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Synthesis of coumarins via Pechmann reaction using Antimony chloride immobilized on neutral alumina as a Catalyst under solvent free conditions

M. Hari Krishna and P. Thriveni*

[1]*Department of Chemistry, Vikrama Simhapuri University, Nellore-524003, A.P, India*

ABSTRACT

Synthesis of coumarin derivatives from phenols with ethyl acetoacetate (via Pechmann reaction) in an excellent yield (86-95%) in presence of $SbCl_3$*–*Al_2O_3 *using microwave (MW) irradiation under solvent-free conditions. The present protocol shows some specific advantages such as short reaction times under solvent-free conditions.*

Keywords: *Coumarins, Pechmann reaction, microwave irradiation, Antimony chloride.*

INTRODUCTION

Coumarins are naturally occurring polyphenolics and its derivatives form an important class of benzo-pyrones which are distributed widely in plants, fungi and bacteria. Coumarins play an important role in the synthetic organic chemistry [1]. Coumarin moiety have been used in cosmetic industry [2], optical brighteners [3] and dispersed fluorescent and laser dyes [4], anticoagulants [5] and in the preparation of insecticides [6]. Coumarin and its derivatives possess significant biological activities such as antitumor [7], anti-HIV [8], antioxidative [9], antimicrobial [10], anticancer activity[11].

There are several methods for their synthesis like Perkin [12–14], Knoevenagel [15–20], Reformatsky [21], Wittig [22], and Pechmann [23–26]. The Pechmann condensation reaction is one of the most popular reaction for the preparation of coumarins moiety. Pechmann condensation involves the condensation of phenols with ß-ketoesters usually in the presence of different acid as catalyst to provide 4-substituted coumarins [27]. However, most of the procedures require harsh reaction conditions, a large amount of catalyst and high temperature to complete the reaction. Therefore, the search continues for a better catalyst for the synthesis of coumarins. Herein, we have focused our attention on $SbCl_3$–Al_2O_3 using microwave (MW) irradiation under solvent-free conditions.

MATERIALS AND METHODS

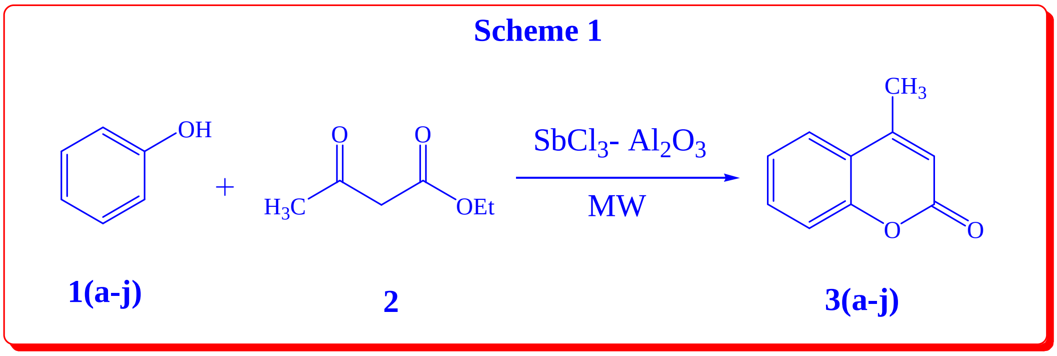
Melting points were determined in open-end capillaries and are uncorrected. Compounds were checked for their purity by TLC on silica gel G plates and spots were located by iodine vapors. The NMR spectra were measured with a 400 MHz Bruker Avance spectrometer at 400.1 and 100.6 MHz. Chemical shifts are given in ppm (δ) and spectra (^1H NMR and ^{13}C NMR) were recorded using tetramethylsilane (TMS) in the solvent of $CDCl_3$-*d* or DMSO-*d6* as the internal standard (^1H NMR: TMS at 0.00 ppm, $CDCl_3$ at 7.26 ppm, DMSO at 2.50 ppm; ^{13}C NMR: $CDCl_3$ at 77.16 ppm, DMSO at 40.00 ppm. The IR spectra were recorded on Perkin-Elmer spectrum RX IFT-IR System using KBr pellets.

General Procedure for the Preparation of Coumarins:

To a mixture of the phenolic compound (10 mmol) and ethyl acetoacetate (1.3g 10 mmol), 3.0 g of catalyst (5 mol% with respect to $SbCl_3$) were mixed thoroughly in a 100 ml beaker with glass rod and then irradiated in the MW oven for about 10 min at power level 800 W with 30 sec pause after every one min. the reaction progress was monitored by the appropriate time (TLC). After completion of the reaction, ethyl acetate (100 ml) was added and stirred well. The resultant product was collected by filtration under suction, The organic layer was dried over anhydrous Na_2SO_4 and evaporated under reduced pressure. The crude material was purified by column chromatography over silica gel to afford products 3(a-j) with high purity. All the products were identified by spectral (IR, ^{1}H NMR, ^{13}C NMR) and analytical data.

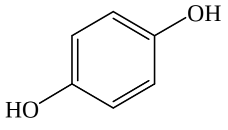
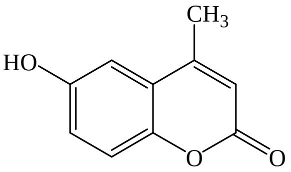
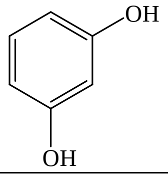
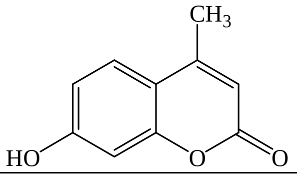
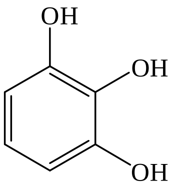
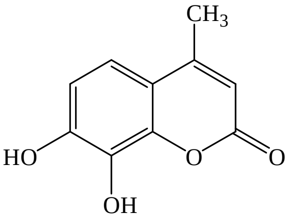
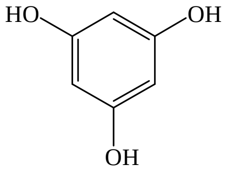
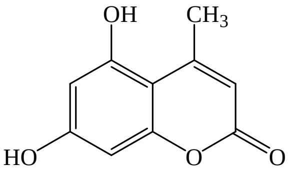
RESULTS AND DISCUSSION

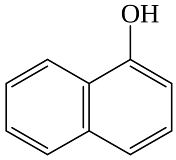
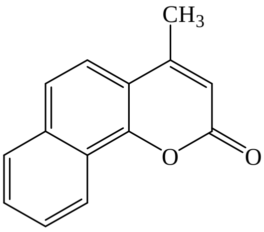
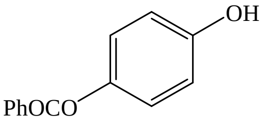
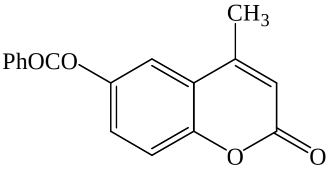
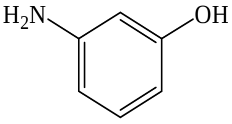
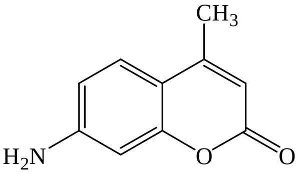
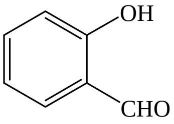
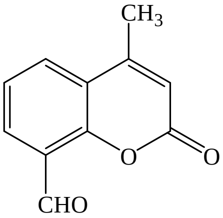
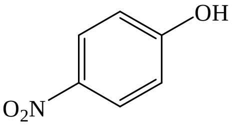
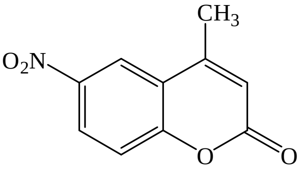
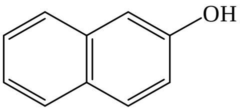
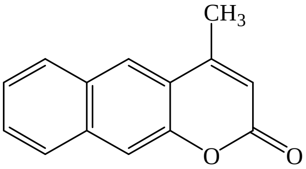
To study the feasibility of the $SbCl_3$–Al_2O_3 catalyzed Pechmann condensation, the reaction of phenolic compound with ethyl acetoacetate was selected as a model. The results indicated that only 5 mol% $SbCl_3$ could effectively catalyze the reaction which could be completed under microwave irradiation. Comparing with other catalysts $SbCl_3$–Al_2O_3 has some advantages such as low catalyst loading. Any excess of $SbCl_3$–Al_2O_3 beyond this loading did not show any substantial improvement in the yield. So 5 mol% $SbCl_3$ chosen as the optimal loading of the catalyst. The results indicated that a wide range of structurally varied phenols reacted smoothly to give the coumarins in good yields (scheme 1). As indicated in Table 1, the reaction works easily for a vast range of phenols with electron-donating groups with ethyl acetoacetate and reaction give low yields in the case of phenols with electron withdrawing groups like nitro (Table 1).



Scheme 1: The synthesis of substituted coumarins in the presence of $SbCl_3$- Al_2O_3

Table 1: Synthesis of Coumarin derivatives (3a-j)

Entry	Phenolic compound	Product	Yield(%)
1			89
2			93
3			92
4			91

5			78
6			79
7			92
8			83
9			75
10			88

Spectral data for selected compounds

6-Hydroxy-4-methylcoumarin (3a):
IR (KBr): 3258, 1516, 1473, 1689, 1209, 1096 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.4 (s, 1H) 7.5 (d, J=8.4 Hz, 1H),6.8 (d, J=8.8 Hz, 1H), 6.2 (s, 1H), 3.0 (s, 1H), 2.2 (s, 3H).

7-Hydroxy-4-methyl-2H-chromen-2-one (3b):
IR (KBr): 3260-3080, 1690, 1383, 1237, 1067, 985, 856, 525, 426 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.52 (brs, 1H), 7.35 (d, J=8.4 Hz, 1H), 6.78 (d, J=8.0 Hz, 1H), 6.65 (s, 1H), 6.10 (brs, 1H), 2.29 (brs, 3H).

7,8-Dihydroxy-4-methyl-2H-chromen-2-one (3c):
IR (KBr): 3260, 1675, 1385, 1235, 1060, 985, 856, 758, 572, 525, 426 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 10.04 (br, 1H), 9.30 (br, 1H), 7.10 (d, J=8.0 Hz, 1H), 6.80 (d, J=8.8 Hz, 1H), 6.10 (s, 1H), 2.37 (s, 3H).

5,7-Dihydroxy-4-methyl-2H-chromen-2-one (3d):
IR (KBr): 3185, 1675, 1380, 1227, 1067, 985, 856, 758, 572, 525, 426 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.35 (d, J=1.8 Hz, 1H), 6.25(d, J=1.8 Hz, 1H), 5.90 (s, 1H), 3.90–4.30 (br, s, 2H), 2.44 (s, 3H).

4-Methyl-2H-benzo[h]chromen-2-one (3e):
IR (KBr): 1675, 1360, 1240, 1060, 926 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50–8.91 (*m*, 6H), 6.51 (*s*, 1H), 2.71 (*s*, 3H).

4-Methyl-2-oxo-2*H*-chromen-6-yl benzoate (3f):
IR (KBr): 3060-3100, 1720, 1688, 1480, 1225, 840 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06 (dd, J = 7.9 Hz, 2H), 7.72 (dd, J = 8.0 Hz, 1H), 7.67 (d, J= 2.1 Hz, 1H), 7.46 (dd, J = 8.0 Hz, 2H), 7.35(d, J = 7.6 Hz, 1H), 7.21 (dd, J= 7.6 Hz, 1H),6.04 (s, 1H), 2.42 (s, 3H).

7-Amino-4-methyl-2H-chromen-2-one (3g):
IR (KBr): 3436, 3353, 3250, 1617, 1543, 1448, 1389, 1263, 1213, 1155, 1056, 835, 710, 649, 539, 452 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 (d, J=8.0 Hz, 1H), 6.43 (dd, J=7.2 Hz, 1H), 6.42 (d, J=2.5 Hz, 1H), 6.12 (brs, 2H), 5.92 (s, 1H), 2.26 (s, 3H).

8-Formyl-4-methylcoumarin (3h):
IR (KBr): 1606, 1558, 1474, 1716, 1610, 1211, 1091. ^{1}H NMR (400 MHz, $CDCl_3$): δ10.0 (s, 1H), 7.8 (d, J=8.4 Hz, 1H), 6.9 (d, J=8.7 Hz, 1H), 6.7 (d, 1H), 6.1 (s, 1H), 2.8 (s, 3H).

6-Nitro-4-methylcoumarin (3i):
IR (KBr): 1500, 1496, 1613, 1592, 1335, 1294, 1199 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.1 (d, J=8.4 Hz, 1H), 7.2 (s, 1H), 6.9 (d, J=8.7 Hz, 1H), 6.4 (s, 1H), 1.9 (s, 3H).

6,7-Benzo-4-methylcoumarin (3j):
IR (KBr): 1601,1512, 1466, 1631, 1277, 1216 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.7 (s, 2H), 7.6 (m, 1H), 7.2-7.4 (m, 2H), 7.1 (d, J=7.8 Hz, 1H), 5.2 (s, 1H), 1.7 (s, 3H, CH_3).

CONCLUSION

In conclusion, the efficient use of $SbCl_3$–Al_2O_3 as catalyst in the Pechmann condensation reaction using microwave (MW) irradiation in solvent-free media has been reported. This reaction leads to the formation of coumarin derivatives in excellent yields.

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