Pergamon

Tetrahedron Vol. 51, No. 41, pp. 11149-11164, 1995
Elsevier Science Ltd
Printed in Great Britain
0040-4020/95 $9.50+0.00

0040-4020(95)00676-1

Enantiomerically Pure 6-Substituted 2-Oxo-cyclohexanecarboxylates by Conjugate Addition of Cuprates to Asymmetric Shielded 2-Oxo-cyclohexenecarboxylates

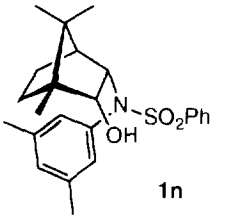
Ernst Urban*[a], Gerhard Riehs[a] and Guido Knühl[b]

[a] Institut für Pharmazeutische Chemie der Universität Wien,
Althanstraße 14, A-1090 Wien, Austria

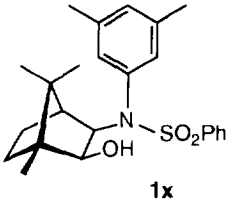
[b] Organisch-Chemisches Institut der Universität Heidelberg,
Im Neuenheimer Feld 270, D-69120 Heidelberg, Germany

Abstract: Asymmetric shielded 2-oxo-cyclohexenecarboxylates **6n** and **6x** were prepared by transesterification of 2-oxo-cyclohexanecarboxylate **2** with camphor derived concave alcohols **1n** and **1x** and by subsequent introduction of a double bond via phenylselenides. Diastereoselective conjugate addition of equimolar amounts of mixed cuprates at -78 °C and deprotection by methanolysis gave enantiomerically pure 6-substituted 2-oxo-cyclohexanecarboxylates **14-19** and *ent*-**14-19**, valuable as chiral building blocks in natural product synthesis.

The conjugate addition of cuprates to asymmetric shielded enoates developed into an important and well known method[1] for assembling structural complex organic molecules. Particularly successful was the conjugate addition of organocopper compounds to enoates of camphor derived chiral auxiliaries.[1-3] Best results were obtained by Helmchen[3] on additions to enoates derived from concave alcohols **1n** and **1x**, which generally proceeded with an extremely high diastereoselectivity (>99%) and in excellent yields (>90%).



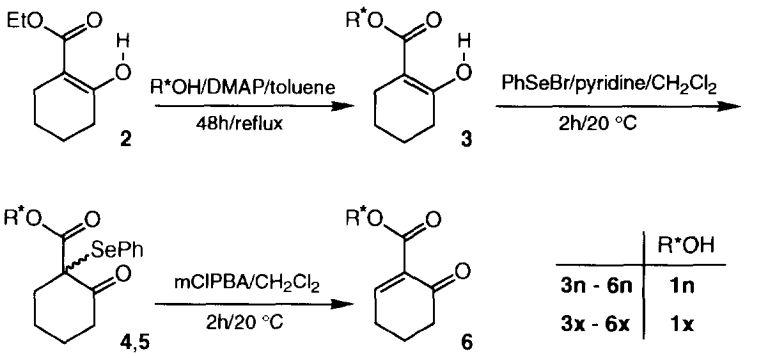
1n



1x

In conjunction with projects aiming at the EPC syntheses of the natural products (-)-chokol A[4] and (+)-heptelidic acid,[5] we investigated the preparation of enantiomerically pure 5-substituted 2-oxo-cyclopentanecarboxylates and 6-substituted 2-oxo-cyclohexanecarboxylates starting from asymmetric protected cyclic enoates. In the present article we want to report on conjugate addition of mixed cuprates to asymmetric protected 2-oxo-cyclohexenecarboxylates derived from the chiral auxiliaries **1n** and **1x**.

Asymmetric shielded 2-oxo-cyclohexanecarboxylates were readily available from auxiliaries **1n** or **1x** and racemic 2-oxo-cyclohexanecarboxylate **2**. We obtained the well crystallizing esters **3n** (94%) and **3x** (94%) in excellent yields using a DMAP[6] mediated transesterification reaction[7] first reported by Taber.[8]



Scheme 1

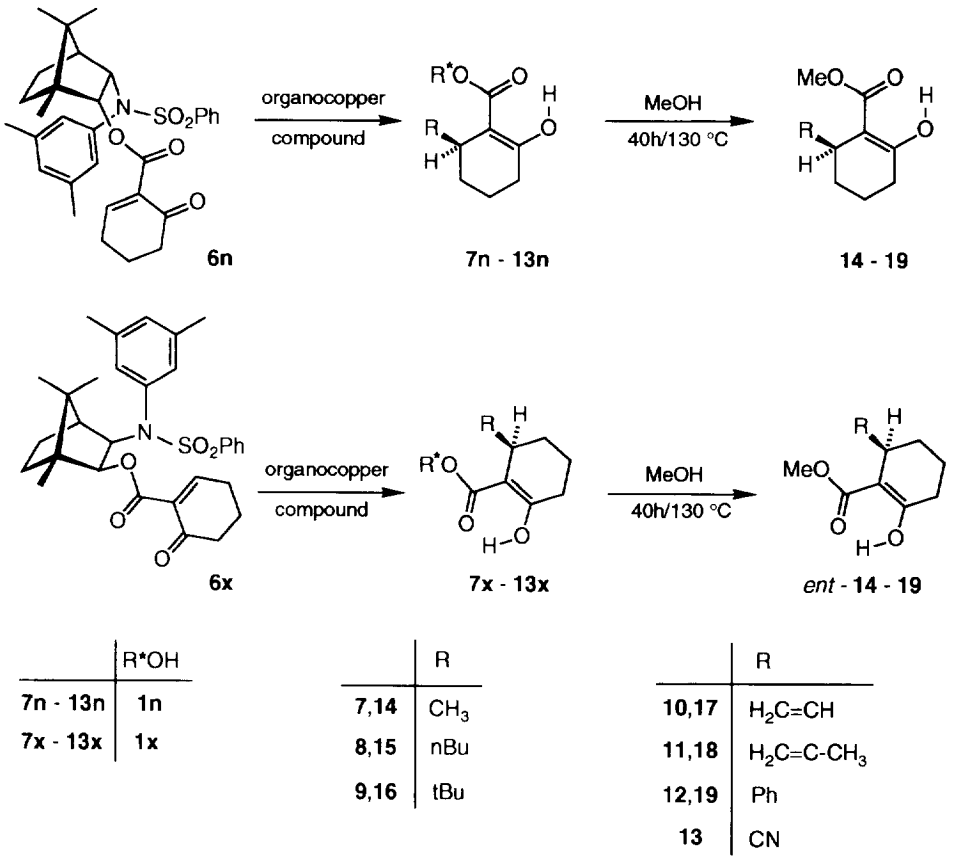
Phenylselenylation[9] of **3n** and **3x** gave mixtures of diastereomeric selenides (**4n**:**5n** = **4x**:**5x** = 60:40) which were separated by chromatography. Oxidative deselenylation of **4n** or **5n** and **4x** or **5x** afforded enoates **6n** and **6x** in good yields (85-91%), respectively. Preparative scale synthesis of enoates **6n** (60%) and **6x** (68%) was manufactured by a one pot procedure starting from **3n** and **3x** without isolation of the intermediate selenides.

Next we studied the addition of Lipshutz cuprates[10] to **6n** and **6x** (see Table 1) and obtained 6-substituted 2-oxo-cyclohexanecarboxylates **7n**-**12n** and **7x**-**12x** in good yields (62-78%), with one significant exception, the reaction of **6n** and **6x** with the bulky t-butyl-2-thienyl-cyanocuprate which led to mixtures of t-butyl adducts **9n** (26%) and **9x** (37%) with β-cyano adducts **13n** (16%) and **13x** (14%), respectively. Nevertheless we were able to prepare **9n** (66%) and **9x** (56%) in good yields using tBu_2CuLi which proved to be the more reactive cuprate.

Table 1. Cuprate Addition to Asymmetric Shielded Enoates and Deprotection by Methanolysis.

Enone	R	Cuprate Precursor	Cuprate Adduct	Yield (%)	Methyl-ester	Yield (%)	R*OH	Yield (%)
6n	CH_3	R-Li	**7n**	64	**14**	70	**1n**	82
6n	nBu	R-Li	**8n**	62	**15**	90	**1n**	79
6n	tBu	R-Li	**9n**	26[a]	**16**	56	**1n**	91
6n	H_2C=CH	R-MgBr	**10n**	70	**17**	81	**1n**	81
6n	H_2C=C(CH_3)	R-Li	**11n**	62	**18**	77	**1n**	71
6n	Ph	R-Li	**12n**	66	**19**	80	**1n**	82
6x	CH_3	R-Li	**7x**	78	*ent*-**14**	62	**1x**	63
6x	nBu	R-Li	**8x**	70	*ent*-**15**	76	**1x**	88
6x	tBu	R-Li	**9x**	37[a]	*ent*-**16**	52	**1x**	94
6x	H_2C=CH	R-MgBr	**10x**	62	*ent*-**17**	75	**1x**	95
6x	H_2C=C(CH_3)	R-Li	**11x**	78	*ent*-**18**	69	**1x**	95
6x	Ph	R-Li	**12x**	63	*ent*-**19**	78	**1x**	91

[a] After separation of **13n** and **13x**; reaction with tBu_2CuLi gave **9n** (66%) and **9x** (56%) as single products.



	R*OH
7n - 13n	1n
7x - 13x	1x

	R
7,14	CH_3
8,15	nBu
9,16	tBu

	R
10,17	H_2C=CH
11,18	H_2C=C-CH_3
12,19	Ph
13	CN

Scheme 2

NMR analysis of unpurified cuprate addition products outlined excellent diastereoselectivities (>95%). After purification of the raw products by flash chromatography and crystallization we were in fact unable, with help of HPLC and NMR, to find more but single diastereomers.

^{1}H and ^{13}C NMR spectroscopic studies of **7n-13n** (Table 2) and **7x-13x** (Table 3) revealed great differences in the degree of enolization depending on the nature of the substituent at C-6'. While compounds with a planar group (**10-13**) showed exclusively signals of the enol form, compounds with a bulky substituent (**7-9**) provided both resonances of the keto and the enol form.

Noteworthy are the special spectroscopic properties of the phenyl substituted derivative **12x**. The ^{1}H NMR signals of the methyl groups attached at the bornane skeleton were shifted upfield (0.5-0.6 ppm) in comparison with the usual values. Obviously the phenyl ring at C-6' and the methyl groups are situated close enough to cause a ring current induced upfield shift of the methyl resonances.

Cleavage of the chiral auxiliary from the sterically highly crowded 2-oxo-cyclohexanecarboxylates **7n-12n** and **7x-12x** was accomplished by transesterification with MeOH at 125 °C, which allowed recycling of **1n** and **1x** and gave the enantiomerically pure methylesters **14-19** and *ent*-**14-19** in good yields (Table 1).

Table 2. ^{13}C NMR Shifts ($CDCl_3$, δ in ppm) of the Auxiliary Protected Derivatives **3n-13n**.[a]

	3n[b]	**4n**[c]	**5n**[c]	**6n**[c]	**7n**[c]	**8n**[c]	**9n**[c]	**10n**[b]	**11n**[b]	**12n**[b]	**13n**[b]
C-1	51.06	52.30	51.64	51.38	51.53	51.57	51.46	51.19	51.04	50.55	51.44
C-2	75.13	77.30	77.96	76.72	76.96	77.01	77.33	75.65	75.22	75.57	77.55
C-3	59.18	59.12	58.49	59.24	59.42	59.27	59.09	59.32	59.24	59.17	59.76
C-4	50.00	49.04	48.90	49.77	49.25	49.28	49.21	49.98	50.03	49.86	49.35
C-5	19.62	19.45	19.33	19.64	19.47	19.51	19.44	19.57	19.84	19.48	19.59
C-6	27.40	26.73	26.73	27.07	26.63	25.02	26.90	26.97	26.72	25.58	27.11
C-7	45.47	45.64	46.00	45.67	45.71	45.72	45.68	45.52	45.30	45.23	45.69
Ar-CH_3	21.03	21.23	21.08	21.05	21.13	21.12	21.20	21.16	21.20	21.19	21.23
Ar-CH_3	21.03	20.93	20.97	21.05	20.90	21.12	21.20	21.16	21.09	21.19	20.95
CH_3	19.49	19.63	19.67	19.60	19.53	19.51	19.55	19.46	19.42	19.37	19.54
CH_3	19.45	19.12	19.14	19.56	19.36	19.35	19.26	19.41	19.39	19.25	19.37
CH_3	13.95	14.35	14.67	14.23	14.14	14.19	14.44	13.96	13.81	13.61	14.36
NAr C-1	136.44	135.91	138.01	136.90	137.42	137.39	136.86	136.30	136.23	136.28	137.03
NAr C-2	128.34	131.11	131.90	128.97	129.99	129.91	130.53	128.08	127.92	127.93	129.82
NAr C-3	137.91	138.68	139.12	138.12	138.11	138.11	138.41	137.90	137.85	137.84	138.45
NAr C-4	129.03	129.15	128.89	129.23	129.24	129.28	129.47	129.01	128.94	128.99	129.42
NAr C-5	137.16	136.61	136.87	137.06	137.10	137.09	136.95	137.17	137.20	137.16	136.17
NAr C-6	127.55	126.92	126.91	127.89	127.50	127.55	127.49	127.70	127.59	127.93	127.43
SO_2Ar C-1	139.45	138.57	138.33	139.26	138.98	139.03	138.71	139.45	139.50	139.48	138.72
SO_2Ar C-2, C-6	128.34	128.48	128.30	128.20	128.07	128.08	128.25	128.34	128.33	128.07	128.21
SO_2Ar C-3, C-5	128.10	128.19	128.14	128.16	127.99	128.05	128.14	128.08	128.06	127.93	128.15
SO_2Ar C-4	132.53	132.80	132.40	132.50	132.33	132.33	132.51	132.55	132.54	132.55	132.71
COO	171.44	169.40	169.21	164.15	169.54	169.74	170.61	171.77	171.64	171.69	170.67
C-1'	97.98	61.82	61.60	133.51	64.56	63.37	57.55	99.23	100.41	99.80	95.07
C-2'	171.44	205.71	203.65	194.45	207.02	207.28	209.13	173.06	172.62	173.62	174.75
C-3'	29.03	42.04	41.61	38.83	41.55	41.28	39.10	29.00	29.00	29.25	28.63
C-4'	22.50	23.17	23.57	22.28	25.41	22.51	21.01	16.74	16.85	16.59	18.80
C-5'	22.39	26.39	26.56	26.14	32.41	28.67	23.82	27.69	25.50	31.53	26.46
C-6'	21.91	37.93	37.98	155.41	35.47	40.80	47.25	35.12	38.96	38.07	25.14

[a] Further data are presented in the experimental part.

[b] **3n** (ketone:enol = 33:67); **10n-13n** showed exclusively signals of the enol form.

[c] **4n-6n** and **9n** showed exclusively signals of the keto form; **7n** (ketone:enol = 85:15); **8n** (ketone:enol = 83:17).

^1H and ^{13}C NMR spectra pointed out that bulky substituted methyl esters **14-16** and *ent*-**14-16** provided mainly signals of the keto form, while the planar substituted esters **17-19** and *ent*-**17-19** showed preferable resonances of the enol form, but in all cases both forms were present and ratios strongly depended on concentration and choice of the solvent, however. Repeated detection of ^1H NMR spectra on the other hand proved that the ketone-enol ratios were constant in $CDCl_3$ solutions, even on storage over a week. Thus we measured the optical rotations of **17-19** and *ent*-**17-19** in $CDCl_3$ solutions and determined subsequently the ketone-enol ratios by ^1H NMR.

Table 3. ^{13}C NMR Shifts ($CDCl_3$, δ in ppm) of the Auxiliary Protected Derivatives **3x**-**13x**.[a]

	3x[b]	**4x**[c]	**5x**[c]	**6x**[c]	**7x**[c]	**8x**[b]	**9x**[c]	**10x**[b]	**11x**[b]	**12x**[b]	**13x**[b]
C-1	50.17	51.88	50.70	50.44	50.73	50.74	50.56	50.56	50.72	50.30	50.65
C-2	80.15	82.46	83.27	81.46	82.44	82.46	82.44	80.58	80.61	80.86	80.67
C-3	67.42	67.82	67.14	67.44	67.66	67.58	67.41	67.67	67.63	67.43	67.86
C-4	48.68	48.84	48.28	48.62	48.38	48.43	48.43	48.60	48.63	48.49	48.33
C-5	27.65	28.31	28.76	27.74	27.75	27.94	27.94	27.85	27.77	27.66	27.49
C-6	32.04	32.64	32.55	32.11	32.34	32.34	32.97	32.36	32.39	32.30	32.36
C-7	47.36	47.35	47.29	47.32	47.33	47.32	47.25	47.37	47.31	46.80	47.50
Ar-CH_3	21.05	21.11	21.03	21.04	21.00	21.06	21.06	21.22	21.08	21.07	21.30
Ar-CH_3	21.05	21.11	21.03	21.04	21.00	21.06	21.06	21.22	21.13	21.07	21.30
CH_3	21.33	21.34	21.34	21.35	21.27	21.20	21.30	22.00	21.88	20.27	21.92
CH_3	20.75	20.53	20.68	20.70	20.72	20.74	20.58	20.71	20.59	20.27	20.49
CH_3	11.33	12.30	12.22	11.30	11.57	11.62	11.33	11.52	11.37	10.95	11.39
NAr C-1	136.84	135.64	137.67	136.97	136.83	136.89	136.81	136.83	136.87	136.80	136.66
NAr C-2	129.14	d	d	d	d	d	d	129.88	130.31	130.93	130.62
NAr C-3	137.38	d	d	d	d	d	d	137.86	137.83	137.78	138.43
NAr C-4	129.20	129.10	128.98	129.31	129.32	129.38	129.49	129.25	129.25	129.30	129.52
NAr C-5	137.38	d	d	d	d	d	d	137.86	136.80	136.65	136.99
NAr C-6	129.14	d	d	d	d	d	d	129.00	129.00	128.96	128.71
SO_2Ar C-1	139.13	138.35	37.93	138.81	138.84	138.67	138.29	138.86	138.79	138.54	138.54
SO_2Ar C-2, C-6	128.41	128.43	128.42	128.30	128.10	128.22	128.47	128.36	128.35	128.27	128.30
SO_2Ar C-3, C-5	128.07	128.14	128.16	128.05	128.04	128.07	128.06	128.04	128.03	128.04	128.12
SO_2Ar C-4	132.48	132.64	132.40	132.46	132.35	132.39	132.50	132.47	132.45	132.48	132.67
COO	171.74	169.57	168.81	163.83	169.32	169.40	170.34	172.05	172.19	172.29	170.54
C-1'	97.92	61.78	61.78	133.49	64.60	63.17	57.62	99.13	100.42	99.54	95.21
C-2'	171.67	205.70	203.19	194.31	206.85	207.07	208.66	173.54	173.44	174.38	175.54
C-3'	29.89	41.90	41.24	38.81	41.62	41.71	39.11	29.06	29.14	29.32	28.62
C-4'	22.31	22.90	23.30	22.24	25.29	22.48	20.96	16.60	16.79	16.40	18.76
C-5'	22.57	26.63	26.47	26.15	32.47	28.18	23.63	27.29	25.30	31.70	26.42
C-6'	21.88	38.46	38.10	155.48	36.50	40.53	46.72	34.76	39.14	37.50	25.17

[a] Further data are presented in the experimental part.

[b] **3x**, **10x**-**13x** showed exclusively signals of the enol form; **8x** (ketone:enol = 24:76).

[c] **4x**-**6x** showed exclusively signals of the keto form; **7x** (ketone:enol = 58:42); **9x** (ketone:enol = 80:20).

[d] Signals were not detectable due to signal broadening caused by hindered rotation.

The steric course of cuprate additions to **6n** and **6x** can be rationalized by an attack of the organocopper nucleophile from the less hindered halfspace of the *s-trans* enoate reactive species (Scheme 2), as it has been found for simpler acyclic enoates by Helmchen[3]. Quite obviously the additional keto function does not seem to influence the reaction, apart from increased reactivity.

In conclusion, the present conjugate addition approach to 6-substituted 2-oxo-cyclohexanecarboxylates enables a short and extremely stereoselective route to valuable intermediates in natural product synthesis.

EXPERIMENTAL SECTION

Melting points were determined with a Büchi glass capillary melting point apparatus (Dr. Tottoli) and are uncorrected. ^1H NMR and ^{13}C NMR spectra were measured with a Bruker AC 300 or a Varian unity plus 300 spectrometer using TMS as an internal standard. The HPLC system consisted of a Knauer pump type 64, a Reodyne injection valve, a Knauer column (Eurosper 80-5, 250x5 mm, 5 μm), a Knauer UV/VIS photometer (detection at 254 nm), and a Hewlett Packard integrator (3393 A). Optical rotations were measured on a Perkin Elmer 241 polarimeter. Microanalyses were determined at the Institute of Organic Chemistry, University of Heidelberg or at the Institute of Physical Chemistry, University of Vienna.

General Procedure A: *Esterification of* **1** *to* **3**. A solution of **1** (40.0 g, 97 mmol), **2** (32.9 g, 193 mmol) and DMAP (23.6 g, 193 mmol) in toluene (600 ml) was refluxed. After 300 ml of the solvent were distilled off within 2 d the mixture was evaporated *in vacuo*, the residue dissolved in CH_2Cl_2. The organic layer was washed with 1 M HCl, dried (Na_2SO_4) and the solvent removed at reduced pressure. Excess **2** was distilled off at 90 °C/0.03 mbar and the residue recrystallized from ether to yield pure **3**.

General Procedure B: *Phenylselenylation of* **3** *to* **4** *and* **5**. A solution of PhSeBr (1.35 g, 5.70 mmol) in CH_2Cl_2 (50 ml) was cooled to 0 °C, pyridine (0.46 g, 5.80 mmol) and a solution of **3** (3.06 g, 5.70 mmol) in CH_2Cl_2 (50 ml) were added and the mixture was stirred for 2 h at 20 °C. After extraction with 1 M HCl, the organic layer was dried (Na_2SO_4) and the solvent removed under reduced pressure to give a mixture of crude selenides (**4n**:**5n** = **4x**:**5x** = 60:40).

General Procedure C: *Oxidative Elimination of* **4** or **5** *to Enoates* **6**. To a solution of the selenide (0.51 g, 0.72 mmol) in CH_2Cl_2 (20 ml) a solution of mCPBA (120 mg, 0.72 mmol) in CH_2Cl_2 (10 ml) was added. The mixture was stirred for 2 h at 20 °C, extracted with saturated $NaHCO_3$ and $NaHSO_3$ solution, the organic layer was dried (Na_2SO_4), the solvent distilled off *in vacuo* and the residue crystallized from ether.

General Procedure D: *Preparation of Enoates* **6**. A solution of PhSeBr (4.72 g, 20.0 mmol) in CH_2Cl_2 (100 ml) was cooled to 0 °C, pyridine (1.61 g, 20.4 mmol) and a solution of **3** (10.75 g, 20.0 mmol) in CH_2Cl_2 (100 ml) was added and the mixture was stirred for 2 h at 20 °C. After extraction with 1 M HCl, the organic layer was dried (Na_2SO_4) and a solution of mCPBA (3.97 g, 23.0 mmol) in CH_2Cl_2 (100 ml) was added. The mixture was stirred for 2 h at 20 °C, extracted with saturated $NaHCO_3$ and $NaHSO_3$ solution, the organic layer was dried (Na_2SO_4), the solvent distilled of *in vacuo* and the residue was crystallized from ether to yield **6**.

General Procedure E: *Conjugate Addition of Lipshutz Cuprates to* **6**. A solution of lithium 2-thienylcyanocuprate (8 ml, 0.25 M in THF, 2 mmol) was cooled to −78 °C, a solution of the organolithium (organomagnesium) compound (2 mmol) was added and the mixture was stirred at −78 °C for 1 h. A solution of **6** (1.05 g, 2 mmol) in THF (20 ml) was added and stirring was continued at −78 °C for 2 h. The reaction mixture was quenched with NH_4Cl solution (5%), stirred at 20 °C for 1 h and extracted with CH_2Cl_2. The organic layer was dried (Na_2SO_4) and the solvent distilled off *in vacuo*. Purification of the residue by flash chromatography (100 g, silica gel, hexane/EtOAc = 9:1) and crystallization gave pure adducts **7**–**13**.

General Procedure F: *Conjugate Addition of* tBu_2CuLi *to* **6**. A suspension of CuI (381 mg, 2.00 mmol) in THF (20 ml) was cooled to −78 °C, a solution of tBuLi (2.30 ml, 1.74 M in pentane, 4 mmol) was added and the resulting mixture stirred for 1 h at −78 °C. A solution of **6** (1.07 g, 2.00 mmol) in THF (20 ml) was added and stirring was continued for 2 h at −78 °C. The reaction mixture was quenched with saturated NH_4Cl solution, stirred at 20 °C for 1 h and extracted with CH_2Cl_2. The organic layer was dried (Na_2SO_4) and the solvent distilled off *in vacuo*. Purification of the residue by flash chromatography (100 g, silica gel, hexane/EtOAc = 9:1) and crystallization gave pure adducts **9n** and **9x**.

General Procedure G: *Transesterification of* **7-12** *to* **14-19**. The camphor derived esters (2.00 mmol) were dissolved in methanol (25 ml) and heated in an autoclave (125-140 °C, 16-100 h). Then the solvent was evaporated at reduced pressure and the auxiliary (**1n** or **1x**) was recovered by crystallization from methanol. Kugelrohr distillation of the filtrate afforded the enantiomerically pure methylesters **14-19**.

(1R,2R,3S,4S)-{3-[N-Benzenesulfonyl-N-(3,5-dimethylphenyl)-amino]-2-bornyl}-2-hydroxy-cyclohexene-carboxylate (**3n**)

Esterification of **1n** (procedure A) gave **3n** (49.0g, 94%), colourless crystals, mp 181 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ketone:enol = 33:67) δ(ketone, separated signals) = 0.85 (s, 3H, CH_3), 0.92 (s, 3H, CH_3), 1.01 (s, 3H, CH_3), 2.12 (s, 3H, Ar-CH_3), 2.26 (s, 3H, Ar-CH_3), 3.39 (dd, *J* = 10.4 and 5.7 Hz, 1H, 1'-H), 5.36 (d, *J* = 8.4 Hz, 1H, 2-H); δ(enol) = 0.81 (s, 3H, CH_3), 0.87 (s, 3H, CH_3), 1.02 (s, 3H, CH_3), 1.10-1.35 (m, 2H), 1.40-1.85 (m, 7H), 1.90-2.05 (m, 2H), 2.09 (s, 3H, Ar-CH_3), 2.24 (s, 3H, Ar-CH_3), 2.30-2.70 (m, 2H), 4.14 (m_c, 1H, 3-H), 5.38 (d, *J* = 8.0 Hz, 1H, 2-H), 6.17 (s, 1H, NAr 2-H), 6.73 (s, 1H, NAr 4-H), 6.81 (s, 1H, NAr 6-H), 7.34-7.42 (m, 4H, SO_2ArH), 7.52 (m_c, 1H, SO_2ArH), 12.01 (s, 1H, =C-OH). ^{13}C NMR (75 MHz, $CDCl_3$, ketone:enol = 33:67) δ(ketone, separated signals) = 13.82 (CH_3), 19.40 (CH_3), 19.45 (CH_3), 19.50 (C-5), 21.03 (2 Ar-CH_3), 23.56 (C-4'), 26.84 (C-5'), 27.40 (C-6), 29.75 (C-6'), 41.94 (C-3'), 45.53 (C-7), 50.00 (C-4), 51.16 (C-1), 57.04 (C-1'), 59.08 (C-3), 76.36 (C-2), 127.73 (NAr C-2), 128.00 (NAr C-6), 128.13 (SO_2Ar C-3, C-5), 128.20 (SO_2Ar C-2, C-6), (NAr C-6), 129.00 (NAr C-4), 132.53 (SO_2Ar C-4), 136.67 (NAr C-1), 137.16 (NAr C-3), 138.10 (NAr C-5), 139.78 (SO_2Ar C-1), 169.48 (COO), 206.44 (C-2'); δ(enol) see table 2. Anal. Calcd for $C_{31}H_{39}NO_5S$: C, 69.24; H, 7.33; N, 2.60; S, 5.95. Found C, 69.20; H, 7.30, N, 2.71; S, 5.98.

(1R,2S,3R,4S)-{3-[N-Benzenesulfonyl-N-(3,5-dimethylphenyl)-amino]-2-bornyl}-2-hydroxy-cyclohexene-carboxylate (**3x**)

Esterification of **1x** (procedure A) gave **3x** (49.1g, 94%), colourless crystals, mp 171 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 0.64 (s, 3H, CH_3), 0.79 (s, 3H, CH_3), 1.00 (s, 3H, CH_3), 1.08 (m_c, 1H), 1.34 (m_c, 1H), 1.54 (m_c, 1H), 1.60-1.83 (m, 5H), 1.90-2.10 (m, 3H), 2.14 (d, *J* = 4.4 Hz, 1H, 4-H), 2.18-2.50 (m, 6H), 2.69 (m_c, 1H), 3.79 (d, *J* = 7.1 Hz, 1H, 3-H), 5.28 (d, *J* = 7.1 Hz, 1H, 2-H), 5.91 (s, br., 1H, NAr 2-H), 6.83 (s, 1H, NAr 4-H), 6.87 (s, br., 1H, NAr 6-H), 7.30-7.42 (m, 4H, SO_2ArH), 7.52 (m_c, 1H, SO_2ArH), 12.20 (s, 1H, =C-OH). ^{13}C NMR (75 MHz, $CDCl_3$) see table 3. Anal. Calcd for $C_{31}H_{39}NO_5S$: C; 69.24; H, 7.33; N, 2.60; S, 5.95. Found C, 69.22; H, 7.33; N, 2.77; S, 6.09.

(1R,2R,3S,4S)-{3-[N-Benzenesulfonyl-N-(3,5-dimethylphenyl)-amino]-2-bornyl}-(1R)-2-oxo-1-phenyl-selenyl-cyclohexanecarboxylate* (**4n**)

Phenylselenylation of **3n** (procedure B), separation by flash chromatography (300 g silica gel, hexane:EtOAc = 8:2) and crystallization from ether/hexane yielded **4n** (1.26g, 32%), colourless crystals, mp 168 °C. TLC (silica gel, hexane:EtOAc = 8:2) R_f = 0.34. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 0.79 (s, 3H, CH_3), 1.04 (s, 3H, CH_3), 0.94-1.22 (m, 3H), 1.09 (s, 3H, CH_3), 1.56 (t, *J* = 4.0 Hz, 1H, 4-H), 1.65-1.93 (m, 4H), 2.01 (m_c, 1H), 2.04 (s, 3H, Ar-CH_3), 2.12-2.35 (m, 2H), 2.39 (s, 3H, Ar-CH_3), 2.86 (d, *J* = 14.8 Hz, 1H), 3.65 (m_c, 1H), 4.22 (dd, *J* = 7.9 and 4.0 Hz, 1H, 3-H), 5.59 (s, 1H, NAr 2-H), 5.65 (d, *J* = 7.9 Hz, 1H, 2-H), 6.89 (s, 1H, NAr 4-H), 7.11 (s, 1H, NAr 6-H), 7.26-7.46 (m, 7H, SeArH, SO_2ArH), 7.57 (m_c, 1H, SO_2ArH), 7.61-7.66 (m_c, 2H, SeArH). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 126.65 (SeAr C-1), 128.66 (SeAr C-3, C-5), 129.75 (SeAr C-4), 138.08 (SeAr C-2, C-6), further signals see table 2. Anal. Calcd for $C_{37}H_{43}NO_5SSe$: C, 64.14; H, 6.27; N, 2.02. Found C, 64.33; H, 6.35; N, 2.19.

(1R,2S,3R,4S)-{3-[N-Benzenesulfonyl-N-(3,5-dimethylphenyl)-amino]-2-bornyl}-(1R)-2-oxo-1-phenylselenyl-cyclohexanecarboxylate* (**4x**)

Phenylselenylation of **3x** (procedure B), separation by flash chromatography (300 g silica gel, hexane:EtOAc = 8:2) and crystallization from ether/hexane yielded **4x** (1.94g, 49%), colourless crystals, mp 182 °C. TLC (silica gel, hexane:EtOAc = 8:2) R_f = 0.38. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 0.57 (s, 3H, CH_3), 0.77 (s, 3H, CH_3), 1.00 (m_c, 1H), 1.17 (s, 3H, CH_3), 1.40-2.50 (m, 16H), 2.81 (d, *J* = 15.4 Hz, 1H), 3.64 (ddd, *J* = 16.0, 12.0 and 6.0 Hz, 1H), 3.78 (d, *J* = 7.2 Hz, 1H, 3-H), 5.50 (d, *J* = 7.2 Hz, 1H, 2-H), 6.91 (s, 1H, NAr 4-H), 7.25-7.50 (m, 7H, SeArH, SO_2ArH), 7.58 (m_c, 1H, SO_2ArH), 7.62-7.68 (m, 2H, SeArH). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 127.01 (SeAr C-1), 129.05 (SeAr C-3, C-5), 129.88 (SeAr C-4), 138.14 (SeAr C-2, C-6), further signals see table 3. Anal. Calcd for $C_{37}H_{43}NO_5SSe$: C, 64.14; H, 6.27; N, 2.02. Found C, 64.28; H, 6.42; N, 2.29.

(1R,2R,3S,4S)-{3-[N-Benzenesulfonyl-N-(3,5-dimethylphenyl)-amino]-2-bornyl}-(1S)-2-oxo-1-phenylselenyl-cyclohexanecarboxylate* (**5n**)

Phenylselenylation of **3n** (procedure B), separation by flash chromatography (300 g silica gel, hexane:EtOAc = 8:2) and crystallization from 2-PrOH yielded **5n** (1.03g, 26%), colourless crystals, mp 173 °C. TLC (silica gel, hexane:EtOAc = 8:2) R_f = 0.28. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 0.79 (s, 3H, CH_3), 0.85 (s, 3H, CH_3), 0.90-1.05 (m, 2H), 1.07 (s, 3H, CH_3), 1.53-2.05 (m, 8H), 2.08 (s, 3H, Ar–CH_3), 2.46 (s, 3H, Ar–CH_3), 2.50-2.70 (m, 3H), 4.45 (dd, *J* = 9.0 and 3.3 Hz, 1H, 3-H), 5.61 (d, *J* = 9.0 Hz, 1H, 2-H), 5.79 (s, 1H, NAr 2-H), 6.92 (s, 1H, NAr 4-H), 7.20-7.48 (m, 5H, NAr 6-H, SeArH, SO_2ArH), 7.50-7.64 (m, 4H, SeArH, SO_2ArH), 7.82 (m_c, 2H, SeArH). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 126.84 (SeAr C-1), 128.54 (SeAr C-3, C-5), 129.82 (SeAr C-4), 138.15 (SeAr C-2, C-6), further signals see table 2. Anal. Calcd for $C_{37}H_{43}NO_5SSe$: C, 64.14; H, 6.27; N, 2.02. Found C, 63.95; H, 6.25; N, 2.23.

(1R,2S,3R,4S)-{3-[N-Benzenesulfonyl-N-(3,5-dimethylphenyl)-amino]-2-bornyl}-(1S)-2-oxo-1-phenylselenyl-cyclohexanecarboxylate* (**5x**)

Phenylselenylation of **3x** (procedure B), separation by flash chromatography (300 g silica gel, hexane:EtOAc = 8:2) and crystallization from hexane yielded **5x** (0.67g, 17%), colourless crystals, mp 187 °C. TLC (silica gel, hexane:EtOAc = 8:2) R_f = 0.30. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 0.56 (s, 3H, CH_3), 0.58 (s, 3H, CH_3), 0.89 (s, 3H, CH_3), 1.09 (m_c, 1H), 1.44-1.80 (m, 7H), 1.84 (d, *J* = 4.1 Hz, 1H, 4-H), 1.90-2.52 (m, 8H, 2 Ar–CH_3, aliphatic H), 2.54-2.70 (m, 2H), 4.07 (d, *J* = 7.4 Hz, 1H, 3-H), 5.44 (d, *J* = 7.4 Hz, 1H, 2-H), 5.71 (s, br., 1H, NAr 2-H), 6.90 (s, 1H, NAr 4-H), 7.26-7.45 (m, 6H, SeArH, SO_2ArH, NAr 6-H), 7.49-7.59 (m, 3H, SeArH, SO_2ArH), 7.79 (m_c, 2H, SeArH). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 127.10 (SeAr C-1), 128.35 (SeAr C-3, C-5), 129.70 (SeAr C-4), 138.44 (SeAr C-2, C-6), further signals see table 3. Anal. Calcd for $C_{37}H_{43}NO_5SSe$: C, 64.14; H, 6.27; N, 2.02. Found C, 64.29; H, 6.31; N, 2.23.

(1R,2R,3S,4S)-{3-[N-Benzenesulfonyl-N-(3,5-dimethylphenyl)-amino]-2-bornyl}-2-oxo-cyclohexenecarboxylate (**6n**)

Reaction of **3n** (procedure D) afforded **6n** (6.43 g, 60%); oxidation of **4n** (procedure C) gave **6n** (351 mg, 91%); oxidation of **5n** (procedure C) yielded **6n** (350 mg, 91%); colourless crystals, mp 180 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 0.78 (s, 3H, CH_3), 0.89 (s, 3H, CH_3), 1.04 (s, 3H, CH_3), 1.11-1.23 (m, 2H), 1.37 (m_c, 1H), 1.84 (t, *J* = 3.4 Hz, 1H, 4-H), 1.94 (m_c, 1H), 2.05 (s, 3H, Ar–CH_3), 2.06-2.15 (m, 2H), 2.27 (s, 3H, Ar–CH_3), 2.50-2.62 (m, 4H), 4.22 (dd, *J* = 8.5 and 3.4 Hz, 1H, 3-H), 5.47 (d, *J* = 8.5 Hz, 1H, 2-H),

5.96 (s, 1H, NAr 2-H), 6.82 (s, 1H, NAr 4-H), 6.86 (s, 1H, NAr 6-H), 7.32-7.41 (m, 4H, SO_2ArH), 7.52 (m_c, 1H, SO_2ArH), 7.87 (t, J = 4.1 Hz, 1H, 6'-H). ^{13}C NMR (75 MHz, $CDCl_3$) see table 2. Anal. Calcd for $C_{31}H_{37}NO_5S$: C, 69.50; H, 6.98; N, 2.62; S, 5.97. Found C, 69.44; H, 6.94; N, 2.72; S, 5.98.

(1R,2S,3R,4S)-{3-[N-Benzenesulfonyl-N-(3,5-dimethylphenyl)-amino]-2-bornyl}-2-oxo-cyclohexene-carboxylate (**6x**)

Reaction of **3x** (procedure D) afforded **6x** (7.28 g, 68%); oxidation of **4x** (procedure C) gave **6x** (328 mg, 85%); oxidation of **5x** (procedure C) yielded **6x** (336 mg, 87%); colourless crystals, mp 171 °C. ^1H NMR (300 MHz, $CDCl_3$) δ = 0.61 (s, 3H, CH_3), 0.89 (s, 3H, CH_3), 0.93 (s, 3H, CH_3), 1.07 (m_c, 1H), 1.39 (m_c, 1H), 1.54 (m_c, 1H), 1.70 (m_c, 1H), 1.93 (d, J = 4.4 Hz, 1H, 4-H), 1.96-2.18 (m_c, 5H, Ar–CH_3, aliphatic H), 2.27 (s, br., 3H, Ar–CH_3), 2.48-2.63 (m, 4H), 3.83 (d, J = 7.2 Hz, 1H, 3-H), 5.35 (d, J = 7.2 Hz, 1H, 2-H), 5.75 (s, br., 1H, NAr 2-H), 6.83 (s, 1H, NAr 4-H), 6.92 (s, br., 1H, NAr 6-H), 7.30-7.40 (m, 4H, SO_2ArH), 7.50 (m_c, 1H, SO_2ArH), 7.95 (t, J = 4.1 Hz, 1H, 6'-H). ^{13}C NMR (75 MHz, $CDCl_3$) see table 3. Anal. Calcd for $C_{31}H_{37}NO_5S$: C, 69.50; H, 6.98; N, 2.62; S, 5.97. Found C, 69.22; H, 6.98; N, 2.84; S, 6.01.

(1R,2R,3S,4S)-{3-[N-Benzenesulfonyl-N-(3,5-dimethylphenyl)-amino]-2-bornyl}-(1S,6R)-6-methyl-2-oxo-cyclohexanecarboxylate (**7n**)

Starting material **6n**: procedure E; cuprate precursor MeLi (1.29 ml, 1.55 M in ether); gave **7n** (706 mg, 64%), colourless crystals from 2-PrOH, mp 176 °C. ^1H NMR (300 MHz, $CDCl_3$, ketone:enol = 57:43) δ(ketone) = 0.80 (s, 3H, CH_3), 1.02 (s, 3H, CH_3), 1.06 (s, 3H, CH_3), 1.16 (d, J = 7.3 Hz, 3H, CH_3), 1.46-1.89 (m, 7H), 1.90-2.14 (m, 2H), 1.99 (s, 3H, Ar–CH_3), 2.15-2.51 (m, 3H), 2.32 (s, 3H, Ar–CH_3), 3.42 (d, J = 11.3 Hz, 1H, 1'-H), 4.28 (dd, J = 8.3 and 3.5 Hz, 1H, 3-H), 5.50 (d, J = 8.3 Hz, 1H, 2-H), 5.73 (s, 1H, NAr 2-H), 6.82 (s, 1H, NAr 4-H), 7.13 (s, 1H, NAr 6-H), 7.28-7.40 (m, 4H, SO_2ArH), 7.50 (m_c, 1H, SO_2ArH); δ(enol, separated signals) = 0.85 (s, 3H, CH_3), 0.86 (s, 3H, CH_3), 1.03 (s, 3H, CH_3), 1.19 (d, J = 7.1 Hz, 3H, CH_3), 2.09 (s, 3H, Ar–CH_3), 2.24 (s, 3H, Ar–CH_3), 3.21 (m_c, 1H, 6'-H), 4.16 (dd, J = 8.3 and 3.5 Hz, 1H, 3-H), 5.42 (d, J = 8.3 Hz, 1H, 2-H), 6.09 (s, 1H, NAr 2-H), 6.74 (s, 1H, NAr 6-H), 6.82 (s, 1H, NAr 4-H), 12.21 (s, 1H, =C–OH). ^{13}C NMR (75 MHz, $CDCl_3$, ketone:enol = 85:15) δ(ketone) = 21.13 (CH_3), for further signals see table 2; δ(enol) = 14.14 (CH_3), 16.91 (C-4'), 19.36 (CH_3), 19.53 (CH_3), 19.66 (C-5), 20.90 (Ar–CH_3), 21.13 (Ar–CH_3), 21.45 (CH_3), 26.04 (C-6'), 27.42 (C-6), 29.60 (C-5'), 29.17 (C-3'), 45.54 (C-7), 49.90 (C-4), 51.11 (C-1), 59.17 (C-3), 75.77 (C-2), 103.46 (C-1'), 128.35 (NAr C-2), 127.99 (SO_2Ar C-3, C-5), 128.07 (SO_2Ar C-2, C-6), 128.35 (NAr C-6), 129.09 (NAr C-4), 132.55 (SO_2Ar C-4), 136.31 (NAr C-1), 137.10 (NAr C-3), 137.91 (NAr C-5), 139.30 (SO_2Ar C-1), 171.93 (COO), 172.03 (C-2'). Anal. Calcd for $C_{32}H_{41}NO_5S$: C, 69.65; H, 7.51; N, 2.54; S, 5.80. Found C, 69.35; H, 7.38; N, 2.69; S, 6.05.

(1R,2S,3R,4S)-{3-[N-Benzenesulfonyl-N-(3,5-dimethylphenyl)-amino]-2-bornyl}-(1R,6S)-6-methyl-2-oxo-cyclohexanecarboxylate (**7x**)

Starting material **6x**; procedure E; cuprate precursor MeLi (1.29 ml, 1.55 M in ether); gave **7x** (861 mg, 78%), colourless crystals from 2-PrOH, mp 175 °C. ^1H NMR (300 MHz, $CDCl_3$, ketone:enol = 58:42) δ(ketone) = 0.57 (s, 3H, CH_3), 0.82 (s, 3H, CH_3), 1.06 (s, 3H, CH_3), 1.17 (d, J = 6.2 Hz, 3H, CH_3), 1.35-2.55 (m, 18H), 3.49 (d, J = 10.7 Hz, 1H, 1'-H), 3.85 (d, J = 7.1 Hz, 1H, 3-H), 5.27 (d, J = 7.1 Hz, 1H, 2-H), 5.80 (s, 1H, NAr 2-H), 6.83 (s, 1H, NAr 4-H), 6.91 (s, 1H, NAr 6-H), 7.27-7.40 (m, 4H, SO_2ArH), 7.49 (m_c,

1H, SO_2ArH); δ(enol, separated signals) = 0.64 (s, 3H, CH_3), 0.85 (s, 3H, CH_3), 0.98 (s, 3H, CH_3), 1.20 (d, J = 6.0 Hz, 3H, CH_3), 3.28 (m_c, 1H, 6'-H), 3.83 (d, J = 7.2 Hz, 1H, 3-H), 5.39 (d, J = 7.2 Hz, 1H, 2-H), 5.60 (s, 1H, NAr 2-H), 6.83 (s, 1H, NAr 4-H), 7.10 (s, 1H, NAr 6-H), 12.49 (s, 1H, =C–OH). ^{13}C NMR (75 MHz, $CDCl_3$, ketone:enol = 58:42) δ(ketone) = 21.15 (CH_3), for further signals see table 3; δ(enol) = 11.57 (CH_3), 16.84 (C-4'), 20.63 (CH_3), 21.00 (Ar–CH_3), 21.15 (CH_3), 21.71 (CH_3), 25.76 (C-6'), 27.82 (C-5), 29.19 (C-3'), 29.37 (C-5'), 32.47 (C-6), 47.30 (C-7), 48.57 (C-4), 50.33 (C-1), 67.59 (C-3), 80.44 (C-2), 103.59 (C-1'), 128.04 (NAr C-2, SO_2Ar C-3, C-5), 128.10 (SO_2Ar C-2, C-6), 128.38 (NAr C-6), 129.27 (NAr C-4), 132.46 (SO_2Ar C-4), 136.83 (NAr C-1), 137.50 (NAr C-3), 138.39 (NAr C-5), 138.84 (SO_2Ar C-1), 172.33 (COO, C-2'). Anal. Calcd for $C_{32}H_{41}NO_5S$: C, 69.65; H, 7.51; N, 2.54; S, 5.80. Found C, 69.51; H, 7.51; N, 2.49; S, 5.88.

(1R,2R,3S,4S)-{3-[N-Benzenesulfonyl-N-(3,5-dimethylphenyl)-amino]-2-bornyl}-(1S,6R)-6-butyl-2-oxo-cyclohexanecarboxylate (**8n**)

Starting material **6n**; procedure E; cuprate precursor nBuLi (1.40 ml, 1.43 M in hexane); gave **8n** (736 mg, 62%), colourless crystals from 2-PrOH, mp 149 °C. ^1H NMR (300 MHz, $CDCl_3$, ketone:enol = 83:17) δ(ketone) = 0.80 (s, 3H, CH_3), 0.84 (t, J = 6.2 Hz, 3H, nBu CH_3), 1.00 (s, 3H, CH_3), 1.04 (s, 3H, CH_3), 1.09-1.90 (m, 13H), 1.94-2.17 (m, 2H), 2.01 (s, 3H, Ar–CH_3), 2.20-2.57 (m, 3H), 2.32 (s, 3H, Ar–CH_3), 3.44 (d, J = 10.3 Hz, 1H, 1'-H), 4.26 (dd, J = 8.6 and 3.0 Hz, 1H, 3-H), 5.48 (d, J = 8.6 Hz, 1H, 2-H), 5.77 (s, 1H, NAr 2-H), 6.82 (s, 1H, NAr 4-H), 7.10 (s, 1H, NAr 6-H), 7.30-7.40 (m, 4H, SO_2ArH), 7.49 (m_c, 1H, SO_2ArH); δ(enol, separated signals) = 0.85 (s, 3H, CH_3), 0.86 (s, 3H, CH_3), 0.89 (t, J = 7.1 Hz, 3H, nBu CH_3), 1.04 (s, 3H, CH_3), 2.06 (s, 3H, Ar–CH_3), 2.24 (s, 3H, Ar–CH_3), 2.97 (m_c, 1H, 6'-H), 4.16 (dd, J = 8.6 and 3.2 Hz, 1H, 3-H), 5.48 (d, J = 8.6 Hz, 1H, 2-H), 6.02 (s, 1H, NAr 2-H), 6.82 (s, 1H, NAr 4-H), 6.84 (s, 1H, NAr 6-H), 12.25 (s, 1H, =C–OH). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 13.97 (nBu C-4), 26.64 (nBu C-3), 29.12 (nBu C-2), 34.24 (nBu C-1), for further signals see table 2. Anal. Calcd for $C_{35}H_{47}NO_5S$: C, 70.79; H, 7.99; N, 2.36; S, 5.39. Found C, 70.56; H, 7.92; N, 2.55; S, 5.40.

(1R,2S,3R,4S)-{3-[N-Benzenesulfonyl-N-(3,5-dimethylphenyl)-amino]-2-bornyl}-(1R,6S)-6-butyl-2-oxo-cyclohexanecarboxylate (**8x**)

Starting material **6x**; procedure E; cuprate precursor nBuLi (1.40 ml, 1.43 M in hexane); gave **8x** (831 mg, 70%), colourless crystals from 2-PrOH, mp 168 °C. ^1H NMR (300 MHz, $CDCl_3$) δ = 0.62 (s, 3H, CH_3), 0.77-1.04 (m, 2H), 0.86 (s, 3H, CH_3), 0.92 (t, J = 6.0 Hz, 3H, nBu CH_3), 0.93 (s, 3H, CH_3), 1.10 (m_c, 1H), 1.25-1.80 (m, 11H), 1.94 (d, J = 4.3 Hz, 1H, 4-H), 2.01 (s, br., 3H, Ar–CH_3), 2.20-2.40 (m, 2H), 2.30 (s, br., 3H, Ar–CH_3), 3.12 (m_c, 1H, 6'-H), 3.85 (d, J = 7.2 Hz, 1H, 3-H), 5.41 (d, J = 7.2 Hz, 1H, 2-H), 5.69 (s, br., 1H, NAr 2-H), 6.85 (s, 1H, NAr 6-H), 7.06 (s, br., 1H, NAr 4-H), 7.30-7.40 (m, 4H, SO_2ArH), 7.50 (m_c, 1H, SO_2ArH), 12.64 (s, 1H, =C–OH). ^{13}C NMR (75 MHz, $CDCl_3$, ketone:enol = 24:76) δ(ketone) = 13.98 (nBu C-4), 24.52 (nBu C-3), 29.19 (nBu C-2), 33.72 (nBu C-1), for further signals see table 3; δ(enol) = 11.56 (CH_3), 14.40 (nBu C-4), 16.68 (C-4'), 20.60 (CH_3), 21.06 (2 Ar–CH_3), 21.75 (CH_3), 23.24 (C-5'), 24.38 (nBu C-3), 27.84 (C-5), 29.09 (nBu C-2), 30.58 (C-3'), 31.38 (C-6'), 32.44 (C-6), 34.03 (nBu C-1), 47.28 (C-7), 48.53 (C-4), 50.44 (C-1), 67.58 (C-3), 80.74 (C-2), 103.64 (C-1'), 128.04 (SO_2Ar C-3, C-5), 128.40 (SO_2Ar C-2, C-6), 129.00 (NAr C-2), 129.32 (NAr C-4), 130.87 (NAr C-6), 132.47 (SO_2Ar C-4), 136.89 (NAr C-1), 137.44 (NAr C-3), 138.45 (NAr C-5), 138.67 (SO_2Ar C-1), 172.48 (COO), 172.52 (C-2'). Anal. Calcd for $C_{35}H_{47}NO_5S$: C, 70.79; H, 7.99; N, 2.36; S, 5.39. Found C, 70.86; H, 7.97; N, 2.58; S, 5.39.

(1R,2R,3S,4S)-{3-[N-Benzenesulfonyl-N-(3,5-dimethylphenyl)-amino]-2-bornyl}-(1S,6R)-6-tert-butyl-2-oxo-cyclohexanecarboxylate (**9n**)

Starting material **6n**; procedure E; cuprate precursor tBuLi (1.15 ml, 1.74 M in pentane); gave a mixture of **9n** and **13n**. TLC (silica gel, hexane:EtOAc = 8:2) R_f(**9n**) = 0.41, R_f(**13n**) = 0.28. Separation by flash chromatography (100 g, silica gel, hexane/EtOAc = 9:1) gave **9n** (309 mg, 26%), colourless crystals from hexane, mp 135 °C and **13n** (182 mg, 16%). Starting material **6n**; procedure F; gave **9n** (783 mg, 66%), colourless crystals from hexane, mp 181 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 0.79 (s, 3H, CH_3), 0.85 (s, 3H, CH_3), 1.00-1.08 (m, 4H), 1.01 (s, 9H, tBu CH_3), 1.04 (s, 3H, CH_3), 1.60-1.79 (m, 5H), 2.04 (s, 3H, Ar-CH_3), 2.32 (m_c, 1H), 2.36 (s, 3H, Ar-CH_3), 2.69 (m_c, 1H), 2.93 (m_c, 1H, 6'-H), 3.56 (s, 1H, 1'-H), 4.26 (m_c, 1H, 3-H), 5.49 (d, J = 8.3 Hz, 1H, 2-H), 5.73 (s, 1H, NAr 2-H), 6.87 (s, 1H, NAr 4-H), 7.26 (s, 1H, NAr 6-H), 7.32-7.44 (m, 4H, SO_2ArH), 7.53 (m_c, 1H, SO_2ArH). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 27.51 (tBu CH_3), 34.11 (tBu C), for further signals see table 2. Anal. Calcd for $C_{35}H_{47}NO_5S$: C, 70.79; H, 7.99; N, 2.36; S, 5.39. Found C, 70.54; H, 7.84; N, 2.50; S, 5.47.

(1R,2S,3R,4S)-{3-[N-Benzenesulfonyl-N-(3,5-dimethylphenyl)-amino]-2-bornyl}-(1R,6S)-6-tert-butyl-2-oxo-cyclohexanecarboxylate (**9x**)

Starting material **6x**; procedure E; cuprate precursor tBuLi (1.15 ml, 1.74 M in pentane); gave a mixture of **9x** and **13x**. TLC (silica gel, hexane:EtOAc = 8:2) R_f(**9x**) = 0.42, R_f(**13x**) = 0.30. Separation by flash chromatography (100 g, silica gel, hexane/EtOAc = 9:1) gave **9x** (444 mg, 37%), colourless crystals from 2-PrOH, mp 215 °C and **13x** (155 mg, 14%). Starting material **6x**; procedure F; gave **9x** (665 mg, 56%), colourless crystals from 2-PrOH, mp 215 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ketone:enol = 81:19) δ(ketone) = 0.55 (s, 3H, CH_3), 0.79 (s, 3H, CH_3), 0.80 (s, 3H, CH_3), 0.97 (s, 9H, tBu CH_3), 1.07 (m_c, 1H), 1.38 (m_c, 1H), 1.52 (m_c, 1H), 1.60-1.76 (m, 2H), 1.80 (d, J = 4.0 Hz, 1H, 4-H), 2.00-2.30 (m, 4H), 2.02 (s, br., 3H, Ar-CH_3), 2.33 (s, br., 3H, Ar-CH_3), 2.69 (m_c, 1H), 2.90 (t, J = 8.0 Hz, 1H, 6'-H), 3.66 (s, 1H, 1'-H), 3.84 (d, J = 7.1 Hz, 1H, 3-H), 5.32 (d, J = 7.1 Hz, 1H, 2-H), 5.59 (s, br., 1H, NAr 2-H), 6.87 (s, 1H, NAr 4-H), 7.23 (s, br., 1H, NAr 6-H), 7.30-7.42 (m, 4H, SO_2ArH), 7.52 (m_c, 1H, SO_2ArH); δ(enol, separated signals) = 0.58 (s, 3H, CH_3), 0.85 (s, 3H, CH_3), 0.90 (s, 3H, CH_3), 1.01 (s, 9H, tBu CH_3), 3.21 (m_c, 1H, 6'-H), 3.79 (d, J = 7.2 Hz, 1H, 3-H), 5.41 (d, J = 7.2 Hz, 1H, 2-H), 12.60 (s, 1H, =C-OH). ^{13}C NMR (75 MHz, $CDCl_3$, ketone:enol = 80:20) δ(ketone) = 27.60 (tBu CH_3), 34.12 (tBu C), for further signals see table 3; δ(enol) = 11.65 (CH_3), 19.85 (C-4'), 20.51 (CH_3), 21.06 (2 Ar-CH_3), 22.79 (CH_3), 23.32 (C-5'), 28.12 (C-5), 28.18 (C-3'), 29.00 (tBu CH_3), 32.22 (C-6), 36.61 (tBu C), 40.04 (C-6'), 47.36 (C-7), 48.43 (C-4), 50.41 (C-1), 67.70 (C-3), 82.27 (C-2), 101.29 (C-1'), 128.00 (SO_2Ar C-3, C-5), 128.39 (SO_2Ar C-2, C-6), 129.42 (NAr C-4), 132.43 (SO_2Ar C-4), 136.89 (NAr C-1), 138.29 (SO_2Ar C-1), 173.71 (COO), 173.95 (C-2'). Anal. Calcd for $C_{35}H_{47}NO_5S$: C, 70.79; H, 7.99; N, 2.36; S, 5.39. Found C, 70.54; H, 7.97; N, 2.48; S, 5.41.

(1R,2R,3S,4S)-{3-[N-Benzenesulfonyl-N-(3,5-dimethylphenyl)-amino]-2-bornyl}-(6S)-2-hydroxy-6-vinyl-cyclohexenecarboxylate (**10n**)

Starting material **6n**; procedure E; cuprate precursor H_2C=CHMgBr (2.00 ml, 1.00 M in THF); gave **10n** (789 mg, 70%), colourless crystals from 2-PrOH, mp 156 °C. ^{1}H NMR (300 MHz, $CDCl_3$, ketone:enol = 17:83) δ(ketone, separated signals) = 0.80 (s, 3H, CH_3), 0.99 (s, 3H, CH_3), 1.04 (s, 3H, CH_3), 2.00 (s, 3H, Ar-CH_3), 2.32 (s, 3H, Ar-CH_3), 3.05 (m_c, 1H, 6'-H), 3.61 (d, J = 10.0 Hz, 1H, 1'-H), 4.26 (m_c, 1H, 3-H), 5.08 (d, J = 10.2 Hz, 1H, =CH_2), 5.18 (d, J = 17.1 Hz, 1H, =CH_2), 5.47 (d, J = 9.2 Hz, 1H, 2-H),

5.78 (s, 1H, NAr 2-H), 5.87 (ddd, J = 17.1, 10.2 and 7.0 Hz, 1H, =CH–), 6.82 (s, 1H, NAr 4-H), 7.09 (s, 1H, NAr 6-H); δ(enol) = 0.78 (s, 3H, CH_3), 0.84 (s, 3H, CH_3), 1.00 (s, 3H, CH_3), 1.05-1.98 (m, 11H), 2.08 (s, 3H, Ar–CH_3), 2.25 (s, 3H, Ar–CH_3), 3.78 (m_c, 1H, 6'-H), 4.10 (m_c, 1H, 3'-H), 4.92 (d, J = 17.2 Hz, 1H, =CH_2), 5.08 (d, J = 10.2 Hz, 1H, =CH_2), 5.38 (d, J = 8.7 Hz, 1H, 2-H), 5.98 (ddd, J = 17.1, 10.2 and 5.3 Hz, 1H, =CH–), 6.09 (s, 1H, NAr 2-H), 6.75 (s, 1H, NAr 6-H), 6.82 (s, 1H, NAr 4-H), 7.30-7.40 (m, 4H, SO_2ArH), 7.51 (m_c, 1H, SO_2ArH), 12.37 (s, 1H, =C–OH). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 114.63 (=CH_2), 142.58 (=CH–), for further signals see table 2. Anal. Calcd for $C_{33}H_{41}NO_5S$: C, 70.30, H, 7.34, N, 2.49; S, 5.68. Found C, 70.11, H, 7.26, N, 2.62; S, 5.71.

(1R,2S,3R,4S)-{3-[N-Benzenesulfonyl-N-(3,5-dimethylphenyl)-amino]-2-bornyl}-(6R)-2-hydroxy-6-vinyl-cyclohexenecarboxylate (**10x**)

Starting material **6x**; procedure E; cuprate precursor H_2C=CHMgBr (2.00 ml, 1.00 M in THF); gave **10x** (699 mg, 62%), colourless crystals from 2-PrOH, mp 165 °C. ^1H NMR (300 MHz, $CDCl_3$) δ = 0.60 (s, 3H, CH_3), 0.77 (s, 3H, CH_3), 0.88 (s, 3H, CH_3), 1.07 (m_c, 1H), 1.36 (m_c, 1H), 1.52 (m_c, 1H), 1.58-1.85 (m, 6H), 1.95-2.40 (m, 8H, 2 Ar–CH_3, aliphatic H), 3.80 (d, J = 7.2 Hz, 1H, 3-H), 3.89 (m_c, 1H, 6'-H), 4.92 (d, J = 17.2 Hz, 1H, =CH_2), 5.11 (d, J = 10.3 Hz, 1H, =CH_2), 5.32 (d, J = 7.2 Hz, 1H, 2-H), 5.80 (s, br., 1H, NAr 2-H), 5.98 (ddd, J = 17.2, 10.3 and 4.9 Hz, 1H, =CH–), 6.85 (s, 1H, NAr 4-H), 6.90 (s, br., 1H, NAr 6-H), 7.30-7.40 (m, 4H, SO_2ArH), 7.50 (m_c, 1H, SO_2ArH), 12.62 (s, 1H, =C–OH). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 114.56 (=CH_2), 142.36 (=CH–), for further signals see table 3. $C_{33}H_{41}NO_5S$: C, 70.30; H, 7.34; N, 2.49; S, 5.68. Found C, 70.31; H, 7.38; N, 2.64; S, 5.93.

(1R,2R,3S,4S)-{3-[N-Benzenesulfonyl-N-(3,5-dimethylphenyl)-amino]-2-bornyl}-(6S)-2-hydroxy-6-iso-propenyl-cyclohexenecarboxylate (**11n**)

Starting material **6n**; procedure E; cuprate precursor isopropenyl-lithium which was prepared from 2-bromo-propene (242 mg, 2.00 mmol) dissolved in THF (10 ml) and tBuLi (2.30 ml, 1.74 M, 4 mmol) at –78 °C (2 h); gave **11n** (716 mg, 62%), colourless crystals from 2-PrOH, mp 158 °C. ^1H NMR (300 MHz, $CDCl_3$) δ = 0.74 (s, 3H, CH_3), 0.83 (s, 3H, CH_3), 1.00 (s, 3H, CH_3), 1.06 (m_c, 1H), 1.28 (m_c, 1H), 1.45-1.87 (m, 6H), 1.90 (s, 3H, =C–CH_3), 1.96 (t, J = 4.0 Hz, 1H, 4-H), 2.07 (s, 3H, Ar–CH_3), 2.16-2.38 (m, 2H), 2.24 (s, 3H, Ar–CH_3), 3.58 (m_c, 1H, 6'-H), 4.11 (dd, J = 9.0 and 4.0 Hz, 1H, 3-H), 4.57 (s, 1H, =CH_2), 4.85 (s, 1H, =CH_2), 5.41 (d, J = 9.0 Hz, 1H, 2-H), 6.09 (s, 1H, NAr 2-H), 6.81 (s, 2H, NAr 4-H, NAr 6-H), 7.30-7.40 (m, 4H, SO_2ArH), 7.51 (m_c, 1H, SO_2ArH), 12.35 (s, 1H, =C–OH). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 22.58 (CH_3), 111.69 (=CH_2), 148.44 (=C–), for further signals see table 2. $C_{34}H_{43}NO_5S$: C, 70.67; H, 7.52; N, 2.42; S, 5.54. Found C, 70.66; H, 7.49; N, 2.57; S, 5.54.

(1R,2S,3R,4S)-{3-[N-Benzenesulfonyl-N-(3,5-dimethylphenyl)-amino]-2-bornyl}-(6R)-2-hydroxy-6-iso-propenyl-cyclohexenecarboxylate (**11x**)

Starting material **6x**; procedure E; cuprate precursor isopropenyl-lithium (preparation see **11n**); gave **11x** (901 mg, 78%), colourless crystals from 2-PrOH, mp 163 °C. ^1H NMR (300 MHz, $CDCl_3$) δ = 0.58 (s, 3H, CH_3), 0.76 (s, 3H, CH_3), 0.86 (s, 3H, CH_3), 1.07 (m_c, 1H), 1.36 (m_c, 1H), 1.51 (m_c, 1H), 1.58-1.78 (m, 5H), 1.88 (s, 3H, =C–CH_3), 1.94 (d, J = 4.5 Hz, 1H, 4-H), 2.01 (s, br., 3H, Ar–CH_3), 2.20-2.40 (m, 5H, Ar–CH_3, aliphatic H), 3.74 (m_c, 1H, 6'-H), 3.81 (d, J = 7.2 Hz, 1H, 3-H), 4.63 (s, 1H, =CH_2), 4.91 (s, 1H, =CH_2), 5.36 (d, J = 7.2 Hz, 1H, 2-H), 5.74 (s, br., 1H, NAr 2-H), 6.85 (s, 1H, NAr 4-H), 7.02 (s, br., 1H, NAr 6-H), 7.29-7.37 (m, 4H, SO_2ArH), 7.50 (m_c, 1H, SO_2ArH), 12.76 (s, 1H, =C–OH). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 22.17 (CH_3), 112.26 (=CH_2), 147.69 (=C–), for further signals see table 3. $C_{34}H_{43}NO_5S$: C, 70.67; H, 7.52; N, 2.42; S, 5.54. Found C, 70.49; H, 7.46; N, 2.68; S, 5.27.

(1R,2R,3S,4S)-{3-[N-Benzenesulfonyl-N-(3,5-dimethylphenyl)-amino]-2-bornyl}-(6S)-2-hydroxy-6-phenyl-cyclohexenecarboxylate (**12n**)

Starting material **6n**; procedure E; cuprate precursor PhLi (1.0 ml, 2.0 M in hexane/ether); gave **12n** (810 mg, 66%), colourless crystals from hexane, mp 195 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 0.22 (m_c, 1H), 0.39 (m_c, 1H), 0.53 (s, 3H, CH_3), 0.67 (s, 3H, CH_3), 0.83-1.30 (m, 3H), 0.92 (s, 3H, CH_3), 1.54-1.66 (m, 2H), 1.81 (t, *J* = 4.0 Hz, 1H, 4-H), 1.87 (m_c, 1H), 2.05 (m_c, 1H), 2.08 (s, 3H, Ar-CH_3), 2.35 (s, 3H, Ar-CH_3), 2.38 (m_c, 1H), 4.04 (dd, *J* = 8.6 and 4.0 Hz, 1H, 3-H), 4.41 (m_c, 1H, 6'-H), 5.33 (d, *J* = 8.6 Hz, 1H, 2-H), 6.06 (s, 1H, NAr 2-H), 6.84 (s, 1H, NAr 4-H), 6.91 (s, 1H, NAr 6-H), 7.11 (m_c, 1H, CArH), 7.21-7.40 (m, 8H, SO_2ArH, CArH), 7.52 (m_c, 1H, SO_2ArH), 12.56 (s, 1H, =C-OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 125.69 (Ph C-4), 127.86 (Ph C-2, C-6), 128.35 (Ph C-3, C-5), 146.68 (Ph C-1), for further signals see table 2. $C_{37}H_{43}NO_5S$: C, 72.40; H, 7.08; N, 2.28; S, 5.21. Found C, 72.12; H, 7.30; N, 2.36; S, 5.24.

(1R,2S,3R,4S)-{3-[N-Benzenesulfonyl-N-(3,5-dimethylphenyl)-amino]-2-bornyl}-(6R)-2-hydroxy-6-phenyl-cyclohexenecarboxylate (**12x**)

Starting material **6x**; procedure E; cuprate precursor PhLi (1.0 ml, 2.0 M in hexane/ether); gave **12x** (773 mg, 63%), colourless crystals from 2-PrOH, mp 212 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 0.00 (s, 3H, CH_3), 0.34 (s, 3H, CH_3), 0.45 (s, 3H, CH_3), 0.99 (m_c, 1H), 1.23-1.65 (m, 6H), 1.75 (d, *J* = 4.4 Hz, 1H, 4-H), 1.85-2.50 (m, 3H), 2.00 (s, br., 3H, Ar-CH_3), 2.40 (s, br., 3H, Ar-CH_3), 3.75 (d, *J* = 7.2 Hz, 1H, 3-H), 4.62 (m_c, 1H, 6'-H), 5.29 (d, *J* = 7.2 Hz, 1H, 2-H), 5.64 (s, br., 1H, NAr 2-H), 6.86 (s, 1H, NAr 4-H), 7.08 (s, br., 1H, NAr 6-H), 7.15 (m_c, 1H, CArH), 7.22-7.40 (m, 8H, SO_2ArH, CArH), 7.50 (m_c, 1H, SO_2ArH), 12.94 (s, 1H, =C-OH). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 125.62 (Ph C-4), 127.73 (Ph C-2, C-6), 128.37 (Ph C-3, C-5), 146.35 (Ph C-1), for further signals see table 3. $C_{37}H_{43}NO_5S$: C, 72.40; H, 7.08; N, 2.28; S, 5.21. Found C, 72.19; H, 7.20; N, 2.46; S, 5.27.

(1R,2R,3S,4S)-{3-[N-Benzenesulfonyl-N-(3,5-dimethylphenyl)-amino]-2-bornyl}-(6R)-6-cyano-2-hydroxy-cyclohexenecarboxylate (**13n**)

Preparation see **9n**; colourless crystals from 2-PrOH, mp 202 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 0.83 (s, 3H, CH_3), 0.94 (s, 3H, CH_3), 1.07 (s, 3H, CH_3), 1.10-1.19 (m, 2H), 1.49 (m_c, 1H), 1.73 (t, *J* = 3.0 Hz, 1H, 4-H), 1.83-2.15 (m, 4H), 1.98 (s, 3H, Ar-CH_3), 2.23-2.44 (m, 3H), 2.34 (s, 3H, Ar-CH_3), 4.25 (dd, *J* = 8.5 and 3.0 Hz, 1H, 3-H), 4.52 (m_c, 1H, 6'-H), 5.51 (d, *J* = 8.5 Hz, 1H, 2-H), 5.67 (s, 1H, NAr 2-H), 6.84 (s, 1H, NAr 4-H), 7.10 (s, 1H, NAr 6-H), 7.28-7.41 (m, 4H, SO_2ArH), 7.52 (m_c, 1H, SO_2ArH), 12.55 (s, 1H, =C-OH). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 122.21 (-C≡N), for further signals see table 2. $C_{32}H_{38}N_2O_5S$: C, 68.30; H, 6.82; N, 4.98; S, 5.69. Found C, 68.05; H, 6.87; N, 4.73; S, 5.76.

(1R,2S,3R,4S)-{3-[N-Benzenesulfonyl-N-(3,5-dimethylphenyl)-amino]-2-bornyl}-(6S)-6-cyano-2-hydroxy-cyclohexenecarboxylate (**13x**)

Preparation see **9n**; colourless crystals from 2-PrOH, mp 185 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ = 0.63 (s, 3H, CH_3), 0.94 (s, 3H, CH_3), 1.11 (s, 3H, CH_3), 1.16 (m_c, 1H), 1.42 (m_c, 1H), 1.60 (m_c, 2H), 1.72 (m_c, 1H), 1.84-2.13 (m, 3H), 1.96 (s, 3H, Ar-CH_3), 2.21-2.47 (m, 3H), 2.36 (s, 3H, Ar-CH_3), 3.88 (d, *J* = 7.1 Hz, 1H, 3-H), 4.40 (m_c, 1H, 6'-H), 5.44 (d, *J* = 7.1 Hz, 1H, 2-H), 5.62 (s, br., 1H, NAr 2-H), 6.85 (s, 1H, NAr 4-H), 7.03 (s, br., 1H, NAr 6-H), 7.28-7.40 (m, 4H, SO_2ArH), 7.50 (m_c, 1H, SO_2ArH), 12.68 (s, 1H, =C-OH). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 122.19 (-C≡N), for further signals see table 3. $C_{32}H_{38}N_2O_5S$: C, 68.30; H, 6.82; N, 4.98; S, 5.69. Found C, 68.16; H, 6.87; N, 4.85; S, 5.58.

Methyl-(1S,6R)-6-methyl-2-oxo-cyclohexanecarboxylate (**14**)

Transesterification of **7n** (1.10 g, procedure G, 125 °C, 40 h) gave **1n** (680 mg, 82%) and **14** (280 mg, 82%), colourless oil, bp 70 °C/0.1 mbar. $[\alpha]_D^{20}$ = + 3.6 (*c* = 1.01, $CDCl_3$, ketone:enol = 85:15). ^1H NMR (300 MHz, $CDCl_3$, ketone:enol = 69:31) δ(ketone) = 1.03 (d, *J* = 6.4 Hz, 3H, CH_3), 1.43 (m_c, 1H), 1.60-1.80 (m, 1H), 1.93 (m_c, 1H), 2.05 (m_c, 1H), 2.20-2.38 (m, 2H, 3-H, 6-H), 2.48 (m_c, 1H, 3-H), 3.06 (dd, *J* = 11.4 and 1.1 Hz, 1H, 1-H), 3.77 (s, 3H, OCH_3); δ(enol) = 1.06 (d, *J* = 6.7 Hz, 3H, CH_3), 1.50-1.82 (m, 4H), 2.20-2.38 (m, 2H, 3-H), 2.69 (m_c, 1H, 6-H), 3.77 (s, 3H, OCH_3), 12.32 (s, 1H, =C–OH). ^{13}C NMR (75 MHz, $CDCl_3$) δ = 20.74 (CH_3), 24.88 (C-4), 32.16 (C-5), 36.50 (C-6), 40.74 (C-3), 51.78 (OCH_3), 64.86 (C-1), 170.09 (COO), 205.92 (C-2). Anal. Calcd for $C_9H_{14}O_3$: C, 63.50; H, 8.30. Found C, 63.47; H, 8.44.

Methyl-(1R,6S)-6-methyl-2-oxo-cyclohexanecarboxylate (*ent*-**14**)

Transesterification of **7x** (1.10 g, procedure G, 125 °C, 64 h) gave **1x** (520 mg, 63%) and *ent*-**14** (210 mg, 62%), colourless oil, bp 100 °C/0.05 mbar. $[\alpha]_D^{20}$ = + 0.6 (*c* = 1.02, $CDCl_3$, ketone:enol = 63:37). ^1H NMR (300 MHz, $CDCl_3$, ketone:enol = 69:31) data identical with **14**. ^{13}C NMR (75 MHz, $CDCl_3$, ketone:enol = 83:17) δ(ketone) data identical with **14**; δ(enol) = 17.11 (C-4), 20.99 (CH_3), 29.21 (C-5), 26.47 (C-6), 29.68 (C-3), 51.25 (OCH_3), 102.98 (C-1), not detected (COO and C-2). Anal. Calcd for $C_9H_{14}O_3$: C, 63.50; H, 8.30. Found C, 63.77; H, 8.55.

Methyl-(1S,6R)-6-butyl-2-oxo-cyclohexanecarboxylate (**15**)

Transesterification of **8n** (1.19 g, procedure G, 130 °C, 44 h) gave **1n** (655 mg, 79%) and **15** (383 mg, 90%), colourless oil, bp 70 °C/0.03 mbar. $[\alpha]_D^{20}$ = - 5.5 (*c* = 1.10, $CDCl_3$, ketone:enol = 53:47). ^1H NMR (300 MHz, $CDCl_3$, ketone:enol = 53:47) δ(ketone) = 0.89 (m_c, 3H, CH_3), 1.16-1.50 (m, 7H), 1.60-1.80 (m, 2H), 2.04 (m_c, 1H), 2.14-2.36 (m, 2H, 3-H, 6-H), 2.49 (m_c, 1H, 3-H), 3.13 (dd, *J* = 10.9 and 1.0 Hz, 1H, 1-H), 3.76 (s, 3H, OCH_3); δ(enol, separated signals) = 3.76 (s, 3H, OCH_3), 12.31 (s, 1H, =C–OH). ^{13}C NMR (75 MHz, $CDCl_3$, ketone:enol = 76:24) δ(ketone) = 13.85 (C-4'), 22.58 (C-4), 24.65 (C-3'), 28.50 (C-5), 28.86 (C-2'), 34.54 (C-1'), 40.99 (C-6), 41.06 (C-3), 51.87 (OCH_3), 63.67 (C-1), 170.34 (COO), 206.20 (C-2); δ(enol) = 13.98 (C-4'), 16.96 (C-4), 25.19 (C-3'), 28.86 (C-2'), 28.99 (C-5), 29.89 (C-3), 31.27 (C-6), 33.79 (C-1'), 51.16 (OCH_3), 102.98 (C-1), 172.33 (COO), 173.17 (C-2). Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.88; H, 9.51. Found C, 68.02; H, 9.76.

Methyl-(1R,6S)-6-butyl-2-oxo-cyclohexanecarboxylate (*ent*-**15**)

Transesterification of **8x** (1.19 g, procedure G, 125 °C, 100 h) gave **1x** (730 mg, 88%) and *ent*-**15** (325 mg, 76%), colourless oil, bp 70 °C/0.02 mbar. $[\alpha]_D^{20}$ = + 9.1 (*c* = 1.03, $CDCl_3$, ketone:enol = 68:32). ^1H NMR (300 MHz, $CDCl_3$, ketone:enol = 68:32) and ^{13}C NMR (75 MHz, $CDCl_3$, ketone:enol = 88:12) data identical with **15**. Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.88; H, 9.51. Found C, 67.80; H, 9.25.

Methyl-(1S,6R)-6-tert-butyl-2-oxo-cyclohexanecarboxylate (**16**)

Transesterification of **9n** (1.19 g, procedure G, 140 °C, 16 h) gave **1n** (755 mg, 91%) and **16** (238 mg, 56%), colourless oil, bp 80 °C/0.04 mbar. $[\alpha]_D^{20}$ = + 32.2 (*c* = 0.96, $CDCl_3$, ketone:enol = 97:3). ^1H NMR (300 MHz, $CDCl_3$) δ = 0.91 (s, 9H, tBu CH_3), 1.39 (m_c, 1H), 1.72 (m_c, 1H), 1.94-2.07 (m, 2H), 2.23 (dddd, *J* = 15.4, 12.2, 6.2 and 1.1 Hz, 1H, 3-H), 2.29 (ddd, *J* = 11.4, 9.1 and 4.7 Hz, 1H, 6-H), 2.55 (dddd, *J* = 15.4, 5.1, 3.4 and 1.7 Hz, 1H, 3-H), 3.24 (dd, *J* = 9.1 and 0.9 Hz, 1H, 1-H), 3.74 (s, 3H, OCH_3). ^{13}C NMR (75

MHz, $CDCl_3$) δ = 22.89 (C-4), 24.79 (C-5), 27.56 (tBu CH_3), 33.89 (tBu C), 40.11 (C-3), 49.11 (C-6), 52.15 (OCH_3), 59.21 (C-1), 171.91 (COO), 207.79 (C-2). Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.88; H, 9.51. Found C, 68.17; H, 9.59.

Methyl-(1R,6S)-6-tert-butyl-2-oxo-cyclohexanecarboxylate (*ent*-**16**)

Transesterification of **9x** (1.19 g, procedure G, 140 °C, 16 h) gave **1x** (780 mg, 94%) and *ent*-**16** (220 mg, 52%), colourless oil, bp 70 °C/0.02 mbar. $[\alpha]_D^{20}$ = - 38.4 (*c* = 0.83, $CDCl_3$, ketone:enol = 93:7). ^1H NMR (300 MHz, $CDCl_3$) and ^{13}C NMR (75 MHz, $CDCl_3$) data identical with **16**. Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.88; H, 9.51. Found C, 68.04; H, 9.72.

Methyl-(1S,6S)-2-oxo-6-vinyl-cyclohexanecarboxylate (**17**)

Transesterification of **10n** (1.13 g, procedure G, 140 °C, 16 h) gave **1n** (670 mg, 81%) and **17** (295 mg, 81%), colourless oil, bp 50 °C/0.05 mbar. $[\alpha]_D^{20}$ = + 77.7 (*c* = 0.99, $CDCl_3$, ketone:enol = 34:66). ^1H NMR (300 MHz, $CDCl_3$, ketone:enol = 34:66) δ(ketone, separated signals) = 1.98 (m_c, 1H), 2.08 (m_c, 1H), 2.32 (m_c, 1H, 3-H), 2.48 (m_c, 1H, 3-H), 2.87 (m_c, 1H, 6-H), 3.27 (dd, *J* = 11.4 and 0.9 Hz, 1H, 1-H), 3.72 (s, 3H, OCH_3), 5.03 (dt, *J* = 10.2 and 1.1 Hz, 1H, $=CH_2$), 5.08 (dt, *J* = 17.2 and 1.2 Hz, 1H, $=CH_2$), 5.71 (ddd, *J* = 17.2, 10.2 and 7.2 Hz, 1H, =CH-); δ(enol) = 1.50-1.83 (m, 4H), 2.26 (m_c, 2H, 3-H), 3.27 (m_c, 1H, 6-H), 3.71 (s, 3H, OCH_3), 4.86 (dt, *J* = 17.1 and 1.6 Hz, 1H, $=CH_2$), 5.01 (dt, *J* = 10.2 and 1.6 Hz, 1H, $=CH_2$), 5.81 (ddd, *J* = 17.1, 10.2 and 6.0 Hz, 1H, =CH-), 12.45 (s, 1H, =C-OH). ^{13}C NMR (75 MHz, $CDCl_3$, ketone:enol = 34:66) δ(ketone) = 24.69 (C-4), 30.05 (C-5), 40.87 (C-3), 45.09 (C-6), 51.91 (OCH_3), 62.44 (C-1), 115.62 ($=CH_2$), 139.04 (=CH-), 169.58 (COO), 205.23 (C-2); δ(enol) = 16.91 (C-4), 27.67 (C-5), 28.97 (C-3), 35.32 (C-6), 51.28 (OCH_3), 99.06 (C-1), 114.24 ($=CH_2$), 141.53 (=CH-), 172.95 (COO), 173.48 (C-2). Anal. Calcd for $C_{10}H_{14}O_3$: C, 65.90; H, 7.76. Found C, 66.00; H, 7.89.

Methyl-(1R,6R)-2-oxo-6-vinyl-cyclohexanecarboxylate (*ent*-**17**)

Transesterification of **10x** (1.13 g, procedure G, 130 °C, 29 h) gave **1x** (785 mg, 95%) and *ent*-**17** (275 mg, 75%), colourless oil, bp 40 °C/ 0.02 mbar. $[\alpha]_D^{20}$ = - 58.8 (*c* = 1.03, $CDCl_3$, ketone:enol = 57:43). ^1H NMR (300 MHz, $CDCl_3$, ketone:enol = 57:43) and ^{13}C NMR (75 MHz, $CDCl_3$, ketone:enol = 60:40) data identical with **17**. Anal. Calcd for $C_{10}H_{14}O_3$: C, 65.90; H, 7.76. Found C, 65.78; H, 7.71.

Methyl-(1S,6R)-2-oxo-6-isopropenyl-cyclohexanecarboxylate (**18**)

Transesterification of **11n** (1.16 g, procedure G, 125 °C, 16 h) gave **1n** (590 mg, 71%) and **18** (303 mg, 77%), colourless oil, bp 50 °C/0.05 mbar. $[\alpha]_D^{20}$ = + 52.1 (*c* = 0.99, $CDCl_3$, ketone:enol = 38:62). ^1H NMR (300 MHz, $CDCl_3$, ketone:enol = 38:62) δ(ketone, separated signals) = 1.76 (s, 3H, $=C-CH_3$), 1.98 (m_c, 1H), 2.10 (m_c, 1H), 2.35 (m_c, 1H, 3-H), 2.51 (m_c, 1H, 3-H), 2.82 (dt, *J* = 3.7 and 11.9 Hz, 1H, 6-H), 3.48 (dd, *J* = 11.9 and 0.9 Hz, 1H, 1-H), 3.72 (s, 3H, OCH_3), 4.77 (s, 1H, $=CH_2$), 4.81 (s, 1H, $=CH_2$); δ(enol) = 1.50-1.75 (m, 4H), 1.78 (s, 3H, $=C-CH_3$), 2.27 (m_c, 2H, 3-H), 3.12 (m_c, 1H, 6-H), 3.70 (s, 3H, OCH_3), 4.51 (s, 1H, $=CH_2$), 4.81 (s, 1H, $=CH_2$), 12.39 (s, 1H, =C-OH). ^{13}C NMR (75 MHz, $CDCl_3$, ketone:enol = 31:69) δ(ketone) = 20.21 (CH_3), 25.05 (C-4), 29.94 (C-5), 41.00 (C-3), 48.50 (C-6), 51.88 (OCH_3), 61.70 (C-1), 111.51 ($=CH_2$), 145.73 (=C-), 169.63 (COO), 205.75 (C-2); δ(enol) = 16.95 (C-4), 22.33 (CH_3), 25.74 (C-5), 28.92 (C-3), 39.05 (C-6), 51.32 (OCH_3), 100.15 (C-1), 110.96 ($=CH_2$), 148.14 (=C-), 172.97 (COO), 173.04 (C-2). Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.31; H, 8.23. Found C, 67.60; H, 8.21.

Methyl-(1R,6S)-2-oxo-6-isopropenyl-cyclohexanecarboxylate (*ent*-**18**)

Transesterification of **11x** (1.16 g, procedure G, 125 °C, 20 h) gave **1x** (788 mg, 95%) and *ent*-**18** (270 mg, 69%), colourless oil, bp 50 °C/ 0.05 mbar. $[\alpha]_D^{20} = -61.0$ (*c* = 1.01, $CDCl_3$, ketone:enol = 23:77). ^1H NMR (300 MHz, $CDCl_3$, ketone:enol = 28:72) and ^{13}C NMR (75 MHz, $CDCl_3$, ketone:enol = 26:74) data identical with **18**. Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.31; H, 8.23. Found C, 67.21; H, 8.14.

Methyl-(1S,6R)-2-oxo-6-phenyl-cyclohexanecarboxylate (**19**)

Transesterification of **12n** (1.23 g, procedure G, 130 °C, 48 h) gave **1n** (680 mg, 82%) and **19** (372 mg, 80%), colourless oil, bp 70 °C/0.01 mbar. $[\alpha]_D^{20} = +26.7$ (*c* = 0.99, $CDCl_3$, ketone:enol = 17:83). ^1H NMR (300 MHz, $CDCl_3$, ketone:enol = 17:83) δ(ketone, separated signals) = 3.39 (dt, *J* = 3.6 and 12.2 Hz, 1H, 6-H), 3.55 (s, 3H, OCH_3), 3.69 (dd, *J* = 12.2 and 0.9 Hz, 1H, 1-H); δ(enol) = 1.50-2.00 (m, 4H), 2.33-2.43 (m, 2H), 3.53 (s, 3H, OCH_3), 3.92 (dd, *J* = 5.3 and 3.3 Hz, 1H, 6-H), 7.10-7.33 (m, 5H, ArH), 12.57 (s, 1H, =C–OH). ^{13}C NMR (75 MHz, $CDCl_3$, ketone:enol = 17:83) δ(ketone) = 25.38 (C-4), 32.92 (C-5), 41.03 (C-3), 47.50 (C-6), 51.78 (OCH_3), 63.65 (C-1), 126.87 (C-3', C-5'), 127.04 (C-4'), 128.68 (C-2', C-6'), 142.21 (C-1'), 169.25 (COO), 205.29 (C-2); δ(enol) = 16.78 (C-4), 29.07 (C-5), 31.45 (C-3), 38.25 (C-6), 51.32 (OCH_3), 99.63 (C-1), 125.72 (C-4'), 127.53 (C-3',C-5'), 127.93 (C-2', C-6'), 145.96 (C-1'), 172.89 (COO), 173.95 (C-2). Anal. Calcd for $C_{14}H_{16}O_3$: C, 72.38; H, 6.96. Found C, 72.10; H, 7.19.

Methyl-(1R,6S)-2-oxo-6-phenyl-cyclohexanecarboxylate (*ent*-**19**)

Transesterification of **12x** (1.23 g, procedure G, 130 °C, 45 h) gave **1x** (755 mg, 91%) and *ent*-**19** (363 mg, 78%), colourless oil, bp 70 °C/ 0.03 mbar. $[\alpha]_D^{20} = -46.9$ (*c* = 1.02, $CDCl_3$, ketone:enol = 34:66). ^1H NMR (300 MHz, $CDCl_3$, ketone:enol = 34:66) and ^{13}C NMR (75 MHz, $CDCl_3$, ketone:enol = 34:66) data identical with **19**. Anal. Calcd for $C_{14}H_{16}O_3$: C, 72.38; H, 6.96. Found C, 72.15; H, 7.15.

Acknowledgments: This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. E. Urban thanks Prof. G. Helmchen for the generous support of this project and the Austrian Fonds zur Förderung der wissenschaftlichen Forschung for a scholarship (J0638-CHE).

REFERENCES AND NOTES

1. For a recent review see: Rossiter, B. E.; Swingle, N. M. *Chem. Rev.* **1992**, *92*, 771-806.
2. Oppolzer, W.; Dudfield, P.; Stevenson, T.; Godel, T. *Helv. Chim. Acta* **1985**, *68*, 212-215.
3. Helmchen, G.; Wegner, G. *Tetrahedron Lett.* **1985**, *26*, 6051-6054.
4. Urban, E.; Knühl, G.; Helmchen, G. *Sci. Pharm.* **1994**, *62*, 195.
5. Recently we were successful using conjugate additions of cuprates to an asymmetric protected 2-oxo-cyclohexenecarboxylate as a key step towards EPC synthesis of (+)-heptelidic acid, following the synthesis of (±)-heptelidic acid by Danishefsky, S. J.; Mantlo, N. *J. Am. Chem. Soc.* **1988**, *110*, 8129-8133.
6. Steglich, W.; Höfle, G. *Angew. Chem. Int. Ed. Engl.* **1969**, *8*, 981.
7. Decicco, C. P.; Buckle, R. N. *J. Org. Chem.* **1992**, *57*, 1005-1008.
8. Taber, D. F.; Amedio, J. C.; Patel, Y. K. *J. Org. Chem.* **1985**, *50*, 3618-3619.
9. Liotta, D.; Barnum, C.; Puleo, R.; Zima, G.; Bayer, C.; Kezar, H. S. *J. Org. Chem.* **1981**, *46*, 2920-2923.
10. Lipshutz, B. H.; Koerner, M.; Parker, D. A. *Tetrahedron Lett.* **1987**, *28*, 945-948.

(*Received in Germany* 14 *July* 1995; *accepted* 16 *August* 1995)