Synthesis and Solvolysis of Derivatives of 7-Methyl-7-hydroxynorbornane and the Epimeric 7-Methyl-7-hydroxynorbornenes

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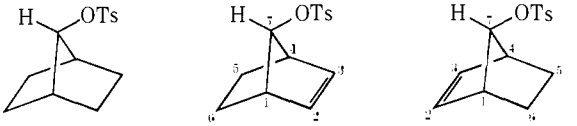
Abstract: The rates of solvolysis of derivatives of 7-methyl-7-hydroxynorbornane (I), *anti*-7-methyl-*syn*-7-hydroxynorbornene (II), and *syn*-7-methyl-*anti*-7-hydroxynorbornene (III) were determined. In addition, the corresponding values for the trideuteriomethyl analogs were measured. The methyl/hydrogen rate ratio was found to vary from 1.3×10^8 for the saturated system (I) to 4.4×10^1 for the *anti*-*p*-nitrobenzoates in the unsaturated cases (III). The methyl/hydrogen rate ratio for the *syn*-*p*-toluenesulfonates (II) was found to be intermediate with a value of 3.0×10^5. Methyl/trideuteriomethyl rate ratios were found to be: I = 1.88 ± 0.03 at 60°, II = 1.23 ± 0.03 at 60°, and III = 0.96 ± 0.03 at 135°. Products were determined in all cases. The presence of the trideuteriomethyl group was found to have a significant effect on product ratios in the case of I.

The role of methyl substitution in the stabilization of positively charged carbon has been the topic of numerous discussions. Streitwieser[1] estimated "the minimum stabilization of a tertiary carbonium ion relative to a secondary in a limiting solvolysis" to be 10^6. Brown and coworkers have suggested[2] that methyl/hydrogen rate ratios for simple aliphatic systems (tertiary cations *vs.* secondary cations) should be about 5.5×10^4. This concept has also been discussed by Tanida[3] and Schleyer,[4] who suggested that in a limiting solvolysis the methyl/hydrogen rate ratios for tertiary *vs.* secondary systems should be of the order of 10^8. In view of our extensive interest in 7-norbornyl and 7-norbornenyl cations,[5] we have carried out a systematic study of the effect of methyl substitution in the 7 position on the solvolytic behavior of derivatives of 7-hydroxynorbornane and the epimeric 7-hydroxynorbornenes. Recent reports of related work from Sunko's[6] and Winstein's[7] laboratories prompts us to report the full details of our investigation at this time.

Among the most quoted cases of neighboring group participation by nonallylic double bonds are those associated with the solvolyses of the *syn*- and *anti*-7-norbornenyl tosylates. When compared to 7-norbornyl tosylates (**1**),[8] *syn*-7-norbornenyl tosylate (**2**) solvolyzes[9] at a relative rate of 10^4, while *anti*-7-norbornenyl tosylate (**3**) undergoes acetolysis[8] at a relative rate of 10^{11}. The rate acceleration noted for **2** was



	1	2	3
k_{rel}	1	10^4	10^{11}

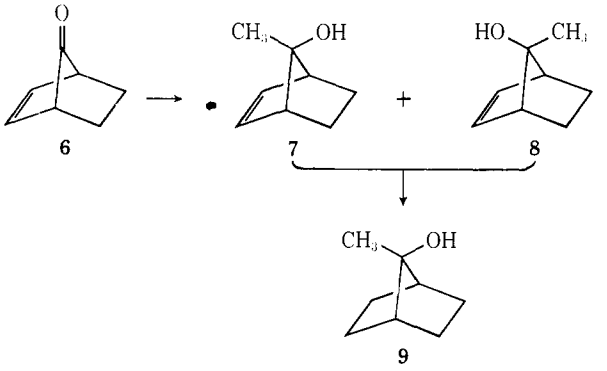
attributed[9] to participation of the C_1–C_6 bonding electrons to yield directly the allylic cation **4**. The much larger acceleration noted for **3** relative to **1** has been attributed[8] to formation of the highly delocalized symmetrical cation **5**. This latter hypothesis has been substantiated solvolytically by Gassman and Patton,[5] and more recently by nmr spectroscopic measurements on the 7-norbornenyl cation.[10] In order to obtain a more detailed insight into the mechanistic details of the formation of these ions, we decided to synthesize and solvolyze the appropriate 7-methylated derivatives.

4 5

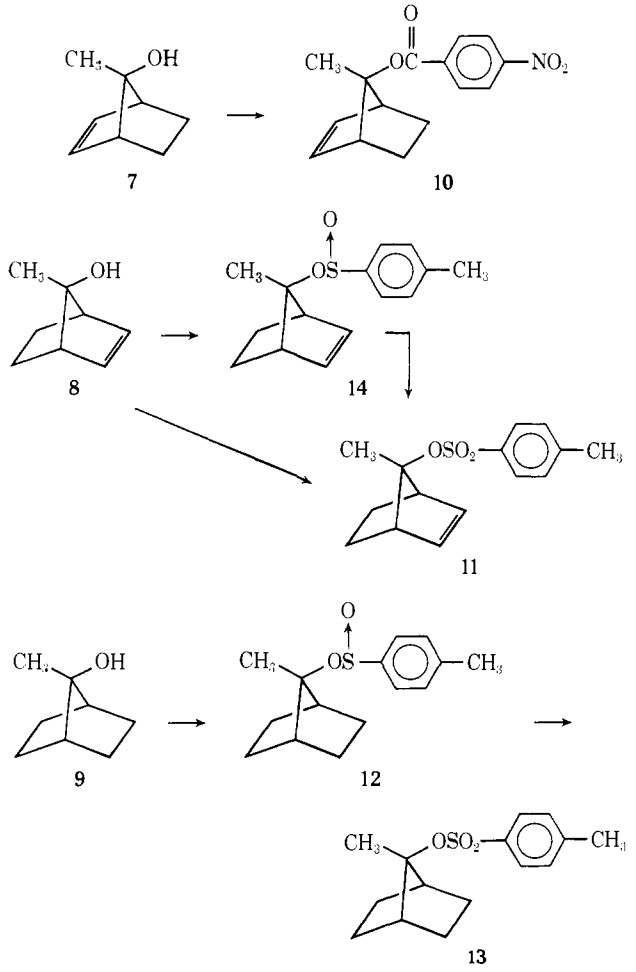
Synthesis

Starting with norbornen-7-one (**6**),[11] we prepared a mixture of **7** and **8** *via* the addition of methyllithium as reported by Erman.[12] Reduction of the mixture over palladium on carbon gave the saturated tertiary alcohol, **9**. In view of the anticipated extreme reactivity of the tosylate of **7**, no attempt was made to prepare this derivative. Instead, **7** was converted into the corresponding *p*-nitrobenzoate ester **10**, in order to have a derivative suitable for solvolytic purposes. The epimeric alcohol, **8**, could be converted into the corresponding tosylate, **11**, *via* reaction with *p*-toluene-

(1) A. Streitwieser, Jr., "Solvolytic Displacement Reactions," McGraw-Hill, New York, N. Y., 1962, p 72.
(2) H. C. Brown, F. J. Chloupek, and M.-H. Rei, *J. Amer. Chem. Soc.*, **86**, 1246, 1247, 1248 (1964); H. C. Brown and M.-H. Rei, *ibid.*, **86**, 5004, 5008 (1964); H. C. Brown and H. M. Bell, *ibid.*, **86**, 5006 (1964).
(3) H. Tanida, Y. Hata, S. Ikegami, and H. Ishitobi, *ibid.*, **89**, 2928 (1967).
(4) J. L. Fry, J. M. Harris, R. C. Bingham, and P. v. R. Schleyer, *ibid.*, **92**, 2540 (1970).
(5) P. G. Gassman and J. L. Marshall, *ibid.*, **88**, 2599 (1966); (b) P. G. Gassman and J. M. Hornback, *ibid.*, **89**, 2487 (1967); (c) P. G. Gassman, J. M. Hornback, and J. L. Marshall, *ibid.*, **90**, 6238 (1968); (d) P. G. Gassman and A. F. Fentiman, *ibid.*, **91**, 1545 (1969); (e) P. G. Gassman and D. S. Patton, *ibid.*, **91**, 2160 (1969); (f) P. G. Gassman, J. L. Marshall, and J. M. Hornback, *ibid.*, **91**, 5811 (1969); (g) P. G. Gassman and J. M. Hornback, *ibid.*, **91**, 5817 (1969); (h) P. G. Gassman and A. F. Fentiman, *ibid.*, **92**, 2549 (1970).
(6) D. E. Sunko, I. Szele, and M. Tomić, *Tetrahedron Lett.*, 1827 (1972); D. E. Sunko and I. Szele, *ibid.*, 3617 (1972).
(7) R. K. Lustgarten, J. Lhomme, and S. Winstein, *J. Org. Chem.*, **37**, 1075 (1972).
(8) S. Winstein, M. Shatavsky, C. Norton, and R. B. Woodward, *J. Amer. Chem. Soc.*, **77**, 4183 (1955); S. Winstein and M. Shatavsky, *ibid.*, **78**, 592 (1956).
(9) S. Winstein and E. T. Stafford, *ibid.*, **79**, 505 (1957).
(10) R. L. Lustgarten, M. Brookhart, S. Winstein, P. G. Gassman, D. S. Patton, H. G. Richey, Jr., and J. D. Nichols, *Tetrahedron Lett.*, 1699 (1970).
(11) P. G. Gassman and J. L. Marshall, *Org. Syn.*, **48**, 25 (1968).
(12) W. F. Erman, *J. Org. Chem.*, **32**, 765 (1967).



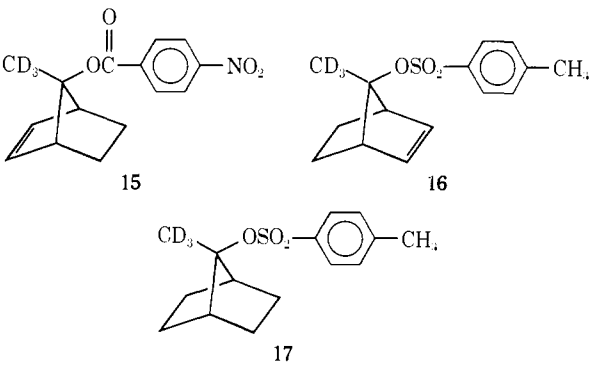
sulfonyl chloride in pyridine for 2 weeks at room temperature. Formation of the tosylate of **9** was accomplished according to the method of Coates and Chen.[13] This involved the use of *p*-toluenesulfinyl chloride to prepare the *p*-toluenesulfinate, **12**, followed by oxidation with *m*-chloroperbenzoic acid to produce the known[3] tosylate **13**. This method proved so superior that it



was then evaluated for the formation of **11** *via* **14**. It was found that **14** could be oxidized to **11** with *m*-chloroperbenzoic acid with no adverse epoxidation of the double bond. Hence, the preferred method for the formation of **11** was also by way of the Coates–Chen procedure.

The corresponding 7-trideuteriomethyl compounds **15**, **16**, and **17** were prepared from **6** and trideuteriomethyllithium according to the methods outlined above.

(13) R. M. Coates and J. P. Chen, *Tetrahedron Lett.*, 2705 (1969).



Solvolytic Studies

Table I lists the rates of solvolysis of **10**, **11**, and **13**.

Table I. Rates of Solvolysis of 7-Norbornyl Esters[a]

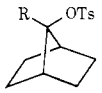
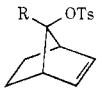
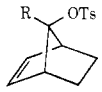
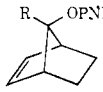
Compd	Temp, ±0.02°C	Rate, sec^{-1}	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, eu
19	190.0	$(2.63 \pm 0.03) \times 10^{-4}$	27.7	−15.9
	175.0	$(1.04 \pm 0.01) \times 10^{-4}$		
	160.0	$(3.03 \pm 0.03) \times 10^{-5}$		
	145.0	$(9.74 \pm 0.01) \times 10^{-6}$		
	(135.0)[b]	4.15×10^{-6}		
	(25.0)[b]	1.01×10^{-11}		
10	135.0	$(4.13 \pm 0.03) \times 10^{-4}$	29.4	−2.4
	130.0	$(2.52 \pm 0.05) \times 10^{-4}$		
	120.0	$(1.13 \pm 0.02) \times 10^{-4}$		
	110.0	$(3.51 \times 0.03) \times 10^{-5}$		
	(25.0)[b]	4.44×10^{-10}		
	(25.0)[b,c]	2.38×10^{-9}		
13	75.0	$(1.72 \pm 0.01) \times 10^{-3}$	25.8	2.8
	60.0	$(3.11 \pm 0.02) \times 10^{-4}$		
	45.0	$(4.63 \pm 0.02) \times 10^{-5}$		
	(25.0)[b]	2.81×10^{-6}		
	(25.0)[b,c]	3.36×10^{-6}		
11	70.0	$(1.94 \pm 0.01) \times 10^{-3}$	24.3	−0.2
	55.0	$(3.62 \pm 0.01) \times 10^{-4}$		
	40.0	$(5.78 \pm 0.01) \times 10^{-5}$		
	(25.0)[b]	7.69×10^{-6}		
18	(25.0)[d]	1.62×10^{-2}		
	(25.0)[e]	2.80		

[a] Tosylates (**11** and **13**) were solvolyzed in 0.01–0.02 *M* solutions of anhydrous acetic acid buffered with sodium acetate. *p*-Nitrobenzoates (**10** and **19**) were solvolyzed in 30:70 v/v water–dioxane. [b] Extrapolated from higher temperatures. [c] Reference 7. [d] Extrapolated from the rate of solvolysis of **10**, utilizing the tosylate/*p*-nitrobenzoate ratio obtained from the secondary systems *anti*-7-tosyloxynorbornene (**3**) and the *p*-nitrobenzoate, **19** (3.66×10^{7}). [e] Extrapolated from the rate of solvolysis of **10**, utilizing the tosylate/*p*-nitrobenzoate rate ratio of 6.3×10^{9} observed for *syn*-7-aryl-*anti*-7-norbornenyl esters by Gassman and Fentiman (ref 5h).

Also included in this table are the calculated rate for *syn*-7-methyl-*anti*-7-tosyloxynorbornene (**18**) and the measured rate of solvolysis of the *anti*-7-*p*-nitrobenzoate **19**. Table II lists the relative rates of solvolysis and the methyl/hydrogen rate ratios for the 7-norbornyl

and 7-norbornenyl ring systems. Examination of Table II shows that the conversion from a secondary to **a** tertiary center at the 7 position of the norbornyl system tends to decrease the amount of participation provided

Table II. Relative Rates of Solvolysis and α-CH_3/H Rate Ratios for 7-Substituted Norbornyl Compounds at 25°

System	$k_{R=H}$, sec^{-1}	k_{rel}	$k_{R=CH_3}$, sec^{-1}	k_{rel}	k_{CH_3}/k_H
 20	2.1×10^{-14} [a]	1	2.81×10^{-6}	1	1.3×10^{8}
 21	2.6×10^{-11} [b]	1.2×10^{3}	7.69×10^{-6}	2.74	3.0×10^{5}
 22	3.7×10^{-4} [c]	1.8×10^{10}	2.80×10^{0}	1.00×10^{6}	7.6×10^{3}
 23	1.01×10^{-11} 4.15×10^{-6} [d]		4.44×10^{-10} 4.13×10^{-4} [d]		4.4×10^{1} 1.0×10^{2} [d]

[a] Calculated from the rate of the corresponding brosylate[3] at 25°, assuming a brosylate:tosylate ratio of 2.90; ref 7. [b] Reference 9. [c] Reference 8. [d] Comparison made at 135° rather than at 25°.

by the syn and anti double bond. Alternatively, this could be viewed in terms of the effectiveness of the syn and anti double bonds in "leveling" the ability of a methyl group to stabilize a cation. This "leveling effect"[5h] of the double bond resulted in a factor of 4.4×10^2 in the case of 7-*syn*-tosyloxynorbornene and in a factor of 1.8×10^4 for the 7-*anti*-tosyloxynorbornenyl system (in the case of the 7-*anti*-*p*-nitrobenzoates this factor can be estimated at 3×10^6). These observations again illustrate the concept that the degree of stabilization provided to a cationic center is a function of the electron demand (stability) of that incipient carbonium ion center.[5h]

The methyl/hydrogen rate ratios for the series **20**, **21**, and **22** represent an interesting comparison. For **20**, this ratio is close to that postulated as the theoretical maximum.[3,4,14] It would appear that the highly strained nature of the 7-cation in the norbornyl system extracts the maximum possible stabilization from the added methyl group in the absence of the stabilizing influence of a double bond. The methyl/hydrogen rate ratio for **21**, although large, is considerably less than the theoretical maximum. Since the C_1–C_7–C_4 bond angles in the norbornyl and norbornenyl systems vary very little,[15] it is anticipated that, in the absence of any form of neighboring group assistance, the demand for stabilization by the incipient cation from the added methyl group should be the same in **20**, **21**, and **22**. The decreased methyl/hydrogen rate ratio in **21**, as compared to **20**, indicates that some residual neighboring group participation must exist in **21**. The concept is supported by the faster rate of solvolysis of **11** as compared to **13**, in spite of the electron-withdrawing effect of the homoallylic double bond.[16]

The methyl/hydrogen rate ratio for **22** was the hardest to evaluate because of the extrapolations involved. Using the value of 3.7×10^{-4} sec^{-1} for the rate of **3** at 25° and 2.8 sec^{-1} for the rate[17] of **18** at 25°, we obtained a ratio of 7.6×10^3. For the corresponding *p*-nitrobenzoate derivatives, **23**, we obtained a methyl/hydrogen rate ratio of 44 at 25° and 100 at 135°. The value at 25° can be compared to a value of 400 at 25° reported recently[7,18] for *p*-nitrobenzoates and 240 at 25° for solvolysis of the corresponding chlorides.[7] It is interesting to note that the methyl/hydrogen rate ratio appears to increase in going from *p*-nitrobenzoates (44) to chlorides (240) to tosylates (7600). Whether this apparent trend is a function of the leaving group and/or of the different solvent systems used for the different solvolyses is difficult to evaluate at this time.

In order to gain a greater insight into the effect of methyl substitution at an incipient cationic center, we also studied the rates of solvolysis of the trideuterated compounds **15**, **16**, and **17**. Table III lists the rates of solvolysis of these compounds and of the corresponding nondeuterated compounds. All rates were determined titrimetrically and are the average of five determinations. The deuterium isotope effect of the trideuteriomethyl group of **20** was 1.88 ± 0.03. This is the largest such effect of which we are aware for a tosylate solvolysis in anhydrous acetic acid. It is considerably larger than the value of 1.41 reported by Schleyer and coworkers for the CH_3/CD_3 rate ratio of the 2-methyl-

(14) Our value of 1.3×10^5 compares quite well with the previously reported[3,7] value of 1.6×10^5.

(15) For leading references, see A. Yokozeki and K. Kuchitsu, *Bull. Chem. Soc. Jap.*, **44**, 2356 (1971); J. F. Chiang, C. F. Wilcox, Jr., and S. H. Bauer, *J. Amer. Chem. Soc.*, **90**, 3149 (1968); G. Dallinga and L. H. Tonman, *Recl. Trav. Chim. Pays-Bas*, **87**, 795, 805 (1968); T. P. DeLacy and C. H. L. Kennard, *J. Chem. Soc., Perkin Trans. 2*, 2153 (1972), and references therein.

(16) For a discussion of the inductive effect of a homoallylic double bond, see M. Hanack and K. Keberle, *Ber.*, **96**, 2937 (1963); M. Hanack and H.-J. Schneider, *Angew. Chem., Int. Ed. Engl.*, **6**, 666 (1967); C. F. Wilcox, Jr., and H. D. Banks, *J. Amer. Chem. Soc.*, **94**, 8231 (1972); P. D. Bartlett and M. R. Rice, *J. Org. Chem.*, **28**, 3351 (1963).

(17) The value of 2.8 sec^{-1} for **18** was used on the assumption that the rate comparison of two tertiary systems would be more reliable than the comparison of a secondary and a tertiary system (see footnotes *d* and *e* of Table I). If the rate calculated from the secondary–tertiary rate comparison (footnote *d*) is used, the methyl/hydrogen rate ratio for **22** becomes 4.4×10^1. As a result of the method of calculation, this ratio must be the same as the corresponding ratio for **23** at 25°.

(18) The factor of 9 which differentiates our value at 25° from that of Winstein and coworkers[7] is probably a result of the large temperature range over which the rates were extrapolated. Comparison at a higher temperature, where very little extrapolation was required, showed very little difference between our methyl/hydrogen rate ratio (100 at 135°) and that of Winstein and coworkers[7] (88 at 135°).

Table III. Rates of Solvolysis of 7-Methyl- and 7-Trideuteriomethyl-7-norbornyl Esters

Compd	Temp, ±0.01 °C	k_{CH_3}, 10^4 sec^{-1}	k_{CD_3}, 10^4 sec^{-1}	k_{CH_3}/k_{CD_3}
20[a]	60.0	3.108 ± 0.025	1.652 ± 0.025	1.88 ± 0.03
21[a]	60.0	6.45 ± 0.03	5.25 ± 0.02	1.23 ± 0.03
23[b]	135.0	4.13 ± 0.03	4.28 ± 0.02	0.96 ± 0.03

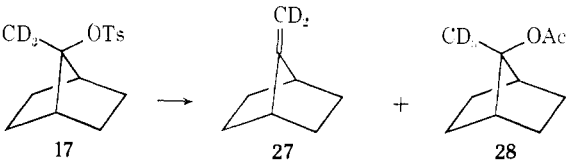
[a] Rates measured in anhydrous acetic acid buffered with sodium acetate. [b] Rates measured in 30:70 v/v water–dioxane.

2-bromoadamantanes,[19] a case which has been discussed in terms of "limiting" solvolyses. Our value agrees well with the value of 1.86 reported[6] by Sunko, Szele, and Tomić for the solvolysis of **20** in 80% ethanol. The sensitivity of these isotope effects to solvent has been clearly demonstrated by the observation[6] of CH_3/CD_3 isotope effects for **20** of 2.33, 2.27, 2.22, and 2.10 in 97% 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP), 80% HFIP, 70% HFIP, and 97% 2,2,2-trifluoroethanol, respectively.

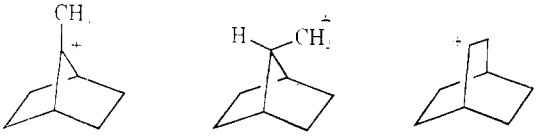
For the acetolysis of **21**, a substantial, but not uncommon, CH_3/CD_3 isotope effect was noted. This correlated well with the typical α-CH_3/H rate ratio noted for this system. The CH_3/CD_3 isotope effect noted for the hydrolysis of **23** was somewhat unexpected. This inverse isotope effect was consistent with a small difference between the inductive effects of the methyl and trideuteriomethyl groups.[20]

Product Studies

The acetolysis of **13** gave 61% of 7-methylenenorbornane (**24**) and 25% of 7-acetoxy-7-methylnorbornane (**25**). The products were identified by comparison with authentic samples. Reaction of 7-ketonorbornane (**26**)[21] with the ylide formed from methyltriphenylphosphonium bromide and dimsyl anion[22,23] gave **24**, while acetylation of **9** with acetyl chloride in pyridine produced **25**. Similar solvolysis of **17** gave a 43% yield of **17** and a 41% yield of **28**. The significant amount of olefin formed in the solvolysis of **13** coupled with the large decrease in olefin formation in going to **17** was consistent with the large methyl/hydrogen and methyl/trideuteriomethyl rate ratios observed for **20**.



All three factors indicate that the incipient cation is deriving fairly massive stabilization from the methyl group, presumably *via* a hyperconjugative interaction of the β hydrogens (deuteriums) with the incipient cation. With the trideuteriomethyl group this hyperconjugative stabilization should be less, due to the increased strength of the C–D bond as compared to the C–H bond. Thus, a large isotope effect would be expected for the product ratio in view of the large rate effect.[24] From the substantial percentage of olefin formed from both **13** and **17**, it could be argued that both the product composition and the methyl/hydrogen and methyl/trideuteriomethyl rate ratios were a reflection of hydrogen participation by the methyl hydrogens.[25] Such hydrogen participation, as contrasted with a hyperconjugative interaction, involves hydrogen migration to the incipient cationic center. This generally requires that the new cationic center, which results from the hydrogen shift, be either comparable in stability or more stable than the ion resulting if no hydrogen participation were to occur. In our case, this would require a comparison of the tertiary carbocation **29** with the primary system **30**. It appears unlikely that **29** would be less stable than **30**. If **30** were formed, we should have been able to detect products derived from it, or from the ion **31** which would result from ring expansion of **30**.[28] In fact, we were unable



to detect any products which might have been derived from either **30** or **31**. Thus, we feel that our observation should not be interpreted in terms of "hydrogen participation." An alternate possibility, which we have not been able to rule out on the basis of our experimental data, is whether **27** is formed by a concerted elimination of *p*-toluenesulfonic acid in the rate-determining step (or by some other elimination mechanism which involves considerable C–H(D) bond breaking in the rate-determining step). The incursion of such an elimination would result in a contribution to the overall isotope effect which would make it appear abnormally large.

Product analysis of the solvolysis of **10** and **15** gave only the starting alcohols **7** and **32** in 91 and 100%

(19) J. L. Fry and P. v. R. Schleyer, Abstracts, 157th National Meeting of the American Chemical Society, Minneapolis, Minn., April 1969, ORGN-133.

(20) For excellent discussions of deuterium isotope effects, see V. J. Shiner, Jr., in "Isotope Effects in Chemical Reactions," A. C. S. Monograph Series No. 167, C. J. Collins and N. S. Bowman, Ed., 1970, pp 90–159; and D. E. Sunko and S. Borcic, *ibid.*, pp 160–212.

(21) P. G. Gassman and P. G. Pape, *J. Org. Chem.*, **29**, 160 (1964).

(22) R. Greenwald, M. Chaykovsky, and E. J. Corey, *ibid.*, 28, 1128 (1963).

(23) A. Maercher, *Org. React.*, 14, 270 (1965).

(24) Again, our results parallel those of Sunko and coworkers[6] who found a significant change in the product ratio from 13 and 17 on solvolysis in 97% 2,2,2-trifluoroethanol.

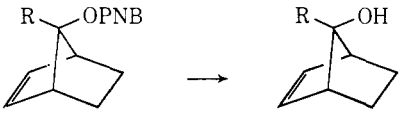
(25) Examples of β-hydrogen participation have been well established in the literature.[26,27] β-Hydrogen/deuterium isotope effects in excess of 2.0 have been observed in these reactions.

(26) V. J. Shiner, Jr., and J. G. Jewett, *J. Amer. Chem. Soc.*, **87**, 1382 (1965).

(27) S. Winstein and J. Takahashi, *Tetrahedron*, **2**, 316 (1958).

(28) J. A. Berson, D. S. Donald, and W. J. Libbey, *J. Amer. Chem. Soc.*, **91**, 5580 (1969).

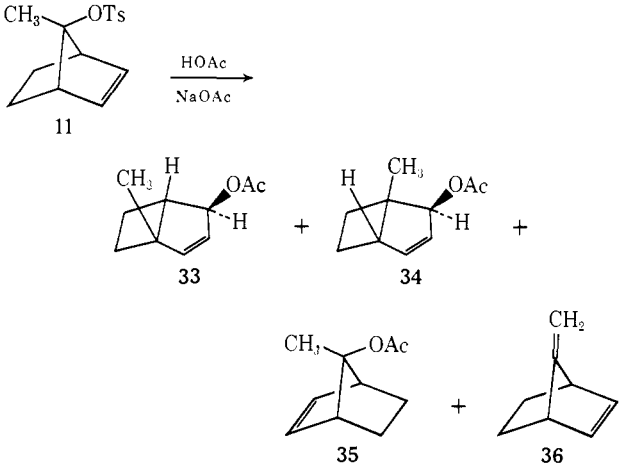
yields, respectively. This was consistent with the relatively small methyl/hydrogen rate ratio and with a negative deuterium isotope effect for the solvolysis of **10**



10, R = CH_3 **7**, R = CH_3
15, R = CD_3 **32**, R = CD_3

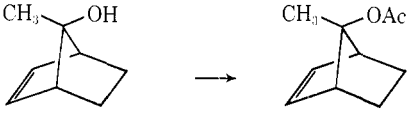
compared to **15**. This indicated that the neighboring group participation of the anti double bond was the overwhelming factor in the solvolysis of both **10** and **15**. Thus, both **10** and **15** appear to solvolyze with relatively little hyperconjugative stabilization of the incipient cationic center by the 7-methyl group.

In both methyl/hydrogen and methyl/trideuteriomethyl rate ratios, the syn system, **21**, was intermediate between **20** and **23** (or **22**). This suggested that the product study might also produce results that cannot be interpreted as easily as either of the extreme cases, **20** and **23**. In confirmation of our expectations, acetolysis of **11** gave 48% of *exo*-4-acetoxy-1-methylbicyclo-



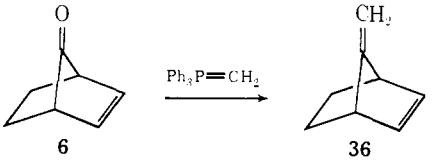
11 **33** **34** **35** **36**

[3.2.0]hept-2-ene (**33**), 13% of *exo*-4-acetoxy-5-methylbicyclo[3.2.0]hept-2-ene (**34**), 27% of 7-*anti*-acetoxy-7-*syn*-methylbicyclo[2.2.1]hept-2-ene (**35**), and 3% of 7-methylenenorbornene (**36**). All of the products were



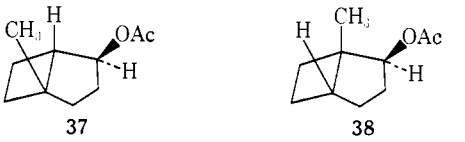
7 **35**

identified either through comparison with authentic samples or through comparison of their reduction products with authentic samples. The acetate, **35**, was prepared by acetylation of **7** with acetyl chloride in pyridine. The Wittig reaction of triphenylphosphonium methylide with 7-ketonorbornene[11] (**6**) gave **36**. The identification of **33** and **34** proved to be a much more formidable task. Although the nmr and ir spectra of **33** and **34**



6 **36**

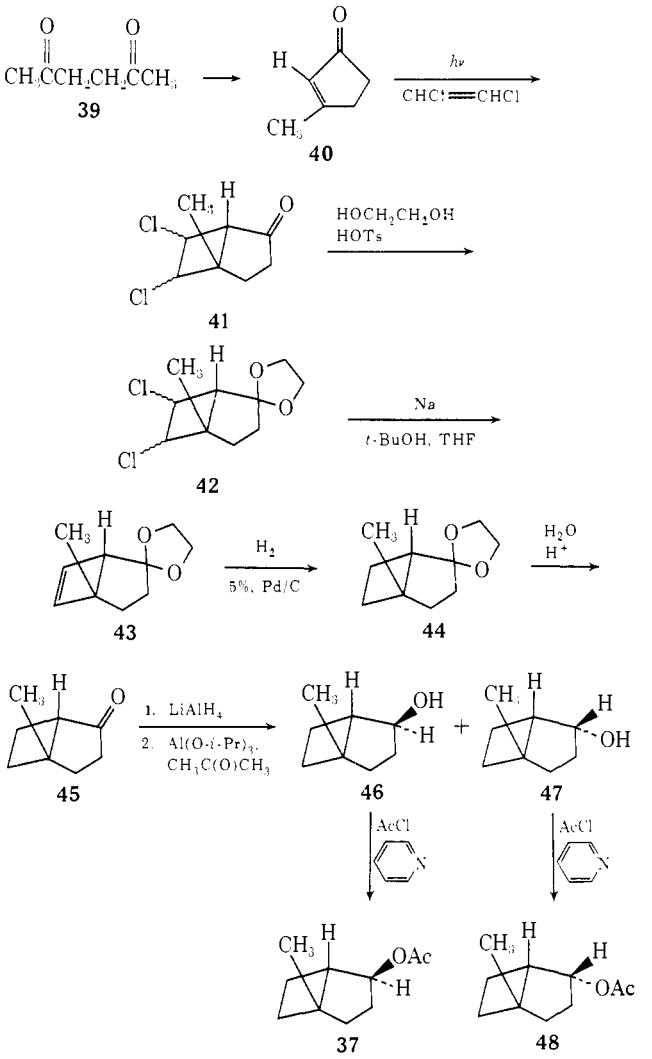
were consistent with the assigned structures, we did not feel that the spectral properties provided sufficient evidence for positive structural assignment. Thus, **33** and **34** were catalytically reduced to the corresponding saturated esters, **37** and **38**, respectively. The syn-



37 **38**

thesis of **37** is outlined in Scheme I. Acetonylacetone

Scheme I



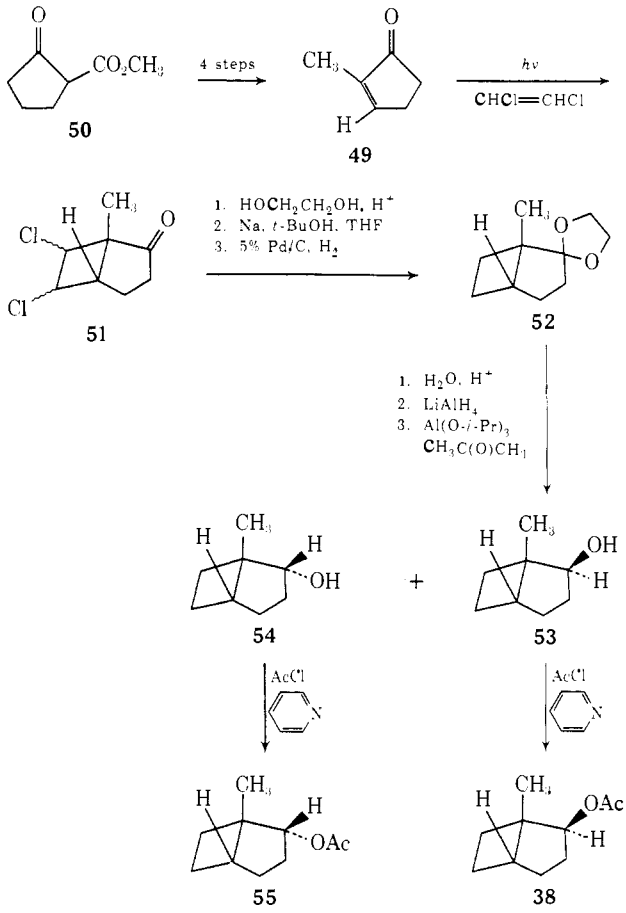
(**39**) was cyclized to 1-methylcyclopenten-3-one (**40**) according to the procedure of Acheson and Robinson.[29] Irradiation of **40** using a mixture of *cis*- and *trans*-1,2-dichloroethylene as the solvent gave **41** as a mixture of isomers in 68% yield. Reaction of **41** with ethylene glycol in the presence of *p*-toluenesulfonic acid gave **42**, which was treated with sodium in tetrahydrofuran–*tert*-butyl alcohol to give **43** in 64% yield. Reduction of **43** over palladium on carbon gave **44** (89%). Hydrolysis of **44** to **45** was accomplished in 92% yield utilizing 5% sulfuric acid at room temperature. Lithium aluminum hydride reduction of **45** gave **46** and **47** in the ratio of 2:98. Refluxing these alcohols for 24 hr with aluminum isopropoxide in the presence of a

(29) R. M. Acheson and R. Robinson, *J. Chem. Soc.*, 1127 (1952).

trace of acetone in toluene permitted equilibration of the mixture to give **46** and **47** in the ratio of 67:33. Although this mixture of alcohols could be separated by vpc, it was found to be most convenient to acetylate the mixture of alcohols to give a mixture of **37** and **48** and to separate this mixture. The sample of **37** prepared in this manner was found to be identical in all respects with the sample of **37** obtained from the catalytic reduction of **33**.

An analogous route to that used for the synthesis of **37** was used to prepare **38**. As shown in Scheme II, 2-

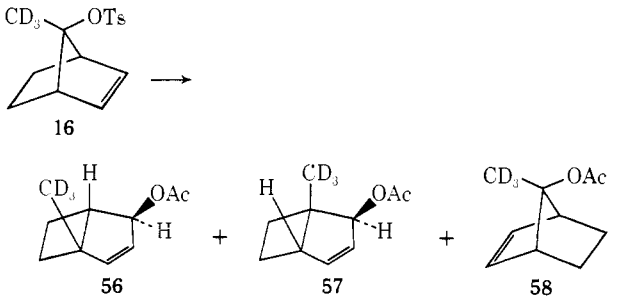
Scheme II



50 49 51 52 54 53 55 38

methylcyclopenten-3-one (**49**) was prepared by a four-step sequence from 2-carbomethoxycyclopentanone. Photochemical addition of 1,2-dichloroethylene gave **51**, which on ketalization, dehalogenation, and subsequent reduction gave **52**. Hydrolysis of the ketal function of **52** followed by lithium aluminum hydride reduction of the resulting ketone gave a mixture of **53** and **54** in the ratio of 1:99. Equilibration of this mixture of alcohols with aluminum isopropoxide gave a 38:62 mixture of **53** and **54**. Acetylation of this mixture followed by separation of the epimeric acetates, **38** and **55**, gave pure **38**, which was identical in all respects with the sample of **38** obtained from the catalytic reduction of **34**. Thus, the structures of all of the solvolysis products were firmly established.

The products from the solvolysis of **16** differed very little from those obtained from **11**. The major difference was that **16** failed to give any trace of the elimination product, 7-dideuteriomethylenenorbornene. The yields of **56**, **57**, and **58** were 50, 14, and 22%, respec-



16 56 57 58

tively. These values agreed closely with the yields obtained in the solvolysis of **11**.

Discussion

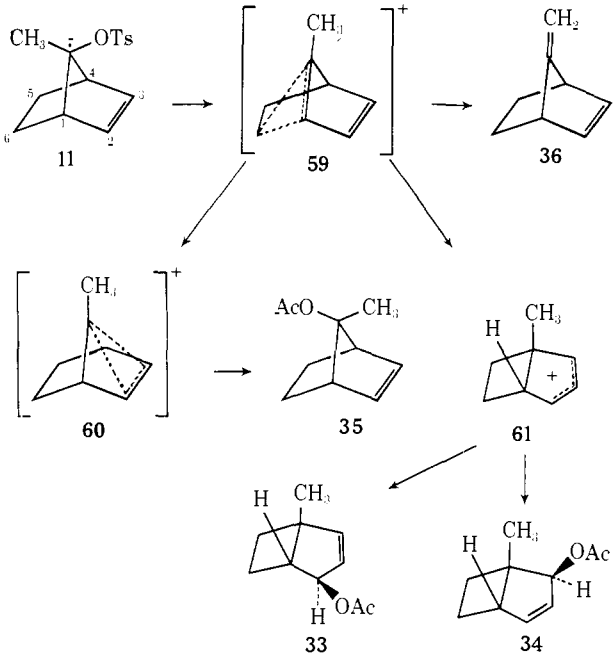
The results obtained and discussed above for the methylated 7-norbornyl, 7-*syn*-norbornenyl, and 7-*anti*-norbornenyl ring systems allow us to produce a fairly general picture of each of the three different methyl-substituted cations. In the acetolysis of **1**, the instability of the developing cation is apparent from the rate of ionization.[30] The overwhelming effect of methyl substitution on the rate of solvolysis of this system indicates to us that the tertiary cation **29** is probably devoid of any stabilization in a "neighboring group sense" by any other part of the norbornyl skeleton.[31] The methyl/hydrogen and methyl/trideuteriomethyl rate ratios and the product studies are consistent with this concept.

The acetolysis of **11** appears to be much more complicated than that of **2**. The added methyl group at the 7 position appears to compete closely with the syn double bond as a stabilizing factor. Both the methyl/hydrogen and methyl/trideuteriomethyl rate ratios are consistent with some hyperconjugative stabilization of the incipient cationic species by the added methyl group in the 7 position. The formation of a small amount of the diene, **36**, in the methyl-substituted case and the absence of any diene in the trideuteriomethylated molecule also indicate a hyperconjugative interaction of the methyl group. However, comparison of the rates of solvolysis of **13** and **11** indicates that the syn double bond is still playing some role, albeit small, in the ionization of **11**. The large amount of rearranged product obtained in the solvolysis of **11** was also consistent with a substantial interaction of the syn double bond with the developing cationic intermediate. In view of all the data available, we feel that the ionization of **11** probably proceeds to give an ion which is best represented by **59**. It is assumed that the positive character of **59** is stabilized at C-7 *via* a hyperconjugative interaction with the methyl group and at C-1 *via* delocalization of charge by the double bond. The formation of **36** is readily explained in terms of the loss of a proton from the methyl group of **59**. The formation of **35** cannot readily be conceived as occurring directly from **59**. Instead, it seems likely that **59** "leaks" to the ion **60** which should be very stable (*vide post*).[32] This "leakage" can

(30) The nature of the cation derived from 1 is still poorly understood.[5b,g] From the available data, it would appear that this cation is greatly in need of a stabilizing influence and is receptive to almost any type of stabilization.

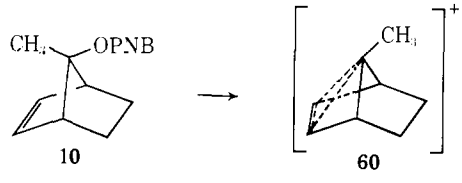
(31) Neighboring group participation in the solvolysis of 1 has been discussed previously.[5b,c]

(32) Ample precedent exists for this type of ion interconversion in the studies of the solvolysis of the brosylate of outside 9-hydroxy-1,2,3,4,-



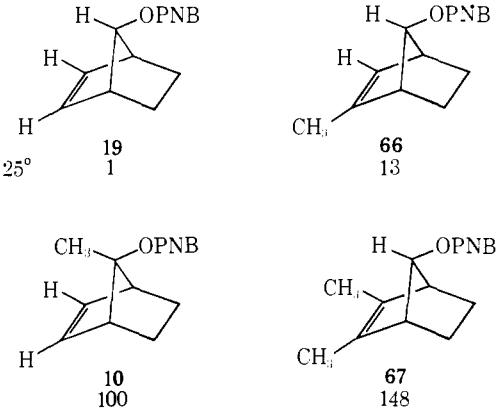
be viewed as a backside attack of the double bond on the ion **59** to give **60**. Attack of solvent on **60** would then produce **35**. The formation of both **33** and **34** implies the intermediacy of an ion such as **61**. However, the exclusive exo stereochemistry of the acetate function in both **33** and **34** implies that this allylic cation must be interacting to some extent with the cyclobutane ring. This idea is supported by our equilibration studies (*vide supra*) which showed that endo substitution was the thermodynamically more stable situation for the corresponding alcohols related to **34**.

The relatively meager effect of the methyl group in the 7 position on the relative rates of solvolysis of **10** and **19**



(a factor of 10^2 at 135°) demonstrates the powerful stabilizing influence of the anti double bond. The methyl/hydrogen rate ratio, the methyl/trideuteriomethyl rate ratio, and the product studies all support the hypothesis that the addition of a methyl group has little more than an inductive effect on the very stable cation, **60**. In particular, the small negative deuterium isotope effect observed for the trideuteriomethyl substituted *p*-nitrobenzoate, **15**, is consistent with this picture.[33] Added support for the nature of **60** has been provided by the nmr studies[34] of **60**, and comparison of the spectra of **60** with that of **5**. All of these studies support the contention that the 7-methyl group does little to stabilize the incipient cation generated when a suitable leaving group is solvolytically ionized from the side anti to the norbornenyl double bond.

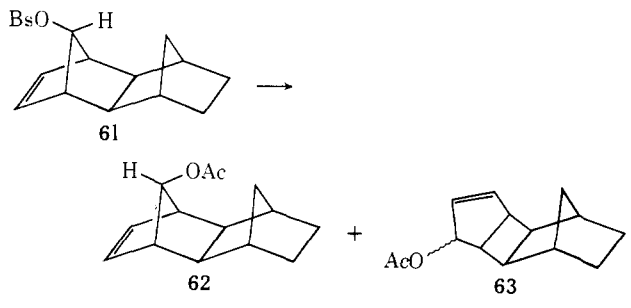
In relation to the postulated purely inductive effect of the methyl at the 7 position it is interesting to compare the relative effects of methyl substitution at the 2 and 3 positions. As shown, monomethyl substitution in the 2 position and dimethyl substitution in the 2 and 3 position give a rate effect that is approximately cumulative.[5e]



The effect of the methyl substitution in the 7 position is slightly more than the effect of the substitution in the 2 position, but less than the effect of dimethyl substitution in the 2 and 3 positions. This indicates that there is very little difference in the effect of methyl substitution at the 2, 3, or 7 positions on the nature of the ion generated from *anti*-7-tosyloxynorbornene. The similarity of the effects of methyl substitution at these various positions is consistent with the methyl playing only an inductive role in each case.

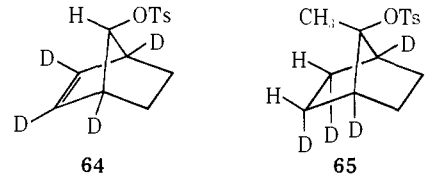
Lastly, it is of interest to compare a plot of log (k_{CH_3}/k_H) *vs.* log (k_{CH_3}/k_{CD_3}) for the systems **20**, **21**, and **22**. Servis, Borčić, and Sunko[35] have shown that for a series of nine different systems an essentially linear relationship was obtained for this type of linear free energy plot. Figure 1 shows that for the three systems studied by us a linear relationship is also observed. It is inter-

4a,5,8,8a-octahydro-1,4-*exo*,*exo*-5,8-dimethanonaphthalene (**61**) which solvolyzes to give substantial amounts of **62**, in addition to **63** [T.



Svensson and S. Winstein, *J. Amer. Chem. Soc.*, **94**, 2336 (1972)]. Although we feel that the direct formation of **35** from **11** or from **59** is extremely improbable, we cannot rigorously exclude such a possibility. The paucity of information which exists concerning the stereochemical aspects of solvolysis in tertiary systems provides little precedent on which to base mechanistic speculation.

(33) The inductive effect of β deuterium has been previously demonstrated in the solvolysis of **64** and **65** which show k_H/k_D of 0.83 and 0.96,



respectively. For a discussion of these effects, see D. E. Sunko and S. Borčić in ref 21.

(34) H. G. Richey, Jr., and R. K. Lustgarten, *J. Amer. Chem. Soc.*, **88**, 3136 (1966); R. K. Lustgarten, P. G. Gassman, D. S. Patton, M. Brookhart, S. Winstein, H. G. Richey, Jr., and J. D. Nicholas, *Tetrahedron Lett.*, 1699 (1970).

(35) K. L. Servis, S. Borčić, and D. E. Sunko, *Tetrahedron*, **24**, 1247 (1968); D. E. Sunko, private communication. We wish to thank Professor Sunko for a helpful discussion of this problem.

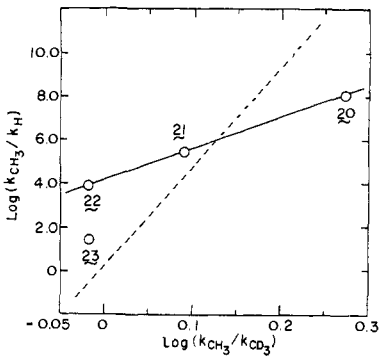


Figure 1. Plot of log (k_{CH_3}/k_H) *vs.* log (k_{CH_3}/k_{CD_3}) for 7-norbornyl tosylates (**20**), *syn*-7-norbornenyl tosylates (**21**), and *anti*-7-norbornenyl tosylates (**22**) represented by solid line. For purposes of comparing our slope with that of Sunko and coworkers (ref 35), their line for the solvolysis of a variety of chlorides is included (-----).

esting that the slope of our plot differs substantially from that previously reported.[35] However, most of the data in the previous study[35] involved the solvolysis of halides, while our study involved the solvolysis of tosylates. Whether this indicates that the slope of the plot may be a function of the leaving group and/or the solvent system used for the solvolyses remains questionable. The value for **22** was extrapolated from the corresponding *p*-nitrobenzoate, **23**, which was included on the plot for comparison. If the isotope effect noted for **20** should have a large component attributable to a concerted elimination, the isotope effect associated with carbonium ion formation would be decreased and the point for **20** would approach the value predicted on the basis of the previously mentioned chloride solvolysis. Thus, the linearity (and associated slope) of the plot obtained for **20**, **21**, and **22** could be fortuitous.

Experimental Section[36]

7-Ketonorbornene (6). The unsaturated ketone, **6**, was prepared according to the method of Gassman and Marshall.[11]

***anti*-7-Hydroxy-*syn*-7-methylnorbornene (7) and *syn*-7-Hydroxy-*anti*-7-methylnorbornene (8).** A mixture of **7** and **8** was prepared according to the method of Erman[12] *via* addition of methyllithium to **6**. Separation of the anti and syn alcohols, **7** and **8**, was accomplished by preparative gas chromatography on 10% Carbowax 20M–KOH (4:1) on 60–80 Chromosorb W at 90°.

7-Hydroxy-7-methylnorbornane (9). A solution of 1.23 g (9.9 mmol) of the mixture of syn and anti alcohols, **8** and **7**, in 50 ml of 95% ethanol was hydrogenated over 50 mg of Pd on carbon. The catalyst was removed by filtration and the solvent removed by distillation. The residue was sublimed (70–80° (15 mm)) to give 0.91 g (73%) of the white crystals, mp 92.0–94.0° (lit.[37] mp 97–98°).

***anti*-Hydroxy-*syn*-7-methylnorbornene *p*-Nitrobenzoate (10).** A solution of 1.50 g (12.1 mmol) of the anti alcohol, **7**, in 25 ml of dry pyridine was cooled to 0° in an ice bath before the addition of 2.47 g (13.3 mmol) of *p*-nitrobenzoyl chloride. After the flask was swirled for several minutes, the reaction was kept at 5° for 3 days. The contents was then poured into 25 ml of water and extracted with three 25-ml portions of chloroform. The combined extracts were washed with saturated sodium bicarbonate solution, water, and saturated salt solution, then dried over anhydrous magnesium sulfate. After filtration, the solvent was removed under reduced pressure to give 3.30 g of the crude *p*-nitrobenzoate. Two recrystallizations from *n*-hexane gave 1.55 g (47% yield): mp 127.0–128.9°; ir (KBr) 3.27 (s), 5.81 (s), 6.20 (m), 6.53 (s), 7.41 (s), 7.69 (s), 7.83 (s), 8.97 (s), 9.10 (s), 9.93 (m), 11.22 (m), 11.50 (m), 11.73 (m), 11.88 (m), 12.79 (m), and 14.00 (s) μ; nmr (CCl_4) τ 1.80 (2 d, AA'XX', 4 H, J = 2 Hz), 3.90 (t, 2 H, J = 2 Hz), 6.90 (m, 2 H), 8.13 (m, 2 H), 8.40 (s, 3 H), and 8.97 (m, 2 H).

Anal. Calcd for $C_{15}H_{15}NO_4$: C, 65.92; H, 5.53; N, 5.13. Found: C, 65.94; H, 5.58; N, 5.08.

***anti*-7-Methyl-*syn*-7-tosyloxynorbornene (11).** *p*-Toluenesulfonyl chloride (2.0 g, 10.5 mmol) was added to an ice-cold solution of the syn alcohol, **8** (1.0 g, 8.06 mmol), in 30 ml of dry pyridine. After storing the solution at room temperature for 2 weeks, the contents was poured into 300 ml of water and extracted three times with 100-ml portions of chloroform. The combined extracts were successively washed with 100-ml portions of dilute hydrochloric acid, water, saturated sodium bicarbonate solution, water, and saturated salt solution. After drying over anhydrous magnesium sulfate and filtering, the solvent was removed at reduced pressure to give 1.86 g of a yellow oil. Crystallization from *n*-hexane gave 0.78 g (35% yield): mp 49.0–51.0°; ir (KBr) 7.48 (s), 8.38 (m), 8.47 (s), 8.53 (s), 11.00 (s), 11.50 (s), 12.18 (m), 13.89 (m), 14.23 (m), and 14.70 (m) μ; nmr (CCl_4) τ 2.36 and 2.77 (2 d, AA'XX', 4 H, J = 8 Hz), 4.28 (t, 2 H, J = 2 Hz), 7.08 (s, 2 H), 7.57 (s, 3 H), 8.27 (m, 2 H), 8.43 (s, 3 H), and 9.05 (m, 2 H).

Anal. Calcd for $C_{15}H_{18}O_3S$: C, 64.72; H, 6.52; S, 11.52. Found: C, 64.57; H, 6.58; S, 11.29.

7-Hydroxy-7-methylnorbornane *p*-Toluenesulfinate (12). The method of Coates and Chen[13] was used to prepare the *p*-toluenesulfinate of **9**. *p*-Toluenesulfinyl chloride[38,39] (1.41 g, 8.06 mmol) was added dropwise to an ice-cold solution of 1.0 g (8.06 mmol) of **9** and 0.64 g (8.06 mmol) of dry pyridine in 10 ml of anhydrous ether, during which time the clear solution turned milky white. After the addition, the reaction was stirred for 2 hr at 0°. The solution was washed with 25-ml portions of 2 *N* hydrochloric acid, water, 5% aqueous sodium bicarbonate solutions, and water, then dried over anhydrous magnesium sulfate. After filtration, the solvent was removed at reduced pressure to give 2.0 g of the crude material. The sulfinate was placed on a silica gel column and eluted with 15% diethyl ether–hexane to give 1.97 g of the pure sulfinate **12** in 92% yield.

7-Methyl-7-tosyloxynorbornane (13). According to the method of Coates and Chen,[13] a solution of *m*-chloroperbenzoic acid (1.84 g, 10.66 mmol) in 40 ml of methylene chloide was added dropwise to 1.97 g (7.46 mmol) of **12** in 50 ml of methylene chloride at 0°. A white precipitate formed after 1.5 hr. The reaction was stirred for 2 hr, then washed with 5% aqueous potassium carbonate solution and water. The methylene chloride solution was dried over anhydrous magnesium sulfate, filtered, and later evaporated at reduced pressure to give 2.17 g of **13**. Crystallization from *n*-pentane gave 1.27 g (60%) of the impure tosylate. Subsequent recrystallizations gave 0.94 g of the pure tosylate **13**, mp 45.5–47° (lit.[3] mp 48–49°).

7-Hydroxy-7-methyl-d_3-norbornane (68). A 100-ml, three-necked Bantamware flask, equipped with a Hirshberg stirrer, dropping funnel with nitrogen inlet, and reflux condenser with drying tube, was charged with 1.86 g (77.6 mmol) of magnesium turnings in 30 ml of anhydrous ether. After the flask was flushed with nitrogen, 5.0 g (34.5 mmol) of methyl-d_3 iodide (99.5% d_3, Stohler Isotopic Chemicals, Inc.) in 20 ml of ether was added at a rate sufficient to maintain a constant reflux. After the mixture was stirred for 15 min, 1.86 g (17.2 mmol) of **6** in 15 ml of ether was added dropwise. The reaction was stirred for another 30 min, whereupon the flask was cooled in an ice bath and 30 ml of saturated ammonium chloride was added slowly. The layers were then separated and the aqueous phase was extracted twice with 25-ml portions of ether. The combined extracts were dried over anhydrous magnesium sulfate, and then filtered. The solvent was removed by distillation through a metal-helices packed column to give a mixture of the epimeric unsaturated alcohols as the residue.

Hydrogenation and work-up were the same as used in the preparation of **9**, giving 1.70 g of the alcohol (77% yield from the ketone).

(36) Elemental analyses were performed by the Scandinavian Microanalytical Laboratory, Herlev, Denmark. Melting points and boiling points are uncorrected. Infrared spectra were taken on a Perkin-Elmer Model 137 Infracord as neat liquids, in solution in carbon tetrachloride, or as powdered solids in potassium bromide disks. Nuclear magnetic resonance spectra were obtained on Varian Associates A-60, A-60-A, or HA-100 spectrometers and are reported in τ units relative to tetramethylsilane (τ 10.00) as the internal standard. Exact mass determinations and isotope abundance were determined on an MS-9 high-resolution mass spectrometer.

(37) R. K. Bly and R. S. Bly, *J. Org. Chem.*, **28**, 3165 (1963).

(38) F. C. Whitmore and F. H. Hamilton, "Organic Synthesis," Collect. Vol. I, Wiley, New York, N. Y., 1932, p 492.

(39) F. Kurzer, "Organic Synthesis" Collect. Vol. IV, Wiley, New York, N. Y., 1963, p 937.

Comparison of this alcohol with **9** by mass spectroscopy showed the methyl to be 99.7% trideuterated.

***anti*-7-Hydroxy-*syn*-7-methyl-d_3-norbornene (32) and *syn*-7-Hydroxy-*anti*-7-methyl-d_3-norbornene (69).** A 100-ml, three-necked Bantamware flask, equipped with a Hirshberg stirrer, a reflux condenser with drying tube, and a pressure-equalizing dropping funnel with gas inlet, was charged with 0.53 g (75.9 mmol) of $^1/_8$-in. pieces of lithium wire under an argon atmosphere. The lithium wire was washed four times with 25-ml portions of *n*-pentane. Anhydrous ether (25 ml) was then added, along with a few drops of methyl-d_3 iodide (**99.5%** d_3) to initiate the reaction. The remainder of the 5.0 g (34.5 mmol) of methyl-d_3 iodide was then added dropwise in 7 ml of ether at a rate to maintain reflux. After stirring the solution for 15 min, the flask was cooled to 0° in an ice bath and 3.35 g (31.0 mmol) of **6** in **7** ml of ether was added slowly. Fifteen minutes after the addition was completed, the reaction was hydrolyzed with 20 ml of water. The layers were separated, and the aqueous layer was extracted twice with 15-ml portions of ether. The combined extracts were dried over anhydrous magnesium sulfate, then filtered. Analysis by gas chromatography on a 2% XF-1150 on 60–80 Chromosorb G column showed that some ketone still remained (*ca.* 10%). The ethereal solution was stirred over three 100-ml portions of saturated sodium bisulfite solution for 25 hr. The ketone was removed in the aqueous phase as the bisulfite addition compound. The alcohols were then separated by preparative gas chromatography on a 10% Carbowax 20M–KOH (4:1) on 60–80 Chromosorb W column at 90° to give 0.53 g (13.5%) of the syn alcohol, **69**, and 1.52 g (39%) of the anti alcohol, **32**. Analysis of the alcohols by mass spectroscopy indicated that they were greater than 99% trideuterated.

***anti*-7-Hydroxy-*syn*-7-methyl-d_3-norbornene *p*-Nitrobenzoate (15).** The *p*-nitrobenzoic acid ester of the anti alcohol, **32**, was prepared in the same manner as described for the nondeuterated compound, **10**. Reaction of 1.50 g (11.8 mmol) of **32** with *p*-nitrobenzoyl chloride gave 3.23 g of crude ester. Recrystallization with *n*-hexane gave 2.70 g (86% yield) of **15**, mp 127.4–128.8°.

***anti*-7-Methyl-d_3-*syn*-7-tosyloxynorbornene (16).** The tosylate of the syn alcohol, **69**, was prepared in the same manner as described for the nondeuterated compound, **11**. After reaction with *p*-toluenesulfonyl chloride and work-up, recrystallization from *n*-pentane gave 0.39 g of **16** in poor yield (35%), mp 48.5–51.0°.

7-Hydroxy-7-methyl-d_3-norbornane *p*-Toluenesulfinate (70). The same procedure used above for the preparation of **12** was followed to convert 1.0 g (7.75 mmol) of 7-hydroxy-7-methyl-d_3-norbornane (**68**) into 1.98 g (96%) of pure sulfinate ester (**70**).

7-Methyl-d_3-7-tosyloxynorbornane (17). The oxidation of the saturated methyl-d_3 sulfinate, **70** (1.98 g, 7.42 mmol), with *m*-chloroperbenzoic acid was accomplished by the procedure used above for the preparation of **13**. Recrystallizations from *n*-pentane gave 1.50 g (71%) of the pure tosylate, **17**, mp 45.5–47.0°. Comparison of the two tosylates (**12** and **17**) by mass spectroscopy showed the methyl to be 99.1% trideuterated.

Kinetic Procedures. Dioxane–Water (70:30) for Solvolysis. Reagent dioxane was prepared by the method of Fieser.[40,41] The dioxane was diluted with water (70% dioxane–30% water), flushed with dry, oxygen-free nitrogen, and stored out of contact with air.

Anhydrous Acetic Acid. A 3-l. flask was charged with 10 g of sodium acetate and 10 ml of acetic anhydride and one bottle (5 lb) of glacial acetic acid. The solution was refluxed for 24 hr and then distilled in a dry atmosphere. A small forerun was discarded and the acetic acid collected.

Anhydrous Acetic Acid Buffered with Sodium Acetate.[42] A 500-ml volumetric flask was charged with 0.53 g of anhydrous sodium carbonate and 5.51 g of acetic anhydride and diluted to the mark with anhydrous acetic acid. The solution was refluxed for 7 hr, and upon cooling a portion was titrated with the standard perchloric acid in acetic acid to the equivalence point.

Standard Perchloric Acid in Acetic Acid. A 500-ml volumetric flask was charged with 7.460 g of acetic anhydride and 1.4378 g of 70% perchloric acid and diluted to the mark with anhydrous acetic acid. The solution was allowed to stand overnight before use. The titrant was standardized against potassium acid phthalate in acetic acid.

(40) L. F. Fieser, "Reagents for Organic Synthesis," Wiley, New York, N. Y., 1967, p 333.

(41) L. F. Fieser, "Experiments in Organic Chemistry," 3rd ed, D. C. Heath, Boston, Mass., 1965, p 284.

(42) P. D. Bartlett and W. P. Giddings, *J. Amer. Chem. Soc.*, **82**, 1240 (1960).

Kinetic Procedure for Solvolysis in 70:30 Dioxane–Water. All glassware was standardized by adding water at a given temperature and weighing the water added. From the density of the water at the given temperature, the exact volume of any given piece of volumetric glassware could be determined. The pure ester, sufficient to form a 0.01–0.04 *M* solution, was accurately weighed in a calibrated 10-ml volumetric flask. The dioxane solvent was purged of oxygen by bubbling pure nitrogen through the solvent for 15–20 min at a moderate rate. The purged dioxane was then added to the volumetric flask containing the ester and flushed with nitrogen before shaking. It was sometimes necessary to heat the flask slightly in order to dissolve the ester. Aliquots (1.2 ml) of the resulting solution were transferred by hyperdermic syringe to solvolysis tubes which had been flushed with nitrogen. The solvolysis tubes were 15 × 125 mm test tubes that had been drawn down to a thin neck near the top. For solvolysis above 150°, thick-walled Carius tubes were used in place of test tubes. The tubes were once again flushed with nitrogen and sealed. For solvolysis above 180°, the solution in each tube was flushed for a minimum of 10 min before sealing. The tubes were then placed all at once into a constant-temperature silicone oil bath (Dow Corning F-1-0143) at the desire temperature and an accurate timer started. The sealed tubes were removed at appropriate intervals and immediately quenched in ice–water. For solvolysis at 180° or above, the tubes were quenched by merely removing them from the bath. To determine the acid generated, a quenched tube was opened and an aliquot removed with a 1-ml calibrated, constant-delivery pipet and immediately titrated with standard sodium hydroxide solution. The end point was taken as the equivalence point of a pH curve obtained on an automatic titrator (Metrohm Potentiograph Model E 436). All these data were then tabulated and a rate constant was calculated.[43]

Kinetic Procedure for Acetolysis of Tosylates. The tosylates were solvolyzed according to the procedure of Winstein.[44] The pure ester, sufficient to form a 0.01–0.02 *M* solution, was accurately weighed in a calibrated 10-ml volumetric flask and sodium acetate buffered acetic acid added. After the ester had dissolved, 1.2-ml aliquots of this solution were transferred to solvolysis tubes which were then sealed. The tubes were placed in a constant-temperature bath at a given temperature and an accurate timer was started. The tubes were removed at intervals and immediately quenched in ice–water. A tube was allowed to warm to room temperature and an aliquot was removed with a calibrated, 1-ml constant-delivery pipet and titrated with the standarized perchloric acid in acetic acid solution. The end point (equivalence point) was determined potentiometrically using a microcombination electrode, Type EA147, and the positive millivolt scale of the Metrohm Potentiograph Model E436. An infinity titer was determined by titrating an aliquot after 10 half-lives. This was compared to the calculated infinity value. This titration gave the amount of remaining sodium acetate buffer, rather than the generated acid directly. However, knowing the initial buffer concentration it was possible to determine the acid generated and finally the remaining tosylate. From these data, the rate of reaction was calculated.[43]

Product Studies. Acetolysis Product Analysis of 7-Methyl-7-tosyloxynorbornane (13). Two solvolysis tubes, charged with 54.0 and 55.3 mg (1.928×10^{-4} and 1.975×10^{-4} mol, respectively) of **13** in 2 ml of 0.1 *M* acetic acid solution buffered with sodium acetate, were sealed and heated at 75° for 10 half-lives (4030 sec). Each tube was then cooled in an ice bath and the contents poured into 10 ml of ice-cold water. The solutions were titrated to neutrality with standard sodium hydroxide solution, followed by extraction with three 10-ml portions of *n*-pentane. The combined extracts were washed with water, dried over anhydrous magnesium sulfate, and filtered. The solvent was carefully distilled through a 12-in. glass-helices column. The residue was analyzed by temperature programming (40–100°; 6°/min) vpc on a 6 ft × $^1/_8$ in. column of SE-30 HiPak silicone rubber using β-pinene as an internal standard.[45] This showed the following percentages of prod-

(43) The least-squares method for the determination of the rate constants and activation parameters was performed on a Wang Electronic Calculator, Model 360 K, using a program from the Wang Program Library as modified by Dr. John Trent. This program also enabled us to determine the rate of reaction at any temperature by extrapolating the least-squares line.

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

(45) Detector response factors for each product relative to the internal standard were obtained on a Varian Associates Gas Chromatograph Model 1200, using a Hewlett-Packard Integrator Model 3370-A.

ucts: 25% of **25** and 61% of **24**. The acetate, **25**, was isolated by preparative gas chromatography on a 10 ft × 3/8 in. column of 15% butanediol succinate on 45–60 Chromosorb G at 120° and compared to an authentic sample. Both products were compared by vpc retention times to authentic samples on SE-30, butanediol succinate, and on a 10 ft × 1/8 in. column of 5% XF-1150 on 60–80 Chromosorb W.

Acetolysis Product Analysis of 7-Methyl-d_3-7-tosyloxynorbornane (17). The same procedure, described above for **13**, was followed for a duplicate run of **17** (55.2 and 56.4 mg; 1.951×10^{-4} and 1.993×10^{-4} mol, respectively). The products were worked up as before and the percentages of products shown to be 41% of 7-acetoxy-7-methyl-d_3-norbornane (**28**) and 43% of 7-methylene-d_2-norbornane (**27**).[45] Although authentic samples of the deuterated compounds were not available, their vpc retention times were identical with the protium products.

Solvolysis Product Analysis of *anti*-7-Hydroxy-*syn*-7-methylnorbornene *p*-Nitrobenzoate (10). Two solvolysis tubes, each containing 27.7 mg (1.01×10^{-4} mol) of **10** in 5 ml of a 70% dioxane–30% water solution, were sealed and heated at 135° for 10 half-lives (16,780 sec). The contents of each tube was then poured into 25 ml of water and titrated to neutrality with standard sodium hydroxide solution. The solutions were then extracted three times with 15-ml portions of ether. The combined extracts were washed with water and brine, then dried over anhydrous magnesium sulfate. After filtration, the solvent was removed by careful distillation through a 12-in. metal-helices column. Only one product was detected, which was shown to be the anti alcohol, **7**, by comparison of vpc retention times with those of an authentic sample. Using 1-octanol as an internal standard, vpc yields were obtained on a 10 ft × 1/8 in. column of 10% Carbowax 20M–KOH (4:1) on 60–80 Chromosorb W at 110°. The average yield of the two runs was 91%.[45] Isolation of the product was by preparative gas chromatography on a 10 ft × 3/8 in. column of 10% Carbowax 20–KOH (4:1) on 60–80 Chromosorb W at 125°. The isolated alcohol had identical infrared and physical properties, mp 79.0–80.5° (lit.[12] mp 79.5–80.5°), mmp 79.0–80.0°, to an authentic sample of the anti alcohol, **7**. No syn alcohol, **8**, or diene, **36**, was detected.

Solvolysis Product Analysis of *anti*-7-Hydroxy-*syn*-7-methyl-d_3-norbornene *p*-Nitrobenzoate (15). Two solvolysis tubes containing 29.4 and 28.3 mg (1.06×10^{-4} and 1.02×10^{-4} mol, respectively) of **15** in 5 ml of a 70% dioxane–30% water solution were sealed and heated at 135° for 10 half-lives (16,190 sec). The solutions were worked up as described above for **10**. Similarly, vpc analysis[45] indicated that the only product was the anti alcohol, **32**, in 100% yield.

Acetolysis Product Analysis of *anti*-7-Methyl-*syn*-7-tosyloxynorbornene (11). The acetolysis and work-up of a duplicate run for tosylate **11** (50.1 and 49.2 mg; 1.802×10^{-4} and 1.770×10^{-4} mol, respectively) for 10 half-lives (3600 sec) at 70° was accomplished in the same manner as described above for **13**. The three acetates observed were isolated by preparative gas chromatography on a 10 ft × 3/8 in. column of 15% butanediol succinate on 45–60 Chromosorb G at 120°. The acetate with the shortest retention time was identical with respect to its ir and nmr spectra, and vpc retention times to an authentic sample of the anti acetate, **35**. The identity of the second and third acetates was established by the procedure shown below.

A solution of 36 mg (2.17×10^{-4} mol) of the second (major) acetate, **33**, which had been collected by vpc, was placed in 5 ml of absolute ethanol, and hydrogenated over 10 mg of prehydrogenated platinum oxide. The solution was filtered through a Celite pad and the solvent evaporated at reduced pressure. The residue was distilled in a molecular still (80–90° (25 mm)) to give 28.4 mg (79%) of the saturated acetate. Spectral and vpc data were identical with that of *exo*-acetoxy-1-methylbicyclo[3.2.0]heptane (**37**).

Since in the unsaturated ester, the proton on the same carbon as the acetoxy group (4-H) was shown to be coupled to the vinyl proton ($J \simeq 2$ Hz) in the nmr and therefore was allylic, the double bond must be between carbons 2 and 3 of **33**: ir (neat) 3.36 (m), 5.74 (s), 6.90 (w), 7.30 (m), 8.07 (s), 8.84 (w), 9.84 (w), 10.50 (m), 11.17 (w), 12.71 (m) μ; nmr (CCl_4) τ 8.76 (s, 3 H), 8.28 (m, 3 H), 8.08 (s, 3 H), 7.75 (m, 2 H), 5.18 (d, 1 H, $J_{3,4} = 2$ Hz), 4.25 (quartet, 1 H, $J_{3,4} = 2$ Hz, $J_{2,3} = 5.5$ Hz), and 4.08 (d, 1 H, $J_{2,3} = 5.5$ Hz).

Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 72.28; H, 8.38.

The same procedure used above for **33** was followed for the third acetate. A sample of 3.6 mg of **34** was hydrogenated and was shown to be identical with that of *exo*-2-acetoxy-1-methylbicyclo-[3.2.0]heptane (**38**); it had the same retention times on 10 ft × 1/8 in. columns of 5% XF-1150 on 60–80 Chromosorb G at 100°, 15% butanediol succinate on 45–60 Chromosorb G at 140° and 15% DEGS on Chromosorb P at 160°. Although the nmr of he unsaturated acetate was more complex, the structure was assigned as **34**, based on analogy with ester, **33**, above: ir (neat) 3.37 (m), 5.75 (s), 6.90 (w), 7.30 (m), 8.10 (s), 9.94 (s), 10.33 (m), 12.80 (w), and 13.40 (w) μ; nmr (CCl_4) τ 8.84 (s, 3 H), 8.30 (m, 3 H), 8.03 (s, 3 H), 7.20 (m, 2 H), 4.78 (m, 1 H), 4.23 (m, 1 H) and 3.95 (m, 1 H).

Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 71.89; H, 8.53.

Using the acetates collected by vpc and an authentic sample of the diene, **36**, the yields of the products were determined using cyclopentanone as an internal standard: 3% of **36**, 27% of **35**, 48% of **33**, and 13% of **34**. No syn acetate, **71**, could be detected.

Acetolysis Product Analysis of *anti*-7-Methyl-d_3-*syn*-7-tosyloxynorbornene (16). Solutions of 26.7 and 26.2 mg (9.502×10^{-4} and 9.324×10^{-4} mol, respectively) of **16** in 1 ml of ~0.1 *M* sodium acetate in anhydrous acetic acid were sealed in solvolysis tubes and heated at 60° for 10 half-lives (13,200 sec). The solutions were worked up as described above for **13**. The yields determined by vpc were: 22% of **58**, 50% of **56**, and 14% of **57**. As in the case of **17**, product identity was based on the similarity of retention times with the protium compounds.[45]

7-Methylenenorbornene (36). A modification of Corey's procedure[33] was used to prepare **36** from 7-ketonorbornene (**6**). In a 100-ml, three-necked flask, equipped with a pressure-equalizing dropping funnel with nitrogen inlet, a septum cap, and a reflux condenser with an isopropyl alcohol–Dry Ice trap and mineral oil bubbler, was placed 1.41 g (33.4 mmol) of a 57% oil dispersion of sodium hydride. The oil was removed by washing several times with *n*-pentane under a nitrogen atmosphere. With a syringe, 15 ml of dry dimethyl sulfoxide was introduced and the mixture heated to 65–80° for *ca.* 45 min or until hydrogen evolution ceased. The solution of methylsulfinyl carbanion was cooled in an ice bath and 11.93 g (33.4 mmol) of methyltriphenylphosphonium bromide in 30 ml of warm dimethyl sulfoxide was added. After the solution was stirred for 10 min at room temperature, 3.97 g (36.8 mmol) of **6** was added giving a bright yellow precipitate. The slurry was heated to *ca.* 80°, whereupon the solution turned clear brown. After cooling to room temperature, the reaction was stirred for 12 hr. The solution was then poured into 700 ml of water, and extracted with four 100-ml portions of ether. The combined extracts were washed four times with 100-ml portions of water and saturated sodium chloride solution, and dried over anhydrous magnesium sulfate. After filtration, the solvent was removed by distillation through a 12-in. metal-helices packed column. During this time a white solid precipitated out of solution (triphenylphosphine oxide). This precipitate was removed by filtration and the residue was distilled at reduced pressure to give 0.13 g of unreacted ketone, **6**, and 1.53 g (39%) of **36**: bp 64–67° (105 mm); n^{24}D 1.4797; ir (neat) 3.22 (m), 3.31 (s), 3.46 (m), 5.90 (s), 7.54 (s), 8.51 (w), 8.96 (w), 11.43 (s), 11.80 (m), 12.46 (m), 12.87 (w), 13.87 (s), and 14.69 (m) μ; nmr (CCl_4) τ 3.87 (t, 2 H, $J = 2$ Hz), 5.86 (s, 2 H), 7.02 (m, 2 H), 8.10–8.47 (m, 2 H), and 8.73–9.12 (m, 2 H).

Anal. Calcd for C_8H_{10}: C, 90.50; H, 9.50. Found: C, 90.49; H, 9.46.

7-Methylenenorbornane (24). The procedure described above for **36** was used to convert 7-ketonorbornane (**26**)[22] (4.0 g, 36.36 mmol) into **24** by reaction with the ylide prepared from 11.80 g (33.06 mmol) of methyltriphenylphosphonium bromide and the methylsulfinyl carbanion. Worked up as before, the reaction was distilled to give 1.16 g (30%) of **24**: bp 65–67° (103 mm); n^{24}D 1.4693; ir (neat) 3.20 (w), 3.30 (s), 3.42 (m), 5.95 (m), 6.89 (m), 8.49 (m), 11.30 (s), 14.63 (s), and 14.86 (s) μ; nmr (CCl_4) τ 5.67 (s, 2 H), 7.90 (m, 2 H), and 8.38–9.00 (m, 8 H).

Anal. Calcd for C_8H_{12}: C, 88.82; H, 11.18. Found: C, 88.77; H, 11.34.

***syn*-7-Acetoxy-*anti*-7-methylnorbornene (71).** A solution of 0.5 g (4.03 mmol) of the syn alcohol **8** in 15 ml of anhydrous tetrahydrofuran was cooled to 5–10° in a 50-ml, three-necked Bantamware flask, equipped with a thermometer, nitrogen inlet, septum cap, and reflux condenser with drying tube. After the flask was flushed with nitrogen, 3.8 ml (0.39 g, 6.05 mmol) of a 15% solution of *n*-butyllithium was added to the cooled solution, which turned cloudy. After the solution was stirred for 30 min, a solution of 0.51 g (6.45 mmol) of acetyl chloride in 5 ml of tetrahydrofuran was added slowly. The yellow solution was allowed to stir overnight before being hydrolyzed with 10 ml of water. The solution was poured into 25 ml of water and extracted three times with 15-ml portions of ether. The combined ethereal extracts were washed with water,

10% aqueous sodium bicarbonate solution, and water, then dried over anhydrous magnesium sulfate. The solution was filtered and the solvent was removed by distillation. The acetate was isolated by preparative gas chromatography on 15% butanediol succinate on 45–60 Chromosorb G (15 ft × 3/8 in.) at 125°. The unreacted alcohol was also obtained (0.13 g) in addition to 0.23 g of the acetate **71**[12] (47% based on unrecovered alcohol).

anti-**7-Acetoxy-*syn*-7-methylnorbornene (35).** A solution of 0.5 g (4.03 mmol) of the anti alcohol **7** in 15 ml of dry pyridine was cooled to 0° in an ice bath, and 0.35 g (4.56 mmol) of acetyl chloride was added. The white precipitate of acylpyridinium chloride formed immediately. After storing for 2 weeks at 5°, this complex disappears, leaving pyridine hydrochloride crystals in the flask. The solution was poured into 50 ml of water and extracted three times with 25-ml portions of chloroform. The combined extracts were washed with dilute hydrochloric acid, water, saturated sodium bicarbonate solution, water, and saturated salt solution, then dried over anhydrous magnesium sulfate. After filtration, the solvent was removed by distillation and the residue distilled at reduced pressure to give 0.49 g (73%) of **35**: bp 77–78° (22 mm).[12]

7-Acetoxy-7-methylnorbornane (25). The procedure used for the anti acetate (**35**) was followed for the conversion of 7-hydroxy-7-methylnorbornane (**9**) into the corresponding acetate, **25**.

1-Methylcyclopenten-3-one (40). Acetonylacetone (**39**) was cyclized to **40** by the procedure of Acheson and Robinson.[29]

6,7-Dichloro-1-methylbicyclo[3.2.0]heptan-4-one (41). A solution of 5.38 g (0.056 mol) of **40** and 50 mg of hydroquinone in 400 ml of freshly distilled *cis*- and *trans*-1,2-dichloroethylene was irradiated with a 450-W Hanovia lamp through Pyrex. The progress of the reaction was followed by gas chromatographic analysis on 10 ft × 1/8 in. columns of 2% XF-1150 on 60–80 Chromosorb G at 100° and 10% SE-30 silicone rubber. Four peaks corresponding to the four possible isomeric (2 + 2) addition products were observed. After 67 hr, the reaction was completed and the solution filtered. The dichloroethylene was removed by distillation and the remaining liquid distilled at reduced pressure to give 7.38 g (68%) of the mixture of epimeric bicyclic chloroketones, **41**, bp 66–87° (0.12 mm). In view of the complex nature of this mixture, no further purification was carried out. The mixture was used directly in the next step of the sequence.

1-Methyl-4,4-dioxolanebicyclo[3.2.0]hept-6-ene (43). A solution of 5.52 g (28.6 mmol) of ketone, **41**, 2.06 (33.2 mmol) of ethylene glycol, and 20 mg of *p*-toluenesulfonic acid monohydrate in 100 ml of benzene was refluxed for 12 hr. The water generated was removed by a Dean–Stark trap. The solution was dried over anhydrous magnesium sulfate and filtered, and the solvent distilled. The residue was distilled at reduced pressure (68–75° (0.02 mm)) to give 4.65 g (70%) of the ketal **42**, as a mixture of epimeric chlorides.

A 250-ml, three-necked flask, equipped with a Hirshberg stirrer, reflux condenser with drying tube, and a pressure-equalizing dropping funnel with nitrogen inlet, was charged with 7.59 g (0.23 mol) of freshly cut, pea-sized pieces of sodium in 85 ml of dry tetrahydrofuran. The flask was flushed with nitrogen, then, while a slow flow of nitrogen was maintained, the solution was brought to reflux. After the addition of 17.0 g of *tert*-butyl alcohol, the reaction was again brought to reflux, whereupon a solution of 4.48 g (19.1 mmol) of the ketal, **42**, in 10 ml of tetrahydrofuran was added dropwise. The reaction was completed after 2 hr, as indicated by the clumping together of the sodium. The hot solution was filtered through a wire screen and the sodium was washed with 60 ml of *n*-pentane. An ice–water mixture (120 g) was added to the filtrate and the solution was shaken. The layers were separated and the top layer was washed twice with 25-ml portions of saturated salt solution, and then dried over anhydrous magnesium sulfate. After filtering, the solvents were removed by distillation and the remaining liquid was distilled at reduced pressure to give 2.06 g (64%) of **43**, bp 79.0–79.5° (13 mm). The ketal, **43**, could be further purified by preparative gas chromatography on a 10 ft × 3/8 in. column of 10% SE-30 on 60–80 Chromosorb W at 110°: $n^{18.5}$D 1.4728; ir (neat) 3.36 (s), 7.48 (s), 8.60 (s), 9.00 (s), 9.26 (s), 9.85 (m), and 13.33 (s) μ; nmr (CCl_4) τ 3.97 (unresolved s, 2 H), 6.20 (s, 4 H), 7.63 (s, 1 H), 7.58–8.62 (m, 4 H), and 8.73 (s, 3 H).

Anal. Calcd for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49. Found: C, 71.89; H, 8.52.

1-Methyl-4,4-dioxolanebicyclo[3.2.0]heptane (44). A solution of 2.49 g (15.0 mmol) of the unsaturated ketal, **43**, in 25 ml of absolute ethanol was hydrogenated over 50 mg of 5% palladium on carbon. The solution was then filtered through a Celite pad and the solvent was removed by distillation. The remaining liquid was distilled at reduced pressure to give 2.24 g (89%) of the saturated ketal, **44**, bp 90–93° (19 mm). An analytical sample was prepared by preparative gas chromatography on a 10% SE-30 on 60–80 Chromosorb W column at 110°: $n^{13.5}$D 1.4683; ir (neat) 3.34 (s), 3.42 (m), 6.84 (m), 7.43 (s), 8.19 (m), 9.02 (s), 9.79 (s), and 11.04 (m) μ; nmr (CCl_4) τ 6.23 (sharp m, 4 H), 7.50–8.73 (m, 9 H), and 8.82 (s, 3 H).

Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.25; H, 9.62.

1-Methylbicyclo[3.2.0]heptan-4-one (45). To a solution of 25 ml of 5% aqueous sulfuric acid was added 1.29 g (7.68 mmol) of the ketal, **44**. After stirring for 2 hr, the solution was extracted three times with 25-ml portions of ether. The combined extracts were washed with saturated sodium bicarbonate solution, water, and saturated salt solution, and dried over anhydrous magnesium sulfate. After filtering and removal of the solvent, the ketone, **45**, was distilled to give 0.87 g (92%): bp 68–69° (13.5 mm); $n^{14.5}$D 1.4651; ir (neat) 3.44 (s), 3.52 (m), 5.72 (s), 6.85 (m), 7.05 (w), 7.24 (w), 7.80 (m), 8.57 (m), 9.09 (w), 9.65 (m), and 10.70 (w) μ; nmr (CCl_4) τ 7.40–8.45 (m, 9 H) and 8.70 (s, 3 H).

Anal. Calcd for $C_8H_{12}O$: C, 77.37; H, 9.74. Found: C, 77.23; H, 9.87.

***exo*- and *endo*-4-Hydroxy-1-methylbicyclo[3.2.0]heptane (46 and 47, respectively).** To a slurry of 0.15 g (4.03 mmol) of lithium hydride in 35 ml of anhydrous ether was added dropwise 0.50 g (4.03 mmol) of 1-methylbicyclo[3.2.0]heptan-4-one (**45**) in 5 ml of ether. The reaction was stirred for 1 hr, then hydrolyzed with 0.60 g of 10% aqueous sodium hydroxide. After the reaction was stirred for 12 hr, the precipitate was removed by filtration and the ethereal solution was dried over anhydrous magnesium sulfate. The solution was filtered and the ether was removed by distillation. The residue was distilled at reduced pressure (93–94° (23 mm)) to give 0.46 g (90%) of an epimeric mixture of alcohols. Analysis by gas chromatography on a 2% XF-1150 on 60–80 Chromosorb G column at 80° showed that the ratio of endo to exo alcohols was 98:2.

Epimerization of *exo*- and *endo*-4-Hydroxy-1-methylbicyclo-[3.2.0]heptane (46 and 47). A solution of 0.30 g (2.38 mmol) of the epimeric alcohols, **46** and **47**, 1.10 g (5.41 mmol) of anhydrous aluminum isopropoxide, and 0.80 ml of acetone in 25 ml of toluene was brought to reflux. After the solution was stirred for 18 hr, an aliquot was shaken with ether and an equal portion of 5% aqueous sodium hydroxide. Analysis on a 2% XF-1150 on 60–80 Chromosorb G vpc column at 80° showed the endo/exo ratio to be 30:70. Refluxing for 24 more hr failed to change this ratio. The solution was cooled and poured into 150 ml of 5% aqueous sodium hydroxide, then extracted with three 30-ml portions of ether. The combined ethereal extracts were washed with water and saturated salt solution, and dried over anhydrous magnesium sulfate. After filtration, the solvents were removed by distillation and the residue was distilled at reduced pressure to give 0.307 g of **46** and **47** (contaminated with some toluene), bp 99–101° (29 mm). The alcohols were separated by preparative gas chromatography on a 10% Carbowax 20M–KOH (4:1) on 60–80 Chromosorb W column at 90° to give 80 mg of the exo alcohol, **46**: mp 172.5–175.5°; ir (neat) 2.95 (s), 3.37 (s), 6.89 (m), 7.07 (w), 8.32 (w), 8.61 (w), 9.66 (s), 9.83 (s), 10.04 (s), 10.40 (s), 11.67 (w), and 14.35 (w) μ; nmr (CCl_4) τ 6.11 (d, 1 H, J = 4 Hz), 7.72 (s, OH), 7.78–8.63 (m, 9 H), and 8.73 (s, 3 H).

The endo alcohol, **47** (20 mg), was obtained in the same manner: n^{25}D 1.4729; ir (neat) 2.95 (s), 3.36 (s), 3.45 (s), 6.87 (s), 7.45 (m), 7.88 (m), 9.36 (s), and 9.57 (m) μ; nmr (CCl_4) τ 5.83 (complex q, 1 H, J = 8 Hz), 6.80 (s, OH), 7.63–8.63 (m, 9 H), and 8.83 (s, 3 H); exact mass (exo), *m/e* 126.1046; (endo), *m/e* 126.1046 (calcd for $C_8H_{14}O$, *m/e* 126.1044).

Anal. Calcd for $C_8H_{14}O$: C, 76.14; H, 11.18. Found: (exo) C, 75.73; H, 11.19; (endo) C, 76.07; H, 11.21.

***exo*- and *endo*-4-Acetoxy-1-methylbicyclo[3.2.0]heptane (37 and 48, respectively).** The same procedure as is described above for the preparation of the 2-acetoxy derivatives was used. The initial product ratio from the reduction with aluminum isopropoxide was 91:9 (endo/exo). The solution was refluxed for 24 hr to give a 33:67 ratio. In this way, 0.5 g (4.03 mmol) of ketone **45** was reduced to the epimeric mixture of alcohols and then converted to the acetates (0.62 g, 80–90° (24 mm)) in good yield (91%) on treatment with acetyl chloride. Separation by vpc on a 15% butanediol succinate on 45–60 Chromosorb G column at 120° gave 0.097 g (14%) of the endo acetate, **48**, and 0.178 g (26%) of the exo acetate,

37. Endo acetate:[46] $n^{24.5}$D 1.4502; ir (neat) 3.36 (s), 3.46 (m), 5.73 (s), 6.90 (w), 7.27 (m), 8.06 (s), 8.85 (w), and 9.60 (s) μ; nmr (CCl_4) τ 5.08 (complex q, 1 H, J = 8 Hz), 7.80–8.66 (m, 9 H), 7.06 (s, 3 H), and 8.80 (s, 3 H). Exo acetate:[46] $n^{24.5}$D 1.4472; ir (neat) 3.34 (s), 3.45 (m), 5.72 (s), 6.87 (m), 7.26 (m), 8.05 (s), and 9.77 (m) μ; nmr (CCl_4) τ 5.20 (d, 1 H, J = 4 Hz), 7.66–8.58 (m, 9 H), 8.10 (s, 3 H), and 8.76 (s, 3 H).

Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: (exo) C, 71.41; H, 9.51; (endo) C, 71.66; H, 9.64.

2-Methylcyclopentanone (72). A 2-l., three-necked flask, equipped with a mechanical stirrer, a reflux condenser with drying tube, and a pressure-equalizing dropping funnel with nitrogen inlet, was charged with 23.2 g (0.55 mol) of a 57% oil dispersion of sodium hydride under a nitrogen atmosphere. The oil was removed by washing three times with dry ether. After the addition of 400 ml of ether, a solution of 75 g (0.50 mol) of the mixed methyl and ethyl esters of cyclopentanone-2-carboxylic acid (**50**) in 200 ml of ether was added dropwise to the rapidly stirred slurry. During this time an off-white pasty precipitate formed. It was important to have sufficient stirring and solvent to keep the salt mobile. After the mixture was stirred for 15 min, 142 g (1 mol) of methyl iodide in 100 ml of ether was added and the slurry refluxed for 36 hr. The progress of the reaction was followed by gas chromatography on 10% SE-30 silicone rubber. At the end of the reaction, the precipitate was now a finely divided, white solid (NaI). The reaction was then poured onto 300 g of ice and 100 ml of saturated ammonium chloride solution. The two layers were separated and the aqueous layer was extracted three times with 100-ml portions of ether. The combined ethereal extracts were washed with water, and dried over anhydrous magnesium sulfate. After filtration, the ether was removed at reduced pressure to give 80.4 g of crude material.

The crude product was placed in a 500-ml flask, with 300 ml of 48% hydrobromic acid solution, and 7.5 g of sand. The reaction was heated over a steam bath for 2 hr (until no more carbon dioxide evolved). The contents was then poured onto 500 g of ice and extracted three times with 150-ml portions of ether. The combined extracts were dried over anhydrous calcium chloride and filtered. After the solvent was evaporated at reduced pressure, the remaining liquid was distilled, bp 63–64° (53 mm), to give 26.8 g (55%) of 2-methylcyclopentanone (**72**).

2-Methylcyclopenten-3-one (49). A modified procedure of Johnson and coworkers[47] was followed. A 100-ml, three-necked Bantamware flask, equipped with a magnetic stirrer, a reflux condenser with drying tube, and a pressure-equalizing dropping funnel with nitrogen inlet, was charged with 9.80 g (0.1 mol) of 2-methylcyclopentanone (**72**) in 50 ml of dry carbon tetrachloride. A solution of 14.85 g (0.11 mol) of sulfuryl chloride in 15 ml of carbon tetrachloride was added dropwise. The exothermic reaction was moderated with a water bath at room temperature. After the addition was completed, the reaction was stirred for 2–3 hr, washed with 25-ml portions of water, saturated sodium bicarbonate solution, water, and saturated salt solutions, and then dried over anhydrous magnesium sulfate. Analysis by gas chromatography on 10% SE-30 silicone rubber column at 70° showed that none of the starting material remained. The solution was filtered and the carbon tetrachloride was removed by distillation. During this time, the clear solution turned dark red with the evolution of hydrochloric acid. Distillation at reduced pressure gave 7.62 g (79%) of pure 2-methylcyclopenten-2-one (**49**): bp 73–75° (32 mm); $n^{23.0}$D 1.4755 [lit.[47] bp 48–50° (14 mm); n^{20}D 1.4744].

6,7-Dichloro-1-methylbicyclo[3.2.0]heptan-2-one (51). The same procedure was used as described above for **41**. The irradiation of 7.0 g (0.073 mol) of **49** was complete in 9 hr. Worked up as before, the compounds were distilled to give 9.19 g (65%) of **51**, bp 61–67° (0.07 mm).

1-Methyl-2,2-dioxolanebicyclo[3.2.0]hept-6-ene (73). The same procedure was used as described above for **43**. The ketone, **51** (9.19 g, 47.6 mmol), was converted to the corresponding ketal, **74**, with some difficulty due to the steric hindrance of the α-methyl group. Distillation gave 8.46 g (76%) of a mixture of the four isomeric ketals, **74**, bp 75–85° (0.07 mm). Dechlorination of 10.35 g (0.044 mol) of **74** with sodium gave two products. The desired unsaturated ketal, **73** (87–90° (19 mm)), was obtained in 43% yield (3.16 g), along with an unidentified product (2.51 g). The ketal was further purified on 10% SE-30 on a column of 60–80 Chromosorb W at 110°: $n^{17.0}$D 1.4793; ir (neat) 3.35 (s), 3.44 (m), 7.60 (s), 8.59 (s), 8.91 (m), 9.33 (s), 9.57 (s), 10.61 (m), 13.24 (w), and 13.70 (s) μ; nmr (CCl_4) τ 3.85 and 4.04 (2 d, AB, 2 H, J = 3 Hz), 6.13 (unresolved s, 4 H), 7.25 (m, 1 H), 7.73–8.37 (m, 4 H), and 8.87 (s, 3 H); exact mass, m/e 166.0995 (calcd for $C_{10}H_{14}O_2$, m/e 166.0993).

1-Methyl-2,2-dioxolanebicyclo[3.2.0]heptane (52). The hydrogenation of 1.23 g (7.41 mmol) of **73**, as described above for **43**, gave 1.14 g (92%) of **52** after distillation: bp 99–100° (22 mm); n^{17}D 1.4716; ir (neat) 3.33 (s), 3.42 (m), 8.13 (m), 8.62 (m), 8.89 (s), 9.47 (s), 9.80 (m), 10.24 (m), and 10.53 (m) μ; nmr (CCl_4) τ 6.18 (s, 4 H), 7.66–8.75 (m, 9 H), and 8.94 (s, 3 H).

Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.24; H, 9.55.

1-Methylbicyclo[3.2.0]heptan-2-one (75). The same procedure, as described above for **45**, was followed to convert 1.14 g (6.78 mmol) of the ketal, **52**, to 0.68 g (81%) of the desired ketone, **75**: bp 75–77° (21 mm); n^{17}D 1.4638; ir (neat) 3.37 (s), 3.46 (m), 5.75 (s), 6.89 (m), 7.09 (w), 7.57 (w), 8.75 (w), 9.10 (m), 9.58 (m), and 11.32 (w) μ; nmr (CCl_4) τ 7.24–7.83 (m, 4 H), 7.90–8.40 (m, 5 H), and 8.88 (s, 3 H); exact mass, m/e 124.0890 (calcd for $C_8H_{12}O$, m/e 124.0888).

The 2,4-dinitrophenylhydrazone derivative was prepared from **75**, mp 132.5–133.5°.

Anal. Calcd for $C_{14}H_{16}N_4O_4$: C, 55.26; H, 5.30; N, 18.41. Found: C, 55.09; H, 5.33; N, 18.29.

Epimeric *exo*- and *endo*-2-Hydroxy-1-methylbicyclo[3.2.0]heptane (53 and 54, respectively). The same procedure was used as was described for the reduction of the ketone, **45**. Conversion of 0.25 g (2.02 mmol) of 1-methylbicyclo[3.2.0]heptan-2-one (**75**) to the epimeric alcohols (0.24 g), bp 91–92° (28 mm), was accomplished in good yield (96%). Analysis by gas chromatography showed the ratio of endo to exo alcohols was 99:1.

Epimerization of *endo*- and *exo*-2-Hydroxy-1-methylbicyclo[3.2.0]heptane (54 and 53). Using aluminum isopropoxide, as described above for **46** and **47**, the alcohols were epimerized in 17 hr to give 0.17 g (83%) of **54** and **53** with an endo/exo ratio of 62:38. The alcohols, however, could not be preparatively separated, and were isolated as the acetates.

***exo*- and *endo*-2-Acetoxy-1-methylbicyclo[3.2.0]heptane (38 and 55, respectively).** A 100-ml, three-necked Bantamware flask was charged with 0.355 g (2.86 mmol) of 1-methylbicyclo[3.2.0]heptan-2-one (**75**), 1.28 g (6.30 mmol) of anhydrous aluminum isopropoxide, and 30 ml of isopropyl alcohol. The stirred reaction was heated until the isopropyl alcohol began to distill slowly, while more alcohol was added to replace that which was lost. Aliquots were removed and shaken with ether and an equal amount of 5% aqueous sodium hydroxide, then analyzed by vpc on a 5% XF-1150 on 60–80 Chromosorb G column until no ketone remained (1.5 hr). The ratio of endo to exo alcohols was 68:32. The solution was immediately cooled and poured into 50 ml of ether, and washed with 50 ml of 5% aqueous sodium hydroxide. The aqueous layer was extracted with two 25-ml portions of ether, and the combined ethereal extracts were washed with water and brine. After drying over anhydrous sodium sulfate and filtering, the ether was removed by distillation and the remaining isopropyl alcohol removed at reduced pressure to give 0.40 g of the mixture of **53** and **54**.

To an ice-cold solution of the mixture of alcohols in 10 ml of dry pyridine was added 0.45 g (5.73 mmol) of acetyl chloride. After swirling for several minutes, the reaction was stored at 5° for 24 hr. The contents of the flask was then poured into 150 ml of water and extracted with three 35-ml portions of chloroform. The combined extracts were washed with dilute hydrochloric acid, water, saturated sodium bicarbonate solution, water, and brine, and then dried over anhydrous magnesium sulfate. After filtering, the solvent was removed by careful distillation through a metal-helices-packed column. The residue was distilled in a molecular still (80–90° (24 mm)) to give 0.38 g (79%) of a mixture of acetates. Gas chromatographic analysis with a 15% diethylene glycol succinate on 60–80 Chromosorb P column at 120° indicated that the ratio was the same as that of the alcohols. The acetates were isolated by preparative gas chromatography using a column of 25% diethylene glycol succinate on 60–80 Chromosorb P at 140° to give 0.113 g (23%) of the

(46) The exo and endo stereochemical assignments were based on the α-hydroxy and α-acetoxy proton coupling constants and *via* comparison of the spectral properties of *endo*- and *exo*-2-hydroxybicyclo[3.2.0]-heptane and *endo*- and *exo*-2-acetoxybicyclo[3.2.0]heptane prepared by J. M. Hornback, Ph.D. Dissertation, The Ohio State University, 1968: *exo*-2-acetoxybicyclo[3.2.0]heptane, nmr τ 5.14 (d, 1 H, J = 4 Hz); *endo*-2-acetoxybicyclo[3.2.0]heptane, nmr τ 5.06 (complex q, 1 H, J = 8 Hz).

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endo acetate, **55**, and 0.056 g (12%) of the exo acetate, **38**. Exo acetate:[46] ir (neat) 3.31 (s), 3.42 (w), 5.71 (s), 6.90 (w), 7.28 (m), 7.96 (s), 8.06 (s), 9.56 (w), 9.80 (m), and 10.32 (m) μ; nmr (CCl_4) τ 5.23 (d, 1 H, J = 4 Hz), 7.66–8.66 (m, 9 H), 8.07 (s, 3 H), and 8.88 (s, 3 H). Endo acetate:[46] $n^{24.5}D$ 1.4501; ir (neat) 3.33 (s), 3.44 (m), 5.72 (s), 6.89 (w), 7.25 (m), 7.90 (s), 8.05 (s), 8.22 (m), and 9.60 (s) μ; nmr (CCl_4) τ 5.41 (complex q, 1 H, J = ~9 Hz), 7.70–8.70 (m, 9 H), 8.03 (s, 3 H), and 8.82 (s, 3 H).

Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: (exo) C, 71.02; H, 9.57; (endo) C, 70.90; H, 9.63.

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New Synthetic Methods. A Rational Synthesis of 7,8-Diazatetracyclo[3.3.0.0^{2,4}.0^{3,6}]oct-7-ene[1]

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Abstract: Alkylation of sodium cyclopentadienide with *N*-(bromomethyl)benzamide followed by Diels–Alder addition of dimethyl azodicarboxylate generated dimethyl 7-*anti*-benzamidomethyl-2,3-diazabicyclo[2.2.1]hept-5-ene-2,3-dicarboxylate. Nitrosation followed by base converted the benzamido group to a diazo grouping. Quenching of this diazo compound with acetic acid produced the 7-*anti*-acetoxymethyl-2,3-diazabicyclo[2.2.1]-hept-5-ene-2,3-dicarboxylate also available by an analogous alkylation Diels–Alder route using bromomethyl acetate. This quench served to allow assignment of stereochemistry at C-7. Carbene generation by photolysis of the diazo compound led by double bond insertion to dimethyl 7,8-diazatetracyclo[3.3.0.0^{2,4}.0^{3,6}]octane-7,8-dicarboxylate. Hydrolysis, decarboxylation, and oxidation by cupric chloride generated the title compound. The flexibility of the approach should permit applicability to the all carbon system as well.

A continuing challenge for synthetic organic chemistry resides in the construction of the valence tautomers of cyclic polyenes. Among the unlimited number of candidates having the formula $(CH)_n$, the isomers of benzene, $(CH)_6$, and cyclooctatetraene, $(CH)_8$, hold special interest. In spite of the great stability of benzene and the high degree of strain embodied in its valence tautomers, two of the four possible isomers, namely Dewar benzene[4] (**1**) and benzvalene[4b,5] (**2**), had been synthesized at the initiation of our work. Although substituted derivatives of all four were known,[6] the parent prismane[7] (**3**) and 3,3′-biscyclopropenyl[8] (**4**) remained undetected in several attempts at their generation.[9] Similarly, many of the 18 possible[10] $(CH)_8$ isomers have been prepared, but the most highly strained member of this series, tetracyclo[3.3.0.0^{2,4}.0^{3,6}]oct-7-ene (**5**), is known only in the form of derivatives.[11]

Encouraged by the then recent synthesis of Dewar benzene,[4a] we were led in 1965 to attempt a synthesis of the parent prismane molecule. In the course of this

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(2) Henry and Camille Dreyfus Teacher-Scholar Grant Recipient.

(3) National Science Foundation and National Institutes of Health Predoctoral Fellow.

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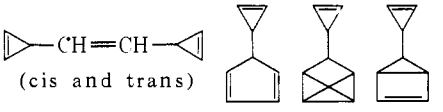

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