Discriminative Synthesis of Fused and Spiro Ring Systems from a Common Intermediate[1]

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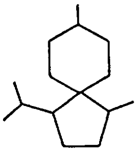
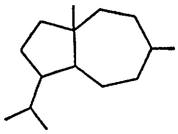
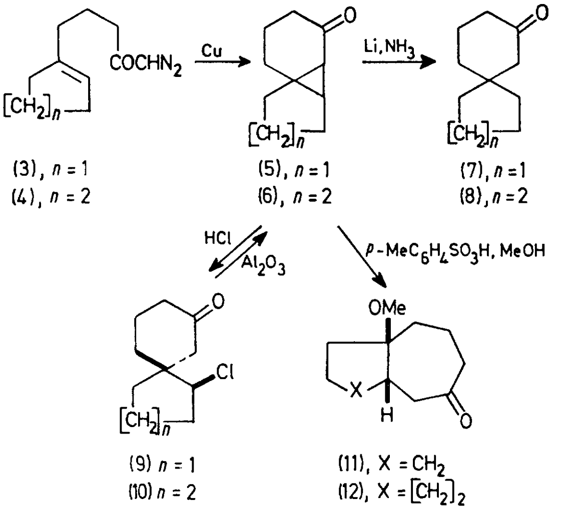
Summary The tricyclic ketones (**5**) and (**6**) are converted selectively into spiro or fused ring systems upon reduction with lithium–ammonia or acidic methanolysis respectively

Skeletal types among sesquiterpenes include a number of structural pairs, in which ring frames are differentiated by a single carbon–carbon bond transposition.[2] For example, the acorane (**1**)–carotane (**2**) pair contain the spiro[5.4] decane[3] and perhydroazulene[4] skeletons, respectively.[5] The synthesis of spiro and fused systems of this type[6] in a controlled fashion from a common intermediate should be both economic and versatile. Tricyclic structures, such as (**5**) and (**6**), are logical candidates for this purpose since selective fission of the cyclopropane ring can, in principle, afford direct entry to either spiro or fused skeletons.[7] (±)-Chamigrene, a spiro[5.5]undecane, has recently been synthesised by this type of approach.[1] There remain, however, crucial questions concerning (i) the regioselectivity to be expected from the two ring-cleavage modes and (ii) the configuration at spiro centre and ring fusion, as well as


(1)


(2)

adjacent centres, resulting from the projected fragmentation. The work described herein is relevant to both these questions.



(3), n = 1
(4), n = 2
(5), n = 1
(6), n = 2
(7), n = 1
(8), n = 2
(9) n = 1
(10) n = 2
(11), X = CH$_2$
(12), X = [CH$_2$]$_2$

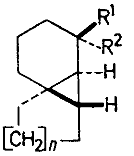
The tricyclodecanone (**5**) (1685 cm^{-1}; 2,4-dinitrophenylhydrazone, m.p. 171—174 °C) was obtained by decomposition of the diazo-ketone (**3**),[8] prepared from 4-cyclopentenylbutyric acid[9] [NaH, (COCl)$_2$, followed by CH$_2$N$_2$], in the presence of copper bronze (refluxing cyclohexane; 4 h). An analogous sequence, starting from the corresponding cyclohexenylbutyric acid, gave (**4**) and the crystalline tricycloundecanone (**6**) (m.p. 50—51 °C; 1690 cm^{-1}). With lithium in ammonia–ether, (**5**) and (**6**) were converted (*ca.* 55% after chromatography on alumina) into the spiro-[5.4] and [5.5] ketones (**7**) and (**8**), respectively. As noted previously,[1] conformational analysis of (**5**) and (**6**), together with application of the well established principle of stereoelectronic control in the dissolving-metal reduction of cyclopropyl ketones,[10] dictates that cleavage of the peripheral bond should be strongly preferred.

TABLE

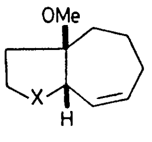
Alcohols (**15**) : (**16**)	Yield of (**18**) (%)	*cis* : *trans* ratio of product
47 : 53[a,b]	69	3 : 1
5 : 95[a,b]	75	3 : 1
20 : 80[a,c]	75	9 : 1

[a] Reactions were carried out for 0·5 h in methanol containing one drop of 70% perchloric acid. [b] At 20 °C. [c] At 0 °C.

Fission of the cyclopropane ring in (**5**) and (**6**), when carried out in a two-phase system of concentrated hydrochloric acid and ether, led in each case to a single, bicyclic chloro-ketone, the structures of which were established as (**9**) and (**10**) on the basis of spectral evidence (ketone CO band at 1715 cm^{-1}; secondary chloride resonance at δ 3·8, 1H, m), and also from the finding that chromatography on alumina (neutral, activity II) regenerated the tricyclic precursor (**5**) and (**6**) in quantitative yield in each case. The latter result strongly implies the configuration indicated in (**9**) and (**10**), in which the ready displacement of chloride results from a stereoelectronically favourable relationship of leaving group and internal enolate anion.



(13), R^1 = H, R^2 = OH, n = 1
(14), R^1 = OH, R^2 = H, n = 1
(15), R^1 = H, R^2 = OH, n = 2
(16), R^1 = OH, R^2 = H, n = 2



(17), X = CH$_2$
(18), X = [CH$_2$]$_2$

In contrast, treatment of (**5**) and (**6**), in methanol, with toluene-p-sulphonic acid gave (**11**) and (**12**) respectively. The formation of fused structures in this case was indicated by the presence of a tertiary methyl ether (δ 3·3, 3H, s), and is consistent with ring opening of the cyclopropyl ketone *via* a carbonium ion, which is subsequently trapped by solvent. Each ketone (**11**) and (**12**), was found by g.l.c. to consist of a pair of stereoisomers (*cis*/*trans* fusion; only the *cis*-isomer is shown), but these could not be separated. However, reduction of (**5**) and (**6**) (NaBH$_4$, MeOH) to *exo* (**13**, **15**) and *endo* (**14**, **16**) alcohols,† followed by acid-catalysed (HClO$_4$) methanolysis, gave (**17**) and (**18**), which were shown to be predominantly the *cis* fused isomers in each instance. The data in the Table show that the *cis*: *trans* product ratio in the case of (**18**) is independent of the configuration of the hydroxy-group in the starting material and, when taken with the observation that *cis* isomers of (**17**) and (**18**) are slowly converted into their more stable *trans* counterparts under the reaction conditions, indicate that *cis* stereoisomers are initially formed in this reaction with virtually complete stereoselectivity.

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† *Exo*/*endo* ratio was 1 : 3 for (**5**) and 1 : 4 for (**6**) as determined by n.m.r. spectroscopy [the proton C*H*OH in *endo* isomers (**14**), (**16**) resonates upfield (δ 3·90—3·95) of that in *exo* isomers (**13**), (**15**) (δ 4·1—4·2)].

[1] For previous paper in the series 'Annelation *via* Cyclopropyl Ketones,' see J. D. White, S. Torii, and J. Nogami, *Tetrahedron Letters*, 1974, 2879.

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