

Clean synthesis of ethyl α -cyanocinnamates catalysed by hexadecyltrimethyl ammonium bromide in aqueous media

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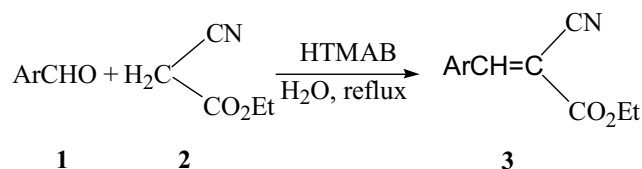
An efficient and convenient approach to the synthesis of ethyl α -cyanocinnamates in water using hexadecyltrimethyl ammonium bromide (HTMAB) as the phase-transfer catalyst (10 mol %) is described. This method provides several advantages such as neutral conditions, high yields and simple work-up procedure.

Keywords: ethyl α -cyanocinnamates, hexadecyltrimethylammonium bromide, green synthesis

With the increasing environmental concerns and the regulatory constraints faced by the chemical and pharmaceutical industries, development of environmentally benign organic reactions has become a crucial and demanding research area in modern organic chemical research.¹ Therefore, more and more chemists involved with research in “green synthesis”, which means that the reagent, solvent and catalyst are environmentally friendly in the reactions. Recently, organic reactions in aqueous media without the use of harmful organic solvents have attracted much attention, because water is a cheap, safe and environmentally-benign solvent.² In the course of our investigations in the development of new green synthetic methods, we have examined the synthesis of ethyl α -cyanocinnamates in water.

Ethyl α -cyanocinnamates are an important class of organic compounds. For instance, ethyl α -cyano-*m*-nitrocinnamate is used in photosensitive compositions³ and as an intermediate for a plant growth regulator.⁴ Ethyl α -cyanocinnamate with a alkoxy or hydroxy group in the benzene ring is used as part of an ultraviolet filter composition for protecting light-sensitive foods, wood-products, paper, dyes, fibres, plastics, etc.⁵ The preparation of ethyl α -cyanocinnamates is usually completed by a Knoevenagel condensation between ethyl cyanoacetate and various aromatic aldehydes. The usual catalysts for the preparation are primary and secondary amines, and their salts.⁶ Subsequently, the use of pyridine,⁷ ZnCl₂,⁸ CdI₂,⁹ TiCl₄,¹⁰ Al₂O₃,¹¹ MgO,¹² AlPO₄-Al₂O₃,¹³ and KF-Al₂O₃¹⁴ has been reported.

As a good phase-transfer catalyst, hexadecyltrimethyl ammonium bromide (HTMAB) has been used in a number of organic reactions. However, the use of HTMAB as a phase-transfer catalyst in water for the synthesis of ethyl α -cyanocinnamates has not been reported. In this article, we report a general and highly efficient route for the synthesis of ethyl α -cyanocinnamates using an inexpensive and



Scheme 1

commercially available HTMAB as catalyst. This method, using water as a green solvent, not only preserves the simplicity but also consistently gives the corresponding products in good to excellent yields (see the Scheme 1).

In a typical experimental procedure, a solution of aromatic aldehyde **1** and ethyl cyanoacetate **2** in water was heated in the presence of a catalytic amount of HTMAB, and the corresponding ethyl α -cyanocinnamates were obtained in good to excellent yields. The results are summarised in Table 1.

From Table 1, we found that electron donating groups such as -OH, -OCH₃, -OCH₂O-, -CH₃ and -N(CH₃)₂ in the aromatic ring can undergo the desired transformation without much difficulty (Entries f, g, h, i and k). Electron withdrawing groups such as -Cl, -NO₂ in the aromatic ring increased the activity of aldehydes, so the condensation reactions can be carried out in relatively shorter times (Entries b, c, d and e).

The catalyst HTMAB plays an important role in the success of the reaction in terms of the rate and the yields. We examined several experiments and found that the amount of the catalyst had a crucial effect on these condensation reactions. For example, 3-nitrobenzaldehyde reacted with ethyl cyanoacetate in the presence of 1 mol % HTMAB to give the product **3d** in modest yield (79 %) at reflux in water after 42 minutes of reaction time. Increasing the amount of the catalyst to 5 mol %, 10 mol % and 15 mol %

Table 1 Synthesis of ethyl α -cyanocinnamates catalysed by HTMAB in aqueous media

Entry	Ar	Reaction Time/min	Yield ^a /%	M.p./°C	
				Found	Reported
a	C ₆ H ₅ 1a	70	86	48–49	48–50 ¹⁴
b	4-ClC ₆ H ₄ 1b	45	97	89–90	90 ⁹
c	3-ClC ₆ H ₄ 1c	50	92	100–101	101–102 ¹⁵
d	3-NO ₂ C ₆ H ₄ 1d	42	97	133–135	134–136 ¹⁶
e	4-NO ₂ C ₆ H ₄ 1e	35	99	171–172	172–173 ¹⁴
f	4-HOC ₆ H ₄ 1f	75	93	168–169	169–170 ¹⁸
g	4-CH ₃ OC ₆ H ₄ 1g	170	86	78–79	79–81 ¹⁸
h	4-(CH ₃) ₂ NC ₆ H ₄ 1h	65	90	122–124	124–125 ¹⁴
i	4-CH ₃ C ₆ H ₄ 1i	90	94	93–94	94–95 ¹⁸
j	4-OH-3-CH ₃ OC ₆ H ₃ 1j	130	91	108–111	110–111 ¹⁴
k	3,4-(OCH ₂ O)C ₆ H ₃ 1k	60	97	106–107	106–108 ¹⁷
l	C ₆ H ₅ CH=CH 1l	80	72	114–115	115–116 ¹⁸

^aIsolated yield.

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Table 2 Reuse of the catalyst HTMAB for the synthesis of **3d**

Entry	1	2	3	4	5
Yield (%)	97	96	96	95	94

results in increasing the reaction yields to 92 %, 97 % and 97 %, respectively. Use of just 10 mol % HTMAB at reflux in water is sufficient to push the reaction forward. Higher amounts of the catalyst did not improve the results to a greater extent. Therefore, 10 mol % HTMAB was chosen as the catalyst for the reactions.

The catalyst could be reused five times for the synthesis of **3d** without significant loss of activity. The results are summarised in Table 2. In addition, it should be emphasised that all of these reactions were carried out in water, a green solvent.

In summary, we have shown that HTMAB is an efficient catalyst for the Knoevenagel condensation between ethyl cyanoacetate and aromatic aldehydes in boiling water giving operational simplicity, short reaction times and high yields.

Experimental

The ethyl α -cyanocinnamates prepared were characterised by ^1H NMR, IR and MS. IR spectra were recorded on a Bio-rad FIS-40 spectrometer (KBr). ^1H NMR spectra were measured on an AVANCE-400 spectrometer using TMS as internal standard and CDCl_3 as solvent.

General procedure for the synthesis of ethyl α -cyanocinnamates: A mixture of aldehyde **1** (1 mmol), ethyl cyanoacetate **2** (1 mmol), HTMAB (10 mol %) and water (10 ml) was added to a 50 ml flask. It was stirred with a magnetic stirrer and refluxed for the appropriate time as indicated in Table 1. The reaction was monitored by TLC. After completion of the reaction, the mixture was cooled to room temperature and the solid was filtered off and washed with H_2O (50 ml). The crude product was washed with 5 % aqueous alcohol and then purified by recrystallisation with ethanol (95 %). Data of some compounds are shown as follows: (For the aromatic AA 'XX' systems $J^* = J_{23} + J_{25}$)

3f: IR (KBr): 3,450–3,180, 3,070–2,900, 2,230, 1,710, 1,590, 1,510, 1,440, 1,370, 1,260, 1,200, 1,185, 1,100 cm^{-1} ; ^1H NMR (CDCl_3): δ 10.50 (s, H, OH), 8.19 (s, 1H, CH=), 7.92 (m, 2H, $J^* = 8.1$, Ar-H), 6.99 (m, 2H, $J^* = 8.1$, Ar-H), 4.39 (q, 2H, $J = 7.3$, OCH_2CH_3), 1.40 (t, 3H, $J = 7.3$, OCH_2CH_3); MS (m/e): 217 (M^+ , 100), 189 (50), 172 (98), 144 (45), 117 (25), 89 (45), 63 (8).

3g: IR (neat): 3,100–2,800, 2,210, 1,705, 1,600, 1,505, 1,260, 1,170 cm^{-1} ; ^1H NMR (CDCl_3): δ 8.21 (s, 1H, CH=), 7.95 (m, 2H, $J^* = 8.4$, Ar-H), 6.96 (m, 2H, $J^* = 8.4$, Ar-H), 4.40 (q, 2H, $J = 7.4$, OCH_2CH_3), 3.91 (s, 3H, OCH_3), 1.40 (t, 3H, $J = 7.4$, OCH_2CH_3); MS (m/e): 231 (M^+ , 45), 200 (3), 170 (89), 143 (90), 115 (100), 89 (10), 70 (7), 65 (9).

3i: IR (neat): 3,100–2,850, 2,220, 1,710, 1,600, 1,460, 1,370, 1,270, 1,200, 1,100 cm^{-1} ; ^1H NMR (CDCl_3): δ 8.21 (s, 1H, CH=), 7.91 (m, 2H, $J^* = 8.1$, Ar-H), 7.31 (m, 2H, $J^* = 8.1$, Ar-H), 4.38 (q, 2H, $J = 7.1$, OCH_2CH_3), 2.43 (s, 3H, CH_3 -Ar), 1.40 (t, 3H, $J = 7.1$, OCH_2CH_3); MS (m/e): 215 (M^+ , 100), 200 (28), 187 (42), 170 (78), 142 (32), 115 (63), 89 (20), 65 (25).

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