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$Mn(OAc)_2$/Schiff base as a new efficient catalyst system for the Henry reaction of nitroalkanes with aldehydes

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Abstract

A series of novel Schiff bases bearing triazole structure were synthesized and characterized by IR and NMR. $Mn(OAc)_2$/Schiff base efficiently catalyzed Henry reaction of nitroalkanes with aldehydes to produce the corresponding products of β-nitroalcohols, under mild conditions with high yields (up to 99%). A reaction mechanism is proposed based on the experimental results.

Keywords: Schiff base; Henry reaction; Aldehydes; Nitroalkanes

The Henry reaction, an aldol-type reaction, has been recognized as one of the most fundamental carbon–carbon bond-forming reactions [1–3]. Products afforded by this reaction can be transformed into various valuable nitrogen-containing building blocks, such as α-hydroxy ketones, aldehydes, carboxylic acids, azides, sulfides, and other important bifunctional compounds [4,5], through either oxidation, reduction [6] or dehydration [7,8]. In particular, a group of β-amino alcohol derivatives [9–11], which have been widely used as catalyst and important building blocks of natural products [12] or pharmaceuticals [13], can be conveniently obtained by the reduction of β-hydroxy nitroalkanes. Recent efforts have been focused on the development of catalytic systems due to the most important role they play in above-mentioned reaction. According to previous reports, this type of C–C bond-forming reaction has been demonstrated can be catalyzed by a range of inorganic, organic bases [14] and earth metal complexes [15–18]. In the past few years, many chemists demonstrated that metal complexes such as copper [19–21], zinc [22,23], chromium, indium, cobalt [24,25], cesium [26], ytterbium [27], and magnesium [28,29] catalyze Henry reaction. However, several drawbacks, such as moisture or air sensitivity, necessity for bases, and difficult preparation of the catalysts, still was lie ahead [30].

Our groups have successfully synthesized a series of triazole-containing Schiff base ligands L1–L6 (chemical structure of these ligands are shown in Fig. 1) and demonstrated that such ligands can act as bi-functional organocatalysts in Friedel–Crafts alkylation of indoles [31,32]. In continuation of our ongoing interest, we find that

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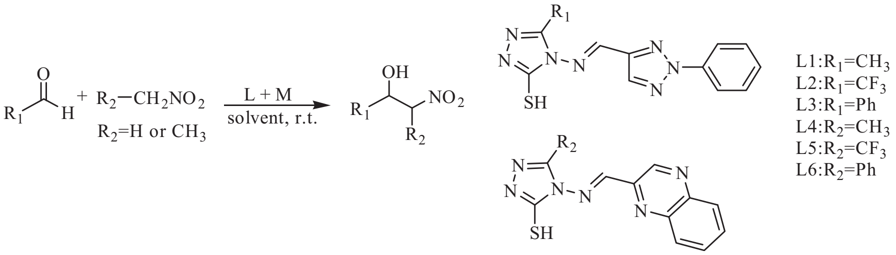


Fig. 1. Ligands used in the Henry reaction of benzaldehyde derivatives with nitroalkanes.

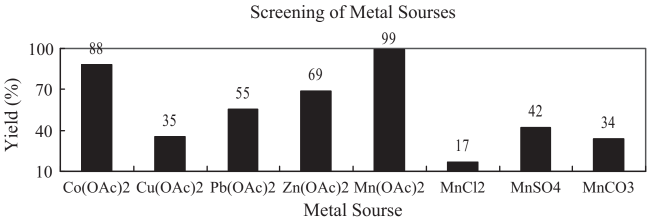


Fig. 2. Screening of metal sources (all the reactions were carried out with L1 (5 mol%), metal salt (5 mol%) and 2-nitrobenzaldehyde (0.2 mmol), nitromethane (0.6 mmol) in EtOH at room temperature for 24 h. Isolated yield by column chromatography).

complexes of these bases and some metal salts can effectively activate the reaction between nitroalkanes with various aldehydes, and the corresponding nitroalcohol-derivative target products have been successfully obtained.

1. Results and discussion

The Henry reaction of 2-nitrobenzaldehyde (0.2 mmol) with nitromethane (0.6 mmol) as model substrate was investigated by using L1–L6 (5 mol%) as catalyst (Fig. 1) in EtOH. L2–L6 as catalyst showed the worst potential in this reaction, no product was obtained. However, only 6% yield was obtained with application of L1 as catalyst.

Previous report demonstrated that weak Lewis acidic metal bearing moderately basic charged ligands would facilitate the reaction of nitroalkanes with aldehydes. Inspired by this finding, we used several L/metal salts complexes to catalyze the same reaction, and the corresponding results were summarized in Figs. 2 and 3. The best result was achieved when using L1/Mn(OAc)$_2$, and the very high yield (99%) implying its promising potential in such reaction in the polar solvent, EtOH.

Table 1 listed the yield results of various nitroalkanols (**3a**–**3t**) afforded by condensation between different aldehydes and nitroalkanes using L1–Mn(II) (5 mol%, 1:1) as a catalyst. In general, high yields (91–99%) were observed when benzaldehyde derivatives bearing electron-withdrawing groups (Table 1, entries 2–8). In contrast,

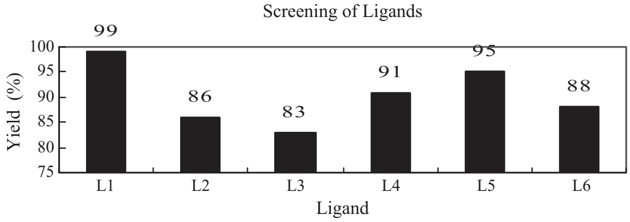
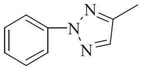
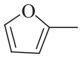
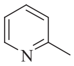
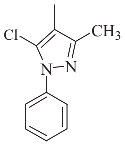
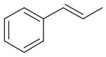


Fig. 3. Screening of ligands (all the reactions were carried out with L (5 mol%), Mn(OAc)$_2$ (5 mol%) and 2-nitrobenzaldehyde (0.2 mmol), nitromethane (0.6 mmol) in EtOH at room temperature for 24 h. Isolated yield by column chromatography).

Table 1

Henry reaction of benzaldehyde derivatives with nitromethane using L1/Mn(OAc)$_2$ in the presence of ethanol.[a]

Entry	R_1	R_2	Prod.	Yield[b] (%)	Entry	R_1	R_2	Prod.	Yield[b] (%)
1	Ph	H	**3a**	71	12	$CH_3CH_2CH_2$	H	**3l**	57
2	4-$NO_2C_6H_4$	H	**3b**	95	13		H	**3m**	88
3	3-$NO_2C_6H_4$	H	**3c**	99	14		H	**3n**	71
4	2-$NO_2C_6H_4$	H	**3d**	99	15		H	**3o**	80
5	4-ClC_6H_4	H	**3e**	91	16		H	**3p**	72
6	3-ClC_6H_4	H	**3f**	93	17	3-$NO_2C_6H_4$	CH_3	**3q**	85
7	3-BrC_6H_4	H	**3g**	92	18	2-$CH_3OC_6H_4$	CH_3	**3r**	12
8	2,4-$Cl_2C_6H_4$	H	**3h**	97	19	2, 4-$Cl_2C_6H_4$	CH_3	**3s**	35
9	2-OHC_6H_4	H	**3i**	98	20	Ph	CH_3	**3t**	10
10	4-$CH_3OC_6H_4$	H	**3j**	78	21		H	**3u**	47
11	2-$CH_3OC_6H_4$	H	**3k**	89					

[a] All the reactions were carried out using L1 (5 mol%), Mn(OAc)$_2$ (5 mol%) as catalyst in ethanol at room temperature. benzaldehyde derivatives and other aldehydes (0.2 mmol), nitromethane (0.6 mmol).

[b] Isolated yield by column chromatography.

aromatic aldehydes containing electron-donating groups gave the corresponding product in relatively low yield (Table 1, entry 10). And in the reaction of aromatic aldehydes containing both electron-withdrawing and electron-donating groups in the aromatic ring's *ortho*-position, the reaction proceeded smoothly in high yields (Table 1, entries 4, 9, and 11). Aliphatic branched, heteroaromatic and cinnamic aldehydes were also acceptable substrates, affording nitro alcohol adducts in good yields (Table 1, entries 12–16, 21). Surprisingly, benzaldehyde derivative containing hydroxyl group was converted to nitroaldol product **3h** in almost quantitative yield (Table 1, entry 9). When nitroethane was used, relatively low yields of corresponding nitroalcohols were obtained under the same condition in EtOH, implying the significant influence brought by the electronic nature of nitroethane, regardless of the substituent on the ring is

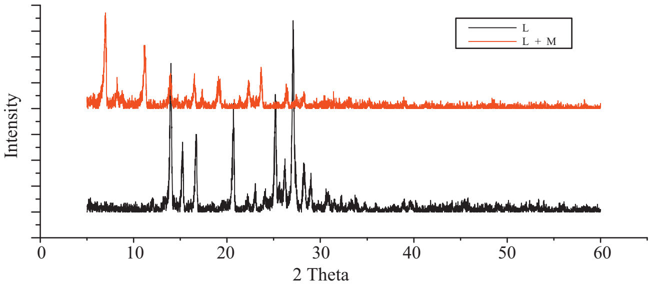


Fig. 4. Powder X-ray diffraction patterns of (L) Schiff base (L + M) corresponding manganese complex.

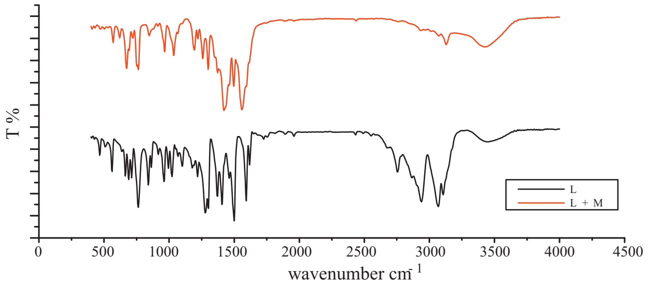


Fig. 5. FT-IR spectra of (L) Schiff base (L + M) corresponding manganese complex.

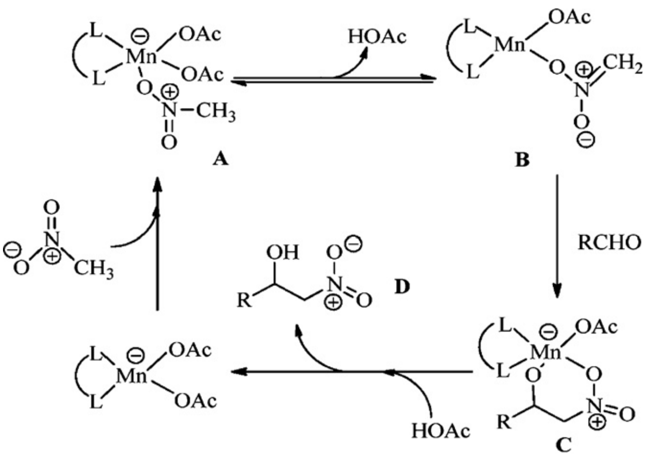


Fig. 6. Plausible transition structures for the Henry reaction.

electron-withdrawing or electron-donating (Table 1, entries 17–20). The reason might be explained by the lower pK_a value of nitroethane than nitromethane (8.456 and 10.211 at 25 °C, respectively) [9].

Powder X-ray diffraction (XRD) patterns were collected with XRD, D8, Advance, Bruker, AXS, using a nickel-filtered Cu Kα (0.154056 nm) radiation source at 40 kV and 50 mA in the range of $2\theta = 5$–60°. XRD spectra (Fig. 4) of the L before and after manganese loading showed a change. IR spectrum of the complex showed that 1619 cm^{-1} for ν(C=N) and 2552 cm^{-1} for ν(S–H) were disappeared in Fig. 5. In addition, IR spectrum of the complex showed an absorption bands at 501 cm^{-1}, which was attributed to the formation of Mn–N. These variations could be confirmed the coordination of manganese ion with the Schiff base ligand.

Although attempts to detail the reaction mechanism have not been undertaken, a possible cycle can be proposed (Fig. 6). From the mechanistic point of view, the initial step involves deprotonation of nitromethane by catalyst to give the intermediate A. Consequent stripping of HOAc moiety to give the intermediate B that can make nitromethane more nucleophilic and liable to attack on aldehydes to give the intermediate C. Then with the HOAc moiety, the corresponding products D will be afforded and the catalyst is recovered to its initial state.

In summary, our results showed that the complex of Mn(II)–Schiff base L1 was an effective catalyst for the Henry reaction and produced β-hydroxy nitroalkanes in high yield. The procedure with above-mentioned catalyst has several merits including simplicity of operation, mild reaction condition and easy isolation. What's more, the insight into the mechanism will provide useful information to synthesize β-nitroalcohols. Further work is in under progress with the aim of expanding the applications of these inexpensive ligands to other catalytic processes.

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