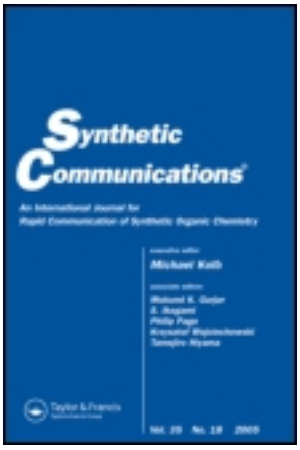

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A Simple and Efficient Method for Selective Single Aldol Condensation Between Arylaldehydes and Acetone

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A Simple and Efficient Method for Selective Single Aldol Condensation Between Arylaldehydes and Acetone

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Abstract: A simple and efficient method has been developed for selective single aldol condensation between acetone and various aromatic/heterocyclic aldehydes using aqueous sodium hydroxide at 5–10°C.

Keywords: Acetone, aldol condensation, aqueous sodium hydroxide, arylaldehydes, chalcones, selectivity

INTRODUCTION

The aldol condensation is an important method for forming C—C bond.[1] The reaction involves the condensation of arylaldehydes with ketones. Both acidic[2] and basic[2,3] catalysts have been used with variable results, however, under classical aldol condensation reaction conditions including basic media, dimer, polymer, and self-condensation products often formed as well. Recently, improved methods have been reported for this type of reaction, which results in the synthesis of chalcones and related enones.[4] The method was simple and works well for the condensation of arylaldehydes and ketones. However, in acetone where α and α'-H are present, reaction didn't stop at one α-carbon atom but extends for α' also; as a result, double condensation reaction takes place. So there is a need to develop a simple and selective procedure for single aldol condensation between acetone and arylaldehydes to benzylidene acetone, because these compounds are

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important intermediates in the synthesis of various natural products[5–8] and heterocyclic compounds.[9–11]

In continuation of our interest[12–15] to devise economic and environmentally friendly procedures for organic reactions, we report a simple and selective procedure for the single aldol condensation between acetone and aryl/heterocyclic aldehydes using aqueous sodium hydroxide at 5–10°C.

In 1999, Kad et al. reported rate enhancement in aldol condensation under microwave irradiation using aqueous sodium hydroxide.[17] In this method, single aldol condensation has been reported in acetone and arylaldehydes. However, the method is limited to small number of aldehydes and also workup is not so simple because it requires extraction with organic solvents. Our method is much more superior than other reported methods because no energy-consuming device is required, pure products crystallize out, and there is no need of further purification. This method is general and can be applied to both aromatic and hereocyclic aldehydes. Furthermore, the formation of Cannizaro product of aromatic aldehydes and self-condensation products of ketones was negligible.

We have successfully applied our new method for the synthesis of single chalcones from acetone and aromatic as well as heterocyclic aldehydes. First, the aldol condensation between benzaldehyde and acetone was examined under different conditions to get single chalcones selectively such as 1 : 2, 1 : 3, and 1 : 4 ratio of benzaldehyde and acetone, respectively, using 1) ethanolic sodium hydroxide under microwave irradiation; 2) ethanolic sodium hydroxide under stirring at room temperature; 3) aqueous sodium hydroxide under stirring at room temperature; and 4) aqueous sodium hydroxide under microwave irradiation. It has been found that in all cases, dichalcones were formed. However, when the reaction of benzaldehyde and acetone in 1 : 4 ratio was carried out by using aqueous sodium hydroxide at 5–10°C, we were able to get single chalcones as pure product in nearly quantitative yield. Thus, in all other examples, 1 : 4 equivalents of aldehyde and acetone were used in aqueous sodium hydroxide at 5–10°C. Among 2-chloro-3-formylquinolines (entries 18 and 19) and 2-aryl-3-formylindoles (entries 16 and 17), quinoline ring deactivates, while indole ring activates the –CHO group. In cinnamaldehydes (entries 12–15), the electron-withdrawing and electron-releasing groups have little effect on the rate of the reaction, whereas in aromatic aldehydes, no specific structure-reactivity relationship can be drawn.

EXPERIMENTAL

General

All reagents were obtained from commercial sources and used without further purification unless mentioned elsewhere. ^{1}H NMR spectra were recorded in

$CDCl_3$ on Jeol JNM-PMX 60 NMR spectrometer (60 MHz) using TMS as internal standard (chemical shifts in δ ppm) and IR spectra as KBr pellets on Hitachi 270–30 spectrophotometer (ν_{max} in cm^{-1}). Elemental analysis was determined on Elemental Analysensysteme GmbH Vario EL. Melting points were determined by using Buchi melting point apparatus and are uncorrected. Purity of all analytical samples was checked by TLC.

General Procedure for Single Aldol Condensation Between Acetone and Arylaldehydes

Arylaldehyde (1 mmol) and acetone (4 mmol) were taken in a borosil beaker (100 mL) containing 15 mL of 10% aqueous sodium hydroxide solution. The beaker containing the reaction mixture was covered with a watch glass, and the reaction mixture was maintained at 5–10°C using crushed ice. The reaction mixture was stirred after every interval of 15 min). After the appropriate time (Table 1), the solid product so obtained was filtered, washed with water until the washings were neutral. It was dried and crystallized from EtOAc: pet. ether, or EtOH.

The structures of the products were confirmed by IR, ^{1}H NMR, elemental analysis, and comparison with authentic samples prepared according to literature methods.

Spectral and Analytical Data of Some Selected Compounds

Entry 10

^{1}H NMR ($CDCl_3$): δ 2.7 (s, 3H), 6.7 (d, J = 13.8 Hz, 1H, –CH═C), 7.2–7.9 (m, 4H, Ar-H & –CH═); IR (KBr, ν_{max} in cm^{-1}): 1665 (C═O). Anal. calcd. for $C_{10}H_8Cl_2O$: C, 56.00%; H, 3.70%. Found: C, 55.78%; H, 3.63%.

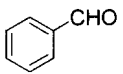
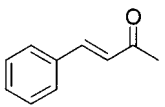
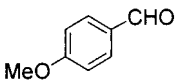
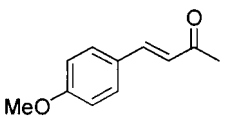
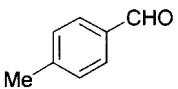
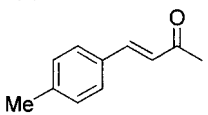
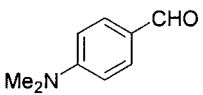
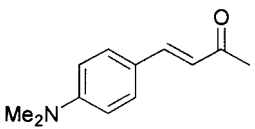
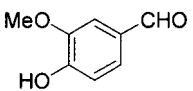
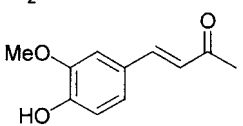
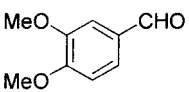
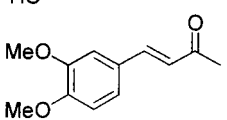
Entry 11

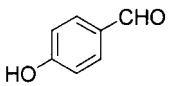
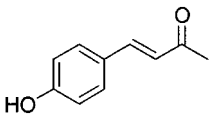
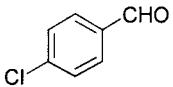
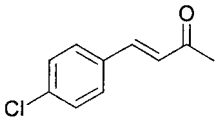
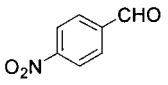
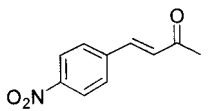
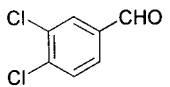
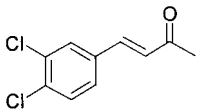
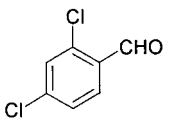
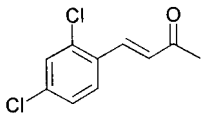
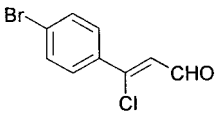
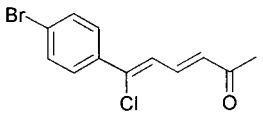
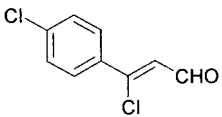
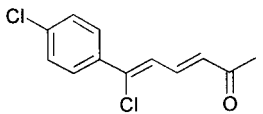
^{1}H NMR ($CDCl_3$): δ 2.8 (s, 3H), 6.8 (d, J = 14.2 Hz, 1H, –CH═C), 7.2–7.85 (m, 4H, Ar-H & –CH═); IR (KBr, ν_{max} in cm^{-1}): 1670 (C═O). Anal. calcd. for $C_{10}H_8Cl_2O$: C, 56.00%; H, 3.70%. Found: C, 55.58%; H, 3.73%.

Entry 12

^{1}H NMR ($CDCl_3$): δ 2.65 (s, 3H), 6.82 (d, J = 14.0 Hz, 1H, –CH═C), 7.0–7.72 (m, 6H, Ar-H & 2x –CH═); IR (KBr, ν_{max} in cm^{-1}): 1630 (C═O). Anal. calcd. for $C_{12}H_{10}BrClO$: C, 52.50%; H, 3.70%. Found: C, 55.78%; H, 3.53%.

Table 1. Single aldol condensation between acetone and arylaldehydes using aqueous sodium hydroxide

Entry	Aldehyde	Product	Time (min)	Yield (%)	m.p./lit. m.p. (°C)
1			140	85	79–80
2			120	98	71–72/73 [18]
3			80	90	33–34/35 [18]
4			35	98	97–98/97[18]
5			120	75	114–115/115[18]
6			20	60	60–61/61[16]

7			90	80	105–107/102–03[18]
8			55	89	106–107/110[18]
9			20	80	117–18/116[18]
10			35	97	162–63
11			25	98	170–171
12			35	95	120–21
13			15	60	122–23

(*continued*)

Table 1. Continued

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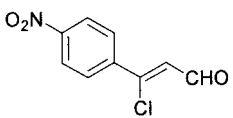
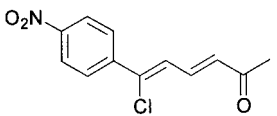
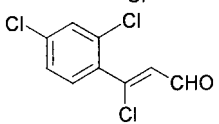
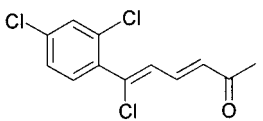
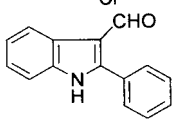
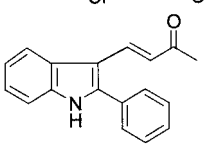
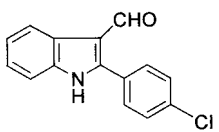
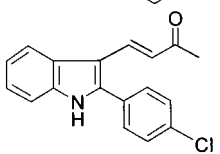
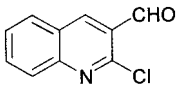
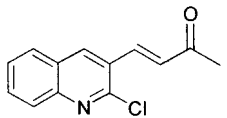
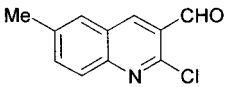
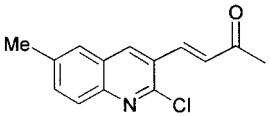
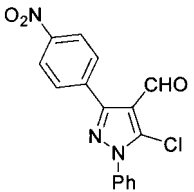
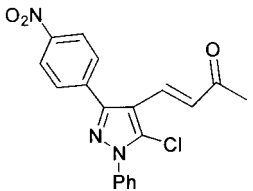
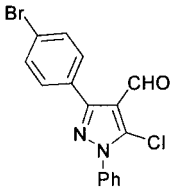
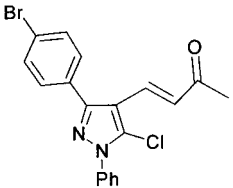
14			20	65	139–40
15			30	70	210–12 (d)
16			15	89	142–43
17			30	88	162–63

18			180	70	110–12
19			75	60	110–11
20			15	70	136–37
21			10	90	157–58

Entry 13

^{1}H NMR ($CDCl_3$): δ 2.7 (s, 3H), 6.78 (d, J = 14.0 Hz, 1H, –CH═C), 7.2–7.72 (m, 6H, Ar-H & 2x –CH═); IR (KBr, ν_{max} in cm^{-1}): 1620 (C═O). Anal. calcd. for $C_{12}H_{10}Cl_2O$: C, 60.00%; H, 4.10%. Found: C, 60.18%; H, 3.95%.

Entry 14

^{1}H NMR ($CDCl_3$): δ 2.74 (s, 3H), 6.57 (d, J = 13.0 Hz, 1H, –CH═C), 7.2–8.2 (m, 4H, Ar-H & 2x –CH═); IR (KBr, ν_{max} in cm^{-1}): 1630 (C═O). Anal. calcd. for $C_{12}H_8ClNO_3$: C, 57.30%; H, 3.90%; N, 5.5%. Found: C, 57.38%; H, 3.98%; N, 5.56.

Entry 15

^{1}H NMR ($CDCl_3$): δ 2.72 (s, 3H), 6.56 (d, J = 13.0 Hz, 1H, –CH═C), 7.3–8.6 (m, 5H, Ar-H & 2x –CH═); IR (KBr, ν_{max} in cm^{-1}): 1630 (C═O). Anal. calcd. for $C_{12}H_9Cl_3O$: C, 43.10%; H, 2.60%. Found: C, 42.98%; H, 2.48%.

Entry 16

^{1}H NMR ($CDCl_3$): δ 2.58 (s, 3H), 6.55 (d, J = 12.5 Hz, 1H, –CH═C), 7.1–7.68 (m, 10H, Ar-H & –CH═), 8.6 (bs, 1H, indole NH); IR (KBr, ν_{max} in cm^{-1}): 1650 (C═O). Anal. calcd. for $C_{18}H_{14}NO$: C, 81.81%; H, 5.70%; N, 5.3%. Found: C, 81.88%; H, 5.78%; N, 5.26%.

Entry 17

^{1}H NMR ($CDCl_3$): δ 2.64 (s, 3H), 6.52 (d, J = 12.5 Hz, 1H, –CH═C), 7.25–7.72 (m, 10H, Ar-H & –CH═), 8.63 (bs, 1H, indole NH); IR (KBr, ν_{max} in cm^{-1}): 1660 (C═O). Anal. calcd. for $C_{18}H_{14}NClO$: C, 73.21%; H, 4.70%; N, 4.70%. Found: C, 73.18%; H, 4.76%; N, 4.66%.

Entry 18

^{1}H NMR ($CDCl_3$): δ 2.54 (s, 3H), 6.54 (d, J = 14.0 Hz, 1H, –CH═C), 7.2–8.4 (m, 5H, Ar-H & –CH═); IR (KBr, ν_{max} in cm^{-1}): 1650 (C═O). Anal. calcd. for $C_{13}H_{10}ClNO$: C, 67.53%; H, 4.30%; N, 6.0%. Found: C, 67.38%; H, 4.37%; N, 5.96%.

Entry 19

^{1}H NMR ($CDCl_3$): δ 2.35 (s, 3H, CH_3), 2.72 (s, 3H, $COCH_3$), 6.55 (d, J = 12.5 Hz, 1H, –CH═C), 7.2–8.4 (m, 4H, Ar-H & –CH═); IR (KBr, ν_{max} in cm^{-1}): 1650 (C═O). Anal. calcd. for $C_{14}H_{12}ClNO$: C, 68.80%; H, 4.90%; N, 5.7%. Found: C, 68.73%; H, 4.98%; N, 5.56%.

Entry 20

^{1}H NMR ($CDCl_3$): δ 2.48 (s, 3H), 6.8 (d, J = 13.0 Hz, 1H, –CH═C), 6.5–8.0 (m, 10H, Ar-H & –CH═); IR (KBr, ν_{max} in cm^{-1}): 1665 (C═O). Anal. calcd. for $C_{19}H_{14}ClN_3O_3$: C, 62.0%; H, 3.80%; N, 11.4%. Found: C, 62.08%; H, 3.98%; N, 5.56.

Entry 21

^{1}H NMR ($CDCl_3$): δ 2.47 (s, 3H), 6.77 (d, J = 13.0 Hz, 1H, –CH═C), 6.7–8.1 (m, 10H, Ar-H & –CH═); IR (KBr, ν_{max} in cm^{-1}): 1660 (C═O). Anal. calcd. for $C_{19}H_{14}BrClN_2O$: C, 58.0%; H, 3.50%; N, 4.0%. Found: C, 57.89%; H, 3.48%; N, 4.06%.

CONCLUSION

We have developed a simple, safe, and economic method for selective single aldol condensation between acetone and aryl/heterocyclic aldehydes. In addition, high yields of the products, ease of workup and low cost make the above method advantageous in comparison to other existing methods.

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