

## Direction of Ring-opening of Ring-substituted Cyclopropyl(stannyloxy)-methyl and Cyclopropyl(hydroxy)methyl Radicals: Preferential Formation of Primary Alkyl Radicals

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*cis*- and *trans*-2-Methylcyclopropyl-stannyloxymethyl and -hydroxymethyl radicals (A) have been generated by treating either the corresponding tin alkoxides or alcohols with *t*-butoxyl radicals, or the corresponding ketones with tributylstannyl radicals. The e.s.r. spectra show that, at low temperature (< -60°C), the *cis*- (A) radicals undergo ring-opening to give principally secondary alkyl radicals, but the *trans*- (A) radicals give only *primary* alkyl radicals.

If a reaction can lead to the alternative formation of primary or secondary or tertiary alkyl radicals, it is normally observed that the primary radicals are formed least readily and the tertiary radicals most readily.<sup>1</sup> The few known exceptions to this rule have attracted much attention, and the interpretation of the anomalies has contributed to our understanding of the steric and electronic factors which control homolytic reactivity.<sup>†</sup>

One such anomaly has been identified in the ring-opening of certain methylcyclopropylstannyloxymethyl

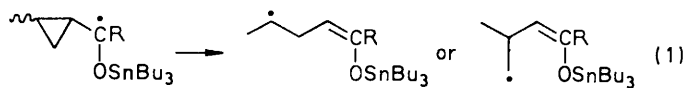
† An important example is the ring closure of the hex-5-enyl radical to the cyclopentylmethyl radical.<sup>2</sup>

‡ The formulae as drawn should not be taken to imply whether the enolates have *cis*- or *trans*-configuration.

<sup>1</sup> D. C. Nonhebel and J. C. Walton, 'Free Radical Chemistry,' Cambridge University Press, 1974, ch. 5.

<sup>2</sup> A. L. J. Beckwith, 'Essays on Free Radical Chemistry,' Chem. Soc. Special Publ. No. 24, 1970, pp. 255—263.

radicals [equation (1)].<sup>3-6,‡</sup> These radicals can be generated by causing (a) trialkylstannyl radicals to add



to the appropriate ketone,<sup>3-5</sup> or (b) *t*-butoxyl radicals to abstract hydrogen from the appropriate alkoxytin compounds,<sup>5,6</sup> under the conditions shown in equations (2) [(a) and (b)] and (3) [(a) and (b)].

<sup>3</sup> J.-Y. Godet and M. Pereyre, *J. Organometallic Chem.*, 1972, **40**, C23.

<sup>4</sup> J.-Y. Godet and M. Pereyre, *Tetrahedron Letters*, 1970, 3653; *Compt. rend.*, 1971, **273C**, 1183; 1973, **277C**, 211.

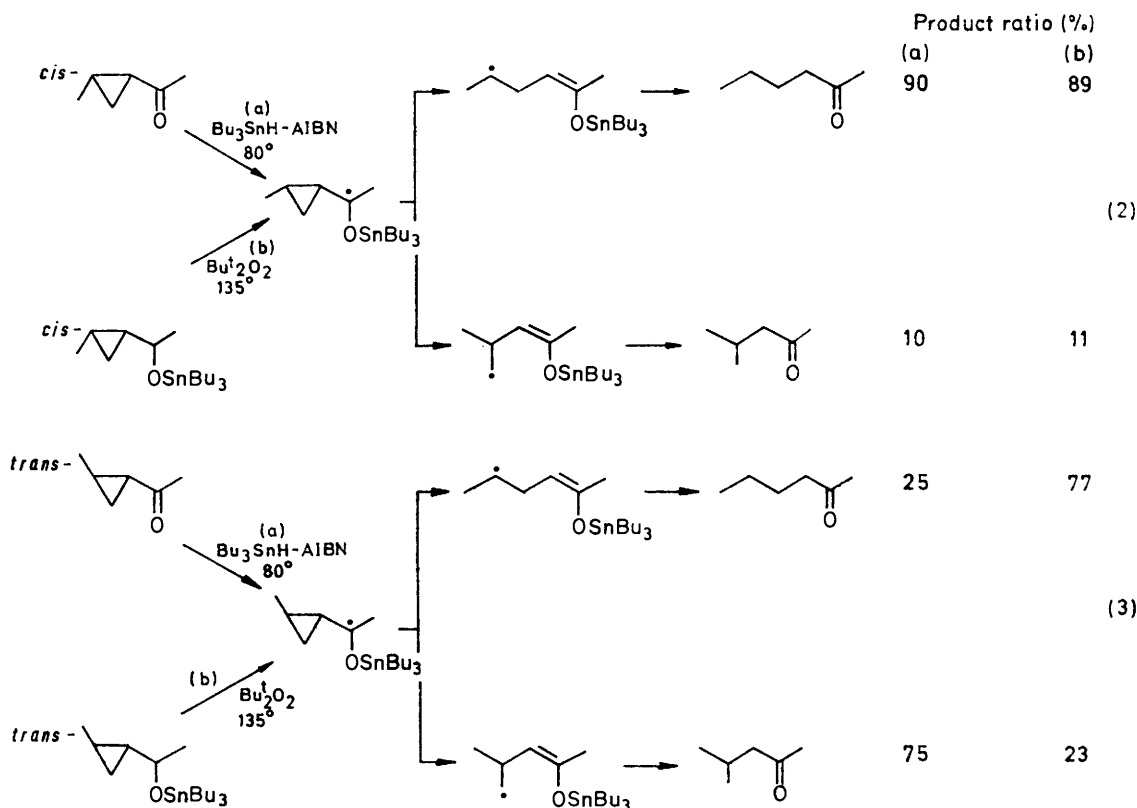
<sup>5</sup> J.-Y. Godet, Thesis, Bordeaux, 1974.

<sup>6</sup> J.-Y. Godet, M. Pereyre, J.-C. Pommier, and D. Chevolleau, *J. Organometallic Chem.*, 1973, **55**, C15.

Analysis by g.l.c. of the ketones formed after hydrolysis of the products showed that, whereas the principal product was normally hexan-2-one derived from the secondary alkyl radical, in the particular case of the reaction of tributyltin hydride with *trans*-2-methylcyclopropylmethyl ketone, there was a preponderance of 4-methylbutan-2-one (75%) which would result from the *primary* alkyl radical. The bias in favour of the non-linear carbonyl compound was greater (92%) when the reactant was *trans*-2-methylcyclopropanecarbaldehyde, but it decreased with the higher *trans*-2-methylcyclopropyl alkyl ketones.

by Brown.<sup>9</sup> The alcohols were converted into the corresponding tributyltin derivatives by exchange with tributyltin methoxide. The results are summarised in Table 1. 1-(*cis*-2-Methylcyclopropyl)ethanol and *cis*- and *trans*-2-methylcyclopropyl methyl ketones were purified before use by preparative g.l.c. on a Carbowax 20M column (3 m × 4 mm; 20% on 60–80 mesh Supasorb) at 130 °C.

*E.s.r. Spectroscopy.*—E.s.r. spectra were recorded on a Varian E4 instrument fitted with a 1 kW d.c. Mazda ME/D or 500 W a.c. Philips SP 500 high-pressure mercury discharge lamp and lens system for carrying out photolysis in the cavity. The reaction mixtures were of three types: they consisted of either a tin alkoxide and di-*t*-butyl



We now report a complementary study of this system and of the corresponding hydroxyalkyl radicals, in which the reactions have been carried out photolytically at relatively low temperatures, and the intermediate ring-opened radicals have been monitored by e.s.r. spectroscopy.

#### EXPERIMENTAL

The cyclopropylmethanols were prepared by Simmons-Smith methylenation of the corresponding unsaturated alcohols, by using the zinc-copper couple described by Rawson and Harrison,<sup>7</sup> and Julia's<sup>8</sup> technique. *cis*- and *trans*-2-Methylcyclopropyl methyl ketone were obtained from the corresponding alcohols by the method described

peroxide, or of an alcohol and di-*t*-butyl peroxide, or of a ketone, hexabutylditin, and di-*t*-butyl peroxide. Each sample was prepared in cyclopropane solvent in a quartz (Suprasil) sample tube connected to a vacuum line, and thoroughly out-gassed before sealing.

#### RESULTS

The cyclopropylstannyloxymethyl or cyclopropylhydroxymethyl radicals (IV) were generated in the e.s.r. cavity by irradiating di-*t*-butyl peroxide in the presence of the appropriate tin alkoxide (I) or alcohol (II), or a mixture of di-*t*-butyl peroxide and hexabutylditin in the presence of the appropriate ketone (III), according to equation (4).

<sup>7</sup> R. J. Rawson and I. T. Harrison, *J. Org. Chem.*, 1970, **35**, 2058.


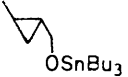

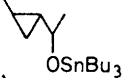


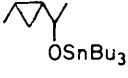


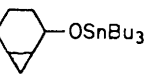
<sup>8</sup> M. Julia and Y. Noel, *Bull. Soc. chim. France*, 1968, 3756.

<sup>9</sup> H. C. Brown and C. P. Gary, *J. Amer. Chem. Soc.*, 1961, **83**, 2952.

Although some simple cyclopropylmethyl hydrocarbon radicals have been observed by e.s.r. spectroscopy below  $-130^{\circ}\text{C}$ ,<sup>10</sup> in the present study the minimum working

coupling constants  $a(\text{H}\alpha)$  21.0 G (1 H),  $a(\text{H}\beta)$  23.6 G (5 H) (at  $-75^{\circ}\text{C}$ ).<sup>\*</sup> Using this as a model for (VI), the

TABLE I

Preparation of starting materials			Ref.
Compound	Yield (%)	B.p. ( $^{\circ}\text{C}$ ) [mm Hg]	
(1) 	53	78 [80]	8
(2) 	80	90 [0.2] <sup>a</sup>	
(3) 	45	129 [764]	e
(4) 	90	120 [1] <sup>b</sup>	
(5) 	68	76 [80]	e
(6) 	30	79 [90]	e
(7) 	92	105 [0.1] <sup>c</sup>	
(8) 	70	80 [85]	e
(9) 	60	72 [7]	f
(10) 	89	135 [0.3] <sup>d</sup>	

I.r. ( $\text{cm}^{-1}$ )		N.m.r.
$\nu(\text{CH})$	$\nu(\text{COSn})$	$\tau(\text{CHOSn})$
<sup>a</sup> 3 060	1 070	6.60 (d)
<sup>b</sup> 3 060	1 070	6.75 (m)
<sup>c</sup> 3 060	1 070	6.78 (m)
<sup>d</sup> 3 065	1 065	5.93 (m)

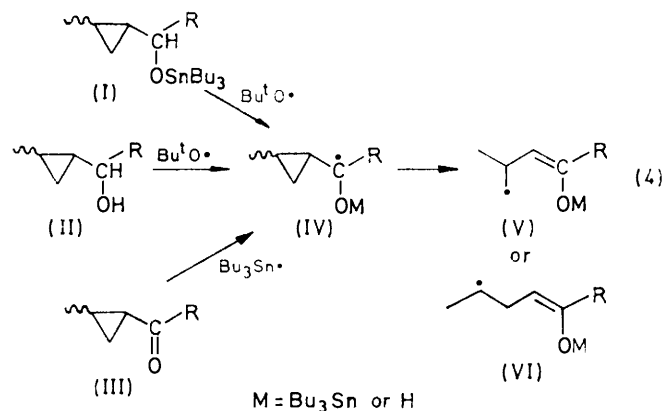
<sup>a</sup> W. G. Dauben, L. Schutte, and R. E. Wolf, *J. Org. Chem.*, 1969, **34**, 1849.

<sup>f</sup> W. G. Dauben and G. H. Berezin, *J. Amer. Chem. Soc.*, 1963, **85**, 468.

temperature was usually about  $-100^{\circ}\text{C}$ , and only the ring-opened radicals (V) or (VI) were observed.

The spectra of the primary alkyl radicals (V) consist of a simple doublet of triplets, and were readily identified. To confirm the identification of the more complex spectrum of the secondary alkyl radicals (VI) the radical  $\text{CH}_3\dot{\text{C}}\text{HCH}_2\text{CH}=\text{CH}_2$  was prepared (from the corresponding bromide, tri-ethylsilane, and di-*t*-butyl peroxide) and the spectrum analysed in terms of the hyperfine

<sup>\*</sup> We are grateful to Mr. P. Blum for carrying out this experiment, and the ones involving alkoxy silanes.



relative concentrations of the radicals (V) and (VI) from the reactions (4) were determined from careful measurements of the intensities of all the relevant signals. Similarly the spectrum of the cycloheptyl radical [ $a(\text{H}\alpha)$

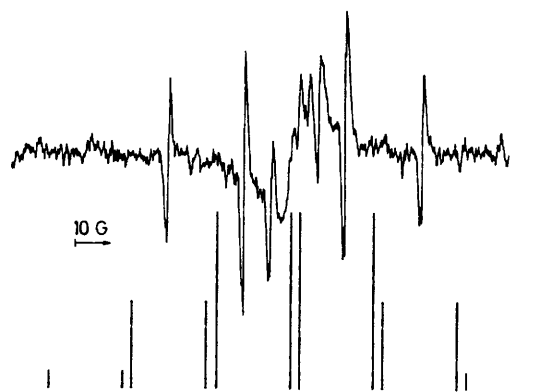


FIGURE 1

E.s.r. spectrum of the primary alkyl radical  $\dot{\text{C}}\text{H}_2\text{CHMeCH}=\text{CHOSnBu}_3$  formed by ring-opening of the *trans*-2-methylcyclopropyl(tributylstannyl ether)methyl radical (IV; R = H, M =  $\text{Bu}_3\text{Sn}$ ) at  $-78^{\circ}\text{C}$ . The stick spectrum illustrates the approximate appearance of the secondary alkyl radical  $\text{Me}\dot{\text{C}}\text{HCH}_2\text{CH}=\text{CHOSnBu}_3$  if it were formed in equal concentration, with the hyperfine couplings  $a(\text{H}\alpha)$  21.0 G (1 H) and  $a(\text{H}\beta)$  23.6 G (5 H)

21.8 G (1 H), 24.7 G (5 H)] was used as a model for interpreting the spectrum derived from the bicyclo[4.1.0]heptyloxytin compound [Table I, compound (10)]. The results are summarised in Table 2.

All the tin alkoxides and alcohols with a *trans*-methyl group in the cyclopropyl ring gave strong spectra of the primary alkyl radicals (V); in no case was there any evidence for the secondary alkyl radicals (VI), and the yield quoted in Table 2 represents the limit of accuracy imposed by the instrumental noise. The intensity of the spectrum derived from *trans*-2-methylcyclopropyl

<sup>10</sup> J. K. Kochi, P. J. Krusic, and D. R. Eaton, *J. Amer. Chem. Soc.*, 1969, **91**, 1877, 1879; K. S. Chen, D. J. Edge, and J. K. Kochi, *J. Amer. Chem. Soc.*, 1973, **95**, 7036.

methyl ketone [compound (5)] was less, and the uncertainty in the ratio of [(V)] to [(VI)] is correspondingly high. The normal quality of the spectra is illustrated in Figure 1 for tributyltin 1-(*trans*-2-methylcyclopropyl)-methoxide [Table 1, compound (2)].

We have shown previously that ring-opening of the radicals derived from cyclopropylmethanols is followed,

trations of the secondary alkyl radical (VI) and the derived enoxyl radical (VIII) are below the limits of detection.

The spectra obtained from 1-(*cis*-2-methylcyclopropyl)-ethanol [compound (6)] and its tributyltin derivative [compound (7)] were less well defined partly because the intensity of the spectra of the secondary radical (VI) is

TABLE 2

Products (V) and (VI) of the ring-opening of cyclopropylstannyloxymethyl and cyclopropylhydroxymethyl radicals (IV) in cyclopropane

Radical (I)	Source (Compd. no. in Table 1)	Radical observed [(V) or (VI)]	Temp. (°C)	$a(\text{H}\alpha)^a$ (G)	$a(\text{H}\beta)^a$ (G)	Yields of (V)/(VI) (%)
	(2)		-78	21.6(2)	28.7(1) <sup>b</sup>	93/7
	(3)		-86	21.7(2)	27.8(1)	96/4
	(4)		-67	21.4(2)	28.8(1)	94/6
	(5)		-84	21.8(2)	28.5(1)	83/17
	(6)		-87	ca. 21.5(1)	24.5(3) 27.0(2)	15/85
	(7)		-112		See text	
	(10)		-87	21.5(2)	25.7(1) <sup>c</sup>	90/10

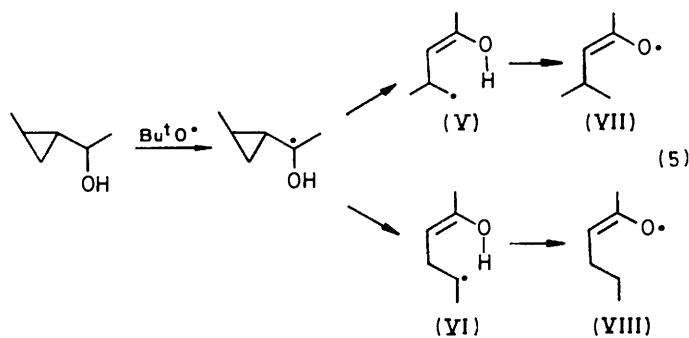
<sup>a</sup> The number of hydrogens coupling are given in parentheses. <sup>b</sup> Also  $a$  0.6 G (3 H). <sup>c</sup> Also  $a$  0.7 G (3 H).

above *ca.* -40 °C, by 1,5-hydrogen transfer to give enoxyl radicals,<sup>11</sup> and the spectra of those enoxyl radicals provide further evidence of the direction of ring opening.\* The spectra of the radicals (V) and (VII)

subdivided amongst more signals than that of the primary radical (V), and the signal-to-noise ratio is thus reduced. In the spectrum from the alcohol [compound (6)], the signals of the secondary radical could clearly be identified, and there was some inconclusive evidence for the presence of relatively weak lines arising from the primary radical (V): the upper limit to the relative concentration of (V) was estimated (Table 2) to be 15%.

The corresponding tributyltin derivative [compound (7)] gave a relatively weak spectrum. The lines to be ascribed to the secondary radical (VI) could be identified, and the presence of any substantial concentration of the primary radical could be excluded, but the most that can be said is that the secondary radical constitutes the major product. The reaction was also attempted between the corresponding ketone [compound (8)] and the tributylstannyl radical, but the signal-to-noise ratio was too low to allow the spectrum to be interpreted.

The spectrum obtained from the bicycloheptyl derivative [compound (10)] showed the presence of a doublet of triplets arising from the primary radical (X), and the relative intensities of the lines were correct, but

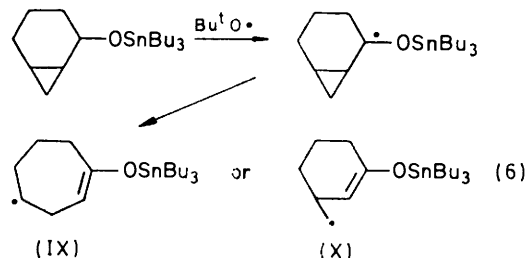


obtained from the reaction of 1-(*trans*-2-methylcyclopropyl)ethanol [compound (3)] were illustrated in reference 11 and again it will be seen that the concen-

\* The equivalent 1,5-transfer of a trialkyltin or trialkylsilyl radical from enoxyl oxygen to carbon in radicals such as (V) and (VI) ( $M = \text{R}_3\text{Sn}$  or  $\text{R}_3\text{Si}$ ) does not occur.

<sup>11</sup> A. G. Davies and B. Muggleton, *J.C.S. Perkin II*, 1976, 502.

the inner lines of the spectrum of the secondary radical (IX) might be obscured, and the presence of up to 10% of the secondary radical cannot be excluded.



#### DISCUSSION

The selectivity which we observe by monitoring the radical intermediates at low temperature is in the same direction but much greater than that found by analysing the products of the reactions carried out at higher temperatures.<sup>4-6</sup> In particular, and most remarkably, the ring-opening of the *trans*-2-methylcyclopropylalkyl radicals is seen to be completely selective in favour of the *primary* alkyl radical, within the sensitivity of the e.s.r. technique.

This increased selectivity at low temperature can be interpreted in terms of the enthalpy diagram of Figure 2. At low temperature, the ring-opening is essentially irreversible and one observes the kinetically controlled ratio of primary and secondary homoallylic radicals (V) and (VI). At higher temperatures, the ring-opening is reversible, the radicals (V) and (VI) can equilibrate through the *trans*-2-methylcyclopropyl isomer (IVb), and the ultimate products depend on the relative rates of this equilibration and the trapping of the radicals (V) and (VI) by hydrogen transfer. Tributyltin

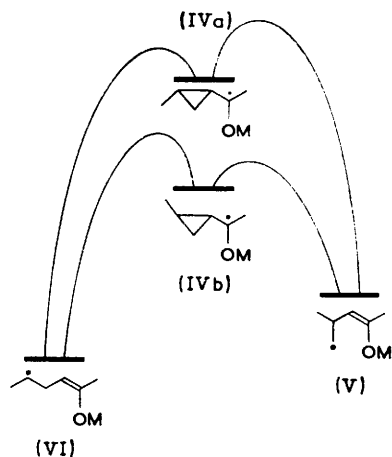
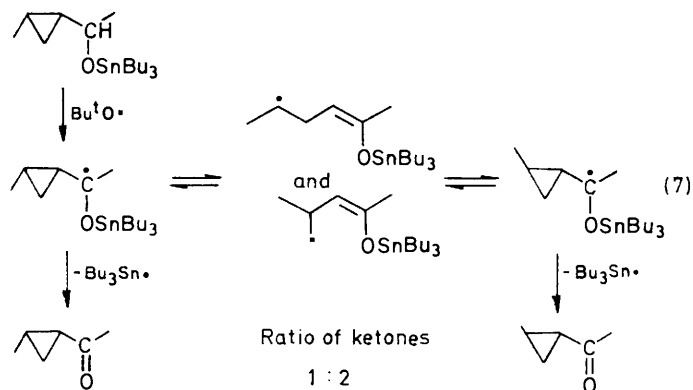


FIGURE 2 Enthalpy diagram for the ring-opening of *cis*- and *trans*-2-methylcyclopropylalkyl radicals (IVa and b)

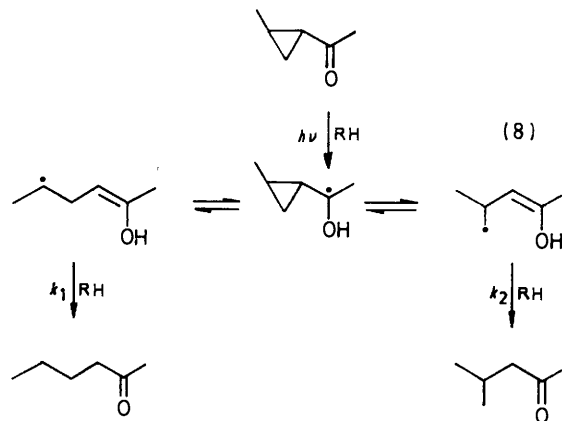
hydride reacts very readily with alkyl radicals, and traps (V) and (VI) before equilibration is very significant [reactions (2)(a) and (3)(a)], but, in the absence

of such a good hydrogen donor, equilibration is extensive and the ratio of products approaches that of thermodynamic control [equations (2)(b) and (3)(b)].

Evidence for this equilibration is given by the *cis-trans* isomerisation of the cyclopropyl compound during the reaction; when di-*t*-butyl peroxide is thermolysed in the presence of the tin alkoxide, *cis*- (I; R = Me), some of the reactant is recovered as a 1:2 mixture of the corresponding *cis*- and *trans*-ketones [equation (7)].<sup>6</sup>



Dauben's work on the photoreduction of the ketones<sup>12</sup> in hydrogen-donating solvents is interesting in this



context [equation (8)]. Photolysis of *trans*-methylcyclopropyl methyl ketone in isopropyl alcohol gave *n*-butyl methyl ketone and isobutyl methyl ketone in the molar ratio 3:1, but, in pentane as solvent, the ratio was 2:3 [equation (8)]. These authors suggested that the ratio of the products in isopropyl alcohol reflected the relative stability of the equilibrating radicals ( $k_1 \approx k_2$ ), but pentane, being a poorer hydrogen donor, reacted preferentially with the primary alkyl radical ( $k_2 > k_1$ ).

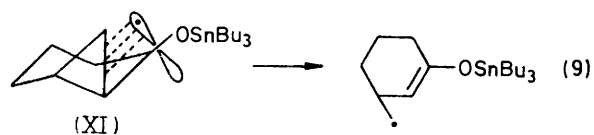
If equilibration is indeed rapid compared with the rate of hydrogen donation, this mechanism would not be

<sup>12</sup> W. G. Dauben, L. Schutte, and R. E. Wolf, *J. Org. Chem.*, 1969, **34**, 1849.

incompatible with our present results, although we now have evidence<sup>11</sup> that a substantial proportion of the hydrogen donation occurs by intramolecular 1,5-transfer from the OH group [equation (5)]. We attempted to observe by e.s.r. the radical intermediates involved in the photolysis of *trans*-2-methylcyclopropyl methyl ketone in isopropyl alcohol, but the intensities of the spectra were inadequate. This problem would warrant a more thorough investigation.

The factors which control the direction of ring-opening of the cyclopropylalkyl radicals described here are not completely understood. The similar problems connected with the reductive (Li-NH<sub>3</sub>) ring-opening of cyclopropyl ketones have been discussed by Dauben, but the degree to which his interpretation is relevant to the reactions of electrically neutral radicals is not clear.

The direction of ring-opening in the bicyclo[4.1.0]heptan-2-ones was ascribed to the preferential overlap of the 2*p* orbital on C(2) with the C(1)-C(7) bond of the cyclopropane ring when the cyclohexane ring is in the more stable chair conformation,<sup>13</sup> and it seems reasonable to apply the same argument to the corresponding stannyloxyalkyl radical (XI).<sup>6</sup>

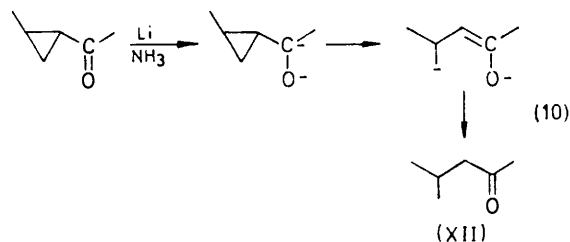


The reduction of *trans*-2-methylcyclopropyl methyl ketone gave 88–94% of 4-methylpentan-2-one (XII) and 6–12% of hexan-2-one; this was ascribed to the preferential formation of the more stable primary carbanion [equation (10); the same principle would apply if ring-opening occurred on the radical anion].<sup>14</sup>

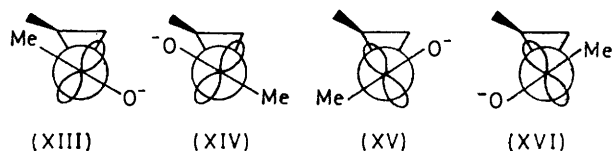
<sup>13</sup> W. G. Dauben, L. Schutte, R. E. Wolf, and E. J. Deviny, *J. Org. Chem.*, 1969, **34**, 2512.

<sup>14</sup> W. G. Dauben and R. E. Wolf, *J. Org. Chem.*, 1970, **35**, 374.

The corresponding *cis*-ketone however gave 91–95% of hexan-2-one; it was suggested that the overriding factor here was the destabilising *syn*-interaction with the methyl substituent in the conformations (XIII) and



(XIV) which caused ring-opening to take place through the conformations (XV) and (XVI) which yield the secondary carbanion.<sup>14</sup> The latter of these two factors



may well be relevant to the ring-opening of the radicals which we have studied,<sup>4-6</sup> but if the former principle were to be carried over one would have to invoke the partial polar character of the O-H or O-Sn bonds to confer some anionic character on the incipient radical in the transition state.<sup>5</sup>

We thank the International Tin Research Council for the award of a Research Studentship (to B. M.) and Dr. B. P. Roberts for discussions. We thank Dr. M. Ratier for preparing some of the cyclopropyl compounds, and Professor W. P. Neumann (Dortmund) for carrying out some of the initial e.s.r. experiments.

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