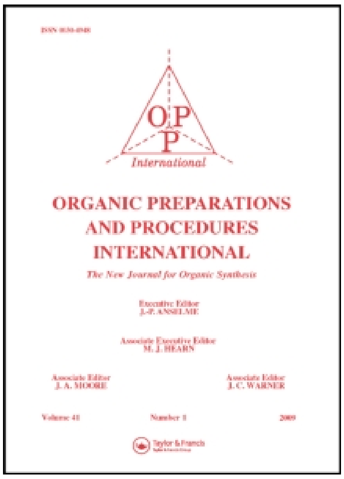

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ONE-POT CONVERSION OF CARBOXYLIC ACIDS TO ALDEHYDES BY TREATMENT OF ACYLOXY-9-BORABICYCLO[3,3,1]NONANES WITH LITHIUM *tris*(DIETHYLAMINO)ALUMINUM HYDRIDE

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ONE-POT CONVERSION OF CARBOXYLIC ACIDS TO ALDEHYDES BY TREATMENT OF ACYLOXY-9-BORABICYCLO[3.3.1]NONANES WITH LITHIUM *tris*(DIETHYLAMINO)ALUMINUM HYDRIDE[†]

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The development of simple routes to aldehydes from carboxylic acids is an important goal in organic synthesis. Several reagents[1] including thexylhaloboranes[2] appear to be promising for such direct conversion. In addition, new methodology utilizing the commercially available 9-borabicyclo[3.3.1]nonane (9-BBN) provides another convenient route to aldehydes.[3] The acyloxy moiety of acyloxy-9-BBNs (**1**), readily formed from carboxylic acids and 9-BBN with evolution of 1 equiv of hydrogen (Eq. 1), is readily converted to the aldehyde through treatment with lithium 9-borabicyclo[3.3.1]nonane (Li 9-BBNH) or *tert*-butyllithium and 9-BBN. The acyloxy group of **1** is also readily reduced by lithium aluminum hydride (LAH) in the presence of pyridine and the reduction stops at the aldehyde stage.[4] This interesting reaction suggests that **1** possesses structural and electronic features which facilitate the selective reduction. We found that lithium tris(diethylamino)aluminum hydride (LTDEA, **2**) in the presence of excess pyridine effects this transformation in excellent yields.

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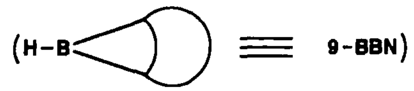

LTDEA can be prepared readily from the reaction of LAH and 3 equiv of diethylamine in THF (Eq. 2).[5] The reagent shows unique reducing characteristics.[6] The acyloxy group of **1** is reduced

$$\mathrm{LiAlH_4} + 3\ \mathrm{Et_2NH} \xrightarrow{0^\circ} \underset{\mathbf{2}}{\mathrm{Li(Et_2N)_3AlH}} + 3\,\mathrm{H_2}\uparrow \qquad (2)$$

by **2** to the aldehyde in fair yields (Table 1). However, in the presence of 2 equiv of pyridine the reduction stops at the aldehyde stage and hydrolysis affords very high yields of the aldehydes (Eq. 3).

$$\mathbf{1} \xrightarrow{\text{(2 equiv.) pyridine}} \xrightarrow{\text{LTDEA}} \xrightarrow{H_3O^+} \text{RCHO} \qquad (3)$$

This system reduces aliphatic carboxylic acids to aldehydes in approximately 0.5 hr at 0° in yields of more than 90%. Alicyclic derivatives, such as cyclopropane- and cyclohexanecarboxylic acids, give yields of 90%. α-Substituted acids and bromoacetic acid also readily undergoes the reaction to the aldehyde in 87% yield. Diacids, such as succinic, adipic, 1,10-decanedicarboxylic, and maleic, are converted to the corresponding dialdehydes in yields of 91-95%.

The reduction of aromatic carboxylic acids, except for nitrobenzoic, affords the corresponding aldehydes in 90-98% yields. Unsubstituted acids, such as benzoic and naphthoic, are readily reduced to aldehydes in essentially quantitative yields. Alkyl, alkoxy and halo groups on the benzene ring are readily accommodated to yield more than 90%. However, the yields for nitrobenzoic acids are somewhat lower (about 80%) possibly due to reduction of the nitro group itself. Dicarboxylic aromatic acids, such as phthalic and terephthalic, are also readily reduced to the dialdehydes in greater than 90% yields.

TABLE 1. Yields of Aldehydes by LTDEA Reduction of Carboxylic Acids[a]

Acid	Yield (%)[b]	Acid	Yield (%)[b]
acetic	92	maleic	91
butyric	93	benzoic	96 (81)[c] (85)[d]
caproic	91 (70)[c] (80)[d]	*o*-toluic	92
decanoic	90	*m*-toluic	90
pentadecanoic	93	*p*-toluic	94 (98)[c]
palmitic	92	*o*-anisic	92
stearic	93 (72)[c]	*m*-anisic	91
isobutyric	90 (49)[c]	*p*-anisic	98 (80)[c]
isopentanoic	90	*o*-chlorobenzoic	92
cyclopropanecarboxylic	90	*m*-chlorobenzoic	94
cyclohexanecarboxylic	91 (78)[d]	*p*-chlorobenzoic	96 (81)[c] (88)[d]
phenylacetic	93	*o*-nitrobenzoic	81
diphenylacetic	94 (81)[c]	*m*-nitrobenzoic	80
triphenylacetic	96	*p*-nitrobenzoic	85 (58)[c]
bromoacetic	90	α-naphthoic	97
6-bromohexanoic	87	β-naphthoic	98
succinic	92	phthalic	90
adipic	94	terephthalic	93
1,10-decanedicarboxylic	95		

a) Two equivalents of pyridine were added to **1** which was then treated with one equiv of LTDEA for 0.5 hr. b) Yields based on 2,4-dinitrophenylhydrazones. c) No pyridine added. d) Yields based on the analytically pure aldehydes isolated by the sodium bisulfite procedure.[2b]

The presence of pyridine in the reduction with LTDEA provides significant yield enhancement. At present, the role of pyridine in this reduction is not clear, but we believe that it coordinates to the boron atom of **1** resulting in a borane-pyridine complex which inhibits hydride transfer from LTDEA to the boron atom.

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 purity, which were carefully purified by standard methods before use. The carboxylic acids were commercial products and were purified either by distillation or by recrystallization. Tetrahydrofuran (THF) was distilled from benzophenone-sodium ketyl and all other solvents (*n*-pentane and diethyl ether) were thoroughly dried over molecular sieves and distilled. 9-Borabicyclo[3.3.1]nonane (9-BBN) and lithium aluminum hydride (LAH) were used directly as received from Aldrich.

All of the compounds prepared have been fully characterized by ^{1}H and ^{27}Al NMR spectra. Yields reported in all cases are of analytically pure compounds unless otherwise specified. Melting points and boiling points reported are uncorrected. ^{1}H NMR spectra were recorded on a Varian EM-360A instrument. ^{27}Al NMR spectra were recorded on a Bruker WP 80SY spectrometer. ^{27}Al NMR chemical shifts are with reference to $Al(H_2O)_6^{6+}$. GC analyses were carried out using a Hewlett-Parkard Model 5790A FID chromatograph equipped with a Hewlett-Parkard 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 stopcock leading to mercury bubbler was added 100 mL of a 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 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 ^{27}Al NMR spectrum of the solution showed a broad singlet at δ 120.

Reduction of Carboxylic Acids.- The following reduction is typical of the procedure utilized in the quantitative analysis with 2,4-dinitrophenylhydrazine. Benzoic acid (6.47 g, 53 mmol) and 9-BBN (12.93 g, 53 mmol) were placed in an oven-dried, 200-mL flask fitted with a side arm and a bent adapter, which was connected to a mercury bubbler. To this mixture was added 50 mL of THF and the slurry was stirred at room temperature until hydrogen was no longer evolved. The reaction mixture was then cooled to 0° and 8.56 g (106 mmol) of pyridine and 53 mL of LTDEA (1.0 M, 53 mmol) in THF were injected in sequence at 0°. The reaction mixture was withdrawn and subjected to analysis with 2,4-dinitrophenylhydrazine, showing a yield of 96% : mp of the hydrazone 235-236° (lit. mp 237°). The rest of the reaction mixture (50 mmol) was further tested for isolating the aldehyde. In a small-scale (3 mmol) blank experiment without addition of pyridine, the analysis with 2,4-dinitrophenylhydrazine showed a yield of 81%.

Sodium Bisulfite Adduct Formation and Regeneration of Aldehydes.- The procedure for the adduct formation and regeneration of benzaldehyde in the reaction mixture is representative. After reaction of benzoyloxy-9-BBN (53 mmol) with the reagent for 0.5 hr at 0° (*vide supra*), an aliquot of the reaction mixture was withdrawn for analysis with 2,4-dinitrophenylhydrazine. Then the remaining reaction mixture was hydrolyzed with 70 mL of 3 N HCl at room temperature. The mixture was saturated with NaCl, and the organic layer was separated, and poured into 75 mL of a saturated aqueous $NaHSO_3$ solution. The mixture was stirred for 1 hr and cooled in an ice-water bath to ensure complete crystallization of the bisulfite adduct, which was then collected by filtration and washed with 3x25 mL of pentane and dried. The solid adduct was placed in 50 mL of a 37% formaldehyde solution were added. The mixture was stirred for 1 hr. The pentane layer was separated and dried with anhydrous $MgSO_4$. Evaporation gave an 85% yield (4.5 g) of analytically pure benzaldehyde. GC analysis showed >99% purity and the ^1H NMR spectrum agreed with that of an authentic sample.

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†. This paper is dedicated to Professor Herbert C. Brown, Wetherill Research Professor of Chemistry, Purdue University on the occasion of his 80th birthday. This is the first in a series of papers dealing with the Selective Reduction with Lithium *tris*(dialkylamino)aluminum Hydrides.

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5. The ^{27}Al NMR spectrum showed a broad singlet at δ 120 ppm relative to $Al(H_2O)_6^{3+}$.

6. The selective reducing characteristics of LTDEA will be described further in this series.

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