vacuum. Then the products were separated by column chromatography on silica gel. Elution with ether–benzene (1:99) gave (α-methoxycyclohexyl)methyl hydroperoxide (**10**) (185 mg; 94% yield): oil; $^1$H NMR $\delta$ 0.8–2.4 (m, 11 H), 3.57 (s, 3 H), 4.40 (d, $J$ = 6 Hz, 1 H), 9.44 (br s, 1 H). Subsequent elution with methanol–ether (1:9) gave nitrone (*Z*)-**4f** (215 mg).

**Thermolysis of Dihydro-3-phenyl-5-benzyl-6-heptyl-1,2,4,5-trioxazine (5h).** A solution of **5h** (95 mg, 0.27 mmol) in benzene (10 mL) was kept with stirring under reflux for 8 h. After evaporation of the solvent, the products were separated by column chromatography on silica gel. Elution with benzene–hexane (3:7) gave first the unreacted **5h**. The second fraction (elution with benzene) contained a mixture of octanal (**6b**) and benzaldehyde (**6a**). From the final fraction (elution with ether–benzene (1:4)) was obtained benzaldehyde oxime (**13**): mp 34–36 °C; $^1$H NMR $\delta$ 7.2–7.6 (m, 5 H), 8.04 (s, 1 H), 8.14 (br s, 1 H).

**Reaction of 5h with Sodium Ethoxide in Ethanol.** A solution of **5h** (94 mg, 0.26 mmol) and sodium ethoxide (3.3 mmol; prepared from 77 mg of sodium) in ethanol (10 mL) was kept with stirring at room temperature for 24 h. Then, the mixture was poured into aqueous potassium hydroxide, and the products were extracted with ether. By column chromatography of the crude product on silica gel were isolated **6b**, **13**, and then **4c**. By neutralization with aqueous HCl, benzoic acid (**14**) was obtained from the aqueous layer.

**Reaction of 5h with Grignard Reagents.** The reaction with phenylmagnesium bromide is representative. A mixture of **5h** (173 mg, 0.49 mmol) and phenylmagnesium bromide (49 mmol) in ether (30 mL) was kept with stirring at room temperature for 20 h. Then, the mixture was poured into ice-cold, aqueous HCl, neutralized with aqueous KOH, and extracted with ether. By column chromatography on silica gel (elution with ether–benzene (1:50)) was obtained *N*-hydroxylamine **16a** first. Subsequent elution yielded benzhydrol (**15a**).

***N*-Benzyl-*N*-(1-phenyloctyl)hydroxylamine (16a)**: mp 82–83 °C (from methanol); $^1$H NMR $\delta$ 0.7–2.2 (m, 15 H), 3.51 (d, $J$ = 14 Hz, 1 H), 3.64 (t, $J$ = 5 Hz, 1 H), 3.69 (d, $J$ = 14 Hz, 1 H), 5.40 (br s, 1 H), 7.2–7.5 (m, 10 H); IR 3445, 3030, 2930, 2852, 759, 734, 698 cm$^{-1}$. Anal. Calcd for $C_{21}H_{29}NO$: C, 80.98; H, 9.38; N, 4.50. Found: C, 81.08; H, 9.47; N, 4.54.

***N*-Benzyl-*N*-(1-methyloctyl)hydroxylamine (16b)**: mp 50–51 °C; $^1$H NMR $\delta$ 0.8–1.7 (m, 18 H), 2.4–2.7 (m, 1 H), 3.62 (s, 2 H), 6.40 (br s, 1 H), 7.2–7.5 (m, 5 H); IR 3200, 3045, 2940, 2855, 1458, 1389, 1143, 981, 937, 814, 738, 696 cm$^{-1}$. Anal. Calcd for $C_{16}H_{27}NO$: C, 77.06; H, 10.91; N, 5.62. Found: C, 77.29; H, 10.92; N, 5.64.

**Reaction of 5h with Lithium Aluminum Hydride.** A mixture of **5h** (308 mg, 0.87 mmol) and lithium aluminum hydride (7.9 mmol) in ether (20 mL) was kept with stirring at room temperature for 18 h. After working as above, the products were separated by column chromtography on silica gel. Elution with ether–benzene (1:50) gave first *N*-benzyl-*N*-octylhydroxylamine (**16c**) and then benzyl alcohol (**15c**).

***N*-Benzyl-*N*-octylhydroxylamine (16c)**: mp 31–33 °C; $^1$H NMR $\delta$ 0.8–1.7 (m, 13 H), 2.52 (t, $J$ = 7 Hz, 2 H), 3.61 (s, 2 H), 6.90 (br s, 1 H), 7.15 (s, 5 H); IR 3422, 2929, 2855, 1465, 1076, 808, 740, 695 cm$^{-1}$; MS (EI) $m/z$ 235 (M$^+$). Anal. Calcd for $C_{15}H_{25}NO$: C, 76.55; H, 10.71; N, 5.95. Found: C, 76.56; H, 10.72; N, 5.93.

**16c**-$\alpha$-$d$: $^1$H NMR $\delta$ 0.8–1.7 (m, 13 H), 2.53 (t, $J$ = 7 Hz, 1 H), 3.64 (s, 2 H), 6.80 (br s, 1 H), 7.19 (s, 5 H); MS (EI) $m/z$ 236 (M$^+$).

**Reaction of 5h with Trifluoroacetic Acid.** A mixture of **5h** (1 mmol) and trifluoroacetic acid (3 mmol) in methylene chloride (10 mL) was kept with stirring at room temperature for 15 h. The mixture was poured into aqueous HCl and extracted with ether. After evaporation of the solvent, the products were separated by column chromatography on silica gel. Elution with benzene–hexane (1:1) gave 3,6-diphenyl-1,2,4,5-tetroxane (**18**): mp 201–202 °C.[17] From the second fraction (elution with benzene) was obtained a mixture of **6a** and **6b**. The third fraction (elution with ether–benzene 1:4) contained benzoic acid (**14**). From the final fraction (elution with methanol–ether (1:9)) was obtained nitrone **4c**.

After neutralization of the aqueous layer with aqueous KOH, the products were extracted with ether. Evaporation of the solvent and the subsequent column chromatography on silica gel (elution with ether–benzene (1:1)) gave *N*-benzylhydroxylamine (**17**): oil; $^1$H NMR $\delta$ 4.01 (s, 2 H), 5.52 (br s, 2 H), 7.28 (s, 5 H); IR 3266, 2920, 2850, 1598, 1491, 1451, 1204, 1068, 1017, 960, 842, 740, 681, 600 cm$^{-1}$.[16]

**Supplementary Material Available:** Tables of fractional coordination parameters for hydrogen and anisotropic vibrational parameters for **5t** and **5f** (4 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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# Enthalpy of Hydrogenation of the Hexadienes and *cis*- and *trans*-1,3,5-Hexatriene

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We present results for the enthalpies of hydrogenation ($\Delta H_h$) and enthalpies of formation of the cyclic unbranched hexadienes and the two hexatrienes by a method that is consistent with our earlier studies on the unbranched hexenes and which gives essentially gas-phase values. The $\Delta H_h$ values are as follows: *cis*-hexa-1,3-diene, −53.9 ± 0.3; *trans*-hexa-1,3-diene, −52.9 ± 0.3; *cis*-hexa-1,4-diene, −58.4 ± 0.4; *trans*-hexa-1,4-diene, −57.6 ± 0.4; hexa-1,5-diene −60.3 ± 0.4; *cis,cis*-hexa-2,4-diene, −52.4 ± 0.4; *cis,trans*-hexa-2,4-diene, −51.4 ± 0.4; *trans,trans*-hexa-2,4-diene, −50.5 ± 0.4; *cis*-hexa-1,3,5-triene, −81.0 ± 0.6; *trans*-hexa-1,3,5-triene, −80.0 ± 0.6 kcal/mol. Results are compared with the three compounds for which literature values exist. A new hydrogenation calorimeter is briefly described. The device yields results as precise as those presently in the literature, but uses samples of 20–100 mg.

The enthalpies of hydrogenation ($\Delta H_h$) of the unbranched, acyclic hexenes have been thoroughly studied.[1,2] Because the enthalpy of formation of *n*-hexane is accurately known, the enthalpies of formation ($\Delta H_f$) of the monoenes follow routinely. Accurate $\Delta H_f$ values have considerable value in parameterizing molecular mechanics force fields and in evaluating semiempirical molecular orbital methods.

The $\Delta H_h$ values of the unbranched dienes and trienes are not so well-known.[3] In particular, $\Delta H_h$ has not been measured for 1,3-hexadiene, and the values for *cis*- and

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**Table I. Molar Enthalpies of Hydrogenation at 298 K of Unbranched Hexadienes and the Hexatrienes in Units of kcal/mol. $\Delta H_h$ Values Are Relative to a Standard Value of −30.2 ± 0.2 kcal/mol for 1-Hexene. Sample Purity Is Given below the Compound Name**

| | $\Delta H_h$ | | | |
|---|---|---|---|---|
| | this work | mean | lit. | $\Delta H_f$ |
| hexa-1,3-diene (cis and trans) | | | | |
| 99.9 | −53.7 ± 0.3<br>−54.0 ± 0.3 | −53.9 ± 0.3 | | |
| cis-hexa-1,3-diene | | −53.9 ± 0.3 | | 14.0 ± 0.4 |
| trans-hexa-1,3-diene | | −52.9 ± 0.3 | | 13.0 ± 0.4 |
| cis-hexa-1,4-diene | | | | |
| 99.8 | −58.2 ± 0.4<br>−58.6 ± 0.3 | −58.4 ± 0.4 | | 18.5 ± 0.4 |
| trans-hexa-1,4-diene | | | | |
| 99.5 | −57.3 ± 0.4<br>−57.9 ± 0.4 | −57.6 ± 0.4 | | 17.7 ± 0.4 |
| hexa-1,5-diene | | | | |
| 99.9 | −60.3 ± 0.4<br>−60.3 ± 0.5 | −60.3 ± 0.4 | −60.2 ± 0.4[a]<br>−60.5 ± 0.1[b] | 20.4 ± 0.4<br>(−20.1 ± 0.2)[c] |
| cis-cis-hexa-2,4-diene | | | | |
| 99.9 | −52.4 ± 0.4<br>−52.4 ± 0.3 | −52.4 ± 0.4 | | 12.5 ± 0.4 |
| cis,trans-hexa-1,4-diene | | | | |
| 99.8 | −51.4 ± 0.5<br>−51.3 ± 0.3 | −51.4 ± 0.4 | | 11.5 ± 0.4 |
| trans,trans-hexa-2,4-diene | | | | |
| 99.9 | −50.3 ± 0.4<br>−50.6 ± 0.3 | −50.5 ± 0.4 | −51.1 ± 0.3[d] | 10.6 ± 0.4 |
| hexa-1,3,5-triene (cis and trans) | | | | |
| 99.9 | −80.6 ± 0.5<br>−80.3 ± 0.7 | −80.5 ± 0.6 | | |
| cis-hexa-1,3,5-triene | | −81.0 ± 0.6 | −80.5 ± 0.2[a] | 41.1 ± 0.6 |
| trans-hexa-1,3,5-triene | | −80.0 ± 0.6 | −79.4 ± 0.3[a] | 40.1 ± 0.6 |

[a] Reference 4. [b] Reference 14. [c] Reference 6. [d] Rogers, D. W.; Kok, R. A.; Allinger, N. L. unpublished results.

*trans*-1,3,5-hexatriene were obtained using glacial acetic acid (GAA) as the calorimeter fluid,[4] which exerts a solvent effect of unknown magnitude on the measured $\Delta H_h$. One can guess the $\Delta H_h$ for 1,3,5-hexatriene to within 2 or 3 kcal/mol from results obtained in GAA, but because of its theoretical importance as the acyclic analogue of benzene, one would like to have a more accurate value. Accordingly, we have carried out $\Delta H_h$ determinations (which lead to $\Delta H_f$) on all the acyclic unbranched hexadienes and the two hexatrienes by a method that is consistent with earlier studies on the unbranched hexenes[2] and which gives essentially gas-phase values.

## Results and Discussion

The molar $\Delta H_h$ and $\Delta H_f$ of the linear hexadienes and hexatrienes, exclusive of the 1,2- and 2,3-hexadienes, are given in Table I. We have presented arguments[5] that $\Delta H_h$ of an alkene, measured in dilute solution with a nonpolar solvent, shows a negligible solvent effect and is within experimental error of the gas-phase value.

Our method involves measurement of $\Delta H_h$ of an unknown relative to a thermochemical standard, for which the $\Delta H_h$ is assumed to be known. These results were measured against the standard 1-hexene, for which $\Delta H_h = -30.2$ kcal/mol.[6] The $\Delta H_f$ values in Table I were calculated using ($\Delta H_f[n\text{-hexane}] = -39.9 \pm 0.2$ kcal/mol.[7] The experimental error estimates given for $\Delta H_h$ are 95% confidence limits. Each estimated error for $\Delta H_f$ is the root mean square (square root of the summed variances) of the errors of $\Delta H_h$ and $\Delta H_f[n\text{-hexane}]$. Although measurement of $\Delta H_h$ in solution in an isoperibol calorimeter does not conform to standard-state conditions, our values of $\Delta H_f$ are, in many cases, the best available approximations to $\Delta H_f{}^\circ(298)$.

Neither 1,3-hexadiene nor 1,3,5-hexatriene was available as the pure cis or trans isomer. The ratio of cis to trans isomer was, however, readily determined by wide-bore capillary GLC. The ratios were 3:97 (1,3-hexadiene) and 48:52 (1,3,5-hexatriene). The difference in $\Delta H_h$ for the cis and trans isomers of 1,3,5-hexatriene is known to be 1.0 kcal/mol from Turner's work.[4] Although the results for both the cis and trans isomers in Turner's studies include a solvent effect, it is reasonable to assume that the solvent effect is nearly the same for both;[8] hence, the difference between two of Turner's measured $\Delta H_h$ values is reliable. With this information, one can calculate the values given in Table I from $\Delta H_h$ of the mixture and the ratio of the isomers.

The enthalpy of hydrogenation of the middle double bond in *cis*-1,3,5-hexatriene is $\Delta H_h[1,3,5\text{-hexatriene}] - \Delta H_h[1,5\text{-hexadiene}] = -80.1 - (-60.30) = -20.7$ kcal/mol. This compares with the enthalpy of hydrogenation of cyclohexene (−28.4 ± 0.2)[9] and *cis*-3-hexene (−28.9 ± 0.2)[10] to yield about 8 kcal/mol of stabilization enthalpy or 4 kcal/mol for each conjugated double bond. This is significantly larger than the value of 3 kcal/mol for the mutual stabilization of the double bonds in 1,3-butadiene

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(8) Accurate measurements suggest a smaller value, $\Delta H_s = 0.7\text{–}0.8$ kcal/mol, for $C_6$ alkenes and larger.[2] We anticipate a slight difference, cis > trans, and hope to measure it with more sensitive apparatus now under construction. In any case, the approximation of 1.0 kcal/mol is probably justifiable within the overall experimental error.

(9) Roth, W. R.; Lennartz, H.-W. *Chem. Ber.* **1980**, *113*, 1806, 1818.

(10) Rogers, D. W.; Crooks, E. L. *J. Chem. Thermodyn.* **1983**, *15*, 1087.

relative to 1-butene that is often quoted as the conjugative stabilization enthalpy in linear molecules.[11] Small strain changes during hydrogenation have been ignored in this calculation. By the same reasoning, conjugative stabilization of the middle double bond in 1,3-hexadiene is 3.7 kcal/mol relative to 1-hexene (−30.2 ± 0.2).[6] It is an artifice to lump all the conjugative stabilization into the central double bond, however, when much current theory stresses bond interaction in concert, not as individual entities.

The $\Delta H_h$ values in Table I are in accord with Liebman's observation that the enthalpy of reaction to form a conjugated dialkene from its component parts is small. He

$$RCH{=}CH_2 + R'CH{=}CH_2 \rightarrow RCH{=}CH{-}CH{=}CHR' + H_2$$

cites combination of 2 ethylene molecules to form 1,3-butadiene which yields $\Delta H_r = 1.2$ kcal/mol. An example from Table I is formation of 2,4-hexadiene from 2-propene molecules, which has $\Delta H_r = -10.6 - 2(-4.8 = -1.0$ kcal/mol. See ref 3 for further discussion.

**Solvent Correction.** The $\Delta H_h$ of both 1,5-hexadiene and 1,3,5-hexatriene were determined by Turner's group,[4] using GAA as the calorimeter fluid. We have pointed out[12] that one can correct for the solvent effect by measuring the difference in enthalpies of solution ($\Delta H_s$) of reactant and product. The enthalpy of solution of *n*-hexane in GAA is 1.4 kcal/mol for very dilute solutions.[13] We have measured $\Delta H_s$ for 1-hexene, 1,5-hexadiene, and 1,3,5-hexatriene to give a dilute GAA solution. The results were 1.1, 0.9, and 0.6 kcal/mol, respectively. This yields correction factors of 0.3, 0.5, and 0.8 kcal/mol. Thus, Turner's value for 1,5-hexadiene corrected for solvent effects is −60.7 ± 0.4 kcal/mol as compared to our value of −60.3 ± 0.4 kcal/mol and Kistiakowsky's value of $\Delta H_h$(gas) = −60.5 ± 0.1 kcal/mol.[14] The present results for *cis*-and *trans*-1,3,5-hexatriene (−81.0 ± 0.6 and −80.0 ± 0.6 kcal/mol) compare with Turner's values (with solvent correction) of −81.3 ± 0.3 and −80.2 ± 0.4 kcal/mol.

Up to now,[15] we have taken the correction factor for cyclopentene (0.7 kcal/mol) and multiplied it by the number of double bonds to obtain an estimate of the solvent correction for polyenes. Our present results indicate, however, that $\Delta H_s$ in GAA is a more complicated function of molecular geometry than this procedure suggests. The correction factor for 1-hexene is smaller than it is for cyclohexene and cyclopentene, and it is not a simple multiple of the number of double bonds in the diene or triene.

The relatively few available literature values show some similarities to our work.[16] The reported difference in $\Delta H_s$ between reactant and product in GAA for cyclohexene is 0.6 kcal/mol, but for 1,3,5-cycloheptatriene it is only 1.1 kcal/mol. Thus, the second and third double bonds in cycloheptatriene contribute less together to $\Delta H_s$ than the lone double bond in cyclohexene. The difference in $\Delta H_s$ for cyclooctatetraene and cyclooctane is only 1.2 kcal/mol, also indicating that $\Delta H_s$ is not the sum of equal parts. Fuchs and Peacock[13] observed a difference of only 0.1 kcal/mol for di(*tert*-butyl)ethylene and its hydrogenation product, an example of the influence of molecular complexity on $\Delta H_s$.

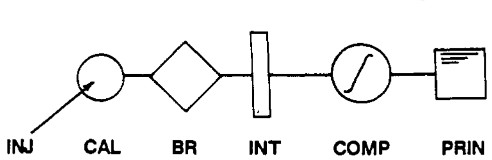

**Figure 1.** Block diagram of the calorimeter.

**Table II. Typical Test Results of the Calorimeter System**

| aliquot samples | mg/aliquot | $\Delta H_h$, kcal/mol |
|---|---|---|
| 1-hexene | | |
| 9 | 1.35 | −29.9 ± 0.4, −29.9 ± 0.2, −30.2 ± 0.2 |
| 5 | 1.44 | −30.2 ± 0.2, −30.0 ± 0.4 |
| 4 | 1.55 | −30.4 ± 0.4, −29.8 ± 0.3 |

Cis–trans isomerization enthalpies, in the absence of structurally complicated groups adjacent to the double bond, are about 1.0 kcal/mol at this level of accuracy, measured in either GAA[4] or in the gas phase.[14] (See, however, ref 8.)

## Experimental Section

The calorimeter system (Figure 1) is the most recent in a series designed and built in this laboratory. The calorimeter consists of a closed isoperibol reaction flask with a rubber septum through which protrudes a steel-jacketed thermistor probe and a needle that conveys hydrogen into the flask from a constant pressure (2-atm) source. The flask also contains 8–20 mL of a slurry of Pd–C catalyst in an inert solvent (cyclohexane or hexane) that is magnetically stirred.

A sample solution is injected into the calorimeter (CAL), in which hydrogenation takes place, causing a temperature change. The ratio of the moles of diene or triene to moles of 1-hexene reference standard was roughly 0.5 or 0.33 as appropriate to obtain an approximate thermochemical equivalence between sample and standard. The temperature ($T$) is converted to a voltage by the bridge (BR), thence to a digital signal by an analog-to-digital interface (INT) and stored in computer memory (COMP). The computer displays the experimental curve of $T$ vs time at the CRT to permit a visual check for irregularities. This is repeated, alternating injections of unknown solution with those of a standard, each result being recorded by a printer (PRIN). Completeness of reaction and absence of side reactions are tested for by gas–liquid chromatography.

Typical test results using the new calorimeter are shown in Table II for the known test compound 1-hexene measured against cyclohexene as the thermochemical standard ($\Delta H_h$[cyclohexene] = −28.4 ± 0.2 kcal/mol).[9] The uncertainties are 95% confidence limits. The accuracy of these results is similar to comparable literature values[2] but they were obtained at higher sensitivity. For 1-hexene a complete study requires about 20 mg for hydrogenation runs on 10 replicate 16 μL aliquots, each aliquot containing 1.4 mg of 1-hexene dissolved in cyclohexane. Other samples require more or less, depending on the number of double (or triple) bonds and the molecular weight.

**Sample Purity.** The source of all dienes was Wiley Organics. Hexa-1,3,5-triene was obtained from Aldrich Chemical Co. Isolation of pure cis and pure trans isomers of hexa-1,3-diene and hexa-1,3,5-triene was not feasible using the packed column preparative GLC system at our disposal. Determination of the cis–trans ratio was, however, possible using a 60-m wide-bore capillary analytical column with a flame-ionization detector.

One of the difficulties in thermochemistry of polyenes is their tendency to polymerize. Analytical gas-phase chromatography is not likely to detect contamination by polymeric compounds because their retention time may be very much longer than that of the desired monomer and they may simply never emerge from the column for detection.

This disadvantage is, however, an advantage in preparative GLC purification. Accordingly, we purified the samples of 1,3,5-hex-

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atriene reported in Table I using a Perkin-Elmer 154 vapor fractometer with a $^1/_4$-in. packed column. Although the purity, as judged from analytical GLC, only increased from ca. 98 to 99%, the thermochemical results increased by about 5%, indicating some contamination by a component (probably a polymer) that was not detected by analytical GLC using a capillary column and a flame ionization detector. Old samples showed a distinct turbidity or tendency to precipitate from solutions in *n*-hexane, due, presumably, to polymer formation.

Completeness of reaction and absence of side reactions was indicated by a single hexane peak in the GLC trace of the reaction product. A competing polymerization reaction in the calorimeter would not have been detected by this method.

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**Registry No.** (*Z*)-1,3-Hexadiene, 14596-92-0; (*E*)-1,3-hexadiene, 20237-34-7; (*Z*)-1,4-hexadiene, 7318-67-4; (*E*)-1,4-hexadiene, 7319-00-8; 1,5-hexadiene, 592-42-7; (*Z,Z*)-2,4-hexadiene, 6108-61-8; (*E,Z*)-2,4-hexadiene, 5194-50-3; (*E,E*)-2,4-hexadiene, 5194-51-4; (*Z*)-1,3,5-hexatriene, 2612-46-6; (*E*)-1,3,5-hexatriene, 821-07-8.

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# Design of Modified Pyrroline *N*-Oxide Derivatives as Spin Traps Specific for Hydroxyl Radical

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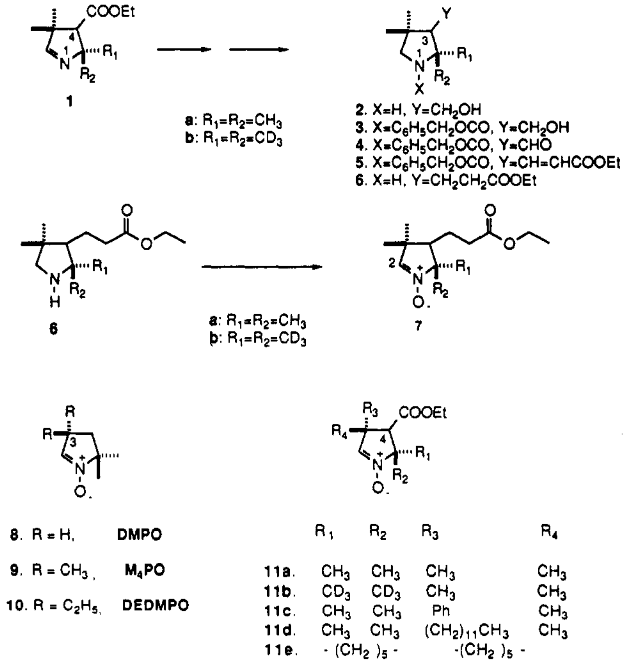
Nitrones, 4-[2-(ethoxycarbonyl)ethyl]-3,3,5,5-tetramethyl-1-pyrroline *N*-oxide (**7a**) and 4-[2-(ethoxycarbonyl)ethyl]-5,5-di([$^2H_3$]methyl)-3,3-dimethyl-1-pyrrolidine *N*-oxide (**7b**) have been synthesized. The ability of the nitrone (**7a**) to spin trap hydroxyl and superoxide radicals has been compared with nitrones **11a** and 5,5-dimethyl-1-pyrroline *N*-oxide (DMPO, **8**). Nitrone **11a** bears a carbethoxy group at C-4, whereas nitrone **7a** has a spacer of two methylene units between the carbethoxy and the basic nitrone ring skeleton. Nitrone **11a** trapped both hydroxyl and superoxide radicals, while nitrone **7a** trapped only hydroxyl radical. The hydroxyl radical adducts of **7a** and **11a** were more resistant toward superoxide-mediated reduction than the hydroxyl radical adduct of DMPO (**8**).

In recent years reduced oxygen species, including superoxide and hydroxyl radical, have been proposed as mediators in a variety of cellular responses, such as phagocytosis, ischemia/reperfusion injury, aging, and cancer.[1] Despite numerous efforts to study the role of these free radicals in initiating tissue injury, the most difficult obstacle remains to be the unambiguous identification of these reactive species. Among the different methods for detecting superoxide and hydroxyl radicals in biological systems, electron spin resonance (ESR) spectroscopy combined with spin trapping offers the opportunity to simultaneously measure and characterize these oxygen-centered free radicals.[2-5] In this technique, transient free radicals are trapped by nitrone and nitroso compounds to give a persistent nitroxide spin trapped adduct that can be observed using a conventional ESR spectrometer.

Among several nitrones employed as spin traps, 5,5-dimethyl-1-pyrroline 1-oxide (DMPO, **8**) is most frequently used in biological systems to detect superoxide and hydroxyl radicals.[6-12] However, DMPO has several limitations.[4,5] To circumvent some of these problems, a family of 5,5-disubstituted, pyrroline 1-oxides have been prepared with enhanced sensitivity,[13] lipophilicity, and decreased susceptibility toward air oxidation.[14] More recently we have synthesized a spin trap, 3,3-diethyl-5,5-dimethylpyrroline 1-oxide (DEDMPO, **10**), which was found to be specific for hydroxyl radical.[15] It does not spin trap superoxide. However, the preparation of DEDMPO (**10**) is

**Scheme I**



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(1) Halliwell, B., Gutteridge, J. M., Eds. In *Free Radicals in Biology and Medicine*; Clarendon Press: Oxford, 1989.