structure of the enzymic intermediates is correct. In general, catalase and peroxidase reactions can be related to similar reactions of the ferric–catechol system, but a detailed discussion of these similarities is outside the realm of this paper.

The enzyme variously known as tyrosinase, phenolase, etc.,[20] also bears some resemblance to the ferric–catechol system. This copper enzyme will catalyze the hydroxylation of phenols to catechols by O_2 but only in the presence of catalytic amounts of catechols.[21] It is not difficult to visualize mechanisms for obtaining from O_2 and the catechol a copper-containing intermediate like **3**, which possibly is the hydroxylating agent in this enzymic reaction.

[20] For a review see D. Kertesz and R. Zito in "Oxygenases," O. Hayaishi, Ed., Academic Press Inc., New York, N. Y., 1962, p 307.

[21] S. H. Pomerantz and M. C. Warner, *Biochem. Biophys. Res. Commun.*, **24**, 25 (1966), and references therein.

Formation and Thermal Decomposition of Bicyclo[1.1.0]butane-2-*exo*-d_1[1]

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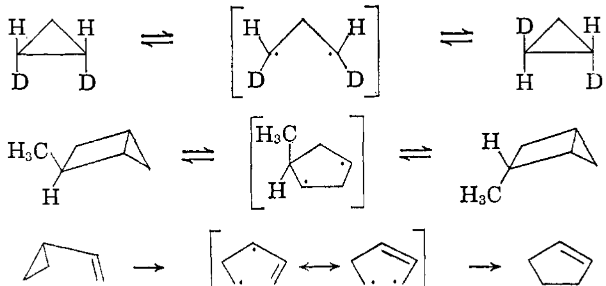
Contribution from the Department of Chemistry, Yale University, New Haven, Connecticut. *Received June 8, 1966*

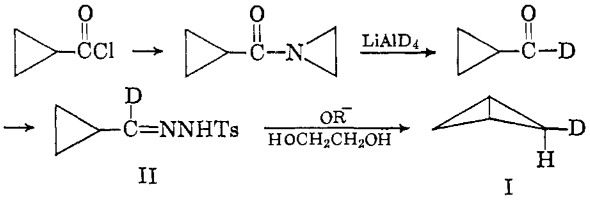
Abstract: The mechanism of the thermal decomposition of bicyclo[1.1.0]butane has been studied using a deuterium-labeled derivative. The reaction giving butadiene appears to involve partial cleavage of both carbon–carbon bonds in the activated complex, and conforms to the Woodward–Hoffmann rules for electrocyclic reactions. The formation of bicyclo[1.1.0]butane-*exo*-2-*d*, from the tosylhydrazone of cyclopropanecarboxaldehyde-*d*, is discussed. It appears that the cyclopropylcarbinyl cation, as such, is not involved in the reaction.

The thermal rearrangement of most cyclopropane derivatives may be rationalized in terms of the formation of a 1,3-diradical intermediate. Thus, the thermal reactions of cyclopropane[3] and bicyclo[2.1.0]pentane[4] both lead to *cis–trans* isomerization of the reactants. Similarly, the rearrangement of vinyl cyclopropane to cyclopentene[5] appears to be best explained as involving a 1,3-diradical intermediate.



Analogy with the reaction of bicyclo[2.1.0]pentane might lead one to expect that the initial reaction in the thermal decomposition of bicyclo[1.1.0]butane would involve the formation of the 1,3 diradical. The fact that 1,3-dimethylbicyclo[1.1.0]butane[6] and 1,3-bis(trifluoromethyl)-2,2,4,4-tetrafluorobicyclo[1.1.0]butane[7] undergo thermal rearrangement to 2,3-disubstituted butadienes indicates the central bond to be intact in the product. Thus, if the 1,3 diradical is formed, it is not involved in the formation of products.

The possibility that any diradical is formed in the reaction in equilibrium with the reactant could be tested by examining the reaction of a 2-labeled bicyclo[1.1.0]butane.[8] A deuterium label is preferred since this will not introduce extraneous steric effects. The synthesis of bicyclo[1.1.0]butane-*exo*-2-*d* (I) is



The final step in the synthesis and the evidence for the position of deuterium in the product will be discussed below. For now we shall simply state that I had at least 90% of the deuterium in the *exo* position.

The bicyclobutane, I, was heated in the gas phase at the reaction temperature of 200°, and the nmr spectrum of the reaction mixture was examined at times corresponding to 6, 21, 30, 45, 58, and 75% reaction. Because of the large chemical shift between the butadiene and bicyclobutane protons, the spectrum of the latter could

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[1] This investigation was supported by the Army Research Office (Durham).

[2] National Institutes of Health Predoctoral Fellow 1963–1966; taken from the Ph.D. thesis of J. M. L., 1966.

[3] B. S. Rabinovitch, E. W. Schlag, and K. B. Wiberg, *J. Chem. Phys.*, **28**, 504 (1958); E. W. Schlag and B. S. Rabinovitch, *J. Am. Chem. Soc.*, **82**, 5996 (1960).

[4] J. P. Chesick, *ibid.*, **84**, 3250 (1962).

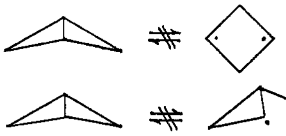
[5] M. C. Flowers and H. M. Frey, *J. Chem. Soc.*, 3547 (1961); C. A. Wellington, *J. Phys. Chem.*, **66**, 1671 (1962).

[6] W. von E. Doering and J. F. Coburn, Jr., *Tetrahedron Letters*, 991 (1965).

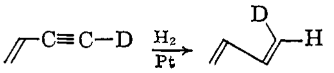
[7] W. Mahler, *J. Am. Chem. Soc.*, **84**, 4600 (1962).

[8] It should be noted that the 2-methylbicyclo[1.1.0]butanes (G. Closs, private communication) and the 2,3-dimethylbicyclo[1.1.0]butyl 1-cyanides (A. Cairncross and E. P. Blanchard, Jr., *J. Am. Chem. Soc.*, **88**, 496 (1966)) do not undergo thermal *cis–trans* equilibration. However, steric factors could intervene in these cases since an *endo*-methyl group would probably give an unfavorable 1,3-nonbonded interaction with the cross-ring methylene group.

easily be seen in the mixtures. Although the spectrum is fairly sensitive to the location of the deuterium, no change in spectrum could be observed at any point in the reaction. Thus, *endo–exo* isomerization does not occur to a significant extent during the reaction and the following equilibria are not established during the reaction.

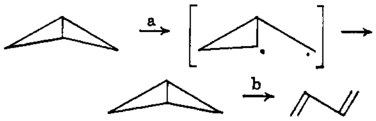


The butadiene formed in the reaction also was examined. The nmr spectrum of the butadiene formed at the initial stages of the reaction was identical with the product of complete reaction. In order to determine the stereochemistry of the butadiene, vinylacetylene-*d* was prepared and catalytically hydrogenated to butadiene-*cis*-1-*d* (III). The nmr spectrum of III was


III

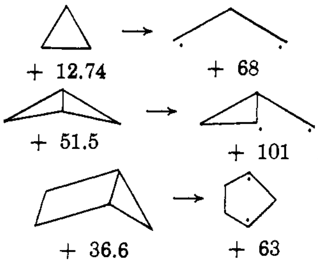
different than that of the butadiene formed from I, and III was found to be unchanged on heating under the reaction conditions used for I. However, when III was heated in the presence of nitric oxide at 220° for 27 hr, it equilibrated to a mixture of *cis*- and *trans*-deuterium-labeled butadienes. This mixture had an nmr spectrum identical with that of the butadiene formed from I.

The result allows two interpretations. First, a diradical may be formed as an intermediate, and rapidly be converted to butadiene. It would not be surprising if the second step were rapid, for unlike the rearrangement of the trimethylene diradical to propylene, which involves a hydrogen shift, the further reaction of the diradical from bicyclobutane would require only an electronic reorganization. The second possibility is that the reaction is synchronous, no intermediate is involved, and the two methylene groups move in a conrotatory fashion.



The problem might be resolved if a 2,4-dilabeled bicyclobutane were available. If the diradical formed *via* path a had a sufficiently long lifetime to permit rotation of the methylene group, the product would be a mixture of isomers, whereas path b would give only butadiene-1-*cis*-4-*trans*-d_2 from bicyclo[1.1.0]butane-*exo*-2,4-d_2. If the lifetime of the intermediate in path a were very short, the process might be indistinguishable from path b. The dilabeled bicyclobutane is, however, not now available and may be difficult to prepare.

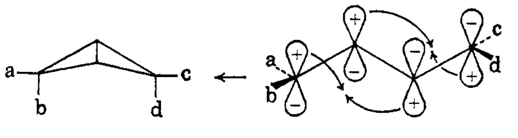
The energetics of the process merit consideration. The heats of formation of propane (−24.82 kcal/mole),[9] cyclopropane (12.74),[10] cyclobutane (6.4),[11] and cyclopentane (−18.46)[9] are known. The heats of hydrogenation of bicyclo[2.1.0]pentane to cyclopentane (−55.1 kcal/mole)[12] and of bicyclo[1.1.0]butane to cyclobutane (−45.1)[13] are also known. Using the normal increment for replacing a secondary hydrogen with a methyl (−7.0 kcal/mole),[6] a bond dissociation energy of 98 kcal/mole for a primary C–H bond, of 94 kcal/mole for a secondary C–H bond, of 100 kcal/mole for a cyclopropane C–H bond,[14] and a correction of 2 kcal/mole for the relief of torsional strain in converting cyclopentane to a cyclopentyl radical,[15] the following may be estimated.



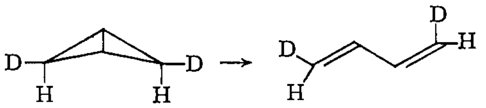
ΔH = 55 kcal/mole;[16] E_a = 46[3]
ΔH = 49 kcal/mole; E_a = 41[17]
ΔH = 26 kcal/mole; E_a = 39[4]

Along with the enthalpy changes are given the observed activation energies. The reverse reaction, reforming the hydrocarbon from the diradical, must have an activation energy. Correspondingly, the reactions of cyclopropane and of bicyclo[2.1.0]pentane have activation energies greater than the enthalpy change. Bicyclo[1.1.0]butane is strikingly different in that the activation energy is considerably less than the enthalpy change in going to a diradical. Even though the enthalpy changes have an uncertainty of several kcal/mole, it seems clear that the isomerization of bicyclo[1.1.0]butane cannot involve the diradical as an intermediate. Consequently, it must be assumed that the thermal decomposition is a concerted process in which both bonds are partially cleaved in the activated complex. With this conclusion, it would appear that the Woodward–Hoffmann rules for electrocyclic reactions[18] should apply.

The application of these rules is probably more easily seen in considering the reverse of the thermal isomerization



which corresponds to



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(9) American Petroleum Institute, Project 44, Tables of Thermodynamic Properties.

(10) J. W. Knowlton and F. D. Rossini, *J. Res. Natl. Bur. Std.*, **43**, 113 (1949).

(11) S. Kaarsemaker and J. Coops, *Rec. Trav. Chim.*, **71**, 261 (1952).

(12) R. B. Turner, *Kekule Symposium*, 67 (1958).

(13) R. B. Turner, P. Goebel, W. von E. Doering, and J. F. Coburn, Jr., *Tetrahedron Letters*, 997 (1965). The heat of hydrogenation was determined on the 1,3-dimethyl derivative, and we shall assume that alkyl substitution affects bicyclobutane and cyclobutane equally.

(14) The activation energy for the abstraction of a hydrogen from cyclopropane by a chlorine atom (J. H. Knox and R. L. Nelson, *Trans. Faraday Soc.*, **55**, 937 (1959)) is about that for methane, and is much higher than that for other methylene groups.

(15) For example, the heat of hydrogenation of cyclopentanone is 1.5 kcal/mole less negative than that of acetone.

(16) The calculation for cyclopropane was first made by S. W. Benson, *J. Chem. Phys.*, **34**, 521 (1961).

(17) H. M. Frey and I. D. R. Stevens, *Trans. Faraday Soc.*, **61**, 90 (1965).

(18) R. B. Woodward and R. Hoffmann, *J. Am. Chem. Soc.*, **87**, 395, 2511 (1965); R. Hoffmann and R. B. Woodward, *ibid.*, **87**, 2046, 4388, 4389 (1965).

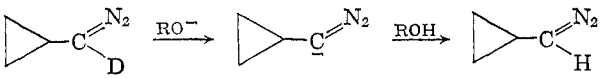
and agrees with our experimental observations. The rearrangement of bicyclobutane to butadiene is then quite similar to the corresponding rearrangement of cyclobutene.

We shall now consider the formation of bicyclo-[1.1.0]butane-2-d_1 (I). The formation of bicyclobutane from cyclopropanecarboxaldehyde tosylhydrazone was first described by Frey and Stevens,[19] and has been investigated in some detail by Friedman, Shechter, and co-workers.[20] The synthesis of the deuterium-labeled tosylhydrazone (II) was described above. When II was heated to 150° in ethylene glycol containing 0.9 equiv of sodium alkoxide, bicyclobutane (I) was formed. The nmr spectrum was examined, and whereas the bands at τ 9.56 (*endo* protons) and τ 8.63 (bridgehead protons) were essentially unchanged from those of unlabeled bicyclobutane, the band at τ 8.53 (*exo* protons) was found to be substantially reduced in intensity.[21]

The deuterium content of I could not be determined satisfactorily by mass spectrometry. Therefore, I was thermally rearranged to butadiene. Low-voltage mass spectrometry indicated 92 atom % deuterium. The nmr bands at τ 8.53 and 8.63 were not sufficiently separated to permit an unambigous separate integration of each. However, since the method of synthesis would not be expected to introduce deuterium at the bridgehead position of II, it was possible to integrate the two bands together, and compare the area for the *endo* protons. Unlabeled II gave a ratio of 2:1 for the downfield to upfield protons. If the deuterium were scrambled between the *exo* and *endo* positions, a ratio of 2.3:1 would be expected, whereas a ratio of 1.54:1 would be expected if all the deuterium were in the *exo* position. Repeated integrations of the spectrum gave ratios between 1.6 and 1.7. This corresponds to 87–95% of the deuterium in the *exo* position.

When the reaction was carried out using 1.1 equiv of sodium alkoxide, the bicyclobutane contained only 64% deuterium. Integration of the nmr spectrum gave area ratios between 1.7 and 1.8:1. If all the deuterium were in the *exo* position, a ratio of 1.7:1 would have been expected. Thus, here again, the deuterium is essentially all in the *exo* position.[22]

It seems fairly certain that the anionic decomposition of tosylhydrazones proceeds *via* an intermediate diazo compound.[23] The decrease in deuterium content of I on addition of excess base to the reaction medium probably results from a base-catalyzed hydrogen exchange with hydrogens from the solvent. The acidity of protons α to a diazo group has been demonstrated.[24]



The reaction of unlabeled cyclopropanecarboxaldehyde tosylhydrazone with base in ethylene glycol-d_2 was also examined. Contrary to our earlier report,[21,22] deuterium is introduced from the solvent. The results are summarized in Table I. The values of per cent *exo-d* and *endo-d* are based on the assumption that essentially all of the deuterium derived from the tosylhydrazone is in the *exo* position and essentially all the deuterium derived from the solvent is in the *endo* position. These percentages are in agreement with the nmr integrals. It is important to note that no d_3 product is obtained, indicating that exchange does not occur at the bridgehead of bicyclobutane under the conditions used.

Table I. Reaction of Cyclopropanecarboxaldehyde Tosylhydrazone with Base in Ethylene Glycol

Reactant	Solvent (%)	Equiv of base	% d_0	% d_1	% d_2	% d_3
d_0	d_2 (98)	0.8	29	69	2	0
d_0	d_2 (88)	0.8	48	49	3	0
d_0	d_2 (98)	0.5	22	69	9	0
d_0	d_2 (98)	2.7	3	27	70	0
d_1	d_0	0.9	8	92	0	0
d_1	d_0	1.1	36	64	0	0
d_1	d_2 (98)	2.5	1	19	81	0

Nmr ratio	% *exo-d*	% *endo-d*
2.8–2.9:1	2	71
. . .	3	52
. . .	9	78
2.5–2.6:1	97	70
1.6–1.7:1	92	0
1.7–1.8:1	64	0
2.4–2.5:1	100	81

It is interesting to note that, whereas high deuterium content may be found in the *exo* position, the per cent in the *endo* position is uniformly lower than the deuterium content of the solvent. Starting with ethylene glycol-d_2 containing 98% deuterium, the addition of the tosylhydrazone will reduce the deuterium content to 96.7%. Transfer operations and protons adsorbed on the glassware would reduce this further, perhaps to about 95% deuterium. Bicyclobutane formed in this solvent had 22–29% unlabeled material. Similarly, starting with 88% deuterium in the solvent, the deuterium content will be reduced to 87% by addition of the tosylhydrazone. Here, the bicyclobutane contained 48% unlabeled material. The marked change in the deuterium content of the product bicyclobutane may be rationalized only by assuming a solvent isotope effect for which k_H/k_D is $\sim$4.

The requirements for a mechanism for the conversion of diazomethylcyclopropane (the reaction intermediate) to bicyclobutane are then: (1) rate-determining proton transfer from the solvent to the diazomethyl carbon; (2) no geometrical equilibration between the protons on the carbinyl carbon; and (3) a geometry for the activated complex which will place the hydrogen originally on the tosylhydrazone in the *exo* position of the product. One possibility is

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[19] H. M. Frey and I. Stevens, *Proc. Chem. Soc.*, 144 (1964).

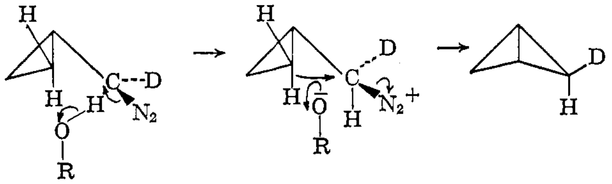
[20] J. Bayless, L. Friedman, J. A. Smith, F. B. Cook, and H. Shechter, *J. Am. Chem. Soc.*, **87**, 661 (1965); J. A. Smith, H. Shechter, J. Bayless, and L. Friedman, *ibid.*, **87**, 659 (1965).

[21] A preliminary report of these results has been given by K. B. Wiberg and J. Lavanish, *ibid.*, **88**, 365 (1966).

[22] Recently F. Cook, H. Shechter, J. Bayless, L. Friedman, R. L. Foltz, and R. Randall, *ibid.*, **88**, 3870 (1966), have reported a confirmation of the stereochemical result. However, they observed only 76% of the deuterium in the *exo* position. Under our conditions, our result is completely reproducible. Possibily, the difference in stereospecificity results from the higher temperature (180°) used by these workers.

[23] G. M. Kaufman, J. A. Smith, G. G. Vander Stouw, and H. Shechter, *ibid.*, **87**, 935 (1965).

[24] *Cf.* H. Zollinger, "Azo and Diazo Chemistry," Interscience Publishers, Inc., New York, N. Y., 1961, p 45.



IV

If the ion pair, IV, formed on the rate-determining step, were to decompose rapidly to products, the observed stereochemistry would result. One may then ask: why should the ethylene glycol approach the molecule in the indicated fashion rather than from the other side? A reasonable hypothesis is that the rearrangement is synchronous with the proton transfer. If that were the case, only the indicated geometry would apply. It is also possible that the proton is transferred to either side, but that transfer to the other side leads to a diazonium ion which prefers to return the proton to the anion.

Experimental Section[25]

Cyclopropanecarboxaldehyde. The general procedure of Brown and Tsukamoto[26] was used. A solution of 7.95 g (0.182 mole) of aziridine and 18.2 g (0.182 mole) of triethylamine in 100 ml of dry ether was placed in a 300-ml, three-necked flask equipped with a stirrer and an addition funnel. A solution of 19.1 g (0.182 mole) of cyclopropanecarbonyl chloride (bp 115–118°) in 50 ml of dry ether was added with ice-bath cooling over the course of 3 hr. The reaction mixture was stirred for 0.5 hr at room temperature. The precipitate was filtered and washed with 100 ml of dry ether. The combined ether fraction was placed in a 300-ml, three-necked flask equipped with stirrer, addition funnel, and condenser, and was cooled in an ice bath. Lithium aluminum hydride (2.0 g) in 100 ml of dry ether was added over 0.5 hr and the mixture was sitrred at 0° for an additional 0.5 hr. Cold 5% sulfuric acid was added slowly until no solid remained. The ether layer was separated, dried over anhydrous magnesium sulfate, filtered, and distilled, giving 3.3–5.6 g (26–44%) of cyclopropanecarboxaldehyde, bp 100–102°.

Cyclopropanecarboxaldehyde-d_1. The method described above was used, except that lithium aluminum deuteride was used in place of lithium aluminum hydride. The yield was 4.6–5.6 g. The nmr spectrum indicated the absence of aldehyde protons.

Cyclopropanecarboxaldehyde Tosylhydrazone. Cyclopropanecarboxaldehyde (5.1 g, 73 mmoles) was added to a solution of 13.5 g (73 mmoles) of *p*-toluenesulfonhydrazide in 25 ml of 60% methanol at about 60°. The solution was placed in a refrigerator. After standing overnight, the solid was filtered and washed with 60% methanol, giving 15.8 g (91%) of the tosylhydrazone, mp 95–97°. Recrystallization from methanol raised the melting point to 96.5–98°. The deuterium-labeled tosylhydrazone was prepared in the same fashion.

2-Phenyl-1,3-dioxolane. Benzaldehyde (212 g, 2 moles), 155 g of ethylene glycol, and about 0.1 g of *p*-toluenesulfonic acid were heated to reflux in a flask equipped with a Dean–Stark trap until no further water was collected. After cooling to room temperature, the solution was washed with saturated sodium bicarbonate solution, water, and saturated sodium chloride solution. The benzene layer was dried over anhydrous sodium sulfate and was distilled, giving 2-phenyl-1,3-dioxolane, bp 90–94° (1.5 mm). Its nmr spectrum was identical with that of an authentic sample.

Ethylene Glycol-d_2. A mixture of 162 g (1.08 moles) of 2-phenyl-1,3-dioxolane, 42 g of deuterium oxide, and about 0.1 g of *p*-toluenesulfonyl chloride was stirred overnight. Potassium carbonate (0.5 g) was then added and the two layers were separated. The aqueous layer was washed with two 100-ml portions of benzene. About 100 ml of benzene was added to the aqueous fraction and excess deuterium oxide was removed azeotropically. The remaining benzene was removed by distillation and the residue was distilled, giving 42 g (63%) of ethylene glycol-d_2, bp 71–72° (2.6 mm). The deuterium content was determined by adding 50.0 μl of ethylene glycol to 400 μl of ethylene glycol-d_2. The area of the hydroxyl band in the nmr spectrum increased by a factor of 5.85 over that of the ethylene glycol-d_2, indicating the presence of 2% hydroxyl protons in the latter.

Butadiene-*cis*-1-d_1. Sodium vinylacetylide was prepared using the procedure of Croxall and Van Hook[27] starting with 2.5 g of 1,4-dichloro-2-butene. After the ammonia had been replaced with dry ether, 10 ml of deuterium oxide was added, and the effluent gas was collected in a Dry Ice–acetone cooled trap. The nmr spectrum of the material in the trap indicated only ether and vinylacetylene. The terminal acetylene band was absent.

The ether solution was added to a flask containing 0.5 g of 10% palladium on calcium carbonate catalyst and 0.2 g of quinoline at liquid nitrogen temperature. The flask was attached to an atmospheric pressure hydrogenation apparatus, and hydrogenation was effected at −10 to −5° until about two-thirds of the theoretical amount of hydrogen had been absorbed. The butadiene was separated from the mixture by vpc using a β,β'-oxydipropionitrile column. The mass spectrum using 11.0-v electrons indicated 28% d_0, 69% d_1, and 3% d_2.

Decomposition of Tosylhydrazones in Ethylene Glycol. The appropriate amount of sodium to give the desired equivalents of base was weighed under benzene and transferred to 25–30 ml of ethylene glycol or ethylene glycol-d_2. Then 5 g of the tosylhydrazone was added and the flask was slowly immersed in a Wood's metal bath at 150°. The gas which was evolved was collected in a Dry Ice–acetone cooled trap. The bicyclobutane was separated and purified *via* vpc using a β,β'-oxydipropionitrile column. The deuterium content was determined by thermal rearrangement to butadiene followed by mass spectrometric analysis using 11-v electrons.

Isomerization of Bicyclo[1.1.0]butane-*exo*-2-d_1. In a typical run, about 70 mg of bicyclobutane was transferred to a 90-ml, cylindrical reaction vessel by bulb-to-bulb distillation and sealed under vacuum. The vessel was placed in a tube furnace heated to 200°. At 2–5-hr intervals, the vessel was removed from the furnace and its contents distilled into a heavy-wall nmr tube. After the determination of the spectrum, the material was distilled back into the reaction vessel and returned to the furnace.

Equilibration of Butadiene-*cis*-1-d_1. Butadiene-d_1 (64%) was distilled into a 90-ml reaction vessel (200 mm) and then nitric oxide (160 mm) was added. The vessel was sealed under vacuum and heated to 220° for 27 hr. The butadiene was separated from nitric oxide *via* vpc and distilled into a heavy-wall nmr tube. The spectrum was different than that of the starting butadiene, indicating that rearrangement had occurred. The spectrum was identical with that of the butadiene formed from bicyclo[1.1.0]butane-*exo*-1-d_1, (64%). The isomerization of butadiene occurred without the formation of detectable amounts of side products.

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(25) The nmr spectra which are referred to as well as the mass spectral data may be found in the Ph.D. thesis of J. M. L., which is available through University Microfilms.

(26) H. C. Brown and A. Tsukamoto, *J. Am. Chem. Soc.*, 83, 2016 (1961).

(27) W. J. Croxall and J. O. Van Hook, *ibid.*, 76, 1700 (1954).