



Yb(OⁱPr)₃, a highly efficient catalyst for the nitro-Mannich reaction

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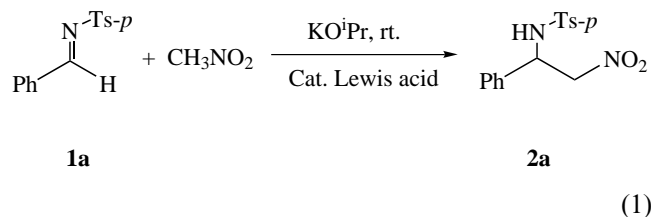
Received 8 January 2001; accepted 11 May 2001

Abstract—A catalytic amount of Yb(OⁱPr)₃ (5 mol%) was found to be an excellent and practical catalyst for the nitro-Mannich reaction of nitromethane with sulfonylimines affording the corresponding adducts in 81–100% isolated yields under extremely mild reaction conditions. © 2001 Elsevier Science Ltd. All rights reserved.

The nitro-Mannich reaction can provide β-nitroamines which can be further converted into several useful building blocks in organic synthesis such as α-amino acids and 1,2-diamines. Although this reaction has been reported before,¹ only a few examples have been described in recent years. Anderson et al. have reported that alkyl nitronate anions can be added to a *N*-(4-methoxybenzyl) imine (PMB imine) in the presence of a Brønsted acid,² or a stoichiometric amount of a Lewis acid.³ In addition, they also reported the addition reaction of 1-trimethylsilyl nitropropanate with *N*-(4-methoxybenzyl) imine (PMB imine) catalyzed by scandium triflate (4 mol%).³ However, as for the typical catalytic version of the nitro-Mannich reaction (direct addition of nitromethane to an imine), there are no reports so far except the work by Shibasaki et al., who reported the first catalytic asymmetric nitro-Mannich type reaction of *N*-phosphinylimines with nitromethane promoted by a heterobimetallic complex (20 mol%).⁴ Herein, we report the first examples of catalytic nitro-Mannich reactions of a sulfonylimine with nitromethane catalyzed by lanthanide alkoxides.

In our initial study of the nitro-Mannich reaction of a sulfonylimine with nitromethane (Eq. (1)) neither KOⁱPr nor a single Lewis acid such as Y(OTf)₃ or Ti(OⁱPr)₄ was found to promote the addition of nitromethane to sulfonylimines. However, the addition

product could be obtained in 33% yield if a mixture of 1.1 equiv. KOⁱPr and 0.1 equiv. Y(OTf)₃ was used (Table 1).



The choice of base is crucial for the Henry reaction.⁵ 1,2-Nitroamines are prone to retroaddition⁶ and in the Henry reaction, the 2-nitroalkanol formed may undergo base-catalyzed elimination of water to give nitroalkenes, which can easily undergo polymerization.⁷ Rare earth metal alkoxides exhibit some basic character, and have been applied in the catalytic C–C bond forming nitroaldol reactions.⁸ Therefore, we proposed that these rare earth alkoxides could also serve as the

Table 1. Nitro-Mannich reactions of sulfonylimine **1a** catalyzed by Lewis acids

Entry	Cat. (10 mol%)	Base (1.1 equiv.)	Yield (%)
1	Ti(O ⁱ Pr) ₄	None	–
2	Y(OTf) ₃	None	–
3	None	K(O ⁱ Pr)	–
4	Ti(O ⁱ Pr) ₄	K(O ⁱ Pr)	34
5	Y(OTf) ₃	K(O ⁱ Pr)	33

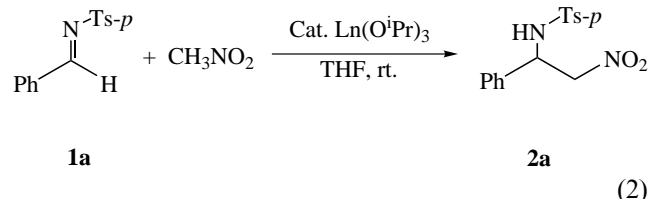
Keywords: catalytic nitro-Mannich reaction; rare earth metal alkoxides; sulfonylimine.

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Table 2. Effect of different kinds and amounts of catalyst on the reaction

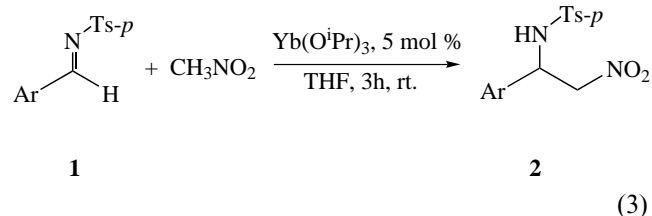
Entry	Ln(O ⁱ Pr) ₃	Cat. (mol%)	Time (h)	<i>r</i> _m ³⁺ (Å)	Yield (%)
1	Sc	20	5	0.810	83
2	La	20	5	1.061	60
3	Gd	20	5	0.938	68
4	Yb	20	1.5	0.858	98
5	Yb	10	3	0.858	100
6	Yb	5	5	0.858	100
7	Yb	1	5	0.858	95

proper catalysts for this nitro-Mannich reaction (Eq. (2)).



At first, several representative alkoxides were screened using the following conditions:⁹ imine (1 mmol) and alkoxide (20 mol%) were stirred for 10 min in 5 ml of THF at room temperature under Ar, then nitromethane (5 mmol) was syringed into the mixture. The results are summarized in Table 2. The radius of the rare earth metal ion strongly affected the reaction. In general, the acidity of rare earth metals depends on their ionic radius. The activity of the catalyst was improved with decreasing radius of the lanthanide metal (Table 2, entries 2–4). Among all of the lanthanide alkoxides screened, Yb gave the best results, which were similar to the results obtained in the addition reaction of *N*-phosphinoylimine.⁴ In addition, the amount of Yb(OⁱPr)₃ catalyst was examined: even with 1 mol% Yb(OⁱPr)₃, the product would be isolated in 95% yield within 5 h (Table 2, entry 7).

Several examples of the nitro-Mannich reaction with various sulfonylimines are listed in Table 3. In all cases, the reactions proceeded smoothly to give the corresponding addition products in excellent yields in the presence of a catalytic amount of Yb(OⁱPr)₃ (5 mol%) under extremely mild reaction conditions (Eq. (3)).



In conclusion, Yb(OⁱPr)₃ was found to be an excellent and practical catalyst for the nitro-Mannich reaction of sulfonylimines. The corresponding adducts of sulfonylimines with nitromethane can be isolated in excellent yields under extremely mild reaction conditions with 5 mol% Yb(OⁱPr)₃. Further work on the lanthanide alkoxides catalytic activity in organic synthesis is underway in our laboratory.

Table 3. Nitro-Mannich reaction of sulfonylimines catalyzed by Yb(OⁱPr)₃ (5 mol%)

Entry	Sulfonylimine	Adduct	Yield (%)
1	1a , C ₆ H ₅	2a , C ₆ H ₅	100
2	1b , 2-MeOC ₆ H ₄	2b , 2-MeOC ₆ H ₄	95
3	1c , 4-MeOC ₆ H ₄	2c , 4-MeOC ₆ H ₄	95
4	1d , 4-MeC ₆ H ₄	2d , 4-MeC ₆ H ₄	91
5	1e , 1-C ₁₀ H ₇	2e , 1-C ₁₀ H ₇	81
6	1f , 4-ClC ₆ H ₄	2f , 4-ClC ₆ H ₄	92
7	1g , 4-NO ₂ C ₆ H ₄	2g , 4-NO ₂ C ₆ H ₄	92

Acknowledgements

Financial support from the National Natural Sciences Foundation of China and the State Key Project of Basic Research (Project 973, No. G2000048007) is gratefully acknowledged.

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- Experimental section: Under an argon atmosphere, **1a** (130 mg, 0.5 mmol) and Yb(OⁱPr)₃ (0.5 ml, 0.5 M in THF) were dissolved in 2 ml THF and stirred for 20 min at room temperature. Then CH₃NO₂ (0.12 ml, 2.5 mmol) was added to the solution and stirred for 5 h at room temperature. The resultant mixture was quenched with five drops of water, dried with MgSO₄. The organic solvent was evaporated, and purified by column chromatography on silica gel (petroleum ether:ethyl acetate, 3:1) to afford **2a**.

(157 mg, 98%) as an off-white solid. Mp 155–157°C; ^1H NMR (300 MHz, CDCl_3 , 25°C, TMS): δ = 7.65 (d, J = 8.3 Hz, 2H), 7.27–7.24 (m, 5H), 7.10 (d, J = 8.3 Hz, 2H), 5.50 (d, J = 7.57 Hz, 1H), 4.99 (m, 1H), 4.84 (dd, J = 13.08, 6.64 Hz, 1H), 4.66 (dd, J = 13.07, 6.34 Hz, 1H), 2.40 (s, 3H); IR

(KBr): ν = 3426, 1550, 1380, 1167 cm^{-1} ; ESI-MS ($\text{CH}_3\text{OH}-\text{H}_2\text{O}$): m/z (%): 338.1 ($\text{M}+\text{H}_2\text{O}^+$, 100), 260.0 (4.9); MS: m/z (%): 274 (0.7), 260 (14), 91 (100); anal. calcd for $\text{C}_{15}\text{H}_{16}\text{N}_2\text{O}_4\text{S}$: C, 56.24; H, 5.03; N, 8.74; S, 10.00. Found: C, 56.50; H, 4.95; N, 8.82; S, 10.15.