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Truly Catalytic Meerwein-Ponndorf-Verley (MPV) Reduction

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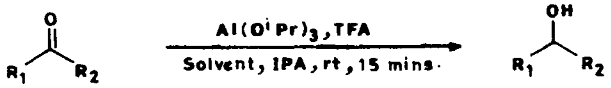
Abstract : A truly catalytic version of MPV reduction system has been developed. Herein p-nitrobenzaldehyde has been completely reduced at room temperature within 15 minutes using catalytic amounts of aluminium isopropoxide modified by trifluoroacetic acid and just one mole equivalent of isopropyl alcohol as external hydride source.

Classical Meerwein-Ponndorf-Verley methodology for selective reduction of aldehydes and ketones involves the use of aluminium alkoxides, particularly aluminium isopropoxide[1,2]. The use of alkali metal alkoxides[3] and more recently lanthanide alkoxides[4], transition metal complexes[5] of zirconium, hafnium, iridium and also heterogenous catalysts[6] have been reported with promising results. Traditional aluminium catalysts show too slow a ligand exchange to enable the use of catalytic amounts. The reaction using aluminium catalysts needs the use of reagent in stoichiometric or excess amounts, as well as high temperatures and provision for removal of acetone in order to achieve satifactory yields in a reasonably short time of a few hours.

Recently we have reported an accelerated MPV reduction where the aluminium isopropoxide is modified by addition of trifluoroacetic acid[7]. This system brings about complete reduction of p-nitrobenzaldehyde at room temperature in 15 minutes, in the absence of external hydride source such as isopropyl alcohol. Thus, in this modified system, aluminium isopropoxide (AIP) is used as reagent rather than as catalyst.

We have further studied this reagent and found that the reagent can be used in catalytic amounts and it very efficiently catalyses hydride transfer from isopropyl alcohol in MPV reduction. We report this truly catalytic MPV reduction in this paper.



Scheme I - Catalytic MPV reduction.

In our studies with modified reagent, TFA had been used in stoichiometric amounts with AIP which markedly enhanced the rate of reaction. We continued the study to determine the minimum amount of TFA that is required to accelerate the reduction.

p-Nitrobenzaldehyde, a reactive carbonyl compound, was chosen as a model substrate for the study and subjected to reduction with decreasing amounts of TFA using the standard procedure developed earlier. The results are summarised in Table - 1.

Table - 1 : Reduction of PNB using Decreasing Amounts of TFA[a]

Entry	Concentration in mole ratios			Conversion (%)
	PNB	AIP	TFA	
1.	1	1	0	36
2.	1	1	1	100
3.	1	1	0.8	100
4.	1	1	0.4	100
5.	1	1	0.2	100
6.	1	1	0.0329	100
7.	1	1	0.0196	100

a - Standard procedure[8] was followed. Reactions were quenched after 15 minutes.

TFA in as low a mole ratio as 0.0196 was sufficient to bring about complete reduction of PNB in 15 minutes at room temperature (Entry 7).

This indicated the possibility of using the reagent in catalytic amounts in the presence of suitable hydride donors.

Various experiments were then carried out to explore this possibility. The results are summarised in Table - 2.

The experiments were performed as follows : PNB (9.9 millimoles) was added to a suspension of AIP in benzene. To this system the calculated amount of TFA was added, followed by 1 mole equivalent of IPA. The reactions were stirred at room temperature for 15 minutes and were quenched by addition of dilute HCl. Usual work up procedure was followed[8] and conversions were determined by ^{1}H NMR (60 MHz) analysis.

Table - 2 : Accelerated Reduction of PNB With Decreasing Amounts of AIP and TFA in Presence of One Mole Ratio of IPA

Entry	Concentration in mole ratios				Conversion (%)
	PNB	IPA	AIP	TFA	
1.	1	1	0.33	0.026	100
2.	1	1	0.166	0.013	100
3.	1	1	0.0833	0.0032	100

As can be seen from entry 3, Table 2, AIP and TFA in as low a ratio as 0.0833 and 0.0032 were sufficient to cause complete reduction of PNB within 15 minutes, in the presence of just 1 mole equivalent of IPA as hydride donor at room temperature. Thus this catalytic system is highly efficient with regard to utilisation of IPA for hydride transfer.

Using these catalytic conditions, various other carbonyl compounds were subjected to reduction. It was noticed that with these substrates the reduction was slow as compared to PNB. The reactions were maintained for longer periods of time to achieve reasonably good conversions at room temperature.

The results are summarised in Table - 3.

Table - 3 : Reductions of Carbonyl Compounds Using Catalytic Accelerated MPV System

Concentration in Mole ratios.

Substrate	IPA	AIP	TFA
1	1	0.083	0.0032

Entry	Carbonyl Compound	Time (hrs)	Conversion (%)
1.	Benzaldehyde	0.75	93
2.	m-Nitrobenzaldehyde	0.50	97
3.	4-Methoxybenzaldehyde	4	61
4.	3,4-Dimethoxybenzaldehyde	2	72
5.	Acetophenone	22	44
6.	Propiophenone	24	20
7.	Ethyl 3-benzoyl, prop-2-enoate	24	45
8.	1,3-Diphenyl-prop-2-en-1-one	24	6
9.	Cyclohexanone	6	80

Among the substrates studied, the best results were obtained with m-nitrobenzaldehyde, while 1,3-diphenyl-prop-2-en-1-one gave conversion of only 6%.

Thus we have been successful in developing a modified MPV reduction system that is truly catalytic in nature and yields good conversions at room temperature and has good potential for general application. Work is in progress to further optimise the reduction system and study its catalytic nature.

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8. To a stirred solution of aluminium isopropoxide and carbonyl compound in benzene at room temperature was added TFA and the reaction was stirred for a further 15 minutes. The reaction was then quenched with dilute HCl (20 mL) and extracted with methylene chloride (3x30 mL). The combined methylene chloride extracts were washed with dilute sodium bicarbonate solution (2x30 mL), water (1x30 mL) and dried over Na_2SO_4. Solvent was removed *in vacuo*. The residue obtained was dissolved in CCl_4 and the percentage conversions were determined by ^1H NMR (60 MHz).

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