Protoadamantyl–Adamantyl Rearrangement. Methyl-d_3 Isotope Effects and Product Compositions in the Solvolysis of 4-*endo*- and 4-*exo*-4-Methylprotoadamantyl and 1-Methyl-2-adamantyl Derivatives. Evidence for Bridging

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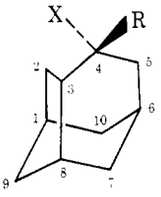
Methyl-d_3 isotope effects and product compositions in the solvolysis of 4-*endo*- (**1b**) and 4-*exo*-4-methylprotoadamantyl dinitrobenzoate (**2b**) and 1-methyl-2-adamantyl tosylate (**3b**) were determined in 60% aqueous dioxane. All three esters yield the same four products, 4-methyl-4-protoadamantene, 4-methyleneprotoadamantane, 4-*exo*-4-methylprotoadamantanol, and 1-methyl-2-adamantanol, but in significantly different ratios. The substitution product with the skeleton of the starting ester is formed preferentially. The titrimetrically determined isotope effects of **1b** (1.47) and **2b** (1.30) are larger than the "true" secondary isotope effects, owing to the primary isotope effect contribution. The calculated "true" values of the secondary methyl-d_3 effects of **1b** (1.37), **2b** (1.16), and **3b** (1.05) are consistent with an anchimerically unassisted solvolysis of **1b** and anchimerically assisted solvolyses of **2b** and **3b**. The substitution products are probably formed by collapse of the solvent-separated ion pairs rather than by nucleophilic attack on these ion pairs. The endo ester (**1b**) appears to solvolyze through a "classical" cationic species which turns subsequently into the same bridged intermediate as formed from the exo ester (**2b**). This intermediate is similar to, but not identical with, the intermediate arising from **3b**.

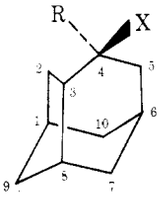
Interconversions of 2-adamantyl and 4-protoadamantyl substrates are well documented,[3-8] but the mechanism of these reactions is still controversial. Thermodynamically controlled reactions of 2-adamantyl and 4-protoadamantyl derivatives exclusively yield 2-adamantyl products[3-5,8] since the protoadamantane skeleton is 11 kcal/mol more strained than the adamantane skeleton.[5,9] However, kinetically controlled reactions produce both 2-adamantyl and 4-protoadamantyl products.[3-7] Schleyer,[4,5] Whiting,[3] and Lenoir[6] postulated the intermediacy of a common bridged 2-adamantyl cation in the solvolyses of 2-adamantyl and 4-*exo*-protoadamantyl substrates, the degree of bridging being highly dependent on the substituent at positions 1 and 4, respectively. The solvolysis of unsubstituted 4-*endo*-protoadamantyl substrates may be anchimerically assisted,[4] while the solvolysis of 4-*endo*-4-methylprotoadamantyl substrates appears to be unassisted[5] but may lead indirectly by "leakage" to the bridged 1-methyl-2-adamantyl cation. Recently, Fărcaşiu[7] questioned the intervention of bridged ions in the solvolyses of 1-substituted 2-adamantyl derivatives and suggested, as at least an equally plausible alternative, a rapidly equilibrating pair of the corresponding "classical" 2-adamantyl and 4-protoadamantyl ions formed by limiting ionization (k_c). Both of these interpretations are based on the product analyses and the substituent influence on the solvolysis rates of 2-adamantyl and 4 protoadamantyl substrates. However, the reaction mechanism can be significantly altered by replacement of substituents in the neighborhood of the reaction center, so that a direct comparison of the results obtained with different substituents could be misleading.

In this work we studied the solvolysis mechanism of 4-*endo*- and 4-*exo*-4-methylprotoadamantyl and 1-methyl-2-adamantyl substrates by methyl-d_3 isotope effects in combination with product analyses. Isotopic substitution induces only small changes in rates and mechanisms[10a] compared with the gross effects caused by replacement of one substituent by another.

Methods and Results

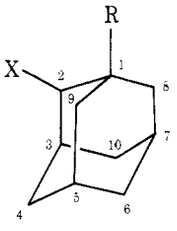
The starting materials 4-*endo*- ($\mathbf{1b_H}$) and 4-*exo*-4-methylprotoadamantyl dinitrobenzoates ($\mathbf{2b_H}$) and 1-methyl-2-adamantyl tosylate ($\mathbf{3b_H}$), as well as their methyl-d_3 analogues ($\mathbf{1b_D}$, $\mathbf{2b_D}$, and $\mathbf{3b_D}$), were obtained from the corresponding alcohols by standard procedures.[11] The purities of all esters were ≥96% (by ^{1}H NMR). 4-*endo*- ($\mathbf{1a_H}$,$\mathbf{1a_D}$) and 4-*exo*-4-methylprotoadamantanols ($\mathbf{2a_H}$,$\mathbf{2a_D}$) were prepared by methyl Grignard addition[8a,b] to 4-protoadamantanone[12] followed by column chromatography separation. Both 1-methyl-2-adamantanol ($\mathbf{3a_H}$) and 1-methyl-d_3-2-adamantanol ($\mathbf{3a_D}$) were obtained by sulfuric acid catalyzed isomerization





$\mathbf{1a_H}$, X = OH; R = CH_3
$\mathbf{1a_D}$, X = OH; R = CD_3
$\mathbf{1b_H}$, X = ODNB; R = CH_3
$\mathbf{1b_D}$, X = ODNB; R = CD_3

$\mathbf{2a_H}$, X = OH; R = CH_3
$\mathbf{2a_D}$, X = OH; R = CD_3
$\mathbf{2b_H}$, X = ODNB; R = CH_3
$\mathbf{2b_D}$, X = ODNB; R = CD_3



$\mathbf{3a_H}$, X = OH; R = CH_3
$\mathbf{3a_D}$, X = OH; R = CD_3
$\mathbf{3b_H}$, X = OTs; R = CH_3
$\mathbf{3b_D}$, X = OTs; R = CD_3

of the respective mixtures of 4-*endo*- and 4-*exo*-4-methylprotoadamantanols.

Esters $\mathbf{1b_H}$, $\mathbf{1b_D}$, $\mathbf{2b_H}$, $\mathbf{2b_D}$, $\mathbf{3b_H}$, and $\mathbf{3b_D}$ were solvolyzed in 60% aqueous dioxane at 60 °C. The solvolysis rates were measured potentiometrically on an automatic recording pH-stat. For the product studies, the esters were solvolyzed through 8 half-lives in the presence of 2,6-lutidine; the resulting solutions of the products were diluted with dioxane and directly analyzed by a gas chromatograph coupled to a data processor using authentic samples as standards. The

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solvolysis rates and the methyl-d_3 isotope effects are given in Table I, while the compositions of the solvolysis products are shown in Table II. Esters **1b** and **3b** produced the same four products, 4-methyl-4-protoadamantene (**4**), 4-methyleneprotoadamantane (**5**), 4-*exo*-4-methylprotoadamantanol (**2a**), and 1-methyl-2-adamantanol (**3a**), in almost quantitative total yields. However, **2b** produced, in addition to the solvolysis products **4, 5, 2a,** and **3a,** 15–20% (by ^{1}H NMR) of 1-methyl-2-adamantyl dinitrobenzoate[13] by the internal-return reaction. In no case was 4-*endo*-4-methylprotoadamantanol (**1a**) detected in the product mixture. All products were stable under the reaction conditions used.

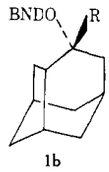
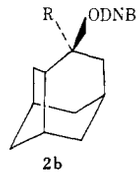
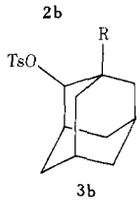
Discussion

The methyl-d_3 isotope effect of 4-*endo*-4-methylprotoadamantyl dinitrobenzoate (**1b**; Table I) is one of the largest methyl-d_3 effects ever observed, comparable with that of 2-methyl-2-adamantyl chloride.[14a] The effect of the exo dinitrobenzoate (**2b**) is considerably smaller, while the effect of 1-methyl-2-adamantyl tosylate (**3b**) is very small but still "normal" (not inverse)! Such methyl-d_3 isotope effects are consistent with the postulated[5] intermediacy of an incipient bridged cation(s) in the solvolysis of **2b** and **3b** and the anchimerically unassisted solvolysis of **1b.** However, the product compositions (Table II) indicate that the mechanism is more complex. All three esters (**1b, 2b,** and **3b**) yield the same four solvolysis products, i.e., 4-methyl-4-protoadamantene (**4**), 4-methyleneprotoadamantane (**5**), 4-*exo*-4-methylprotoadamantanol (**2a**), and 1-methyl-2-adamantanol (**3a**), but in significantly different ratios, contrary to the results reported[5,15] previously. Consequently, solvolyses of **1b, 2b,** and **3b** cannot lead to the same intermediate either directly from **2b** and **3b** or indirectly from **1b** ("leakage").

The elimination/substitution product ratio of the dinitrobenzoates (**1b** and **2b**) is approximately three times larger than the ratio for the tosylate (**3b**; see Table II). This strongly indicates that some elimination occurs in the tight ion pairs of **1b** and **2b,** involving the rather basic dinitrobenzoate leaving group as a proton acceptor. With the tosylate (**3b**), the low basicity of the counterion should highly reduce the elimination in the tight ion pair. This is consistent with the ratio of 4-methyleneprotoadamantane (**5**)/4-methyl-4-protoadamantene (**4**) determined in the solvolysis of the endo (**1b**) and exo dinitrobenzoates (**2b**). The ratio **5/4** is considerably larger for **2b,** which is expected[5] to solvolyze through the bridged transition state and intermediate. Owing to the bridging in the tight ion pair of **2b,** the methyl group should be tilted toward the exo side, coming close to the dinitrobenzoate group and favoring elimination. In the case of the endo dinitrobenzoate (**1b**), where no bridging is expected,[5] the distance between the methyl and the dinitrobenzoate group is larger. In addition, the dinitrobenzoate group in the tight ion pair of **2b** is more removed from the methylene hydrogen at postion 5 than in the case of **1b.** All of these effects should be considerably less pronounced in the solvent-separated ion pairs.

The relative amounts of 4-methyleneprotoadamantane (**5**) formed from the deuterio esters ($\mathbf{1b}_D$, $\mathbf{2b}_D$, and $\mathbf{3b}_D$) are, because of the primary isotope effect, twice smaller than those formed from the protio analogues ($\mathbf{1b}_H$, $\mathbf{2b}_H$, and $\mathbf{3b}_H$). All other products (**2a, 3a,** and **4**) arise in approximately equal amounts from both the deuterio and protio esters. If the elimination leading to **5** is a rate-determining process, the experimentally determined values of the isotope effects (Table I) are larger than the "true" methyl-d_3 secondary isotope effects. Since the tosylate group is a very weak base, it may be assumed that essentially all elimination from 1-methyl-2-adamantyl tosylate (**3b**) occurs in the solvent-separated ion pair and is not a rate-determining process. Elimination from the dinitrobenzoates (**1b** and **2b**) occurs in both the tight and

Table I. Solvolysis Rates and Methyl-d_3 Isotope Effects in 60% Aqueous Dioxane at 60 °C

Compd	R	$k \times 10^4$, s^{-1} [a,b]	$(k_H/k_D)_{exptl}$ [b]
 1b	CH_3	0.397 (5)	1.47 (5)
	CD_3[c]	0.270 (8)	
 2b	CH_3	4.62 (9)	1.30 (3)
	CD_3[c]	3.56 (6)	
 3b	CH_3	1.22 (1)	1.05 (1)
	CD_3[c]	1.16 (1)	

[a] Average values of 7–9 individual rate constants. [b] The uncertainties are standard errors; e.g., 0.397 (5) = 0.397 ± 0.005 and 1.47 (5) = 1.47 ± 0.05. [c] Deuterium content was 99.5%.

solvent-separated ion pairs, while the substitution products of all three esters (**1b, 2b,** and **3b**) are derived exclusively from the solvent-separated ion pairs (see later). Assuming that the fractions of the elimination products arising from the solvent-separated ion pairs of all three esters are essentially equal, fractions of the solvolysis products formed from the tight (x) and solvent-separated ion pairs ($1 - x$) of dinitrobenzoates **1b** and **2b** can be calculated by

$$f_{DNB} = x + (1 - x)f_{Ts} \quad (1)$$

where f_{DNB} and f_{Ts} are the experimentally determined fractions of the elimination products (Table II) derived from the corresponding dinitrobenzoates (**1b** and **2b**) and tosylate **3b,** respectively.

The "true" values of the methyl-d_3 secondary isotope effect, $(k_H/k_D)_{true}$, of 4-*endo*- (**1b**) and 4-*exo*-4-methylprotoadamantyl dinitrobenzoates (**2b**) can be calculated from the experimentally determined isotope effects, $(k_H/k_D)_{exptl}$ (Table I), using the modified Shiner's[14a] expression:

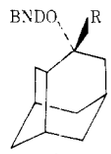
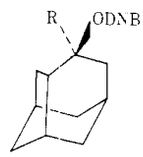
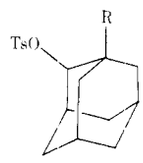
$$(k_H/k_D)_{true} = (k_H/k_D)_{exptl}(1 - x_H)/(1 - x_D) \quad (2)$$

Fractions of the solvolysis products derived from the solvent-separated ion pairs of the respective protio ($1 - x_H$) and deuterio ($1 - x_D$) dinitrobenzoates have been computed by expression 1. The obtained "true" values of the isotope effects (Table III) are in good agreement with the values of the methyl-d_3 secondary isotope effects estimated from the solvolysis rate constants[4,5] of the methyl-substituted (k_{CH_3}) and unsubstituted (k_H) esters using the SBS correlation:[14]

$$\log (k_H/k_D)_{SBS} = 0.02024 \log (k_{CH_3}/k_H) \quad (3)$$

The "true" values of the methyl-d_3 β-secondary isotope effect of 4-*endo*- (**1b**) and 4-*exo*-4-methylprotoadamantyl dinitrobenzoate (**2b**) are lower than the titrimetrically determined isotope effects (Table III), owing to the contribution of the rate-determining elimination. The magnitude of the "true" isotope effect of **1b** is close to the "limiting value"[16] for the methyl-d_3 β-secondary isotope effect and considerably larger compared with the "true" isotope effect of **2b.** The β-secondary isotope effects are generally reduced by positive charge delocalization in a solvolysis transition state since the

Table II. Solvolysis Products in 60% Aqueous Dioxane at 60 °C

Starting Material	R	Products, %[a] 4	5	2a	3a
 1b	CH_3	9.2 (3)	14.3 (3)	44.5 (4)	32.0 (4)
	CD_3[b]	10.3 (3)	6.5 (3)	45.4 (4)	37.8 (4)
 2b	CH_3	5.8 (2)	23.0 (2)	46.4 (2)	24.8 (4)
	CD_3[b]	6.9 (2)	11.3 (2)	52.2 (3)	29.6 (3)
 3b	CH_3	3.0 (2)	7.8 (4)	33.2 (9)	56.0 (7)
	CD_3[b]	4.2 (3)	5.2 (3)	42.5 (6)	48.1 (3)

[a] Average values of 2–4 independent experiments with 5–10 GLC analyses of each product mixture. The uncertainties are standard errors; e.g., 9.2 (3) = 9.2 ± 0.3. [b] Deuterium content was 99.5%.

Table III. Methyl-d_3 Isotope Effects of 4-*endo*-(1b), 4-*exo*-4-Methylprotoadamantyl Dinitrobenzoate (2b), and 1-Methyl-2-adamantyl Tosylate (3b) Corrected for the Primary Isotope Effect Contribution [$(k_H/k_D)_{true}$]

Compd	(k_H/k_D)-$_{exptl}$[a]	$1 - x_H$[b]	$1 - x_D$[b]	$(k_H/k_D)_{true}$[c]	(k_H/k_D)-$_{SBS}$[d]
1b	1.47	0.86	0.92	1.37 (6)	1.39
2b	1.30	0.80	0.90	1.16 (4)	1.19
3b	1.05	1.0	1.0	1.05 (1)	1.06

[a] Methyl-d_3 isotope effects determined titrimetrically in 60% dioxane at 60 °C (see Table I). [b] Computed by eq 1. [c] Computed by eq 2. [d] Methyl-d_3 secondary isotope effects estimated by the SBS correlation (eq 3); k_{CH_3} and k_H are calculated from the values[4,5] at other temperates using for **1b** the conversion factor[4] $k_{OTs}/k_{ODBN} = 2 \times 10^7$.

hyperconjugative interaction is better the larger the electron deficiency at the reaction center.[16] Factors, other than σ participation, which might possibly influence positive charge location in the transition state of 4-*endo*- and 4-*exo*-methylprotoadamantyl substrates, would be essentially equal. Consequently, positive charge in the transition state of the exo dinitrobenzoate (**2b**) should be more strongly delocalized than that in the endo isomer (**1b**). Both the exo C_4–ODNB bond in **2b** and the endo C_4–ODNB bond in **1b** are stereochemically well situated for σ participation, i.e., antiperiplanar relative to the C_2–C_3 and C_3–C_8 bonds, respectively. However, σ participation is far more favored for the exo dinitrobenzoate (**2b**) since the bridging resulting from the C_3–C_8 bond participation would require a considerable distortion of the skeleton and the resulting bridged species would be a highly unfavorable intermediate between a secondary and a tertiary 4-protoadamantyl cation.[17,18]

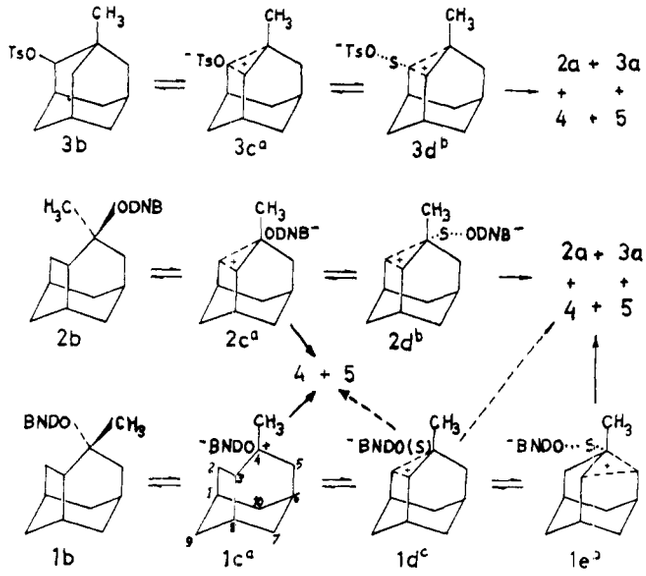
The γ-secondary deuterium isotope effect is generally inverse ($k_H/k_D < 1$) if there is no special mechanistic complication associated with the solvolysis.[10] However, the methyl-d_3 γ-secondary isotope effect of 1-methyl-2-adamantyl tosylate (**3b**) is significantly higher than unity; i.e., the effect is "normal", not inverse! Since the reaction center is at the γ position relative to the deuterium atoms, no contribution of the primary isotope effect to the measured effect should be expected. (Elimination occurs in the solvent-separated ion pair and is not rate determining; see the preceding text.) Consequently, some positive charge must be located at the β carbon relative to the deuterium atoms in the transition state of **3b.** In other words, positive charge is delocalized between the carbon atoms at positions 1 and 2; the solvolysis of **3b** is assisted by σ participation involving the C_1–C_8 (C_1–C_9) bond anti to the C_2–OTs bond.

Contrary to the solvolysis of 4-*endo*-4-methylprotoadamantyl substrate (**1b**), the solvolyses of both 4-*exo*-4-methylprotoadamantyl (**2b**) and 1-methyl-2-adamantyl (**3b**) substrates are anchimerically assisted, but fractions of positive charge located at the carbon atom adjacent to the methyl group in the transition states of **2b** and **3b** are rather different.

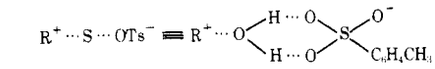
The substitution products, 4-*exo*-4-methylprotoadamantanol (**2a**) and 1-methyl-2-adamantanol (**3a**), of all three esters (**1b, 2b,** and **3b**) are formed from the solvent-separated ion pairs. Nucleophilic attack on the tight ion pairs arising from tertiary substrates as well as from secondary 2-adamantyl substrates[19] is unlikely to occur owing to steric hindrance. The ratio of the substitution products **2a/3a** depends on the structure of the starting ester (Table II). This ratio is considerably higher for 4-methyl-4-protoadamantyl dinitrobenzoates (exo, 1.9; endo, 1.4) than for 1-methyl-2-adamantyl tosylate (0.6), indicating a "memory" effect.

Both 1-methyl-2-adamantyl tosylate (**3b**) and 4-*exo*-4-methylprotoadamantyl dinitrobenzoate (**2b**) solvolyze through tight and solvent-separated ion pairs involving a common bridged cationoid[19a] resulting from the C_1–C_8 and

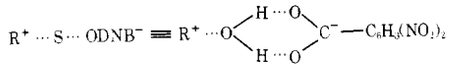
Scheme I



[a] The tight ion pairs. [b] The solvent-separated ion pairs:

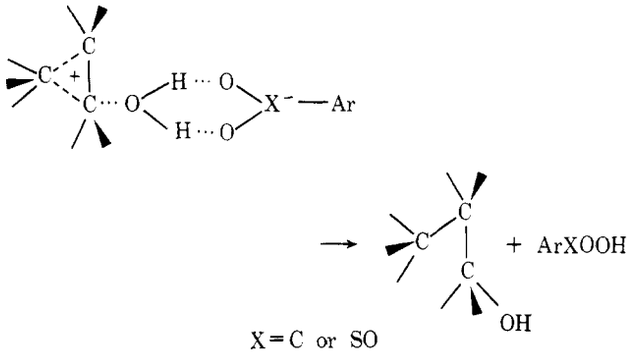


and



[c] The solvent may be "incorporated" into the ion pair.

C_2–C_3 bond participation, respectively (see the preceding text and Scheme I). The preferential formation of the substitution product with the same structure as the starting ester (Table II) may be explained by the influence of the leaving group location in the solvent-separated ion pairs. The substitution products are probably formed by collapse of the solvent-separated ion pairs rather than by nucleophilic attack on these ion pairs. This is consistent with the prevailing retention of the configuration observed in the solvolyses of secondary 2-adamantyl derivatives.[20]



The relative amounts of the substitution products, **2a** and **3a**, arising from the endo and exo dinitrobenzoates (**1b** and **2b**) are almost equal, suggesting that these products are formed from similar intermediates, solvent-separated ion pairs. The solvolysis course of 4-*endo*-4-methylprotoadamantyl dinitrobenzoate (**1b**) could be interpreted (see Scheme I) by the initial formation of an essentially "classical" cationic intermediate (**1c**), which turns subsequently into a more stable bridged species **1d** by formation of the C_2–C_4 bond and simultaneous weakening of the C_2–C_3 bond. The leaving group is located on the "wrong", endo side of the cationoid. However, this intermediate may isomerize rapidly into the isomer **1e** with the leaving group on the exo side, which is "identical"[21] to the solvent-separated ion pair **2d** formed from the exo dinitrobenzoate (**2b**). Therefore, it should yield the same substitution products as **2b**.[22] The small difference in the substitution product compositions of **1b** and **2b** indicates that the substitution products of **1b** arise preferably (but not exclusively) from the intermediate **1e**.

The formation of no 4-*endo*-4-methylprotoadamantanol (**1a**) in the solvolyses of all three esters, **1b, 2b,** and **3b,** is consistent with the bridging on the endo side and cannot be explained by the steric hindrance resulting from the hydrogen and carbon atoms neighboring the reaction center. Reduction of 4-protoadamantanone by $LiAlH_4$,[4] as well as methyl Grignard addition to this ketone,[5] do not involve the bridged intermediates and yield both the exo and endo products.

Internal return generally occurs at the tight ion pair stage. According to the mechanism proposed, the internal return to 1-methyl-2-adamantyl dinitrobenzoate should be expected to be more important for the exo dinitrobenzoate (**2b**) than for the endo ester (**1b**) since the cationoid in the tight ion pair arising from **2b** is bridged and that of **1b** is essentially "classical". The experimental results agree well with these predictions; solvolysis of **2b** gave 15–20% of 1-methyl-2-adamantyl dinitrobenzoate, while solvolysis of **1b** yielded less than 2% (if any) of the rearranged ester.

In conclusion, we would like to point out that contrary to the solvolysis of 4-*endo*-4-methylprotoadamantyl substrate, the solvolyses of both 4-*exo*-4-methylprotoadamantyl and 1-methyl-2-adamantyl substrates are anchimerically assisted. Our results are consistent with the mechanism proposed by Schleyer[5] and Lenoir[6] and cannot be explained by the equilibrating pair of the "classical" 1-methyl-2-adamantyl and 4-methyl-4-protoadamantyl ions as suggested by Fărcaşiu.[7] However, the real solvolysis mechanism is more complex than that postulated by Schleyer. All three substrates yield the same solvolysis products, but in significantly different ratios, contrary to the results reported[5] previously. The substitution products with the skeleton of the starting substrate are produced preferentially; these products are probably formed by collapse of the solvent-separated ion pairs rather than by nucleophilic attack on these ion pairs. The dinitrobenzoates yield considerably more elimination products than the tosylate, indicating that some elimination occurs in the tight ion pairs of the dinitrobenzoates involving the leaving group as a proton acceptor.

Experimental Section

General. Dioxane (p.a.) was purified as described previously.[23] Methyl-d_3 iodide (Merck) contained ≥99% of the theoretical amount of deuterium. All other chemicals were analytical grade. Melting points were determined on a Perkin-Elmer 1B differential scanning calorimeter and are uncorrected. ^1H NMR spectra were recorded on a Varian A-60A spectrometer using $CDCl_3$ as solvent, IR spectra were taken on a Perkin-Elmer 377 spectrophotometer, and mass spectra were obtained on a Varian CH-7 mass spectrometer. GLC analyses were carried out on a Varian Aerograph 1440 gas chromatograph coupled to a Perkin-Elmer processor PEP-1. Deuterium contents were determined by mass spectroscopy.

4-*endo*-4-Methylprotoadamantanol ($1a_H$) and 4-*exo*-4-Methylprotoadamantanol ($2a_H$). A crude mixture of epimeric 4-methyl-4-protoadamantanols ($1a_H$, 37%; $2a_H$, 63%) was obtained in 98% yield by methyl Grignard addition to 4-protoadamantanone[12] using the standard procedure.[8a,b] The mixture of alcohols (226 mg) was chromatographed on 40 g of silica gel using benzene with 1% of ether as eluent. Pure epimeric alcohols $1a_H$ and $2a_H$ (≥98% by GLC) were obtained in 27 (61 mg) and 65% (147 mg) yield, respectively. The ^1H NMR and the mass spectral data were in complete agreement with those reported previously[5] for these alcohols. $1a_H$: mp 86–88 °C (after sublimation in vacuo); IR (KBr) 3300 (s), 2924 (s), 1462 (m), 1372 (m), 1322 (m), 1130 (m), 1117 (s), and 917 (s) cm^{-1}. $2a_H$: mp 82–83 °C (after sublimation); IR (KBr) 3360 (s), 2920 (s), 1458 (m), 1370 (m), 1100 (m), 1090 (m), 914 (m), and 846 (m) cm^{-1}.

4-*endo*-4-Methyl-d_3-protoadamantanol ($1a_D$) and 4-*exo*-4-methyl-d_3-protoadamantanol ($2a_D$) were prepared in the same

manner as the protio analogues. The purity of $1a_D$ and $2a_D$ was higher than 99 and 97% (by GLC), respectively; the deuterium content of both alcohols was 99.5% of the theoretical amount of deuterium.

1-Methyl-2-adamantanol ($3a_H$). A crude mixture of $1a_H$ and $2a_H$ (90 mg, 0.54 mmol) was dissolved in 4 mL of 80% aqueous acetone; one drop of concentrated H_2SO_4[24] was added, and the reaction mixture was refluxed for 30 min. The resulting solution was concentrated in vacuo and extracted with ether (3 × 20 mL), the combined extracts were washed with water and dried, and the solvent was evaporated. The crude product was sublimed to give 80 mg (89%) of pure $3a_H$ (≥97% by GLC): mp 158–160 °C; IR (KBr) 3450 (s), 2900 (s), 2822 (s), 1452 (m), 1050 (m), 1034 (m), 980 (m), and 940 (m) cm^{-1}. The ^1H NMR and mass spectral data were in good agreement with those reported previously[8a] for this compound.

1-Methyl-d_3-2-adamantanol ($3a_D$) was obtained in the same manner as the protio analogue; the purity was higher than 97% (by GLC), and the deuterium content was 99.5% of the theoretical amount.

4-*endo*-4-Methylprotoadamantyl 3,5-Dinitrobenzoates ($1b_H$ and $1b_D$) and 4-*exo*-4-Methylprotoadamantyl 3,5-Dinitrobenzoates ($2b_H$ and $2b_D$). The protio and the methyl-d_3 dinitrobenzoates were prepared from the corresponding alcohols by the standard 3,5-dinitrobenzoyl chloride–pyridine method.[11a] Freshly recrystallized 3,5-dinitrobenzoyl chloride and pyridine dried over CaH_2 were used. The crude dinitrobenzoates were recrystallized twice from a 1:1 ether–pentane mixture at −80 °C (dry ice–acetone). Pure esters were obtained in the following yields: $1b_H$, 61% (mp 130–131 °C); $1b_D$, 74% (mp 131–133 °C); $2b_H$, 72% (mp 113–114 °C); and $2b_D$, 65% (mp 114–115 °C). The IR spectra (KBr) of all four dinitrobenzoates showed no absorption owing to the OH group [$1b_H$ 3111 (m), 3100 (m), 2917 (s), 1718 (s), 1630 (m), 1540 (s), 1175 (s), 742 (s), and 712 (s) cm^{-1}; $2b_H$ 3120 (m), 3099 (w), 2910 (s), 1720 (s), 1548 (s), 1342 (s), 1200 (m), 723 (s), and 711 (s) cm^{-1}]. The ^1H NMR spectral data of $1b_H$ and $2b_H$ agree with those reported previously[5] for these compounds.

1-Methyl-2-adamantyl Tosylates ($3b_H$ and $3b_D$). The protio and the methyl-d_3 tosylates were obtained by the pyridine method[11b] from the corresponding alcohols. The crude tosylates were recrystallized twice from 1:1 ether–pentane at −80 °C. Pure $3b_H$ was obtained in 69% yield (mp 113–114 °C) and $3b_D$ in 60% yield (mp 114–116 °C). The IR spectra (KBr) of both tosylates showed no absorption owing to the OH group [$3b_H$ 3060 (w), 2905 (s), 2851 (m), 1601 (m), and 1452 (m) cm^{-1}]. The ^1H NMR spectral data of $3b_H$ agree with those reported[5] for this tosylate.

Kinetic Measurements. The solvolysis rates were determined by continuous potentiometric titration using a Radiometer Copenhagen SBR2/TTT11 pH-stat, maintaining the pH of the reaction solution at 6.8. The initial concentration of the starting ester was ca. 0.004 M (20 mg in 15 mL of solvent) in all kinetic measurements. The protio and deuterio analogues were titrated at random in order to minimize the influence of temperature variations in the isotope effects. At least seven individual measurements were conducted for each ester. The rate constants were calculated from the standard integrated first-order law using a nonlinear least-squares program.

Product Studies. In a typical experiment, ester (120 mg, 0.33 mmol) was dissolved in 12 mL of 60% aqueous dioxane, an equivalent amount of 2,6-lutidine was added, and the resulting solution was stirred for 8 half-lives at 60 °C. The reaction mixture was allowed to cool down, diluted with 12 mL of dioxane, and then analyzed directly by gas chromatography on a 6 ft × ⅛ in 10% Carbowax 20M (Chromosorb W 100/120) column at a temperature programmed from 70 to 180 °C at a rate of 6 °C/min. The product study of each ester was performed at least twice. Each product mixture was analyzed by GLC 5–10 times, giving a total of at least 10 analyses for each ester.

All three esters (**1b, 2b,** and **3b**) yielded the same four solvolysis products, 4-methyl-4-protoadamantene (**4**), 4-methyleneprotoadamantane (**5**), 4-*exo*-4-methylprotoadamantanol (**2a**), and 1-methyl-2-adamantanol (**3a**), but in significantly different ratios (see Table II). No other products were detected in the solvolyses of **1b** and **3b,** but **2b** produced, in addition to the solvolysis products, 15–20% of 1-methyl-2-adamantyl dinitrobenzoate by the internal return reaction. The solvolysis products were identified by GLC comparison with authentic samples, and the products were proved to be stable under the solvolytic conditions used, as well as on the GLC column. Samples of pure compounds **2a, 3a, 4,** and **5,** with an adequate quantity of 2,6-lutidine added, were treated separately with an equivalent amount of *p*-nitrobenzoic acid in the same manner as the esters in the product studies. In all cases, the gas chromatograms revealed only the compound tested.

For the internal return studies of dinitrobenzoates **1b** and **2b,** the crude solvolysis product mixture was concentrated to a small volume in vacuo at 25 °C and then saturated with Na_2CO_3 and extracted with ether. The extracts were dried, and the solvent was evaporated. The ^1H NMR spectrum of the residue was compared with the spectrum of an authentic sample of 2-methyl-2-adamantyl dinitrobenzoate (**3**-ODNB). The spectrum of the crude product mixture of **2b** indicated the presence of 15–20% of **3**-ODNB, while essentially no **3**-ODNB (less than 2%) was detected in the product mixture of **1b.**

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Registry No.—$1a_H$, 52746-23-3; $1a_D$, 66900-44-5; $1b_H$, 28846-71-1; $1b_D$, 66842-11-3; $2a_H$, 28840-89-3; $2a_D$, 66842-15-7; $2b_H$, 29845-45-2; $2b_D$, 66900-43-4; $3a_H$, 28786-69-8; $3a_D$, 66842-16-8; $3b_H$, 28786-70-1; $3b_D$, 66842-12-4; 4_H, 66842-13-5; 4_D, 66842-14-6; 5_H, 39762-63-5; 5_D, 66901-80-2.

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(2) To whom correspondence should be addressed.
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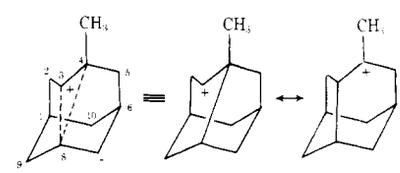
(17)



(18) Supposing there was no contribution of the rate-determining elimination to the values of the methyl-d_3 isotope effect of 4-*endo*- (**1b**) and 4-*exo*-4-methylprotoadamantyl dinitrobenzoate (**2b**), the "true" methyl-d_3 β-secondary isotope effects of *both* **1b** and **2b** would be proportionally larger (and equal to the corresponding titrimetrically determined isotope effects). Consequently, the discussion and conclusions based on the values of the titrimetrically determined isotope effect would be essentially the same as those reached from the corrected ("true") values of the β-secondary effects.
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(22) Such isomerizations of bridged intermediates are well known, for example, see J. E. Baldwin and W. D. Foglesong, *J. Am. Chem. Soc.*, **90**, 4303 (1968), and references therein.
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(24) When concentrated HCl was used[8a] instead of H_2SO_4, some 1-methyl-2-chloroadamantane was also produced.

Roles of Heteroatoms in Solvolytic Reactions. 4. Solvolysis of the Exo and Endo Esters of 2-Thiabicyclo[2.2.1]heptan-6-ols[1]

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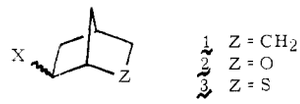
Diels–Alder cyclization of cyclopentadiene with thiophosgene yielded 3,3-dichloro-2-thiabicyclo[2.2.1]hept-5-ene, which was directly converted to 2-thiabicyclo[2.2.1]hept-5-ene in high yield by reduction with lithium aluminum hydride. Hydrochlorination of the olefin, followed by hydrolysis in a neutral or basic medium, gave 2-thiabicyclo[2.2.1]heptan-6-*exo*-ol in satisfactory overall yield. Acidic hydrolysis of 6-*exo*-chloro-2-thiabicyclo[2.2.1]heptane resulted in the major formation of a dimeric ether. The alcohol was oxidized with *tert*-butyl chromate, followed by reduction, to afford pure endo alcohol. Both alcohols were converted to esters, *p*-nitrobenzoate for the exo and tosylate for the endo, and the esters were solvolyzed. An exo/endo rate ratio of 3.7×10^{14} was observed, after correction for a leaving group as well as the solvent system, and 3.1×10^{10} and 1/43, respectively, for the rate ratios of the exo and endo esters against the corresponding parent carbon systems. This unusually high exo/endo rate ratio is attributed to β-S participation for the exo ester and the rate-retarding effect for the endo ester. In a product study, only an exo isomer was found as the solvolysis product from both esters. Isolation of a tricyclic episulfonium ion, 1-thioniatricyclo[1.1.1.$0^{2,6}$]heptane perchlorate, a solvolysis intermediate from the exo ester, was possible; its structure was confirmed by ^1H and ^{13}C NMR spectra.

Generally, it is well known that the amount of neighboring-group participation in solvolytic reactions varies with the spatial circumstances of molecules. C_2–C_6 interaction in the norbornyl system (**1**) has been observed in many kinetic, mechanistic, and structural studies.[3]

In the solvolysis of the 2-oxabicyclo[2.2.1]hept-6-*exo*-yl system (**2**), a relatively large amount of β-O-participation has



been observed.[4] It is considered that the structural peculiarity of the bicyclo[2.2.1]heptyl system gives rise to this unusual neighboring-group participation. Usually the effect of a β-oxygen atom resulting from direct nucleophilic participation is extremely small,[5] although the precise evaluation of the effect is difficult because of the large inductive character of oxygen.

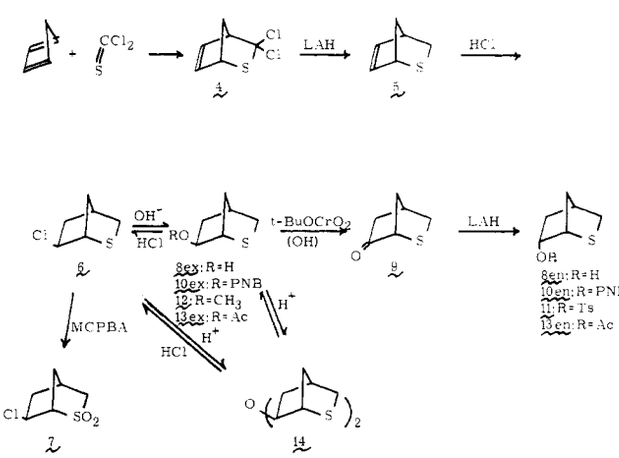
The 2-thiabicyclo[2.2.1]heptyl system (**3**) may exhibit a large amount of neighboring-group participation in solvolytic reactions and allow the isolation of a stable episulfonium ion when a carbocation is formed at the 6 position. This work was designed to examine mechanistic and structural effects in the solvolysis of the exo and endo stereoisomers of 2-thiabicyclo[2.2.1]heptan-6-ol esters and to isolate a tricyclic episulfonium ion.

Results

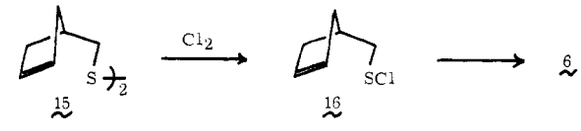
Synthesis. Originally the 2-thiabicyclo[2.2.1]heptane skeleton was prepared by Middleton[6] and several analogues were studied by Johnson and co-workers[7] in an investigation of stereochemical aspects.

As shown in Scheme I, 3,3-dichloro-2-thiabicyclo[2.2.1]-hept-5-ene (**4**), prepared according to the known procedure,[6] was directly reduced with lithium aluminum hydride ($LiAlH_4$)

Scheme I



to give 2-thiabicyclo[2.2.1]hept-5-ene (**5**) in high yield; chemical shifts of **5** in the ^1H NMR spectrum were consistent with those of reported values.[7] Hydrochlorination of the olefin (**5**) in methylene chloride with dry hydrogen chloride at −30 ~ −50 °C gave a single isomer (**6**), in which the configuration of the chlorine atom was determined to be exo on the basis of its reactivity, stereochemistry on HCl addition, and the NMR pattern of the 6-endo proton (4.74 ppm, doublets of doublet, $J_{5en,6}$ = 6.5 Hz, $J_{5ex,6}$ = 3.0 Hz) of the corresponding sulfone (**7**). This chloride was also prepared quantitatively by the intramolecular addition of sulfenyl chloride (**16**) generated in situ from the reaction of 3-cyclopentenylmethyl disulfide (**15**).[8]



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