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Catalysis Communications 9 (2008) 349–354

CATALYSIS COMMUNICATIONS

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Polymer-supported sulphonic acid catalyzed cross-aldol condensation: An expeditious synthesis of α,α′-bis(substituted benzylidene) cycloalkanones

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Received 24 December 2006; received in revised form 19 May 2007; accepted 6 June 2007
Available online 12 June 2007

Abstract

Polymer-supported sulphonic acid (NKC-9) efficiently catalyzed the cross-aldol condensation of arylaldehydes and cycloketones to afford α,α′-bis(substituted benzylidene) cycloalkanones in good yields. The catalyst can be recovered simply and reused.

Keywords: Cross-aldol condensation; Aromatic aldehyde; Cyclic ketone; Solid acid; α,α′-Bis(substituted benzylidene) cycloalkanones

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1. Introduction

Cross-aldol condensation of aromatic aldehydes with cyclic ketones is an important protocol for the synthesis of α,α′-bis(substituted benzylidene) cycloalkanones, which are the important intermediates for synthesis of pyrimidines [1], agrochemicals, pharmaceuticals, perfumes [2], liquid-crystalline polymers [3] and bis-spiropyrrolidines [4,5]. Usually, the aldol reaction is catalyzed by strong acid or base, however, the yield is low in common due to reverse and side-reactions [6]. Therefore, much efforts on improvement of the reaction yield were performed, the main progress was the following: (1) The aldol reaction was catalyzed by organometallic complexes but the yields were not satisfactory [7] or required long reaction time [8]. (2) Using Lewis acid such as $RuCl_3$ [9], SmI_3 [10], $BF_3 \cdot Et_2O$ [11,12], $FeCl_3 \cdot 6H_2O$ [13], $Mg(HSO_4)_2$ [14], $Yb(OTf)_3$ [15], $InCl_3 \cdot 4H_2O$ [16] as catalyst promoted the aldol reaction. (3) I_2 [17], TMSCl/NaI [18], LiOH [19], KF/Al_2O_3 [20] and BMPTO [21] were also found to accelerate this type reaction. However, most of the above-mentioned process generated a large amount of toxic waste and involved tedious separation procedures since the reactions were homogeneous and the catalysts were destroyed or discarded on the work-up procedure.

Recently, because of increased environmental concerns and strong economic driver in chemical research and industry, great efforts have been made on heterogeneous catalysis [22,23], which allows the catalyst for easy isolation and recycling. Thus, solid catalysts have drawn considerable attention in organic synthesis due to their advantages such as environmental compatibility, reusability, high selectivity, simple operation, non-corrosiveness and low cost. Among of many solid catalysts employed, polymeric sulfonic acid, one of the important polymer-supported catalysts [24,25] has already been developed in organic chemistry [26–29].

To the best of our knowledge, there is no report on polymer-supported catalyst for promoting the cross-aldol condensation. Herein, authors wish to report a new and effective method for synthesis of α,α′-bis(substituted benzylidene) cycloalkanones catalyzed

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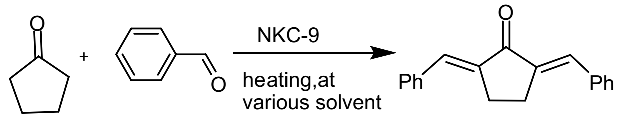
doi:10.1016/j.catcom.2007.06.004

by polystyrene-supported sulphonic acid (NKC-9). It is a macroreticular strongly acidic cation-exchange resin H^+ form (more information about NKC-9, see Section 2).

Initially, the reaction of cyclopentanone with benzaldehyde was tested in the presence of polystyrene supported sulphonic acid (NKC-9) in acetonitrile (Scheme 1). The reactants kept unchanged even under reflux for 12 h (Table 1, entry 1). Then, we turned to choose chloroform as solvent, interestingly, the reaction took place and gave α,α′-bis(benzylidene) cyclopentanone (**3a**) in 17% yield for 4 h at 20 °C (Table 1, entry 2). Followed by increasing the reaction temperature to reflux, we found that the yield reached 84% (Table 1, entry 3). When the catalyst loading increased to 0.17 g, the product was obtained in 90% yield (Table 1, entry 4), continue to increase the catalyst loading, the yield was not improved greatly (Table 1, entry 5). Thus, we think that 0.17 g NKC-9 may be sufficient for satisfactory result. In order to understand the action of catalyst NKC-9, the same reaction was carried out for 6 h in refluxing chloroform without NKC-9, but no reaction was observed (Table 1, entry 6). It is obvious that NKC-9 is necessary for this reaction. Furthermore, different solvents were screened, eventually, chloroform was found to be the best (Table 1, entries 4, 7–10).

The catalyst NKC-9 could be recovered easily by filtration after completion of the reaction, followed by drying at 100 °C for 2 h prior to the next run, it could be reused for three times without obvious activity loss (Table 2). The slight loss in activity may be due to the leakage of sulfonic group from the matrix. When the yield drops, the catalyst can be activated to recover its activity by simple activation procedure (Table 3).



3a

Scheme 1.

Table 1
Effect of the solvents on the yield of α,α′-bis(benzylidene) cyclopentanone[a]

Entry	Solvent	Temperature (°C)	Time (h)	Yield (%)[b]
1	CH_3CN	82 (reflux)	12	0[c]
2	$CHCl_3$	r.t.	4	17[c]
3	$CHCl_3$	62 (reflux)	4	84[c]
4	$CHCl_3$	62 (reflux)	4	90
5	$CHCl_3$	62 (reflux)	4	92[d]
6	$CHCl_3$	62 (reflux)	6	0[e]
7	$CH_3COOC_2H_5$	77 (reflux)	6	53
8	C_6H_6	80 (reflux)	6	28
9	$CH_3C_6H_5$	80	6	34
10	CH_2Cl_2	40 (reflux)	6	65

[a] *Reaction conditions:* 1 mmol cyclopentanone, 2.2 mmol benzaldehyde, 0.17 g NKC-9 resin unless otherwise mentioned.
[b] Isolated yield.
[c] *Reaction conditions:* 1 mmol cyclopentanone, 2.2 mmol benzaldehyde, 0.08 g NKC-9 resin.
[d] *Reaction conditions:* 1 mmol cyclopentanone, 2.2 mmol benzaldehyde, 0.34 g NKC-9 resin.
[e] *Reaction conditions:* 1 mmol cyclopentanone, 2.2 mmol benzaldehyde, in the absence of NKC-9.

Table 2
The activity of the recovered catalyst in the reaction of cyclopentanone with benzaldehyde[a]

Entry	Run	Time (h)	Yield[b] (%)
1	1st	4	90[c]
2	2nd	4	90[d]
3	3rd	4	85[d]
4	4th	4.5	83[d]

[a] Reaction condition: 1 mmol cyclopentanone, 2.2 mmol benzaldehyde, 0.17 g NKC-9.
[b] Isolated yield.
[c] Fresh resin.
[d] Used resin.

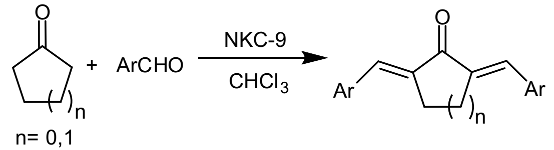
To evaluate the reaction scope and generality of the catalyst, the reactions of cyclopentanone with other aryl aldehydes were conducted. The results were summarized in Scheme 2 and Table 4, which demonstrated that the substituted groups of aryl aldehydes, such as methyl, methoxy, fluoro, chloro groups could be tolerated under the reaction conditions and good yields were obtained (Table 4, entries 2–6). An interesting example was observed that 2-fluorobenzaldehyde gave higher yield than 4-fluorobenzaldehyde (Table 4, entries 2 and 3) when they reacted with cyclopentanone. As for cyclohexanone, the result was quite inverse (Table 4, entries 11 and 12). In addition, conjugated aryl aldehyde such as cinnamaldehyde, could also afford the desired product in 83% yield (Table 4, entry 7).

Inspired by the results of aromatic aldehydes, we extended the reaction to aliphatic aldehydes, in which paraformaldehyde, acetaldehyde, *n*-butylaldehyde, *iso*-butyral-

Table 3
The activity of the regenerated catalyst in the reaction of cyclopentanone with benzaldehyde

Entry	Run	Time (h)	Yield[a] (%)
1	1st	4	89[b]
2	2nd	4	87[b]
3	3rd	4	83[b]

[a] Isolated yield.
[b] Reaction condition: 1 mmol cyclopentanone, 2.2 mmol benzaldehyde, 0.17 g NKC-9, which was obtained by the activation of used NKC-9 in Table 2 after running four times (For regenerated procedure, see Section 2).



3b-30

Scheme 2.