3,3-Dimethylchlorocyclohexane-2,2,6,6-d_4 was prepared from the alcohol by treatment with thionyl chloride in pyridine.[26] The product was separated from the alcohol and olefins by preparative gc. The mass spectrum (20 eV) showed parent peaks at m/e 150 ($C_8H_{11}D_4{}^{35}Cl$] and 152 ($C_8H_{11}D_4{}^{37}Cl$) in a 3:1 ratio, with intensities less than 1% of the base peak at m/e 99 ($M-CH_2Cl$).

4,4-Dimethylchlorocyclohexane-2,2,6,6-d_4 was prepared as given for the above chloride and purified by gc.

3,3-Dimethylbromocyclohexane-2,2,6,6-d_4 was prepared from the corresponding alcohol by reaction with (C_6H_5)$_3$PBr$_2$ following Wiley.[7] The reaction proceeded in substantially lower yield (20%)

than is common with this reaction and large amounts of alcohol were recovered. The product was purified by gc.

4,4-Dimethylbromocyclohexane-2,2,6,6-d_4 was prepared in 80% yield and purified in a manner analogous to the 3,3 isomer. The mass spectrum of the purified product gave parent peaks at 196 ($C_8H_{11}D_4{}^{81}Br$) and 194 ($C_8H_{11}D_4{}^{79}Br$) in an approximate 1:1 ratio, with intensities less than 1% of the base peak at 115 ($M-Br$).

3,3-Dimethyliodocyclohexane-2,2,6,6-d_4 was prepared following Wiley[7] from the alcohol and (C_6H_5)$_3$PI$_2$. Again the yield was only 20%. The mass spectrum of the distilled product had a parent peak at m/e 242 ($C_8H_{11}D_4I$) with an intensity of 2% relative to the base peak at 115 ($M-{}^{127}I$).

4,4-Dimethyliodocyclohexane-2,2,6,6-d_4 was prepared in 70% yield in a manner analogous to the 3,3-dimethyl isomer. The mass spectrum had a peak at m/e 242 with an intensity of 4% of the base peak at 115.

(26) F. C. Whitmore and F. A. Karnatz, J. Amer. Chem. Soc., 60, 2536 (1938).

Nitrous Acid Deamination of 2-(Aminomethyl)cyclohexanol. The Question of a 1,3-Hydride Shift or Two Consecutive 1,2-Hydride Shifts[1]

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Abstract: The nitrous acid deamination of cis- and trans-2-(aminomethyl)cyclohexanol leads to the formation of the corresponding substitution products (cis- and trans-2-(hydroxymethyl)cyclohexanols, respectively), an elimination product (2-methylenecyclohexanol), and three rearrangement products (2-methylcyclohexanone and cis- and trans-2-methylcyclohexane-1,2-diol), albeit in different proportions from the two isomers. The differences are rationalized in terms of the reaction taking place from the most stable conformer and the subsequent reactions of the intermediate carbonium ions being more rapid than ring inversion. Contrary to an earlier claim, deuterium-labeling experiments indicate that 2-methylcyclohexanone arises from trans-2-(aminomethyl)cyclohexanol by way of two 1,2-hydride shifts rather than by a 1,3-hydride shift.

The nitrous acid deamination of 2-(aminomethyl)-cyclohexanol (1) has been described by Mousseron and coworkers.[3] The cis isomer 1a was reported to give the corresponding diol, cis-2-(hydroxymethyl)-cyclohexanol (2a), and cyclohexanecarboxaldehyde (3) (eq 1). The latter was claimed to arise by a 1,3-alkyl shift. Likewise, from trans-2-(aminomethyl)-cyclohexanol (1b), trans-2-(hydroxymethyl)cyclohexanol (2b) was obtained, together with 2-methylcyclohexanone (4) as the only rearrangement product (eq 2). Furthermore, optically active 1b was found to yield optically active 4. It was argued that since 4 was optically active the asymmetric carbon was not touched during the reaction, and therefore a 1,3-hydride shift had occurred in carbonium ion 5b (eq 3).[3c] However, this finding does not rule out a reaction path involving two consecutive 1,2-hydride shifts. Only if the configurational relationship between the reactant 1b and the product 4 is known can a conclusion be drawn concerning the reaction mechanism. A 1,3-hydride shift would
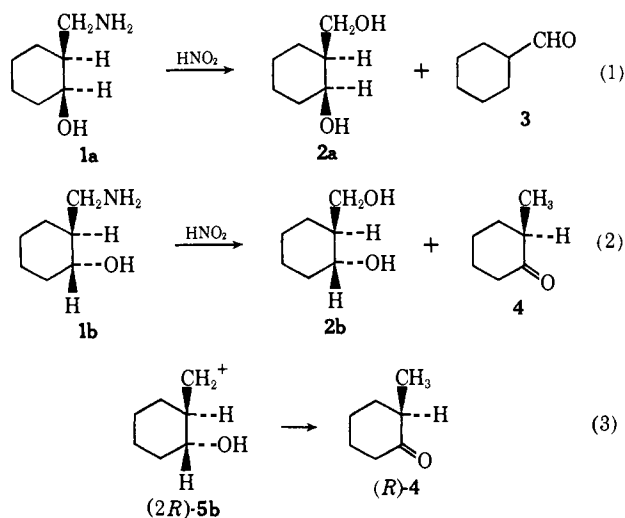

result in retention (eq 3), while two consecutive 1,2-hydride shifts would result in inversion at C-2 (eq 4).[4] Since this configurational relationship had not been established in the previous work, we decided to reinvestigate the nitrous acid deamination of 1b.

(3) (a) M. Mousseron, J. Jullien, and F. Winternitz, C. R. Acad. Sci. Paris, 226, 1909 (1948); (b) M. Mousseron, R. Jacquier, and J. Jullien, Bull. Soc. Chim. Fr., C89 (1951); (c) M. Mousseron, M. Mousseron-Canet, and R. Jacquier, Ann. Chim. (Paris), 8, 5 (1953).

(4) This sequence implies that the intramolecular hydride migration in 6 is favored over proton elimination to give the enol, a process which would destroy the asymmetry.

$$\text{(2R)-5b} \xrightarrow{} \text{6} \xrightarrow{} \text{(S)-4} \quad (4)$$
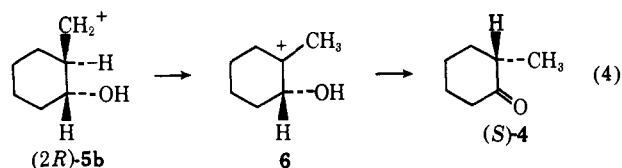
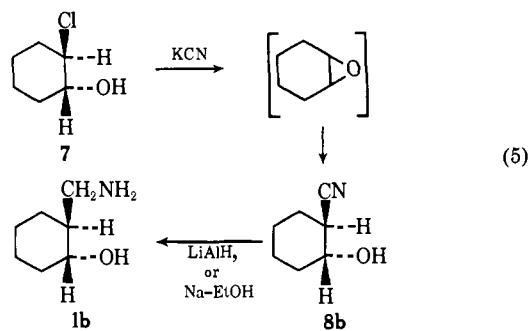To differentiate between a 1,3-hydride shift and two consecutive 1,2-hydride shifts, we studied the nitrous acid deaminations of specifically labeled amino alcohols **1b**-*2*-*d* and **1b**-*1,7*-*d₃*. The results expected from the two mechanisms are shown in Scheme I.

Scheme I

$$\text{4-7-}d_1 \xleftarrow{2(\sim1,2\text{-H})} \text{1b-2-}d \xrightarrow{\sim1,3\text{-H}} \text{4-2-}d$$

$$\text{4-2,7-}d_3 \xleftarrow{2(\sim1,2\text{-H})} \text{1b-1,7-}d_3 \xrightarrow{\sim1,3\text{-H}} \text{4-7-}d_3$$
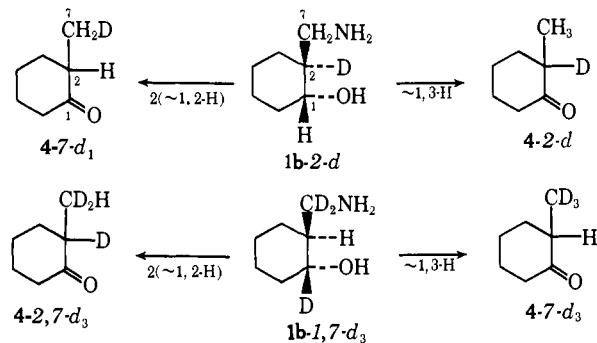
Synthesis and Stereochemistry of the 2-(Aminomethyl)cyclohexanols (1a and 1b). Both **1a** and **1b** have been previously described by Mousseron and coworkers. The trans isomer **1b** was obtained from *trans*-2-chlorocyclohexanol (7) by way of the corresponding 2-cyanocyclohexanol (8b) (eq 5).[5] Its stereo-

$$\text{7} \xrightarrow{\text{KCN}} \text{[epoxide]} \quad (5)$$

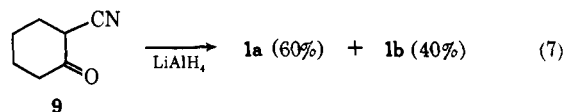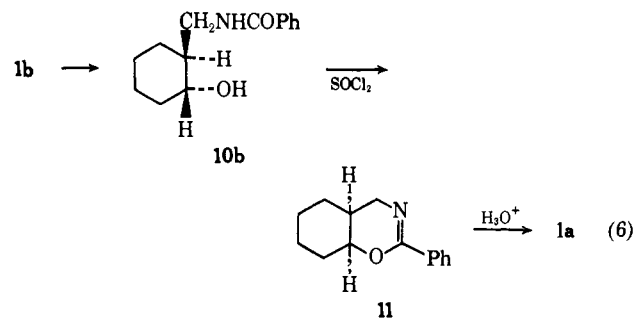$$\text{1b} \xleftarrow[\substack{\text{or} \\ \text{Na-EtOH}}]{\text{LiAlH}_4} \text{8b}$$

chemistry was subsequently shown to be correct.[6] The lithium aluminum hydride reduction of 2-cyanocyclohexanone (9) was also claimed to yield **1b**.[5b] This last reaction seemed well suited for our needs, because the reduction of 9 with lithium aluminum deuteride would give *trans*-2-(aminomethyl-*d₂*)cyclohexanol-*2*-*d* (**1b**-*1,7*-*d₃*). However, the products obtained from **8b** and 9 with lithium aluminum hydride possessed different nmr spectra. A comparison with authentic *cis*-2-(aminomethyl)cyclohexanol (**1a**) prepared from the *N*-benzoyl derivative of the trans isomer **10b** (eq 6)[7] indicated that the reduction product from 9 was actually a mixture of **1a** and **1b** (eq 7).[8]

(5) (a) M. Mousseron, F. Winternitz, and J. Jullien, *C. R. Acad. Sci. Paris*, **226**, 91 (1948); *Bull. Soc. Chim. Fr.*, 878 (1948); (b) M. Mousseron, R. Jacquier, M. Mousseron-Canet, and R. Zagdoun, *C. R. Acad. Sci. Paris*, **235**, 177 (1952); *Bull. Soc. Chim. Fr.*, 1042 (1952).

(6) E. J. Moriconi and P. H. Mazzocchi, *J. Org. Chem.*, **31**, 1372 (1966).

(7) (a) M. Mousseron, F. Winternitz, and M. Mousseron-Canet, *Bull. Soc. Chim. Fr.*, 737 (1953); (b) W. S. Johnson and E. N. Schubert, *J. Amer. Chem. Soc.*, **72**, 2187 (1950); (c) M. T. Leffler and R. Adams, *ibid.*, **59**, 2252 (1937).

$$\text{1b} \xrightarrow{} \text{10b} \xrightarrow{\text{SOCl}_2} $$

$$\text{11} \xrightarrow{\text{H}_3\text{O}^+} \text{1a} \quad (6)$$

$$\text{9} \xrightarrow{\text{LiAlH}_4} \text{1a (60\%)} + \text{1b (40\%)} \quad (7)$$

The nmr spectra of amino alcohols **1a** and **1b** agreed with the previously assigned stereochemistry.[5a,6] Especially relevant was the signal for the hydrogen α to the hydroxyl group. A comparison of the nmr parameters for this hydrogen in **1a**, **1b**, and some other 2-substituted cyclohexanols of known stereochemistry is given in Table I. Chemical shifts[9] and coupling

Table I. Nmr Parameters for H-1 in 2-Substituted Cyclohexanols[a]

Compound	τ (H-1)	J, Hz	W, Hz[b]	Preferred conformation[c]
cis-2-(Aminomethyl)-cyclohexanol (1a)	5.97		(8)	e
trans-2-(Aminomethyl)-cyclohexanol (1b)	6.61	9; 4.5	22.5	a
cis-2-(Hydroxymethyl)-cyclohexanol (2a)	5.89		(7.5)	e
trans-2-(Hydroxymethyl)-cyclohexanol (2b)[d]	6.7		(21)	a
cis-2-Cyanocyclo-hexanol (8a)	6.91		(13–14)	a
trans-2-Cyanocyclo-hexanol (8b)	6.28	9; 4	22	a
cis-2-Carboxycyclo-hexanol (12a)[e]	5.78		(9)	e
trans-2-Carboxycyclo-hexanol (12b)[f]	6.18	10; 4	24	a
1-Methyl-*cis*-1,2-cyclohexanediol (13a)	6.58	8; 5	13	a
1-Methyl-*trans*-1,2-cyclohexanediol (13b)	6.53	9.5; 4.5	14	a

[a] 60 MHz, CDCl₃, internal TMS. [b] *W* = bandwidth (sum of the coupling constants); when this could not be measured, the width at half-height is given (in parentheses). [c] e = equatorial H-1; a = axial H-1. [d] Determined for the methylene-dideuterated compound (**2b**-*7*-*d₂*); in the unlabeled compound the 7-methylene signal is superimposed on the H-1 signal. [e] Literature values:[11] τ 5.73; *W*, 8.5. [f] Literature values:[11] τ 6.29; *J*, 10.2, 4.5; *W*, 25.0.

constants (or bandwidths)[10,11] of the hydrogens α to

(8) Treatment of this mixture with hydrogen chloride in ether gave a hydrochloride whose melting point rose after purification to 148°. This could be the explanation of why the previous investigators[5b] considered this product to be the trans isomer **1b**, the hydrochloride of which melts at 151°.[5a]

(9) E. L. Eliel and M. H. Gianni, *Tetrahedron Lett.*, 97 (1962); A. H. Levin and S. Winstein, *J. Amer. Chem. Soc.*, **84**, 2464 (1962); J. Reisse, J. C. Celotti, D. Zimmerman, and C. Chiurdoglu, *Tetrahedron Lett.*, 2145 (1964).

(10) (a) N. C. Franklin and H. Feltkamp, *Angew. Chem.*, *Int. Ed. Engl.*, **4**, 774 (1965), and references therein; (b) H. Feltkamp and N. C. Franklin, *Tetrahedron*, **21**, 1541 (1965); J. Klein and E. Dunkelblum, *ibid.*, **24**, 5701 (1968).

(11) H. Baumann, N. C. Franklin, and H. Möhrle, *ibid.*, **23**, 4331 (1967).

the hydroxyl group have been used to determine the preferred conformation of substituted cyclohexanols. For all but one compound studied the most stable conformations predicted by our nmr data are those expected from a consideration of the conformational free energies of substituents of a cyclohexane ring.[10a] For 2-methylcyclohexane-*trans*-1,2-diol (13b), the ΔG values would predict similar stability for the two conformations. Apparently, the intramolecular hydrogen bond, which is possible only for the conformation with equatorial hydroxyl groups, determines the observed preference for this conformation (Table I). It was previously suggested, based on infrared data, that intramolecular hydrogen bonds are present in 13a and 13b.[12] It is also the intramolecular hydrogen bond which could bring about a cyclohexane chair distortion suggested by the values of the coupling constants for the cis isomer 13a.

Contrary to previous reports,[5] nmr spectra showed that the amino alcohol obtained from cyano alcohol 8b was not pure 1b but contained 16–17% of 1a. By glc, the content of 1a in the mixture was found to be 19–20%. This could possibly arise from an isomerization during the reduction with lithium aluminum hydride. On the other hand basic hydrolysis of cyano alcohol 8b gave a mixture of hydroxy acids consisting of (by nmr) 16% 12a and 84% 12b. These results could also be explained by an isomerization, this time during hydrolysis. However, the spectrum of the starting cyano alcohol (8b) exhibited a band at τ 6.91 which could not be assigned to any hydrogen of 8b, but which was consistent with the α hydrogen of the cis isomer 8a. The bands present at τ 6.28 and 6.91 integrated together for one hydrogen, and their ratio was about 85:15. Consequently, the band at τ 6.91 was assigned to the cis isomer 8a. The presence of 8a in 8b thus accounts for the production of 12a and 1a above.

These results suggest a dual mechanism for the formation of 8 from *trans*-2-chlorocyclohexanol (7).[13,13a] Most of 7 reacts through the epoxide (eq 5) to give *trans*-cyano alcohol (8b),[5a] while a minor portion gives *cis*-cyano alcohol (8a), probably by a S_N2 mechanism.

Deamination Products of 1a and 1b. This reaction was previously reported to give only unrearranged and 1,3-rearranged products.[3] No other products generally expected from carbonium ion intermediates, such as 1,2-rearrangement products or elimination products, were reported. However, we obtained from both 1a and 1b substitution products (1,3-diols 2a and 2b, respectively), an elimination product (2-methylenecyclohexanol (14)), and three rearrangement products (2-methylcyclohexanone (4) and cis- and trans-2-methylcyclohexane-1,2-diol (13a and 13b, respectively). In each case, identification was based on a comparison of glc retention times and nmr and ir spectra with those of authentic material.

The deamination reactions were carried out with sodium nitrite and phosphoric acid at room temperature.[14] The use of sodium nitrite and oxalic acid[3a,15]

gave similar results, but the reaction was slower, the system was heterogeneous, and the large amount of water required hampered the isolation of the diols, which were quite soluble in this medium. The pH of the diazotization mixture was *ca.* 4 for the oxalic acid mixture and 5–6 for the phosphoric acid mixture.

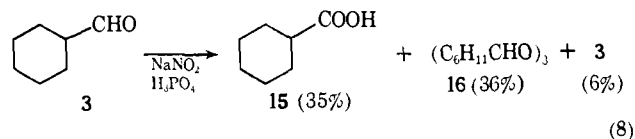The ratios of the reaction products obtained from 1a and 1b are given in Table II. The values for 1b were

Table II. Diazotization Products from *cis*- and *trans*-2-(Aminomethyl)cyclohexanol (1a and 1b, respectively)

Product	From 1a, $\%^{a,b}$	From 1a + 1b, (20:80), $\%^{a,b}$	From 1b (calcd), $\%^{b}$
2a	33	5.1	0
2b	0	36	41
4	1.9	9.5	11
13a	3.0	16	18
13b	47	19	16
14	16	14	14

^{a} Obtained from peak areas (glc). ^{b} The values given do not represent absolute yields, but the per cent of each compound, the sum being taken as 100. This approach was preferred because the reaction mixture also contained several other minor products in amounts too small to allow their identification. These could possibly be other diols, unsaturated alcohols, 7-oxabicyclo[4.2.0]-octane (L. J. Dolby, F. A. Meneghini, and T. Koizumi, *J. Org. Chem.*, **33**, 3060 (1968); A. Rosowski and D. S. Tarbell, *ibid.*, **26**, 2255 (1961); H. B. Henbest and B. B. Millward, *J. Chem. Soc.*, 3578 (1960); H. Rupe and O Klemm, *Helv. Chim. Acta*, **21**, 1538 (1938)), phosphate esters (E. H. White and D. J. Woodcock in "The Chemistry of the Amino Group," S. Patai, Ed., Interscience, London, 1968, Chapter 8), etc. The recovery of crude product was similar from 1a and 1b and was approximately 65–80%.

obtained by extrapolation of the results from pure 1a and from the mixture of 1a and 1b.

The reaction mixtures did not contain any significant quantities of cyclohexanecarboxaldehyde (3). Actually, this compound was not stable under the diazotization conditions. When treated with sodium nitrite and phosphoric acid, 3 gave a mixture of cyclohexanecarboxylic acid (15) and the trimer of 3, 16 (eq 8). Neither

$$3 \xrightarrow[\text{H}_3\text{PO}_4]{\text{NaNO}_2} 15 \ (35\%) + (\text{C}_6\text{H}_{11}\text{CHO})_3 + 3$$
$$16 \ (36\%) \quad (6\%)$$

(8)

of these species could be identified from the deamination of 1a or 1b. We cannot explain the discrepancy between our findings and the previous ones.[3]

The Mechanism of 2-Methylcyclohexanone (4) Formation. The formation of diols 13a and 13b suggests, contrary to the earlier claim,[3] that a 1,2-hydride shift does take place in 5, to give 6.[16] It was next necessary

(12) A. Cole and P. Jefferies, *J. Chem. Soc.*, 4391 (1956); H. Buc, *Ann. Chim. (Paris)*, **8**, 409 (1963).

(13) The 2-chlorocyclohexanol used was shown by nmr spectroscopy to consist of only the trans isomer.

(13a) NOTE ADDED IN PROOF. G. Bernath, K. Kovacs, and K. L. Lang (*Acta Chim. (Budapest)*, **64**, 183 (1970)) have recently concluded that 8 formed from 7 is a mixture of cis and trans isomers.

(14) E. J. Corey and R. L. Dawson, *J. Amer. Chem. Soc.*, **85**, 1782 (1963).

(15) M. Godchot and M. Mousseron, *C. R. Acad. Sci., Paris*, **198**, 2000 (1934).

(16) For convenience, the reaction is pictured as proceeding through carbonium ion 5. This work does not allow us to distinguish between the intermediacy of ion 5 and a concerted pathway involving the corresponding diazonium ion or other nitrogen-containing intermediate.[17] This problem was recently reviewed by Friedman[18] who concluded that the products from primary amines can be understood in terms of synchronous reactions of primary diazonium ions without involving the intermediacy of primary carbonium ions.

(17) H. Maskill, R. M. Southam, and M. C. Whiting, *Chem. Commun.*, 496 (1965).

(18) L. Friedman in "Carbonium Ions," Vol. II, G. A. Olah and P. v. R. Schleyer, Ed., Wiley, New York, N. Y., 1970, Chapter 16.

to establish if the 2-methylcyclohexanone (4) was formed by a second 1,2-hydride shift or by a concurrent 1,3-hydride shift. This question was answered by labeling experiments (Scheme I). As discussed above, 2-cyano-cyclohexanone (9) was a good starting material for the preparation of the necessary specifically deuterated amino alcohols. Taking into account the difference in the amount of 4 obtained from 1a and 1b (Table II) (about 5.5 times more 4 from 1b than from 1a), we concluded that the mixture of 1a and 1b (6:4) obtained from the lithium aluminum hydride reduction of 9 could be used directly in the deamination reaction.

In our initial experiments, 9 was deuterated by exchange with deuterium oxide at room temperature to give 2-deuterio-2-cyanocyclohexanone (9-2-d). As evidenced by nmr analysis of the crude deuterated mixture, after two exchanges the deuteration was virtually complete. However, due to the lability of the hydrogen at the 2 position,[19] part of the deuterium was lost during the work-up and the subsequent reduction with lithium aluminum hydride. A mixture of partly deuterated amino alcohols 1a and 1b was finally obtained (eq 9).
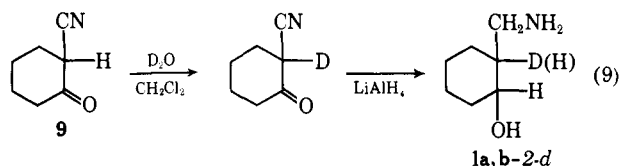
The *trans*-amino alcohol 1b-2-d would give 4-2-d by a 1,3-hydride shift and 4-7-d_1 by two 1,2-hydride shifts (Scheme I). In order to avoid deuterium exchange in 4-2-d, the deaminations of labeled compounds were carried out in the presence of pentane in which 4 and 14 were quite soluble. This procedure was checked by running the deamination of unlabeled 1b in deuterium oxide solution. An upper limit of 3.5% deuterium incorporation in the product, 4, was found by mass spectrometric analysis. Considering the deuterium isotope effect, it can be concluded that the deuterium loss from 4-2-d would be even smaller.

In a second series of experiments, a mixture of 1a,b-1,7-d_3 which was obtained from 9 by reduction with lithium aluminum deuteride (eq 10) was subjected to
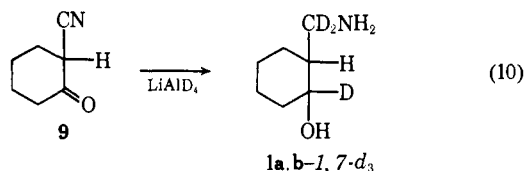

the deamination conditions.

The deuterium distribution in the 2-methylcyclohexanone (4) obtained was studied by mass spectrometry. The fragmentation scheme of 4 had previously been studied by Siebl and Gaumann,[20] who on the basis of labeled compounds assigned structures 17 and 18 to ions of m/e 68 and 69, respectively.

The mass spectrum of 4-d_1 (55–57% d_1 and 43–45% d_0) from 1a,b-2-d (eq 9) showed the base peak at m/e 69 and a peak of 45% relative intensity at m/e 70. These figures are consistent with a mixture of 4 and 4-7-d_1 rather than a mixture of 4 and 4-2-d. The deuterium was therefore located at the methyl group.

(19) S. S. Kulp, *Can. J. Chem.*, **45**, 1981 (1967).
(20) J. Siebl and T. Gaumann, *Z. Anal. Chem.*, **197**, 33 (1963).

m/e 68, intensity 100

m/e 69, intensity 45
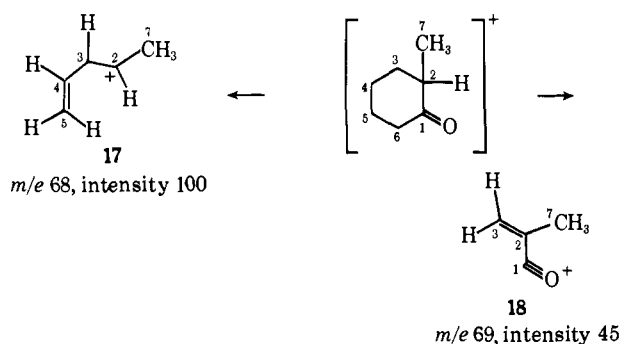
In the case of 4-d_3, obtained from 1a,b-1,7-d_3 (eq 10),[21] the base peak appeared at m/e 71. At the same time, no significant increase in the relative intensity of the peak at m/e 72 was observed, over that found for the dilabeled material 4-7-d_2 which was obtained from 1b-

1b-7-d_2

4-7-d_2
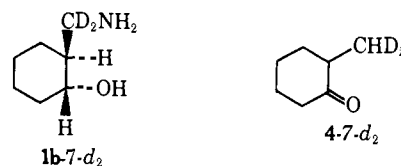
7-d_2. Consequently, in 4-d_3, only two deuterium atoms are located at the methyl group, and the third is on C-2.

In order to ascertain the amount of 4 which is formed from cation 6 by way of an enol,[4] the deuterium loss during the deamination of 1a,b-1,7-d_3 must be determined. However, the deuterium content could not be accurately measured for the starting amino alcohol due to ion–molecule reactions in the mass spectrometer. Consequently, the deuterium content of the diol products 2 and 13 was determined and used as a measure of the deuterium content of the starting material. The diol mixtures from the deamination experiments were treated with acetone and p-toluenesulfonic acid to give the bicyclic ketals 19a, 19b, and 20 of diols 2a, 2b, and 13a, respectively. (The *trans*-1,2-diol 13b did not yield a ketal and was recovered unchanged.)

19a

19b

20
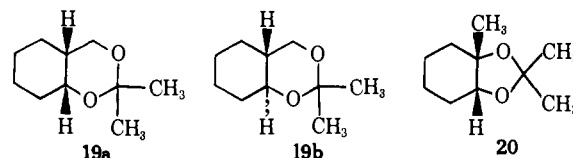
The deuterium content of the ketals was determined using the (M − CH₃)⁺ peak. (19a and 19b gave no molecular ion peaks and 20 gave a very small one.) That the expelled methyl group comes exclusively from the acetone moiety was established from the mass spectra of ketals prepared from the unlabeled diols and hexadeuterioacetone. These ketals exhibited (M − CD₃)⁺ peaks but no (M − CD₂H)⁺, (M − CDH₂)⁺, or (M − CH₃)⁺ peaks. Using this method, diols 2a, 2b, and 13a from the deamination of 1-1,7-d_3 were found to contain 6–7% dideuterated material.[22] Since the ketone 4 obtained from this amino alcohol contained 8–9% 4-d_2, an upper limit of 2% can be estimated for the sum of the contributions of the enol

(21) Two runs were performed with virtually identical results.
(22) Because of the primary kinetic isotope effect involved in the rearrangement of 5[18] to 6, and the fact that 1-2-d prepared by the route shown in eq 9 contained appreciable quantities of undeuterated material, this method could not be used for assessing the deuterium content of 1-2-d.

pathway in the conversion of **6** to **4** and the hydrogen-deuterium exchange at the 2 position of **4** with the solvent.

For nmr studies, **4-d_1** from **1-2-d** was isolated by distillation under moderate vacuum in a short-path assembly. The nmr spectrum of the distillate which contained **4-d_1** (55–57% d_1) and some 2-methylenecyclohexanol **(14)** showed a methyl doublet (τ 8.97, J = 6.5 Hz) for the unlabeled material and a slightly shifted (partially superimposed on the previous signal) doublet of triplets (τ 9.00, J = 6.5, 1.8 Hz) corresponding to **4-7-d_1**, the second splitting being produced by geminal coupling with one deuterium atom.

With trilabeled material, the ketone **(4-d_3)** was isolated by preparative glc. Its nmr spectrum at 90 MHz exhibited a closely spaced quintet (τ 9.02, J = 1.8–2.0 Hz) which integrated for one proton. This clearly indicates the presence of the $CDCHD_2$ group, as in **4-2,7-d_3**, and rules out the $CHCD_3$ group, as in **4-7-d_3**.

Discussion

The results presented above can be understood in terms of the low-activation energy for the decomposition of diazonium ions, which causes the so-called "ground-state control" of deamination reactions.[23,24] Consequently, carbonium ions **5a** and **5b** are formed in the conformation which is most stable for **1a** and **1b**, respectively.[16] It was shown above (Table I) that the most stable conformation of **1a** involves the hydroxyl group of the ring in an axial position, whereas in **1b** the hydroxyl group is in an equatorial position. The transformations undergone by ions **5a** and **5b** are presented in Charts I and II, respectively. Both carbonium ions

**Chart I.** Deamination of cis-2-(Aminomethyl)cyclohexanol[a]
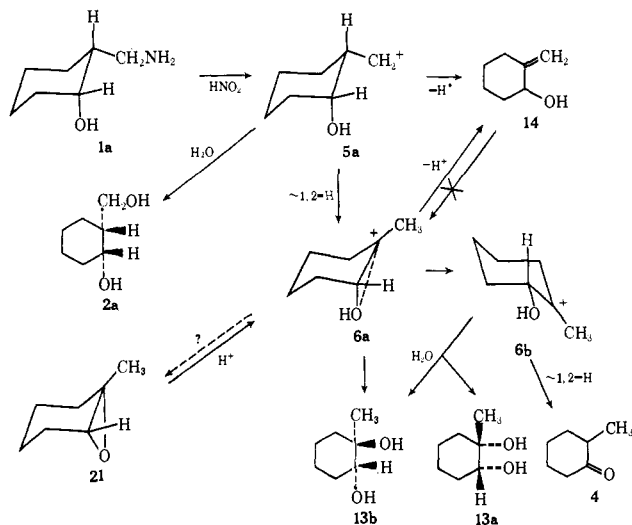
[a] See ref 16.

5a and **5b** form the corresponding diols **(2a** and **2b,** respectively) by reaction with water. By a 1,2-hydride shift, ions **5a** and **5b** are converted into tertiary ions **6a** and **6b,** respectively. The difference in the ratios of rearranged products **(4, 13a, 13b)** formed from **1a** and **1b** requires that the subsequent reactions of ions **6a** and **6b** be more rapid than the ring inversion which interconverts these ions.

(23) D. V. Banthorpe, "Elimination Reactions," Elsevier, Amsterdam, 1963, p 158.

(24) See White and Woodcock in Table II, footnote b.

Chart II. Deamination of trans-2-(Aminomethyl)cyclohexanol[a]
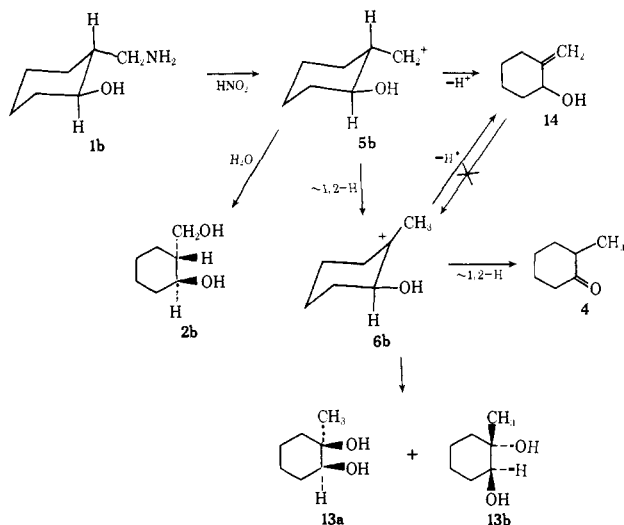
[a] See ref 16.

Ion **6a** should be the same as that obtained by acid-catalyzed ring opening of 1-methylcyclohexene oxide **(21).** The acidic hydrolysis of **21** was previously reported to yield **13b.**[25] We repeated this hydrolysis under conditions similar to our deamination conditions (sodium nitrite and phosphoric acid, buffered with K_2HPO_4 to pH 5) and obtained 68% **13b**[26] together with small amounts of **13a** (ca. 3%), **4** (ca. 3%), traces of **14,** and other minor, unidentified products.[27] A small amount of **6a** apparently leaks to the other conformation, **6b,** which is the source of **13a** and **4.**

In the second tertiary ion, **6b,** the equatorial hydroxyl group is close to eclipsing the methyl group, and this should tend to destabilize **6b.** On the other hand one p orbital of the oxygen is parallel to the empty p orbital of the neighboring ring carbon, and this could stabilize **6b.**[30] The fact that **1b** leads to almost equal quantities of **13a** and **13b** suggests that ion **6b** is attacked at both sides with comparable facility.[31] In addition, the adjacent axially oriented hydrogen in **6b** can readily migrate to the positive center, forming ketone **4.** This migration could be (partly) synchronous with the first migration **(5b → 6b).** Both concerted and nonconcerted shifts are compatible with the preservation of optical activity in **4.**[3c]

2-Methylenecyclohexanol **(14)** could arise most simply by the loss of a proton from the initial cation, **5.**[16] However, an examination of the mass spectrum of this product formed from **1-2-d** revealed that some of the deuterium remained in **14.** In addition, **14** obtained from **1b-7-d_2** lost some deuterium from the exocyclic methylene group. These findings suggest that part of **14** arises from the rearranged tertiary ion **6.** The reverse process, **14 → 6,** does not occur during the deami-

(25) J. Boeseken, Chem. Ber., **56,** 2409 (1923).

(26) Isolated yield. Considering the losses involved in the work-up, the actual yield was certainly higher.

(27) Analysis by glc. Actually, 1-methylcyclohexene oxide obtained from 1-methylcyclohexene by epoxidation already contained (glc) traces of **4**[28] and **14.**[29]

(28) R. Filler, B. R. Camara, and S. M. Naqvi, J. Amer. Chem. Soc., **81,** 658 (1959).

(29) V. S. Joshi, N. P. Damodaran, and S. Dev, Tetrahedron, **24,** 5817 (1968).

(30) We thank Professor Paul von R. Schleyer for this suggestion.

(31) Our results do not give us any information on the leakage of **6b** to **6a.**

nation. When subjected to the reaction conditions, **14** did not yield any **4**, **13a**, or **13b**. It was recovered unchanged.

Experimental Section[32]

trans-2-Cyanocyclohexanol (**8b**) was prepared as previously described,[5a] except that the ethereal extract containing the product was washed with water, 1.5% NaOH, and again with water, before drying and evaporation: bp 122–125° (4.5 mm), mp 46.5–47.0° (lit.[5a] bp 145–146° (16 mm), mp 46°); yield 60%; nmr spectroscopy indicated the product to consist of 85% **8b** and 15% **8a**, τ 6.28 (0.85 H, m, CHO trans isomer), 6.91 (0.15 H, m, CHO cis isomer), 7.30–8.90 (9 H, broad envelope, CH_2 and CH), 6.16 (1 H, s, OH).

trans-2-Carboxycyclohexanol (**12b**) was prepared in 55% yield by basic hydrolysis of **8b**:[5a] crude mp 99–102° (lit.[38] mp 109–111°); nmr spectroscopy indicated the product to consist of 84% **12b** and 16% **12a** (see Table I for chemical shifts).

cis-2-Carboxycyclohexanol (**12a**) was prepared in 42% yield from ethyl 2-cyclohexanonecarboxylate by catalytic hydrogenation followed by hydrolysis of the ester group:[34] mp 74–76° (lit.[34] mp 81°). Nmr spectroscopy indicated the product to consist of 90% **12a** and 10% **12b**.

Methyl *cis*- (**22a**) and *trans*-2-hydroxycyclohexanecarboxylate (**22b**) were obtained by esterification of **12a** and **12b**, respectively, with diazomethane.[33] The cis ester was obtained in 90% crude yield. The trans ester was obtained in 70% yield, bp 108–113° (9 mm) (lit.[33] bp 87.5–88.5 (3 mm)).

cis- (**2a**) and *trans*-2-(hydroxymethyl)cyclohexanol (**2b**) were obtained by reduction of esters **22a** and **22b** with lithium aluminum hydride. The cis isomer **2a** was obtained in 87% yield: bp 117–120° (3 mm); mp 47–49° (lit.[33] bp 124° (2 mm), mp[35] 49–50°); nmr τ 5.89 (1 H, broad, CHO), 6.33 (2 H, d, $J = 4$ Hz, CH_2O), 7.90–8.85 (9 H, broad envelope, CH_2, CH), 6.29 (2 H, broad s, OH). The trans isomer **2b** was obtained in 88% yield: bp 113–115° (2 mm) (lit.[33] bp 103.5–104° (0.9 mm)); nmr τ 6.7 (1 H, broad, CHO), 6.32 (2 H, broad doublet, CH_2O), 7.85–9.10 (9 H, broad envelope, CH_2, CH), 5.60 (2 H, broad s, OH).

1-Methylcyclohexene oxide (**21**) was prepared by epoxidation of 1-methylcyclohexene with *m*-chloroperbenzoic acid in CH_2Cl_2[36] in 40% yield: bp 137–139° (lit.[37] bp 137.5–138°); nmr τ 7.55 (1 H, t, $J = 2$ Hz, CHO), 8.47 (4 H, m, CH_2), 8.87 (4 H, m, CH_2), 8.92 (3 H, s, CH_3). Glc analysis indicated the product to contain traces of **4** and **14**.

1-Methyl-*cis*-1,2-cyclohexanediol (**13a**) was synthesized in 26% yield from 1-methylcyclohexene by oxidation with potassium permanganate at −20 to −30°:[38] mp 62–63° (from petroleum ether) (lit.[39] mp 68°); nmr τ 6.58 (1 H, m, CHO), 8.0–8.8 (8 H, broad envelope, CH_2), 8.75 (3 H, s, CH_3), 7.39 (2 H, s, OH).

1-Methyl-*trans*-1,2-cyclohexanediol (**13b**) was prepared in 78% yield by the hydrolysis of 1-methylcyclohexene oxide (**21**) with 0.05 N sulfuric acid:[25] mp 81.5–83° (lit.[39] mp 85°); nmr τ 6.53 (1 H, m, CHO), 7.95–9.00 (8 H, broad envelope, CH_2), 8.80 (3 H, s, CH_3), 6.58 (2 H, s, OH).

2-Methylenecyclohexanol (**14**). Ethyl 2-cyclohexanonecarboxylate (10 g) was reduced with 6.7 g of lithium aluminum hydride in 95 ml of ether.[40] After completion of the reaction, the mixture

was treated with 31 ml of a 35% sodium potassium tartrate solution with stirring and cooling for 45 min. After an additional 30 min of stirring at room temperature, the white, granular solid was filtered off and thoroughly washed with ether. Evaporation of the combined ether solutions gave 7.2 g of a liquid which consisted of (glc) ca. 60% **14**, together with 1-(hydroxymethyl)cyclohexene, *cis*-(**2a**) and *trans*-2-(hydroxymethyl)cyclohexanol (**2b**). For ir and nmr spectra, samples of **14** were isolated by prepatative glc: nmr τ 5.08 (1 H, m, C=CH), 5.23 (1 H, m, C=CH), 5.88 (1 H, m, CHO), 7.45–8.70 (8 H, broad envelope, CH_2), 7.88 (1 H, s, OH).

2-Cyanocyclohexanone (**9**). The imino derivative of **9** was prepared from 1,5-dicyanopentane.[19] After decomposing the lithium salt of the imine with water, the product was extracted with ether. Evaporation of the ether in the cold gave several crops of imino derivative melting in the range 90–94° (lit.[19] mp 94–95°): yield, 70–85%; nmr τ 5.6 (2 H, broad s, NH_2), 7.82 (4 H, m, CH_2), 8.35 (4 H, m, CH_2).

Treatment of the imino derivative with 2.5 N HCl gave **9** in 65% yield: bp 122–125° (4 mm) (lit.[19] bp 128–133° (8 mm)); nmr τ 5.4 (0.1 H, broad singlet, OH (enol)), 6.35 (0.9 H, m, CHCN), 7.0–8.2 (8 H, broad envelope, CH_2). The semicarbazone derivative had mp 172° (lit.[41] mp 162°).

Anal. Calcd for $C_8H_{12}N_4O$: C, 53.32; H, 6.71; N, 31.09. Found: C, 53.32; H, 6.54; N, 30.87.

2-Deuterio-2-cyanocyclohexanone (**9**-*2*-*d*). The solvents used for this preparation were shaken with several small portions of deuterium oxide before use. A solution of 7.1 g (58 mmol) of **9** in 25 ml of CH_2Cl_2 was stirred with 20 ml of deuterium oxide at room temperature for 14 hr. The deuterium oxide was replaced by 20 ml of fresh deuterium oxide, and the stirring was continued for an additional 13 hr. Nmr spectroscopy of the organic layer indicated virtually complete exchange at the 2 position. The organic layer was dried and the solvent was removed to yield **9**-*2*-*d* (97%). Mass spectroscopy indicated ca. 82% d_1 and 18% d_0 (direct inlet, possibly exchange is occurring in the mass spectrometer).

trans-2-(Aminomethyl)cyclohexanol (**1b**).[5b] A solution of 20.1 g (0.16 mol) of **8b** in 60 ml of ether was slowly added, with stirring, to a suspension of 18.25 g (0.48 mol) of lithium aluminum hydride in 250 ml of ether, under nitrogen. After addition of an additional 90 ml of ether, the mixture was heated under reflux for 3.5 hr and left at room temperature overnight. Sodium potassium tartrate solution (81 ml, 35%) was added to the ice-cold reaction mixture with stirring over a period of 2 hr. After an additional 1 hr of stirring, the mixture was filtered, and the solid was washed with ether. After evaporation of the solvent, the residue was dissolved in 100 ml of 2.5 N HCl. The acidic solution was extracted with chloroform and ether, brought to pH 11 with solid sodium hydroxide, and extracted with ether. The ethereal solution was dried (sodium hydroxide) and concentrated, and the residue was distilled to yield 17.7 g (85%) of **1b** (nmr spectroscopy indicated the presence of 16–17% **1a**; glc analysis indicated 19–20% **1a** to be present): bp 109–111° (6 mm) (lit.[5a] bp 133° (17 mm); nmr τ 6.61 (0.83 H, m, CHO of **1b**), 5.97 (0.17 H, m, CHO of **1a**), 7.20 (2 H, concentration-dependent m, CH_2N), 7.85–9.30 (9 H, broad multiplet, CH_2 and CH), 6.88 (3 H, s, OH and NH_2); mass spectral base peak at m/e 30 (CH_2NH_2). The forerun contained a small amount of 1-(aminomethyl)cyclohexene (**23**).[42]

trans-2-(Aminomethyl-d_2)cyclohexanol (**1b**-*7*-*d*$_2$) was prepared in a similar fashion from **8b** and lithium aluminum deuteride in 78% yield: bp 104–106° (5 mm); mass spectral base peak at m/e 32 (CD_2NH_2). The nmr spectrum showed no absorption in the CH_2N region. Mass spectral analysis of the ketals (**19** and **20**) prepared from the diols (**2** and **13**) obtained from the deamination of this material showed that **1**-*7*-*d*$_2$ contained 5–6% monodeuterated material.

Reduction of 2-Cyanocyclohexanone (**9**) under the same conditions as used for **8b** gave a mixture of **1a** and **1b** (6:4 by glc) in 60–65% yield: bp 105–111° (5 mm). The forerun contained some 1-(aminomethyl)cyclohexene (**23**).

cis- (**1a**-*2*-*d*) and *trans*-2-(Aminomethyl)cyclohexanol-*2*-*d* (**1b**-*2*-*d*). A mixture of **1a**-*2*-*d* and **1b**-*2*-*d* (6:4) was prepared in 64% yield by reduction of **9**-*2*-*d* with lithium aluminum hydride: bp 108–

(32) Nmr spectra were determined in a $CDCl_3$ solution at 60 MHz using Varian A-60 and Jeolco C-60HL spectrometers with tetramethylsilane as internal standard. Nmr spectra of deuterated compounds were determined at 90 MHz using a Brucker HFX-2/0 spectrometer. Infrared spectra of liquids were determined as thin films between NaCl plates. Infrared spectra of solids were determined in KBr discs. Mass spectra were determined at 70 eV with a Varian CH5 spectrometer. Most glc separations were performed using a QF-1 (fluorosilicone) column (10%, 10 ft × ¹/₈ in.). Compounds **14** and **21** were not separated under these conditions; a 10%, 10 ft × ¹/₈ in. OV-17 (methylphenylsilicone (50%)) column was used for this separation. Microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn. Melting points are corrected.

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(42) J. Colonge and H. Daunis, *C. R. Acad. Sci. Paris*, **251**, 1080 (1960).

115° (4 mm). The deuterium content could not be measured exactly.[22]

cis- (1a-*1,7-d₃*) and *trans*-2-(Aminomethyl-*d₂*)cyclohexanol-2-*d* (1b-*1,7-d₃*). A mixture of 1a-*1,7-d₃* and 1b-*1,7-d₃* (6:4) was prepared in 58% yield by reduction of 9 with lithium aluminum deuteride: bp 110–115° (4 mm). Mass spectral analysis of the ketals 19 and 20 prepared from the diols 2 and 13 obtained from the deamination of this material showed that 1-*1,7-d₃* contained 6–7% dideuterated material.

N-Benzoyl derivative of 1b (10b) was prepared as previously described[7c] in 90% yield: mp 120–122.5° (petroleum ether–benzene) (lit.[7a] mp 123–124°).

cis-2-(Aminomethyl)cyclohexanol (1a). The inversion at C-1 was accomplished by treating 10b with thionyl chloride.[7b] The acidic hydrolysis of the intermediate, 11, gave 1a in 40% yield: bp 105–108° (5 mm); nmr τ 5.97 (1 H, m, CHO), 7.18 (2 H, m, CH₂N), 8.0–9.0 (9 H, broad m, CH₂, CH), 7.31 (3 H, s, OH and NH₂). No 1b was detected in the product by glc (<5%). The forerun consisted mainly of 1-(aminomethyl)cyclohexene (23).

Deamination Procedure. A solution of 31.5 mmol of sodium nitrite in 15 ml of water was added at once to an ice-cold solution of 30 mmol of amino alcohol (1) and 30 mmol of phosphoric acid in 30 ml of water. The resulting solution was stirred for 1.5 hr at 0° and 93–95 hr at room temperature. For product analysis, the solution was saturated with sodium chloride and thoroughly extracted with ether. The dried (MgSO₄) extract was concentrated and analyzed by glc (Table II). For identification, the components were isolated by preparative glc and subjected to ir and nmr analysis. Mass spectra were run directly from the mixture by glc–mass spectrometry.

In experiments with deuterated compounds, 25 ml of pentane was added immediately after the nitrite solution. At the end of the reaction, the water was frozen in a Dry Ice-acetone bath, and the pentane solution was separated. The aqueous solution was extracted two times with pentane by thawing–stirring–freezing cycles. The products 13a,b and 2a,b were isolated from the aqueous solution, as above. Products 4 and 14 were isolated from the pentane solution by concentration followed by either distillation in a short-path assembly at 100 mm or preparative glc. Mass spectra were determined by glc–mass spectrometry. In order to avoid errors due to isotopic fractionation during the chromatographic process, several mass spectra were run during the elution of each peak. No significant isotope fractionation was observed for any of the compounds investigated.

Attempts to isolate cyclohexanecarboxylic acid (15) from the deamination of 1a by extraction with alkali led to a few milligrams of an unidentified oil. Similarly, dilution of the reaction product with alcohol did not precipitate any cyclohexanecarboxaldehyde trimer 16 (see below).

Reaction of Cyclohexanecarboxaldehyde (3) with Nitrous Acid. The same procedure as that used for amino alcohol 1 was followed. A partly solid, crude product was obtained which on dilution with ethanol gave 36% solid 16: mp 199–200° (acetone) (lit.[43] mp 202–203°); nmr τ 5.49 (3 H, d, J = 4.5 Hz, CHO₂), 8.10–9.10 (33 H, broad envelope, CH₂, CH). Extraction of the mixture with base gave 35% cyclohexanecarboxylic acid (15). The remainder of the product consisted mainly of unreacted 3 (6%).

Reaction of 2-Methylenecyclohexanol (14) with Nitrous Acid. This reaction was performed with the mixture obtained from the lithium aluminum hydride reduction of ethyl 2-cyclohexanone-carboxylate. The same procedure as that used for amino alcohol 1 was followed except that K₂HPO₄ was used to buffer the reaction mixture at pH 5–6. The usual work-up procedure was used. The pentane extract contained mainly unreacted 14 and 1-(hydroxymethyl)cyclohexene (together 77% of the starting weight). No more than traces of 1-methylcyclohexanone (4) were found. The ether extract contained 2a, 2b, some 1-(hydroxymethyl)cyclohexene, and other minor compounds (all together 14% of the starting weight).

Reaction of 1-Methylcyclohexene Oxide (21) with Nitrous Acid. The same procedure as that used for 2-methylenecyclohexanol (14) was followed to yield 13a (3%), 13b (68%), and 4 (3%). Minor amounts of 14 and other unidentified products were also present.[25]

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Kinetic Evidence for Both Quenching and Reaction of Singlet Oxygen with Triethylamine in Pyridine Solution

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Abstract: Kinetic evidence is presented which shows that, in pyridine solution, triethylamine is approximately 16 times as reactive an acceptor of singlet oxygen as 2-methyl-2-pentene, that it is as good a quencher of singlet oxygen as 1,4-diazabicyclo[2.2.2]octane, and that approximately nine quenching acts occur for every molecule of triethylamine which is destroyed by singlet oxygen.

Although it is well established that aliphatic amines may *quench* singlet oxygen,[1,2] it is not so well established that aliphatic amines may also *react* with singlet oxygen. Ogryzlo and Tang[2] found that, in the gas phase, reaction of singlet oxygen with aliphatic amines must be at least 100 times less efficient than quenching of the amines by singlet oxygen. Ouannes and Wilson[1] reported that the tertiary amines 1,4-diazabicyclo[2.2.2]octane (DABCO), ethyldiisopropylamine, *N,N,N',N'*-tetramethylethylenediamine, and *N*-allylpiperidine were "apparently unreactive toward ¹O₂" in bromobenzene solution, yet retarded the oxidation of 1,3-diphenylisobenzofuran, a known singlet oxygen acceptor.

There have been several reports of dye-sensitized oxygenations of amines. The earliest was that of Gaffron,[3] who found that erythrosin photosensitized the oxygenation of *n*-propylamine, and that chlorophyll photosensitized the oxygenation of isoamylamine. More recently Schenck[4] reported that dye-sensitized photooxygenation of primary, secondary, and tertiary amines results in the uptake of one, two, or three molecules of O₂, respectively, indicating that the number of α-CH groups determines the stoichi-

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