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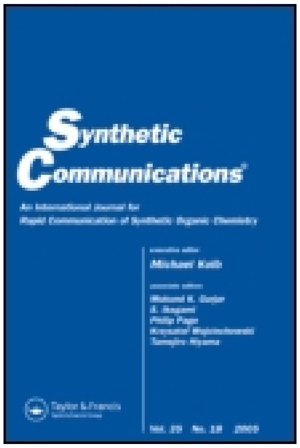

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Michael Addition Catalyzed by Potassium Hydroxide Under Ultrasound

Ji-Tai Li [a] , Yong Cui [a] , Guo-Feng Chen [a] , Zhao-Li Cheng [a] & Tong-Shuang Li [a]

[a] College of Chemistry and Environmental Science, Hebei University, Baoding, P.R. China

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Michael Addition Catalyzed by Potassium Hydroxide Under Ultrasound

Ji-Tai Li,* Yong Cui, Guo-Feng Chen, Zhao-Li Cheng, and Tong-Shuang Li

College of Chemistry and Environmental Science,
Hebei University, Baoding, P.R. China

ABSTRACT

Michael addition of chalcone with active methylene compound such as diethyl malonate, nitromethane and ethyl acetoacetate catalyzed by potassium hydroxide in anhydrous ethanol results Michael adducts in 75–98% yield under ultrasound irradiation in 25–90 min.

Key Words: Michael addition; Chalcone; Ultrasound irradiation.

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*Correspondence: Ji-Tai Li, College of Chemistry and Environmental Science, Hebei University, Baoding 071002, P.R. China; E-mail: orgsyn@mail.hbu.edu.cn.

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Michael addition reaction of appropriate carboanionic reagents to α,β-unsaturated carbonyl compounds is of great synthetic interest for C-C bond formation.[1] The versatile Michael reactions have numerous applications to remote functionalization in the synthesis of fine chemicals.[2]

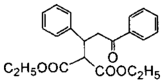
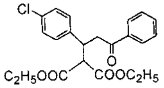
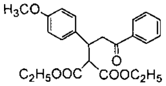
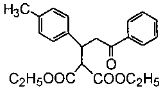
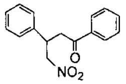
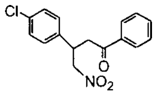
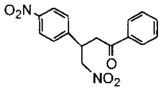
Michael reaction is classically catalyzed by bases or suitable combination of amines and carboxylic or Lewis acids under homogeneous conditions. Some catalysis such as $Ba(OH)_2$,[3] KF/Al_2O_3,[4] metal (Zn, Co, Ni etc.)(II) complexes,[5] Mg-Al-O-*t*-Bu hydrotalcite,[6] and phase-transfer catalysis[7] have been reported to be effective to the Michael reactions, and good results were obtained. However, there were some disadvantages due to long reaction time or difficult work-up or low yield.

Ultrasound has increasingly been used in organic synthesis in last three decades.[8] Compared with traditional methods, this method is more convenient and easily controlled. A large number of organic reactions can be carried out in a higher yield, shorter reaction time or milder conditions under ultrasonic irradiation. And it had been reported that ultrasound could facilitate Michael reactions in the presence of phase transfer catalyst in heterogeneous system.[9] All of the results stated above prompt us to study the possibility of Michael addition of chalcone with active compound such as diethyl malonate, nitromethane and ethyl acetoacetate under ultrasonitation. Herein we wish to report a facile sonochemical Michael addition.

As shown in Table 1 and Sch. 1, Michael additions were carried out in good yield catalyzed by KOH in ethanol under ultrasound irradiation. For example, compound **5j** was previously prepared in 75% yield catalyzed by $Ba(OH)_2$ in ethanol at reflux temperature for 5 h,[11] whereas under ultrasonication, **5j** was obtained in 97% yield at 28–38°C for 1.5 h; Compound **3h** was previously prepared in 72% yield, catalyzed by NaOH in ethanol at r.t. for 2–4 h,[13] whereas present procedure results in the similar yield at 19–24°C for 25 min. In addition, products **4i** and **5i** were given within 15 min and 30 min, respectively, which proved **5i** was obtained via the intermediate product **4i**. We also did the experiments in the absence of ultrasound, the addition of **1e** and CH_3NO_2 (**2e**) was carried out in 90% yield (**3e**) using the stirring for 2.5 h, while the reaction of **1i** and $CH_3COCH_2CO_2C_2H_5$ (**2i**) was carried out in 92% yield (**4i**) using the stirring for 1 h. It is apparent that Michael addition can be finished in shorter reaction time under ultrasound.

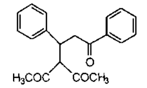
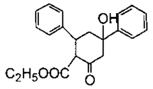
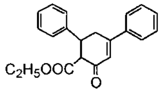
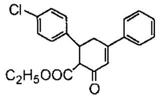
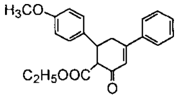
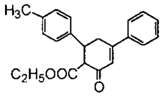
From these results we can deduce that the yields are, in general, similar or higher than those described in literature.[5,11,12] Compared

Table 1. Michael addition of active methylene compounds (**2**) to chalcone (**1**) under ultrasound.

	1	2^a						
Entry	*X*	R_1	R_2	T (°C)/ *t* (min)		Product	Yield, (lit.) (%)	M.p., (lit.) (°C)
a	H	$CO_2C_2H_5$	$CO_2C_2H_5$	27–32/25	**3a**		97 (95)[11]	65–67 (65–67)[11]
b	Cl	$CO_2C_2H_5$	$CO_2C_2H_5$	27–32/60	**3b**		92 (90)[11]	96–98 (96–98)[11]
c	OCH_3	$CO_2C_2H_5$	$CO_2C_2H_5$	27–32/60	**3c**		89 (85)[11]	62–64 (60–62)[11]
d	CH_3	$CO_2C_2H_5$	$CO_2C_2H_5$	27–32/90	**3d**		89 (90)[11]	68–70 (66–67)[11]
e	H	H	NO_2	28–35/90	**3e**		98^b (95)[11]	98.5–100 (100–101)[11]
f	Cl	H	NO_2	28–35/60	**3f**		95 (78)[5]	94–96 (97–98)[5]
g	NO_2	H	NO_2	28–35/60	**3g**		75 (73)[5]	103–104 (105–106)[5]

(*continued*)

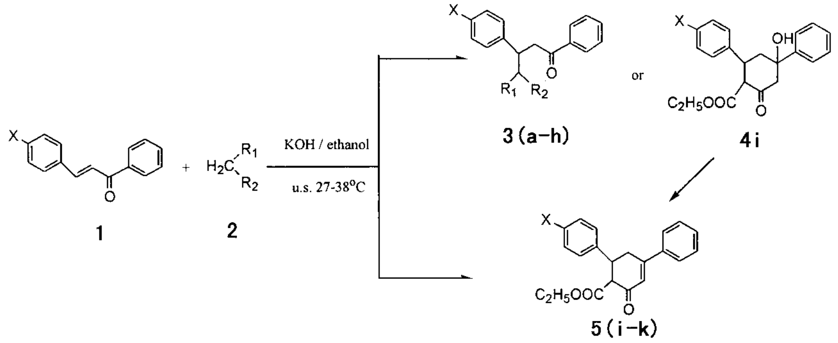
Table 1. Continued.

	1	2^a						
Entry	*X*	R_1	R_2	T (°C)/ t, (min)		Product	Yield, (lit.) (%)	M.p., (lit.) (°C)
h	H	$COCH_3$	$COCH_3$	19–24/25	**3h**		72 (72)[13]	142–144 (146)[13]
i	H	$COCH_3$	$CO_2C_2H_5$	28–38/15	**4i**		97^c (95)[11]	159–162 (162–164)[11]
				28–38/30	**5i**		96 (80)[11]	110–112 (111–112)[11]
j	Cl	$COCH_3$	$CO_2C_2H_5$	28–38/90	**5j**		97 (75)[11]	139–142 (141–143)[11]
k	OCH_3	$COCH_3$	$CO_2C_2H_5$	28–38/90	**5k**		90 (75)[11]	105–107 (106–108)[11]
l	CH_3	$COCH_3$	$CO_2C_2H_5$	28–38/90	**5l**		87 (80)[11]	140–142 (139–142)[11]

[a] Nitromethane was 20 mmol.

[b] Without ultrasound, stirred for 2.5 h at 28–35°C, in 90% yield.

[c] Without ultrasound, stirred for 1 h at 28–38°C, in 92% yield.



Scheme 1.

with reported, the mainly advantages of the present procedure are milder conditions, higher yield and shorter reaction period.

In conclusion, ultrasound can accelerate the Michael addition of chalcone with active methylene compound to furnish adducts in high yield catalyzed by potassium hydroxide with easy work-up.

EXPERIMENTAL

Apparatus and Analysis

All chalcones were synthesized according to literature,[10] melting point, ^{1}H NMR and MS data agreed to the reported. Diethyl malonate and ethyl acetoacetate were purified by distillation prior to use. Melting points were uncorrected. Sonication was performed in a Shanghai Branson-CQX ultrasonics cleaner with a frequency of 25 KHz and a normal power of 500 W. The reaction flask was located in the maximum energy area in the cleaner and addition or removal of water was used to control the temperature of the water bath.

General Procedure

To a 50 mL Pyrex flask was added chalcone (**1**, 1 mmol), active methylene compound (**2**, 1.2 mmol), KOH (0.2 mmol), and anhydrous ethanol (1 mL). The mixture was irradiated in the water bath of an ultrasonic cleaner at the temperature for the period as indicated in Table 1 (sonication was continued until crystals were appeared or chalcone was disappeared indicated by TLC). After cooling a period of time, the precipitate was isolated by filtration, washed with cool water to neutral, dried, and crystallized from ethanol. The authenticity of the products was established by comparison the melting points with literature value.

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