Comparison of Two Initiators of Cyclisation derived from Cyclohexen-1-ones

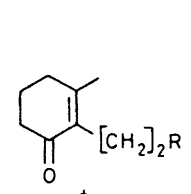
By JOSEPH AMUPITAN, ALBERT SANTOS, and JAMES K. SUTHERLAND*
(*Chemistry Department, The University, Manchester* M13 9PL)

Summary The use of the enol trifluoroacetates of cyclohex-2-en-1-ones for initiating alkene cyclisation is compared with results from cyclisation of the related 2,3-epoxycyclohexanones.

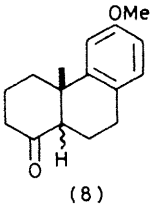
HARDING'S demonstration[1] that protonation of cyclohexadienol acetates provided efficient initiating cations for monocyclisations prompted us to try this route where our Lewis acid–epoxide-induced cyclisations had given poor results.[2] The success of dienol trifluoroacetate in our hands and, independently, in Harding's[3] prompted us to make a more extensive comparison of the alternative methods. Compounds (**3**), (**5**), and (**6**) gave comparable results in both types of cyclisation. Reaction of (**3**) with $(CF_3CO)_2O$–CF_3CO_2H at 0 °C gave, after hydrolysis, the *cis*- and *trans*-isomers† of (**8**) (56%) as an inseparable 2:1 mixture [τ ($CDCl_3$) 2·8—3·5 (3H, m), 8·66 (s), and 8·94 (s)] while the 2,3-epoxide with $SnCl_4$–CH_2Cl_2 at −20 °C, gave the related β-hydroxy compound in 88% yield [ν_{max} 1710 cm^{-1}; τ ($CDCl_3$) 2·95 (1H, dd, J 8 and 1·3 Hz), 3·24 (brs), 3·29 (1H, dd, J 8 and 3·0 Hz), and 8·72 (3H, s)]. Cyclisation of (**5**) gave, after hydrolysis ($NaHCO_3$–H_2O), a mixture (49%) of (**9**) [ν_{max} 1710 cm^{-1}; τ ($CDCl_3$) 7·89 (3H, s) and 8·95 (3H, s)] and (**10**) [ν_{max} 1710 cm^{-1}; τ ($CDCl_3$) 7·81 (3H, s) and 8·72 (3H, s)]. Hydrolysis of the cyclisation product under more vigorous conditions (NaOH–H_2O) gave the aldol product (**11**) [ν_{max} 3580 and 1705 cm^{-1}; τ ($CDCl_3$) 7·43 (1H, d, J 17·5 Hz), 7·81 (1H, d, J 17·5 Hz), and 9·03 (3H, s)].

The same products (30%) were obtained from cyclisation of (**6**) while the corresponding epoxide reacted with BCl_3–CH_2Cl_2 to yield (**12**) (54%) [ν_{max} 3470 and 1710 cm^{-1}; τ ($CDCl_3$) 7·80 (3H, s) and 8·85 (3H, s)]. The related vinyl chloride was obtained from the epoxide of (**5**)[4] (95%). We have already reported[5] that cyclisation of the 2,3-epoxide of (**1**) with BF_3–OEt_2 or $SnCl_4$ yields the mixture of isomers (**13**); BCl_3–CH_2Cl_2 also forms some (**13**) but the major product (84%) is formulated as (**14**) [ν_{max} 3600 cm^{-1}; m.s. 1H exchangeable with D_2O; τ ($CDCl_3$) 8·79 (3H, s), and 9·10 (3H, s)]. $(CF_3CO)_2O$–CF_3CO_2H cyclisation of (**1**) yields (**15**)† (26%) [ν_{max} 3600 and 1710 cm^{-1}; τ ($CDCl_3$) 6·65 (1H, m, $\omega_{1/2}$ 27 Hz), 9·00 (3H, d, J 7 Hz), and 9·35 (3H, s)], (**16**) (15%) [ν_{max} 3600 and 1710 cm^{-1}; τ ($CDCl_3$) 6·55 (1H, m, $\omega_{1/2}$ 25 Hz), 9·01 (3H, s), 9·12 (3H, d, J 8 Hz)], and (**17**) (23%) [$\lambda_{max}^{(MeOH)}$ 245 nm (ϵ 12,600) ν_{max} 1670 and 1610 cm^{-1};

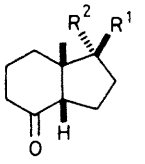
† Stereochemistry was assigned using the chemical shifts of the angular methyl groups; see L. M. Jackman and S. Sternhell, 'Applications of NMR Spectroscopy in Organic Chemistry,' 2nd edn., Pergamon, Oxford and New York, 1969, p. 243.



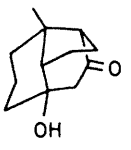
(1) R = CH=CHMe
(2) R = CH=CMe$_2$
(3) R = C$_6$H$_4$OMe-*p*
(4) R = [CH$_2$]C≡CMe
(5) R = C≡CMe
(6) R = CH=C(Cl)Me
(7) R = CH=CH$_2$



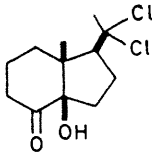
(8)



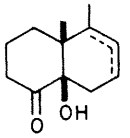
(9) R^1 = Ac, R^2 = H
(10) R^1 = H, R^2 = Ac



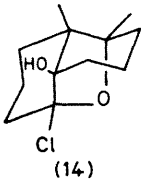
(11)



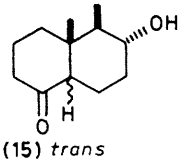
(12)



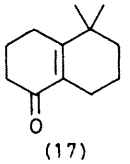
(13)



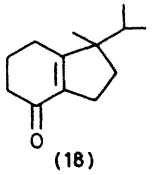
(14)



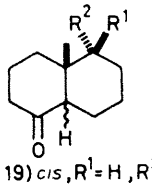
(15) *trans*
(16) *cis*



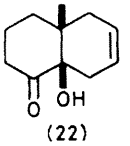
(17)



(18)



(19) *cis*, R^1 = H, R^2 = Ac
(20) *cis*, R^1 = Ac, R^2 = H
(21) *trans*, R^1 = Ac, R^2 = H



(22)

τ ($CDCl_3$) 8·91 (6H, s)] That the latter product arose from hydride migration, rather than addition–elimination, was established by cyclisation using CF_3CO_2D when monodeuterio-(**17**) (ν_{max} 2170 cm^{-1}) was obtained, on treatment with NaOH–H_2O dioxan this deuterium atom was removed

Prior work[6] had established that cyclisation of the epoxide of (**2**) gave a bicyclo[3·3·1]nonane derivative Cyclisation of the dienone (**2**) took a more expected course but the intermediate cation underwent hydride and methyl migration to give (**18**) (51%) [$\lambda_{max}^{(EtOH)}$ 249 nm (ϵ 12,500), ν_{max} 1660 cm^{-1}, τ ($CDCl_3$) 8·92 (3H, s) and 9·10 (6H, d, J 7 Hz)] to a larger extent than in the previous case This reflects the well-established propensity to rearrangement of cyclopentyl methyl cations In the case of the epoxide of the acetylene (**4**) attempted cyclisation led only to ring contraction Cyclisation of the enone (**4**) was more successful, giving (in 50% yield) the decalone (**19**) [ν_{max} 1705 cm^{-1}, τ ($CDCl_3$) 7·98 (3H, s) and 8·79 (3H, s)] and an inseparable 2 : 1 mixture of (**20**)† [τ ($CDCl_3$) 7·90 (s) and 9·01 (s)] and (**21**) [τ ($CDCl_3$) 7·92 (s) and 9·14 (s)], the *cis-trans* ratio changed to 1 : 3 on equilibration with K_2CO_3–MeOH Cyclisation, hydrolysis, and chromatographic isolation of the products from (**7**) gave an unusual result, the products, (**22**), and the related hydration product (40%), were identical with those obtained from cyclisation of the 2,3-epoxide The reaction is reproducible but we have been unable to ascertain at what stage oxidation is occurring

These and earlier results show that the alternative strategies of using Harding's dienol acylates[3] or our 2,3-epoxycyclohexanones[4,5] are both useful in initiating cyclisations and show the flexibility of 2-substituted-3-methylcyclohex-2-enones in approaches of this type, especially as, in addition, they are readily convertible into cyclohexenols, allowing use of the powerful methods which Johnson[7] has developed

We thank the University of Ahmadu Bello, Zaria, Nigeria for leave of absence to J A and the S R C for financial support to A S

(*Received, 6th February* 1980; *Com.* 130.)

[1] J L Cooper and K E Harding, *Tetrahedron Lett*, 1977, 3321
[2] J Amupitan and J K Sutherland, *J Chem Soc, Chem Commun*, preceding communication
[3] K E Harding, J L Cooper, P M Puckett, and J D Ryan, *J Org Chem*, 1978, **43**, 4363
[4] M Mellor, A Santos, E G Scovell, and J K Sutherland, *J Chem Soc, Chem Commun*, 1978, 529
[5] E Huq, M Mellor, E G Scovell, and J K Sutherland, *J Chem Soc, Chem Commun*, 1978, 526
[6] E G Scovell and J K Sutherland, *J Chem Soc, Chem Commun*, 1978, 529
[7] W S Johnson, *Angew Chem, Int Ed Engl*, 1976, **15**, 9