

An Efficient and Green Synthesis of 5-Oxo-5, 6, 7, 8-tetrahydro-4H-benzo-[b]-pyran Derivatives Promoted by $\text{InCl}_3 \cdot 4\text{H}_2\text{O}$ Under Microwave Irradiation

Xue Yuan HU^{1,2}, Xue Sen FAN^{1*}, Xin Ying ZHANG¹, Gui Rong QU¹, Yan Zhen LI¹

¹ School of Chemical and Environmental Sciences, Henan Key Laboratory for Environmental Pollution Control, Henan Normal University, Xinxiang 453007

² Chongqing University of Medical Sciences, Chongqing 400016

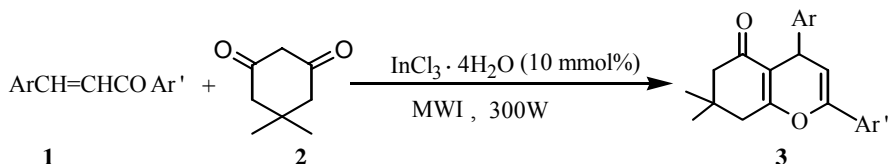
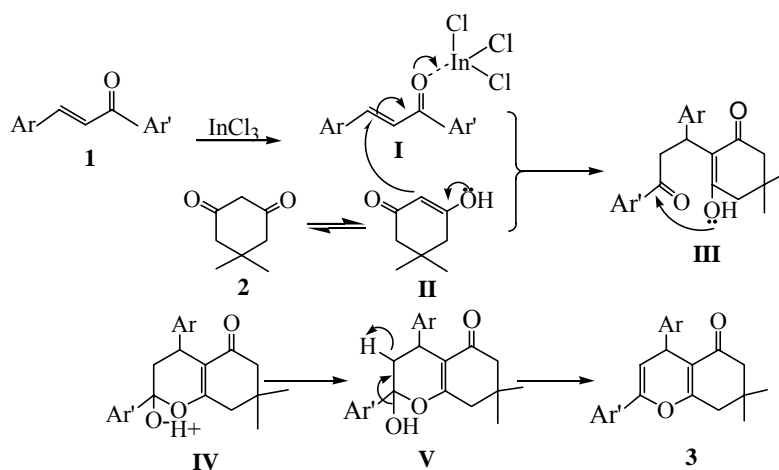
Abstract: A rapid and facile preparation of benzo-[b]-pyran derivatives through condensation of chalcone and 5, 5-dimethyl-1,3-cyclohexandione under microwave irradiation in the presence of catalytic amount of $\text{InCl}_3 \cdot 4\text{H}_2\text{O}$ has been developed. With its high efficiency, operational simplicity and environmental benignancy, this method may provide a useful alternative for the preparation of benzo-[b]-pyran derivatives.

Keywords: Pyran derivatives, indium trichloride, microwave irradiation.

Construction of tetrahydropyran rings has attracted a great deal of interests in organic synthesis in recent years¹, since tetrahydropyran moiety constitutes a structural unit in a number of natural products². In addition, tetrahydropyran derivatives possess wide range of biological activities and pharmacological properties, such as anticancer activity³ and antihypersensitivity⁴. Many methods for the preparation of such compounds have already been developed⁵. Among them, condensation of α , β -unsaturated ketones **1** with 5, 5-dimethyl-1, 3-cyclohexandione **2** with various catalysts has appeared as a novel alternative. In this respect, several procedures have been reported^{5b, 5c}. However, these methods often suffered from long reaction time, poor yields, and/or harsh reaction conditions. Thus, there are still needs to find more practical and more efficient methods for the preparation of benzo-[b]-pyran derivatives.

Recently, indium trichloride has emerged as potential Lewis acid catalyst imparting high regio- and chemoselectivity in various chemical transformations in both aqueous and non-aqueous media and has been offered promising protocols for green organic synthesis⁶. On the other hand, in the past few years, the utilization of microwave irradiation in chemical transformations has attracted considerable interest and is of significant importance in the search for green synthesis and sustainable chemistry. Many microwave assisted reactions demonstrated much shorter reaction time, higher yield and selectivity compared to conventional methods⁷. In continuation of our efforts to pursue green procedures for organic synthesis⁸, we report herein for the first time a fa-

* E-mail: fanxs88@263.net

Scheme 1**Scheme 2**

cile and efficient synthesis of benzo-[b]-pyran derivatives (**3**, **Scheme 1**) through condensation of 5,5-dimethyl-1,3-cyclohexanedione **2** and chalcones **1** through the protocol of coupling MWI with $\text{InCl}_3 \cdot 4\text{H}_2\text{O}$ under solvent free conditions. The probable mechanism for this $\text{InCl}_3 \cdot 4\text{H}_2\text{O}$ promoted condensation process is shown in **Scheme 2**.

General experimental procedure: Chalcone **1** (1 mmol), 5, 5-dimethyl-1, 3-cyclohexanedione **2** (1 mmol) and $\text{InCl}_3 \cdot 4\text{H}_2\text{O}$ (0.1 mmol) were mixed together without solvent in a 10 mL open flask. The flask was then placed in a domestic microwave oven. The mixture was irradiated at 300W for a certain period of time as required to complete the reaction (monitored by TLC). At completion, the reaction mixture was allowed to cool to room temperature. Then water was added and the mixture was extracted with ethyl acetate. The organic phase was dried over Na_2SO_4 and concentrated. The residue was recrystallized from the mixture of ethyl acetate and hexane to give products **3** in good yields (shown in **Table 1**). All the products were fully characterized by their IR, ^1H NMR and MS⁹. On the other hand, the aqueous phase containing $\text{InCl}_3 \cdot 4\text{H}_2\text{O}$ was concentrated under reduced pressure to recover the catalyst for reuse. It has been demonstrated that the recovered catalyst could be reused for at least 6 times without obvious loss in activity. Finally, it should also be noted that in the absence of $\text{InCl}_3 \cdot 4\text{H}_2\text{O}$, this reaction was reluctant to proceed and afforded **3** in low yield even with long reaction time.

Table 1 Preparation of benzo-[b]-pyran derivatives promoted by $\text{InCl}_3 \cdot 4\text{H}_2\text{O}$ under microwave irradiation

Products	Ar	Ar'	Reaction Time (min)	Isolated Yield (%)	mp °C (lit.)
3a	C_6H_5	C_6H_5	13	86 (41 ^a , 64 ^b)	140 - 142 (141) ^{5b}
3b	C_6H_5	<i>p</i> -ClC ₆ H ₄	10	85	172 - 174 (175 - 176) ^{5b}
3c	C_6H_5	<i>p</i> -NO ₂ C ₆ H ₄	10	80	148 - 150
3d	C_6H_5	<i>p</i> -CH ₃ OC ₆ H ₄	15	83	134 - 136
3e	C_6H_5	<i>p</i> -BrC ₆ H ₄	15	86	180 - 182
3f	<i>p</i> -ClC ₆ H ₄	C_6H_5	10	81	108 - 110
3g	<i>p</i> -CH ₃ C ₆ H ₄	C_6H_5	15	80	84 - 86
3h	<i>m</i> -NO ₂ C ₆ H ₄	C_6H_5	10	90	142 - 144
3i	<i>p</i> -NO ₂ C ₆ H ₄	C_6H_5	10	92	148 - 150
3j	<i>m</i> -NO ₂ C ₆ H ₄	<i>p</i> -ClC ₆ H ₄	10	91	194 - 196
3k	<i>p</i> -ClC ₆ H ₄	<i>p</i> -NO ₂ C ₆ H ₄	10	93	202 - 204

^a Irradiated 25 min in the absence of $\text{InCl}_3 \cdot 4\text{H}_2\text{O}$; ^b Refluxed 4 hours in toluene employing 10 mmol % $\text{InCl}_3 \cdot 4\text{H}_2\text{O}$.

Acknowledgments

This work was financially supported by the National Natural Science Foundation of China (No. 20372018) and the Science Foundation of Henan Normal University for Young Scholars (No. 0307032).

References and Notes

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- Spectral and analytical data for representative products:
Compound **3h**: ¹H NMR (CDCl₃, 400 MHz, δ ppm): 0.91 (s, 3H, CH₃), 1.14 (s, 3H, CH₃), 2.23~2.67 (m, 4H, 2×CH₂), 4.66 (d, 1H, *J* = 4.8 Hz, CH), 5.57(d, 1H, *J* = 4.8 Hz, =CH), 7.34~7.49 (m, 4H, ArH), 7.62 (d, 2H, *J* = 7.6 Hz, ArH), 7.72 (d, 1H, *J* = 7.6 Hz, ArH), 8.07 (d, 1H, *J* = 8.4 Hz, ArH), 8.19 (s, 1H, ArH); IR (KBr), (cm⁻¹): 3094, 2953, 2933, 2874, 1683, 1658, 1629, 1527, 1494, 1382, 1348, 1275, 1217, 1169, 1056, 874, 741; MS (70eV) *m/z* (%): 374 (M⁺, 20), 358 (100), 328 (43), 253 (96), 197 (8), 141 (8), 105 (8), 77(7).

Received 19 July, 2004