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An Efficient Solid-Phase Green Synthesis of Chromen-2-one Derivatives

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An efficient route for the synthesis of chromen-2-one derivatives (**3a-h**) *via* Knoevenagel condensation under solid phase by the condensation of salicylaldehydes (**1**) with various ethyl acetate derivatives (**2**) is described. The reaction has been done under conventional method as well as under solid-phase method. The later method has been found to be much better in terms of time and yield. The structures of all the compounds were confirmed by spectral and analytical data.

Key Words: Salicylaldehyde, Various derivatives of ethyl acetate, $ZrOCl_2.8H_2O$ (10 mol %), Mortar and pestle.

INTRODUCTION

The preparation and screening of small molecules libraries based on natural products have attracted in recent years[1]. Chromen-2-ones (2*H*-1-benzopyran-2-ones) are well-known structural unit present in several natural products[2]. Chromen-2-one derivatives have been used as therapeutic agents[3], optical bleaching agents[4] and active media for tunable dye lasers[5]. In view of the above observations and in continuation of our studies in the field of oxygen heterocycles, the present investigation deals the synthesis of chromen-2-one derivatives.

Various methods are known for the synthesis of substituted chromen-2-ones in the literature including the Pechmann[6], Perkin[7], Knoevenagel[8], Claisen[9], Reformatsky[10] and Wittig reactions[11]. Chromen-2-ones have been synthesized by the Kostanecki-Robinson reaction of *o*-hydroxyarylalkyl ketones with acid anhydrides, which proceeds through an ester enolate intermediate[12]. Most of the procedures suffer from several disadvantages like harsh reaction conditions, such as the use of stoichiometric amount of minerals, Lewis acids or toxic reagents, often under high temperatures and with longer reactions time, poor substituent tolerance and low yields[13]. Thus, it is clearly evident that development of new and flexible protocols is required.

EXPERIMENTAL

Melting points are uncorrected and were determined in open capillary tubes in sulphuric acid bath. TLC was performed on silica gel-G and spotting was done using UV-light. IR spectra were recorded with Perkin- Elmer 1000 instrument in KBr phase. ^{1}H NMR was recorded on VARIAN 400 MHz instrument and Mass spectra were recorded on Agilent-LC-MS instrument.

Synthesis of 3 (conventional method): A mixture of **1** (3 mmol), **2** (3 mmol) and $ZrOCl_2.8H_2O$ (10 mol %) was heated under neat conditions for 0.5 h. The reaction was monitored by TLC. After the complete disappearance of the starting material spot on TLC, the reaction mixture was cooled to room temperature and poured in to ice-cold water (100 mL). The separated solid was filtered, thoroughly washed with water and dried to obtain the crude product. The latter was recrystallized from ethanol to yield pure **3**.

Compound 3a. Yellow solid; m.p. 119-121 ºC;

Compound 3b. Yellow solid; m.p. 91-92 ºC; IR (KBr): 1722 cm^{-1} (strong, sharp, -CO- of coumarin ring), 1662 cm^{-1} (strong, sharp, CO of $COOC_2H_5$); ^{1}H NMR (DMSO-d_6/TMS) δ: 1.43 (t, 3H, CH_3), 4.43 (q, 2H, CH_2), 7.39-8.58 (complex, m, 5H aryl protons); MS: *m/z* = 218 (M^{+}+1): Elemental analysis (%): found C 66.17, H 4.49; $C_{12}H_{10}O_4$ requires C 66.05, H 4.58.

Compound 3c. Yellow solid; m.p. 159-161 ºC; IR (KBr): 1724 cm^{-1} (strong, sharp, -CO- of coumarin ring), 1656 cm^{-1} (strong, sharp, CO of $COCH_3$); ^{1}H NMR (DMSO-d_6/TMS): δ 2.52 (s, 3H, $-CH_3$), 7.33-8.55 (complex, m, 4H aryl protons), 11.7 (s, 1H, D_2O exchangeable -OH); MS: *m/z* = 205 (M^{+}+1). Elemental analysis (%): found C 66.17, H 4.49; $C_{12}H_{10}O_4$ requires C 66.05, H 4.58.

Compound 3d. Yellow solid; m.p. 97-98 ºC; IR (KBr): 1728 cm^{-1} (strong, sharp, -CO- of coumarin ring), 1668 cm^{-1} (strong, sharp, CO of $COOC_2H_5$); ^{1}H NMR (DMSO-d_6/TMS) δ: 1.55 (t, 3H, CH_3), 4.31 (q, 2H, CH_2), 7.27-8.42 (complex,

m, 4H aryl protons), 11.7 (s, 1H, D_2O exchangeable -OH); MS: *m/z* = 234 (M^{+} + 1). Elemental analysis (%): found C 60.59, H 4.27; $C_{12}H_{10}O_5$ requires C 61.54, H 4.30.

Compound 3e. Yellow solid; m.p. 139-140 ºC; IR (KBr): 1732 cm^{-1} (strong, sharp, CO of coumarin ring), 1660 (strong, sharp, CO of $COCH_3$); ^1H NMR (DMSO-d_6/TMS): δ 2.68 (s, 3H, $-CH_3$), 3.88 (s, 3H, $-OCH_3$), 7.38-8.48 (complex, m, 4H, aryl protons); MS: *m/z* = 218 (M^{+}+1). Elemental analysis (%): found C 65.02, H 4.58; $C_{12}H_{10}O_4$ requires C 66.05, H 4.62.

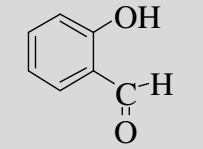
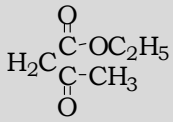
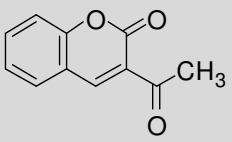
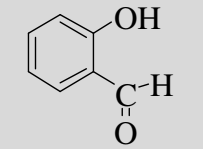
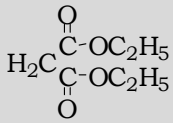
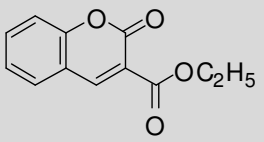
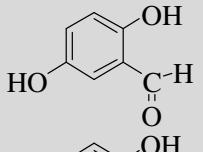
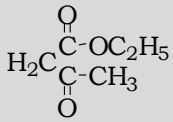
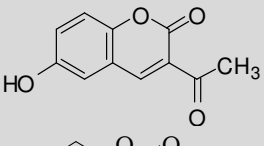
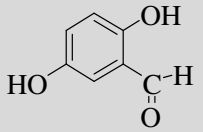
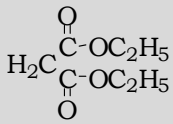
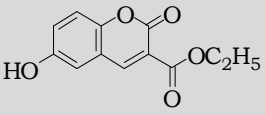
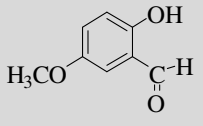
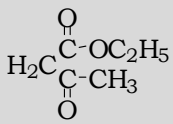
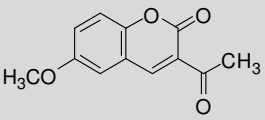
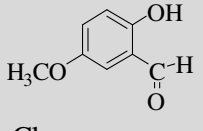
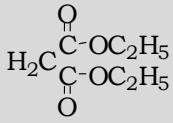
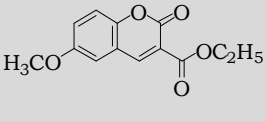
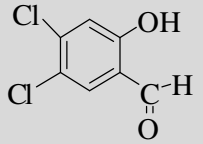
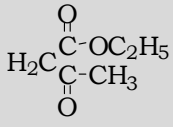
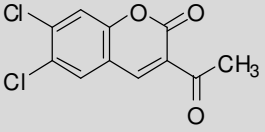
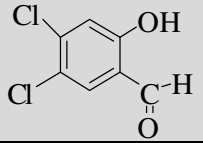
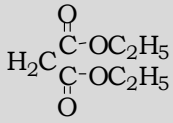
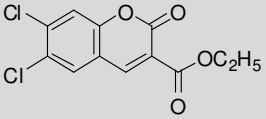
Compound 3f. Yellow solid; m.p. 89-91 ºC; IR (KBr): 1731 cm^{-1} (strong, sharp, -CO- of coumarin ring), 1655 cm^{-1} (strong, sharp, CO of $COOC_2H_5$); ^1H NMR (DMSO-d_6/TMS) δ: 1.55 (t, 3H, CH_3), 3.80 (s, 3H, $-OCH_3$), 4.29 (q, 2H, CH_2), 7.23-8.38 (complex, m, 4H aryl protons); MS: *m/z* = 248 (M^{+} + 1). Elemental analysis (%): found C 61.88, H 4.66; $C_{13}H_{12}O_5$ requires C 62.90, H 4.87.

Compound 3g. Yellow solid; m.p. 151-53 ºC; IR (KBr): 1742 cm^{-1} (strong, sharp, CO of coumarin ring) 1662 (strong, sharp, CO group of $COCH_3$); ^1H NMR (DMSO-d_6/TMS): δ 2.55 (s, 3H, $-CH_3$), 7.34-8.44 (complex, m, 3H, aryl protons); MS: *m/z* = 255 (M^{+} + 1). Elemental analysis (%): found C 51.39, H 2.35, Cl 27.58; $C_{11}H_6O_3Cl_2$ requires C 50.90, H 2.2, Cl 26.98.

Compound 3h. Yellow solid; m.p. 131-133 ºC; IR (KBr): 1735 cm^{-1} (strong, sharp, -CO- of coumarin ring), 1670 cm^{-1} (strong, sharp, CO of $COOC_2H_5$); ^1H NMR (DMSO-d_6/TMS) δ : 1.51 (t, 3H, CH_3), 4.31 (q, 2H, CH_2), 7.27-8.41 (complex, m, 3H aryl protons); MS: *m/z* = 285 (M^{+}+1). Elemental analysis (%): found C 50.20, H 2.81, Cl 24.70; $C_{12}H_8O_4Cl_2$ requires C 49.90, H 2.77, Cl 23.88.

Alternative general procedure for the preparation of 3 (solid-phase grinding method): In the solid-phase synthesis method **3a** (*i.e.*, **3**, $R^1 = R^2 = R^3 = H$), has been synthesized. Thus, when equimolar quantities of ^{1a} (*i.e.*, **1**, $R^1 = R^2 = H$) and **2a** (*i.e.*, **2**, $R^3 = H$) were ground along with $ZrOCl_2 \cdot 8H_2O$ (10 mol %) in a mortar with the help of pestle at room temperature, the reaction was completed within 13 min as shown by TLC analysis of crude mixtures. The mp and the spectral data of the obtained product were coincided with **3a**.

TABLE-1
PHYSICAL DATA OF COMPOUNDS (**3a-h**)

S. No.	Substrates 1	Substrates 2	Products	Method-A Time (min)	Method-A Yield (%)	Method-B Time (min)	Method-B Yield (%)
a				30	86	13	92
b				60	84	30	91
c				40	81	20	93
d				90	82	30	90
e				30	83	15	92
f				90	81	40	94
g				45	84	20	92
h				60	80	40	90

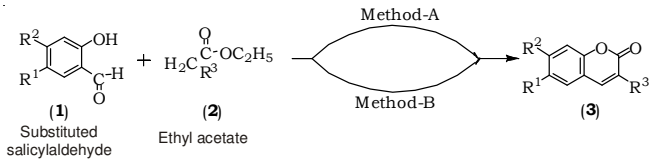
Method-A is conventional method & Method-B is Physical grinding method

RESULTS AND DISCUSSION

Salicylaldehyde (**1a**, *i.e.*, **1**, $R^1 = R^2 = H$) on heating with ethyl acetate (**2a**, *i.e.*, **2**, $R^3 = COCH_3$) and $ZrOCl_2 \cdot 8H_2O$ (10 mol %) for 0.5 h, gave the previously reported 3-acetylchromen-2-one (**3a**, *i.e.*, **3**, $R^1 = R^2 = H$, $R^3 = COCH_3$)[14] homogenous on TLC and different from the starting material. The structure of this compound was supported by spectral and analytical data. Thus, its IR (KBr): 1725 cm^{-1} (strong, sharp, -CO- of coumarin ring), 1668 cm^{-1} (strong, sharp, CO of $COCH_3$); ^1H NMR (DMSO-d_6/TMS) δ: 2.77 (S, 3H, CH_3), 7.19-8.88 (complex, m, 5H aryl protons); Its mass spectrum when recorded in CI method showed a molecular ion peak at m/z (*i.e.*, $M.^+$+1) 188 (base peak) corresponding to a molecular mass of 187 **(Scheme-1)**.

By adopting the same procedure, other compounds namely ethyl 2-oxo-2H-chromene-3-carboxylate (**3b**, *i.e.*, **3**, R^1, $R^2 = H$, $R^3 = COC_2H_5$), 3-acetyl-6-hydroxy-2H-chromen-2-one (**3c**, *i.e.*, **3**, $R^1 = OH$, $R^2 = H$, $R^3 = COCH_3$), ethyl 6-hydroxy-2-oxo-2H-chromene-3-carboxylate (**3d**, *i.e.*, **3**, $R^1 = OH$, $R^2 = H$, $R^3 = COC_2H_5$), 3-acetyl-6-methoxy-2H-chromen-2-one (**3e**, *i.e.*, **3**, $R^1 = OCH_3$, $R^2 = H$, $R^3 = COCH_3$), ethyl 6-methoxy-2-oxo-2H-chromene-3-carboxylate (**3f**, *i.e.*, **3**, $R^1 = OCH_3$, $R^2 = H$, $R^3 = COC_2H_5$), 3-acetyl-6,7-dichloro-2H-chromen-2-one (**3g**, *i.e.*, **3**, $R^1 = Cl$, $R^2 = Cl$, $R^3 = COCH_3$) and ethyl 6,7-dichloro-2-oxo-2H-chromene-3-carboxylate (3 h, *i.e.*, **3**, $R^1 = Cl$, $R^2 = Cl$, $R^3 = COC_2H_5$) have been synthesized. All the products were assigned structures based on the spectral and analytical data. (For details, please see experimental section).

3a (*i.e.*, **3**, $R^1 = R^2 = H$, $R^3 = COCH_3$) could also be prepared by an alternative method. Thus **1a** (*i.e.*, **1**, $R^1 = R^2 = H$) and **2a** (*i.e.*, **2**, $R^3 = COCH_3$) were ground in mortar with the help of pestle in the presence of $ZrOCl_2.8H_2O$ (10 mol %) at room temperature. The product obtained on processing the solid reaction mixture was found to be identical in all respects (m.p., m.m.p. and co-TLC analysis) with 3a obtained earlier above **Scheme-I**. The results are summarized in Table-1. A comparison between the two methods shows that in the physical grinding technique the time is drastically reduced and the yields are comparable.



Scheme-I

Method-A is conventional
Method-B is solid-phase grinding
$R^1 = R^2 = H$, OH, OCH_3, Cl.
$R^2 = Cl$,
$R^3 = COCH_3$, $COOC_2H_5$.

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REFERENCES

1. (a) J. Nielsen, *Curr. Opin. Chem. Biol.*, **6**, 297 (2002). (b) L.A. Wessjohann, *Curr. Opin. Chem. Biol.*, **4**, 303 (2000). (c) D.G. Hall, S. Manku and F.J. Wang, *Comb. Chem.*, **3**, 125 (2001). (d) M.-L. Lee and G.J. Schneider, *Comb. Chem.*, **3**, 284 (2001).
2. R.D.H. Murray, J. Mendez and S.A. Brown, The Natural Coumarins: Occurrence, Chemistry and Biochemistry, Wiley & Sons, New York (1982).
3. (a) C.M. Kessler, *Chest*, **99**, 97S (1991). (b) R. O'Kennedy and R.D. Thornes, Eds. Coumarins Biology (1997).
4. L.E. Jusinski and C.A. Taatjes, *Rev. Sci. Instrum.*, **72**, 2837 (2001).
5. A.E. Siefrist, H. Hefti, H.R. Meyer and E. Schmidt, *Rev. Prog. Coloration*, **17**, 39 (1987).
6. V.H. Pechmann and C. Duisherg, *Chem. Ber.*, **17**, 929 (1884).
7. W.H. Perkin and E.S. Henry, *J. Chem. Soc.*, **28**, 10 (1875).
8. G. Brufola, F. Fringuelli, O. Piermatti and F. Pizzo, *Heterocycles*, **43**, 1257 (1996).
9. N. Cairns, L.M. Harwood and D.P. Astles, *J. Chem. Soc. Perkin Trans. I*, 3101 (1994).
10. R.L. Shriner, *Org. React.*, **1**, 15 (1942).
11. I. Yavari, R. Hekmatshoar and A. Zonouzi, *Tetrahedron Lett.*, **39**, 2391 (1998).
12. D.N. Shah and N.M. Shah, *J. Am. Chem. Soc.*, **77**, 1699 (1955).
13. A. De La Hoz, A. Moreno and E. Vazquez, *Synlett.*, 608-610 (1999).
14. N. Siddiqui, M.F. Arshad and A.S. Khan, *Acta Poloniae Pharm.-Drug Res.*, **66**, 161 (2009).