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Enantioselective Dreiding–Schmidt reactions: asymmetric synthesis and analysis of α-methylene-γ-butyrolactones †

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Abstract: The zinc/silver-graphite mediated Dreiding–Schmidt reactions between aldehydes and the 2-bromomethyl-acrylate derived sultamamides (+)/(−)-**28** or (+)/(−)-**30** gave the corresponding substituted α-methylene-γ-butyrolactones with ee's up to 90%. Enantiomerically pure compounds were obtained by semipreparative HPLC using a chiral stationary phase. © 1997 Elsevier Science Ltd

Introduction

α-Methylene-γ-butyrolactones possess a wide range of biological activities[1], particularly cytotoxic and antitumor activity[2], fungitoxicity[3] as well as plant growth inhibition.[4] Many different approaches for their efficient synthesis have been elaborated.[1,5,6] Due to the strong dependance between absolute configuration and biological activities of many natural occuring α-methylene-γ-butyrolactones several methods have been developed for their stereoselective synthesis[7] but most of these approaches use starting materials that already contain the stereogenic centers.[8] To the best of our knowledge no non-racemic 2-bromomethyl-acrylates have been prepared and tested for their potential use as chiral reagents in Dreiding–Schmidt reactions.[9–12]

Results and discussion

The racemic α-methylene-γ-butyrolactones **1–7** were easily obtained from the corresponding aldehydes **8–14** (*cf.* Table 1) by their zinc/silver-graphite mediated reaction with ethyl 2-bromomethyl-acrylate (**15**),[13] whereas their reaction with ethyl (*Z*)-2-bromomethyl-2-butenoate **16**[14] afforded the products **17–23** possessing an additional methyl substituent at position C(3) of the butyrolactone moiety.

For the Dreiding–Schmidt reaction at least four reasonable transition states (transition states Figure 1) can be drawn. Whereas *re–re* and *si–si*-attacks lead to six-membered chair-like transition states **B** and **C** showing the residue R^1 in an unfavourable axial position (leading to a *trans*-orientation of R^1 and R^2 in the final products) for *si–re* and *re–si* attacks the transition states become more favourable: the products from transition states **A** and **D**, however, lead to *cis*-configurated products with respect to R^1 and R^2.

Following previous experiments with Reformatsky reactions several chiral alkyl 2-bromomethyl-acrylates were prepared and tested for their use in Dreiding–Schmidt reactions. Unfortunately, the ee's obtained were rather disappointing. A breakthrough was observed, however, on altering the alcohol part of the ester into an amide moiety[15] by using Oppolzer's sultam as the amino part.

Thus, reaction of 2-bromomethyl-acrylic acid **24** with oxalyl dichloride gave a mixture of the corresponding chlorides **25**[16] and **26** which was allowed to react with the in situ prepared sodium

† Dedicated to Professor Dr. Dieter Seebach, ETH Zürich, on the occasion of his 60th birthday.

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Table 1. Synthesis of racemic α-methylene-γ-butyrolactones

aldehyde	R^1	acrylate	product $R^2 = H$	yield [%]	acrylate	product $R^2 = Me$	yield [%] (*cis*/*trans*)
8	Ph	**15**	**1**	87	**16**	**17**	86 / 0
9	*o*-OMe-Ph	**15**	**2**	84	**16**	**18**	40 / 13
10	*m*-OMe-Ph	**15**	**3**	79	**16**	**19**	82 / 0
11	*p*-OMe-Ph	**15**	**4**	80	**16**	**20**	76 / 13
12	1-naphthyl	**15**	**5**	87	**16**	**21**	88 / 0
13	2-naphthyl	**15**	**6**	90	**16**	**22**	84 / 6
14	isobutyl	**15**	**7**	79	**16**	**23**	86 / 7

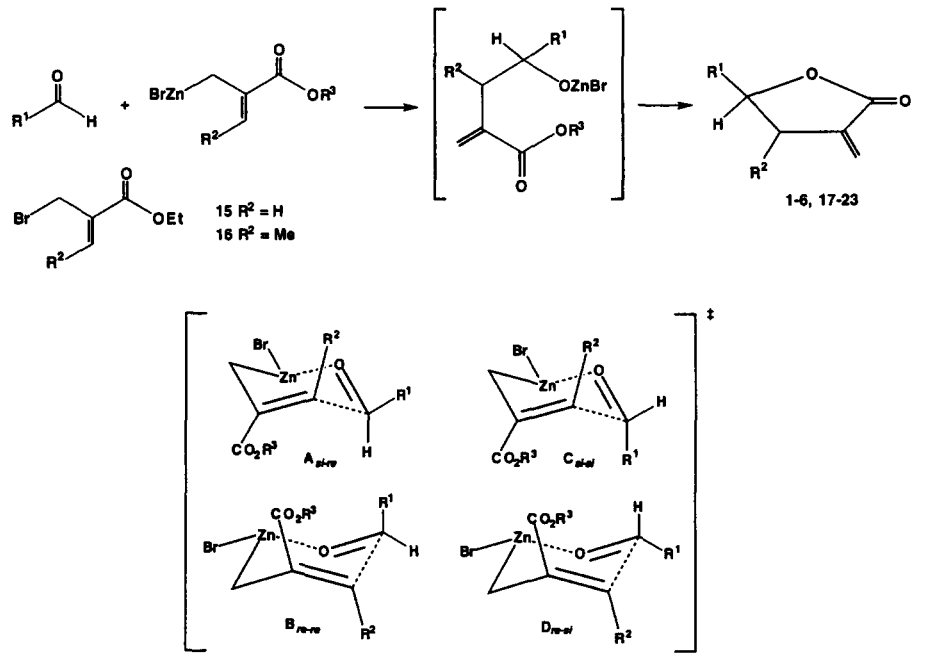
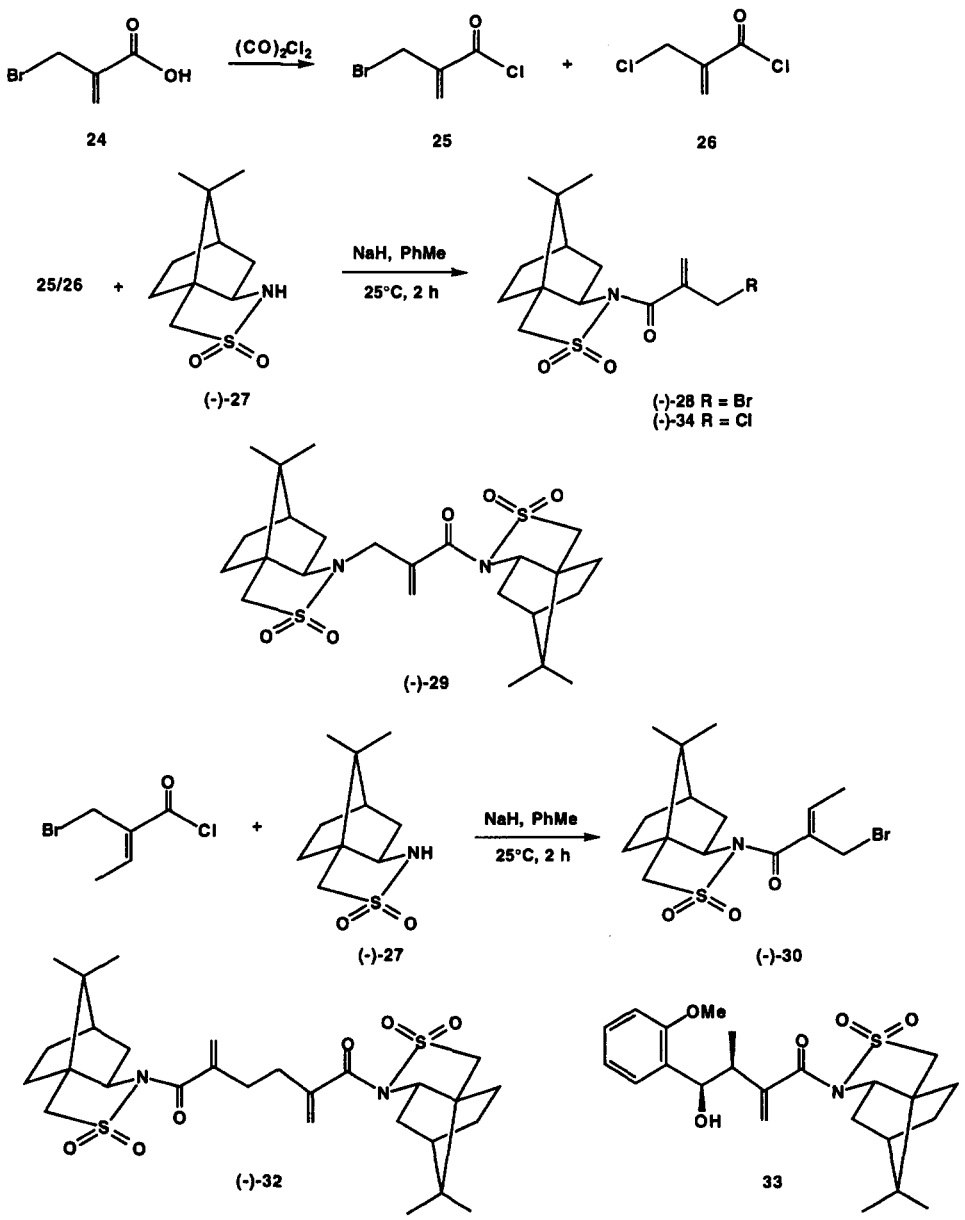


Figure 1. Transition states for the Dreiding–Schmidt reaction.

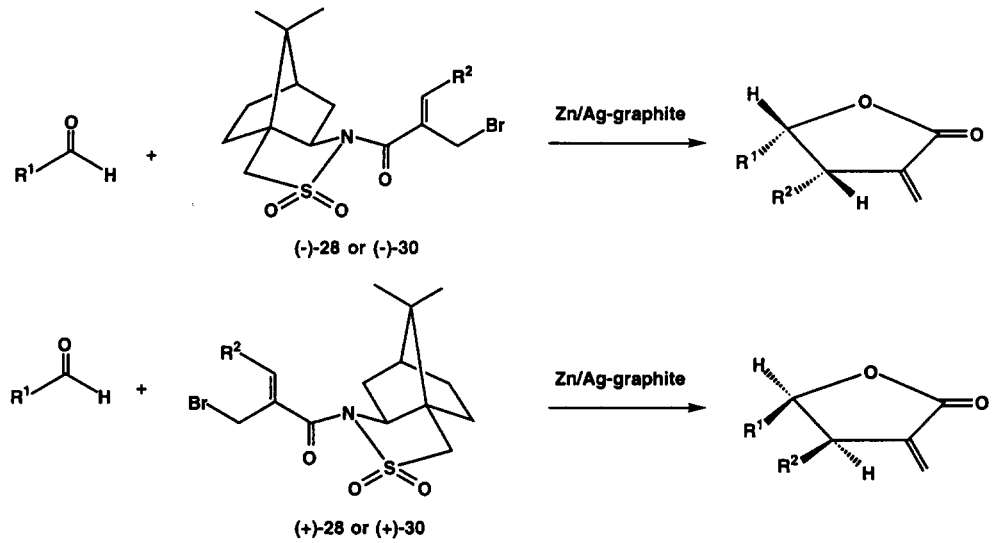
salt of (*R*) -or (*S*)-Oppolzer sultam (−)-**27** or (+)-**27** to yield yield (−)-**28** and (+)-**28**, respectively. (Schemes 1 and 2).[17] In addition, some **29** resulting from a double addition of the sultam with both the carboxylic chloride as well as with the bromosubstituent was obtained. Similarly, from 2-bromomethyl-3-methyl-acrylic acid and the sultams the methacrylamides (−)-**30** and (+)-**30** were obtained.[18] Reaction of the sultamamide (−)-**28** with **8** afforded the monosubstituted butyrolactone (**4** ***R***)-**1** with an ee of 62% besides some **32** resulting from a Wurtz-type dimerization reaction. Upon reaction of **8** with the substituted sultamamide (−)-**30** the disubstituted butyrolactone (**3** ***S***, **4** ***R***)-**17** was obtained in 95% yield with an ee of 69%. Yields and ee's of the products are summarized in Tables 2 and 3. It is worthwhile mentioning that the chiral auxiliary (+)- or (−)-**27** can be recovered from these reactions in good yields.

From Diels–Alder reactions of sultam substituted starting materials it is well established that the two



Scheme 1.

oxygen substituents of the sultam moiety are pseudo-axially/pseudo-equatorially oriented.[19] Whereas in the solid state an *anti*-orientation **E** is preferred[20] in the presence of Lewis acids a *syn* -orientation **F** seems more favourable (Figure 2).[21] Hence, it can be assumed that in the presence of zinc a chelation takes place and a rational structure for the zinc organic reagents is depicted in Figure 2.[22] The conformation of the organometallic species derived from **30** (R^2=Me) is similar to its unsubstituted analogue derived from **28**. Due to the geometry of the double bond a $si_{reagent}$–$re_{aldehyde}$ attack will bring the methyl group into a *cis*-orientation with the phenyl moiety and this relative configuration is also found in the final products. An attack of the *si*-face of the zinc organic reagent is preferred due to steric crowding of the campher skeleton. Assuming the existence of a six-membered chair-



Scheme 2.

Table 2. Reaction of the aldehydes with sultamamides (+)-28 and (−)-28

aldehyde	R^1	sultamamide	product[a]	yield [%]	ee [%]
8	Ph	(−)-28	(4 *R*)-1	85	62
8	Ph	(+)-28	(4 *S*)-1	86	54
9	*o*-OMe-Ph	(−)-28	(4 *R*)-2	89	39
9	*o*-OMe-Ph	(+)-28	(4 *S*)-2	87	42
10	*m*-OMe-Ph	(+)-28	(4 *S*)-3	89	71
11	*p*-OMe-Ph	(+)-28	(4 *S*)-4	90	58
12	1-naphthyl	(+)-28	(4 *S*)-5	93	61
13	2-naphthyl	(−)-28	(4 *R*)-6	95	83
13	2-naphthyl	(+)-28	(4 *S*)-6	94	83
14	isobutyl	(+)-28	(4 *R*)-7	89	59

[a] stereochemical descriptor for the major product

like transition state for these reactions[23] the residue R^1 of the aldehyde is brought into the favorable equatorial position when the carbonyl group reacts with its *re*-face (→**J**) whereas for an attack with the *si*-face (→**I**) 1,3-diaxal interactions are expected. Hence, the most favorable transition state should result in the formation of a (3 *S*, 4 *R*)-configured product (from (−)-**30**) whereas the reaction of the aldehydes with (+)-**30** should lead to the corresponding (3 *R*, 4 *S*) enantiomers.

In as much as the isobutyl moiety is less space demanding than the phenyl group one would expect a smaller ee of the resulting product whereas the highest ee should result from the reaction of **13**. Simulation of the reaction (software CAChe 3.8; individual conformations optimized by AM1 calculations after having performed a systematic conformational search by application of a MM2 force

Table 3. Reaction of the aldehydes with sultamamides (+)-**30** and (−)-**30**

aldehyde	R^1	sultamamide	product[a]	yield [%]	ee [%]
8	Ph	(−)–**30**	(3 *S*, 4 *R*)–**17**	95	69
8	Ph	(+)–**30**	(3 *R*, 4 *S*)–**17**	96	90
9	*o*–OMe–Ph	(−)–**30**	(3 *S*, 4 *R*)–**18**[b]	68	c
10	*m*–OMe–Ph	(+)–**30**	(3 *R*, 4 *S*)–**19**	86	62
11	*p*–OMe–Ph	(+)–**30**	(3 *R*, 4 *S*)–**20**	81	75
12	1–naphthyl	(+)–**30**	(3 *R*, 4 *S*)–**21**	81	61
13	2–naphthyl	(−)–**30**	(3 *S*, 4 *R*)–**22**	89	82
13	2–naphthyl	(+)–**30**	(3 *R*, 4 *S*)–**22**	88	82
14	isobutyl	(+)–**30**	(3 *R*, 4 *R*)–**23**	87	60

[a] stereochemical descriptor for the major product; [b] some uncylized **33** was recovered from this reaction; [c] mixture of *cis*/*trans* isomers that could not be separated by HPLC

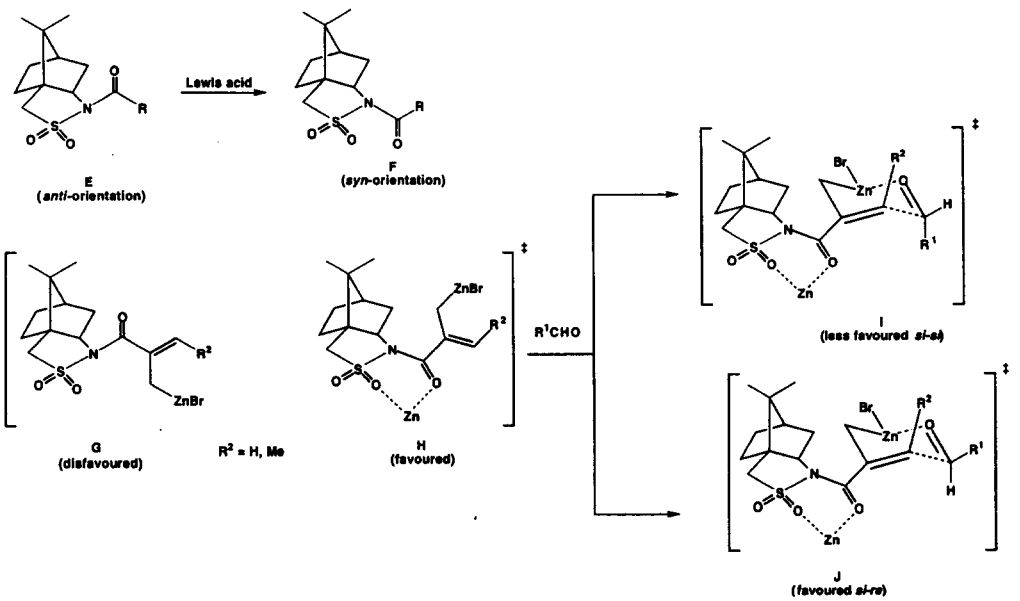


Figure 2. Possible transition states.

field) make it reasonable that the influence of a substituent bridging the *ortho*- and *meta*-position onto the ee of the product is smaller than of the same substituent occupying the *meta*- and *para*- position: Upon consideration of the unfavourable *si–si* approaches (leading to the minor enantiomer) of **12** and **13** the transition state for the reaction of **13** shows both aromatic rings parallel to the carboxamide moiety whereas for **12** the aromatic residue is arranged orthogonal to the carboxamide hence resulting in less steric interactions. From these considerations it is conceivable that the products obtained from **12** should possess a lower ee than those analogs resulting from **13**.

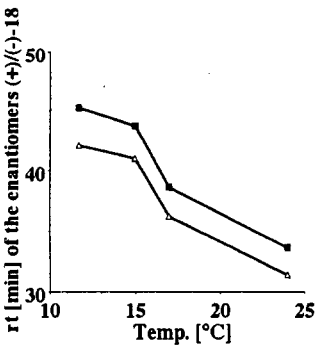


Figure 3. Dependence of the retention time (rt) from the temperature as exemplified for of the enantiomers of (±)-**18**: column (*R*, *R*)-Whelk O1®, hexane/prop-2-OH 98:2.

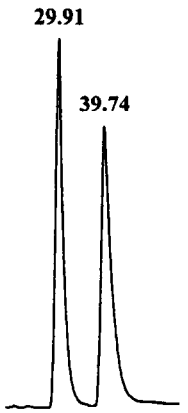


Figure 4. Typical chromatogramm; (±)-**22**, (*S*, *S*)-Whelk O1®, 1.0 *ml*/min, 34 bar, 20°C, hexane/prop-2-OH 98:2.

To determine the enantiomeric purity of the obtained compounds a suitable HPLC system had to be established and (*S*, *S*)- and (*R*, *R*)-Whelk O1® columns possessing the chiral selector (3 *R*, 4 *R*) or (3 *S*, 4 *S*)-4-(3,5-dinitro-benzamido)-1,2,3,4-tetrahydrophenanthrene using hexane/prop-2-OH mixtures as eluents were shown to give excellent results. The retention times were shown to depend as well on the polarity of the eluent as on the temperature of the column (*cf.* Figure 3).

A typical chromatogram is shown in Figure 4. Interestingly enough, compounds possessing a methyl group at C(3) in general show shorter retention times than their unsubstituted analogues; similary, the separation factor α is lower for the methylated compounds (Figure 5). It is of interest to note in this context that the enantiomers of (±)-**31** (Scheme 3)[24,25] possessing two methyl groups at C(3) under these chromatographic conditions are not separated at all.

To obtain several of these compunds not only in an enantiomerically enriched but in an enantiomerically pure form the conditions of the analytical HPLC were applied for semipreparative HPLC separations. Thus, the pure enantiomers of **1**, **4**, **6**, **20** and **22** were obtained and their enantiomeric purity was rechecked by analytical HPLC.

Experimental

Melting points are uncorrected (Reichert hot stage microscope), optical rotations were obtained using a Perkin–Elmer 243B polarimeter (1 cm micro-cell), NMR spectra (internal Me_4Si) were recorded using either a Bruker AM250 or a Varian XL300 instrument (δ given in ppm, *J* in Hz, internal Me_4Si), IR spectra (film or KBr pellet) on a Perkin–Elmer 298 instrument or on a Perkin–Elmer 1605 FT-IR,

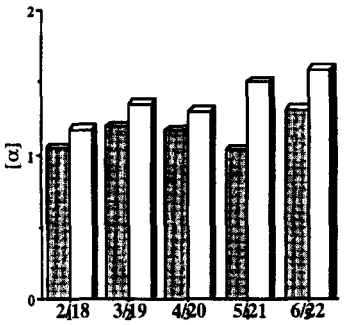
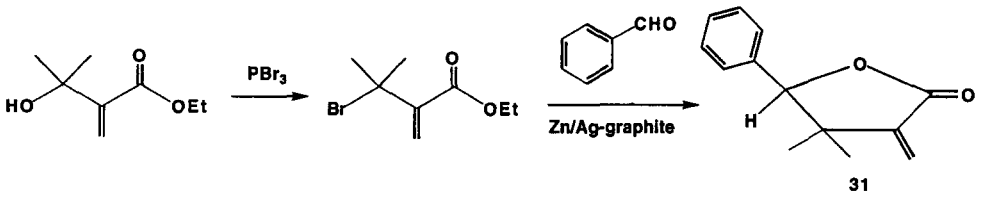


Figure 5. Dependence of the separation factor [α] *vs* substituent at C(3), column (*S, S*)-Whelk O1®, 20°C, hex/prop-2-OH 90:10.



Scheme 3.

MS spectra were taken either on a MAT311A or a Varian-112S instrument; for elemental analysis a Foss–Heraeus Vario EL instrument was used. TLC was performed on silica gel (Merck 5554, detection by dipping in a solution containing 10% sulfuric acid (400 *ml*), ammonium molybdate (20 g) and cerium(IV) sulfate (20 mg) followed by heating to 150°C. For the HPLC either a Merck LaChrom L7100/L7250/L7450/D7000 system or a Merck–Hitachi L6200A/L4000/D-2500 system was used. The tetrahydrofuran used throughout for all reactions was freshly distilled from sodium/benzophenone; all reactions were performed under dry argon.

General procedure for the synthesis of racemic α-methylene-γ-butyrolactones

Graphite (Fluka AG, Buchs, 0.90 g, 75.0 mmol) is degassed at 150° C under argon for 1 h and then clean potassium (0.35 g, 8.82 mmol) is added in several portions under vigorous stirring. After cooling to 25° C the bronze-colored C_8K is suspended in dry THF (30 *ml*) and a mixture of anhydrous zinc chloride (0.60 g, 4.41 mmol) and silver(I) acetate (0.06 g, 0.36 mmol) is added causing the solvent to reflux. After heating under reflux for an additional 30 min the suspension is cooled to −5 °C and a solution of the corresponding aldehyde in abs. THF (5 *ml*) and of the corresponding bromoester in THF (5 *ml*) is added and stirring is continued at −5 °C → 0 °C until the reaction has come to completion (as checked by TLC). The reaction mixture is filtered through a pad of Celite, the filter cake is washed with ethyl acetate (150 *ml*), the filtrates are combined and washed with aqueous hydrochloric acid (1 M, 10 *ml*) and brine (10 *ml*), the organic layer is dried ($MgSO_4$), filtered, the solvents are evaporated under diminished pressure and the residue is subjected to column chromatography (silica, hexane/ethyl acetate 10:1 → 3:1).

General procedure for the synthesis of the enantiomerically enriched compounds

Following the procedure for the synthesis of the racemic compounds to a suspension of Zn/Ag-graphite (5.6 mmol) in dry THF (25 *ml*) at 0 °C the aldehyde is added and then at 0 °C a solution of **28** or **30** in dry THF (10 *ml*) is slowly added within 15 min. Work up as above and chromatography affords the products.

General conditions for the determination of the ee by analytical HPLC

20 µl of a filtered solution of the compound (*c*=0.03 mg/*ml*) in the respective eluent was used for the analysis; column: (*S, S*)- or (*R, R*)-Whelk O1® (Merck, Darmstadt), 250×4 mm.

General conditions for the separation of the enantiomers by semipreparative HPLC

Column (*S, S*)-Whelk O1® (Merck, Darmstadt, 250×10 mm), 3 *ml*/min, *c*=10 mg/*ml*).

(±)-2-Methylene-4-phenyl-γ-butyrolactone ***1***

From **8** (0.23 g, 2.21 mmol) and **15** (0.43 g, 2.21 mmol) **1** (0.35 g, 92%) was obtained as an oil; R_F 0.55 (hexane/ethyl acetate 3:1); IR (film): ν 1756*s*, 1700*w*, 1685*w*, 1663*w*, 1653*w*, 1635*w*, 1560*w*, 1539*w*, 1521*w*, 1506*w*, 1496*w*, 1459*w*, 1437*w*, 1398*w*, 1376*w*, 1320*m*, 1277*m*, 1241*m*, 1200*w*, 1176*m*, 1130*m*, 1063*w*, 1021*m*, 991*m*; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.91 (*ddt*, *J*=17.1, 6.6, 2.9, 1 H, H_A–C(3)), 3.40 (*ddt*, *J*=17.1, 8.0, 2.5, 1 H, H_B–C(3)), 5.52 (*dd*, *J*=8.0, 6.6, 1 H, H–C(4)), 5.69 (*dd* (virt *t*), *J*=2.5, 1 H, H_A–C(2′)), 6.30 (*dd* (virt *t*), *J*=2.9, 1 H, H_B–C(2′)), 7.29–7.42 (*m*, 5 H, CH (phenyl)); ^{13}C NMR (50 MHz, $CDCl_3$): δ 36.28 (*t*, C(3)), 77.94 (*d*, C(4)), 122.39 (*t*, C(2′), 125.38 and 128.84 (each *d*, CH (phenyl)), 128.84 (*d*, CH (*p*-phenyl)), 134.22 (*s*, C_q (phenyl)), 139.83 (*s*, C(2)), 170.05 (*s*, C(1)); MS (ei, 80 eV, 20 °C): 174(33.3), 129(10.5), 115(11.4), 114(18.8), 107(24.6), 105(16.9), 91(6.3), 79(23.8), 77(38.6), 68(100.0).

(4 R*)-2-Methylene-4-phenyl-γ-butyrolactone (4* **R**)-***1*** *and 1,6-bis-((5* R*)-10,10-dimethyl,-3,3-dioxo-3$^{\lambda 6}$-thia-4-aza-tricyclo[5.2.1.0^{1,5}]dec-4-yl)-2,5-dimethylene-hexane-1,6-dione (−)-**32***

Following the general procedure from **8** (0.3 g, 2.83 mmol) and (−)-**28** (1.0 g, 2.76 mmol) after chromatography (hexane/ethyl acetate 10:1) (***R***)-**1** (0.39 g, 85%) and (−)-**32** (0.14 g, 13%) were obtained.

Data for (**4*R***)-**1**: ee 62% (by HPLC (*R, R*)-Whelk O1®, 1.0 *ml*/min, 34 bar, 20°C, hexane/prop-2-OH, 98:2, t_R(*S*) 25 min, t_R(*R*) 31 min).

Data for (−)-**32**: colorless crystals; mp 232–234 °C, $[\alpha]_D^{25}$=−103.3 (*c*=1.0, $CHCl_3$), R_F 0.29 (hexane/ethyl acetate 3:1); IR (KBr): 2970m, 2938m, 1585s, 1671s, 1653w, 1646w, 1634m, 1616w, 1576w, 1569w, 1559w, 1540w, 1521w, 1506w, 1457w, 1448w, 1420w, 1407w, 1391w, 1373w, 1338w, 1327s, 1284w, 1259w, 1235w, 1211m, 1165w, 1146w, 1135m, 1111m, 1065m, 1037m, 1006w; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.99, 1.22 (each *s*, 6 H, H_3–C(10_{C1}′A, 10_{C2}′A, 10_{C1}′B, 10_{C2}′B)), 1.24–1.46 (*m*, 4 H), 1.85–2.09 (*m*, 10 H, (H–C(7_{C1}′, 7_{C2}′), H_2–C(6_{C1}, 6_{C2}, 8_{C1}, 8_{C2}, 9_{C1}, 9_{C2})), 3.39 (*d*, *J*=13.7, 1 H, H_A–C(2_{C1}, 2_{C2})), 3.50 (*d*, *J*=13.7, 1 H, H_B–C(2_{C1}, 2_{C2})), 4.05 (*dd*, *J*=7.5, 5.0, 2 H, H–C(5_{C1}, 5_{C2})), 5.70 (*s*, 2 H, H_A–C(2′, 5′)), 5.79 (*s*, 2 H, H_B–C(2′, 5′)); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 19.85, 21.28 (each *q*, C(10_{C1}′A, 10_{C2}′A, 10_{C1}′B, 10_{C2}′B)), 30.54 (*t*, C(3, 4)), 26.43, 33.16, 38.31 (each *t*, C(6_{C1}, 6_{C2}, 8_{C1}, 8_{C2}, 9_{C1}, 9_{C2})), 45.14 (*d*, C(4_{C1}, 4_{C2})), 47.62, 47.85 (each *s*, C(1_{C1}, 1_{C2}, 7_{C1}, 7_{C2})), 53.51 (*t*, C(2_{C1}, 2_{C2})), 65.43 (*d*, C(5_{C1}, 5_{C2})), 124.10 (*t*, C(2′, 5′)), 141.92 (*s*, C(2, 5)), 170.53 (*s*, C(1, 6)); MS (ei, 80 eV, 254 °C): 564(6.0), 500(3.0), 436(1.1), 350(56.3), 322(10.4), 218(10.6), 152(29.5), 135(100.0), 107(55.0), 93(42.3), 79(49.4), 67(18.9), 55(17.8), 43(19.1), 41(21.1); Anal. calcd. for $C_{28}H_{40}N_2O_6S_2$ (564.75): C, 59.55; H, 7.14; N, 4.96; found: C, 59.66; H, 7.09; N, 4.75.

(4 S*)-2-Methylene-4-phenyl-γ-butyrolactone (4* **S**)-***1*** *and 1,6-bis-((5* S*)-10,10-dimethyl,-3,3-dioxo-3$^{\lambda 6}$-thia-4-aza-tricyclo[5.2.1.0^{1,5}]dec-4-yl)-2,5-dimethylene-hexane-1,6-dione (+)-**32***

Following the general procedure from **8** (0.3 g, 2.83 mmol) and (+)-**28** (1.0 g, 2.76 mmol) after chromatography (hexane/ethyl acetate 10:1) (***S***)-**1** (0.51 g, 86%) and (+)-**32** (0.14 g, 13%) were obtained.

Data (**4*S***)-**1**: ee 54% (by HPLC (*S, S*)-Whelk O1®, 1.0 *ml*/min, 38 bar, 20 °C, hexane/prop-2-OH, 90:10, t_R(*R*) 16.2 min, t_R(*S*) 18.9 min).

Data for (+)-**32**: mp 233-235 °C; $[\alpha]_D^{25}$=+102.8 (*c*=1.0, $CHCl_3$); Anal. calcd. for $C_{28}H_{40}N_2O_6S_2$ (564.75): C, 59.55; H, 7.14; N, 4.96; found: C, 59.62; H, 7.12; N, 4.78.

(4 R)-2-Methylene-4-phenyl-γ-butyrolactone (4 R)-1 and (4 S)-2-methylene-4-phenyl-γ-butyrolactone (S)-1

From semipreparative HPLC of the racemate both compounds were obtained with ee ≥ 99%.

Data **(4 *R*)-1**: colorless crystals; mp 43–44 °C, $[\alpha]_D^{25}$=−20.8 (*c*=1.0, $CHCl_3$); Anal. calcd. for $C_{11}H_{10}O_2$ (174.07): C, 75.84; H, 5.79; found: C, 75.63; H, 5.89.

Data **(*S*)-1**: colorless crystals; mp 42–44 °C, $[\alpha]_D^{25}$=+20.2 (*c*=1.0, $CHCl_3$); Anal. calcd. for $C_{11}H_{10}O_2$ (174.07): C, 75.84; H, 5.79; found: C, 75.92; H, 5.88.

(±)-4-(2-Methoxyphenyl)-2-methylene-γ-butyrolactone 2

From **9** (0.30 g, 2.21 mmol) and **15** (0.43 g, 2.21 mmol) **2** (0.38 g, 84%) was obtained as a solid; mp 29 °C; R_F 0.50 (hexane/ethyl acetate 3:1); IR (film): ν 2941*w*, 1766*s*, 1664*w*, 1604*m*, 1590*m*, 1494*m*, 1465*m*, 1439*m*, 1322*m*, 1278*m*, 1249*s*, 1130*m*, 1029*s*, 756*m*; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.82 (*dddd* (virt *ddt*), *J*=17.4, 5.7, 2.9, 1 H, H_A–C(3)), 3.41 (*dddd* (virt *ddt*), *J*=17.4, 8.4, 2.7, 1 H, H_B–C(3)), 3.82 (*s*, 3H, OCH_3)), 5.61 (*dd* (virt *t*), *J*=2.6, 1 H, H_A–C(2′)), 5.72 (*dd*, *J*=8.4, 5.7, 1 H, H–C(4)), 6.26 (dd (virt *t*), *J*=2.9, 1 H, H_B–C(2′)), 6.88–6.98 (*m*, 2 H, H–C(3, 5) (phenyl)), 7.27–7.33 (*m*, 2 H, H–C(4, 6) (phenyl)); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 34.94 (*t*, C(3)), 55.21 (*q*, OCH_3)), 74.80 (*d*, C(4)), 110.43 (*d*, C(3) (phenyl)), 120.40 (*d*, C(5) (phenyl)), 121.50 (*t*, C(2′)), 125.70 (*d*, C(4) (phenyl)), 128.18 (*s*, C(1) (phenyl)), 134.62 (*s*, C(2)), 155.96 (C(2) (phenyl)), 170.37 (*s*, C(1)); MS (ei, 80 eV, 60 °C): 204(39.4), 159(9.3), 129(5.3), 115(6.9), 91(7.8), 77(10.2), 68(100.0), 51(3.7), 41(5.6); Anal. calcd. for $C_{12}H_{12}O_3$ (204.23): C, 70.58; H, 5.92; found: C, 70.42; H, 6.00.

(4 R)-4-(2-Methoxyphenyl)-2-methylene-γ-butyrolactone (4 R)-2

From **9** (0.30 g, 2.21 mmol) and **(−)-28** ((1.0 g, 2.76 mmol) **2** (0.39 g, 86%) was obtained; ee 39% (by HPLC: (*S, S*)-Whelk O1®, 1 *ml*/min, 38 bar, 20 °C, hexane/prop-2-OH 90:10, t_R(*R*)=16.5 min, t_R(*S*) 19.8 min).

(4 S)-4-(2-Methoxyphenyl)-2-methylene-γ-butyrolactone (4 S)-2

From **9** (0.30 g, 2.21 mmol) and **(+)-28** (1.0 g, 2.76 mmol) **2** (0.41 g, 89%) was obtained; ee 42% (by HPLC: (*S, S*)-Whelk O1®, 1 *ml*/min, 35 bar, 20 °C, hexane/prop-2-OH 95:5, t_R(*R*)=27.4 min, t_R(*S*) 32.1 min).

(±)-4-(3-Methoxyphenyl)-2-methylene-γ-butyrolactone 3

From **10** (0.30 g, 2.21 mmol) and **15** (0.43 g, 2.21 mmol) **3** (0.26 g, 58%) was obtained as an oil; R_F 0.40 (hexane/ethyl acetate 3:1); IR (film): 1766*s*, 1665*w*, 1603*m*, 1491*m*, 1458*m*, 1438*m*, 1321*m*, 1275*s*, 1157*m*, 1129*s*, 1025*m*; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.89 (*dddd*, (virt *ddt*), *J*=17.1, 6.4, 2.9, 1 H, H_A–C(3)), 3.39 (*dddd*, (virt *ddt*), *J*=17.1, 8.0, 2.5, 1 H, H_B–C(3)), 3.80 (*s*, 3 H, OCH_3), 5.49 (*dd*, *J* =8.0, 6.4, 1 H, H–C(4)), 5.68 (*dd* (virt *t*), *J*=2.5, 1 H, H_A–C(2′)), 6.29 (*dd* (virt *t*), *J*=2.9, 1 H, H_B–C(2′)), 6.85–6.89 (*m*, 3 H, H–C(2, 4, 6) (phenyl)), 7.26–7.32 (*m*, 1 H, H–C(5) (phenyl)); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 36.28 (*t*, C(3)), 55.31 (*q*, OCH_3)), 77.75 (*d*, C(4)), 110.82 (*d*, C(4) (phenyl)), 113.87 (*d*, C(2) (phenyl)), 117.38 (*d*, C(6) (phenyl)), 122.33 (*t*, C(2′)), 129.85 (*d*, C(5) (phenyl)), 134.04 (*s*, C(2)), 141.34 (*s*, C(1) (phenyl)), 159.81 (*s*, C(3) (phenyl)), 170.15 (*s*, C(1)); MS (ei, 80 eV, 99 °C): 204(42.3), 135(7.4), 115(6.3), 92(4.3), 91(4.2), 77(7.6), 68(100.0), 51(3.6), 41(6.9); Anal. calcd. for $C_{12}H_{12}O_3$ (204.23): C, 70.58; H, 5.92; found: C, 70.77; H, 5.97.

(4 S)-4-(3-Methoxyphenyl)-2-methylene-γ-butyrolactone (4 S)-3

From **10** (0.30 g, 2.21 mmol) and (+)-**28** (1.0 g, 2.76 mmol) **(4 *S*)-3** (0.41 g, 89%) was obtained; ee 72% (by HPLC: (*S, S*)-Whelk O1®, 1 *ml*/min, 38 bar, 20 °C, hexane/prop-2-OH, 90:10, t_R(*R*) 25.0 min, t_R(*S*) 31.2 min).

(±)-4-(4-Methoxyphenyl)-2-methylene-γ-butyrolactone 4

From **11** (0.30 g, 2.21 mmol) and **15** (0.43 g, 2.21 mmol) **4** (0.36, 80%) was obtained as a solid; mp 47 °C; R_F 0.24 (hexane/ethyl acetate 3:1); IR (KBr): ν 1750*s*, 1659*m*, 1612*m*, 1519*m*, 1438*m*, 1337*m*,

1286*m*, 1261*s*, 1178*m*, 1130*s*, 1020*m*, 978*m*, 952*m*, 834*s*; ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.89 (*dddd*, (virt ddt), *J*=17.1, 6.5, 2.9, 1 H, H_A–C(2)), 3.34 (*dddd*, (virt *t*), *J*=17.1, 7.9, 2.4, 1 H, H_B–C(2)), 3.79 (*s*, 3 H, OCH_3), 5.45 (*dd*, *J*=7.9, 6.5, 1 H, H–C(4)), 5.67 (*dd* (virt *t*), *J*=2.4, H_A–C(2′)), 6.27 (*dd* (virt *t*), *J*=2.9, 1 H, H_B–C(2′)), 6.86–6.92 (*m*, 2 H, H–C(2, 6) (phenyl)), 7.21–7.25 (*m*, 2 H, H–C(3, 5) (phenyl)); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 36.15 (*t*, C(3)), 55.32 (*q*, OCH_3), 78.06 (*d*, C(4)), 114.20 (*d*, C(3, 5) (phenyl)), 122.11 (*t*, C(2′)), 127.10 (*d*, C(2, 6) (phenyl)), 131.67 (*s*, C(1) (phenyl)), 134.66 (*s*, C(2)), 159.87 (*s*, C(4) (phenyl)), 170.17 (*s*, C(1)); MS (ei, 80 eV, 75 °C): 204(51.4), 173(1.2), 159(8.0), 145(4.4), 135(17.5), 129(4.9), 115(7.2), 92(5.2), 77(10.4), 68(100.0), 51(4.3), 41(5.7); Anal. calcd. for $C_{12}H_{12}O_3$ (204.23): C, 70.58; H, 5.92; found: C, 70.53; H, 5.89.

(4 S)-4-(4-Methoxyphenyl)-2-methylene-γ-butyrolactone (4 S)-4

From **11** (0.30 g, 2.21 mmol) and (+)-**28** (0.8 g, 2.21 mmol) (**4** *S*)-**4** (0.39, 90%) was obtained; ee 58% (by HPLC: (*S, S*)-Whelk O1®, 1.0 *ml*/min, 38 bar, 20°C, hexane/prop-2-OH, 90:10, t_R(*R*) 31.5 min, t_R(*S*) 39.5 min).

(4 R)-4-(4-Methoxyphenyl)-2-methylene-γ-butyrolactone (4 **R***)-4 and (4 S)-4-(4-methoxy-phenyl)-2-methylene-γ-butyrolactone (4* **S***)-4*

By semipreparative HPLC from the racemate (eluent: hexane/prop-2-OH 95:5) (**4** *R*)-**4** and (**4** *S*)-**4** were obtained as colorless oils.

Data for (**4** *R*)-**4**: $[\alpha]_D^{25}$=−31.9 (*c*=1.0, $CHCl_3$); Anal. calcd. for $C_{12}H_{12}O_3$ (204.23): C, 70.58; H, 5.92; found: C, 70.62; H, 5.81.

Data for (**4** *S*)-**4**: $[\alpha]_D^{25}$=+31.3 (*c*=1.0, $CHCl_3$); Anal. calcd. for $C_{12}H_{12}O_3$ (204.23): C, 70.58; H, 5.92; found: C, 70.75; H, 5.79.

(±)-2-Methylene-4-naphthalen-1-yl-γ-butyrolactone 5

From **12** (0.35 g, 2.21 mmol) and **15** (0.43 g, 2.21 mmol) **5** (0.44 g, 87%) was obtained as a solid; mp 59 °C, R_F 0.47 (hexane/ethyl acetate 3:1); IR (KBr): 1752*s*, 1700*w*, 1695*w*, 1684*w*, 1653*w*, 1597*w*, 1559*w*, 1540*w*, 1534*w*, 1507*w*, 1457*w*, 1432*w*, 1398*w*, 1361*w*, 1334*w*, 1308*w*, 1284*m*, 1252*m*, 1233*m*, 1167*w*, 1121*s*, 1051*m*, 1028*m*, 1011*m*, 967*m*, 801*m*, 773*s*; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.95 (*dddd*, (virt ddt), *J*=17.1, 5.6, 2.8, 1 H, H_A–C(3)), 3.63 (*dddd*, (virt *ddt*, *J*=17.1, 8.3, 2.7, 1 H, H_B–C(3)), 5.67 (*dd* (virt *t*), *J*=2.7, 2.4, 1 H, H_A–C(2′)), 6.25 (*dd*, *J*=8.3, 5.6, 1 H, H–C(4)), 6.35 (*dd* (virt *t*), *J*=2.9, 1 H, H_B–C(2′)), 7.45–7.60 (*m*, 4H), 7.77–7.94 (*m*, 3 H) (CH (naphthalene)); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 35.77 (*t*, C(3)), 75.32 (*d*, C(4)), 122.81 (*t*, C(2′)), 121.51, 122.17, 125.20, 125.78, 126.42, 128.56, 128.97 (each *d*, CH (naphthalene)), 129.14, 133.59 (2×) (each *s*, C_q (naphthalene)), 135.41 (*s*, C(2)), 170.00 (*s*, C(1)); MS (ei, 80 eV, 86 °C): 224(46.7), 179(7.2), 178(7.5), 165(5.6), 155(6.4), 128(14.5), 127(15.8), 68(100.0); Anal. calcd. for $C_{15}H_{12}O_2$ (224.26): C, 80.35; H, 5.39; found: C, 80.46; H, 5.29.

(4 S)-2-Methylene-4-naphthalen-1-yl-γ-butyrolactone (4 **S***)-5*

From **12** (0.35 g, 2.21 mmol) and (+)-**28** (0.80, 2.21 mmol) (**4** *S*)-**5** (0.40 g, 93%) was obtained; ee 61% (by HPLC: (*S, S*)-Whelk O1®, 1 *ml*/min, 38 bar, 20°C, hexane/prop-2-OH, 90:10, t_R(*R*) 22.6 min, t_R(*S*) 33.1 min).

(±)-2-Methylene-4-naphthalen-2-yl-γ-butyrolactone 6

From **13** (0.35 g, 2.21 mmol) and **15** (0.43 g, 2.21 mmol) **6** (0.45 g, 90%) was obtained as a solid; mp 83–85 °C, R_F 0.42 (hexane/ethyl acetate 3:1); IR (KBr): 1755*s*, 1700*w*, 1684*w*, 1653*w*, 1647*w*, 1635*w*, 1602*w*, 1560*w*, 1540*w*, 1521*w*, 1509*w*, 1472*w*, 1457*w*, 1438*w*, 1407*w*, 1279*m*, 1250*m*, 1183*w*, 1158*w*, 1127*m*, 1020*w*, 982*m*, 901*w*, 867*w*, 824*m*, 755*m*; ^{1}H NMR (300 MHz, $CDCl_3$): δ 2.95 (*dddd*,, *J*=17.1, 5.9, 3.1, 2.8, 1 H, H_A–C(3)), 3.43 (*dddd*,, *J*=17.1, 8.1, 2.6, 2.3, 1 H, H_B–C(3)), 5.63–5.69 (*m*, 2 H, H_A–C(2′), H–C(4)), 6.32 (*dd*, *J*=3.1, 2.6, 1 H, H_B–C(2′)), 7.34–7.37 (*m*, 1H), 7.45–7.52 (*m*, 2 H), 7.70–7.86 (*m*, 4 H) (CH (naphthalene)); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 36.25 (*t*, C(3)),

78.11 (*d*, C(4)), 122.65 (*t*, C(2′)), 122.84, 124.61, 126.58, 126.70, 127.80, 128.13, 129.03 (each *d*, CH (naphthalene)), 133.11, 133.25, 134.21 (each *s*, C_q (naphthalene)), 137.16 (*s*, C(2)), 170.20 (*s*, C(1)); MS (ei, 80 eV, 86 °C): 224(51.2), 178(8.4), 165(5.0), 155(8.2), 127(15.5), 69(100.0); Anal. calcd. for $C_{15}H_{12}O_2$ (224.26): C, 80.34; H, 5.39; found: C, 80.06; H, 5.30.

(4 R*)-2-Methylene-4-naphthalen-2-yl-γ-butyrolactone (4* **R***)-6)*

From **13** (0.35 g, 2.21 mmol) and (−)-**28** (0.8 g, 2.21 mmol) **15** (0.43 g, 2.21 mmol) (4 *R*)-**6** (0.40 g, 95%) was obtained; ee 83% (by HPLC: (*S, S*)-Whelk O1®, 1.0 *ml*/min, 38 bar, 20°C, hexane/prop-2-OH, 90:10, t_R(*R*) 26.0 min, t_R(*S*) 45.6 min).

(4 S*)-2-Methylene-4-naphthalen-2-yl-γ-butyrolactone (4* **S***)-6*

From **13** (0.35 g, 2.21 mmol) and (+)-**28** (0.80, 2.21 mmol) (**4** ***S***)-**6** (0.39 g, 94%) was obtained; ee 82.7% (by HPLC: (*R, R*)-Whelk O1®, 1.0 *ml*/min, 38 bar, 20°C, hexane/prop-2-OH 90:10, t_R(*S*) 29.1 min, t_R(*R*) 46.2 min).

(4 R*)-2-Methylene-4-naphthalen-2-yl-γ-butyrolactone (4* **R***)-6 and (4* S*)-2-methylene-4-naphthalen-2-yl-γ-butyrolactone (4* S*)-6)*

By semipreparative HPLC from the racemate (eluent: hexane/prop-2-OH 95:5) (**4** ***R***)-**6**) and (**4** ***S***)-**6**) were obtained as colorless crystals.

Data for (**4** ***R***)-**6**: mp 72–73 °C; $[\alpha]_D^{25}$=−54.5 (*c*=1.0, $CHCl_3$); Anal. calcd. for $C_{15}H_{12}O_2$ (224.26): C, 80.34; H, 5.39; found: C, 80.23; H, 5.33.

Data for (**4** ***S***)-**6**: mp 72–73°C; $[\alpha]_D^{25}$=+54.5 (*c*=1.0, $CHCl_3$); Anal. calcd. for $C_{15}H_{12}O_2$ (224.26): C, 80.34; H, 5.39; found: C, 80.45; H, 5.49.

(±)-4-(2-Methyl-propyl)-2-methylene-γ-butyrolactone 7

From **14** (0.30 g, 3.49 mmol) and **15** (0.67 g, 3.49 mmol) **7** (0.48 g, 89%) was obtained as an oil; R_F 0.27 (hexane/ethyl acetate 5:1); IR (film): ν 2959*m*, 2872*w*, 1764*s*, 1666*w*, 1469*w*, 1437*w*, 1399*w*, 1369*w*, 1353*w*, 1336*w*, 1275*m*, 1186*w*, 1158*w*, 1119*m*, 1067*w*, 1023*w*, 1004*w*; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.95, 0.97 (each *d*, *J*=6.6, 3 H, H_3–C(4‴A, 4‴B), 1.41 (*ddd*, *J*=14.0, 8.1, 5.1, 1 H, H_A–C(4′)), 1.69 (*ddd*, *J*=14.0, 8.6, 6.0, 1 H, H_B–C(4′)), 1.79–1.90 (*m*, 1 H, H–C(4″)), 2.55 (*dddd*, (virt *ddt*), *J*=17.0, 6.1, 3.0, 1 H, H_A–C(3)), 3.08 (*dddd*, (virt *ddt*), *J*=17.0, 7.6, 2.5, H_B–C(3)), 4.60 (*dddd*, *J*=8.6, 7.6, 6.1, 5.1, 1 H, H–C(4)), 5.63 (*dd* (virt *t*), *J*=2.6, 1 H, H_A–C(2′)), 6.22 (*dd* (virt *t*), *J*=2.8, 1 H, H_B–C(2′)); ^{13}C NMR; MS (ei, 80 eV, 46 °C): 154(10.8), 139(3.1), 111(4.6), 97(100.0), 69(47.0), 68(35.6), 55(9.3), 43(20.5), 41(88.5).

(4 R*)-4-(2-Methyl-propyl)-2-methylene-γ-butyrolactone (4* **S***)-7*

From **14** (0.30 g, 3.49 mmol) and (+)-**28** (0.76 g, 2.1 mmol) (**4** ***S***)-**7** (0.43 g, 79%) was obtained; ee 59% (by HPLC: (*S, S*)-Whelk O1®, 0.1 *ml*/min, 35 bar, 20°C, hexane/prop-2-OH, 95:5, t_R(*R*) 14.4 min, t_R(*S*) 16.1 min).

cis-*(±)-3-Methyl-2-methylene-4-phenyl-γ-butyrolactone* ***17***

From **8** (0.23 g, 2.21 mmol) and **16** (0.46 g, 2.21 mmol) **17** (0.35 g, 87%) was obtained as an oil; R_F 0.48 (hexane/ethyl acetate 3:1); IR (film): ν 3064*w*, 3034*w*, 2968*m*, 2879*w*, 1763*s*, 1677*m*, 1604*w*, 1498*w*, 1457*m*, 1408*m*, 1331*s*, 1295*w*, 1265*w*, 1246*s*, 1212*m*, 1193*w*, 1119*s*, 1089*m*, 991*s*; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.79 (*d*, *J*=7.1, 3 H, H_3–C(3′)), 3.42–3.47 (*m*, 1 H, H–C(3)), 5.58 (*d*, *J*=2.6, 1 H, H_A–C(2′)), 5.62 (*d*, *J*=8.1, 1 H, H–C(4)), 6.33 (*d*, *J*=2.9, H_B–C(2′)), 7.15–7.18 (*m*, 2 H), 7.32–7.39 (*m*, 3 H) (CH (phenyl)); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 15.32 (*q*, C(3′)), 38.84 (*d*, C(3)), 82.00 (*d*, C(4)), 121.52 (*t*, C(2′)), 125.79, 128.17, 128.25 (each *d*, CH (phenyl)), 136.09 (*s*, C_q (phenyl), 139.84 (*s*, C(2)), 170.32 (*s*, C(1)); MS (ei, 80 eV, 40 °C): 188(8.8), 173(0.5), 143(3.5), 128(6.1), 115(4.6), 105(9.3), 82(84.7), 77(20.1), 54(100.0); Anal. calcd. for $C_{12}H_{12}O_2$ (188.23): C, 76.57; H, 6.43; found: C, 76.69; H, 6.56.

cis-(3 S, 4 R)-3-Methyl-2-methylene-4-phenyl-γ-butyrolactone (3 S, 4 R)-17

From **8** (0.9 g, 8.49 mmol) and **(-)-30** (1.10 g, 2.83 mmol) after chromatography (hexane/ethyl acetate 10:1) **(3 *S*, 4 *R*)-17** (0.50 g, 95%) was obtained; ee 69% (by HPLC, (*S, S*)-Whelk O1®, 1.0 *ml*/min, 34 bar, 20°C, hexane/prop-2-OH, 98:2, $t_R(S)$ 27.4 min, $t_R(R)$ 30.6 min).

cis-(3 R, 4 S)-3-Methyl-2-methylene-4-phenyl-γ-butyrolactone (3 R, 4 S)-17

From **8** (0.3 g, 2.83 mmol) and **(+)-30** (1.10 g, 2.83 mmol) after chromatography (hexane/ethyl acetate 10:1) **(3 *R*, 4 *S*)-17** (0.51 g, 96%) was obtained; ee 90% (by HPLC *vide supra*).

(±)-4-(2-Methoxyphenyl)-3-methyl-2-methylene-γ-butyrolactone 18

From **9** (0.30 g, 2.21 mmol) and **16** (0.46 g, 2.21 mmol) **18** (0.25 g, 53%) was obtained as an inseparable mixture of *cis/trans* isomers (3:1 by ^{1}H NMR and HPLC ((*S,S*)-Whelk O1®, 1 *ml*/min, 33 bar, 17°C, hexane/prop-2-OH 99:1, $t_R(R^1)$ 51.0 min, $t_R(R^2)$ 54.9 min, $t_R(S^1)$ 60.6 min, $t_R(S^2)$ 71.0 min)); mp 54 °C, R_F 0.57 (hexane/ethyl acetate 3:1); IR (KBr): ν 3048*w*, 1008*w*, 2979*m*, 2926*w*, 1897*w*, 1757*s*, 1684*w*, 1662*m*, 1636*w*, 1617*w*, 1602*m*, 1588*w*, 1560*w*, 1540*w*, 1492*m*, 1466*w*, 1442*m*, 1409*w*, 1388*w*, 1370*w*, 1355*w*, 1329*m*, 1298*m*, 1271*w*, 1252*s*, 1240*w*, 1198*w*, 1164*s*, 1116*w*, 1092*m*, 1066*m*, 1048*m*, 1036*m*, 1023*m*, 979s; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.77 (*d*, *J*=7.1, 2.1 H, H_3–C(3′), A), 1.34 (*d*, *J*=6.9, 0.9 H, H_3–C(3′), B), 3.02 (*m*, 0.3 H, H–C(3), B), 3.50 (*m*, 0.7 H, H–C(3), A), 3.82 (*s*, 2.1 H, OCH_3, A), 3.83 (*s*, 0.9 H, OCH_3, B), 5.30 (*d*, *J*=5.8, 0.3 H, H–C(4), B), 5.55 (*d*, *J*=2.0, 0.3 H, H_A–C(2′), B), 5.56 (*d*, *J*=2.4, 0.7 H, H_A–C(2′), A), 5.87 (*d*, *J*=7.8, 0.7 H, H–C(4), A), 6.27 (*d*, *J*=2.7, 0.3 H, H_B–C(2′), B), 6.28 (*d*, *J*=2.6, 0.7 H, H_B–C(2′), A), 6.87–6.98 (*m*, 2H), 7.21 (*m*, 2H) (CH (phenyl)); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 15.67 (*q*, C(3′), A), 18.24 (*q*, C(3′), B), 37.81 (*d*, C(3), A), 42.02 (*d*, C(3), B), 55.16 (*q*, OCH_3, A), 55.32 (*q*, OCH_3, B), 78.47 (*d*, C(4), A), 82.03 (*d*, C(4), B), 109.98 (*d*, CH (phenyl), A), 110.63 (*d*, CH (phenyl), B), 120.42 (*d*, CH (phenyl), A), 120.55 (*d*, CH (phenyl), B), 120.79 (*t*, C(2′), B), 121.02 (*t*, C(2′), A), 124.67 (*s*, C(1) (phenyl), A), 126.40 (*d*, CH (phenyl), A), 126.44 (*d*, CH (phenyl), B), 127.25 (*s*, C(1) (phenyl), B), 129.05 (*d*, CH (phenyl), A), 129.49 (*d*, CH (phenyl), B), 140.87 (*s*, C(2), B), 140.94 (*s*, C(2), A), 155.93 (*s*, C(2) (phenyl), A), 156.52 (*s*, C(2) (phenyl), B), 170.54 (*s*, C(1), A and B); MS (ei, 80 eV, 50 °C): 218(23.0), 203(6.2), 173(3.7), 135(6.7), 115(4.8), 91(6.1), 82(88.6), 77(10.4), 65(4.8), 54 (100.0); Anal. calcd. for $C_{13}H_{14}O_3$ (218.25): C, 71.54; H, 6.47; found: C, 71.71; H, 6.37.

(3 S, 4 R)-4-(2-Methoxyphenyl)-3-methyl-2-methylene-γ-butyrolactone (3 S, 4 R)-18 and 1-N-((5R)-10,10-dimethyl-3,3-dioxo-3$^{\lambda 6}$-thia-4-aza-tricyclo[5.2.1.01.5]dec-4-yl)-2-[(1 S, 2 R) (2-hydroxy-1-methyl-2-(2-methoxyphenyl)-ethyl)]-prop-2-en-1-one 33

From **9** (0.3 g, 2.21 mmol) and (−)-**30** (1.10 g, 2.83 mmol) **(3 *S*, 4 *R*)-18** (0.34 g, 68%) and **33** (0.08 g, 8.8%) were obtained.

Data for **(3 *S*, 4 *R*)-18**: HPLC: (*S,S*)-Whelk O1®, 1 *ml*/min, 33 bar, 20°C, hexane/prop-2-OH, 99:1, $t_R(R^1)$ 45.3 min, $t_R(R^2)$ 48.0 min, $t_R(S^1)$ 51.9 min, $t_R(S^2)$ 62.6 min.

Data for **33**: mp 138–140 °C, $[\alpha]_D^{25}$=−100.6 (*c*=1.2, $CHCl_3$), R_F 0.48 (hexane/ethyl acetate 3:1); IR (KBr): ν 3540*s*, 2967*m*, 1767*m*, 1683*s*, 1628*w*, 1602*w*, 1588*w*, 1491*m*, 1457*m*, 1408*m*, 1330*s*, 1275*s*, 1246*s*, 1183*m*, 1169*m*, 1129*s*, 1082*w*, 1063*w*, 1050*m*, 1027*m*, 756*m*; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.89 (*d*, *J*=7.1, 3 H, H_3–C(3′)), 1.01, 1.26 (each *s*, 3 H, H_3–C(10_C′A, 10_C′B)), 1.33–1.49 (*m*, 2 H), 1.86–2.15 (*m*, 5 H) (H–C(7_C), H2–C(6_C, 8_C, 9_C)), 3.24 (*m*, 1 H, H–C(3)), 3.44 (*d*, *J*=13.7, 1 H, H_A–C(2_C)), 3.55 (*d*, *J*=13.7, 1 H, H_B–C(2_C)), 3.65 (*bs*, 1 H, OH), 3.85 (*s*, 3 H, OCH_3), 4.14 (*dd*, *J*=7.6, 4.9, 1 H, H–C(5_C)), 5.11 (*d*, *J*=2.2, 1 H, H–C(4)), 5.82 (*d*, *J*=1.4, 1 H, H_A–C(2′)), 5.99 (*d*, *J*=0.7, 1 H, H_B–C(2′)), 6.82–6.85, 6.93–6.99 (each *m*, 1 H, H–C(3, 5) (phenyl)), 7.19–7.25, 7.51–7.54 (each *m*, 1 H, H–C(4, 6) (phenyl)); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 9.83 (*q*, C(3′)), 19.85, 21.46 (each *q*, C(10_C′A, 10_C′B)), 26.37, 33.21, 38.41 (each *t*, C(6_C, 8_C, 9_C)), 41.45 (*d*, C(3)), 45.27 (*d*, C(4_C)), 47.65, 47.79 (each *s*, C(1_C, 10_C)), 53.63 (*t*, C(2_C)), 55.15 (*q*, OCH_3)), 65.81 (*d*, C(5C)), 70.35 (*d*, C(4)), 109.69 (*d*, C(3) (phenyl)), 119.99 (*d*, C(5) (phenyl)), 126.40 (*t*, C(2′)), 127.17 (*d*,

C(4) (phenyl)), 127.41 (*d*, C(6) (phenyl)), 130.76 (*s*, C(1) (phenyl)), 145.95 (*s*, C(2)), 155.45 (*s*, C(2) (phenyl)), 170.86 (*s*, C(1)); MS (ei, 80 eV, 135 °C): 433(2.0), 369(0.5), 344(0.5), 297(46.5), 218(23.2), 151(13.5), 137(33.8), 135(63.2), 119(20.8), 108(29.4), 107(30.5), 93(30.5), 83(100.0), 82(93.5), 77(26.3), 67(20.2), 55(30.6), 54(79.6), 43(85.1); Anal. calcd. for $C_{23}H_{31}NO_5S$ (433.56): C, 63.72; H, 7.21; N, 3.23; found: C, 63.42; H, 7.19; N, 2.99.

cis-*(±)-4-(3-Methoxyphenyl)-3-methyl-2-methylene-γ-butyrolactone* ***19***

From **10** (0.30 g, 2.21 mmol) and **16** (0.46 g, 2.21 mmol) **19** (0.40 g, 82%) was obtained as an oil; R_F 0.42 (hexane/ethyl acetate 3:1); IR (film): ν 2970*w*, 1767*s*, 1664*w*, 1603*m*, 1587*w*, 1491*m*, 1455*m*, 1438*w*, 1406*w*, 1406*w*, 1360*w*, 1195*w*, 1150*m*, 1121*m*, 1089*w*, 1049*m*, 994*m*; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.81 (*d*, *J*=7.1, 3 H, H_3–C(3′)), 3.42 (*m*, 1 H, H–C(3)), 3.79 (*s*, 3 H, OCH_3)), 5.58 (*m*, 2 H, H–C(4), H_A–C(2′)), 6.31 (*d*, *J*=2.8, 1 H, H_B–C(2′)), 6.71 (*m*, 2 H), 6.83 (*m*, 1 H), 7.27 (*t*, *J*=7.9, 1 H) (CH (phenyl)); ^{13}C NMR (75.4 MHz, $CDCl_3$): d 15.28 (*q*, C(3′)), 38.80 (*d*, C(3)), 55.15 (*q*, OCH_3), 81.82 (*d*, C(4)), 111.57 (*d*, C(4) (phenyl)), 113.41 (*d*, C(2) (phenyl)), 118.06 (*d*, C(6) (phenyl)), 121.46 (*t*, C(2′)), 129.36 (*d*, C(5) (phenyl)), 137.71 (*s*, C(1) (phenyl)), 139.89 (*s*, C(2)), 159.46 (*s*, C(3) (phenyl)), 170.23 (C(1)); MS (ei, 80 eV, 85 °C): 218(27.9), 136(7.6), 135(9.5), 128(5.3), 115(4.7), 107(4.8), 92(5.0), 86(24.8), 84(39.5), 82(100.0), 77(10.6), 65(5.9), 54(93.9), 47(12.9), 43(8.3); Anal. calcd. for $C_{13}H_{14}O_3$ (218.25): C, 71.54; H, 6.47; found: C, 71.39; H, 6.52.

cis-*(3* R, *4* S*)-4-(3-Methoxyphenyl)-3-methyl-2-methylene-γ-butyrolactone (3* **R**, *4* **S***)-**19***

From **10** (0.3 g, 2.21 mmol) and **(+)-30** (0.89 g, 2.21 mmol) after chromatography (hexane/ethyl acetate 10:1) **(3** ***R*****, 4** ***S*****)-19** (0.41 g, 86%) was obtained; ee 62% (by HPLC: (*S, S*)-Whelk O1®, 1 *ml*/min, 33 bar, 20°C, hexane/prop-2-OH, 99:1, t_R(*R*) 59.7 min, t_R(*S*) 69.7 min).

trans-*(±)-4-(4-Methoxyphenyl)-3-methyl-2-methylene-γ-butyrolactone* ***20a*** *and* cis-*(±)-4-(4-methoxyphenyl)-3-methyl-2-methylene-γ-butyrolactone* ***20b***

From **11** (0.30 g, 2.21 mmol) and **16** (0.46 g, 2.21 mmol) **20a** (60 mg, 13%) and **20b** (0.37 g, 77%) were obtained.

Data for **20a**: mp 73–75 °C, R_F 0.36 (hexane/ethyl acetate 3:1); IR (KBr): ν 2969*m*, 2936*w*, 2838*w*, 1762*s*, 1662*w*, 1615*m*, 1584*w*, 1516*s*, 1493*m*, 1441*w*, 1411*w*, 1365*w*, 1295*m*, 1251*s*, 1181*m*, 1173*m*, 1142*s*, 1110*w*, 1029*s*, 1013*w*, 999*s*, 963*m*, 824*m*; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.28 (*d*, *J*=6.8, 3 H, H_3–C(3′)), 2.91–2.97 (*m*, 1 H, H–C(3)), 3.81 (*s*, 3 H, OCH_3), 4.84 (*d*, *J*=7.9, 1 H, H–C(4)), 5.57 (*d*, *J*=2.9, 1 H, H_A–C(2′)), 6.29 (*d*, *J*=3.2, 1 H, H_B–C(2′)), 6.89–6.94 (*m*, 2 H, H–C(2, 6) (phenyl)), 7.26–7.30 (*m*, 2H, H–C(3, 5) (phenyl)); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 15.56 (*q*, C(3′)), 43.22 (*d*, C(3)), 55.23 (*q*, OCH_3), 85.80 (*d*, C(4)), 113.99 (*d*, C(3, 5) (phenyl)), 120.47 (*t*, C(2′)), 127.37 (*d*, C(2, 6) (phenyl)), 129.92 (*s*, C(1) (phenyl)), 140.57 (*s*, C(2)), 159.81 (*s*, C(4) (phenyl)), 169.82 (*s*, C(1)); MS (ei, 80 eV, 71 °C): 218(23.5), 159(2.4), 135(13.5), 115(5.1), 92(4.3), 82(87.8), 77(9.4), 54(100.0); Anal. calcd. for $C_{13}H_{14}O_3$ (218.25): C, 71.54; H, 6.47; found: C, 71.84; H, 6.32.

Data for **20b**: mp 67–69 °C; R_F 0.31 (hexane/ethyl acetate 3:1); IR (KBr): ν 2970*m*, 2935*w*, 2838*w*, 2057*w*, 1767*s*, 1684*w*, 1664*w*, 1653*w*, 1613*m*, 1586*w*, 1559*w*, 1516*s*, 1457*m*, 1400*w*, 1364*w*, 1329*w*, 1298*m*, 1253*s*, 1180*m*, 1148*m*, 1117*m*, 1088*w*, 1033*m*, 986*m*, 816m; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.81 (*d*, *J*=7.1, 3 H, H_3–C(3′)), 3.35–3.44 (*m*, 1 H, H–C(3)), 3.80 (*s*, 3 H, OCH_3), 5.56 (*d*, *J*=2.6, 1 H, H_A–C(2′)), 5.57 (*d*, *J*=8.7, 1 H, H–C(4)), 6.31 (*d*, *J*=2.9, 1 H, H_B–C(2′)), 6.85–6.94 (*m*, 2 H, H–C(2, 6) (phenyl)), 7.05–7.10 (*m*, 2H, H–C(3, 5) (phenyl)); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 15.18 (*q*, C(3′)), 38.97 (*d*, C(3)), 55.19 (*q*, OCH_3), 85.02 (*d*, C(4)), 113.69 (*d*, C(3, 5) (phenyl)), 121.30 (*t*, C(2′)), 127.16 (*d*, C(2, 6) (phenyl)), 128.18 (*s*, C(1) (phenyl)), 140.03 (*s*, C(2)), 159.40 (*s*, C(4) (phenyl)), 170.39 (*s*, C(1)); MS (ei, 80 eV, 60 °C): 218(18.7), 159(1.4), 135(13.3), 115(4.8), 92(4.6), 82(73.2), 77(9.9), 54(100.0); Anal. calcd. for $C_{13}H_{14}O_3$ (218.25): C, 71.54; H, 6.47; found: C, 71.38; H, 6.33.

cis-*(3* R, *4* S*)-4-(4-Methoxyphenyl)-3-methyl-2-methylene-γ-butyrolactone (3* **R**, *4* **S***)-20b*

From **11** (0.30 g, 2.21 mmol) and **(+)-30** (0.8 g, 2.21 mmol) **[(3 R, 4 S)-20b]** (0.39 g, 81%) was obtained; ee 75% (by HPLC: (S, S)-Whelk O1®, 1 *ml*/min, 38 bar, 20°C, hexane/prop-2-OH, 90:10, $t_R(R)$ 21.0 min, $t_R(S)$ 26.2 min).

cis-*(3* R, *4* S*)-4-(4-Methoxyphenyl)-3-methyl-2-methylene-γ-butyrolactone (3* **R**, *4* **S***)-20b and* cis-*(3* S, *4* R*)-4-(4-methoxyphenyl)-3-methyl-2-methylene-γ-butyrolactone (3* **S**, *4* **R***)-20b*

By semipreparative HPLC from the racemate (eluent: hexane/prop-2-OH 95:5) **(3 *R*, 4 *S*)-20b** and **(3 *S*, 4 *R*)-20b** were obtained as colorless crystals.

Data for **(3 *R*, 4 *S*)-20b**: mp 31–33 °C; $[\alpha]_D^{25}=-39.8$ (*c*=1.0, $CHCl_3$); Anal. calcd. for $C_{13}H_{14}O_3$ (218.25): C, 71.54; H, 6.47; found: C, 71.42; H, 6.52.

Data for **(3 *S*, 4 *R*)-20b**: mp 31–33 °C; $[\alpha]_D^{25}=+41.1$ (*c*=1.0, $CHCl_3$); Anal. calcd. for $C_{13}H_{14}O_3$ (218.25): C, 71.46; H, 6.47; found: C, 71.38; H, 6.67.

cis-*(±)-3-Methyl-2-methylene-4-naphthalen-1-yl-γ-butyrolactone 21*

From **12** (0.35 g, 2.21 mmol) and **16** (0.46 g, 2.21 mmol) **21** (0.47 g, 88%) was obtained as a solid; mp 106–107 °C, R_F 0.53 (hexane/ethyl acetate 3:1); IR (KBr): ν 3093*w*, 2974*w*, 2929*w*, 1753*s*, 1658*w*, 1598*w*, 1510*w*, 1446*w*, 1404*w*, 1329*m*, 1295*w*, 1272*m*, 1251*w*, 1166*m*, 1158*m*, 1100*m*, 1072*w*, 1051*m*, 784*m*, 733*s*; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 0.64 (*d*, *J*=7.2, 3 H, H_3–C(3′)), 3.65–3.73 (*m*, 1 H, H–C(3)), 5.65 (*d*, *J*=2.0, 1 H, H_A–C(2′)), 6.30 (*m*, 2 H, H–C(4), H_B–C(2′)), 7.45–7.57 (*m*, 4 H), 7.76–7.91 (*m*, 3 H), (CH (naphthalene)); ^{13}C NMR (62.9 MHz, $CDCl_3$): d 16.46 (*q*, C(3′)), 38.68 (*d*, C(3)), 79.09 (*d*, C(4)), 122.43 (*t*, C(2′)), 122.00, 123.09, 125.34, 125.87, 126.57, 128.53, 129.19 (each *d*, CH (naphthalene)), 129.95, 131.89, 133.42 (each *s*, C_q (naphthalene)), 140.80 (*s*, C(2)), 170.22 (*s*, C(1)); MS (ei, 80 eV, 88 °C): 238(46.6), 178(3.9), 165(3.1), 155(7.6), 127(18.0), 82(100.0); Anal. calcd. for $C_{16}H_{14}O_2$ (238.29): C, 80.65; H, 5.92; found: C, 80.69; H, 5.82.

cis-*(3* S, *4* R*)-3-Methyl-2-methylene-4-naphthalen-1-yl-γ-butyrolactone (3* **S**, *4* **R***)-21*

From **12** (0.35 g, 2.21 mmol) and (−)-**30** (0.90 g, 2.39 mmol) **(3 *S*, 4 *R*)-21** (0.36 g, 81%) was obtained; ee 61% (by HPLC: (*S*, *S*)-Whelk O1®, 1.0 *ml*/min, 33 bar, 20°C, hexane/prop-2-OH 99:1, $t_R(R)$ 52.0 min, $t_R(S)$ 57.7 min).

cis-*(±)-3-Methyl-2-methylene-4-naphthalen-2-yl-γ-butyrolactone 22*

From **13** (0.35 g, 2.21 mmol) and **16** (0.46 g, 2.21 mmol) **22** (0.45 g, 84%) was obtained as a solid; mp 64–65 °C, R_F 0.47 (hexane/ethyl acetate 3:1); IR (KBr): 3058*w*, 2973*w*, 2934*w*, 2885*w*, 1754*s*, 1700*w*, 1696*w*, 1684*w*, 1675*w*, 1653*w*, 1647*w*, 1635*m*, 1617*w*, 1601*w*, 1576*w*, 1570*w*, 1560*w*, 1540*w*, 1521*w*, 1507*w*, 1457*m*, 1424*w*, 1404*w*, 1379*w*, 1345*w*, 1315*w*, 1183*w*, 1108*m*, 1089*w*, 991*m*, 958*m*, 817*m*; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 0.78 (*d*, *J*=7.1, 3 H, H_3–C(3′)), 3.42–3.50 (*m*, 1 H, H–C(3)), 5.57 (*d*, *J*=2.5, 1 H, H_A–C(2′)), 5.74 (*d*, *J*=8.1, 1 H, H–C(4)), 6.35 (*d*, *J*=2.8, 1 H, H_B–C(2′)), 7.20 (*dd*, *J*=8.6, 1.7, 1 H), 7.45–7.51 (*m*, 2 H), 7.60 (*d*, *J*=0.7, 1 H), 7.79–7.82 (*m*, 3 H), (CH (naphthalene)); ^{13}C NMR (75.4 MHz, $CDCl_3$): d 15.44 (*q*, C(3′)), 38.81 (*d*, C(3)), 82.08 (d. C(4)), 121.62 (*t*, C(2′)), 123.35, 124.99, 126.18. 126.32. 127.50. 127.82. 128.07 (each *d*, CH (naphthalene)), 132.77, 132.91, 133.90 (each *s*, C_q (naphthalene)), 139.90 (*s*, C(2)), 170.32 (*s*, C(1)); MS (ei, 80 eV, 88 °C): 238(37.3), 202(4.4), 178(4.5), 155(7.7), 127(14.1), 82(100.0); Anal. calcd. for $C_{16}H_{14}O_2$ (238.29): C, 80.65; H, 5.92; found: C, 80.35; H, 5.78.

cis-*(3* S, *4* R*)-3-Methyl-2-methylene-4-naphthalen-2-yl-γ-butyrolactone (3* **R**, *4* **S***)-22*

From **13** (0.35 g, 2.24 mmol) and (−)-**30** (0.8 g, 2.21 mmol) **(3 *R*, 4 *S*)-22** (0.47 g, 89%) was obtained; ee 82% (by HPLC: (*S*, *S*)-Whelk O1®; 1.0 *ml*/min, 38 bar, 20°C, hexane/prop-2-OH, 90:10, $t_R(R)$ 20.4 min, $t_R(S)$ 28.4 min).

cis-*(3 R, 4 S)-3-Methyl-2-methylene-4-naphthalen-2-yl-γ-butyrolactone (3* **S, 4 R)-22**

From **13** (0.35 g, 2.24 mmol) and **(+)-30** (0.8 g, 2.21 mmol) **(3 *S*, 4 *R*)-22** (0.46 g, 88%) was obtained; ee 82% (by HPLC: (*R, R*)-Whelk O1®; 1.0 *ml*/min, 38 bar, 20°C, hexane/prop-2-OH, 90:10, $t_R(S)$ 19.6 min, $t_R(R)$ 25.8 min).

cis-*(3 R, 4 S)-3-Methyl-2-methylene-4-naphthalen-2-yl-γ-butyrolactone (3* **R, 4 S)-22** *and* cis-*(3 S, 4 R)-3-methyl-2-methylene-4-naphthalen-2-yl-γ-butyrolactone (3* **S, 4 R)-22**

From the racemate by semipreparative HPLC **(3 *R*, 4 *S*)-22** and **(3 *S*, 4 *R*)-22** were obtained as colorless crystals.

Data for **(3 *R*, 4 *S*)-22:** mp 86–88°C, $[\alpha]_D^{25}=-52.5$ (*c*=1.0, $CHCl_3$); Anal. calcd. for $C_{16}H_{14}O_2$ (238.29): C, 80.65; H, 5.92; found: C, 80.46; H, 5.93.

Data for **(3 *S*, 4 *R*)-22** mp 86–88 °C, $[\alpha]_D^{25}=+51.8$ (*c*=1.0, $CHCl_3$); Anal. calcd. for $C_{16}H_{14}O_2$ (238.29): C, 80.65; H, 5.92; found: C, 80.39; H, 5.98.

cis-*(±)-3-Methyl-2-methylene-4-(2-methylpropyl)-γ-butyrolactone* **23**

From **14** (0.30 g, 3.49 mmol) and **16** (0.72 g, 3.49 mmol) **23** (0.50 g, 86%) was obtained as an oil; R_F 0.37 (hexane/ethyl acetate 5:1); IR (film): ν 2959*m*, 2872*m*, 1762*s*, 1700*w*, 1664*w*, 1637*w*, 1560*w*, 1540*w*, 1507*w*, 1468*m*, 1387*w*, 1351*w*, 1322*w*, 1267*m*, 1248*m*, 1168*m*, 1120*m*, 966*m*; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.96 (*d*, *J*=6.7, 3 H, H_3–C(4‴A)), 0.96 (*d*, *J*=6.6, 3 H, H_3–C(4‴B)), 1.15 (*d*, *J*=7.1, 3 H, H_3–C(3′)), 1.26 (*ddd*, *J*=14.2, 9.2, 3.4, 1 H, H_A–C(4′)), 1.47 (*ddd*, *J*=14.2, 10.9, 4.7, 1 H, H_B–C(4′)), 1.82–1.92 (*m*, 1 H, H–C(4″)), 3.17 (*m*, 1 H, H–C(3)), 4.36 (*ddd*, *J*=10.9, 7.5, 3.4, 1 H, H–C(4)), 5.54 (*d*, *J*=2.5, 1 H, H_A–C(2′)), 6.20 (*d*, *J*=2.7, 1 H, H_B–C(2′)); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ 13.87 (*q*, C(3′)), 21.42, 23.54, 24.42 (*d* resp. *q*, C(4″, 4‴A, 4‴B)), 37.62 (*d*, C(3)), 39.30 (*t*, C(5)), 79.16 (*d*, C(4)), 120.33 (*t*, C(2′)), 140.86 (*s*, C(2)), 170.18 (*s*, C(1)); MS (ei, 80 eV, 20 °C): 168(3.7), 153(10.3), 139(0.4), 125(0.8), 111(23.5), 82(100.0), 69(3.1), 54(47.7), 41(12.1); Anal. calcd. for $C_{10}H_{16}O_2$ (168.24): C, 71.39; H, 9.58; found: C, 71.32; H, 9.32.

cis-*(3 R, 4 R)-3-Methyl-2-methylene-4-(2-methylpropyl)-γ-butyrolactone (3* **S, 4 R)-23**

From **14** (0.30 g, 3.49 mmol) and **(+)-30** (1.31 g, 3.49 mmol) **(3 *R*, 4 *R*)-23** (0.51 g, 87%) was obtained; ee 60% (by HPLC: (*S, S*)-Whelk O1®, 1.0 *ml*/min, 35 bar, 20°C, hexane/prop-2-OH, 95/5, $t_R(R)$ 12.2 min, $t_R(S)$ 15.3 min).

*2-Bromomethyl-1-*N*-((5 R)-10,10-dimethyl-3,3-dioxo-3$^{\lambda 6}$-thia-4-aza-tricyclo[5.2.1.0$^{1.5}$]dec-4-yl)-prop-2-en-1-one (-)-28, 1-*N*-((5 R)-10,10-dimethyl-3,3-dioxo-3$^{\lambda 6}$-thia-4-aza-tricyclo [5.2.1.0$^{1.5}$]dec-4-yl)-2-((5 R)-10,10-dimethyl-3,3-dioxo-3$^{\lambda 6}$-thia-4-aza-tricyclo[5.2.1.0$^{1.5}$]-dec-4-yl-methyl)-propen-1-one (−)-29 and 2-chloromethyl-1-((5 R)-10,10-dimethyl-3,3-dioxo-3$^{\lambda 6}$-thia-4-aza-tricyclo[5.2.1.0$^{1.5}$]dec-4-yl)-prop-2-en-1-one (−)-34*

A mixture of 2-bromomethyl-acrylic acid (15.0 g, 91.0 mmol) and oxalyl dichloride (8.7 *ml*, 100 mmol) is stirred at 25°C until the evolution of gases has ceased (ca 100 h). Distillation of the reaction mixture (1 mbar, 29-32°C) afforded an inseparable mixture (by ^{1}H NMR and MS) consisting of **25** (60%) and **26** (40%). Sodium hydride (0.52 g, 17.4 mmol, as 80% dispersion in mineral oil) is suspended in dry toluene (30 *ml*) and (−)-**27** (Oxford Asymmetry, 2.50 g, 11.61 mmol, ee 99%, used as received) is slowly added at 25 °C. Stirring is continued for 1 h and a toluene solution of the mixture of the propenoyl chlorides (4.3 g) is slowly added. After warming to 25 °C stirring is continued for another 2 h and then the excess of the hydride is destroyed at 0 °C by the careful addition of ice water (20 *ml*). The aqueous layer is extraced twice with toluene (30 *ml* each) and the combined organic phases are washed with brine (2×20 *ml*), dried ($MgSO_4$), the solvent is removed under reduced pressure and the residue subjected to chromatography (hexane/ethyl acetate 5:1 → 3:1) to afford (−)-**28** [1.2 g, 39%, containing 40% of (−)-**34**] and **29** (0.75 g, 36%).

Data for (−)-**28**: R_F 0.56 (hexane/ethyl acetate); IR (KBr): ν 2971*m*, 1684*s*, 1653*w*, 1627*w*, 1457*w*, 1437*w*, 1410*w*, 1392*w*, 1368*w*, 1324*s*, 1262*w*, 1233*w*, 1220*w*, 1198*m*, 1164*m*, 1136*m*, 1111*m*, 1062*m*,

1033*w*, 973*m*, 917*w*, 764*m*; ^{1}H NMR (300 MHz, d_6-acetone): δ 1.04, 1.23 (each *s*, 3 H, H_3–C(10_C'A, 10_C'B), 1.36–1.43 (*m*, 1 H), 1.54–1.62 (*m*, 1 H), 1.87–2.00 (*m*, 5 H), (H–C(7_C), H_2–C(6_C, 8_C, 9_C)), 3.58 (*d*, *J*=13.9, 1 H, H_A–C(2_C)), 3.72 (*d*, *J*=13.9, 1 H, H_B–C(2_C)), 4.07 (*dd* (virt *t*), *J*=6.2, H–C(5_C)), 4.18 (*d*, *J*=11.1, 0.6 H, H_A–C(2'), A), 4.30 (*d*, *J*=12.8, 0.4 H, H_A–C(2'), B), 4.44 (*d*, *J*=11.1, 0.6 H, H_B–C(2'), A), 4.48 (*d*, *J*=12.8, 0.4 H, H_B–C(2'), B), 5.99 (*m*, 1 H, H_A–C(3)), 6.05 (*m*, 1 H, H_B–C(3)); ^{13}C NMR (75.4 MHz, d_6–acetone): δ 20.04, 20.06, 21.45, 21.49 (each *q*, C(10_C'A, 10_C'B)), 30.94 (*t*, C(2'), A), 26.97, 33.34, 38.98 (each *t*, C(6_C, 8_C, 9_C)), 43.86 (*t*, C(2'), B), 45.85, 45.91 (*d*, C(7_C)), 48.27, 48.30, 48.91, 48.92 (each *s*, C(1_C, 10_C)), 53.65 (*t*, C(2_C)), 65.96 (*d*, C(5_C), B), 66.01 (*d*, C(5_C), A), 126.83 (*t*, C(3), B), 127.76 (*t*, C(3), A), 140.37 (*s*, C(2), B), 140.63 (*s*, C(2), A), 168.05 (*s*, C(1), A), 168.07 (*s*, C(1), B); MS (ei, 80 eV, 105 °C): 363(0.1), 361(0.1), 348(0.2), 346(0.1), 319(0.9), 317(2.3), 282(100.0), 256(1.5), 254(2.7), 218(68.6), 190(5.5), 162(2.5), 149(46.5), 147(46.8), 135(50.8), 134(41.7), 121(17.6), 119(19.9), 108(36.3), 103(69.5), 93(28.3), 75(25.2), 68(23.5), 55(18.6), 43(23.6), 41(45.7); Anal. calcd. for $C_{14}H_{20}Cl_{0.4}Br_{0.6}NO_3S$ (344.51): C, 48.91; H, 5.85; N, 4.07; S, 9.31; found: C, 48.93; H, 5.99; N, 3.97; S, 9.56.

Data for (−)-**29**: colorless crystals; mp 187–188 °C, $[\alpha]_D^{25}$=−90.9 (*c*=1.3, $CHCl_3$), R_F 0.19 (hexane/ethyl acetate 3:1); IR (KBr): ν 3108*w*, 3008*w*, 2987*w*, 2955*m*, 2876*m*, 1695*s*, 1682*s*, 1653*w*, 1647*w*, 1624*w*, 1576*w*, 1559*w*, 1539*w*, 1521*w*, 1472*w*, 1457*m*, 1436*w*, 1407*w*, 1390*w*, 1374*w*, 1340*s*, 1324*s*, 1310*w*, 1285*s*, 1258*m*, 1244*w*, 1227*w*, 1196*w*, 1174*w*, 1156*m*, 1131*s*, 1103*m*, 1079*w*, 1058*w*, 1002*w*; ^{1}H NMR (300 MHz, $CDCl_3$): δ 0.92, 0.99, 1.15, 1.22 (each *s*, 3 H, H_3–C(10_{C1}'A, 10_{C2}'A, 10_{C1}'B, 10_{C2}'B)), 1.35–1.47 (*m*, 5 H), 1.60–1.67 (*m*, 1 H), 1.84–2.12 (*m*, 8 H) (H–C(7_{C1}', 7_{C2}'), H_2–C(6_{C1}, 6_{C2}, 8_{C1}, 8_{C2}, 9_{C1}, 9_{C2})), 3.17 (*s*, 2 H, H_2–C($10_{C1/2}$)), 3.22 (*dd*, *J*=8.1, 4.6, 1 H, H–C($5_{C1/2}$)), 3.41 (*d*, *J*=13.7, H_A–C($2_{C2/1}$)), 3.52 (*d*, *J*=13.7, 1 H, H_B–C($2_{C2/1}$)), 3.69 (*d*, *J*=16.6, 1 H, H_A–C(2')), 4.03 (*dd*, *J*=6.2, 5.9, 1 H, H–C($5_{C2/1}$)), 4.05 (*d*, *J*=16.6, 1 H, H_B–C(2')), 6.01 (*s*, 1 H, H_A–C(3)), 6.05 (*s*, 1 H, H_B–C(3)); ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 19.84, 20.02, 20.47, 21.13 (each *q*, C(10_{C1}'A, 10_{C2}'A, 10_{C1}'B, 10_{C2}'B)), 26.42, 26.86, 32.10, 33.04, 34.87, 38.16 (each *t*, C(6_{C1}, 6_{C2}, 8_{C1}, 8_{C2}, 9_{C1}, 9_{C2})), 43.38 (*t*, C(2')), 44.52, 45.05 (each *d*, C(4_{C1}, 4_{C2})), 47.55, 47.67, 48.04, 49.75 (each *s*, C(1_{C1}, 1_{C2}, 7_{C1}, 7_{C2})), 49.45, 53.39 (each *t*, C(2_{C1}, 2_{C2})), 65.43, 67.55 (each *d*, C(5_{C1}, 5_{C2})), 127.72 (*d*, C(3)), 138.03 (*s*, C(2)), 168.90 (*s*, C(1)); MS (ei, 80 eV, 193 °C): 496(0.1), 480(0.3), 432(31.0), 368(14.4), 282(17.3), 219(61.3), 190(36.7), 159(42.1), 135(100.0); Anal. calcd. for $C_{24}H_{36}N_2O_5S_2$ (496.68): C, 58.04; H, 7.31; N, 5.64; S, 12.91; found: C, 57.76; H, 7.08; N, 5.48; S, 12.59.

Data for (−)-**34**: colorless crystals; mp 157–159 °C, $[\alpha]_D^{25}$=−109.1 (*c*=1.3 $CHCl_3$), R_F 0.56 (hexane/ethyl acetate); IR (KBr): ν 2977*m*, 2908*w*, 2892*w*, 1687*s*, 1631*w*, 1458*w*, 1437*w*, 1409*w*, 1392*w*, 1376*w*, 1368*w*, 1324*s*, 1267*m*, 1233*w*, 1199*s*, 1165*m*, 1134*s*, 1113*m*, 1063*m*, 1033*w*, 974*m*, 950*w*, 917*w*, 798*w*, 766*m*; ^{1}H NMR (250 MHz, d_6-acetone): δ 1.05, 1.23 (each *s*, 3 H, H_3–C(10_C'A, 10_C'B), 1.35–1.43 (*m*, 1 H), 1.54–1.63 (*m*, 1 H), 1.88–2.01 (*m*, 5 H), (H–C(7_C), H_2–C(6_C, 8_C, 9_C)), 3.57 (*d*, *J*=13.9, 1 H, H_A–C(2_C)), 3.73 (*d*, *J*=13.9, 1 H, H_B–C(2_C)), 4.06 (*dd* (virt *t*), *J*=6.2, H–C(5_C)), 4.30 (*ddd*, *J*=12.8, 1.1, 0.4, 1 H, H_A–C(2')), 4.48 (*ddd*, *J*=12.8, 1.5, 0.8, 1 H, H_B–C(2')), 5.99 (*ddd*, *J*=13.6, 0.8, 0.4, 1 H, H_A–C(3)), 6.04 (*ddd*, *J*=13.6, 1.5, 1.1, 1 H, H_B–C(3)); ^{13}C NMR (62.9 MHz, d_6-acetone): δ 20.07, 21.53 (each *q*, C(10_C'A, 10_C'B)), 26.97, 33.34, 38.98 (each *t*, (6_C, 8_C, 9_C)), 43.94 (*t*, C(2')), 46.00 (*d*, C(7_C)), 48.37, 49.01 (each *s*, C(1_C, 10_C)), 53.78 (*t*, C(2_C)), 66.10 (*d*, C(5_C)), 127.06 (*t*, C(3)), 140.65 (*s*, C(2)), 168.57 (*s*, C(1)); MS (ei, 80 eV, 92 °C): 319(1.5), 317(3.9), 282(9.9), 219(10.5), 218(62.4), 210(4.9), 190(3.8), 135(36.6), 134(33.6), 119(10.3), 108(30.7), 105(41.2), 103(100.0), 93(18.5), 79(11.6), 77(17.0), 75(38.5), 67(11.9), 55(10.4), 43(10.4), 41(22.0); Anal. calcd. for $C_{14}H_{20}ClNO_3S$ (317.92): C, 59.42; H, 6.34; N, 4.41; S, 10.09; found: C, 59.28; H, 6.30; N, 4.58; S, 10.28.

*2-Bromomethyl-1-*N*-((5 S)-10,10-dimethyl-3,3-dioxo-3$^{\lambda 6}$-thia-4-aza-tricyclo[5.2.1.0$^{1.5}$]dec-4-yl)-prop-2-en-1-one* **(+)-28**, *1-*N*-((5 S)-10,10-dimethyl-3,3-dioxo-3$^{\lambda 6}$-thia-4-aza-tricyclo-[5.2.1.0$^{1.5}$]dec-4-yl)-2-((5 S)-10,10-dimethyl-3,3-dioxo-3$^{\lambda 6}$-thia-4-aza-tricyclo[5.2.1.0$^{1.5}$]dec-4-yl-methyl)-propen-1-one* **(+)-29** *and 2-chloromethyl-1-((5 S) 10,10-dimethyl-3,3-dioxo-3$^{\lambda 6}$-thia-4-aza-tricyclo[5.2.1.0$^{1.5}$]dec-4-yl)-prop-2-en-1-one* **(+)-34**

Obtained as above starting from 2-bromo-methyl-acrylic acid (15.0 g, 91.0 mmol), oxalyl dichloride (8.7 *ml*, 100 mmol) and **(+)-27** (Oxford Asymmetry, 2.50 g, 11.61 mmol, ee 99%, used as received).

Data for **(+)-(29)**: mp 187–188 °C, $[\alpha]_D^{25}$=+89.5 (*c*=1.1, $CHCl_3$); Anal. calcd. for $C_{24}H_{36}N_2O_5S_2$ (496.68): C, 58.04; H, 7.31; N, 5.64; S, 12.91; found: C, 57.84; H, 7.11; N, 5.63; S, 12.71.

Data for (+)-**34**: colorless crystals; mp 156–158 °C, $[\alpha]_D^{25}$=+108.3 (*c*=1.2, $CHCl_3$); Anal. calcd. for $C_{14}H_{20}ClNO_3S$ (317.92): C, 59.42; H, 6.34; N, 4.41; S, 10.09; found: C, 59.39; H, 6.44; N, 4.63; S, 10.17.

*(Z) 2-Bromomethyl-1-*N*-((5 R)-10,10-dimethyl-3,3-dioxo-3$^{\lambda 6}$-thia-4-aza-tricyclo[5.2.1.0$^{1.5}$]-dec-4-yl)-but-2-en-1-one (−)-30*

A mixture of 2-bromomethyl-3-methyl-acrylic acid (20.0 g, 110.0 mmol) and oxalyl dichloride (10.7 *ml*, 120.0 mmol) is stirred at 25 °C for 100 h. Distillation of the reaction mixture (1 mbar, 32–35 °C) affords 2-bromomethyl-3-methyl-2-propenoyl chloride (19.1 g, 87%). To a suspension of sodium hydride (1.4 g, 46.5 mmol) in dry toluene (100 *ml*) (−)-(***R***)-**27** (5.0 g, 23.3 mmol) is slowly added. Stirring is continued for 1 h, the reaction mixture is cooled to 0 °C and a toluene solution (30 *ml*) of the 2-bromomethyl-3-methyl-2-propenoyl chloride (9.2 g, 46.5 mmol) is slowly added. After warming to 25 °C stirring is continued for an additional 3 h and then the excess of the hydride is destroyed by the careful addition of ice water (20 *ml*). The aqueous layer is extracted twice with toluene (30 *ml*) and the combined organic layers are washed with brine (2×20 *ml*), dried ($MgSO_4$), the solvent is removed under reduced pressure; the residue is subjected to chromatography (hexane/ethyl acetate 5:1 → 3:1) to afford (−)-**30** (6.5 g, 74.3%); mp 135–137 °C, $[\alpha]_D^{25}$=−99.0 (*c*=1.3 $CHCl_3$), R_F 0.55 (hexane/ethyl acetate); IR (KBr): ν 2958*s*, 2876*m*, 1784*w*, 1666*s*, 1639*m*, 1559*w*, 1540*w*, 1507*w*, 1486*w*, 1469*w*, 1458*m*, 1402*m*, 1377*m*, 1352*w*, 1329*s*, 1299*s*, 1258*w*, 1220*m*, 1189*s*, 1135*s*, 1051*m*, 853*m*, 755*s*; ^{1}H-NMR (300 MHz, $CDCl_3$): δ 0.99, 1.22 (each *s*, 3 H, H_3–C(10$_C$′A, 10$_C$′B), 1.33–1.49 (*m*, 2 H), 1.86–2.09 (*m*, 5 H), (H–C(7$_C$), H_2–C(6$_C$, 8$_C$, 9$_C$)), 1.96 (*d*, *J*=7.1, 3 H, H_3–C(4)), 3.42 (*d*, *J*=13.7, 1 H, H_A–C(2$_C$)), 3.51 (*d*, *J*=13.7, 1 H, H_B–C(2$_C$)), 4.09 (*dd*, *J*=7.8, 4.5, H–C(5$_C$)), 4.10 (*d*, *J*=10.5, 1 H, H_A–C(2′)), 4.30 (*d*, *J*=10.5, 1 H, H_B–C(2′)), 6.75 (*q*, *J*=7.1, 1 H, H–C(3)); ^{13}C-NMR (75.4 MHz, $CDCl_3$): δ 14.59 (*q*, C(4)), 19.84, 21.07 (each *q*, C(10$_C$′A, 10$_C$′B)), 24.28 (*t*, C(2′)), 26.48, 32.95, 38.06 (each *t*, (6$_C$, 8$_C$, 9$_C$)), 44.92 (*d*, C(7$_C$)), 47.66, 47.84 (each *s*, C(1$_C$, 10$_C$)), 53.42 (*t*, C(2$_C$)), 65.39 (*d*, C(5$_C$)), 132.43 (*s*, C(2)), 143.89 (*t*, C(3)), 169.05 (*s*, C(1)); MS (ei, 80 eV, 100 °C): 377(0.2), 375(0.2), 333(0.6), 331(1.7), 296(100.0), 232(26.5), 163(86.2), 161(90.3), 135(40.0), 117(31.9), 107(16.8), 93(23.1), 82(31.6), 81(28.4), 54(69.3)), 53(96.8), 41(27.2); Anal. calcd. for $C_{14}H_{20}BrNO_3S$ (376.31): C, 47.88; H, 5.89; N, 3.72; found: C, 48.10; H, 5.83; N, 3.42.

*(Z) 2-Bromomethyl-1-*N*-((5 R)-10,10-dimethyl-3,3-dioxo-3$^{\lambda 6}$-thia-4-aza-tricyclo[5.2.1.0$^{1.5}$]-dec-4-yl)-but-2-en-1-one (+)-30*

Following the procedure given for the preparation of (−)-**30** from (Z)-2-bromomethyl-but-2-enoic acid (20.0 g, 110.0 mmol) and **(+)-(S)-27** **(+)-30** (6.6 g, 75%) was obtained; mp 135–137 °C, $[\alpha]_D^{25}$=+99.3 (*c*=1.1, $CHCl_3$); Anal. calcd. for $C_{14}H_{20}BrNO_3S$ (376.31): C, 47.88; H, 5.89; N, 3.72; found: C, 48.08; H, 5.92; N, 3.56

(±)-3,3-Dimethyl-2-methylene-5-phenyl-γ-butyrolactone 31

Methyl 3-hydroxy-3-methyl-2-methylene-but-2-enoate (prepared according to refs[24,25]) (0.5 g, 5.9 mmol) was brominated with PBr_3 (0.86 g, 3.2 mmol) for 15 min at 25 °C to afford methyl 2-(bromomethyl)-3-methyl-but-2-enoate [(0.98 g, 80%); R_F 0.53 (hexane/ethyl acetate 5:1); IR (film): ν

2996*m*, 2951*m*, 1719*s*, 1627*m*, 1435*s*, 1372*m*, 1318*s*, 1292*s*, 1232*s*, 1159*s*, 1135*s*, 1067*s*, 988*m*, 846*m*, 791m; ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.99, 2.17 (each *s*, 3 H, H_3–C(3′, 4)), 3.79 (*s*, 3 H, OCH_3), 4.31 (*s*, 2 H, H_2–C(2′)); ^{13}C NMR (75.4 MHz, $CDCl_3$): d 22.95, 23.86 (each *q*, C(3′, 4)), 29.32 (*t*, C(2′)), 51.61 (*q*, OCH_3), 124.47 (*s*, C(3′)), 153.66 (*s*, C(2)), 166.77 (*s*, C(1)); MS (ei, 80 eV, 30 °C): 208(0.1), 206(0.1), 177(3.3), 175(3.5), 149(0.4), 147(0.4), 127(65.1), 95(43.9), 73(31.6), 67(100.0), 53(21.8), 41(49.3); Anal. calcd. for $C_7H_{11}BrO_2$ (207.07): C, 40.60; H, 5.35; found: C, 40.37; H, 5.40]. From **8** (0.30 g, 2.83 mmol) and methyl 2-(bromomethyl)-3-methyl-but-2-enoate (0.55 g, 2.66 mmol) **31** (0.36 g, 63%) was obtained as a solid; mp 39 °C, R_F 0.38 (hexane/ethyl acetate 3:1); IR (KBr): ν 1770*s*, 1662*s*, 1605*m*, 1499*m*, 1463*m*, 1407*m*, 1368*m*, 1313*s*, 1296*s*, 1243*m*, 1194*s*, 1120*s*, 1080*s*, 1019*s*, 1001*s*; ^{1}H-NMR (300 MHz, $CDCl_3$): d 0.73, 1.38 (each *s*, 3 H, H_3–C(3′A, 3′B)), 5.14 (*s*, 1 H, H–C(4)), 5.54 (*s*, 1 H, H_A–C(2′)), 6.26 (*s*, 1 H, H_B–C(2′)), 7.23–7.41 (*m*, 5H, CH (phenyl)); ^{13}C NMR (75.4 MHz, $CDCl_3$): d 24.30, 25.87 (each *q*, C(4′A, 4′B)), 43.57 (*s*, C(4)), 87.91 (*d*, C(5)), 119.96 (*t*, C(3′)), 125.66, 128.15, 128.20 (each *d*, CH (phenyl)), 135.49 (*s*, C_q (phenyl)), 145.28 (*s*, C(3)), 170.06 (*s*, C(2)); MS (ei, 80 eV, 49 °C): 202(18.6), 165(2.0), 141(1.2), 128(2.3), 115(3.0), 105(7.0), 96(97.6), 77(11.7), 68(100.0); Anal. calcd. for $C_{13}H_{14}O_2$ (202.26): C, 77.20; H, 6.98; C, 77.20; H, 7.00.

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16. MS spectra and elemental analysis revealed **25** to consist as a 60:40 mixture of **25** and **26** that could not be separated either by distillation or chromatography. The formation of **26** results from a bromine → chlorine substitution during the formation of the acid chloride. To avoid this side reaction attempts were undertaken to synthesize the correponding 2-bromometacrylic bromide by the reaction of **24** with oxalyl dibromide. These reactions, however, did not result in the formation of significant amounts of the desired product but huge deterioration took place.
17. Under these conditions the product contains approx. 40% of **34** (*cf.* 16). In the following reactions only **28** gave the desired reactions very quickly but **34** was partially recovered.
18. Interestingly enough, neither a halogen exchange reaction occurs nor products resulting from a double addition reaction have been observed.
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