussion

A general method of synthesizing α-alkoxynitrones from hydroxamic acids was developed as outlined in Scheme I, where alkylation with methyl or ethyl trifluoromethanesulfonate (triflate or OTf) produced the nitrone hydrotriflate, and deprotonation gave the nitrone. Examples include derivatives of aldo-(R = H) and ketonitrones (R = Me, Ph) with steric extremes of *N*-substitution (R_1 = Me, *t*-Bu).

Regioselective Alkylation. Alkylations of N-substituted hydroxamic acids under basic conditions occur at the OH group via the more nucleophilic hydroxamate anion, and in fact **1a** with methyl iodide in the presence of sodium methoxide gave **4** (see Scheme II). The only previously reported alkylation of a hydroxamic acid under neutral conditions[9] was one utilizing diazomethane, which reacted at the carbonyl oxygen. For these reasons, alkylations were carried out in neutral media where the less reactive carbonyl oxygen might be more competitive as a nucleophile. After this work was completed Coates and Firsan reported that neutral alkylation of *thio*hydroxamic acids occurred at the sulfur atom.[10]

Alkylation of **1a** with the very reactive methyl triflate in methylene chloride gave **2a** in 95% yield. Spectroscopic evidence for **2a** includes downfield shifts of *tert*-butyl and phenyl protons relative to **1a** and IR absorptions at 3500–2500 cm^{-1} (OH) and 1619 cm^{-1} (C=N^+), which is significantly higher than the 1584 cm^{-1} C=O stretch of **1a**. Although somewhat lower than C=N^+ stretches for corresponding *N,N*-diethyl[11] (1640 cm^{-1}) and *N*-ethyl[12] (1658 cm^{-1}) imidate salts, the absorption in the 1619 cm^{-1} region for **2a** compares favorably with results for other hydrotriflates (1626 cm^{-1} for **2d** and 1682 cm^{-1} for **2e**). Indeed, the effect of substitution on $\nu_{C=N^+}$ of these compounds (α-H > α-Me > α-Ph) is the same as the well-known trend in $\nu_{C=O}$ with aldehydes > aliphatic ketones > aromatic ketones.[13] Finally, deprotonation of **2a** gave a neutral material with spectral properties markedly different from those of **4**, as discussed below.

Structure **2a** was confirmed by chemical degradation. Hydrolysis in CD_3CN gave methyl benzoate and *N-tert*-butylhydroxylamine hydrotriflate quantitatively. These are expected products from breakdown of tetrahedral intermediate **5** shown in Scheme II, while isomers of **2a** would have given *N-tert*-butylhydroxylamine bearing also an *N*- or *O*-methyl group. Loss of MeO^- from **5** to produce MeOH and **1a** was not observed, presumably because the protonated N group[14] would be a better leaving group than MeO^-.[15] Other positive-charged substrates such as α-ethoxy iminium salts[16] also show this preference for cleavage under neutral hydrolysis.

Alkylation at the carbonyl oxygen of **1** (instead of N to give a protonated amine oxide) is thus analogous to reactions of amides with trialkyloxonium tetrafluoroborates,[17] dialkyl sulfates,[18] carboxonium ions,[19] alkyl fluorosulfonates,[20] and alkyl trifluoromethanesulfonates.[21] For amides, MO calculations have shown that the highest electron density is at the carbonyl oxygen.[17]

Other hydroxamic acids underwent similar alkylations. Configuration isomers were observed for **2b** in $CDCl_3$ at room temperature where a 3:1 *E:Z* ratio was present on the basis of NOE assignments.[22] Except for the *N*-methyl derivatives **2f** and **2h**, which showed a complex mixture, all other nitrone hydrotriflates exhibited only one alkoxy NMR signal under these conditions. NOE experiments showed that the signals for **2e** corresponded to the *Z* isomer.

Nitrone Formation. The formation of nitrones **3** was accomplished by deprotonation by three methods: (1) silica gel preparative thin layer chromatography (TLC) with a 9/1 (v/v), CH_2Cl_2/MeOH mobile phase, (2) reaction with triethylamine in either $CDCl_3$ or CH_2Cl_2, or (3) treatment with the free base form of a weakly basic anion exchange resin. Yields for the formation of **3a** were 74%, 85%, and 58% for these methods, respectively.

Evidence for nitrone formation consisted of ^1H NMR, ^{13}C NMR, IR, UV, and mass spectral data. The ^1H NMR of **3a** displayed *tert*-butyl and methoxy signals at 1.62 ppm and 3.63 ppm, respectively. These values were upfield from the corresponding signals of the hydrotriflate (1.71 and 4.00 ppm) due to higher electron density provided by the nitrone oxygen and different from those for the *N*-O-CH_3 isomer **4** (1.56 and 3.37 ppm). The aromatic region, with multiplets at ca. 7.4 (3 H) and 7.9 (2 H) ppm, was different from that of the hydrotriflate (singlet at 7.6 ppm) and resembled that for α-phenyl-*N-tert*-butylnitrone.

The ^{13}C NMR of **3a** showed, in addition to aromatic signals, characteristic *tert*-butyl signals at 27.7 (CH_3) and 70.4 (quaternary carbon) ppm, an *O*-methyl signal at 59.5 ppm, and an α-carbon signal at 152.1 ppm, which is considerably downfield from that of aldonitrones due to the electronegativity of the methoxy oxygen.

The strongest band in the IR of **3a**, assigned to the N–O stretch, which apparently can occur over a wide range from 1070 to 1280 cm^{-1},[2e] was at 1184 cm^{-1} in $CDCl_3$, and there was no absorption in the 1500–1600 cm^{-1} region. This is directly comparable to the spectrum of α-phenyl-*N-tert*-

(9) Shchukin, G. I.; Volodarski, L. B. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1979**, *28*, 228; *Engl. Ed.* **1979**, *28*, 214–217.
(10) Coates, R. M.; Firsan, S. J. *J. Org. Chem.* **1986**, *51*, 5198–5209.
(11) Merenyi, R. In *Imminium Salts in Organic Chemistry*; Bohme, H., Viehe, H. G., Eds.; Wiley: New York, 1976; Part I, pp 23–105.
(12) Pilotti, A.; Reuterhall, A.; Torssell, K. *Acta Chem. Scand.* **1969**, *23*, 818–824.
(13) Silverstein, R. M.; Bassler, G. C.; Morril, T. C. *Spectromeric Identification of Organic Compounds*, 4th ed.; Wiley: New York, 1981; pp 95–180.
(14) The estimated acidities of O-protonated (Gunthrie, J. P. *J. Am. Chem. Soc.* **1978**, *100*, 5892–5904) vs N-protonated (Rosenberg, S.; Silver, S. M.; Sayer, J. M.; Jencks, W. P. *J. Am. Chem. Soc.* **1974**, *96*, 7986–7998) tetrahedral intermediates lead to the conclusion that the N-protonated form would be favored by about 4 orders of magnitude.
(15) Lowry, T. H.; Richardson, K. S. In *Mechanism and Theory in Organic Chemistry*; Harper and Row: New York, 1976; pp 170–212.
(16) Deslongchamps, P.; Taillfefer, R. J. *Can. J. Chem.* **1975**, *53*, 3029–3037.
(17) Kantlehner, W. In *Imminium Salts in Organic Chemistry*; Bohme, H., Viehe, H. G., Eds.; Wiley: New York, 1979; Part 2, pp 181–277.
(18) Bredereck, H.; Gomper, R.; Rempfer, H.; Klemm, K.; Keck, H. *Chem. Ber.* **1959**, *92*, 329–337.
(19) Kabuss, K. *Angew. Chem., Int. Ed. Engl.* **1966**, *5*, 675–676.
(20) Ahmed, M. G.; Alder, R. W.; James, G. H.; Sinnott, M. L.; Whiting, M. C. *Chem. Commun.* **1968**, *32*, 1533–1534.
(21) Arnarp, J.; Lonngren, J. *Acta Chem. Scand. B* **1978**, *32*, 465–467.
(22) Gallis, D. E. Unpublished work.

Table I. Nucleophilic Substitution Products YHC=N(O)-*t*-Bu from α-Methoxynitrone 3e

Y	yield, %	NMR shifts, ppm α-H	NMR shifts, ppm α-C(CH_3)	NMR shifts, ppm α-C	M^+, m/z	$\nu_{C=N}$, cm^{-1}
PhNH	24	8.0	1.54		192	1642
n-BuN	25	7.24	1.44	136.97	172	1670
PhS	28	7.49	1.53		209	
n-BuS	86	7.38	1.51	133.74	189	1545
CN	80	6.85	1.55		126	1659
						1527

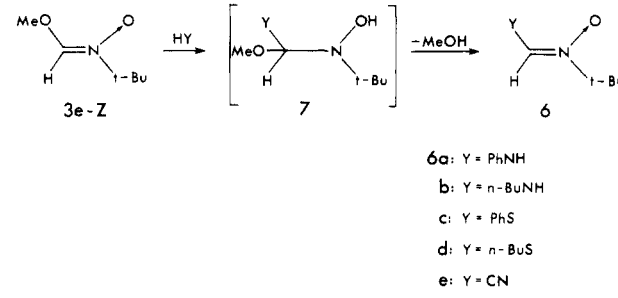
butylnitrone, which had the largest band at 1131 cm^{-1} in CCl_4 and also was transparent in the normal C=N region of nitrones. This lack of C=N absorption may be a consequence of the *N-tert*-butyl group, since **3h** shows medium absorption at 1603 cm^{-1} as previously reported.[7] In contrast, the IR of isomeric **4** shows strongest absorption at 1651 cm^{-1} assigned to the amide carbonyl stretch. The UV spectrum at **3a**, with λ_{max} = 321 nm (ϵ = 11 000) in benzene, was similar to that of α-phenyl-*N-tert*-butylnitrone (λ_{max} = 301 nm, ϵ = 17 000). The mass spectrum of **3a** showed a molecular ion at m/z 207, a base peak corresponding to the loss of *tert*-butyl radical, and a second most intense peak rationalized as the phenylacylium ion. Accurate mass analysis confirmed the molecular formula.

As final confirmation of the structure of **3a**, it was found that the ^1H NMR spectrum of this material was the same as that obtained by treatment of 2-*tert*-butyl-3-methoxy-3-phenyloxaziridine in methanol at 5 °C. Such a ring opening is a well-known thermal reaction for oxaziridines,[23] although higher temperatures are usually required.

Attempts to prepare **3a** in larger scale by flash chromatography[24] of **2a** on silica gel were unsuccessful. From the resulting complex mixture, only methyl benzoate could be identified. Two decomposition pathways were suggested by following the ^1H NMR of a solution of **3** in $CDCl_3$ at 25 °C, one of which was hydrolysis, giving methyl benzoate and *N-tert*-butylhydroxylamine. After 62 h, only 10% of the nitrone remained. Similar decomposition results were obtained for **3g**. In the case of **3e**, the nitrone could not be isolated by TLC and therefore was generated in situ by deprotonation with triethylamine. In general, yields of *N-tert*-butylnitrones were greater than those of *N*-methylnitrones with the exception of **3c**. In all cases the spectral data were analogous to those for **3a**. The ^1H NMR of **3e** was the same as that of material obtained by treatment of 2-*tert*-butyl-3-methoxyoxaziridine with methanol at 60 °C.

Configuration isomers were observed for *N*-methylnitrone **3f**, and the *E*/*Z* isomers could be separated by preparative TLC. The ^1H NMR of material from each band taken after 30 min in $CDCl_3$ at room temperature displayed four singlets (two per isomer) in the region between 3.40 to 4.00 ppm. These singlets correspond to two pairs of *N*-methyl and *O*-methyl signals for **3f**. Further, the ratio of isomers from both bands was 1.8/1 on the basis of integration of *N*-methyl signals[7] at 3.83 and 3.51 ppm, respectively. Consequently, the isolation of either nitrone isomer results in equilibration with the other isomer. Similar equilibration results were observed for **3h** and as previously reported.[7] All *N-tert*-butylnitrones, on the other hand, showed only one signal for *O*-methyl and one signal for *N-tert*-butyl protons in $CDCl_3$ at room temperature. NOE experiments showed that **3a**, **3b**, and **3c** exist exclusively in the *E* configuration in $CDCl_3$,[22] while **3e** exclusively as the *Z* isomer.

Scheme III



Reactions of α-Methoxy-*N-tert*-butylnitrones. Preliminary screening results for α-methoxynitrones with various test nucleophiles showed a reactivity order of α-H (**3e**) > α-Ph (**3a**). Thus, while substitution reactions occurred readily for **3e** as discussed below, **3a** was unreactive despite longer reaction times, and higher temperatures led to its decomposition. For these reasons, reactions of **3e**, generated in situ from the hydrotriflate with triethylamine, with nucleophiles and other reagents were investigated in more detail.

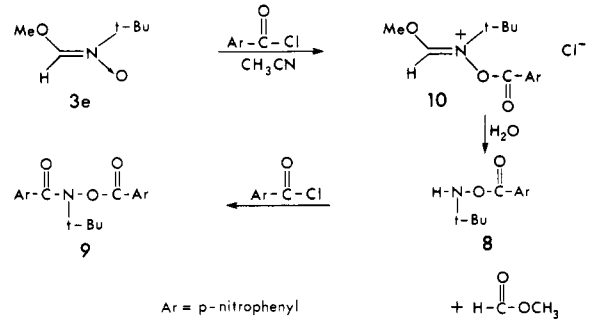
With aniline, *n*-butylamine, thiophenol, *n*-butyl mercaptan, and cyanide as nucleophiles, **3e** gave substitution products **6** (see Scheme III). Yields for these reactions, carried out in acetonitrile at ambient temperature ranged from 24 to 86%. Products are assumed to have the *Z* configuration based on their structural similarity to **3e**.

Evidence for this type of product lies in consistent ^1H NMR, mass spectra, and IR data as summarized in Table I. For example, **6a** shows very strong IR absorption at 1642 cm^{-1} (C=N), which is comparable to that of 1653 cm^{-1} for an *N*-phenylamidine,[25] as well as at 3315 and 1097 cm^{-1} assigned to N–H and to N–O, respectively. The ^1H NMR of **6a** displays signals at 1.54 ppm (singlet, 9 H, N-*t*-Bu), 7.05–7.32 ppm (multiplet, 5 H, Ar H) and 7.99 ppm (singlet, 1 H, N=CH). The mass spectrum gives a molecular ion at m/z 192 and a base peak at m/z 119, which has been assigned to the $PhNH^+C{=}NH$ ion. The present displacement of methoxide by aniline is directly analogous to the reaction of *p*-toluidine with ethyl *N*-phenylformimidate to give an amidine in a substitution reaction.[26]

Mercapto-substituted nitrones **6c,d**, formed in 28% and 86% yields, respectively, both showed strong absorbance at ca. 1115 cm^{-1}, which was assigned to the N–O stretch.[2e] For **6d**, IR absorbances at 3080 (α-C—H) and 1545 cm^{-1} (C=N) were also observed, and the chemical shift of SCH_2 protons occurred at 2.79 ppm comparable to values of 2.2–2.4 ppm reported for the *E*/*Z* isomers of methyl *N*-ethylthioacetimidate.[27] The ^{13}C NMR of **6d** showed expected signals with the α-carbon occurring at 133.74 ppm. Both **6c** and **6d** displayed characteristic α-H signals at ca. 7.4 ppm and molecular ions in their MS, with base peaks

(23) Emmons, W. D. *J. Am. Chem. Soc.* **1957**, *79*, 5739–5754.
(24) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923–2925.
(25) Leplawy, M. T.; Jones, D. S.; Kenner, G. W.; Sheppard, R. C. *Tetrahedron* **1960**, *11*, 39–51.
(26) Roberts, R. M. *J. Am. Chem. Soc.* **1950**, *72*, 3603–3608.
(27) Fodor, G.; Philips, B. A. In *The Chemistry of Amidines and Imidates*; Patai, S., Ed.; Wiley: New York, 1975; pp 85–156.

Scheme IV



at m/z 57 corresponding to *tert*-butyl ion. Spectral data for **6d** compare reasonably with those reported[10] for α-(ethylthio)-α-phenyl-*N*-methylnitrone, which showed C=N$^+$ IR absorption at 1560 cm^{-1}, SCH_2 protons at 2.30 ppm, and an α-^{13}C signal at 149.55 ppm.

Cyano-substituted nitrone **6e**, formed in 80% yield, showed IR absorbances at 3157, 2223, and 1263 cm^{-1}, which were assigned to α-C—H, C≡N, and N—O stretches, respectively. These absorbances are similar to those observed for α-isopropyl-*N*-(α-cyanopropyl)nitrone.[28] The ^{1}H NMR of **6e** exhibited singlets at 1.55 ppm (9 H, *N*-*t*-Bu) and 6.85 ppm (1 H, α-C–H), and the mass spectrum showed a parent ion and base peak due to *tert*-butyl ion.

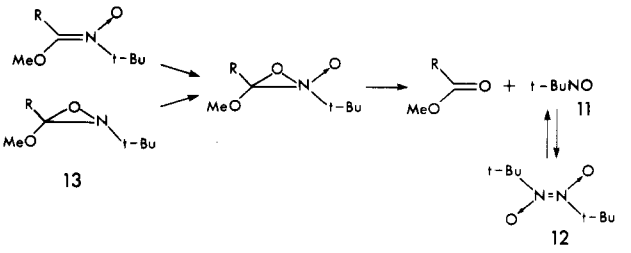
The reaction with mercaptans is of special interest, since the products with an α-thio group are new examples of a recently discovered family of nitrones. After the completion of the present work, Coates and Firsan reported the first in-depth study[10,29] of a synthesis and characterization of this class of nitrones. Their examples, prepared by alkylation of thiohydroxamic acids followed by deprotonation, included *N*-methyl, *N*-ethyl, and *N*-isopropyl derivatives, all with α-alkyl or α-phenyl groups. Previous to their work, the only reported examples, to our knowledge, contained *N*-benzyl[30a] or α-amido groups.[30b] With regard to other products in the present study, although other α-amino[31] and α-cyano nitrones[32] are known, the specific examples **6a**, **6b**, and **6e** in the present study are previously unreported.

Nucleophilic displacement of alkoxide in α-alkoxynitrones is directly analogous to nucleophilic substitution reactions of esters, and consequently we propose an addition–elimination mechanism[33] via intermediate **7** (Scheme III). The well-known similar reactivity of nitrones to ketones therefore has a parallel similarity of α-alkoxynitrones to esters, as first indicated by the "transesterification" reaction.[8a]

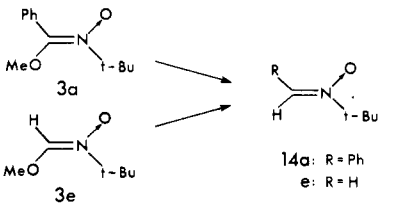
With *p*-nitrobenzoyl chloride as an electrophilic reagent, nitrone **3e** gave acylated products **8** (38%) and **9** (29%) after chromatography (Scheme IV, Ar = *p*-nitrophenyl).

The IR of **8** exhibited very strong absorption at 1724 cm^{-1}, which corresponds to the ester carbonyl group, and a ^{1}H NMR spectrum with a singlet at 1.26 ppm (*t*-Bu) and an AB system (4 H) from 8.18 to 8.34 ppm. The IR of **9** showed strong absorptions at both 1774 and 1661 cm^{-1}, corresponding to ester and amide carbonyl groups, respectively, and a consistent ^{1}H NMR spectrum.

Scheme V



Scheme VI



These acylated products probably arose from further reactions of **10**, which would be formed by electrophilic attack at the nitrone oxygen. One would expect **10** to be very susceptible to hydrolysis,[34] which would give **8** in the presence of adventitious moisture. In a similar reaction, α-phenyl-*N*-*tert*-butylnitrone was reported[34] to give **8** and benzaldehyde on treatment with *p*-nitrobenzoyl chloride in moist acetone.

3a was treated with 1.4 equiv of MCPBA in $CDCl_3$ to investigate the behavior of α-alkoxynitrones with oxidizing agents. After 4 min at room temperature the ^{1}H NMR spectrum showed the absence of **3a** and the appearance of new signals due to methyl benzoate (85%), 2-methyl-2-nitrosopropane **11** (56%), and nitroso dimer **12** (6%) (Scheme V, R = Ph). At longer times, the ratio of dimer to monomer increased due to equilibration,[35] which was observed in a separate experiment with independently synthesized[36] **12**.

A similar result was found for the oxidation of **3e**. After 25 min the ^{1}H NMR spectrum showed the absence of nitrone and the presence of methyl formate (64%), 2-methyl-2-nitrosopropane (70%), and the nitroso dimer (9%). These were the same products reported[37] for the oxidation of 2-*tert*-butyl-3-methoxyoxaziridine (**13**) (Scheme V, R = H) by MCPBA in methylene chloride. It seems reasonable that the present oxidation proceeds through the same alkoxyoxaziridine *N*-oxide previously postulated.[37]

Reduction of α-alkoxynitrones with sodium borohydride was found to give the corresponding nitrones as shown in Scheme VI. For **3a**, prepared in situ by deprotonation of the hydrotriflate, reaction with 4.6 equiv of borohydride gave α-phenyl-*N*-*tert*-butylnitrone (**14a**) in 30% yield after chromatography. The structure was determined by comparison of IR and ^{1}H NMR spectra to those of authentic material. Similarly, **3e** gave nitrone **14e** in 17% yield by comparison of the ^{1}H NMR spectrum of crude product

(28) Masui, M.; Yijima, C. *J. Chem. Soc. C* **1967**, 2022–2023.
(29) In footnote 4 in ref 7, mention is made of methyl *N*-methylbenzenecarboximidothioate *N*-oxide.
(30) (a) Kerr, D. A.; Wilson, D. A. *J. Chem. Soc. C* **1970**, 1718–1725. (b) Pennings, M. L. M.; Reinhoudt, D. N. *J. Org. Chem.* **1982**, *47*, 1816–1823.
(31) (a) Aurich, H. G. *Chem. Ber.* **1965**, *98*, 3917–3923. (b) Aurich, H. G.; Baer, F. *Tetrahedron Lett.* **1965**, 2517–2520. (c) Aurich, H. G.; Wabmuth, G. *Liebigs Ann. Chem.* **1975**, 1307–1316.
(32) (a) Bonnett, R.; Brown, R. F. C.; Clark, V. M.; Sutherland, I. O.; Todd, A. R. *J. Chem. Soc.* **1959**, 2094–2102. (b) Barrow, F.; Thorneycroft, F. J. *J. Chem. Soc.* **1939**, 769–773.
(33) Koskikallio, J. In *The Chemistry of Carboxylic Acids and Esters*; Patai, S., Ed.; Wiley: New York, 1969; p 103.
(34) Heistand, R. H.; Stahl, M. A.; Heine, H. W. *J. Org. Chem.* **1978**, *43*, 3613–3615.
(35) Stowell, J. C. *J. Org. Chem.* **1971**, *36*, 3055–3056.
(36) Calder, A.; Forrester, A. R.; Hepburn, S. P. *Org. Synth.* **1972**, *52*, 77–82.
(37) Aue, D. A.; Thomas, D. *J. Org. Chem.* **1974**, *39*, 3855–3862.

with that of **14e** prepared independently.[38]

These reductions, which can be viewed as hydride displacements of methoxide, seem analogous to the nucleophilic displacements described above and to the probable first step in reduction of ethyl *N*-ethylbenzimidate with $NaBH_4$.[39]

In a preliminary experiment with a typical organometallic reagent, **3e** was formed in the presence of excess phenylmagnesium bromide. Of the seven products detected by *TLC*, five were isolated by flash chromatography. These were identified as benzhydrol (9%), α-phenyl-*N*-*tert*-butylnitrone (**14a**) (1%), *N*-*tert*-butyldiphenylmethanimine (1.5%), benzophenone, and an appreciable quantity of phenol attributed to oxidation of the Grignard reagent. Of special interest is the nitrone, which was probably formed in the same manner as nucleophilic substitution products **6** and analogous to the reaction of cyclic α-alkoxynitrones.[6]

As shown in Scheme VI this nitrone **14a** is a common product from two different α-methoxynitrones treated with either borohydride or phenyl Grignard reagent. It is also probably the precursor of the imine, formed by addition of phenyl anion[40] and then loss of MgBrOH.[41] Benzophenone could arise from hydrolysis of the imine, and the carbinol from Grignard addition to methyl formate possibly present as an impurity in the starting material. Phenol most likely is produced by air oxidation of the Grignard reagent.[42] Reaction of **2e** with phenyllithium gave **14a** in higher yield (20%), but this reaction unfortunately was not reproducible.

Experimental Section

Instrumentation. ^1H and ^{13}C NMR spectra were run at 300 or 75.47 MHz, respectively. IR spectra of nitrones were obtained on a Nicolet 7000 Series Fourier transform spectrometer in a Beckman 12-mm liquid cell with solvent absorptions subtracted. All melting points are uncorrected.

Chromatography. Preparative TLC was done by eluting 0.5-mm silica gel plates (60-F-254, Merck, EM Reagents) with 9/1 (v/v) CH_2Cl_2/MeOH. Flash chromatography was done on silica gel (60–200 μm, Baker), silica Woelm (32–64 μm, Universal Scientific), or Kieselgel 60, (40–63 μm, Merck EM Reagents) at 10–20 psi nitrogen pressure. Analytical TLC was done on 0.25-mm silica gel plates (60-F-254, Merck, EM Reagents) and these R_f values are given with spectral data.

Materials. Hydroxamic Acids. *N*-Hydroxy-*N*-(1,1-dimethylethyl)benzamide (**1a**) was prepared[43] from *N*-*tert*-butylhydroxylamine hydrochloride:[36,43] mp 112–114 °C (lit.[43] mp 113 °C); IR ($CHCl_3$) 3239 (br), 1584 (s), 1464 (m), 1365 (vs), 1076 (w) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.31 (s, 9 H, N-*t*-Bu), 7.41 (s, 5 H, Ar*H*); MS (70 eV), *m/z* (rel intensity) 193 (1.0, M^+), 105 (100), 77 (32).

N-Hydroxy-*N*-(1,1-dimethylethyl)-4-methoxybenzamide (**1b**) was prepared[44] from *N*-*tert*-butylhydroxylamine:[45] mp 113–115 °C (lit.[46] mp 113–114 °C); IR ($CHCl_3$) 3253 (br), 1612 (vs), 1464 (m), 1365 (s), 1175 (w) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.32 (s, 9 H, N-*t*-Bu), 3.83 (s, 3 H, OCH_3), 6.80–7.50 (m, 4 H, Ar*H*), 8.01 (s, 1 H, O*H*).

N-Hydroxy-*N*-(1,1-dimethylethyl)-4-nitrobenzamide (**1c**) was prepared[44] from *tert*-butylhydroxylamine:[45] mp 138–142 °C (lit.[47] mp 142 °C); IR ($CHCl_3$) 3181 (br), 1640 (m), 1605 (s), 1344 (vs), 1105 (w), cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.40 (s, 9 H, N-*t*-Bu), 7.60–7.65 (d, 2 H, Ar*H*), 8.20–8.27 (d, 2 H, Ar*H*).

N-Hydroxy-*N*-(1,1-dimethylethyl)ethanamide (**1d**) was prepared[44] from *N*-*tert*-butylhydroxylamine[45] as an oil of >95% purity: IR ($CHCl_3$) 3274 (br), 1654 (vs), 1457 (m), 1379 (s), 1365 (s), 1098 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.47 (s, 9 H, N-*t*-Bu), 2.20 (s, 3 H, CH_3).

N-Hydroxy-*N*-(1,1-dimethylethyl)methanamide (**1e**) was prepared[48] from *N*-*tert*-butylhydroxylamine.[45] Flash chromatography with 97:3 CH_2Cl_2–MeOH and sublimation at 25 °C (1 Torr) gave the product in 16% yield: mp 61–63 °C (lit.[48] mp 60 °C); IR (CCl_4) 3394–2633 (br), 1661 (vs), 1372 (s), 1351 (s), 1083 (m), 1034 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.43 (s, 9 H, N-*t*-Bu), 8.11 (s, 1 H, O=C*H*).

N-Hydroxy-*N*-methylbenzamide (**1f**) was prepared[49] from *N*-methylhydroxylamine hydrochloride as an oil of >95% purity by NMR: TLC R_f 0.79 (16:1, CH_2Cl_2–MeOH); IR ($CHCl_3$) 3260 (br), 1619 (vs), 1577 (s), 1457 (m), 1386 (m), 1372 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.41 (s, 3 H, NCH_3), 7.25–7.60 (m, 5 H, Ar*H*).

General Procedure for Preparation of α-Alkoxynitrones. To a solution of the hydroxamic acid in P_2O_5-dried CH_2Cl_2 was added a 20% molar excess of methyl or ethyl triflate. After standing at room temperature for several days, the solvent and excess alkylating agent were removed in vacuo to yield the crude nitrone hydrotriflate. Generation of the free nitrone was accomplished by three methods. **Method 1 (Preparative TLC).** A solution of crude **2** in CH_2Cl_2 was chromatographed, and then the nitrone band was scraped from the plate and extracted into dry MeOH. After evaporation of solvent under a stream of dry argon or nitrogen at 0 °C, the nitrone was dissolved in the appropriate solvent for further work. **Method 2 (Triethylamine).** To a solution of the nitrone hydrotriflate in either CH_2Cl_2, $CDCl_3$, MeCN, or MeOH was added a 20% molar excess of BaO-dried triethylamine. **Method 3 (Resin).** The free base form (19 equiv) of the weakly basic anion exchange resin Bio-rad AG3-X4 was added to dry MeOH and the resulting heterogeneous mixture stirred for 5 min. To this slurry was added the nitrone hydrotriflate and stirring was continued for 5 min. Removal of resin by filtration gave a solution of the nitrone in MeOH.

All nitrones in the present study, with the exception of **6d**, were too unstable for elemental analysis. For example, neat samples of **3a** decomposed rapidly at room temperature, **3e** could not be isolated by TLC, and attempts at recrystallization of the somewhat more stable nitrones **6** were unsuccessful. Consequently, molecular formulas were determined by accurate mass measurements on pure samples (by TLC, proton NMR).

Methyl *N*-(1,1-dimethylethyl)benzenecarboximidate *N*-oxide (**3a**) was prepared from **1a** (5.1 g, 0.026 mol) and methyl triflate (5.2 g, 0.032 mol) in 65 mL of CH_2Cl_2. After 48 h, product workup gave 9.0 g (95%) of **2a** as a white solid, 97% pure by NMR. A small quantity was further purified by extensive washing under nitrogen with CCl_4: mp 45–50 °C; IR ($CHCl_3$) 3500–2500 (br), 1619 (vs), 1302 (s), 1154 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.71 (s, 9 H, N-*t*-Bu), 4.00 (s, 3 H, OCH_3), 7.62–7.67 (s, 5 H, Ar*H*). Deprotonation (method 1) of 0.17 g (97%, 0.46 mmol) of **2a** produced the **3a** nitrone band at R_f 0.61, 98% pure by NMR: IR ($CDCl_3$) 1600 (w), 1445 (m), 1339 (s), 1223 (m), 1212 (m), 1184 (vs) cm^{-1}; ^1H NMR *E* isomer ($CDCl_3$) δ 1.63 (s, 9 H, N-*t*-Bu), 3.63 (s, 3 H, OCH_3), 7.37–7.47 (m, 3 H, Ar*H*), 7.87–7.93 (m, 2 H, Ar*H*); ^{13}C NMR ($CDCl_3$) δ 27.7 ($C(CH_3)_3$), 59.5 (OCH_3), 70.4 ($C(CH_3)_3$), 127.8, 128.1, 129.3, 130.0 (Ar), 152.1 (C=N); UV (benzene, 0.01 M) λ_{max} 321 nm (ε 11 000); MS (70 eV), *m/z* (rel intensity) 207 (32.9, M^+), 151 (69.7), 150 (100.0), 105 (93.2), 104 (73.3), 77 (74.0), 57 (66.4); molecular ion calcd for $C_{12}H_{17}NO_2$ *m/z* 207.1259, found 207.1269; MS(CI) 209 (4.1, M + 2), 208 (30.6, M + 1); R_f 0.64 (16:1, CH_2Cl_2–MeOH). For yield calculations 2.0 μL of CaH_2-dried toluene as an internal standard was added to the above solution of the nitrone in $CDCl_3$. Integration showed the yield of the nitrone to be 78% with respect to the hydrotriflate salt and 74%

(38) Druelinger, M. L.; Shelton, R. W.; Lammert, S. R. *J. Heterocycl. Chem.* **1976**, *13*, 1001–1007.
(39) Borch, R. F. *Tetrahedron Lett.* **1968**, 61–65.
(40) Janzen, E. G.; Blackburn, B. J. *J. Am. Chem. Soc.* **1969**, *91*, 4481–4490.
(41) Singh, N.; Mohan, S. *Chem. Commun.* **1969**, 868.
(42) Hock, H.; Kropf, H.; Ernst, F. *Angew. Chem.* **1959**, *71*, 541–545.
(43) Exner, O.; Kakac, B. *Collect. Czech. Chem. Commun.* **1963**, *28*, 1656–1663.
(44) Uchida, Y.; Hashimoto, Y.; Kozuka, S. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 2309–2314.
(45) Green, F. D.; Pazos, J. F. *J. Org. Chem.* **1969**, *34*, 2269–2274.
(46) Alewood, P. F.; Hussain, S. A.; Jenkins, T. C.; Perkins, M. J.; Sharma, A. H.; Siew, N. P. Y.; Ward, P. *J. Chem. Soc., Perkin Trans. I* **1978**, 1066–1076.
(47) Exner, O.; Holubek, J. *Collect. Czech. Chem. Commun.* **1965**, *30*, 940–951.
(48) Aurich, H. G.; Trosken, J. *Chem. Ber.* **1973**, *106*, 3483–3494.
(49) Plapinger, R. E. *J. Org. Chem.* **1959**, *24*, 802–804.

with respect to **1a**. Deprotonation (method 2) of 26.0 mg (97%, 0.072 mmol) of **2a** in 1 mL of $CDCl_3$ yielded the nitrone in 85% yield with respect to **1a**. Also present were triethylammonium triflate, methyl benzoate (15%), and *N*-*tert*-butylhydroxylamine (15%). Deprotonation (method 3) was also accomplished by adding 0.25 g of the resin to 3.0 mL of MeOH with stirring. After stirring 5 min, 27.0 mg (0.073 mmol) of **2a** was added. After filtration and evaporation of MeOH, **3a** was taken up in 1 mL of $CDCl_3$ and NMR showed a 58% yield with respect to **1a**.

Methyl *N*-(1,1-dimethylethyl)-4-methoxybenzenecarboximidate *N*-oxide (**3b**) was prepared from **1b** (21.0 mg, 0.092 mmol) with methyl triflate (24.0 mg, 0.15 mmol) in 1 mL of CH_2Cl_2. Product workup after 48 h on a 0.1-mL aliquot showed that **2b** was formed in 76% yield as a 3/1 mixture of *E* and *Z* isomers: IR of both isomers ($CHCl_3$) 3521–2600 (br), 1610 (vs), 1300 (s), 1159 (m) cm^{-1}. Predominant isomer **2bE**: ^1H NMR ($CDCl_3$) δ 1.69 (s, 9 H, N-*t*-Bu), 3.90 (s, 3 H, ArOCH_3), 4.02 (s, 3 H, N=COCH_3), 7.07–7.11 (m, 2 H, Ar*H*), 7.53–7.68 (m, 2 H, Ar*H*). Minor isomer **2bZ**: ^1H NMR ($CDCl_3$) δ 1.35 (s, 9 H, N-*t*-Bu), 3.85 (s, 3 H, N=COCH_3), 3.91 (s, 3 H, ArOCH_3), 7.08–7.26 (m, 2 H, Ar*H*), 7.53–7.56 (m, 2 H, Ar*H*). Deprotonation of a 0.25-mL aliquot (method 1) yielded **3b** at R_f 0.46: IR ($CDCl_3$) 1606 (s), 1509 (s), 1254 (vs), 1197 (m) cm^{-1}; ^1H NMR *E* isomer ($CDCl_3$) δ 1.61 (s, 9 H, N-*t*-Bu), 3.63 (s, 3 H, N=COCH_3), 3.84 (s, 3 H, ArOCH_3), 6.90–6.95 (d, 2 H, Ar*H*), 7.90–7.95 (d, 2 H, Ar*H*); MS (70 eV), *m/z* (rel intensity) 237 (2.9, M^+), 181 (23.2), 135 (100), 134 (28.4), 133 (45.0), 92 (24.7), 90 (22.9), 86 (20.0), 84 (35.4), 77 (29.0); molecular ion calcd for $C_{13}H_{19}NO_3$ *m/z* 237.1365, found 237.1371; R_f 0.56 (16:1, CH_2Cl_2/MeOH); yield 50% with respect to **1b** by NMR.

Methyl *N*-(1,1-dimethylethyl)-4-nitrobenzenecarboximidate *N*-oxide (**3c**) was prepared from **1c** (23.0 mg, 0.097 mmol) and methyl triflate (34.0 mg, 0.21 mmol) in 25 mL of CH_2Cl_2. Product workup after 10 days and ^1H NMR of the reaction mixture revealed a complex mixture with signals at 1.72 ppm (s, N-*t*-Bu) and 4.08 ppm (s, O-CH_3) due to **2c**. Concentration in vacuo left 30 mg of a brown solid, which was taken up in 0.5 mL of CH_2Cl_2 and deprotonated by method 1, giving **3c** at R_f 0.45: IR ($CDCl_3$) 1603 (m), 1528 (vs), 1508 (s), 1287 (m), 1202 (m), 1182 (m) cm^{-1}; ^1H NMR *E* isomer ($CDCl_3$) δ 1.64 (s, 9 H, N-*t*-Bu), 3.68 (s, 3 H, OCH_3), 8.1–8.35 (m, 4 H, Ar*H*); MS (70 eV), *m/z* (rel intensity) 252 (5.4, M^+), 196 (36.0), 150 (100), 102 (50.3), 76 (40.9), 75 (34.2), 57 (93.3); molecular ion calcd for $C_{12}H_{16}N_2O_4$ *m/z* 252.1111, found 252.1116; R_f 0.69 (16:1, CH_2Cl_2–MeOH); yield 4% with respect to **1c** by NMR.

Methyl *N*-(1,1-dimethylethyl)ethanimidate *N*-oxide (**3d**) was prepared from **1d** (0.12 g, 0.92 mmol) and methyl triflate (0.19 g, 1.16 mmol) in 10 mL of CH_2Cl_2. Product workup after 24 h gave **2d** as an oil, 98% pure by NMR: IR ($CHCl_3$) 3591–2478 (br), 1626 (vs), 1295 (s), 1207 (s), 1161 (s), 1154 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.57 (s, 9 H, N-*t*-Bu), 2.70 (s, 3 H, N=COCH_3). A sample of **2d**, prepared from 5.9 mg of **1d**, was dissolved in 1 mL of $CDCl_3$ and deprotonated (method 2) with triethylamine (6.0 mg, 0.06 mmol), giving **3d**: ^1H NMR ($CDCl_3$) δ 1.50 (s, 9 H, N-*t*-Bu), 2.33 (s, 3 H, N=CCH_3), 3.80 (s, 3 H, N=COCH_3); R_f 0.48 (9:1, CH_2Cl_2–MeOH); yield 51% with respect to **1d** by NMR. **3d** (method 1): MS (70 eV), *m/z* (rel intensity) 145 (3.1, M^+), 89 (17.5), 57 (53.9), 56 (37.8), 41 (100).

Methyl *N*-(1,1-dimethylethyl)methanimidate *N*-oxide (**3e**) was prepared from **1e** (0.29 g, 2.5 mmol) and methyl triflate (0.49 g, 3.0 mmol) in 25 mL of CH_2Cl_2. Product workup after 48 h gave 0.65 g of a brown oil consisting of *N*-*tert*-butylhydroxylamine hydrotriflate (15%) and **2e** (80%): IR ($CHCl_3$) 3598–2494 (br), 1682 (vs), 1323 (s), 1288 (m) cm^{-1}; ^1H NMR *Z* isomer ($CDCl_3$) δ 1.53 (s, 9 H, N-*t*-Bu), 4.42 (s, 3 H, OCH_3), 8.61 (s, 1 H, N=C*H*). A sample of **2e**, prepared from 5.8 mg of **1e**, was dissolved in 1 mL of $CDCl_3$ and deprotonated (method 2) with triethylamine (8.0 mg, 0.079 mmol), giving **3e**: ^1H NMR *Z* isomer ($CDCl_3$) δ 1.48 (s, 9 H, N-*t*-Bu), 4.08 (s, 3 H, OCH_3), 7.80 (s, 1 H, N=C*H*); MS (70 eV) on **2e**, molecular ion calcd for **3e** *m/z* $C_6H_{13}NO_2$ 131.0946, found 131.0947; R_f 0.37 (9:1, CH_2Cl_2–MeOH); yield 68% with respect to **1e** by NMR.

Methyl *N*-methylbenzenecarboximidate *N*-oxide (**3f**) was prepared from **1f** (0.365 g, 2.42 mmol) and methyl triflate (0.49 g, 3.0 mmol) in 24 mL of CH_2Cl_2. Deprotonation of 0.5 mL of the resulting complex reaction mixture after 5 days (method 1) yielded two bands for **3f** at R_f 0.30 and R_f 0.50. The isolation and subsequent ^1H NMR of each band resulted in identical 1.75/1 mixtures of nitrone isomers based on the integrated ratio of *N*-methyl groups at 3.83 and 3.51 ppm; IR ($CDCl_3$) 1602 (m), 1281 (m), 1224 (vs), 1065 (m) cm^{-1}; MS (70 eV), *m/z* (rel intensity) 165 (14.1, M^+), 149 (47.5), 105 (100), 104 (28.2), 77 (83.2); R_f 0.28 and 0.62 (9:1, CH_2Cl_2–MeOH); yield (total of both isomers): 4% with respect to **1f** by NMR. Predominant isomer: ^1H NMR ($CDCl_3$) δ 3.74 (s, 3 H, OCH_3), 3.83 (s, 3 H, NCH_3), 7.35–8.22 (m, 5 H, Ar*H*). Minor isomer: ^1H NMR ($CDCl_3$) δ 3.51 (s, 3 H, NCH_3), 3.76 (s, 3 H, OCH_3), 7.35–8.22 (m, 5 H, Ar*H*).

Ethyl *N*-(1,1-dimethylethyl)benzenecarboximidate *N*-oxide (**3g**) was prepared from **1a** (0.50 g, 2.6 mmol) and ethyl triflate (0.57 g, 3.2 mmol) in 26 mL of CH_2Cl_2. Product workup of an aliquot after 10 days showed a complex mixture by ^1H NMR in $CDCl_3$ with signals at 1.69 ppm (s, N-*t*-Bu) and 4.29 ppm (q, OCH_2CH_3) due to **2g**. Deprotonation of 1 mL of the above reaction mixture (method 1) gave **3g** at R_f 0.51, greater than 95% pure by NMR: IR ($CDCl_3$) 1341 (s), 1232 (m), 1176 (s), 1153 (s), 1074 (w) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.36 (t, 3 H, OCH_2CH_3), 1.64 (s, 9 H, N-*t*-Bu), 3.81 (q, 2 H, CH_2CH_3), 7.37–7.47 (m, 3 H, Ar*H*), 7.82–7.88 (m, 2 H, Ar*H*); MS (70 eV), *m/z* (rel intensity) 221 (1.1, M^+), 105 (100), 77 (47.1), 57 (11.4); R_f 0.60 (16:1, CH_2Cl_2–MeOH); yield 24% with respect to **1a** by NMR.

Ethyl *N*-methylbenzenecarboximidate *N*-oxide (**3h**) was prepared from **1f** (0.35 g, 2.3 mmol) and ethyl triflate (0.50 g, 28 mmol) in 23 mL of CH_2Cl_2. Deprotonation of the complex mixture after 10 days (method 1) gave two nitrone bands at R_f 0.3 and 0.51. The NMR of each band showed identical 2/1 mixtures of nitrone isomers based on the integrated ratio of *N*-methyl groups at 3.83 and 3.51 ppm; IR ($CDCl_3$) 1603 (m), 1346 (m), 1214 (vs), 1068 (m) cm^{-1}; MS (70 eV), *m/z* (rel intensity) 179 (3.6, M^+), 105 (100), 104 (25.2), 77 (63.6), 51 (20.7); R_f 0.25 and 0.67 (9:1, CH_2Cl_2–MeOH); yield (for both isomers) 8% with respect to **1f** by NMR. Predominant isomer: ^1H NMR ($CDCl_3$) δ 1.39 (t, 3 H, OCH_2CH_3), 3.83 (s, 3 H, NCH_3), 3.94 (q, 2 H, OCH_2CH_3) 7.35–8.20 (m, 5 H, Ar*H*). Minor isomer: ^1H NMR ($CDCl_3$) δ 1.35 (t, 3 H, OCH_2CH_3), 3.51 (s, 3 H, NCH_3) 4.05 (q, 2 H, OCH_2CH_3), 7.35–8.20 (m, 5 H, Ar*H*).

Structure Confirmation of 3a. Regioselective alkylation of **1a** was shown by hydrolysis of **2a** (25 mg, 0.07 mmol) in 1 mL of CD_3CN with H_2O (5 mg, 0.28 mmol). After 24 h at ambient temperature the ^1H NMR spectrum showed complete conversion to methyl benzoate and *N*-*tert*-butylhydroxylamine hydrotriflate by comparison to the ^1H NMR of authentic materials in the same solvent. Methyl benzoate: ^1H NMR (CD_3CN) δ 3.87 (s, 3 H, OCH_3), 7.40–7.50 (m, 2 H, Ar*H*), 7.52–7.65 (m, 1 H, Ar*H*), 7.95–8.01 (m, 2 H, Ar*H*). *N*-*tert*-Butylhydroxylamine hydrotriflate was prepared by adding triflic acid (0.37 g, 2.5 mmol) to a solution of *N*-*tert*-butylhydroxylamine (0.22 g, 2.5 mmol) in 10 mL of ether under nitrogen. After 5 h the ether and excess triflic acid were removed in vacuo, yielding 0.55 g (93%) of the crude hydrotriflate: ^1H NMR (CD_3CN) δ 1.34 (s, N-*t*-Bu). In a larger scale hydrolysis, **2a** (0.5 g, 1.42 mmol) was reacted with water (0.56 g, 0.03 mol) in 25 mL of CH_3CN for 2 days. Removal of solvent by distillation and flash chromatography with CH_2Cl_2 (0.5 L) and then CH_2Cl_2–MeOH (1.5 L, 9:1) gave 85 mg of methyl benzoate (44%) and 27 mg (22%) of *N*-*tert*-butylhydroxylamine by comparison of IR and NMR with those of authentic samples.

For comparison of properties of **3a** with an isomer, *N*-(1,1-dimethylethyl)-*N*-methoxybenzamide (**4**) was prepared[50] from **1a** (1.0 g, 5.2 mmol) and methyl iodide (1.5 g, 0.01 mol) in 50 mL of MeOH containing 0.01 mol of NaOMe. Distillation of the product after 24 h at ambient temperature gave 0.3 g (29%): bp 91–93 °C (0.8 Torr) [lit.[50] bp 83–85 °C (0.1 Torr)]; IR (CCl_4) 3084 (w), 3063 (w), 2971 (s), 2964 (s), 2936 (m), 1651 (vs), 1445 (m), 1393 (m), 1362 (vs), 1206 (m), 1089 (m), 1028 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.56 (s, 9 H, N-*t*-Bu), 3.37 (s, 3 H, OCH_3), 7.35–7.63 (m, 5 H, Ar*H*).

An alternate synthesis of **3a** was achieved by treating 91.5 mg (0.44 mmol) of 2-*tert*-butyl-3-methoxy-3-phenyloxaziridine with 0.5 mL of anhydrous MeOH for 24 h at 5 °C. NMR showed a 91% rearrangement to **3a**: ^1H NMR (MeOH) δ 1.61 (s, 9 H, *N*-*t*-Bu), 3.66 (s, 3 H, OCH_3), 7.39–8.26 (m, 5 H, Ar*H*).

(50) Ito, Y.; Yokoya, H.; Umehora, Y.; Matsuura, T. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 2407–2408.

Reactions of 3e with Nucleophiles. General Procedure. Solutions ca. 0.1 M in **3e** were made by dissolving a known weight of **2e** in P_2O_5-dried CH_3CN. The solution was stirred for 5 min and then 1.5 equiv of BaO-dried triethylamine was added with continuous stirring followed by addition of 2 equiv of the nucleophile. After 24 to 48 h at ambient temperature the reaction mixture was concentrated in vacuo and the products were isolated by flash chromatography.

The reaction of aniline (0.40 g, 4.3 mmol) with **3e** (0.80 g, 80%, 2.28 mmol) for 24 h gave a mixture containing eight components by TLC. Concentration and flash chromatography on 125 g of silica Woelm with 47:3 CH_2Cl_2–MeOH at 10 psi gave 105 mg (24%) of **6a**: IR (CCl_4) 3315 (w), 3060 (w), 1642 (vs), 1606 (w), 1506 (s), 1207 (m), 1097 (s) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.54 (s, 9 H, N-*t*-Bu), 7.05–7.35 (m, 5 H, Ar*H*), 8.00 (s, 1 H, N=C*H*); MS (70 eV), *m/z* (rel intensity) 192 (4.5, M^+), 120 (36.9), 119 (100), 118 (32.7), 93 (84.5), 77 (45.5), 58 (38.2), 57 (33.3); molecular ion calcd for $C_{11}H_{16}N_2O$ *m/z* 192.1263, found 192.1263.

The reaction of *n*-butylamine (0.37 g, 4.6 mmol) with **3e** (0.96 g, 80%, 2.7 mmol) for 24 h gave four components by TLC. Concentration and flash chromatography on 150 g of Kieselgel silica gel with 9:1 CH_2Cl_2–MeOH at 15 psi gave 40 mg (9%) of **6b**: IR (CCl_4) 2950 (s), 2920 (s), 1670 (s), 1460 (m), 1160 (w), 1090 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.93 (t, 3 H, $N(CH_2)_3CH_3$), 1.37 (sextuplet, 2 H, $N(CH_2)_2CH_2CH_3$), 1.44 (s, 9 H, N-*t*-Bu), 1.56 (p, 2 H, $NCH_2CH_2CH_2CH_3$), 3.23 (t, 2 H, $N\text{-}CH_2(CH_2)_2CH_3$), 7.24 (s, 1 H, N=C*H*); ^{13}C NMR ($CDCl_3$) 27.18 ($C(CH_3)_3$), 62.49 $C(CH_3)_3$, 13.53, 19.61, 33.00, 44.90 (C_4H_9), 136.97 (C=N); MS (70 eV), *m/z* (rel intensity) 172 (6.7, M^+), 84 (30.8), 73 (22.3), 58 (55.1), 57 (100).

The reaction of thiophenol (0.30 g, 2.7 mmol) with **3e** (0.53 g, 80%, 1.5 mmol) for 48 h gave 1.12 g of a brown oil after removal of solvent. Flash chromatography of 0.92 g on 135 g of silica Woelm with 97:3 CH_2Cl_2–MeOH at 10 psi gave 0.11 g (28% calculated yield) of **6c**, 80% pure by NMR: IR (CCl_4) 2925 (s), 1311 (s), 1197 (m), 1119 (vs), 1026 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.53 (s, 9 H, N-*t*-Bu), 7.35–7.40 (m, 3 H, Ar*H*), 7.49 (s, 1 H, N=C*H*), 7.50–7.60 (m, 2 H, Ar*H*); MS (70 eV), *m/z* (rel intensity) 209 (1.4, M^+), 110 (37.8), 109 (20.3), 57 (100); molecular ion calcd for $C_{11}H_{15}NSO$ *m/z* 209.0874, found 209.0866. Also obtained was 0.24 g (21%) of phenyl disulfide identified by comparison of IR and NMR with those of authentic material.

The reaction of *n*-butyl mercaptan (0.27 g, 3.0 mmol) with **3e** (0.54 g, 80%, 1.54 mmol) for 24 h gave 0.92 g of a yellow oil after removal of solvent. Flash chromatography over 125 g of silica Woelm with 97:3 CH_2Cl_2–MeOH at 10 psi gave 0.25 g (86%) of **6d**: IR (KBr) 3080 (w), 3030 (m), 1545 (s), 1205 (s), 1110 (vs) cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.94 (t, 3 H, $S(CH_2)_3CH_3$), 1.45 (sextuplet, 2 H, $S(CH_2)_2CH_2CH_3$), 1.51 (s, 9 H, N-*t*-Bu), 1.65 (p, 2 H, $SCH_2CH_2CH_2CH_3$), 2.79 (t, 2 H, $SCH_2(CH_2)_2CH_3$), 7.38 (s, 1 H, N=C*H*); ^{13}C NMR ($CDCl_3$) 27.87 ($C(CH_3)_3$), 68.59 ($C(CH_3)_3$), 13.53, 21.61, 27.87, 30.87 (C_4H_9), 133.74 (C=N); MS (70 eV), *m/z* (rel intensity) 189 (6.1, M^+), 101 (33.7), 77 (22.2), 57 (100); molecular ion calcd for $C_9H_{19}NOS$ *m/z* 189.1187, found 189.1187. Anal. Calcd for $C_9H_{19}NOS \cdot {}^1/_4H_2O$ (193.82): C, 55.77; H, 10.14; N, 7.23. Found: C, 55.77; H, 10.02, N, 7.22.

The reaction of potassium cyanide (0.11 g, 1.66 mmol) with **3e** (0.31 g, 80%, 0.89 mmol) was carried out under stirring for 48 h. Removal of solvent gave 0.22 g of an off-white solid. Flash chromatography of material soluble in 1 mL of CH_2Cl_2 (1.39 mg) on 125 g of Kieselgel with 99:1 CH_2Cl_2–MeOH at 10 psi gave 90 mg (80%) of **6e**: IR (CCl_4) 3157 (w), 1659 (m), 1527 (vs), 1369 (vs), 1263 (vs), 1193 (m), 1122 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.55 (s, 9 H, N-*t*-Bu), 6.85 (s, 1 H, N=C*H*); MS (70 eV), *m/z* (rel intensity) 126 (2.5, M^+), 57 (100) 41 (59.6), 39 (22.9); MS (CI) M + 1 ion calcd for $C_6H_{11}N_2O$ *m/z* 127.0871, found 127.0838.

Transesterification. When an equimolar amount of absolute EtOH was added to a 20% solution of **3e** in $CDCl_3$ at 40 °C, transesterification was observed as indicated by the change in the position of the OCH_2CH_3 signals from δ 3.70 (q) to δ 4.29 (q) and the formation of methanol by the change in δ from 4.04 (s) to δ 3.45 (s). The reaction proceeded to 74% completion (by NMR integration) after 48 h at room temperature.

Acylation. Anhydrous *p*-nitrobenzoyl chloride (0.42 g, 2.3 mmol) was added to a solution of **3e** prepared by adding triethylamine (0.185 g, 1.8 mmol) to 0.42 g (80%, 1.2 mmol) of **2e** in 25 mL of CH_3CN. After 24 h, removal of solvent gave 0.95 g of a solid. Flash chromatography of this material on 130 g of Kieselgel silica with gradient elution (CH_2Cl_2–MeOH) gave 101 mg (35%) of *O*-(*p*-nitrobenzoyl)-*N*-*tert*-butylhydroxylamine (**8**) and 130 mg (28%) of *N,O*-bis(*p*-nitrobenzoyl)-*N*-*tert*-butylhydroxylamine (**9**). For **8**: mp 74–74.5 °C (lit.[34] mp 69–71 °C, lit.[47] mp 78 °C); IR ($CHCl_3$) 1724 (vs), 1612 (m), 1534 (m), 1365 (m), 1274 (vs), 1097 (m) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.26 (s, 9 H, N-*t*-Bu), 8.18–8.22 (d, J = 8.8 Hz, 2 H, Ar*H*), 8.30–8.34 (d, J = 8.8 Hz, 2 H, Ar*H*). For **9**: mp 170–171 °C (ethanol) (lit.[47] mp 170 °C); IR ($CHCl_3$) 1774 (s), 1661 (s), 1605 (m), 1534 (m), 1351 (vs) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.61 (s, 9 H, N-*t*-Bu), 7.97–8.27 (m, 8 H, Ar*H*).

Oxidation. Nitrone **3a**, prepared from 17 mg (97%, 0.05 mmol) of **2a** by method 1, in 1 mL of $CDCl_3$ was treated with 10 mg (85%, 0.05 mmol) of MCPBA. The solution turned a deep blue, and after 4 min ^1H NMR signals for **3a** at 1.63 and 3.63 ppm had disappeared, while new signals at 1.26 ($PhCOOCH_3$, 85%), 1.26 (**11**, 56%), and 1.61 (**12**, 6%) appeared. Assignments were made by comparison to values for authentic methyl benzoate and **12** synthesized by oxidation of *N*-*tert*-butylhydroxylamine with sodium hypobromate.[36] A solution of **12** in $CDCl_3$ displayed signals at 1.59 and 1.26 ppm. With time the signal at 1.59 ppm (for **12**) decreased and that at 1.26 ppm (for **11**) increased, corresponding to the approach to equilibrium between nitroso dimer and monomer. Yields were calculated from integrations using toluene as an internal standard.

Nitrone **3e**, prepared from 60 mg (80%, 0.17 mmol) of **2e** by method 2, in 2 mL of $CDCl_3$ was treated with 50 mg (85%, 0.25 mmol) of MCPBA. As described for **3a**, the ^1H NMR of the resulting blue solution showed no signals due to **3e** after 25 min, but new singlets at 1.26 (**11**, 70%), 1.61 (**12**, 9%), 3.75 ($HCOOCH_3$, 64%), and 8.07 (*H*COOMe, 64%) ppm.

Reduction. Nitrone **3a**, prepared from 0.25 g (0.70 mmol) of **2a** by method 3, in 25 mL of MeOH was treated with $NaBH_4$ (0.12 g, 3.2 mmol). After 30 min, removal of solvent, extraction of the resulting solid with 25 mL of ether, and flash chromatography on 125 g of silica gel at 10 psi gave 36 mg (30%) of **14a** by comparison of IR and NMR with authentic material: IR (CCl_4) 1365 (s) 1133 (s); ^1H NMR ($CDCl_3$) δ 1.62 (s, 9 H, N-*t*-Bu), 7.40–7.50 (m, 3 H, Ar*H*), 7.55 (s, 1 H, N=C*H*), 8.24–8.32 (m, 2 H, Ar*H*).

Nitrone **3e**, prepared from 56 mg (80% 0.16 mmol) of **2e** in 2 mL of MeOH, was treated with $NaBH_4$ (22 mg, 0.58 mmol). After 30 min, removal of solvent and extraction of the resulting solid with 1 mL of $DCCl_3$ gave **14e** in 17% yield: ^1H NMR ($CDCl_3$) δ 1.52 (s, 9 H, N-*t*-Bu), 6.49 (d, J = 6.96 Hz, 1 H, N=CH_a), 6.56 (d, J = 6.93 Hz, 1 H, N=CH_b); R_f 0.5 (9:1, CH_2Cl_2–MeOH). Authentic **14e** for comparison was prepared by reaction of **12** with diazomethane.[38]

Reaction with Organometallic Reagents. Nitrone hydrotriflate **2e**, 0.61 g (80%, 1.7 mmol), in 20 mL of ether, was treated with 5 equiv of phenylmagnesium bromide in 5 mL of ether. After 2 h, 5 mL of water was added and the product extracted with ether. Drying with Na_2SO_4, removal of solvent, and flash chromatography on 125 g of silica Woelm with gradient elution by CH_2Cl_2–MeOH gave the following, identified by comparison of ^1H NMR and IR with those of authentic samples or literature spectra: 60 mg (37%) of phenol; 30 mg (9%) of benzhydrol; and (after preparative TLC) 3.1 mg (1%) of **14a**. An additional product that was separated from phenol by TLC was 0.62 mg (1.5%) of *N*-*tert*-butyldiphenylmethanimine: IR (KBr) 3055 (w), 1220 (s); ^1H NMR ($CDCl_3$) δ 1.44 (s, 9 H, N-*t*-Bu), 7.20–7.75 (m, 10 H, Ar*H*); acid hydrolysis in CH_3CN–2.0 M HCl yielded two aromatic compounds, one of which had an identical ^1H NMR spectrum and R_f value as benzophenone. In addition to other unidentified reaction products, the presence of benzophenone was indicated by IR, NMR, and R_f values.

Acknowledgment. This research was supported by an NSF Chemical Instrumentation Grant CHE-8406088, an equipment grant from the W. M. Keck Foundation, and fellowships from the ARCS Foundation. We especially thank Dr. Kyoichi A. Watanabe of Sloan-Kettering Institute for supplying certain chemicals and making facilities available to one of us (J.A.W.) and Prof. Frank H.

Field of Rockefeller University for mass spectra. Accurate mass analyses on unstable nitrones were run by Noel Whittaker, and his cooperation and expertise are most gratefully acknowledged.

Registry No. **1a**, 7419-56-9; **1b**, 58621-81-1; **1c**, 1613-78-1; **1d**, 51338-95-5; **1e**, 51338-94-4; **1f**, 2446-50-6; (*E*)-**2a**, 118891-41-1; (*E*)-**2b**, 118891-43-3; (*Z*)-**2b**, 118891-45-5; (*E*)-**2c**, 118891-47-7; (*E*)-**2d**, 118891-49-9; (*Z*)-**2e**, 118891-51-3; (*E*)-**2g**, 118891-53-5; (*E*)-**3a**, 118891-54-6; (*E*)-**3b**, 118891-55-7; (*E*)-**3c**, 118891-56-8; (*E*)-**3d**, 118891-57-9; (*Z*)-**3e**, 118891-58-0; (*E*)-**3f**, 118891-59-1; (*Z*)-**3f**, 118891-60-4; (*E*)-**3g**, 118891-61-5; (*E*)-**3h**, 96915-25-2; (*Z*)-**3h**, 96915-26-3; **4**, 76204-26-7; **6a**, 118891-62-6; **6b**, 118891-63-7; **6c**, 118920-06-2; **6d**, 118891-64-8; **6e**, 118891-65-9; **8**, 1746-98-1; **9**, 1613-84-9; **14a**, 52392-70-8; **14e**, 41012-82-2; *N*-*tert*-butylhydroxylamine hydrotriflate, 118891-66-0; 2-*tert*-butyl-3-methoxy-3-phenyloxaziridine, 118891-67-1; phenol, 108-95-2; benzhydrol, 91-01-0; *N*-*tert*-butyldiphenylmethanimine, 27126-13-2.

Notes

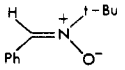
Acyclic α-Alkoxynitrones. A New Class of Spin-Trapping Agents

Bruce J. Acken,[1a] James A. Warshaw, David E. Gallis,[1b] and DeLanson R. Crist*

Department of Chemistry, Georgetown University, Washington, D.C. 20057

Received March 16, 1987

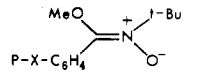
One of the major branches of nitrone chemistry is that of trapping radicals to produce long-lived spin adducts whose ESR spectra can be obtained and analyzed.[2] Nitrones most frequently used for this purpose include α-phenyl-*N*-*tert*-butylnitrone (PBN) (**1**) and 5,5-dimethyl-1-pyrroline *N*-oxide (DMPO) (**2**). Recently, much attention has been given to spin trapping in biological systems,[3] in specific areas of biphasic media,[4] in electrochemical processes,[4b] and photochemical reactions.[5]



1

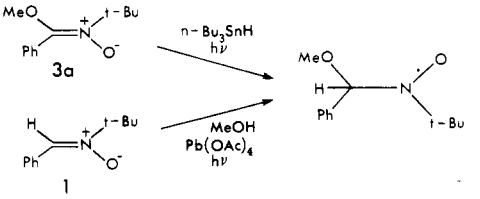
2

This paper describes our results on acyclic α-alkoxynitrones **3**, which represent a new class of spin traps. The nitrones were prepared by alkylation of hydroxamic acids with methyl trifluoromethanesulfonate followed by deprotonation with silica gel/MeOH as previously described.[7]



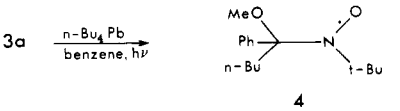
3a: X = H
b: X = OMe
c: X = NO_2

Scheme I



Spin adducts of nitrones with H• have been observed when solutions containing $(n\text{-Bu})_3SnH$ are irradiated.[1b] In this manner, a benzene solution of **3a**, irradiated in the presence of $(n\text{-Bu})_3SnH$, exhibited an ESR spectrum consisting of the triplet of doublets expected for the H• spin adduct (a_N = 13.76 G, a_H^β = 1.98 G). This spin adduct, shown in Scheme I, confirms the structure postulated for the addition of MeO• to PBN,[6] since irradiation of a benzene solution of **1** containing MeOH and $Pb(OAc)_4$ gave essentially the same spectrum with a_N = 13.73 G and a_H^β = 1.93 G. Errors in hyperfine splitting constants are considered to be ±0.05 G. Similarly, α-ethoxy-α-phenyl-*N*-*tert*-butylnitrone trapped H• (a_N^β = 13.79 G, a_H = 1.86 G) corresponding to the spin adduct postulated for the trapping of the ethoxy radical by PBN (a_N = 13.75 G, a_H^β = 1.91 G).[6]

Carbon-centered radicals are also trapped by **3a**. The methyl spin adduct (a_N = 13.85 G) was obtained by irradiation of a benzene solution of **3a** containing tetramethyltin.[1b] This structure was confirmed by observing the same spectrum upon irradiation of a solution containing α-methoxy-α-methyl-*N*-*tert*-butylnitrone and phenylazotriphenylmethane or phenylmercuric chloride[1b] (a_N = 13.87 G). Similarly, *n*-Bu• from $n\text{-Bu}_4Sn$ or $n\text{-Bu}_4Pb$[1b] was trapped by **3a** (a_N = 13.73 G) as was phenyl radical from $PhPb(OAc)_3$[1b] (a_N = 13.75 G). Only triplets expected for adducts such as **4** were obtained except for the case of $n\text{-Bu}_4Sn$, which produced a second weak triplet (a_N = 8.13 G).



4

Solutions of nitrones with no added radical source did not produce ESR signals upon irradiation except for α-

(1) (a) Taken, in part, from the Ph.D. Dissertation of B. J. Acken, Georgetown University, 1987. (b) Present address: Environmental Resources Management, Inc., Exton, PA 19341.

(2) (a) Janzen, E. G.; Blackburn, B. J. *J. Am. Chem. Soc.* **1968**, *90*, 5909–5910. (b) Janzen, E. G.; Blackburn, B. J. *J. Am. Chem. Soc.* **1969**, *91*, 4481–4489. (c) Janzen, E. G. *Methods in Enzymology*; Academic Press: Orlando, FL, 1984; Vol. 105, pp 188–198. (d) Perkins, M. *J. Adv. Phys. Org. Chem.* **1980**, *17*, 1–63. (e) Janzen, E. G.; Evans, C. A.; Davis, E. R. *Organic Free Radicals, ACS Symposium Series*, No. 69; American Chemical Society: Washington, DC, 1978; pp 433–446.

(3) (a) Kalyanaramon, B. *Rev. Biochem. Toxicol.* **1982**, *4*, 73. (b) Janzen, E. G. *Free Radicals Biol.* **1980**, *4*, 115.

(4) (a) Janzen, E. G.; Coulter, G. A. *J. Am. Chem. Soc.* **1984**, *106*, 1962–1968. (b) Walter, T. H.; Bancroft, E. E.; McIntire, G. L.; Davis, E. R.; Gierasch, L. M.; Blount, H. N.; Stronks, H. J.; Janzen, E. G. *Can. J. Chem.* **1982**, *60*, 1621–1636.

(5) (a) Carmichael, A. J.; Samuni, A.; Riesz, P. *Photochem. Photobiol.* **1985**, *41*, 635–642. (b) Carmichael, A. J.; Makino, K.; Riesz, P. *Radiation Res.* **1984**, *100*, 222–234.

(6) Bluhm, A. L.; Weinstein, J. *J. Org. Chem.* **1972**, *37*, 1748–1753.

(7) Warshaw, J. A.; Gallis, D. E.; Acken, B. J.; Gonzalez, O. J.; Crist, D. R. *J. Org. Chem.*, accompanying article in this issue.

0022-3263/89/1954-1743$01.50/0