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THE REDUCTION OF BICYCLOBUTANES TO CYCLOBUTANES BY LITHIUM IN PRIMARY AMINES[1a]

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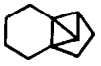
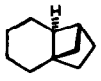
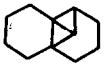
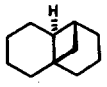
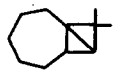
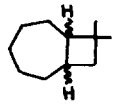
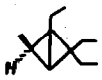
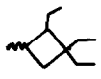
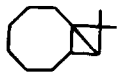
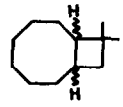
Bicyclobutanes undergo ready catalytic hydrogenation, but in general, mixtures of reduction products are obtained and the predominant mode of cleavage varies from compound to compound.[2] Although the central bond is presumably the most strained, cleavage of this bond to give a cyclobutane, which would be stable to further hydrogenation, is usually not observed or is found as a minor pathway. Based on considerations of the nature of the bonding in bicyclobutanes, we felt that it should be possible to cleave the central bond selectively by some type of reduction based on electron transfer and that any such method would be of considerable theoretical interest.

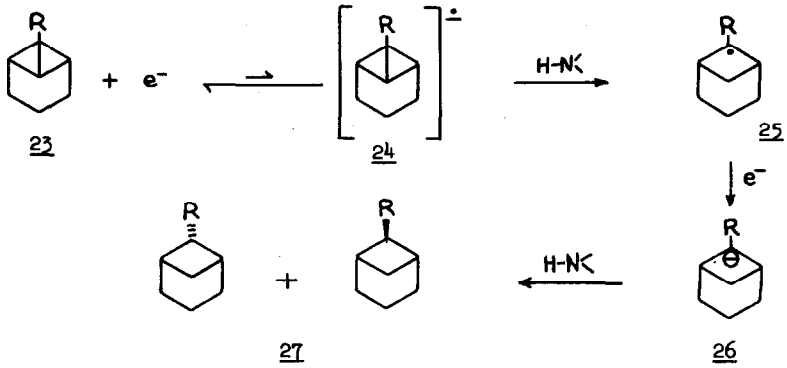
In related studies we have prepared a number of alkyl-substituted bicyclobutanes via cyclopropylidene insertion reactions employing procedures similar to those we have reported previously.[2b,3] We have investigated the reactivity of several of these bicyclobutanes toward alkali metal reduction. Sodium in refluxing ammonia with or without added tert-butyl alcohol caused no reduction; starting materials were recovered. However all of the bicyclobutanes listed in Table I can be reduced quantitatively to cyclobutanes with lithium in refluxing ethylamine[4] or ethylenediamine.[5] The latter appears to be the reagent of choice since it gives a more potent reducing system which will effect reduction quickly where ethylamine fails.

The products have been characterized as cyclobutanes by combined spectral methods.[6] Mass spectra have established the molecular formulas and, in addition, the fragmentation patterns can be interpreted in terms of the assigned structures and are consistent with the presence of cyclobutane rings. In every case the nmr and ir spectra unequivocally establish the absence of cyclopropyl protons and unsaturation. Although the nmr spectra tend to be complex, in many cases reasonably detailed nmr assignments can be made and in all cases the signals expected for unique groups such as $CH_3CH<$, $(CH_3)_2C<$, $(CH_3)_2CH-$, $(CH_3CH_2)_2C<$, $(CH_3)_3C-$,

TABLE I. Reduction of Bicyclobutanes with Lithium and an Amine

Reactants[4,5] (ref.)		Products (ratio of stereoisomers	Reactants (ref.)		Products (ratio of stereoisomers)
 1	EA (2b)	 2	 13	EA (3g,h)	 14
 3	EA (3a,b)	 4	 15	EDA (3i)	 35:65 16
 5	EA (3a,c,j)	 6	 17	EDA (3i)	 50:50 18
 7	EA (3d,e)	 8	 19	EDA (3i)	 68:32 20
 9	EA (3f)	 10	78 trans 22 cis		
 11	EA (3f)	 12	72 trans 28 cis		
			 21	EDA (3i)	 50:50 22

SCHEME I



etc., are observed.[7]

Although the first seven bicyclobutanes in Table I underwent complete reduction after 8 hr in ethylamine, under the same conditions reduction of compound 15 was only 62% complete (giving a 30:70 mixture of stereoisomers) and 17 underwent no reduction. Both compounds, however, were quantitatively reduced in ethylenediamine.[5] Whether this difference reflects a solvent effect or simply the large temperature difference (ca 100°) is not known.

In cases where only a single cyclobutane can be formed, only one product is observed (2, 8, 14). Compounds 4 and 6 also appear to be free of stereoisomers. In both compounds the bicyclo[4.2.0]octane ring systems could be either cis or trans fused. Examination of molecular models indicates that in each case the cis configuration must be substantially lower in energy than the trans. In view of the proposed mechanism for the reduction (below), we have assigned the cis configuration to both 4 and 6.[9] In all other cases, the two possible stereoisomers are formed. Based on nmr and mass spectral data we have assigned the trans configuration to the major isomers of 10 and 12. In other examples (16, 18, 20, 22) at present we have made no stereochemical assignment.

At this time we suggest the mechanism for this reaction outlined in Scheme I. A bicyclobutane such as 23 must have an antibonding orbital sufficiently low in energy to permit formation of a radical anion 24 having the electron density concentrated in the central bond. Protonation at the unsubstituted terminus of this bond to give the more stable radical 25 would account for the ultimate formation of both possible stereoisomers 27 because the addition of an electron to 25 gives an anion 26 which should protonate from either side unless the molecule is conformationally constrained in a manner which permits protonation from only one side.[9b] We believe that the fact that increasing the bulk of a group R on a central bridgehead position inhibits reduction (15 and 17 in ethylamine) indicates hindrance to proton rather than electron transfer, implying that the second step is rate determining.

REFERENCES

(1) (a) Supported in part by the National Science Foundation (GP-8181); (b) National Institutes of Health Predoctoral Fellow 1964-1967; (c) National Institutes of Health Predoctoral Fellow 1968-1970.

(2) Representative examples: (a) K. B. Wiberg and R. P. Ciula, J. Am. Chem. Soc., 81, 5261 (1959); (b) W. R. Moore, H. R. Ward, and R. F. Merritt, ibid., 83, 2019 (1961); (c) J. Meinwald, C. Swithenbank, and A. Lewis, ibid., 85, 1880 (1963); (d) S. Masamune, ibid., 86, 735 (1964); (e) W. von E. Doering and M. Pomerantz, Tetrahedron Letters, 961 (1964); (f) D. M. Lemal and K. Shin, ibid., 3231 (1964); (g) W. von E. Doering and J. F. Coburn, Jr., ibid., 991 (1965).

(3) A series of papers describing the chemistry of these systems is in preparation. All of the bicyclobutanes referred to here have been completely characterized by elemental analysis and mass, nmr, and infrared spectra. The bicyclobutanes have been prepared in our laboratories by the following coworkers: (a) Sr. Eleanor Robert Boardway, (b) Thomas C. Jensen, (c) William J. Steffy, (d) Zalman L. F. Gaibel, (e) K. Grant Taylor, (f) John B. Hill, (g) John L. Marshall, (h) Stan S. Hall, (i) Corey Largman. Compound 5 has also been reported by (j) R. Vaidyanathaswamy and D. Devaprabhakara, Chem. Ind. (London), 515 (1968).

(4) The bicyclobutane was added to a well-stirred, dark-blue solution of (excess) lithium in ethylamine under helium, and the mixture was allowed to stand for 8 hr at reflux (ca 17°) before processing in the usual way. Significantly shorter reaction times led to incomplete reduction.

(5) The bicyclobutane was dissolved in ethylenediamine at room temperature under helium and, while stirring, excess lithium was added, bringing the solution to reflux (ca 117°). After ca 5 min the blue color was discharged at which time the mixture was cooled and processed in the usual way.

(6) In addition, reduction product 8 has been shown to be identical with a sample synthesized independently in our laboratories by P. Müller.

(7) For example, the nmr spectrum of 2, a crystalline solid, mp 28.5-29.5°, is very similar to that of bicyclo[2.1.1]heptane[8] and related assignments can be made.

(8) (a) R. Srinivasan, J. Am. Chem. Soc., 83, 2590 (1961); (b) J. Meinwald and A. Lewis, ibid., 83, 2769 (1961); (c) K. B. Wiberg, B. R. Lowry, and B. J. Nist, ibid., 84, 1594 (1962).

(9) (a) A cis-bicyclo[4.2.0]octane system corresponds to a trans-perhydroindane system (4) and a trans-decalin system (6). (b) We suggest that the intermediate anion related to 26 would be constrained to the cis configuration.