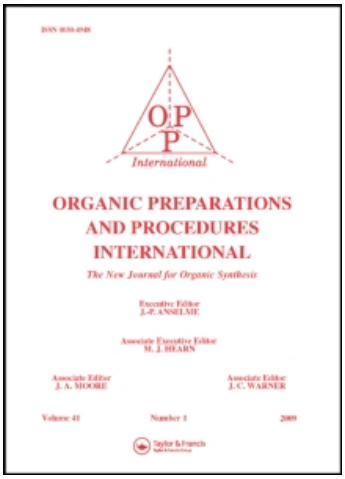

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A CONVENIENT PREPARATION OF (+)-5(S)-METHYL-2(5H)-FURANONE. SYNTHESIS OF (S)-(+)-SULCATOL

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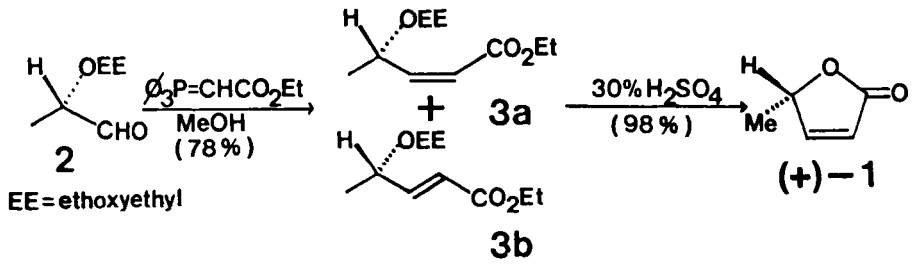
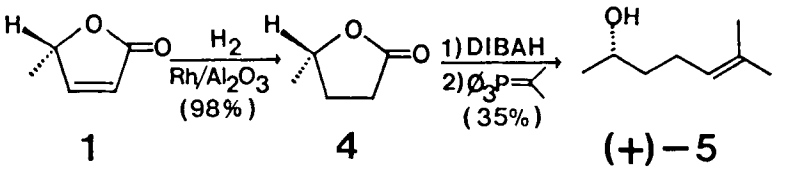
(+)-5-Methyl-2(5H)-furanone (1), (S-(+)–β-angelica lactone), has been shown to be an important synthon for the synthesis of substituted γ-valerolactonic natural products by regio- and stereocontrolled functionalization at the C_2 and C_3 carbon atoms of the γ-lactone moiety.[1] Lactone (+)-1 has been prepared starting from diethyl L-(+)-tartarate in nine steps[2] and from unnatural (R)-(-)-glutamic acid in nine steps.[1] In connection with our synthetic program directed toward chiral syntheses of natural products, we needed a large amount of (+)-1, and we have developed a brief and convenient route to (+)-1 of high optical purity starting from the readily available ethyl (S)-(-)-lactate in five steps.



Scheme 1

Aldehyde 2, $[\alpha]_D^{23}$ = -57.3° (c = 3.0, $CHCl_3$),[3] was prepared in three steps from ethyl (S)-(-)-lactate in 69% overall yield. Stereoselective Wittig olefination[4] of the aldehyde 2 with (ethoxycarbonylmethylene)triphenylphosphorane in methanol afforded a mixture of the (E)- and (Z)-pentenoates 3a and 3b (82:18 ratio) after column chromatography. The (Z)-pentenoate 3a was treated with a catalytic amount of sulfuric acid (30%) in methanol at room temperature for 0.5 hr to give (+)-5(S)-methyl-2(5H)-furanone (Scheme 1);[5] the overall yield of (+)-1 from ethyl (S)-(-)-lactate was 47%.

Using the lactone (+)-1 as a chiral synthon, we have developed an enantiospecificsynthesis of (S)-(+)-6-methyl-5-hepten-1-ol (5) [(S)-(+)-sulcatol],[6] the aggregation pheromone of Gnathotrichus retusus.[6b,7] G. retusus is sensitive to the S enantiomer of 5, and its response seems to be inhibited by the R enantiomer.[8] Catalytic hydrogenation of the unsaturated lactone (+)-1 with rhodium on alumina furnished (S)-(-)–γ-butyrolactone (4)[1,6a,9] in 98% yield. In our hands, catalytic hydrogenation of (+)-1 with Pd/C or PtO_2 failed to give (+)-4 of high optical purity. Reduction of the lactone (+)-4 with i-Bu_2AlH, followed by Wittig reaction with isopropylidenetriphenylphosphorane in THF afforded (S)-(+)-sulcatol (5) (Scheme 2).



Scheme 2

EXPERIMENTAL SECTION

All chemicals and solvents were analytical grade. IR spectra were recorded on a Shimadzu IR-440 spectrophotometer and were calibrated. ^1H NMR spectra were obtained in chloroform-d_1 at 80MHz on a Bruker WP 80 SY spectrometer. ^{13}C NMR spectra (^1H decoupled) were taken in $CDCl_3$ at 22.6 MHz using TMS as an internal standard. Mass spectra were obtained using Hewlett-Packcard 5890 GC/MS system at 70 eV. Optical rotations were measured on a JASCO DIP-360 polarimeter. Column chromatography was performed on Merck silica gel (70-230 mesh).

Ethyl (Z- and E-)-(S)-4-Ethoxyethyloxy-2-pentenoate (3a and 3b).- A mixture of aldehyde 2 (1.10 g, 6.87 mmol) and (ethoxycarbonylmethylene)triphenylphosphorane (5.22 g, 14.9 mmol) in MeOH (12 ml) was stirred at 0° for 5 hrs. The solvent was evaporated and the residue was extracted with pentanes and the solution was filtered through a silica gel pad. The organic solution was dried over $MgSO_4$, and concentrated in vacuo. Distillation of the residue gave a colorless liquid, 1.15 g (78%), which consisted of a 82:18 mixture of 3a and 3b as determined by GLC analysis. Chromatography on silica gel (elution with 4:1 hexanes/ethyl acetate), afforded 0.93 g (63%) of 3a, bp. 65°/8 mm [TLC: $R_f \sim 0.62$ (hexanes/ethyl acetate 4:1)]; $[\alpha]_D^{18} = +5.0°$ (c = 3.8, $CHCl_3$); IR (neat): 3050, 1730 cm^{-1}; ^1H NMR (80 MHz, $CDCl_3$): δ 1.05-1.50 (m, 12H), 2.25-2.80 (m, 2H), 4.18 (q, J = 7Hz), 4.70 (m, 1H), 5.32 (q, 1H, J = 6.5Hz), 5.70 (dd, 1H, J = 11, 1.6Hz), 6.25 (dd, 1H, J = 11, 9Hz); ^{13}C NMR (22.6 MHz, $CDCl_3$): δ 14.84,15.78, 15.92, 21.45, 60. 77, 62.10, 69.00, 69.31, 100.20, 118.56, 153.49; MS (m/e): 216 (M^+), 201 (M^+-15), 171, 144, 127, 115, 99, 73 (base peak), 45] and 0.18 g (15%) of 3b, bp. 65°/8 mm. [TLC: $R_f \sim 0.50$ (hexanes/ethyl acetate 4:1)]; $[\alpha]_D^{22} = +8.3°$ (c = 3.3, $CHCl_3$); IR (neat): 3050, 1730 cm^{-1}; ^1H NMR (80 MHz, $CDCl_3$): δ 1.05-1.50 (m, 12H),2.30-2.80 (m, 2H), 4.20 (q, 2H, J = 7Hz), 4.72 (m, 1H), 5.28 (q, 1H, J = 6.5Hz), 5.98 (dd, 1H, J = 15Hz, 1Hz), 6.85 (dd, 1H, J = 15Hz, 8Hz)].

Anal. Calcd. for $C_{11}H_{20}O_4$ (3a): C, 61.13; H, 9.25. Found: C, 61.15; H, 9.40

5(S)-Methyl-2(5H)-furanone (1).- To a stirred solution of 3a (1.02 g 4.72 mmol) in MeOH (5 ml) was added sulfuric acid (30%, 6 drops). The reaction mixture was stirred for 1 hr at RT and the solvent was removed in vacuo and the residue was extracted with CH_2Cl_2 (2 x 10 ml). The extract was dried over $MgSO_4$ and evaporated in vacuo to yield an oil. Chromatography on silica gel [elution with CH_2Cl_2 ($R_f \sim 0.35$)] afforded 0.47 g (98%) of (+)-1, bp. 98-100°/12 mm; $[\alpha]_D^{22} = +100°$ (c = 3.0, $CHCl_3$), [lit.[2] $[\alpha]_D^{20} = +93.8°$ (c = 0.5, $CHCl_3$)]; IR (neat): 1770 cm^{-1}; ^1H NMR (80 MHz,

$CDCl_3$): δ 1.40 (d, 3H, J = 7Hz), 5.08 (m, 1H), 6.02 (dd, 1H, J = 5.5, 1.5Hz), 7.41 (dd, 1H, J = 5.5, 1.8Hz).The IR spectrum and ^1H NMR spectrum of (+)-1 were identical in all respects to those reported previously.[1]

(S)-5-Methyldihydro-2(3H)-furanone (4).- To a stirred solution of (+)-1 (0.250 g, 2.50 mmol) in ethyl acetate (5 ml) was added 5% Rh/Al_2O_3 (10 mg). The mixture was stirred under hydrogen atmosphere for 6 hrs and filtered through Celite to remove the catalyst. Ethyl acetate was evaporated in vacuo to give an oil. Column chromatography on silica gel (elution with 5:2 hexanes/ethyl acetate), afforded 0.250 g (98%) of 4; [TLC: R_f ~ 0.38 (hexanes/ethyl acetate 5:2)]; $[\alpha]_D^{23}$ = -30.9° (c = 0.75, $CHCl_3$), lit.[6a] $[\alpha]_D^{23}$ = -29.6° (c = 1.29, CH_2Cl_2)]; IR (neat): 1780, 1210 cm^{-1}; ^1H NMR (80 MHz, $CDCl_3$): δ 1.40 (d, 3H, J = 7Hz), 1.70-2.69 (m, 4H), 4.57 (m, 1H). The IR spectrum and ^1H NMR spectrum of 4 are consistent with those previously published.[1,6a]

(S)-(+)-6-Methyl-5-hepten-2-ol (5).- To a stirred solution of 4 (0.200 g, 2.00 mmol) in dry THF (4 ml) at -78° under nitrogen atmosphere was added DIBAL-H (20% in n-hexane, 1.42 ml) dropwise and stirring was continued for 40 min. The reaction mixture was quenched with a saturated NH_4Cl solution (0.5 ml) at -78°. The Dry Ice-acetone bath was removed and the mixture was diluted with ether (5 ml) at RT. The solution was dried over $MgSO_4$ and filtered through a Celite pad. The filtrate was concentrated in vacuo to afford (S)–γ-methyl–γ-butyrolactol (0.178 g, 87%); TLC: R_f ~ 0.22 (hexanes/ethyl acetate 1:1); IR (neat): 3400 cm^{-1}. The lactol was employed in the next step without purification.

To a suspension of isopropyltriphenylphosphonium iodide (1.73 g, 4.00 mmol) in THF (20 ml) at -40° was added n-BuLi (1.6M in n-hexane, 2.50 ml, 4.00 mmol) dropwise and the reaction was stirred for 30 min. The lactol (0.178 g, 1.70 mmol) in THF (3 ml) was added at -40° and the mixture was warmed to RT and stirred for 16 hrs. After quenching with solid NH_4Cl (1 g), the mixture was filtered through a Celite pad. The filtrate was concentrated in vacuo . The residue was extracted with ether and the organic phase was washed with water and a saturated NH_4Cl solution then dried over $MgSO_4$. Concentration in vacuo gave a liquid which was chromatographed on silica gel [elution with 3:1 hexanes/ethyl acetate], afforded 94 mg (42%) of (S)-(+)-sulcatol (5); TLC: R_f ~ 0.39 (hexanes/ethyl 3:1); $[\alpha]_D^{24}$ = +18.0° (c = 2.00, EtOH), lit.[6a] $[\alpha]_D^{23}$ = +14.4° (c = 0.998, EtOH); IR (neat): 3350 cm^{-1}; ^1H NMR (80 MHz, $CDCl_3$): δ 1.18 (d, 3H, J = 6Hz), 1.27-1.58 (m, 2H), 1.65 (s, 3H), 1.70 (s, 3H), 1.90-2.20 (m, 2H), 3.81 (sextet, 1H, J = 6Hz), 5.14 (tq, 1H, J = 6, 1Hz). Spectral data (^1H NMR, IR) of 5 were consistent with those reported.[6a]

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REFERENCES

1. R. M. Ortuno, D. Alonso, J. Cardellach and J. Font, Tetrahedron, 43, 2191 (1987) and references therein.

2. R. M. Ortuno, D. Alonso and J. Font, Tetrahedron Lett., 27, 1079 (1986).

3. T. Hiyama, K. Nishida and K. Kobayashi, ibid., 25, 569 (1984).

4. Z-Stereoselective Wittig olefination reaction of 2,3-O-isopropylidene-D-glyceraldehyde with ethoxycarbonylmethylenetriphenylphosphorane in methanol is known; B. Häfele and V Jäger, Ann., 85 (1987) and references therein.

5. The mixture could, without separation of geometrical isomers 3a and 3b, be lactonized to obtain (+)-1, after separation of unreacted 3b.

6. Known synthesis: a) K. Mori, Tetrahedron, 31, 3011 (1975); b) H. R. Schuler and K. N. Slessor, Can. J. Chem., 55, 3280 (1977); c) B. D. Johnston and K. N. Slessor, ibid., 57, 233 (1979); d) K. Mori, Tetrahedron, 37, 1341 (1981); e) A. Belan, J. Bolte, A. Fauve, J. G. Gourcy and H. Veschambre, J. Org. Chem., 52, 256 (1987); f) C. M. Afonso, M. T. Barros, L. Godinho and C. D. Maycock, Tetrahedron Lett., 30, 2707 (1989).

7. Another species, Gnathotrichus sulcatus, responds to a 65/35 mixture of (S)-(+)- and (R)-(-)-sulcatol; K. J. Byrne, A. A. Swigar, R. M. Silverstein, J. H. Borden and E. J. Stokkink, J. Insect. Physiol., 20, 1895 (1974).

8. a) J. H. Borden, L. Chong, J. A. Mclean, K. N. Slessor and K. Mori, Science, 192, 894 (1976); b) J. H. Borden, J. R. Haudley, J. A. Mclean R. M. Silverstein, L. Chong, K. N. Slessor, B. D. Johnston and H. R. Schuler, J. Chem. Ecol., 6, 445 (1980).

9. a) P. A. Levene, H. L. Haller and A. Walt, J. Biol. Chem., 72, 591 (1927); b) P. A. Levene and H. L. Haller, ibid., 77, 555 (1928); c) K. Takeda and H. Minato, Tetrahedron Lett., 22, 33 (1960); d) T. Reschke, ibid., 3434 (1969).

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