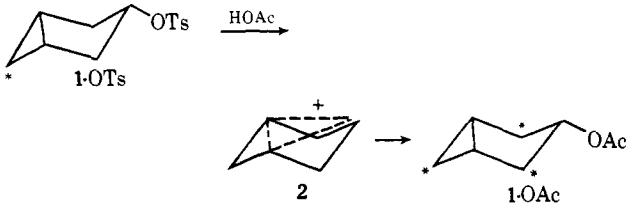
Solvolysis of Tetracyclo[11.1.0.0^{3,5}.0^{7,9}]tetradecan-11-yl *p*-Toluenesulfonates, Possible Heptahomotropylium Ion Precursors[1]

Richard W. Thies,*[2] Mitsuru Sakai, Dale Whalen, and S. Winstein[3]

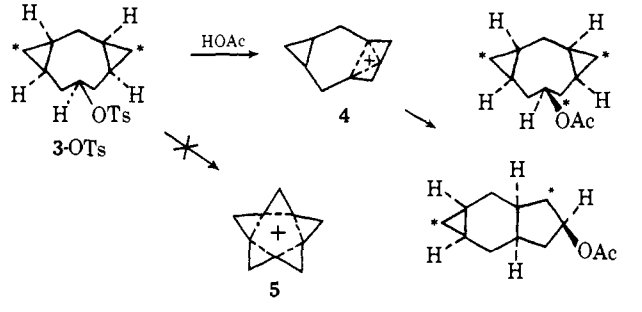
Contribution No. 2960 from the Department of Chemistry, University of California, Los Angeles, California 90024, and the Department of Chemistry, Oregon State University, Corvallis, Oregon 97330. *Received June 4, 1971*

Abstract: Solvolysis of *endo,endo,endo*-tetracyclo[11.1.0.0^{3,5}.0^{7,9}]tetradecan-11-yl *p*-toluenesulfonate (**7**-OTs) results in 97% 1,2 elimination products. Neither heptahomotropylium ion nor trishomocyclopropenyl ion intermediates are formed although the system is geometrically constructed to favor these intermediates. The propensity of medium-sized rings to undergo syn elimination to trans olefins provides a rationalization for the behavior of this system relative to its eight-membered analog.

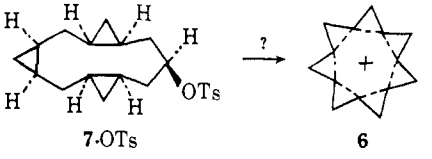
We have previously reported the solvolyses of two compounds which are geometrically arranged to yield symmetrical homoaromatic[4,5] or antihomoaromatic ions.[4,6] *cis*-Bicyclo[3.1.0]hex-3-yl *p*-toluenesulfonate (**1**-OTs) gives rates, products, stereochemistry, special salt effects, substituent effects, and deuterium scrambling results which are most consistent with the intermediacy of the threefold symmetric, trishomocyclopropenium ion, **2**. Solvolysis of *endo,endo*-tricyclo-



[7.1.0.0^{3,5}]decan-7-yl *p*-toluenesulfonate (**3**-OTs) gives rates, products, and deuterium scrambling that suggest the intermediacy of a twofold symmetric trishomoaromatic ion **4**, rather than the fivefold symmetric ion **5**. Since ion **5** would be antihomoaromatic, it is not surprising that the trishomocyclopropenyl species is preferentially formed.



The present study has examined whether a higher order homoaromatic species, the sevenfold symmetric heptahomotropylium ion **6**, could be an intermediate in the solvolysis of *endo,endo,endo*-tetracyclo[11.1.0.0^{3,5}.0^{7,9}]tetradecan-11-yl *p*-toluenesulfonate (**7**-OTs). The



synthesis and stereochemical assignment of the corresponding alcohol **7**-OH and its epimer epi-**7**-OH have been described earlier.[7]

Results and Discussion

Three types of evidence have been used previously to detect homoaromatic ion intermediates: rates, products, and deuterium scrambling. Rate comparisons have been of least value since formation of a delocalized intermediate will not necessarily result in an appreciably enhanced rate.[8] For example, tosylate **1** shows little rate acceleration because the conformation necessary for participation is not preferred. In the present case, **7**-OTs, the compound that is geometrically constructed to favor homoaromatic ion formation, solvolyzes approximately 15-fold faster than its epimer, epi-**7**-OTs (Table I). This rate enhancement has little meaning without considering products of the reaction.

Table I. Rates of Solvolysis in 80% Aqueous Acetone of *endo,endo,endo*- and *endo,endo,exo*-Tetracyclo[11.1.0.0^{3,5}.0^{7,9}]tetradecanyl *p*-Toluenesulfonates (**7**-OTs and epi-**7**-OTs)

Compd	Temp, °C	10^5k, sec^{-1}
7-OTs	50	1.68 + 0.03
epi-**7**-OTs	75	1.88 + 0.02

The epimer for which cyclopropyl interaction is not geometrically favorable, epi-**7**-OTs, gives a product

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(2) At Oregon State University, to whom inquiries should be addressed. NIH Postdoctoral Fellow, June 1967–Sept 1968.

(3) Deceased Nov 23, 1969.

(4) S. Winstein, *Quart. Rev., Chem. Soc.*, **23**, 141 (1969), and references therein.

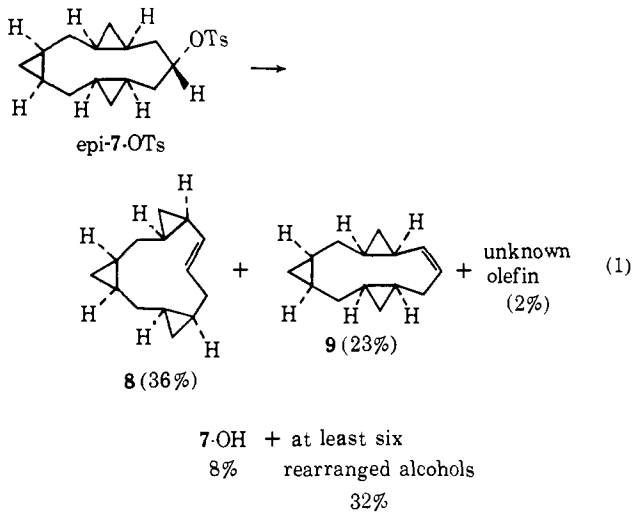
(5) S. Winstein, E. C. Friederich, R. Baker, and Y. Lin, *Tetrahedron, Suppl.*, **No. 8** (Part II), 621 (1966), and references therein.

(6) S. Winstein, P. Bruck, P. Radlick, and R. Baker, *J. Amer. Chem. Soc.*, **86**, 1867 (1964); unpublished results of P. Bruck.

(7) R. W. Thies, M. Gasic, D. Whalen, J. B. Grutzner, M. Sakai, B. Johnson, and S. Winstein, *ibid.*, **94**, 2262 (1972).

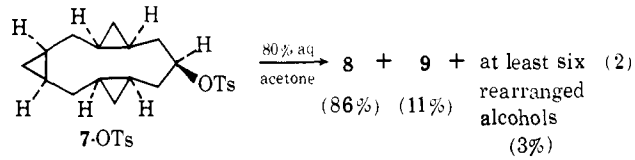
(8) A. F. Diaz and S. Winstein, *ibid.*, **91**, 4300 (1969); H. C. Brown, C. J. Kim, C. J. Lancelot, and P. v.R. Schleyer, *ibid.*, **92**, 5244 (1970).

mixture that indicates a classical ion intermediate (eq 1). Thus, elimination gives trans and cis olefins, **8** and



9, substitution results in inverted alcohol **7**-OH with no detectable (<4%) retained alcohol epi-**7**-OH, and rearrangement leads to a mixture of other alcohol products. Elimination and predominant inversion have been observed previously with most classical ions.[4,5,9] Although the structures of the other alcohols were not completely assigned, the major rearranged alcohols resulted from a combination of 1,2 or 1,5 hydride shifts and homoallylic ring expansion followed by solvent capture. The same types of products were observed with the "wrong epimers" of the analogous five- and eight-membered ring systems, epi-**1**-OTs and epi-**3**-OTs.

The products from solvolysis of **7**-OTs are somewhat surprising (eq 2).[10] The *trans*-olefin **8** is almost the



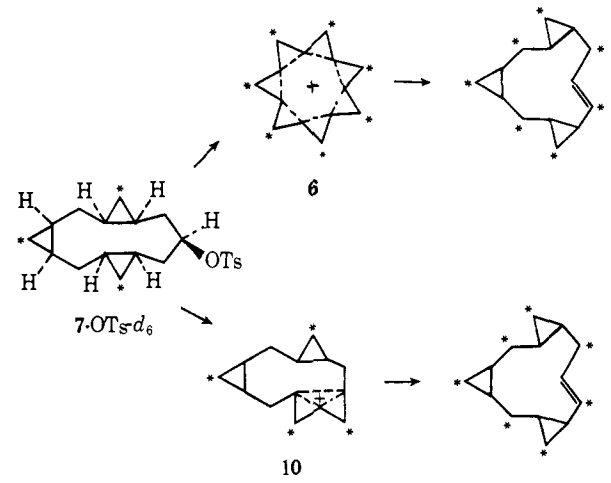
exclusive product. Neither **7**-OH nor epi-**7**-OH could be positively identified in the reaction mixture and neither could be present in greater than 1%.

The products suggest that delocalized intermediates are unimportant. To make certain that this is the case, deuterated compounds, **7**-OTs-d_6 and epi-**7**-OTs-d_6, were prepared and solvolyzed. If either tosylate solvolyzed *via* a heptahomotropylium ion (**6**), or trishomocyclopropenyl ion (**10**), deuterium scrambling would result as shown in Scheme I. *No scrambling was observed in either the olefin or alcohol products from either* **7**-*OTs-*d_6 *or epi-***7**-*OTs-*d_6. This rules out the delocalized intermediates **6** and **10**. Scrambling of deuterium *via* **6** or **10** would be detectable for the olefin products in both the vinyl and the high-field cyclopropane regions but only in the latter region for the alcohols. Delocalized intermediates such as **11**, that might result from hydride shifts, would not scramble deuterium and thus are not ruled out.

(9) H. Weiner and R. A. Sneen, *ibid.*, 87, 287 (1965); A. Streitwieser and T. D. Walsh, *Tetrahedron Lett.*, 27 (1963); S. Winstein and N. J. Holness, *J. Amer. Chem. Soc.*, 77, 5562 (1955).

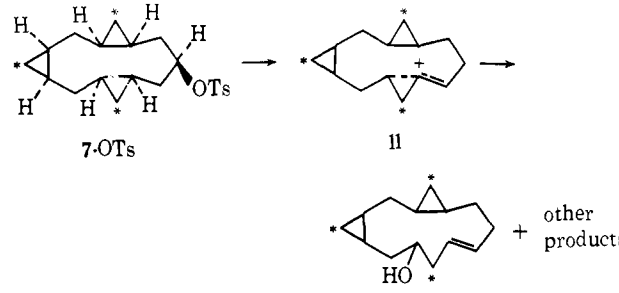
(10) Acetolysis followed by lithium aluminum hydride reduction gave a very similar product mixture to that shown.

Scheme I[a]



[a] Asterisks represent complete or partial deuteration of the position shown.

Why is a homoaromatic ion not formed? It is instructive to compare this system, **7**-OTs, with the similar system, **3**-OTs. Both systems could give trishomocyclopropenyl ions, **4** and **10**, but only **3**-OTs does so. One possible reason is that the increased ring size spreads



the angle between the developing carbonium ion and the nearest cyclopropane ring. Molecular models indicate that the more distant cyclopropane carbon is approximately 3.7 Å from the carbon bearing the tosylate for **7**-OTs compared to 3.4 Å for **3**-OTs. Thus the geometry is somewhat less favorable for cyclopropane delocalization in the present system, regardless of whether interaction by one or three cyclopropanes is to be considered.

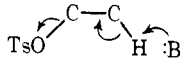
A more important factor is probably the efficiency of elimination. An almost coplanar arrangement exists between the bonds to the tosylate group and the hydrogen that must be lost to produce trans olefin. The nmr coupling constant data[7] indicate a dihedral angle of approximately 10°. Thus as the tosylate bond ionizes, orbital overlap is nearly ideal for trans olefin formation. The geometry of the eight-membered analog, **3**-OTs, is quite similar but the transition state would be a high-energy one since it would lead to an eight-membered ring compound with a trans double bond, which is highly strained. In medium-sized rings similar to **7**-OTs, syn[11] elimination to a trans olefin is particularly favorable as noted by Sicher[12] for base-catalyzed reactions and by Prelog[13] for solvolytic cases.

(11) Syn refers to the relative orientation of the tosylate and hydrogen removed.

(12) M. Svoboda, J. Zavada, and J. Sicher, *Collect. Czech. Chem. Commun.*, 1415 (1968), and references therein; J. Zavada, J. Krupicka, and J. Sicher, *Chem. Commun.*, 66 (1967).

(13) V. Prelog, *Pure Appl. Chem.*, **6**, 545 (1963), and references therein.

The exact elimination mechanism cannot be determined from the data available. Clearly the two epimers do not go through a common intermediate since the product ratios from each are quite different. The products from the wrong epimer, epi-7-OTs, implicate a classical ion pair as discussed above. The all endo isomer, 7-OTs, may also solvolyze *via* a classical ion pair where the only difference is the position of the counterion. Previous work[14] has demonstrated that the counterion position affects the products and in this case, elimination from a classical ion pair resulting from 7-OTs would require almost no rotation. In the other epimer, rotations of *ca.* 50 and 70° would be required to place the leaving hydrogen coplanar with the carbonium ion orbital. The proton eliminated could be removed by departing anion, solvent or buffer (2,6-lutidine or sodium acetate). It is also possible that the elimination is synchronous (**12** or **13**), involving solvent, buffer,



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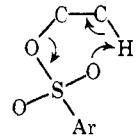

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or the tosylate itself for proton removal. The latter mechanism is apparently possible for syn elimination of cyclodecyl tosylate[15] which eliminates readily even as a solid.

To summarize, homoaromatic ions are not formed in the present case. This may be partly attributed to a slightly less favorable geometry for cyclopropyl participation and partly to the availability of a low-energy pathway leading to olefin. This does not argue against the homoaromatic theory but does indicate that generating these species in medium-sized ring systems will be difficult because of their propensity toward elimination.

Experimental Section

All melting points are uncorrected. Infrared spectra were measured on a Perkin-Elmer Model 421 instrument and nmr spectra were determined on a Varian Associates Model A-60 instrument. Microanalyses were performed by Mrs. Heather King.

endo,endo,endo-**Tetracyclo[11.1.0.0^{3,5}.0^{7,9}]tetradecan-11-yl *p*-Toluenesulfonate (7-OTs).** This material was prepared in the usual manner from the alcohol[7] and *p*-toluenesulfonyl chloride in pyridine and recrystallized from ether–pentane: mp 89.5–90.0°; ir (CS_2) 3055, 1361, 1183, 1172 cm^{-1}.

Anal. Calcd for $C_{21}H_{28}SO_3$: C, 69.96; H, 7.83. Found: C, 70.03; H, 7.84.

endo,endo,exo-**Tetracyclo[11.1.0.0^{3,5}.0^{7,9}]tetradecan-11-yl *p*-Toluenesulfonate (epi-7-OTs).** This material was prepared as above and recrystallized from ether–pentane: mp 127–128°; ir (CS_2) 3055, 1360, 1186, 1175 cm^{-1}.

Anal. Calcd for $C_{21}H_{28}SO_3$: C, 69.96; H, 7.83. Found: C, 70.19; H, 7.88.

Deuterated Tosylates 7-OTs-d_6 and epi-7-OTs-d_6. *endo,endo*-Tetracyclo[11.1.0.0^{3,5}.0^{7,9}]tetradecan-11-one (**7** ketone) was prepared by a sequence described previously[7] except that CD_2I_2, prepared as before,[5] was used in the Simmons–Smith[16] reaction. Thus, *cis,cis,cis*-3,6,9-cycloundecatrien-1-yl acetate was allowed to react with Zn–Cu couple[17] and CD_2I_2, then reduced with $LiAlH_4$, and oxidized with CrO_3. The resulting ketone-d_6 gave a parent peak at *m/e* 210 ($C_{14}H_4OD_6^+$) and no nmr signal in the τ 10–11 region (cyclopropyl).

Reduction of the deuterated **7** ketone with $NaBH_4$ in methanol at −40° as before[7] gave epi-**7**-OH-d_6 and **7**-OH-d_6 (91:9 ratio). Recrystallization from ether–pentane gave pure epi-**7**-OH-d_6; mp 98–99°. The tosylate was prepared as above; mp 96.5–97.0°.

Reduction of the deuterated **7** ketone with Al(*i*-PrO)$_3$ in isopropyl alcohol as before[7] gave 99% pure **7**-OH-d_6 which was recrystallized from ether–pentane; mp 129.5–130.5°. The tosylate was prepared as above; mp 136.0–137.0°.

Deuterated Tosylate epi-7-OTs-d_1. Reduction of **7** ketone with $NaBD_4$ in methanol at −40° followed by recrystallization as above gave epi-**7**-OTs-d_1; mp 94.5–95.5°. The mass spectrum gave a parent peak at *m/e* 207 ($C_{14}H_{21}OD^+$) and no nmr signal in the τ 5.2 region. The tosylate was prepared as above; mp 95.0–96.5°.

Solvolysis Kinetics. Aqueous acetone (80%) was prepared by mixing 1 vol of conductivity water and 4 vol of reagent acetone at 25°. Rates were followed by the ampoule method described previously[18] except that 2-ml aliquots were titrated to brom thymol blue endpoint with 0.0104 *M* aqueous sodium hydroxide. In all cases, the experimental infinity titers were within 5% of the theoretical values.

Product Studies. Solvolyses were run to 10 half-lives in either 80% aqueous acetone (0.05 *M* ROTS and 0.055 *M* 2,6-lutidine) or in anhydrous acetic acid (0.011 *M* ROTS and 0.015 *M* NaOAc). The products were analyzed on $^1/_8$ in. × 10 ft 2.5% KOH–2.5% Carbowax 4000 on Chromosorb W or 0.01 in. × 50 ft capillary DEGS glc column and were separated on a $^1/_4$ in. × 2 m 10% DEGS on Chromosorb W column.

Olefin Products, 8 and 9. Hydroborations[19] (see below) of either **8** or **9** gave a mixture of **7**-OH and epi-**7**-OH which elucidates their structure except for the stereochemistry of the double bond. The double bond stereochemistry was assigned from the infrared spectra. It has been noted previously[20] that medium-sized ring olefins show a strong band at *ca.* 960 cm^{-1} for the trans isomers whereas the cis isomers absorb in the 700-cm^{-1} region. This has been substantiated in the laboratories of two of the authors (S. W. and R. W. T.) for at least ten different systems.[21] The major olefin **8** was clearly the trans isomer (968 cm^{-1}). Olefin **9** could not be isolated in a pure state but was clearly the cis isomer (ir, neat, 695 cm^{-1}).

Olefin 8 showed the following characteristics: ir (CS_2) 3045, 968 cm^{-1}; nmr (CS_2) 4.5 (m,2), 7–10 (m, 17), 10.4 (m, 1)

Anal. Calcd for $C_{14}H_{20}$: C, 89.29; H, 10.71. Found: C, 89.33; H, 10.80.

Hydroboration[19] of Olefins 8 and 9. A mixture of 5 mg of $NaBH_4$, 40 ml of diglyme, and 10 mg of olefins was stirred at −10° as 10 ml of BF_3–etherate was added over 10 min. After 1 hr, 10 ml of water was added, followed by 10 ml each of 3 *N* sodium hydroxide and 30% hydrogen peroxide, and the reaction mixture was stirred 1 hr at 30°. The mixture was extracted into ether solution which was washed with water and dried. This gave only two alcohols, **7**-OH and epi-**7**-OH, in 90% yield. The ratio varied with the amount of cis isomer **9** in the mixture (see Table II).

Table II

Olefin ratio **8**:**9**	Alcohol ratio **7**-OH:epi-**7**-OH
99:1	77:23
87:13	69:31
75:25	60:40
Calcd for pure **8**	79:21
Calcd for pure **9**	2:98

(14) P. S. Skell and W. L. Hall, *J. Amer. Chem. Soc.*, **85**, 2851 (1963); S. Winstein and M. Cocivera, *ibid.*, **85**, 1702 (1963); D. J. Cram and M. R. V. Sahyun, *ibid.*, **85**, 1257 (1963).

(15) V. Prelog, W. Kueng, and T. Tomljenovic, *Helv. Chim. Acta*, **45**, 1352 (1962).

(16) H. E. Simmons, E. P. Blanchard, and R. D. Smith, *J. Amer. Chem. Soc.*, **86**, 1347 (1964), and references therein.

(17) E. LeGoff, *J. Org. Chem.*, **29**, 2048 (1964).

(18) S. Winstein, E. Grunwald, and L. Ingraham, *J. Amer. Chem. Soc.*, 70, 821 (1948).

(19) G. Zweifel and H. C. Brown, *Org. React.*, **13**, 1 (1963).

(20) A. T. Bloomquist, L. H. Liu, and J. C. Bohrer, *J. Amer. Chem. Soc.*, **74**, 3643 (1952).

(21) (a) M. Gasić, D. Whalen, B. Johnson, and S. Winstein, *ibid.*, **89**, 6383 (1967); (b) C. D. Poulter, E. C. Friedrich, and S. Winstein, *ibid.*, **92**, 4274, 4282 (1970); (c) unpublished results of M. Gasić and D. Whalen; (d) unpublished results of R. W. Thies and J. Billigmeier.

Alcohol Products. Alcohol epi-7-OH was identified by spectral comparison. The other alcohol products show very complex spectra that only allow partial assignment of structure, *viz.*, the two major alcohol products, A and B, both contain two cyclopropane rings and one trans double bond: unknown alcohol A, ir (CS_2) 3590, 3300, 960 cm^{-1}; nmr (CS_2, τ) 4.4 (m, 2), 6.4 (m, 1), 7.5–9.6 (m, 17), 9.7–10.5 (m, 2); ketone corresponding to A, ir (CS_2) 3060, 1717, 970 cm^{-1}; unknown alcohol B, ir (CS_2) 3600, 3400, 3050, 965 cm^{-1}; nmr (CS_2, τ) 4.5 (m, 2), 6.3 (m, 1), 7.5–9.8 (m, 18), 10.15 (m, 1); ketone corresponding to B, 3057, 1710, 965 cm^{-1}.

The Vinyl Anion[1]

H. M. Walborsky* and L. M. Turner

Contribution from the Department of Chemistry, Florida State University, Tallahassee, Florida 32306. *Received September 2, 1970*

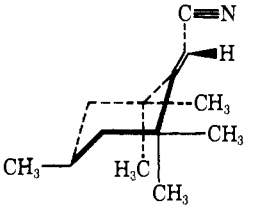
Abstract: The chiral molecule, 2,2,4,6,6-pentamethylcyclohexylideneacetonitrile (**1**), was synthesized in order to study the stereochemistry of the vinyl anion in protonic solvents. At 90° the vinyl anion exhibits a very high degree of retention of configuration (>99%) in methanol using sodium methoxide as the base, $k_e/k_r = 140$. Evidence is provided to show that the proton is abstracted directly from the vinyl carbon rather than being exchanged by an addition–elimination mechanism. A small kinetic isotope effect ($k_H/k_D \approx 2$) is observed. It is suggested that in neither the exchange nor the racemization of **1** is proton abstraction rate determining.

Recently there have been reports from this laboratory on the stereochemical fate of the cyclopropyl anion.[2,3] It was found that the 1-cyano-2,2-diphenylcyclopropyl anion, generated by sodium methoxide in methanol, was capable of maintaining its configuration. On the other hand, the anion derived from the optically active acyclic analog, 2-methyl-3,3-diphenylpropionitrile, was totally racemized under the same conditions. A number of factors influence the energy barrier for the racemization of carbanions including, among others, (1) the initial hybridization of the central carbon atom and (2) constraint in a small ring (I strain).[4] In order for these factors to be evaluated (cyclopropyl *vs.* vinyl) information was needed on a corresponding vinyl system. This article presents the data obtained on the stereochemical fate of the anion derived from 2,2,4,6,6-pentamethylcyclohexylideneacetonitrile.

Results and Discussion

Studies have been made on the configurational stability of vinyl anions by Miller[5] and by Cram.[6] The systems used and the results of those investigations are insufficient for present purposes since a number of complicating factors are involved: (1) *cis–trans* energy differences with its concomitant driving force for isomerization; (2) the competing addition–elimination mechanism or thermal isomerization; (3) delocalization energy differences due to different substituents attached to the carbanion site.

In order to study the vinyl anion a suitable system had to be chosen. There were several necessary qualities for the molecule to possess. Obviously it had to have a double bond with at least one vinyl hydrogen. Second, a suitable molecule would need an acidifying substituent on the double bond to make the olefinic proton more readily removable. Third, there should be no allylic hydrogens in the system so that rearrangements would be avoided. Furthermore, it was desirable to have the β-carbon of the double bond as sterically hindered as possible so that the addition–elimination mechanism (*vide infra*) could be avoided. Lastly, a chiral molecule would be useful since the rate of isomerization could be measured directly by measuring the rate of racemization and, moreover, it would obviate the problem of cis–trans energy differences with its resulting chemical potential difference. A molecule which meets all those requirements is 2,2,4,6,6-pentamethylcyclohexylideneacetonitrile (**1**).



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It is readily seen that the molecule is chiral, possesses a double bond with no allylic hydrogens, and that it has an acidified vinyl hydrogen. Furthermore, it is certainly sterically hindered since it is analogous to a dineopentyl-substituted olefin. The nitrile group was chosen as the acidifying substituent because nitrile substitution increases the kinetic acidity of the carbon–hydrogen bond and also it permits a comparison with our previous studies on the cyclopropylnitrile.[2]

Syntheses. The synthesis of 2,2,4,6,6-pentamethylcyclohexylideneacetonitrile (**1**) was attempted by several different routes, all of which used 2,2,4,6,6-pentamethylcyclohexanone (**2**) as the starting point. Pentamethyl ketone **2** was obtained by a sodium hydride–methyl iodide alkylation of the commercially available

(1) The support of this work by grants from the National Science Foundation and the Public Health Service, Grant No. 04065 from the National Cancer Institute, is gratefully acknowledged.

(2) H. M. Walborsky and J. M. Motes, *J. Amer. Chem. Soc.*, **92**, 2445 (1970).

(3) J. M. Motes and H. M. Walborsky, *ibid.*, **92**, 3697 (1970).

(4) H. C. Brown, *et al.*, *ibid.*, 73, 212 (1951); H. C. Brown and M. Borkowsky, *ibid.*, **74**, 1894 (1952).

(5) S. I. Miller and W. G. Lee, *ibid.*, **81**, 6316 (1959).

(6) D. H. Hunter and D. J. Cram *ibid.*, **86**, 5478 (1964).