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CYCLOBUTANE–BICYCLOBUTANE SYSTEM—6

AN *AB INITIO* CALCULATION OF THE PREFERRED PATHWAY FOR NUCLEOPHILIC ATTACK ON BICYCLOBUTANE

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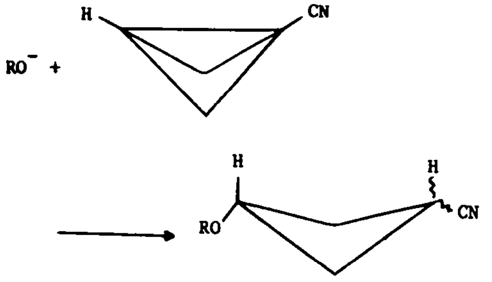
Abstract—The stereochemistry of the nucleophilic attack of H^- on bicyclobutane was studied by *ab initio* calculations of various possible pathways. Three directions of approach; axial, equatorial and sidewise, were examined by using a split levels basis set. Relative to an axial or sidewise approach, the equatorial was found to be significantly favored.

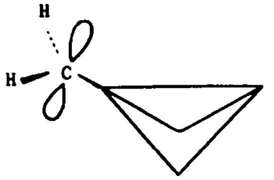
In the course of studies on cyclobutane–bicyclobutane system, we became interested in various aspects of nucleophilic attack on bicyclobutane (BCB).[2,3] The central bond of BCB closely resembles a π bond in its ability, when suitably activated, to undergo nucleophilic addition. We have shown[3] that for the bridgehead cyano activated compound, the central bond is cleaved during the course of a nucleophilic attack, as shown in eqn (1).



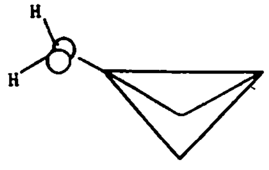
(1)

Since the product, 1,3 disubstituted cyclobutane, can exist as two geometrical isomers, the direction of addition of the nucleophile may be determinative of the stereochemical outcome of the reactions (and therefore of their reversal as well). Nucleophilic attack on C–C double bonds takes place in a plane perpendicular to that of the olefin. Due to the planarity of the latter, the nucleophile can approach the molecule from either side with equal probability. Since, structurally, BCB differs significantly from an olefin one should carefully consider possible alternative directions of approach for a nucleophile reacting with BCB.

An in-plane attack on an olefin (orthogonal to the π system) is to the best of our knowledge, not known. In nucleophilic vinylic substitution reactions such an attack would result in an inversion of configuration. Yet these reactions show mainly retention of configuration and in some cases, where long-lived carbanions are involved, stereoconvergence is observed.[4] No pure inversion has been reported and no evidence for in-plane attack has ever been found. However, unlike an olefinic C, an acetylenic C is susceptible to attack in the orthogonal plane as well. In this context, the bridgehead C of BCB may somewhat resemble an acetylenic one. This resemblance is manifested, for example, in the hybridization of its bond to the H atom[5] ($sp^{1.58}$). Another manifestation of this feature of the bridgehead C is found in the rotational barrier of methylenebicyclobutyl anion (1).



1a



1b

Greenberg reported several years ago[6] an unexpectedly low rotational barrier for **1** (taken as the energy difference between structures **1a** and **1b**). We have recently found[7] that this low barrier does not result from the lack of ability of the π^*-like orbital of the central bond to stabilize the negative charge in the **1a** conformation but is due rather to an effective stabilization of **1b** as a result of an interaction between the p orbital on the methylene C and a combination of the two σ^* orbitals of the two side C–C bonds. Thus, like in acetylene, one should consider the possibility of nucleophilic approach both in the XY and the XZ planes (Fig. 1). Since however, the two faces of BCB (above and below the XZ plane) are not identical, one must also consider the possibility of two different directions of approach, namely axial and equatorial in the XY plane.

In our previous papers,[2,3] we have tentatively assumed an equatorial approach for *nucleophilic* reactions on BCB. Interestingly, Lehn[8] has calculated that this equatorial approach is the preferred mode for *electrophilic* attacks (H^+) on BCB. In order to determine whether the equatorial approach is indeed as we have assumed, the preferred one for nucleophilic reactions as well, we have performed an *ab initio* study of the reaction of H^- with BCB testing the axial, equatorial and sidewise approaches as shown in Fig. 1.

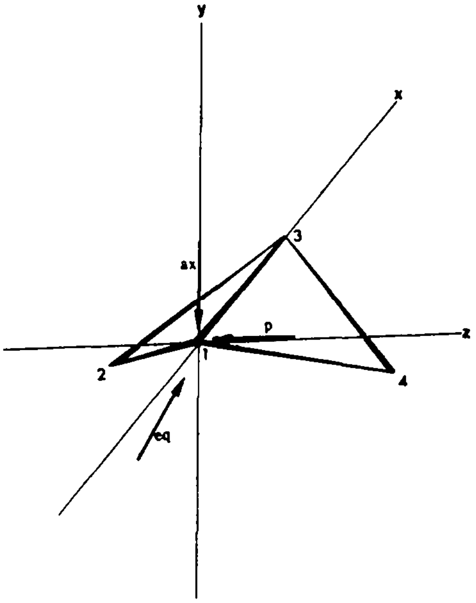


Fig. 1. General directions of H^- approach to bicyclobutane.

METHODS AND RESULTS

In order to find the preferred direction of the nucleophilic attack on bicyclobutane we have used H^- as a nucleophile and unsubstituted bicyclobutane as a substrate.

Three approach directions were studied: (a) the axial approach (ax) in the XY plane from above the molecule; (b) an equatorial approach (eq) from the lower side in the XY plane; and (c) a sidewise approach (p) in the XZ plane. These general directions are shown in Fig. 1. In each zone of approach the H^- was located at several points on each of a series of three arcs centered on the bridgehead C. The radii of these arcs were chosen as 1.25, 1.5 and 1.75 Å. The energy of each configuration was determined by an *ab initio* calculation using the HONDO program[9] with an energy optimized $(9^s4^p)/[3^s2^p]$ split valence basis set.[10] The geometry of the bicyclobutane employed in the present calculations was that determined by Wiberg *et al.*[11] This geometry was maintained constant and was not optimized for each of the H^- locations. Although this procedure does not give the exact optimal track, it can still provide a reliable indication as to the preferred mode of approach, especially if the various approach lines differ significantly in their energy.

The location of the minimum of energy on each of the arcs was found in several steps. In the first step the energy of four to six points equally spaced on each arc was calculated. In the consecutive steps additional points were sampled in the area shown by the previous steps to contain the minimum in energy on the arc. This procedure was repeated until the energy separation between adjacent points at the zone of minimum energy did not exceed 2 kcal/mol. Finally, the minimum was found by solving a quadratic equation for three neighboring points in the minimum zone. Results are given in Table 1.

In addition, the energy of BCB with H^- at r = 1.25 Å along the C1–C2 bond (anti to C2) was calculated to be −154.952326 au.

DISCUSSION

As can be clearly seen from the graphical presentation of the change in energy as a function of the distance between H^- and the BCB molecule (Fig. 2), the equatorial approach is greatly preferred over

Table 1. Total energies as a function of the distance of H^- from BCB for the optimal approach in each of the three directions

		E_{au} [a,b,c]	
r Å [d]	eq [e]	ax [e]	p [e]
1.25	-155.120602 (-1.100,0.594,0.0)	-154.94768 (0.204,-1.238,0.0)	-155.063989 (-1.25,0.0,0.0)
1.5	-155.146130 (-1.346,0.662,0.0)	-155.053613 (0.149,-1.493,0.0)	-155.111490 (-1.50,0.0,0.0)
1.75	-155.167485 (-1.585,0.742,0.0)	-155.132242 (0.0,-1.75,0.0)	-155.150858 (-1.75,0.0,0.0)

a. Numbers in parentheses are coordinates (X,Y,Z respectively) of H^-.

b. The coordinates of carbon atoms of BCB are C1 (0.0,0.0,0.0); C2 (0,748,0.623,1.139); C3 (1.497,0.0,0.0); C4 (0.748,0.623,-1.139).

c. The energy of separated reactants is -155.20552 a.u.

d. r - distance of H^- from C1.

e. eq. - equatorial approach; ax - axial approach; p - perpendicular - sidewise approach, see arrows on Figure 1.

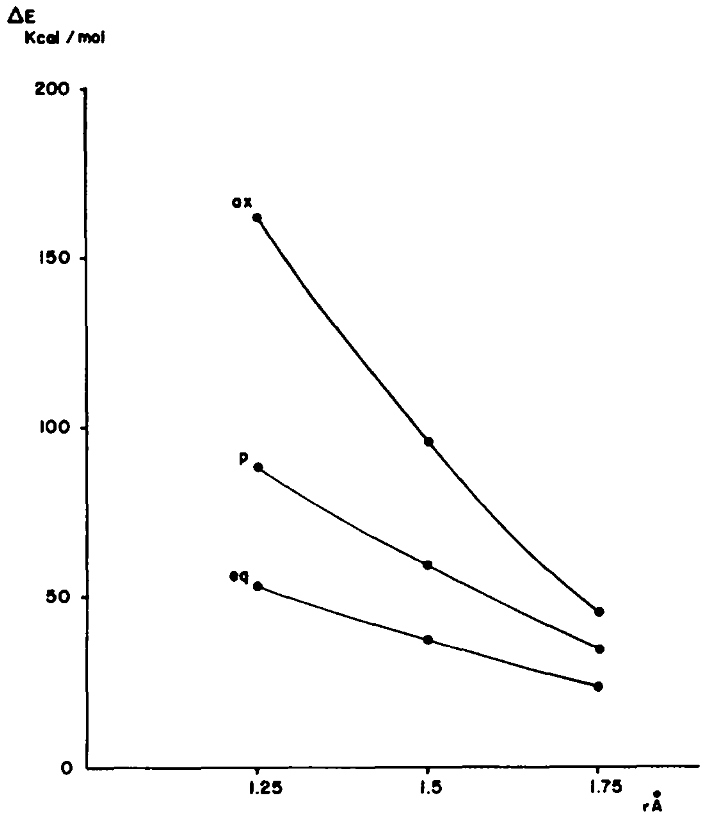


Fig. 2. Change in energy of H⁻ + BCB at various distances of H⁻ from C-1 compared to the separated reactants; ax, eq and p are axial equatorial and sidewise approaches.

the axial one. Although the BCB geometry has not been reoptimized during the various steps, the large energy separation between the two pathways (108.7 kcal/mol at r = 1.25 Å) lends much support to the hypothesis that the nucleophile will prefer the equatorial approach in an actual reaction.

Regarding C-3 of BCB as a leaving group in this system, one can draw an analogy between the reaction with H^- and an SN2 displacement. The preferred back side approach in SN2 reactions is generally attributed to two main factors.[12] One is the repulsion between the nucleophile and the charge density at the bond to the leaving group. The other is due to the nodal plane in the LUMO of the substrate. During the course of a front side attack, the bonding overlap between the HOMO of the nucleophile and one of the LUMO lobes is largely compensated by an anti-bonding interaction with the other one. It is difficult to estimate the repelling effect of the charge concentrated in the central bond of BCB. Nevertheless, it is clear that even if this effect is smaller here than the one existing in a typical SN2 substrate such as methyl bromide, it contributes at least in part to the overall preference for an equatorial attack. As to the second effect, an obvious difference between methyl bromide and BCB lies in the concentration of the LUMO on the electrophilic C. Since the electronegative bromine atom polarizes the σ bond onto itself, the anti-bonding orbital in methyl bromide resides largely on the C. In BCB, the two groups on the two sides of the central bond are of equal electronegativity and therefore the coefficients on both C atoms are equal. Thus the anti-bonding component in the axial approach is expected to be larger than in the model compound methyl bromide. On the other hand, for the same reason, the energetic advantage of a rear side approach is probably somewhat diminished. It is therefore difficult to draw an unambiguous conclusion as to the origin of the preferred equatorial approach. Our method of calculation does not provide a clear insight as to the origin of this preference. However a comparison of the amount of charge transferred (based on Mulliken populations) from the H^- to BCB reveals that while only 0.37 e^- is transferred to the substrate from H^- when r = 1.25 Å in the axial direction, 0.69 e^- are transferred to BCB from an H^- at the same distance in equatorial direction. If the amount of charge transferred to BCB by H^- can be taken as an indication of the degree of orbital interaction, it is clear that one of the major reasons for the preferred rear side approach is a better orbital interaction as compared to that in an axial approach.[13] An additional factor which is likely to play an important role in actual reactions is the bulkiness of the nucleophile. This factor is likely to play an important role in the reactions with BCB since the axial and the equatorial approaches differ from each other by their steric susceptibilities. The bridgehead C of BCB has an inverted geometry[11] (all four bonds are contained in a single hemisphere). An equatorial approach is thus sterically favored as this is the exposed side of the molecule. Since the majority of the nucleophiles are larger than H^-, this factor is likely to contribute significantly more to the overall equatorial preference in an actual reaction.

The stereochemical implications of the preferred line of approach will manifest themselves in the 1,3-elimination reactions as well as in the nucleophilic ring cleavage reactions. In the latter type of reactions, the final stereochemistry is determined by the preferred direction of protonation. If one assumes that the lifetime of the carbanion is long enough for it to undergo rapid inversions and the ring can flip-flop (barrier for this process is 0.9 kcal/mol for BCB[14]) before it is protonated, then the direction of the nucleophilic approach is practically, stereochemically insignificant. In cases of a very short lived carbanion, when the proton donor may be preassociated[15] with the BCB, no doubt the stereochemistry of the products will be determined by the preferred direction of the nucleophilic approach.

The third conceivable line of approach, the perpendicular one, will ultimately lead to a cleavage of a side C–C bond. It should be pointed out that the relief of the strain will hardly differentiate between a central bond cleavage to give a cyclobutanic system and a side bond cleavage which results in the formation of a cyclopropylcarbinyl moiety. This results from the similarity of the strain associated with the two systems; 26.9 kcal/mol for cyclobutane and 28.13 kcal/mol for cyclopropane.[16] Thus, thermodynamic strain factors are not likely to determine the actual direction of a nucleophilic approach. However, it is interesting to note that the optimal approach in the XZ plane is along the X axis. Thus, the preferred line of approach in the XZ plane is in fact also in the XY plane where the HOMO of the nucleophile can effectively interact with the LUMO of the central bond of BCB (for $r = 1.25$, deviation of 45° from the X-axis in the XZ plane, gives a 44 kcal/mol rise in energy. A deviation of 60° results in an energy rise of 88 kcal/mol). We have also determined the energy of the system where H^- is located colinearly with the C1–C2 axis with $r = 1.25$ Å. This is the "classical" anti position required for an SN2 reaction on the side bond. However in spite of the absence of any strain factor constraints, its energy was found to be higher by *ca* 105 kcal/mol than that of the optimal equatorial approach at the same distance, showing that central bond cleavage is strongly preferred over side bond cleavage in nucleophilic reactions. (At this configuration only $0.22\,e^-$ are transferred from the H^- to the BCB molecule.)

In conclusion, it is clearly shown that orbital interactions direct the nucleophile in its reaction with BCB toward an equatorial rather than an axial or a sidewise approach.

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