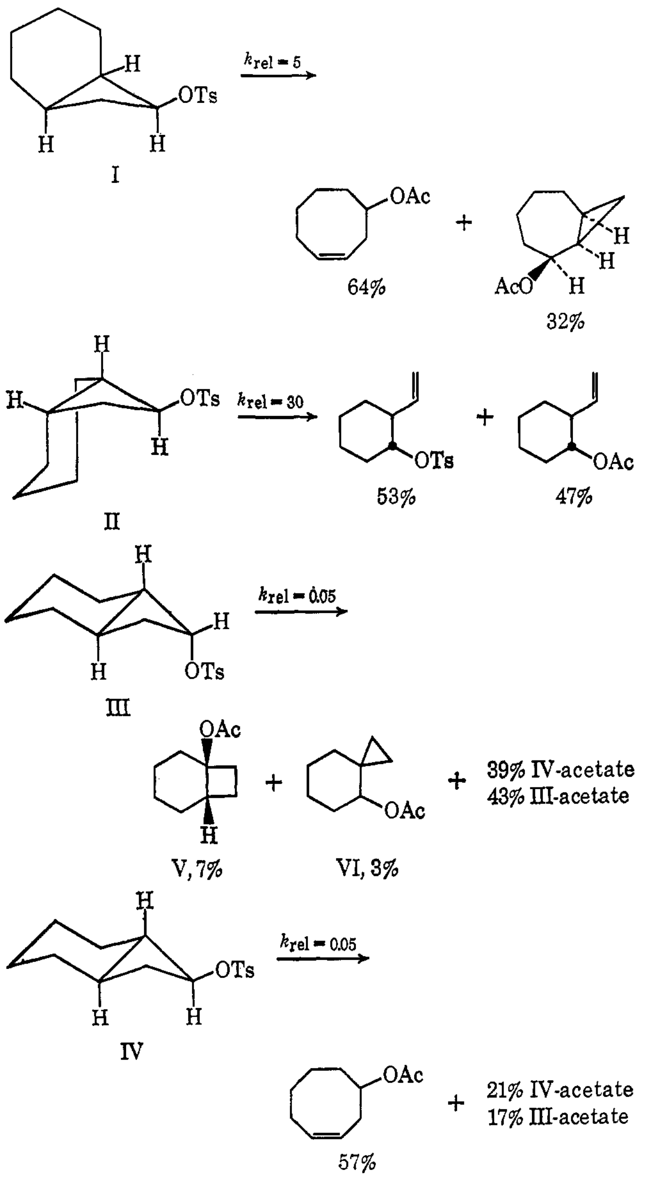
Orbital Factors in Cyclobutyl Solvolyses[1]

Sir:

Our molecular orbital calculations[2] suggest that the activated complex for cyclobutyl solvolyses may be stabilized by a cross-ring interaction. A corollary of this is that bond cleavage should occur in such a way as to maximize bonding at all times. This suggestion has also been made by DePuy.[3] We believe we have now found a case in which this effect is dramatically demonstrated.

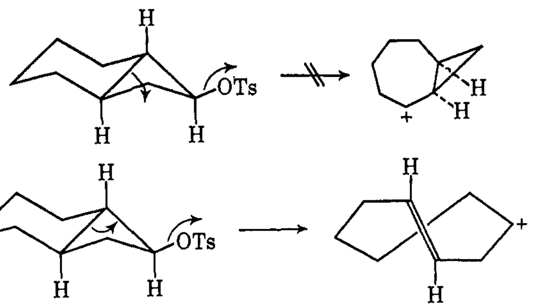
We have examined the acetolyses of the *cis*- and *trans*-fused bicyclo[4.2.0]octyl 7-tosylates (I–IV). The products derived from the *cis*-fused derivatives have been determined by Cope, *et al.*,[4] and we obtain corresponding results except that *cis*-bicyclo[4.2.0]octyl *trans*-7-tosylate (II) was found to give only vinylcyclohexyl products. The other products previously reported were derived from the internal return product, vinylcyclohexyl tosylate.



The *trans*-fused derivatives III and IV were obtained *via* the photochemical condensation of cyclohexenone with benzyl vinyl ether[5] (giving 55% *trans*-fused and 45% *cis*-fused 7- and 8-benzyloxybicyclo[4.2.0]octan-2-ones), lithium aluminum hydride reduction, conversion to the tosylate, lithium aluminum hydride hydrogenolysis, and debenzylation. The mixture of isomers was separated by preparative vpc. The isomer which led to hydrogen migration from the bridgehead position was assumed to have an axial tosyl group (III), whereas the other isomer was assumed to have an equatorial tosyl group (IV).[6] The results are summarized above. The rates given are relative rates as compared to cyclobutyl tosylate.

The reactions of I and III appear quite normal. Participation of the bridging bond in I would lead to the observed products with the correct stereochemistry. The increase in rate over cyclobutyl tosylate may result either from the stabilizing effect of alkyl substitution on the activated complex or from the relief of strain associated with the second ring. The reaction of III gives as rearranged products V and VI, which are also the products obtained in the solvolysis of *trans*-bicyclo[4.2.0]octyl 1-(3,5-dinitrobenzoate).[7] These products arise from the migration of the axial bridgehead hydrogen which is correctly situated for migration. The unrearranged products may arise either from a cyclobutyl cation or from a hydrogen-bridged species formed by migration of the axial hydrogen at the adjacent methylene position. The difference in rate between I and III might reasonably be expected.

The reactions of II and IV are not as easily described. II gives only vinylcyclohexyl derivatives, whereas it might be expected also to give bicyclo[4.1.0]heptane-7-methyl acetate.[8] Of more significance, the reaction of IV would be expected to give the bicyclo[5.1.0]octyl 2-acetate, whereas none is found. Further, the rearrangement to a cyclooctenyl derivative would be expected to lead to a *trans*-fused double bond which is destabilized by 9 kcal/mol.[9] It might be noted that the *trans* derivative, if formed, would be converted to *cis* under the reaction conditions.



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[1] This investigation was supported by Public Health Service Grant GM12800 from the National Institutes of General Medical Science.

[2] K. B. Wiberg, *Tetrahedron*, 24, 1083 (1968).

[3] C. H. DePuy, *Accounts Chem. Res.*, 1, 33 (1968).

[4] A. C. Cope, R. W. Gleason, S. Moon, and C. H. Park, *J. Org. Chem.*, 32, 942 (1967).

[5] E. J. Corey, J. D. Bass, R. LeMahieu, and R. B. Mitra, *J. Am. Chem. Soc.*, 86, 5570 (1964).

[6] All new compounds gave satisfactory elemental analyses and had nmr spectra in accord with the assigned structures. The products were identified by vpc separation and comparison of spectra with those of authentic samples.

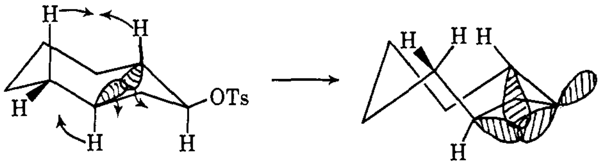
[7] Unpublished results, J. E. Hiatt.

[8] This would be in analogy with the results of the solvolysis of the corresponding bicyclo[3.2.0]heptyl tosylate: H. L. Goering and F. F. Nelson, private communication; F. F. Nelson, Ph.D. thesis, University of Wisconsin, 1960.

[9] R. B. Turner and W. R. Meador, *J. Am. Chem. Soc.*, 79, 4133 (1957).

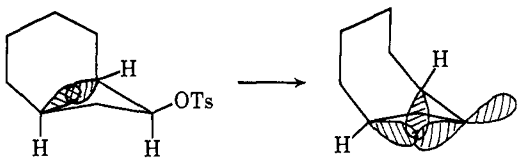
Using conditions which permitted the isolation of *trans*-2-cycloocten-1-ol from *exo*-bicyclo[5.1.0]oct-8-yl bromide (aqueous dioxane with calcium carbonate)[10] the solvolysis of IV was found to give *trans*-3-cycloocten-1-ol. This was identified by its rapid reaction with phenyl azide to give a triazoline. The *cis* isomer is quite unreactive toward this reagent.[11]

If one accepts the postulate that maximum boiling must be maintained during the reaction,[12] the observations are explicable.



The type of rotation shown above, which is required in order to give the bicyclo[5.1.0]oct-2-yl cation, is opposed by hydrogen–hydrogen repulsion, as well as carbon–carbon repulsion. On the other hand, a process leading to the *trans*-3-cycloocten-1-yl cation need not involve such interaction. Similar considerations apply to the reaction of II. The formation of the bicyclo[4.1.0]-heptane-7-methyl cation *via* the type of rotation described above would require a marked distortion of the cyclohexane ring. However, the process leading to the vinylcyclohexyl cation does not pose such difficulty.

The situation with I is quite different than that for IV. Here the rotation will relieve strain in the cyclohexane ring. In I, the ring is flattened by fusion onto a cyclobutane ring, and the rotation is in a direction to restore the normal conformation of the cyclohexane ring. Thus it is not unreasonable that the process will occur.



These ideas appear to correlate a variety of observations which have been made concerning the solvolyses of cyclobutyl derivatives. They will accommodate the difference in reactivity and mode of reaction which has been observed with the *cis*- and *trans*-3-substituted cyclobutyl derivatives[13] and also predict a specific stereochemistry for the ring opening to a homoallyl derivative. This will be discussed in detail at a later time.

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(10) G. H. Whiham and M. Wright, *Chem. Commun.*, 294 (1967).

(11) The use of phenyl azide was based on the observation that *trans*-cyclooctene reacts rapidly with this reagent (K. Ziegler and H. Wilms, *Ann.*, **567**, 1 (1950)) whereas *cis*-cyclooctene reacts only slowly (K. Alder and G. Stein, *ibid.*, **501**, 41 (1933). The triazoline was identified by its ultraviolet spectrum and mass spectrum, which were very similar to those for the adduct from *trans*-2-cycloocten-1-ol.

(12) This is, of course, the explanation used for the stereochemistry of the solvolytic ring opening of cyclopropyl derivatives: R. B. Woodward and R. Hoffmann, *J. Am. Chem. Soc.*, **87**, 395 (1965); C. H. DePuy, L. G. Schnack, and J. W. Hausser, *ibid.*, **88**, 3343 (1966); U. Schollkopf, K. Fellenberger, M. Patsch, P. von R. Schleyer, T. Su, and G. W. van Dine, *Tetrahedron Letters*, 3639 (1967).

(13) I. Lillien and R. A. Doughty, *ibid.*, 3953 (1967); I. Lillien, G. F. Reynolds, and L. Handloser, *ibid.*, 3475 (1968).

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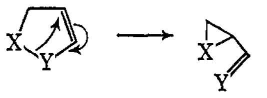
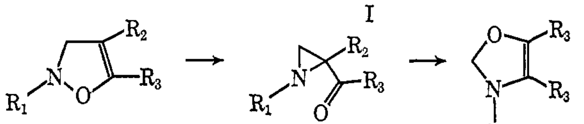
Valence Rearrangement of Hetero Systems. The 4-Isoxazolines

Sir:

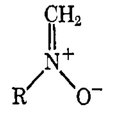
When two hetero atoms of higher electronegativity than carbon, *e.g.*, nitrogen, oxygen, halogens, are linked together through a single bond, it is well known that such linkages are considerably weaker than similar bonds with carbon.[1] The origins of this effect are not at present clear, but repulsion between the necessarily higher nuclear charges and/or the nonbonded electron pairs may be responsible. Whatever its source, this effect was considered to be a potential driving force in the development of new synthetic procedures, *e.g.*, eq 1, where X and Y are atomic species of the types mentioned.[2] Accordingly we have examined the 4-isoxazolines (II), since they were readily available from nitrones and acetylenes, and have herein demonstrated the existence of the facile thermal valence rearrangements of 4-isoxazolines (II) to 2-acylaziridines (III) and subsequently to 4-oxazolines (IV).[3] The relative rates of the two steps are dependent on the various substituents R_1, R_2, and R_3, and so we have used a series of substituting functions to allow the isolation of the separate steps.



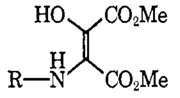
I (1)



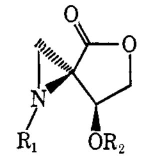
II III IV



V



VI



VII

Addition of *t*-butylmethylenenitrone[4] (V, R = *t*-butyl) to dimethyl acetylenedicarboxylate proceeded rapidly and quantitatively at 0° (nmr control) to the isoxazoline[5] II (R_1 = *t*-butyl; $R_2 = R_3 = CO_2Me$; λ_{max} (ethanol) 289 mμ (ϵ 3260); ν_{max} (neat) 1760, 1715, 1660 cm^{-1}; nmr (carbon tetrachloride), τ 8.88 (9 H, singlet), 6.33 (3 H, singlet), 6.18 (3 H, singlet), 5.82 (2

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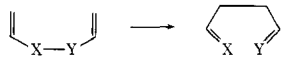
(1) Data on bond dissociation energies that have been determined, with criticisms of the methods and results, are listed in several places, *e.g.*, T. I. Cottrell, "The Strengths of Chemical Bonds," 2nd ed., Butterworth & Co. (Publishers) Ltd., London, 1958; J. A. Kerr, *Chem. Rev.*, **66**, 496 (1966).

(2) System I may be regarded as an example of a more general process, *i.e.*



which is exemplified by the well-known benzidine rearrangement and Fischer indole synthesis (X = Y = N). Aryl peroxides are only reported as very unstable reaction intermediates; *cf.* C. Walling and S. A. Buckler, *J. Am. Chem. Soc.*, **77**, 6032 (1955).

(3) This work was initiated at Imperial College, London, and we thank Professor D. H. R. Barton for the use of facilities.

(4) J. E. Baldwin, A. K. Qureshi, and B. Sklarz, *Chem. Commun.*, 373 (1968).

(5) Satisfactory analytical data have been obtained. *Anal.* Found: C, $<\pm0.2$; H, $<\pm0.3$; N, $<\pm0.5$.