Di-*n*-butylcadmium was prepared by the rapid addition of 50.4 g. (0.275 mole) of cadmium chloride to the cooled solution of *n*-butylmagnesium bromide formed from 12.15 g. (0.5 mole) of magnesium and 75.4 g. (0.55 mole) *n*-butyl bromide in 550 ml. of diethyl ether. Following the addition, the mixture was stirred in an ice-bath for two hours. The di-*n*-butylcadmium reaction mixture, including the precipitate, was then added to a stirred solution of 85.9 g. (0.625 mole) of phosphorus trichloride in 100 ml. of ether over a period of twenty-five minutes. The phosphorus trichloride reaction mixture was maintained at −20° by means of a Dry Ice and acetone bath. After the addition, 100 ml. of ether was flushed through the cadmium reaction vessel into the main reaction mixture from which the delivery tube was then withdrawn. The cooling bath was removed and the stirred reaction mixture allowed to warm to room temperature (0.5 hour) subsequent to refluxing for 2.5 hours.

The reaction was worked up by allowing the mixture to stand overnight at room temperature followed by decantation of the main portion of the ethereal solution. The residual precipitate was diluted with 100 ml. of ether, filtered by gravity and washed with ether. (Care must be taken in the disposal of this precipitate, since hydrolysis of traces of residual dichlorophosphine in the precipitate yields some alkylphosphine. Careful addition to a large volume of water in an efficient fume hood is necessary.) Ether was removed from the combined decantate, filtrate, and washings by distillation at atmospheric pressure, and the residue was distilled under reduced pressure to yield the crude dichlorophosphine. Fractionation of the crude through an 18-inch glass-helices packed column gave 37.4 g. (47% based on magnesium) of *n*-butyldichlorophosphine, b. p. 58–60° at 22 mm.

Properties of Alkyldichlorophosphines.—The alkyldichlorophosphines are water-white liquids with obnoxious odors. On standing, particularly in contact with atmospheric moisture, they deposit a yellow amorphous solid which was not identified. Both the odor and the tendency to deposit a solid decrease as the length of the carbon chain increases. A sample of *n*-amyldichlorophosphine in a sealed bottle was kept at room temperature for seven months without appreciable change in purity. *n*-Amyldichlorophosphine and its lower homologs can be distilled at atmospheric pressure without decomposition of the still-pot residue.

Physical Measurements.—Boiling points at various pressures were determined by distilling a fractionated sample of constant boiling range through an 18-inch glass helices-packed column and observing the vapor temperature in the still head; a high reflux ratio was maintained at all times. A closed-tube mercury manometer was used for pressure observations. Boiling points at atmospheric pressure were made by sand-bath distillation of a constant-boiling sample in a Claisen flask with all-glass joints. These data are shown on the Cox Chart (Fig. 1) and indicate that the vapor pressure curve of log *p* *vs.* $1/T$ is not quite a straight line function. Refractive indices were measured on an Abbe-type refractometer, and densities were determined in a Weld pycnometer of approximately 10 ml. capacity.

Summary

The synthesis of a series of alkyldichlorophosphines by reaction of dialkylcadmium compounds with phosphorus trichloride has been developed.

WASHINGTON, D. C. RECEIVED MARCH 6, 1950

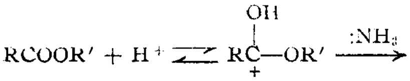
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE POLYTECHNIC INSTITUTE OF BROOKLYN]

The Aminolysis of Esters. A Preliminary Study

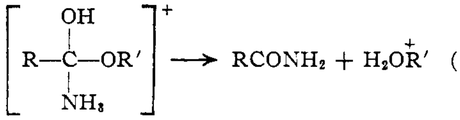
BY RICHARD BALTZLY, IRVING M. BERGER[1] AND ARNOLD A. ROTHSTEIN[1]

Although the ammonolysis of esters has received considerable attention, relatively little has been published on the kinetics of the kindred reaction of aminolysis. Glasoe, Kleinberg and Audrieth[2] examined the reaction of ethyl phenylacetate in *n*-butylamine (serving as solvent and reactant). Grunfeld[3] determined reaction rates of some long-chain aliphatic amines with esters in ethanol and petroleum ether as solvents.

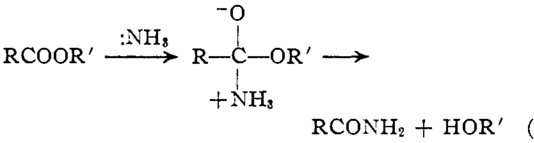
While an additional variable, the structure of the amine, is involved in the reaction with amines, there is no reason to suppose that the mechanism differs essentially from ammonolysis. *A priori* the reaction might be uncatalyzed or subject to acid or basic catalysis according to Equations 1–3



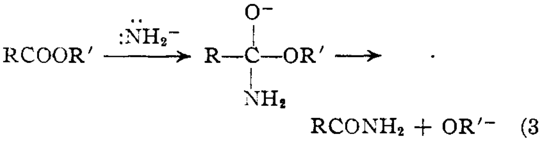
$$\mathrm{RCOOR' + H^+ \rightleftharpoons R\overset{OH}{\underset{+}{C}}{-}OR' \xrightarrow{:NH_3}}$$



$$\left[\mathrm{R{-}\overset{OH}{\underset{NH_3}{C}}{-}OR'}\right]^+ \longrightarrow \mathrm{RCONH_2 + H_2\overset{+}{O}R'} \quad (1)$$



$$\mathrm{RCOOR' \xrightarrow{:NH_3} R{-}\overset{^-O}{\underset{+NH_3}{C}}{-}OR' \longrightarrow RCONH_2 + HOR'} \quad (2)$$



$$\mathrm{RCOOR' \xrightarrow{:\ddot{N}H_2^-} R{-}\overset{O^-}{\underset{NH_2}{C}}{-}OR' \longrightarrow RCONH_2 + OR'^-} \quad (3)^4$$

Simultaneous operation of the mechanisms of Equations 1 and 3 would not be expected but either mechanism could be concurrent with that

---

[1] From theses presented by I. M. Berger and A. A. Rothstein to the School of Graduate Study of the Polytechnic Institute of Brooklyn in partial fulfillment of the requirements for the degree of Master of Science, May, 1948, and May, 1949.

[2] Glasoe, Kleinberg and Audrieth, THIS JOURNAL, **61**, 2387 (1939).

[3] Grunfeld, *Ann. chim. phys.*, [10], **20**, 351 (1933).

[4] A variant of this mechanism, suggested by Gordon, Miller and Day (THIS JOURNAL, **71**, 1245 (1949)) involves attack by a hydrogen-bonded complex. For catalysis by methylate anion in methanol this would be written as $\mathrm{RNH{-}H{\cdots}{}^-OCH_3}$. Since an amide anion in methanol would also be subject to hydrogen bonding and should be written as: $\mathrm{RNH^-{\cdots}H{-}OCH_3}$, it is our opinion that the distinction is academic.

of Equation 2. Betts and Hammett[5] deduced that in methanolic solution about two-thirds of the amide produced resulted from the reaction of Equation 3. From the results of Audrieth[2,6] it would appear that when ammonia or an amine is the solvent, the reaction of Equation 1 is dominant.

Disagreement centers chiefly about the effect of solvent upon the reaction, and because of this we felt it necessary to examine a number of solvents in order to determine the best conditions for kinetic studies. Audrieth found his reactions to be hastened by the presence of water (which presumably acted as an acid in his systems). Other investigators, notably Morrell[7] and Gordon, Miller and Day[8,4] have stated that useful rates are not obtained in anhydrous solvents (other than polyhydric alcohols). On the other hand, Betts and Hammett[5] performed their experiments in methanol which was as nearly anhydrous as extreme precautions could render it. An intermediate position was occupied by Grunfeld[3] who, on the basis of his experience with ethanol and petroleum ether, concluded that the solvent did not make much difference. This conclusion is actually justified as between those two solvents, but is not generally valid.

Experimental

The reactions were carried out in volumetric flasks into which appropriate quantities of amine and ester were weighed, the volume being completed by addition of the solvent. Reaction Id (Table I) shows that no significant error is introduced by the time required for this procedure. After mixing, the flasks were thermostated and duplicate aliquots removed for titration. Further aliquots were taken for titration at convenient intervals thereafter. The concentrations of amine and ester were in the range from 1–2 molar and were approximately equal. This is not the generally preferred condition but in the relatively high concentrations necessary with slow reactions a large excess of either reactant would modify the character of the solution unduly. Titrations were performed by running the aliquot into methanol and titrating against 0.1 or 0.05 *N* hydrochloric acid using a solution of methyl red and methylene blue as indicator.

The thermostat employed in the latter part of this work was set at 25.2 ± 0.2°. While more precise control is desirable, the nature of these reactions is such that extreme precautions are unprofitable. During the earlier work while orienting runs were being made it was not possible to operate at that temperature, and thermostating was at lower temperatures, mainly at 22°. The results of these runs have been corrected to 25.2° and are included in Table I for purposes of comparison.

Of the amines used, *n*-butylamine, isobutylamine, piperidine and morpholine were of "C. P." commercial grade. They were redistilled from solid potassium hydroxide and middle fractions of constant boiling point taken for the kinetic runs. Methyl-*n*-butylamine and methyl-isobutylamine were prepared by the Decker method from the corresponding primary amines. The bases were liberated by sodium methylate from their purified salts dissolved in methanol. The bases and methanol were distilled together, some concentration being achieved in the process. Since the reactions were to be run in methanol, the most concentrated fractions were further dried by distillation from magnesium methylate, and the concentration of base in the distillate was determined by titration.

Methyl caproate was prepared from caproyl chloride and methanol and purified by distillation. The other esters used were of good commercial grade. They were dried over magnesium sulfate and redistilled, constant boiling middle fractions being employed in the reactions.

Methanol was distilled from magnesium methylate, ethanol from calcium oxide, dioxane from sodium (after a reflux period) and isopropyl alcohol from aluminum isopropylate. Petroleum ether was a 30–60° boiling fraction obtained from Merck.

Since most of the runs were in anhydrous solvents, no attempt was made to estimate the extent of hydrolysis. Previous work[4,6] has shown that it would be negligible in the faster reactions. In the slower reactions this could not be assumed but any considerable hydrolysis results in an uncertain end-point in titrations, and this was not observed.

Results

Bimolecular rate constants obtained in the present work are shown in Table I. The particular difficulty with this type of reaction is a tendency for k to diminish as the reaction proceeds. Extrapolation to zero time suffers from the disadvantage that the earlier titration values, which are the least accurate, receive the greatest weight. Comparison of k in different reactions after fixed intervals of time has the effect of comparing fast and slow reactions in very different states of completion. We have therefore taken the reaction rate at 10% completion ($k_{10\%}$) as most satisfactory for purposes of comparison. The results of earlier exploratory runs at 22° have been re-calculated for 25.2° by use of the Arrhenius equation in which E was assumed to be 12,000 cal./mole.[9] The resultant figures are not seriously in error *because of this* since the possible error in the correction is less than the variation of the rate-constants during the reaction. Such re-calculated values are denoted by asterisks.

In certain cases, however, $k_{10\%}$ is higher rather than lower than the initial rate. This arises from two causes. When a non-methyl ester reacts in methanol the rate increases rapidly, presumably due to ester-exchange. With ethyl acetate in methanol the maximum rate is observed at 15% completion and is there about twice as large as near the beginning. Again, when methyl acetate reacts in petroleum ether or when excess ester is employed with no other solvent, the rate increases, presumably because the character of the solution is favorably altered by the methanol released in the reaction. In these cases initial values for k were also deduced and these are shown in Table I in parentheses.

In Tables II–IV are shown typical data for runs with methyl acetate and *n*-butylamine in meth-

---

[5] Betts and Hammett, THIS JOURNAL, **59**, 1568 (1937).

[6] Fellinger and Audrieth, *ibid.*, **60**, 579 (1938); Audrieth and Kleinberg, *J. Org. Chem.*, 3, 312 (1938); Glasoe and Audrieth, *ibid.*, 4, 54 (1939).

[7] Morrell, *J. Chem. Soc.*, 2701 (1914).

[8] Gordon, Miller and Day, THIS JOURNAL, **70**, 1946 (1948).

[9] Gordon, Miller and Day (ref. 8) give 10,800 as the average of ten reactions of ammonolysis. Harfenist and Baltzly (THIS JOURNAL, **69**, 362 (1947)) found 12,700 as an average of eight reactions of ester exchange. Studies, as yet incomplete, for the present reactions suggest that E is in the same range.

TABLE I

BIMOLECULAR REACTION RATES[a] FOR AMINOLYSIS OF ESTERS IN VARIOUS SOLVENTS

Reaction	Amine	Ester	Solvent	$k_{10\%} \times 10^3$
Ia	*n*-Butylamine	Methyl acetate	Methanol	15.1
Ib	*n*-Butylamine	Methyl acetate	Methanol and water (0.5 *M*)	14.0
Ic*	*n*-Butylamine	Methyl acetate	Methanol and $C_4H_9NH_3Cl$ (0.045–0.11 molar)	7.9
Id*	*n*-Butylamine	Methyl acetate	Methyl acetate	0.1(0.09)
Ie*	*n*-Butylamine	Methyl acetate	Ethanol	3.5
If*	*n*-Butylamine	Methyl acetate	Isopropyl alc.	1.3
Ig	*n*-Butylamine	Methyl acetate	Dioxane	0.11
Ih	*n*-Butylamine	Methyl acetate	Dioxane–water (80–20)	4.7
Ii*	*n*-Butylamine	Methyl acetate	Petroleum ether	2.9
IIa*	*n*-Butylamine	Ethyl acetate	Methanol	7.9(4.7)
IIb*	*n*-Butylamine	Ethyl acetate	Ethanol	0.25
IIc*	*n*-Butylamine	Ethyl acetate	Isopropyl alc.	0.22
IId*	*n*-Butylamine	Ethyl acetate	Dioxane	0.036
IIIa*	*n*-Butylamine	Isopropyl acetate	Methanol	2.6(1.3)
IIIb*	*n*-Butylamine	Isopropyl acetate	Ethanol	0.054
IIIc*	*n*-Butylamine	Isopropyl acetate	Isopropyl alc.	0.011
IIId*	*n*-Butylamine	Isopropyl acetate	Dioxane	0.022
IVa	*n*-Butylamine	Methyl caproate	Methanol	1.62
IVb*	*n*-Butylamine	Methyl caproate	Isopropyl alc.	0.22
V	Isobutylamine	Methyl acetate	Methanol	6.3
VIa	Piperidine	Methyl acetate	Methanol	0.47
VIb	Piperidine	Methyl acetate	Methanol and $NaOCH_3$ (0.019 *M*)	5.2
VIIa	Morpholine	Methyl acetate	Methanol	0.13
VIIb	Morpholine	Methyl acetate	Methanol and $NaOCH_3$ (0.019 *M*)	6.7
VIII	Methyl *n*-butylamine	Methyl acetate	Methanol	0.11
IX	Methylisobutylamine	Methyl acetate	Methanol	0.018

[a] Values for $k_{10\%}$ in the lines marked with an asterisk are recalculated from data obtained at 22°. Figures in parentheses were obtained by extrapolation to zero time.

TABLE II

TITRATION DATA FOR THE REACTION OF *n*-BUTYLAMINE WITH METHYL ACETATE

In methanol at 25.2°; methyl acetate, 1.283 molar; *n*-butylamine, 1.118 molar

Time, hours	0.05 *N* HCl, cc.	Amine reacted, %	$k \times 10^3$ (liters/mole/hour)
0.00	44.70	0.00	...
1.50	43.40	2.91	15.3
3.00	42.20	5.59	15.3
24.50	31.30	29.98	13.3
26.75	30.65	31.43	13.0
Methyl acetate, 1.005 molar; *n*-butylamine, 1.108 molar			
0.00	44.30	0.00	...
24.00	33.50	24.38	13.6
49.50	28.10	36.57	12.0
72.67	24.85	43.91	11.3
96.42	22.50	49.21	10.7
169.50	18.20	58.92	9.29
194.67	17.25	61.06	8.93
218.75	16.40	62.98	8.71
238.75	15.90	64.11	8.42

TABLE III

TITRATION DATA FOR THE REACTION OF *n*-BUTYLAMINE WITH METHYL ACETATE

In methanol containing water; at 25.2°; methyl acetate, 0.994 molar; *n*-butylamine, 1.072 molar; water, 0.514 molar

Time, hours	0.05 *N* HCl required, cc.	Amine reacted, %	$k \times 10^3$ (liters/mole/hour)
0.00	42.88	0.00	...
24.00	33.10	22.81	12.5
47.42	28.45	33.65	11.0
69.50	25.60	40.30	9.00
140.50	20.15	53.01	8.53
166.88	19.05	55.57	8.03
190.88	18.10	57.79	7.74

anol, methanol containing added water, and in a dioxane–water mixture.

The errors in determinations of this sort have been adequately discussed by Betts and Hammett and by Gordon, Miller and Day. The actual experimental error is rather small and *k* in the faster reactions is probably accurate within 1–2%. In the slower reactions the inherent errors are greater and the estimation of $k_{10\%}$ less precise. In some of these the uncertainty might easily amount to 100%. In the runs with piperidine and morpholine against methyl acetate in methanol containing·sodium methylate (VIb and VIIb) the rate changed very rapidly during the reaction. The figures given in Table I are reasonable estimates but we do not assign to them greater validity than to indicate that the catalyst increased the rate of the piperidine reaction about ten and that of the morpholine reaction about fifty times.

TABLE IV

TITRATION DATA FOR THE REACTION OF *n*-BUTYLAMINE WITH METHYL ACETATE

In dioxane–water (80% dioxane: 20% water) at 25.2°; methyl acetate 1.196, molar; *n*-butylamine, 1.126 molar

Time, hours	0.05 *N* HCl required, cc.	Amine reacted, %	$k \times 10^3$ (liters/mole/hour)
0.00	45.05	0.00	..
20.75	40.35	10.43	4.64
44.75	36.25	19.53	4.54
68.75	32.85	27.08	4.50
92.75	30.20	32.96	4.43
164.50	24.65	45.28	4.25
188.50	23.20	48.50	4.25
212.50	22.05	51.05	4.18

Discussion

Compared to the rate constants given by Gordon, Miller and Day[8] for the reactions of some of these esters with ammonia, it appears that simple primary amines react rather more readily than ammonia. Electronic factors in the amines should favor reaction while steric factors should discourage it. The secondary amines are very much less reactive than either primary amines or ammonia. This is in accord with occasional preparative experience of the unreactivity of secondary amines toward esters. Apparently, the increase in basicity is not enough to compensate for the greater hindrance (very likely it is the crowding in the reaction complex that is critical). Some indication of the effect of an increase in basicity alone is shown by the comparison of Reactions VIa and VIIa. The bases employed, piperidine and morpholine, should be nearly identical sterically, while K_B for piperidine is a thousand times greater than for morpholine. The reaction with methyl acetate is three to four times faster with piperidine.

The extent to which these stronger bases can be expected to react by the amide anion scheme (Equation 3) of Betts and Hammett is uncertain in the absence of a more complete study of the effect of added amine salts. Reaction Ic shows, however, that amine salts do inhibit the reaction, and Reactions VIb and VIIb demonstrate a marked catalysis by methylate anion, which, as expected, is greater for morpholine than for piperidine.

The chief discrepancy between our results and those anticipated on the basis of previously published work is in the superiority we have found for methanol as the reaction solvent and in the minor effect of water, when added, upon the rate. The runs (Reaction Ih) with 80–20 dioxane–water as solvent approximate the conditions employed by Gordon, Miller and Day[8,10] and the rate in those runs was markedly below that obtained in Ia. Further, since ammonolysis in methanol is a satisfactory preparative method[11] we are unable to understand the statement that methyl acetate and ammonia do not react together,[4,8] at a useful rate in that solvent. The use of anhydrous methanol as a solvent has the particular advantage of permitting catalysis by sodium methylate with esters that react sluggishly.[12] The fact that the runs with methyl acetate in dioxane did not accelerate as they proceeded is, however, in agreement with the report of Gordon, Miller and Day[4] that small amounts of methanol added to dioxane did not increase the rate of ammonolysis.

Summary

1. Kinetic studies have been made of the reactions of several primary and secondary amines with esters in various solvents.

2. *n*-Butylamine and isobutylamine react rather more rapidly than ammonia, secondary amines much more slowly.

3. Methanol has been found to be the solvent of choice for aminolyses of methyl esters.

BROOKLYN 2, NEW YORK RECEIVED DECEMBER 3, 1949

---

(10) Gordon, Miller and Day used solutions 10 molar in water or 18% (wt./vol.). In Reaction Ih the concentration of water was 16%.

(11) A methanolic solution 8 molar in ammonia and 0.5 molar in methyl acetate afforded a 90% yield of acetamide after standing twenty-four hours at room temperature (the solvent being removed *in vacuo* below 30°). This indicates a rate-constant comparable to those obtained by Gordon, Miller and Day under their conditions.

(12) Russell, THIS JOURNAL, **72**, 1853 (1950).