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A FACILE AND ECO-FRIENDLY ALUM [KAl $(SO_4)_2.12H_2O$] CATALYZED MULTICOMPONENTSYNTHESIS OF BIS-COUMARINS

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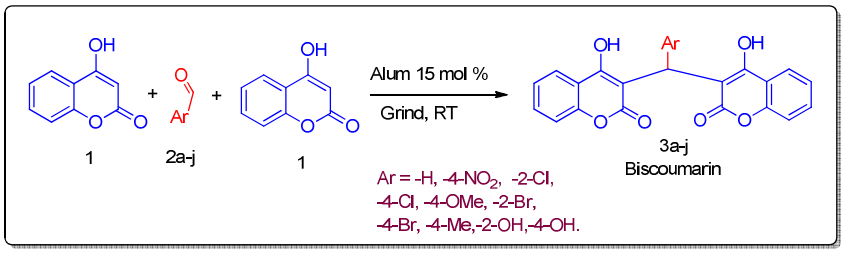
Abstract: A simple single stage, environmentally benign, an efficient condition for synthesis of bis-coumarins involving simple grinding technique of 4-hydroxy coumarins and substituted aromatic aldehyde under solvent free condition, at room temperature by naturally occurring environmentally benign catalyst has been described. The remarkable features of this environmentally benign protocol are short reaction time, use of commercially in expensive alum [KAl $(SO_4)_2.12H_2O$] catalyst with high yield of product by simple experimental procedure.

Keywords: Alum, bis-coumarins, solvent free condition, multicomponent, grinding technique, room temperature.

Introduction:

Coumarin scaffold[i] is central part of biologically active, pharmaceutically important compounds with various applications and uses such as inhibition of platelet aggregation,[ii]anticancer,[iii] antibacterial,[iv] anti-inflammatory,[v] antipyretic, antifungal[vi] and also reported for exhibiting photochemical properties.[vii] In particular bis-coumarins is an important class of coumarins derivatives due to their prominent pharmacological activities.[viii-xi] In our literature survey, previously reported for synthesis of biscoumarins from 4-hydroxycoumarins and substituted aromatic aldehydes using various catalyst like Ruthenium (III) chloride,[xii]Nanosilicachloride,[xiii] Cobalt (II) chloride,[xiv] Trichloroacetic acid,[xv] DBSA,[xvi] Cellulose sulphuric acid,[xvii] Magnesium oxide nanoparticles.[xviii]

In our continuation of research work[xix-xxvii] here, we report the synthesis of bis-coumarins by simple grinding technique using alum as a green catalyst from 4-hydroxycoumarins and aromatic aldehydes, catalyst having many advantages such as ease of handling, non-corrosiveness, low cost, regeneration, easily available etc. Many researchers have been devote for the use of alum catalyst in organic transformation for example the Beginelli[xxviii] and coumarins,[xxix] and also used for the synthesis of 1,8-dioxo-octahydroxanthenes,[xxx] isoquinolonic acids,[xxx] trisubstituted dimidazoles,[xxxii] 1*H*-spiro[isoindoline-1,2'-quinazoline]-3,4'(3*H*)-diones,[xxxiii]1,3,4-oxadiazoles,[xxxiv]and1,5 benzodiazepines.[xxxv] Finally all the compound were confirmed by spectral data such as IR, ^{1}H-NMR, physical properties and compared with those reported in literature.[xxxvi]



Scheme 1 Synthesis of 3,3'-(argiomethylene)bis(4-hydroxy-2*H*-chromen-2-one)using alum catalysedby simple grinding techniques

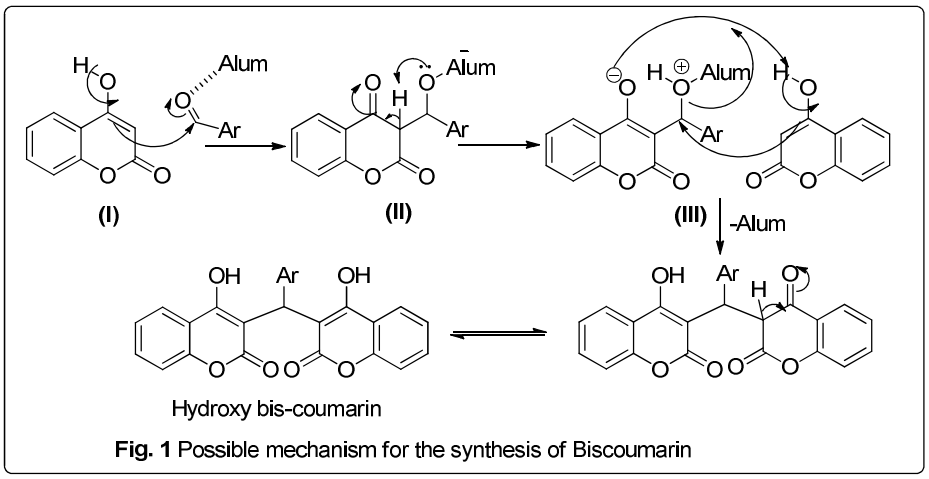


Fig. 1. Possible mechanism synthesis of Biscoumarin Derivatives

Experimental section:

All the compounds used in synthesis were of analytical grade, the melting points of the compounds were determined in open head capillary and are uncorrected. The IR spectra of the compounds were recorded in the region of 4000-400 cm-[1] by using KBr pallet on FT-IR Perkin spectrophotometer. ^{1}H NMR spectra were recorded on a DRX-300Bruker FT-NMR spectrophotometer in $CDCl_3$. Satisfactory elemental analysis was obtained on a Perkin Elmer CHN analyzer. The values of chemical shift are expressed in δ ppm as a unit. All the compounds were checked for purity by thin layer chromatography (TLC).

***General procedure for the synthesis of Bis-coumarin derivatives(3a-j)*:**

A mixture of 4-hydroxy coumarin (0.021 mol, 3.40 gm), substituted aromatic aldehydes (0.01 mol) and Alum (15 mol %) was mixed into a mortar and grind by pestle for the period of appropriate time (**Table 1**) the completion of reaction was monitor by TLC, after completion of reaction, water was added, filtered to removed catalyst, solid product was obtained and purified by silicagel column chromatography and recrystalized from aq. alcohol.

Result and Discussion

A series of reactions arranged by keeping focus on green protocols, synthesises of bis-coumarins by simple grinding method and using 4-hydroxy coumarins and benzaldehyde as model reaction. Without catalyst reaction did not detect (Table 1. entry 1). Various catalyst were screened to different mole% and with different time of reaction, (Table 1.) among these 15 mol% alum was most prominent catalyst togive an excellent yield. (Table 1, entry 8.)If we decreasing amount of catalyst to 5 and 10 mol % reaction yield was fall down with essentially increase in reaction time, whereas on increasing catalyst upto 20 mol % no significant effect was observed on the yield of product. Thus, we decide all the examples were tested reasonably good to excellent yield (Table 2.)could be achieved in a simple grinding technique at room temperature for 25-30 minutes.Finally, the structures of compound were substantiated by FTIR, ^{1}H NMR and Mass spectral analysisand characterised data were comparedwith those reported literature.[xxxvi]

Table 1 Optimisation of reaction condition[b] for synthesis of biscoumarin (**3g**) using alum catalyst by simple grinding technique.

Entry	Catalyst	Mol %	Time (min.)	Yield[a] (%)
1.	Neat	-	30 min.	00
2.	Montmorillonite	5 mol %	30 min.	48
3.	Montmorillonite	10 mol %	30 min.	65
4.	Montmorillonite	15mol %	30 min.	87
5.	Montmorillonite	20 mol %	30 min.	86
6.	Alum	5mol %	30 min.	68
7.	Alum	10 mol %	25 min.	86
8.	**Alum**	**15 mol %**	**25 min.**	**97**
9.	Alum	20 mol %	25 min.	96
10.	Glacial acetic acid	10 mol %	30 min.	80
11.	Glacial acetic acid	15 mol %	25 min.	89
12.	Glacial acetic acid	20 mol %	25 min.	89

[a] Isolated yield
[b] reaction condition: 4-hydroxy coumarins (**1,** 0.021 mol), 4-bromo benzaldehyde (**2**, 0.01 mol) and Alum catalyst, grinding at r.t.

Table 2. Physical data of biscoumarin derivatives.

Sr. no.	Compound	Ar	Molecular Formula	Time (min)	M.P. (°C) (Reported xxviii)	Yield[a] (%)
1	3a	-H	$C_{25}H_{16}O_6$	25	231-233 (231-34)	93
2	3b	-4-NO_2	$C_{25}H_{15}NO_8$	30	233-235 (232-34)	85
3	3c	-2-Cl	$C_{25}H_{15}ClO_6$	30	220-222 (224-26)	89
4	3d	-4-Cl	$C_{25}H_{15}ClO_6$	25	251-253 (254-56)	90
5	3e	-4-OMe	$C_{26}H_{18}O_7$	30	245-247 (246-48)	87
6	3f	-2-Br	$C_{25}H_{15}BrO_6$	25	251-253 (256-58)	94
7	3g	-4-Br	$C_{25}H_{15}BrO_6$	25	268-270 (266-68)	**97**
8	3h	-4-Me	$C_{26}H_{18}O_6$	30	264-266 (266-68)	84
9	3i	-2-OH	$C_{25}H_{16}O_7$	30	252-254 (254-56)	86
10	3j	-4-OH	$C_{25}H_{16}O_7$	30	221-223 (222-24)	88

[a] Isolated yield

Conclusion

Herein, we report the multicomponent synthesis of bis-coumarin derivatives from 4-hydroxy coumarins and substituted aryl aldehyde in the presence of alum catalyst by simple grinding technique at room temperature. This present green approach offers several advantages such as, excellent yield, short reaction time, simple reaction procedure to avoided electrical and thermal energy and with solvent free condition by using commercially available green biodegradable Alum as total environmentally benign catalyst. We believe that, this method found to be useful addition to present methodologies for the synthesis of biscoumarin derivatives.

Spectral data:

3,3'-(benzylidene)-bis-[4-hydroxycoumarin] ***(3a):***
Yield 93 %
IR (KBr, cm^{-1}): 3035, 1650, 1608, 756
^{1}H NMR (300 MHz, $CDCl_3$): δ 6.16 (s, 1H, CH), 6.84 to 7.58 (m, 13H, Ar), 10.70(brs, 2H, OH) ppm.
Mass: [M^++1]; 413.39

3,3'-(4-Nitrobenzylidene)-bis-[4-hydroxycoumarin] ***(3b):***
Yield 85 %

IR (KBr, cm^{-1}): 3030, 1650, 1615, 1530,1345, 7610
^{1}H NMR (300 MHz,$CDCl_3$): δ 6.58 (s, 1H, CH), 7.14 to 8.36 (m, 12H, Ar), 11.23(brs, 2H, OH) ppm.
Mass: [M^++1]; 458.07

3,3'-(4-Methylbenzylidene)-bis-[4-hydroxycoumarin](***3h***)*:
Yield 84%
IR (KBr, cm^{-1}): 3450, 3070, 1670, 1620, 1608, 1565, 1350, 765
^{1}H NMR (300 MHz, $CDCl_3$): δ 2.21 (s, 3H, CH_3), 6.23 (s, 1H, CH), 7.01-7.93 (m, 12H, Ar), 11.89 (br s, 2H, OH) ppm.
Mass: [M^++1]; 427.41

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