ketone. This mixture was carried through to the hydrocarbon as before. The pyrolysis product in this case, despite scrupulous vacuum drying of the sodium salt, was contaminated with about 30% of tetrahydrofuran. The other products consisted of about 6% 3-*endo*-methyl-2-norbornanone (**12**), 1.5% 2-methyl-2-norbornene, 1.5% of an unidentified compound, and the remainder 3-methylnortricyclene. The tricyclic hydrocarbon was again separated by preparative vpc on column G-1 at 130°, shown by infrared to be identical with material obtained from previous preparations, and its purity checked by capillary vpc. It had $[\alpha]^{23.2}D$ −16.4° (95% ethanol), a value essentially identical in magnitude and opposite in sign with that of hydrocarbon obtained above in Scheme I directly from 7-*anti*-methyl-2-*exo*-norbornyl acetate (**2b**).

The Chemistry of Methylnorbornyl Cations. IV. Ratios of Rates of Nucleophilic Capture of the Cations at Wagner–Meerwein-Related Sites[1]

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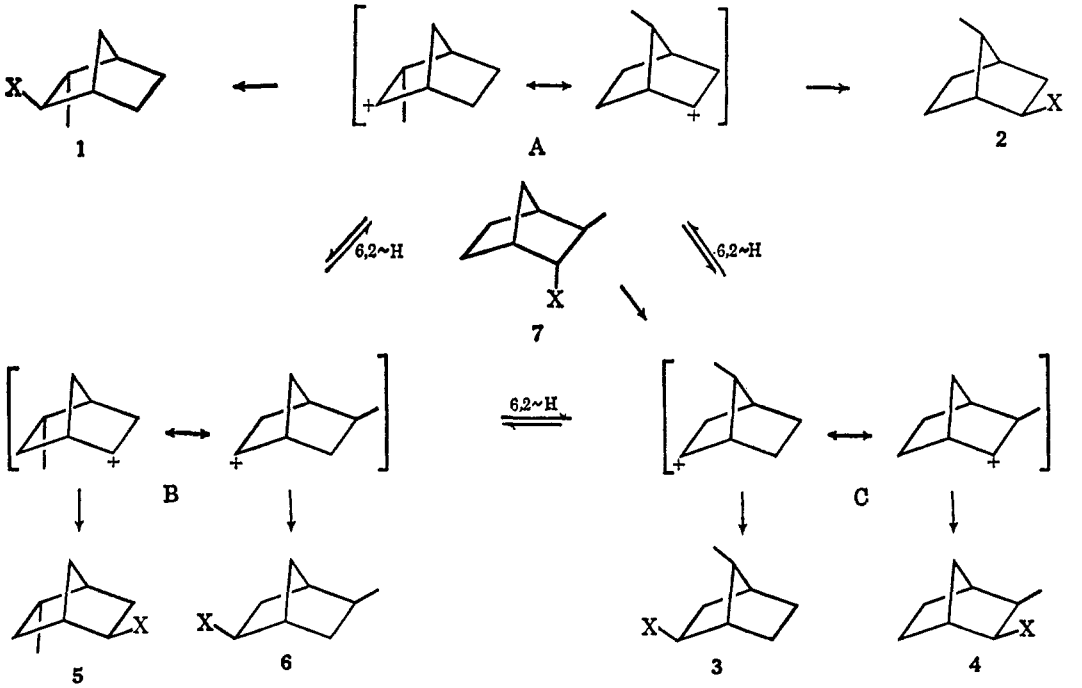
Contribution from the Department of Chemistry, University of Wisconsin, Madison, Wisconsin. *Received October 31, 1966*

Abstract: A detailed study of the product distributions from solvolyses and deaminations of a number of precursors of methylnorbornyl cations permits the evaluation of the relative rates of capture of these species at each of the two Wagner–Meerwein-related sites. A direct steric effect on nucleophilic approach and another effect which opposes developing hydrogen–methyl repulsions in the transition state are noted. The characteristic capture ratios observed in the solvolytically produced ions apply also to the deaminatively produced ones, the major difference between the two processes being the excess of "direct substitution" observed in deamination. A comparison of the deamination results with those obtained earlier in the unsubstituted norbornyl case reveals that the "direct substitution" is very sensitive to a β-methyl steric effect, which causes a complete reversal of the stereochemistry of the process.

The summarizing rearrangement scheme given in paper I[3] of this series outlines the interconversions of a set of "core" methylnorbornyl cations A, B, and C by 6,2-hydride shifts (Chart I) and their escape to "periphery" cations A_1, B_1 (≡B_2), and C_1 by 3,2-hydride shifts. The present paper provides evidence for this scheme from studies of the products derived from solvolyses of various methylnorbornyl derivatives.

Chart I. "Core" System



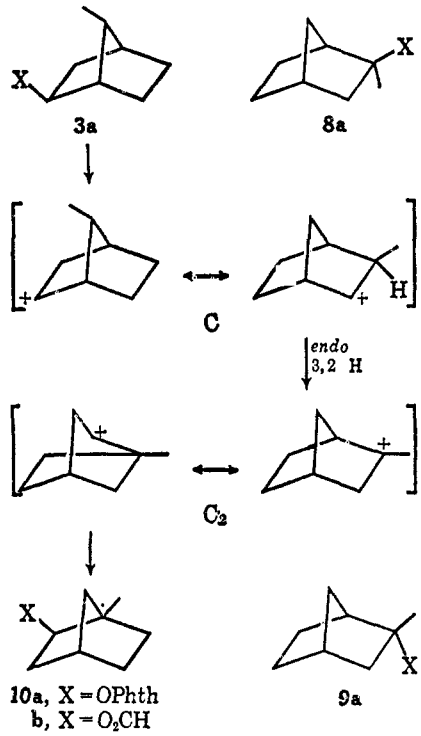
a, X = OPhth; b, X = O_2CH; c, X = OAc; d, X = OH; e, X = OBs; f, X = NH_2

(1) (a) Support of part of this work by the National Institute of Arthritis and Metabolic Diseases through Grant No. AM-07505 and by the National Science Foundation is gratefully acknowledged. (b) A preliminary report of some of this work has appeared: J. A. Berson, A. W. McRowe, and R. G. Bergman, *J. Am. Chem. Soc.*, **88**, 1067 (1966).

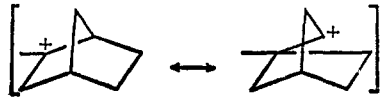
(2) National Institutes of Health Predoctoral Fellow, 1964–1966.

(3) J. A. Berson, J. H. Hammons, A. W. McRowe, R. G. Bergman, A. Remanick, and D. Houston, *J. Am. Chem. Soc.*, **89**, 2561 (1967).

In a previous study,[4] entry into the "core" set of cations was effected *via* cation C, generated by formolysis of *syn*-7-methyl-2-*exo*-norbornyl acid phthalate (**3a**). The major products reported[4] were the formates

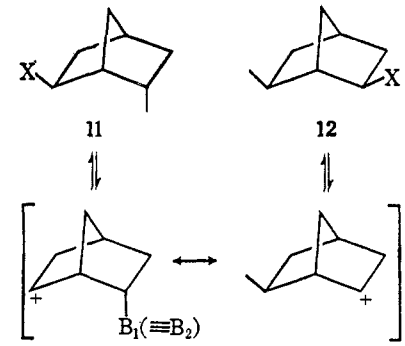


of 5-*exo*-methyl-2-*exo*-norborneol (**6b**), assumed[4] to be derived by 6,2-hydride shift, and 1-methyl-2-*exo*-norborneol (**10b**), assumed[4] to be derived by *endo*-3,2-hydride shift. Longer exposure of the products to the formolysis conditions caused conversion to **10b** in high yield. It seemed likely, however, that a number of other products might be formed, at least under kinetically controlled conditions.[5] Gas chromatography provides a means of demonstrating this and now reveals the presence in such solvolysis mixtures of all six products expected from the "core" set of cations as well as three additional ones with structures **10**, **8**, and **9** derived from the "periphery" cation A_1. The origin of the latter products from A_1 rather than from the enantiomerically related cation C_2 can be demonstrated in the optically active series,[6] but for the present, the distinction between **10**, **8**, and **9** on the one hand and their respective enantiomers on the other is ignored.



A_1

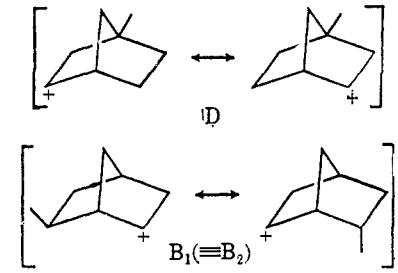
Entry into the "core" cycle is effected *via* cation A when 3-*endo*-methyl-2-*exo*-norbornylamine (**1f**) is nitrosated or when the corresponding *p*-bromobenzenesulfonate (**1e**) is solvolyzed; *via* cation C by deamination of 3-*exo*-methyl-2-*endo*-norbornylamine (**7f**) or the corresponding *p*-bromobenzenesulfonate (**7e**); and *via* cation B by solvolysis of 5-*exo*- or 5-*endo*-methyl-2-*exo*-norbornyl *p*-bromobenzenesulfonate (**6e** or **5e**). The "periphery" cation A_1 (C_2) is encountered in solvolyses of 1-methyl-2-*exo*-norbornyl *p*-toluenesulfonate, in deamination of 2-*endo*-methyl-2-*exo*-norbornylamine,[7] in solvolysis of the corresponding chloride,[8] and also in leakage to the "periphery" from the "core" series. Solvolyses of 6-*endo*-methyl-2-*exo*-norbornyl *p*-bromobenzenesulfonate (**11e**) generate cation B_1 ($\equiv B_2$), which is captured to give **11c** or **11d** and the 6-*exo*-methyl isomer **12c**, or **12d**, in addition to products derived from 6,2-H shift.



a, X = OPhth; b, X = O_2CH; c, X = OAc; d, X = OH; e, X = OBs

Solvolyses. Table I lists the product distributions from solvolytic generation of cations A, B, and C (the "core" series) at 95–100° in several solvent systems. The cations generated at the points of entry into and exit from the scheme are indicated alongside each starting material and product. The percentages of products derived by capture of the *initial* cation (without hydride shift) are given in boldface type.

Very little leakage from the "core" to the "periphery" series of cations by vicinal hydride shift occurs under kinetically controlled conditions (excess of buffer). When the acid generated in solvolysis is allowed to accumulate, however, the kinetically controlled product composition shifts, and the "core" products are gradually converted to 1-methyl-2-*exo* product **10** derived from secondary–tertiary cation A_1, which represents a thermodynamic valley. The accumulation of product **10** under reversible conditions had been observed[4] qualitatively in unbuffered solvolysis of **3a**. The very low yield of products from cation A_1 (Table I) under buffered conditions results therefore from the escape of the bulk of the material at earlier exits in the mechanism. Under prolonged exposure of the 1-methyl-2-*exo* product **10** to equilibrating conditions, still slower processes occur. One of these is secondary–secondary 3,2-hydride shift to give cation D, which



(4) S. Beckmann and G. Eder, *Chem. Ber.*, 91, 2878 (1958).
(5) J. A. Berson in "Molecular Rearrangements," Vol. I, Part 3, P. de Mayo, Ed., Interscience Publishers, Inc., New York, N. Y., 1963.
(6) Papers V and VI of this series: J. A. Berson, J. H. Hammons, A. McRowe, R. G. Bergman, and A. Remanick, *J. Am. Chem. Soc.*, 89, 2581, 2590 (1967).
(7) S. Beckmann, R. Schaber, and R. Bamberger, *Chem. Ber.*, 87 997 (1954).
(8) N. J. Toivonen, E. Siltanen, and K. Ojala, *Ann. Acad. Sci. Fennicae, Ser. AII*, No. 64 (1955).

Table I. Solvolyses

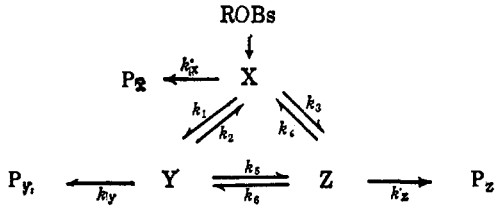
Product, 2-*exo*	Cation	Starting material (ROBs) and conditions: 5-*endo*-Me (B) HOAc[c]	3-*exo*-Me (C) HOAc[c]	3-*exo*-Me (C) HCO_2H[c]	3-*exo*-Me (C) Aq EtOH[d]	3-*endo*-Me (A) HOAc[c]	3-*endo*-Me (A) Aq dioxane[d]	7-*syn*-Me[a] (C) HCO_2H[f]	1-Me (A_1) HOAc[b]	6-*endo*-Me (B_1) HOAc[d]	6-*endo*-Me (B_1) Aq EtOH[d]
		Product, %									
3-*endo*-Me	A	16	18	18	10	**30**	**41**	2	0	0	0
7-*anti*-Me	A	14	17	15.4	9	**31**	**41**	3	0	0	0
5-*exo*-Me	B	**25**	14	11	8	11	4	6	0	0	0
5-*endo*-Me	B	**33**	16	12	10	12	6	3	0	0	0
3-*exo*-Me	C	Trace	**5**	**4**	**14**	Trace	Trace	**1**	0	0	0
7-*syn*-Me	C	9	**28**	**34**	**49**	8	4	**1**	0	0	0
2-*endo*-Me	A_1 (C_2)	4	3.4	1	1.4	7	4	1	**92.7**	68	48
2-*exo*-Me	A_1 (C_2)	0	Trace	?	0	0	0	?	**2.8**	Trace	0
1-Me	A_1	0	Trace	5	0	0	0	73	0	3.1	Trace
Others		0	0	0	0	0	0	10[g]	0	**29**[h]	**52**[i]

[a] Acid phthalate. [b] *p*-Toluenesulfonate, fourfold excess sodium acetate buffer. [c] *p*-Nitrobenzenesulfonate, fourfold excess sodium formate buffer. [d] *p*-Bromobenzenesulfonate, 25-fold excess pyridine buffer, 40–50% by volume ethanol or 50% by volume dioxane. [e] *p*-Bromobenzenesulfonate, 2.5-fold excess sodium acetate buffer. [f] *p*-Bromobenzenesulfonate, 10% molar excess sodium acetate buffer. [g] About 60% of this fraction was 6-*exo*-methyl-2-*exo* product (**12b**). The remainder was a mixture of about equal parts of 6-*endo*-methyl-2-*exo* (**11b**), 1-methyl-2-*endo*, and 1-methyl-3-*exo* products. [h] This fraction consisted of a 9.8:1 mixture of 6-*exo*-methyl-2-*exo*-norbornyl acetate and **11c**. [i] A mixture (8.2:1) of the 6-methyl-2-*exo* norbornanols, the *endo* isomer **11d** being the minor component.

leads to 1-methyl-3-*exo* product, and cation B_1 ($\equiv B_2$), which leads to 6-*exo*- and 6-*endo*-methyl-2-*exo* products. Significantly, under buffered conditions in all the media examined, only the first nine products listed in Table I are formed. These are the ones expected from Scheme I of paper I.

6,2-Hydride Shift *vs.* Solvent Capture. Table I shows that regardless of the point of entry into the scheme, products from each of the "core" cations A, B, and C are always found. Thus, 6,2-hydride shift is competitive with capture by solvent. The transannular shifts are intramolecular. Sodium acetate buffered acetolysis of 3-*exo*-methyl-2-*endo*-norbornyl *p*-bromobenzenesulfonate (entry *via* cation C) in acetic acid-O-*d* gives the typical mixture of products, about two-thirds of which (Table I) arise from hydride shift, but these contain only about 0.03 D per molecule. In contrast, the 1-methyl-2-*exo*-norbornyl product that accumulates in unbuffered medium incorporates substantial amounts of deuterium.

The per cent of product derived from the cation generated at entrance (boldface entries in Table I) is greater in aqueous medium than in acetic or formic acid. In a crude sense, this effect suggests that capture by solvent becomes relatively more important as the solvent nucleophilicity increases. Similar behavior is observed in the 7,7-dimethyl–3,3-dimethyl–5,5-dimethyl series[9] and in the 2,3-di-^{14}C-labeled norbornyl[10a] and 7-chloronorbornyl cases.[10b] In terms of the adjacent scheme, this interpretation amounts to the proposal that k_x, the rate constant (which includes a solvent concentration term) for capture of the initial cation X, is greater in the more nucleophilic solvent. Strictly speaking, this is applicable to the observed result only in the "unsubstituted" (isotopically labeled) norbornyl case, where the fractions of the total product derived without (F_x) and with ($F_y + F_z$) hydride shift are given by eq 1 and 2. If it is assumed that the hydride shift rate k_1 is insensitive to solvent, the fraction of X captured as P_x necessarily increases as k_x increases. The



$$F_x = P_x/(P_x + P_y + P_z) = (k_1 + k_x)/(3k_1 + k_x) \quad (1)$$

$$F_y + F_z = (P_y + P_z)/(P_x + P_y + P_z) = 2k_1/(3k_1 + k_x) \quad (2)$$

simplicity of eq 1 arises from symmetry; in the "unsubstituted" norbornyl system, where X, Y, and Z are structurally equivalent, all the hydride shift rate constants (k_1 through k_6) are identical (except for a negligible isotope effect), as are all the capture rate constants (k_x k_y, and k_z). Furthermore, these respond equally to a change of solvent. The symmetrical situation is discussed further elsewhere,[6] but we note here that in the general case the equivalences are perturbed by substitution, and large changes in the rate constants result. The solvent effect is then less readily interpretable, since the fraction $P_x/(P_x + P_y + P_z)$ is a much more complex function of the rate constants, any or all of which (k_x, k_y, and k_z in particular) may have varying solvent sensitivity.

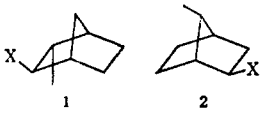
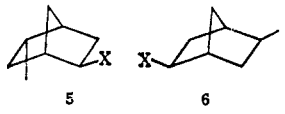
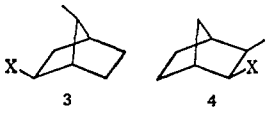
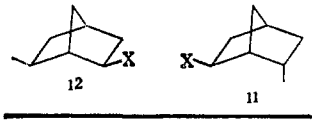
The general pattern of Table I makes it clear that the rates of solvent capture, 6,2-hydride shift, and tertiary–secondary 3,2-hydride shift are all competitive. Were 6,2 shift overwhelmingly fast relative to the other two processes, the product distribution would be insensitive not only to solvent variation but also to the point of entry into the "core" cycle. This is clearly not the case. Even with cation B_1 ($\equiv B_2$) derived from 6-methyl substrate, where 6,2-hydride shift is especially favorable because it leads to tertiary cation C_2, one still sees a substantial amount of direct solvent capture (Table I).

Tertiary cation C_2 (A_1), whether generated from the 6-methyl system B_1 by hydride shift or directly from 1-methyl-2-*exo* precursor, does not revert to any of the

(9) A. Colter, E. C. Friedrich, N. J. Holness, and S. Winstein, *J. Am. Chem. Soc.*, 87, 378 (1965), and references cited therein.

(10) (a) J. D. Roberts, C. C. Lee, and W. H. Saunders, Jr., *ibid.*, 76, 4501 (1954); (b) W. G. Woods, R. A. Carboni, and J. D. Roberts, *ibid.*, 78, 5653 (1956).

Table II. Products Derived from Capture of Methylnorbornyl Cations

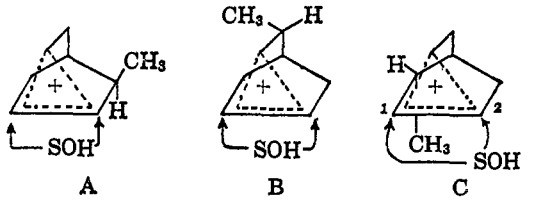
Wagner–Meerwein pair[a]	Cation	Starting material and conditions[b]: HOAc	HCO_2H[c]	HOAc	Aq EtOH	HOAc	Aq dioxane	HOAc	EtOH
		Product ratio							
 1 2	A	1.15	1.13	1.05	1.13	1.03	0.98	...	...
 5 6	B	1.33	1.10	1.13	1.30	1.1	1.4	...	...
 3 4	C	...	8 ± 2	5 ± 0.5	4 ± 0.5	...	...	...	...
 12 11	B_1	...	...	...	...	...	...	9.9	8.1

[a] In acetolyses, X = OAc; in aqueous ethanol or aqueous dioxane, X = OH. [b] Acetolyses at 95–100°, NaOAc buffered; hydrolyses at 95°, pyridine buffered. Product ratios do not change under reaction conditions. [c] Formolysis at 95–100°, sodium formate buffered. Product ratios do not change under reaction conditions.

secondary cations of Table I under kinetically controlled conditions.

Relative Rates of Capture of the Cations at Wagner–Meerwein-Related Sites. Each of the "core" cations A, B, and C can be captured at two nonequivalent Wagner–Meerwein-related sites. Arrangement of the products of Table I in Wagner–Meerwein pairs permits an inspection of the relative rates of capture at the two available positions in each. The data are given in Table II, where the results of solvolyses that generate the 6-methyl cation B_1 are also listed. Note that B_1 also suffers extensive hydride shift into the tertiary system (cation C_2).

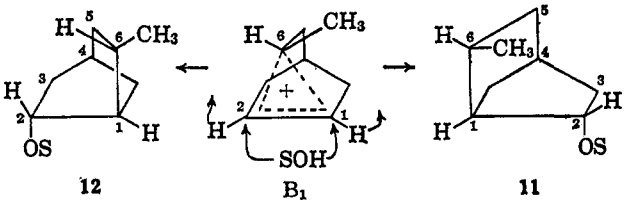
With cations A and B, the capture ratios show virtually no position selectivity and, furthermore, are quite insensitive to solvent or to the point of entry into the "core" cycle. Thus, cation A gives 3-*endo*-methyl- and 7-*anti*-methyl-2-*exo* products (**1** and **2**) in the ratio 1.08 ± 0.06, and cation B gives 5-*endo*-methyl- and 5-*exo*-methyl-2-*exo* products (**5** and **6**) in the ratio 1.23 ± 0.12, the values being the averages of results obtained by generating the cations in six different ways each. The methyl group in both cations is remote from the reaction site and can exert little effect on the approach of a nucleophilic solvent molecule (SOH) from the *exo* direction.



As an alternative, one might consider a trivial explanation for the constancy of the ratios based on the assumption that equilibration of starting arenesulfonate *via* ion-pair return provides a common pool of mixed substrates regardless of the point of entry. This can be ruled out immediately, since it would require not only constant capture ratios for each cation but constant ratios of *all* products, in conflict with the data of Table I. The invariance of the product ratios from cations A and B is most simply explained in terms of characteristic ratios for cation capture. These seem to be quite insensitive to solvent.

Cation C shows a marked preference for attack at C-2 to give *syn*-7-methyl-2-*exo* product rather than at C-1 to give 3-*exo*-methyl-2-*exo* product, as would be expected from the more severe steric shielding of C-1 by the methyl group. The apparent fluctuation in the product ratio from C is probably attributable to the lower accuracy of analyses for these two products. The data also suggest a slower over-all rate of capture (or a higher rate of hydride shift) for cation C than for cations A or B, since the total amount of C-derived products (**3** and **4**) when entry is made at C is substantially less than the total amount of A-derived or B-derived products when entry is made at either of those points.

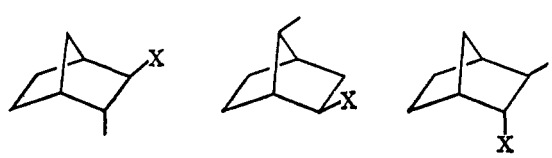
In cation B_1 even though the methyl group now does not interfere directly with the line of approach of solvent to the *exo* side of C-1 or C-2, there is an 8- to 10-fold preference for attack at C-2 to give 6-*exo*-methyl-2-*exo*



(12) rather than at C-1 to give 6-*endo*-methyl-2-*exo* (11) product. A simple interpretation of the preference is based on the repulsive interactions that develop in the transition states. One of these involves the site of attack, where a hydrogen is driven upwards toward either another hydrogen or a methyl group at C-6. It seems reasonable to assume that the $H-CH_3$ repulsion generated during attack at C-1 would be the more serious one, and that consequently attack at C-2 would predominate.

The steric effect in the product-forming step is associated with a difference in free energy between the transition states leading to **12** and **11**, since the ground states are either the same or effectively the same (a common nonclassical ion B_1, or if the opponents of such species insist, a pair of rapidly equilibrating classical ions). Whatever its detailed nature, a kind of specific destabilization similar to that in the transition state leading to 6-*endo*-methyl-2-*exo product* must also be present, by virtue of an approximately microscopically reverse relationship, in the solvolysis of a corresponding 6-*endo*-methyl-2-*exo substrate*. If this energy increment is the predominant one and if it is greater in the transition state than in the solvolysis ground state, the result would be a lower solvolysis rate for a 6-*endo*-methyl derivative than for the unsubstituted norbornyl system itself. The observation[11] that 6,6-dimethyl-2-*exo*-norbornyl *p*-toluenesulfonate acetolyzes 25 times slower than the corresponding norbornyl derivative is consistent with these requirements. It is tempting to conclude, as a referee has urged, that the steric interference in question *is* greater in the transition state, which would be attributable to a decreased C-2:C-6 distance resulting from carbon bridging in a nonclassical structure. In our opinion, however, this probably would be an overinterpretation, since substitution of methyl for hydrogen in the norbornyl system unavoidably introduces numerous steric interactions (in addition to the one depicted in B_1) in both ground and transition states. The net increase or decrease in solvolysis rate as compared to the parent system is a resultant of these difficultly separable effects. For the present, we merely point out that the results given here provide experimental evidence for transition-state steric effects in 6-*endo*-methyl-2-*exo*-norbornyl solvolyses. Future analyses of substituent effects on solvolysis rates in norbornyl derivatives must take factors of this kind into account.

Deamination of 3-*exo*-Methyl-2-*endo*-norbornylamine (7f) and 3-*endo*-Methyl-2-*exo*-norbornylamine (1f). Komppa and Beckmann[12] prepared these two amines in what must have been[13] essentially pure form from the corresponding acids. From deamination with sodium nitrite in aqueous acetic acid they reported isolation



1 **3** **7**

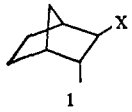
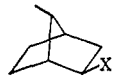
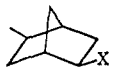
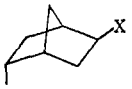
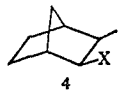
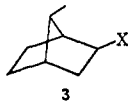
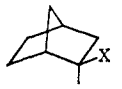
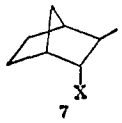
c, X = OAc; d, X = OH; f, X = NH_2

(as acid phthalates) of two alcohols, *syn*-7-methyl-2-*exo*-norborneol (**3d**) and 3-*exo*-methyl-2-*endo*-norborneol (**7d**). In addition, they inferred that another product, *anti*-7-methyl-2-*exo*-norborneol (**2d**), was present in the reaction mixture from one (or both) of the amines.[14] In our hands, substantial quantities of the *endo* alcohol **7d**, the *syn*-7-methyl-2-*exo* alcohol **3d**, or the corresponding acetates are formed only from *endo* amine **7f**. The product distributions from the two amine hydrochlorides are given in Table III. The conditions for deamination of **1f** are those of Komppa and Beckmann[12] (aqueous acetic acid, sodium nitrite); these give a mixture of alcohols and acetates. Deamination of **7f** is effected in dry acetic acid or in water, where the products are acetates or alcohols, respectively.

The most striking difference between the deamination (Table III) and solvolysis (Table I) results is the large amount of 3-*exo*-methyl-2-*endo*-norbornyl derivative (**7d** or **7c**) formed in deaminations of 3-*exo*-methyl-2-*endo*-norbornylamine **7f**. This product is not formed in deaminations of the 3-*endo*-methyl-2-*exo* amine **1f** or in solvolyses of any of the substrates of Table I. Qualitatively, formation of **7c** with retention of configuration from amine **7f** recalls previous observations with the unsubstituted parent compound *endo*-norbornylamine.[15,16] The deamination of that substance in acetic acid gave [16] acetate products 21–23% of which were formed by a path in which substitution (by some mechanism not yet clear[16]) occurred at the site of the original amino group and 77–79% of which came from "racemizing" processes involving nonclassical ions or their structural equivalents. The 21–23% "direct substitution" figure is matched fairly well by the 28% of product **7c**, 3-*exo*-methyl-2-*endo*-norbornyl acetate. Another 4% of product with unrearranged structure, 3-*exo*-methyl-2-*exo*-norbornyl acetate (**4c**), is also formed, but it seems likely that most if not all of this material results from capture of the familiar cation C rather than by "direct substitution." This conclusion is based on the demonstrably reasonable assumption that the characteristic cation capture ratios observed for Wagner–Meerwein pairs in solvolyses of arenesulfonates (Table II) apply, at least roughly, to deaminations as well. For example, the **1**:**2** ratios of Table III from amine **7f** (where neither **1** nor **2** can be formed by direct substitution) are 1.28 and 0.94. Although measured on minor components and hence not very accurate, these are in agreement with the average value 1.08 of Table II. Similarly, the **5**:**6** ratio of 1.6, again measured on a minor pair of products, corresponds moderately well to the value 1.23 found in Table II. Thus, if any appreciable fraction of the *cis-exo* product **4** were being formed by "direct substitution," the **3**:**4** ratio should be less than that found in solvolysis. This solvolytic value, which because of experimental difficulties is not very accurately measurable, ranges between 4 and 8 (Table II), whereas the deaminative **3**:**4** ratio (Table III) is in the range 11–12. Although the discrepancy, if real, is not readily interpretable, the data argue against the idea of an

(11) P. von R. Schleyer, M. M. Donaldson, and W. E. Watts, *J. Am. Chem. Soc.*, 87, 375 (1965).
(12) G. Komppa and S. Beckmann, *Ann.*, **523**, 68 (1936).
(13) S. Beckmann and R. Mezger, *Chem. Ber.*, **90**, 1559, 1564 (1957).
(14) For further discussion, see paper II of this series: J. A. Berson, A. W. McRowe, R. G. Bergman, and D. Houston, *J. Am. Chem. Soc.*, **89**, 2563 (1967).
(15) E. J. Corey, J. Casanova, Jr., P. A. Vatakencherry, and R. Winter, *J. Am. Chem. Soc.*, **85**, 169 (1963).
(16) J. A. Berson and A. Remanick, *ibid.*, **86**, 1749 (1964).

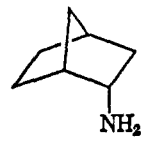
Table III. Deaminations of 3-Methylnorbornylamines

	Me gp	Cation	Starting material and conditions: 1f, Aq HOAc, X = OH (Product, %)	1f, Aq HOAc, X = OAc (Product, %)	7f, Dil HCl, X = OH (Product, %)	7f, HOAc, X = OAc (Product, %)
 1	3-*endo*	A	34	21	4.5	5.7
 2	7-*anti*	A	23	14	3.5	6.1
 6	5-*exo*	B	~1	1	<1	3.5
 5	5-*endo*	B	~1	1	3.7	5.5
 4	3-*exo*	C	1	Trace	3.1	4.3
 3	7-*syn*	C	1	1	38.4	46.4
 8	2-*endo*	C_s (A_1)	1	1	0	0
 7	3-*exo*		0	0	46.8	28.4

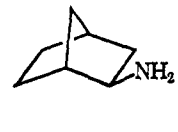
origin of a substantial amount of product **4** in a "direct substitution" path.

In the deamination of 3-*endo*-methyl-2-*exo*-norbornylamine (**1f**), at most a small amount of the product seems to arise from direct substitution. The ratios of products **2**:**1** in both the alcohols (X = OH) and acetates (X = OAc) are about 1.5, and if this is assumed to be meaningfully higher than the ratio 1.08 found in solvolyses (Table II), as much as 9% of the alcohol and 6% of the acetate of the 3-*endo*-methyl-2-*exo* structure (**1d** or **1c**) might be "direct substitution" product. There is no 3-*endo*-methyl-2-*endo* product (less than 1% would have been detected), so that the 6–9% figures represent the total "direct substitution." Thus, "direct substitution" is considerably less important with the 3-*endo*-methyl-2-*exo* amine **1f** than with the 3-*exo*-methyl-2-*endo* isomer **7f**. This corresponds to the pattern in the unsubstituted norbornylamine case,[16] where the *exo* amine gave less "direct substitution" product than the *endo*.

The division of the "direct substitution" products between inversion (*exo* amine → *endo* alcohol, *endo* amine → *exo* alcohol) and retention modes for the two *trans*-3-methylnorbornylamines (**7f** and **1f**) and for the two unsubstituted cases (**13** and **14**) are summarized in Table IV. The major effect of substituting a 3-*trans*-methyl for 3-hydrogen in both the *endo*- and *exo*-amino



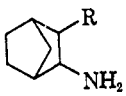
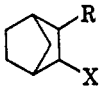
13



14

compounds (**13** → **7f**, **14** → **1f**) is to suppress the inverting deaminative "direct substitution." The result is consistent with several mechanistic rationalizations for the process and hence not decisive. Nevertheless, it does demonstrate a rather high degree of steric sensitivity to β substitution. This sensitivity is particularly pronounced in the case of 3-*exo*-methyl-2-*endo*-norbornylamine (**7f**), where the *exo*-methyl group forces virtually exclusive *endo* substitution (retention), a complete reversal of the result obtained[16] in the unsubstituted

Table IV. Inversion and Retention in the Deaminative "Direct Substitution"

Starting amine		Total % "direct subst" in		Fraction of "direct subst"	
					
R	NH_2	X = OH	X = OAc	Retn	Invn
H	*endo* (13)[a]	...	21–23	0.14–0.22	0.78–0.86
H	*exo* (14)[a]	...	13	0.85	0.15
exo-CH_3	*endo* (7f)	47[b]	28[c]	1.00, 1.00	0
endo-CH_3	*exo* (1f)	9[d]	6[d]	1.00, 1.00	0

[a] Reference 16. [b] In water. [c] In dry acetic acid. [d] In aqueous acetic acid.

case. The stereochemistry of "direct substitution" in **7f** contrasts markedly with that in the lithium aluminum hydride reduction of the corresponding ketone, 3-*exo*-methyl-2-norbornanone, which gives predominantly the product of *exo*-hydride attack, 3-*exo*-methyl-2-*endo*-norbornanol (**7d**).[13,14,17] The observed stereochemistry of hydride reduction of 2-norbornanones has been used[5,18] as a model of the stereochemistry to be expected in the nucleophilic capture of hypothetical classical 2-norbornyl cations. The discrepancy between the results in the 3-*exo*-methyl system must mean either that the model is not uniformly applicable or that a classical carbonium ion is not the product-forming intermediate in the "direct substitution." In view of the widespread intervention of ion pair or other complex intermediates in deaminations[19] which might well produce the observed stereochemical pattern, it seems unnecessary to abandon the stereochemical model.

Experimental Section

Acetic acid and formic acid were dried according to procedures in the literature.[20,21]

Solvolyses were carried out at 95–100° under the conditions given in Table I. Cold solutions of reactive substrates were injected into preheated solvolysis media. The preparation of the substrates is described elsewhere.[22] Acetolyses and formolyses were carried out at initial concentrations of about 0.5 *M* buffer and 0.1 *M* substrate. Hydrolyses used about 2.5 *M* pyridine and about 0.1 *M* substrate. As has been shown elsewhere,[6] the material balance in acetolysis of 3-*exo*-methyl-2-*endo*-norbornyl *p*-bromobenzenesulfonate is essentially quantitative. Product identification was achieved for the runs of Table I by actual isolation[6] and/or by co-vpc with known samples[22] on two different capillary columns using procedures already described. Detector response to isomers was considered uniform. Samples of 0.2 μl were injected with splitting ratios of 100:1 to 400:1. Detector response was linear with this size sample if column "bleed" was not excessive.

Peak areas were determined by triangulation and were reproducible to better than 0.5% between two major well-resolved peaks and to 1–2% between minor ones. Comparisons between peaks of very different size were subject to greater error. Analyses were carried out with columns L and N^{22} on acetate mixtures. Alcohols were acetylated and formates were saponified to alcohols and acetylated for analysis. Most of the peaks were resolved to base line, but *syn*-7-methyl-, 5-*exo*-methyl-, and 3-*exo*-methyl-2-*exo*-norbornyl acetates emerged within 1 min of each other and were difficult to analyze with high accuracy. The tertiary acetate, 2-*endo*-methyl-2-*exo*-norbornyl acetate, separated from its epimer 2-*exo*-methyl-2-*endo*- and from its Wagner–Meerwein relative 1-methyl-2-*exo*-norbornyl acetate, whereas the alcohol 1-methyl-2-*exo*-norbornanol separated well from the two tertiary alcohols. All three of these separated well from the remainder of the product mixture. The amount of 2-*exo*-methyl-2-*endo* material was, therefore, determined by difference between the acetate and alcohol chromatograms.

Except for the slow conversion among these three "tertiary-related" acetates,[6] the remainder of the product composition was essentially unchanged upon reexposure to the reaction conditions in buffered medium. In particular, no interconversion between the "tertiary-related" products and the group of secondary products derived from the "core" cations occurred, nor was there appreciable interconversion among the latter secondary products, at least in buffered acetolyses and hydrolyses. In formolysis, even in the presence of buffer, slow conversion to 1-methyl-2-*exo* product was observed. Entry *via* cation C in Table I was effected by a brief (5 min) formolysis of 3-*exo*-methyl-2-*endo*-norbornyl *p*-nitrobenzenesulfonate. This sufficed to achieve essentially complete reaction, but the product mixture was essentially unchanged after 20-min additional exposure and therefore presumably reflects rate control. After 2 hr of further exposure, however, the accumulation of 1-methyl-2-*exo* product became detectable. Unbuffered formolysis of the *p*-bromobenzenesulfonate gave 1-methyl-2-*exo* formate as the major product.

3-*exo*-Methyl-2-*endo*-norbornylamine (7f). A mixture of 13.1 g (85 mmoles) of pure racemic 3-*exo*-methyl-2-*endo*-norbornanecarboxylic acid, 95 ml of concentrated sulfuric acid, and 175 ml of reagent grade chloroform was chilled below 0°. In small portions, 6.5 g (100 mmoles) of sodium azide was added. The mixture was stirred at room temperature for 4 hr with a slow evolution of bubbles. Refluxing on a steam bath for 1.5 hr completed the reaction. The reaction mixture was cooled and 300 ml of 6 *N* sodium hydroxide solution was added to half-neutralize the acid; the addition of 350 ml of water was necessary to dissolve the salts formed.

The chloroform layer was drawn off from the chilled mixture, and the aqueous phase was washed with another 50 ml of solvent. The solution was made basic and more water was added. The free amine was extracted four times with a total of 600 ml of ether; the combined organic layers were washed once with 1 *N* sodium hydroxide solution and twice with saturated brine and dried over sodium sulfate.

The hydrochloride was precipitated by passing anhydrous hydrogen chloride gas over the chilled ether solution of the amine. The solid was filtered off and dried *in vacuo*. The yield of white, crystalline, nondeliquescent material was 12.5 g (91%). The material could be recrystallized from absolute ethanol.

The urea prepared in the manner described[12] gave sharply melting platelets, mp 204–205° (lit.[12] mp 200–201°).

3-*endo*-Methyl-2-*exo*-norbornylamine (1f) was prepared in a similar manner from the corresponding acid. The urea melted at 209–210° (lit.[12] mp 206–207°).

Aqueous Deamination of 3-*exo*-Methyl-2-*endo*-norbornylamine (7f). A solution of 1.9 g (27.5 mmoles) of sodium nitrite in 8 ml of water was added over a period of 10 min to a solution of 2.0 g (12.3 mmoles) of amine hydrochloride in 20 ml of water and five drops of 10% hydrochloric acid at 0°. The mixture, which became cloudy after 1 hr, was allowed to stand at 25° for 4 hr. No reddish nitrogen oxide fumes were noticed throughout the reaction course.

The acid solution was extracted with pentane three times; the combined organic layers were washed with saturated brine twice and dried over sodium sulfate. Careful concentration of the pentane solution yielded 1.5 g (96%) of a yellow oil as crude residue with the characteristic alcohol odor. An intense infrared spectrum of the neat liquid film indicated very strong hydroxyl peaks, no acetate at 5.75 or 8.0 μ, and only a very weak nitrate ester peak (6.1 μ). Capillary vpc on columns L or N indicated only one major peak (≥90% of total area). No 5-*exo* alcohol was present.

(17) S. Beckman, A. Durkop, R. Bamberger, and R. Mezger, *Ann.*, **594**, 199 (1955).
(18) R. Howe, E. C. Friedrich, and S. Winstein, *J. Am. Chem. Soc.*, **87**, 379 (1965).
(19) (a) E. H. White and C. A. Aufdermarsh, *ibid.*, **83**, 1179 (1961); E. H. White and F. W. Bachelor, *Tetrahedron Letters*, 77 (1965); (b) T. Cohen and E. Jankowski, *J. Am. Chem. Soc.*, **86**, 4217 (1964); (c) R. Huisgen and C. Rüchardt, *Ann.*, **601**, 1 (1956).
(20) L. F. Fieser, "Experiments in Organic Chemistry," 3rd ed, D. C. Heath and Co., Boston, Mass., 1957, p 281.
(21) P. D. Bartlett, C. E. Dills, and H. G. Richey, Jr., *J. Am. Chem. Soc.*, **82**, 5414 (1960).
(22) See ref 14.

The crude product was acetylated directly with excess pyridine and acetic anhydride for 1.2 hr at 98°. After the reaction mixture was cooled to 25°, the excess anhydride was hydrolyzed with water for 2 hr. The mixture was then extracted three times with pentane, and the combined organic layers were washed with 10% hydrochloric acid, 10% sodium carbonate solution, and twice with saturated brine and dried over sodium sulfate.

The solution was carefully concentrated to yield a yellow residue which was distilled bulb to bulb at room temperature (3×10^{-2} mm) The yield of colorless product was 1.8 g (90%) with the characteristically fruity odor. The infrared spectrum indicated it was all acetate; no hydroxyl absorptions remained. Analysis by capillary vpc on column L indicated two major peaks with small amounts of other acetate and unidentified olefins. The distribution of acetate products is given in Table III, in which the approximately 1% olefin formed is omitted. The errors in these percentages are estimated to be ±0.5% absolute, although similar sized components can be compared with greater accuracy. The 5-*exo*-methyl-2-*exo* acetate **6c** emerges between **4c** (3-*exo*) and **3c** (7-*syn*), and while it may be present to some extent, the limit of the determination of this component is about 1% for this case.

The two major components **3c** and **7c** could be preparatively separated on column E. After two successive passes, component **7c** was free of any contamination. Its infrared spectrum was identical with that of the acetate prepared by the Baeyer–Villiger oxidation of 3-*exo*-methyl-2-*endo*-acetylnorbornane. It was reduced to 3-*exo*-methyl-2-*endo*-norbornanol (**7d**) with lithium aluminum hydride. The acid phthalate was prepared with equimolar quantities of phthalic anhydride and pyridine at 100° for 2 hr. This product, recrystallized thrice from hexane–benzene, melted at 126.5–128.0° (lit.[12] mp 131–132° for apocamphenilyl acid phthalate). Mixture melting point with the acid phthalate from the Baeyer–Villiger product gave no depression.

Three passes of component **3c** through column E still gave material contaminated with several per cent each of **4c** and **5c**. Reduction to the alcohols with lithium aluminum hydride and preparation of the acid phthalate were carried out in the usual manner. Four recrystallizations from hexane–benzene yielded material, mp 163.5–166.0° (lit.[12] mp 165–166° for "isoaposantenyl acid phthalate"). Two more recrystallizations did not change the melting point. Saponification of the purified acid phthalate by alkaline steam distillation, ether extraction, drying, concentration, and acetylation in the usual manner gave back 7-*syn*-methyl-2-*exo*-norbornyl acetate (**3c**) contaminated with 3% **4c**.

Deamination of 3-*exo*-Methyl-2-*endo*-norbornylamine in Acetic Acid. To 20 ml of dry acetic acid was added 0.43 g (2.66 mmoles) of amine hydrochloride. The solution was stirred and chilled to *ca.* 4° (solidification occurred at any lower temperature), and 0.43 g (6.2 mmoles) of finely crystalline sodium nitrite was added over a 20-min period. The solution became cloudy after 10 min and was allowed to stand at room temperature for 2 hr.

Ice water was added, and the mixture was extracted four times with pentane. The combined organic layers were washed once each with 2 *N* hydrochloric acid, saturated bicarbonate, and saturated brine, dried over sodium sulfate, and carefully concentrated. The pale yellow, mobile liquid product weighed 0.38 g (85%) and was directly analyzed on capillary columns L and N. Several per cent olefin and about 3% alcohols were formed in addition to the acetates. The minor classes of components were not readily identified. Only the relative acetate composition is reported in Table III.

A small portion of the acetate mixture was reduced with lithium aluminum hydride to the alcohol mixture. Analysis on capillary column L indicated the presence of a trace, estimated to be 0.02%, of the *t-exo* alcohol. No 1-methyl-2-*exo*-acetate or *t-endo* acetate was detected.

Deamination of 3-*endo*-Methyl-2-*exo*-norbornylamine Hydrochloride. A solution of 32.0 g of sodium nitrite in 100 ml of water was added dropwise to a stirred solution of 10.0 g of the amine hydrochloride in 75 ml of 50% (by volume) water–acetic acid at room temperature. Gas evolved at a moderate rate and an organic phase quickly separated. The mixture was allowed to stir at room temperature for 5 hr; it was then extracted four times with pentane. The pentane extracts were combined and washed with water and sodium bicarbonate until the washings were basic; they were then washed with saturated sodium chloride solution and dried over magnesium sulfate. Filtration and solvent evaporation with a Vigreux column left 6.0 g (67% yield) of a mixture whose composition is described in Table III. Distillation of the mixture bulb to bulb and acetylation of the distillate by the usual method gave a mixture of acetates whose composition was identical with the "acetate fraction" of Table III.

On column E at 180°, 3-*endo*-methyl-2-*exo*-norbornyl acetate (**1c**) and 7-*anti*-methyl-2-*exo*-norbornyl acetate (**2c**) could be separated from the minor products and obtained in relatively pure form. After reduction of **1c** with lithium aluminum hydride, the alcohol **1d** obtained was converted to its acid phthalate derivative **1a**. Compounds **1c** and **1d** were identified by comparison of their infrared spectra and retention times on vpc with those of authentic materials.[22] Compound **1a** had mp 89.5–90°, alone or mixed with an authentic sample[22] of 3-*endo*-methyl-2-*exo*-norbornyl acid phthalate. Compound **2c** had a retention time on vpc different from that of 3-*exo*-methyl-2-*endo*-norbornyl acetate (**7c**) or 7-*syn*-methyl-2-*exo*-norbornyl acetate (**3c**). By lithium aluminum hydride reduction and treatment with phthalic anhydride, it was converted to 7-*anti*-methyl-2-*exo*-norbornyl acid phthalate (**2a**), mp 105.5–107.5° (from heptane).

Anal. Calcd for $C_{16}H_{18}O_4$: C, 70.06; H, 6.61. Found: C, 70.20; H, 6.57.