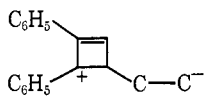
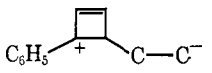
reaction with the dienophile proceeds *via* the more reactive isomer, namely B. However with the extremely reactive dienophiles the rate of interconversions is relatively slow and the two types of adducts are observed. Unless tetracyanoethylene and dicyanomaleimide accidentally have the same relative reactivity, it follows that the equilibrium constant for eq 1 is approximately 7 in favor of isomer A.[8]

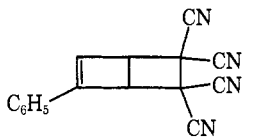
If cyclobutadiene were square and only one 1,2-diphenyl derivative existed then it could be argued that the different types of adducts result from a switch in mechanism from a concerted Diels–Alder reaction with benzoquinone and N-phenylmaleimide to a dipolar or diradical type addition with tetracyanoethylene and dicyanomaleimide. With tetracyanoethylene the intermediate 1,2-diphenylallyl cation (or radical) derivative VII would then be required to close preferentially to yield the isomer IV; such also would be required with dicyanomaleimide and it would be then held accidental



VII



VIII



IX

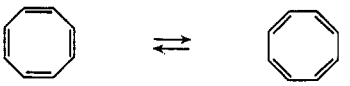
that both reagents yield the same distribution of isomeric adducts. We are however inclined to reject this alternative explanation. In other molecules when given a choice between 1,2 and 1,4 addition, tetracyanoethylene prefers to react in the normal concerted Diels–Alder manner.[9] In particular we find that with 2,3-diphenylbutadiene, tetracyanoethylene adds completely in a 1,4 manner and no evidence of 1,2 addition can be found.[4] Furthermore this argument would suggest that addition to phenylcyclobutadiene should also proceed *via* the allylic cation (or radical) VIII and that this would also then be expected to ring close in a manner analogous to VII. However, this is not the case. We find that tetracyanoethylene reacts with phenylcyclobutadiene to produce predominantly, if not exclusively, the adduct IX;[10] this is the isomer to be expected on the basis of a normal Diels–Alder addition to phenylcyclobutadiene.

(8) Using the data of Sauer, *et al.* (ref 6), as a basis for the diene reactivity of cyclobutadiene one obtains a value in the vicinity of 5 kcal/mol for the orbital-symmetry forbidden interconversion of the rectangular forms of cyclobutadiene. This neglects any effects due to the phenyl groups.

(9) J. K. Williams, D. W. Wiley, and B. C. McKusick, *J. Amer. Chem. Soc.*, 84, 2210 (1962). The only established exceptions of which we are aware is the case of dimethylenecyclobutene where the normal Diels–Alder reaction would be required to yield a derivative of cyclobutadiene (A. T. Blomquist and Y. C. Meinwald, *ibid.*, 81, 667 (1959); R. Criegee, *Angew. Chem.*, 74, 703 (1962)) and where large amounts of strain energy are involved (C. A. Stewart, *J. Amer. Chem. Soc.*, 84, 117 (1962)).

(10) Phenylcyclobutadieneiron tricarbonyl was prepared by addition of lithiocyclobutadieneiron tricarbonyl to cyclohexenone followed by dehydration and dehydrogenation. The total crude product in the addition of phenylcyclobutadiene to tetracyanoethylene shows ethylenic hydrogen absorptions centered at τ 3.82 and two allylic hydrogen absorptions at τ 5.11 and 5.61 in the ratio 1:1:1. Similar stereochemical results are seen with other monosubstituted cyclobutadienes, *e.g.*, the methyl-, ethyl-, isopropyl-, and iodo derivatives.

Although perhaps not imperative we consider that the above results are more consistent with the hypothesis that cyclobutadiene is rectangular in its ground state, in which case this molecule would then fit in with the pattern that has now emerged for other cyclic polyenes. Those cyclic polyenes which possess $(4n + 2)$ π electrons are "aromatic" and possess equal carbon–carbon bonds while those having $4n$ π electrons are "nonaromatic" and have alternating short double bonds and long single bonds. Anet, *et al.*,[11] have recently shown that the inversion of cyclooctatetraene from one tub form to the other proceeds faster than the rearrangement of the double bonds within the molecule. If it can be assumed that the inversion of the tub form proceeds *via* a planar structure then it follows that the planar cyclooctatetraene exists as an irregular octagon and that equilibrium 2, which is entirely analogous to 1, should also exist. Recent X-ray data confirm that [16]annulene, another member of the $4n$ series, also possesses



(2)

alternating short double and long single bonds.[12]

It is of interest to note that when complexed to a transition metal *via* the entire conjugated system, the cyclobutadiene and cyclooctatetraene ligands now adopt a square[13] and regular octagon[14] configuration, respectively. This change in shape presumably arises because of the back donation of electrons from the metal to the antibonding orbitals of the ligands, these levels being of lower energy when the carbon–carbon distances become equal.

(11) F. A. L. Anet, A. J. R. Bourn, and Y. S. Lin, *J. Amer. Chem. Soc.*, 86, 3576 (1964).

(12) S. M. Johnson and I. C. Paul, *ibid.*, 90, 6555 (1968).

(13) J. D. Fitzpatrick, L. Watts, G. F. Emerson, and R. Pettit, *ibid.*, 87, 3254 (1965).

(14) H. Dietrich and H. Dierks, *Angew. Chem. Intern. Ed. Engl.*, 5, 899 (1966).

(15) The authors thank the National Science Foundation, The Petroleum Research Foundation, the U. S. Army (Durham, N. C.), and the Robert A. Welch Foundation for financial assistance. We also thank Badische Anilin und Soda Fabrik for a generous gift of cyclooctatetraene.

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Unique Intermolecular and Intramolecular Exchange Reactions of Hexaborane(10)

Sir:

The apparent inconsistency between the X-ray diffraction study of crystalline hexaborane(10) and boron-11 nmr studies on the neat liquid or its solutions in inert solvents has long been known. In the crystalline solid (Figure 1)[1-3] hexaborane(10) has four different types of borons; two are unique and situated on the mirror plane (1, 2) and two pairs (3 and 6, 4 and 5) are related by the mirror plane. The boron-11 nmr consists of

(1) K. Eriks, W. N. Lipscomb, and R. Schaeffer, *J. Chem. Phys.*, 22, 754 (1954).

(2) F. L. Hirshfeld, K. Eriks, R. E. Dickerson, E. L. Lippert, Jr., and W. N. Lipscomb, *ibid.*, 28, 56 (1958).

(3) Nomenclature and numbering follow the "Rules for Nomenclature of Boron Compounds," *Inorg. Chem.*, 7, 1945 (1968).

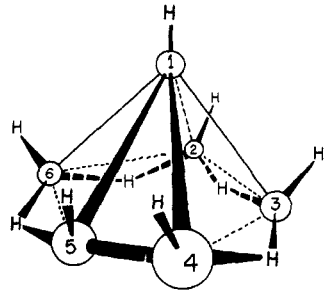

Figure 1. Structure and numbering convention of hexaborane(10).

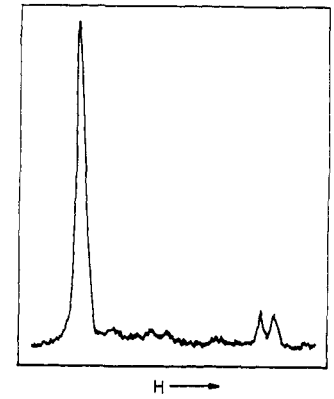

Figure 2. ^{11}B nmr spectrum of $B_6H_5D_5$ at 32.1 MHz and −30° in methylcyclohexane.

two doublets, the one at lower field being five times larger than the other.[4] The high-field doublet has been assigned to the apical boron (1). The apparent equivalence of the five basal borons may be rationalized in several ways; the two most commonly used arguments are accidental degeneracy and hydrogen-atom migration.[5] The former has the disadvantage that degeneracy of three types of borons with very different environments is required whereas, experimentally, the peaks of the low-field doublet are among the sharpest and most symmetrical found for any of the boron hydrides at both 19.3 and 32.1 MHz. The latter suffers when compared to the octahydrotriborate(1−) ion which is assumed to undergo a similar migration of hydrogen atoms. The boron-11 nmr spectrum of the $B_3H_8^-$ ion is a nonet[6,7] which indicates a single type of boron coupled to all hydrogens (both bridge and terminal) of the ion. The three borons are not identical when examined in crystalline solids.[8] It has been reported[9] that the terminal hydrogens of hexaborane(10) exchange more rapidly with B_2D_6 than the bridge hydrogens, but no experimental details were given to allow comparison with this present study.

We wish to report preliminary results of a study on exchange reactions between hexaborane(10) and isotopically labeled diborane(6) and their bearing on the nmr equivalence of the basal borons. Hexaborane(10) undergoes hydrogen exchange with B_2D_6 at low temperatures in a variety of solvents. The low temperature at which exchange occurs is in sharp contrast to the exchange between pentaborane(9) and diborane(6) which occurs only at much higher temperatures. We feel certain the mechanisms of the two reactions are different and the short boron–boron bond between atoms 4 and 5 of hexaborane(10) is involved in the reaction intermediate.

Under the conditions of our experiments, a maximum of five hydrogens of B_6H_{10} exchange to give $B_6H_5D_5$. The positions of the deuteriums were determined by a combination of boron-11 and proton nmr data. The boron-11 nmr of an exchanged sample ($B_6H_5D_5$) is shown in Figure 2. The high-field doublet is unchanged, indicating no exchange at that position. The low-field doublet collapses to a singlet indicating exchange of all hydrogens to which the basal borons are coupled. Evidence that the exchange involved the base terminal hydrogens but *not* the bridging hydrogens is available from the proton spectrum. The peaks attributed to the bridge and apex terminal hydrogens remain unchanged, whereas the base terminal hydrogen peaks decrease in size as the exchange progresses. Evidence that boron atoms do not exchange was obtained by using diborane(6) labeled with boron-10 isotope. The possibility of intermolecular exchange was eliminated by examining changes in the low-temperature spectra using different solvents and with fourfold changes in concentration.

Several conclusions may be drawn from these and other observations concerning the structure and intramolecular migration of hydrogens in hexaborane(10). The apical boron is coupled only to its terminal hydrogen. This hydrogen does not exchange with any base terminal or bridge hydrogen. Each base boron is coupled to one and only one terminal hydrogen. No coupling is observed between the base borons and the bridge hydrogens. The base terminal hydrogens exchange fairly rapidly at low temperatures with diborane(6). No exchange occurs between base terminal hydrogens and bridge hydrogens. The base terminal hydrogens do not exchange with each other. The apparent equivalence of the basal borons in the nmr is a result of migration of the bridge hydrogens (and thus the short boron–boron bond) which occurs by a mechanism requiring a specific stereochemistry and which does not involve any terminal hydrogens.

The last two statements are particularly important and require additional discussion. If rapid exchange between base terminal hydrogens, or base terminal and bridge hydrogens, occurred, the boron-11 spectrum should be related to that of $B_3H_8^-$ ion; one would expect spin–spin coupling between boron and hydrogen to show the boron coupled to at least five, if not nine, hydrogens rather than the one found. The lack of any apparent difference in the exchange rate of the five base terminal hydrogens agrees with a rapid migration of the bridge hydrogens. We suggest that intermolecular exchange of hydrogen occurs at the short boron–boron bond, and rapid migration of the bridge hydrogens results in an equal probability of this bond being adjacent to any base boron. The failure of the base terminal hydrogens to exchange with the bridge hydrogens may now be rationalized by examining the three-dimensional location of the hydrogen (Figure 1). The

(4) R. E. Williams, S. G. Gibbins, and I. Shapiro, *J. Chem. Phys.*, 30, 333 (1959).
(5) R. E. Williams, *J. Inorg. Nucl. Chem.*, 20, 201 (1961).
(6) W. D. Phillips, H. C. Miller, and E. L. Muetterties, *J. Am. Chem. Soc.*, 81, 4496 (1959).
(7) B. M. Graybill, J. K. Ruff, and M. F. Hawthorne, *ibid.*, 83, 2669 (1961).
(8) C. R. Peters and C. E. Nordman, *ibid.*, 82, 5758 (1960).
(9) S. G. Gibbins and I. Shapiro, *J. Chem. Phys.*, 30, 1483 (1959).

terminal hydrogens lie approximately on an extension of the line joining each boron with the center of the icosahedron of which the boron framework may be imagined to be a part. The bridge hydrogens lie approximately in the surface of the same icosahedron and below the base borons. The rupture of one end of a hydrogen-bridge bond gives a hydrogen quite different from the terminal hydrogen already present. Only the "new terminal hydrogen" is in a position to re-form as a bridge, either in its previous position or over what was previously the short boron–boron bond. This provides a consistent explanation of both the products of the exchange reaction with diborane(6) and the nmr spectrum. Both the intermolecular and intramolecular exchange reactions described here are of types not previously observed for boron hydrides.

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(10) National Aeronautics and Space Administration Predoctoral Trainee.

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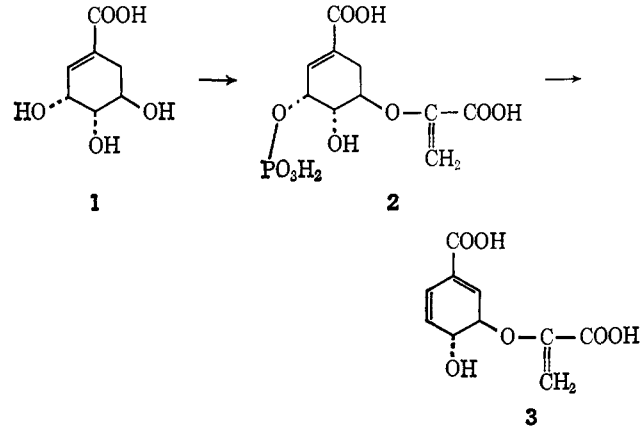
Stereochemistry of Chorismic Acid Biosynthesis[1]

Sir:

The pathway of aromatic ring biosynthesis in bacteria from glucose *via* shikimic acid (**1**) has been elucidated in considerable detail.[2] In this sequence chorismic acid (**3**) plays a central role as branch point,[3] leading to many important groups of aromatic natural products: the aromatic amino acids (phenylalanine, tyrosine, and tryptophan), anthranilic acid and (in some organisms) nicotinic acid, *p*-aminobenzoic acid and folic acid, *p*-hydroxybenzoic acid and ubiquinone, vitamin K_2, and salicylic acid and its hydroxylated derivatives.[4]

The steps from shikimic acid to chorismic acid have been clarified by Sprinson and coworkers,[5] who showed that shikimate 5-phosphate is converted to the 3-enolpyruvate **2**, which then undergoes 1,4 elimination of phosphoric acid. This elimination, mediated by chorismate synthetase, presents an interesting stereochemical question with which this communication deals: does such a 1,4-conjugate elimination show a preference for proceeding *cis* or *trans?* Theory[6] predicts that a concerted 1,4-conjugate elimination should be *cis*, but studies in nonenzymatic systems have led to conflicting conclusions.[7] By using stereospecifically deuterated shikimic acids as substrates, we have now been able to show that the chorismate synthetase reaction is a stereospecific *trans*-1,4 elimination.



Our approach to this problem was to prepare samples of shikimic acid in which each of the hydrogens at C-6 was in turn replaced by deuterium. The Diels–Alder route[8] to shikimic acid was followed to ensure stereospecific introduction of the label. Addition of *trans,trans*-1,4-diacetoxybutadiene to methyl α,*trans*-β-dideuterioacrylate[9] (**4**) (98% of two deuteriums by nmr analysis) afforded adduct[10] **5**, which was converted by the published procedure[5] to 6α-deuterioshikimic acid (**6**α-*d*). In a similar fashion, methyl *cis*-β-deuterioacrylate[9] (**6**) was converted through adduct **7** to 6β-deuterioshikimic acid (**6**β-*d*) containing 85% of one deuterium. All synthetic intermediates were characterized by ir, nmr, and mass spectroscopy, and had melting or boiling points identical with the published values. The deuterated shikimic acids were pure, recrystallized products.

Incorporation experiments were conducted with *E. coli* mutant 156-53M31, doubly blocked both immediately before and after dehydroshikimic acid, to minimize the possibility of back mutation.[11] The mutant was grown in medium A with 0.5% glucose supplemented by deuterated or natural shikimate. Growth rates on **6**α-*d* and **6**β-*d* showed that both racemic deuterated shikimic acids supported growth to exactly one-half the extent of natural (−)-shikimate. Cells were harvested after 12 hr, denatured with trichloroacetic acid, and hydrolyzed with acid. Phenylalanine and tyrosine were isolated from the hydrolysate by the method of Partridge;[12] tyrosine was then purified by recrystallization, while phenylalanine was converted to its ethyl ester and purified by preparative vpc.

(1) This investigation was supported in part by a research grant (GM-06568) from the Public Health Service, to whom we express our appreciation.

(2) (a) B. D. Davis, *Advan. Enzymol.*, **16**, 247 (1955); (b) D. B. Sprinson, *Advan. Carbohyd. Chem.*, **15**, 235 (1960); (c) B. A. Bohm, *Chem. Rev.*, **65**, 435 (1965); (d) F. Lingens, *Angew. Chem. Intern. Ed. Engl.*, 7, 350 (1968).

(3) M. I. Gibson and F. Gibson, *Biochem. J.*, **90**, 248 (1964); F. Gibson, *ibid.*, **90**, 256 (1964).

(4) C. Ratledge in "Biosynthesis of Aromatic Compounds," G. Billek, Ed., Pergamon Press, London, 1966.

(5) (a) J. G. Levin and D. B. Sprinson, *J. Biol. Chem.*, **239**, 1142 (1963); (b) H. Morell, M. J. Clark, P. F. Knowles, and D. B. Sprinson, *ibid.*, **242**, 82 (1967).

(6) (a) N. G. Anh, *Chem. Commun.*, 1089 (1968); (b) K. Fukui, *Tetrahedron Lett.*, 2427 (1965).

(7) (a) H. D. Orloff and A. J. Kolka, *J. Amer. Chem. Soc.*, **76**, 5484 (1954); (b) S. J. Cristol, W. Barasch, and C. H. Tieman, *ibid.*, **77**, 583 (1955).

(8) (a) E. E. Smissman, J. T. Suh, M. Oxman, and R. Daniels, *ibid.*, **84**, 1040 (1962); **81**, 2909 (1959); (b) R. McCrindle, K. H. Overton, and R. A. Raphael, *J. Chem. Soc.*, 1560 (1960); (c) B. Chabannes, L. Pichat, M. Herbert, and H. Pacheco, *J. Label. Compounds*, **1**, 102 (1965).

(9) R. K. Hill and G. R. Newkome, *J. Org. Chem.*, **34**, 740 (1969).

(10) For recent proof of the configuration of the Diels–Alder adduct, see (a) R. McCrindle, K. H. Overton, and R. A. Raphael, *Tetrahedron Lett.*, 1847 (1968); (b) R. K. Hill and G. R. Newkome, *ibid.*, 1851 (1968); (c) E. E. Smissman and J. P. Li, *ibid.*, 4601 (1968); J. P. Li, Ph.D. Dissertation, University of Kansas, 1966.

(11) We are particularly grateful to Dr. Bernard D. Davis, Harvard Medical School, for his advice in selecting this mutant and for providing a slant.

(12) S. M. Partridge, *J. Biol. Chem.*, **44**, 521 (1949).