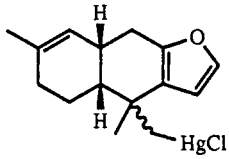
as the eluant to separate the high R_f material containing (-)-**3a**. Chromatography of this fraction on silica (medium-pressure liquid chromatography) afforded 24 mg (10% yield) of colorless spears, which were spectroscopically identical, although opposite in optical rotation, with an authentic sample of natural (+)-furodysinin: $[\alpha]_D$ = -54° (c = 0.5, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.18 (s, 3 H), 1.19 (s, 3 H), 1.32 (overlapping m, 2 H), 1.66 (s, 3 H), 1.54 (bd, 1 H), 2.03 (m, 2 H), 2.29 (m, 1 H), 2.73 (m, 2 H), 5.57 (bs, 1 H), 6.24 (d, J = 2, 1 H), 7.21 (d, J = 2, 1 H); ^{13}C NMR ($CDCl_3$) δ 19.3, 23.1, 26.2, 27.6, 29.7, 31.3, 31.7, 33.9, 44.7, 108.2, 124.7, 126.2, 133.6, 140.5, 147.5; IR (cm^{-1}, KBr pellet) 2962, 2907, 2863, 1634, 1506, 1446, 1361, 1262, 1197, 1130, 1055, 1027, 897, 839, 799, 728; high resolution MS m/z (M^+ - H) calcd for $C_{15}H_{19}O$ 215.1435, found 215.1430.

Organomercurial Intermediate in the 44 → (-)-2a Conversion. This intermediate could be isolated in 14% yield by flash chromatography on silica, eluting with 2:1 hexane/CH_2Cl_2. Conversion of this substance to (-)-**2a** could be accomplished quantitatively by reduction with aqueous basic $NaBH_4$ solution. The organomercurial appears to be a 2:1 mixture of isomers at C1: ^1H NMR ($CDCl_3$) δ 7.22 (br s), 6.26 (br s), 5.61 (m), 2.74



(overlapping m), 2.30 (overlapping m), 2.07 (m), 1.80 (m), 1.67 (s), 1.49 (m), 1.67 (s), 1.49 (m), 1.34 (s), 1.32 (s); ^{13}C NMR ($CDCl_3$) δ 147.6, 141.4, 141.0, 133.8, 133.6, 125.6, 125.5, 124.1, 107.6, 107.5, 53.0, 47.5, 46.4, 38.3, 36.1, 31.7, 31.5, 31.3, 31.1, 29.5, 27.6, 23.1, 19.9, 19.7; IR (neat oil) 3143, 3103, 2964, 2911, 2858, 1629, 1503, 1463, 1443, 1384, 1198, 1131, 1058, 905, 733 cm^{-1}; low resolution mass spectrometry 215 ($C_{15}H_{19}O$, M^+ - HgCl).

Acknowledgment. We wish to acknowledge the support of an Atlantic Richfield grant from Research Corporation We also acknowledge the support of the National Institutes of Health (Biomedical Research Support).

Registry No. (-)-**2a**, 129783-56-8; (-)-**3a**, 98672-90-3; **9**, 464-49-3; **10**, 129594-57-6; **14** (R = Me), 129594-67-8; **14** (R = Et), 129594-68-9; **14** (R = *i*-Pr), 129594-70-3; **14** (R = *t*-Bu), 129618-70-8; **14** (R = Ph), 60300-67-6; **14** (R = $PhCH_2$), 129594-74-7; **14** (R = 2-furyl), 129594-58-7; **15** (R = Me), 129704-48-9; **15** (R = Et), 129594-69-0; **15** (R = *i*-Pr), 129594-71-4; **15** (R = *t*-Bu), 129594-72-5; **15** (R = Ph), 129594-73-6; **15** (R = $PhCH_2$), 129594-75-8; **15** (R = 2-furyl), 129594-59-8; **18**, 10293-09-1; **20**, 5989-27-5; **21**, 129704-41-2; **22**, 129594-60-1; **23**, 129594-61-2; **24**, 129704-42-3; **25**, 129704-43-4; **26**, 129704-44-5; **27**, 129704-44-5; **28**, 28974-17-6; **29a**, 129704-46-7; **30a**, 20347-65-3; **30b**, 464-43-7; **30** (R = Ms), 129704-47-8; **31**, 122763-76-2; **32**, 122763-77-3; *endo*-**32**, 129594-78-1; **32** alcohol, 122763-80-8; *endo*-**32** alcohol, 129594-76-9; **33**, 122763-78-4; **34**, 122763-79-5; **35**, 129594-62-3; **36** (isomer 1), 129594-63-4; **36** (isomer 2), 129594-79-2; **42**, 129594-64-5; *endo*-**42**, 129594-77-0; **43**, 129594-65-6; **44**, 129594-65-6; MeCHO, 75-07-0; EtCHO, 123-38-6; *i*-PrCHO, 78-84-2; *t*-BuCHO, 630-19-3; PhCHO, 100-52-7; $PhCH_2CHO$, 122-78-1; 2-furaldehyde, 98-01-1; (+)-*endo*-3-bromocamphor, 10293-06-8; (+)-*endo*-3,9-dibromocamphor, 10293-10-4; 3-furaldehyde, 498-60-2.

Supplementary Material Available: Proton and ^{13}C spectral data on all synthetic intermediates (34 pages). Ordering information is given on any current masthead page.

On the Diastereofacial Selectivity of Lewis Acid Catalyzed Carbon–Carbon Bond Forming Reactions of Conjugated Cyclic Enones Bearing Electron-Withdrawing Substituents at the γ-Position

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Lewis acid catalyzed reactions of several cyclic enones are described. The γ-OTBS enones **1** and **2** give products where carbon–carbon bond formation at the β carbon occurs with high stereoselectivity favoring attack syn to the resident OTBS group. In the case of enone **24** bearing an additional dioxolane ring, the products correspond to addition anti to the resident carbon–oxygen bond at the γ carbon. The reaction of **24** with lithium dimethylcuprate also occurs in an anti sense. The starting materials in this study are available in quantity in optically pure form. Given the excellent stereoselectivity of the reactions, these compounds are useful intermediates for synthesis.

Introduction

Recently we had occasion to study Lewis acid catalyzed Michael-type addition reactions of silyl ketene acetals to the γ-OTBS cyclenones **1**[1] and **2**.[2] In each instance, carbon–carbon bond formation was accompanied by group transfer of the silyl function.[3,4] The resultant silyl enol ethers, reacted with suitable aldehydes in highly stereoselective reactions to produce products that lent themselves to conversion to prostaglandin $F_{2\alpha}$[1,5] and compactin,[2,6] respectively (Scheme I).

(1) Danishefsky, S. J.; Cabal, M. P.; Chow, K. *J. Am. Chem. Soc.* **1989**, *111*, 3456.
(2) Danishefsky, S. J.; Simoneau, B. *J. Am. Chem. Soc.* **1989**, *111*, 2599.
(3) Webster, O. W.; Hertler, W. R.; Sogah, D. Y.; Farnham, W. B.; Rajan Babu, T. J. *J. Am. Chem. Soc.* **1983**, *105*, 5706.
(4) Kobayashi, S.; Mukaiyama, T. *Chem. Lett.* **1986**, 1805.
(5) See also: Chow, K.; Danishefsky, S. J. *J. Org. Chem.* **1989**, *54*, 6016.
(6) Danishefsky, S. J.; Simoneau, B. *Pure Appl. Chem.* **1988**, *60*, 1155.

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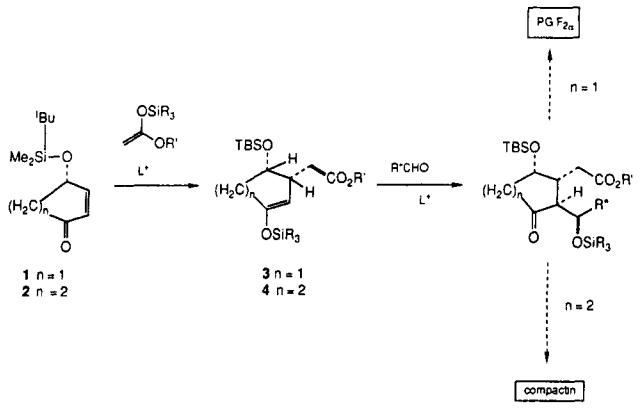
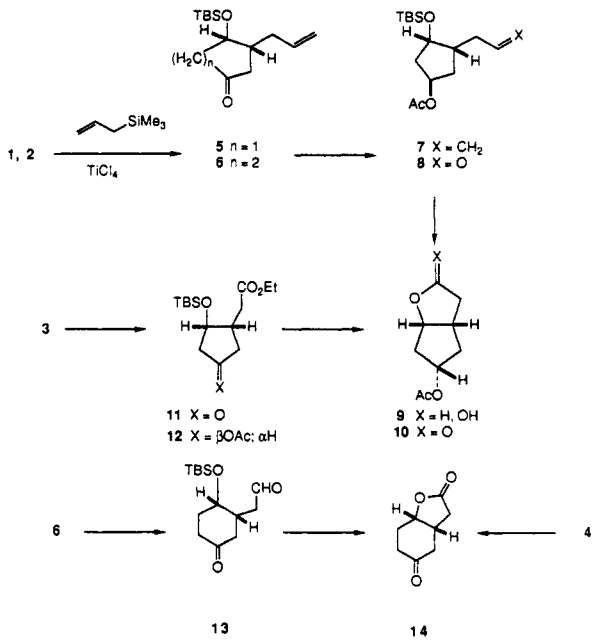
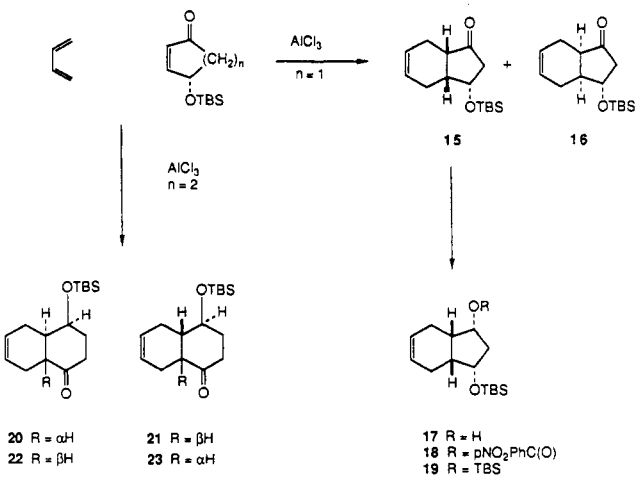
Scheme I



Scheme II



Scheme III



The antipode shown as compound **1** was generated via a simple route, which started with the enantiotopically specific monohydrolysis of *cis*-1,4-diacetoxycyclopentene.[7,8] Compound **2**, in the absolute configuration shown, was obtained via quinic acid.[9,10] While the optically homogeneous versions of **1** and **2** are readily obtained, racemic compounds were used in this study. Compound **24**, used later in this investigation, was employed as a homogeneous enantiomer in the configuration shown.

Of great interest to us was the face selectivity in the original addition step. Surprisingly, in each case the Michael-type reactions had occurred syn to the resident OTBS group with selectivity margins of >15:1. These results, in of themselves surprising, at first glance, also stand in striking contrast to the anti delivery of carbon ligands in 1,4-addition reactions of the same enones with various organometallic species. In the case of **1**, such anti delivery has been the basis of many earlier prostaglandin syntheses.[11] Similarly, anti attachment of a methyl group from lithium dimethylcuprate to **2** was demonstrated in our laboratory in an early route to FK-506.[12]

Discussion of Results

Naturally we wondered whether the particular syn directivity encountered in the formation of **3** and **4** arose from the Lewis acid catalyzed nature of the reaction.[13] Accordingly we examined the feasibility and steric sense of Sakurai[14] reactions of compounds **1** and **2**. In the event, addition of allyltrimethylsilane to these enones under catalysis by titanium tetrachloride afforded **5** (54%) and **6** (74%), respectively. Though the yields are far from quantitative, these reactions must have been highly stereoselective since no other products were identified that were chromatographically similar to **5** or **6**.

The cis relationships shown in these products were verified by chemical correlation with **3** and **4**, respectively. Thus, upon reduction (L-Selectride) and acetylation, **5** afforded **7** (Scheme II). The latter was subjected to ozonolysis followed by reductive processing of the ozonide with dimethyl sulfide. Aldehyde **8** thus generated in 80% yield, upon desilylation, afforded bicyclic hemiacetal **9** (72%), which, upon Jones oxidation, gave rise to acetoxy lactone **10** in 57% yield.

The same lactone was elaborated from **3**. De-silylation (aqueous acetic acid), affording ketone **11**, was followed by reduction (L-Selectride) and acetylation, providing an 80% yield of **12**. Treatment of **12** with TBAF afforded a 75% yield of the same lactone, **10**.

By much the same methodology, compounds **6** and **4** were correlated. Thus **6** was converted to aldehyde **13** ((i) OsO_4, (ii) $Pb(OAc)_4$), which, after desilylation and Jones oxidation, provided keto lactone **14**. The same compound had been obtained in 79% yield by treatment of **4** with HF in acetonitrile.

Having demonstrated high syn selectivity in the Sakurai reaction, we examined Lewis acid catalyzed Diels–Alder reactions.[15] Reaction of compound **1** with 1,3-butadiene

(7) Deardorf, D. R.; Myles, D. C.; MacFerren, K. D. *Tetrahedron Lett.* **1985**, *26*, 5615. Deardorf, D. R.; Matthews, A. J.; McMeekin, D. S.; Craney, C. L. *J. Org. Chem.* **1988**, *53*, 3614.

(8) Johnson, C. R.; Penning, T. D. *J. Am. Chem. Soc.* **1984**, *106*, 5655.

(9) Trost, B. M.; Romero, A. G. *J. Org. Chem.* **1986**, *51*, 2332.

(10) Audia, J. E.; Boisvert, L.; Patten, A. D.; Villalobos, A. *J. Org. Chem.* **1989**, *54*, 3738.

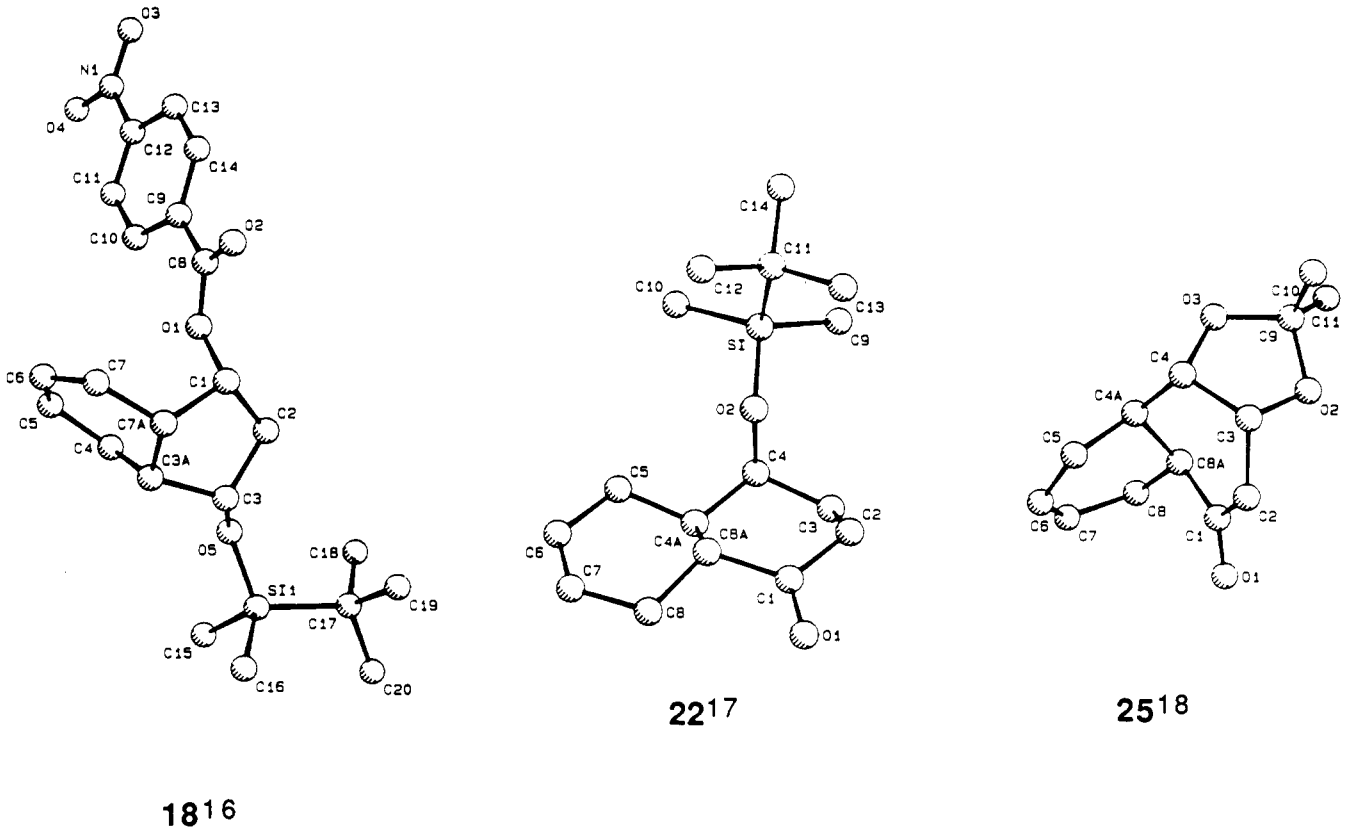
(11) See: Morita, Y.; Suzuki, M.; Noyori, R. *J. Org. Chem.* **1989**, *54*, 1987 and references therein.

(12) Jones, A. B.; Yamaguchi, M.; Patten, A.; Danishefsky, S. J., Ragan, J. A.; Smith, D. B., Schreiber, S. L. *J. Org. Chem.* **1989**, *54*, 17.

(13) For previous instances of high face selectivity in Lewis acid catalyzed carbon–carbon construction, see: (a) Danishefsky, S. J.; Kato, N.; Askin, A.; Kerwin, J. F. *J. Am. Chem. Soc.* **1982**, *104*, 360. (b) Heathcock, C. H.; Flippin, L. A. *J. Am. Chem. Soc.* **1983**, *105*, 1667. (c) Heathcock, C. H.; Davidson, S. K.; Hug, K. T.; Flippin, L. A. *J. Org. Chem.* **1986**, *51*, 3027.

(14) (a) Sakurai, H. *Pure Appl. Chem.* **1982**, 54. (b) Hosomi, A.; Sakurai, H. *J. Am. Chem. Soc.* **1977**, *99*, 1673.

(15) (a) Yates, P.; Eaton, P. *J. Am. Chem. Soc.* **1960**, *82*, 4436. (b) Fringuelli, F.; Pizzo, F.; Taticchi, A.; Halls, T. D. J.; Wenkert, E. *J. Org. Chem.* **1982**, *47*, 5056.



18[16] 22[17] 25[18]

Figure 1. Pluto plots for compounds 18, 22, and 25.

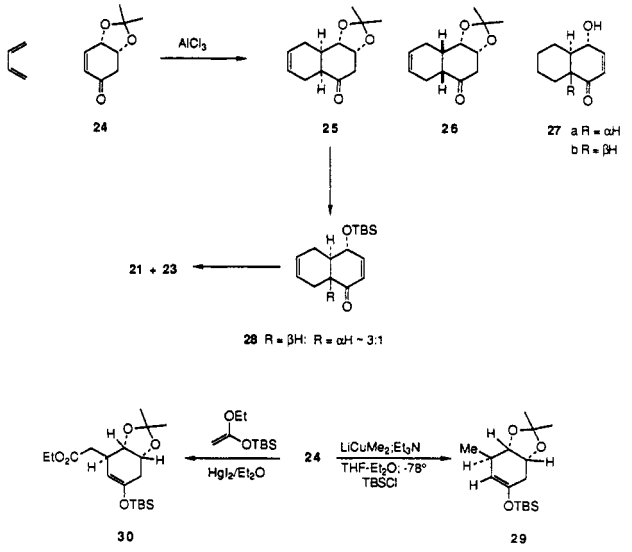
in toluene at room temperature in the presence of aluminum chloride afforded, as the principal product adduct, **15**. In addition there was obtained, in 4% yield, a minor isomer provisionally formulated as **16**. Reaction of **15** with L-Selectride afforded a 90% yield of **17**, contaminated by ca. 5% of the epimeric β-hydroxy compound (not shown here). Characterization of **17** was best achieved as its *p*-nitrobenzoate derivative **18** (Figure 1). The stereochemistry assigned to **18** was corroborated by a single-crystal determination.[16] Silylation of **17** (TBSCl, DBU) afforded the bis-silyl derivative **19**, whose symmetry was well reflected in its ^{13}C NMR spectrum.

Reaction of 1,3-butadiene with **2** under similar conditions in toluene for 1 h afforded a 76% yield of **20** (Scheme III). In addition, there was obtained a 6% yield of the other cis-fused isomer **21** and traces of another product. This latter compound is the principal product (40%) when the aluminum chloride catalyzed Diels–Alder reaction is carried out at 40 °C in toluene for 4 h. These conditions apparently favor epimerization of an initially formed cis-fused adduct. This product was shown to be **22** by an X-ray crystallographic determination.[17] In a separate experiment **20** was converted to **22** via treatment with sodium methoxide. In a similar vein, **21** suffered epimerization to **23** under the same conditions. These exper-

(16) A suitable crystal (0.25 mm × 0.20 mm × 0.06 mm) of compound **18** was selected and mounted in a random orientation in a glass capillary. Diffraction measurements were made on a Rigaku AFC5S fully automated diffractometer using graphite-monochromated Cu Kα (λ = 1.54178 Å). The cell parameters were obtained from 10 carefully centered reflections in the range of $21.84 \leq 2\theta \leq 41.57°$, which corresponded to a monoclinic cell with dimensions a = 23.746 (4) Å, b = 7.591 (1) Å, c = 12.442 (4) Å, and β = 95.98 (2)°. On the basis of systematic absences, packing considerations, a statistical analysis of intensity distribution, and the successful solution and refinement of the structure, the space group was determined to be $P2_1/c$ (No. 14), Z = 4, with one molecule of $C_{22}H_{31}O_5NSi$ forming the asymmetric unit. The volume was 2230 (2) Å^3 and the calculated density was 1.243 g/cm^3. There were 3298 unique reflections collected with $2\theta \leq 114°$; of those reflections, 1233 (37%) with $I \geq 3(\sigma)I$ were adjudged observed. The structure was solved by using a combination of MITHRIL and DIRDIF programs. Nineteen out of twenty-five hydrogens were located in a difference Fourier calculation; the rest were calculated and located at their idealized positions and included in the refinement with isotropic thermal parameters that were 20% greater than the equivalent value of the atom to which they were bonded. The hydrogen positions were not refined. The final cycle of full-matrix least-squares refinement was based on 1233 observed reflections $I \geq 3(\sigma I)$ and 262 variable parameters. The refinement has converged with the following conventional crystallographic values: R = 0.059 and R_w = 0.070. All calculations were performed by using TEXSAN: Single Crystal Analysis Software, Version 5.0 (1989), a crystallographic software package developed by Molecular Structure Corporation, Woodlands, TX, 77381. Tables containing fractional coordinates, temperature factors, bond distances, torsional angles, and anisotropic temperature factors for compound **18** are available as supplementary material.

(17) A suitable crystal (0.45 mm × 0.30 mm × 0.25 mm) of compound **22** was selected and mounted in a random orientation in a glass capillary. Diffraction measurements were made on a Rigaku AFC5S fully automated diffractometer using graphite-monochromated Cu Kα (λ = 1.54178 Å). The cell parameters were obtained from 25 carefully centered reflections in the range of $83.66 \leq 2\theta \leq 99.09°$, which corresponded to a triclinic cell with dimensions a = 9.9293 (6) Å, b = 12.717 (1) Å, c = 6.8968 (5) Å, and α = 94.512 (6)°, β = 91.448 (6)°, γ = 101.906 (6)°. On the basis of packing considerations, a statistical analysis of intensity distribution, and the successful solution and refinement of the structure, the space group was determined to be $P1$ (No. 2), Z = 2, with one molecule of $C_{16}H_{28}O_2Si$ forming the asymmetric unit. The volume was 848.7 (1) Å^3 and the calculated density was 1.097 g/cm^3. There were 2526 unique reflections collected with $2\theta \leq 120°$; of those reflections, 2109 (83%) with $I \geq 3(\sigma)I$ were adjudged observed. The structure was solved by using the VERY HARD option in MITHRIL. The hydrogens were located in two successive difference Fourier syntheses and included in the refinement with isotropic thermal parameters, which were 20% greater than the equivalent value of the atom to which they were bonded. The hydrogen positions were not refined. The final cycle of full-matrix least-squares refinement was based on 2109 observed reflections $I \geq 3(\sigma I)$ and 172 variable parameters. The refinement has converged with the following conventional crystallographic values: R = 0.044 and R_w = 0.069. All calculations were performed by using TEXSAN: Single Crystal Structure Analysis Software, Version 5.0 (1989), a crystallographic software package developed by Molecular Structure Corporation, Woodlands, TX 77381. Tables containing fractional coordinates, temperature factors, bond distances, torsional angles and anisotropic temperature factors for compound **22** are available as supplementary material.

Scheme IV



iments provide support for the assignment of structure **20** and suggest the relationship between **21** and **23** to be as shown. These latter assignments are further supported by the sequence that started with compound **24** (vide infra).

Thus six Lewis acid catalyzed reactions of compounds **1** and **2** resulting in carbon–carbon bond formation at the β-carbon occur with high stereoselectivity syn to the resident OTBS groups at the γ-carbon. It was of interest to probe the applicability of this effect to a system that might be expected to manifest a greater steric constraint against syn addition. Toward that end, we studied the aluminum chloride catalyzed Diels–Alder reaction of substrate **24** (of the absolute configuration shown). This compound had been an intermediate in the synthesis of the optically pure (4*S*) enantiomer of **2**.[10] Treatment of **24** with 1,3-butadiene in toluene at room temperature in the presence of aluminum chloride afforded a 16:1 mixture of 1:1 adducts (Scheme IV). The structure of the major adduct (67%) was shown by an X-ray crystallographic determination to be **25**.[18] The minor Diels–Alder product **26** was isolated in 4% yield. In addition, a third product (13%) was isolated as a 12:1 mixture of cis:trans junction isomers (**27a,b**). System **27** now as a 3:1 mixture of cis:trans junction isomers was generated more efficiently from the reaction of **25** with lithium diisopropylamide.

Treatment of **25** with *tert*-butyldimethylsilyl chloride in the presence of DBU afforded system **28** as a 3:1 mixture of trans:cis junction stereoisomers. Conjugate reduction of the enone linkage was achieved with sodium dithionite in the presence of Aliquat 336,[19] thus giving rise to the optically pure versions of the previously encountered compounds **21** and **23** as a 1:6 mixture. This sequence serves to correlate the stereochemistry of **21** (and **23**) with the rigorously determined **25**.

Thus, it has been demonstrated that with **24**, even in a Lewis acid catalyzed Diels–Alder reaction, anti addition is favored over the syn mode. In this case syn addition would have corresponded to an attack from the hindered concave face of the bicyclic system. We explored other conjugate additions leading to β-bond forming reactions with **24**. Reaction of **24** with lithium dimethylcuprate and concurrent silylative trapping[20] afforded a 72% yield of a product formulated as **29**. Similarly, group transfer addition of 1-ethoxy-1-[(*tert*-butyldimethylsilyl)oxy]ethene (HgI_2–ether) afforded an 89% yield of adduct **30**. The ^1H NMR multiplicities and couplings of the vinylic and dioxolane bound hydrogens in the two compounds are virtually identical, suggesting that in this instance, unlike the situation with compounds **1** and **2**, the Lewis acid catalyzed ketene acetal group transfer reaction[3,4] occurred in the same (anti) sense as did the cuprate addition.

We conclude with a proposal to explain the remarkable syn selectivity in the three Lewis acid catalyzed reactions resulting in C–C bond formation at the β carbon of enones **1** and **2**. Precedents from similar reactions under Lewis acid catalysis with alkyl substituents at the γ carbon do not indicate a trend toward syn additions.[21] In these cases the reactions exhibit either the expected anti addition or are not particularly selective. Moreover, non Lewis acid mediated nucleophilic additions to the same γ-OTBS substrates in fact occur with the expected anti selectivity.[11,12] Hence the powerful syn effect seems to require the confluence of Lewis acid catalysis and an electron-withdrawing γ-function, and even with these conditions generalization to other systems may not be appropriate.[22,23]

Mindful of the elegant formulations of Cieplak,[24] we

(18) A suitable crystal (0.42 mm × 0.25 mm × 0.20 mm) of compound **25** was selected and mounted in a random orientation in a glass capillary. Diffraction measurements were made on a Rigaku AFC5S fully automated diffractometer using graphite-monochromated Cu Kα (λ = 1.54178 Å). The cell parameters were obtained from 25 carefully centered reflections in the range of $22.86 \leq 2\theta \leq 52.19°$, which corresponded to an orthorhombic cell with dimensions a = 9.832 (1) Å, b = 19.060 (2) Å, c = 6.4617 (5) Å, and $\alpha = \beta = \gamma = 90.0°$. On the basis of systematic absences, packing considerations, a statistical analysis of intensity distribution, and the successful solution and refinement of the structure, the space group was determined to be $P2_12_12_1$ (No. 19), Z = 4, with one molecule of $C_{13}H_{18}O_3$ forming the asymmetric unit. The volume was 1210.9 (2) Å^3 and the calculated density was 1.219 g/cm^3. There were 1097 unique reflections collected with $2\theta \leq 120°$; of those reflections, 685 (63%) with $I \geq 3(\sigma)I$ were adjudged observed. The structure was solved by using a combination of MITHRIL and DIRDIF programs. Thirteen out of eighteen hydrogens were located in a difference Fourier calculation, the rest were calculated and located at their idealized positions and included in the refinement with isotropic thermal parameters, which were 29% greater than the equivalent value of the atom to which they were bonded. The hydrogen positions were not refined. The final cycle of full-matrix least-squares refinement was based on 685 observed reflections $I \geq 3(\sigma I)$ and 145 variable parameters. The refinement has converged with the following conventional crystallographic values: R = 0.063 and R_w = 0.077. All calculations were performed by using TEXSAN: Single Crystal Structure Analysis Software, Version 5.0 (1989), a crystallographic software package developed by Molecular Structure Corporation, Woodlands, TX 77381. Tables containing fractional coordinates, temperature factors, bond distances, torsional angles, and anisotropic temperature factors for compound **25** are available as supplementary material.

(19) Cf. (a) Louis-Andre, O.; Gelbard, G. *Tetrahedron Lett.* **1985**, *26*, 831. (b) Camps, F.; Coll, J.; Guitart, J. *Tetrahedron* **1986**, *42*, 4603.

(20) Cf. (a) Corey, E. J.; Boaz, N. W. *Tetrahedron Lett.* **1985**, *26*, 6015. (b) Corey, E. J.; Boaz, N. W. *Tetrahedron Lett.* **1985**, *26*, 6019.

(21) For face selectivity of Lewis acid catalyzed reactions of 4-alkylcyclohexenones, see: (a) Blumenkopf, T. A.; Heathcock, C. H. *J. Am. Chem. Soc.* **1983**, *105*, 234. (b) Fringuelli, F.; Pizzo, F.; Taticchi, A.; Ferreira, V. F.; Michelotti, E. L.; Porter, B.; Wenkert, E. *J. Org. Chem.* **1985**, *50*, 890. (c) Angill, E. C.; Fringuelli, F.; Halls, T. D. J.; Pizzo, F.; Porter, B.; Taticchi, A.; Tourris, A. P.; Wenkert, E. *Ibid.* **1985**, *50*, 4691.

(22) It should be noted that the results described here are different from those observed by Wenkert and co-workers[23] in the case of Lewis acid catalyzed Diels–Alder reaction of 3-methyl-4 substituted-cyclohexenones. In the Wenkert case, only marginal selectivity is observed for the 4-alkyl and 4-acetoxy substituents and their behavior is virtually identical. Whether the variation arises as a consequence of the 3-alkyl group or derives from different effects of an acetoxy vs an OTBS group remains to be determined. We note that the results in our case are the same for cyclopentenones and cyclohexenones. Thus we prefer interpretations that do not rely on the particular conformation of either ring system. The proposal offered here accounts for the cases that we have studied. However, attempts to generalize it to other systems are not appropriate till more data are available.

(23) (a) Angell, E. C.; Fringuelli, F.; Pizzo, F.; Porter, B.; Taticchi, A.; Wenkert, E. *J. Org. Chem.* **1986**, *51*, 2642. (b) Angell, E. C.; Fringuelli, F.; Minuti, L.; Pizzo, F.; Porter, B.; Taticchi, A.; Wenkert, E. *J. Org. Chem.* **1989**, *54*, 1217.

(24) Cieplak, A. S. *J. Am. Chem. Soc.* **1981**, *103*, 4540.

hypothesize that in Lewis acid catalyzed processes, the importance of stabilizing the emerging σ^* orbital at the β carbon by interaction with the σ bonds of the γ carbon becomes particularly critical. Carbon–carbon bond formation syn to the electron-withdrawing resident OR group places the emerging σ^* orbital syn to the σ CH bond at the γ carbon. In the alternate sense of attack, where nucleophile would attack anti to the OR group, a less favorable and possibly destabilizing syn interaction between the emerging σ^* orbital at the β carbon and the electron σ C-OR function at the γ carbon would be engendered. Therefore, syn face addition is favored. The nonextendability of this effect to the case of compound **24** might reflect the dominance of a massive steric effect favoring anti attack. Alternatively, the bicyclic system of **24** might carry with it conformational restrictions on the nature of the interaction between the emerging σ^* at C_β and the σ bonds of the resident groups at the γ carbon.

While the theoretical basis of the effects remains to be explicated in greater detail, the availability of stereoselective reactions on significantly functionalized enones that are available in enantiomerically pure form will be valuable for purposes of synthesis.

Experimental Section

General Procedure for the Allyltrimethylsilane Conjugate Additions. (3*SR*,4*RS*)-4-Allyl-3-(*tert*-butyldimethylsiloxy)cyclopentanone (5). A well-stirred solution of the cyclopentenone **1** (0.22 g, 1.03 mmol) in dry CH_2Cl_2 (8 mL) was cooled to −78 °C. Titanium tetrachloride (0.12 mL, 1.03 mmol) was added in one portion via syringe. After 5 min, a solution of allyltrimethylsilane (0.196 mL, 1.26 mmol) in 1 mL of CH_2Cl_2 was added dropwise over a 5-min period. The dark purple mixture was stirred an additional 70 min, and 5 mL of saturated aqueous $NaHCO_3$ was then added over a 5-min period. The reaction mixture was allowed to warm to room temperature, during which time it became colorless. Water (30 mL) was added and the mixture was extracted with Et_2O (5 × 50 mL). The organic solution was washed with brine (2 × 25 mL) and dried ($MgSO_4$). Removal of the solvent gave an oil (0.25 g), which was flash chromatographed using hexanes–ethyl acetate (10:1) as eluent to give 0.142 g (53.8%) of **5** as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.82 (dddd, 1 H, J = 17.0, 10.2, 6.5, 6.5 Hz), 5.08 (dd, 1 H, J = 17.0, 1.2 Hz), 5.03 (dt, 1 H, J = 10.2, 1.2 Hz), 4.43 (m, 1 H, $W_{1/2} \approx$ 8 Hz), 2.40–2.09 (m, 7 H), 0.88 (s, 9 H), 0.099 and 0.055 (2s, 2 × 3 H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 216.8, 136.4, 115.7, 71.2, 49.0, 42.7, 40.7, 33.8, 25.5, 17.8, −4.7, −5.2; IR ($CHCl_3$) 2955, 2929, 2899, 2857, 1743, 1470, 1268, 1261, 1255, 1157, 1112, 1040, 910, 832, 746, 722 cm^{-1}; EIMS (20 eV) m/z (relative intensity) 254 (0.5), 239 (37), 212 (2), 200 (23), 198 (28), 197 (100), 187 (3), 179 (10), 167 (5), 155 (34), 153 (15), 143 (30), 131 (10), 129 (10), 115 (28), 105 (28), 101 (15), 75 (43); CIHRMS calcd for $C_{14}H_{27}O_2Si$ (M + H) 255.1781, found 255.1791. Anal. Calcd for $C_{14}H_{26}O_2Si$: 66.09; H, 10.30. Found: C, 66.17; H, 10.16.

(3*RS*,4*SR*)-3-Allyl-4-(*tert*-butyldimethylsiloxy)cyclohexanone (6). The procedure used for the preparation of **5** was followed. The reaction was performed with 0.68 g (3.0 mmol) of the cyclohexenone **2**, 0.39 mL (3.55 mmol) of titanium tetrachloride, and 0.73 mL (4.56 mmol) of allyltrimethylsilane in 30 mL of CH_2Cl_2. The crude product (0.79 g) was purified by flash chromatography using hexanes–ethyl acetate (10:1) as eluent to afford 0.602 g (74.7%) of **6** as a colorless oil: ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.77–5.69 (m, 1 H), 5.07–5.02 (m, 2 H), 4.85 (bs, 1 H), 2.66 (td, 1 H, $J \approx$ 13.7, 6.5 Hz), 2.47 (t, 1 H, J = 13.5 Hz), 2.29–2.18 (m, 3 H), 2.07 (dddd, 1 H, J = 13.7, 6.5, 3.3, 3.3 Hz) 1.99 (ddd, 1 H, J = 14.3, 7.2, 7.2 Hz), 1.86 (m, $W_{1/2} \approx$ 25 Hz), 1.77 (tdd, 1 H, J = 13.7, 4.7, 1.8 Hz), 0.94 (s, 9 H), 0.11 (s, 6 H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 211.3, 136.0, 116.5, 67.7, 43.6, 42.1, 36.9, 35.7, 33.0, 25.8, 18.1, −4.3, −4.9; IR ($CHCl_3$) 2955, 2929, 2886, 2849, 1716, 1634, 1470, 1456, 1441, 1418, 1366, 1254, 1090, 1053, 778 cm^{-1}; EIMS (20 eV) m/z (relative intensity) 268 (0.1), 253 (0.1), 211 (100), 169 (9), 157 (12), 141 (4), 131 (4), 129 (43), 119 (22), 115 (17), 91 (17), 75 (50); CIHRMS calcd for $C_{15}H_{29}O_2Si$ (M + H) 269.1938, found 269.1948. Anal. Calcd for $C_{15}H_{28}O_2Si$: C, 67.11; H, 10.51. Found: C, 67.08; H, 10.31.

General Procedure for the Diels–Alder Reactions of the Enones 1, 2, and 24 with 1,3-Butadiene. (3*SR*,3a*RS*,7a*SR*)-3-(*tert*-Butyldimethylsiloxy)-2,3,3a,4,7,7a-hexahydro-1*H*-inden-1-one (15) and (3*SR*,3a*SR*,7a*RS*)-3-(*tert*-Butyldimethylsiloxy)-2,3,3a,4,7,7a-hexahydro-1*H*-inden-1-one (16). A solution of the cyclopentenone **1** (1.52 g, 7.15 mmol) in toluene (20 mL) was slowly added to a suspension of $AlCl_3$ (0.88 g, 6.6 mmol, 0.92 equiv) in toluene (35 mL) at room temperature under nitrogen. After stirring at room temperature for ca. 40 min, a solution of 1,3-butadiene (10 mL) in toluene (30 mL) was added via a cannula. The resulting solution was stirred at room temperature for 1 h or until TLC indicated complete consumption of the enone. The reaction mixture was poured into ice-saturated aqueous $NaHCO_3$ (200 mL). The layers were separated and the aqueous mixture was extracted with Et_2O (3 × 100 mL). The combined organic layer was washed with saturated aqueous $NaHCO_3$ (1 × 80 mL) and brine (1 × 100 mL), dried over $MgSO_4$, and concentrated to give a yellow oil (1.63 g). ^{1}H NMR analysis of this product showed a ca. 13:1 ratio of **15**/**16**. Flash chromatography eluting with hexanes–ethyl acetate (19:1) afforded 0.082 g (4.3%) of the less polar isomer **16** and 1.36 g (71.4%) of the more polar isomer **15**.

Compound 15: colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.73–5.69 (m, 1 H), 5.66–5.62 (m, 1 H), 4.52 (ddd, 1 H, J = 7.5, 7.5, 5.6 Hz), 2.58–2.48 (m, 3 H, one of the H is a dd centered at δ 2.53, J = 19.0, 7.5 Hz), 2.38 (td, 1 H, J = 7.6, 2.5 Hz), 2.22 (dd, 1 H, J = 19.0, 7.5 Hz), 2.18–2.11 (m, 2 H), 1.95–1.88 (m, 1 H), 0.90 (s, 9 H), 0.098 and 0.077 (2s, 2 × 3 H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 215.5, 125.5, 124.9, 70.6, 47.1, 43.6, 37.9, 25.7, 21.3, 20.5, 18.0, −4.8; IR ($CHCl_3$) 2970, 2940, 2900, 2870, 1740, 1255, 1140, 1110, 840 cm^{-1}, EIMS (20 eV) m/z (relative intensity) 209 (100), 191 (3), 179 (2), 155 (8), 143 (7), 131 (4), 117 (5), 105 (3), 101 (3), 75 (5); CIHRMS calcd for $C_{15}H_{27}O_2Si$ (M + H) 267.1781, found 267.1794. Anal. Calcd for $C_{15}H_{26}O_2Si$: C, 67.62; H, 9.83. Found: C, 67.76; H, 10.01.

Compound 16: colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.68–5.60 (m, 2 H), 4.19 (ddd, 1 H, $J \approx$ 5.8, 2.6, 2.6 Hz), 2.81 (td, 1 H, J = 7.5, 1.7 Hz), 2.48 (dd, 1 H, J = 19.0, 5.8 Hz), 2.43–2.39 (m, 2 H), 2.24–2.16 (m, 3 H), 1.55 (dddd, 1 H, $J \approx$ 18.0, 8.9, 3.0, 3.0 Hz), 0.89 (s, 9 H), 0.095 and 0.077 (2s, 2 × 3 H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 217.7, 125.7, 124.4, 72.2, 44.6, 43.5, 41.1, 25.7, 23.7, 21.0, 18.0, −4.8; IR ($CHCl_3$) 3010, 2950, 2930, 2890, 2850, 1740, 1260, 1120, 1080, 845 cm^{-1}; EIMS (20 eV) m/z (relative intensity) 209 (100), 191 (5), 185 (4), 181 (4), 179 (4), 165 (13), 155 (17), 143 (11), 131 (10), 129 (6), 117 (10), 105 (6), 101 (7), 89 (3), 75 (14); CIHRMS calcd for $C_{15}H_{27}O_2Si$ (M + H) 267.1781, found 267.1798. Anal. Calcd for $C_{15}H_{26}O_2Si$: C, 67.62; H, 9.83. Found: C, 67.83; H, 9.89.

(4*SR*,4a*RS*,8a*SR*)-4-(*tert*-Butyldimethylsiloxy)-3,4,4a,5,8,8a-hexahydro-1(2*H*)-naphthalenone (20), (4*SR*,4a*SR*,8a*RS*)-4-(*tert*-Butyldimethylsiloxy)-3,4,4a,5,8,8a-hexahydro-1(2*H*)-naphthalenone (21), and (4*SR*,4a*RS*,8a*RS*)-4-(*tert*-Butyldimethylsiloxy)-3,4,4a,5,8,8a-hexahydro-1(2*H*)-naphthalenone (22). The general procedure was followed, using 0.728 g (3.21 mmol) of the cyclohexenone **2** dissolved in 85 mL of toluene, 0.40 g (3.0 mmol) of $AlCl_3$ in 16 mL of toluene, and 5 mL of 1,3-butadiene in 12 mL of toluene). After workup, a yellow oil was obtained (0.95 g). ^{1}H NMR analysis showed the presence of a 10:1 ratio of **20**/(**21** + **22**). The crude mixture was purified by chromatography using hexanes–ethyl acetate (10:1) as eluent. First to elute was **21** (0.069 g, 7.65%) contaminated with ca. 15% of **22**, followed by pure **20** (0.689 g, 76.3%). Careful chromatography of the mixture of **21** and **22** using hexanes–ethyl acetate (19:1) as eluent gave first pure **22** (0.008 g, 0.9%) and **21** (0.052 g, 5.8%) (ca. 95% pure).

Compound 20: isolated as a colorless oil, which solidified on standing in the freezer, mp 33–34 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.67–5.61 (m, 2 H), 4.31 (ddd, 1 H, J = 10.0, 5.0, 5.0 Hz), (2.76 app t, 1 H, J = 5.5 Hz), 2.57 (dm, 1 H, $J \approx$ 17.8 Hz), 2.43 (dddd, 1 H, J = 10.0, 5.0, 5.0, 5.0 Hz), 2.37–2.34 (m, 2 H), 2.17 (~dt, 1 H, $J \approx$ 17.8, 5.0 Hz), 2.08–1.93 (m, 3 H), 1.83 (m, 1 H, $J \approx$ 17.8, 10.0 Hz), 0.90 (s, 9 H), 0.10 (s, 6 H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 209.9, 124.7, 71.2, 45.7, 41.5, 37.7, 30.9, 25.7, 23.7, 21.4, 17.9, −4.8, −4.9; IR ($CHCl_3$) 2995, 2967, 2935, 2895, 1735, 1490, 1485, 1445,

1380, 1275, 1130, 1080, 875, 865 cm^{-1}; EIMS (20 eV) m/z (relative intensity) 280 (1), 265 (2), 223 (100), 205 (8), 149 (2), 131 (78), 129 (22), 105 (11); EIHRMS calcd for $C_{16}H_{28}O_2Si$ 280.1858, found 280.1839. Anal. Calcd for $C_{16}H_{28}O_2Si$: C, 68.52; H, 10.06. Found: C, 68.26; H, 10.11.

Compound 21: colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.69–5.65 (m, 1 H), 5.59–5.56 (m, 1 H), 3.91 (app dd, 1 H, $J \approx$ 6.4, 3.2 Hz), 3.24 (app t, 1 H, $J \approx$ 5.7 Hz), 2.69 (td, 1 H, $J \approx$ 13.2, 6.6 Hz), 2.60 (dm, 1 H, $J \approx$ 18.0 Hz), 2.38 (app dddd, 1 H, $J \approx$ 10.7, 5.7, 5.2, 1.8 Hz), 2.24 (ddd, 1 H, J = 13.7, 5.1, 3.2 Hz), 2.10 (app tdd, 1 H, $J \approx$ 13.2, 5.1, 2.8 Hz), 1.99–1.89 (m, 3 H), 1.73–1.67 (m, 1 H), 0.94 (s, 9 H), 0.11 (s, 6 H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 211.7, 125.6, 123.9, 69.1, 44.0, 42.9, 36.4, 31.7, 26.0, 25.7, 23.1, 18.0, -4.8, -4.9; IR ($CHCl_3$) 2945, 2925, 2885, 2850, 1705, 1470, 1460, 1445, 1370, 1255, 1085, 1035, 840 cm^{-1}; EIMS (20 eV) m/z (relative intensity) 280 (0.2), 265 (13), 273 (100), 205 (5), 181 (13), 169 (17), 129 (30), 131 (76), 105 (20), 91 (11), 75 (22); CIHRMS calcd for $C_{16}H_{29}O_2Si$ (M + H) 281.1938, found 281.1943. Anal. Calcd for $C_{16}H_{28}O_2Si$: C, 68.52; H, 10.06. Found: C, 68.77; H, 10.00. For the physical data of **22**, see below.

When the Diels–Alder reaction of the enone **2** was carried out for 15 h at room temperature and then 4 h at 40 °C on a 1-mmol scale, the compounds **20** (2% isolated yield), **21** (3%), and **22** (40%) were obtained.

Isomerization of 20. Compound 22. To a solution of **20** (0.116 g) in dry MeOH (7 mL) was added 2 M methanolic NaOMe (5 mL) at room temperature. After 1 h at room temperature, TLC showed absence of the starting material. Solid CO_2 was added and the MeOH evaporated. The residue was mixed with H_2O (10 mL) and extracted with Et_2O (3 × 20 mL). The Et_2O solution was washed with brine (1 × 15 mL) and dried ($MgSO_4$). Concentration furnished the trans-fused Diels–Alder adduct **22** (0.112 g) as a light yellow solid, which was purified by flash chromatography eluting with hexanes–ethyl acetate (10:1) to give **22** (0.105 g, 87.5%) as a colorless oil, which solidified on standing. Recrystallization (hexane, −22 °C) afforded colorless crystals, mp 62–64 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.68–5.63 (m, 2 H), 3.93 (bs, 1 H), 2.85 (td, 1 H, J = 13.9, 5.8 Hz), 2.68 (dt, 1 H, J = 12.3, 8.2 Hz), 2.41–2.34 (m, 1 H), 2.27–2.21 (m, 3 H), 2.10 (dddd, 1 H, J = 13.9, 5.9, 3.4, 2.5 Hz), 1.94–1.78 (m, 3 H), 0.94 (s, 9 H), 0.12 (s, 6 H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 212.2, 125.6, 125.3, 68.3, 44.2, 44.0, 35.9, 33.7, 28.6, 25.8, 24.5, 18.1, -4.4, -4.9; IR ($CHCl_3$) 3020, 2945, 2925, 2890, 2850, 1705, 1470, 1460, 1435, 1365, 1255, 1135, 1085, 1050, 1000, 990, 835 cm^{-1}; EIMS (20 eV) m/z (relative intensity) 280 (0.2), 265 (14), 223 (100), 205 (4), 181 (2), 179 (2.5), 169 (4), 157 (4), 149 (3), 131 (48), 129 (11), 105 (13), 91 (7), 75 (15); CIHRMS calcd for $C_{16}H_{29}O_2Si$ (M + H) 281.1938, found 281.1930. Anal. Calcd for $C_{16}H_{28}O_2Si$: C, 68.52; H, 10.06. Found: C, 68.45; H, 10.05.

Isomerization of 21. (4*SR*,4a*SR*,8a*SR*)-4-(*tert*-Butyldimethylsiloxy)-3,4,4a,5,8,8a-hexahydro-1(2*H*)-naphthalenone (23). The procedure used for the isomerization of **20** was followed, using 0.048 g of **21**. After 3 h, workup and chromatography (hexanes–ethyl acetate, 15:1) yielded 0.042 g (87%) of a mixture of **23** and **21** (ca. 7:1) as a colorless oil: ^{1}H NMR (250 MHz, $CDCl_3$) (major isomer **23**) δ 5.71–5.63 (m, 2 H), 3.75 (ddd, 1 H, J = 10.8, 9.2, 4.2 Hz), 2.53–2.35 (m, 3 H), 2.32–2.08 (m, 4 H), 1.98–1.70 (m, 3 H); IR ($CHCl_3$) 3025, 2950, 2926, 2885, 2850, 1702, 1456, 1351, 1253, 1148, 1107, 1072, 837 cm^{-1}; EIMS (20 eV) m/z (relative intensity) 280 (0.2), 265 (1.4), 223 (100), 181 (6), 169 (9), 131 (31), 129 (12), 105 (5), 75 (6); CIHRMS calcd for $C_{16}H_{29}O_2Si$ (M + H) 281.1938, found 281.1950. Anal. Calcd for $C_{16}H_{28}O_2Si$: C, 68.52; H, 10.06. Found: C, 68.63; H, 10.08.

(3*R*,4*S*,4a*R*,8a*S*)-3,4-*O*-Isopropylidene-3,4-dihydroxy-3,4,4a,5,8,8a-hexahydro-1(2*H*)-naphthalenone (25), (3*R*,4*S*,4a*S*,8a*R*)-3,4-*O*-Isopropylidene-3,4-dihydroxy-3,4,4a,5,8,8a-hexahydro-1(2*H*)-naphthalenone (26), and (4*S*,4a*R*)-4-Hydroxy-4a,5,8,8a-tetrahydro-1(4*H*)-naphthalenone (27). The general procedure was followed, using 1.56 g (9.27 mmol) of the chiral cyclohexenone **24** dissolved in 25 mL of toluene, 1.14 g (8.53 mmol) of $AlCl_3$ in 40 mL of toluene, and 12 mL of 1,3-butadiene in 35 mL of toluene. After workup, a thick yellow oil was obtained (2.21 g). ^{1}H NMR analysis of this mixture showed a ca. >10:1 ratio of **25**/**26** and the presence of the elimination product **27**. The crude was purified by chromatography using a stepwise gradient of hexanes–ethyl acetate (4:1 and 7:3) as eluent. First to elute was **25** (1.39 g, 67.4%), followed by **26** (0.091 g, 4.4%), and then the hydroxy enone **27** (0.198 g, 13%).

Compound 25: off-white solid; recrystallization (hexane, −22 °C) afforded colorless needles, mp 67.5–68.5 °C; $[\alpha]^{23}_D$ +30.0° (c 1.3, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.70–5.66 (m, 1 H), 5.59–5.54 (m, 1 H), 4.62 (ddd, 1 H, J = 7.1, 4.8, 3.2 Hz), 4.26 (dd, 1 H, J = 7.1, 2.4 Hz), 2.85 (ddd, 1 H, $J \approx$ 6.6, 3.4, 3.4 Hz), 2.70 (dd, 1 H, J = 18.4, 3.2 Hz), 2.69 (dm, 1 H, $J \approx$ 17.9 Hz), 2.56 (dd, 1 H, J = 18.4, 4.8 Hz), 2.42 (dddd, 1 H, J = 11.4, 6.6, 4.6, 2.4 Hz), 2.16 (dm, 1 H, $J \approx$ 18.0 Hz), 2.04 (dm, 1 H, $J \approx$ 17.9 Hz), 1.77 (m, 1 H, $J \approx$ 18.0, 11.4 Hz), 1.50 and 1.37 (2s, 2 × 3 H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 208.9, 126.6, 124.3, 107.8, 75.5, 72.5, 41.6, 40.5, 36.5, 26.7, 25.8, 24.1, 23.8; IR ($CHCl_3$) 3050, 2990, 2920, 1715, 1445, 1430, 1380, 1260, 1215, 1165, 1045 cm^{-1}; EIMS (20 eV) m/z (relative intensity) 222 (21), 207 (51), 165 (100), 164 (80), 147 (20), 146 (15), 119 (45), 107 (25), 91 (13), 79 (14); EIHRMS calcd for $C_{13}H_{18}O_3$ 222.1256, found 222.1254. Anal. Calcd for $C_{13}H_{18}O_3$: C, 70.25; H, 8.16. Found: C, 70.38; H, 8.29.

Compound 26: off-white solid; recrystallization (hexane, −22 °C) afforded colorless needles, mp 63–64 °C; $[\alpha]^{23}_D$ −31° (c 0.7, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.68 (m, 2 H), 4.63 (ddd, 1 H, J = 7.5, 6.2, 4.8 Hz), 4.54 (dd, 1 H, J = 7.5, 4.8 Hz), 2.75 (dd, 1 H, J = 17.1, 6.2 Hz), 2.62 (dd, 1 H, J = 17.1, 4.8 Hz), 2.56–2.50 (m, 2 H), 2.45–2.38 (m, 2 H), 2.25–2.20 (m, 1 H), 2.12–2.07 (m, 1 H), 1.46 and 1.36 (2s, 2 × 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 209.9, 125.4, 125.0, 108.6, 76.3, 72.8, 43.4, 42.7, 33.3, 26.1, 25.6, 24.9, 23.8; IR ($CHCl_3$) 3020, 2980, 2905, 1715, 1450, 1435, 1405, 1385, 1370, 1265, 1210, 1170, 1065, 1035 cm^{-1}; EIMS (20 eV) m/z (relative intensity) 222 (53), 207 (73), 175 (41), 165 (68), 164 (63), 147 (30), 146 (59), 145 (26), 119 (74), 107 (83), 105 (47), 104 (32), 100 (39), 97 (100), 91 (43), 80 (52), 79 (81); EIHRMS calcd for $C_{13}H_{18}O_3$ 222.1256, found 222.1265. Anal. Calcd for $C_{13}H_{18}O_3$: C, 70.25; H, 8.16. Found: C, 70.36; H, 8.15.

Compound 27: colorless oil; ^{1}H NMR analysis showed a ca. >12:1 mixture of cis/trans-fused diastereoisomers; $[\alpha]^{23}_D$ +38° (c 1.2, $CHCl_3$); ^{1}H NMR (250 MHz, $CHCl_3$) (major isomer, cis) δ 6.87 (dd, 1 H, J = 10.2, 2.6 Hz), 5.91 (ddd, 1 H, J = 10.2, 1.8, 0.8 Hz), 5.78–5.64 (m, 2 H), 4.44 (app tdd, 1 H, $J \approx$ 7.4, 2.6, 1.8 Hz), 2.82 (app ddd, $J \approx$ 9.7, 6.1, 4.1 Hz), 2.52 (d, 1 H, J = 7.0 Hz, HO), 2.44–2.08 (m, 5 H); IR ($CHCl_3$) 3417, 3010, 2915, 2890, 2840, 1667, 1441, 1378, 1210, 1040 cm^{-1}; EIMS (20 eV) m/z (relative intensity) 164 (26), 146 (17), 136 (29), 123 (8), 118 (7), 110 (100), 107 (11), 84 (34), 79 (12); EIHRMS calcd for $C_{10}H_{12}O_2$ 164.0837, found 164.0847. Anal. Calcd for $C_{10}H_{12}O_2$: C, 73.15; H, 7.37. Found: C, 73.01; H, 7.48.

Reaction of 25 with LDA. To a solution of LDA (0.142 mmol) in THF–hexane (4:1) (0.25 mL) cooled to −78 °C was slowly added a solution of **25** (0.030 g, 0.135 mmol) in THF (0.8 mL). After 2.5 h at −78 °C, TLC analysis showed the absence of the starting material and the presence of a more polar spot. The reaction was then quenched at −78 °C with saturated aqueous NH_4Cl (2 mL), and after warming to room temperature, water (2 mL) was added and the mixture extracted with Et_2O (5 × 5 mL). The organic layer was washed with brine (1 × 5 mL), dried (Na_2SO_4), and concentrated to a yellow oil (0.018 g). ^{1}H NMR analysis showed the presence of the hydroxy enone **27** as a mixture of stereoisomers (cis/trans, ca 3:1). Chromatography of the crude mixture eluting with hexanes–ethyl acetate (3:1) afforded 0.013 g (58.6%) the pure hydroxy enone **27** (cis/trans, ca. 3:1) as a colorless oil: ^{1}H NMR (250 MHz, $CDCl_3$) selected signals for the minor trans isomer, δ 6.92 (dd, 1 H, J = 10.2, 1.8 Hz, H-3, partially superimposed to H-3 of the major isomer), 5.98 (dd, 1 H, J = 10.2, 2.4 Hz, H-2), 4.30 (bt, 1 H, $W_{1/2} \approx$ 15 Hz, H-4).

When the reaction was carried out as above but stopped at 40% conversion, a 10:1 ratio (cis/trans) could be observed by ^{1}H NMR analysis of the crude reaction mixture.

Reaction of 25 with *tert*-Butyldimethylsilyl Chloride/DBU. (4*S*,4a*R*)-4-(*tert*-Butyldimethylsiloxy)-4a,5,8,8a-tetrahydro-1(4*H*)-naphthalenone (28). To the acetonide **25** (0.184 g, 0.82 mmol) in benzene (10 mL) were added *tert*-butyldimethylsilyl chloride (0.187 g, 1.24 mmol) and DBU (0.28 mL, 1.82 mmol). The mixture was stirred at room temperature for 30 min and heated to reflux for 6 h. The reaction mixture was cooled to room temperature and diluted with Et_2O (80 mL). The organic layer was washed with H_2O (1 × 20 mL), 0.1 M aqueous

HCl (2 × 15 mL), saturated aqueous $NaHCO_3$ (2 × 10 mL), and brine (2 × 10 mL). The solution was dried over $MgSO_4$ and concentrated to give a yellow oil (0.25 g). Flash chromatography using hexanes–ethyl acetate (10:1) gave 0.206 g (89.2%) of an unseparable mixture of the diastereoisomeric silyl ethers **28** (trans/cis, 3:1) as a colorless oil: $[\alpha]^{23}_D$ −177° (*c*, 1.5, $CHCl_3$); ^1H NMR (250 MHz, $CDCl_3$) δ 6.80 (dd, 1 H, *J* = 10.3, 1.7 Hz, H-3, major isomer), 6.75 (dd, 1 H, *J* = 10.2, 2.6 Hz, H-3, minor isomer), 5.95 (dd, 1 H, *J* = 10.3, 2.3 Hz, H-2, major isomer), 5.88 (ddd, 1 H, *J* = 10.2, 1.7, 0.7 Hz, H-2, minor isomer), 5.78–5.64 (m, 2 H, olefinic protons H-6 and 7, both isomers), 4.41 (dt, 1 H, *J* = 7.9, 2.2 Hz, H-4, minor isomer), 4.27 (dt, 1 H, *J* = 9.1, 2.0 Hz, H-4, major isomer), 2.88–2.84 (m, 1 H, minor isomer), 2.58–2.01 (m, 5 H, both isomers), 1.95–1.86 (m, 1 H, major isomer), 0.94 (s, 9 H, major isomer), 0.93 (s, 9 H, minor isomer), 0.15 and 0.14 (2s, 2 × 3 H, major isomer), 0.12 and 0.10 (2s, 2 × 3 H, minor isomer); IR ($CHCl_3$) 3026, 2949, 2926, 2890, 2854, 1675, 1651, 1468, 1434, 1378, 1250, 1150, 1105, 1078 cm^{-1}; EIMS (20 eV) *m/z* (relative intensity) 278 (8), 263 (2), 221 (100), 203 (7), 167 (9), 129 (9), 113 (9), 75 (12); EIHRMS calcd for $C_{16}H_{26}O_2Si$ 278.1702, found 278.1707. Anal. Calcd for $C_{16}H_{26}O_2Si$: C, 69.01; H, 9.41. Found: C, 69.13; H, 9.45.

Selective Reduction of 28. To a solution of **28** (0.045 g, 0.16 mmol) in benzene (6 mL) were added Aliquat 336 (20 μL, 0.042 mmol) and a soluton of $NaHCO_3$ (0.220 g, 2.58 mmol) and $Na_2S_2O_4$ (0.227 g, 1.3 mmol) in H_2O (6 mL). The biphasic system was heated to 80 °C with vigorous stirring under nitrogen. After 1.5 h the reaction was complete. The benzene layer was separated and the aqueous was extracted with Et_2O (3 × 5 mL). The combined organic layer was washed with brine (1 × 5 mL) and dried ($MgSO_4$) and the solvent was evaporated. Chromatography (hexanes–ethyl acetate, 16:1) of the residual oil afforded 0.028 g (62.7%) of a diastereoisomeric mixture of **21** and **23** (**21**/**23**, ca. 1:6) [$[\alpha]^{23}_D$ −39° (*c* 0.8, $CHCl_3$)], which presented identical chromatographic and spectroscopic properties as that of the racemic **21**/**23** mixture obtained before.

(3*R*,4*S*,5*R*)-1-(*tert*-Butyldimethylsiloxy)-4,5-*O*-isopropylidene-4,5-dihydroxy-3-methylcyclohexene (29). To a suspension of copper(I) iodide (0.484 g, 2.54 mmol) in THF (12 mL) cooled to 0 °C was added a 1.37 M solution of methyllithium in Et_2O (3.05 mL, 4.16 mmol). The white suspension turned immediately into an orange suspension, gradually becoming a clear colorless solution. The cuprate solution was stirred at 0 °C for 30 min and cooled to −78 °C. Triethylamine (0.87 mL, 6.24 mmol) and a solution of *tert*-butyldimethylsilyl chloride (0.75 g, 5 mmol) in THF (2 mL) were added and the mixture was stirred at −78 °C for 10 min. A solution of the enone **24** (0.350 g, 2.08 mmol) in THF (4 mL) was added dropwise and the resulting orange suspension was stirred at −78 °C for 1 h and then warmed to room temperature over 2 h. The reaction mixture was poured into a 1:1 mixture of saturated aqueous NH_4Cl and 3% aqueous NH_3 (15 mL) and Et_2O (15 mL). The aqueous layer was separated and extracted with Et_2O (3 × 15 mL). The combined organic solution was washed with 1:1 saturated aqueous NH_4Cl and 3% aqueous NH_3 (1 × 10 mL), 0.4 M aqueous HCl (1 × 10 mL), saturated aqueous $NaHCO_3$ (1 × 15 mL) and dried ($MgSO_4$). Concentration in vacuo gave 0.70 g of a yellow liquid. Flash chromatography of the residue afforded **29** as a colorless oil (0.448 g, 72%): $[\alpha]^{23}_D$ −40° (*c* 1.8, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 4.64 (dd, 1 H, *J* = 3.6, 1.8 Hz), 4.39 (dd, 1 H, *J* = 6.9, 6.9, 4.6 Hz), 3.76 (app t, 1 H, *J* = 6.5 Hz), 2.46 (ddd, 1 H, *J* = 16.5, 7.0, 0.8 Hz), 2.32–2.26 (m, 2 H), 1.46 and 1.34 (2s, 2 × 3 H), 1.09 (d, 3 H, *J* = 7.1 Hz), 0.91 (s, 9 H), 0.138 and 0.136 (2s, 2 × 3 H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 148.4, 108.1, 106.6, 80.1, 73.6, 34.1, 33.2, 27.6, 25.6, 25.1, 19.1, 18.0, −4.4, −4.5; IR ($CHCl_3$) 2955, 2925, 2885, 2855, 1655, 1475, 1465, 1385, 1375, 1260, 1210, 1180, 1060, 845 cm^{-1}; EIMS (20 eV) *m/z* (relative intensity) 298 (13), 283 (6), 240 (5), 225 (19), 223 (29), 211 (11), 197 (6), 185 (10), 184 (13), 183 (58), 169 (10), 165 (20), 156 (8), 155 (15), 143 (12), 142 (67), 141 (33), 127 (26), 115 (6), 109 (7), 100 (100), 85 (8), 75 (17), 73 (6); EIHRMS calcd for $C_{16}H_{30}O_3Si$ 298.1964, found 298.1970.

Ethyl (1*R*,5*R*,6*S*)-[3-(*tert*-Butyldimethylsiloxy)-5,6-*O*-isopropylidene-5,6-dihydroxy-2-cyclohexen-1-yl]acetate (30). To a solution of isopropylidenecyclohexenone **24** (0.280 g, 1.66 mmol) in anhydrous Et_2O (17 mL) was added HgI_2 (0.058 g, 0.12 mmol) under nitrogen. After being stirred at room temperature for 30 min, the mixture was cooled to −78 °C, and a solution of 1-(*tert*-butyldimethylsiloxy)-1-ethoxyethene (0.420 g, 2.07 mmol) in Et_2O (1 mL) was added over 5 min. After 19 h at −78 °C, triethylamine (0.1 mL) was added and the cold bath removed. The mixture was allowed to warm to room temperature and then filtered through a short column (5 cm) of silica gel (deactivated with a 5% triethylamine solution of hexanes–ethyl acetate, 10:1), eluting with hexanes–ethyl acetate (9:1). The solvent was evaporated and the residue was rechromatographed (hexanes–ethyl acetate, 9:1) to give 0.547 g (88.9%) of silyl enol ether **30** as a colorless oil: $[\alpha]^{23}_D$ −43.5° (*c* 1.2, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 4.70 (dd, 1 H, *J* = 3.7, 1.7 Hz), 4.41 (ddd, 1 H, *J* = 6.8, 6.8, 4.2 Hz), 4.13 (2q, 1 H, *J* = 7.1 Hz), 3.88 (dd, 1 H, *J* = 6.4, 6.4 Hz), 2.69 (m, 1 H, $W_{1/2} \approx 27$ Hz), 2.54 (dd, 1 H, *J* = 14.8, 5.8 Hz), 2.46 (ddd, 1 H, *J* = 17.0, 7.0, 1.0 Hz), 2.32 (dddd, 1 H, *J* = 17.0, 4.1, 1.8, 1.8 Hz), 2.28 (dd, 1 H, *J* = 14.8, 8.8 Hz), 1.47 and 1.34 (2s, 2 × 3 H), 1.27 (t, 3 H, *J* = 7.1 Hz), 0.92 (s, 9 H), 0.15 and 0.14 (2s, 2 × 3 H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 172.2, 149.5, 108.4, 103.4, 77.7, 73.4, 60.4, 38.1, 35.9, 33.9, 27.6, 25.6, 25.2, 18.0, 14.2, −4.5; IR ($CHCl_3$) 2970, 2945, 2925, 2885, 2850, 1725, 1660, 1470, 1465, 1385, 1375, 1350, 1260, 1210, 1165, 1055, 845 cm^{-1}; EIMS (20 eV) *m/z* (relative intensity) 370 (35), 355 (10), 325 (7), 313 (8), 312 (28), 297 (6), 296 (13), 295 (53), 294 (14), 283 (30), 267 (20), 255 (20), 238 (15), 237 (24), 225 (100), 221 (74), 209 (19), 181 (22), 165 (7), 100 (14), 75 (3); EIHRMS calcd for $C_{19}H_{34}O_5Si$ 370.2175, found 370.2170.

(1*RS*,3*SR*,3a*RS*,7a*SR*)-3-(*tert*-Butyldimethylsiloxy)-2,3,3a,4,7,7a-hexahydro-1*H*-inden-1-ol (17). To a 1 M solution of lithium tri-*sec*-butylborohydride (L-Selectride, Aldrich) (1 mL) in THF cooled to −78 °C was slowly added a solution of **15** (0.222 g, 0.83 mmol) in THF (3.5 mL). After 1 h at −78 °C, the reaction was quenched by the addition of H_2O (0.2 mL) and the resulting mixture was allowed to warm to 0 °C. Ethanol (0.7 mL) and a 3 M aqueous solution of NaOH (0.9 mL) were added followed by a 30% aqueous solution of hydrogen peroxide (0.7 mL). After 20 min the mixture was diluted with H_2O (5 mL), saturated with K_2CO_3, and extracted with Et_2O (5 × 20 mL). The organic phase was dried over Na_2SO_4 and concentrated. The residue was subjected to flash chromatography (hexanes–ethyl acetate, 4:1) to afford 0.206 g (92%) of the alcohol **17** (1α-HO/1β-HO, 20:1) as a colorless oil: ^1H NMR (250 MHz, $CDCl_3$) δ 5.94–5.83 (m, 2 H), 4.17 (bm, 1 H, $W_{1/2} \approx 15$ Hz), 4.10 (bm, 1 H, $W_{1/2} \approx 15$ Hz), 2.28–2.05 (m, 8 H), 1.81 (ddd, 1 H, *J* = 14.3, 4.4, 3.2 Hz), 0.89 (s, 9 H), 0.071 and 0.063 (2s, 2 × 3 H); IR ($CHCl_3$) 3488, 3010, 2948, 2928, 2900, 2849, 1470, 1460, 1437, 1360, 1260, 1130, 1117, 1095, 1060, 1010, 880, 845 cm^{-1}; EIMS (20 eV) *m/z* (relative intensity) 268 (0.6), 250 (0.4), 211 (47), 193 (30), 157 (34), 119 (100), 118 (17), 117 (22), 91 (93), 75 (22); CIHRMS calcd for $C_{15}H_{29}O_2Si$ (M + H) 269.1938, found 269.1936. Anal. Calcd for $C_{15}H_{28}O_2Si$: C, 67.11; H, 10.51. Found: C, 67.36, H, 10.70.

(1*RS*,3*SR*,3a*RS*,7a*SR*)-3-(*tert*-Butyldimethylsiloxy)-2,3,3a,4,7,7a-hexahydro-1*H*-inden-1-yl 4-Nitrobenzoate (18). To a solution of **17** (0.111 g, 0.41 mmol) in 5 mL of CH_2Cl_2 cooled to 0 °C was added triethylamine (0.069 mL, 0.49 mmol), 4-nitrobenzoyl chloride (0.085 g, 0.45 mmol), and DMAP (0.006 g, 0.045 mmol). The ice bath was removed and the mixture was stirred at room temperature for 2 h. Then, Et_2O (90 mL) was added and the organic phase was washed with H_2O (1 × 15 mL), 0.1 M aqueous HCl (1 × 15 mL), saturated aqueous $NaHCO_3$ (1 × 15 mL), and brine (1 × 15 mL). The solution was dried over $MgSO_4$, and the solvent was removed in vacuo. The solid residue was purified by flash chromatography (hexanes–ethyl acetate, 4:1) to afford the 4-nitrobenzoate **18** as a solid (0.159 g, 92%). Recrystallization from ethanol gave pale yellow plates, mp 127–128 °C: ^1H NMR (500 MHz, $CDCl_3$) δ 8.28 (app d, 2 H, $J \approx 8.8$ Hz), 8.18 (app d, 2 H, $J \approx 8.8$ Hz), 5.88 (app d, 1 H, $J \approx 10.5$ Hz), 5.74 (d, 1 H, $J \approx 10.5$ Hz), 5.34 (m, 1 H, $W_{1/2} \approx 17$ Hz), 4.27 (m, 1 H, $W_{1/2} \approx 19$ Hz), 2.68 (ddd, 1 H, *J* = 15.4, 7.7, 7.7 Hz), 2.31–2.10 (m, 6 H), 1.81 (ddd, 1 H, *J* = 15.4, 6.4, 3.7 Hz), 0.89 (s, 9 H), 0.067 and 0.053 (2s, 2 × 3 H); IR ($CHCl_3$) 2945, 2920, 2880, 2845, 1715, 1525, 1350, 1280, 1250, 1120, 835 cm^{-1}; EIMS (20 eV) *m/z* (relative intensity) 417 (0.1), 360 (12), 266 (1.3), 224 (100), 193 (6), 150 (6), 119 (50), 118 (9), 117 (8), 91 (13), 75 (2); CIHRMS calcd for $C_{22}H_{32}O_5NSi$ (M + H) 418.2051, found 418.2058. Anal. Calcd for $C_{22}H_{31}O_5NSi$: C, 63.28; H, 7.48; N, 3.35. Found: C, 63.03; H, 7.44; N, 3.17.

(1*RS*,3*SR*,3a*RS*,7a*SR*)-1,3-Bis(*tert*-butyldimethylsiloxy)-2,3,3a,4,7,7a-hexahydro-1*H*-indene (19). To a solution of **17** (0.014 g, 0.052 mmol) in 1 mL of CH_2Cl_2 were added *tert*-butyldimethylsilyl chloride (0.010 g, 0.066 mmol) and DBU (10.9 μL, 0.072 mmol). After 24 h at room temperature, the reaction mixture was diluted with Et_2O (20 mL). The organic layer was washed with H_2O (1 × 5 mL), 0.1 M aqueous HCl (1 × 5 mL), saturated aqueous $NaHCO_3$ (1 × 5 mL), and brine (1 × 5 mL). The solution was dried over $MgSO_4$, and the solvent was removed in vacuo. Flash chromatography (stepwise gradient of hexanes–ethyl acetate, 20:1 and 7:3) of the residue gave **19** (0.031 g, 60%) as a colorless oil and recovered starting material **17** (0.011 g, 20%): ^1H NMR (250 MHz, $CDCl_3$) δ 5.69 (t, 2 H, J = 1.5 Hz), 4.08 (app ddd, 2 H, J = 7.9, 5.7, 5.7 Hz), 2.33 (dt, 1 H, J = 14.2, 7.9 Hz), 2.07–2.04 (m, 4 H), 1.94–1.89 (m, 2 H), 1.63 (dt, 1 H, J = 14.2, 5.7 Hz), 0.87 (br s, 9 H), 0.022 (br s, 6 H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 126.4, 74.1, 43.4, 39.2, 25.8, 22.9, 18.0, -4.6, -5.0; IR ($CDCl_3$) 2945, 2925, 2885, 2845, 1250, 1130, 1065, 860, 840 cm^{-1}; EIMS (20 eV) m/z (relative intensity) 382 (0.2), 325 (100), 271 (8), 224 (6), 193 (17), 189 (13), 175 (11), 167 (12), 147 (70), 119 (94), 118 (15), 117 (25), 91 (58), 75 (18); CIHRMS calcd for $C_{21}H_{43}O_2Si_2$ (M + H) 383.2803, found 383.2809.

Obtention of the Lactone 14 from the Allyl Derivative 6. (1*RS*,2*SR*)-2-[2-(*tert*-Butyldimethylsiloxy)-5-oxocyclohex-1-yl]ethanal (13). A solution of **6** (0.101 g, 0.37 mmol), osmium tetraoxide (0.15 mmol), and *N*-methylmorpholine *N*-oxide (0.088 g, 0.75 mmol) in 8:1 THF–H_2O (8 mL) was stirred at room temperature for 2 h. The reaction was quenched by the addition of saturated aqueous $NaHCO_3$ (4 mL), and the mixture was diluted with ethyl acetate (150 mL). The organic solution was washed with saturated aqueous solution of $NaHSO_3$ (2 × 10 mL) and brine (2 × 10 mL) and dired (Na_2SO_4). Evaporation of the solvent in vacuo gave a yellow oil (0.114 g), which was dissolved in dry CH_2Cl_2 (10 mL). The solution was cooled to 0 °C, and $NaHCO_3$ (0.032 g, 0.38 mmol) followed by lead tetraacetate (0.172 g, 0.37 mmol) were added. After 15 min of vigorous stirring, saturated aqueous solution of $NaHCO_3$ (4 mL) was added. The mixture was diluted with ethyl acetate (150 mL) and washed with saturated aqueous solution of $NaHCO_3$ (1 × 15 mL) and brine (1 × 15 mL). The organic solution was dried (Na_2SO_4) and concentrated in vacuo to give an oil (0.089 g). Flash chromatography eluting with hexanes ethyl–acetate (7:3) afforded the aldehyde **13** as a colorless oil (0.077 g, 77%): ^1H NMR (250 MHz, $CDCl_3$) δ 9.77 (t, 1 H, J = 1.6 Hz), 4.08 (bs, 1 H), 2.75–2.16 (m, 7 H), 2.12–2.01 (m, 1 H), 1.86 (tdd, 1 H, J = 13.6, 4.8, 2.1 Hz), 0.93 (s, 9 H), 0.10 and 0.078 (2s, 2 × 3 H); IR ($CDCl_3$) 2955, 2930, 2885, 2858, 2726, 1712, 1471, 1368, 1254, 1100, 1053, 1019 cm^{-1}; EIMS (20 eV) m/z (relative intensity) 213 (100), 195 (17), 185 (12), 169 (8), 155 (47), 121 (15), 93 (10), 75 (12); CIHRMS calcd for $C_{14}H_{26}O_3Si$ (M + H) 271.1729, found 271.1737.

3a,6,7,7a-Tetrahydro-2,5(3*H*,4*H*)-benzofurandione (14). A solution of aldehyde **13** (0.075 g, 0.277 mmol) in acetonitrile (5 mL) was treated with 5 mL of a 95:5 (acetonitrile/48% HF in H_2O) soloution. After 3 h at room temperature, the reaction was quenched by the addition of saturated aqueous solution of $NaHCO_3$ (15 mL). The mixture was extracted with ethyl acetate (6 × 20 mL). The organic layer was washed with brine (2 × 15 mL), dried (Na_2SO_4), and concentrated in vacuo. Flash chromatography (chloroform–ethyl acetate, 1:1) of the residual oil gave the lactol as a colorless oil (mixture of diastereoisomers) (0.030 g, 68.5%). A cold (0 °C) solution of this lactol (0.028 g, 0.18 mmol) in acetone (1 mL) was treated with Jones reagent. The excess of reagent was decomposed with 2-propanol (1 mL) and the mixture was evaporated in vacuo. The residue was taken with CH_2Cl_2 (30 mL) and the organic mixture was washed with a saturated aqueous solution of $NaHSO_3$ (1 × 5 mL), saturated aqueous $NaHCO_3$ (1 × 10 mL), and brine (1 × 5 mL). The solution was dried ($MgSO_4$), and concentrated at reduced pressure. The residue was chromatographed (chloroform–ethyl acetate, 1:1) to afford **14** (0.0175 g, 61.5%) as a solid: mp 52–53 °C; ^1H NMR (250 MHz, $CDCl_3$) δ 4.85 (ddd, 1 H, J = 6.7, 4.5, 4.5 Hz), 3.09–2.95 (m, 1 H), 2.58–2.15 (m, 7 H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 208.6, 175.5, 76.7, 41.6, 36.0, 34.2, 33.8, 26.6; IR ($CHCl_3$) 2960, 2925, 1775, 1720, 1425, 1350, 1190, 1015 cm^{-1}; EIMS (20 eV) m/z (relative intensity) 154 (100), 126 (30), 113 (31), 99 (45), 85 (23), 71 (21), 68 (36); EIHRMS calcd for $C_8H_{10}O_3$ 154.0630, found 154.0628. Anal. Calcd for $C_8H_{10}O_3$: C, 62.33; H, 6.54. Found: C, 62.38; H, 6.59.

Obtention of the Lactone 14 from Ethyl (1*RS*,6*SR*)-[3,6-Bis(*tert*-butyldimethylsiloxy)-2-cyclohexen-1-yl]acetate (4). A solution of the enol ether **4** (0.091 g, 0.21 mmol) in acetonitrile (3 mL) was treated with 3.5 mL of a 9:1 (acetonitrile/48% HF in H_2O) solution. After 3 h at room temperature, the reaction was quenched by the addition of saturated aqueous solution of $NaHCO_3$ (15 mL). The mixture was extracted with ethyl acetate (3 × 20 mL). The organic layer was washed with brine (2 × 10 mL), dried ($MgSO_4$), and concentrated in vacuo. Flash chromatography (chloroform–ethyl acetate, 1:1) of the residual solid gave the lactone **14** (0.026 g, 79%) as a solid; mp and mixture mp 51–53 °C, which presented the same chromatographic and spectroscopic characteristics as that of the lactone obtained starting with the allyl derivative **6**.

Obtention of (3a*SR*,5*SR*,6a*SR*)-5-Acetoxyhexahydro-2*H*-cyclopenta[*b*]furan-2-one (10) from the Allyl Derivative 5. The allyl ketone **5** (0.093 g, 0.36 mmol) in THF (2 mL) was reduced with L-Selectride (0.44 mmol), following the procedure used for the reduction of compound **15**. After the usual workup, the residue was chromatographed (hexanes–ethyl acetate, 9:1) to afford the alcohol as a colorless oil (0.073 g, 77%). To a solution of this alcohol (0.060 g, 0.23 mmol) in CH_2Cl_2 (2 mL) was added pyridine (47 μL, 0.58 mmol), DMAP (3 mg), and acetic anhydride (50 μL, 0.53 mmol). The mixture was stirred for 2 h at room temperature and then CH_2Cl_2 (50 mL) was added. The mixture was washed with H_2O (1 × 10 mL), 1 M aqueous HCl (1 × 10 mL), saturated aqueous $NaHCO_3$ (1 × 10 mL), and brine (1 × 10 mL). The solution was dried over $MgSO_4$, and the solvent was removed in vauco. Flash chromatography (hexanes–ethyl acetate, 10:1) of the residual oil afforded the acetate **7** (0.066 g, 95%) as a colorless oil (not characterized).

Ozone was bubbled through a cold (-78 °C) solution of **7** (0.064 g, 0.21 mmol) in a 2:1 solution of CH_2Cl_2–MeOH (6 mL), until a blue color persisted (ca. 3 min). Excess ozone was purged by bubbling nitrogen through the reaction mixture for 2 min. Dimethyl sulfide (1.5 mL) was then added, and the reaction was allowed to warm slowly to room temperature and stirred overnight at that temperature. The solvent was evaporated and the residue was purified by flash chromatography (hexanes–ethyl acetate, 9:1) to give the unstable aldehyde **8** (0.052 g, 80%) as an oil.

Tetrabutylammonium fluoride (0.32 mL, 1 M solution in THF) was added under nitrogen to a solution of aldehyde **8** (0.050 g, 0.16 mmol) in anhydrous THF (2 mL) at 0 °C. The cold bath was removed when the addition was finished. After 1.5 h the solvent was evaporated in vacuo and the crude was chromatographed (hexanes–ethyl acetate, 2:3) to afford the lactol **9** (0.023 g, 72%) as a colorless oil (mixture of diastereoisomers).

A cold (0 °C) solution of the lactol **9** (0.023 g, 0.12 mmol) in acetone (2 mL) was treated with Jones reagent. The excess of reagent was decomposed with 2-propanol (1 mL) and the mixture was evaporated in vacuo. The residue was mixed with Et_2O (35 mL) and the organic mixture was washed with a saturated aqueous solution of $NaHSO_3$ (1 × 5 mL), a saturated aqueous $NaHCO_3$ (1 × 10 mL), and brine (1 × 5 mL). The solution was dried ($MgSO_4$) and concentrated at reduced pressure. The residue was chromatographed (chloroform–ethyl acetate, 4:1) to give the lactone **10** (0.013 g, 57%) as a solid: mp 80–81 °C; ^1H NMR (250 MHz, $CDCl_3$) δ 5.24 (bt, 1 H, $J \approx$ 4.6 Hz), 5.10 (t, 1 H, J = 6.6 Hz), 3.16–3.03 (m, 1 H), 2.88 (dd, 1 H, J = 18.2, 11.2 Hz), 2.43 (dd, 1 H, J = 18.2, 2.9 Hz), 2.37 (bd, 1 H, $J \approx$ 14.4 Hz), 2.13 (ddd, 1 H, J = 14.5, 9.4, 4.6 Hz), 2.00 (s, 3 H), 2.01–1.84 (m, 2 H); ^{13}C NMR (62.9 MHz, $CDCl_3$) δ 176.9, 170.4, 84.6, 76.0, 39.7, 39.5, 36.7 (2 C's), 21.1; IR ($CHCl_3$) 2970, 2935, 1773, 1734, 1445, 1425, 1380, 1365, 1335, 1245, 1190, 1095, 1045 cm^{-1}; EIMS (20 eV) m/z (relative intensity) 142 (32), 124 (100), 114 (11), 96 (20), 68 (10); CIHRMS calcd for $C_9H_{13}O_4$ 185.0814, found 185.0809. Anal. Calcd for $C_9H_{12}O_4$: C, 58.69; H, 6.57. Found: C, 58.77; H, 6.53.

Obtention of the Lactone 10 from Ethyl (1*RS*,5*SR*)-[5-(*tert*-Butyldimethylsiloxy)-3-(triethylsiloxy)-2-cyclopenten-1-yl]acetate (3). The enol ether **3** (0.100 g, 0.24 mmol) was treated with a 10:1:3.3 mixture of AcOH/THF/H_2O (1 mL) at room temperature for 40 min. The reaction mixture was diluted with ethyl acetate (70 mL) and washed with saturated aqueous $NaHCO_3$ (2 × 15 mL) and brine (1 × 15 mL). The solution was

dried ($MgSO_4$), and the solvent was evaporated in vacuo. Chromatography (hexanes–ethyl acetate, 4:1) of the residual oil afforded **11** (0.059 g, 81%) as a colorless oil. This ketone (0.052 g, 0.17 mmol) was reduced with L-Selectride (0.21 mmol), following the procedure used for the reduction of compound **15**. After the usual workup, the corresponding alcohol was obtained as a colorless oil (0.048 g, 91%), which was not purified and was carried directly into the next step. The crude alcohol (0.044 g, 0.14 mmol) was acetylated following the same procedure employed for the preparation of **7**. After workup, the crude product was chromatographed (hexanes–ethyl acetate, 4:1) to afford the acetate **12** (0.049 g, 98.2%) as a colorless oil.

Tetrabutylammonium fluoride (0.26 mL, 1 M solution in THF) was added under nitrogen to a solution of acetate **12** (0.045 g, 0.13 mmol) in anhydrous THF (2 mL) at 0 °C. The cold bath was removed when the addition was finished. After 2 h, the solvent was evaporated in vacuo and the crude was chromatographed (chloroform–ethyl acetate, 4:1) to give the lactone **10** (0.018 g, 75%) as a solid; mp and mixture mp 79–81 °C, which presented the same chromatographic and spectroscopic characteristics as that of the lactone obtained starting with the allyl derivative **5**.

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Registry No. **1**, 61740-33-8; **2**, 119414-47-0; **3**, 130193-05-4; **4**, 119414-48-1; **5**, 130096-86-5; **6**, 130096-87-6; **7**, 130096-88-7; **8**, 130096-89-8; **9** (isomer 1), 130096-90-1; **9** (isomer 2), 130193-11-2; **10**, 130193-06-5; **11**, 130096-91-2; **12**, 130096-92-3; **13**, 130096-93-4; **14**, 130096-94-5; **15**, 130096-95-6; **16**, 130096-96-7; **17** (1α-OH), 130096-97-8; **17** (1β-OH), 130193-10-1; **18**, 130096-98-9; **19**, 130096-99-0; **20**, 130097-00-6; **21**, 130097-01-7; **22**, 130097-02-8; **23**, 130097-03-9; **24**, 121651-99-8; **25**, 130097-04-0; **26**, 130193-07-6; **27a**, 130193-08-7; **27b**, 130193-09-8; **28** (R = βH), 130097-05-1; **28** (R = αH), 130120-60-4; **29**, 130097-06-2; **30**, 130097-07-3; H_2C=C(OEt)OSi(Me_2)Bu-*t*, 42201-84-3; 3a,6,7,7a-tetrahydro-2-hydroxy-(3*H*,4*H*)-benzofuran-5-one (isomer 1), 130097-08-4; 3a,6,7,7a-tetrahydro-2-hydroxy-(3*H*,4*H*)-benzofuran-5-one (isomer 2), 130193-12-3; 4-allyl-3-(*tert*-butyldimethylsiloxy)cyclopentanol, 130097-09-5; allyltrimethylsilane, 762-72-1; 1,3-butadiene, 106-99-0.

Supplementary Material Available: X-ray crystallographic data for compounds **18**, **22**, and **25** (35 pages). Ordering information is given on any current masthead page.

Racemic Resolution of Free Sugars with Macroporous Polymers Prepared by Molecular Imprinting. Selectivity Dependence on the Arrangement of Functional Groups versus Spatial Requirements[1]

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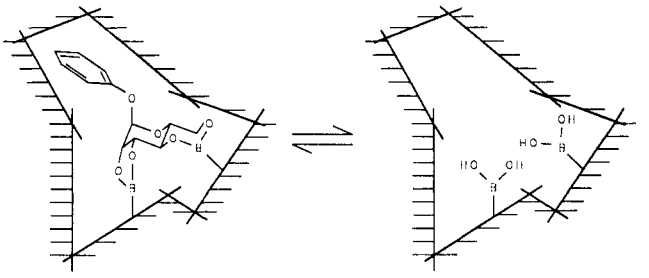
A molecular imprinting procedure was adopted to prepare highly cross-linked polymers for racemic resolution of free sugars. This is the first example illustrating a racemic resolution of free sugars on a support. For this purpose β-D-fructopyranose 2,3:4,5-bis-*O*-((4-vinylphenyl)boronate) **2** and α-D-galactopyranose 1,2:3,4-bis-*O*-((4-vinylphenyl)boronate) **3**, easily prepared from their parent free sugars in a single step, were copolymerized with a large amount of cross-linking agent. After splitting off the respective templates these polymers were used for racemic resolution of the racemates of the templates with separation factors α as high as α = 2.36 in the batch procedures. Surprisingly, polymers prepared from **2** preferably absorb D-fructose from D,L-fructose, but L-galactose from D,L-galactose. Similarly, polymers prepared from **3** preferably absorb D-galactose but L-fructose from the corresponding racemates. From these results and similar studies carried out with mannose derivatives, important conclusions can be drawn with regard to the separation mechanism on polymers prepared by molecular imprinting with templates. The influence of the arrangement of functional groups within the cavities versus the spatial requirements (shape selectivity) on selectivity is discussed in detail. In the examples presented here, the orientation of the functional groups inside the cavity is the dominating factor; shape selectivity is only of secondary importance. These findings offer new possibilities for the construction of selective adsorbents and enzyme-analogue-built catalysts.

Introduction

Several years[2,3] ago we introduced a new synthetic methodology to prepare specific binding sites in cross-linked polymers having a predetermined shape as well as an arrangement of functional groups with a defined steric orientation. For this purpose an imprinting procedure was used with the aid of template molecules. Suitable polymerizable binding groups were linked to a template molecule, and this was copolymerized to form highly cross-linked polymers. Removal of the templates leaves behind cavities

Scheme I. Schematic Representation of the Polymerization of the Template Monomer 1 and the Removal of the Template



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