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Chemistry

Mechanism of thermal rearrangement of the spiro bicyclo[2.1.0]-pentane-5,2′-methylenecyclopropanes to 6- and 7-methylenebicyclo[3.2.0]hept-1-enes

(peripheral bond cleavage/interconversion of biradical intermediates/isotopic position labeling)

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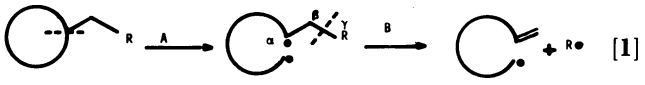
ABSTRACT **The thermal rearrangements of the bicyclo[2.1.0]pentane-5,2′-methylenecyclopropanes fall into two classes. The first occurs near 80°C and consists of a double epimerization ("bridge flip") which is initiated by cleavage of the bridge bond. An alternative mechanism by way of a trimethylenemethane intermediate is ruled out by an isotopic position-marking experiment. The second rearrangement begins to be detected above 120°C. It gives the isomeric 6- and 7-methylenebicyclo[3.2.0]hept-1-enes. Two possible mechanisms can operate in this complex change, but a choice between them is not yet possible.**

Thermally induced multiple rearrangements of certain alicyclic hydrocarbons may be formulated mechanistically as sequential cleavages of two or more covalent bonds. Typically, the first step (schematically shown in Eq. **1A**) is strongly endothermic and may lead to a biradical intermediate. This species can undergo further reaction by rupture (Eq. **1B**) of a second bond which has a β,γ-relationship to one of the odd-electron sites. The second step is of special interest in mechanistic organic



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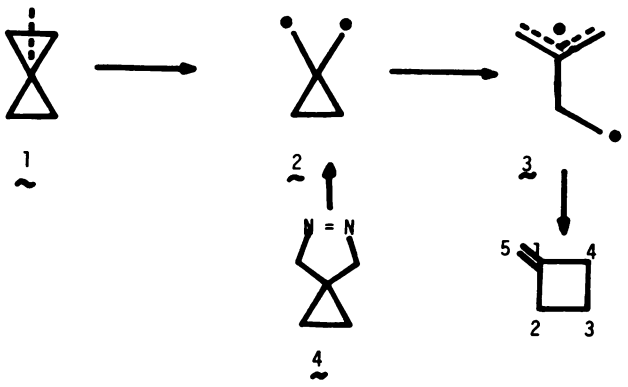
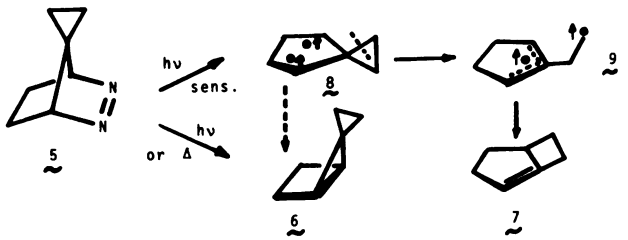
chemistry because it involves a bond so weak as to be on the borderline of covalency (1–5). As part of a study of such multiple rearrangements, we report here on the thermal reorganizations of two new methylenespiropentane derivatives which provide some information on the timing and reversibility of the sequential bond cleavages.

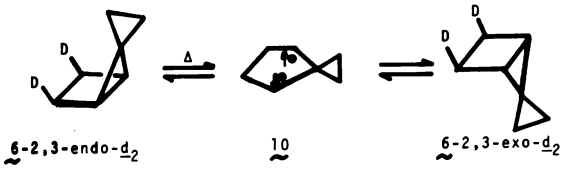
Some known thermal rearrangements of spiropentanes and methylenespiropentanes

In the structural isomerization of spiropentane **1**, the peripheral bond breaks first to give the 1,3-biradical **2** which, by fission of a β,γ bond, is converted to the allylically stabilized 1,4-biradical **3** (6–10). The latter species also is postulated as an intermediate in the degenerate rearrangement of methylenecyclobutane-5,5-d_2 to the 2,2-d_2 isomer (3, 11). Biradical **2** also may be involved in the gas phase decomposition of the diazene **4** (12).

In a closely related tricyclic spiropentane system (13), the thermolysis or direct photolysis of the diazene **5** gives mixtures of two hydrocarbon products, **6** (99% and 90%, respectively) and **7** (1% and 10%). Benzophenone-sensitized photolysis of **5** gives the same two products, but **7** now is dominant (98:2 at −50°C). It is a plausible hypothesis (13) that the triplet state of the spiro biradical **8**, which is generated efficiently in the sensitized photolysis, rearranges to triplet biradical **9** by bond fission faster than it can cyclize to the tricyclic hydrocarbon **6**. The singlet state **10** of the spiro biradical presumably is the intermediate or transition state in the thermal endo → exo isomerization of **6**-2,3-endo-d_2 (13).







Pyrolysis of methylenespiropentane **11** at 320°C gives both 1,2- and 1,3-bismethylenecyclobutane, **12** and **13**, in the kinetic ratio of about 7:1(14, 15) (**Scheme I**). The reaction leading to **12** may be formulated (14, 15) *via* the trimethylenemethane **14**, formed by cleavage of the allylic radial bond (reaction A). This step is followed by cleavage of the peripheral bond to give the tetramethyleneethane **15**. An alternative, albeit energetically less attractive, path might be imagined (14, 15) in which the order of bond cleavages is reversed, so that the peripheral bond breaks first (reaction B) to give biradical **16**.

The formation of 1,3-bismethylenecyclobutane **13** in competition with the pathways leading to **12** is quite surprising because it apparently requires rupture of a presumably strong

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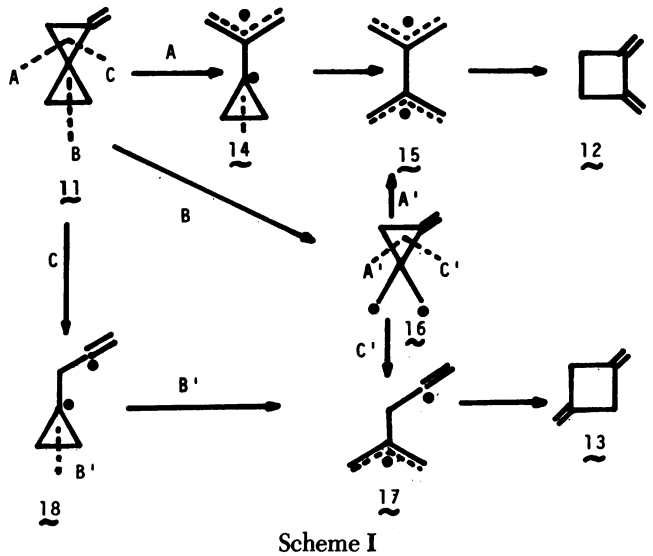
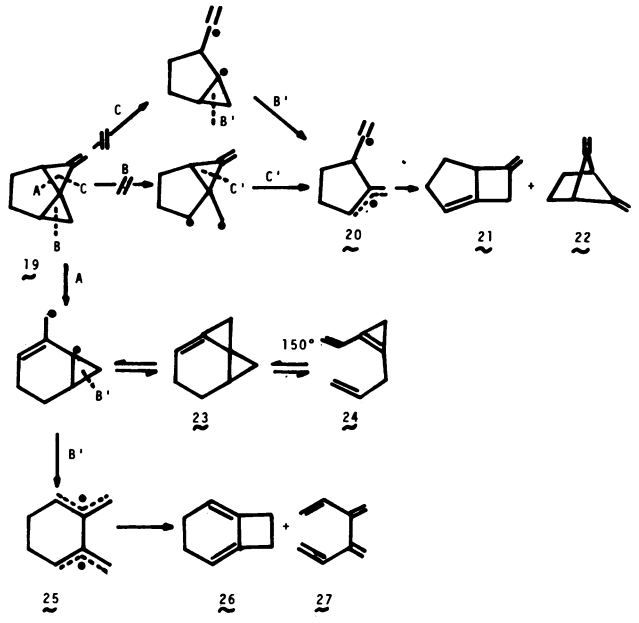


Scheme I

bond, C, with high s-character, at a rate only slightly less than that of the weak allylic bond at A. It has been suggested (14, 15) that this reaction may involve the allylic-vinylic radical **17** and that the puzzling ease with which it apparently is formed may be rationalized by the path **11** → **16** → **17**. Hypothetically, cleavages A′ and C′ in **16** would be more nearly matched in rate than would cleavages A and C in **11** because **16** is a high-energy intermediate, and the activation energies leading to the cleavage transition states are both small (14, 15).

In the pyrolysis of the analogous bridged spiropentane **19** (16, 17) (**Scheme II**), however, the corresponding B + C′ (or C + B′) sequence, which would give the allylic-vinylic biradical **20**, does not seem to occur because neither **21** nor **22**, the two possible 1,3-bismethylenecyclobutanes, is among the products. The major product at 120°C is the spiro olefin **23**, which rearranges by a reversible retro Diels–Alder reaction to the triene **24** at 150°C. At still higher temperatures (180°C), **23** gives the 1,2-bismethylenecyclobutane **26** and its cycloreversion product **27**. The path **23** → **26** presumably involves the tetramethylene ethane intermediate **25** (16, 17).

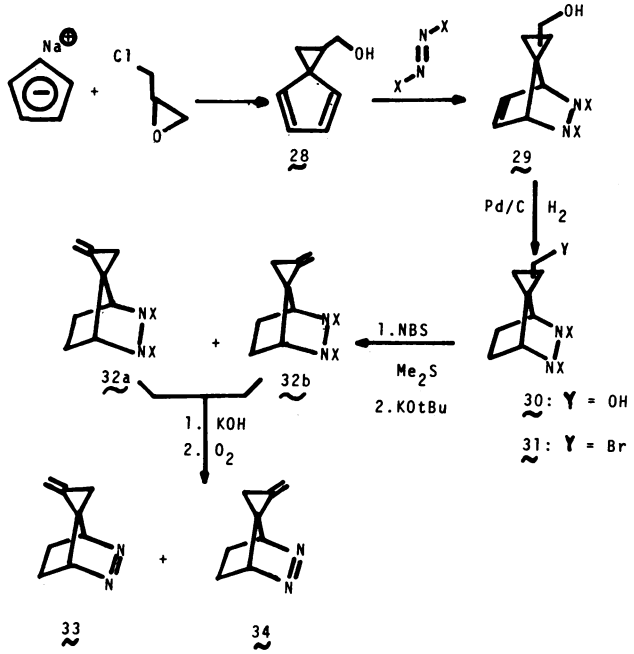


Scheme II

Synthesis and pyrolysis of the *syn*- and *anti*-spiro(bicyclo[2.1.0]pentane)-5-2′-methylenecyclopropanes

The spiro dienol **28**, prepared (**Scheme III**) from cyclopentadienyl sodium and epichlorohydrin (18, 19),† was converted to the diazenes **33** and **34** as shown. One of the isomers, m.p. 68–69°C, could be separated by fractional crystallization from pentane at −40°C.

Irradiation of the crystalline diazene, arbitrarily assigned the *anti* configuration **33**, in pentane solution at 350 nm gave a mixture that could be fractionated by gas chromatography. The



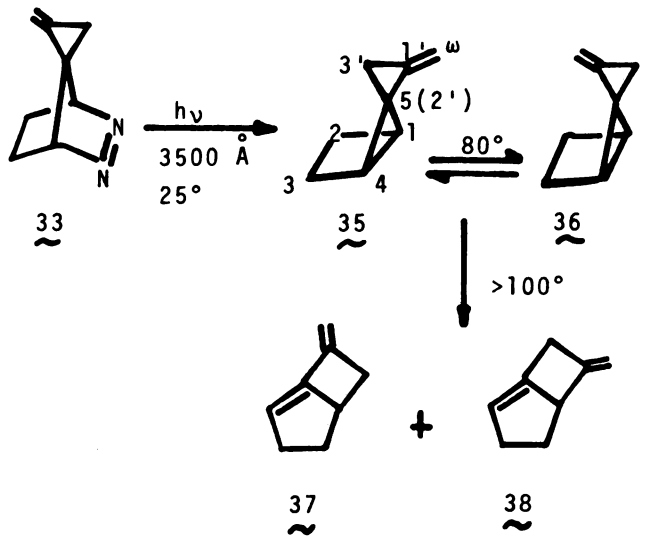
Scheme III (X = CO_2Me or CO_2Et)

major products were the tricyclic hydrocarbons *anti*- and *syn*-spiro(bicyclo[2.1.0]pentane)-5,2′-methylenecyclopropane, **35** and **36**, in a ratio of about 4:1. The structures shown here were assigned by comparison of the NMR spectra with those of model compounds (see *Experimental*). The assignments of gross structure seem firm, although the spectra provide only a suggestive basis for a stereochemical assignment (**35** vs. **36**), which in any case is not crucial to the present study. Two minor products subsequently were identified as 6- and 7-methylenebicyclo[3.2.0]hept-1-ene, **37** and **38**.

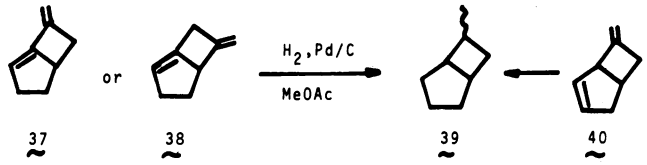
Pyrolysis of either spiro hydrocarbon **35** or **36** at 80°C in deuteriochloroform caused interconversion of the two isomers to give an equilibrium mixture of 65% of **35** and 35% of **36**. At 100°C, further slow rearrangement to **37** and **38** occurred. These substances, particularly the conjugated diene **37**, polymerized readily under the solution phase pyrolysis conditions, and it was difficult to isolate pure samples from the reaction mixtures. For this purpose, a set of pyrolysis conditions was developed that simultaneously effected rearrangement of the spiro compounds **35** and **36** and permitted separation of the products. Thus, injection of **35** and **36** onto a 10-ft × ¼-in. 15% OV-17 preparative gas chromatography column maintained at 60°C with the injection port at 240°C cleanly brought about the **35** ⇌ **36** double epimerization. When the injection port temperature was raised to 340°C, **37** and **38** were formed in a ratio of 6 parts of **37** to 1 part of **38** and could be isolated.

Identification of the products **37** and **38** was achieved by

† The correct structure is shown in ref. 19.



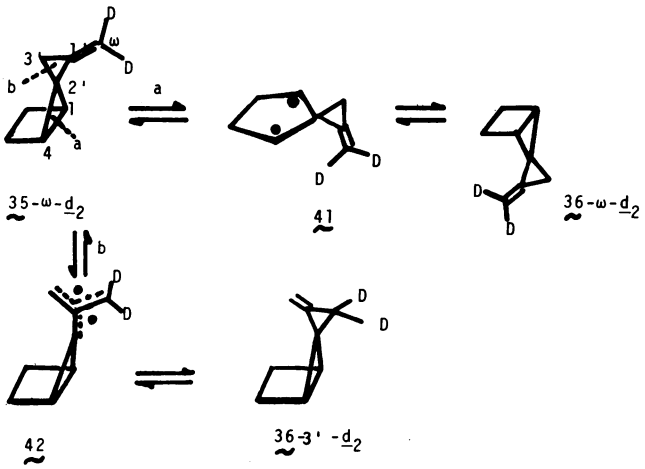
low-temperature NMR (to prevent polymerization of **37**). The structural assignments were confirmed by comparisons of the spectra with those of model compounds (see *Experimental*) and also by catalytic hydrogenation of **37** and **38** to the mixture of saturated bicyclic hydrocarbons **39** which also were obtained by hydrogenation of the known (20, 21) closely related diene **40.**



Mechanisms of the rearrangements

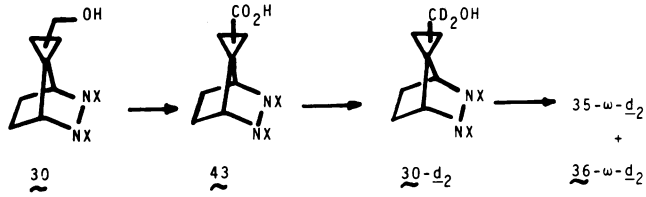
Two plausible pathways may be imagined for the stereomutation of the spiro hydrocarbons **35** and **36.** The first is a "bridge-flip" process, which involves cleavage of the C-1—C-4 bond (a) giving the spiro biradical **41** which can cyclize in either stereochemical sense. The second involves cleavage of the C-2′—C-3′ bond (b) giving the trimethylenemethane biradical **42** which can recyclize, joining the original C-2′ to the original exocyclic methylene carbon.

These two mechanisms can be distinguished by an isotopic labeling experiment, as shown (**Scheme IV**). Rearrangement of a labeled isomer **35**-ω-d_2 with deuterium in the exocyclic methylene position would give the epimer **36**-ω-d_2 by the bridge-flip mechanism (a) but would lead to ring-labeled epimer **36**-3′-d_2 by the trimethylenemethane mechanism (b).



Scheme IV

Syntheses of the labeled spiro hydrocarbons **35**-ω-d_2 and **36**-ω-d_2 were effected by the route shown here (X = CO_2Et), starting with the alcohols **30** which were oxidized with potassium permanganate in benzene containing a catalytic amount of dicyclohexo-18-crown-6 (22) to the carboxylic acids **43.** Reduction with hexadeuteriodiborane gave the deuterated alcohol **30**-d_2, which was converted to the deuterated spiro

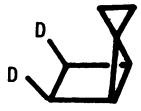
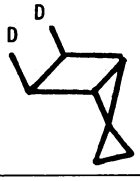


compounds **35**-ω-d_2 and **36**-ω-d_2 as before. The major isomer (arbitrarily assigned stereochemistry **35**-ω-d_2) was separated by gas chromatography and pyrolyzed at 240°C under the flow conditions described above to give a mixture of **35**-ω-d_2 and **36**-ω-d_2. Isolation and NMR analysis of the epimer **36**-ω-d_2 showed the deuterium label to be exclusively affixed to the exocyclic carbon. This result is consistent with the "bridge-flip" mechanism (a) but not with the trimethylenemethane mechanism (b).

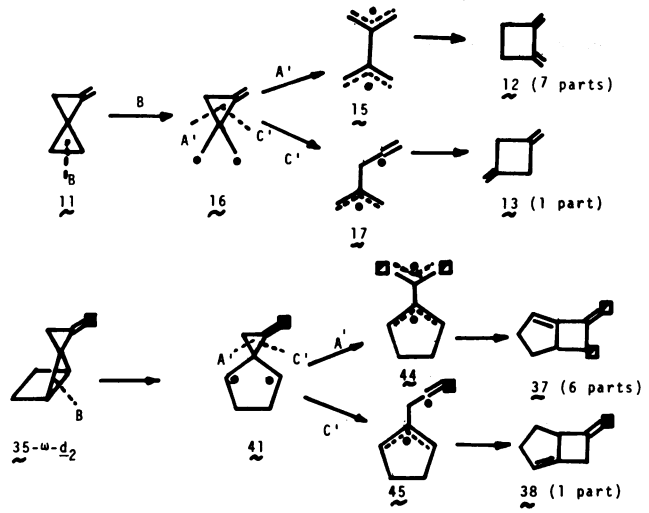
Although the incorporation of the spiropentane and methylenecyclopropane systems into the tricyclic framework of **35** and **36** may introduce nonadditive strain effects that are difficult to predict, nevertheless the qualitative relative reactivities of these moieties in the present systems are correctly predicted by modeling them on appropriate simpler cases. The activation energies for the transformations of the model compounds shown (Table 1) suggest that the bridge bond (C-1—C-4) of **35** should be more reactive than the radial bond (C-2′—C-3′) by a large factor.

There is a striking similarity in the relative amounts of 1,2- and 1,3-bismethylenecyclobutane products from the **35/36** pair and from methylenespiropentane itself (**11**). The 1,2 product predominates by a factor of 6 from **35/36** and of 7 from **11.** It is tempting to suggest a common mechanistic basis for this parallelism. A simple rationalization (**Scheme V**) would be that pyrolysis of both **35/36** and **11** is initiated by cleavage of the remote bond B (**11** → **16** from **Scheme I,** and **35** → **41** from **Scheme IV**). The product distribution then is determined by the relative rates **16** → **15** vs. **16** → **17** in the parent spiropentane system and **41** → **44** vs. **41** → **45** in the tricyclic case. These rate ratios represent competitions between similar pairs and might well be roughly equal. For the purpose of the present

Table 1. Activation energies for pyrolytic rearrangements

Reactant	Product	E_a*	Ref.
		46.4	23
		38.8	24
		29.0	25

* In kcal/mol.



Scheme V (■ = CD_2, ◪ = $CD_2/2$)

discussion, the similarity in product distributions might be expected regardless of the details of the pathways leading to the 1,2- and 1,3-bismethylenecyclobutane products. In particular, the biradical species derived by cleavages A′ and C′ need not be true intermediates.

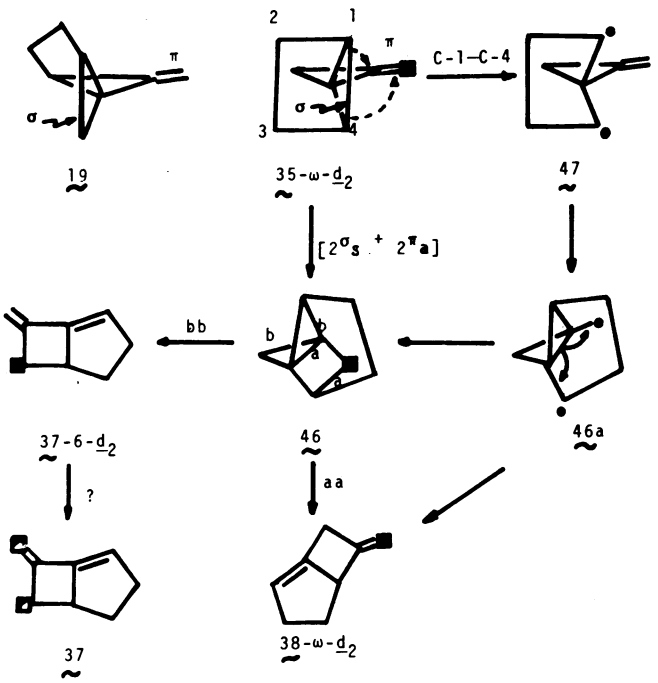
On the basis of this rationalization, the absence of 1,3-bismethylenecyclobutane products **21** and **22** from the pyrolysis of the tricyclic compound **19** (see **Scheme II**) could be attributed to preferential initial cleavage to a trimethylenemethane biradical by path A instead of to a cyclopropylbiscarbinyl radical by path B.

A conceivable alternative mechanism is outlined in **Scheme VI.** This involves a [2.1.1]propellane as a common intermediate for both the 1,2- and 1,3-bismethylenecyclopropane products. In the case of **35,** for example, this would be **46,** which could be formed either by cyclization of the biradical **41** or by a symmetry-allowed $[_2\sigma_s + {}_2\pi_a]$ cycloaddition. Note that, in the analogous tricyclic compound **19,** the ethano bridge tends to distort the methylenespiropentane structure and pull the σ bond away from its π partner. On the other hand, neither isomer in the present series, **35** or **36,** suffers this difficulty.

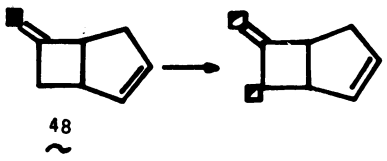
Starting from **35**-ω-d_2, **46** would be labeled as shown. Cleavage of bonds aa of **46** (compare the analogous change bicyclo[2.2.2]propellane → 1,4-bismethylenecyclohexane) (26–29) would give **38**-ω-d_2, the same product predicted from the allylic-vinylic biradical **45** in **Scheme V.** However, cleavage of bonds bb of **46** (compare the analogous rearrangement of bicyclo[1.1.0]butane to 1,3-butadiene) (30, 31) would lead to **37**-6-d_2 rather than to the **37** product with the label scrambled between the ring (C-6) and exocyclic methylene, which would be expected from the tetramethyleneethane intermediate **44** of **Scheme V.**

A variant of this mechanism, which would lead to the same connectivity in the product, involves cleavage at C-1—C-4 of **35**-ω-d_2 followed by cyclization of the biradical **47** (≡**41**) to another biradical **46a** and cleavage of the bridge bond in the latter.

The labeling experiment would be directly decisive only if regiospecifically labeled **37**-6-d_2 were the observed product. If the label were completely scrambled between the exocyclic and endocyclic methylene groups, it would be necessary to show that **37**-6-d_2 does not suffer a secondary methylenecyclobutane rearrangement. Because **37**-6-d_2 is not yet available by an independent synthesis, a control experiment could not be done, but kinetic measurements (20) on the analogous compound **48** show the half-life for deuterium scrambling to be about 10 sec at 340°C, the temperature at which our flow pyrolysis of **35** occurs. Of course one cannot equate the scrambling rates for **48** and **37**-6-d_2, but if they are even roughly similar, the implication for the success of our experiment is unfavorable because the residence time of the sample in the heated zone under our conditions is about 6 sec. A choice between the pathways of **Scheme V** and **Scheme VI** therefore necessitated an experimental gamble that the correct mechanism corresponds to **Scheme VI** and that the secondary label scrambling in the product **37**-6-d_2 is slow.



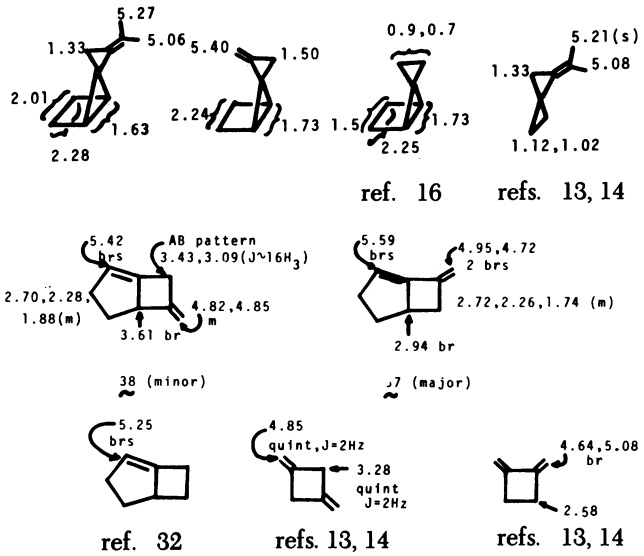
Scheme VI (■ = CD_2)



In the event, the gamble failed. We found that **38** recovered from the pyrolysis had all of the original deuterium label in the exocyclic position, as would be predicted by either mechanism, but **37,** the potentially decisive product, had suffered complete scrambling of its label between the exocyclic and C-6 methylene groups. This was best detected in the ^2H NMR spectrum which showed only four signals of equal intensity: two at δ 4.93 and 4.70 (=CD_2) and two at 3.71 and 2.24 (saturated CH_2).

Conclusions

The energy surface for the thermal rearrangements of the methylenespiropentanes **35** and **36** is complex. So far, the lowest energy transition state we have been able to detect involves cleavage of the C-1—C-4 bond, leading to a "bridge-flip." A conceivable alternative pathway in which the radial bond C-2′—C-3′ cleaves to give a trimethylenemethane biradical is not competitive. At higher temperatures, deep-seated rearrangements of **35** and **36** to the methylenebicyclo[3.2.0]heptenes **37** and **38** occur.



Experimental

Elemental compositions for new compounds **33** (or **34**), **35, 36, 39,** and the methyl ester of **43** were established by combustion analyses or high-resolution mass spectrometery. The NMR chemical shift assignments (δ values, $CDCl_3$ or CCl_4 solutions) and those of model compounds are shown.

The spectrum of **38** (Bruker HX-270) was unexceptional, but the vinyl proton resonance at δ 5.59 of **37** integrated to only half the expected intensity under Fourier transform acquisition, even with pulse delays of 10 sec. It was necessary to increase the pulse delays to 60 sec in order to compensate for the slow relaxation and obtain the correct integration.

We thank Prof. Peter B. Dervan, California Institute of Technology, for the suggestion of the variant sequence **47** → **46a** → **46** of **Scheme VI.** Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this work. We also thank the National Science Foundation (CHE 76-00416) for partial support and the Biotechnology Resources Program of the National Institutes of Health (RR-798) for its support of the Southern New England High-Field NMR Facility.

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