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The effect of coordination on the reaction of *N*-tosyl imines with diethylzinc

Feifeng Gao, Minzhi Deng and Changtao Qian*

State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Road, Shanghai 200032, China

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Abstract—The effect of coordination on the reaction of *N*-tosyl imines and diethylzinc was studied in detail. It showed that there was strong coordination between *N*-tosyl imine and diethylzinc. Due to this coordination, *N*-tosyl imines could be reduced directly through the β-H transferring mechanism by diethylzinc in nonpolar solvents to afford the corresponding secondary amines in excellent yields at mild conditions. The coordination of diethylzinc and *N*-tosyl imine was hindered by reacting in polar solvents or adding TMEDA to the reaction, it afforded ethylating product partially or exclusively.

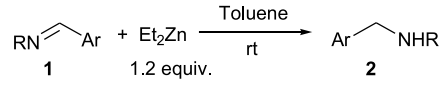
1. Introduction

The reduction of imines to amines is an important transformation in organic chemistry. Most of the methods involve borohydride reagents or transition metal hydrogenation catalysts;[1] Few general methods employing main group Lewis acid catalysts have appeared.[2] Imines also could be reduced by Grignard reagents bearing β-H. Thies et al. have observed that *N*-benzylidene-*N*-butylimine could be partially reduced to amines by *i*-PrMgI during the addition reaction.[3] Davis et al. have also found that *N*-sulfinylimine could be slightly reduced to amines by *n*-BuMgCl during the addition reaction.[4] Crowe et al. have even reported that, in the presence of a catalytic amount of Cp_2TiCl_2, *n*-BuMgCl could be used as the reductive reagent in the reduction of imine.[5]

Diethylzinc has been widely applied in organic synthesis, such as addition to aldehydes,[6] ketones[7] and imines,[1a] radical addition as chain-transfer agent[2b,8] and catalytic enantioselective reduction of ketones as the precatalyst.[9]

Though diethylzinc could reduce benzaldehyde to afford benzyl alcohol as the byproduct in the addition reaction to benzaldehyde,[10] there are also a few reports about the reduction of imines by diethylzinc during the enantioselective addition to the imines.[11]

Table 1. Reduction of imines by diethylzinc in toluene



Entry	Ar	R	Time (h)	Yield[a] of **2** (%)
1	**1a**, Ph	Ts	1	**2a**, 98
2	**1b**, 4-$MeOC_6H_4$		1	**2b**, 96
3	**1c**, 2-$MeOC_6H_4$		1	**2c**, quant.
4	**1d**, 4-MeC_6H_4		2	**2d**, 71
5	**1e**, 4-ClC_6H_4		1	**2e**, 98
6	**1f**, 1-$C_{10}H_7$		5	**2f**, 70
7	**1g**, Ph	Ms	1	**2g**, 86
8	**1h**, Ph	$P(O)Ph_2$	24	—
9	**1i**, Ph	Ph	24	—
10	**1j**, Ph	2-$MeOC_6H_4$	24	—

[a] Isolated yield.

Various imines were allowed to react with diethylzinc in toluene at rt, the results were summarized in Table 1. All *N*-tosyl imines afforded the corresponding reduction products with good to excellent yields exclusively (entry 1–7, Table 1) while there was no reductive or addition reaction product under the same conditions in the case of *N*-aryl aldimines and *N*-phosphinylimine (entry 8–10, Table 1). For *N*-phosphinylimine had the similar structure to *N*-tosyl imine, it was possible due to the bond length differences between *N*-tosyl-imine and *N*-phosphinylimine.

The effect of solvents on the reaction of *N*-tosyl imine and diethylzinc was studied. The results were shown in Table 2. It turned out that solvents had strong effect on the reaction.

Keywords: *N*-Tosyl imines; Diethylzinc; Reduction; Ethylation; Solvent effect; Coordination.
* Corresponding author. Tel.: +86 21 54925030; fax: +86 21 64166148; e-mail: qianct@mail.sioc.ac.cn

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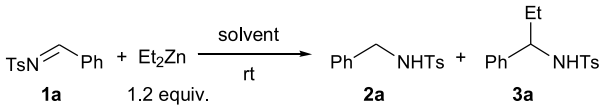
Table 2. Effect of the solvents



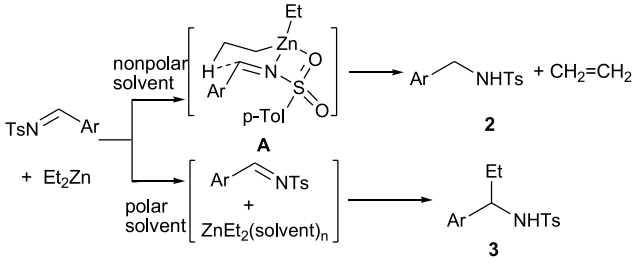
Entry	Solvent	Time (h)	**2a**[a] (%)	**3a**[a](%)
1	Hexane	3	92	—
2	Toluene	1	98	—
3	THF	6	27	40
4	Et_2O	6	65	14
5	CH_3CN	6	51	18
6	CH_2Cl_2	6	85	14

[a] Isolated yield.

It was found that *N*-tosyl imine **1a** could be readily reduced by diethylzinc at very mild conditions in nonpolar solvents (entry 1–2, Table 2). Though the *N*-tosyl imine **1a** and the corresponding reduction product **2a** were almost insoluble in hexane, the reduction reaction still proceeded smoothly (entry 1, Table 2). The reaction phenomenon in toluene was especially interesting. Those *N*-tosyl imines could not be dissolved in toluene completely under the reaction conditions (entry 1–7, Table 1). After diethylzinc was added into the mixture, the turbid mixture became clear. About 30 min later, white precipitates came out in company with a releasing gas which was trapped by liquid N_2 and proved to be ethylene by GC–MS.

But in polar solvents, ethylating product was also found in the reaction along with reduction product (entry 3–6, Table 2).

According to the reaction phenomenon and results, we proposed the reaction of *N*-tosyl imines and diethylzinc in different solvents may proceed as Scheme 1.

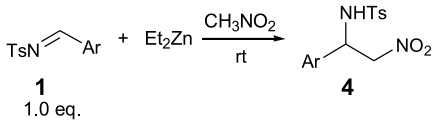


Scheme 1.

In nonpolar solvent diethylzinc and the *N*-tosyl imine brought out a zinc specie with the presumed structure **A**, then the β-hydrogen atom of the ethyl group was transferred to the C=N double bond with release of ethylene, therefore the reduction product **2** was formed. The product **2** was obtained exclusively in toluene and hexane.

On the contrary, the polar solvent such as THF, which could coordinate predominately with diethylzinc and activate diethylzinc in some extent, led to the addition reaction. As a result, the addition product **3** became the main product (entry 3, Table 2). When weaker coordination solvent such as Et_2O was used, it was still predominated by the reduction reaction was still the (entry 4, Table 2).

Table 3. Nitro-Mannich reaction in CH_3NO_2

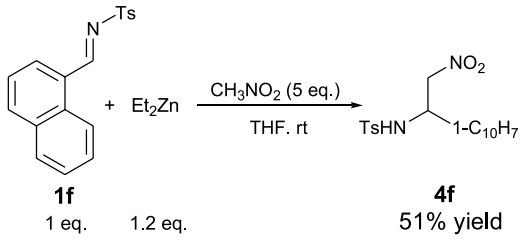


Entry	Ar	Amount of Et_2Zn (equiv)	Time (h)	Yield[a] of 4 (%)
1	**1a**, Ph	1.2	6	**4a**, 73
2		0.5	18	**4a**, 62
3		0.2	24	**4a**, 25
4	**1b**, 4-$MeOC_6H_4$	1.2	6	**4b**, 86
5	**1c**, 2-$MeOC_6H_4$		6	**4c**, 59
6	**1d**, 4-MeC_6H_4		6	**4d**, 79
7	**1e**, 4-ClC_6H_4		6	**4e**, 75
9	**1f**, 1-$C_{10}H_7$		12	**4f**, 50[b]

[a] Isolated yield.
[b] 47% Reduction product **2f** was isolated.

The coordination between *N*-tosyl imine and diethylzinc was shown more obviously in nitro-Mannich reaction when CH_3NO_2 was used as the reaction solvent (Table 3). In those reaction, it was found that dialkylzinc could only promote but not catalyze the nitro-Mannich reaction either in CH_3NO_2 (entry 1–3, Table 3) or in other solvents such as toluene, hexane, CH_2Cl_2, Et_2O and THF, while even Et_3N (20 mol%) could catalyze the nitro-Mannich reaction of *N*-tosyl imine with a yield of 74%.[12]

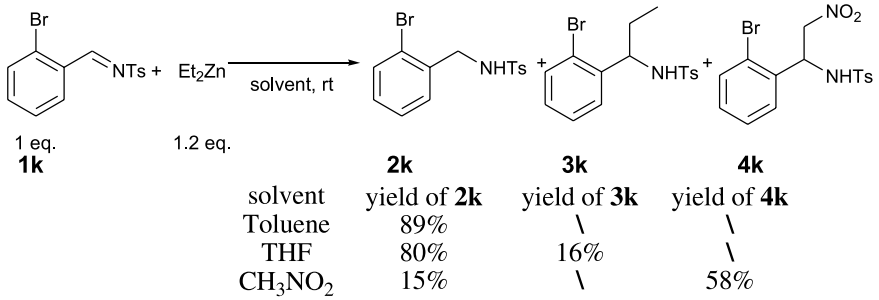
Interestingly, when imine **1f** and diethylzinc were reacted in CH_3NO_2, the product ratio between **4f** (nitro-Mannich adduct) and **2f** (reduction product) was almost 1:1 (entry 9, Table 3). We thought it might be caused by the steric effect, which suppressed the nitro-Mannich reaction. If a stronger coordination ligand was added to break the coordination between imine **1f** and diethylzinc, it would reduce the amount of reduction product. Indeed, when this reaction was taken place in THF, no reduction product was detected other than 51% nitro-Mannich addition product **4f** (Scheme 2). These were all in accordance with the β-H transferring mechanism also.



Scheme 2.

This could be confirmed by the results of another steric hindered imine **1k** (Scheme 3). Similar to the imine **1f**, it took much longer time, 12 h, for imine **1k** to be reduced in toluene than other imines **1a**–**1e** and the reduction product **2k** was also isolated with 15% yield when imine **1k** and diethylzinc was reacted in CH_3NO_2. Unlike imine **1a**, the reduction product **2k** was the major one when it was reacted in THF.

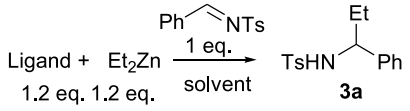
The coordination effects could be proven by following experiments more clearly. Diethylzinc with an equiv of

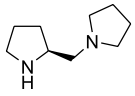


solvent	yield of **2k**	yield of **3k**	yield of **4k**
Toluene	89%	\	\
THF	80%	16%	\
CH_3NO_2	15%	\	58%

Scheme 3.

TMEDA (tetramethyl ethylene diamine) or (*S*)-1,2′-methylenedipyrrolidine, which could prevent the coordination of diethylzinc with *N*-tosyl imine, were stirred for 30 min at rt, and then 1 equiv of *N*-tosyl imine was added to the reaction mixture. It was found all gave ethylating product in good yield without detection of the reduction product in NMR whether in THF or toluene. In the case of the chiral ligand (*S*)-1,2′-methylenedipyrrolidine, it gave 98% yield with 77% ee in toluene (Scheme 4).



Solvent	Ligand	Temp.	Yield(%)
THF	Me_2N ⟋⟍ NMe_2	rt	69
Toluene	Me_2N ⟋⟍ NMe_2	rt	83
Toluene		-78°	98(77%ee)

Scheme 4.

In conclusion, we studied the effect of solvents on the reaction of *N*-tosyl imines and diethylzinc in detail and found there was strong coordination between *N*-tosyl imine and diethylzinc. The *N*-tosyl imines were reduced directly by diethylzinc in nonpolar solvents to give corresponding secondary amines in good to excellent yields through the β-H transferring mechanism. The coordination of diethylzinc and *N*-tosyl imine was hindered by using the polar solvents or addition of TMEDA or (*S*)-1,2′-methylenedipyrrolidine to the reaction, it afforded ethylating product partially or exclusively. This coordination could be used in the further study.

2. Experimental

2.1. General

All reactions were performed under a nitrogen atmosphere using oven-dried glassware. Unless otherwise stated, all reagents were employed as received. Solvents were distilled on CaH_2 or Na/benzophenon. NMR spectrums were made on BRUCKER AMX-300 for proton. IR spectra were obtained on a Shimadzu IR-440 infrared spectrophotometer. Mass spectra were determined on a Finnigan 8230 mass spectrometer. Elemental analyses were performed on a Foss-Heraeus Vario EL instrument.

2.1.1. General procedure (for reduction of Imine 1a–1k by diethylzinc). Under N_2 atmosphere, imine **1a** (260 mg, 1 mmol) was dissolved in 5 mL toluene at rt. Diethylzinc (1.2 mL, 1 M in hexane) was syringed into the solution. The turbid mixture soon became clear in 5 min. After about 30 min, white precipitates came out while bubbling. When no gas was released, the reaction was treated with 1 M HCl, 15 mL ethyl acetate was added, washed with water and brine, dried over Na_2SO_4, evaporated in vacuum to give a white solid **2a**, *N*-Benzyl-4-methylbenzenesulfonamide (254 mg, 98% yield), no need for further purification. Mp 111.1 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ=7.69 (d, J=8.25 Hz, 2H), 7.26–7.12 (m, 7H), 4.64 (t, J=6.1 Hz, 1H), 4.05 (d, J=6.1 Hz, 2H), 2.37 (s, 3H); IR (KBr): ν=3271, 1599, 1381, 1163 cm^{-1}; MS (*m*/*z*) 262, 135. Anal. Calcld for $C_{14}H_{15}NO_2S$: C: 64.34, H: 5.79, N: 5.38, S: 12.27. Found: C: 64.62, H: 5.78, N: 5.23, S: 12.42.

2.1.2. *N*-(4-Methoxybenzyl)-4-methylbenzenesulfonamide 2b. The product was obtained according to the general procedure, isolated as a white solid in quantitative yield. Mp 116.6 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ=7.76 (d, J=7.63 Hz, 2H), 7.31 (d, J=7.73 Hz, 2H), 7.10 (d, J=7.91 Hz, 2H), 6.80 (d, J=7.86 Hz, 2H), 4.63 (br s, 1H), 4.05 (d, J=3.34 Hz, 2H), 3.77 (s, 3H), 2.44 (s, 3H); IR (KBr): ν=3253, 1612, 1381, 1160 cm^{-1}; MS (*m*/*z*) 291, 135. Anal. Calcld for $C_{15}H_{17}NO_3S$: C: 61.83, H: 5.88, N: 4.81, S: 11.01. Found: C: 61.57, H: 5.76, N: 4.81, S: 11.29.

2.1.3. *N*-(2-Methoxybenzyl)-4-methylbenzenesulfonamide 2c. The product was obtained according to the general procedure, purified by silica gel chromatography (petroleum ether/acetate ethyl=5:1) and isolated as a pale oil in 96% yield; ^{1}H NMR (300 MHz,$CDCl_3$, 25 °C, TMS): δ=7.58 (d, J=8.20 Hz, 2H), 7.12–7.09 (m, 3H), 6.98 (t, J=7.4 Hz, 1H), 6.72 (t, J=7.4 Hz, 1H), 6.64 (d, J=8.2 Hz, 1H), 5.13 (t, J=6.4 Hz, 1H), 4.05 (d, J=6.4 Hz, 2H), 3.64 (s, 3H), 2.37 (s, 3H); IR (KBr): ν=3362, 1599, 1381, 1162 cm^{-1}; MS (*m*/*z*) 291, 136; HRMS: Calcld for $C_{15}H_{17}NO_3S$: 291.0929, found: 291.0956.

2.1.4. 4-Methyl-*N*-(4-methylbenzyl)benzenesulfonamide 2d. The product was obtained according to the general

procedure, purified by silica gel chromatography (petroleum ether/acetate ethyl=5:1) and isolated as a white solid in 71% yield. Mp 86.7 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ=7.76 (d, J=8.23 Hz, 2H), 7.30 (d, J=8.10 Hz, 2H), 7.08 (s, 4H), 4.69 (t, J=5.93 Hz, 1H), 4.07 (d, J=5.93 Hz, 2H), 2.44 (s, 3H), 2.33 (s, 3H); IR (KBr): ν=3250, 1598, 1378, 1167 cm^{-1}; MS (*m/z*) 274, 120. Anal. Calcld for $C_{15}H_{17}NO_2S$: C: 65.45, H: 6.18, N: 5.09, S: 11.64. Found: C: 65.27, H: 6.17, N: 5.22, S: 11.38.

2.1.5. *N*-(4-Chlorobenzyl)-4-methylbenzenesulfonamide 2e. The product was obtained according to the general procedure, purified by silica gel chromatography (petroleum ether/acetate ethyl=5:1) and isolated as a white solid in 70% yield. Mp 101.6 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ=7.71 (d, J=8.3 Hz, 2H), 7.27 (d, J=8.10 Hz, 2H), 7.21 (d, J=8.5 Hz, 2H), 7.12 (d, J=8.4 Hz, 2H), 5.17 (t, J=6.2 Hz, 1H), 4.07 (d, J=6.4 Hz, 2H),2.43 (s, 3H); IR (KBr): ν=3330, 1597, 1392, 1157 cm^{-1}; MS (*m/z*) 296, 140. Anal. Calcld for $C_{14}H_{14}ClNO_2S$: C: 56.85, H: 4.47, N: 4.74, S: 10.84. Found: C: 56.95, H: 4.61, N: 4.61, S: 11.12.

2.1.6. 4-Methyl-*N*-(naphthalen-1-ylmethyl)benzenesulfonamide 2f. The product was obtained according to the general procedure, isolated as a white solid in 98% yield. Mp 151.9 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ=7.81–7.61 (m, 5H), 7.40–7.39 (m, 2H), 7.24–7.17 (m, 4H), 4.61 (t, J=5.7 Hz, 1H), 4.46 (d, J=5.7 Hz, 2H), 2.35 (s, 3H); IR (KBr): ν=3330, 1597, 1392, 1157 cm^{-1}; MS (*m/z*) 311, 154. Anal. Calcld for $C_{18}H_{17}NO_2S$: C: 69.43, H: 5.50, N: 4.50, S: 10.30. Found: C: 69.38, H: 5.50, N: 4.37, S: 10.35.

2.1.7. *N*-(2-Bromobenzyl)-4-methylbenzenesulfonamide 2k. The product was obtained according to the general procedure, purified by silica gel chromatography (petroleum ether/acetate ethyl=5:1) and isolated as a white solid in 70% yield. Mp 73.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ=7.71 (d, J=8.1 Hz, 2H), 7.46 (d, J=7.8 Hz, 1H), 7.32–7.08 (m, 6H), 4.97 (t, J=6.3 Hz, 1H), 4.23 (d, J=6.3 Hz, 2H), 2.41 (s, 3H); IR (KBr): ν=3258, 1597, 1438,1392, 1155 cm^{-1}; MS (*m/z*) 342, 340, 260, 184. Anal. Calcld for $C_{14}H_{14}BrNO_2S$: C: 49.42, H: 4.15, N: 4.12. Found: C: 49.32, H: 4.07, N: 3.96.

2.2. General procedure (for reaction between diethylzinc and *N*-tosyl imine 1a and 1k in THF)

Under N_2 atmosphere, imine **1a** (1 mmol) was dissolved in 5 mL THF at rt. Diethylzinc (1.2 mL, 1 M in hexane) was syringed into the mixture. After about 6 h, the reaction was treated with 1 M HCl, 30 mL ethyl acetate was added, washed with water and brine, dried over Na_2SO_4, evaporated in vacuum and purified by silica gel chromatography.

2.2.1. 4-Methyl-*N*-(1-phenylpropyl)benzenesulfonamide 3a. The product was obtained according to the general procedure, purified by silica gel chromatography(petroleum ether/acetate ethyl=5:1) and isolated as a white solid **3a** in 40% yield along with **2a** in 27% yield. Mp 109–110 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ=7.54 (d, J=8.33 Hz, 2H), 7.32–6.99 (m,7H), 5.09 (d, J=7.29 Hz, 1H), 4.22–4.15 (m, 1H), 2.35 (s, 3H), 1.86–1.64 (m, 2H), 0.78 (t, J=7.39 Hz, 3H); IR (KBr): ν=3059, 1598, 1368, 1130 cm^{-1}; MS (*m/z*) 289, 260, 91. Anal. Calcld for $C_{16}H_{19}NO_2S$: C: 66.40, H: 6.62, N: 4.84, S: 11.08. Found: C: 66.46, H: 6.64, N: 4.68, S: 11.26.

2.2.2. *N*-(1-(2-Bromophenyl)propyl)-4-methylbenzenesulfonamide 3k. According to the general procedure, purified by silica gel chromatography(petroleum ether/acetate ethyl=5:1) and isolated a mixture of **3k** in 16% yield and **2k** in 80% yield which were hard to separate. The pure **3k** was obtained by following: Diethylzinc (1.2 mL, 1 M in hexane) and TMEDA were stirred in THF at rt for 1 h. Imine **1k**(1 mmol) was added into the reaction mixture. After 10 h, the reaction was treated with 1 M HCl, 30 mL ethyl acetate was added, washed with water and brine, dried over Na_2SO_4, evaporated in vacuum and purified by silica gel chromatography(petroleum ether/acetone=6:1) to a white solid **3k** in 89% yield. Mp 131.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ=7.63–7.61 (m, 2H), 7.36–7.32 (m, 1H), 7.18–6.93 (m, 5H), 5.93 (d, J=7.8 Hz, 1H), 4.70 (d, J=7.2 Hz, 1H), 2.32 (s, 3H), 1.76–1.66 (m, 2H), 0.84 (t, J=7.5 Hz, 3H); IR (KBr): ν=3273, 1438, 1335, 1159 cm^{-1}; MS (*m/z*) 370, 368, 155. Anal. Calcld for $C_{16}H_{18}BrNO_2S$: C: 52.18, H: 4.93, N: 3.80. Found: C: 52.29, H: 5.11, N: 3.76.

2.3. General procedure (for Nitro-Mannich reaction of Imine 1a–1k in CH_3NO_2)

Under N_2 atmosphere, imine **1** (1 mmol) was dissolved in 5 mL CH_3NO_2 at rt. Diethylzinc (1.2 mL, 1 M in hexane) was syringed into the mixture solution. After about 24 h, the reaction was treated with 1 M HCl, 20 mL ethyl acetate was added, washed with water and brine, dried over Na_2SO_4, evaporated in vacuum and purified by silica gel chromatography.

2.3.1. 4-Methyl-*N*-(2-nitro-1-phenylethyl)benzenesulfonamide 4a. The product was obtained according to the general procedure, purified by silica gel chromatography (petroleum ether/acetone=4:1) and isolated as a white solid in 70% yield. Mp 155–157 °C; ^{1}H 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), 5.03–4.96 (m, 1H), 4.84 (d-d, J=13.08, 6.64 Hz, 1H), 4.66 (d-d, J=13.07, 6.34 Hz, 1H), 2.40 (s, 3H); IR (KBr): ν=3426, 1550, 1380, 1167 cm^{-1}; MS (*m/z*) 274, 260, 91. Anal. Calcld for $C_{15}H_{16}N_2O_4S$: 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.

2.3.2. *N*-(1-(4-Methoxyphenyl)-2-nitroethyl)-4-methylbenzenesulfonamide 4b. The product was obtained according to the general procedure, purified by silica gel chromatography (petroleum ether/acetone=4:1) and isolated as a white solid in 86% yield. Mp 142.4 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ=7.64 (d, J=8.2 Hz, 2H), 7.24 (d, J=8.0 Hz, 2H), 7.00 (d, J=8.62 Hz, 2H), 6.76 (d, J=8.62 Hz, 2H), 5.43 (d, J=6.92 Hz, 1H), 4.93–4.89 (m, 1H), 4.83 (d-d, J=12.83, 6.67 Hz, 1H), 4.64 (d-d, J=12.71, 6.57 Hz, 1H), 3.76 (s, 3H), 2.41 (s, 3H); IR (KBr): ν=3255, 1615, 1380, 1163 cm^{-1}; MS (*m/z*) 350, 91. Anal.

Calcld for $C_{16}H_{18}N_2O_5S$: C: 54.85, H: 5.18, N: 7.99, S: 9.15. Found: C: 54.88, H: 5.31, N: 7.89, S: 9.29.

2.3.3. *N*-(1-(2-Methoxyphenyl)-2-nitroethyl)-4-methylbenzenesulfonamide 4c. The product was obtained according to the general procedure, purified by silica gel chromatography (petroleum ether/acetone=4:1) and isolated as a white solid in 59% yield. Mp 142.4 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ=7.56 (d, J=8.3 Hz, 2H), 7.21–7.16 (m, 1H), 7.10 (d, J=8.0 Hz, 2H), 6.95–6.93 (m, 1H), 6.78–6.72 (m, 2H), 6.00 (br s, 1H), 5.1 (br s, 1H), 4.81 (d-d, J=12.60, 7.5 Hz, 1H), 4.64 (d-d, J=12.60, 6.70 Hz, 1H), 3.80 (s, 3H), 2.33 (s, 3H); IR (KBr): ν=3289, 1601, 1368, 1159 cm^{-1}; MS (*m*/*z*) 354, 91. Anal. Calcld for $C_{16}H_{18}N_2O_5S$: C: 54.85, H: 5.18, N: 7.99, S: 9.15. Found: C: 54.99, H: 5.02, N: 8.12, S: 9.44.

2.3.4. 4-Methyl-*N*-(2-nitro-1-p-tolylethyl)benzenesulfonamide 4d. The product was obtained according to the general procedure, purified by silica gel chromatography (petroleum ether/acetone=4:1) and isolated as a white solid in 79% yield. Mp 192.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ=7.67 (d, J=8.2 Hz, 2H), 7.26 (d, J=8.0 Hz, 2H), 7.01 (d, J=7.9 Hz, 2H), 6.98 (d, J=6.9 Hz, 2H), 5.24 (d, J=7.1 Hz, 1H), 4.92 (q, J=6.7 Hz, 1H), 4.84 (d-d, J=13.0, 6.4 Hz, 1H), 4.67 (d-d, J=12.9, 6.7 Hz, 1H), 2.41 (s, 3H), 2.39 (s, 3H); IR (KBr): ν=3248, 1552, 1378, 1167 cm^{-1}; MS (*m*/*z*) 335, 91. Anal. Calcld for $C_{16}H_{18}N_2O_4S$: C: 57.47, H: 5.43, N: 8.38, S: 9.59. Found: C: 57.49, H: 5.50, N: 8.33, S: 9.36.

2.3.5. *N*-(1-(4-Chlorophenyl)-2-nitroethyl)-4-methylbenzenesulfonamide 4e. The product was obtained according to the general procedure, purified by silica gel chromatography (petroleum ether/acetone=4:1) and isolated as a white solid in 75% yield. Mp 193.8 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ=7.41 (d, J=8.1 Hz, 2H), 7.16–7.08 (m, 6H), 5.04–4.99 (m, 1H), 4.68 (d, J=7.5 Hz, 2H), 2.34 (s, 3H); IR (KBr): ν=3242, 1599, 1380, 1168 cm^{-1}; MS (*m*/*z*) 355, 91. Anal. Calcld for $C_{15}H_{15}ClN_2O_4S$: C: 50.85, H: 4.26, N: 7.90, S: 9.04. Found: C: 51.04, H: 4.12, N: 7.97, S: 9.33.

2.3.6. 4-Methyl-*N*-(1-(naphthalen-1-yl)-2-nitroethyl)benzenesulfonamide 4f. The product was obtained according to the general procedure, purified by silica gel chromatography (petroleum ether/acetone=4:1) and isolated as a white solid in 50% yield along with **2f** in 47% yield. Mp 164.6 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ=7.84–7.74 (m, 3H), 7.57–7.26 (m, 6H), 7.08 (d, J=7.99 Hz, 2H), 5.88–5.86 (m, 1H), 5.74 (d, J=7.28 Hz, 1H), 4.99 (d-d, J=13.14, 7.35 Hz, 1H), 4.64 (d-d, J=13.14, 5.94 Hz, 1H), 2.33 (s, 3H); IR (KBr): ν=3359, 1597, 1402, 1157 cm^{-1}; MS (*m*/*z*) 350, 154. Anal. Calcld for $C_{19}H_{18}N_2O_4S$: C: 61.61 H: 4.90, N: 7.56, S: 8.65. Found: C: 61.62, H: 4.92, N: 7.47, S: 8.75.

2.3.7. *N*-(1-(2-Bromophenyl)-2-nitroethyl)-4-methylbenzenesulfonamide 4k. The product was obtained according to the general procedure, purified by silica gel chromatography (petroleum ether/acetone=4:1) and isolated as a white solid in 58% yield along with **2k** in 15% yield. Mp 137.7 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ=7.61 (d, J=7.8 Hz, 2H), 7.44 (d, J=7.8 Hz, 1H), 7.26–7.06 (m, 5H), 6.21 (d, J=8.7 Hz, 1H), 5.52–5.45 (m, 1H), 4.78–4.64 (m, 2H), 2.35 (s, 3H); IR (KBr): ν=3244, 1554, 1341, 1158 cm^{-1}; MS (*m*/*z*) 340, 338, 319, 91. Anal. Calcld for $C_{15}H_{15}BrN_2O_4S$: C: 45.12 H: 3.79, N: 7.02. Found: C: 45.01, H: 3.95, N: 7.04.

2.4. General procedure (for nitro-Mannich reaction of Imine 1f in THF)

Under N_2 atmosphere, imine **1a** (1 mmol) was dissolved in 5 mL THF and 5 equiv CH_3NO_2 at rt for 10 min. Diethylzinc (1.2 mL, 1 M in hexane) was syringed into the solution. After about 12 h, the reaction mixture was treated with 1 M HCl, 30 mL of ethyl acetate was added, washed with water and brine, dried over Na_2SO_4, evaporated in vacuum and purified by silica gel chromatography (petroleum ether/acetone=4:1) and **4f** was isolated as a white solid **4f** in 51% yield.

Procedure (for the ethylating reaction of imine **1a** *with TMEDA (Scheme 4))*. Diethylzinc (1.2 mL, 1 M in hexane) and TMEDA were stirred in THF at rt for 1 h. Imine **1a** (1 mmol) was added. After 10 h, the reaction was treated with 1 M HCl, 30 mL of ethyl acetate was added, washed with water and brine, dried over Na_2SO_4, evaporated in vacuum and purified by silica gel chromatography(petroleum ether/acetate ethyl=5:1) to give **3a** as a white solid in 69% yield.

Procedure (for the ethylating reaction of Imine **1a** *with (S)-1,2′-methylenedipyrrolidine (Scheme 4))*. Diethylzinc (1.2 mL, 1 M in hexane) and (*S*)-1,2′-methylenedipyrrolidine were stirred in toluene at −78 °C for 1 h. Imine **1a** (1 mmol) was added. After 10 h, the reaction was treated with 1 M HCl, 30 mL of ethyl acetate was added, washed with water and brine, dried over Na_2SO_4, evaporated in vacuum and purified by silica gel chromatography (petroleum ether/acetate ethyl=5:1) to afford an optical **3a** in 98% yield and 77% ee (determined by HPLC analysis on a chiralcel OD column with ^{i}PrOH/hexane=20/80 as the eluent).

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