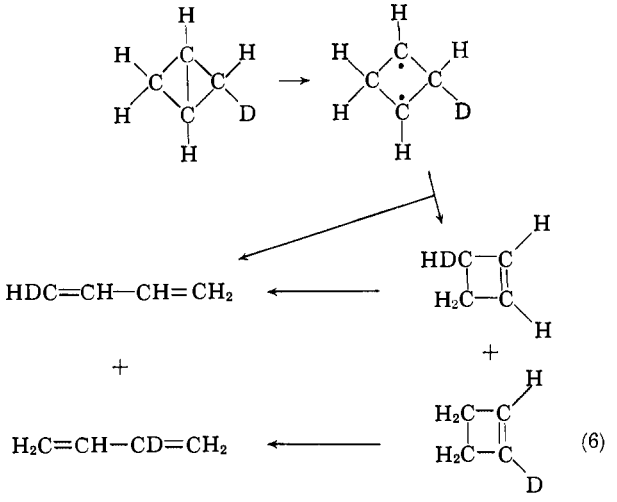

Decomposition of the dry salt (125°, 8 mm.) yields only cyclobutene-1-*d* (44%) and 1,3-butadiene-2-*d* (56%) as C_4 products. The deuterio hydrocarbons formed are thus consistent with that derived by carbon-skeleton rearrangement of cyclopropylmethylidene-*d* as in eq. 4.[6b] A similar mechanism is apparently involved in vacuum thermolysis of sodium 1-phenylcyclopropanecarboxaldehyde-*d* tosylhydrazone in that 1-phenylcyclobutene (78%) is formed containing deuterium only at the vinyl position.[6] The 2-phenyl-1,3-butadiene obtained (16%), however, contains most of its deuterium at the 1 and 4 positions and thus may be derived by isomerization of intermediate 1-phenylbicyclo[1.1.0]butanes-2-*d*.

(6) (a) The positions and ratios of hydrogen and deuterium in the products were determined by n.m.r. methods. (b) An alternate but unlikely mechanism being investigated with other systems involves insertion of cyclopropylmethylidene-*d* between its methylene carbons to give bicyclo[1.1.0]butane-1-*d* which reorganizes *via* its external bonds to cyclobutene-1-*d* and 1,3-butadiene-2-*d*.

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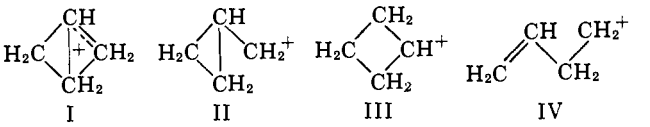
Intramolecular Reactions of Cyclopropylcarbinyl, Cyclobutyl, and Allylcarbinyl Cationic Systems

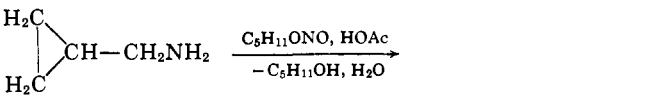
Sir:

Carbonium ion reactions of cyclopropylcarbinyl, cyclobutyl, and allylcarbinyl compounds result in extensive rearrangement.[1] The intermolecular products and the detailed mechanisms of such solvolyses vary according to the reagents and their environment.[1] In general, mixtures of cyclopropylcarbinyl, cyclobutyl, allylcarbinyl, and less frequently 1-buten-3-yl and 3-buten-1-yl derivatives are formed, possibly as derived from interconverting bicyclobutonium ions (I) and/or energetic classical cations (II–IV).[1] Recently decomposition of sodium cyclopropanecarboxaldehyde *p*-tosylhydrazone in proton-donor solvents was found to give bicyclo[1.1.0]butane as a major product along with cyclobutene, 1,3-butadiene, acetylene, and ethylene.[2] Bicyclo[1.1.0]butane and its isomeric C_4 hydrocarbons are apparently derived from intramolecular decomposition of high-energy cyclopropylmethyldiazonium ion intermediates. Since such processes have not been recognized previously, a study has been initiated (Table I) of the intramolecular reactions of cyclopropylcarbinyl, cyclobutyl, and allylcarbinyl cationic systems as generated from various sources. The disciplines of such processes are contrasted with those of analogous carbenic systems.

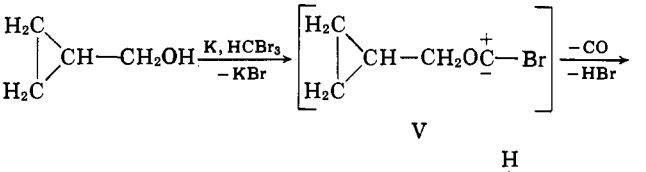


I II III IV

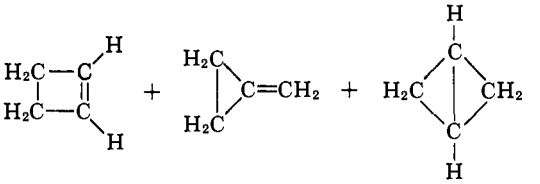
Deamination of cyclopropylcarbinylamine hydrochloride with amyl nitrite gives low yields (7%) of hydrocarbons derived from intramolecular processes. Bicyclo[1.1.0]butane is not formed; the product is primarily a mixture of cyclopropylcarbinyl chloride (72%), cyclobutyl chloride (13%), and allylcarbinyl chloride (15%). Aprotic diazotization[3] of cyclopropylcarbinylamine by amyl nitrite and acetic acid in chloroform results in extensive intramolecular insertion in which bicyclo[1.1.0]butane is the principal product (eq. 1).[4] The intramolecular products are similar to that in cationic decomposition of sodium cyclopropanecarboxaldehyde *p*-tosylhydrazone in proton-donor solvents (Table I) and appear to be derived from poorly solvated cyclopropylmethyldiazonium ion intermediates which are highly energized. Alkaline deoxidation of potassium cyclopropylcarbinol by bromoform,[5] a reaction involving dibromocarbene and apparent collapse of a subsequent intermediate such as V, yields



(1)



V



+ $H_2C{=}CH{-}CH{=}CH_2$ + $HC{\equiv}CH$ + $H_2C{=}CH_2$

(2) J. A. Smith, H. Shechter, J. Bayless, and L. Friedman, *ibid.*, 87, 659 (1965).

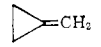
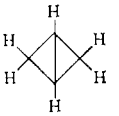
(3) (a) L. Friedman and F. M. Logullo, *ibid.*, 85, 1549 (1963); (b) aprotic diazotization of various amines will be described in subsequent publications by J. Bayless and L. Friedman.

(4) Cyclopropylcarbinyl (67%), cyclobutyl (20%), and allylcarbinyl (13%) acetates are formed *via* solvolytic routes.

(5) J. Hine, E. L. Pollitzer, and H. Wagner, *J. Am. Chem. Soc.*, 75, 5607 (1953); P. S. Skell and I. Starer, *ibid.*, 81, 4117 (1959).

(1) K. L. Servis and J. D. Roberts, *J. Am. Chem. Soc.*, 86, 3773 (1964), and references therein.

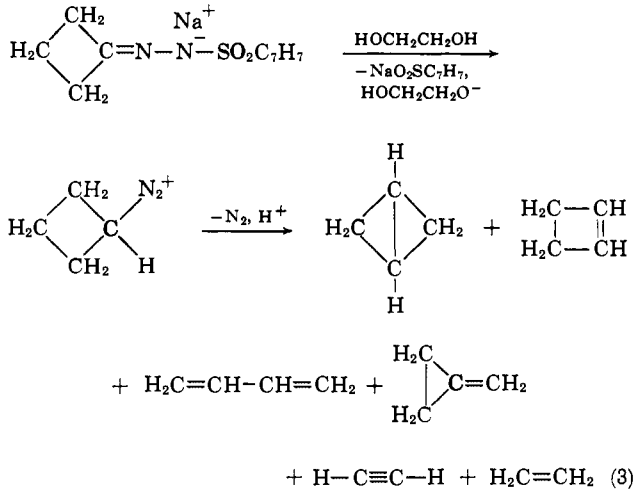
Table I. Intramolecular Products of Cationic Reactions of Cyclopropylcarbinyl, Cyclobutyl, and Allylcarbinyl Systems

System[b]	Yield, %	% composition of hydrocarbons[a]			
					$H_2C{=}CH{-}CH{=}CH_2$
c-$C_3H_5CH_2NH_2$, $C_5H_{11}ONO$, HCl	7		91		8
c-$C_3H_5CH_2NH_2$, $C_5H_{11}ONO$, HOAc	48	0.3	3	97	
c-$C_3H_5CH{=}N{-}NNa{-}O_2SC_7H_7$[c,d]	27–76	20–50	3–8	34–79	
c-$C_3H_5CH_2OH$, $CC_3H_5CH_2OH$, $HCBr_3$[d,e]	11	1	7	38	46
c-$C_4H_7NH_2$, $C_5H_{11}ONO$, HCl	13	40	56		
c-$C_4H_7NH_2$, $C_5H_{11}ONO$, HOAc	31	17	2	79–82	
c-$C_4H_6{=}NNHO_2SC_7H_7$, $NaOCH_3$, $HOCH_2CH_2OH$[d]	86	12	6	60	0
c-C_4H_7OK, c-C_4H_7OH, $HCBr_3$[d]	8	10	2	20	45
$H_2C{=}CHCH_2CH_2NH_2$, $C_5H_{11}ONO$, HCl[e]	30				96
$H_2C{=}CHCH_2CH_2NH_2$, $C_5H_{11}ONO$, HOAc[f]	30			8	88
$H_2C{=}CHCH_2CH_2OK$, $H_2C{=}CHCH_2CH_2OH$, $HCBr_3$[g]	12		2	2	77

[a] Small amounts of other C_4 hydrocarbons are formed. [b] Representative data. [c] Ref. 2. [d] Ethylene and acetylene are formed. [e] Similar results were obtained at −40 to 25°. [f] The principal intermolecular product is allylcarbinyl chloride. [g] Allylcarbinyl acetate (95%), cyclopropylcarbinyl acetate (2.5%), and cyclobutyl acetate (2.5%) are formed.

cyclobutene, methylenecyclopropane, bicyclo[1.1.0]-butane, 1,3-butadiene, ethylene, and acetylene. Details of decomposition of an intermediate such as V have not yet been established; however, it is apparent that the process involves highly energetic intramolecular cationic paths involving carbon–hydrogen insertion, carbon-skeleton rearrangement, and fragmentation. The present results indicate that the intramolecular routes for reaction of cyclopropylcarbinyl cationic intermediates depend on their energy contents. The principal internal reaction of lesser stabilized intermediates gives bicyclo[1.1.0]butane with expulsion of hydrogen ion; the analogous carbenic process for cyclopropylmethylidene results primarily in ring expansion to cyclobutene.[2]

Intramolecular processes in deamination of cyclobutylamine hydrochloride with amyl nitrite (Table I) lead in low yield to methylenecyclopropane by ring shrinkage along with cyclobutene and 1,3-butadiene; the intramolecular products are cyclobutyl chloride (26%), cyclopropylcarbinyl chloride (61%), and allylcarbinyl chloride (13%). Aprotic diazotization of cyclobutylamine or cationic decomposition of sodium cyclobutanone p-tosylhydrazone in ethylene glycol



+ $H_2C{=}CH{-}CH{=}CH_2$ +

+ $H{-}C{\equiv}C{-}H$ + $H_2C{=}CH_2$ (3)

(eq. 3) however yields bicyclo[1.1.0]butane as the principal C_4 hydrocarbon. Cyclobutene, 1,3-butadiene, and methylenecyclopropane along with ethylene and acetylene are minor intramolecular or fragmentation products; cyclobutyl acetate (48%), cyclopropylcarbinyl acetate (34%), and allylcarbinyl acetate (10%) are also formed. Alkaline deoxidation of cyclobutanol (excess) by bromoform gives bicyclo[1.1.0]butane, cyclobutene, and 1,3-butadiene in near-equivalent yields[6]; methylenecyclopropane, acetylene, and ethylene are also produced. It is of particular note that highly energetic cyclobutyl cationic processes result in such extensive transannular insertion to yield bicyclo[1.1.0]butane, whereas the principal carbenic process of cyclobutyl systems allows ring contraction to methylenecyclopropanes.[6]

1,3-Butadiene, ethylene, and acetylene are the major hydrocarbons derived from deamination of allylcarbinylamine or alkaline deoxidation of allylcarbinol (Table I). Intramolecular reactions of these allylcarbinyl cationic systems also yield bicyclo[1.1.0]-butane and methylenecyclopropane; however, insertion and carbon-skeleton rearrangement are much more prevalent in decomposition of cyclopropylcarbinyl and cyclobutyl cationic systems. The conversion of highly energized allylcarbinyl cationic intermediates to 1,3-butadiene, acetylene, and ethylene rather than bicyclo[1.1.0]butane, cyclobutene, and methylenecyclopropane may be rationalized on the basis that the "hot" cations lose much of their initial energies by the time they can undergo ring closure to the intermediate(s) that lead to the cyclic hydrocarbons.[7] The patterns of decomposition of allylcarbinyl cations thus differ from that for allylmethylene from which only 1,3-butadiene and bicyclo[1.1.0]butane are formed.[8]

Bicyclo[1.1.0]butane reacts rapidly with acidic reagents to give cyclopropylcarbinyl, cyclobutyl, and allylcarbinyl derivatives.[9] The present results thus raise questions as to the involvement of the bicyclic hydrocarbon as an intermediate in solvolytic reactions of cyclopropylcarbinyl, cyclobutyl, and allylcarbinyl cationic systems. Reaction of 1,2,2,4,4-pentadeuteriocyclobutanol-d and phosphorus pentachloride[10] gives

(6) L. Friedman and H. Shechter, *J. Am. Chem. Soc.*, **82**, 1002 (1960).
(7) E. Renk and J. D. Roberts, *ibid.*, **83**, 878 (1961).
(8) D. M. Lemal, F. Menger, and G. W. Clark, *ibid.*, **85**, 2579 (1963).
(9) K. B. Wiberg, private communication.
(10) H. Kim and W. D. Gwinn, *Tetrahedron Letters*, 2535 (1964).

1,2,2,4,4-pentadeuteriocyclobutyl chloride and 1,2,2,3,3-pentadeuteriocyclobutyl chloride in a 1:2 ratio. The rearranged dideuteriomethylene groups are statistically distributed among the 2, 3, and 4 positions as derived by interconversion of bicyclobutonium ion intermediates. There is no rearrangement involving transfer of hydrogen as required if bicyclo[1.1.0]butanes were reaction intermediates in this system. It may well be however that bicyclobutanes are significant intermediates in solvolytic reactions of highly energized cyclopropylcarbinyl and cyclobutyl cationic systems in environments of limited nucleophilicity. It will be of interest to determine if bicyclo[1.1.0]butane and its solvolytic products are formed *via* classical or nonclassical intermediates; upon extension of previous theory,[7] it is probable that bicyclo[1.1.0]butane will be formed from highly energized sources by classical rather than by nonclassical processes.

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The Role of Dipole Interactions in Determining Polypeptide Configurations

Sir:

As a consequence of the planar, *trans* conformation of the peptide linkage,[1,2] the distance between neighboring α-carbon atoms in the polypeptide is fixed within narrow limits, and the chain, shown in Figure 1, may be treated legitimately as a sequence of n_p virtual bonds of length l_p joining the α-carbons.[3] The mutual orientation of each pair of connecting virtual bonds, and hence the spatial configuration of the chain, is determined by the angles of rotation, φ''' and φ', about the two single bonds adjoining the intervening α-carbon. For a given such pair of single bonds, hindrances to rotation about one of the bonds are strongly dependent on the angle of rotation of the other, as is readily verified from molecular models. In contrast to the marked interdependence of rotations for the bonds comprising a given pair, the rotations of one pair are not significantly dependent on the angles of rotation of bonds in neighboring pairs.

A characteristic measure of the unperturbed dimensions[4] of the random polypeptide chain is given by $\langle r^2\rangle_0/n_p l_p^2$, the ratio of the actual mean square end-to-end distance, $\langle r^2\rangle_0$, to the mean square end-to-end distance for the random flight chain of virtual bonds, $n_p l_p^2$. Replacement of the continuous distribution of angles for rotations about the chain single bonds by sets of discrete rotation angles enables one to calculate theoretical values of $\langle r^2\rangle_0/n_p l_p^2$ from bond angles, bond lengths, and rotational potential functions using methods recently developed.[5] Because of the

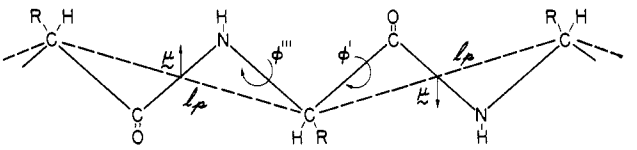

Figure 1. Virtual bonds are shown by dashed lines. Peptide group dipole moment vectors, $\boldsymbol{\mu}$, are depicted as arrows originating at the location of the dipole.

rotational interdependence within the pair of chain bonds adjoining an α-carbon, the potential function adopted must depend jointly on both rotation angles for the pair.

Calculations of $\langle r^2\rangle_0/n_p l_p^2$ based on small inherent sixfold torsional potentials and repulsive van der Waals interactions between nonbonded atoms yielded results smaller by a factor of about three than values estimated from the limited experimental data in the literature.[6] We therefore undertook experiments to determine $\langle r^2\rangle_0$ for poly-β-benzyl-L-aspartate in *m*-cresol at 100°, for poly-L-glutamic acid in aqueous 0.3 *M* sodium phosphate at pH 7.85 and 37°, and for poly-L-lysine hydrobromide in aqueous 1.0 *M* sodium bromide at pH 4.54 and 37°. The mean square end-to-end distances have been calculated from measured intrinsic viscosities, $[\eta]$, and osmotic molecular weights using the familiar relationship[4] $\langle r^2\rangle^{3/2} = [\eta]M/\Phi$, where $\Phi \cong 2.1 \times 10^{21}$ with $[\eta]$ in dl. g.$^{-1}$. Θ-Solvent conditions,[4] under which $\langle r^2\rangle$ assumes its unperturbed value $\langle r^2\rangle_0$, appear to be unattainable for these random polypeptides owing to the preference of the molecules for ordered configurations in poor solvents. The measurements were therefore conducted in the good solvents cited above, and the values of $\langle r^2\rangle$ obtained were corrected to $\langle r^2\rangle_0$ on the basis of measured second virial coefficients.[7,8] The polymers were unfractionated. A Poisson molecular weight distribution ($\bar{M}_w/\bar{M}_n \cong 1$) was assumed for the aspartate and lysine polymers; the most probable distribution ($\bar{M}_w/\bar{M}_n = 2$) was ascribed to the glutamic acid polymer. Errors attributable to departures from these assumed distributions affect the values of $\langle r^2\rangle_0/n_p l_p^2$ by no more than a few per cent.

A characteristic ratio of 9 ± 1 was found for all three polymers. Previously published results for poly-γ-benzyl-L-glutamate[6] yield a value in the same range. The experimental result is much larger than the value of 1.93 calculated assuming free rotation about the single bonds adjoining the α-carbons.[3,9] Thus, the same value of $\langle r^2\rangle_0/n_p l_p^2$ holds within experimental error for the four systems studied, marked differences in solvents and in amino acid side chains notwithstanding. It would appear that specific interactions between side chains, between side chains and backbone, or between polymer and solvent exert little effect on the unperturbed dimensions of these four molecules.

Further efforts to rationalize the experimental unperturbed dimensions in terms of the chain struc-

(1) L. Pauling, R. B. Corey, and H. R. Branson, *Proc. Natl. Acad. Sci. U. S.*, 37, 205 (1951).
(2) L. A. LaPlanche and M. T. Rogers, *J. Am. Chem. Soc.*, **86**, 337 (1964).
(3) P. J. Flory, *Brookhaven Symp. Biol.*, **13**, 89 (1960).
(4) P. J. Flory, "Principles of Polymer Chemistry," Cornell University Press, Ithaca, N. Y., 1953.
(5) For a review and extension of these methods, see P. J. Flory, *Proc. Natl. Acad. Sci. U. S.*, **51**, 1060 (1964).
(6) P. Doty, J. H. Bradbury, and A. M. Holtzer, *J. Am. Chem. Soc.*, **78**, 947 (1956).
(7) T. A. Orofino and P. J. Flory, *J. Chem. Phys.*, **26**, 1067 (1957).
(8) T. A. Orofino and P. J. Flory, *J. Phys. Chem.*, **63**, 283 (1959).
(9) W. G. Crewther, *J. Polymer Sci.*, **A2**, 123 (1964).