Supplementary Information

Asymmetric transfer hydrogenation over Ru/TsDPEN catalysts supported on siliceous mesocellular foam

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General Experimental Procedures

All reactions were carried out under an argon atmosphere. Di-μ-chlorobis[(*p*-cymene)chlororuthenium(II)] $[RuCl_2(p\text{-Cymene})]_2$ and (*S*,*S*)-DPEN were purchased from Strem Chemical Co., and used without further purification. Poly(ethylene oxide)-poly(propylene oxide)-poly(ethylene oxide) triblock copolymer ($EO_{20}PO_{70}EO_{20}$, Pluronic P123) used for MCF preparation was obtained from BASF. Silica gel 60 with 40–63 μm particle size was purchased from EMD Chemicals Inc. Dichloromethane was purchased from Sigma-Aldrich in Sure/Seal™ bottles, and used without further purification. All other reagents were bought from commercial sources, and used without further purification.

^{1}H NMR spectra were recorded on a Varian XL 300 or Bruker Avance DPX-400 NMR spectrometer with chemical shifts reported in ppm relative to the residual deuterated solvent or the internal standard tetramethylsilane. ^{13}C and ^{29}Si solid state magic angle spinning nuclear magnetic resonance (MAS NMR) spectra were obtained by Spectral Data Services, Inc. using a 7-mm probe with a spin speed of 7.5 and 4.0 kHz, respectively. Nitrogen and ruthenium analyses were performed by Atlantic Microlab, Inc. and Desert Analytics, Inc., respectively. Gas chromatography analyses were performed on a Hewlett Packard 5890 instrument with a FID detector and a Hewlett Packard 50 m × 0.32 mm I.D. HP-1 capillary column. Nitrogen adsorption isotherms were collected at 77 K on a Micromeritics ASAP 2010 Gas Sorption and

Porosimetry system using samples degassed under high vacuum at 150°C for ≥ 3 h. BET (Brunauer-Emmett-Teller) surface areas were determined over a relative pressure range of 0.05–0.30. Mesopore size distributions were calculated from the nitrogen adsorption isotherms using the BJH (Brunauer-Joyner-Halenda) method. Enantiomeric excess was determined on a HPLC system comprising a Waters 1525 Binary HPLC Pump, a Waters 2487 Dual λ Absorbance Detector and a Waters In-Line Degasser AF. Raman spectra were obtained on a Kaiser Hololab 5000R Raman Spectrometer with Raman Microprobe attachment. IR spectra were obtained on a Bio-Rad FTS-60A spectrometer with a MTEC model 200 photoacoustic detector. Optical rotations were recorded on Jasco Model 1010 Polarimeter. The absolute configuration was determined from the sign of rotation of the product.

Catalyst Preparation

*Synthesis of **1**:* 4-ethyl benzenesulfonyl chloride-functionalized silica gel (0.50 g, 0.45 mmol) was added slowly to a solution of (*S*,*S*)-DPEN (106 mg, 0.500 mmol) and Et_3N (0.28 mL, 2.0 mmol) in CH_2Cl_2 (5 mL). The reaction mixture was stirred at room temperature for 24 h, and then filtered through a fritted funnel. The solid was washed with CH_2Cl_2 (10 mL × 3) and dried *in vacuo*.

*Syntheses of **2** and **3**:* To prepare **2** and **3**, silica gel (1.0 g) and MCF (1.0 g), respectively, were added to a solution of phenethyltrimethoxysilane (0.87 mL, 4.0 mmol) in toluene (15 mL). The reaction mixture was refluxed under argon for 24 h. It was then cooled to room temperature, and filtered through a fritted funnel. The solid was washed with CH_2Cl_2 (10 mL × 3) and dried *in vacuo*. Chlorosulfonic acid (0.66 mL, 10 mmol) was added to the dispersion of 4-ethyl benzene-functionalized silica in CH_2Cl_2 (10 mL). The reaction mixture was stirred at room temperature under argon for 24 h, and then filtered through a fritted funnel. The solid was washed with CH_2Cl_2 (10 mL × 3) and dried *in vacuo*. Oxalyl chloride (2.0 M in CH_2Cl_2, 5.0 mL, 10 mmol) and DMF (0.12 mL, 1.5 mmol) were added dropwise to the dispersion of 4-ethyl benzenesulfonic acid-functionalized silica in CH_2Cl_2 (10 mL). The reaction mixture was stirred at room temperature under argon for 24 h, and then filtered through a fritted funnel. The solid was washed with CH_2Cl_2 (10 mL × 3), dried *in vacuo*, and added to a solution of (*S*,*S*)-DPEN (0.21 g, 1.0 mmol) and Et_3N (0.28 mL, 2.0 mmol) in CH_2Cl_2 (10 mL). The reaction mixture was

stirred at room temperature for 24 h, and then filtered through a fritted funnel. The solid was washed with CH_2Cl_2 (10 mL × 3), and dried *in vacuo*.

*Characterization of **3**:* IR (cm^{-1}) 3067, 3031, 2985, 1599, 1495, 1476, 1456, 1400, 1079, 961, 807, 699. Raman (cm^{-1}) 417, 621, 637, 745, 813, 904, 1005, 1034, 1122, 1161, 1209, 1603. The great resemblance of **3** and TsDPEN in Raman spectra (see Figures S1 and S2) confirmed that **3** was successfully synthesized as MCF-immobilized TsDPEN. Elemental analysis: C, 13.27; H, 2.27; N, 1.35; S, 1.72. Ligand loading (0.5 mmol/g) was calculated based on nitrogen analysis. CP-MAS ^{13}C NMR (91 MHz) δ 127.3 (aromatic carbons), 67.3 (-*C*HNHSO$_2$-), 62.5 (-*C*HNH$_2$), 28.3 (-SiCH$_2$*C*H$_2$-), 8.1 (-Si*C*H$_2$CH$_2$-). CP-MAS ^{29}Si NMR (54 MHz) δ -42.1 (T^2), -54.6 (T^2), -65.1 (T^3), -90.7 (Q^2), -100.2 (Q^3), -110.2 (Q^4).

General Procedure for Transfer Hydrogenation

Immobilized ligand on silica (**3**, 50 mg) and [RuCl$_2$(*p*-Cymene)]$_2$ (1.5 mg, 2.5 μmol) were loaded into a crimp top vial containing a stir bar. The vial was flushed with argon and sealed with a PTFE/silicone septum. A needle connected to a flow of argon was inserted through the septum. Triethylamine (Et_3N, 14 μL, 0.10 mmol) and CH_2Cl_2 (1.0 mL) were injected into the vial. The reaction mixture was stirred at room temperature for 1 h. The layers were separated by centrifuge, and the liquid was removed by a syringe. The imine or ketone (0.50 mmol) in CH_2Cl_2 or isopropanol (1.0 mL) and the HCO_2H/Et_3N complex (5:2, 0.25 mL, 0.60 mmol) were injected into the vial. The reaction mixture was stirred at either room or elevated temperature for 12 h. CH_2Cl_2 (3.0 mL) was added into the vial and the mixture was centrifuged. The liquid layer was removed by a syringe under a flow of argon. The wash and centrifuge sequence was repeated twice. The liquid layer after each wash was combined, washed with aqueous Na_2CO_3 solution and brine, dried over Na_2SO_4, and concentrated under reduced pressure. The product was isolated and analyzed with GC to determine the conversion and yield, and with HPLC to determine the enantioselectivity. Another batch of fresh imine or ketone and HCO_2H/Et_3N complex was added to the solid catalyst remaining in the vial. After the same reaction duration, the reaction mixture was treated and analyzed in the same way as the first run.

Products Characterization

(R)-Salsolidine[1]*:* Pale-yellow oil. HPLC condition: CHIRALCEL® OD-H column (0.46 cm ∅ × 25 cm) from Daicel Chemical Ind., Ltd. Hexane:isopropanol:diethylamine = 90:10:0.1 (v/v/v), 1.0 mL/min. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.63 (s, 1H), 6.57 (s, 1H), 4.12–4.01 (m, 1H), 3.86 (s, 3H), 3.85 (s, 3H), 3.32–3.20 (m, 1H), 3.06–2.95 (m, 1H), 2.87–2.74 (m, 1H), 2.72–2.60 (m, 1H), 1.95 (br s, 1H), 1.45 (d, J = 6.6 Hz, 3H). $[\alpha]_D^{23}$ = 50.0 (c = 1.0, $CHCl_3$). Lit.[1] $[\alpha]_D^{25}$ = 59.5 (c = 0.9, EtOH).

(R)-2-Chloro-1-phenylethanol[2]*:* Colorless oil. HPLC condition: CHIRALCEL® OD-H column (0.46 cm ∅ × 25 cm) from Daicel Chemical Ind., Ltd. Hexane:isopropanol = 90:10 (v/v), 0.80 mL/min. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42–7.30 (m, 5H), 4.91 (dt, J = 9.0, 3.0 Hz, 1H), 3.75 (dd, J = 11.4, 3.3 Hz, 1H), 3.65 (dd, J = 11.4, 9.0 Hz, 1H), 2.64 (d, J = 3.0 Hz, 1H). $[\alpha]_D^{23}$ = -59.1 (c = 1.0, $CHCl_3$). Lit.[3] $[\alpha]_D^{25}$ = -56.2 (c = 1.1, $CHCl_3$).

(R)-2-Chloro-1-(2,4-dichlorophenyl)ethanol[4]*:* White solid. HPLC condition: (R,R) Whelk-O 1 column (0.46 cm ∅ × 25 cm) from Regis Technologies, Inc. Hexane:isopropanol = 90:10 (v/v), 0.80 mL/min. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59 (d, J = 8.4 Hz, 1H), 7.38 (d, J = 1.8 Hz, 1H), 7.32 (dd, J = 8.4, 1.8 Hz, 1H), 5.31–5.22 (m, 1H), 3.88 (dd, J = 11.4, 3.0 Hz, 1H), 3.52 (dd, J = 11.4, 8.7 Hz, 1H), 2.76 (d, J = 3.6 Hz, 1H). ^{13}C NMR ($CDCl_3$, 75 MHz) δ 136.0, 134.8, 132.7, 129.5, 128.7, 127.8, 70.5, 49.4. IR (cm^{-1}) 2955, 1587, 1561, 1470, 1383, 1074, 866, 784. $[\alpha]_D^{23}$ = -59.1 (c = 1.2, $CHCl_3$). Lit.[4] $[\alpha]_D^{20}$ = -50.9 (c = 1.2, EtOH).

(R)-2-Chloro-1-(4-methoxyphenyl)ethanol[2]*:* Colorless oil. HPLC condition: CHIRALCEL® OD-H column (0.46 cm ∅ × 25 cm) from Daicel Chemical Ind., Ltd. Hexane:isopropanol = 90:10 (v/v), 0.80 mL/min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (d, J = 8.4 Hz, 2H), 6.90 (d, J = 8.4 Hz, 2H), 4.85 (dd, J = 8.8, 3.6 Hz, 1H), 3.81 (s, 3H), 3.70 (dd, J = 11.2, 3.6 Hz, 1H), 3.63 (dd, J = 11.2, 8.8 Hz, 1H), 2.65 (br s, 1H). $[\alpha]_D^{23}$ = -59.8 (c = 1.0, $CHCl_3$). Lit.[2] $[\alpha]_D^{22}$ = 40.2 (c = 2.2, $CHCl_3$) for 90.5% ee of (*S*).

(R)-Methyl mandelate[5]*:* Colorless oil. HPLC condition: CHIRALCEL® OD-H column (0.46 cm ∅ × 25 cm) from Daicel Chemical Ind., Ltd. Hexane:isopropanol = 90:10 (v/v), 0.80 mL/min. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44–7.31 (m, 5H), 5.19 (s, 1H), 3.77 (s, 3H). $[\alpha]_D^{23}$ = -116 (c = 1.0, $CHCl_3$). Lit.[6] $[\alpha]_D^{23.5}$ = -168 (c = 0.5, $CHCl_3$).

(R)-Ethyl 3-hydroxy-3-phenylpropanoate[7]*:* Colorless oil. HPLC condition: CHIRALCEL® OD-H column (0.46 cm ∅ × 25 cm) from Daicel Chemical Ind., Ltd. Hexane: isopropanol = 90:10 (v/v), 0.80 mL/min. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.42–7.23 (m, 5H), 5.18–5.11 (m, 1H), 4.19 (q, J = 7.2 Hz, 2H), 3.27 (d, J = 3.3 Hz, 1H), 2.82–2.66 (m, 2H), 1.27 (t, J = 7.2 Hz, 3H). $[\alpha]_D^{23}$ = -50.6 (c = 1.0, $CHCl_3$). Lit.[7] $[\alpha]_D$ = -52 (c = 1, $CHCl_3$).

Ru and N Analysis of Complex ***6****:* Before the reaction: %N, 1.35; %Ru, 1.01. After six consecutive runs: %N, 1.25; %Ru, 0.84.

Ru Analysis of Organic Solution (3 mL) After Each Run: 1st Run, 4.0 ppm; 2nd run, 3.0 ppm; 3rd run, 2.4 ppm; 4th run, 2.7 ppm; 5th run, 2.6 ppm; 6th run, 3.0 ppm.

Physical Mixture of Ru/TsDPEN and MCF (Table S1, Entry 7 & 8)

Transfer hydrogenation reaction was also catalyzed by the Ru complex prepared from $RuCl_2$[*p*-Cymene)]$_2$ and TsDPEN in the presence of MCF. This study involved a physical mixture of the Ru complex and the MCF support, whereby the Ru complex could either be entrapped within the pores of MCF or be on the external surface of MCF. The yield and ee obtained with this catalyst system in the first run were the same as those achieved by catalyst **6** in Table 1. However, the MCF recovered after filtration and washing did not exhibit any significant catalytic activity and enantioselectivity in the subsequent run, indicating the severe leaching of Ru complex when it was prepared as a physical mixture with the support. The poor reusability of this case was in sharp contrast with that of catalyst **6** reported in Table 1, illustrating the covalent nature of the complex immobilization in catalyst **6**.

Notes and references

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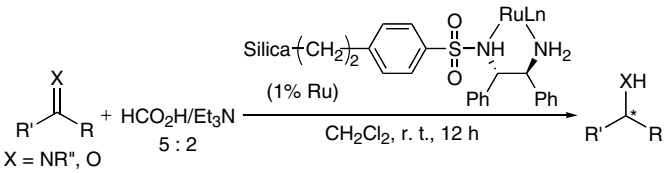
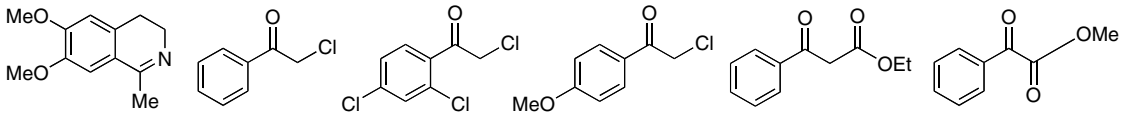
Table S1. Asymmetric Transfer Hydrogenation over Immobilized Chiral Ru/TsDPEN Catalyst



Substrate



A B C D E F

Entry	Substrate	Solvent/ Temperature	Ru Complex	Ru Loading (%)	Yield (%)[a]	ee (%)[b]	Run #
1	A	CH_2Cl_2/rt	**4**	1	94–95	78–81	1–2
2	A	CH_2Cl_2/rt	**4**	1	80	79	3
3	A	CH_2Cl_2/rt	**5**	1	95–97	86–87	1–3
4	A	CH_2Cl_2/rt	**5**	1	80	86	4
5	A	CH_2Cl_2/rt	**6**	1	95–100	90–91	1–6
6	A	CH_2Cl_2/rt	**6**	0.1	< 3	n.d.	1
7	A	CH_2Cl_2/rt	Ru/TsDPEN/MCF	1	95	91	1
8	A	CH_2Cl_2/rt	Ru/TsDPEN/MCF	1	< 1	n.d.	2
9	A	CH_2Cl_2/0°C	**6**	1	10	n.d.	1
10	A	CH_3CN/rt	**6**	1	> 99	90	1
11	A	CH_3CN/rt	**6**	1	24	90	2
12	A	DMF/rt	**6**	1	98	87	1
13	A	DMF/rt	**6**	1	64	88	2
14	A	THF/rt	**6**	1	> 99	81	1
15	A	EtOAc/rt	**6**	1	> 99	76	1
16	A	EtOAc/rt	**6**	1	50	77	2
17	A	Neat/rt	**6**	1	98	78	1
18	A	Neat/rt	**6**	1	86	78	2
19	A	CH_2Cl_2/rt	**6**[c]	1	20	82	1
20	A	CH_2Cl_2/rt	**6**[d]	1	97	58	1

21[e]	A	CH_2Cl_2/rt	**6**	1	30	n.d.	1
22[f]	A	CH_2Cl_2/rt	**6**	1	20	n.d.	1
23	B	CH_2Cl_2/rt	**6**	1	94–100	97–98	1–6
24	C	CH_2Cl_2/rt	**6**	1	97–99	90–92	1–6
25	D	CH_2Cl_2/rt	**6**	1	88–94	97	1–6
26	E	^{i}PrOH/45°C	**6**	1	90–95	96–97	1–6
27	F	^{i}PrOH/rt	**6**	1	95–98	71–73	1–6

[a]Yields were based on GC analysis and isolated material. [b]Enantiomeric excess was determined by HPLC analysis (Chiralcel OD-H). [c]Silanol groups on MCF were capped with TMS using 1-(trimethylsilyl)imidazole. [d]Silanol groups on MCF were capped with TMS using hexamethyldisilazane. [e]Formic acid/triethylamine complex (2:1) was used. [f]Formic acid/triethylamine complex (1:1) was used.

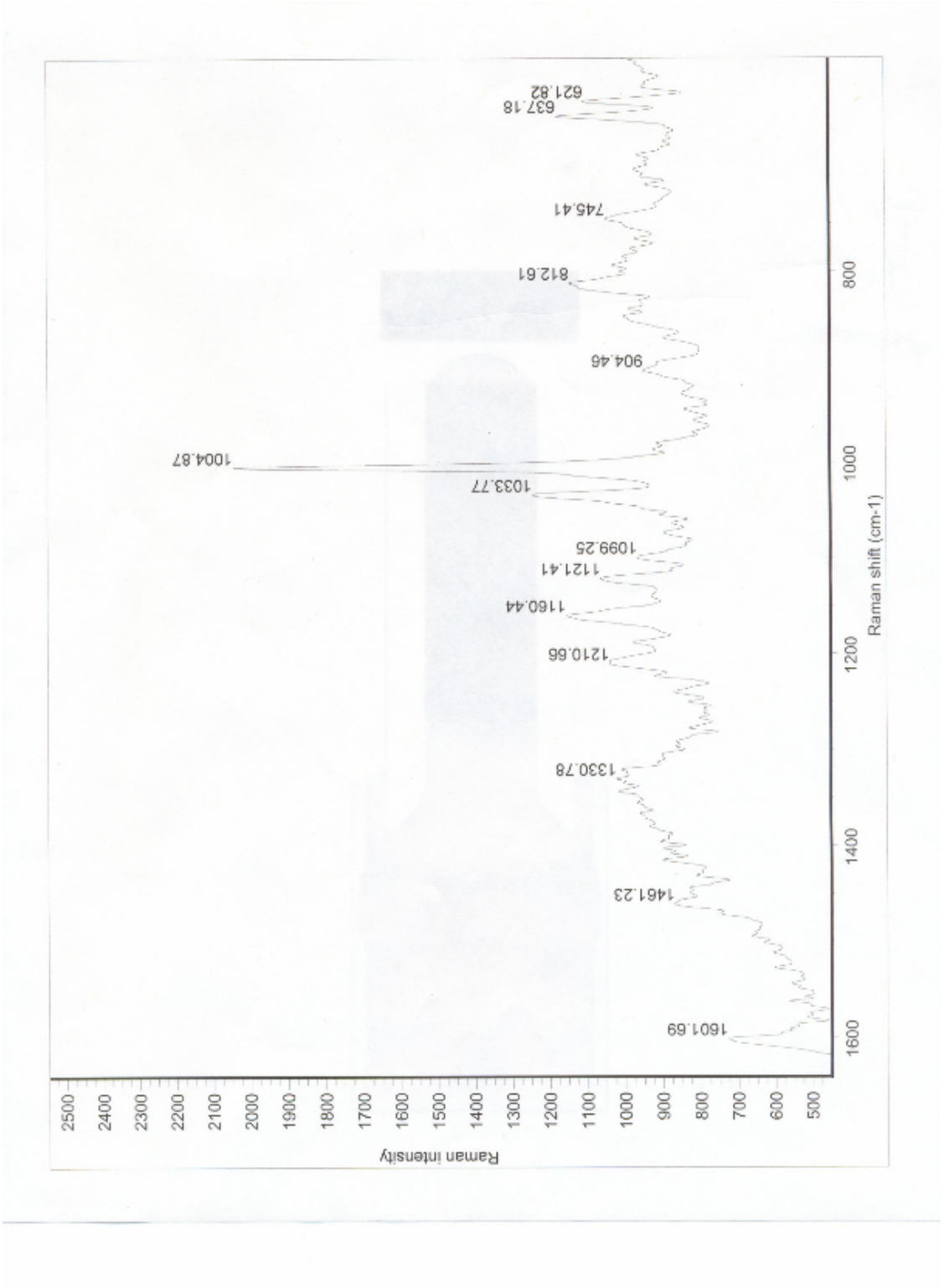


Figure S1. Raman spectrum of **3**.

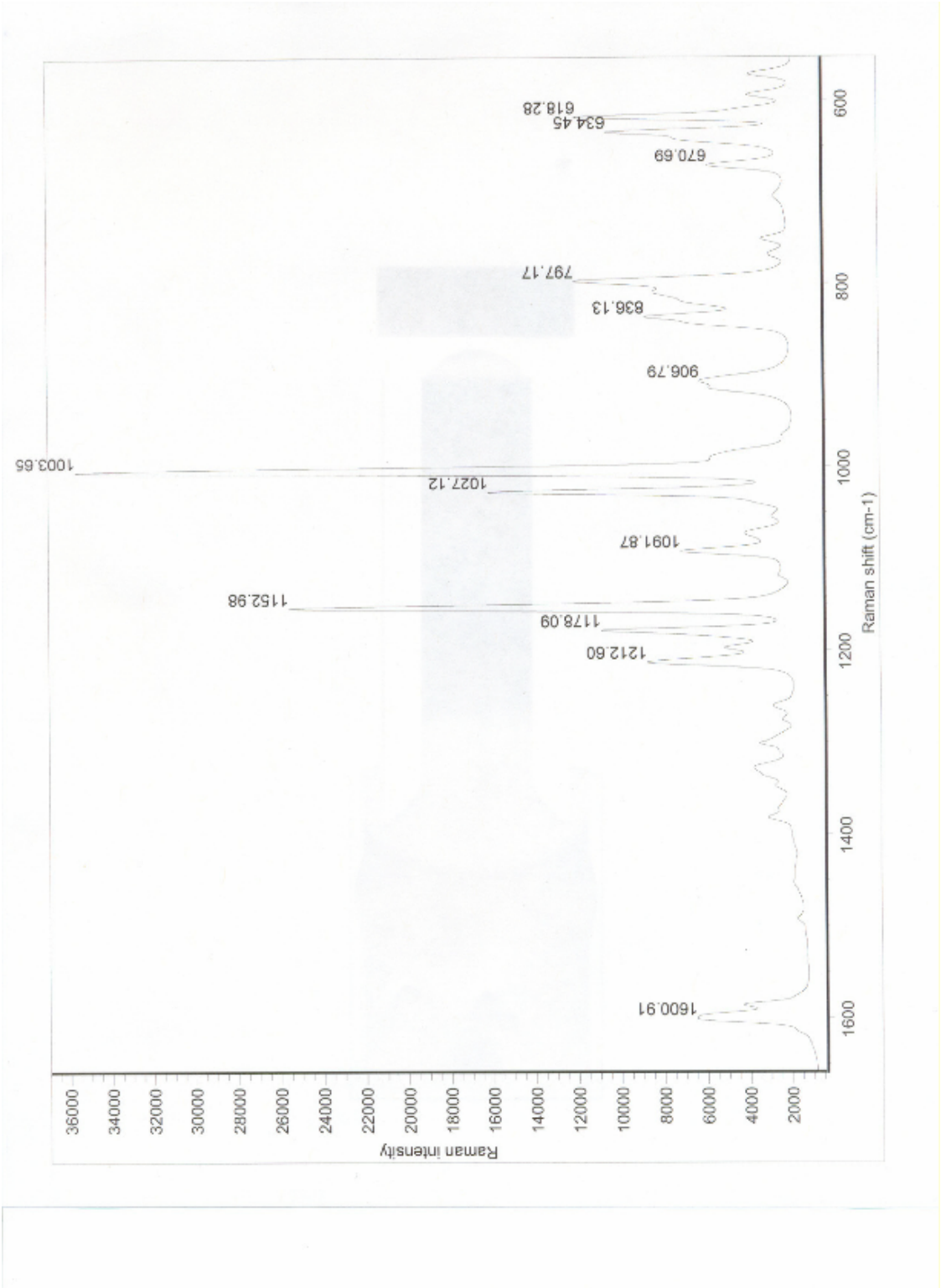


Figure S2. Raman spectrum of TsDPEN.