An Improved Procedure for the Preparation of Chalcones and Related Enones

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The conditions employed to condense aryl aldehydes with ketones are legion[1]. Both acidic[2] and basic[2,3] catalysts have been used with variable results. Although 'the last word'[4] on benzalacetophenone preparation has recently been claimed[4], we wish to report an even simpler procedure.

Our method, wherein the analytically pure product **3** crystallises out as formed, involves the addition of sodium hydroxide pellets to a well stirred solution of the reactants **1** and **2** in absolute ethanol. This method is superior due to a simple isolation procedure and to the fact that no further purification is required. The yields are at least as good as those obtained by others (see Table). The advantages of the method are clearly seen in entries 2 and 3 (Table). When the method of Kohler and Caldwell[3] was employed for the synthesis of the chalcone (entry 11, Table) a 50% yield was obtained compared with a 90% yield by the present method. This procedure is suited to products which are crystalline and which have no free phenolic or acidic groups. It was noted that 18-crown-6 accelerated the reaction (see entry 4, Table).

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Table. Aldol Condensation Reactions

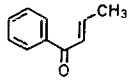
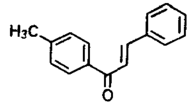
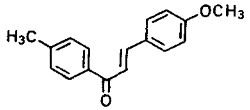
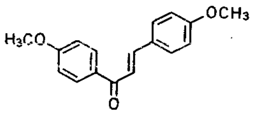
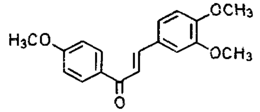
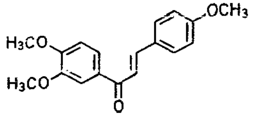
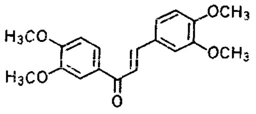
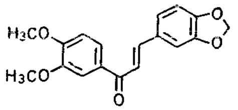
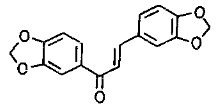
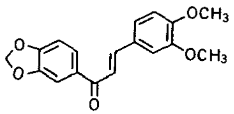
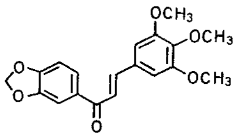
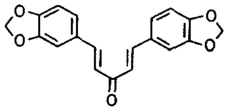
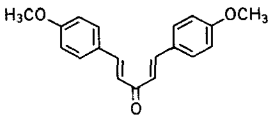
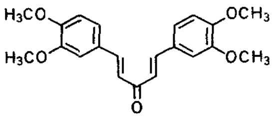
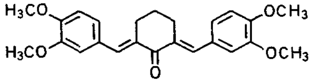
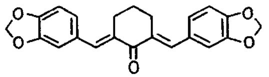
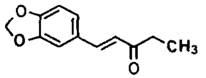
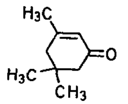
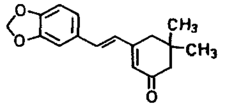
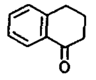
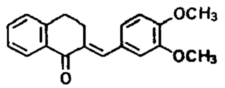
Entry	Ketone 1 R^1 (mol)	Aldehyde 2 R^2 (mol)	Reaction conditions	Product 3	m.p. [°C] found	m.p. [°C] reported	Yield [%] found[a]	Yield [%] reported[b]
1	C_6H_5 (1)	H (1)	1. r.t./1h 2. 0°C/0.5h		56–57°	57°[5]	75	50–80[4]
2	4-H_3C–C_6H_4 (1)	H (1)	1. r.t./2h 2. 5°C/20 min		57–58°	59°[6,7]; 75°[8]; 77°[7]	72	0[9]; 22–42[2]
3	4-H_3C–C_6H_4	4-H_3CO	r.t./5h		95–96°	91°[2]; 94°[10]	92	45[10]; 48–55[2]
4	4-H_3CO–C_6H_4 (1)	4-H_3CO (1)	r.t./10h		102–103°	97–99°[11]; 102–103°[12]	92;	92[11]; 35[12]; 72[12];
			r.t./35 min				33[c]	
			r.t./35 min/18-crown-6				50[d]	
5	4-H_3CO–C_6H_4 (1)	3,4-di-H_3CO (1)	r.t./10h		92–93°	91°[13]	90	–[e], 13
6	3,4-di-H_3CO–C_6H_3 (1)	4-H_3CO (1)	r.t./10h		85–86°	86°[10]; 80–81°[15]	90	–[e], 14
7	3,4-di-H_3CO–C_6H_3 (1)	3,4-di-H_3CO (1)	r.t./10h		105–106°	110°[14]	99	–[e], 14
8	3,4-di-H_3CO–C_6H_3 (1)	3,4-OCH_2O (1)	r.t./10h		143–144°	123°[16]; 144°[14]	99	87[16]; –[e], 14
9	3,4-OCH_2O–C_6H_3 (1)	3,4-OCH_2O (1)	r.t./10h		176–178°	–[f]	90[f]	–

Table. (Continued)

Entry	Ketone 1 R^1 (mol)	Aldehyde 2 R^2 (mol)	Reaction conditions	Product 3	m.p. [°C]		Yield [%]	
					found	reported	found[a]	reported[b]
10	3,4-$OCH_2O-C_6H_3$ (1)	3,4-di-H_3CO (1)	r.t./10h		134–136°	133–135°[7]	90	–[e, 17]
11	3,4-$OCH_2O-C_6H_3$ (1)	3,4,5-tri-H_3CO (1)	r.t./10h		153–154.5°	–[g]	90[g]	–
12	H_3C (1)	3,4-OCH_2O (2)	r.t./10h		198–200°	185°[18]	91	–[e, 18]
13	H_3C (1)	4-H_3CO (2)	r.t./10h		136–138°	129–130°[19]	90	–[e, 19]
14	H_3C (1)	3,4-di-H_3CO (2)	r.t./10h		83–85°	84°[20]	88	fair[20]
15	cyclohexanone (1)	3,4-di-H_3CO (2)	r.t./10h		155–157°	–[h]	87[h]	–
16	cyclohexanone (1)	3,4-OCH_2O (2)	r.t./10h		190–192°	189°[21]	90	–
17	C_2H_5	3,4-OCH_2O (1)	r.t./1.5h		98–101°	101–102°[22]	30–40	–[e, 22]
18	 (1)	3,4-OCH_2O (1)	r.t./10h		151–152.5°	–[i]	76[i]	–
19	 (1)	3,4-di-H_3CO (1)	r.t./10h		105–107°	–[j]	75[j]	–

Footnotes to Table:

[a] Yield of precipitated product; the mother liquors were not investigated.

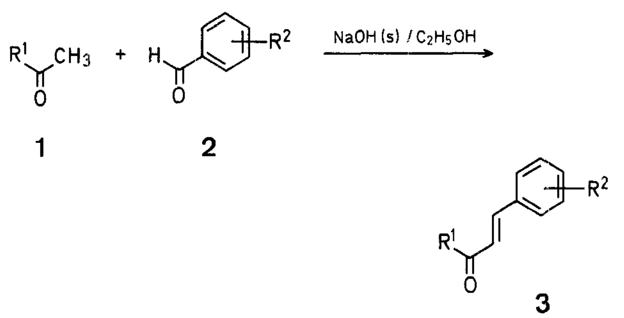
[b] Same starting materials and a base catalyst were used.

[c] The product starts to precipitate after 30 min.

[d] The product starts to precipitate after 19 min; 18-Crown-6 (20 mg) per 0.01 mol of ketone used.

[e] Yield not stated.

[f]	$C_{17}H_{12}O_5$ (296.3)	calc. found	C 68.91 69.12	H 4.08 4.19
[g]	$C_{19}H_{18}O_6$ (342.3)	calc. found	C 66.66 67.07	H 5.30 5.47
[h]	$C_{24}H_{26}O_5$ (394.5)	calc. found	C 73.07 73.50	H 6.64 6.78
[i]	$C_{17}H_{18}O_3$ (270.3)	calc. found	C 75.53 75.54	H 6.71 6.94
[j]	$C_{19}H_{18}O_3$ (294.3)	calc. found	C 77.53 77.86	H 6.16 6.19



Aldol Condensation; General Procedure:

To a solution of the ketone **1** and aldehyde **2** in absolute methanol (about 10 ml per 0.01 mol ketone) either in a closed system or under nitrogen at room temperature (19–20 °C) is added a catalytic quantity of solid sodium hydroxide (2–3 pellets) and the mixture is vigorously stirred at room temperature. [Normally, the product starts to precipitate within 1 h except chalcone (entry 1, Table) and 3′-methylchalcone (entry 3, Table), which requires cooling to initiate. Stirring was maintained throughout.] The crystalline product is filtered, washed with cold ethanol, water, and dried (under vacuum and heat) and is shown to be of high purity by melting point, spectroscopic data, and analysis.

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