ORGANIC AND BIOLOGICAL CHEMISTRY

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF SOUTHERN CALIFORNIA, LOS ANGELES 7, CALIF.]

The Ring Expansion Route to Bicyclic Carbonium Ions.
I. The Multiple Rearrangement of the *endo*-2-Norbornylcarbinyl System[1a,b]

BY JEROME A. BERSON[1c] AND P. REYNOLDS-WARNHOFF[1d]

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For geometric reasons, the ring expansions of 2-norbornylcarbinyl to 2-bicyclo[3.2.1]octyl cations are unlikely to lead directly to nonclassical species. The intervening classical stage of one of the 2-bicyclo[3.2.1]octyl cations has now been detected and its chemistry elucidated by the application of symmetry criteria (using both optical and tracer methods) to the results of the nitrosative deamination of optically active *endo*-2-norbornylcarbinylamine and the acetolysis of the corresponding *p*-bromobenzenesulfonate. When water captures the classical cation, which has a chair cyclohexane ring, attack from the *endo-equatorial* direction is favored by a rather small factor (4 or less) over that from the *exo-axial* side. Competing with these processes are two others, the more important of which is reversible transformation of the classical cation to its nonclassical counterpart. The remaining mode of disposal of the classical cation is crossover into the set of ions derived from the *exo*-2-norbornylcarbinyl system. The symmetrical nonclassical species derived from the *endo* system reverts to the classical form at a rate that is competitive with solvent attack. This contrasts with the behavior of the next lower homolog, the nonclassical 2-bicyclo[2.2.1]heptyl cation, reversion of which to classical species has a rate imperceptibly slow in comparison to solvent attack.

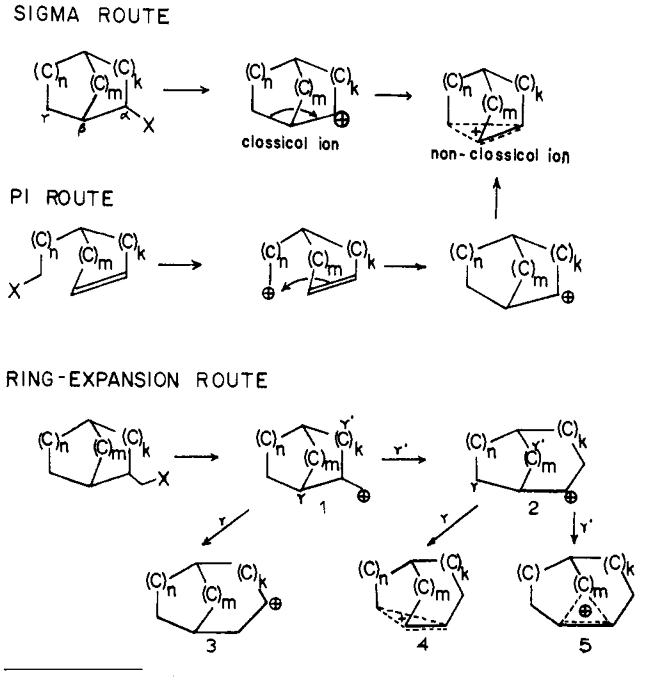
Carbonium ions derived from bridged bicyclic systems usually have been generated by the detachment of a group and its binding electron pair from an already constructed bicyclic framework; involvement of a σ-bond β-γ to the positive charge so created at C-α can occur in concert with or subsequent to the departure of the leaving group and frequently results in the familiar Wagner–Meerwein rearrangement.[2] In many cases particularly with derivatives of the norbornyl(bicyclo[2.2.1]heptyl) system, the product-forming intermediates are best formulated with nonclassical structures, *i.e.*, with three-center bonding between C-α, C-β, and C-γ[2] (Chart 1).

More recently, it has been possible to generate the same (or at least closely related) species by interaction of a π-electron system with the cationic site[2,3–6] in ring closures (Chart 1). In the examples of both the σ- and π-routes, the fragment X is a conventional leaving group such as halide or sulfonate ion or a nitrogen molecule. For completeness, the ionization and delocalization steps are shown here as distinct processes, but they frequently occur simultaneously. Regardless of the details of the act of ionization, the weight of evidence[2] in all previous cases suggests that the classical ion, when involved at all, is converted rapidly to the nonclassical ion, and that the latter, once formed, does not revert to the classical one at a rate competitive with its conversion to stable product by capture of a nucleophile. Thus, an energy barrier separates the nonclassical ion from its classical counterpart, and under conditions of irreversible product formation, the chemistry of classical ions in these systems is virtually unknown.

The present paper describes the results of a study of a third method of generating bicyclic carbonium ions, the *ring-expansion route* (Chart 1). Here the role of leaving group is played by a portion of the molecule that migrates to a new position of attachment, leaving behind an electron-deficient site at the origin of migration. As will become evident, the resulting entity is frequently a classical carbonium ion, which requires a finite time for conversion to the nonclassical ion. In the proper circumstances, generation of the cations in this way allows an inspection of the behavior of classical species. Further, the systems examined here and in the companion paper[7] manifest a hitherto unobserved phenomenon, the reversible interconversion of the classical and nonclassical forms of a bicyclic cation under conditions that do not regenerate cations from products.

In the multiple rearrangement route, there are in principle two kinds of carbon shift open to the species **1**, only one of which (involving the β–γ' bond) leads to a species (**2**) that readily can become nonclassical. The alternative migration path (involving the β–γ bond) leads to **3** and is of minor interest in the present con-

CHART 1



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(1) (a) The support of part of this work by the National Science Foundation through Grant NSF-G11386 is gratefully acknowledged. (b) For preliminary reports, see J. A. Berson and P. Reynolds-Warnhoff, *J. Am. Chem. Soc.*, **84**, 682 (1962); ref. 2, pp. 221–226; *cf.* also Abstracts of the Eighteenth National Organic Chemistry Symposium of the American Chemical Society, Columbus, Ohio, June 16–20, 1963, pp. 23–30. (c) To whom inquiries should be directed at Department of Chemistry, University of Wisconsin, 1112 W. Johnson St., Madison, Wis. (d) This paper was taken in part from the dissertation submitted by Patricia Reynolds-Warnhoff in partial fulfillment of the requirements for the Ph.D degree.

(2) For a review, see J. A. Berson in "Molecular Rearrangements," edited by P. de Mayo, Interscience Publishers, Inc., New York, N. Y., 1963, Part 1, p. 111.

(3) G. Le Ny, *Compt. rend.*, **251**, 1526 (1960).

(4) R. G. Lawton, *J. Am. Chem. Soc.*, **83**, 2399 (1961).

(5) P. D. Bartlett and S. Bank, *ibid.*, **83**, 2591 (1961).

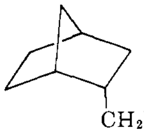
(6) S. Winstein and P. Carter, *ibid.*, **83**, 4485 (1961).

(7) J. A. Berson and D. Willner, *ibid.*, **86**, 609 (1964).

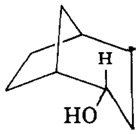
text, although its occurrence can constitute a serious nuisance in practice.[7] There is a further point at which the system is confronted with a choice—when the classical ion **2** is converted to one of the two nonclassical ions **4** or **5** by delocalization of bonds β–γ or β–γ', respectively. Both decisions are predetermined, as will be shown, by the stereochemistry of the starting system.

Ring Expansion of the *endo*-2-Norbornylcarbinyl System.—The nitrosative deamination of *endo*-2-norbornylcarbinylamine (**6a**) previously had been studied by Alder and Reubke[8a] who used as starting material a liquid amine derived by hydrogenation of an apparently homogeneous *endo*-2-cyanonorbornane.[9] The latter reaction, however, was carried out in the presence of ammonia (conditions that suppress the formation of secondary and tertiary amine by-products), and it was therefore possible that some epimerization might have occurred prior to reduction. For the present study of this system, an alternative method[10] of preparing the amine **6a** avoids this problem.

Deamination of **6a** with nitrous acid in aqueous acetic acid led[8] to an alcohol that could be oxidized to 2-bicyclo[3.2.1]octanone (**9**) and was therefore one of the epimers of 2-bicyclo[3.2.1]octanol (**7** or **8**) or possibly a mixture of both.[8] Subsequently, a repetition of the deamination[11] and infrared examination of the product showed both epimers to be present in the ratio of 9:1, the major product being the *endo-equatorial* isomer **7**.[12] Since, however, the amine **6a** used[11] apparently was prepared by Alder's method,[9] and since the *exo-axial* product **8** is formed in substantial amounts from the epimeric *exo*-norbornylcarbinylamine,[7] it was still not clear whether the small amount of **8** observed[11] was an authentic product from **6a** or an artifact arising from contamination of the starting material with *exo*-norbornylcarbinylamine.



6a, X = NH$_2$
b, X = OH
c, X = OBs



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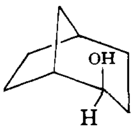

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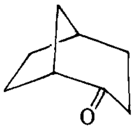

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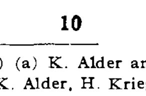
Deamination of our epimerically homogeneous **6a** leads to a high yield of a mixture of products. Preliminary examination of this mixture by vapor chromatography on a 2 m. × 7 mm. column packed with tri-β-(cyanoethoxy)-propane (TCEP) on firebrick shows the presence of small amounts (7.5%) of materials with low retention times (presumably hydrocarbons) and 92.5% of a mixture of alcohols. The alcohol fraction shows two partially overlapping peaks in the approximate proportions 90–92:8–10. After testing the efficacy of a large number of other stationary phases in a fruitless attempt to improve the analytical resolution, we find that vapor chromatography with a TCEP-coated 50-m. capillary column cleanly resolves the alcohol fraction into four distinct peaks which correspond in retention time to *endo-equatorial* alcohol **7** (83%), *exo-axial* alcohol **8** (9%), 2-bicyclo[2.2.2]octanol (**10**) (7%), and the *meso*-alcohol 3-bicyclo[3.2.1]octanol (**11**) (1%). The first three products **7**, **8**, and **10** are formed in amounts much too large to have resulted from contamination of the starting *endo*-amine **6a** with its epimer; the maximum limit of such contamination (see Experimental) and the yield of these materials from the alleged contaminant under the same conditions of deamination[7] are known and do not allow more than a small fraction of the product mixture to have been formed in this way. Products **7**, **8**, and **10** are therefore authentic results of the deamination of *endo*-amine **6a**. We are less certain that the trace of *meso*-alcohol **11** observed is truly derived from **6a**; accordingly, 1% may be taken as an upper limit for the amount of 11 formed from **6a**. We have no information at present on the epimeric configuration of **11**, and it is not impossible that, despite its apparent homogeneity by vapor chromatographic and other criteria,[7] it may be a mixture of both possible epimers. The alcohol **6b** with the skeleton of the starting material is not among the products.



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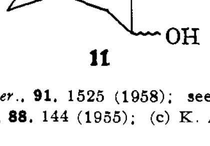

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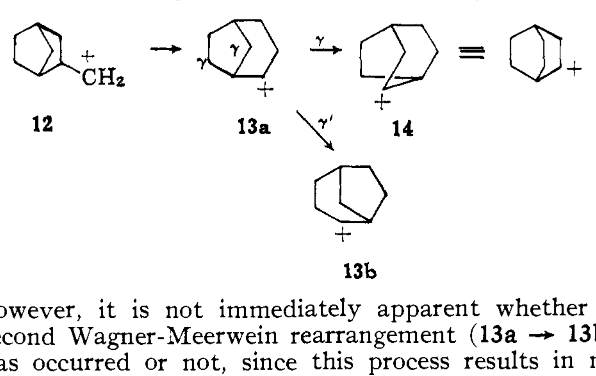
That all of the above products are kinetically controlled and do not result from equilibration subsequent to their formation in other proportions is evident from appropriate control experiments reported in the literature[14] and from confirmatory findings (see below) in acetolysis.

Acetolysis of the corresponding *p*-bromobenzenesulfonate **6c** results in a mixture of acetates, the proportions being similar to but not identical with those observed in deamination: 77% of **7**, 12.5% of **8**, 10.5% of **10**, 0% of **11** (all with OH = OAc). These acetates constitute 92% of the total product, the remaining 8% of material being hydrocarbon.

Detailed Stereochemistry of the Rearrangement.—In a formal sense, the conversion of the norbornylcarbinyl system to the 2-bicyclo[2.2.2]octyl system is a double rearrangement, **12** → **13** → **14**, terminating in product **10** or its acetate. The second step **13** → **14** is of a familiar[14–16] type. In the case of the products **7** and **8** having the 2-bicyclo[3.2.1]octyl skeleton, however, it is not immediately apparent whether a second Wagner-Meerwein rearrangement (**13a** → **13b**) has occurred or not, since this process results in no change in structure. A simple way of discerning such a rearrangement, which formally involves merely the interconversion of an enantiomeric pair of cations, is to use optically active starting material.



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[8] (a) K. Alder and R. Reubke, *Chem. Ber.*, **91**, 1525 (1958); see also (b) K. Alder, H. Krieger, and H. Weiss, *ibid.*, **88**, 144 (1955); (c) K. Alder and E. Windemuth, *ibid.*, **71**, 2404 (1938).

[9] K. Alder, K. Heimbach, and R. Reubke, *ibid.*, **91**, 1516 (1958).

[10] (a) J. A. Berson, J. S. Walia, A. Remanick, S. Suzuki, P. Reynolds-Warnhoff, and D. Willner, *J. Am. Chem. Soc.*, **83**, 3986 (1961); (b) J. A. Berson and D. A. Ben-Efraim, *ibid.*, **81**, 4083 (1959).

[11] A. A. Youssef, M. E. Baum, and H. M. Walborsky, *ibid.*, **81**, 4709 (1959).

[12] For the assignments of configuration to the epimers **7** and **8**, see ref. 11 and 13.

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

[14] H. L. Goering and M. F. Sloan, *ibid.*, **83**, 1397 (1961).

[15] H. M. Walborsky, M. E. Baum, and A. A. Youssef, *ibid.*, **83**, 988 (1961).

[16] W. von E. Doering and M. Farber, *ibid.*, **71**, 1514 (1949); M. Farber, Dissertation, Columbia University 1949.

Optically active (−)-hydrochloride of *endo*-2-norbornylcarbinylamine (**6a**), 52.4% optically pure, prepared by our previously described method,[10] is deaminated in aqueous acetic acid under the same conditions used in the racemic series. Preparative vapor chromatographic isolation of the 2-bicyclo[3.2.1]-octanols (**7** and **8**) is achieved by repetitive cycling to constant rotation. Both products are optically active, the *endo* isomer **7** with $[\alpha]_D$ +0.684° (ethanol), +0.858° (chloroform), and the *exo* isomer **8** with $[\alpha]_D$ −3.67° (ethanol). The *exo* isomer can be obtained in the homogeneous state and shows only one peak on capillary vapor chromatography. The *endo* isomer **7**, despite repeated cycling, is very difficult to obtain free of small amounts of 2-bicyclo[2.2.2]octanol (**10**), the vapor chromatographic retention times of **7** and **10** being very close together on the preparative column. Similarly, isolation of pure **10**, which has a retention time between those of **7** and **8**, is extremely difficult from these mixtures, in which it is present in small quantity. Our best sample of **7** obtained from deamination is free of **8** but still contains 4% of **10**. Nevertheless, for two reasons the small rotation observed for this sample cannot be solely attributable to **10**: (i) oxidation of the sample gives an optically active ketone (were the rotation of the alcohol solely due to contamination of racemic **7** with active **10**, the derived ketone would be an optically inactive mixture of racemic 2-bicyclo[3.2.1]octanone and 2-bicyclo[2.2.2]-octanone, the latter substance being incapable of optical activity); (ii) the sign of rotation of **10** would be the same as that of the *axial*-alcohol **8**,[7] *i.e.*, (−), and opposite to that observed for the **7** sample. The rotation of the **7** sample is thus a minimum value for the specific activity of the pure **7** in it. Although the rotation of the contaminant **10** is unknown, there is good reason (see Experimental) to conclude that its contribution is small and that the per cent retention in **7** is not seriously in error. Even in the worst possible case, *i.e.*, even if **10** were formed with complete retention of optical purity, the conclusions given below would be unaffected.

From the highest rotation reported[15] for the *endo-equatorial*-alcohol **7**, the minimum value for 52.4% optically pure material can be calculated to be 4.25° (chloroform). The **7** formed in the deamination–rearrangement of **6a** is thus at least 80% racemized. Similarly, from data obtained elsewhere,[7] the minimum value $[\alpha]_D$ 6.76° (ethanol) can be calculated for 52.4% optically pure *exo-axial* alcohol **8**, and the **8** sample from the rearrangement is therefore at least 46% racemized.

These minimum figures suffice to demonstrate substantial racemization in both products, but give no information on whether the extents of racemization are the same. This point is settled by relating the optical rotations of the two epimeric alcohols at identical levels of optical purity. Oppenauer oxidation of an optically active, chemically homogeneous preparation[7] of the *exo*-alcohol **8**, $[\alpha]_D$ +5.25° (ethanol), gives (−)-2-bicyclo[3.2.1]octanone, $[\alpha]_D$ −50.3° (ethanol), which upon lithium aluminum hydride reduction gives a mixture of **8** (22%) and **7** (78%), $[\alpha]_D$ −4.24°. The rotation of the **7** in this mixture is thus −6.95° (ethanol) and the ratio of rotations **7**/**8** is thus 1.33 in ethanol for materials of identical optical purity. As is shown above, the **7**/**8** ratio of rotations for the two alcohols derived from the deamination–rearrangement is 0.186 (with a possible upper limit of 0.36 if the extreme assumption is made that contaminant **10** is formed with complete retention). It is thus apparent that the two alcohols **7** and **8** formed in the rearrangement have different optical purities, the *endo-equatorial*-alcohol **7** retaining only about a third to a seventh as much optical purity as the *exo-axial*-alcohol **8**. This result has profound mechanistic implications.

Exact values for the actual percentage retention in the products **7** and **8** can now be calculated by combining the above correlations with the value for the maximum rotation of **7**. The latter figure is available from the work of Goering and Fickes,[17] who find $[\alpha]_D$ 23.5° ($CHCl_3$) as the rotation of optically pure **7** by the isotopic dilution technique.[7,10b,18] Thus, alcohol **8** has $[\alpha]_D$ 14.0° (ethanol) when optically pure or 7.35° when 52.4% optically pure. The **8** formed in the deamination of 52.4% optically pure **6a** has $[\alpha]_D$ −3.67° (ethanol) and is therefore formed with 50% retention of the original optical purity. The **7** formed in the same reaction retains 7–13% of optical purity.

What appears to be a similar pattern is observed in the acetolysis (sodium acetate buffered) of optically active *endo*-2-norbornylcarbinyl *p*-bromobenzenesulfonate (**6c**). The mixture of acetates so obtained is first subjected to lithium aluminum hydride reduction and the resulting mixture of alcohols separated by preparative vapor chromatography. From (−)-*p*-bromobenzenesulfonate of 46.1% optical purity (configuration[10] enantiomeric with that of the (−)-amine hydrochloride used for the deamination) there are obtained: racemic *endo-equatorial* alcohol **7** (isolated with difficulty but this time free of **8** and **10**), $[\alpha]_D$ 0.00°; (+)-*exo-axial*-alcohol **8**, $[\alpha]_D$ +0.90° (ethanol); (+)-2-bicyclo[2.2.2]-octanol (**10**), $[\alpha]_D$ +1.14 ± 0.3° ($CHCl_3$). The latter is obtained only in admixture with **7**, but the rotation reported here is that calculated for the pure substance by correcting the observed value for dilution by the optically inactive contaminant. The result corresponds to 6 ± 1% retention of optical purity in **10** based on the known[7] value of the maximum rotation. Acetolysis leads to much more nearly complete racemization of both **7** and **8**, the former alcohol being essentially 100% racemic from acetolysis and the latter retaining only about a quarter as much optical purity in acetolysis as in aqueous deamination. Nevertheless, although the extremely low levels of optical activity of **7** and **8** in the acetolysis experiment do not inspire much confidence in a quantitative estimate of the ratio of rotations, the discrepancy in optical purities observed in deamination seems to persist qualitatively in acetolysis (see below, however). The products **7**, **8**, and **10** (OH = OAc) are all chemically and optically stable under the acetolysis conditions.

Although *meso*-alcohol **11** is formed to the extent of about 1% in the acetolysis of optically active **6c**, we suspect that it is an artifact arising from contamination of the starting *endo*-*p*-bromobenzenesulfonate **6c** with a trace of the *exo* epimer. Judging by the behavior of the *exo* system when examined separately,[7] we calculate that as little as 5% contamination of this type would suffice to produce the 1% of **11**. The contaminant probably is introduced by a small amount of epimerization during the lithium aluminum hydride reduction of *endo*-2-norbornanecarboxylic acid to the *endo*-carbinol **6b**, which is the starting material for the preparation of the *p*-bromobenzenesulfonate. Since the latter cannot be recrystallized when prepared from partially resolved material for fear of optical fractionation, *exo* contaminant is not separated. Unfortunately, detection of the presence of small amounts of

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(17) H. L. Goering and G. Fickes, private communication. We are indebted to Professor Goering for this information and for permission to cite it here.

(18) *Cf.* (a) S. Graff, D. Rittenberg, and G. L. Foster, *J. Biol. Chem.*, **133**, 745 (1940); (b) J. A. Berson and S. Suzuki, *J. Am. Chem. Soc.*, **81**, 4088 (1959); (c) H. L. Goering and J. T. Doi, *ibid.*, **82**, 5850 (1960).

exo-norbornylcarbinol in *endo* is difficult by vapor chromatographic or infrared techniques below about 5% contamination. The strongest evidence that **11** is a spurious product in the acetolysis is provided by an experiment in the deuterated series to be described below, in which the acetolysis products of **6c** known to be free of *exo* contaminant contain no **11**.

In contrast to the deamination product, the acetate mixture derived from acetolysis does contain a small amount (2–3%) of the acetate of alcohol **6b** with the skeleton of the starting material. Again, the authenticity of this product is dubious since it may well result from simple acetylation of a small amount of carbinol that escapes esterification in the preparation of the *p*-bromobenzenesulfonate **6c** (although **6b** acetate is formed even from recrystallized **6c** in the deuterated series). Whatever its source, the presence of **6b** is a serious nuisance, since it has virtually the same retention time as the *equatorial*-alcohol **7** and cannot be detected in the latter by vapor chromatography. In the acetolytic experiments, the parent carbinol **6b** is dextrorotatory, while the product **7**, if it were optically active at all, would be levorotatory. Thus, the **7** could have a small rotation that is just cancelled by the trace of **6b** contaminant with much higher rotation to produce the observed zero rotation. On the assumption that the contamination of this type is about 3% (the amount revealed by vapor chromatography on the original acetate mixture), the rotation of the **7** could have been as high as −0.1°. This leaves unchanged our earlier conclusion that racemization of **7** is more extensive in acetolysis than in deamination and reinforces the opinion already expressed regarding the uncertainty in the ratio of rotations **7**/**8** in the acetolysis experiment.

The product distributions and stereochemical results of the deamination and acetolysis are summarized in Table I.

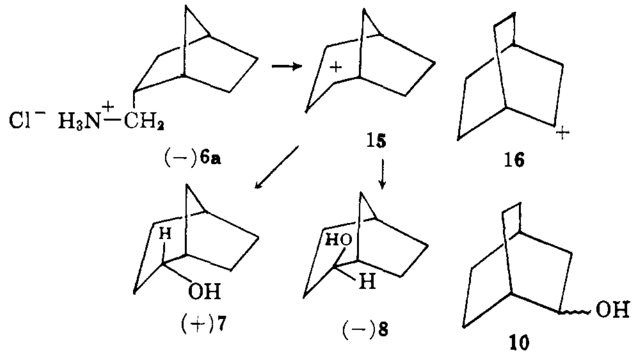
TABLE I

PRODUCT DISTRIBUTIONS AND STEREOCHEMICAL RESULTS FROM THE RING EXPANSIONS OF THE *endo*-2-NORBORNYLCARBINYL SYSTEM

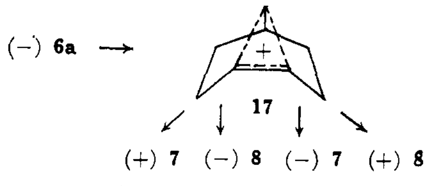
Product	Deamin.	Acetol.	Deamin.	Acetol.
	Yield, %		Retn. of opt. purity, %	
2-*endo*-[3.2.1], **7**	83^{a,c}	77^{a,c}	7–13	0
2-*exo*-[3.2.1], **8**	9^{a,c}	12.5^{a,c}	50	14
[2.2.2], **10**	7^{a,c}	10.5^{a,c}	?	6
3-*meso*-[3.2.1], **11**	0	1^{a,c}	*meso*	*meso*
Unrearr. **6b**	0	2.9^{d}	..	..
Hydrocarbons	7.5^{b}	8^{b}	..	..

[a] % of alcohol product. [b] % of total product. [c] Relative area of peak in vapor chromatogram of alcohol fraction. [d] Relative area of peak in vapor chromatogram of acetate mixture, possibly an artifact (see text).

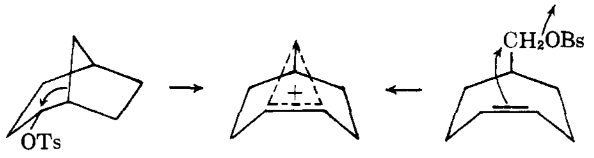
Mechanism (i)



Mechanism (ii)

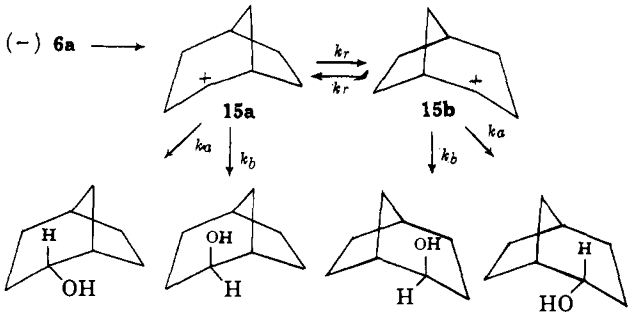


The Mechanism of the Rearrangement.—In the discussion that follows, optically active materials are assigned structural formulas in the correct[10a] absolute configurations. We first discard four simple schemes with some *a priori* plausibility as descriptions of the chemistry of these rearrangements. The details of the first rearrangement step (**6a** → **15**) are unspecified for the present but will be discussed below. Also, the origin of cation **16** which is a potential source of 2-bicyclo[2.2.2]octyl product **10**, is left for later consideration. Mechanism (i), involving optically active classical cation **15** as the sole source of **7** and **8**, can be rejected on the simple grounds that it does not account for the extensive racemization observed in both **7** and **8**. This mechanism involves the symmetrical nonclassical cation **17** as the product-forming intermediate. Cation **17** has been postulated previously to account for the solvolytic behavior of *endo*-2-bicyclo[3.2.1]octyl *p*-toluenesulfonate (**18**)[14] and of 4-cycloheptenylcarbinyl *p*-bromobenzenesulfonate (**19**),[3] but it cannot be the *sole* product-forming intermediate in the present cases, for then both **7** and **8** would be completely rather than only partially racemized. There is the additional difficulty that opening of the mesomeric bridge to give *exo-axial* product **8** would have to occur with retention of configuration, rather than the normal inversion observed in all other such reactions.[2]



18 **17** **19**

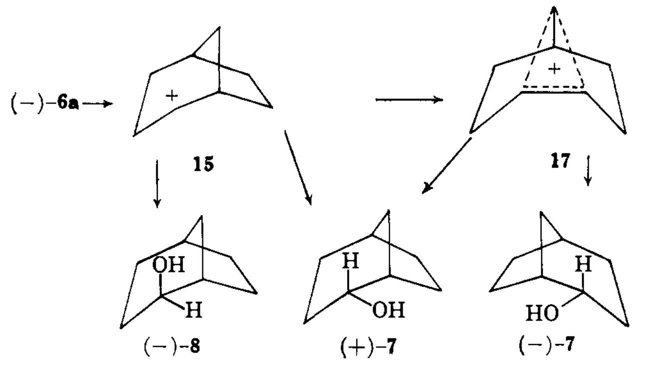
Mechanism (iii)



Reversible interconversion of the enantiomeric forms of classical cation **15** provides a device for partial racemization of both products **7** and **8** as long as the rearrangement rate (characterized by k_r) is not very much faster than the rate of capture of the cations by solvent (characterized by k_a and k_b). The mechanism nevertheless cannot account for all the results, for the properties of enantiomers require that the ratio of rate constants k_a/k_b from both of the antipodal forms of **15** be the same and consequently that the product ratio **7**/**8** from both be the same. This would produce **7** and **8** with identical optical purities, which is in conflict with experiment. In fact, *the observed nonidentity of the optical purities of* **7** *and* **8** *requires that there be at least two discrete product-forming intermediates* and that the ratio of products **7**/**8** from both be different. Further, whatever intermediates are postulated must also account for a ratio of optical purities **7**/**8** less than unity.

One way of meeting this requirement is provided by mechanism (iv), which postulates irreversible conversion of classical ion **15** to nonclassical ion **17** and adheres to the rule that opening of the mesomeric bridge of the latter occurs stereospecifically to give *endo-equatorial* product **7**. The mechanism fails in another respect, however, since it does not account for the observed extensive racemization of the *axial*-alcohol **8**.

Mechanism (iv)

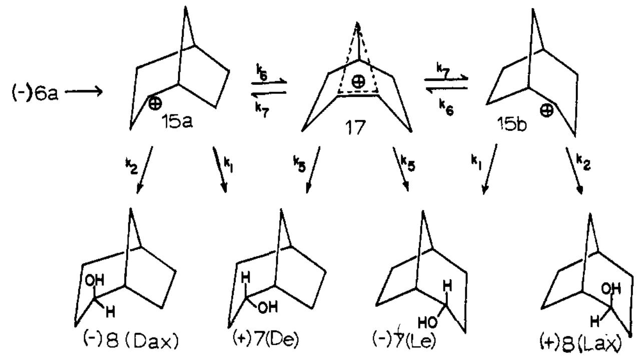


To formulate mechanisms compatible with our results in terms of cations **15** and **17**, mechanism (iv) must be modified by abandoning either of its two restrictions: it must be assumed that either (a) the **15** → **17** reaction is reversible, and product can thus arise from *both enantiomers* of **15**, or (b) that opening of the mesomeric bridge of **17** is not stereospecific but gives some axial alcohol **8** as well as *equatorial*-alcohol **7**. The argument using assumption (b) requires the subsidiary hypothesis that the **7**/**8** product ratio from **17** is not the same as that from **15**.

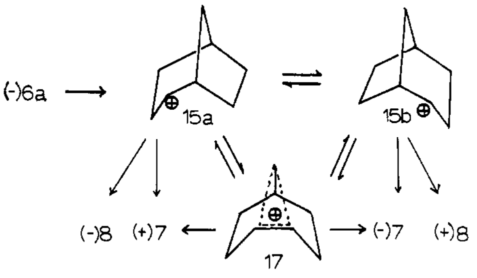
Reversions of nonclassical cations to the classical ones, analogous to the postulated **17** → **15** reaction, do not seem to occur in simple bicyclo[2.2.1]heptyl (norbornyl) derivatives under kinetically controlled conditions; the only circumstances in which it is necessary or even permissible to postulate such processes in norbornyl systems are those in which the cations are repeatedly formed in the reaction medium, thus providing an opportunity for slow reactions to become discernible.[2] Similarly, the evidence[2] is very strong that nucleophiles open the mesomeric bridge of nonclassical cations of the norbornyl series with exclusive inversion. Thus, both assumptions (a) and (b) above are without experimental precedent in the most extensively studied group of bridged bicyclic substances. Nevertheless, assumption (a) seems to us less disagreeable, because adoption of assumption (b) leaves one in the dubious logical position of having abandoned one of the major arguments[2] for the very existence of nonclassical ions. In other words, it seems to us unjustifiable, at least at present, to use a nonclassical structure for the necessary second intermediate in the system without accepting the corollary that its reactions with nucleophiles be stereospecific.

The two simplest partial mechanisms that are consistent with the experimental results are (v) and (vi). We prefer mechanism (v) on the admittedly intuitive grounds that mechanism (vi) involves a true product-forming intermediate **17** which has a structure that is conceptually difficult to distinguish from that of the transition state for the **15a** ⇄ **15b** reaction. Note that this objection applies only if the **15a** ⇄ **15b** reaction of mechanism (vi) is a Wagner–Meerwein rearrangement, but does not apply if the transformation is effected by 4,2-hydrogen shift. Evidence on the latter problem is described below.

Mechanism (v)



Mechanism (vi)



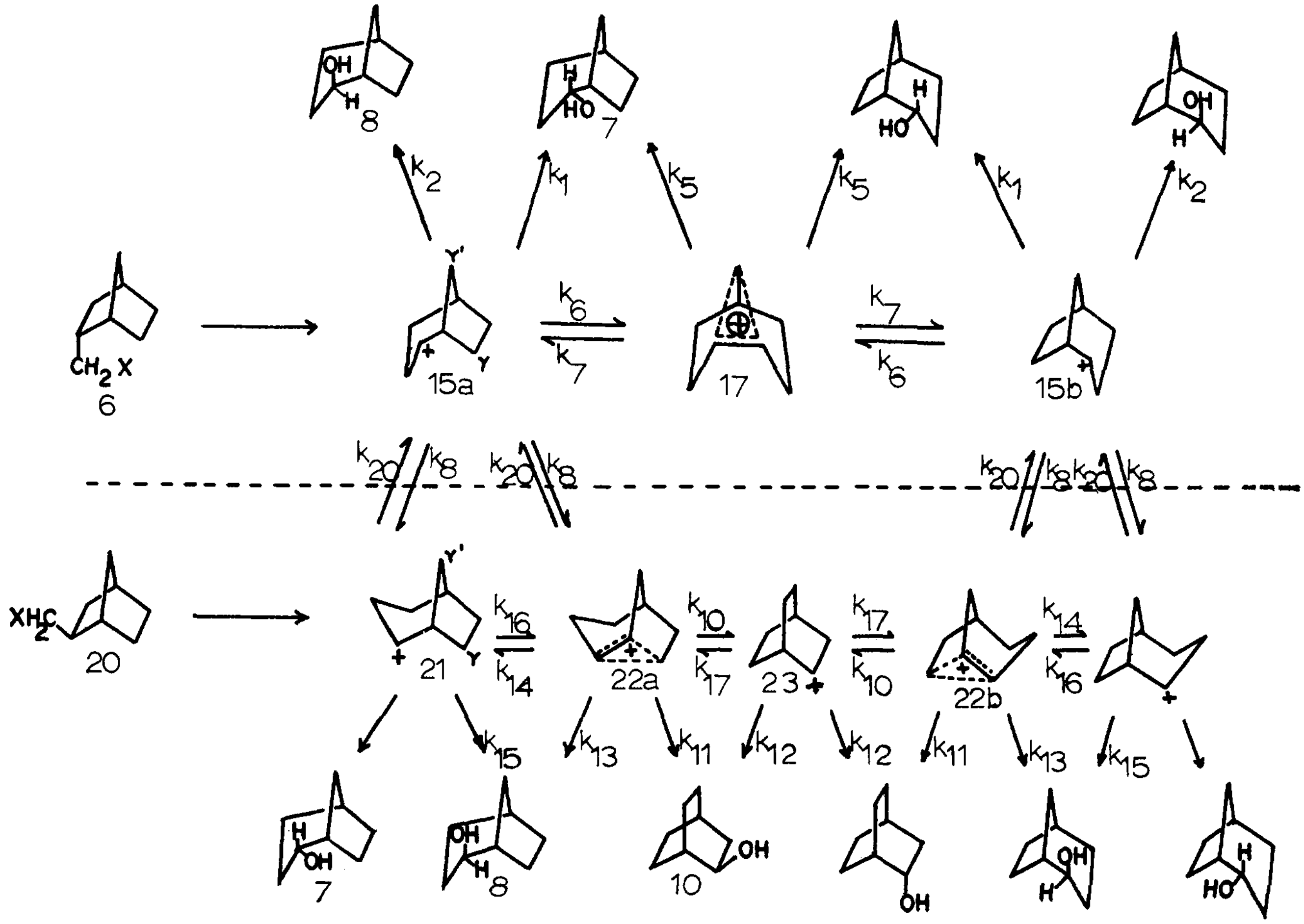
That mechanism (v) fits the data may be deduced by inspection. Since in this scheme the optically inactive nonclassical cation **17** is considered to give only *endo-equatorial* product **7** and occurs in the scheme *between* the enantiomeric forms of the classical cation **15** (which are the sole sources of *exo-axial* product **8**), product **7** will always be more highly racemized than product **8**. This result may also be shown analytically by assuming that all the cationic intermediates may be treated by steady-state methods and that the form of the rate-law for conversion of the cations to products is the same for each. The theoretical ratio of optical purities is then given by eq. 1. The symbols D and L are arbitrary configurational designations. When $k_5 = 0$, that is, when nonclassical ion **17** is not a product-forming intermediate, the ratio is unity. When $k_5 > 0$, the term on the right of eq. 1 becomes less than unity, which is in accord with experiment.

$$\frac{\text{Opt. purity of } \mathbf{7}}{\text{Opt. purity of } \mathbf{8}} = \left[\frac{\mathrm{D_e} - \mathrm{L_e}}{\mathrm{D_e} + \mathrm{L_e}}\right] \Big/ \left[\frac{\mathrm{D_{ax}} - \mathrm{L_{ax}}}{\mathrm{D_{ax}} + \mathrm{L_{ax}}}\right] = \frac{k_1(k_5 + k_7)}{k_1(k_5 + k_7) + k_5k_6} \quad (1)$$

As is usually the case with mechanisms involving nonclassical ions, mechanism (v) can be modified to one in which cation **17** is replaced or supplemented by two lop-sided, unsymmetrical nonclassical cations in rapid equilibrium. Mechanism (v) is suggested as the working hypothesis with the greatest economy of intermediates.

Crossover between the Rearrangement Paths.—Mechanism (v) is incomplete in that the source of the small amount of 2-bicyclo[2.2.2]octanol (**10**) is not indicated. This product seems to be derived by way of a slow leak connecting the *endo*- (**6**) and *exo*- (**20**) 2-norbornylcarbinyl rearrangement paths. The *exo*-amine **20** shows a drastically different pattern,[7] the two major products being the *axial*-alcohol **8** and 2-bicyclo[2.2.2]octanol (**10**). If crossover between the two systems occured at the classical cation stage (**15a** ⇄ **21**, Chart 2), but this reversible chair–boat con-

CHART 2

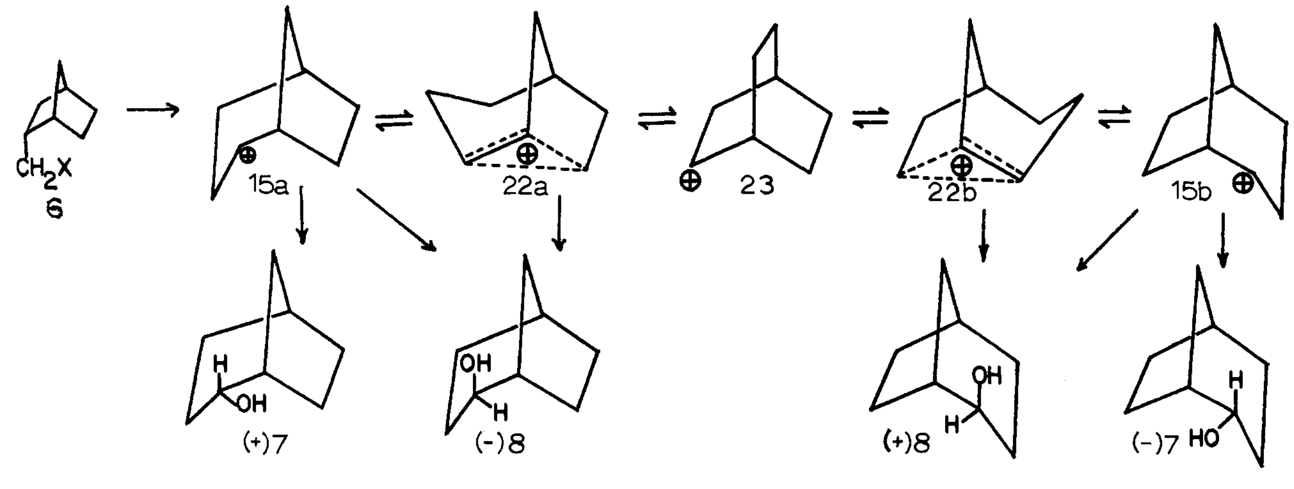


formational isomerization were slow enough to provide partial mechanistic insulation between the two systems, differing product distributions would result. Alternatively, one can account for the inefficient connection between the two systems with the postulate that bond delocalization in the conversions of classical to nonclassical ions are partially rather than wholly stereospecific, with $k_{\mathrm{Y}'}/k_{\mathrm{Y}} >> 1$ for **15a**, and $k_{\mathrm{Y}}/k_{\mathrm{Y}'} >> 1$ for **21**, but that in neither case does the less favored rate constant actually vanish. Some specificity in the bond delocalization is reasonable on the stereoelectronic grounds discussed below.

As is shown elsewhere,[7] the *exo-axial*-alcohol **8** is a companion product to 2-bicyclo[2.2.2]octanol (**10**) in the deamination of *exo*-2-norbornylcarbinylamine (**20**). It is therefore necessary to examine the possibility that the sole origin of the small amount of *exo*-alcohol **8** observed in the deamination of *endo*-amine **6a** is the same as that of the small amount of **10**, namely crossover into the rearrangement path that starts with *exo*-amine **20** *via* **15a** → **21** (Chart 2). Were this the sole origin of **8**, the **8**/**10** ratio from either amine under the same conditions would be the same. This is not what is observed, however, the ratio being 1.3 from **6a** and 0.9 from **20**, in aqueous acetic acid deamination. The greater proportion of **8** formed from *exo*-amine is consistent with an origin of about a third of the *axial*-alcohol **8** in the trapping of the classical intermediate **15** in mechanism (v). This calculation is based on the assumption that the observed 7% of 2-bicyclo[2.2.2]-octanol measures the amount of crossover and that it is accompanied by (0.9)(7%) or 6% of *axial*-alcohol **8** of the same provenance, the difference between the latter figure and the total observed 9% of **8** being attributed to trapping of **15**. On the other hand, leakage *via* the alternative path **15a** → **22a** (Chart 2) as the sole source of *axial*-alcohol **8** would not necessarily produce a **8**/**10** ratio the same as that observed (0.9) in the deamination of *exo*-amine **20**; in general, this ratio would be smaller, since the first source **21** of **8** from **20** would be by-passed. In other words, entry into the **20** → **21** ⇄ **22** path at **22** rather than at **21** would reduce the ratio. Therefore, the fraction of the **8** arising from **15a** in the deamination of **6a** would be greater than the one-third calculated on the basis of **15a** → **21** as the leakage mechanism.

The recognition of crossover as a factor in determining the course of the reaction requires a reconsideration of the mechanism at a higher level of complexity. Can the intricate maze of reactions that evidently occur be formulated with a scheme totally different from mechanism (v)? In particular, does crossover provide an alternative to our earlier postulates that a nonclassical cation **17** is involved and that it is reversibly transformed to its classical counterpart **15**? Several formulations attempting to employ crossover as a device for escaping the previous conclusions can be rejected. In mechanism (vii), which is a variant of mechanism (i), racemization of both **7** and **8** is achieved, without invoking nonclassical ion **17**, by way of the inactive classical ion **23**. The mechanism is incompatible with the results because racemization of *exo-axial*-alcohol **8** occurs earlier in the sequence than that of *endo-equatorial*-alcohol **7**. This would produce a lower retention of optical purity in **8** than in **7**, rather than the observed result, which is the converse. The same objection applies if the nonclassical ion **22** is replaced by any intermediate (*e.g.*, the boat classical ion **21**) that is cap-

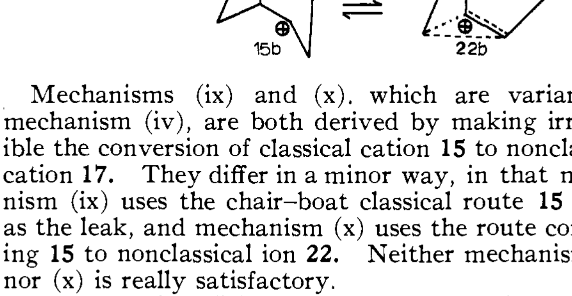
Mechanism (vii)



tured by solvent to give less equatorial product **7** than axial product **8**.

Mechanism (viii) is a variant of mechanism (iii) and, like the latter, postulates direct interconversion of the enantiomorphic forms of the classical cation **15** without the intervention of another product-forming intermediate. Insertion of a leak by conversion of **15** to nonclassical ion **22** or to the boat classical ion **21**, reversibly or irreversibly, does not remove the objection that has already eliminated mechanism (iii). Products **7** and **8** would be formed with identical optical purities, as may readily be shown by a steady-state analysis. In fact, there is no way out of this impasse with any mechanism that uses only direct interconversion of the optical antipodes of classical ion **15**.

Mechanism (viii)



Mechanisms (ix) and (x), which are variants of mechanism (iv), are both derived by making irreversible the conversion of classical cation **15** to nonclassical cation **17**. They differ in a minor way, in that mechanism (ix) uses the chair–boat classical route **15** → **21** as the leak, and mechanism (x) uses the route connecting **15** to nonclassical ion **22**. Neither mechanism (ix) nor (x) is really satisfactory.

In mechanism (ix), all of the racemization of *axial* product **8** is effected by channeling through the symmetrical classical ion **23**. Since this process is entered, starting with *endo*-reactant **6**, at classical ion **21**, which is also the point of entry into the rearrangement path from *exo*-reactant **20**, the degree of retention of optical purity of *axial*-alcohol **8** derived from **6** should be equal to or greater than that from **20**. This is in conflict with the experimental observations; deamination of **6a** in aqueous acetic acid and acetolysis of **6c** in acetic acid both yield **8** with substantial racemization (Table I), but deamination of **20** in acetic acid yields virtually unracemized **8**.[7] (Although a direct comparison with identical solvents and leaving groups is not yet available, it seems reasonable to assume that deamination of **6a** in glacial acetic acid would produce **8** at least as highly racemized as that obtained in aqueous acetic acid.) Note that mechanism (ix) cannot be modified by by-passing nonclassical ion **22** and permitting direct **21** → **23** conversion since **22** is needed to account for the optical activity observed in the 2-bicyclo[2.2.2]octyl product **10**.

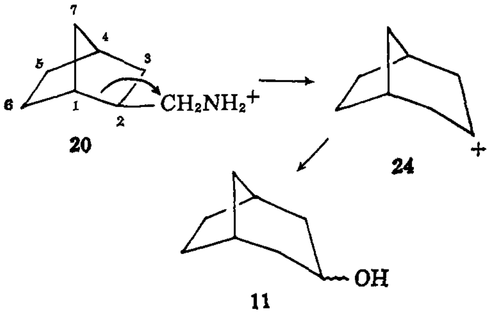
With mechanism (x), it is difficult to account for the almost complete racemization of the 2-bicyclo[2.2.2]-octyl product **10** obtained from acetolysis of *endo-p*-bromobenzenesulfonate **6c**. Product **10** retains much more optical purity when formed from *exo*-amine **20** in acetic acid.[7] Although the leaving groups in the two experiments are different, it is hard to see how any difference in the nature of the cations resulting from this difference could survive the numerous vibrations and collisions that must occur by the time ions **22** and **23** are reached. Accordingly, some mechanism must exist for racemizing **10** derived from *endo* (**6**) starting material more completely than **10** derived from *exo* (**20**) starting material. This mechanism is provided by allowing the **15** → **17** step of Chart 1 to be reversible. Finally, it is shown later in this paper that no appreciable fraction of the racemization in the precursors of *equatorial* product **7** occurs by passage through the classical 2-bicyclo[2.2.2]octyl cation **23**. If the **15** → **17** step is to be irreversible, there is then no way of generating **15b** cations in the system, and it must be assumed that none of the *axial* product **8** arises from **15a**. This seems unlikely.

We conclude that Chart 2, despite its intricate detail, is the simplest and most satisfactory scheme for the mechanism of the reactions discussed here. One minor aspect of the scheme that cannot yet be specified concerns the exact description of the crossover (*via* **21** or **22**?).

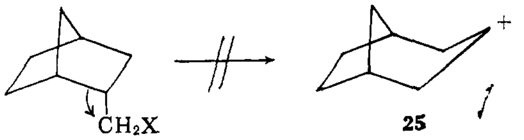
That far more racemization accompanies the acetolysis of *endo*-2-norbornylcarbinyl *p*-bromobenzenesulfonate than deamination in aqueous acetic acid of the corresponding amine is reasonably explained in terms of the mechanism of Chart 2 as a solvent effect. Although the two experiments are not strictly comparable because the leaving groups are different, the results are just what would be anticipated from a change from a highly "ionizing," strongly nucleophilic medium to a nonaqueous, weakly nucleophilic one. In the more nucleophilic aqueous medium, the rate of capture of classical ion **15a** should be greater than in acetic acid. Further, the system with greater "ionizing" power should favor the dispersal of charge to a smaller extent than the one with poorer "ionizing" power; conversion of the classical ion **15** with localized charge to the nonclassical one **17** with dispersed charge should be more favorable in glacial acetic acid. Both of these effects would cooperate to make the efficiency with which the classical ion **15a** is trapped greater in aqueous medium. It remains to be seen whether some of the differences in behavior are the result of ion-pair phenomena. For example, acetolysis of the *endo-p*-bromobenzenesulfonate **6c** could conceivably be accompanied by ion-pair return to a rearranged sulfonate of the *endo-equatorial* 2-bicyclo[3.2.1]octyl structure. Racemization of the latter by ion-pair return is a reasonable possibility during acetolysis but has no counterpart in deamination.

Origin of the Stereospecificity of the Rearrangements.—Even before the detailed stereochemical results of this and the companion paper[7] were available, it was already clear from the work of Alder and Reubke[8] that the stereochemistry (*endo* or *exo*) of the starting primary carbinyl system exerts a profound effect on the distribution of products. This genetic memory guides the rearrangements through highly (although not completely) specific courses.

The most obvious manifestation of these effects is the difference in the yield of the *meso* substance 3-bicyclo[3.2.1]octanol (**11**) resulting from migration of C-1 to the methylene side chain. This product is formed in substantial amount from *exo* starting material **20**[7] but is virtually absent in the product mixture from *endo* starting material **6**. These results are presumably attributable to conformational effects, at least in part. A further discussion of this point is given in the accompanying paper.[7]



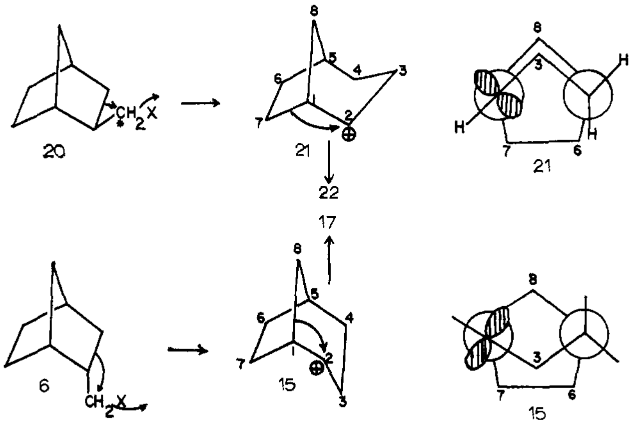
20 **24** **11**



6a, X = NH_2
c, X = OBs

25

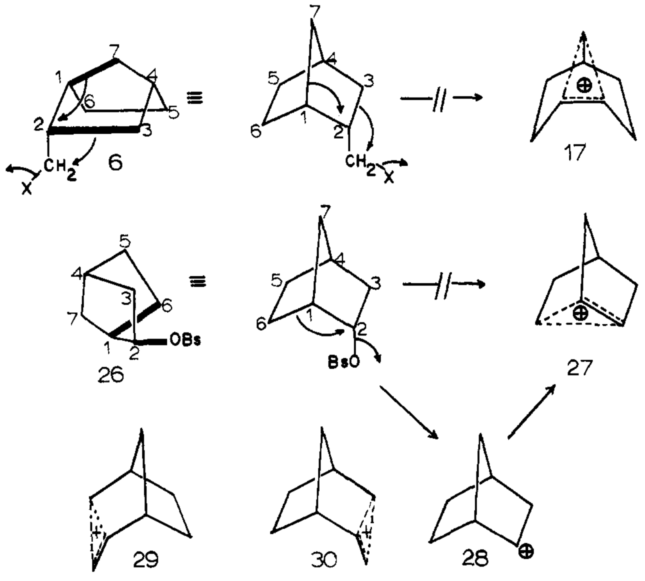
In the double rearrangements initiated by migration of C-3 from C-2 to the methylene side chain, conformational factors are again at work to produce specificity. The cation **21** that results from this change presents the axis of its empty p-orbital at C-2 more nearly parallel to the C-1–C-7 bond than to the C-1–C-8 bond, with the result that delocalization to give **22** rather than **17** occurs. It is not clear whether formation of **17** directly from the boat-like **21** is possible without prior conformational isomerization of the latter to the chair-like **15**. Similarly, it is not certain that delocalization in **21** to give **22** must await "completion" of the **20** → **21** rearrangement, or whether it occurs at a stage when C-3 of **20** has become bonded to $\overset{*}{C}H_2$ but cation **21** has not yet assumed its equilibrium posture. When the first rearrangement step has proceeded far enough so that C-3 is effectively detached from C-2 and close enough to $\overset{*}{C}H_2$ to be strongly bonded, the system may be imagined to represent a vibrationally excited state of **21** in which the axis of the p-orbital is quite accurately parallel to the C-1–C-8 bond. How critical this alignment is for the second rearrangement **21** → **22** is unclear.



20 **21** **21** **6** **15** **15**

In the rearrangement of **6**, the *equilibrium* geometry of chair cation **15** is such that interaction of the C-1–C-8 bond with the empty p-orbital does not seem to be very much more favorable stereoelectronically than that of the C-1–C-7 bond. Nevertheless, in the initial ring expansion of **6**, the axis of the developing p-orbital at C-2 gradually tilts, as migration proceeds, until it passes through an orientation parallel to the C-1–C-8 bond. Completion of the process eventually leads to **15** in its equilibrium configuration, but it is conceivable that involvement of the C-1–C-8 bonding electron pair in delocalization occurs at the distorted stage corresponding to optimum alignment of the p-orbital axis. If this is the correct explanation for C-1–C-8 rather than C-1–C-7 delocalization, the specificity results from a kind of intramolecular "trapping" of the cation **15** while it is in a vibrationally distorted conformation. Alternatively, the specificity could arise from more subtle effects. For example, if cation **17** is more stable than **22**, *e.g.*, because of lower angle or nonbonded strain, C-1–C-8 delocalization in **15** leading to the former could be more favorable than C-1–C-7 delocalization leading to the latter merely because the respective transition states are affected by corresponding sorts of strain factors. It does not seem possible to specify the precise nature of these hypothetical strain effects at present.

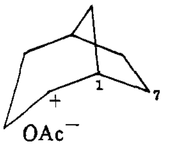
The rearrangements observed here and in the companion study[7] are all characterized by detectable caesurae at the classical cation stage. Apparently there is an activation energy required for conversion of classical ion **15a** to mesomeric ion **17**. Departure of nitrogen or of *p*-bromobenzenesulfonate ion from **6a** or **6c** does not lead directly to the inactive mesomeric species **17** but instead passes through interceptable intermediate stages. The stepwise nature of the rearrangement is probably a consequence of the geometry of the **6** structure, which does not fulfill the antiparallel stereoelectronic requirement presumably necessary for a concerted multiple rearrangement in which C-7 displaces C-3 from C-2. Thus, the C-1–C-7 and C-2–C-3 bonds of **6** make a projected angle of about 60° with each other rather than the 180° that would be favorable for concerted migration. The stereoelectronic situation in **6** is very similar to that in *endo*-norbornyl *p*-bromobenzenesulfonate **26**, where the dihedral angle between the C-1–C-6 bond and the C-2–OBs bond (the latter bond being functionally analogous to the C-2–C-3 bond of 6) is also about 60°. The behavior of 26 on solvolysis reflects this stereoelectronic inadequacy: the reaction does not proceed directly from 26 to the mesomeric cation 27 but instead pauses at a discrete interceptable stage, the classical ion **28**.[19]



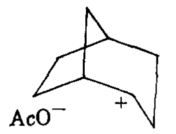
The geometric parallel between 6 and 26 thus results in mechanistically analogous consequences.

In a formal sense, the optically active classical cations **15a** and **15b** of Chart 2 may be replaced by mesomeric optically active cation **29** and its mirror image **30**. This substitution would have no effect on the conclusions derived earlier, but has the disagreeable feature that direct conversion of **29** to the axial product **8** requires opening of the mesomeric bridge of **29** with retention of configuration. Such an assumption, while perhaps not rigorously excluded, at least has no precedent and appears to us unnecessarily drastic. We therefore prefer the formulation in terms of **15**. There are no grounds at present for excluding **29** as a possible intermediate lying between **6** and **15** and giving only *equatorial* product **7**. Note that the absence of *endo*-norbornylcarbinyl derivatives (**6b** or its acetate) as products is not a valid argument against **29**, since this cation would be expected to react at the more highly substituted center with high specificity.[2]

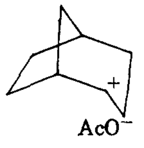
Although the stereochemical pattern observed in the products of the ring-expansion reactions of *endo*-norbornylcarbinyl derivatives is well accommodated by the concept of two structurally different ions, classical **15** and nonclassical **17**, there are certain features of the results that may be described by a formal alternative in which only classical ions are involved. If the concept of "structure" is expanded to include the counter-ions that might be imagined to accompany the cations, the roles of **15a**, **17**, and **15b** in Chart 2 can be assumed, for example, by ion-pair species **15c**, **17a**, and **15d**, respectively. Species **15c** and **15d** are enantiomeric, but species **17a** is structurally different from either, the counter-ion being further removed from the locus of positive charge in **17a** than in **15c** or **15d**. The unequal optical purities observed in products **7** and **8** are then explicable if it is assumed that the ratios of the rates of formation of products **7**/**8** from **17a** is greater than that from **15c** or **15d**. Although such an assumption might be valid, there is no obvious reason why it should be, in contrast to the formulation of Chart 2, where the appropriate relationships are direct consequences of the structures of the cations involved.



15c

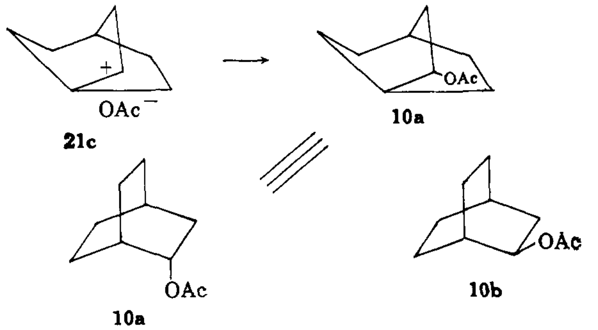


17a

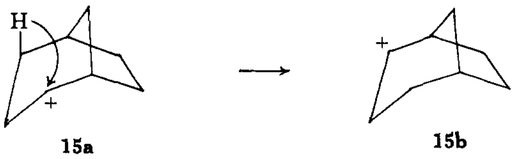


15d

A further difficulty with this alternative mechanism is encountered when one attempts to apply it to the problem of cross-over between the *endo*-derived and *exo*-derived systems. If this is imagined to occur by movement of the C-1–C-7 bond of **15c**, the resulting ion-pair, **21c** would give, by the most direct route of collapse, a product **10a** that is the *enantiomer* of that which is found to predominate[7] in the 2-bicyclo[2.2.2]octyl acetate derived from the *exo* system. Formation of the experimentally observed product **10b** would require some such additional hypothesis as (i) leakage occurs only from **17a** but not from **15c**, or (ii) the ion-pair **15c** must be transformed into another one in which the counter-ion is on the *exo* side of the ring system before leakage can occur, or (iii) ion-pair **21c** does not collapse directly to product but is preferentially attacked by solvent from the side opposite the counter-ion. Although none of these hypotheses is obviously incorrect, it is clear that by this stage the entire argument invoking them has acquired a teleological flavor. Recognizing the important role that counter-ion effects may play in many carbonium ion phenomena, we nevertheless can see no advantage to assigning them the responsibility for the results obtained here. In our opinion, the scheme of Chart 2, involving differences in carbonium ion structure, encompasses the whole pattern of the data far more simply and directly.



On the Question of Hydride Shift.—Wagner–Meerwein rearrangement is not the only racemizing mechanism hypothetically available to the cation **15**. The occurrence of intramolecular transannular hydride shift analogous to those established in norbornyl[21] and fenchyl[22,23] cations would also convert **15a** to its mirror image **15b**. For the reasons already given, this process



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[19] S. Winstein and D. Trifan, *J. Am. Chem. Soc.*, **74**, 1147 (1952).

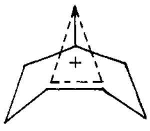
[20] (a) P. Beltrame, C. A. Bunton, and D. Whittaker, *Chem. Ind.* (London), 557 (1960); (b) J. A. Berson, *Tetrahedron Letters*, **No. 16**, 17 (1960); (c) J. D. Roberts, Abstracts of Papers, Sixteenth National Organic Chemistry Symposium of the American Chemical Society, Seattle, Wash., June, 1959; (d) M. S. Silver, M. C. Caserio, H. E. Rice, and J. D. Roberts, *J. Am. Chem. Soc.*, **83**, 3671 (1961).

[21] J. D. Roberts and C. C. Lee, *ibid.*, **73**, 5009 (1951); J. D. Roberts, C. C. Lee, and W. H. Saunders, Jr., *ibid.*, **76**, 4501 (1954).

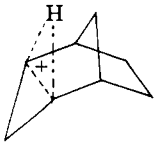
[22] W. von E. Doering and A. P. Wolf, *Perfumery Essent. Oil Record*, **42**, 414 (1951).

[23] Even cyclohexyl cations suffer small amounts of hydride shift, although it is not yet clear whether these are transannular or vicinal [*cf.* O. A. Reutov and T. N. Shatkina, *Tetrahedron*, **18**, 237 (1962)].

is insufficient to account for all the results in our system, but must be combined with the intervention of another product-forming intermediate, which could in principle be either the Wagner–Meerwein mesomeric cation **17** or the hydrogen-bridged cation **31**. To evaluate the importance of 4,2-hydride shift and to distinguish it from Wagner–Meerwein rearrangement, isotopic position-tagging experiments are helpful.

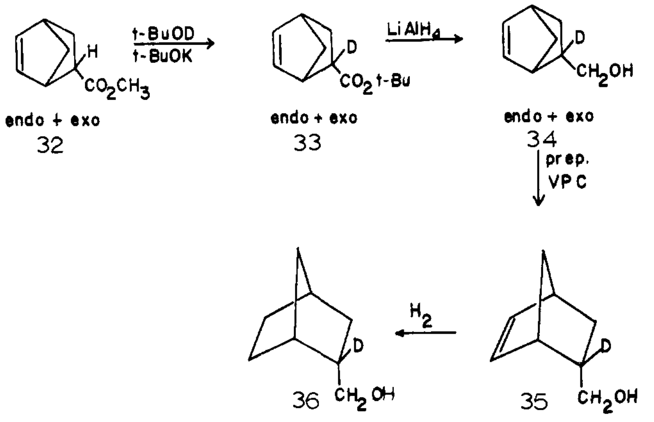


17



31

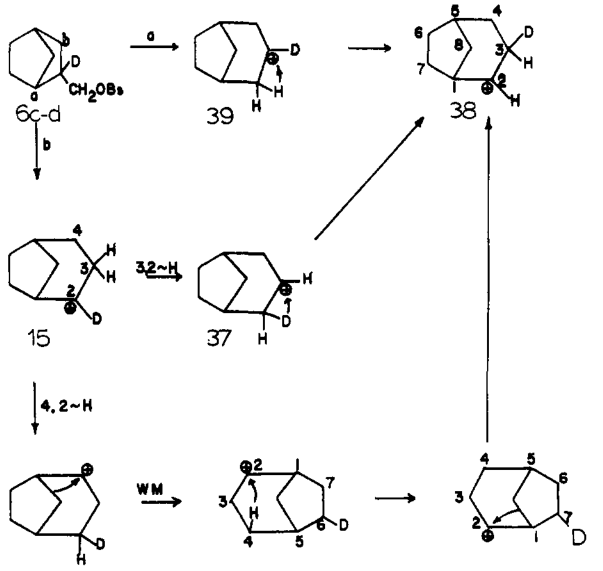
exo-2-Deuterio-*endo*-2-hydroxymethylnorbornyl *p*-bromobenzenesulfonate (**6c**–*d*) is prepared from the mixture of epimeric unsaturated methyl esters **32** obtained by Diels–Alder addition of cyclopentadiene and methyl acrylate. With twice-sublimed potassium *t*-butoxide in a 20-fold excess of hot *t*-butyl alcohol-*d*, **32** is converted to a mixture of epimeric 2-deuterio-*t*-butyl esters **33**, which upon lithium aluminum hydride reduction gives a mixture of unsaturated 2-deuterio-2-hydroxymethylnorbornanes **34**. The *endo* isomer **35** is obtained completely free of *exo* material (>99.9% homogeneous) by two passes through a preparative vapor chromatographic column. Catalytic hydrogenation of **35** gives **36** in a reaction that control experiments show to occur without appreciable deuterium exchange. The pure deuterated carbinol **36** gives a *p*-bromobenzenesulfonate **6c**–*d* which infrared analysis shows to contain not more than about 2% of unreacted carbinol **36**.

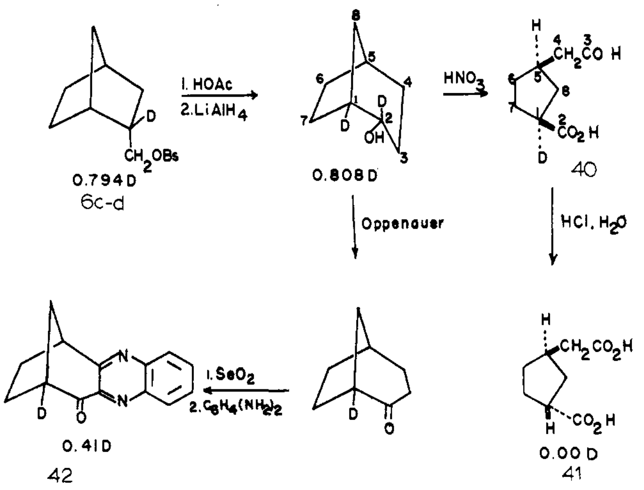


Acetolysis of the deuterated *p*-bromobenzenesulfonate **6c**–*d* under the same conditions used in the optically active case gives an acetate mixture containing 2% of the acetate of unrearranged structure (*endo*-2-norbornylcarbinyl acetate, possibly carried through from the bromobenzenesulfonate preparation), 12.7% of *exo-axial*-2-bicyclo[3.2.1]octyl acetate (**8**, OH = OAc), 76.5% of *endo-equatorial*-2-bicyclo[3.2.1]octyl acetate (**7**, OH = OAc), 10.8% of 2-bicyclo[2.2.2]octyl acetate (**10**, OH = OAc), and no observable *meso*-3-bicyclo[3.2.1]octyl acetate (**11**, OH = OAc). The latter compound would readily have been detected if present to the extent of 0.3%. The absence of this material in the product mixture from *p*-bromobenzenesulfonate known to be free of *exo* contaminant supports the conclusion that the 1% of **11** (OH = OAc) observed in acetolysis of optically active *p*-bromobenzenesulfonate is spurious. The remainder of the product distribution is identical within experimental error with that found in the optically active case.

Lithium aluminum hydride cleavage of the mixture of acetates and then two cycles of preparative vapor chromatography afford the *equatorial*-alcohol **7** virtually pure, the only contaminants being 0.8% of *axial*-alcohol **8** and 2% of 2-bicyclo[2.2.2]octanol (**10**). The material thus isolated has the same deuterium enrichment as the *p*-bromobenzenesulfonate starting material.

Distribution of the Label. C-3.—There are three formally conceivable ways in which deuterium might arrive at C-3. The first involves vicinal shifts of hydrogen and deuterium (C-3 → C-2 and C-2 → C-3) in the 2-bicyclo[3.2.1]octyl cation (*i.e.*, **15** → **37** → **38**), and the second an initial ring expansion of **6c** leading directly to the 3-bicyclo[3.2.1]octyl system (*i.e.*, **6c** → **39**) by movement of atom a, followed by vicinal shift of hydrogen to **38**. Both of these processes involve development of cationic character at C-3 and suggest that the *meso* product 3-bicyclo[3.2.1]octyl acetate should be found in the reaction mixture. Its absence is strong presumptive evidence against these mechanisms. The third way for deuterium to get to C-3 involves sequential Wagner–Meerwein and 4,2-hydrogen shift, as illustrated in the attached scheme. This series of changes does not involve cationic C-3, but is objectionable on the ground that it would distribute deuterium not only to C-3 but also to C-6 and C-7, and eventually to C-5. As is shown below, these positions are deuterium-free in the product, and the process therefore is not a factor. The same objection applies if the initial rearrangement is imagined to be Wagner–Meerwein rather than hydride shift.

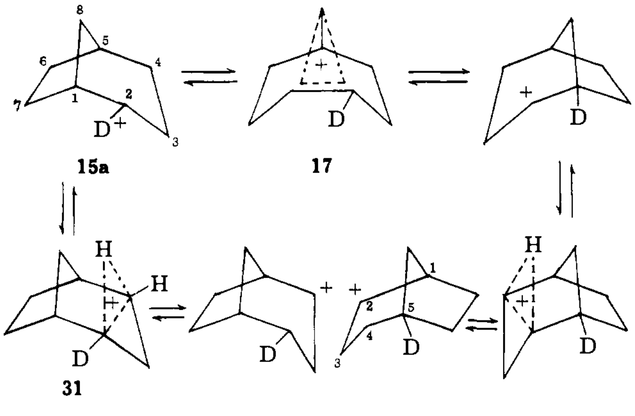




C-5–C-8.—Nitric acid oxidation[8b] of a sample of the deuterated product alcohol **7** gives *cis*-3-carboxycyclopentaneacetic acid (**40**). Heating this substance in a sealed tube with hydrochloric acid converts it to the *trans* isomer **41**, a process that must involve hydrogen–deuterium exchange at the inverted asymmetric center, since the epimerization passes over an enol. Exchange at the α-hydrogens of the acetic acid side chain is also expected. and direct evidence for exchange of three hydrogens α to carboxyl is provided by the reaction of synthetic undeuterated *cis*-acid **40** (D = H) with deuterium chloride in deuterium oxide under the above conditions. From this control experiment, *trans*-acid is isolated containing 2.90 atoms of deuterium per mole (after removal of carboxyl deuterium during work-up) and showing a degraded nuclear magnetic resonance spectrum in which the low-field signals due to α-carboxyl protons have all but vanished. The *trans*-acid **41** isolated from the oxidation of deuterated alcohol **7** therefore corresponds in deuterium content to carbons 5, 6, 7, and 8 of **7**. Analysis shows that this acid has only the natural deuterium abundance (0.01 atom % excess), and therefore C-5–C-8 of **7** *bear no deuterium.* This result eliminates the possibility that *both* 4,2-hydride shift and Wagner–Meerwein rearrangement occur *in sequence,* regardless of which process is imagined to precede the other, for then deuterium would appear at C-5 or C-6 and eventually at all the carbon atoms of the ring system except C-8.

C-1, C-2, and C-4.—The rearrangement that leads to completely racemic acetate of **7** must therefore involve either (i) all Wagner–Meerwein shift; (ii) all 4,2-hydride shift; or (iii) *competitive* carbon and hydrogen shift.

Alternative (iii) is unlikely, since it becomes equivalent to *sequential* carbon and hydrogen shift in respect to the labeling pattern it produces when an attempt is made to fit it into the scheme of Chart 2. For reasons already given, a reversible sequence of cations (classical ⇄ nonclassical ⇄ classical) is required in the mechanism. Racemization alternative (iii) could then be formulated as in the attached scheme (or with **17** and **31** interchanged).

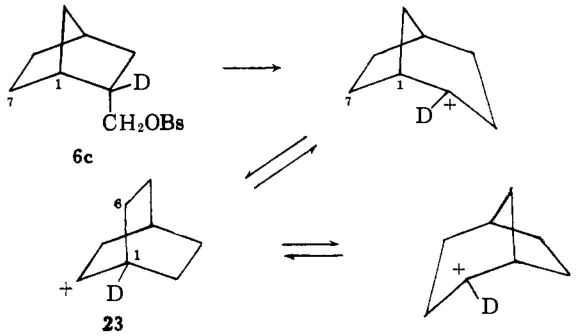


The symmetry of the system ensures that whatever reactions are accessible to classical cation **15a** are also accessible to its mirror image. The net result would be to spread deuterium label to C-5 and eventually over the entire carbon skeleton except C-8. This is in conflict with the experimental observations, and if the reversibility of the scheme of Chart 2 is correct, competitive carbon and hydrogen shift can be ruled out.

Decisive evidence against any contribution from hydrogen shift is provided by a further degradation. Carbon shift (Wagner–Meerwein) alone would produce a deuterium distribution with 50% of the original label at C-1, 50% at C-2, and 0% at C-4; hydrogen shift alone would put 0% at C-1, 50% at C-2, and 50% at C-4. Thus, any substantial contribution of hydrogen shift would reduce the share of deuterium label at C-1 to less than 50%.

Oppenauer oxidation of the **7** isolated from solvolysis gives 2-bicyclo[3.2.1]octanone,[24] which upon further oxidation with selenium dioxide in xylene gives the triketone 2,3,4-bicyclo[3.2.1]octantrione (previously reported[8]), isolated and purified as the quinoxaline **42**. This material has a deuterium enrichment 51 ± 1% of that in the original sample of **7**. Since any deuterium at C-2, C-3, and C-4 in **7** is removed in the quinoxaline, the entire deuterium content of the latter must be at C-1. The observed enrichment is exactly that predicted by exclusive Wagner–Meerwein rearrangement and eliminates the possibility of hydrogen shift as the cause of any appreciable fraction of the racemization.

The deuterium tracer results also establish that little if any of the racemization observed in the acetolysis of *endo*-2-norbornylcarbinyl *p*-bromobenzenesulfonate (**6c**) can be attributed to diversion of some of the cations through the classical 2-bicyclo[2.2.2]octyl cation (**23**), *e.g.*, by over-all migration of the C-1–C-7 bond, regardless of mechanistic details.



The latter process followed by movement of C-1–C-6 of **23** would cause racemization of an initially optically active 2-bicyclo[3.2.1]octyl cation *but no scrambling of deuterium.* Any significant contribution of this path would produce *endo*-2-bicyclo[3.2.1]octanol (**7**) with more than 50% of the deuterium label at C-2 and less than 50% at C-1. The observed C-2/C-1 distribution of 49 ± 1/51 ± 1 thus does not permit any of the **7** to have its origin in this path. Yet a substantial fraction of the total product mixture in the acetolysis of **6c** does come from the series of cations below the dotted line of Chart 2, *i.e.*, by crossover into the *exo*-derived path. If one takes the results in the *exo* system[7] as indicative of the behavior of the cations in this path, the 2-bicyclo[2.2.2]octyl product is accompanied by an approximately equal amount of *exo*-2-bicyclo[3.2.1]octyl product. The formation of 10.5% (see Table I) of 2-bicyclo[2.2.2]octyl acetate **10** in the acetolysis of **6c** thus suggests that some 21% of the total reaction is diverted into the path below the dotted line of Chart 2. In order for this leakage to affect the deuterium distribution appreciably, however, it would be necessary for passage across the barrier to be fast *in both directions:* this we already know not to be the case, for were it so, the *endo*- and *exo*-derived over-all product distributions would be similar or identical. In effect then, the deuterium scrambling data support the earlier conclusions based on optical and structural information: crossover is slow in comparison to reactions on a given side of the barrier.

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(24) The oxidation does not involve exchange at C-1 of the ketone. This position, although formally α to carbonyl, cannot readily become part of an enol without violation of Bredt's rule. Even a deliberate attempt to exchange the C-1 proton of the ketone under strongly basic conditions fails, only the two protons at C-3 being replaced by deuterium. Under the conditions of Oppenauer oxidation, this dideuterio ketone loses a large fraction of its deuterium, as is expected. *Cf.* W. von E. Doering and T. C. Aschner, *J. Am. Chem. Soc.*, **75**, 393 (1953).

Partitioning of the Classical Ion 15a.—In the scheme of Chart 2, the classical ion **15a** is partitioned among three paths: conversion to *axial* product **8** with rate constant k_2, to equatorial product **7** with rate constant k_1, and to symmetrical nonclassical ion **17** with rate constant k_6. (The "rate constants" k_1 and k_2 actually include a solvent concentration term which we assume to be identical for both processes.) The experimental data can be analyzed with the aid of the steady-state assumption to give an estimate of the ratio k_2/k_1, which measures the relative importance of *axial vs. equatorial* capture of the substituted chair cyclohexyl cation **15a.** For this analysis, the following symbols for experimental quantities apply.

$R_n{}^a$ = ratio of *axial* product **8** to 2-bicyclo[2.2.2]octyl product **10** from *endo* starting material **6**
$R_x{}^a$ = ratio of **8**/**10** from *exo* starting material **20**
$R_n{}^e$ = ratio of **7**/**10** from **6**
$P_n{}^a$ = fract. of optical purity retained in **8** from **6**
$P_n{}^e$ = fract. of optical purity retained in **7** from **6**
$R_x{}^e$ = ratio of **7**/**10** from **20**

The optical purity of the *i*th product is given by $(\mathrm{D}_i - \mathrm{L}_i)/(\mathrm{D}_i + \mathrm{L}_i)$, where D and L are arbitrary configurational symbols.

We assume (i) that all of the cationic intermediates may be treated by steady-state kinetics; (ii) that no *equatorial* product **7** arises from the *boat* classical cation **21,** which cannot be seriously in error, since only a trace of this material is found in the product from *exo* starting material **20;** and (iii) that the conversion of nonclassical ion **22a** to symmetrical classical ion **23** is essentially irreversible, *i.e.*, that $k_{17} = 0$. The justification for the latter assumption rests on the observed[7] high degree of retention of optical purity (94%) in the *axial* product **8** derived from *exo* starting material **20**; if k_{17} were important, conversion of classical ion **23** to the nonclassical ion **22b** enantiomeric with that of **22a** first generated in the system would occur and product **8** would be extensively racemized.

The algebraic form of the relationship between the ratio k_2/k_1 and experimental quantities depends on which mode of crossover occurs. Since there is presently no evidence that permits a decision on this point, we derive both cases.

Case I. Crossover between Classical Ion 15a and Classical Ion 21.—For this path it may be shown that

$$\frac{(R_n{}^a - R_x{}^a)(P_n{}^a/P_n{}^e)}{R_n{}^e} = \frac{k_2}{k_1}\left(1 - \frac{k_8\gamma k_{20}\beta}{\rho\omega}\right) \qquad (2)$$

where

$$\begin{aligned}\gamma &= k_{14} + k_{13} + k_{10} + k_{11}\\ \rho &= \alpha\beta - 2k_6k_7\\ \alpha &= k_1 + k_2 + k_6 + k_8\\ \beta &= 2k_5 + 2k_7\\ \omega &= (k_{20} + k_{15} + k_{16})\gamma - k_{14}k_{16}\end{aligned}$$

If case I applies, the term on the right of eq. 2 is essentially k_2/k_1, for the modifying element $k_8\gamma k_{20}\beta/\rho\omega$ can be shown to be very small. This term is evaluated for case I by the relationship of eq. 3. The

$$k_8\gamma k_{20}\beta/\rho\omega = R_x{}^e/R_n{}^e \qquad (3)$$

experimental quantity $R_x{}^e/R_n{}^e$ is only of the order 10^{-2} (see Table I), and therefore k_2/k_1 is given by the experimental quantity of eq. 2 to an excellent approximation. On this basis, k_2/k_1 is about 0.24 in the aqueous acetic acid solvent used for the deaminations (Table I).

Case II. Crossover between Classical Ion 15a and Nonclassical Ion 22a.—In this path, the branching point that connects the *exo*-derived to the *endo*-derived set of cations occurs not at the boat cation, which is proximal to *exo* starting material, but further on in the sequence. For this system

$$\frac{(R_n{}^a - R_x{}^a)(P_n{}^a/P_n{}^e)}{R_n{}^e} = \frac{k_2}{k_1}\left(1 - \frac{k_8\beta k_{20}\phi}{\rho\mu}\right) + \frac{k_8k_{15}}{k_1k_{16}}\left(\frac{k_8\beta k_{20}\phi}{\rho\mu} - 1\right) \qquad (4)$$

where $\phi = k_{15} + k_{16}$, $\mu = \phi\epsilon - k_{14}k_{16}$, and $\epsilon = k_{14} + k_{10} + k_{11} + k_{13} + k_{20}$. Here again, a very small modifying term may be evaluated experimentally

$$k_8\beta k_{20}\phi/\rho\mu = R_x{}^e/R_n{}^e \cong 0.01 \qquad (5)$$

Thus, to a good approximation, eq. 4 reduces to

$$\frac{(R_n{}^a - R_x{}^a)(P_n{}^a/P_n{}^e)}{R_n{}^e} = \frac{k_2}{k_1} - \frac{k_8k_{15}}{k_1k_{16}} \qquad (6)$$

The experimental quantity (0.24) is thus a minimum measure of k_2/k_1 in case II and a direct measure in case I. This fourfold or smaller preference for *equatorial* (k_1) over *axial* (k_2) attack of water on the substituted chair cyclohexyl classical cation **15a** is to be compared to the estimated[25] fivefold preference in the same sense for attack of water on the unsubstituted chair cyclohexyl cation itself. The apparent correspondence is probably fortuitous. The experimental value reported here is quite rough, since it involves a small difference between large numbers ($R_n{}^a - R_x{}^a$) as well as considerable uncertainty in the value of $P_n{}^e$; the estimate[25] for cyclohexyl cation is also only approximate. On purely steric grounds, the preference for *equatorial* attack on **15a** might be expected to be less than that on cyclohexyl cation. Scale models reveal that the C-7 methylene group of **15a** provides substantial hindrance to *equatorial* attack, thus decreasing the normal preference for this path that exists in the unsubstituted cyclohexyl cation.

Conclusions.—The ring expansion route to the 2-bicyclo[3.2.1]octyl carbonium ion system evidently generates classical cations **15** from *endo*-norbornylcarbinyl derivatives. These cations are separated from their carbon-bridged nonclassical counterparts **17** by an energy barrier roughly comparable in magnitude to that which must be overcome to give solvolysis product, and consequently some of them can be intercepted. The nonclassical cation **17** is not very much (if any) more stable than the classical one **15,** since its rate of reversible interconversion with the latter is large enough to compete readily with capture by solvent. This relationship is to be contrasted with that prevailing in the next lower homologous member of the bridged cation series, the 2-bicyclo[2.2.1]heptyl system, where reversions of nonclassical to classical ions seem to be observed only under conditions of repeated regeneration of the cationic intermediates.[2]

Entry into bridged bicyclic carbonium ion systems by the ring expansion route promises to provide a variety of further examples of the chemistry of classical ions. These should help to define the factors that control the relative importance of classical and nonclassical ions in specific cases. Some additional results in this area are described in the accompanying paper,[7] and further experiments along these lines are under way.

Experimental[26]

Deamination of *endo*-2-Aminomethylnorbornane Hydrochloride 6a. A. Racemic Series.—A sample of 17.0 g. of the amine hydrochloride[10a] was dissolved in a mixture of 50 ml. of water and 20 ml. of glacial acetic acid in a 300-ml. round-bottomed flask

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(25) A. Streitwieser, Jr., and C. E. Coverdale, *J. Am. Chem. Soc.*, **81**, 4275 (1959).

(26) Melting points were corrected (micro-hot stage); boiling points were uncorrected. Microanalyses were by Joseph F. Alicino, Metuchen, N. J. Deuterium analyses by the falling drop method were by Josef Nemeth, Urbana, Ill. Optical rotations were measured with a Rudolph Model 80 high-precision polarimeter. Ultraviolet spectra (ethanol solutions) were

fitted with an addition funnel and condenser. The solution was cooled to 5° in an ice–salt bath and treated with a solution of 13.9 g. of sodium nitrite in 30 ml. of water, while the mixture was stirred. Stirring was continued in the cold for 30 min., at room temperature for 30 min., and then on the steam bath for 90 min. The mixture was diluted with water, extracted with three portions of ether, the ethereal extract washed with 10% potassium bicarbonate, then with brine, and dried over magnesium sulfate. Evaporation of the solvent through a Vigreux column on the steam bath left 13.0 g. of a mixture of hydrocarbons (7.5%) and alcohols (92.5%), with less than 1% of other contaminants, which may have been acetates, nitrates, or nitrites. A small portion of the mixture was acetylated and the resulting acetate mixture analyzed with the 6-mm. column. The chromatogram showed no peak in the region where *endo*-2-norbornylcarbinyl acetate would have emerged, as determined with an authentic sample. Under these conditions, 1% of this product could have been detected. Analysis of the deamination product with the capillary column gave the results shown in Table I.

Authentic samples of *equatorial*- and *axial*-2-bicyclo[3.2.1]-octanols (**7** and **8**) were obtained by preparative vapor chromatography. The infrared spectra of these alcohols corresponded well to those of **7** and **8** prepared by Goering and co-workers,[13] to whom we are indebted for copies.

B. Optically Active Series.—A sample of 14.1 g. of (−)-*endo*-2-aminomethylnorbornane hydrochloride (**6a**), $[\alpha]^{26}\mathrm{D}$ −3.87° (*c* 5.37 in 95% ethanol), prepared[10a] from (+)-*endo*-2-norbornanecarboxylic acid, $[\alpha]^{26}\mathrm{D}$ +16.05° (*c* 6.64 in 95% ethanol, 52.4% optically pure),[10b] was dissolved in 50 ml. of water and 20 ml. of glacial acetic acid, stirred at 5°, and treated during 45 min. with a solution of 11.5 g. of sodium nitrite in 20 ml. of water. Completion of the reaction and isolation of the product were carried out as in the racemic case to give 10.0 g. of a 92:8 mixture of alcohols and olefins.

Preparative gas chromatographic fractionation of the mixture was carried out with the column described above. The *axial*-2-bicyclo[3.2.1]octanol (**8**) emerged earlier than the *equatorial* isomer **7**. Alcohol **8** was obtained after successive passes; $[\alpha]^{25}\mathrm{D}$ −3.67° (*c* 3.6 in 95% ethanol, *l* 1), homogeneous in capillary vapor chromatography under conditions where 1% contamination by **7** or **10** would easily have been detected. Alcohol **7** was successively refractionated with the same technique; four successive passes were required to give material of $[\alpha]^{26}\mathrm{D}$ +0.684° (*c* 3.76 in 95% ethanol, *l* 4), $[\alpha]^{31}\mathrm{D}$ +0.858° (*c* 7.0 in $\mathrm{CHCl_3}$, *l* 1) containing 4% of **10**; the rotations of the material from the third and fourth successive cuts were identical within experimental error, the third cut having $[\alpha]\mathrm{D}$ +0.699° (*c* 5.4 in 95% ethanol, *l* 4).

Correlation of the Rotations of *equatorial* (7) and *axial* (8) 2-Bicyclo[3.2.1]octanol *via* 2-Bicyclo[3.2.1]octanone (9).—A sample (225 mg., 1.78 mmoles) of the above specimen of **7**, $[\alpha]^{26}\mathrm{D}$ +0.684° (95% ethanol), in 25 ml. of sodium-dried benzene was treated with 392 mg. (3.62 mmoles) of *p*-benzoquinone and 780 mg. (3.16 mmoles) of aluminum *t*-butoxide. The heterogeneous mixture was boiled at reflux for 72 hr. with protection from moisture, cooled, filtered, and the insoluble material washed with benzene. The combined filtrate and washings were washed with cold 5% sulfuric acid, then with 10% sodium hydroxide, and then with brine. After having been dried over magnesium sulfate, the benzene was removed by azeotropic distillation with methanol through a Vigreux column. The residue was transferred to a 10-cm. test tube, the last traces of solvent removed by brief, cautious warming on the steam bath, and the ketone **9** (85 mg., 39%) obtained by stoppering the test tube and subliming the residue in an oil bath at 125°. Thus obtained, **9** had $[\alpha]^{28}\mathrm{D}$ +5.34° (*c* 4.53 in 95% ethanol, *l* 1). Vapor chromatography showed it to be free of unreacted alcohols.

A sample of 244 mg. (1.93 mmoles) of *axial*-2-bicyclo[3.2.1]-octanol (**8**),[7] $[\alpha]^{29}\mathrm{D}$ +5.21° (95% ethanol), in 25 ml. of benzene was treated with 425 mg. (3.92 mmoles) of *p*-benzoquinone and 845 mg. (3.42 mmoles) of aluminum *t*-butoxide. The oxidation was carried out as for the *equatorial* isomer to give 87.5 mg. (37%) of ketone **9**, $[\alpha]^{28}\mathrm{D}$ −50.3° (*c* 4.46 in 95% ethanol, *l* 1), $[\alpha]\mathrm{D}$ −53.7° (*c* 0.8 in $\mathrm{CHCl_3}$, *l* 1). Vapor chromatography showed it to be free of unreacted alcohols. The retention times of the two optically active samples of **9** thus prepared were identical with that of an authentic sample of racemic **9**, which had m.p. 128.5–130°, semicarbazone m.p. 173° (reported[8] m.p. 129°; semicarbazone, m.p. 175°).

A solution of 41.5 mg. (0.334 mmole) of the above optically active sample of ketone **9**, $[\alpha]\mathrm{D}$ −50.3° (95% ethanol), in dry ether was added dropwise during 45 min. to a stirred mixture of excess lithium aluminum hydride in ether. The reaction mixture was stirred overnight at room temperature and then cautiously treated with small portions of saturated sodium sulfate solution until the solid material became white and granular. The mixture was filtered and the filter cake was washed several times with fresh ether. The combined filtrate and ether solutions were treated with water, the ether layer was separated, and the aqueous layer was washed with fresh ether. The combined ethereal extracts were washed with brine, dried over magnesium sulfate, distilled to dryness under a Vigreux column, and sublimed to give a mixture of 78% of *equatorial*-**7** and 22% of *axial*-**8** alcohols; the mixture showed no other components by vapor chromatographic analysis. It had $[\alpha]^{24}\mathrm{D}$ −4.24° (*c* 2.62 in 95% ethanol, *l* 1). The specific rotation of the pure *equatorial*-alcohol **7** in this mixture was calculated from the equation $0.78[\alpha]\mathrm{D} + 0.22°(5.21) = -4.24°$ and is therefore $[\alpha]\mathrm{D}$ −6.95° (95% ethanol). The ratio of rotations **7**/**8**, when both have same optical purity, is therefore 1.33. This value is more reliable than the value 1.23 calculated from the correlation described above in which **7** and **8** both were oxidized to **9**, since the sample of **7** used there contained 4% of **10**. Nevertheless, since both correlations agree to within about 8%, the contribution of **10** to the rotation of this sample of **7** must be small. Furthermore, its presence can have no substantial effect on the correlation of the rotation of **7** in alcohol with that in chloroform, since this solvent change is virtually without effect on the rotation of **10**.[7]

Preparation of (−)-*endo*-2-Hydroxymethylnorbornane *p*-Bromobenzenesulfonate (6c).—Preparation of (+)-*endo*-2-hydroxymethylnorbornane (**6b**), $[\alpha]^{26}\mathrm{D}$ +3.54° (*c* 3.45 in 95% ethanol, *l* 1), was achieved by lithium aluminum hydride reduction of (−)-*endo*-2-norbornanecarboxylic acid, $[\alpha]^{26}\mathrm{D}$ −14.1° (*c* 3.44 in 95% ethanol, *l* 1), 46.1% optically pure,[10b] by the procedure already described.[10a] The ratio of rotations acid/carbinol was thus 3.98, in exact agreement with the value found in the enantiomeric series used for the preparation of the amine.[10a]

A solution of 8.2 g. of the above carbinol **6b** in 25 ml. of pyridine (freshly distilled from potassium hydroxide pellets) was cooled in ice–water and treated dropwise during 30 min. with a solution of 35.2 g. of *p*-bromobenzenesulfonyl chloride, m.p. 75°, in 25 ml. of dry pyridine. The mixture was stirred and slowly allowed to come to room temperature. After 23 hr., it was poured onto 20 ml. of concentrated hydrochloric acid and 100 g. of cracked ice, whereupon a solid separated. The entire mixture was extracted with three portions of ether, and the ethereal extract was washed successively with several portions of 10% potassium bicarbonate solution and then with brine. After having been dried over magnesium sulfate, the ether solution was distilled to dryness to give 19.8 g. (96%) of crude sulfonate ester **6c**, m.p. 89–90°, $[\alpha]^{28}\mathrm{D}$ −2.01° (*c* 9.15 in $\mathrm{CHCl_3}$, *l* 1).

A sample of racemic **6c**, m.p. 87–87.5° (from hexane), was prepared in the same manner for elemental analysis. The infrared spectra of the active and racemic materials were identical.

Anal. Calcd. for $\mathrm{C_{14}H_{17}O_3BrS}$: C, 48.64; H, 4.96. Found: C, 48.92; H, 5.22.

Acetolysis of Optically Active 6c.—A solution of 19.06 g. of **6c**, $[\alpha]^{28}\mathrm{D}$ −2.01°, in 620 ml. of 0.72 *M* sodium acetate in glacial acetic acid was kept at 110° under a reflux condenser for 47 hr., cooled, and poured onto cracked ice. The cold mixture was carefully neutralized with solid sodium carbonate and extracted with three portions of ether. The ethereal extract, after having been washed with 10% potassium bicarbonate and with brine, was dried over magnesium sulfate and evaporated to give 7.76 g. of a mixture of olefins (8.2%) and acetates (91.8%). The olefin/acetate ratio may be in error because the volatility of the olefins makes their quantitative recovery in evaporative procedures difficult. Capillary vapor chromatographic analysis showed the presence of 2.9% of *endo*-2-norbornylcarbinyl acetate (**6b**, OH = OAc). The solvolysis product was dissolved in 30 ml. of dry ether and reduced with lithium aluminum hydride, according to the procedure described above for reduction of the ketone **9**, to give 5.2 g. of material. The composition of the alcohol fraction, determined by capillary vapor chromatography, is given in Table I.

Preparative vapor chromatographic separation of the alcohol components was carried out as in the case of the deamination product described above. In this manner, there were obtained: (1) *equatorial*-alcohol **7**, $[\alpha]^{24}\mathrm{D}$ 0.00° (*c* 30 in $\mathrm{CHCl_3}$, *l* 1), homogeneous by capillary v.p.c.; (2) *axial*-alcohol **8**, $[\alpha]^{24}\mathrm{D}$ +0.90° (*c* 2.77 in 95% ethanol, *l* 1), vapor chromatographically homo-

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measured with a Cary spectrophotometer, Model 14PM. Infrared spectra were taken with a Perkin–Elmer Infracord spectrophotometer Model 137 and were calibrated for wave length with a polystyrene reference. Nuclear magnetic resonance spectra were taken with a Varian A-60 instrument.

Vapor chromatographic analyses were carried out with two instruments: (i) Perkin–Elmer fractometer Model 154C, using a 2 m. × 6 mm. column of 20% tri-(β-cyanoethoxy)-propane (TCEP) on 40–60 mesh Johns–Manville Chromosorb-P at a column temperature of 115° and a helium flow rate of *ca.* 85 ml./min.; (ii) Barber–Colman gas chromatograph Model 20, using a 46-m. stainless steel capillary coated with TCEP at a column temperature of 100° and an argon pressure of 45 p.s.i. Preparative vapor chromatographic separations were carried out with a 4 m. × 22 mm. 20% TCEP-coated Chromosorb-P column in the apparatus previously described,[27] using column temperatures of about 130° and helium flow rates of 1100 ml./min.

[27] J. A. Berson, C. J. Olsen, and J. S. Walia, *J. Am. Chem. Soc.*, **84**, 3337 (1962).

geneous; (3) a mixture of 0.9% of **8**, 84.1% of **7**, and 15% of **10**, which had an observed rotation of +0.038 ± 0.02° (*c* 22.73 in $CHCl_3$, *l* 1). The specific rotation of the **10** in this mixture is thus $[\alpha]^{25}\mathrm{D}$ +1.13 ± 0.6° ($CHCl_3$); (4) a mixture of 1.8% of **8**, 21.2% of **10**, and 77.0% of **7**, which had an observed rotation +0.049 ± 0.01° (*c* 20.0 in $CHCl_3$, *l* 1). The specific rotation of the **10** in this mixture is thus $[\alpha]^{26}\mathrm{D}$ +1.15 ± 0.3° ($CHCl_3$).

Control Experiment on Optical and Chemical Stability of Solvolysis Products.—A synthetic mixture of **7**, **8**, and **10** (each optically active) was prepared. It had $[\alpha]^{24}\mathrm{D}$ −5.02° (*c* 9.6 in 95% ethanol, *l* 1) and consisted of 17.5% of **8**, 23.0% of **10**, and 59.5% of **7**. A sample (95.8 mg.) of this mixture, 0.6 ml. of acetic anhydride, and 200 mg. of potassium *p*-bromobenzenesulfonate in 3 ml. of a solution of 0.72 *M* sodium acetate in glacial acetic acid was held at 115° for 60 hr. After work-up and lithium aluminum hydride reduction in the manner used in the solvolysis of **6c**, the alcohol mixture recovered had $[\alpha]^{24}\mathrm{D}$ −5.05° and a composition of 17.3% of **8**, 23.2% of **10**, and 59.5% of **7**.

Preparation of ***exo*****-2-Deuterio-2-*****endo*****-norbornylcarbinyl *p*-Bromobenzenesulfonate (6c-*d*).**—*t*-Butyl alcohol-O-*d* was prepared by the reaction of equimolar quantities of twice-sublimed potassium *t*-butoxide and 99.5% deuterium oxide (General Dynamics Corp.). The deuterated alcohol was distilled at atmospheric pressure through a Vigreux column and stored in a paraffin-sealed glass-stoppered flask in a desiccator.

A 13.0-g. sample of mixed *endo*- and *exo*-2-carbomethoxynorbornene (b.p. 78–88° at 35 mm., prepared from cyclopentadiene and methyl acrylate) was treated with 12.53 g. of twice-sublimed potassium *t*-butoxide and 128.0 g. of *t*-butyl alcohol-O-*d*. The mixture was kept at 105° in a nitrogen atmosphere under an air condenser for 22 hr. Distillation of the methanol and *t*-butyl alcohol at atmospheric pressure was followed by vacuum distillation of the residue at 120° and 35 mm. to give 11.96 g. of a mixture of deuterated *t*-butyl esters (95%) and methyl esters (5%). This material was dissolved in 100 ml. of dry ether and the solution was added during 30 min. to a stirred suspension of 6.0 g. of lithium aluminum hydride in 250 ml. of dry ether under a reflux condenser. The mixture was stirred at room temperature for 2 hr. and then at reflux (bath at 42–45°) for 21 hr. After hydrolysis, isolation of the product was accomplished in the same manner described[10a] for the undeuterated alcohols. This material consisted of a 2:1 mixture of *endo*-2-deuterio-2-*exo*-hydroxymethylnorbornene-5 and the *exo*-deuterio-*endo*-carbinol isomer (capillary v.p.c.). Two passes through the preparative vapor chromatography column gave 1.30 g. of epimerically pure *exo*-2-deuterio-*endo*-2-hydroxymethylnorbornene-5. Capillary vapor chromatography showed no contamination with the epimeric carbinol under conditions where 0.1% could have been detected. The infrared spectrum showed C–D stretching absorption at 2175 cm.$^{-1}$.

The pure deuterated carbinol was dissolved in 10 ml. of methanol containing a trace of water and hydrogenated over 0.105 g. of platinic oxide at room temperature and atmospheric pressure. The reaction ceased after consumption of 256 ml. (1.05 moles) of gas, whereupon the catalyst was filtered off, washed with methanol, and the filtrate evaporated to give a quantitative yield (1.303 g.) of *exo*-2-deuterio-*endo*-2-hydroxymethylnorbornane. The vapor chromatographic retention time was identical with that of an undeuterated sample.

The above saturated carbinol in 7 ml. of dry pyridine was chilled in an ice–water bath, stirred, and treated dropwise with 5.6 g. of *p*-bromobenzenesulfonyl chloride. After 2 hr. in the cold and 16 hr. at room temperature, the mixture was worked up as in the preparation of undeuterated **6c** to give 3.106 g. of **6c-*d***, m.p. 81–87°. This material was free of unreacted carbinol (<2%) as judged by its infrared spectrum. A small sample recrystallized to constant m.p. (86.5–87.5° from hexane) was analyzed in duplicate for deuterium by the falling drop method. It had 4.64 and 4.70 atom % excess D (0.794 atom of D per molecule).

In a control experiment to check the possibility of exchange of deuterium during catalytic hydrogenation, a sample of distilled mixed unsaturated *exo*- and *endo*-2-deuteriocarbinols **34** was hydrogenated under the same conditions as above. Samples of the original **34** and the distilled product saturated carbinols **35** were analyzed by the falling drop method. The sample of **34** had 7.57 atom % excess D (0.91 atom of D per molecule); the sample of **35** had 6.41 atom % excess D (0.90 atom of D per molecule).

Acetolysis of ***exo*****-2-Deuterio-*****endo*****-2-norbornylcarbinyl *p*-Bromobenzenesulfonate.**—The above sample (3.1 g.) of **6c-*d*** was dissolved in 100 ml. of a 0.72 *M* solution of sodium acetate in glacial acetic acid and heated at reflux for 45 hr. (bath at 125°). After work-up according to the procedure used in the acetolysis of undeuterated material **6c**, there was obtained 1.33 g. (97% calculated as acetates) of a mixture of hydrocarbon (7%) and acetates (93%). Capillary v.p.c. showed that 2.1% of the acetate portion of the product was *endo*-2-norbornylcarbinyl acetate (**6b**, OH = OAc). Lithium aluminum hydride reduction according to the procedure used in the undeuterated series and capillary v.p.c. analysis indicated the composition 12.7% of **8**, 10.8% of **10**, and 76.5% of **7**, in agreement with the previous results. No *meso*-alcohol **11** was observed under conditions that permitted detection of as little as 0.3%.

Preparative v.p.c. of the alcohol mixture gave two fractions of deuterio-**7**: (A) 97.2% **7**, 0.8% **8**, 2% **10**; (B) 88% **7**, 2% **8**, 10% **10**. Fraction A had 5.77 atom % excess deuterium (falling drop) or 0.808 atom of D per molecule.

cis**-3-Carboxycyclopentaneacetic acid**[8c] was prepared by adding in small portions 340 mg. of a mixture of alcohols derived from acetolysis of racemic **6c** to 2.0 ml. of concentrated nitric acid cooled in an ice–water bath. Brown fumes appeared at once. The solution was allowed to warm to room temperature, then was warmed on the steam bath for 45 min. and poured onto a small amount of ice. The mixture was extracted with three portions of ether; the extract was dried over magnesium sulfate and evaporated to give 302 mg. of crude acid. Recrystallization from ethyl acetate–hexane gave material of m.p. 137–139°, reported[8c] m.p. 139°.

trans**-3-Carboxycyclopentaneacetic acid** was obtained by heating 128 mg. of the *cis* isomer in a sealed tube with 1 ml. of 1 *N* hydrochloric acid at 180° for 6 hr. The mixture was diluted with water and extracted with ether, and the extract was dried over magnesium sulfate. Evaporation gave 109 mg. of crude *trans*-acid, m.p. 124.5–128°. Several recrystallizations from ethyl acetate–hexane gave material, m.p. 129.5–131°, unchanged upon further recrystallization.

Anal. Calcd. for $C_8H_{12}O_4$: C, 55.74; H, 7.03. Found: C, 55.86; H, 7.09.

trans**-3-Carboxycyclopentaneacetic acid-d_3** was prepared by repeating the above experiment with 85 mg. of the *cis*-acid and 1 ml. of 1 *N* deuterium chloride in deuterium oxide. The deuterium chloride was generated by the action of deuterium oxide on phosphorus pentachloride. Isolation of the product as before gave 76 mg. of crude deuterated *trans*-acid, which after having been twice evaporated to dryness from solution in ordinary water, was recrystallized from ethyl acetate–hexane and had m.p. 129–130.5°. This material had 24.14 atom % excess D (falling drop) or 2.9 atoms D per molecule. The nuclear magnetic resonance (n.m.r.) spectrum of undeuterated *trans*-acid in deuterium oxide showed the methinyl proton absorption as a complex multiplet centered about 1.86 p.p.m. upfield from the sharp O–H peak and the methylene protons as a broad intense peak centered at about 0.5 p.p.m. still further upfield. The areas of the two peaks were in the approximate ratio 1:2. In the trideuterio acid, both peaks had all but vanished.[28]

Degradation of Deuterated *equatorial*-Alcohol 7 from the Acetolysis. A. *trans*-3-Carboxycyclopentaneacetic Acid.—Nitric acid oxidation of 100 mg. of fraction A of the reaction mixture from acetolysis of *exo*-2-deuterio-2-*endo*-norbornylcarbinyl *p*-bromobenzenesulfonate gave 88 mg. of *cis*-3-carboxycyclopentaneacetic acid, which was heated at 185° for 15.5 hr. with 1 *N* hydrochloric acid. The *trans*-acid, isolated as in the preparation of the trideuterio acid, showed 0.01 atom % excess D (falling drop) or 0.00 atom of D per molecule.

B. 2-Bicyclo[3.2.1]octanone (9).—Oppenauer oxidation of 310 mg. of fraction B with 585 mg. of quinone and 1.07 g. of aluminum *t*-butoxide in 15 ml. of benzene was carried out as in the optically active series described above, whereupon 98 mg. of ketone was obtained free of unreacted alcohols as judged by capillary v.p.c. Analysis (falling drop) of a sublimed sample showed 3.91 atom % excess D or 0.47 atom of D per molecule.

Application of the same procedure to fraction A gave 80 mg. of ketone **9**.

C. Quinoxaline of 2,3,4-bicyclo[3.2.1]octanetrione (42)[8b] was prepared by heating 120 mg. of 2-bicyclo[3.2.1]octanone (**9**) (unlabeled) in 1.5 ml. of xylene to 145–150° (oil bath temperature) and adding in small portions 270 mg. of selenium dioxide which had been freshly sublimed after moistening with a drop of nitric acid. After 6 hr. at reflux and overnight at room temperature, the xylene was filtered off and the gray metallic selenium was washed throughly with hot benzene. The combined xylene and benzene solutions were carefully evaporated and the residue (126 mg.) was sublimed at 130–140° at 1 mm. to give 12.5 mg. of dark red crystals and 10.0 mg. of yellow crystals. Conversion of the red material to the quinoxaline **42** was accomplished by treating it with 9.0 mg. of *o*-phenylenediamine in 1 ml. of acetic acid. The product, after recrystallization from ethyl acetate–hexane, weighed 10 mg. and had m.p. 146.5–149° (reported[8b] m.p. 143°). The infrared spectrum showed bands at 1720 (carbonyl) and 765 cm.$^{-1}$ (four adjacent hydrogens on a benzene ring); the ultraviolet spectrum showed $\lambda_{\max}$ 238 mμ (ϵ 21,000), 242 (21,600), 251 (16,000), and 316 (7850).

When the same procedure was carried out on the ketone **9** derived by oxidation of fraction A, there were obtained 2 mg. of quinoxaline **42**. Mass spectrometric analyses of this material were carried out by Dr. K. Biemann of the Massachusetts Institute of Technology. They were run at 70, 18, and 13 e.v.

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[28] We are indebted to Dr. E. W. Warnhoff for the spectra.

and showed the composition 59 ± 1% d_0 species and 41 ± 1% of d_1 species, corrected for the M − 1 and ^{13}C isotope peaks. The two major peaks in the parent peak region occurred at M = 224 (**42**) and M = 225 (**42**-d_1). The quinoxaline **42** thus retains 0.41/0.808 or 51 ± 1% of the deuterium label originally present in the **7** derived by acetolysis.

Control Experiment on Exchange in 2-Bicyclo[3.2.1]octanone.—A solution of 0.40 g. of the ketone and 1.03 g. of sodium methoxide in 4.0 ml. of 99.5% deuterium oxide and 1.0 ml. of methanol-*d* (prepared from the reaction of equivalent amounts of dry sodium methoxide and deuterium oxide) was sealed in a sturdy tube and heated at 100° for 12 hr. The contents of the tube were diluted with deuterium oxide and the ketone was extracted with three portions of sodium-dried ether. After having been washed to neutrality with several portions of deuterium oxide, the solution was dried over anhydrous magnesium sulfate and evaporated through a Vigreux column. The residue was sublimed and the product analyzed for deuterium by the falling drop method. It had 15.25 atom % excess D, or 1.83 atoms of D per molecule. The n.m.r. spectrum[28] of this material in carbon disulfide showed, by comparison with that of an undeuterated sample, very little change in the broad α-carbonyl methinyl multiplet centered about 2.5 p.p.m. (downfield from tetramethylsilane) but a marked diminution in the intensity of the higher field α-carbonyl methylene multiplet centered roughly at 2.1 p.p.m. When this sample of deuterated ketone was submitted to the above-described Oppenauer oxidation conditions, it was recovered (in 30% yield) with only 4.04 atom % excess D (0.49 atom of D per molecule), as shown by analysis using the falling drop method.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF SOUTHERN CALIFORNIA, LOS ANGELES 7, CALIF.]

The Ring Expansion Route to Bicyclic Carbonium Ions.
II. The Multiple Rearrangement of the *exo*-2-Norbornylcarbinyl System[1a–c]

BY JEROME A. BERSON[1d] AND DAVID WILLNER[1e]

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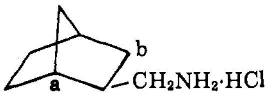
The carbonium ions derived by ring expansion in the *exo*-2-norbornylcarbinyl system are distinct from and only inefficiently converted to those of the corresponding *endo* series. In the *exo* series, the major products have the Wagner–Meerwein related pair of structures 2-*exo-axial*-bicyclo[3.2.1]octyl and 2-bicyclo[2.2.2]octyl. Substantial amounts of product with the 3-bicyclo[3.2.1]octyl structure also occur, but very little of the 2-*endo-equatorial*-bicyclo[3.2.1]octyl product is found. From optically active *exo*-2-norbornylcarbinylamine there are obtained by the nitrous acid deamination in glacial acetic acid optically active *exo-axial*-2-bicyclo[3.2.1]octyl acetate with nearly complete retention of optical purity and substantially but incompletely racemized 2-bicyclo-[2.2.2]octyl acetate. The results are most simply embodied in a mechanism that involves sequential formation of both classical and nonclassical ions.

The rearrangements of cations derived from the 2-*exo*-norbornylcarbinyl ring system provide instructive comparisons with those derived from the *endo* isomer described in the accompanying paper.[2] In qualitative accord with a previous report,[3] we find that nitrous acid in aqueous acetic acid converts racemic 2-*exo*-norbornylcarbinylamine hydrochloride (**1**) to a mixture of alcohols, among which are readily identified (by capillary gas chromatography) 2-*exo-axial*-bicyclo[3.2.1]-octanol (**2**, 37%)), 2-bicyclo[2.2.2]octanol (**4**, 41%), 3-bicyclo[3.2.1]octanol (**3**, 19%), and 2-*endo-equatorial*-bicyclo[3.2.1]octanol (**5**, 3%).

Three products corresponding to the gross structures **2**, **3**, and **4** were reported by Alder and Reubke,[3] although the method of identification (by oxidation to the ketones and isolation of benzylidene derivatives) precluded any stereochemical assignments in the cases (**2** and **3**) in which epimeric products might have been formed.[3] Alcohol **3**, isolated as described below, is a crystalline solid with a sharp melting point, and it emerges from vapor chromatograms as a single symmetrical peak. These properties suggest but do not prove that the **3** formed in the deamination is a single stereoisomer.

Similar results are observed when the deamination is carried out in glacial acetic acid, the corresponding acetates being formed in about the same proportions as the alcohols in aqueous deamination. In the acetic acid deamination, about 3% of nitrogenous contaminants, probably nitrate esters,[4,5] and traces of alcohol and hydrocarbon also accompany the major products.



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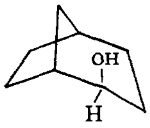

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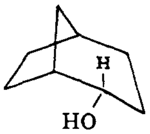

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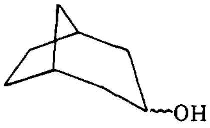

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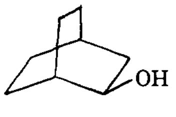

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Final identification of the three major products **2**, **3**, and **4**, is achieved by preparative vapor chromatographic isolations and comparisons of melting points, mixture melting points, and infrared spectra with those of authentic samples prepared by methods described in the Experimental section.

As was already clear from the work of Alder and Reubke,[3] the *endo*- and *exo*-norbornylcarbinyl cations both lead into the bicyclo[3.2.1]octyl system by ring expansion, but the two reaction courses retain specificity to a substantial degree. The differences in product distribution are summarized for a variety of reaction conditions and methods of generating the cations in Table I. Also given are the results of experiments with optically active **1** to be discussed later.

As the starting material is changed from *endo*-**6** to *exo*-**1** the yield of the *equatorial*-alcohol **5** falls drastically, and the proportions of products **2**, **3**, and **4** increase. The substance of unrearranged structure, *exo*-2-norbornylcarbinyl acetate (**1**, X = OAc), is

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[1] (a) The support of part of this work by the National Science Foundation through Grant NSF-G11386 is gratefully acknowledged. For preliminary reports, see (b) J. A. Berson and D. Willner, *J. Am. Chem. Soc.*, **84**, 675 (1962); (c) J. A. Berson in "Molecular Rearrangements," P. de Mayo, Ed., Interscience Publishers, Inc., New York, N. Y., 1963, pp. 221–226; *cf.* also Abstracts of the Eighteenth National Organic Chemistry Symposium of the American Chemical Society, Columbus, Ohio, June 16–20, 1963, pp. 23–30. (d) To whom inquiries should be addressed at Department of Chemistry, University of Wisconsin, 1112 W. Johnson St., Madison, Wis. (e) On leave of absence from the Weizmann Institute of Science, Rehovoth, Israel.

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

[3] K. Alder and R. Reubke, *Chem. Ber.*, **91**, 1525 (1959).

[4] *Cf.* A. Streitwieser, Jr., and W. D. Schaeffer, *J. Am. Chem. Soc.*, **79**, 2888 (1957).

[5] J. A. Berson and D. A. Ben-Efraim, *ibid.*, **81**, 4094 (1959).