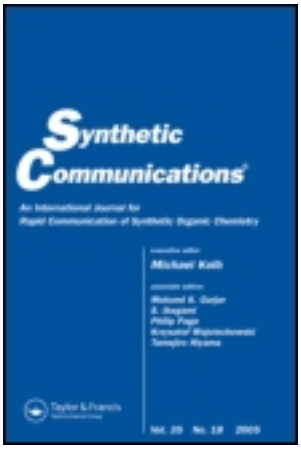


Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

Aldol Condensations Catalyzed by PEG400 and Anhydrous K_2CO_3 Without Solvent

Yu-Qing Cao [a], Zhi Dai [a], Rui Zhang [b] & Bao-Hua Chen [a]

[a] College of Chemistry and Environmental Science, Hebei University, Hebei, P.R. China

[b] Hebei Changtian Pharma, Baoding, P.R. China

Version of record first published: 16 Aug 2006

To cite this article: Yu-Qing Cao, Zhi Dai, Rui Zhang & Bao-Hua Chen (2005): Aldol Condensations Catalyzed by PEG400 and Anhydrous K_2CO_3 Without Solvent, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 35:8, 1045-1049

To link to this article: http://dx.doi.org/10.1081/SCC-200054198

Synthetic Communications®, 35: 1045–1049, 2005

ISSN 0039-7911 print/1532-2432 online
DOI: 10.1081/SCC-200054198

Aldol Condensations Catalyzed by PEG400 and Anhydrous K_2CO_3 Without Solvent

Yu-Qing Cao and Zhi Dai
College of Chemistry and Environmental Science, Hebei University, Hebei, P.R. China

Rui Zhang
Hebei Changtian Pharma, Baoding, P.R. China

Bao-Hua Chen
College of Chemistry and Environmental Science, Hebei University, Hebei, P.R. China

Abstract: Aldol condensations of aromatic aldehydes with ketones under solvent-free conditions to synthesize α,β-unsaturated ketones in good to excellent yields using PEG400 and powdered anhydrous K_2CO_3 as catalysts at 90 °C and 120 °C are described.

Keywords: Aldol condensation, anhydrous K_2CO_3, PEG400, solvent-free

α,β-Unsaturated ketones are very important intermediates in organic synthesis and some of them exhibit important pharmacological and biological activities. Aldol condensation is a common approach to prepare α,β-unsaturated ketones and is usually carried out in organic solvents catalyzed by strong acids, bases,[1] or some metal salts.[2]

Organic synthesis in the absence of solvent is a powerful tool for the generation of structurally diverse molecules because of its low pollution, special

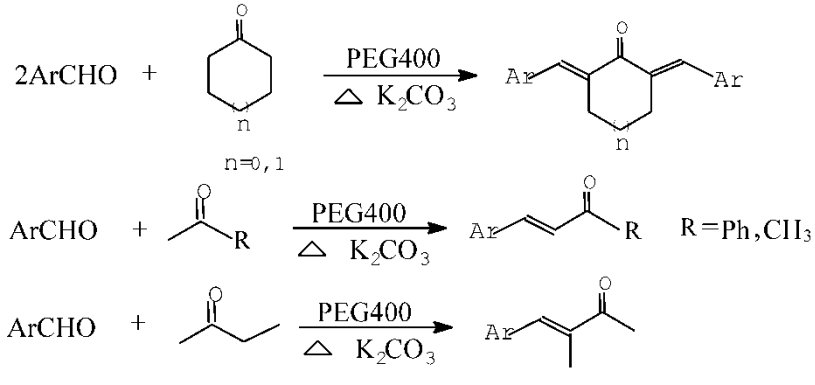
Received in Poland October 15, 2004
Address correspondence to Yu-Qing Cao, College of Chemistry and Environmental Science, Hebei University, Hebei, P.R. China. E-mail: chemistry_hbu@yahoo.com

selectivity, and ease of setup and workup.[3] It was reported in earlier literatures that Aldol condensation reactions in the absence of solvent under microwave irradiation afforded high yields of products in a short time.[4] Up until now, this was suitable only for small-scale preparation, not for large-scale industrial preparation. Polyethylene glycols (PEG) have been widely used as phase-transfer catalysts in many organic reactions because of their stability, low cost, environmental friendliness, and easy availability. It has been proved that PEGs incorporating 7–9 units are more effective in catalyzing reactions in which K^+ or Na^+ salts participated.[5] Especially because of their liquid property and the two terminal hydroxy groups, PEG 400–600 are more suitable for solid–liquid organic reactions under solvent-free conditions.

In the continuation of our previous work,[6] we report a practical and convenient approach for the Aldol condensations catalyzed by anhydrous K_2CO_3 and PEG400 in satisfactory yields without solvent. The reactions are shown in Scheme 1 and the results are summarized in Table 1.

As shown in Table 1, longer reaction periods were needed in the reactions for the products with high melting points. Higher yields could be obtained in the condensation of ketones and aldehydes with electron-withdrawing groups in the aromatic ring, such as –Cl, –Br, and NO_2, than with electron-donating groups, such as $-CH_3$ and $-OCH_3$, mainly because the aldehyde group with electron-donating groups in the aromatic ring was easily oxidized. The reason that the condensation of aromatic aldehydes has higher yields and longer reaction periods with cyclopentanone than with cyclohexanone remains to be investigated further.

When the reaction was carried out in the ratio of 1:1 (aromatic aldehyde/cycloalkanone), the main products were α,α'-bis (substituted benzylidene) cycloalkanones with less α-mono (substituted benzylidene) cycloalkanones. The condensation of aromatic aldehydes with acetone in the ratio of 1:1



Scheme 1.

Table 1. Aldol condensation of aromatic aldehydes with ketones in solvent-free condensations

Entry	Aldehyde	Ketone	Time (h)	Yield (%)	mp, °C	
					Found	Lit.
a	C_6H_5CHO	Cyclohexanone	2[b]	85	116–117	117[7]
b	4-$CH_3C_6H_4CHO$	Cyclohexanone	3[a]	82	199–200	202[7]
c	4-$CH_3OC_6H_4CHO$	Cyclohexanone	3[a]	84	169–170	170[7]
d	4-ClC_6H_4CHO	Cyclohexanone	2.5[a]	90	146–147	147[8]
e	4-$NO_2C_6H_4CHO$	Cyclohexanone	2.5[a]	91	158–159	159[7]
f	Furfural	Cyclohexanone	3[a]	82	143–144	144[9]
g	Cinnamaldehyde	Cyclohexanone	3[a]	86	179–180	180[10]
h	Furfural	Cyclopentanone	2.5[a]	84	164–165	165[9]
i	C_6H_5CHO	Cyclopentanone	3[a]	89	188–189	189[8]
j	4-$CH_3C_6H_4CHO$	Cyclopentanone	3.5[a]	85	183–184	184[10]
k	3-$CH_3C_6H_4CHO$	Cyclopentanone	3[b]	87	135–136	136[10]
l	4-$CH_3OC_6H_4CHO$	Cyclopentanone	3.5[a]	86	209–210	210[10]
m	3-BrC_6H_4CHO	Cyclopentanone	3[a]	94	179–180	180[10]
n	4-ClC_6H_4CHO	Cyclopentanone	3.5[a]	93	223–224	223[10]
o	C_6H_5CHO	Acetophenone	2[b]	88	54–55	55[10]
p	4-$CH_3C_6H_4CHO$	Acetophenone	2[b]	88	95–96	96[10]
q	4-$CH_3OC_6H_4CHO$	Acetophenone	2[b]	89	75–76	76[10]
r	4-ClC_6H_4CHO	Acetophenone	2[b]	91	111–112	112[11]
s	4-$NO_2C_6H_4CHO$	Acetophenone	2.5[a]	93	164–165	165[11]
t	C_6H_5CHO	Acetone	2[b]	90	39–40	41[12]
u	4-$CH_3C_6H_4CHO$	Acetone	1.5[b]	91	27–28	28–29[12]
v	furfural	Acetone	2[b]	89	33–34	33–35[13]
w	C_6H_5CHO	2-Butanone	2.5[b]	78	36–37	37–38[13]

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

provided the main product α-mono (substituted benzylidene) acetone. When the ratio of aromatic aldehydes to acetones was 2:1, α,α'-bis (substituted benzylidene) acetone was obtained in the yield of only 53%, possibly because of some by-products being formed. The condensation of benzaldehyde with 2-butanone was selective and the main product was 4-phenyl-3-methyl-3-buten-2-one with less 5-phenyl-4-penten-3-one because of thermodynamic dominating.

Effects of alkalies on the condensation were apparently different. Taking the reactions of benzaldehyde with cyclopentanone as an example, the yields using K_2CO_3, Na_2CO_3, KF, or KOH as bases were respectively 85%, 68%, 55%, and 38% under the same reaction conditions.

Using PEG400 as phase-transfer catalyst allowed us to perform the condensation under mild conditions without solvent. The amount of PEG400 was 3–5 mol% to aromatic aldehydes (larger amounts were used in the reactions for the products with higher melting points). A longer reaction period would be necessary with less PEG400 and more products would be lost during the course of washing with water with the larger amount of PEG400.

In summary, a novel method for Aldol condensation catalyzed by PEG400 and anhydrous K_2CO_3 without solvent was developed. The advantages of our method are safety, high selectivity, environmental friendliness, and ease of workup.

EXPERIMENTAL

Thin layer chromatography (TLC) was GF_{254} with petroleum ether/diethyl ether (2:1) as eluent. Aromatic aldehydes and ketones were obtained from commercial suppliers and were not purified. Melting points were determined on a microscopy apparatus and are uncorrected.

Typical procedure for the synthesis of compound **a**: A mixture of benzaldehyde (0.2 mol), cyclohexanone (0.1 mol), anhydrous K_2CO_3 (0.01 mol), and PEG-400 (2 mL) were put into a 50-ml, three-necked, round-bottomed flask equipped with a mechanical stirrer and drying tube filled with KOH. The reaction was processed with vigorous stirring and heating at the assigned temperature. The completion of the reaction was monitored by TLC. The reaction mixture was cooled and treated with cool water. The product was filtered, dried, recrystallized with ethanol, and identified by comparison of melting point.

REFERENCES

1. Fuentes, A.; Marinas, J. M.; Sinisterra, J. V. Catalyzed synthesis of chalcones under interfacial solid–liquid conditions with ultrasound. *Tetrahedron Lett.* **1987**, *28*, 4541.

2. Deng, G. S.; Ren, T. G. Indium trichloride catalyzes aldol-condensations of aldehydes and ketones. *Synth. Commun.* **2003**, *33*, 2995.
3. Tanaka, K.; Toda, F. Solvent-free organic synthesis. *Chem. Rev.* **2000**, *100*, 1025.
4. Wang, J. X.; Kang, L.; Hu, Y. L.; Wei, B. G. Synthesis of bis(substituted benzylidene) cycloalkanone using supported reagents and microwave irradiation. *Synth. Commun.* **2002**, *32*, 1691.
5. Wang, M.; Chang, K. R. Effect of polyethylene glycol 400 on the allylation of phenoxide in a homogeneous phase. *Ind. Eng. Chem. Res.* **1990**, *29* (1), 40.
6. (a) Cao, Y. Q.; Pei, B. G. Etherification of phenols catalyzed by solid–liquid phase transfer catalyst PEG400 without solvent. *Synth. Commun.* **2000**, *30*, 1759; (b) Cao, Y. Q.; Chen, B. H.; Pei, B. G. Cyanidation of halogen compounds and esters catalyzed by PEG400 without solvent. *Synth. Commun.* **2001**, *31*, 2202; (c) Cao, Y. Q.; Dai, Z.; Zhang, R.; Chen, B. H. A practical Knoevenagel condensation catalyzed by PEG400 and anhydrous K_2CO_3 without solvent. *Synth. Commun.* **2004**, *34*, 2965.
7. Iranpoor, N.; Kazemi, F. $RuCl_3$ catalyses aldol condensations of aldehydes and ketones. *Tetrahedron* **1998**, *54*, 9475.
8. Huitric, A. C.; Kulmler, W. D. The dipole moments, spectra and structure of some new 2-phenyl-,2-benzyl-,2-(*p*-halobenzylidene) and 2,6-bis-(*p*-halobenzylidene)-cyclohexanones. *J. Am. Chem. Soc.* **1956**, *78*, 614.
9. Alexander, K.; Hafner, L. S.; Smith, G. H. The partial hydrogenation of difurfuralacetone and related compounds. *J. Am. Chem. Soc.* **1950**, *72*, 5506.
10. Zheng, X. L.; Zhang, Y. M. SmI_3 catalyzed condensation of aliphatic cycloketones and aldehydes in ionic liquid. *Synth. Commun.* **2003**, *33*, 161.
11. Kumar, C. V.; Ramaiah, D.; Kas, P. K.; George, M. V. Photochemistry of aromatic α,β-epoxy ketones: Substituent effects on oxirane ring-opening and related ylide behavior. *J. Org. Chem.* **1985**, *50*, 2818.
12. Gilman, H. Chalcone. *Org. Syn. Coll.*; John Wiley & Sons, 1941; Vol. 1, p. 77.
13. Hauser, C. R.; Lindsay, J. K. Some typical aldehyde addition and condensation reactions of formylferrocene. *J. Org. Chem.* **1957**, *22*, 906.