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.

Acknowledgment.—We are much indebted to Dr. K. Biemann, Massachusetts Institute of Technology, for the mass spectrometric analyses.

[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]

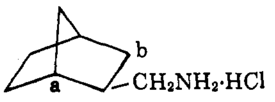
BY JEROME A. BERSON[1d] AND DAVID WILLNER[1e]

RECEIVED AUGUST 26, 1963

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.



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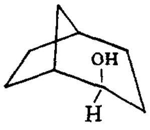

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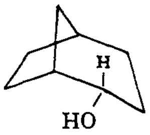

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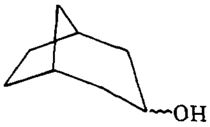

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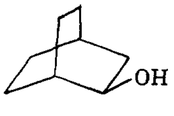

4

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.

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).

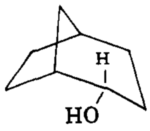
[3] K. Alder and R. Reubke, *Chem. Ber.*, **91**, 1525 (1959).

[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).

Table I

Distribution of Products from the *endo*- and *exo*-2-Norbornylcarbinyl Systems



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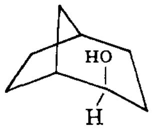

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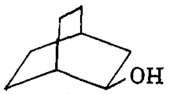

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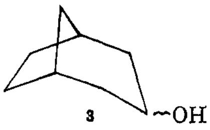

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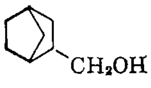
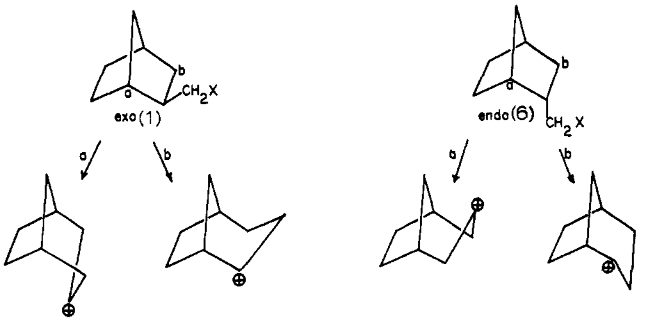


	5		**2**		**4**		**3**	
Reactants	Yield, %	O.P.[a]	Yield, %	O.P.[a]	Yield, %	O.P.[a]	Yield, %	Yield, %[d]
endo-NH_2 + HONO + H_2O + HOAc	83	7–13	9	50	7	[b]	0	0
endo-OBs + HOAc + NaOAc[c]	77	0	12.5	14	10.5	6	0	2.9
exo-NH_2 + HONO + H_2O + HOAc	3		37	[b]	41	[b]	19	~0
exo-NH_2 + HONO + HOAc[c]	<5	[b]	35–40	94	35–40	55 ± 7	17–20	~0

[a] O.P. = % optical purity retained. [b] Not determined. [c] Product distribution refers to acetates in this case. [d] Stereochemistry of this product corresponds to that of the starting material.

absent from the product of the deamination of *exo*-2-norbornylcarbinylamine, a result that corresponds to that in the *endo* series, where the products also arise virtually exclusively from ring expansion (Table I).



Conformational effects seem to play a large role in determining which of the two possible modes of ring expansion (a or b) predominates in the *endo* and *exo* systems. On purely electronic grounds, migration of carbon a (secondary) of **1** or **6** should be preferred over that of carbon b (primary).[6,7] As is shown in Table II and the accompanying diagram, however, migration a leads to a boat-like ring expansion product in the case of *endo* starting material **6**. Some of the disadvantages of this conformation probably come into play even in the transition state for its formation, thereby counteracting the electronic effect and increasing the energy of this transition state relative to that of the alternative one for migration b, which leads to a chair-like ring-expanded cation from the *endo* starting material. The conformational effects are reversed in the *exo* case **1**, where migration a leads to a chair and b to a boat. In a qualitative sense, the greater a/b ratio observed in the *exo* case (product **3** being a measure of migration a) is therefore reasonable. This analysis is nevertheless clearly oversimplified, since if the a/b ratio were merely the result of a composite of the electronic and conformational effects discussed above, migration a in the *exo* case, where the effects reinforce each other, should actually predominate over b. Experimentally, the process a is less than a fifth as important as b (see Table II). At present, it does not seem fruitful to speculate on the influence of such subtle but potentially decisive additional factors as the relative populations of the various conformations available to the side chain, the role of anchimeric assistance in the ring expansion, and the effects of differing extents of bond-angle distortion in the four transition states.

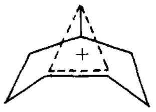
Table II

Starting material	Migration	Subst. type of mig. group	Conform. of new cation	Found, %
exo-**1**	a	2°	Chair	18[a]
exo-**1**	b	1	Boat	82[b]
endo-**6**	a	2	Boat	<1[a]
endo-**6**	b	1	Chair	~100[b]

[a] Percentage of product **3**. [b] Percentage of products **2** + **4** + **5**.

Migration b in the *exo* starting material **1** gives a 2-bicyclo[3.2.1]octyl cation that is clearly different from that derived by migration b in the *endo* system **6**. From the *endo* derived cation, the major product has the *endo-equatorial*-2-bicyclo[3.2.1]octyl structure and stereochemistry, whereas the *exo*-derived cation gives very little of this material and, for the most part, is partitioned nearly equally between products of the *exo-axial*-2-bicyclo[3.2.1]octyl and 2-bicyclo[2.2.2]octyl structures. The possible origins of this efficient but not quite perfect insulation between the two cation systems are discussed in the accompanying paper.[2] We are primarily concerned here with the formulation of detailed structures for the *exo*-derived cations.

As in the *endo* case,[2] we employ the symmetry properties of the system as a mechanistic probe. Operationally, the symmetry criterion in the *exo* case is the converse of that in the *endo*. In the latter example,[2] racemization was linked to the intervention of a mesomeric cation (**7**), but the corresponding cation in the *exo* case (**8**) would be optically active if formed from active starting material; it is one of the classical species, the symmetrical 2-bicyclo[2.2.2]octyl cation **9**, that can lead to racemization here.



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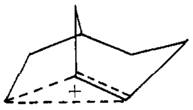

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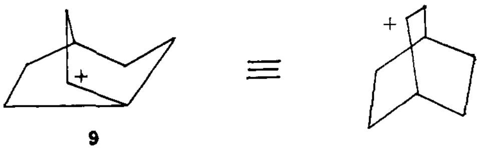

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Results

By a sequence similar to that described[2] in the *endo* series, (−)-*exo*-2-norbornanecarboxylic acid[9] is converted[10] to (−)-*exo*-2-norbornylcarbinylamine hydrochloride (**1**). Deamination in glacial acetic acid gives a mixture of the four acetates **2**, **3**, **4**, and **5** (OH =

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(6) M. Stiles and R. P. Mayer, *J. Am. Chem. Soc.*, **81**, 1497 (1959).

(7) S. Winstein, P. Magee, and K. Nelson, unpublished work, cited by P. Magee, Dissertation, University of California at Los Angeles, 1955, and in ref. 8.

(8) J. A. Berson and S. Suzuki, *J. Am. Chem. Soc.*, **81**, 4088 (1959).

(9) J. A. Berson and D. A. Ben-Efraim, *ibid.*, **81**, 4083 (1959).

(10) J. A. Berson, J. S. Walia, A. Remanick, S. Suzuki, P. Reynolds-Warnhoff, and D. Willner, *ibid.*, **83**, 3986 (1961).

OAc), which lithium aluminum hydride converts to a mixture of the corresponding alcohols.

The *endo-equatorial*-2-bicyclo[3.2.1]octanol (**5**) is present in only minute amount, and we have not yet succeeded in isolating a fraction sufficiently enriched in it for a determination of its optical rotation. The remaining three alcohols are separated by repeated cycles of preparative vapor chromatography. Although capillary vapor chromatography separates the three alcohols well enough to produce distinct peaks with very little overlap, the packed columns necessary for preparative work have much inferior resolving power, and the three peaks overlap seriously. The preparative isolation of the components of the mixture is therefore exceptionally tedious and difficult, five cycles being required for the *exo-axial*-2-bicyclo[3.2.1]-octanol (**2**) and eight for 2-bicyclo[2.2.2]octanol (**4**). By the criteria described in the Experimental section, these alcohols are obtained substantially homogeneous. Both are optically active. From starting material 40.7% optically pure, there are obtained **2** with $[\alpha]_D$ +5.25° (ethanol), and **4** with $[\alpha]_D$ +8.97° (chloroform), $[\alpha]_D$ +8.79° (ethanol). In addition, the *meso*-alcohol 3-bicyclo[3.2.1]octanol (**3**) is obtained optically inactive, $[\alpha]_D$ 0.00° (ethanol). The accurately zero rotation of **3** provides a measure of confidence in the efficacy of the separations that is independent of and supplementary to the other criteria described in the Experimental section.

Calculation of the fraction of the original 40.7% of optical purity persisting in the product alcohols **2** and **4** requires a knowledge of the rotations of enantiomerically pure materials. Although an optical activation of 2-bicyclo[2.2.2]octanol (**4**) *via* the brucine salt of the acid phthalate is reported[11] to lead to **4** of $[\alpha]_D$ −7.45° (chloroform), it is apparent that this rotation does not represent optical purity. The value at optical purity must be at least 22°, since 8.97° represents a maximum of 40.7% optical purity. In a repetition of the reported[11] optical activation of **4** acid phthalate, we find that the resolution proceeds very slowly and is made still more difficult by the peculiar solubility properties of the system, which concentrate the more highly resolved salt in the mother liquors of each crystallization. The problem is soluble in principle with the isotopic dilution technique,[8,9,12] which in the original applications[8,9] involves reisolation of racemic material by fractionation of a labeled, partially resolved sample. In the present case, partially resolved **4** acid phthalate does not fractionate upon recrystallization, the rotation remaining virtually unchanged. A variation of the technique, first used by Goering and Doi,[13] involves adding x g. of labeled racemic carrier of specific radioactivity C_0 to B g. of optically active material of specific rotation α_0 and re-resolution. When the resolution is carried to the point where α_0 is again achieved,[13] the weight E_1 of excess enantiomer in the starting sample is given by eq. 1, where C is the specific radioactivity of the reisolated sample. In the more general case of

$$E_1^2 = \frac{B[(x + B)^2 - (C_0/C)x(x + B)]}{B - (C_0/C)x} = J \qquad (1)$$

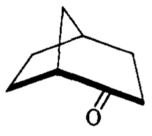
resolution to some specific rotation α other than α_0, eq. 2 becomes appropriate. Application of eq. 2 to a

$$E_2^2 = (\alpha_0/\alpha)J \qquad (2)$$

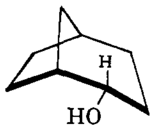
reisolated sample of **4** acid phthalate after the steps described above leads to the conclusion that enantiomerically pure **4** acid phthalate has $[\alpha]_D$ 30.5 ± 3.7° (chloroform); regeneration of **4** from partially resolved acid phthalate establishes the relative rotary powers of alcohol and acid phthalate of identical optical purities, whence the rotation of enantiomerically pure **4** alcohol is 40.0 ± 4.8° (chloroform). The stereochemical result in the deamination of **1** to **4** (OH = OAc) is thus 55 ± 7% retention of optical purity and 45 ± 7% racemization.

The specific rotation of optically pure *exo-axial*-2-bicyclo[3.2.1]octanol (**2**) in ethanol is 13.8°; it is derived from that of the epimer *endo-equatorial*-2-bicyclo[3.2.1]octanol (**5**), determined by Goering and Fickes,[14] and the relative rotatory powers of **2** and **5**.[2] Deamination of **1** thus gives **2** with 94% retention of optical purity. Since the maximum rotation of **2** is determined only indirectly, two correlations[2] as well as an isotopic dilution analysis[14] being involved, there is a greater than usual uncertainty in the specification of per cent retention of optical purity for this product. We estimate that this number could be as low as 85% or as high as 100%. Further, the *relative* optical purities of products **2** and **4** are only indirectly established, in contrast to those of **2** and **5**.[2]

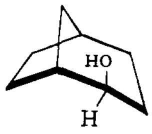
Absolute Configurations.—By application of the octant rule,[15] the absolute configuration **10** is assigned[11] to (−)-2-bicyclo[3.2.1]octanone (signs of rotation in this section refer to the sodium D line). (−)-Ketone **10** is obtained by oxidation of (−)-*endo-equatorial*-2-bicyclo[3.2.1]octanol (**5**), which must therefore have the configuration shown. This relationship is confirmed[2] in the enantiomeric series by the conversion of (+)-**5** to (+)-**10**, and the absolute configurations of **10** and **5** are also confirmed chemically by the relationship[2] of **5** to *endo*-2-norbornanecarboxylic acid of known[10] absolute configuration. The original assignment[11] of configuration to *exo-axial*-2-bicyclo[3.2.1]octanol (**2**), must now be reversed, since it is (+)-**2**, not (−), that gives (−)-**10**.[2] This relationship has now also been established recently by Walborsky.[16] Since (+)-**4** and (+)-**2** are Wagner–Meerwein related, acetates of both having been formed in the deamination of (−)-**1**, it is reasonable to assume that (+)-**4** has the configuration shown. This is supported by its relationship to (−)-2-bicyclo[2.2.2]oct-5-ene-2-one (**11**), the enantiomer of which has an optical rotatory dispersion curve (sign and amplitude) in excellent agreement with that predicted on theoretical grounds.[17]



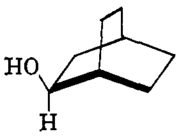
(−)**10**



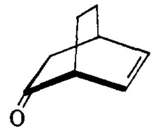
(−)-**5**



(+)-**2**



(+)-**4**



(−)**11**

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[11] H. M. Walborsky, M. E. Baum, and A. A. Youssef, *J. Am. Chem. Soc.*, **83**, 988 (1961).

[12] S. Graff, D. Rittenberg, and G. L. Foster, *J. Biol. Chem.*, **133**, 745 (1940).

[13] H. L. Goering and J. T. Doi, *J. Am. Chem. Soc.*, **82**, 5850 (1960).

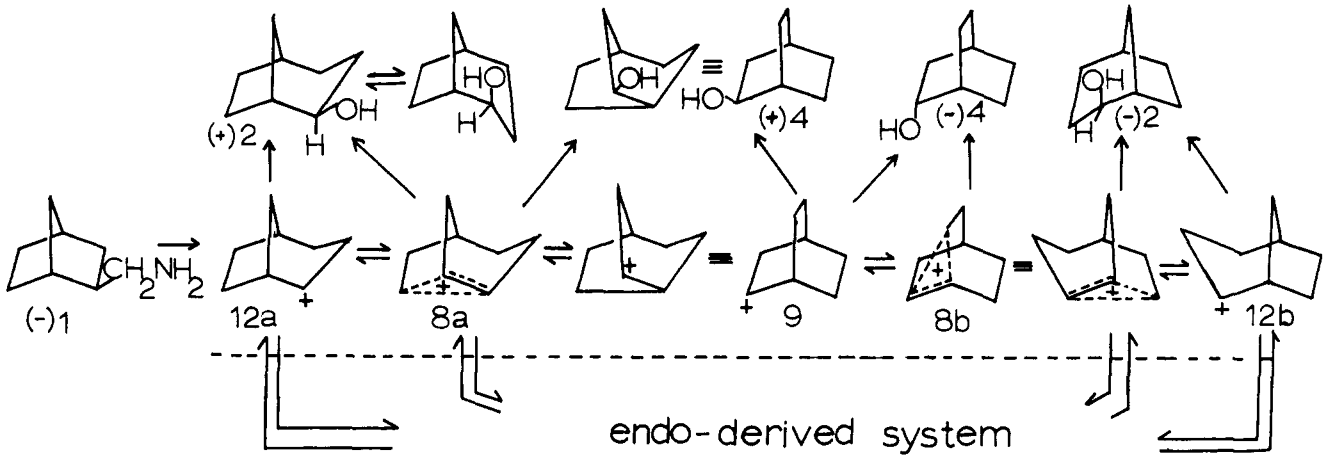
[14] H. L. Goering and G. Fickes, personal communication. We are indebted to Professor Goering for this information and for permission to cite it in advance of publication.

[15] W. Moffitt, R. B. Woodward, A. Moscowitz, W. Klyne, and C. Djerassi, *J. Am. Chem. Soc.*, **83**, 4013 (1961).

[16] H. M. Walborsky, personal communication. We are indebted to Professor Walborsky for informing us of this result before publication. *Cf.* H. M. Walborsky, J. Webb, and C. G. Pitt, *J. Org. Chem.*, **28**, 3214 (1963).

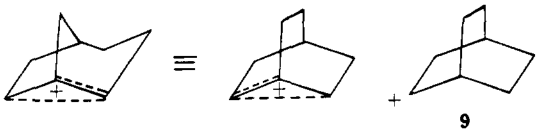
[17] K. Mislow and J. G. Berger, *J. Am. Chem. Soc.*, **84**, 1956 (1962).

CHART I



Discussion

exo-axial-2-Bicyclo[3.2.1]octyl (**2**) and 2-bicyclo[2.2.2]octyl (**4**) products are formed in other carbonium ion processes; arenesulfonates of either structure give mixtures of both products in solvolysis[11,18] and are interconverted by ion-pair return.[18b] Solvolyses of 3-cyclohexenylethyl *p*-bromobenzenesulfonate give products of both structures in addition to varying amounts (depending on solvent) of uncyclized product,[19] and nitrous acid converts 2-bicyclo[2.2.2]octylamine to a mixture of **2** and **4**.[18a] In all these reactions, the nonclassical mesomeric cation **8** is invoked as an intermediate.[11,18,19] The survival of at least some optical activity in the acetolysis product (**4**, OH = OAc) from optically active **4** (OH = OBs)[11,16] and the specific formation of *exo-axial*-2-bicyclo[3.2.1]octyl product (**2**) rather than the epimer **5**[11,18,19] are experimental observations consistent with **8** but not with a simple picture of classical cationic species as the product-forming intermediates.



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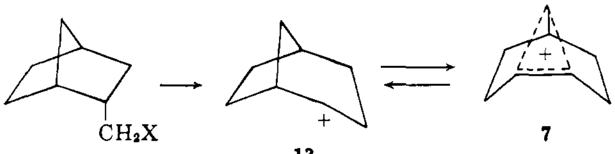
9

Nevertheless, nonclassical cation **8** clearly cannot be the sole product-forming intermediate in the deaminative ring expansion of *exo*-2-norbornylcarbinylamine (**1**). Cation **8**, when formed from optically active precursors, is optically active and must give products with complete retention of optical purity. Although product **2** (OH = OAc) is formed with high or perhaps even complete retention (*ca.* 94%), product **4** (OH = OAc) is definitely partially racemized. Similarly, the optically inactive classical cation **9** cannot be the sole precursor of 2-bicyclo[2.2.2]octyl product, since this would result in racemic **4**. Just as is the case in the *endo*-2-norbornylcarbinyl ring expansion,[2] at least two product-forming intermediates seem to be required. We propose the attached scheme (Chart 1), involving both nonclassical **8** and classical **9** ions, as the simplest formulation of the mechanism.

It is likely that movements of the C-2–C-3 and C-1–C-6 bonds of **1** occur in discrete steps, *i.e.*, that **1** is not converted directly to nonclassical ion **8**. The stereoelectronic situation in **1** is entirely analogous to that already discussed for the *endo* analog,[2] and is unfavorable for the simultaneous delocalization that presumably would be required for a concerted double rearrangement. There is, however, a difference in the degree of certainty with which the first-formed classical cations (**12a** from *exo*-**1** and **13** from *endo*-**6** starting materials) can be identified as *product-forming* intermediates. In the *endo* case, where the mesomeric ion **7** is optically inactive, interception of **13** is revealed in the survival of optical activity in the product *equatorial*-alcohol **5**.[2] This criterion is inapplicable in the *exo*-derived system, since both classical **12a** and nonclassical **8a** ions are optically active. The scheme could therefore be modified to eliminate either (but not both) of the product-forming steps **12** → **2** or **8** → **2**.



6

13

7

Crossover from the set of cations **12**–**8**–**9** associated with the *exo* system into the set **13**–**7** derived from *endo* seems to be a minor path, the characteristic product with the *endo-equatorial*-bicyclo[3.2.1]octyl structure from the *endo* system[2] constituting only 3% of the total in aqueous acetic acid; in contrast, crossover in the reverse direction, *i.e.*, *endo*-derived cation **13** into the *exo* set, is substantially more important.[2] It is not clear that even the small amount of *endo-equatorial*-[3.2.1]octyl product that does result from the ring expansion in the case of *exo* starting material **1** is derived by crossover to the **13**–**7** set of cations, another possible source being the classical boat cations **12a** and **12b**. The 3% figure is therefore an upper limit for crossover. In principle, it would be possible to specify the source of the small amount of *endo-equatorial* product **5** in more detail by determining its optical purity, for if it came entirely from cations **12a** and **12b**, it would retain optical purity to at least the same extent as the companion *axial* product **2**. Unfortunately, the very small amount of product **5** formed has so far prevented us from establishing its optical purity.

The higher retention of optical purity in the *exo-axial*-2-bicyclo[3.2.1]octyl product **2** (OH = OAc) than in the Wagner–Meerwein-related **4** (OH = OAc) is a direct consequence of the sequential formation of cations **8a**, **9**, and **8b**, the symmetry of the scheme of Chart 1 being directly analogous to that in the *endo*-derived series,[2] where corresponding stereochemical relationships hold. That very little racemization is

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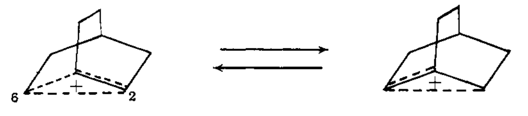
[18] (a) H. L. Goering and M. F. Sloan, *J. Am. Chem. Soc.*, **83**, 1397 (1961); (b) *ibid.*, **83**, 1992 (1961).

[19] S. Winstein and P. Carter, *ibid.*, **83**, 4485 (1961).

observed in the *axial* product **2** (OH = OAc) is presumably a consequence of the slow rate of conversion of classical ion **9** to nonclassical ion **8b** relative to the rate at which **9** is captured to give 2-bicyclo[2.2.2]octyl acetate (**4**, OH = OAc). An alternative way of accounting for the apparent near-absence of racemization in product **2** is to postulate that all of it comes from classical ion **12a** and none from nonclassical ion **8a**. This would allow the **9** → **8b** conversion to be fast but would require that **8b** → **12b** conversion be slow. This alternative seems less satisfactory than that given in Chart 1, since it is hard to see why **8a** should react at only one of the two cationic sites.

At present, the optically inactive classical ion **9** appears to provide the simplest and best explanation for the partial racemization observed in product **4** (OH = OAc). The two other most readily envisioned racemizing processes involve hydride shift and are less satisfactory. One of these, 4 → 2 shift in either or both ions **12a** and **8a**, is a reaction that has already been shown[2] not to occur in the closely analogous cations derived from the *endo*-norbornylcarbinyl system. Although we do not have matching experimental evidence yet for the *exo*-derived system, there are at least no firm grounds for anticipating that this process, which is completely absent in one series, would become of major importance in the other. The second conceivable kind of racemization alternative involves direct interconversion of the enantiomeric nonclassical cations **8a** and **8b** by 6,2-hydride shift without the intervention of classical cation **9**. This process, while not directly excluded, seems unlikely since **8b**, which would then be the only precursor providing a source of racemized product **4**, also would be a potential source of racemized **2**. Since product **2** does not seem to be appreciably racemized, adherence to this mechanism would again require the dubious postulate that nonclassical ion **8** reacts at only one cationic site.

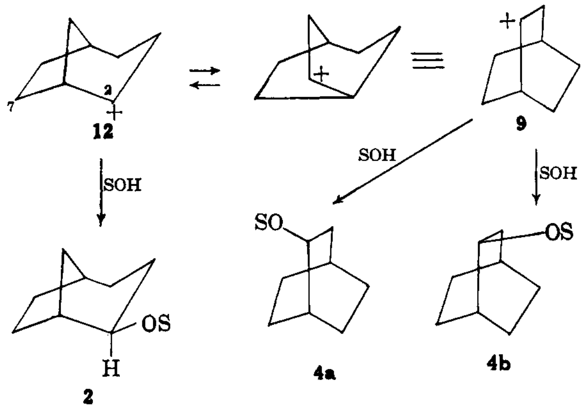


8a **8b**

The formulation in Chart 1 of the precursor of optically active 2-bicyclo[2.2.2]octyl acetate (**4**, OH = OAc) as the nonclassical ion **8a** is again offered as the simplest explanation of the facts. There are several alternative hypotheses that might conceivably be proposed. None of these is, in our view, as satisfactory in the present case as the nonclassical formulation.

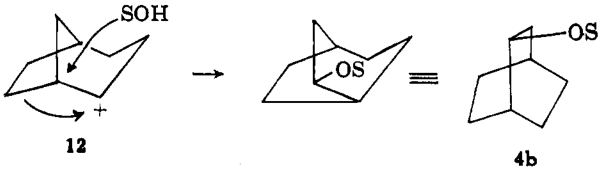
For example, it is asserted that retention of stereochemistry in Wagner–Meerwein processes (*e.g.*, the exclusive formation of *exo* products in norbornyl solvolyses[20]) is not a criterion for the existence of nonclassical ions and that rapid interconversion of the Wagner–Meerwein-related pair of classical cations would produce the same stereochemical pattern.[21] (This hypothetical phenomenon has been referred to as the "windshield wiper" effect.) Without expressing an opinion here on the validity of the idea in the general case, we attempt to apply it to the specific system of cations derived from the *exo*-norbornylcarbinyl ring expansion.

It must first be made clear that the hypothesis cannot be formulated in terms of conventional kinetics, in which the rate of capture of an intermediate is given by the product of a rate constant, the concentration of the intermediate, and the macroscopic concentration of solvent. Thus, in the Wagner–Meerwein-related pair of cations **12** and **9**, conventional kinetics would require that the symmetrical cation **9** be converted with equal probability to the two enantiomeric products **4a** and **4b**, since the rate constants and solvent concentrations for attack on either side of the cationic site are identical, regardless of whether the 12 ⇄ 9 equilibrium is fast or slow. The hypothesis rests on the assumption that if rearrangement (*i.e.*, movement of C-7) is fast relative to the rate at which solvent relaxation occurs, the effective concentration of solvent at one side of the rearranged cation **9** is abnormally low, and thus attack occurs from the side opposite that to which the migrating carbon was attached.



To fit the present results on this basis, we must assume that the postulated back-and-forth movement of C-7 is fast enough to prevent solvent relaxation, since more **4b** is formed than **4a**. This necessarily implies that 12 ⇄ 9 is fast *in both directions* before symmetrical solvation of **9** occurs. The partial racemization observed in **4** would presumably be a result of the escape from capture of some of the unsymmetrically solvated **9** cations and their survival long enough to become symmetrically solvated. But now it must be assumed that the 12 ⇄ 9 reaction, which was enormously fast with unsymmetrically solvated **9**, becomes very slow with symmetrically solvated **9**; were it fast, product **2** would have been highly racemized, but in fact it seems to be formed with almost complete retention of optical purity. Further, the type of rapid Wagner–Meerwein interconversion postulated cannot account for the results in the *endo*-derived system, where the Wagner–Meerwein related 2-bicyclo[3.2.1]octyl cations (**13** and its mirror image) are *enantiomeric;* this would lead to equal optical purities of the *equatorial*- and *axial*-2-bicyclo[3.2.1]octyl products, in conflict with experiment.[2]

A second way of formulating the mechanism without nonclassical intermediates would propose that the first-formed optically active boat cation **12** is attacked stereospecifically by a nucleophile at the site (C-1) *adjacent* to the positive charge,[22] producing rearranged optically active product **4b**. An additional hypothesis



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(20) For a review, see J. A. Berson in "Molecular Rearrangements," P. de Mayo, Ed., Interscience Publishers, Inc., New York, N. Y., p. 111.

(21) (a) H. C. Brown in "The Transition State," Chemical Society Special Publication No. 16, The Chemical Society, Burlington House, London, 1962, pp. 140–158, 174–178; (b) P. S. Skell and R. J. Maxwell, *J. Am. Chem. Soc.*, **84**, 3963 (1962).

(22) This reaction has been postulated in the case of dibenzo-2-bicyclo[3.2.1]octyl cation.[23]

(23) S. J. Cristol, Abstracts of the Eighteenth National Organic Chemistry Symposium of the American Chemical Society, Columbus, Ohio, June 16–20, 1963, pp. 12–22.

is required to keep this mechanism consistent with the facts. Since some of the enantiomer of **4b** is also formed, the postulated stereospecific concerted nucleophilic attack-*cum*-rearrangement mechanism must be supplemented by a racemizing process. The simplest such process would be rearrangement of **12** to the inactive 2-bicyclo[2.2.2]octyl cation **9**. But if this is the case, still another condition must be imposed to account for the high retention of optical purity observed in product **2**, namely that although cation **12** is readily subject to the attack-*cum*-rearrangement process, cation **9** for some reason is not.

As in our discussion[2] of alternatives to nonclassical ions in the *endo*-norbornylcarbinyl system, we do not take the view that some such combination of hypothesis and *ad hoc* subsidiary hypothesis is incapable of accounting for our results, or that nonclassical ions are necessarily the "correct" explanation. We do feel, however, that the alternatives at present have a patchwork and purposive air, and that the nonclassical species we invoke provide the simpler and clearer picture.

There remains one further alternative, which is derived from what is roughly the converse of the "windshield wiper" hypothesis. If solvent relaxation, instead of being slow, is extremely fast—in fact, competitive in rate with molecular skeletal vibrations—it is just possible to imagine a formulation of our results involving no mesomeric ions. If the cation **9**, when *freshly formed* by rearrangement of cation **12**, reacts with solvent before it has a chance to take up a symmetrical conformation, it will give optically active product. In other words, the *nascent* cation **9** need not be strictly symmetrical and may conceivably be trapped before it becomes so. Its geometry in this twisted state would lie between that of the mesomeric cation **8** and the fully symmetrical form of **9**, the major conceptual difference between **8** and twisted, nascent **9** being that in the latter the carbon atom that was originally C-7 of **12** has "completed" its migration and is bound only to the migration terminus rather than to both terminus and origin.

Although the minimum in the vibrational potential curve of skeletal motions of the bicyclo[2.2.2]octyl system may not coincide with the completely symmetrical conformation,[24] there can be no doubt that this conformation is achieved in each molecular vibration. It is therefore necessary that solvent trap the nascent cation in less than about 10^{-13} sec. At present, we can offer no further information on how likely this alternative is, but we hope to report later on experiments designed to detect such twisted nonmesomeric species. These questions bear on the whole use of symmetry criteria in mechanism studies. It has usually been assumed that the structures of nonisolable intermediates could be inferred from their symmetry properties, but this has required the further implicit assumption that the intermediates were long lived on the molecular vibrational time scale. Symmetry criteria often can be so cleanly decisive in limiting mechanistic hypotheses that on pragmatic grounds, we have no compunction in continuing to apply them until evidence against the underlying assumption is forthcoming.

The results of this and the companion work[2] provide some insight into the effect of structure on bicyclic carbonium ion properties. In particular, there is now a strong implication that reactivities of bicyclic nonclassical ions may fall into a graded series. Thus there can be wide variations in the degree to which the stereochemical and structural outcome of a carbonium ion process is dominated by such species. In a qualitative way, we can begin to discern the outlines of the series by observing that, *relative to capture by solvent*, nonclassical → classical cation conversion is slow with norbornyl, but fast with chair-derived 2-bicyclo[3.2.1]octyl (**7**) and fast with 2-bicyclo[2.2.2]octyl-boat-2-bicyclo[3.2.1]octyl (**8**). Evidently norbornyl represents that extreme of behavior in which the nonclassical ion is sovereign,[25] while the cations **7** and **8** encountered in the present work are only roughly equal in importance to their classical counterparts. It seems likely that continued examination of additional structures will reveal the other limit of behavior in which the nonclassical ion becomes subordinate and exerts only a feeble influence (or none at all) on the course of the reaction.

Experimental[26]

Deamination of *exo*-2-Norbornylcarbinylamine Hydrochloride (1). A. Racemic Amine in Aqueous Acetic Acid.—A solution of 18 g. of the amine hydrochloride[10] in 200 ml. of water was heated to boiling, stirred under reflux, and treated dropwise with a solution of 10 g. of sodium nitrite in a small amount of water. Glacial acetic acid (10 g.) was added dropwise followed by additional small portions of sodium nitrite and acetic acid until the mixture gave a positive test with starch–iodide paper. The mixture was heated at reflux for an additional 30 min., kept overnight at room temperature, and extracted with ether. After having been washed with sodium bicarbonate solution and water and dried over magnesium sulfate, the ether was evaporated, leaving 13.3 g. (92% calculated as alcohols) of solid residue. This material contained small amounts of acetates (infrared absorption at 1724 cm.$^{-1}$; two small v.p.c. peaks with retention times less than those of the alcohols), hydrocarbons (two more small v.p.c. peaks with short retention times), and nitrate esters (infrared absorption at 1638 cm.$^{-1}$).

Most of this material (13.0 g.) was dissolved in 150 ml. of ether and added dropwise to a stirred suspension of 5 g. of lithium aluminum hydride in 150 ml. of dry ether. After having been heated at reflux for 1 hr., the mixture was worked up in the usual manner.[2] A 2-g. sample of the resulting mixture of alcohols was chromatographed on 60 g. of Merck alumina. After removal of traces of oily material from the column with pentane and with ether–pentane 3:1, the alcohols were eluted with 10% acetone in ether. The analysis of this materal by capillary v.p.c. is given in Table I.

B. Racemic 1 in Glacial Acetic Acid.—A solution of 1.5 g. of amine hydrochloride 1 in 25 ml. of glacial acetic acid was stirred, cooled to 16°, and treated with portions of sodium nitrite (2 g. total) at such a rate that the temperature did not rise above 20°. Cooling was necessary, even after completion of the addition, to keep the temperature below 30°. After 1 hr., a further quantity (1 g.) of sodium nitrite was added, and the mixture was heated on the steam bath for 15 min. The mixture was poured into water, extracted with ether, and then worked up as in part A. The residual oil was distilled at 90–92° (20–22 mm.) to give 79% (calculated as acetate) of colorless liquid. In addition to a strong acetate peak, the infrared spectrum showed nitrate absorption at 1635 cm.$^{-1}$ and a very weak band in the 3500 cm.$^{-1}$ region suggesting the presence of a small amount of alcohol. A nitrogen analysis showed 0.25% N, indicating about 3% contamination by nitrate. The mixture of acetates was cleaved with lithium aluminum hydride in the usual manner,[2] and the alcohols were analyzed with a 7 mm. × 300 cm. tri-β-cyanoethoxypropane (TCEP) v.p.c. column. The results are shown in Table I. Analytical separation of the alcohols on this column was superior to that of the corresponding acetates. Similar results were observed with a variety of other stationary phases, although the resolution with TCEP was substantially better than with any of the other packings tried. The latter included: (1) tetracyanoethoxyneopentane (cyanoethylation product of pentaerythritol), (2) dicyanoethyl-1-nitropropane, (3) Hyprose AN (cyanoethylation product of Dow Chemical Co. Hyprose SD-8D), (4) tetrahydroxyethylethylenediamine, (5) Tide (a commercial detergent), (6) Ucon LB 550X (a product of Union Carbide).

A small sample of the original mixture of acetates was saponified with aqueous sodium hydroxide and the resulting alcohols examined in the infrared. The spectrum showed only a trace of absorption in the 5.8 μ region. By comparison with spectra of

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[24] R. B. Turner, W. R. Meador, and R. E. Winkler, *J. Am. Chem. Soc.*, **79**, 4116 (1957).

[25] Reference 1c, pp. 111–139.

[26] Spectrophotometric, gas chromatographic (v.p.c.), and polarimetric techniques are the same as those described in the companion paper.[2] Melting points are corrected; boiling points are uncorrected. Elemental analyses are by Joseph Alicino, Metuchen, N. J.

synthetic mixtures of the alcohols and their corresponding ketones, we estimate the maximum amount of ketone that could have been formed in the deamination as about 1%.

C. Optically Active 1 in Glacial Acetic Acid.—The deamination was carried out with two batches of optically active amine hydrochloride. The first batch had been prepared[10] from (−)-*exo*-5-norbornene-2-carboxylic acid of $[\alpha]_D$ −11.02° (*c* 5.24 in 95% ethanol, *l* 1), 64.0% optically pure,[9] and the second from (−)-*exo*-5-norbornene-2-carboxylic acid of $[\alpha]_D$ −3.89 ° (*c* 9.38 in 95% ethanol, *l* 1), 22.6% optically pure.[9] The deamination products from each batch were examined separately by v.p.c. and found to be identical in chemical composition with each other and to the product from the racemic run. A mixture of 7.3806 g. of product from the 22.6% optically pure starting material and 5.6642 g. from the 64.0% optically pure starting material was used for subsequent work. The optical purity of products derived from this mixture is calculated on the basis of the weighted average optical purity of the starting materials, 40.7%.

Separation of the Products. A. Racemic Series.—The mixture of alcohols from part A were preparatively vapor chromatographed with the TCEP column previously described.[2] Samples injected were 250–350 mg. in 1–2 ml. of ether. The three major products emerged in the sequence: A, *axial*-alcohol **2**; B, 2-bicyclo[2.2.2]octanol (**4**); C, *meso*-alcohol **3**. Peaks A and B overlapped badly, but peaks B and C were more cleanly separated. *meso*-Alcohol **3** was therefore obtained in pure form with the least difficulty.

Fraction A was recycled until analytical v.p.c. indicated homogeneity and then recrystallized from pentane to give pure **2**, m.p. 198–199°, reported[18a] 199.9–200.2°, reported[27] 200–201°. The infrared spectrum showed the band at 1015 cm.$^{-1}$ that is typical of authentic **2**.[27]

Fraction B was cycled thrice but still contained a small amount of contaminant. It was recrystallized from pentane to give **4**, m.p. 217–219°, undepressed on admixture with authentic **4** of m.p. 215–217°. The authentic sample of **4** was prepared from its acetate obtained by Baeyer–Villiger oxidation of 2-acetylbicyclo[2.2.2]octane[28] according to the procedure used[8] for the oxidation of 2-acetylnorbornane. The 2-acetylbicyclo[2.2.2]-octane was prepared[29] from 2-bicyclo[2.2.2]octanecarboxylic acid, m.p. 83–84° (from pentane), reported[29] m.p. 84–85°, which was converted to the acid chloride and thence, with dimethylcadmium according to the procedure used in the analogous case,[8] to the ketone. The latter had b.p. 94° (8 mm.), n^{24}_D 1.4843; reported[28] b.p. 99–100° (9 mm.), n^{20}_D 1.4852. The semicarbazone had m.p. 198–200°, reported[28] 196–197°. Baeyer–Villiger oxidation[8] with perbenzoic acid–chloroform gave 2-bicyclo[2.2.2]-octyl acetate, b.p. 58° (0.5 mm.), which upon saponification with methanolic sodium hydroxide gave, after sublimation and recrystallization from pentane, pure **4**, m.p. 215–217° (sealed capillary). This alcohol was more conveniently prepared by the procedure of Goering and Sloan[18a] *via* Diels–Alder reaction of cyclohexadiene[30] and vinyl acetate, followed by hydrogenation and saponification.

Fraction C (300 mg.) which consisted largely of *meso*-alcohol **3**, was oxidized with chromium trioxide–acetone reagent[31] to give crude 3-bicyclo[3.2.1]octanone which was dissolved in 4 ml. of 5% ethanolic sodium hydroxide and treated with 1 ml. of freshly distilled benzaldehyde. The mixture was kept overnight and the resulting yellow crystals recrystallized from ethyl acetate and from isopropyl alcohol to give **2,4-bis-benzylidene-3-bicyclo[3.2.1]octanone**, $\lambda\lambda_{max}$ 232 mμ (ϵ 15,200), 332 mμ (ϵ 27,300), m.p. 190–191°, reported[3] m.p. 187°.

B. Optically Active Series.—The mixture of alcohols from the deaminations of optically active 2-*exo*-norbornylcarbinylamine hydrochloride was subjected to vapor chromatographic separation in the same manner as the racemic alcohols. Recycling of fractions A and B was carried to constant optical rotation of each.

Four cycles gave fraction A, $[\alpha]_D$ +5.29° (*c* 10.24 in 95% ethanol). A fifth pass gave 500 mg. of pure *exo-axial*-2-bicyclo[3.2.1]octanol (**2**), $[\alpha]_D$ +5.21° (*c* 11.55 in 95% ethanol, *l* 1), vapor chromatographically homogeneous (capillary column). We are indebted to Dr. P. Reynolds-Warnhoff for this chromatogram.

After seven cycles, fraction B had $[\alpha]_D$ +9.06° (*c* 6.32 in chloroform, *l* 1). The eighth pass gave about 0.6 g. of 2-bicyclo[2.2.2]octanol (**4**), $[\alpha]_D$ +8.87° (*c* 2.61 in chloroform, *l* 1), $[\alpha]_D$ +8.79° (95% ethanol). This material was homogeneous by conventional v.p.c. on the 7-mm. packed column, but this column was incapable of detecting small amounts of *meso*-alcohol **3** or unrearranged alcohol (*exo*-2-norbornylcarbinol). The infrared spectrum of fraction B suggested, by comparison with the spectra of authentic mixtures, the presence of a total of about 2% of alcohol **3** and/or unrearranged carbinol. Conversion of a small sample of fraction B to the acetate with acetic anhydride–pyridine and vapor chromatographic analysis of the acetate under conditions where the acetates of **3** and 2-*exo*-norbornylcarbinol have identical retention times but are separated from the acetate of **4**, also showed the presence of 2% of impurity. The infrared spectrum of the acetate suggested that the 2% impurity was more probably the acetate of **3** rather than that of *exo*-2-norbornylcarbinol. In either case, the effect on the rotation of fraction B was negligible. Contamination by **3** would mean that the actual rotation of pure **4** was 2% higher (0.18°) than observed, since **3** is optically inactive. The maximum effect that could be caused by *exo*-2-norbornylcarbinol is calculated on the assumption that it retains all of the original 40.7% optical purity. From the value[10] of the maximum rotation and the fact that this alcohol has the same sign of rotation as *exo*-2-norbornanecarboxylic acid of the same configurational series,[10] 2% of the carbinol would contribute a specific rotation of −0.087°. The rotation of pure **4** would then be in error by 0.19° or about 2%. These uncertainties are within the experimental errors of measuring the specific rotations themselves.

Fraction C, 1.4 g. obtained from the preparative vapor chromatogram, was repeatedly sublimed to give **3-bicyclo[3.2.1]octanol** (**3**), m.p. 112.5–114.5°, $[\alpha]_D$ 0.00° (*c* 11.3 in 95% ethanol, *l* 1).

Anal. Calcd. for $C_8H_{14}O$: C, 76.19; H, 11.11. Found: C, 76.31; H, 11.23.

Optical Activation of 2-Bicyclo[2.2.2]octyl Acid Phthalate.—The racemic acid phthalate, m.p. 154.5–156.5° (from benzene), reported[11] m.p. 155°, was converted in trial experiments to a number of alkaloidal salts including those of cinchonine, strychnine, and brucine. Exploratory attempts to fractionate each of these were made from acetone, ethyl alcohol, and ethyl acetate. We were unable to find conditions for the resolution that were appreciably better than those reported,[11] and accordingly we adopted the earlier procedure[11] of recrystallization of the brucine salt from ethyl acetate. Four different batches of acid phthalate were partially resolved. A typical run was carried out by the following procedure. A mixture of 36.3 g. of pure acid phthalate and 52.5 g. of brucine was dissolved in 200 ml. of hot ethyl acetate. Cooling and seeding with a small quantity of crystalline brucine salt (obtained by vigorous scratching of an aliquot) gave a crop of crystals and a mother liquor. Concentration of the mother liquor deposited a second crop of crystals. This procedure was repeated several times, the more highly resolved material concentrating in the mother liquor. The acid phthalate regenerated from the fourth crop of crystals (by shaking with ether–dilute sulfuric acid, washing of the ether layer with dilute sulfuric acid and water, drying over magnesium sulfate, and evaporation) had $[\alpha]_D$ +3.1° (chloroform). An aliquot of the fourth mother liquor gave acid phthalate of $[\alpha]_D$ +8.02° (*c* 7.67 in chloroform). Recrystallization of the brucine salt corresponding to acid phthalate of $[\alpha]_D$ +3.1° gave a mother liquor from which acid phthalate of $[\alpha]_D$ +6.59° was obtained. In two of the four resolutions, *levorotatory* acid phthalate appeared at about the third or fourth level of fractionation. The difficulty of reproducing the behavior of the salt and the inconvenient tendency of the more active salt to accumulate in the mother liquors made the system quite unsuitable for a systematic attempt at complete resolution. Furthermore, the partially resolved acid phthalate itself did not fractionate appreciably upon recrystallization from benzene–pentane, samples of $[\alpha]_D$ +3.55 and −7.62° having $[\alpha]_D$ +3.78° and −7.45°, respectively, after recrystallization.

Isotopic Dilution Analysis of Optically Active Acid Phthalate.—Racemic ^{14}C-labeled 2-bicyclo[2.2.2]octyl acid phthalate was prepared by dissolving 0.95 g. of pure 2-bicyclo[2.2.2]octanol and 1.11 g. of *carbonyl*-^{14}C-phthalic anhydride[8] in 20 ml. of pyridine (freshly distilled from barium oxide) and heating the solution at 100–110° in an oil bath for 4 hr. After having been cooled and allowed to remain at room temperature for 3 days, the solution was heated an additional hour at 100–110°, cooled, and poured into 1 l. of water. The product was extracted with ether–benzene, and the extract was washed with 10% sulfuric acid and water and dried over magnesium sulfate. Evaporation left the phthalate as a solid residue. The products from two such runs were combined and dissolved in sodium bicarbonate; the aqueous solution was washed with ether, and then carefully acidified to regenerate the acid phthalate. Recrystallization from benzene–pentane gave material of m.p. 156–157°, unchanged by further recrystallization. This sample had a specific radioactivity of 1280 ± 11 counts/min./mg., as determined by the liquid scintil-

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(27) A. A. Youseef, M. Baum, and H. M. Walborsky, *J. Am. Chem. Soc.*, **81**, 4709 (1959).

(28) B. A. Kazanskii and P. I. Zabeshenskaya, *Doklady Akad. Nauk S.S.S.R.*, **72**, 57 (1950); *Chem. Abstr.*, **45**, 1544 (1951), prepared this substance by another method.

(29) R. Seka and O. Tramposch, *Ber.*, **75**, 1379 (1942).

(30) C. A. Grob, H. Kny, and A. Gagneux, *Helv. Chim. Acta*, **40**, 137 (1957).

(31) R. G. Curtis, I. Heilbron, E. R. H. Jones, and G. F. Woods, *J. Chem. Soc.*, 457 (1953); A. Bowers, T. G. Halsall, E. R. H. Jones, and A. J. Lemin, *ibid.*, 2548 (1953); T. B. Halsall, P. Hodges, and E. R. H. Jones, *ibid.*, 3019 (1953).

lation counting method previously described.[32] The value given is the average of three separate determinations, each one involving weighing, dilution, and counting. Each sample was counted three to six times. The activity is corrected for background, the usual precautions[32] being taken to minimize instrumental fluctuations by counting background and sample within a short time of each other and by taking background counts before and after a set of counts. Background counts were usually 190–200 dis./min., and sample counts were in the range 2,000–10,000 dis./min. A standard sample was periodically checked to determine instrumental drift. This amounted to only about 1%, but the drift correction was nevertheless applied in comparisons of samples counted at different times.

A sample of 5.2645 g. of optically active 2-bicyclo[2.2.2]-octyl acid phthalate, $[\alpha]_{\mathrm{D}}$ +7.75°, +7.72° (*c* 5 in $\mathrm{CHCl_3}$, two separate determinations), was mixed with 1.0088 g. of the above racemic labeled acid phthalate, the whole was dissolved in ether–ethanol, the solution was evaporated, and the residue dissolved, along with 9.05 g. of brucine, in 35 ml. of hot ethyl acetate. Upon cooling, the solution deposited about 13 g. of salt from which acid phthalate of $[\alpha]_{\mathrm{D}}$ +5.48° ($\mathrm{CHCl_3}$) could be regenerated. From the mother liquor, there was obtained 2 g. of salt which gave after the usual work-up a sample of acid phthalate. Recrystallization from benzene–pentane gave 0.7 g. of material (sample 1), which was recrystallized twice more from benzene–pentane giving samples 2 and 3. These materials had the following properties ($[\alpha]_{\mathrm{D}}$ in $\mathrm{CHCl_3}$, *c* 4; specific radioactivity in c./min./mg.): sample 1, +11.91°, 194; sample 2, +11.49°, 200; sample 3, +11.85°, 199. From these data and eq. 1, it can be calculated that *E*, the weight of enantiomer in the original optically active sample, is 1.3325 ± 0.17 g. (the uncertainty shown is the experimental average deviation), whence the optical purity is 25.3%. The rotation of optically pure acid phthalate is thus 30.5 ± 3.7° ($\mathrm{CHCl_3}$). The uncertainty shown is that calculated from probability theory as described earlier.[9]

Correlation of 2-Bicyclo[2.2.2]octanol with its Acid Phthalate.—A solution of 5.5 g. of the acid phthalate, $[\alpha]_{\mathrm{D}}$ +4.86° (*c* 8.475 in $\mathrm{CHCl_3}$), and 19 g. of sodium hydroxide in 75 ml. of water was subjected to steam distillation. The distillate was saturated with sodium chloride and extracted with ether. After having been dried over sodium sulfate and evaporated under a Vigreux column, the solution left 2.0 g. (80%) of 2-bicyclo[2.2.2]octanol which was sublimed *in vacuo* at 130–140°. The resulting material had m.p. 209–211°, infrared spectrum identical with that of the racemate, $[\alpha]_{\mathrm{D}}$ +6.20° (*c* 8.075 in $\mathrm{CHCl_3}$), +6.52° (*c* 8.34 in $\mathrm{CHCl_3}$). The alcohol thus has 1.31 times the rotatory power of the acid phthalate, and $[\alpha]_{\mathrm{D}}$ for optically pure alcohol is 40.0 ± 4.7° ($\mathrm{CHCl_3}$). An indirect correlation[17] gives the ratio 1.18 for the relative rotatory powers; on this basis optically pure alcohol would have $[\alpha]_{\mathrm{D}}$ 36°.

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[32] J. A. Berson and W. A. Mueller, *J. Am. Chem. Soc.*, **83**, 4940 (1961).

[Contribution from the Converse Memorial Laboratory, Harvard University, Cambridge 38, Mass.]

Cycloaddition. I. The 1,2-Addition of 1,1-Dichloro-2,2-difluoroethylene to Some Dienes[1]

By Paul D. Bartlett, Lawrence K. Montgomery, and Bernhard Seidel

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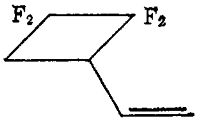
In sealed tubes at 80° with 1,1-dichloro-2,2-difluoroethylene in excess and a polymerization inhibitor (hydroquinone or di-*n*-butylammonium picrate) butadiene, *cis*-piperylene, and *trans*-piperylene each yielded a single 1,2-addition product. From isoprene (2-methylbutadiene), 1,2- and 3,4-cycloaddition products were obtained in the ratio of 5.4 to 1; from chloroprene (2-chlorobutadiene) the ratio of 1,2- and 3,4-addition products was 4.0 to 1. Cyclopentadiene and a fourfold excess of 1,1-dichloro-2,2-difluoroethylene yielded a product consisting of the 1,4-adduct 2,2-dichloro-3,3-difluorobicyclo[2.2.1]heptene-5 (44%), the 1,2-adduct 6,6-difluoro-7,7-dichlorobicyclo[3.2.0]heptene-2 (9%), and *endo*-dicyclopentadiene (47%). The butadiene, isoprene, and chloroprene adducts were degraded by oxidation to the corresponding cyclobutanecarboxylic acids. The structure of 2,2-dichloro-3,3-difluorocyclobutane-1-carboxylic acid was shown by its ease of conversion under acid conditions into 2-chloro-3,3-difluoro-1-cyclobutene-1-carboxylic acid and under basic conditions into 2-chloro-3,3-difluoro-1-cyclobutene. The establishment of these structures provided bases of n.m.r. and infrared comparison from which it is concluded that all the 1,2-cycloadducts have the chlorine atoms adjacent to the unsaturated substituent in the cyclobutane ring. These results are consistent with the hypothesis that a bifunctional ("biradical") intermediate is formed as the first step in 1,2-cycloaddition.

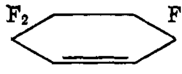
Introduction

Fluorinated olefins generally undergo thermal cycloaddition reactions with 1,3-butadienes to give vinylcyclobutanes.[2] In the present series of papers we report studies of some of the properties of these cycloaddition reactions bearing upon the mechanism of the reaction in the case of 1,1-dichloro-2,2-difluoroethylene.

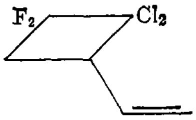
One of the most remarkable facts about these cycloadditions is the almost complete dichotomy among the known reagents which add to butadiene. With few exceptions a reagent reacts either entirely by 1,4-addition (Diels–Alder reaction), like maleic anhydride, or entirely by 1,2-addition, like tetrafluoroethylene. In the latter case,[3] there is only a single 1,2-addition product (I) and none of the isomeric 1,4-addition product (II).



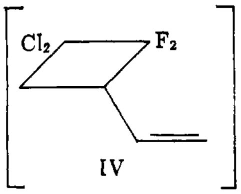
I



II



III



IV

The use of the less symmetrical reagent, 1,1-dichloro-2,2-difluoroethylene (to be called here "1122" for brevity) introduces the possibility of simple orientation isomerism (III *vs.* IV). Here, too, existing evidence[2] presents a simple picture: wherever the structures have been established they represent the type III and not IV. This fact is covered by the generalization[2,4] that the structure is that which would be formed *via* the most stable "biradical" intermediate. In the present paper we add something to the existing evidence and find that this rule predicts correctly the orientations in the case of butadiene and 1122.

With 1- and 2-substituted butadienes selectivity between the double bonds gives rise to a further structural variation in the products. In this paper we find that the product from piperylene is entirely V (a or b) with the configuration of the propenyl group being that of the initial piperylene, while isoprene (R = $\mathrm{CH_3}$) and

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[1] Presented at the National Organic Symposium, Columbus, Ohio, June 18, 1963.

[2] J. D. Roberts and C. M. Sharts in "Organic Reactions," Vol. 12, John Wiley and Sons, Inc., New York, N. Y., 1962, p. 1.

[3] D. D. Coffman, P. L. Barrick, R. D. Cramer, and M. S. Raasch, *J. Am. Chem. Soc.*, **71**, 490 (1949).

[4] E. C. Coyner and H. S. Hillman, *ibid.*, **71**, 324 (1949).