Memory Effects in Multiple Carbonium Ion Rearrangements. II. Behavior of the Potentially Symmetrical Cation in the Ring-Expansion Reactions of 7-Norbornylcarbinyl Systems[1,2a,b]

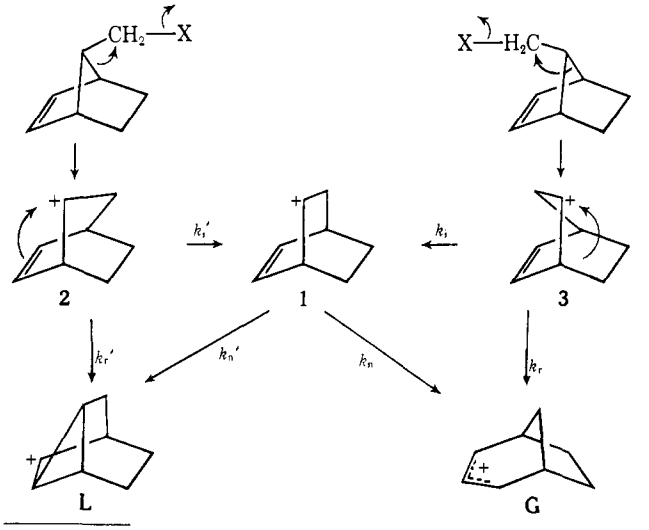
Jerome A. Berson,[2c] Mohindar Singh Poonian, and William J. Libbey

Contribution from the Department of Chemistry, University of Wisconsin, Madison, Wisconsin 53706. *Received March 29, 1969*

Abstract: Carbonium ion ring expansions of stereospecifically labeled *syn*- and *anti*-7-norbornylcarbinyl-2,3-d_2 derivatives lead to bicyclo[2.2.2]oct-2-yl and bicyclo[3.2.1]oct-*exo*-2-yl products. The ratio of these two products is barely higher in the ring expansions than in "conventional" entry into this system from bicyclo[2.2.2]oct-2-yl or bicyclo[3.2.1]oct-*exo*-2-yl substrates. External nucleophilic capture of an "extra" precursor of bicyclo[2.2.2]oct-2-yl product in the ring expansions thus is rather inefficient. The distribution of the deuterium label in the bicyclo-[3.2.1]oct-*exo*-2-yl product demonstrates the existence of a memory effect in the second rearrangement step. The first-formed potentially symmetrical ring-expanded cation behaves unsymmetrically: the bond that migrates preferentially in the second rearrangement step is the one remote from the initial site of reaction in the starting material. The magnitude of this preference in solvolytic ring expansion is rather insensitive to environmental factors, and the small changes produced by large changes in solvent ionizing power are opposite in direction to those expected for ion-pair return phenomena. Deaminative ring expansions at room temperature give higher memory effect selectivities than solvolytic ones at elevated temperature. Independent synthesis and solvolysis of the hypothetical ion-pair return product, stereospecifically labeled bicyclo[2.2.2]oct-2-yl-5,6-d_2 *p*-bromobenzenesulfonate, show that this cannot be the sole intermediate in the ring expansion of the labeled 7-norbornylcarbinyl *p*-bromobenzenesulfonate.

The difference in the distribution of products obtained from the ring expansions of *syn*- and *anti*-2-norbornenyl-7-carbinyl systems amounts to a qualitative demonstration of the existence of a memory effect in those reactions.[3] Despite the opportunity for the formation of identical product mixtures from both substrates by way of the common cation **1**, each ring expansion passes first over a separate "twisted" cation (**2** or **3**), the disposition of which is determined by a competition between quasi-symmetrization to **1** and further bond rearrangement (Scheme I). Attempts to evaluate the competition ratios k_r/k_i and k_r'/k_i', which measure the efficiency with which memory is preserved, are doomed to frustration. The system is inherently complex because of the presence of two such ratios, but more significantly the experimental product ratios are determined not only by the competition k_r/k_i (or k_r'/k_i') but also by the "natural" ratio k_n'/k_n for rearrangement of the quasi-symmetrical cation **1**. Unless one of these ratios is known independently, the other two cannot be deduced from the product ratios. So far, no method is available for the needed independent determination.

Scheme I



The present study of the ring expansions of deuterium-labeled 7-norbornylcarbinyl derivatives circumvents this problem. The intermediate **4** (Scheme II) mechanistically corresponding to **1** in the previous system now is truly symmetrical, and its "natural" competition ratio for further rearrangement is unity. Further, the twisted cations **6** and **7** now have identical properties, so that except for small secondary isotope effects, the same symmetrization rates (k_S) and rearrangement rates (k_R) apply.

The potentially symmetrical system resulting from 7-norbornylcarbinyl ring expansions nevertheless is not free of disadvantages. The most severe of these concerns the twice-rearranged cation **9** and its isotope-position isomer **10**, which for convenience we have formulated in nonclassical notation. Cation **9** is the precursor of 2-bicyclo[3.2.1]octyl product **11**, which is the substance that is to reveal the memory effect by its predominance over the isotope-position isomer **12** derived from cation **10**. A serious complication here that was absent in the unsaturated analogs (Scheme I) is that the reactive intermediates of the 2-bicyclo[2.2.2]octyl-2-bicyclo-[3.2.1]octyl system (**9**, **10**) do not maintain fully their stereochemical integrity.[4-7] Although the products

(1) This work was supported in part by grants from the National Institute of Arthritis and Metabolic Diseases (AM-07505) and the National Science Foundation (GP-6212X).

(2) (a) For preliminary reports, see J. A. Berson and M. S. Poonian, *J. Am. Chem. Soc.*, **88**, 170 (1966), and (b) J. A. Berson, *Angew. Chem. Intern. Ed. Engl.*, 7, 779 (1968). (c) Please address inquiries to this author at Sterling Chemistry Laboratory, Yale University, New Haven, Conn. 06520.

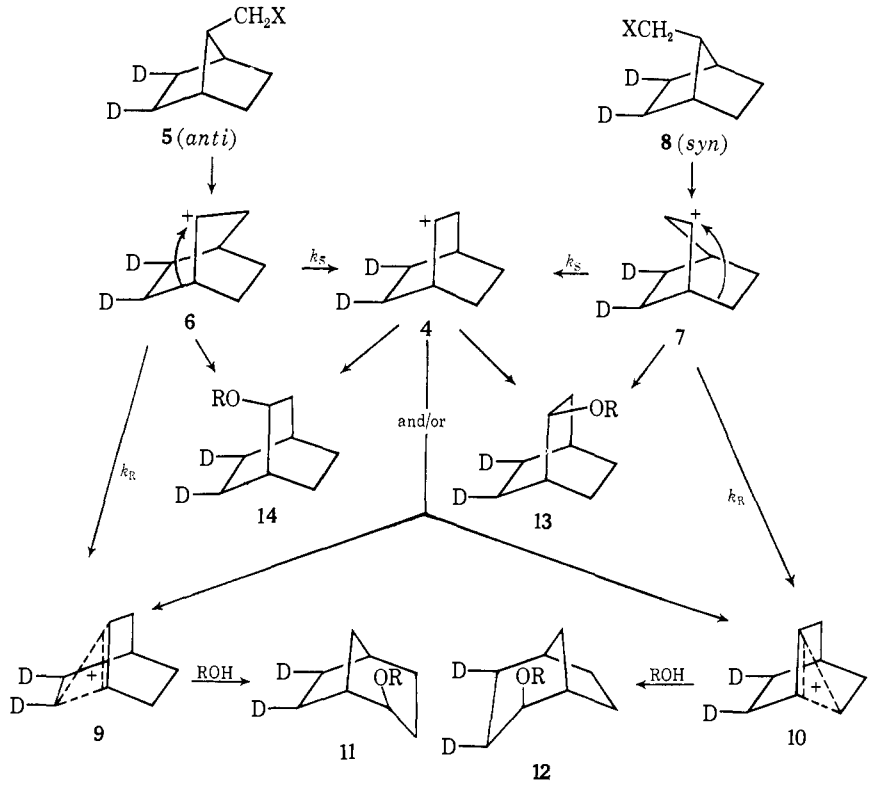
(3) (a) J. A. Berson and J. J. Gajewski, *J. Am. Chem. Soc.*, **86**, 5020 (1964); (b) J. A. Berson, J. J. Gajewski, and D. Donald, *ibid.*, **91**, 5550 (1969).

(4) (a) J. A. Berson and D. Willner, *ibid.*, **84**, 675 (1962); (b) *ibid.*, **86**, 609 (1964).

(5) H. L. Goering and G. N. Fickes, *ibid.*, **90**, 2862, 2865 (1968).

(6) H. M. Walborsky, J. Webb, and C. G. Pitt, *J. Org. Chem.*, **28**, 3214 (1963).

Scheme II

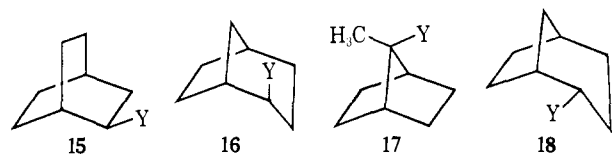


themselves (**11**, **12**) are stable, the cationic intermediates reversibly interconvert with symmetrical species, among which is very probably the classical 2-bicyclo[2.2.2]octyl cation **4**.[4-6] Therefore, the observed predominance of 6,7-dideuterio product **11** over 2,3-dideuterio product **12** from the ring expansion of *anti* substrate **5** only provides the basis for a *minimum* measure of the true rate constant ratio k_R/k_S. We defer further discussion of this point, but note here that corrections for this kind of "leakage" are not easy to make. Nevertheless, although these cations are not ideally suited for quantitative evaluation of memory effects, their previously recorded properties[4-6] give assurance that "leakage" is not severe enough to erase completely whatever memory survives. Thus, at least a qualitative demonstration of the phenomenon is feasible. Beyond this, the symmetry of the system eliminates the "natural ratio" problem which occurs in unsymmetrical cases[3] and permits a further examination of the effect of ionic concentration. The results of such studies bear on possible asymmetric ion-atmosphere interpretations of memory effects.

As is usually the case in studies of memory effects, mechanisms like that in Scheme II are not distinguishable from alternatives in which crossover occurs directly from "twisted" cations **6** and **7** to the "wrong" doubly rearranged ions **10** and **9**, respectively, rather than by way of a symmetrical intermediate **4**.

Results

The products of solvolyses of 7-norbornylcarbinyl *p*-bromobenzenesulfonate and of deaminations of 7-norbornylcarbinylamine (Table I) in aqueous and in carboxylic acid solvents vary with conditions but always include alcohol or ester of unrearranged (7-norbornylcarbinyl) skeleton as well as ring-expansion products of the formally singly rearranged 2-bicyclo[2.2.2]octyl (**15**) and formally doubly rearranged *exo*-2-bicyclo[3.2.1]-octyl (**16**) series. Small amounts of tertiary product 7-methyl-7-norbornanol or its acetate (**17**) resulting from hydride shift, and traces of *endo*-2-bicyclo[3.2.1]-octyl product (**18**) also are present. There are varying



15 16 17 18

but generally small amounts of hydrocarbons. Control experiments establish the stability of the major products to the reaction conditions.[8]

Although bimolecular displacement contributes to the proportion of primary 7-norbornylcarbinyl product in acetolysis, as is revealed by the increase in the fraction of this material with increasing buffer concentration (Table I), the ring-expanded products **15**, **16**, and **18** occur in proportions relative to each other that are essentially invariant with buffer concentration or indeed with other reaction conditions (Table I).

Search for Evidence of an "Extra" Capturable Intermediate. The **15**/**16** ratios in the ring expansions of 7-norbornylcarbinyl *p*-bromobenzenesulfonate are only

(7) For entry into this system by the π route, see (a) S. Winstein and P. Carter, *J. Am. Chem. Soc.*, **83**, 4485 (1961). For entry *via* 2,7-hydride shift in the bicyclo[3.2.1]oct-7-yl cation, see (b) R. A. Appleton, J. C. Fairlie, R. McCrindle, and W. Parker, *J. Chem. Soc., C*, 1716 (1968).

(8) It is possible to imagine mechanisms of formation of the products involving reversible deprotonation of carbonium ion intermediates, but this would result in incorporation of deuterium when the reaction was carried out in deuterated solvent. Deamination of 7-norbornylcarbinylamine hydrochloride in deuterioacetic acid gives an acetate product mixture containing only 0.05 D. The small amount of incorporation may result from a side reaction reversibly interconverting diazonium salt and diazoalkane, but whatever its source, its effect on the evaluation of the selectivity would be conservative and virtually within experimental error. Similarly, acetolysis of **15**-OBs in acetic acid-O-*d* at 100° gives **15**-OAc and **16**-OAc without measurable incorporation of deuterium.

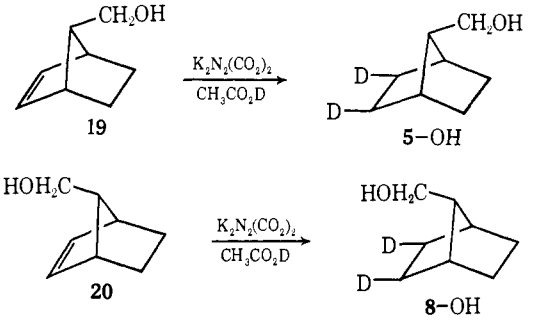
Table I. Products[a] from Reactions of 7-Norbornylcarbinyl Derivatives, RX

Reactant RX	Conditions: Solvent and temp, °C	Conditions: Buffer or salt concn, *M*	Products, % yield[b,n]: 15	16	18		17
A. Solvolyses							
ROBs	HOAc, 100	0.066[c]	22.8	16.6	Trace	58.5	2.3
ROBs	HOAc, 120	0.066[c,d]	23.2	16.7	Trace	58.3	1.7
ROBs	HOAc, 100	0.14[c]	21.2	15.3	Trace	61.2	2.2
ROBs	HOAc, 120	0.128[c]	20	15	Trace	63	2
ROBs	HOAc, 120	0.245[c]	12	9	Trace	78	1.4
ROBs	HOAc, 120	0.383[c]	4.8	3.5	Trace	91	0.9
ROBs	HCO_2H, 100	*e*	39	30	2	26	3
ROBs	Aq EtOH, 100[g]	0.011[h]	4.8	3.2	Trace	92	~0
ROBs	Aq EtOH, 100[g]	0.011[i]	1.8	1.2	Trace	97	~0
RBr[m,o]	Aq dioxane,[j] 100	0.066[h]	8.8	6.1	Trace	84.4	1.0
	$AgClO_4$[k]						
B. Deaminations[f,l]							
RNH_2[q,r]	Aq HOAc[p]	None	46.2	34.1	Trace	11.1	0
RNH_2[q,s]	Aq HOAc[p]	1.0[t]	43.3	33.4	Trace	9.7	0
RNH_2[u]	HOAc	None	51.8	29.9	Trace	18.3	Trace
RNH_2[u]	HOAc	1.0[v]	54.2	37.0	Trace	8.9	Trace
RNH_2[o,u]	HOAc	2.0[v]	55	38	Trace	7.2	Trace

[a] Compare R. K. Bly and R. S. Bly, *J. Org. Chem.*, **31**, 1577 (1966) [b] In acetic acid, Y = OAc; in aqueous solvents, Y = OH, in formic acid, Y = OCOH. Percentage of volatile product (acetate or alcohol) exclusive of hydrocarbons. [c] Sodium acetate. [d] Polyvinyl acetate sufficient to cause 15-fold viscosity increase at 120°. [e] Formic acid–pyridine 9:1 (v/v). [f] At 25°. [g] Ethanol–water 77:23 (v/v). [h] Pyridine. [i] Potassium hydroxide. [j] Dioxane–water 67:33 (v/v). [k] 0.13 *M*. [l] Nitrosating agent sodium nitrite; salt concentrations given refer to salt in addition to this. [m] *Ca.* 40% of unreacted bromide also was present. [n] A few per cent of hydrocarbon was formed unless otherwide indicated. [o] *Ca.* 20% (by uncalibrated vpc peak area) hydrocarbon was formed. [p] Acetic acid–water 6:94 (v/v). [q] *Ca.* 4–5% of acetates present. [r] 8.7% 2-bicyclo[2.2.2]octanone present. [s] 13.8% 2-bicyclo[2.2.2]octanone present. [t] Sodium fluoroborate. [u] *Ca.* 2% alcohols present. [v] Lithium perchlorate.

slightly higher in both formic and acetic acids than the values that might be considered "typical" for the 2-bicyclo[2.2.2][3.2.1]octyl cation system. These "typical" values are derived from solvolyses of 2-bicyclo-[2.2.2]octyl or *exo*-2-bicyclo[3.2.1]octyl substrates **15**- and **16**-OBs and -OTs (Table II). The ratio is still higher in hydrolytic ring expansion in aqueous dioxane. It is tempting to conclude that these trends follow changes in the nucleophilicity of the media, but the deamination results (Table II) do not support this idea very well. The more significant observation to be made is that even if the apparent slight "excess" of preference for bicyclo[2.2.2]octyl product **15** in the ring expansions is real, there is only inefficient capture of the "extra" precursor (*e.g.*, **7** or **6** of Scheme II) of product **15** (**13** and/or **14** of Scheme II) that is not produced in conventional entry *via* substrates **15**-OBs or **16**-OBs. Moreover, the most nucleophilic solvents are only slightly more effective than the least nucleophilic ones.[9]

Ring Expansions of *anti*- and *syn*-Norbornylcarbinyl-2,3-d_2 Derivatives. The *anti* (**5**) and *syn* (**8**) deuterated starting materials for the ring expansions result from the reaction of the olefinic carbinols **19** and **20**[10] with



dideuteriodiimide (N_2D_2), which is generated from acetic acid-O-*d* and potassium azodicarboxylate in solvent methanol-O-*d*. The deuteration procedure introduces label only at the site of the double bond of the starting material. This is expected on chemical grounds and is confirmed by the mass spectrum of the derived *anti*-phthalimide **21**, which shows no species more highly deuterated than d_2.

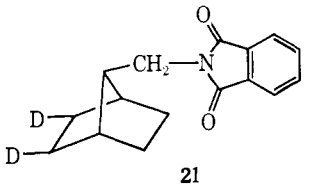
(9) (a) Table II shows that the **15**/**16** ratio is slightly higher in deaminations than in solvolyses of 7-norbornylcarbinyl substrates. Although the cause of this is not clear, the reactions show no evidence of the solvent-sorting effects that produce a disproportionately large share of alcohol product in the glacial acetic acid deamination of decalylamines.[9b] A total of only about 2% alcohols is produced in the deaminations of 7-norbornylcarbinylamine in glacial acetic acid, and control experiments show the stability of the alcohols under the conditions of deamination. Similarly, the only important products in the aqueous acetic acid media (94% water, 6% acetic acid) are alcohols. The total of acetates produced amounts to about 2%. Depending on the deamination conditions (see Experimental Section) some 2-bicyclo[2.2.2]octanone and apparently smaller amounts of 2-bicyclo[3.2.1]octanone also are formed, presumably by oxidation of the corresponding alcohols (**15** and **16**). Therefore, the observed **15**/**16** ratio in aqueous deamination probably is a minimum value. (b) T. Cohen and E. Jankowski, *J. Am. Chem. Soc.*, **86**, 4217 (1964).

(10) (a) The 2-norbornene-7-carbinols, **19** and **20**, are made by two methods. The first follows known[10b] steps and affords both isomers but requires careful spinning band and vpc separations of the methyl ester precursors to obtain the isomers pure. The second, which gives only the *syn* isomer **20**, is an adaptation of the method devised by Foley[10c] to prepare 1-methylnorborn-2-ene-*syn*-7-carbinol. It involves the bromination of norbornan-2-one-*syn*-7-carboxylic acid[10d] to the 3-bromo derivative, conversion to the methyl ester, lithium aluminum hydride reduction to the bromodiol, and zinc reduction to the *syn*-carbinol **20**. (b) R. R. Sauers, *Chem. Ind.* (London), 176 (1960); R. R. Sauers and R. M. Hawthorne, Jr., *J. Org. Chem.*, **29**, 1685 (1964); (c) J. W. Foley, Ph.D. Thesis, University of Wisconsin, 1969; (d) S. Beckmann and H. Geiger, *Chem. Ber.*, **94**, 48 (1961).

Table II. Ratios of 2-Bicyclo[2.2.2]octyl to *exo*-2-Bicyclo[3.2.1]octyl Products (**15**/**16**) Obtained from 7-Norbornylcarbinyl (7-Nor-CH_2X) and Bicyclooctyl Substrates

Starting material	Solvent	Other reagents	*T*, °C	**15**/**16**	Ref
15-OBs	HOAc	NaOAc	120	1.20	*a*
15-OBs	HOAc	NaOAc	50	1.26	*b*
15-OTs	HOAc	NaOAc	49	1.16	*c*
16-OTs	HOAc	NaOAc	49	1.18	*c*
15-OBs	HCO_2H	Py	100	1.20 ± 0.02	*a*, *d*
15-OTs	Aq acetone	Py	49	1.34	*c*
16-OTs	Aq acetone	Py	49	1.33	*c*
7-Nor-CH_2OBs	HCO_2H	Py	100	1.29	*a*,
7-Nor-CH_2OBs	HOAc	NaOAc	100	1.39	*a*, *f*
7-Nor-CH_2OBs	HOAc	NaOAc	120	1.33 ± 0.03	*a*, *e*
7-Nor-CH_2Br	Aq dioxane[g]	$AgClO_4$	100	1.41 ± 0.03	*a*, *d*
7-Nor-CH_2NH_2	Aq HOAc[h]	$NaNO_2$	25	1.44 ± 0.05	*a*, *i*
7-Nor-CH_2NH_2	HOAc	$NaNO_2$	25	1.55 ± 0.12	*a*, *e*

[a] Present work. [b] Reference 6. [c] Reference 5. [d] Average of two determinations. [e] Average of three determinations. [f] Single determination. [g] 40% water, 60% dioxane v/v. [h] 94% water, 6% HOAc. [i] Average of four determinations.



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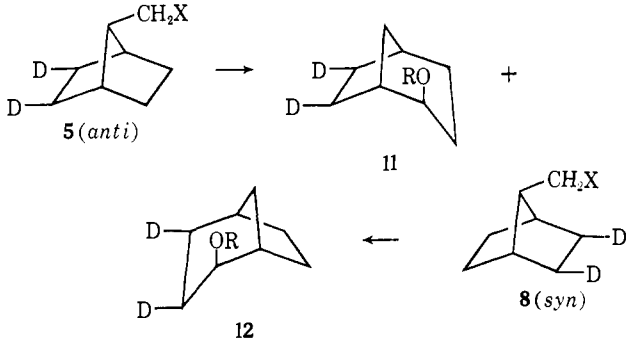
Combustion analyses[11] by the falling drop method provide routine assays for total deuterium in starting materials and products. The results agree within experimental error (1–3%) with parallel mass spectrometric determinations.

In terms of Scheme II, the efficiency with which memory is preserved in the case of *anti*-deuterio substrate **5** can be expressed as a ratio $(\mathbf{11}/\mathbf{12})_{anti}$ of 6,7-labeled to 3,4-labeled *exo*-2-bicyclo[3.2.1]octyl product, whereas the inverse ratio $(\mathbf{12}/\mathbf{11})_{syn}$ gives the memory effect from *syn*-dideuterio substrate **8**. Except for a small secondary isotope effect, these ratios should be identical.

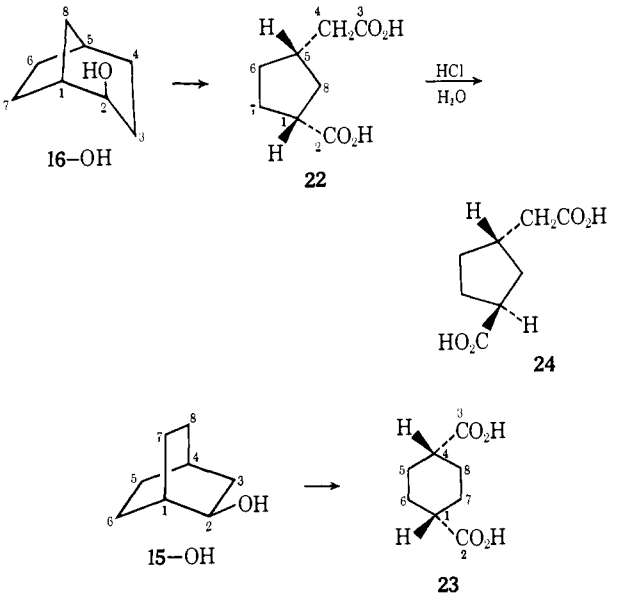


5 (*anti*) **11** **12** **8** (*syn*)

That they are found to be so in the cases where comparisons are available (Table III) provides an important test of the internal consistency of the data. An alternative way to express the memory effect is the "per cent excess" of the favored position isomer; *i.e.*, from **5** (*anti*) this parameter is calculated as 100[(**11** − **12**)/(**11** + **12**)].

Isolation of *exo*-2-bicyclo[3.2.1]octan-*exo*-2-ol (**16**-OH) and 2-bicyclo[2.2.2]octanol (**15**-OH) is achieved by vapor chromatography (vpc), either directly upon the products in the case of aqueous reaction media, or after lithium aluminum hydride treatment of the mixture of esters formed in carboxylic acid media. Control experiments show that the chromatography does not cause significant isotopic fractionation. Previous control experiments[4] demonstrate that the acetate products derived in acetolyses do not revert to their carbonium ion precursors appreciably under the conditions of solvolysis. This conclusion is supported by the present observation that bicyclo[3.2.1]octan-*exo*-2-yl acetate **16**-OAc does not form any bicyclo[2.2.2]octan-2-yl acetate **15**-OAc under the solvolysis conditions.

Degradation follows a procedure previously used for *endo* isomer:[12] nitric acid oxidation of the separated alcohols gives *cis*-3-carboxycyclopentaneacetic acid (**22**) from **16**-OH and *cis*-1,4-cyclohexanedicarboxylic acid (**23**) from **15**-OH, the carbon atoms of which are numbered here to correspond to the positions they occupy in the precursor alcohols. Hot hydrochloric acid converts the *cis*-3-carboxycyclopentaneacetic acid **22** to the *trans* isomer **24**, simultaneously exchanging for protium any deuterium bound to C-1 or C-4. The completeness of this exchange under these conditions is verified by control experiments on independently prepared deuterated acid **22**. The total deuterium content of **24** thus represents the amount of 6,7-labeled product **16**-OH (**11**-OH of Scheme II), provided three conditions are

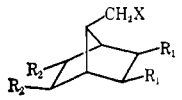
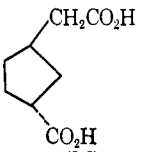


16–OH **22** **24** **15**–OH **23**

(11) By Mr. Josef Nemeth, Urbana, Ill.

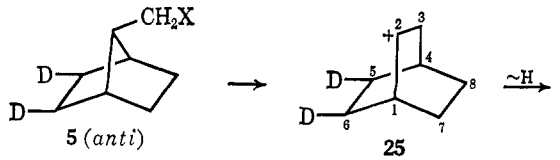
(12) J. A. Berson and P. Reynolds-Warnhoff, *J. Am. Chem. Soc.*, **86**, 595 (1964).

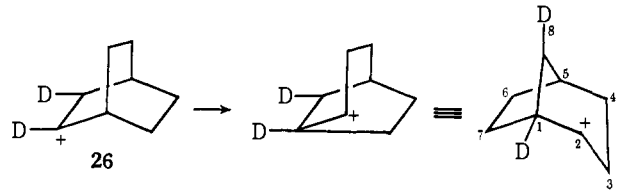
Table III. Selectivities in Ring Expansions of 7-Norbornylcarbinyl-2,3-d_2 Derivatives

Reactant 	Exptl conditions	D/molecule[c] of reactant (N)	D/molecule[c]  (M)	Selectivity Ratio, α[e]	Selectivity % excess[f]
X = OBs R_1 = D; R_2 = H	HOAc, NaOAc 120°	1.334 1.334	0.549[a] 0.547[a]	1.4 1.4	18 18
X = OBs R_1 = D; R_2 = H	HOAc, NaOAc 100°	1.576	0.534	2.0	34
X = OBs R_1 = H; R_2 = D	HOAc, NaOAc 120°	1.414	0.872	1.6	24
X = OBs R_1 = H; R_2 = D	HCO_2H, Py 100°	1.810	1.290	2.5	42
X = NH_2 R_1 = D; R_2 = H R_1 = H; R_2 = D	Aq HOAc $NaNO_2$, 25°	1.460 (1.499)[d] 1.460 (1.461)[d]	0.193 1.242	6.6 5.7	74 70
X = NH_2 R_1 = D; R_2 = H	Aq HOAc $NaNO_2$, 25°	1.403 (1.396)[d]	0.232	5.1	68
X = NH_2 R_1 = D; R_2 = H	Aq HOAc $NaNO_2$, 25° 1 *M* $NaBF_4$	1.403 (1.396)[d]	0.236	5.0	66
X = NH_2 R_1 = D; R_2 = H	HOAc $NaNO_2$, 25°	1.518	0.580[b] 0.524[b]	1.6[b] 1.9[b]	24[b] 32[b]
X = OBs R_1 = H; R_2 = D	HOAc Polyvinyl acetate 120°	1.841	1.224	2.0	34

[a] Separate runs. [b] Duplicate analyses, performed on small samples (9 and 6 mg). Deuterium content for these samples is probably accurate to 10%. [c] Deuterium content (probable error ±2%) determined by combustion and falling drop analysis. [d] Mass spectrometric analysis in parentheses. [e] When R_1 = D, α = (N/M) − 1; when R_1 = H, α = M/(N − M). [f] 100[2α/(α + 1) − 1].

satisfied. (1) The ratio of 6,7-dilabeled/3,4-dilabeled materials is the same as the ratio of 6- (and/or 7-) monolabeled/3- (and/or 4-) monolabeled materials. (2) No deuterium resides at C-5 or C-8. (3) Transannular hydride or deuteride shifts (*e.g.*, **25** → **26**) do not occur.





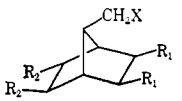
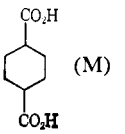
Condition 1 does not seem to be a major concern, since its contravention would imply either a large kinetic isotope effect or an extra chemical reaction not encompassed in Scheme II. The kinetic isotope effect is a secondary one and therefore is expected to be small. Moreover, the already mentioned compatibility of the results from *syn*- and *anti*-labeled starting materials indicates that it is negligible. The other conceivable source of difficulty under condition (1) seems of remote concern, since no mechanistically significant superfluous products are observed. This also argues for condition (2), the absence of deuterium at C-5 and C-8, since it is difficult to devise mechanisms for significant labeling at those sites which also would not lead to extra products. An even stronger argument against location of deuterium at C-5 and C-8 again derives from the observation in Table III that the selectivities calculated from results with the *syn*-2,3-dideuterio substrate correspond well to those from the *anti* system. This would require some far-fetched coincidences were an appreciable fraction of the deuterium undergoing position exchange with hydrogens at C-5 or C-8.

The absence of transannular hydride shifts (condition 3) appears to be experimentally established by the deuterium content of the 1,4-cyclohexanedicarboxylic acid (**23**), which within experimental error is always the same as that of the starting material (Table IV). The average retention of deuterium in the ten runs for which such data are available is 99.1%. Transannular shift of either hydrogen or deuterium as in **25** → **26** would inevitably result in a lower deuterium content in **23**.[13]

On the Role of Ion-Pair Return Product 15-OBs. The product of ion-pair return with rearrangement in the solvolysis of 7-norbornylcarbinyl *p*-bromobenzenesulfonate **8-OBs** (*syn*) would be the 2-bicyclo[2.2.2]octyl isomer **15-OBs**-*syn*-5,6-d_2. Since the rearranged ester

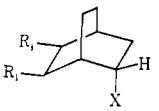
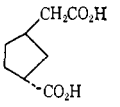
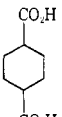
(13) However, the experimental error in the deuterium analyses is sufficient to permit several per cent of transannular hydride shift to go undetected. Furthermore, *syn*-labeled substrate does not provide a suitable test for such processes. In a closely related system,[10c] more accurate analytical techniques now have revealed the occurrence of a few per cent of hydride shift. Since the presence of such reactions in this work would diminish the memory effects, the selectivities reported here should be considered minimum values.

Table IV. Retention of Deuterium in *cis*-1,4-Cyclohexanedicarboxylic Acid Samples Obtained from 2-Bicyclo[2.2.2]octanol Isolated from Ring Expansions

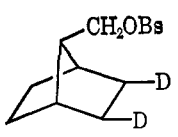
Reactant 	Exptl conditions	D/molecule[a] of reactant (N)	D/molecule[a]  (M)	% D retained[b]
X = OBs R_1 = D; R_2 = H	HOAc, NaOAc 120°	1.771 1.334	1.723 1.362	97 102
X = OBs R_1 = H; R_2 = D	HOAc, NaOAc 120°	1.414 1.827 (1.850)[c]	1.437 1.750	102 98
X = OBs R_1 = H; R_2 = D	HCO_2H, Py 100°	1.810	1.746	97
X = NH_2 R_1 = H; R_2 = D	Aq HOAc $NaNO_2$, 25°	1.460 (1.461)[c]	1.494	102
X = NH_2 R_1 = D; R_2 = H	Aq HOAc $NaNO_2$, 25°	1.460 (1.499)[c] 1.403 (1.396)[c]	1.500 1.344	103 96
X = NH_2 R_1 = D; R_2 = H	Aq HOAc $NaNO_2$, 25° 1 *M* $NaBF_4$	1.403 (1.396)[c]	1.338	95
X = NH_2 R_1 = D; R_2 = H	HOAc, $NaNO_2$ 25°	1.518	1.554	102

[a] Deuterium content determined by combustion and falling drop analysis with a probable error of ±2%. [b] 100(M/N). [c] Value in parentheses determined mass spectrometrically.

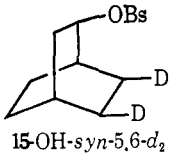
Table V. Selectivities for *anti* Migration in Solvolyses of Bicyclo[2.2.2]oct-2-yl *p*-Bromobenzenesulfonate **15**-OBs-*syn*-5,6-d_2 and of Its Optically Active Analog

D/molecule in reactant 	Exptl conditions	% D retained in  M	% D retained 	% retention of config (or equiv)
R_1 = D; X = OBs 1.701	HOAc, NaOAc 120°	24.7	97	51[a]
R_1 = D; X = OBs 1.652	HCO_2H, Py 100°	20.9	95	58[a]
R_1 = H; X = OTs optically active	HOAc, NaOAc 49°			63[b]
R_1 = H; X = OTs optically active	Aq acetone, Py 49°			87[b]

[a] 100 − 2M. [b] Reference 5. A comparable result is obtained with X = OBs (ref 6).



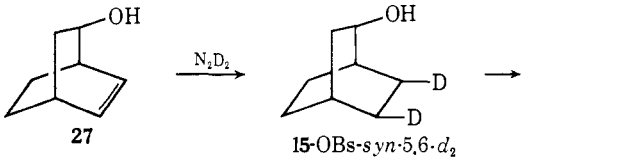
8-OBs(*syn*)



15-OH-*syn*-5,6-d_2

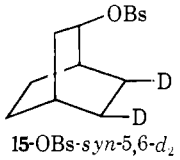
is by far more reactive in solvolysis,[5,6] it would not accumulate, and hence its intervention as an intermediate could not be established by isolation. To evaluate what role **15**-OBs-*syn*-5,6-d_2 may play in the ring expansion of **8**-OBs (*syn*), it is necessary to carry out the solvolysis of independently synthesized **15**-OBs-*syn*-5,6-d_2 and to determine the specificity of labeling in the 2-bicyclo[3.2.1]octyl product. Some information bearing on this question is already available from studies[5,6] of solvolyses of optically active 2-bicyclo[2.2.2]octyl substrates, but these report experiments at temperatures well below those necessary to observe conveniently the solvolysis of **8**-OBs, and a closer comparison is to be preferred.

Synthesis of **15**-OBs-*syn*-5,6-d_2 is readily achieved by dideuteriodiimide reduction of bicyclo[2.2.2]oct-5-en-2-*endo*-ol (**27**) followed by arenesulfonylation. Injection



27

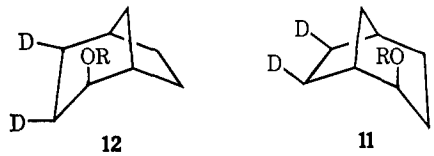
15-OBs-*syn*-5,6-d_2



15-OBs-*syn*-5,6-d_2

of a concentrated solution of **15**-OBs-*syn*-5,6-d_2 into a stirred, preheated, buffered sample of the solvent provides an approximation of the conditions that would prevail were **15**-OBs-*syn*-5,6-d_2 generated in the solvo-

lytic ring expansion of **8**-OBs at 120°. The specificity of formation of the two position isomers of 2-bicyclo[3.2.1]octyl product **12** and **11** is determined by the isolation and degradation procedure already described.



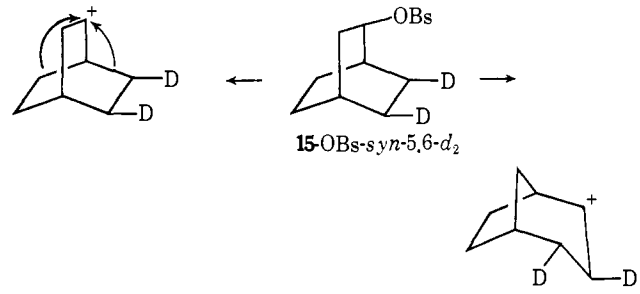
12 **11**

Similarly, the absence of significant deuteride shift is established by isolation and degradation of the 2-bicyclo[2.2.2]octyl product. The results obtained in acetolysis and formolysis are given in Table V. In both solvents, the selectivity of migration of the *anti* bond is *higher* from **15**-OBs-*syn*-5,6-d_2 than from **8**-OBs (*syn*). The once-rearranged sulfonate **15**-OBs thus cannot be the sole intermediate in the ring expansion of **8**-OBs (*syn*).

Discussion. The data of Table III clearly indicate the operation of a memory effect. As in all the previously examined cases,[3,4,12] the bond that migrates preferentially in the second rearrangement step is the one remote from the site of the initial heterolysis.

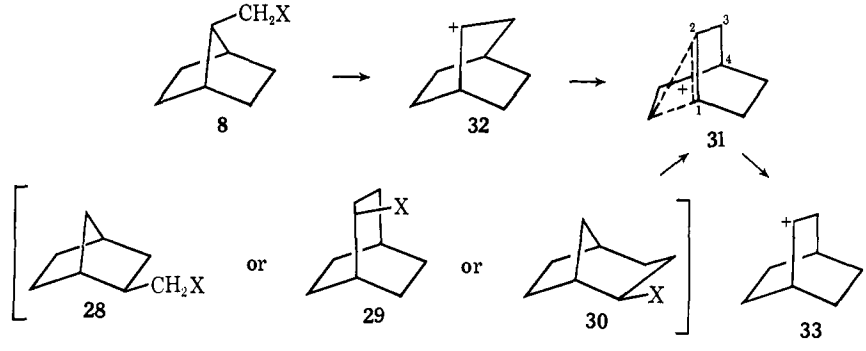
The deuterium distribution in the 2-bicyclo[3.2.1]octyl products shown in Table III give too pessimistic an estimate of the selectivity, because the doubly rearranged specifically labeled 2-bicyclo[2.2.2][3.2.1]octyl cation system suffers crossover. Solvolyses of optically active 2-bicyclo[2.2.2]octyl (**29**) or *exo*-2-bicyclo[3.2.1]octyl (**30**) substrates give products with substantial amounts of racemization,[5,6] and similar behavior is observed in the corresponding bicyclooctyl products derived from ring expansion in the 2-*exo*-norbornylcarbinyl system (**28**).[4] The optically active nonclassical cation **31** formed by bond delocalization in the "twisted" species **32** is expected to suffer the same partial symmetrization as the (presumably identical) cation generated by other means. At present, the favored mechanism for most of the symmetrization that competes with solvent capture of cations derived from **28**, **29**, and **30** involves "leakage" of nonclassical ion **31** to classical ion **33**.[4,5,14] In solvolyses of optically active **29** and **30**, there is additional racemization which occurs at the ion-pair stage.[5]

In the case of 2-bicyclo[2.2.2]octyl substrate **29**, a small amount of racemization also may stem from a competing solvolysis to the classical 2-bicyclo[2.2.2]octyl cation.[5] These types of symmetrization have no direct counterparts in the ring-expansion route. It follows that no accurate value is available for how much "leakage" to expect of cation **31** itself. As rough guides, we might use the values for deuterium distribution in the *exo*-2-bicyclo[3.2.1]octyl product of the already mentioned solvolyses of bicyclo[2.2.2]oct-2-yl *p*-bromobenzenesulfonate **15**-OBs-*syn*-5,6-d_2. The data of Table V show that in acetic acid solvent, 51% of the 2-bicyclo[3.2.1]octyl product is formed by net migration of the *anti* bridge and 49% by net symmetrization (this is indistinguishable from 76% *anti* and 24% *syn* migration). The result in formic acid is 58% *anti* migration and 42% symmetrization. The net *anti* migration in excess of symmetrization would correspond to net retention of enantiomeric purity in solvolysis of an optically active **15**-OBs. Some data of Goering and Fickes[5] from such experiments are given in Table V along with the tracer results.



15-OBs-*syn*-5,6-d_2

Correction for "Leakage." If it is assumed that symmetrization in the solvolyses of **15**-OBs-*syn*-5,6-d_2 and in the ring expansion of **8**-OBs (*syn*) have the same cause (Scheme III), the selectivity in the ring expansion can be corrected to derive a "true" measure of what the memory effect would be were there no "leakage" of cation **31**.



8 **32** **31** **28** **29** **30** **33**

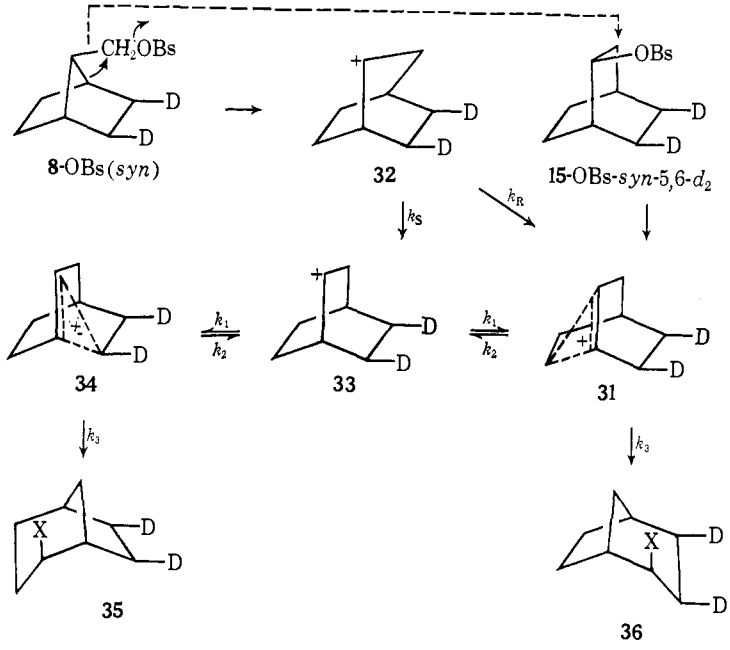
Use of the steady-state assumption with respect to the cationic intermediates of this scheme permits the expression of the ratio of 3,4-labeled (**36**) to 6,7-labeled (**35**) 2-bicyclo[3.2.1]octyl product from the ring-expansion route (starting material **8**) as in eq 1.[15] This equa-

$$(36/35)_8 - 1 = \frac{2k_3/k_2}{(k_S/k_R)[1 + (k_3/k_2)] + 1} = b \quad (1)$$

(14) Part of the racemization may occur by transannular shift.[13] One possible mechanism not previously ruled out is vicinal (C-3–C-2) hydride shift in **31**, but it now seems unlikely that this can be a major contributor, since solvolyses of 1-methyl-3-bicyclo[2.2.2]octyl derivatives give no more than 1% of products derived from 1-methyl-2-bicyclo[2.2.2]octyl cation.[10c] Racemization by reversible deprotonation of the carbonium ion intermediates to either or both of the symmetrical hydrocarbons, bicyclo[2.2.2]oct-2-ene or tricyclo[3.2.1.$0^{2,7}$]octane, is ruled out by the observation that acetolysis of bicyclo[2.2.2]oct-2-yl *p*-bromobenzenesulfonate in acetic acid-O-*d* gives bicyclo[2.2.2]- and -[3.2.1]oct-2-*exo*-yl acetates without incorporation of deuterium.

(15) Capture of cation **33** by solvent in Scheme III is assumed to be negligible in the present sense. There is firm experimental support for this view.[5]

Scheme III



tion can be rearranged to give an expression (eq 2) for the

$$k_R/k_S = \frac{b[(k_3/k_2) + 1]}{(2k_3/k_2) - b} \qquad (2)$$

ratio k_R/k_S, which measures the competition between stereospecific migration and symmetrization in the "twisted" cation **32**. In eq 2, the term b is known from the experimental product ratio (eq 1) in the ring expansion of **8**-OBs-*syn*-2,3-d_2, and the term $2k_3/k_2$, the competition ratio for solvent capture *vs.* "leakage" of the nonclassical ions **31** and **34**, can be evaluated from the experimental product ratio (Table V) in solvolysis of bicyclo[2.2.2]oct-2-yl substrate, **15**-OBs-*syn*-5,6-d_2 (eq 3).[16]

$$2k_3/k_2 = (\mathbf{36}/\mathbf{35})_{15} - 1 \qquad (3)$$

Application of eq 2 and 3 to the data gives values, corrected for leakage, of 1.4 in acetic acid and 2.8 in formic acid for the competition ratio k_R/k_S between rearrangement and symmetrization of the twisted cations at 100°.

The correction for "leakage" given here is very sensitive to experimental error and moreover probably is not strictly accurate for reasons already stated. At first glance, it would appear that perhaps a closer approach to the desired correction could be achieved by entering the cation scheme through solvolysis of *exo*-2-bicyclo[3.2.1]octyl *p*-bromobenzenesulfonate, **35**-OBs, since in this way one might hope to obviate any racemization associated with ionization of the bicyclo[2.2.2]octyl substrate (**15**-OBs) directly to classical ion **33**. However, the well-known fast interconversion of these two substrates by ion-pair return[5] would largely negate the supposed advantage.

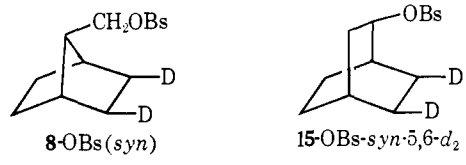
(16) As Table III shows, there is a small temperature effect in the ring expansions of **8**-OBs-*syn*-2,3-d_2, which changes b (eq 1) from an average value of 0.5 at 120° to 0.95 at 100°. A similar increase in selectivity with declining temperature is noted in the solvolyses of the bicyclo[2.2.2]oct-2-yl system (Table V), where acetolysis of **15**-OBs-5,6-d_2 at 120° gives a value for $2k_3/k_2$ (eq 3) of 2.0, while acetolysis of optically active **15**-OBs at 50° gives $2k_3/k_2 = 3.4$. If we assume that the deuterium-labeling and optical activity experiments with **15**-OBs measure the same processes (Scheme III), and that the temperature effect is roughly linear, an approximate value of 2.3 for $2k_3/k_2$ can be calculated for acetolysis at 100°.

The efficiency with which memory is preserved, which is measured by the ratio k_R/k_S, is derived on the assumption (Scheme III) that bond rearrangement (**32** → **31**) is completely stereospecific. To the extent that some direct trapping in the opposite stereochemical sense (**32** → **34**) occurs, the calculation overemphasizes the importance of the symmetrization path (**32** → **33**).

Although these uncertainties preclude a quantitative evaluation of the "true" selectivity, they do not obscure the existence of the memory effect. The selectivities of Table III are minimum measures of the "true" values.

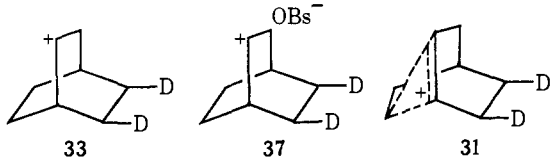
Ring Expansion by Two Competitive Rearrangements or One Bifurcated One? The observed memory effects in the bond-migration steps are interpreted in Scheme III as the result of a branching point in the mechanism, "twisted" cation **32**. In an alternative scheme, the memory effects might be accounted for by an earlier branching point, namely the starting substrate **8**. Such a scheme would involve competition between two or more parallel paths of ring expansion, one leading directly to symmetrical 2-bicyclo[2.2.2]octyl ion **33** and the other to doubly rearranged 2-bicyclo[3.2.1][2.2.2]octyl ion **31** (or to **31** and some combination of its isotope-position isomer **34** and symmetrical ion **33**). A full discussion of such alternatives is deferred,[17] but it is already clear that they cannot provide a generally satisfactory rationale for all the memory effects.[4,17]

Possible Origins of the Memory Effect. Tables III and V show that formolysis and acetolysis of the 7-norbornylcarbinyl substrate **8**-OBs-*syn*-2,3-d_2 do not proceed exclusively by stereospecific ion-pair return (dashed line, Scheme III) to the once-rearranged 2-bi-



(17) A brief outline of part of the argument has been given.[2b] Further details will be available in forthcoming papers of this series with J. Foley, J. M. McKenna, and H. Junge.

cyclo[2.2.2]octyl isomer **15**-OBs-*syn*-5,6-d_2, since the selectivity, as measured by the ratio of 3,4-labeled to 6,7-labeled *exo*-2-bicyclo[3.2.1]octyl products (**36**/**35**), is *higher* in both solvents from the alleged intermediate, **15**-OBs-*syn*-5,6-d_2, than from the starting material, **8**-OBs (*syn*). It follows that solvolytic ring expansion of **8**-OBs (*syn*) traverses some extra intermediate capable of symmetrization. Although this might be formulated as a ion pair, with an intrinsically symmetrical 2-bicyclo-[2.2.2]octyl cation rendered unsymmetrical by the counterion (**37**), there is again difficulty in reconciling



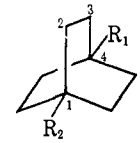
33 **37** **31**

this with the data of Table III. The large increase in the ionizing power of the solvent that is entailed by a shift from acetic acid to formic acid evokes a small *increase* in the memory effect selectivities, which can be interpreted (as above) as an approximately twofold increase in k_R/k_S. If the memory effect were simply due to a competition between memory-preserving processes like stereospecific rearrangement of **37** to **31** (either directly or after return to covalent **15**-OBs) on one hand and memory-destroying symmetrization by dissociation of **37** to separate ions (OBs^- and **33**) on the other, a substantial *decrease* in the ratio of rearrangement to symmetrization (k_R/k_S) should result from a change to a more highly ionizing solvent. Arguments similar to those given in a discussion of the ring expansions of the unsaturated analogs[3] can be invoked to oppose variants of the ion-pair rationalization. With the exception of the deaminations conducted in aqueous acetic acid, which show higher selectivities than the other ring expansions, the data of Table III are noteworthy for how little effect variations of environmental factors cause.

Similarly, there is no significant effect of added salt on the selectivities in aqueous acetic acid deamination, a result in accord with the previous finding[3] from similar experiments in the unsaturated series. For reasons already given,[3] this argues against an asymmetric ion atmosphere explanation of the memory effect.

In an experiment to test the possibility that symmetrization might be a diffusion-controlled process involving readjustments of solvent networks in the vicinity of the cations, solvolysis of **8**-OBs (*syn*) is conducted in a medium of acetic acid containing enough polyvinyl acetate to cause a 15-fold increase in viscosity as compared to that of pure acetic acid. Although a slight increase in selectivity in the viscous solvent is observed (Table III), it is barely more than the experimental error and suggests that any contributions to the memory effect by slow solvent readjustments probably involve only the immediate vicinity of the cation and are not associated with long-range diffusion through the bulk of the medium. As in the case of the ring expansions in the unsaturated series,[3] there does not seem to be an obvious interpretation of the memory effects in terms of extramolecular processes.

Among the conceivable intramolecular interpretations of memory effects, the simplest would involve the use of the "twisted" 2-bicyclo[2.2.2]octyl cation structure (heretofore merely a convenient symbolism) to represent a true conformational energy minimum. What is known of the geometry of the bicyclo[2.2.2]octane ring system does not encourage the idea of a deep minimum at the twisted conformation. Recent X-ray crystallographic analyses of the 1-*p*-bromobenzenesulfonoxymethyl derivative and the 1,4-dicarboxylic acid **38**[18a] and **39**[18b] indicate projected angles between the C-1–C-2

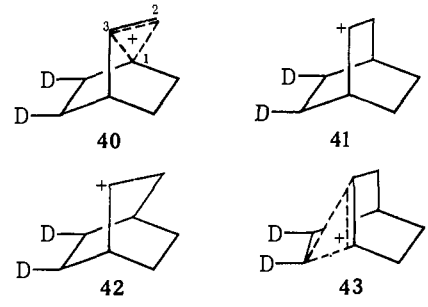


38, $R_1 = H$; $R_2 = CH_2OBs$
39, $R_1 = R_2 = CO_2H$

and C-4–C-3 bonds of 3° in the case of **38** and 0° in the case of **39**. These results are compatible with a nearly or exactly eclipsed structure. Of course, these derivatives may not be good models for the classical 2-bicyclo-[2.2.2]octyl cation, and there is the usual possibility that crystal lattice forces may influence the conformation in the solid phase. However, the results suggest that the cation, even if slightly twisted, probably is separated by at most a small barrier from the enantiomeric twisted form or from the symmetrical one.

The effect of replacement of one tetrahedral carbon atom by a trigonal one on the conformational mobility of the bicyclo[2.2.2]octane ring system is not obviously predictable, but it seems unlikely that the barrier should be appreciably raised. The closest analogy we are aware of is the cyclohexane system, where the conformational barrier to chair-to-boat isomerization in the hydrocarbon (11 kcal/mol[19a]) is actually *lowered* to 4.9 kcal/mol[19b] in the radical.

Nonclassical bonding is one way of stabilizing the first-formed unsymmetrical intermediate. Such a cation (**40**), the symmetrical classical 2-bicyclo[2.2.2]octyl cation (**41**), and the conformationally twisted cation (**42**) would differ from each other in subtle but distinct senses. The symmetrical and twisted cations **41** and **42** would have normal bond lengths, and the nonclassical one would involve partial (and therefore, presumably abnormally long) bonds between the bridging C-1 and the ends of the nonclassical bridge, C-2 and C-3. The specificity of migration of the bridge *anti* to the



40 **41**

42 **43**

site of initiation of the rearrangement in either **40** or **42** is to be expected on the stereoelectronic grounds already discussed for the unsaturated cases.[3] The major difference between the formulations **40** and **42** for the

(18) (a) A. F. Cameron, G. Ferguson, and D. G. Morris, *Chem. Commun.*, 316 (1968); (b) O. Ermer and J. D. Dunitz, *ibid.*, 567 (1968).
(19) (a) F. R. Jensen, D. S. Noyce, C. H. Sederholm, and A. J. Berlin, *J. Am. Chem. Soc.*, **84**, 386 (1962), and references cited therein; (b) S. Ogawa and R. W. Fessenden, *J. Chem. Phys.*, **41**, 999 (1964).

first-formed ions is that the nonclassical bonding in **40** would provide self-evident grounds for the postulate of an energy barrier to symmetrization. If twisted cation **42** really represents at best a shallow minimum in the conformational potential energy curve, the follow-up rearrangement step would have to be exceedingly fast to compete with symmetrization.

Studies[20,21] of the rates of solvolysis of 7-norbornylcarbinyl derivatives give no more than a hint of the pronounced anchimeric assistance that would be expected if a strongly stabilized nonclassical intermediate were formed in the rate-determining step. Moreover, only small amounts of "extra" 2-bicyclo[2.2.2]octyl product are formed, which suggests that any first-formed nonclassical ion (*e.g.*, **40**) is much less stable than the 2-bicyclo[3.2.1][2.2.2] ion **43**, the major product-forming cation of the ring expansion.

Conclusions. The ring-expansion route from 7-norbornylcarbinyl derivatives to 2-bicyclo[2.2.2][3.2.1]-octyl cations produces as the first-formed intermediate an unsymmetrical ion. This species is not identical with either the classical 2-bicyclo[2.2.2]octyl cation or the nonclassical ion of the 2-bicyclo[2.2.2][3.2.1]octyl series. Conversion to the latter ion in the second rearrangement step competes with symmetrization of the first-formed intermediate; it is this competition which leads to a memory effect. Qualitatively, the results parallel those observed in other ring expansions[3,4,12] and permit the conclusion that such memory effects are a characteristic feature of this mode of generation of many bridged bicyclic cations. The memory effect provides an intramolecular carbonium ion rearrangement as a calibrating rate process with which to compare the rate of symmetrization of the first-formed intermediate.

The weight of evidence so far favors an intramolecular cause of the unsymmetrical nature of this memory-preserving species, but regardless of whether this is correct or even whether the cause is the same in each case, the detection of such fleeting intermediates establishes the memory effect as an exceedingly sensitive probe for small, hitherto undetectable, minima in the energy surface of carbonium ion reactions.

Experimental Section

Routine procedures for purification of solvents, standard reactions, and vpc analyses follow those previously described.[3] The vpc columns used are designated by the same code.[3] Falling drop analyses for deuterium were performed by Mr. J. Nemeth, Urbana, Ill. Deuterium contents on *p*-bromobenzenesulfonates were determined directly and checked occasionally against that of precursor alcohols. Deuterium contents of amine reactants were taken to be the same as those of the precursor phthalimides, which were directly analyzed. Microanalyses were by Spang Microanalytical Laboratory or by Micro-Tech Laboratory, Skokie, Ill. Mass spectra were recorded with a Consolidated Electrodynamics Model 21-103C instrument.

Acetic acid-O-*d* was prepared by the reaction of equivalent amounts of freshly distilled acetic anhydride and deuterium oxide (>99.5% isotopic purity). Distillation gave acetic acid-O-*d* *ca.* 94–97% isotopically pure. Methanol-O-*d*, 90–96% isotopically pure, was prepared by the procedure of Streitwieser, *et al.*[22]

Norborn-2-*exo*-ol-*syn*-7-carboxylic acid was prepared by a modification of the method of Beckmann and Geiger.[10d] To 2800 ml of stirred, precooled (15°) 75% sulfuric acid–25% water (v/v) was added dropwise (during 30 min) 280 g of norborn-5-ene-2-carboxylic acid while the temperature of the reaction mixture was kept below 25°. After an additional 3.5 hr at 25°, the solution was poured in three equal portions onto 4.5 l. of ice–water, and each portion was continuously extracted with ether for 40 hr. After having been washed with sodium bicarbonate solution, the ether extracts were concentrated to a reddish brown mixture of oil and solid, which was stirred at 85° for 1.8 hr with 800 ml of 4 *M* sodium hydroxide. The solution was cooled and brought to pH 2 with cold 4 *M* sulfuric acid while the temperature was kept below 25°. The mixture was immediately made basic with solid sodium bicarbonate and extracted continuously with ether for 16 hr. The bicarbonate solution was made acidic to pH 2 with cold 4 *M* sulfuric acid, while the temperature was kept below 25°, and the solid that precipitated was filtered off. The filtrate was continuously extracted with ether for 4 hr, and after the ether extract had been dried over sodium sulfate, it was evaporated. The residue was combined with the previous solid material and the whole recrystallized from acetone to give 28 g (8.8%) of the hydroxy acid: mp 151–152° (lit.[10d] mp 155–156°); ir (KBr) 3.0 (alcohol OH), 3.0–4.0 (acid OH), 5.93 (acid C=O), 8.30, 9.25, 9.62, 10.25, and 14.20 μ; nmr ($CDCl_3$) δ 6.36 (s, 2, CO_2H and O*H*), 3.8 (m, 1, α to OH), 2.52 (complex, 3), and 2.0–1.0 ppm (complex, 6).

***syn*-7-Carboxynorbornan-2-one.** To a 5-l. erlenmeyer flask was added 32.2 g (0.206 mol) of *syn*-7-carboxybicyclo[2.2.1]heptan-*exo*-2-ol, 25 g of sodium sulfate, and 42. l. of acetone, and this solution was cooled to 0°. To the rapidly swirled solution was added 58.5 ml (0.181 mol) of Jones reagent in ten portions over a 3.5-min period. The solution then was swirled for an additional 4.5 min and the excess Jones reagent was quenched with ethanol. The green mixture was filtered using a Büchner funnel with Filter Cel. The filtrate was shaken with Norit, then filtered through a fritted-glass funnel using Filter Cel. The acetone was stripped from the clear, colorless solution on a rotary evaporator, giving a liquid with a small amount of green solid present. Ether was added to this mixture, and the green material was removed by washing with water and saturated brine. The ether solution was dried (Na_2SO_4), and the ether removed on a rotary evaporator giving a solid which upon recrystallization from acetone gave 24 g (75%) of the desired ketonic acid: mp 120–124° (lit.[10d] mp 122–123°); ir (KBr) 2.8–4.2 (broad, acid OH), 5.71 (ketone C=O), 5.90 (acid C=O), 7.71, 8.01, 8.10, 8.22, 10.6–10.9 (broad), 11.40, 12.57, and 13.80 μ; nmr (hexadeuteriodimethyl sulfoxide) δ 12.7–12.0 (broad, 1, CO_2H), 2.75 (broad singlet, 2), 2.53 (complex, 1), 2.2–1.2 ppm (complex, 6). The semicarbazone derivative had mp 217–219° (lit.[10d] mp 218–220°).

3-Bromo-*syn*-7-carboxynorbornan-2-one. To a 3-l. three-necked flask previously flushed with nitrogen and wrapped in aluminum foil to exclude light was added 77.2 g (0.50 mol) of *syn*-7-carboxynorbornan-2-one (**102**) in 1220 ml of chloroform. The system was kept under nitrogen while 88.8 g (0.553 mol) of bromine in 250 ml of chloroform was added dropwise to the stirred solution over a 30-min period, while simultaneously for the first 20 min hydrogen chloride gas was passed over the solution. Stirring was continued at room temperature for 3 hr after the addition was completed, then the solid which formed was filtered off and washed four times with chloroform. Recrystallization from acetone gave 69 g (59%) of the product: mp 203.5–205.5°; ir (KBr) 2.8–4.2 (broad, acid OH), 5.70 (ketone C=O), 5.87 (acid C=O), 7.70, 7.78, 7.99, 8.19, 9.14, 10.92, 12.61, and 13.87 μ; nmr (hexadeuteriodimethyl sulfoxide) δ 11.3–9.7 (broad, 1 CO_2H), 4.25 (d, 1, J = 2 Hz, α to Br), 3.1–2.7 (complex, 3, bridgehead 1,4 protons and α to CO_2H), and 2.2–1.0 ppm (complex, 4, methylene protons).

Anal. Calcd for $C_8H_9O_3Br$: C, 41.22; H, 3.89; Br, 34.29. Found: C, 41.13; H, 3.86; Br, 34.25.

3-Bromo-*syn*-7-carbomethoxynorbornan-2-one. An ether solution of diazomethane was added by pipet to a stirred solution of 28.5 g of 3-bromo-*syn*-7-carboxynorbornan-2-one until the yellow color persisted. The solution was allowed to stir overnight. Removal of the ether and recrystallization from methanol gave 27.1 g (90%) of the white, crystalline product: mp 74–75.5°; ir ($CHCl_3$) 5.69 (ketone C=O), 5.79 (ester C=O), 7.00, 7.76, 8.3 (broad), 9.2, and 9.8 μ; nmr ($CDCl_3$) δ 3.84 (d, 1, J = 2 Hz, α to Br), 3.69 (s, 3, CO_2CH_3), 3.25–2.80 (complex, 3, to CO_2CH_3 and bridgehead 1,4 protons), and 2.3–1.4 ppm (complex, 4, methylene protons).

2-Bromo-3-hydroxynorbornane-*syn*-7-carbinol. To a stirred suspension of 8.0 g (0.211 mol) of lithium aluminum hydride in 600 ml of anhydrous ether under a nitrogen atmosphere at 5° was added 14.6 g (0.059 mol) of the above bromoketonic ester in 450 ml of anhydrous ether dropwise over a 1-hr period. The solution was

(20) R. K. Bly and R. S. Bly, *J. Org. Chem.*, **31**, 1577 (1966).
(21) J. A. Berson, D. S. Donald, and W. J. Libbey, *J. Am. Chem. Soc.*, **91**, 5580 (1969).
(22) A. Streitwieser, Jr., L. Verbit, and P. Stang, *J. Org. Chem.*, **29**, 3706 (1964).

stirred an additional 3.3 hr at 0° maintaining a nitrogen atmosphere at all times. The reaction mixture was worked up using the standard procedure employing a saturated sodium sulfate solution. The ether was removed, giving 12.7 g (97%) of the white, solid product: mp 100–103°; ir ($CHCl_3$) 2.84 (OH), 8.38, 9.48, 10.00, 10.26, 10.47, and 11.62 μ; nmr ($CDCl_3$) δ 4.2–3.75 (complex, 4, α to the two hydroxyls and α to Br), 2.7–2.35 (complex including sharp singlet at 2.47, 4, two O*H* and bridgehead 1.4 protons), 2.2–1.0 (complex, 5, methylenes and α to CH_2OH).

Anal. Calcd for $C_8H_{13}O_2Br$: C, 43.46; H, 5.92; Br, 36.15. Found: C, 43.28; H, 5.81; Br, 36.15.

***syn*-7-Hydroxymethylnorbornene (20-OH).** A mixture of 33.4 g of 2-bromo-3-hydroxynorbornane-*syn*-7-carbinol, 33.4 g of zinc powder, 334 ml of ethanol, and 66.8 ml of glacial acetic acid was heated at reflux under nitrogen for 19.5 hr. The zinc was then filtered off and most of the ethanol removed by distillation. To the remaining colorless, clear liquid, was added 600 ml of 2.7 *M* sodium hydroxide solution, giving a white precipitate. This mixture was heated at reflux with stirring for 2.75 hr, then cooled and extracted five times with 200-ml portions of ether. The ether solution was washed once with saturated brine and dried (Na_2SO_4). The majority of the ether was removed by distillation through a Vigreux column. A short-path vacuum distillation then gave 15.58 g (82.4%) of the desired alcohol, which distilled at 95–98° (15 mm). Vpc analysis on column B at 117° showed only one peak. The ir and nmr spectra matched those reported.[20] On one occasion, a contaminant, apparently 3-oxatricyclo[4.3.0^{1,6}0^{4,9}]nonane, was found.

7-Norbornylcarbinol. A solution of 1.45 g (0.0116 mol) of *anti*-2-norbornene-7-carbinol (**19**) in 50 ml of methanol was hydrogenated over 250 mg of Pt catalyst under 40 lbs pressure. The uptake of hydrogen was rapid and 1 molar equiv of the gas was absorbed. The shaking was continued for about 1 hr after the gauge reading had become constant. The catalyst was carefully filtered out and the solvent evaporated with a Vigreux column. The crude product was distilled at 11 mm and 70–110° to give 1.20 g of a colorless liquid (81.4% yield): ir (neat) strong band at 3.0 μ, no absorptions between 3.24 and 3.28 or 13.90 and 14.05 μ; nmr δ 3.46, methylene doublet (J = 8 cps, 2 H), 3.06 sharp singlet (OH proton, 1 H), 0.94–2.19 complex multiplet (11 H).

Anal. Calcd for $C_8H_{14}O$: C, 76.19; H, 11.11. Found: C, 76.15; H, 11.15.

The alcohol was found homogeneous by vpc (column B).

7-Norbornylcarbinyl *p*-bromobenzenesulfonate, prepared by the standard procedure, had mp 89.5–90.3° (from methanol).

Anal. Calcd for $C_{14}H_{17}O_3SBr$: C, 48.72; H, 4.96; S, 9.28; Br, 23.15. Found: C, 48.43; H, 5.16; S, 9.25; Br, 22.95.

Preparation of Dipotassium Azodicarboxylate. After cooling 3.1 l. of 40% potassium hydroxide by weight aqueous solution to below 5°, 500 g of azodicarbonamide (Aldrich Chemical Co.) was added to the solution in small portions with stirring over a 1.75-hr period. The temperature was kept below 8° during the addition. After being stirred an additional 5 hr, the bright yellow dipotassium azodicarboxylate was filtered off using a Büchner funnel, and the solid was then washed 20 times with a total of 2 gallons of methanol, precooled to 0°, in order to wash out the potassium hydroxide. The solid was freed of residual methanol on a rotary evaporator, and since the compound was to be used for a deuterium reduction, 25 ml of methanol-O-*d* was added and the flask, fitted with a calcium sulfate drying tube, was allowed to stand overnight in a refrigerator. The methanol-O-*d* was removed on a rotary evaporator. The solid was dried at 0.5 mm for 24 hr over phosphorus pentoxide and stored in a desiccator over $CaSO_4$. It should be noted that the 24-hr vacuum drying period is apparently necessary; on two occasions when the vacuum drying periods were only 2 and 5.5 hr, respectively, the dipotassium azodicarboxylate decomposed to a white solid within a few days. Fortunately the decomposition was not a detonation, but there was the danger of the storage vessel exploding if no pressure release mechanism was available.

2,3-Dideuterio-*syn*-7-norbornylcarbinol (8-OH (*syn*)). To a 5-l, three-necked flask fitted with a dropping funnel and two condensers in series was added 14.6 g (0.117 mol) of *syn*-7-hydroxymethylnorbornene (**20-OH**), *ca.* 1.3 kg (7.65 mol) of dipotassium azodicarboxylate, and *ca.* 1.5 l. of methanol-O-*d* (90% O-*d*). The system was kept under a nitrogen atmosphere. The slurry was stirred very rapidly with a mechanical stirrer while *ca.* 650 ml of glacial acetic acid-O-*d* (94% O-*d*) was added dropwise over a 1.7-hr period. Vigorous gas evolution was noted and the contents of the flask rapidly became warm, accompanied by reflux of the methanol-O-*d*. The acetic acid-O-*d* was added at a rate necessary to maintain reflux. The yellow color was discharged upon addition of *ca.* 450 ml of the acetic acid-O-*d* and copious amounts of a white solid had formed, but an additional 200 ml was added since gas evolution continued although the temperature dropped. The solution was stirred an additional 5.5 hr, then *ca.* 700 ml of methanol-O-*d* was distilled off with considerable gas evolution accompanying the first half of the distillation. The solution was cooled and 800 ml of water was added, dissolving the solid and giving a light yellow, cloudy liquid. The aqueous solution was extracted ten times with 500-ml portions of pentane, then the pentane extracts were washed twice with 200 ml of 1 *M* sodium bicarbonate solution (second wash was basic) and dried (Na_2SO_4). Removal of the pentane on a rotary evaporator gave a yellow liquid. This liquid was distilled through a tantalum wire column, and 11.88 g (79%) of a colorless liquid which distilled at *ca.* 100° at 25 mm was collected. Vpc analysis on column B at 117° showed only one peak with no starting material remaining.

This procedure normally gives *ca.* 10–15% unreacted starting material. The method of choice for separating the two compounds in that event is to wash out the unsaturated compound using aqueous silver nitrate solution. As an example of the procedure to be followed, in one case of a poor reduction, *ca.* 4.9 g of alcohols which contained 23% unreduced alcohol were obtained. The alcohols were dissolved in 50 ml of pentane and the pentane solution was washed 20 times with 10-ml portions of a 30% aqueous silver nitrate solution, once with 3 ml of water, once with saturated brine, and dried (Na_2SO_4). Removal of the pentane gave 3.35 g of a cloudy, colorless liquid, and vpc analysis on column B at 118° showed that <1% of unsaturated alcohol was present. Distillation gave 3.06 g of the clear, colorless alcohol, which represents a recovery of 81% of the original amount of saturated alcohol present after reduction. Alternatively the alcohols can be separated by vpc using column R.

2,3-Dideuterio-*anti*-7-norbornylcarbinol (5-OH (*anti*)) was prepared in a similar manner from the *anti*-unsaturated carbinol **19-OH**.

2,3-Dideuterionorbornyl-*syn*- and -*anti*-7-carbinyl *p*-bromobenzenesulfonates (8-OBs and 5-OBs) prepared from the corresponding alcohols in the usual manner, had mp 90–92°.

7-Norbornylcarbinyl Bromide. A solution of 630 mg (1.83 mmol) of norbornyl-7-carbinyl *p*-bromobenzenesulfonate and 392 mg (3.30 mmol) of potassium bromide in 11.7 ml of dimethylformamide was heated at 60° under nitrogen with stirring for 12 hr and then was cooled and diluted with 20 ml of water. The solution was extracted four times with 9-ml portions of ether, washed twice with water and once with saturated brine, and dried (Na_2SO_4).

The ether was distilled through a Vigreux column, leaving 350 mg of a slightly yellow liquid. Vpc analysis on column A at 112° showed one major peak and two minor contaminants totaling *ca.* 1%. The products were separated on a 14 ft × 0.25 in. Carbowax column (column temperature 123°, helium flow rate 120 ml/min). The minor peak of short retention times was identified as dimethylformamide and the other minor peak at a slightly longer retention time than the major peak appeared to be 7-norbornylcarbinyl formate.

The major product was collected in 67% yield (233 mg) and was identified as 7-norbornylcarbinyl bromide: ir (neat) 6.81, 6.90, 7.71, 8.15, 8.30, 9.43, and 11.50 μ; nmr (CCl_4) δ 3.30 (d, 2, J = 8 cps, α to Br), 2.25–1.0 ppm (complex, 11).

Anal. Calcd for $C_8H_{13}Br$: C, 50.81; H, 6.93; Br, 42.26. Found: C, 51.17; H, 7.02; Br, 42.05.

N-7-Norbornylcarbinylphthalimide. To a solution of 0.5175 g (0.0015 mol) of 7-norbornylcarbinyl *p*-bromobenzenesulfonate (**40**) in 20 ml of dimethylformamide was added 207 mg (0.0015 mol) of anhydrous potassium carbonate and 441 mg (0.003 mol) of phthalimide. The reaction mixture was heated at reflux with stirring for 10 hr in a dry atmosphere. It was cooled and diluted with 40 ml of ice-cold water. The stirring was continued for additional 0.5 hr. The white solid was filtered under aspirator vacuum and washed several times with water. After having been dried in air, the solid was taken up in ether and the ether solution was washed with a 2% aqueous solution of potassium hydroxide. Subsequent washings were given with 1 *N* HCl and brine. The organic extract was dried over anhydrous sodium sulfate and the solvent removed in a rotary evaporator under vacuum. The crude white material on recrystallization from methanol gave colorless, crystalline 7-phthalimidomethylnorbornane (**51**): mp 90–90.5°; 85% yield; ir ($CHCl_3$) 1773, 1715 cm^{-1}; nmr δ 7.71 (d, J = 3 cps, 4 H, aromatic), 3.56 (d, J = 8 cps, 2 H, CH_2N), 0.85–2.13 (m, 11 H, aliphatic); mass spectrum significant

peaks at *m/e* 255, 227, 226, 186, 161, 160, 148, 108, 105, 104, 95, 93, 80, 79, 78, 77, 76, 67, 65, 64, 55, 54, 53, 52, 51, 50.

Anal. Calcd for $C_{16}H_{17}NO_2$: C, 75.29; H, 6.66; N, 5.49. Found: C, 75.28; H, 6.61; N, 5.46.

2,3-Dideuterio-N-norbornyl-*syn*-7-carbinylphthalimide (**8-NC$_2$O$_2$C$_6$H$_4$**) was prepared in the same manner from the deuterated *p*-bromobenzenesulfonate **8-OBs** (*syn*). It had mp 90.5–92°. The *anti* isomer was prepared from **5-OBs** (*anti*) and had the same melting point. A mass spectrum of the *anti* isomer showed the following composition: d_0, 7.9%; d_1, 38.1%; d_2, 54.0%; d_3, 0.0%. This corresponds to 1.461 D/molecule. A falling drop analysis on this material showed 8.32 atom % excess, or 1.414 D/molecule.

2,3-Dideuterionorbornyl-*syn*-7-carbinylamine (**8-NH$_2$** (*syn*)), the *anti* isomer **5-NH$_2$**, and the undeuterated analog were prepared by alkaline hydrolysis of the phthalimide precursors. A typical procedure follows. A solution of 5.45 g (0.0202 mmol) of 2,3-dideuterio-*syn*-7-phthalimidomethylnorbornane and 43 g (1.07 mmol) of sodium hydroxide in 109 ml of methanol and 35.8 ml of water was heated to reflux under nitrogen with stirring. After 72 hr the solution was cooled while nitrogen was bled in, and diluted with 60 ml of saturated brine and 60 ml of water. The solution was extracted five times with 100-ml portions of pentane, with care being taken to keep the solutions under a nitrogen atmosphere since the amine very rapidly forms a solid amine carbonate when it comes in contact with air. The pentane extracts were washed once with saturated brine and dried (Na_2SO_4). The pentane was removed through a Vigreux column under a nitrogen atmosphere giving a yellow liquid. The liquid was distilled at 30–60° (0.5 mm) using a short-path distillation apparatus. Again care was taken to ensure that the amine did not come into contact with air. This yielded 2.41 g (95%) of the clear, colorless liquid: ir (neat) 3.0 (NH), 3.07 (NH), 4.65 (CD), 6.24, 6.84, 7.20, 7.42, 7.71, 8.44, 9.32, 11.42 (broad), 12.04 (broad), and 12.70 μ (broad). The spectrum for the nondeuterated amine has absorptions at 2.98, 3.04, 6.31, 6.86, 7.25, 7.32, 7.63, 8.32, 9.31, 11.49, 12.22, and 12.58 μ.

Solvolyses of Norbornylcarbinyl Derivatives. A typical procedure follows. A solution of 5.00 g (14.42 mmol) of 2,3-dideuterio-norbornyl-*syn*-7-carbinyl *p*-bromobenzenesulfonate (**8-OBs**, 1.576 atoms of D/molecule) and 1.30 g (15.84 mmol) of sodium acetate in 113.5 ml of glacial acetic acid was heated at 100° in a nitrogen atmosphere for 232 hr (*ca.* five half-lives[16]). The reaction mixture was cooled and treated with 200 ml of water, 50 ml of brine, and solid sodium chloride until saturated. The solution was filtered and extracted with four 100-ml portions of pentane. The pentane solution was washed with sodium bicarbonate and then with brine, dried over sodium sulfate, and concentrated by distillation of the solvent through a Vigreux column. The residue, 2.1 g (86%) of a clear, colorless oil, showed acetate absorption bands at 5.76 and 8.10 μ in the ir. The acetate mixture was dissolved in 120 ml of anhydrous ether and reduced to alcohols with lithium aluminum hydride in the usual manner.

Isolation of Products. The mixture of alcohols was subjected to vpc fractionation. In each case the requirement was to isolate bicyclo[3.2.1]octan-*exo*-2-ol and bicyclo[2.2.2]octan-2-ol, in greater than 99% purity, from a mixture containing the desired two alcohols in addition to usually a small amount of bicyclo[3.2.1]octan-*endo*-2-ol, 7-norbornylcarbinol, in some cases several per cent of the acetates of the above alcohols, and in some cases bicyclo[2.2.2]-octan-2-one. Some olefins and other minor short-retention time peaks were also normally present. The compounds emerged from the columns used in the separation in the order: olefins, other short retention time peaks such as 7-hydroxy-7-methylnorbornane **17-OH**, the acetates of the alcohols, the *exo*-[3.2.1] alcohol, the [2.2.2] alcohol, the *endo*-[3.2.1] alcohol, 7-norbornyl carbinol, and last the [2.2.2] ketone. Column Q was satisfactory for cases where no acetates were present (the acetates came off at the beginning of the *exo*-[3.2.1] alcohol peak, thereby contaminating it on this column. The retention times and separation were reasonable (*ca.* 73 min for the [3.2.1] alcohol and 81 min for the [2.2.2] alcohol) at the conditions used (column temperature 105°, helium flow rate 110 ml/min), but sample size had to be limited so that one could only collect *ca.* 1.5 mg of the [3.2.1] alcohol and 2.0 mg of the [2.2.2] alcohol on each injection. Two passes were required to obtain the alcohols in greater than 99% purity, with larger sample size possible on the second pass.

Column O-1 also was satisfactory, but it likewise could only separate small samples on each pass.

The column of choice was column D. The retention times were somewhat longer than for the above columns (110 min for the [3.2.1] alcohol and 120 min for the [2.2.2] alcohol at a column temperature of 137° and a helium flow of 120 ml/min), but considerably larger amounts could be separated on each injection. On the first pass sample size was such that *ca.* 5 mg of the [3.2.1] alcohol and 7 mg of the [2.2.2] alcohol could be separated on each injection. Again two passes were required to obtain the desired alcohols in greater than 99% purity, but total separation time was reduced considerably.

Deaminations. A typical procedure follows. 2,3-Dideuterio-norbornyl-*syn*-7-carbinylamine (**8-NH$_2$**) was prepared as previously described by basic hydrolysis of 2,3-dideuterio-*syn*-7-phthalimidomethylnorbornane which had been analyzed for deuterium content. In the falling drop deuterium analysis, atom % excess deuterium = 8.32, which corresponds to 1.403 deuteriums per molecule. Mass spectral analysis of the phthalimide gave a deuterium content of 1.396 deuteriums per molecule.

A solution of 0.853 g (6.81 mmol) of the amine **8-NH$_2$** in 4.62 ml of glacial acetic acid and 60 ml of water under a nitrogen atmosphere was treated with 0.940 g (13.61 mmol) of sodium nitrite in 4 ml of water dropwise over a 3.2-hr period at room temperature. The solution was stirred an additional 20 hr under nitrogen at room temperature, then extracted five times with 40-ml portions of pentane. The pentane extracts were washed once with 12 ml of 1 *M* sodium bicarbonate solution (wash was basic), once with saturated brine, and dried (Na_2SO_4). The pentane was distilled through a Vigreux column, leaving 600 mg (70%) of a light yellow solid. The composition of this neutral fraction is given in Table I. Unreacted amine was recovered from the aqueous layer by addition of sodium hydroxide, extraction with pentane, washing with brine, and drying over sodium sulfate. After filtration, the pentane solution was chilled to −78° and treated with dry hydrogen chloride to precipitate the amine hydrochloride. In several runs, the material balance was quantitative based on unreacted starting amine.

Products were isolated by vpc in the same manner used in the solvolyses.

In some of the deaminations (Table I), bicyclo[2.2.2]octan-2-one appeared as a minor product. It was identified by vpc retention time and also by isolation and spectroscopic comparison with an authentic sample. At least some if not all of this material must arise from oxidation of bicyclo[2.2.2]octan-2-ol under the deamination conditions. Control experiments established the occurrence of this reaction and also showed the stability of the other products.

Control Experiment. Deamination of 7-norbornylcarbinylamine in acetic acid-O-*d* (95.5% O-*d*) followed by normal work-up gave an acetate product mixture which contained 0.32 atom % excess D (0.051 atom of D/molecule).

***syn*-5,6-Dideuteriobicyclo[2.2.2]octan-*endo*-2-ol** (**15-OH-*syn*-5,6-d_2**) was prepared from bicyclo[2.2.2]oct-5-en-*endo*-2-ol (**27**)[23] by the above-described diimide reduction procedure used for the preparation of **5-OH** and **8-OH**. The *endo*-alcohol **27** was first separated from the *exo* isomer by vpc on column H and was obtained 99.5% pure (column R). The *p*-bromobenzenesulfonate, **15-OBs-*syn*-5,6-d_2**, was prepared in the usual manner. The alcohol was analyzed for deuterium content, and the deuterium content of the *p*-bromobenzenesulfonate was assumed to be the same. This assumption cannot be seriously in error, since the 2-bicyclo[2.2.2]-octyl product recovered from solvolysis has essentially the same deuterium content as the starting **15-OH-*syn*-5,6-d_2** (Table V).

Solvolyses of 15-OBs-*syn*-5,6-d_2. A 50-ml flask fitted with a reflux condenser and containing 19.08 ml of formic acid (Aldrich Chemical Co., 97+% formic acid) was heated to 101° in an oil bath. The system was kept under nitrogen throughout the reaction. A solution of 1.167 g (3.38 mmol) of **15-OBs-*syn*-5,6-d_2** (deuterium content: 1.652 deuteriums per molecule) in 2.12 ml of pyridine, with this solution at 25°, was added to the stirred formic acid. The resulting solution was stirred at 100° under nitrogen for 2 hr, and was then cooled and diluted with 80 ml of 1 *M* sodium bicarbonate solution. This solution was extracted five times with 45-ml portions of pentane, then the pentane extracts were washed once with 1 *M* sodium bicarbonate solution (wash was basic). The sodium bicarbonate solution was extracted once with pentane, and the combined pentane solutions were dried (Na_2SO_4). Removal of the solvent through a Vigreux column gave a clear liquid. The infrared spectrum had strong bands at 5.81 (formate C=O) and 8.50 μ (formate C—O), typical of formate absorptions. The vpc analysis on column B showed a small amount of olefins and two

(23) H. L. Goering, R. W. Greiner, and M. F. Sloan, *J. Am. Chem. Soc.*, **83**, 1391 (1961).

other poorly resolved peaks of approximately equal intensity. The liquid was dissolved in 30 ml of anhydrous ether and added dropwise to a stirred suspension of 0.8 g of lithium aluminum hydride in 20 ml of anhydrous ether, at room temperature under a nitrogen atmosphere. This mixture was stirred for 2 hr, then worked up by the standard saturated sodium sulfate solution procedure. Removal of the ether through a Vigreux column gave 365 mg (85.5%) of a white solid. The infrared spectrum had no carbonyl absorption and absorptions at 2.78 (OH) and 3.0 μ (OH). A vpc analysis on column B showed that 45.1% bicyclo[3.2.1]-octan-*exo*-2-ol and 53.9% bicyclo[2.2.2]octan-2-ol, plus *ca.* 1% bicyclo[3.2.1]octan-*endo*-2-ol was present. The two major alcohols were isolated by vpc on column Q in the manner already described for the norbornylcarbinyl solvolyses.

Acetolysis of **15**-OBs-*syn*-5,6-d_2 was carried out in a similar manner, the only difference being that a solution of sodium acetate in acetic acid was substituted for formic acid, and the substrate was added in acetic acid solution rather than in pyridine.

Control Experiment.[24] **Acetolysis of bicyclo[2.2.2]oct-2-yl *p*-bromobenzenesulfonate in acetic acid-O-*d*** (*ca.* 93% isotopically pure) was carried out at 100° in the same manner. The bicyclo-[3.2.1]octan-*exo*-2-ol (**16**-OH) and bicyclo[2.2.2]octan-2-ol (**15**-OH) were isolated in the usual manner and analyzed separately for deuterium. Each showed 0.00 atom % excess D.

(24) We are indebted to Dr. Dieter Wege for this experiment.

Location of the Label. Oxidation of Bicyclo[3.2.1]octan-*exo*-2-ol (16-OH) to *cis*-3-Carboxycyclopentaneacetic Acid (22). The procedure was essentially that previously reported.[12] Conversion to the *trans*-acid **24** was effected by heating with 3.58 *M* (or preferably with 1.19 *M*) hydrochloric acid at 180° in a sealed tube. The more strongly acidic conditions caused some resinification, and after a control experiment had shown the milder acid sufficient to effect complete exchange of α-hydrogens, the milder conditions were adopted as standard.

Control Experiments. Stability of Bicyclo[3.2.1]octan-*exo*-2-yl Acetate (16-OAc) to Solvolysis Conditions. The acetolysis conditions were simulated by a solution of 0.022 mmol of sodium acetate and 0.062 mmol of sodium *p*-bromobenzenesulfonate in 0.57 ml of acetic acid. Acetate (*ca.* 0.065 mmol) was added, and the mixture was heated for 72 hr at 120°. The acetate compositions in two runs were as follows: run 1—(before heating) 75% **16**-OAc, 25% **15**-OAc, (after heating) 77% **16**-OAc, 23% **15**-OAc; run 2—(before heating) 99% **16**-OAc, 1% **15**-OAc, (after heating) 99% **16**-OAc, 1% **15**-OAc.

Similarly, heating a mixture of 51.6% of **16**-OCOH, 7.1% tertiary formate **17**-OCOH, and 1.3% **15**-OCOH in formic acid–pyridine at 100° for 6 hr followed by the usual work-up gave a mixture consisting of 52.5% **17**-OCOH, 46.1% **17**-OCOH, and 1.3% **15**-OCOH.

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