



Aluminium Isopropoxide - TFA, a Modified Catalyst for Highly Accelerated Meerwein - Ponndorf - Verley (MPV) Reduction.

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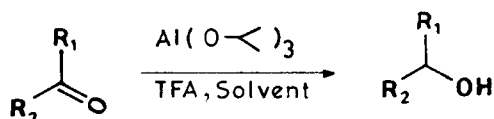
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Abstract : Aldehydes and ketones have been reduced very rapidly in good yields at room temperature by addition of trifluoroacetic acid (TFA) to aluminium isopropoxide (AIP) in MPV reduction.

Recently, interest is being regenerated in MPV reduction as evidenced by a recent review article¹. This is a mild and relatively inexpensive method for reduction of aldehydes and ketones. In the classical method this reduction employs aluminium alkoxides². Recently however transition metal complexes also have been used³. For the reduction aluminum alkoxides are required in more than stoichiometric ratios and very often high temperatures are needed. The reaction is generally completed with in a period of 3 to 8 hours by shifting of equilibrium in the direction of products by a suitable procedure.

With a view for application in asymmetric synthesis we were interested in developing a MPV reduction system using aluminium alkoxide which functions efficiently at room temperature. Literature reports a few studies where replacement of alkoxy groups by electronegative ligands are found to enhance the rate of the reduction⁴. Also there is a report by Rathke et al⁵ who observed good acceleration of rate in Oppenauer oxidation of cyclohexanol by aluminum-t-butoxide with benzaldehyde in presence of protic acids. They found trifluoro acetic acid to be the best catalyst though greatly enhanced aldol condensation by this agent was found to be a large drawback for general application.

We report here a highly practical accelerated MPV reduction system which uses as reducing agent aluminium isopropoxide that is modified by addition of TFA. This modified catalyst is useful for reduction of a number of aldehydes and ketones (Table-1). The attractive features of this system include 1) extremely rapid reaction at room temperature. 2) practically no condensation products are observed. The typical procedure employed for reduction is as follows: To a stirred solution of aluminium isopropoxide and carbonyl compound in benzene, (toluene or methylene chloride may also be used) at room temperature was added trifluoro acetic acid and the reaction was stirred for further 15 minutes. The reaction was then quenched with dil.HCl and worked up by usual procedures to give the carbinols. The % conversions of carbinols were analysed by ¹H NMR spectroscopy.

Table I : Accelerated reduction of aldehydes and ketones to carbinols catalysed by aluminium isopropoxide-TFA.

Sr. No.	Substrate Name	Conc ^a	AIP Conc ^a	TFA Conc ^a	% conversion
1.	Benzaldehyde	1	1	1	100
2.	p-Nitrobenzaldehyde	1	1	1	100
3.	Heptanal	1	1	1	80
4.	Acetophenone	1	1	1	36
5.	Acetophenone	1	3	3	74
6.	Propiophenone	1	1	1	33
7.	Propiophenone	1	4	4	81
8.	Cyclohexanone	1	1	1	100
9.	Estrone methyl ether	1	5	5	66

a) Concentration in mole ratios, b) Reaction time of 15 mins, at room temperature.

Minimum time required for maximum conversions were checked by repeating experiments of entries 2, 4 & 6 and quenching at the interval of one minute. Conversions obtained within a minute were same as those obtained with quenching after 15 minutes, indicating extremely rapid reduction⁶. With less reactive carbonyl compounds conversions could be improved by the use of an excess of reducing agent (entry 5, 7 & 9). An important finding was the absence of condensation products as determined in ¹H NMR 60 MHz analysis of the products.

Thus we are successful in developing an extremely fast modified MPV reduction system useful for reduction of aldehydes and ketones to corresponding carbinols in good to excellent conversions. Work is in progress to use this system in asymmetric reduction.

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References & Notes :

- De graauw, C.F.; Peters, J.A.; Bekkum, H.V.; Huskens, J. *Synthesis*, 1994, 10, 1007.
- Wilds, A.L. *Org. React.* 1944, 2, 178.
- Zassinovich, G.; Mestroni, G.; *Chem.Rev.* 1992, 92, 1051.
- (a) Gal, G.; Kruzsnai, I.; *Magyar. Kem. Foly. Oirat*, 1956, 62, 155. [*Chem. Abstr.* 52, 0872d (1958)].
(b) Rodinov, N.P.; Mairanovsku, S.G.; Gultai, V.P.; Proskurouskaya, I.V. *Izv. Akad. Nauk. Ussr. Ser. Khim.* 1976, 6, 155. [*Chem. Abstr.* 85, 772758 (1976)].
- Rathke, M.W.; Kow, R.; Nygren, R.; *J. Org. Chem.* 1977, 42, 826.
- These reactions were performed in the absence of TFA also. Except for p-nitrobenzaldehyde (conversion 36%) others did not show significant conversion within 15 minutes.

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