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Bismuth(III) Chloride-Mediated, Efficient, Solvent-Free, MWI-Enhanced Doebner Condensation for the Synthesis of (E)-Cinnamic Acids

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BISMUTH(III) CHLORIDE–MEDIATED, EFFICIENT, SOLVENT-FREE, MWI-ENHANCED DOEBNER CONDENSATION FOR THE SYNTHESIS OF (E)-CINNAMIC ACIDS

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A bismuth(III) chloride–mediated green process for the production of (E)-cinnamic acid derivatives using microwave irradiation under solvent-free conditions is described. The (E)-cinnamic acids are obtained in excellent yields. This protocol is green because it employs an established environmentally benign procedure, microwave irradiation. Solvent vapor pollution is not there because it is solvent free, and bismuth(III) chloride is an established nontoxic catalyst.

Keywords: Bismuth(III) chloride; (E)-cinnamic acids; MWI; solvent free

INTRODUCTION

trans-Cinnamic acids are of current interest because they are useful synthons in organic chemistry and for several industrial products. Notably these are required in the production of cosmetics and hair protection agents.[1,2] Because of these significant uses in industry as well as organic synthesis, there has been considerable interest for developing facile efficient processes for their production. The previous procedures employed conventional heating, catalysts such as pyridine and piperidine,[3] and organic bases. Organic bases are established carcinogenic materials and have been replaced by several inorganic salts.[4] Several methods have been reported for synthesis of cinnamic acids, which involve the Claisen–Schmidt condensation of aldehydes with acetates,[5] the Knoevenagel reaction of aldehydes with malonic acid,[6] the Wittig reaction of aldehydes with a phosphorus ylide derived from a-bromoacetate,[7] and more recently the Heck reaction between aryl halides and acrylates.[8] Evidently, these procedures are not facile and cheap. Considering the cost of the reagents and ease of operation, especially on a practical, large-scale preparation, herein we report the time-effective synthesis of cinnamic acids in excellent yield by Doebner condensation of aryl aldehydes and malonic acid. We and others[9] have been developing bismuth(III) chloride as an efficient nontoxic catalyst in organic synthesis. Guided by the nontoxic behavior of this salt and our requirement

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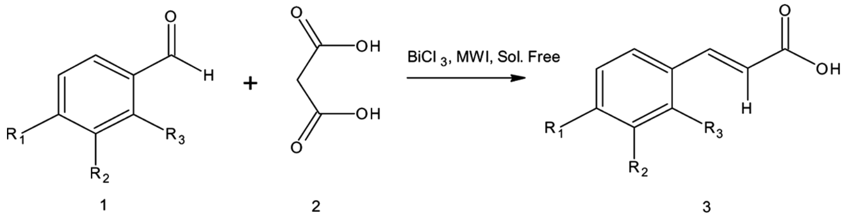

Scheme 1. Doebner condensation of aryl aldehydes and malonic acid.

for *trans*-cinnamic acids (we needed this material in the development of enaminone chemistry of uracils),[10] we disclose an efficient protocol for the production of (E)-cinnamic acids through Doebner modification as shown in Scheme 1.

RESULTS AND DISCUSSION

We initiated our investigation with pilot experiments using 5 mol% $BiCl_3$ in condensation of anisaldehyde (5 mmol) and malonic (5.05 mmol) without solvent under microwaves, which proceed smoothly in a short time, but the obtained yields of *trans*-cinnamic acids were not excellent. To optimize the yields, we performed experiments to quantify the catalyst and established 10 mol% $BiCl_3$ catalyst as enough to have the optimum yields. In a typical procedure, aryl aldehydes, malonic acid, and $BiCl_3$ (1:1.1:0.1) were mixed properly and treated under microwave irradiation (MWI) using solvent-free conditions (for times, see Table 1) to obtain *trans*-cinnamic acids **3a** in 98% yields. To check the efficacy and applicability of this catalyst, we could successfully obtain a range of desired products in 89–98% yields (Table 1) in 3–8 min. Catalyst more than 5 mol% (up to 10 mol%) did not effect any drastic change in reaction time and yields. Electron-withdrawing and

Table 1. $BiCl_3$-catalyzed synthesis of (E)-cinnamic acids

Entry	R1	R2	R3	Product[a]	Time (min)	Yield (%)[b]	Mp (lit.[11]) (°C)
1	H	H	H	3a	3	98	132 (133)
2	MeO	H	H	3b	4	97	170–171 (172)
3	H	H	Cl	3c	5	95	209–210 (208–210)
4	Me	H	H	3d	3.5	97	196–197 (197)
5	Cl	H	H	3e	6	94	249–251 (248–250)
6	H	NO_2	H	3f	7.5	92	196–197 (197)
7	Cl	H	Cl	3g	6.5	89	232–233 (233–235)
8	NO_2	H	H	3h	7	90	286 (286)
9	OH	H	H	3i	5	94	213–215 (214–215)
10	H	OH	H	3k	6.5	89	198 (197–198)
11	OH	MeO	H	3l	5	93	166–168 (168)
12	Meo	MeO	H	3m	4	90	181–182 (181–183)
13	Me_2N	H	H	3n	8	91	215–216 (216)

[a] The products were characterized by comparison of their melting points and spectral (IR, ^1H NMR) data with those of authentic samples.

[b] Isolated yields after recrystallization.

electron-donating substituents on aryl aldehydes did not affect product yields and reaction rate; clearly the catalyst was effective over a wide range of aryl aldehydes.

CONCLUSION

In summary, the present method employing $BiCl_3$ is a mild, efficient, and environmentally benign protocol for the synthesis of (E)-cinnamic acids. Products are obtained in excellent yields in short reaction times. The factor in favor of the present protocol is that the catalyst used is a cheap, well-known, and nontoxic inorganic salt. Operational simplicity and easy workup are the other attractive features of this procedure. These features place this protocol superior to the existing ones. During aqueous workup, no hazardous, unsafe, or corrosive by-products were formed, as is the case with strong, metallic, conventional Lewis acids.

EXPERIMENTAL

Melting points were determined in open capillaries and are uncorrected. Reagent-grade chemicals were purchased from a commercial source and used without further purification. Infrared (IR) spectra were recorded in KBr discs on a Perkin-Elmer 240C analyzer. ^1H NMR spectra were recorded on a Varian Gemini 300-MHz spectrometer using trimethylsilane (TMS) as internal standard. The progress of the reaction was monitored by thin-layer chromatography (TLC) using silica gel G (Merck).

General Procedure for Preparation of *trans*-Cinnamic Acids

Aryl aldehydes (10 mmol), malonic acid (10 mmol), and $BiCl_3$ (0.1 mmol) were mixed for 3–4 min in an Erlenmeyer flask. This reaction mixture was treated with MWI for the times given in Table 1 using solvent-free conditions. After completion of the reaction (monitored via TLC), the crude product was cooled, washed with water, and filtered, then recrystallized from ethanol.

Representative Spectral Data

Compound 3a. ^1H NMR ($CDCl_3$) δ 7.70 (d, $J = 16.0$ Hz, 1H), 7.55–7.48 (m, 2H), 7.45–7.34 (m, 3H), 6.44 (d, $J = 16.0$ Hz, 1H), 3.81 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 167.8 (s), 145.3 (d), 134.8 (s), 130.7 (d), 129.3 (d), 128.5 (d), 118.2 (d), 52.1 (q); IR (KBr) 1720, 1638, 981, 769 cm^{-1}; MS m/z 162 (M^+).

Compound 3b. ^1H NMR ($CDCl_3$) δ 7.65 (d, $J = 16.0$ Hz, 1H), 7.49–7.45 (m, 2H), 6.92–6.88 (m, 2H), 6.31 (d, $J = 16.0$ Hz, 1H), 3.83 (s, 3H), 3.79 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 168.1 (s), 161.8 (s), 144.9 (d), 130.1 (d), 127.5 (s), 115.7 (d), 114.7 (d), 55.7 (q), 51.9 (q); IR (KBr) 1718, 1639, 1604, 985, 839, 824 cm^{-1}; MS m/z 192 (M^+).

Compound 3c. ^1H NMR ($CDCl_3$) δ 7.64 (d, $J = 16.0$ Hz, 1H), 7.46 (dd, $J = 6.4$, 2.1 Hz, 2H), 7.35 (dd, $J = 6.4$, 1.9 Hz, 2H), 6.41 (d, $J = 16.0$ Hz, 1H), 3.81 (s, 3H); ^{13}C NMR ($CDCl_3$) δ 167.6 (s), 143.8 (d), 136.6 (s), 133.3 (s), 129.6

(d), 129.6 (d), 118.8 (d), 52.2 (q); IR (KBr) 1710, 1635, 1006, 82 cm^{-1}; MS m/z 196 (M^{+}).

Compound 3d. ^{1}H NMR (CDCl$_3$) δ 7.67 (d, $J = 16.0$ Hz, 1H), 7.42 (d, $J = 8.1$ Hz, 2H), 7.19 (d, $J = 8.0$ Hz, 2H), 6.40 (d, $J = 16.0$ Hz, 1H), 3.80 (s, 3H), 2.37 (s, 3H); ^{13}C NMR (CDCl$_3$) δ 167.6 (s), 144.9 (d), 140.7 (s), 130.7 (s), 129.6 (d), 128.1 (d), 116.7 (d), 51.6 (q), 21.5 (q); IR (KBr) 1712, 1634, 818 cm^{-1}; MS m/z 176 (M^{+}).

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