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Abstract: Knoevenagel condensation of aromatic aldehydes with active methylene compounds under solvent-free conditions to synthesize arylidene compounds by grinding in the presence of TEBA at room temperature has been described. This method is simple, efficient, and environmentally friendly.

Keywords: Aromatic aldehydes, Knoevenagel condensation, methylene compounds, TEBA

Developing green chemical methods is one of the most important purposes of organic synthesis at present. Organic synthesis in the absence of solvent is a powerful tool for the generation of structurally diverse molecules. Because of their special selectivity, the ease of setup, and workup, they are arousing

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great interest.^[1-3] Moreover, solvent-free reactions sometimes are faster, taking just a few minutes rather than hours to complete, because the reactants are in close contact with each other. This aspect, coupled with the lower overall costs of running a reaction without solvent, including no special equipment, could become a decisive factor in industry.

Knoevenagel condensations are one of the most useful and widely employed reactions for carbon–carbon formation in organic synthesis.^[4] A number of methods have been developed for this reaction.^[5–13] However, most of them were carried out in organic solvent and created much waste. As environmental consciousness in chemical research and industry has increased, efficient, economic, and clean procedures have received increased attention in recent years. For example, many kinds of heterogeneous basic catalysts were used in Knoevenagel condensations under solvent-free conditions.^[14–23]

 α ,β-Unsaturated nitriles and their derivatives are important precursors of potentially bioactive pyrimidine derivatives^[24] and also are versatile tools for the construction of a variety of novel complex heterocycles.^[25] They can be prepared via Knoevenagel condensation between malononnitrile or methyl (ethyl) cyanoacetate and various aromatic aldehydes. The reaction is usually catalyzed by various amines or their corresponding ammonium salts.^[5–13] In recent years, a grinding method under solvent-free conditions used in Knoevenagel condensation has rapidly increased. Many catalysts have been used in the synthetic procedure, for example, K₂O-Al₂O₃,^[26] CaO,^[27] ZnCl₂,^[28] and NH₄OAC.^[29] Herein, and we report a convenient preparation of some arylidene derivatives by Knoevenagel condensation using aromatic aldehydes with malononnitrile or ethyl cyanoacetate under solvent-free conditions, including phase-transfer catalysis of triethylbenzy-lammonium chloride (TEBA) (Scheme 1).

Encouraged by the literature, recently we have studied the reaction of Knoevenagel condensation under solvent-free conditions. We tried to use various catalysts in this reaction. Surprisingly, when we chose and used phase-transfer catalysis in the reaction of aromatic aldehydes with active methylene compounds at room temperature under solvent-free condition using a grinding method, we found the reaction was very efficient and gave high yields.

As an extension of this study, first we decided to investigate the use of different phase-transfer catalysts, such as hexadecyl trimethyl ammonium bromide (HTMAB), 4-dodecylbenzenesulfonic acid (DBSA), and

ArCHO +
$$H_2C \swarrow_Y \xrightarrow{CN} \frac{TEBA}{\text{grinding r.t.}} ArC = C \swarrow_Y$$

1 2 3

Scheme 1.

Entry	Catalyst	Amount of catalyst (mmol)	Time (min)	Yield (%) of 3a	
1	HTMAB	4	15	70	
2	DBSA	4	15	55	
3	TEBA	4	15	90	
4	TEBA	2	6	89	
5	TEBA	2	10	90	

Table 1. Catalytic activity of phase-transfer catalysis in solvent-free conditions

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triethylbenzylammonium chloride (TEBA). We found they all had catalytic activity but triethylbenzylammonium chloride (TEBA) displayed the best catalytic effect. The result is shown in Table 1.

We have examined the reaction by various aromatic aldehydes containing electron-withdrawing or electron-donating groups as reactants. They all gave the expected results with good to excellent yields for almost all the tested substracts. The results are listed in Table 2. From Table 2, we not only could see that all the reactions were completed within a few minutes, but we could also see that the condensation of aldehydes with electron-withdrawing groups such as -Cl and $-NO_2$ in the aromatic ring, with active methylene compounds,

			Time	Vield	Mp (°C)	
Entry	Ar	Y	(min)	(%)	Found	Lit.
3a	C ₆ H ₅	CN	10	90	81-83	82-84 ^[13d]
3b	$4-CH_3C_6H_4$	CN	15	95	132-134	133-135 ^[12]
3c	$4-ClC_6H_4$	CN	5	97	160-162	159–161 ^[12]
3d	$2-ClC_6H_4$	CN	5	93	96-98	95–96 ^[12]
3e	$4-BrC_6H_4$	CN	5	97	153-154	153-155 ^[13c]
3f	2,3-(CH ₃ O) ₂ C ₆ H ₃	CN	15	85	100-102	$101 - 103^{[13c]}$
3 g	3,4-Cl ₂ C ₆ H ₃	CN	5	95	144-146	145-147 ^[13c]
3 h	$2-NO_2C_6H_4$	CN	5	96	134-136	137-138 ^[13c]
3i	$4-N(CH_3)_2C_6H_4$	CN	15	82	182-183	$180 - 182^{[12]}$
3j	C ₆ H ₅	CO ₂ Et	10	87	50-52	$49-50^{[27]}$
3 k	4-ClC ₆ H ₄	CO ₂ Et	5	90	86-88	86-87 ^[27]
31	$4-NO_2C_6H_4$	CO ₂ Et	5	92	167-168	168–169 ^[27]
3 m	3,4-(CH ₃ O) ₂ C ₆ H ₃	CO ₂ Et	15	89	154-156	155–157 ^[27]
3n	$4-OHC_6H_4$	CO ₂ Et	15	78	170 - 172	170–171 ^[27]
30	$4-N(CH_3)_2C_6H_4$	CO ₂ Et	15	86	121-123	$122 - 123^{[27]}$
3р	4-CH ₃ OC ₆ H ₄	CO ₂ Et	15	89	83-85	$80 - 84^{[13b]}$
3q	3-ClC ₆ H ₄	CO ₂ Et	5	92	102-103	102-103 ^[27]
3r	4-OH-3-CH ₃ OC ₆ H ₃	CO ₂ Et	15	90	98-99	97–98 ^[27]

Table 2. Reaction time, yields, and melting points of products 3

could be carried out in relatively shorter times and higher yields than electron-donating groups such as $-N(CH_3)_2$ and $-OCH_3$. The product was identified by comparison of physical data and ¹H NMR and IR spectra with those described in the literature.

In summary, we have developed an environmentally friendly Knoevenagel condensation between various aldehydes and active methylene compounds in the presence of phase-transfer catalyst TEBA in the absence of solvent at room temperature using a grinding method. To our knowledge, TEBA is first used in the Knoevenagel condensation reaction. Compared with the classical heating reactions, the main advantages of the procedure are milder reaction condition, better yield, shorter reaction time, and easier workup.

EXPERIMENTAL

All the reagents and aromatic aldehydes were obtained from suppliers and were not purified. Melting points were determined on XT-5 microscopic melting-point spectrometer and are uncorrected.

General Procedure

A mixture of aromatic aldehydes 1 (1 mmol), active methylene compounds 2 (1 mmol), and TEBA (2 mmol) were ground at room temperature with a glass mortar and pestle. The reactions were monitored by TLC. The crude mixture was treated with water. The product was filtered, dried, recrystallized from ethanol, and dried at room temperature.

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