Microwave Assisted Synthesis of Coumarins *Via* Potassium Carbonate Catalyzed Knoevenagel Condensation in 1-*n*-Butyl-3-methylimidazolium Bromide Ionic Liquid

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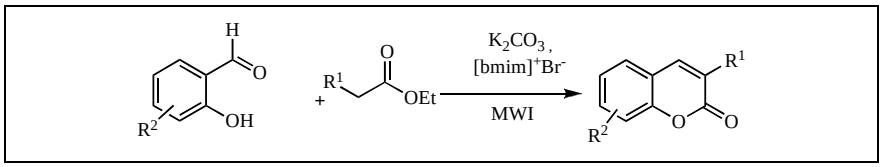

A variety of substituted coumarins have been prepared *via* an inexpensive and efficient potassium carbonate catalyzed Knoevenagel condensation of salisylaldehydes with acidic methylene compounds in ionic liquid media. 1-*n*-Butyl-3-methylimidazolium bromide has been employed as an alternative reaction medium in this procedure. The reaction proceeds smoothly under mild and solvent-free conditions and the products are obtained in excellent yields. Mild reaction conditions and good to excellent yields of the products are the noteworthy advantages of the method.

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INTRODUCTION

Coumarins are an important group of organic compounds that are used as additives to food and cosmetics [1] and optical brightening agents [2]. Many derivatives of coumarin have pharmacological properties [3] and occur as secondary metabolites present in seeds, root, and leaves of many plant species. Their function is far from clear, though suggestions include waste products, plant growth regulators, fungistats and bacteriostats [4]. It is therefore of utmost importance that the synthesis of coumarin and its derivatives should be achieved by a simple and effective method.

Organic reactions under solvent-free [5,6] and aqueous [7-9] conditions have increasingly attracted chemists' interests, particularly from the viewpoint of green chemistry [10]. As an important carbon-carbon bond forming reaction, the Knoevenagel condensation has been extensively studied. Generally, this type of reaction is catalyzed by base or Lewis acid in the liquid-phase system. In recent years, chemists paid more and more attention to the clean synthesis of alkenes by Knoevenagel condensations. The Knoevenagel condensations between aldehydes and malononitrile in dry media catalyzed by $ZnCl_2$ [11], silica gel [12] and ammonium acetate (NH_4OAc)-basic alumina [13] have been reported. Knoevenagel reaction has been the object of a complete study [14], recently the enhancement of the yield of this reaction by microwave heating has been reported by several groups [15].

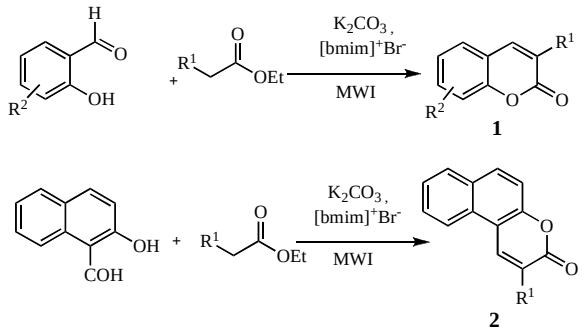
However, previously both the Knoevenagel reaction [16] and synthesis of coumarin by the Knoevenagel condensation [17] have been the subject of microwave induced reactions. Surprisingly, a survey of the literature revealed that the use of K_2CO_3 as an inexpensive catalyst for the synthesis of coumarins *via* Knoevenagel condensation has not been previously.

In order to carry out the Knoevenagel condensation in a faster and more inexpensive procedure, we investigated the influence of MW irradiation, K_2CO_3 and a variety of solid supports such as basic alumina, molecular sieves, silica gel and montemorllonite on the reaction of ß-ketoester and arylaldehydes. An attempted K_2CO_3 catalyzed reaction in several organic solvents and the presence of solid supports and MW irradiation proved to be unsuccessful and the reactions are sluggish and considerable amounts of starting materials are recovered unchanged even after prolonged exposure to microwave irradiation. Room temperature ionic liquid (RTIL) is no longer more a new concept to the scientific community. Rising numbers of publications are indicative of the potential of RTILs as 'neoteric solvents' for various chemical reactions. These include Friedel-Crafts reactions [18], enzyme catalyzed reactions [19], hydrogenations [20], benzoylation [21], Heck reaction [22], Fischer indole synthesis [23], *etc.*

In view of the emerging importance of the ionic liquids as reaction media and our general interest in microwave-assisted and green chemical processes [24], we decided to explore the synthesis of coumarins in ionic liquid using microwave (MW) irradiation under solvent-free conditions. In the present paper, we would like to report the remarkably fast synthetic method for preparation of 3-substituted coumarins *via* Knoevenagel condensation of arylaldehydes with acidic methylene compounds using K_2CO_3 in ionic liquid as the reaction media by microwave irradiation (Scheme 1). We have shown that, by using the

ionic liquid as reaction media, high product yields can be obtained, and a reduced amount of waste is produced in the Knoevenagel given reaction. Also, the reactions in ionic liquid are not difficult to perform and usually require no special apparatus or methodologies.

Scheme 1



($bmim^+Br^-$) = 1-*n*-butyl-3-methylimidazolium bromide

The reaction is conducted by exposure of a mixture of arylaldehydes with acidic methylene compounds, K_2CO_3 and 1-*n*-butyl-3-methylimidazolium bromide($bmim^+Br^-$) ionic liquid to microwave irradiation. Most of aryl-aldehydes disappeared within the first 2 min as determined by TLC. It is noteworthy to mention that in the absence of 1-*n*-butyl-3-methylimidazolium bromide and K_2CO_3 the reactions are sluggish and considerable amounts of starting materials are recovered unchanged even after prolonged exposure to microwave irradiation. Inorganic bases such as K_2CO_3 are insoluble in organic solvents so can not be use as catalyst of organic reactions in solvent systems, however this work shows that K_2CO_3 can be use as a good catalyst for the Knoevenagel condensation in ionic liquid as reaction media.

EXPERIMENTAL

All of the melting points were determined on a stuart scientific apparatus and are uncorrected. Infrared spectra were measured on a FTIR spectrometer. ^{1}H-NMR spectra were recorded on a Bruker Avance 500 MHz or JEOL FX90 MHz instruments. MIele Electronic M720 domestic oven was used for microwave irradiation. Mass spectra and elemental analyses were not obtained because all of products are known compounds that have been synthesized and reported in the literature.

General Proceedure. An equimolar mixture of arylaldehyde, methylene compound, K_2CO_3 and an excess of freshly prepared [25] 1-butyl-3-methylimidazolium bromide were mixed thoroughly in a mortar. Then the reaction mixture was transferred to a pyrex test tube and subjected to microwave irradiation in a domestic microwave oven. The cooled reaction mixture was taken up in cold water and extracted with ethylacetate. The extract was concentrated by evaporation and was directly subjected to flash chromatography using *n*-hexane:ethylacetate as eluent to obtain the related coumarins Table 1.

Selected Spectroscopic Data.

1a: ^{1}HNMR δ ($CDCl_3$): 1.51(t, 3H, Me), 4.55(q, 2H, OCH2), 7.23(dd, 1H, ArH), 7.42(m, 1H, ArH), 7.25(m, 1H, ArH), 7.65(dd, 1H, ArH), 8.68(s,1H,olefinic CH), IR, ν (KBr disc): 1725, 1685 cm^{-1}, EIMS (70ev) m/z: (M^+ 218), Anal. Calcd. for $C_{12}H_{10}O_4$: C, 66.05%; H, 4.58%; found C, 65.90%; H, 4.52%.

1b: ^{1}HNMR δ ($CDCl_3$): 2.76(s, 3H, Me), 7.23(dd, 1H, ArH), 7.43(m, 1H, ArH), 7.25(m, 1H, ArH), 7.66(dd, 1H, ArH), 8.78(s,1H,olefinic CH), IR, ν (KBr disc): 1712, 1672 cm^{-1}, EIMS (70ev) m/z: (M^+ 188), Anal. Calcd. for $C_{11}H_8O_3$: C, 70.21%; H, 4.25%; found C, 69.50%; H, 4.19%.

1c: ^{1}HNMR δ ($CDCl_3$): 7.22(dd, 1H, ArH), 7.42(m, 1H, ArH), 7.26(m, 1H, ArH), 7.65(dd, 1H, ArH), 8.57(s,1H,olefinic CH), IR, ν (KBr disc): 2230, 1685 cm^{-1}, EIMS (70ev) m/z: (M^+ 171), Anal. Calcd. for $C_{10}H_5NO_2$: C, 70.17%; H, 2.92%; N, 8.18%; found C, 69.50%; H, 2.89%; N, 8.10%.

1d: ^{1}HNMR δ (DMSO d_6): 1.52(t, 3H, Me), 4.45(q, 2H, OCH2), 6.69(d, 1H, ArH), 6.70(dd, 1H, ArH), 7.15(dd, 1H, ArH),

Table 1

Coumarin	Yield (%)[a]	Time (min)	Substituent		m.p. (° C)	Lit. m.p. (° C)
			R^1	R^2		
1a	85	1.5	CO_2Et	H	90-93	94-97 [25]
1b	87	1.2	COMe	H	119-121	120-122 [26]
1c	82	1	CN	H	180-184	182-184 [26]
1d	79	1.7	CO_2Et	7-OH	173-176	173-175 [25]
1e	80	1.7	CO_2Me	7-OH	264-267	265-267 [25]
1f	79	1.5	CN	7-OH	250-252	249-251 [25]
1g	75	2	CO_2Et	7- Et_2N	79-82	77-78 [27]
1h	77	2	COMe	7- Et_2N	150-153	150-152 [28]
1i	72	2	CO_2Et	8-OMe	87-89	88-90 [29]
1j	70	2	COMe	8-OMe	165-168	173-174 [29]
2a	89	1.2	CO_2Et	-	113-116	110-112 [25]
2b	87	1.2	COMe	-	181-185	192-195 [25]
2c	91	1	CN	-	290-294	292-295 [25]
2d	85	1.5	CO_2Me	-	169-171	168-170 [25]

Yield, m.p. and literature m.p. of coumarins which were prepared *via* Knoevenagel reaction in 1-*n*-butyl-3-methyl-imidazolium bromide by MWI. [a] Isolated yield.

8.95(s,1H,olefinic CH), 11.15(1H, s, OH), IR, ν (KBr disc): 3300-3100, 1725,1685 cm^{-1}, EIMS (70ev) m/z: (M^+ 234), *Anal.* Calcd. for $C_{12}H_{10}O_5$: C, 61.53%; H, 4.27%; found C, 60.98%; H, 4.20%.

1e: ^{1}HNMR δ (DMSO d_6): 4.15(s, 3H, OMe), 6.71(d, 1H, ArH), 6.72(dd, 1H, ArH), 7.17(dd, 1H, ArH), 8.68(s,1H,olefinic CH), 11.25(1H, s, OH), IR, ν (KBr disc): 3305-3150, 1725,1685 cm^{-1}, EIMS (70ev) m/z: (M^+ 220), *Anal*. Calcd. for $C_{11}H_8O_5$: C, 60.00%; H, 3.63%; found C, 59.40%; H, 3.50%.

1f: ^{1}HNMR δ (DMSO d_6): 6.69(d, 1H, ArH), 6.70(dd, 1H, ArH), 7.15(dd, 1H, ArH), 8.35(s,1H, olefinic CH), 11.05(1H, s, OH), IR, ν (KBr disc): 3300-3140, 2220, 1675 cm^{-1}, EIMS (70ev) m/z: (M^+ 187), *Anal*. Calcd. for $C_{10}H_5NO_3$: C, 67.11%; H, 2.67%; N, 7.48%; found C, 66.60%; H, 2.61%; N, 7.41%.

1g: ^{1}HNMR δ ($CDCl_3$): 1.13(t, 6H, $N(CH_2\mathit{Me})_2$), 1.41(t, 3H, $OCH_2\mathit{Me}$), 3.39(q, 4H, $N(\mathit{CH}_2Me)_2$), 4.45(q, 2H, OCH2), 6.55(d, 1H, ArH), 6.57(dd, 1H, ArH), 7.15(d, 1H, ArH), 8.95(s, 1H, olefinic CH),); IR, ν (KBr disc): 1735, 1687 cm^{-1}, EIMS (70ev) m/z: (M^+ 289), Anal. Calcd. for $C_{16}H_{19}NO_4$: C, 66.43%; H, 6.57%; N, 4.84%; found C, 65.92%; H, 6.30%; N, 4.72%.

1h: ^{1}HNMR δ ($CDCl_3$): 1.23(t, 6H, $N(CH_2\mathit{Me})_2$), 3.33(q, 4H, $N(\mathit{CH}_2Me)_2$), 2.76(s, 3H, Me), 6.56(d, 1H, ArH), 6.57(dd, 1H, ArH), 7.17(d, 1H, ArH), 8.73(s, 1H, olefinic CH),); IR, ν (KBr disc): 1732, 1672 cm^{-1}, EIMS (70ev) m/z: (M^+ 259), *Anal*. Calcd. for $C_{15}H_{17}NO_3$: C, 69.49%; H, 6.56%; N, 5.40%; found C, 68.25%; H, 6.26%; N, 5.28%.

1i: ^{1}HNMR δ ($CDCl_3$): 1.47(t, 3H, Me), 4.38(q, 2H, OCH2), 3.68(3H, s, OMe), 6.82(dd, 1H, ArH), 7.10(dd, 1H, ArH), 7.18(dd, 1H, ArH), 8.74(s,1H,olefinic CH), IR, ν (KBr disc): 1718,1690 cm^{-1}, EIMS (70ev) m/z: (M^+ 248), Anal. Calcd. for $C_{13}H_{12}O_5$: C, 62.90%; H, 4.83%; found C, 62.06%; H, 4.70%.

1j: ^{1}HNMR δ ($CDCl_3$): 2.75(s, 3H, Me), 3.65(3H, s, OMe), 6.83(dd, 1H, ArH), 7.11(dd, 1H, ArH), 7.17(dd, 1H, ArH), 8.72(s,1H,olefinic CH), IR, ν (KBr disc): 1715,1677 cm^{-1}, EIMS (70ev) m/z: (M^+ 218), *Anal*. Calcd. for $C_{12}H_{10}O_4$: C, 66.05%; H, 4.58%; found C, 65.55%; H, 4.41%.

2a: ^{1}HNMR δ ($CDCl_3$): 1.37(t, 3H, Me), 4.35(q, 2H, OCH2), 6.98(d, 1H, ArH), 7.29(m, 1H, ArH), 7.38(m, 1H, ArH), 7.58(d, 1H, ArH), 7.61(dd, 1H, ArH), 7.72(dd, 1H, ArH), 9.32(s, 1H, olefinic CH),); IR, ν (KBr disc): 1745, 1680 cm^{-1}, EIMS (70ev) m/z: (M^+ 268), *Anal*. Calcd. for $C_{16}H_{12}O_4$: C, 71.64%; H, 4.47%; found C, 71.15%; H, 4.39%.

2b: ^{1}HNMR δ ($CDCl_3$): 2.75(s, 3H, Me), 7.01(d, 1H, ArH), 7.32(m, 1H, ArH), 7.41(m, 1H, ArH), 7.62(d, 1H, ArH), 7.66(dd, 1H, ArH), 7.76(dd, 1H, ArH), 9.21(s, 1H, olefinic CH),); IR, ν (KBr disc): 1705, 1679 cm^{-1}, EIMS (70ev) m/z: (M^+ 267), *Anal.* Calcd. for $C_{15}H_{10}O_3$: C, 75.63%; H, 4.20%; found C, 75.05%; H, 4.15%.

2c: ^{1}HNMR δ ($CDCl_3$): 7.12(d, 1H, ArH), 7.35(m, 1H, ArH), 7.42(m, 1H, ArH), 7.61(d, 1H, ArH), 7.67(dd, 1H, ArH), 7.76(dd, 1H, ArH), 9.35(s, 1H, olefinic CH),); IR, ν (KBr disc): 2230, 1675 cm^{-1}, EIMS (70ev) m/z: (M^+ 221), *Anal*. Calcd. for $C_{14}H_7NO_2$: C, 76.01%; H, 3.16%; N, 6.33%; found C, 75.61%; H, 3.08%; N, 6.21%.

2d: ^{1}HNMR δ ($CDCl_3$): 4.15(s, 3H, OMe), 6.99(d, 1H, ArH), 7.30(m, 1H, ArH), 7.39(m, 1H, ArH), 7.59(d, 1H, ArH), 7.62(dd, 1H, ArH), 7.72(dd, 1H, ArH), 8.98(s,1H,olefinic CH), IR, ν (KBr disc): 1735, 1685 cm^{-1}, EIMS (70ev) m/z: (M^+ 283, *Anal.* Calcd. for $C_{15}H_{10}O_4$: C, 70.86%; H, 3.93%; found C, 69.90%; H, 3.90%.

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