and chemical ionization mass spectra were determined on a VG Micromass 7070 H machine. UV–vis spectra were determined in MeCN solution on a Perkin-Elmer 202 spectrometer. Elemental analyses were performed by Galbraith Laboratories, Inc., Knoxville, TN.

o-Xylene-α,α′-diylidenebis(4,5-dicarbomethoxy-1,3-dithiole) (7). To a stirred mixture of (4,5-dicarbomethoxy)thiolyl triphenyl phosphonium fluoborate[5] (10.5 g) and o-phthalaldehyde (1 g) in dry acetonitrile (100 mL) under argon was added excess Et_3N (10 mL). After 4–5 h of stirring under argon, the mixture was diluted carefully with water until no more crystals precipitated. The crystalline product was filtered, washed with water and methanol successively, and dried to give crude tetraester 7, mp, 130 °C with prior shrinking at 114 °C (3.7 g, 92%); an analytical sample was obtained by recrystallization from methanol–methylene chloride and had mp 130 °C; mass spectrum, m/e 538 (14%): UV–vis spectrum λ_{max} 235 nm (log ε 4.083), 310 sh (4.106), 365 (4.208). Anal. Calcd for $C_{22}H_{18}O_8S_4$: C, 49.05; H, 3.37; S, 23.82. Found: C, 49.01; H, 3.50; S, 26.05.

Dithiino Fulvene Tetraester (10). To a solution of bisfulvene tetraester 7 (1.076 g) in CCl_4 (10 mL) under argon was added a solution of Br_2 (0.32 g) in CCl_4 (4 mL). Upon stirring at room temperature, HBr evolved and it was observed that light increased the rate of HBr evolution. After HBr evolution slackened, the dark solution was filtered through a short column of alumina, and the eluant was evaporated in vacuo. The crystalline residue (1 g) was recrystallized from benzene to give very dark red rhombs of tetraester 10: mp 198 °C (0.85 g; 79.3%); mass spectrum (EI), m/e 504 (100%) (CI) 536 (15%); UV–vis spectrum, λ_{max} 235 nm (log ε 4.221), 258 br (4.253), 300 sh (3.855), 400 (4.309). Anal. Calcd for $C_{22}H_{16}O_8S_4$: C, 49.24; H, 3.00; S, 23.90. Found: C, 49.49; H, 3.06; S, 23.7.

Acknowledgment. This work was supported by a grant from the National Science Foundation (NSF CHE 82-03897).

Registry No. 7, 88430-83-5; 9, 88430-82-4; 10, 88430-84-6; o-phthalaldehyde, 643-79-8.

Supplementary Material Available: Full X-ray data for compound 10 (5 pages). Ordering information is given on any current masthead page.

Communications

Two New Asymmetric Epoxidation Catalysts. Unusual Stoichiometry and Inverse Enantiofacial Selection

Summary: Use of $TiCl_2(O\text{-}i\text{-}Pr)_2$ instead of $Ti(O\text{-}i\text{-}Pr)_4$ with tartrate diesters (in a 2:1 ratio) affords the chloro diols arising from regiospecific opening of intermediate epoxides of *opposite* enantioselectivity to those produced in the standard asymmetric epoxidation. These "inverse" epoxides are also obtained in oxidations catalyzed by $Ti(O\text{-}i\text{-}Pr)_4$ and tartramide ligands in the 2:1 ratio.

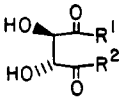
Sir: We have recently reported evidence for the dimeric nature of the standard (2:2) titanium–tartrate asymmetric epoxidation catalysts.[1] During the past several months we have discovered three new asymmetric catalyst systems that depend on a titanium to tartrate ligand ratio of 2:1.[2] Furthermore, the two systems that involve epoxidation of an allylic alcohol effect this transformation with an enantiofacial selection that is opposite to that of the standard catalyst. These two systems are the subject of this report.

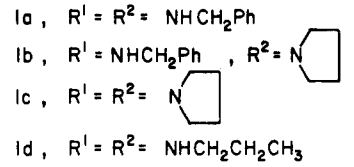
Tartramide Ligands. The first of these new systems evolved from work that began at Stanford on modified tartrate ligands. Initially, erratic results were obtained with the amides derived from tartaric acid,[3] but careful reinvestigation of amide ligands such as 1a has led to the remarkable discovery revealed in eq 1 and 2.

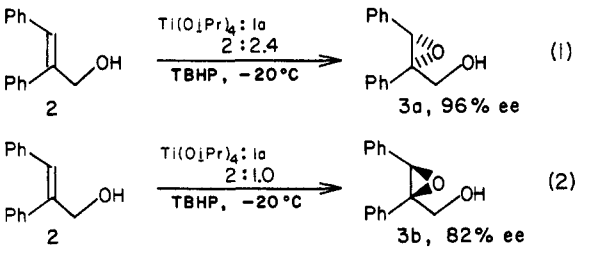
Table I. Epoxidation of (E)-α-Phenylcinnamyl Alcohol with Various 2:1 $Ti(O\text{-}i\text{-}Pr)_4$-Tartramide Complexes

(+)-tartramide	epoxy alcohol,[a] % ee (2R, 3R)
1b	84
1c	53
1d	66

[a] Enantiomeric excess (ee) determined by HPLC on two ionically bound Pirkle type 1-A column in series (Regis Chemical Co. Hi-Chrom reversible HPLC column).







(1) (a) Sharpless, K. B.; Woodard, S. S.; Finn, M. G. *Pure Appl. Chem.* **1984**, *55*, 1823–1836. (b) The standard asymmetric epoxidation conditions include the use of slightly greater than 1 equiv of tartrate per equiv of Ti.[18] We denote this sytem as "2:2", however, because it is the complex with the 2:2 Ti:tartrate stoichiometry that is the active catalyst under these conditions.

(2) (a) Miyano, S.; Lu, L. D.; Viti, S. M.; Sharpless, K. B. *J. Org. Chem.* **1983**, *48*, 3608–3611. (b) Hill, J. G.; Rossiter, B. E.; Sharpless, K. B. *Ibid.* **1983**, *48*, 3607–3608. (c) Altering the titanium–tartrate ratio in the opposite direction (i.e., Ti:tartrate = 2:4) gives an effective reagent for the asymmetric oxidation of certain sulfides (H. B. Kagan and P. Pitchen, private communication). We had earlier shown that the 2:4 Ti:tartrate species is completely inactive as an epoxidation catalyst for allylic alcohols (Woodard, S. S. Ph.D. Dissertation, Stanford University, Stanford, CA, 1981).

(3) Zilenovsky, J.; Sharpless, K. B., unpublished results.

0022-3263/84/1949-0728$01.50/0

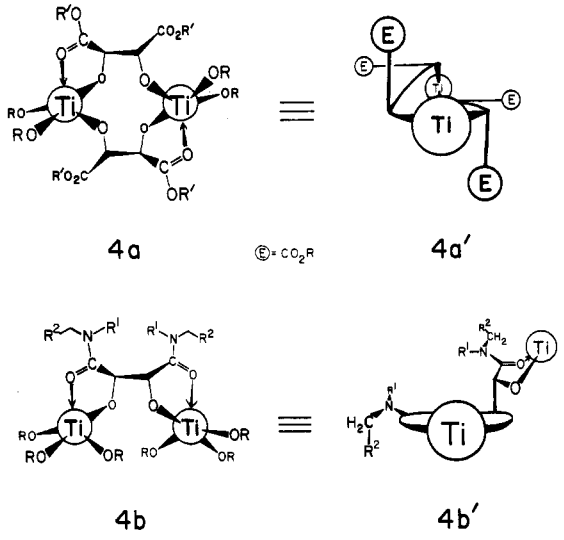


Figure 1.

When the standard ratio (i.e., 2:2.4) of Ti(O-*i*-Pr)$_4$ to ligand **1a** is used and sufficient time for complex formation is allowed,[4] excellent enantiofacial selection in the usual sense is obtained in the epoxidation of (*E*)-α-phenylcinnamyl alcohol **2**, (see eq 1). However, when the ratio is 2:1, a strong inverse enantiofacial selection is observed (see eq 2). Careful variation of the ratio proved that, as might be expected, the 2:1 ratio is optimal for the inverse enantiofacial selection process. We then examined the effects of varying the structure of the amide ligand used under the inverse selectivity conditions (i.e., the 2:1 Ti:ligand ratio) of eq 2. Several examples are given in Table I, and many additional results may be found in the supplementary material to this communication.

This discovery suggested that we might be able to access either enantioface of an allylic alcohol using the appropriate derivative of the inexpensive L-(+)-tartaric acid. However, the effectiveness of the 2:1 system appears to be rather substrate dependant. For example, the inverse face selection was maintained for (*E*)-cinnamyl alcohol, but the ee was only 65%. With a good substrate like **2**, the 2:1 Ti:**1a** system proved very effective even in catalytic amounts. For example, the same yield (90%) and enantioselectivity (80% ee) were realized when the 2:1 catalyst system was reduced from 100 to 2.5 mol %. Another practical advantage is that amide **1a** is very polar and therefore easy to separate from most epoxy alcohols during nonhydrolytic workup procedures.[5]

While more work is needed to decide on the practical utility of the tartramide ligands, we are highly intrigued by the mechanistic implications of these results. How can a simple change in stoichiometry effect such a dramatic inversion in catalyst selectivity? Clearly the two ratios afford very different catalysts. The 2:2.4 system is likely

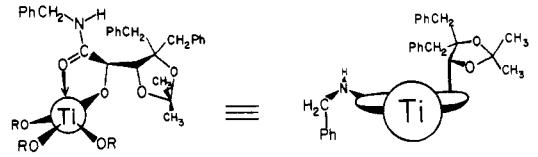
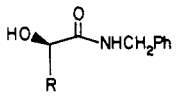
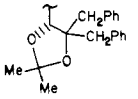


Figure 2. Presentation analogous to Figure 1 of the complex formed from a 1:1 mixture of Ti(OR)$_4$ and ligand **5e**.

Table II. α-Hydroxy Amides Used with 1 Equiv of Ti(O-*i*-Pr)$_4$ in the Oxidation of Allylic Alcohol **2** to Epoxy Alcohols **3a** and **3b**



ligand	R	3a/3b
5a	Me	50/50
b	Ph	52/48
c		45/55
d	t-Bu	44/56
e		25/75

the amide analogue of the normal Ti(O-*i*-Pr)$_4$–tartrate ester dimer system. Present evidence best supports the structures proposed in Figure 1 for the 2:2 and the new 2:1 catalyst.[1a,6]

An attractive rationale for the inverse selection is readily forthcoming from structures such as **4**, which are derived from CPK space-filling models. Drawings **4a′** and **4b′** are simplified versions of **4a** and **4b** from a perspective in the plane defined by one of the two equivalent titanium atoms and its two least labile, "framework", ligands. In the case of the 2:2 complex, these ligands are the alkoxide oxygens of the two tartrates in the ten-membered ring. In the 2:1 system, the framework ligands of each Ti atom are the amide carbonyl and its α-alkoxide that form a five-membered chelate ring. Upon comparing **4a′** and **4b′** more closely, one notices that, although they have the same L-(+)-tartaric acid backbone, the quadrants in which blocking groups are located have a mirror image relationship, leading to mirror image epoxy alcohol products. While the group in the upper right quadrant of **4b′** is huge, the blocking group in the lower left quadrant is smaller and conformationally flexible. We believe the *N*-alkyl group (CH_2R) will prefer to occupy the lower left quadrant in the conformation shown, since that is the position farthest away from the large titanium blocking group on the upper right. The poorer enantioselectivities observed with the 2:1 catalyst may reflect the inferior blocking effect in the lower left quadrant.

Use of α-hydroxy benzyl amides **5a–d** as ligands in the epoxidation of **2** resulted in little or no enantioselectivity as shown in Table II.[7] In these ligands, R serves to substitute for the large group found in the upper right-hand quadrant of **4b′**. We reasoned that in these ligands R may be too small to provide (a) an adequate blocking effect in

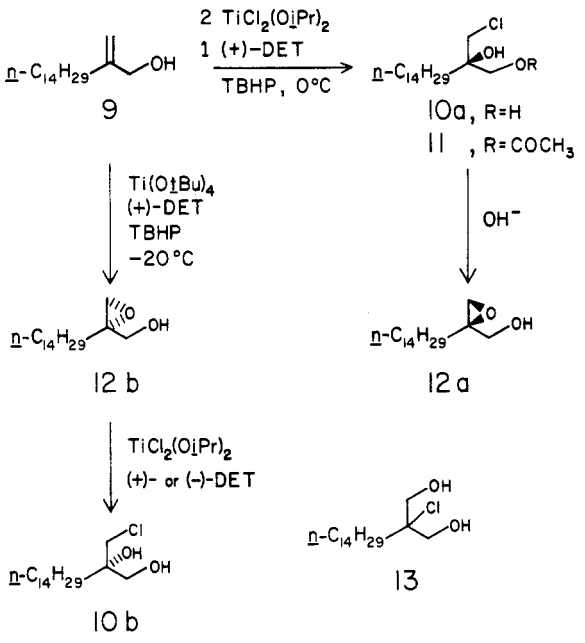
(4) The solution of Ti(O-*i*-Pr)$_4$ and **1a** must be aged for at least 30 min at 0 °C. If less time is allowed, the enantiomeric excess of the reaction is greatly diminished. The assembly of the 2:2 catalyst is apparently much slower with these tartramide ligands than with the standard tartrate ester ligands.

(5) In a typical procedure, 2.0 equiv of Ti(O-*i*-Pr)$_4$ are added to a stirred suspension of 1.0 equiv of tartramide **1a** in CH_2Cl_2. After being stirred for at least 30 min at 0 °C, the homogeneous solution is cooled to −20 °C, and 1.0 equiv of allylic alcohol **2** is added. After several minutes, ca. 2.0 equiv of anhydrous TBHP in toluene[2b] is added. All manipulations are done under anhydrous conditions. The final reaction solution is usually ca. 0.05–0.10 M in Ti. The reaction is complete within an hour and is quenched by stirring with saturated aqueous Na_2SO_4 (1 mL per mmol Ti used) and ether (the same volume as the reaction solution) for at least 1 h, followed by filtration through Celite. The epoxy alcohol is then isolated by chromatography.

(6) Structures **4b** and **4b′** apply directly to the bis(dialkylamido) ligands (such as **1c**). The structures of complexes of titanium with (alkylamido)tartrates (such as **1a**, **1b**, and **1d**) are more complex. Ligand **1a**, for example, has in principle two labile protons that a tartrate diester does not. Our evidence in this case suggests that a mixture of tautomeric and fluxional forms is present, involving amide, imidate, and bridging alkoxide species. We believe, however, that the average structure closely resembles that of **4b**. **Note Added in Proof**: The molecular weights of the 2:2 and 2:1 Ti:tartramide **1a** complexes in CH_2Cl_2 solution have been measured by the isopiestic Signer method (Clark, E. P. *Ind. Eng. Chem., Anal. Ed.* **1941**, *13*, 820–822). The results (2:2 obsd = 997, calcd = 985; 2:1 obsd = 819, calcd = 777) are consistent with structures **4a** and **4b**.

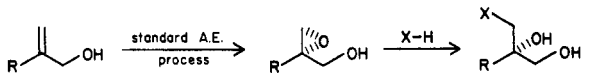
(7) These reactions are performed with a Ti:ligand ratio of 1.0:1.0 at −20 °C in CH_2Cl_2 with 2 equiv of TBHP.

Scheme I



the upper right quadrant and (b) the necessary steric bulk required to force the *N*-benzyl group in the lower left quadrant into an effective blocking conformation. To simulate the steric requirements of model **4b'**, ligand **5e** was designed and prepared from L-dimethyltartrate. Chelation of titanium with **5e** in the manner shown by Figure 2 may be expected to enhance the enantioselectivity in the same sense as for the 2:1 Ti:L-tartramide system (**4b**). This is indeed observed, as epoxidation of **2** with TBHP and a 1:1.1 mixture of $Ti(O\text{-}i\text{-}Pr)_4$ and **5e** at −20 °C gives epoxy alcohol **3** in 50% ee.[8]

$TiCl_2(O\text{-}i\text{-}Pr)_2$. Certain epoxy alcohols are difficult to obtain in the standard asymmetric epoxidation process because they are sensitive to opening under the reaction conditions. An important class of allylic alcohols that often suffers from this limitation is the 2-alkyl series **6**.[9] De-



pending on the R group, the yields of **7** may vary from 80% to almost nothing. The problem has been traced to titanium alkoxide catalyzed opening of **7** by X-H (where X-H may be *i*-PrOH, TBHP, allyl alcohol, epoxy alcohol, and perhaps even *tert*-butyl alcohol). The opened products might be useful except that they are formed as a mixture.[10] The use of $Ti(O\text{-}t\text{-}Bu)_4$ instead of $Ti(O\text{-}i\text{-}Pr)_4$ is a partial solution to this problem. The yield of epoxy alcohol **12b** (shown in Scheme I), for example, increases from approximately 15% with $Ti(O\text{-}i\text{-}Pr)_4$ to 51% with $Ti(O\text{-}t\text{-}Bu)_4$. Similar yield improvements have been observed for other allylic alcohols in the 2-alkyl class upon switching from $Ti(O\text{-}i\text{-}Pr)_4$ to $Ti(O\text{-}t\text{-}Bu)_4$.[11]

We reasoned that intentional and selective opening of the epoxy alcohols **7** might serve to rescue these chiral intermediates in a useful form. Halide capture seemed especially desirable and was easily tried by substituting the readily available $TiCl_2(O\text{-}i\text{-}Pr)_2$[12] for $Ti(O\text{-}i\text{-}Pr)_4$ in the standard asymmetric epoxidation process. This approach was successful and our best result to date is outlined in Scheme I. From allylic alcohol **9**[13] a single chloro diol (**10a**) was obtained in 76% yield, and, through the acetate derivative **11**, was found to have an ee of 73%. When the chloro diols (e.g., **10**) are treated with base, they close cleanly to the epoxides (e.g., **12**).[14] Upon correlation of **10a** and **12a** with samples **10b** and **12b** prepared by the standard asymmetric epoxidation procedure (see Scheme I), we again found that the face selection was opposite of normal. This inverse induction suggested that a 2:1-type catalyst might be the effective species in the reaction. When the oxidation of **9** was carried out as before except with a 2:1 $TiCl_2(O\text{-}i\text{-}Pr)_2$: (+)-DET ratio, virtually identical results were observed (73% yield and 68% ee), consistent with the action of a 2:1-type catalyst.[15]

Although epoxides (e.g., **12**) have not been detected in these reactions, we have no evidence to indicate that they should be excluded as likely intermediates. Authentic epoxide **12** reacts rapidly in the $TiCl_2(O\text{-}i\text{-}Pr)_2$–DET system to give the chloro diol **10** in a highly regioselective manner. Interestingly, when DET is excluded and only $TiCl_2(O\text{-}i\text{-}Pr)_2$ is used, the opening reaction is less selective and both regioisomeric chloro diols (i.e., **10** and **13**) are formed.[16]

This chlorohydroxylation process has been applied to six other allylic alcohols including geraniol and various cinnamyl alcohols. Reversed face selection was observed in every case and the enantiomeric excesses ranged from 20% to 68%, the cinnamyl alcohols being among the best substrates (see supplementary material for details).

More work is clearly needed to elucidate the special nature of the 2:1 titanium:tartrate system in the presence of chloride ligands. However, it seems possible that the inverse inductions in the 2:1 systems may require a stronger metal-to-carbonyl-oxygen bond, which could be achieved with a metal of greater Lewis acidity, as in the titanium chloride catalysts, or by virtue of the more basic carbonyl of the tartramide ligands.

We must now ask what happens in the parent asymmetric epoxidation system if a 2:1 catalyst system is em-

(8) Replacing the two *C*-benzyl groups of ligand **5e** with methyl groups gives a ligand (**5f**) that induces only 15% ee (in favor of enantiomer **3b**) under the same conditions as the reaction involving **5e**.

(9) Other epoxy alcohols that are very sensitive to opening in situ include cinnamyl alcohols with electron-donating substituents (e.g., 4-methyoxycinnamyl alcohol) and conjugated dienols (e.g., (*E,E*)-2,4-decadien-1-ol).

(10) The main components of this mixture are usually isopropoxy, *tert*-butylperoxy, or allyloxy diols resulting from epoxide opening by isopropanol, TBHP, and the allylic alcohol, respectively.

(11) Solutions of $Ti(O\text{-}t\text{-}Bu)_4$ and tartrate must be allowed a longer time to reach equilibrium before being used in asymmetric epoxidation reactions (at least 30 min at room temperature), due to the slower nature of alkoxide exchange reactions involving the *tert*-butoxide ligand.

(12) Weingarten, H.; Van Wazer, J. R. *J. Am. Chem. Soc.* **1965**, *87*, 724–730.

(13) We thank Dr. Winston Ho of McNeil Pharmaceutical for a generous sample of methyl 2-methylenehexadecanoate, the precursor to alcohol **9**.

(14) The closure of **10** to **12** proceeds cleanly and rapidly with potassium carbonate in methanol. An alternate procedure, which minimizes exposure of the epoxy alcohol to base (and hence possible Payne rearrangement[19]), was used in the closure of the analogous chloro diols leading to the cinnamyl epoxides. In this procedure, the chloro diol was dissolved in ether and stirred with brine containing NaOH added as pellets to generate an ca. 2 N solution (see supplementary material).

(15) In the recommended procedure, 1.0 equiv of L-(+)-DET is added to 2.0 equiv of $TiCl_2(O\text{-}i\text{-}Pr)_2$ in CH_2Cl_2. The stirred solution is cooled to 0 °C and 1.0 equiv of allylic alcohol **9** is added. After several minutes, ca. 2 equiv of anhydrous TBHP in toluene[2b] is added. The reactions are usually complete within 4 h and are quenched as noted in ref 5. The crude product is purified by chromatography. The enantiomeric excesses are determined by ^1H NMR in benzene-d_6 on the corresponding epoxy acetates (Ac_2O/pyridine) in the presence of $Eu(hfc)_3$.

(16) In the reaction of epoxide **12** with $TiCl_2(O\text{-}i\text{-}Pr)_2$ alone, the chloro diols **10** and **13** are found in a 93:7 ratio. Propylene oxide is opened nonselectively (56:44 1-chloride:2-chloride) with $TiCl_2(OEt)_2$: Choukroun, R. *Inorg. Chim. Acta* **1981**, *58*, 121–122.

ployed. This has been done with (*E*)-α-phenylcinnamyl alcohol, geraniol, and *trans*-2-decen-1-ol. All give normal face selection (i.e., 2*S* with (+)-DET) to the extent of 78, 70, and 65% ee, respectively. We cannot yet explain why the normal enantioselection is preserved to such a high degree in these reactions.

Many questions remain to be answered about these epoxidation catalysts in both the 2:1 and 2:2 systems. Kinetic studies of these processes are under way, and we are increasing our efforts to obtain crystalline derivatives for X-ray structural analysis.

These new 2:1 inverse induction systems are already useful in special cases,[17] and, if the enantioselectivities can be further enhanced, they could become truly valuable additions to the already popular parent asymmetric epoxidation process.

Acknowledgment. This work was supported by grants from the National Institutes of Health (GM28384), Eli Lilly and Company, and Exxon Chemical Company. We also acknowledge the excellent assistance of Mr. Jonathan Ellman in the preparation and characterization of ligand **5e**, as well as the MIT undergraduate research opportunities program for his financial support.

Supplementary Material Available: Results of epoxidations mediated by tartrate amide derivatives and other chiral ligands (45 ligands in all); preparation and properties of ligand **5e**; experimental details of chlorohydroxylation reactions (16 pages). Ordering information is given on any current masthead page.

(17) The chlorohydroxylation system is probably the most useful as it allows asymmetric oxidation of certain sensitive substrates (e.g. **9**, see also ref 8) that are either very poor or fail completely in the standard asymmetric epoxidation process. For research purposes the 2:1 tartramide system is clearly inferior to the standard system because it is less enantioselective. However, in a commercial application it could prove superior to the normal catalyst in cases where the substrate is favorable and the required enantioselection is that based on use of the unnatural tartrate ester in the standard asymmetric epoxidation process.

(18) (a) Martin, V. S.; Woodard, S. S.; Katsuki, T.; Yamada, Y.; Ikeda, M.; Sharpless, K. B. *J. Am. Chem. Soc.* **1981**, *103*, 6237–6240. (b) Katsuki, T.; Sharpless, K. B. *Ibid.* **1980**, *102*, 5974–5976.

(19) Payne, G. B. *J. Org. Chem.* **1962**, *27*, 3819–3822.

(20) On sabbatical leave from The Upjohn Company, Kalamazoo, MI, Sept 1, 1982–Aug 31, 1983.

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Ikarugamycin: Total Synthesis of the Decahydro-*as*-indacene Portion

Summary: An efficient, stereoselective synthesis of octahydro-*as*-indacenone **2**, the carbocycle fragment of the antibiotic ikarugamycin, is described. The prominent step in this sequence is an intramolecular Diels–Alder reaction, which establishes the relative stereochemistry of **2**.

Sir: Ikarugamycin (**1**) was isolated in 1972 by Jomon et al.[1] from a culture broth of *Streptomyces phaeochromogens var. ikarugamycin* Sakai and was fully characterized in 1977 by Ito and Hirata.[2] Its biological properties include strong specific antiprotozoal activity, in vitro antiamoebic activity, and activity against some Gram-positive bacteria.[1] Structurally ikarugamycin is a unique natural product that embodies an enoyltetramic acid containing macrocyclic lactam and a rare *trans-anti-cis*-decahydro-*as*-indacene system.[3] These structural features have recently attracted synthetic investigation.[4]

We have undertaken a synthetic approach to ikarugamycin, which at its focal point relies on the intermediacy of octahydro-*as*-indacenone **2**. Our strategy for the synthesis of **2** is outlined retrosynthetically in Scheme I. Key features in this analysis include (a) efficient access to trienoate **4** by rational manipulation of the terminal functionalities of pentenoic acid **5**, (b) a stereoselective intramolecular Diels–Alder reaction yielding tetrahydroindan **3**, and (c) regioselective ring C annulation. Examination of molecular models for the two diastereomeric endo-Diels–Alder transition states of **4** suggested that the steric demands of the vicinal chiral centers in this trienoate would dictate cycloaddition via the sterically preferred transition state A.[5] Subsequent ring C elaboration was envisaged via routes including a Collman carbonyl insertion sequence (**2a**, X = H) and a homologation/condensation sequence (**2b**, X = SO_2Ar). In this report, we describe an efficient procedure that delivers the crucial carbocyle **2** appropriately disposed for elaboration to ikarugamycin.

Our plan for the synthesis of **2** was conjunctive with the ready availability of intramolecular Diels–Alder precursor **4** from pentenoic acid **5**. Thus, **5**,[6] prepared in 83% yield by ester enolate Claisen rearrangement[7] of (*E*)-crotyl butanoate (LDA, THF, −78 °C; Me_3SiCl; −78 → 40 °C; H_3O^+), was reduced with lithium aluminum hydride to the corresponding alcohol (Scheme II). Parikh-modified[8] Moffatt oxidation followed by immediate condensation of the resulting aldehyde with the lithio salt of methyl 4-(diethylphosphono)crotonate at −40 °C in THF furnished the (*E,E*)-triene ester. Diisobutylaluminum hydride reduction afforded trienol **6**[6] in 49% overall yield from acid **5**. Regioselective hydroboration of the *tert*-butyldimethylsilyl ether of **6** with 9-BBN[9] gave as expected the terminal

(1) Jomon, K.; Kuroda, Y.; Ajsaka, M.; Sakai, H. *J. Antibiot.* **1972**, *25*, 271.

(2) (a) Ito, S.; Hirata, Y. *Bull. Soc. Chem. Jpn.* **1977**, *50*, (a) 227; (b) 1813.

(3) To our knowledge, the only other natural product containing the *trans-anti-cis-as*-hydrindacene system is the related antibiotic capsimycin: Aizawa, S.; Akutsu, H.; Satomi, T.; Nagatsu, T.; Taguchi, R.; Mogami, M.; Komuro, H.; Seino, A. *J. Antibiot.* **1979**, *32*, 193.

(4) (a) Since submission of this manuscript, a stereoselective preparation of a tetracyclic intermediate for ikarugamycin has been reported: Boeckman, R. K., Jr.; Napier, J. J.; Thomas, E. W.; Sato, R. I. *J. Org. Chem.* **1983**, *48*, 4152. (b) Progress toward the *as*-hydrindacene skeleton of ikarugamycin was recently described: Whitesell, J. K.; Minton, M. A.; Fisher, M. "Abstract of Papers", 186th National Meeting of the American Chemical Society, Washington, DC, Aug 1983, American Chemical Society: Washington, DC: 1983; ORGN 300. (c) A preparation of phosphonate-activated 3-acetyltetramic acids has been reported: Boeckman, R. K., Jr.; Thomas, A. J. *J. Org. Chem.* **1982**, *47*, 2823.

(5) For related intramolecular Diels–Alder strategies, see: (a) Roush, W. R.; Meyers, A. G. *J. Org. Chem.* **1981**, *46*, 1509. (b) Nicolaou, K. C.; Magolda, R. L. *Ibid.* **1981**, *46*, 1506.

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