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Accelerated Reduction of Carbonyl Compounds under Microwave Irradiation

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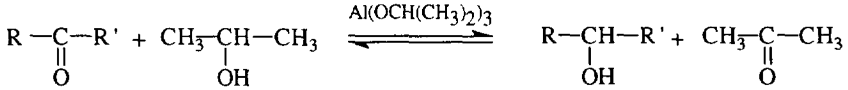
Abstract : Aldehydes and ketones are quickly reduced to alcohols by aluminum isopropoxide under microwave irradiation. © 1997 Elsevier Science Ltd.

The Meerwein-Ponndorf-Verley reaction[1-3] is the chemoselective reduction of carbonyl compounds by aluminum alkoxides, generally aluminum isopropoxide. In this reaction, a hydride transfer from the alcoholate to the carbonyl group via a six-membered transition state is initiated by the activation of the carbonyl upon coordination to the metal[4]; the most important side reactions are the aldol condensation and the Tishchenko reaction[5] which leads to the formation of carboxylic esters, especially with the more reactive carbonyl of aldehydes.



$$R-\underset{\underset{O}{\|}}{C}-R' + CH_3-\underset{\underset{OH}{|}}{CH}-CH_3 \xrightleftharpoons{Al(OCH(CH_3)_2)_3} R-\underset{\underset{OH}{|}}{CH}-R' + CH_3-\underset{\underset{O}{\|}}{C}-CH_3$$

In its earlier form[6], acetone was distilled off during several hours to shift this equilibrated reaction towards the formation of alcohol. The more recent improvements of this reaction are the use of catalytic amounts of lanthanide alkoxides[7,8] and the addition of trifluoroacetic acid to the aluminum isopropoxide to accelerate the reduction[9,10].

We here report that this reaction takes place in good yields and short reaction times under microwave irradiation (Table 1). These results require the following comments :

a) Microwave irradiation gives always a better yield of about 20% than classical heating (oil bath) when both of these reactions are led under reflux of isopropanol. Superheating of the solvent under microwave irradiation may lead to the observed rate enhancement [11].

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Table 1 - Meerwein-Ponndorf-Verley reduction of carbonyl compounds under microwave irradiation[a].

Substrate	Aluminum isopropoxide[b]	Time (mn)	Yields[c] %
Cyclohexanone	1	2	51
	1	10	79
	2	2	76
Cyclopentanone	5	10	69
Benzaldehyde	1	2	84
Hexanal	1	2	55
(E)-Cinnamaldehyde	1	5	78
(E)-4-Phenyl-3-buten-2-one	1	10	48[d]

[a] *Typical procedure* : a mixture of aluminum isopropoxide (2.04g, 10 mmol), isopropanol (20ml) and the corresponding carbonyl compound (10 mmol) is introduced in a pyrex spherical flask placed in a multimode microwave oven under a reflux condenser and irradiated for 2 mn (450W). The solvent is removed and the residue is hydrolysed with 6N hydrochloric acid ; after saturation with sodium chloride, the aqueous layer is extracted thrice with 10ml of ether. The organic layers are washed with a sodium hydrogen carbonate solution and water, dried over magnesium sulfate and distilled. [b] equivalent with regard to the carbonyl compound. [c] isolated yields ; similar results are obtained starting from five times the amount of carbonyl compound. [d] with 38% recovered ketone ; no improvement is observed when more than one equivalent of alkoxide is used.

b) Side reactions can occur especially with aldehydes ; the reaction of hexanal with aluminum alkoxide yields only 4% of the product of aldol condensation (followed by dehydration), traces of ester (Tishchenko reaction) and 20% of tar (with regard to the carbonyl compound).

c) Whereas an excess of alkoxide leads to the improvement of the reduction of saturated ketones, no such effect is observed for aldehydes : side reactions become more important and the yield of alcohol is lowered.

d) Same results are obtained with a new alkoxide and an old reagent.

e) The work-up of the reaction with cyclopentanone is peculiar because cyclopentanol and isopropanol form an azeotropic mixture : prior to the distillation, 30 ml of cyclohexane are added to the organic layer, the cyclohexane-isopropanol mixture is removed and then cyclopentanol can be distilled.

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