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A Green and Efficient Synthesis of Xanthenedione Derivatives Promoted by $InCl_3 \cdot 4H_2O$ in Ionic Liquid

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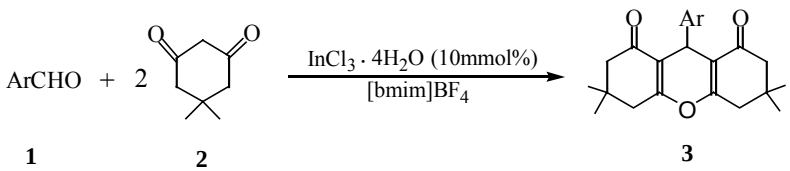
Abstract: Xanthenedione derivatives were prepared through $InCl_3 \cdot 4H_2O$ promoted condensation of aldehydes with 5, 5-dimethyl-1, 3-cyclohexandione in [bmim][BF_4]. The advantages of this method are: simple operation, environmental benign and high efficiency. Moreover, the reaction media and the catalyst can be recovered and reused effectively for at least six times.

Keywords: Ionic liquid, xanthenedione derivatives, indium trichloride.

Xanthenedione derivatives have held considerable interests in recent years, since they constitute a structural unit in a number of natural products[1] and have been used as versatile synthons because of the inherent reactivity of the inbuilt pyran ring[2]. Usually, poly-hydrogenated xanthenediones (**3**, **Scheme 1**) can be obtained through the acid or base catalyzed condensation of appropriate active methylene carbonyl compounds with aldehydes. But this method is not very satisfactory because of the prolonged reaction time, poor yields and side reactions of aldehydes[3]. As an improvement, Singh has reported a novel method for the preparation of this kind of compounds by using carbon transfer reactions of 1, 3-oxazianes and oxazolidines with carbon nucleophiles[4a]. Very recently, the reaction of aldehyde and 5, 5-dimethyl-1, 3-cyclohexanedione for the preparation of **3** in glycol under microwave irradiation has also been reported[4b]. However, to develop novel methods for the preparation of xanthenedione derivatives is still needed, these compounds play important role in organic synthesis.

Scheme 1



1 **2** **3**

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Table 1 Preparation of xanthenediones promoted by $InCl_3 \cdot 4H_2O$ in [bmim][BF_4] at 80℃

Products	Ar	Reaction time (h)	Isolated yield (%)	M. p. (lit.) (℃)
3a	C_6H_5	4	87	199 - 201 (198 - 200) [4b]
3b	*p*-ClC_6H_4	5	95	237 - 239 (230 - 231) [4b]
3c	p-$CH_3C_6H_4$	4	90	210 - 212 (218 - 220) [4b]
3d	*o*-ClC_6H_4	10	83	225 - 227 (228 - 229) [4b]
3e	*p*-BrC_6H_4	4	93	234 - 236
3f	*p*-$NO_2C_6H_4$	5	86	222- 224 (222 - 224) [4b]
3g	*p*-FC_6H_4	4	90	224 - 226 (225 - 227) [8]
3h	p-$CH_3OC_6H_4$	5	87	241 - 243 (227 - 228) [8]
3i	*m*-$NO_2C_6H_4$	4	92	145 - 147
3j	*o*-BrC_6H_4	10	76	226 - 228

In recent years, ionic liquids have attracted extensive interests as excellent alternatives of organic solvents[5] because of their favorable properties, such as no measurable vapor, non-flammability, high thermal stability, reusability and easy to handle. In many cases, the products are weakly soluble in the ionic phase so that the products can be easily separated by simple filtration or extraction with ether. As continuation of our interest in the area of clean synthesis using ionic liquids[6], we herein wish to report a very simple and green method for the preparation of poly-hydrogenated xanthenediones **3** (**Scheme 1**) through $InCl_3 \cdot 4H_2O$ promoted cascade reaction of aldehydes **1** and 5,5-dimethyl-1,3-cyclohexanedione **2** in ionic liquid, 1-butyl-3-methyl-imidazolium tetrafluoroborate ([bmim][BF_4]).

The experimental procedure: Aldehyde **1** (1 mmol), 5, 5-dimethyl-1, 3-cyclo-hexanedione **2** (2 mmol) and $InCl_3 \cdot 4H_2O$ (0.1 mmol) were added to a 10 mL round-bottom flask containing 1 mL [bmim][$BF]_4$. Then the mixture was stirred at 80℃ for a certain period of time as required to complete the reaction (monitored by TLC). At completion, the reaction mixture was added with water and the solid was collected by suction and then rinsed with cold ethanol to give the products **3** in good yields (shown in **Table 1**). All the products were fully characterized by IR, ^{1}H NMR, MS and elemental analysis[7]. In addition, [bmim][BF_4] together with the catalyst could be recovered easily by concentrating the filtrate under reduced pressure, and could be reused for at least 6 times without obvious decrease the amount of [bmim][BF_4] and the catalytic activity of catalyst In (III).

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References and Notes

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7. Spectral and analytical data for representative products:
   Compound **3a**: m.p. 199~201℃ (198~200℃)[4b]; ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 0.99 (s, 6H, 2×CH_3), 1.10 (s, 6H, 2×CH_3), 2.08 ~2.49 (m, 8H, 4×CH_2), 4.67 (s, 1H, CH), 7.06 (t, 1H, *J* = 7.6 Hz, ArH), 7.17 (t, 2H, *J* = 7.6 Hz, ArH), 7.33 (d, 2H, *J* = 7.6 Hz, ArH); IR (KBr) ν: 2958, 1685, 1660, 1627, 1467, 1357, 1203 cm^{-1}; MS (70eV) *m/z* (%): 350 (M^+, 71.21), 273 (100), 217(13.64), 161(8.33); Anal. Calcd. for $C_{23}H_{26}O_5$: C, 78.83; H, 7.47. Found: C, 78.73; H, 7.31.
   Compound **3i**: m.p. 145~147℃; ^{1}H NMR ($CDCl_3$, 400 MHz, δ ppm): 1.02 (s, 6H, 2×CH_3), 1.14 (s, 6H, 2×CH_3), 2.17 ~2.53 (m, 8H, 4×CH_2), 4.86 (s, 1H, CH), 7.43 (t, 1H, *J* = 8.0 Hz, ArH), 7.84 (d, 1H, *J* = 7.6 Hz, ArH), 7.99 ~ 8.04 (m, 2H, ArH); IR (KBr) ν: 2958, 1677, 1655, 1622, 1525, 1475, 1363, 1202 cm^{-1}; MS (70eV) *m/z* (%): 395 (M^+, 16.00), 378 (100), 348 (33.33), 273(54.67), 217(12.00), 161(12.00); Anal. Calcd for $C_{23}H_{25}NO_5$: C, 69.86; H, 6.37; N, 3.54. Found: C, 69.66; H, 6.29; N, 3.51.
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