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

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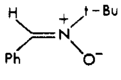
One of the major branches of nitrone chemistry is that of trapping radicals to produce long-lived spin adducts whose ESR spectra can be obtained and analyzed.[2] Nitrones most frequently used for this purpose include α-phenyl-*N-tert*-butylnitrone (PBN) (1) and 5,5-dimethyl-1-pyrroline *N*-oxide (DMPO) (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]



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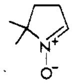

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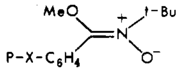
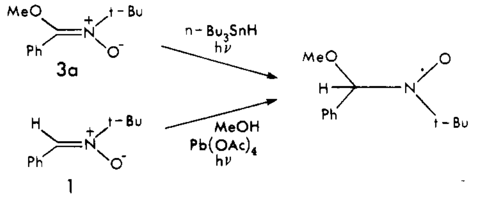
This paper describes our results on acyclic α-alkoxynitrones **3**, which represent a new class of spin traps. The nitrones were prepared by alkylation of hydroxamic acids with methyl trifluoromethanesulfonate followed by deprotonation with silica gel/MeOH as previously described.[7]



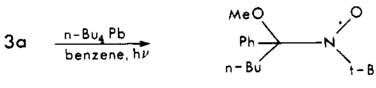
3a: X = H
b: X = OMe
c: X = NO$_2$

Scheme I



Spin adducts of nitrones with H$^•$ have been observed when solutions containing $(n\text{-Bu})_3$SnH are irradiated.[1b] In this manner, a benzene solution of **3a**, irradiated in the presence of $(n\text{-Bu})_3$SnH, 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*-Bu$_4$Sn or *n*-Bu$_4$Pb[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*-Bu$_4$Sn, which produced a second weak triplet (a_N = 8.13 G).



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

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(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.

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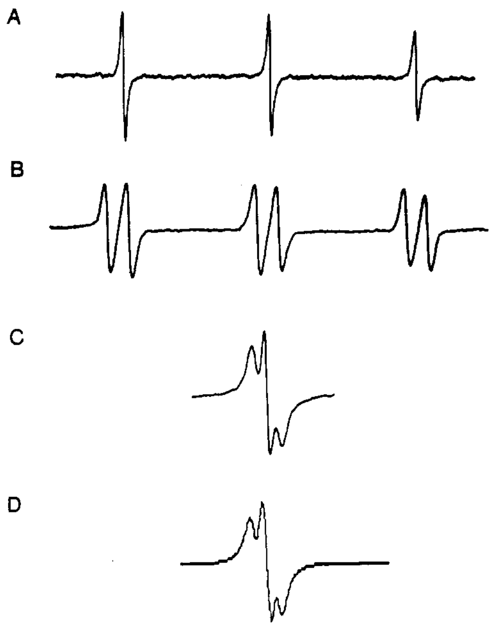


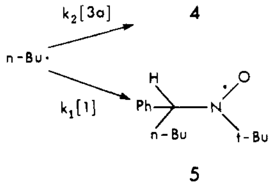
Figure 1. ESR spectra of *n*-Bu$^\bullet$ spin adducts. (A) With alkoxynitrone **2**. (B) With PBN. (C) With both **2** and PBN present under kinetic run conditions. (D) Simulated spectrum of (C).

methyl-α-methoxy-*N*-*tert*-butylnitrone, which showed a weak triplet ($a_N = 13.85$ G). However, the signal did not increase upon continued irradiation.

Trapping of heteroatom-centered radicals by **2** was not as successful. Attempts to trap the succinimidyl radical,[8] phenylthiyl radical,[8] and methoxy[6] radical did not produce solutions having ESR signals.

Para-substituted derivatives of **3** also acted as spin traps. α-Methoxy-α-(*p*-nitrophenyl)-*N*-*tert*-butylnitrone (**3c**) trapped *n*-butyl radicals from $(n\text{-Bu})_4Pb$, giving only the expected triplet ($a_N = 13.70$ G), as did α-methoxy-α-(*p*-methoxyphenyl)-*N*-*tert*-butylnitrone (**3b**) ($a_N = 13.43$ G).

For determination of the trapping efficiency of alkoxynitrones relative to PBN, the rates of formation of spin adducts **4** and **5** were measured in a competition[9] for *n*-Bu$^\bullet$.



The central multiplet of the overlapping spectra of **4** and **5** (see Figure 1) was scanned at 60-s intervals, and computer simulation[10] was used to determine relative peak areas.

Curves of the relative areas of spin adducts vs time were linear in initial stages of reaction (see Figure 2), which permitted determination of initial rates $d[4]_0/dt$ and $d[5]_0/dt$ of trapping *n*-Bu$^\bullet$. Following established procedures,[9] substitution of these values and initial nitrone concentrations into eq 1 gave the relative rate ratio for the trapping reaction. From these data, it was found that the rate constant for trapping *n*-Bu$^\bullet$ by **3a** is 5.0 ± 1.0 times faster than that of PBN.

$$\frac{d[4]_0/dt}{d[5]_0/dt} = \frac{k_2[\mathbf{3a}]_0}{k_1[\mathbf{1}]_0} \qquad (1)$$

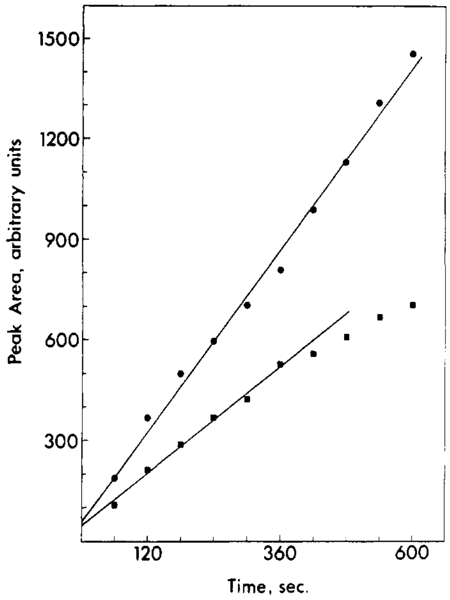


Figure 2. Rate of formation of *n*-Bu$^\bullet$ spin adducts **4** (●) and **5** (■) for a solution 1.4 mM in **3a** and 3.6 mM in **1**. Areas calculated from simulated curves of the center band region.

Table I. Substituent Effect on the Relative Rates[a] of Trapping *n*-Bu$^\bullet$ Relative to PBN (1)

nitrone	k_2/k_1	$\delta(^{13}C)$ α-carbon[b]
3c	4.8 ± 1.4	151.93
3a	5.0 ± 1.0	152.00
3b	9.6 ± 2.3	152.74
1	(1.0)	129.53

[a] Rate data taken at 25.0 °C in benzene. [b] In $CDCl_3$, downfield from Me_4Si. Data from ref 7.

A competition study was also carried out with para-substituted derivatives of **3** to gain information on the electronic effect on spin-trapping efficiency of α-alkoxynitrones. As indicated by the data in Table I, a *p*-nitro group has very little effect, while a *p*-methoxy group doubles the spin-trapping efficiency.

It is interesting to note that an increase in spin-trapping efficiency goes along with a downfield shift in the α-carbon ^{13}C chemical shift, also shown in Table I. Since ^{13}C NMR is a sensitive probe of local electron density, it would appear that the most reactive α-alkoxynitrone has the most electrophilic α-carbon. This trend is in keeping with that of the addition of α-hydroxyalkyl,[11] primary alkyl,[12] and *tert*-butoxy[13] radicals to PBN in which electron-withdrawing groups on PBN enhanced the rate, but unlike the case for the more electrophilic benzoyloxy radicals in which electron-withdrawing groups retarded addition.[14]

The α-carbon ^{13}C chemical shifts of the α-alkoxynitrones are approximately 23 ppm downfield from that of PBN. Thus it is not surprising that α-alkoxynitrones **3** are more efficient at trapping nucleophilic alkyl radicals than PBN.

The present results indicate that acyclic α-alkoxynitrones are efficient spin traps and may serve as useful

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precursors to alkoxy radical spin adducts for structure confirmation.

Experimental Section

Instrumentation. ESR spectra were recorded on a Varian E-4 spectrometer equipped with a Varian temperature control unit. Spectra were calibrated by using the stable nitroxide 3-carbamoyl-2,2,5,5-tetramethyl-3-pyrrolin-1-yloxy (Aldrich). ^1H and ^{13}C NMR spectra were recorded at 30 and 75.47 MHz, respectively.

Spin-Trapping Procedure. Solutions of the nitrones were generated from the hydrotriflate salts by TLC on silica gel plates (Merck) using 9:1 CH_2Cl_2–MeOH solvent as previously described.[7] In a typical experiment a millimolar benzene solution of the α-alkoxynitrone was deoxygenated with argon for 20 min at which time a small amount of the radical source was added. The solutions were then irradiated in the cavity of the spectrometer by using a Spectroline low pressure mercury vapor lamp.

Kinetic Procedure. The α-alkoxynitrone solution was generated as above and its concentration determined by UV absorbance. In this manner, a solution containing both traps at millimolar concentrations was prepared and deoxygenated with argon. For kinetic runs, the temperature of the cavity was maintained at 25.0 ± 0.2 °C. Identical spectrometer settings, cells, and lamp position were used for each experiment. After computer simulation of each spectrum, the program of Oehler and Janzen[10] gave the relative peak areas used in kinetic plots. The relative rate ratios reported are an average of five kinetic experiments for each nitrone.

UV extinction coefficients of α-alkoxynitrones were measured in benzene: **3a**, λ_{max} 321 (ϵ 11000); **3b**, λ_{max} 319 (ϵ 17500); **3c**, λ_{max} 393 (ϵ 11000). Concentrations of the α-alkoxynitrones for this purpose were determined by integration of NMR signals of the α-alkoxynitrone and an internal standard of known concentration.

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Registry No. 1, 3376-24-7; 3a, 118949-64-7; 3b, 118949-65-8; 3c, 118949-66-9; 4, 118949-68-1; 5, 21999-41-7; Bu_3SnH, 688-73-3; Me_4Sn, 594-27-4; Bu_4Pb, 1920-90-7; Bu_4Sn, 1461-25-2; $PhPb(OAC)_3$, 3076-54-8; $Ph(MeO)CHN(O^{\bullet})Bu$-*t*, 34234-86-1; $Ph(EtO)CHN(O^{\bullet})Bu$-*t*, 34280-35-8; $Ph_2(MeO)CN(O^{\bullet})Bu$-*t*, 118949-70-5; $4\text{-}O_2NC_6H_4(Bu)C(OMe)N(O^{\bullet})Bu$-*t*, 118949-71-6; $4\text{-}MeOC_6H_4(Bu)C(OMe)N(O^{\bullet})Bu$-*t*, 118949-72-7; $Ph(MeO)C(Me)N(O^{\bullet})Bu$-*t*, 118949-73-8; α-ethoxy-α-phenyl-*N*-*tert*-butylnitrone, 118949-67-0; α-methoxy-α-methyl-*N*-*tert*-butylnitrone, 118949-69-2; phenylazotriphenylmethane, 981-18-0; phenylmercuric chloride, 100-56-1.

Theoretical (MM2) Conformational Analysis of 1,4-Dioxepane

A. Entrena, C. Jaime,† A. Espinosa,* and M. A. Gallo

Departamento de Química Orgánica, Facultad de Farmacia, Universidad de Granada, 18071 Granada, Spain, and Departamento de Química, Química Orgánica, Facultad de Ciencias, Universidad Autónoma de Barcelona, 08193 Bellaterra, Spain

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Introduction

Molecular mechanics calculations have proven to be very useful in molecular dynamics studies for organic compounds.[1] The pseudorotational equilibria in seven-membered rings have already been studied by different force field methods. Cycloheptane itself, **1**, was studied by Hendrickson,[2] and the twist-chair (TC) conformation was found to be the most stable. These results were confirmed by Bocian[3] and, more recently, by Ōsawa[4] who used MM2′,[5] a modification of Allinger's force field.[6] Bocian[7] also studied 1,3-dioxepane, **2**, finding a TC conformation again as the most stable. Recently, Kamalov[8] has carried out a theoretical study on the conformational transitions for this compound, confirming Bocian's results. In contrast, 1,4-dioxepane, **3**, has not been conformationally studied, although related compounds 1,5-benzodioxepins, **4**, have been experimentally studied (NMR)[9] and show preference for chair (C) or twist-boat (TB) conformations, depending on the substituents on C-3. In this paper we described the MM2 results on the conformational analysis of **3**.

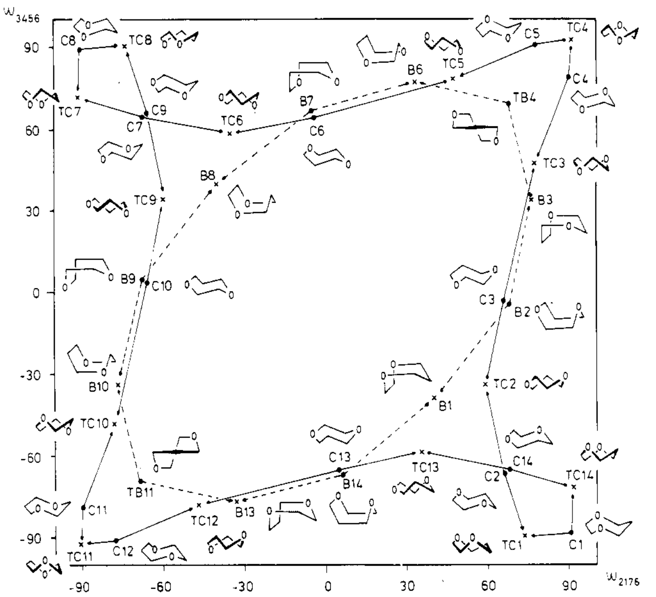
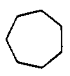


Figure 1. Schematic representation of the T/TC and B/TB pseudorotational pathways as a function of the two internal dihedral angles $\omega(2176)$ and $\omega(3456)$. Points represent saddle points while x represent energy minima.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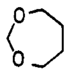
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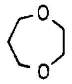
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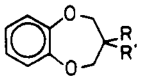

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Results and Discussion

The conformational analysis has been carried out in two well-defined steps: (i) calculation of the torsional energy

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† Universidad Autónoma de Barcelona.

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