Stereoselectivity of Ring Closure of Substituted Hex-5-enyl Radicals

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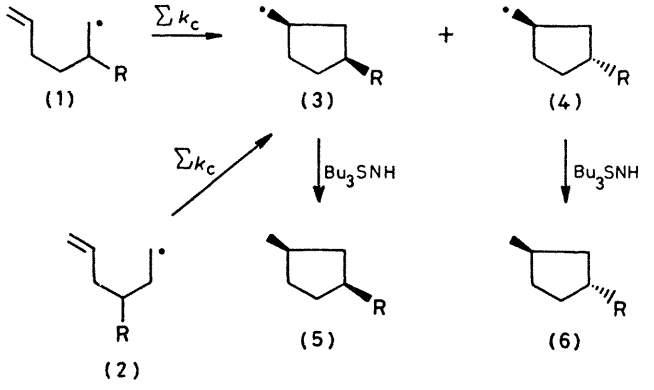
Summary 1,5-Ring closure of 1- or 3-substituted hex-5-enyl radicals affords mainly *cis*-disubstituted cyclic products, whereas 2- or 4-substituted species give mainly *trans*-products; the significance of this stereoselectivity is demonstrated in the formation of the norbornane system from acyclic precursors.

INTRAMOLECULAR addition in the 1-methylhex-5-enyl radical and in related species substituted at C-1 occurs regiospecifically in the *exo*-mode and affords mainly *cis*-disubstituted cyclic products.[1] We now report that ring closures of 2-, 3-, or 4-substituted hex-5-enyl radicals are also stereoselective.

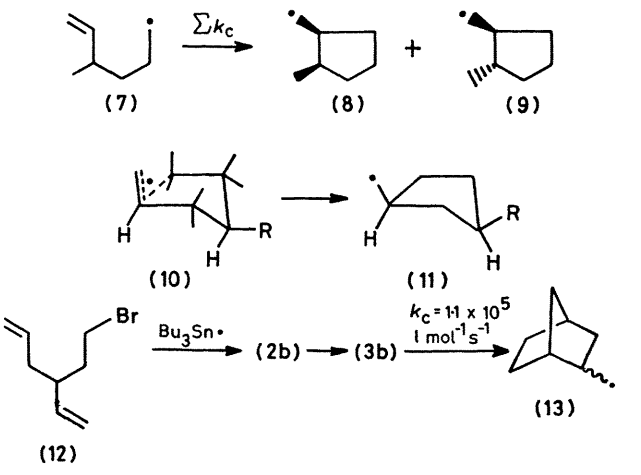
Treatment of appropriate bromoalkenes with tributylstannane in benzene or decalin at 80 °C gave, by the usual mechanism,[2] mixtures of acyclic and cyclic products which were identified by comparison with authentic samples and quantitatively determined by g.l.c. Application of the integrated rate equation[3] to the results gave values of $\Sigma k_c/k_H$ ($\Sigma k_c = k_{trans} + k_{cis}$) from which k_c can be derived on the reasonable assumption that k_H for substituted hex-5-enyl radicals is close to the value of that for the parent system ($k_H = 2{\cdot}2 \times 10^6$ l mol^{-1} s^{-1} at 80 °C).†



a; R = Me
b; R = CH=CH$_2$
c; R = CH$_2$–CH=CH$_2$
d; R = Pr

Each of the substituted radicals (**1a**), (**1b**), (**2a**—**d**), and (**7**) underwent regiospecific (>96%), 1,5-ring closure with a rate constant (Σk_c) greater than that for hex-6-enyl radical. The rate enhancements, which are ascribed to the 'gem-dialkyl' effect,[5] are consistent with previously reported values for substituted hex-5-enyl radicals.[6]

The data presented in the Table show that the 3-substituted radicals (**2a**—**d**) preferentially form *cis*-products (**3a**—**d**) whereas the 2-substituted radicals (**1a**) and (**1b**) and 4-methylhex-5-enyl radical (**7**) give mainly the appropriate *trans*-radicals [(**4a**), (**4b**), and (**9**), respectively]. The stereoselective formation of (**3c**) from the 3-allylhex-5-enyl radical (**2c**) was previously ascribed to the effect of homoconjugation between the two olefinic bonds.[7] This hypothesis cannot be valid because the closely related radical (**2d**) exhibits similar stereoselectivity and because the radical (**1b**) containing a 1,6-diene system preferentially forms a *trans*-product (**4b**). Nor does the observed stereoselectivity reflect the relative thermodynamic stabilities of the product radicals.



We suggest therefore that the stereoselectivity of ring closure derives from the shape of the transition state in which, since the distance between C-1 and C-5 is not much

TABLE. Rate constants for ring closure at 80 °C.

Radical	$10^5 \Sigma k_c$/s^{-1}	$10^5 k_{cis}$/s^{-1}	$10^5 K_{trans}$/s^{-1}	k_{cis}/k_{trans}	Ref.
Hex-5-enyl	5·2	—	—	—	4
(**1a**)	12·8	4·6	8·2	0·56	This work
(**1b**)	7·5	2·7	4·8	0·56	" "
(**2a**)	16·5	12·1	4·6	2·53	" "
(**2b**)	9·8	7·5	2·3	3·3	" "
(**2c**)[a]	31·9	*ca.* 25·5	*ca.* 6·4	*ca.* 4·0	7
(**2d**)[a]	23·0	*ca.* 18·7	*ca.* 4·2	*ca.* 4·5	This work
(**7**)	9·7	1·6	7·8	0·21	" "

[a] Ratio of *cis*/*trans* determined by ^{13}C n.m.r. spectroscopy.

† Values of k_H, the rate constant for the reaction R• + Bu$_3$SnH → RH + Bu$_3$Sn• were obtained by combining kinetic data for the cyclization of hex-5-enyl radical (ref. 4) with the results of a product study on the reaction of hex-5-enyl radical with tributyltin hydride (ref. 3) and further unpublished results.

less[8] than that between C-1 and C-3 in cyclohexane, the hexenyl system assumes a chair-like conformation (**10**) with substituents preferentially occupying pseudo-equatorial positions. Thus, the most stable conformation of the transition state for a 3-substituted radical (**2**) will be that (**10**) which, on completion of the 1,5-bond, affords the *cis*-product (**11**). Similarly the preferred transition state for (**1**) or (**7**) will bear the substituent in a pseudo-equatorial position and hence will lie on the pathways to *trans*-product.

The hypothesis that the stereochemical outcome of 1,5-ring closure in hex-5-enyl systems is determined by conformational effects in a chair-like transition state, should be of wide generality and should apply equally to related hetero-atom centred radicals. Furthermore, since the degree of stereoselectivity is related to the conformational preference of the substituent it should be most pronounced with bulky groups. Recent examples of the cyclization of alkenylperoxyl radicals support these predictions.[9]

The stereoselectivity of cyclization of substituted hexenyl radicals has important implications for the practicability of forming bicyclic systems from acyclic radicals by two successive ring closures. Thus, treatment of the bromo-compound (**12**) with tributylstannane (0·009 M) affords moderate yields (71%) of *exo*- and *endo*-2-methylnorbornane *via* (**13**) because the initially formed 3-substituted radical (**2b**) preferentially forms the *cis*-product (**3b**) in which the reactive centres are correctly disposed to undertake further ring closure. Conversely, the 2-substituted radical (**1b**) under the same conditions gives a poor yield (33%) of bicyclic products; the major product is *trans*-3-methyl(vinyl)cyclopentane (**6b**).

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