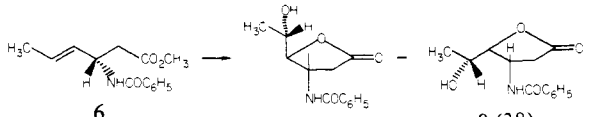
the sulfoxides is stereospecific and that of the sulfone is not demonstrates that oxidation of the sulfoxide to a sulfone does not take place prior to hydroxylation of the olefin. Additional evidence which indicates that a complex initially forms between the osmium and the sulfoxide group was derived from a study of the hydroxylation of **1** and **3** with 2 or less equiv of TMNO. In every instance, only the diol sulfones **2** and **4** and the respective starting materials were isolated. No products of incomplete oxidation or hydroxylation such as the diol sulfoxide or olefinic sulfone **5** were found.[13] Apparently, once complexation of the osmium occurs, complete conversion to products results.

Further studies have been initiated to establish the generality of this methodology and to extend it to achieve diastereo- and enantioselective total syntheses of natural products.

Acknowledgment. We express our appreciation to Drs. Richard Finke and John Baldwin (University of Oregon) and G. Doyle Daves, Jr. (Lehigh University), for their comments. This work was generously supported by the National Institutes of Health of the Department of Health, Education and Welfare (GM 26754 and CA 24487).

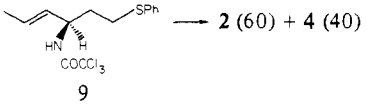
Supplementary Material Available: An ORTEP drawing and tables of fractional coordinates, bond distances, and bond angles (6 pages). Ordering information is given on any current masthead page.

(12) In related work, hydroxylation of the allyl amide **6** gave a 62:38 ratio of lactones **7** and **8**.[7] A parallel explanation accounts for this result.



6 7 (62) 8 (38)

(13) Upon hydroxylation of the olefinic sulfide **9** (catalytic OsO_4, 4 equiv of TMNO) and subsequent acetylation, a 60:40 ratio of the diacetate sulfones



2 and **4** were obtained as the only products of reaction. The relative rate of oxidation is: sulfone > sulfoxide ≫ sulfide.

Sulfoximine-Directed Osmylation: Synthesis of Enantiomerically Pure Dihydroxycycloalkanones

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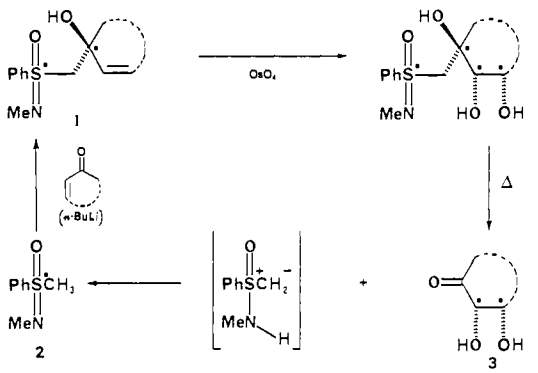
Of the existing methods for the conversion of alkenes to *cis*-1,2-diols, the most reliable method continues to be the reaction of alkenes with osmium tetroxide in either catalytic[1a] or stoichiometric[1b,2] modes. The stereochemical outcome of alkene osmylations with respect to existing substituents in the substrate is dependent on several factors. Steric considerations are of demonstrated importance.[3] The importance of allylic

Scheme I



substituents—especially heteroatom-containing groups such as hydroxyl or alkoxyl—in the determination of diastereoface selectivity has also become evident.[4-7]

Osmium tetroxide is known to reversibly form stable adducts with basic ligands such as pyridine[1b] and quinuclidine.[8] Behrman and co-workers[9] have invoked this complexation to account for a sequence-selective osmylation in polynucleotides in which the cyclosine residues are modified by attaching an osmiophilic diamino residue. We anticipated that the methylimino group of adducts **1**[10] of *N*,*S*-dimethyl-*S*-phenylsulfoximine (**2**) and cycloalkenones would facilitate and direct[14] osmylation of the adjacent carbon–carbon double bond. Furthermore, the antiperiplanar effect[7] of the allylic hydroxyl group should provide a synergistic enhancement of the diastereoface selectivity. A novel dihydroxy ketone optical activation method was envisioned involving (1) directed osmylation and (2) thermal reversal[12] of the sulfoximine addition to afford optically pure dihydroxy ketones **3** and the recyclable resolving agent **2** (Scheme I).

As an initial probe of this concept, (*S*)-**2** was added to 3,5,5-trimethyl-2-cyclohexenone and the resulting diastereomers **4** were separated by silica gel chromatography using ethyl acetate/hexanes as eluent.[10,12] Treatment of the individual diastereomers[13] in water/tetrahydrofuran solutions containing trimethylamine *N*-oxide dihydrate (1.5 equiv) with solutions of osmium tetroxide (5 mol %) in tetrahydrofuran for 24–72 h at room temperature afforded crude triols. In each case, analytical HPLC revealed a single diastereomeric product, which was isolated in 78% yield after flash chromatography as a white amorphous solid. Stoi-

(1) (a) Van Rheenen, V.; Kelly, R. C.; Cha, D. Y. *Tetrahedron Lett.* **1976**, 1973. Ray R.; Matteson, D. S. *Ibid.* **1980**, 449. (b) Criegee, R. *Justus Liebigs Ann. Chem.* **1936**, *522*, 75. Criegee, R.; Marchand, B.; Wannowius, H. *Ibid.* **1942**, *550*, 99.

(2) Schroder, M. *Chem. Rev.*, **1980**, *80*, 187.

(3) Danishefsky, S.; Hirama, M.; Gombatz, K.; Harayama, T.; Berman, E.; Schuda, P. *J. Chem. Soc.* **1978**, *100*, 6536; *Ibid.* **1979**, *101*, 7020. (b) Smith, A. B., III; Boschelli, D. *J. Org. Chem.* **1983**, *48*, 1217. For a related result, see: Kon, K.; Isoe, S. *Tetrahedron Lett.* **1980**, *3399*.

(4) For a discussion of factors affecting the stereochemistry of osmylations of allylic alcohol systems, see: (a) Cha, J. K.; Christ, W. J.; Kishi, Y. *Tetrahedron Lett.* **1983**, 3943, 3947. (b) Stork, G.; Kahn, M. *Ibid.* **1983**, 3951.

(5) Smith, A. B., III; Branca, S. J.; Pilla, N. N.; Guaciara, M. A. *J. Org. Chem.* **1982**, *47*, 1855.

(6) Posternak, T.; Friedli, H. *Helv. Chim. Acta* **1953**, *36*, 251.

(7) For a discussion of the "antiperiplanar effect" and its role in controlling the stereochemistry of additions to allylic systems see: Caramella, P.; Rondan, N. G.; Paddon-Row, M. N.; Houk, K. N. *J. Am. Chem. Soc.* **1981**, *103*, 2438. Paddon-Row, M. N. Rondan, N. G., Houk, K. N. *Ibid.* **1982**, *104*, 7162. Houk, K. N. *Pure Appl. Chem.* **1983**, *55*, 277. See also: Franck, R. W.; John, T. V.; Olejniczak, K.; Blount, J. F. *J. Am. Chem. Soc.* **1982**, *104*, 1106.

(8) Cleare, M. J.; Hydes, P. C.; Griffith, W. P.; Wright, M. J. *J. Chem. Soc., Dalton Trans.* **1977**, 941.

(9) Ford, H.; Chang, C.-H.; Behrman, E. *J. J. Am. Chem. Soc.* **1979**, *101*, 2251; **1981**, *103*, 7773.

(10) Johnson, C. R.; Barbachyn, M. R. *J. Am. Chem. Soc.* **1982**, *104*, 4290. This paper describes the preparation of enantiomerically pure cyclopropyl ketones utilizing the hydroxyl group of enantiomerically pure β-hydroxysulfoximines of type **1** to provide diastereoface selection in the Simmons–Smith reaction.

(11) The directive effect of a basic group in this reaction could be the result of guidance of the reagent to one diastereoface of the alkene or of nucleophilic triggering of osmate ester formation from equilibrating oxametallacyclobutane intermediates. For recent discussions of osmium tetraoxide mechanisms, see: Hentges, S. G.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 4263. Sharpless, K. B.; Teranishi, A. Y.; Backvall, J.-E. *Ibid.* **1977**, *99*, 3120. Casey, C. P. *J. Chem. Soc., Chem. Commun.* **1983**, *126*. Schroder, M.; Constable, E. C. *Ibid.* **1982**, 734.

(12) Johnson, C. R.; Zeller, J. R. *J. Am. Chem. Soc.* **1982**, *104*, 4021; *Tetrahedron*, in press.

(13) In some cases it was found to be more expedient to osmylate the mixture of diastereomers **1** and then separate the triol diasteromers by chromatography.

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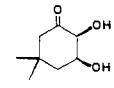
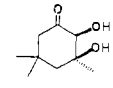
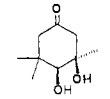
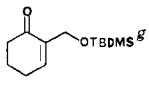
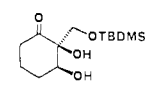
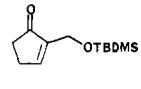
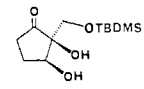
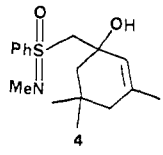
Table I. Preparation of Dihydroxycycloalkanones

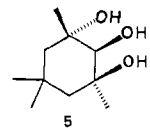
ketone	adduct 3 yield, %[d]	adduct 3 no.[b]	osmylation yield, %[c]	thermolysis yield, %	product 5	$[\alpha]^{25}_D$ (conc) $CHCl_3$
	84	(+)-I[d]	(74)	81		+0.7° (1.01)[h]
		(−)-I[e]	(73)	70		−0.8° (1.06)
	94	e,f	87[f]	85		−21.2° (1.08)[i]
				76		+21.6° (0.36)[j]
	96	(+)-I[e]	87	83		−29.3° (1.09)[k]
		(−)-II[e]	90	97		+28.6° (1.05)[l]
	47	(+)-I[e]	94	82		−24.2° (0.39)[m]
		(+)-II[e]	98	89		+24.0° (0.92)[n]
	92	(+)-I[d]	87 (78)	96		−52.3° (1.34)
			89 (78)	65		+51.2° (1.01)
	83	(−)-I[e]	97	96		+35.2° (1.04)
		(+)-II[e]	84	95		−34.7° (1.00)

[a] Combined yield of adducts after purification by flash chromatography on silica gel with hexane/ethyl acetate. [b] Entry designates sign of rotation of diastereomer; I indicates faster eluting diastereomer. [c] Yields in parenthesis were obtained in catalytic procedures using trimethylamine *N*-oxide. [d] Adduct from (−)-(*R*)-4. [e] Adduct from (+)-(*S*)-4. [f] A mixture of diastereomers was oxidized. Separation of the diastereomeric triols was achieved by silica gel chromatography; a small amount of a third diastereomer was formed in the osmylation reaction. [g] TBDMS = *tert*-butyldimethylsilyl. [h] Colorless oils unless otherwise stated. [i] mp 47–48 °C. [j] mp 48–49 °C. [k] mp 57–58 °C. [l] mp 65–67 °C. [m] mp 129–130 °C. [n] mp 132–133 °C.

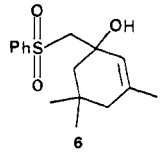
chiometric osmylation of the adducts in tetrahydrofuran/pyridine afforded the same products but in somewhat higher yields (87% and 90%). Desulfurization[14] of each of the above triols provided, in 87% isolated yield, a white crystalline solid (mp 86.5–88 °C) that exhibited 10 resonances in the decoupled ^{13}C NMR spectrum and four methyl singlets in the ^1H NMR spectrum. The spectra are only consistent with the unsymmetrical structure **5**. These



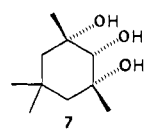
4



5



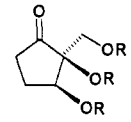
6



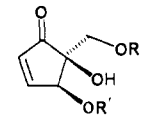
7

results show that osmylation occurs in the above cases anti to the original hydroxyl and syn to the sulfoximine moiety. In order to ascertain whether the diastereoface selectivity could be ascribed to the presence of the sulfoximine group, the corresponding sulfone adduct **6** was prepared and subjected to osmylation. The sulfone and sulfoximine moieties should exhibit similar steric and electronegative properties. The triol produced in the sulfone case was a 2:1 mixture of diastereomers. Desulfurization of the major diastereomer gave the unsymmetrical triol **5**; desulfurization of the minor diastereomer afforded a new triol **7** exhibiting only seven lines in the decoupled ^{13}C NMR and two methyl singlets in the ^1H NMR.

The application of the methodology to sulfoximine adducts of other cycloalkeneones was examined. Optically active cis-hydroxylated β-hydrosulfoximines undergo clean thermal elimination[12] of the sulfoximine in refluxing solvent (2-butanol, toluene, or xylene). The progress of the thermolysis is easily monitored by thin-layer chromatography. Generally, reaction times of 12–48 h necessary. When the reaction was complete the solvent was removed under vacuum and the nonracemic dihydroxy ketones were separated from the recyclable sulfoximine **2** by flash chromatography or recrystallization. The results are tabulated in Table I. To our knowledge these dihydroxy ketones have not been previously prepared in optically active form. The optical purities are assumed to be ca. 100%. This assumption is based on the criteria that the precursor β-hydroxysulfoximines were shown to be pure compounds by analytical HPLC and ^{13}C and ^1H NMR and that the magnitudes of the observed specific rotations of the enantiomeric dihydroxycycloalkanones exhibited consistency.



8 R = H
9 R = Ac



10 R=R′=H
11 R=H; R′=Ac

A variety of naturally occurring substances—carbohydrates, antibiotics, toxins, etc.—contain cis vicinal oxygenated centers. The methodology outlined here shows considerable promise for involvement in the synthesis of such chiral nonracemic targets. The preparation of (+)- and (−)-**8** represents formal total syntheses of both optical isomers of the antibiotics pentenomycin I and II (**10** and **11**) since Smith and co-workers[5] have successfully converted racemic material to these substances. We transformed both enantiomers of **8** into dihydropentenomycin I triacetate (**9**) with mp 60–61 °C and $[\alpha]_D^{21}$ +164.0° (*c* 0.34, EtOH) and −162.0° (*c* 0.10, EtOH). Material derived from naturally occurring pentenomycin I has $[\alpha]^{21}_D$ +164.0° (*c* 0.34, EtOH) and mp 60 °C.[15] At this time attempts to extend this oxidation methodology

(14) Johnson, C. R.; Stark, C. J., Jr. *J. Org. Chem.* **1982**, *47*, 1193.

(15) Umino, K.; Takeda, N.; Ito, Y.; Okuda, T. *Chem. Pharm. Bull.* **1974**, *22*, 1233.

to the preparation of enantiomerically pure acyclic diol ketones has been less successful.[16,17]

Acknowledgment is made to the National Science Foundation (Grant CHE83-06594) and to the Monsanto Company for support ot this research.

(16) Satisfactory microanalysis and/or high-resolution mass spectra were obtained on all new compounds involved in this study.

(17) A remote sulfoxide group has been found to control the stereospecific hydroxylation at an olefinic center by osmium tetroxide. Hauser, F. M.; Ellenberger, S. R.; Clardy, J. D.; Bass, L. S. *J. Am. Chem. Soc.*, Preceding paper in this issue.

Isotopic Multiplets in the ^{13}C NMR Spectra of Polyols with Partially Deuterated Hydroxyls. 2.[1] Effects of Cis–Trans Isomerism in Cyclic Vicinal Diol Systems

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The assignment of carbon-13 NMR spectra of polyols in general and carbohydrates in particular is greatly facilitated by the characteristic multiplets in the proton-decoupled spectra of Me_2SO solutions of materials with partially deuterated hydroxyls.[1-4] These multiplets are due to upfield deuterium isotope effects on the carbon-13 chemical shifts: 0.09–0.12 ppm for directly bonded hydroxyls (β-effect, Δ_β) and 0.07 ppm or less for hydroxyls on vicinal carbons (γ-effect, Δ_γ).[1-6] Thus, if only part of the molecules are deuterated, the resonance of a hydroxylated carbon will be split into a doublet with a spacing of Δ_β. In partially deuterated vicinal diols, the ^{13}C NMR spectral line of each hydroxylated carbon appears as a quartet (with components corresponding to the HH, HD, DH, and DD species) with spacings of Δ_β and Δ_γ. Up to eight components (octet) can be observed for a hydroxylated carbon flanked by two hydroxylated carbons.[1,4]

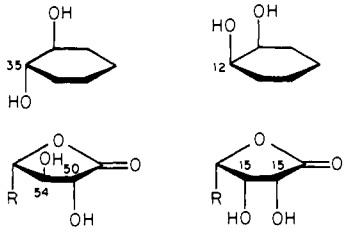
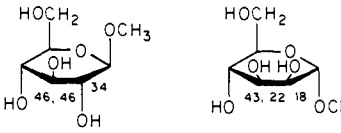
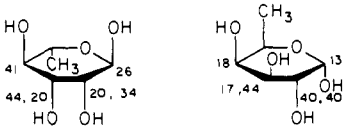
This communication presents results on the dependence of the γ-effect in cyclic vicinal diol systems on the relative orientation, cis or trans, of the hydroxyls. On the basis of this finding, one can use the approach of isotopic multiplets for more detailed structural interpretations as well as for spectral assignments. Examples showing the effects of cis–trans isomerism on the magnitude of the γ-effect, Δ_γ, are given in Table I. The data show that in general

$$\Delta_\gamma(\text{trans}) > \Delta_\gamma(\text{cis}) \qquad (1)$$

Since the isotopic state ("light" or "heavy") of a hydroxyl is analogous to the spin state ($+^1/_2$ or $-^1/_2$) of a spin $^1/_2$ nucleus in a magnetic field, there is a remarkable similarity between isotopic multiplets and those due to spin–spin couplings.[1] Owing to the cis–trans relationship of eq 1, this analogy can been carried one step further: *isotopic multiplets of vicinal hydroxylated carbons have similar spacings*. Thus, from the multiplicity and spacings in the isotopic multiplets, one can trace the pairwise connectivity of such atoms. Note, however, that, unlike spin–spin interactions, the Δ_β and the Δ_γ values are not necessarily the same for both carbons.

The isotopic multiplets in the ^{13}C NMR spectra of α-L-rhamnopyranose (**1**) and α-D-fucopyranose (**2**) with partially deuterated hydroxyls are shown in Figure 1.[7] These molecules

Table I. Effects of Cis–Trans Isomerism on the Three-Bond Isotope Shift (Δ_γ in ppb) due to Hydroxyl Deuteration

	Δ_γ(trans) – Δ_γ(cis)
	C-1: 23
	C-2: 35 C-3: 39
R = CHOHCH$_2$OH	
	C-2: 16 C-3: 24
	C-1: 13 C-2: 20, –6 C-3: 24, 27 C-4: 23
I	2

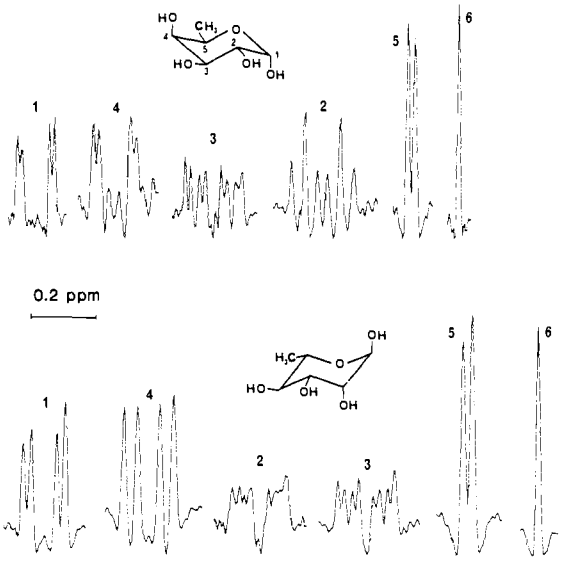


Figure 1. Isotopic multiplets in the 90.55-MHz ^{13}C NMR spectra (resolution enhanced) of Me_2SO solutions of α-L-rhamnopyranose (**1**) (bottom) and α-D-fucopyranose (**2**) (top) with partially deuterated hydroxyls. The chemical shifts (in ppm from TSP) of the protio forms (leftmost component of each multiplet): (**1**) 95.77, 74.15, 73.27, 72.16, 69.46, 19.79; (**2**) 94.26, 73.54, 71.23, 70.16, 66.84, 18.35.

form an interesting pair: the configuration of each vicinal diol fragment, as well as the configuration at carbon 5, changes from cis to trans in going from one molecule to the other. As a result, the resonances of the carbon atoms involved show conspicuous differences in the Δ_γ spacings in comparing the spectrum of one with that of the other. For C-2 of α-rhamnose (**1**), the isotope effect due to the trans hydroxyl on C-1 (34 ppb) is smaller than that (40 ppb) in a α-fucose (**2**), where the configuration is cis. This anomaly, which has also been observed by Pfeffer et al.,[5] seems to occur only when the anomeric carbon is part of a diaxial array. For diequatorial trans hydroxyls in similar positions, much larger γ-effects have been observed, e.g., 67 ppb for C-2 in β-D-glucopyranose.[1]

(1) Part 1: Reuben, J. *J. Am. Chem. Soc.* **1983**, *105*, 3711–3713.
(2) Gagnaire, D.; Vincendon, M. *J. Chem. Soc., Chem. Commun.* **1977**, 509–510.
(3) Newmark, R. A.; Hill, J. R. *Org. Magn. Reson.* **1980**, *13*, 40–44.
(4) Christofides, J. C.; Davies, D. B. *J. Am. Chem. Soc.* **1983**, *105*, 5099–5105; *J. Chem. Soc., Chem. Commun.* **1983**, 324–326.
(5) Pfeffer, P. E.; Valentine, K. M.; Parrish, F. W. *J. Am. Chem. Soc.* **1979**, *101*, 1265–1274.
(6) Ho. S. C.; Koch, H. J.; Stuart, R. S. *Carbohydr. Res.* **1978**, *64*, 251–256.

(7) The assignment of such spectra is a fairly simple matter.[1,4] The acronym SIMPLE, which stands for secondary isotope multiplets of partially labeled entities, emphasizes this point.[4]

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