Direction of Ring-opening of 2-Methyl-substituted Cyclopropyl(stannyloxy)methyl and Cyclopropyl(hydroxy)methyl Radicals: Kinetic and Thermodynamic Control

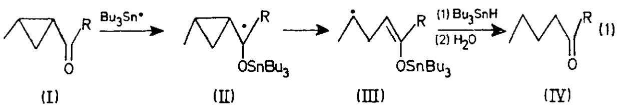
By Alwyn G. Davies,* Jean-Yves Godet,† Brenda Muggleton, and Michel Pereyre*†

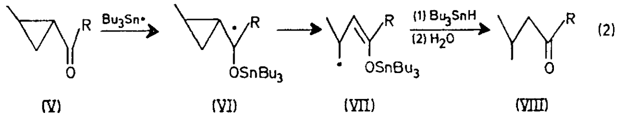
(*Chemistry Department, University College London, 20 Gordon Street, London* WC1H 0AJ; *and* † *Laboratoire de Chimie Organique, Université Bordeaux I,* 351 *cours de la Liberation,* 33405 *Talence, France*)

Summary *trans*-2-Methylcyclopropyl(stannyloxy or hydroxy)methyl radicals undergo ring-opening to give principally the thermodynamically less stable primary alkyl radicals; use has been made of this effect to establish the conditions under which the cyclopropylmethyl → homo-allyl rearrangement is reversible.

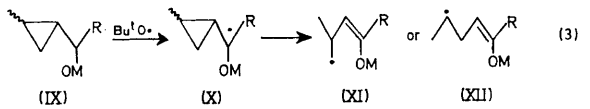
There has been considerable interest in the ring-opening of cyclopropylmethyl radicals to give homoallyl radicals,[1] and in the potential reversibility of the reaction.[2,3] We have now shown that the presence of a 2-methyl substituent in the ring can exert a remarkable directive effect on the ring-opening, and have made use of this effect to demonstrate the reversibility of the process.

The reductive homolytic ring-opening of *cis*- and *trans*-2-methylcyclopropyl ketones with tributyltin hydride at 80 °C is known to occur with partial regioselectivity, the *cis* reactants (I) giving principally the n-butyl ketones (IV) *via* the secondary alkyl radicals (III), but, surprisingly, the *trans*-reactants (V) give principally the isobutyl ketones (VIII) *via* the primary alkyl radicals (VII).[4]



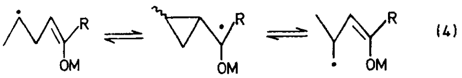


However, when the same radicals (II) or (VI) (equation 3; M = Bu_3Sn) were generated by thermolysis of di-t-butyl peroxide at 130 °C in the presence of the corresponding cyclopropylmethoxytin compounds (*i.e.* in the absence of a good hydrogen-donor), the ketone (IV) was the chief product from both the *cis*- and *trans*-reactants.[3]

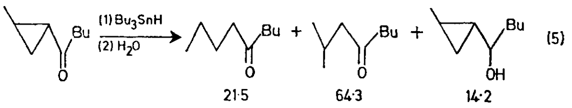


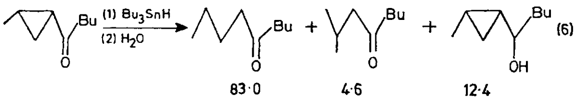
We have generated a series of stannyloxymethyl radicals (*trans*-X: M = Bu_3Sn, R = H or Me; *cis*-X: M = Bu_3Sn, R = Me) and of the corresponding hydroxymethyl radicals (*trans*-X: M = H, R = Me; *cis*-X: M = H, R = Me) at −67 to −112 °C by photolysing di-t-butyl peroxide in the presence of the appropriate precursor.[5] The spectra of the ring-opened radicals (XI) or (XII) were monitored by e.s.r. spectroscopy.‡

All the reactions were now regiospecific within the limits of detection of the minor component (estimated to be 4—15%) imposed by the noise level of the spectrometer: *cis*-(IX) gave the secondary alkyl radical (XII) and, particularly, *trans*-(IX) gave the less thermodynamically stable primary alkyl radical (XI). Any substantial equilibration of the primary and secondary alkyl radicals through the cyclopropylalkyl radical (equation 4, M = Bu_3Sn or H) can therefore be excluded under these conditions. These reactions provide one of the very few examples of the selective formation of a primary rather than a secondary alkyl radical. The origin of this effect, and its dependence on the structure of the reactant, is discussed in the succeeding paper.[6]



Experiments were also conducted to determine the effect of temperature and of concentration on the proportions of the ultimate products (analysed by g.l.c.) from the reduction of the cyclopropyl ketones.



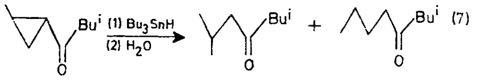


‡ Above *ca.* −30 °C, the radicals (XI) or (XII), (M = H), undergo 1,5-transfer of hydrogen from oxygen to carbon. The e.s.r. spectra of the enoxyl radicals which are formed confirm the structures of (XI) and (XII) (ref. 5).

At −29 °C, using neat tributyltin hydride with u.v. initiation, and a tin hydride to ketone ratio of 2 : 1, the results shown in equations (5) and (6) were obtained; the percentage composition of the products is given under the formulae.

The products still appear to be kinetically controlled under these conditions: the regioselectivity is in the same sense as that observed in the e.s.r. experiments at lower temperature, and the alcohol which is formed at this low temperature by trapping of the initially formed cyclopropylmethyl radical has the same configuration as that of the original ketone.§ If equilibration by equation (4) were now significant, the *cis*-ketone would be expected to show the formation of the *trans*-alcohol.

At 80 °C, using neat tributyltin hydride and azoisobutyronitrile as initiator, and with a tin hydride to ketone ratio of 1 : 1, *trans*-2-methylcyclopropyl isobutyl ketone is reduced with a similar regioselectivity (equation 7), and the ratio of branched chain to straight chain product [(XIII)]/[(XIV)] = 1·63, and is unchanged if the proportion of tin hydride is increased.



(XIII) (XIV)

However, if the reaction is conducted in benzene solution with a relatively low concentration of tin hydride, the ratio [(XIII)]/[(XIV)] decreases rapidly as shown in the Figure, reaching a value of about 0·2 at 0·1 M Bu_3SnH, *i.e.* the reaction now proceeds with an inversed regioselectivity. We conclude that under these latter conditions the products of the reactions are thermodynamically controlled, the radicals avoiding capture by the tin hydride for long enough to permit their equilibration by reaction (4) to favour the secondary alkyl radical.

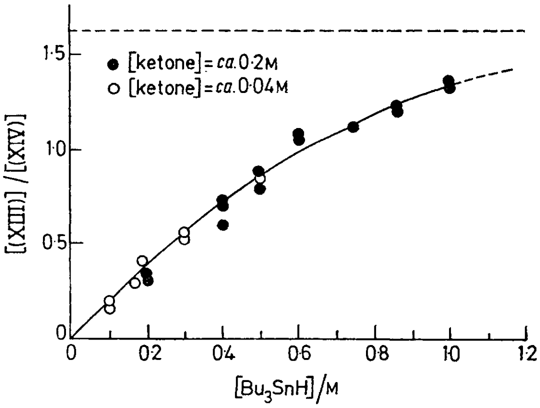


FIGURE. Plot of regioselectivity of ring opening of *trans*-2-methylcyclopropyl isobutyl ketone, [(XIII)]/[(XIV)], *vs.* tributyltin hydride concentration at 80 °C.

We thank the International Tin Research Council for support (B.M.).

(*Received, 23rd June* 1976; *Com.* 706.)

---

§ G.l.c. showed the presence of both diastereoisomers of the *cis*-alcohol.

[1] Reviewed by J. W. Wilt, 'Free Radicals,' Vol. 1, ed. J. K. Kochi, Wiley-Interscience, New York, 1973, Ch. 8.

[2] E. Renk, P. R. Shafer, W. H. Graham, R. H. Mazur, and J. D. Roberts, *J. Amer. Chem. Soc.*, 1961, **83**, 1987; L. K. Montgomery and J. W. Matt, *ibid.*, 1967, **89**, 934, 3050; T. A. Halgren, M. E. H. Howden, M. E. Medof, and J. D. Roberts, *ibid.*, p. 3051; J. K. Kochi, P. J. Krusic, and D. R. Eaton, *ibid.*, 1969, **91**, 1877, 1879; W. G. Dauben, L. Schutte, and R. E. Wolf, *J. Org. Chem.*, 1969, **34**, 1849.

[3] J.-Y. Godet, M. Pereyre, J.-C. Pommier, and D. Chevolleau, *J. Organometallic Chem.*, 1973, **55**, C15.

[4] M. Pereyre and J.-Y. Godet, *Tetrahedron Letters*, 1970, 3653; J.-Y. Godet and M. Pereyre, *Compt. rend.* (*C*), 1971, **273**, 1183; 1973, **277**, 211; *Bull. Soc. Chim. France*, in the press.

[5] *Cf.* A. G. Davies and B. Muggleton, *J.C.S. Perkin II*, 1976, 502; A. G. Davies, J.-Y. Godet, B. Muggleton, M. Pereyre and J.-C. Pommier, *ibid.*, in the press.

[6] P. Blum, A. G. Davies, M. Pereyre, and M. Ratier, following communication.