

# Diisopropoxyaluminium Trifluoroacetate: A New off the Shelf Metal Alkoxide Type Reducing Agent for Reduction of Aldehydes and Ketones

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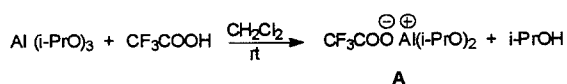
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**Abstract:** A new off the shelf reducing agent, diisopropoxyaluminium trifluoroacetate, has been prepared by reacting aluminium isopropoxide with trifluoroacetic acid in dichloromethane. It is a white solid and stable when stored under dry conditions. Using this reagent various aldehydes and ketones have been reduced to the corresponding alcohols in moderate to quantitative yields, at room temperature in short time.

Aldehydes and ketones can be reduced to alcohols using variety of reagents such as lithium aluminium hydride<sup>1</sup>, sodium borohydride<sup>2</sup>, sodium dithionite<sup>3</sup>, tetra-n-butylammonium cyanoborohydride<sup>4</sup> and others<sup>5</sup> which are commercially available.

Metal alkoxide catalysed transfer hydrogenation is another method that was very often used before the advent of metal hydrides as reducing agents. Amongst these, the Meerwein-Ponndorf-Verley (MPV) reaction using aluminium isopropoxide as catalyst and isopropyl alcohol as hydride source was the preferred method. This is because of its chemoselectivity, mild reaction conditions, ready adaptation in the laboratory and on a large scale<sup>6</sup>. However there are some practical problems in the reaction, such as need for excess of alkoxide, low reaction rate, formation of condensation products, and frequently it is necessary to employ higher reaction temperatures with concurrent removal of acetone. Recently we have reported an accelerated MPV reaction system where aluminium isopropoxide is modified by addition of trifluoroacetic acid<sup>7</sup>. This modified system brings about complete reduction of 4-nitrobenzaldehyde at room temperature within 15 min, in the absence of an added hydride source such as isopropyl alcohol. Thus, in the modified system, aluminium isopropoxide is used as a reagent rather than as a catalyst. In this paper we report preparation of the envisaged reagent as a dry powder that can be stored and used conveniently. This is a new reagent belonging to metal alkoxide class that can be made readily available off the shelf for the reduction of aldehydes and ketones to the corresponding alcohols.

The reagent was prepared by reacting a solution of aluminium isopropoxide in dichloromethane with trifluoroacetic acid followed by removal of volatiles by distillation *in vacuo*<sup>8</sup>.



We believe the reagent could be a salt and have considered the tentative structure **A**. Further studies are in progress to confirm the structure. In order to document the efficiency of preparation of the reagent on larger scale, 50.00 g (250 mmol) of aluminium isopropoxide was reacted with 28.50 g (250 mmol) of trifluoroacetic acid to afford 64.10 g of the reagent (yield: 99.4%).

Various aldehydes and ketones have been reduced using this reagent (Table-1). In the course of our studies for the utility of the reagent, we found that benzaldehyde and 4-nitrobenzaldehyde (entry 1 & 2) were reduced to give their corresponding alcohols in quantitative yields at room temperature and within 15 min, by employing 1 equivalent of the reagent and dichloromethane as solvent<sup>9</sup>. However with other aromatic aldehydes it was noticed that the reduction was comparatively slow and in some cases needed a longer reaction time to achieve reasonably good conversion. 4-Dimethylaminobenzaldehyde and 2-pyridinecarboxaldehyde (entry 8 & 9) could also be reduced and the reactions were complete within half an hour and one hour respectively. This is a striking observation because these substrates contain basic nitrogen and are expected to form a complex with the reagent and to slow down the reaction rate considerably.

**Table 1. Reduction of Aldehydes and Ketones to Alcohols<sup>a</sup>**

entry	aldehyde/ketone	time (h)	alcohol yield (%) <sup>b</sup>
1	Benzaldehyde	0.25	100
2	4-Nitrobenzaldehyde	0.25	100
3	2-Fluorobenzaldehyde	0.50	100
4	Anisaldehyde	0.50	85
5	Salicylaldehyde	2.00	33
6	3,4-Dimethoxybenzaldehyde	0.50	97
7	3-Hydroxy-4-methoxybenzaldehyde	6.00	40
8	4-Dimethylaminobenzaldehyde	0.25	94
9	2-Pyridinecarboxaldehyde	1.00	98
10	Lauraldehyde	0.25	98
11	Isobutyraldehyde	0.25	95
12	2-Phenylpropanal	0.25	98
13	Acetophenone <sup>c</sup>	8.00	85
14	4-Nitroacetophenone <sup>c</sup>	6.00	95
15	Propiophenone <sup>c</sup>	24.00	66
16	Benzophenone <sup>c</sup>	24.00	77
17	Cyclohexanone <sup>d</sup>	3.00	100

<sup>a</sup>Unless otherwise noted, reductions were carried out by using 1 equiv. of reagent in CH<sub>2</sub>Cl<sub>2</sub> at rt. <sup>b</sup>The isolated yields after column chromatography.

<sup>c</sup>The reactions were performed by using 5 equiv of the reagent. <sup>d</sup>The reaction was performed by using 3 equiv of the reagent.

For all the aliphatic aldehydes the reaction was complete within 15 min and yields were very high (entry 10, 11 & 12). Unlike aldehydes, reductions of ketones were very slow. Nevertheless, a good conversion could be achieved by employing the reagent in larger quantity and in a reasonable period of time.

To study the effect of prolonged storage, the reagent was stored in a desiccator for three months before use. No difference in reactivity towards the reduction was observed. This implies that the reagent is stable when stored under dry conditions.

In conclusion a new reagent for the reduction of aldehydes and ketones has been developed. This reagent is effective at room temperature. The reaction conditions are mild, the workup procedure is simple, and the reagent can be stored. This new reagent will make a very valuable addition to the existing reducing agents.

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## References and Notes

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- (8) **Preparation of the reagent:** To a stirred solution of aluminium isopropoxide (10.00 g, 49.02 mmol) in 15 mL of dry dichloromethane in a 100 mL round bottom flask, equipped with a pressure equalizing dropping funnel fitted with calcium chloride guard tube was added dropwise trifluoroacetic acid (5.58 g, 49.02 mmol) over a period of half an hour and stirred for further one hour during which the reaction mixture becomes viscous. This was followed by removal of volatiles by distillation *in vacuo* to get diisopropoxyaluminium trifluoroacetate (DIPAT) as a white powder (12.56 g, 99.31%). DIPAT is highly soluble in dichloromethane, soluble in acetonitrile (22.5 mg/mL), moderately soluble in chloroform, benzene, toluene and insoluble in hexane. (a) mp decomp > 185°C, Anal: C, 36.84; H, 5.28; Al 10.87; (C<sub>8</sub>H<sub>14</sub>O<sub>4</sub>AlF<sub>3</sub> requires C, 37.22; H, 5.47; Al, 10.45) (b) Aluminium was analysed by complexometry, see *Encyclopedia of Industrial Chemical Analysis*; Snell F. D.; Hilton C. L. Eds.; Interscience Publications (John Wiley & Sons, Inc.): New York, **1967**, Vol. 5, p 163.
- (9) **General Procedure for the Reduction:** To a stirred solution of aldehyde (10 mmol) in dichloromethane (20 mL) was added the reagent (10 mmol). The progress of the reaction was monitored by TLC. After being stirred for the specific time interval, the reaction mixture was diluted by addition of dichloromethane (30 mL) and immediately followed by dilute HCl (20 mL) to quench the reaction. The organic layer was separated and aqueous layer was extracted with dichloromethane (2 x 20 mL). The combined organic layers was washed with dilute sodium bicarbonate solution (2 x 30 mL), water (1 x 30 mL) and dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. Solvent was removed *in vacuo* and the residue obtained was chromatographed to isolate the product.