[CONTRIBUTION FROM THE JOHN HARRISON LABORATORY OF CHEMISTRY, UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA, PA.]

Kinetic Isotope Effect in the Reaction of N-Methylaniline-N-*d* and 3-Chloro-1-butene[1]

BY DONALD C. DITTMER[2] AND ARNOLD F. MARCANTONIO[3]

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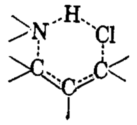
The reaction of 3-chloro-1-butene with $C_6H_5NDCH_3$ at 80.2° and at 102.3° in *n*-heptane in the presence of 2,4,6-collidine is slower than the reaction with $C_6H_5NHCH_3$. The over-all rate of reaction is given by $k_2 \cdot [RCl][R_2NH] + k_3[RCl][R_2NH]^2$ and the kinetic isotope effect is observed only in the third-order term, $k_{3H}/k_{3D} = 1.38(80.2°), 1.34(102.3°)$. A possible interpretation of the data is that the reaction is proceeding by two paths. One path is taken by a reaction which corresponds to the second-order term (SN2′ reaction) which does not involve an isotope effect; the other path involves an extra molecule of N-methylaniline which may be assisting the reaction by hydrogen bonding with the leaving chloride ion. An ion-pair intermediate may be involved in this latter path.

Introduction

An attractive mechanism for the displacement reaction of a primary or secondary amine on an allylic halide which occurs with rearrangement, the SN2′ reaction,[4] has involved hydrogen bonding to the leaving halide ion.[5] This hydrogen-bonding mechanism has been widely disseminated.[6] It has since been shown that tertiary amines also take part in the SN2′ reaction, but the possible facilitation of reactions of primary and secondary amines by such hydrogen bonding has been suggested.[7]



Information concerning the importance of hydrogen bonding in the transition states of SN2′ reactions might be obtained from observation of the presence or lack of a kinetic hydrogen isotope effect when N-deuterated amines are used. If the proton attached to the nitrogen atom is significantly involved in the transition state, one may observe an isotope effect.

Previous work indicated that there was no difference in rate between the reaction of N,N-diethylamine and N,N-diethylamine-N-*d* and α-methylallyl chloride (3-chloro-1-butene).[8] However, the lack of an isotope effect does not mean necessarily that hydrogen bonding does not occur in the transition state.[9] In order to provide for a more favorable substrate for hydrogen bonding, N-methylaniline was used as the amine. It was felt that the electron-withdrawing character of the phenyl ring would make the proton on nitrogen more acidic and more prone to engage in hydrogen bonding.[10] From a study of the effect of solvent on the fluorine nuclear magnetic resonance in *m*-fluoroaniline and in *m*-fluorobenzylamine, Taft and co-workers concluded that *m*-fluoroaniline showed the characteristics of a proton donor while *m*-fluorobenzylamine showed the characteristics of a proton acceptor.[11] Thus, with the aromatic amine there may be a more favorable opportunity to observe an SN2′ reaction proceeding through the hydrogen-bonded transition state.

Results

Diethylamine and Diethylamine-N-*d*.—As previously reported,[8] the average second-order rate constant (2.07×10^{-2} M^{-1} hr.$^{-1}$) for the reaction of diethylamine-N-*d* (0.103–0.196 *M*) with 3-chloro-1-butene (0.088–0.298 *M*) in benzene at 60.10 ± 0.04° was identical within experimental error with the average second-order rate constant ($2.08 \times 10^{-2} M^{-1}$ hr.$^{-1}$) of the reaction of diethylamine (0.187–0.478 *M*) with 3-chloro-1-butene (0.069–0.295 *M*). The product of the reaction was *trans*-N-1-(2-butenyl)-N,N-diethylamine with some *cis* isomer being formed also. The experimental activation energy for the reaction of diethylamine with 3-chloro-1-butene was 15.3 kcal./mole, the enthalpy of activation 14.6 kcal./mole (60.1°), and the entropy of activation −39.0 e.u. (60.1°).[12]

N-Methylaniline and N-Methylaniline-N-*d*.—The kinetics of the reaction of both amines with 3-chloro-1-butene was measured at 60.1, 80.2, and 102.3° in *n*-heptane in the presence of 2,4,6-collidine. The collidine, being more basic than N-methylaniline, removes hydrogen chloride and prevents the Hofmann–Martius reaction,[13] in which demethylation of the amine occurs followed by further complicating reactions of the methyl chloride produced. Variation of the collidine concentration had no effect on the observed rates, and it was concluded that the collidine was functioning only as a scavenger of hydrogen chloride and was not involved in the rate-determining step.

Most kinetic runs were followed to at least 60% completion. Many were followed beyond 80%.

The rate data were not represented well by a second-order expression, although within a given run second-

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[1] Reported at the 139th National Meeting of the American Chemical Society, St. Louis, Mo., March, 1961. For complete details see A. F. Marcantonio, Ph.D. Thesis, University of Pennsylvania, 1961.

[2] Department of Chemistry, Syracuse University, N. Y. 13210.

[3] Walter T. Taggard Memorial and University of Pennsylvania Fellow, 1958. Allied Chemical and Dye Corporation Fellow, 1959.

[4] The SN2′ reaction has been reviewed: R. H. deWolfe and W. G. Young, *Chem. Rev.*, **56**, 769 (1956).

[5] (a) W. G. Young, I. D. Webb, and H. L. Goering, *J. Am. Chem. Soc.*, **73**, 1076 (1951); (b) R. E. Kepner, S. Winstein, and W. G. Young, *ibid.*, **71**, 115 (1949).

[6] C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, p. 592.

[7] W. G. Young, R. A. Clement, and C.-H. Shih, *J. Am. Chem. Soc.*, **77**, 3061 (1955).

[8] D. C. Dittmer and A. F. Marcantonio, *Chem. Ind.* (London), 1237 (1960).

[9] (a) L. Melander, "Isotope Effects on Reaction Rates," The Ronald Press Co., New York, N. Y., 1960, p. 15. (b) See the arguments cited in S. D. Ross and M. Finkelstein, *J. Am. Chem. Soc.*, **85**, 2603 (1963).

[10] Infrared frequency shifts for N–H stretching vibrations are generally greater for N-methylaniline than for diethylamine in a variety of solvents: R. E. Dodd and G. W. Stephenson, "Hydrogen Bonding," D. Hadzi, Ed., Pergamon Press, New York, N. Y., 1959, p. 177.

[11] R. W. Taft, E. Price, I. R. Fox, I. C. Lewis, K. K. Anderson, and G. T. Davis, *J. Am. Chem. Soc.*, **85**, 709 (1963).

[12] Values previously reported for the reaction of dimethylamine in benzene and trimethylamine in acetone with 3-chloro-1-butene were, respectively: ΔE exp = 18.3, 14.5 kcal./mole; $\Delta H^* = 17.6, 13.9$ kcal./mole; $\Delta S^* = -26.2, -38$ e.u. (50°) [W. G. Young and I. J. Wilk, *J. Am. Chem. Soc.*, **79**, 4793 (1957)].

[13] A. W. Hofmann, *Ber.*, **5**, 720 (1872).

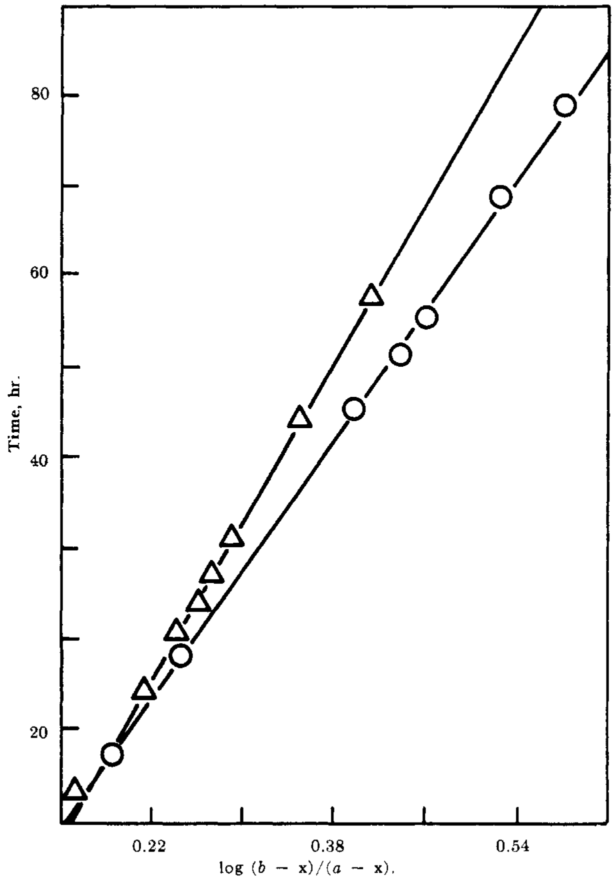

Fig. 1.—Typical second-order rate plots for the reaction of 0.987 M 3-chloro-1-butene with 1.344 M N-methylaniline and 1.326 M N-methylaniline-N-*d*, respectively, in the presence of 1.862 and 1.826 M 2,4,6-collidine, respectively, in *n*-heptane at 102.3 ± 0.05°: ○, reaction involving N-methylaniline; △, reaction involving N-methylaniline-N-*d*; a = initial concentration of halide; b = initial concentration of amine; x = concentration of product at time t.

order rate constants calculated from

$$-\mathrm{d}[R_2NH]/\mathrm{d}t = \mathrm{d}[Cl^-]/\mathrm{d}t = k_{2\mathrm{obsd}}[RCl][R'_2NH]$$

were reasonably constant.[14] The observed second-order rate constant was dependent on the concentration of N-methylaniline but not on the concentration of 3-chloro-1-butene. There are few reactions in the literature in which the rate of reaction of a halide with an amine shows greater than first-order dependence on the amine concentration: the rate of the reaction of aniline or *p*-toluidine with 2,4-dinitrochlorobenzene was reported to be strongly dependent on the concentration of excess amine[15]; the rate expression for the reaction of certain amines with 2,4-dinitrochlorobenzene required a term second order with respect to the amine concentration which was interpreted as indicating that a second molecule of amine was functioning as a base in proton removal[16]; the rate of reaction of benzhydryl chloride with *m*-chloroaniline appeared to be greater than first order with respect to amine concentration.[17] Attempts to correlate all the rate data by five-halves and third-order rate equations were not successful. All the data, however, can be represented by

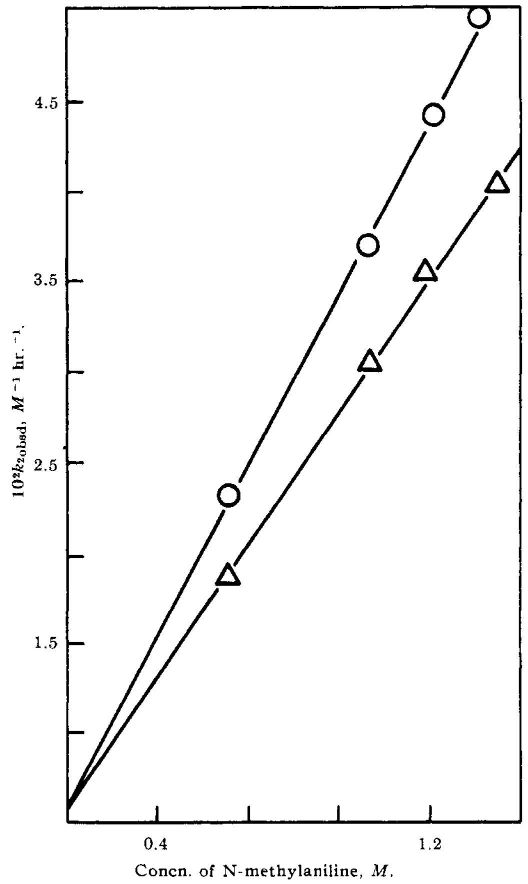

Fig. 2.—Observed second-order rate constants *vs.* concentration of N-methylaniline for the reaction of N-methylaniline with 3-chloro-1-butene in the presence of 2,4,6-collidine in *n*-heptane at 102.3 ± 0.05°: ○, reaction involving N-methylaniline; △, reaction involving N-methylaniline-N-*d*.

$$\text{rate} = k_{2\mathrm{obsd}}[RCl][R'_2NH] = k_2[RCl][R'_2NH] + k_3[RCl][R'_2NH]^2 \quad (1)$$

where

$$k_{2\mathrm{obsd}} = k_2 + k_3[R'_2NH]$$

The values of $k_{2\mathrm{obsd}}$ are satisfactorily constant although the values at later stages of the reaction show greater deviations. The rate expression can be integrated to give

$$\frac{1}{b-a}\ln\frac{a(b-x)}{b(a-x)} - \frac{k_3}{k_2}\left[\ln\frac{b}{b-x} - \ln\frac{b+(k_2/k_3)}{(b-x)+(k_2/k_3)}\right] = [k_2 + k_3(b-a)]t$$

where a is the initial concentration of allyl halide, b the initial concentration of amine, and x the concentration of product at time t. As Ross and Petersen have pointed out, the second term on the left will be small, particularly near the beginning of the reaction.[16b]

Values of $k_{2\mathrm{obsd}}$ for the reaction of N-methylaniline are given in Table I and for N-methylaniline-N-*d* in Table II. Figure 1 shows typical second-order rate plots of the reaction of both deuterated and undeuterated N-methylaniline with 3-chloro-1-butene. Figure 2 shows a plot of the observed second-order rate con-

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[14] [RCl] = concentration of 3-chloro-1-butene; [R'₂NH] = concentration of N-methylaniline.

[15] L. Nicolini, *Boll. sci. facolta chim. ind. Bologna*, **3**, 221 (1942); *Chem. Abstr.*, **38**, 6277 (1944).

[16] (a) S. D. Ross, J. E. Barry, and R. C. Petersen, *J. Am. Chem. Soc.*, **83**, 2133 (1961); S. D. Ross, M. Finkelstein, and R. C. Petersen, *ibid.*, **81**, 5336 (1959); S. D. Ross and M. Finkelstein, *ibid.*, **79**, 6547 (1957); (b) S. D. Ross and R. C. Petersen, *ibid.*, **80**, 2447 (1958).

[17] C. G. Swain and D. C. Dittmer, *ibid.*, **77**, 3924 (1955).

stants *vs.* the concentration of N-methylaniline at 102.3°. The intercept on the *Y*-axis is k_2 and the slope of the line is k_3. The isotope effect occurs in the third-order term only since the intercepts of the lines for the two isotopic amines are equal within experimental error.

TABLE I

OBSERVED SECOND-ORDER RATE CONSTANTS FOR THE REACTION OF N-METHYLANILINE WITH 3-CHLORO-1-BUTENE IN *n*-HEPTANE AND 2,4,6-COLLIDINE

N-Methylaniline, *M*	3-Chloro-1-butene, *M*	2,4,6-Collidine, *M*	*T*, °C.	$10^3k_{2\text{obsd}}$, M^{-1} hr.$^{-1}$
0.456	0.989	0.597	60.1	0.975
.728	.475	.742	60.1	1.32
.827	.481	.899	60.1	1.45
.455	.973	1.871	80.2	5.02
.810	.986	1.880	80.2	7.94
1.356	.980	3.014	80.2	11.6
1.360	.978	2.406	80.2	12.1
1.367	.982	1.871	80.2	12.2
1.832	.983	1.884	80.2	16.3
0.704	.986	1.847	102.3	22.9
1.334	.987	1.862	102.3	36.8
1.611	.985	1.855	102.3	44.1
1.807	.987	1.858	102.3	49.4
1.808	2.470	1.860	102.3	48.8
1.810	0.493	1.856	102.3	49.0

TABLE II

OBSERVED SECOND-ORDER RATE CONSTANTS FOR THE REACTION OF N-METHYLANILINE-N-*d* WITH 3-CHLORO-1-BUTENE IN *n*-HEPTANE WITH 2,4,6-COLLIDINE

N-Methylaniline-N-*d*, *M*	Mole % N-*d*-amine[a]	3-Chloro-1-butene, *M*	2,4,6-Collidine, *M*	*T*, °C.	$10^3k_{2\text{obsd}}$, M^{-1} hr.$^{-1}$
0.388	91.7	0.747	0.514	60.1	0.853
.446	91.7	.480	0.587	60.1	0.968
.584	60.0	.985	1.826	80.2	4.88
1.314	60.0	.984	1.822	80.2	9.64
1.773	60.0	.984	1.815	80.2	12.7
0.706	86.0	.987	1.848	102.3	18.2
1.326	86.0	.986	1.826	102.3	30.1
1.576	86.0	.984	1.816	102.3	35.0
1.773	86.0	.985	1.806	102.3	39.7

[a] Determined by infrared spectroscopic analysis.

The concentrations of N-methylaniline-N-*d* in runs at 60.1° were not varied sufficiently to ascertain if an isotope effect was present, although if an effect of the magnitude of that observed at 80.2 or 102.3° were present it ought to have been observed at the *ca.* 0.4 *M* amine concentration used in these runs.[18]

Products of the reaction of N-methylaniline and 3-chloro-1-butene were N-1-(2-butenyl)-N-methylaniline (**1**), N-2-(3-butenyl)-N-methylaniline (**2**), and collidine hydrochloride.

$$\mathrm{CH_2{=}CHCH(CH_3)Cl + C_6H_5NHCH_3} \xrightarrow[\text{heptane}]{s\text{-collidine}}$$

$$\underset{\mathbf{1}}{\mathrm{C_6H_5N(CH_3)CH_2CH{=}CHCH_3}} +$$

$$\underset{\mathbf{2}}{\mathrm{CH_2{=}CHCH(CH_3)N(CH_3)C_6H_5}} + \mathrm{C_8H_{11}N{\cdot}HCl}$$

N-1-(2-Butenyl)-N-methylaniline was identified by its physical properties which agreed with those reported in the literature and by conversion to a picrate. N-2-(3-Butenyl)-N-methylaniline (**2**) is not reported in the literature. Its structure was assigned on the basis of the analysis of its picrate and its infrared spectrum. The amine had the same empirical formula as N-1-(2-butenyl)-N-methylaniline, but differences were observed in the melting point of its picrate, its infrared spectrum, and its gas chromatographic retention time. This new amine was not believed to be N-1-(1-butenyl)-N-methylaniline (**3**) because its infrared spectrum was significantly different from that of N,N-divinylaniline.[19]

$$\underset{\mathbf{3}}{\mathrm{CH_3CH_2CH{=}CHN(CH_3)C_6H_5}}$$

Table III illustrates the yields of products obtained from the reaction of 3-chloro-1-butene and N-methylaniline. Yields were determined by gas chromatography and were averaged for several runs. The principal product of the reaction of 1-chloro-2-butene with N-methylaniline in heptane in the presence of collidine was N-1-(2-butenyl)-N-methylaniline. Less than 10% of N-2-(3-butenyl-N-methylaniline was obtained. Neither 3-chloro-1-butene nor the allylic products isomerized under the reaction conditions.

Discussion

Two paths appear to be taken by the reaction of 3-chloro-1-butene with N-methylaniline. The rates at which these reactions occur are given, respectively, by the two terms on the right of eq. 1. A small isotope effect is observed in the third-order expression. Table IV gives the values of k_2, $k_{3\text{H}}$, and $k_{3\text{D}}$ as well as the ratio of rate constants, $k_{3\text{H}}/k_{3\text{D}}$, for the two isotopic species, where $k_{3\text{H}}$ and $k_{3\text{D}}$ are, respectively, rate constants for the third-order term in eq. 1 for N-methylaniline and N-methylaniline-N-*d*. The values of k_3 were obtained from slopes of plots of $k_{2\text{obsd}}$ *vs.* the concentration of N-methylaniline.

Although in the reaction of diethylamine with 3-chloro-1-butene, the amine concentration was not varied as greatly as in the reaction with N-methylaniline, there clearly was no dependence of the observed second-order rate constant on the concentration of diethylamine. Equation 1, therefore, seems peculiar to the reactions of N-methylaniline.

The reaction path corresponding to k_2 may be taken to exemplify the well-known SN2′ reaction.

The third-order reaction may be a reversible ionization of the allylic chloride assisted by one mole of N-methylaniline followed by a relatively slow reaction of the ion pair with a second molecule of N-methylaniline. This explanation is analogous to that proposed for the methanolysis of trityl chloride in which under certain conditions the order with respect to methanol was about two.[20]

$$\begin{tikzcd}
\mathrm{RCl{-}{-}{-}HNR_2'} \arrow[r, shift left, "k_1"] & \mathrm{[R^+Cl^-{-}{-}{-}HNR_2']} \arrow[l, shift left, "k_{-1}"] \arrow[r, "\mathrm{R_2'NH}", "k_s"'] \arrow[d] & \mathrm{RNHR_2'} \\
 & \text{rearrangement} &
\end{tikzcd}$$

Electrophilic catalysis and nucleophilic attack may be synchronous, but this does not allow for formation of N-2-(3-butenyl)-N-methylaniline which may occur *via* attack at the more hindered position of the allylic

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[18] Runs at 60.1° were quite slow, half-lives being of the order of 30 days.

[19] The infrared spectrum of N,N-divinylaniline was made available to us by Dr. C. C. Price and Dr. E. Y. C. Chang of the University of Pennsylvania.

[20] C. G. Swain and E. E. Pegues, *J. Am. Chem. Soc.*, **80**, 812 (1958).

TABLE III

YIELDS OF REACTION PRODUCTS IN *n*-HEPTANE

Concentration of reactants, *M*			Temp., °C.	Products, mole %		
					$C_6H_5N(CH_3)CH_2CH{=}CHCH_3$	
$CH_2{=}CHCH(CH_3)Cl$	$C_6H_5NHCH_3$	Collidine		$CH_2{=}CHCH(CH_3)N(CH_3)C_6H_5$	*trans*	*cis*
1	2	2	60.1	8.8	85.1	6.1
1	4	4	80.2	15.6	73.6	10.8
1	2	4	80.2	12.9	79.5	7.6
1	2	2	80.2	11.5	78.8	9.7
3	1	2	80.2	10.2	81.2	8.6
3	1	1	80.2	7.1	86.7	6.9
1	2	2	102.3	15.7	72.0	12.3

TABLE IV

RATE CONSTANTS FOR THE REACTION OF DEUTERATED AND UNDEUTERATED N-METHYLANILINE WITH 3-CHLORO-1-BUTENE

T, °C.	10^4k_2, M^{-1} hr.$^{-1}$	$10^3k_{3\text{H}}$, M^{-2} hr.$^{-1}$	$10^3k_{3\text{D}}$, M^{-2} hr.$^{-1}$	$(k_{3\text{H}})/k_{3\text{D}})_{\text{obsd}}$	$(k_{3\text{H}})/k_{3\text{D}})^a$
80.2	14.0	8.00	6.67[b]	1.20	1.38
102.3	58.0	24.0	18.8[c]	1.28	1.34

[a] Corrected to the values which would be observed if 100% pure N-methylaniline-N-*d* were used. [b] The amine was deuterated to the extent of 60%. [c] The amine was deuterated to the extent of 86%.

carbonium ion. The kinetics also are consistent with nucleophilic attack by R'_2N^- and electrophilic attack by $R'_2NH_2^+$, although this possibility was considered unlikely by Ross and Finkelstein for reactions of 2,4-dinitrochlorobenzene.[16]

The rate expression for this mechanism, if the intermediate is assumed not to accumulate, is

$$\frac{d[\mathrm{Cl}^-]}{dt} = \frac{k_1k_s\,[\mathrm{RCl}][\mathrm{R'_2NH}]^2}{k_{-1} + k_s\,[\mathrm{R'_2NH}]}$$

The over-all rate is the sum of the rates of the reactions proceeding by both the second-order and third-order mechanisms and if $k_{-1} >> k_s[\mathrm{R'_2NH}]$

$$\frac{d[\mathrm{Cl}^-]}{dt} = k_2[\mathrm{RCl}][\mathrm{R'_2NH}] + (k_1k_s/k_{-1})\,[\mathrm{RCl}][\mathrm{R'_2NH}]^2$$

The isotope effect would arise from the hydrogen bonding of an amine hydrogen to chlorine in the transition state. Hydrogen bonding to acetone involving the protons on nitrogen in aniline has been deduced from n.m.r. studies,[21] and hydrogen bonding to dioxane by aniline has been suggested as the result of studies of molecular polarization.[22] Intramolecular hydrogen bonding in *o*-haloanilines has been postulated on the basis of $-NH_2$ stretching vibrations[23] and basicity constants.[24]

If the origin of the kinetic isotope is as indicated in the above mechanism, then its small magnitude[25] may be caused in part by increased N–H deformation frequencies in the transition state. If the transition state is approximated by a linear system

$$\overset{+\delta}{\mathrm{C}}\text{-----}\overset{-\delta}{\mathrm{Cl}}\text{-----}\overset{+\delta}{\mathrm{H}}\text{-----}\overset{-\delta}{\mathrm{N}}$$

bending motions of the N–H–Cl bond perpendicular to the line joining the centers of the nitrogen and chlorine atoms would tend to increase the electrostatic energy of the system since any vibration which tended to remove the hydrogen atom from between the two partially negative atoms would result in a decrease in attractive energy.

Another possible explanation for the small isotope effect is that the rate decrease caused by net loss of zero point energy in the stretching vibrations is offset by a rate increase caused by an inductive effect of deuterium,[26] although the latter is likely to be small. A rate increase caused by deuterium substitution also might be offset by a rate increase (for $C_6H_5NHCH_3$) caused by proton tunnelling.

Lastly, the small isotope effect may be caused simply by considerable zero point energy in the symmetric vibration in the transition state.[27]

Table III shows that as the temperature is increased the proportion of **2** and the proportion of *cis*-**1** increase.[28] This would be expected if at the higher temperature there was a greater degree of ionization to an ion pair. The ion pair may be attacked at the 3-position as well as at the 1-position to give the products observed.

$$[\mathrm{CH_3\overset{3}{C}H{=}\overset{2}{C}H{=}\overset{1}{C}H_2}]^+\mathrm{Cl}^-$$

As the ratio of amine concentration to halide concentration is increased at a given temperature, a greater proportion of **2** is formed relative to **1**. The greater the ratio of N-methylaniline to 3-chloro-1-butene, the greater is the amount of excess amine available for electrophilic assistance to ionization and, once an ion is formed, **2** may be produced. Some of **2** could arise, of course, by an S_N2 mechanism.

A mechanism in which the second molecule of N-methylaniline functions as a base by removing a proton from the N-methylaniline which is attacking the double bond seems unlikely since the stronger base, 2,4,6-collidine, has no effect on the rate.[29] The third-order term also could arise by reaction of a dimer of the amine with the allylic halide. However, while aliphatic amines appear to be associated, there is no evidence for significant association of aniline derivatives.[30]

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[21] I. Yamaguchi, *Bull. Chem. Soc. Japan*, **34**, 1606 (1961).

[22] A. V. Few and J. W. Smith, *J. Chem. Soc.*, 753, 2663 (1949).

[23] P. J. Krueger, *Can. J. Chem.*, **41**, 363 (1963).

[24] L. Otvos and F. Sirokman, *Acta Univ. Szegediensis, Acta Phys. Chem.*, [N.S.], **2**, 118 (1956); *Chem. Abstr.*, **51**, 16472 (1957).

[25] The isotope effect is calculated to be 5.4 if there is no change in bending frequencies on going from reactants to transition state and 7.8 if the bending frequencies vanish in the transition state (ref. 9a, pp. 20, 21).

[26] The greater rate of reaction of $C_6H_5ND_2$ over that of $C_6H_5NH_2$ with benzoyl chloride has been attributed to an inductive effect [J. J. Elliott and S. F. Mason, *Chem. Ind.* (London), 488 (1959); see also E. A. Halevi, *Tetrahedron*, **1**, 174 (1957)].

[27] F. H. Westheimer, *Chem. Rev.*, **61**, 265 (1961).

[28] Yields of 5–10% of *cis*-alcohol are obtained in the silver ion assisted hydrolysis of 3-chloro-1-butene, a reaction obviously involving an intermediate carbonium ion [W. G. Young, S. H. Sharman, and S. Winstein, *J. Am. Chem. Soc.*, **82**, 1376 (1960)].

[29] The collidine is 550 times stronger as a base in water than N-methylaniline [H. C. Brown, S. Johnson, and H. Podall, *ibid.*, **76**, 5556 (1954); A. Albert and E. P. Serjeant, "Ionization Constants of Acids and Bases," Methuen and Co., London, 1962, p. 144].

[30] J. Feeney and L. H. Sutcliffe, *J. Chem. Soc.*, 1123 (1962); C. Giessner-Prettre, *Compt. rend.*, **252**, 3238 (1961).

Experimental

Reagents.—Reagent-grade benzene was distilled through a 2-ft. column packed with glass helices and dried over sodium. *n*-Heptane (Phillips Pure grade) also was distilled through the same column and dried over sodium. Diethylamine (reagent grade) was distilled from sodium hydroxide followed by distillation from calcium hydride through a 2-ft. column packed with glass helices. It was stored over calcium hydride.

N-Methylaniline (Eastman White Label) was distilled over calcium hydride and zinc dust through the 2-ft. column. The colorless amine was stored in a nitrogen atmosphere in a refrigerator over calcium hydride. 2,4,6-Collidine (Eastman White Label or Matheson Coleman and Bell reagent grade) was distilled and was found to be pure by gas chromatography. One sample of commercial material was found to be highly contaminated with other pyridine derivatives and was partially purified by treatment with boron trifluoride etherate.[29] 3-Chloro-1-butene (Columbia Organic Chemical Co.) was distilled in the presence of 2 ml. of 2,4,6-collidine through a Podbielniak Minical semiautomatic high temperature distillation apparatus equipped with a 1 ft. × 13 mm. Heli-grid column with Hastelloy B packing. The column was preflooded for 30 min. at a pot temperature of 66° and then the allylic chloride was distilled at atmospheric pressure at a reflux ratio of 25:1. The second fraction was collected, b.p. 63.2–63.8° (761 mm.), n^{27}D 1.4118 (lit.[7] b.p. 63.5–64.2°, n^{25}D 1.4120). Analysis by gas chromatography showed only a single peak.

N,N-Diethylamine-N-*d*.—Lithium diethylamide was prepared by adding diethylamine (21.6 g., 0.295 mole) dropwise to an ethereal solution of phenyllithium (0.295 mole) in 445 ml. of ether in apparatus protected from moisture. Volatile substances were removed on a rotary evaporator and the lithium diethylamide was subjected to a pressure of 7 mm. (vacuum pump) for several hours. The salt was treated with 20 ml. (1 mole) of deuterium oxide (purity in excess of 99.9%) which was added dropwise. An excess of calcium oxide was added and the N,N-diethylamine-N-*d* was distilled, b.p. 56°. The yield was quantitative. The purity varied from 87–100%.

N-Methylaniline-N-*d*.—N-Methylaniline (35.4 g., 0.331 mole) was treated with phenyllithium (0.331 mole in 850 ml. of ether) as above. The lithium N-methylanilide was refluxed 24 hr. with 20 ml. (1 mole) of deuterium oxide (purity in excess of 99.9%). The N-methylaniline-N-*d* was distilled over calcium oxide under nitrogen to yield 32.3 g. (90%), b.p. 69–73° (6–7 mm.). The purity of both N,N-diethylamine-N-*d* and N-methylaniline-N-*d* was determined by an infrared method which has been described elsewhere.[1] The purity of N-methylaniline-N-*d* varied from 60–92%.

Reaction Products from 3-Chloro-1-butene and N,N-Diethylamine.—The reactions were allowed to go to completion and the mixtures were analyzed by gas chromatography. Every reaction was repeated several times. Every component of the reaction mixture was purified or synthesized independently and these standard compounds were used in the identification of the reaction components by gas chromatography. Every constituent of the reaction mixture was isolated on passage through the chromatographic column, and its infrared spectrum obtained. Derivatives were prepared and identified. Retention times were obtained for the various components of the reaction mixture when they were subjected to gas chromatography under these conditions: detector (Burrell Corp. Model SS, No. 340-148) temperature, 100 ± 0.1°; detector current, 135 ma.; flow rate (He), 64 ml./min.; bath temperature, 100 ± 1°, glass U-column, 3.64 m. × 7 mm.; alkaline Polar Carbowax 20 M (25% by weight) on Chromosorb (30/60 mesh). The following retention times in minutes were obtained: diethylamine, 3.6; 3-chloro-1-butene, 5.6; N,N-diethyl-α-methylallylamine,[31] 9.0; 1-chloro-2-butene, 10.0; benzene, 10.3; *trans*-N,N-diethyl-γ-methylallylamine, 13.6; toluene, 17.0. Toluene was used as solvent instead of benzene because the latter interfered with the identification of 1-chloro-2-butene.

No N,N-diethyl-α-methylallylamine was isolated from any reaction, and the amine was stable under the reaction conditions. Both *cis*- and *trans*-N,N-diethyl-γ-methylallylamines were isolated from the reaction mixture. They were separated and identified by their infrared spectra which were identical except for the *trans*-C–H out-of-plane deformation at 965 cm.$^{-1}$, which was completely absent in the *cis* isomer. Picrates were prepared: *trans*, m.p. 83.5–84.0°; *cis*, m.p. 73.0–74.0°. *trans*-Product was obtained in amounts from 85 to 100 mole %, any difference being accounted for by the *cis* product.

Isomerization of 3-chloro-1-butene to 1-chloro-2-butene occurs under the reaction conditions only after all the diethylamine is consumed, and thus, as had been found previously,[5a] isomerization is not an important factor in the kinetic runs.

The amine hydrochloride precipitate which formed in the reaction mixture was shown to be diethylamine hydrochloride by its infrared spectrum and by conversion to diethylamine.

Reaction Products from 3-Chloro-1-butene and N-Methylaniline.—Gas chromatographic analyses of products were done as described above except that for determination of the less volatile material the detector temperature was 200 ± 0.1°, the detector current 95 ma., and the bath temperature 215 ± 2°. Retention times in minutes at 200° were *n*-heptane, 1.4; 3-chloro-1-butene, 2.0; 1-chloro-2-butene, 2.6; 2,4,6-collidine, 7.0; N-methylaniline, 19.6; N-2-(3-butenyl)-N-methylaniline, 21.6; *trans*-N-1-(2-butenyl)-N-methylaniline, 28.6; *cis*-N-1-(2-butenyl)-N-methylaniline, 30.6.

In a preparative run, 3-chloro-1-butene was treated with N-methylaniline in the absence of solvent. The reaction mixture was treated with dilute sodium hydroxide and extracted with ether. The ether extract was treated with benzenesulfonyl chloride followed by extraction with 5% sodium hydroxide and dilute hydrochloric acid. The aqueous acid extract of tertiary amines was made basic with sodium carbonate and extracted with ether; the ether was removed under vacuum and the oil remaining was distilled at 2 mm. through a 30-mm. Vigreux column. The third fraction, b.p. 85–94°, n^{25}D 1.5489, was converted into a picrate, m.p. 132–133°, which analyzed for the picrate of N-2-(3-butenyl)-N-methylaniline.

Anal. Calcd. for $C_{17}H_{18}N_4O_7$: C, 52.31; H, 4.65; N, 14.35. Found: C, 52.29; H, 4.62; N, 14.35.

The picrate was decomposed by treatment with 0.1 *N* sodium hydroxide and the infrared spectrum of the free amine was taken.

The residue from the above distillation was fractionated through a Podbielniak distillation column with Heli-grid packing of Hastelloy B. The first fraction, b.p. 97–105° (13.5 mm.), gave a picrate whose analysis is given above. A second fraction, b.p. 117–118° (13.5 mm.), n^{25}D 1.5501, was identified as N-1-(2-butenyl)-N-methylaniline [lit.[32] b.p. 118–120° (14 mm.), 119° (14 mm.), n^{25}D 1.5503] by means of a mixture melting point of its picrate, m.p. 79–81° (lit.[32] m.p. 80–82°) with the picrate derivative of the major product of the reaction of N-methylaniline with 1-chloro-2-butene.

The same two products in addition to collidine hydrochloride were obtained when the reaction was done in heptane in the presence of 2,4,6-collidine.

Gas chromatographic analysis partially separated *cis*- and *trans*-N-1-(2-butenyl)-N-methylaniline. By analogy with the reaction of 3-chloro-1-butene with diethylamine the major product was assumed to be the *trans* isomer. The melting point of the mixed picrates was 81–82°.

The reaction products were stable under the reaction conditions and did not isomerize. Only after all the N-methylaniline was consumed did 3-chloro-1-butene isomerize to 1-chloro-2-butene.

Kinetic Procedure.—Stock stolutions of reactants were prepared in the appropriate solvent. The reactants were mixed and 5-ml. aliquots were pipetted into Pyrex glass test tubes which had been drawn out to give a neck for easy sealing. Every tube was stoppered immediately with a calcium chloride tube, immersed in a Dry Ice–acetone bath, and sealed. In the runs with N-methylaniline, the tubes were flushed with dry nitrogen. The sealed tubes were placed in a constant-temperature bath, several tubes being opened at once and analyzed to give a zero time point. Three tubes were prepared containing 5 ml. of the reaction mixture, 5 ml. of water, and excess amine and these were used as a check on the initial concentration of 3-chloro-1-butene since they were allowed to go to completion of the reaction. The chloride ions produced in these runs were determined by the Volhard method.

At various time intervals, a sealed tube was withdrawn from the bath, immersed in a Dry Ice–acetone bath, and opened. In the runs with diethylamine, the reaction mixture was washed out

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(31) Prepared as described in ref. 5a.

(32) R. F. Kleinschmidt and A. C. Cope, *J. Am. Chem. Soc.*, **66**, 1929 (1944); J. Braun and W. Schirmacher, *Ber.*, **56**, 538 (1923).

with distilled water into a 50-ml. separatory funnel containing petroleum ether. The petroleum ether layer was extracted with cold, dilute nitric acid, and the chloride content of the aqueous solution was determined by the Volhard method. The initial concentration of diethylamine was determined by titration of a 5-ml. aliquot of the benzene solution with standard hydrochloric acid with methyl red as indicator. In the runs with N-methylaniline the reaction mixture was washed out with acetic acid, and the amine concentration determined by titration with a standard solution of perchloric acid in acetic acid with methyl violet as indicator.[33] Some runs were followed by potentiometric titration of the weak organic bases in glacial acetic acid with standard perchloric acid. The results obtained by this method agreed well with those obtained by potentiometric titration of chloride ion with standard silver nitrate.

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[33] J. S. Fritz and G. S. Hammond, "Quantitative Organic Analysis," John Wiley and Sons, Inc., New York, N. Y., 1957, pp. 28-43, 265.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, CAMBRIDGE 39, MASS.]

Molecular Asymmetry of Olefins. II. The Absolute Configuration of *trans*-Cyclooctene[1,2]

BY ARTHUR C. COPE AND ANIL S. MEHTA[3]

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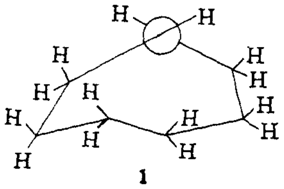
The absolute configuration of *trans*-cyclooctene has been determined and the levorotatory enantiomer is assigned the (*R*)-configuration. (1*S*:2*S*)-(+)-1,2-Dimethoxycyclooctane was synthesized from (2*R*:3*R*)-(+)-tartaric acid and its rotation was shown to be identical with that of the same diether obtained from (−)-*trans*-cyclooctene.

Although it has long been recognized that *trans* cyclic olefins of medium ring size should exhibit molecular asymmetry[4] the first resolution of such an olefin was reported only recently.[5] *trans*-Cyclooctene was resolved as the *trans*-dichloro(*trans*-cyclooctene)-(α-methylbenzylamine)platinum(II) complex containing optically active α-methylbenzylamine. The object of the present work was to assign absolute configurations to the enantiomeric *trans*-cyclooctenes.

(−)-*trans*-Cyclooctene was treated with osmium tetroxide and the resulting osmate ester was decomposed with sodium sulfite to give (+)-*trans*-1,2-cyclooctanediol-(**10**).[6] Methylation of the glycol **10** with diazomethane in the presence of fluoroboric acid[7] afforded *trans*-1,2-dimethoxycyclooctane (**9**) having $[\alpha]^{31}\mathrm{D}$ + 49.5° (*c* 4.337, chloroform).

The same compound of known absolute configuration (1*S*:2*S*)-(+)-1,2-dimethoxycyclooctane (**9**) [$[\alpha]^{31.8}\mathrm{D}$ +50.3° (*c* 4.63, chloroform)] was synthesized from (2*R*:3*R*)-(+)-tartaric acid (**2**) by the sequence of reactions summarized in Fig. 1.[8] Since the signs of rotation of the relay compounds **9** were the same, it followed that (−)-*trans*-cyclooctene was related to (2*R*:3*R*)-(+)-tartaric acid and has the (*R*)-configuration as indicated in the Newman projection formula **1**.



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The synthesis of (1*S*:2*S*)-(+)-1,2-dimethoxycyclooctane (**9**) involved use of the C$_2$- and C$_3$-hydroxyl groups of (2*R*:3*R*)-(+)-tartaric acid (**2**) as the source of the adjacent *trans*-methoxyl groups in **9**.

(2*R*:3*R*)-(+)-Tartaric acid was esterified[9] by methanolic hydrogen chloride and the resulting dimethyl (2*R*:3*R*)-(+)-tartrate was methylated[10] with methyl iodide and silver oxide. Lithium aluminum hydride reduction of dimethyl (2*R*:3*R*)-(+)-2,3-dimethoxysuccinate (**3**) using the minimum amount of aqueous base for decomposition of the aluminate salt[11] gave (2*S*:3*S*)-(+)-2,3-dimethoxy-1,4-butanediol[12] (**4a**) in 62% yield. The crystalline ditosylate **4b**[12] was prepared (94% yield) and converted to the diiodide (2*R*:3*R*)-(−)-2,3-dimethoxy-1,4-diiodobutane[12] (**4e**) by treatment with sodium iodide in anhydrous acetone (94% yield).

Alkylation of acetonitrile with either the ditosylate **4b** or the diiodide **4e** gave a poor yield of the dinitrile **5c**; the major product appeared to be *trans*-3,4-dimethoxycyclopentyl cyanide. Attempts to alkylate **4b** or **4e** with lithium ethoxyacetylene to give a diyne that on hydrolysis would give the dicarboxylic ester **5e** also were unsuccessful.

Posternak and Susz[12] on attempting the conversion of the diiodide **4e** to the dinitrile **4c** with sodium cyanide were able to obtain only a difficultly separable mixture consisting essentially of an iodonitrile (from the iodine and nitrogen content) and a small amount of the desired dinitrile which was not analyzed. No experimental details were given. In this work the dinitrile **4c** was obtained by the reaction of the ditosylate **4b** with sodium cyanide under carefully controlled conditions. Optimum yields (65–78%) were obtained with purified dimethyl sulfoxide as solvent and a reaction time of 6 days at 20 ± 3°. Higher temperatures gave markedly lower yields and made purification more difficult. Other solvents (acetone, methanol, or dimethylformamide) gave either a good recovery of the starting material or a poor yield of the product.

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[1] For a preliminary communication on this work see A. C. Cope and A. S. Mehta, *J. Am. Chem. Soc.*, **86**, 1268 (1964).

[2] Supported in part by the Army Research Office (Durham) under Grant No. DA-ARO(D)31-124-G404.

[3] Postdoctoral Fellow, 1963–1964.

[4] A. T. Blomquist, L. H. Liu, and J. C. Bohrer, *J. Am. Chem. Soc.*, **74**, 3643 (1952); V. Prelog in A. Todd, Ed., "Perspectives in Organic Chemistry," Interscience Publishers, Inc., New York, N. Y., 1956, p. 129.

[5] A. C. Cope, C. R. Ganellin, H. W. Johnson, Jr., T. V. Van Auken, and H. J. S. Winkler, *J. Am. Chem. Soc.*, **85**, 3276 (1963).

[6] A. C. Cope, R. A. Pike, and C. F. Spencer, *ibid.*, **75**, 3212 (1953).

[7] M. Neeman, M. C. Caserio, J. D. Roberts, and W. S. Johnson, *Tetrahedron*, **6**, 36 (1959).

[8] The nomenclature for absolute configuration used throughout is that of R. S. Cahn, C. K. Ingold, and V. Prelog, *Experientia*, **12**, 81 (1956).

[9] A. Skrabal and L. Hermann, *Monatsh.*, **43**, 633 (1922).

[10] T. Purdie and J. C. Irvine, *J. Chem. Soc.*, **79**, 957 (1901).

[11] V. M. Mićović and M. Lj. Mihailović, *J. Org. Chem.*, **18**, 1190 (1953).

[12] Th. Posternak and J. Ph. Susz, *Helv. Chim. Acta*, **39**, 2032 (1956).