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FACILE METHOD FOR ACETALISATION AND KETALISATION OF AROMATIC CARBONYL COMPOUNDS

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ABSTRACT

Calcium oxide and calcium sulphate were mixed with silica at different percentage ranges, 55% w/w - 80% w/w to obtain homogenous powdered materials. The powdered materials were employed as catalysts as well as dehydrating agents in the acetalisation and ketalisation of some aromatic carbonyl compounds using ethylene glycol. The aromatic carbonyl compounds, calcium salt-silica mixtures, and ethylene glycol were mixed using pestle and mortar in the absence of solvent. After simple work up procedure, various yields of the corresponding acetals and ketals were obtained where calcium sulphate-silica mixture, 75% w/w provided the optimum condition for the method. Among the aromatic carbonyl compounds studied, it was found that vanillin furnished the highest acetal yield (73%). This investigation proved that calcium oxide and calcium sulphate when mixed with silica can effectively catalysed the acetalisation and ketalisation of aromatic carbonyl compounds in a solvent-free condition, and with relatively good yields.

Keywords: Acetalisation, Calcium oxide, Calcium sulphate, Ethylene glycol, Silica, Ketalisation, Solvent-free.

INTRODUCTION

Acetalisation or ketalisation is the routine method employed for the protection of carbonyl functional groups in aldehydes or ketones during organic synthesis. The method provides a convenient way to protect carbonyl compounds from metal hydrides, Grignard reagents, hydrogenation reagents, and oxidants [1, 2]. Normally, the approach involved the use of alcohol and a catalytic amount of protic acid with continuous removal of by-product water either physically or chemically [1-2]. Recent advances have led to the development of metal complexes [3-6], Lewis acids [7-15], and other heterogenous catalysts as mediators [16-21]. However, those methods suffered from limitations such as poor substrate scope, high reaction temperature, use of expensive and toxic reagents, long duration, and tedious purification [3-21]. The successful applications of a mixture of reagents with silica as mediators for various transformations have been reported. This includes synthesis of bis-(4-hydroxycoumarin-3-yl) methane [22], Diels–Alder reaction [23], alkylation reaction [24], chemoselective hydrogenation [25], chemoselective formylation of indoles [26], and direct amination of dodecanol [27]. Here, we reported the use of the mixture of silica with calcium oxide and calcium sulphate to mediate the acetalisation or ketalisation of aromatic carbonyl compounds in a simple way.

EXPERIMENTAL

General

FTIR spectra were recorded on Agilent Cary 630. Vanillin, 4-methoxybenzaldehyde, 4-bromobenzaldehyde, 4-hydroxybenzaldehyde were purchased from Sigma-Aldrich. Other chemicals were purchased from different manufacturers: 3-nitrobenzaldehyde (JN Chem., India), Benzophenone (Burgoyne Burbidges, India), ethylene glycol (Park Sci. Ltd, UK), calcium oxide and calcium sulphate were purchased from Loba Chimie, India. Silica gel, 60-120 mesh was purchased from Sisco Research Laboratories Pvt. Ltd., India.

General Procedure for Preparation of Salt-Silica Mixture

Typically, calcium oxide-silica mixture (75% w/w) was prepared by grinding calcium oxide (0.285 g) with silica (0.095 g) using pestle and mortar until a homogenous, free-flowing powder was obtained. The appropriate ratios were varied to obtain the corresponding 50%, 55%, 60%, 65 %, 70%, 75%, and 80% w/w. This method was also used for the preparation of calcium sulphate-silica mixtures [28].

General Procedure for Acetalisation/Ketalisation of Aromatic Carbonyl Compounds

Aromatic carbonyl compound (2 mmol), salt-silica powder [(75 % w/w), 0.3g] were gently mixed, and ethylene glycol (2.4 mmol) was added. The mixture was ground using pestle and mortar in the absence of solvent. After the appropriate reaction time, the mixture was treated with diethyl ether (10 ml) and filtered. The filtrate was allowed to dry and then washed with ethanol (10 ml) followed by distilled water (5 ml). After drying, different solid products were obtained. The FTIR spectra of the acetals and the ketals were then recorded.

RESULTS AND DISCUSSION

As a model reaction, the acetalisation of vanillin (4-hydroxy-3-methoxybenzaldehyde) was investigated using various percentages of the salt-silica mixture. Thus by varying the percentages, 55% w/w – 80% w/w, it was found that the best yield of vanillin acetal was obtained at 75% w/w (Table 1). However, when the percentage weight was increased to 80% w/w, the yield of the acetal depreciated to 61%. This might be as a result of the inefficiency of the silica to activate the carbonyl group due to the high concentration of the salt. On the other hand, when the percentage weights were decreased, the yields of the acetals were found to be low (70% w/w to 55% w/w). There was a negligible formation of the acetal at 50% w/w. This might be attributed to the fact that the salts which act as the dehydrating agents to remove the water by-product were not reasonably available; hence, the reaction tends to move backward in favour of the formation of the aldehyde. The FTIR spectroscopic analysis of vanillin and the corresponding acetal was monitored to confirm the successful conversion of the C=O group to the corresponding acetal group. It could be seen that the C=O band at 1663 cm^{-1} (Figure 1) has clearly disappeared in the FTIR spectrum of the acetal (Figure 2). The C-O band appeared very strong at 1097 cm^{-1} which signified the contribution of the absorption by the two C-O bonds in the acetal group (Figure 2).

Table 1. Acetalisation of Vanillin[a]

Salt-Silica	Yield (%)[b]						
	50% w/w	55% w/w	60% w/w	65% w/w	70% w/w	75% w/w	80% w/w
CaO-Silica	Traces	12	18	45	47	51	38
$CaSO_4$-Silica	Traces	17	21	27	33	73	61

[a] Reaction mixture ground using pestle and mortar for 5 minutes.

[b] Isolated acetals as confirmed by the disappearance of C=O band and appearance of C-O band in the FTIR spectra.

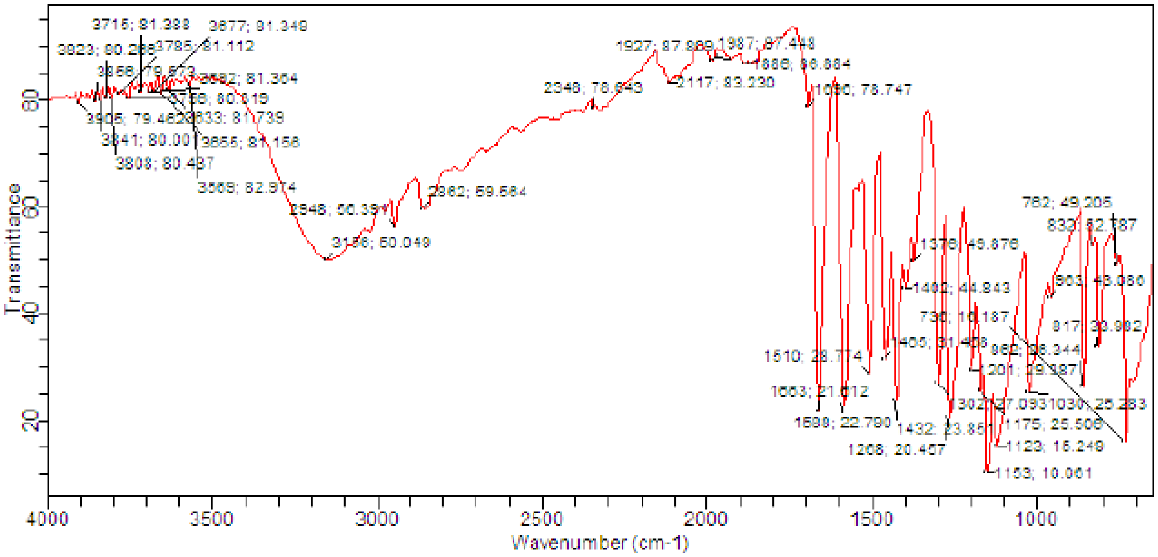


Figure 1: FTIR Spectrum of Vanillin

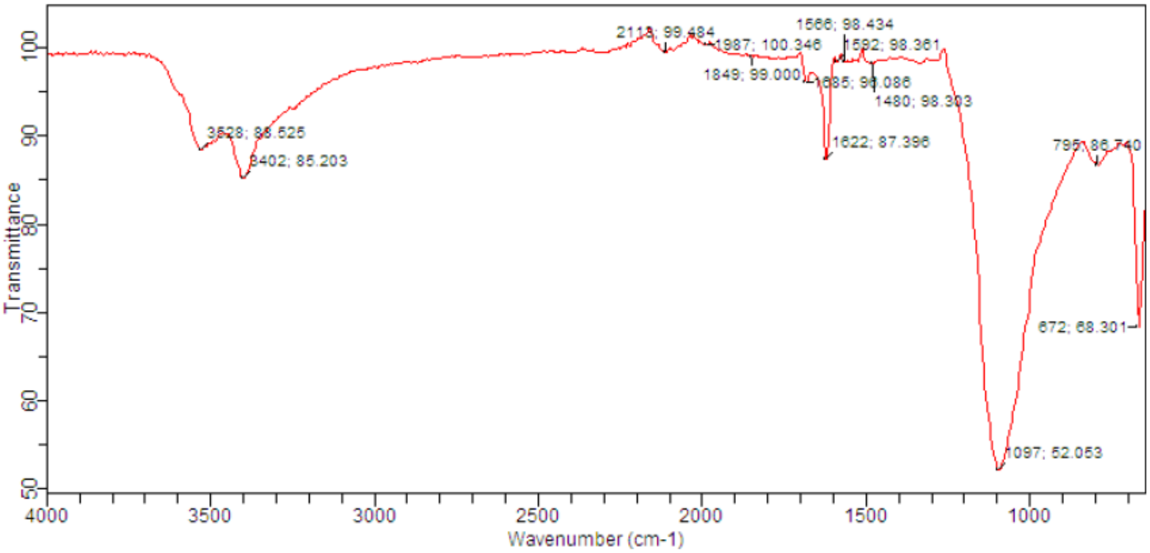


Figure 2: FTIR Spectrum of Vanillin Acetal

The calcium sulphate-silica mixture (75% w/w) was further investigated at different time intervals to ascertain the effect of the reaction duration. However, it was found that the yield of the acetal at longer duration (30 minutes) was not significantly different from the shorter duration of 5 minutes.

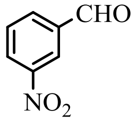
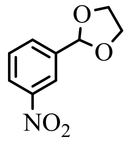
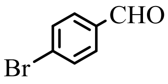
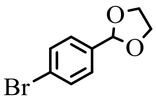
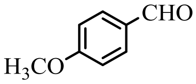
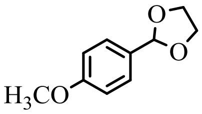
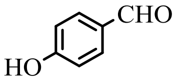
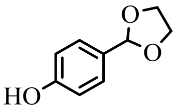
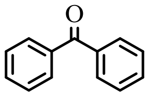
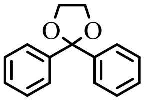
Table 2: Acetalisation of Vanillin using $CaSO_4$-Silica (75% w/w) at Different Times

Time (min)	Yield (%)[a]
10	73
15	73
20	73
25	75
30	75

[a] Isolated acetals as confirmed by the disappearance of C=O band and appearance of C-O band in the FTIR spectra

To explore the substrate scope, some structurally different aldehydes and one aromatic ketone were subjected to the reaction condition, and the corresponding products were obtained in different yields (Table 2).

Table 3: Acetalisation and Ketalisation of Carbonyl compounds using $CaSO_4$-Silica, 75 % w/w[a]

S/N	Carbonyl Compound	Product	Yield (%)[b]
1			50
2			71
3			41
4			69
5			43

[a] Reaction mixture ground using pestle and mortar for 5 minutes

[b] Isolated acetals as confirmed by the disappearance of C=O band and appearance of C-O band in the FTIR spectra

The yield of the products indicated that 4-bromo benzaldehyde and 4-hydroxy benzaldehyde formed the corresponding acetals with good yields, 71% and 69% respectively. This was followed by 3-nitro benzaldehyde (50%) and benzophenone (43%). The substituted aldehydes seemed to have exhibited an irregular pattern because 4-bromo benzaldehyde which contained the less deactivating group (bromine) gave the highest yield (71%), while the 4-methoxy benzaldehyde containing the strongest activating group (methoxy) gave the lowest yield (41%). The only ketone considered was benzophenone, and it appeared to be ketalised with a fair yield (43%).

CONCLUSION

A simple method for the acetalisation and ketalisation of six aromatic carbonyl compounds mediated by calcium oxide-silica and calcium sulphate-silica mixtures has been explored. The appropriate acetals and ketals were successfully obtained in various yields with vanillin (4-

hydroxy-3-methoxy benzaldehyde) giving the highest acetal product. This concept proved that inexpensive dehydrating agents mixed with silica could effectively serve both as catalyst and dehydrating agent in the acetalisation and ketalisation of carbonyl compounds using ethylene glycol as the alcohol.

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