Synthesis of *cis-transoid-cis-* and *cis-cisoid-cis-* Tricyclo[6.3.0.0^{2,6}]undecan-1-ols

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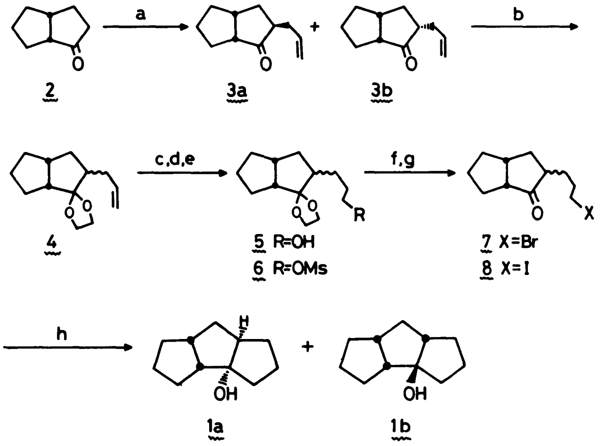
Synopsis. Two isomeric linear triquinanes, *cis-transoid-cis-* and *cis-cisoid-cis-*tricyclo[6.3.0.0^{2,6}]undecan-1-ols, were effectively synthesized by means of the modified Barbier cyclization.

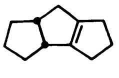
Recently, much attention has been focused on linearly fused triquinanes (tricyclo[6.3.0.0^{2,6}]undecanes), since a lot of natural products which possess this ring system have been found out and some of them, such as hirsutic acid and coriolin, display significant levels of biological activities.$^{1)}$ In this connection, we wish to report here the facile synthesis of two isomeric linear triquinanes, *cis-transoid-cis-* and *cis-cisoid-cis-*tricyclo[6.3.0.0^{2,6}]undecan-1-ols (**1a**) and (**1b**) by means of a new cyclopentane annelation, that is, the modified Barbier cyclization.$^{2)}$



Scheme 1.

a) CH_2=$CHCH_2OH$, $CH_3C(OCH_3)_2CH_3$, TsOH, △; b) $HO(CH_2)_2OH$, TsOH; c) B_2H_6; d) H_2O_2; e) CH_3SO_2Cl (MsCl), Et_3N; f) LiBr; g) NaI; h) Mg, $HgCl_2$.

An ingenious adaptation of the Claisen rearrangement$^{3)}$ of a diquinane, *cis*-bicyclo[3.3.0]octan-2-one (**2**),$^{4)}$ gave the 3-allyl derivatives **3a** and **3b** (an approximate 1:1 ratio) in 73% yield. The mixture **3a** and **3b** was readily transformed to the 3-iodopropyl derivatives **8** as follows: i) acetalization, ii) hydroboration-oxidation of the acetals **4**, iii) mesylation of the alcohols **5**, iv) reaction of the mesylates **6** with lithium bromide,$^{5)}$ and v) treatment of the bromides **7** with sodium iodide. Finally, reaction of **8** with magnesium activated by $HgCl_2$ afforded the desired alcohols **1a** and **1b** in 17% and 11% isolated yields from **3a** and **3b**, which were readily separated by column chromatography on silica gel.



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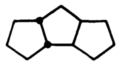
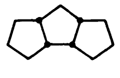
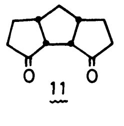


10a



10b



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Their structures were elucidated on the basis of spectroscopic data and the following chemical transformations. Elimination of the mesylates of **1a** and **1b** with $LiAlH_4$$^{6)}$ gave the same olefin, *cis*-tricyclo[6.3.0.0^{2,6}]undec-1(8)-ene (**9**), in 65% and 67% yields, respectively. Hydrogenation of **9** with Pd on charcoal gave two hydrocarbons, tricyclo[6.3.0.0^{2,6}]undecanes (**10a**) and (**10b**), in 43% and 35% yields. The hydrocarbon **10b** was also obtained in 45% yield by reductive deoxygenation$^{7)}$ of the diethyl phosphate of **1b** with lithium in diethylamine. The *cis-cisoid-cis* stereochemistry of **10b** was determined by comparison with the authentic sample derived from *cis-cisoid-cis*-tricyclo[6.3.0.0^{2,6}]undecane-3,11-dione (**11**)$^{8)}$ by Wolff-Kishner reduction. Consequently, **1b** was established to be the *cis-cisoid-cis*-isomer, and **1a** and **10a** were characterized to be *cis-transoid-cis*-isomers.

Experimental

All boiling points are uncorrected. Measurements of IR, MS, ^1H NMR, and ^{13}C NMR as well as analytical and preparative GLC were done on the same instruments as in the previous work.$^{6)}$ Column chromatography was carried out with silica gel (Wakogel C-200). Yields were calculated from the isolated products based on the consumed starting materials.

exo- *and* endo-*3-(2-Propenyl)-*cis-*bicyclo[3.3.0]octan-2-ones (3a) and (3b).* A solution composed of **2** (10.0 g, 80.6 mmol), allyl alcohol (11.2 g, 193 mmol), 2,2-dimethoxypropane (10.0 g, 96.2 mmol), and *p*-toluenesulfonic acid monohydrate ($TsOH \cdot H_2O$) (10 mg) and benzene (44 ml) was distilled through a spinning band column and operated at a reflux ratio of 10. After 19 ml of distillate had been collected at 55—60 °C, the distillation was continued with a reflux ratio of 3 until the overhead temperature reached 95 °C. Yellow residue was distilled *in vacuo* to give the recovered **2** (3.59 g; bp 51 °C/2 mmHg (mmHg=133.322 Pa)) and the allyl ketones **3a** and **3b** (6.21 g, 73%; bp 70 °C/1 mmHg) which were purified by column chromatography. Since **3a** and **3b** could not be separated by GLC or column chromatography, they were characterized as a mixture (an approximate 1:1 ratio calculated from ^{13}C NMR spectrum). **3a** and **3b**: IR 3080, 1740, 1640, 915 cm^{-1}; MS *m/z* 164 (M^+), 68 (base); ^{13}C NMR ($CDCl_3$) δ=223.4 (s), 220.9 (s), 136.1 (d), 135.9 (d), 116.2 (t), 115.9 (t), 52.2 (d), 51.3 (d), 49.8 (d), 46.6 (d), 38.5 (d), 37.8 (d), and ten triplets. Found: C, 80.56; H, 10.05%. Calcd for $C_{11}H_{16}O$: C, 80.44; H, 9.83%.

cis-transoid-cis- *and* cis-cisoid-cis-*Tricyclo[6.3.0.0^{2,6}]undecan-1-ols (1a) and (1b).* Reaction[9] of **3a** and **3b** (6.39 g, 39 mmol), ethylene glycol (12.2 g, 194 mmol), and TsOH·H_2O (194 mg) in toluene (220 ml) gave the acetals **4**: IR 3070, 1040, 915 cm^{-1}. Hydroboration[6] of the crude acetals **4** with diborane generated from $NaBH_4$ (2.94 g, 26.0 mmol) and $BF_3·Et_2O$ (4.24 g, 31.2 mmol) in THF (170 ml), and the subsequent oxidation with H_2O_2 gave the alcohols **5**: IR 3400, 1040 cm^{-1}. Mesylation[9] of the crude alcohols **5** with methanesulfonyl chloride (9.1 ml, 116 mmol) and triethylamine (27.2 ml, 194 mmol) in dry ether (300 ml) gave the mesylates **6**: IR 1345, 1170 cm^{-1}. Reaction[9] of the crude mesylates **6** with lithium bromide (12.5 g, 119 mmol) in acetone (320 ml) gave the bromides **7**: 6.24 g, 65% from **3a** and **3b**; bp 120—122 °C/1.5 mmHg; IR 1735 cm^{-1}.

A suspension of **7** (25.5 mmol) and sodium iodide (7.65 g, 51.0 mmol) in acetone (93 ml) was stirred at room temperature for 2 h. The reaction mixture was concentrated *in vacuo* and ether was added. The organic layer was washed with 10% $NaHSO_3$ solution, water, and dried ($MgSO_4$). The solvent was removed *in vacuo* to give the crude iodides **8**: IR 1735 cm^{-1}.

A mixture of magnesium (1.7 g, 70.0 mmol) and $HgCl_2$ (0.4 g) in THF (90 ml) was heated to 45 °C. A solution of the above iodides **8** in THF (55 ml) was added over a period of *ca.* 30 min. During addition the temperature of the reaction mixture was maintained at 45—50 °C. After refluxing for 24 h, the mixture was hydrolyzed with water and decanted from the excess magnesium. The solution was extracted with ether and the organic layer was washed with water, dried ($MgSO_4$), and concentrated *in vacuo*. The residue was chromatographed to give the alcohols **1a** and **1b**. **1a**: 1.08 g, 26% from **8**; IR 3350 cm^{-1}; MS *m/z* 166 (M$^+$), 84 (base); ^{1}H NMR (CCl_4) δ=1.3—2.6 (m); ^{13}C NMR ($CDCl_3$) δ=92.0 (s), 53.1 (d), 50.4 (d), 42.9 (d), 41.5 (t), 37.7 (t), 34.1 (t), 30.8 (t), 28.1 (t), 26.6 (t), 23.7 (t). Found: C, 79.33; H, 11.21%. Calcd for $C_{11}H_{18}O$: C, 79.46; H, 10.92%. **1b**: 0.65 g, 17% from **8**; IR 3350 cm^{-1}; MS *m/z* 166 (M$^+$) 119 (base); ^{1}H NMR (CCl_4) δ=0.78 (q, 1H), 1.2—3.0 (m, 17H); ^{13}C NMR ($CDCl_3$) δ=93.6 (s), 55.4 (d), 55.0 (d), 44.8 (d), 39.6 (t), 35.9 (t), 31.8 (t), 29.6 (t), 28.0 (t), 26.6 (t), 25.4 (t). Found: C, 79.16; H, 11.19%. Calcd for $C_{11}H_{18}O$: C, 79.46; H, 10.92%.

cis-*Tricyclo[6.3.0.0^{2,6}]undec-1(8)-ene (9).* Mesylation of **1a** (50 mg, 0.30 mmol) as described above followed by treatment[6] of the crude mesylate with $LiAlH_4$ (23 mg, 0.60 mmol) gave the olefin **9**: 29 mg, 65% from **1a**; MS *m/z* 148 (M$^+$), 119 (base); ^{1}H NMR (CCl_4) δ=1.2—2.4 (m, 14H), 2.6—3.2 (m, 2H); ^{13}C NMR ($CDCl_3$) δ=148.2 (s), 144.4 (s), 47.6 (d), 46.8 (d), 37.4 (t), 35.7 (t), 30.3 (t), 29.4 (t), 28.2 (t), 27.9 (t), 26.0 (t). Found: C, 88.89; H, 11.14%. Calcd for $C_{11}H_{16}$: C, 89.12; H, 10.88%. The isomeric alcohol **1b** (50 mg, 0.30 mmol) was dehydrated as described for **1a** to give **9** (30 mg, 67%).

cis-transoid-cis- *and* cis-cisoid-cis-*Tricyclo[6.3.0.0^{2,6}]undecanes (10a) and (10b).* The olefin **9** (217 mg, 1.46 mmol) was hydrogenated as described previously[6] to give the two hydrocarbons **10a** and **10b**. **10a**: 95 mg, 43%; MS *m/z* 150 (M$^+$), 67 (base); ^{13}C NMR ($CDCl_3$) δ=52.3 (d, 2C), 44.8 (d, 2C), 40.1 (t), 33.9 (t, 2C), 32.9 (t, 2C), 26.1 (t, 2C). Found: C, 87.76; H, 12.32%. Calcd for $C_{11}H_{18}$: C, 87.92; H, 12.08%. **10b**: 78 mg, 35%; MS *m/z* 150 (M$^+$), 67 (base); ^{13}C NMR ($CDCl_3$) δ=47.3 (d, 2C), 47.2 (d, 2C), 40.2 (t), 31.5 (t, 2C), 28.4 (t, 2C), 27.2 (t, 2C). Found: C, 87.78; H, 12.36%. Calcd for $C_{11}H_{18}$: C, 87.92; H, 12.08%.

*Synthesis of **10b** by Reductive Deoxygenation from **1b**.* The reaction of the lithium alkoxide [derived from **1b** (486 mg, 2.93 mmol) and butyllithium (1.56 M hexane solution (1 M=1 mol dm^{-3}), 3.9 ml, 5.96 mmol)] with diethyl phosphorochloridate (506 mg, 2.93 mmol) gave the diethyl phosphate: IR 1250, 1010 cm^{-1}. Treatment of the crude phosphate with lithium (200 mg) in dry diethylamine (140 ml) followed by *t*-BuOH (1.5 ml) and THF (40 ml) gave 199 mg (45% from **1b**) of **10b** after usual workup.[7]

*Synthesis of an Authentic Sample of **10b**.* Wolff-Kishner reduction of the diketone **11**[8] (500 mg, 2.81 mmol) as described previously[6] gave the hydrocarbon (165 mg, 39%) whose Mass and ^{13}C NMR spectra were identical with those of **10b**.

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