Synthesis and X-ray Analysis of Dihydro-1,2,4,5-trioxazine. Evidence of a Stepwise Mechanism for the [3 + 3] Cycloaddition of Carbonyl Oxides with Nitrones

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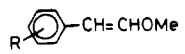
Carbonyl oxides, derived by ozonolysis of vinyl ethers, readily undergo [3 + 3] cycloaddition reactions with nitrones affording dihydro-1,2,4,5-trioxazines in fair to excellent yield. The structures of dihydro-3,5,6-triphenyl-1,2,4,5-trioxazine (**5f**) and dihydro-3-cyclohexyl-5-methyl-6,6-diphenyl-1,2,4,5-trioxazine (**5t**) were unambiguously determined by X-ray analysis. Ozonolysis of 1-cyclohexyl-2-methoxyethene in the presence of either (*E*)- or (*Z*)-α-(4-methylphenyl)-α-phenyl-*N*-methylnitrone gave a 1:1 mixture of two stereoisomeric cycloadducts. This result, in conjunction with the structure of the relevant **5t**, suggests that the [3 + 3] cycloaddition proceeds by a stepwise mechanism.

[3 + 3] cycloadditions between two different 1,3-dipoles have been shown in a limited number of cases to be useful for the synthesis of six-membered heterocyclic compounds.[2] In this respect, carbonyl oxides, which are well-known to undergo dimerization to give 1,2,4,5-tetraoxanes,[3] have recently been shown by us to undergo cycloadditions with nitrones, affording the corresponding novel dihydro-1,2,4,5-trioxazine derivatives.[4] The observed nonstereospecificity of these cycloaddition reactions with configurationally stable nitrones, (*E*)- and (*Z*)-α-(4-methylphenyl)-α-phenyl-*N*-methylnitrone, indicates that the mechanism is stepwise. We now report in detail the results of our synthetic and mechanistic studies of the aforementioned [3 + 3] cycloaddition process.

Results and Discussion

Synthesis and X-ray Analysis of Dihydro-1,2,4,5-trioxazine. After ozonation (2 mmol of ozone) of a mixture of the appropriate vinyl ether **1** (2 mmol) and nitrone



1g: R = 2-CF_3

1h: R = 4-MeO

4 (1 mmol) in methylene chloride at 0 °C, the products were isolated by rapid column chromatography on silica gel (Scheme I and Table I). Although dihydrotrioxazines were generally stable enough to be isolated in this manner, adduct **5j**, derived from benzaldehyde *O*-oxide (**2b**), and α,α-diphenyl-*N*-methylnitrone (**4e**), which was present in the crude product mixture as determined by ^{1}H NMR analysis [δ 2.80 (s, NCH_3), 6.69 (s, H-3)], had decomposed

Table I. Synthesis of Dihydro-1,2,4,5-trioxazine[a]

vinyl ether	nitrone	trioxazine (% yield)	others (% yield)
1a: $R^1 = R^2 = H$, $R^3 = CH_2CH(CH_3)_2$	**4a**: $R^4 = R^6 = Ph$, $R^5 = H$	**5a** (84)	
	4b: $R^4 = Ph$, $R^5 = H$, $R^6 = CH_2Ph$	**5b** (71)	
	4c: $R^4 = (CH_2)_6CH_3$, $R^5 = H$, $R^6 = CH_2Ph$	**5c** (52)	**5m** (16)
	4d: $R^4 = R^5 = R^6 = Ph$	**5d** (80)	
	4e: $R^4 = R^5 = Ph$, $R^6 = CH_3$	**5e** (91)	
1b: $R^1 = Ph$, $R^2 = H$, $R^3 = CH_3$	**4a**	**5f** (38)	**6b** (16), **7b** (31)[b]
	4b	**5g** (41)	**6b** (20), **7b** (25)[b,c]
	4c	**5h** (42)	**5m** (18)
	4d	**5i** (96)	
	4e	**5j** (90)[d]	
1c: $R^1 = (CH_2)_6CH_3$, $R^2 = H$, $R^3 = CH_3$	**4a**	**5k** (86)[e]	
	4b	**5l** (69)[f]	
	4c	**5m** (70)[g]	
	4d	**5n** (90)	
	4e	**5o** (81)	
1d: R^1 = cyclohexyl, $R^2 = H$, $R^3 = CH_3$	**4a**	**5p** (69)[h]	
	4b	**5q** (62)[f]	
	4c	**5r** (80)[i]	
	4d	**5s** (92)	
	4e	**5t** (97)	
1e: $R^1,R^2 = -(CH_2)_5-$, $R^3 = CH_3$	**4a**	**5u** (36)	**6b** (32), **6e** (33)[b]
	4b	**5v** (12)[j]	**6e** (39)
	4c	**5w** (68)	
1f: $R^1 = R^2 = Ph$, $R^3 = CH_3$	**4c**	**5x** (8)[k]	

[a] The reaction of a vinyl ether (400 mg) in CH_2Cl_2 (10 mL) in the presence of a nitrone (0.5 equiv) at 0 °C. [b] The yield was based on the vinyl ether. [c] Recovered **4b**; 30%. [d] The trioxazine was labile on silica gel, and therefore, by column chromatography of the crude product, nitrone **4e** was isolated in 96% yield. [e] The isomer ratio = 51:49. [f] The ^{1}H NMR spectra showed that two isomers might have been produced; the minor isomer was, however, not well assigned. [g] The ratio of two isomers was 66:34. [h] The isomer ratio = 71:29. [i] The isomer ratio = 67:33. [j] Recovered **4b**; 60%. [k] Recovered **4c**; 72%.

(1) Osaka University. (b) Heriot-Watt University; all the correspondence for X-ray analysis should be addressed to K.J.M.

(2) (a) Moody, C. J. *Comprehensive Heterocyclic Chemistries*; Katritzky, A. R., Rees, C. W., Eds.; Pergamon Press: Oxford, 1984; Vol. 3. (b) Crabb, J. N.; Storr, R. C. *1,3-Dipolar Cycloaddition Chemistry*; Padwa, A., Ed.; Wiley: New York, 1984; Vol. 2. (c) Heine, H. W.; Heitz, L. *J. Org. Chem.* **1974**, *39*, 3192. (d) Kliegel, W. *Chem.-Ztg.* **1976**, *100*, 236. Relevant [3 + 3] cycloaddition involving a 1,3-dipole: (e) Schultz, A. G.; Macielag, M.; Plummer, M. *J. Org. Chem.* **1988**, *53*, 391. (f) Calcagno, M. A.; Heine, H. W.; Kruse, C.; Krofke, W. A. *J. Org. Chem.* **1974**, *39*, 162. (g) Brandi, A.; Guarna, A.; Goti, A.; De Sarlo, F. *Tetrahedron Lett.* **1986**, *27*, 1727. (h) Saso, H.; Ando, W. *Tetrahedron* **1989**, *45*, 1929. (i) Tsuge, O.; Watanabe, H. *Heterocycles* **1977**, *7*, 907.

(3) (a) Bunnelle, W. H. *Chem. Rev.* **1991**, *91*, 335. (b) Kuczkowski, R. L. In *Advances in Oxygenated Processes*; Baumstark, A. L., Ed.; JAI Press: Greenwich, 1991; Vol. 3, p 1. (c) Kuczkowski, Chiang C.; Butler, W.; Kuczkowski, R. L. *J. Chem. Soc., Chem. Commun.* **1988**, 465.

(4) A part of this work has been reported in preliminary form: Mori, M.; Sugiyama, T.; Nojima, M.; Kusabayashi, S.; McCullough, K. J. *J. Am. Chem. Soc.* **1989**, *111*, 6884.

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Scheme I

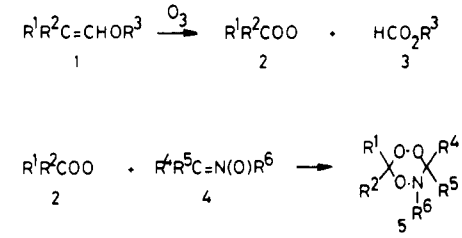


Table II. Reaction of Stereoisomeric Dihydrotrioxazines[a]

trioxazine	reagent	reaction time, h	recovered 5,[d] %	products (% yield)
t,t-**5k**[b]	$ClSO_3H$	1	88	
c,c-**5k**[c]	$ClSO_3H$	1	80[e]	
5m	$ClSO_3H$	1	88	
5p	$ClSO_3H$	1	85	
5r	$ClSO_3H$	1	85	
t,t-**5k**[b]	PPh_3	7200	50	**4a** (43), **6b** (38)
t,t-**5k**[b]	PPh_3	65	90	**4a** (8), **6b** (8)
c,c-**5k**[c]	PPh_3	65		**4a** (85), **6b** (92)
5m	PPh_3	40	61	**4c** (32), **6b** (30)
5p	PPh_3	40	65	**4a** (27), **6c** (20)
5r	PPh_3	24	60	**4c** (35), **6c** (25)

[a] The reaction with 0.1 equiv of $ClSO_3H$ in methylene chloride at 0 °C or the reaction with 1 equiv of triphenylphosphine in $CDCl_3$ at room temperature. Unless otherwise noted, the dihydrotrioxazine used for the reaction was a mixture of two stereoisomers; for the ratio see the footnotes in Table I. [b] *trans,trans*-**5k**. [c] *cis,cis*-**5k**. [d] Only the more stable isomer was recovered unless otherwise noted. [e] A mixture of *trans,trans*- and *cis,cis*-**5k**, the ratio being 77:23.

completely, resulting in recovery of the starting material **4e** (96%).

The substituents R^4 and R^5 were found to influence the reactivity of the nitrone **4**. For the coupling reactions with aldehyde *O*-oxides **2a–d**, increasing the steric bulk of the substituents R^4 and R^5 appeared to increase the reactivity of the corresponding nitrone **4** toward carbonyl oxides (as judged from the yield of trioxazines **5**), which is contrary to the reactivity of carbonyl compounds; under similar circumstances, aldehydes would be expected to be more reactive than ketones.[3a,b] Consistent with this, ozonolysis of a 1:1:1 mixture of vinyl ether **1b**, α,*N*-diphenylnitrone (**4a**) and α,α,*N*-triphenylnitrone (**4d**) resulted in exclusive formation of dihydrotrioxazine **5i** (33% yield), derived from capture of bulkier **4d** by benzaldehdye *O*-oxide (**2b**). Although treatment of a 2:1:1 mixture of **1b**, **4a**, and **4d** with ozone gave **5f** together with **5i**, the yield of **5f** (14%) was significantly lower than that of **5i** (58%). However, more reactive formaldehyde *O*-oxide (**2a**) underwent cycloaddition with both nitrones **4a** and **4d** in a similar rate, thereby producing a mixture of **5a** and **5d** in yields of 43% and 49%, respectively.

In competition experiments, nitrones were found to be more reactive than carbonyl compounds toward carbonyl oxides since the corresponding dihydrotrioxazines **5** were obtained as the sole isolable product, albeit in reduced yields. Thus, for example, ozonolysis of 1-phenyl-2-methoxyethylene (**1b**) carried out in the presence of a 1:1 mixture of nitrone **4d** and benzophenone (**6e**) afforded **5i** in 46% yield. Similarly, **5f** was isolated in 30% yield from the ozonolysis of **1b** in the presence of a 1:1 mixture of nitrone **4a** and benzaldehyde (**6a**).

In contrast to the nitrones **4**, the reactivity of the carbonyl oxides **2** was found to decrease significantly with increasing substitution (Table I). Thus, the aldehyde

$R^1R^2C{=}O$
6

a: R^1 = Ph, R^2 = H

b: R^1 = heptyl, R^2 = H

c: R^1 = cyclohexyl, R^2 = H

d: $R^1, R^2 = -(CH_2)_5-$

e: $R^1 = R^2$ = Ph

f: R^1 = 4-$CH_3C_6H_4$, R^2 = Ph

g: R^1 = 2-$CF_3C_6H_4$, R^2 = H

h: R^1 = 4-$CH_3OC_6H_5$, R^2 = H

O-oxides **2a–d** underwent cycloadditions to both α,*N*-disubstituted- and α,α,*N*-trisubstituted nitrones **4a–e**, yielding in each case the corresponding dihydrotrioxazines **5** in fair to excellent yield. With cyclohexanone *O*-oxide (**2e**), cycloadducts were formed only with the less sterically hindered α,*N*-disubstituted nitrones **4a–c**. The more sterically encumbered benzophenone *O*-oxide (**2f**) reacted only with nitrone **4c** producing the dihydrotrioxazine **5x** in low yield (8%). The above trends in reactivity are very similar to those observed for the analogous cycloaddition reactions between carbonyl oxides and imines in which ketone *O*-oxides and imines did not generally give cycloadducts.[5]

Cycloadditions involving unsymmetrically substituted dipolar components would be expected to give rise to the dihydrotrioxazines such as **5f–h, k–m, p–r** as mixtures of stereoisomers. In reality, the reaction of benzaldehyde *O*-oxide (**2b**) with nitrones **2a–c** afforded trioxazines **5f–h** as single isomers; this was confirmed by the X-ray analysis of the crystalline dihydro-3,5,6-triphenyl-1,2,4,5-trioxazine (**5f**) (vide infra). On the other hand, octanal *O*-oxide (**2c**) and cyclohexanecarboxaldehyde *O*-oxide (**2d**) with nitrones **4a,c** gave the corresponding dihydrotrioxazines **5k,m** and **5p,r**, respectively, as mixtures of isomers. In the case of **5k**, the two isomers could be separated by either column chromatography on silica gel or recrystallization from methanol.

The crystalline material, tentatively assigned as *cis,cis*-**5k** on the basis of the ^1H NMR spectra (Figure 1),[6] was extremely labile. On (a) treatment with 0.1 equiv of chlorosulfonic acid in methylene chloride at 0 °C for 1 h, it isomerized to *trans,trans*-**5k**, and (b) reduction with 1 equiv of triphenylphosphine at room temperature for 65 h, a mixture of octanal (**6b**) and α,*N*-diphenylnitrone (**4a**) was obtained quantitatively. Under similar conditions, the more stable isomer, *trans,trans*-**5k** could be recovered in ca. 90% yield.

Despite several attempts, pure samples of the minor isomers of dihydrotrioxazines **5m,p,r** could not be isolated. The isomer ratios were determined by ^1H NMR analysis (see the footnotes to Table I). As for **5m,p,r** treatment of the isomer mixtures led to selective isomerization of the minor isomer in each case, with recovery of the major

(5) As an exception, the very reactive dihydroisoquinoline is efficiently captured by **2e** yielding the corresponding 1,2,4-dioxazolidines in excellent yield; (a) Mori, M.; Nojima, M.; Kusabayashi, S.; McCullough, K. J. *J. Chem. Soc., Chem. Commun.* **1988**, 1550. (b) Mori, M.; Tabuchi, T.; Nojima, M.; Kusabayashi, S.; McCullough, K. J. Unpublished results.

(6) We have tentatively assigned the stereochemistry on the basis that in ^1H NMR spectra the equatorial proton would appear at a lower field compared with the axial one: Halls, P. J.; Jones, R. A. Y.; Katritzky, A. R.; Snarey, M.; Trepanier, D. L. *J. Chem. Soc. B* **1971**, 1320.

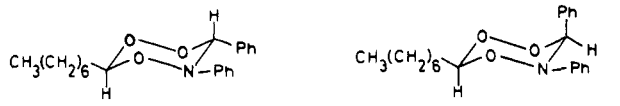
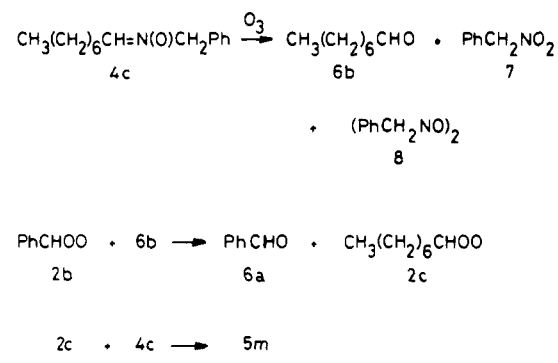


Figure 1. X-ray crystal structure of dihydrotrioxazine **5t** (ORTEP,[23] 50% probability ellipsoids). Hydrogen atom labels have been omitted for clarity.

Scheme II



isomer in ca. 85% yield. Similarly, the minor isomer in the mixture was preferentially reduced by triphenylphosphine to produce a mixture of the corresponding aldehyde **6** and nitrone **4** (Table II). Owing to the complexity of the ^{1}H NMR spectra of the crude mixtures of dihydrotrioxazines **5l,q** it was not possible to assign signals unambiguously to the minor isomer in each case. Thus, although a minor isomer may have also been formed, only the major isomers of **5l,q** were isolated and satisfactorily characterized.

The ozonolysis of vinyl ether **1a** or **1b** in the presence of α-heptyl-*N*-benzylnitrone (**4c**) unexpectedly afforded in small but significant quantities the 3,6-diheptyl-5-benzyl derivative **5m** which is formally derived from the cycloaddition of octanal *O*-oxide (**2c**) to nitrone (**4c**). Although nitrones do not react rapidly with ozone under normal circumstances,[7,8] ozonolysis (1 equiv of O_3, CH_2Cl_2, 0 °C) of nitrone (**4c**) resulted in the formation of a mixture of octanal (**6b**, 53%), (nitromethyl)benzene (**7**, 6%), and the nitroso dimer **8** (45%), together with unreacted nitrone (**4c**, 29%). Since the dihydrotrioxazine **5m** was not obtained in this case, it seems unlikely that the necessary carbonyl oxide **2c** had been generated directly by ozonolysis of **4c** in the previous reaction. As an alternative explanation, outlined in Scheme II, it is tentatively suggested that the carbonyl oxides derived from the enol ethers **1a** and **1b**, respectively, transfer an oxygen atom to octanal **6c**,[9] produced by ozonolysis of **4c**, to give the carbonyl oxide **2c** which in turn reacts with nitrone **4c** to give the adduct **5m**.

As an intrinsic part of our study, it was important to establish the nature of the dihydro-1,2,4,5-trioxazine ring system, and, for later stereochemical studies, the preferred locations of the ring substituents. The molecular structures of the dihydrotrioxazine derivatives **5t** and **5f**, as determined by X-ray crystallographic analysis, are depicted

(7) Bailey, P. S. *Ozonation in Organic Chemistry*; Academic Press: New York, 1982; Vol. 2, Chapter 8.

(8) The reaction of nitrone **4a** with 1 equiv of ozone in methylene chloride at 0 °C gave a mixture of benzaldehyde (**6a**) and nitrobenzene in yields of 45% and 50%, respectively; the unreacted **4a** was recovered in 44%. The reaction of nitrone **4d** under the same conditions gave rise to the formation of benzophenone (**6e**) and nitrobenzene in yields of 50% and 45%, respectively; the unreacted nitrone **4d** was recovered in 48%.

(9) Murray, R. W.; Agarwal, S. K. *J. Org. Chem.* **1985**, *50*, 4698.

Table III. Fractional Coordinates of Non-Hydrogen Atoms with Estimated Standard Deviations for Dihydrotrioxazine 5t

	x	*y*	*z*	U_{eq}
O(1)	0.351 16 (11)	0.626 38 (15)	0.478 35 (15)	0.0528 (9)
O(2)	0.324 11 (11)	0.785 72 (15)	0.508 35 (16)	0.0528 (9)
O(3)	0.135 86 (10)	0.706 48 (15)	0.489 45 (14)	0.0480 (8)
N(1)	0.158 75 (13)	0.547 68 (18)	0.439 99 (17)	0.0452 (9)
C(1)	0.210 94 (16)	0.789 58 (23)	0.589 14 (21)	0.0493 (12)
C(2)	0.278 87 (15)	0.542 30 (22)	0.370 01 (21)	0.0457 (11)
C(3)	0.124 27 (17)	0.472 60 (24)	0.573 17 (24)	0.0574 (13)
C(4)	0.181 61 (17)	0.952 18 (23)	0.634 37 (22)	0.0509 (12)
C(5)	0.261 37 (20)	1.0483 (3)	0.7413 (3)	0.0638 (15)
C(6)	0.228 57 (22)	1.2115 (3)	0.7956 (3)	0.0720 (17)
C(7)	0.104 97 (24)	1.2190 (3)	0.8710 (3)	0.0788 (18)
C(8)	0.026 67 (21)	1.1235 (3)	0.7670 (3)	0.0759 (17)
C(9)	0.057 58 (19)	0.9593 (3)	0.7127 (3)	0.0639 (15)
C(10)	0.389 34 (17)	0.333 52 (24)	0.4081 (3)	0.0580 (14)
C(11)	0.413 23 (19)	0.1830 (3)	0.3746 (3)	0.0698 (16)
C(12)	0.356 23 (21)	0.0763 (3)	0.2732 (3)	0.0687 (16)
C(13)	0.275 62 (22)	0.1211 (3)	0.2041 (3)	0.0705 (16)
C(14)	0.252 42 (20)	0.2703 (3)	0.2352 (3)	0.0628 (15)
C(15)	0.308 85 (16)	0.378 27 (23)	0.338 06 (22)	0.0468 (11)
C(16)	0.214 77 (19)	0.6138 (3)	0.140 32 (23)	0.0600 (14)
C(17)	0.238 84 (22)	0.6608 (3)	0.001 (3)	0.0756 (18)
C(18)	0.349 16 (25)	0.6973 (3)	−0.0617 (3)	0.0823 (19)
C(19)	0.435 54 (23)	0.6865 (3)	0.0163 (3)	0.0777 (18)
C(20)	0.412 33 (18)	0.6396 (3)	0.1570 (3)	0.0641 (15)
C(21)	0.301 29 (16)	0.60275 (22)	0.219 88 (22)	0.0480 (12)

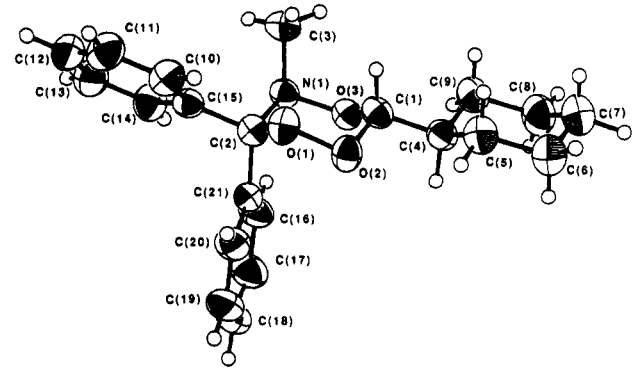


Figure 2. X-ray crystal structure of dihydrotrioxazine **5f** (ORTEP,[23] 50% probability ellipsoids). Hydrogen atom labels have been omitted for clarity.

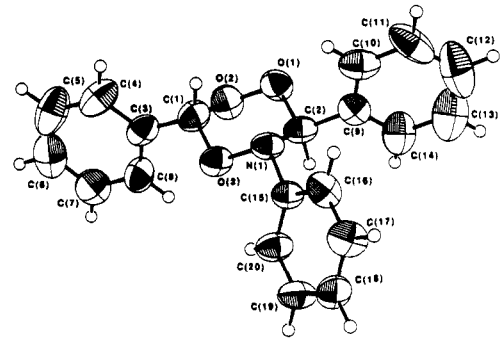


Figure 3.

in Figures 2 and 3, respectively. Tables III–VI contain the refined atomic coordinates and selected derived geometrical parameters for compounds **5t** and **5f** as appropriate.

The central six-membered rings adopt a slightly distorted conformation in each case. The O–O and N–O bond lengths are close to expected values for related saturated heterocyclic systems.[10] In **5t** (Figure 2), the cyclohexyl

(10) Riddell, F. G. *The Conformational Analysis of Heterocyclic Compounds*; Academic Press: London, 1980.

Table IV. Derived Geometrical Parameters for Dihydrotrioxazine 5t

(a) Bond Lengths (Å) with Estimated Standard Deviations

O(1)-O(2)	1.4757 (19)	C(6)-C(7)	1.518 (4)
O(1)-C(2)	1.4432 (23)	C(7)-H(7A)	0.906 (4)
O(2)-C(1)	1.4193 (24)	C(7)-H(7B)	1.100 (4)
O(3)-N(1)	1.4546 (20)	C(7)-C(8)	1.502 (4)
O(3)-C(1)	1.4133 (23)	C(8)-H(8A)	0.822 (4)
N(1)-C(2)	1.466 (3)	C(8)-H(8B)	1.069 (4)
N(1)-C(3)	1.473 (3)	C(8)-C(9)	1.529 (4)
C(1)-H(1)	1.003 (3)	C(9)-H(9A)	0.929 (3)
C(1)-C(4)	1.508 (3)	C(9)-H(9B)	0.953 (3)
C(2)-C(15)	1.526 (3)	C(10)-C(11)	1.386 (3)
C(2)-C(21)	1.528 (3)	C910)-C(15)	1.382 (3)
C(3)-H(3A)	0.915 (3)	C(11)-C(12)	1.378 (4)
C(3)-H(3B)	0.823 (3)	C(12)-C(13)	1.378 (4)
C(3)-H(3C)	1.014 (3)	C(13)-C(14)	1.372 (4)
C(4)-H(4)	1.069 (3)	C(14)-C(15)	1.388 (3)
C(4)-C(5)	1.531 (3)	C(16)-C(17)	1.383 (3)
C(4)-C(9)	1.529 (3)	C(16)-C(21)	1.382 (3)
C(5)-H(5A)	0.926 (3)	C(17)-C(18)	1.372 (4)
C(5)-H(5B)	0.973 (3)	C(18)-C(19)	1.371 (4)
C(5)-C(6)	1.528 (4)	C(19)-C(20)	1.387 (4)
C(6)-H(6A)	0.926 (4)	C(20)-C(21)	1.383 (3)
C(6)-H(6B)	1.060 (4)		

(b) Angles (deg) with Standard Estimated Deviations

O(2)-O(1)-C(2)	106.11 (13)	C(5)-C(6)-C(7)	111.97 (21)
O(1)-O(2)-C(1)	105.95 (13)	H(6A)-C(6)-H(6B)	112.2 (3)
N91)-O(3)-C(1)	112.04 (13)	H(6A)-C(6)-C(7)	109.6 (3)
O(3)-N(1)-C(2)	107.42 (13)	H(6B)-C(6)-C(7)	109.4 (3)
O(3)-N(1)-C(3)	109.15 (14)	C(6)-C(7)-H(7A)	102.3 (3)
C(2)-N(1)-C(3)	115.29 (15)	C(6)-C(7)-H(7B)	109.8 (3)
O(2)-C(1)-O(3)	109.34 (15)	C(6)-C(7)-C(8)	111.63 (23)
O(2)-C(1)-H(1)	104.77 (20)	H(7A)-C(7)-H(7B)	113.7 (4)
O(2)-C(1)-C(4)	108.37 (16)	H(7A)-C(7)-C(8)	110.0 (3)
O(3)-C(1)-H(1)	113.07 (20)	H(7B)-C(7)-C(8)	109.4 (3)
O(3)-C(1)-C(4)	108.58 (16)	C(7)-C(8)-H(8A)	122.2 (3)
H(1)-C91)-C(4)	112.54 (21)	C(7)-C(8)-H(8B)	116.0 (3)
O(1)-C(2)-N(1)	110.79 (15)	C(7)-C(8)-C(9)	112.65 (22)
O(1)-C(2)-C(15)	105.62 (15)	H(8A)-C(8)-H(8B)	93.9 (3)
O(1)-C(2)-C(21)	110.58 (15)	H(8A)-C(8)-C(9)	96.5 (3)
N(1)-C(2)-C(15)	108.22 (15)	H(8B)-C(8)-C(9)	113.1 (3)
N(1)-C(2)-C(21)	110.76 (15)	C(4)-C(9)-C(8)	110.97 (19)
C(15)-C(2)-C(21)	110.72 (16)	C(4)-C(9)-H(9A)	105.2 (3)
N(1)-C(3)-H(3A)	112.57 (23)	C(4)-C(9)-H(9B)	106.13 (25)
N(1)-C(3)-H(3B)	99.34 (24)	C(8)-C(9)-H(9A)	106.3 (3)
N(1)-C(3)-H(3C)	103.97 (21)	C(8)-C(9)-H(9B)	104.3 (3)
H(3A)-C(3)-H(3B)	116.5 (3)	H(9A)-C(9)-H(9B)	123.8 (3)
H(3A)-C(3)-H(3C)	102.6 (3)	C(11)-C(10)-C(15)	120.06 (20)
H(3B)-C(3)-H(3C)	121.5 (3)	C(10)-C(11)-C(12)	120.58 (22)
C(1)-C(4)-H(4)	103.91 (20)	C(11)-C(12)-C(13)	119.24 (23)
C(1)-C(4)-C(5)	110.89 (17)	C(12)-C(13)-C(14)	120.53 (23)
C(1)-C(4)-C(9)	109.67 (17)	C(13)-C(14)-C(15)	120.60 (22)
H(4)-C(4)-C(5)	110.16 (21)	C(2)-C(15)-C(10)	122.54 (18)
H(4)-C(4)-C(9)	11.08 (21)	C(2)-C(15)-C(14)	118.48 (18)
C(5)-C(4)-C(9)	110.93 (18)	C(10)-C(15)-C(14)	118.98 (20)
C(4)-C(5)-H(5A)	104.0 (3)	C(17)-C(16)-C(21)	120.56 (21)
C(4)-C(5)-H(5B)	107.93 (25)	C(16)-C(17)-C(18)	120.31 (24)
C94)-C(5)-C(6)	111.54 (19)	C917)-C(18)-C(19)	119.5 (3)
H(5A)-C(5)-H(5B)	118.0 (3)	C(18)-C(19)-C(20)	120.63 (25)
H(5A)-C(5)-C(6)	105.3 (3)	C(19)-C(20)-C(21)	120.10 (21)
H(5B)-C(5)-C(6)	109.9 (3)	C(2)-C(21)-C(16)	122.12 (18)
C(5)-C(6)-H(6A)	108.0 (3)	C(2)-C(21)-C(20)	118.90 (18)
C(5)-C(6)-H(6B)	105.6 (3)	C(16)-C(21)-C(20)	118.88 (19)

substituent attached to C(1) adopts an equatorial position whereas the *N*-methyl substituent shows preference for an axial position, similar to that noted previously for **5e**.[4] Although *N*-methyl substituents in saturated heterocyclic systems would normally be found in the equatorial position, the observed arrangement in both **5t** and **5e** minimizes steric interactions with the geminal phenyl groups at C(2). The equatorial phenyl group in **5t** rotates out of the bisecting ring plane through C(1) and C(2) by almost 58° to accommodate the axial methyl group (cf. 51° in **5e**).

In the triphenyl derivative **5f**, which was isolated as a single isomer, the substituents all lie in equatorial positions with the phenyl ring planes almost perpendicular to the dihydrotrioxazine ring plane (Figure 3). This arrangement appears to be close to what would be notionally regarded as the lowest energy conformation.

Stereochemistry of [3 + 3] Cycloaddition between Carbonyl Oxide and (*E*)- or (*Z*)-α-(4-Methylphenyl)-α-4-phenyl-*N*-methylnitrone. [3 + 3] Cycloadditions between two 1,3-dipoles are predicted to be stepwise, unless one of the components is antarafacial. To investigate the stereochemistry of the [3 + 3] cycloaddition processes described above, the ozonolysis of vinyl ether 1 was carried out in the presence of the conformationally

Table V. Fractional Coordinates of Non-Hydrogen Atoms with Estimated Standard Deviations for Dihydrotrioxazine 5f

	x	y	z	U_{eq}
O(1)	0.21060 (0)	0.13477 (17)	0.08804 (13)	0.072 (4)
O(2)	0.0462 (14)	0.10151 (19)	0.08732 (14)	0.074 (5)
O(3)	0.1777 (14)	0.0827 (18)	0.02851 (13)	0.063 (4)
N(1)	0.3416 (16)	0.11323 (21)	0.02812 (17)	0.059 (5)
C(1)	0.1440 (22)	0.0684 (3)	0.06740 (24)	0.072 (7)
C(2)	0.2412 (20)	0.14785 (25)	0.04932 (19)	0.058 (6)
C(4)	0.0344 (16)	−0.0021 (3)	0.09045 (16)	0.089 (8)
C(5)	−0.1176 (16)	−0.0346 (3)	0.09218 (16)	0.113 (10)
C(6)	−0.3161 (16)	−0.0316 (3)	0.07211 (16)	0.104 (10)
C(7)	−0.3626 (16)	0.0037 (3)	0.05032 (16)	0.087 (8)
C(8)	−0.2105 (16)	0.0362 (3)	0.04860 (16)	0.081 (8)
C(3)	−0.0121 (16)	0.0333 (3)	0.06866 (16)	0.067 (7)
C(10)	0.6058 (20)	0.17799 (22)	0.0763 (17)	0.081 (8)
C(11)	0.7465 (20)	0.21196 (22)	0.07487 (17)	0.103 (9)
C(12)	0.6819 (20)	0.25109 (22)	0.06170 (17)	0.126 (12)
C(13)	0.4767 (20)	0.25624 (22)	0.04429 (17)	0.113 (10)
C(14)	0.3359 (20)	0.22227 (22)	0.04006 (17)	0.085 (8)
C(9)	0.4005 (20)	0.18315 (22)	0.05323 (17)	0.058 (7)
C(16)	0.5756 (15)	0.13893 (16)	−0.02350 (15)	0.066 (6)
C(17)	0.6105 (15)	0.15003 916)	−0.06190 (15)	0.077 (7)
C(18)	0.4422 (15)	0.14502 (16)	−0.08890 (15)	0.076 (7)
C(19)	0.2391 (15)	0.12892 (16)	−0.07749 (15)	0.074 (7)
C(20)	0.2043 (15)	0.11783 (16)	−0.03908 (15)	0.068 (6)
C(15)	0.3725 (15)	0.12283 (16)	−0.01209 (15)	0.053 (5)

Table VI. Derived Geometrical Parameters for Dihydrotrioxazine 5f

(a) Bond Lengths (Å) with Standard Deviations

O(1)–O(2)	1.464 (8)	N(1)–C(15)	1.441 (10)
O(1)–C(2)	1.419 (10)	C(1)–H(1)	1.034 (15)
O(2)–C(1)	1.403 (13)	C(1)–C(3)	1.474 (13)
O(3)–N(1)	1.455 (10)	C(2)–H(2)	1.100 (13)
O93)–C(1)	1.417 (12)	C(2)–C(9)	1.498 (13)
N(1)–C(2)	1.467 (12)		

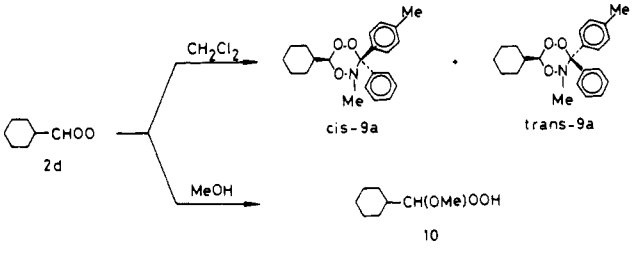
(b) Angles (deg) with Standard Deviations

O(2)–O(1)–C(2)	106.8 (5)	C(5)–C(4)–C(3)	120.0 (7)
O(1)–O(2)–C(1)	106.0 (6)	C(5)–C(4)–H(4)	120.0 (9)
N(1)–O(3)–C(1)	107.7 (7)	C(3)–C(4)–H(4)	120.0 (9)
O(3)–N(1)–C(2)	105.3 (6)	C(4)–C(5)–C(6)	120.0 (7)
O(3)–N(1)–C(15)	104.7 (6)	C(4)–C(5)–H(5)	120.0 (9)
C(2)–N(1)–C(15)	112.1 (7)	C(6)–C(5)–H(5)	120.0 (9)
O(2)–C(1)–O(3)	108.9 (8)	C(5)–C(6)–C(7)	120.0 (7)
O(2)–C(1)–H(1)	104.4 (10)	C(5)–C(6)–H(6)	120.0 (9)
O(2)–C(1)–C(3)	107.2 (8)	C(7)–C(6)–H(6)	120.0 (9)
O(3)–C(1)–H(1)	107.7 (10)	C(6)–C(7)–C(8)	120.0 (7)
O(3)–C(1)–C(3)	109.2 (8)	C(6)–C(7)–H(7)	120.0 (9)
H(1)–C(1)–C(3)	119.2 (11)	C(8)–C(7)–H(7)	120.0 (9)
O(1)–C(2)–N(1)	107.7 (7)	C(7)–C(8)–C(3)	120.0 (7)
O(1)–C(2)–H(2)	118.2 (9)	C(7)–C(8)–H(8)	120.0 (9)
O(1)–C(2)–C(9)	102.9 (7)	C(3)–C(8)–H(8)	120.0 (9)
N(1)–C(2)–H(2)	111.6 (9)	C(1)–C(3)–C(4)	120.7 (8)
N(1)–C(2)–C(9)	110.6 (7)	C(1)–C(3)–C(8)	119.3 (8)
H(2)–C(2)–C(9)	105.4 (9)	C(4)–C(3)–C(8)	120.0 (7)

stable (*E*)- or (*Z*)-α-(4-methylphenyl)-α-phenyl-*N*-methylnitrone ((*E*)-**4f** and (*Z*)-**4f**, respectively).[11]

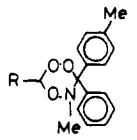
The ozonolysis of 1-cyclohexyl-2-methoxyethene (**1d**) (2 mmol) in the presence of 1 mmol of α,α-diphenyl-*N*-methylnitrone (**4e**) gave the adduct **5t** in 90% yield as a single isomer as shown by X-ray analysis (Figure 2). In contrast, the ozonolysis of a mixture of vinyl ether **1d** (2 mmol) and (*Z*)-nitrone (*Z*)-**4f** in methylene chloride at −70 °C produced an equimolar mixture of the corresponding isomeric adducts **9a** in 87% yield, together with a 1:1 mixture of the unreacted (*E*)- and (*Z*)-**4f** (13%). A similar result was obtained using the isomeric nitrone (*E*)-**4f** (Table VII and Scheme III). Although the two isomers of **9a** were not separable, it is reasonable to expect that, by analogy with the structure of **5t**, the *N*-methyl and cyclohexyl groups are located in axial and equatorial positions, respectively, and the isomerism arises from the interchanging of the phenyl and 4-methylphenyl groups.

Scheme III



The cis–trans isomer ratios of dihydrotrioxazines were essentially invariant with the vinyl ether to ozone ratio (Table VII, entries 1–7). As judged from ^{1}H NMR analysis, similar results were obtained from the ozonolyses of mixture of **1b** or 1-(4-methoxyphenyl)-2-methoxyethene (**1h**) and nitrone (*Z*)-**4f** though the actual dihydrotrioxazines

(11) Dobashi, T. S.; Goodrow, M. H.; Grubbs, E. J. *J. Org. Chem.* 1973, *38*, 4440.



9b; R = heptyl
9c; R = 2-$CF_3C_6H_4$
9d; R = Ph
9e; R = 4-$MeOC_6H_4$

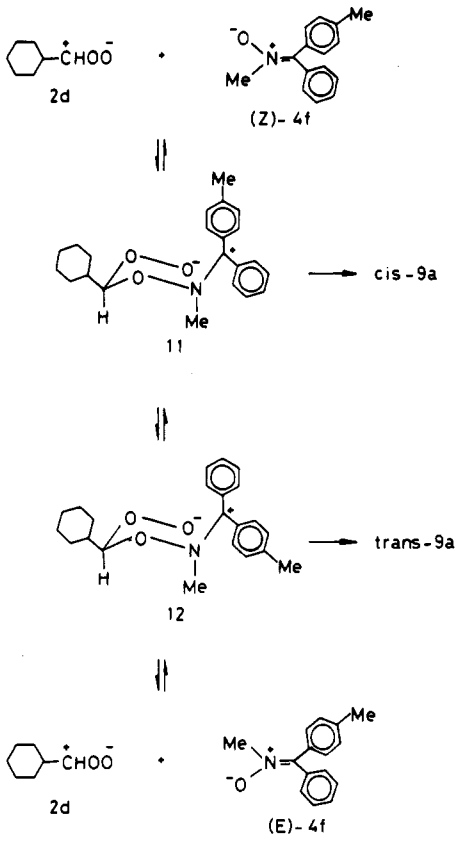
9d [^{1}H NMR δ 2.24 (s, *p*-Me), 2.31 (s, *p*-Me), 2.80 (s, NMe), 6.69 (s, H-3)] and **9e** [^{1}H NMR δ 2.28 (s, *p*-Me), 2.34 (s, *p*-Me), 2.82 (s, NMe), 3.70 (s, OMe), 6.10 (s, H-3)] were too labile to be isolated by column chromatography on silica gel (Table VII, entries 8–10). The *E*/*Z* ratios of the recovered nitrones were observed to vary significantly with the ratio of ozone to enol ether substrate (Table VII, column 5).

When a solution of **1d** and (*Z*)-**4f** in methanol–methylene chloride was ozonized, the solvent-derived product, α-methoxycyclohexylmethyl hydroperoxide (**10**), was obtained quantitatively, suggesting that capture of the intermediate carbonyl oxide **2d** by solvent was significantly faster than the reaction of **2d** with nitrone **4f** (Scheme III).[3b,12] Consistent with this, the recovered nitrone **4f** was not contaminated with the (*E*)-isomer. Nitrone (*Z*)-**4f** reacted only slowly with ozone; after the passage of 1 equiv, 4-methylbenzophenone (**6f**) was obtained in 38% yield, together with unreacted **4f** (61%). No significant isomerization of the (*Z*)-**4f** was observed.

Taken together, the above stereochemical observations suggest that the [3 + 3] cycloaddition process between the carbonyl oxide **2d** and the nitrone **4f** should be faster than the isomerization of nitrone **4f** which in turn implies that the nitrone **4f** must lose the stereochemical integrity during the cycloaddition process. Thus, the most probable cycloaddition process would be a stepwise as proposed in Scheme IV.[13]

Ozone attacks preferentially the electron-rich vinyl ether **1d** providing cyclohexanecarboxaldehyde *O*-oxide (**2d**) and methyl formate (**3b**). In the first step of the cycloaddition process, there are two possible ways in which the dipolar carbonyl oxide **2d** and nitrone **4f** could combine. Since the steric requirements of the nitrone substituents, unlike those of the carbonyl oxide component, have been found to have a little effect on the overall rate of reaction, it seems likely that the terminal oxygen of the nitrone **4f** attacks the electrophilic carbon of carbonyl oxide **2d** to produce the zwitterionic intermediate **11**. Although subsequent ring closure would give the *cis*-dihydrotrioxazine *cis*-**9a** selectively, this would be inconsistent with the formation of a 1:1 mixture of the *cis*- and *trans*-**9a**. There must, therefore, be rapid interconversion between the zwitterionic intermediates **11** and **12** by bond rotation from which *cis*- and *trans*-**9a** are derived respectively. To account for the isomerization of the nitrone **4f** requires that

Scheme IV



the intermediates **11** and **12** can revert reversibly to the carbonyl oxide and the nitrone **4f** as indicated in Scheme IV.

Decomposition of Dihydro-3-phenyl-5-benzyl-6-heptyl-1,2,4,5-trioxazine (5h). The results of the decomposition studies on dihydro-3-phenyl-5-benzyl-6-heptyl-1,2,4,5-trioxazine (**5h**), presumed to be a typical dihydrotrioxazine derivative, are summarized in Table VIII.

Thermolysis of a solution of **5h** in benzene at reflux for 8 h afforded a mixture of ring cleavage products, benzaldehyde (**6a**) (78%), octanal (**6b**) (78%), and benzaldehyde oxime (**13**) (20%), together with recovered **5h** (11%) (eq 1).

$$\mathbf{5h} \xrightarrow{\text{heat}} \mathbf{6b} + \mathbf{6c} + \underset{\mathbf{13}}{\text{PhCH=NOH}} \qquad (1)$$

Treatment of **5h** with triethylamine (10 equiv) at room temperature for 90 h resulted in the formation of a mixture of nitrone **4c** and benzoic acid (**14**) in yields of 34% and 59%, respectively (eq 2). With excess sodium ethoxide

$$\mathbf{5h} \xrightarrow{\text{Et}_3\text{N}} \mathbf{4c} + \underset{\mathbf{14}}{\text{PhCO}_2\text{H}} \qquad (2)$$

in ethanol at room temperature for 24 h, **5h** gave nitrone **4c** (49%) and benzoic acid (**14**) (93%) as before but also octanal (**6b**) (18%) and benzaldehyde oxime (**13**) (20%). The base-catalyzed decomposition results are generally consistent with an initial abstraction of the acidic C-3 hydrogen followed by reorganization of the ring system. This reaction sequence is very similar to that observed for the decomposition of the relevant 1,2,4-trioxanes under similar conditions.[14]

(12) (a) Griesbaum, K.; Kim, W.; Nakamura, N.; Mori, M.; Nojima, M.; Kusabayashi, S. *J. Org. Chem.* **1990**, *55*, 6153; (b) Keul, H.; Kuczkowski, R. L. *J. Am. Chem. Soc.* **1984**, *106*, 5370; (c) Wojciechowski, B. J.; Pearson, W. H.; Kuczkowski, R. L. *J. Org. Chem.* **1989**, *54*, 115.

(13) An alternative explanation would be possible for the formation of a 1:1 mixture of the stereoisomeric trioxazinanes *cis*-**9a** and *trans*-**9a** from the configurationally stable nitrone (*Z*)-**4f**. Four concerted processes shown in Scheme VI could competitively participate; *cis*-**9a** would be formed by pathways a and b, while the isomeric *trans*-**9a** would be formed by pathways c and d. If the steric interactions between cyclohexyl and *N*-methyl groups are important in the transition states in paths c and d, however, the formation of *cis*-**9a** could predominate. This expectation is inconsistent with the experimental observations.

(14) (a) Fujisaka, T.; Miura, M.; Nojima, M.; Kasabayashi, S. *J. Chem. Soc., Perkin Trans. 1* **1989**, 1031; (b) Jefford, C. W.; Rossier, J.; Boukouvalas, J. *J. Chem. Soc., Chem. Commun.* **1986**, 1701; **1987**, 1593.

Table VII. Ozonolysis of Vinyl Ether 1 in the Presence of (*E*)- and (*Z*)-α-(4-Methylphenyl)-α-phenyl-*N*-methylnitrone (4f) in Methylene Chloride at 0 °C

			dihydrotrioxazine		recovered 4f	
vinyl ether (mmol)	nitrone (mmol)	ozone (mmol)	(% yield)	cis/trans	(%)	*E*/*Z*
1d (2)	(*Z*)-**4f** (1)	(1)	**9a** (87)	1:1	(13)	1:1
1d (2)	(*E*)-**4f** (1)	(1)	**9a** (89)	1:1	(11)	1:1
1d (1)	(*Z*)-**4f** (1)	(1)	**9a** (79)	1:1	(21)	2:3
1d (1)	(*Z*)-**4f** (1)	(0.7)	**9a** (59)	1:1	(41)	3:7
1d (1)	(*Z*)-**4f** (1)	(0.5)	**9a** (47)	1:1	(53)	1:9
1c (2)	(*Z*)-**4f** (1)	(2)	**9b** (73)	1:1	(27)	1:1
1g (2)	(*Z*)-**4f** (1)	(2)	**9c** (66)	1:1	(13)	1:1
1b (2)	(*Z*)-**4f** (1)	(2)			(90)	1:1[a]
1b (1)	(*Z*)-**4f** (1)	(0.5)			(88)	1:1[a]
1h (2)	(*Z*)-**4f** (1)	(2)			(76)	1:1[a]

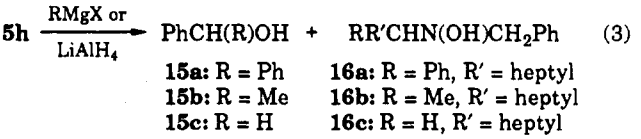
[a] The ^{1}H NMR spectra of the crude products showed the formation of dihydrotrioxazines, **9d** or **9e**, in significant amounts.

Table VIII. Reaction of Dihydro-3-phenyl-5-benzyl-6-heptyl-1,2,4,5-trioxazine (5h)

reagent (equiv)	solvent	reaction time, h	products (% yield)	recovered **5h** (%)
heat	benzene	8	**6a** (78), **6b** (78), **13** (53)	(11)
Et_3N (10)	CH_2Cl_2	90	**4c** (34), **14** (59)	(1)
NaOEt (13)	EtOH	24	**4c** (49), **6b** (18), **13** (20), **14** (93)	
PhMgBr (10)	ether	20	**15a** (93), **16a** (68)	
MeMgI (10)	ether	20	**4c** (17), **15b** (77), **16b** (54)	
LAH[c] (9)	ether	20	**15c** (63), **16c** (57)	
LAD[d] (4)	ether	20	**15c**-α-*d* (48), **16c**-α-*d* (52)	(15)
PPh_3 (1)	benzene	90	**4c** (17), **6a** (11)	(80)
$TiCl_4$ (1)	CH_2Cl_2	0.5	**4c** (28), **6a** (89), **6b** (44)	
TFA[e] (3)	CH_2Cl_2	15	**4c** (25), **6a** (30), **6b** (26), **14** (16), **17** (25), **18** (11)	

[a] The reaction was conducted at room temperature unless otherwise noted. [b] The reaction at 80 °C. [c] Lithium aluminum hydride. [d] Lithium aluminum deuteride. [e] Trifluoroacetic acid.

The reaction of **5h** with nucleophiles such as Grignard reagents and lithium aluminum hydride proceeded smoothly. When **5h** was treated with phenylmagnesium bromide (10 equiv) in ether for 20 h at room temperature, benzhydrol (**15a**) and *N*-benzyl-*N*-(1-phenyloctyl)-hydroxylamine (**16a**) were obtained in yields of 93% and 68%, respectively. Similar results were obtained for the reaction between **5h** and methylmagnesium iodide and lithium aluminum hydride (eq 3). These results suggest



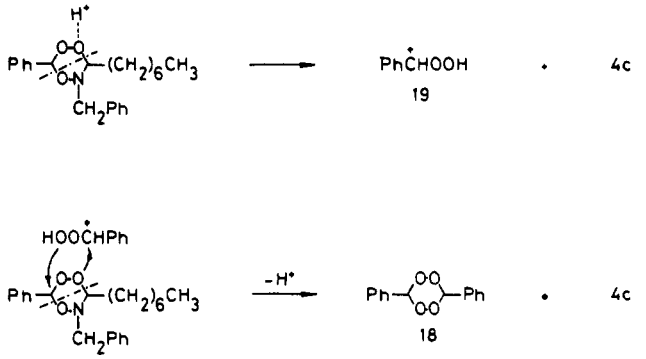
(3)

that the dihydrotrioxazine is initially deoxygenated by the nucleophilic reagent to yield a mixture of benzaldehyde (**6a**) and α-heptyl-*N*-benzylnitrone (**4c**), which react in turn with excess reagent to produce the observed alcohols **15a–c** and *N*-hydroxylamines **16a–c**.[15] Consistent with this, reduction of **5h** with lithium aluminum deuteride resulted in the formation of a mixture of **15c**-α-*d* and **16c**-α-*d*.

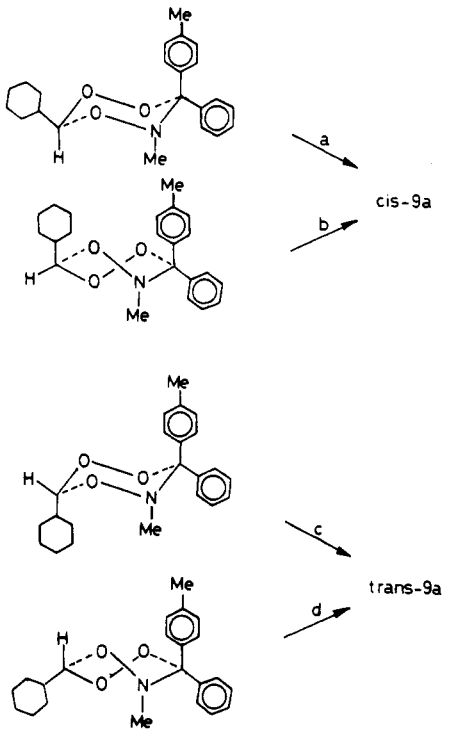
Although the reduction of **5h** with lithium aluminum hydride proceeded smoothly, deoxygenation of **5h** with triphenylphosphine was very slow. Thus, treatment of **5h** with 1 equiv of triphenylphosphine in benzene at room temperature for 90 h gave a mixture of benzaldehyde (**6a**) (11%) and the nitrone **4c** (17%); the starting material was recovered in 80% yield. Under similar reaction conditions, **5h** did not react with thioanisole.

Titanium tetrachloride catalyzed decomposition of **5h** was rapid. After 30 min, the peroxide **5h** was completely consumed, producing a product mixture consisting of the nitrone **4c**, benzaldehyde (**6a**), and octanal (**6b**) in isolated yields of 28%, 89%, and 44%, respectively. With trifluoroacetic acid as catalyst, the decomposition product mixture was more complex. In addition to the ring-cleavage products **4c**, **6a**, and **6b** observed previously,

Scheme V



Scheme VI



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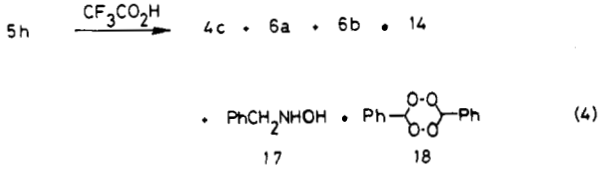
benzoic acid (14), *N*-benzylhydroxylamine (17) and the 3,6-diphenyl-1,2,4,5-tetraoxane (18, 11%) were also obtained. The hydroxylamine 17 was produced by the acidolysis of the corresponding nitrone.[16] The formation of the tetraoxane 18 is noteworthy. It is probably formed via the protonated carbonyl oxide **19**, as outlined in Scheme V, in a similar fashion to that proposed for the formation of tetraoxanes from the acid-catalyzed rearrangement of 3,5-disubstituted 1,2,4-trioxolanes (ozonides).[17]



(4)

Experimental Section

General. ^1H and ^{13}C NMR spectra in $CDCl_3$ were obtained with a JNM-PS-100 spectrometer and a JEOL JNM-GSX-400 spectrometer, respectively. Mass data were obtained with a JEOL JMS-DX303 spectrometer and infrared with a Hitachi 215 spectrometer. The method of preparation of the vinyl ethers **1b–h** is described elsewhere.[12a] α-*N*-Diphenylnitrone (**4a**),[18] α-phenyl-*N*-benzylnitrone (**4b**),[16] α-heptyl-*N*-benzylnitrone (**4c**),[19] α,α,*N*-triphenylnitrone (**4d**),[20] α-diphenyl-*N*-methylnitrone (**4e**),[21] and (*E*)- and (*Z*)-α-(4-methylphenyl)-α-phenyl-*N*-methylnitrone, (*E*)-**4f**, and (*Z*)-**4f**[21] were prepared by the reported methods.

(*E*)-**4f**: mp 109–112 °C (from benzene–hexane); ^1H NMR δ 2.46 (s, 3 H), 3.75 (s, 3 H), 7.0–7.5 (m, 7 H), 7.8–8.1 (m, 2 H).

(*Z*)-**4f**: mp 93–95 °C (from benzene–hexane); ^1H NMR δ 2.36 (s, 3 H), 3.73 (s, 3 H), 7.0–7.6 (m, 7 H), 7.89 (d, *J* = 8 Hz, 1 H).

Ozonolysis of a Vinyl Ether in the Presence of a Nitrone. Reaction of a mixture of vinyl ether **1c** and nitrone **4a** is representative. A solution of **1c** (2 mmol) and nitrone **4a** (1 mmol) in methylene chloride (20 mL) was treated with 2 mmol of ozone at 0 °C. After evaporation of the solvent, the products were separated by column chromatography on silica gel. Elution with benzene–hexane (3:7) gave a mixture of two isomeric dihydro-3-heptyl-5,6-diphenyl-1,2,4,5-trioxazines (**5k**). Subsequent elution with benzene gave a mixture of benzaldehyde and octanal. The isomers of the dihydrotrioxazine **5k** were separated by repeated column chromatography on silica gel. Elution with benzene–hexane (1:4) yielded first *cis,cis*-**5k** and then *trans,trans*-**5k**. The former trioxazine was purified by recrystallization from methanol.

Dihydro-5,6-diphenyl-1,2,4,5-trioxazine (5a): mp 75–77 °C (from methanol); ^1H NMR δ 5.52 (d, *J* = 9 Hz, 1 H), 6.10 (s, 1 H), 6.14 (d, *J* = 9 Hz, 1 H), 7.0–7.4 (m, 10 H). Anal. Calcd for $C_{14}H_{13}NO_3$: C, 69.14; H, 5.35; N, 5.76. Found: C, 68.94; H, 5.38; N, 5.73.

Dihydro-5-(phenylmethyl)-6-phenyl-1,2,4,5-trioxazine (5b): mp 96.5–97.5 °C (from methanol); ^1H NMR δ 3.65 (d, *J* = 15 Hz, 1 H), 3.83 (d, *J* = 15 Hz, 1 H), 5.56 (d, *J* = 8 Hz, 1 H), 5.79 (s, 1 H), 5.94 (d, *J* = 8 Hz, 1 H), 7.2–7.6 (m, 10 H). Anal. Calcd for $C_{15}H_{15}NO_3$: C, 70.04; H, 5.84; N, 5.45. Found: C, 69.87; H, 5.90; N, 5.46.

Dihydro-5-(phenylmethyl)-6-heptyl-1,2,4,5-trioxazine (5c): oil; ^1H NMR δ 0.8–1.5 (m, 15 H), 3.74 (d, *J* = 14 Hz, 1 H), 4.07 (d, *J* = 14 Hz, 1 H), 4.8–5.1 (m, 2 H), 5.6–5.7 (m, 1 H), 7.1–7.3 (m, 5 H); MS (CI; isobutane) *m/z* 280 (M^+ + 1). Anal. Calcd for $C_{16}H_{25}NO_3$: C, 68.82; H, 8.96; N, 5.02. Found: C, 69.25; H, 9.16; N, 5.07.

Dihydro-5,6,6-triphenyl-1,2,4,5-trioxazine (5d): mp 93.5–95 °C (from ethyl acetate–hexane); ^1H NMR δ 5.10 (br s, 1 H), 5.91 (br s, 1 H), 7.0–7.8 (m, 15 H). Anal. Calcd for $C_{20}H_{17}NO_3$: C, 75.24; H, 5.33; N, 4.39. Found: C, 75.20; H, 5.60; N, 4.26.

Dihydro-5-methyl-6,6-diphenyl-1,2,4,5-trioxazine (5e): mp 102–103.5 °C (from methanol); ^1H NMR δ 2.76 (s, 3 H), 4.94 (br s, 1 H), 6.18 (br s, 1 H), 7.3–7.7 (m, 10 H); ^{13}C NMR δ 35.77, 89.97, 100.01, 125.33–132.36 (12 C); MS (CI; isobutane) *m/z* 258 (M^+ + 1). Anal. Calcd for $C_{15}H_{15}NO_3$: C, 70.04; H, 5.84; N, 5.45. Found: C, 69.81; H, 5.88; N, 5.48.

Dihydro-3,5,6-triphenyl-1,2,4,5-trioxazine (5f): mp 108–109 °C (from methanol); ^1H NMR δ 6.10 (s, 1 H), 6.91 (s, 1 H), 7.1–7.6 (m, 15 H); ^{13}C NMR δ 101.06, 106.30, 124.45–130.34 (18 C); MS (CI; isobutane) *m/z* 320 (M^+ + 1). Anal. Calcd for $C_{20}H_{17}NO_3$: C, 75.24; H, 5.33; N, 4.39. Found: C, 75.07; H, 5.36; N, 4.43.

Dihydro-3,6-diphenyl-5-(phenylmethyl)-1,2,4,5-trioxazine (5g): mp 117–120 °C (from methanol); ^1H NMR δ 3.87 (s, 2 H), 5.81 (s, 1 H), 6.69 (s, 1 H), 7.1–7.7 (m, 15 H). Anal. Calcd for $C_{21}H_{19}NO_3$: C, 75.68; H, 5.71; N, 4.20. Found: C, 75.21; H, 5.71; N, 4.18.

Dihydro-3-phenyl-5-(phenylmethyl)-6-heptyl-1,2,4,5-trioxazine (5h): oil; ^1H NMR δ 0.8–1.5 (m, 15 H), 3.87 (d, *J* = 14 Hz, 1 H), 4.16 (d, *J* = 14 Hz, 1 H), 4.7–4.9 (m, 1 H), 6.36 (s, 1 H), 7.1–7.4 (m, 10 H); MS (CI; isobutane) *m/z* 356 (M^+ + 1).

Dihydro-3,5,6,6-tetraphenyl-1,2,4,5-trioxazine (5i): mp 120.5–122 °C (from ethyl acetate–hexane); ^1H NMR δ 6.65 (s, 1 H), 7.1–7.9 (m, 20 H). Anal. Calcd for $C_{26}H_{21}NO_3$: C, 78.99; H, 5.32; N, 3.54. Found: C, 78.95; H, 5.29; N, 3.51.

Dihydro-*cis,cis*-3-heptyl-5,6-diphenyl-1,2,4,5-trioxazine (*cis,cis*-5k): mp 60–62 °C (from methanol); ^1H NMR δ 0.8–1.6 (m, 15 H), 5.66 (t, *J* = 5 Hz, 1 H), 6.46 (s, 1 H), 6.9–7.6 (m 10 H); MS (CI; isobutane) *m/z* 342 (M^+ + 1). Anal. Calcd for $C_{21}H_{27}NO_3$: C, 73.90; H, 7.92; N, 4.11. Found: C, 73.61; H, 8.02; N, 4.09.

Dihydro-*trans,trans*-3-heptyl-5,6-diphenyl-1,2,4,5-trioxazine (*trans,trans*-5k): oil; ^1H NMR δ 0.8–1.6 (m, 15 H), 5.69 (s, 1 H), 5.82 (t, *J* = 5 Hz, 1 H), 6.9–7.2 (m, 10 H); MS (CI; isobutane) *m/z* 342 (M^+ + 1). Anal. Calcd for $C_{21}H_{27}NO_3$: C, 73.90; H, 7.92; N, 4.11. Found: C, 74.04; H, 8.17; N, 4.27.

Dihydro-3-heptyl-5-(phenylmethyl)-6-phenyl-1,2,4,5-trioxazine (5l): mp 21–24 °C; ^1H NMR δ 0.8–1.7 (m, 15 H), 3.54 (d, *J* = 14 Hz, 1 H), 3.81 (d, *J* = 14 Hz, 1 H), 5.46 (s, 1 H), 5.60 (t, *J* = 5 Hz, 1 H), 7.1–7.5 (m, 10 H). Anal. Calcd for $C_{22}H_{29}NO_3$: C, 74.37; H, 8.17; N, 3.94. Found: C, 74.37; H, 8.29; N, 4.13.

Dihydro-3,6-heptyl-5-(phenylmethyl)-1,2,4,5-trioxazine (5m; major isomer): oil; ^1H NMR δ 0.8–1.7 (m, 30 H), 3.73 (d, 14 Hz, 1 H), 4.06 (d, *J* = 14 Hz, 1 H), 4.7–4.8 (m, 1 H), 5.45 (t, *J* = 5 Hz, 1 H), 7.2–7.4 (m, 5 H); MS (CI; isobutane) *m/z* 378 (M^+ + 1). Anal. Calcd for $C_{23}H_{39}NO_3$: C, 73.21; H, 10.34; N, 3.71. Found: C, 73.36; H, 10.40; N, 3.88.

Minor 5m (in admixture with the major isomer, the ratio being 34:66): oil; ^1H NMR δ 0.8–1.7 (m, 30 H), 3.73 (d, *J* = 14 Hz, 1 H), 4.06 (d, *J* = 14 Hz, 1 H), 4.1–4.2 (m, 1 H), 5.67 (t, 5 Hz, 1 H), 7.2–7.4 (m, 5 H). Anal. Calcd for $C_{23}H_{39}NO_3$: C, 73.21; H, 10.34; N, 3.71. Found: C, 73.40; H, 10.41; N, 3.73.

Dihydro-3-heptyl-5,6,6-triphenyl-1,2,4,5-trioxazine (5n): oil; ^1H NMR δ 0.7–1.3 (m, 15 H), 5.68 (t, *J* = 5 Hz, 1 H), 6.8–7.7 (m 15 H); MS (CI; isobutane) *m/z* 418 (M^+ + 1). Anal. Calcd for $C_{27}H_{31}NO_3$: C, 77.70; H, 7.43; N, 3.36. Found: C, 77.76; H, 7.59; N, 3.38.

Dihydro-3-heptyl-5-methyl-6,6-diphenyl-1,2,4,5-trioxazine (5o): oil; ^1H NMR δ 0.8–1.3 (m, 15 H), 2.69 (s, 3 H), 5.58 (t, *J* = 5 Hz, 1 H), 7.1–7.7 (m, 10 H); MS (CI; isobutane) *m/z* 356 (M^+ + 1). Anal. Calcd for $C_{22}H_{29}NO_3$: C, 74.37; H, 8.17; N, 3.94. Found: C, 74.41; H, 8.32; N, 4.06.

Dihydro-3-cyclohexyl-5,6-diphenyl-1,2,4,5-trioxazine (5p; *major isomer*): mp 75–77 °C (from methanol); ^1H NMR δ 1.4–2.1 (m, 11 H), 5.71 (d, *J* = 6 Hz, 1 H), 5.74 (s, 1 H), 6.9–7.5 (m, 10 H). Anal. Calcd for $C_{20}H_{23}NO_3$: C, 73.85; H, 7.08; N, 4.31. Found: C, 73.48; H, 7.14; N, 4.29.

Minor 5p (in admixture with the major one, the ratio being 29:71): an oil; ^1H NMR δ 1.1–2.0 (m, 11 H), 5.49 (d, *J* = 6 Hz, 1 H), 6.54 (s, 1 H), 7.0–8.0 (m, 10 H). Anal. Calcd for $C_{20}H_{23}NO_3$: C, 73.85; H, 7.08; N, 4.31. Found: C, 74.03; H, 7.05; N, 4.30.

Dihydro-3-cyclohexyl-5-(phenylmethyl)-6-phenyl-1,2,4,5-trioxazine (5q): mp 121–124 °C (from ethyl acetate–hexane); ^1H NMR δ 1.1–1.7 (m, 11 H), 3.69 (d, *J* = 13 Hz, 1 H), 3.81 (d, *J* = 13 Hz, 1 H), 5.53 (d, *J* = 5 Hz, 1 H), 5.59 (s, 1 H), 7.2–7.5 (m, 10 H). Anal. Calcd for $C_{21}H_{25}NO_3$: C, 74.34; H, 7.37; N, 4.13. Found: C, 74.01; H, 7.40; N, 4.11.

Dihydro-3-cyclohexyl-5-(phenylmethyl)-6-heptyl-1,2,4,5-trioxazine (5r; major isomer): oil; ^1H NMR δ 0.9–1.7 (m, 26 H), 3.73 (d, *J* = 14 Hz, 1 H), 4.07 (d, *J* = 14 Hz, 1 H), 4.7–4.8 (m,

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1 H), 5.22 (d, J = 5 Hz, 1 H), 7.1–7.2 (m, 5 H). Anal. Calcd for $C_{21}H_{33}NO_3$: C, 72.62; H, 9.51; N, 4.03. Found: C, 73.04; H, 9.82; N, 3.83.

Minor 5r (in admixture with the major isomer, the ratio being 33:67): oil; ^{1}H NMR δ 0.9–1.7 (m, 26 H), 3.73 (d, J = 14 Hz, 1 H), 4.07 (d, J = 14 Hz, 1 H), 4.2–4.3 (m, 1 H), 5.42 (d, J = 5 Hz, 1 H), 7.1–7.2 (m, 5 H). Anal. Calcd for $C_{21}H_{33}NO_3$: C, 72.62; H, 9.51; N, 4.03. Found: C, 72.95; H, 9.70; N, 4.00.

Dihydro-3-cyclohexyl-5,6,6-triphenyl-1,2,4,5-trioxazine (5s): mp 100–102 °C (from ethyl acetate–hexane); ^{1}H NMR δ 1.0–1.6 (m, 11 H), 5.57 (d, J = 5 Hz, 1 H), 7.0–7.5 (m, 13 H), 7.7–7.8 (m, 2 H). Anal. Calcd for $C_{26}H_{27}NO_3$: C, 77.81; H, 6.73; N, 3.49. Found: C, 77.48; H, 6.76; N, 3.46.

Dihydro-3-cyclohexyl-5-methyl-6,6-diphenyl-1,2,4,5-trioxazine (5t): mp 104–106 °C (from ethyl acetate–hexane); ^{1}H NMR δ 1.0–1.6 (m, 11 H), 2.75 (s, 3 H), 5.72 (d, J = 5 Hz, 1 H), 7.2–7.4 (m, 8 H), 7.6–7.7 (m, 2 H). Anal. Calcd for $C_{21}H_{25}NO_3$: C, 74.34; H, 7.37; N, 4.13. Found: C, 74.23; H, 7.43; N, 4.16.

3,4-Diphenyl-1,2,5-triox-4-azaspiro[5.5]undecane (5u): mp 126–126.5 °C (from ether–hexane); ^{1}H NMR δ 1.5–1.7 (m, 10 H), 5.87 (s, 1 H), 7.1–7.4 (m, 10 H). Anal. Calcd for $C_{19}H_{21}NO_3$: C, 73.31; H, 6.75; N, 4.50. Found: C, 73.24; H, 6.84; N, 4.51.

3-Phenyl-4-benzyl-1,2,5-triox-4-azaspiro[5.5]undecane (5v): mp 116–117 °C (from methanol); ^{1}H NMR δ 1.2–2.8 (m, 10 H), 3.54 (d, J = 14 Hz, 1 H), 3.72 (d, J = 14 Hz, 1 H), 5.54 (s, 1 H), 7.1–7.6 (m, 10 H). Anal. Calcd for $C_{20}H_{23}NO_3$: C, 73.85; H, 7.08; N, 4.31. Found: C, 73.72; H, 7.12; N, 4.37.

3-Heptyl-4-benzyl-1,2,5-triox-4-azaspiro[5.5]undecane (5w): an oil; ^{1}H NMR δ 0.8–2.4 (m, 25 H), 3.57 (d, J = 14 Hz, 1 H), 3.95 (d, J = 14 Hz, 1 H), 4.56 (t, J = 4 Hz, 1 H), 7.2–7.4 (m, 5 H). Anal. Calcd for $C_{21}H_{33}NO_3$: C, 72.62; H, 9.51; N, 4.03. Found: C, 72.61; H, 9.58; N, 4.07.

Dihydro-3,3-diphenyl-5-(phenylmethyl)-6-heptyl-1,2,4,5-trioxazine (5x): an oil; ^{1}H NMR δ 0.9–1.6 (m, 15 H), 3.82 (d, J = 14 Hz, 1 H), 4.10 (d, J = 14 Hz, 1 H), 4.98 (t, J = 5 Hz, 1 H), 7.2–7.4 (m, 15 H).

Competition Reaction between Two Nitrones 4a and 4d. A solution of **1b** (268 mg, 2 mmol), **4a** (197 mg, 1 mmol), and **4d** (273 mg, 1 mmol) in methylene chloride (15 mL) was treated with ozone (2 mmol) at 0 °C. After evaporation of the solvent, the products were separated by column chromatography on silica gel. Elution with benzene–hexane (1:4) gave a mixture of dihydrotrioxazines **5f** (δ 6.17) and **5i** (δ 6.75) in yields of 14% and 58%, respectively (the ratio was determined by comparing the pear areas of the characteristic signals in ^{1}H NMR spectra cited in the blankets).

Treatment of a mixture of **1a** (100 mg, 1 mmol), **4a** (197 mg, 1 mmol), and **4d** (273 mg, 1 mmol) in methylene chloride with ozone (1 mmol) at 0 °C, followed by column chromatography on silica gel (elution with benzene–hexane, 1:4), afforded a mixture of dihydrotrioxazines **5a** (δ 5.52 (d), 6.14 (s), 6.19 (br d)) and **5d** (δ 5.0–6.3 (br s)) in yields of 43% and 49%, respectively.

Competition Reaction between Nitrone 4d and Benzophenone (6e). Over a solution of **1b** (268 mg, 2 mmol), **4d** (273 mg, 1 mmol), and **6e** (182 mg, 1 mmol) in methylene chloride (15 mL) was passed a slow stream of ozone (2 mmol) at 0 °C. After evaporation of the solvent, the products were separated by column chromatography on silica gel. Elution with benzene–hexane (1:4) gave **5i** (182 mg, 46% yield). Subsequent elution with benzene gave benzaldehyde (**6a**, 75 mg) and then benzophenone (**6e**, 170 mg). From the final fraction (elution with methanol–ether (1:10)) was obtained **4d** (137 mg, 50%).

Chlorosulfonic Acid-Catalyzed Isomerization of *cis,cis*-5k. A mixture of *cis,cis*-**5k** (1 mmol) and chlorosulfonic acid (0.1 mmol) in methylene chloride (10 mL) was kept with stirring at 0 °C for 30 min. The mixture was poured into aqueous potassium hydroxide, extracted with ether, and dried over anhydrous magnesium sulfate. Column chromatography on silica gel (elution with benzene–hexane (1:4)) gave a mixture of *trans,trans*- and *cis,cis*-**5k** in 80% yield, the ratio being 77:23.

Reaction of Dihydrotrioxazine 5m with Triphenylphosphine. A $CDCl_3$ solution (1 mL) of **5m** (100 mg, the isomer ratio = 66:34) and triphenylphosphine (70 mg) was kept in a NMR tube at room temperature. By measuring the ^{1}H NMR spectra periodically, it was found that after 40 h the signals attributable to the minor isomer of **5m** disappeared completely. The mixture was then column chromatographed on silica gel. The first fraction (elution with benzene–hexane (1:1)) contained the major isomer of **5m**. From the second fraction (elution with benzene) was obtained **6b**. The final fraction (elution with ether) contained nitrone **4a**.

Reaction of Nitrone 4c with Ozone. A methylene chloride solution of **4c** (2 mmol) was treated with 2 mmol of ozone at 0 °C. By column chromatography (elution with benzene–hexane (1:1)) was obtained (nitromethyl)benzene (**7**) first. The second fraction (elution with benzene) contained octanal (**6b**). From the third fraction (elution with ether–benzene (2:3)) was obtained the nitroso dimer **8**. The final fraction (elution with methanol–ether (1:9)) contained the nitrone **4c**.

(Nitromethyl)benzene (7): an oil; ^{1}H NMR δ 5.34 (s, 2 H), 7.35 (s, 5 H); IR 2920, 1552, 1372, 700 cm^{-1}.[22]

α-Nitrosotoluene dimer 8: mp 129–131 °C (lit.[23] mp 116–118 °C); ^{1}H NMR d 5.39 (s, 4 H), 7.40 (s, 10 H); MS (EI) m/z 242 (M^+); IR 3025, 1498, 1457, 1424, 1347, 1308, 1285, 1174, 1160, 1029, 750, 693 cm^{-1}. Anal. Calcd for $C_{14}H_{14}N_2O_4$: C, 69.42; H, 5.79; N, 11.57. Found: C, 69.13; H, 5.87; N, 11.43.

Ozonolysis of a Vinyl Ether in the Presence of (*E*)- or (*Z*)-α-(4-Methylphenyl)-α-phenyl-*N*-methylnitrone (4f) in Methylene Chloride. Ozonolysis of **1d** in the presence of (*E*)-**4f** is representative. In a 50-mL flask, equipped with a magnetic stirrer and a gas-inlet tube, was added a solution of 1-cyclohexyl-2-methoxyethene (**1d**) (280 mg, 2 mmol) and (*E*)-**4f** (225 mg, 1 mmol) in methylene chloride (15 mL), and the mixture was cooled to −70 °C in a methanol–dry ice bath. Into the mixture was passed a slow stream of O_3/O_2 (2 mmol of ozone), and then the solvent was immediately evaporated in vacuo. Then, the products were separated by column chromatography on silica gel. Elution with benzene–hexane (3:7) gave a cis–trans mixture of the dihydrotrioxazine **9a**. By the subsequent elution with ether–methanol (9:1) was obtained nitrone **4f** (a 1:1 mixture of (*E*)- and (*Z*)-isomer).

Dihydro-3-cyclohexyl-5-methyl-6-(4-methylphenyl)-6-phenyl-1,2,4,5-trioxazine (9a; a 1:1 mixture of cis and trans isomer): mp 70–74 °C (from ether–hexane); ^{1}H NMR δ 0.7–2.0 (m, 11 H), 2.25 (s, *p*-Me), 2.30 (s, *p*-Me), 2.70 (s, 3 H, NMe), 5.61 (br d, J = 5 Hz, 1 H, H-3), 6.9–7.7 (m, 9 H); ^{13}C NMR δ 21.05 (*p*-Me), 21.11 (*p*-Me), 25.44, 25.48, 25.50, 26.09, 26.57, 26.67, 26.77, 26.83, 36.47 (NMe), 36.57 (NMe), 39.26, 39.34, 98.60 (C-6), 98.67 (C-6), 99.49 (C-3), 99.63 (C-3), 125.21, 125.46, 126.90, 127.70, 127.74, 127.80, 127.95, 128.30, 128.58, 129.02, 136.57, 137.14, 137.81, 139.56, 140.20, 142.62; IR 2940, 2860, 1450, 1240, 1210, 1181, 1102, 1080, 1015, 990, 808, 755, 698, 680 cm^{-1}. Anal. Calcd for $C_{22}H_{27}NO_3$: C, 74.76; H, 7.70; N, 3.96. Found: C, 74.91; H, 7.74; N, 4.02.

Dihydro-3-heptyl-5-methyl-6-(4-methylphenyl)-6-phenyl-1,2,4,5-trioxazine (9b; a 1:1 mixture of cis and trans isomer): oil; ^{1}H NMR δ 0.7–1.8 (m, 15 H), 2.23 (s, *p*-Me), 2.30 (s, *p*-Me), 2.73 (s, 3 H, NMe), 5.8–6.0 (m, H-3), 6.9–7.8 (m, 9 H); IR 2930, 2860, 1450, 968, 808, 750, 698 cm^{-1}. Anal. Calcd for $C_{22}H_{27}NO_3$: C, 74.76; H, 8.46; N, 3.79. Found: C, 74.64; H, 8.50; N, 3.90.

Dihydro-3-[2-(trifluoromethyl)phenyl]-5-methyl-6-(4-phenylmethyl)-6-phenyl-1,2,4,5-trioxazine (9c; a 1:1 mixture of cis and trans isomer): oil; ^{1}H NMR δ 2.27 (s, *p*-Me), 2.35 (s, *p*-Me), 2.88 (s, 3 H, NMe), 6.6–7.7 (m, 14 H). Anal. Calcd for $C_{23}H_{20}F_3NO_3$: C, 66.50; H, 4.85; N, 3.37. Found: C, 68.15; H, 5.05; N, 3.11.

Ozonolysis of Vinyl Ether 1d in the Presence of (*Z*)-4f in Methanol–Methylene Chloride. A solution of **1d** (210 mg, 1.5 mmol) and (*Z*)-**4f** (225 mg, 1 mmol) in methanol–methylene chloride (20 mL, 1:1 v/v) was treated with 1 mmol of ozone at −70 °C. Then the mixture was poured into ice-cold aqueous potassium dihydrogen phosphate, and the products were extracted with ether. The organic layer was separated and dried over anhydrous magnesium sulfate, and the solvent was removed under

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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 δ 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 δ 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 δ 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 δ 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 δ 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-α-*d*: ^{1}H NMR δ 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 δ 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.

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 (ΔH_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 ΔH_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 (ΔH_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 (ΔH_f) of the monoenes follow routinely. Accurate ΔH_f values have considerable value in parameterizing molecular mechanics force fields and in evaluating semiempirical molecular orbital methods.

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

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