The Determination of the Preferred Stereochemistry and the Magnitude of the Hydrogen Isotope Effect for 1,3 Elimination in the Locked Norbornyl System Methyl *exo*-2-Bromo-1-norbornanecarboxylate-*endo,endo*-5,6-d_2[1]

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Methyl *exo*-2-bromo-1-norbornanecarboxylate-*endo,endo*-5,6-d_2 (**1***b*) has been prepared and solvolyzed at 112° in 80:20 EtOH-H_2O buffered with NaOAc. The loss of 85–90% of the deuterium available on the front face of **1***b* in the formation of the tricyclic ester **6**D coupled with a novel analysis established that the *endo*:*exo* preference for 1,3 elimination is at least 15:1 to 20:1. A comparison of the solvolytic kinetic isotope effect (1.18 ± 0.04) for **1***b* and the 1,3-elimination kinetic isotope effect (1.45–1.6) with data for 1,2 eliminations indicates that elimination occurs from the classical, perhaps 1,3 hyperconjugatively stabilized carbocation **20**. The *endo*:*exo* preference established in this study is used to reinterpret 1,3-elimination data determined by Collins in the solvolysis of deuteriohydroxyphenyl norbornyl tosylates.

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On a préparé et solvolysé l'ester méthylique de bromo-2-*exo* norbornanecarboxylique-1 *endo,endo*-5,6-d_2 (**1***b*) à 112° avec une solution tamponnée de 80:20 EtOh–H_2O avec NaOAc. La perte de 85–90% du deutérium disponible sur la face avant de **1***b* dans la formation de l'ester tricyclique **6**D couplée avec une analyse nouvelle établit que la préférence *endo*:*exo* pour une élimination 1,3 est au moins de 15:1 à 20:1. Une comparaison de l'effet isotopique solvolytique et cinétique (1.18 ± 0.04) pour **1***b* et de l'effet isotopique pour la cinétique de l'élimination 1,3 (1.45–1.6) avec les résultats pour les éliminations 1,2 indique que l'élimination se produit d'une façon classique, peut-être par une carbocation stabilisé par hyperconjugaison 1,3 **20**. La préférence *endo*:*exo* établie dans cette étude est utilisée pour réinterpréter les résultats de l'élimination 1,3 déterminés par Collins dans la solvolyse des tosylates de deutériohydroxyphényl norbonyle.

[Traduit par le journal]

Introduction

The intricacies of the mechanisms of 1,2 (β) elimination have been probed extensively through kinetic and solvent isotope effect studies, through changes in base strength, leaving group and solvent polarity, and studies on stereospecifically deuterium labelled substrates. Many substantial reviews are available presently on this subject (2–9). However, 1,3- and 1,4-elimination reactions have not been studied as extensively, although there is presently activity in the area of 1,3 eliminations, prefaced by the work of Nickon and Werstiuk (*10*).

1,3 Elimination occurs in acyclic and alicyclic systems through E1cb-like, E-2-like, and E-1-like transition states. For example, there are a multitude of three-membered ring-forming reactions both in acyclic and alicyclic systems which involve prior anion formation followed by 1,3 displacement of the leaving group. A recent publication by Bordwell and Jarvis (11) describes some of the latest mechanistic information that has been accumulated on these E1cb-like 1,3 eliminations. An example of a fully concerted E-2-like 1,3 elimination has not yet been documented but studies under selected conditions on 5-*oxo*-*exo*-2-norbornyl derivatives (12) may prove fruitful. There are many examples documented in the literature (12–21) of E-1-like 1,3 elimination especially in bicyclo[2.2.1]heptyl derivatives. However, little mechanistic detail has been established for these 1,3 processes.

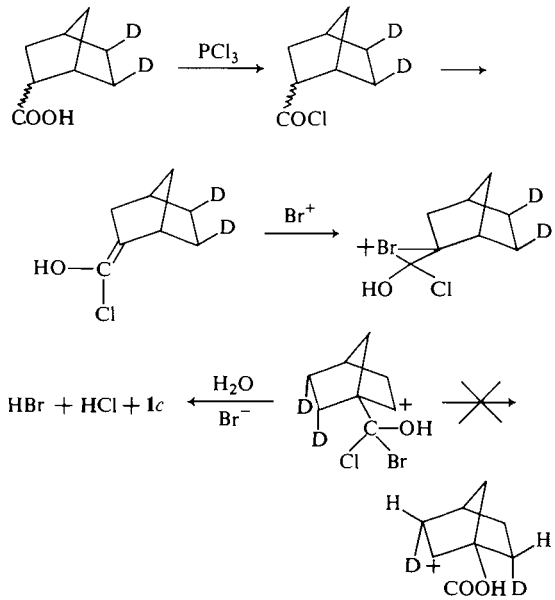
This paper describes in detail a study of 1,3 elimination in the norbornyl system methyl *exo*-2-bromo-1-norbornanecarboxylate (**1***a*). The study was undertaken to establish the preferred stereochemistry for the E-1-like 1,3 elimination in this locked norbornyl substrate, where the ubiquitous 1,2 Wagner–Meerwein rearrangement and/or norbornonium ion formation which scrambles C—H stereochemistry at C-6 is precluded or at least diminished. The results of this study would then serve as a basis for the interpretation of the stereochemical preference

[1]For a preliminary account see ref. 1.

data for 1,3 elimination in norbornyl systems in general. A specific case that deals with the work of Collins and Benjamin (15) will be discussed subsequently in the text of this paper. Also, the present study would establish both product and solvolysis kinetic isotope effects for the purpose of providing a comparison with those of 1,2 effects. Eventually, it would be desirable to decide through the magnitude of the effects whether or not the *exo* or *endo* C—H bonds at C-6 participate directly in a 1,3 manner in the ionization step during solvolysis. The bromoester **1***a* was chosen for the study because it is a locked system (1) that yields 43% of tricyclic material on solvolysis (13) and the synthesis of the deuterated substrate **1***b* is straightforward.

Preparation of Substrates: Determination of Stereochemical Purity

Compound **1***a* was prepared by the method of Boehme (22, 23). The dideuterated bromoester **1***b* was prepared by using a 1,2 Wagner–Meerwein shift to move *exo* deuterium to the *endo* position (24). Reduction of 5-norbornene-2-carboxylic acid (**2**) (80% *endo*, 20% *exo*) both with dideuteriodimide and deuterium on palladium-on-charcoal gave good yields of a mixture of *exo*-2- and *endo*-2-norbornanecarboxylic-*exo*, *exo*-5, 6-d_2 acid (**3**). Bromination of the acid gave *exo*-2-bromo-1-norbornanecarboxylic-*endo*,*endo*-5,6-d_2 acid (**1***c*) that was esterified with diazomethane. Although the mechanism of the bromination rearrangement sequence for the conversion of **3** → **1***c* has not been established, undoubtedly, the Hell–Volhard–Zelinsky reaction involves enolization of the acid chloride followed by electrophilic attack of bromine on the enol. As charge is developed at C-2, rearrangement occurs to the 1-carboxy system that is captured by bromide ion. Interestingly, a 6,2 hydride (deuteride) shift does not occur significantly in this case. This was established by n.m.r. integration analysis (Fig. 1) of the olefinic region of methyl 1-norbornenecarboxylate-*endo*,*endo*-5,6-d_2 isolated from NaOMe-catalyzed elimination of HBr from **1***b*. Since 1,2 elimination of HBr from **1***b* is specifically *cis-exo* (25) the bromoester, in which a 6,2 deuteride shift has occurred, would give olefin in which a hydrogen at C-3 is replaced by deuterium. From integration analysis an upper limit of 5% is set on the extent of deuteride shift. The presence of a deuteride shifted product,



SCHEME I

however, does not affect the interpretation of the stereochemistry studies since the deuterium must necessarily remain 1,3 and *endo* with respect to the bromine.

It is of interest that the 1,2-elimination product is the major component (80%) of the reaction of **1***b* under E-2 conditions. Three other products, listed in order of increasing retention time, were tricyclic ester (8%), unknown (4%), and methyl 2 methoxy-1-norbornanecarboxylate (8%). That methyl 2 methoxy-1-norbornanecarboxylate was one of the minor components (isolated by preparative g.l.p.c.) was established by mass spectrometry which showed a parent ion at *m/e* 186

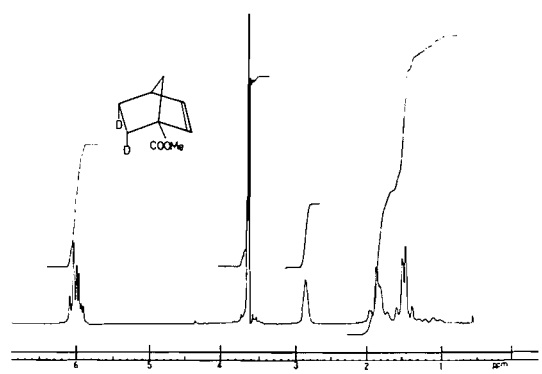


FIG. 1. Nuclear magnetic resonance spectrum (100 MHz; CCl_4) of 4D obtained from NaOMe-catalyzed elimination of HBr from **1***b*.

($C_{10}H_{14}O_3D_2$) and a fragmentation pattern consistent with the proposed structure. The methoxy group is likely situated *exo* at C-2. That the 1,2-elimination product predominates under E-2 conditions supports our claim that under solvolysis conditions 1,3 elimination is E-1-like and is preceded by ion pair formation. The integration analysis on the olefin **4D** obtained from base-catalyzed elimination also established that the deuterium in the bromoester was at least 95% stereochemically pure *endo* at C-5 and C-6. This reflects the stereospecific *exo* reduction of the norbornenecarboxylic acid which is expected for the system (26). The multiplets centered at 1.8 and 1.5 δ (Fig. 1) are what would be expected for the *exo*-5,6 and C-7 hydrogens, respectively, in the [2.2.1] system (24, 26). The residual of the *endo* hydrogens is centered at around 1.1 δ. Further support for the stereochemistry of the deuterium is obtained from the proton n.m.r. spectrum (Fig. 2) of methyl 2-norbornene-2-carboxylate-*exo*,*exo*-5,6-d_2 (**5***b*) obtained from CH_2N_2 esterification of the product obtained from elimination of HBr from the carboxylic acid **1***c*. Since the rearrangement to **5***a* shifts *endo* deuterium to the *exo* position, the relative intensities of the peaks at around 1.8 and 1.1 δ should interchange. The n.m.r. spectrum (Fig. 2) of **5***b* indicates this to be the case.

Results

Solvolysis of **1***a* and **1***b* in 80:20, v/v, EtOH–H_2O buffered with NaOAc gave the products **4**H, **6**H, **7**H, **8**H, and **4**D, **6**D, **7**D, **8**D respectively as described in Table 1. The deuterium content of both **1***b* and tricyclic material was established by mass spectrometry and n.m.r. spectroscopy

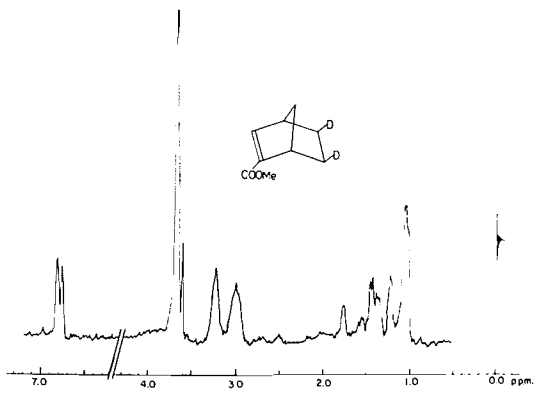
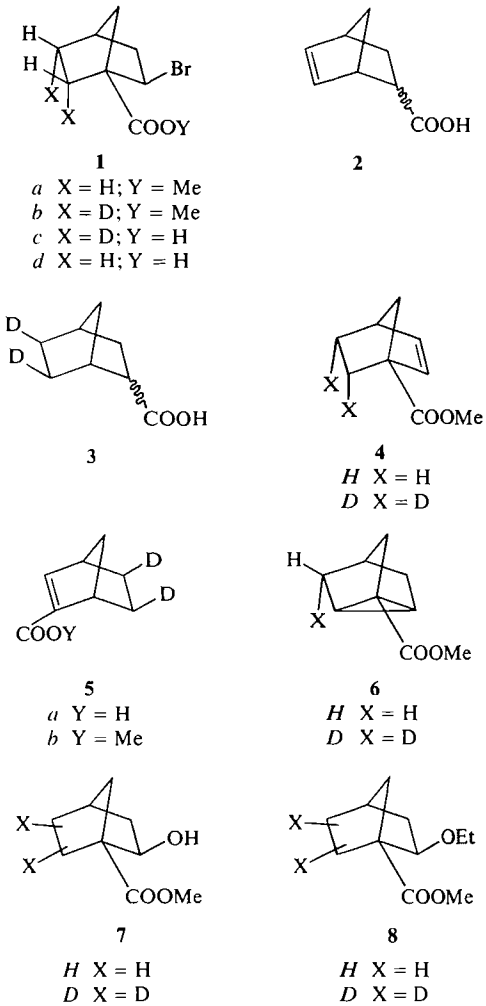


FIG. 2. Nuclear magnetic resonance spectrum (60 MHz; CCl_4) of **5***b*.



1
a X = H; Y = Me
b X = D; Y = Me
c X = D; Y = H
d X = H; Y = H

2

3

4
H X = H
D X = D

5
a Y = H
b Y = Me

6
H X = H
D X = D

7
H X = H
D X = D

8
H X = H
D X = D

(Fig. 3). As indicated in Table 1 an isotope effect operates in the elimination to decrease the quantity of tricyclic material and increase the amount of the other products. This, coupled with the loss of approximately 90% of the deuterium available on the front face of **1***b*, establishes a large preference for cleavage of the *endo*-C—H bond over the *exo*-C—H bond at C-6 in the 1,3 elimination. The γ-kinetic isotope effect (Table 2) for solvolysis of **1***a* and *b* is 1.18 ± 0.04 in the range of 115°. The data for run 3 is plotted in Fig. 4. The rate constant of 1.04×10^{-5} s^{-1} at 115° for **1***a* (0.03 *M* **1***a*; 0.09 *M* NaOAc) compares favorably with the rate constants of 0.85×10^{-5} s^{-1} (112.6°) and 1.28×10^{-5} s^{-1} (119.5°) reported for **1***a* (0.01–0.04 *M* **1***a*; 0.01–0.04 *M* NaOAc) by Wilt (13). The increased rate

TABLE 1. Product and deuterium loss data for solvolysis of **1***a* and **1***b* in 80:20 EtOH–H_2O

Entry	Substrate	Conditions	Relative % products*					Fractional % loss of one deuterium
				Δ	ROH	ROEt	Other	
1	**1***a*	0.09 *M* **1***a* 0.10 *M* NaOAc 112 ± 2°	7.4	43.0	13.8	31.8	4.0	
2	**1***b*	0.14 *M* **1***b* 0.16 *M* NaOAc 112 ± 2°	9.9	32.0	16.7	38.4	3.0	87†
3	**1***b*	0.07 *M* **1***b* 0.11 *M* NaOAc 112 ± 2°						92‡
4	**1***b*	0.32 *M* **1***b* 0.35 *M* NaOAc 112 ± 2°						86§

*Run consecutively during the same g.l.c. analysis: the average of two analyses integrated electronically.
†A composite of 8.6% d_2, 79.4% d_1, and 12.0% d_0 species (average 0.97 excess D per molecule). Starting **1***b* a composite of 73.7% d_2, 24.5% d_1, and 1.8% d_0 species (average 1.72 excess D per molecule).
‡The 6D a composite of 5.7% d_2, 81.0% d_1, and 13.3% d_0 species (average 0.92 excess D per molecule). Compound **1***b* a composite of 73.7% d_2, 24.5% d_1, and 1.8% d_0 species.
§Compound 6D a composite of 1% d_3, 13.4% d_2, 76.5% d_1, and 9.3% d_0 species (average 1.06 excess D per molecule). Compound **1***b* a composite of 2.3% d_3, 84.2% d_2, 11.2% d_1, and 2.5% d_0 species (average 1.87 excess D per molecule).

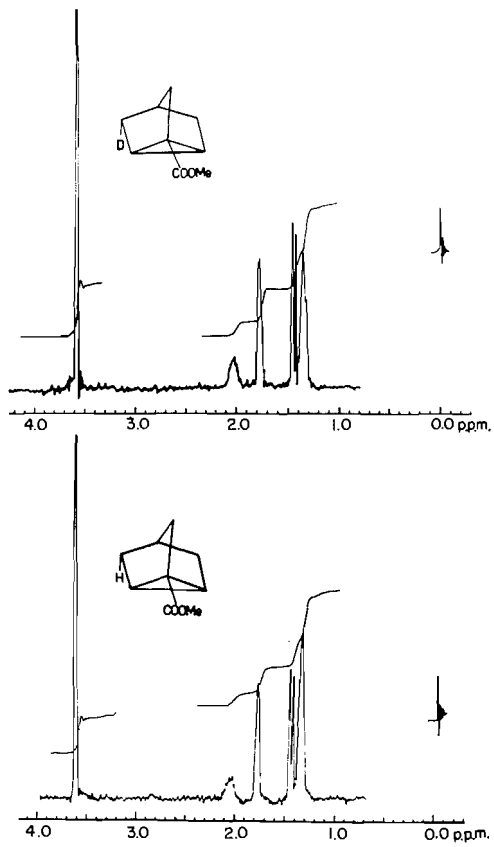


FIG. 3. Nuclear magnetic resonance spectra (60 MHz; CCl_4) of 6H and D obtained from solvolysis of **1***a* and *b*, respectively (entries 1 and 2, Table 1).

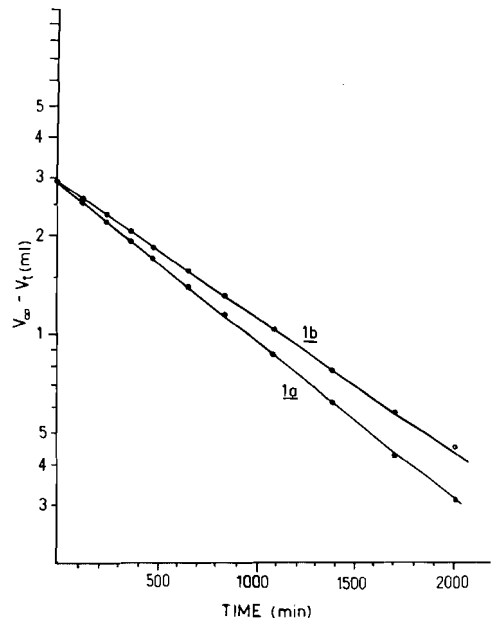


FIG. 4. Semilogarithmic plot of kinetic data for run 3 (Table 2).

constants for runs 2 and 3 likely are a consequence of the higher salt concentration. Nevertheless, the comparison establishes the validity of the kinetic procedure used in this study. The bromoesters used for the kinetic studies were purified by preparative liquid chromatography (l.c.) using a Waters Model 200

TABLE 2. γ-Kinetic isotope effect for solvolysis of **1***a*,**1***b**

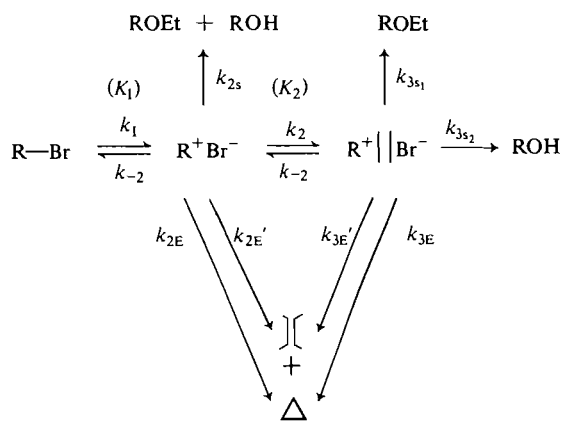
Run	Conditions	$k_H \times 10^5$ (s^{-1})†	$k_D \times 10^5$ (s^{-1})	k_H/k_D
1	0.03 *M* **1***a*,**1***b* 0.09 *M* NaOAc 115.00 ± 0.03°	1.09 ± 0.02	0.92 ± 0.02	1.14 ± 0.04
2	0.05 *M* **1***a*,**1***b* 0.14 *M* NaOAc 116.20 ± 0.03°	1.85 ± 0.02	1.52 ± 0.02	1.21 ± 0.04
3	0.05 *M* **1***a*,**1***b* 0.14 *M* NaOAc 116.10 ± 0.04°	1.86 ± 0.02	1.54 ± 0.02	1.20 ± 0.04
	Mean			1.18 ± 0.04

*Five additional preliminary runs were used to establish the validity of the kinetic procedure. Compounds **1***a* and **1***b* were run simultaneously in the same constant temperature bath and aliquots were removed at the same time.
†The rate constants were obtained by least-squares analysis of the data; the standard deviation of the slope was taken as the error in the slope.

High Pressure Liquid Chromatograph. The solvent system 15–20% $CHCl_3$ – 85–80% hexane (v/v) was used with a 3/8 in. × 3 ft Porasil A column (column volume 34 ml). A flow rate of 0.7 ml/min was used with the pressure being 800 p.s.i. The bromoester was eluted after approximately 80 ml of flow. Although there was some tailing when a 60–70 mg (45 μl neat liquid) sample was injected, careful g.l.p.c. and n.m.r. analysis of the tail fraction showed that no other compound was present. Also, a l.c. analysis of a 4 μl sample showed a symmetrical peak. After a total of 10–12 samples each of **1***a* and *b* were injected and collected, the appropriate fractions were combined and the solvent was taken off on the rotatory evaporator. The residue was distilled under vacuum bulb to bulb twice for final purification. In this case l.c. is far superior to gas chromatography in terms of degree of separation, ease of handling and recovery of materials. This is however offset to some degree by the somewhat lengthy period required to establish conditions.

Discussion

When an ion pair scheme is considered for the solvolysis (Scheme 2) and the formation of products from tight ion pairs (TIP) and solvent separated ion pairs (SSIP) is describable on the basis of pseudo first-order processes, the following analysis can be made.[2] Since it has been established that k_{2S} is negligible in the



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[2.2.1] system (27), attack of solvent on TIP to give ether and alcohol products is not important in the solvolysis of **1***a*. If the steady state approximation can be applied in this case, then in the scheme, K_1 would be affected by deuterium substitution but K_2 would not, since k_{2H}/k_{-2H} and k_{2D}/k_{-2D} should remain constant. This is so because the electronic and hybridization changes at C-6 (compared to R_H-Br) in R_H^+ in the $SSIP_H$ should be essentially identical to those in R_H^+ in TIP_H. Also, the changes at C-6 (from R_D-Br) in R_D^+ in $SSIP_D$ should be essentially identical to those for R_D^+ in TIP_D. Therefore, since $[TIP]_H/[SSIP]_H \simeq [TIP]_D/[SSIP]_D \simeq$ constant, the difference in the relative amounts of products from **1***a* and *b* would be governed by the relative magnitudes of the product rate constants and not by a variation in

[2]A hydride shift sequence is omitted from the scheme since the ion which results from an $H^-(D^-)$ shift should exhibit the reactivity of a SSIP even in the case of **1***b*.

the magnitude of K_2. This is reasonably important since it is not yet established which of k_{2E} and k_{3E} is most important or whether they both contribute equally to the 1,3 elimination. However, it is likely that for an E-1-like elimination k_{2E} and k_{3E} are of comparable magnitude since the force constant changes in the TIP and SSIP at C-6 should be essentially identical (28). For the same reason, the elimination isotope effects should also be identical for both species. Thus, k_{2E} and k_{3E} (1,3 elimination) are combined into $k_{E\ total}$.[3] Therefore, assuming the equilibrium between TIP and SSIP is fast

$$\frac{k_{HE\ total}}{k_{H3S_1} + k_{H3S_2}} \simeq \frac{\mathbf{6H}}{\mathbf{7H + 8H}}$$

and

$$\frac{k_{DE\ total}}{k_{D3S_1} + k_{D3S_2}} \simeq \frac{\mathbf{6D}}{\mathbf{7D + 8D}}$$

On the assumption that the isotope effect for capture of SSIP by solvent is negligible so that $k_{H3S_1} + k_{H3S_2} \simeq k_{D3S_1} + k_{D3S_2}$

$$\frac{k_{HE\ total}}{k_{DE\ total}} \simeq \frac{\dfrac{\mathbf{6H}}{\mathbf{7H + 8H}}}{\dfrac{\mathbf{6D}}{\mathbf{7D + 8D}}} \simeq 1.6$$

If an isotope effect does indeed operate on k_{3S} then it is likely inverse (28). Since there is no information available on the magnitude of such a γ-effect, only an estimate is possible presently based on a β-isotope effect. Humski *et al.* (28) have recently reported a value of 0.90 for the β-isotope effect for the collapse of cyclopentyl-*cis*-β-*d* brosylate ion pairs in 80:20 ethanol–water. If this is considered as the maximum value for a collapse isotope effect then $k_{D3S} \simeq 1.10\ k_{H3S}$. Substituting this in the expression for $k_{HE\ (total)}/k_{DE\ (total)}$, a value of 1.45 is obtained for the elimination isotope effect. The value of 1.45–1.60 compares favorably with the values reported for 1,3 elimination in the [2.2.1] system (10).

[3]The sum of k_{3S_1} and k_{3S_2} is used since the elimination process likely also involves both solvent bases. This comparison is an attempt to take into account the pseudo first-order nature of the product steps involving both EtOH and H_2O.

A novel analysis[4] that combines in [1] the initial distribution of deuterated species, the elimination isotope effect (1.6), the stereochemical purity (95–98%), an assumed preference, and the amount of tricyclic material (43%) formed from **1***a*, is used to predict the yield and the distribution of deuterated species of tricyclic material from **1***b*. The data in Table 3 clearly validate the method and establish that for a stereochemical purity of 98–95% there is at least a 15:1 to 20:1 preference for cleavage of the *endo*-C—H bond at C-6.

[4]Described herein is a sample calculation (assumed preference 20:1; isotope effect 1.6) that uses [1] for analysis of *endo vs. exo* cleavage for **1***b* (73.7% d_2, 24.5% d_1, 1.8% d_0) in which the deuterium is taken to be 95% stereochemically pure *endo* and the secondary isotope effect for cleavage of a C—H bond is assumed to be negligible.

endo,endo-5,6-d_2 component

endo cleavage $\left(\frac{73.7}{100}\right)(0.95)\left(\frac{20}{20}\right)\left(\frac{1}{1.6}\right)(43) = 18.80\ d_1$

exo cleavage $\left(\frac{73.7}{100}\right)(0.95)\left(\frac{1}{20}\right)(43) = 1.51\ d_2$

exo,exo-5,6-d_2 component

endo cleavage $\left(\frac{73.7}{100}\right)(0.05)\left(\frac{20}{20}\right)(43) = 1.59\ d_2$

exo cleavage $\left(\frac{73.7}{100}\right)(0.05)\left(\frac{1}{20}\right)\left(\frac{1}{1.6}\right)(43) = 0.05\ d_1$

endo-6-d_1-component

endo cleavage $\left(\frac{\frac{1}{2}\times 24.5}{100}\right)(0.95)\left(\frac{20}{20}\right)\left(\frac{1}{1.6}\right)(43) = 3.12\ d_0$

exo cleavage $\left(\frac{\frac{1}{2}\times 24.5}{100}\right)(0.95)\left(\frac{1}{20}\right)(43) = 0.25\ d_1$

exo-6-d_1 component

endo cleavage $\left(\frac{\frac{1}{2}\times 24.5}{100}\right)(0.05)\left(\frac{20}{20}\right)(43) = 0.25\ d_1$

exo cleavage $\left(\frac{\frac{1}{2}\times 24.5}{100}\right)(0.05)\left(\frac{1}{20}\right)\left(\frac{1}{1.6}\right)(43) =$ Negligible

5-d_1-component

$\left(\frac{\frac{1}{2}\times 24.5}{100}\right)(43) = 5.30\ d_1$

d_0-component

$\left(\frac{1.8}{100}\right)(43) = 0.77\ d_0$

Distribution of species 3.10 d_2 (9.8%), 24.65 d_1 (77.9%), 3.89 d_0 (12.3%); Σ relative yields d_x species = 31.6.

TABLE 3. Relative % yields and distribution of deuterated species: comparison of experimental and calculated values

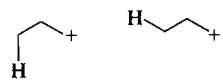
	Stereochemical purity	*Endo*:*exo* preference	Relative % yield 4D	$\%d_2$	$\%d_1$	$\%d_0$	Excess D remaining per molecule
Experimental*			32	8.6	79.4	12.0	0.97
Calculated using eq.	98%	10:1	33.2	11.1	76.8	12.1	0.99
1 with isotope effect	98%	15:1	31.9	8.2	79.2	12.6	0.96
of 1.6			(34)†	(7.9)	(80.3)	(11.9)	(0.96)
	98%	20:1	31.3	6.8	80.5	12.8	0.94
	95%	10:1	33.5	13.7	74.5	11.7	1.02
	95%	15:1	32.3	11.5	76.4	12.2	0.99
	95%	20:1	31.6	9.8	77.9	12.3	0.97
			(33)†	(9.4)	(78.3)	(12.3)	(0.97)

*Compound 1*b* was a composite of 73.7% d_2, 24.5% d_1, and 1.8% d_0 species; an average of 1.72 excess D per molecule. Deuterium analysis was done mass spectrometrically at low voltage.
†Using an isotope effect of 1.5.

$$\left(\frac{\%\ d_n \text{ species}}{100}\right)\left(\begin{matrix}\text{fractional amount}\\ \text{each stereoisomer}\end{matrix}\right)\left(\begin{matrix}\text{assumed}\\ \text{preference}\end{matrix}\right)\left(\frac{1}{\text{isotope effect}}\right)43 = \text{Relative yield of } d_x \text{ species } (x = 0, 1, 2) \quad [1]$$

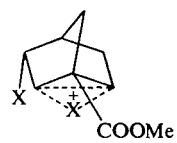
$$\text{Relative \% yield of } \mathbf{6D} = \frac{\text{Relative yields of } d_x \text{ species}}{\sum}$$

The *endo* preference for elimination from **1***a* establishes that the semi-U pathway (**A**) (10) is preferred for an E-1-like 1,3 process in locked [2.2.1] systems with $\Delta G^{\ddagger}$ being a *minimum* of 1.5–2 kcal/mol less than that for the semi-W pathway (**B**). Whether or not a symmetrical

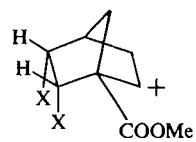


A B

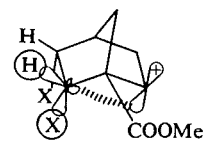
edge-protonated nortricyclane (**9**H, **9**D) is an intermediate from which loss of a proton (deuteron) occurs is a point of interest. This problem is discussed in more detail subsequently in the text. That is, the ion **10**H (**10**D) may be the intermediate and **9**H (**9**D) represents only a transition state for the elimination and $H^-(D^-)$ shift. That a hydride (deuteride) shift does occur during solvolysis of **1***a* (**1***b*) is supported by the following facts. Nuclear magnetic resonance integration analysis of the olefinic region of **4**D, obtained from solvolysis of **1***b*, showed that deuterium was located at C-3 and established that 10–20% of the olefin arises after a deuteride shift occurs. Furthermore, partial collapse of the *endo*-2-C–H multiplet in the n.m.r. spectrum (Fig. 5) of **7**D



9*H* X = H
9*D* X = D

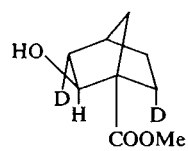


10*H* X = H
10*D* X = D



11*H* X = H
11*D* X = D

is consistent with loss of *cis–endo* coupling (29) which would be expected from **12**. That a hydride (deuteride) shift would be expected in this system is supported by Muneyuki's (19) study on the acetolysis of optically active **13** which established that the product acetate racemized partially.



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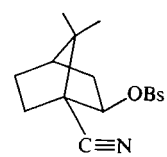


13

The *endo* preference established in this study shows conclusively that the overlap of the back-lobe of *exo*-C-6—H with the p-orbital at C-2 as described in **11**H (**11**D) *does not* play an important role in the stereochemical outcome of an E-1-like 1,3 elimination in the [2.2.1] system.

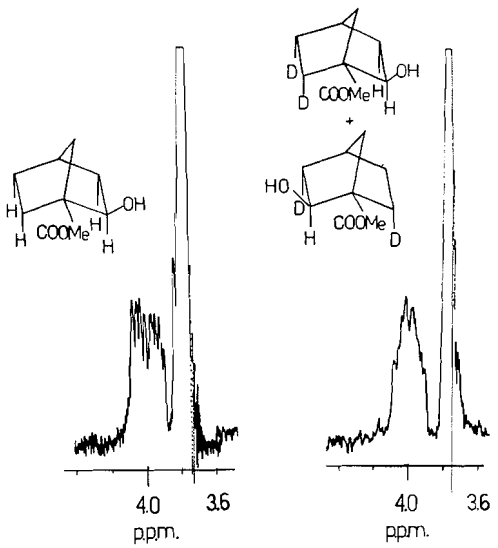


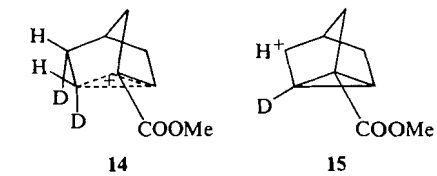
FIG. 5. Nuclear magnetic resonance spectra (60 MHz; $CDCl_3$) (sweep width 250 Hz) of 7H and D obtained from solvolysis of **1***a* and *b*.

This is of interest for two reasons. Farnum and Mehta (30) and Olah and co-workers (31, 32) have reported that this type of overlap operates in the norbornyl system and is the cause of the deshielding of the *exo* over the *endo* proton at C-6 in norbornyl cations generated in strong acids. Apparently, this overlap is not sufficient to preferentially activate *exo*-C—H over *endo*-C—H for 1,3 elimination. Also, *exo* approach of reagents to the [2.2.1] system is preferred, especially for proton transfer in homoenolization and homoketonization (33) processes.

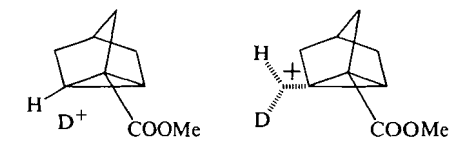
The magnitude (1.45–1.6) of the primary 1,3-elimination isotope effect established in this study parallels closely the few examples documented in the literature (10, 15, 21, 34–38) for E-1 1,2 and 1,3 eliminations (Table 4).

Since the magnitude of the isotope effect for an E-2-like 1,3 elimination has not been determined because there is as yet no experimental support for a concerted 1,3 elimination and no theoretical studies have been carried out on 1,3 processes the usual correlation between the magnitude of the isotope effect and concertedness is difficult to establish in this case. However, the low value observed for **1***b* does fall in the range for 1,2 eliminations and 1,3 eliminations from carbocations (*vide supra*).

The γ-kinetic isotope effect is of interest since the presence of the carbomethoxy group should preclude significant neighboring group (non-vertical) participation of C-1—C-6 bond via **14**. Thus, the γ-effect may arise from any one, or some combination of the three effects. Possibly, 1,3 hyperconjugation to both the *exo*- and *endo*-C—H bonds at C-6 as described by the

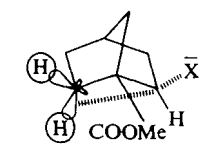


14 **15**



16 **17**

limiting forms **15** and **16** is important in the ionization step. Perhaps the sum of **15** and **16** is equivalent to the H-nortricyclonium ion **17**, the unsubstituted form of which Olah has proposed as a contributor to the structure of the norbornyl cation. Also likely is the direct involvement, as described by **18**, of only the *endo*-C—H(D) bond in the ionization step. Presently, the relative importance of each effect cannot be established although **15** + **16** = **17** may be important in the solvolysis of 7-chloro-*exo*-2-norbornyl- 6-*endo*-*d* and -*exo*,*exo*-5,6-d_2 brosylates (21). Lastly, it is possible that the

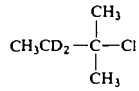
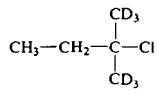
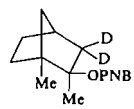
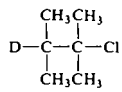
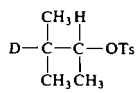
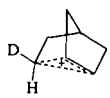


18

kinetic isotope effect is a manifestation of the elimination isotope effects only. If the ion pair scheme (Scheme 2, *vide supra*) is considered and the steady state approximation is applied, then it can be shown that when $k_{2S} = 0$ (27)

$$\left(\frac{k_H}{k_D}\right)_{obs} = \left(\frac{k_{H1}}{k_{D1}}\right)\left(\frac{1 + Y_D}{1 + Y_H}\right) \times \frac{\frac{k_{H2E}}{k_{H2}} + \left[\left(\frac{k_{H3E}}{k_{H3S}} + 1\right)\left(\frac{1}{1 + Z_H}\right)\right]}{\frac{k_{D2E}}{k_{D2}} + \left[\left(\frac{k_{D3E}}{k_{D3S}} + 1\right)\left(\frac{1}{1 + Z_D}\right)\right]} = (IIE)(R)(S)$$

TABLE 4. Tabulation of β-kinetic isotope effects and 1,2 and 1,3 elimination isotope effects for solvolysis reactions

Entry	Deuterated substrate	Conditions	Kinetic isotope effect per D	Primary isotope effect for olefin formation	Reference No.
1		80:20 EtOH–H_2O 25°	1.19	1.8	34
2		75:25 HOAc–H_2O 57°		2.5–2.8	37
3		50:50 Dioxane–H_2O 69.3°	1.14* 1.28	1.92	39
4		80:20 EtOH–H_2O 40°	1.18	1.32	28
5		80:20 EtOH–H_2O 55°	1.16	≃1.07†	35
6		HOAc–NaOAc 75°	1.93	1.2–1.6‡	36
7		0.054 *M* KO*t*Bu *t*-BuOH 60°		2.1§	10

*The value of 1.14 is based on the *exo* and *endo* effect being identical. The value of 1.28 is the total observed kinetic effect.
†Based on the ratio of olefin fraction from H substrate and D substrate.
‡The value of 1.2 is obtained from the ratio of 2-methylbutene-2 fractions. The value of 1.6 is obtained using the tertiary acetate ratio as well as the olefin ratio in the analysis developed in this paper.
§This is the isotope effect for nortricyclane formation.

where

$$Y = \frac{k_{-1} + k_{2E}}{k_2}$$

and

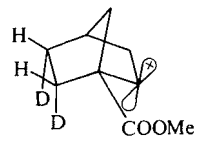
$$Z = \frac{k_{-2} + k_{3E}}{k_{3S}}$$

If the ionization isotope effect (IIE) $k_{H1}/k_{D1} \simeq 1.0$ then through a consideration of the effect of deuterium substitution on the rate constants k_{2E}, k_2, k_{-2}, k_{3E}, and k_{3S} it is seen that $k_{H2E} > k_{D2E}$, $k_{H2} \simeq k_{D2}$, $k_{H-2} \simeq k_{D-2}$, $k_{H3E} > k_{D3E}$, and $k_{H3S} \simeq k_{D3S}$. Therefore, the R and S terms could control the observed isotope effect but with some mutual attenuation since $1 + Y_D$ is $< 1 + Y_H$ in the R term and the numerator is larger than the denominator in the S term. That the observed kinetic isotope effect can vary with the amount of elimination has been established by Humski (38) through studies on the solvolysis of 1,2-dimethyl-*exo*-2-norbornyl-*p*-nitrobenzoate. This however is not general since in the solvolysis of cyclopentyl brosylate-*trans*-β-*d* in ethanol–water the kinetic isotope effect does not vary significantly with a change in the amount of olefin formed and in fact in trifluoroethanol–water actually increases slightly as the amount of olefin decreases (28).

Nevertheless, 1,3 elimination at some point would involve a transition state which resembles

an edge-protonated nortricyclane[5], the overall process being characterized by an isotope effect of 1.45–1.6. If the kinetic isotope effect (1.18 ± 0.04) in fact predominantly reflects the ionization isotope effect then that k_H/k_D (elim) > k_H/k_D (kinetic) indicates that the C—H bonds at C-6 undergo a force constant change during ionization either through **15** + **16** = **17** or **18** or both but the change does not approach that in **9**D. That is, if involvement of the endo-C—D bond at C-6 at ionization approached the extent depicted in **9**D then k_H/k_D (kinetic) > k_H/k_D (elim). There is some support for this concept available in the literature at least for 1,2 eliminations. For example, in Table 4 in entries 1, 3, and 4 where k_H/k_D (obs) > k_H/k_D (elim), elimination is considered to occur from classical species with the β-C—H bonds being perturbed only through hyperconjugation (vertical participation). It must be pointed out here that it is understood that the primary elimination isotope effects are inflated somewhat in entries 1, 2, and 3 because a secondary effect (≃ 1.2) operates in each case as well. However, k_H/k_D (obs) would still be less than k_H/k_D (elim). In the solvolysis of 2-substituted-2,3-dimethylbutanes (entry 5), however, k_H/k_D (obs) > k_H/k_D (elim). In the case of the solvolysis of the tosylate in entry 6, Winstein and Takahashi (36) proposed that neighboring group participation (nonvertical participation) of the C—H(D) leading to an ethonium ion was important. In this case it is reasonable that k_H/k_D (obs) > k_H/k_D (elim) since elimination should now occur from an ethonium ion. The isotope effect for loss of D^+ from such a species would be expected to be less than that for loss of D^+ from a classical ion since the C—H(D) force constants in the former are already lowered substantially. Significantly, Cram and Tadanier (40) proposed that the ethonium ion was formed in the solvolysis of 3-cyclohexyl-2-butyl tosylate where k_H/k_D (obs) is in the order of 1.7–1.8. Unfortunately the olefin ratios were not reported for the deuterated compounds so that an elimination isotope effect cannot be evaluated. However, this author predicts that k_H/k_D (obs) should be greater than k_H/k_D (elim).

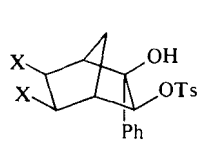
Thus from the stereochemical preference data, the relative magnitudes of the kinetic and elimination isotope effects the author proposes that 1,3 elimination in **1***b* occurs from a species which closely resembles the classical ion **20** where the C—H, C—D bonds at C-6 may be involved in 1,3 hyperconjugative stabilization



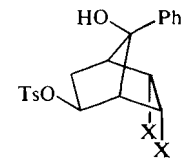
20

but that the transition state for 1,3 elimination and the 6,2 H(D) shift resembles an edge-protonated nortricyclane, the isotope effect for the 1,3 process being around 1.6.

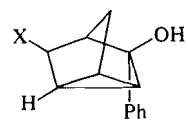
That the semi-U pathway is preferred for E-1-like 1,3 elimination in the [2.2.1] system where rearrangement is precluded provides a basis for the reinterpretation of other 1,3 preference data (15). Collins found that the tosylates **21**H and **22**H gave essentially identical product compositions including the nortricyclanol



21*H* X = H
21*D* X = D



22*H* X = H
22*D* X = D



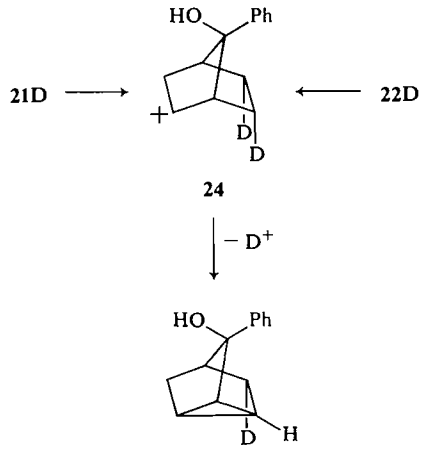
23*H* X = H
23*D* X = D

23H (26%). When **21**D and **22**D were solvolyzed in each case one deuterium atom was lost in the formation of **23**D. That the product composition

[5]E-1-like 1,3 elimination in the [2.2.1] system should be essentially the reverse of the protonation of the appropriately substituted nortricyclane. Although **6**H has not been opened with D^+ to check this, the D^+

opening of nortricyclyl chloride occurs by edge-protonation of bond *a* (39). This correlates very well with the finding that cleavage of *endo*-C—H(D) at C-6 is preferred for 1,3 elimination in solvolysis of the 7-chloro-*exo*-2-norbornyl-6-*endo*-*d* brosylate (21).

was identical within experimental error from **21**H and **22**H indicated that common intermediates were involved. The authors interpreted the deuterium loss data on the basis of elimination of *exo* deuterium from **21**D and *endo* deuterium from **22**D and stated that the solvolysis results could be accounted for on the basis of either nonclassical or classical ions and that the edge-protonated nortricyclane could be either an intermediate or transition state. On the basis of previous discussion (*vide supra*) the results can be accounted for in the following manner.



Cleavage of the C—OTs bond in **21**D followed by a 1,2 alkyl shift gives **24**. Solvolysis of **22**D gives **24** directly. In this case the hydroxyl and phenyl groups provide the necessary lock through an inductive effect and perhaps OH-4 participation for the former and an inductive and steric effect for the latter. Ion **24** need be classical and stabilized only through 1,3 hyperconjugation (*vide supra*). Reaction of **24** with an *endo* preference as expected would then lead directly to **23** with a loss of one deuterium in both cases. The point here is that the C—D bond originally *exo* in **21**D is cleaved as an *endo* bond in **24**. That **24** resembles a classical ion and elimination occurs from this species is supported by value of 1.8 for magnitude of the elimination isotope effect which was evaluated from Collins' product data by the method described previously in this paper.

Experimental

General

Melting points were taken on a Kofler hot stage melting point apparatus and are uncorrected. The i.r. spectra were recorded on a Perkin–Elmer Model 337 spectrometer. The n.m.r. spectra were recorded on Varian A-60, T-60 and HA-100 spectrometers on solutions in CCl_4 or $CDCl_3$ with tetramethyl silane as internal standard. Mass spectra were obtained on a Hitachi Model RMU6-A spectrometer. Preparative and analytical gas liquid chromatography was carried out on Varian 90-P-3 and 204 instruments, respectively, with He as carrier gas. High pressure liquid chromatography was accomplished on a Waters Model 200 liquid chromatograph. All solutions were dried over anhydrous Na_2SO_4 or $MgSO_4$.

Dipotassium Azodicarboxylate

To a vigorously stirred solution of 600 ml of 40% KOH maintained at 0–3° was added azodicarbonamide (110 g) portionwise. After the addition was complete the mixture was stirred for 1 h and the salt was filtered through a sintered glass funnel. The salt was washed with 8 l of anhydrous methanol, cooled to 0–5°, and vacuum dried (rotatory pump) for 2 days. The salt that was used for the deuterations was washed with (2 × 50 ml; 1 × 75 ml) MeOD and pumped on for 2 days.

Dideuteriodimide Reduction of Norbornenecarboxylic Acid

Norbornenecarboxylic acid (14 g, 80:20 *endo*:*exo*) was added to a slurry of dipotassium azodicarboxylate (54 g) in MeOD (300 ml, 95%-O-*d*) contained in a three-necked 1-l flask equipped with a condenser, dropping funnel, and stirrer. To the vigorously stirred mixture was added DOAc (26 g, 95–97%-O-*d*) in MeOD (30 ml) over a period of 1 h. After the addition was complete the mixture was stirred for an additional 1.5 h at room temperature. An aliquot was worked up and analyzed by infrared spectroscopy. The absence of an initially strong band at 710 cm^{-1} showed that the reduction was at least 98–99% complete. The MeOD was recovered by distillation through a 14 in. glass helices column to yield a viscous residue of approximately 75 ml. Ether (100 ml) and water (175 ml) were added and after shaking the ether layer was drawn off. The aqueous layer was extracted with additional ether (10 × 50 ml). The combined ethereal layers were washed with water, dried, and the ether was distilled off. Distillation of the residue gave 9 g of the dideuterioacid, b.p. 103–104° (1–8 mm), which solidified to a viscous mass on standing. Nuclear magnetic resonance (60 MHz, $CDCl_3$) δ 11.0 (bs, 1H, COOH), 2.75 (bm, 1H, C-2—*exo*-H), 2.55 and 2.25 (m, 2H, bridgehead C—Hs), 1.8–1.1 (norbornyl envelope, approximately 6H).

Deuteration of Norbornenecarboxylic Acid

Norbornenecarboxylic acid (30 g, 0.218 mol, Aldrich Chemical Co., 80:20 *endo*:*exo*) was dissolved in anhydrous methanol (125 ml) in a 250 ml conical flask. Palladium (10%) on charcoal (4 g) was added and the mixture was connected to a gas burette. The mixture was stirred vigorously while approximately 5 l of D_2 was taken up by the warm solution. The mixture was stirred for 4 h longer and the catalyst was filtered off. The methanol was distilled off through a 12 in. Vigreux column. The residue which remained was distilled under vacuum as above to give 26 g of the dideuteriocarboxylic acid. Nuclear magnetic resonance (60 MHz, CCl_4) δ 12.0 (s, 1H, COOH), 2.88 (m, approximately 1H, C-2—*exo*-H), 2.70 (m, 1H, bridgehead C—H), 2.35 (m, 1H, C-4—H), 1.75 (m, 2H, *syn*- and *anti*-7-H), 1.5 (bs, approximately 4H, norbornyl envelope).

Dimide Reduction of Norbornenecarboxylic Acid

To a slurry of dipotassium azodicarboxylate (36 g, freshly prepared) in methanol (distilled from sodium) was added norbornenecarboxylic acid (10 g, 80:20 *endo*:*exo*). To the vigorously stirred solution was added glacial acetic acid (17.5 g, in 20 ml of dry methanol) over a period of 1.5 h. After the addition was complete analysis of an aliquot by i.r. showed the absence of an intense peak at 710 cm^{-1} and indicated that the reduction was complete. Ether was added (700 ml) and the KOAc which precipitated was filtered off. The solvent was distilled off to a volume of 20 ml, then water was added (150 ml) and the solution was extracted with ether (1 × 200 ml; 3 × 50 ml). The ethereal solution was dried and the solvent evaporated. Vacuum distillation of the residue gave 7.6 g of 2-norbornanecarboxylic acid (b.p. 108–109°/2 mm) which solidified to a semi-solid on standing. Nuclear magnetic resonance (60 MHz, $CDCl_3$) δ 12.0 (s, 1H, COOH), 2.75 (bm, < 1H, C-2—*exo*-H), 2.58 (bs, 1H, C-1—H), 2.26 (bs, 1H, C-4—H), 1.45 (norbornyl envelope, 8H). There was no detectable olefinic signal in the n.m.r.

Bromination of 2-Norbornanecarboxylic Acid

The 2-norbornanecarboxylic acid (6.4 g, > 95% pure) was heated on the steam bath with bromine (8.8 g) and PCl_3 (0.1 ml) for 7 h. After the initial time an additional amount of bromine was added (4.0 g) and the mixture was heated for an additional 3 h. The mixture was poured onto water (250 ml) and ether (50 ml). An additional amount of ether was added (100 ml) followed by 6 g of $Na_2S_2O_4$. The ethereal layer was washed with water (50 ml) and dried. The ether was concentrated and the solid mass (5.0 g) was crystallized from toluene to give 3.9 of the bromoacid, m.p. 148–150° (lit. (22, 23) 150–151°).

Bromination of 2-Norbornanecarboxylic-exo,exo-5,6-d_2 Acid

Run 1. The deuteriocarboxylic acid (2.0 g, 0.014 mol), obtained from the dideuteriodimide reduction, was mixed with Br_2 (2.7 g, 0.016 mol) and PCl_3. The mixture was heated on the steam bath for 9 h, then poured into a dilute aqueous solution of $Na_2S_2O_4$, extracted with ether (1 × 100, 2 × 50 ml) and decolorized with charcoal. The residue was recrystallized from toluene to give 1.1 g of the deuterated *exo*-2-bromo-1-norbornanecarboxylic acid, m.p. 148–150°. Nuclear magnetic resonance ($CDCl_3$) δ 11.63 (s, COOH, 1H), 4.19 (m, H—C—Br, 1H), 2.5–1.4 (m, norbornyl envelope, 7.2 H). The n.m.r. showed considerable simplification in the region of 1.5–1.6 δ when compared to that of **1*d***, consistent with the replacement of *endo*-5,6-C—H with deuterium. Mass spectrum (80 eV), *m/e* 218–223 (M^+), 189–192 ($M^+ - C_2H_2D_2$), 139–141 ($M^+ - Br$).

Run 2. The acid (16 g, > 95% pure) prepared by catalytic deuteration of norbornenyl carboxylic acid was heated on the steam bath for 8 h with 1 ml of PCl_3 and 20 g of Br_2 as described previously. An additional 10 g of Br_2 were added and the mixture was heated for an additional 4 h at 75–80°. The reaction mixture was worked up as described previously and recrystallized from toluene to give 6.7 g of the dideuteriobromoacid, m.p. 150–152°.

*Esterification of the Dideuteriobromoacid **1c***

Run 1. The deuterated acid obtained from dideuteriodimide reduction (0.9 g, 0.004 mol, m.p. 148–150°) was dissolved in ether (50 ml) and treated with an ether solution of CH_2N_2 prepared from Diazald. The ether was evaporated and the viscous oil was purified by a bulb-to-bulb distillation at 5 mm to give 0.60 g of the bromoester. Analytical gas chromatography showed the ester to be > 98% pure; n.m.r. ($CDCl_3$) δ 4.18 (m, H—C—Br, 1H) 3.73 (s, —COOMe, 3H), 2.4–1.3 (m, norbornyl envelope, 7.3 H). The n.m.r. showed considerable simplification of the spectrum in the region of 1.7 δ as compared to the nondeuterated ester consistent with the replacement of *endo*-5,6-C—H with deuterium. Mass spectrum (80 eV), *m/e* 232–237 (M^+), 201–206 (M^+ – OMe), 173–178 (M^+ – COOMe), 153–157 (M^+ – Br). Analysis of the M^+ – Br peaks at 10 eV showed that the ester was composed of 73.7% d_2, 24.5% d_1, and 1.8% d_0 species, a total of 1.72 excess D per molecule.

Run 2. The bromoacid (3.8 g) obtained from the Pd-on-charcoal reduction was esterified with diazomethane as described previously. Analytical g.l.p.c. on 10 ft × 1/8 in. 10% Carbowax on Chromosorb W at 175° showed the ester to be > 98% pure with two minor components, one (< 1%) of slightly shorter retention time and another (< 1%) of longer retention time. Mass spectrum (14 eV, sample purified by preparative g.l.c.) 2.3% d_3, 84.2% d_2, 11.2% d_1, and 2.5% d_0 species; 1.87 excess D per molecule.

*Esterification of the Bromoacid **1d***

Run 1. The bromoacid (0.14 g) was treated with an ether solution of diazomethane prepared in the usual manner and after work-up gave the methyl ester. Nuclear magnetic resonance ($CDCl_3$) δ 4.20 (m, H—C—Br, 1H), 2.80 (s, COOMe, 3H), 2.5–1.2 (m, norbornyl envelope, 9H). Mass spectrum (80 eV, sample purified by preparative g.l.p.c.) 232–235 (M^+), 201–204 (M^+ – OMe), 173–176 (M^+ – COOMe) 153–154 (M^+ – Br). Analysis of M^+ – Br peak at 10 eV established that 153 and 154 were 9.45 and 0.80% of the 152 peak, respectively.

Run 2. The bromoacid (3.5 g, m.p. 148–150°) was esterified as described previously. Gas chromatographic analysis on a 10 ft × 3/8 in. 10% SE-30 on Chromosorb W column at 160° showed the ester to be 95–97% pure with two minor components present.

*Solvolysis of the Dideuteriobromoester **1b***

Run 1. The deuteriobromoester (0.16 g, purified by preparative g.l.p.c.) obtained from dideuteriodimide reduction sequence was dissolved in EtOH (4 ml) and H_2O (1 ml) containing NaOAc (0.065 g) and the mixture was sealed in a tube which was suspended in refluxing toluene (112°) for 4 days. The tube was opened, the contents poured into water (50 ml), and extracted with pentane (1 × 25 ml, 2 × 15 ml). The dried solution was analyzed by analytical g.l.p.c. with electronic area integration on a 5 ft × 1/8 in. 5% SE-30 Chromosorb W column with temperature programming from 100–150° at 80 min. The following product distribution, listed in order of increasing retention time, was established; methyl deuterio-1-norbornenecarboxylate 9.9%, methyl deuterio-1-nortricyclanecarboxylate 32.0%, methyl deuterio-*exo*-2-hydroxynorbornane-1-carboxylate 16.7%, methyl deuterio-*exo*-2-ethoxynorbornane-1-carboxylate 38.4%, unknown 1.6%, unknown 1.4% (entry 2, Table 1). The pentane was distilled off to yield an oily residue which

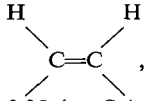
was separated into the four major components by preparative gas chromatography on a 5 ft × 1/4 in. 20% SE-30 on Chromosorb W column at 155°. Nuclear magnetic resonance (CCl_4) (Fig. 3) methyl deuterio-1-nortricyclanecarboxylate: δ 3.60 (s, COOMe, 3H), 2.06 (m, C-4—H, 1H), 1.78 (m, C-7, 2H) 1.47 (d, C-2, C-6—H, <2H), 1.37 (m, C-3, C-5—H, >3H). Mass spectrum methyl 1-nortricyclanecarboxylate (10 eV); a composite of 8.6% d_2, 79.4% d_1, and 12.0 d_0 species, corresponding to 0.97 excess D per molecule.

Nuclear magnetic resonance integration analysis (average of two integrations) utilizing the ester methyl and the total of the signals at 1.47 and 1.37 established that essentially only one deuterium remained in the nortricyclane with reduction of the signal at 1.37 being pronounced. A slight decrease in the relative intensity of the signal at 1.78 was consistent with some deuterium positioned on the cyclopropane ring (Fig. 3).

Run 2. The deuteriobromoester (0.080 g) obtained from the dideuteriodimide reduction sequence and purified by preparative g.l.p.c. was dissolved in EtOH (4 ml) and H_2O (1 ml) and anhydrous NaOAc (0.043 g) was added. The mixture was refluxed for 4 days and poured into water (10 ml) and extracted with ether (3 × 10 ml). The ether was distilled off after drying and the oily residue was separated by preparative gas chromatography on a 5 ft × 1/4 in. 20% SE-30 on Chromosorb W column at 140° into the four major products, in the following order of elution; methyl deuterio-1-norbornenecarboxylate, methyl deuterio-1-nortricyclanecarboxylate, methyl deuterio-*exo*-2-hydroxynorbornanecarboxylate, and methyl deuterio-1-*exo*-2-ethoxynorbornanecarboxylate. Mass spectrum methyl deuterio-1-nortricyclanecarboxylate (80 eV): *m/e* 153 (M^+, $C_9H_4O_2D$); analysis at 10 eV of M^+ showed the tricyclic material to be a composite of 5.7% d_2, 81.0% d_1, and 13.3% d_0 species, a total of 0.92 excess D per molecule.

Large Scale Solvolysis of the Dideuteriobromoester 1b

The dideuteriobromoester (1.5 g, >98% pure) prepared by CH_2N_2 esterification of the dideuterio acid obtained by catalytic deuteration was dissolved in 20 ml of 80:20, v/v, EtOH–H_2O (0.35 *M* in NaOAc) and the solution was sealed in a tube and suspended in refluxing toluene. After 14 days the tube was removed and the contents were poured into water (50 ml, saturated with NaCl) and the mixture was extracted with purified pentane (1 × 20 ml, 2 × 10 ml). The aqueous layer was then extracted with ether (1 × 20, 2 × 10 ml). The two solutions were washed with water and dried. Distillation of the solvent in each case through a 2 ft helices packed column gave 1–1.5 ml of residue in each case. The products were isolated by preparative g.l.p.c. (5 ft × 1/4 in., 20% Carbowax on Chromosorb W, 180°). The norbornenyl ester which was difficult to collect because of its volatility was collected with the aid of a collector that contained glass wool in the inlet and $CDCl_3$ in a bulb at the bottom. After every collection the tube was inverted carefully in order to dissolve the collected ester. Compound **4D** n.m.r. (60 MHz, $CDCl_3$) δ 6.18 (m,

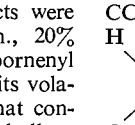


, 1.90 ± 0.10 H), 3.70 (s, —O—Me, 3.0 H), 2.95 (m, C-4—H, 1.0 H) 1.90 (unresolved quartet with fine structure, C-6, C-5 *exo*-H, *ca.* 2.0 H), 1.55 (m, C-7-*syn*- and *anti*-H, 2.0 H). The other products were also collected with a V-tube in which glass wool was placed in the part of the collector that was inserted into the preparative g.l.c. Compound **6D**; n.m.r. (60 MHz, CCl_4) δ 3.72 (s, —OMe, 3.0 H) 2.15 (m, C-4—H, 1.0 H), 1.90 (s, C-2; C-6—H, 1.90 H), 1.58 (d, C-7—H, 2.0 H), 1.45 (s, C-3; C-5—H, approximately 3H). Compound **7D** n.m.r. δ 3.70 (s, COOMe, 3H), 3.5 (m, H—C—O—CH_2—, 3H), 2.5 (m, C-4—H, 1H), 1.6 (m, norbornyl envelope, approximately 6H), 1.10 (t, —CH_3, 3H). Compound **8D** n.m.r. δ 4.0 (m, H—C—OH, 1H), 3.80 (s, COOMe, 3H), 3.0 (bs, —O—H, 1H), 2.30 (m, C-4—H, 1H), 2.0–1.1 (m, norbornyl envelope, approximately 6H). There was considerable simplification of the H—C—OH signal at 4.0 δ (Fig. 5) indicating that a deuteride shift results in the positioning of a deuterium *endo* at C-3. Compound **6D** mass spectrum (14 eV) 1.0% d_3, 13.4% d_2, 76.5% d_1, 9.3% d_0; 1.06 excess D per molecule.

Solvolysis of the Bromoester 1a

Run 1. The bromoester (0.1 g) was mixed with EtOH (4 ml), H_2O (1 ml), and NaOAc (0.040 g) and sealed in a tube. The tube was heated in refluxing toluene (112°) for 4 days and the contents were poured into water (50 ml) and extracted with pentane (1 × 25 ml, 2 × 15 ml). Analytical g.l.p.c. analysis on a 5 ft × 1/8 in. 5% SE-30 on Chromosorb W column with temperature programming (100–150° at 8°/min) and electronic area integration established the product distribution; methyl 1-norbornenecarboxylate 7.4%, methyl 1-nortricyclanecarboxylate 43.0%, unknown 0.2%, methyl *exo*-2-hydroxynorbornane-1-carboxylate 13.8%, methyl *exo*-2-ethoxynorbornane-1-carboxylate 31.8%, unknown 3.0%, unknown 0.6%, unknown 0.2%.

Run 2. The bromoester (1.24 g, 95–97% pure) was dissolved in 30 ml of solvolysis solution (EtOH 80 ml, H_2O 20 ml, NaOAc 1.6 g) and the solution (0.18 *M* ester, 0.2 *M* NaOAc) was sealed in a tube and heated on the steam bath (95°) for 6 days. The contents were poured into water (100 ml) saturated with NaCl and extracted with pentane (2 × 30, 3 × 20 ml). Analytical g.l.p.c. analysis on the 5 ft, 5% SE-30 column showed the four major products and *ca.* 15% starting material. The pentane layers were dried and distilled through a 1.5 ft helices packed column. Preparative g.l.p.c. on a 5 ft × 1/4 in. 20% SE-30 on Chromosorb W column at 165° gave the pure norbornenyl and nortricyclyl esters. The ether and alcohol were collected together then separated on a 10 ft × 3/8 in. 15% Carbowax on Chromosorb W column at 190°. Nuclear magnetic resonance (60 MHz, CCl_4): methylnorbornene-1-carboxylate, δ 6.05 (m,



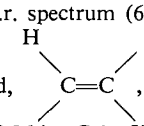
, 2H), 3.70 (s, COOMe, 3H), 2.90 (m, C-4—H, 1H), 1.9 (m, C-5, C-6—*exo*-H, 2H), 1.5 (m, C-7-H, 2H), 1.1 (m, C-5, C-6—*endo*-H, 2H); methyl 1-nortricyclane-1-carboxylate δ 3.70 (s, COOMe, 3H), 2.10 (m, C-4—H, 1H), 1.90 (s, C-2, C-6—H, 2H), 1.5 (d, C-7—H, 2H), 1.20 (s, C-3, C-5-H, 4H); methyl *exo*-2-ethoxynorbornane-1-carboxylate δ 3.70 (s, COOMe, 3H), 3.3 (m, H—C—O—Et, 3H), 2.25 (m, C-4—H, 1H), 2.0–1.2 (m, norbornyl envelope, 8H), 1.10 (t, —O—CH_2—CH_3, 3H); methyl *exo*-2-hydroxynorbornane-1-carboxy-

late δ 4.0 (m, H—C—OH, 1H), 3.0 (bs, —O—H, 1H), 2.30 (m, C-4-H, 1H), 2.1–1.0 (m, norbornyl envelope, 8H).

Methoxide-catalyzed Elimination of HBr from **1b**

The bromoester obtained via dideuteriodimide reduction (0.23 g, 0.00096 mol) was dissolved in 10 ml of a saturated solution of NaOMe in MeOH and the solution was refluxed for 24 h. The mixture was poured into water (30 ml) and extracted with ether (2 × 30 ml). The aqueous layer was acidified with dilute aqueous HCl and extracted with ether (2 × 30 ml). The ethereal layers were dried and the solvent was taken off on the rotatory evaporator to yield a solid. The solid was taken up in ether and treated with diazomethane. Analytical g.l.p.c. of the solution showed that the product ester had the same retention time as the material obtained from extraction of the basic solution. The two ethereal solutions were combined and the volume was reduced to *ca.* 3 ml by distillation through a 1-ft helices packed column. The methyl deuterionorbornene-1-carboxylate (0.075 g) was isolated by preparative g.l.p.c. In addition to the norbornenyl ester there were three minor products, the deuterionortricyclyl ester < 8%, unknown 4%, and *exo*-2-methoxynorbornyl ester < 8%. The latter product was isolated and its structure inferred from the mass spectrum (80 eV): *m/e* 186 (M^+, $C_{10}H_4O_2D_2$). Compound **4D** (Fig. 1) n.m.r. (100 MHz, CCl_4): δ 6.18 (d, C-2-H, J = 5 Hz), 6.03 (pair of doublets, C-3-H, J = 5.3 Hz), 3.70 (s, COOMe, 3H), 2.95 (m, C-4-H, 1H), 1.87 (A, B quartet with fine structure with higher field position coupled more than low-field position, C-6,C-5—*exo*-H's, respectively, < 2H), 1.5 (A, B quartet with fine structure, C-7-*syn*- and *anti*-H's, 2H), 1.2 (m, C-5, C-6-*endo*-H's < 0.3 H). Area integration analysis of the olefinic and methyl ester protons (average of 8 integrals) showed that there was only 1.95 hydrogens at C-2, C-3. This establishes that a deuteride shift occurs only to the extent of 5% during bromination of the dideuterionorbornylcarboxylic acid.

t-Butoxide-catalyzed Elimination of HBr from **1c**

The deuteriobromoacid (0.25 g, m.p. 144–146°) was dissolved in a saturated solution of KO*t*Bu in *t*-BuOH (30 ml) and the mixture was refluxed for 7 h. The mixture was poured into water (25 ml) and acidified with dilute aqueous hydrochloric acid and extracted with ether (1 × 50, 2 × 25 ml). The ethereal layer was dried and treated with diazomethane. Analytical g.l.p.c. 5 ft × 1/8 in. 5% SE-30 on Chromosorb W column with temperature programming (100–150°) at 10°/min showed in order of increased retention time, methyl deuterio-2-norbornene-1-carboxylate (20%), unknown < 1%, methyl deuterio-2-norbornene-2-carboxylate 60%, unknown 1%, unknown 10%, unknown 10% as well as 3% of bromoester. The ester **5D** was isolated by preparative g.l.p.c. on a 5 ft × 1/4 in. 20% SE-30 on Chromosorb W column maintained at 160°. The n.m.r. spectrum (60 MHz, CCl_4) showed signals at δ 6.83 (d,  , J = 3.5 Hz, 1H), 3.70 (s, COOMe, 3H), 3.26 (m, C-1—H, 1H), 3.03 (m, C-4—H, 1H), 1.77 (m, C-5,C-6—*exo*-H's, 0.3 H), 1.42 (m, C-7-*syn*-H, 1H), 1.15 (m, C-7—*anti*-H, 1H), 1.09 (m, C-5, C-6—*endo*-H's, 1.86 H). Integration analysis of the methyl ester signal at 3.70 and the signals at 1.77 (*exo*-C—H) and 1.09 (*endo*-C—H) gave ratios which were consistent with the deuterium being 95% stereochemically pure *exo*.

Kinetic Procedure

Sample tubes were made from 10 mm pyrex tubing and washed exhaustively with distilled water and absolute ethanol and dried in an oven. The bromoesters used for the exploratory runs and run 1 (Table 2) were purified by preparative g.l.p.c. on a 5 ft × 1/4 in. 20% SE-30 on Chromosorb W at 170–180°. The bromoesters used in runs 2 and 3 (Table 2) were purified by high pressure liquid chromatography using a Waters Model 200 Chromatograph. The solvent system 15–20% $CHCl_3$ – 85–80% hexane (v/v) was used with a 3/8 in. × 3 ft Porasil A column (column volume 34 ml). At a flow rate of 0.7 ml/min (800 p.s.i.) the bromoester was eluted after approximately 80 ml of flow. After 10–12 injections of 45 μl of neat liquid the appropriate fractions were combined and the solvent was removed on the rotatory evaporator. Final purification was achieved by two bulb-to-bulb vacuum distillations. The 0.09 and 0.135 *M* NaOAc in 80:20 EtOH–H_2O solvolysis solutions were prepared by dissolving 0.68 g of NaOAc·$3H_2O$ and 0.79 g of anhydrous NaOAc, respectively, in 100 ml of 80:20 EtOH–H_2O solution which was 0.04 *M* in NaOAc. The water used in the EtOH–H_2O solution was distilled then doubly distilled from $KMmO_4$. The absolute ethanol was distilled prior to use. In a typical kinetic run 0.10–0.17 g of each ester was dissolved in 15.00 ml of solvolysis solution transferred by means of 10 and 5 ml volumetric pipettes. The solution was mixed and approximately 1.2 ml of the solution of each of the esters was transferred to the ampoules (10–12) which were flushed with dry nitrogen. The ampoules containing the deuterated and nondeuterated esters were sealed and simultaneously submerged completely in a Haake Model NBe bath maintained at around 115.00 ± 0.03° with ethylene glycol as solvent. Both deuterated and nondeuterated aliquots were withdrawn simultaneously at appropriate intervals and stored in the freezer. After the kinetic run was complete and infinity samples were obtained by suspending two samples in refluxing toluene for 1–2 weeks, the samples were removed and equilibrated to room temperature. An exact portion (1.00 ml) was removed from each aliquot, distilled water (1.0 ml), and 6 *N* HOAc (1.0 ml) and 2 drops of 0.1% eosin in 95% EtOH was added and the aliquot was titrated to a pink end point (41) with 0.0100–0.0150 *N* $AgNO_3$ using a 5.00 ml burette. Titers ranged from 0.4 to 3.5 ml. The results were subjected to least-squares analysis. An example of the data is described in Fig. 4.

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