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[CONTRIBUTION FROM THE RICHARD B. WETHERILL LABORATORY OF PURDUE UNIVERSITY]

A New Aldehyde Synthesis—The Reduction of Acid Chlorides by Lithium Tri-*t*-butoxyaluminohydride[1]

BY HERBERT C. BROWN AND B. C. SUBBA RAO[2,3]

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The addition of lithium tri-*t*-butoxyaluminohydride in diglyme solution to acid chlorides at −78° provides a convenient synthesis of aldehydes. The scope of this synthesis was explored by applying it to thirty representative acid chlorides exhibiting widely varying structural characteristics. Aromatic acid chlorides containing substituents in the *meta* and *para* positions form aldehydes in yields of 60–90%. Many types of substituents can be tolerated, including those which might be considered sensitive to reduction, such as nitro, cyano and carbethoxy. Substituents in the *ortho* position tend to reduce the yield. Polycyclic (α- and β-naphthyl), heterocyclic (nicotinyl), unsaturated (cinnamoyl) and polyfunctional (terephthalyl) acid chlorides may be utilized in the synthesis. In the case of aliphatic and alicyclic acid chlorides (isobutyryl, adipyl, cyclopropanecarboxyl, fumaryl) the yields fall within the range 40–60%. The simplicity and wide applicability of this synthesis should provide a valuable new preparative route from the carboxylic acids to the corresponding aldehydes.

The relatively ready availability of carboxylic acids has made a simple synthetic route from such acids to the corresponding aldehydes highly desirable. The catalytic reduction of acid chlorides to aldehydes has provided one such route.[4] This valuable reaction suffers from two serious disadvantages: the difficulty of reproducing the precise poisoning of the catalyst to obtain good yields, and the sensitivity of some substituents to the hydrogenation conditions.[5]

Wittig and Hornberger observed that the reduction of the N-acylcarbazoles by lithium aluminum hydride provided a convenient route to the aldehydes, and they made use of this procedure in the synthesis of unsaturated derivatives, $C_6H_5(CH{=}CH)_nCHO$ (n = 2, 4 and 6).[6] Weygand has demonstrated that the related reduction of the N-methylanilides is applicable to a wide range of aldehyde preparations.[7,8]

Recently, lithium tri-*t*-butoxyaluminohydride was synthesized and observed to be a far milder reducing agent than lithium aluminum hydride itself. Moreover, in a few representative cases it reduced acid chlorides to aldehydes in reasonable yields.[9,10] The procedure is exceedingly simple. Consequently, it appeared desirable to explore the scope and possible limitations of this new aldehyde synthesis.

Results and Discussion

In the earlier procedure lithium tri-*t*-butoxyaluminohydride was precipitated from a solution of lithium aluminum hydride in ethyl ether by addition of a slight excess of *t*-butyl alcohol (3.1 moles of alcohol per mole of lithium aluminum hydride). The product, a white solid, was separated from the solvent and stored in that form. To carry out a reduction, a weighed quantity of the hydride was dissolved in diglyme (dimethyl ether of diethylene glycol) and the solution (1.0 M) was added to an equimolar quantity of the acid chloride in diglyme (2.0 M) maintained at −78°. The reaction mixture was allowed to warm to room temperature, hydrolyzed, and the aldehyde isolated by appropriate techniques.

It appeared desirable to simplify the procedure by circumventing the isolation of the reagent. Accordingly, alternative procedures were followed to obtain the reagent in solution and the yields realized in the reduction of *p*-nitrobenzoyl chloride compared. The five procedures examined were: A. Preparation and isolation of the solid lithium tri-*t*-butoxyaluminohydride, followed by solution in diglyme. B. Precipitation of the reagent by addition of 3 moles of *t*-butyl alcohol to 1 mole of lithium aluminum hydride in ether, followed by decantation of the ether, and addition of diglyme to dissolve the ether-wet residue. C. Preparation of the reagent as in B, but retaining the ether, followed by sufficient diglyme to provide a clear solution. D. Direct preparation of the reagent in diglyme by adding 3 moles of *t*-butyl alcohol to 1 mole of lithium aluminum hydride in diglyme. E. Direct preparation of the reagent in tetrahydrofuran by adding 3 moles of *t*-butyl alcohol to 1 mole of lithium aluminum hydride in tetrahydrofuran.

The results of these five comparative studies are summarized in Table I.

TABLE I

REDUCTION OF *p*-NITROBENZOYL CHLORIDE BY LITHIUM TRI-*t*-BUTOXYALUMINOHYDRIDE AT −78°

Procedure used for preparation of reagent	Yield of *p*-nitrobenzaldehyde, %: By estimation as 2,4-dinitrophenylhydrazone	By isolation: Crude	By isolation: Pure
A. Solid reagent		81	67
B. Ether decanted		80	67
C. Ether-diglyme soln.		78	63
D. Prepared in diglyme	84	80	66
E. Prepared in tetrahydrofuran	70	65	53

(1) Addition Compounds of the Alkali Metal Hydrides. XI.

(2) The Upjohn Co. Post-doctorate Fellow at Purdue University, 1955–1956.

(3) The Parke, Davis and Co. Post-doctorate Fellow at Purdue University, 1955–1956.

(4) K. W. Rosenmund, *Ber.*, **51**, 585 (1918).

(5) For a survey of the scope and limitations of the Rosenmund reduction, see E. Mosettig, "Organic Reactions," Vol. IV, John Wiley and Sons, Inc., New York, N. Y., 1948, pp. 362–377.

(6) G. Wittig and P. Hornberger, *Ann.*, **577**, 11 (1952).

(7) F. Weygand, *et al.*, *Angew. Chem.*, **65**, 525 (1953).

(8) For a general review of these and other synthetic routes from carboxylic acid derivatives to the corresponding aldehydes, see E. Mosettig, "Organic Reactions," Vol. VIII, John Wiley and Sons, Inc., New York, N. Y., 1954, pp. 218–257.

(9) H. C. Brown and R. F. McFarlin, THIS JOURNAL, **78**, 252 (1956).

(10) H. C. Brown and R. F. McFarlin, *ibid.*, **80**, 5372 (1958).

These results indicate that tetrahydrofuran as the solvent is less effective than diglyme. The yields in diglyme are quite comparable. It is somewhat inconvenient to isolate the solid reagent. Consequently, procedures B, C and D appear preferable, with C the preferred procedure in cases where it is desired to have ether present in the isolation of the aldehyde, and B or D preferred in cases where the aldehyde is to be isolated in the absence of ether.

The effect of the reaction temperature was noted with several representative acid chlorides. Reductions were carried out under identical conditions at −78°, −40° and −10°. In all cases the reagent was added slowly, over a period of approximately an hour. It was observed that rapid addition, over a period of 10 minutes instead of the usual 60, led to somewhat lower yields. The results are summarized in Table II.

TABLE II

EFFECT OF REACTION TEMPERATURE ON THE ALDEHYDE YIELD

Acid chloride	Yield of aldehyde, %[a] −78°	−40°	−10°
Benzoyl	81	74	58
p-Nitrobenzoyl	84	66	53
o-Chlorobenzoyl	41	44	35
Cinnamoyl	71	67	64
Pivalyl	58	57	46
Pivalyl	16[b]	54[b]	44[b]

[a] By analysis with 2,4-dinitrophenylhydrazine. [b] Triglyme as solvent.

It is clear that the yield is favored by lower temperatures. It is probable that we are dealing with two competitive reactions, with the first being faster than the second

$$RCOCl + LiAlH[OC(CH_3)_3]_3 \longrightarrow RCHO + LiCl + Al[OC(CH_3)_3]_3$$

$$RCHO + LiAlH[OC(CH_3)_3]_3 \longrightarrow LiRCH_2OAl[OC(CH_3)_3]_3$$

Apparently, the lower the temperature the greater is the rate of reaction of the reagent with the acid chloride relative to the rate of the reaction with the aldehyde.

We also examined the possibility that triglyme (dimethyl ether of triethylene glycol) might possess advantages over diglyme as the solvent. In this case the yields at −40° and −10° were comparable, but at −78° the yield was much lower (Table II). It is probable that the much higher viscosity of triglyme at −78° was a factor in the low yield.

Finally, we applied the reagent at −78° in diglyme to thirty representative acid chlorides to establish the scope and possible limitations of the reduction. In all cases the yield was established by the isolation and weighing of the 2,4-dinitrophenylhydrazine with the melting point of the hydrazone checked to establish its identity and essential purity. In practically all cases, the hydrazone appeared to be of high purity as isolated from the reaction mixture. In a few cases, the melting point of the crude 2,4-dinitrophenylhydrazone was slightly low and the product was recrystallized. In a representative number of cases the aldehydes were isolated as such and the yields of crude and purified products noted to check the analytical data. The results are summarized in Table III.

TABLE III

ALDEHYDE YIELDS IN THE REDUCTION OF ACID CHLORIDES BY LITHIUM TRI-*t*-BUTOXYALUMINOHYDRIDE

Acid chloride	Yield of aldehyde, % Analysis with 2,4-dinitrophenylhydrazine: Direct	Purified	Yield by isolation: Crude	Purified
Benzoyl	81		85	73
p-Toluyl	61			
p-*t*-Butylbenzoyl	77		70	63
p-Nitrobenzoyl	84		81	67
m-Nitrobenzoyl	88			
o-Nitrobenzoyl	77	64	74	61
p-Cyanobenzoyl	87	77	80	68
p-Carbethoxybenzoyl	48			
p-Chlorobenzoyl	81		80	70
m-Chlorobenzoyl	76			
o-Chlorobenzoyl	41			
p-Methoxybenzoyl	60		57	50
m-Methoxybenzoyl	66			
o-Methoxybenzoyl	27			
Terephthalyl	82		85	77
Isophthalyl	77		80	64
α-Naphthoyl	84	68		
β-Naphthoyl	58			
Nicotinyl	69			
Cinnamoyl	71		65	50
n-Butyryl	37		23	
Isobutyryl	57	48		
Pivalyl	58			
Caproyl	41	32		
Crotonyl	48			
Adipyl	53			
Fumaryl	59			
Cyclopropanecarboxyl	42		52	
Cyclobutanecarboxyl	46			
Cyclohexanecarboxyl	56			

The yields realized in the case of benzoyl chloride and its *meta* and *para* substituted derivatives averaged approximately 80%, ranging from 60% for *p*-methoxybenzoyl chloride to 88% for *m*-nitrobenzoyl chloride.[11] Various types of substituents can be tolerated, even those which might be considered susceptible to reduction by complex hydrides, such as nitro, cyano and carbethoxy. Since the reduction of terephthalyl and isophthalyl chlorides presumably proceeds through two individual stages, the excellent yields of dialdehydes realized in these reductions suggests that even the sensitive aldehyde group can be tolerated as a substituent.

Ortho substituents result in lower yields. These range from 77% for *o*-nitrobenzoyl chloride to 41% for *o*-chlorobenzoyl chloride to a low of 27% for *o*-methoxybenzoyl chloride. A similar low yield was observed by Weygand for the *o*-methoxy derivative in his reduction of the N-methylanilide.[7]

Numerous changes in the aromatic nucleus

(11) We do not believe that the 48% yield observed in the case of *p*-carbethoxybenzoyl chloride represents the maximum realizable in this reaction. Unfortunately, the synthesis of the acid chloride involved several steps and we had sufficient material for a single experiment only.

appear possible. Thus equally good yields were realized with polycyclic (α- and β-naphthyl) and heterocyclic (nicotinyl) derivatives.

The presence of double bonds conjugated with the carbonyl group appears to offer no difficulty. A 71% yield of aldehyde was indicated in the reduction of the cinnamoyl chloride and the yields in the case of crotonyl (48%) and fumaryl (59%) chlorides are approximately the same as those observed for the related saturated derivatives.

In the case of both representative aliphatic and alicyclic derivatives the yields fall within the range of 40–60%, definitely lower than the average yields of 60–80% realized for the majority of the aromatic derivatives.

In conclusion the yields obtained in the present procedure appear to be comparable in the case of the aromatic derivatives to those realizable in the Rosenmund reduction of acid chlorides and in the Weygand reduction of the N-methylanilides. In the case of the aliphatic derivatives, the yields appear to be slightly lower. However, the present procedure is an exceedingly simple one experimentally, and for that reason may be preferable even in cases where there may be no advantage in yield.

Experimental

Preparation of Lithium Tri-*t*-butoxyaluminohydride.—The five procedures examined for preparing the reagent are: A. Lithium aluminum hydride, 1.00 mole in 2.5 l. of ether, was placed in a flask equipped with a stirrer, reflux condenser and separatory funnel. Anhydrous *t*-butyl alcohol, 3.15 moles (231 g.) in 1 l. of ether, was added slowly through the separatory funnel. (The hydrogen evolved was conducted to a vent.) During the addition of the last third of the alcohol, a white precipitate formed. The solvent was decanted, and the flask was evacuated with heating on the steam-cone to remove the last traces of ether and excess *t*-butyl alcohol. The solid was collected and stored in bottles with careful protection from atmospheric moisture. Solutions 0.2 *M* in reagent were prepared as required by dissolving the solid in diglyme.

B. The reagent was prepared as in A, but on a smaller scale, in a 1-l. flask, using 0.60 mole of *t*-butyl alcohol in 250 ml. of ether and 0.20 mole of lithium aluminum hydride in 500 ml. of ether. After addition was complete, stirring was halted, and the precipitate allowed to settle. The supernatant ether was decanted. To the residue, wet with ether, diglyme was added to make 200 ml. of solution (1.0 *M*).

C. The reagent was prepared in ether as in B, using a 2-l. flask. Sufficient diglyme, approximately 600 ml., was added to the ether suspension to dissolve the lithium tri-*t*-butoxyaluminohydride. The resulting solution was approximately 0.2 *M* in reagent.

D. In a flask fitted with a pressure equilibrated dropping funnel and stirrer, 150 ml. of diglyme was placed and 0.2 mole of finely powdered lithium aluminum hydride was added. The material was stirred for a period to facilitate partial solution of the hydride. Through the separatory funnel was added over a period of 1 hour 0.60 mole of *t*-butyl alcohol with stirring. Hydrogen was evolved and the suspended lithium aluminum hydride went into solution. (The final solution was light gray in color, presumably due to minor impurities in the lithium aluminum hydride usually removed by the prior solution of the material in ether in the other procedures.) The resulting solution was used directly for the reduction.

E. The procedure was the same as in D, with tetrahydrofuran substituted for the diglyme.

Identical results were obtained by the four procedures utilizing diglyme (A–D). If the solid reagent is not available, procedures B and D appear to be the more convenient. Tetrahydrofuran gave somewhat lower yields, so its use appears less desirable. The results are summarized in Table I.

Reduction of Acid Chlorides.—The acid chlorides were either commercial products, distilled or recrystallized before use, or they were synthesized by standard methods.

These reductions are typical of the procedures utilized. *p*-Nitrobenzoyl chloride (0.200 mole, 37.1 g.) was dissolved in 100 ml. of diglyme and placed in a flask fitted with a stirrer, separatory funnel, low temperature thermometer and nitrogen inlet and outlet. The flask was flushed with dry nitrogen and cooled to approximately −78° by immersing in a cooling bath of solid carbon dioxide and trichloroethylene. To the stirred flask the reagent, 0.200 mole of lithium tri-*t*-butoxyaluminohydride in sufficient diglyme to make 200 ml. of solution, was added over a period of 1 hr., avoiding any major rise in temperature. The cooling bath was then removed and the flask allowed to warm up to room temperature over a period of approximately 1 hr. The contents were then poured onto crushed ice. The precipitated aldehyde (with some unreacted product) was filtered, pressed dry, and then extracted several times with 95% ethanol. Distillation of the solvent gave 24.5 g. of crude aldehyde, m.p. 103–104°, a yield of 81%. Recrystallization from hot water (or aqueous ethanol) gave 20.3 g. of light yellow flakes, m.p. 104–105°, a yield of 67%.

p-*t*-Butylbenzoyl chloride, b.p. 86–87° at 1 mm., was prepared from the acid with thionyl chloride. The acid chloride (0.200 mole, 39.3 g.) was dissolved in 100 ml. of diglyme and reduced with 0.200 mole of lithium tri-*t*-butoxyaluminohydride in 200 ml. of solution as described above. The reaction product was hydrolyzed and the crude aldehyde was taken up in ether. On distillation there was obtained 22.9 g., b.p. 123–125° at 20 mm., a yield of 70%. Estimation of an aliquot of the reaction mixture with 2,4-dinitrophenylhydrazine gave the hydrazone, m.p. 248–250°, in a yield of 77%.

p-Cyanobenzoyl chloride, m.p. 65°, was prepared from the acid. Reduction of the acid chloride, 16.6 g. in 50 ml. diglyme, was accomplished over 25 min. with 0.1 mole of the reagent. The crude aldehyde, 10.5 g., 80% yield, was recrystallized from aqueous ethanol to give 8.95 g. of the pure *p*-cyanobenzaldehyde, m.p. 92–93°, a yield of 68%. Estimation as the 2,4-dinitrophenylhydrazone, m.p. 295–298°, indicated a yield of 87% of crude, 77% of product recrystallized from acetic acid.

Anal. Calcd. for $C_{14}H_8N_6O_4$: C, 54.0; H, 2.90; N, 22.5. Found: C, 53.99; H, 3.11; N, 22.63.

Terephthalyl chloride, m.p. 81–82°, was prepared from the acid. The acid chloride, 0.200 mole, 40.6 g., in 200 ml. of diglyme was treated with 0.4 mole of reagent at 78°, utilizing 2 hours for the addition. On hydrolysis, the crude dialdehyde, 23.0 g., m.p. 112–115°, was obtained in 85% yield. Recrystallization from hot water gave 20.9 g. of pure terephthalaldehyde, m.p. 114–115°, a yield of 77%. By estimation as the 2,4-dinitrophenylhydrazone, the yield was 81.5%.

Similarly, isophthalyl chloride, m.p. 42–43°, was converted into 22.4 g., 80% yield, of crude aldehyde. Recrystallization from aqueous ethanol produced 17.2 g., 64% yield, of isophthalaldehyde, m.p. 89–90°.

Cinnamoyl acid chloride was prepared from the acid, b.p. 100° at 1 mm. The acid chloride (33.3 g., 0.200 mole) was reduced in the usual manner. The aldehyde, taken up in ether, was recovered by distillation. There was obtained 16.2 g., b.p. 95–105° at 3–4 mm., a yield of 64.5%. Refractionation yielded 13.3 g. of pure cinnamaldehyde, b.p. 98–100° at 3–4 mm., 50% yield.

A number of acid chlorides were reduced on a small scale and the yield of aldehyde established by the quantitative estimation of the 2,4-dinitrophenylhydrazone. The identity of the hydrazones was checked through their melting points. When these differed significantly from literature values, the hydrazones were purified by recrystallization from glacial acetic acid or some other suitable solvents to obtain the pure derivatives. The yields of both the crude and purified hydrazones are recorded in Table III.

The following procedure was used. In a flask fitted with stirrer, thermometer and dropping funnel was placed 0.025 mole of the acid chloride in 15 ml. of diglyme. The reagent, 0.025 mole in 25 ml. of solution, was added slowly to the cold (−78°) acid chloride. At the end of the reaction, 5-ml. samples of the supernatant liquid were added to 100 ml. of saturated solutions of the 2,4-dinitrophenylhydrazine in 2 *M* hydrochloric acid. The precipitated derivative was

filtered, washed, dried and weighed, following the procedure described by Iddles.[12] The results are included in Table III.

Three of the 2,4-dinitrophenylhydrazones are new: (1) 2,4-dinitrophenylhydrazone of *p*-carbethoxybenzaldehyde, m.p. 248–249° dec. *Anal.* Calcd. for $C_{16}H_{14}N_4O_6$: C, 53.6; H, 3.94; N, 15.6. Found: C, 53.61; H, 3.93; N, 15.37. (2) Bis-2,4-dinitrophenylhydrazone of fumaric dialdehyde, m.p. 260° dec. *Anal.* Calcd. for $C_{16}H_{12}N_8O_8$: C, 43.2; H, 2.80; N, 25.2. Found: C, 43.90; H, 2.76; N, 22.7. (3) 2,4-Dinitrophenylhydrazone of cyclobutanecarboxaldehyde, m.p. 155–156°. *Anal.* Calcd. for $C_{11}H_{11}N_4O_4$: C, 50.1; H, 4.2; N, 21.2. Found: C, 50.28; H, 4.25; N, 21.27.

(12) H. A. Iddles, A. W. Low, B. D. Rosen and R. T. Hart, *Anal. Ed.*, **11**, 103 (1939).

LAFAYETTE, IND.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, ILLINOIS INSTITUTE OF TECHNOLOGY]

Intramolecular Catalysis of Hydrolytic Reactions. II. The Hydrolysis of Phthalamic Acid[1,2]

BY MYRON L. BENDER, YUAN-LANG CHOW AND FRANK CHLOUPEK

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The hydrolysis of phthalamic acid in aqueous solution exhibits kinetic dependence on the undissociated phthalamic acid and independence of external hydrogen ion from *p*H 1 to 5. At *p*H 3 the hydrolysis of phthalamic acid is about 10^5 faster than the hydrolysis of benzamide and about 10^6 faster than the hydrolysis of *o*-nitrobenzamide. On the other hand the hydrolysis of terephthalamic acid is somewhat slower than that of benzamide. The large rate enhancements in the former case suggest that the *o*-carboxylic acid group does not exert a substituent effect but rather catalyzes the amide hydrolysis by a direct intramolecular process. It is suggested that this process is an electrophilic–nucleophilic catalyzed reaction involving the intermediate formation of phthalic anhydride. A tracer experiment involving the hydrolysis of phthalamic acid-*carboxamide*-C^{13} in H_2O^{18} provides indirect evidence for the formation of a symmetrical phthalic anhydride intermediate. The hydrolysis of phthalamic acid in concentrated hydrochloric acid exhibits a rate maximum and appears to involve the direct attack of water on the protonated amide; apparently the undissociated carboxylic acid group cannot function as a nucleophile toward a protonated amide group as effectively as the carboxylate ion can.

Introduction

Recently nucleophilic catalysis[3] of ester hydrolysis has been demonstrated in the hydrolyses of *p*-nitrophenyl acetate, 2,4-dinitrophenyl acetate, phenyl acetate, ethyl thiolacetate and methyl pyrrolidylacetylsalicylate hydrochloride using the nucleophiles pyridine, 3- and 4-picoline, trimethylamine, imidazole, N-methylimidazole, a number of 4,5-substituted imidazoles, quinoline and acetate ion.[4–7]

Investigations of intramolecular catalysis have now been initiated.[2] The purpose of these investigations is to compare the kinds and effectiveness of intramolecular and intermolecular catalysis. Intramolecular catalysis implies that there are groups attached to a molecule that can catalyze the reactions of other groups. This interpretation immediately excludes consideration of hydronium ion and hydroxide ion as intramolecular catalysts (except for certain ion exchange resins) and focuses attention on general (Brönsted) catalysts.

The earlier experiments described above suggested that in favorable systems nucleophilic catalysis of the hydrolysis of carboxylic acid derivatives can occur. It was then thought feasible to investigate the possibility of nucleophilic and/or electrophilic catalysis in intramolecular cases where steric factors would favor such processes. Much work has been done on anchimeric or synartetic assistance to the solvolysis at saturated carbon atoms.[8] The present research is an extrapolation of such intramolecularly-assisted reactions to the hydrolysis of carboxylic acid derivatives.

Leach and Lindley observed that the hydrolysis of two aliphatic amides is subject to what they have called an internal mechanism.[9] They determined the kinetics of the hydrolysis of the amide links of glycyl-L-asparagine and L-leucyl-L-asparagine in aqueous solution from *p*H 1.2 to 3.5. Each reaction was first order in organic reactant with an undissociated carboxyl group and was independent of the external hydrogen ion concentration over this *p*H range. These authors concluded that the first-order character of the reactions, the independence of the external hydrogen ion concentration and the small, negative entropies of activation were consistent with an internal mechanism of hydrolysis involving an (internal) proton transfer from the un-ionized carboxyl group at one end of the molecule to the amide group at the other end. It was postulated that the peptides exist in solution in a six-membered cyclic hydrogen-bonded structure which is close to the postulated activated complex of a protonated amide group. In order to

(1) This research was supported by Grant H-2416 of the National Institutes of Health.

(2) A preliminary report of part of this research was given by M. L. Bender, THIS JOURNAL, **79**, 1258 (1957), and was presented at a symposium on "Reaction Mechanisms and Solvent Effects" at Queen Mary College, London, July, 1957.

(3) Originally the term general basic catalysis was used to describe this phenomenon but it is suggested that nucleophilic catalysis be adopted as the proper term in order to distinguish a mechanism involving the addition of a nucleophile to the substrate producing an unstable intermediate from the classical mechanism of general basic catalyses involving a rate-determining proton transfer.

(4) M. L. Bender and B. W. Turnquest, THIS JOURNAL, **79**, 1656 (1957).

(5) T. C. Bruice and G. L. Schmir, *Arch. Biochem. & Biophys.*, **63**, 484 (1956); THIS JOURNAL, **79**, 1663 (1957).

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(7) E. R. Garrett, THIS JOURNAL, **79**, 3206 (1957).

(8) S. Winstein, C. R. Lindegren, H. Marshall and L. L. Ingraham, *ibid.* **75**, 147 (1953); C. K. Ingold, "Structure and Mechanisms in Organic Chemistry," Cornell Univ. Press, Ithaca, N. Y., 1953, p. 511.

(9) S. J. Leach and H. Lindley, *Trans. Faraday Soc.*, **49**, 921 (1953).