(*E*/*Z*)-oxime geometry for diastereofacial selectivity contrasts with previous results of lithium aluminum hydride reductions.[4] Derivatives resulting from acetylation or ether protection of the proximate hydroxyl gave oximino benzyl ethers which were not reduced by TABH. Parent oximes (C═N̈—OH) and oximino benzyl ethers lacking a proximate (α or β) hydroxy function were also recovered unchanged.

Three independent investigations corroborate the stereochemical assignments of our products. Firstly, the aminoolefin cyclizations (I_2, CH_2Cl_2, $NaHCO_3$, 22 °C) of **3** and **4** followed by dehydrohalogenations with subsequent reactions leading to reductive cleavage of the N–O bond afforded materials which were spectroscopically (^1H and ^{13}C) compared to substances available via the nitrone cycloaddition route from substituted 2,3,4,5-tetrahydropyridine 1-oxides and terminal alkenes.[6] Secondly, our 1,3-amino alcohols were converted to their corresponding six-membered *N*-benzyloxy carbamates (1,1′-carbonyldiimidazole, benzene, reflux) for extensive proton decoupling studies.[7] Finally, unambiguous stereochemical assignments were directly available from the X-ray diffraction study of the *anti*-1,3-*N*-benzyloxyamino alcohol from entry 3 of Table I.[8]

An additional chiral center at C-2 has a profound effect on the course of our TABH reductions. The anti arrangement of vicinal hydroxyl and methyl substitutents of entries 5 and 6 overcame the influence of oxime geometry, delivering predominantly the 1,3-syn product. On the other hand, entries 7 and 8 (vicinal syn OH/CH_3) exhibited enhancement of the usual mode of stereocontrol. The (*E*)- and (*Z*)-oxime isomers of the primary alcohol (entries 11 and 12) were cleanly reduced to a single amino alcohol.

In summary, our reductions of acyclic β-hydroxyoximino ethers demonstrate the importance of the proximate hydroxyl as well as the geometry (*E*/*Z*) of the starting oxime for stereocontrolled production of 1,3-*syn*- and 1,3-*anti*-amino alcohols in high yields. Further efforts and rationalizations of these results are in progress.

Acknowledgment. We gratefully acknowledge financial assistance provided by the National Institutes of Health (GM-41560) and the National Science Foundation (CHE86-18955).

Supplementary Material Available: Data of (*E*)- and (*Z*)-oximes and the pure 1,3-*syn*- and 1,3-*anti*-amino alcohol products are provided with a general experimental procedure for these TABH reductions (12 pages). Ordering information is given on any current masthead page.

2,2-Dialkoxy-Δ³-1,3,4-oxadiazolines: Convenient Thermal Sources of Dialkoxycarbenes

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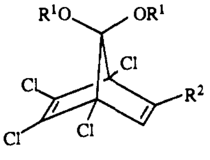
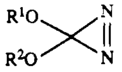
Dialkoxy- and diaminocarbenes are species with low chemical reactivity[1] and a large singlet/triplet energy gap.[2] Both properties are attributed to resonance stabilization of the singlet (Scheme I), which imparts nucleophilic properties to dimethoxycarbene (DMC).[2,3]

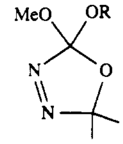
There are only two well-established precursors of dialkoxycarbenes.[4] The one based on thermolysis of **1**[5,6] has at least two limitations. First, only DMC has been generated effectively by that route, and it is unsuitable, in any case, for unsymmetric carbenes, $R^1O\ddot{C}OR^2$. Second, there are major coproducts of high molecular mass that must be separated from products of reaction of DMC with a substrate in a synthetic application of DMC. The other method, involving the decomposition of dialkoxydiazirines (**2**), has been restricted, to date, to dimethoxycarbene[3g,7] and methoxyphenoxycarbene.[8] Although compounds **2** have an advantage, because the carbenes can be generated photochemically for low-temperature and matrix isolation studies, they are poor sources for studies of the chemistry of dialkoxycarbenes because compounds **2** are obtained as relatively unstable materials, highly diluted with hydrocarbon solvent.



1



2



3 **a**: R=Me; **b**: R=Et;
c: $R=CH_2CH_2C{\equiv}CH$

Dialkoxycarbenes are particularly interesting as potential synthons of carbonyl compounds. Conventional carbene cycloadditions to alkenes and alkynes lead, at least in principle, to cyclopropanone[3a,h,8] and cyclopropenone ketals while insertion reactions would afford masked, acyclic carbonyl compounds (Scheme II).

We now report that 2-alkoxy-2-methoxy-Δ³-1,3,4-oxadiazolines (**3**) are readily accessible, shelf-stable liquids that serve as convenient sources of dialkoxycarbenes, by thermolysis at 100 °C in solution.

Compounds **3** were prepared by oxidative cyclization[9] of the (methoxycarbonyl)hydrazone of acetone (**4**) with lead tetraacetate in alcohol ROH (for **3a**, **3b**) or in CH_2Cl_2 containing ROH (for **3c**), in yields ranging from 40 to 80% (reaction 1). Their

$$\underset{\mathbf{4}}{Me_2C{=}NNHCO_2Me} \xrightarrow[ROH]{Pb(OAc)_4} \mathbf{3} \tag{1}$$

structures were established by ^1H and ^{13}C NMR spectroscopy ($CDCl_3$, δ: C2, 136.7–137.9; C5, 118.7–119.4) and by mass spectrometry.[10]

Thermolysis of **3a** in benzene (sealed NMR tube) at 100 °C followed the first-order rate law with $k = 1.2 \times 10^{-5}\ s^{-1}$. Both **3a** and **3b** afforded acetone (>80%) and the appropriate tetraalkoxyethene(s) (70–88%) as major products. Dimerization of ethoxymethoxycarbene occurred with little or no discrimination;

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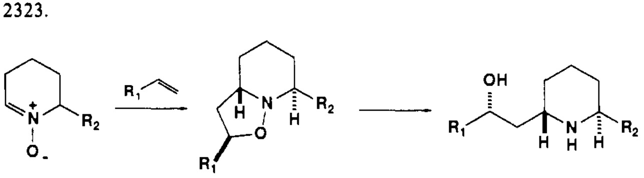
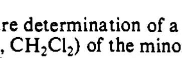
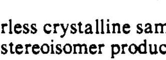
(6) Cycloadditions of terminal alkenes with 2,3,4,5-tetrahydropyridine-*N*-oxide take place exclusively in the exo mode. Tufariello, J. J. 1,3-Dipolar Cycloaddition Chemistry; Padwa, A., Ed.; Wiley: 1984; Vol. 2, p 83. Carruthers, W.; Coggins, P.; Weston, J. B. *J. Chem. Soc., Perkin Trans 1* **1990**, 2323.



(7) The 1,3-syn isomers **5** demonstrated the expected trans diaxial proton coupling (J_{DE} = 11 Hz), whereas **6** provided coupling constants in keeping with the usual data for vicinal axial–equatorial (J_{DE} = 7–8 Hz) and equatorial–equatorial (J_{CE} = 2–4 Hz) arrangements. Modeling indicates a small dihedral angle for the vicinal axial HD–equatorial HE hydrogens of **6** resulting from planarization of the six-membered carbamate. This accounts for the relatively large coupling constant J_{DE} compared to J_{CE}. A similar relationship exists in **5** for protons HC and HE.



5



6

(8) Structure determination of a colorless crystalline sample $C_{19}H_{25}NO_2$ (mp 58–60 °C, CH_2Cl_2) of the minor diastereoisomer produced as illustrated in entry 3 of Table I was established by X-ray diffraction at −172 °C. All atoms, including hydrogens, were refined by full-matrix least-squares to final residuals of $R(F) = 0.0347$ and $R_w(F) = 0.0422$. Crystallographic data are available from Indiana University Chemistry Library. Request Molecular Structure Center Report 90257.

† McMaster University undergraduate, 1992 (K.K.), 1989 (T.T.).

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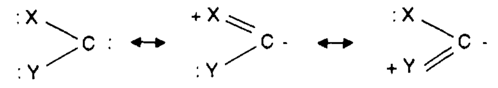
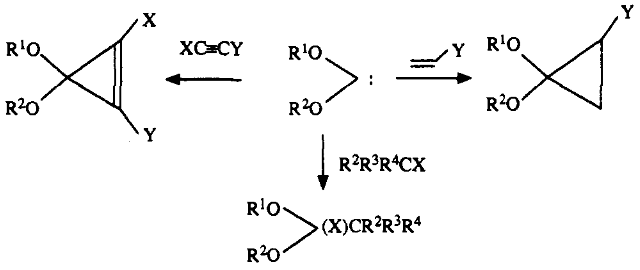
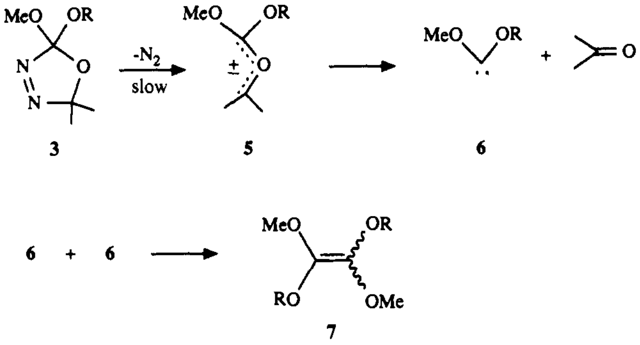
Scheme I



Scheme II



Scheme III[a]

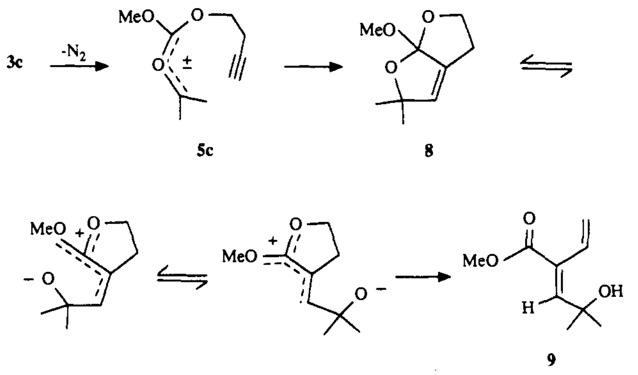


[a] **a**: R = Me. **b**: R = Et. **c**: R = $CH_2CH_2C{\equiv}CH$.

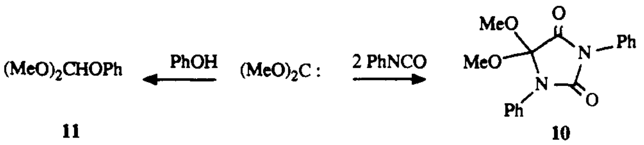
within experimental error the E:Z ratio was 1.0 (Scheme III). The mechanism that fits these observations, and that is in keeping with precedents,[9a,11] involves concerted, irreversible, 1,3-dipolar cycloreversion in the first step, forming N_2 and a carbonyl ylide (**5**).[12] Ylide fragmentation, exclusively in one sense,[13] yields acetone and dialkoxycarbene (**6**), which undergoes bimolecular reaction to form the major product(s), **7**.[14]

The intermediacy of ylide **5**, with a significant lifetime in benzene at 100 °C, was demonstrated with **3c**. A minor product from its thermolysis in benzene was firmly identified as (E)-3-(methoxycarbonyl)-5-methyl-1,3-hexadien-5-ol (**9**) (9%) (Scheme IV). Although the mechanism for formation of **9** is tentative, the connectivity leaves no doubt that intramolecular, 1,3-dipolar cycloaddition afforded **8** in the second step. Thus **5c** and, by analogy, **5a** and **5b** have appreciable lifetimes although their major fate is fragmentation to acetone and carbene. Confirmation of the dialkoxycarbene intermediate of Scheme III, inferred from the observation of **7**, was based on interception of **6a** with phenyl isocyanate and with phenol to afford **10**[15] (65–80%) and dimethyl phenyl orthoformate (**11**)[2] (50%), respectively (Scheme V).

Scheme IV



Scheme V



Extension of the use of oxadiazolines to generate other dialkoxycarbenes, including cyclic analogues, is in progress. New chemistry of both known and unreported dialkoxycarbenes will be disclosed in due course.

Acknowledgment. This work was supported by NSERC, Canada. We are indebted to Dr. Don Hughes for assistance with the identification of **9** by NMR spectroscopy.

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(12) Two ylides are possible from both **3b** and **3c**, from different senses of conrotatory cycloreversion.[11e,f]

(13) Neither propene, from 2-propylidene, nor dimethyl carbonate were detectable by ^{1}H NMR spectroscopy or by GC of the pyrolysate from **3a**.

(14) Formation of tetramethoxyethene from **3a**, from **1**, and from reaction of (aryloxy)dimethoxymethanes with sodium hydride[4c] is evidence that it is formed by coupling of two DMC, rather than by attack of DMC on its precursors. Major products from **3c** (not yet fully identified) do not include **7c**.

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