A solution of 3,7-dimethyl-8-methylthiohypoxanthine (10,[6] 100 mg) and phosphorus pentasulfide (200 mg) in pyridine (10 ml) was refluxed for 30 min. The solvent was removed in vacuo and the residue was treated with boiling water for 30 min. The insoluble portion was recrystallized from water. The physical properties of this compound were identical with those of the product resulting from thiohydrolysis of 3 (see Table I).

II. Hydrolysis of 6 to 3,7-dimethyl-8-methylthioxanthine (7). A suspension of 6 in 2 *N* NaOH was stirred and refluxed for 20 min. The clear solution was acidified with acetic acid. The precipitate was identified by comparison with an authentic sample of 7.[2]

9-Methyl-6,8-dimethylthiopurine (4). A. 9-Methyl-8-thiohypoxanthine. An intimate mixture of 5-amino-6-hydroxy-4-methylaminopyrimidine[16] (2 g) and thiourea (6 g) was heated to 250° for 45 min and then to 280° for 15 min. The cake was dissolved in dilute NaOH and the solution was neutralized with acetic acid. Repeated reprecipitation and finally recrystallization from water gave colorless needles (56%): mp >300° dec; λ_{max} (pH 1) 234 sh, 289 nm (log ϵ_{max} 4.30); R_f (B) 0.48, (C) 0.51; violet fluorescence.

Anal. Calcd for $C_6H_6N_4OS$: C, 39.6; H, 3.3; N, 30.8; S, 17.6. Found: C, 40.0; H, 3.1; N, 30.6; S, 17.3.

B. 9-Methyl-6,8-dithiopurine. A mixture of 9-methyl-8-thiohypoxanthine (5 g) and phosphorus pentasulfide (20 g) in pyridine (800 ml) was refluxed for 3.5 hr. Already after the first 20 min a homogeneous solution was obtained. After removal of the solvent in vacuo, the mixture was heated with water (150 ml) for 2.5 hr. The brown, insoluble portion was dissolved in 1 *N* NaOH and the product was precipitated by addition of glacial acetic acid. Final purification was by ammonia–acetic acid: yield 45%; mp >300° dec; λ_{max} (pH 1) 269, 357 nm (log ϵ_{max} 4.47, 4.42); λ_{max} (pH 8) 263, 337 nm (log ϵ_{max} 4.23, 4.39); R_f (B) 0.68, (C) 0.66; yellow fluorescence.

Anal. Calcd for $C_6H_6N_4S_2$: C, 36.4; H, 3.0; N, 28.3; S, 32.3; Found: C, 36.4; H, 3.1; N, 28.1; S, 32.35.

C. 9-Methyl-6,8-dimethylthiopurine (4). A solution of the foregoing dithio derivative (2 g) in 5% NaOH (30 ml) was stirred with methyl iodide (3 ml). After 5 min, a white precipitate formed as colorless needles (ethanol): mp 166°; yield 75%; λ_{max} (pH 0) 248, 331 nm; R_f (B) 0.83, (C) 0.75; sky-blue fluorescence.

Anal. Calcd for $C_8H_{10}N_4S_2$: C, 42.5; H, 4.4; N, 24.8; S, 28.3. Found: C, 42.5; H, 4.5; N, 25.0; S, 28.5.

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Registry No.—**1**, 55800-42-5; **2**, 55800-43-6; **3**, 55800-44-7; **3** picrate, 55800-45-8; **4**, 55800-46-9; **5**, 38759-27-7; **6**, 40848-24-6; **9**, 55800-47-0; **10**, 55800-48-1; **11**, 42930-79-0; **12**, 39008-31-6; **13**, 55800-49-2; 3-methyl-6,8-dimethylthio-2-oxopurine 39013-78-0; phosphorus pentasulfide, 1314-80-3; 9-methyl-8-thiohypoxanthine, 55800-50-5; 5-amino-6-hydroxy-4-methylaminopyrimidine, 45751-74-4; thiourea, 62-56-6; 9-methyl-6,8-dithiopurine, 55800-51-6.

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(6) Synthesis of this compound will be described in a separate publication.
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Solvolysis of *exo*- and *endo*-2-Bicyclo[3.2.0]hept-6-enyl Tosylates and the Corresponding 1,4,4- and 4,4,6-Trimethyl Derivatives. Steric and Conformational Effects on the Ring Enlargements of the Resulting Carbocations[1]

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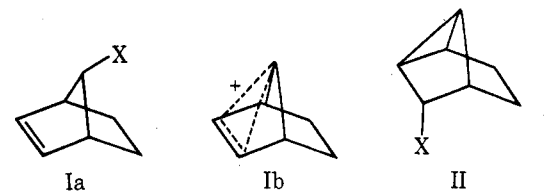
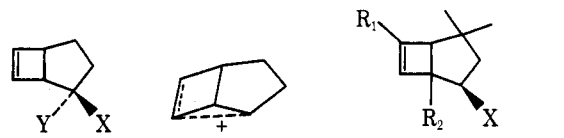
The kinetics of acetolysis and the products from solvolysis in acetic acid, aqueous acetone, and 4.0 *M* sodium methoxide in methanol of the title compounds were determined. An exo/endo rate ratio, corrected for the observed yield of products formed via a solvent-assisted pathway during acetolysis of the endo tosylate, of 2400 was observed. Solvolysis of the endo tosylate yields unrearranged exo-2-substituted and ring-enlarged products, with product ratios dependent on the nucleophilicity of the solvolysis medium. Solvolysis of the exo tosylate yields only products derivable from the ring-enlarged 7-norbornenyl cation. Acetolysis of the *exo*-1,4,4- and 4,4,6-trimethylbicyclo[3.2.0]hept-6-enyl tosylates has been shown to yield small amounts of the corresponding unrearranged exo 2-acetates. The differences in the rates for ring enlargement of the first formed cations from these solvolyses are explained in terms of steric and conformational effects.

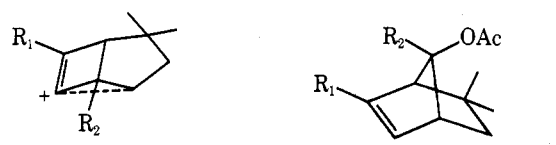
Winstein[3] and Tufariello[4] have elegantly delineated two routes which result in direct formation of the 7-norbornenyl cation (Ib). The π route involves solvolysis of *anti*-7-norbornenyl tosylate (Ia, X = OTs)[3a,b] or treatment of the corresponding alcohol (Ia, X = OH) with fluorosulfonic acid (FSO_3H) at low temperatures.[3c,d] The other, termed the σ route, involves treatment of *endo*-tricyclo[3.2.0.0^{2,7}]hept-3-yl methyl ether (II, X = OMe) with dilute acid[3c] or FSO_3H



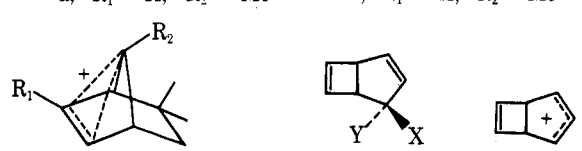
Ia Ib II



IIIa, Y = H; b, X = H IIIc IVa, R_1 = Me; R_2 = H; b, R_1 = H; R_2 = Me



IVc, R_1 = Me; R_2 = H; d, R_1 = H, R_2 = Me Va, R_1 = Me; R_2 = H; b, R_1 = H; R_2 = Me



Vc, R_1 = Me; R_2 = H; d, R_1 = H; R_2 = Me VIa, X = Y = H; b, Y = H; c, X = H VId

at low temperatures,[3d] and solvolysis of the corresponding aryl esters[3e,4] (II, X = OPNB, OPMB). In the preliminary communication[5] describing this work, we noted that SN1 solvolysis of *exo*-2-bicyclo[3.2.0]hept-6-enyl tosylate (IIIa, X = OTs) yields only products derivable from the 7-norbornenyl cation (Ib), furnishing an interesting alternate π route to this cation. Analysis of the appropriate kinetic data and relative energies of the substrates showed that the solvolytic transition states for acetolysis of IIIa and Ia, X = OTs, differ in energy by ca. 18–19 kcal/mol, showing that the new π route is not direct, and that bridged cation IIIc is probably involved as the first-formed intermediate.[5] We now present this more detailed report on the solvolysis of *exo*- and *endo*-2-bicyclo[3.2.0]hept-6-enyl tosylates (IIIa, X = OTs; IIIb, Y = OTs), noting that the data from acetolysis of the endo tosylate agrees well with those independently published by Coates[6a] and Svensson.[6b] Whitham[7] noted that acetolysis of *exo*-1,4,4- and -4,4,6-trimethylbicyclo[3.2.0]hept-6-en-2-yl tosylates (IVa, IVb, X = OTs) yields small amounts of the corresponding unrearranged exo acetates along with major proportions of the corresponding ring-enlarged acetates (Va and Vb, respectively), indicating that the exceedingly rapid ring enlargement (IIIc → Ib) noted during solvolysis of our exo tosylate (IIIa, X = OTs) is retarded by the methyl substituents to the extent that first-formed cations IVc and IVd can be trapped even in such a weakly nucleophilic medium as acetic acid before rearrangement is complete. The rather dramatic reactivity differences shown by these cations can be explained using the conformational arguments presented below.

Experimental Section

Melting points were determined using a Varian capillary melting point apparatus and are uncorrected. Elemental analyses were performed by Midwest Microlabs, Inc.

Nuclear magnetic resonance (NMR) spectra were recorded using either a Varian HA-100 or A-60 nuclear magnetic resonance spectrometer on carbon tetrachloride (CCl_4) solutions (Me_4Si internal standard). Infrared (ir) spectra were recorded using either the Perkin-Elmer Model 621 or 257 recording infrared spectrophotometer. Mass spectra were recorded using a Hitachi Perkin-Elmer RMU-6E single focusing mass spectrometer.

Analytical and preparative gas chromatography (GC) separations were performed using either the Varian A-90-P3 or HiFi-III Model gas chromatographs. Columns packed with either Carbowax 20M or 1500 were found to be satisfactory for all separations described herein. Detector responses were determined prior to each analytical determination by injecting known volumes of standard solutions of *anti*-7-norbornenol (Ia, X = OH) or the corresponding acetate.

All solvents and reagents used were commercially available and not further purified, with the following exceptions. Methanol was purified by distillation from magnesium turnings, and *p*-toluenesulfonyl (tosyl) and *p*-bromobenzenesulfonyl (brosyl) chlorides were recrystallized from pentane. Pyridine was dried by distillation from barium oxide and stored over potassium hydroxide pellets.

Titrimetric rate constants for acetolysis were determined on weighed amounts of tosylates in 0.0753 *M* sodium acetate in 5% acetic anhydride in acetic acid by the ampoule method. The excess sodium acetate was back-titrated with 0.0156 *M* perchloric acid–acetic acid solutions to the Crystal Violet end point. Least-squares treatment of the data was used in the calculation.

***endo*-2-Bicyclo[3.2.0]hept-6-enyl tosylate (IIIb, Y = OTs)** was prepared in yields as high as 80% from samples of the corresponding alcohol[8] (IIIb, Y = OH) by treatment with tosyl chloride in pyridine, followed by aqueous work-up, mp 53.0–53.6° (hexane) (lit.[6a] mp 52.5–54°). Anal. Calcd for $C_{14}H_{16}O_3S$: C, 63.61; H, 6.10; S, 12.13. Found: C, 62.81; H, 6.39; S, 11.70. ν_{max}(neat) 3040, 1600, 1365, 1190, 1178, 752, 670 cm^{-1}; δ 7.47 (ab q, ArH), 4.50 (d of t, J = 6, 8 Hz), 3.09 (m, 2 H), 2.40 (s, 3 H, $ArCH_3$), 1.98 (m, 2 H), 1.40 (m, 2 H). Kinetic determinations on 100-mg samples (0.380 mmol) yielded the following values for the rate constants: $k = 1.11 \pm 0.1 \times 10^{-7}$ (50.0°), $3.60 \pm 0.1 \times 10^{-6}$ (75.03°), and $1.11 \pm 0.016 \times 10^{-4}$ sec^{-1} (106.8°).

***endo*-2-Bicyclo[3.2.0]hept-6-enyl brosylate (IIIb, Y = OBs)** was prepared in similar fashion, mp 75° (hexane) (lit.[6b] mp 76–77°). Anal. Calcd for $C_{13}H_{13}O_3BrS$: C, 47.43; H, 3.98; S, 9.74; Br, 24.27. Found: C, 47.47; H, 4.00; S, 9.85; Br, 24.50. ν_{max}(CCl_4) 3040, 1620, 1375, 1187, 1172, 718, 692 cm^{-1}. The NMR spectrum is very similar to that for the corresponding tosylate, and matches the published spectrum of Svensson.[6b]

***exo*-2-Bicyclo[3.2.0]hept-6-enyl tosylate (IIIa, X = OTs)** was synthesized in 82% yield by the same procedure used for the endo tosylate (IIIb, Y = OTs). The product was isolated as an oil. Attempts to induce crystallization from hydrocarbon failed, as did attempts to further purify the product by elution chromatography from silica gel or alumina, which resulted in bulk decomposition of the sample. The following spectral properties were noted: ν_{max}(neat) 3040, 1600, 1370, 1195, 1183, 704, 670 cm^{-1}; δ 7.46 (ab q, ArH, 4 H), 5.86 (2 H), 4.69 (d, J = 3 Hz, 1 H), 3.30 (1 H), 3.19 (1 H), 2.40 (s, 3 H), 1.2–2.1 (m, ca. 4 H). Samples of exo alcohol (IIIa, X = OH) used in this preparation were obtained by large-scale hydrolysis of exo tosylate (IIIa, X = OTs) in 50% aqueous acetone and purified by elution chromatography (silica gel, with pentane and pentane–diethyl ether mixtures as eluent). GC analysis showed these samples to be of 99% or higher purity.

Kinetic determinations were carried out on 61.5-mg (0.233 mmol) and 67.0-mg (0.254 mmol) samples of the tosylate at 50.0°. The following values were obtained for the rate constant: $k = 1.79 \pm 0.08$ and $1.99 \pm 0.13 \times 10^{-4}$ sec^{-1}.

***anti*-7-Norbornenyl tosylate (Ia, X = OTs)** was prepared in 50% yield according to the procedure of Winstein,[3a] and used without further purification.

Acetolysis of Endo Tosylate (IIIb, Y = OTs). A 264-mg sample (1 mmol) of endo tosylate was treated with 15 ml of 5% acetic anhydride–acetic acid and 0.25 g of sodium acetate in a sealed tube at 101° for 8 hr. The resulting slurry was extracted with three portions of methylene chloride, and the organic layer was dried (sodium sulfate) and concentrated to a known volume. GC analysis showed the presence of a ca. 72:28 mixture (56% yield) of *anti*-7-norbornenyl acetate (Ia, X = OAc), whose ir spectrum matched that of an authentic sample,[3a] and *exo*-2-bicyclo[3.2.0]hept-6-enyl-acetate (IIIa, X = OAc). Reduction of a portion of the crude acetate mixture with ethereal $LiAlH_4$ formed a 68:32 mixture (82% yield) of the corresponding alcohols, Ia, X = OH, mp 116–117° (lit.[3a] mp 117–118°), and IIIa, X = OH: ν_{max}(neat) 3340 (br), 3030, 1565, 1060, 738 cm^{-1}; δ 5.89 (two lines, separated by 2 Hz, 2 H),

3.94 (d, J = 3.5 Hz, 1 H), 3.26 (m, 1 H), 2.96 (m, 1 H), 1.2–2.1 (m, 4–5 H). Anal. Calcd for $C_7H_{10}O$: C, 76.33; H, 9.15. Found: C, 75.81; H, 9.22.

Hydrolysis of Endo Tosylate (IIIb, Y = OTs) in 50% Aqueous Acetone.[9] A 264-mg sample (1 mmol) of endo tosylate was treated with 252 mg of sodium bicarbonate and 20 ml of 50% (by volume) aqueous acetone in a sealed tube at 101° for 8 hr. After cooling, the contents were poured into saturated salt solution. The resulting slurry was extracted with three 30-ml portions of CH_2Cl_2. The organic layers were combined and washed with salt, sodium bicarbonate, and salt solutions, dried (sodium sulfate), and concentrated at reduced pressure for GC analysis, which showed the presence of a 57:43 mixture (91% yield) of anti alcohol (Ia, X = OH) and exo alcohol (IIIa, X = OH).

Basic Methanolysis of Endo Brosylate (IIIb, Y = OBs). A 100-mg sample (0.304 mmol) of endo brosylate was treated with 15 ml of 4.1 M sodium methoxide in methanol, prepared by dissolving the appropriate amount of sodium metal in methanol, in a sealed tube at 101° for 9 hr. The contents were subjected to aqueous work-up, and the resulting slurry was extracted with four 25-ml portions of hexane. Organic layers were separated and dried (sodium carbonate) and concentrated by distillation. GC analysis showed the presence of bicyclo[3.2.0]hepta-2,6-diene (VIa) (8% yield), identified by comparison of its ir spectrum with that of an authentic sample,[10] and *exo*-2-methoxybicyclo[3.2.0]hept-6-ene (IIIa, X = OMe) (78% yield): $\nu_{max}(CCl_4)$ 3030, 1100, 735 cm^{-1}; δ 5.92 (2 H), 3.48 (d, J = 3 Hz, 1 H), 3.26 (m, 1 H), 3.20 (s, 3 H), 2.98 (m, 1 H), 1.2–2.1 (m, ca. 4 H); m/e 124 (P^+), 123, 109 ($P - CH_3$), 91 (base peak).

Acetolysis of Exo Tosylate (IIIa, X = OTs). An 18.2-mg (0.069 mmol) sample of exo tosylate was treated with 20 mg of sodium acetate and 1.5 ml of 2% acetic anhydride in acetic acid under the conditions described above. GC and ir analysis of the crude product showed the presence of anti acetate (Ia, X = OAc) (81% yield) as the only GC volatile product.

Hydrolysis of Exo Tosylate (IIIa, X = OTs) in 50% Aqueous Acetone.[9] A 16.5-mg sample (0.065 mmol) of exo tosylate was treated with 50 mg of sodium bicarbonate and 1.3 ml of 50% aqueous acetone under the conditions described above for 12 hr. Analysis using GC and ir showed the presence of anti alcohol (Ia, X = OH) as the only GC volatile product (80% yield).

Basic Methanolysis of Exo Tosylate (IIIa, X = OTs). A 110-mg (0.418 mmol) sample of exo tosylate was treated with 10 ml of 4.3 M sodium methoxide in methanol at 50.0° for 8 hr. Work-up and GC analysis as described above showed the presence of four components, characterized as bicyclo[3.2.0]hepta-2,6-diene (VIa)[10] (10% yield), *anti*-7-methoxynorbornene (Ia, X = OMe) (39% yield), $\nu_{max}(CCl_4)$ 3050, 1114, 713 cm^{-1}, matching that of an authentic sample,[3c] *endo*-2-methoxybicyclo[3.2.0]hept-6-ene (IIIb, Y = OMe) (30% yield), $\nu_{max}(CCl_4)$ 3025, 1560, 1098, 734, 708 cm^{-1}, δ 5.95 (ab q, 2 H), 3.40 (q, J = 7.7 Hz, 1 H), 3.21 (s with 2 m, 5 H), 1.78 (m, 2 H), 1.36 (m, 2 H), m/e 124 (P^+), 123, 91 (base peak), and *endo*-6-methoxytricyclo[3.2.0.$0^{2,7}$]heptane (II, X = OMe) (20% yield), δ 3.66 (q, J = 3.8 Hz), matching that of an authentic sample.[3e] Yield ratio for Ia, X = OMe:II, X = OMe, is 65:35.

Basic Methanolysis of *anti*-7-Norbornenyl Tosylate (Ia, X = OTs). A 106.8-mg sample (0.405 mmol) of anti tosylate was treated with 10 ml of 4 M sodium methoxide in methanol at 50.0° for 2 hr. Usual work-up and analysis procedures showed the presence of an unidentified hydrocarbon (11% yield), *anti*-7-methoxynorbornene (Ia, X = OMe) (46% yield), and endo tricyclic ether II, X = OMe (27% yield). Yield ratio for Ia, X = OMe:II, X = OMe, is 63:37.

Results and Discussion

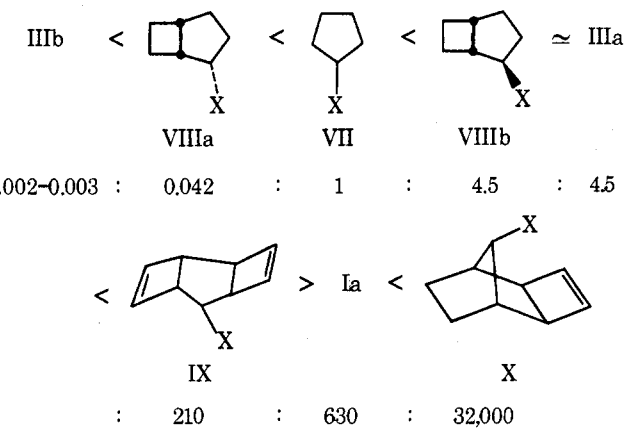
The kinetics of acetolysis of *endo*-2-bicyclo[3.2.0]hept-6-enyl tosylate (IIIb, X = OTs) were studied at three temperatures. The following results were obtained: 50.0°, k = $1.11 \pm 0.1 \times 10^{-7}$ sec^{-1}; 75.03°, k = $3.60 \pm 0.1 \times 10^{-6}$ sec^{-1}; 106.8°, k = $1.11 \pm 0.016 \times 10^{-4}$ sec^{-1}. This is in good agreement with the results of Coates[6a] (50°, k = 1.21×10^{-7} sec^{-1}; extrapolated from data at higher temperatures) and those of Svensson[6b] from the more reactive corresponding brosylate (50°, k = 4.45×10^{-7} sec^{-1}). Samples of the exo tosylate (IIIa, X = OTs) could only be obtained as oils despite extensive attempts at purification using column chromatography, and recrystallization from hydrocarbon solvents, so the kinetic results cannot be accepted without some reservation. It should be pointed out that high-purity (99% or better) samples of alcohol were used in its preparation. Also, the spectral results are consistent with the assigned structure, especially those from the NMR, which shows no extraneous signals, and integration peak heights in ratios expressable as integral numbers within experimental error. This is consistent with 95% or better purity. Also, first-order plots of the rate data did not deviate from linearity over at least 2 half-lives. Replicate determinations of the rate constant for acetolysis of the exo tosylate at 50.0° yielded the following average value: k = $1.9 \pm 0.1 \times 10^{-4}$ sec^{-1}. Thus, the exo tosylate undergoes acetolysis at a rate some 1600 times faster than does the endo epimer. Since at least 30% of the products from acetolysis of the latter appear to be formed via a solvent-assisted pathway, rather than unassisted ionization (see below), a corrected rate ratio of 2400 is probably a more accurate representation of the reactivity difference. Either ratio, being close to the corresponding rate difference (7600) in the dehydronorbornenyl system,[11] is consistent with homoallylic participation to form bridged cation IIIc, analogous in structure to the bridged 2-norbornenyl cation,[12] as the first-formed intermediate from solvolysis of exo tosylate IIIa. In a study of the solvolysis of *exo*- and *endo*-2-bicyclo[3.2.0]hepta-3,6-dienyl p-nitrobenzoates (VIb, X = OPNB, and VIc, Y = OPNB, respectively), we noted[14] that the allylic double bond in the five-membered ring levels the exo/endo rate ratio to unity and also swamps out homoallylic participation in the product-forming step. This indicates that homoallylic participation in the solvolysis of exo tosylate results in nonvertical[15] or distortional[16] stabilization in bridged cation IIIc. The rate data from acetolysis of the title compounds and some related substrates are presented in Table I. Consideration of the relative reactivities is informative in several respects.

The endo tosylate (IIIb, Y = OTs) undergoes acetolysis some 300–500 times slower than does cyclopentyl tosylate

Table I
Rate Constants for Acetolysis of Various Tosylates

Substrate	Temp, °C	k, sec^{-1}	Relative rate	Ref
VII, X = OTs[a]	50	4.23×10^{-5}	1	17
VIIIa, X = OTs[b]	50	2×10^{-6}	0.042	18
VIIIb, X = OTs[b]	50	1.9×10^{-4}	4.5	18
IIIb, Y = OTs[c,d]	50.0	$(1.11 \pm 0.1) \times 10^{-7}$	0.0027	*e*
	50[f,g]	1.21×10^{-7}		6a
	75.03[c,d]	$(3.6 \pm 0.12) \times 10^{-6}$		*e*
	100[f]	4.90×10^{-5}		6a
	106.8[c,d]	$(1.11 \pm 0.02) \times 10^{-4}$		*e*
IIIa, X = OTs[c,h]	50.0	$(1.9 \pm 0.1) \times 10^{-4}$	4.5	*e*
Ia, X = OTs[i]	50	2.7×10^{-2}	630	3a
IX, X = OTs[i]	50	9×10^{-3}	210	6a
X, X = OTs[j]	50	1.4	3.2×10^4	6a

[a] [NaOAc] = 0.117 M. [b] Calculated from rate data on the corresponding brosylate using a factor of 3 to relate the relative reactivities. [c] [NaOAc] = 0.0756 M. [d] Result of a single determination. Error is standard deviation. [e] This work. [f] [NaOAc] = 0.045 M. [g] Extrapolated from data at higher temperatures. [h] Average of two determinations. Error is average deviation. [i] Extrapolated from data at lower temperatures. [j] Calculated from the data on Ia, X = OTs, assuming that the reactivity ratio for hydrolysis of the corresponding p-nitrobenzoates (50, ref 6a) is applicable to acetolysis at 50°.



(VII, X = OTs).[17] That this difference is due in part to the electron-withdrawing powers of the double bond is shown by the fact that the corresponding reactivity difference for *endo*-2-bicyclo[3.2.0]heptyl tosylate (VIIa, X = OTs),[18] the saturated analog, is decreased to ca. 25. The exo tosylate (IIIa, X = OTs), on the other hand, reacts 4.5 times faster than VII, X = OTs, as does *exo*-2-bicyclo[3.2.0]heptyl tosylate (VIIIb, X = OTs),[18] the saturated analog. The latter observation would appear to argue against significant homoallylic participation in the solvolysis of exo tosylate IIIa, but the solvolysis of VIIIb, X = OTs, is itself thought to be anchimerically assisted ($k_{VIIIb}/k_{VIIIa} = 10^2$),[18] rendering it a poor model compound for comparisons of this type.

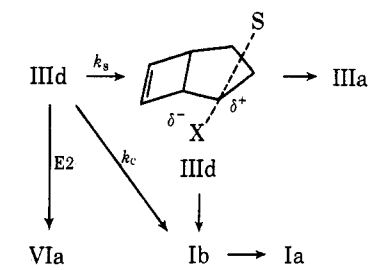
Svensson[6b] noted that attempts to prepare exo brosylate IIIa (X = OBs) resulted in mixtures of the desired compound and *anti*-7-norbornenol (Ia, X = OH) and made the reasonable proposal that exo brosylate, which partially hydrolyzed during work-up, was probably somewhat more reactive than anti 7-brosylate Ia (X = OBs), which survives such work-up intact. This seems plausible, since *anti*-tricyclo[5.2.0.0^{2,5}]nona-3,8-dien-6-yl tosylate (IX, X = OTs)[6a] undergoes acetolysis some 6.8×10^4 times faster than endo tosylate IIIb (X = OTs) at 25°. Our results show, however, that exo tosylate IIIa (X = OTs) is in fact some 140 times *less* reactive than *anti*-7-norbornenyl tosylate (Ia, X = OTs), and some 47 times less reactive than tricyclic tosylate IX (X = OTs). The latter compound exhibits a reactivity ca. 150 times slower than that projected for *exo-syn*-tricyclo[4.2.1.0^{2,5}]nona-3,7-dien-9-yl tosylate. Since exo tosylate and anti 7-tosylate (IIIa and Ia, X = OTs) are structurally related in the same fashion as the tricyclic tosylates (IX and X, X = OTs), the good agreement between the relative rates is probably significant, demonstrating that incorporation of an additional ethylenic bridge in exo tosylate and anti 7-tosylate (forming IX and X, respectively) results in a ca. 50-fold solvolytic rate enhancement ($k_{IX}/k_{IIIa} = 47$; $k_X/k_{Ia} = 50$[6a]).

The results from the product studies involving the endo tosylate IIIb are presented in Table II. Acetolysis and hydrolysis in 50% aqueous acetone produce mixtures of *exo*-2-bicyclo[3.2.0]hept-6-enyl and *anti*-7-norbornenyl derivatives (IIIa and Ia, X = OAc and OH, respectively). Our results from the acetolysis (IIIa:Ia, X = OAc 32:68) agree well with those of Svensson[6b] (IIIa:Ia, X = OAc 33:67). Hydrolysis in 50% aqueous acetone, a more nucleophilic medium, results in an increase in the ratio of yields of unrearranged to ring-enlarged products (IIIa:Ia X = OH 57:43). Methanolysis in 4 *M* sodium methoxide of the more reactive endo brosylate (IIIb, Y = OBs) yielded the corresponding exo methyl ether (IIIa), along with small amounts of bicyclo[3.2.0]hepta-2,6-diene (VIa).

Table II
Products from Solvolysis of *endo*-2-Bicyclo[3.2.0]hept-6-enyl Tosylate (IIIb, X = OTs)

Solvolysis medium (temp, °C)	Products (relative yield)	Total yield, %
HOAc[a] (101)	IIIa, X = OAc (32); Ia, X = OAc (68)	82
HOAc[b] (75)	IIIa, X = OAc (33); Ia, X = OAc (67)	100
50% aqueous acetone[c] (101)	IIIa, X = OH (57); Ia, X = OH (43)	91
4 *M* NaOMe in MeOH[d] (101)	IIIa, X = OMe (90); VIa (10)	86

[a] Buffered with a ca. threefold excess of NaOAc; reaction time 8 hr. [b] Run in 0.07 *M* NaOAc for 170 hr (ref 6b). [c] Buffered with a ca. threefold excess of $NaHCO_3$; reaction time 8 hr. [d] Reaction carried out on corresponding brosylate (IIIb, Y = OBs); reaction time 8 hr.



The stereospecific Walden inversion observed in the formation of unrearranged products is more consistent with a solvent-assisted pathway (k_s) than with reaction of solvent with a "classical" cation, as observed[14] during the nonstereospecific solvolysis of the closely related *exo*- and *endo*-dienyl *p*-nitrobenzoates VIb and VIc (X and Y = OPNB, respectively), presumably involving allyl cation VId. We concur, therefore, with Svensson's view[6b] that the endo tosylate undergoes solvolysis at least in part via transition state IIId which collapses to form the exo products (IIIa, X = OAc, OH). Since nucleophilic solvent participation occurs to an extent sufficient to influence the stereochemistry, it also probably influences the reactivity of the endo substrate. The rearranged anti 7 products (Ia, X = OAc, OH) can arise either from unassisted ionization (k_c), with rearrangement to the more stable 7-norbornenyl cation (Ib) probably occurring within a tight ion pair before solvent can intervene, or solvent-assisted ionization via leakage from IIId to Ib.[6b] This ambiguity cannot be resolved using the data at hand, but disappears when 4 *M* sodium methoxide in methanol is employed; in this strongly nucleophilic medium, rearrangement is not observed, IIId becomes the classical SN2 transition state with little ionic character, and E2 elimination, forming VIa, occurs to a limited extent.

The results from product studies on the solvolysis of the exo tosylate are given in Table III. Hydrolysis of this substrate, *anti*-7-norbornenyl tosylate (Ia, X = OTs), and *endo*-tricyclo[3.2.0.0^{2,7}]hept-3-yl *p*-nitrobenzoate (II, X = OPNB) in 50% aqueous acetone produces anti 7-alcohol, with the latter substrate also furnishing some of the less reactive corresponding ester (Ia, X = OPNB). Thus, the 7-norbornenyl cation (Ib) appears to be the product-forming intermediate in the solvolysis of all three substrates. The latter two (Ia, X = OTs, and II, X = OPNB) are thought[3,4] to yield this cation directly. In our preliminary communication[5] of these results, we showed that the solvolytic transition state for the exo tosylate was ca. 18–19 kcal/mol higher in energy than that from anti tosylate, suggesting the involvement of another species, presumably bridged cation

Table III
Products from Solvolysis of *exo*-2-Bicyclo[3.2.0]hept-6-enyl Tosylate and Related Substrates in Various Media

Substrate	Solvolysis medium	Products (% yield)	Ref
Ia, X = OTs	50% aqueous acetone[a]	Ia, X = OH (100)	3b
II, X = OPNB	50% aqueous acetone[a]	Ia, X = OH (76); Ia, X = OPNB (23)	4
IIIa, X = OTs	50% aqueous acetone[b]	Ia, X = OH (80)	c
IIIa, X = OTs	4 *M* NaOMe–MeOH[d]	Ia, X = OMe (39); II, X = OMe (20); IIIb, X = OMe (30); VIa (10) (Ia:II 65:35)	c
Ia, X = OTs	4 *M* NaOMe–MeOH[e]	Ia, X = OMe (46); II, X = OMe (27) (Ia:II 63:37)	c

[a] Buffered by excess $NaHCO_3$. [b] Buffered by a threefold excess of $NaHCO_3$. [c] This work. [d] 50° for 6 hr. [e] 50° for 2 hr. An unidentified hydrocarbon (10% yield) was also detected.

Table IV
Products from Acetolysis of Various *exo*-2-Bicyclo[3.2.0]hept-6-enyl Tosylates[a]

Substrate	Products (% yield)	Ref
IVa, X = OTs[b]	IVa, X = OAc (12); Va, X = OAc (82)	7
IVb, X = OTs[b]	IVb, X = OAc (11); Vb, X = OAc (83)[c]	7
IIIa, X = OTs[d]	Ia, X = OAc (80)	e

[a] Buffered by a threefold excess of NaOAc. [b] 98°. The crude product was reduced to the corresponding alcohols using $LiAlH_4$ prior to GC analysis. [c] Also detected in 5% yield was 7-methylene-5,5-dimethylbicyclo[2.2.1]hept-2-ene, bringing the total yield of ring-enlarged products to 88%. [d] 101°. [e] This work.

IIIc, as the first-formed intermediate,[19] which undergoes a very facile rearrangement.

Strong nucleophiles are often employed to trap[3e,20] rapidly rearranging cations; thus a study of the solvolysis of exo tosylate (IIIa, X = OTs) in 4 *M* sodium methoxide in methanol was undertaken. The products were found to be bicyclo[3.2.0]hepta-2,6-diene (VIa) (10% yield) and endo methyl ether IIIb (Y = OMe) (30% yield), formed via E2 and SN2 pathways, respectively, as well as a 65:35 mixture of *anti*-7-norbornenyl and *endo*-tricyclo[3.2.0.$0^{2,7}$]hept-3-yl methyl ethers (Ia and II, X = OMe, respectively) (59% yield). The latter products are known to arise from similar treatment of anti tosylate at 25° (as a 51:49 mixture)[3e]. As a control experiment, the latter reaction was studied at 50°, the conditions employed for the methanolysis of exo tosylate IIIa. A virtually identical (63:37) mixture of Ia and II was observed (73% yield).

Thus, the ring enlargement of bridged cation IIIc to the 7-norbornenyl cation is exceedingly rapid, being complete before reaction with solvent or added strong nucleophile occurs to a detectable extent. Whitham[7] found that acetolysis of *exo*-4,4,6- and -1,4,4-trimethylbicyclo[3.2.0]hept-6-en-2-yl tosylates (IVa and IVb, X = OTs, respectively) yields mixtures of the corresponding ring-enlarged acetates (Va and Vb, X = OAc) along with small amounts of the unrearranged exo acetates (see Table IV). Acetolysis of exo tosylate IIIa yields, as expected, only *anti*-7-norbornenyl acetate (Ia, X = OAc). The first-formed cations (IVc and IVd) from solvolysis of the exo trimethyl tosylates are, therefore, seen to be partially trapped even by the weak nucleophile, buffered acetic acid, showing that they undergo ring enlargement at a much slower rate than does cation IIIc. Comparison of the relative free energies of activation (calculated directly from the solvolytic product ratios) for ring enlargement vs. solvent capture for these cations (Figure 1) is instructive.

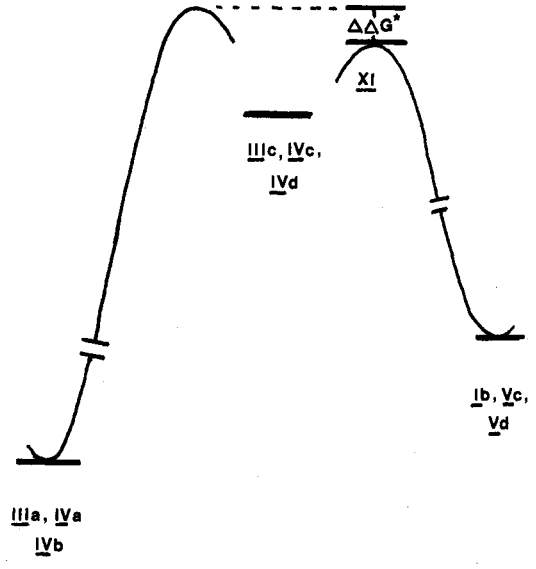


Figure 1. Relative free energies of activation for ring enlargement of various 2-bicyclo[3.2.0]hept-6-enyl cations vs. capture by solvent: $\Delta\Delta G^*_{IIIc} > 4$ kcal/mol, $\Delta\Delta G^*_{IVc} = 1.41$ kcal/mol, $\Delta\Delta G^*_{IVd} = 1.53$ kcal/mol.

For the 4,4,6-trimethylbicyclo[3.2.0]heptenyl cation (IVc), the transition state for solvent capture is higher in energy than that for ring enlargement ($\Delta\Delta G^*_{IVc}$) by 1.41 kcal/mol; the corresponding value ($\Delta\Delta G^*_{IVd}$) for the 1,4,4-trimethylbicyclo[3.2.0]heptenyl cation (IVd) is 1.53 kcal/mol. Since no unrearranged products were observed in the solvolysis of exo tosylate IIIa, an accurate value for the corresponding free energy difference ($\Delta\Delta G^*_{IIIc}$) is not available. A lower limit, however, can be assigned as follows: if, along with the 80% yield of anti 7-acetate (Ia, X = OAc), unrearranged products were formed in yields as high as 0.3–0.5%, but escaped detection, then this energy difference is at least ca. 4 kcal/mol, differing by ca. 2.5 kcal/mol from the value for both trimethyl derivatives.

In cation IVc, the methyl group at C-6 should have a similar stabilizing effect on the transition states for both solvent capture and ring enlargement (XI, $R_1 = R_2 = Me$; $R_3 = H$). The relative free energies for ring enlargement of cations IVc and IIIc should be similar. They are not. More significantly, the methyl group at C-1 in cation IVd should have little or no effect on the energy of the transition state for solvent capture (or the cation itself), but should significantly stabilize the ring-enlarged cation (Vd). Gassman[21] noted that substitution of a methyl group at C-7 enhances the rate of solvolysis of *anti*-7-norbornenyl tosylate (Ia, X = OTs) by a factor of 7600 (25°), corresponding to a 5.4 kcal/mol decrease in the free energy of activation with a similar enhancement in stability of the intermediate cation, closely related to Vd. The transition state for ring enlargement (XI, $R_1 = R_3 = Me$; $R_2 = H$) should be stabilized by a similar amount, rendering the relative free energy for ring enlargement vs. solvent capture for cation IVd ($\Delta\Delta G^*_{IVd}$) larger than for cation IVc ($\Delta\Delta G^*_{IVc}$). The predicted energy difference is observed ($\Delta\Delta G^*_{IVd} - \Delta\Delta G^*_{IVc} = 0.11$ kcal/mol), but is so small as to be insignificant. Thus, neither single methyl gives rise to the predicted effect. The retar-

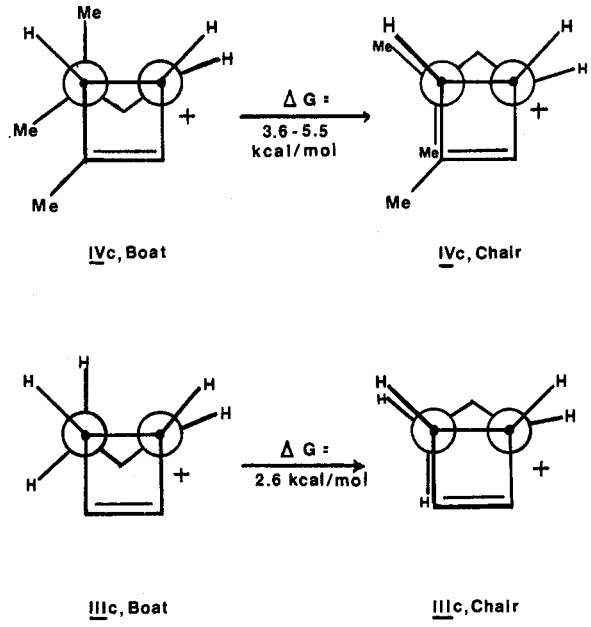
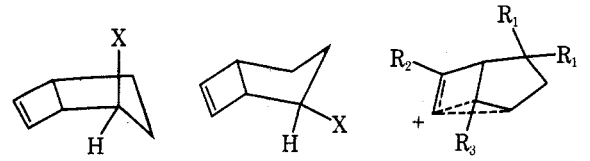


Figure 2. Chair- and boat-like conformations for the 2-bicyclo-[3.2.0]hept-enyl cation (IIIc) and the 4,4,6-trimethyl derivative (IVc).

dation is, therefore, probably best explained in terms of steric–conformational effects arising from the *gem*-dimethyl group at C-4.

Svensson[6b] noted that the NMR data on the endo brosylate (IIIb, X = OBs) are consistent with a boat-like conformation. We note in all *exo*-2-bicyclo[3.2.0]hept-6-enyl derivatives (IIIa) that the methine proton at C-2 gives rise to a doublet, J = 3.5 Hz [X (δ): OTs (4.69), OH (3.94), OMe (3.48)] with the splitting apparently due to the endo proton at C-3, with similar observations being made by Whitham[7] concerning trimethyl derivatives IVa and IVb. These observations are consistent with a boat-like conformation for the exo derivatives (IIIa, IVa, IVb) also. Inspection of molecular models of these derivatives shows that (a) orbital interactions between the developing positive charge and the homoallylic double bond are more favorable in the boat-like conformation than the chair, suggesting the former conformation for the first-formed cations (IIIc, IVc, IVd) also, and (b) ring enlargement must be concomitant with or preceded by ring flipping to the chair-like conformation.



Examination of the Newman projections of cations IIIc and IVc (Figure 2) shows that in the latter case this ring flipping gives rise to eclipsing between C-6 and the endo methyl at C-4, and should be endothermic by ca. 3.6–5.5 kcal/mol, the energy difference between butane in the gauche and cisoid conformation.[22] The corresponding interaction in cation IIIc, involving the endo hydrogen at C-4, is less unfavorable; the ring flipping in this case should only be endothermic by ca. 2.6 kcal/mol, the energy difference between the gauche and lower energy eclipsed forms of butane.[22] Thus, a difference in the relative free energies of activation for ring enlargement between cations IIIc and IVc (as well as IVd) ($\Delta\Delta G^*_{IIIc} - \Delta\Delta G^*_{IVc}$) of ca. 1–3 kcal/mol would be expected. The reasonably good agreement between expectation and experiment ($\Delta\Delta G^*_{IIIc} - \Delta\Delta G^*_{IVc} \geq$ 2.5 kcal/mol) demonstrates the validity of these steric–conformational arguments.

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Registry No.—Ia (X = OTs), 13111-74-5; Ia (X = OH), 694-70-2; Ia (X = OMe), 13041-10-6; Ia (X = OAc), 13426-55-6; II (X = OMe), 38452-05-0; II (X = OPNB), 23211-61-2; IIIa (X = OTs), 53585-69-6; IIIa (X = OH), 52759-75-8; IIIa (X = OAc), 55682-01-4; IIIa (X = OMe), 54594-93-3; IIIb (Y = OTs), 41326-98-1; IIIb (Y = OH), 41398-41-8; IIIb (Y = OBs), 52743-48-3; IIIb (Y = OMe), 53934-56-8; tosyl chloride, 98-59-9; brosyl chloride, 98-58-8.

References and Notes

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(12) Brown[13] has strongly questioned the bridged structure for the 2-norbornenyl cation, but has recently found evidence for weak homoallylic participation in the solvolysis of certain 5-methyl-2-norbornenyl derivatives.[13b] In both cases, the arguments rested on significant exo/endo rate ratios observed during solvolysis of various 2-aryl derivatives. In a previous paper, we noted[14] that the allylic double bond in the 2-bicyclo-[3.2.0]hepta-3,6-dienyl *p*-nitrobenzoates (VIb, Y = OPNB, and VIc, X = OPNB) levels the exo/endo solvolytic rate ratio for the title compounds to unity. Thus, whatever the structure of the 2-norbornenyl cation, this, plus the information in the paper, establishes a bridged structure for cation IIIc.
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