the injector of the high-pressure LC system. The injector lever was turned exactly at the lapse of the desired time, which caused the aliquot to rapidly mix with the methanolic elution solvent and be transported to the high-pressure LC column.

The high-pressure LC system consisted of a Waters μ-Bondapak C_{18} column (30 cm × 3.9 mm i.d.) with 50% MeOH buffered to pH 3.5 with 0.01 M KH_2PO_4 and containing 0.01% desferal mesylate as the elution solvent at a flow rate of 1.5 mL/min.[6] Detection was made at 254 nm, and the signal peak height of the *N*-hydroxyformanilide product converted to micromoles by comparison with the peak height of a known amount of the standard *N*-hydroxyformanilide. Standard calibration curves for each product were prepared immediately prior to the analysis and were always linear in the range in which the studies were conducted.

Special Reaction Method for Time-Course Studies. For those studies that required sequential analyses at given times exceeding 15 min, the above general methodology was modified in the following manner. A 25-mL, round-bottomed flask (Kontes K-294000) fitted with a syringe-needle adapter (Kontes K-275750) was filled with 30.0 mL of 0.05 M, pH 6.0, KH_2PO_4 buffer containing 5.0 mM sodium glyoxylate. After equilibration to 30 °C in a heated water bath, the flask was placed in a New Brunswick Model G-24 shaker and further allowed to equilibrate to 30 °C for about 15 min. The reaction was initiated by the addition of 3 μmol of the nitroso aromatic in 300 μL of ethanol. Rapid mixing was achieved within 15 s by agitation at 400 rpm, after which the agitation rate was lowered to 200 rpm. Aliquots for analysis were taken by temporarily stopping the agitation and then inserting a high-pressure LC syringe needle through the septum.

Radiotracter Experiments with Sodium [1-^{14}C]Glyoxylate. Approximately 50 μCi of sodium [1-^{14}C]glyoxylate (specific activity 8.33 mCi/mmol; Amersham Corp.) was diluted with 499 mg of sodium glyoxylate to give sodium [1-^{14}C]glyoxylate with a specific activity determined to be 9.18 μCi/mmol. The diluted sodium [1-^{14}C]glyoxylate was dissolved in 5.0 mL of H_2O and kept frozen until needed. Incubations were conducted under N_2 in Thunberg tubes by placing 10.0 mL of pH 5.0, 0.05 M, KH_2PO_4 buffer containing 50 μL (0.48 μCi total radioactivity, 52 μmol) of the diluted sodium [1-^{14}C]glyoxylate solution in the reaction tube. The top reservoir was charged with 200 μL of Protosol (New England Nuclear), and the reaction was initiated by the addition of sufficient 4-methylnitrosobenzene as a 100-mM solution in EtOH to achieve the desired reaction concentration. The tubes were incubated in a water bath at 25 °C for 4 h, and then 100 μL of 10% H_2SO_4 was carefully added through the side arm of the tube. After further incubation for 4 h, the Protosol was quantitatively transferred into 12 mL of Aquasol (New England Nuclear) in a glass LSC vial and counted after chemiluminescence effects had disappeared (16 h). Counting efficiency was determined by recounting each vial after the addition of 45 000 dpm of [^{14}C]toluene standard. High-pressure LC analysis of the reaction product was used to quantitatively determine the amount of *N*-hydroxy-*N*-(4-methylphenyl)formamide (**5e**) produced during the incubation. The isolation of **5e** from a large-scale radiotracer experiment (60 mL with 4-methylnitrosobenzene at 0.50 mM) conducted in an identical manner was achieved by extraction twice with 60 mL of Et_2O after the 4-h incubation period. The combined Et_2O extract was washed with 50 mL of saturated NaCl solution, dried (Na_2SO_4), and evaporated in vacuo. The residue was chromatographed on silica gel (11 cm × 9 mm bed size) with 10 mL of $CHCl_3$ and then 50 mL of 2% $MeOH/CHCl_3$. Fractions containing **5e** were identified by the use of high-pressure LC analysis and were combined and evaporated. The residue was dissolved in 2.0 mL of EtOH, of which 0.5 mL was analyzed by LSC in Aquasol. High-pressure LC analysis indicated that the yield of **5e** was 3.3 mg (73% of theory).

Registry No. **1a**, 586-96-9; **1b**, 3623-23-2; **1c**, 932-98-9; **1d**, 932-78-5; **1e**, 623-11-0; **1f**, 611-23-4; **1g**, 352-15-8; **1h**, 1516-21-8; **1i**, 7476-79-1; **2**, 298-12-4; **5a**, 31335-69-0; **5b**, 1836-27-7; **5c**, 1613-88-3; **5d**, 4070-53-5; **5e**, 73747-07-6; **5f**, 73747-08-7; **5g**, 456-07-5; **5h**, 73747-09-8; **5i**, 73747-10-1; sodium glyoxylate, 2706-75-4.

Nitrous Acid Deamination of Axial and Equatorial *trans*-2-Decalylamines in Mixed Solvents[1,2]

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Received August 20, 1979

The nitrous acid deamination of the axial *trans,trans*-2-decalylamine and the equatorial *trans,cis*-2-decalylamine has been performed in water, dioxane, and sulfolane, each containing increasing concentrations of acetic acid. The nitrosation conditions were found to destroy substantial proportions of the elimination and alcohol products, and discrepancies in earlier work may be due to this phenomenon; the alcohols, but not the alkenes, can be nearly completely regenerated by ebullition of nitrogen through the solution, a procedure which is strongly recommended for future work. It is shown that the stereochemical results as well as the acetate/alcohol distribution are essentially identical for the two amines in solutions in nonhydroxylic solvents containing low concentrations of acetic acid; the retained substitution product (60–65% of the total and consisting of about one-half alcohol and one-half acetate) is believed to be formed by collapse of an ion pair containing the carbocation, an acetate ion, and a water molecule produced in the diazotization, whereas the inverted product, which is very largely acetate, is believed to arise by collapse of an inverted ion pair. Very little of the small yield of inverted alcohol is formed by solvent attack on the backside of some intermediate since greatly increasing the concentration of water in the solvent has a negligible influence on the proportion of inverted alcohol produced. The stereochemical results for the two amines diverge as the solutions in nonhydroxylic solvents become richer in acetic acid and the divergence becomes more pronounced with increasing water content of the acetic acid; the more hydroxylic the solvent, the greater the equatorial/axial ratio of substitution products. These results are attributed to unpairing of ion pairs as the hydroxylic nature of the solvent increases; the resulting, symmetrically solvated cations form mainly equatorial products. In the mixtures of acetic acid with nonhydroxylic solvents, only those ion pairs (or their precursors) in which the cation has become stereochemically inverted appear to undergo unpairing.

Ever since the principles of conformational analysis were developed and applied to six-member alicyclic systems,[5] nucleophilic substitution reactions in cyclohexane derivatives have intrigued organic chemists. It is now known

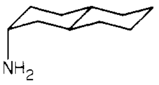
0022-3263/80/1945-2839$01.00/0

that acetolysis of both equatorial and axial cyclohexyl arenesulfonates gives mainly elimination product and that the substitution product is very predominantly inverted.[6]

The results are very different for nitrous acid deaminations[7,8] in which equatorial amines give little elimination and largely retained substitution product while axial amines give mainly elimination and the substitution product is approximately equally inverted and retained. The original explanation for the difference in elimination/substitution ratios between equatorial and axial amines, based on a preferred trans-diaxial transition state for elimination, became moot when it was shown that the elimination is mainly cis.[9a] A tentative explanation for these ratio differences based on isotope effects has been proposed;[9b] it involves a competition in retained ion pairs between removal of the cis proton by the anion and nucleophilic attack to give retained product. However, despite the great effort devoted to the study of deaminations in general[7] and those in conformationally homogeneous cyclohexyl systems in particular,[8] a fairly satisfactory and complete explanation for the difference in the stereochemistry of substitution in deaminations of equatorial and axial amines has not been advanced.[10]

At the time this work was started, most nitrous acid deaminations were conducted in acetic acid or aqueous acetic acid solutions and no reports had appeared of deaminations in conformationally homogeneous cyclohexyl systems in which the stereochemistry of both the alcohols and acetates, starting from either epimeric amine, had been determined. The ratio of total acetate to alcohol had been reported for deamination of the epimeric 4-methylcyclohexylamines.[13] In addition, two intriguing reports had appeared[14,15] that deaminations in cyclic systems, conducted in acetic acid, yielded alcohol of more highly retained configuration than the acetate produced.

Our approach was to determine the stereochemical composition of both the alcohols and acetates upon nitrous acid deamination of the conformationally rigid epimeric trans-fused 2-decalylamines (1 and 2) in solvents containing varying proportions of acetic acid. The *trans*-decalyl system was chosen instead of the 4-*tert*-butylcyclohexyl system, which has been studied by others,[4,8b,e,f] because of the possibility only in the former of regiospecific and stereospecific deuterium labeling at a single one of the β positions[8e,9] and because of the possibility of comparison with the deamination of steroidal amines.



1
trans,trans-2-decalylamine

2
trans,cis-2-decalylamine

Results

In addition to the epimeric *trans*-2-decalols and *trans*-2-decalyl acetates produced from both amines by nitrous acid deamination, the axial amine 1 also yielded a mixture of *trans*-1- and *trans*-2-octalin and two unidentified components. The latter have lower retention times on GLC than either of the *trans*-1-decalols or *trans*-1-decalyl acetates, compounds which were not produced (GLC and IR evidence, authentic samples in hand). These unknowns, which constituted 1–3% of the total substitution product, are probably 9-decalols and acetates resulting from two successive 1,2 hydride shifts.[4,6]

Control tests conducted in 10, 75, and 100 vol % acetic acid in water in the absence of sodium nitrite indicated that neither of the *trans*-2-decalyl acetates were subject to hydrolysis, nor were the epimeric *trans*-2-decalols subject to esterification. The absence of transesterification reactions and the stability of the elimination products in these solutions were also established.

However, when control tests were conducted in the presence of added sodium nitrite, GLC analysis indicated a very substantial loss of both epimeric decalols and of octalin. The loss of the epimeric *trans*-2-decalols was shown to decrease with increasing reaction time and was accompanied by the appearance of two new infrared bands at 1600 and 1639 cm^{-1}; the intensities of these bands were also shown to decrease with increasing reaction time. Since secondary alcohols become reversibly nitrosated in the presence of nitrous acid,[16] it is believed that at least one of the new infrared peaks is due to nitrite esters which are formed rapidly and which slowly revert to alcohol as fumes of nitrogen oxides escape from the solution. Treatment of *trans,cis*-2-decalol with a deficiency of nitrosyl chloride in pyridine produced, upon workup, a yellow solid, which is presumably a mixture of *trans,cis*-2-decalol and *trans,cis*-2-decalyl nitrite and which exhibits a strong IR

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[1] Taken from the Ph.D. theses of A. D. Botelho and E. J. Jankowski, submitted to the University of Pittsburgh in 1970 and 1966, respectively.

[2] A preliminary account of the deamination of the axial amine in aqueous acetic acid mixtures has appeared: T. Cohen and E. Jankowski, *J. Am. Chem. Soc.*, **86**, 4217 (1964). In addition, as a result of private communications, the results for the equatorial amine in aqueous acetic acid have been given exposure in reviews[3] and in one original article.[4]

[3] (a) E. H. White and D. J. Woodcock in "Chemistry of the Amino Group", S. Patai, Ed., Wiley, New York, 1968, p 441; (b) W. H. Saunders, Jr., and A. F. Cockerill, "Mechanism of Elimination Reactions", Wiley-Interscience, New York, 1973, pp 303–305; (c) J. M. Williams, *Adv. Carbohydrate Chem.*, **31**, 9 (1975).

[4] H. Maskill and M. C. Whiting, *J. Chem. Soc., Perkin Trans. 2*, 1462 (1976).

[5] D. H. R. Barton, *Experientia*, **6**, 316 (1950).

[6] N. C. G. Campbell, D. M. Muir, R. R. Hill, J. H. Parish, R. M. Southam, and M. J. Whiting, *J. Chem. Soc. B*, 355 (1968), and references cited there.

[7] For reviews of nitrous and related deaminations, see ref 3 and (a) W. Kirmse, *Angew. Chem., Int. Ed. Engl.*, **15**, 251 (1976); C. J. Collins, *Chem. Soc. Rev.*, **4**, 251 (1975); (b) R. A. Moss, *Acc. Chem. Res.*, **7**, 421 (1974); (c) J. T. Keating and P. S. Skell in "Carbonium Ions", Vol. 2, G. A. Olah and P. R. Schleyer, Eds., Wiley-Interscience, New York, 1970, p 573; L. Friedman, *ibid.*, p 655; R. J. Baumgarten, *J. Chem. Educ.*, **43**, 398 (1966); J. H. Ridd, *Q. Rev., Chem. Soc.*, **15**, 418 (1961).

[8] For recent work on the deamination of conformationally homogeneous axial and equatorial amines, see ref 4, 9, and (a) F. W. Bachelor and E. H. White, *Can. J. Chem.*, **50**, 364 (1972); E. H. White and F. W. Bachelor, *Tetrahedron Lett.*, 77 (1965); (b) C. W. Shoppee, C. Culshaw, and R. E. Lack, *J. Chem. Soc. C*, 506 (1969); (c) C. W. Shoppee, J. G. Feher, R. M. Hall, R. E. Lack, and L. Tarasoff, *ibid.*, 2211 (1969); (d) C. W. Shoppee, R. E. Lack, and P. Ram, *ibid.*, 1018 (1966); (e) G. Lamaty, C. Tapiero, and R. Wylde, *Bull Soc. Chim. Fr.*, 2039 (1968); (f) W. Hückel and K. Heyder, *Chem. Ber.*, **96**, 220 (1963).

[9] (a) T. Cohen and A. R. Daniewski, *J. Am. Chem. Soc.*, **91**, 533 (1969); (b) T. Cohen, A. R. Daniewski, G. M. Deeb, and C. K. Shaw, *ibid.*, **94**, 1786 (1972).

[10] Explanations put forth some time ago based on the presumed relative lifetimes of diastereomeric cations[8d] or on frontside S_N2-type displacements[11] do not seem consonant with modern theory. The more viable concept[12] that frontside-solvated carbonium ions derived from axial amines are shorter lived than those derived from equatorial amines and tend to collpase to symmetrically solvated species does not take into account more recently discovered concepts such as the intermediacy of ion pairs, frontside exchange or intramolecular inversion.[3a] White and Woodcock[3a] have given a satisfactory explanation, based on a common cationic intermediate, for the inversion and retention, respectively, in the products of deamination of axial and equatorial amines in highly aqueous solvents, but they have not dealt with the differences in product distribution in solvents such as acetic acid.

[11] (a) J. A. Mills, *J. Chem. Soc.*, 260 (1953); (b) C. W. Shoppee, D. E. Evans, and G. H. R. Summers, *J. Chem. Soc.*, **97**, (1957).

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[13] W. Hückel and K. D. Thomas, *Justus Liebigs Ann. Chem.*, **645**, 177 (1961).

[14] E. H. White and J. E. Stuber, *J. Am. Chem. Soc.*, **85**, 2168 (1963).

[15] R. Huisgen and C. Rüchardt, *Justus Liebigs Ann. Chem.*, **601**, 1, 21 (1956).

[16] J. Tadanier and W. Cole, *J. Org. Chem.*, **27**, 4615 (1962).

Table I. Nitrous Acid Deamination of *trans,trans*- (Axial) and *trans,cis*-2-Decalylamine (Equatorial) in Acetic Acid-Water[a]

			composition of substitution product in 2-position, %			
entry	amine	vol % (mol %) AcOH	axial alcohol	axial acetate	equatorial alcohol	equatorial acetate
1	axial	100 (100)	26.1 ± 0.7[b]	32.4 ± 0.1[b]	1.9 ± 0.3[b]	39.5 ± 0.5[b]
2	axial[c]	100 (100)	25.2	33.9	2.2	40.3
3	axial	91 (75)	31.3	29.3	5.1	34.3
4	axial	77 (50)	33.0 ± 0[d]	24.9 ± 0.1[d]	12.0 ± 0.5[d]	30.0 ± 0.6[d]
5	axial	77 (50)[e]	32.8	24.3	12.7	30.2
6	axial[c]	77 (50)	34.2	26.1	11.5	28.2
7	axial	53 (25)	32.8	17.2	26.7	23.4
8	axial	50 (23)	34.5	16.8	25.8	22.9
9	axial	27 (10)	32.5	8.0	45.0	14.5
10	axial	10 (3.4)	30.8 ± 2.5[f]	2.6 ± 0.3[f]	62.2 ± 2.5[f]	4.4 ± 0.7[f]
11	equatorial	100 (100)	0.7	18.4	26.3	54.6
12	equatorial	91 (75)	1.2	14.4	35.6	48.8
13	equatorial	77 (50)	2.8	10.3	40.9	46.0
14	equatorial	53 (25)	3.6	6.2	53.1	37.1
15	equatorial	10 (3.4)	2.7	3.2	68.0	26.1

[a] Temperature = 30.5 ± 0.2 °C; 5 mol of nitrite used per mole of amine; reaction time 12-15 h. [b] Average of 3 deaminations. [c] *trans,trans*-2-Decalylamine-*2-d*. [d] Average of 2 deaminations. [e] Sodium acetate present in same molar quantity as sodium nitrite. [f] Average of 4 deaminations. This result differs from that in ref 2. See text.

band at 1639 cm^{-1}. Analysis by GLC revealed only one peak having the retention time of the alcohol; the nitrite ester is apparently destroyed in the injection port. It was shown that the process of denitrosation could be accelerated by ebullition of nitrogen through the aqueous acetic acid solutions of the alcohols which had been treated with sodium nitrite; the equatorial decalol could be completely regenerated as could over 98% of the axial decalol. This technique failed to regenerate the elimination products destroyed by the nitrosating conditions.

In all of the deaminations reported here the decalols were regenerated by passing nitrogen through the solution, then through a dry ice trap, and finally into a 15-20% aqueous solution of potassium iodide. When the iodine color was no longer developed over a 20-min period, the denitrosation was considered complete. Less than 1 h of ebullition was necessary for deaminations conducted in glacial acetic acid and at least 3 h or more of rapid ebullition for those conducted in 10 vol % acetic acid.

Since much of the olefin is destroyed under the reaction conditions, only the composition of the substitution product was regularly monitored. In Table I are summarized the results of the deaminations of the two amines in acetic acid and aqueous acetic acid. Also included are the results of deaminations at two solvent compositions of the axial amine bearing a deuterium atom on the carbinyl carbon atom (entries 2 and 6). The result of adding sodium acetate to the deamination medium of the axial amine is shown in entry 5.

The yield of substitution products from axial amine in acetic acid was 26%. We suspect that most of the remainder was olefin which was partially destroyed by nitrous acid. A 41% yield of *trans*-1- and *trans*-2-octalin was determined; no 1,9-octalin or 9,10-octalin could be detected. In the case of the equatorial amine in 100% acetic acid, the yield of substitution products was 86%; no olefin could be detected. The far higher total recoveries attained in the present work than in the deamination of 4-*tert*-butylcyclohexylamine[4] are probably largely due to the use in our work of 2.2 times larger excesses of sodium nitrite and far longer reaction times. Such conditions were required in order to attain substantially complete deaminations.

Table II. Nitrous Acid Deamination of *trans,trans*- (Axial) and *trans,cis*-2-Decalylamine (Equatorial) in Acetic Acid-Dioxane[a]

		composition of substitution product in 2-position, %			
amine	vol % AcOH	axial alcohol	axial acetate	equatorial alcohol	equatorial acetate
axial	100	26.1	32.4	1.9	39.5
axial	64.1	24.0	30.4	4.8	40.8
axial	29.1	24.1	31.0	5.9	39.0
axial	20.4	23.3	34.2	4.9	37.6
eq	100	0.7	18.4	26.3	54.6
eq	51.1	~ 0[b]	27.0	27.2	45.8
eq	10.3	~ 0[b]	38.0	22.3	39.7
eq	10.0	2.6	36.0	27.6	33.8

[a] Conditions as in Table I. [b] In the analytical method used in these particular experiments, the numbers are estimated by difference and are rather inaccurate for small values; the actual value could be as high as 2%.

The compositions of the products from deamination of the axial amine were used to test the reproducibility of the results. Repetitions of some of the deaminations by the same worker and of all of the deaminations by a second worker some years later revealed that all the results were highly reproducible except those in 10 vol % acetic acid. In this case, the originally homogeneous deamination medium becomes cloudy as deamination proceeds. Furthermore, because of the slow rate of regeneration of alcohols from nitrites, it is difficult to determine the "end point" in the reaction of the nitrogen oxides with potassium iodide. Indeed, the values for 10 vol % (3.4 mol %) acetic acid in the preliminary communication[2] were found to be incorrect;[17] apparently the nitrogen ebullition was not vigorous enough in this particular case. The corrected values (entry 10, Table I), which were found to be acceptably reproducible, indicate considerably higher yields of alcohols and lower yields of acetates than the earlier data.[2]

The aqueous acetic acid system, though common for deaminations, is a complex one for mechanistic study because both components of the solvent are capable of substitution at the cationic center and vast changes in solvent polarity occur as the water content is changed. Therefore, deaminations of the two amines were performed in acetic acid at different concentrations in two presumably inert solvents, the relatively nonpolar dioxane ($\epsilon = 2.2$) and the polar tetramethylene sulfone (sulfolane, $\epsilon = 44$). The

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[17] An error was suspected when a sharp discontinuity appeared in plots of product composition against solvent composition. Such plots of the data in Table I now give smooth curves.

Table III. Nitrous Acid Deamination of *trans,trans-* (Axial) and *trans,cis-*2-Decalylamine (Equatorial) in Acetic Acid-Sulfolane[a]

entry	amine	vol % AcOH	composition of substitution product in 2-position, %			
			axial alcohol	axial acetate	equatorial alcohol	equatorial acetate
1	axial	100	26.1	32.4	1.9	39.5
2	axial	67.8	29.7	31.0	4.3	35.0
3	axial	37.6	28.6	32.9	5.6	32.9
4	axial	1.76	27.2	37.9	6.1	28.8
5	axial	1.74	29.4	36.0	7.3	27.3
6	axial	1.42[b]	38.0	30.2	8.8	23.0
7	eq	100	0.7	18.4	26.3	54.6
8	eq	49	2.9 ± 0.1[c]	24.3 ± 0.1[c]	32.2 ± 2.0[c]	40.6 ± 1.8[c]
9	eq	2.3	3.0	37.5	30.7	28.8

[a] Conditions as in Table I. [b] This solution was also 3.3 vol % in water. [c] Average of two deaminations.

results are displayed in Tables II and III. Concentrations of acetic acid in dioxane of less than 10% were not used because of the insolubility of sodium nitrite in such mixtures. In one of the deaminations of the axial amine (1) in sulfolane at very low acetic acid concentrations, water (3.3 vol %) was added to the medium (Table III, entry 6). It was also demonstrated that in acetic acid–sulfolane mixtures, as in the aqueous acetic acid solutions, much of the olefin is irreversibly destroyed by the nitrosation conditions.

Discussion

Perhaps the most far-reaching consequence of this study is the finding that under nitrous acid deamination conditions olefins and alcohols are to a substantial extent destroyed and that only the alcohols are regenerated slowly on standing and more rapidly upon nitrogen ebullition. Thus, all literature olefin yields and many of the alcohol yields for this type of reaction are probably understated, but the extent must depend not only on the quantity of sodium nitrite used but also on the duration of the experiment; longer reaction times tend to give more accurate yields of alcohols. This nitrosation may be responsible to a large extent for discrepancies in the literature with respect to product distributions in the deaminations of conformationally homogeneous cyclohexylamines.[18] For quantitative analysis of alcohols, regeneration by nitrogen ebullition is strongly recommended. Comparisons[4] of product distribution determined in different laboratories (with the possible exception of ratios of inverted to retained acetates) are of questionable significance unless this procedure is used.

There is a possibility that the intermediate diazonium ions are being epimerized via proton loss to form a diazoalkane followed by reprotonation of the latter. The conventional test for this process has been the determination of the extent of proton–deuterium exchange between the carbinyl position and the medium.[3a,4,8a,19,20] It is conceivable, however, that in some cases the process would be "intramolecular" and would not be detected by this test; thus, the carboxylic acid formed when the carboxylate anion removes the proton from the diazonium ion may, before diffusing away from the diazoalkane, reprotonate the latter to give the epimeric diazonium ion. Such a process should be readily detected by noting differences in product distribution between deamination of amine labeled with deuterium on the carbinyl carbon atom and unlabeled amine. Since proton removal is nearly always accompanied by a substantial isotope effect,[9,21,22] the extent of epimerization of the diazonium ion should be less in the deuterated substrate and a change in product composition should result. The insignificant change which occurs (Table I, entries 2 and 6) rules out all but a very minor role for diazoalkane intermediates, in agreement with conclusions from the deuterium-exchange criterion in the nitrous acid and *N*-nitrosoamide deamination of simple secondary alkyl amines.[3a,20b] We reported earlier that some of the olefinic but none of the ester products had lost an α-deuterium atom in the deamination of 1 and 2 by the *N*-nitrosocarbamate method.[9b]

While the substitution product which results from a 1,2 hydride shift would be readily identified as a *trans*-1-decalyl compound (or, if two successive hydride shifts are involved, as a 9-decalyl compound), the substitution product arising from a 3,2 hydride shift can not be distinguished from unrearranged substitution product because both are *trans*-2-decalyl derivatives. However, there is reason to believe that the broad trends in product distribution found here may not be influenced to a major extent by this complication. It is clear that the deamination of equatorial amines results in almost completely unrearranged substitution product.[4,8a] However, more rearrangement is expected in the case of axial amines. Maskill and Whiting[4] have found that the total extent of rearrangement in the acetate products from nitrous acid deamination of *cis*-4-*tert*-butylcyclohexylamine in acetic acid is only 18%. In their case, two equivalent rearrangement positions are available. Since, in our system, we are concerned only about rearrangement to a single position (the 3-position), we can probably expect even less.[23] Even if total rearranged acetate is included along with unrearranged acetate in the calculation of the ratio of equatorial to axial acetate in the work of Maskill and Whiting,[4] the value (1.1) does not differ greatly from the ratio (1.3) of unrearranged equatorial to axial acetate. Finally, Bachelor and White[8a] were unable to detect re-

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[18] For example, one group[8d] reported the production of no alcohol in the deamination of 3α-aminocholestane while another[8a] reported that 37% of the substitution product was alcohol. For another,[8b] the ratio of acetate to alcohol in the retained product of deamination of *trans*-4-*tert*-butylcyclohexyl amine was reported to be 1.0[8b] and 3.8[4] by two different groups.

[19] A. Streitwieser and W. D. Schaeffer, *J. Am. Chem. Soc.*, **79**, 2893 (1957).

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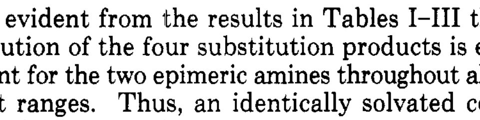
[21] J. Bigeleisen, *Science*, **147**, 463 (1965); W. H. Saunders, *Surv. Prog. Chem.*, **3**, 109 (1966); W. P. Jencks, "Catalysis in Chemistry and Enzymology", McGraw-Hill, New York, 1969, Chapter 4; "Isotope Effects in Chemical Reactions", C. J. Collins and N. S. Bowman, Eds., Van Nostrand-Reinhold, New York, 1970.

[22] J. A. Jenkins and T. Cohen, *J. Org. Chem.*, **40**, 3566 (1975).

[23] Another, but weaker, indication that rearrangement is not substantial in the present system is the absence of 1-decalyl products, the very small quantity (1–3%, maximum) of 9-decalyl product, and the absence of rearranged olefin. However, there is a possibility that rearrangement to the 1-position is rapidly followed by a hydride migration from the angular position to form a tertiary carbocation which mainly gives elimination product and that the latter, being tri- and tetrasubstituted olefins, are selectively destroyed by nitrous acid.

arranged products in the 3α-aminocholestane system, one which is quite analogous to ours but in which rearrangement to either branch would give products which differ from unrearranged material.[24] Since the complexity of the process precludes great precision in the description of the mechanism, we are probably justified, as a first approximation, in ignoring the rearrangement problem in the deamination of the axial amine.

It is evident from the results in Tables I–III that the distribution of the four substitution products is entirely different for the two epimeric amines throughout all of the solvent ranges. Thus, an identically solvated common intermediate in the deamination of the two amines does not play a predominant role, although it can not be ruled out as a significant intermediate. One of the effects which stimulated this research and which had been reported for acyclic systems[14,15] is that the alcohol products are more highly retained than the acetates produced in deaminations in acetic acid. The present results demonstrate this strikingly in the decalyl system. Starting with the axial or equatorial amine, in acetic acid, 93% and 97%, respectively, of the alcohol is retained whereas the acetates are only 55% and 75% retained, respectively. Furthermore about one quarter of the substitution product is alcohol, although the mole percent of water in the medium is probably in the range 1–3% and the volume percent is about one-third of this.[25] The formation of such highly retained alcohol is readily rationalized by the scheme of White and Stuber,[3a,14,26] modified to avoid the postulation of diazonium ions, which, it has been pointed out,[4] may not exist in secondary carbinyl systems or, at least, may have too short a lifetime to be readily detectable.



3

As expected for such a scheme, the proportion of retained alcohol in the substitution product is essentially independent of the acetic acid concentration in dioxane or sulfolane (Tables II and III). A somewhat more surprising result is that the proportion of retained alcohol from axial amine remains essentially unchanged throughout the range of 10–100 vol % acetic acid in water; on the other hand, the proportion of retained alcohol from equatorial amine increases with increasing water content of the medium (Table I). These trends will be rationalized below.

One of the most intriguing questions concerning deamination in these cyclohexyl systems concerns the genesis of the inverted products. White and Woodcock, in their outstanding review,[3a] have outlined several possible paths for inverted product based on White's thorough and elegant studies of deamination reactions: (1) nucleophilic displacement on some diazo intermediate, a mechanism of minor importance in most secondary systems; (2) intramolecular inversion, in which the cation from which N_2 is being expelled rotates in such a way that the counterion becomes positioned close to the former backside of the cation;[27] (3) collapse of the solvent shell around an ion-pair intermediate to yield solvolysis products of mostly inverted configuration; and (4) in highly aqueous solvents conversion of the ion pairs lacking backside solvation to normal solvated cations. In enantiomeric systems the latter process would lead to racemization but in the present diastereomeric system it would be expected to yield mainly the less hindered equatorial product.[3a,12] The nucleophilic displacement mechanism can be ruled out on the basis of the insensitivity of the product ratios to enough dissolved sodium acetate to more than double the acetate concentration in the solution (Table I, entry 5) but more convincingly by the results in Tables II and III to be discussed below.

At first glance, the inverted product in 100% acetic acid appears to be formed by a mechanism other than intramolecular inversion.[3a,27] One might expect an ion pair such as **3** (or a precursor still retaining the N_2) to give an analogous ion pair in which the carbonium ion center has been inverted and which should lead to inverted product with a similar alcohol/acetate ratio to that of the retained product; in fact, for both epimeric amines, the ratio of alcohol to acetate in the inverted product is only a small fraction of that in the retained product. Moreover, throughout most of the solvent composition range in aqueous acetic acid, there is a satisfactory correspondence between the fraction of acetate in the inverted product (F_{ai}) and the volume percent (V %$_{\mathrm{a}}$) of acetic acid in the solvent; F_{ai} (V %$_{\mathrm{a}}$) for axial amine: 95 (∼99),[25] 87 (91), 71 (77), 47 (53), 47 (50), 24 (27), 7 (10); F_{ai} (V %$_{\mathrm{a}}$) for equatorial amine: 96 (∼99),[25] 92 (91), 79 (77), 63 (53), 54 (10). The only marked deviation is for deamination of the equatorial amine in 10 vol % acetic acid, but because of the difficulty of regeneration of the alcohol in that particular mixture (see above), the values in entry 15 are undoubtedly the least accurate in Table I.

However, the absence of the intramolecular inversion mechanism would be most surprising in view of its extensive occurrence, particularly in the very closely related *N*-nitrosoamide decompositions.[3a] Bachelor and White[8a] have provided strong evidence for substantial intramolecular inversion in the *N*-nitrosoamide decomposition in cyclohexane and in methylene chloride–acetic acid (9:1) of 3β-cholestanylamine, which is closely related structurally to *trans,cis*-2-decalylamine (**2**). Furthermore, as indicated in the following paper,[28] it would be difficult to rationalize the production of substantial inverted ester upon deamination of **1** and **2** (by the *N*-nitrosoamide method) in a solvent as nonpolar as cyclohexane without involving the intramolecular inversion pathway. Finally, the results in Tables II and III, now to be discussed, are best explained by processes which indeed involve such an inversion.

The effects on the composition of substitution products of varying the concentration of acetic acid in dioxane and sulfolane (Tables II and III) are striking and unexpected, and they provide important evidence about the nature of the inversion processes. If, in these reactions, acetolysis of an ion pair with inversion of configuration were occurring, then one would expect that the importance of this route would increase as the concentration of acetic acid is raised from a very low value to 100%. Not only is this trend nonexistent or barely discernible in the products from the axial amine but also just the opposite trend occurs, in pronounced fashion, upon deamination of the equatorial amine; as the acetic acid concentration *increases*

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[24] Shoppee, Lack, and Ram,[8d] did not mention the detection of rearranged product from the same amine.

[25] Water is produced during the deamination and by the reaction of sodium nitrite with the acetic acid.

[26] Evidence for a somewhat related mechanism in which "internal" water gives mainly retained alcohol has been found by Moss[7b] in his excellent studies of the decomposition of alkanediazotates.

[27] E. H. White and C. A. Aufdermarsh, Jr., *J. Am. Chem. Soc.*, **83**, 1179 (1961).

[28] T. Cohen, A. R. Daniewski, and J. Solash, *J. Org. Chem.*, following paper in this issue.

in either solvent there is a sharp *decrease* in the proportion of inverted acetate and a corresponding increase in that of retained acetate. This is hardly the result expected if the acetic acid is attacking a diazo species or a retained ion pair in a nucleophilic manner in competition with the usual retention mechanisms. What makes this striking response of the product distributions to acetic acid concentration in dioxane and sulfolane so intriguing is that it appears to be confined to the equatorial amine; the product distribution from the axial epimer is rather insensitive to acetic acid concentration. Another interesting result is that at low concentrations of acetic acid in dioxane and sulfolane, a very substantial portion of inverted (axial) acetate is produced from equatorial amine; the yield of inverted acetate is actually greater than that of retained acetate.

Before the results in Tables II and III were acquired, we were baffled by the fact that although in 100% acetic acid retained alcohol constitutes 26% of the substitution product starting with either amine, the ratio of retained acetate to retained alcohol is almost twice as great in the case of equatorial amine (2.1) than in the case of axial reactant (1.2). It is now seen, however, that the ratio of acetate to alcohol and in fact the percentages of each in the retained product are essentially identical for the two amines when the deaminations are conducted at very low concentrations of acetic acid. It thus appears that under these conditions, we have finally reached a point at which *there is no major difference between the deamination behavior of axial and equatorial amines* with regard to retention/inversion ratios and the compositions of retained and inverted products. The differences grow as the solvents become more hydroxylic. At 100% acetic acid, as mentioned above, the ratio of acetate/alcohol from equatorial amine has grown to 2 while the ratio of slightly greater than 1 has not changed for deamination of the axial amine. Also in that solvent, the ratio of retention to inversion is >4 for equatorial amine and only <1.5 for axial amine. These differences are further exacerbated as the water content increases. At 53 vol % acetic acid in water, the retention/inversion ratio is 9.2 and 1.0, respectively, in the product from equatorial and axial amine. It appears that the greater the hydroxylic nature of the solvent the more equatorial product is formed.[29] A similar trend is evident with regard to *N*-nitrosoamide decomposition in the following paper;[28] in proceeding from cyclohexane to the more hydroxylic solvent acetic acid or to the more polar solvents, acetonitrile and sulfolane, a significant increase in the ratio of equatorial to axial product is observed.

Returning now to the low alcohol content of the inverted product in acetic acid, it is seen that this value is considerably higher in nonhydroxylic solvents containing low concentrations of acetic acid. It is clear that the 7.3% of inverted alcohol formed from axial amine in 1.7% acetic acid in sulfolane (Table III, entry 5) is not due predominantly to solvolysis of some intermediate, since a vast increase of water content of the medium (entry 6) causes only a slight increase in the proportion of equatorial alcohol in the product. We conclude that most of the inverted alcohol formed at low acetic acid concentrations in sulfolane, and presumably in dioxane as well, is formed by intramolecular inversion. Indeed, it is likely that nearly all of the products formed at low acetic acid concentrations in sulfolane and dioxane are from intramolecular processes. Apparently, the expectation that a specifically aquated ion pair such as **3**, or its precursor, would undergo intramolecular inversion to yield an inverted ion pair which would result in the same alcohol/acetate ratio as **3** is mistaken. Maskill and Whiting[4] have also come to this conclusion from other considerations; they suggest that the inefficiency of production of intramolecularly inverted alcohol may be due to the monodentate nature of water. Possible explanations of the interesting phenomenon are given below.

The simplest explanation of the results in Tables II and III is that as the acetic acid concentration in the solvent is increased there is an increased tendency of some of the ion pairs to unpair and for the cationic component to become a normal, symmetrically solvated cation which would then collapse preferentially to the more stable equatorial substitution product.[31] The proclivity of an ion pair to unpair rather than to form intramolecular substitution product must depend on the detailed structure of the ion pair as well as on the nature of the solvent. We can explain the present results most simply if we assume that inverted ion pairs have a far greater tendency to unpair in acetic acid than do retained ion pairs. It has been pointed out previously[9b] that there is no reason to expect an inverted ion pair from an equatorial reactant to behave in a fashion identical with that of a retained ion pair from an axial reactant, and our previous isotope-effect study[9b] appeared to reveal differences in such species.

A slightly different alternative picture is that the *precursor* of the inverted ion pair is more readily unpaired than the retained ion pair or its precursor. It seems likely that in the array of nitrogen-separated ion pairs[32] some would be most likely to collapse by nitrogen expulsion to retained tight ion pairs and others to inverted tight ion pairs. The latter type of nitrogen-separated ion pair may have its anions oriented rather far from the cationic center and may be more susceptible both to intramolecular inversion and unpairing. For the sake of simplicity, we shall use the more easily discussed former picture, but we consider the latter one at least as likely and the reader can readily translate the discussion into terms of the latter picture.

To a first approximation, it appears from the results in Tables II and III that the extent of intramolecular inversion is not dependent on the concentration of acetic acid. Thus, in 2.3% acetic acid in sulfolane (Table III), about 40% (3.0 + 37.5) of the retained, equatorial ion pairs from equatorial amine undergo intramolecular inversion;[33] this is, in fact, comparable to the extent of intramolecular inversion found by White[3a] in a number of secondary systems. When the acetic acid concentration is raised to 49%, one-third or more of these intramolecularly inverted ion pairs become unpaired and the resulting ions, solvated almost completely by acetic acid and sulfolane (there is very little water in the medium), are rapidly converted mainly to equatorial (retained) acetate. In 100% acetic acid, at least one-half of the inverted ion pairs undergo unpairing and end up mainly as equatorial acetate. In deamination of equatorial amines, the results of unpairing of inverted ion pairs are easily discernible because ion pairs which had been destined to yield axial product are diverted to equatorial product.

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[29] The increase in equatorial product with increasing water concentration explains the older belief [11a,30] that the substitution product from axial amine is very predominantly inverted while that from equatorial amine is almost completely retained.

[30] A. Streitwieser, *Chem. Rev.*, **22**, 861 (1957). See also A. K. Bose, *Experientia*, **9**, 256 (1953).

[31] White and Woodcock[3a] and Saunders[3b] have put forth a somewhat similar hypothesis but with respect to deaminations in highly aqueous systems. A fairly similar concept was enunicated by Dauben.[12]

[32] E. H. White and K. W. Field, *J. Am. Chem. Soc.*, **97**, 2148 (1975).

[33] This number could be greater if even in 2.3% acetic acid some of the intramolecularly inverted ion pairs are becoming unpaired.

In 1.74% acetic acid in sulfolane, approximately 35% (7.3 + 27.3) of the original axial ion pairs from the axial amine becomes inverted. As the acetic acid concentration is increased, an increasing number of these inverted ion-pairs become unpaired and end up reacting with the nucleophilic component of the solvent (acetic acid) to yield mainly equatorial (inverted) acetate. In this case, the only noticeable difference as the acetic acid concentration is increased is a decrease in the small yield of intramolecularly inverted alcohol and a corresponding slight increase in the yield of equatorial acetate; this trend is just discernible in sulfolane and nearly undiscernible in dioxane in which the range of acetic acid concentrations used was smaller. The reason that unpairing of inverted ion pairs is hardly noticeable in the deamination of axial amine is that ion pairs which had been destined to yield equatorial product (mainly acetate) end up reacting with acetic acid in the solvent to yield equatorial acetate. According to this picture, there is no reason to expect the addition of 3.3% of water to the medium to have a pronounced effect on the proportion of inverted alcohol formed and it does not. Because the effect on product composition of unpairing of inverted ion pairs starting with axial amine is expected to be small and because of complications due to rearrangement, we can not be sure to what extent this unpairing actually occurs.

At first glance, the very similar results in solutions of acetic acid in sulfolane and dioxane, solvents of very different polarity, may appear surprising. However, the polarities of mixtures of these solvents with acetic acid may be far different from those of the pure solvents.

If we accept that differences exist in structure and behavior between retained and inverted ion pairs, at least two explanations for the low alcohol/acetate ratio in the inverted product become evident: (1) In the inverted ion pairs, the juxtaposition of the cation, the water molcule, and the acetate ion may be such that collapse to an alkyl acetate may be more favorable than collapse to alcohol (here the bidentate character of acetate or Coulombic attraction between the acetate and the carbocation may play a role). (2) As has been suggested[32] for retained ion pairs, there may be an array of structural types among the inverted ion pairs, and some of those in which the water molecule is closest to the cationic center may behave as solvent-separated ion pairs and become unpaired more readily than those with acetate ion close to the cationic center; the latter type may behave like tight ion pairs and readily collapse to ester.[34]

If considerable unpairing occurs in acetic acid, then proceeding to more aqueous solvents would very likely accelerate the process. Even retained ion pairs probably fall prey to the unpairing phenomenon and the ratio of equatorial/axial substitution product increases as the water content increases. It is of interest, however, that even in 90% water solution, the axial amine yields 31% of axial alcohol; this probably means that some of the retained ion pairs have structures which are particularly resistant to unpairing.

Conclusions

When care is taken to regenerate the alcohols that are destroyed during nitrosation, changes in the composition of the substitution product with changes in the acetic acid concentration of the medium lead to significant new insights into the mechanism of nitrous acid deamination of homogeneously axial and equatorial amines. When the deaminations are conducted in dioxane containing small quantities of acetic acid, axial and equatorial amines exhibit essentially identical behaviors with regard to inversion/retention ratios as well as acetate/alcohol ratios. It is of considerable interest that the much discussed differences in the degree of inversion and retention observed in the deamination of axial and equatorial amines are only manifested in solvents of high hydroxylic character; they are apparently the result of solvent-induced unpairing of intramolecularly inverted ion pairs or their precursors, which has the effect of converting axial ion pairs into equatorial products. In solvents of low hydroxylic content, the similar ratios starting with epimeric amines, the changes that occur in product composition as the acetic acid content of the dioxane and sulfolane media is increased, and the low response of product composition to added water in the solvent all imply that most of the product mix is derived by intramolecular decomposition of ion pairs. Any substantial component of nucleophilic attack on the backside of some intermediate seems to be ruled out by the effects of added acetic acid, sodium acetate, or water. Another interesting phenomenon has been uncovered and rationalized in which a retained ion pair, containing an acetate ion and a water molecule produced in the deamination, is capable of either direct collapse, to produce almost equal quantities of retained alcohol and acetate, or conversion to an intramolecularly inverted ion pair which collapses almost completely to inverted acetate.

Finally, we should comment on an interesting difference between the results of deamination of cyclohexylamines and of acyclic secondary alkylamines. In the cyclohexyl systems, there appears to be far less attack of solvent on intermediates to give mainly inverted product.[3a,35] This is presumably a result of the considerably greater steric hindrance to backside solvent participation in cyclohexyl systems than in acyclic systems.[36]

Experimental Section

Infrared spectra were taken on a Beckman IR-8 or Perkin-Elmer 21 spectrophotometer. Proton magnetic resonance spectra were taken on a Varian A-60 instrument. Gas–liquid chromatography (GLC) was performed on an F and M 1609 or a Varian 1520 A instrument, both equipped with flame-ionization detectors and disc integrators.

The preparation of the epimeric *trans*-2-decalols and the corresponding acetates are described in the following paper.[28] The corresponding 1-decalyl derivatives were prepared by a literature procedure.[37] A mixture of *trans*-1- and *trans*-2-octalin and another of *trans*-1-octalin and 1,9-octalin were prepared by the method of Powell and Whiting;[38] this octalin mixture, which could be separated into its components by GLC on a 24-ft 17% Apiezon-L column at 102 °C, was used to identify the olefins produced in the deamination. *trans*-2-Decalone was prepared by dichromate oxidation of *trans,cis*-2-decalol.[39]

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[34] This latter explanation would require that significant unpairing of inverted ion pairs is occurring even at very low acetic acid concentrations in dioxane and sulfolane at which the alcohol/acetate ratio in the inverted product, although significantly higher than in pure acetic acid, is still well below that in the retained product.

(35) R. A. Moss, C. J. Talkowski, D. W. Reger, and C. E. Powell, *J. Am. Chem. Soc.*, **95**, 5215 (1973). For evidence of S_N2 attack of a weakly nucleophilic anion on a fluorinated secondary alkyldiazonium ion, see J. R. Mohrig, K. Keegstra, A. Maverick, R. Roberts, and S. Wells, *J. Chem. Soc., Chem. Commun.*, 780 (1974).

(36) J. E. Nordlander and T. J. McCrary, *J. Am. Chem. Soc.*, **94**, 5133 (1972).

(37) I. Moritani, S. Nishida, and M. Murakami, *J. Am. Chem. Soc.*, 81, 3420 (1959).

(38) J. W. Powell and M. C. Whiting, *Tetrahedron*, 12, 163, 168, 278, (1961).

(39) V. I. Nikitin, *Izv. Acad. Nauk SSSR*, **2**, 123 (1952); *Chem. Abstr.*, 48, 657*g* (1954).

***trans,cis*-2-Decalol-*2-d*.** A solution of 6.0 g (40 mmol) of *trans*-2-decalone in 50 mL of anhydrous ether was added dropwise over a 20-min period to a mechanically stirred slurry of 0.47 g (11 mmol) of lithium aluminum deuteride in 70 mL of anhydrous ether under a nitrogen atmosphere. After 3.5 h of stirring, the reaction was quenched by dropwise addition of 20 mL of 10% sulfuric acid. The ether layer was washed twice with saturated sodium chloride solution and dried (magnesium sulfate). Gas chromatographic analysis indicated the presence of 17% *trans,trans*- and 83% *trans,cis*-2-decalol in the solution. Removal of the solvent and two recrystallizations from pentane provided 4.1 g (66%) of *trans,cis*-2-decalol-*2-d*, the melting point (74–75 °C) of which was identical with that of an authentic sample of unlabeled alcohol.[28] Analysis by ^{1}H NMR indicated nearly complete deuteration of the carbinyl position.

Preparation of the *trans*-2-Decalylamines. *trans,trans*-2-Decalylamine was prepared by ammonolysis of *trans,cis*-2-decalyl tosylate;[40] it was found that the reported yields could be considerably improved by continuing the heating for at least 48 h rather than for 22.5 h as recommended.[40,41] The 2-deuterio analogue was prepared in the same way from labeled alcohol (see above). *trans,cis*-2-Decalylamine was prepared by reduction of the oxime[42] of *trans*-2-decalone with sodium in alcohol according to Hückel.[43]

Product Analysis. All of the *trans*-2-decalols and acetates and the *trans*-1-decalols and acetates could be separated from each other and from the olefins, albeit at a sacrifice of time, by the use of a 10-ft column of 3% Carbowax 20M on Gas Chrome Q at 82 °C. A somewhat less time-consuming method consisted of using a 10-ft 10% OV 17 column at 130 °C to separate all of the products except *trans,trans*- and *trans,cis*-2-decalol and the 3% Carbowax 20M column to separate these two alcohols; hexadecane was used as an internal standard on both columns. In some earlier work, a 22% Carbowax 20M column at 142 °C was occasionally used to separate all of the products except *trans,-trans*-2-decalol and *trans,cis*-2-decalyl acetate, which were not completely separated, followed by the use of a flow splitter and a 100-ft 0.1-mm column coated with Carbowax 20M to determine ratios of products (the peak of the internal standard overlapped with that of the solvent at the temperature used); the ratio of *trans,trans*-2-decalol to the corresponding acetate was found by subtracting the ratio of *trans,cis*-2-decalyl acetate to *trans,-trans*-2-decalyl acetate from the ratio (sum of *trans,cis*-acetate plus *trans,trans*-alcohol) to *trans,trans*-2-decalyl acetate.

Tests of Product Stability. A. In the Absence of Sodium Nitrite. A synthetic mixture of the GLC standard, *n*-hexadecane, and the substitution and elimination products was dissolved in 77 vol % acetic acid in water and the solution was subjected to the workup conditions; analysis by GLC indicated that the distribution in the mixture had not changed. Equimolar mixtures of *trans,cis*-2-decalol and *trans,trans*-2-decalyl acetate containing *n*-hexadecane were dissolved in three solvent mixtures ranging from 10 to 100 vol % acetic acid in water, and the mixtures were allowed to remain at the deamination temperature for at least 40% longer than the time used in the deaminations; the recovered compounds contained no octalins, *trans,trans*-2-decalol, or *trans,cis*-2-decalyl acetate, indicating that acid-catalyzed elimination, ester interchange, esterification, and ester hydrolysis were not occurring.

B. In the Presence of Sodium Nitrite. A mixture of *trans*-1- and *trans*-2-octalin and *n*-hexadecane was stirred in 91 vol % acetic acid in water containing sodium nitrite at the concentration used in the deaminations for 17 h at 30.8 °C; no new products were detectable by GLC, indicating that addition of water and acetic acid to the octalins does not occur, but the area ratio of the octalin signal to that of the standard had decreased by 45% and new strong absorptions appeared in the IR spectrum at 1748 and 1543 cm^{-1}. When a mixture of the epimeric 2-decalols, containing standard, was subjected to the nitrosating conditions in 77 vol % acetic acid in water for 45 min at 31 °C, no new products were detected by GLC, but the signals for *trans,cis*- and *trans,trans*-2-decalol had decreased by 67% and 30%, respectively, relative to that of *n*-hexadecane and strong new IR bands appeared at 1600 and 1639 cm^{-1}; when the reaction time was extended to 16 h, the loss in the signal areas was reduced to 26% and 16%, respectively, and the two IR bands were weaker.

A mixture of *trans,cis*-2-decalol and *trans,cis*-2-decalyl nitrite was prepared by the addition of 0.71 g (11 mmol) of nitrosyl chloride to a solution of 2.00 g (13 mmol) of *trans,cis*-2-decalol in 40 mL of pyridine at −16 °C. After remaining at ambient temperature for 50 min, the mixture was equilibrated between ether and dilute hydrochloric acid, and the ether solution was washed with two portions of acid. Evaporation of the solvent yielded an intensely yellow sweet-smelling crystaline solid, the IR spectrum of which displayed very strong new bands at 1639, 810, and 784 cm^{-1}. A gas chromatogram of this mixture exhibited a single peak with the retention time of *trans,cis*-2-decalol.

A mixture of the epimeric *trans*-2-decalols and standard in 77% acetic acid–water was again treated with sodium nitrite at 30.8 °C and stirred for 16 h. Nitrogen gas was passed through the solution with stirring and the escaping gas was passed through a large cold finger immersed in a dry ice–acetone bath. After 4 h of such ebullition, the gas which had passed through the trap failed to produce significant iodine color on passage through 20 mL of 15–20% aqueous potassium iodide solution for 20 min. The combined contents of the reaction vessel and trap were worked up in the usual way. The IR spectrum no longer showed the peaks at 1600 and 1639 cm^{-1} and GLC analysis indicated that *trans,-cis*-2-decalol was quantitatively recovered and *trans,trans*-2-decalol was recovered to the extent of at least 98%, the remainder going to a material of retention time equal to that of *trans,cis*-2-decalyl acetate.

A mixture of the epimeric *trans*-2-decalols and acetates, *trans*-1- and 2-octalins, and *n*-hexadecane was dissolved in 37.6 vol % acetic acid in sulfolane containing a large excess of dissolved sodium nitrite, and the solution was maintained at 30.6 °C for 42 h. After nitrogen ebullition as above, it was determined by GLC analysis that the peak areas of the acetates and alcohols were the same as those of the original mixture in relation to that of the standard, but the olefin peak had decreased to 25% of its former value. A similar experiment in 50 vol % acetic acid in dioxane gave similar results.

Deamination Procedure. The following procedure is representative. A solution of 0.293 g (1.91 mmol) of *trans,trans*-2-decalylamine in 13.6 g of 37.6 vol % acetic acid in sulfolane was prepared in a three-neck 50-mL flask fitted with a mechanical stirrer, a thermometer, and an angle adapter attached to a 5-mL flask (which allowed admission of solid sodium nitrite while the system remained closed). The reaction vessel was immersed in a constant temperature bath at 30.5 ± 0.2 °C and the sodium nitrite (0.660 g, 9.5 mmol), contained in the 5-mL flask, was added in portions with stirring over a 20-min period by turning the angle adapter in the joint attaching it to the reaction vessel. The reaction mixture was stirred in the closed system at the same temperature for an additional 20 h. Nitrogen was then passed through the acetic acid solution at room temperature as described in the previous section; nitrogen ebullition was continued for 1 h after the iodine color failed to be produced (in this case 1.5 h).

The contents were removed from the flask and the latter and cold trap were rinsed with pentane and water. The combined liquids were cooled to 0 °C and a solution of 4 g (0.1 mol) of sodium hydroxide in 50 mL of water was added dropwise with stirring over a period of 15–20 min until the aqueous layer was slightly basic. After the aqueous and pentane layers had been further equilibrated in a separatory funnel, the aqueous layer was washed with fresh pentane. The combined organic layer was washed with saturated brine and the wash added to the aqueous layer. The combined aqueous layer was washed with pentane and the wash was combined with the organic layer which was washed twice with 20 mL of 0.4 N aqueous HCl. The acid wash was extracted with pentane and the organic phases were again combined. A weighed quantity (∼0.12 g) of the internal standard *n*-hexadecane was added to the pentane solution and the latter was concentrated to a volume of ca. 1 mL by distillation. The concentrate was

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(40) J. L. Pinkus, G. Pinkus, and T. Cohen, *J. Org. Chem.*, **27**, 4356 (1962).

(41) More recent work by Dr. J. L. Pinkus has shown that a higher ratio of substitution to elimination can be attained by employing the mesylate in place of the tosylate.

(42) E. Müller and U. Heuschkel, *Chem. Ber.*, **92**, 71 (1959).

(43) W. Hückel, *Justus Liebigs Ann. Chem.*, **533**, 1 (1938).

analyzed by GLC, the peak area ratios of product to standard being converted to molar ratios by detector-response calibration charts constructed by using authentic materials. The qualitative analysis of several reaction mixtures indicated the absence of 1,9-octalin, the *trans*-1-decalols, and the *trans*-1-decalyl acetates. The product distribution was essentially independent of the concentration of the amine within the limits 0.030–0.17 M for amine and 0.15 to 1.15 M for nitrite; the same molar ratio of nitrite to amine was always used. All experiments were run in duplicate.

Acknowledgment. This work was supported in part by Grant AM 06419 from the National Institutes of Health and Grant B-19 from the Health Research and Services Foundation, Pittsburgh, PA. T.C. thanks the Chemistry Department of the University of North Carolina at Chapel Hill for its hospitality while he was on leave there during the writing of this paper.

Registry No. 1, 936-35-6; 2, 23017-71-2; *trans,cis*-2-decalol, 2529-06-8; *trans,trans*-2-decalol, 5779-35-1; *trans,cis*-2-decalyl acetate, 66964-88-3; *trans,trans*-2-decalyl acetate, 66964-89-4; *trans*-2-decalone, 16021-08-2; *trans,cis*-2-decalol-2-*d*, 73688-54-7; *trans,cis*-2-decalyl nitrite, 73688-55-8; *trans,trans*-2-decalyl nitrite, 73688-56-9; nitrous acid, 7782-77-6.

Deamination of Axial and Equatorial *trans*-2-Decalylamines by the *N*-Nitrosoamide Method in Various Solvents. Remarkable Stereochemistry and Efficiency of Capture of a Cationic Intermediate by Acetonitrile[1]

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Received August 20, 1979

Product distributions have been determined for thermal decomposition of the axial ethyl *N*-(*trans,trans*-2-decalyl)-*N*-nitrosocarbamate (3) and the equatorial epimer (4) in cyclohexane, acetic acid, acetonitrile, and sulfolane. In cyclohexane, the axial substrate gives mainly elimination and the substitution product is predominantly the ester of retained configuration; the equatorial epimer gives almost equal quantities of elimination and substitution product, the latter consisting of 1.7 times more retained than inverted ester. In the other three solvents, the retention–inversion ratios for the two substrates are nearly interchanged due to an increase in the ratio of equatorial to axial product which occurs in these more hydroxylic or polar solvents. It is believed that the preference for equatorial product formation in these solvents is due to (1) unpairing of an inverted ion pair or its precursor with attack of carboxylic acid or acetonitrile on the relatively free carbocation mainly to give the more stable equatorial substitution product and (2) in the case of the axial isomer, increased rearrangement to give largely equatorial 2-decalyl product. The results in acetic acid and acetonitrile are rather similar except that acetonitrile is more effective at scavenging the cationic intermediate (via a nitrilium ion which is converted to an imide), and there is evidence for a significant degree of cation capture from the frontside, probably by a solvent molecule which is closely associated with the diazo function. The decrease in olefin yield which occurs in the equatorial but not in the axial case in proceeding from cyclohexane or sulfolane to acetic acid or acetonitrile is believed to be due to decreased removal of α- and cis β-protons by the counterion due to the decreased basicity of the latter and/or its greater distance from these protons in the ion pair intermediate; previous work indicates that in the axial case this decrease in olefin production is compensated for by the removal of a trans β-proton by these somewhat basic solvents.

Our approach to the investigation of the mechanistic details of deaminations by nitrous acid diazotization and related methods[3] has been the study of the product distributions upon deamination of the conformationally homogeneous trans-fused 2-decalylamines in systematically varied solvent systems[4] or of regiospecifically and stereospecifically α- and β-deuterated derivatives in invariant solvents.[5,6]

We were particularly interested in the well-known generalizations about the differences in product array between axial and equatorial amines. Early generalizations[9] held that axial amines give nearly all elimination and the small yield of substitution product is nearly all inverted while equatorial amines give nearly all substitution product of retained configuration. More recently, it has been held that the substitution product in the case of the axial amine is approximately equally inverted and retained.[10,11] This contrasts sharply with the solvolysis of cyclohexyl sulfonate esters, both axial and equatorial epimers of which give a large yield of olefin and a small yield of largely inverted substitution product.[12] In contrast to such generalizations, it is shown in the preceding paper[4a] that upon nitrous acid deamination in nonhydroxylic solvents containing small amounts of acetic acid, axial and equatorial amines actually behave in a remarkably similar manner with regard to the distribution of substitution products; they give 59–65% of an approximately equimolar mixture of retained alcohols and acetates and 35–41% of inverted product which is very predominantly acetate. As the acetic acid concentration

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[1] Taken in part from the Ph.D. thesis of J. Solash, University of Pittsburgh, 1972.

[2] Andrew Mellon Predoctoral Fellow.

[3] For leading general references to deamination in nonaromatic systems, see the preceding paper.[4a]

[4] (a) T. Cohen, A. D. Botelho, and E. J. Jankowski, *J. Org. Chem.*, preceding paper in this issue; (b) T. Cohen and E. Jankowski, *J. Am. Chem. Soc.*, **86**, 4217 (1964).

[5] (a) T. Cohen and A. R. Daniewski, *J. Am. Chem. Soc.*, **91**, 533 (1969); (b) T. Cohen, A. R. Daniewski, G. M. Deeb, and C. K. Shaw, *ibid.*, **94**, 1786 (1972).

[6] The *trans*-decalyl system was chosen in preference to the 4-*tert*-butylcyclohexyl system[7] largely because of the ease and certainty of labeling in specific fashion at one of the two β-positions.[5] An additional consideration was that meaningful comparison of the results in the related steroid system would be possible.

[7] The 4-*tert*-butylcyclohexyl system has been studied by others. See ref 8 of this paper and ref 8b, e, and f of the preceding paper.[4a]

[8] H. Maskill and M. C. Whiting, *J. Chem. Soc., Perkin Trans. 2*, 1462 (1976).

[9] J. A. Mills, *J. Chem. Soc.*, 260 (1953); A. Streitwieser, Jr., *Chem. Rev.*, **56**, 571 (1956); see also A. K. Bose, *Experientia*, **9**, 256 (1953).

[10] See footnotes 7 and 8 of the preceding paper.[4a]

[11] F. W. Bachelor and E. H. White, *Can. J. Chem.*, **50**, 364 (1972); E. H. White and F. W. Bachelor, *Tetrahedron Lett.*, 77 (1965).

[12] N. C. G. Campbell, D. M. Muir, R. R. Hill, J. H. Parish, R. M. Southam, and M. J. Whiting, *J. Chem. Soc. B*, 355 (1968), and references cited therein.

0022-3263/80/1945-2847$01.00/0