HETEROCYCLES, Vol. 71, No. 12, 2007, pp. 2721 - 2733. © The Japan Institute of Heterocyclic Chemistry
Received, 18th July, 2007, Accepted, 27th August, 2007, Published online, 28th August, 2007. COM-07-11175

$Al_2O_3/MeSO_3H$ (AMA) AS A NOVEL HETEROGENEOUS SYSTEM FOR SYNTHESIS OF COUMARINS UNDER MILD CONDITIONS

Hashem Sharghi* and Mahboubeh Jokar

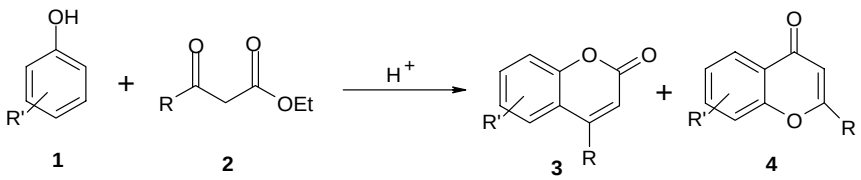
Department of Chemistry, Shiraz University, Shiraz, 71454, I.R.Iran

Fax:+98 711 2280926; E-mail: shashem@chem.susc.ac.ir.

Abstract – $Al_2O_3/MeSO_3H$ (AMA) is found to be an efficient reagent for the Pechman condensation reaction of phenols and β- ketoesters under solvent free conditions. The reaction protocol is simple, cost- effective, solvent free and gives good isolated yield with high purity and good regioselectivity.

INTRODUCTION

Coumarins are structural units of several products,[1] and feature widely in pharmacologically and biologically active compounds.[2-6] They have been used as additives in food and cosmetics, [7] and in the preparation of insecticides, optical brighteners [8] anticoagulants,[9a, b] and dispersed fluorescent and laser dyes.[9c] There have been many synthetic routes to coumarins, including Pechmann,[10a] Perkin,[10b] Knoevenagel,[10c] Reformatsky,[10d] Witting reaction[10e] and Flash Vacuum Pyrolysis[10f] the first of which is one of the most famous and valuable methods of synthesis. The Pechmann reaction has been studied with homogeneous acid catalysts such as sulfuric, hydrochloric, phosphoric[7] and trifluoroacetic acid,[11a] and with Lewis acids such as $FeCl_3$, $ZnCl_2$, $AlCl_3$, $ZrCl_4$, and also with P_2O_5, PPA, montmorillonite and other clays. [12] Solvents such as alcohol, ether, and benzene have been favored. Under some conditions, chromones (**4**) may be also formed (Scheme 1).[13]

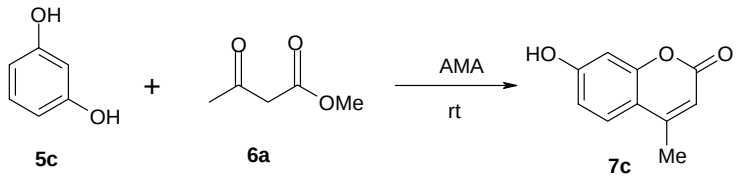


Scheme 1

However, these methods are associated with one or more disadvantages such as long reaction time, tedious work up, low yields, acidic waste, high temperature and expensive reagent.

In recent years, the use of inorganic solid oxides as catalysts, reagents, and reaction media have received considerable attention because of their high level of chemoselectivity and environmental compatibility as well as simplicity of operation and their use of availability at low cost. Thus, a number of heterogeneous reactions using inorganic oxides such as SiO_2, Al_2O_3, zeolite, etc. have already been reported.[14]

In our last work it was reported that a mixture of Al_2O_3/$MeSO_3H$ (AMA) is an effective reagent for Fries rearrangement,[15] Beckmann rearrangement,[16] direct conversion of aromatic aldehydes to the corresponding glycol monoesters,[17] hydration of nitriles into amides,[18] synthesis of macrocyclic polyether-diesters,[19] synthesis of new hydroxythioxanthone derivatives[20] and direct sulfonyltion of phenloes with *p*-toluensulfonic acid.[21] When this protocol was applied to the Pechmann synthesis, the expected coumarins were obtained as pure products in high yield by solvent-free stirring (Scheme 2).



Scheme 2

RESULTS AND DISCUSSION

To exploit simple and suitable condition for synthesis of coumarin derivatives, the reaction of resorcinol **(5c)** with methyl acetoacetate (**6a**) was chosen as a model, and its behavior was studied under a variety of conditions via TLC and ^{1}H NMR and ^{13}C NMR spectroscopy (Table 1).

Table 1. Results of the reactions[a] of **5c** and **6a** in the presence of different conditions

Entry	Conditions	Time (h)	Temp. °C	Yield (%)[b]
1	graphite (0.2 g)	5	100	5
2	Al_2O_3(0.2 g acidic)	5	rt	0
3	Al_2O_3(0.2 g acidic)	5	100	0
4	ZnO_2 (0.2 g)	5	100	0
5	SiO_2 (0.2 g)	5	100	0
6	TiO_2 (0.2 g)	5	100	0
7	AcOH (3 mmol)	5	rt	0
8	AcOH (3 mmol)	5	100	0
9	CF_3CO_2H (3 mmol)	5	rt	15
10	CF_3CO_2H (3 mmol)	5	100	20

Table 1. *Continued*

Entry	Conditions	Time (h)	Temp. °C	Yield (%)[b]
11	$MeSO_3H$ (3 mmol)	5	100	10 [c]
12	$MeSO_3H$ (3 mmol)	2	rt	78
13	$MeSO_3H$ (0.5 mmol) + (0.2 g) graphite	3.30	rt	75
14	$MeSO_3H$ (0.5 mmol) + (0.2 g)TiO_2	5	rt	10
15	$MeSO_3H$ (0.5 mmol) + (0.2 g) ZnO_2	5	rt	15
16	$MeSO_3H$ (0.5 mmol) + (0.2 g) SiO_2	3.30	rt	70
17	$MeSO_3H$ (0.5 mmol) + (0.2 g) basic Al_2O_3	4	rt	70
18	$MeSO_3H$ (0.5 mmol) + (0.2 g) neutral Al_2O_3	3	rt	75
19	$MeSO_3H$ (0.5 mmol) + (0.2 g) acidic Al_2O_3	20 min	rt	96

[a]: **5c** (1 mmol) and **6a** (1.2 mmol). [b]: Isolated yield. [c]: The reaction mixture decomposed.

According to Table 1, the best results were obtained when a mixture of Al_2O_3 (0.2 g) and $MeSO_3H$ (0.5 mmol) at room temperature for 20 minutes was used. The results also emphasize the importance of using, Al_2O_3 and $MeSO_3H$ concomitantly (compare entries 2, 3, 11, 12 with 19). The use of two equivalents of phenol **5c** and 1.2 equivalent of methyl acetoacetate (**6a**) for 7-hydroxyl-4-methylcoumarin (**7c**) does not improve the yield of coumarin in comparison with the case with one equivalent of phenol **5c** and 1.2 equivalent of methyl acetoacetate (**6a**).

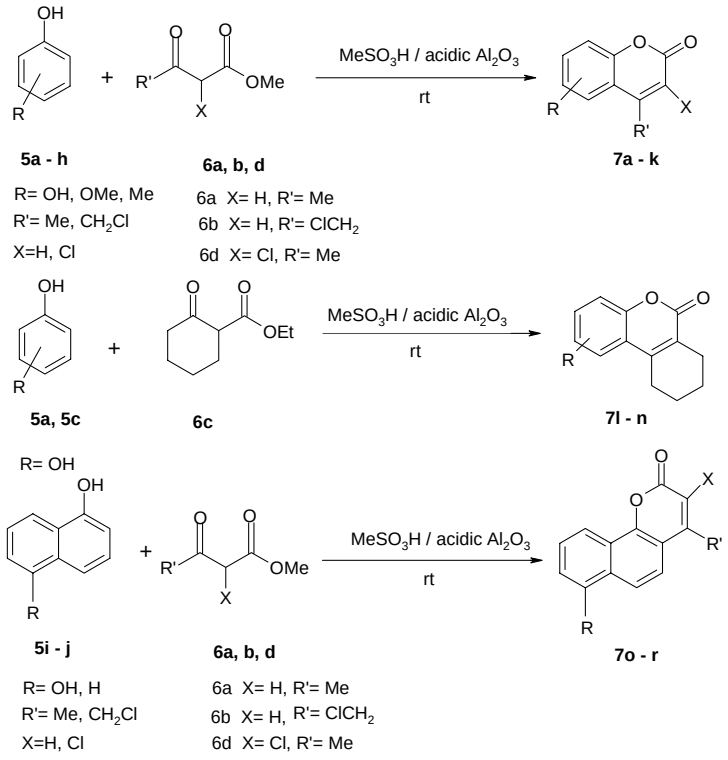
In the absence of Al_2O_3 (Table 1, entry 11) the reaction was conducted at 100 °C for 10 hours, affording the 7-hydroxyl-4-methylcoumarin (**7c**) , in 10 % yield; extension of the reaction time and increase of the reaction temperature resulted in the decomposition of the reaction mixture[22] to a dark solution.

Both the acetoacetic esters (ethyl and methyl) reacted almost similarly to produce coumarins.

The results also show the importance of using acidic Al_2O_3 in comparison with basic and neutral Al_2O_3 (compare entry 19 with entries 18, 17).

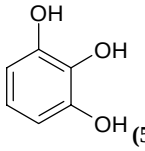
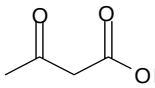
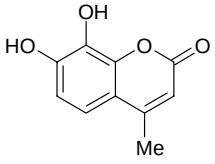
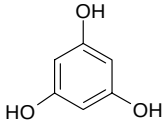
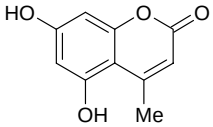
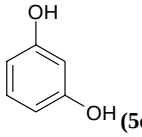
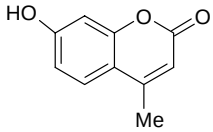
The above mentioned results show the advantages of this method as a new and more suitable way to coumarins synthesis.

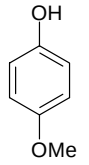
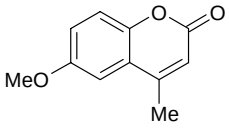
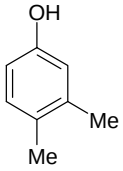
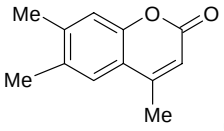
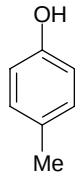
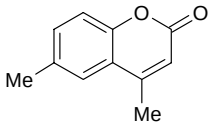
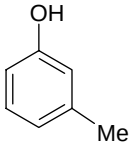
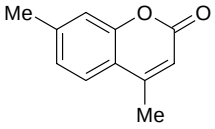
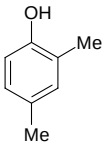
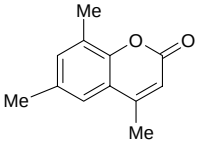
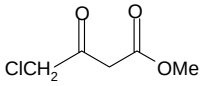
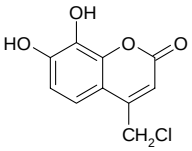
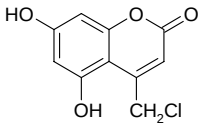
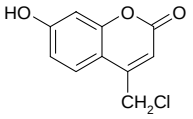
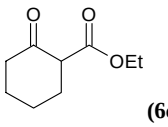
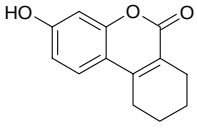
To establish the generality and applicability of this method we have carried out these reactions with a series of monohydric and polyhydric phenols with various β-ketoesters such as methyl acetoacetate, ethyl acetoacetate methyl 4-chloroacetoacetate, 2-carbethoxycylcohexanone and also 2-chloromethyl acetoacetate to furnish the corresponding coumarins in good yields. Short reaction times were observed (5 min–3 h) regardless of structural variations in the phenols or β-ketoesters (Scheme 3, Table 2). Thus, several pharmacologically relevant substituent patterns could be introduced with high efficiency under the present conditions.

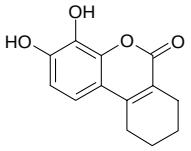
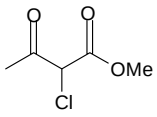
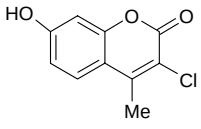
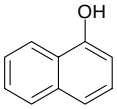
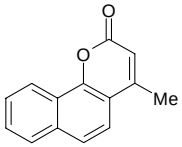
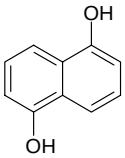
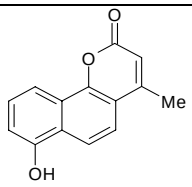
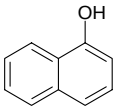
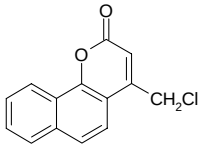
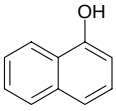
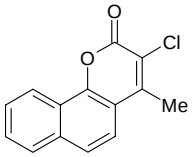
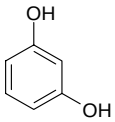
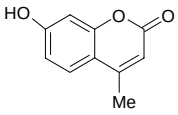


Scheme3

Table 2. The results of reaction **5** and **6** in the presence of AMA reagent

Entry	Phenols	β-Ketoesters	Product[a]	$MeSO_3H$ (mmol)	Time (h)	Yield (%)[b]
1	 **(5a)**	 **(6a)**	 **(7a)**	0.5	15 min	96
2	 **(5b)**	**(6a)**	 **(7b)**	0.5	20 min	97
3	 **(5c)**	**(6a)**	 **(7c)**	0.5	20 min	96

4	 **(5d)**	**(6a)**	 **(7d)**	1	2.30	84
5	 **(5e)**	**(6a)**	 **(7e)**	1	3	80
6	 **(5f)**	**(6a)**	 **(7f)**	1	2.45	85
7	 **(5g)**	**(6a)**	 **(7g)**	1	3	75
8	 **(5h)**	**(6a)**	 **(7h)**	0.5	2.50	80
9	**(5a)**	 **(6b)**	 **(7i)**	0.5	15 min	93
10	**(5b)**	**(6b)**	 **(7j)**	0.5	15 min	94
11	**(5c)**	**(6b)**	 **(7k)**	0.5	30 min	88
12	**(5c)**	 **(6c)**	 **(7l)**	0.5	10 min	96

13	**(5a)**	**(6c)**	 **(7m)**	0.5	5 min	95
14	**(5c)**	 **(6d)**	 **(7n)**	0.5	8 min	96
15	 **(5i)**	**(6a)**	 **(7o)**	0.5	2.30	79
16	 **(5j)**	**(6a)**	 **(7p)**	0.5	2.10	84
17	 **(5i)**	**(6b)**	 **(7q)**	0.5	35 min	90
18	 **(5i)**	**(6d)**	 **(7r)**	0.5	40 min	86
19		**(6a)**		0.5	20 min	94[c]

[a] a) Products were characterized by their IR and NMR spectra. b) Yields refer to isolated products. c) The reaction was carried out on a 100 mmol scale.

Pyrogallol **5a**, phloroglucinol **5b**, resorcinol **5c** and α-naphthol **5i** were subjected to the reaction with different β-ketoesters as shown in Table 2.

Yields of 4-(chloromethyl)-7-hydroxy-2*H*-chromen-2-one (**7k**), 3-hydroxy-7,8, 9,10-tetrahydro-6*H*-benzo[c]chromen-6-one (**7l**) and 3-chloro-7-hydroxy-4-methylcoumarin (**7n**) from resorcinol (**5c**) were similar to those obtained from unsubstituted methyl acetoacetate (Table 2, entries 11, 12, 14).

The nature of the substituent in the starting phenol seems to have relevant effect on the yield. Some phenols having electron-donating groups in the *para* position to the site of electrophilic substitution gave

maximum yields under reaction conditions in short periods of time. Some phenols having an electron-withdrawing group such as NO_2 and/or Cl did not produce any coumarin. Increase of the reaction time to 24 hours or more did not improve the yield of the reaction. Similarly naphthols (Table 2, entries 15-18) required longer reaction times due to presence of another phenyl moiety.

As expected, β-naphthol was less reactive than the alpha-isomer, yielding no more than 7% of 4-methyl-2*H*-benzo[*g*]chromen-2-ones in AMA at room temperature.

Naphthalene-1, 5-diol (**5j**) was subjected to the reaction with methyl acetoacetate as shown in Table 2(entry 16). Electron-acceptor effect of the α-pyrone ring in molecule **7p** hampers the second heterocyclization with participation of the hydroxy group in position *7*; however, it is known[23] that such heterocyclization does occur under more severe conditions.

p-Methoxyphenol showed no detectable demethylation under the reaction conditions (Table 2, entry 4).

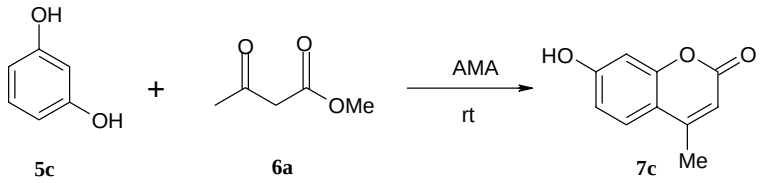
In the case of phenols that can form two products, regioselectivity is governed by less steric hindrance factors. As illustrated in Table 2, when resorcinol (**5c**), 3-methylphenol (**5g**) and 3,4-dimethylphenol (**5e**) were employed, 7-hydroxy-4-methyl-2*H*-chromen-2-one (**7c**), 4,7-dimethyl-2*H*-chromen-2-one(**7g**) and 4,6,7-trimethyl-2*H*-chromen-2-one(**7e**) were isolated as regioselective isomers in 96%, 75% and 80% yields, respectively (Table 2, entries 3, 7 and 5). Similar regiochemical behavior was observed in the reaction of resorcinol (**5c**) with methyl 4-chloroacetoacetate (**6b**), 2-carbethoxycylcohexanone (**6c**) and methyl 2-chloroacetoacetate (**6d**) affording 4-(chloromethyl)-7-hydroxy-2*H*-chromen-2-one (**7k**), 3-hydroxy-7,8,9,10-tetrahydro-6*H*-benzo[c]chromen-6-one(**7l**) and 3-chloro-7-hydroxy-4-methyl-2*H*-chromen-2-one (**7n**) in 88%, 96% and 96% yields, respectively (Table 2, entries 11, 12, 14).

The Pechmann reaction of resorcinol with methyl acetoacetate on a 100 mmol scale (Table 2, entry 19) proceeded just as well as the 1 mmol reaction.

From Table 2, it is observed that for most of the substrates, the reaction time is reduced drastically even at ambient conditions in contrast to reported methods,[10a] with an excellent yield of the coumarins. The reactions are remarkably clean, and no chromatographic separation is necessary to get the spectra-pure compounds.

Furthermore, the catalytic activity of the recovered catalyst (Al_2O_3) was examined. As shown in Table 3, the yield of coumarin product in the second and third cycles was almost the same as the first run. In every case alumina was easily recovered from the reaction mixture by simple washing with EtOH. It should be noted that $MeSO_3H$ was not adsorb onto Al_2O_3 during the reaction and extraction with EtOH. No attempt has been made to probe the mechanism of the reaction or gain a greater understanding of catalysis by alumina. Obviously, some other reports[7, 11a, b] showed that Brønsted acid could catalyze Pechmann condensation; however, our data demonstrated that $MeSO_3H$ only is not working. We assume that due to the absorption properties of alumina by bringing to together the two substrates together.

Table 3: Recycling of alumina



5c **6a** **7c**

Run	$MeSO_3H$ (0.5 mmol)	Yields (%)
1	0	0
1	0.5	96
2	0.5	93
3	0.5	91

In summary, we have demonstrated an efficient and simple alternative for the preparation of coumarin derivatives via the Pechmann condensation using AMA as reagent. The present method has the following advantages: (a) The reagent is readily available, safe to handle and inexpensive; (b) the procedure is simple; (c) work up is easy; (d) the reaction is carried out at room temperature. In fact, alumina can be re-used after simple washing with EtOH that renders a more economic process. All of these facts make this method a useful addition to the present methodologies. Hence, we believe that it will find wide application in organic synthesis as well as industry.

EXPERIMENTAL

Instrumentation, Analysis and Starting Material

NMR spectra were recorded on a Bruker Avance DPX-250 (^{1}H-NMR 250 MHz and ^{13}C NMR 62.9 MHz) spectrometer in pure deuterated solvents with tetramethylsilane as an internal standard. IR spectra were obtained using a Shimadzu FT-IR 8300 spectrophotometer. Mass spectra were determined on a Shimadzu GCMS-QP 1000 EX instruments at 70 or 20 ev. Melting points determined in open capillary tubes in a Büchi-535 circulating oil melting point apparatus. The purity determination of the substrates and reaction monitoring were accomplished by TLC on silica gel PolyGram SILG/UV 254 plates. Chemical materials were purchased from Fluka, Aldrich and Merck Companies. Acidic alumina (Al_2O_3) type 540 C was purchased from the Fluka-company

General procedure

To a mixture of $MeSO_3H$ (98%, 0.5-1 mmol and Al_2O_3, acidic type, 0.2 g), phenol (1 mmol) and β-ketoesters (1.2 mmol) were added. The mixture was stirred at rt**.** The reaction progress was monitored by TLC. After completion of the reaction (Table 2), EtOH (10 mL) was added and heated at 70°C and then

filtered. The ethanol solution was then put into a 100 mL beaker containing ice-cold water (30 mL). Crystalline product was collected by filtration to give coumarin derivatives, the crude crystals thus obtained were recrystallized from EtOH

Preparation of 7-Hydroxy-4-methyl-2*H*-chromen-2-one (7c): Prepared according to the general procedure using $MeSO_3H$ (98%, 1.06 mL, 7.5 mmol and Al_2O_3, acidic type, 3 g), resorcinol (1.65 g, 15 mmol) and methyl acetoacetate (2.23 mL, 18 mmol). The reaction progress was monitored by TLC. After the completion of the reaction (Table 2), EtOH (150 mL) was added and heated at 70ºC and then filtered. The ethanol solution was then put into a 100 mL beaker containing ice-cold water (450mL). Crystalline was collected by filtration to give 7-hydroxyl-4-methylcoumarin in 96% yield; the crude crystals thus obtained were recrystallized from EtOH to give pure 7-hydroxyl-4- methylcoumarin as colorless prisms.

The produced coumarins were known. Specific detailed data for each of the compounds are given below:

1) 7,8-Dihydroxy-4-methyl-2*H*-chromen-2-one (7a) White solid, mp 236-239 °C, (lit.,[25] 236-238 ºC); yield 96 %. ^{1}H NMR (250 MHz, DMSO-d_6): δ 2.35 (s, 3H), 6.12 (s, 1H), 6.82 (d, 1H, J =8.6 Hz), 7.09 (d, 1H, J =8.6 Hz), 9.30 (s, 1H), 10.10 (s, 1H). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ 18.2, 110.1, 112.0, 112.7, 115.4, 132.1, 143.2, 149.3, 153.9, 160.2. IR (KBr, cm^{-1}): 3227 (OH), 1668 (C=O). MS: m/z=192 (M+), 176, 164, 147, 136, 118, 89, 77, 63.

2) 5,7-Dihydroxy-4-methyl-2*H*-chromen-2-one (7b) White solid, mp 280-284 °C; (lit.,[24] 281-284 ºC); yield 97 %. ^{1}H NMR (250 MHz, DMSO-d_6): δ 2.24 (s, 3H); 5.83 (s, 1H); 6.13 (s, 1H); 6.16 (s, 1H); 10.28 (s, 1H); 10.50 (s, 1H). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ 23.4, 94.4, 99.0, 102.1, 108.8, 154.92, 156.42, 157.87, 160.03, 160.99. IR (KBr, cm^{-1}): 3252 (OH), 1668 (C=O).

3) 7-Hydroxy-4-methyl-2*H*-chromen-2-one(7c) Colorless prisms, mp 185-188 °C; (lit.,[24] 185 ºC); yield 96 %. ^{1}H NMR (250 MHz, DMSO-d_6): δ 2.13 (s, 3H), 5.88 (s, 1H), 6.31 (s, 1H), 6.59 (d, 1H, J =8.7 Hz), 7.34 (d, 1H, J =8.7 Hz), 10.32 (s, 1H). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ 18.00, 102.0, 110.15, 111.910, 112.75, 126.44, 153.39, 154.73, 160.22, 161.06. IR (KBr, cm-1): 3500 (OH), 1681 (C=O).

4) 6-Methoxy-4-methyl-2*H*-chromen-2-one(7d) Colorless prisms, mp 164-165 °C; yield 84 %. ^{1}H NMR (250 MHz, DMSO-d_6): δ 2.30 (s, 3H), 3.81 (s, 3H), 6.36 (s, 1H), 7.14 (s, 1H), 7.17 (d, 1H, J =8.3 Hz), 7.68 (d, 1H, J =8.3 Hz). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ 18.2, 55.7, 108.1, 114.6, 117.4, 119.0, 120.0, 145.1, 152.9, 155.5, 161. IR (KBr, cm^{-1}): 1705 (C=O).

5) 4,6,7-Trimethyl-2*H*-chromen-2-one(7e)[27]White solid, mp 167-169 °C; yield 80 %. ^{1}H NMR (250 MHz, DMSO-d_6): δ 2.15 (s, 3H), 2.19 (s, 3H), 2.26 (s, 3H), 6.26 (s, 1H), 7.16 (s, 1H), 7.49 (s, 1H). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ 22.8, 23.5, 24.3, 115.0, 121.5, 121.9, 122.5, 129.9, 131.8, 133.4, 140.6, 157.6. IR (KBr, cm^{-1}): 1706 (C=O).

6) 4,6-Dimethyl-2*H*-chromen-2-one(7f) Colorless prisms, mp 151-153 °C; (lit.,[12f] 150-151 ºC) yield 85 %. ^{1}H NMR (250 MHz, DMSO-d_6): δ 2.35 (s, 6H), 6.40 (s, 1H), 7.24 (d, 1H, *J* =8.40 Hz), 7.40 (d, 1H, *J* =8.40 Hz), 7.58 (s, 1H). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ 18.0, 20.3, 114.2, 116.1, 119.2, 125.0, 132.7, 133.5, 150.9, 153, 159. 8. IR (KBr, cm^{-1}): 1719 (C=O).

7) 4,7-Dimethyl-2*H*-chromen-2-one(7g) Colorless prisms, mp 131-132 °C; (lit.,[12f] 131.5-132 ºC); yield 75 %. ^{1}H NMR (250 MHz, DMSO-d_6): δ 2.36 (s, 6H), 6.26 (s, 1H), 7.22(s, 1H), 7.26 (d, 1H, *J*=8.7 Hz), 7.58 (d, 1H, *J*=8.7 Hz). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ 17.9, 20.93, 113.2, 116.3, 117.1, 124.9, 125.3, 142.6, 152.9, 153.1, 159. 8. IR (KBr, cm^{-1}): 1703 (C=O).

8) 4, 6, 8-Trimethyl-2*H*-chromen-2-one (7h) White solid, mp 129-132 °C ; yield 80 %. ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.30(s, 3H); 2.36 (s, 6H); 6.18 (s, 1H); 7.12 (s, 2H). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 15.58, 18.8, 20.9, 114.7, 119.4, 122.0, 126.0, 133.1, 134.1, 150.1, 152.6, 161.2. Anal Calcd for $C_{12}H_{12}O_2$ (188.222): C, 76.57; H, 6.43. Found: C, 76.51; H, 6.40.IR (KBr, cm^{-1}): 1708 (C=O)**.**

9)4-(Chloromethyl)-7,8-dihydroxy-2*H*-chromen-2-one (7i) White solid, mp 128-133 °C, (lit.,[28a] 133-135 ºC); yield 93 %. ^{1}H NMR (250 MHz, DMSO-d_6): δ 4.47 (s, 2H),6.23 (s, 1H),6.60 (d, 1H, *J* =8.7 Hz), 6.9 (d, 1H, *J* =8.7 Hz), 9.37(s, 1H), 10.07 (s, 1H). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ 41.4, 110.0, 110.9, 112.2, 115.4, 132.4, 134.0, 149.8, 151.3, and 160.1. Anal Calcd for $C_{10}H_7ClO_4$ (226.613): C, 53.00; H, 3.11. Found: C, 53.07; H, 3.09. IR (KBr, cm^{-1}): 3225(OH), 1701 (C=O)

10) 4-(Chloromethyl)-5,7-dihydroxy-2*H*-chromen-2-one (7j) White solid, mp 246-248°C; (lit.,[28b] 243-245ºC); yield 94 %. ^{1}H NMR (250 MHz, DMSO-d_6): δ 5.01 (s, 2H), 6.19 (s, 2H), 6.25 (s, 1H), 10.43 (s, 1H), 10.89 (s, 1H). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ 44.91, 94.75, 99.17, 99.74, 108.79, 152.01, 156.47, 157.09, 160.02, 161.470. Anal Calcd for $C_{10}H_7ClO_4$ (226.613): C, 53.00; H, 3.11. Found: C, 52.98; H, 3.15. IR (KBr, cm-1): 3300(OH), 1662(C=O).

11) 4-(Chloromethyl)-7-hydroxy-2*H*-chromen-2-one (7k) Colorless prisms, mp 178-181°C; (lit.,[28c] 180-181ºC); yield 88 %. ^{1}H NMR (250 MHz, DMSO-d_6): δ 4.68 (s, 2H), 6.26 (s, 1H), 6.48 (d, 1H, *J* =2.2 Hz), 6.58 (dd, 1H, J =8.74 Hz, *J* =2.2), 7.40 (d, 1H, *J* =8.72 Hz), 10.40 (s, 1H). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ 41.3, 102.2, 109.2, 111.0, 113.0, 126.5, 150.9, 155.23, 160.1, 161.4. Anal Calcd for $C_{10}H_7ClO_3$ (210.613): C, 57,03; H, 3.35. Found: C, 57.07; H, 3.38. IR (KBr, cm^{-1}): 3363(OH), 1740(C=O).

12) 3-Hydroxy-7,8, 9,10-tetrahydro-6*H*-benzo[c]chromen-6-one (7l) White solid, mp 217-220°C ; yield 96 %.^{1}H NMR (250 MHz, $CDCl_3$): δ 1.72-1.79 (m, 4H), 2.50 (t, 2H, *J* =5.8 Hz), 2.68 (t, 2H, *J* =5.8 Hz), 6.76 (d, 1H, *J* =8.7 Hz), 6.90 (s. 1H), 7.38(d, 1H, *J* =8.7 Hz). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 21.3, 21.6, 23.7, 25.3, 103.1, 106.1, 112.9, 118.0, 124.5, 143.0, 147.0, 158.5, 162. Anal Calcd for $C_{13}H_{12}O_3$ (216.233): C, 72.21; H, 5.59. Found: C, 72.27; H, 5.49. IR (KBr, cm^{-1}): 3280 (OH), 1678 (C=O)

13) 3,4-Dihydroxy-7,8,9,10-tetrahydro-6*H*-benzo[c]chromen-6-one (7m) White solid, mp 265-268 °C; yield 95 %. ^{1}H NMR (250 MHz, DMSO-d_6): δ 1.68-1.70 (m, 4H), 2.34 (t, 2H, *J* =5.7 Hz), 2.68 (t, 2H, *J* =5.7 Hz), 6.77 (d, 1H, *J* =8.6 Hz), 6.90(d, 1H, *J* =8.6 Hz), 9.67 (s, 2H). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ 20.9, 21.2, 23.5, 24.6, 111.9, 112.7, 113.8, 118.2, 131.8, 142.0, 148.0, 153.0, 160.0. Anal Calcd for $C_{13}H_{12}O_4$ (232.232): C, 67.23; H, 5.21. Found: C, 67.20; H, 5.23. IR (KBr, cm $^{-1}$): 3463 (OH), 1678 (C=O).

14) 3-Chloro-7-hydroxy-4-methyl-2*H*-chromen-2-one (7n) White solid, mp 236-240 °C; (lit;[29] 236 ºC) yield 96 %. ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.49 (s, 3H), 6.78 (s, 1H), 6.80 (d, 1H, *J* =9.4 Hz), 7.45 (d, 1H, *J* =9.4 Hz). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ 15.6, 101.8, 103.1, 111.6, 113.5, 127.1, 149.0, 152.7, 158.0, 161.2. IR (KBr, cm^{-1}): 3325 (OH), 1759, 1693 (C=O), 840.

15) 4-Methyl-2*H*-benzo[h]chromen-2-one (7o) Light brown solid, mp 168-171 °C; (lit.,[12f] 170 ºC) yield 79 %. ^{1}H NMR (250 MHz, DMSO-d_6): δ 2.44 (s, 3H), 6.40 (s, 1H), 7.4 -7.67 (m, 4H), 7.93 (d, 1H, *J* =9.1 Hz), 8.24 (d, 1H, *J* =9.1 Hz). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ 18.6, 113.8, 121.1, 121.5, 122.1, 123.7, 126.4, 127.3, 127.9, 128.5, 134.3, 142.2, 154.0, 159. 90. IR (KBr, cm^{-1}): 1711 (C=O).

16)7-Hyroxy-4-methyl-2*H*-benzo[h]chromen-2-one (7p) Light green solid, mp 296-298 °C; (lit.,[30a] 298-300 ºC) yield 84 %. ^{1}H NMR (250 MHz, DMSO-d_6): δ 2.45 (s, 3H), 6.41 (s, 1H), 7.05 (d, 1H, *J* =8.3 Hz), 7.42 (t, 1H, *J* =8.02 Hz), 7.53 (d, 1H, *J* =8.9 Hz), 7.9 (d, 1H, J =8.3 Hz), 8.08 (d, 1H, *J* =8.9 Hz), 10.47 (s, 1H). ^{13}C NMR (62.9 MHz, DMSO-d_6): δ 18.6, 110.9, 111.9, 113.7, 115.1, 118.1, 119.4, 123.5, 125.4, 127.9, 149.5, 153.3, 154.1, 159.7. Anal Calcd for $C_{14}H_{10}O_3$ (226.227): C, 74.33; H, 4.46. Found: C, 74.37; H, 4.49. IR (KBr, cm^{-1}): 3220 (OH), 1678 (C=O).

17) 4-(Chloromethyl)-2*H*-benzo[h]chromen-2-one (7q) White solid, mp 160-165 °C; (lit.,[30b] 165-167ºC) yield 90 %. ^{1}H NMR (250 MHz, $CDCl_3$): δ 4.73 (s, 2H), 6.76 (s, 1H), 7.4-7.61 (m, 4H), 7.81 (d, 1H, *J* =9.4 Hz), 8.49 (d, 1H, *J* =9.4 Hz). ^{13}C NMR (62.9 MHz, $CDCl_3$): δ 41.6, 111.0, 112.7, 115.0, 119.5, 122.6, 123.2, 124.5, 127.4, 127.7, 129.0, 134.0, 150.4, 160.0. IR (KBr, cm^{-1}): 1716 (C=O).

18) 3-chloro-4-methyl-2*H*-benzo[h]chromen-2-one (7r) White solid, mp 247-248 °C; yield 86 %. ^{1}H NMR (250 MHz, $CDCl_3$): δ 2.64 (s, 3H), 7.25-7.85 (m, 5H), 8.50 (t 1H, *J* =9.1 Hz). ^{13}C NMR (250 MHz, $CDCl_3$): δ 16.7, 113.8, 120.5, 122.4, 122.1, 124.9, 126.4, 127.3, 127.9, 128.8, 134.3, 145.2, 154.1, 159.8. Anal. Calcd for $C_{14}H_9ClO_2$ (244.673): C, 68.72; H, 3.71. Found: C, 68.81; H, 3.66. IR (KBr, cm^{-1}): 1719 (C=O).

ACKNOWLEDGEMENTS

We gratefully acknowledge the support of this work by the Shiraz University Research Council. We are also grateful to Mr. H. Sajedian Fard for helpful cooperation.

REFERENCES (AND NOTES)

1. (a) R. D. H. Murray, *Prog. Chem. Org. Nat. Prod*., 1991, **58**, 84. (b) S. M. Kovalenko, S. V. Valsov, and V. P. Chernykh, *Heteroatom Chem*., 2007, **18**, 341. (c) M. Dabiri, P. Salehi, M. A. Zolfigol, and M. baghbanzadeh, *Heterocycles*, 2007, **71**, 677. (d) S. K. De and R. A. Gibbs, *Synthesis*, 2005, 1231. (e) M. K. Potdar, S. S. Mohile, and M. M. Salunkhe, *Tetrahedron Lett.*, 2001, **42**, 9285. (f) W. Jie, D. Tianning, S. Wei, and L. Yizhe, *Synth. Commun.,* 2006, **36**, 2949.
2. A. Mitra, S. K. Misra, and A. Patra, *Synth. Commun.,* 1980, **10**, 915.
3. L. A. Singer and N. P. Long, *J. Am. Chem. Soc*., 1966, **88**, 5213.
4. R. D. H. Murray, J. Mendez, and S. A. Brown, 'The Natural Coumarins: Occurrence, Chemistry and Biochemistry', Wiley & Sons, New York, 1982.
5. M. J. Brites, C. Santos, S. Nacimento, B. Giante, and M. N. Berberan-Santos, *Tetrahedron Lett*., 2004, **45**, 6927.
6. (a) K. Hara, K. Sayama,Y. Ohga, A. Shinpo, S. Suga, and H. Arakawa, *Chem. Commun*., 2001, 569. (b) C. Jiao, L. Chen, G. Shen, and R. Yu, *Sens. Actuators*, 2003, **94**, 176. (c) Y. Kashman, K. R. Gustafson, R. Fuller, J. H. Cardellina, J. B. McMahon, M. J. Currens, R. W. Buckheit, S. H. Hughes, G. M. Cragg, and M. R. Boyd, *J. Med. Chem*., 1992, **35**, 2735.
7. R. O. Kennedy and R. D. Thornes, 'Coumarins: Biology, Applications and Mode of Action', Wiley & Sons, Chichester, 1997.
8. M. Zahradnik, 'The Production and Application of Flourescent Brightening Agents', Wiley & Sons, 1992.
9. (a) A. K. Mitra, A. De, N. Karchaudhuri, S. K. Misra, and A. K. Mukopadhyay, *J. Indian Chem. Soc*., 1998, 75, 666. (b) G. Cravotto, G. M. Nano, G. Palmisano, and S. Tagliapietra, *Tetrahedron: Asymmetry*, 2001, **12**, 707. (c) M. Maeda, 'Laser Dyes', Academic, New York, 1994.
10. (a) S. Sethna and R. Phandka, *Org. React*., 1953, **7**, 1. (b) J. R. Jonhnson, *Org*. *React*., 1942, **1**, 210. (c) F. Jones, O. Piermatti, and F. Pizzo, *Heterocycles*, 1996, **43**, 1257. (d) R. L. Shirner, *Org. React*., 1942, **1**, 1. (e) I. Yavari, R. Hekmat-Shoar, and A. Zonouzi, *Tetrahedron Lett*., 1998, **39**, 2391. (f) G. A. Cartwright and H. J. McNab, *J. Chem. Res. (S).*, 1997, 296.
11. (a) L. L. Woods and J. Sapp, *J. Org. Chem*., 1962, **27**, 3703. b) W. C. Sun, K. R. Gee, and R. P. Haugland, *Bioorg. Med. Chem. Lett*., 1998, 3107.
12. (a) H. Appel, *J. Chem. Soc*., 1935, 1031. (b) Z. S. Ahmad and R. D. Desai, *Proc. Indian Acad. Sci*., 1937, *5A*, 277 (*Chem. Abstr*., 1937, **31**, 5785). (c) R. Robinson and F. Weygand, *J. Chem. Soc*., 1941, 386. (d) A. J. Nadkarni and N. A. Kudav, *Ind. J. Chem. Sect. B*, 1981, **20**, 719. (e) B. Gangadasu, P. Narender, B. China Raju, and V. Jayathirtha Rao, *J. Chem. Res*., 2004, 480. (f) T. S. Li, Z. H. Zhang, F. Yang, and C. G. Fu, *J. Chem. Res. (S)*, 1998, 38.

13. M. S. Manhas, S. N. Ganguly, S. Mukherjee, A. K. Jain, and A. K. Bose, *Tetrahedron Lett*., 2006, **47**, 2423.
14. M. Mihara, Y. Ishino, S. Minakata, and M. Komatsu, *Synlett*, 2002, 1526.
15. H. Sharghi and B. Kaboudin, *J. Chem. Res. (S)*, 1998, 628.
16. H. Sharghi and M. Hosseini Sarvari, *J. Chem. Res. (S)*, 2001, 446.
17. H. Sharghi and M. Hosseini Sarvari, *J. Org. Chem*., 2003, **68**, 4096.
18. H. Sharghi and M. Hosseini Sarvari, *Synth. Commun*., 2003, **33**, 207.
19. H. Sharghi and M. Hosseini Sarvari, *Tetrahedron*, 2003, **59**, 3627.
20. H. Sharghi and A. R. Salimi Beni, *Synthesis,* 2004, 17, 2900.
21. H. Sharghi and Z. Shahsavari-Fard, *J I C S*., 2005, **2**, 47 (http://www.ics-ir.org/ jics /).
22. M. Ueda, M. Sato, and A. Mochizuki, *Macromolecules*, 1985, **18**, 2723.
23. R. Robinson and F. Weygand, *J. Chem. Soc*., 1941, 387.
24. A. C. Khanderkar and B. M. Khadikar, *Synlett,* 2002, 152.
25. M. Maheswara, V. Siddaiah, G. L. Vasantha Damu, Y. K. Rao, and C. V. Rao, *J. Mol. Cat. A: Chem*., 2006, **255**, 49.
26. S. S. Bahekar and D. B. Shinde, *Tetrahedron Lett*., 2004, **45**, 7999.
27. G. P. Romanelli, D. Bennardi, D. M. Ruiz, G. Baronetti, H. J. Thomas, and J. C. Autino, *Tetrahedron Lett*., 2004, **45**, 8935.
28. (a) M. S. Khaikin, N. L. Petrova, and V. A. Kukhtin, *Zh. Obshch. Khim*., 1963, **33**, 3941. (b) G. Smitha and C. Sanjeeva, *Synth. Commun*., 2004, **34**, 3997. (c) G. Zagotto, O. Gia, F. Baccichetti, E. Uriarte, and M. Palum, *Photochem. Photobiol*., 1993, **58**, 486.
29. J. C. Rodrıguez-Domınguez and G. Kirsch, *Tetrahedron Lett*., 2006, **47**, 3279.
30. V. V. Mezheritskii, R. V. Tyurin, L. G. Minyaeva, A. N. Antonov, and A. P. Zadorozhnaya, *Russ. J. Org. Chem*., 2006, **42**, 1458. (b) G. V. M. Sharma, J. Janardhan Reddy, P. Sree Lakshmi, and P. Radha Krishna, *Tetrahedron Lett*., 2005, **46**, 6119.