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Novel Cyclopenta[*c*]benzofuran Intermediates for the Synthesis of Acorane–Alaskane Sesquiterpenes: Total Synthesis of (±)-β-Acorenol and (±)-Acorenone

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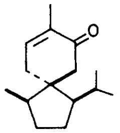
Cyclopenta[*c*]benzofuran derivatives (**5a**) and (**5b**) were synthesized from spirodienone esters (**6a**) and (**6b**), respectively, and the utility of these intermediates in acorane–alaskane sesquiterpene synthesis is illustrated by their conversion into (±)-β-acorenol (**4a**) and (±)-acorenone (**1**).

The acorane–alaskane family is a large group of sesquiterpenes having the spiro[4.5]decane skeleton.[1] This family is important as members are intermediates in terpene biogenesis and constituents of essential oils. Although synthetic studies of this family, for example acorenone (**1**) and acorenone B (**2**), have been reported,[2] only two groups have reported the synthesis of the compounds bearing tertiary hydroxy groups, *e.g.*, α- (**3**) and β-acorenol (**4a**).[2c,3] We now present a new, flexible synthetic route to this family using the reductive fission of the novel cyclopenta[*c*]benzofuran derivatives (**5a**) and (**5b**).

The *trans*- (**6a**) and *cis*-spirodienone esters (**6b**)[4] were treated with methyl-lithium (5 equiv.) to give diols (**7a**) and (**7b**) which afforded tricyclic dienes (**5a**) and (**5b**) by treatment with Lewis acids [SiO_2 for (**7a**) and $Mg(ClO_4)_2$ for (**7b**)] in 35 and 90% yields, respectively.† The A–C ring junction is *cis*, by



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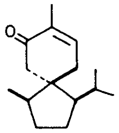

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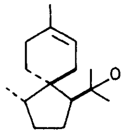

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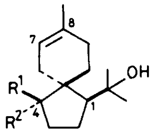
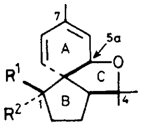
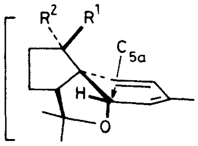
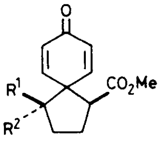


(4a)
(4b)

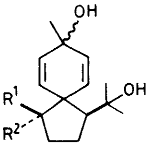


(5a)
(5b)

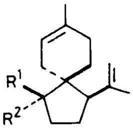




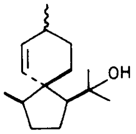
(6a)
(6b)



(7a)
(7b)



(8a)
(8b)



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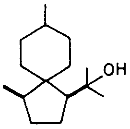

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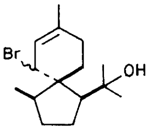

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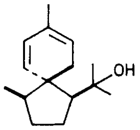

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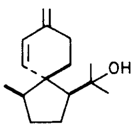

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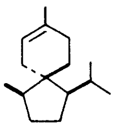

(14)

a; $R^1 = H, R^2 = Me$; **b**; $R^1 = Me, R^2 = H$

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† *Selected spectral data.* (**5a**): $\nu_{max.}$ 1670 cm^{-1}; $\lambda_{max.}$ 259 nm; δ 0.87 (3 H, d, *J* 6.5 Hz, 1-Me), 1.10, 1.13 (6 H, 2 × s, 4-Me_2), 1.77 (6 H, s, 7-Me), 5.40 (1 H, m, 6-H), 5.5—5.8 (2 H, AB q, 8- and 9-H); M^+ *m/z* 218. (**5b**): $\nu_{max.}$ 1675 cm^{-1}; $\lambda_{max.}$ 259 nm; δ 0.76 (3 H, d, *J* 6.0 Hz, 1-Me), 1.09, 1.12 (6 H, 2 × s, 4-Me_2), 1.78 (3 H, s, 7-Me), 4.02 (1 H, br. d, *J* 5 Hz, 5a-H), 5.3—5.6 (1 H, m, 6-H), 5.46 (1 H, d, *J* 9.5 Hz, 9-H), 5.71 (1 H, dd, *J* 9.5 and 1 Hz, 8-H); M^+ *m/z* 218. (**4b**): $\nu_{max.}$ 3440 cm^{-1}; δ 0.92 (3 H, d, *J* 7 Hz, 4-Me), 1.18, 1.23 (6 H, 2 × s, CMe_2OH), 1.62 (3 H, br. s, 8-Me), 5.21 (1 H, m, 7-H); $M^+ - H_2O$ *m/z* 204. (**9**), $\nu_{max.}$ 3620 and 3575 cm^{-1}; δ 0.94 (3 H, d, *J* 6.3 Hz, 4-Me), 0.96 (3 H, d, *J* 6.5 Hz, 8-Me), 1.13, 1.22 (6 H, 2 × s, CMe_2OH), 5.11, 5.44 (2 H, 2 × br. d, *J* 10 Hz, 6- and 7-H); M^+ *m/z* 222. (**11**): $\nu_{max.}$ 3400 cm^{-1}; δ 0.93 (3 H, d, *J* 6.3 Hz, 4-Me), 1.16, 1.19 (6 H, 2 × s, CMe_2OH), 3.55 (1 H, br. d, *J* 5.5 Hz, 6-H), 5.43 (1 H, m, 7-H); $M^+ - HBr$ *m/z* 220. (**8b**): $\nu_{max.}$ 3070, 3010, 1640, and 895 cm^{-1}; δ 0.95 (3 H, d, *J* 6 Hz, 4-Me), 1.59 (6 H, br. s, $CMe{=}CH_2$ and 8-Me), 4.68, 4.77 (2 H, 2 × br. s, $C{=}CH_2$), 5.24 (1 H, m, 7-H); M^+ *m/z* 204.

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considering the reaction mechanism and the coupling constant of the allylic methine proton (5a-H).[5] The *J* value (5 Hz) of the 5a-H of (**5b**) shows that this proton is quasi-equatorial. If the A–C rings fusion was *trans*, this proton could only be quasi-axial. Although the *J* value of this proton in (**5a**) is uncertain, the A–C ring fusion would be expected to be *cis* as in (**5b**).

The reductive fission of the allylic ether bond and the 1,4-reduction of the conjugated diene of (**5a**) with lithium (20 equiv.) in liquid ammonia containing t-butyl alcohol at −40 °C afforded stereoselectively (±)-β-acorenol (**4a**) in 81% yield and the dehydration of (**4a**) by a known method[6] gave (±)-β-acoradiene (**8a**).

Reduction of compound (**5b**) under the same conditions gave 4-*epi*-β-acorenol (**4b**), the spiro-alkene (**9**),† and the perhydro compound (**10**) in 23, 34, and 43% yields, respectively. The conditions for the reduction of (**5b**) were varied (Li, Na, K, and Ca; −20, −33, −40, and −60 °C), but the yields of (**4b**) were always in the range 20—25%, and under certain conditions [*e.g.*, K (20 equiv.), −33 °C] the spiro-alkene (**9**) was the major product (54%). Bromination of (**9**) followed by dehydrobromination with 1,8-diazabicyclo[5.4.0]undec-7-ene afforded the allylic bromide (**11**) in 63% yield.† Attempted reductive debromination of (**11**) under various conditions failed. Further dehydrobromination (NaI–pyridine–dimethylformamide) of (**11**) afforded the dienes (**12**) [$\lambda_{max.}$ 269 nm; M^+ m/z 220] and (**13**) [$\lambda_{max.}$ 235 nm; M^+ m/z 220] in 32 and 27% yields, respectively. Metal–ammonia reduction of (**13**) afforded 4-*epi*-β-acorenol (**4b**) in 90% yield, while unexpectedly the same reduction of (**12**) afforded mainly compound (**9**).

Dehydration (Al_2O_3–pyridine, 200 °C) of (**4b**) gave 4-*epi*-β-acoradiene (**8b**) in 78% yield.† Selective reduction (Li–$EtNH_2$, room temp.) of the terminal olefin[7] of (**8b**) afforded a mono olefin (**14**) (100%), [δ 5.27 (1 H, m, 7-H); M^+ m/z 206] which was oxidized with selenium dioxide in ethanol to give (±)-acorenone (**1**)[8] in 75% yield.

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