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TETRAHEDRON

Enantioselective Copper-Catalyzed Cyclopropanation of Silyl Enol Ethers

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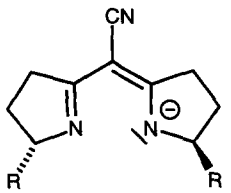
Abstract: Copper(I) complexes derived from semicorrins, azasemicorrins and bisoxazolines are efficient catalysts for the enantioselective cyclopropanation of silyl enol ethers with diazoacetates. The resulting cyclopropanes can be converted to γ-ketocarboxylates by acid-induced ring cleavage. In this way methyl (2-oxocyclopentyl)- and (2-oxocyclohexyl)acetates have been prepared with up to 90 and 80% ee, respectively. © 1998 Elsevier Science Ltd. All rights reserved.

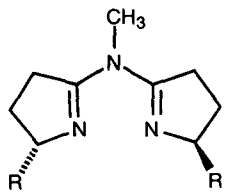
INTRODUCTION

Metal-catalyzed cyclopropanation has become one of the most versatile methods for enantioselective C-C bond formation.[1-5] The most efficient and most general catalysts are chiral dinuclear rhodium(II) complexes[3] and copper complexes with chiral heterocyclic nitrogen ligands such as semicorrins **1**[4], azasemicorrins **2**[4c] or bisoxazolines of type **3**.[2g,4de,5]



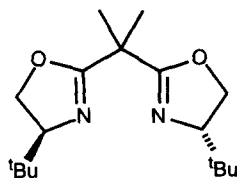
R = CMe_2OH

1



R = CMe_2OSiMe_3

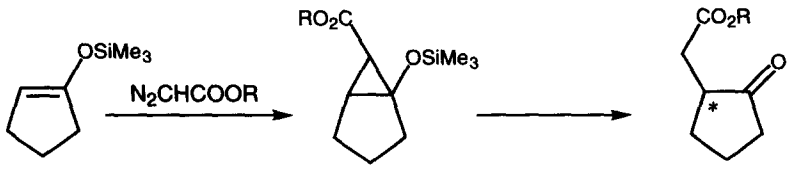
2



3

An interesting class of substrates for the enantioselective cyclopropanation are silyl enol ethers. *Reißig et al.* have carried out extensive studies of the cyclopropanation of these substrates with diazoacetates.[6] They have also shown that subsequent ring cleavage leads to γ-ketocarboxylates which are useful precursors for organic synthesis (Scheme 1).

Scheme 1



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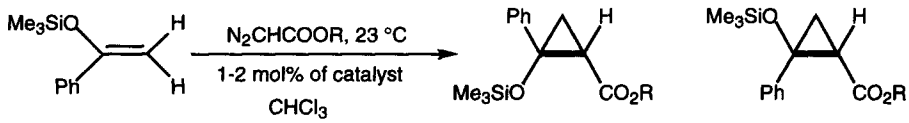
The best enantioselectivities (>95% ee) have been reported for the cyclopropanation of 1-(trimethylsilyloxy)styrene derivatives bearing electron-withdrawing *para*-substituents and 2-(trimethylsilyloxy)-1,3-butadiene using the bisoxazoline ligand **3**.[6ab] However, the enantioselectivities achieved so far in the transformation shown in Scheme 1 are unsatisfactory. Here, we report that under optimized conditions, synthetically useful ee's and yields can be obtained in the conversion of 1-(silyloxy)cyclopentene and -hexene to the corresponding γ-ketocarboxylates using Cu complexes with azasemicorrins **2** or bisoxazolines **3** as catalysts.

ENANTIOSELECTIVE CYCLOPROPANATION

The synthesis of ligands **1-3** has been previously described.[4,5] During the course of this work, we developed a convenient alternative procedure for the preparation of the bis(*tert*-butyl)oxazoline **3** from dimethylmalonodinitrile in one step using the method of *Witte* and *Seeliger*.[7]

As a test reaction, the cyclopropanation of 1-(trimethylsilyloxy)styrene with different alkyl diazoacetates was chosen (Table 1). The reactions were carried out at room temperature using standard procedures.[4ac,5]

Table 1. Enantioselective Cyclopropanation of 1-(Trimethylsilyloxy)styrene



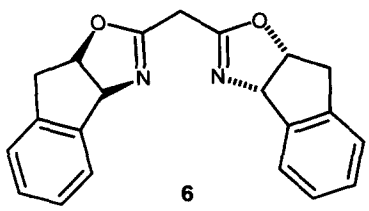
4 **5**

Catalyst	Diazoacetate R	Solvent	% Yield 4 + 5	*cis* / *trans*[a] 4 : 5	% ee[a] 4	% ee[a] 5
$[Cu(\mathbf{1})_2]$[b]	Methyl	$Cl(CH_2)_2Cl$	74	28 : 72	63	80
2 / Cu(I)OTf	Methyl	$Cl(CH_2)_2Cl$	70	36 : 64	68	64
3 / Cu(I)OTf	Methyl	$CHCl_3$	82	48 : 52	96	89
2 / Cu(I)OTf	Ethyl	$Cl(CH_2)_2Cl$	81	32 : 68	77	77
3 / Cu(I)OTf	Ethyl	$CHCl_3$	77	44 : 56	95	90
2 / Cu(I)OTf	*tert*-Butyl	$Cl(CH_2)_2Cl$	82	35 : 65	60	70

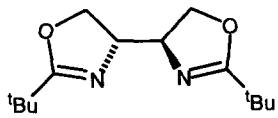
a) Determined by GC; *cis/trans* assignments: see ref. 6c. b) The catalyst was activated by treatment with phenylhydrazine (see exp. procedure in ref. 4a).

Interestingly, the *trans/cis* selectivity is dependent on the ligand (ca. 5:2 with **1**, 1:1 with **3**), in contrast to the cyclopropanation of styrene which affords essentially identical *trans/cis* ratios with ligands **1-3**. On the other hand, as observed by *Reißig et al.*,[6] very similar *trans/cis* ratios are obtained with methyl, ethyl and *tert*-butyl diazoacetate whereas in analogous reactions with styrene, more bulky esters such as *tert*-butyl diazoacetate give significantly higher *trans/cis* selectivities than methyl or ethyl diazoacetate.

In chloroform with methyl diazoacetate, 96% ee for the *cis* and 89% ee for the *trans* product were obtained, whereas in 1,2-di-chloroethane or dichloromethane the ee's were lower. Consistent with our findings,[8] *Reißig et al.* reported 77% ee for the *cis* and 56% ee for the *trans* product in this cyclopropanation with ligand **3** in 1,2-di-chloroethane.[6a]



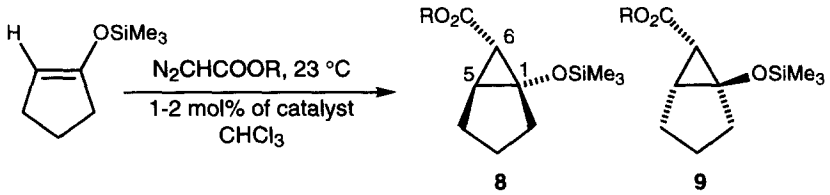
6



7

Table 2 summarizes the results for the cyclopropanation of 1-(trimethylsilyloxy)cyclopentene. The best enantioselectivities were recorded in the reaction with methyl diazoacetate and ligand **3**. The azasemicorrin **2** gave higher yields but lower ee's. In addition, ligands **6**[9] and **7**[10] were also tested. An interesting reversal of the *cis/trans* ratio was observed with the indanolamine ligand **6**, however, the chemical yields were low. The bisoxazoline **7** and related derivatives gave only very low ee's.

Table 2. Enantioselective Cyclopropanation of 1-(Trimethylsilyloxy)cyclopentene



8 9

Catalyst	Diazoacetate R	% Yield 8 + 9	*cis* / *trans*[a] 8 : 9	% ee[a] 8	% ee[a] 9	Configuration 8	Configuration 9
[Cu(**1**)$_2$][b]	Methyl	54	81 : 19	79	11	1R, 5S, 6S	1S, 5R, 6S
2 / Cu(I)OTf	Methyl	90	68 : 32	85	43	1R, 5S, 6S	1S, 5R, 6S
3 / Cu(I)OTf	Methyl	56	73 : 27	92	87	1S, 5R, 6R	1R, 5S, 6R
6 / Cu(I)OTf	Methyl	35	41 : 59	41	63	1S, 5R, 6R	1R, 5S, 6R
7 / Cu(I)OTf	Methyl	53	70 : 30	24	6	1R, 5S, 6S	1S, 5R, 6S
2 / Cu(I)OTf	Ethyl	70	73 : 27	56	56	1R, 5S, 6S	1S, 5R, 6S
3 / Cu(I)OTf	Ethyl	46	75 : 25	85	40	1S, 5R, 6R	1R, 5S, 6R
7 / Cu(I)OTf	Ethyl	60	65 : 35	0	0	-	-

a) Determined by GC. b) The catalyst was generated from [Cu(**1**)$_2$] by treatment with phenylhydrazine (ref. 4a). The reaction was performed in Cl(CH$_2$)$_2$Cl.

The relative configuration of the products was determined by NOE experiments. For the *cis* isomer **8** a distinct NOE between the trimethylsilyl protons and the methyl protons of the ester function was observed, while the *trans* isomer **9** exhibited no NOE between these groups.

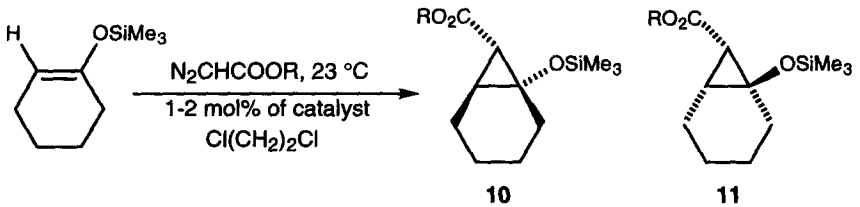
After screening of different ligands and reaction conditions, we worked out a suitable procedure for preparative scale reactions. We observed that with increasing scale a side reaction leading to methyl [2-(trimethylsilyloxy)cyclopenten-1-yl]acetate gained importance. It seemed likely that this rearrangement of the products **8** and **9** (R = Me) was catalyzed by the copper complex acting as a Lewis acid. By addition of 2 mol% of 2,2,6,6-tetramethylpiperidine, it was possible to suppress this side reaction.

Another problem encountered with increasing scale is the instability of the products **8** and **9** during flash column chromatography on silica gel. It is essential to cleanly separate the *cis/trans* isomers **8** and **9** before subjecting them to the ring-opening procedure (Scheme 2). As shown in Table 2 and Scheme 2, the absolute configuration of the two isomers at C(5) is different and, consequently, ring-opening of **8** and **9** leads to opposite enantiomers of **14**. This implies that the use of a *cis/trans* mixture of **8** and **9** results in a ring-opened product of low enantiomeric purity. Therefore it was necessary to find a suitable chromatographic method for

separating the two isomers. Using a florisil™ column and hexane/Et_2O (95:5) as eluent, it was possible to obtain the pure *cis* and *trans* isomers in satisfactory yield. In an experiment with 15 mmol of 1-(trimethylsilyloxy)cyclopentene, 30 mmol of methyl diazoacetate, 2 mol% of CuOTf/**3** and 2 mol% of 2,2,6,6-tetramethylpiperidine in chloroform, the two isomeric products were isolated in a total yield of 43% (**8**:**9** = 66:34, **8**: 90% ee, **9**: 84% ee).

As an alternative solution of this problem, we decided to increase the stability of the labile silyl ether function by replacing the trimethylsilyl by a triisopropylsilyl group. Cyclopropanation of 1-(triisopropylsilyloxy)cyclopentene with methyl diazoacetate under standard conditions led to the products in good yield and the ee's were essentially the same as in the cyclopropanation of the corresponding trimethylsilyl derivatives. The *cis* and *trans* products proved to be sufficiently stable to allow separation by MPLC on silica gel (hexane/EtOAc 97:3). In this way, the pure *cis* and *trans* isomers could be isolated in a total yield of 56% (*cis*:*trans* = 52:48; 89 and 84% ee, respectively) in an experiment on a 5.0 mmol scale with 2 mol% of **3**/CuOTf.

Table 3. Enantioselective Cyclopropanation of 1-(Trimethylsilyloxy)cyclohexene



10 **11**

Catalyst	Diazoacetate R	% Yield **10** + **11**	*cis* / *trans*[a] **10** : **11**	% ee[a] **10**	% ee[a] **11**	Configuration **10**	Configuration **11**
2 / Cu(I)OTf[b]	Methyl	47	61 : 39	69	n.d.	1R, 6S, 7S	1S, 6R, 7S
2 / Cu(I)OTf	Methyl	40	76 : 24	76	n.d.	1R, 6S, 7S	1S, 6R, 7S
3 / Cu(I)OTf[c]	Methyl	7	27 : 73	11	n.d.	1S, 6R, 7R	1R, 6S, 7R
3 / Cu(I)OTf[d]	Methyl	13	78 : 22	18	n.d.	1S, 6R, 7R	1R, 6S, 7R
2 / Cu(I)OTf	Ethyl	25	67 : 33	72	n.d.	1R, 6S, 7S	1S, 6R, 7S
2 / Cu(I)OTf	*tert*-Butyl	39	68 : 32	65	n.d.	1R, 6S, 7S	1S, 6R, 7S

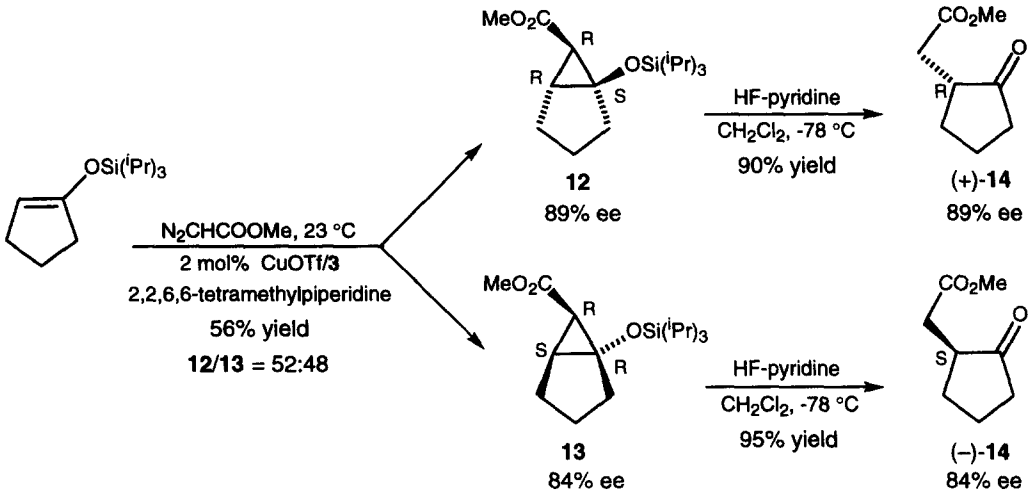
a) Determined by GC. b) At 82 °C. c) In $CHCl_3$. d) In boiling toluene.

The cyclopropanation of 1-(trimethylsilyloxy)cyclohexene (Table 3) proved to be difficult because the enol ether and the resulting silyloxycyclopropanes were found to decompose much more readily than the five-membered ring analogues. With catalyst **3**/CuOTf only very low yields were obtained and the *cis*/*trans* ratios fluctuated considerably from one experiment to the next. The azasemicorrin **2** was the ligand of choice in this case, giving ee's of up to 76% ee with yields ranging between 40 and 50%. Unfortunately, no suitable method for determining the ee of the *trans* product was found. Better results were obtained with the corresponding triisopropylsilyl enol ether. In a reaction on a 5.5 mmol scale with subsequent purification by MPLC, the pure *cis* and *trans* isomers were obtained in a total yield of 50% (*trans*:*cis* = 69:31) with 81 and 86% ee, respectively (Scheme 3).

CLEAVAGE OF THE CYCLOPROPANE RING

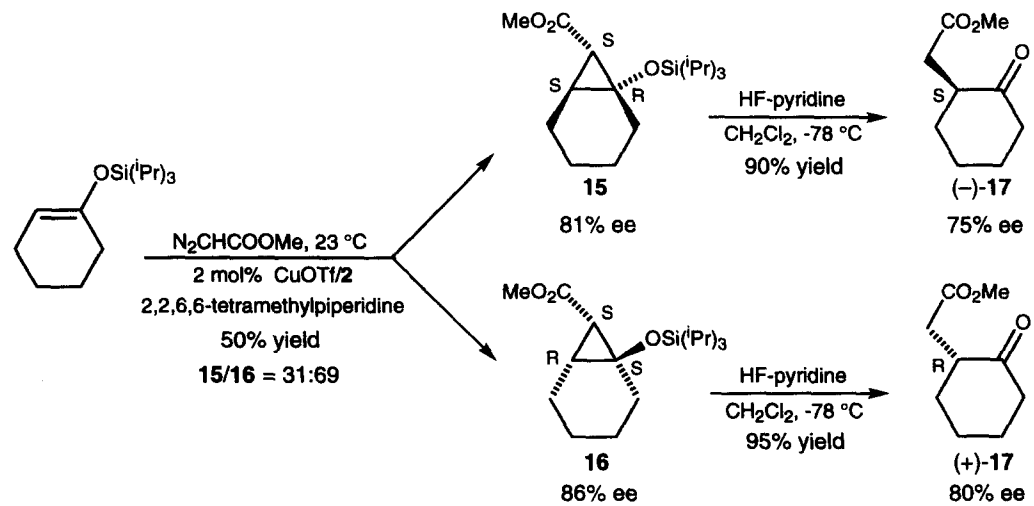
The *cis*- and *trans*-silyloxycyclopropanes could be converted to the corresponding γ-ketocarboxylates in high yield (Schemes 2 and 3).

Scheme 2



The trimethylsilyl derivatives readily underwent electrophilic ring-opening in refluxing methanol containing a few drops of acetic acid. For the ring-opening of the more stable triisopropylsilyl ethers it was more difficult to find a suitable method leading to the desired product without concomitant racemization. After extensive screening of reagents and conditions, the following procedure was worked out: a solution of the (triisopropyloxy)cyclopropane and 25 equivalents of HF-pyridine complex was stirred in dichloromethane at –78 °C for a few hours and then directly filtered through silica gel. After purification by flash column chromatography or Kugelrohr distillation, the product could be isolated in high yields of up to 95%. Using this procedure, methyl (2-oxocyclopentyl)acetate and the corresponding six-membered ring analogue were prepared with ee's of up to 90 and 80%, respectively. As shown in Scheme 3, racemization could not be fully suppressed in the reactions of the cyclohexane derivatives **15** and **16**.

Scheme 3



The absolute configuration of products **14**[11] and **17**[12] was determined based on the optical rotation values reported in the literature. Consequently, the absolute configuration of the silyloxycyclopropanes could be assigned by correlation with the ring-opened products as shown in Schemes 2 and 3.

CONCLUSION

We have shown that silyl enol ethers can be converted to optically active silyloxycyclopropanes with good enantioselectivities by copper-catalyzed cyclopropanation using chiral azasemicorrin or related bisoxazoline ligands. Problems caused by the instability of the trimethylsilyl ethers were overcome by replacing the trimethylsilyl by a triisopropylsilyl group. Starting from triisopropylsilyl enol ethers, the two step sequence, cyclopropanation - ring-opening, allows the enantioselective introduction of an acetic acid side chain at the α-position of cycloalkanones.

Acknowledgement. Financial support by the Swiss National Science foundation and the Max Planck Society is gratefully acknowledged. We thank Dr. David Miller for preparing ligand **7**.

EXPERIMENTAL

General: [Cu(OTf)•$(C_6H_6)_{0.5}$]: Fluka, pract.; chlorobenzene: Fluka, purum.; 1-(trimethylsiloxy)cyclohexene: Fluka, purum; 1-(trimethylsiloxy)cyclopentene: Fluka, purum; 1-phenyl-1-(trimethylsiloxy)ethene: Fluka, purum; methyl and *tert*-butyl diazoacetate: ref. 13 and 14; ethyl diazoacetate: Fluka, purum; L-*tert*-leucinol: prepared from L-*tert*-leucine (Fluka) according to ref. 15; (triisopropyl)silyl enol ethers: prepared according to ref. 16. All reactions were carried out under an argon atmosphere using dried glassware. Flash column chromatography: silica gel 60, Merck; florisil™: 30-60 mesh, Fluka. TLC: silica gel 60, Merck, 0.25 mm. Specific rotations were measured on a Perkin Elmer 241 polarimeter at room temperature or on a Jasco DIP-360 Digital Polarimeter, estimated error ±5%. IR ($CHCl_3$): selected bands in cm^{-1}. NMR ($CDCl_3$): δ in ppm *vs.* TMS, *J* in Hz; ^1H: 300 or 200 MHz; ^{13}C: 75 MHz or 50 MHz, assignments based on DEPT or APT spectra. MS: selected peaks; *m/z* (%). GC: OV-1701, 30 m x 0.25 mm, 0.25 μm (Restek Co.); chiral column (β-CD): Wcot fused silica coated with CP cyclodextrin B 236M , 25 m x 0.25 mm, 0.25 μm (Chrompack).

Synthesis of Bisoxazoline 3. *General procedure: 2,2-Bis[2-{(4S)-4,5-dihydro-4-(tert-butyl)oxazolyl}]-propane* (**3**). A mixture of 1.53 g (13.1 mmol, 2.4 eq) of L-*tert*-leucinol, 0.507 g (5.4 mmol) of dimethylmalonodinitrile[17], and 0.750 g (5.5 mmol) of anhydrous $ZnCl_2$ in 25 ml of chlorobenzene was refluxed for 72 h. The reaction was monitored by TLC. After removal of the solvent *in vacuo*, the residue was dissolved in CH_2Cl_2 and carefully washed with aqueous KOH (3 x 20 ml, 10%). After drying of the organic layer (Na_2SO_4) the solvent was evaporated and the residue dissolved in pentane and filtered. After removal of the pentane *in vacuo* 1.66 g of yellowish crystals were obtained. Recrystallization from pentane yielded 1.25 g of **3** (80%) as colorless crystals. mp.: 90-91 °C. $[\alpha]_D$ = -108 (c = 0.975, CH_2Cl_2), $[\alpha]_{365}$ = -383 (c = 0.975, CH_2Cl_2). IR: 1660 s, 1480 m, 1395 w, 1365 m. ^1H-NMR: 4.15 (dd, J = 10.0, 8.7, 2H, $H_AC(5,5')$), 4.08 (dd, J = 8.7, 7.0, 2H, HC(4,4')), 3.85 (dd, J = 10.0, 7.0, 2H, $H_BC(5,5')$), 1.52 (s, 6H, $C(CH_3)_2$), 0.88 (s, 18H, $C(CH_3)_3$). ^{13}C-NMR: 168.4 (C(2,2'), 75.6 (HC(4,4')), 69.0 ($H_2C(5,5')$), 38.5 ($\underline{C}(CH_3)_2$), 33.9 ($\underline{C}(CH_3)_3$), 25.7 ($C(\underline{C}H_3)_3$), 24.5 ($C(\underline{C}H_3)_2$). MS (EI): 294 (<1, M^+), 279 (7, M^+- CH_3), 237 (100, M^+- $C(CH_3)_3$), 169 (49), 137 (44), 111(20), 57 (43, $C(CH_3)_3^+$), 41 (41). TLC (hexane / EtOAc 7:3): R_f = 0.20. Anal. Calcd. for $C_{17}H_{30}N_2O_2$: C, 69.35, H, 10.27; N, 9.51. Found: C, 69.39; H, 10.27; N, 9.54.

Cyclopropanation. *General procedure for 4 and 5:* Reactions were carried out according to the general procedure in ref. 4a (ligand **1**) and refs. 4c and 5 (ligands **2** and **3**). After evaporation of the solvent *i.v.* the crude mixture was filtered through a short column of florisil™ (hexane/Et_2O 90:10). The solvent was removed and the crude product was purified by column chromatography (silica gel, hexane/EtOAc 98:2).

cis/trans-mixture of Methyl [2-phenyl-2-(trimethylsilyloxy)]cyclopropane-1-carboxylate 4 and 5 (R = Me). IR: 1730 s, 1680 w, 1600 w, 1450 w, 1440 m, 1370 m, 1325 w, 1280 w, 1260 m, 1250 s, 1165 s, 1105 w, 1075 w, 1055 w, 1040 w, 1000 w, 980 w, 950 w, 910 m, 840 s, 700 m. ^{1}H-NMR: 7.98-7.95 (m, 0.8H, arom. H), 7.56-7.25 (m, 5H, arom. H), 3.73 (s, 1.15H, OCH_3/*cis*), 3.41 (s, 1.85H, OCH_3/*trans*), 2.30 (dd, J = 9.3, 7.0, 0.6H, CH_2/*cis*), 1.99-1.93 (m, 1.4H, CH_2/*trans*), 1.69 (dd, J = 7.9, 5.0, 0.4H, CH/*cis*), 1.53 (dd, J = 9.3, 5.8, 0.6H, CH/*trans*), 0.07 (s, 3.5H, $Si(CH_3)_3$/*cis*), -0.05 (s, 5.4H, $Si(CH_3)_3$/*trans*). ^{13}C-NMR: 170.5 (C=O/*trans*), 169.5 (C=O/*cis*), 137.9 (arom. C/*cis*), 132.9 (arom. C/*trans*), 128.6, 128.4, 128.2, 127.9, 127.8, 127.1, 125.6, 125.1, (arom. CH), 65.5 (C(1)/*trans*), 63.5 (C(1)/*cis*), 51.7 (OCH_3/*cis*), 51.4 (OCH_3/*trans*), 30.9 (C(2)/*cis*), 30.2 (C(2)/*trans*), 20.4 (C(3)/*cis*), 19.6 (C(3)/*trans*), 0.8 ($Si(CH_3)_3$). MS (CI, NH_3): 266 (20), 265 (100, M^++1), 233 (45), 193 (18), 175 (59), 161 (14), 121 (15), 105 (23), 90 (42), 73 (12). TLC (hexane/EtOAc 9:1): R_f = 0.40. Anal. Calcd. for $C_{14}H_{20}O_3Si$: C, 70.79; H, 11.88. Found: C, 70.04; H, 11.94. GC: OV 1701, 0.6 bar H_2, 90 °C, 1 °C/min, t_R = 33.2 min (*trans*), t_R = 37.2 min (*cis*); β-CD, 0.6 bar H_2, 120 °C, 0.3 °C/min, t_R = 24.4/24.9 min (*trans*), t_R = 29.2/29.7 min (*cis*).

Ethylesters 4 and 5 (R = Et). IR: 1720 s, 1600 w, 1450 m, 1380 m, 1175 s, 1080 w, 970m, 930 m, 860 s, 840 s, 700 m. ^{1}H-NMR: 7.44-7.41 (m, 1H, arom. H), 7.34-7.24 (m, 4H, arom. H), 4.19 (q, J = 7.1, 0.77H, $\underline{CH_2}CH_3$/*cis*), 3.85 (sym. m, 1.27H, $\underline{CH_2}CH_3$/*trans*), 2.28 (dd, J = 9.2, 7.0, 0.59H, H_2C(3)/*cis*), 1.99-1.91 (m, 1.5H, H_2C(3)/*trans*), 1.66 (dd, J = 8.1, 5.2, 0.4H, HC(2)/*cis*), 1.51 (dd, J = 9.3, 5.9, 0.68H, HC(2)/*trans*), 1.28 (t, J = 7.1, 1.3H, $CH_2\underline{CH_3}$/*cis*), 0.96 (t, J = 7.1, 1.9H, $CH_2\underline{CH_3}$/*trans*), 0.07 (s, 3.1H, $Si(CH_3)_3$/*cis*), –0.05 (s, 5.0H, $Si(CH_3)_3$/*trans*). ^{13}C-NMR: 170.1 (C=O/*trans*), 169.0 (C=O/*cis*), 142.8 (arom. C/*cis*), 138.0 (arom. C/*trans*), 128.8, 128.2, 127.9, 127.8, 127.1, 125.6 (arom. CH), 65.3 (C(1)/*trans*), 63.5 (C(1)/*cis*), 60.5 ($\underline{CH_2}CH_3$/*cis*), 60.1 ($\underline{CH_2}CH_3$/*trans*), 31.0 (C(2)/*cis*), 30.3 (C(2)/*trans*), 20.1 (C(3)/*cis*), 19.2 (C(3)/*trans*), 14.3 ($CH_2\underline{CH_3}$/*cis*), 13.9 ($CH_2\underline{CH_3}$/*trans*), 0.75 ($Si(CH_3)_3$/*cis*), 0.70 ($Si(CH_3)_3$/*trans*). MS (CI, NH_3): 280 (21), 279 (100, M^++1), 233 (32), 207 (27), 189 (38), 161 (9), 90 (57). TLC (hexane/EtOAc 9:1): R_f = 0.36. GC: OV 1701, 0.6 bar H_2, 90 °C, 1 °C/min, t_R = 48.0 min (*trans*), t_R = 51.4 min (*cis*); β-CD, 0.7 bar H_2, 90 °C, 0.1 °C/min, t_R = 128.5/134.0 min (*trans*), t_R = 146.9/148.2 (*cis*).

tert-Butylesters 4 and 5 (R = tert-Bu). IR: 1720 s, 1460 w, 1450 w, 1420 w, 1390 m, 1370 m, 1320 w, 1300 w, 1250 s, 1150 s, 1105 w, 1075 w, 1050 w, 1030 w, 1020 w, 970m, 860 m, 840 s, 700 m. ^{1}H-NMR: 7.45-7.42 (m, 1H, arom. H), 7.33-7.23 (m, 4H, arom. H), 2.20 (dd, J = 9.2, 7.0, 0.5H, H_2C(3)/*cis*), 1.93-1.85 (m, 1.4H, H_2C(3)/*trans*), 1.60-1.51 (m, 0.4H, HC(1)/*cis*), 1.48 (s, 4H, $C(CH_3)_3$/*cis*), 1.44-1.39 (m, 0.6H, HC(1)/*trans*), 1.13 (s, 5H, $C(CH_3)_3$/*trans*), 0.06 (s, 3H, $Si(CH_3)_3$/*cis*), –0.05 (s, 5H, $Si(CH_3)_3$/*trans*); additional signals at 1.32-1.27, 0.91-0.87 (ca. 0.2 equivalents of di(*tert*-butyl) fumarate and maleate). ^{13}C-NMR: 169.1 (C=O/*trans*), 168.0 (C=O/*cis*), 143.1 (arom. C/*cis*), 138.3 (arom. C/*trans*), 129.0, 127.7, 127.0, 125.7 (arom. CH), 80.1 ($\underline{C}(CH_3)_3$/*cis*), 79.9 ($\underline{C}(CH_3)_3$/*trans*), 65.0 (C(1)/*trans*), 62.9 (C(1)/*cis*), 32.1 (C(2)/*cis*), 31.3 (C(2)/*trans*), 28.2 ($C(\underline{CH_3})_3$/*cis*), 27.7 ($C(\underline{CH_3})_3$/*trans*), 19.3 (C(3)/*cis*), 18.7 (C(3)/*trans*), 0.78 ($Si(CH_3)_3$/*cis*), 0.71 ($Si(CH_3)_3$/*trans*). MS (CI, NH_3): 323 (6.7, M^++NH_3), 252 (20), 251 (100, M^+–$C(CH_3)_3$+2), 250 (8.2), 233 (18), 179 (9.3), 161 (31), 90 (30). TLC (hexane/EtOAc 9:1): R_f = 0.34. GC: OV 1701, 0.6 bar H_2, 90 °C, 1 °C/min, t_R = 53.2 min (*trans*), t_R = 55.3 min (*cis*); β-CD, 0.7 bar H_2, 120 °C, isotherm, t_R = 49.6/50.7 min (*trans*), t_R = 54.6/55.3 (*cis*).

cis- and trans-Methyl 1-(trimethylsilyloxy)bicyclo[3.1.0]hexane-6-carboxylates 8 and 9 (R = Me). A mixture of [Cu(OTf)•$(C_6H_6)_{0.5}$] (74.0 mg, 0.294 mmol) and ligand **3** (95.2 mg, 0.323 mmol, 1.1 eq.) in 5 ml of $CHCl_3$ was stirred for 3 h. After filtration through a micro filter (pore diameter 0.2 μm) under an argon atmosphere the solution was transferred to another flask. A solution of 1-trimethylsiloxycyclopentene (2.62 ml, 14.7 mmol) and 2,2,6,6-tetramethylpiperidine (50 μl, 2 mol%) in 15 ml $CHCl_3$ was added. Using a syringe pump, a solution of methyldiazoacetate (2.94 g, 29.4 mmol, 2.0 eq.) in 7 ml of $CHCl_3$ was added over a period of 4 h. After completion of the addition the reaction mixture was allowed to stir for an additional

12 h. The solvent was removed *in vacuo*, and the resulting brownish oil was rapidly flushed through a small column of florisil™ (1.5x7 cm, hexane/Et_2O 95:5), yielding 4.0 g of a colorless oil. The separation of *cis/trans*-isomers by chromatography (7x25 cm, hexane/Et_2O 97:3) with florisil™ was conducted twice giving 0.49 g of the pure *trans*- and 0.97 g of the pure *cis*-isomer (43% total yield).

trans-Methylester ***9*** *(R = Me).* $[\alpha]_D$ = - 49.5 (c = 0.45, $CHCl_3$, at 80% ee). IR: 1725 s, 1640 w, 1530 w, 1470 w, 1435 m, 1400 m, 1350 m, 1310 w, 1300 w, 1250 s, 1220 b s, 1170 m, 1080 m, 1040 m, 925 m, 840 s. ^{1}H-NMR: 3.67 (s, 3H, OCH_3), 2.25 (ddd, J = 12.8, 9.0, 2.2, 1H, $H_AC(2)$), 2.08-1.97 (m, 3H,$H_BC(2)$, $H_AC(4)$, HC(6)), 1.81-1.71 (m, 3H, $H_AC(3)$, $H_BC(4)$, HC(5)), 1.34-1.23 (m, 1H, $H_BC(3)$), 0.16 (s, 9H, $Si(CH_3)_3$). ^{13}C-NMR: 170.5 (C=O), 70.6 (C(1)), 51.4 (OCH_3), 32.9 (C(2)), 31.76, 31.72 (C(5), C(6)), 24.7 (C(4)), 22.7 (C(3)), 0.7 ($Si(CH_3)_3$). MS (CI, NH_3): 229 (34, M^++1), 197 (14), 169 (15), 139 (100, M^+-$OSi(CH_3)_3$), 107 (12), 90 (22). TLC (hexane/EtOAc 9:1): R_f = 0.40. GC: β-CD, 0.55 bar H_2, 80 °C, 0.2 °C/min, t_R = 48.8/50.2 min (1S, 5R, 6S/1R, 5S, 6R).

cis-Methylester ***8*** *(R = Me).* $[\alpha]_D$ = - 26.3 (c = 0.54, $CHCl_3$, at 81% ee). ^{1}H-NMR: 3.64 (s, 3H, OCH_3), 2.13-1.85 (m, 4H, $H_2C(2)$, $H_AC(4)$, HC(6)), 1.70-1.57 (m, 3H, $H_AC(3)$, $H_BC(4)$, HC(5)), 1.14-1.02 (m, 1H, $H_BC(3)$); 0.11 (s, 9H, $Si(CH_3)_3$). ^{13}C-NMR: 170.6 (C=O), 71.8 (C(1)), 51.3 (OCH_3), 34.6 (C(2)), 31.9 (C(6)), 28.5 (C(5)), 26.2 (C(4)), 20.5 (C(3)); 0.6 ($Si(CH_3)_3$). TLC (hexane/EtOAc 9:1): R_f = 0.32. GC: β-CD, 0.55 bar H_2, 80 °C, 0.2 °C/min, t_R = 60.5/61.5 min (1S, 5R, 6R/1R, 5S, 6S).

trans-Ethylester ***9*** *(R = Et).* IR: 1725 s, 1407 m, 1370 m, 1350 m, 1254 s, 1232 m, 1175 m, 1160 m, 890 m, 845 m. ^{1}H-NMR: 4.14/4.12 (2q, J = 7.2, 1.5, 2H, $\underline{CH_2}CH_3$), 2.26 (ddd, J = 12.8, 8.8, 1.9, 1H, $H_AC(2)$), 2.09-1.97 (m, 3H, $H_BC(2)$, $H_AC(4)$, HC(6)), 1.84-1.62 (m, 3H, $H_AC(3)$, $H_BC(4)$, HC(5)), 1.27 (m with t, J = 7.1, 4H, $H_BC(3)$, $CH_2\underline{CH_3}$), 0.17 (s, 9H, $Si(CH_3)_3$). ^{13}C-NMR: 170.1 (C=O), 70.5 (C(1)), 60.2 ($\underline{CH_2}CH_3$), 32.9 (C(2)), 31.9, 31.6 (C(6), (C(5)), 24.8 (C(4)), 22.7 (C(3)), 14.3 ($CH_2\underline{CH_3}$); 0.7 ($Si(CH_3)_3$). MS (CI, NH_3): 244 (11), 243 (14, M^++1), 197 (15), 171 (32), 169 (14), 154 (10), 153 (100, M^+ –$OSi(CH_3)_3$), 90 (32, $HOSi(CH_3)_3$). TLC (hexane/EtOAc 9:1): R_f = 0.28. GC: OV 1701, 0.6 bar H_2, 90 °C, 1 °C/min, t_R = 24.6 min; β-CD, 0.55 bar H_2, 80 °C, 0.2 °C/min, t_R = 66.1/68.0 (1S, 5R, 6S/1R, 5S, 6R).

cis-Ethylester ***8*** *(R = Et).* ^{1}H-NMR: 4.10 (q, J = 7.1, 2H, $\underline{CH_2}CH_3$), 2.13-1.89 (m, 4H, $H_2C(2)$, $H_AC(4)$, HC(6)), 1.68-1.58 (m, 3H, $H_AC(3)$, $H_BC(4)$, HC(5)), 1.24 (t, J = 7.1, 3H, $CH_2\underline{CH_3}$), 1.18-1.00 (m, 1H, $H_BC(3)$), 0.12 (s, 9H, $Si(CH_3)_3$). ^{13}C-NMR: 170.2 (C=O), 71.8 (C(1)), 60.1 ($\underline{CH_2}CH_3$), 34.6 (C(2)), 31.9, 28.4 (C(6), (C(5)), 26.3, 20.6 (C(3), C(4)), 14.3 ($CH_2\underline{CH_3}$), 0.71 ($Si(CH_3)_3$). TLC (hexane/EtOAc 9:1): R_f = 0.22. GC: OV 1701, 0.6 bar H_2, 90 °C, 1 °C/min, t_R = 28.3 min; β-CD, 0.55 bar H_2, 80 °C, 0.2 °C/min, t_R = 77.9/78.7 (1S, 5R, 6S/1R, 5S, 6R).

Methyl 1-(triisopropylsilyloxy)bicyclo[3.1.0]hexane-6-carboxylates ***12*** *and* ***13***. A mixture of $[Cu(OTf)\bullet(C_6H_6)_{0.5}]$ (25.8 mg, 0.102 mmol) and ligand **3** (33.2 mg, 0.113 mmol, 1.1 eq.) in 5 ml of $CHCl_3$ was stirred for 2 h. The solution was filtered using a micro filter (pore diameter 0.2 μm) under an argon atmosphere and transferred to another flask. A solution of 1-tri(isopropyl)silyloxycyclopentene (1.20 g, 5.0 mmol) and 2,2,6,6-tetramethylpiperidine (17 μl, 2 mol%) in 25 ml $CHCl_3$ was added. A solution of methyl diazoacetate (1.10 g, 11.0 mmol, 2.2 eq.) in 4 ml of $CHCl_3$ was added at 23 °C over a period of 5 h by a syringe pump. To start the reaction it was sometimes necessary to heat the mixture to 60 °C for a short time until N_2-evolution occurred. After completion of the addition the reaction mixture was allowed to stir for an additional 12 h. The solvent was removed *in vacuo* , and the resulting brownish oil was rapidly flushed through florisil™ (1.5x7 cm, hexane/Et_2O 90:10), yielding 1.45 g of a colorless oil. Separation of the *cis/trans*-isomers by MPLC (4x20 cm, Silica 100 Sichroprep Merck, hexane/Et_2O 99:1, flow 30 ml/min) gave 0.36 g of the pure *trans*- and 0.51 g of the pure *cis*-isomer (55% total yield).

trans-Methylester ***13*** *(R = Me).* $[\alpha]_D$ = –53.5 (c = 0.53, $CHCl_3$, at 86% ee). IR: 2947 s, 2890 s, 1727 s, 1602 w, 1464 m, 1438 m, 1402 m, 1353 s, 1271 m, 1172 s, 1150 m, 1079 m, 884 m, 856 m. ^{1}H-NMR: 3.67 (s, 3H, OCH_3), 2.31 (dd, J = 9.0, 2.5, 1H, $H_AC(2)$), 2.13-2.03 (m, 3H, $H_BC(2)$, $H_AC(4)$, C(6)), 1.82-1.74 (m, 3H, $H_AC(3)$, $H_BC(4)$, HC(5)), 1.44-1.39 (m, 1H, $H_BC(3)$), 1.10-1.06 (m, 21H, $OSi\underline{CH}(CH_3)_2$, $OSiCH(\underline{CH_3})_2$). ^{13}C-NMR: 170.8 (C=O), 71.5 (C(1)), 51.4 (OCH_3), 33.1 (C(2)), 33.0, 32.5 (C(6), C(5)), 25.0 (C(4)), 22.9 (C(3)), 18.0 ($SiCH(\underline{CH_3})_2$), 12.5 ($Si\underline{CH}(CH_3)_2$). MS: 312 (1, M^+), 281 (1), 269 (100), 253 (14), 239 (14), 157 (11),

145 (30), 115 (22), 89 (12), 75 (18), 73 (17), 59 (26). TLC (hexane/EtOAc 9:1): R_f = 0.55. GC: OV 1701, 0.6 bar H_2, 90 °C, 1 °C/min, t_R = 69.2 min; β-CD, 0.55 bar H_2, 80 °C, 0.5 °C/min, t_R = 122.7/123.3 (1S, 5R, 6S/1R, 5S, 6R).

cis-Methylester ***12*** *(R = Me).* $[\alpha]_D$ = –27.4 (c = 0.48, $CHCl_3$, at 84% ee). ^{1}H-NMR: 3.64 (s, 3H, OCH_3), 2.20-1.85 (m, 5H, $H_AC(3)$, $H_2C(2)$, $H_BC(4)$, C(6)), 1.75-1.55 (m, 3H, $H_BC(4)$, HC(5), $H_BC(3)$), 1.10-1.06 (m, 21H, $OSi\underline{CH}(CH_3)_2$, $OSiCH(\underline{CH_3})_2$). ^{13}C-NMR: 170.6 (C=O), 72.1 (C(1)), 51.4 (OCH_3)), 34.4 (C(2)), 32.2 (C(6)), 28.9 (C(5)), 26.2 (C(4)), 20.5 (C(3)), 18.0 ($SiCH(\underline{CH_3})_2$), 12.9 ($Si\underline{CH}(CH_3)_2$). TLC (hexane/EtOAc 9:1): R_f = 0.49. GC: OV 1701, 0.6 bar H_2, 90 °C, 1 °C/min, t_R = 74.3 min; β-CD, 0.55 bar H_2, 80 °C, 0.5 °C/min, t_R = 131.3 (no separation of enantiomers).

cis- and trans-Methyl 1-(trimethyl)bicyclo[3.1.0]heptane-7-carboxylates ***10*** *and* ***11*** *(R = Me). General procedure for* ***10*** *and* ***11****:* Reactions were carried out according to the general procedure in refs. 4c and 5 (ligands **2** and **3**). After evaporation of the solvent *i.v.* the crude mixture was filtered through a short column of florisil™ (hexane/Et_2O 90:10). The solvent was removed and the crude product was purified by column chromatography (silica gel, hexane/EtOAc 98:2). All reactions were carried out on a 1.0 mmol scale.

trans-Methylester ***11*** *(R = Me).* IR: 2935 s, 2866 m, 1737 s, 1437 m, 1415 m, 1363 m, 1310, m, 1251 s, 1193 s, 1160 s, 1108 m, 1079 w, 1053 w, 1005 s, 952 w, 931 w, 895m, 876 m, 843 s. ^{1}H-NMR: 3.65 (s, 3H, OCH_3), 2.19-2.12 (m, 1H, $H_AC(2)$), 1.96-1.85 (m, 2H, $H_BC(2)$, HC(7)), 1.72-1.55 (m, 2H, HC(6), $H_AC(5)$), 1.44-1.30 (m, 5H, $H_2C(3)$, $H_2C(4)$, $H_BC(5)$), 0.13 (s, 9H, $Si(CH_3)_3$). ^{13}C-NMR: 170.8 (C=O), 60.7 (C(1)), 51.2 (OCH_3), 31.3 (C(7)), 29.2 (C(2)), 26.1 (C(6)), 21.3, 20.9, 18.9 (C(3), C(4), C(5)), 1.15 ($Si(CH_3)_3$). MS(EI): 242 (11), 227 (21), 211 (18), 210 (58), 184 (10), 183 (56), 182 (30), 169 (13), 168 (23), 167 (8), 137 (11), 121 (11), 110 (11), 109 (13), 89 (24), 82 (10), 81 23), 75 (21), 73 (100), 59 (15), 55 (8), 45 (24), 41(8). TLC (hexane/EtOAc 9:1): R_f = 0.40. GC: OV 1701, 1.2 bar H_2, 90 °C, 1 °C/min, t_R = 27.3 min; β-CD, 0.6 bar H_2, 80 °C, 0.5 °C/min, t_R = 48.2 min (no separation of enantiomers).

cis-Methylester ***10*** *(R = Me).* ^{1}H-NMR: 3.64 (s, 3H, OCH_3), 2.19 (dt, J = 5.1, 14.0, 1H, $H_AC(2)$), 2.05-1.97 (m, 2H, HC(6), HC(7)), 1.94-1.84 (m, 1H, $H_BC(2)$), 1.54-1.42 (m, 3H, $H_AC(3)$, HC(4)), 1.28-1.20 (m, 2H, $H_BC(3)$, $H_AC(5)$), 1.18-1.07 (m, 1H, $H_BC(5)$), 0.12 (s, 9H, $Si(CH_3)_3$). ^{13}C-NMR: 170.9 (C=O), 63.6 (C(1)), 51.4 (OCH_3), 32.8 (C(2)), 32.0 (C(7)), 27.8 (C(6)), 23.5 (C(5)), 21.4, 20.9 (C(3), C(4)), 1.01 ($Si(CH_3)_3$). TLC (hexane/EtOAc 9:1): R_f = 0.28. GC: OV 1701, 0.6 bar H_2, 90 °C, 1 ° /min, t_R = 31.9 min; β-CD, 0.6 bar H_2, 80 °C, 0.5 °C/min, t_R = 56.5/57.3 (1S, 6R, 7S/1R, 6S, 7R).

trans-Ethylester ***11*** *(R = Et).* IR: 2937 s, 1729 s, 1464 w, 1447 m, 1413 m, 1370 w, 1349 m, 1252 s, 1202 s, 1153 s, 1110 s, 1045 w, 986 m, 877 s, 842 s. ^{1}H-NMR: 4.20-4.05 (m, 2H, $\underline{CH_2}CH_3$), 2.30-2.05 (m, 1H, $H_AC(2)$), 1.95-1.18 (m, 12H, $H_BC(2)$, $H_2C(4)$, HC(6), $H_2C(3)$, $H_2C(5)$, $CH_2\underline{CH_3}$), 0.10 (s, 9H, $Si(CH_3)_3$). ^{13}C-NMR: 169.9 (C=O), 60.1 (C(1)), 59.5 ($\underline{CH_2}CH_3$), 31.0 (C(7)), 28.8 (C(2)), 25.5 (C(6)), 21.0 (C(4)), 20.5 (C(5)), 18.5 (C(3)), 14.0 ($CH_2\underline{CH_3}$); 0.76 ($Si(CH_3)_3$). MS (EI): 256 (32, M^+), 227 (33), 211 (18), 210 (30) 184 (9), 183 (54), 182 (15), 169 (9), 168 (18), 137 (31), 121 (9), 109 (8), 75 (25), 73 (100), 45 (15). TLC (hexane/EtOAc 9:1): R_f = 0.53. GC: OV 1701, 0.6 bar H_2, 90 °C, 1 °C/min, t_R = 32.8 min; β-CD, 0.60 bar H_2, 80 °C, 0.5 °C/min, t_R = 58.7 (no separation of enantiomers).

cis-Ethylester ***10*** *(R = Et).* ^{1}H-NMR: 4.09 (dq, J = 7.1, 1.0, 2H, $\underline{CH_2}CH_3$), 2.25-1.75 (m, 4H, $H_2C(2)$, $H_AC(5)$, HC(7)), 1.55-1.35 (m, 3H, $H_AC(3)$, $H_BC(5)$, HC(6)), 1.25 (m with t, J = 7.1, 6H, $CH_2\underline{CH_3}$, $H_2C(4)$, $H_BC(3)$), 0.05 (s, 9H, $Si(CH_3)_3$). ^{13}C-NMR: 170.1 (C=O), 63.2 (C(1)), 59.8 ($\underline{CH_2}CH_3$), 32.5 (C(2)), 31.7 (C(7)), 27.2 (C(6)), 23.1, 21.1 (C(4), C(5)), 20.6 (C(3)), 14.3 ($CH_2\underline{CH_3}$), 0.67 ($Si(CH_3)_3$). TLC (hexane/EtOAc 9:1): R_f = 0.44. GC: OV 1701, 0.6 bar H_2, 90 °C, 1 °C/min, t_R = 37.4 min; β-CD, 0.6 bar H_2, 80 °C, 0.5 °C/min, t_R = 67.0/67.8 (1S, 6R, 7S/1R, 6S, 7R).

trans-tert-Butylester ***11*** *(R = tert-Bu).* IR: 2950 s, 1725 s, 1448 m, 1411 m, 1392 m, 1367 m, 1252 s, 1212 s, 1147 s, 1111 s, 990 m, 951 w, 877 s, 842 s. ^{1}H-NMR: 2.28-2.12 (m, 1H, $H_AC(2)$), 1.95-1.62 (m, 4H, $H_BC(2)$, HC(7), HC(6), $H_AC(5)$), 1.53-1.27 (m with s, 14H, $C(CH_3)_3$, $H_2C(3)$, $H_2C(4)$, $H_BC(5)$), 0.13 (s, 9H, $Si(CH_3)_3$). ^{13}C-NMR: 169.1 (C=O), 79.6 ($\underline{C}(CH_3)_3$), 59.5 (C(1)), 31.7 (C(7)), 29.0 (C(2)), 27.9 (C(6)), 24.6 ($C(\underline{CH_3})_3$), 21.0, 20.6, 18.4 (C(3), C(4), C(5)), 0.78 ($Si(CH_3)_3$). MS (EI): 284 (2), 229 (15), 228 (85), 213 (13), 212 (8), 211 (32), 210 (67), 184 (12), 183 (64), 182 (34), 169 (20), 168 (38), 155 (8), 139 (8), 138 (51),

137 (9), 121 (12), 110 (9), 75 (30), 73 (100), 57 (27), 45 (15), 41 (14). TLC (hexane/EtOAc 9:1): R_f = 0.62. GC: OV 1701, 0.6 bar H_2, 90 °C, 1 °C/min, t_R = 37.4 min; β-CD, 0.6 bar H_2, 80 °C, 0.5 °C/min, t_R = 58.7 min (no separation of enantiomers).

cis-tert-Butylester ***10*** *(R = tert-Bu).* ^{1}H-NMR: 2.20-1.80 (m, 4H, $H_AC(2)$, HC(7), HC(6), $H_AC(5)$), 1.60-1.20 (m with s, 15H, $H_BC(2)$, $C(CH_3)_3$, $H_2C(3)$, $H_2C(4)$, $H_BC(5)$), 0.07 (s, 9H, $Si(CH_3)_3$). ^{13}C-NMR: 164.1 (C=O), 81.3 ($\underline{C}(CH_3)_3$), 62.7 (C(1)), 32.8 (C(7)), 32.5 (C(2)), 27.7 (C(6)), 26.3 ($C(\underline{CH_3})_3$), 23.1, 21.2, 20.7 (C(3), C(4), C(5)), 0.75 ($Si(CH_3)_3$).TLC (hexane/EtOAc 9:1): R_f = 0.51. GC: OV 1701, 0.6 bar H_2, 90 °C, 1 °C/min, t_R = 32.8 min; β-CD, 0.60 bar H_2, 80 °C, 0.5 °C/min, t_R = 67.0/67.8 min (1S, 6R, 7S/1R, 6S, 7R).

Methyl 1-(triisopropylsilyloxy)bicyclo[3.1.0]heptane-7-carboxylates ***15*** *and* ***16***. A mixture of $[Cu(OTf)\bullet(C_6H_6)_{0.5}]$ (34.4 mg, 0.137 mmol) and ligand **2** (66.8 mg, 0.157 mmol, 1.1 eq.) in 11 ml of $Cl(CH_2)_2Cl$ was stirred for 3.5 h. The solution was filtered using a micro filter (pore diameter 0.2 μm) in an argon atmosphere and transferred to another flask. A solution of 1-(triisopropylsilyloxy)cyclohexene (1.39 g, 5.5 mmol) and 2,2,6,6-tetramethylpiperidine (23 μl, 2 mol%) in 20 ml of 1,2-dichloroethane was added. Using a syringe pump, a solution of methyl diazoacetate (2.50 g, 25.0 mmol, 4.5 eq.) in 7.5 ml of 1,2-dichloroethane was added at 23 °C over a period of 2.5 h. To start the reaction it was sometimes necessary to heat the mixture to 60 °C for a short time until N_2-evolution occurred. After completion of the addition the reaction mixture was allowed to stir for an additional 12 h. The solvent was removed *in vacuo*, and the resulting brownish oil was rapidly flushed through florisil™ (1.5x7 cm, hexane/Et_2O 90:10), yielding 2.1 g of a colorless oil. The *cis/trans*-isomers were separated by MPLC (4x20 cm, Silica 100 Sichroprep Merck, hexane/Et_2O 99:1, flow 30 ml/min) giving 0.28 g of the pure *cis*- and 0.68 g of the pure *trans*-isomer (50% total yield). *trans-Methylester* ***16***. $[\alpha]_D$ = + 52.1 (c = 0.665, $CHCl_3$, at 81% ee). IR: 2944 s, 2867 s, 1733 s, 1464 m, 1447 m, 1436 m, 1407 m, 1360 m, 1206 s, 1171 s, 1154 s, 1114 s, 1086 m, 997 m, 883 s, 865 m, 803 w. ^{1}H-NMR: 3.66 (s, 3H, OCH_3), 2.30-2.17 (m, 1H, $H_AC(2)$), 2.01-1.83 (m, 3H, HC(6), HC(7), $H_BC(2)$), 1.74-1.61 (m, 2H, $H_2C(3)$), 1.53-1.34 (m, 4H, $H_2C(5)$, $H_2C(4)$), 1.07-0.97 (m, 21H, OSi^iPr_3). ^{13}C-NMR: 170.6 (C =O), 60.6 (C(1)), 50.8 (OCH_3), 31.5 (C(7)), 28.8 (C(2)), 26.7 (C(6)), 21.1 (C(5)), 20.4 (C(4)), 18.6 (C(3)), 17.7 ($Si(CH(\underline{CH_3})_2$), 12.8 ($Si(\underline{CH}(CH_3)_2$). MS: 326 (1, M^+), 295 (4), 284 (21), 283 (100), 145 (36), 117 (18), 115 (12), 114 (12), 103 (8), 89 (9), 87 (9), 75 (17), 73 (13), 59 (22). TLC (hexane/EtOAc 9:1): R_f = 0.62. GC: OV 1701, 0.6 bar H_2, 90 °C, 1 °C/min, t_R = 77.5 min. HPLC: Chiralcel OD-H, n-heptane/2-propanol (99.9:0.1), t_R = 10.6/11.2 min (1S, 6R, 7S/1R, 6S, 7R).

cis-Methylester ***15***. $[\alpha]_D$ = + 28.1 (c = 0.95, $CHCl_3$, at 86% ee). ^{1}H-NMR: 3.64 (s, 3H, OCH_3), 2.22-2.15 (m, 2H, $H_AC(2)$, HC(7)), 2.02-1.87 (m, 3H, HC(6), $H_AC(5)$, $H_BC(2)$), 1.52-1.43 (m, 3H, $H_2C(3)$, $H_BC(5)$), 1.24-1.19 (m, 2H, $H_2C(4)$), 1.05-0.98 (m, 21H, OSi^iPr_3). ^{13}C-NMR: 170.4 (C=O), 63.1 (C(1)), 51.1 (OCH_3), 32.4 (C(2)), 32.0 (C(7)), 27.4 (C(6)), 23.2 (C(5)), 21.2 (C(4)), 20.6 (C(3)), 17.7 (CH_3), 12.8 (SiCH). TLC (hexane/EtOAc 9:1): R_f = 0.54. GC: OV 1701, 0.6 bar H_2, 90 °C, 1 °C/min, t_R = 83.9 min. HPLC: Chiralcel OD-H, n-heptane/2-propanol (99.9:0.1), t_R = 11.5/16.7 min (1R, 6S, 7S/1S, 6R, 7R).

Rearrangement product. *Methyl [2-(trimethylsilyloxy)cyclopenten-1-yl]acetate.* ^{1}H-NMR: 3.66 (s, 3H, OCH_3), 3.04 (s, 2H, CH_2), 2.34-2.26 (m, 4H, C(3), C(5)), 1.86-1.81 (m, 2H, C(4)), 0.18 (s, 9H, $OSi(CH_3)_3$). ^{13}C-NMR: 172.3 (C=O), 149.6 (C(1)), 109.5 (C(2)), 51.5 (OCH_3), 33.4, 32.2, 31.1 (C(5), C(3), C(2)), 19.9 (CH_2), 0.51 ($Si(CH_3)_3$). MS (EI): 228 (5, M^+), 169 (67), 89 (16), 75 (13), 73 (100, $Si(CH_3)_3$), 68 (17), 45 (11). TLC (hexane/EtOAc 9:1): R_f = 0.35. GC: OV 1701, 0.6 bar H_2, 90 °C, 1 °C/min, t_R = 32.6 min; β-CD, 0.55 bar H_2, 80 °C, 0.2 °C/min, t_R = 56.6 min.

Ring cleavage. *General procedure 1:* To a solution of **8** (R = Me, 0.50 g, 2.19 mmol) in 20 ml of methanol were added four drops of anhydrous acetic acid. The mixture was heated to reflux and the reaction was monitored by TLC over a period of 1 h. After completion of reaction, the solvent was evaporated *in vacuo* and the residue purified by column chromatography (2x18 cm, hexane/EtOAc 85:15) or distillation in a

Kugelrohr apparatus. Average yield was 95%. *Methyl (2-oxocyclopentane)acetate* : see ref. 11. GC: OV 1701, 0.6 bar H_2, 90 °C, 1 °C/min, t_R = 27.5; β-CD, 0.6 bar H_2, 80 °C, 0.2 °C/min, t_R = 49.6/51.0 min (2S/2R).

General procedure 2: A solution of **15** (0.28 g, 0.86 mmol) was stirred in 5 ml of CH_2Cl_2 at –78 °C. HF-pyridine-complex (1.0 ml, 25 equiv.) was added using a syringe over a period of 2 min. Upon completion of the reaction (ca. 2-4 h at –78 °C, checked by TLC), the mixture was poured on an ice-cold column filled with silica gel (hexane/ethylacetate 7:3) and filtered rapidly through the column. The solvent was removed *i.v.* and the product purified as described above. Average yield was 90%. *Methyl (2-oxocyclohexane)-acetate.* (R)-**17**: $[\alpha]_D$ = + 21.7 ($CHCl_3$, c = 0.87, at 75% ee); (S)-**17**: $[\alpha]_D$ = - 23.3 ($CHCl_3$, c = 0.91, at 80% ee). IR: 1739 s, 2862 s, 1739 s, 1711 s, 1437 s, 1437 s, 1356 s, 1341 m, 1311 m, 1277 s, 1168 s, 1132 m, 1101 w, 1075 w, 1003 m, 962 w, 931 w, 886 w, 845 w, 818 w. ^{1}H-NMR: 3.64 (s, 3H, OMe), 2.91-2.68 (m, 2H, $\underline{H_A}$CCOOMe, C(2)), 2.39-2.30 (m, 2H, H_2C(6)), 2.19-2.02 (m, 3H, $\underline{H_A}$CCOOMe, H_AC(3), H_AC(5)), 1.92-1.27 (m, 4H, H_BC(3), H_2C(4), H_BC(5)). ^{13}C-NMR: 210.6 (C=O Ketone), 172.7 (C=O Ester), 51.3 (OMe), 46.7 (CH), 41.4 (C(6)), 33.8 ($\underline{H_2}$CCOOMe), 33.5 (C(3)), 27.4 (C(5)), 24.8 (C(4)). MS(EI): 170 (24, M^+), 139 (51), 138 (100), 127 (16), 121 (11), 110 (23), 97 (40), 82 (12), 74 (32), 67 (21). TLC (hexane/EtOAc 9:1): R_f = 0.10. GC: OV 1701, 0.6 bar H_2, 90 °C, 1 °C/min, t_R = 27.6 min. HPLC: Chiracel OB-H, n-heptane/2-propanol (80:20), t_R = 15.5/17.1 min (2S/2R).

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