

A New Route to Tricyclane Sesquiterpenoids: Total Synthesis of α -Ekasantalic acid

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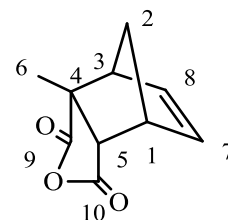
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Experimental procedures

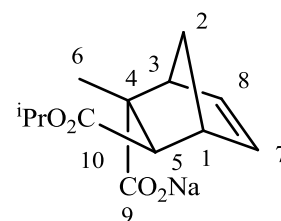
2-Methyl-4-oxa-tricyclo[5.2.1.0^{0,0}]dec-8-ene-3,5-dione, **16**.

Freshly distilled cyclopentadiene (150 mL) was added to stirred neat citraconic anhydride (102 g, 0.91 mol) at such a rate to maintain the temperature below 20 °C (Caution: Delayed exothermic reaction! External cooling is necessary from time to time). After the addition was complete, petroleum ether (500 mL) was added to the gelatinous reaction mixture and stirring was continued for two hours at room temperature. The reaction mixture was filtered and the solid was dried under vacuum to afford a white powder (160 g, 99%). Mp 139-140 °C (Lit¹ 138 °C); δ_{H} (CDCl₃) 1.63 (3H, s, H-6CH₃), 1.79-1.86 (2H, m, CH₂), 3.04 (1H, m, H-3), 3.13 (1H, d, J = 4.7, H-5), 3.47 (1H, m, H-1), 6.31 (1H, dd, J = 3, 5.7 Hz, H-8/H-7), 6.39 (1H, dd, J = 3, 5.7 Hz, H-8/H-7); δ_{C} {H} (CDCl₃) 21.8 (CH₃, C-6), 47.1 (CH, C-5), 51.1 (CH₂, C-2), 52.4 (CH, C-3), 53.9 (CH, C-1), 54.2 (C, C-4), 133.7 (CH, C-8/C-7), 136.6 (CH, C-8/C-7), 173.8 (C, C-9), 177.7 (C, C-10).



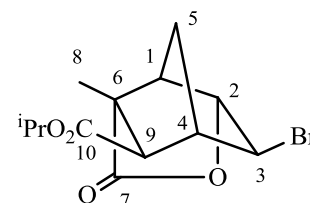
2-Methylbicyclo[2.2.1]hept-5-ene-2,3-dicarboxylic acid 3-isopropyl ester, **17**.

Sodium hydride (36.0 g of a 60% w/w suspension in mineral oil, 0.90 mol) was added over 45 minutes to stirred isopropanol (1.2 L) maintained at 0 °C (Caution: Vigorously exothermic reaction!). To the resulting solution was added compound **16** (160 g, 0.90 mol) in eight portions over a 15 min period. And the resulting mixture was stirred at room temperature overnight. The reaction mixture was reduced in volume to about 200 mL under reduced pressure and diethyl ether (600 mL) was added with vigorous stirring. After an hour, solid was filtered off, washed with ether and dried under vacuum to afford the title compound as an off white powder (202 g, 87%). A second crop (12.2 g, 5%) was secured after leaving the filtrate at 4 °C overnight. δ_{H} (CDCl₃) 1.20 (3H, d, J = 6.8 Hz, CH₃CH), 1.22 (3H, d, J = 6.8 Hz, CH₃CH), 1.36 (1H, d, J = 8.5 Hz, H-2a), 1.52 (3H, s, CH₃C), 1.57 (1H, d, J = 8.5 Hz, H-2b), 2.69 (2H, m, H-5 and H-3), 2.91 (1H, m, H-1), 4.94 (1H, sept, J = 6.8 Hz, CHMe₂), 6.18 (1H, dd, J = 3, 5 Hz, H-8/H-7), 6.48 (1H, dd, J = 3, 5 Hz, H-8/H-7); δ_{C} {H} (CDCl₃) 20.4 (CH₃CH), 20.8 (CH₃CH), 24.1 (CH₃, C-6), 44.0 (CH₂, C-2), 44.1 (CH, C-5), 51.0 (C-3), 54.3 (C-1), 58.4 (C-4), 64.0 (CHMe₂), 132.6 (C-7/C-8), 135.4 (C-7/C-8); 172.5 (C, C-10), 176.7 (C, C-9); $\nu_{\text{max}}/\text{cm}^{-1}$ 2590, 1779, 1660, 1442, 1294; m/z (EI) 238 [MH(-Na)⁺, 100]; HRMS: calculated for C₁₃H₁₈O₄Na 261.2694, found 261.2692.



2-Bromo-6-methyl-5-oxo-4-oxatricyclo[4.2.1.0^{0,0}]nonane-9-carboxylic acid isopropyl ester, **18**.

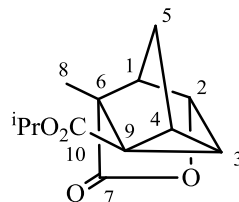
Bromine (21.5 mL) was added over a period of fifteen minutes to a vigorously stirred solution of compound **17** (100 g, 0.42 mol) in distilled water (1 L). After the completion of the addition, the reaction mixture was left in a cold room at 4 °C over night. The white solid was filtered and dried under vacuum to afford the title compound as a white solid (130 g, 98%). Mp 92-94 °C; δ_{H} (CDCl₃) 1.18 (3H, d, J = 6.3 Hz, CH₃CH), 1.19 (3H, d, J = 6.3 Hz, CH₃CH), 1.28 (3H, s, CH₃C), 1.74 (1H, dd, J = 1.7, 11.8 Hz, H-5a), 2.36 (1H, dt, J = 1.4, 11.8 Hz, H-5b), 2.58 (1H, d, J = 3.4, H-3), 2.78 (1H, m, H-4), 2.85 (1H, dd, J = 1.4, 5.5, H-1), 4.21 (1H, d, J = 2.4 Hz, H-9), 4.87 (1H, d, 5.5 Hz, H-2), 4.94 (1H, sept, J = 6.3 Hz, CHMe₂); δ_{C} {H} (CDCl₃) 20.6 (CH₃CH), 22.1 (CH₃CH), 22.2 (CH₃, C-6), 35.0 (CH₂, C-2), 46.2 (C-6), 49.1 (CH, C-9), 49.8 (CH, C-1), 53.3 (CH, C-3), 56.9 (CH, C-4), 69.7 (CH, C-2), 85.0 (CHMe₂), 170.1 (C, C-10), 178.3 (C, C-7); $\nu_{\text{max}}/\text{cm}^{-1}$ 2984, 1772, 1720, 1012, 686; m/z (EI) 318 (M⁺, 18), 316 (18), 238 (100); HRMS: calculated for C₁₃H₁₈O₃Na (MNa⁺ - Br) 261.1103, found 261.1101.



¹ Diels, O.; Alder, K. *Justus Liebigs Ann. Chem.*, **1928**, 430, 98-122

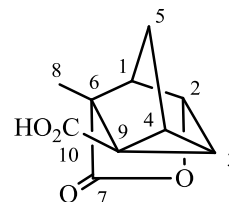
Tricyclane 19.

Bromide **18** (38.86 g, 168.9 mmol) was dissolved in anhydrous THF (600 mL) and tBuOK (20.37 g, 181.5 mmol) was added. The mixture was stirred under nitrogen for 4 days until tlc had indicated consumption of all the starting material. Solvent was evaporated and the residue was partitioned with water (100 mL) and dichloromethane (250 mL). The aqueous layer was extracted with more dichloromethane (3 x 100). The combined organic extractes were washed with brine (100 mL), dried over MgSO₄ and evaporated. The residue was chromatographed on silica (eluting with 20 % v/v ethyl acetate in petroleum ether) to give the *title compound* as a gum (25.91 g, 65%); δ_{H} (CDCl₃) 1.21 (3H, d, J = 6.8 Hz, CH₃CH), 1.23 (3H, d, J = 6.8 Hz, CH₃CH), 1.36 (3H, s, H-8), 1.88 (2H, m, H-5), 2.36 (2H, m, H-3 and H-4), 2.50 (1H, m, H-1), 4.76 (1H, d, J = 3 Hz, H-2), 5.00 (1H, sept, J = 6.3 Hz, CHMe₂); δ_{C} {H} (CDCl₃) 10.9 (CH₃, C-8), 22.1 (CH₃CH), 22.2 (CH₃CH), 29.3 (CH₂, C-5), 32.1 (CH, C-3), 33.3 (CH, C-4), 35.7 (C, C-9), 51.6 (CH, C-1), 52.6 (C, C-6), 69.0 (CH, C-2), 82.3 (CHMe₂), 169.8 (C, C-7), 178.1 (C, C-10); ν_{max} /cm⁻¹ 2923, 1778, 1464, 1377, 1338, 1278, 1081, 1026, 910.; m/z (EI) 237 (MH⁺, 100); HRMS: calculated for C₁₃H₁₆O₄Na 259.0946, found 259.0944.



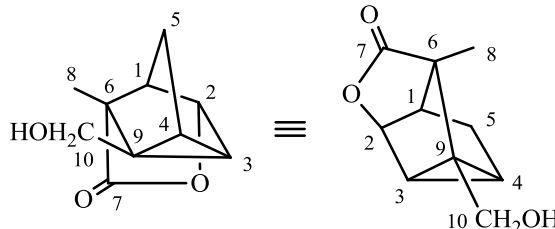
Acid 20.

Water (100 mL) and conc hydrochloric acid (80 mL) were carefully added to a round-bottomed flask containing tricyclane **19** (16.06 g, 68.0 mmol) and a stirrer bar. The resulting mixture was heated at reflux until it became homogenous (5 hours) and the heating was continued for a further 5 hours. The reaction flask was cooled first to room temperature and then in an ice bath. The solid was filtered to afford the *title compound* as white crystals (11.23 g, 85%). The filtrate was reduced in volume to about 30 mL to secure a second crop of slightly beige crystals (1.52 g, 11%); Mp 205 °C δ_{H} (CDCl₃) 1.23 (3H, s, H-8), 1.81 (2H, m, H-5), 2.36-2.52 (3H, m, H-1, H-3 and H-4), 3.39, (1H, bs, exchanges with D₂O, CO₂H), 4.87 (1H, t, J= 2.2 Hz, H-2); δ_{C} {H} (CDCl₃) 9.92 (CH₃, C-8), 28.4 (CH₂, C-5), 31.3 (CH, C-3), 32.2 (CH, C-4), 34.3 (C, C-9), 50.2 (C, C-1), 50.3 (C, C-6), 81.5 (CH, C-2), 171.3 (C, C-10), 177.6 (C, C-7); ν_{max} /cm⁻¹ 2594, 1779, 1673, 1440, 1284, 972; m/z (ESI) 210 (M⁺, 100); HRMS: calculated for C₁₀H₁₀O₄Na 217.0477, found 217.0475.



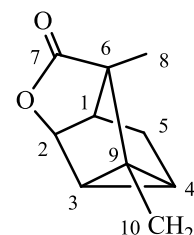
Hexahydro-3-hydroxymethyl-7-methyl-3,5,6-metheno-2H-cyclopenta[b]furan-2-one, 15.

Borane-methyl sulphide complex (17.2 ml of a 2 M solution in THF) was added over a period of 15 minutes to a stirred solution of acid **20** (4.45g, 22.9 mmol) in dry methylene chloride maintained under an argon atmosphere at 0 °C. The reaction was warmed to room temperature and stirring was continued for 15 hours. Water (70 ml) was added and the organic phase was separated. The aqueous phase was further extracted with DCM (3 x 40 ml). The combined extracts were dried (MgSO₄) and the solvent was evaporated at reduced pressure. The crude product was purified by flash chromatography (eluting with 20 % v/v petroleum ether / ethyl acetate) to give the *title compound* as fine white crystals (3.66 g, 89 %) Mp 180 °C; δ_{H} (CDCl₃) 1.24 (3H, s, H-8), 1.69 – 1.78 (4H, m, H-3, H-4, H-5), 2.30 (1H, s, H-1), 2.37 (1H, s, exchanges with D₂O, OH), 3.71 (1H, d, J= 12.4 Hz, H-10a), 3.92 (1H, d, J= 12.4 Hz, H-10b), 4.76 (1H, m, H-2); δ_{C} {H} (CDCl₃) 10.3 (CH₃, C-8), 25.7 (CH, C-3), 26.9 (CH, C-4), 29.7 (CH₂, C-5), 36.0 (C, C-9), 51.6 (CH, C-1), 54.1 (C, C-6), 59.6 (CH₂, C-10), 83.7 (CH, C-2), 180.8 (C, C-7); ν_{max} /cm⁻¹ 3486, 2923, 2852, 1746, 1346, 1246, 1092, 1038, 962; m/z (EI) 180 (M⁺, 18), 162 (88), 134 (36), 117 (34), 106 (33), 105 (93), 91 (100); HRMS: calculated for C₁₀H₁₂O₃Na 203.0679, found 203.0678.



Hexahydro-3-iodomethyl-7-methyl-3,5,6-metheno-2H-cyclopenta[b]furan-2-one, 21.

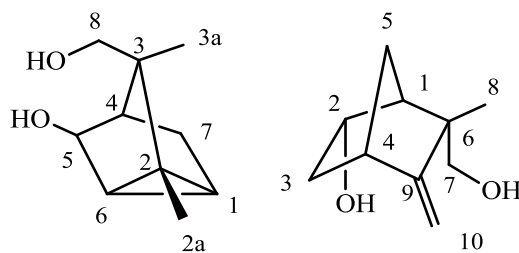
Iodine (3.93 g, 15.5 mmol) was slowly added in small portions over a period of 10 minutes to a vigorously stirred solution of alcohol **15** (2.80 g, 15.5 mmol), triphenylphosphine (4.08g, 15.5 mmol) and imidazole (1.06 g, 15.5 mmol) in dry THF (80 ml) maintained at room temperature under an argon atmosphere. Stirring was continued for an additional 10 minutes and then the solvent was removed at reduced pressure. The residue was partitioned between water (80 ml) and DCM (40 ml). The organic phase was separated and the aqueous phase was further extracted with DCM (2 x 40 ml). The extracts were combined, dried (MgSO₄) and stripped of solvent at reduced pressure. The residue was subjected to flash chromatography (eluting with 50 % v/v petroleum ether / ether) to afford the *title compound* as white crystals that quickly turn yellow on standing (3.62 g, 83 %). δ_{H} (CDCl₃) 1.30 (3H, s, H-8), 1.80 – 1.88 (2H, m, H-3 and H-4), 1.95 – 1.99 (2H, m, H-5), 2.39 (1H, s, H-1), 3.40 (1H, d, J= 11.2 Hz, H-5a), 3.51 (1H, d, J= 11.2, H-5b), 4.73 (1H, m, H-2); δ_{C} {H} (CDCl₃) 2.1 (CH₂, C-10), 9.9 (CH₃, C-8), 29.5 (CH₂, C-5), 32.8 (CH, C-3), 33.0 (CH, C-4), 34.3 (C, C-9), 51.5 (CH, C-1), 54.9 (C, C-6), 83.1 (CH, C-2), 178.9 (C, C-7); ν_{max} /cm⁻¹ 2991, 1764, 1462, 1377, 1183, 968, 953; m/z (CI) 308 (MNH₄⁺, 100); HRMS: calculated for C₁₀H₁₁O₂ 290.9876, found 290.9881.



3-hydroxymethyl-2,3-dimethyl-tricyclo[2.2.1.0^{2,6}]heptan-5-ol (**22**), and 6-hydroxymethyl-6-methyl-5-methylene bicyclo[2.2.1]heptan-2-ol (**23**)

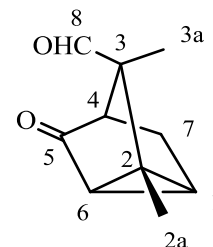
A solution of the iodide **21** (17.4 g, 60 mmol) in dry THF (100 ml) was added over a period of 20 minutes to a stirred suspension of lithium aluminium hydride (8.0 g, 210.0 mmol) in dry THF (200 ml), maintained under an argon atmosphere at 0 °C. When the addition was complete the reaction mixture was refluxed for one hour and was then cooled in an ice / water bath. The excess hydride was destroyed by the careful addition of water (8.0 ml), 15 % aqueous NaOH (8.0 ml) and finally water (24.0 ml).

The solids were removed by filtration and the filtrate was concentrated by evaporation at reduced pressure. The residue was partitioned between water (100 ml) and DCM (100 ml), the organic phase was separated and the aqueous phase was further extracted with DCM (2 x 100 ml). The combined organic extracts were dried (MgSO₄) and stripped of solvent at reduced pressure to leave a solid residue. The residue was subjected to flash chromatography (eluting with 20 % v/v petrol / ethyl acetate). The first compound to be eluted from the column was 6-hydroxymethyl-6-methyl-5-methylene bicyclo[2.2.1]heptan-2-ol (0.16 g, 2 %); Mp 81-84 °C; δ_H (CDCl₃) 1.08 (1H, m, H-3a), 1.11 (3H, s, H₈), 1.37 (1H, d, J = 10.3, H-5a), 1.62 (1H, m, H-5b), 2.15 (1H, s, H-1), 2.23 (1H, ddd, J = 5.2, 10.7, 12.8 Hz, H-3b), 2.71 (1H, m, H-4), 3.15 (1H, broad, exchanges with D₂O, OH), 3.60 (1H, d, J = 11.7 Hz, H-7a), 3.76 (1H, d, J = 11.7 Hz, H-7b), 4.00 (1H, broad, exchanges with D₂O, OH), 4.29 (1H, ddd, J = 4, 5.2, 10.7 Hz, H-5), 4.55 (1H, s, H_{10β}), 4.93 (1H, s, H_{10α}); δ_C {H} (CDCl₃) 26.5 (CH₃, C-8), 36.3 (CH₂, C-5), 37.5 (CH₂, C-3), 46.0 (CH, C-1), 47.9 (C, C-6), 51.4 (CH, C-4), 68.6 (CH₂, C-7), 73.8 (CH, C-2), 100.9 (CH₂, C-10), 161.6 (C, C-9); m/z (CI) 186 (MNH₄⁺, 100), 168 (37), 150 (29); HRMS: calculated for C₁₀H₁₆O₂Na 191.1043, found 191.1042. The second compound to be eluted from the column was 3-hydroxymethyl-2,3-dimethyl-tricyclo[2.2.1.0^{2,6}]heptan-5-ol (8.45 g, 84 %); Mp 165 °C; δ_H (CDCl₃) 0.97 (3H, s, H-2a), 0.99 (1H, m, H-6), 1.08 (1H, d, J = 6 Hz, H-4), 1.11 (3H, s, H-3a), 1.26 (1H, d, J = 10.9, H-7a), 1.64 (1H, dt, J = 1.5, 10.9 Hz, H-7b), 1.70 (1H, s, H₄), 3.40 (1H, broad, exchanges with D₂O, OH), 3.57 (1H, d, J = 11 Hz, H_{8a}), 3.75 (1H, exchanges with D₂O, OH), 3.87 (1H, s, H₅), 4.01 (1H, d, J = 11 Hz, H_{8b}); δ_C {H} (CDCl₃) 10.8 (CH₃, C-3a), 18.4 (CH₃, C-2a), 20.2 (CH, C-1), 24.7 (CH, C-6), 25.9 (C, C-2), 29.3 (CH₂, C-7), 45.0 (CH, C-4), 49.2 (C, C-3), 68.0 (CH₂, C-8), 78.7 (CH, C-5); ν_{max}/cm⁻¹ (Nujol mull) 3314, 2960, 1465, 1134, 1052, 1026, 880; m/z (EI) 168 (M⁺, 16), 137 (100), 109 (46), 107 (67), 91 (50); HRMS: calc. for C₁₀H₁₆O₂Na 191.1043, found 191.1079.



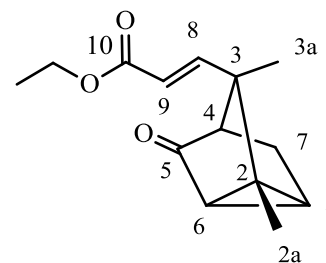
2,3-Dimethyl-5-oxo-tricyclo[2.2.1.0^{2,6}]heptan-3-carbaldehyde, **24**.

A stirred solution of oxalyl chloride (1.71 ml, 19.6 mmol) and dry DCM (40 ml), in an oven dried flask, fitted with a CaCl₂ drying tube was cooled to -60 °C. Dry DMSO (3.03 ml) in dry DCM (9.0 ml) was added over a period of 2 minutes and the reaction conditions maintained for an additional 2 minutes. Alcohol **22** (1.50 g, 8.92 mmol) in dry DCM (9.0 ml) was added over a period of 5 minutes and the reaction conditions were maintained for an additional 15 minutes. Following the dropwise addition for triethyl amine (12.4 ml, 89.2 mmol) the reaction was held at -61 °C for 5 minutes before being allowed to warm to room temperature. Water (70 ml) was added and the organic layer separated. The aqueous layer was further extracted with DCM (2 x 50 ml). The combined extracts were washed, in the following order with 0.1 M HCl (70 ml), water (70 ml), 5 % Na₂CO₃ (70 ml), and finally with water (70 ml). Drying (MgSO₄) removal of the solvent by evaporation and purification of the residue by flash chromatography (elution with 50 % petroleum / ethyl acetate) afforded the title compound as an oil (1.38 g, 95 %). δ_H (CDCl₃) 1.19 (3H, s, H-2a), 1.28 (3H, s, H-3a), 1.55 (1H, d, J = 5.5, H-1), 1.90 (1H, s, H-4), 2.05 (1H, d, J = 11 Hz, H-7b), 2.07 (s, 1H, d, J = 1.6 Hz, H-6), 2.16 (1H, dd, J = 1.6, 11 Hz, H-7a), 9.61 (1H, s, CHO, H-8); δ_C {H} (CDCl₃) 11.6 (CH₃, C-2a), 11.8 (CH₃, C-3a), 26.2 (CH, C-1), 27.9 (CH, C-6), 30.8 (CH₂, C-7), 35.4 (C, C-2), 48.5 (CH, C-4), 58.8 (C, C-3), 204.6 (CH, C-8), 210.5 (C, C-5); ν_{max}/cm⁻¹ 2947, 1752, 1716, 1466, 922, 880; m/z (ESI) 165 (MH⁺, 100), HRMS calc. for C₁₀H₁₂NaO₂ 187.0735; found 187.0731.



3-(2,3-Dimethyl-5-oxo-tricyclo[2.2.1.0^{2,6}]hept-3-yl)-acrylic acid ethyl ester.

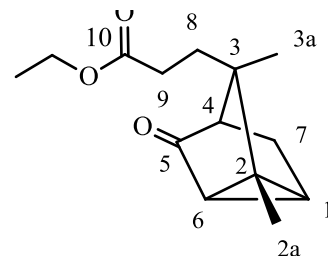
A solution of (ethoxycarbonylmethylene)triphenylphosphorane (3.18 g, 9.14 mmol) and aldehyde **21** (1.0 g, 6.10 mmol) in dry THF (50 ml) were refluxed for 22 hours under a dry argon atmosphere. The solvent was removed by evaporation and the residue was subjected to chromatography (eluting with 20 % v/v ethyl acetate / petrol). The title compound was isolated as a clear oil (1.39 g, 97 %). δ_H (CDCl₃) 1.18 (3H, s, H-2a), 1.25 (3H, s, H-3a), 1.29 (3H, t, J = 7.2 Hz, CH₃ of Et), 1.37 (1H, d, J = 5.4, H-1), 1.74 (1H, s, H-4), 1.98 (1H, d, J = 11.3, H-7a), 2.02 (1H, d, J = 5.4, H-6), 2.14 (1H, d, J = 11.3, H-7b), 4.18 (2H, q, J = 7.2, CH₂ of Et), 5.92 (1H, d, J = 16 Hz, H-8), 6.92 (1H, d, J = 16 Hz, H₉); δ_C {H} (CDCl₃) 11.2 (CH₃, C-2a), 14.6 (CH₃, Et), 16.4 (CH₃, C-3a), 28.0 (CH, C-1), 28.2 (CH, C-6), 30.1 (CH₂, C-7), 37.5 (C, C-2), 50.1 (C, C-3), 50.8 (CH, C-4), 60.8 (CH₂, Et), 122.4 (CH, C-9), 150.5 (CH, C-8), 166.6 (C, C-10), 211.7 (C, C-5); ν_{max}/cm⁻¹ 2979, 2885, 1755, 1719,



1651, 1448, 1368, 1311, 1188, 1035, 987, 878, 827, 732. m/z (EI) 234 (M^+ , 60), 189 (81), 188 (72), 161 (69), 144 (80), 133 (100), 105 (54); HRMS calc. for $C_{14}H_{18}NaO_3$ 234.1256; found 234.1254.

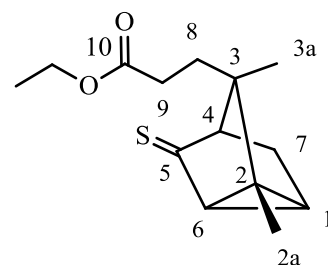
3-(2,3-Dimethyl-5-oxo-tricyclo[2.2.1.0^{2,6}]hept-3-yl)-propionic acid ethyl ester, 25.

Palladium on charcoal (10% w/w, 65 mg) was added to a solution of 3-(2,3-Dimethyl-5-oxo-tricyclo[2.2.1.0^{2,6}]hept-3-yl)-acrylic acid ethyl ester (1.30 g, 5.55 mmol) in ethyl acetate (50 ml). The resulting suspension was stirred under a hydrogen atmosphere for 18 hours. The catalyst was removed by filtration through a pad of celite® and the solvent was removed by evaporation to afford the title compound as a clear oil (1.30 g, 100%). δ_H ($CDCl_3$) 1.00 (3H, s, H-2a), 1.24 (3H, s, H-3a), 1.25 (3H, t, $J = 7$ Hz, CH_3 of Et), 1.54 – 1.61 (1H, m, H-8), 1.65 (1H, s, H-1), 1.83 – 1.90 (3H, m, H-8, H-7a and H-6), 1.98 – 2.02 (2H, m, H-7b and H-4), 2.27 – 2.32 (2H, m, H-9), 4.12 (2H, q, $J = 7$ Hz, CH_2 of Et); δ_C {H} ($CDCl_3$) 11.0 (CH_3 , C-2a), 14.6 (CH_3 , Et), 16.6 (CH_3 , C-3a), 28.2 (CH, C-1), 29.6 (CH, C-6), 29.8 (CH_2 , C-8), 30.7 (CH_2 , C-9), 30.8 (CH_2 , C-7), 39.9 (C, C-2), 46.9 (C, C-3), 48.7 (CH, C-4), 60.8 (CH_2 , Et), 173.8 (C, C-10), 213.5 (C, C-5); ν_{max}/cm^{-1} 2959, 1752, 1458, 1376, 1185, 1023, 878, 828; m/z (EI) 236 (M^+ , 10), 191 (8), 188 (72), 163 (6), 135 (10), 107 (5); HRMS calc. for $C_{14}H_{20}NaO_3$ 259.1305; found 259.1304.



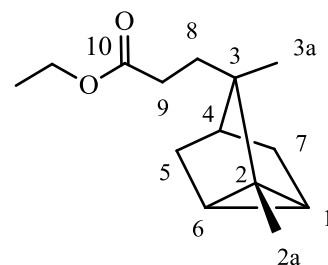
3-(2,3-Dimethyl-5-thio-tricyclo[2.2.1.0^{2,6}]hept-3-yl)propionic acid ethyl ester, 26.

Ester 25 (1.05 g, 4.44 mmol) and Lawessons reagent (0.99 g, 2.45 mmol) were refluxed in dry toluene (50 mL) under an argon atmosphere for 24 hours. The yellow mixture was cooled and the volatiles were removed under vacuum. The residue was subjected to silica gel chromatography (elution with 10% ethyl acetate in petroleum ether). The title compound was isolated as a yellow oil (0.89 g, 80%). δ_H ($CDCl_3$) 1.02 (3H, s, H-2a), 1.24 (3H, s, H-3a), 1.26 (3H, t, $J = 7$ Hz, CH_3 of Et), 1.62 (1H, ddd, $J = 6, 12, 14$ Hz, H-8a), 1.76 (1H, ddd, $J = 5, 11, 14$ Hz, H-8b), 1.90 (1H, m, H-1), 1.90-2.40 (4H, 2 x CH_2 , m, H-7, H-9), 2.10 (1H, m, H-4), 2.3 (1H, m, H-6), 4.10 (2H, q, $J = 7$ Hz, CH_2 of Et); δ_C {H} ($CDCl_3$) 10.8 (CH_3 , C-2a), 14.2 (CH_3 , Et), 16.8 (CH_3 , C-3a), 30.7 (2 x CH_2 , C-7 and C-8), 32.8 (CH_2 , C-9), 36.0 (CH, C-1), 45.4 (CH, C-6), 46.7 (C, C-2), 50.1 (C, C-3), 59.7 (CH, C-4), 60.8 (CH_2 , Et), 173.5 (C, C-10), 260 (C, C-5); ν_{max}/cm^{-1} 2956, 2874, 1732, 1455, 1340, 1181, 1098, 1078, 1026, 868, 815; m/z (EI) 253 (23), 252 (M^+ , 100), 151 (47), 145 (38); HRMS calc. for $C_{14}H_{20}NaO_2S$ 275.1078; found 275.1076.



3-(2,3-Dimethyl-tricyclo[2.2.1.0^{2,6}]hept-3-yl)propionic acid ethyl ester, 27.

Ester 26 (0.18 g, 0.71 mmol) and nickel(II) chloride (0.28 g, 2.16 mmol) were stirred in absolute ethanol (20 mL) under an argon atmosphere. Sodium borohydride (0.25 g, 6.61 mmol) was added portionwise over five minutes, after which the mixture was brought to reflux. After one hour, the black mixture was cooled and filtered through a bed of Celite®. The filtrate was concentrated *in vacuo* and the residue was subjected to silica gel chromatography (elution with 10% ethyl acetate in petroleum ether). The title compound was isolated as a colourless oil (0.12 g, 75%). δ_H ($CDCl_3$) 0.81 (3H, s, H-3a), 0.85 (2H, m, H-4 and H-6), 1.02 (3H, s, H-2a), 1.05 (1H, m, H-8a), 1.26 (3H, t, $J = 7$ Hz, CH_3 of Et), 1.40-1.50 (4H, CH_2 , m, H-5 & H-7), 1.60 (2H, m, H-1 and H-8b), 2.21 (2H, m, H-9), 4.12 (2H, q, $J = 7$ Hz, CH_2 of Et); δ_C {H} ($CDCl_3$) 9.4 (CH_3 , C-2a), 13.6 (CH_3 , Et), 16.5 (CH_3 , C-3a), 18.8 (CH, C-1), 18.9 (CH, C-6), 26.7 (C, C-2), 28.8 (CH_2 , C-5), 29.6 (CH_2 , C-8), 30.3 (CH_2 , C-7), 30.9 (CH_2 , C-9), 37.4 (CH, C-4), 44.9 (C, C-3), 59.6 (CH_2 , Et), 173.8 (C, C-10); ν_{max}/cm^{-1} 2946, 2876, 1738, 1462, 1372, 1179, 1113, 853; m/z (EI) 222 (M^+ , 63), 121 (85), 93 (100); HRMS calc. for $C_{14}H_{22}NaO_2$ 245.1512; found 245.1514.



3-(2,3-Dimethyl-tricyclo[2.2.1.0^{2,6}]hept-3-yl)propionic acid (α -ekasantalic acid), 14.

Aqueous sodium hydroxide (1 M, 1 mL) was added to a solution of ester 27 (0.10 g, 0.45 mmol) in THF (9 mL). After 24 hour, solvent was removed and hydrochloric acid (0.2 M, 6 mL) was added. The resulting solution was extracted with dichloromethane (5 x 10 mL). The title compound was isolated as a foam (83 mg, 95%). δ_H ($CDCl_3$) 0.82 (3H, s, H-3a), 0.87 (2H, m, H-4 and H-6), 1.02 (3H, s, H-2a), 1.09 (1H, m, H-8a), 1.45-1.50 (4H, CH_2 , m, H-5 & H-7), 1.59 (2H, m, H-1 and H-8b), 2.22 (2H, m, H-9); δ_C {H} ($CDCl_3$) 11.0 (CH_3 , C-2a), 17.6 (CH_3 , C-3a), 19.8 (CH, C-1), 19.9 (CH, C-6), 27.7 (C, C-2), 29.82 (CH_2 , C-5), 30.6 (CH_2 , C-9), 31.3 (CH_2 , C-7), 31.9 (CH_2 , C-8), 38.4 (CH, C-4), 45.9 (C, C-3), 174.8 (C, C-10); ν_{max}/cm^{-1} 2956, 2866, 1724, 1452, 1382, 873; m/z (EI) 217 (M^+ , 33), 93 (83); HRMS calc. for $C_{12}H_{18}NaO_2$ 217.1204; found 217.1205.

