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An Efficient and Green Procedure for the Preparation of Acylals from Aldehydes Catalyzed by Alum [$KAl(SO_4)_2{\cdot}12H_2O$]

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ABSTRACT

Alum [$KAl(SO_4)_2{\cdot}12H_2O$] is an inexpensive, efficient, non-toxic and mild catalyst for the preparation of acylals from aromatic and heteroaryl aldehydes with acetic anhydride at room temperature under solvent-free conditions. This method gives remarkable advantages such as excellent chemoselectivity, mild reaction conditions, short reaction times and excellent yields, and offers a green synthetic solution by avoiding toxic catalysts and hazardous solvents.

KEYWORDS

Alum, acylals, aromatic and heteroaryl aldehydes, solvent-free synthesis, room temperature.

1. Introduction

The protection of carbonyl groups is often necessary during the synthesis of multi-functional complex molecules and natural products. Acylal formation is one of the most useful methods to protect carbonyl groups due to the stability of the resulting acylals. They are stable in neutral and basic media.[1] Acylals are synthetically important precursors for the preparation of 1-acetoxydienes for Diels–Alder reaction.[2] Chiral allylic esters have been obtained using palladium catalysts by an asymmetric allylic alkylation of gem-diesters.[3] The preparation of homoallyl acetates by allylation of acylals has also been reported.[4]

Generally, acylals have been prepared by the reaction of aldehydes with acetic anhydride catalyzed by sulphuric, phosphoric and methanesulphonic acids,[5] I_2,[6] $InCl_3$,[7] $Cu(OTf)_3$,[8] $H_6P_2W_{18}O_{62}{\cdot}24H_2O$,[9] [Hmim]$HSO_4$,[10] $SnCl_4/SiO_2$,[11] $GaCl_3$[12] and ceric ammonium nitrate (CAN).[13] However, in the references above some methods suffer from one or more drawbacks such as prolonged reaction times, use of environmentally unfavourable solvents and sometimes low yields. Thus, the development of a new method for the preparation of acylal derivatives would be highly desirable.

In recent years, solvent-free organic syntheses have offered some advantages compared with their homogeneous counterparts, due to the growing concern over the influence of organic solvents on the environment as well as on the human body, economic demands and simplicity of the processes.[14]

Alum [$KAl(SO_4)_2{\cdot}12H_2O$] was found to be effective in the synthesis of *cis*-isoquinolic acids,[15a] mono- and disubstituted 2,3-dihydroquinazolin-4(1*H*)-ones,[15b] dihydropyrimidine via the Biginelli reaction,[15c] coumarins,[15d] 1,3,4-oxadiazoles,[15e] dibenzoxanthenes,[15f] 1,5-benzodiazepines[15g] and 2,4,5-trisubstituted imidazoles.[15h] Alum has been exploited in organic synthesis, as a non-toxic, inexpensive, eco-friendly, easily handled and mild catalyst. It was therefore decided to investigate alum as a catalyst for the synthesis of acylals. It was found that alum is an effective promoter in the synthesis of acylals from various aromatic and 4-oxo-(4*H*)-1-benzopyran-3-carbaldehydes and acetic anhydride.

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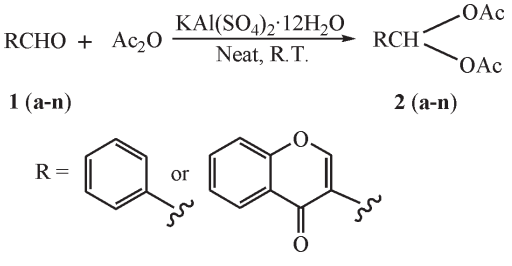
2. Results and Discussion

In continuation of our work on the protection of aldehydes and ketones,[13,16] the study of 4-oxo-(4*H*)-1-benzopyran-3-carbaldehydes[17] and an interest in the development of novel synthetic methodology,[18] we report herein a simple, mild, efficient and rapid method for the preparation of acylals from a variety of aromatic and heteroaryl aldehydes with acetic anhydride in the presence of a catalytic amount of alum at room temperature under solvent-free conditions (Scheme 1).

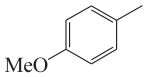
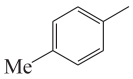
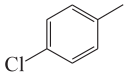
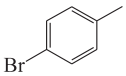
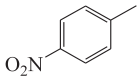
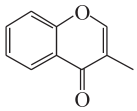
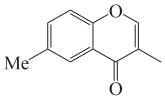
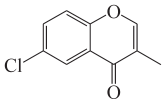
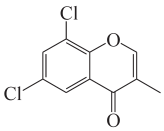
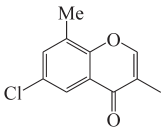
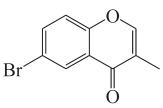
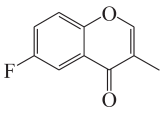
To optimize the reaction conditions, the reaction of benzaldehyde **(1a)** and acetic anhydride was selected as a model to investigate the effects of different amounts of catalyst on the yield. The best result was obtained by carrying out the reaction with a 1:2 mol ratio of benzaldehyde:acetic anhydride and 1 mol % of alum at room temperature under solvent-free conditions. Under these conditions **2a** was obtained in 97 % yield after 10 min (see Table 1, compound **2a**). To determine the role of alum, the model reaction was carried out in the absence of catalyst at room temperature under solvent-free conditions; the desired product was not obtained after 120 min. This result indicates that alum exhibits a high catalytic activity in this transformation.

The substrate, 4-oxo-(4*H*)-1-benzopyran-3-carbaldehyde has three active centres, an α, β-unsaturated carbonyl group, a carbon– carbon double bond and a formyl group. Of these three reactive centres, the reaction occurs chemoselectively at the formyl group. Table 1 shows that aromatic and heteroaryl aldehydes, having different substituents, such as chloro, nitro, methoxy, methyl, bromo, fluoro, etc., are converted to the corre-

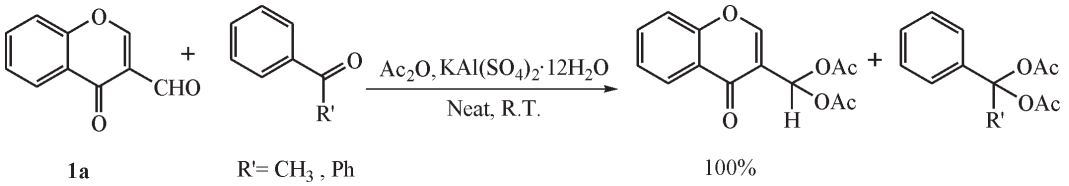


Scheme 1

Table 1 Alum catalyzed preparation of acylals [a].

Compound[b]	R	Time/min	Yield/% [c]	M.p./°C	
				Found	Reported
2a		10	97	44–46	44–46 [11]
2b		15	93	64–65	64–65 [11]
2c		15	95	82–83	81–82 [11]
2d		10	93	80–82	79–81 [11]
2e		10	94	92–94	93–95 [11]
2f		15	95	124–126	125–126 [11]
2g		10	89	52–54	52–53 [10]
2h		15	94	130–132	131–132 [12]
2i		20	92	148–150	150 [13]
2j		15	87	170–171	170 [13]
2k		15	95	190–191	189 [13]
2l		20	91	160–162	162 [13]
2m		10	90	170–172	171 [13]
2n		10	93	154–156	156 [13]

[a] Reaction conditions: aromatic and heteroaryl aldehydes (1 mmol), acetic anhydride (2 mmol), alum (1 mol %) at room temperature under solvent-free conditions.
[b] Compounds were characterized by IR, ^{1}H NMR and ^{13}C NMR spectroscopy and compared with reported methods.[10–13]
[c] Isolated yield based on starting aldehyde.



1a

Scheme 2

Table 2 Comparison of the present method with some other procedures for acylal synthesis [a].

Entry	Catalyst	Mol %	Time	Yield/%	Reference
	4-nitrobenzaldehyde (**1f**)				
1	I_2	10	2 h	99	6
2	$InCl_3$	10	4 h	88	7
3	$Cu(OTf)_3$	2.5	4 h	94	8
4	$H_6P_2W_{18}O_{62}\cdot 24H_2O$	1	30 min	92	9
5	$[Hmim]HSO_4$	3.8	40 min	89	10
6	$KAl(SO_4)_2\cdot 12H_2O$	1	15 min	95	–
	4-oxo-(4*H*)-1-benzopyran-3-carbaldehyde (**1h**)				
1	$GaCl_3$	5	12 min	92	12
2	CAN	6	2 h	89	13
3	$KAl(SO_4)_2\cdot 12H_2O$	1	15 min	94	–

[a] Reaction conditions: aldehydes (1 mmol), acetic anhydride (2 mmol), alum (1 mol %) at room temperature.

sponding acylal derivatives with high yields.

The acylals were prepared at room temperature and isolated by simple quenching in water and neutralization with $NaHCO_3$. All the reactions were completed within 10–20 min with excellent yields (87–97 %). This methodology avoids the use of corrosive acids and solvents, and requires only a catalytic amount of the alum to promote the reaction. The identities of compounds **2a–n** were established by comparison of their physical and spectroscopic properties with those reported earlier.[11,13]

In order to demonstrate the high selectivity of the procedure, we investigated competitive reactions for the preparation of the acylals from 4-oxo-(4*H*)-1-benzopyran-3-carbaldehyde in the presence of acetophenone or benzophenone using a catalytic amount of alum at room temperature under solvent-free conditions. It was found that ketones did not produce any acylals under the optimized reaction conditions. This result suggested that chemoselective protection of aromatic and heteroaryl aldehydes in the presence of ketones could be achieved with this procedure (Scheme 2).

In Table 2, our results are compared with results obtained by some other procedures for the synthesis of compounds **2f** and **2h**.

The data presented in this table show the promising features of this method in terms of molar ratio of the catalyst, reaction time and yield of the product compared with those reported in the literature.

3. Experimental

The uncorrected melting points of all compounds were measured in an open capillary in a paraffin bath. The progress of the reaction was monitored by TLC. IR spectra were recorded in a matrix of KBr with a Perkin-Elmer 1430 spectrometer (Manasquan, NJ, USA). ^{1}H and ^{13}C NMR spectra were recorded on Varian NMR spectrometers (300 and 75 MHz) (Lake Forest, CA, USA) using $CDCl_3$ as a solvent and TMS as an internal standard. All the compounds were characterized by IR, ^{1}H NMR and ^{13}C NMR spectroscopy, and compared with literature data.[10–13]

3.1. General Procedure for the Preparation of 2a–n

1a–n (1 mmol), acetic anhydride (2 mmol) and alum (1 mol %) were added to a round bottom flask and stirred at room temperature. The time required for each reaction is indicated in Table 1. The reaction was followed by TLC (*n*-hexane:EtOAc, 9:1). After completion of the reaction, the mixture was diluted with ethyl acetate (15 mL). The organic layer was washed with 10 % $NaHCO_3$ solution and water and then dried over anhydrous Na_2SO_4. The solvent was evaporated under reduced pressure to give pure **2a–n** in excellent yields without further purification. The spectral data of the principal compounds are as follows.

3.2. Spectral Data of Principal Compounds

(**2a**) IR (KBr): 3060, 1755, 1605, 1470, 1375, 1245, 1205, 1065, 1010, 760, 700 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 7.6 (s, 1H), 7.4–7.2 (m, 5H), 1.92 ppm (s, 6H).

(**2f**) IR (KBr): 3124, 1762, 1610, 1529, 1345, 1210, 1200, 1090, 1000, 960, 850 cm^{-1}. ^{1}H NMR ($CDCl_3$): δ 8.07 (d, J = 8.4 Hz, 2H), 7.54 (s, 1H), 7.51 (d, J = 8.4 Hz, 2H), 1.96 ppm (s, 6H).

(**2h**) IR (KBr): 3070 (ArC-H), 1656 (C=O, chromone), 1768 cm^{-1} ($OCOCH_3$). ^{1}H NMR ($CDCl_3$): δ 2.13 (s, 6H), 7.4 (s, 1H), 8.2 (s, 1H), 7.5– 7.82 ppm (m, 4H). ^{13}C NMR ($CDCl_3$): δ 175.47, 168.77, 154.88, 153.77, 135.68, 130.90, 126.88, 124.27, 119.79, 118.22, 85.64, 21.37 ppm.

(**2k**) IR (KBr): 3080 (ArC-H), 1657 (C=O, chromone), 1776 ($OCOCH_3$), 990 cm^{-1} (C-Cl). ^{1}H NMR ($CDCl_3$): δ 2.13 (s, 6H), 7.77 (s, 1H), 7.72 (d, 1H, J = 2.20 Hz), 8.06 (d, 1H, J = 2.20 Hz), 8.18 ppm (s, 1H). ^{13}C NMR ($CDCl_3$): δ 173.58, 168.59, 155.31, 150.95, 134.68, 131.90, 126.31, 124.94, 124.45, 120.60, 84.91, 21.08 ppm.

(**2m**) IR (KBr): 3060 (ArC-H), 1650 (C=O, chromone), 1750 ($OCOCH_3$), 1016 cm^{-1} (C-Br). ^{1}H NMR ($CDCl_3$): δ 2.14 (s, 6H), 7.40

(d, 1H, J = 8.78 Hz), 7.80 (dd, 2H, J = 2.30 and 8.70 Hz), 8.19 (s, 1H), 8.4 ppm (s, 1H). ^{13}C NMR ($CDCl_3$): δ 173.56, 168.17, 154.93, 137.09, 128.53, 125.38, 120.07, 119.84, 77.63, 76.36, 20.68 ppm.

(**2n**) IR (KBr): 3055 (ArC-H), 1660 (C=O, chromone), 1770 ($OCOCH_3$), 900 cm^{-1} (C-F). ^{1}H NMR ($CDCl_3$): δ 2.13 (s, 6H), 7.30 (d, 1H, J = 8.78 Hz), 7.79 (dd, 2H, J = 2.30 and 8.70 Hz), 8.20 (s, 1H), 8.5 ppm (s, 1H). ^{13}C NMR ($CDCl_3$): δ 173.58, 168.23, 154.85, 137.25, 128.65, 125.30, 120.15, 119.90, 84.88, 77.55, 76.32, 20.63 ppm.

4. Conclusion

In conclusion, we have described a facile and efficient method for the preparation of acylals from a variety of aromatic and heteroaryl aldehydes with acetic anhydride in the presence of a catalytic amount of alum at room temperature under solvent-free conditions. This method is highly selective for the synthesis of acylals from aromatic and heteroaryl aldehydes in the presence of ketones. The notable merits of the present method are short reaction times, mild reaction conditions, excellent chemoselectivity, simple work-up procedure and excellent yield of products. Moreover, the catalyst used is easily available, inexpensive, mild, non-toxic and eco-friendly in nature. It is thus a rapid, convenient and environmentally benign method for the preparation of compounds of type **2a-n**.

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