6.23, EtOH). **9**-(*R,S*): thick oil, R_f 0.30 (B); $[\alpha]^{25}_D$ -8.6° (*c* 6.1, EtOH).

2(*S*)-[Bis(2-chloroethyl)amino]-3-[(*S*)-α-methylbenzyl]-1,3,2-oxazaphosphorinane 2-Oxide [7-(*S,S*)] and Its Diastereomers 7-(*S,R*), 7-(*R,R*), and 7-(*R,S*). To a stirred solution of thionyl chloride (7.14 g, 60 mM) in dichloromethane (30 mL) was added dropwise a solution of **9**-(*S,S*) (6.57 g, 20 mM) and hexamethylphosphoric triamide (5.4 g, 30 mM) under cooling in an ice bath. The mixture was then refluxed for 30 min. After the mixture was cooled, the excess thionyl chloride was decomposed by the addition of a mixture of acetic acid (3 mL) and MeOH (15 mL). The solvent was evaporated, and water (200 mL) was added to the residue. The mixture was extracted with carbon tetrachloride. The organic layer was washed (10% HCl, water, 10% NaOH, water) and dried (Na_2SO_4). The solvent was removed by evaporation, and the residue was purified on a short silica gel column [benzene–$CHCl_3$–acetone (10:2:1)] to afford thick colorless oil of **7**-(*S,S*): 6.3 g (86%); $[\alpha]^{25}_D$ -70° (*c* 2.6, benzene). The other diastereomers were similarly prepared: **7**-(*S,R*), $[\alpha]^{25}_D$ -0.94° (*c* 1.28, benzene); **7**-(*R,R*), $[\alpha]^{25}_D$ +73.5° (*c* 8.3, benzene); **7**-(*R,S*), $[\alpha]^{25}_D$ +1.2° (*c* 2.6, benzene). These compounds were identified by the direct comparison with the authentic samples prepared by the Stec method[3] (IR, NMR, MS, and TLC).

(*R*)-(+)-Cyclophosphamide [1-*R*(+)] and (*S*)-(-)-Cyclophosphamide [1-*S*(-)]. (1) Hydrogenolysis of **7**-(*S,S*) or **7**-(*R,S*) according to the Stec method[3] afforded **1**-[*R*(+)]: 60–65% yield; mp 67–68 °C (AcOEt–*i*-Pr_2O); $[\alpha]^{25}_D$ +2.48° *c* 10, MeOH). Hydrogenolysis of **7**-(*R,R*) of **7**-(*S,R*) or **7**-(*S,R*) gave **1**-[*S*(-)]: 55–67% yield; mp 67–68 °C (AcOEt–*i*-Pr_2O); $[\alpha]^{25}_D$ -2.46° (*c* (AcOEt–*i*-Pr_2O); MeOH).

(2) 2-(*S*)-[Bis(2-chloroethyl)amino]-3-[(*S*)-α-methylbenzyl]-2-oxo-1,3,2-oxazaphosphorinane [**9**-(*S,S*), 37 g] was dissolved in toluene (300 mL) and cooled in an ice–salt bath. Under stirring with a mechanical stirrer, 37 g of concentrated sulfuric acid was added dropwise at a rate so that the temperature did not exceed 10 °C. After the completion of the addition, the mixture was stirred for 15 min. The mixture was then poured into ice–water (500 mL), hexane (300 mL) was added, and the organic layer was separated. The organic layer was extracted with water (2 × 200 mL). The combined water layer was extracted with chloroform (3 × 200 mL), and the chloroform layer was dried over anhydrous magnesium sulfate and evaporated to dryness under reduced pressure to give crude crystals of (*R*)-(+)-cyclophosphamide. Recrystallization of the crude material from ethyl acetate and isopropyl ether afforded pure (*R*)-(+)-cyclophosphamide: 21 g (81%); mp 67–68 °C; $[\alpha]^{25}_D$ +2.46° (*c* 9.3, MeOH).

Acknowledgment. Valuable discussions and encouragements by Dr. Akio Sonoda of Otsuka Pharmaceutical Co. and Dr. T. Higuchi of Inter$_x$ Research Corp. are greatly acknowledged. We thank Mr. Iwao Miura[1a] for the measurements of ^{1}H NMR (200 mHz) and ^{13}C NMR (50 MHz) spectra and Mr. Hideo Mori[1a] for the mass spectra.

Registry No. (±)-(*R*)-**1**, 60030-72-0; (-)-(*S*)-**1**, 60007-96-7; (*S*)-**5**, 59198-54-8; (*R*)-**5**, 58028-69-6; (*S,S*)-**7**, 58028-73-2; (*S,R*)-**7**, 58028-72-1; (*R,R*)-**7**, 58028-71-0; (*R,S*)-**7**, 58028-70-9; (*S,S*)-**8**, 72578-63-3; (*S,R*)-**8**, 72578-62-2; (*R,R*)-**8**, 73834-61-4; (*R,S*)-**8**, 73834-62-5; (*S,S*)-**9**, 73837-99-7; (*S,R*)-**9**, 73834-60-3; (*R,R*)-**9**, 74457-85-5; (*R,S*)-**9**, 83862-09-3.

Preparation and Acetolysis of 7-Norbornadienylmethyl and (7-Methyl-7-norbornadienyl)methyl Brosylates. An Intramolecular Retro-Diels–Alder Reaction following Laticyclic Participation[1]

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Received May 27, 1982

The title compounds, **19**- and **20**-OBs, respectively, have been prepared and their acetolysis rates and products determined. At 99.2 °C the acetolysis of **19**-OBs ($k_t = 3.63 \times 10^{-6}$ s^{-1}) produces 40% unrearranged acetate, **19**-OAc, by direct displacement and 60% tetracyclo[3.3.0.0^{3,8}.0^{4,6}]oct-7-yl acetate. Under identical conditions **20**-OBs is 97 times as reactive ($k_t = 3.53 \times 10^{-4}$ s^{-1}) and yields 56% of approximately equal amounts of *syn*- and *anti*-1-methyltetracyclo[3.3.0.0^{3,8}.0^{4,6}]oct-7-yl acetates and a total of 44% of a mixture of *endo*-1-methyltricyclo-[3.3.0.0^{2,7}]oct-3-en-6-yl acetate (**28**-OAc) and its retro-Diels–Alder product, 3-(1-methyl-2,4-cyclopentadien-1-yl)-*trans*-1-propenyl acetate (**29**-OAc). Comparison of these results with those of other norbornenyl and norbornadienyl derivatives suggests that unsymmetrical ($2^0 + 2^0 + 1^+$) laticyclic stabilization is enhanced relative to ($2^0 + 1^+$) pericyclic stabilization in the acetolysis of **19**- and **20**-OBs. Such stabilization is appreciably greater in **20**-OBs than in **19**-OBs. The intramolecular retro-Diels–Alder reaction that converts **28**- to **29**-OAc under acetolytic conditions is discussed, and its comparative rarity is emphasized by citing other norbornadienyl derivatives known to behave in this manner.

An appropriately situated, remote double bond enhances solvolytic reactivity and therefore is usually presumed to stabilize the resulting carbocation.[2] The solvolytic reactivity of **2**-OTs is 10^{11} times that of **1**-OTs,[3] for example, while **5**-OBs is $10^{5.3}$ times as reactive as **4**-OBs[4] (Chart I). Whether a second, remote double bond provides additional stabilization is less clear. The doubly unsaturated **3**-Cl is 10^3 times more reactive than **2**-Cl,[5] but **6**-OBs and **5**-OBs react at comparable rates.[6]

In an attempt to understand and predict the overall effect of several such isolated "ribbons" of unsaturation within a molecule, Goldstein and Hoffmann have developed a symmetry-based, topological model for their ho-

(1) Portions of this work have been reported at: (a) The 30th Southeastern Regional Meeting of the American Chemical Society, Savannah, GA, Nov 8–10, 1978, Abstract No. 252; (b) The 178th National Meeting of the American Chemical Society, Washington, DC, Sept 9–14, 1979, Abstract ORGN 142; (c) The Second Chemical Congress of the North American Continent, Las Vegas, NV, Aug 24–29, 1980, Abstract ORGN 360.

(2) For a recent summary with leading references see: Lowery, T. H.; Richardson, K. S. "Mechanism and Theory in Organic Chemistry", 2nd ed.; Harper & Row: New York, 1981; pp 396–436.

(3) Winstein, S.; Shatavsky, M.; Norton, C.; Woodward, R. B. *J. Am. Chem. Soc.* **1955**, *77*, 4183.

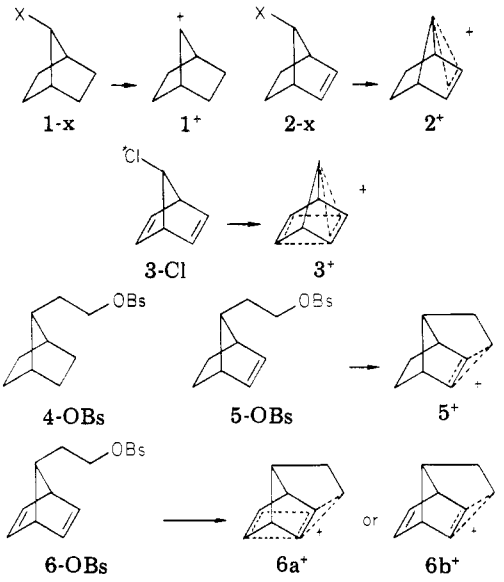
(4) Bly, R. S.; Bly, R. K.; Bedenbaugh, A. O.; Vail, O. R. *J. Am. Chem. Soc.* **1967**, *89*, 880.

(5) Winstein, S.; Ordronneau, C. *J. Am. Chem. Soc.* **1960**, *82*, 2084.

(6) Bly, R. S.; Bly, R. K.; Konizer, G. B.; Jindal, S. P. *J. Am. Chem. Soc.* **1976**, *98*, 2953.

0022-3263/83/1948-0101$01.50/0

Chart I



k_{rel} R-Cl(EtOH, 25 °C): 1 (1.0), 2 (10^{11}), 3 (10^{14})
k_{rel} R-OBs(HOAc, 25 °C): 4 (≤1.0), 5 ($10^{5.3}$), 6 ($10^{5.3}$)

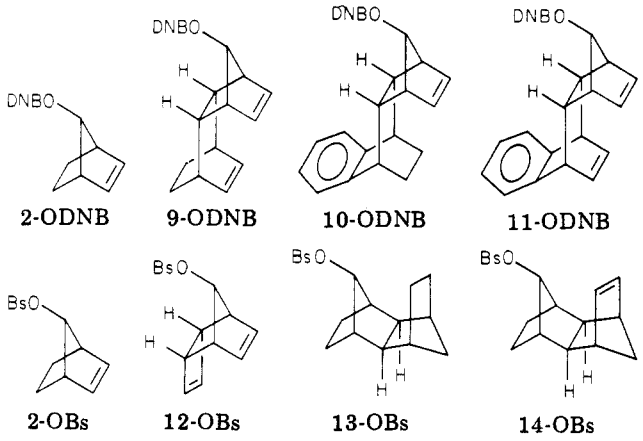
moconjugative interaction.[7] Using this theory, it is possible to analyze and to compare in a qualitative way the "pericyclic" interaction (7) of the two ribbons (the double

bond and the empty p orbital) in a singly homounsaturated carbocation with the unsymmetrical "laticyclic" interaction (8) of the three ribbons in a doubly homounsaturated carbocation. In topological terminology 2^+ and 5^+ are pericyclic (2,0) or ($2^0 + 1^+$) cases while 3^+ and 6^+ are laticyclic (2,2,0) or unsymmetrical, laticyclic ($2^0 + 2^0 + 1^+$) examples. The theory suggests that carbocations of the latter type might be somewhat more stable than those of the former.

This prediction is not clearly supported by experiment. Certainly, 3-Cl is much more reactive than 2-Cl (see above), and 9-ODNB is about $10^{2.3}$ times as reactive as 2-ODNB (Chart II), but 11-ODNB is only 0.9 times as reactive as 10-ODNB[8] (though they are both considerably more reactive than 2-ODNB under comparable conditions), and 12-OBs is but 6.7 times as reactive as 2-OBs.

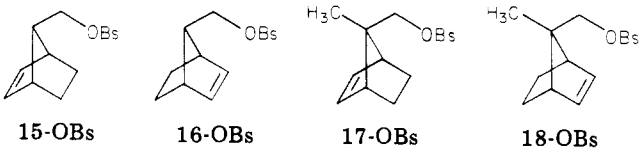
Paquette and Dunkin, after a detailed consideration of these and other data, suggest that "despite the theoretical attractiveness of the concept ... the lack of accelerating influences by the laticyclically positioned double bond ... shows that extended ionic stabilization above that associated with the *anti*-7-norbornenyl moiety is not operative".[8b] They reason that since the "enormous electron demand" at the developing cationic site which is created by solvolysis of a 7-norbornyl derivative can be satisfied quite effectively by bishomoaromatic (pericyclic) delocalization of an *anti*-2-norbornenyl double bond, there is little call for laticyclic stabilization by a more remote double bond.[8b] Only when the developing charge cannot be stabilized in this way, as in the case of 13-OBs, they believe, is electron demand sufficient to promote more

Chart II



k_{rel} R-ODNB (80% actn, 100 °C): 2 (1.0), 9 ($10^{2.3}$), 10 ($10^{2.6}$), 11 ($10^{2.5}$)
k_{rel} R-OBs (HOAc, 25 °C?): 2 (1.0), 12 ($10^{0.8}$), 13 ($10^{-7.5}$), 14 ($10^{-0.5}$)

Chart III



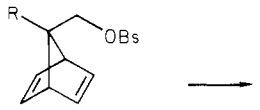
k_{rel} R-OBs (HOAc, 120 °C): 15 (1.0), 16 ($10^{0.13}$), 17 ($10^{0.63}$), 18 ($10^{0.95}$)

distant pericyclic or laticyclic participation, e.g., 14-OBs.[8b] Paquette and Dunkin conclude that: "There would appear to be a definite upper limit to the amount of stabilization which a remote double bond can provide to delocalization of a positive charge by laticyclic interaction. If ... massive levels of stabilization are required, all of the traditional characteristics of neighboring-group influences will be made manifest ... [but] should the potential stabilization of the adjacent bridge not exceed that already provided to the positive charge ..., neighboring-group involvement will cease, and the rate ratios will be effectively leveled".[8b] This latter suggestion is prophetically fulfilled in the solvolyses of 4-, 5-, and 6-OBs.[4,6]

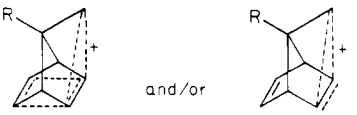
If unsymmetrical ($2^0 + 2^0 + 1^+$) laticyclic stabilization is indeed potentially greater than pericyclic ($2^0 + 1^+$) stabilization and if the analysis of Paquette and Dunkin is correct, participation by a second remote double bond might be expected to become more evident in the solvolysis of a 7-norbornadienylmethyl brosylate. Should concerted ring enlargement be inhibited, electron demand would certainly be great at the developing primary cationic center. Although the absence of appreciable anchimeric effects in the acetolyses of 16- and 18-OBs[9a,c] (Chart III) suggests that the electron deficit at the primary carbon of these relatively unreactive *syn*-7-norbornenylmethyl brosylates is not decreased significantly by pericyclic delocalization,[9a] the formation of substantial amounts of tricyclic products in the case of 18-OBs[9c] hints of possible pericyclic stabilization lurking subliminally at the threshold of kinetic detection. Hoping to ascertain whether the unsymmetrical ($2^0 + 2^0 + 1^+$) laticyclic cations $\mathbf{19a}^+$ and $\mathbf{20a}^+$ are indeed stabilized relative to their pericyclic (2^0

(7) Goldstein, M. J.; Hoffmann, R. *J. Am. Chem. Soc.* **1971**, *93*, 6193.
(8) (a) Battiste, M. A.; Deyrup, C. L.; Pincock, R. E.; Haywood-Farmer, J. *J. Am. Chem. Soc.* **1967**, *89*, 1954. (b) Paquette, L. A.; Dunkin, I. R. *Ibid.* **1975**, *97*, 2243.
(9) (a) Bly, R. K.; Bly, R. S. *J. Org. Chem.* **1966**, *31*, 1577. (b) Berson, J. A.; Gajewski, J. J.; Donald, D. S. *J. Am. Chem. Soc.* **1969**, *91*, 5550. (c) Berson, J. A.; Donald, D. S.; Libbey, W. J. *Ibid.* **1969**, *91*, 5580.

+ 1⁺) counterparts **19b**⁺ and **20b**⁺, we have prepared and investigated the acetolyses of 7-norbornadienylmethyl and 7-methyl-7-norbornadienylmethyl brosylates, **19**- and **20**-OBs, respectively (eq 1). Herein we report the results of this study.



19-OBs, R = H
20-OBs, R = CH_3



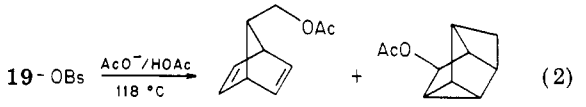
19a⁺, R = H
20a⁺, R = CH_3

and/or

19b⁺, R = H
20b⁺, R = CH_3

(1)

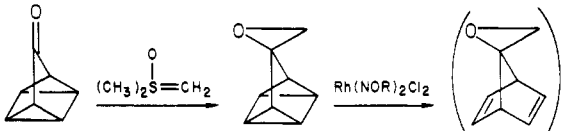
While our work was in progress the independent synthesis and acetolysis of **19**-OBs were communicated by von Angerer.[10] Although no kinetic data were included, we were greatly encouraged by the fact that nearly half of the product is the tetracyclic acetate **21**-OAc (eq 2), a clear implication of laticyclic stabilization!



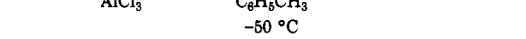
19-OBs $\xrightarrow[118\ °C]{AcO^-/HOAc}$ **19**-OAc + **21**-OAc (2)

Results

Starting Materials. Alcohols **19**- and **20**-OH were prepared from quadricyclanone (**22**) as outlined in eq 3 and 4 and converted into brosylates **19**- and **20**-OBs in the usual manner.[9a]

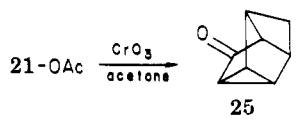


22 $\xrightarrow{(CH_3)_2S{=}CH_2}$ **23** $\xrightarrow{Rh(NOR)_2Cl_2}$ **24** (3)



19-OH $\xleftarrow[AlCl_3]{LiAlH_4}$ (**24**) $\xrightarrow[C_6H_5CH_3,\ -50\ °C]{Al(CH_3)_3}$ **20**-OH (4)

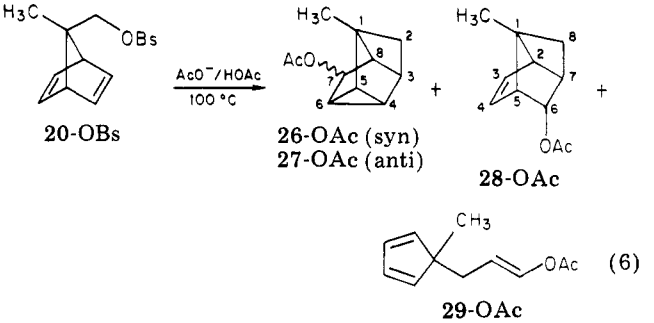
Acetolysis Products. Solvolysis of **19**-OBs at 100 °C in anhydrous acetic acid buffered with 0.024 M sodium acetate gives a mixture consisting of 40% **19**-OAc and 60% **21**-OAc. von Angerer, who carried out the reaction at 118 °C in the presence of 0.033 M sodium acetate, reports 53% **19**-OAc and 47% **21**-OAc. The structures of these two acetates were assigned by von Angerer: **19**-OAc from its identity with the acetylation product of **19**-OH[10] and **21**-OAc by comparison of its ^1H NMR spectrum and that of its oxidation product, **25** (eq 5), with those of several other



21-OAc $\xrightarrow[acetone]{CrO_3}$ **25** (5)

tetracyclooctyl derivatives.[11] The $^{13}C\{H\}$ NMR spectrum of **21**-OAc is identical (see Experimental Section) with that reported by Jefford et al.[12] for 7-tetracyclo[3.3.0.0^{3,8}.0^{4,6}]-octyl acetate prepared in an unequivocal manner from 7-*tert*-butoxynorbornadiene.[12b]

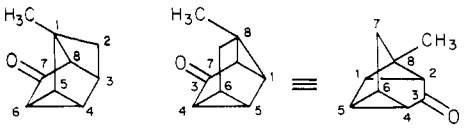
Acetolysis of **20**-OBs at 100 °C gives a mixture of *syn*- and *anti*-1-methyltetracyclo[3.3.0.0^{3,8}.0^{4,6}]oct-7-yl acetates (**26**- and **27**-OAc, respectively), *endo*-1-methyltricyclo[3.3.0.0^{2,7}]oct-3-en-6-yl acetate (**28**-OAc), and 3-(1-methyl-2,4-cyclopentadien-1-yl)-*trans*-1-propenyl acetate (**29**-OAc) (eq 6). The composition of the product mixture,



20-OBs $\xrightarrow[100\ °C]{AcO^-/HOAc}$ **26**-OAc (syn) + **27**-OAc (anti) + **28**-OAc + **29**-OAc (6)

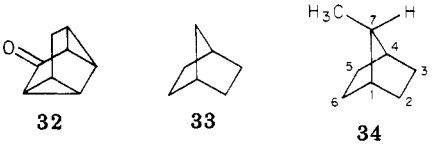
estimated from the ^1H NMR spectrum of the crude solvolysis mixture (see Experimental Section), is time and temperature dependent (Figure 1). An attempt to separate the products by GLC yielded two fractions: an equimolar mixture of **26**- and **27**-OAc and pure **29**-OAc. The tricyclic acetate **28**-OAc is converted to **29**-OAc by gas chromatography (see below). The structures of these products were assigned as follows.

The two tetracyclic acetates, **26**- and **27**-OAc, collected together as a mixture by GLC, where shown to be present in essentially equal amounts by analytical GLC on a 20-ft Carbowax 20M capillary column where they are completely resolved (see Experimental Section). The infrared, ^1H NMR, and $^{13}C\{H\}$ NMR spectra of this mixture reveal the total absence of double bonds, thus indicating the tetracyclic nature of both components. In addition to the acetate absorptions, the $^{13}C\{H\}$ spectrum exhibits a total of 17 resonances, 16 of which appear in "pairs" (Table IV). This suggests that both of these two components are asymmetric but that they probably have similar skeletal structures. In fact, reduction of this mixture with lithium aluminum hydride followed by Jones oxidation yields a single ketone having nine nonequivalent carbons. Either of the two mechanistically acceptable possibilities, **30** or **31**, can, a priori, be reconciled with the spectral data of this ketone.



30 **31**

To decide between them and thus to confirm the skeletal structure of **26**- and **27**-OAc, we compared the $^{13}C\{H\}$ NMR spectra of our methylated ketone and acetates with those of several nonmethylated tetracyclo[3.3.0.0^{3,8}.0^{4,6}]oct-7-yl derivatives,[12] including **21**-OAc and **25**, and with that of tetracyclo[3.3.0.0^{2,8}.0^{4,6}]octan-3-one (**32**), a sample of which



32 **33** **34**

(10) von Angerer, E. *Tetrahedron Lett.* **1977**, 3245.
(11) Freeman, P. K.; Ziebarth, T. D.; Rao, V. N. M. *J. Org. Chem.* **1973**, *38*, 3823.
(12) (a) Jefford, C. W.; Rossier, J.-C.; Zuber, J. A.; Suri, S. C.; Mehta, G. *Tetrahedron. Lett.* **1980**, *21*, 4081. (b) Kwantes, P. M.; Klumpp, G. W. *Ibid.* **1976**, 707.

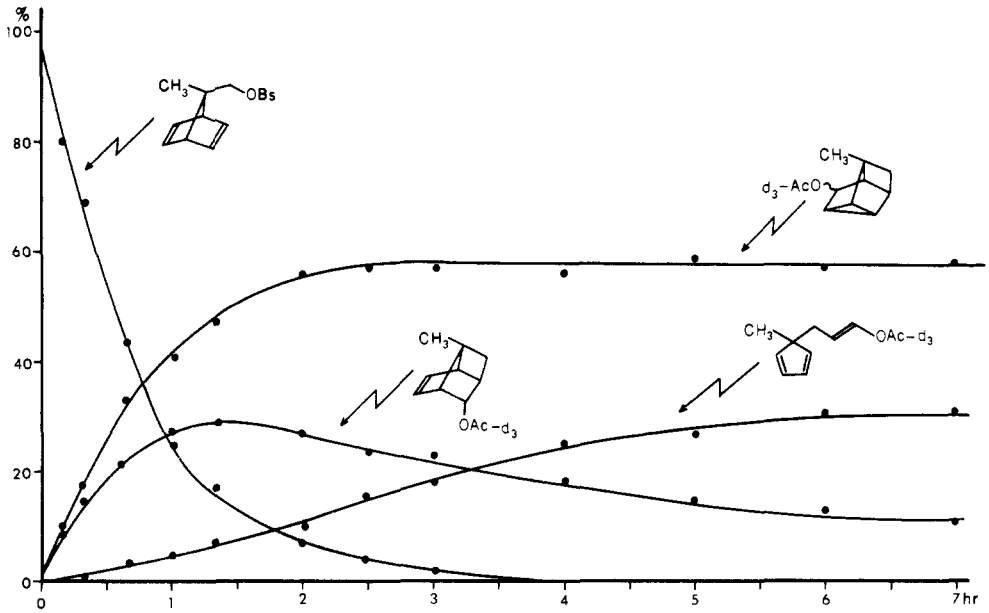


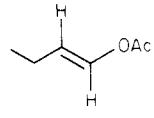
Figure 1. Relative concentration of reactant and products during the perdeuterioacetolysis of (7-methyl-7-norbornadienyl)methyl brosylate (**20**-OBs) at 99.2 °C as determined by repetitive ^1H NMR scans at 25 °C.

was kindly provided by Professor Jefford.[13] The chemical shift differences caused by the methyl group in our methylated acetates and ketone are compared with those due to the 7-methyl substituent in norbornane,[14] i.e., with those of **33** and **34**, in Table IV. From these collations it is clear that the epimeric acetates formed from **20**-OBs are tetracyclo[3.3.0.$0^{3,8}$.$0^{4,6}$]oct-7-yl rather than tetracyclo-[3.3.$0^{2,8}$.$0^{4,6}$]oct-3-yl derivatives.[15]

Quantitative catalytic hydrogenation of **29**-OAc reveals the presence of three carbon-to-carbon double bonds. That one of these is present as an enol acetate is suggested by the fact that mild alkaline hydrolysis of **29**-OAc (eq 7)

$$\textbf{29}\text{-OAc} \xrightarrow[H_2O,\ 25\ ^\circ C]{NaHCO_3} RCH_2CHO \qquad (7)$$

yields an aldehyde as evidenced by the appearance of an aldehydic hydrogen resonance in the ^1H NMR spectrum of the hydrolysis mixture. The infrared and ^1H NMR spectra of **29**-OAc exhibit absorptions and vinyl-hydrogen coupling constants, respectively, similar to those of *trans*-1-butenyl acetate (**35**;[17] cf. Experimental Section),



35

implying a trans arrangement about the double bond of the enol acetate. The $^{13}C\{H\}$ NMR spectrum reveals two pairs of equivalent vinylic carbons, two other nonequivalent vinylic carbons, and three nonequivalent saturated carbons. In the off-resonance decoupled carbon-13 spectrum, all of the vinylic carbons appear as doublets while the saturated carbons appear as a singlet, a triplet, and a quartet, respectively. Taken collectively, these data suggest that **29**-OAc is 3-(1-methyl-2,4-cyclopentadien-1-yl)-*trans*-1-propenyl acetate.[18] More detailed data and individual peak assignments are included in the Experimental Section.

Thus far we have been unable to isolate **28**-OAc free of the other acetolysis products. While column chromatography on silica gel enabled us to separate **29**-OAc, it did not individually resolve **26**-, **27**-, and **28**-OAc. A 400-MHz ^1H NMR spectrum of this three-component mixture, in addition to resonances due to the epimeric tetracyclic acetates **26**- and **27**-OAc, clearly shows completely or partially resolved signals attributable to each type hydrogen in **28**-OAc. We can distinguish and unequivocally assign the vinyl, the C-6, the C-5 bridgehead, the 1-methyl, and the acetate hydrogens (see Experimental Section). The 20-MHz $^{13}C\{H\}$ spectrum of this mixture shows eight resonances (in addition to those of **26**- and **27**-OAc) which can be attributed to the eight nonequivalent carbons of **28**-OAc.

The most convincing evidence of the structure of this tricyclic acetate is probably the facility of its conversion to **29**-OAc. When a triene-free, liquid chromatography

(13) Private communication from Prof. C. W. Jefford dated Dec 8, 1980.

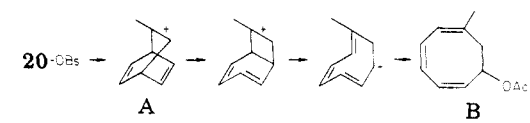
(14) Grutzner, J. L.; Jautelat, M.; Dence, J. B.; Smith, R. A.; Roberts, J. D. *J. Am. Chem. Soc.* **1970**, *92*, 7107.

(15) Were the latter to be the case, the mean change in chemical shift attributable to the methyl group would be 9.8 rather than 3.3 ppm, and the three low-field resonances would have to have been shifted by at least 19.3, 18.9, and 18.6 ppm, respectively (Table IV). These effects are too large to be caused by the replacement of a hydrogen with a methyl,[16] thus we discount tetracyclo[3.3.0.$0^{2,8}$.$0^{4,6}$]octane as the skeletal structure of the tetracyclic acetolysis products.

(16) Levy, G. C.; Lichter, R. L.; Nelson, G. L. "Carbon-13 Nuclear Magnetic Resonance Spectroscopy", 2nd ed.; Wiley-Interscience: New York, 1980; p 50 ff, Table 3.7. The fact that the average chemical shift caused by the 7-methyl on norbornane is 1.43 ppm, considerably less than the 3.30 ppm observed here, probably simply reflects the greater number of different "routes" between methyl and a given atom that obtains in a small tetracyclic carbon framework; cf. problem 3.3, p 57.

(17) Bigley, B. D.; Paying, D. W. *J. Chem. Soc.* **1965**, 3974. (b) Dauben, W. G.; Wolf, R. E. *J. Org. Chem.* **1970**, *35*, 2361. (c) Jackman, L. M.; Sternhell, S. "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry", 2nd ed.; Pergamon Press: Oxford, 1969; p 301 ff.

(18) This product was initially thought to be a 1-methyl-1,3,5-cyclooctatrien-7-yl acetate[1c] (B) formed by ring enlargement through the Möbius-like 2-methyl-2-bicyclo[2.2.2]octadienyl cation (A). This is clearly not the case; no products from A are detected in the acetolysis mixture.



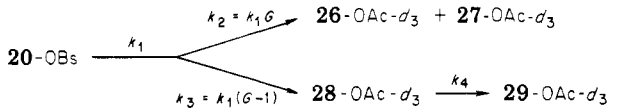
A B

Table I. Titrimetric First-Order Rate Constants and Activation Parameters for the Acetolysis of the 7-Norbornadienylmethyl Brosylates 19- and 20-OBs[a]

compd	temp, °C	10^4k_t, s^{-1}	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, eu
19-OBs	115.0	0.173	27.9	−8.8
		0.179		
	99.2	0.0363		
		0.0362		
20-OBs	99.2	3.56	26.9	−2.6
		3.50		
	83.8	0.768		
	70.5	0.154		

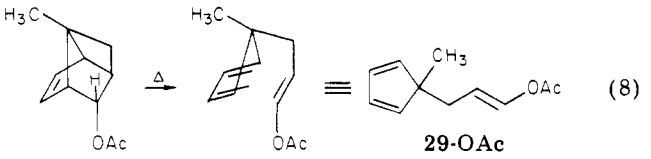
[a] Solutions contained 1% acetic anhydride, 0.025–0.027 M ROBs, and 0.027–0.030 M NaOAc in acetic acid.

Scheme I. Perdeuterioacetolysis of 7-Methyl-7-norbornenylmethyl Brosylate[a]



[a] G = the fraction of perdeuterio acetates 26- and 27-OAc-d_3.

fraction of the acetolysis mixture is subjected to gas chromatography, 29-OAc is formed. Since both tetracyclic acetates, 26- and 27-OAc, are stable to this treatment, it is apparent that 29-OAc is formed from 28-OAc, presumably by a thermally initiated retro-Diels–Alder reaction (eq 8) which probably occurs in the heated injection port of the gas chromatograph.



28-OAc 29-OAc (8)

Acetolysis Rates. First-order titrimetric rate constants, k_t, for the reaction of 19- and 20-OBs in anhydrous, buffered acetic acid and the derived activation parameters are listed in Table I.

When the perdeuterioacetolysis of 0.23 M 20-OBs is carried out in a sealed NMR tube, the relative concentrations of the starting material and each of the products can be determined as a function of time by proton magnetic resonance (cf. Figure 1). In this manner it is possible to observe the build up of 28-OAc-d_3 and its subsequent conversion to 29-OAc-d_3.

The enol acetate 29-OAc is not in equilibrium with the tricyclic acetate 28-OAc under these conditions. The ^{1}H NMR spectrum of a solution of pure 29-OAc in perdeuterioacetic acid buffered with sodium perdeuterioacetate and heated in a sealed NMR tube at 100 °C for 12 h is virtually unchanged. No 28-OAc can be detected.

On the assumption that the perdeuterioacetolysis follows the course outlined in Scheme I, rate constants for the disappearance of 20-OBs (k_1), for the formation of 26- and 27-OAc-d_3 (k_2), and for the formation of 28-OAc-d_3 (k_3) and its conversion to 29-OAc-d_3 (k_4) can be calculated[4,19] (cf. Experimental Section). The rate constants of the pmr-determined perdeuterioacetolysis at three different temperatures and the derived activation parameters are listed in Table II.

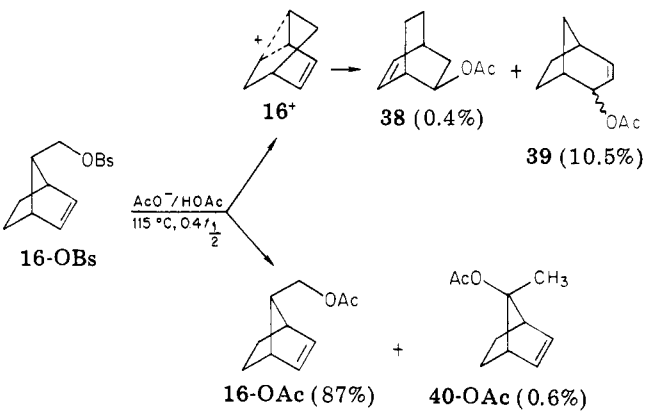
(19) Moore, J. W.; Pearson, R. G. "Kinetics and Mechanism", 3rd ed.; Wiley: New York, 1981; p 290 ff.

Table II. ^{1}H NMR Estimated Rate Constants for the Perdeuterioacetolysis of (7-Methyl-7-norbornadienyl)methyl Brosylate (20-OBs)[a]

temp, °C	G[b]	10^4k_1, s^{-1}[c]	10^4k_2, s^{-1}[d]	10^4k_3, s^{-1}[e]	10^4k_4, s^{-1}[f]
99.2	0.57	3.6	2.05	1.6	2.5
83.8	0.57	0.96	0.55	0.41	0.61
70.5	0.58	0.21	0.12	0.088	0.098

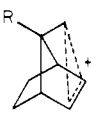
[a] 0.23 M 20-OBs and 0.30 M sodium perdeuterioacetate in perdeuterioacetic acid. [b] Fraction of tetracyclic acetates 26- and 27-OAc-d_3. [c] $\Delta H^{\ddagger}$ = 24.4 kcal/mol; $\Delta S^{\ddagger}$ = −9.0 eu. [d] $\Delta H^{\ddagger}$ = 24.4 kcal/mol; $\Delta S^{\ddagger}$ = −10.2 eu. [e] $\Delta H^{\ddagger}$ = 24.9 kcal/mol; $\Delta S^{\ddagger}$ = −9.2 eu. [f] $\Delta H^{\ddagger} \approx 28$ kcal/mol, $\Delta S^{\ddagger} \approx -0.3$ eu.

Scheme II



Discussion

The introduction of a second, remote double bond increases the unimolecular solvolytic reactivity of a *syn*-7-norbornenylmethyl derivative. The dissected kinetic data in Table III indicate that the ionization rate of norbornadienylmethyl brosylate in acetic acid is about 10 times that of the syn analogue; i.e., k_r (19-OBs)/k_r(16-OBs) = 9.5. As anticipated from the earlier data of Berson et al.[9c] the effect is larger in the case of the 7-methylated derivative: k_r(20-OBs)/k_r(18-OBs) = 34. Since a substantial portion of the unimolecular acetolysis product in each of the norbornadienyl cases is tetracyclic, these rate accelerations presumably result from unsymmetrical ($2^0 + 2^0 + 1^+$) laticyclic stabilization of the developing cations **19a**$^+$ and **20a**$^+$, respectively. Clearly, the additional double bond stabilizes the weakly coupled, pericyclic, norbornenylmethyl cations **36**$^+$ and **37**$^+$ more effectively than

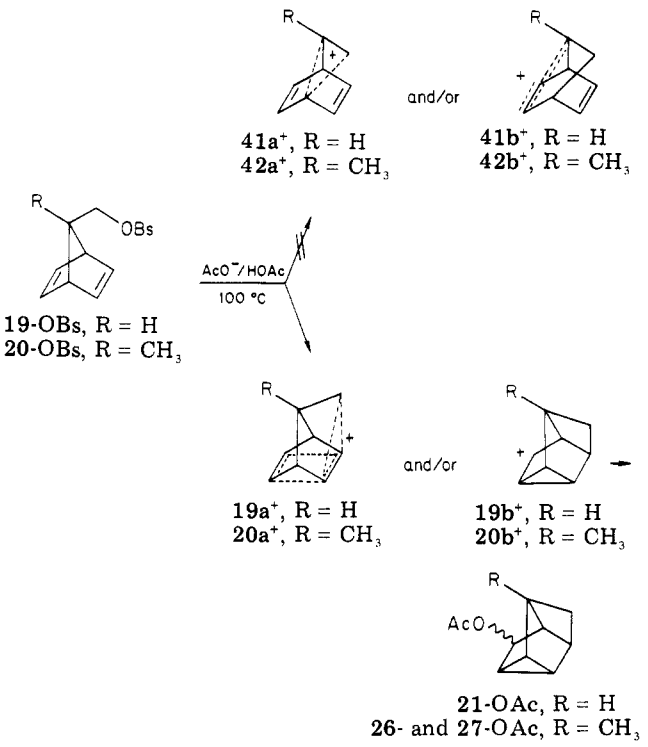


36$^+$, R = H
37$^+$, R = CH_3

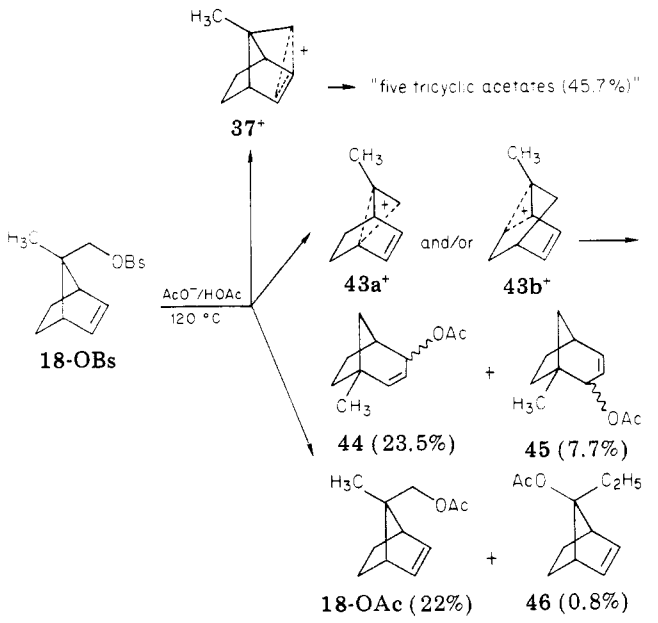
it does the strongly coupled β-(7-norbornenyl)ethyl cation, **5**$^+$.[4] Thus, our data support Paquette and Dunkin's analysis[8b] though perhaps less forcefully than we (or they) might have hoped.

Not only does the additional, remote double bond accelerate the acetolysis of 19-OBs relative to that of 16-OBs but it also alters dramatically the course of the unimolecular reaction (Scheme II). Whereas ring enlargement via the skewed bicyclooctenyl cation **16**$^+$ occurs in the case of 16-OBs,[9a,b] ring closure to the highly strained,[20] tetra-

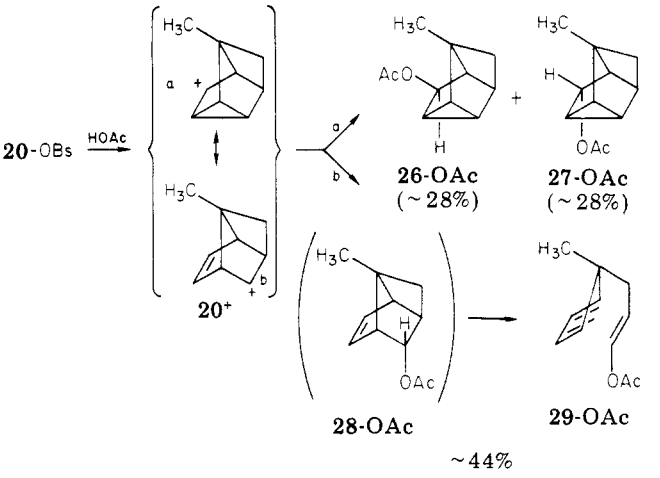
Scheme III



Scheme IV



Scheme V

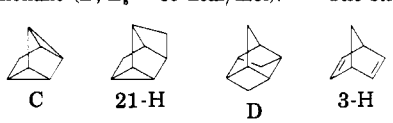


cyclic acetate **21**-OAc dominates the solvolysis of **19**-OBs. In this latter case, we estimate from kinetic data (Table III) that the transition state for ring enlargement, presumably via the Möbius-type bicyclooctadienyl cation **41**$^+$ (Scheme III), is at least 2.5 kcal/mol less favorable than that of ring closure via **19**$^+$. We presume that this difference is due largely[22] or completely to increased stabilization of **19a**$^+$ and/or **19b**$^+$ relative to **16**$^+$.

The 7-methyl and the adjacent double bond of **20**-OBs act synergistically to enhance its unimolecular solvolysis rate. Were the effects merely multiplicative, i.e., independent of each other, **20**-OBs should be $[k_r(\textbf{19}\text{-OBs})k_r(\textbf{18}\text{-OBs})]/[k_r(\textbf{16}\text{-OBs})]^2$ or ~360 times as reactive as **16**-OBs. It is actually $k_r(\textbf{20}\text{-OBs})/k_r(\textbf{16}\text{-OBs})$ or ~1300 times more reactive. Apparently, the methyl group promotes laticyclic stabilization of **20**$^+$ more effectively than it does pericyclic stabilization of **37**$^+$. We presume the effect to be steric in origin.[9c]

As our incorrect preliminary report illustrates,[1c,18] we were unprepared for the combined impact of the 7-methyl group and the remote double bond on the acetolysis course of **20**-OBs. Berson et al.[9c] had found that the acetolysis of **18**-OBs not only produces substantial amounts of tricyclic acetates via ring closure but also is accompanied by less solvolytic displacement and more ring enlargement than is observed in the case of **16**-OBs (e.g., Scheme IV). Thus, we had naively expected that the methyl group in **20**-OBs might induce some ring enlargement via **42**$^+$ during acetolysis. It does not. Instead, after promoting laticyclic stabilization by the remote double bond, the 7-methyl group hinders exo attack by nucleophile at "a" of the resulting cation, **20**$^+$ (Scheme V), causing a decrease in the relative amount **26**-OAc and an increase in the proportion of **27**- and **28**-OAc produced by endo attack at a and b, respectively. The endocyclic double bond of **28**-OAc then provides a low-energy path of strain relief for this unstable[23] tricyclic ester, an intramolecular retro-Diels–Alder

(20) The "strain energy" of tetracyclo[3.3.0.0^{3,8}.0^{4,6}]octane (**21**-H) is apparently not known but may be intermediate between those of tetracyclo[2.2.1.0^{2,6}.0^{3,5}]heptane (C; E_s = 97.1 kcal/mol)[21a] and tetracyclo[4.3.0.0^{3,9}.0^{4,7}]nonane (D; E_s = 85 kcal/mol).[21b] The strain energy of

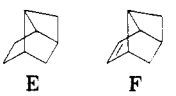


bicyclo[2.2.1]heptadiene (**3**-H) is estimated to be 30.7 kcal/mol.[21a] The enthalpy of isomerization of **3**-H to C is -26 kcal/mol.[21c] Clearly, the acetolytic conversion of **19**-OBs to **21**-OAc must be a kinetically controlled, endothermic process accompanied by a substantial increase in strain energy.

(21) (a) Osawa, E.; Aigami, K.; Inamoto, Y. *J. Org. Chem.* **1977**, *42*, 2621; cf. Table I, footnote *ee*. (b) Osawa, E.; Aigami, K.; Inamoto, Y. *J. Chem. Soc. Perkin Trans. 2* **1979**, 181. (c) Wiberg, K. B.; Connon, H. A. *J. Am. Chem. Soc.* **1976**, *98*, 5411.

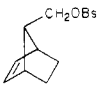
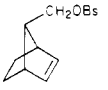
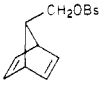
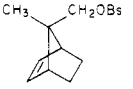
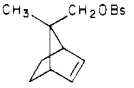
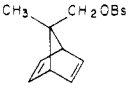
(22) The extent to which this minimum difference may reflect some destabilization of the Möbius cation **41**$^+$ relative to **16**$^+$ is not known.

(23) The strain energy of tricyclo[3.3.0.0^{2,7}]octane (E) is estimated to be at least 48.3 kcal/mol,[24] while the difference in strain energy of norbornene and norbornane is at least 5 kcal/mol;[21a] thus, the strain energy of tricyclo[3.3.0.0^{2,7}]oct-2-ene (F) is probably at least 53 kcal/mol.



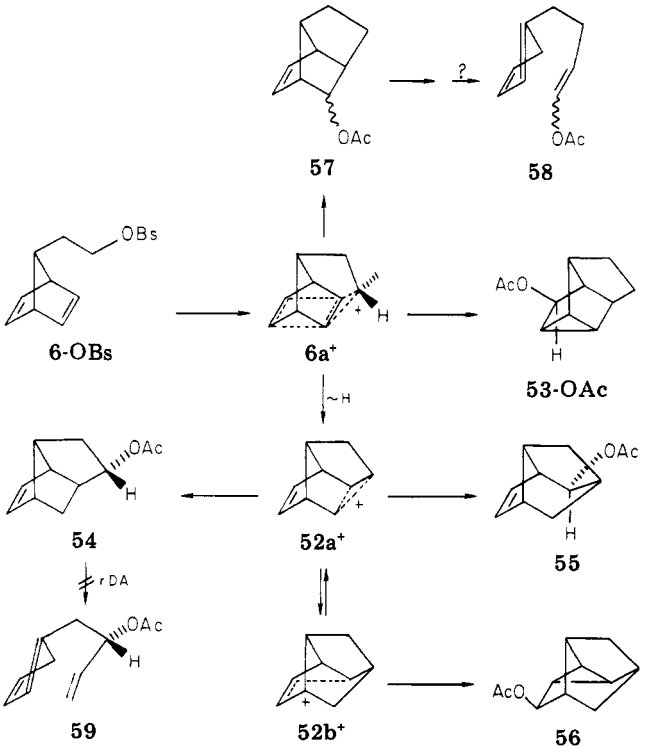
(24) Engler, E. M.; Andose, J. D.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1973**, *95*, 8005.

Table III. Titrimetric Rate Constants for the Formation of Rearranged and Nonrearranged Products during the Acetolysis of 7-Norbornenyl- and 7-Norbornadienylmethyl Brosylates at 120.4 °C

compd	$10^5 k_t$, s^{-1}	fraction of primary acetate	$10^5 k_d$,[g] s^{-1}	$10^5 k_r$,[h] s^{-1}	rel k_r
 15-OBs	1.05[a]	0.92[d]	0.97	0.084	1.0
 16-OBs	1.43[a]	0.87[d]	1.2	0.19	2.3
 19-OBs	3.07[b]	0.40[e]	1.2	1.8	21
 17-OBs	4.45[c]	0.33[c,f]	1.5	3.0	36
 18-OBs	9.40[c]	0.22[c,f]	2.1	7.3	87
 20-OBs	250[b]	<0.01	<3	250	3000

[a] Extrapolated from the data of ref 9a. [b] Extrapolated from the data of Table I. [c] Reference 9c. [d] At 115 °C.[9a] [e] At 99.2 °C, this work. [f] At 120 °C. [g] $k_d = k_t \times$ (fraction of primary acetate). [h] $k_r = k_t \times$ (1 − fraction of primary acetate).

Scheme VI



reaction which produces the monocyclic enol acetate **29**-OAc. The methyl group ultimately wins its stereoelectronic tug-of-war with the double bond: it blocks the thermal [1,5] sigmatropic hydrogen shifts that would normally isomerize a nongeminally substituted cyclopentadiene under these conditions.[25] The enol acetate **25**-OAc can thus be isolated without further rearrangement.

Intramolecular retro-Diels–Alder reactions rarely occur during solvolysis.[26] Aside from the present case we are aware of but three well-documented examples: the aqueous enthanolysis of **3**-Cl in the presence of excess sodium cyanide (eq 9),[27] the hydrolysis of **48**-OPNB in 70% aqueous acetone (eq 10),[28] and the trifluoroethanolysis of **50**-OTs (eq 11).[29] In each of these instances a 7-norbornadienyl derivative solvolyzes with laticyclic participation to produce a highly strained tricyclo[3.2.0.0^{2,7}]hept-3-en-6-yl intermediate[30] which opens to a cyclopentadienyl derivative (eq 12) that can be trapped

(25) Cf.: (a) Mironov, V. A.; Sobolev, E. V.; Elizarovna, A. N. *Tetrahedron* **1963**, *19*, 1939. (b) McLean, S.; Haynes, P. *Ibid.* **1965**, *21*, 2329. (c) McLean, S.; Webster, C. J.; Rutherford, R. T. D. *Can. J. Chem.* **1969**, *47*, 1555.

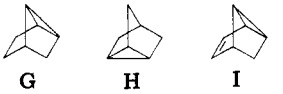
(26) Cf.: Ripoll, J. L.; Rouessac, A.; Rouessac, F. *Tetrahedron* **1948**, *34*, 19 and references cited therein.

(27) Tanida, H.; Hata, Y. *J. Org. Chem.* **1965**, *30*, 977.

(28) Lustgarten, R. K.; Lhomme, J.; Winstein, S. *J. Org. Chem.* **1978**, *37*, 1075.

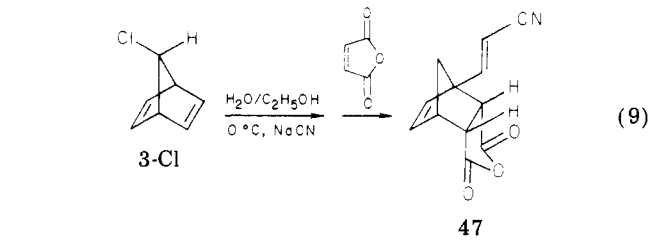
(29) Gassman, P. G.; Talley, J. J. *J. Am. Chem. Soc.* **1980**, *102*, 4138.

(30) On the assumption that tricyclo[3.2.0.0^{2,7}]heptane (G) must be at least as strained as tricyclo[2.2.1.0^{2,6}]heptane (H), whose strain energy is about 43 kcal/mol,[31] the introduction of an endocyclic double bond to produce tricyclo[3.2.0.0^{2,7}]hept-3-ene (I) would be expected to increase the strain energy to at least 48 kcal/mol.[21a]

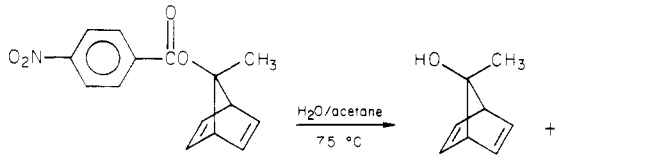


G H I

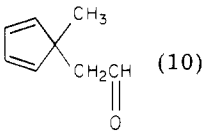
(31) Turner, R. B.; Goebel, P.; Mallon, B. J.; Doering, W. v. E.; Coburn, J. F., Jr.; Pomerantz, M. *J. Am. Chem. Soc.* **1968**, *90*, 4315.



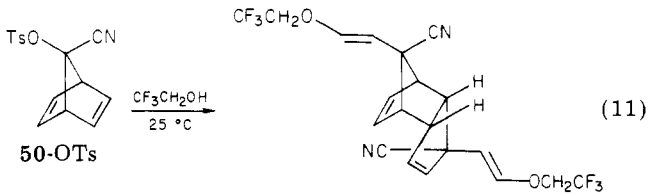
3-Cl 47 (9)



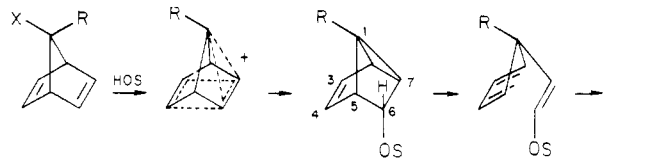
48-OPNB 48-OH



49 (10)



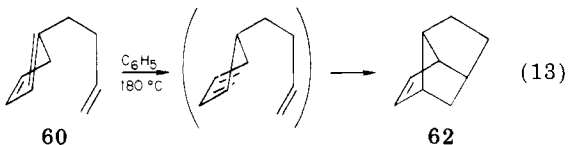
50-OTs 51 (11)



R = H, CH_3, CN; OS = CN, OH, OCH_2CF_3 (12)

as a Diels–Alder adduct (**47**), that tautomerizes (**49**), or that dimerizes (**51**). When, as in the case of **3**-Cl, the starting material bears a 7-hydrogen, the initial retro-Diels–Alder product undergoes a [1,5] sigmatropic hydrogen shift before reacting further.[32]

Laticyclic participation during the solvolysis of a norbornadienyl derivative does not lead inevitably to an intramolecular retro-Diels–Alder reaction; a highly strained, unsaturated, tricyclic intermediate must first be formed. The acetolysis of β-(7-norbornadienyl)ethyl brosylate (**6**-OBs, Scheme VI), for example, is certainly anchimerically assisted, probably involves an unsymmetric ($2^0 + 2^0 + 1^+$) laticyclic cation, $\mathbf{6a}^+$, but yields no retro-Diels–Alder products.[6] Although the acetolysis of **6**-OBs produces no 2-brexenyl acetates (**57**) which would yield the enol acetates **58** upon retro-Diels–Alder reaction, it does form *exo*-4-brexenyl acetate (**54**). This isomeric ester shows no tendency to undergo an intramolecular retro-Diels–Alder reaction. Perhaps this is not surprising in view of the fact that 4-brexene (**62**) is much less strained[36] than tricyclo[3.2.0.0^{2,7}]heptene (I)[30] and can, in fact, be prepared quantitatively by the intramolecular Diels–Alder reaction of 1-(3-butenyl)-1,3-cyclopentadiene (**60**, eq 13).[37] Apparently, an unsaturated tricyclic intermediate must be more highly strained than 2-brexene if an intramolecular retro-Diels–Alder is to accompany solvolysis.



60 61 62 (13)

(7-Methyl-7-norbornadienyl)methyl brosylate (**20**-OBs) is solvolytically unique. Like **6**- and **19**-OBs it yields strained but kinetically stable tetracyclic acetolysis products,[38] yet, like **3**-Cl, **48**-OPNB, and **50**-OTs, it produces a labile, unsaturated tricyclic intermediate[30] which undergoes an intramolecular retro-Diels–Alder reaction under solvolytic conditions. The kinetic and thermodynamic factors that govern the reaction path and products are nicely balanced; its acetolysis is modestly accelerated by laticyclic delocalization and produces essentially equivalent amounts of **26**-, **27**-, and **28**-OAc. Hence, (7-methyl-7-norbornadienyl)methyl derivatives offer an unusual opportunity to explore the effect of relatively small stereoelectronic perturbations upon laticyclic participation, strained tetracyclic product formation, intramolecular retro-Diels–Alder reactions, and possibly even Möbius cation formation and reactivity during solvolysis.

Experimental Section[40]

Spiro[quadricyclane-7,2′-oxacyclopropane] (23). Trimethyloxosulfonium iodide (2.20 g, 10.0 mmol) was added, under a nitrogen atmosphere, to a stirred suspension of 0.245 g (10.2 mmol) of sodium hydride, obtained by several washings with dry hexane of 0.430 g of a commercially available (Alfa/Ventron) ~57% suspension of NaH in mineral oil, in 10 mL of dimethyl sulfoxide (Me_2SO). When the evolution of hydrogen had ceased, the reaction mixture was cooled to ~15 °C, and a solution of 0.700 g (9.43 mmol) of quadricyclanone (**22**)[42] in 5 mL of Me_2SO was added dropwise during ~5 min. The reaction mixture was stirred at room temperature for 20 minutes, poured into ~30 mL of

(32) It is possible that a related cyclization–ring opening sequence may be responsible for the highly labile and/or unknown products formed during the solvolysis of 7-quadricyclyl β-naphthalenesulfonate in acetic acid,[33] the corresponding chloride in buffered, 50% aqueous ethanol,[34] or norbornadienyl chloride (**3**-Cl) in basic methanol.[35]

(33) Richey, H. G., Jr.; Buckley, N. C. *J. Am. Chem. Soc.* **1963**, *85*, 3057.

(34) Story, P. R.; Fahrenholtz, S. R. *J. Am. Chem. Soc.* **1964**, *86*, 527.

(35) Tanida, H.; Tsuji, T.; Irie, T. *J. Am. Chem. Soc.* **1966**, *88*, 864.

(36) The strain energy of brexane (J) is calculated to be 25.5 kcal/mol;[24] that of 2-brexene (**62**) must be at least 30 kcal/mol[21a,30] but surely is much less than that of tricyclo[3.2.0.0^{2,7}]hept-3-ene (I).[30]

J

(37) (a) Brieger, G.; Anderson, D. R. *J. Org. Chem.* **1971**, *36*, 243. (b) Tam, J. C. L.; Yates, P. *J. Chem. Soc., Chem. Commun.* **1975**, 739.

(38) The tetracyclic acetates formed in this and a previous study,[6] i.e., **21**-, **26**-, **27**-, and **53**-OAc, though highly strained appear to be kinetically stable under solvolysis conditions. In fact, **53**-OAc is the only product reported from the acetolysis of 5-deltacyclyl brosylate (**53**-OBs).[39]

(39) Schleyer, P. v. R.; Leone, R. E. *J. Am. Chem. Soc.* **1968**, *90*, 4164.

(40) Microanalyses were performed by Bernhardt Mikroanalitisches Laboratorium, Elbach über Engelskirchen, West Germany. Infrared spectra were determined on a Beckman Model IR 4210 spectrophotometer and ultraviolet spectra on a Beckman Model 35 UV-visible spectrophotometer. Nuclear magnetic resonance spectra were determined on Varian Associates Models EM360 and CFT-20 and Bruker Model WH-400 spectrometers. Gas–liquid partition chromatography (GLC) was performed on a Varian Aerograph Series 1800 chromatograph by using a 12 ft × 0.25 in. copper column packed with 20% diethylene glycol succinate (DEGS) on 60/80-mesh Chromosorb W or a 10 ft × 0.25 in. column packed with a 2:1 mixture of Quadrol/SAIB[41] on 60/80-mesh Chromosorb W or on a Hewlett-Packard Model 5830A chromatograph with a 20-m glass capillary column coated with Carbowax.

(41) Cf.: Broderick, F. H. "Aerograph Research Notes"; Wilkinson Instrument and Research: Walnut Creek, CA, 1960; Fall issue.

(42) Gassman, P. G.; Patten, D. S. *J. Am. Chem. Soc.* **1968**, *90*, 7276.

ice–water, and extracted with several portions of pentane. The pentane extract was dried (Na_2SO_4) and concentrated very slowly at atmospheric pressure to ~10 mL. The product crystallized from the concentrated solution at dry ice–acetone temperature. The supernatant solution was withdrawn with a pipet, and the crystals were washed with a small volume of cold pentane. The residual solvent was allowed to evaporate slowly at room temperature. The yield was 0.408 g (52%) of *very volatile* white needles: mp 63–65 °C; IR (CCl_4) 3082, 3042, 3015, 3002, 2950, 2910, 1495, 1428, 1238, 1032, 1005, 980, 968, 933, 914, 858 cm^{-1}; ^1H NMR (CCl_4) δ 3.08 (s, >$\overline{CCH_2O}$), ~1.75 (m, 4 H, >CH), 0.84 (t, 2 H, >CH, bridgehead at C_1 and C_4). Anal. Calcd for C_8H_8O: C, 79.97; H, 6.75. Found: C, 79.81; H, 6.56.[43]

Spiro[norbornadiene-7,2′-oxacyclopropane] (24). Spiro[quadricyclane-7,2′-oxacyclopropane] (**23**; 0.134 g, 1.1 mmol) was dissolved in ~0.6 mL of deuteriochloroform contained in a 5-mm NMR tube. Approximately 10 mg of the dimer of (η^4-norbornadiene)rhodium(I) chloride[45] was added, causing a mildly exothermic reaction. The tube was cooled intermittently in an ice bath as necessary to maintain the temperature below 25 °C. The isomerization was complete in 20 minutes as indicated by the proton magnetic resonance spectrum of the solution: δ 6.55 (m, 4 H, =CH), 3.23 (quintet, 2 H, >CH, bridgehead), 2.77 (s, >$\overline{CCH_2O}$).[44] The chloroform solution was poured into ~3 mL of hexane. The resulting suspension was treated with charcoal and filtered through a Celite mat. The colorless filtrate was used for the preparation of alcohol **19-OH** without isolation of the epoxide.

7-Norbornadienylmethanol (19-OH). To a stirred slurry of 0.187 g (4.92 mmol) of lithium aluminum hydride in 15 mL of anhydrous ether was added a solution of 0.454 g (3.44 mmol) of aluminum trichloride in 10 mL of ether. The mixture was stirred at room temperature for 1 h and then cooled to −25 °C. A solution of 0.451 g (3.70 mmol) of the quadricyclic epoxide **23** in 10 mL of ether was added dropwise while the temperature was maintained at −20 to −30 °C. The solution was allowed to warm slowly to −10 °C and then cooled again to −30 °C. About 1.5 mL of 15% aqueous sodium hydroxide was added with rapid stirring. The mixture was allowed to warm to room temperature, and the suspended inorganic salts were removed by filtration. The ethereal solution was concentrated to ~2 mL under reduced pressure, 5 mL of deuteriochloroform was added, and the mixture was again concentrated to ~2 mL. The ^1H NMR spectrum of the deuteriochloroform solution showed the product to be identical with 7-quadricyclylmethanol, prepared previously in a different manner by Dauben and Vinson.[46] The solution was cooled in ice, and ~20 mg of the dimer of (η^4-norbornadiene)rhodium(I) chloride[45] was added in one portion. The solution was allowed to warm to room temperature. The proton magnetic resonance spectrum, determined after about 10 min, indicated complete isomerization to 7-norbornadienylmethanol (**19-OH**): ^1H NMR (CCl_4) δ 6.87 (t, 2 H, =CH), 6.58 (t, 2 H, =CH), 3.39 [d (>CHC$\mathbf{H_2}$O) superimposed upon a br s at 3.42 (2 H, >CH, bridgehead)], 2.69 (t >C$\mathbf{H}$CH$_2$O), ~2 (concentration-dependent s, OH). The chloroform solution was combined with ~30 mL of pentane, and the resulting suspension was treated with charcoal and filtered through Celite to give a clear, colorless solution. The solvent was removed under aspirator pressure and the residue distilled in a short-path still at a 1.3-mm pressure and an oil-bath temperature of 90 °C. The yield of colorless liquid was 0.197 g (43% based upon epoxide).[47]

7-Norbornadienylmethyl *p*-bromobenzenesulfonate (19-OBs) was prepared by the method of Tipson:[49] 72% yield; mp 65–67 °C (lit.[10] mp 64–65 °C) IR (CCl_4) 3085, 2988, 2980, 1580, 1395, 1380, 1192, 1100, 1073, 1028, 963, 825, 653 cm^{-1}; ^1H NMR (CCl_4) δ 7.68 (4 H, aromatic), 6.78 (t, 2 H, =CH), 6.52 (t, 2 H, =CH), 3.83 (d, >CHC$\mathbf{H_2}$O), 3.39 (m, 2 H, bridgehead), 2.75 (t, >C$\mathbf{H}$CH$_2$O); $^{13}C\{H\}$ NMR (CD_3COCD_3) δ 145.0 (2 C), 140.8 (2 C), 136.4, 133.6 (2 C), 130.4 (2 C), 129.1, 82.4, 72.4, 51.9 (2 C).

Acetolysis Products of 7-Norbornadienylmethyl Brosylate (19-OBs). A solution of 0.217 g (0.636 mmol) of **19-OBs** in 30 mL of anhydrous acetic acid buffered with sodium acetate (0.0243 M) was heated at 100 °C for 96 h (1.8 half-lives). The solution was poured into 50 mL of ice–water and extracted with five 20-mL portions of pentane. The pentane solution was washed to neutrality with saturated sodium chloride and sodium bicarbonate and dried (Na_2SO_4). The solvent was removed at atmospheric pressure and the residue distilled in a short-path still (1 mm pressure, oil-bath temperature 80 °C), giving 32 mg (44%, based upon 1.8 half-lives) of clear distillate. GLC analysis on the DEGS column showed two components. The first component comprised 40% of the mixture and was identified as **19-OAc**:[10] ^1H NMR ($CDCl_3$) δ 6.65 (t, 2 H, =CH), 6.38 (t, 2 H, =CH), 3.98 (d, >CHC$\mathbf{H_2}$O), 3.14 (m, 2 H, bridgehead), 2.73 (t, >C$\mathbf{H}$CH$_2$O); $^{13}C\{H\}$ NMR ($CDCl_3$) δ 173.3, 144.4, 140.0, 82.6, 64.8, 51.4 (2 C). The second component comprised 60% of the acetate mixture; its $^{13}C\{H\}$ NMR spectrum was identical with that of **21-OAc** reported by Jefford.[12a]

Tetracyclo[3.3.0.0^{3,8}.0^{4,6}]octan-7-one (25). The distilled acetolysis mixture from **19-OBs** was combined with 2.5 mL of ether and 2.5 mL of pentane. The solution was stirred for two 20-min periods with 1-mL portions of saturated aqueous silver nitrate. The ether–pentane solution was dried over sodium sulfate and concentrated to ~2 mL. GLC analysis showed that the mixture now contained only ~10% of **19-OAc** and ~90% of **21-OAc**. The mixture was then reduced with excess lithium aluminum hydride and, without isolating the intermediate alcohol, oxidized to **25**, as described in detail for the preparation of ketone **30** (vide infra). Ketone **25** was isolated by GLC on the DEGS column: IR (CCl_4) 3075, 2992, 2943, 2875, 1745, 1602, 1285, 1268, 1160, 1150, 969, 896, 851 cm^{-1}; the $^{13}C\{H\}$ NMR spectral data are listed in Table IV.

(7-Methyl-7-norbornadienyl)methanol (20-OH). A 2 M solution of trimethylaluminum in toluene (5 mL; Aldrich) was diluted with toluene to 20 mL and cooled under a nitrogen atmosphere to −50 °C. To the cooled solution was added dropwise during 15 min a solution of 0.500 g (4.16 mmol) of the epoxide **24** in 10 mL of a 1:5 chloroform–hexane mixture.[50] The reaction mixture was allowed to warm to 0 °C and hydrolyzed by adding 4 mL of 15% aqueous sodium hydroxide.[51] The layers were separated, and the organic phase was washed twice with water and dried over anhydrous sodium sulfate. The solvent was removed under aspirator pressure, and the residue was sublimed at 50 °C (1.5 mm). The product was further purified by recrystallization from pentane, giving 0.279 g (49%) of white crystals: mp 88–89 °C (lit.[48,52] mp 85 °C); IR (CCl_4) 3635, ~3200–3500 (br), 3125, 3100, 3065, 2964, 2922, 2871, 1459, 1371, 1310, 1270, 1186, 1019, 956, 914, 873 cm^{-1}; ^1H NMR (CCl_4) δ 6.55 (m, 4 H, =CH), 3.54 (s, >CCH$_2$O), 3.12 (quintet, 2 H, >CH, bridgehead), ~2 (s, concentration dependent, OH), 1.14 (s, CH_3). Anal. Calcd for $C_9H_{12}O$: C, 79.37; H, 8.88. Found: C, 79.39; H, 8.86.

(7-Methyl-7-norbornadienyl)methyl *p*-Bromobenzenesulfonate (20-OBs). A solution of 0.641 g (4.71 mmol) of the alcohol (**20-OH**) in 10 mL of anhydrous pyridine was cooled to 0 °C, and 1.405 g (5.5 mmol) of *p*-bromobenzenesulfonyl chloride was added in small portions, under a nitrogen atmosphere.[49] The mixture was swirled at this temperature for 15 min and then

(43) When we first prepared this epoxide we were unaware of its earlier preparation[44] and of the admonition not to use trimethyloxosulfonium iodide as a source of the ylide. In fact, we encountered no difficulty with the iodide; our ^1H NMR spectrum agrees with that reported earlier.

(44) Hoffmann, R. W.; Schüttler, R. *Chem. Ber.* **1975**, *108*, 844.

(45) Abel, E. W.; Bennett, M. A.; Wilkinson, G. *J. Chem. Soc.* **1959**, 3178.

(46) Dauben, W. G.; Vinson, J. W. *J. Org. Chem.* **1975**, *40*, 3756.

(47) This compound and its 7-deuterio analogue have been reported by von Angerer[10] and by Klumpp et al.[48] Neither of these preparations is similar to that reported here; no spectral details are included in either case.

(48) Stapersma, J.; Rood, I. D. C.; Klumpp, G. W. *Tetrahedron* **1982**, *38*, 191.

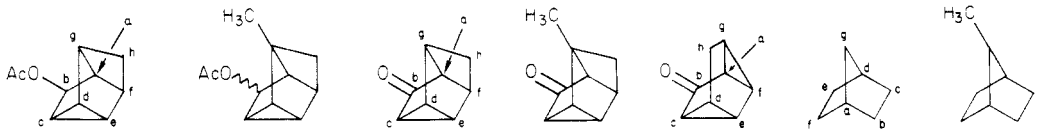
(49) Tipson, R. S. *J. Org. Chem.* **1944**, *9*, 235.

(50) Cf.: Kennedy, F.; Lundeen, A. U.S. Patent 3 024 287. Mole, T.; Jeffery, E. A. "Organoaluminum Compounds"; Elsevier: Amsterdam, 1979; pp 361–363.

(51) Micovic, V. M.; Mihailovic, M. L. *J. Org. Chem.* **1953**, *18*, 1190.

(52) This compound, prepared in a different manner, has recently been reported by Klumpp et al.[48] Our infrared and ^1H NMR spectra appear generally to agree with those reported by Klumpp except that the positions are shifted by about 10 cm^{-1} in the case of the IR and 0.1–0.2 ppm in the case of the ^1H NMR spectral data.

Table IV. Observed $^{13}C\{H\}$ NMR Spectra



21-OAc 26- and 27-OAc 25 30 32 33 34

compd		^{13}C chemical shift, δ										
		a	b	c	d	e	f	g	h	g-CH_3	g-$COCH_3$	g-$COCH_3$
33[14]		36.8	30.1	30.1	36.8	30.1	30.1	38.7				
34[14]		41.0	27.2	27.2	41.0	31.0	31.0	44.3		12.7		
	Δδ ^{13}C	+4.2	−2.9	−2.9	+4.2	+0.9	+0.9	+5.6				
21-OAc[b]		46.6	81.1	32.5	20.2	20.7	39.5	41.3	43.5		171.3	20.8
26-OAc		50.9	81.9	32.4	24.9	23.2	39.3	48.2	48.9	17.5	171.3	20.8
27-OAc		50.4	80.4	32.3	24.4	22.4	37.4		48.8	18.1		
	Δδ ^{13}C	+3.8	−0.7	−0.2	+4.2	+1.7	−2.1	+7.2	+5.3			
		+4.3	+0.8	−0.1	+4.7	+2.6	−0.2		+5.4			
25		44.9	212.5	31.2	23.8	23.8	40.7	40.7	44.5			
30		49.7	213.5	31.4	28.2	26.0	37.9	50.1	49.4	17.6		
	Δδ ^{13}C	+4.8	+1.0	+0.2	+4.4	+2.2	−2.8	+9.4	+4.9			
32[c]		27.0	206.1	27.0	30.8	30.8	30.8	30.8	26.8			

[a] Measured in perdeuteriobenzene relative to Me_4Si. [b] The chemical shifts reported here are virtually identical with those measured by Jefford et al.[12] [c] Measured from a sample supplied by C. W. Jefford.[13] Because of the symmetry plane a = c, d = g, and e = f. We presume that accidental degeneracy of d-g is responsible for the four-carbon singlet at δ 30.8.

allowed to stand at 5 °C overnight. The solution was poured into ice–water, and the crystalline precipitate was separated by filtration. The product was recrystallized from pentane to give 1.129 g (67.5%) of the brosylate: mp 81.5–82.2 °C; IR (CCl_4) 3073, 2973, 2879, 1575, 1470, 1378, 1357, 1306, 1286, 1189, 1097, 1070, 1013, 962, 916, 848, 828, 651 cm^{-1}; ^1H NMR (CCl_4) δ 7.60 (s, 4 H, aromatic), 6.50 (t, 2 H, =CH), 6.42 (t, 2 H, =CH), 4.06 (s, $>CH_2O$), 3.16 (m, 2 H, bridgehead), 1.20 (s, CH_3). Anal. Calcd for $C_{15}H_{15}O_3BrS$: C, 50.70; H, 4.22. Found: C, 50.83, H, 4.26.

Acetolysis Products of (7-Methylnorbornadienyl)methyl *p*-Bromobenzenesulfonate (20-OBs). Procedure A. A solution of 1.54 g (4.36 mmol) of the brosylate **20**-OBs in 120 mL of anhydrous acetic acid buffered with 0.04 M sodium acetate was heated at 100 °C for 7 h (11 half-lives). The solution was poured into 150 mL of ice–water and extracted with four 50-mL portions of pentane. The combined extract was washed twice with saturated sodium chloride and dried over anhydrous sodium sulfate. The pentane solution was concentrated to ~1 mL by distillation of the solvent at atmospheric pressure. GLC analysis on the Quadrol/SAIB column showed the presence of two fractions (labeled A and B) with relative retention times and areas (percent, given in parentheses) of 1 (57) to 1.3 (43). The products were collected, giving 0.267 g (34.4%) of the first and 0.189 g (24.3%) of the second material.

Fraction A. The collected product, when reinjected on the 20-ft capillary column, was further separated into equal parts of two components, which were subsequently assigned structures **26**- and **27**-OAc. Since we were not able to separate these two isomers on a preparative scale, the spectra reported are those of the mixture: IR (neat) 3060, 2950, 2870, 1735, 1450, 1375, 1355, 1246, 1059, 1030, 987 cm^{-1}; ^1H NMR (CCl_4) δ 4.77 (s, >CHO, **26**-OAc + **27**-OAc), 2.52 (br s, 2 H, >C**H**C(OAc)<, **26**-OAc or **27**-OAc), 2.30 (br s, 2 H, >C**H**C(OAc)<, **26**- or **27**-OAc), 1.90 (s, CO**CH$_3$**, **26**-OAc + **27**-OAc), 1.25 (s, >CCH_3, **26**- or **27**-OAc), 1.14 (s, >CCH_3, **26**- or **27**-OAc), 2.13–1.03 (m, $>CH_2$ + >CH, **26**-OAc + **27**-OAc); $^{13}C\{H\}$ NMR (C_6D_6) δ 171.3 (C=O), 81.9, 80.4, 50.9, 50.4, 48.9, 48.8, 48.5, 39.3, 37.2, 32.4, 32.3, 24.9, 24.4, 23.3, 22.4, 20.8 (CO**CH$_3$**), 18.1, 17.3.

Fraction B. The second collected fraction, a pure compound by capillary GLC, was assigned structure **29**-OAc: IR (neat) 3080, 2979, 2930, 2870, 1760, 1675, 1452, 1434, 1373, 1230, 1160, 1103, 1045, 1035, 935, 905, 752 cm^{-1}; ^1H NMR (CCl_4) δ 7.06 (d, J_{ab} = 12.5 Hz, CH_b=C**H$_a$**OAc, trans), 6.23 (s, 4 H, =CH), 5.27 (dt, J_{ab} = 12.5 Hz, J_{bc} = $J_{bc'}$ = 8 Hz, $CH_cH_{c'}$C**H$_b$**=C**H$_a$**OAc, trans), 2.20 (d, J = 8 Hz, C**H$_c$H$_{c'}$**CH_b=), 2.11 (s, CO**CH$_3$**), 1.14 (s, =CCH_3); $^{13}C\{H\}$ NMR ($CDCl_3$, with multiplicity of the off-resonance decoupled peaks shown in parentheses) δ 168.1, 144.7 (d, 2 C), 136.5 (d), 128.9 (d, 2 C), 111.5 (d), 55.8 (s), 33.7 (t), 20.7 (q), 19.7 (q); UV (EtOH) λ_{max} 250 nm. Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.16; H, 7.84. Found: C, 73.86; H, 7.90.

For confirmation of the presence of an enol acetate a solution containing ~10 mg of collected fraction B, a mixture of a few drops of 2% aqueous sodium bicarbonate and ~0.5 mL of acetone contained in a 5-mm NMR tube was allowed to stand at room temperature. The δ 9–10 region was observed intermittently. A signal at δ 9.46, attributable to an aldehydic proton,[17c] appeared within ~24 h. The product was not isolated.

1-Methyltetracyclo[3.3.0.0^{3,8}.0^{4,6}]octan-7-one (30). A solution of 0.265 g (1.5 mmol) of the mixed acetates (**26**- and **27**-OAc) in 0.5 mL of ether was added to a slurry of 50 mg (1.3 mmol) of lithium aluminum hydride in 10 mL of ether. The mixture was stirred at room temperature for ~10 min and decomposed in the usual manner by using water and 15% sodium hydroxide.[51] The ethereal solution was dried (Na_2SO_4) and most of the ether removed under atmospheric pressure. About 2 mL of spectroscopic grade acetone was added and the last of the ether removed by distillation under nitrogen. A GLC analysis on the DEGS column at 175 °C with a helium flow of ~75 mL/min showed two overlapping peaks with retention times and relative areas of 12.7 (~48%) and 13.9 min (~52%). The solution of the mixed isomeric alcohols was oxidized to a ketone (**30**) without isolation of the individual components by using the following procedure as described by Dauben and Berezin.[53] The acetone solution of **26**- and **27**-OH was placed in a water bath at 20 °C, and chromic acid reagent[53] (deoxygenated by bubbling through nitrogen for 15 min) was added dropwise under nitrogen with stirring until the orange color of the reagent persisted for ~5 min. The excess reagent was decomposed with methanol. The acetone solution was decanted from the gummy green precipitate into a separatory funnel containing 3 mL of pentane and 3 mL of saturated aqueous sodium chloride. The product was extracted with two additional 3-mL portions of pentane. The extract was washed with saturated sodium bicarbonate, dried (Na_2SO_4), and concentrated to ~0.5 mL at atmospheric pressure. A GLC analysis on the DEGS column at 175 °C with a helium flow of 75 mL/min showed a single peak with a retention time of 16 min. Collection from the DEGS column yielded ketone **30**: 60 mg (30%, based upon the acetates); IR (neat) 3075, 3024, 2992, 2960, 2937, 2878, 1740, 1450, 1382, 1335, 1299, 1281, 1208, 1157, 1112, 1039, 975, 896, 881, 862, 842, 804, 785, 652 cm^{-1}; ^1H NMR ($CDCl_3$, determined on the 400-MHz spectrometer) δ 2.70 (q), 2.38 (septet), 2.11 (q), 2.00 (d), 1.86 (sextet), 1.60 (m), 1.55 (br d), 1.19 (s); $^{13}C\{H\}$ NMR (C_6D_6) δ 213.4, 50.1, 49.7, 49.4, 37.9, 31.4, 28.2, 26.0, 17.6 (cf. Table IV);

(53) Dauben, W. G.; Berezin, G. H. *J. Am. Chem. Soc.* **1963**, *85*, 468.

Table V

fraction	vol, mL	wt of residue, mg	composition, % 26- and 27-OAc	28-OAc	29-OAc	20-OBs
1	180	0				
2	50	139	63	29	8	0
3	50	120	57	38	5	0
4	50	75	47	53	0	0
5	150	141	34	55	0	21
6	100	51	30	23	0	47
7	100	17	16	0	0	84

UV (EtOH) λ_{max} 289 nm (ϵ 41.5). Anal. Calcd for $C_9H_{10}O$: C, 80.60; H, 7.46. Found: C, 80.27; H, 7.46. The 2,4-dinitrophenylhydrazone, recrystallized from ethanol, melts at 170–171 °C.

Quantitative Catalytic Hydrogenation of 29-OAc. A solution containing 93 mg (0.52 mmol) of fraction B (the enol acetate) in 5 mL of methanol was hydrogenated at 22 °C (759 mm) by using 10% Pd/C catalyst. The hydrogen uptake was 37.1 mL (1.53 mmol). The mixture was filtered and the solvent distilled at atmospheric pressure. The residue was distilled in a micro short path apparatus at an oil bath temperature of 75 °C (0.4 mm), giving 62 mg (69%) of a colorless liquid identified as 3-(1-methyl-1-cyclopentyl)propyl acetate on the basis of the following spectral data:[17] IR (neat) 2960, 2900, 2870, 1739, 1450, 1420, 1385, 1363, 1285, 1245, 868, 693 cm^{-1}; ^1H NMR (CCl_4) δ 3.90 (t, J = 6 Hz, CH_2CH_2O), 1.90 (s, $COCH_3$), 1.80–1.05 (m, 12 H), 0.9 (>CCH_3); $^{13}C\{H\}$ NMR (C_6D_6) δ 170.1, 65.2, 41.8, 39.5 (2 C), 38.6, 25.9, 25.1, 24.8 (2 C), 20.5.

Acetolysis of 20-OBs. Procedure B. A solution of 1.206 g (3.397 mmol) of the brosylate in 150 mL of anhydrous acidic acid buffered with 0.04 M sodium acetate was heated at 70 °C for 53 h (~6 half-lives). The work up was as described in procedure A. A small sample of the product-containing pentane concentrate was withdrawn, and the last of the solvent was removed under aspirator pressure. The ^1H NMR spectrum of the residue, determined in carbon tetrachloride solution, showed unreacted starting material, acetates **26-**, **27-**, and **29-**OAc, and another unsaturated material, presumably **28-**OAc. The composition of the mixture, calculated from the areas of selected ^1H NMR signals (δ values given in parentheses) was as follows: **20-**OBs, 10% (7.60); **29-**OAc, 2% (6.23); **28-**OAc (?), 33% (5.86); **26-** and **27-**OAc, 55% (4.77). The remaining solvolysis mixture was chromatographed on a 24 × 2.5 cm column packed with 60 g of silica gel (Fisher Scientific Co., 100–200 mesh) in pentane. The column was eluted with 3% ether in pentane. The collected fractions were analyzed by ^1H NMR. Only partial separation was achieved as summarized in Table V. GLC of fraction 3 on the DEGS column showed two peaks with retention times identical with those of components A and B obtained in procedure A in relative abundances of 48% and 52%, respectively. The spectra of the collected materials did, in fact, confirm that the first fraction (A) was a mixture of **26-** and **27-**OAc and that the second fraction (B) was pure **29-**OAc, apparently formed by thermal rearrangement of **28-**OAc during GLC. Fraction 5 was distilled in a micro short path still (0.5 mm, 70 °C), and the magnetic resonance spectrum of **28-**OAc was deduced from that of the mixture by subtracting the contributions of the tetracyclic acetates: ^1H NMR (400-MHz, $CDCl_3$) δ 5.86 (br, s, 2 H, =CH), 4.71 (d, J = 4 Hz, >CHO), 2.93 (br, m, 1 H), 2.48 (br s, 2 H), ~2.1–1.0 (m, 2 H), 1.86 (s, $COCH_3$), 0.85 (s, >CCH_3); $^{13}C\{H\}$ NMR δ 169.9, 77.8, 68.2, 58.8, 52.2, 42.0, 33.5, 20.5, 14.7.

Perdeuterioacetolysis Rates and Products of 20-OBs by ^1H NMR. Samples containing 25 mg (0.070 mmol, 0.23 M) of **21-**OBs, 8 mg (0.09 mmol) of sodium perdeuterioacetate, and 0.3 mL of perdeuterioacetic acid were sealed in 5-mm NMR tubes. The samples were placed in constant-temperature baths at 99.2, 83.8, and 70.5 °C. Each sample was periodically withdrawn, cooled, and washed, and its ^1H NMR spectrum was determined on a Varian EM-360 spectrometer. The relative amounts of starting material and each of the products were determined by repeated integral scans of the pertinent hydrogen resonance regions: δ 6.42 and 6.50 for **21-**OBs, 6.23 for **29-**OAc, 5.86 for **28-**OAc-d_3, and 4.77 for **26-** and **27-**OAc-d_3. From the intensity measurements of the intermediates and products relative to that of the starting material (**21-**OBs) and the time of maximum concentration of **28-**OAc-d_3 (Figure 1), the first-order constants, defined as shown in Scheme I, were calculated[19] (cf. Table II).

Titrimetric Acetolysis Rates of 19- and 20-OBs. Anhydrous acetic acid was prepared by mixing Baker and Adamson analytical reagent acetic acid with 1% by volume acetic anhydride, refluxing overnight, and distilling through a 3-ft helix-packed column. To the center cut (bp 118.0–118.3 °C) were added 1% by volume analytical reagent acetic anhydride and enough freshly fused reagent grade sodium acetate to make an ~0.03 M solution. A weighed sample of the brosylate (~90 mg) contained in a 10-mL volumetric flask was dissolved in this solution and diluted to the mark at 25 °C. Aliquots (1 mL) of this solution were sealed in test tubes and placed in a thermostated bath. At measured intervals, tubes were removed and dropped into an ice–water bath to quench the reaction. Tubes were washed, cracked, and titrated immediately with standard perchloric acid to a crystal violet end point. Standard solutions were protected from moisture at all times. First-order rate constants, computed in the usual manner,[9a] are summarized in Table I.

Skeletal Structure of the Tetracyclic Products from the Acetolysis of 20-OBs. As outlined in the Results, it is clear from their $^{13}C\{H\}$ NMR's (Table IV) that the tetracyclic acetolysis products (**26-** and **27-**OAc) of **20-**OBs and the ketone derived from them (**30**) are tetracyclo[3.3.0.$0^{3,8}$.$0^{4,6}$]- rather than [3.3.0.$0^{2,8}$.$0^{4,6}$]octyl derivatives.[15]

Acknowledgment. It is a pleasure to acknowledge Professor Charles W. Jefford of the University of Geneva for his help in the product identification,[13] Professor Stephen L. Morgan of this department for the use of and his help with the Hewlett-Packard 5830A capillary gas chromatograph, the staff of the National Science Foundation Regional Nuclear Magnetic Facility at the University of South Carolina (Grant No. CHE78-18723), Professor Paul D. Ellis, Director, for the 400-MHz spectra reported here, and the National Science Foundation for their partial support of this work.

Registry No. **19-**OH, 63603-20-3; **19-**OAc, 65844-32-8; **19-**OBs, 65844-33-9; **20-**OH, 82478-37-3; **20-**OBs, 83831-01-0; **21-**OAc, 59530-83-5; **21-**OBs, 83816-72-2; **22**, 1072-92-0; **23**, 55314-34-6; **24**, 55314-36-8; **25**, 59530-91-5; **26-**OAc, 83816-73-3; **26-**OAc-d_3, 83816-78-8; **27-**OAc, 83860-72-4; **27-**OAc-d_3, 83860-73-5; **28-**OAc, 83816-76-6; **28-**OAc-d_3, 83816-77-7; **29-**OAc, 83816-74-4; **30**, 83816-75-5; trimethyloxosulfonium iodide, 1774-47-6; trimethylaluminum, 75-24-1; 3-(1-methyl-1-cyclopentyl)propyl acetate, 83816-79-9.