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Preparation of Optically Active 3,9-disubstituted Spiro[5.5]undecane Derivatives and the Determination of their Absolute Configuration

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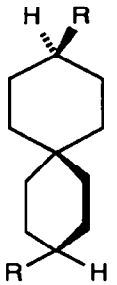
Abstract: The enantiomerically pure 3,9-disubstituted spiro[5.5]undecane derivatives **1** to **8** have been prepared by resolution and their absolute configuration determined by chemical correlation with the known (*aS*)-(–)-spiro[5.5]undecane-3,9-diol (**9**).

Aschan[1] recognized for the first time that symmetrically substituted spiro[5.5]undecanes of the general type **1** to **9** are chiral molecules with C_2 symmetry without a stereogenic C atom. The compounds **1** to **8** have not yet been prepared in optically active form and their theoretically interesting chiroptical properties are unknown. We have synthesized the dicarboxylic acid dimethylester (±)-**2** starting from the known[2] spiro[5.5]undecane-3.9-dione (**10**) by reacting it with 2-lithio-2-trimethylsilyl-1,3-dithiane[3] to give the ketene dithioacetal **11**. Methanolysis of **11** in the presence of mercury(II)-nitrate produced the dimethylester (±)-**2**, that could be reduced to the 3,9-bis(hydroxymethyl)spiro[5.5]undecane (±)-**3**. The diol (±)-**3** was esterified with (1*S*,4*R*)-(–)-camphanoyl chloride[4] to yield the diastereomeric esters. Recrystallization from cyclohexane/benzene (1:1) gave the diastereomerically pure ester (–)-**12**. Repeating the procedure with (1*R*,4*S*)-(–)-camphanoyl chloride[5] gave the diastereomerically pure ester (+)-**12**. The purity of (–)-**12** and (+)-**12** can be monitored by means of the ^{1}H NMR spectra, showing that signals of the more soluble diastereomer are disappearing during recrystallization. Transesterification of the pure biscamphanoates (–)-**12** or (+)-**12** with methanol yielded the enantiomerically pure diols (–)-**3** or (+)-**3** and (–)- or (+)-methyl camphanoate[6].

The (–)-bis(hydroxymethyl)spiro[5.5]undecane **3** was converted into (*aS*)-(–)-spiro[5.5]undecane-3,9-diol [(–)-**9**] of known absolute configuration[7] by the following sequence of reactions: Oxidation of the diol (–)-**3** with sodium periodate and $RuCl_3$ as catalyst by the method of Sharpless[8] yielded the dicarboxylic acid (*aS*)-(–)-**1** that could be transformed into the (*aS*)-(–)-3,9-bis(acetyl)spiro[5.5]undecane (**4**) by reacting its dicarboxylic acid chloride with Meldrum's acid followed by hydrolysis and decarboxylation of the product.



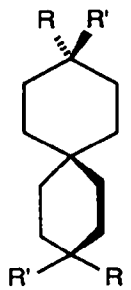
(a*S*) - (–) - **1** R = -CO_2H (*aS*) - (–) - **6** R = -Me

(*aS*) - (–) - **2** R = -CO_2Me (*aS*) - (+) - **7** R = 4-$MeOC_6H_4$-

(*aS*) - (–) - **3** R = -CH_2OH (*aS*) - (+) - **8** R = 4-HOC_6H_4-

(*aS*) - (–) - **4** R = -COMe (*aS*) - (–) - **9** R = -OH

(a*S*) - (–) - **5** R = -CH_2Br



10 R + R' = O **11** R + R' = -$S(CH_2)_3S$-

(–) - **12** R = H, R' = (1*S*,4*R*)-camphanoyl-OCH_2-

(±) - **13** R = OH, R' = 4-$MeOC_6H_4$-

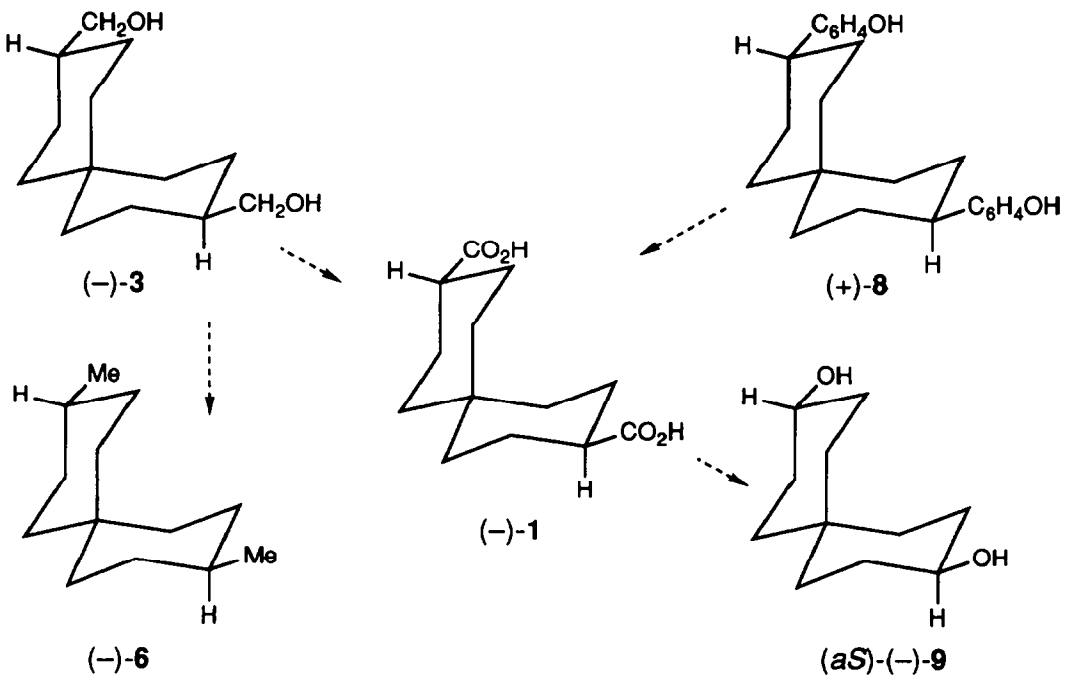
(+) - **14** R = H, R' = 4-(1*S*,4*R*)-camphanoyl-OC_6H_4-

Scheme 1

Oxidation of (–)-**4** with peracetic acid and H_2SO_4 yielded a diacetate that could be saponified to give (*aS*)-(-)-spiro[5.5]undecane-3,9-diol **9** with 25% ee (cp. lit.[7]). Under the strongly acidic conditions of the Baeyer-Villiger oxidation (–)-**4** has partially racemized via enolization.

The diol (*aS*)-(–)-**3** could be converted into (*aS*)-(–)-3,9-bis(bromomethyl)spiro[5.5]undecane [(–)-**5**] and then by hydrogenolysis into (*aS*)-(–)-3,9-bis(methyl)spiro[5.5]undecane [(–)-**6**]. The specific rotation of compound (–)-**6**, $[\alpha]_D^{20} = -31.1$ (c = 0.69 in pentane), is unexpectedly high.

We attempted to synthesize also spiro[5.5]undecanes with aryl groups in 3,9-positions. Reaction of the dione **10** with 4-methoxyphenylmagnesium bromide produced the diol (±)-**13** with tertiary hydroxy groups. Ionic hydrogenation of **13** with triethylsilane and $Et_2O{\cdot}BF_3$ gave the 3,9-bis(4-methoxyphenyl)-spiro[5.5]undecane [(±)-**7**] that could be demethylated by aqueous hydrogen iodide to yield the 3,9-bis(4-hydroxyphenyl)spiro[5.5]undecane [(±)-**8**]. The bisphenol **8** was reacted with (1*S*,4*R*)-(–)-camphanoyl chloride to give the diastereomeric esters. Recrystallization from toluene produced the diastereomerically pure ester (+)-**14** that yielded the bisphenol (+)-**8** upon methanolysis. Oxidation of (+)-**8** with periodic acid and $RuCl_3$ as catalyst led to (*aS*)-(–)-spiro[5.5]undecane-3,9-dicarboxylic acid [(–)-**1**] and its methylester (*aS*)-(–)-**2**. This



Scheme 2

chemical correlation with (*aS*)-(−)-**1** shows, that (+)-**8** is enantiomerically pure and has (*aS*)-absolute configuration.

EXPERIMENTAL SECTION

^{1}H (500.13 MHz) and ^{13}C (125.77 MHz) NMR spectra were recorded on a Bruker AM-500-FT instrument (δ in ppm calibrated to residual solvent signal, with chemical shifts referred to TMS; J in Hz, ^{1}H NMR signals were assigned by COSY experiments, ^{13}C signal multiplicities were determined from DEPT spectra). Optical rotations were measured on a Perkin Elmer 241 polarimeter. IR spectra were recorded on a Perkin Elmer 297 instrument. UV spectra were obtained using a Kontron Uvikon 860 instrument. CD spectra were recorded on a Jobin-Yvon-Mark III Dichrograph. Mass spectra were measured with a MAT 312 mass spectrometer [70 eV, m/z (%)] (Varian). Melting points were determined on a Büchi 510 melting point apparatus. Kieselgel 60 F_{254} glass plates (Merck) were used for TLC; separated compounds were visualized by conc. H_2SO_4/5min 160 °C. All solvents were distilled before use. Ether and THF were filtered through ICN Alox B. Elemental analyses were performed by the Microanalytical Laboratory of Ilse Beetz, D-96317 Kronach.

Spiro[5.5]undecane-3,9-dione (**10**): An aqueous solution of 240 mL (0.319 mmol) 1.33 M NaOCl was added within 55 min to 24.6 g (134 mmol) (±)-**9**[2,7] in 120 mL acetic acid. The mixture was stirred for 90 min. Thereafter 20 mL (0.3 mol) 2-propanol were added and the mixture was stirred for an additional 15 min. After addition of 1.4 L 2 M KOH the mixture was extracted with 1.5 L toluene. The combined extracts were washed with 200 mL of 2 M $KHCO_3$ and dried (Na_2SO_4). Evaporation of the solvent gave 21.42 g of crude material which yielded 20.1 g (83%) **10** after recrystallization from cyclohexane/AcOEt (2:1) as colourless crystals, m.p. 110.8-111.4 °C (lit.[2] 110-111 °C).

3,9-Bis-(2,6-dithiacyclohexylidene)spiro[5.5]undecane (**11**): A solution of 100 mL (155 mmol) of 1.55 M nBuLi in hexane was added under N_2 at 0 °C to a solution of 25 g (0.13 mol) 2-trimethylsilyl-1,3-dithiane[3] in 250 mL dry THF. The resulting yellow solution was stirred at 0 °C for 30 min, cooled to -60 °C, and treated slowly with 10.45 g (58.0 mmol) of **10** in 50 mL dry THF. The mixture was allowed to reach room temperature overnight. Then 200 mL of water were added and the product was extracted with 1.8 L of toluene. The extract was washed with water and 2 M $KHCO_3$, dried (Na_2SO_4), and the solvent was removed under reduced pressure. Filtration of the residue (22.3 g) on 100 g silica gel (elution with benzene) gave 17.0 g (76%) **11** as colourless crystals, which were used without further purification for the next step; R_f = 0.80, m.p. 149.2-157.9 °C. A sample for analysis was prepared by sublimation (145 °C/0.001Torr). - IR (CCl_4): 2925 cm^{-1} (CH_2), 2845 (CH_2). - ^1H NMR ($CDCl_3$): 1.37-1.45 (m, 8 H, 1-H, 5-H, 7-H, 11-H), 2.10 (m, 4 H, $CH_2(CH_2S)_2$), 2.44 (m, 8 H, 2-H, 4-H, 8-H, 10-H), 2.83 (m, 8 H, SCH_2). - ^{13}C NMR ($CDCl_3$): 25.2 (t, 2 C), 27.1 (t, 4 C), 30.3 (t, 4 C), 32.5 (s, C-6), 36.4 (t, 4 C), 115.9 (s, 2 C), 144.4 (s, 2 C). - MS: 384 (100) [M^+], 351 (4), 310 (4), 309 (8), 277 (9), 211 (4), 192 (4), 171 (8), 159 (7).
Analysis calculated for $C_{19}H_{28}S_4$ (384.7): C, 59.32; H, 7.34; S, 33.34. Found C, 59.37; H, 7.34; S, 33.31.

(±)-Dimethyl spiro[5.5]undecane-3,9-dicarboxylate [(±)-**2**]: A solution of 60.0 g (0.22 mol) of $HgCl_2$ in 300 mL methanol/water (9:1) was added to a suspension of 17.0 g (44 mmol) of **11** in 200 mL methanol/water (9:1). The mixture was stirred and heated under reflux overnight. After cooling, the precipitate was filtered off (celite) and washed with methanol and CH_2Cl_2. The filtrate was concentrated and the oily residue was dissolved in 0.8 L diethyl ether, washed with 0.5 M NaCN, dried (Na_2SO_4) and the solvent was evaporated. The residue, 8.57 g (72%) (±)-**2** as a colourless oil, was used without further purification for the next step. A sample for analysis was prepared by distillation *in vacuo*. R_f = 0.40 (cyclohexane/AcOEt, 9:1), b.p. 120 °C/0.03 Torr. - IR (CCl_4): 1735 cm^{-1} (C=O). - ^1H NMR ($CDCl_3$): 0.89 (td, J = 13.3, J = 3.7 Hz, 2 H, 1-H_a, 7-H_a), 1.10 (td, J = 13.3, J = 4.2 Hz, 2 H, 5-H_a, 11-H_a), 1.29 (m, 2 H, 5-H_e, 11-H_e), 1.45 (m, 2 H, 2-H_a, 8-H_a), 1.53 (m, 2 H, 4-H_a, 10-H_a), 1.58-1.67 (4 H, 2-H_e, 4-H_e, 8-H_e, 10-H_e), 1.83 (m, 2 H, 1-H_e, 7-H_e), 2.15 (m, 2 H, 3-H, 9-H), 3.55 (s, 6 H, OCH_3). - ^{13}C NMR ($CDCl_3$): 23.7, 23.8 (t, 2 C, t, 2 C, C-2, C-8, C-4, C-10), 31.0 (t, 2 C, C-1, C-7), 31.1 (s, C-6), 39.1 (t, 2 C, C-5, C-11), 43.1 (d, 2 C, C-3, C-9), 51.2 (q, 2 C, OCH_3), 176.1 (s, 2 C, C=O).- MS: 268 (2) [M^+], 236 (100), 208 (21), 204 (28), 176 (30), 87 (45).
Analysis calculated for $C_{15}H_{24}O_4$ (268.4): C, 67.14; H, 9.01. Found C, 67.21; H, 8.99.

(±)-3,9-Bis(hydroxymethyl)spiro[5.5]undecane [(±)-**3**]: A solution of 8.57 g (32.0 mmol) (±)-**2** in 30 mL diethyl ether was added to a boiling solution of 7.0 g (0.18 mol) $LiAlH_4$ in 300 mL diethyl ether within 1 h.

The mixture was heated unter reflux for 3 h. After cooling, the mixture was treated with 42 mL satd. K_2CO_3 solution, stirred for additional 2 h and filtrated. The white solids were washed several times with diethyl ether (500 mL) and the combined organic solutions were dried and evaporated. Purification of the residue (6.8 g) by column chromatography (200 g silicagel, AcOEt) gave 4.11 g (61%) (±)-**3** as colourless crystals, R_f = 0.60, m.p. 81.7-85.0 °C. - IR ($CHCl_3$): 3620 cm^{-1} (OH), 3470 (OH, br). - ^1H NMR (CD_3OD): 0.91 (td, J = 13.2, J = 3.1 Hz, 2 H, 1-H_a, 7-H_a), 1.03 (m, 2 H, 5-H_a, 11-H_a), 1.11-1.30 (4 H, 2-H_a, 5-H_e, 8-H_a, 11-H_e), 1.30-1.42 (4 H, 3-H_a, 4-H_a, 9-H_a, 10-H_a), 1.38-1.63 (4 H, 2-H_e, 4-H_e, 8-H_e, 10-H_e), 1.99 (m, 2 H, 1-H_e, 7-H_e), 3.36 (d, J = 6.3 Hz, 4 H, CH_2O). - ^{13}C NMR (CD_3OD): 25.6, 25.7 (t, 2 C, t, 2 C, C-2, C-8, C-4, C-10), 32.4 (t, 2 C, C-1, C-7), 33.5 (s, C-6), 41.9 (t, 2 C, C-5, C-11), 42.1 (d, 2 C, C-3, C-9), 68.6 (t, 2 C, CH_2O). - MS: 212 (10) [M^+], 194 (100), 176 (12), 163 (76), 147 (28), 93 (57).
Analysis calculated for $C_{13}H_{24}O_2$ (212.3): C, 73.54; H, 11.89. Found C, 73.53; H, 11.85.

(–)-Spiro[5.5]undecane-3,9-dimethyldiyl-bis-(1S,4R)-camphanoate [(–)-**12**]: A solution of 3.27 g (15.4 mmol) (±)-**3** in 40 mL pyridine was added to 10.1 g (47.7 mmol) (1*S*,4*R*)-(-)-camphanoyl chloride[4] in 40 mL pyridine. The mixture was stirred for 16 h, 800 mL of 1 M H_2SO_4 were added, and the solution was extracted twice with CH_2Cl_2 (1 L). The extracts were washed with 2 M $KHCO_3$, dried (Na_2SO_4) and the solvent was evaporated; yield: 8.86 g (100%) mixture of the diastereomeric esters, m.p. 144.9-148.0 °C. Recrystallization from 288 mL of a mixture of cyclohexane/benzene (1:1) gave 2.97 g (33%) crystals after 3.5 h at room temperature; m.p. 168.7-172.6 °C. These crystals were dissolved in a boiling mixture of 116 mL cyclohexane/benzene (1:1). Crystallization (3.5 h at room temperature) afforded 2.13 g (25%) (–)-**12** as colourless needles, R_f = 0.45 (cyclohexane/AcOEt, 2:1), m.p. 172.6-175.1 °C, $[\alpha]_D^{20}$ = –2.1 (c = 1.11 in $CHCl_3$). - IR ($CHCl_3$): 1790 cm^{-1} (C=O), 1780 (C=O), 1740 (C=O), 1720 (C=O). - ^1H NMR (C_6D_6, 300 MHz): 0.61 (td, J = 13.4, J = 3.4 Hz, 2 H), 0.72 (s, 6 H, CH_3), 0.75-0.84 (2 H), 0.86 (s, 6 H, CH_3), 0.87 (s, 6 H, CH_3), 0.94-1.18 (6 H), 1.20-1.28 (4 H), 1.28-1.50 (6 H), 1.64 (m, 2 H), 1.73 (m, 2 H), 2.09 (m, 2 H), 3.89 (dd, J = 8.7, J = 6.3 Hz, 2 H), 3.94 (dd, J = 8.6, J = 6.3 Hz, 2 H). Mixture of the diastereomeric esters: additional signal at 3.91 (d, J = 6.3 Hz, 4 H, CH_2O) which disappears upon recrystallization.
Analysis calculated for $C_{33}H_{48}O_8$ (572.7): C, 69.20; H, 8.45. Found C, 69.28; H, 8.50.

(+)-Spiro[5.5]undecane-3,9-dimethyldiyl-bis-(1R,4S)-camphanoate [(+)-**12**]: Prepared by reaction of (±)-**3** with (1*R*,4*S*)-(+)-camphanoyl chloride[5] and subsequent recrystallization of the mixture of diastereomeric esters as described above; (+)-**12** as colourless needles, m.p. 175.4-176.4 °C, $[\alpha]_D^{20}$ = +2.1 (c = 1.14 in $CHCl_3$).

(aS)-(-)-3,9-Bis(hydroxymethyl)spiro[5.5]undecane [(–)-**3**]: A solution of 2.32 g (4.05 mmol) (–)-**12** in 100 mL 0.1 M NaOMe/MeOH was boiled under reflux for 20 min. The mixture was cooled to room temperature and 10 mL of 1 M HCl/MeOH were added. Evaporation of the solvent followed by column chromatography (100 g silicagel, cyclohexane/AcOEt, 1:1) gave 757 mg (88%) of (–)-**3** as colourless crystals. R_f = 0.30, m.p. 105.4-107.4 °C from AcOEt, $[\alpha]_D^{20}$ = –30.0 (c = 1.07 in MeOH). - Spectral data cp. (±)-**3**.

(aR)-(+)-3,9-Bis(hydroxymethyl)spiro[5.5]undecane [(+)-**3**]: This compound was prepared as described above from 358 mg (0.63 mmol) of (+)-**12**: 130 mg (98%) (+)-**3** as colourless crystals; R_f = 0.3 (cyclohexane/AcOEt, 1:1); m.p. 106.1-106.6 °C from AcOEt; $[\alpha]_D^{20}$ = +31.2 (c = 2.45 in MeOH).

(aS)-(–)-Spiro[5.5]undecane-3,9-dicarboxylic acid [(–)-**1**]: A solution of 351 mg (1.65 mmol) of (–)-**3** was added within 30 min to 2.06 g (9.67 mmol) $NaIO_4$ and 25 mg (0.096 mmol) $RuCl_3 \cdot 3\ H_2O$ in 4.5 mL acetonitrile, 7.5 mL CCl_4, and 10 mL water. The mixture was stirred for 2.5 h at room temperature. The mixture was concentrated *in vacuo* and 20 mL 0.1 M H_2SO_4 were added and repeatedly extracted with AcOEt. The extracts were dried (Na_2SO_4) and the solvent was evaporated under reduced pressure. The residue, 294 mg (74%) (–)-**1** as colourless crystals, was used without further purification for the following step; m.p. 241-245 °C [cp. lit.[9] (±)-**1** m.p. 241.0-242.5 °C], $[\alpha]_D^{20}$ = –9.8 (c = 1.83 in MeOH).

(aS)-(–)-Dimethyl spiro[5.5]undecane-3,9-dicarboxylate [(–)-**2**]: A solution of 22 mg (0.09 mmol) of (–)-**1** in 2.0 mL MeOH was treated with a solution of diazomethane in diethyl ether. After reacting for 30 min at room temperature, the volatile materials were removed. The residue (39 mg) was purified by column chromatography on 10 g silica gel. Elution with cyclohexane/AcOEt (4:1) afforded 24 mg (99%) of (–)-**2** as a colourless oil, $[\alpha]_D^{20}$ = –7.5 (c = 0.5 in cyclohexane). - Spectral data cp. (±)-**2**.

(aS)-(–)-3,9-Bis(acetyl)spiro[5.5]undecane [(–)-**4**]: 110 mg (0.46 mmol) of (–)-**1** were added in portions under stirring at room temperature to 0.7 mL (9.6 mmol) of thionyl chloride and the reaction mixture was heated under reflux for 3 h. After cooling, the mixture was repeatedly treated with CCl_4 and concentrated *in vacuo* to give 128 mg of (*aS*)-(–)-spiro[5.5]undecane-3,9-dicarboxylic acid-dichloride, orange-coloured oil, $[\alpha]_D^{20}$ = –9.7 (c = 0.70 in cyclohexane), IR (CCl_4): 1800 cm^{-1} (C=O). A solution of 128 mg (0.46 mmol) of the acid chloride in 4.0 mL dry CH_2Cl_2 was added dropwise to a solution of 159 mg (1.10 mmol) of Meldrum's acid in 0.5 mL dry CH_2Cl_2 and 0.23 mL (2.8 mmol) of pyridine at 0 °C. After stirring for 90 min at 0 °C, followed by stirring at room temperature for 2 h, the mixture was diluted with 5 mL CH_2Cl_2 and poured into 3 mL of cold 1 M H_2SO_4. The mixture was extracted three times with CH_2Cl_2 (45 mL). The organic layer was washed with 1 M H_2SO_4, dried (Na_2SO_4) and the solvent was evaporated. The residue (306 mg) was dissolved in 4.5 mL of 66% AcOH and heated under reflux for 90 min. After cooling to room temperature, the mixture was extracted three times with diethyl ether (45 mL). The organic layer was washed successively with water, 2 M KOH, and water, dried (Na_2SO_4) and evaporated. The residue (52 mg) was chromatographed on 6 g silicagel (cyclohexane/AcOEt, 4:1) to provide 33 mg (31%) (–)-**4** as a colourless oil, R_f = 0.31, b.p. 99-104 °C/0.001 Torr, $[\alpha]_D^{20}$ = –10.6 (c = 0.55 in cyclohexane). - IR (CCl_4): 1710 (C=O). ^1H NMR ($CDCl_3$): 0.94 (dt, J = 3.6, J = 13.3 Hz, 2 H, 1-H_a, 7-H_a), 1.21 (dt, J = 4.3, J = 13.2 Hz, 2 H, 5-H_a, 11-H_a), 1.34-1.47 (m, 4 H, 2-H_a, 5-H_e, 8-H_a, 11-H_e), 1.51 (m, 2 H, 4-H_a, 10-H_a), 1.58-1.70 (m, 4 H, 2-H_e, 4-H_e, 8-H_e, 10-H_e), 1.93 (m, 2 H, 1-H_e, 7-H_e), 2.11 (s, 6 H, MeCO), 2.27 (m, 2 H, 3-H, 9-H). - ^{13}C NMR ($CDCl_3$): 23.3 (t, 2 C), 23.4 (t, 2 C), 28.1 (q, 2 C, CH_3CO), 31.1 (t, 2 C, C-1, C-7), 31.6 (s, C-6), 39.8 (t, 2 C, C-5, C-11), 51.6 (d, 2 C, C-3, C-9), 212.2 (s, 2 C, CO). - MS: 236 (10) [M^+], 218 (16), 190 (7), 175 (17), 71 (25), 43 (100).

Analysis calculated for $C_{15}H_{24}O_2$ (236.4): C, 76.23; H, 10.23. Found C, 76.28; H, 10.29.

(aS)-(–)-Spiro[5.5]undecane-3,9-diol [(–)-**9**]: To a solution of 33 mg (0.14 mmol) of (–)-**4** in 0.24 mL AcOH was added dropwise 0.1 mL conc. H_2SO_4 at 0 °C. After cooling to –7 °C, 0.09 mL (97 mg, 0.42 mmol) of 32% peroxyacetic acid was added dropwise. After stirring for 3 h at 10 °C, 1 g crushed ice was added and the mixture was extracted three times with diethyl ether (20 mL). The organic phases were washed with 2 M K_2CO_3, dried (Na_2SO_4), and the solvent was evaporated. The residue (34 mg) was dissolved in a mixture of 0.3 mL 2 M KOH and 1.4 mL EtOH, and heated under reflux for 30 min. The mixture was concentrated *in vacuo*. After addition of 1.4 mL 1 M H_2SO_4, the products were extracted with AcOEt. The solvent was removed *in vacuo* and the residue (34 mg) was chromatographed on 5 g silica gel. Elution with AcOEt provided 15 mg (58%) of (–)-**9** (25% ee) as colourless crystals, R_f = 0.40, m.p. 132.6-139.7 °C [lit.[7] 149.2-149.9 °C for (*aS*)-(–)-**9** with 100% ee, 133.7-135.5 °C for (±)-**9**], $[\alpha]_D^{20}$ = –3.6 (c = 0.22 in MeOH) [lit.[7] –14.2 (c = 1.13 in MeOH) for (*aS*)-(–)-**9** with 100% ee] .

(+)-Spiro[5.5]undecane-3,9-diyl-bis-(4-bromobenzoate): colourless crystals, m.p. 156.2-161.5 °C [lit.[7] 165.7-166.1 °C with 100% ee], $[\alpha]_D^{20}$ = +13.9 (c = 0.62 in dioxane) [lit.[7] +49.7 (c = 0.67 in dioxane) with 100% ee].

(aS)-(–)-3,9-Bis(bromomethyl)spiro[5.5]undecane [(–)-**5**]: At 0 °C, 479 mg (1.83 mmol) of triphenylphosphine was added in portions under stirring to a solution of 128 mg (0.60 mmol) of (–)-**3** and 504 mg (1.52 mmol) tetrabromomethane in 5.0 mL CH_2Cl_2. The yellow solution was stirred at 0 °C for 5 min and then 2 h at room temperature. Then the solvent was evaporated and the residue was extracted three times with cyclohexane, and the extracts were concentrated *in vacuo*. Chromatography of the residue (340 mg) on 10 g silica gel with cyclohexane gave 171 mg (84%) (–)-**5** as a colourless oil, R_f = 0.42, b.p. 94-104 °C/0.001 Torr, $[\alpha]_D^{20}$ = -21.4 (c = 1.69 in cyclohexane). - IR (CCl_4): 2920 cm^{-1} (CH), 2840 (CH), 655 (CBr). - ^1H NMR ($CDCl_3$): 0.90 (dt, J = 2.5, J = 13.3 Hz, 2 H, 1-H_a, 7-H_a), 1.18 (m, 2 H), 1.16-1.35 (6 H), 1.51-1.68 (6 H), 1.92 (m, 2 H, 1-H_e, 7-H_e), 3.29 (d, J = 5.9 Hz, 4 H, CH_2Br). - ^{13}C NMR ($CDCl_3$): 26.6 (t, 2 C), 26.7 (t, 2 C), 31.0 (t, 2 C), 31.8 (s, C-6), 40.2 (t, 2 C), 40.3 (d, 2 C, C-3, C-9), 40.6 (t, 2 C).
Analysis calcd. for $C_{13}H_{22}Br_2$ (338.1): C, 46.18; H, 6.56; Br, 47.26. Found C, 46.11; H, 6.50; Br, 47.25.

(aS)-(–)-3,9-Bis(methyl)spiro[5.5]undecane [(–)-**6**]: A mixture of 170 mg (0.46 mmol) of (–)-**5**, 1.2 mL 2 M KOH and 141 mg 5% of Pd/C as a catalyst in 20 mL ethanol was stirred under H_2 (1 bar). After the hydrogen absorption had ceased, the catalyst was removed by filtration (celite). The filtrate was diluted with 10 mL water, extracted twice with pentane (50 mL), and the solvent was evaporated. The residue was distilled and yielded 72 mg (87%) of (–)-**6** as a colourless oil, R_f = 0.85 (cyclohexane), b.p. 103-110 °C/11 Torr, $[\alpha]_D^{20}$ = -31 (c = 0.69 in pentane). - IR (CCl_4): 2930 cm^{-1} (CH), 2900 (CH), 2840 (CH). - ^1H NMR ($CDCl_3$): 0.85 (d, J = 6.4 Hz, 6 H, CH_3), 0.86 (m, 2 H, 1-H_a, 7-H_a), 0.95-1.34 (10 H), 1.35-1.47 (4 H), 1.87 (m, 2 H, 1-H_e, 7-H_e). - ^{13}C NMR: 22.5 (q, 2 C, CH_3), 30.3, 30.4 (t, 2 C, t, 2 C, C-2, C-8, C-4, C-10), 31.6 (s, C-6), 31.9 (t, 2 C, C-1, C-7), 33.2 (d, 2 C, C-3, C-9), 41.3 (t, 2 C, C-5, C-11). - MS: 180 (42) [M^+], 125 (47), 110 (99), 95 (64), 81 (100), 67 (42), 55 (34). -

Analysis calculated for $C_{13}H_{24}$ (180.3): C, 86.58; H, 13.41. Found C, 86.58; H, 13.46.

(±)-3,9-Bis(4-methoxyphenyl)spiro[5.5]undecane-3,9-diol [(±)-**13**]: A solution of 5.6 g (31 mmol) of **10** in benzene was added dropwise within 15 min to a solution of the Grignard reagent made from 14.96 g (80.4 mmol) 4-bromoanisole and Mg in 320 mL diethyl ether. After stirring overnight at room temperature, the mixture was quenched with 100 mL water and extracted with 800 mL diethyl ether. The organic layer was washed with 1 M H_2SO_4 and 2 M $KHCO_3$, dried (Na_2SO_4) and evaporated. The residue (12.5 g) was purified by column chromatography on 700 g silicagel with cyclohexane/AcOEt (2:1) to afford (±)-**13** as a colourless glassy substance (7.74 g, 63%), R_f = 0.50, m.p. 113-118 °C. - IR ($CHCl_3$): 3600 cm^{-1} (OH), 3640 (OH, br). - ^1H NMR ($CDCl_3$): 1.37 (m, 2 H), 1.49-1.60 (2 H), 1.62-1.71 (4 H), 1.75 (td, J = 13.2, J = 3.8 Hz, 2 H), 1.82 (m, 2 H), 1.91 (td, J = 13.6, J = 3.9 Hz, 2 H), 2.05 (td, J = 13.6, J = 4.1 Hz, 2 H), 3.79 (s, 6 H, OCH_3), 6.87 (d, J = 8.8 Hz, 4 H, arom. 3-H), 7.42 (d, J = 8.8 Hz, 4 H, arom. 2-H). - ^{13}C NMR ($CDCl_3$): 27.3 (t, 2 C), 30.9 (t, 2 C), 34.3 (t, 2 C), 34.5 (t, 2 C), 36.0 (s, C-6), 55.2 (q, 2 C, OCH_3), 72.9 (s, 2 C, C-3, C-9), 113.5 (d, 4 C, arom. C), 125.8 (d, 4 C, arom. C), 141.3 (s, 2 C, arom. C-1), 158.4 (s, 2 C, arom. C-4). - MS: 396 (1) [M^+], 378 (5), 360 (100), 331 (12), 212 (11), 200 (25), 160 (14), 121 (10). -
Analysis calculated for $C_{25}H_{32}O_4$ (396.5): C, 75.73; H, 8.13. Found C, 75.79; H, 8.09.

(±)-3,9-Bis(4-methoxyphenyl)spiro[5.5]undecane [(±)-**7**]: A solution of 5.00 g (12.6 mmol) of (±)-**13** and 8.00 mL (50.2 mmol) triethylsilane in 130 mL CH_2Cl_2 was treated at 0 °C with 6.28 mL (50 mmol) $Et_2O{\cdot}BF_3$ under N_2. Stirring was continued for 10 min at 0 °C and for 50 min at room temperature. The reaction mixture was quenched with 20 mL of 2 M $KHCO_3$. The aqueous layer was extracted twice with CH_2Cl_2. The extracts were washed with 2 M $KHCO_3$, dried (Na_2SO_4), and the solution was evaporated to give 4.47 g (97%) of (±)-**7** as colourless crystals, which were used without further purification for the next step; R_f = 0.55 (cyclohexane/AcOEt, 9:1), m.p. 130.1-131.0 °C. A sample for analysis was prepared by sublimation (120 °C/0.001 Torr). - IR (CCl_4): 2830 cm^{-1} (OMe). - ^1H NMR ($CDCl_3$): 1.06 (td, J = 13.4, J = 3.4, 2 H, 1-H_a, 7-H_a), 1.39-1.45 (4 H), 1.54 (qd, J = 13.3, J = 3.4 Hz, 2 H), 1.62-1.73 (6 H), 2.22 (dm, J = 13.4 Hz, 2 H, 1-H_e, 7-H_e), 2.43 (m, 2 H, 3-H, 9-H), 3.78 (s, 6 H, OCH_3), 6.83 (d, J = 8.7 Hz, 4 H, arom. H), 7.14 (d, J = 8.7 Hz, 4 H, arom. H). - ^{13}C NMR ($CDCl_3$): 29.5, 29.6 (t, 2 C, t, 2 C, C-2, C-8, C-4, C-10), 31.4 (s, C-6), 32.0 (t, 2 C, C-1, C-7), 42.0 (t, 2 C, C-5, C-11), 44.1 (d, 2 C, C-3, C-9), 55.2 (q, 2 C, OCH_3), 113.7 (d, 4 C, arom. C), 127.6 (d, 4 C, arom. C), 140.0 (s, 2 C, arom. C-1), 157.7 (s, 2 C, arom. C-4). - MS: 364 (100) [M^+], 217 (7), 160 (7), 147 (12), 134 (12), 121 (22). -
Analysis calculated for $C_{25}H_{32}O_2$ (364.5): C, 82.37; H, 8.85. Found C, 82.46; H, 8.84.

(±)-3,9-Bis(4-hydroxyphenyl)spiro[5.5]undecane [(±)-**8**]: A solution of 3.34 g (9.18 mmol) of (±)-**9** in 175 mL (1.80 mol) of 67% aqueous hydrogen iodide was heated under reflux for 4 h. Water (900 mL) was added and the products were extracted twice with diethyl ether (900 mL). The extracts were washed with 50% $Na_2S_2O_3$ and water, dried (Na_2SO_4), and evaporated to give a residue (6.22 g) which, after column chromatography [700 g silica gel, eluant cyclohexane/AcOEt (4:1)], afforded (±)-**8** (2.71 g, 88%) as colourless crystals, R_f = 0.24, m.p. 214-216 °C. - IR (KBr): 3350 cm^{-1} (OH, br.), 3010 (arom. H). - ^1H NMR (CD_3OD): 1.09 (dt, J = 3.6, J = 15.9 Hz, 2 H, 1-H_a, 7-H_a), 1.41 (m, 4 H), 1.51-1.70 (8 H), 2.26 (dm, J = 13.6, 2 H, 1-H_e, 7-H_e), 2.37 (tt, J = 12.0, J = 3.8 Hz, 2 H, 3-H_a, 9-H_a), 6.67 (d, J = 8.5 Hz, 4 H,

arom. H), 7.02 (d, J = 8.5 Hz, 4 H, arom. H). - ^{13}C NMR (CD_3OD): 30.9, 31.0 (t, 2 C, t, 2 C, C-2, C-8, C-4, C-10), 32.6 (s, C-6), 33.2 (t, 2 C, C-1, C-7), 43.4 (t, 2 C, C-5, C-11), 45.7 (d, 2 C, C-3, C-9), 116.0 (d, 4 C, arom. C), 128.6 (d, 4 C, arom. C), 140.0 (s, 2 C, arom. C-1), 156.3 (s, 2 C, arom. C-4). -
Analysis calculated for $C_{23}H_{28}O_2$ (336.4): C, 82.10; H, 8.39. Found C, 82.20; H, 8.39.

(+)-3,9-Diphenyl-spiro[5.5]undecane-4',4'-di-(1S,4R)-camphanoate [(+)-**14**]: A solution of 2.57 g (7.65 mmol) of (±)-**8** in 19 mL of dry pyridine was added to 5.02 g (23.1 mmol) of (1*S*,4*R*)-(–)-camphanoyl chloride[5] in 19 mL of pyridine. After stirring for 4 h at room temperature, the mixture was dropped into 800 mL 1 M H_2SO_4. The mixture was extracted twice with CH_2Cl_2 (1000 mL). The extracts were washed with 2 M $KHCO_3$, dried (Na_2SO_4), and the solvent was evaporated to yield a mixture of the diastereomeric esters, 4.99 g (94%), m.p. 251-274 °C. Crystallization from hot toluene (480 mL) gave within 12 h at room temperature 2.07g (39%) colourless crystals; m.p. 254-286 °C. Subsequent recrystallization of these crystals from 200 mL of toluene afforded 1.22 g (23%) (+)-**14** as colourless crystals, m.p. 291-295 °C, $[\alpha]_D^{20}$ = +3.4 (c = 1.12 in $CHCl_3$). - IR ($CHCl_3$): 1790 (C=O), 1750 (C=O). -
Analysis calculated for $C_{43}H_{52}O_8$ (696.9): C, 74.11; H, 7.52. Found C, 74.05; H, 7.58.

(aS)-(+)-3,9-Bis(4-hydroxyphenyl)spiro[5.5]undecane [(+)-**8**]: A solution of 537 mg (0.77 mmol) of (+)-**14** in 55 mL of 0.1 M NaOMe/MeOH was boiled under reflux for 25 min. The reaction mixture was cooled to room temperature and 2.2 mL of 1 N HCl/MeOH was added. Evaporation of the solvent followed by column chromatography of the residue (15 g silicagel, CH_2Cl_2/acetone, 19:1) gave 239 mg (92%) of (+)-**8** as colourless crystals, R_f = 0.41, m.p. 221-223 °C, $[\alpha]_D^{20}$ = +12.2 (c = 1.20 in MeCN). - UV (MeCN): λ_{max} (lg ε) = 283 nm (3.548), 278 nm (3.461). - CD (MeCN): $\Delta\varepsilon_{max}$ = –0.30 (285 nm), –0.39 (278 nm). - Spectral data cp. (±)-**8**.

(aS)-(+)-3,9-Bis(4-methoxyphenyl)spiro[5.5]undecane [(+)-**7**]: A solution of 80 mg (0.24 mmol) of (+)-**8** in 5.0 mL CH_2Cl_2/MeOH (2:1) was treated with a solution of diazomethane in diethyl ether. After reaction for 16 h at room temperature, the volatile materials were removed *in vacuo* and the residue was chromatographed on 10 g silicagel with cyclohexane/AcOEt (4:1) as eluent to give 38 mg (49%) of (+)-**7** as colourless crystals, R_f = 0.70, m.p. 137.2-138.3 °C, $[\alpha]_D^{20}$ = +6.2 (c = 0.76 in $CHCl_3$).- Spectral data cp. (±)-**7**.

(aS)-(–)-Spiro[5.5]undecane-3,9-dicarboxylic acid [(–)-**1**] *and (aS)-(–)-dimethyl spiro[5.5]undecane-3,9-dicarboxylate* [(–)-**2**] *by oxidation of the bisphenol* (+)-**8**: A mixture of 336 mg (1.0 mmol) of (+)-**8**, 9.63 g (45 mmol) $NaIO_4$, 22 mg (0.09 mmol) of $RuCl_3 \cdot 3\ H_2O$ as a catalyst in 17 mL acetonitrile, 17 mL CCl_4, and 23 mL water was stirred at room temperature for 2 d. The mixture was concentrated in vacuo and 10 mL of 0.1 M H_2SO_4 was added. After repeated extractions with AcOEt, the extracts were dried (Na_2SO_4), and the solvent was evaporated *in vacuo*. The residue (110 mg) was sublimed *in vacuo* (150 °C/0.001 Torr) to yield 76 mg of (–)-**1** as colourless solid; m.p. 220-235 °C, $[\alpha]_D^{20}$ = –9.5 (c = 1.12 in MeOH). The ester was synthesized from a solution of 76 mg (0.30 mmol) of (–)-**1** in 30 mL CH_2Cl_2, 12 mL MeOH, and 0.3 mL conc. H_2SO_4 by boiling for 16 h under reflux. Thereafter 10 mL of toluene and 10 mL of water were added and

the mixture was concentrated *in vacuo*. The residue was extracted twice with cyclohexane (20 mL), the extracts were washed with 2 M $KHCO_3$, dried, and evaporated. The oily residue (85 mg) was chromatographed on 10 g silicagel with cyclohexane/AcOEt (4:1), as an eluant to yield 57 mg (20%) of (–)-**2** (100% ee) as a colourless oil; $[\alpha]_D^{20} = -7.5$ (c = 1.13 in cyclohexane).

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