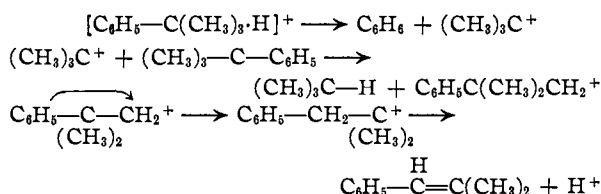


replaceable hydrogen are present to take part in the bimolecular displacement reaction. However, at 166°, hexaethylbenzene reacts to give ethane, isobutane, ethylbenzene, polyethylbenzenes and tar. Under severe conditions, ethylcarbonium ions appear to split off from the aromatic cation. Some of these highly reactive ions abstract a hydride ion from an alkyl side-chain and are converted to ethane. Some dissociate to a proton and ethene; others, after reaction with ethene, form isobutane. The hydrogen-poor alkylaromatics condense to tar.

The change in mechanism with increase in temperature is also illustrated by experiments 9 and 10. At 0°, *t*-butylbenzene disproportionates smoothly into benzene, 1,3-di-*t*-butylbenzene and 1,3,5-tri-*t*-butylbenzene.¹¹ However, at 45°, *t*-butylbenzene forms a complicated mixture including isobutane, benzene and β -alkylstyrenes boiling mostly in the range 220 to 280°. Hydrogen-transfer reactions occur, possibly according to the scheme



The mechanism of alkyl-group transfer in disproportionation reactions therefore depends upon the severity of reaction conditions. Under moderate conditions, simple alkyl disproportionation is a bimolecular reaction between an aromatic cation and a neutral aromatic molecule. Under severe conditions, the aromatic cation dissociates unimolecularly into a neutral aromatic molecule and an alkyl carbonium ion. The carbonium ion then reacts further by isomerization, alkylation, polymerization and hydride-ion abstraction. Disproportionation by the unimolecular mechanism is accompanied by a considerable amount of side reaction and may lead to a complex product.

(11) This material, a white crystalline solid, m.p. 73°, b.p. 248°, is apparently a new compound not previously reported in the literature. Evidence for its identification will be presented in a subsequent paper.

WHITING, INDIANA

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF MERCK & Co., INC.]

Reduction of Lactones to Hydroxyaldehydes with Lithium Aluminum Hydride

BY GLEN E. ARTH

RECEIVED JANUARY 22, 1953

The addition of a solution of one-fourth of a mole of lithium aluminum hydride to a solution of one mole of α -methyl- δ -caprolactone has provided a good yield of α -methyl- δ -hydroxycaproaldehyde. The latter compound was dehydrated to 3,4-dihydro-2,5-dimethyl-2,H-pyran. This new partial reduction reaction has been successfully applied to γ -valerolactone and (-)- α -hydroxy- β , β -dimethyl- γ -butyrolactone (pantoyllactone).

Hexoses have been prepared in a practical manner by the partial reduction of polyhydroxy- γ -lactones with sodium amalgam.¹ This partial reduction fails when applied to non-hydroxylated lactones.² Lithium aluminum hydride³ in excess reduces saturated γ - and δ -lactones to 1,4- and 1,5-diols, respectively. The same reagent is reported⁴ to reduce α -angelica lactone to γ -acetopropanol and β -angelica lactone to the diol. In 1949, Friedman⁵ described an interesting partial reduction of amides and nitriles to aldehydes. Similarly Claus and Morgenthau⁶ disclosed the partial reduction of orthoesters to the corresponding acetals using lithium aluminum hydride and Wolfrom and Wood⁷ used sodium borohydride to replace sodium amalgam in the classical partial reduction of sugar lactones.

An attractive synthesis of γ - and δ -hydroxyaldehydes would be provided by a partial reduction of the corresponding lactones. The latter are, in

many cases, readily prepared. For this partial reduction to be successful the intermediate must be less easily reduced than the starting lactone. It is clear that an aldehyde would not fulfill this condition. However, should an intermediate in this reduction, such as II (R = LiAlH₄), arising from I by addition of lithium aluminum hydride to the lactone carbonyl,³ prove more resistant to reduction than the starting lactone, or if an intermediate should precipitate then the desired effect could be achieved. *The addition of lithium aluminum hydride to the lactone (one-fourth mole of reducing agent per mole of lactone) does indeed effect the desired partial reduction in good yield.* Since all of the available hydrogen is used, it would appear that II (R = LiAlH₄) is first formed, is soluble, and reacts successively with three more molecules of lactone until V (whatever its fine structure) is formed and precipitates. The hydroxyaldehydes are isolated by extraction of the acidified reaction mixture and purified by distillation. In this manner α -methyl- δ -caprolactone (I) was reduced to α -methyl- δ -hydroxycaproaldehyde (II, R = H) or IIa; γ -valerolactone gave γ -hydroxyvaleraldehyde (III, R = H) or IIIa; (-)- α -hydroxy- β , β -dimethyl- γ -butyrolactone (pantoyllactone) gave α , γ -dihydroxy- β , β -dimethylbutyraldehyde (one-half mole of lithium aluminum hydride per mole of lactone was used in this case). All of the hydroxy-

(1) Cf. E. Fischer, *Ber.*, **22**, 2204 (1889); N. Sperber, H. Zaugg and W. Sandstrom, *THIS JOURNAL*, **69**, 915 (1947).

(2) F. C. Whitmore, "Organic Chemistry," D. Van Nostrand Co., Inc., New York, N. Y., 1931, pp. 146, 420-444.

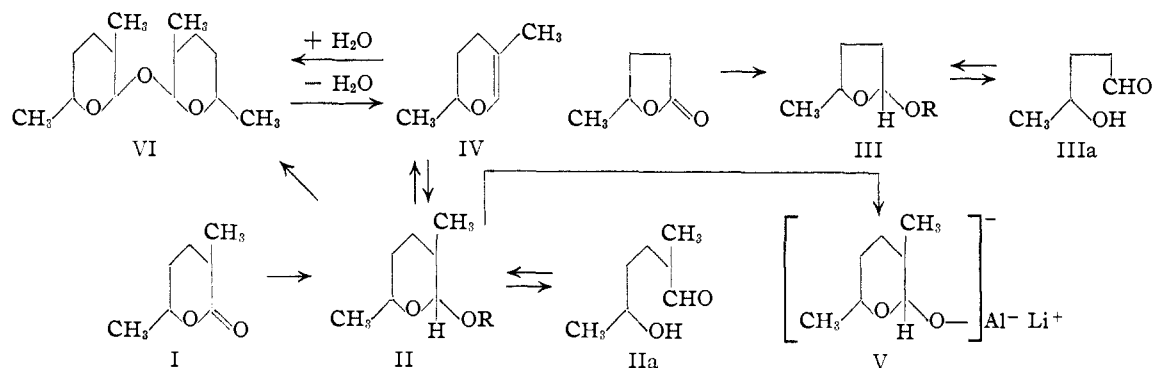
(3) W. G. Brown in R. Adams, "Organic Reactions," Vol. VI, John Wiley and Sons, Inc., New York, N. Y., 1951, p. 469.

(4) F. A. Hochstein, *THIS JOURNAL*, **71**, 305 (1949).

(5) L. Friedman, Abstracts of Papers, 116th Meeting A.C.S., Sept., 1949, p. 5M.

(6) C. J. Claus and J. L. Morgenthau, Jr., *THIS JOURNAL*, **73**, 5005 (1951).

(7) M. L. Wolfrom and Harry B. Wood, *ibid.*, **73**, 2933 (1951).



aldehydes formed nicely crystalline 2,4-dinitrophenylhydrazones and were analyzed as such. Phthalide, subjected to the same reducing conditions, gave only small amounts of *o*-hydroxymethylbenzaldehyde (shown by 2,4-dinitrophenylhydrazone formation), starting material and the usual diol being isolated in approximately equal quantities.

The dehydration of α -methyl- δ -hydroxycaproaldehyde (II, R = H)⁸ by distillation from fused potassium bisulfate provided 3,4-dihydro-2,5-dimethyl-2,4-pyran (IV) in 72% yield. The latter compound could be converted to its parent hydroxyaldehyde by treatment with aqueous acid. Though γ - and δ -hydroxyketones⁹ have been dehydrated to dihydrofurans and dihydropyrans, respectively, this dehydration of a δ -hydroxyaldehyde to a dihydropyran as a preparative method appears, curiously enough, to have been overlooked. Thus Paul¹⁰ in discussing the preparation of δ -hydroxyvaleraldehyde from dihydropyran claimed that the former tended to give the latter when heated with acid but did not describe an experiment in which dihydropyran was actually isolated. It is possible that the first step in the dehydration is the formation of the anhydro dimer VI¹¹ and that this compound then loses water to give the dihydropyran.

Acknowledgment.—The author gratefully acknowledges the valuable suggestions and encouragement received from Dr. Lewis H. Sarett during the course of this work.

Experimental¹²

α -Methyl- β -hydroxycaproaldehyde (IIa).—A solution of 12.8 g. (0.1 mole) of α -methyl- β -caprolactone¹³ in 30 ml. of dry tetrahydrofuran was cooled to -10 to -15° and stirred while 25 ml. of a 4% solution of lithium aluminum hydride (1 g., slightly over 0.025 mole) in tetrahydrofuran was slowly added over a 20-minute period. The initial temperature was maintained during the addition. After the reducing agent had been added, stirring was continued for an hour while the reaction mixture gradually warmed to room tem-

perature. Approximately two-thirds of the solvent was evaporated *in vacuo* and the semi-solid residue was added to a mixture of ice (40 g.) and 11 ml. of 5 *M* sulfuric acid (0.055 mole). The product was extracted into ether. The ethereal extract was washed once with saturated aqueous sodium sulfate, dried and distilled. The product, α -methyl- β -hydroxycaproaldehyde, IIa or II (R = H), 8.4 g. (64.5%), boiled at $39-40^\circ$ (0.3 mm.). A sample of the product was converted to its 2,4-dinitrophenylhydrazone, m.p. $102-103^\circ$, by conventional methods.

Anal. Calcd. for $C_{13}H_{18}N_4O_5$: C, 50.32; H, 5.85; N, 18.06. Found: C, 50.17; H, 5.59; N, 18.33.

When the reaction was repeated using ether or tetrahydrofuran or mixtures of these solvents the yields varied between 64 and 84%. Initially, solutions of lithium aluminum hydride were standardized by the method of Krytnitsky.¹⁴ Later results showed that in most cases the hydride would provide a reduction capacity equivalent to 85% of the weight of the hydride taken.

γ -Hydroxyvaleraldehyde (IIIa).—Using conditions as described above, 20 g. (0.2 mole) of γ -valerolactone was reduced with 65 ml. of an 0.84 *M* solution of lithium aluminum hydride in tetrahydrofuran. The product, IIIa or III (R = H), b.p. 83° (13 mm.), weighed 11.8 g.; 2,4-dinitrophenylhydrazone, m.p. $125-127^\circ$.

Anal. Calcd. for $C_{11}H_{14}N_4O_5$: C, 46.81; H, 5.0; N, 19.85. Found: C, 46.52; H, 4.82; N, 19.87.

α,γ -Dihydroxy- β,β -dimethylbutyraldehyde.—A solution of 6 g. (0.05 mole) of (–)- α -hydroxy- β,β -dimethyl- γ -butyrolactone (pantoylactone) in 30 ml. of tetrahydrofuran was stirred and cooled to -30° while 34 ml. (10% excess over 0.025 mole) of an 0.84 *M* solution of lithium aluminum hydride in tetrahydrofuran was added during the course of 30 minutes. The mixture was stirred for an additional hour while it attained room temperature. Approximately half of the solvent was removed by evaporation *in vacuo* (15 mm.). To the remaining semi-solid material was added a mixture of 3.1 ml. of concentrated sulfuric acid and 50 g. of ice. Two layers formed. The upper layer contained the product dissolved in tetrahydrofuran and was separated. Distillation of the product, α,γ -dihydroxy- β,β -dimethylbutyraldehyde, b.p. 70° (0.05 mm.), was accompanied by decomposition. Its 2,4-dinitrophenylhydrazone, m.p. $172-174^\circ$, was prepared in the usual manner.

Anal. Calcd. for $C_{12}H_{16}N_4O_5$: C, 46.15; H, 5.17; N, 17.94. Found: C, 46.40; H, 5.05; N, 18.21.

3,4-Dimethyl-2,5-dihydro-2,4-pyran (IV).—In a 10-ml. distilling flask (Claisen) was placed 100 mg. of fused and powdered potassium acid sulfate and 6.7 g. of α -methyl- δ -hydroxycaproaldehyde (II, R = H) or IIa. The flask was heated to $160-180^\circ$ by means of an oil-bath. The dihydropyran-water mixture distilled quite rapidly at $110-120^\circ$. The distillate, in ether, was washed once with saturated sodium bicarbonate and dried with sodium sulfate. The solvent was evaporated and the product, IV, was distilled at atmospheric pressure; yield, 4.5 g. (72%), b.p. $112-123^\circ$, n_D^{25} 1.4375.

Anal. Calcd. for $C_7H_{12}O$: C, 74.95; H, 10.79. Found: C, 75.06; H, 11.10.

To a mixture of 5 ml. of ethanol and 5 ml. of 2.5 *N* hy-

(8) B. Helferich, *Ber.*, **52**, 1123, 1801 (1919). See also C. D. Hurd and W. H. Saunders, *This Journal*, **74**, 5324 (1952), who have shown that γ - and δ -hydroxyaldehydes, at equilibrium, are predominantly in their cyclic hemiacetal form such as II (R = H) or III (R = H).

(9) A. Lipp, *Ber.*, **22**, 1199 (1889); *Ann.*, **289**, 187 (1896).

(10) R. Paul, *Bull. soc. chim.*, [5] **1**, 971 (1934).

(11) Reported in many other analogous cases, cf. R. Paul reference 10. High boiling products are always present as still residues.

(12) The microanalyses are the contributions of L. M. Anderson, G. E. Clinton, L. E. May, W. K. Humphrey and R. N. Boos. All melting points were determined on the Koffler micro-hot stage and are therefore corrected.

(13) L. Ruzicka, *Helv. Chim. Acta*, **2**, 744 (1919).

(14) J. A. Krytnitsky, J. E. Johnson and W. H. Carhart, *Ind. Eng. Chem., Anal. Ed.*, **20**, 311 (1948).

drochloric acid saturated with 2,4-dinitrophenylhydrazine was added 0.1 ml. of the pyran IV. The mixture was heated to its boiling point for a few minutes. From the

cooled solution was obtained the 2,4-dinitrophenylhydrazone of IIa (see above), m.p. and mixed m.p. 102–103°. RAHWAY, N. J.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, DUKE UNIVERSITY]

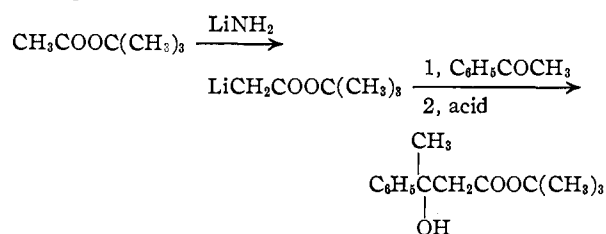
Synthesis of N,N-Dialkyl- β -hydroxyamides from N,N-Dialkylamides and Ketones Using Lithium Reagents¹

BY W. H. PUTERBAUGH² AND CHARLES R. HAUSER

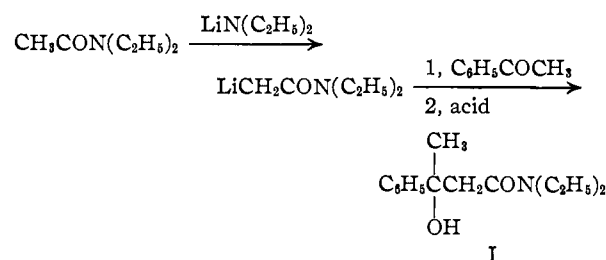
RECEIVED JANUARY 19, 1953

The aldol condensation method described previously for preparing β -hydroxy esters from esters and ketones or aldehydes by means of lithium amide has been adapted to the synthesis of N,N-dialkyl- β -hydroxyamides from N,N-dialkylamides and ketones by employing the appropriate lithium dialkylamide. This new method appears to be as satisfactory as the extension of the Reformatsky reaction described by other workers. Certain of the β -hydroxy amides were dehydrated to form the corresponding α,β -unsaturated amides.

Recently, we³ described a new method for the synthesis of β -hydroxy esters that involved an aldol condensation between esters and ketones or aldehydes. The reaction, which was effected by lithium amide, may be illustrated with *t*-butyl acetate and acetophenone.



The present paper describes the analogous aldol condensation of certain N,N-dialkylamides with ketones by means of the corresponding lithium dialkylamide (prepared from lithium phenyl and dialkylamine) to form N,N-dialkyl- β -hydroxyamides. The method may be illustrated with N,N-diethylacetamide and acetophenone.



An α -hydrogen of the N,N-diethylacetamide was first metalated, and the resulting lithio derivative then condensed with the ketone. In contrast to esters which may self-condense unless the intermediate lithio ester is soon treated with the ketone,³ N,N-diethylacetamide showed no such tendency for self-condensation.⁴

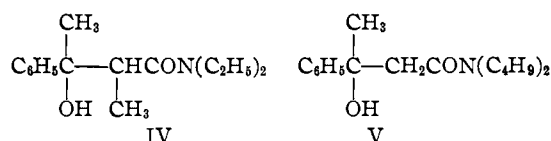
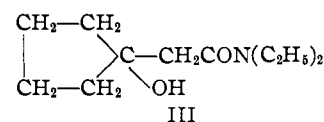
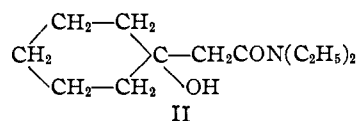
(1) Paper XLIX on Condensations.

(2) Carbide and Carbon Chemicals Company Fellow, 1950–1952.

(3) C. R. Hauser and W. H. Puterbaugh, *THIS JOURNAL*, **76**, 1068 (1953).

(4) Whereas isopropyl acetate gave a 54% yield of self-condensation product on treatment with lithium amide for 15 minutes in liquid ammonia followed by 40 minutes in ether at -70° , N,N-diethylacetamide gave none of its self-condensation product on treatment with lithium diethylamide for 40 minutes in ether at room temperature.

N,N-Diethylacetamide was also condensed with cyclohexanone and cyclopentanone to form β -hydroxyamides II and III, respectively. Similarly, N,N-diethylpropionamide and N,N-di-*n*-butylacetamide were condensed with acetophenone to give β -hydroxyamides IV and V, respectively. The yields were reasonably good (Table I).



However, N,N-diethylacetamide and N,N-diethylpropionamide failed to condense satisfactorily with *p*-nitroacetophenone even on application of the inverse addition technique, which was previously applied successfully in corresponding condensations with esters.³

In most of these reactions, considerable amounts of the original ketones were recovered. This has been taken into account in the calculations of the yields of condensation products given in parentheses in Table I. The recovery of ketone may indicate either that the reaction time was not sufficient for complete condensation or that part of the ketone underwent, with the reactive intermediate, "enolization" involving an α -hydrogen of the ketone. Since the reaction of *p*-nitroacetophenone with the intermediate was permitted to proceed longer than usual and yet the ketone was largely recovered, enolization appears to have predominated. Such enolizations have been observed previously with lithio *t*-butyl isobutyrate and acetophenone,³ and in certain Reformatsky reactions.⁵

The reaction of N,N-diethylacetamide with acetophenone was also effected by means of lithium

(5) See M. S. Newman, *THIS JOURNAL*, **64**, 2131 (1942).