

1,6-Methano[10]annulene-Stabilized
Radicals

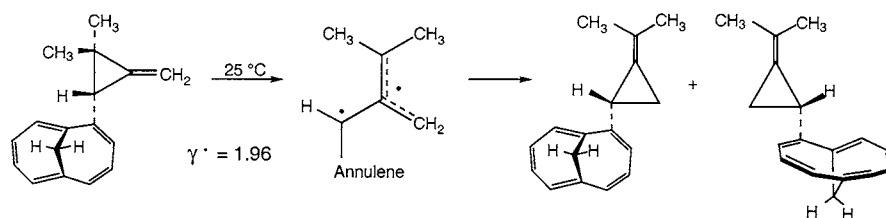
Xavier Creary* and Kevin M. Miller

Department of Chemistry and Biochemistry, University of Notre Dame,
Notre Dame, Indiana 46556

creary.1@nd.edu

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ABSTRACT



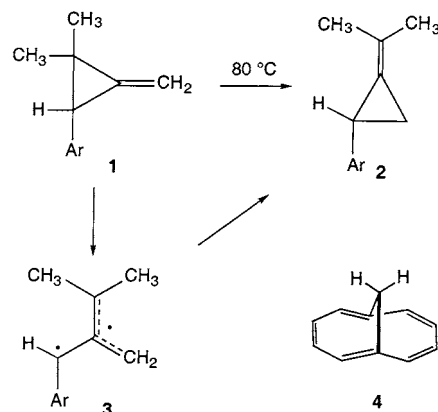
The rate of the methylenecyclopropane rearrangement is remarkably enhanced by the 1,6-methano[10]annulene group, which greatly stabilizes the biradical intermediate. The diastereomeric products argue against a concerted rearrangement mechanism and support a stabilized biradical intermediate that lives long enough to undergo rotation before ring closure.

Over the years, we¹ and others² have undertaken a number of studies designed to quantitatively evaluate the effect of various substituents on the stability of free radicals. This has led to the development of σ^* radical stability scales. Aromatic groups themselves are outstanding radical stabilizers and related γ^* values, which are a measure of radical-stabilizing abilities of groups, have been determined.³ Our probe utilizes the methylenecyclopropane rearrangement of substrates **1** to the corresponding isopropylidenecyclopropanes **2** (Scheme 1). These rearrangements are proposed to occur via the biradicals **3**, where the aromatic group can stabilize the biradical, thereby enhancing the rearrangement rate. This probe has been applied to many conventional aromatic groups, including phenyl, pyridyl, naphthyl, pyrenyl, furanyl, thienyl,

and ferrocenyl. In an attempt to find outstanding radical stabilizers, we have now turned our attention to the 1,6-methano[10]annulene system **4** as a potential radical stabilizing group. This system, first prepared by Vogel in 1964,⁴ has aromatic properties as judged by NMR and chemical reactivity criteria. Reported here are the results of this study.

The desired methylenecyclopropane was prepared as shown in Scheme 2. The 1,6-methano[10]annulene **4** was

Scheme 1

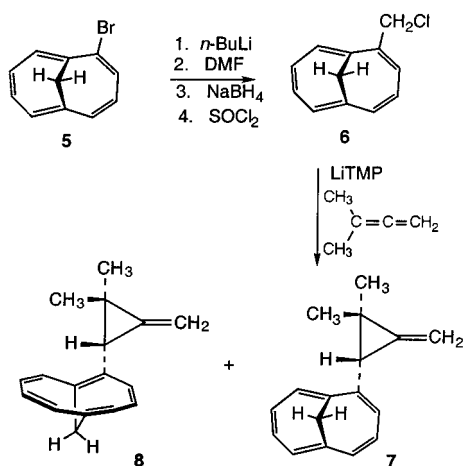


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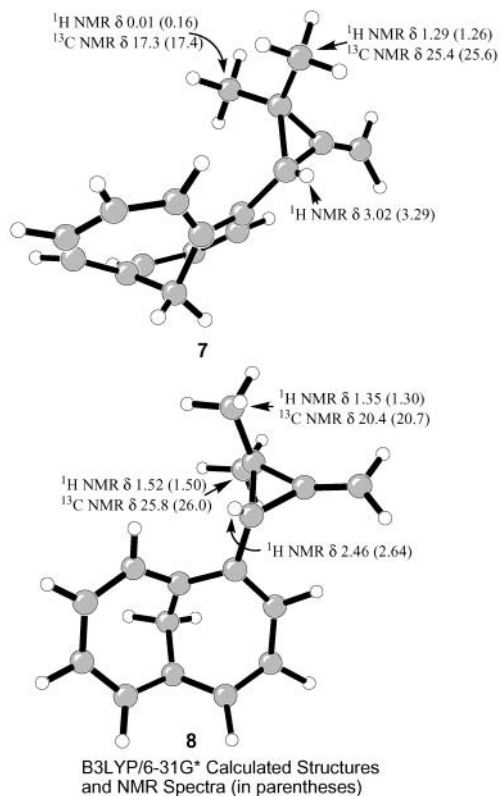
(2) (a) Adam, W.; Harrer, H. M.; Kita, F.; Nau, W. M. *Adv. Photochem.* **1998**, *24*, 205. (b) Adam, W.; Harrer, H. M.; Kita, F.; Korth, H.-G.; Nau, W. M. *J. Org. Chem.* **1997**, *62*, 1419. (c) Jackson, R. A.; Sharifi, M. *J. Chem. Soc., Perkin Trans. 2* **1996**, 775. (d) Jackson, R. A. *J. Organomet. Chem.* **1992**, *437*, 77. (e) Jiang, X. K.; Ji, G. Z. *J. Org. Chem.* **1992**, *57*, 6051. (f) Luedtke, A.; Meng, K.; Timberlake, J. W. *Tetrahedron Lett.* **1987**, *28*, 4255. (g) Wayner, D. D. M.; Arnold, D. R. *Can. J. Chem.* **1985**, *63*, 2378. (h) Engel, P. S.; Bishop, D. J. *J. Am. Chem. Soc.* **1975**, *97*, 6754. (i) Engel, P. S.; Bishop, D. J. *J. Am. Chem. Soc.* **1975**, *97*, 6754.

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Scheme 2

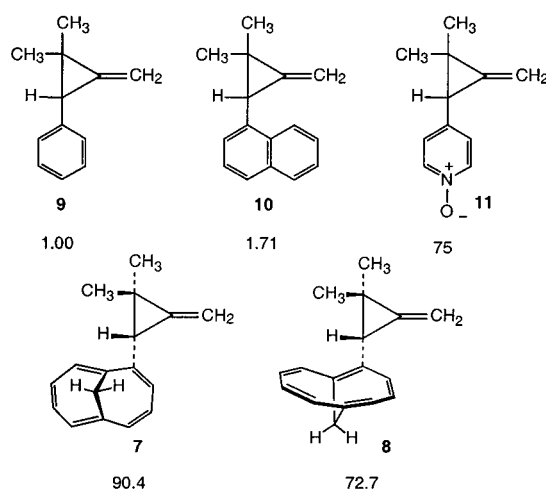


brominated⁵ and then reacted with *n*-BuLi. The organolithium reagent was then formylated using DMF, and the corresponding aldehyde was reduced with NaBH₄. Conversion to the chloride (56% yield from **5**) was followed by carbenoid generation in the presence of 1,1-dimethylallene. This reaction gave a 35% yield of racemic mixtures of diastereomeric methylenecyclopropanes **7** and **8** in a 2.6:1 ratio. These diastereomers could be separated by silica gel chromatography.



The structures of **7** and **8** were established by NMR spectroscopic methods which involved comparison of actual spectra with *ab initio* calculated spectra.⁶ The major diastereomer **7** showed an upfield methyl singlet at δ 0.01. The

Chart 1



Relative Rearrangement Rates at 80.0 °C

B3LYP/6-31G*-calculated minimum energy structure of **7** showed that the methyl group that is *cis* to the annulene system is also in the shielding region of the annulene ring with a calculated chemical shift of δ 0.16. The other methyl group has a measured shift of δ 1.29 and a calculated shift of δ 1.26. The calculated ¹³C NMR shifts of δ 17.4 and 25.6 for the methyl carbons also correspond quite well with the actual shifts of δ 17.3 and 25.4.

The minor product **8** shows methyl group ¹H NMR shifts of δ 1.35 and 1.52 while the calculated values are δ 1.30 and 1.50. The actual ¹³C NMR shifts of δ 20.4 and 25.8 also correspond well with the calculated values of δ 20.7 and 26.0.

Methylenecyclopropanes **7** and **8** rearrange thermally at reasonable rates in benzene-*d*₆ at 25 and 50 °C.⁷ Rates are significantly faster than the phenyl analogue **9**. In fact, **7** rearranges even faster than the pyridine *N*-oxide system **11**, which was our previous record holder as the most activating aromatic group (Chart 1). These rates for **7** and **8** correspond to γ^* values of 1.96 and 1.86.

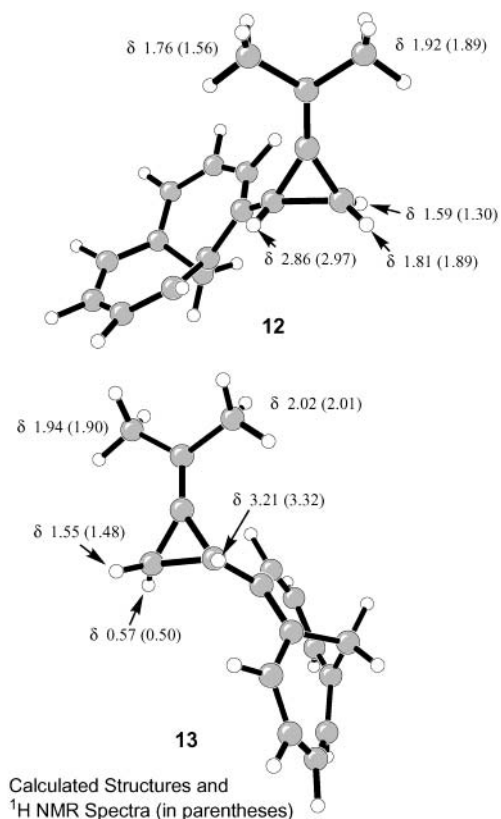
The rearrangement of **7** gives a mixture of two diastereomeric isopropylidenecyclopropanes **12** and **13** in a 93:7 ratio. The product **12** is one of net inversion at the carbon bearing the annulene group, while **13** is a product of net

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retention at this center. Rearrangement of **8** also gives a mixture of **12** and **13** (enantiomers of **12** and **13**), but in a far different ratio of 2.5:97.5. There is no interconversion of **7** and **8** under the reaction conditions. As before, structures were determined by NMR spectra of **12** and **13**, which differ substantially (Scheme 3).

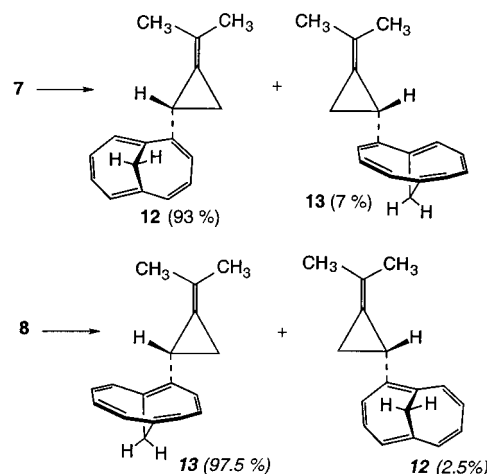
The cyclopropyl hydrogens of **12** appear at δ 2.86, 1.81, and 1.59, while those of **13** appear at δ 3.21, 1.55, and 0.57. The calculated minimum energy structure of **13** shows that the cyclopropyl hydrogen that is cis to the annulene ring is also in the shielding region of the annulene system with a calculated ^1H shift of δ 0.50. The remainder of the calculated spectrum of **13** (as well as **12**) fits well with the actual spectrum. Computational chemistry has therefore proven to be a powerful tool for discerning subtle differences in structure in systems such as **7** and **8**, as well as **12** and **13**.



Scheme 4 is proposed to account for the diastereomeric mixture of products formed in the thermal rearrangement of **7**. Fragmentation of the cyclopropane bond gives the biradical **14**, which can close to give the major product **12** (93%). It is suggested that this biradical is greatly stabilized by the 1,6-methano[10]annulene system and can live long enough to undergo rotation about the indicated carbon–carbon bond to give the biradical **15**. Subsequent closure of **15** leads to the 7% of the diastereomeric product **13**. Methylene-cyclopropane **8** is proposed to undergo an analogous process. The

(7) For **7**: $k = 7.45 \times 10^{-6} \text{ s}^{-1}$ at 25.0 °C and $1.89 \times 10^{-4} \text{ s}^{-1}$ at 50.0 °C. For **8**: $k = 5.22 \times 10^{-6} \text{ s}^{-1}$ at 25.0 °C and $1.42 \times 10^{-4} \text{ s}^{-1}$ at 50.0 °C. ΔH^\ddagger and ΔS^\ddagger values are 24.1 kcal/mol and -1.0 eu for **7** and 24.7 kcal/mol and 0.1 eu for **8**.

Scheme 3

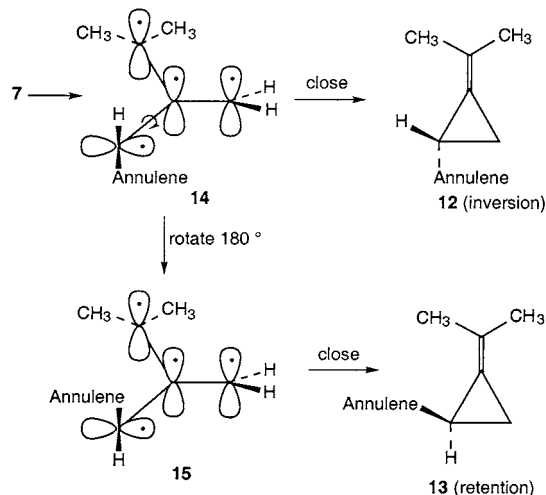


fact that completely different product ratios are observed from **7** and **8** suggests that **14** and **15** have not equilibrated; i.e., biradical **14** remains a very short-lived intermediate.

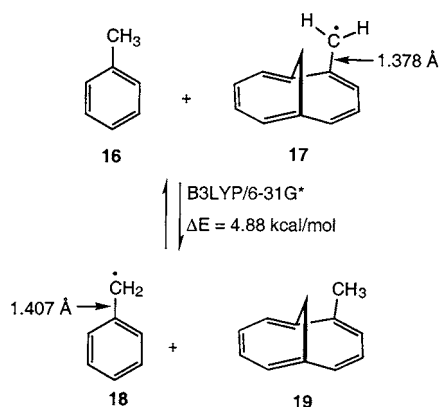
This product study provides strong evidence that the methylenecyclopropane rearrangement that we have used as the basis for σ^* values is not a concerted process. A concerted process, which has always been a possibility in the methylenecyclopropane rearrangement, must proceed with complete inversion at the migrating center.⁸ On the other hand, a stepwise process, proceeding via a biradical intermediate that lives long enough to undergo rotation, nicely accounts for the stereochemical behavior presently observed in the thermal rearrangements of **7** and **8**.

B3LYP/6-31G* computational studies on radical **17** give further insight into radical stabilization by the 1,6-methano[10]annulene system. The radical stabilization energy of **17** relative to the benzyl radical, **18**, is calculated via the isodesmic reaction in Scheme 5. The ΔE value of 4.88 kcal/mol is one of the largest radical stabilization energies for a

Scheme 4



Scheme 5



simple aromatic system calculated to date. Spin density at the CH_2 carbon of **17** is only 0.559, and this compares to a spin density of 0.792 at the benzylic carbon of **18**. Spin is more extensively delocalized into the annulene ring of **17** than into the benzene ring of **18**. The $\text{H}_2\text{C}-\text{C}$ bond length of 1.378 Å in **17** is considerably shorter than the analogous bond length in **18** (1.407 Å) and also in line with extensive spin delocalization.

Why is the 1,6-methano[10]annulene system such a potent radical stabilizer relative to other aromatic rings? While the computational studies verify extensive spin delocalization and resultant stabilization by the annulene ring, a more

fundamental explanation is still needed. It is suggested that the aromatic nature of the 1,6-methano[10]annulene system holds the answer. Spin delocalization by the annulene ring necessarily results in disruption of aromaticity. The aromatic character of the 1,6-methano[10]annulene system,⁹ which is not completely planar,¹⁰ is less than that of a benzene ring involved in delocalization. Hence, the cost for disruption of aromaticity in radicals such as **17** is less than must be paid for disruption of benzene aromaticity in **18**.

In summary, the 1,6-methano[10]annulene group is an extremely effective radical stabilizing group as determined from its rate enhancing effect on the methylenecyclopropane rearrangement of **7** and **8**. Rearrangements of **7** and **8** give product mixtures that argue against a concerted 1,3-sigmatropic shift mechanism. The products formed implicate a 1,6-methano[10]annulene-stabilized biradical intermediate that lives long enough to rotate before ring closure. B3LYP/6-31G* computational studies also support the suggested large spin delocalizing and stabilizing effect of the 1,6-methano[10]annulene system on radicals.

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