iments were run: 1 drop (10 mg, 0.08 mmol), 3 drops, 5 drops (0.4 mmol), and 0.5 g (4 mmol). Kinetic runs in MeOH-d_4: concentrations identical; data was accumulated every 30 s over 15 min. Acquisition parameters: number scans, 4; acquisition time, 4.76 s/scan; relaxation delay, 2.24 s/scan; 2 drops $CHCl_3$ were added to each reaction mixture as an integration standard. Kinetic runs with DBN: solutions were diluted 1:10; an equilmolar amount of DBN was added to the solution containing **2a** just prior to mixing.

Cyclic Voltammetry. General Procedure. One milliliter of the substrate (0.01 M in EtOH) was added to 9 mL of deaerated buffer/EtOH (70:30) and deaerated with N_2 bubbling for 15 min (buffer systems are listed in Table V). The glassy carbon electrode was polished with 0.05 μm alumina prior to each scan. The scan rate was 50 mV s^{-1}. The reported data (Table V) are the average of two runs.

Acknowledgment. This investigation was partially supported by Zambon Farmaceutici, S.P.A., Milano, Italy.

Supplementary Material Available: Spectroscopic parameters for **4a**, **5**, 12, and 4,6-di-*tert*-butyl-2-nitrophenol (^1H and ^{13}C NMR, IR, UV/vis (12) and MS (12)); MNDO-MO optimized geometries (Cartesian coordinates) for *un*substituted **1**, **5**, and model systems **7–9**; IR and ^1H-NMR direct comparisons of **4a** from **1** and **2a** vs **5** and **6a**; cyclic voltammetry plot of **5** in acidic media, kinetic plots (13 pages). Ordering information is given on any current masthead page.

The 1-Aza-Cope Rearrangement. 2[1]

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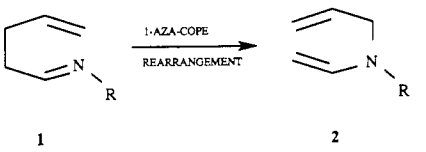
The 1-aza-Cope rearrangement of 4-vinylcyclohexene analogues has been studied with respect to substituents on C-3 of the 1-aza diene. The 1-aza-Cope rearrangement was unsuccessful with an electron-donating methoxy substitution at C-3 of the aza diene. The origin of this effect is believed to be due to thermodynamic rather than kinetic factors; that is, the reactant 1-aza diene is more stable than the product. The electron-withdrawing methoxycarbonyl group on C-3 of the aza diene accelerates the 1-aza-Cope rearrangement. Both an electron-donating group (OCH_3) at C-4 and an electron-withdrawing group (CO_2CH_3) at C-3 result in an extremely reactive substrate for the 1-aza-Cope rearrangement. All of the results to date on the 1-aza-Cope rearrangement are consistent with the dipolar transition state depicted in Scheme III.

The 1-aza-Cope rearrangement (Scheme I) is unknown as a general transformation in organic chemistry.[2] The primary reason for this situation is probably due to thermodynamic rather than kinetic factors. Compared to carbon–carbon bonds, the carbon–nitrogen π-bond is relatively strong whereas the carbon–nitrogen σ-bond is relatively weak.[3] Thus, the imine reactants are usually more stable than the enamine product. For this reason there are a number of examples known of the 3-aza-Cope rearrangement.[4]

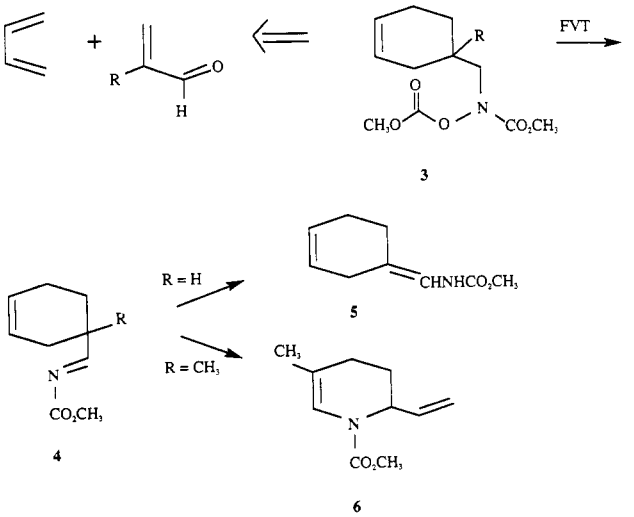
We have recently observed examples of the 1-aza-Cope rearrangement when an acyl function is present on the nitrogen atom of the imine.[5] The thermodynamic driving force for this reaction is presumably due to the resonance stabilization of the amide functionality present in the product. This scheme represents a new and potentially useful synthetic method. Its utility is further enhanced

Scheme I



1 2

Scheme II



3 4 5 6

(1) For part 1, see ref 5b.

(2) We apply the term 1-aza-Cope rearrangement to reactions where C-1 of the reacting 1,5-diene has been replaced by nitrogen. Although the term aza Claisen has also been used for the reverse of this process this designation is probably a misuse of the "replacement nomenclature". (*Nomenclature of Organic Compounds. Principles and Practice*; Fletcher, J. H., Cermer, O. C., Fox, R. B., Eds.; American Chemical Society: Washington, DC, 1974; Chapter 7. An aza Claisen rearrangement would be applied to those processes where one of the *carbon* atoms has been replaced by nitrogen. It is interesting to note that some aza Claisen rearrangements have also been called aza-Cope rearrangements. For example, see: (a) Mundy, B. P.; Bornmann, W. *Tetrahedron Lett.* **1978**, 957. (b) Lipkowitz, K. B.; Scarpone, S.; McCullouth, D.; Barney, C. *Tetrahedron Lett.* **1979**, 2241. (c) Kurth, M. J.; Soares, C. J. *Tetrahedron Lett.* **1987**, *28*, 1031.

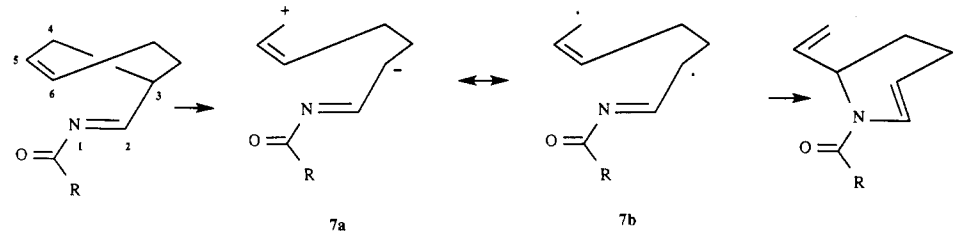
(3) For example, the σ-bond strengths of CH_3–CH_3 and CH_3–NH_2 are 88 and 79 kcal/mol respectively, whereas the π-bond strengths for CH_2=CH_2 and CH_2=NH_2 have been calculated to be 59.4 and 74.3 kcal/mol respectively (*Handbook of Organic Chemistry*; Dean, J. A., Ed.; McGraw-Hill: New York, 1987; p 3–18, and *The Chemical of Double Bonded Functional Groups*; Shaw, R., Patai, S., Eds.; Wiley: New York, 1977; p 131). For a recent theoretical analysis of the relative strengths of these bonds, see: Schleyer, P.v.R.; Kost, D. *J. Am. Chem. Soc.* **1988**, *110*, 2105.

(4) (a) Heimgartner, H.; Schmid, H. In *Advances in Organic Chemistry*; Taylor, E. C., Ed.; Academic: New York, 1979; Vol. 9, Part 2, p 656. (b) Winterfeldt, E. *Fortshr, Chem. Forsch.* **1971**, *16*, 75. (c) Przheval'skii, G. *Russ. Chem. Rev.* **1987**, *56*, 477.

(5) (a) Chu, M.; Wu, P.-L.; Givre, S.; Fowler, F. W. *Tetrahedron Lett.* **1986**, *27*, 461. (b) Wu, P.-L.; Chu, M.; Fowler, F. W. *J. Org. Chem.* **1988**, *53*, 963.

0022-3263/88/1953-5998$01.50/0

Scheme III



7a 7b

by the recognition that many *N*-acyl-1-aza 1,5-dienes are accessible using the Diels–Alder reaction as a key synthetic step. However, the simplest member of this series, **4** (R = H), avoided the Cope rearrangement completely by producing the enamide **5** rather than the Cope rearranged product (Scheme II). This result was not surprising since inspection of molecular models indicates that a synchronous mechanism would possess considerable strain energy, and it is also known that the all-carbon analogue of this Cope rearrangement has a very high activation energy.[6]

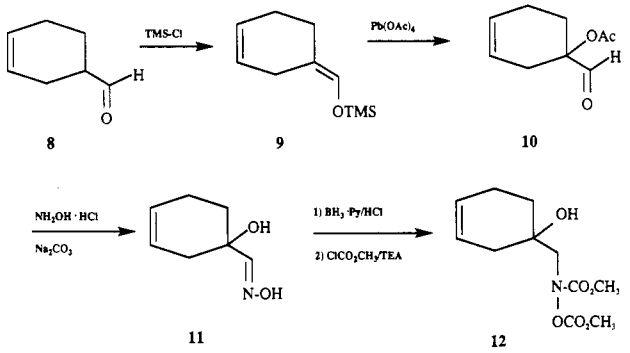
We have observed that the 1-aza-Cope rearrangement can be accelerated by suitable substituents.[1] For example, placement of a methoxy substituent at C-4 of the aza diene or the introduction of ground-state strain energy result in successful 1-aza-Cope rearrangements. We have used both of these effects to incorporate the 1-aza-Cope rearrangement as a key step in a formal total synthesis of aspidospermine.[1] Because of the potential utility of this new strategy, the Diels–Alder reaction and 1-aza-Cope rearrangement, for the synthesis of heterocycles we have investigated the effect of other substituents on the 1-aza-Cope rearrangement.

As a working model for our studies, we assume that the 1-aza-Cope and the Claisen rearrangement pass through similar transition states. The mechanism of the Claisen rearrangement has been the focus of a number of excellent studies in recent years, and much insight has been gained into the nature of this reaction.[7] Although there is still disagreement regarding the best electronic description of the transition state as well as the possibility that the reaction mechanism may be sensitive to substituents, we believe a reasonable model is emerging. The electronic configuration of the transition state can be represented by a species involving two polarized allyl fragments with partial bonding at their termini. Representative resonance structures for this transition state are **7a** and **7b** (Scheme III).

Because of factors such as the sensitivity of the Claisen rearrangement to solvent effects, a polar transition state has been proposed.[8] However, the data are not consistent with an extreme situation as represented by dipolar structure **7a**, leading to the conclusion diradical structures, such as **7b**, must also contribute to the electronic description of the transition state.

If electronic configurations such as **7b** are important, then a π-electron-donating group at C-3 of the aza diene may lower activation energy for the aza-Cope rearrangement. It has been postulated that a synergistic stabilizing effect occurs when an electron-donating and an electron-withdrawing group are both present on radical center.[9] For this reason we considered it of interest to study the 1-aza-Cope rearrangement of the 3-hydroxy-1-aza diene **13**.

Scheme IV



8 9 10 11 12

The synthesis of this compound was initiated by formation of the enol ether of the Diels–Alder adduct **9** under standard conditions.[10] Treatment of the enol ether **9** with lead tetraacetate gave the α-acetoxy aldehyde **10**.[11] The aza diene precursor **12** was prepared from the aldehyde by using Scheme IV. Attempts to purify **12** by silica gel chromatography resulted in transfer of the methoxycarbonyl group from the oxygen of the hydroxamic acid to the tertiary alcohol.

Flash vacuum thermolysis of **12** did not result in the anticipated Cope rearranged product **16**. Instead, a mixture of two cycloheptenones, **14** and **15**, was produced. A single product was obtained by reduction of the double bond with catalytic hydrogenation. The transformation of **13** to **14** and **15** can be viewed as a pericyclic reaction competing with the 1-aza-Cope rearrangement (Scheme V). The observed pericyclic reaction is facilitated by a relatively unstrained transition state as well as the formation of the stable carbamate function in the product.

It should be possible to retain the desired substitution pattern but to suppress the above reaction by the use of a methoxy rather than hydroxy substituent. Compound **19** was prepared according to Scheme VI. Because of the instability of the hydroxy aldehyde,[12] it was necessary to protect the carbonyl group before the liberation of the alcohol and its conversion into its methyl ether derivative.

Evaporation of **19** through the thermolysis tube under conditions previously successful for the rearrangement of

(6) The activation energy of the degenerate Cope rearrangement of 4-vinylcyclohexene is 52.3 kcal/mol (Doering, W.v.E.; Brenner, D. M. *Tetrahedron Lett.* **1977**, 899).

(7) For a recent theoretical paper on this reaction and a leading reference to other work in the area, see: Vance, R. L.; Rondan, N.; Houk, K. N.; Jensen, F.; Borden, W. T.; Komornicki, A.; Wimmer, E. *J. Am. Chem. Soc.* **1988**, *110*, 2314.

(8) For recent examples, see: (a) Wilcox, C.; Babston, R. E. *J. Am. Chem. Soc.* **1986**, *108*, 6636. (b) Coates, R. M.; Rogers, B. D.; Hobbs, S. J.; Peck, D. R.; Curran, D. P. *Ibid.* **1987**, *109*, 1160. (c) Gajewski, J. J.; Jurayj, J.; Kimbrough, D. R.; Gande, M. E.; Ganem, B.; Carpenter, B. K. *Ibid.* **1987**, *109*, 1170.

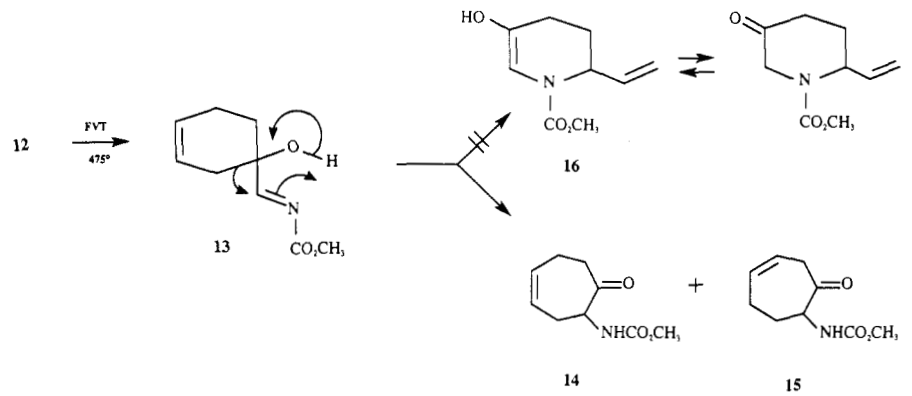
(9) This phenomenon has often been referred to as the captodative effect. For a recent paper concerned with this effect on the homolysis of 1,5-hexadienes, see: Van Hoecke, M.; Borgese, A.; Penelle, J.; Merényi, R.; Viehe, H. G. *Tetrahedron Lett.* **1986**, *27*, 4569.

(10) House, H. O.; Czuba, L. J.; Gall, M.; Olmstead, H. D. *J. Org. Chem.* **1969**, *34*, 2324.

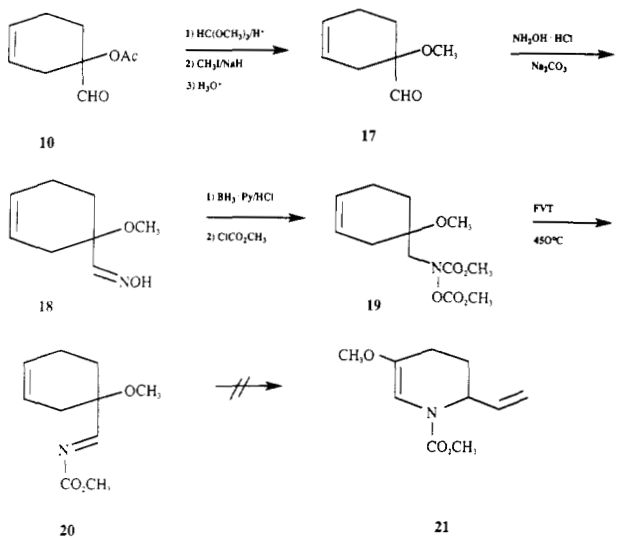
(11) Rubottom, G. M.; Marrero, R.; Gruber, J. *Tetrahedron* **1983**, *39*, 861.

(12) Blumbergs, P.; La Montagne, M. P. *J. Org. Chem.* **1972**, *37*, 1248.

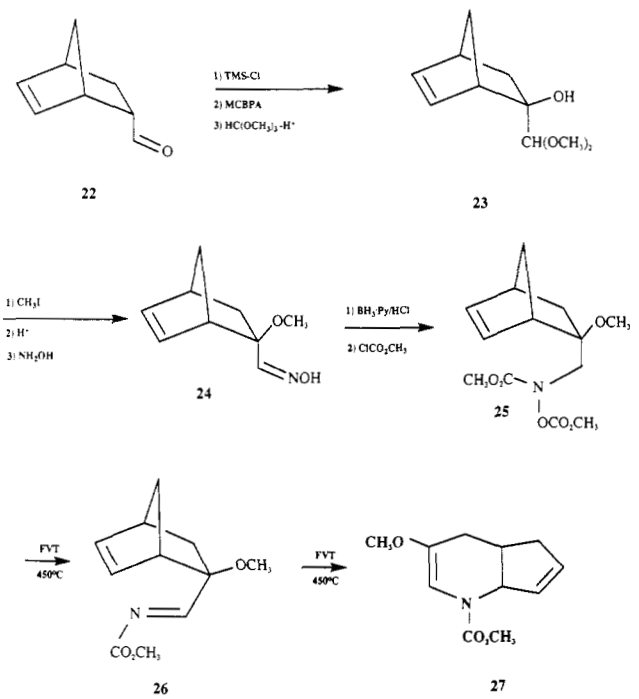
Scheme V



Scheme VI



Scheme VII



4 (R = CH_3) gave only the aza diene **20**, the reactant for the 1-aza-Cope rearrangement. Raising the temperature of the oven still did not induce the Cope rearrangement but ultimately resulted in the elimination of methanol followed by rearrangement to methyl *N*-benzylcarbamate.[13] Possible explanations for this result are either that the methoxy substituent raises the activation energy of the 1-aza-Cope rearrangement or that the 1-aza-Cope rearrangement occurs but the position of the equilibrium favors the azadiene. We presently believe the latter explanation is responsible for our inability to observe the piperidine product **21**.

From thermochemical data it has been estimated that the 1-aza-Cope rearrangement is *unfavorable* by 8–10 kcal/mol.[14] From NMR measurement of carbonyl rotational barriers, it can be estimated that the carbamate stabilization energy in these piperidine derivatives provides about a 12 kcal/mol driving force for this rearrangement.[15] Thus, the 1-aza-Cope of *N*-(methoxycarbonyl)-1,5-aza dienes is estimated to be favorable by only 2–4 kcal/mol.[16]

A possible destabilizing interaction present in **21** is the repulsion of the nitrogen and oxygen lone pairs of electrons through the double bond. It is known that NO bonds are relatively weak, and repulsion of the heteroatomic lone pairs is believed to be an important factor responsible for these weak bonds.[17] Compound **21** is a vinylgous hydroxamic acid.

In an attempt to provide more information on why **20** failed to undergo the 1-aza-Cope rearrangement, the thermal chemistry of aza diene **26** was studied. It was reasoned that the additional strain energy (19.2 kcal/mol) associated with the bicyclo[2.2.1]heptene ring system[18] may be sufficient to facilitate the 1-aza-Cope rearrangement. The synthesis of the required azadiene precursor **25** was prepared from the Diels–Alder adduct **22** according to Scheme VII.

Evaporation of hydroxamic acid derivative **25** through the thermolysis oven at 450 °C produced the Cope rearranged product **27** in 24% yield. Thus, the methoxy substituent on C-3 of the aza diene does not appear to be inhibiting the 1-aza-Cope rearrangement, and the failure

(13) We have previously observed[1] the formation of methyl *N*-benzylcarbamate during the thermolysis of the isomeric compound where the methoxy substituent is on C-4 rather than C-3 of the aza diene.

(14) Heimgartner, H.; Schmid, H. In *Advances in Organic Chemistry*; Taylor, E. C., Ed.; Academic: New York, 1979; Vol. 9, part 2, p 656.

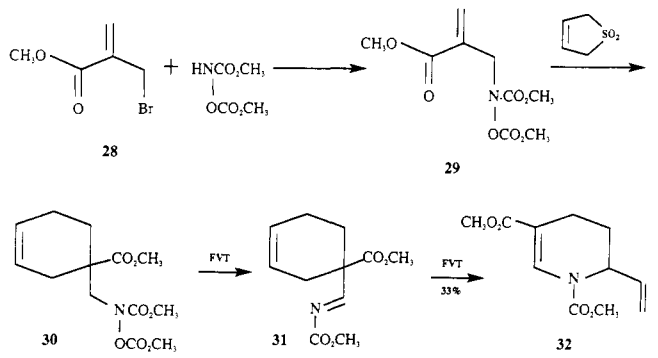
(15) Hirsch, J. A.; Augustine, R. L.; Koletar, B.; Wolf, H. G. *J. Org. Chem.* **1975**, *40*, 3547.

(16) This driving force would only be decreased by any stabilization resulting from the interaction of the carbonyl group with the imine. (Allman, R.; Kupfer, R.; Nagel, M.; Wurthwein, E.-U. *Chem. Ber.* **1984**, *117*, 1597.)

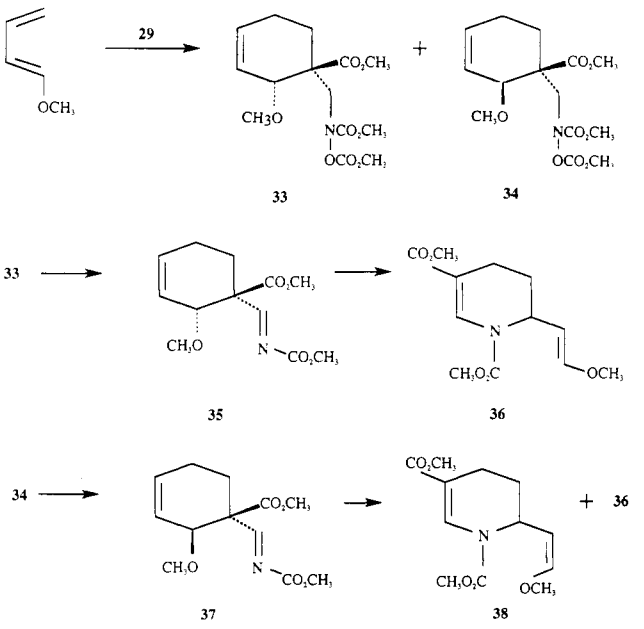
(17) Lowry, T. H.; Richardson, K. S. *Mechanism and Theory in Organic Chemistry*, 2nd ed.; Harper and Row: New York, **1981**, p 147.

(18) Wiberg, K. B. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 312.

Scheme VIII



Scheme IX



to observe 1-aza-Cope rearrangement with the monocyclic aza diene **20** is probably due to the product being thermodynamically less stable than the reactant.[19]

If the proposed model for the transition state possesses dipolar character (Scheme III), then an electron-withdrawing group at C-3 of the aza diene should facilitate the 1-aza-Cope rearrangement. A suitable aza diene precursor to explore this possibility is the methoxycarbonyl derivative **31**. The dienophile **29**, for the Diels–Alder reaction, was readily obtained from methyl α-(bromomethyl)acrylate and *N,O*-bis(methoxycarbonyl)hydroxyamine. Heating the dienophile **29** with sulfolene, a butadiene precursor, produced the desired aza diene precursor **30** (Scheme VIII).

Evaporation of **30** through the thermolysis oven at 500 °C gave a 33% yield of the 1-aza-Cope rearranged product **32**. Both qualitatively and quantitatively, the methoxycarbonyl group at C-3 of the aza diene appears to be facilitating the 1-aza-Cope rearrangement. For example, the derivative with a methyl group at C-3 (**4**, R = CH_3) gave the 1-aza-Cope rearranged product with a lower yield (5%) and required a higher temperature (525 °C).[5b]

We have previously observed that a methoxy substituent at C-4 of the aza diene has a rate-accelerating effect on the 1-aza-Cope rearrangement.[5b] This effect is consistent with a transition state, described earlier, possessing considerable dipolar character. Presumably the interaction of the positive end of the dipolar transition state with the electron lone pairs of the oxygen atom results in stabilization of the transition state. If the dipolar species **7** is an accurate model for the transition state then it would be anticipated that an electron-donating group at C-4 combined with an electron-withdrawing group at C-3 of the aza diene would greatly facilitate the 1-aza-Cope rearrangement.[20] In order to evaluate this possibility we prepared aza dienes with a methoxy substituent at C-4 of the aza diene and a methoxycarbonyl substituent at C-3 according to Scheme IX.

The Diels–Alder reaction showed little preference for either the exo or endo transition states giving about a 1:1 mixture of the *E* and *Z* stereoisomers **33** and **34**. Evaporation of **33** through the thermolysis oven at 425 °C, the minimum temperature required to form the aza diene, gave a 71% yield of the rearranged product **36**. This result clearly indicates that an electron-withdrawing group at C-3 in combination with an electron-donating group at C-4 has a dramatic effect on the 1-aza-Cope rearrangement consistent with the transition-state model described in Scheme III.

Interestingly, evaporation of **34** through the thermolysis oven gave a low yield (18%) of a 1:1 mixture of **36** and **38**. The difference in behavior of **33** compared to **34** is probably reflecting additional nonbonding interactions present along the reaction coordinate. These interactions can be seen by using the transition state model in Figure 1. In the *Z* isomer **37**, a significant trans annular interaction occurs, involving the methoxy substituent. This interaction is absent with the *E* isomer **35**.

In summary, it has been previously shown that an *N*-methoxycarbonyl substituent is capable of providing sufficient product stability to facilitate the 1-aza-Cope rearrangement. A methoxycarbonyl substituent on C-3 of the aza diene accelerates the rearrangement compared to a methyl group at this same position. Both a π-electron-withdrawing group on C-3 (methoxycarbonyl) and a π-electron-donating group on C-4 (methoxy) of the aza diene combine to produce a fast and efficient 1-aza-Cope rearrangement. However, a methoxy substituent at C-3 of the aza diene appears to produce sufficient product instability to suppress the 1-aza-Cope rearrangement. The 1-aza-Cope rearrangement of vinylcyclohexene analogues appear to be very sensitive to substituents on C-3 as well as C-4 of the aza diene.

Experimental Section

General Procedures. Melting points were recorded on a Fischer-Johns melting point apparatus and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 567 spectrometer as either thin films or KBr solid solutions. The absorption intensities are described as strong (s), medium (m), weak (w), or broad (br), and the absorption of polystyrene at 1944 or 1601 cm^{-1} was used as a reference. Proton NMR spectra were recorded on either a Varian HFT-80 or a Nicolet-300 spectrometer. Carbon NMR spectra were recorded on either a Varian CFT-20 or a Nicolet-300 spectrometer. All chemical shifts are reported in ppm from tetramethylsilane as internal standard and described as singlet (s), doublet (d), triplet (t), quartet (q), quintet (q'), multiplet (m), or broad (br). Low-resolution mass spectra were recorded on a Hewlett-Packard 5980A spectrometer. High-resolution mass spectra were recorded on an AEI MS-30 spectrometer. Elemental analyses were performed by MicAnal Organic Microanalysis, Tucson, AZ, or M-H-W Laboratories, Phoenix, AZ.

(19) We cannot make this statement with absolute certainty because the formation of the aza diene is the slow step for all of the bicyclo[2.2.1]oct-2-enes. Since we did not observe the aza diene **26** there does not appear to be a significant rate retardation due to the methoxy substituent.

(20) This substitution pattern has been observed to accelerate the Claisen rearrangement (see ref 8b) providing support for the dipolar transition state.

Analytical gas chromatographic analyses were performed on a Hewlett-Packard 5710A chromatograph equipped with a flame ionization detector. Thin-layer chromatography was carried out using Analtech silica gel HLF precoated thin-layer chromatography plates. Flash column chromatography was carried out using 230–400 mesh silica gel 60 (E. Merck). Dry tetrahydrofuran and diethyl ether were freshly distilled over sodium benzophenone ketyl under nitrogen.

1-Hydroxy-3-cyclohexene-1-carbaldoxime (11). Sodium carbonate (1.91 g, 18 mmol) was added to a solution of hydroxylamine hydrochloride (1.25 g, 18 mmol) in a minimum amount of water. The aldehyde **10**[11] (2.02 g, 12 mmol) in ethyl alcohol (3 mL) was added to the aqueous solution and stirred at room temperature for 3 h. The reaction mixture was extracted with diethyl ether. The combined extracts were washed with saturated sodium chloride solution, dried over anhydrous magnesium sulfate, and concentrated in vacuo.[21] The pure product **11** was obtained by flash column chromatography as a single isomer isomer (1.21 g, 72%): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.6–2.5 (m, 6 H, 3 CH_2), 3.2–3.7 (br, 1 H, COH), 5.5–5.8 (m, 2 H, CH=CH), 7.50 (br s, 1 H, CH=N), 9.0 (br, 1 H, NOH); IR (film) 3350 (br), 3040 (m), 2937 (s), 2860 (m), 1653 (w), 1440 (s), 1350 (w), 1081 (s), 945 (s), 920 (s), 742 (s) cm^{-1}; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 22.35, 32.22, 35.93, 69.90, 123.00, 126.46, 154.04.

***N,O*-Bis(methoxycarbonyl)-*N*-[(1-hydroxy-3-cyclohexen-1-yl)methyl]hydroxylamine (12).** A mixture of oxime **11** (0.55 g, 3.9 mmol) and pyridine–borane (0.45 g, 4.9 mmol) in ethanol (4 mL) was kept at 0 °C. To this mixture was added dropwise a 10% HCl solution (4 mL), and the mixture was stirred for 20 min at room temperature. The solution was made alkaline with sodium carbonate or sodium hydroxide (with cooling) and extracted with diethyl ether.[22] The ether solution was dried over anhydrous magnesium sulfate and concentrated in vacuo to a volume of 40 mL. Triethylamine (0.79 g, 7.8 mmol) was added to the diethyl ether solution, then methyl chloroformate (0.76 g) in dry diethyl ether (4 mL) was added dropwise at 0 °C. The mixture was stirred for 1.5 h at room temperature and then acidified with 10% HCl and extracted with diethyl ether. These extracts were combined, dried over anhydrous magnesium sulfate, and concentrated in vacuo. The resulting crude product was purified by flash column chromatography to give the pure colorless diacylated hydroxamic acid **12** (0.33 g, 32%): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.6–2.3 (m, 6 H, 3 CH_2), 2.6 (br, 1 H, OH), 3.70 (s, 2 H, CH_2N), 3.79 (s, 3 H, NCO_2CH_3), 3.89 (s, 3 H, OCO_2CH_3), 5.53–5.73 (m, 2 H, CH=CH); IR (film) 3500 (br), 3040 (w), 2978 (m), 2942 (m), 2870 (w), 1785 (s), 1730 (s), 1445 (s), 1385 (m), 1238 (s), 1132 (s), 940 (m), 780 (m) cm^{-1}; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 22.41, 31.07, 35.58, 53.99, 56.25, 59.91, 70.12, 123.45, 126.33, 155.17, 156.96; MS, *m/z* (relative intensity) 183 (1, M^+ – $HOCO_2CH_3$), 166 (16), 150 (15), 104 (23), 93 (58), 91 (77), 88 (35), 79 (100), 77 (57), 59 (56).

2-[*N*-(Methoxycarbonyl)amino]-4-cycloheptenone and 2-[*N*-(Methoxycarbonyl)amino]-5-cycloheptenone (14 and 15). By the general method for FVT previously described,[1] **12** (20 mg, 0.08 mmol) gave **14** and **15** (8.8 mg, 32%) at the optimum oven temperature of 475 °C: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 2.0–2.8 (m, 6 H, 3 CH_2), 3.67 (s, 3 H, NCO_2CH_3), 4.15–4.3 (m, 1 H, CHN), 5.7–6.0 (m, 3 H, NH and CH=CH); IR (film) 3400 (br), 3042 (m), 2970 (s), 2860 (m), 1720 (s), 1705 (s), 1500 (s), 1450 (m), 1375 (m), 1270 (m), 1205 (m), 1080 (s), 790 (w) cm^{-1}; ^{13}C NMR ($CDCl_3$, 75 MHz) of one isomer δ 22.66, 32.92, 41.19, 52.15, 58.47, 127.44, 130.13, 156.06, 208.44; ^{13}C NMR ($CDCl_3$, 75 MHz) of the other isomer δ 24.56, 31.08, 41.01, 52.30, 61.30, 121.62, 132.51, 156.13, 204.66; MS, *m/z* (relative intensity) 183 (27, M^+), 151 (11), 140 (22), 127 (54), 108 (44), 101 (100), 96 (20), 80 (46), 76 (49), 68 (31), 59 (42); HRMS, *m/e* 183.0891 ($C_9H_{13}NO_3$ requires 183.0896).

The above mixture (18.3 mg) was dissolved in absolute ethyl alcohol (5 mL), 4 mg of 5% of Pd/C was added, and the mixture was stirred at room temperature under 1 atm of hydrogen for 12 h.[23] The catalyst was filtered, and the solvent was removed under vacuum. The crude product was purified by flash column chromatography to afford 2-[*N*-(methoxycarbonyl)amino]cycloheptanone (18.1 mg, 98%): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.2–2.7 (m, 10 H, 5 CH_2), 3.61 (s, 3 H, NCO_2CH_3), 4.43 (m, 1 H, CHN), 5.83 (br, 1 H, NH); IR (film) 3350 (br), 2930 (s), 2860 (m), 1700 (s), 1500 (m), 1455 (m), 1370 (w), 1235 (m), 1070 (w), 738 (w) cm^{-1}; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 23.09, 27.35, 28.88, 32.83, 41.24, 51.95, 60.15.

1-Methoxy-3-cyclohexene-1-carboxaldehyde (17). Trimethyl orthoformate (3.14 g, 29.6 mmol) was added dropwise over a period of 20 min to a solution of **10**[11] (3.98 g, 24 mmol) and *p*-toluenesulfonic acid monohydrate (14 mg) in absolute methanol (5 mL) while the reactants were maintained under gentle reflux.[24] After 6 h, the mixture was neutralized with saturated Na_2CO_3, dried over anhydrous magnesium sulfate, and concentrated in vacuo. The crude product was purified by vacuum distillation to give the pure α-hydroxy acetal (3.33 g, 81%) as a colorless liquid: bp 49–51 °C (0.7 mm); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.6–2.35 (m, 6 H, 3 CH_2), 3.3 (br, 1 H, OH), 3.53 (s, 6 H, 2 OCH_3), 4.03 (s, 1 H, CH), 5.5–5.8 (m, 2 H, CH=CH); IR (film) 3450 (br), 3035 (m), 2935 (s), 2850 (m), 1652 (w), 1445 (m), 1350 (m), 1260 (m), 1200 (m), 1085 (s), 976 (m), 933 (m), 883 (m), 670 (s) cm^{-1}; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.47, 27.85, 32.44, 57.58, 57.89, 72.33, 109.66, 123.49, 126.30.

In a flask was placed sodium hydride (1.73 g, 36 mmol, 50% in oil). The oil was removed with three successive washes of dry hexanes. Then dry THF was added under nitrogen. The suspension was heated in an oil bath at 40–50 °C, and methyl iodide (5.11 g, 36 mmol) was added. A solution of the above acetal (3.1 g, 18 mmol) in dry THF (4 mL) was added dropwise.[25] After a further 1 h of heating, the reaction mixture was cooled and sufficient water was added to dissolve any precipitate. The mixture was the extracted with diethyl ether, washed with saturated NaCl solution, dried over anhydrous magnesium sulfate, and concentrated in vacuo. The crude product was purified by vacuum distillation to give the methyl ether as a colorless liquid (2.99 g, 89%): bp 45–57 °C (0.1 mm); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.6–2.2 (m, 6 H, 3 CH_2), 3.32, 3.50, 3.52 (s, 9 H, 3 OCH_3), 4.13 (s, 1 H, CH), 5.5–5.8 (m, 2 H, CH=CH); IR (film) 3030 (w), 2930 (s), 2845 (m), 1660 (w), 1450 (m), 1365 (w), 1270 (m), 1198 (m), 1105 (s), 938 (w) cm^{-1}; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.89, 25.88, 28.24, 50.86, 57.65, 57.97, 76.37, 109.24, 123.48, 126.69.

A mixture of the above methyl ether (0.3 g, 1.6 mmol), acetone (15 mL), and 2 drops of concentrated sulfuric acid was refluxed for 1 h.[26] It was then neutralized by sodium carbonate, filtered, and concentrated in vacuo. Pure **17** (0.18 g, 77%) was obtained by flash column chromatography: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.75–2.45 (m, 6 H, 3 CH_2), 3.29 (s, 3 H, OCH_3), 5.6–5.8 (m, 2 H, CH=CH), 9.57 (s, 1 H, CHO); IR (film) 3040 (w), 2935 (m), 2838 (w), 2705 (w), 1730 (s), 1655 (w), 1435 (w), 1375 (w), 1095 (s), 725 (w) cm^{-1}; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.66, 25.40, 28.34, 51.95, 79.86, 122.16, 126.68, 203.43.

1-Methoxy-3-cyclohexene-1-carbaldoxime (18). By use of the procedure described for **11**, **17** (0.14 g, 1 mmol) gave **18** as a solid (0.12 g, 90%) and a single isomer: mp 77–78 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.8–2.5 (m, 6 H, 3 CH_2), 3.25 (s, 3 H, OCH_3), 5.55–5.75 (m, 2 H, CH=CH), 7.33 (s, 1 H, CH=N), 8.4 (br, 1 H, NOH); IR (KBr) 3300 (br), 3050 (w), 2940 (m), 2850 (w), 1690 (w), 1430 (s), 1285 (s), 1080 (s), 940 (s), 735 (s), 670 (s) cm^{-1}; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 22.50, 29.05, 32.40, 50.69, 74.63, 122.80, 126.69, 153.22.

***N,O*-Bis(methoxycarbonyl)-*N*-[(1-methoxy-3-cyclohexen-1-yl)methyl]hydroxylamine (19).** By use of the procedure described for the preparation of **12**, **18** (0.93 g, 6 mmol) gave **19** (0.97 g, 59%) after a longer time (8 h) for the acylating step: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.7–2.4 (m, 6 H, 3 CH_2), 3.20 (s, 3 H, OCH_3), 3.65, 3.82 (d, 2 H, CH_2N, J = 16 Hz), 3.78 (s, 3 H, NCO_2CH_3), 3.89 (s, 3 H, OCO_2CH_3), 5.5–5.7 (m, 2 H, CH=CH); IR (film) 3030 (m), 2940 (s), 2840 (m), 1780 (s), 1715 (s), 1650 (w), 1440 (s), 1380 (s), 1240 (s), 1115 (s), 935 (m), 765 (m) cm^{-1}; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 22.64, 27.54, 31.93, 48.75, 52.92, 53.67,

(21) We used the method for preparing the oximes described in the following paper: Bousquet, E. W. *Organic Syntheses*; Wiley: New York: 1943; Collect. Vol. II, p 313.
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55.88, 76.57, 123.31, 126.37, 154.39, 156.67; MS, *m/z* (relative intensity) 111 (100), 79 (56), 77 (13), 59 (14). Anal. Calcd for $C_{12}H_{18}NO_6$: C, 52.74; H, 7.01. Found: C, 52.51; H, 6.76.

***N*-[(1-Methoxy-3-cyclohexen-1-yl)methylene]-*N*-(methoxycarbonyl)amine (20).** By the previously described FVT procedure,[1] **19** (20 mg, 0.07 mmol) gave **20** (14 mg, 97% by GC) at the optimum temperature of 450 °C. Purification was not possible because of the instability of the imine: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.7–2.5 (m, 6 H, 3 CH_2), 3.26 (s, 3 H, OCH_3), 3.83 (s, 3 H, NCO_2CH_3), 5.6–5.8 (m, 2 H, CH=CH), 8.15 (s, 1 H, CH=N); IR (film) 3040 (w), 2950 (m), 2840 (w), 1728 (s), 1628 (m), 1505 (w), 1440 (m), 1358 (w), 1250 (s), 1095 (m) cm^{-1}; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.97, 27.54, 30.73, 51.36, 53.84, 76.52, 122.31, 126.62, 163.22, 176.90; MS, *m/z* (relative intensity) 197 (13, M^+), 182 (18), 150 (39), 122 (37), 111 (85), 91 (25), 86 (30), 79 (100), 77 (32), 59 (22); HRMS, *m/e* 197.1060 ($C_{10}H_{15}NO_3$ requires 197.1052).

2-Hydroxybicyclo[2.2.1]hept-5-ene-2-*endo*-carboxaldehyde Dimethyl Acetal (23). Anhydrous powdered zinc chloride (200 mg) was added to triethylamine (25.45 g, 0.24 mmol). The mixture was cooled to 0 °C, and a solution of 5-norbornene-2-carboxaldehyde (25.62 g, 0.21 mmol) in benzene (50 mL) was added followed by trimethylsilyl chloride (27.34 g, 0.24 mmol).[11] The mixture was refluxed for 1 day. After cooling, the reaction mixture was extracted with diethyl ether and filtered to remove the salt. The filtrate and the combined washings were concentrated in vacuo. Distillation gave the pure trimethylsilyl enol ether as a mixture of cis and trans isomers (27.01 g, 66%): bp 58–60 °C (0.5 mm), major:minor = 2:1); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.14 (s, 9 H, OTMS of major isomer), 0.16 (s, 9 H, OTMS of minor isomer), 1.25–2.3 (m, 4 H, 2 CH_2), 2.95 and 3.08 (br s, 2 H, 2 CH), 5.97–6.32 (m, 3 H, 3 CH=C); IR (film) 3060 (w), 2960 (s), 2860 (w), 1695 (m), 1565 (w), 1505 (m), 1450 (w), 1350 (w), 1250 (s), 1165 (s), 1145 (s), 1115 (m), 880 (s), 840 (s), 750 (m), 715 (m) cm^{-1}; ^{13}C NMR ($CDCl_3$, 75 MHz) of the major isomer δ −0.44, 30.26, 41.68, 45.89, 50.40, 124.17, 129.52, 134.43, 135.58; ^{13}C NMR ($CDCl_3$, 75 MHz) of the minor isomer δ −0.53, 29.89, 41.63, 43.46, 49.32, 124.00, 129.18, 134.25, 135.65.

To a stirred solution of the above trimethylsilyl enol ether (9.70 g, 50 mmol) in methylene chloride (30 mL) was added, portionwise, 80–85% *m*-chloroperbenzoic acid (1.14 g).[27] After the resulting solution was stirred for 1 h, aqueous Na_2SO_3 was added to destroy excess peroxide. The solution was washed with aqueous $NaHCO_3$, and the organic layer was dried over anhydrous magnesium sulfate and concentrated in vacuo. The crude hydroxy aldehyde derivative was difficult to purify and was converted to **23** as follows. The crude product was dissolved in methanol (30 mL), and a catalytic amount of *p*-toluenesulfonic acid was added. During the gentle reflux, trmethyl orthoformate was added dropwise. Then the resulting mixture was refluxed for 2 h and concentrated in vacuo. After vacuum distillation, the distillate showed the desired endo aldehyde acetal almost pure according to the ^{1}H NMR spectrum. Column chromatography gave the pure endo aldehyde acetal **23** (4.86 g, 53%): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.4–2.0 (m, 4 H, 2 CH_2), 2.64, 2.67 and 2.82 (br s, 3 H, 2 CH and OH), 3.46 and 3.50 (s, 6 H, 2 OCH_3), 3.91 (s, 1 H, $CH(OCH_3)_2$), 6.00 and 6.23 (dd, 2 H, CH=CH, *J* = 3, 6 Hz); IR (film) 3480 (br), 3060 (w), 2970 (s), 2940 (s), 2835 (m), 1575 (w), 1445 (w), 1330 (m), 1115 (s), 1070 (s), 975 (s), 720 (s) cm^{-1}; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 38.84, 41.05, 47.44, 51.39, 55.65, 56.17, 83.44, 107.89, 133.29, 139.73.

2-Methoxybicyclo[2.2.1]hept-5-ene-2-*endo*-carbaldoxime (24). By use of the method previously described for the preparation of **17**, **23** (3.68 g, 20 mmol) gave 3.28 g (83%) of the *O*-methyl derivative: bp 40–42 °C (0.05 mm); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.25–1.8 (m, 4 H, 2 CH_2), 2.81 and 3.05 (br s, 2 H, 2 CH), 3.46 (s, 3 H, OCH_3), 3.48 (s, 6 H, OCH_3), 3.94 (s, 1 H, $CH(OCH_3)_2$), 5.98 and 6.23 (dd, 2 H, CH=CH, *J* = 3, 6 Hz); IR (film) 3060 (w), 2970 (s), 2940 (s), 2830 (s), 1575 (w), 1440 (m), 1330 (m), 1095 (s), 1065 (s), 720 (s) cm^{-1}; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 37.44, 41.03, 47.19, 47.57, 53.08, 56.68, 57.24, 87.92, 111.11, 133.32, 140.07.

The above *O*-methyl acetal (2.97 g, 15 mmol) was added to 30 mL of 1% oxalic acid in acetone–H_2O (10:1). The resulting mixture was refluxed for 1 day, neutralized with $NaHCO_3$ (s), dried over anhydrous magnesium sulfate, and concentrated in vacuo. The crude product was chromatographed to give aldehyde (1.95 g, 86%): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.6–1.9 (m, 4 H, 2 CH_2), 2.97 and 3.06 (br s, 2 H, 2 CH), 3.34 (s, 3 H, OCH_3), 5.95 and 6.34 (dd, 2 H, CH=CH, *J* = 3, 6 Hz), 9.51 (s, 1 H, CHO); IR (film) 3060 (w), 2980 (m), 2940 (m), 2830 (w), 2710 (w), 1730 (s), 1435 (w), 1330 (w), 1110 (m), 1090 (m), 1075 (m), 715 (w) cm^{-1}; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 34.44, 41.72, 48.08, 49.07, 53.37, 91.88, 131.45, 141.00, 202.35.

By the method previously described for the preparation of **11**, the above aldehyde (1.09 g, 7.2 mmol) gave **24** as a solid (0.61 g, 51%): mp 103.5–104.5 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.6–2.0 (m, 4 H, 2 CH_2), 2.88 and 2.97 (br s, 2 H, 2 CH), 3.26 (s, 3 H, OCH_3), 5.92 and 6.25 (dd, 2 H, CH=CH, *J* = 3, 6 Hz), 7.36 (s, 1 H, CH=N), 8.19 (br s, 1 H, NOH); IR (KBr) 3280 (br), 3080 (w), 2940 (s), 2870 (m), 1445 (s), 1335 (m), 1065 (s), 935 (s), 855 (m), 770 (m), cm^{-1}; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 36.48, 41.53, 47.33, 50.38, 51.93, 85.67, 132.79, 140.36, 153.04.

***N*,*O*-Bis(methoxycarbonyl)-*N*-[(2-methoxybicyclo-[2.2.1]hept-5-en-2-*endo*-yl)methyl]hydroxylamine (25).** By the previously described method for the preparation of **12**, **24** (0.92 g, 5.5 mmol) gave **25** (0.81 g, 52%): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.8–1.9 (m, 4 H, 2 CH_2), 2.8–3.1 (br, 2 H, 2 CH), 3.26 (s, 3 H, OCH_3), 3.79 (s, 3 H, NCO_2CH_3), 3.92 (s, 3 H, OCO_2CH_3), 3.3–4.1 (br, 2 H, CH_2N), 6.0–6.3 (br, 2 H, CH=CH); IR (film) 3060 (w), 2960 (m), 2870 (w), 2830 (w), 1795 (s), 1725 (s), 1445 (s), 1380 (m), 1275 (s), 1255 (s), 1230 (s), 1120 (m), 930 (w), 850 (w), 735 (m) cm^{-1}; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 34.91, 37.99, 41.25, 47.53, 50.22, 51.57, 53.28, 55.67, 86.07, 133.57, 139.58, 154.24, 156.10; MS, *m/z* (relative intensity) 285 (1, M^+), 220 (35), 210 (20), 144 (100), 123 (71), 116 (47), 91 (35), 66 (77), 59 (64). Anal. Calcd for $C_{13}H_{19}NO_6$: C, 54.73; H, 6.71. Found: C, 54.96; H, 6.57.

Thermolysis of 25. By use of the previously described FVT method,[1] **25** (590 mg, 2.1 mmol) gave, after purification by flash chromatography (hexanes–ether, 8:1), the pyrindine **27** (104 mg, 24%), *N*,*O*-Bis(methoxycarbonyl)-2-methoxyallylhydroxylamine (33 mg, 7%) and *N*-(methoxycarbonyl)-1,2-dimethoxyallylamine (40 mg, 11%) at the optimum temperature of 450 °C.

***N*-(Methoxycarbonyl)-3-methoxy-1,4,8,9-tetrahydropyrindine (27).** Two rotamers of the amide are clearly visible in the NMR spectra: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.9–2.9 (m, 5 H, 2 CH_2 and CH), 3.53 and 3.55 (s, 3 H, OCH_3), 3.75 and 3.77 (s, 3 H, NCO_2CH_3), 4.81 and 4.94 (br d, 1 H, NH, *J* = 8 Hz), 5.7–5.8 and 5.8–5.9 (br, 2 H, CH=CH), 6.00 and 6.24 (s, 1 H, C=CHN); IR (film) 3120 (w), 3050 (w), 2945 (m), 2845 (m), 1700 (s), 1445 (s), 1390 (s), 1375 (s), 1340 (s), 1225 (s), 1120 (s), 1000 (m), 885 (w), 765 (m), 735 (m) cm^{-1}; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 28.78 and 28.60, 35.92 and 35.81, 38.27 and 38.12, 52.38, 54.45, 60.95 and 60.40, 100.81 and 101.34, 131.71 and 131.47, 131.94 and 132.63, 145.32 and 145.88, 154.00; MS, *m/z* (relative intensity) 209 (100, M^+), 194 (32), 144 (47), 119 (26), 79 (28), 66 (39), 59 (19). Anal. Calcd for $C_{11}H_{15}NO_3$: C, 63.14; H, 7.23. Found: C, 62.97; H, 7.12.

***N*,*O*-Bis(methoxycarbonyl)-*N*-(2-methoxyallyl)-hydroxylamine**: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.57 (s, 3 H, OCH_3), 3.80 (s, 3 H, NCO_2CH_3), 3.89 (s, 3 H, OCO_2CH_3), 4.09 and 4.15 (d, 2 H, CH_2=C, *J* = 2 Hz), 4.24 (s, 2 H, CH_2N); IR (film) 3120 (w), 2960 (m), 2850 (w), 1795 (s), 1730 (s), 1640 (w), 1445 (s), 1370 (m), 1250 (s), 1220 (s), 1115 (m), 1070 (m), 930 (m), 820 (w), 780 (w) cm^{-1}; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 53.33, 53.65, 55.04, 55.95, 84.07, 154.56, 156.04, 157.11; MS, *m/z* (relative intensity) 219 (6, M^+), 144 (71), 116 (29), 59 (100). Anal. Calcd for $C_8H_{13}NO_6$: C, 43.84; H, 5.98. Found: C, 44.00; H, 5.89.

***N*-(Methoxycarbonyl)-1,2-dimethoxyallylamine**: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.39 and 3.61 (s, 6 H, 2 OCH_3), 3.71 (s, 3 H, NCO_2CH_3), 4.12 and 4.30 (d, 2 H, CH_2=C, *J* = 3 Hz), 5.2–5.3 and 5.55–5.65 (br d, 2 H, CH and NH); IR (film) 3330 (br), 3120 (w), 2950 (m), 2830 (w), 1730 (s), 1645 (m), 1515 (s), 1450 (m), 1330 (m), 1235 (s), 1080 (s), 995 (m), 825 (m), 730 (w) cm^{-1}; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 52.17, 55.01, 55.15, 83.13, 83.67, 156.30, 158.44; MS, *m/z* (relative intensity) 175 (31, M^+), 160 (61), 144 (78), 118 (100), 101 (39), 75 (23), 59 (100), 42 (55); HRMS, *m/e* 175.0846 ($C_7H_{13}NO_4$ requires 175.0845).

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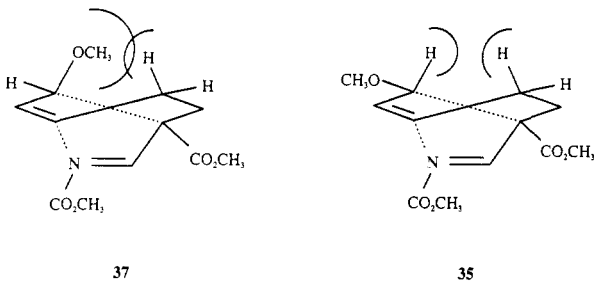

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Figure 1.

Methyl α-[[*N*-[(Methoxycarbonyl)oxy]-*N*-(methoxycarbonyl)amino]methyl]acrylate (29). To a solution of *N*,*O*-bis(methoxycarbonyl)hydroxylamine[28] (0.44 g, 3 mmol) in dry benzene (10 mL) was added methyl α-(bromomethyl)acrylate[29] (0.36 g, 2 mmol). Then a solution of triethylamine (0.30 g, 3 mmol) in dry diethyl ether (5 mL) was added dropwise over $^1/_2$ h. The solution was made alkaline with 10% NaOH, and then the organic layer was washed twice with 10% HCl, dried over magnesium sulfate, and concentrated in vacuo. Pure **29** (0.33 g, 67%) was obtained by flash column chromatography: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.78 (s, 3 H, CCO_2CH_3), 3.82 (s, 3 H, NCO_2CH_3), 3.90 (s, 3 H, OCO_2CH_3), 4.54 (s, 2 H, CH_2N), 5.89 (d, 1 H, CH=C trans to CO_2CH_3, J = 1 Hz), 6.37 (d, 1 H, CH=C, cis to CO_2CH_3, J = 1 Hz); IR (film) 3005 (w), 2955 (m), 1790 (s), 1720 (s), 1640 (w), 1440 (s), 1350 (m), 1270 (s), 1220 (s), 1160 (s), 1100 (m), 930 (m), 735 (m) cm^{-1}; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 50.88, 51.80, 53.66, 56.00, 127.69, 133.83, 154.32, 155.59, 165.57.

***N*,*O*-Bis(methoxycarbonyl)-*N*-[[1-(methoxycarbonyl)-3-cyclohexen-1-yl]methyl]hydroxylamine (30).** A solution of 3-sulfolene (0.94 g, 8 mmol) and **29** (0.99 g, 4 mmol) in benzene (20 mL) was sealed in a tube under nitrogen.[30] This was heated at 125 °C for 2.5 days, cooled to room temperature, washed with saturated sodium carbonate solution, dried over anhydrous magnesium sulfate, and concentrated in vacuo. Pure **30** (0.59 g, 49%) was obtained by flash column chromatography: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.7–2.6 (m, 6 H, 3 CH_2), 3.65 (s, 3 H, CCO_2CH_3), 3.76 (s, 3 H, NCO_2CH_3), 3.88 (s, 3 H, OCO_2CH_3), 3.9 (br, 2 H, CH_2N), 5.6–5.7 (m, 2 H, CH=CH); IR (film) 3020 (w), 2950 (m), 1790 (s), 1725 (s), 1440 (s), 1390 (m), 1260 (s), 1108 (s), 930 (m), 735 (m) cm^{-1}; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 21.81, 26.96, 30.45, 44.44, 51.86, 53.69, 55.82, 56.05, 123.76, 125.98, 154.04, 155.87, 175.44; MS, m/z (relative intensity) 301 (2, M$^+$), 269 (9), 238 (7), 166 (20), 153 (22), 139 (22), 111 (100), 91 (36), 79 (46), 77 (29), 59 (28).

***N*,5-Bis(methoxycarbonyl)-2-vinyl-1,2,3,4-tetrahydropyridine (32).** By use of previously described method for FVT,[1] **30** (20 mg, 0.07 mmol) gave **32** (4.8 mg, 33%) at the optimum temperature of 500 °C: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.6–2.5 (m, 4 H, 2 CH_2), 3.72 (s, 3 H, CCO_2CH_3), 3.82 (s, 3 H, NCO_2CH_3), 4.85 (br, 1 H, CHN), 4.95 (d, 1 H, trans proton of C=CH_2, J = 17 Hz), 5.13 (d, 1 H, cis proton of C=CH_2, J = 10 Hz) , 5.68 (ddd, 1 H CH=C, J = 5, 10, 17 Hz), 8.1 (br, 1 H, C=CHN); IR (film) 3020 (w), 2960 (m), 2908 (w), 2856 (w), 1725 (s), 1690 (s), 1635 (s), 1440 (s), 1390 (s), 1344 (s), 1310 (s), 1250 (s), 1198 (s), 1134 (s), 1108 (m), 952 (m), 928 (m), 772 (m), 750 (m) cm^{-1}; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 16.99, 24.45, 51.29, 52,82, 53.62, 108.06, 115.29, 134.37, 134.67, 154, 167.60; MS, m/z (relative intensity) 225 (92, M$^+$), 210 (33), 194 (75), 182 (45), 166 (100), 150 (30), 134 (41), 106 (66), 91 (43), 79 (37), 59 (55); HRMS, m/e 225.0990 ($C_{11}H_{15}NO_4$ requires 225.1001).

(*E*)- and (*Z*)-*N*,*O*-Bis(methoxycarbonyl)-*N*-[[1-(methoxycarbonyl)-2-methoxy-3-cyclohexen-1-yl]methyl]-hydroxylamine (33 and 34). A mixture of 1-methoxy-1,3-butadiene (0.32 g, 3.8 mmol), compound **29** (0.79 g, 32 mmol), hydroquinone (10 mg), and benzene (10 mL) in a heavy wall glass tube was sealed under nitrogen. The mixture was heated at 120 °C for 2 days and concentrated in vacuo. The crude product contained both **33** and **34**. Flash column chromatography gave pure **33** as a solid (0.36 g, 34%): mp 71–72 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.7–2.1 (m, 4 H, 2 CH_2), 3.35 (s, 3 H, OCH_3), 3.64 (s, 3 H, CO_2CH_3), 3.75 (s, 3 H, NCO_2CH_3), 3.88 (s, 3 H, OCO_2CH_3), 3.5–4.0 (br, 2 H, CH_2N), 4.01 (br d, 1 H, C*H*OCH_3, J = 5 Hz), 5.83–6.04 (m, 2 H, CH=CH); IR (KBr) 3030 (w), 2960 (m), 2830 (w), 1795 (s), 1740 (s), 1440 (s), 1395 (m), 1350 (m), 1265 (s), 1200 (s), 1120 (s), 1090 (s), 930 (m), 895 (w), 845 (w), 780 (s) cm^{-1}; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 23.00, 23.79, 49.74, 51.84, 53.66, 54.27, 55.94, 56.60, 73.25, 125.06, 130.97, 154.37, 156.03, 173.79; MS, m/z (relative intensity) 300 (0.3, M$^+$ – OCH_3), 256 (2), 172 (12), 169 (16), 162 (20), 137 (50), 91 (34), 84 (100), 59 (56). Anal. Calcd for $C_{14}H_{21}NO_8$: C, 50.75; H, 6.39. Found: C, 50.80; H, 6.43.

From the above crude product, **34** was obtained by flash column chromatography as a solid (0.32 g, 30%): mp 47–49 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.9–2.2 (m, 4 H, 2 CH_2), 3.31 (s, 3 H, OCH_3), 3.47 (br d, 1 H, C*H*OCH_3, J = 5 Hz), 3.68 (s, 3 H, CO_2CH_3), 3.74 (s, 3 H, NCO_2CH_3), 3.87 (s, 3 H, OCO_2CH_3), 3.6–4.1 (br, 2 H, CH_2N), 5.55–6.0 (m, 2 H, CH=CH); IR (film) 3030 (w), 2980 (m), 2830 (w), 1795 (s), 1735 (s), 1445 (s), 1385 (m), 1360 (m), 1335 (m), 1265 (s), 1095 (s), 930 (m), 845 (w), 780 (w) cm^{-1}; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 19.81, 22.10, 49.40, 51.62, 51.80, 53.75, 56.05, 57.13, 75.23, 122.58, 132.23, 154.07, 156.10, 174.17; MS, m/e (relative intensity) 272 (0.1, M$^+$ – CO_2CH_3), 256 (0.3), 212 (5), 169 (28), 162 (26), 137 (52), 91 (40), 84 (100), 59 (66). Anal. Calcd for $C_{14}H_{21}NO_8$: C, 50.75; H, 6.39. Found: C, 50.90; H, 6.28.

(*E*)-*N*,5-Bis(methoxycarbonyl)-2-(2-methoxyvinyl)-1,2,3,4-tetrahydropyridine (36). By the previously described method for FVT,[1] **33** (60 mg, 0.18 mmol) gave **36** as a solid (33 mg, 71%) as the sole isolated product at the optimum temperature of 425 °C: mp 54–56 °C; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.7–2.5 (m, 4 H, 2 CH_2), 3.48 (s, 3 H, OCH_3), 3.73 (s, 3 H, CO_2CH_3), 3.81 (s, 3 H, NCO_2CH_3), 4.66 (dd, 1 H, C*H*=$COCH_3$, J = 8, 12 Hz), 4.7–4.8 (br, 1 H, CHN), 6.50 (d, 1 H, C=C*H*OCH_3, J = 12 Hz), 8.01 (br s, 1 H, C=CHN); IR (KBr) 3100 (w), 3000 (w), 2960 (m), 2840 (w), 1730 (s), 1715 (s), 1650 (s), 1625 (s), 1435 (s), 1335 (s), 1250 (s), 1185 (s), 1145 (s), 1120 (m), 1090 (m), 1050 (m), 945 (s), 850 (m), 760 (m), 740 (m), 635 (m) cm^{-1}; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 17.09, 26.40, 49.87, 51.11, 53.34, 55.91, 99.90, 107.73, 134.38, 150.13, 153.06, 167.59; MS, m/z (relative intensity) 255 (8, M$^+$), 197 (14), 196 (17), 180 (16), 121 (14), 118 (17), 97 (9), 84 (100), 69 (42), 59 (21). Anal. Calcd for $C_{12}H_{17}NO_5$: C, 56.46; H, 6.71. Found: C, 56.39; H, 6.63.

Flash Vacuum Thermolysis of 34. By use of the same method for FVT as was used above, **34** (60 mg, 0.18 mmol) gave **36** (4 mg, 9%) and **38** (4 mg, 9%) at an optimal oven temperature of 425 °C, which could be separated by flash column chromatography.

(*Z*)-*N*,5-Bis(methoxycarbonyl)-2-(2-methoxyvinyl)-1,2,3,4-tetrahydropyridine (38): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.6–2.5 (m, 4 H, 2 CH_2), 3.62 (s, 3 H, OCH_3), 3.73 (s, 3 H, CO_2CH_3), 3.81 (s, 3 H, NCO_2CH_3), 4.28 (dd, 1 H, CH=$COCH_3$, J = 6, 8 Hz), 5.2–5.3 (br, 1 H, CHN), 5.90 (dd, 1 H, C=C*H*OCH_3, J = 1, 6 Hz), 8.03 (br s, 1 H, C=CHN); IR (film) 3110 (w), 3000 (w), 2950 (m), 2860 (w), 1725 (s), 1700 (s), 1660 (m), 1640 (s), 1445 (s), 1385 (s), 1245 (s), 1185 (s), 1115 (s), 1080 (s), 770 (m), 748 (m) cm^{-1}; ^{13}C NMR ($CDCl_3$, 75 MHz) δ 17.64, 25.95, 47.23, 51.23, 53.44, 60.01, 104.98, 108.07, 134.74, 147.25, 149.26, 167.86; MS, m/z (relative intensity) 255 (8, M$^+$), 197 (15), 196 (18), 180 (14), 121 (14), 118 (17), 84 (100), 69 (45), 59 (22); HRMS, m/e 255.1104 ($C_{12}H_{17}NO_5$ requires 255.1107).

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Registry No. **10**, 55638-24-9; **11**, 117370-76-0; **12**, 117370-77-1; **14**, 117370-79-3; **15**, 117370-80-6; **17**, 117370-82-8; **18**, 117370-83-9; **19**, 117370-84-0; **20**, 117370-85-1; **22**, 19926-90-0; **23**, 117370-87-3; **24**, 117370-88-4; **25**, 117370-89-5; **27**, 117370-91-9; **28**, 4224-69-5; **29**, 117370-92-0; **30**, 117370-93-1; **32**, 117370-94-2; **33**, 117370-95-3; **34**, 117370-96-4; **36**, 117370-97-5; **38**, 117370-98-6; $H_3CO_2CONHCO_2CH_3$, 51216-94-5; (*E*)-H_2C=CHCH=$CHOCH_3$, 3036-66-6; 2,5-dihydrothiophene 1,1-dioxide, 77-79-2; *N*-(methoxycarbonyl)-1,2-dimethoxyallylamine, 117370-70-4; 2-methoxy-

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bicyclo[2.2.1]hept-5-ene-2-*endo*-carboxaldehyde, 117370-71-5; 2-methoxybicyclo[2.2.1]hept-5-ene-2-*endo*-dimethoxymethane, 117370-72-6; bicyclo[2.2.1]hept-5-ene-(*E*)-[(trimethylsilyl)oxy]-2-methylene, 117370-73-7; bicyclo[2.2.1]hept-5-ene-(*Z*)-[(trimethylsilyl)oxy]-2-methylene, 117370-74-8; 4-methoxy-4-(dimethoxymethyl)cyclohexene, 117370-75-9; *N*-(methoxycarbonyl)-2-oxocycloheptanamine, 117370-78-2; 4-hydroxy-4-(dimethoxymethyl)cyclohexene, 117370-81-7; 2-hydroxybicyclo[2.2.1]hept-5-ene-2-carboxaldehyde, 117370-86-2; *N*,*O*-bis(methoxycarbonyl)-*N*-(2-methoxyallyl)hydroxylamine, 117370-90-8.

The Chemistry of L-Ascorbic and D-Isoascorbic Acids. 2. *R* and *S* Glyceraldehydes from a Common Intermediate[1]

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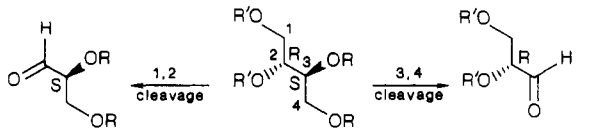
(*R*)- and (*S*)-glyceraldehyde and glycerol derivatives have been prepared from (2*R*,3*S*)-1,2-*O*-isopropylidenebutane-1,2,3,4-tetrol. (2*R*,3*S*)- and (2*S*,3*S*)-1,2-*O*-benzylidenebutane-1,2,3,4-tetrol have been prepared and cleaved to give (*R*)- and (*S*)-1,2-*O*-benzylideneglyceraldehydes and -glycerols. The conservation of chirality and conversion to PAF analogues are also demonstrated.

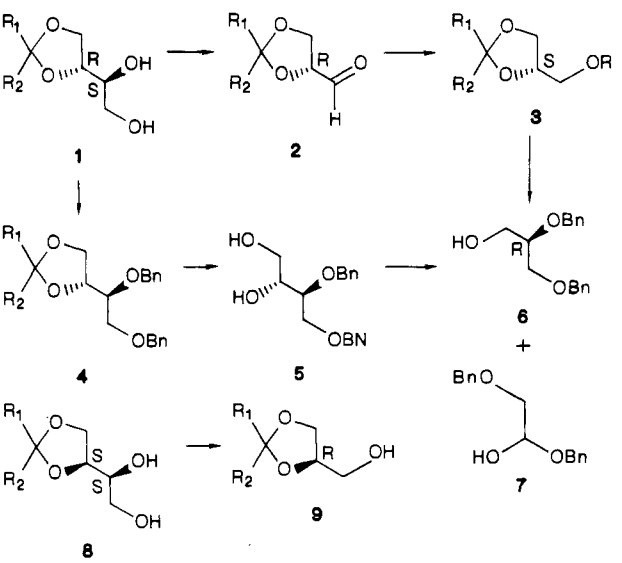
(*R*)- and (*S*)-glyceraldehyde and glycerol derivatives are common building blocks for a number of chiral natural[2] and synthetic[3] products. The enantiomers are usually prepared by degradative methods of the proper starting materials,[4] or, in the case of glycerols, by exchange of substituents between the oxygens at C-1 and C-3.[5] The latter procedure for inversion of chirality is rather lengthy and requires selective blocking of a primary hydroxyl group in a 1,2-diol system, a process that is not always totally selective and proceeds in variable yields.[5,6] More recently the use of enzymes has been reported for the preparation of chiral glycerols that have been suitably protected for further synthetic manipulations.[7] This paper describes a novel and simple approach for the preparation of (*R*)- and (*S*)-glyceraldehydes and glycerols from a *single* compound that contains both chiral centers, and in high yields. Also reported is a practical approach to the hitherto unknown (*R*)- and (*S*)-1,2-*O*-benzylideneglyceraldehydes, which are readily converted to the corresponding glycerol derivatives.

Conceptually both (*R*)- and (*S*)-glyceraldehyde derivatives can be prepared by selective cleavage of either the C-1, C-2 or C-3, C-4 bonds in a properly protected, and thus chiral, (2*R*,3*S*)-butane-1,2,3,4-tetrol derivative (Scheme I).

Scheme I



Scheme II[a]



[a] Bn = $CH_2C_6H_5$. **a** series: $R_1 = R_2 = CH_3$. **b** series: $R_1 = H$; $R_2 = C_6H_5$.

We have recently reported the preparation of (2*S*,3*S*)-1,2-*O*-isopropylidenebutane-1,2,3,4-tetrol from 5,6-*O*-isopropylidene-L-ascorbic acid.[8] Other chiral butanetetrols are accessible from either D- or L-tartaric acids.[9] However, the isomeric (2*R*,3*S*)-1,2-*O*-isopropylidene- and -benzylidenebutane-1,2,3,4-tetrols, which are derivable

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