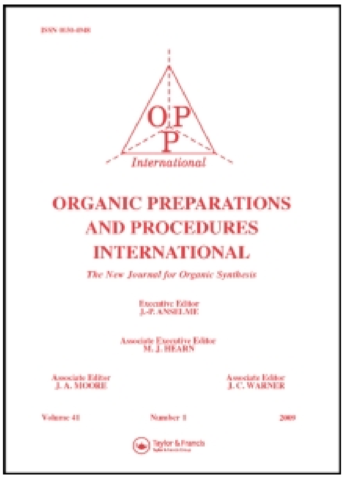

Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

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To cite this Article Cha, Jin Soon , Min, Soo Jin , Lee, Jae Cheol , Lee, Heung Soo and Lee, Sung Eun(1992) 'TRANSFORMATION OF CARBOXYLIC ESTERS TO ALDEHYDES WITH LITHIUM *tris*(DIETHYLAMINO)ALUMINUM HYDRIDE', Organic Preparations and Procedures International, 24: 3, 335 — 337

To link to this Article: DOI: 10.1080/00304949209355895

URL: http://dx.doi.org/10.1080/00304949209355895

ORGANIC PREPARATIONS AND PROCEDURES INT., 24 (3), 335-368 (1992)

OPPI BRIEFS

TRANSFORMATION OF CARBOXYLIC ESTERS TO ALDEHYDES WITH LITHIUM *tris*(DIETHYLAMINO)ALUMINUM HYDRIDE

Submitted by (1/21/92)

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The development of a simple synthetic route to aldehydes from carboxylic esters is an important goal in organic chemistry. Many useful reducing agents for such a transformation have been reported, e. g., lithium tri-*tert*-buthoxyaluminum hydride,[1] diisobutylaluminum hydride,[2] sodium diisobutylaluminohydride,[3] and *bis*(4-methyl-1-piperazinyl)aluminum hydride.[4] Recently, we have synthesized a new class of reducing agents, dialkylamino-substituted derivatives of lithium aluminum hydride, and applied them for selective reduction of organic functionalities.[5] In the course of this study, we found that lithium *tris*(diethylamino)aluminum hydride (LTDEA) effects the transformation of esters to aldehydes in good yields at -78°.

$$RCO_2R' \; + \; Li(Et_2N)_3AlH \longrightarrow RCHO$$

The reagent reduces aliphatic carboxylic esters to aldehydes in yields of 55-80%. Diethyl adipate is converted to the corresponding dialdehyde with 2.2 equiv of LTDEA in a yield of 70%. α,β-Unsaturated esters such as ethyl crotonate and ethyl cinnamate also undergo the reduction to afford the corresponding olefinic aldehydes in yields of 60-80%. The reduction of aromatic esters by this reagent provides the corresponding aldehydes in 65-99% yields. The unsubstituted benzoates with a variety of alcohol portions are reduced to benzaldehyde in yields of 70-80%, showing no significant difference in the yields. Methyl-substituted benzoates such as ethyl 3- and 4-methylbenzoates afford the corresponding aldehydes in 73-75% yields. Finally, chloro and nitro groups on the benzene ring are readily accommodated, giving the aldehydes in better than 95% yield.

The reaction also provides a simple procedure for the isolation of the aldehydes products, by removal of the diethylammonium salt formed after hydrolysis of the reaction mixture.

TABLE 1. Yields of Aldehydes in the Reduction of Representative Carboxylic Esters with Lithium *tris*(Diethylamino)aluminum Hydride in Tetrahydrofuran at -78°[a]

Ester	Reaction Time, hrs	Yield of Aldehyde (%)[b]
Isopropenyl acetate	1	79
Ethyl butyrate	3	56, 54[c]
Ethyl isobutyrate	3	60
Ethyl isovalerate	3	76 (64)[e]
Ethyl caproate	1	67, 64[c]
Ethyl caprylate	1	76 (63)[e]
Diethyl adipate	1	70
Ethyl crotonate	1	68
Ethyl cinnamate	3	60
Methyl benzoate	3	70
Ethyl benzoate	3	79, 70[d]
Butyl benzoate	3	70
Phenyl benzoate	3	76
Ethyl 3-methylbenzoate	3	73
Ethyl 4-methyl benzoate	3	75, 72[d]
Methyl 3-chlorobenzoate	3	95, 90[d]
Methyl 4-chlorobenzoate	3	99, 94[d] (90)[e]
Ethyl 4-nitrobenzoate	3	95

a) Treated with 1 equiv of reagent for aliphatic and 1.1 equiv for aromatic esters. b) Analysis with 2,4-dinitrophenylhydrazine. c) 1 Equiv of reagent was added. d) 1.1 Equiv of reagent was added. e) Isolated yield. f) 2.2 Equiv of reagent was added.

EXPERIMENTAL SECTION

All glassware used was dried thoroughly in a drying oven, assembled hot, and cooled under a stream of dry nitrogen prior to use. All reactions and manipulations of air- and moisture-sensitive materials were carried out under a dry nitrogen atmosphere. All chemicals were commercial products of the highest available purity, which were further purified by standard methods before use. Tetrahydrofuran (THF) was distilled from benzophenone-sodium ketyl. Lithium aluminum hydride (LAH) was used directly as received from Aldrich. Yields reported in all cases are of analytically pure compounds unless otherwise specified. Melting points and boiling points reported here are uncorrected. Al-27 NMR spectra were recorded on a Bruker WP 80 SY spectrometer. The chemical shifts are with reference to $Al(H_2O)_6^{3+}$. GC analyses were carried out using a Hewlett-Packard 3390A integrator/plotter.

Preparation of Lithium *tris*(Diethylamino)aluminum Hydride (LTDEA) in THF.- To an oven-dried, 500-mL flask fitted with a side arm and a reflux condenser leading to a mercury bubbler was added 100 mL of 2 M solution of LAH in THF and the solution was cooled to 0°. To this solution was added 46 g of diethylamine (630 mmol, 5% excess) dropwise with vigorous stirring. The reaction mixture was then stirred for 3 hrs at 0° until the evolution of hydrogen was complete. The resulting LTDEA solution in THF was diluted with THF to be 1.0 M. The Al-27 NMR spectrum of the solution showed a broad singlet at δ 120 ppm and the IR spectrum showed an absorption band at 1695 cm^{-1} for the Al-H stretching vibration.

Reduction of Carboxylic Esters.- The following procedure for the reduction of methyl 4-chlorobenzoate is illustrative. An oven-dried 25-mL flask, fitted with a side-arm and a bent adaptor connected to a mercury bubbler, was charged with 5 mL of 1 M methyl 4-chlorobenzoate solution in THF (0.85 g, 5 mmol). The flask was immersed into a Dry Ice-acetone bath. To this solution was added 5 mL of 1M LTDEA solution in THF (5 mmol) dropwise with vigorous stirring, and the reaction mixture was stirred for 3 hrs at -78°. Analysis with 2,4-dinitrophenylhydrazine indicated a yield of 99%.

The following procedure was used for a larger scale reaction. In the assembly described above, a solution of 8.53 g of methyl 4-chlorobenzoate (50 mmol) in 40 mL of THF solution was charged in the flask and the solution was cooled to -78°. To this solution was injected 50 mL of 1 M LTDEA solution in THF (50 mmol) slowly with vigorous stirring and the mixture was stirred for 3 hrs at -78°. THF was removed at reduced pressure, and then 50 mL of diethyl ether and 50 mL of 4N HCl solution were added. The mixture was stirred overnight at room temperature, saturated with NaCl, and then filtered. The organic layer was washed with 2N HCl solution three times and dried over $MgSO_4$. All the volatile materials were removed at reduced pressure to yield 6.3 g of analytically pure 4-chlorobenzaldehyde (90%), mp. 48-50°. The PMR spectrum agreed with that of an authentic sample.

Acknowledgment.- The authors thank the Organic Chemistry Research Center-KOSEF for the financial support.

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