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FORMATION OF SOME BICYCLIC SYSTEMS BY RADICAL RING-CLOSURE

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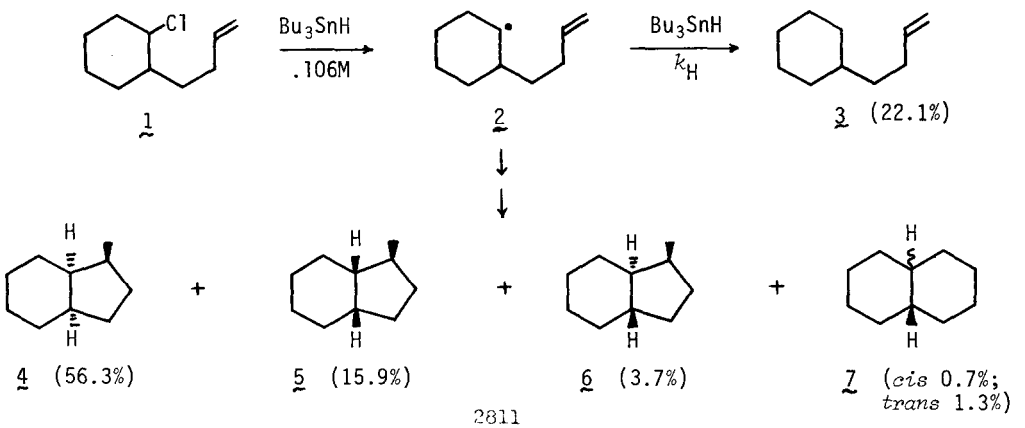
Summary: *The rates and stereochemistry of ring closure of the radicals (2), (9), (10), and (16) have been determined and rationalised.*

Recently,[1] we suggested that 1,5-ring closures of substituted hex-5-enyl radicals and related acyclic species are stereoselective: 1- or 3-substituted systems give mainly *cis*-disubstituted cyclic products whereas 2- or 4-substituted systems give mainly *trans*. Cyclizations of acyclic substituted hex-5-enyl radicals generally conform to this guideline but ring-closures of cyclic systems sometimes appear exceptional. We now give an example of such an exception and show how it can be reconciled with the fundamental stereo-electronic basis of the guideline, namely, that intramolecular addition requires effective overlap between the semi-occupied orbital and the vacant π* orbital.[3]

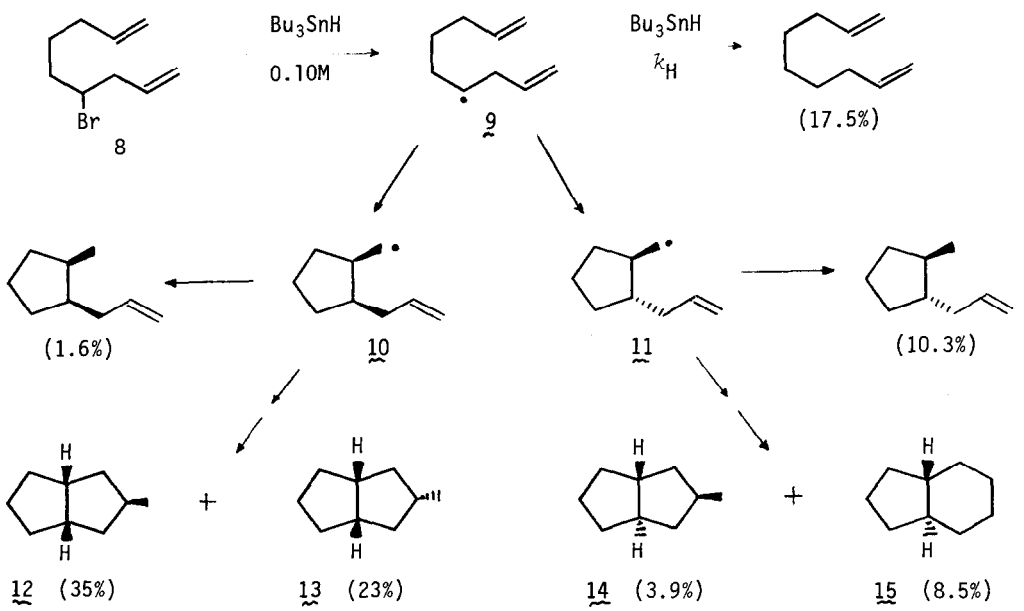
The radical (2) generated in the usual way[2] from the chloro compound (1) is formally a 1,2-disubstituted hexenyl system and is therefore predicted to give mainly the product (6) of *exo*-ring closure in which the newly formed methyl group is in a *cis*-relationship to the 1-substituent and a *trans*-relationship to the 2-substituent. However, the experimental results show that the major product (4) has the all *cis*-configuration. The cyclopentyl analogue of radical (2) behaves similarly.[4]



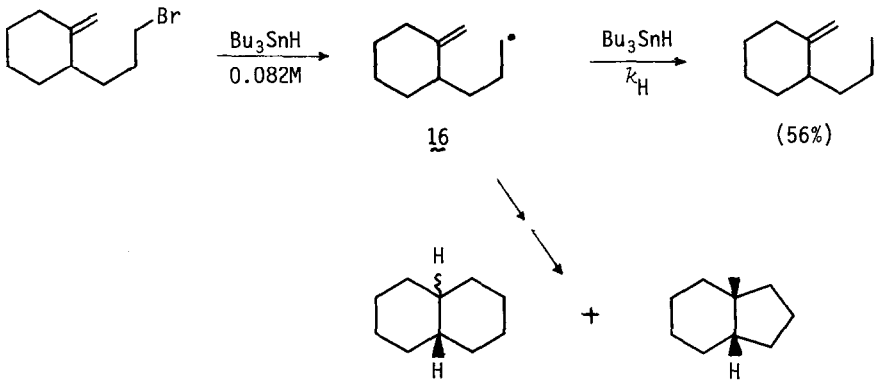
The predominant formation of 4 from 2, although it contravenes the guideline, is not unexpected, since the fact that the radical centre already resides in a ring imposes steric constraints on the reaction which do not apply to simple acyclic systems. Inspection of models indicates that the chair-like conformation of 2 in which the butenyl substituent occupies an equatorial position allows poor overlap of the semi-occupied and π* orbitals. Maximum interaction is achieved when ring-closure occurs through the conformation in which the substituent is axial. Such a conformation necessarily affords *cis*-fused products (4) and (5), of which the major, as predicted by the guideline, is that (4) containing the methyl group *cis* to the formal 1-substituent in 2.

Trans-fused products must arise through ring closure of that conformer of the radical (2) in which the butenyl group is equatorial. As predicted, the predominant *trans*-fused product is that (6) in which the methyl group is *cis*- to the 1-substituent and *trans* to the 2-substituent.

In some cyclic systems the presence of a ring determines the relative stereochemistry of two formal substituents on a hex-5-enyl radical. This is the case for 10, the major product formed in conformity with the guideline by ring closure of 9. Radical (10) is formally a 2,3-disubstituted hex-5-enyl system in which the two substituents are expected to exert opposing effects on the stereochemistry of further ring closure. Consequently, cyclization of 10 is relatively stereo-random and affords only a slight preponderance of the *endo*-product (12) (k_{endo}/k_{exo} = 1.4). Cyclization of the radical (11) is relatively slow (see Table) and occurs mainly in the *endo*-mode presumably because of the strain engendered in formation of the *trans*-[3,3,0]bicyclooctane system by *exo*-ring-closure.



Some cyclic systems, e.g. the 4,5-disubstituted radical (16), undergo ring closure in strict conformity with the guidelines. As predicted,[1] the 5-substituent disfavours 1,5-ring closure, and the major products (7) arise, therefore, via *endo*-cyclization. However, the *exo*-process, in accord with the guidelines, gives only the product (17) in which the methyl group and the formal 4-substituent are in the *trans*-relationship.



7 (*cis*, 3.9%; *trans*, 24.9%) 17 (15.1%)

Appropriate substitution of the integrated rate equation[5] gives values of Σk_c relative to k_H (approximately 2×10^6 l mol^{-1} s^{-1} at these temperatures)[2,6] from which relative rates of *exo*- and *endo*-ring closure can be readily calculated (see Table). A feature of interest is the high relative rate of *exo*-cyclization of 10, ascribed to the fact that the relative lack of conformational freedom in (10) maintains a favourable disposition of the reactive centres. Conversely, the radical 16, as expected for a 5-substituted hex-5-enyl system, undergoes 1,5-ring closure relatively slowly.

Table: Relative Rate Constants for Radical Ring Closure

Radical	T/°C	$\Sigma k_{1,5}.k_H^{-1}$/mol l^{-1}	$\Sigma k_{1,6}.k_H^{-1}$/mol l^{-1}
hex-5-enyl	65	0.17	0.004
hex-5-enyl	80	0.22	0.005
2	65	0.17	0.003
9	80	0.22	<0.002
10	80	1.90	<0.02
11	80	0.013	0.028
16	65	0.009	0.019

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References

1. A.L.J. Beckwith, C.J. Easton, and A.K. Serelis, J.Chem.Soc.,Chem.Commun., 1980, 482.

2. A.L.J. Beckwith and G. Phillipou, J.Chem.Soc.,Chem.Commun., 1973, 280.

3. A.L.J. Beckwith, 'Essays on Free-Radical Chemistry', Special Publication No. 24, The Chemical Society, London, 1970, p.239.

4. S. Wolff and W.C. Agosta, personal communication.

5. A.L.J. Beckwith and G. Moad, J.Chem.Soc.,Chem.Commun., 1974, 472.

6. D.J. Carlsson and K.U. Ingold, J.Amer.Chem.Soc., 1968, 90, 7047.

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