Communications to the Editor

Concerted, Backside Displacement and *exo*:*endo* Stereospecificity on Deamination of Substituted Norbornylamines[1]

Sir:

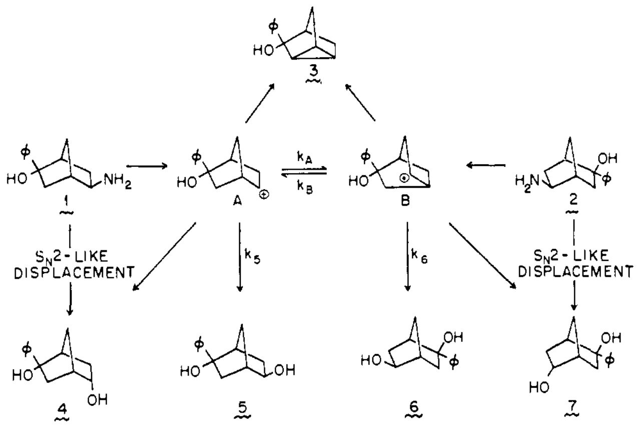
We have measured the stereospecificity (166–650) for *exo*:*endo* attack on the classical 5-phenyl-5-hydroxy-2-norbornyl cations (A and B) during deamination and, in addition, have strong evidence for S$_N$2-like processes during these reactions. Our experiments clearly require open ions, but exclude nonclassical ions as necessary intermediates.

There have been arguments both for[2,3] and against[4] S$_N$2-like processes during deaminations of the *exo*- and *endo*-2-norbornylamines, and although there seems to be general agreement[2–5] that classical cations can be formed,[6] the consensus as to what happens to them is summed up by Bartlett:[7] "The principal fate of the classical ion is conversion to the nonclassical ion, from which the racemic *exo*-acetate comes."

The high ratio of *exo*:*endo* product formation during solvolysis of 2-*exo*-norbornyl esters is an important criterion for the existence of nonclassical norbornyl ions,[8] although there has been no clear-cut measurement of such stereospecificity for the classical unsubstituted 2-norbornyl ion. The problems involved in such an experiment have been partially discussed by Bartlett[7] and appear to be formidable. For this reason we decided to study *exo*:*endo* product ratios and the possibility of S$_N$2-like processes with the substituted 2-*exo*-norbornylamines **1** and **2**.

The ratio of the yields of the diols **5**:**6**[9,10] upon hydrolysis of both of the tosylates (NH_2 = OTs) corresponding to **1** and **2** is 1.4:1,[10] a result consistent either with a common nonclassical carbonium ion intermediate or with an interconverting pair of classical ions ($A \rightleftharpoons B$) which have already reached equilibrium. During the deaminations of **1** and **2** the counterions formed on decomposition of the diazonium acetates[11] should be so situated[12] that they can directly attack the positively charged positions of the cations A and B. Thus if the Wagner–Meerwein pair $A \rightleftharpoons B$ is classical and has not yet reached equilibrium before anion attack occurs, we might expect amine **1** to yield the monoacetates of the diols **5**:**6** in a ratio greater than 1.4:1, and the amine **2** to yield them in a ratio less than 1.4:1. If, on the contrary, the pair $A \rightleftharpoons B$ is a single, nonclassical ion, both **1** and **2**—like the tosylates—should yield the acetates of **5** and **6** in the same proportions. Further a concerted, backside displacement during deamination of **1** should form *endo*-**4**-acetate and not *endo*-**7**-acetate, which could only be produced by *endo* attack on ion B. Starting with amine **2**, just the reverse would be expected: an S$_N$2-like process should produce the acetate of **7** but not of **4**.

We prepared[13] the amines **1** and **2** and subjected them to deaminating conditions[11] in acetic acid or in acetic acid–sodium acetate solutions. The product mixture was treated with lithium aluminum hydride, and the yields of the products **3**–**7** were determined by isotope dilution analysis[14] with carbon-14 and, when possible, by nmr spectroscopy. The results are summarized in Table I. From these data we can draw the following important conclusions.



(1) The carbonium ion intermediates are best interpreted as the classical Wagner–Meerwein pair $A \rightleftharpoons B$ which do not reach equilibrium before they suffer attack to yield the products, for from **1** the ratio **5**:**6** is 2.3:1, whereas from **2** this ratio is 1:1.7.[15]

(2) The *rearranged* ion B (from **1**) and the *rearranged* ion A (from **2**) produce much smaller yields of *endo* products than the *unrearranged* ions (A from **1** and B from **2**), and we interpret these results to mean that pathways **1** → **4** and **2** → **7** take place[2,3] through S$_N$2-like processes.

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[1] Research sponsored by the U. S. Atomic Energy Commission under contract with the Union Carbide Corporation.

[2] J. A. Berson and D. A. Ben-Efriam, *J. Amer. Chem. Soc.*, **81**, 4094 (1959).

[3] J. A. Berson and A. Remanick, *ibid.*, **86**, 1749 (1964).

[4] E. J. Corey, *et al.*, *ibid.*, **85**, 169 (1963).

[5] J. D. Roberts, C. C. Lee, and W. H. Saunders, Jr., *ibid.*, 76, 4501 (1954).

[6] There is overwhelming evidence for a classical ion in the deamination of 3-*endo*-hydroxy-3-phenyl-2-*endo*-norbornylamine: C. J. Collins, V. F. Raaen, B. M. Benjamin, and I. T. Glover, *ibid.*, **89**, 3940 (1967).

[7] P. D. Bartlett, "Nonclassical Ions," W. A. Benjamin, New York, N. Y., 1965, pp 463, 464.

[8] S. Winstein, E. Clippinger, R. Howe, and E. Vogelfanger, *J. Amer. Chem. Soc.*, **87**, 376 (1965), for example, report the *exo*:*endo* product ratio for acetolysis of the brosylate is greater than 5000.

[9] Compounds **3**, **5**, and **6** have been characterized by C. J. Collins and B. M. Benjamin, *ibid.*, **89**, 1652 (1967).

[10] B. M. Benjamin and B. S. Benjaminov, unpublished work.

[11] C. J. Collins, J. B. Christie, and V. F. Raaen, *J. Amer. Chem. Soc.*, **83**, 4267 (1961); R. Huisgen and Ch. Rüchardt, *Justus Liebigs Ann. Chem.*, 601, 21 (1956); E. H. White and C. A. Aufdermarsh, *J. Amer. Chem. Soc.*, **80**, 2597 (1958).

[12] C. J. Collins, V. F. Raaen, and M. D. Eckart, *ibid.*, **92**, 1787 (1970).

[13] We synthesized the amines by oxidation of the diols[9] **5** and **6** to the corresponding ketones followed by reduction with lithium aluminum hydride to the *endo* diols **4** and **7**. These diols were converted to the *endo* tosylates which were treated with sodium azide. The *exo* azides were reduced to the amines **1** and **2**. C and H analyses and nmr spectra of all compounds are consistent with the assigned structures.

[14] V. F. Raaen, G. A. Ropp, and H. P. Raaen, "Carbon-14," McGraw-Hill, New York, N. Y., 1968, Chapter 2.

[15] The reactants, intermediates, and products shown in the chart lend themselves to the same type of mechanistic analysis employed previously by us [see C. J. Collins and M. H. Lietzke, *J. Amer. Chem. Soc.*, **89**, 6565 (1967)]. If we assume $k_5 = k_6$, then the equilibrium constant $k_B/k_A = 1.1$ can be calculated from the data in Table I.

Table I. Yields of Products and Product Ratios on Deamination of Amines **1** and **2**[a]

Products[b]	From **1** HOAc (glacial)	From **1** HOAc–NaOAc	From **2** HOAc–NaOAc
3	43.5	35.0	29.6
4	3.4[c]	2.4[c]	0.039[c]
5	36.7	43.5	25.6
6	16.5	19.0	42.6
7	0.075[c]	0.114	2.2[c]
Ratio			
5:**6**	2.2:1	2.3:1	1:1.7
5:**4**	10.5:1	18:1	650:1
6:**7**	220:1	166:1	19:1
4:**7**	45:1	21:1	1:56

[a] Deaminations were performed at ambient temperature. [b] The monoacetates of **4–7** were obtained on deamination, and these were converted to the diols with lithium aluminum hydride. Smaller yields of three other compounds[a] resulting from hydride shift in the ions A and B. [c] These products were crystallized repeatedly with the addition of hold-back carrier[14] until the radioactivity contents were constant.

(3) The product ratios **6**:**7** (from **1**) of 166 and **5**:**4** (from **2**) of 650 provide the first measurement of a lower limit for the stereospecificity of *exo*:*endo* attack by anion (or solvent) on a classical, substituted norbornyl carbonium ion. Because of steric hindrance to *endo* attack by the 5-*endo*-phenyl or -hydroxyl groups, one might guess that these ratios are higher than the stereospecificity for *exo vs. endo* attack on the unsubstituted norbornyl cation.

Since the yields of *endo* products formed from A and B through the long routes (**1** → A → B → **7**; **2** → B → A → **4**) are so small and were measured by an indirect method[14] rather than by isolation, the question naturally arises whether these yields are real or merely reflect the limits of our experimental methods. Phrased differently, is it possible for a classical, substituted norbornyl cation to undergo 1,2-Wagner–Meerwein rearrangement to another classical ion which can then suffer *endo* attack? That the answer to this question is "yes" can be seen from the accompanying communication.[16]

(16) B. M. Benjamin and C. J. Collins, *J. Am. Chem. Soc.*, **92**, 3183 (1970).

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Wagner–Meerwein Rearrangements of Substituted Classical Norbornyl Cations[1]

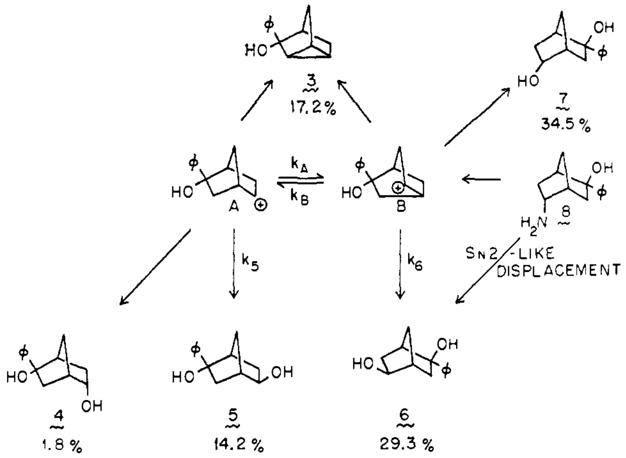
Sir:

In the preceding communication[2] we presented evidence for SN2-like processes during deaminations of the substituted 2-*exo*-norbornylamines **1** and **2**.[3] We reported our measurements of the stereospecificities for *exo vs. endo* attack on the classical ions A and B and concluded that bridged nonclassical ions were unimportant during the deaminations investigated.

We report here the results of our studies of the deamination, in acetic acid–sodium acetate solution, of the *endo* amine **8**. The deamination proceeds through rearrangement of the classical ion B to the classical ion A; A then undergoes some *endo* attack to produce an isolable quantity (about 2%) of *endo*-**4**-acetate. We consider this result to be incontrovertible evidence for the survival of the classical ion A even *after* 1,2-Wagner–Meerwein rearrangement of the initially formed classical ion B; we also consider it further evidence for the unimportance of substituted, nonclassical 2-norbornyl cations during the reaction.

Previously we reported evidence that formation of the counterion by decomposition of the diazonium acetate is an important factor in the control of stereospecificity during deaminations.[4–7] We now present additional evidence and contend that it is primarily the counterion which is responsible for the "memory effects"[8] during our deaminations.

The amine **8** was subjected to deamination[9] in acetic acid–sodium acetate solution at room temperature. The mixture of products **3** and **4–7** (as the acetates) was treated with lithium aluminum hydride, and the yields of **3** and the diols **4–7** were determined spectrally (these yields are shown under the appropriate structures). In addition, the products were isolated by column chromatography. In a second deamination of **8** the yield of **4** was determined with a carbon-14 isotope dilution experiment to be 1.8%, in agreement with our estimation of the yield by isolation.



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(1) Research sponsored by the U. S. Atomic Energy Commission under contract with the Union Carbide Corporation.

(2) C. J. Collins and B. M. Benjamin, *J. Amer. Chem. Soc.*, **92**, 3182 (1970).

(3) We preserve the same numbering system as used in the preceding paper.[2]

(4) C. J. Collins and J. B. Christie, *J. Amer. Chem. Soc.*, **82**, 1255 (1960).

(5) C. J. Collins, J. B. Christie, and V. F. Raaen, *ibid.*, **83**, 4267 (1961).

(6) C. J. Collins, V. F. Raaen, B. M. Benjamin, and I. T. Glover, *ibid.*, **89**, 3940 (1967).

(7) C. J. Collins, V. F. Raaen, and M. D. Eckart, *ibid.*, **92**, 1787 (1970).

(8) J. A. Berson, *Angew. Chem.*, **80**, 765 (1968). We disagree with Berson's argument against counterion control of "memory effects" during deamination, for he assumes that since the leaving group is N_2 such control cannot be important. In his argument Berson overlooks the very strong configuration-holding effect[4–6] of the acetate anion formed on decomposition of the diazonium acetate. See also R. Huisgen and Ch. Rüchardt, *Justus Liebigs Ann. Chem.*, **601**, 1 (1956); E. H. White, *J. Amer. Chem. Soc.*, **77**, 6011, 6014 (1955); E. H. White and C. A. Aufdermarsh, *ibid.*, **80**, 2597 (1958); **83**, 1174, 1179 (1961).

(9) The synthesis was through the following route: norbornenone + PhMgBr → 2-*exo*-phenyl-2-norbornenol (borohydration) → 2-*exo*-phenyl-2-*endo*-hydroxy-5-*exo*-norborneol (mixture) → 2-*exo*-phenyl-2-*endo*-hydroxy-5-*exo*-norbornyl tosylate (hydrolysis) → mixture of diols **5** and **6** (plus smaller yields of several other products). Diol **6** was oxidized with chromic acid to the ketone, which was converted to the oxime. The oxime was then treated with lithium aluminum hydride to yield the amine **8**. Elemental analyses and spectral data were consistent with the assigned structure.