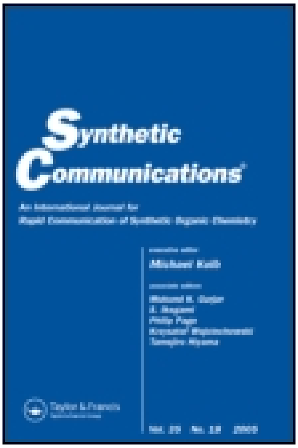

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A Practical Knoevenagel Condensation Catalyzed by PEG400 and Anhydrous K_2CO_3 Without Solvent

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ABSTRACT

Knoevenagel condensation of aromatic aldehydes with active methylene compounds under solvent-free conditions to synthesize arylidene compounds in good to excellent yields using powdered anhydrous K_2CO_3 and PEG400 as catalysts has been described.

Key Words: Aromatic aldehydes; Methylene compounds; PEG400; Solvent-free.

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INTRODUCTION

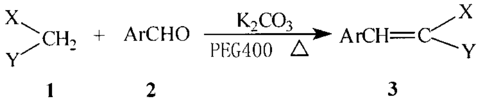
Developing green chemistry is one of the most important purposes of organic synthesis at present. Organic synthesis in the absence of solvent is a powerful tool for the generation of structurally diverse molecules, due to their special selectivity, the ease of set-up and work-up, arousing great interest.[1–3] Moreover, solvent-free reactions sometimes are faster, taking just a few minutes rather than hours to complete because the reactants are close contact with each other. This aspect, coupled with the lower overall costs of running a reaction without solvent and no specially needed equipment, could become a decisive factor in industry.

Polyethylene glycols (PEGs) have been widely used as PTC in many organic reactions[4,5] owing to their stability, low cost, environment-friendly, and easy availability. It has been proved that PEGs incorporating 7–9 units are more effective in catalyzing the reactions in which K^+ or Na^+ salts participate.[6] Especially, due to their liquid property and the two hydroxy groups, PEG 400–600 was more suitable for liquid–liquid or solid–liquid phase solvent-free organic reactions. As a continuance of our study,[7,8] we take a primary investigation on using PEGs as PTC in condensation catalyzed by alkali without solvent.

Knoevenagel condensation of carbonyl compounds with active methylene compounds is one of the most important methods for the preparation of substituted alkenes.[9–11] Recently, Knoevenagel reaction under solvent-free conditions carried out by microwave irradiation and by grinding has rapidly increased.[12–14] But microwave irradiation process is difficult to apply in the industrial process until now and the grinding reaction is only suitable to some active solid reactants. We wish to report a convenient preparation of some arylidene derivatives by Knoevenagel condensation of aromatic aldehydes with active methylene compounds under solvent-free conditions using PEG400 and K_2CO_3 as catalysts (Sch. 1). The results are listed in Table 1.

RESULTS AND DISCUSSION

Anhydrous K_2CO_3 was more satisfied to obtain excellent yield in short time than other inorganic alkalies. KOH and NaOH were too strong bases



Scheme 1.

Table 1. Knoevenagel condensation of aromatic aldehydes with active methylene compounds.

Entry	Ar	X–CH_2–Y	Time (min)	Yield (%)	M.p. (°C) or b.p. (°C/Torr)	
					Found	Lit.
3a	C_6H_5	$CH_2(CN)_2$	60^a	89	82–83	83.5–84[15]
3b	4-$NO_2C_6H_4$	$CH_2(CN)_2$	90^b	92	159–160	159–160[15]
3c	3-$NO_2C_6H_4$	$CH_2(CN)_2$	60^a	93	103–104	104–105[15]
3d	4-ClC_6H_4	$CH_2(CN)_2$	90^b	90	161–162	162–163[15]
3e	4-HOC_6H_4	$CH_2(CN)_2$	120^b	86	186–187	187.5–188[15]
			180^a	72	186–187	187.5–188[15]
3f	3-CH_3O–4-HOC_6H_4	$CH_2(CN)_2$	100^b	88	136–137	137–138[15]
3g	4-$(CH_3)_2NC_6H_4$	$CH_2(CN)_2$	120^b	88	179–180	180–181[15]
3h	4-$CH_3OC_6H_4$	$CH_2(CN)_2$	90^b	87	113–114	114–115[15]
3i	C_6H_5	$NCCH_2COOEt$	60^a	84	48–50	49[16]
3j	4-$NO_2C_6H_4$	$NCCH_2COOEt$	90^b	88	167–169	168[16]
3k	3-$NO_2C_6H_4$	$NCCH_2COOEt$	90^b	89	134–135	134–136[17]
3l	4-ClC_6H_4	$NCCH_2COOEt$	60^a	90	89–90	90[17]
3m	4-$(CH_3)_2NC_6H_4$	$NCCH_2COOEt$	120^b	85	123–125	124–126[17]
3n	4-$CH_3OC_6H_4$	$NCCH_2COOEt$	90^a	88	79–80	79–81[17]
3o	4-HOC_6H_4	$NCCH_2COOEt$	150^b	76	168–169	169–170[17]
3p	3-CH_3O–4-HOC_6H_4	$NCCH_2COOEt$	90^b	83	110–111	111–112[17]
3q	C_6H_5	$CH_2(COOEt)_2$	90^a	74	184/17	185–186/17[18]
3r	4-$NO_2C_6H_4$	$CH_2(COOEt)_2$	120^a	82	91–93	93[18]
3s	3-$NO_2C_6H_4$	$CH_2(COOEt)_2$	120^a	83	74–75	75–76[18]
3t	4-ClC_6H_4	$CH_2(COOEt)_2$	120^a	84	85–86	87[18]

(*continued*)

Table 1. Continued.

Entry	Ar	X–CH_2–Y	Time (min)	Yield (%)	M.p. (°C) or b.p. (°C/Torr)	
					Found	Lit.
3u	4-$(CH_3)_2NC_6H_4$	$CH_2(COOEt)_2$	150^b	78	109–110	110[18]
3v	C_6H_5	CH_3COCH_2COOEt	120^a	76	58–59	59–60[19]
3w	4-$NO_2C_6H_4$	CH_3COCH_2COOEt	150^b	80	163–164	164[19]

[a] The reactions were processed at 90°C.
[b] The reactions were processed at 120°C.

to result in more by-products. KF and AcONa cannot catalyze effectively this reaction under the same conditions. Low yield was obtained and long reaction time is needed using MgO and CaO as base catalysts. Using K_2CO_3, KOH, KF, and MgO as catalyst for the condensation of benzaldehyde with ethyl cyanoacetate, a yield of 84%, 46%, 51%, and 55% was, respectively, obtained under the same reaction conditions. The appreciable amount of PEG400 was between 3 and 5 mol% to aromatic aldehydes. A longer reaction time will be necessary and lower yield obtained with less PEG. The more amount of PEG400 employed, the more products would be lost during the cause of washing with water.

From Table 1, it was shown that the condensation of aldehydes with electron withdrawing groups such as $-Cl$ and $-NO_2$ in the aromatic ring, with active methylene compounds can be carried out in relatively shorter time and higher yield than with electron donating groups such as $-N(CH_3)_2$ and $-OCH_3$. A longer reaction time was necessary for the reactants with $-OH$ owing to $-OH$ can partly react with alkali to form salt and the reaction resulted in high melting point of the product. The rate would slow down along with increasing amount of the high melting point of products, so a high reaction temperature was needed. However, higher temperature will result in low yield especially for the products containing group $-OH$ and ester bond due to the oxidation and hydrolysis of some reactant and product by water generating in reaction. But when nitromethane and nitroethane as active methylene compounds, arylidene compounds cannot be obtained under this condition.

In summary, this method was safe, environment-friendly, and working-up easily. The distinct advantages of this process lie in being easily practiced in industry without needing special equipment.

EXPERIMENTAL

TLC was GF_{254} thin layer chromatography with petroleum ether/diethyl ether (2/1) used as eluent. All the reagents and aromatic aldehydes were obtained from commercial suppliers and were not purified. Melting points were determined on a microscopy apparatus and uncorrected.

General Procedure

A mixture of aromatic aldehyde **2** (0.1 mol), active methylene compound **1** (0.1 mol), anhydrous K_2CO_3 (0.02 mol), and PEG-400 (1.5 mL) were taken into a 50 mL three-necked, round-bottomed flask equipped with mechanical stirrer and drying tube filled with KOH. The reaction was processed with vigorous stirring and heating at assigned temperature. The completion of the reaction was monitored by TLC. The reaction mixture was cooled to room temperature and treated with cool water (acidifying needed for the products with –OH). The product was filtered, dried, recrystallized from ethanol, and identified by comparison of physical data and ^{1}H NMR and IR spectra with those described in the literatures.

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