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# Selective synthesis of nitroalcohols in the presence of Ambersep 900 OH as heterogeneous catalyst

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**Abstract** A green protocol has been developed for the selective synthesis of  $\beta$ -nitroalcohols using commercially available Ambersep 900 OH as reusable heterogeneous catalyst. The reaction between aldehyde and nitromethane was performed under solvent-free condition at room temperature within a short time (70–150 min) in the presence of 10 wt % of Ambersep 900 OH to produce corresponding nitroalcohols in high yield (72–91 %). After the reaction is over, the catalyst can be separated and reused (3 cycles) without appreciable loss in its activity. *Graphical Abstract* 



**Keywords** Henry reaction · Aldehyde · Nitroalcohol · Nitromethane · Ambersep 900 OH

#### Introduction

The Henry reaction of carbonyl compounds with alkyl nitro compounds bearing  $\alpha$ -hydrogen atoms is one of the most fundamental and widely utilized methods for the construction of carbon-carbon bonds that leads to the formation of  $\beta$ -nitroalcohols which in turn can be used as valuable building blocks in organic synthesis [1–9]. From the synthetic point of view,  $\beta$ -nitroalcohols are very important difunctional compounds as they are versatile precursors for the preparation of a great variety of pharmaceutically active compounds such as  $\beta$ -aminoalcohols,  $\alpha$ -hydroxycarboxylic acids, 2-nitroketones, or nitroalkenes [1–11]. Classical methods for preparing  $\beta$ -nitroalkanols include the condensation of the carbonyl compounds and a nitroalkane in the presence of a base such as alkali metal hydroxides, carbonates, bicarbonates, alkaline earth oxides, alkaline earth hydroxides or magnesium and aluminum alkoxides, rhodium complex, potassium exchanged zirconium phosphate and also organic bases such as primary, secondary, and tertiary amines [1–9]. Competitive reactions such as Cannizzaro reaction, Tishchenko reaction, and Nef-type reactions were also observed during the course of this particular reaction [1-11]. In certain cases, base catalyzed elimination of water leads to the formation of nitroalkenes which further undergo nitration to yield 1,3dinitro compounds [12–14]. Different solid catalysts such as alumina [15, 16], alumina-KF [17], Amberlyst A21 [18, 19], SiO<sub>2</sub> [20], hydrotalcites [21-24], etc. were found to promote nitroaldol reaction. Some metal incorporated heterogeneous phases such as polyacrylic acid template [25], carbon nanotubes [26], and metal organic frame works [27] were also developed. Phase transfer catalyst has also been utilized for this particular reaction to improve the selectivity [28]. Some of the former approaches require

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longer reaction time and in some cases, the reaction produces condensed olefin as one of the products [29–31]. Apart from these, some more catalytic systems have also been developed, which include the use of tetramethylguanidine [32], dendritic catalysts [33], rhodium complex [34], and proazaphosphatranes [3c]. Due to the importance of this particular transformation in organic synthesis, several asymmetric synthetic approaches were developed using metallic catalyst in the presence of a chiral ligand [1-9, 35-40]. There are also reports for the nitroaldol reaction in aqueous media [18, 19, 28, 41-45] and under solvent-free conditions [46–53]. However, long reaction time and formation of nitroalkene as side product are the major issues for many of these methods. Hence, the development of a convenient protocol using commercially available heterogeneous catalyst for selective synthesis of  $\beta$ -nitroalcohol is a prime concern for many chemical processes.

Heterogeneous catalysts are getting importance in organic transformations under solvent-free condition [54–56]. From industrial point of view, heterogeneous catalysts are important in organic transformation due to their easy separation process and economically favorable reusability. Similar to Amberlyst A21, Ambersep<sup>®</sup> 900 OH is also an anionic macromolecular ion-exchange resin, but it is strongly basic in comparison to Amberlyst A21. The utility of Ambersep 900 OH is very limited with a very few reported reactions [57–60]. Herein, we are reporting a new protocol for selective synthesis of nitroalcohols using Ambersep 900 OH as heterogeneous green catalyst (Scheme 1).

### **Results and discussion**

To begin with, the condensation of benzaldehyde with nitromethane (1.2 equiv.) was examined at room temperature in the presence of 5 wt % of Ambersep 900 OH (Table 1, entry 1) under solvent-free condition. The reaction selectively produced corresponding nitro alcohol in 43 % yield after 2 h of reaction. When the catalyst loading was increased to 10 wt %, the reaction completes in 1.5 h with 86 % isolated yield (Table 1, entry 2).

 Table 1 Optimization condition of nitroaldol reaction of benzaldehyde

Entry	Catalyst loading/wt %	Time/h	Yield/% <sup>a</sup>	
1	5	2	43	
2	10	1.5	86	
3	15	1.5	84	

Reaction conditions: 10 mmol benzaldehyde, 12 mmol nitromethane, room temperature

<sup>a</sup> Isolated yield

Further increase of catalyst amount did not improve the yield significantly. So the use of 10 wt % of the catalyst at room temperature was chosen as the best reaction condition for optimum yield.

After optimizing the reaction condition, the process was extended to a number of aldehydes. Results are summarized in Table 2. Aryl aldehydes with large -I effect (or small +R effect) requires less time than aldehydes with a large +R effect. However, the positions of substituent on the phenyl ring do not have considerable effect on rate of the reaction. Aromatic aldehydes such as 3-nitrobenzaldehyde, 4-methylbenzaldehyde, 4-methoxybenzaldehyde, and 3,4-dimethoxybenzaldehyde produced lower yield of the product. Moreover, for these particular substrates the transformations took relatively longer reaction time for completion. Reaction with heterocyclic aldehydes such as furan-2-carbaldehyde produced low yield of corresponding

 Table 2 Henry reaction of nitromethane with various aldehydes (Scheme 1)

Entry	R	Prod.	Time/min	Yield/% <sup>a</sup>	References
1	C <sub>6</sub> H <sub>5</sub>	1b	90	86	[61]
2	4-Cl-C <sub>6</sub> H <sub>4</sub>	2b	70	91	[62]
3	$4-F-C_6H_4$	3b	80	87	[63]
4	4-Br-C <sub>6</sub> H <sub>4</sub>	4b	90	82	[62]
5	4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	5b	70	86	[ <mark>61</mark> ]
6	3-Cl-C <sub>6</sub> H <sub>4</sub>	6b	80	91	[ <mark>61</mark> ]
7	3-Br-C <sub>6</sub> H <sub>4</sub>	7b	90	88	[ <mark>61</mark> ]
8	2-Cl-C <sub>6</sub> H <sub>4</sub>	8b	80	78	[ <mark>61</mark> ]
9	3-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub>	9b	80	72	[ <mark>61</mark> ]
10	4-CH <sub>3</sub> -C <sub>6</sub> H <sub>4</sub>	10b	120	76	[63]
11	4-CH <sub>3</sub> O-C <sub>6</sub> H <sub>4</sub>	11b	120	77	[63]
12	2-Naphthyl	12b	120	78	[ <mark>61</mark> ]
13	C <sub>6</sub> H <sub>5</sub> CH <sub>2</sub> CH <sub>2</sub>	13b	120	78	[ <mark>61</mark> ]
14	2-Furanyl	14b	120	72	[ <mark>61</mark> ]
15	3,4-(CH <sub>3</sub> O) <sub>2</sub> -C <sub>6</sub> H <sub>3</sub>	15b	150	75	[45]

Reaction conditions: 1.2 equiv. nitromethane and 10 wt % Ambersep 900 OH at room temperature

<sup>a</sup> Isolated yield



Fig. 1 Bar diagram representing the reproducibility of the catalyst in terms of yield after each consecutive cycles

nitroalcohol. Aliphatic aldehydes, such as 3-phenylpropanal, also produced low yield of the corresponding product.

Since we are using a solid resin catalyst, we were interested to examine the feasibility of recycling the catalyst. The catalyst was recovered from the reaction mixture just by filtration and then it was washed with ethanol for 2–3 times. The recyclability experiment was carried out for condensation of *p*-nitrobenzaldehyde and nitromethane under the optimized reaction conditions for three consecutive cycles. During the first two consecutive cycles, the similar yield (85 %) was recorded (Fig. 1). In the third round of catalytic cycle, though the yield was found to be lower (82 %), the change was not detrimental.

## Conclusions

In conclusion, an efficient, green, and controlled methodology for the synthesis of  $\beta$ -nitroalcohols has been developed using Ambersep 900 OH as heterogeneous catalyst. Moreover, the reaction is very easy to carry out and

Table 3 Activity of different reusable catalysts for Henry reaction

Entry	Catalyst	Condition	Time/ h	Yield/ %	References
1	Ambersep 900 OH	r.t.	1-2.5	72–91	This work
2	Amberlyst A21	r.t.	3–20	70–95	[18, 19]
3	Phosphate buffer	r.t., pH 7	12–40	91–95	[45]
4	KF/alumina	0 °C	5-15	50-78	[17]
5	Mg-Al Hydrotalcites	Reflux	6–8	72–95	[22]
6	Zr(KOPO <sub>3</sub> ) <sub>2</sub>	r.t.	6–25	62–89	[52]
7	DNA	r.t., pH 5.5	8–72	64–96	[43]

the catalyst can be recovered just by filtration of the reaction mixture with the aid of small amount of dichloromethane. The catalyst could be recycled for the same process without having detrimental effect. Both aromatic and aliphatic aldehydes undergo the Henry reaction with high yield within a short time. The advantages of our methods can be easily realized by comparing the recent results on the use of reusable catalysts for selective synthesis of nitroalcohols via Henry reaction, which are presented in Table 3.

# Experimental

All reagents were purchased from Sigma–Aldrich. The catalyst Ambersep 900 OH was obtained from Alfa Aesar. The solvents were purified through distillation prior to use. All reactions were carried out under indicated conditions. NMR spectra were recorded using Bruker 300 MHz instruments (300 MHz for <sup>1</sup>H, 75.3 MHz for <sup>13</sup>C). Chemical shifts are given in  $\delta$  units relative to the tetramethylsilane (TMS) signal as an internal reference. IR spectra were recorded on Perkin Elmer Spectrum RX I FT-IR System.

# General procedure

To a solution of aldehyde (10 mmol) in nitromethane (12 mmol) was added Ambersep 900 OH (10 wt %). The solution was stirred for appropriate time and progress of the reaction was monitored by TLC. After completion of the reaction, 5 cm<sup>3</sup> dichloromethane was added and the catalyst was filtered off and washed with 2 cm<sup>3</sup> ethanol twice. The combined organic extract was evaporated under reduced pressure and the crude product was purified by flash column chromatography using petroleum ether and ethyl acetate as eluent.

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