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On the Mechanism of the Dimerization of Benzocyclobutadiene

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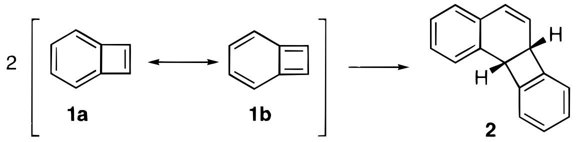
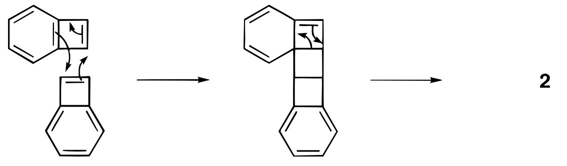
The dimerization of benzocyclobutadiene (**1**), generated by the fluoride ion-induced elimination of trimethylsilyl mesylate from 2-(trimethylsilyl)benzocyclobutenyl-1 mesylate (**5**), was carefully studied by flow NMR spectroscopy. Only formation of the final dimer, 6a,10b-dihydrobenzo[*a*]biphenylene (**2**), was observed; no evidence for the formation of transient intermediates was obtained. Benzocyclobutadiene with a deuterium atom on position 1, **1**-d_1, was prepared and allowed to dimerize. It is shown by several NMR spectroscopic techniques that **1**-d_1 dimerizes to produce six dideuterated isotopomers. It is proposed that the deuterium distribution is explained by a dimerization mechanism involving the formation of [4 + 2] dimer **3** followed by opening of **3** to form dibenzo[*a*,*d*]cyclooctatetraene (**6**) which closes to final dimer **2**.

Benzocyclobutadiene (**1**), first prepared in 1956 by Cava and Napier,[1] is a very reactive molecule that rapidly dimerizes to form 6a,10b-dihydrobenzo[*a*]biphenylene (**2**), the so-called "angular" dimer.[1,2] Cava and Napier proposed[1] that the mechanism for the formation of **2** involves the [4 + 2] cycloaddition of two molecules of **1** followed by rearrangement of the initially formed dimer, **3**, to dimer **2**.





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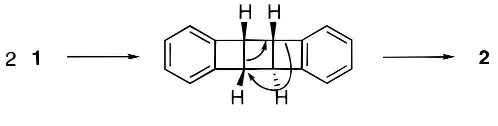
Recently we observed the ^{1}H NMR spectrum of **1** using the technique of flow NMR spectroscopy.[3,4] We confirmed that the stable dimer formed is **2**, and we detected weak transient signals that we tentatively assigned to a short-lived intermediate. From the NMR signals it appeared that the transient intermediate did not have olefinic hydrogens[4] so we proposed that **1** initially forms dimer **4**, a dimer with no olefinic protons, and that dimer **4** rearranges rapidly to dimer **2**. Dimerization of **1** to form **4** could proceed by a thermally allowed [2s + 2a] cycloaddition.[5]



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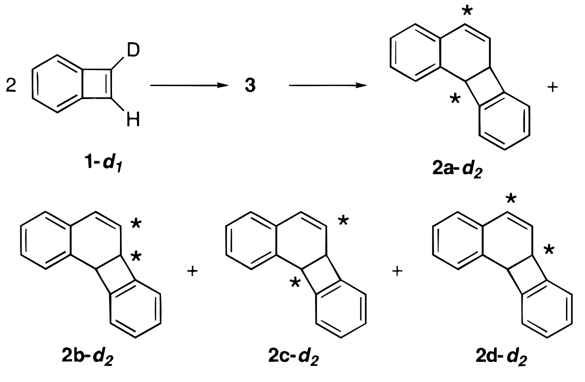
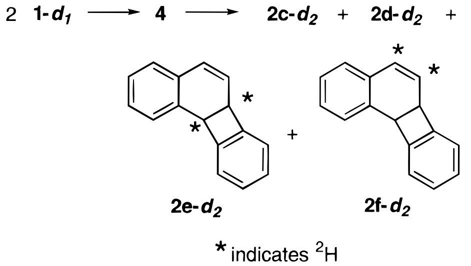
We noted that it should be possible to determine whether dimerization involves dimer **3** or **4** because the four-membered ring atoms of each monomer are distributed differently in **2** (Scheme 1).

In this study we have reinvestigated the dimerization of **1** by flow NMR spectroscopy searching carefully for signals from a transient intermediate. We have also investigated the dimerization of an isotopically labeled benzocyclobutadiene, **1**-d_1. Dimerization of **1**-d_1 would produce the four isotopomers **2a**-d_2, **2b**-d_2, **2c**-d_2, and **2d**-d_2 if dimerization proceeds via dimer **3** (Cava's mechanism), but a different set of four isotopomers would be obtained if the dimerization proceeds through **4**. Note that two isotopomers are common to each set of four, and that there are only six isotopomers possible (**2a**-d_2 to **2f**-d_2).



* indicates ^{2}H



* indicates ^{2}H

[⊗] Abstract published in *Advance ACS Abstracts,* September 1, 1996.

[1] (a) Cava, M. P.; Napier, D. R. *J. Am. Chem. Soc.* **1956**, *78*, 500. (b) Cava, M. P.; Napier, D. R. *J. Am. Chem. Soc.* **1957**, *79*, 1701.

[2] (a) Cava, M. P.; Mitchell, M. J. *Cyclobutadiene and Related Compounds*; Academic Press: New York, 1967; pp 1−87, 188−218. (b) Shepherd, M. K. *Cyclobutarenes The Chemistry of Benzocyclobutene, Biphenylene, and Related Compounds*; Elsevier: New York, 1991; pp 68−108. (c) Toda, F.; Garrat, P. *Chem. Rev.* **1992**, *92*, 1685. (d) Toda, F. in *Advances in Strain in Organic Chemistry*; Halton, B., Ed.; JAI Press LTD: Greenwich, Connecticut, 1993; Vol. 3, pp 161−167.

[3] Trahanovsky, W. S.; Fischer, D. R. *J. Am. Chem. Soc.* **1990**, *112*, 4971.

[4] Fischer, D. R. Ph. D. Dissertation, Iowa State University, Ames, IA, 1990; pp 91−121.

[5] Woodward, R. B.; Hoffmann, R. *Angew. Chem., Int. Ed. Engl.* **1968**, *8*, 781.

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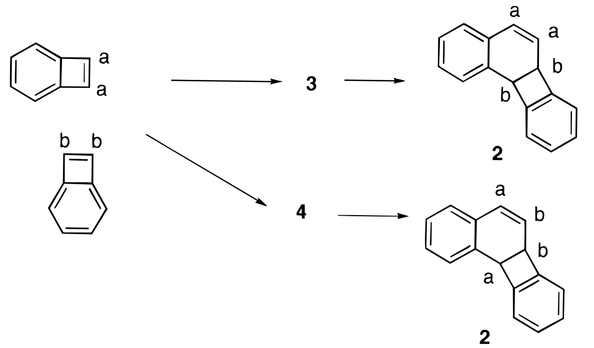
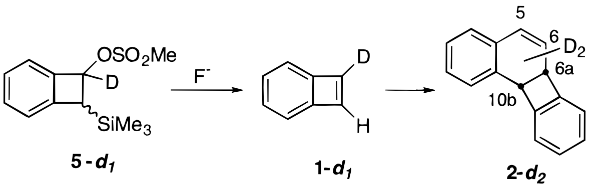
Scheme 1



Results

Flow NMR Spectroscopy Studies. The dimerization of **1** was carefully studied by ^{1}H flow NMR spectroscopy with the objective of obtaining signals that could be assigned to a transient intermediate. In these experiments, benzocyclobutadiene (**1**) was generated by mixing CD_3CN solutions of 2-(trimethylsilyl)benzocyclobutenyl-1 mesylate (**5**) and tetrabutylammonium fluoride. If the conversion of **1** to **2** involves the formation of a transient dimer, the relative concentration of the transient dimer should be favored by working at higher concentrations since the transient dimer is formed by a second-order reaction, but it would rearrange to the final dimer by a first-order reaction. Thus the NMR spectra of solutions at a higher concentration ([**5**] = 0.0068 M and [F$^-$] = 0.28 M before mixing) as well as the original concentration ([**5**] = 0.0012 M and [F$^-$] = 0.05 M before mixing) were obtained at flow rates of 0.03−20 mL/min. For the higher concentration solutions, at the faster flow rates (1.5−20 mL/min) **1** was the predominate species and at the slower flow rates (0.03-1.0 mL/min) **2** was the predominant species. At a flow rate of 1 mL/min the amounts of **1** and **2** were comparable. Under all conditions studied, no signals were obtained that could be assigned to a transient intermediate.

Labeling Study. A sample of **5** was prepared with a deuterium atom on position 1 (**5**-d_1). Desilylation of **5**-d_1 using cesium fluoride in acetonitrile resulted in the generation of highly enriched dideuterated species **2**-d_2. GC/MS/CI analysis of compound **2**-d_2 shows that the sample was essentially 100% dideuterated.



Investigation of this sample by ^{1}H NMR spectroscopy revealed the presence of four broad singlets for the hydrogen atoms on positions 5, 6, 6a, and 10b at δ 6.26, 6.13, 4.37, and 4.78, respectively. The relative integrations of these signals are 1.00:0.92:0.98:1.05, which indicates that the hydrogen atoms were evenly distributed among the four positions. A ^{2}H NMR spectrum of the same sample shows a set of four broad singlets, two of which are not completely resolved, in a 2.2:0.99:1.00 ratio which again is consistent with the even distribution of deuterium atoms among positions 5, 6, 6a, and 10b. The six possible isotopomers can be divided into three pairs (**a** and **b**, **c** and **d**, and **e** and **f**), each pair having a deuterium atom and a hydrogen atom on each of the four positions 5, 6, 6a, and 10. The even distribution of deuterium atoms among these four positions requires that the members of each pair occur in equal amounts; the amount of each pair is unrestricted.

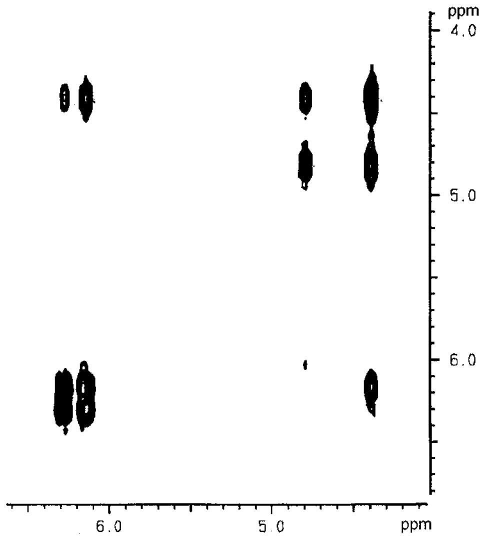


Figure 1. ^{1}H DQCOSY of the **2**-d_2 isotopomer mixture.

A ^{1}H DQCOSY was performed on the dideuterated species (Figure 1) and on a sample of nondeuterated dimer. Both of these spectra contain off-diagonal signals for the hydrogen atoms on positions 5 and 6 (for **2e**-d_2), on positions 6 and 6a (for **2a**-d_2), on positions 6a and 10b (for **2f**-d_2), and on positions 5 and 6a (for **2c**-d_2). There are no off-diagonal peaks seen for the hydrogen atoms on positions 5 and 10b, nor on positions 6 and 10b. These data show that dimers **2a**-d_2, **2c**-d_2, **2e**-d_2, and **2f**-d_2 were present in the deuterated sample; the presence of dimers **2b**-d_2 and **2d**-d_2 could not be confirmed, but because of the even distribution of deuterium atoms among the four positions the amounts of **2b**-d_2 and **2d**-d_2 must equal the amounts of **2a**-d_2 and **2c**-d_2, respectively. Thus these results indicate that all six isotopomers were produced.

As a means of gaining additional information about the deuterium distribution, a second two-dimensional experiment, ^{1}H/^{2}H correlated spectroscopy, was run (Figure 2).[6] In this type of experiment, coupling between a ^{1}H and a ^{2}H is revealed. For example, if there were a peak at the intersection of 6.17 ppm on the *x*-axis and 6.27 ppm on the *y*-axis, it would indicate that a deuterium atom is on position 6 and a hydrogen atom is on position 5. From this ^{1}H/^{2}H correlated spectrum the following information was obtained: ^{2}H/^{1}H interactions were found between positions 5,6; 6,5; 6,6a; 10b,6a; 6a,6; and 6a,10b. The signal resulting from a deuterium atom on position 6a and a hydrogen atom on position 10b is consistent with only two isotopomers: **2b**-d_2 and **2d**-d_2. These data thus provide direct evidence for the presence of isotopomers **2a**-d_2, **2c**-d_2, **2e**-d_2, **2f**-d_2, and either **2b**-d_2 or **2d**-d_2.

Since neither mechanism proposed above can account for the formation of six isotopomers, a new mechanism was needed. A variation of Cava's mechanism which would produce all six isotopomers involves the ring opening of **3**, the first formed dimer of Cava's mechanism, to one of the valence isomers of dibenzo[*a*,*d*]cyclooctatet-

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[6] (a) Gould, S. J.; Planiswamy, V. A.; Bleich, H.; Wilde, J. *J. Chem. Soc., Chem. Commun.* **1984**, 1075. (b) Bleich, H.; Gould, S.; Pitner, P.; Wilde, J. *J. Magn. Reson.* **1984**, *56*, 515.

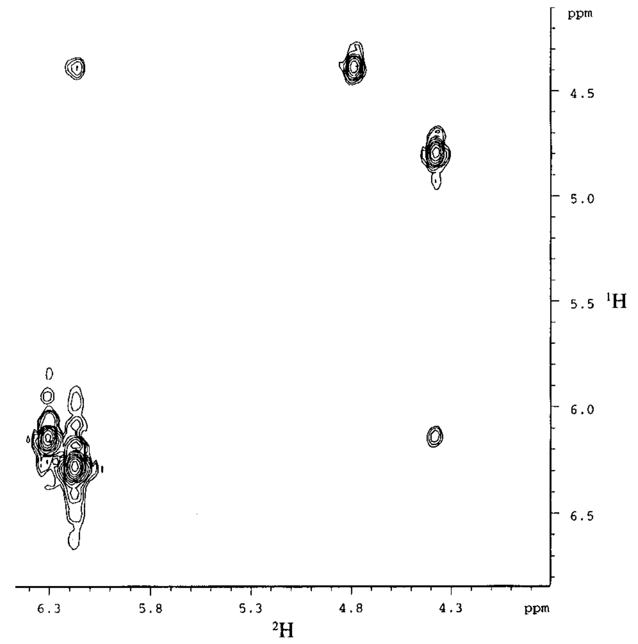
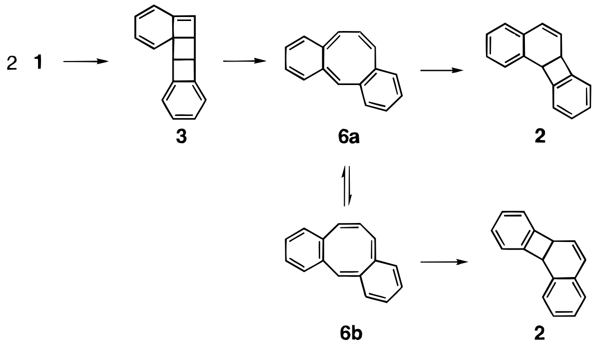


Figure 2. $^1H/^2H$ correlated spectrum of the **2**-d_2 isotopomer mixture.

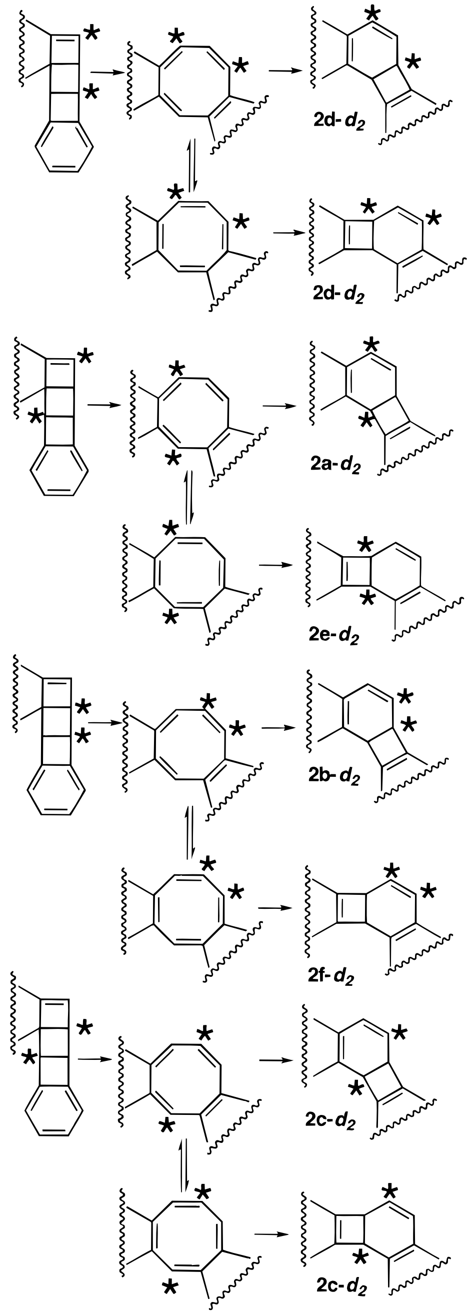
Scheme 2



raene, **6a**. The initially formed valence isomer of dibenzo[*a*,*d*]cyclooctatetraene, **6a**, should be able to isomerize readily to the other valence isomer, **6b**.[7] A 6π electrocyclic ring closure of **6a** and **6b** would produce **2** (see Scheme 2).[5,7] If dimerization of **1** proceeds by this third mechanism, dimerization of **1**-d_1 would produce all six isotopomers with the ratio of **2a**-d_2 to **2f**-d_2 being 1:1:2:2:1:1 (see Scheme 3), a distribution which accounts for the even distribution of deuterium in the four positions.

In order to gain further evidence for the formation of all six isotopomers and to quantify the amounts of the isotopomers, detailed analysis of the four ^1H NMR signals was undertaken.[8] The signals of each d_2 isotopomer are slightly different because of the spin–spin splitting difference of hydrogen and deuterium atoms. The ^1H NMR spectrum of each of the six isotopomers and **2** were simulated on an SGI Indy computer using the program NUMMARIT found in the Xsim software package. The chemical shifts and coupling constants used in the calculations were obtained from the high resolution ^1H NMR spectrum of **2**-d_0. These values were entered into the program, and a noniterative calculation was performed.

Scheme 3



The ^1H spectrum of a d_2 isotopomer was generated by replacing two hydrogen atoms with two deuterium atoms and adjusting the coupling constants to the appropriate $J_{H/D}$ values. Small adjustments (<0.008 ppm; the simulated spectrum of the isotopomer was compared to the experimental spectrum of the mixture of isotopomers) were also made to the chemical shifts to take into account the effects of the deuterium atoms. This procedure was repeated until all six isotopomers had been simulated. The individual d_2 ^1H NMR spectra were added and a scaling factor (×2) used for isotopomers **2c**-d_2 and **2d**-d_2 to obtain a spectrum containing the signals associated with all six isotopomers. This was done using Xwin NMR software. The ^1H NMR spectra for the four-isotopomer mixtures associated with each of the first two mechanisms were also generated. The four signals associated with positions 5, 6, 6a, and 10b were enlarged and compared to enlargements of the actual ^1H NMR spectrum of the d_2 dimer mixture. The experimental d_2

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(7) (a) Grimme, W.; Lex, J.; Schmidt, T. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 1268. (b) Fray, G. I.; Saxton, R. G. *The Chemistry of Cyclooctatetraene and its Derivatives*; Cambridge University Press: New York, 1978; pp 143, 137, 157.

(8) This analysis was suggested by Professor John B. Grutzner.

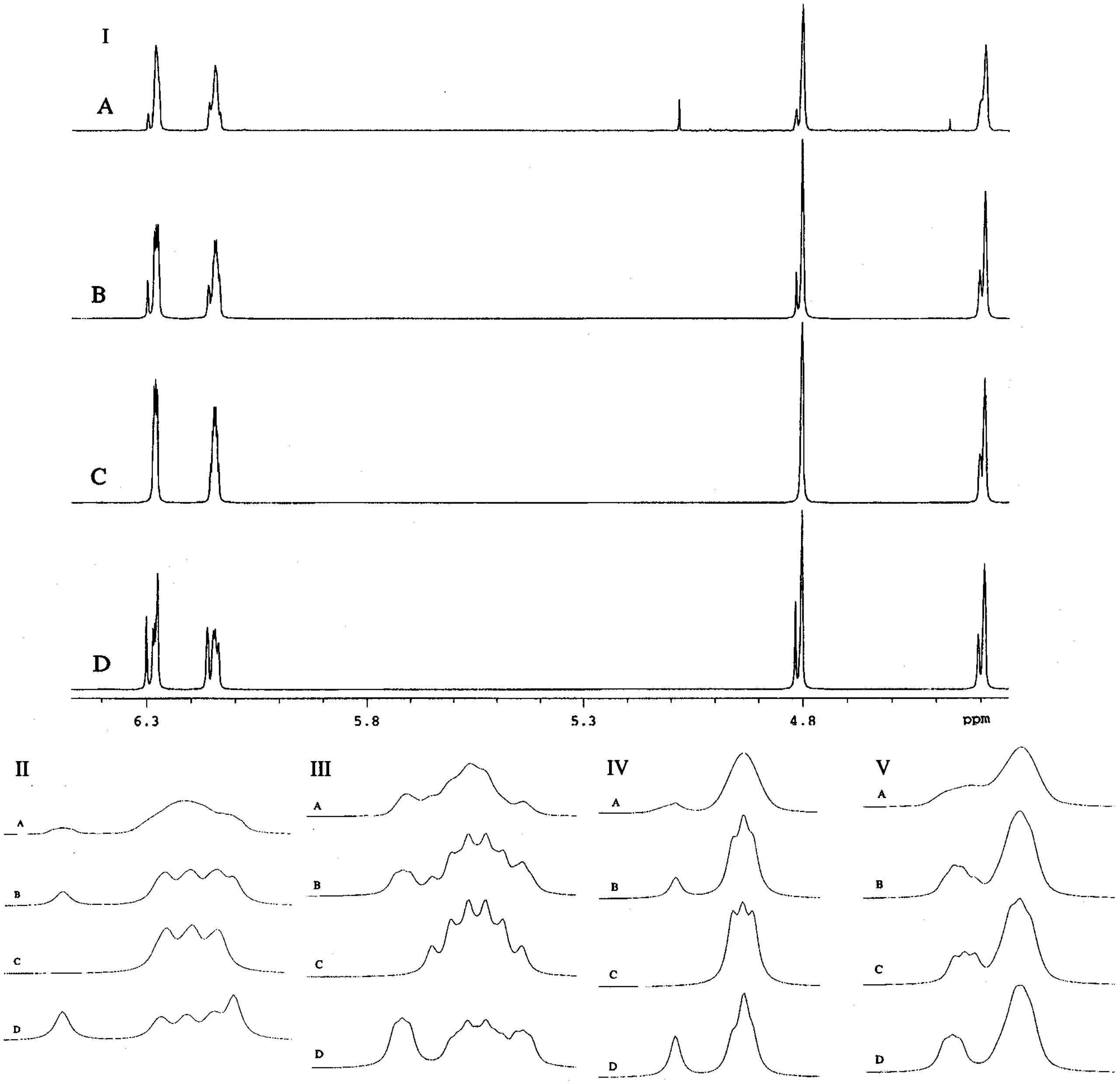


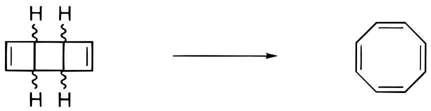
Figure 3. I is a composite of (A) the ^{1}H NMR spectrum of the **2**-d_2 isotopomer mixture, (B) the simulated spectrum of the six isotopomers **2a**-d_2 to **2f**-d_2 in the ratios 1:1:2:2:1:1, (C) the simulated spectrum of the four isotopomers consistent with Cava's mechanism, and (D) the simulated spectrum of the four isotopomers consistent with the mechanism which involves **4** as an intermediate. II−V are enlargements of the signals in I in the order in which they appear in I.

spectrum is in good agreement with the simulated spectrum for the six isotopomers obtained by the third mechanism but does not correspond well to the simulated spectra for the two four-isotopomer mixtures associated with the first two mechanisms (see Figure 3).

Discussion

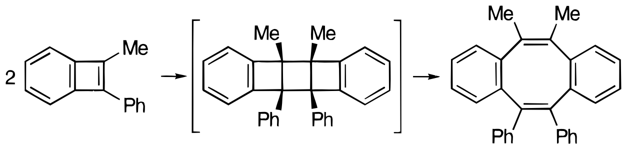
Careful reinvestigation of the dimerization of **1** by flow NMR spectroscopy failed to reveal any transient intermediates; only the final dimer, dimer **2**, was detected.

The d_2 isotopomers obtained from the dimerization of **1**-d_1 are not consistent with the dimerization mechanism proposed by Cava or our mechanism involving intermediate **4**, but are consistent with the mechanism shown in Scheme 2 in which the initially formed dimer, **2**, undergoes ring opening to form the cyclooctatetraene intermediate **6**. The parent system of **1**, *syn*- and *anti*-tricyclo[4.2.0.0^{2,4}]octa-3,7-diene (**7**), readily opens to cyclooctatetraene (**8**) when heated above 100 °C.[2a] Some



7 **8**

substituted benzocyclobutadienes, e.g., the 1-methyl-2-phenyl derivative, dimerize to give the syn-isomer of a dibenzo analog of **7** which rapidly opens to a substituted cyclooctatetraene, the so called "linear" dimer (**9**).[2a,b] The highly hindered 3,4,5,6-tetramethyl-1,2-diphenylbenzocyclobutadiene (**10**) gives two dimers, the "linear" dimer and a dibenzosemibullvalene (**12**) which is proposed to come from the rearrangement of a dibenzo[*a*,*d*]cyclooctatetraene (**11**). However, Grimme et al.[7] have studied a monodeuterated sample of **2** with a deuterium atom in the 5 position and have shown that it rapidly intercon-



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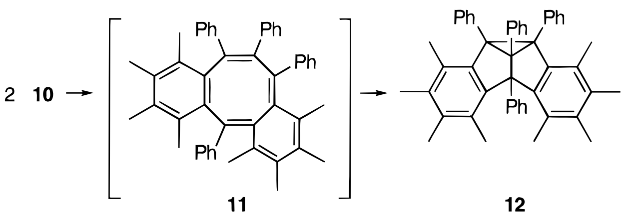


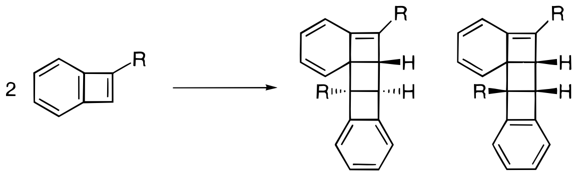
11

12

verts with the isotopomer with the deuterium atom in the 6a position at 100 °C. It is proposed[7] that this interconversion proceeds via **6**. Thus if **11** is the precursor of **12** the rearrangement must be a result of the steric effects of the large substituents.

The heats of formation of **3** and **6a** have been calculated using PCMODEL[9] to be 170 kcal/mol and 113 kcal/mol, respectively, indicating a large driving force for the opening of **3** to **6a**. In Grimme et al.'s study of the rapid interconversion of the isotopomers of **2** via **6**, they determined the free energy of activation for ring opening to the eight-membered ring to be 29.6 kcal/mol. Wilcox, Carpenter, and Dolbier have also investigated the ring opening of **2**. They estimated the enthaply of activation for ring opening to be 22 kcal/mol.[10] Using the calculated heat of formation of **2** (102 kcal/mol) and that of **6** (113 kcal/mol) and the free energy of activation for ring opening (29.6 kcal/mol), our estimate of the energy of activation for ring closure to **2** is 19 kcal/mol. This E_a is low enough to be surmounted at room temperature.

Several workers[11] have worked with a number of substituted benzocyclobutadienes and have found that a bulky substituent such as an isopropyl, a *tert*-butyl, or even a methyl group on the one position of **1** resulted in the formation of an angular dimer with the alkyl substituents on the 5 and 10b positions. These results are consistent with our proposed mechanism. For example, an alkyl-substituted cyclobutadiene (**13**) would form [4 + 2] dimers **14** or **15**. Either dimer would open to an eight-membered ring which could either close to the 5,10b isomer or to the sterically crowded 6a,10b isomer. Clearly the 5,10b dimer would be favored.



13 14 15

Conclusion

No evidence for the formation of transient intermediates in the conversion of **1** to **2** was obtained by flow NMR spectroscopy studies. We have shown by several NMR spectroscopic techniques that **1**-d_1 dimerizes to produce six dideuterated isotopomers **2a**-d_2 to **2f**-d_2, in a ratio of 1:1:2:2:1:1. We propose that this deuterium distribution is explained by a dimerization mechanism involving the formation of [4 + 2] dimer **3** followed by opening of **3** to form the cyclooctatetraene dimer **6** which closes to final dimer **2**.

Experimental Section

General Information. The residual CHD$_2$CN was used as the internal reference for all ^{1}H NMR spectra unless noted otherwise. All flow NMR experiments were performed on a 300 MHz wide-bore (5 cm) spectrometer using acetonitrile-d_3 as a solvent and the residual CHD$_2$CN as an internal reference (1.93 ppm). Acetonitrile-d_3 was obtained from Cambride Isotope Labs. GC/CI/MS analyses were performed on a GC/MS equipped with a 30 m DB-1 capillary column and used ammonia as the ionization gas. All starting materials were purchased from Aldrich Chemical Co. The heat of formations of compounds **2**, **3**, and **6** were calculated using PCMODEL v. 4.0.

2-(Trimethylsilyl)benzocyclobutenyl-1 mesylate (5) was prepared as described by Trahanovsky and Fischer.[3,4] Compound **5** was stored under argon at −75 °C.

1-Deutero-2-(trimethylsilyl)benzocyclobutenyl-1 mesylate (5-*d*$_1$) was prepared in the same fashion as **5** with the exception that the ketone was reduced with AlD$_3$. ^{1}H NMR (CD$_3$CN, 300 MHz) δ 7.35−7.09 (m, 4H), 3.48 (s, 1H), 3.13 (s, 3H), 0.049 (s, 9H). Compound **5**-d_1 was stored under argon at −75 °C.

6a,10b-Dihydrobenzo[*a*]biphenylene-*d*$_2$ (2-*d*$_2$). Mesylate **5**-d_1 (0.0497 g, 0.194 mmol) was placed in a flask containing 0.8 mL of CD$_3$CN (freshly distilled from CaH$_2$, and deaerated with argon). To this solution was added CsF (0.173 g, 1.14 mmol), and the reaction mixture was stirred overnight under argon. ^{1}H NMR (CD$_3$CN, 300 MHz) δ 7.35−6.99 (m, 64H), 6.26 (s broad, 4H), 6.13 (s broad, 4H), 4.78 (s broad, 4H), 4.37 (s broad, 4H); ^{2}H NMR (CH$_3$CN, 46 MHz, internal reference CD$_3$CN) δ 6.30 (s broad, 1H), 6.17 (s, 1H), 4.79 (s broad, 1H), 4.38 (s, 1H); GC/MS (CI/NH$_3$) *m*/*e* (% base peak) 224.1 $[M + NH_4]^+$ (100), 225 (16), 226 (2), 241 (48), 242 (9), 243 (1).

6a,10b-Dihydrobenzo[*a*]biphenylene (2). Compound **2** was prepared in the same way as **2**-d_2. ^{1}H NMR (CD$_3$CN, 400 MHz) δ 7.40−7.00 (m, 8H), 6.28 (d, J = 10.0 Hz, 1H), 6.15 (dd, J = 10.0 Hz, J^1 = 4.4 Hz, 1H), 4.81, (d, J = 6 Hz, 1H), 4.40 (m, 1H); ^{13}C NMR (CD$_3$CN, 75.4 MHz, internal reference CN of CD$_3$CN) δ 128.88, 128.83, 128.64, 128.56, 128.41, 128.23, 127.73, 126.27, 122.30, 121.85, 45.35, 43.98; (CDCl$_3$, 100.6 MHz, 7.7 mg/mL Cr(acac)$_3$ added,[12] internal reference TMS) δ 149.18, 148.58, 134.81, 131.24, 127.83 (2C), 127.72 (3C), 126.86, 126.79, 125.99, 121.61, 120.86, 43.82, 43.28.

Flow NMR Experiments. A description of the flow NMR apparatus and a procedure for flow NMR have previously been described.[3,4,13] Tetrabutylammonium fluoride (TBAF) was purchased as its hydrate from Aldrich Chemical Co. Excess water was removed from the TBAF by placing it into a desiccator and pulling a vacuum (0.1 mmHg/25 °C) on it for 12 h. The acetonitrile-d_3 was purified and dried before use by consecutive distillations from sulfuric acid, calcium hydride, and phosphorus pentoxide through a Vigreux column. A

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typical experiment would consist of preparing two 50 mL CD_3-CN solutions: one containing the starting material, *e.g.* **5** (0.0583 g, 0.2155 mmol), and the other containing the flouride source, tetrabutylammonium fluoride trihydrate (2.97 g, 9.430 mmol). Flow rates were varied from 0.3 mL/min to 20 mL/min during various flow NMR experiments.

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Supporting Information Available: NMR spectra for compounds **2**, **2**-d_2, **5**, and **5**-d_1, GC/MS/CI of **2**-d_2, and simulated ^1H NMR spectra of **2**, and chemical shift and coupling constant values used in the simulation of the NMR spectra (18 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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