

Steric Effects in Cyclization Reactions

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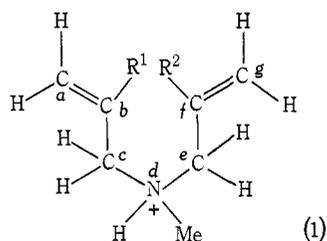
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Abstract

Calculations of geometric probability factors indicate that steric effects are important in determining whether the cyclization of β -substituted diallylmethylammonium ions results in five- or six-membered rings. Evidence is obtained of the direction of intramolecular attack.

Recent experimental results obtained in these laboratories¹ have shown that in the radical cyclization of β -substituted diallylmethylammonium ions (1) five-membered rings are formed in preference to six-membered rings except when there are two bulky β -substituents R^1 and R^2 (see Table 1). That result is contrary to predictions based on the thermodynamic stabilities of the products and indicates that a kinetic factor is important. An examination of molecular models suggests that this factor may arise from steric effects.

In this note, we report the results of model calculations of *geometric probability factors*, $P(5)$ and $P(6)$, for the formation of five- and six-membered rings respectively. The calculations have been made for the following simplified skeletal arrangements. The atom b carries the free electron contributed by addition of a radical to a in (1), and cyclization occurs by the attack of b upon f or g to give a five- or six-membered ring respectively. Clearly, such attack can only occur if b is in a suitable position with respect to f or to g , and our calculations have been aimed at estimating the probability of its being in that position. We have assumed (i) that the bond lengths and bond angles have the normal values for aliphatic compounds² and are fixed, and (ii) that there is free rotation about the single bonds. Three rotation angles are therefore needed to specify the internal configuration of the total skeleton. We have allowed each of these three angles to change, independently, by increments of 4° from 0° to 360° so that the skeleton could assume a total of $(360/4)^3 = 729000$ configurations.



¹ Hawthorne, D. G., Johns, S. R., Solomon, D. H., and Willing, R. I., *Aust. J. Chem.*, 1976, 29, 1955; Beckwith, A. L. J., Hawthorne, D. G., and Solomon, D. H., *Aust. J. Chem.*, 1976, 29, 995.

² Bowen, H. J. M., *et al.*, 'Tables of Interatomic Distances and Configurations in Molecules and Ions' (Chemical Society: London 1958).

We have defined geometric probability factor $P(5)$ as the ratio of the number of these configurations in which b is in a suitable position to attack f , to the total number. $P(6)$ is the corresponding ratio for attack of b upon g .

Table 1. Cyclization of β -substituted diallylmethylammonium ions (1)—experimental results

R ¹	R ²	Non-propagating ring type	Polymer ring type	R ¹	R ²	Non-propagating ring type	Polymer ring type
H	H	5	5	CMe ₃	H	5+6	5+6
Me	H	5	5	CMe ₃	CMe ₃	nil	acyclic
Me	Me	5 > 6	5+6	CO ₂ Et	H	nil	5 \gg 6
Et	H	5	5	CO ₂ Et	CO ₂ Et	nil	6
Et	Et	6	5+6	Ph	H	5	5 \gg 6
CHMe ₂	H	5	5	Ph	Ph	nil	5+6
CHMe ₂	CHMe ₂	6	acyclic				

We have considered three models for the cyclization step. The first is based on skeleton (2) and assumes that b can react with f or g if it approaches within a particular distance r from them, in any direction. It can be seen from the results in Table 2 that this simple model favours the formation of five-membered rings in all circumstances.

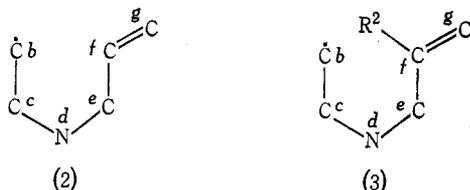


Table 2. Geometric probability factors $P(5)$ and $P(6)$ for reaction of b with f or g if it approaches within a particular distance r in any direction

r/nm	$P(5)$	$P(6)$
0.2	0.05	0.05
0.3	0.22	0.16
0.4	0.39	0.29

But, of course, it is much too simple. The attack leading to reaction is thought to depend on direction as well as distance. One suggestion,^{3,4} later discounted⁵ by indirect evidence from transition state theory, was that the direction of attack is approximately end-on to the double bond fg . We have therefore considered a second model, also based on the skeleton (2), in which we have calculated the proportion of the total possible configurations which place b within cones emanating from f and g with their axes in the line fg and with cone angles θ . The results in Table 3 show that

³ Bader, A., Buckley, R. P., Leavitt, F., and Szwarc, M., *J. Am. Chem. Soc.*, 1957, **79**, 5621.

⁴ Szwarc, M., and Binks, J. H., in 'Theoretical Organic Chemistry' p. 277, The Kekulé Symposium (Butterworths: London 1959).

⁵ Matsuoka, M., and Szwarc, M., *J. Am. Chem. Soc.*, 1961, **83**, 1260.

this model predicts that no six-membered rings can be formed and is therefore inconsistent with the experimental evidence.

Table 3. Geometric probability factors $P(5)$ and $P(6)$ for reaction of b with f or g if it approaches within a particular distance r and within cones (angle θ) emanating from f and g with their axes in the line fg

r/nm	$P(5)$			$P(6)$		
	$\theta = 10^\circ$	$\theta = 20^\circ$	$\theta = 30^\circ$	$\theta = 10^\circ$	$\theta = 20^\circ$	$\theta = 30^\circ$
0.2	0	0	0.00017	0	0	0
0.3	0.0017	0.0067	0.017	0	0	0
0.4	0.0074	0.033	0.070	0	0	0

The third model supposes that the attack has to take place in a direction roughly perpendicular to the double bond,⁶⁻⁸ that is, perpendicular to the plane containing e, f, g and R^2 in (3). In this case we have calculated the proportion of configurations which place b within cones of angle θ emanating from f and g in directions perpendicular to that plane, on each side of it. To allow for the steric effect of the substituent group R^2 , it was represented by a sphere of radius s and any configuration which placed b within that sphere was forbidden. The trends of the calculated results in Table 4 are consistent with the experimental results. Five-membered rings are favoured in almost all cases, but there is the possibility of the formation of six-membered rings.

Table 4. Geometric probability factors $P(5)$ and $P(6)$ for the reaction of b with f or g if it approaches within a particular distance r and within cones (angle θ) emanating from f and g and perpendicular to the double bond. The substituent R^2 is represented by a sphere s

s/nm	r/nm	$P(5)$			$P(6)$		
		$\theta = 10^\circ$	$\theta = 20^\circ$	$\theta = 30^\circ$	$\theta = 10^\circ$	$\theta = 20^\circ$	$\theta = 30^\circ$
0	0.2	0.0021	0.010	0.017	0	0.0079	0.019
	0.3	0.011	0.035	0.063	0	0.014	0.040
	0.4	0.012	0.052	0.11	0	0.014	0.057
0.2	0.2	0.0021	0.0086	0.012	0	0.0079	0.020
	0.3	0.011	0.036	0.058	0	0.014	0.042
	0.4	0.013	0.053	0.11	0	0.015	0.054
0.3	0.2	0	0	0	0	0.0020	0.0063
	0.3	0.0032	0.011	0.024	0	0.0072	0.022
	0.4	0.0048	0.027	0.071	0	0.0078	0.039
0.4	0.2	0	0	0	0	0	0
	0.3	0	0	0	0	0	0.0017
	0.4	0	0.0067	0.027	0	0.00011	0.012

Our conclusion from these model calculations is that steric factors are important in cyclization reactions. Furthermore, the results suggest strongly that the free radical addition occurs by attack perpendicular to the double bond.

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⁶ Capon, B., and Rees, C. W., *Annu. Rep. Prog. Chem.*, 1964, **61**, 221.

⁷ Richey, H. G., and Rothman, A. M., *Tetrahedron Lett.*, 1968, 1457.

⁸ Struble, D. L., Beckwith, A. L. J., and Gream, G. E., *Tetrahedron Lett.*, 1968, 3701.