Some Cation-induced Bicyclisations

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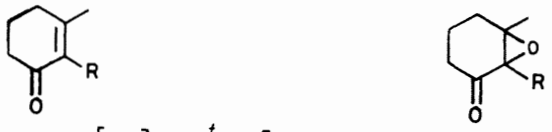
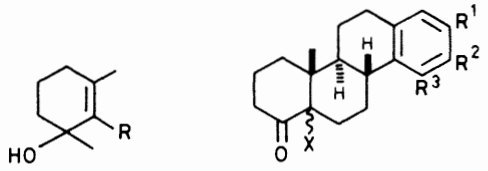
Summary Cyclisations of the enones (**1**)—(**3**) and the related epoxides (**4**)—(**6**) have been investigated and shown to give tetra- and tri-cyclic compounds in variable yield.

IN continuation of our work[1] on polyene cyclisations we have examined the bicyclisations of compounds (**1**)—(**7**), which are readily available by a route previously described.[2] Cyclisation of (**5**) with BCl_3–CH_2Cl_2 at −78 °C gave† partially cyclised (**13**) (57%) [ν_{max} 3560 and 1715 cm^{-1}; τ ($CDCl_3$) 2·80 (1H, m), 3·28 (3H, m), 5·82 (1 H, m, $\omega_{1/2}$ 23 Hz), and 9·03 (3H, s)], and the tetracycle‡ (**8**) (9%) [ν_{max} 3590 and 1710 cm^{-1}; τ ($CDCl_3$) 2·82 (1H, d, J 9 Hz), 3·29 (1H, dd, J 9 and 3 Hz), 3·40 (1H, d, J 3 Hz), and 8·93 (3H, s)]. The epoxide (**4**), under identical conditions, gave equally disappointing results, the major product (51%) being assigned structure (**14**) on mechanistic and spectroscopic grounds [ν_{max} 3600 cm^{-1}; τ ($CDCl_3$) 3·05 (4H, m), 9·08 (3H, s)] while the tetracycle (**9**) [ν_{max} 3590 and 1710 cm^{-1}; τ ($CDCl_3$) 3·04 (1H, d, J 8·5 Hz), 3·80 (1H, d, J 2·5 Hz), 3·34 (1H, dd, J 8·5 and 2·5 Hz), and 8·92 (3H, s)] was formed in only 4% yield.§

Harding's demonstration[3] that protonation of enol-acetates of cyclohexenones provided good initiating cations for monocyclisation prompted us to investigate this system for bicyclisations, and we found, as did Harding,[4] that enol-trifluoroacetates were superior. Reaction of (**1**) with $(CF_3CO)_2O$–CF_3CO_2H at 0 °C gave, after hydrolysis (KOH–MeOH), the tetracycle (**10**) (81%) [ν_{max} 1710 cm^{-1}; τ ($CDCl_3$) 2·98 (1H, d, J 8·4 Hz), 3·10 (1H, d, J 2·4 Hz), 3·28 (1H, dd, J 8·4 and 2·4 Hz), 9·22 (3H, s)]. Cyclisation of (**2**) under similar conditions yielded (**11**) (56%) [ν_{max} 1710 cm^{-1}; τ ($CDCl_3$) 2·75 (1H, d, J 8·4 Hz), 3·24 (1H, dd, J 8·4 and 2·4 Hz), 3·34 (1H, d, J 2·4 Hz) and 9·22 (3H, s)], and (**12**)¶ (14%) [ν_{max} 1710 cm^{-1}; τ ($CDCl_3$) 2·82 (1H, d, J 6·7 Hz), 3·2—3·5 (2H, m), 9·20 (3H, s)]. In order to compare these

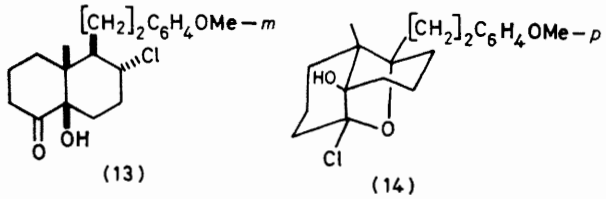


(1) R = $[CH_2]_2CH{=}^{t}CH[CH_2]_2C_6H_4OMe-p$ (4)
(2) R = $[CH_2]_2CH{=}^{t}CH[CH_2]_2C_6H_4OMe-m$ (5)
(3) R = $[CH_2]_2CH{=}^{t}CH[CH_2]_2C{\equiv}CH$ (6)



(7) R as in (1)

(8) R^1=OMe, R^2=R^3=H, X=β-OH
(9) R^1=R^3=H, R^2=OMe, X=β-OH
(10) R^1=R^3=H, R^2=OMe, X=α-H
(11) R^1=OMe, R^2=R^3=H, X=α-H
(12) R^1=R^2=H, R^3=OMe, X=α-H



(13) (14)

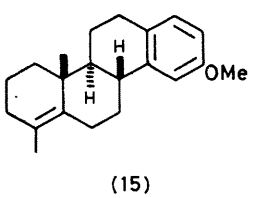
† Other products isolated were the ring-contracted cyclopentanone (14%) and the chlorohydrin (17%).

‡ Other products isolated were the ring-contracted cyclopentanone (18%), the chlorohydrin (3%), and the partially cyclised chloride [*cf.*(**14**) (10%)].

§ A-B Ring junction stereochemistry was assigned by our previously established results (ref. 1). The absence of intramolecular hydrogen bonding (i.r.) supports cyclisation *via* an A-B 'steroid' conformation, *i.e.* diaxial ring opening of the epoxide.

¶ Stereochemistry of the A–B ring systems was assigned using the chemical shifts of the angular Me groups; see L. M. Jackman and S. Sternhell, 'Applications of NMR spectroscopy in Organic Chemistry,' 2nd edn., Pergamon, Oxford and New York, 1969, p. 243. B-C Ring stereochemistry was assumed by analogy, but confirmation is being sought by *X*-ray structure determination.

initiating cations with Johnson's highly successful allyl cations,[5] (**1**) was allowed to react with MeLi to give (**7**) which was cyclised smoothly with HCO_2H–pentane to (**15**) (60%) [τ ($CDCl_3$) 3·05 (1H, d, J 8·4 Hz), 3·17 (1H, d, J 2·7 Hz), 3·38 (1H, dd, J 8·4 and 2·7 Hz), 8·39 (3H, s), and 8·99 (3H, s)].



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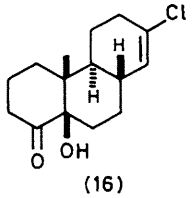

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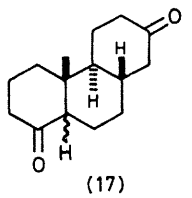

(17)

Cyclisation of the enyne (**6**) with BCl_3–CH_2Cl_2 at −78 °C yielded (**16**) (36%) [ν_{max} 3590 and 1710 cm^{-1}; τ ($CDCl_3$) 4·52 (1H, m) and 9·01 (3H, s)]; here there was no evidence of partially cyclised products. Comparable results were obtained in cyclisation of the enynone (**3**) by the $(CF_3CO)_2O$ –CF_3CO_2H procedure when the *cis*- and *trans*-isomers of (**17**) [*trans*: τ ($CDCl_3$) 9·28 (3H, s); *cis*: 8·94 (3H, s)] were obtained in a combined yield of 40%.

Most of our results can be rationalised on the basis of initial monocyclisation to an intermediate carbonium ion which can react by an inter- or intra-molecular process to give the observed products. However, there are a number of puzzling features; in the cation from monocyclisation of (**4**) the major decomposition pathway is elimination–addition or hydride migration–addition, pathway (a), in the cation from (**5**) it is intermolecular attack by Cl^- pathway (b), and in those from (**1**) and (**2**) it is intramolecular attack by the anisyl rings, pathway (c). Since process (a) is that which occurs in the absence of the *p*-anisyl group it would appear that the *m*-anisyl group somehow allows (b) to become a lower energy process than (a). The virtual absence of pathway (c) in the epoxide cyclisations may be due to the nucleophilicity of the anisyl rings being reduced by complexation with the excess Lewis acid present.

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