Supporting Information

Selective Diethylzinc Reduction of Imines in the Presence of Ketones Catalyzed by $Ni(acac)_2$

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Contents of Supporting Information

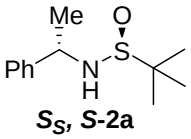
General methods.

All reagents were purchased from commercial suppliers and used without further purification. Solvents were dried according to standard procedures. The dr value of the reduction products were determined by HPLC and ^{1}H NMR. Chromatography refers to flash chromatography on silica gel (300–400 mesh). Thin-layer chromatography (TLC) was performed on glass plates silica gel sheets (SilicaGel F254) and visualised under UV light or colored in I_2.

tert-Butanesulfinyl ketimines **1** were prepared according to the literature procedure[1]

General procedure for the reduction of imines 1 by Et_2Zn and $Ni(acac)_2$.

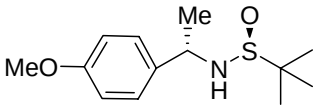
Under N_2, to a 5 mL solution of imine 1 (0.5 mmol) in dioxane was injected diethylzinc (1.5 mmol, 1.1 M in toluene), followed by adding a solution of $Ni(acac)_2$ (0.025 mmol) in 0.5 ml dioxane. The mixture was stirred at room temperature for a certain time indicated in Table 1, Table 2 and Table 3 and was monitored by thin-layer chromatography. The reaction mixture was quenched by adding saturated aq. NH_4Cl (10 mL). The aqueous layer was extracted twice with CH_2Cl_2 (3 X 10 mL). The combined organic layers were dried over Na_2SO_4. After removing the solvent, the residue was directly subjected to HPLC or ^{1}H NMR analysis to determine the dr value. The residue was then purified by column chromatography to afford sulfonamide **2**. The chromatography fractions containing major isomer were collected and used to measure the rotation after removing the *tert*-butanesulfinyl group by 6 N HCl. The absolute configuration of major isomer of resulting amine was determined by comparison of its rotation with the data of known amine.



***S*$_S$, *S*-2a**

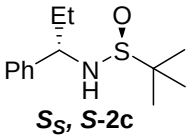
(*Ss*, *S*)-*N*-(*tert*-Butanesulfinyl) 1-phenylethylamine 2a.[2] Purified by flash chromatography on silica gel (ethyl acetate/petroleum 1:4). Colorless oil. The

diastereomeric ratio was determined by HPLC analysis (DIKAMA Inertsil SIL-100A column; 90:10 hexanes/IPA, 0.8 ml/min, 227 nm; t_R = 7.6 min (major), 9.5 min (minor)). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.24 (s, 9H), 1.51 (d, *J* = 8 Hz, 3H), 3.42 (b, 1H), 4.52-4.58 (m, 1H), 7.25-7.33 (m, 5H) ppm. The chromatography fractions containing major isomer were collected and used to measure the rotation after removing the *tert*-butanesulfinyl group. (*S*)-1-Phenylethylamine hydrochloride $[\alpha]_D^{23}$ -3.0°(c 2.8, MeOH) (lit.[7] $[\alpha]_D^{23}$ -4.6°(c 4.0, MeOH)).



***S*$_S$, *S*-2b**

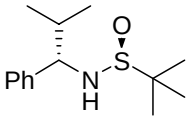
(*Ss*, *S*)-*N*-(*tert*-butanesulfinyl) 1-(4'-methoxyphenyl)ethylamine 2b. Purified by flash chromatography on silica gel (ethyl acetate/petroleum 1:4). Colorless oil. The diastereomeric ratio was determined by HPLC analysis (DIKAMA Inertsil SIL-100A column; 93:7 hexanes/IPA, 0.8 ml/min, 227 nm; t_R = 12.0 min (major), 14.5 min (minor)). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.23 (s, 9H), 1.48 (d, *J* = 6.4 Hz, 3H), 3.37 (d, *J* = 1.6 Hz, 1H), 3.8 (s, 3H), 4.50-4.52 (m, 1H), 6.86-6.90 (m, 2H), 7.26-7.29 (m, 2H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.6, 22.8, 53.4, 55.3, 55.4, 114.1, 127.8, 136.3, 159.2 ppm; IR (film) 1039, 1247, 1513, 2968, 3217 cm^{-1}; HRMS: calcd for $C_{13}H_{21}NO_2SNa$ $(M+Na)^+$ 278.1185. Found 278.1177. The chromatography fractions containing major isomer were collected and used to measure the rotation after removing the *tert*-butanesulfinyl group. (*S*)-1-(4'-Methoxyphenyl)ethylamine $[\alpha]_D^{22}$ -32°(c 1.0, MeOH) (lit.[8] $[\alpha]_D^{22}$ -28°(c 3.2, MeOH)).



***S*$_S$, *S*-2c**

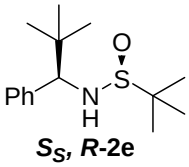
(*Ss*, *S*)-*N*-(*tert*-Butanesulfinyl) 1-phenylpropylamine 2c[2]. Purif Purified by flash chromatography on silica gel (ethyl acetate/petroleum 1:3). Colorless oil. The diastereomeric ratio was determined by HPLC analysis (DIKAMA Inertsil SIL-100A

column; 93:7 hexanes/IPA, 0.8 ml/min, 227 nm; t_R = 8.2 min (major), 10.1 min (minor)). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.80 (t, *J* = 7.6 Hz, 3H), 1.23 (s, 9H), 1.70-1.82 (m, 1H), 2.00-2.10 (m, 1H), 3.39 (br, 1H), 4.26-4.30 (m, 1H), 7.27-7.37 (m, 5H) ppm. The chromatography fractions containing major isomer were collected and used to measure the rotation after removing the *tert*-butanesulfinyl group. (*S*)-1-Phenylpropylamine $[\alpha]_D^{23}$ -14.9°(c 1.0, $CHCl_3$) (lit.[9] $[\alpha]_D^{23}$ -36.6°(c 1.0, $CHCl_3$)).



***S*$_S$, *S*-2d**

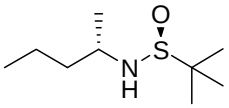
(*Ss*, *S*)-*N*-(*tert*-Butanesulfinyl) 2-methyl-1-phenylpropylamine 2d[2]. Purifi Purified by flash chromatography on silica gel (ethyl acetate/petroleum 1:4). White solid. The diastereomeric ratio was determined by ^{1}H NMR (δ 2.23 (major), 1.98 (minor)). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.80 (d, *J* = 6.8 Hz, 3H), 0.93 (d, *J* = 6.8 Hz, 3H), 1.25 (s, 9H), 2.19-2.27 (m, 1H), 3.45 (br, 1H), 4.17 (d, *J* = 5.4 Hz, 1H), 7.24-7.35 (m, 5H) ppm. The chromatography fractions containing major isomer were collected and used to measure the rotation after removing the *tert*-butanesulfinyl group. (*S*)-2-Methyl-1-phenylpropylamine $[\alpha]_D^{23}$ –10.8°(c 1.0, $CHCl_3$) (lit.[10] $[\alpha]_D^{23}$ -11.5°(c 1.0, $CHCl_3$)).



***S*$_S$, *R*-2e**

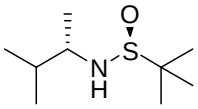
(*Ss*, *R*)-*N*-(*tert*-Butanesulfinyl) 2,2-dimethyl-1-phenylpropylamine 2e. Purified by flash chromatography on silica gel (ethyl acetate/petroleum 1:4). White solid. The diastereomeric ratio was determined by HPLC analysis (DIKAMA Inertsil SIL-100A column; 95:5 hexanes/IPA, 1 ml/min, 227 nm; t_R = 6.7 min (minor), 7.5 min (major)). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.95 (s, 9H), 1.21 (s, 9H), 3.60 (b, 1H), 4.14 (d, *J* = 2.0 Hz, 1H), 7.24-7.31 (m, 5H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 22.6, 26.7, 35.2, 55.5, 67.2, 127.5, 128.1, 129.5, 139.2 ppm; IR (KBr) 1067, 2956, 3338 cm^{-1}; HRMS: calcd

for $C_{15}H_{25}NOSNa$ $(M+Na)^+$ 290.1549. Found 290.1561. The chromatography fractions containing major isomer were collected and used to measure the rotation after removing the *tert*-butanesulfinyl group. (*R*)-2,2-Dimethyl-1-phenylpropylamine $[\alpha]_D^{23}$ +3.3°(c 1.0, $CHCl_3$) (lit.[10] $[\alpha]_D$ -5.5°(c 1.0, $CHCl_3$) for *S* configuration amine).



***S*S, *S*-2f**

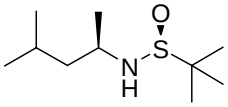
(*Ss*, *S*)-*N*-(*tert*-Butanesulfinyl) 1-methylbutylamine 2f. Purified by flash chromatography on silica gel (ethyl acetate/petroleum 1:2). Colorless oil. The diastereomeric ratio was determined by HPLC analysis (DIKAMA Inertsil SIL-100A column; 98:2 hexanes/IPA, 1.5 ml/min, 227 nm; t_R = 13.0 min (major), 15.7 min (minor)). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.93 (t, *J* = 7.2 Hz, 3H), 1.16 (d, *J* = 6.4 Hz, 3H), 1.20 (s, 9H), 1.33-1.46 (m, 2H), 1.51-1.60 (m, 2H), 3.04 (b, 1H), 3.34-3.42 (m ,1H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$) δ 13.6, 18.9, 21.3, 22.4, 40.5, 50.9, 55.1 ppm; IR (film) 1055, 1458, 2959, 3215 cm^{-1}; HRMS: calcd for $C_9H_{21}NOSNa$ $(M+Na)^+$ 214.1236. Found 214.1228. The chromatography fractions containing major isomer were collected and used to measure the rotation after removing the *tert*-butanesulfinyl group. (*S*)-1-Methylbutylamine hydrochloride $[\alpha]_D^{24}$ –1.8°(c 1.7, EtOH) (lit.[11] $[\alpha]_D^{24}$ +7.2°(c 2.3, EtOH) for *R* configuration amine hydrochloride).



***S*S, *S*-2g**

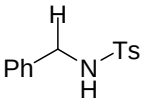
(*Ss*, *S*)-*N*-(*tert*-Butanesulfinyl) 1,2-dimethyl-propylamine 2g[2]. Purified by flash chromatography on silica gel (ethyl acetate/petroleum 1:2). Colorless oil. Crude The diastereomeric ratio was determined by ^{1}H NMR (δ 3.11 (major), 2.81 (minor)). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.92 (t, *J* = 6.8 Hz, 6H), 1.09 (d, *J* = 6.4 Hz, 3H), 1.21 (s, 9H), 1.73-1.79 (m, 1H), 3.11 (b, 1H), 3.25-3.30 (m, 1H) ppm. The chromatography fractions containing major isomer were collected and used to measure the rotation after

removing the *tert*-butanesulfinyl group. (*S*)-1,2-Dimethylpropylamine hydrochloride $[\alpha]_D^{23}$ -1.1°(c 1.2, MeOH) (lit.[12] $[\alpha]_D^{23}$ -2.16°(c 4.0, MeOH)).



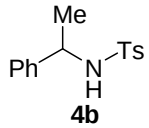
***S*$_S$, *R*-2h**

(*Ss*, *R*)-*N*-(*tert*-Butanesulfinyl) 1,3-dimethyl-butylamine 2h[3]. Purified by flash chromatography on silica gel (ethyl acetate/petroleum 1:2). White crystals. The diastereomeric ratio was determined by HPLC analysis (DIKAMA Inertsil SIL-100A column; 95:5 hexanes/IPA, 1 ml/min, 227 nm; t_R = 7.5 min (major), 8.7 min (minor)). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.91 (dd, *J* = 6.8, 8 Hz, 6H), 1.16 (d, *J* = 6.4 Hz, 3H), 1.20 (s, 9H), 1.27-1.35 (m, 1H), 1.41-1.48 (m, 1H), 1.67-1.74 (m, 1H), 3.01 (b, 1H), 3.38-3.50 (m, 1H) ppm. The chromatography fractions containing major isomer were collected and used to measure the rotation after removing the *tert*-butanesulfinyl group. (R)-1,3-Dimethylbutylamine hydrochloride $[\alpha]_D^{25}$ -3.5°(c 1.0, MeOH) (lit.[13] $[\alpha]_D^{25}$ +3.7°(c 1.0, MeOH) for *S* configuration amine hydrochloride).



4a

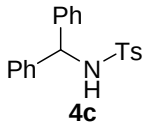
***N*-Ts Benzylamine 4a[4]**. Purified by flash chromatography on silica gel (ethyl acetate/petroleum 1:7). White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.44 (s, 3H), 4.12 (d, *J* = 6.4 Hz, 2H), 4.64 (s, 1H), 7.10-7.21 (m, 2H), 7.26-7.32 (m, 5H), 7.76 (d, *J* = 8 Hz, 2H) ppm.



4b

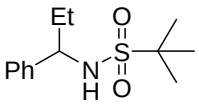
***N*-Ts Methylbenzylamine 4b[5]**. Purified by flash chromatography on silica gel (ethyl acetate/petroleum 1:8). Yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.42 (d, *J* = 6.8 Hz, 3H), 2.39 (s, 3H), 4.42-4.48 (m, 1H), 4.19 (d, *J* = 6.8 Hz, 1H), 7.09-7.11 (m, 2H),

7.17-7.21 (m, 5H), 7.61 (d, *J* = 8.4 Hz, 2H) ppm.



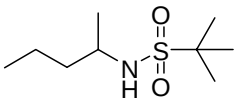
4c

***N*-Ts Phenylbenzylamine 4c[6]**. Purified by flash chromatography on silica gel (ethyl acetate/petroleum 1:10). White solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.29 (s, 3H), 5.00 (d, *J* = 6.8 Hz, 1H), 5.48 (d, *J* = 6.8 Hz, 1H), 7.00-7.06 (m, 6H), 7.11-7.17 (m, 6H), 7.47 (d, *J* = 8.4 Hz, 2H) ppm.



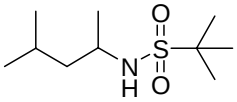
4d

***N*-(*tert*-Butanesulfonyl) ethylbenzylamine 4d.** Purified by flash chromatography on silica gel (ethyl acetate/petroleum 1:9). White solid. mp 86-87□; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.82 (t, *J* = 7.6 Hz, 3H), 1.18 (s, 9H), 1.71-1.81 (m, 2H), 4.30 (b, 1H), 4.31(b, 1H), 7.14-7.20 (m, 3H), 7.24-7.28 (m, 2H) ppm. ^{13}C NMR (50 MHz, $CDCl_3$) δ 10.7, 24.1, 32.5, 59.6, 60.4, 126.4, 127.3, 128.6, 142.5 ppm; IR (KBr) 1121, 1293, 2970, 3285 cm^{-1}; HRMS: calcd for $C_{13}H_{21}NO_2SNa$ $(M+Na)^+$ 278.1185. Found 278.1198.



4e

***N*-(*tert*-Butanesulfonyl) methylbutylamine 4e.** Purified by flash chromatography on silica gel (ethyl acetate/petroleum 1:8). Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.93 (t, *J* = 7.2 Hz, 3H), 1.24 (d, *J* = 6.4 Hz, 3H), 1.34-1.57 (m, 4H), 1.41 (s, 9H), 3.45-3.52 (m, 1H), 3.64(b, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 13.8, 19.2, 22.7, 24.2, 40.7, 51.2, 59.5 ppm; IR (film) 1125, 1301, 2964, 3281 cm^{-1}; HRMS: calcd for $C_9H_{21}NO_2SNa$ $(M+Na)^+$ 230.1185. Found 230.1181.



4f

***N*-(*tert*-Butanesulfonyl) 1,3-dimethyl-butylamine 4f.** Purified by flash chromatography on silica gel (ethyl acetate/petroleum 1:9). White solid. mp 77-78□; ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.92 (dd, *J* = 6.8 Hz, 12.4 Hz, 6H), 1.24 (d, *J* = 6.0 Hz, 3H), 1.27-1.33 (m, 1H), 1.39 (s, 9H), 1.42-1.48 (m, 1H), 1.66-1.74 (m, 1H), 3.52 (b, 1H), 3.54 (b, 1H) ppm; ^{13}C NMR (50 MHz, $CDCl_3$) δ 22.1, 22.6, 23.1, 24.2, 24.6, 48.1, 49.6, 59.5 ppm; IR (KBr) 1116, 1298, 2971, 3281 cm^{-1}; HRMS: calcd for $C_{10}H_{23}NO_2SNa$ $(M+Na)^+$ 244.1342. Found 244.1333.

General procedure for the selective reduction of imines S_S-1a, S_S-1h and 3b by Et_2Zn and $Ni(acac)_2$ in the presence of ketone 5 or 7.

Under N_2, to a 5 mL solution of imine (0.5 mmol) and ketone (0.5 mmol) in dioxane was injected diethylzinc (1.5 mmol, 1.1 M in toluene), followed by adding a solution of $Ni(acac)_2$ (0.025 mmol) in 0.5 ml dioxane. The mixture was stirred at room temperature for 1 h. The reaction mixture was quenched by adding saturated aq. NH_4Cl (10 mL). The aqueous layer was extracted with ether (3 X 10 mL). The combined organic layers were washed with 1 N HCl (5 mL) and were dried over Na_2SO_4. The unchanged ketones **5** and **7** were easily detected by TLC analysis. For the reduction of ***S*$_S$-1h**, the ether was evaporated under 1 atm pressure to give a dioxane solution, which was used for GC analysis. For the reduction of ***S*$_S$-1a** and **3b**, the ether and dioxane were evaporated under 1 atm pressure to give a residue, which was used for HPLC analysis. GC condition: Fuli 9790 instrument with a SE-30 column (Restec, 25m x 0.23mm), T_{inj} = 240□, T_{det} = 260°C, T_{colum} = 60°C hold 5 min, then 15°C/min, t_R= 3.8 min (ketone **7**), 4.2 min (alcohol **8**), 14.2 min (amide *S*$_S$-**2h**). HPLC condition**:** DIKAMA Inertsil SIL-100A column, 90:10 hexanes/IPA, 0.8 ml/min, 210 nm, t_R=5.4 min (ketone **5**), 6.6 min (alcohol **6**), 7.6 min (amide *S*$_S$-**2a**); DIKAMA Inertsil SIL-100A column, gradual eluting with hexanes/IPA from 97:3 (1-8 min) to 90:10 (9-11 min), 1 ml/ min, 210nm, t_R= 4.8 min (ketone **5**), 6.8 min (amide **3b**), 8.9 min

(alcohol **6**); The residue was purified by column chromatography to afford amide **2**.

Mechanism study of the reduction reaction.

Under N_2, to a solution of S_S-**1c** (0.05 mmol) in toluene-d_8 (1 mL) in a NMR tube was injected diethylzinc (0.15 mL, 1.0 M in hexane). Two ^{1}H NMR spectra were recorded at the time right after adding diethylzinc and at 2 h respectively before $Ni(acac)_2$ was added. After adding a solution of $Ni(acac)_2$ (0.0025 mmol) in 0.1 mL of toluene-d_8, The ^{1}H NMR spectra were recorded again at a different time indicated in Figure 4 until **1c** was consumed. Part of those ^{1}H NMR spectra between 2.0 ppm and 6.0 ppm were compiled in Figure 4.

Reference:

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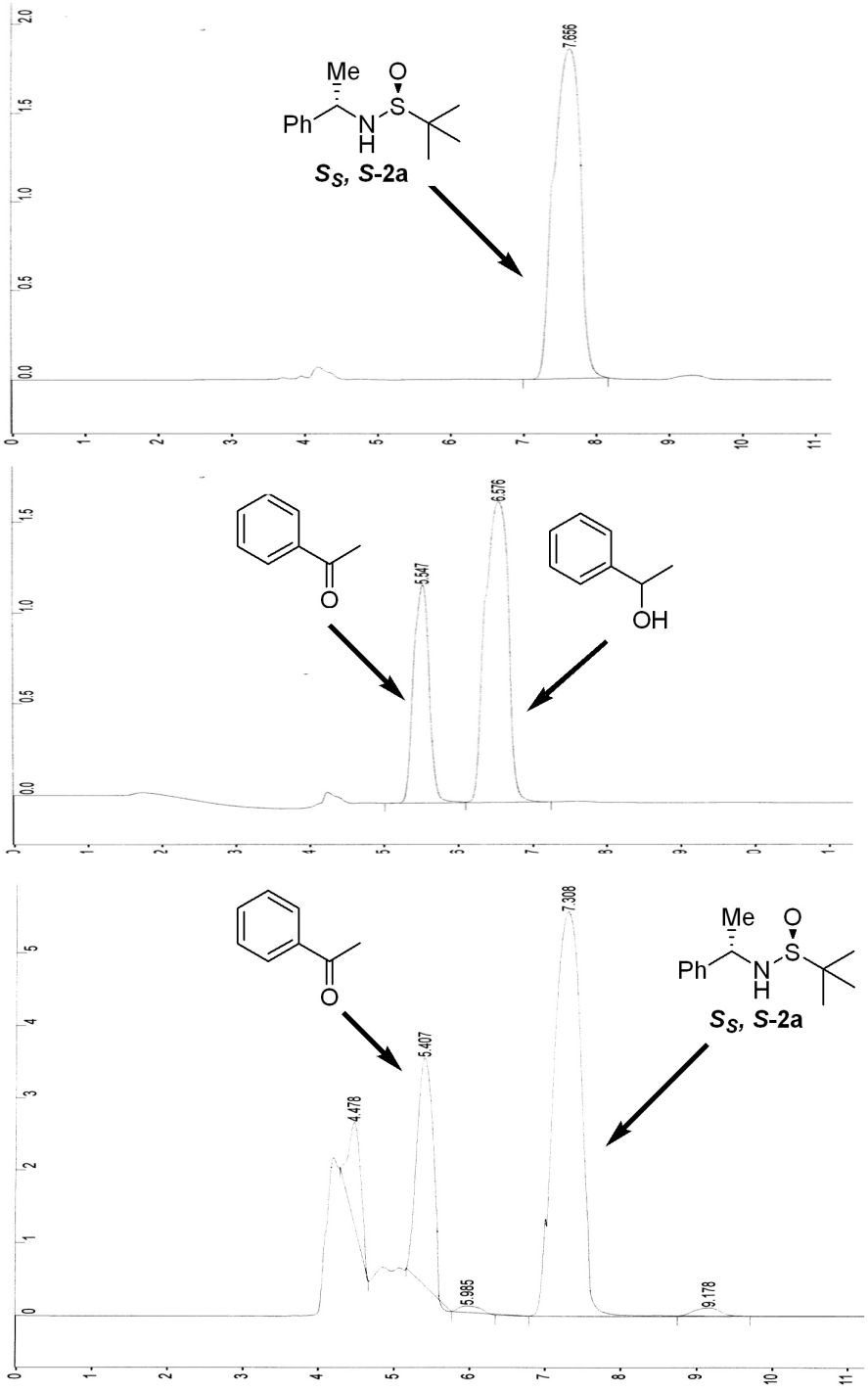
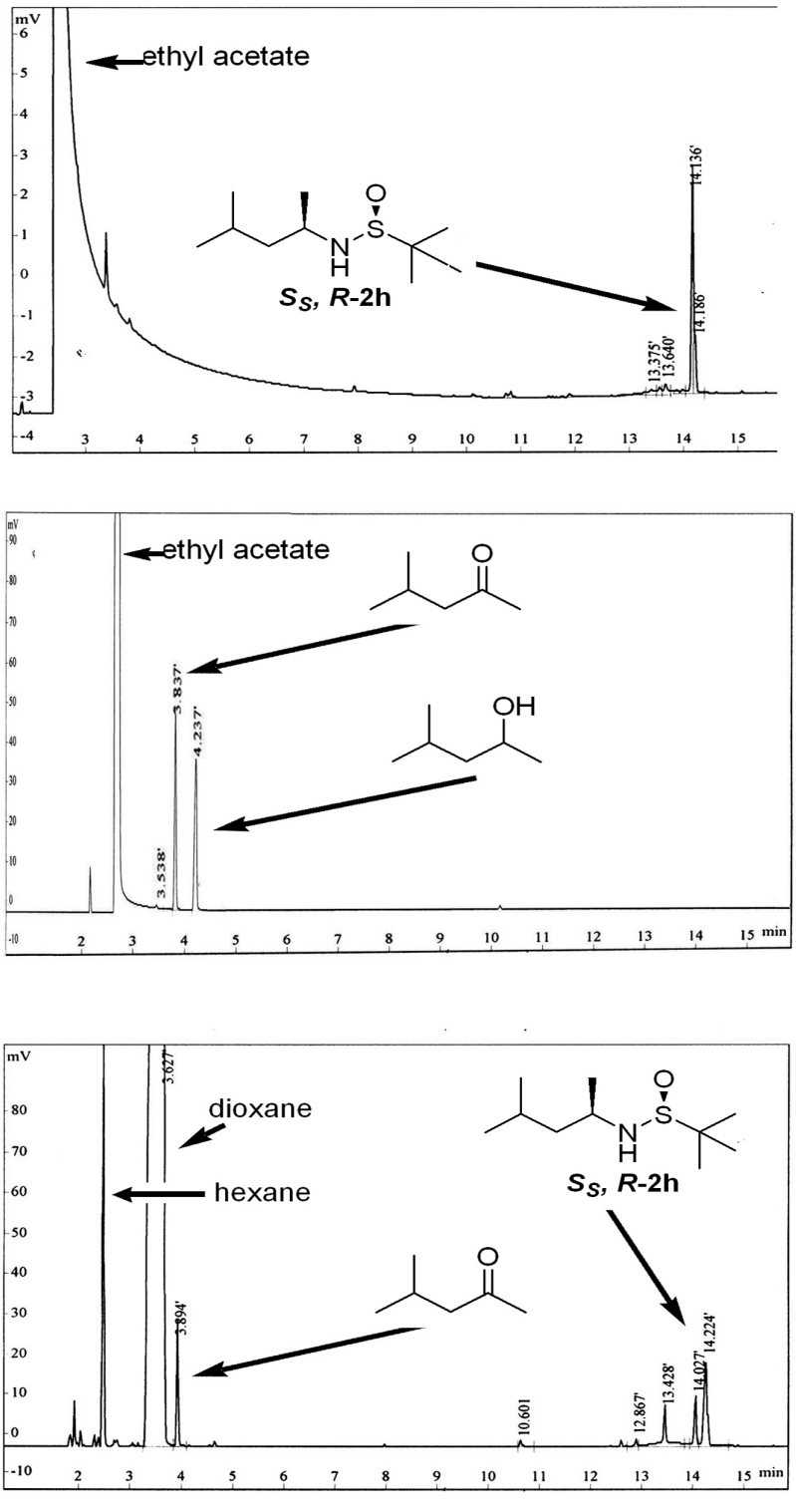
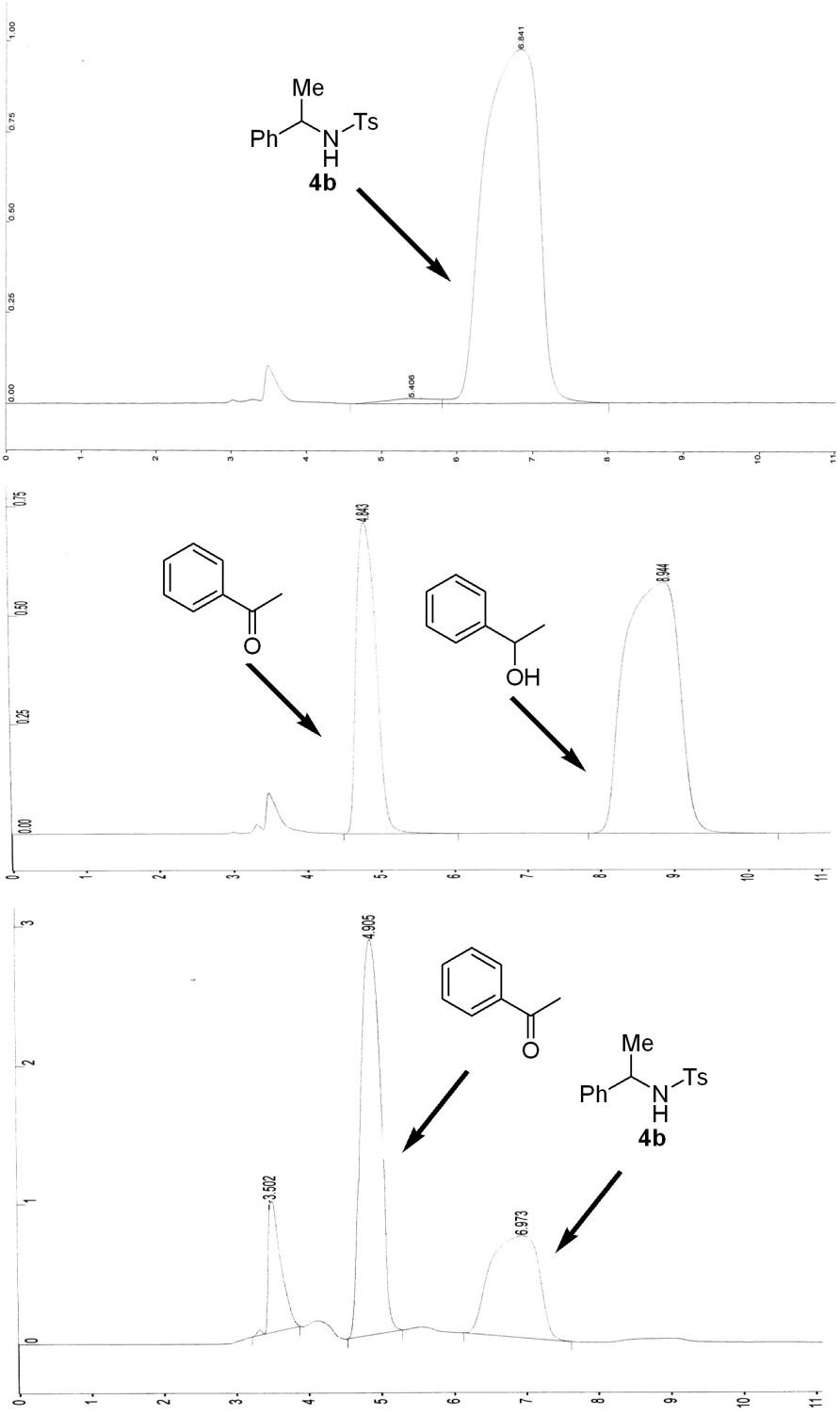


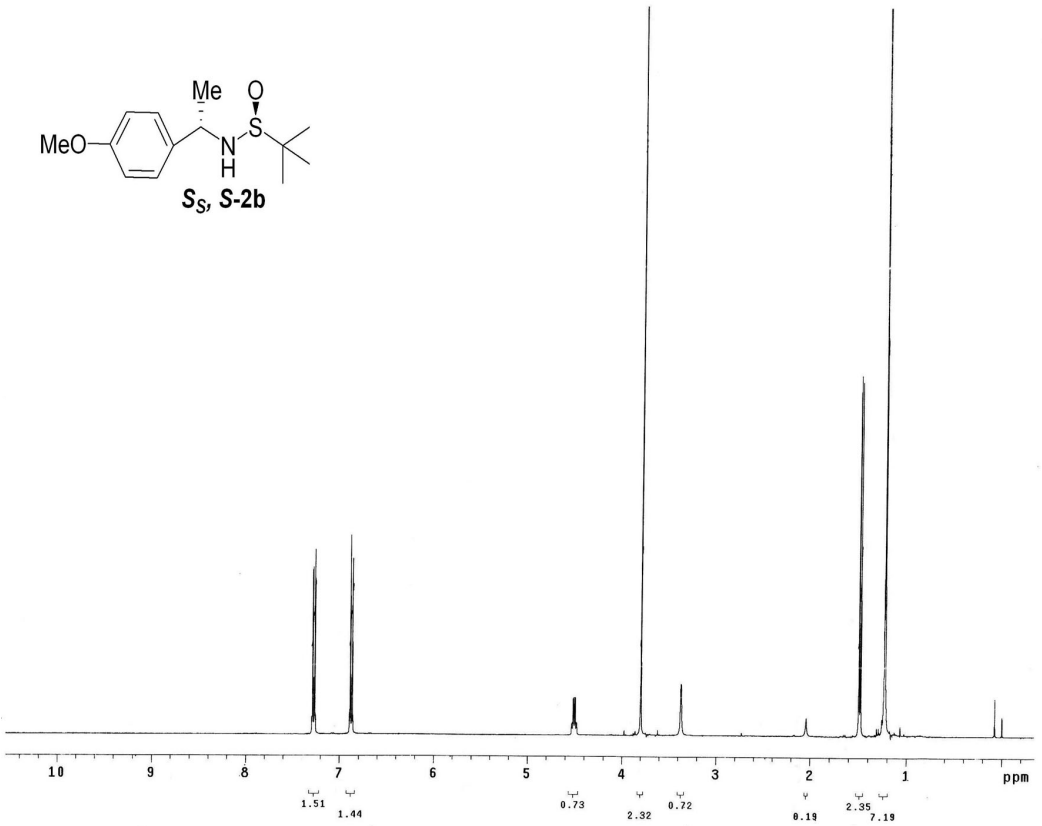
HPLC analysis of selective reduction of S_S-**1a** by Et_2Zn and $Ni(acac)_2$ in the presence of ketone **5**.

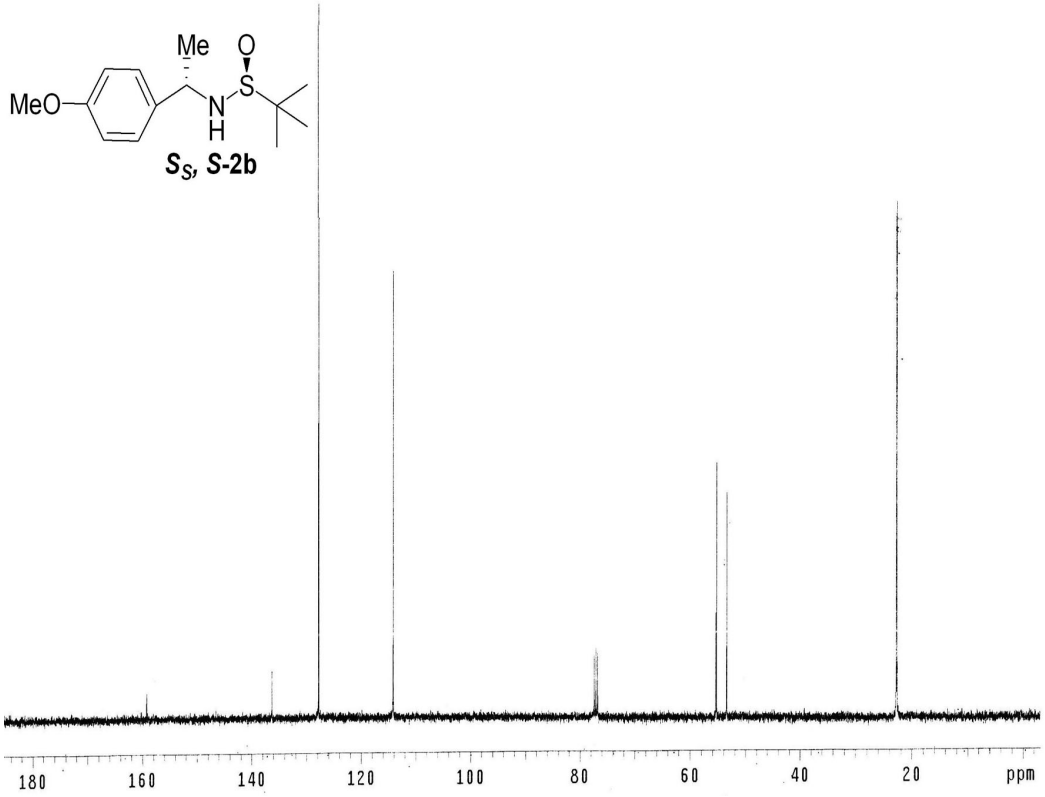


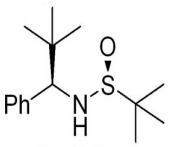
GC analysis of selective reduction of ***S*$_S$-1h** by Et_2Zn and $Ni(acac)_2$ in the presence of ketone **7**.



HPLC analysis of selective reduction of **3b** by Et_2Zn and $Ni(acac)_2$ in the presence of ketone **5**.

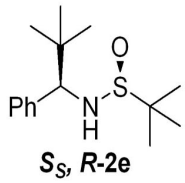

Me
O
MeO
N
S
H
S_S, S-2b
10
9
8
7
6
5
4
3
2
1
ppm
1.51
1.44
0.73
2.32
0.72
0.19
2.35
7.19


Me
O
MeO
N
S
H
S_S, S-2b
180
160
140
120
100
80
60
40
20
ppm


Ph
N
H
S
O

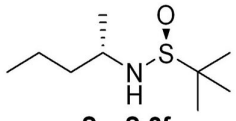
S_S, *R*-2e

10
9
8
7
6
5
4
3
2
1
ppm
6.36
1.09
0.96
16.17
12.71


Ph
N
H
S
O

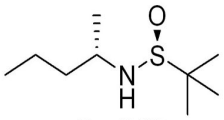
S_S, *R*-2e

180
160
140
120
100
80
60
40
20
ppm



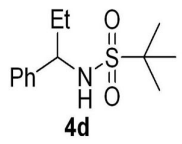
S_S, **S-2f**

9
8
7
6
5
4
3
2
1
0
ppm
0.49
1.01
1.00
1.32
2.03
4.22



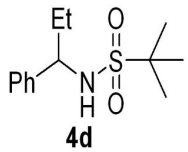
S_S, **S-2f**

0
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
PPM


Et
O
Ph
N
S
H
O

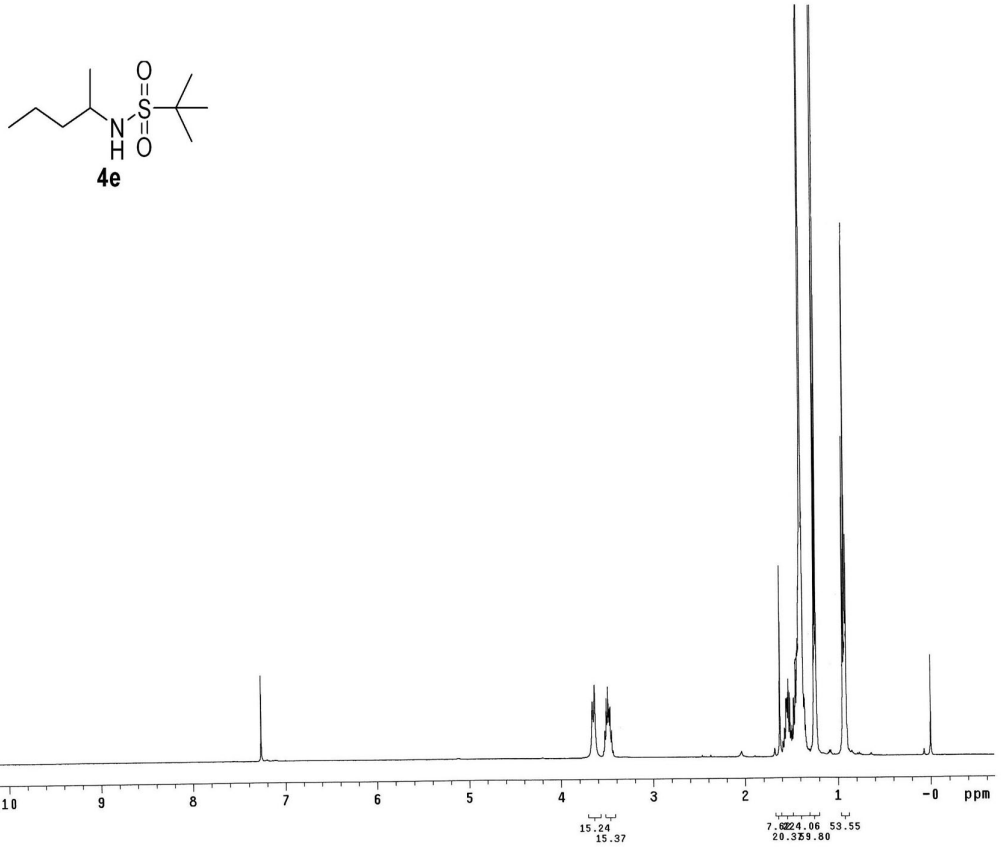
4d

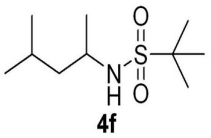
10
9
8
7
6
5
4
3
2
1
-0
ppm
16.71
31.92
21.52
23.51
7.27
105.29
34.12


Et
O
Ph
N
S
H
O

4d

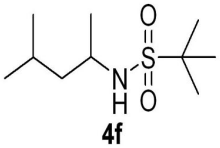
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
PPM


4e
10
9
8
7
6
5
4
3
2
1
-0
ppm
15.24
15.37
53.55
4e
160
140
120
100
80
60
40
20
ppm



4f

10
9
8
7
6
5
4
3
2
1
ppm
2.00
1.11
1.27
7.45
6.82



4f

170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
PPM