108. Asymmetric Catalysis by Vitamin B_{12}: The Isomerization of Achiral Cyclopropanes to Optically Active Olefins

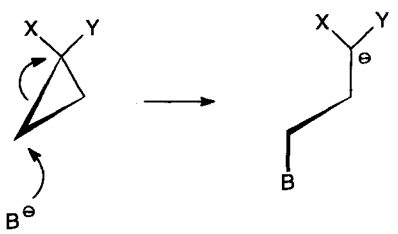
by **Thomas Troxler**[1]) and **Rolf Scheffold***

Institut für organische Chemie, Universität Bern, Freiestrasse 3, CH-3012 Bern

(21.IV.94)

Achiral spiroactivated cyclopropanes are isomerized to optically active (*R*)-(cycloalk-2-enyl)-*Meldrum*'s acids (= (*R*)-5-(cycloalk-2-enyl)-2,2-dimethyl-1,3-dioxane-4,6-diones) in high yield and ee's up to 86% by catalytic amounts of cob(I)alamin in polar protic solvents.

Introduction. – Ring opening of cyclopropanes **A** containing two geminal electron-withdrawing groups X and Y by homoconjugate addition of nucleophiles is a known reaction[2]) (→**B**). *Danishefsky* and *Singh* found that spiroactivated cyclopropanes with X,Y = –C(O)–O–C(Me)$_2$–O–C(O)– (spiroalkylated *Meldrum*'s acids) are especially reactive since the emerging negative charge is optimally delocalized [8]. *Ogoshi et al.* reported on the homoconjugate addition of cob(I)alamin to activated cyclopropanes leading to 3-substituted propylcob(III)alamins [7]. In cases where the two substituents X and Y were different, two diastereoisomeric 3,3-disubstituted propylcob(III)alamins were obtained in ratios up to 2:1. Very likely, this selectivity is due to enantioselective protonation of the intermediate carbanion.



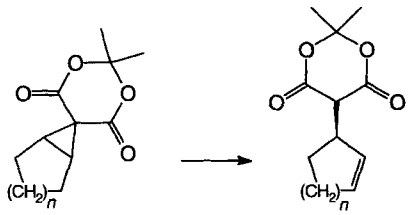
A **B**

Since *sec*-alkylcob(III)alamins easily undergo dehydrocobaltation to olefins, H^+, and cob(I)alamin, we became interested in the reaction of cob(I)alamin with bicyclo[3.1.0]-hexanes and norcaranes (= bicyclo[4.1.0]heptane) bearing electron-withdrawing groups at C(6) and C(7), respectively. As an extension of our previous work on the enantioselective isomerization of epoxides to allylic alcohols [9] and aziridines to allylic amines [10], we report here on the cob(I)alamin-catalyzed conversion of the achiral spiroactivated cyclopropanes **1** to the optically active (*R*)-(cycloalk-2-enyl)-*Meldrum*'s acids **2** (*Scheme 1*).

[1]) Part of the Ph. D. thesis of *T. T.*, University of Bern, 1993.

[2]) Examples of this process are the homoconjugate addition of enolates [1], amines [2], mercaptanes [2], H_2O [3], enamines [4], cuprates [5], Rh(I)porphyrins [6], and cob(I)alamins [7].

Scheme 1[a])



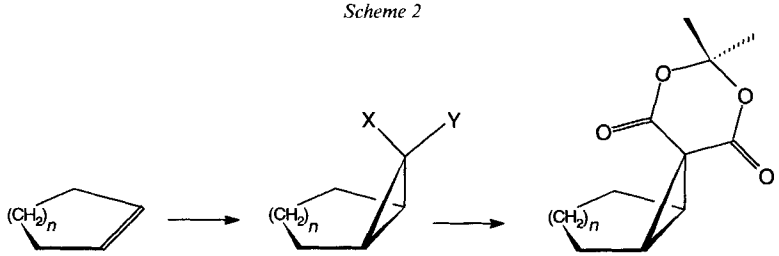
1a $n = 1$ **2a** $n = 1$
b $n = 2$ **b** $n = 2$

[a]) Only one enantiomer of **2** is shown.

These isomerizations favorably complement the Pd^0-catalyzed S_N2' substitution of allylic acetates by soft nucleophiles as a methodology for the enantioselective synthesis of olefins with malonic-acid-derived substituents in allylic position (for reviews, see [11]).

Results and Discussion. – *Starting Materials* (*Scheme 2*). The synthesis of geminally disubstituted cyclopropanes **4** and **5** from olefins proved to be most convenient according to the procedure of *Ohishi* [12]. The cycloalkenes **3** were consecutively treated with methanesulfenyl chloride (prepared *in situ* from Me_2S_2 and SO_2Cl_2), dimethyl sodiomalonate (in case of **4**) or sodiomalonodinitrile (in case of **5**), and dimethyl sulfate and base (NaOMe in case of **4**, and Et_3N in case of **5**), yielding **4a**, **4b**, and **5** in 68, 43, and 26% yield, respectively. Alkaline hydrolysis of **4** to the diacids **6** [13] followed by acid-catalyzed treatment with isopropenyl acetate [14] gave the spiroactivated compounds **1a** and **1b** in 39 and 61% yield, respectively. A mixture of the ethyl norcarane-7-*endo*- and -*exo*-carboxylates **7** and **8** (2:7) was obtained by Rh^{II}-catalyzed reaction of ethyl diazoacetate with cyclohexene in 80% yield [15].

Scheme 2



3a $n = 1$
b $n = 2$

4a X = Y = COOMe, $n = 1$
b X = Y = COOMe, $n = 2$
5 X = Y = CN, $n = 2$
6a X = Y = COOH, $n = 1$
b X = Y = COOH, $n = 2$
7 X = COOEt, Y = H, $n = 2$
8 X = H, Y = COOEt, $n = 2$

1a $n = 1$
b $n = 2$

Cob(I)alamin-Catalyzed Isomerization. If achiral spiroactivated cyclopropanes **1** were dissolved or dispersed in a polar protic solvent containing catalytic amounts of hydroxocob(III)alamin hydrochlorid (= vitamin B_{12a} = OH–Cbl · HCl), Zn powder, and NH_4Cl, optically active (+)-(*R*)-5-(cycloalk-2-enyl)-*Meldrum*'s acids **2** were formed on standing at room temperature under Ar (*Scheme 1*). The reaction rates and enantiomeric excesses (ee's) strongly depended on the solvent polarity (*Table*). The fastest and most selective reactions took place in the most polar solvents, although neither **1** nor **2** were entirely dissolved. These reactions proceeded cleanly (no side products could be detected by ^{1}H-NMR of the crude product) and in nearly quantitative yield. The influence of temperature on the ee was small (*Table, Entries 2* and *3*). Although the crude *Meldrum*'s-acid derivatives **2** obtained by this procedure were crystalline, no substantial enrichment of the (*R*)-enantiomers could be achieved by recrystallization. With the cyclopropanes **4b**, **5**, **7**, and **8**, only non-preparative experiments were performed and monitored by GC. The mono- and diester-activated cyclopropanes showed no reaction, even after prolonged heating with 2 mol-% of OH–Cbl · HCl, Zn, and NH_4Cl in MeOH (*Table, Entries 9* and *10*). The dicyano-activated compound **5** in MeOH gave a complex mixture of products which, according to GC/MS, seem to result from reactions between

Table. *Cob(I)alamin-Catalyzed Isomerization of Cyclopropanes*

Entry	Cyclo-propane	Reaction conditions[a])			Product			
		Solvent (*v*/*v*)	Temp. [°C]	Time [h]	Olefin	Yield [%][b])	ee [%][c])	$[\alpha]_D^{22}$[d])
1	**1a**	MeOH/H_2O 2:1	22	7	**2a**	100	52	+50
2	**1a**	THF/H_2O 1:15	22	2	**2a**	100	83	+96
3	**1a**	THF/H_2O 1:15	0	7	**2a**	92	86	+94
4	**1b**	DMF	22	240	**2b**	[e])	25	
5	**1b**	MeOH/dioxane 1:2	22	96	**2b**	[e])	41	
6	**1b**	MeOH	22	17	**2b**	81	52	+23
7	**1b**	MeOH/H_2O 1:1	22	2	**2b**	98	70	+29
8	**1b**	THF/H_2O 1:15	22	2	**2b**	99	77	+31
9	**4b**	MeOH	65	72	no reaction			
10	**7**/**8**[f])	MeOH	65	42	no reaction			
11	**5**	MeOH	22	115	complex mixture[g])			
12	**5**	2M $LiClO_4$ in DMF	60	48	**9**[h])	6[i])	5	

[a]) Reaction conditions: Hydroxocob(III)alamin hydrochlorid (= vitamin B_{12a}; 2 mol-% with respect to the cyclopropane) dissolved in the indicated solvent was reduced *in situ* by Zn in the presence of NH_4Cl under Ar. A solution of the cyclopropane was injected and the mixture stirred at the given temp. The reaction was monitored by TLC (*Entries 1–8*) and GC (*Entries 9–12*). In the case of *Entries 1–3* and *6–8*, the mixture was diluted with 1M $KHSO_4$ and extracted with Et_2O (see *Exper. Part*).

[b]) Yield of crude **2** ((*R*)- and (*S*)-enantiomers) relative to **1**. The crude product was essentially pure according to TLC and NMR.

[c]) Determined by enantioselective GC: **2a** was converted first to the iodolactone **13a** (*vide infra*), whereas **2b** was injected directly and pyrolized partially on the injector block to cyclohex-2-enyl keten.

[d]) Optical rotation of crude **2** in MeOH (c = 0.1 to 0.4).

[e]) Not isolated.

[f]) Mixture (2:7) of the *endo*- and *exo*-isomers.

[g]) Complex mixture of unidentified products, but practically no **9**.

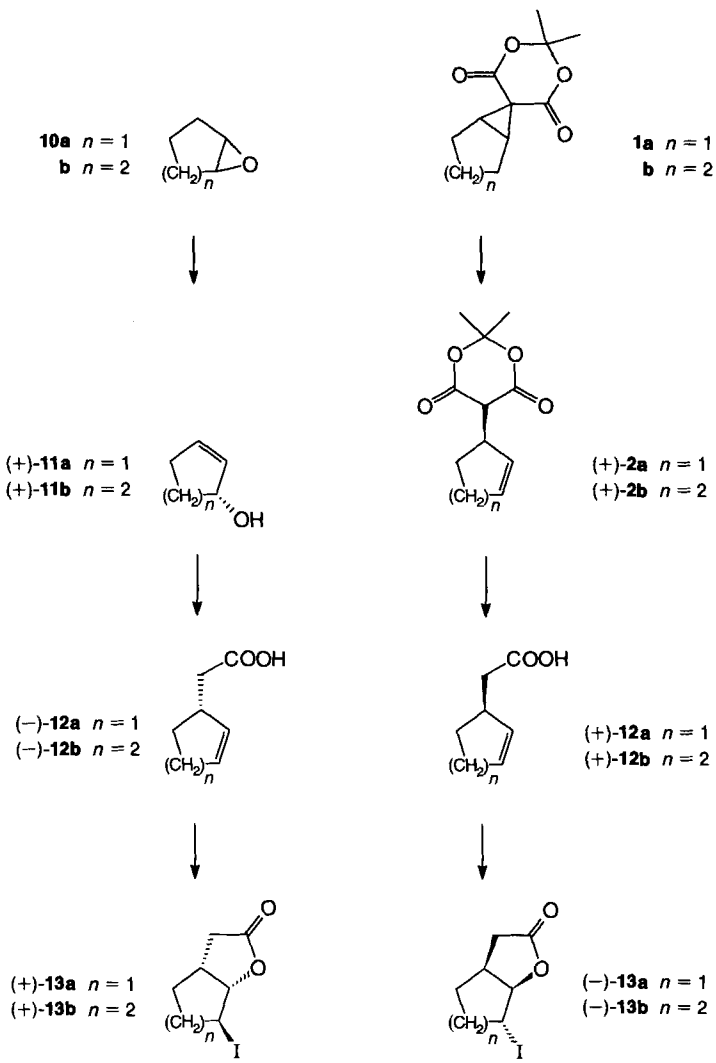
[h]) Identified by comparison (GC retention times) with racemic **9** (independently prepared by reaction of 3-bromocyclohexene with $NaHC(CN)_2$ in THF).

[i]) Not isolated. GC: 91.2% of **5**, 6.3% of **9**, and 2.5% of unidentified products.

the nitrile groups and the solvent (*Table*, *Entry 11*). In a 2M solution of $LiClO_4$ in DMF at 60°, slow isomerization of **5** to 2-(cyclohex-2-enyl)malononitrile (**9** = **2** with NC–CH–CN instead of cyclo[OC(O)–CH–C(O)O–CNe_2]) was observed (*Table*, *Entry 12*).

Configuration by Chemical Correlation. The chirality of the isomerization products (+)-**2a** and (+)-**2b** was established according to *Scheme 3*. The allylic alcohols (+)-**11a** and (+)-**11b**, which were shown earlier to have (*R*)-configuration [9], were converted *via* ester enolate *Claisen* rearrangement [16] to the (–)-(*R*)-(cycloalk-2-enyl)acetic acids

Scheme 3[a])



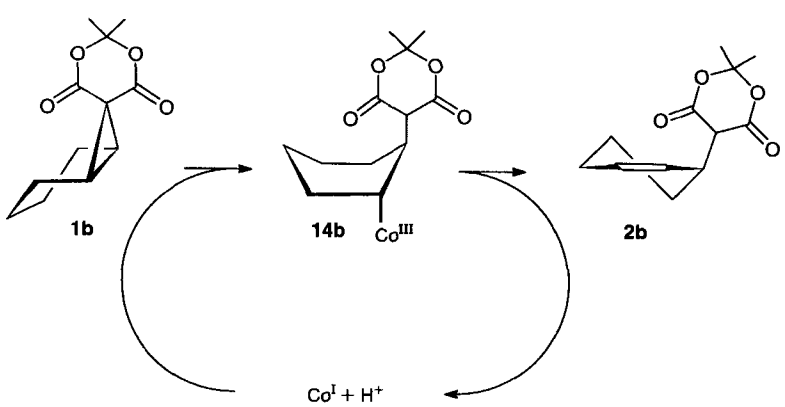
[a]) Only one enantiomer of **2**, **11**, **12**, and **13** is shown. For reaction conditions, see *Exper. Part.*

(−)-**12a** and (−)-**12b**. Since acidic hydrolysis of the *Meldrum*'s acid moiety of **2** gave (+)-**12**, the configuration of (+)-**2a** and (+)-**2b** can be deduced to be (*R*). The liquid acids (+)-**12** were easily converted to the crystalline iodolactones (−)-**13** which, after simple recrystallization, were obtained as enantiomerically pure compounds.

The preparative conversion of (+)-**11a** to (+)-**13a** proved to be more convenient *via* the orthoester variant of the *Claisen* rearrangement [17], which yielded the ethyl ester of **12a** (59%). Hydrolysis of the ester, iodolactonization, and crystallization of the pure enantiomer of (+)-**13a** were accomplished in one pot (11%).

Mechanism of Isomerization. We assume that the mechanism of the isomerization **1**→**2** is similar to that of the Cbl-catalyzed isomerization of epoxides to allylic alcohols [18] and aziridines to allylic amines [10]. However, there are two remarkable observations: *i*) The ee's and the reaction rates of **1**→**2** strongly depend on the solvent polarity, with the fastest and most selective reactions taking place in the most polar solvents (*Table*). *ii*) In the case of **1a**→**2a**, the color of the reacting mixture is orange-red (color of alkylcob(III)alamin), but dark green-brown (color of alkylcob(I)alamin) in the case of **1b**→**2b**. The UV/VIS spectrum of the steady state of **1a**→**2a** shows a distinct absorption signal at *ca.* 470 nm which may be attributed to the base-off form of an alkylcob(III)alamin [19], and only a relatively weak shoulder at *ca.* 390 nm (signal of cob(I)alamin). The spectrum of the steady state of **1b**→**2b**, on the other hand, is dominated by a sharp signal at 390 nm, and only a very weak signal at 470 nm is detected. These observations suggest the following two-step mechanism: In a first step, the cyclopropane ring is opened by nucleophilic attack of the (chiral) cob(I)alamin to afford a mixture of the two diastereoisomeric [(1*R*,2*R*)- and (1*S*,2*S*)-alkyl]cob(III)alamins **14** in a different ratio. In a second step, these intermediates decompose to yield **2**, recycled cob(I)alamin, and H^+ (*Scheme 4*). For the isomerization of the cyclopentane derivative **1a**, the second step seems to be rate-determining, since, in the steady state, alkylcob(III)alamin is the predominant species. The relative rates of the two steps seem to be reversed for the isomerization of the cyclohexane derivative **1b**: The predominance of cob(I)alamin in the steady state indicates that the initial nucleophilic cyclopropane

Scheme 4[a])



[a]) Only one diastereoisomer of **14b** and one enantiomer of **2b** is shown.

opening step is rate-determining. We assume that the attack of the voluminous cob(I)alamin nucleophile results in a sterically congested conformation of the cyclohexane ring of **1b** on the way to the S_N2 transition state.

The first step is responsable for the enantioselectivity. It is believed that the β-axially oriented acetamido side chains of Cbl direct the approach of the substrate **1** to the reactive Co-center. The influence of solvent polarity on the enantioselectivity is not yet fully understood.

The authors are grateful to Mr. *A. Saxer* for anal. GC and enantioselective GC. This work was financially supported by the *Swiss National Science Foundation*.

Experimental Part

1. *General.* Chemicals and solvents: Vitamin B_{12a} (= hydroxocobalamin hydrochloride pyrogen-free *Fr. Ph. BP*, 10.7% loss on drying, < 2% cyanocobalamin) from *Roussel Uclaf*; Et_3N and Zn powder, *Fluka puriss. p.a.*; Zn wool, *Fluka purum*, activated by sequential washing with 5% HCl/H_2O, H_2O, and MeOH; cyclopentene; *Fluka puriss.*; Me_2S_2 and SO_2Cl_2, *Fluka pract.*; NaH, *Fluka pract.*, 55–65%, dispersion in oil; Et_2O and pentane from *Siegfried*, distilled over NaH before use; THF from *Siegfried*, distilled over K before use; all other reagents were *Fluka purum* and all other solvents *Fluka puriss. p.a.* and were used as purchased. Column chromatography: silica gel (30–60 μm) from *Baker*. Anal. TLC: precoated plates, silica gel *60* F_{254} from *Merck*. Anal. GC: *Hewlett-Packard-5794* gas chromatograph; 20-m *Duran* glass cap. column coated with *SE-54* (*df* 0.15 μm); temp. program from 40° to 250°, 3°/min; flame-ionization detector (FID). Enantioselective GC (t_R in min): *Hewlett-Packard-5890* with modified cyclodextrins as chiral stationary phase; column *A*: 10 m, 20% heptakis{2,3-di-*O*-propyl-6-*O*-[(*tert*-butyl)dimethylsilyl]}-β-cyclodextrine in *OV-1701*; column *B*: 10 m, 30% octakis{2,3-di-*O*-acetoxy-6-*O*-[(*tert*-butyl)dimethylsilyl]}-γ-cyclodextrine in *OV-1701*; column *C*: 10 m, 20% heptakis{2,3-di-*O*-methyl-6-*O*-[(*tert*-butyl)dimethylsilyl]}-β-cyclodextrine in *OV-1701*. In all cases, the ee was determined from the % of relative intensities of base-line-separated peaks of enantiomers and checked by analogous measurements of the corresponding racemic compounds. Melting point (uncorrected): *Büchi 510*. $[\alpha]_D$: *Perkin-Elmer-241* polarimeter. UV/VIS: *Hewlett-Packard-8451A* diode array spectrophotometer. IR: *Perkin-Elmer-782* spectrometer; only characteristic absorptions are given. ^{1}H-NMR: *Bruker-AM-400-WB* (400 MHz) and *Bruker-AC-300* (300 MHz) spectrometer; δ-values in ppm with respect to Me_4Si (= 0 ppm) as internal standard. ^{13}C-NMR: *Bruker-AM-400-WB* (100 MHz) and *Bruker-AC-300* (75 MHz) spectrometer; Me_4Si (= 0 ppm) as internal standard. MS (*m/z* (%)): *Varian-MAT-CH-7A*, ionization energy 70 eV; only peaks with intensities > 3% of the base peak are given. GC/MS: *Varian MAT-44S*. Elemental analyses: Mikroelementaranalytisches Laboratorium, ETH, Zürich.

2. *Starting Materials. Dimethyl Bicyclo[3.1.0]hexane-6,6-dicarboxylate* [12] (**4a**). To a soln. of Me_2S_2 (14.12 g, 150 mmol) in CH_2Cl_2 (90 ml), SO_2Cl_2 (20.24 g, 150 mmol) was added at −50°. After stirring for 5 min, cyclopentene (**3a**; 20.43 g, 300 mmol) was added at −50° within 30 min. The solvent and SO_2 were evaporated at r.t., and the residual oil was transferred by means of a pipette into a soln. of dimethyl sodiomalonate (prepared from dimethyl malonat (43.59 g, 330 mmol) and NaOMe (330 mmol) in 300 ml MeOH) and heated under reflux for 2.5 h. The solvent was distilled off, H_2O (300 ml) added, and the mixture extracted with Et_2O (3 × 150 ml). The extracts were washed with brine (100 ml) and dried ($MgSO_4$), and the solvent was distilled off. To the remaining brown oil, dimethyl sulfate (41.61 g, 330 mmol) was added and the mixture allowed to stand at r.t. for 15 h. NaOMe (600 mmol) in MeOH (600 ml) was added and the soln. heated under reflux for 10 min. The solvent and Me_2S were distilled off, H_2O (300 ml) was added and the mixture extracted with Et_2O (4 × 250 ml). The extracts were washed with brine (250 ml), dried ($MgSO_4$), and evaporated, and the brown residue was distilled (68°/0.2 Torr): 40.73 g (68.3%) of **4a**. Colorless oil which crystallized at 4°. An anal. sample was obtained by recrystallization from MeOH. M.p. 47–48°. IR (KBr): 1730*s*, 1440*s*, 1252*m*. ^{1}H-NMR ($CDCl_3$): 0.72–0.93 (*m*, 1 H); 1.60–1.75 (*m*, 1 H); 1.86–2.20 (*m*, 6 H); 3.71 (*s*, 3 H); 3.78 (*s*, 3 H). ^{13}C-NMR ($CDCl_3$): 21.55, 26.46, 34.98, 35.88, 52.61, 52.63, 168.18, 170.70. MS: 198 (14, M^+), 169 (16), 168 (5), 167 (50), 166 (80), 165 (13), 151 (6), 139 (10), 138 (52), 137 (27), 135 (29), 134 (61), 133 (7), 132 (11), 123 (15), 113 (5), 111 (7), 110 (8), 108 (9), 107 (43), 106 (44), 105 (18), 101 (10), 99 (4), 97 (5), 95 (7), 94 (4), 93 (28), 92 (6), 91 (6), 81 (8), 80 (16), *79* (100), 78 (25), 77 (44), 75 (4), 71 (5), 69 (10), 68 (10), 67 (41), 66 (16), 65 (7), 59 (37), 55 (9), 54 (5), 53 (16), 52 (11), 51 (9), 50 (4), 45 (6), 44 (4), 41 (19), 40 (4), 39 (19), 29 (7), 28 (15), 27 (8), 18 (17), 17 (7), 14 (19).

Bicyclo[3.1.0]hexane-6,6-dicarboxylic Acid (**6a**). A soln. of **4a** (9.9 g, 50 mmol) and KOH (50 g) in H_2O/MeOH 1:1 (250 ml) was heated under reflux for 48 h. Most of the MeOH was distilled off under reduced pressure, H_2O (100 ml) added, the clear soln. extracted with Et_2O (100 ml), and the aq. phase acidified with 25% HCl soln. (150 ml) and evaporated. Extraction of the white residue with hot Et_2O (4 × 100 ml) and evaporation gave 8.50 g of a white powder. Recrystallization from H_2O yielded 7.74 g (91%) of **6a**. White crystals. M.p. 190–191° (decarbox.). IR (KBr): 3700–2200 (br.), 1700*s*. ^{1}H-NMR ((D_6)DMSO): 0.94–1.14 (*m*, 1 H); 1.58–1.73 (*m*, 1 H); 1.82–2.06 (*m*, 6 H); 3.50 (br., 1 H); 12.25 (br., 1 H). ^{13}C-NMR ((D_6)DMSO): 21.76, 26.40, 33.73, 36.28, 168.85, 171.91. MS: 170 (7, M^+), 154 (5), 153 (44), *152* (100), 151 (29), 141 (7), 135 (16), 134 (68), 133 (6), 126 (4), 125 (24), 124 (82), 123 (65), 112 (4), 111 (8), 110 (8), 108 (11), 107 (16), 106 (42), 105 (18), 97 (8), 96 (25), 95 (15), 84 (14), 83 (7), 82 (7), 81 (11), 80 (20), 79 (57), 78 (25), 77 (34), 71 (4), 69 (6), 68 (18), 67 (27), 66 (36), 65 (6), 55 (10), 54 (6), 53 (15), 52 (7), 51 (8), 45 (6), 43 (6), 41 (24), 39 (17), 27 (7).

2′,2′-Dimethylspiro{bicyclo[3.1.0]hexane-6,5′-[1,3]dioxane}-4′,6′-dione (**1a**). A suspension of finely powdered **6a** (6.80 g, 40 mmol) in isopropenyl acetate (4.80 g, 48 mmol) was stirred well at 0° under Ar. H_2SO_4 (0.3 ml) was added dropwise within 20 min by means of a syringe, and the resulting brown slurry was stirred at 0° for 1 h. After standing at 4° for 16 h, cold H_2O (10 ml) was added to the partially crystallized dark mixture. The precipitate was filtered off and washed with a 2nd portion of cold H_2O (10 ml). The red-brown solid was extracted with boiling hexane (4 × 40 ml). Recrystallization of the remaining residue from H_2O gave 2.05 g (30%) of recovered diacid **6a** (m.p. 189–190°, decarbox.). The combined hexane extracts were diluted with Et_2O (100 ml), washed with brine (100 ml), dried ($MgSO_4$), and evaporated: 2.55 g (43% rel. to converted **6a**) of **1a**, essentially pure according to ^{1}H-NMR. Yellowish crystals. M.p. 82–85°. An anal. sample was obtained by 2 recrystallizations from hexane. M.p. 87–88°. IR (KBr): 1762*s*, 1740*s*. ^{1}H-NMR ($CDCl_3$): 1.78 (*s*, 6 H); 1.90–2.30 (*m*, 6 H); 2.87–2.93 (*m*, 2 H). ^{13}C-NMR ($CDCl_3$): 26.34, 26.73, 27.39, 35.25, 46.12, 104.01, 164.57, 167.73. MS: 195 (11, $[M - Me]^+$), 154 (4), 153 (49), *152* (100), 151 (11), 135 (20), 134 (94), 125 (8), 124 (90), 123 (46), 109 (4), 108 (6), 107 (8), 106 (27), 105 (9), 96 (12), 95 (10), 81 (5), 80 (12), 79 (39), 78 (7), 77 (16), 68 (7), 67 (19), 66 (33), 59 (15), 55 (7), 53 (4), 52 (4), 43 (15), 41 (4), 39 (4).

Dimethyl Bicyclo[4.1.0]heptane-7,7-dicarboxylate [12] (**4b**). As described for **4a**. The crude product was purified by recrystallization from MeOH instead of distillation. Yield 43%. Yellowish crystals. M.p. 82–87°. An anal. sample was obtained by recrystallization from MeOH. M.p. 87–88.5°. IR (KBr): 1725*s*, 1435*m*, 1255*m*. ^{1}H-NMR ($CDCl_3$): 0.95–1.10 (*m*, 2 H); 1.20–1.35 (*m*, 2 H); 1.80–2.00 (*m*, 6 H); 3.70 (*s*, 3 H); 3.80 (*s*, 3 H). ^{13}C-NMR ($CDCl_3$): 19.70, 20.70, 25.54, 35.36, 52.28, 52.67, 167.99, 171.74. MS: 213 (7), 212 (38, M^+), 185 (4), 184 (43), 182 (10), 181 (69), *180* (100), 179 (7), 170 (10), 169 (63), 165 (18), 159 (4), 158 (59), 156 (4), 154 (4), 153 (32), 152 (88), 151 (8), 150 (12), 149 (62), 148 (68), 147 (9), 139 (31), 138 (4), 137 (26), 135 (4), 134 (12), 133 (75), 132 (12), 127 (5), 126 (44), 125 (8), 124 (37), 123 (14), 122 (51), 121 (33), 120 (65), 119 (9), 113 (26), 111 (8), 109 (7), 107 (14), 105 (7), 101 (14), 99 (4), 98 (34), 97 (4), 96 (6), 95 (9), 94 (20), 93 (48), 92 (20), 91 (27), 85 (5), 83 (4), 82 (5), 81 (42), 80 (50), 79 (37), 78 (6), 77 (18), 71 (10), 69 (9), 68 (11), 67 (11), 66 (10), 65 (11), 59 (30), 55 (13), 54 (4), 53 (9), 45 (4), 43 (4), 41 (16), 39 (9), 27 (4), 18 (12).

Bicyclo[4.1.0]heptane-7,7-dicarboxylic Acid [13] (**6b**). As described for **6a**. Yield 74%. Slightly brown crystals. M.p. 176–177° (decarbox.; [13]: m.p. 186–188°). IR (KBr): 3700–2200 (br.), 1700*s*. ^{1}H-NMR ((D_6)DMSO): 1.00–1.17 (*m*, 2 H); 1.17–1.32 (*m*, 2 H); 1.58–1.68 (*m*, 2 H); 1.80–2.00 (*m*, 4 H); 3.50 (br., 1 H); 12.68 (br., 1 H). ^{13}C-NMR ((D_6)DMSO): 19.55, 20.66, 23.75, 35.48, 168.69, 172.82. MS: 184 (1, M^+), 168 (5), 167 (44), *166* (100), 165 (13), 156 (16), 151 (15), 149 (19), 148 (69), 147 (7), 141 (35), 140 (4), 139 (21), 138 (83), 137 (17), 131 (5), 130 (51), 128 (7), 125 (29), 124 (47), 123 (46), 122 (35), 121 (20), 120 (63), 119 (7), 113 (8), 112 (59), 111 (7), 110 (40), 109 (6), 107 (6), 105 (13), 99 (18), 98 (4), 97 (16), 96 (14), 95 (12), 94 (27), 93 (43), 92 (18), 91 (35), 85 (7), 84 (36), 83 (5), 82 (17), 81 (31), 80 (48), 79 (37), 78 (8), 77 (24), 71 (4), 69 (8), 68 (23), 67 (19), 66 (17), 65 (13), 57 (4), 55 (21), 54 (6), 53 (17), 51 (4), 45 (5), 43 (6), 41 (16), 40 (4), 39 (15), 29 (4), 27 (6), 18 (6).

2′,2′-Dimethylspiro{bicyclo[4.1.0]heptane-7,5′-[1,3]dioxane}-4′,6′-dione [14] (**1b**). As described for **1a**. Yield 83%. Brownish crystals. M.p. 74–78°. An anal. sample was obtained by 2 recrystallizations from hexane. M.p. 80–81° ([14]: m.p. 87–88°). IR (KBr): 1763*s*, 1740*s*. ^{1}H-NMR ($CDCl_3$): 1.27–1.42 (*m*, 2 H); 1.63–1.83 (*m*, 4 H); 1.77 (*s*, 6 H); 1.96–2.12 (*m*, 2 H); 2.58–2.69 (*m*, 2 H). ^{13}C-NMR ($CDCl_3$): 18.08, 20.32, 27.44, 32.73, 35.84, 103.97, 164.77, 169.13. MS: 208 (3, $[M - CH_4]^+$), 167 (17), *166* (100), 165 (5), 149 (19), 148 (62), 139 (13), 138 (95), 137 (8), 125 (7), 124 (8), 123 (23), 122 (21), 121 (15), 120 (62), 112 (15), 110 (17), 109 (6), 107 (5), 99 (6), 97 (4), 96 (5), 95 (7), 94 (27), 93 (43), 92 (9), 91 (16), 84 (15), 83 (4), 82 (9), 81 (34), 80 (24), 79 (54), 78 (8), 77 (19), 69 (5), 68 (49), 67 (8), 66 (12), 65 (11), 59 (17), 57 (6), 56 (4), 55 (12), 54 (5), 53 (13), 52 (7), 51 (4), 44 (4), 43 (29), 42 (5), 41 (18), 40 (5), 39 (11), 29 (6), 28 (14), 27 (8), 18 (18).

Bicyclo[4.1.0]heptane-7,7-dicarbonitrile (**5**). To a soln. of Me_2S_2 (4.71 g, 50 mmol) in CH_2Cl_2 (30 ml) was added SO_2Cl_2 (6.75 g, 50 mmol) at −50°. After stirring for 5 min, cyclohexene (**3b**; 8.22 g, 100 mmol) was added

dropwise at −50° within 15 min. The solvent and SO_2 were evaporated at r.t., and the residual oil was transferred by means of a pipette into a soln. of sodiomalononitrile (prepared from a suspension of NaH (4.8 g, 110 mmol) in THF (50 ml) and malononitrile (7.27 g, 110 mmol) in THF (50 ml)) and heated under reflux for 15 h. The solvent was distilled off, H_2O (100 ml) added, and the mixture extracted with Et_2O (4 × 100 ml). The extracts were washed with brine (100 ml) and dried ($MgSO_4$), and the solvent was distilled off. To the remaining brown oil, dimethyl sulfate (18.90 g, 150 mmol) was added and the mixture allowed to stand at r.t. for 120 h. To the crude solid, Et_3N (15 g, 150 mmol) in DMF (50 ml) was added and stirred at r.t. for 90 min. The solvent was distilled off (80°/50 Torr), 1M HCl (100 ml) added, and the mixture extracted with Et_2O (4 × 100 ml). The combined extracts were washed with aq. $NaHCO_3$ soln. (100 ml) and brine (100 ml) and dried ($MgSO_4$), and the solvent was distilled off. The residue (orange oil) crystallized partially after 17 h at −20°. The supernatant liquid was decanted, the crystals were dissolved in cyclohexane, and the soln. was filtered through SiO_2. Crystallization yielded 3.76 g (26%) of **5**. White plates. M.p. 58.5–59°. An anal. sample was obtained by recrystallization from cyclohexane. M.p. 60.5–61.5°. IR (KBr): 2242*m*, 1450*m*, 1050*m*. ^{1}H-NMR ($CDCl_3$): 1.30–1.60 (*m*, 4 H); 1.80–2.00 (*m*, 2 H); 2.10–2.30 (*m*, 4 H). ^{13}C-NMR ($CDCl_3$): 9.12, 19.57, 19.73, 29.54, 113.52, 116.36. MS: 147 (20), 146 (67, $M^{+\cdot}$), 133 (8), 132 (63), 130 (6), 129 (5), 121 (7), 120 (22), 119 (21), 118 (5), 107 (19), 106 (44), 105 (18), 94 (5), 81 (6), 80 (13), 79 (13), 78 (17), 77 (16), 76 (5), 68 (28), 67 (24), 66 (7), 65 (9), 64 (9), 63 (9), 56 (8), *55* (100), 54 (9), 53 (15), 52 (7), 51 (10), 42 (24), 41 (38), 40 (5), 39 (32), 29 (6), 28 (16), 27 (15), 18 (22), 17 (8).

3. *Cbl-Catalyzed Isomerization. (R)-5-(Cyclopent-2-enyl)-2,2-dimethyl-1,3-dioxane-4,6-dione* ((+)-**2a**). A 500-ml vessel containing H_2O (300 ml), NH_4Cl (2 g), Zn powder (20 g), and a magnetic stirrer bar was sonicated in an ultrasonic bath for 1 min. After Ar had been bubbled through the soln. for 10 min, OH–Cbl·HCl (1.38 g, 1 mmol) was added. Stirring under Ar led to a color change from red to dark green (Cbl(I)) within a few min. To this mixture, a soln. of **1a** (10.5 g, 50 mmol) in THF (25 ml, previously flushed with Ar) was injected at once (→ fine dispersion of **1a**). After 2 h of stirring at r.t. (TLC: no **1a** left), 1M $KHSO_4/H_2O$ (50 ml) was added to the dispersion and the aq. phase extracted with Et_2O (4 × 150 ml). Drying of the extracts ($MgSO_4$) and evaporation yielded 9.08 g (87%) of **2a**. White, fluffy solid. M.p. 117–122°. $[\alpha]_D^{22} = +101.3$ ($c = 0.72$, MeOH). The ee of this crude **2a** was determined to be 81% after conversion to the iodolactone (−)-**13a** and enantioselective GC on column *A* (*vide infra*). An anal. sample of **2a** was obtained by recrystallization from MeOH. M.p. 124–125°. $[\alpha]_D^{22} = +101.6$ ($c = 0.32$, MeOH). IR (KBr): 3070*w*, 1780*s*, 1740*s*. ^{1}H-NMR ($CDCl_3$): 1.77 (*s*, 3 H); 1.80 (*s*, 3 H); 1.80–1.90 (*m*, 1 H); 2.20–2.34 (*m*, 1 H); 2.37–2.43 (*m*, 1 H); 2.46–2.58 (*m*, 1 H); 3.60–3.68 (*m*, 2 H); 5.71–5.75 (*m*, 1 H); 5.89–5.93 (*m*, 1 H). ^{13}C-NMR ($CDCl_3$): 27.41, 27.48, 28.47, 32.31, 45.49, 50.00, 104.88, 129.98, 133.76, 164.90, 164.96. MS: 195 (14, $[M - Me]^+$), 182 (31), 153 (7), 152 (43), 146 (4), 145 (47), 135 (20), 134 (48), 129 (52), 125 (15), *124* (100), 123 (15), 109 (11), 108 (67), 107 (54), 106 (21), 96 (15), 87 (5), 84 (4), 81 (8), 80 (48), 79 (67), 78 (17), 77 (33), 69 (6), 68 (14), 67 (74), 66 (81), 65 (14), 61 (10), 59 (33), 58 (4), 55 (5), 53 (8), 52 (8), 51 (9), 44 (4), 43 (44), 41 (19), 40 (6), 39 (16), 27 (6), 18 (12). Anal. calc. for $C_{11}H_{14}O_4$ (210.23): C 62.85, H 6.71; found: C 62.78, H 6.70.

The ee of crude **2a** from a similar reaction was increased from 78 to 81% by 2 recrystallizations from cyclohexane, and from 81 to 95% by 2 recrystallizations from MeOH.

(R)-5-(Cyclohex-2-enyl)-2,2-dimethyl-1,3-dioxane-4,6-dione ((+)-**2b**). As described for **2a**. Yield 98%. White, fluffy solid. M.p. 126–127°. $[\alpha]_D^{22} = +28.9$ ($c = 0.31$, MeOH). Enantioselective GC (column *C*, 70°) showed 4 signals: t_R 5.71 (8.30%; (*R*)-cyclohex-2-enyl ketene (GC-MS)), 5.94 (46.06%; (*S*)-cyclohex-2-enyl ketene), corresponding to 70% ee of (+)-**2b**; 20.04 (7.30%; (−)-**2b**), 20.50 (38.35%; (+)-**2b**), corresponding to 68% ee of (+)-**2b**. An anal. sample of (+)-**2b** was obtained by recrystallization from MeOH. M.p. 131–132°. $[\alpha]_D^{22} = +30.7$ ($c = 0.14$, MeOH). IR (KBr): 1775*s*, 1742*s*. ^{1}H-NMR ($CDCl_3$): 1.52–1.92 (*m*, 4 H); 1.78 (*s*, 3 H); 1.81 (*s*, 3 H); 1.97–2.18 (*m*, 2 H); 3.21–3.32 (*m*, 1 H); 3.56 (*d*, $J = 3.3$, 1 H); 5.53 (*d*, $J = 8.5$, 1 H); 5.79–5.88 (*m*, 1 H). ^{13}C-NMR ($CDCl_3$): 22.31, 24.52, 25.72, 27.65, 28.28, 36.89, 50.33, 104.85, 127.14, 129.39, 164.76, 164.91. MS: 208 (2, $[M - CH_4]^+$), 166 (8), 148 (7), 139 (9), *138* (100), 129 (6), 123 (8), 122 (41), 121 (18), 120 (12), 110 (9), 107 (15), 95 (5), 94 (54), 93 (45), 92 (8), 91 (15), 82 (4), 81 (36), 80 (47), 79 (42), 78 (7), 77 (23), 68 (6), 67 (4), 66 (23), 65 (8), 60 (7), 59 (15), 55 (7), 53 (8), 51 (4), 44 (5), 43 (28), 41 (13), 40 (4), 39 (8), 28 (8), 27 (7), 18 (9). Anal. calc. for $C_{12}H_{16}O_4$ (224.26): C 64.27, H 7.19; found: C 64.32, H 7.24.

4. *Determination of the Configuration. (R)-Cyclopent-2-en-1-ol* [9] ((+)-**11a**). Through a mixture of MeOH (80 ml), NH_4Cl (8 g), and activated Zn wool (5 g; wrapped around a magnetic stirrer bar), Ar was bubbled for 10 min by means of a syringe needle. After addition of OH–Cbl·HCl (4.15 g, 3.00 mmol) and stirring for 0.5 h, the color changed from red to dark green (cob(I)alamin). Epoxide **10a** [20] (25.25 g, 300 mmol) was injected at once (→ red-brown (alkylcob(III)alamin). After 6 d of stirring under Ar at r.t. (GC: no **10a** left), Et_2O (200 ml) was added, the red-brown precipitation filtered off over *Celite* and washed with Et_2O (2 × 100 ml), the slightly red filtrate dried ($MgSO_4$), filtered through *Celite*, and evaporated, and the residual clear, brownish oil distilled over a 10-cm

Vigreux column (58–59°/18 Torr): 17.25 g (66%) of **11a**. Clear, colorless oil. Purity 97.5% (GC). Enantioselective GC (column *A*, 50°): t_R 7.49 (17.82%; (−)-**11a**), 8.13 (79.82%; (+)-**11a**), corresponding to 62% ee of (+)-**11a**. $[\alpha]_D^{22}$ = +89.7 (neat). IR (film): 3600–2700 (br.), 3060*m*, 1050*m*. ^{1}H-NMR ($CDCl_3$): 1.60–1.82 (*m*, 1 H); 2.15–2.33 (*m*, 2 H); 2.42–2.58 (*m*, 1 H); 2.82 (*d*, *J* = 6.6, OH); 4.80–4.91 (*m*, 1 H); 5.78–5.87 (*m*, 1 H); 5.92–6.00 (*m*, 1 H). ^{13}C-NMR ($CDCl_3$): 31.01, 33.11, 77.35, 133.41, 134.84. MS: 84 (45, M^+), *83* (100), 82 (8), 69 (7), 67 (15), 66 (37), 65 (21), 63 (4), 57 (13), 56 (18), 55 (58), 54 (4), 53 (10), 51 (6), 43 (14), 42 (14), 41 (31), 40 (17), 39 (40).

(S)-(Cyclopent-2-enyl)acetic Acid ((+)-**12a**). A suspension of (+)-**2a** (6.30 g, 30 mmol) in 1M HCl (100 ml) was stirred at 60° until a clear soln. was formed (22 h). Extraction with Et_2O (6 × 50 ml), drying of the extracts ($MgSO_4$), and evaporation gave a white powder (5.84 g, dicarboxylic acid). Heating of the diacid to 200° (15 min, 400 Torr) caused melting and decarboxylation. Bulb-to-bulb distillation (200°/50 Torr) afforded 3.45 g (91%) of (+)-**12a**. Clear, slightly yellow liquid. $[\alpha]_D^{22}$ = +86.6 (neat). IR (film): 3700–2200 (br.), 1700*s*. ^{1}H-NMR ($CDCl_3$): 1.43–1.56 (*m*, 1 H); 2.10–2.23 (*m*, 1 H); 2.27–2.50 (*m*, 4 H); 3.04–3.18 (*m*, 1 H); 5.68–5.72 (*m*, 1 H); 5.77–5.82 (*m*, 1 H); 10.10 (br., 1 H). ^{13}C-NMR ($CDCl_3$): 29.67, 31.64, 40.24, 41.79, 131.77, 133.42, 179.57. MS: 126 (27, M^+), 109 (7), 108 (70), 98 (4), 97 (8), 83 (7), 81 (14), 80 (23), 79 (31), 77 (12), 69 (4), 68 (11), *67* (100), 66 (72), 65 (16), 60 (12), 55 (8), 54 (5), 53 (8), 41 (20), 39 (13), 28 (9), 18 (37), 17 (6).

(3aS,6R,6aR)-Hexahydro-6-iodo-2H-cyclopenta[b]furan-2-one ((−)-**13a**). A soln. of I_2 (12.5 g, 50 mmol) and KI (25 g, 150 mmol) in H_2O (75 ml) was added to a soln. of (+)-**12a** (3.15 g, 25 mmol) in 0.5M aq. $NaHCO_3$ (150 ml, 75 mmol) and allowed to stand at r.t. in the dark for 64 h. A 20% aq. $Na_2S_2O_3$ soln. (150 ml) was added and the nearly colorless soln. extracted with Et_2O (4 × 100 ml). Enantioselective GC of the combined extracts (column *A*, 120°): t_R 30.43 (90.4%; (−)-**13a**), 31.69 (9.6%; (+)-**13a**), corresponding to 81% ee of (−)-**13a**. The Et_2O soln. was dried ($MgSO_4$) and evaporated: yellow oil (6.25 g) that crystallized. Recrystallization from hexane/Et_2O gave 3.84 g (61%) of (−)-**13a**. Long, yellowish needles. M.p. 68–69°. $[\alpha]_D^{22}$ = −51.8 (*c* = 0.39, MeOH). Enantioselective GC (column *A*, 120°): t_R 30.27 (100%; (−)-**13a**). IR (KBr): 1170*s*, 1180*m*, 1000*m*. ^{1}H-NMR ($CDCl_3$): 1.56–1.67 (*m*, 1 H); 2.00–2.23 (*m*, 2 H); 2.39 (*dd*, *J* = 18.4, 2.2, 1 H); 2.40–2.54 (*m*, 1 H); 2.91 (*dd*, *J* = 18.4, 9.9, 1 H); 3.12–3.24 (*m*, 1 H); 4.49 (*d*, *J* = 4.8, 1 H); 5.23 (*d*, *J* = 6.3, 1 H). ^{13}C-NMR ($CDCl_3$): 29.40, 32.09, 34.64, 36.02, 36.10, 92.32, 176.48. MS: 253 (4), 252 (56, M^+), 223 (11), 155 (5), 154 (5), 127 (5), 126 (15), *125* (100), 108 (6), 107 (70), 97 (51), 96 (7), 95 (30), 83 (45), 82 (4), 81 (48), 80 (15), 79 (69), 78 (5), 77 (17), 70 (5), 69 (67), 68 (12), 67 (42), 66 (9), 65 (9), 59 (4), 57 (8), 56 (4), 55 (62), 54 (6), 53 (27), 52 (7), 51 (7), 43 (13), 42 (17), 41 (72), 40 (13), 39 (45), 31 (4), 29 (14), 28 (11), 27 (35), 18 (42), 17 (9).

(S)-(Cyclohex-2-enyl)acetic Acid ((+)-**12b**). As described for (+)-**12a**, (+)-**2b** was hydrolyzed (64 h) and decarboxylated (250°/400 Torr, 15 min). Yield 92%. Clear, slightly yellow liquid. $[\alpha]_D^{22}$ = +38.2 (neat). IR (film): 3700–2200 (br.), 1710*s*. ^{1}H-NMR ($CDCl_3$): 1.27–1.49 (*m*, 1 H); 1.50–1.66 (*m*, 1 H); 1.66–1.79 (*m*, 1 H); 1.82–1.94 (*m*, 1 H); 1.95–2.04 (*m*, 2 H); 2.31 (*dd*, *J* = 15.4, 8.1, 1 H); 2.49 (*dd*, *J* = 15.4, 7.0, 1 H); 2.54–2.69 (*m*, 1 H); 5.53–5.62 (*m*, 1 H); 5.70–5.80 (*m*, 1 H); 10.74 (br., 1 H). ^{13}C-NMR ($CDCl_3$): 20.94, 25.00, 28.77, 32.04, 40.62, 128.41, 129.82, 179.37. MS: 141 (9), 140 (60, M^+), 139 (7), 123 (11), 122 (61), 121 (4), 112 (10), 111 (17), 98 (11), 97 (30), 96 (34), 95 (23), 94 (32), 93 (11), 91 (8), 84 (15), 83 (16), 82 (16), 81 (83), *80* (100), 79 (67), 78 (19), 77 (20), 71 (6), 70 (17), 69 (14), 68 (47), 67 (53), 66 (12), 65 (8), 61 (9), 60 (4), 57 (12), 56 (9), 55 (45), 54 (21), 53 (18), 43 (12), 42 (7), 41 (30), 40 (4), 39 (18), 29 (6), 28 (4), 27 (7), 18 (9).

(3aS,7R,7aR)-Octahydro-7-iodobenzofuran-2-one ((−)-**13b**). A soln. of I_2 (2.50 g, 10 mmol) and KI (5 g, 30 mmol) in H_2O (15 ml) was added to a soln. of (+)-**12b** (0.70 g, 5 mmol) in 0.5M aq. $NaHCO_3$ (30 ml, 15 mmol) and allowed to stand at r.t. in the dark for 22 h. A 20% aq. $Na_2S_2O_3$ soln. (30 ml) was added and the nearly colorless soln. extracted with Et_2O (4 × 20 ml). Enantioselective GC of the combined extracts (column *B*, 150 → 230°, 2°/min): t_R 31.20 (82.89%; (−)-**13b**), 33.68 (17.11%; (+)-**13b**), corresponding to 66% ee of (−)-**13b**. The Et_2O soln. was dried ($MgSO_4$) and evaporated: yellow oil (1.22 g) that crystallized. Recrystallization from hexane/Et_2O yielded 0.61 g (46%) of (−)-**13b**. Yellowish crystals. M.p. 94–96°. Enantioselective GC (column *B*, 150 → 230°, 2°/min): t_R 31.25 (99.48%; (−)-**13b**), 33.87 (0.52%; (+)-**13b**) corresponding to 99% ee of (−)-**13b**. An anal. sample was obtained by a 2nd recrystallization from hexane/Et_2O. Slightly yellow crystals. M.p. 96–96.5°. $[\alpha]_D^{22}$ = −56.6 (*c* = 0.41, MeOH). Enantioselective GC (column *B*, 150 → 230°, 2°/min): t_R 30.84 (100%; (−)-**13b**). IR (KBr): 1768*s*, 1158*m*, 969*m*. ^{1}H-NMR ($CDCl_3$): 1.26–1.41 (*m*, 1 H); 1.49–1.64 (*m*, 1 H); 1.65–1.88 (*m*, 2 H); 1.88–2.02 (*m*, 2 H); 2.30 (*dd*, *J* = 16.9, 3.3, 1 H); 2.59 (*dd*, *J* = 16.9, 6.6, 1 H); 2.75–2.87 (*m*, 1 H); 4.60–4.64 (*m*, 1 H); 4.71 (*t*, *J* = 4.4, 1 H). ^{13}C-NMR ($CDCl_3$): 20.55, 26.47, 27.68, 30.66, 32.60, 37.03, 83.06, 176.08. MS: 267 (11), 266 (90, M^+), 141 (8), 140 (65), 139 (94), 123 (9), 122 (62), 121 (55), 112 (5), 111 (13), 97 (24), 96 (6), 95 (37), 94 (25), 93 (38), 92 (4), 91 (14), 84 (7), 83 (14), 82 (10), 81 (72), *80* (100), 79 (73), 78 (21), 77 (28), 70 (9), 69 (7), 68 (10), 67 (49), 66 (7), 65 (10), 61 (33), 60 (4), 57 (9), 56 (5), 55 (39), 54 (14), 53 (18), 51 (4), 43 (13), 41 (33), 39 (19), 29 (5), 27 (7).

Ethyl (R)-2-(Cyclopent-2-enyl)acetate. A soln. of **11a** (2.88 g, 33.3 mmol; ee (GC) 60.6%), triethyl orthoacetate (25 ml), and hydrochinone (0.11 g, 1 mmol) was stirred in a hot oil bath (140°; 10-cm *Vigreux* column,

distillation head). After 15 h, 2.2 ml of EtOH had been distilled off. The temp. of the oil bath was raised to 170° which led to distillation of most of the excessive orthoacetate (*ca.* 16 ml) within 30 min. After 7 h at 170°, the residual brown mixture was distilled (58–86°/20 Torr) to afford a clear, colorless oil (4.31 g). GC: 70% of ethyl (cyclopentenyl)acetate (*i.e.* 59% yield) and 30% triethyl orthoacetate. $[\alpha]_D^{22} = -16.7$ (neat); ee (GC)[3] 54.7%. An anal. sample was obtained by flash chromatography (SiO_2, AcOEt/hexane 1:9). IR (film): 3060*w*, 1740*s*, 1030*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.27 (*t*, 3 H); 1.43–1.51 (*m*, 1 H); 2.08–2.18 (*m*, 1 H); 2.26–2.43 (*m* 4 H); 3.06–3.14 (*m*, 1 H); 4.15 (*q*, 2 H); 5.65–5.70 (*m*, 1 H); 5.75–5.80 (*m*, 1 H). ^{13}C-NMR (25.2 MHz, $CDCl_3$): 14.29, 29.61, 31.85, 40.50, 42.09, 60.20, 131.41, 133.75, 172.99. MS: 154 (5, $M^{+\cdot}$), 125 (11), 109 (9), 108 (12), 107 (11), 88 (18), 83 (18), 81 (6), 80 (19), 79 (26), 70 (8), 68 (5), *67* (100), 66 (37), 65 (7), 61 (7), 60 (8), 53 (4), 41 (17), 39 (7), *29* (10), 28 (9), 27 (4).

(3aR,6S,6aS)-Hexahydro-6-iodo-2H-cyclopenta[b]furan-2-one ((+)-**13a**). A soln. of the crude ethyl (*R*)-2-(cyclopent-2-enyl)acetate (3.3 g, 70% pure according to GC, 15 mmol; ee 54.7%) in EtOH (90 ml) and 0.5M NaOH (90 ml, 45 mmol) was allowed to stand at r.t. for 2 h. Crushed dry ice (30 g) was added. After the evolution of CO_2 had ceased, a soln. of I_2 (7.5 g, 30 mmol) and KI (15 g, 90 mmol) in H_2O (45 ml) was added and the mixture allowed to stand at r.t. in the dark for 20 h. A 20% $Na_2S_2O_3$ soln. was added slowly until the color of I_2 just disappeared (*ca.* 40 ml). The clear, slightly yellow soln. was kept at 4° for 2 h and then seeded with (+)-**13a**. After 5 d at 4°, enantiomerically pure (enantioselective GC) (+)-**13a** (0.79 g, 21%) crystallized. Long, white needles. M.p. 62–63°. An anal. sample was obtained by recrystallization from hexane/Et_2O. M.p. 68–69°. $[\alpha]_D^{22} = +53.7$ ($c = 0.3$, MeOH). Spectral data: identical with those of (−)-**13**.

REFERENCES

[1] R.W. Kierstead, R.W. Linstead, B.C.L. Weedon, *J. Chem. Soc.* **1952,** 3610; P.L. Fuchs, *J. Am. Chem. Soc.* **1974,** *96,* 1607; W.G. Dauben, *ibid.* **1975,** *97,* 1622.

[2] J.M. Steward, H.H. Westberg, *J. Org. Chem.* **1965,** *30,* 1951.

[3] R.K. Singh, S. Danishefsky, *J. Org. Chem.* **1976,** *41,* 1668.

[4] J.E. Dolfini, K. Menich, P. Corlias, S. Danishefsky, R. Cavanaugh, S. Chakrabartty, *Tetrahedron Lett.* **1966,** 4421.

[5] E.J. Corey, P.L. Fuchs, *J. Am. Chem. Soc.* **1972,** *94,* 4014.

[6] H. Ogoshi, J. Setsune, Z. Yoshida, *J. Chem. Soc., Chem. Commun.* **1975,** 572.

[7] H. Ogoshi, Y. Kikuchi, T. Yamaguchi, H. Toi, Y. Aoyama, *Organometallics* **1987,** *6,* 2175.

[8] S. Danishefsky, R.K. Singh, *J. Am. Chem. Soc.* **1975,** *97,* 3239.

[9] H. Su, L. Walder, Z.-da Zhang, R. Scheffold, *Helv. Chim. Acta* **1988,** *71,* 1073.

[10] Z.-da Zhang, R. Scheffold, *Helv. Chim. Acta* **1993,** *76,* 2602.

[11] C.G. Frost, J. Howarth, J.M.J. Williams, *Tetrahedron: Asymmetry* **1992,** *3,* 1089; O. Reiser, *Angew. Chem.* **1993,** *105,* 576.

[12] J. Ohishi, *Synthesis* **1980,** 690.

[13] H. Musso, *Chem. Ber.* **1968,** *101,* 3710.

[14] S. Danishefsky, R.K. Singh, *J. Org. Chem.* **1975,** *40,* 2969.

[15] A.J. Anciaux, A.J. Hubert, A.F. Noels, N. Petiniot, P. Teyssié, *J. Org. Chem.* **1980,** *45,* 695.

[16] R.E. Ireland, R.H. Müller, *J. Am. Chem. Soc.* **1972,** *94,* 5897.

[17] W.S. Johnson, L. Werthemann, W.R. Bartlett, T.J. Brocksom, T. Li, D. Faulkner, M.R. Peterson, *J. Am. Chem. Soc.* **1970,** *92,* 741.

[18] P. Bonhôte, R. Scheffold, *Helv. Chim. Acta* **1991,** *74,* 1425.

[19] J.N.Grate, G.N. Schrauzer, *J. Am. Chem. Soc.* **1979,** *101,* 4601.

[20] L. Goodman, A. Benitez, B.R. Baker, *J. Am. Chem. Soc.* **1958,** *80,* 1680.

[3]) For determination of the ee, the ethyl (cyclopentenyl)acetate (2 drops) was dissolved in 0.5M NaOH (1 ml). After 1 h, little dry ice, followed by a few drops of an aq. I_2/KI soln. was added. After 10 min, the mixture was decolorized with a $Na_2S_2O_3$ soln. and shaken with Et_2O (0.5 ml). The Et_2O phase containing iodolactone **13** was directly analyzed.