

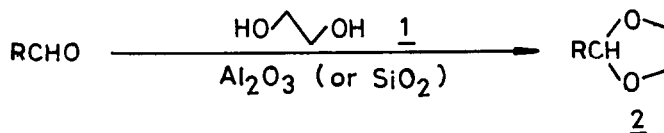
ALUMINA AS AN VERSATILE CATALYST
FOR THE SELECTIVE ACETALIZATION OF ALDEHYDES

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Abstract: Alumina was found to be an effective and convenient catalyst for acetalization of aldehydes to the corresponding 1,3-dioxoranes and 1,3-dioxanes. It can be used for selective protection of only formyl group of ketoaldehydes.

Acetalization is now frequently used as an important synthetic means for protecting ketones or aldehydes in the course of preparations of a variety of multifunctional complex organic molecules. So far a number of catalysts eg., protic acids, Lewis acids and silicon reagents have been developed¹⁾ for this purpose. However little is known about sufficiently selective as well as convenient acetalization method for aldehydes in the presence of the other reactive functional groups. Highly selective acetalization of only formyl group of ketoaldehydes,²⁾ if possible, would be very valuable, which can simplify synthetic processes of many organic compounds. Developments of a new acetalization method applicable to acid-sensitive heterocyclic compounds such as furfural would also be important.

In the course of our studies on the chemoselective reactions promoted by silica gel,³⁻¹³⁾ we tried to use dry silica gel as a new alternative catalyst for acetalization. This is based on the reasoning that since wet silica gel serves as a good deacetalization reagent¹³⁾ dry silica gel would promote the reverse reaction, ie. acetalization. As anticipated reaction of aldehydes with ethylene glycol 1 proceeded quite cleanly in the presence of silica gel, affording 1,3-dioxoranes 2 with a very simple procedure.



In Table 1 are listed the results, together with the results where alumina was used as a catalyst in place of silica gel. As is seen in Table 1 silica gel¹⁴⁾ exhibited effectiveness for acetalization of some aldehydes but the

yields were critically affected by reaction media and substituent groups on the substrates. In contrast, acetalization using alumina was successfully performed in common solvents with various aliphatic as well as aromatic aldehydes, so that corresponding 1,3-dioxoranes¹⁵⁾ were obtained in high yields. All these reactions proceeded cleanly. No esterification was observed in the case of No 11. Even furfural was converted successfully to the corresponding 1,3-dioxorane (97 %). Thus alumina was found to be a more excellent catalyst than silica gel for the purpose of acetalization of aldehydes.

Typical procedure for acetalization of aldehydes using alumina is as follows. To a mixture of 0.25 g of acidic alumina (Alumina Woelm acid TLC)¹⁶⁾ and 1 (5 mmol) in dry toluene (5 ml) was added 2-phenylpropanal (1 mmol), and the whole mixture was stirred for 24 h at the refluxing temperature. Alumina was filtered off and washed thoroughly with CH₂Cl₂. Washings and filtrate were combined, washed twice with water, and dried over MgSO₄. Removal of the solvent afforded practically pure 2g in a quantitative yield. None of by-products as well as the starting aldehyde were detected even by careful inspection of ¹H NMR spectra of the raw products.

Table 1. Acetalization of Aldehydes with the Use of SiO₂ and Al₂O₃.^{a)}

No	RCHO	HO \setminus OH ^{b)} (mmol)	cat. , g	solvent ^{b,c)}	RCH(OCH ₂) ₂ Yield, %
1	PhCHO	10	SiO ₂ , 1	toluene	<u>2a</u> 100
2	p-ClC ₆ H ₄ CHO	10	SiO ₂ , 1	toluene	<u>2b</u> 0 ^{d)}
3		10	SiO ₂ , 1	heptane	<u>2b</u> 99
4	p-O ₂ NC ₆ H ₄ CHO	10	SiO ₂ , 1	heptane	<u>2c</u> 0 ^{d)}
5		10	SiO ₂ , 1	CCl ₄	<u>2c</u> 60 ^{e)}
6	PhCHO	5	Al ₂ O ₃ , 0.25	CCl ₄	<u>2a</u> 100
7	p-ClC ₆ H ₄ CHO	5	Al ₂ O ₃ , 0.25	CCl ₄	<u>2b</u> 95
8	p-O ₂ NC ₆ H ₄ CHO	5	Al ₂ O ₃ , 0.25	CCl ₄	<u>2c</u> 91
9	p-Me ₂ NC ₆ H ₄ CHO	5	Al ₂ O ₃ , 0.25	CCl ₄	<u>2d</u> 94
10	p-HOC ₆ H ₄ CHO	5	Al ₂ O ₃ , 0.25	toluene ^{f)}	<u>2e</u> 78
11	p-HO ₂ CC ₆ H ₄ CHO	5	Al ₂ O ₃ , 0.25	CCl ₄	<u>2f</u> 87
12	CH ₃ (Ph)CHCHO	5	Al ₂ O ₃ , 0.25	CCl ₄	<u>2g</u> 95
13	CH ₂ =CH(CH ₂) ₈ CHO	5	Al ₂ O ₃ , 0.25	CCl ₄	<u>2h</u> 97
14	PhCH=CHCHO	5	Al ₂ O ₃ , 0.25	CCl ₄	<u>2i</u> 100
15	furfural	5	Al ₂ O ₃ , 0.25	CCl ₄	<u>2j</u> 97

a) All reactions were carried out at refluxing temperature for 24h. b) Ethylene glycol and solvents were dried over molecular sieves 4A 1/16 before use. c) For each 1 mmol of substrates 5 ml of solvent was used. d) Complete recovery of starting materials. e) Starting material was recovered in 40 %. f) Higher yield was obtained in toluene than in CCl₄ (41 %).

We then examined acetalization of ketones with the use of alumina and found the reaction proceeded much more slowly than the case of aldehydes. For instance, only 16 % of acetophenone and none of di-isobutylketone were converted to the corresponding 1,3-dioxoranes even under the conditions in which benzaldehyde was converted to 2a completely. This difference in reactivity between aldehydes and ketones were successfully utilized to chemoselective acetalization of only aldehydes in the presence of ketones. As shown in Table 2, excellent chemoselectivity was observed with several equimolar mixtures of aldehydes and ketones studied.

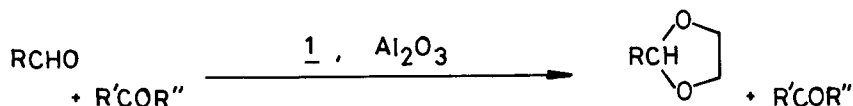


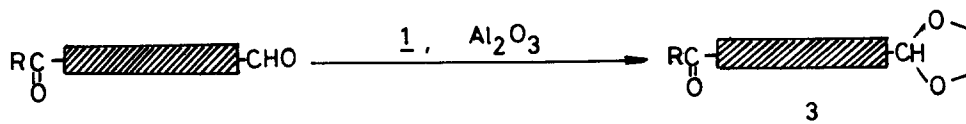
Table 2. Selective Acetalization of Aldehydes by Ethylene Glycol in the Presence of Equimolar Amounts of Ketones. ^{a)}

No	substrates		Al ₂ O ₃ g	conversion, % ^{b)}	
	aldehyde	ketone		RCHO,	R'COR''
1	PhCHO	PhCOCH ₃	0.5	100,	4
2	PhCH ₂ CHO	i-Bu ₂ CO	0.25	100,	0
3	p-TolCHO	i-Bu ₂ CO	0.25	100,	0
4 ^{c)}	CH ₃ (CH ₂) ₈ CHO,	(PhCH ₂) ₂ CO	0.25	100,	3
5 ^{d)}	PhCHO	PhCOCH ₃	0.5	96,	7

a) For 1 mmol/ 1 mmol mixture of substrates 5 mmol of dry ethylene glycol and 5 ml of toluene were used. Reactions were carried out at refluxing temperature of toluene under N₂.

b) Calculated on the basis of ¹H NMR spectra of the raw materials. c) For 1 mmol/ 1 mmol mixture of substrates, 1.1 mmol of dry ethylene glycol and 5 ml of CCl₄ were used. d) 1,3-propanediol was used.

In each case aldehydes afforded corresponding 1,3-dioxoranes in high yields while most of ketones remained unchanged. Selective acetalization of benzaldehyde with 1,3-propanediol also proceeded successfully in the presence of acetophenone (run 5, Table 2). Finally chemoselectivity of the present acetalization was examined with the use of some ketoaldehydes. Satisfactory results were obtained and these are summarized in Table 3.



Thus the present reaction will provide a convenient method of acetalization, particularly useful for the purpose of chemoselective protection of an aldehyde group in the presence of ketocarbonyl groups.

Table 3. Selective Acetalization of Ketoaldehydes with the Use of Al_2O_3 .^{a)}

No	ketoaldehyde	HO \setminus OH, ^{b)} mmol	time h	products ratio, % ^{c)}	
				3,	bis(1,3-dioxorane)
1		1.1	5	88,	12
2		1.1	24	94,	6
3		2.0	24	100,	0
4		1.5	24	83,	13

a) For 1 mmol of ketoaldehyde 0.25g of Al_2O_3 and 5 ml of dry CCl_4 were used. b) Ethylene glycol and CCl_4 were dried over molecular sieves 4A 1/16 before use. c) Calculated on the basis of 1H NMR spectra of the crude materials.

References and Notes

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- 14) Commercial grade silica gel (Wakogel C-300, for column chromatography) was used after dried at 150-170°C for 3 h under vacuum.
- 15) All 1,3-dioxoranes and 1,3-dioxanes obtained here were identified by means of 1H NMR and IR measurements, and hydrolysis of them provided original aldehydes and ketones.
- 16) Commercial grade alumina (Woelm Acid TLC) was used after dried for 3 h at 170-190°C under vacuum.

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