REDUCTION OF SOME DERIVATIVES OF ACIDS TO ALDEHYDES WITH SODIUM DIHYDRODIISOBUTYLALUMINATE

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We have previously described [1-4] the reduction of various carboxylic acid derivatives to aldehydes with diisobutylaluminum hydride. In this investigation we have studied the reduction of esters, nitriles, and N,N-disubstituted amides of carboxylic acids to aldehydes with sodium dihydroiisobutylaluminate $NaAl(i\text{-}C_4H_9)_2H_2$, which is readily prepared from diisobutylaluminum hydride and sodium hydride [5]. It was found that by the reduction of carboxylic esters in diethyl ether at −70 to −60° aldehydes are formed in good yields. A less satisfactory yield of aldehyde (though higher than when diisobutylaluminum hydride is used [4]) was obtained in the reduction of ethyl cinnamate (Table 1). The reduction of esters proceeds by the scheme

$$2RCOOR' + NaAl\,(i\text{-}C_4H_9)_2H_2 \rightarrow [RCH\,(OR')\,O]_2\,Al\,(i\text{-}C_4H_9)_2\,Na \xrightarrow{H_2O} 2RCHO.$$

We also carried out the reduction of 4-hydroxyvaleric acid γ-lactone, and we then obtained a good yield of 4-hydroxyvaleraldehyde.

TABLE 1. Yields of Aldehydes in the Reduction of Carboxylic Derivatives with Sodium Dihydrodiisobutylaluminate

Compound	Reaction temp., °C	Yield of aldehyde
Ethyl butyrate	−70	80
Methyl hexanoate	−70	74
Ethyl benzoate	−70	82
Propyl phenylacetate	−70	94
Ethyl cinnamate	−70	30
Dimethyl sebacate	−70	62
Diisobutyl phthalate	−70	73
4-Hydroxyvaleric lactone	−70	70
Benzonitrile	20	77
Cinnamonitrile	0	55
Butyronitrile	30-35	36
N,N-Diethylbenzamide	0	36
N-Ethylbenzanilide	0	35
N,N-Dimethylbutyramide	0	45
N,N-Diethylhydrocinnamamide	0	26
N,N-Diethylnicotinamide	0	55

The results of the reduction of nitriles to aldehydes and with aid of sodium dihydrodiisobutylaluminate are presented in Table 1. The reduction of nitriles can be represented as follows:

$$2RCN + NaAl(i\text{-}C_4H_9)_2H_2 \rightarrow (RCH = N)_2Al(i\text{-}C_4H_9)_2Na \xrightarrow{H_2O} 2RCHO.$$

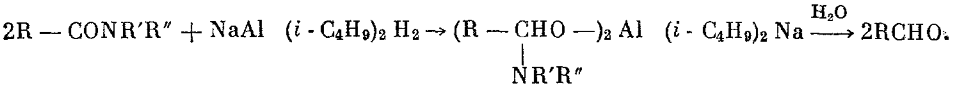
Investigation of the effect of temperature on this reaction showed that at −70° nitriles are scarcely reduced at all by sodium dihydrodiisobutylaluminate. In contrast to this, at this temperature diisobutylaluminum hydride reduces nitriles to aldehydes in good yield (e.g., at −70° benzaldehyde was obtained from benzonitrile in more than 80% yield). It was found also that there is an appreciable difference in the rates of reduction of aromatic and aliphatic nitriles with sodium dihydrodiisobutylaluminate. Thus, in the case of benzonitrile a considerable yield of benzaldehyde (up to 35%) is obtained in five hours even at −30°, and at room temperature the yield of aldehyde is 80%, but in the case of butyronitrile and hexanenitrile scarcely any reduction occurs at −30° and satisfactory results are obtained only at the boiling point of ether, though there is then formed an appreciable amount of amine (Table 2).

The difference in the rates at which ester and nitrile groups are reduced with sodium dihydrodiisobutylaluminate may be applied in the selective conversion of an ester group into an aldehyde group in presence of a nitrile group. Thus, in the reduction of ethyl 5-cyanovalerate in ethereal solution at −60° we obtained a 60% yield of 5-cyanovaleraldehyde:

$$2CN(CH_2)_4COOC_2H_5 + NaAl(i\text{-}C_4H_9)_2H_2 \xrightarrow{H_2O} CN(CH_2)_4CHO.$$

The reduction of N,N-disubstituted amides (see Table 1) leads in satisfactory yields to aldehydes (30-50%). Again a marked temperature dependence of the yield of aldehyde is found: at −70° no aldehyde is formed (see Table 2), and satisfactory yields are obtained only at 0-20°. In this respect sodium dihydrodiisobutylaluminate differs from diisobutylaluminum hydride, which readily reduces amides to aldehydes at −70 to −60°. In the case of the reduction of amides with sodium dihydrodiisobutylaluminate no marked difference is observed between aliphatic and aromatic compounds; there is no substantial difference also between alkylanilides and dialkylamides as in the case of reduction with diisobutylaluminum hydride [2].

The reduction of N,N-disubstituted amides goes by a scheme analogous to that given above:



$$2R-CONR'R'' + NaAl(i\text{-}C_4H_9)_2H_2 \rightarrow (R-\underset{NR'R''}{C}HO-)_2Al(i\text{-}C_4H_9)_2Na \xrightarrow{H_2O} 2RCHO.$$

The difference in the rates at which ester and amide groupings are reduced makes it possible to reduce the ester grouping selectively to an aldehyde group in presence of an amide grouping. By the reduction of ethyl N,N-diethylsuccinamate with sodium dihydrodiisobutylaluminate in ethereal solution at −55° we obtained N,N-diethylsuccinamaldehyde in 47% yield:

$$2(C_2H_5)_2NCOCH_2CH_2COOC_2H_5 + NaAl(i\text{-}C_4H_9)_2H_2 \xrightarrow{H_2O} (C_2H_5)_2NCOCH_2CH_2CHO.$$

We may conclude from our investigation that in reduction reactions sodium dihydrodiisobutylaluminate is a less reactive reducing agent than diisobutylaluminum hydride.

EXPERIMENTAL

Reduction of carboxylic esters. The reduction was carried out by the procedure described for the reduction of carboxylic esters with diisobutylaluminum hydride at −75 to −70°. The reaction mixture was decomposed by the addition of commercial methanol. In some cases, for the rapid determination of the yield and identification of the aldehyde, the reaction solution or an aliquot part of it was decomposed with a cooled sulfuric acid solution of 2,4-dinitrophenylhydrazine. The constants of the aldehydes obtained and of their 2,4-dinitrophenylhydrazones correspond completely to data in the literature.

Reduction of methyl hexanoate. A solution of 7.6 g of sodium dihydrodiisobutylaluminate in 20 ml of dry ether was added dropwise to a solution of 11.7 g of methyl hexanoate in 30 ml of ether at −70°. One hour after the addition of the hydride 30 ml of methanol was added to the reaction mixture at −70°. The temperature of the mixture was cautiously brought up to that of the room, and it was washed with water until neutral to litmus. From the ethereal solution by distillation through a column we obtained 6.7 g (74%) of hexanal, b. p. 128-129°, together with 2.4 g of the original ester.

TABLE 2. Relation of the Yield of Aldehyde in the Reduction of Nitriles and N,N-Disubstituted Amides to the Reaction Temperature (reaction time 5 hours)

Compound	Reaction temp., °C	Yield of aldehyde, %	Compound	Reaction temp., °C	Yield of aldehyde, %
Benzonitrile	−70	< 1	N,N-Diethylbenzamide	−70	0
Ditto	−30	35	Ditto	0	36
"	0	50	N-Ethylbenzanilide	−70	0
"	+20	77	Ditto	0	35
Butyronitrile	−70	< 1	N,N-Dimethylbutyramide	−70	0
Ditto	−30	< 1			
"	+30	36	Ditto	0	45

Reduction of nitriles. The reduction of nitriles was carried out by the usual method by the addition of a solution of sodium dihydrodiisobutylaluminate in dry ether to the corresponding amount of the nitrile in ether at the appropriate temperature. The mixture was stirred for one hour at the same temperature and then decomposed by the addition first of 15-20 ml of methanol and then 10% sulfuric acid. In a number of cases after the ether extraction of the acidic aqueous solution it was made alkaline and the alkaline solution was extracted to isolate any amines formed.

Reduction of butyronitrile. At −70°. A solution of 5.9 g of sodium dihydrodisiobutylaluminate in 20 ml of ether was added at −75 to −70° to 4.9 g of butyronitrile in 20 ml of ether. Four hours after the addition of the hydride one-tenth of the reaction mixture was decomposed at −70° with a sulfuric acid solution of 2,4-dinitrophenylhydrazine, when we isolated 0.0105 g of butyraldehyde 2,4-dinitrophenylhydrazone, m. p. 121-122° (0.58% of the theoretical amount). The rest of the reaction mixture was decomposed at −70° by the addition first of 15 ml of methanol and then of 50 ml of 10% sulfuric acid. From the ethereal solution we isolated 3.8 g of the original nitrile, b. p. 118°. On making the aqueous solution alkaline we isolated traces of butylamine (0.5% of the theoretical amount); phenylthiourea compound, m. p. 65°.

At −30°. In the reduction of 6.9 g of butyronitrile at −30° by an analogous procedure we found only traces of butyraldehyde (0.55%) and butylamine (0.6%), and we obtained 5.8 g of unchanged nitrile.

At 30-40°. In the reaction of 14 g of sodium dihydrodiisobutylaluminate dissolved in 50 ml of ether with 11 g of butyronitrile in 30 ml of ether at the boiling point of the latter for five hours we isolated, by extraction of the acidic solution, 3.5 g of butyraldehyde, b. p. 75°, 3.5 g of unchanged nitrile, b. p. 118°, and 0.55 g of 2-ethyl-2-hexenal, b. p. 122-125° (35 mm) (the 2,4-dinitrophenylhydrazone had m. p. 121-123° [6]); after making the aqueous solution alkaline we obtained 1.5 g of butylamine, b. p. 78°.

Reduction of benzonitrile with diisobutylaluminum hydride at −70°. In the reduction of 3.26 g of benzonitrile in 10 ml of toluene at −70° with a solution of 4.5 g of diisobutylaluminum hydride in 5 ml of toluene we isolated 2.7 g (80%) of benzaldehyde, b. p. 175°. The 2,4-dinitrophenylhydrazone had m. p. 239° (from acetic acid).

Reduction of amides. The reduction of amides was carried out like the reduction of nitriles.

Reduction of N-Ethylbenzanilide at −70°. A solution of 1.66 g of sodium dihydrodiisobutylaluminate in 10 ml of ether was added to 4.5 g of N-ethylbenzanilide in 20 ml of ether at −70°. After four hours 10 ml of methanol was added to the reaction mixture, and then 30 ml of 10% sulfuric acid was added. Ether was driven off, and we obtained 2 g of unchanged anilide, b. p. 140-143° (5 mm), m. p. 54°. No traces of aldehyde or amine could be detected.

At 0°. By the same procedure, but at 0°, from the same amounts of the starting compounds we isolated 0.75 g of benzaldehyde, b. p. 75-76° (18 mm) (2,4-dinitrophenylhydrazone, m. p. 238°), 0.45 g of N-ethyl-N-phenylbenzylamine, b. p. 163-164° (6 mm) (picrate, m. p. 114-115°), and 2 g of unchanged anilide.

Reduction of N,N-dimethylbutyramide with diisobutylaluminum hydride at −60°. From 6.3 g of the amide in 10 ml of toluene and 7.8 g of diisobutylaluminum hydride in 10 ml of toluene we obtained 2.0 g (51%) of butyraldehyde, b. p. 75°. The 2,4-dinitrophenylhydrazone had m. p. 122°.

Reduction of ethyl 5-cyanovalerate. A solution of 3.4 g of sodium dihydrodiisobutylaluminate in 20 ml of ether was added dropwise to 6.2 of ethyl 5-cyanovalerate in 20 ml of ether at −60 to −50°. One hour after the completion of the addition of the hydride the mixture was decomposed, first with 20 ml of methanol and then with 50 ml of 10% sulfuric acid. Solvent was removed, and we obtained 3.6 g of a substance having b. p. 97-101° (5 mm) and $n^{20}D$ 1.4338, which according to chromatographic analysis consisted of 39% of the starting compound and 61% of 5-cyanovaleraldehyde. The latter was also determined quantitatively through the 2,4-dinitrophenylhydrazone (60%), m. p. 89.5-90.5° (from acetic acid). Found: C 49.22; H 4.61; N 24.05%. $C_{12}H_{13}N_5O_4$. Calculated: C 49.46; H 4.50; N 24.04%.

We then obtained 0.6 g of the product of the crotonic condensation of 5-cyanovaleraldehyde, namely 7-cyano-2-(3-cyanopropyl)-2-heptenal, b. p. 200° (5 mm) and $n^{20}D$ 1.4848; it was identified via its 2,4-dinitrophenylhydrazone, m. p. 166-167° (from acetic acid). Found: C 56.30; H 5.24; N 21.72%. $C_{18}H_{20}N_6O_4$. Calculated: C 56.24; H 5.24; N 21.86%.

The structure of 7-cyano-2-(3-cyanopropyl)-2-heptenal was confirmed by its infrared spectrum, which contained strong bands at 1588 and 2253 cm^{-1}.

Reduction of ethyl N,N-diethylsuccinamate. In the reaction of 3.32 g of the hydride dissolved in 20 ml of ether with 8.04 g of ethyl N,N-diethylsuccinamate in 20 ml of ether at −50° we isolated 5 g of a substance of b. p. 112-115° (5 mm), which according to chromatographic analysis consisted of 53% of the original compound and 47% of N,N-diethylsuccinamaldehyde, which was identified via the 2,4-dinitrophenylhydrazone, m. p. 111.5° (from acetic acid). Found: C 49.33; H 5.70; N 21.00%. $C_{14}H_{19}O_5N_5$. Calculated: C 49.84; H 5.67; N 20.76%.

Reduction of 2-hydroxyvaleric acid γ-lactone. A solution of 2.8 g of the hydride in 15 ml of ether was added at −70° to 3.2 g of 4-hydroxyvaleric lactone. Thirty minutes after the hydride had been added the mixture was decomposed by the addition of 15 ml of methanol and then 50 ml of 10% sulfuric acid. Solvent was removed, and we obtained 2.25 g (70%) of 4-hydroxyvaleraldehyde, b. p. 70° (10 mm). 2,4-Dinitrophenylhydrazone, m. p. 125° (from alcohol) [7].

SUMMARY

1. Sodium dihydrodiisobutylaluminate reduces carboxylic esters to aldehydes in good yields.

2. Sodium dihydrodiisobutylaluminate reduces nitriles and N,N-disubstituted amides to aldehydes in satisfactory yields.

3. With the aid of sodium dihydrodiisobutylaluminate the ester grouping can be selectively reduced to an aldehyde group in presence of a nitrile or amide group.

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