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Highly Functionalized Enantiopure Oxatricyclo[3.3.1.0^{4,6}]nonanes; Selective Opening of an Activated Cyclopropane Ring

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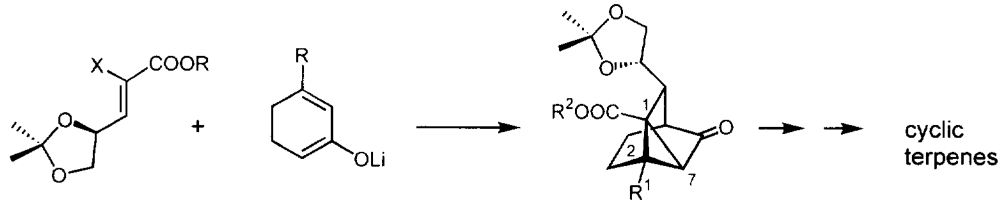
Abstract: Baeyer-Villiger oxidation of **3** gives solely the lactones **4**. The double-pull-push substituted cyclopropane moiety of **4b** is selectively opened upon hydrogenolysis of the benzyl ether to yield ketone **5**. Copyright © 1996 Elsevier Science Ltd

Functionalized tricyclo[3.2.1.0^{2,7}]octanes are valuable starting materials in the total synthesis of terpenoid natural products such as kaurene, gibberellins and grayanotoxin.[1] Enantiopure tricyclo[3.2.1.0^{2,7}]octanes **3** are obtained by a diastereoselective cascade reaction[2] of the chiral Michael acceptors (+)-**1** with the dienolates **2** (d. e. >95%). The absolute configuration of **3b**[3] was deduced from the CD spectrum [CD (methanol): λ_{max} (Θ /$\Delta\epsilon$) = 286.5 nm (+ 14984 / + 4.54)] which is similar to that of **3a** [CD (methanol): λ_{max} (Θ /$\Delta\epsilon$) = 287 nm (+ 13504/ + 4.09)].[4]

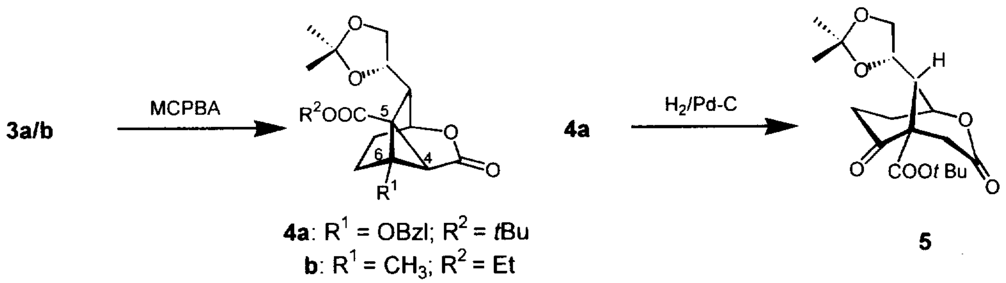


1a: R = *t*Bu; X = Cl
b: R = Et; X = Br

2a: R = OBzl
b: R = CH$_3$

3a: R^1 = OBzl; R^2 = *t*Bu
b: R^1 = CH$_3$; R^2 = Et

In order to extent the range of accessible carbon skeletons starting from **3** we investigated the insertion of additional hetero atoms. Baeyer-Villiger oxidation[5] of **3** with MCPBA in dichloromethane buffered with solid KHCO$_3$ gave exclusively the lactones **4** in good yields.[6] The bridge head C-5 of the parent tricyclo[3.2.1.0^{2,7}]octane **3** migrated in both cases. Hydrogenolysis of the benzyl ether of **4a** gave an intermediate double-pull-push activated cyclopropanol[7] which spontaneously underwent a retro-grade aldol reaction to give the oxabicyclo[3.3.1]nonane **5** (cleavage of the C4-C6 bond).[8] The alternative opening of the C5-C6 bond was not observed:



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3. **3b**: 68 %, oil. - $[\alpha]^{25}_{D}$ = + 54.0° (c = 1.42 in $CHCl_3$). - ^{13}C NMR($CDCl_3$): δ = 13.93 (q), 20.35 (q), 23.88 (t, C-4), 24.67 (t, C-3), 25.53 (q), 26.41 (q), 40.44 (s, C-2), 42.24 (s, C-1), 42.52 (d, C-8), 44.15 (d, C-7), 44.73 (d, C-5), 61.02 (t), 70.10 (t, C-5'), 75. 60 (d, C-4'), 107.85 (s, C-2'), 169.42 (s), 210.49 (s, C-6).
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6. **4a**: 90 %, white crystals, mp 117-119°C. - $[\alpha]^{24}_{D}$ = + 38.1° (c = 1.12 in $CHCl_3$). - ^{13}C NMR($CDCl_3$): δ = 21.61 (t, C-7), 22.12 (t, C-8), 24.67 (q), 26.58 (q), 27.63 (q), 33.53 (d, C-9), 40.17 (d, C-4), 40.40 (s, C-5), 66.72 (s, C-6), 69.98 (t, C-5'), 70.67 (t), 74.35 (d, C-1), 75.65 (d, C-4'), 82.88 (s), 108.83 (s, C-2'), 127.82, 127.93, 128.29 (d), 136.61 (s), 166.01 (s), 168.54 (s, C-3). **4b**: 55 %, oil. - $[\alpha]^{24}_{D}$ = + 43.8° (c = 1.28 in $CHCl_3$). - ^{13}C NMR($CDCl_3$): δ = 13.75 (q), 20.69 (t, C-8), 23.64 (q), 24.15 (t, C-7), 24.79 (q), 26.21 (q), 29.62 (s, C-6), 33.70 (d, C-9), 37.14 (s, C-5), 39.08 (d, C-4), 61.30 (t), 69.63 (t, C-5'), 74.11 (d, C-1), 75. 68 (d, C-4'), 108.42 (s, C-2'), 168.87 (s, C-3), 169.31 (s).
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8. **5**: 96 %, white crystals, mp 123-125°C. - $[\alpha]^{24}_{D}$ = + 58.1° (c = 1.08 in $CHCl_3$). - ^{13}C NMR($CDCl_3$): δ = 24.59 (q), 26.50 (q), 27.82 (q), 28.18 (t, C-8), 33.37 (t, C-7), 37.76 (t, C-4), 48.26 (d, C-9), 58.36 (s, C-5), 71.66 (t, C-5'), 73.83 (d, C-1), 75.05 (d, C-4'), 83.57 (s). 108.96 (s, C-2'), 167.84 (s), 168.54 (s, C-3), 205.00 (s, C-6).

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