[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE SPRAGUE ELECTRIC CO.]

Rates, Products and Salt Effects in the Reactions of 2,4-Dinitrochlorobenzene with Amines in Chloroform and in Ethanol

BY SIDNEY D. ROSS AND MANUEL FINKELSTEIN

RECEIVED AUGUST 13, 1957

The rates of reaction of 2,4-dinitrochlorobenzene with *n*-butylamine, 2-phenylethylamine and di-*n*-butylamine in chloroform and with *n*-butylamine, piperidine, di-*n*-butylamine and pyridine in ethanol have been measured. The effects of added salts in the reactions with *n*-butylamine and pyridine have been investigated. For the primary and secondary amines it is shown that the correct rate expression is d product/dt = k_1(chloride)(amine) + k_6(chloride)(amine).^{2}

Aromatic, nucleophilic substitution reactions involving 2,4-dinitrochlorobenzene and aliphatic amines are generally considered to be straightforward, second-order reactions, except in cases where there is an accompanying attack on the halide by either the solvent or the conjugate base of the solvent.[1] The results of exploratory measurements with 2,4-dinitrochlorobenzene and *n*-butylamine in both chloroform and ethanol proved to be strongly at variance with this expectation. For a fixed, initial chloride concentration, an increase in the amine concentration always resulted in an appreciable increase in the measured bimolecular rate constant. This led to the more detailed study of the reaction of 2,4-dinitrochlorobenzene with amines which is described herein.

Experimental

Materials.—Absolute ethanol, obtained from the U. S. Industrial Chemicals Co., was distilled from calcium hydride before use. Baker and Adamson reagent grade chloroform, lot no. L340, was used without purification. This solvent contains 0.75% ethanol as a stabilizer.

Eastman Kodak Co. white label amines were used, unless otherwise indicated. *n*-Butylamine and di-*n*-butylamine were distilled from calcium hydride, and middle fractions of b.p. 77° and 159°, respectively, were used. Pyridine was distilled first from calcium hydride and then from sodium hydroxide. A middle fraction, b.p. 115°, was taken from both distillations. 2-Phenylethylamine was twice distilled from calcium hydride, b.p. 87° at 13 mm. This amine was used directly after distillation, since it takes up carbon dioxide rapidly. Piperidine, Eastman Kodak Co. practical grade, was refluxed over calcium hydride and then distilled from calcium hydride. A middle cut from this distillation was again refluxed over and distilled from calcium hydride. A middle cut, b.p. 106°, was used.

2,4-Dinitrochlorobenzene, Eastman Kodak Co. white label, was crystallized two times from absolute ethanol; m.p. 51°.

Analytical reagent grade lithium nitrate, lithium chloride and ammonium nitrate were dried *in vacuo* before use.

Benzyltriethylammonium chloride was prepared by refluxing benzyl chloride and triethylamine in acetone for 20 hours. The crude product was filtered, washed with acetone and crystallized from benzene–ethanol; yield 75%, m.p., 188° dec.

Anal. Calcd. for $C_{13}H_{22}NCl$: Cl, 15.57. Found: Cl, 15.63.

Benzyltriethylammonium nitrate was obtained by adding equivalent silver nitrate, as a saturated aqueous solution, to benzyltriethylammonium chloride dissolved in a minimum amount of water. The precipitated silver chloride was filtered, and the water was removed *in vacuo*. The crude product was twice crystallized from benzene containing just sufficient isopropyl alcohol to permit solution while hot; m.p. 108–110°.

Anal. Calcd. for $C_{13}H_{22}N_2O_3$: N, 11.02. Found: N, 10.95.

n-Butylammonium chloride was obtained by adding dry hydrogen chloride to a hexane solution of the amine; m.p. 198° dec.

n-Butylammonium nitrate was prepared by neutralizing an aqueous solution of *n*-butylamine with dilute nitric acid. The water was removed *in vacuo*, and the crude product was crystallized first from isopropyl alcohol and then from benzene–ethanol; m.p. 44–46°.

Anal. Calcd. for $C_4H_{12}N_2O_3$: N, 20.58. Found: N, 20.61.

Tetraethylammonium nitrate was prepared by the method described previously.[2]

Pyridinium nitrate was prepared by adding equivalent dilute nitric acid to an aqueous solution of pyridine. Water was removed *in vacuo*, and the crude salt was crystallized from isopropyl alcohol and dried over phosphorus pentoxide; m.p. 115–118° in a sealed tube.

Anal. Calcd. for $C_5H_6N_2O_3$: neut. equiv., 142. Found: neut. equiv., 141.

Rate Measurements.—Separate, determinate solutions of 2,4-dinitrochlorobenzene and the amines in ethanol, chloroform or solutions of the appropriate salts in these solutions were made up at the temperature of the measurements. The solutions were mixed at zero time, and aliquots were withdrawn at appropriate time intervals and analyzed for chloride ion by the Volhard method. For runs in ethanol, the aliquots were quenched by adding them to 25 ml. of 4 *N* nitric acid. For runs in chloroform, aliquots were quenched by partitioning them between benzene (50 ml.) and 4 *N* nitric acid (25 ml.) and extracting the benzene solution two additional times with water.

In the measurements involving pyridine, determinate solutions of the chloride and amine in ethanol or an ethanolic solution of the appropriate salt were made up and mixed at room temperature. The reaction mixture was then apportioned amongst tubes, which were sealed and placed in a thermostat at 69.4 ± 0.1°. At appropriate time intervals, tubes were withdrawn and cooled quickly to room temperature. An aliquot was taken and analyzed for chloride ion by the Volhard procedure. The concentrations at 69.4°, which are used throughout in this paper, were calculated from the concentrations at room temperature and the known change in volume of ethanol with temperature.

Product Isolation Experiments. N-*n*-Butyl-2,4-dinitroaniline.—A solution of 2,4-dinitrochlorobenzene (2 g.) and *n*-butylamine (5 ml.) in absolute ethanol (100 ml.) was left standing at room temperature for 20 hours. The alcohol was largely removed *in vacuo*, water was added, and the mixture was extracted three times with ether. The ether extracts were washed with water and dried over magnesium sulfate. Removal of the ether gave 1.14 g. (96.4%) of the known N-*n*-butyl-2,4-dinitroaniline,[3] m.p. 86–90°. One crystallization from ethanol raised the m.p. to 89–90°.

The above preparation was repeated using chloroform (100 ml.) as solvent. After standing at room temperature the solution was washed two times with water and dried over magnesium sulfate. Removal of the chloroform gave 1.1 g. (93%) of N-*n*-butyl-2,4-dinitroaniline, m.p. 87–90°. Crystallization from methanol yielded 0.9 g. (80%) of product, m.p. 89–90°.

N-2-Phenylethyl-2,4-dinitroaniline.—A solution of 2,4-dinitrochlorobenzene (2 g.) and 2-phenylethylamine (10

---

[1] (a) J. F. Bunnett and R. E. Zahler, *Chem. Revs.*, **49**, 344 (1951); (b) A. F. Holleman, W. J. deMooy and J. terWeel, *Rec. trav. chim.*, **35**, 1 (1915); (c) J. J. Blanksma and H. H. Schreinemachers, *ibid.*, **52**, 428 (1933); (d) O. L. Brady and F. R. Cropper, *J. Chem. Soc.*, 507 (1950).

[2] S. D. Ross and M. M. Labes, THIS JOURNAL, **79**, 4155 (1957).

[3] E. J. van der Kam, *Rec. trav. chim.*, **45**, 722 (1926).

ml.) in chloroform (200 ml.) was left standing 24 hours at room temperature. The solution was washed two times with water and dried over magnesium sulfate. Removal of the solvent gave 2.3 g. (81%) of the known N-2-phenylethyl-2,4-dinitroaniline,[4] m.p. 155°.

N-2,4-Dinitrophenylpiperidine.—A solution of 2,4-dinitrochlorobenzene (2 g.) and piperidine (8.6 g.) in ethanol (100 ml.) was left standing at room temperature for 2 hr. Benzene (300 ml.) was added, and the solution was washed two times with water and dried over magnesium sulfate. Removal of the solvent gave the crude product, which was crystallized from ethanol yielding 2.38 g. (96.4%) of the known N-2,4-dinitrophenylpiperidine,[5] m.p. 92–93°.

N,N-Di-*n*-butyl-2,4-dinitroaniline.—A solution of 2,4-dinitrochlorobenzene (0.522 g.) and di-*n*-butylamine (5.61 g.) in ethanol (50 ml.) was left standing at room temperature for 25 hr. The solution was poured into a large excess of water and extracted three times with 100-ml. portions of ether. The ether extracts were washed with water and dried over magnesium sulfate. The ether and excess di-*n*-butylamine were removed *in vacuo* leaving the product as a viscous, orange oil, yield 0.68 g. (90%). This oil could not be induced to crystallize and decomposed when distilled in a conventional apparatus. A sample for analysis was distilled in a short-path still built on the cold finger principle, with a central take-off so placed as to allow the condensate drops to fall directly into the receiver. The distillation was carried out at 0.05 mm. with the heating bath at 120°.

Anal. Calcd. for $C_{14}H_{21}N_3O_4$: C, 56.93; H, 7.17; N, 14.23. Found: C, 57.10; H, 7.03; N, 14.62.

2,4-Dinitrophenetole.—A solution of 2,4-dinitrochlorobenzene (2 g.) and pyridine (14 g.) in absolute ethanol (200 ml.) was kept in a thermostat at 69.4 ± 0.1° for 47 hr. It was then poured into water (500 ml.) and extracted with three 150-ml. portions of ether. The ether extracts were washed once with water and dried over magnesium sulfate. Removal of the solvent gave 0.256 g. (12.1%) of crude 2,4-dinitrophenetole. Crystallization from ethanol resulted in 0.133 g. of the product, m.p. 80–81°. Recrystallization gave 0.095 g., m.p. 83–84°, no depression on mix-melting with an authentic sample of 2,4-dinitrophenetole.

In a second experiment a solution of 2,4-dinitrochlorobenzene (2 g.), pyridine (14 g.) and pyridinium nitrate (6 g.) in ethanol (200 ml.) was kept in a thermostat for 88 hr. When worked up, as above, the crude product weighed 0.136 g. Crystallization from ethanol gave 0.030 g. of 2,4-dinitrophenetole, m.p. 81–82°.

Similarly, a solution of 2,4-dinitrophenylpyridinium chloride (2.8 g.) and pyridine (14 ml.) in ethanol (200 ml.) was kept at 69.4° for 48 hr. Isolation as above resulted in 0.283 g. of crude 2,4-dinitrophenetole and 0.158 g. of recrystallized product. Repetition of this experiment with the addition of pyridinium nitrate (6.1 g.) gave 0.080 g. of crude 2,4-dinitrophenetole and 0.012 g. of recrystallized product.

Results

The results of measurements of the rate of reaction of 2,4-dinitrochlorobenzene and *n*-butylamine in chloroform, containing 0.75% ethanol as stabilizer, at 24.8 ± 0.1° are compiled in Table I. To point up the problem with respect to the reaction order, we have tabulated the second-order, the five-halves-order and the third-order rate constants. These constants were calculated from the appropriate rate equations 1, 2 and 3 below, where x is the chloride ion concentration, a is the initial 2,4-dinitrochlorobenzene concentration and b is the initial n-butylamine concentration.

TABLE I

RATES OF REACTION OF 2,4-DINITROCHLOROBENZENE AND *n*-BUTYLAMINE IN CHLOROFORM AT 24.8 ± 0.1°

2,4-Dinitrochlorobenzene, mole/l.	*n*-Butylamine, moles/l.	$k_2 \times 10^4$, l. mole^{-1} sec.$^{-1}$	$k_{5/2} \times 10^4$, l.$^{3/2}$ mole$^{-3/2}$ sec.$^{-1}$	$k_3 \times 10^3$, l.^{2} mole^{-2} sec.$^{-1}$
0.05165	0.1038	2.47	8.10	4.42
.05141	.1866	3.25	8.50	2.33
.05111	.1985	3.07	7.63	1.90
.05061	.4961	4.37	6.47	0.99
.05168	.8018	6.22	7.10	.78
.05108	.9997	7.45	7.07	.82
.05196	1.009	7.20	7.43	.76
.02449	0.9945	7.63	7.33	.79

$$k_2t = \frac{2.303}{b - 2a}\log\frac{a}{b}\frac{(b - 2x)}{(a - x)} \tag{1}$$

$$\frac{2.303}{(b - 2a)^{3/2}}\log\frac{\sqrt{b - 2x} + \sqrt{b - 2a}}{\sqrt{b - 2x} - \sqrt{b - 2a}} - \frac{2}{(b - 2a)\sqrt{b - 2x}} = k_{5/2}t + \frac{2.303}{(b - 2a)^{3/2}}\log\frac{\sqrt{b} + \sqrt{b - 2a}}{\sqrt{b} - \sqrt{b - 2a}} - \frac{2}{(b - 2a)\sqrt{b}} \tag{2}$$

$$\frac{1}{(2a - b)}\left[\frac{1}{(b - 2x)} + \frac{2.303}{(2a - b)}\log\frac{(b - 2x)}{(a - x)}\right] = k_3t + \frac{1}{(2a - b)}\left[\frac{1}{b} + \frac{2.303}{(2a - b)}\log\frac{b}{a}\right] \tag{3}$$

All of the runs in Table I were followed to beyond 60% reaction, and some were followed to beyond 80% reaction. Good linear plots, with very nearly every point falling on a straight line, were obtained for all three reaction orders, and the rate constants were calculated from the slopes of the best straight lines through the experimental points. None of these reaction orders represents a satisfactory fit to the data. The closest fit is obtained with the five-halves-order rate constants, but even in this case, the highest measured rate constant differs from the lowest measured rate constant by almost 24%, and if we take an average value, the maximum deviation from this average value is 14%.

In Table II the second-order rate constants for the reaction of 2,4-dinitrochlorobenzene and *n*-butylamine with added tetraethylammonium nitrate, benzyltriethylammonium nitrate and benzyltriethylammonium chloride, all in chloroform at 24.8 ± 0.1°, are recorded. In this table and in all the following tables only the second-order rate constants will be tabulated, since only these constants will be used in the subsequent discussion.

From a comparison of Tables I and II it is clear that, in chloroform, this reaction is subject to a positive neutral-salt effect.

The effects on the rate resulting from the addition of *n*-butylammonium chloride and *n*-butylammonium nitrate are shown in Table III. These salts are of particular interest since their addition might be expected to result in two effects, a neutral salt effect and a specific effect due to the butylammonium ion, which is a product of reaction. A comparison of Tables I and II indicates that the addition of these salts has almost no effect on the rates. There is, of course, the possibility that this results from the two effects operating in opposite directions, but this question will be reserved for later discussion.

Tables IV and V present the results of rate measurements with two other amines, 2-phenylethylamine and di-*n*-butylamine. The results with the

---

(4) M. P. J. M. Jansen, *Rec. trav. chim.*, **50**, 617 (1931).

(5) R. J. W. LeFevre, S. L. M. Saunders and E. E. Turner, *J. Chem. Soc.*, 1168 (1927).

TABLE II

SALT EFFECTS IN THE REACTION OF 2,4-DINITROCHLOROBENZENE AND *n*-BUTYLAMINE IN CHLOROFORM AT 24.8 ± 0.1°

2,4-Dinitrochlorobenzene, mole/l.	*n*-Butylamine, mole/l.	Added salt, mole/l.	$k_2 \times 10^3$, l. mole^{-1} sec.$^{-1}$
0.05097	0.1981	0.0201 $Et_4N^+NO_3^-$	0.443
.04986	.1991	.0502 $Et_4N^+NO_3^-$	0.690
.05090	.1989	.0983 $Et_4N^+NO_3^-$	1.05
.05047	.3974	.0964 $Et_4N^+NO_3^-$	1.22
.05087	.5003	.0953 $Et_4N^+NO_3^-$	1.32
.05000	.2009	.0495 $PhCH_2NEt_3^+NO_3^-$	0.685
.05030	.2003	.0969 $PhCH_2NEt_3^+NO_3^-$	1.06
.05163	.2002	.1402 $PhCH_2NEt_3^+Cl^-$	1.26
.05038	.3963	.1374 $PhCH_2NEt_3^+Cl^-$	1.50
.05090	.5998	.1345 $PhCH_2NEt_3^+Cl^-$	1.74
.05064	.6014	.1345 $PhCH_2NEt_3^+Cl^-$	1.70

TABLE III

EFFECT OF ADDED *n*-BUTYLAMMONIUM ION ON THE REACTION OF 2,4-DINITROCHLOROBENZENE AND *n*-BUTYLAMINE IN CHLOROFORM AT 24.8 ± 0.1°

2,4-Dinitrochlorobenzene, mole/l.	*n*-Butylamine, mole/l.	Added salt, mole/l.	$k_2 \times 10^4$, l. mole^{-1} sec.$^{-1}$
0.04963	0.1989	0.0383 *n*-$BuNH_3^+Cl^-$	2.98
.05043	.1988	.1504 *n*-$BuNH_3^+Cl^-$	2.90
.05067	.2980	.1471 *n*-$BuNH_3^+Cl^-$	3.68
.04960	.4964	.1457 *n*-$BuNH_3^+Cl^-$	4.97
.04951	.5950	.1471 *n*-$BuNH_3^+Cl^-$	5.55
.05069	.7986	.1471 *n*-$BuNH_3^+Cl^-$	6.70
.05056	.2003	.142 *n*-$BuNH_3^+NO_3^-$	3.27
.05127	.4978	.138 *n*-$BuNH_3^+NO_3^-$	5.35
.05055	.7976	.134 *n*-$BuNH_3^+NO_3^-$	7.57

former amine are very similar to those obtained with *n*-butylamine. With di-*n*-butylamine the closest to a satisfactory fit is obtained with the second-order rate constants, but, in this case, too, the rate constants increase as the amine concentrations increase.

TABLE IV

RATES OF REACTION OF 2,4-DINITROCHLOROBENZENE AND 2-PHENYLETHYLAMINE IN CHLOROFORM AT 24.8 ± 0.1°

2,4-Dinitrochlorobenzene, mole/l.	2-Phenylethylamine, mole/l.	$k_2 \times 10^4$, l. mole^{-1} sec.$^{-1}$
0.02559	0.2352	1.24
.02523	.3908	1.49
.02670	.7835	2.33
.05231	.3922	1.48

TABLE V

RATES OF REACTION OF 2,4-DINITROCHLOROBENZENE AND DI-*n*-BUTYLAMINE IN CHLOROFORM AT 24.8 ± 0.1°

2,4-Dinitrochlorobenzene, mole/l.	Di-*n*-butylamine, mole/l.	$k_2 \times 10^4$, l. mole^{-1} sec.$^{-1}$
0.05147	0.1739	8.70
.05068	.1741	8.90
.05025	.5827	9.43
.05080	.5830	9.40
.05144	.8718	10.3
.05120	.8738	9.70

Turning now to the reactions in ethanol, the results on the reaction of 2,4-dinitrochlorobenzene and *n*-butylamine at 24.8 ± 0.1° are given in Table VI. Once again, for a given chloride concentration, there is a decided increase in the second-order rate coefficient as the amine concentration is increased. In general, for all of the rate measurements in ethanol, the second-order rate constants are more nearly constant than are either the five-halves or the third-order rate constants. In this particular case the bimolecular rate expression, 1, is clearly unsatisfactory, since a fivefold increase in the amine concentration results in an almost 50% increase in the rate constant.

TABLE VI

RATES OF REACTION OF 2,4-DINITROCHLOROBENZENE AND *n*-BUTYLAMINE IN ETHANOL AT 24.8 ± 0.1°

2,4-Dinitrochlorobenzene, mole/l.	*n*-Butylamine, mole/l.	$k_2 \times 10^3$, l. mole^{-1} sec.$^{-1}$
0.05005	0.1724	1.04
.05070	.1779	1.03
.05040	.3326	1.10
.05160	.4942	1.22
.04950	.6607	1.35
.04960	.8838	1.51

Table VII contains all of the data on the effects of added neutral salts on this reaction. In all, four salts, lithium chloride, lithium nitrate, benzyltriethylammonium chloride and benzyltriethylammonium nitrate, were used. With the two lithium salts the salt effects are small and positive. With the two quaternary ammonium salts appreciably larger positive salt effects were observed.

TABLE VII

SALT EFFECTS IN THE REACTION OF 2,4-DINITROCHLOROBENZENE AND *n*-BUTYLAMINE IN ETHANOL AT 24.8 ± 0.1°

2,4-Dinitrochlorobenzene, mole/l.	*n*-Butylamine, mole/l.	Added salt, mole/l.	$k_2 \times 10^3$, l. mole^{-1} sec.$^{-1}$
0.05004	0.1755	0.04832 LiCl	0.98
.05011	.1747	.09792 LiCl	1.08
.04992	.1755	.1003 LiCl	1.01
.05011	.1747	.1452 LiCl	1.09
.04997	.5051	.04672 LiCl	1.24
.04992	.4998	.09487 LiCl	1.40
.04996	.4979	.1405 LiCl	1.41
.04990	.4963	.1406 LiCl	1.40
.04996	.6582	.03255 LiCl	1.47
.04999	.6673	.04931 LiCl	1.45
.05011	.6699	.09431 LiCl	1.43
.04995	.6644	.1381 LiCl	1.49
.04993	.6645	.1425 LiCl	1.43
.04962	.1740	.0262 $LiNO_3$	1.02
.05105	.1736	.1064 $LiNO_3$	1.09
.04990	.1764	.1605 $LiNO_3$	1.14
.05008	.6597	.0468 $LiNO_3$	1.41
.05010	.6598	.1520 $LiNO_3$	1.45
.05010	.6614	.04654 $PhCH_2NEt_3^+Cl^-$	1.51
.04990	.6745	.09303 $PhCH_2NEt_3^+Cl^-$	1.65
.05001	.6748	.1393 $PhCH_2NEt_3^+Cl^-$	1.79
.04994	.1777	.0491 $PhCH_2NEt_3^+NO_3^-$	1.20
.04995	.1775	.0983 $PhCH_2NEt_3^+NO_3^-$	1.31
.05028	.1753	.1474 $PhCH_2NEt_3^+NO_3^-$	1.45
.04981	.6688	.0467 $PhCH_2NEt_3^+NO_2^-$	1.54
.04993	.6677	.0934 $PhCH_2NEt_3^+NO_3^-$	1.66
.04993	.6637	.1402 $PhCH_2NEt_3^+NO_3^-$	1.86

Table VIII presents the results of rate measurements with added *n*-butylammonium chloride and with added *n*-butylammonium nitrate. The results with these two salts are almost identical with those obtained with added lithium nitrate and lithium chloride.

TABLE VIII

EFFECT OF ADDED *n*-BUTYLAMMONIUM ION ON THE REACTION OF 2,4-DINITROCHLOROBENZENE AND *n*-BUTYLAMINE IN ETHANOL AT 24.8 ± 0.1°

2,4-Dinitrochlorobenzene, mole/l.	*n*-Butylamine, mole/l.	Added salt, mole/l.	$k_2 \times 10^3$, l. mole^{-1} sec.$^{-1}$
0.05068	0.1768	0.0974 *n*-$BuNH_3^+Cl^-$	1.04
.04990	.1754	.1472 *n*-$BuNH_3^+Cl^-$	1.05
.04995	.1762	.1959 *n*-$BuNH_3^+Cl^-$	1.13
.04986	.6630	.0323 *n*-$BuNH_3^+Cl^-$	1.30
.05027	.6716	.0487 *n*-$BuNH_3^+Cl^-$	1.28
.04997	.6674	.0928 *n*-$BuNH_3^+Cl^-$	1.38
.04990	.6670	.1381 *n*-$BuNH_3^+Cl^-$	1.46
.05009	.1755	.0494 *n*-$BuNH_3^+NO_3^-$	1.07
.04996	.1735	.0960 *n*-$BuNH_3^+NO_3^-$	1.12
.04993	.1766	.1432 *n*-$BuNH_3^+NO_3^-$	1.15
.04994	.6677	.0469 *n*-$BuNH_3^+NO_3^-$	1.39
.05008	.6647	.0995 *n*-$BuNH_3^+NO_3^-$	1.42
.04999	.6695	.1422 *n*-$BuNH_3^+NO_3^-$	1.46

Tables IX and X present the results of some exploratory measurements with piperidine and with di-*n*-butylamine. The former was studied at 0° and the latter at 24.8 ± 0.1°. Although our data are not extensive, they are, nevertheless, sufficient to indicate that, with these amines too, the second-order rate constants increase with increasing amine concentration. Table X corrects a previous report from this Laboratory[6] to the effect that the bimolecular rate constant for this reaction is independent of the di-*n*-butylamine concentration. The experiment at the lower amine concentration in the earlier work was obviously in error.

TABLE IX

RATES OF REACTION OF 2,4-DINITROCHLOROBENZENE AND PIPERIDINE IN ETHANOL AT 0°

2,4-Dinitrochlorobenzene, mole/l.	Piperidine, mole/l.	$k_2 \times 10^3$, l. mole^{-1} sec.$^{-1}$
0.02441	0.07901	3.23
.02488	.2006	3.58
.02461	.4094	4.70

TABLE X

RATES OF REACTION OF 2,4-DINITROCHLOROBENZENE AND DI-*n*-BUTYLAMINE IN ETHANOL AT 24.8 ± 0.1°

2,4-Dinitrochlorobenzene, mole/l.	Di-*n*-butylamine, mole/l.	$k_2 \times 10^4$, l. mole^{-1} sec.$^{-1}$
0.05011	0.1785	1.88
.05085	.2741	2.02
.05007	.4958	2.08
.05001	.8691	2.47

In order to include a tertiary amine in the present study the rate of reaction of pyridine and 2,4-dinitrochlorobenzene in ethanol at 69.4 ± 0.1° was measured. These results are given in Table XI, and effects resulting from added salts are presented in Table XII.

Discussion

Consider first the results with *n*-butylamine. It is apparent from Tables I and VI that the simple, bimolecular rate equation does not adequately describe this reaction. There are no previously reported measurements in chloroform, but the reaction rate in ethanol has been reported by Blanksma and Schreinemachers[1c] and by Brady and Cropper.[1d] In neither of the above studies were the *n*-butylamine concentrations varied sufficiently to point up the deviations from the second-order treatment.

TABLE XI

RATES OF REACTION OF 2,4-DINITROCHLOROBENZENE AND PYRIDINE IN ETHANOL AT 69.4 ± 0.1°

2,4-Dinitrochlorobenzene, mole/l.	Pyridine, mole/l.	$k_2 \times 10^5$, l. mole^{-1} sec.$^{-1}$
0.04753	0.1889	3.10
.04756	.2855	3.22
.04840	.3837	3.25
.04776	.5242	3.26
.04781	.6796	3.36
.04766	.8488	3.41

TABLE XII

SALT EFFECTS IN THE REACTION OF 2,4-DINITROCHLOROBENZENE AND PYRIDINE IN ETHANOL AT 69.4 ± 0.1°

2,4-Dinitrochlorobenzene, mole/l.	Pyridine, mole/l.	Added salt, mole/l.	$k_2 \times 10^5$, l. mole^{-1} sec.$^{-1}$
0.04769	0.5206	0.048 $LiNO_3$	3.62
.04771	.5265	.096 $LiNO_3$	3.63
.04766	.5247	.144 $LiNO_3$	3.76
.04758	.5302	.183 $LiNO_3$	4.04
.05079	.5229	.076 LiCl	3.68
.04841	.5250	.182 LiCl	3.93
.04949	.8213	.178 NH_4NO_3	4.18
.04941	.8235	.178 $Et_4N^+NO_3^-$	5.12
.04903	.8302	.191 $Et_4N^+NO_3^-$	5.00
.04929	.8330	.188 $Py^+NO_3^-$	5.00

In both solvents the reaction product is entirely or almost entirely N-*n*-butyl-2,4-dinitroaniline, which could be isolated in better than 90% yield. The reaction is a clean one, and no alcoholysis product or other side reaction product could be isolated.

Since the five-halves-order and the third-order rate equations are also inadequate representations for the rate of this reaction, it becomes necessary to explore the possibility that there is more than one reaction path leading to the final product and that these paths differ in that they involve either different numbers of amine molecules or different species derived from the amine. In the ammonolysis of methyl phenylacetate, Hammett and Betts[7] have demonstrated that amide results from reaction of the ester with either ammonia or amide ion. Similarly, in the aminolysis of ethyl formate with *n*-butylamine, the product results from reaction of the ester with either molecular amine or with *n*-butylamide ion.[8] Also, Glasoe, Kleinberg and Audrieth[9] have presented evidence indicating that the aminolysis of ethyl phenylacetate in *n*-butylamine is catalyzed by *n*-butylammonium ion, and Hawkins and Piscalnikow[10] have found evidence for acid catalysis in the aminolysis of α-naphthyl acetate.

---

[6] S. D. Ross and I. Kuntz, THIS JOURNAL, **76**, 3000 (1954).

[7] L. P. Hammett and R. L. Betts, *ibid.*, **59**, 1568 (1937).

[8] W. H. Watanabe and L. R. DeFonso, *ibid.*, **78**, 4542 (1956).

[9] P. K. Glasoe, J. Kleinberg and L. F. Audrieth, *ibid.*, **61**, 2387 (1939).

[10] P. J. Hawkins and I. Piscalnikow, *ibid.*, **77**, 2771 (1955).

For the case at hand, there are, in all, five possible kinetic terms to be considered:

1 $k_1(\mathrm{RCl})(\mathrm{RNH_2})$

2 $k_3(\mathrm{RCl})(\mathrm{RNH^-}) = k_3K_\mathrm{B}(\mathrm{RCl})(\mathrm{RNH_2})^2/(\mathrm{RNH_3^+})$

3 $k_4(\mathrm{RCl})(\mathrm{RNH_2})(\mathrm{RNH_3^+})$

4 $k_5(\mathrm{RCl})(\mathrm{RNH^-})(\mathrm{RNH_3^+}) = k_5K_\mathrm{B}(\mathrm{RCl})(\mathrm{RNH_2})^2$

5 $k_6(\mathrm{RCl})(\mathrm{RNH_2})(\mathrm{RNH_2})$

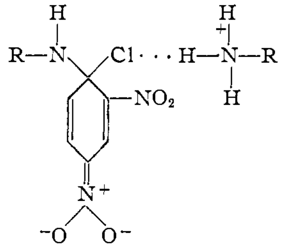
The second and fourth terms have also been written in alternate forms which incorporate the autoprotolysis of the amine

$$2\mathrm{RNH_2} \rightleftarrows \mathrm{RNH_3^+} + \mathrm{RNH^-} \qquad (4)$$

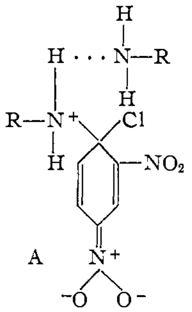
for which the equilibrium constant is

$$K_\mathrm{B} = \frac{(\mathrm{RNH^-})(\mathrm{RNH_3^+})}{(\mathrm{RNH_2})^2} \qquad (5)$$

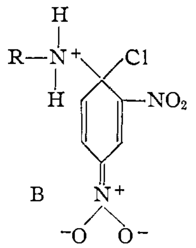
Because of this equilibrium the fourth and fifth terms are kinetically indistinguishable. Nevertheless, these could represent distinctly different reaction paths to the final product. For the fourth term, displacement is by n-butylamide ion, and the breaking of the carbon–chlorine bond may be facilitated by hydrogen bonding of the n-butylammonium ion to the chlorine atom. The transition state for this process might be pictured as



For the fifth term, displacement is by the molecular amine, and the second amine molecule assists the process by participating in breaking a nitrogen–hydrogen bond. This transition state could be pictured as (A).



A



B

For both of the above, it is, of course, to be recognized that a termolecular reaction is not necessarily involved. In the first case the actual mechanism might involve an equilibrium between the chloride and n-butylammonium ion and subsequent reaction of the complex formed with n-butylamide ion. Similarly, for the second case, amine and chloride might form the intermediate (B), which then reacts with a second amine molecule.

If all of the possible terms were involved, the total rate, V, would be given by

$$V = k_1(\mathrm{RCl})(\mathrm{RNH_2}) + k_3K_\mathrm{B}(\mathrm{RCl})(\mathrm{RNH_2})^2/(\mathrm{RNH_3^+}) + k_4(\mathrm{RCl})(\mathrm{RNH_2})(\mathrm{RNH_3^+}) + k_7(\mathrm{RCl})(\mathrm{RNH_2})^2 \qquad (6)$$

where $k_7 = K_5K_\mathrm{B}$, k_6 or the sum of these two constants. The specific rate, k_2, is given by

$$k_2 = k_1 + k_3K_\mathrm{B}(\mathrm{RNH_2})/(\mathrm{RNH_3^+}) + k_4(\mathrm{RNH_3^+}) + k_7(\mathrm{RNH_2}) \qquad (7)$$

where the k_2's are the second-order rate constants which we have tabulated in the previous section. For a fixed n-butylammonium ion concentration, a plot of the k_2's against the initial amine concentrations should be linear with the slope equal to $k_3K_\mathrm{B}/(\mathrm{RNH_3^+}) + k_7$ and the intercept equal to $k_1 + k_4 \cdot (\mathrm{RNH_3^+})$.

In this reaction the n-butylammonium ion is a product, and its concentration increases with time. However, for runs without added salts, the initial n-butylammonium ion concentration is determined by the autoprotolysis equilibrium (5). For all of the runs of Tables I and VI the second-order rate constants are essentially constant throughout the course of the run; *i.e.*, the tabulated rate constants can be taken as initial rate constants.

This constancy of the instantaneous rate constants during the course of each individual run suggests that the k_3K_B and k_4 terms are of minor importance. In Fig. 1 the second-order rate constants are plotted against the initial amine concentrations. The lower line is for the runs in chloroform, and the upper line is for the runs in ethanol. Excellent linear plots are obtained in both solvents. This is in spite of the fact that as we increase the initial amine concentration, we also increase the initial n-butylammonium ion concentration and suggests again that the k_3K_B and k_4 terms do not contribute appreciably.

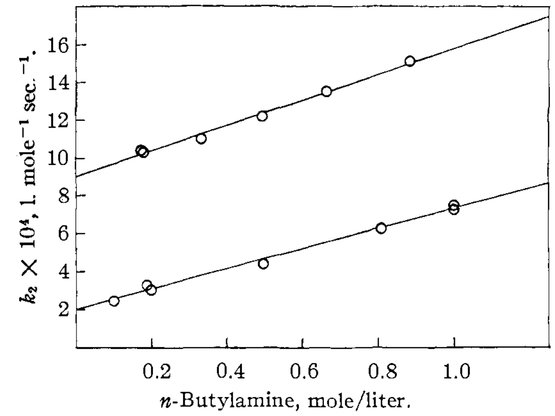


Fig. 1.—Second-order rate constants *vs.* initial amine concentrations for the reaction of n-butylamine and 2,4-dinitrochlorobenzene. The upper line is for the reaction in ethanol, and the lower line is for the reaction in chloroform.

There still remains the possibility that both the k_3K_B and k_4 terms are present, that their magnitudes are comparable and that as the n-butylammonium ion concentration is increased, the decrease in the k_3K_B term is compensated for by an increase in the k_4 term. A decision as to the importance of these terms requires, therefore, a knowledge of the specific effects due to added n-butylammonium ion, and since any n-butylammonium salt can also function as a neutral salt, it is first necessary to determine neutral salt effects in these reactions.

Table II compiles the data on neutral salt effects in chloroform, and Table III shows the effects of added *n*-butylammonium ion in the same solvent. The sparing solubility of salts in chloroform made it necessary to restrict our neutral salt studies to quaternary ammonium salts. In all of the experiments in Table II there is an appreciable acceleration of the rate. If we restrict our attention to the three measurements in which the added tetraethylammonium nitrate was kept roughly constant (0.095–0.098 *M*) and the amine was varied from 0.2–0.8 *M* and plot k_2 *vs.* the initial amine concentration, we again obtain a straight line, with the intercept at 8.9×10^{-4} l. mole^{-1} sec.$^{-1}$ and the slope equal to 8.6×10^{-4} l.^{2} mole^{-2} sec.$^{-1}$. These values are to be compared with the values of 2.0×10^{-4} l. mole^{-1} sec.$^{-1}$ for the intercept and 5.3×10^{-4} l.^{2} mole^{-2} sec.$^{-1}$ for the slope (Fig. 1) in the absence of added salt. On the other hand, if we take the four points in Table III, in which the added *n*-butylammonium ion is nearly constant (0.146–0.147 *M*) and the initial amine concentrations are varied from 0.2–0.8 *M* and plot k_2 *vs.* the initial amine concentration, we obtain a straight line, with the intercept 2.0×10^{-4} l. mole^{-1} sec.$^{-1}$, and the slope 5.7×10^{-4} l.^{2} mole^{-2} sec.$^{-1}$, almost identical with the values obtained in the absence of any added salt.

In this case it is not possible to argue that there is an accelerating salt effect being almost exactly counterbalanced by a decelerating specific *n*-butylammonium ion effect, for, in accordance with equation 7, the intercept $k_1 + k_4(\mathrm{RNH_3^+})$ would be expected to increase both because of a neutral salt effect and the specific *n*-butylammonium ion effect, which, in this case, is a catalysis of the displacement by *n*-butylammonium ion.

An explanation for the complete absence of an effect due to added *n*-butylammonium ion must be sought elsewhere. Experiments with added salts in solvents of low dielectric constant are difficult to interpret quantitatively because the ions involved are so extensively paired and associated into higher aggregates.[11] Unfortunately, quantitative data on the dissociation in chloroform of the salts of interest are not available. However, it is possible to make some roughly qualitative estimates with data in the literature.[11] In general, quaternary ammonium salts are much more highly dissociated than are amine salts. For example, in benzene, which has a dielectric constant of 2.3, the equilibrium constant for ion-pair dissociation for tetraamylammonium picrate is 21.8×10^{-18} mole l.$^{-1}$. In 1,2-dichloroethane, which has a dielectric constant of 10.23, the same salt has a dissociation constant of 2.38×10^{-4} mole l.$^{-1}$. In chloroform, which has a dielectric constant of 4.8, we would estimate an equilibrium constant of 10^{-10} mole l.$^{-1}$ or less. For triamylammonium picrate the dissociation constant in benzene is 4×10^{-21} mole l.$^{-1}$, a value which is 1/5000 as large as that obtained with the quaternary ammonium salt. With the salt of a primary amine the dissociation constant would be smaller still. In view of the foregoing it is not surprising that added *n*-butylammonium salts fail to show even a neutral salt effect in chloroform. In this solvent these salts are probably so highly associated into ion-pairs that only negligible concentrations of the free ions are present.

The difficulties resulting from ion-pairing are very much moderated in ethanol, which has a dielectric constant of 24.3. In this medium neutral salt effects are small and positive (Table VII), yet the quaternary ammonium salts are appreciably more dissociated than are the lithium salts and result in significantly larger salt effects at equivalent molar concentrations.

The effects due to added *n*-butylammonium salts (Table VIII) are indistinguishable, within experimental error, from the effects due to added lithium salts. In Fig. 2 the second-order rate constants at two constant initial amine concentrations (0.67 and 0.17 *M*) have been plotted against the added salt concentrations for the two lithium salts and both *n*-butylammonium salts. The straight lines were drawn visually and made to intersect the Y-axis at the known rate constants (Table VI) in the absence of added salts. The scatter in Fig. 2 is more apparent than real, since the maximum deviation of any point from the appropriate line is less than 8%. Moreover, it seems to us reasonable that the lithium salts and *n*-butylammonium salts should be associated to a comparable extent and should give similar salt effects, since both cations are relatively small, with the charge not highly shielded by alkyl groups.

We conclude, therefore, that there is no specific effect due to the *n*-butylammonium cation in ethanol. Equation 7 may be simplified by eliminating the two terms involving $(\mathrm{RNH_3^+})$ as

$$k_2 = k_1 + k_7(\mathrm{RNH_2}) \qquad (8)$$

where k_1 and k_7 are the slope and intercept, respectively, of the appropriate line in Fig. 1.

Equation 8 is adequate for the runs in chloroform as well. The autoprotolysis constant, K_B, for *n*-butylamine would be considerably lower in chloroform than in ethanol, and any ions formed would be highly paired. The probability of a reaction involving the *n*-butylamide ion is, therefore, almost negligible. For the same reasons a transition state involving the *n*-butylamide ion and the *n*-butylammonium ion is equally improbable, and we conclude that the k_7 term in equation 8 refers to the reaction of 2,4-dinitrochlorobenzene with two molecular amine molecules; *i.e.*, $k_7 = k_6$.

In ethanol this last conclusion is somewhat less certain but still highly probable. Our results definitely eliminate the k_3 term; *i.e.*, there is no reaction of 2,4-dinitrochlorobenzene with *n*-butylamide ion alone to give the final product. If this reaction is unimportant it seems to us improbable that the same reaction catalyzed by *n*-butylammonium ion would be important, particularly since any increase in the *n*-butylammonium ion concentration is accompanied by a decrease in the *n*-butylamide ion concentration and the observed effects due to added *n*-butylammonium ion are small.

The essentials of this mechanism were first suggested by Brady and Cropper.[1d] They found that triethylamine catalyzes the reaction of methylamine with 2,4-dinitrochlorobenzene although it itself does not react with the chloride to an appreciable

---

[11] C. A. Kraus, *J. Phys. Chem.*, **60**, 129 (1956).

extent under the conditions of the experiments. This is additional evidence that the term in $(RNH_2)^2$ involves two amine molecules rather than amide ion and an ammonium ion.

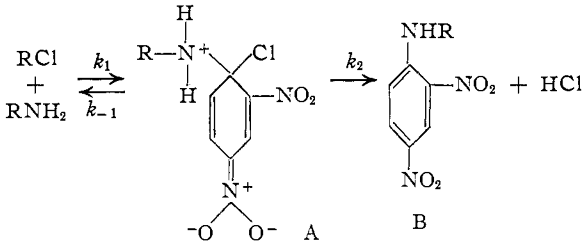
n-Butylamine is in no sense unique. We have studied the reaction of 2,4-dinitrochlorobenzene with 2-phenylethylamine and di-*n*-butylamine in chloroform and with piperidine and di-*n*-butylamine in ethanol. Measurements with both di-*n*-butylamine and piperidine have been reported previously.[1c,d] In all four of these cases the results are very similar to those obtained with *n*-butylamine. At a constant 2,4-dinitrochlorobenzene concentration the second-order rate constants increase with increasing amine concentration and plots of the k_2's *vs.* the initial amine concentrations are linear in every case. Equation 8 is adequate to encompass all of these results, and in Table XIII we have summarized all the results in terms of this equation.[12]

TABLE XIII

RATES OF REACTION OF AMINES WITH DINITROCHLOROBENZENE IN CHLOROFORM AND IN ETHANOL

Amine	Solvent	T, °C.	k_1, l. mole^{-1} sec.^{-1}	k_7, l.^2 mole^{-2} sec.^{-1}
n-$BuNH_2$	$CHCl_3$	24.8 ± 0.1	2.0×10^{-4}	5.3×10^{-4}
n-$BuNH_2$	EtOH	24.8 ± .1	9.0×10^{-4}	6.7×10^{-4}
Di-*n*-BuNH	$CHCl_3$	24.8 ± .1	8.4×10^{-4}	1.8×10^{-4}
Di-*n*-BuNH	EtOH	24.8 ± .1	1.7×10^{-4}	9.0×10^{-5}
$C_6H_5CH_2CH_2NH_2$	$CHCl_3$	24.8 ± .1	7.5×10^{-5}	2.0×10^{-4}
Piperidine	EtOH	0	2.8×10^{-3}	4.4×10^{-3}

These results are in accord with the view[1a,12] that a quinoid type of intermediate is involved in these reactions. Representing the reactions as



$$A + RNH_2 \xrightarrow{k_3} B + RNH_3^+, Cl^-$$

and applying the steady state assumption to A, we obtain

$$A = \frac{k_1(RCl)(RNH_2)}{k_{-1} + k_2 + k_3(RNH_2)} \qquad (9)$$

If $k_{-1} >> k_2 + k_3(RNH_2)$

$$A \cong \frac{k_1}{k_{-1}}(RCl)(RNH_2) \cong K(RCl)(RNH_2) \qquad (10)$$

where K is the equilibrium constant for formation of the intermediate, A. The over-all rate is given by

$$\frac{dB}{dt} = k_2K(RCl)(RNH_2) + k_3K(RCl)(RNH_2)^2 \qquad (11)$$

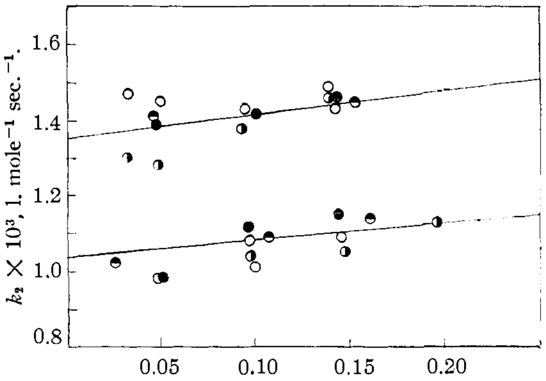


Fig. 2.—Second-order rate constants *vs.* added salt concentrations for the reaction of 2,4-dinitrochlorobenzene with *n*-butylamine in ethanol. For all of the data the initial 2,4-dinitrochlorobenzene concentration is ~0.05 *M*. The initial amine concentrations are ~0.67 *M* for the upper line and ~0.17 *M* for the lower line: ○, lithium chloride; ◒, lithium nitrate; ◑, *n*-butylammonium chloride; ●, *n*-butylammonium nitrate.

and k_1 and k_7 in Table XIII are equal to k_2K and k_3K, respectively.

Studies with a tertiary amine are of particular interest, since, with a tertiary amine, the product is a quaternary ammonium salt, and there is no hydrogen to be removed in going from reactants to products. As a consequence, there is no possibility for the sort of third-order term which we have observed with primary and secondary amines, and the reaction should be bimolecular.

In alcohol both triethylamine and N-methylpiperidine reacted with 2,4-dinitrochlorobenzene at too slow a rate for convenient measurement. We turned, finally, to pyridine, which was studied previously by Cavell and Chapman[13] and measured the reaction rate at 69.4 ± 0.1°. In chloroform, at this temperature, the reaction with pyridine did not proceed at a measurable rate. The results in ethanol are given in Table XI. The average value for the rate constant is 3.27×10^{-5} l. mole^{-1} sec.^{-1}. The maximum deviation from this average value is 5.2%, and the average deviation is 2.4%.

In accordance with expectations, the second-order rate coefficients are constant within experimental error. Nevertheless, there is a disturbing trend in the results, with the rate constants increasing very slightly as the pyridine concentrations increase. We have, therefore, considered the possibility of a slight amount of competing alcoholysis[1,14] as an explanation for this trend.

Cavell and Chapman[13] have presented a convincing, quantitative argument, based on the rates of reaction of 2,4-dinitrochlorobenzene with pyridine and with ethoxide ion and the equilibrium constant for the reaction of pyridine with ethanol to form ethoxide ion and pyridinium ion, to the effect that alcoholysis is negligible. However, as described in the Experimental section, it is possible to isolate

---

[12] Since amines, particularly piperidine, have been widely used in previous studies of the mechanism of aromatic nucleophilic substitution reactions (J. F. Bunnett and G. T. Davis, THIS JOURNAL, **76**, 3011 (1954); J. F. Bunnett and R. J. Morath, *ibid.*, **77**, 5051 (1955); J. F. Bunnett, E. W. Garbisch, Jr., and K. M. Pruitt, *ibid.*, **79**, 385 (1957); E. Berliner and L. C. Monack, *ibid.*, **74**, 1574 (1952); M. F. Hawthorne, *ibid.*, **76**, 6358 (1954)) and since the reactions were generally treated as bimolecular reactions it should be emphasized that the third-order term in equation 7 decreases in importance as the initial amine concentration decreases. Therefore, any conclusions reached from measurements at low initial amine concentrations (below 0.05 *M*) would not be substantially altered because of the present results.

[13] E. A. S. Cavell and N. B. Chapman, *J. Chem. Soc.*, 3392 (1953).

[14] C. A. Lobry deBruyn, *Rec. trav. chim.*, **13**, 101 (1894); J. D. Loudon and T. D. Robson, *J. Chem. Soc.*, 242 (1937); H. S. Forrest and J. Walker, *ibid.*, 1939 (1948).

significant amounts of the alcoholysis product, 2,4-dinitrophenetole, from this reaction. Unfortunately, this isolation experiment does not permit an unambiguous conclusion since, under the conditions of the experiment, 2,4-dinitrophenylpyridinium chloride undergoes alcoholysis to give 2,4-dinitrophenetole. With added pyridinium ion the alcoholysis of both the chloride and the quaternary ammonium salt is in part suppressed. In the absence of quantitative rate studies it is, therefore, not possible to assert that any of the 2,4-dinitrophenetole results from alcoholysis of the chloride rather than the quaternary ammonium salt.

Analysis of our rate data leads to an equally ambiguous result. The instantaneous rates are constant throughout the course of each run. The values in Table XI are, therefore, indistinguishable from the rates at zero time. At zero time, without added pyridinium ion, it can be assumed that the concentrations of ethoxide and pyridinium ion are equal, and it may be shown that

$$k_2(\text{pyridine})^{1/2} = k_1(\text{pyridine})^{1/2} + k_3K^{1/2} \quad (12)$$

where k_2 is the experimental second-order rate constant, k_1 is the rate with pyridine, k_3 the rate with ethoxide ion and K, the equilibrium constant for the reaction of pyridine with ethanol.

In accord with this equation a plot of $k_2(\text{pyridine})^{1/2}$ *vs.* $(\text{pyridine})^{1/2}$ is linear, and every point falls on the line. The intercept, however, is slightly negative, but if we were to draw a line with a slightly positive intercept, giving a reasonable value for $k_3K^{1/2}$, all of the points would still be on this alternate line within experimental error. The effect is thus too small and our results are insufficiently precise to permit a clear decision.

Finally, our results with added salts (Table XII) show that the reaction is subject to a positive salt effect but indicate no effect other than a neutral salt effect due to added pyridinium ion. Both this and the constancy of the instantaneous rate constants during the course of each run support an absence of any appreciable alcoholysis affecting the rate. Within the precision of our results, the best conclusion that can be drawn is that the reaction is truly bimolecular.

NORTH ADAMS, MASSACHUSETTS

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF NORTHWESTERN UNIVERSITY]

The Stereochemistry of Ketonization. IV[1]

BY HOWARD E. ZIMMERMAN

RECEIVED JULY 10, 1957

Irreversible ketonization of the enol of 1-acetyl-2-phenylcyclohexane has been found to yield predominantly the *cis*-ketone. The degree of selectivity compared to closely related examples is rationalized with a concept of specific and non-specific steric hindrance. Acid-catalyzed bromination of *cis*-1-acetyl-2-phenylcyclohexane yields the expected 1-acetyl-1-bromo-2-phenylcyclohexane while *trans*-1-acetyl-2-phenylcyclohexane affords 1-bromoacetyl-2-phenylcyclohexane.

For a thorough understanding of the stereochemistry of the ketonization reaction of enols, previously shown to yield frequently the less stable of two stereoisomers,[2-4] a complete elucidation of the relation between molecular structure and both the direction and degree of stereoselectivity seems necessary. In particular, knowledge of the effect of small structural changes would be extremely useful.[5] The present paper relates details of a study of the 1-acetyl-2-phenylcyclohexane enol, this being one of a number of closely related systems studied in our laboratory with this objective in mind.

Of the two stereoisomeric 1-acetyl-2-phenylcyclohexanes requisite for this study, only one, m.p. 81°, had been reported. This seemed almost certainly to be the *trans* isomer, since it had been synthesized[6] from the 2-phenylcyclohexanecarboxylic acid shown more recently[7] to be *trans*. A synthesis by Kipping and Perkin[8] of the 81° ketone by treatment of ethyl 1-acetyl-2-phenylcyclohexanecarboxylate with alcoholic potassium hydroxide was not incompatible with this view, the drastic conditions sufficing for equilibration.[9]

However, two syntheses, which on mechanistic bases would be expected to lead to the *cis* stereoisomer, had been reported to result in formation of the same 81° 1-acetyl-2-phenylcyclohexane. The first involved hydrogenation of the Diels–Alder product from 1-phenylbutadiene and methyl vinyl ketone.[10-12] In the second[13] the 81° ketone was obtained from the conjugate addition of phenylmagnesium bromide to 1-acetylcyclohexene along with considerable 1,2-addition product. Since the product configuration in such a reaction is determined during enol ketonization,[2] by analogy with the stereochemistry of ketonization in similar systems[2-4] the *cis*-ketone would be predicted unless

---

(1) Part of this material was presented at the Sixth Reaction Mechanism Conference, held at Swarthmore College, September, 1956.

(2) H. E. Zimmerman, *J. Org. Chem.*, **20**, 559 (1955).

(3) H. E. Zimmerman, THIS JOURNAL, **78**, 1168 (1956).

(4) H. E. Zimmerman and H. J. Giallombardo, *ibid.*, **78**, 6259 (1956).

(5) *Cf.* the comparable use of substituent effects in studying resonance and polar factors.

(6) C. D. Gutsche and W. S. Johnson, THIS JOURNAL, **68**, 2239 (1946). This synthesis utilized the reaction of the acid chloride with the conjugate base of diethyl malonate followed by hydrolysis and decarboxylation. Isomerization to the *cis* series is unlikely.

(7) C. D. Gutsche, *ibid.*, **70**, 4150 (1948).

(8) F. S. Kipping and W. H. Perkin, *J. Chem. Soc.*, 304 (1890).

(9) The decarboxylation, which must proceed by way of the enol, would be anticipated to yield largely the *cis* product were it not for the isomerizing conditions.

(10) G. A. Ropp and E. C. Coyner, THIS JOURNAL, **71**, 1832 (1949).

(11) L. Reich and E. I. Becker, *ibid.*, **71**, 1834 (1949).

(12) (a) Some evidence for a second Diels–Alder stereoisomer, in the form of a second semicarbazone, was reported in ref. 11; however, only the 81° hydrogenation product was isolated. (b) The *cis*-ketone is predicted by the Alder rule of maximum accumulation of unsaturation to result from *trans*-1-phenylbutadiene. *cis*-1-Phenylbutadiene has been reported to be unreactive in the diene synthesis by O. Grummitt and F. Cristoph, THIS JOURNAL, **73**, 3479 (1951).

(13) D. Nightingale, E. Milberger and A. Tomisek, *J. Org. Chem.*, **13**, 357 (1948).