Supporting information

Effects of heterocycle sulfonyl groups on the enantioselectivity and reactivity of Noyori-Ikariya catalysts in asymmetric ketone reduction

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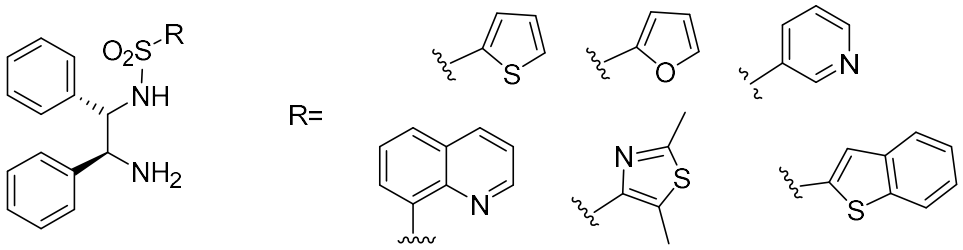
Contents:

General Experimental:

General; Solvents and reagents for the synthesis of complexes and catalytic reactions were degassed prior to use and all reactions were carried out under a nitrogen atmosphere. Reactions at elevated temperature were maintained by thermostatically controlled oil-baths or aluminium heating blocks. A temperature of 0 °C refers to an ice slush bath, -78 °C to a dry ice acetone bath. Reactions were monitored by TLC using aluminium backed silica gel 60 (F254) plates, visualized using UV 254 nm and phosphomolybdic acid (PMA), potassium permanganate as appropriate. Flash column chromatography was performed using silica gel of 230-400 mesh size. Thin layer chromatography was carried out on aluminium backed silica gel 60(F254) plates, visualised using 254nm UV light or potassium permanganate. Reagents were used as received from commercial sources unless otherwise stated. ^{1}H NMR spectra were recorded on a Bruker AV (250 MHz), Bruker DPX (300 or 400MHz) or Bruker DRX (500 MHz). Chemical shifts are reported in δ units, parts per million relative to the singlet at 7.26 ppm for chloroform and at 2.50 ppm for dimethyl sulfoxide for TMS. Coupling constants (J) are measured in Hertz. IR spectra were recorded on a Perkin-Elmer Spectrum One FT-IR Golden Gate. Mass spectra were recorded on a Bruker Esquire2000 or a Bruker MicroTOF mass spectrometer. Melting points were recorded on a Stuart Scientific SMP 1 instrument and are uncorrected. The chiral GC measurements were performed using a Hewlett-Packard 1050 instrument linked to a PC running DataApex Clarity software. HPLC measurements were performed out using a Hewlett Packard 1050 Series with a quaternary pump, autosampler and variable wavelength detector linked to a PC running DataApex Clarity software. Dry solvents were purchased and used as received. Optical rotations were measured on an Optical Activity Ltd. AA-1000 Polarimeter and are reported in deg dm^{-1} cm^{3} g^{-1}.

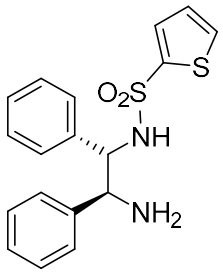
Experimental procedure for complexes, ligands, and substrates with NMR spectra.



Scheme 1 The heterocycle groups that will be used to functionalize DPEN.

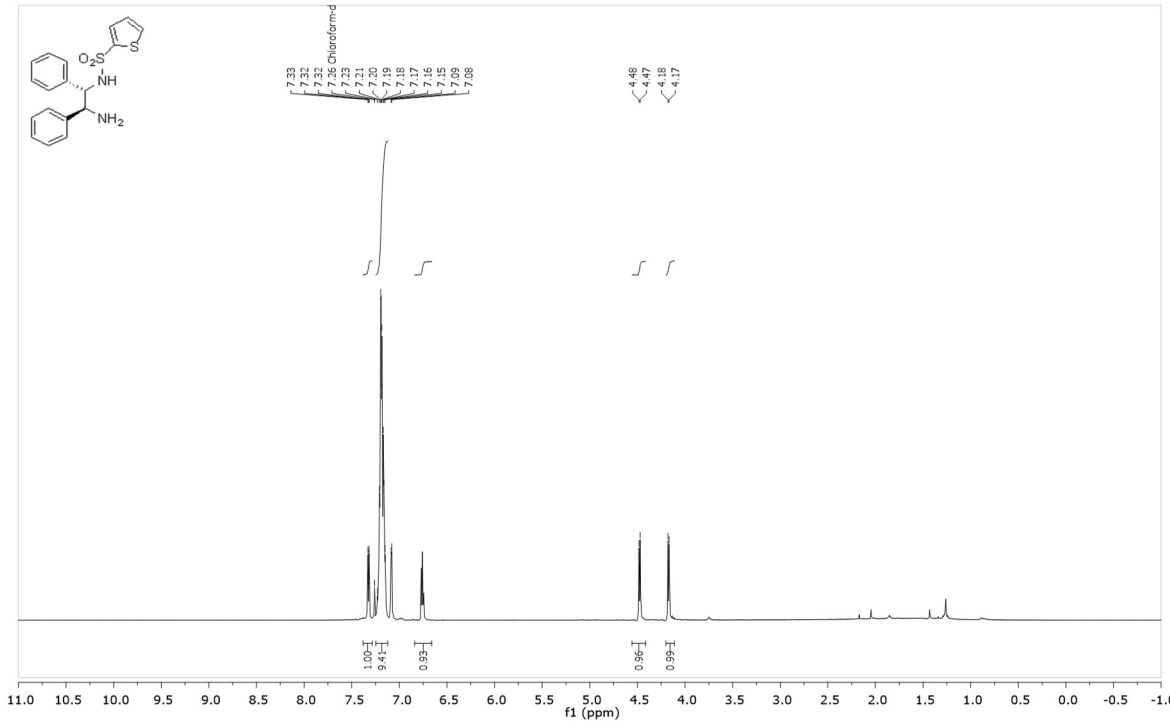
Section 1: Preparation of ligands:

***N*-((*1S,2S*)-2-Amino-1,2-diphenylethyl)thiophene-2-sulfonamide 11a.**



This compound is novel. Under a nitrogen atmosphere, a 100 mL dry round-bottom flask was charged with (*S,S*)-DPEN (150 mg, 0.71 mmol) dissolved in dry THF (6 mL). Triethylamine (218 mg, 2.16 mmol, 300 μL) was added and the resulting solution was cooled to 0 °C using an ice bath. Thiophene 2-sulfonylchloride (129 mg, 0.71 mmol) was dissolved in dry THF (1.5 mL) in a 25 mL dry round flask. This solution was added dropwise to the cooled (*S,S*)-DPEN solution and the resulting solution was stirred overnight at r.t. Saturated $NaHCO_3$ (20 mL) was added to the mixture and the crude product was extracted using DCM (3 x 30 mL). The combined extracts were washed with brine (20 mL), dried using $MgSO_4$ and filtered. The solvent was removed under reduced pressure to afford the crude product. Purification by column chromatography using silica gel (100% EtOAc) gave the pure product (178 mg, 0.498 mmol, 70%) as a yellow solid; TLC: Rf ca 0.40 (100% EtOAc), strong UV and $KMnO_4$; Mp 113 °C, $[\alpha]_D^{25}$ = +24.3 (*c* 0.2 in $CHCl_3$); ν_{max} 3356, 3296, 1593, 1450 cm^{-1} ; δ_H (400 MHz, $CDCl_3$) 7.34 – 7.30 (1 H, m, CH of Thiophene), 7.25 – 7.12 (10 H, m, ArCH), 7.07 (1 H, t, *J* 8.4, CH of Thiophene), 6.79 – 6.73 (1 H, m, CH of Thiophene), 4.48 (1 H, d, *J* 5.1, NCH), 4.17 (1 H, d, *J* 5.1, NCH), NH not observed; δ_C (101 MHz, $CDCl_3$) 141.35 (C), 141.25 (C), 139.17 (C), 131.81 (CH), 131.40 (CH), 128.53 (CH), 128.37 (CH), 127.65 (CH), 127.55 (CH), 126.94 (CH), 126.88 (CH), 126.53 (CH), 63.45 (NCH), 60.48 (NCH); MS (ESI^+): m/z, 359.1 [(M + H) $^+$] ; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{18}H_{19}N_2O_2S_2$ 359.0882; Found 359.0879 (1.0 ppm error).

δ_H (400 MHz,$CDCl_3$)



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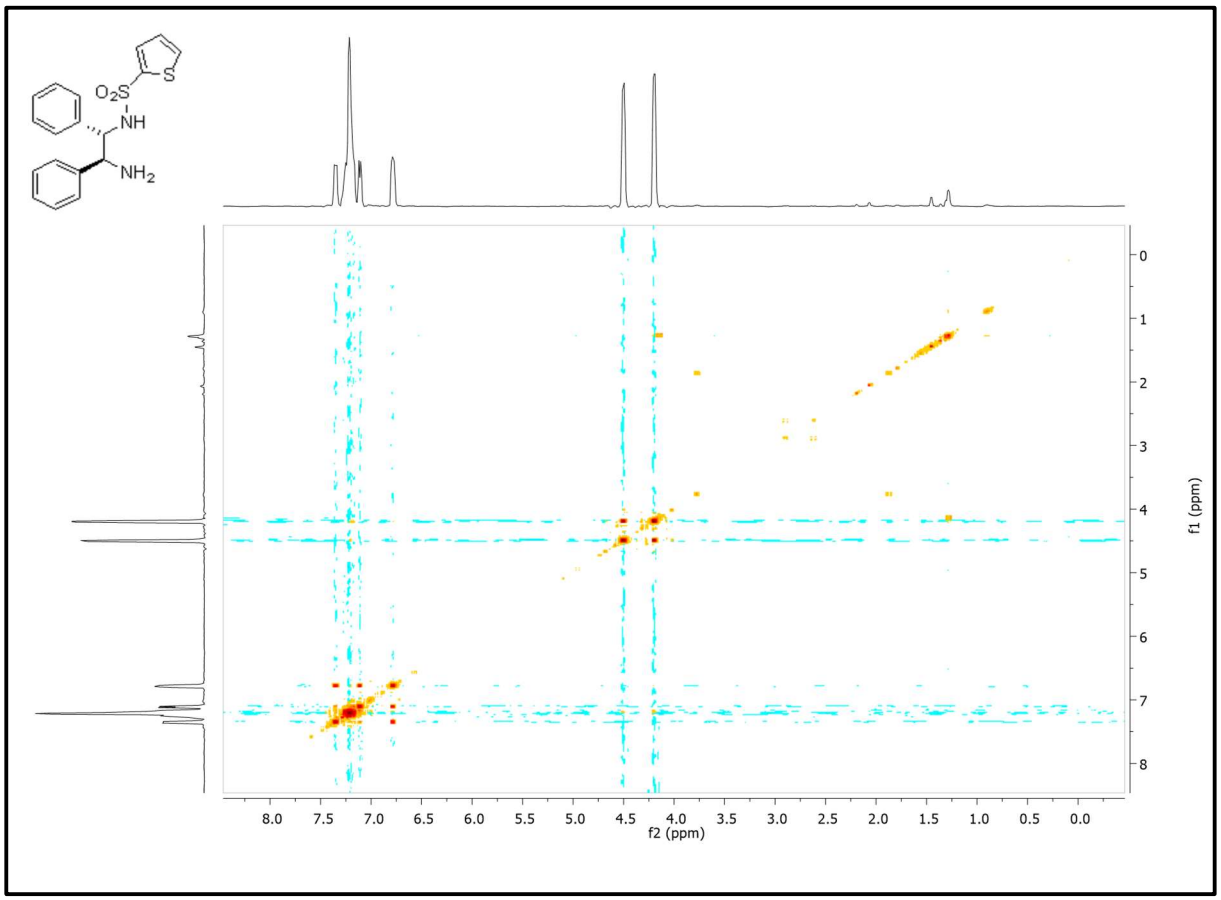
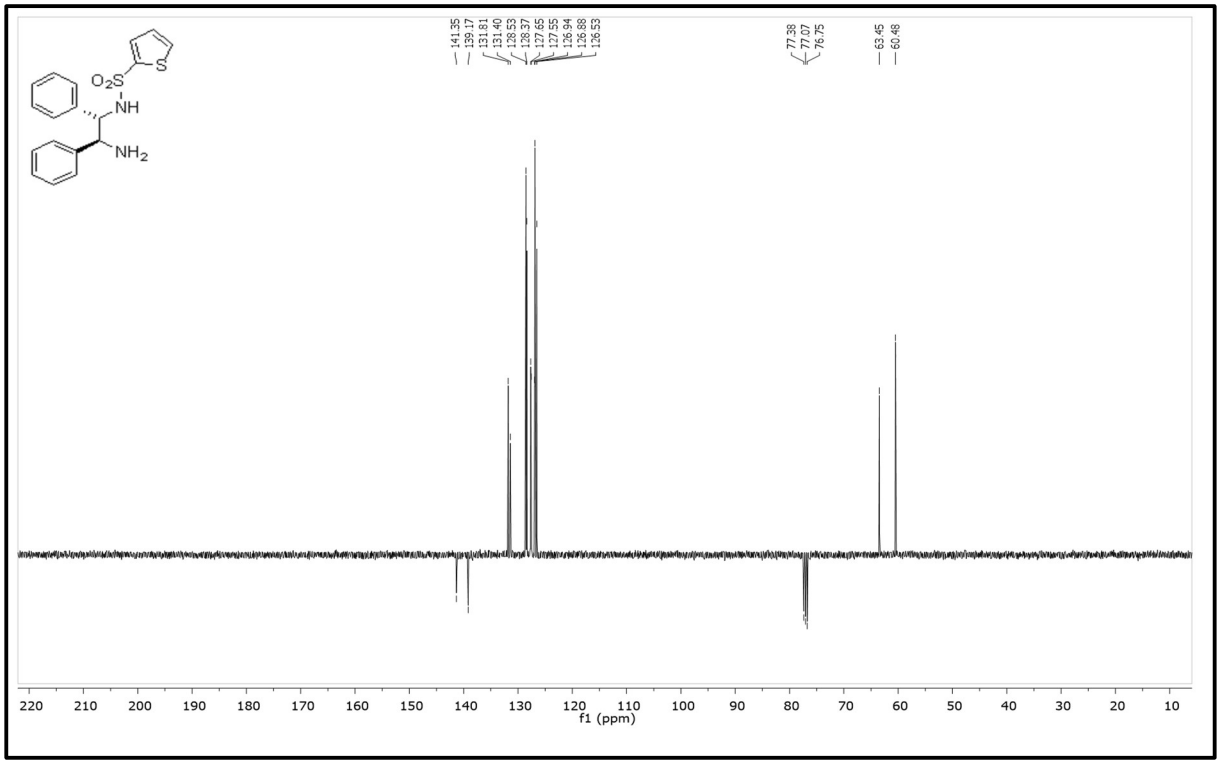
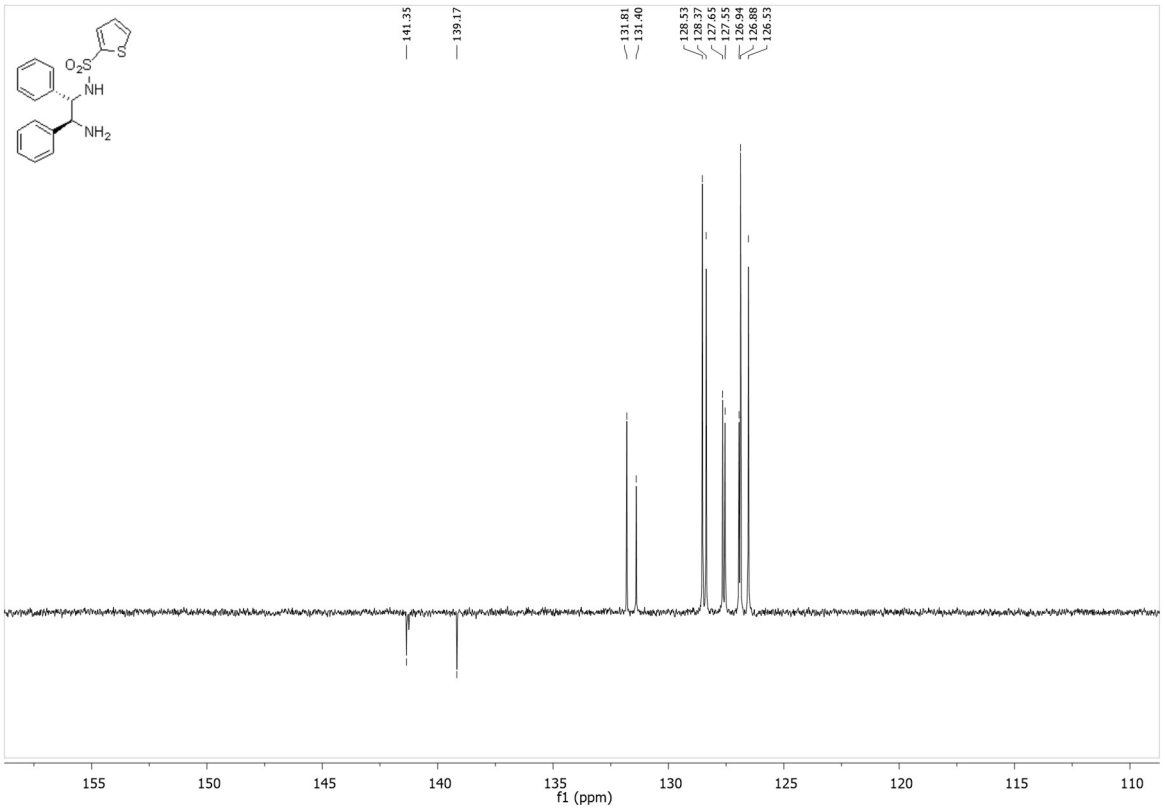
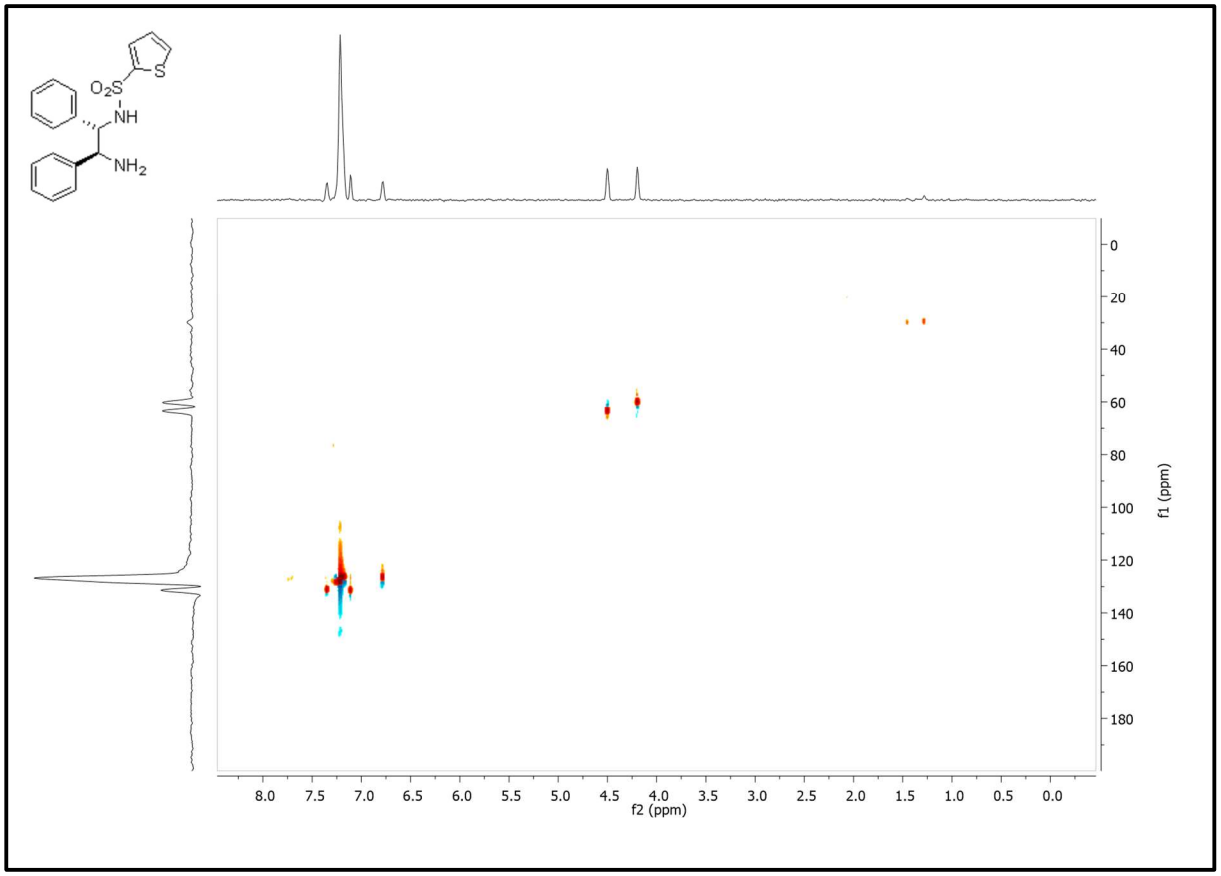


δ_C (101 MHz, $CDCl_3$)

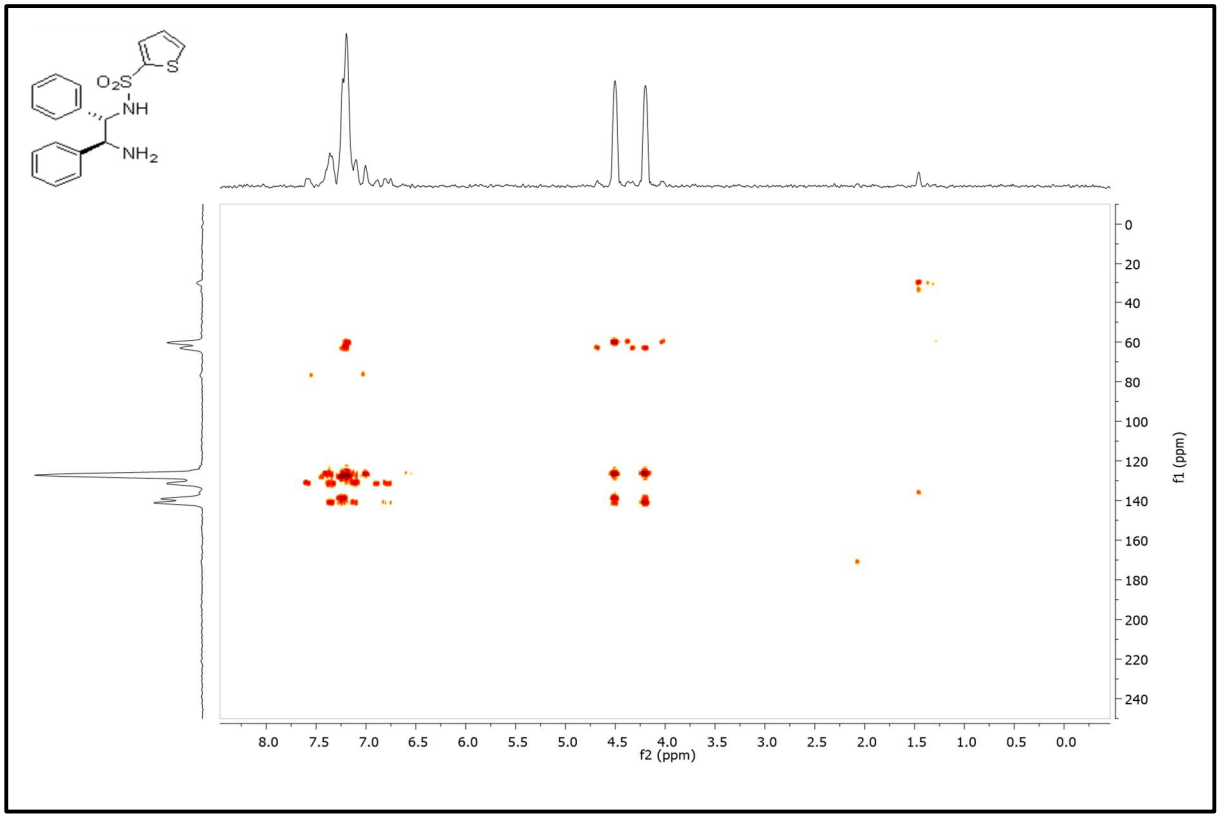




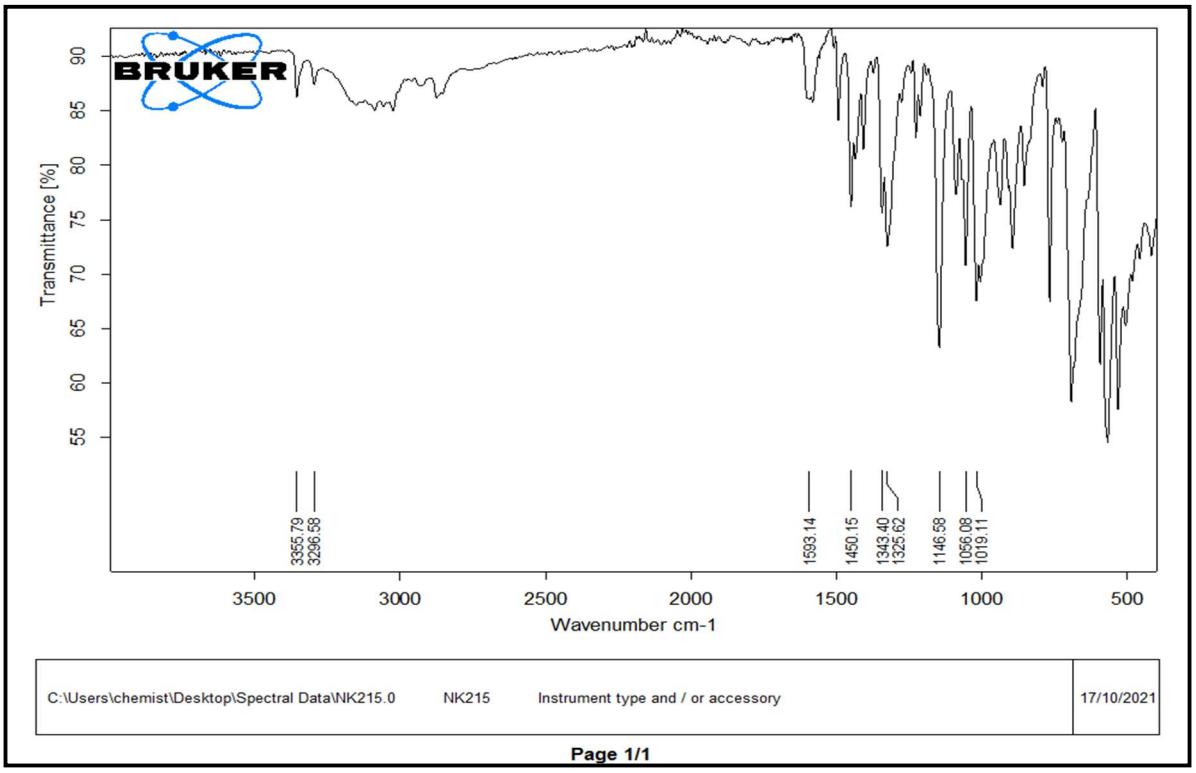
HSQC (400 MHz, $CDCl_3$)



HMBC (400 MHz, $CDCl_3$)



IR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2500
2000
1500
1000
500
Wavenumber cm-1
C:\Users\chemist\Desktop\Spectral Data\NK215.0
NK215
Instrument type and / or accessory
17/10/2021
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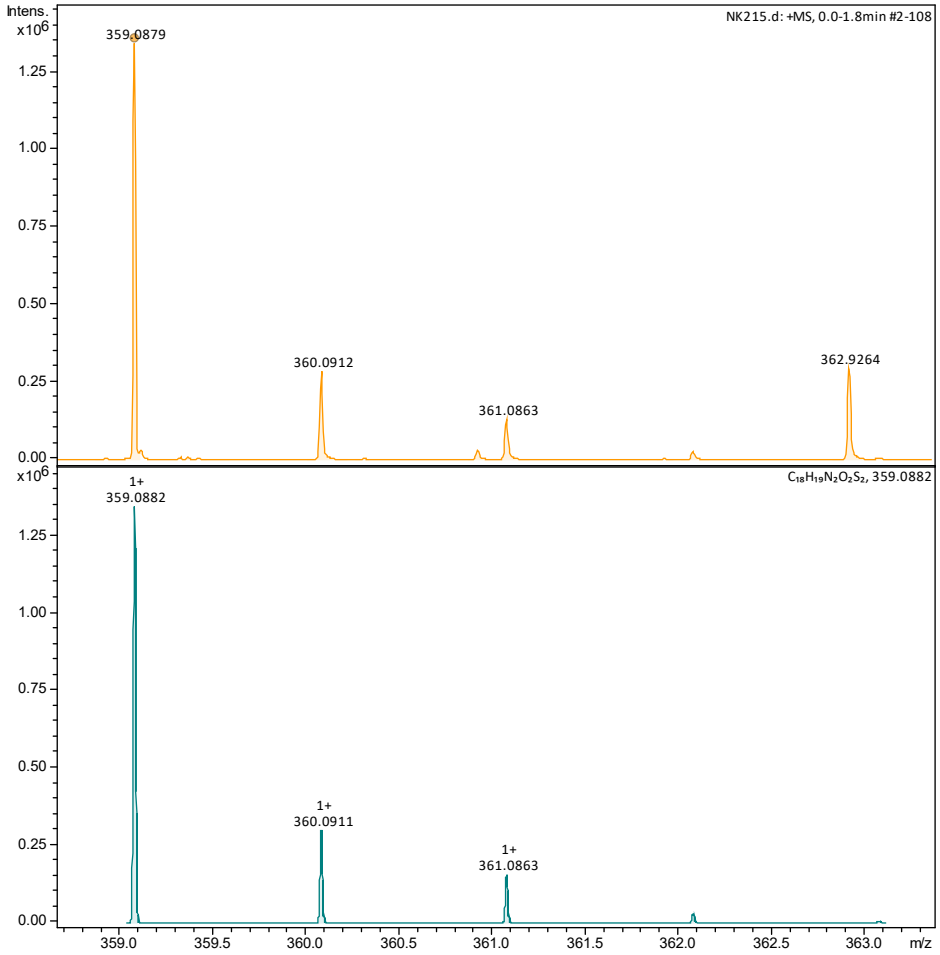
HRMS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0.25
0.00
1+
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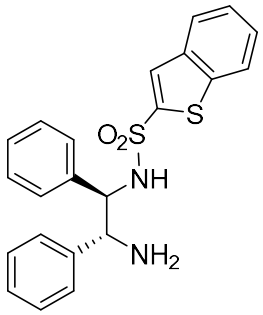
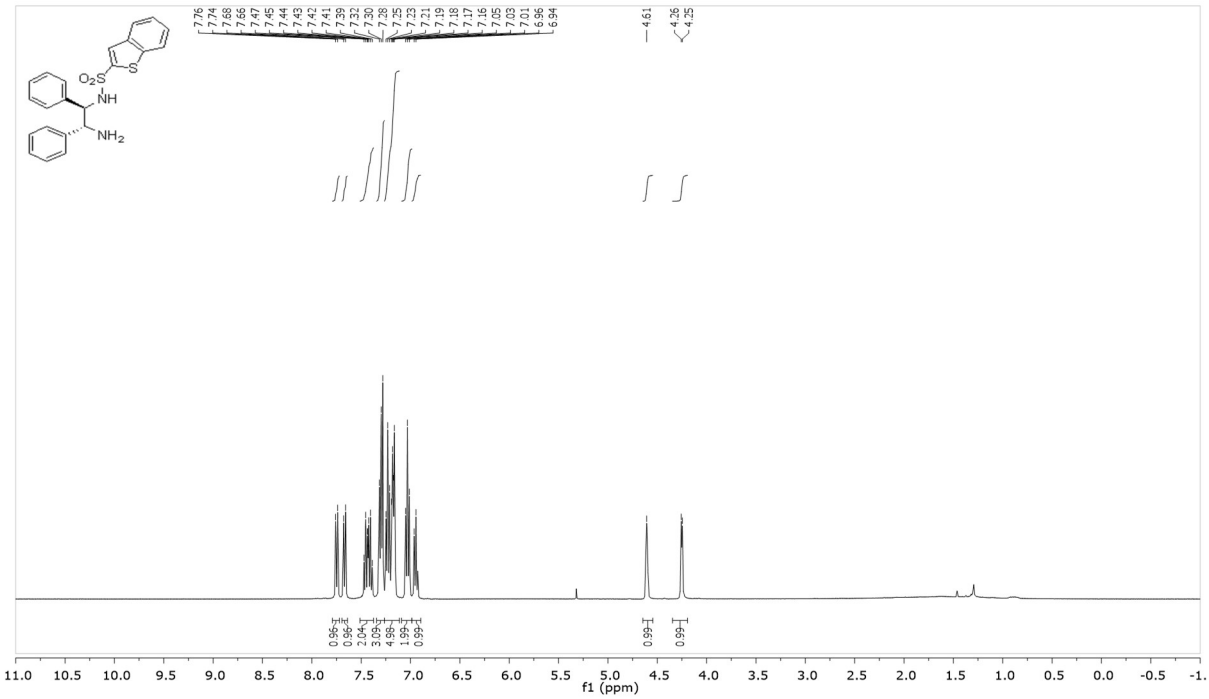
1+
360.0911
1+
361.0863
359.0
359.5
360.0
360.5
361.0
361.5
362.0
362.5
363.0
m/z

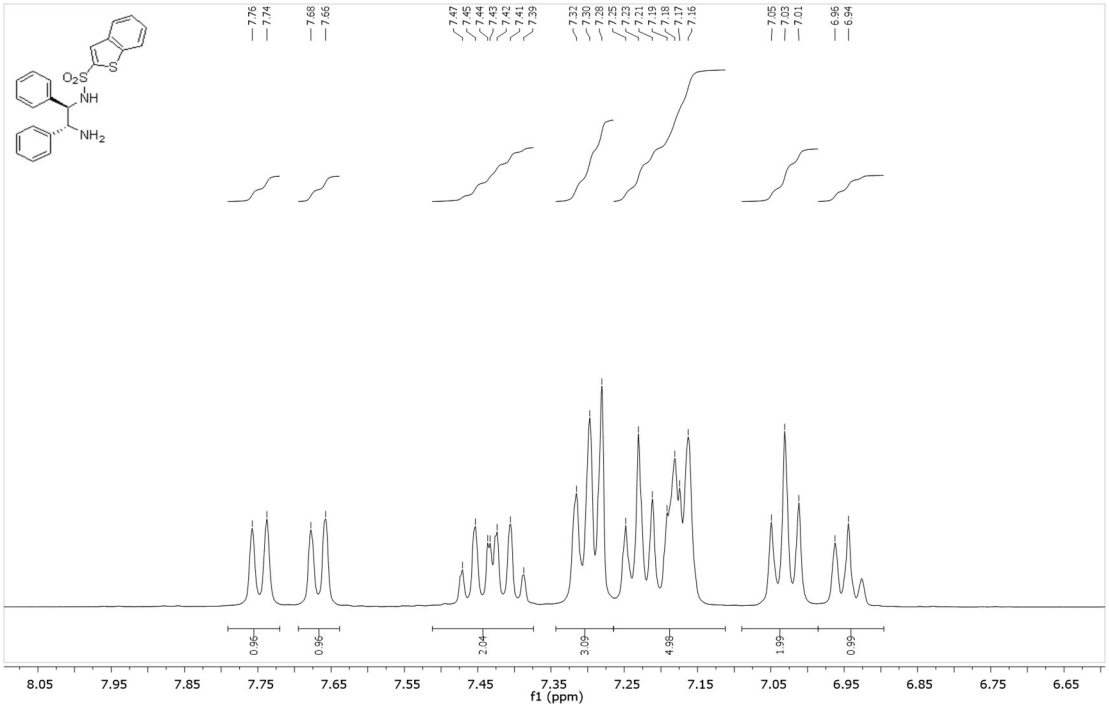
***N*-((*1R,2R*)-2-Amino-1,2-diphenylethyl)benzo[b]thiophene-2-sulfonamide 11b.**



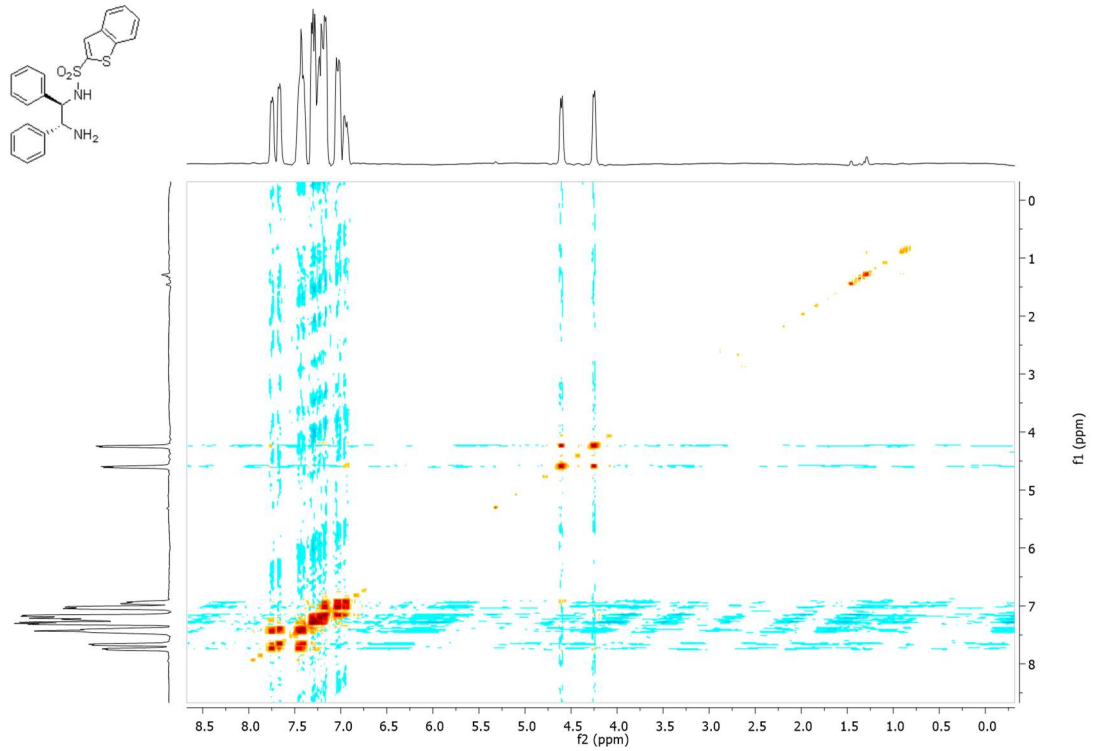
This compound is novel. Under a nitrogen atmosphere, a 100 mL dry round-bottom flask was charged with (*R,R*)-DPEN (109 mg, 0.52 mmol) dissolved in dry THF (5 mL). Triethylamine (156 mg, 1.55 mmol, 215 μL) was added and the solution was cooled to 0 ºC using an ice bath. 1-Benzothiophene-2-sulfonyl chloride (120 mg, 0.52 mmol) was dissolved in dry THF (1.5 mL) in a 25 mL dry round-bottom flask. This solution was added dropwise to the (*R,R*)-DPEN solution and the resulting solution was left overnight at r.t. Saturated $NaHCO_3$ (20 mL) was added to the mixture and the crude product was extracted using DCM (3 x 30 mL). The combined extracts were washed with brine (20 mL) and dried using $MgSO_4$ and filtered. The solvent was removed under reduced pressure to afford the crude product. Purification by column chromatography using silica gel (50% Petroleum ether: 50% EtOAc) gave the pure product (198 mg, 0.484 mmol, 94%) as a white solid; TLC: Rf ca 0.44 (100% EtOAc), strong UV and $KMnO_4$; Mp 140 °C; $[\alpha]_D^{25}$ -62.5 (*c* 0.07 in $CHCl_3$); ν_{max} 3356, 3296, 3151, 3057, 3024, 2877 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.75 (1 H, d, *J* 8.0, CH of benzo[b]thiophene), 7.67 (1 H, d, *J* 8.0, CH of benzo[b]thiophene), 7.51 – 7.37 (2 H, m, CH of benzo[b]thiophene), 7.33 – 7.26 (3 H, m, ArH of DPEN), 7.26 – 7.12 (5 H, m, ArH of DPEN), 7.03 (2 H, t, *J* 7.5, ArH of DPEN), 6.94 (1 H, t, *J* 7.3, CH of benzo[b]thiophene), 4.61 (1 H, br. s, NCH), 4.25 (1 H, d, J 4.3, NCH), NH not observed; δ_C (101 MHz, $CDCl_3$) 141.72 (C), 141.28 (C), 141.11 (C), 139.38 (C), 137.66 (C), 128.66 (CH), 128.40 (CH), 128.27 (CH), 127.62 (CH), 127.50 (CH), 126.76 (CH), 126.32 (CH), 125.50 (CH), 124.99 (CH), 122.45 (CH), 63.48 (NCH), 60.28 (NCH); MS (ESI^+): m/z, 409.1 [$(M + H)^+$]; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{22}H_{21}N_2O_2S_2$ 409.1039, found 409.1032 (1.8 ppm error).

δ_H (400 MHz, $CDCl_3$)

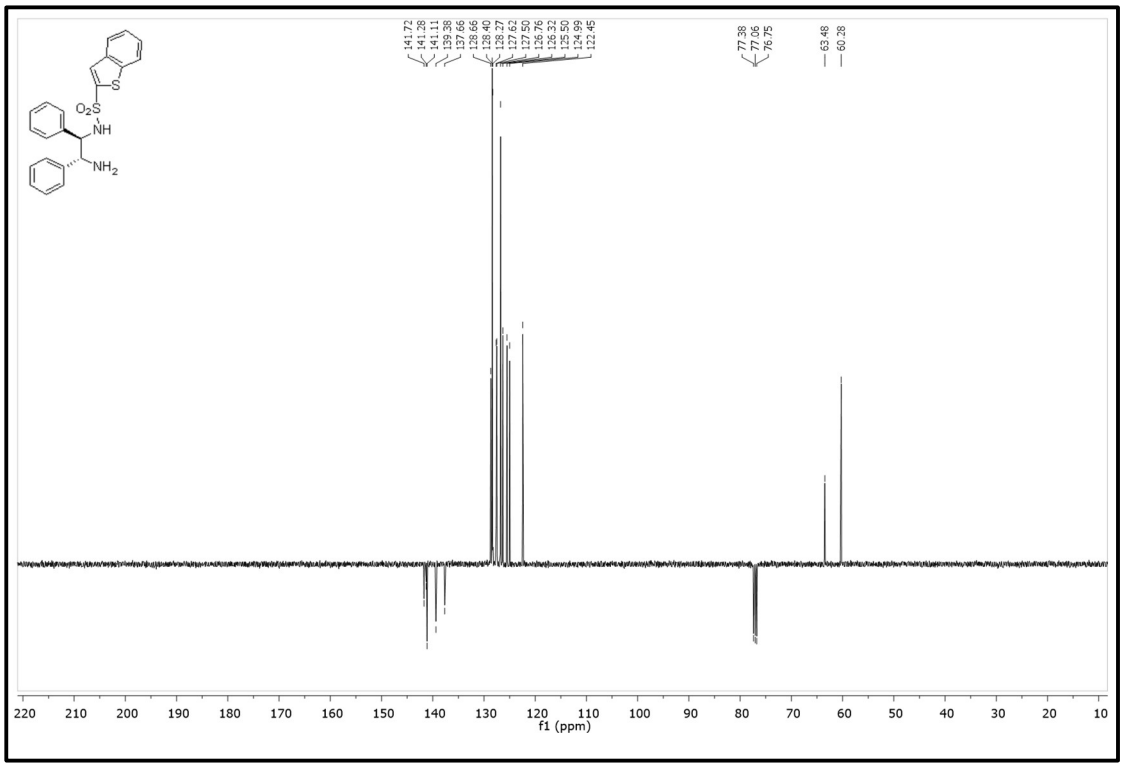


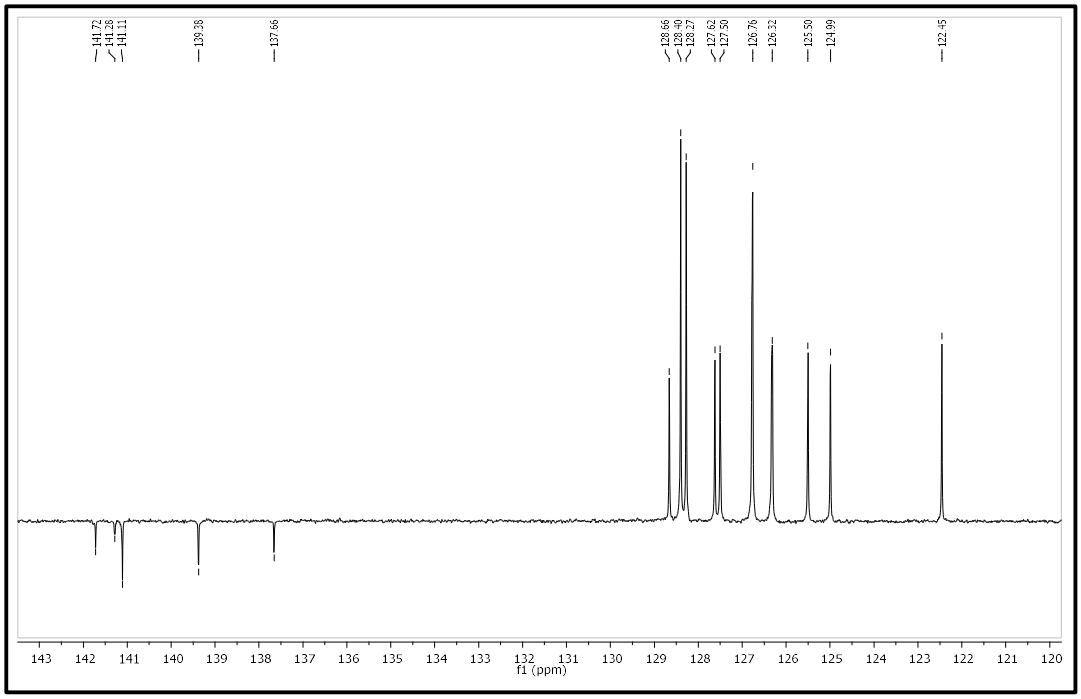


COSY (400 MHz, $CDCl_3$)

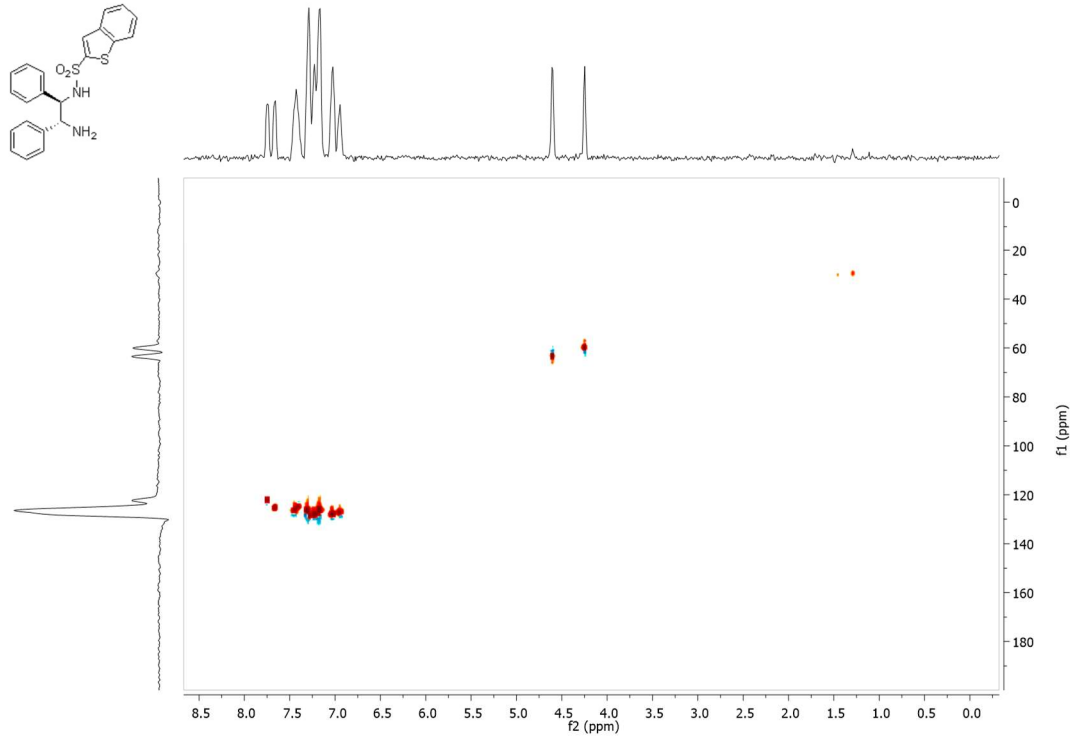


δ_C (101 MHz, $CDCl_3$)

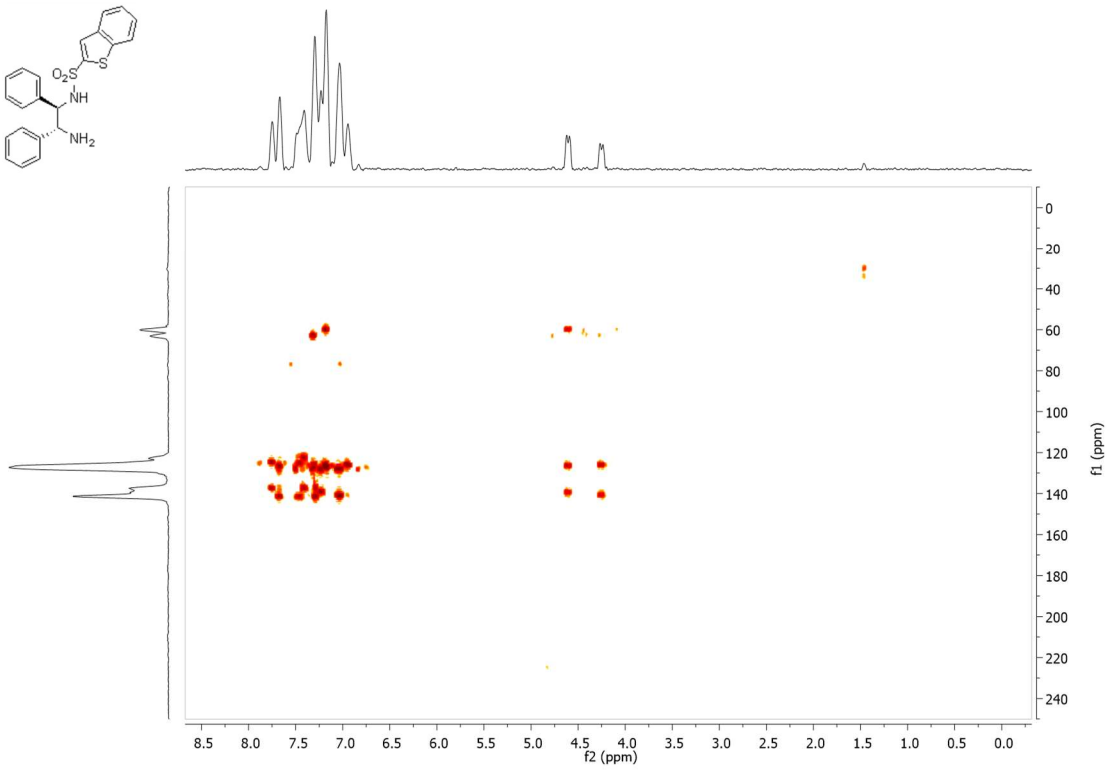




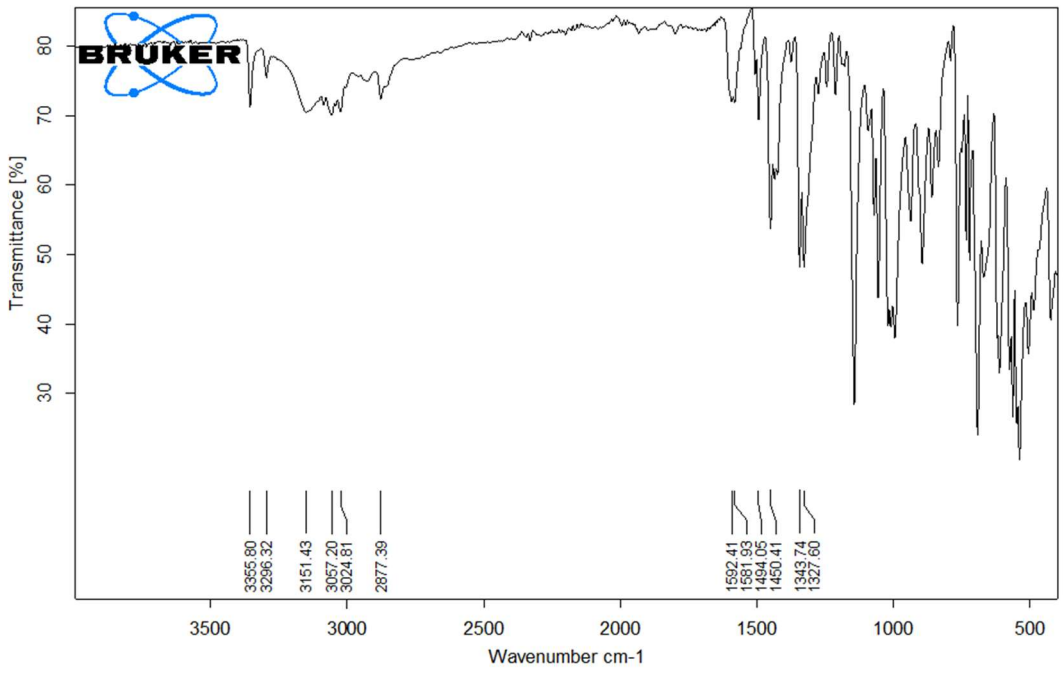
HSQC (400 MHz, $CDCl_3$)



HMBC (400 MHz, $CDCl_3$)



IR spectra



C:\Users\chemist\Desktop\Spectral Data\NK223LIGANDBENZOTHIOPHENE.0	NK223LIGANDBENZOTHIOPHENE	Instrument type and	11/11/2021

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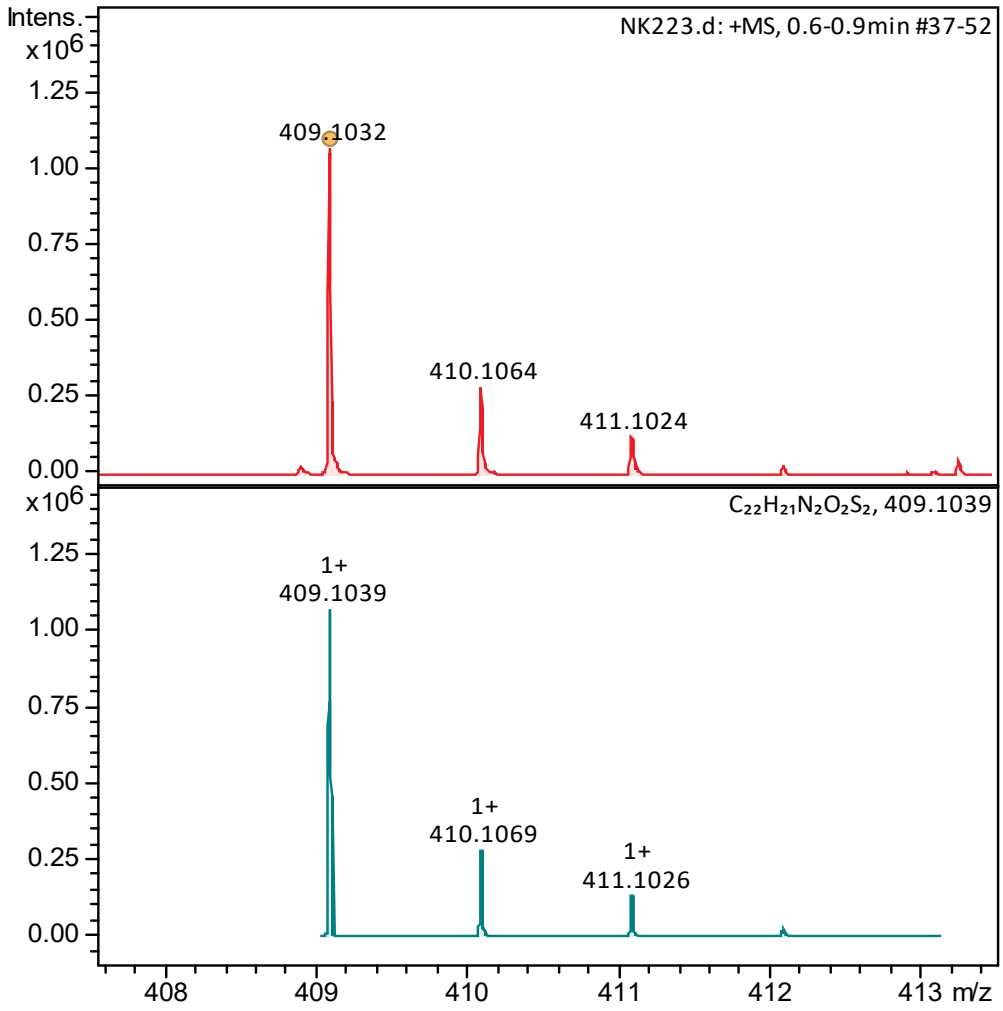
HRMS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0.25
0.00
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x10^6
1.25
1.00
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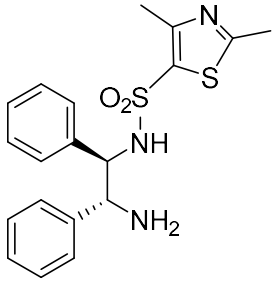
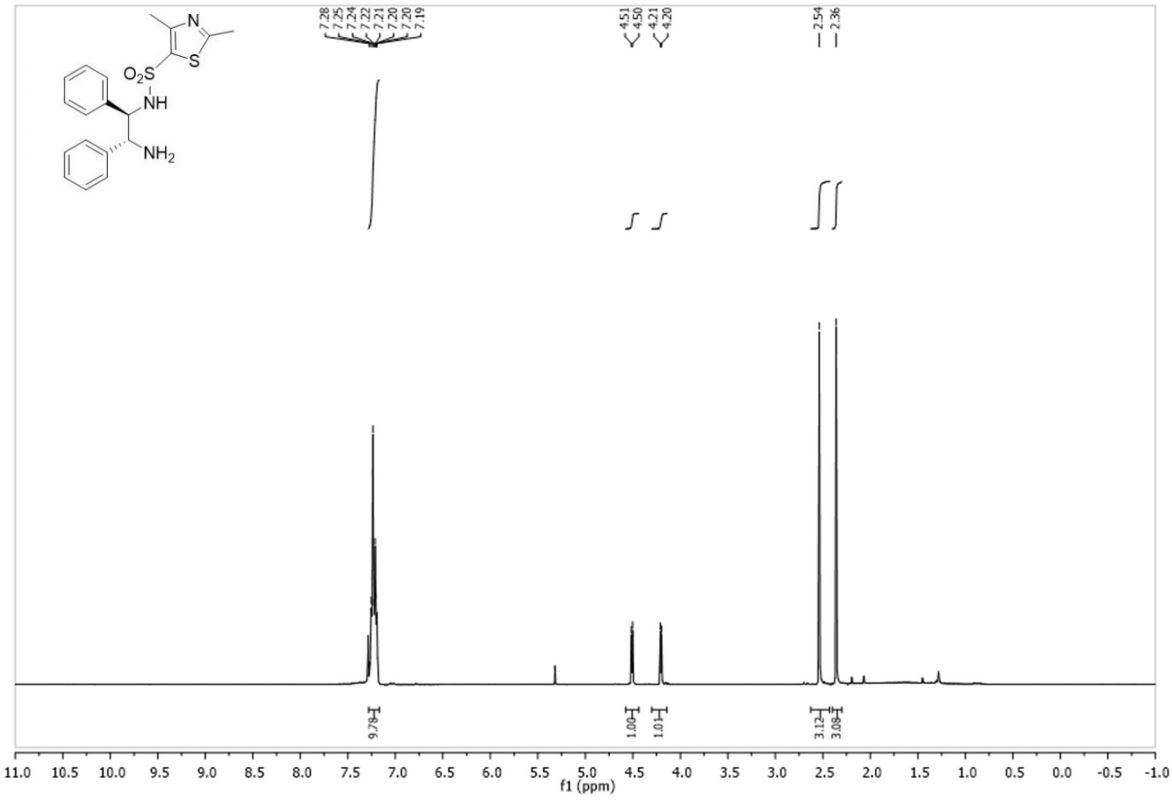
0.25
0.00
C22H21N2O2S2, 409.1039
1+
409.1039
1+
410.1069
1+
411.1026
408
409
410
411
412
413 m/z

***N*-((*1R,2R*)-2-Amino-1,2-diphenylethyl)-2,5-dimethylthiazole-4-sulfonamide 11c.**

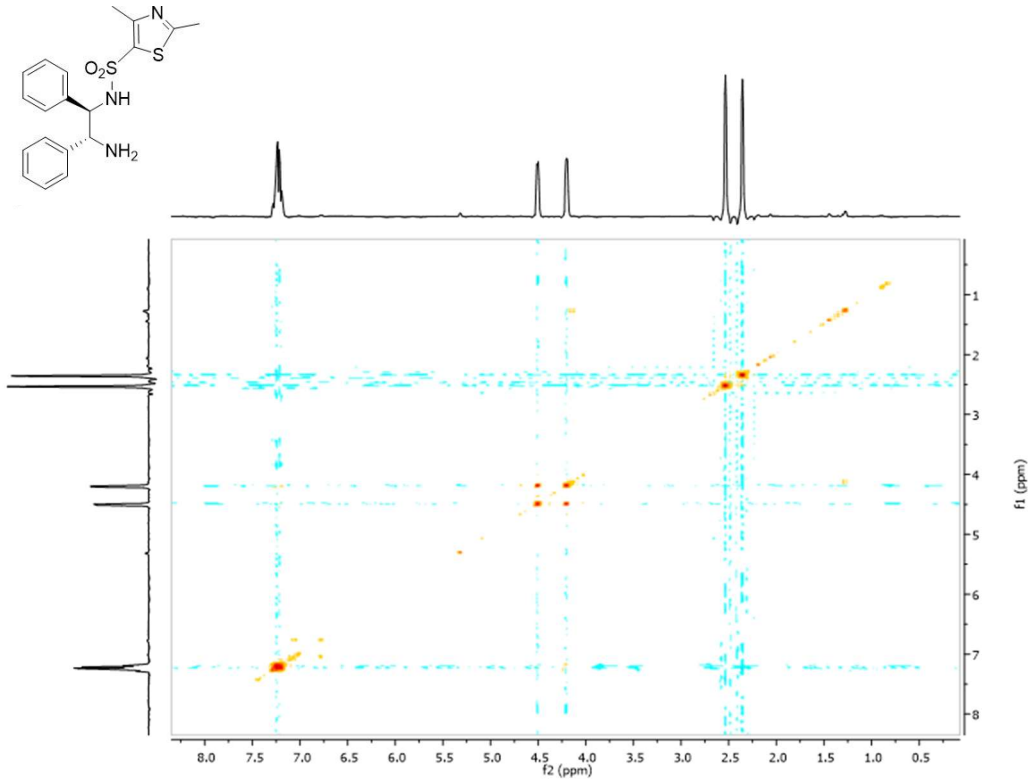


This compound is novel. Under a nitrogen atmosphere, a 100 mL dry round-bottom flask charged with (*R,R*)-DPEN (150 mg, 0.71 mmol) dissolved in dry THF (6 mL). Triethylamine (218 mg, 2.16 mmol, 300 µL) was added and the resulting solution was cooled to 0 ºC using an ice bath. 2,4-Dimethylthiazole-5-sulfonyl chloride (150 mg, 0.71 mmol) was dissolved in dry THF (1.5 mL) in a 25 mL dry round-bottom flask. This solution was added dropwise to the (*R,R*)-DPEN solution and the resulting solution was left overnight at r.t. Saturated $NaHCO_3$ (20 mL) was added to the mixture and the crude product was extracted using DCM (3 x 30 mL) and the combined extracts were washed with brine (20 mL), then dried using $MgSO_4$ and filtered. The solvent was removed under reduced pressure to afford the crude product. Purification by column chromatography using silica gel (50% Petroleum ether : 50% EtOAc, then 20% MeOH: 80% EtOAc) gave the pure product (159.3 mg, 0.412 mmol, 58%) as a yellow solid; TLC: Rf ca 0.24 (100% EtOAc), strong UV and $KMnO_4$; Mp 120 °C; $[\alpha]_D^{25}$ +7.6 (*c* 0.09 in $CHCl_3$); ν_{max} 3335, 3295, 3190, 3087, 3058, 3024, 2922 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.25 – 7.14 (10 H, m, ArH), 4.49 (1 H, t, *J* 5.0, NCH), 4.18 (1 H, d, *J* 5.0, NCH), 2.51 (3 H, s, CH_3), 2.33 (3 H, s, CH_3), NH not observed; δ_C (101 MHz, $CDCl_3$) 168.06 (C), 155.27 (C), 141.28 (C), 139.03 (C), 130.23(C), 128.52 (CH), 128.42 (CH), 127.70 (CH), 127.67 (CH), 126.81 (CH), 126.36 (CH), 63.32 (NCH), 60.35 (NCH), 19.09 (CH_3), 16.20 (CH_3); MS (ESI^+): m/z, 388.1 $[(M + H)^+]$; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{19}H_{22}N_3O_2S_2$ 388.1148, found 388.1142 (1.7 ppm error).

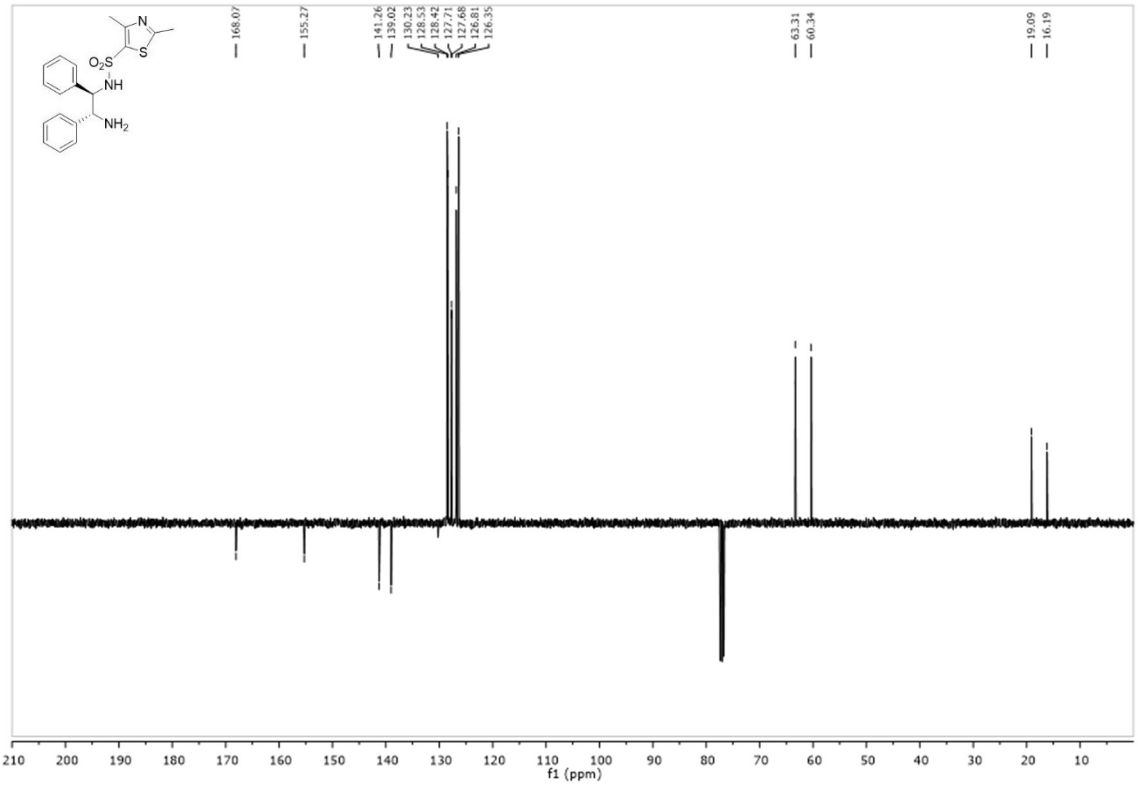
δ_H (400 MHz, $CDCl_3$)

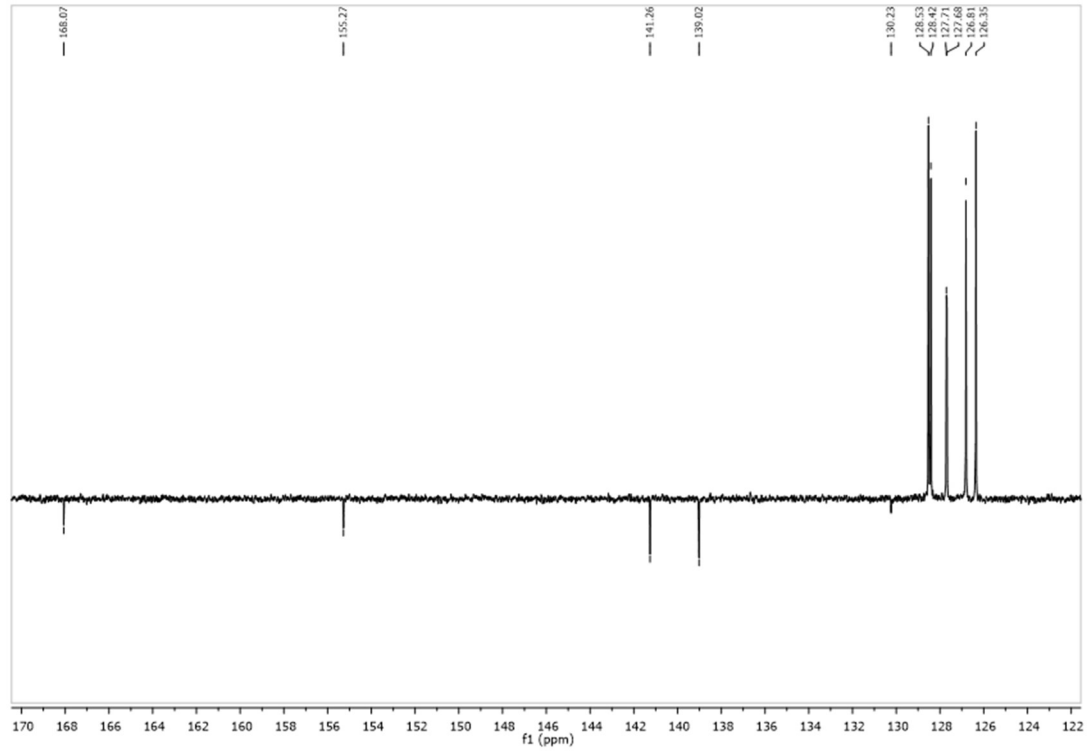


COSY (400 MHz, $CDCl_3$)

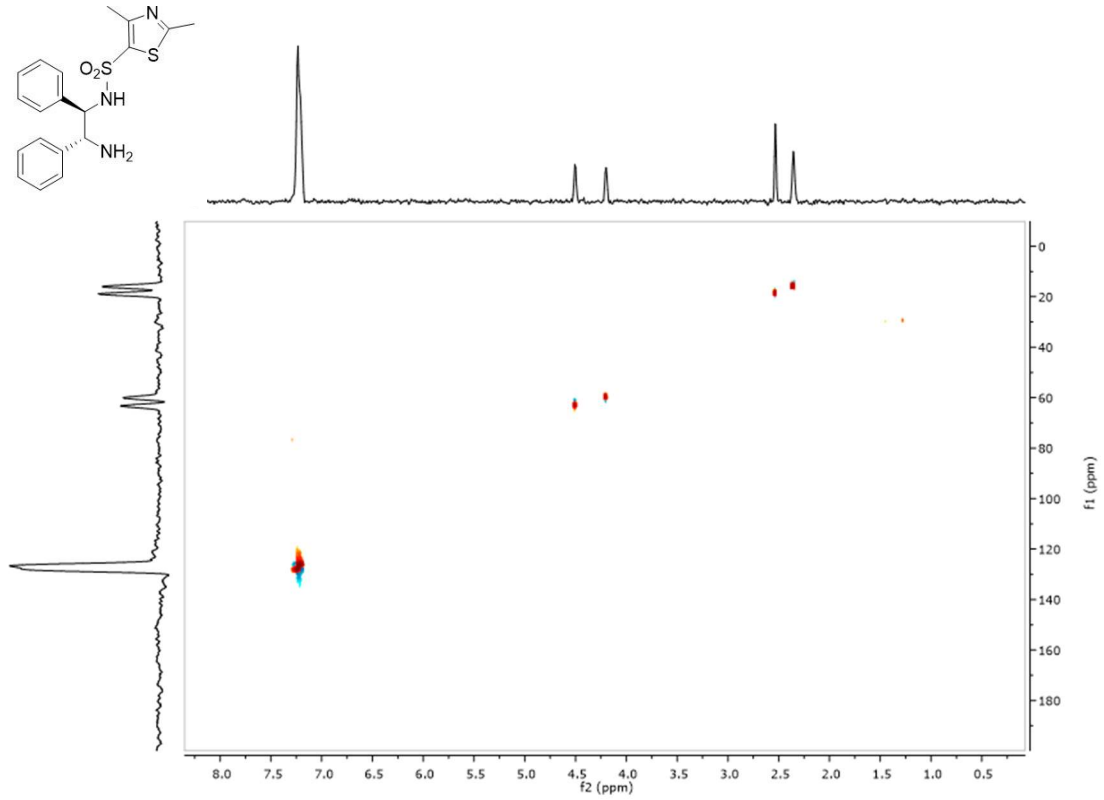


δ_C (101 MHz, $CDCl_3$)

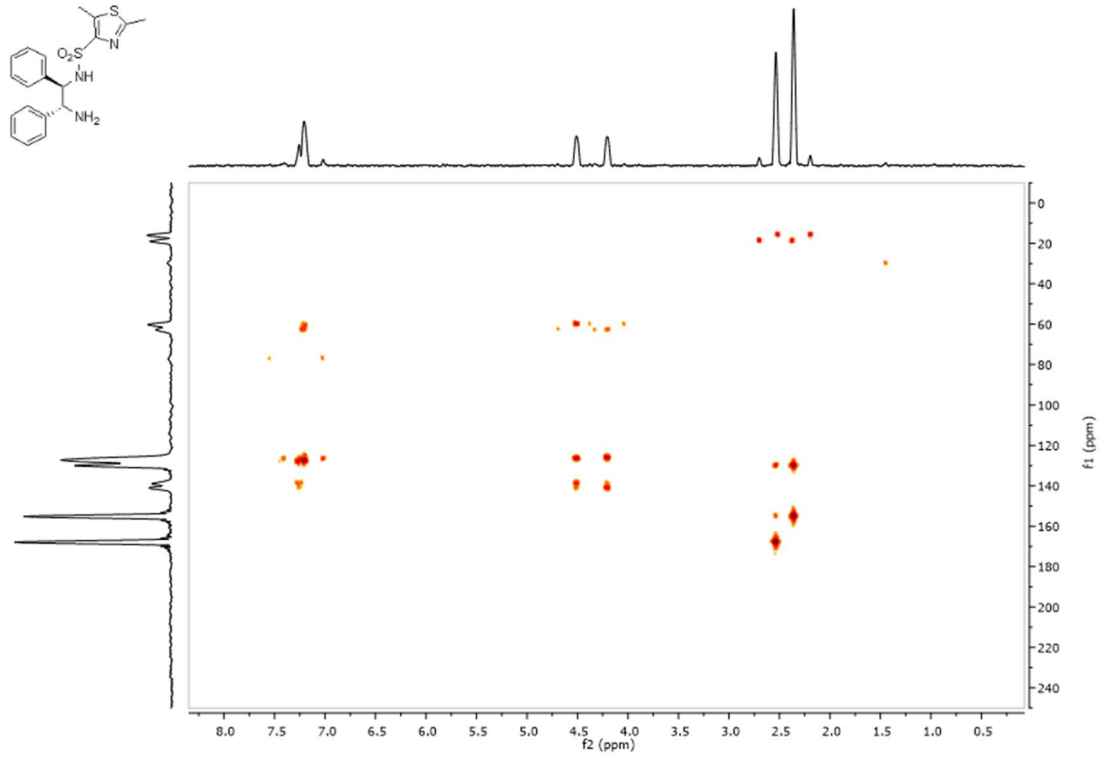




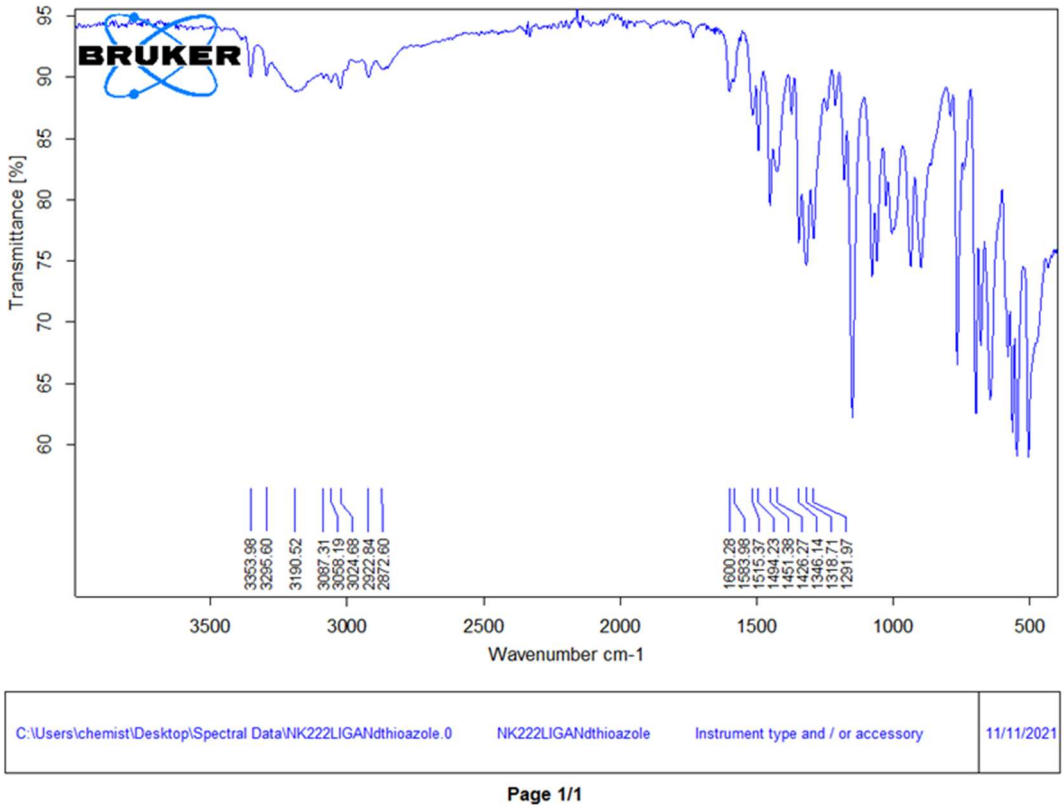
HSQC (400 MHz, $CDCl_3$)



HMBC (400 MHz, $CDCl_3$)



IR


BRUKER
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Instrument type and / or accessory
11/11/2021
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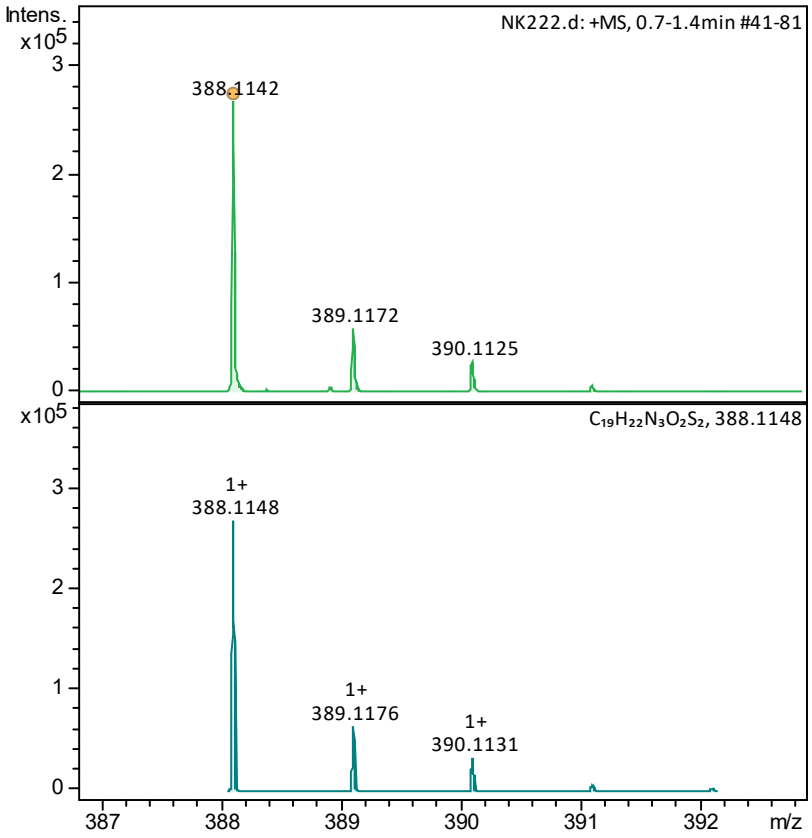
HRMS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1+
390.1131
387
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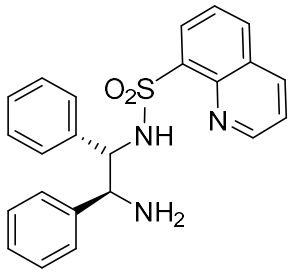
389
390
391
392
m/z

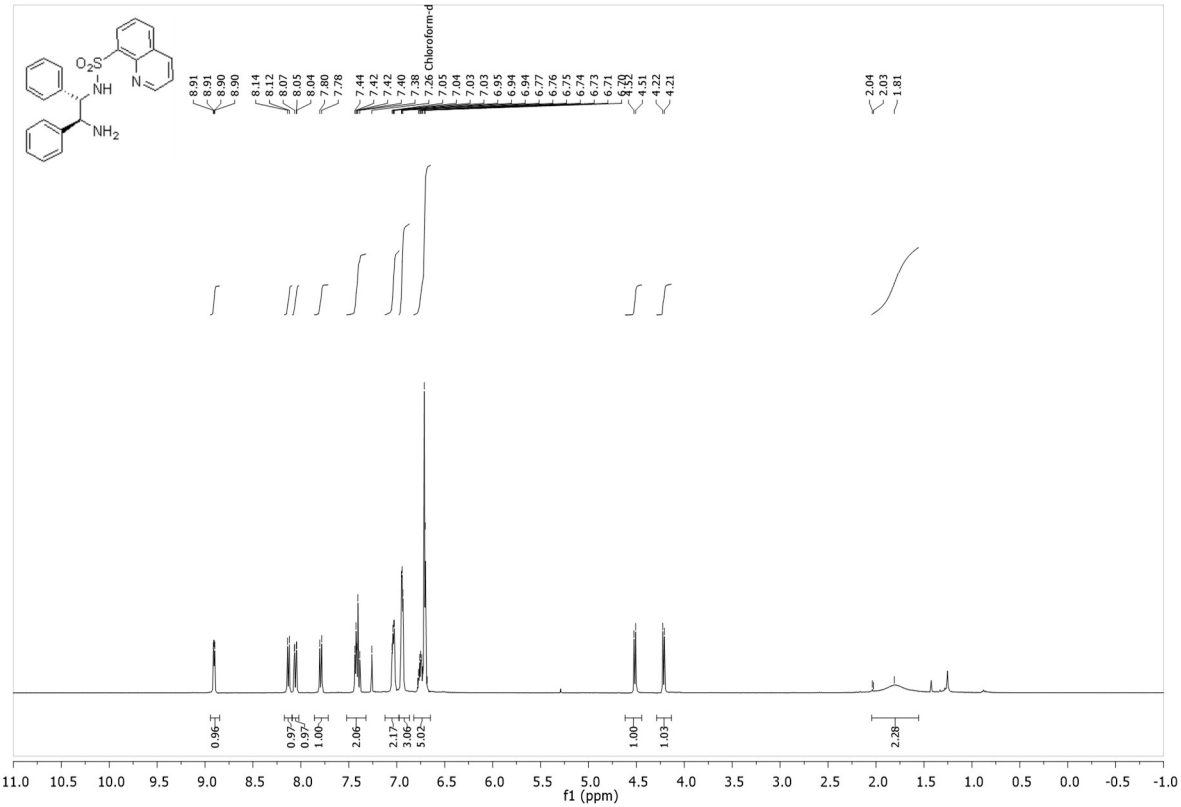
***N*-((*1S,2S*)-2-Amino-1,2-diphenylethyl)quinoline-8-sulfonamide 11d.**

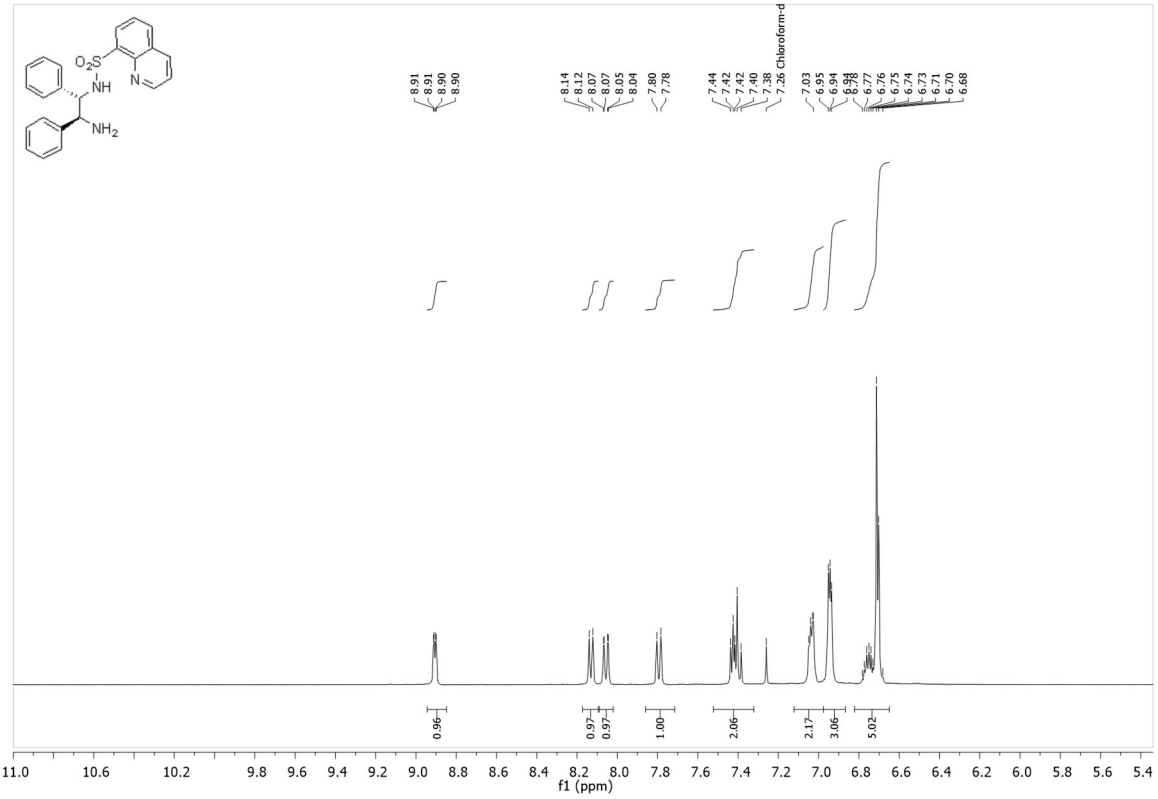


This compound has been reported.* Under a nitrogen atmosphere, in a 100 mL dry round-bottom flask was charged with (*S,S*)-DPEN (150 mg, 0.71 mmol) dissolved in dry THF (6 mL). Triethylamine (218 mg, 2.16 mmol, 300 μL) was added and the resulting solution was cooled to 0 ºC using an ice bath. 8-Quinoline sulfonyl chloride (162 mg, 0.71 mmol) was dissolved in (1.5 mL) dry THF In a 25 mL dry round-bottom flask. This solution was added dropwise to the (*S,S*)-DPEN solution and the resulting solution was left overnight at r.t. $NaHCO_3$ (20 mL) was added to the mixture and the crude product was extracted using DCM (3 x 30 mL) and then washed with brine (20 mL), dried using $MgSO_4$ and filtered. The solvent was removed under reduced pressure to afford the crude product. Purification by column chromatography using silica gel (100% EtOAc to 10% MeOH in EtOAc) gave the pure product (99.7 mg, 0.247 mmol, 35%) as a white solid; TLC: Rf ca 0.16 (100% EtOAc), strong UV and $KMnO_4$; Mp 79.5 °C; $[\alpha]_D^{26}$ -159.2 (*c* 0.2 in $CHCl_3$); ν_{max} 3034, 3005, 1612, 1595, 1564,1493 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 8.91 (1 H, dd, J 4.2, 1.3, CH of quinoline), 8.13 (1 H, d, J 7.2, CH), 8.06 (1 H, dd, J 8.3, 1.3, CH of quinoline), 7.79 (1 H, d, J 8.1, CH of quinoline), 7.47 – 7.35 (2 H, m, CH of quinoline), 7.04 (2 H, dd, J 6.4, 2.7, ArH of Ph), 6.98 – 6.90 (3 H, m, ArH of Ph), 6.80 – 6.67 (5 H, m, ArH of Ph), 4.52 (1 H, d, J 6.8, NCH), 4.22 (1 H, d, J 6.8, NCH), 2.09 – 1.42 (2 H, br.s, NH_2); δ_C (101 MHz, $CDCl_3$) 150.70 (CH), 142.95 (C), 141.15 (C), 138.29 (C), 136.81 (C), 136.49 (CH), 132.74 (CH), 130.12 (CH), 128.49 (C), 127.81 (CH), 127.39 (CH), 127.18 (CH), 126.99 (CH), 126.93 (CH), 126.70 (CH), 125.26 (CH), 121.85 (CH), 65.49 (NCH), 60.27 (NCH); MS (ESI^+): m/z, 404.1 [$(M+H)^+$]; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{23}H_{22}N_3O_2S$ 404.1427, found 404.1420 (1.8 ppm error).

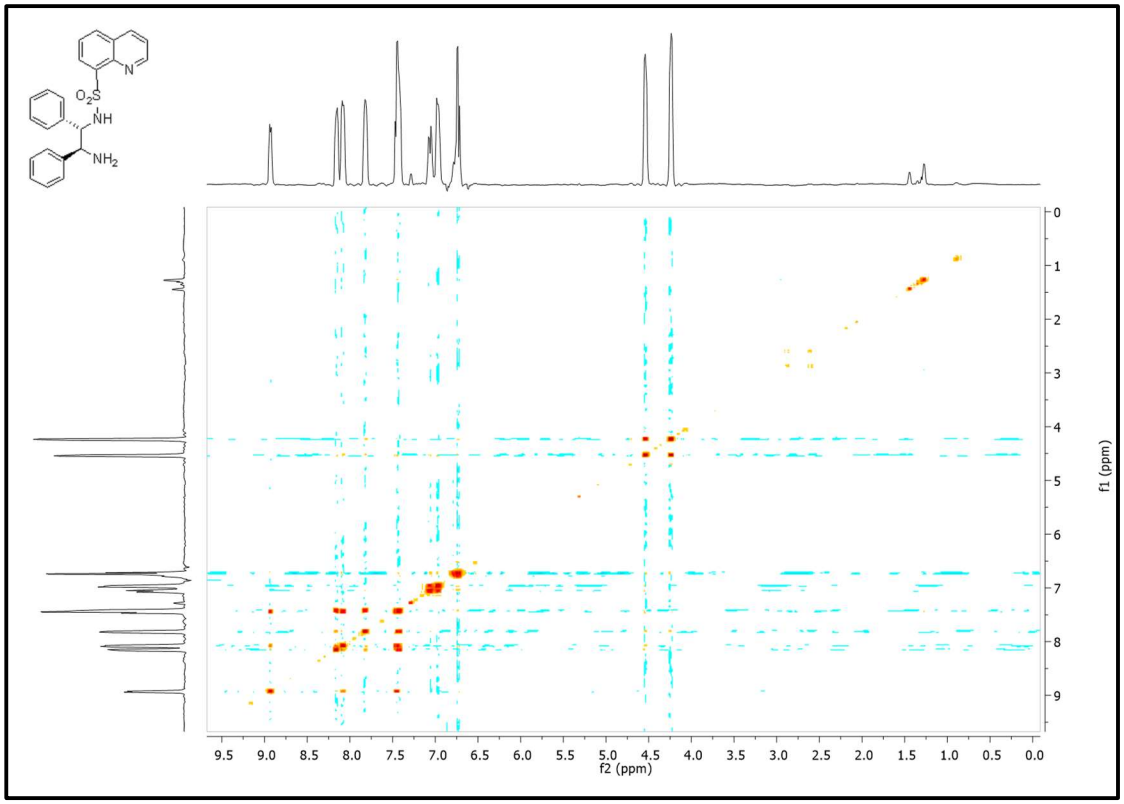
* D. E. Dong, J. L. Zhang, W. Z. Zheng, L. Zuo and L. F. Zhang, *Chen. Chem. Lett.* 2000, **11**, 383-384.

δ_H (400 MHz, $CDCl_3$).

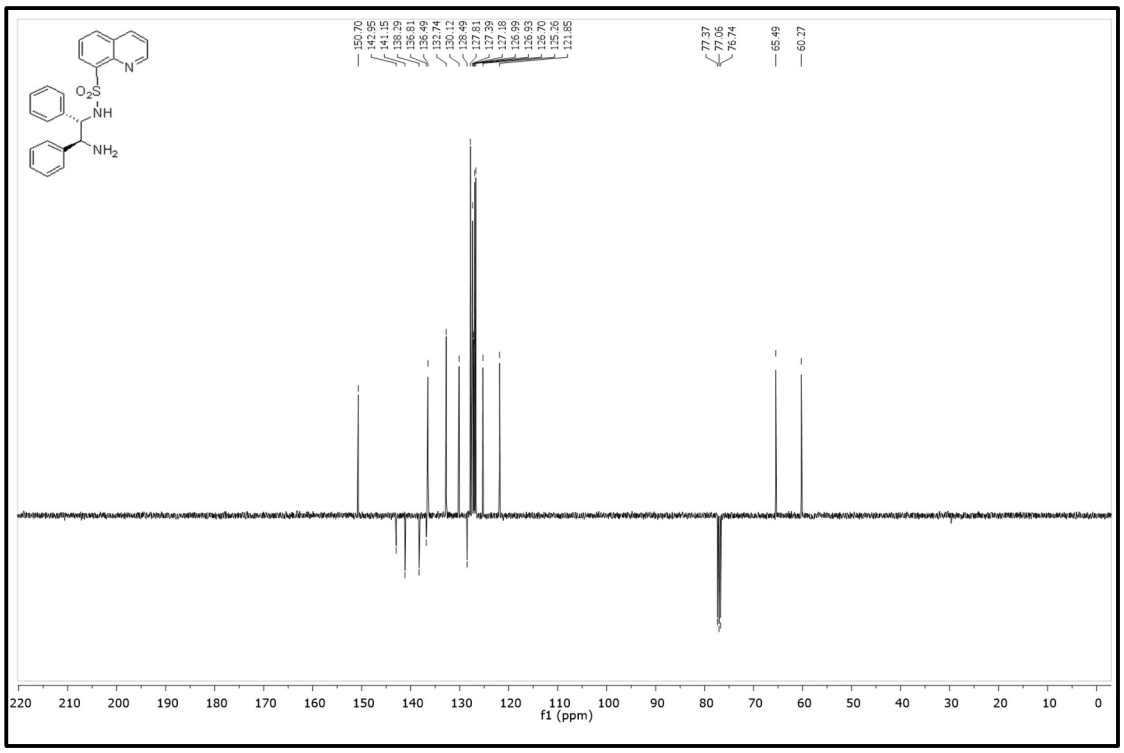


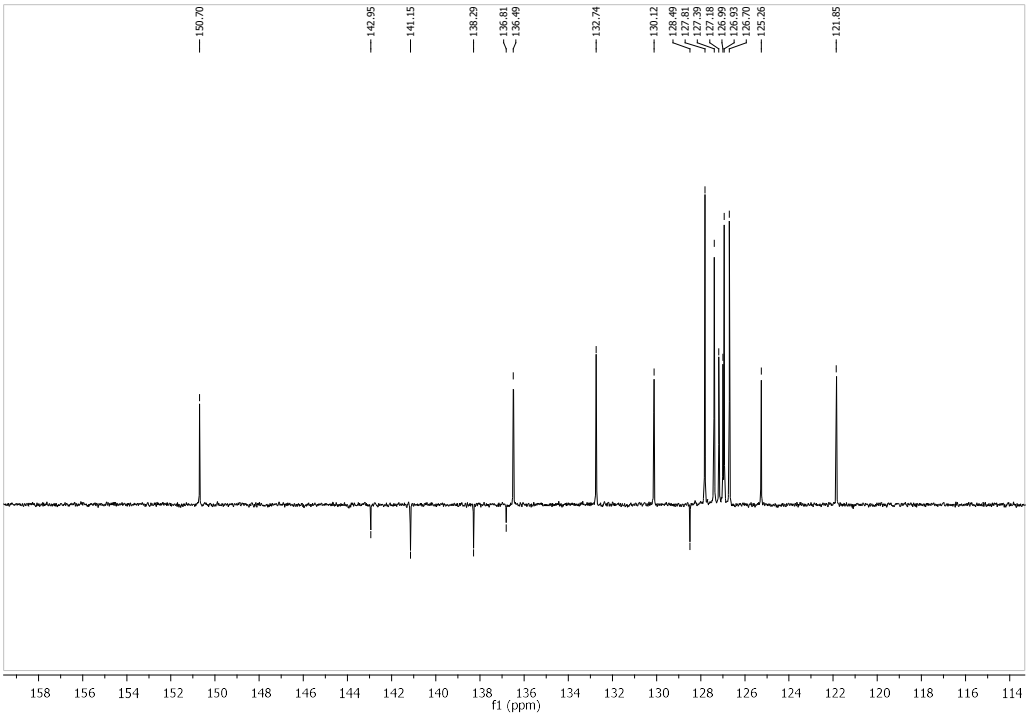


COSY (101 MHz, $CDCl_3$)

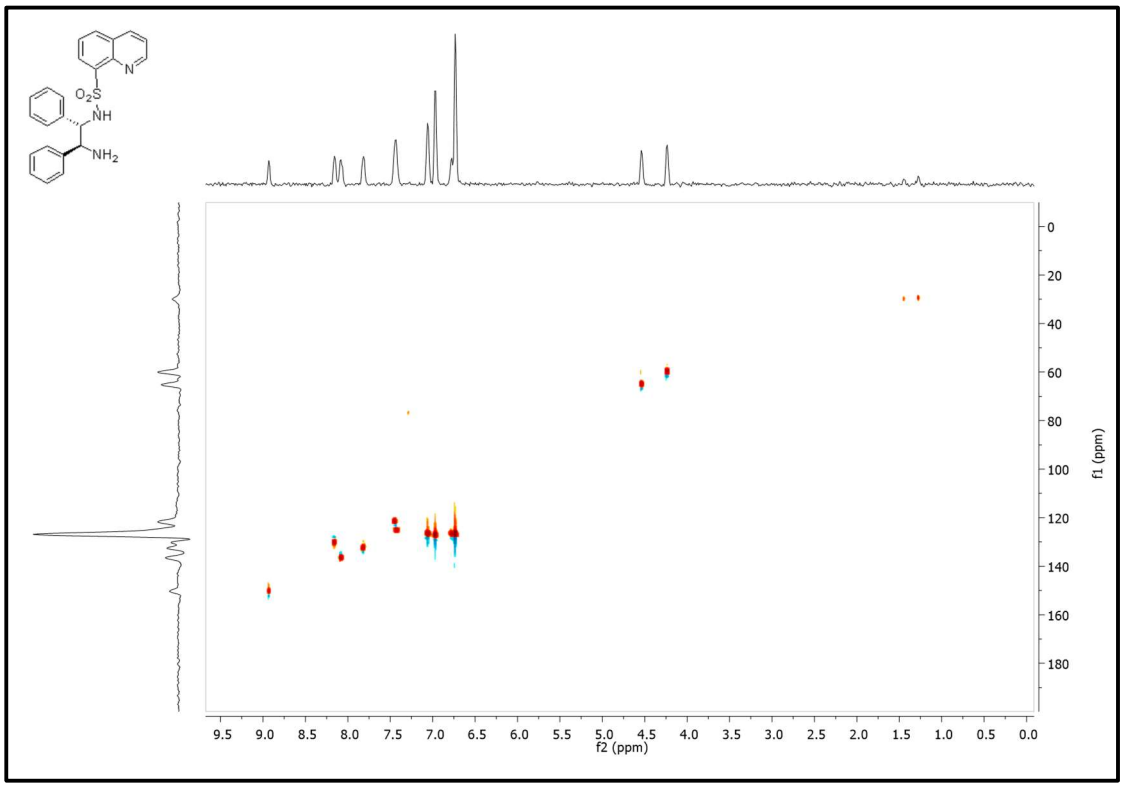


δ_C (400 MHz, $CDCl_3$)

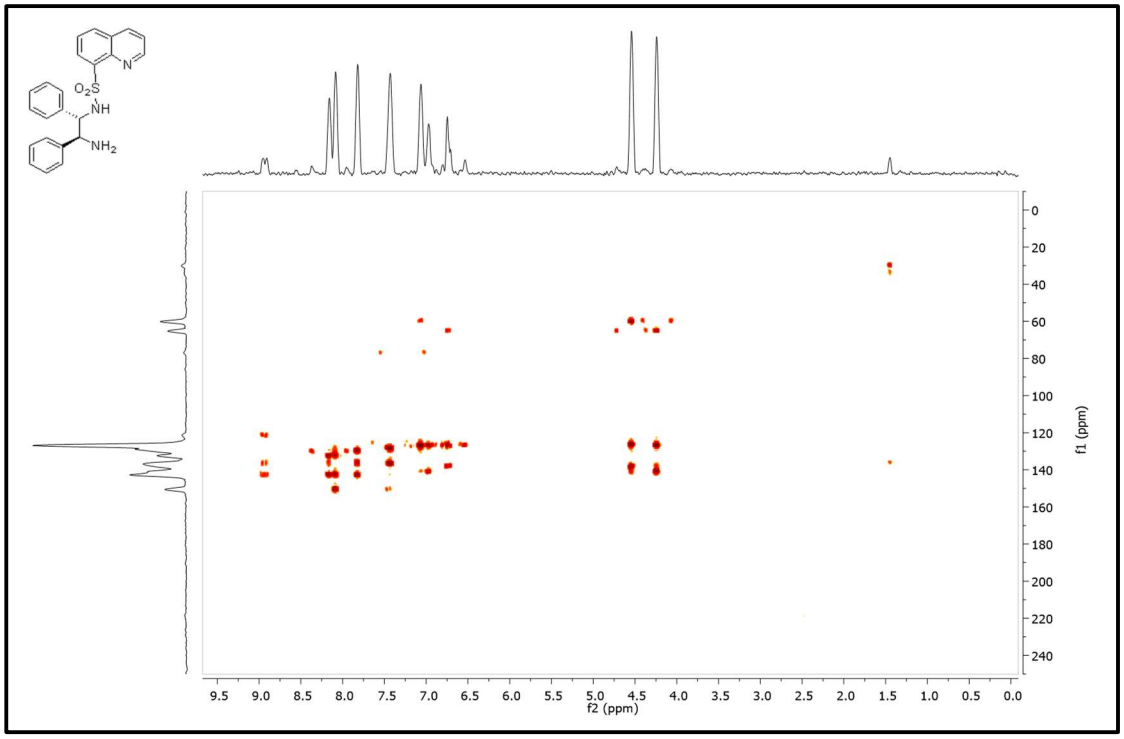




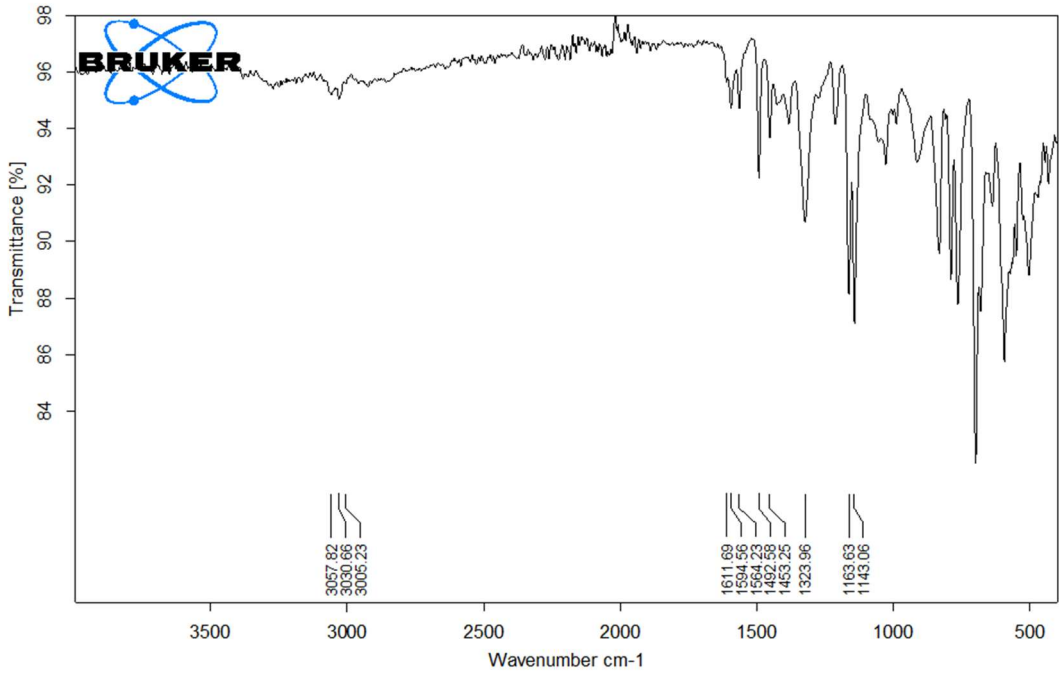
HSQC (400 MHz, $CDCl_3$)



HMBC (400 MHz, $CDCl_3$)



IR spectra



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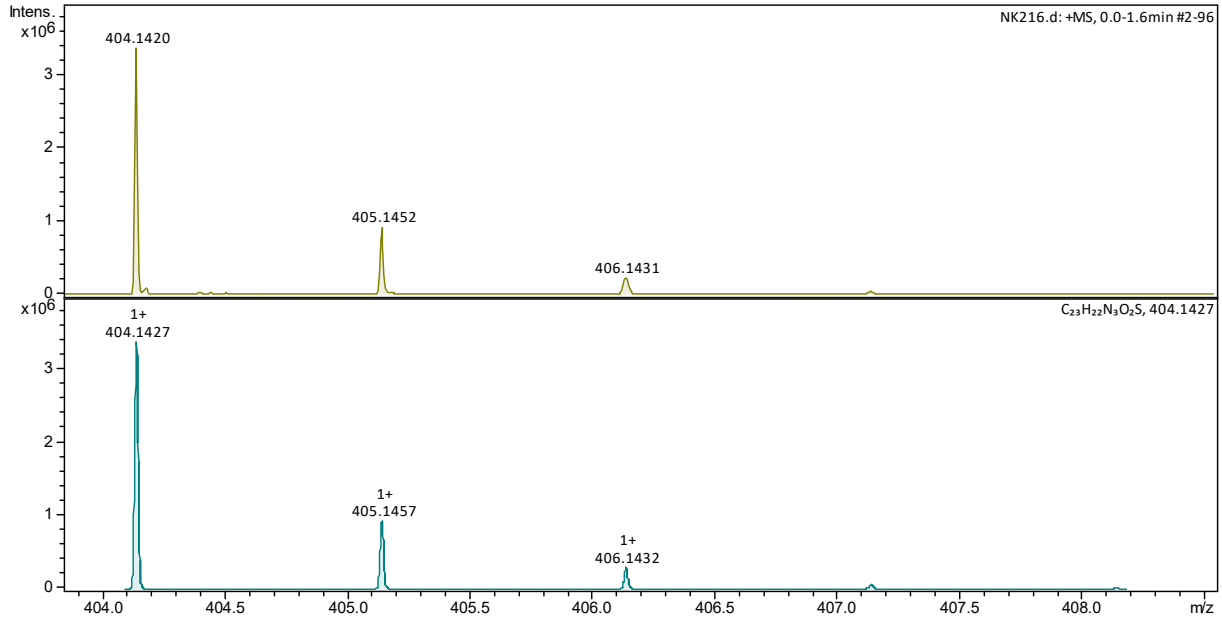
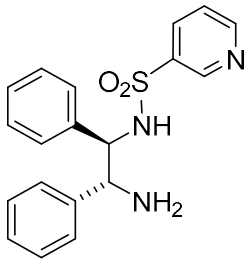
HRMS

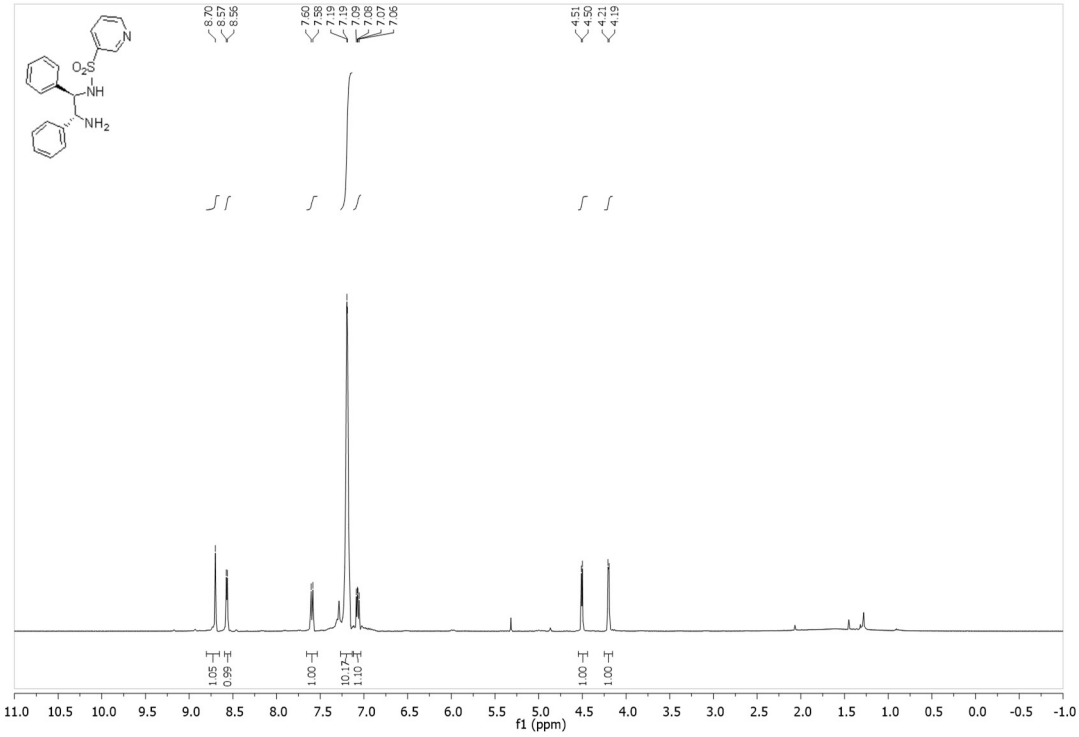

Intens.
x10^6
404.1420
405.1452
406.1431
NK216.d: +MS, 0.0-1.6min #2-96
1+
404.1427
1+
405.1457
1+
406.1432
C23H22N3O2S, 404.1427
m/z

***N*-((*1R,2R*)-2-Amino-1,2-diphenylethyl)pyridine-3-sulfonamide 11f.**

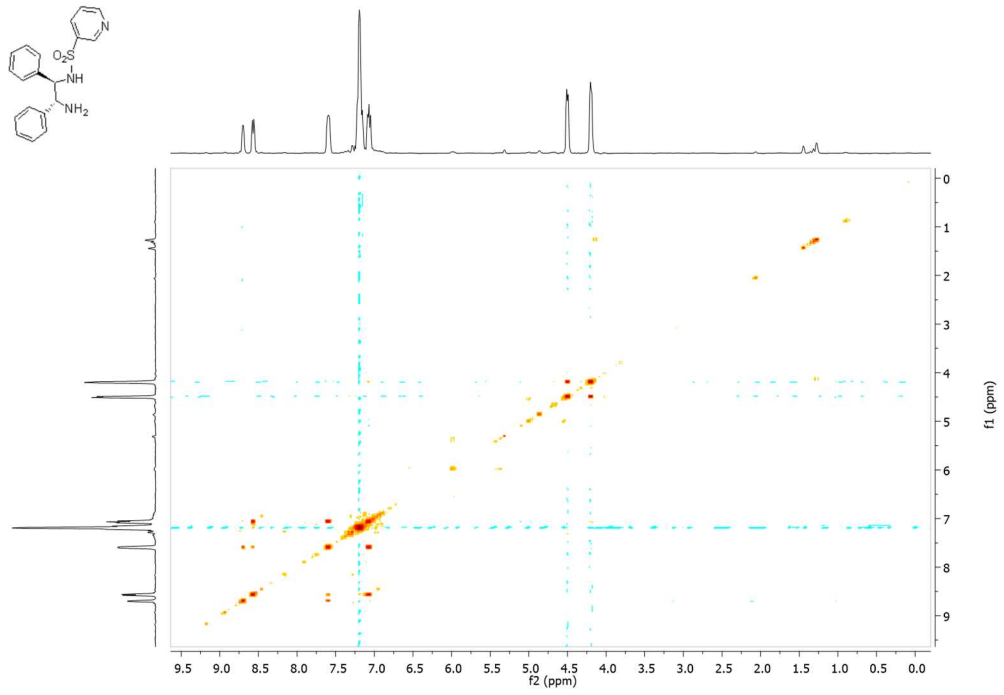


This compound is novel. Under a nitrogen atmosphere, a 100 mL dry round flask was charged with (*R,R*)-DPEN (200 mg, 0.94 mmol) dissolved in dry THF (6 mL). Triethylamine (380 mg, 3.76 mmol, 530 μL) was added to the solution and this was cooled to 0 ºC using an ice bath. In a 25 mL dry round flask, pyridine-3-sulfonyl chloride (201 mg, 1.13 mmol) was dissolved in dry THF (2 mL). The solution of pyridine-3-sulfonyl chloride was added dropwise to the (*R,R*)-DPEN solution and left overnight at rt. Saturated $NaHCO_3$ (20 mL) was added to the mixture and the crude product was extracted using DCM (3 x 30 mL) and then washed with brine (20 mL) and dried using $MgSO_4$. The solvent was removed under reduced pressure to afford the crude product. Purification by column chromatography using silica gel (100% DCM to 100% EtOAc) gave the pure product (119 mg, 0.337 mmol, 36%) as a pale-yellow solid; TLC: Rf ca 0.27 (100% EtOAc), strong UV and $KMnO_4$; Mp 162 °C; $[\alpha]_D^{26}$ +30.8 (*c* 0.05 in $CHCl_3$); ν_{max} 3354, 3296, 2872, 2855, 1573 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 8.70 (1 H, s, ArH of pyridyl ring), 8.57 (1 H, d, *J* 4.8, ArH of pyridyl ring), 7.59 (1 H, d, *J* 8.0, ArH of pyridyl ring), 7.19 (10 H, m, ArH), 7.07 (1 H, m, ArH of pyridyl ring), 4.51 (1 H, d, *J* 4.9, NCH), 4.20 (1 H, d, *J* 5.0, NCH), NH not observed; δ_C (101 MHz, $CDCl_3$) 152.29 (CH), 147.85 (CH), 141.19 (C), 138.68 (C), 136.91 (C), 134.15 (CH), 128.57 (CH), 128.51 (CH), 127.82 (CH), 127.76 (CH), 126.95 (CH), 126.34 (CH), 123.14 (CH), 63.29 (NCH), 60.25 (NCH); MS (ESI^+): m/z, 354.1 $[M + H]^+$; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{19}H_{20}N_3O_2S$ 354.1271, found 354.1267 (1.0 ppm error).

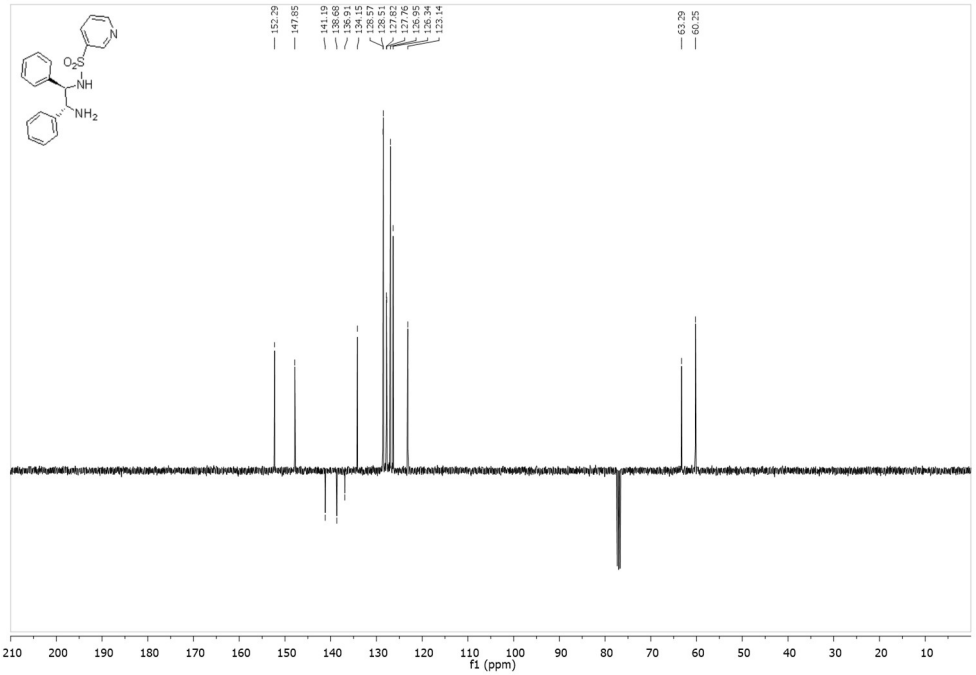
δ_H (400 MHz, $CDCl_3$)

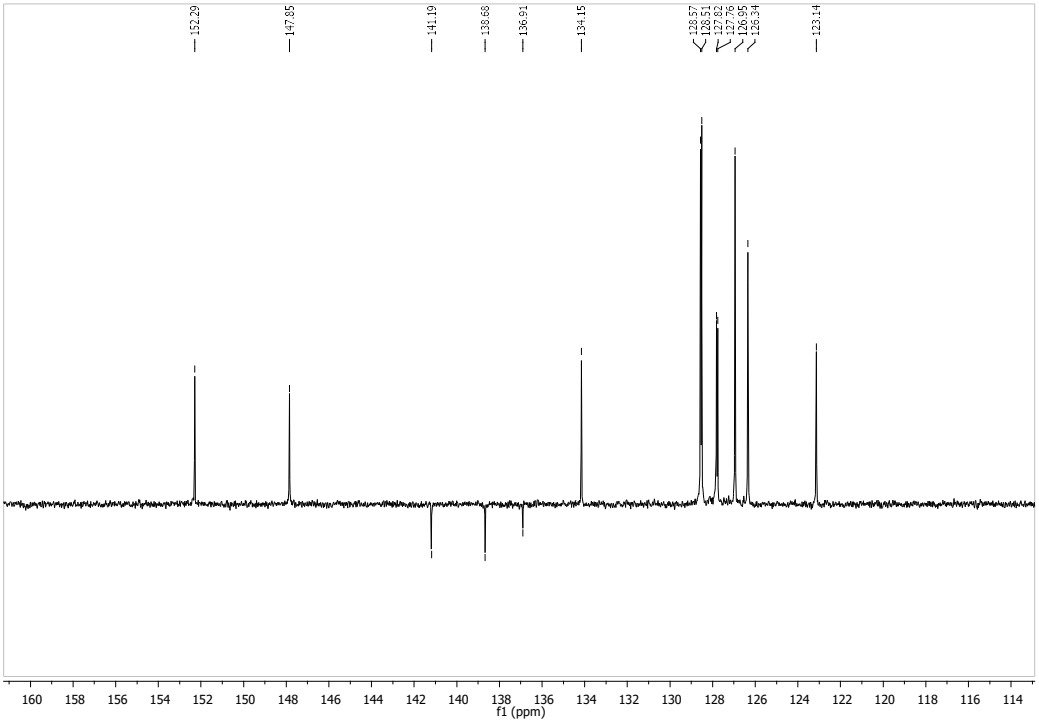


COSY (101 MHz, $CDCl_3$)

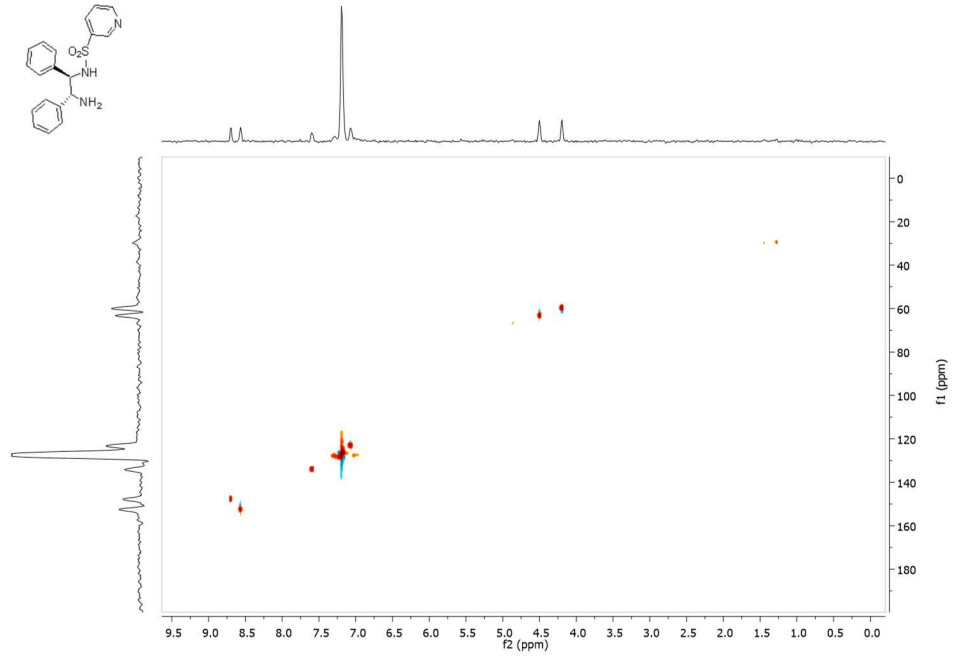


δ_C (400 MHz, $CDCl_3$)

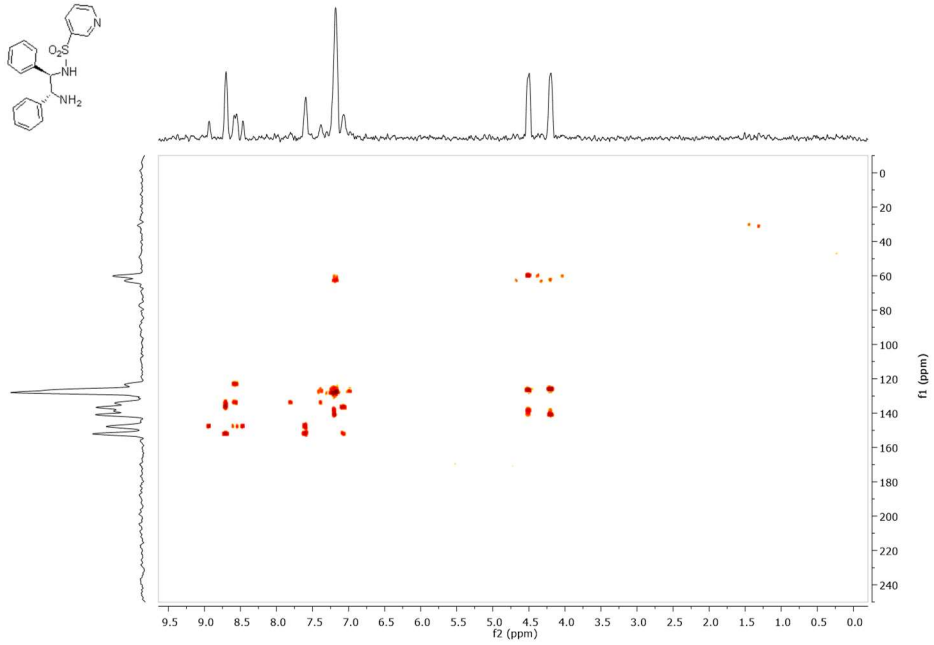




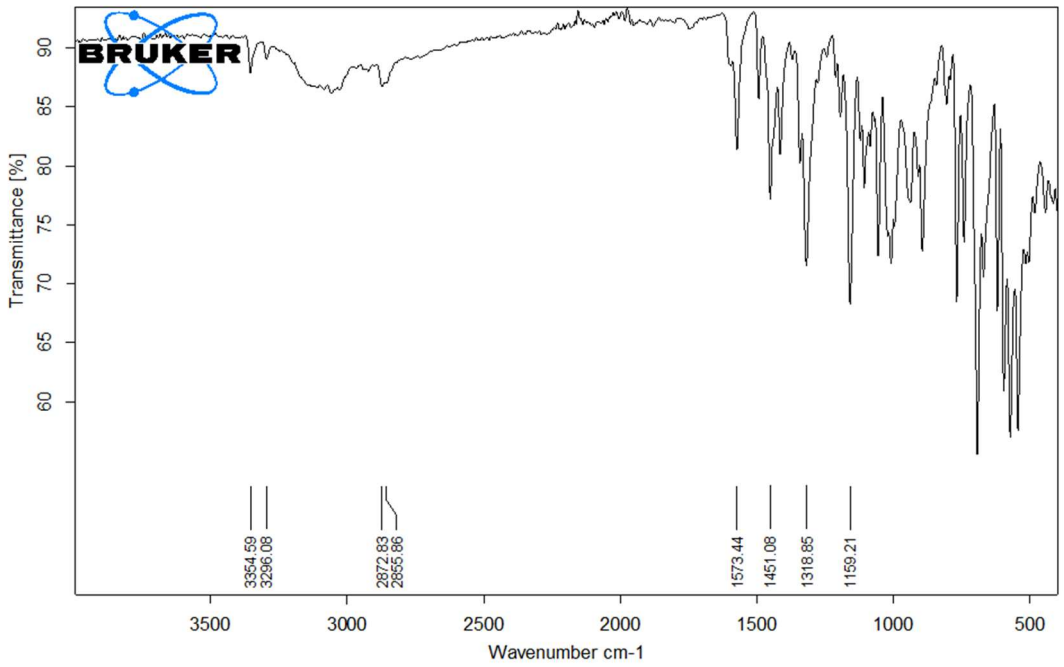
HSQC (400 MHz, $CDCl_3$)



HMBC (400 MHz, $CDCl_3$)



IR spectra



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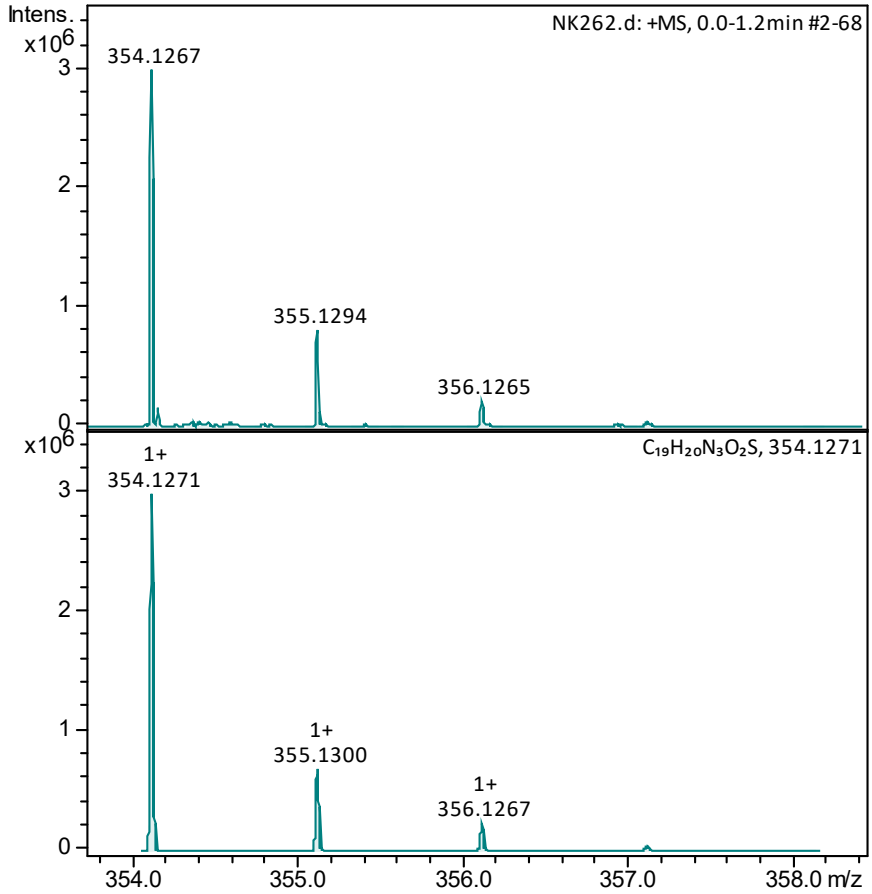
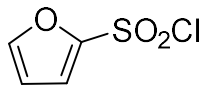
HRMS

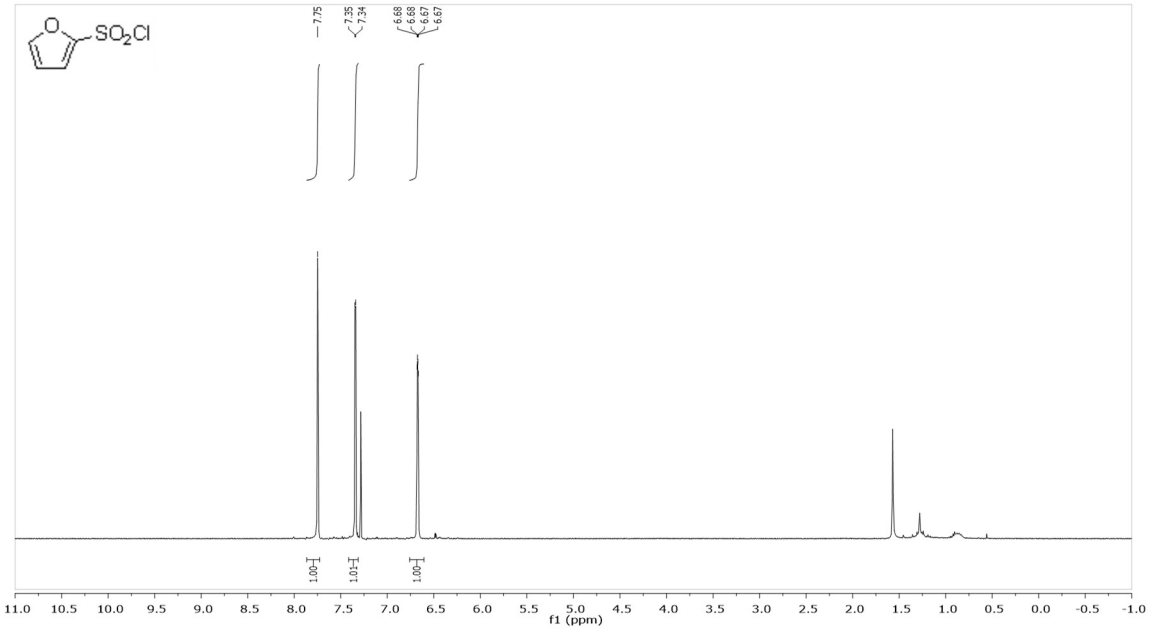


Furan-2-sulfonyl chloride.

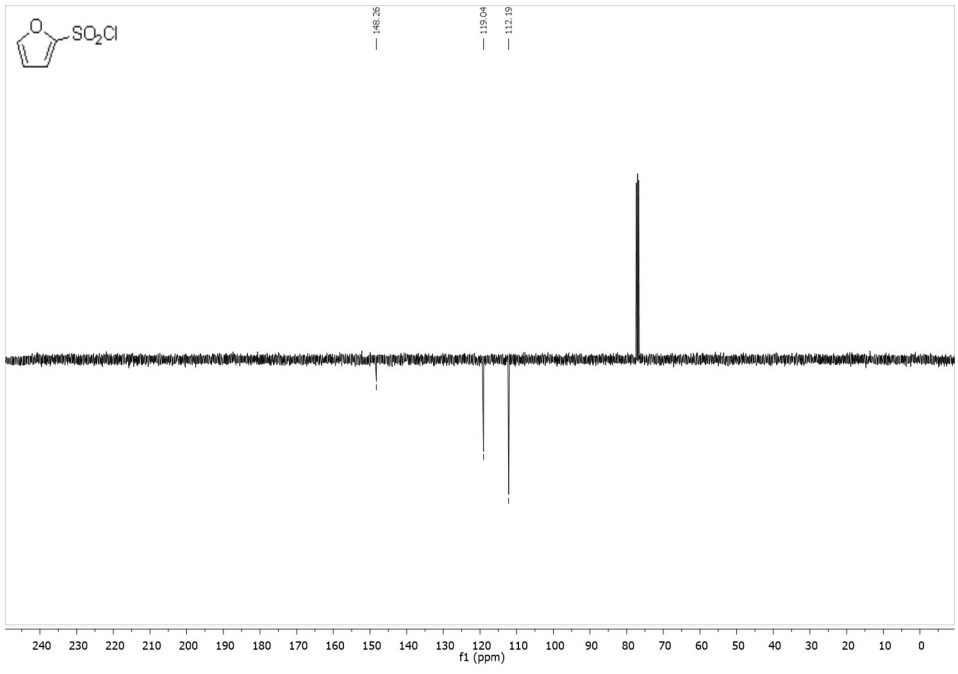


This compound is known. Under a nitrogen atmosphere, In a 25 mL dry round-bottom flask, furan (500 mg, 7.3 mmol) was dissolved in dry THF(6 mL) and cooled to 0 °C using an ice bath, t-BuLi (3.11 mL, 1.7M in pentane, 5.3 mmol) was added dropwise to the solution and left for 15 min at 0 °C. In another 50 mL dry round-bottom flask, 1,4-diazabicyclo[2.2.2]octane bis(sulfur dioxide) adduct (DABSO) (882 mg, 4.41 mmol) was suspended in dry THF (6mL) at 0 °C, then the furan solution was added to this solution dropwise and the mixture was left for 30min. NCS (1.47 g, 11 mmol) was added portionwise to the mixture at 0 °C then left to warm to r.t over 30min. The crude product was evaporated under vacuum. The crude was diluted using water (30 mL) and extracted with EtOAc (3 x 30 mL) and the combined extracts were dried using $MgSO_4$. The solvent was removed under reduced pressure to afford the crude product. Purification by column chromatography using silica gel (5% Petroleum ether: 95% EtOAc) gave the pure product (175.6 mg, 1.05 mmol, 14.4%) as a yellow oil; δ_H (400 MHz, $CDCl_3$) 7.75 (1 H, brs, furan ring), 7.34 (1 H, d, *J* 3.6, furan ring), 6.67 (1 H, m, furan ring); δ_C (101 MHz, $CDCl_3$) 148.26 (CH), 119.04 (CH), 112.19(CH), ipso CH not observed. The data matched that reported.[1]

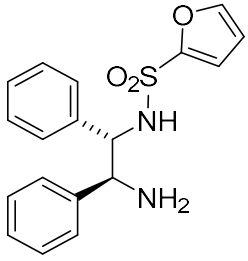
δ_H (400 MHz, $CDCl_3$)



δ_C (101 MHz, $CDCl_3$)

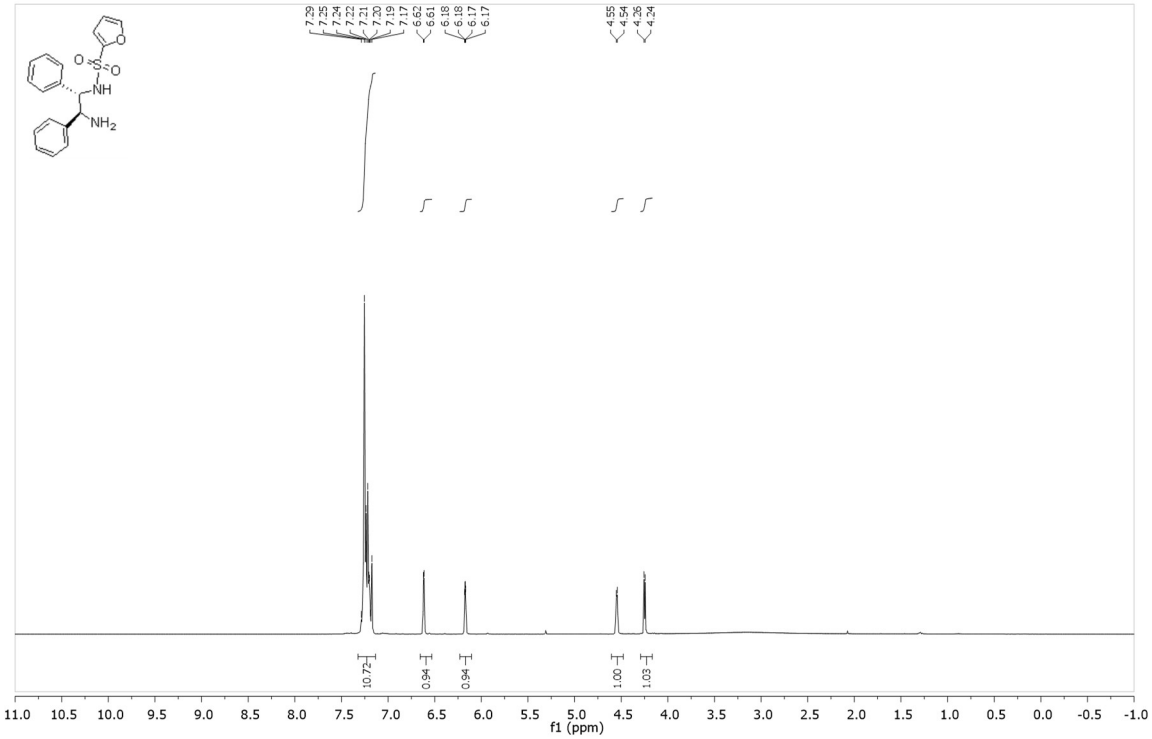


***N*-((*1S,2S*)-2-Amino-1,2-diphenylethyl)furan-2-sulfonamide 11g.**

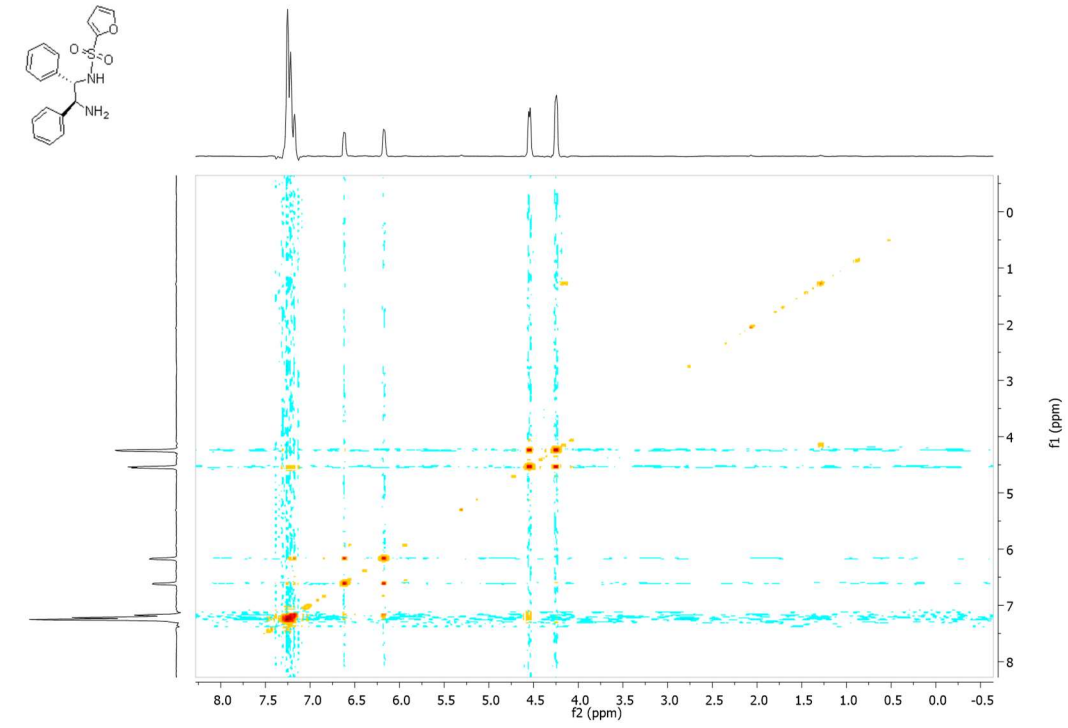


This compound is novel. Under a nitrogen atmosphere, In 100 mL dry round-bottom flask charged with (*S,S*)-DPEN (224 mg, 1.06 mmol) dissolved in dry THF (6mL). Triethylamine (320 mg, 3.17 mmol, 440 μL) was added to the solution and cooled to 0 ºC using an=ice bath. In 25 mL dry round-bottom flask, furan-2-sulfonyl chloride (175.6 mg, 1.06 mmol) was dissolved in dry THF (2 mL). This solution was added dropwise to the (*S,S*)-DPEN solution and left overnight at r.t. Saturated $NaHCO_3$ (20 mL) was added to the mixture and the crude product was extracted using DCM (3 x 30 mL) and the extracts were washed with brine (20 mL) and dried using $MgSO_4$. The solvent was removed under reduced pressure to afford the crude product. Purification by column chromatography using silica in (100% DCM to 60% DCM: 40% EtOAc) gave the pure product (237.1 mg, 0.693 mmol, 66%) as a white solid; TLC: Rf ca 0.3 (100%EtOAc), strong UV and $KMnO_4$; Mp 121 °C; $[\alpha]_D^{26}$ +12.7 (*c* 0.048 in $CHCl_3$); ν_{max} 3355, 3298, 3140, 3106, 3025, 2874 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.35 – 7.12 (11 H, m, ArH + CH of furan ring), 6.62 (1 H, d, J 3.4, CH of furan ring), 6.17 (1 H, m, CH of furan ring), 4.55 (1 H, d, J 4.6, NCH), 4.25 (1 H, d, J 4.9, NCH); δ_C (101 MHz, $CDCl_3$) 148.20 (C), 145.63 (CH), 141.25 (C), 139.34 (C), 128.51 (CH), 128.40 (CH), 127.63 (CH), 127.51 (CH), 126.69 (CH), 126.66 (CH), 115.90 (CH), 110.64 (CH), 63.34 (NCH), 60.38 (NCH); MS (ESI+): m/z, 343.1 $[M + H]^+$; HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{18}H_{19}N_2O_3S$ 343.1111, found 343.1112 (-0.3ppm error).

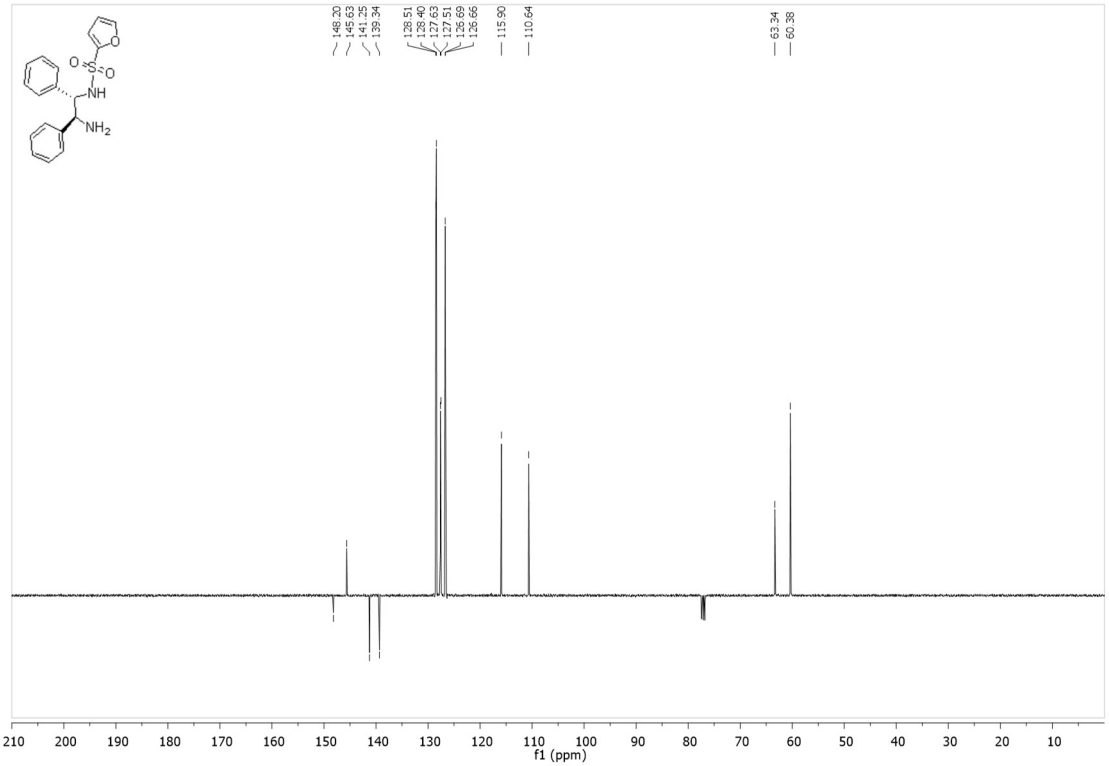
δ_H (400 MHz, $CDCl_3$)

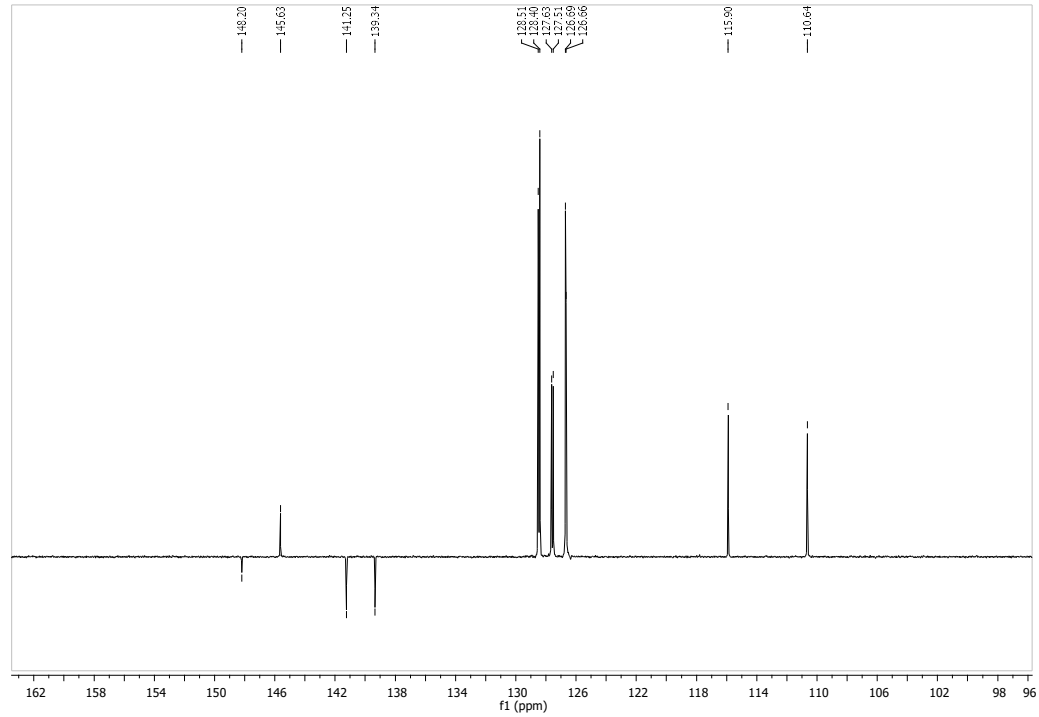


COSY (101 MHz, $CDCl_3$)

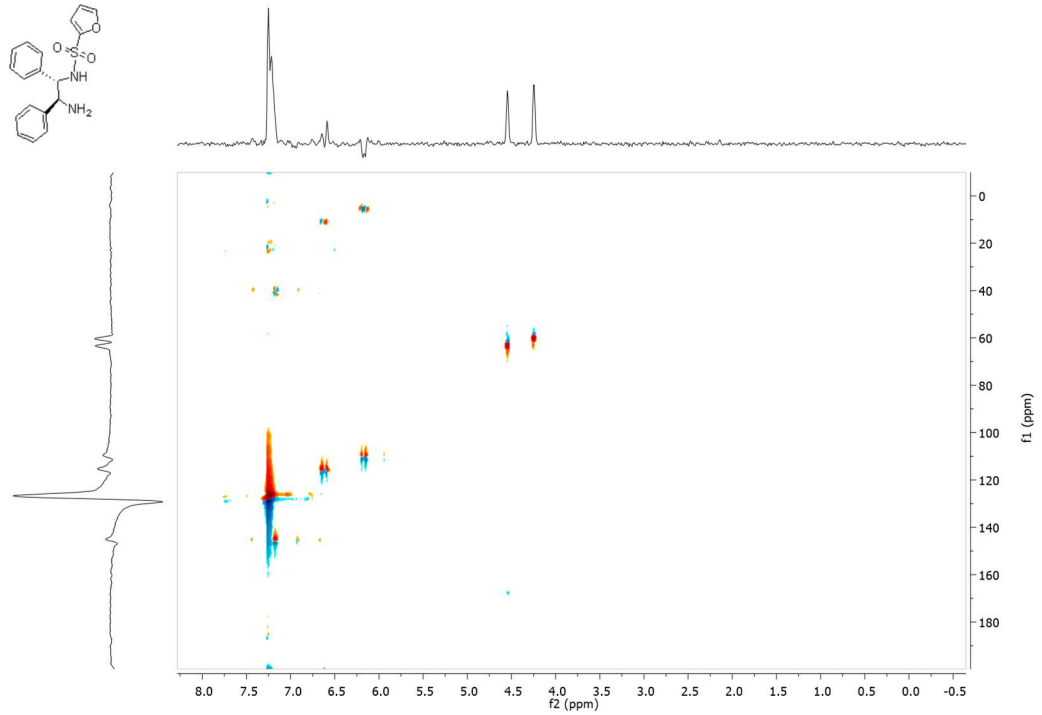


δ_C (400 MHz, $CDCl_3$)

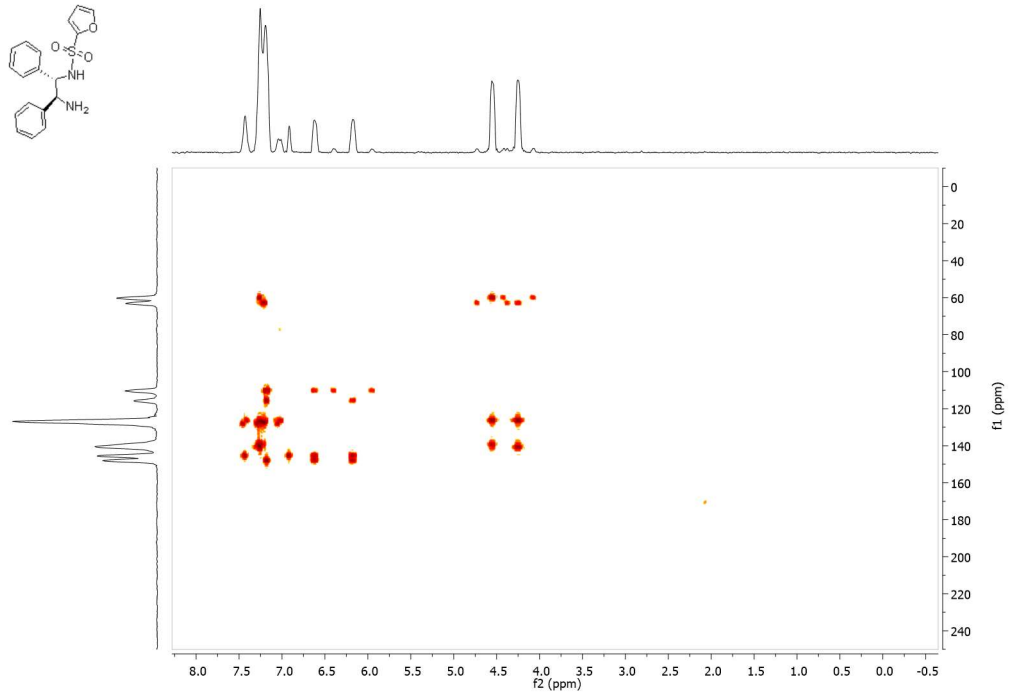




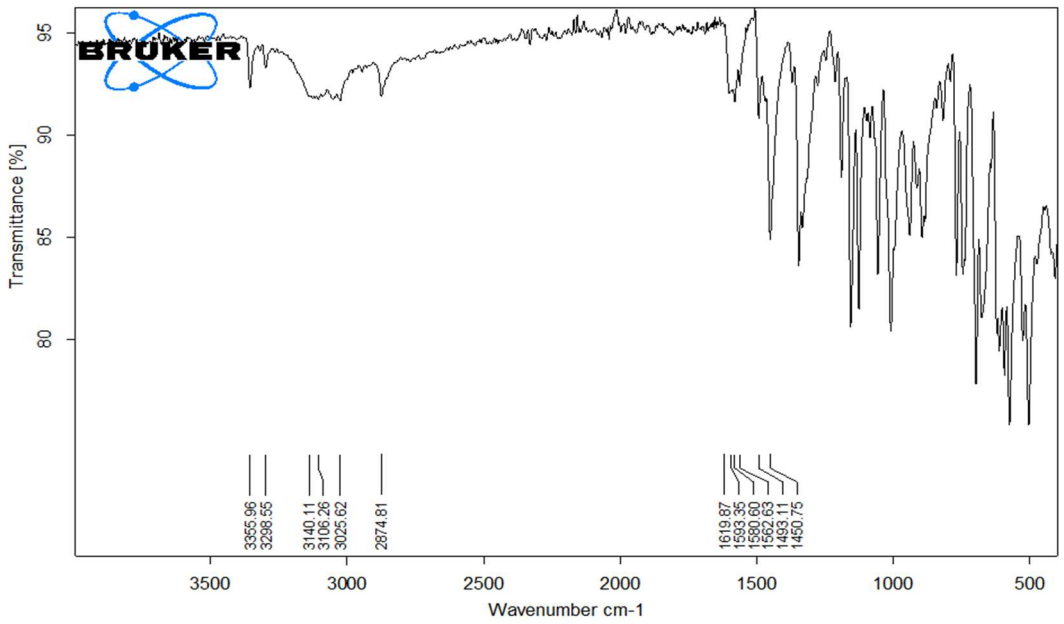
HSQC (400 MHz, $CDCl_3$)



HMBC (400 MHz, $CDCl_3$)



IR spectra



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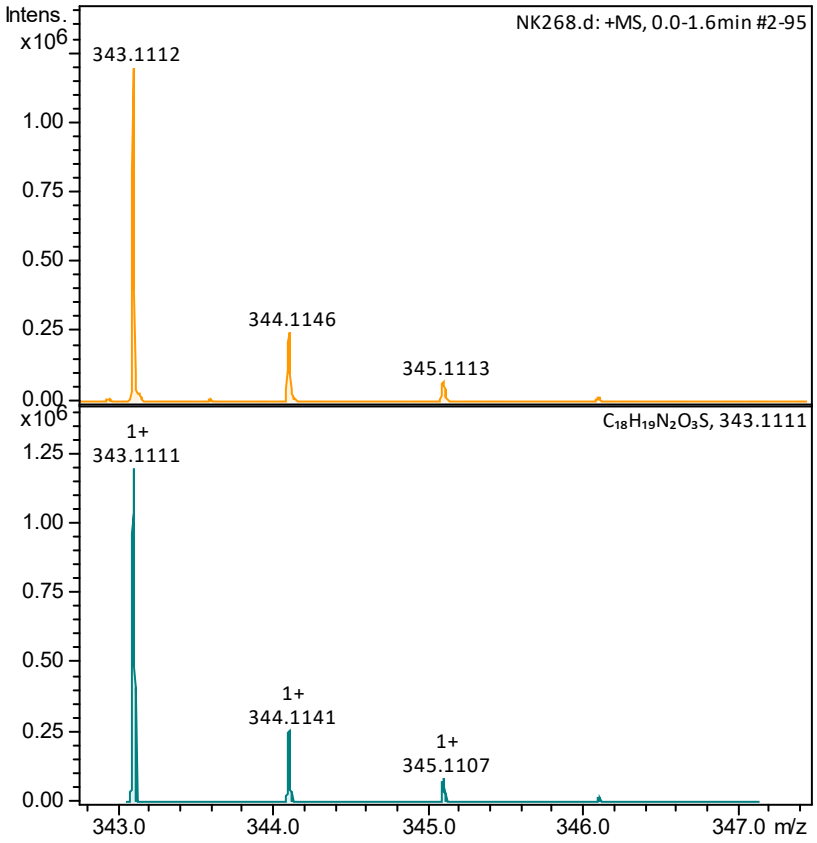
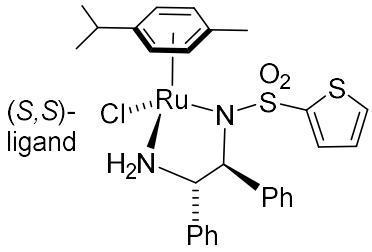
HRMS



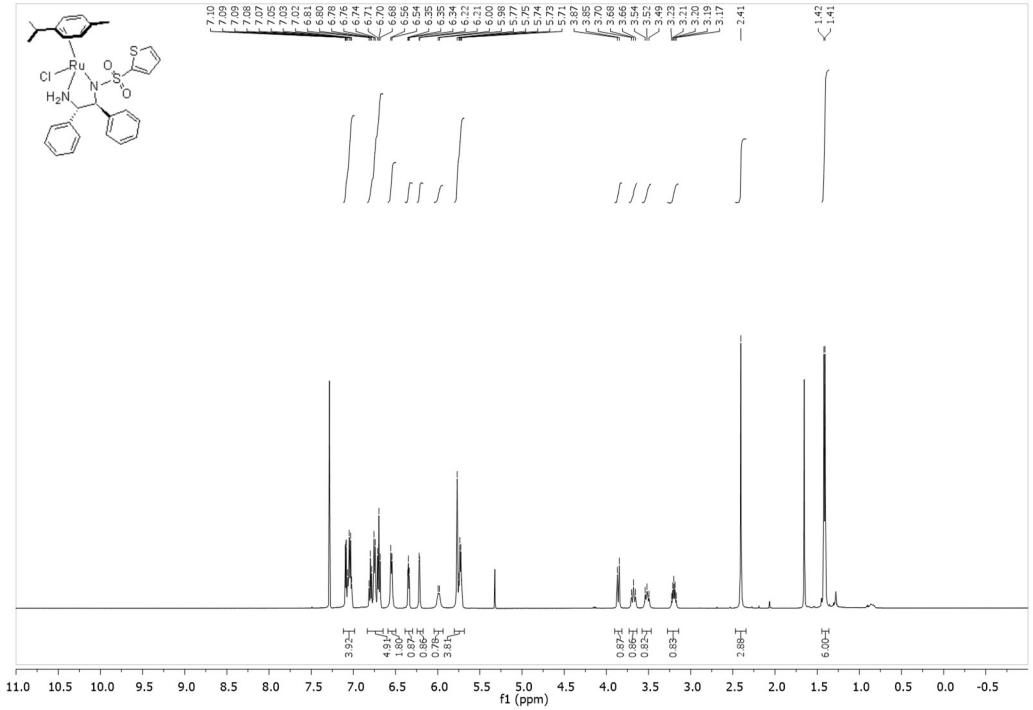
Section 2: Formation of complexes:

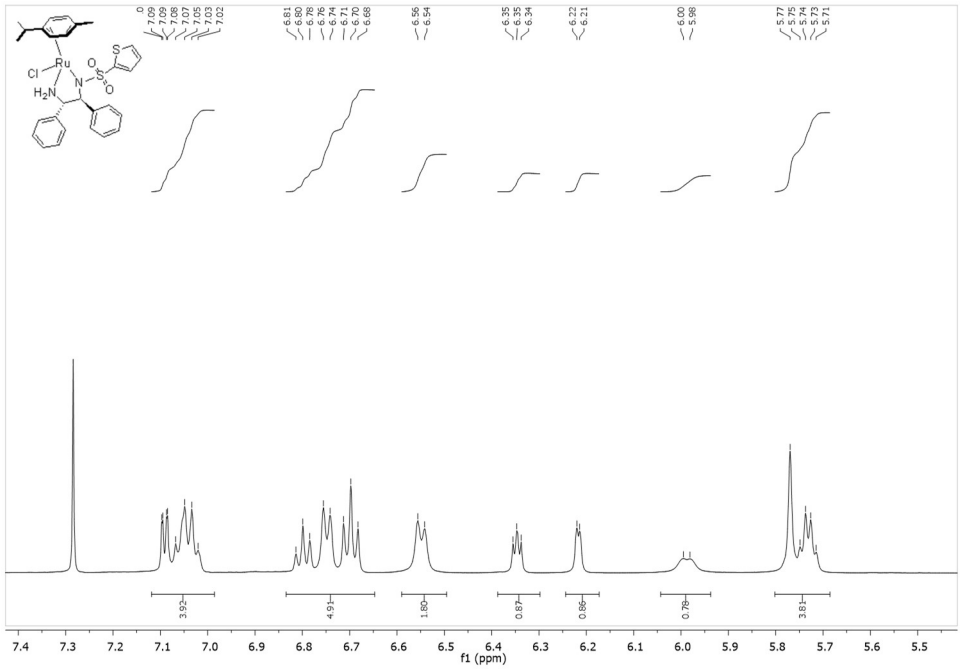
Ru Complex (*S,S,R*^{Ru})-12a, of ligand 11a.

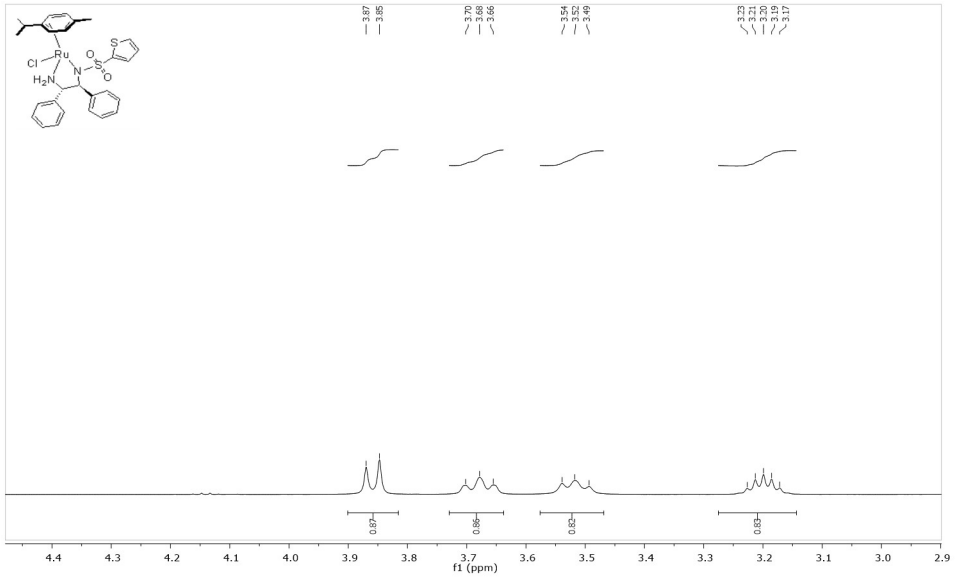


This compound is novel. To a dry 50 mL round-bottom flask charged with a solution of dichloro(p-cymene)ruthenium(II) dimer (85.5 mg, 0.140 mmol) and ligand **11a** (100 mg, 0.279 mmol) in dry 2-propanol (1.5 mL) was added triethylamine (56.5 mg, 0.558 mmol, 79 µL). After stirring at 80 °C for 1 h, the solution was allowed to cool to r.t, and the solvent was removed under reduced pressure. The residue was dissolved in DCM (2 mL) to remove traces of 2-propanoland then dried under vacuum, then the crude product was washed with water (5 mL). The complex was purified by column chromatography on silica gel (100% DCM to 60% DCM: EtOAc) to give the pure product (145 mg, 0.231 mmol, 83%) as a orange solid; TLC: Rf ca 0.6 (1:10 MeOH :DCM), strong UV and $KMnO_4$; Mp 209 °C; $[\alpha]_D^{26}$ = +105.5 (*c* 0.1 in $CHCl_3$); ν_{max} 3285, 3221, 3067, 3027, 2960, 2603, 2498 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.08-7.04 (4 H, m, ArH), 6.86 – 6.59 (5 H, m, ArH), 6.52 (2 H, brd, *J* 7.2, ArH), 6.39 – 6.35 (1 H, m, ArH), 6.19 (1 H, d, *J* 2.8, ArH), 5.96 (1 H, brd, *J* 7.1, NH_2), 5.81 – 5.66 (4 H, m, ArCH of *p*-cymene), 3.83 (1 H, d, *J* 11.5, CH of NSO_2), 3.65 (1 H, t, *J* 11.5, CH of NH_2), 3.54 – 3.44 (1 H, m, NH_2), 3.18 (1 H, dt, *J* 13.7, 6.8, C*H*Me_2 of *p*-cymene), 2.38 (3 H, s, CH_3), 1.39 (6 H, d, *J* 6.8, CH_3); δ_C (126 MHz, $CDCl_3$) 148.41 (ArC), 139.18 (ArC), 138.69 (ArC), 129.93 (ArCH), 128.80 (ArCH), 128.20 (ArCH), 127.76 (ArCH), 127.20 (ArCH), 126.92 (ArCH), 126.14 (ArCH), 125.62 (ArCH), 104.33 (RuArC), 95.38 (RuArC), 84.52 (RuArCH), 82.20 (RuArCH), 81.02 (RuArCH), 79.93 (RuArCH), 71.76 (NCH), 68.90 (NCH), 30.66 (CH of iPr), 22.53 (CH_3), 22.38 (CH_3), 19.05 (CH_3); *m/z* (ESI^+) 593.1 [M - Cl]$^+$; HRMS (ESI-TOF) m/z: [M - Cl]$^+$ calcd for $C_{28}H_{31}N_2O_2{}^{102}RuS_2$ 593.0865, found 593.0860 (1.9 ppm error).

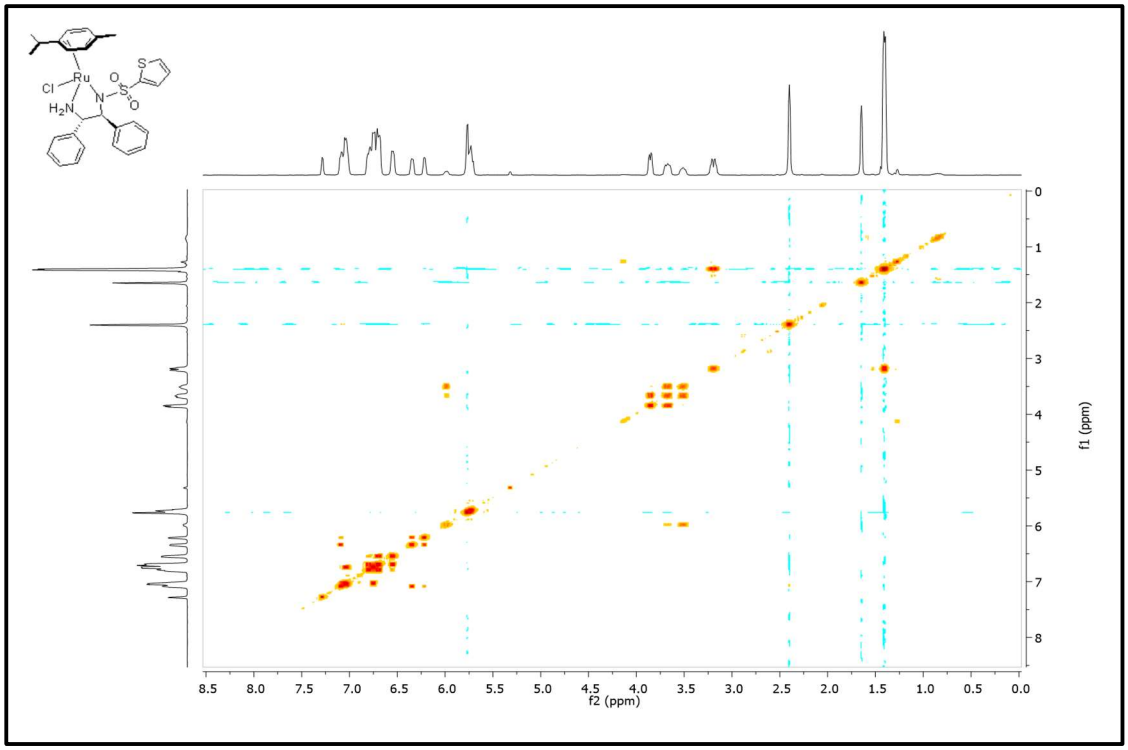
δ_H (500 MHz, $CDCl_3$).



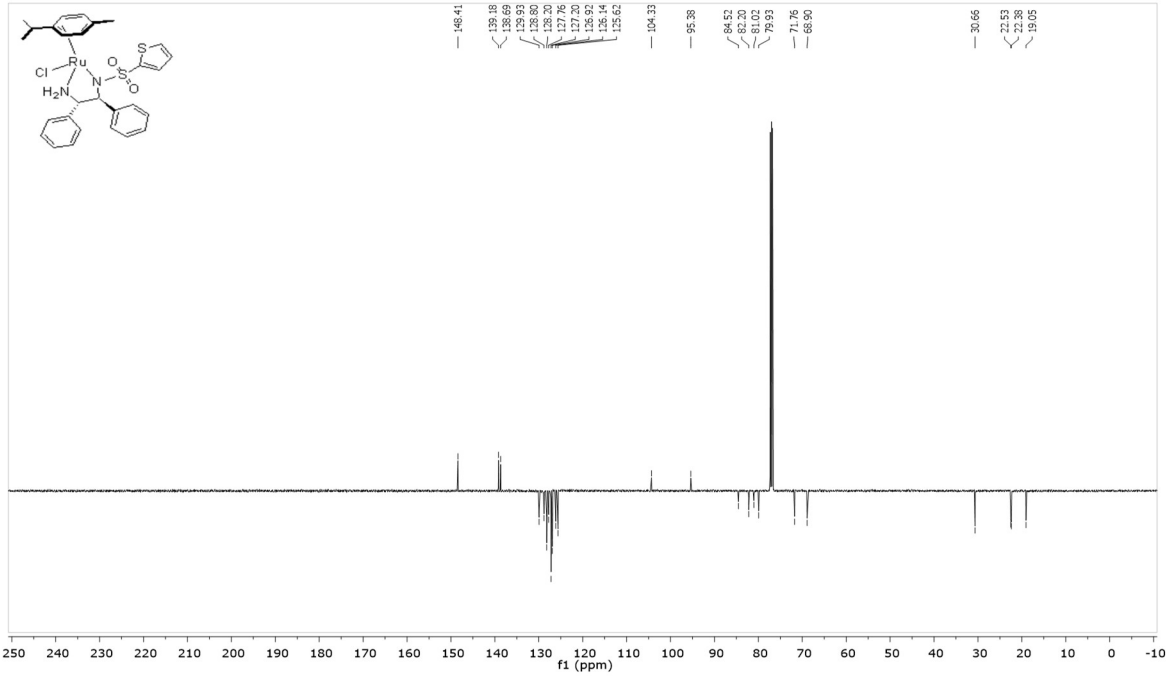


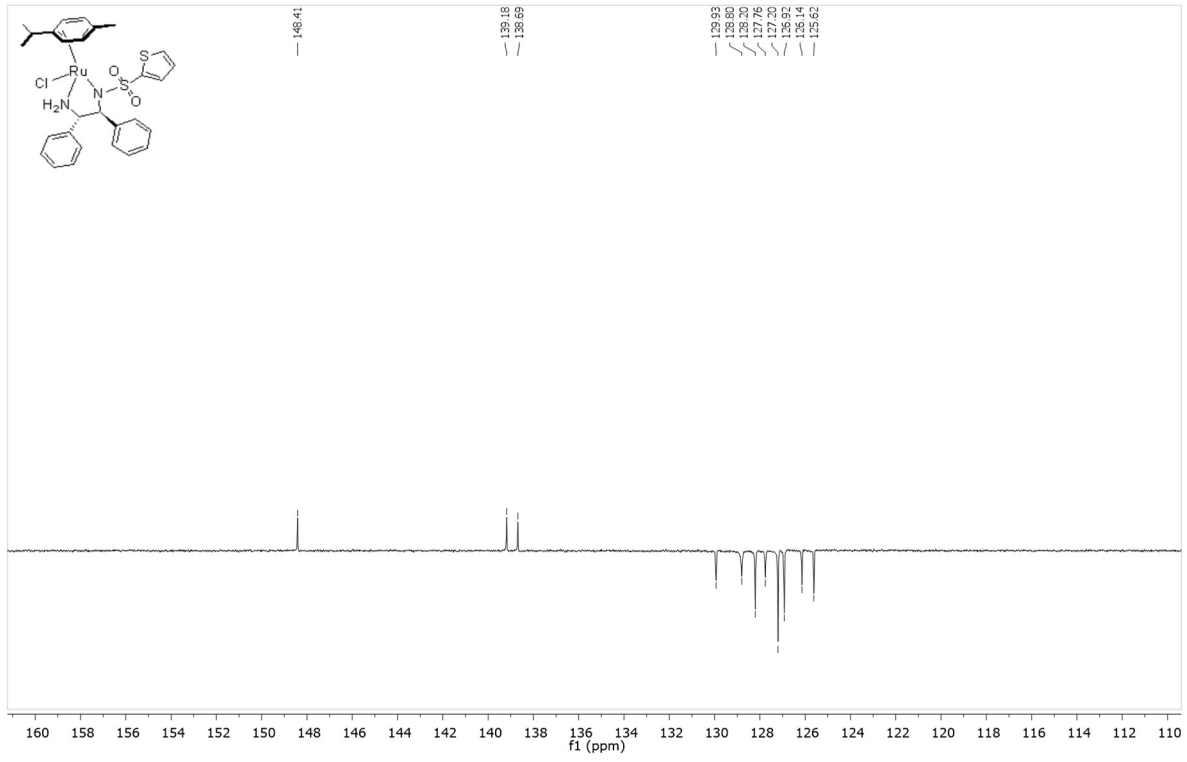


COSY (500 MHz, $CDCl_3$).

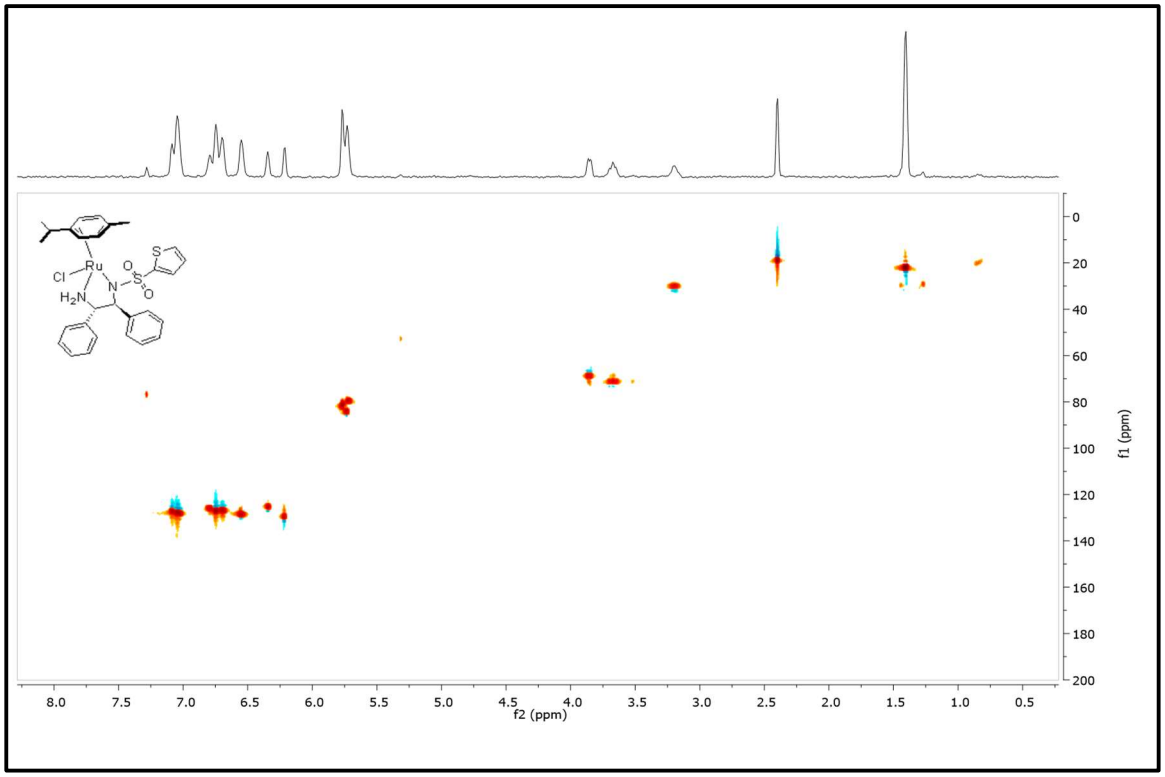


δ_C (126 MHz, $CDCl_3$).

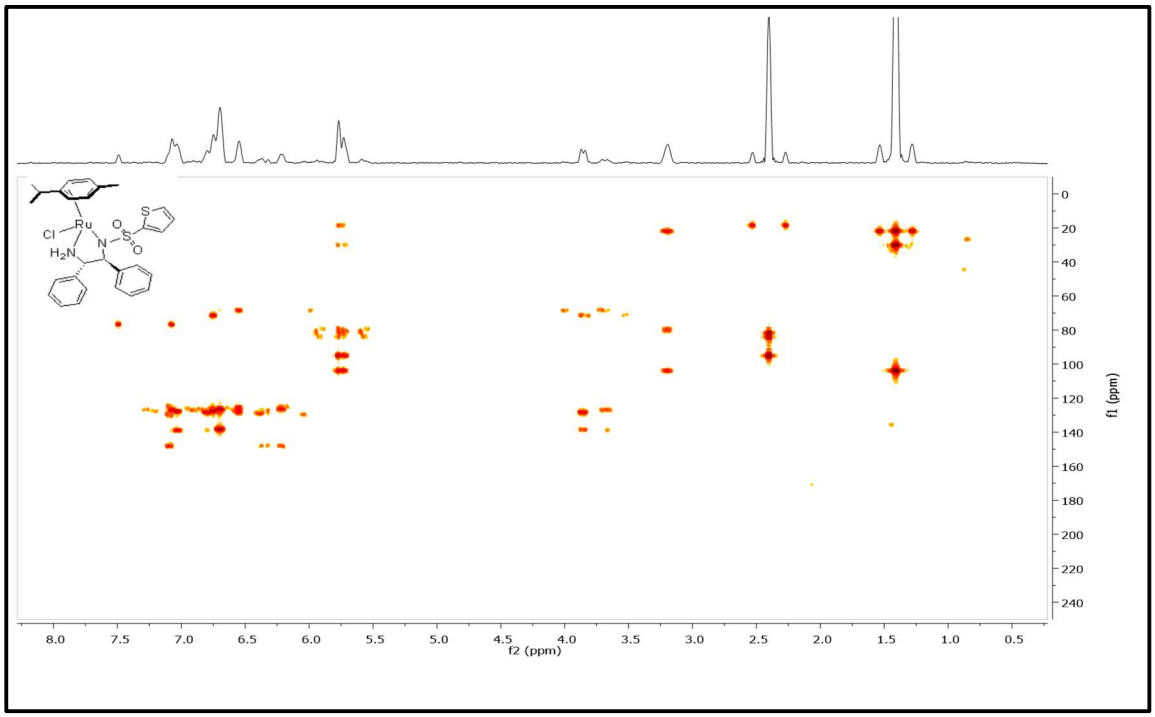




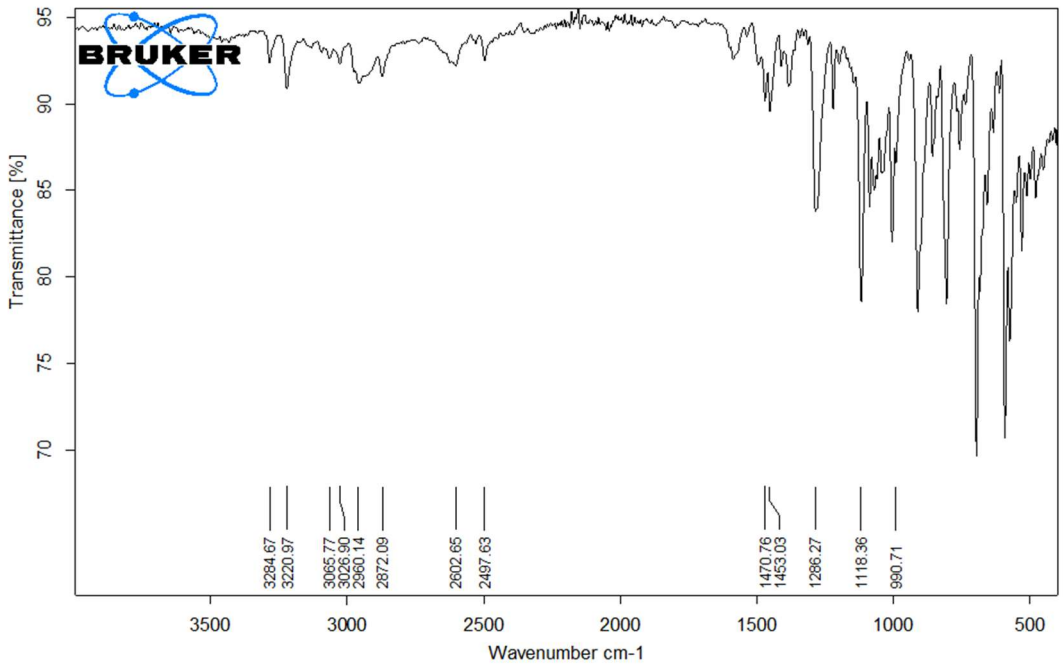
HSQC (500 MHz, $CDCl_3$).



HMBC (500 MHz, $CDCl_3$)



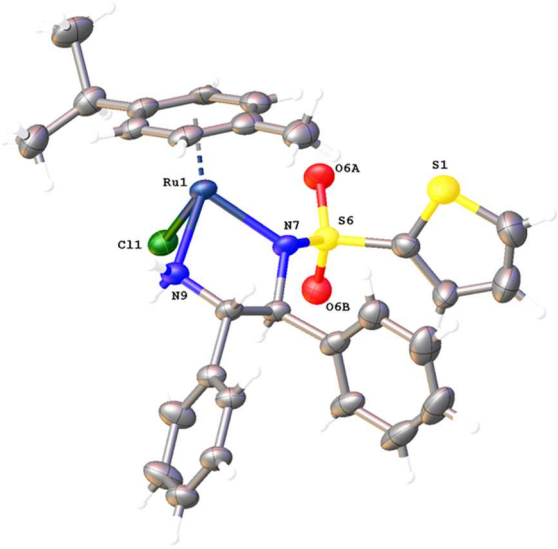
IR spectra



C:\Users\chemist\Desktop\Spectral Data\NK218.0	NK218	Instrument type and / or accessory	20/10/2021

Page 1/1

X-ray of Ru Complex (S,S,R^{Ru})-12a CCDC 2182537 (local code nk3).



solid state structure of CCDC 2182537 with only key atoms labelled and thermal ellipsoids drawn at 50% probability

Crystal structure determination

The asymmetric unit contains the complex and some partially occupied water, there are 4 in the unit cell. The NHs on the amine were located in a difference map and refined with restrains. One of them forms a short contact with a neighbouring sulphonamide oxygen and the other with the partially occupied water O101 shown below

Specified hydrogen bonds (with esds except fixed and riding H)

D-H	H...A	D...A	<(DHA)	
0.91	2.25	2.982(5)	136.9	N9-H9A...O6B_$1
0.91	2.38	3.21(3)	151.6	N9-H9B...O101

symmetry operator used to generate symmetry equivalent atoms discussed in above contact was

$1 0.5+X,0.5-Y,1-Z

There was some electron density between molecules modelled as partially occupied molecules of water. O100 and O101 were both refined at 25% occupancy. No hydrogens were located for these partially occupied solvents.

The Flack parameter and associate Hooft y parameters were

Flack x: -0.018(3) Shelx 2018

Hooft y: -0.027(2) Olex2

These are small with a small error so you can be confident about the assignment of the handedness of the crystal measure. Additionally, the synthesis is from a known chiral diamine.

Experimental

Single crystals of $C_{28.25}H_{31}ClN_2O_{2.25}RuS_2$ [nk3] were grown from methanol. A suitable crystal was selected and mounted on a glass fibre with Fomblin oil and placed on a Rigaku Oxford Diffraction SuperNova diffractometer with a dual source (Cu at zero) equipped with an AtlasS2 CCD area detector. The crystal was kept at 150(2) K during data collection. Using Olex2 [1], the structure was solved with the SHELXT [2] structure solution program using Intrinsic Phasing and refined with the SHELXL [3] refinement package using Least Squares minimisation.

1. Dolomanov, O.V., Bourhis, L.J., Gildea, R.J, Howard, J.A.K. & Puschmann, H. (2009), J. Appl. Cryst. 42, 339-341.

2. Sheldrick, G.M. (2015). Acta Cryst. A71, 3-8.

3. Sheldrick, G.M. (2015). Acta Cryst. C71, 3-8.

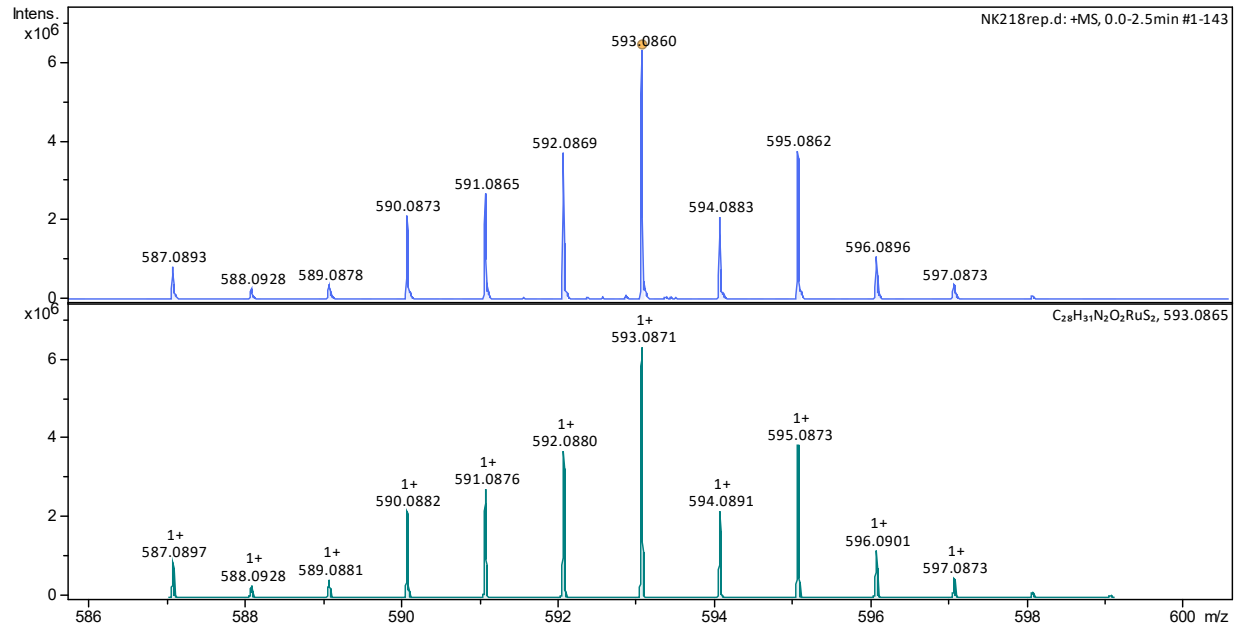
Crystal Data for $C_{28}H_{31}ClN_2O_{2.5}RuS_2$ (M = 636.19 g/mol): orthorhombic, space group $P2_12_12_1$ (no. 19), a = 11.94996(8) Å, b = 12.97812(10) Å, c = 19.21709(12) Å, V = 2980.34(4) Å3, Z = 4, T = 150(2) K, μ(Cu Kα) = 6.620 mm-1, Dcalc = 1.418 g/cm^3, 91422 reflections measured ($8.22° \leq 2\Theta \leq 147.198°$), 5988 unique ($R_{int}$ = 0.0515, R_{sigma}= 0.0176) which were used in all calculations. The final R_1 was 0.0291 ($I > 2\sigma(I)$) and wR_2 was 0.0791 (all data).

Table 1 Crystal data and structure refinement. CCDC 2182537.

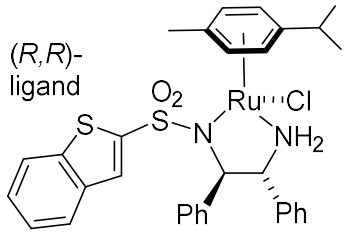
Identification code	nk3
Empirical formula	$C_{28}H_{31}ClN_2O_{2.5}RuS_2$
Formula weight	636.19
Temperature/K	150(2)
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	11.94996(8)
b/Å	12.97812(10)
c/Å	19.21709(12)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	2980.34(4)
Z	4
Pcalc g/cm^3	1.418

μ/mm 1	6.620
F(000)	1304.0
Crystal size/mm^3	0.2 × 0.12 × 0.06 yellow block
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	8.22 to 147.198
Index ranges	-14 ≤ h ≤ 14, -16 ≤ k ≤ 16, -23 ≤ l ≤ 23
Reflections collected	91422
Independent reflections	5988 [R_{int} = 0.0515, R_{sigma} = 0.0176]
Data/restraints/parameters	5988/0/336
Goodness-of-fit on F^2	1.061
Final R indexes [I>=2σ (I)]	R_1 = 0.0291, wR_2 = 0.0789
Final R indexes [all data]	R_1 = 0.0293, wR_2 = 0.0791
Largest diff. peak/hole / e Å^{-3}	0.80/-0.89
Flack parameter	-0.018(3)

HRMS

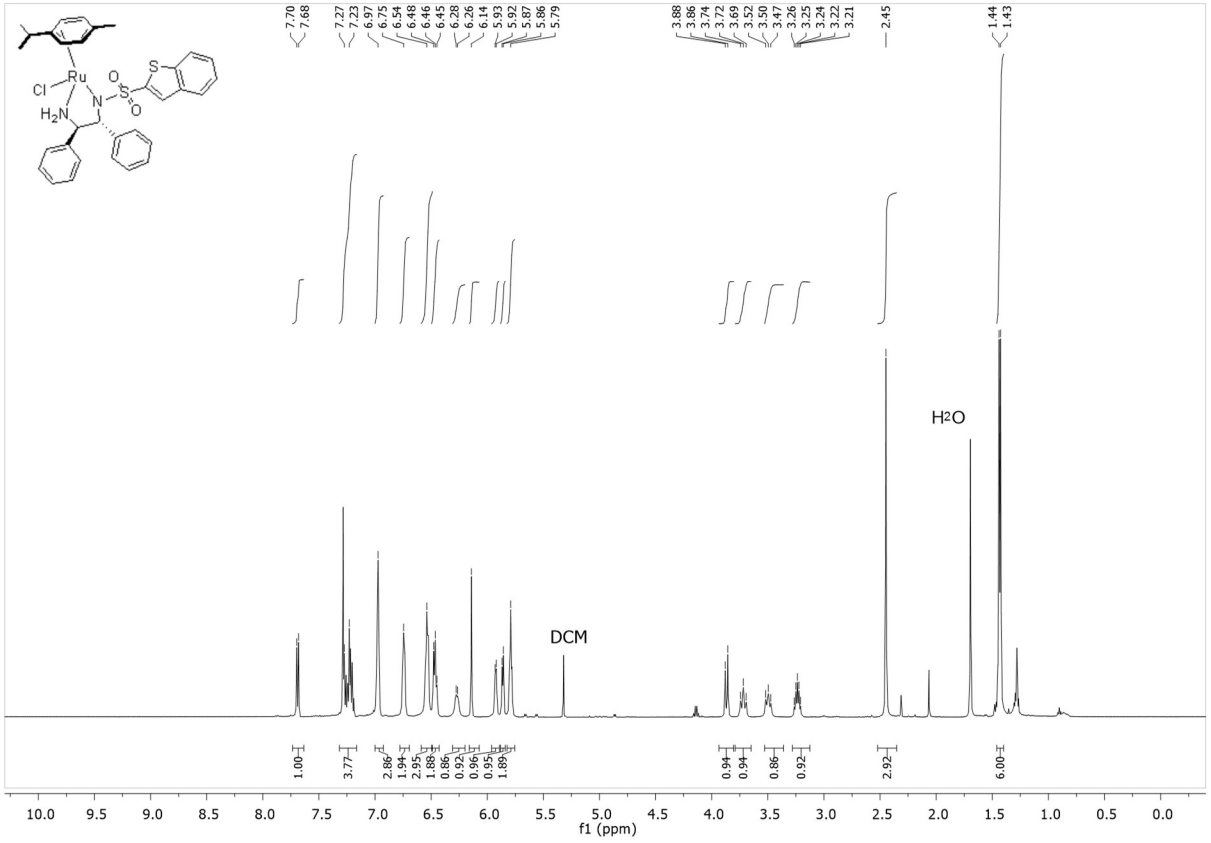


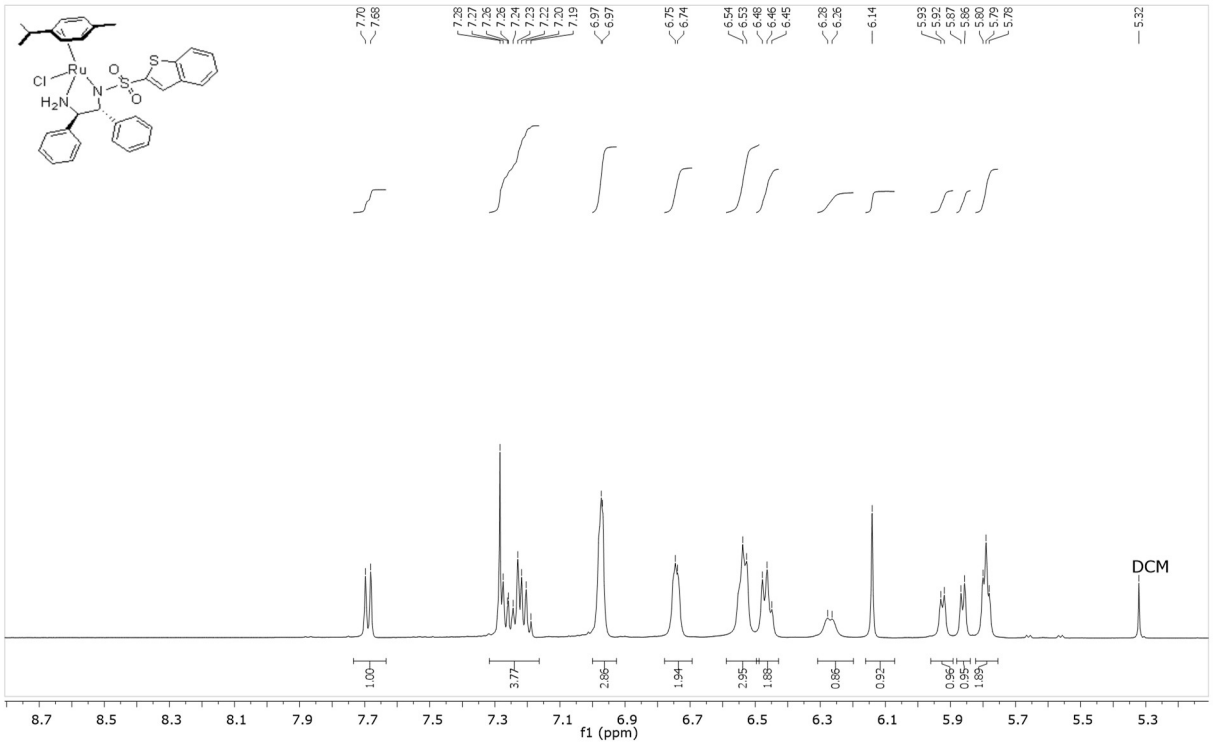
Ru Complex (*R,R,S*^{Ru})-12b of ligand 11b.

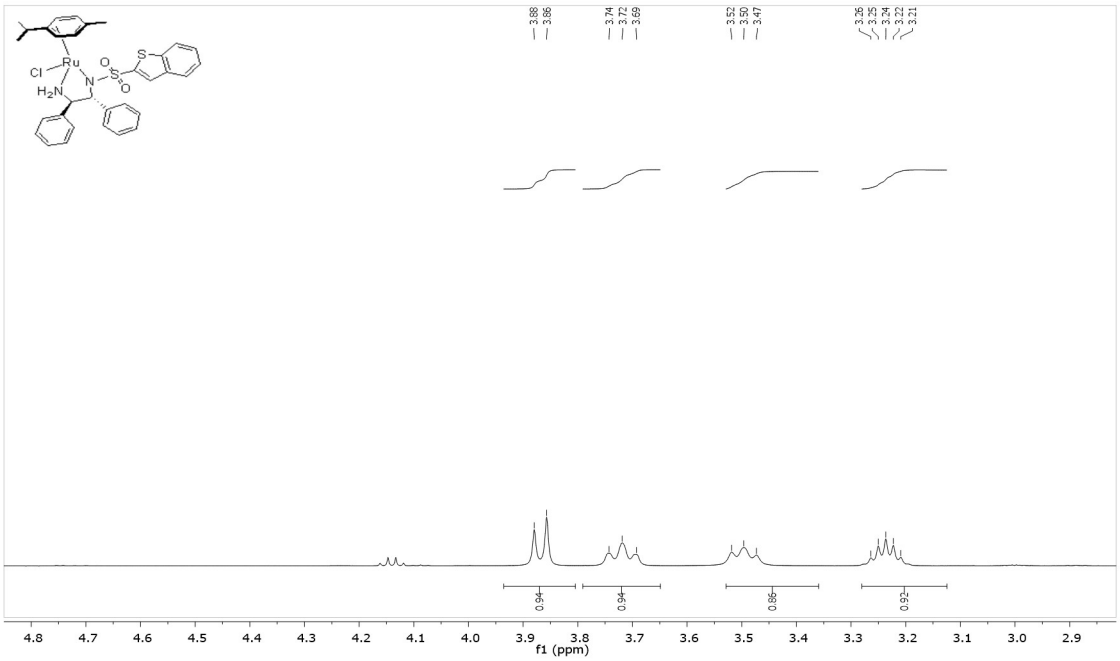


This compound is novel. To a dry 50 mL round-bottom flask charged with a solution of dichloro(p-cymene)ruthenium(II) dimer (75.1 mg, 0.123 mmol) and ligand **11b** (100 mg, 0.245 mmol) in dry 2-propanol (1.5 mL) was added triethylamine (49.6 mg, 0.49 mmol, 68 μL). After stirring at 80 °C for 1 h, the solution was allowed to cool to r.t, and the solvent was removed under reduced pressure. The residue was dissolved in DCM (2 mL) to remove residues of 2-propanol and then dried under vacuum, then the crude product was washed with water (5 mL). The complex was purified by column chromatography on silica gel (100% DCM to 60% DCM: 40% EtOAc) to give the pure product (88 mg, 0.130 mmol, 53%) as an orange solid; TLC: Rf ca 0.6 (1:10 MeOH :DCM), strong UV and $KMnO_4$; Mp =190 °C; $[\alpha]_D^{25}$ = -167.5 (*c* 0.02 in $CHCl_3$); ν_{max} 3354, 3296, 3220, 3087, 3061, 3028, 2960, 2923, 2871 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.69 (1 H, d, *J* 8.0, ArH), 7.32 – 7.14 (3H, m, ArH), 6.98-6.94 (3 H, m, ArH), 6.74 (2 H, d, *J* 3.4, ArH), 6.55-6.51 (3 H, m, ArH), 6.46 (2 H, t, *J* 7.3, ArH), 6.27 (1 H, br. s NH_2), 6.14 (1 H, s, ArH), 5.92 (1 H, d, *J* 5.4, ArCH of *p*-Cymene), 5.86 (1 H, d, *J* 5.7, ArCH of *p*-Cymene), 5.80-5.76 (2 H, m, ArCH of *p*-Cymene), 3.87 (1 H, d, *J* 11.3, NCH of NSO_2), 3.72 (1 H, t, *J* 12.5, NCH of NH_2), 3.57 – 3.38 (1 H, m, NH_2), 3.24 (1 H, m, $CHMe_2$ of *p*-Cymene), 2.45 (3 H, s, CH_3), 1.43 (6 H, d, *J* 6.9,CH_3); δ_C (126 MHz, $CDCl_3$) 147.78 (ArC), 140.36 (ArC), 139.15 (ArC), 138.07 (ArC), 128.83 (ArCH), 128.09 (ArCH), 127.64 (ArCH), 127.18 (ArCH), 127.07 (ArCH), 126.63 (ArCH), 126.48 (ArCH), 125.06 (ArCH), 124.75 (ArCH), 124.01 (ArCH), 122.05 (ArCH), 105.24 (RuArC), 94.54 (RuArC), 85.20 (RuArCH), 82.57 (RuArCH), 80.10 (RuArCH), 79.79 (RuArCH), 71.53 (NCH), 68.85 (NCH), 30.73 (CH of iPr), 22.53 (CH_3), 22.40 (CH_3), 19.06 (CH_3); *m/z* (ESI^+) 643.1 [M - Cl]$^+$; HRMS (ESI-TOF) m/z: [M - Cl]$^+$ calcd for $C_{32}H_{33}N_2O_2{}^{102}RuS_2$ 643.1023, found 643.1032 (-0.5 ppm error).

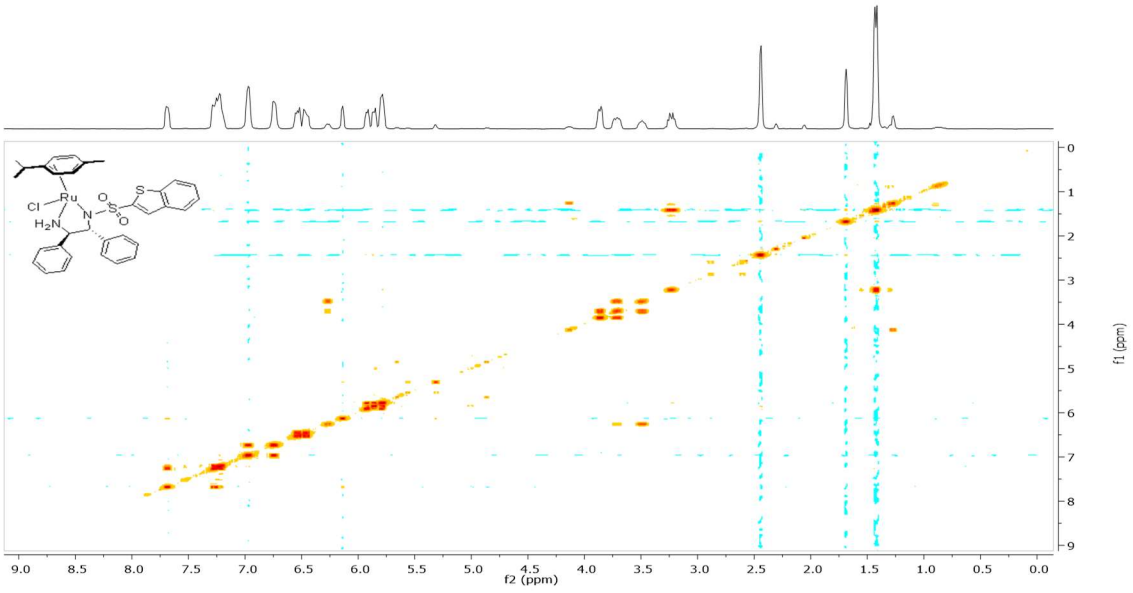
δ_H (500 MHz, $CDCl_3$)



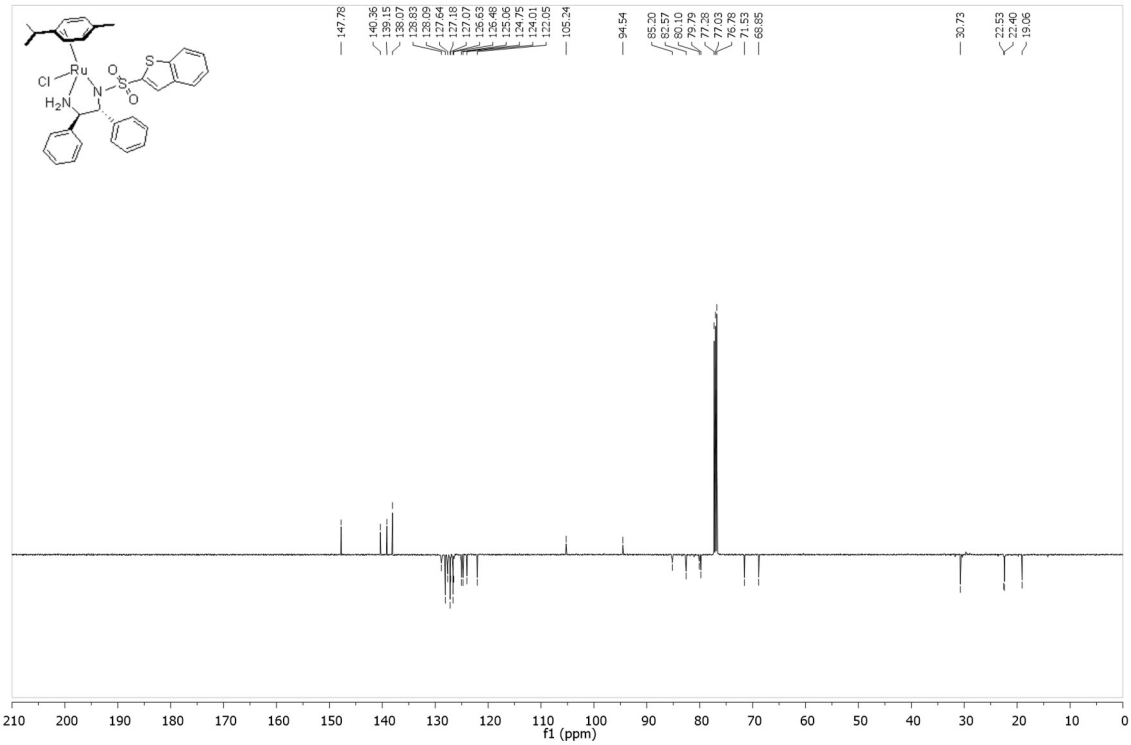


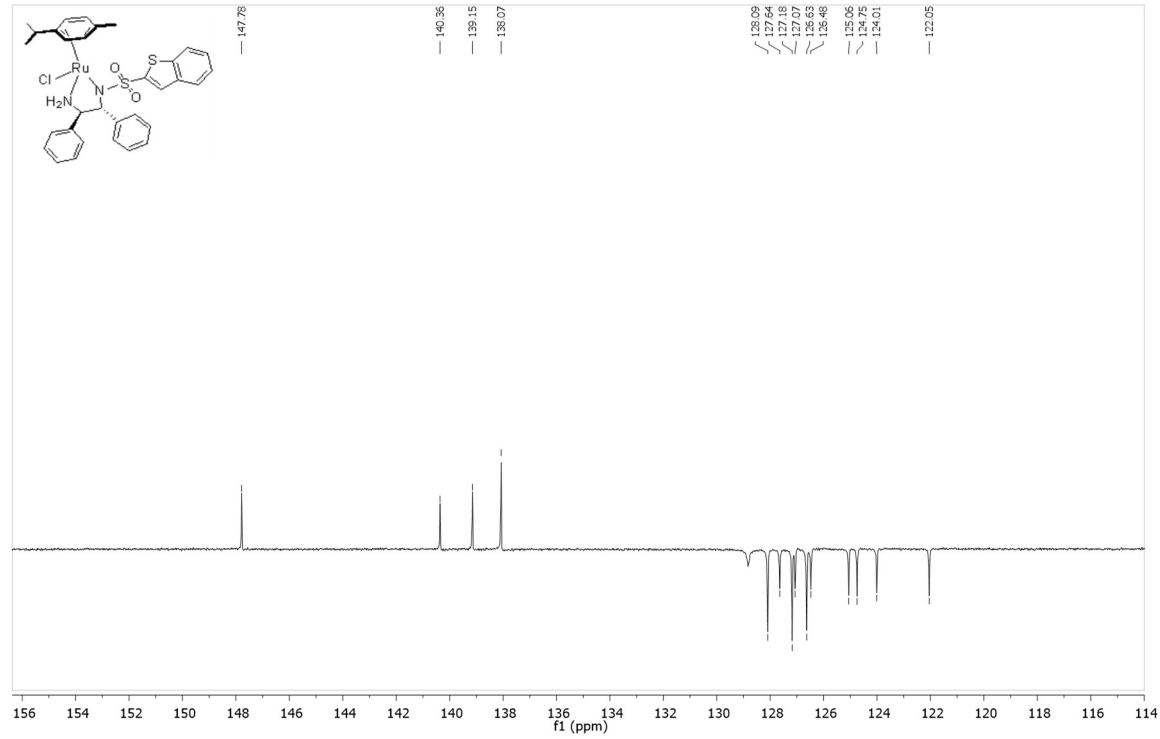


COSY (500 MHz, $CDCl_3$)

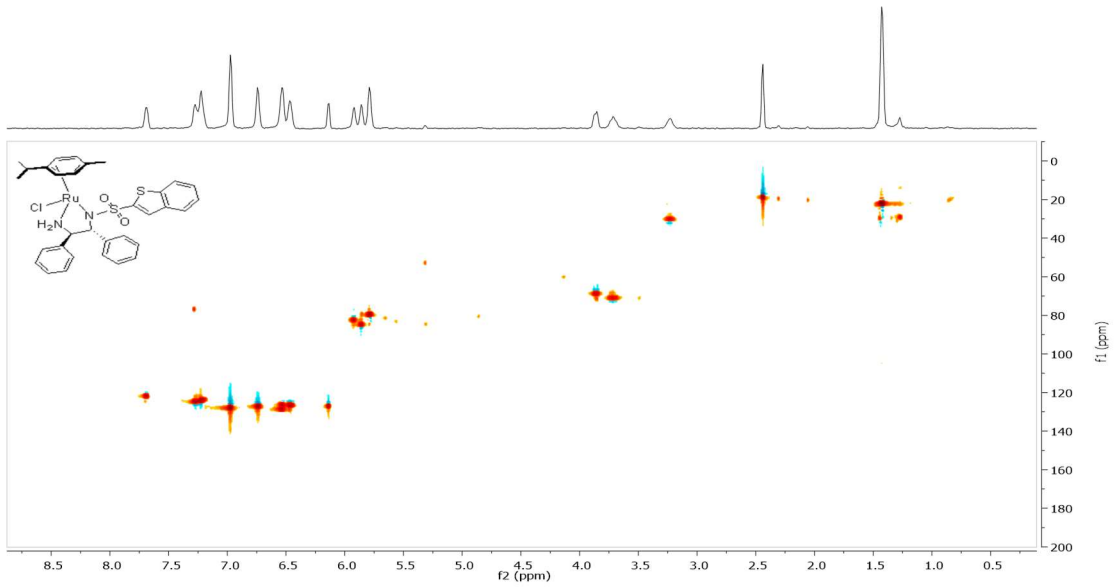


δ_C (126 MHz, $CDCl_3$)

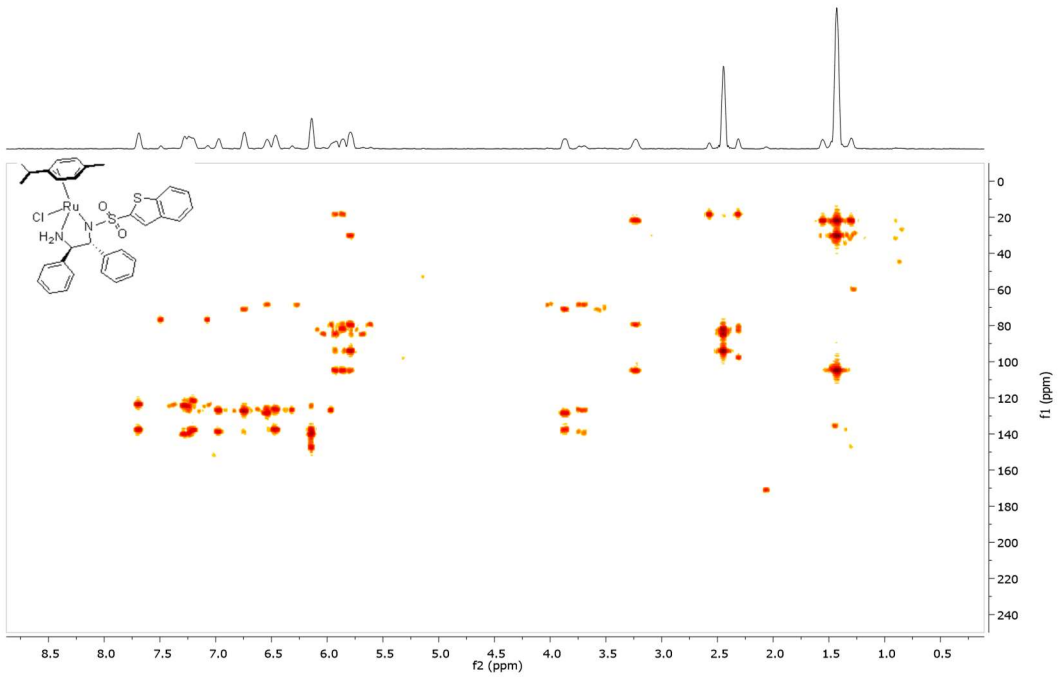




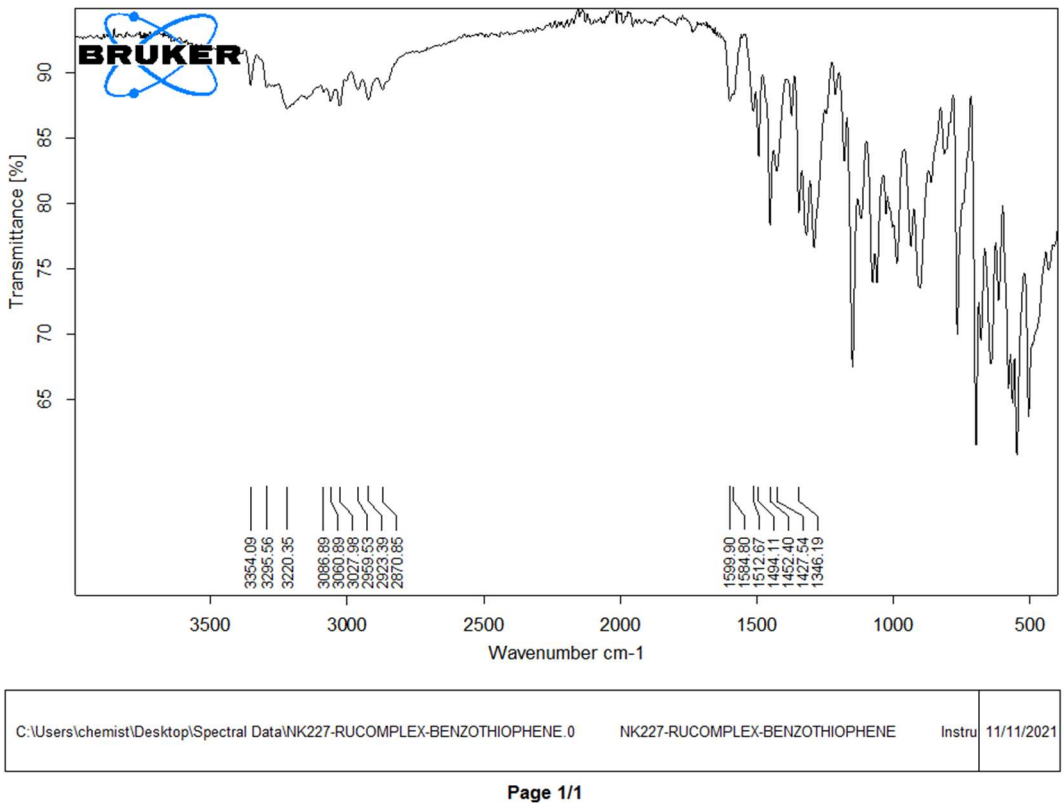
HSQC (500 MHz, $CDCl_3$)



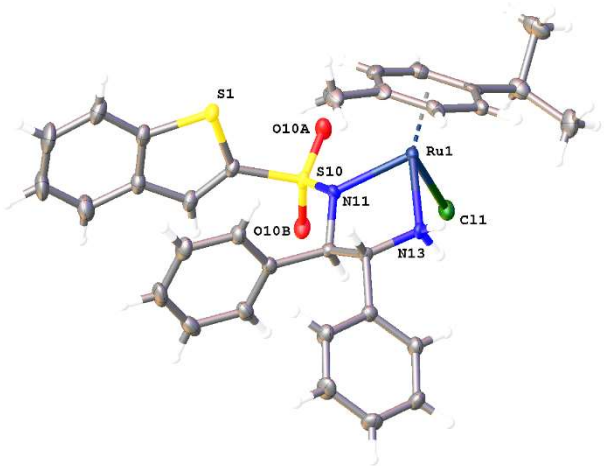
HMBC (500 MHz, $CDCl_3$)



IR spectra



X-ray structure of Complex of ligand (R,R,S^{Ru})-12a CCDC 2182538 (local code nk4).



solid state structure of the complex in CCDC 2182538 with only key atoms labelled and thermal ellipsoids drawn at 50% probability level

Crystal structure determination.

The asymmetric unit contains the complex and some partially occupied methanol (O36-C37) and water (O38). The methanol was refined at 50% occupancy and the water at 25% occupancy

(the occupancy was judged visually by gauging the size of the thermal parameters on refinement). The minor component solvents were refined isotropically. The hydrogens were placed at calculated positions on the methanol but no hydrogens were located on the partially occupied water O31. The hydrogens were located on the amine and refined with restraints.

They form short contacts tabulated below

Specified hydrogen bonds (with esds except fixed and riding H)

D-H	H...A	D...A	<(DHA)	
0.91	2.38	2.982(6)	123.5	N13-H13B...O10B_$1
0.84	2.46	3.268(9)	161.4	O36-H36...Cl1

Symmetry operator used to generate symmetry equivalent atoms in above contacts were $1 2-X,-0.5+Y,1-Z

The other NH (N13-H13A) is pointing towards the partially occupied water but is also lying in the plane of the Ru-Cl bond which is traditional with these compounds (likely a dipole-dipole interaction).

The flack parameter and the associated Hooft y parameter were

Flack x: -0.017(9) Shelx 2018

Hooft y: -0.038(2) Olex2

These are relatively small with a small error so you can be confident in the assignment of the crystal chosen.

The compound is synthesised from a starting material of known chirality

Experimental

Single crystals of $C_{32.5}H_{35}ClN_2O_{2.75}RuS_2$ [nk4] were grown from methanol. A suitable crystal was selected and mounted on a glass fibre with Fomblin oil and placed on a Rigaku Oxford Diffraction SuperNova diffractometer with a dual source (Cu at zero) equipped with an AtlasS2 CCD area detector. The crystal was kept at 150(2) K during data collection. Using Olex2 [1], the structure was solved with the SHELXT [2] structure solution program using Intrinsic Phasing and refined with the SHELXL [3] refinement package using Least Squares minimisation.

1. Dolomanov, O.V., Bourhis, L.J., Gildea, R.J, Howard, J.A.K. & Puschmann, H. (2009), J. Appl. Cryst. 42, 339-341.

2. Sheldrick, G.M. (2015). Acta Cryst. A71, 3-8.

3. Sheldrick, G.M. (2015). Acta Cryst. C71, 3-8.

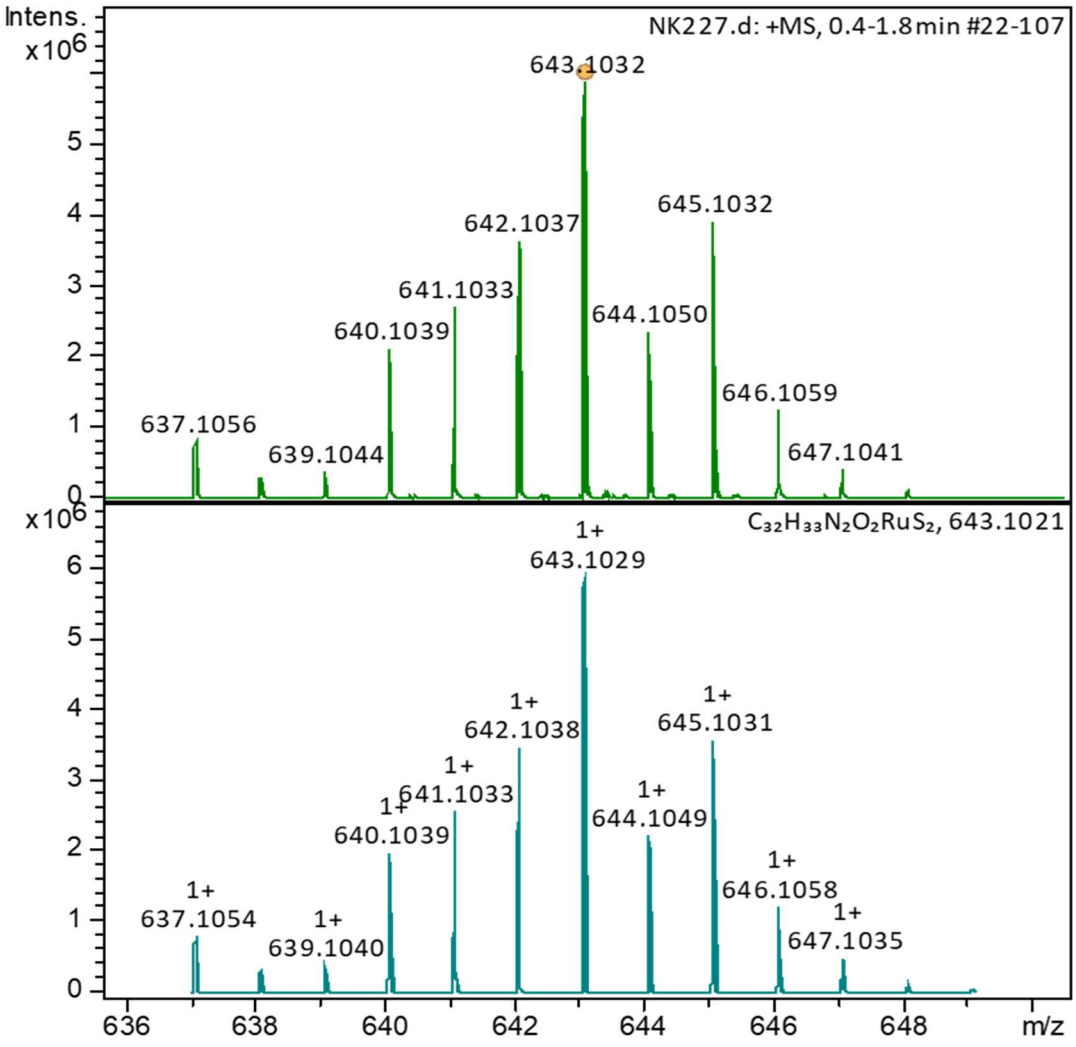
Crystal Data for $C_{32.5}H_{35}ClN_2O_{2.75}RuS_2$ (M =698.26 g/mol): monoclinic, space group $P2_1$ (no. 4), a = 9.78513(4) Å, b = 11.79817(5) Å, c = 14.04533(5) Å, β = 99.3866(4)°, V = 1599.776(11) $Å^3$, Z = 2, T = 150(2) K, μ(Cu Kα) = 6.227 mm-1, Dcalc = 1.450 g/cm^3, 76379 reflections measured (6.378° ≤ 2Θ ≤ 147.368°), 6201 unique (R_{int} = 0.0891, R_{sigma} = 0.0265) which were used in all calculations. The final R_1 was 0.0373 (I > 2σ(I)) and wR_2 was 0.1065 (all data).

Table 1 Crystal data and structure refinement. CCDC 2182538.

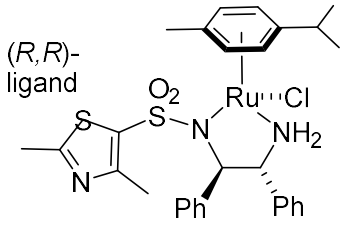
Identification code	nk4
Empirical formula	$C_{32.5}H_{35}ClN_2O_{2.75}RuS_2$
Formula weight	698.26
Temperature/K	150(2)
Crystal system	monoclinic
Space group	$P2_1$
a/Å	9.78513(4)
b/Å	11.79817(5)
c/Å	14.04533(5)
α/°	90
β/°	99.3866(4)
γ/°	90
Volume/$Å^3$	1599.776(11)
Z	2
ρcalcg/cm^3	1.450
μ/mm 1	6.227
F(000)	718.0
Crystal size/mm^3	0.3 × 0.22 × 0.06 yellow block
Radiation	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	6.378 to 147.368
Index ranges	-12 ≤ h ≤ 12, -14 ≤ k ≤ 12, -17 ≤ l ≤ 17
Reflections collected	76379
Independent reflections	6201 [R_{int} = 0.0891, R_{sigma} = 0.0265]
Data/restraints/parameters	6201/2/378
Goodness-of-fit on F^2	1.084
Final R indexes [I>=2σ (I)]	R_1 = 0.0373, wR_2 = 0.1064

Final R indexes [all data]	$R_1 = 0.0373$, $wR_2 = 0.1065$
Largest diff. peak/hole / e Å^{-3}	1.28/-0.79
Flack parameter	-0.017(9)

HRMS

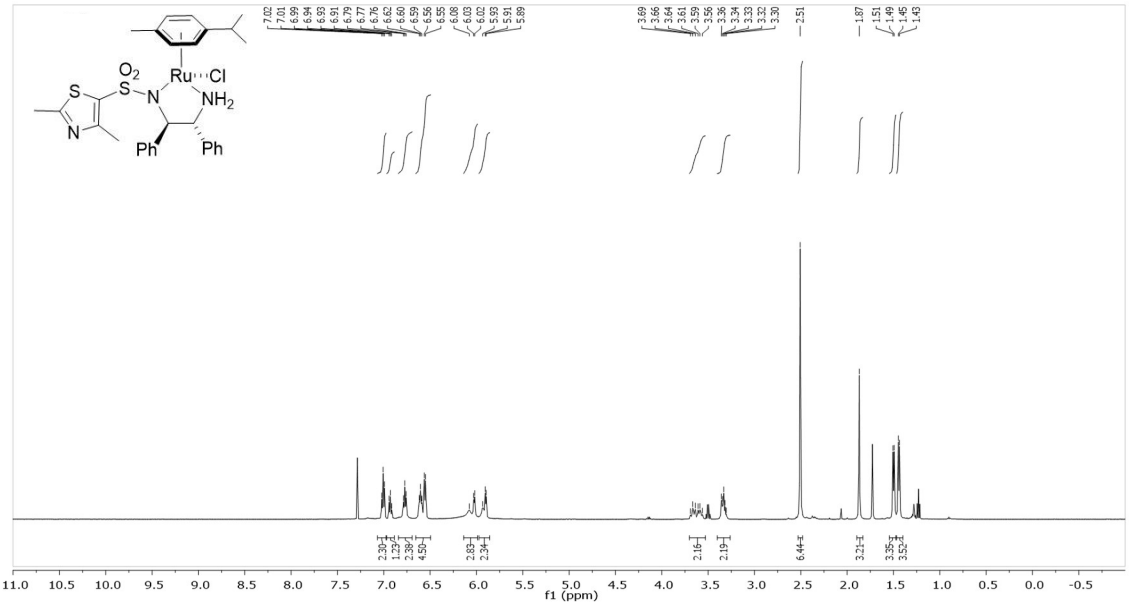


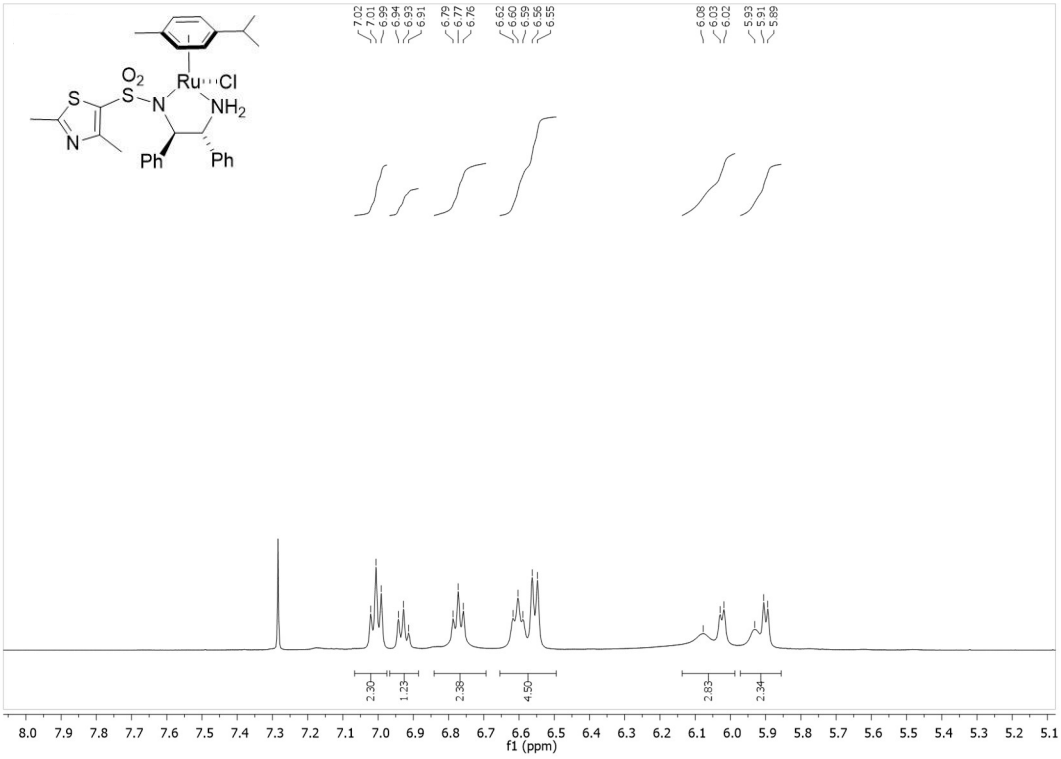
Ru Complex (*R,R,S*^{Ru})-12c of ligand 11c.

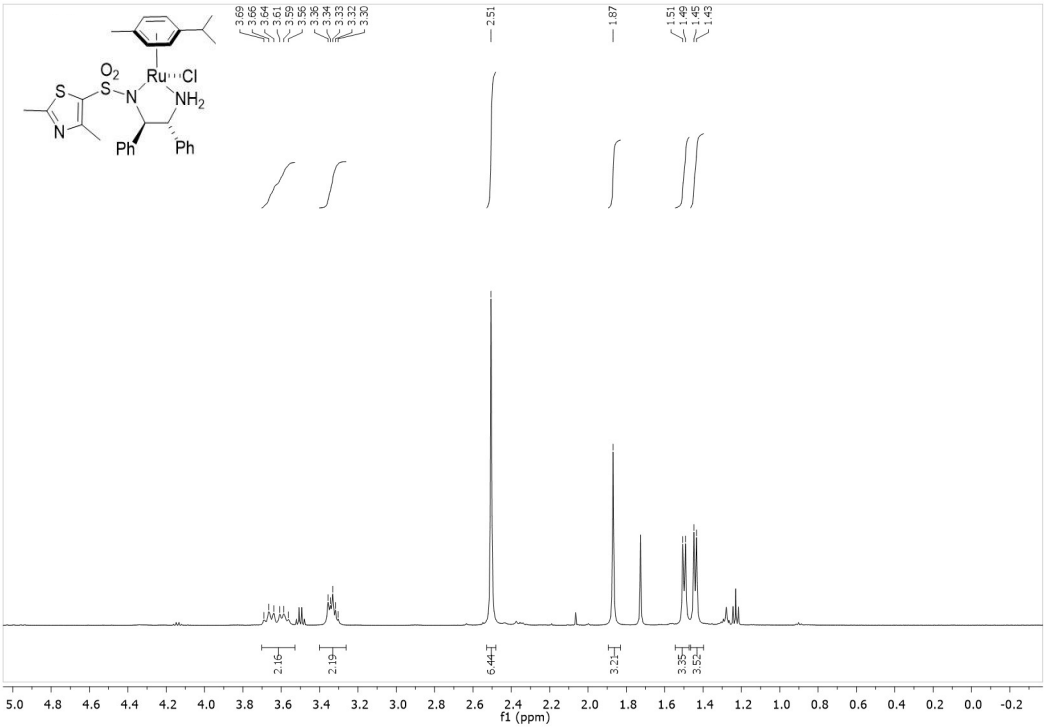


This compound is novel. To a dry 50 mL round-bottom flask charged with a solution of dichloro(p-cymene)ruthenium(II) dimer (85.5 mg, 0.140 mmol) and ligand **11c** (100 mg, 0.258 mmol) in dry 2-propanol (1.5 mL) was added triethylamine (56.5 mg, 0.558 mmol, 79 μL). After stirring at 80 °C for 1 h, the solution was allowed to cool to r.t, and the solvent was removed under reduced pressure. The residue was dissolved in DCM (2mL) to remove residues of 2-propanol and then dried under vacuum, then the crude product washed with water (5 mL). The complex was purified by column chromatography on silica gel (100% DCM to 60% DCM: 40% EtOAc to 5% MeOH: 95% EtOAc) to give the pure product (126 mg, 0.192 mmol, 74.5%) as a orange solid; TLC: Rf ca 0.5 (1:10 MeOH :DCM), strong UV and $KMnO_4$; Mp =234 °C, $[\alpha]_D^{25}$ = +16.39 (*c* 0.072 in $CHCl_3$); ν_{max} 3283, 3217, 3032, 2957 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.01 (2 H, t, *J* 7.4, ArH), 6.93 (1 H, t, *J* 7.2, ArH), 6.77 (2 H, t, *J* 7.2, ArH), 6.68 – 6.45 (5 H, m, ArH), 6.13 – 5.95 (3 H, m, 2 ArCH of *p*-cymene + N*H*H), 5.98 – 5.83 (2 H, m, ArCH of *p*-cymene), 3.65 -3.60 (2 H, m, NCH + NH*H*), 3.38-3.30 (2 H, m, NCH + C*H*Me_2 of *p*-cymene), 2.51 (6 H, s, 2 x CH_3), 1.87 (3 H, s, CH_3), 1.49 (3 H, d, *J* 6.8, CH_3), 1.44 (3 H, d, *J* 6.8, CH_3); δ_C (126 MHz, $CDCl_3$) 164.52 (ArC), 152.02 (ArC), 139.42 (ArC), 138.08 (ArC), 137.24 (ArC), 127.85 (ArCH), 127.09 (ArCH), 126.97 (ArCH), 126.42 (ArCH), 126.33 (ArCH), 83.09 (RuArCH), 79.30 (RuArCH),71.13 (NCH), 69.57 (NCH), 30.64 (C*H*Me_2 of *p*-cymene), 23.05 (CH_3), 21.96 (CH_3), 19.02 (CH_3), 18.90 (CH_3), 15.79 (CH_3), both RuArC and two of the RuArCH not observed; *m/z* (ESI^+) 622.1 $[M - Cl]^+$; HRMS (ESI-TOF) m/z: $[M - Cl]^+$ calcd for $C_{29}H_{34}N_3O_2{}^{102}RuS_2$ 622.1130, found 622.1123 (2.2 ppm error).

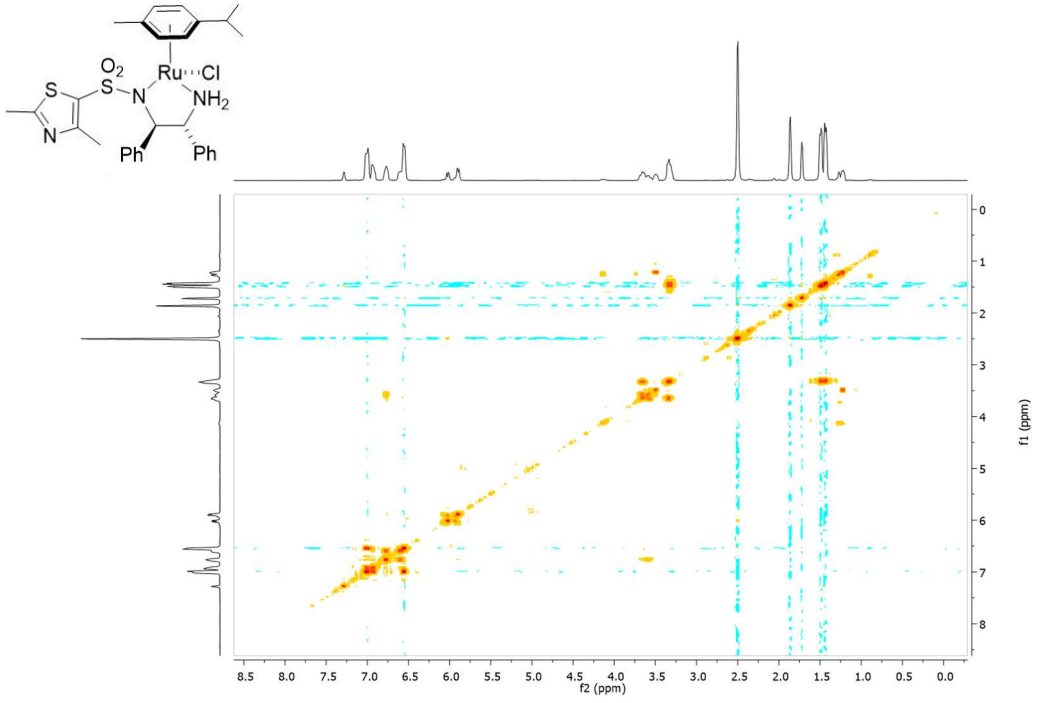
δ_H (500 MHz, $CDCl_3$)



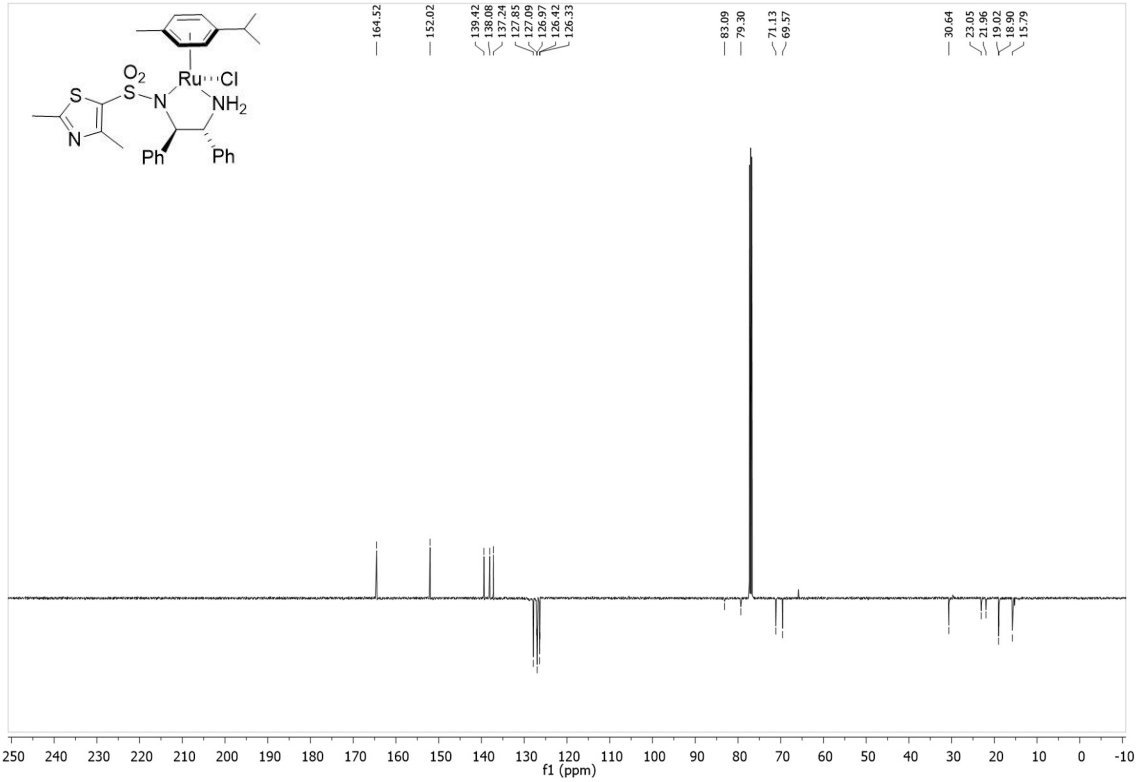


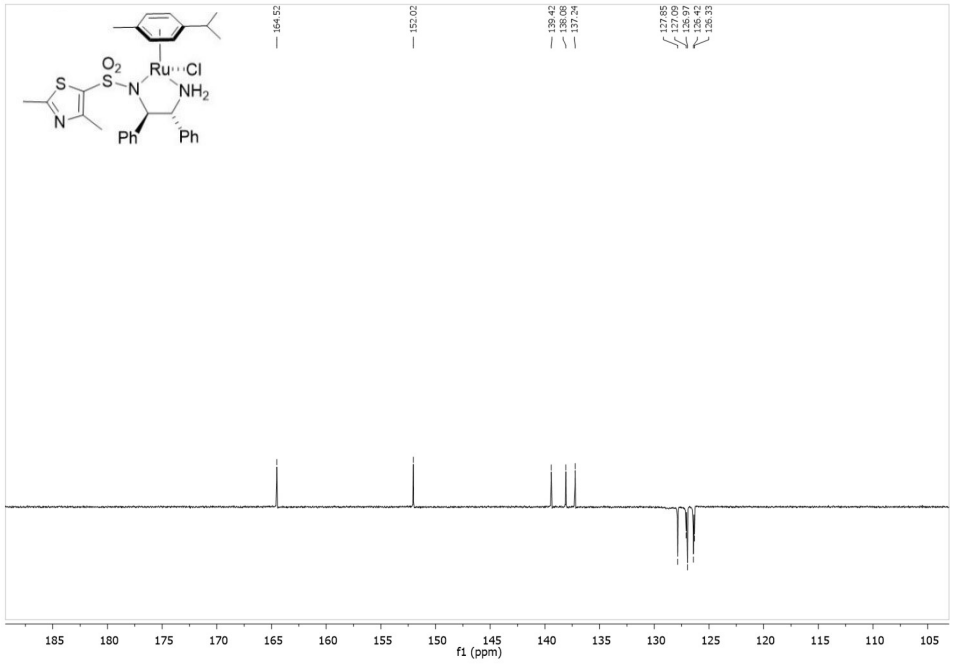


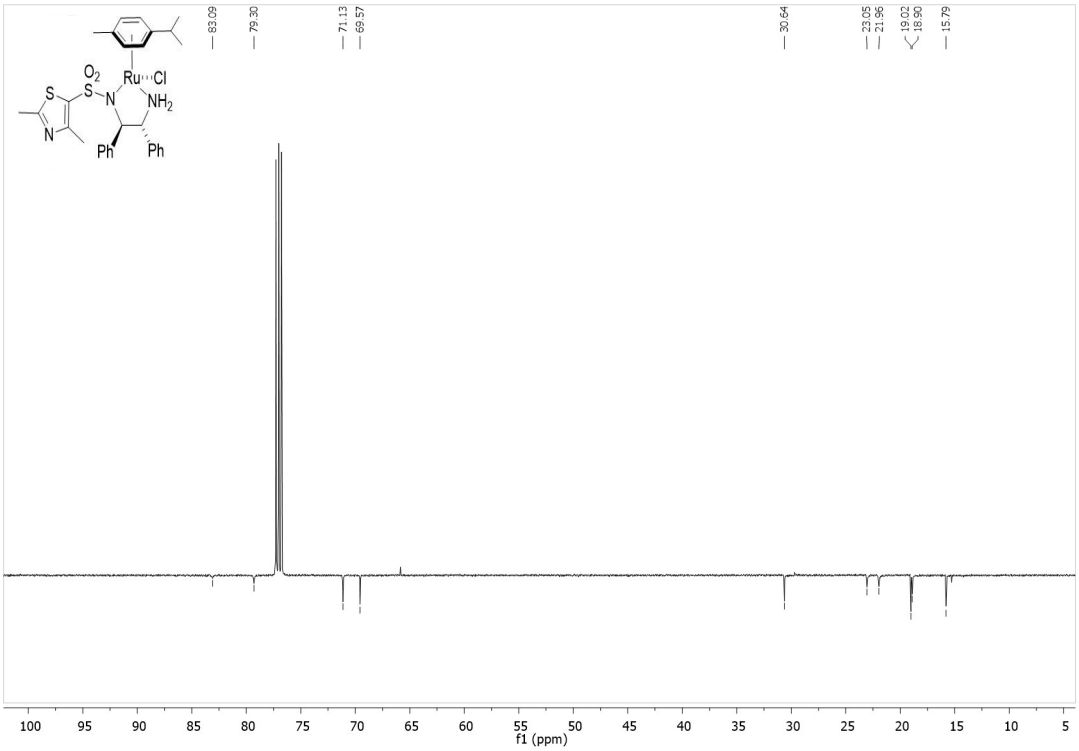
COSY (500 MHz, $CDCl_3$)



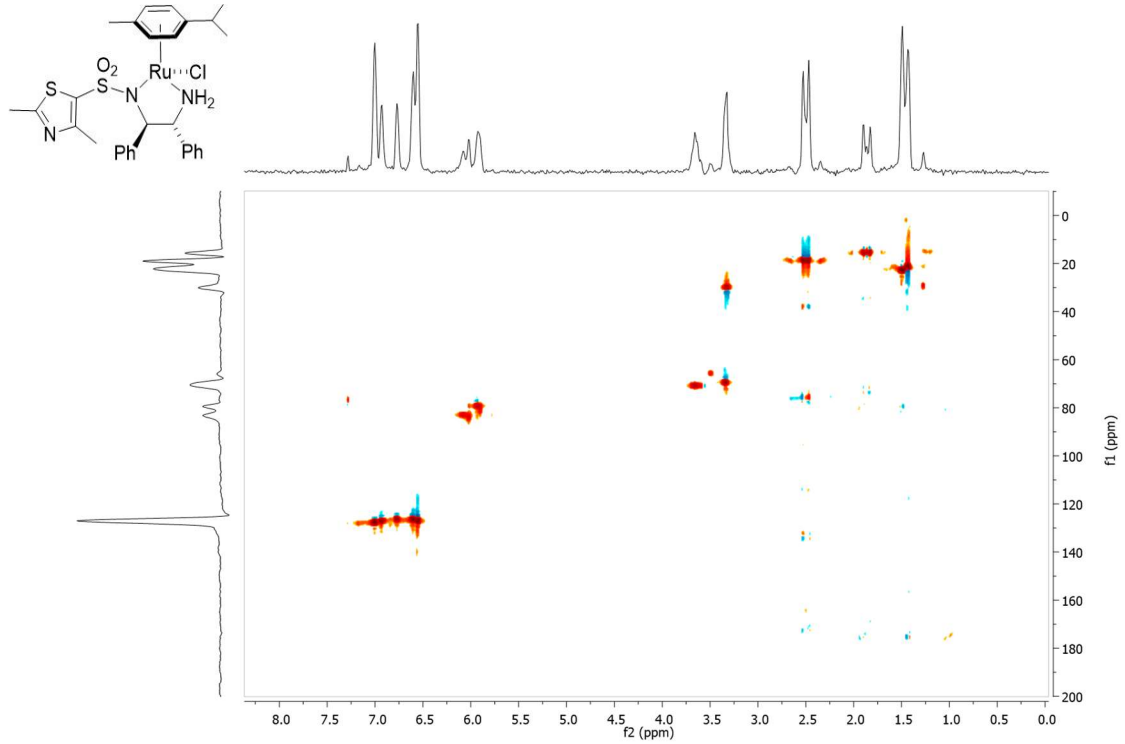
δ_C (126 MHz, $CDCl_3$).



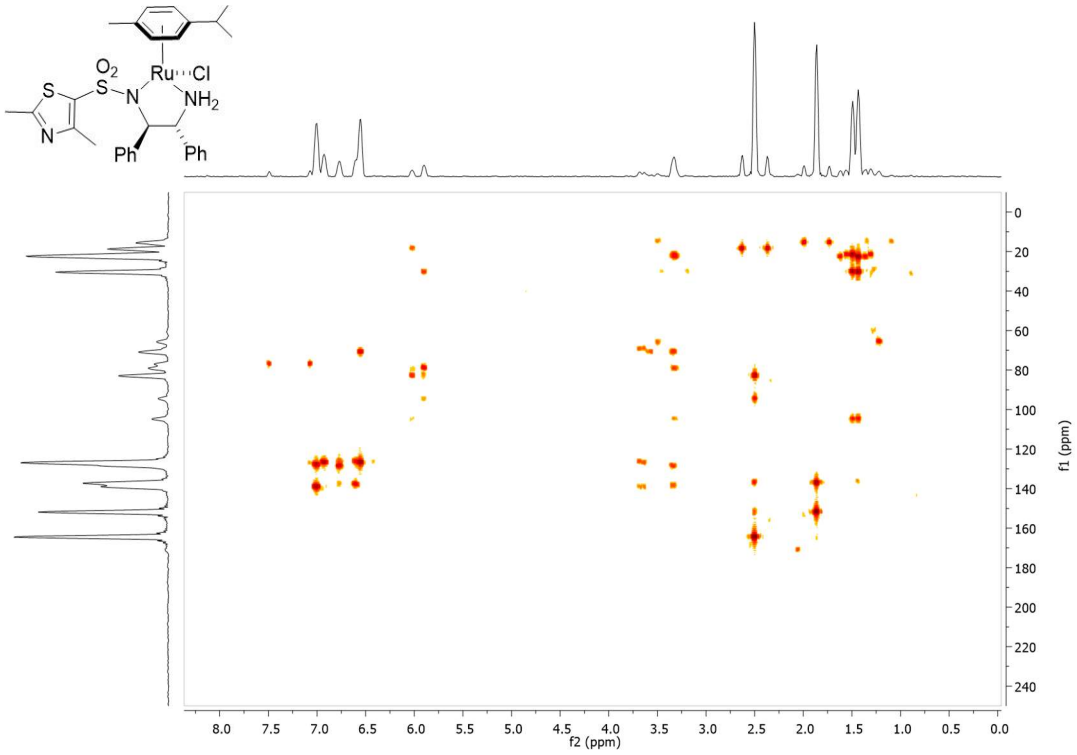




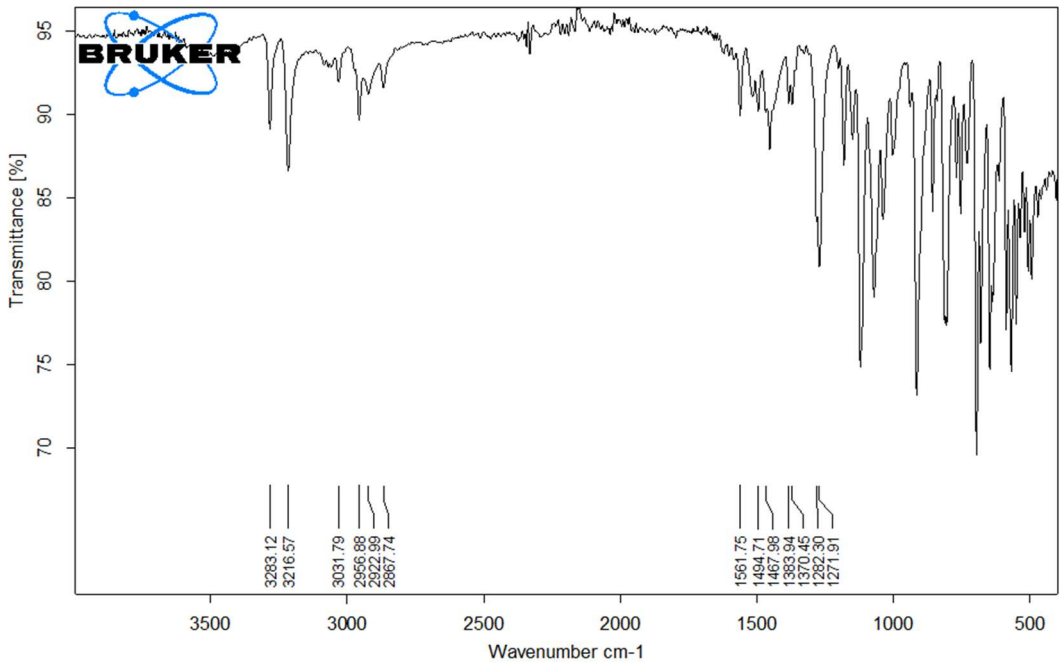
HSQC (500 MHz, $CDCl_3$)



HMBC (500 MHz, $CDCl_3$)



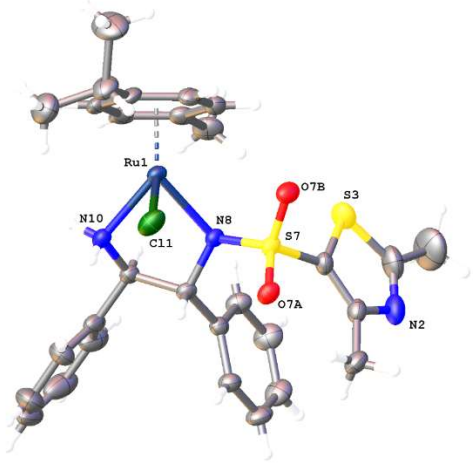
IR spectra



C:\Users\chemist\Desktop\Spectral Data\NK226-ru complex-thioazole.0	NK226-ru complex-thioazole	Instrument type and / or accessor	30/11/2021

Page 1/1

X-ray structure of Ru Complex (*R,R,S*^{Ru})-12c CCDC 2182539 (local code nk5).



solid state structure of the complex in CCDC 2182539 with only key atoms labelled and thermal ellipsoids drawn at 50% probability level

Crystal structure determination.

The asymmetric unit contains the complex and a disordered water. Six times this in the unit cell. The water was modelled as disordered over two closely related positions. The occupancy of the two positions was fixed at 50%. No hydrogens were located on these disordered solvents and they were refined isotropically. The hydrogens were located on the amine but refined restraints. They form short contacts tabulated below

Specified hydrogen bonds (with esds except fixed and riding H)

D-H	H...A	D...A	<(DHA)	
0.91	2.10	2.875(6)	142.0	N10-H10B...O7A_$1

Symmetry operator used to define symmetry related atoms in above contact was $1 -Y+X,+X,-0.167+Z

N10-H10A lies along the bond of the Ru-Cl1 in what seems to be the norm for these compounds in a likely dipole-dipole interaction. Both NHs have a much longer interaction with a symmetry related Cl not detailed above.

The Flack and the associated Hooft y parameter are shown below

Flack x: -0.02(2) Shelx 2018

Hooft y: -0.0278(16) Olex2

These are relatively small with a small error so you can have confidence in the handedness of the structure refined.

Additionally, the molecule is synthesised from a stating material of known configuration

Experimental

Single crystals of $C_{29}H_{34}ClN_3O_3RuS_2$ **[nk5]** were grown from methanol**.** A suitable crystal was selected and mounted on a glass fibre with Fomblin oil and placed on a Rigaku Oxford Diffraction SuperNova diffractometer with a dual source (Cu at zero) equipped with an AtlasS2 CCD area detector. The crystal was kept at 150(2) K during data collection. Using Olex2 [1], the structure was solved with the SHELXT [2] structure solution program using Intrinsic Phasing and refined with the SHELXL [3] refinement package using Least Squares minimisation.

1. Dolomanov, O.V., Bourhis, L.J., Gildea, R.J, Howard, J.A.K. & Puschmann, H. (2009), J. Appl. Cryst. 42, 339-341.
2. Sheldrick, G.M. (2015). Acta Cryst. A71, 3-8.
3. Sheldrick, G.M. (2015). Acta Cryst. C71, 3-8.

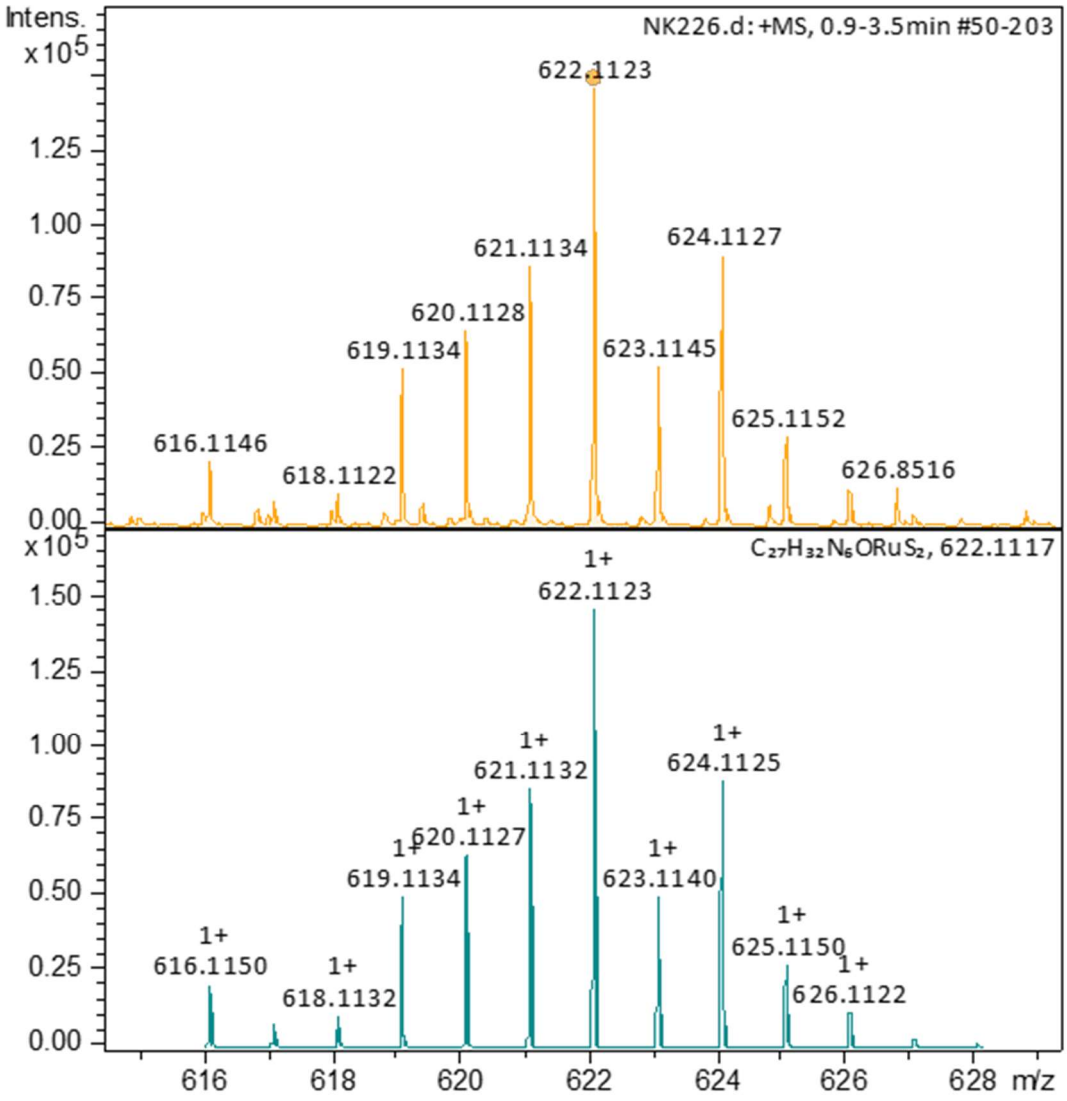
Crystal Data for $C_{29}H_{34}ClN_3O_3RuS_2$ (M =673.23 g/mol): hexagonal, space group $P6_5$ (no. 170), a = 16.90780(10) Å, c = 19.27870(10) Å, V = 4772.90(6) Å^3, Z = 6, T = 150(2) K, μ(Cu Kα) = 6.253 mm^{-1}, *Dcalc* = 1.405 g/cm^3, 96080 reflections measured (7.582° ≤ 2Θ ≤ 147.348°), 6407 unique (R_{int} = 0.0416, R_{sigma} = 0.0134) which were used in all calculations. The final R_1 was 0.0424 (I > 2σ(I)) and wR_2 was 0.1132 (all data).

Table 1 Crystal data and structure refinement. CCDC 2182539.

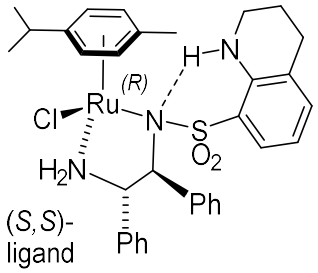
Identification code	nk5
Empirical formula	$C_{29}H_{34}ClN_3O_3RuS_2$
Formula weight	673.23
Temperature/K	150(2)
Crystal system	hexagonal
Space group	$P6_5$
a/Å	16.90780(10)
b/Å	16.90780(10)
c/Å	19.27870(10)
α/°	90
β/°	90
γ/°	120
Volume/Å^3	4772.90(6)
Z	6
ρ_{calc}mg/mm^3	1.405

μ/mm^{-1}	6.253
F(000)	2076.0
Crystal size/mm^3	0.16 × 0.1 × 0.06 yellow block
2Θ range for data collection	7.582 to 147.348°
Index ranges	$-20 \leq h \leq 21$, $-20 \leq k \leq 20$, $-23 \leq l \leq 23$
Reflections collected	96080
Independent reflections	6407[R(int) = 0.0416]
Data/restraints/parameters	6407/1/356
Goodness-of-fit on F^2	1.089
Final R indexes [I>=2σ (I)]	$R_1 = 0.0424$, $wR_2 = 0.1128$
Final R indexes [all data]	$R_1 = 0.0426$, $wR_2 = 0.1132$
Largest diff. peak/hole / e $Å^{-3}$	1.01/-0.74
Flack parameter	-0.027(11)

HRMS


Intens.
x10^5
NK226.d: +MS, 0.9-3.5min #50-203
622.1123
621.1134
624.1127
620.1128
619.1134
623.1145
625.1152
616.1146
618.1122
626.8516
C27H32N6ORuS2, 622.1117
1+ 622.1123
1+ 621.1132
1+ 624.1125
1+ 620.1127
1+ 619.1134
1+ 623.1140
1+ 625.1150
1+ 616.1150
1+ 618.1132
1+ 626.1122
616
618
620
622
624
626
628
m/z

Ru Complex (*S,S,S*^{Ru})-12e of ligand 11d.

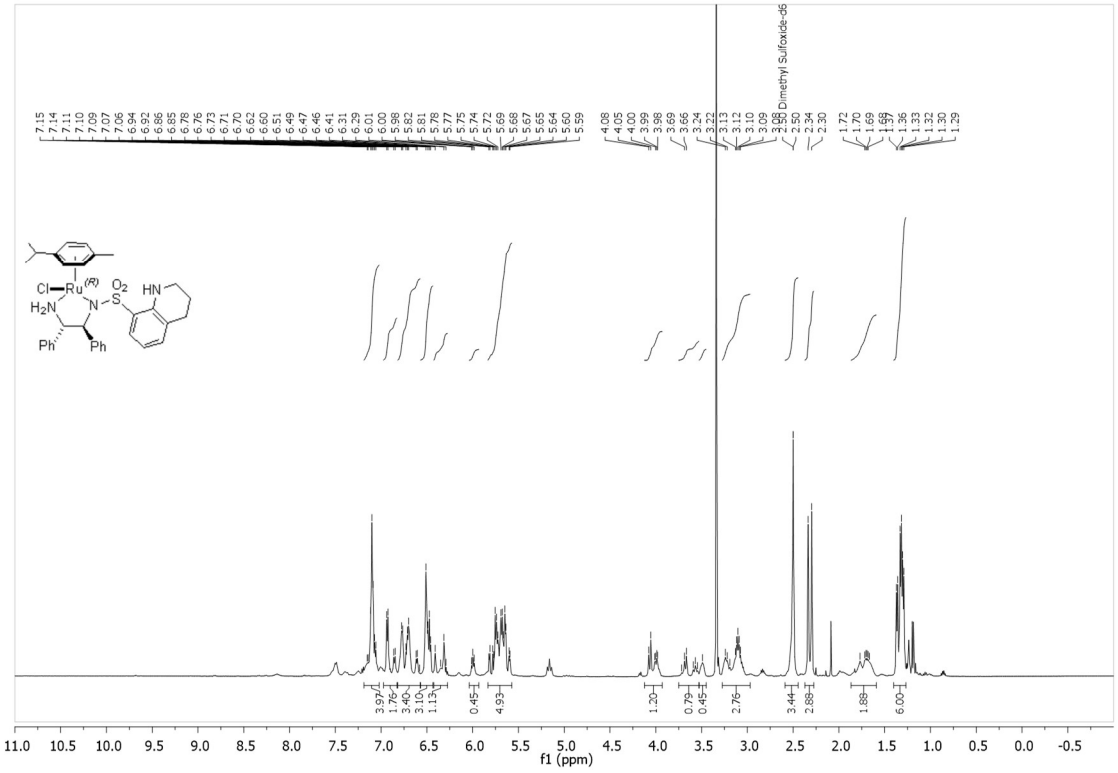


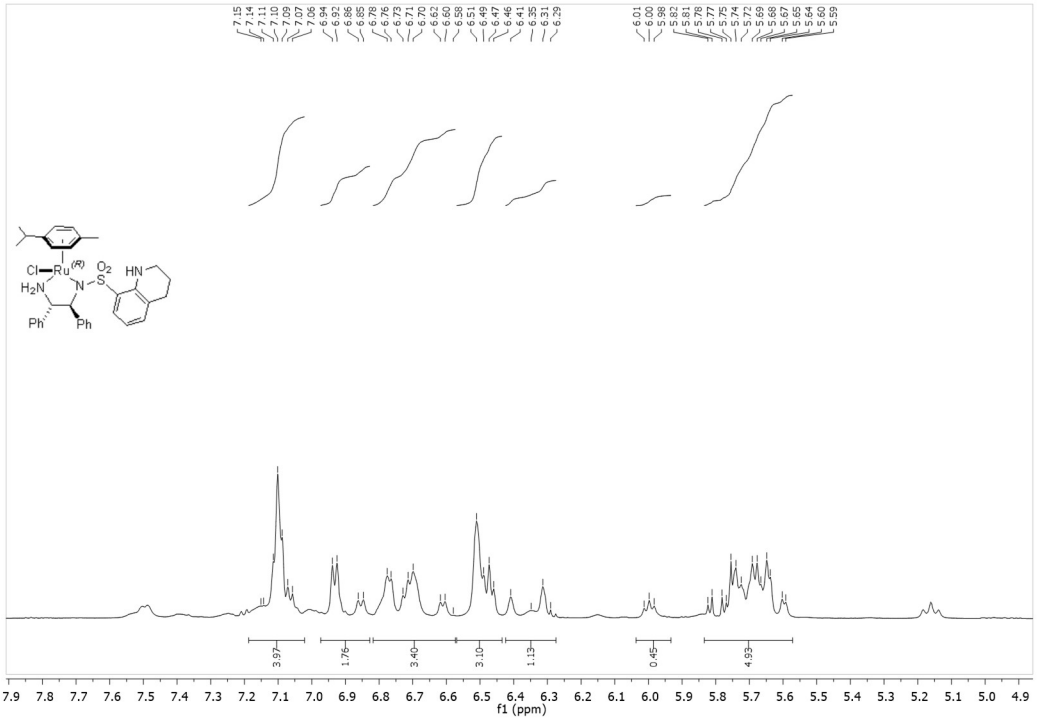
The quinoline ring was reduced to the tetrahydroquinoline upon complexation.

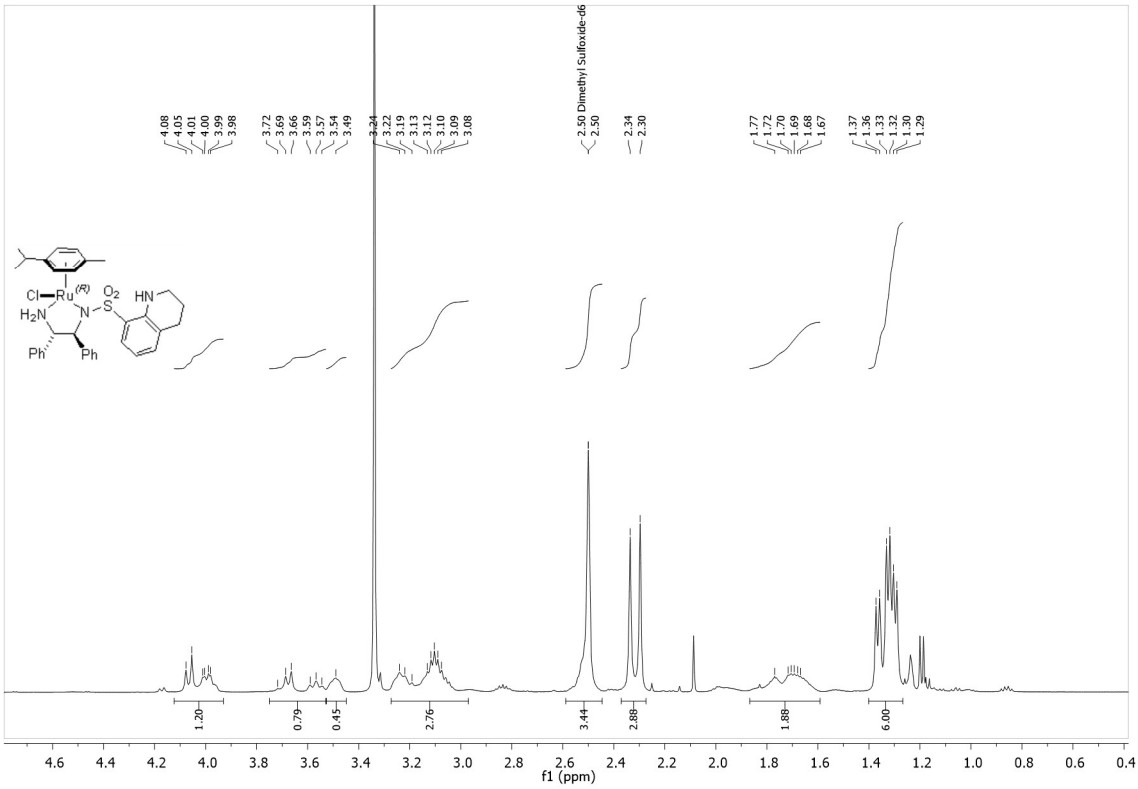
The ^{1}H and ^{13}C NMR spectra indicate the formation of two isomers in a 1:1 ratio, however the X-ray structure is of one isomer and shows an unexpected inversion of the relative configuration of the major diastereoisomer compared to other complexes of this type.

This compound is novel. To a dry 50 mL round-bottom flask charged with a solution of dichloro(p-cymene)ruthenium(II) dimer (92.0 mg, 0.150 mmol) and ligand **11d** (121 mg, 0.300 mmol) in dry 2-propanol (1.5 mL) was added triethylamine (60.8 mg, 0.600 mmol, 80 µL). After stirring at 80 °C for 1 h, the solution was allowed to cool to r.t, and the solvent was removed under reduced pressure. The residue was dissolved in DCM (2 mL) and then dried under vacuum to remove the residues of 2-propanol, then the crude product was washed with water (5 mL). The complex was purified by column chromatography on silica gel (100% DCM to 100% EtOAc) to give the pure product (106 mg, 0.158 mmol, 53%) as an orange solid; TLC: Rf ca 0.5 (1:10 MeOH :DCM), strong UV and $KMnO_4$; Mp = 217.6 °C; $[\alpha]_D^{26}$ = - 675 (*c* 0.016 in $CHCl_3$); ν_{max} 3549, 3442, 3333, 3247 cm^{-1}; δ_H (500 MHz, d^6-DMSO) 7.55-7.45 (0.5 H, m, ArH), 7.15-7.05 (3 H, m, ArH), 6.96-6.92 (1 H, m, ArH), 6.85-6.75 (1 H, m, ArH), 6.75-6.68 (1.5 H, m, ArH), 6.62 (0.5 H, d, J = 8.0 Hz, ArH), 6.58-6.45 (3 H, m, ArH), 6.42 (0.5 H, brs, ArH), 6.38-6.30 (0.5 H, m, ArH), 6.05-5.96 (0.5 H, m, ArH), 5.80-5.63 (4.5 H, m, 4 x RuArH + 0.5 ArH), 4.08 (0.5 H, d, J = 8.0 Hz, NCH), 4.05-3.96 (0.5 H, m, NCH), 4.68 (0.5 H, d, J = 9.0 Hz, NCH), 3.62-3.55 (0.5 H, m, NCH), 3.55-3.47 (1 H, m, quinNCHH), 3.28-3.20 (1 H, m, quinNCHH), 3.18-3.05 (2 H, m, C<u>H</u>Me_2 + NH), 2.55-2.48 (2 H, m, $THQCH_2$), 2.36 (1.5 H, s, cym-Me), 3.30 (1.5 H, s, cym-Me), 1.82-1.62 (2 H, m, CH_2), 1.42-1.28 (6 H, m, CH<u>Me</u>$_2$); δ_C (126 MHz, d^6-DMSO) 142.49 (ArC), 142.15 (ArC), 140.28 (ArC), 140.10 (ArC), 139.34 (ArC), 138.39 (ArC), 130.03 (ArCH), 129.15 (ArCH), 129.04 (ArCH), 128.65 (ArCH), 128.47 (ArCH), 128.38 (ArCH), 128.14 (ArCH), 127.84 (ArCH), 127.45 (ArCH), 127.49 (ArCH), 126.76 (ArCH), 126.55 (ArCH), 126.43 (ArCH), 124.70 (ArC), 122.39 (ArC), 120.78 (ArC), 120.13 (ArC), 113.75 (Quin CH), 112.47 (Quin CH), 106.84 (RuArC), 104.00 (RuArC), 100.55 (RuArC), 95.30 (RuArC), 94.85 (RuArC), 86.84 (RuArCH), 85.98 (RuArCH), 84.16 (RuArCH), 82.49 (RuArCH), 82.32 (RuArCH), 81.49 (RuArCH), 81.07 (RuArCH), 79.85 (RuArCH), 71.87 (NCH), 70.73 (NCH), 69.34 (NCH), 65.98 (NCH), 41.33 (NCH_2), 40.87 (NCH_2), 30.45 (CH_3), 30.29 (CH_3), 27.86 (CH_2), 27.70 (CH_2), 22.85 (CH_3), 22.54 (CH_3), 22.17 (CH_3), 21.97 (CH_3), 21.08 (CH_2), 20.96 (CH_2), 18.68 (CH_3), 18.33 (CH_3); *m/z* (ESI^+) 642.2 [M -Cl] $^+$; HRMS (ESI-TOF) m/z: [M - Cl]$^+$ calcd for $C_{33}H_{38}N_3O_2{}^{102}RuS$ 642.1723, found 642.1720 (1.6 ppm error).

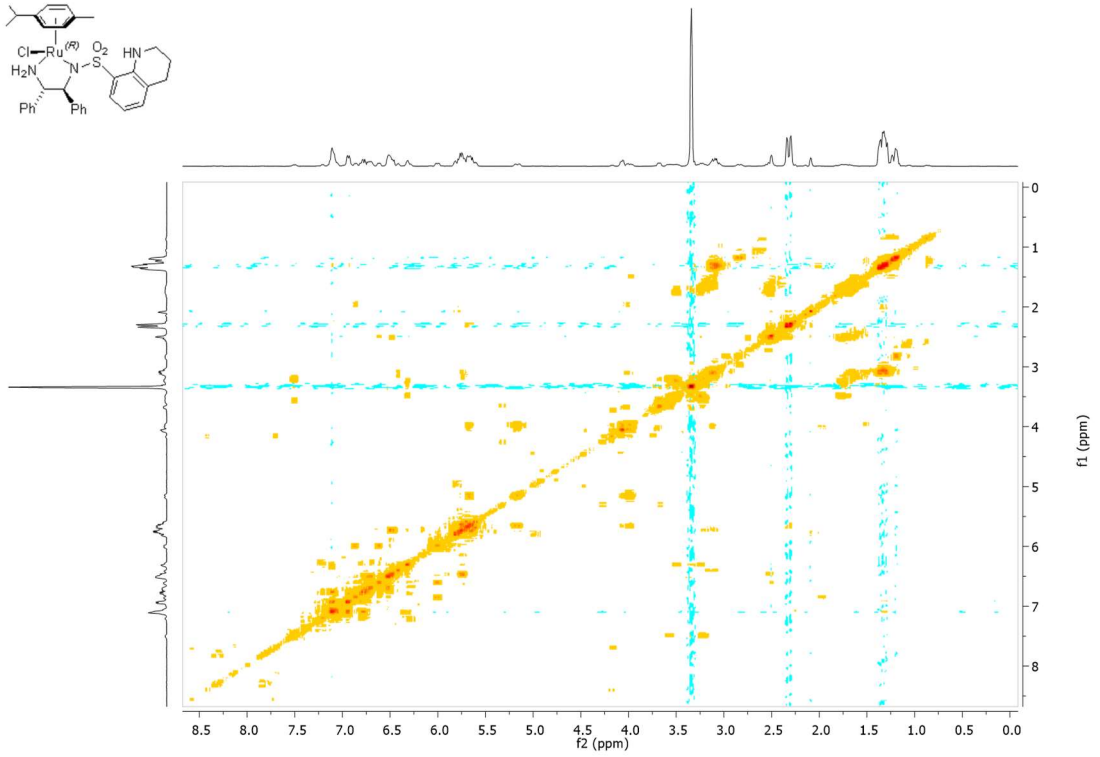
δ_H (500 MHz, d^6-DMSO)

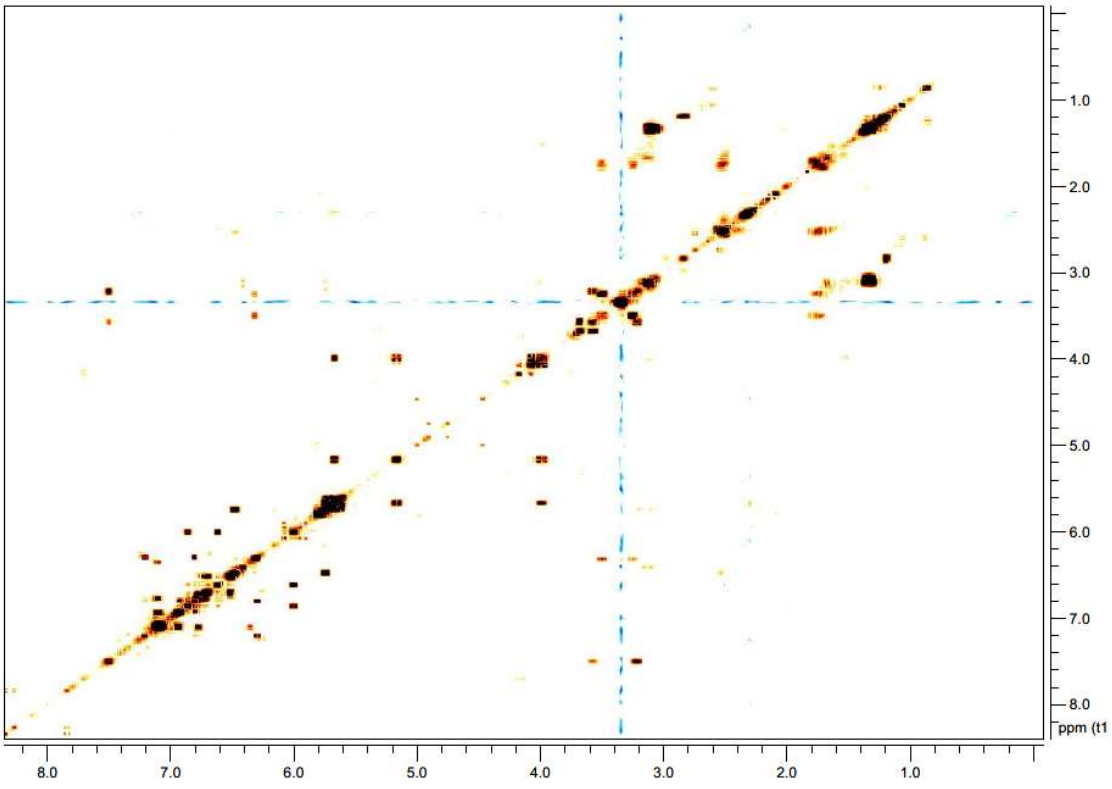


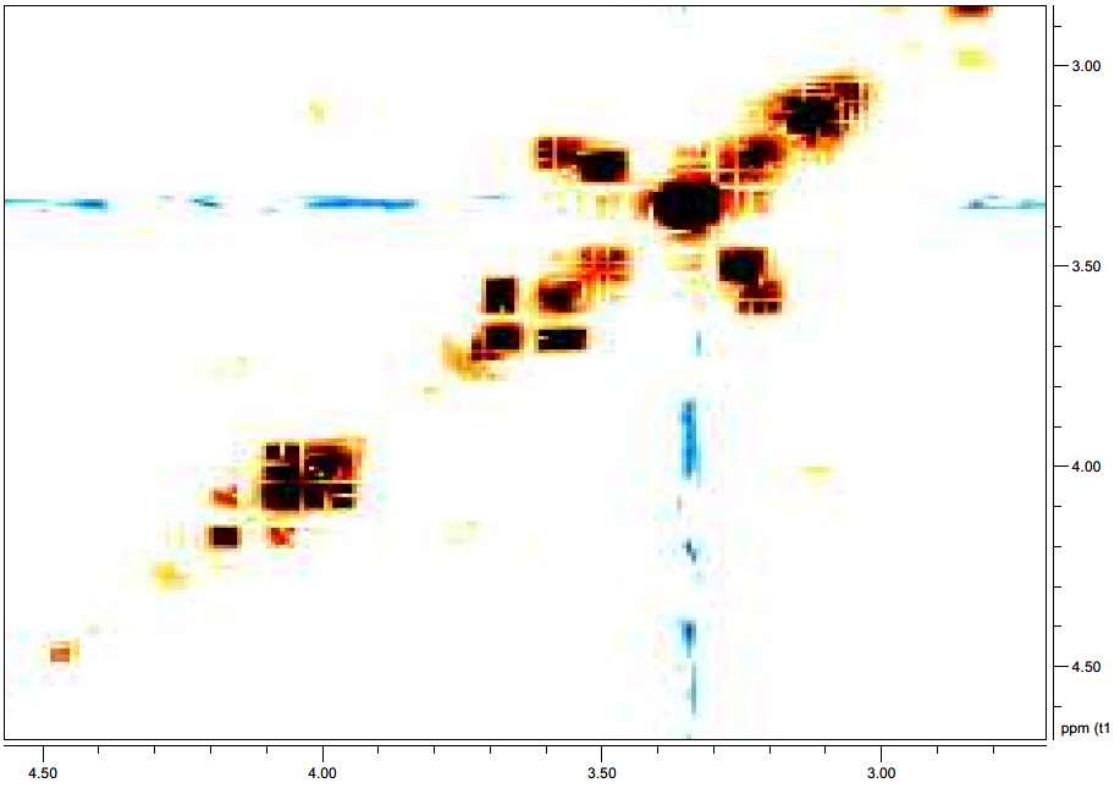




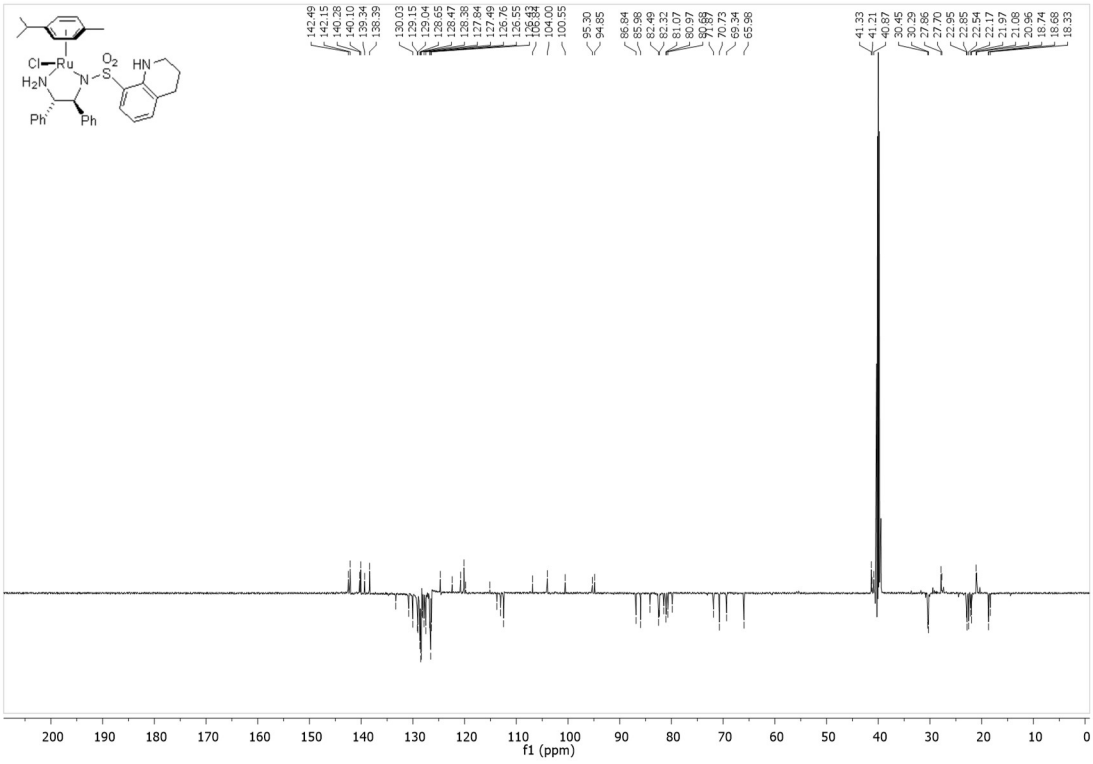
COSY (500 MHz, d⁶-DMSO)

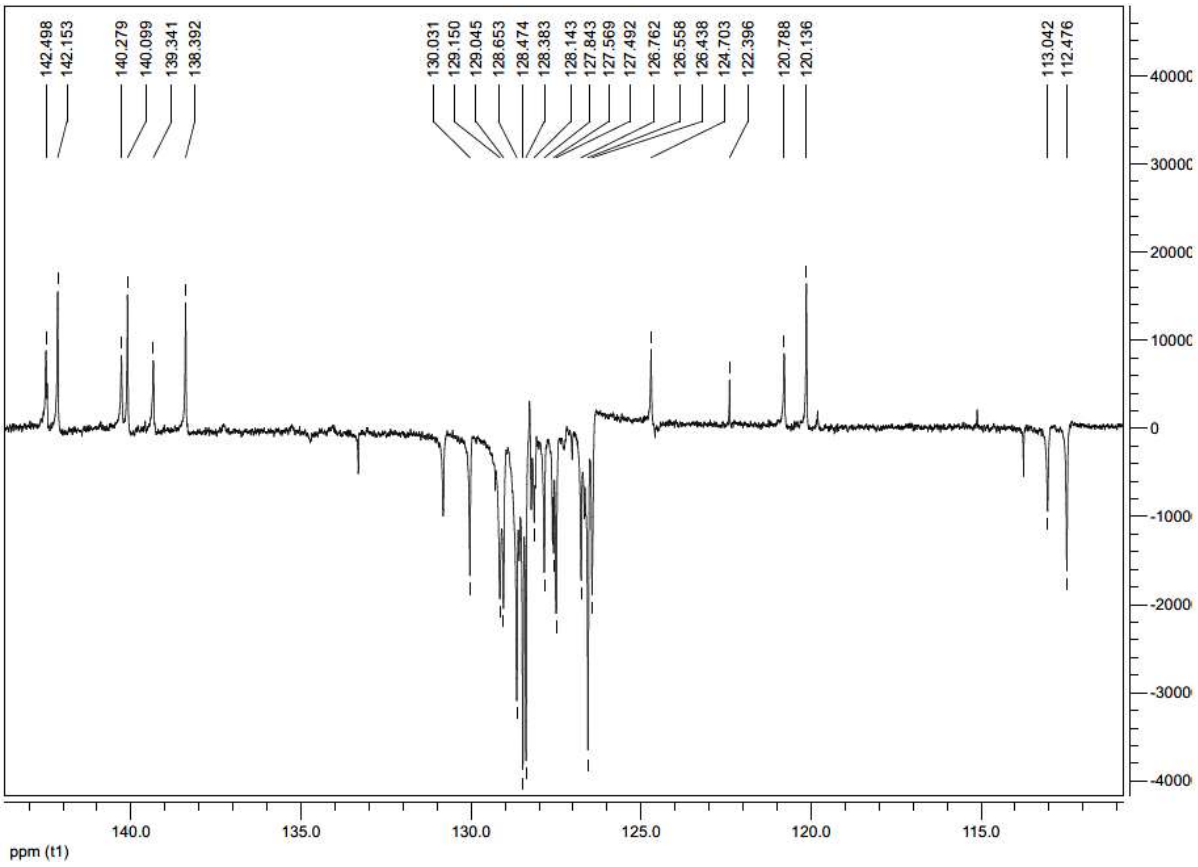


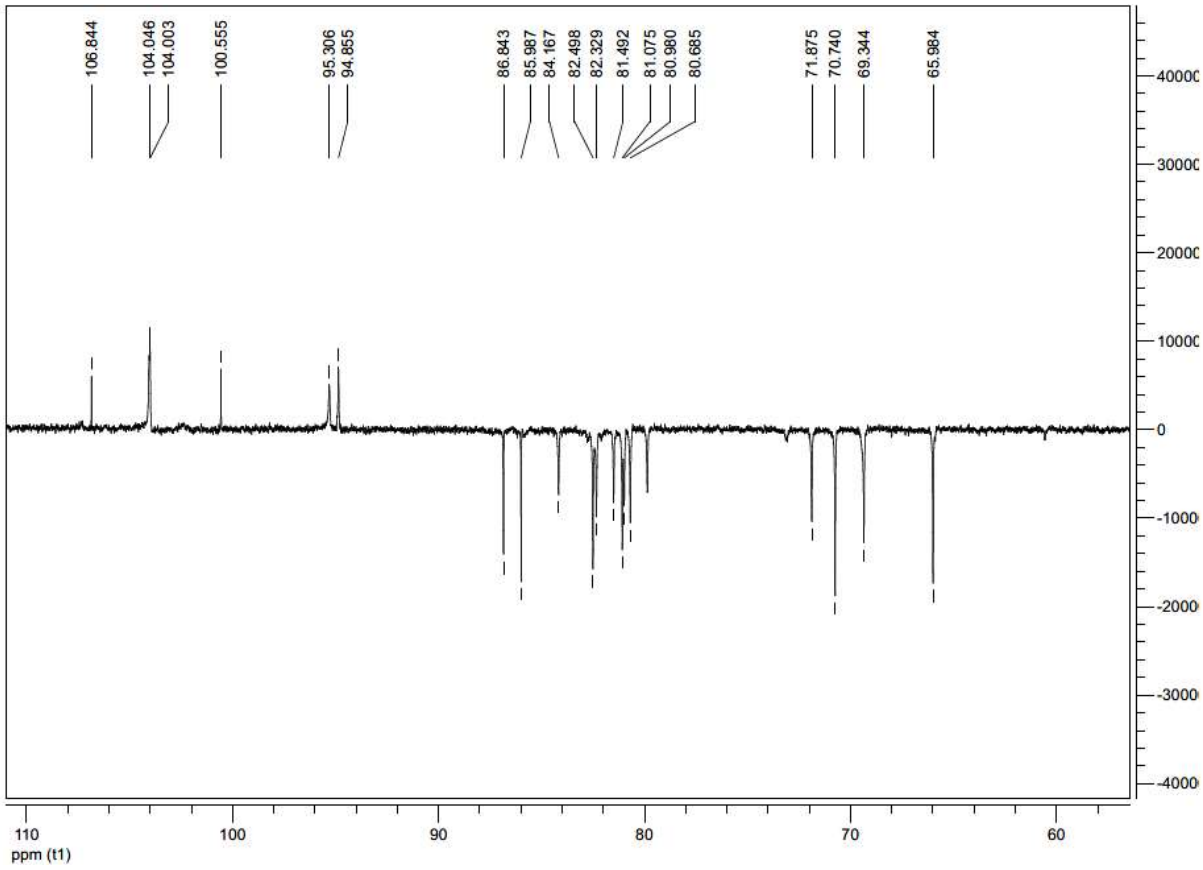

1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
ppm (t1
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0


3.00
3.50
4.00
4.50
ppm (t1
4.50
4.00
3.50
3.00

δ_C (126 MHz, d^6-DMSO)



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104.046
104.003
100.555
95.306
94.855
86.843
85.987
84.167
82.498
82.329
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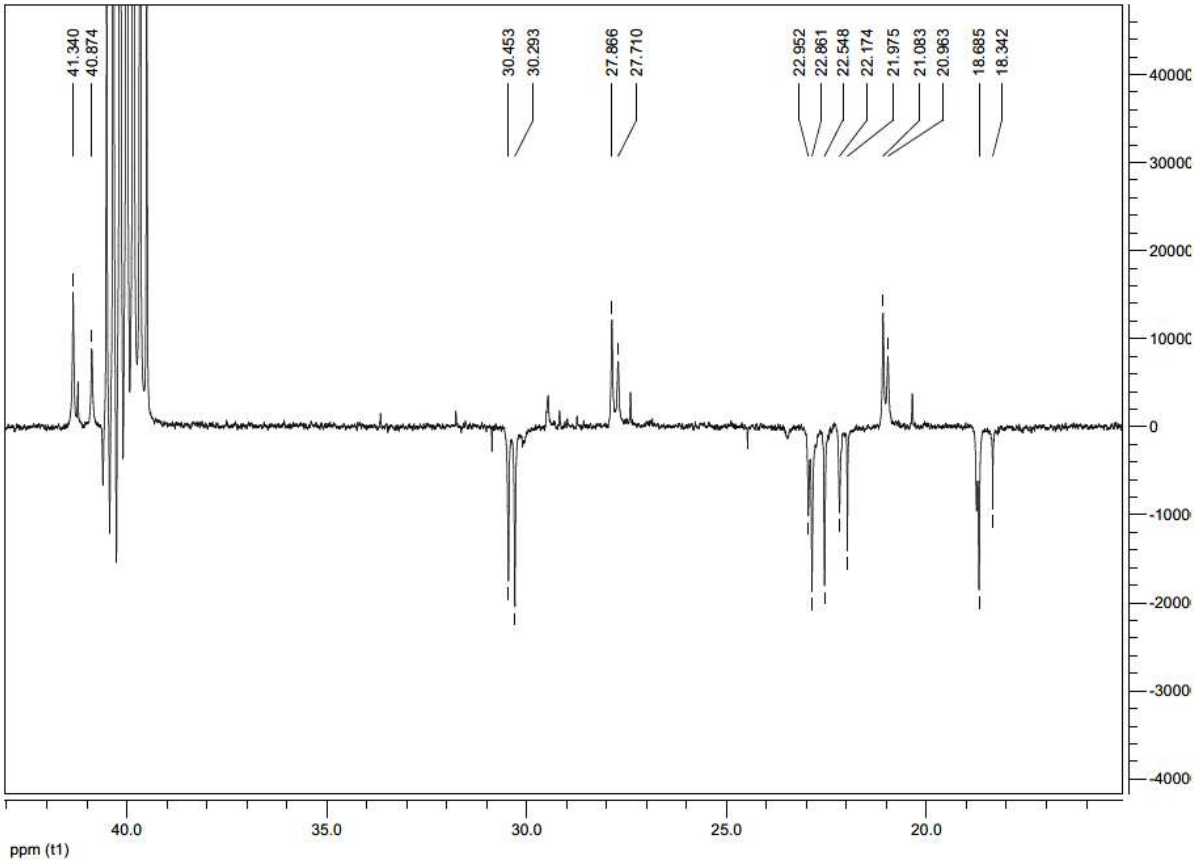
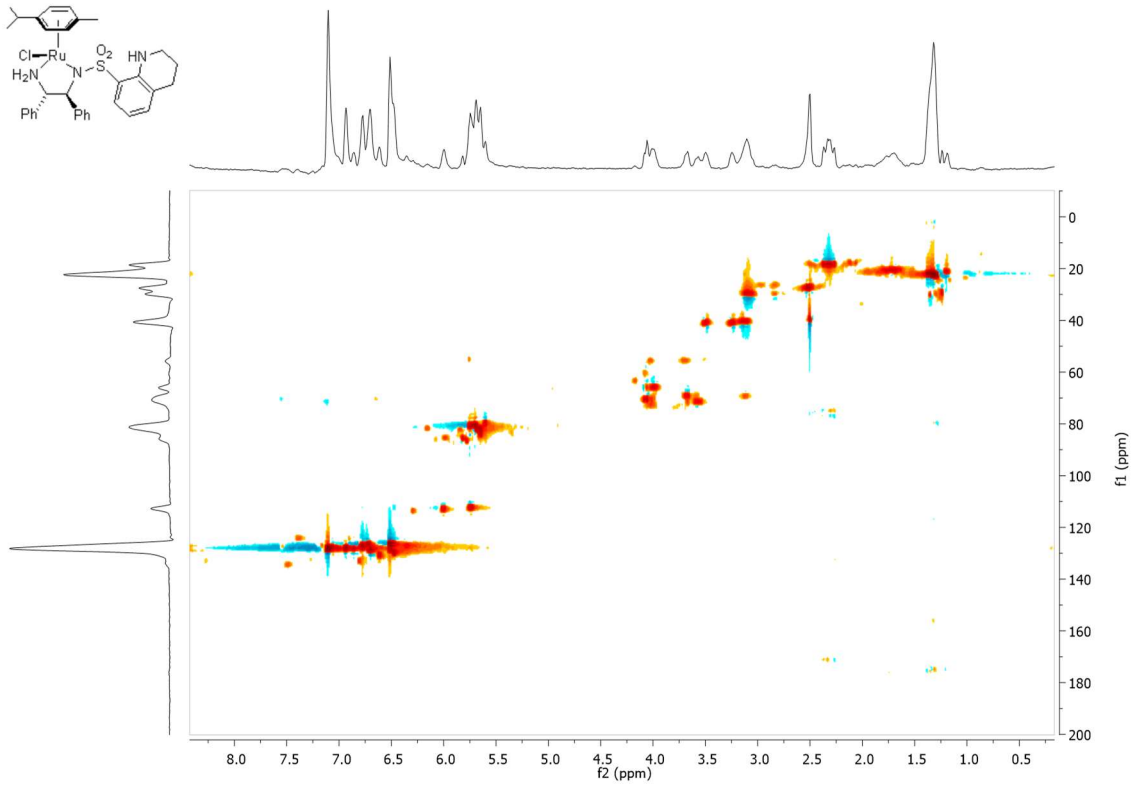
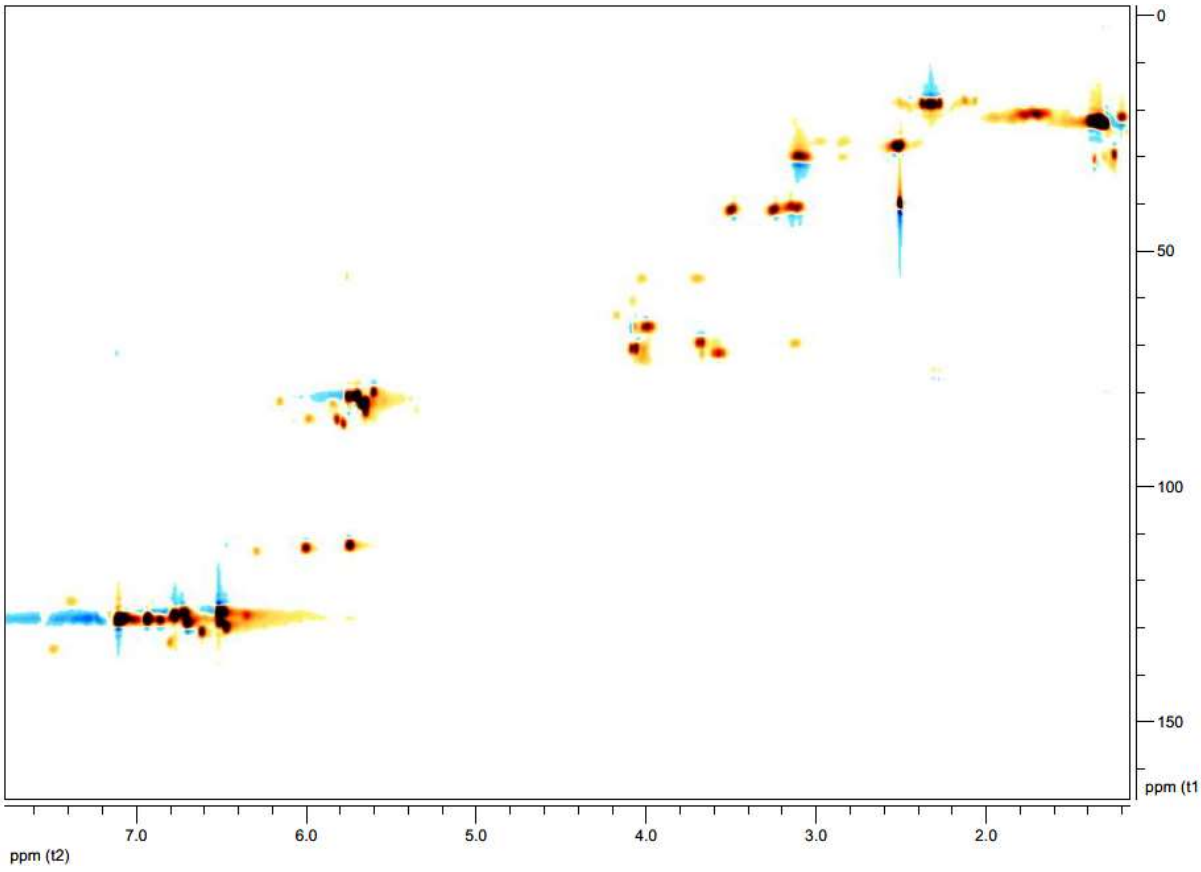
110
100
90
80
70
60
ppm (t1)

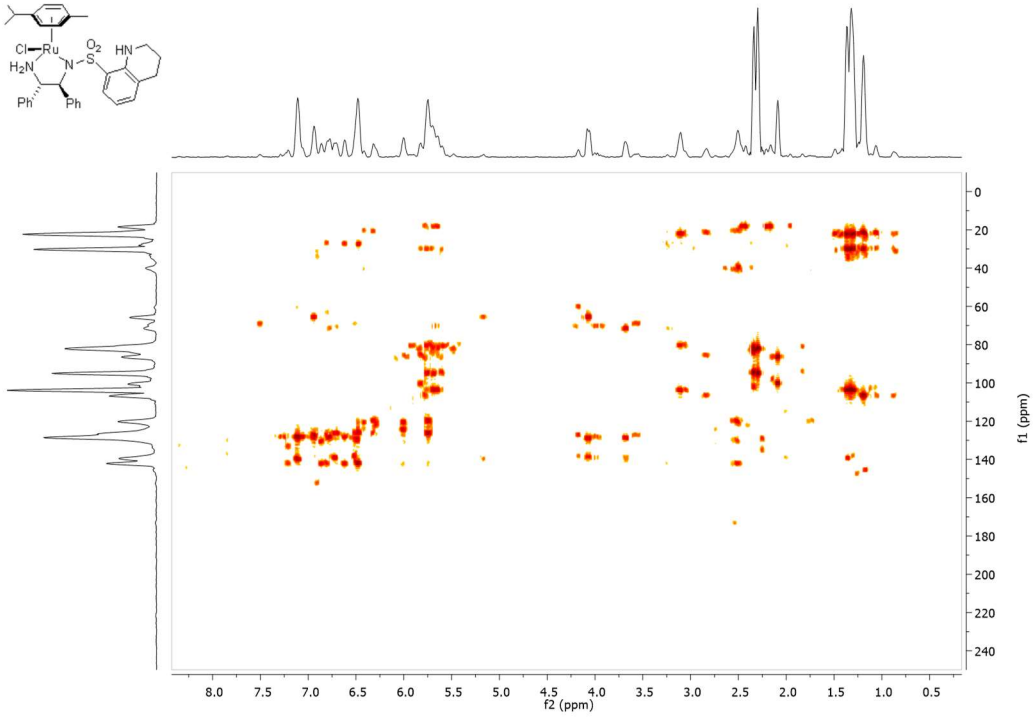

41.340
40.874
30.453
30.293
27.866
27.710
22.952
22.861
22.548
22.174
21.975
21.083
20.963
18.685
18.342
40.0
35.0
30.0
25.0
20.0
ppm (t1)

HSQC (500 MHz, d^6-DMSO)

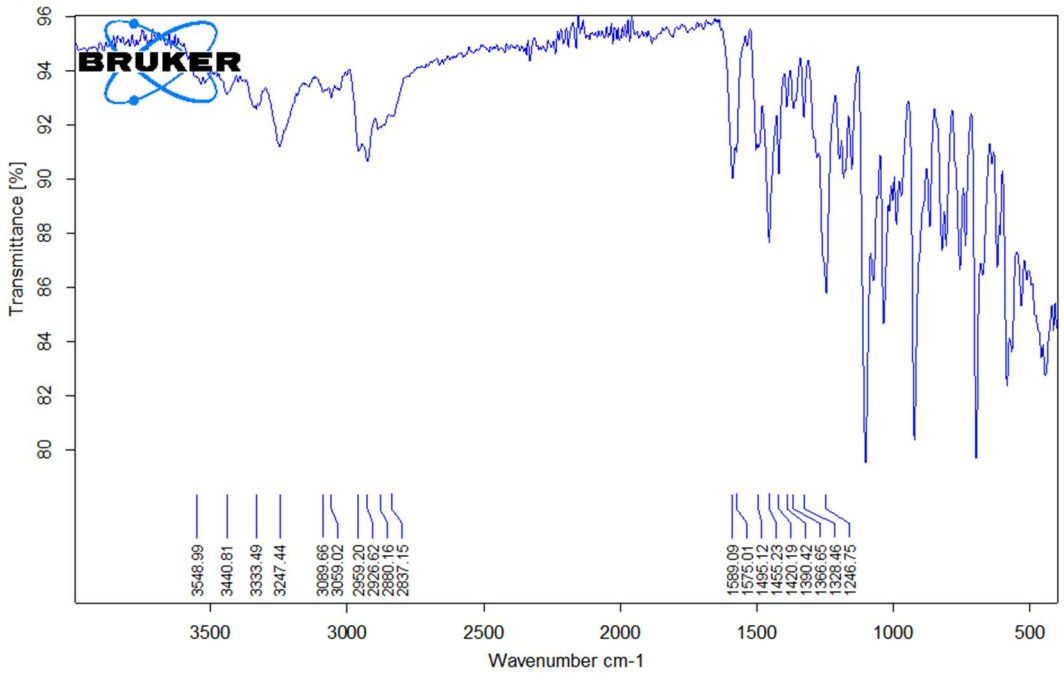




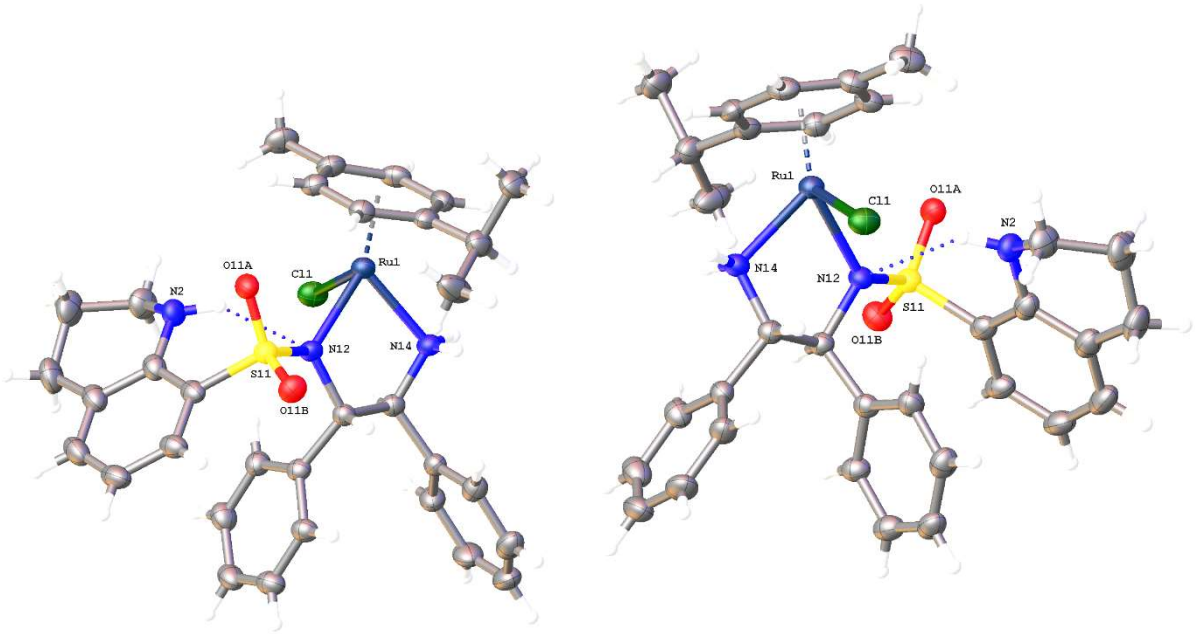
HMBC (500 MHz, d^6-DMSO)



IR spectra



X-Ray structure of Ru Complex (S,S,S^{Ru})-12e CCDC 2182540 (4) (local code nk6).



Two different views of the solid state structure on CCDC 2182540 with only key atoms labelled and thermal ellipsoids drawn at 50% probability level

Crystal structure determination.

The asymmetric unit contains the complex and a molecule of methanol. Twice this in the unit cell. The NHs and the OH on the methanol were located in a difference map and refined with distance restraints. They form short contacts tabulated below.

Specified hydrogen bonds (with esds except fixed and riding H)

D-H	H...A	D...A	<(DHA)	
0.91	2.23	2.974(7)	138.0	N14-H14A...O11A_$1
0.91	2.40	3.205(8)	148.3	N14-H14B...O37_$1
0.95(3)	2.33(3)	3.096(8)	137(4)	N2-H2...N12
0.84	2.12	2.952(9)	170.5	O37-H37...N2

Symmetry operator used to generate symmetry equivalent atom discussed in above contact where $1 1-X,-0.5+Y,1-Z

The Flack parameter and associated Hooft y parameter parameter were

Flack x: -0.011(10) Shelx2018

Hooft y: -0.028(3) Olex2

These are reasonably small with a reasonably small error but not so important as the complex was made from a starting material of known handedness.

Of interest is the unusual orientation of the NH_2 hydrogens. The bond of one of the N-H hydrogens traditionally points along the Ru-Cl bond/vector (see other solid state structures of these types of Ru complexes). This may be because of steric hindrance or what appears to be a close contact/H-bond between the tetrahydroquinolyl N2-H2 and the deprotonated sulphonamide amide N12.

Experimental

Single crystals of $C_{34}H_{42}ClN_3O_3RuS$ [nk6] were grown from methanol**.** A suitable crystal was selected and mounted on a glass fibre with Fomblin oil and placed on a Rigaku Oxford Diffraction SuperNova diffractometer with a dual source (Cu at zero) equipped with an AtlasS2 CCD area detector. The crystal was kept at 150(2) K during data collection. Using Olex2 [1], the structure was solved with the SHELXT [2] structure solution program using Intrinsic Phasing and refined with the SHELXL [3] refinement package using Least Squares minimisation.

1. Dolomanov, O.V., Bourhis, L.J., Gildea, R.J, Howard, J.A.K. & Puschmann, H. (2009), J. Appl. Cryst. 42, 339-341.
2. Sheldrick, G.M. (2015). Acta Cryst. A71, 3-8.
3. Sheldrick, G.M. (2015). Acta Cryst. C71, 3-8.

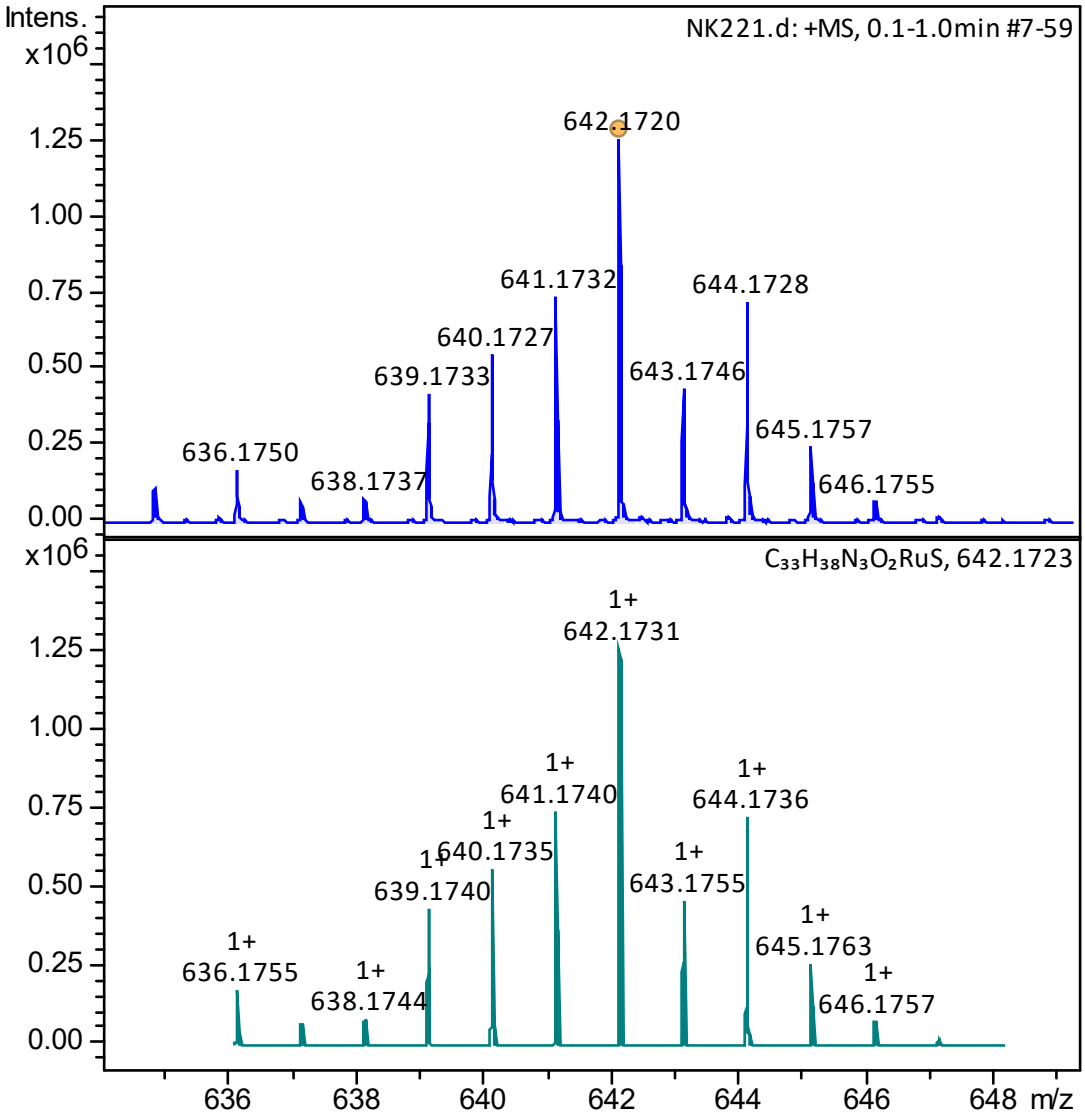
Crystal Data for $C_{34}H_{42}ClN_3O_3RuS$ (M =709.28 g/mol): monoclinic, space group $P2_1$ (no. 4), a = 9.40940(6) Å, b = 14.51707(10) Å, c = 12.09559(8) Å, β = 102.9107(7)°, V = 1610.45(2) Å^3, Z = 2, T = 150(2) K, μ(Cu Kα) = 5.616 mm^{-1}, *Dcalc* = 1.463 g/cm^3, 41114 reflections measured (7.498° ≤ 2Θ ≤ 147.23°), 6469 unique (R_{int} = 0.0384, R_{sigma} = 0.0233) which were used in all calculations. The final R_1 was 0.0422 (I > 2σ(I)) and wR_2 was 0.1132 (all data).

Table 1 Crystal data and structure refinement for nk6. CCDC 2182540.

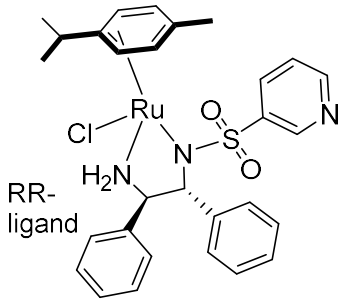
Identification code	nk6
Empirical formula	$C_{34}H_{42}ClN_3O_3RuS$
Formula weight	709.28
Temperature/K	150(2)
Crystal system	monoclinic
Space group	$P2_1$
a/Å	9.40940(6)
b/Å	14.51707(10)
c/Å	12.09559(8)
α/°	90
β/°	102.9107(7)
γ/°	90

Volume/Å^3	1610.45(2)
Z	2
ρ_{calc}mg/mm^3	1.463
μ/mm^{-1}	5.616
F(000)	736.0
Crystal size/mm^3	0.14 × 0.1 × 0.05 yellow block
2Θ range for data collection	7.498 to 147.23°
Index ranges	-11 ≤ h ≤ 11, -18 ≤ k ≤ 17, -15 ≤ l ≤ 15
Reflections collected	41114
Independent reflections	6469[R(int) = 0.0384]
Data/restraints/parameters	6469/4/396
Goodness-of-fit on F^2	1.065
Final R indexes [I>=2σ (I)]	R_1 = 0.0422, wR_2 = 0.1128
Final R indexes [all data]	R_1 = 0.0425, wR_2 = 0.1132
Largest diff. peak/hole / e Å^{-3}	2.20/-0.92
Flack parameter	-0.011(10)

HRMS

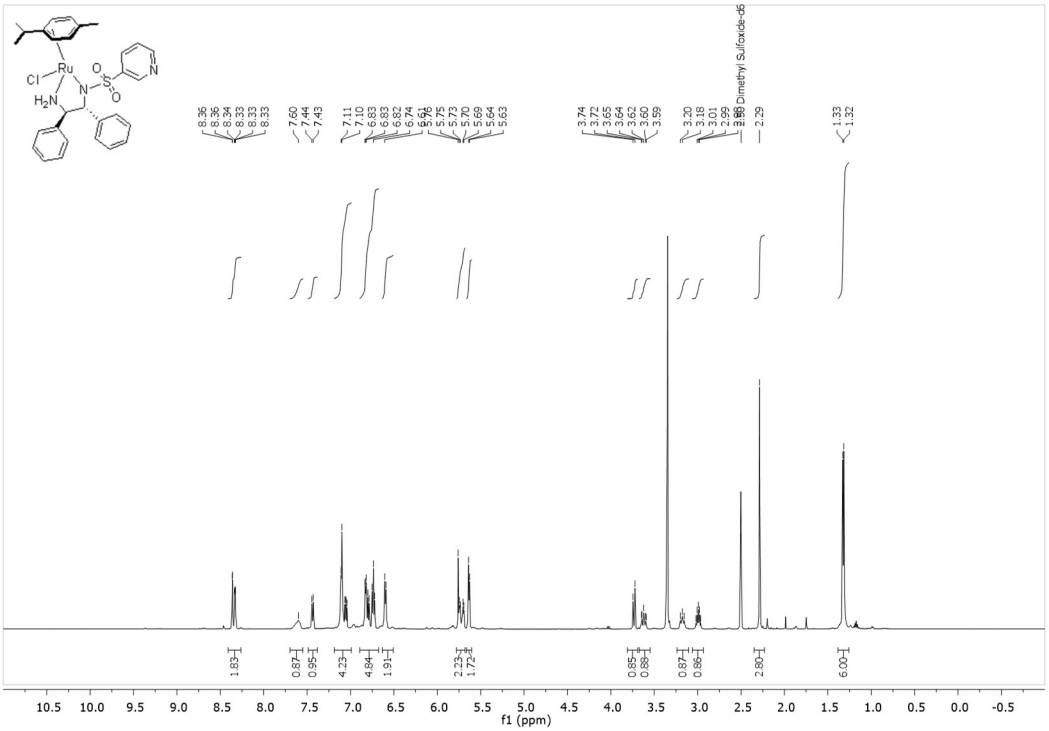

Intens.
x10^6
1.25
1.00
0.75
0.50
0.25
0.00
NK221.d: +MS, 0.1-1.0min #7-59
642.1720
641.1732
644.1728
640.1727
639.1733
643.1746
645.1757
636.1750
638.1737
646.1755
x10^6
C33H38N3O2RuS, 642.1723
1+
642.1731
1+
641.1740
1+
644.1736
1+
640.1735
1+
639.1740
1+
643.1755
1+
645.1763
1+
636.1755
1+
638.1744
1+
646.1757
636
638
640
642
644
646
648
m/z

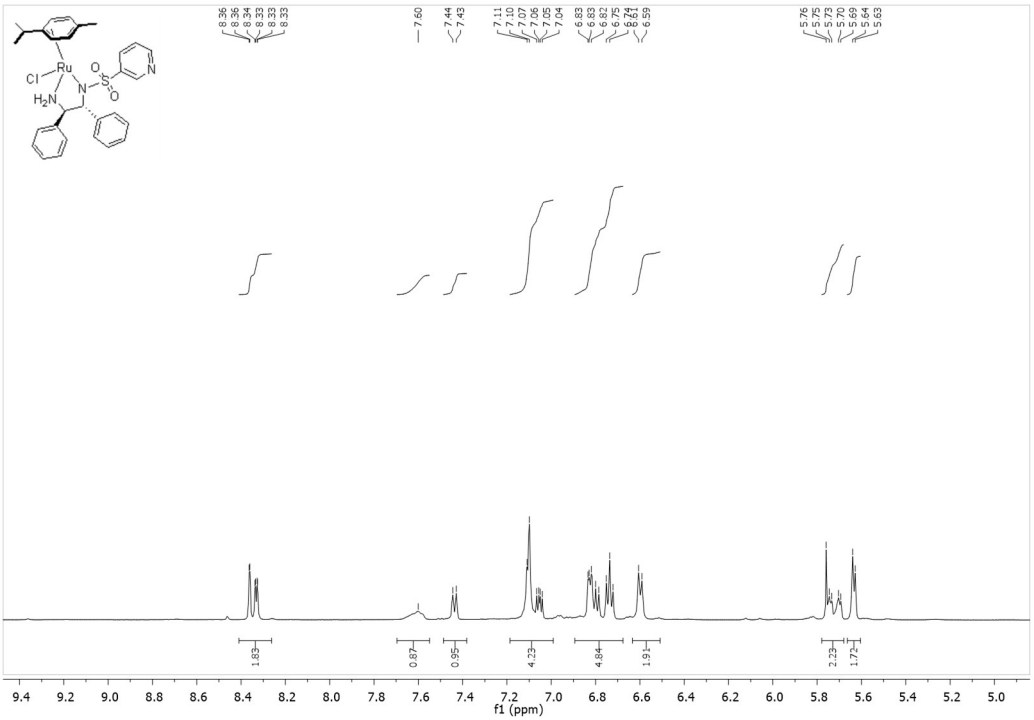
Ru Complex (*R*,*R*,*S*^{Ru})-12f of ligand (*R*,*R*)-11f.

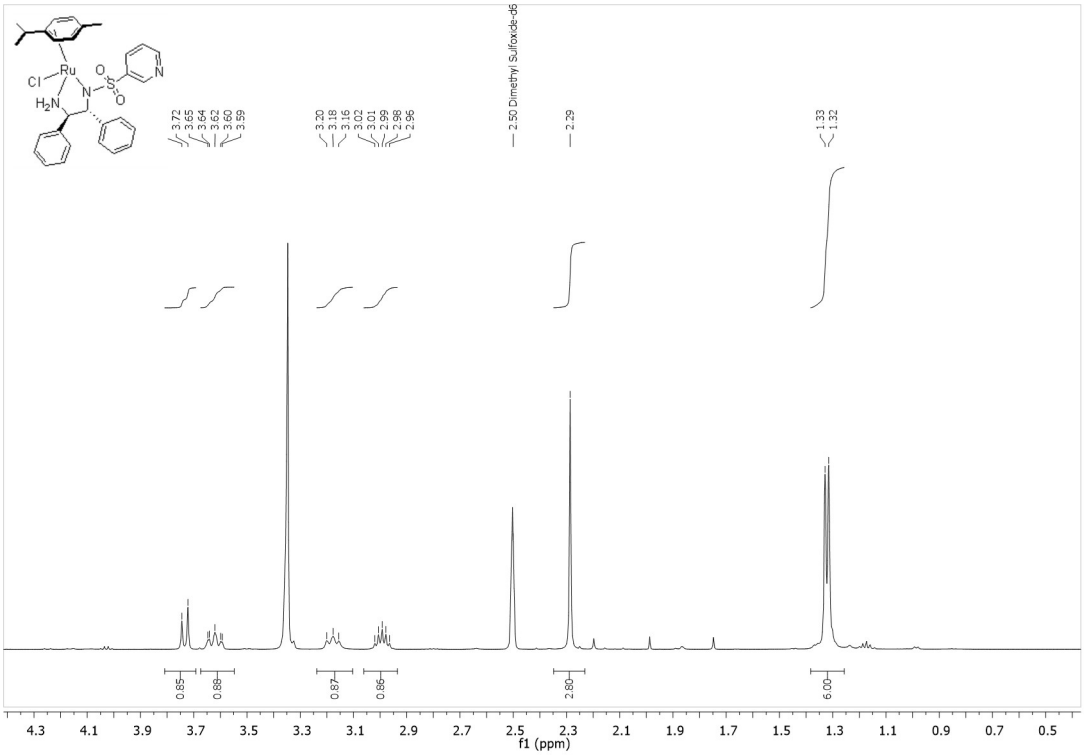


This compound is novel. To a dry 50 mL round-bottom flask charged with a solution of dichloro(p-cymene)ruthenium(II) dimer (347 mg, 0.567 mmol) and ligand **11f** (400 mg, 1.13 mmol) in dry 2-propanol (14 mL) was added triethylamine (229 mg, 2.27 mmol, 400 µL). After stirring at 80 °C for 1 h, the solution was allowed to cool to rt, and the solvent was removed under reduced pressure. The residue was dissolved in DCM (2 mL) to remove residues of 2-propanol and then dried under vacuum, then the crude product was washed with water (5 mL). The complex was purified by column chromatography on silica gel (100% DCM to 10% MeOH: 89% EtOAc and 1% Et_3N), then extracted with DCM (3 x 30 mL) to remove excess Et_3N after adding water (10 mL) and dried using $MgSO_4$ to give the pure product (337 mg, 0.542 mmol, 48%) as a orange solid; TLC: Rf ca 0.6 (1:10 MeOH :DCM), strong UV and $KMnO_4$; Mp =210 °C; $[\alpha]_D^{21}$ = +10.7 (*c* 0.0035 in $CHCl_3$); ν_{max} 3061, 3028, 2961, 2921, 2865, 1593 cm^{-1}; δ_H (500 MHz, DMSO) 8.41 – 8.28 (2 H, m, ArH of pyridyl), 7.61 (1 H,br. s, NH*H*), 7.44 (1 H, d, *J* 7.9, ArH), 7.08 (4 H, m, ArH), 6.79 (5 H, m, ArH), 6.60 (2 H, d, *J* 7.3, ArH), 5.80 – 5.68 (2 H, m, ArCH of *p*-cymene), 5.64 (2 H, d, *J* 5.9, ArCH of *p*-cymene), 3.74 (1 H, d, *J* 11.3 NCH of NSO_2), 3.67 – 3.55 (1 H, m, NCH of NH_2), 3.18 (1 H, t, *J* 11.3,N*H*H), 3.00 (1 H, m, C*H*Me_2 of *p*-cymene), 2.29 (3 H, s, CH_3), 1.33 (6 H, d, *J* 6.8, CH_3); δ_C (126 MHz, DMSO) 149.63 (ArCH pyridine), 147.82 (ArCH pyridine), 142.63 (ArC), 140.14 (ArC), 139.53 (ArC), 134.32 (ArCH), 129.30 (ArCH), 128.66 (ArCH), 128.12 (ArCH), 127.63 (ArCH), 127.35 (ArCH), 126.84 (ArCH), 122.87 (ArCH), 103.23 (RuArC), 95.33 (RuArC), 84.76 (RuArCH), 81.62 (RuArCH), 81.47 (RuArCH), 80.10 (RuArCH), 71.19 (NCH), 68.85 (NCH), 30.52 (C*H*Me_2 of *p*-cymene), 23.20 (CH_3), 21.87 (CH_3), 18.78 (CH_3); *m/z* (ESI^+) 588.1[M - Cl]$^+$; HRMS (ESI-TOF) m/z: [M - Cl]$^+$ calcd for $C_{29}H_{32}N_3O_2{}^{102}RuS$ 588.1253, found 588.1266 (-0.9 ppm error).

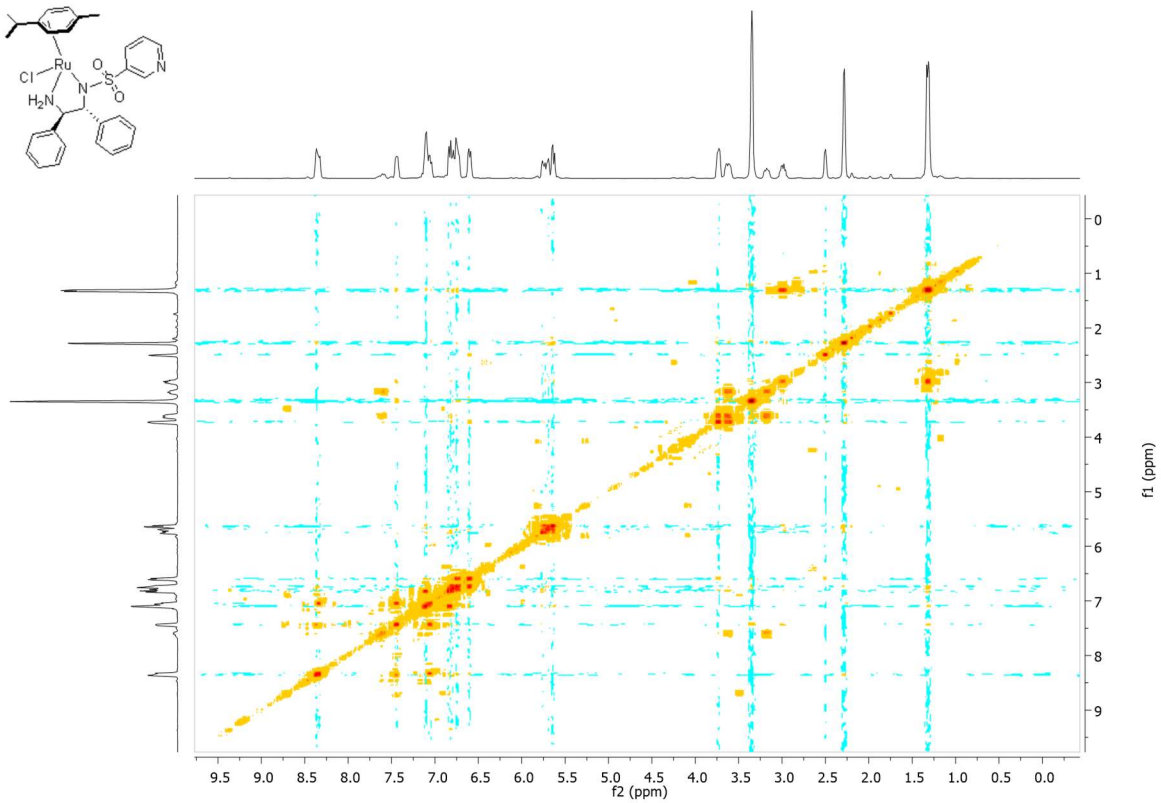
δ_H (500 MHz, DMSO)



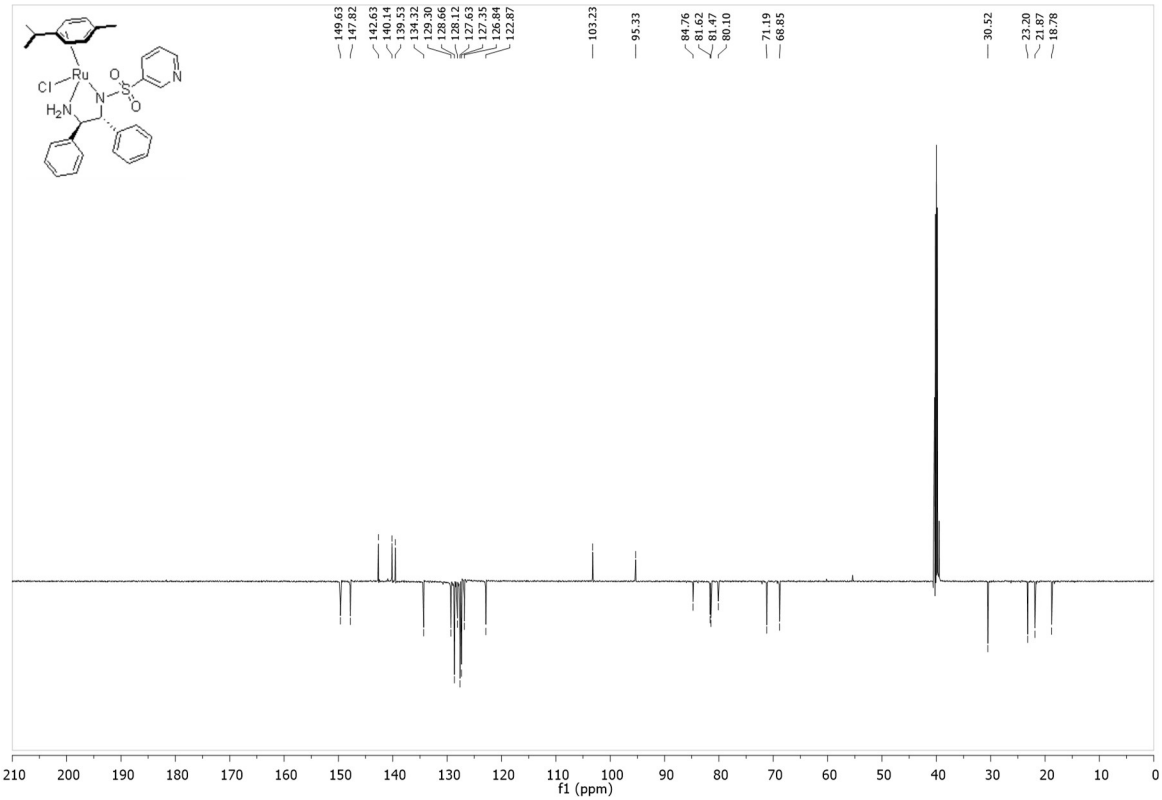


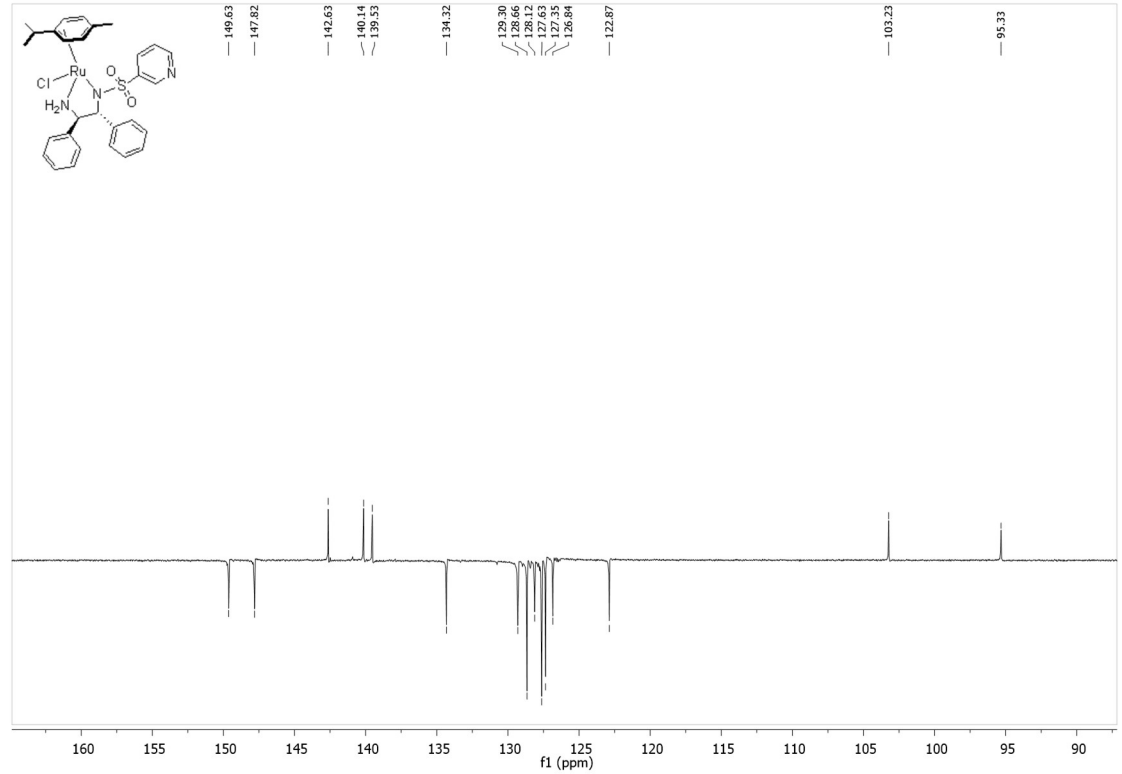


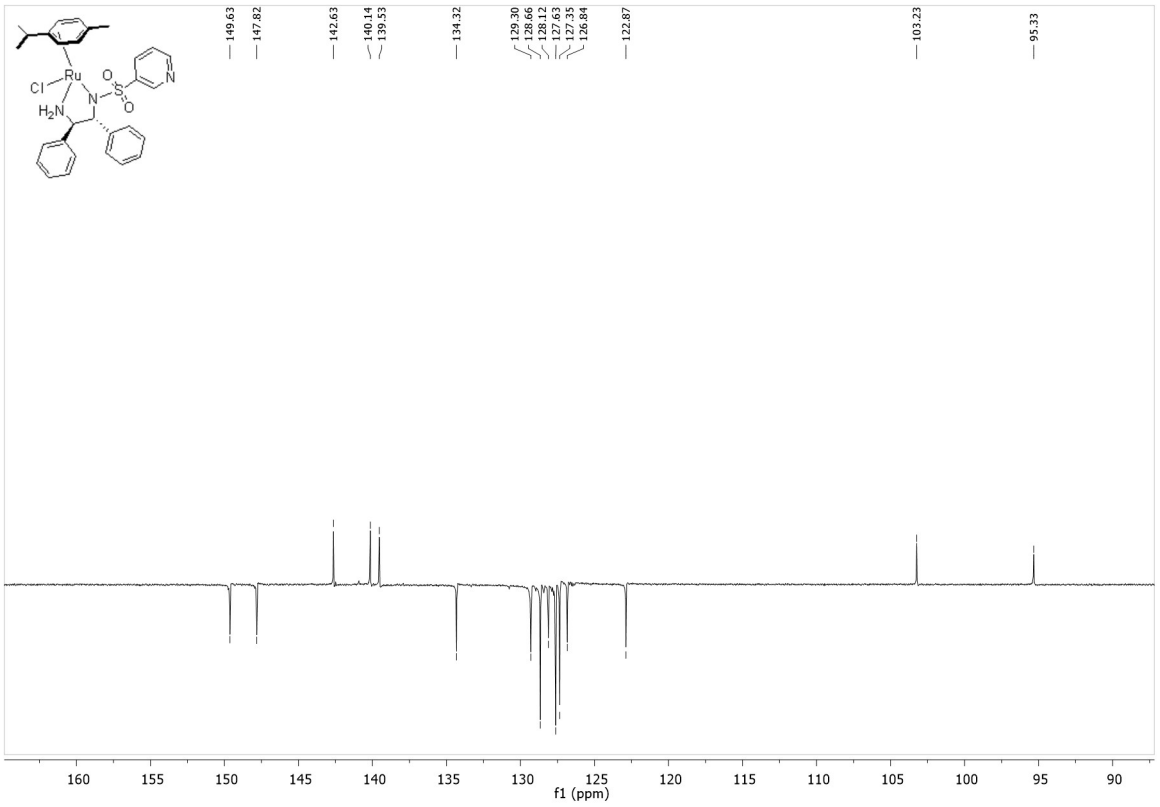
COSY (500 MHz, DMSO)



δ_C (126 MHz, DMSO)






149.63
147.82
142.63
140.14
139.53
134.32
129.30
128.66
128.12
127.63
127.35
126.84
122.87
103.23
95.33
Ru
Cl
H2N
N
S
O
O
N
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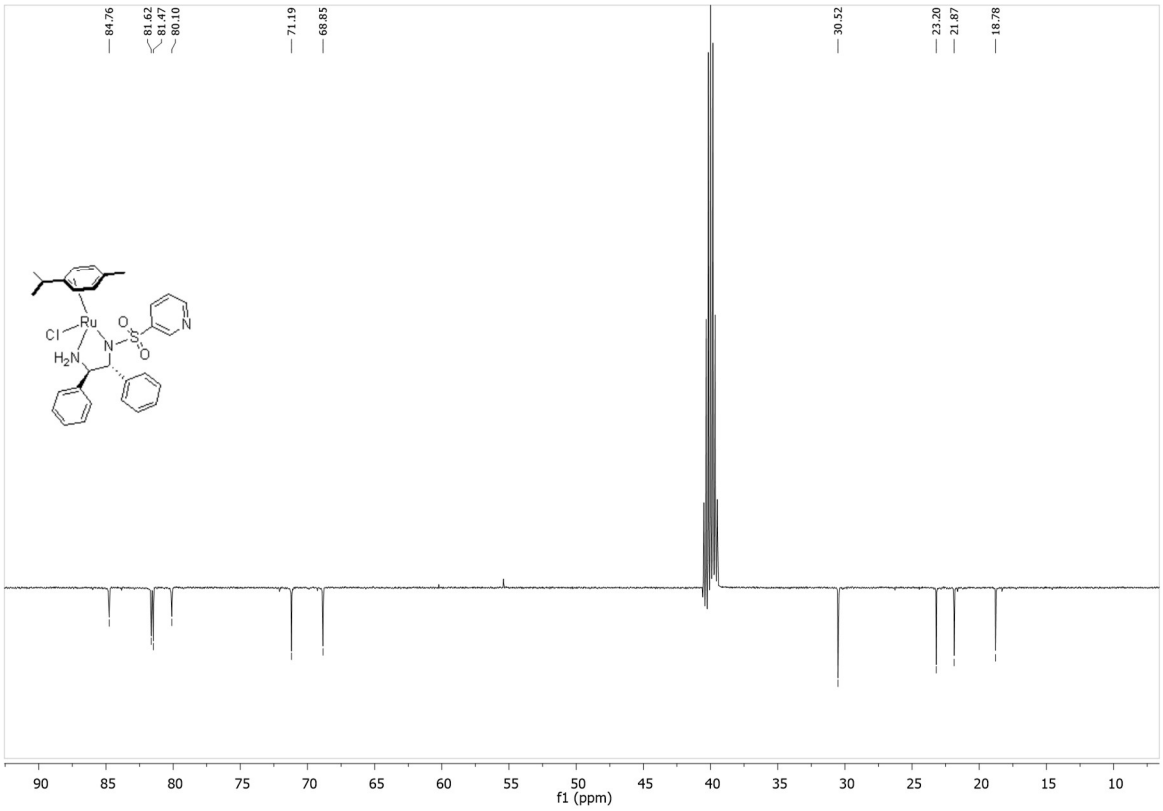
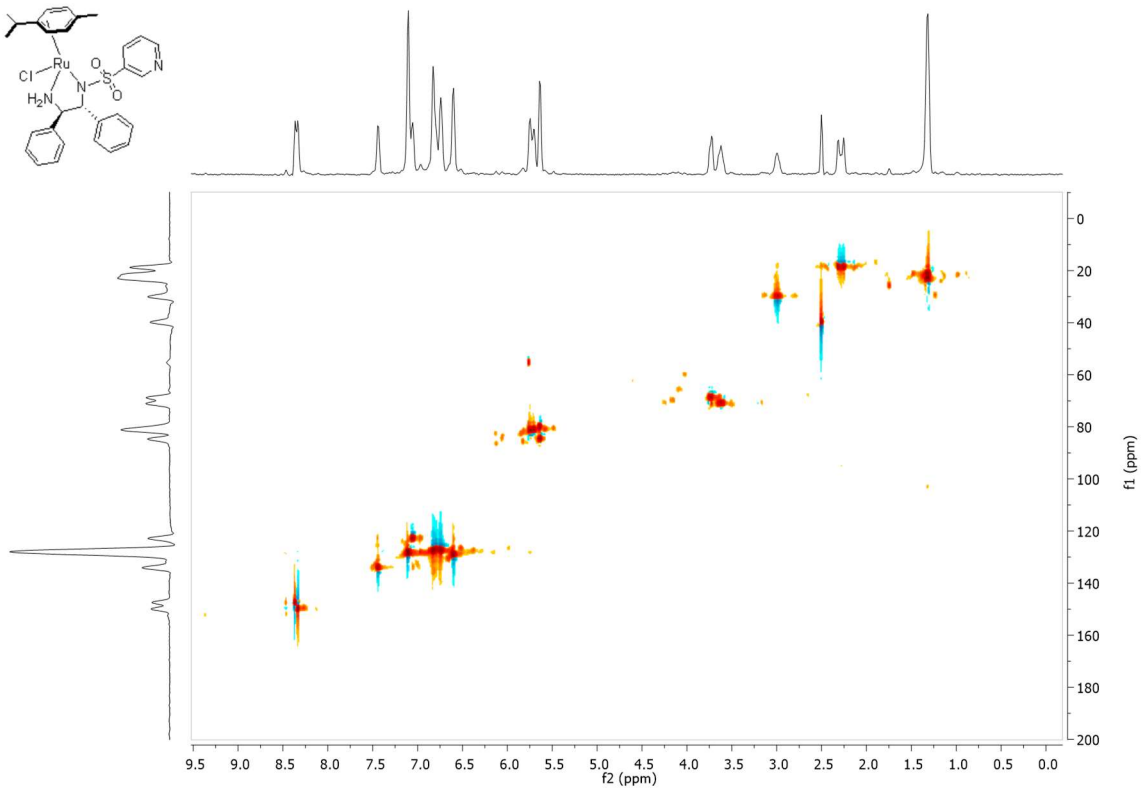
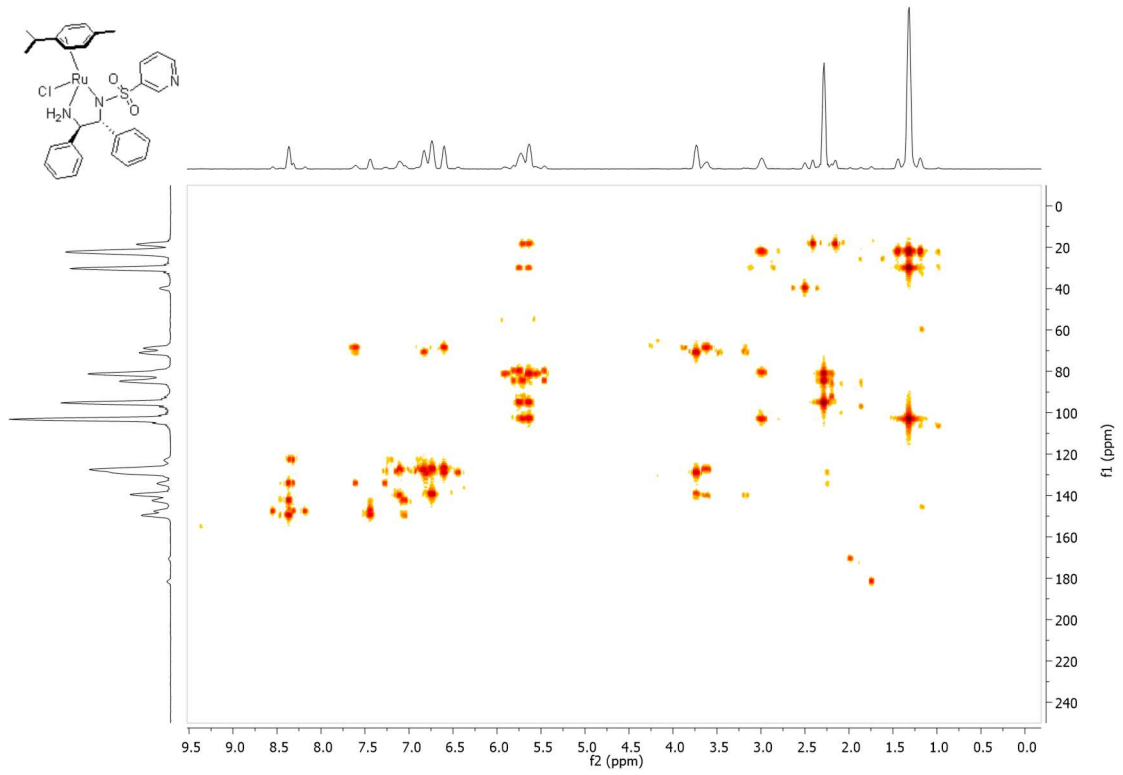
155
150
145
140
135
130
125
120
115
110
105
100
95
90
f1 (ppm)


84.76
81.62
81.47
80.10
71.19
68.85
30.52
23.20
21.87
18.78
Ru
Cl
H2N
N
S
O
O
N
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
f1 (ppm)

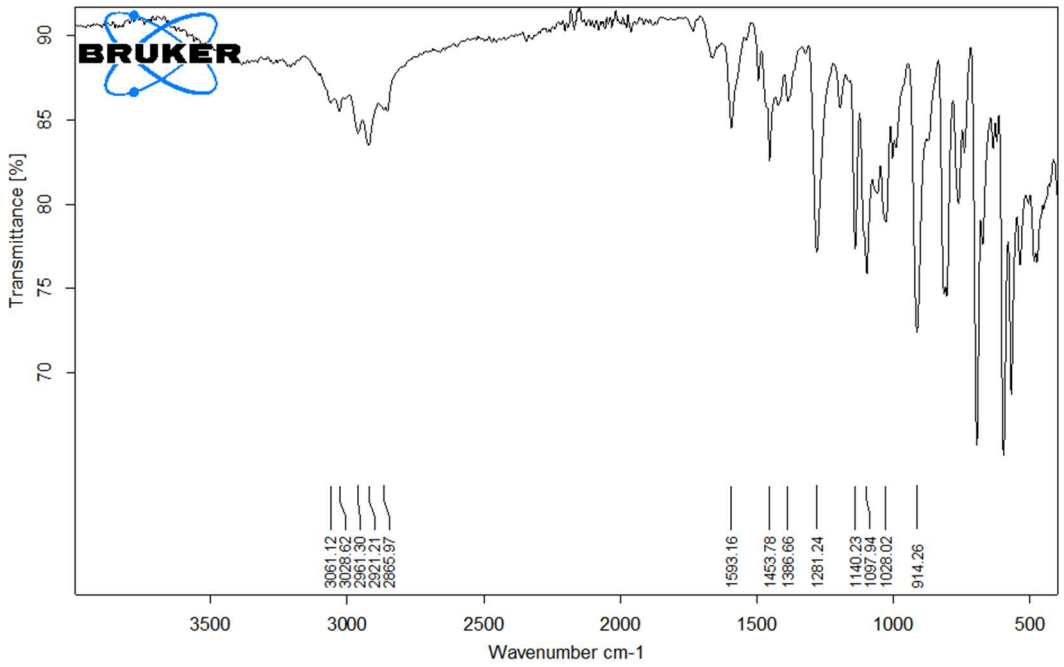
HSQC (500 MHz, DMSO)



HMBC (500 MHz, DMSO)



IR spectra



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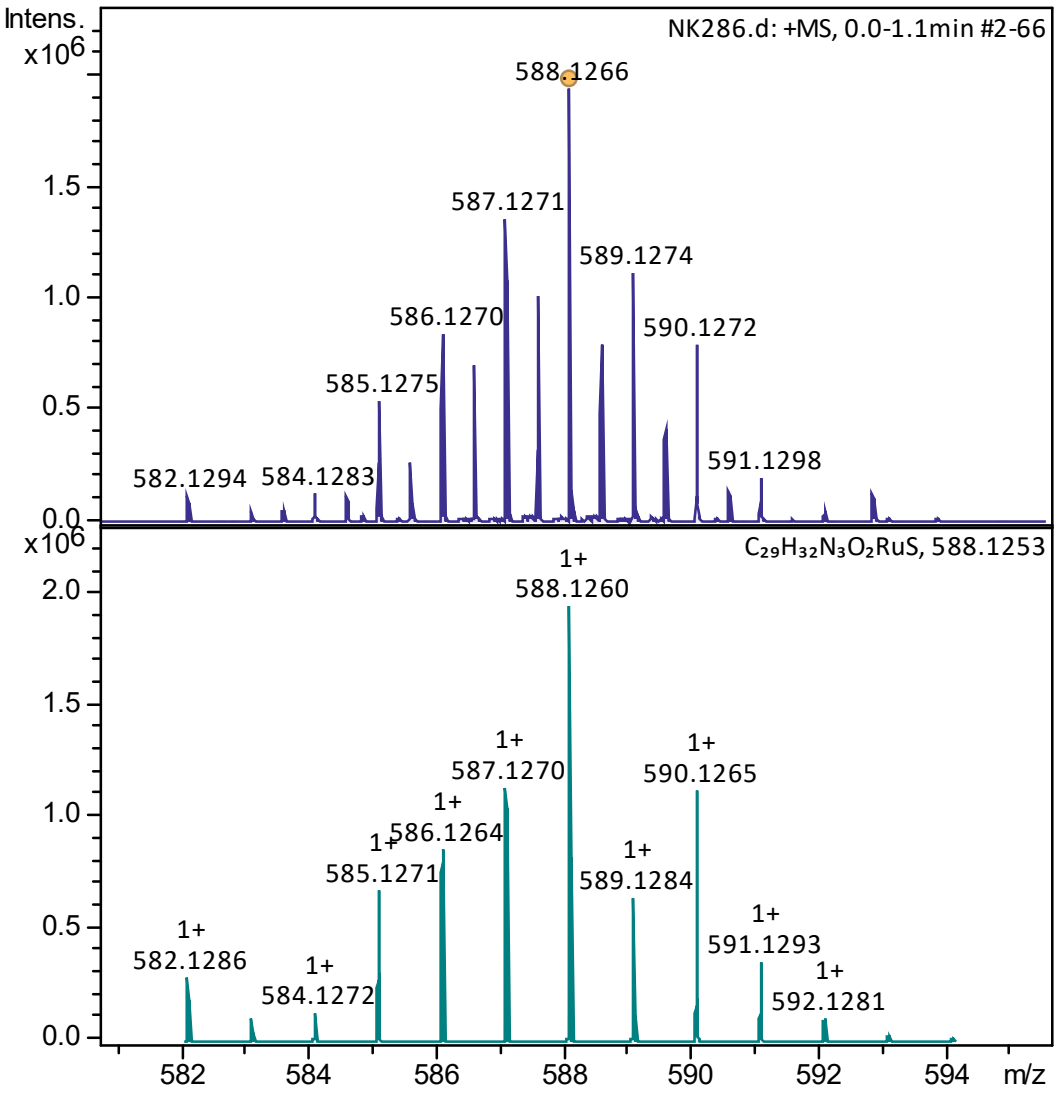
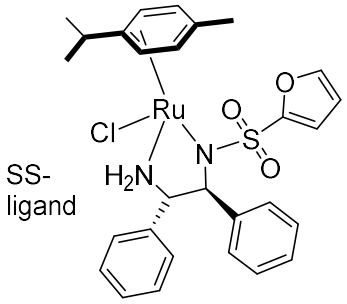
HRMS

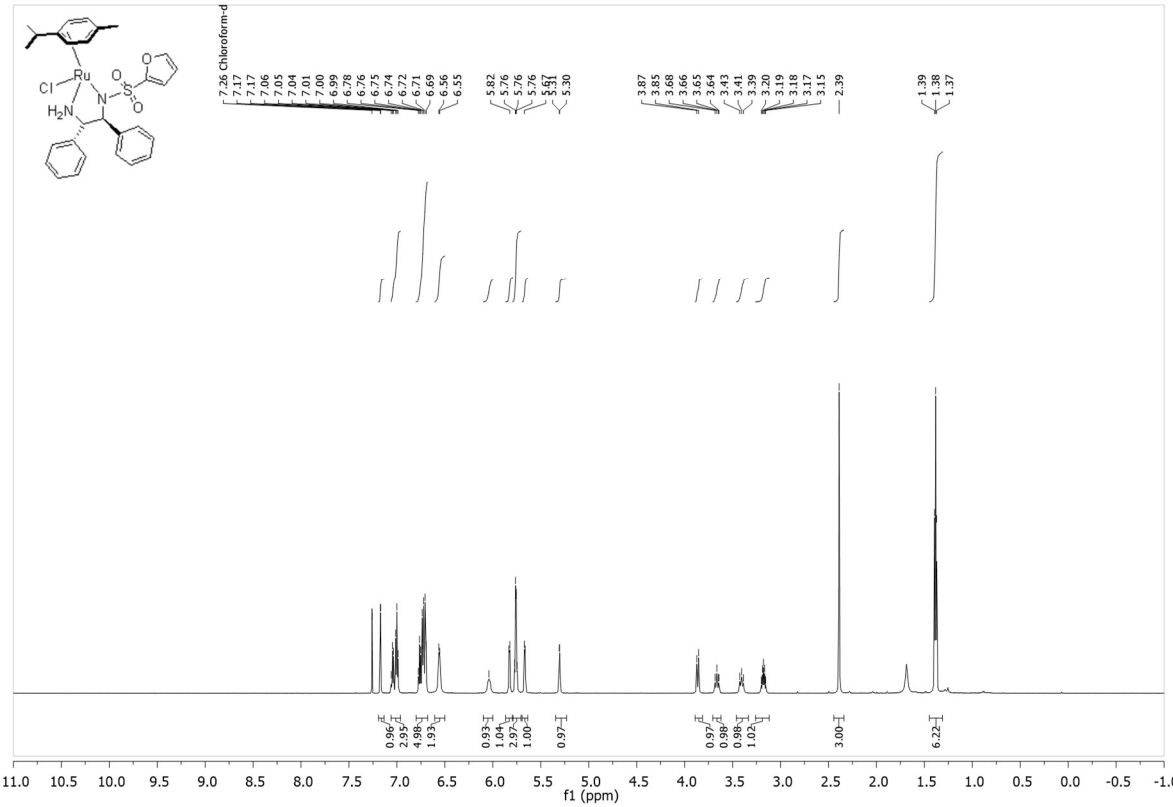

Intens.
x10^6
NK286.d: +MS, 0.0-1.1min #2-66
588.1266
587.1271
589.1274
586.1270
590.1272
585.1275
582.1294
584.1283
591.1298
C29H32N3O2RuS, 588.1253
1+
588.1260
1+
587.1270
1+
590.1265
1+
586.1264
1+
585.1271
1+
589.1284
1+
582.1286
1+
591.1293
1+
584.1272
1+
592.1281
m/z

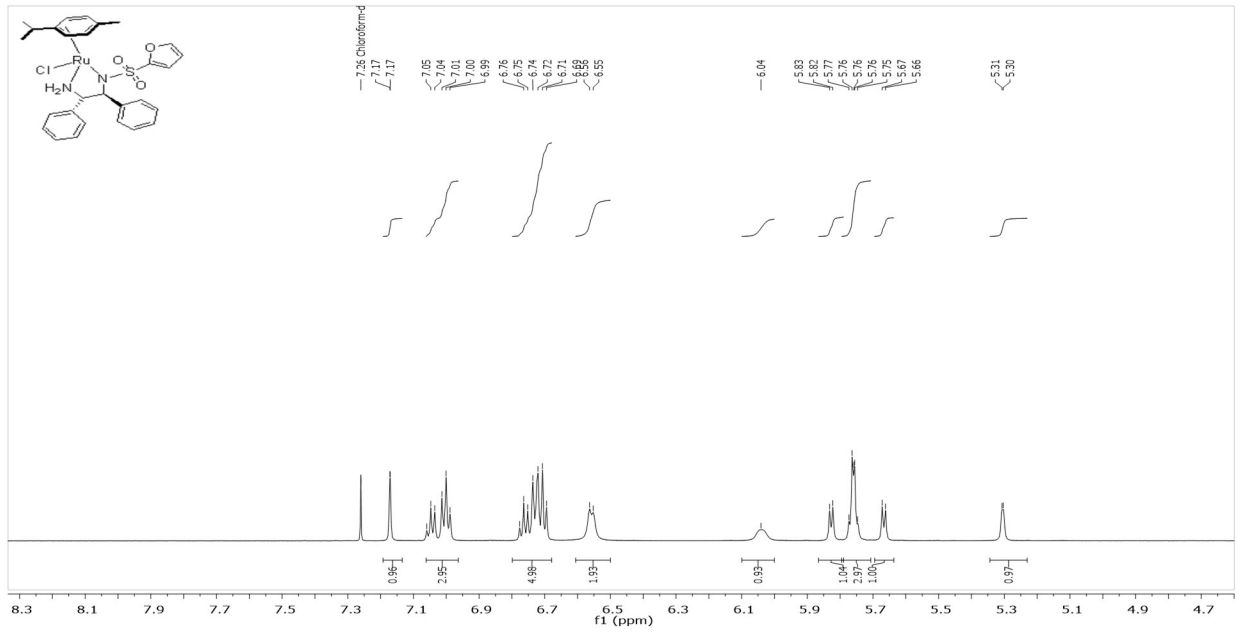
Ru Complex (*S,S,R*^{Ru})-12g of ligand (*S,S*)-11g.

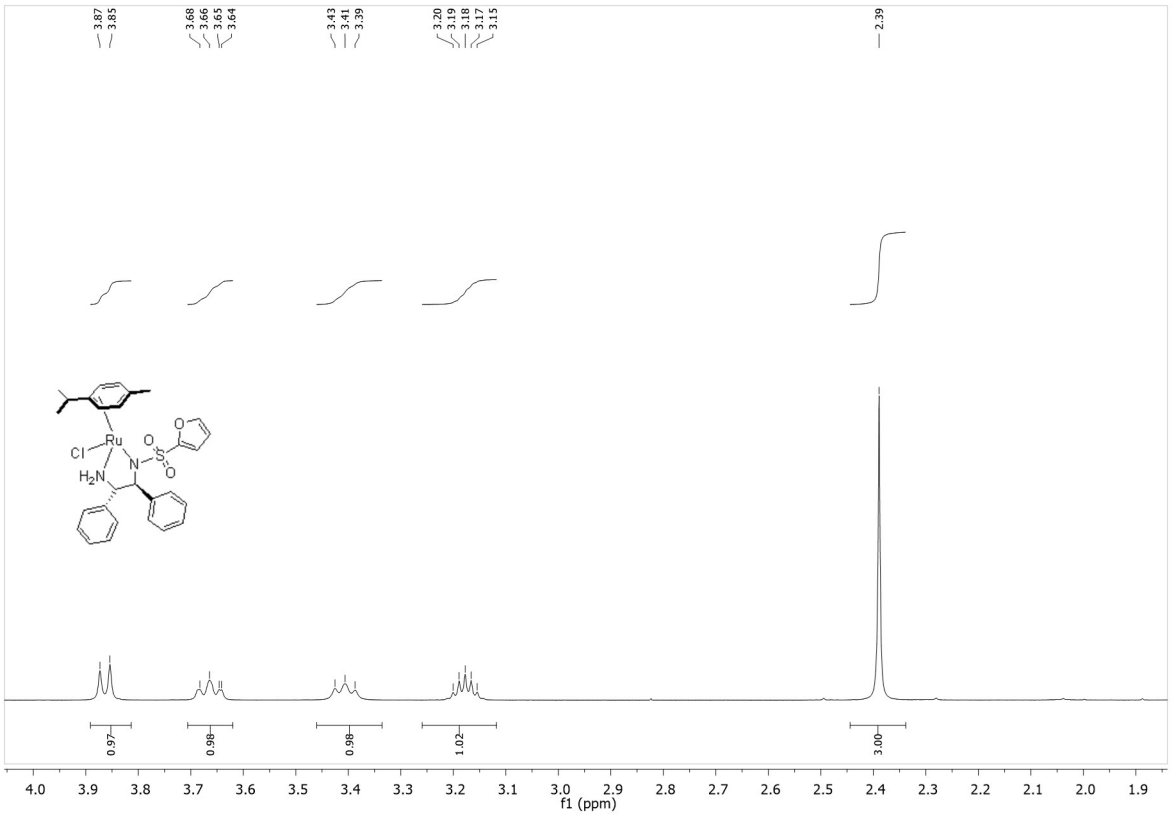


This compound is novel. To a dry 50 mL round-bottom flask charged with a solution of dichloro(p-cymene)ruthenium(II) dimer (212 mg, 0.346 mmol) and ligand **11g** (237 mg, 0.690 mmol) in dry 2-propanol (1.5 mL) was added triethylamine (140 mg, 1.38 mmol, 192 µL). After stirring at 80 °C for 1 h, the solution was allowed to cool to r.t, and the solvent was removed under reduced pressure. The residue was dissolved in DCM (2 mL) to remove residues of 2-propanol and then dried under vacuum, then the crude product was washed with water (5 mL). The complex was purified by column chromatography on silica gel (20% DCM: 80% EtOAc to 40% DCM: 60% EtOAc) to give the pure product (394 mg, 0.645 mmol, 93%) as an orange solid; TLC: Rf ca 0.3 (100% EtOAc), strong UV and $KMnO_4$; Mp =215°C; $[\alpha]_D^{25}$ = +85.8 (*c* 0.02 in $CHCl_3$); ν_{max} 3279, 3222, 2960, 2873, 1574 cm^{-1}; δ_H (600 MHz, $CDCl_3$) 7.17 (1 H, br. s, ArCH), 7.02 (3 H, m, ArCH), 6.81 – 6.65 (5 H, m, ArCH), 6.56 (2 H, br. S, ArCH), 6.04 (1 H, br. S, NH*H*), 5.83 (1 H, d, *J* 5.8, ArCH of *p*-cymene), 5.80 – 5.72 (3 H, m, ArCH of *p*-cymene), 5.67 (1 H, d, *J* 5.9, ArCH), 5.31 (1 H, br. s, ArCH), 3.86 (1 H, d, *J* 11.3, NCH of NSO_2), 3.66 (1 H, m, NCH of NH_2), 3.46 – 3.35 (1 H, m, N*H*H), 3.18 (1 H, m, C*H*Me_2 of *p*-Cymene), 2.39 (3 H, s, CH_3), 1.38 (6 H, t, *J* 6.5, CH_3); δ_C (151 MHz, $CDCl_3$) 153.27 (ArC), 141.77 (ArCH), 139.34 (ArC), 139.02 (ArC),, 128.25 (ArCH), 127.82 (ArCH), 127.19 (ArCH), 127.07 (ArCH), 126.07 (ArCH), 111.97 (ArCH), 110.60 (ArCH), 104.83 (RuArC), 95.07 (RuArC), 85.57 (RuArCH), 81.67 (RuArCH), 80.21 (RuArCH), 71.77 (NCH), 68.32 (NCH), 30.46 (C*H*Me_2 of *p*-cymene), 22.72 (CH_3), 22.14 (CH_3), 18.74 (CH_3); *m/z* (ESI^+) 577.1 [M - Cl]$^+$; HRMS (ESI-TOF) m/z: [M - Cl]$^+$ calcd for $C_{28}H_{31}N_2O_3{}^{102}RuS_2$ 577.1093, found 577.1102 (-0.3 ppm error).

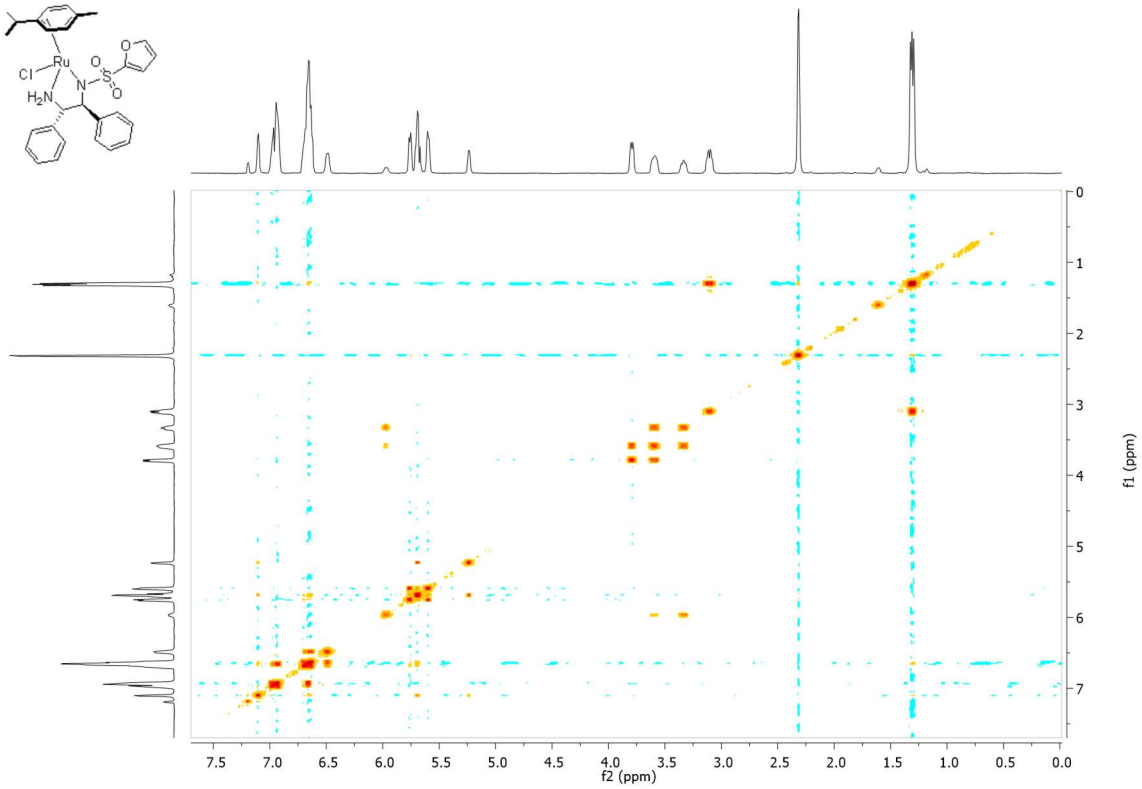
δ_H (600 MHz, $CDCl_3$)



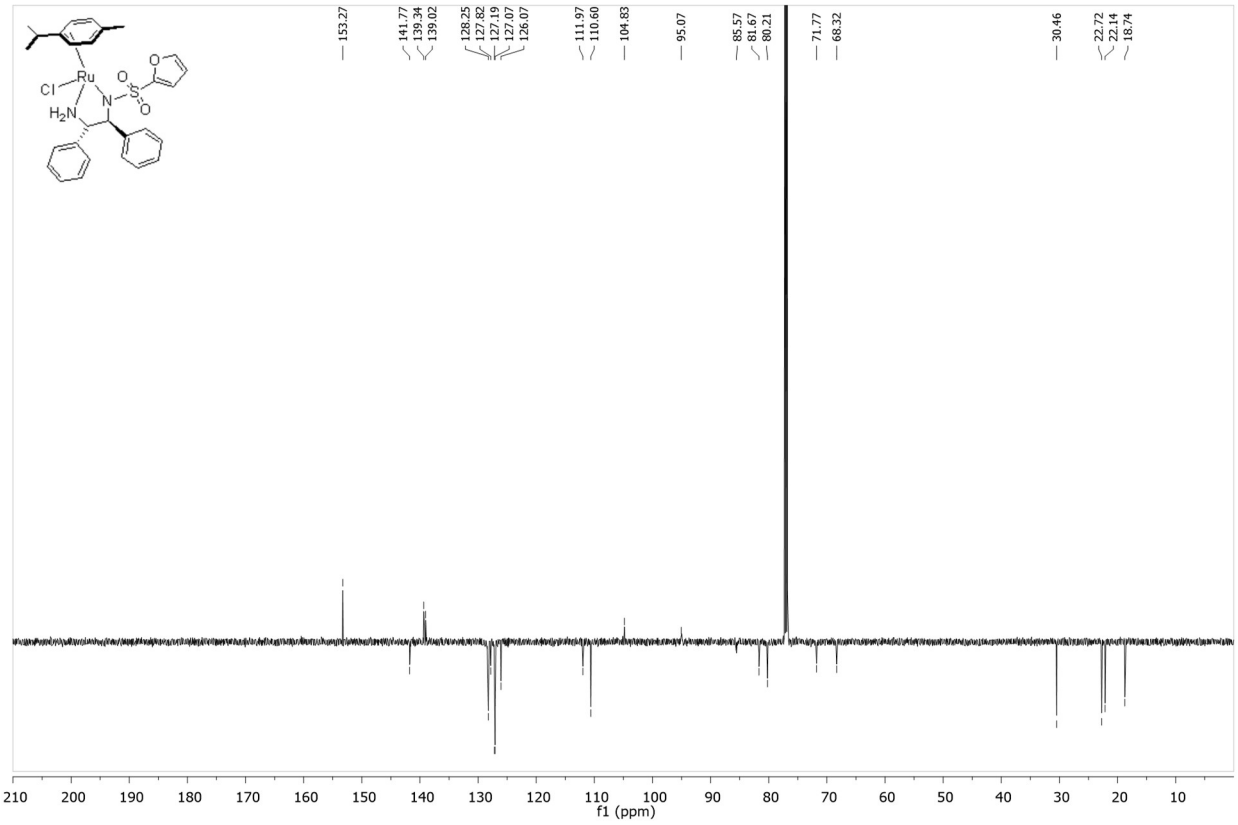


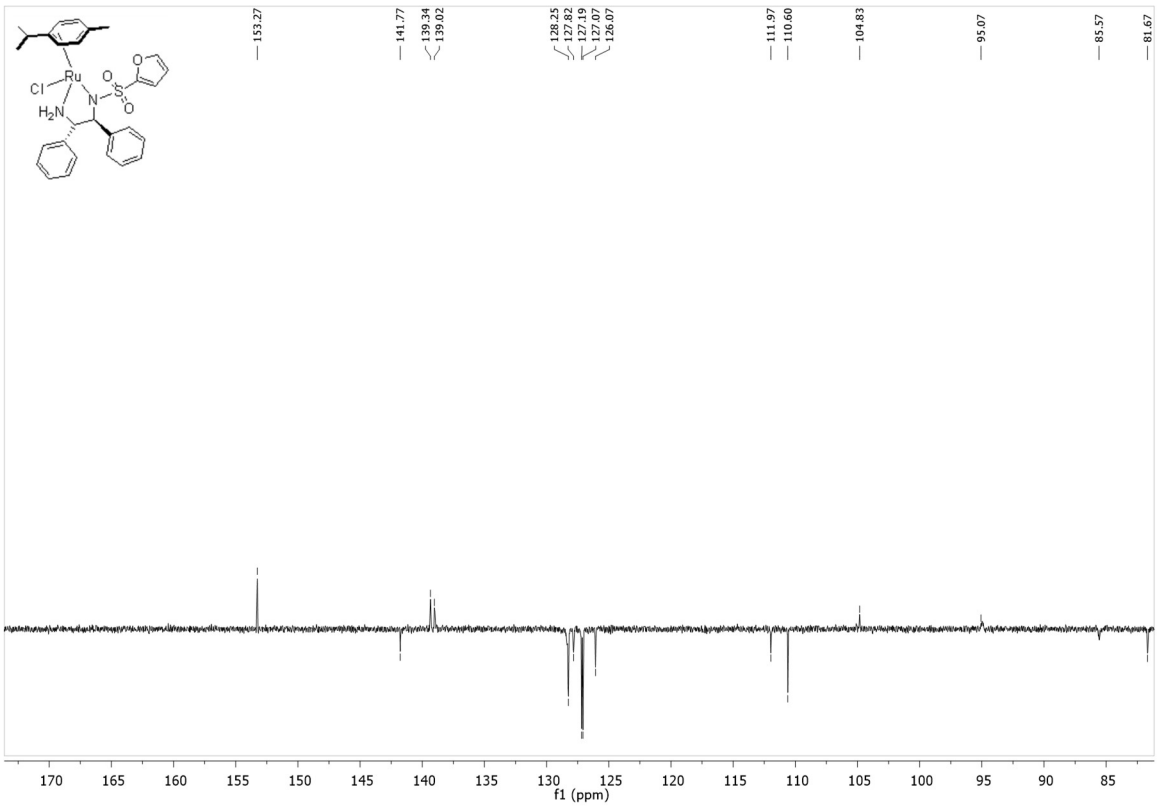


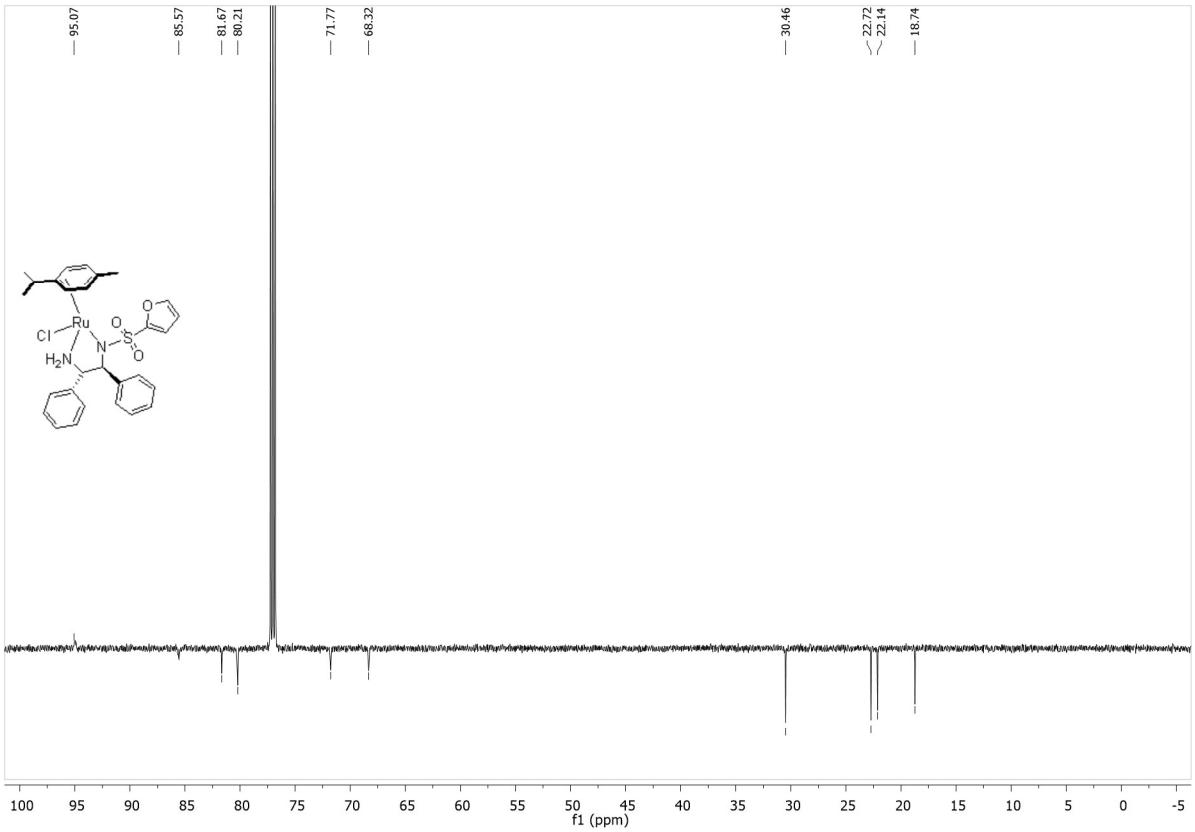
COSY (600 MHz, $CDCl_3$)



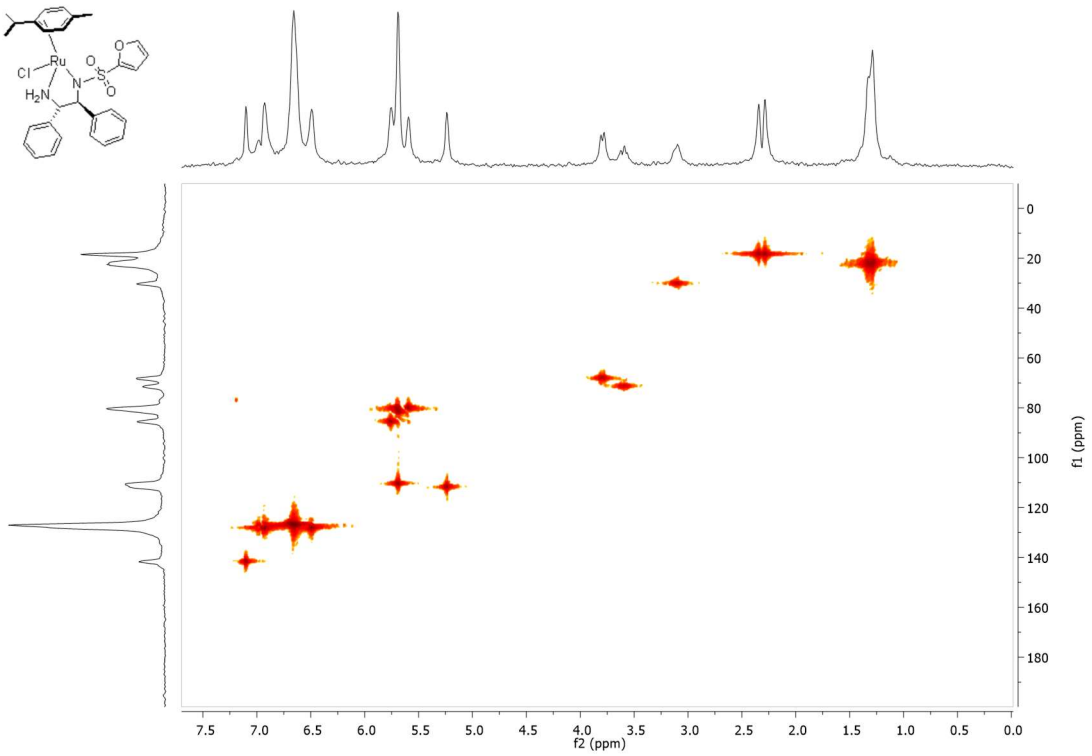
δ_C (151 MHz, $CDCl_3$)



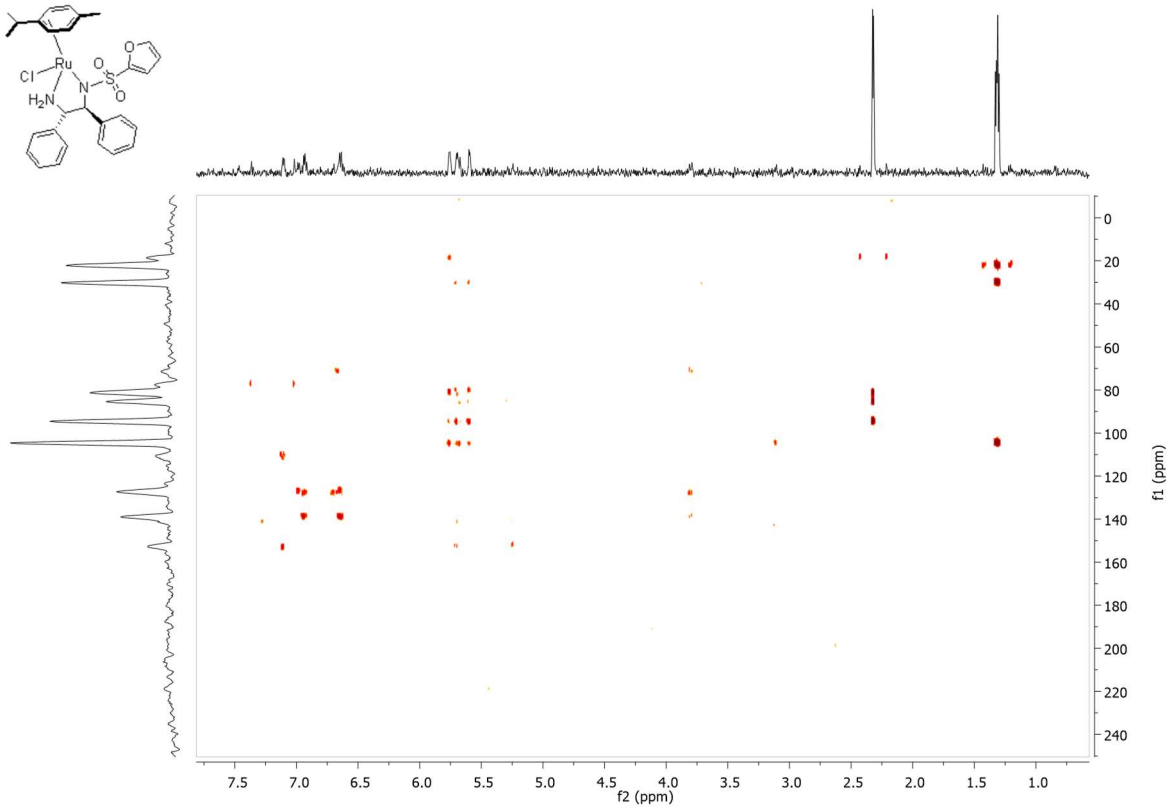




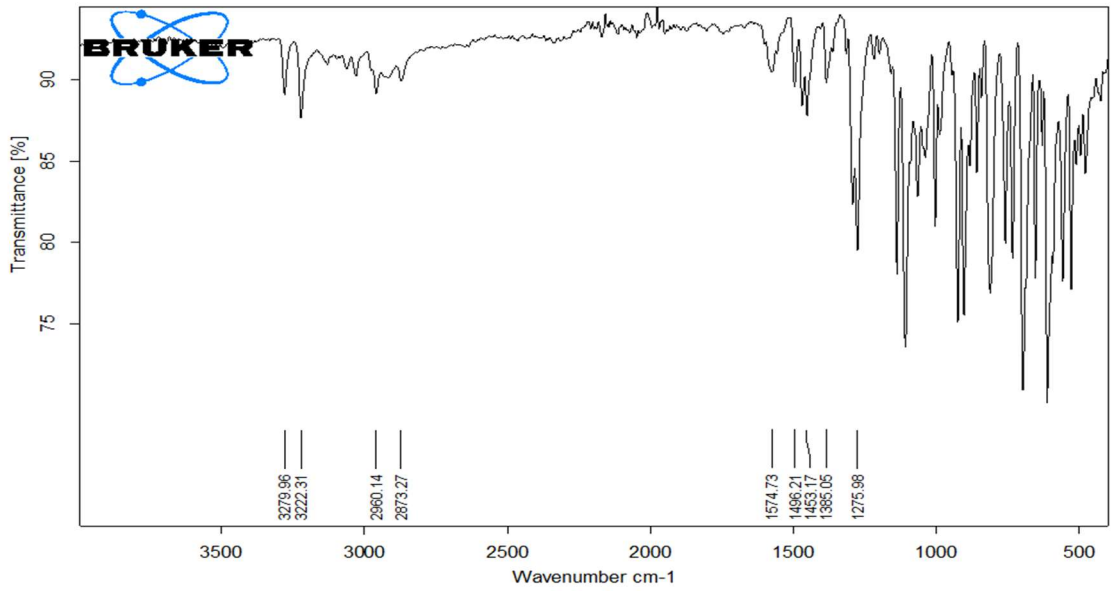
HSQC (600 MHz, $CDCl_3$)



HMBC (600 MHz, $CDCl_3$)



IR spectra



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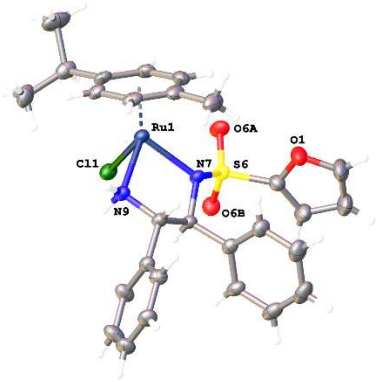
X-ray structure of Ru Complex (*S,S,R*^{Ru})-12g CCDC 2182541 (local code nk7).



Solid state structure of CCDC 2182541 with only key atoms labelled and thermal ellipsoids drawn at 50% probability level

Crystal structure determination.

The asymmetric unit contains the complex, there are four complexes in the unit cell.

The NHs on N9 were located in a difference map and placed at calculated positions for the refinement. One forms a short contact tabulated below and the other lies along the dipole of the Ru-Cl bond.

Specified hydrogen bonds (with esds except fixed and riding H)

D-H	H...A	D...A	<(DHA)	
0.91	2.19	2.932(3)	138.1	N9-H9A...O6B_$1

Symmetry operator used to define symmetry related atom discussed in above contact was $1 0.5+X,1.5-Y,1-Z

The Flack parameter and related Hoofty y parameter were

Flack x: -0.016(2)

Hooft y: -0.026(2)

This is small with a small error so you can be confident in the assignment of the crystal chosen. Additionally, it is made from a molecule of known handedness.

Experimental

Single crystals of $C_{28}H_{31}ClN_2O_3RuS$ **[nk7]** were grown from methanol. A suitable crystal was selected and mounted on a glass fibre with Fomblin oil and placed on a Rigaku Oxford Diffraction SuperNova diffractometer with a dual source (Cu at zero) equipped with an AtlasS2 CCD area detector. The crystal was kept at 150(2) K during data collection. Using Olex2 [1], the structure was solved with the SHELXT [2] structure solution program using Intrinsic Phasing and refined with the SHELXL [3] refinement package using Least Squares minimisation.

1. Dolomanov, O.V., Bourhis, L.J., Gildea, R.J, Howard, J.A.K. & Puschmann, H. (2009), J. Appl. Cryst. 42, 339-341.

2. Sheldrick, G.M. (2015). Acta Cryst. A71, 3-8.
3. Sheldrick, G.M. (2015). Acta Cryst. C71, 3-8.

Crystal Data for $C_{28}H_{31}ClN_2O_3RuS$ (M =612.13 g/mol): orthorhombic, space group $P2_12_12_1$ (no. 19), a = 12.03830(10) Å, b = 12.88610(10) Å, c = 18.52100(10) Å, V = 2873.10(4) Å^3, Z = 4, T = 150(2) K, μ(Cu Kα) = 6.196 mm^{-1}, *Dcalc* = 1.415 g/cm^3, 58813 reflections measured (8.358° ≤ 2Θ ≤ 147.162°), 5770 unique (R_{int} = 0.0390, R_{sigma} = 0.0183) which were used in all calculations. The final $R_1$was 0.0198 (I > 2σ(I)) and wR_2 was 0.0517 (all data).

Table 1 Crystal data and structure refinement. CCDC 2182541.

Identification code	nk7
Empirical formula	$C_{28}H_{31}ClN_2O_3RuS$
Formula weight	612.13
Temperature/K	150(2)
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	12.03830(10)
b/Å	12.88610(10)
c/Å	18.52100(10)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	2873.10(4)
Z	4
ρ_{calc}mg/mm^3	1.415
μ/mm^{-1}	6.196
F(000)	1256.0
Crystal size/mm^3	0.16 × 0.1 × 0.04 yellow block
2Θ range for data collection	8.358 to 147.162°
Index ranges	-14 ≤ h ≤ 14, -14 ≤ k ≤ 16, -23 ≤ l ≤ 23
Reflections collected	58813

Independent reflections	5770[R(int) = 0.0390]
Data/restraints/parameters	5770/0/328
Goodness-of-fit on F^2	1.042
Final R indexes [I>=2σ (I)]	R_1 = 0.0198, wR_2 = 0.0514
Final R indexes [all data]	R_1 = 0.0202, wR_2 = 0.0517
Largest diff. peak/hole / e Å^{-3}	0.66/-0.52
Flack parameter	-0.016(2)

HRMS

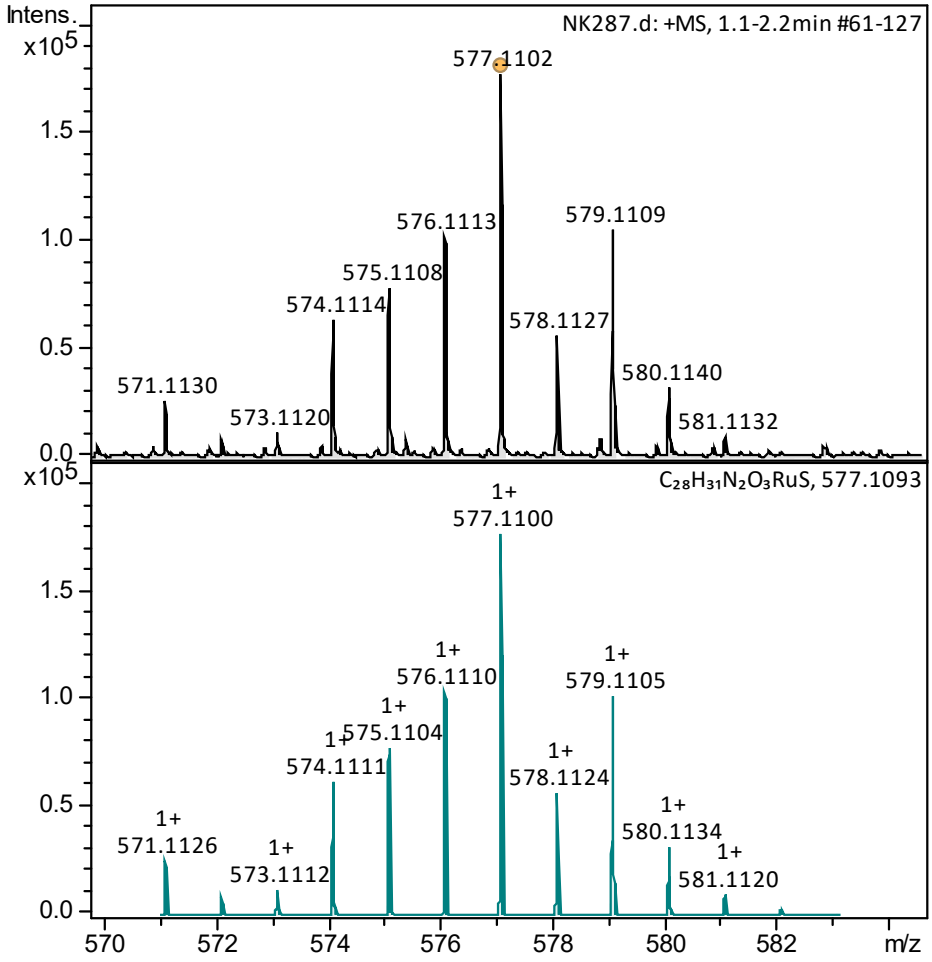
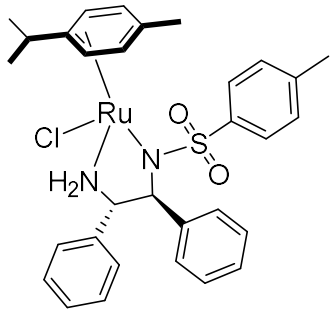


Table Comparative X-ray crystallographic data for Ru complexes.

Compound	(*S,S,R*^{Ru})-**12a** CCDC 2182537	(*R,R, S*^{Ru})-**12b** CCDC 2182538	(*R,R, S*^{Ru})-**12c** CCDC 2182539
Empirical formula	$C_{28}H_{31}ClN_2O_{2.5}RuS_2$	$C_{32.5}H_{35}ClN_2O_{2.75}RuS_2$	$C_{29}H_{34}ClN_3O_3RuS_2$
Formula weight	636.19	698.26	673.23
Temperature/K	150(2)	150(2)	150(2)
Crystal system	orthorhombic	Monoclinic	hexagonal
Space group	$P2_12_12_1$	$P2_1$	$P6_5$
a/Å	11.94996(8)	9.78513(4)	16.90780(10)
b/Å	12.97812(10)	11.79817(5)	16.90780(10)
c/Å	19.21709(12)	14.04533(5)	19.27870(10)
α/°	90	90	90
β/°	90	99.3866(4)	90
γ/°	90	90	120
Volume/Å^3	2980.34(4)	1599.776(11)	4772.90(6)
Z	4	2	6
Pcalc g/cm^3	1.418	1.450	1.405
μ/mm 1	6.620	6.227	6.253
F(000)	1304.0	718.0	2076.0
Reflections collected	91422	76379	96080
Data/restraints/ parameters	5988/0/336	6201/2/378	6407/1/356
Goodness-of-fit on F^2	1.061	1.084	1.089
Final R indexes [I>=2σ (I)]	R_1 = 0.0291, wR_2 = 0.0789	R_1 = 0.0373, wR_2 = 0.1064	R_1 = 0.0424, wR_2 = 0.1128
Final R indexes [all data]	R_1 = 0.0293, wR_2 = 0.0791	R_1 = 0.0373, wR_2 = 0.1065	R_1 = 0.0426, wR_2 = 0.1132
Largest diff. peak/hole / e Å^{-3}	0.80/-0.89	1.28/-0.79	1.01/-0.74
Flack parameter	-0.018(3)	-0.017(9)	-0.027(11)
Compound	(*S,S,S*^{Ru})-**12e** CCDC 2182540	(*S,S,R*^{Ru})-**12g** CCDC 2182541	
Empirical formula	$C_{34}H_{42}ClN_3O_3RuS$	$C_{28}H_{31}ClN_2O_3RuS$	
Formula weight	709.28	612.13	
Temperature/K	150(2)	150(2)	
Crystal system	Monoclinic	orthorhombic	
Space group	$P2_1$	$P2_12_12_1$	
a/Å	9.40940(6)	12.03830(10)	
b/Å	14.51707(10)	12.88610(10)	
c/Å	12.09559(8)	18.52100(10)	
α/°	90	90	
β/°	102.9107(7)	90	
γ/°	90	90	
Volume/Å^3	1610.45(2)	2873.10(4)	
Z	2	4	
Pcalc g/cm^3	1.463	1.415	

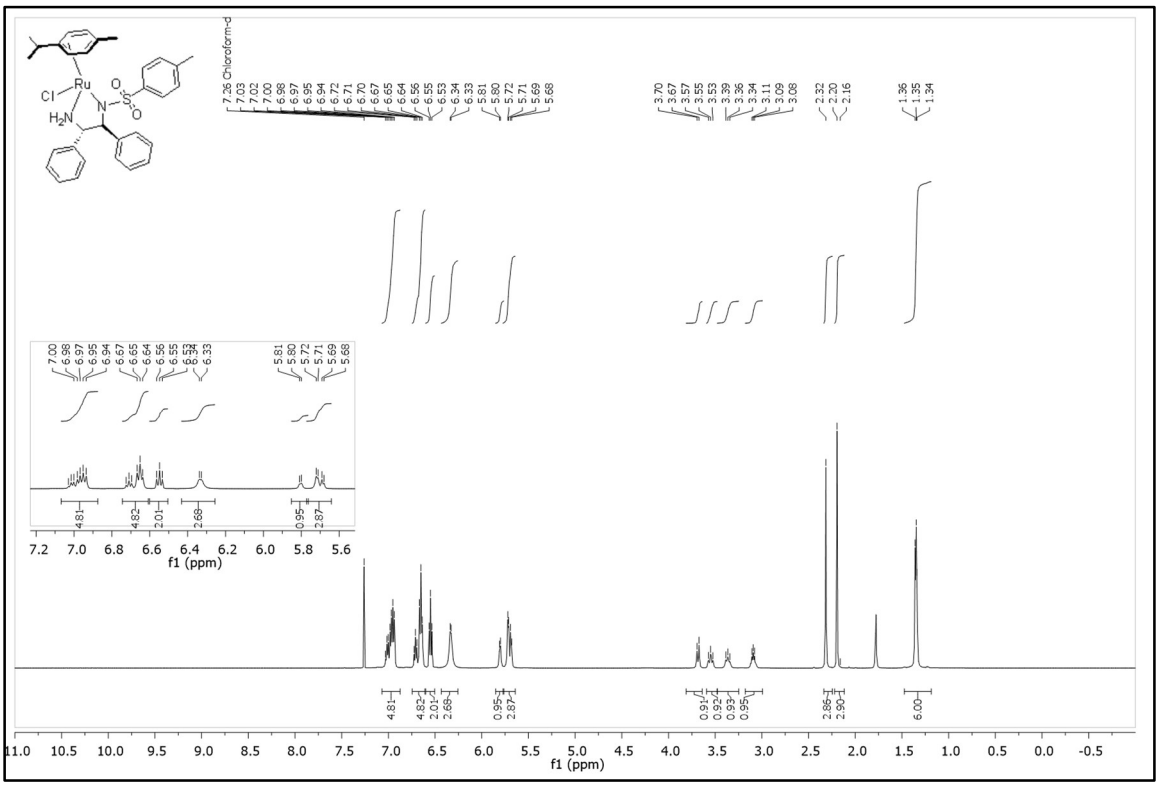
μ/mm 1	5.616	6.196	
F(000)	736.0	1256.0	
Reflections collected	41114	58813	
Data/restraints/ parameters	6469/4/396	5770/0/328	
Goodness-of-fit on F^2	1.065	1.042	
Final R indexes [I>=2σ (I)]	R_1 = 0.0422, wR_2 = 0.1128	R_1 = 0.0198, wR_2 = 0.0514	
Final R indexes [all data]	R_1 = 0.0425, wR_2 = 0.1132	R_1 = 0.0202, wR_2 = 0.0517	
Largest diff. peak/hole / e $Å^{-3}$	2.20/-0.92	0.66/-0.52	
Flack parameter	-0.011(10)	-0.016(2)	

(*S,S*)-Noyori Ru complex 1.

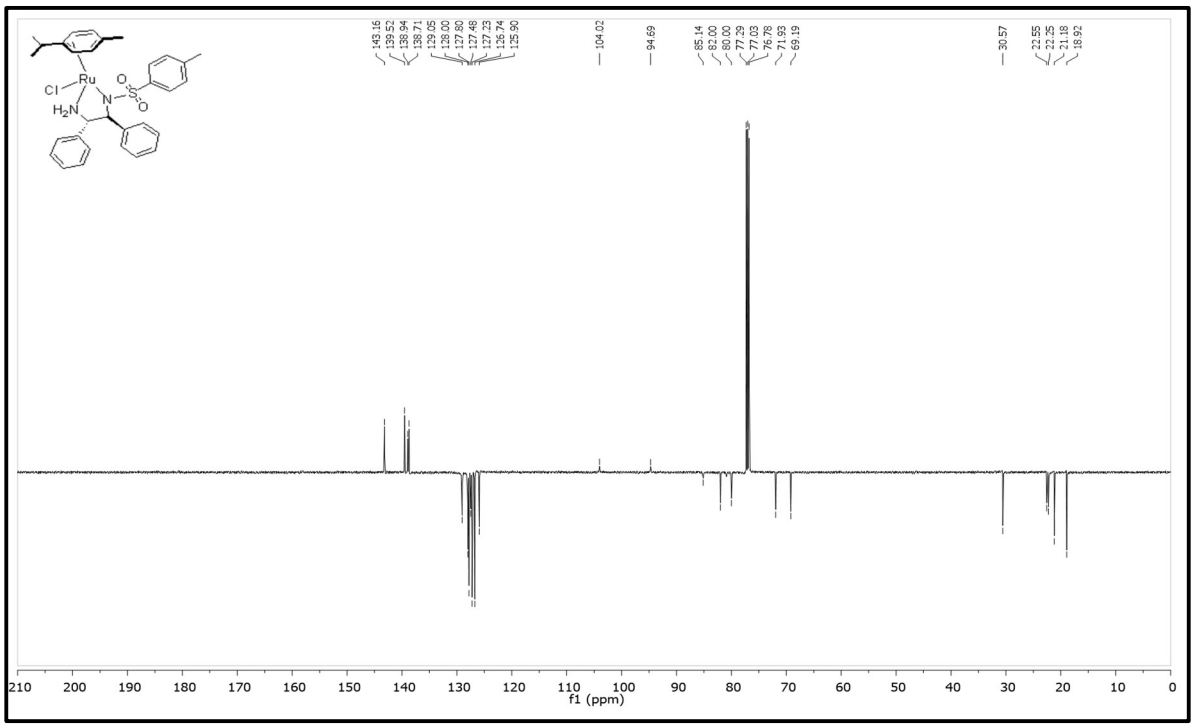


This compound has been reported and fully characterised.* In a dry 50 mL round flask, dichloro(p-cymene)ruthenium(II) dimer (153 mg, 0.250 mmol) and (*S,S*) TsDPEN (183 mg, 0.50 mmol) were dissolved in dry 2-propanol (2 mL). Triethylamine (100 mg, 1.00 mmol, 130 μL) was added to the mixture. After stirring at 80 °C for 1 h, the solution was allowed to cool to r.t, and the solvent was removed under reduced pressure. The residue was dissolved in DCM (2 mL) and then dried under vacuum, then the crude product was washed with water (5 mL). The complex was purified by recrystallization from methanol to afford the pure complex as orange crystals (304 mg, 0.478 mmol, 96%); Mp 233.5 °C; $[\alpha]_D^{25}$ = +24.3 (*c* 0.2 in $CHCl_3$); δ_H (500 MHz, $CDCl_3$) 7.05-6.95 (5 H, m, ArH), 6.70-6.64 (5 H, m, ArH), 6.55 (2 H, t, *J* 7.6, ArH), 6.40-6.28 (3 H, m, ArH+NH), 5.80 (1 H, d, *J* 4.9, CH of *p*-cymene), 5.75-5.65 (3 H, m, CH of *p*-cymene), 3.68 (1 H, d, *J* 11.1, $CHNSO_2$), 3.55 (1 H, t, *J* 11.5, C*H*NH_2), 3.36 (1 H, t, *J* 11.0, NH), 3.19 – 2.95 (1 H, m, CH of *p*-cymene), 2.32 (3 H, s, CH_3 of-*p*-Ts), 2.20 (3 H, s, CH_3 of *p*-cymene), 1.38 – 1.31 (6 H, m, 2 x CH_3 of *p*-cymene); δ_C (126 MHz, $CDCl_3$) 143.16 (C), 139.52 (C), 138.94 (C), 138.71 (C), 129.05 (CH), 128.00 (CH), 127.80 (CH), 127.48 (CH), 127.23 (CH), 126.74 (CH), 125.90 (CH), 104.02 (C), 94.69 (C), 85.14 (CH), 82.00 (CH), 80.00 (CH), 71.93 (CH), 69.19 (CH), 30.57 (CH), 22.55 (CH_3), 22.25 (CH_3), 21.18 (CH_3), 18.92 (CH_3); MS (ESI^+): m/z, 601.1 $[M - Cl]^+$. *K.-J. Haack, S. Hashiguchi, A. Fujii, T. Ikariya and R. Noyori, *Angew. Chem. Int. Ed.*, 1997, **36**, 285-288.

δ_H (500 MHz, $CDCl_3$)



δ_C (500 MHz, $CDCl_3$)



General procedure for racemic reduction of all substrates.

To a solution of ketone (1 mmol) in MeOH (10 mL) was added $NaBH_4$ (75.6 mg, 2mmol) portion-wise. The solution was stirred at rt until the ketone had consumed. The solvent was then removed under reduced pressure and the residue partitioned between water (10 mL) and EtOAc (10 mL). The organic extract were collected and the aqueous layer extracted with EtOAc (2 x 10 mL). The organic layers were combined, dried over $MgSO_4$, filtered and the solvent removed under reduced pressure. Products were purified by column chromatography gradient elution 0-50% EtOAc in Pet. Ether

General procedure for asymmetric transfer hydrogenation of all substrates.

Catalyst (1 mol%) in FA/TEA 5:2 complex (0.5 mL) was stirred under an inert atmosphere at rt for 15 min. The ketone (1 mmol) in DCM (0.5 mL) was then added to the mixture and the reaction was stirred at rt. At the end of the reaction time, sat. $NaHCO_3$ (10 mL) was added to quench the reaction and the product was extracted with EtOAc (3 x 10 mL). The organic fractions were then combined, dried over $MgSO_4$, filtered and the solvent removed under pressure. The crude products were purified by column chromatography (0 – 50% EtOAc in Pet. Ether). The enantiomeric excess was determined by chiral GC or HPLC.

General procedure for asymmetric transfer hydrogenation of all substrates followed by GC.

Catalyst (1 mol%) in FA/TEA 5:2 complex (0.5 mL) was stirred under an inert atmosphere at rt for 15 min. The ketone (1 mmol) in DCM (0.5 mL) was then added to the mixture and the reaction was stirred at rt. A small amount of solution was taken in specific time and quenched using Sat. $NaHCO_3$ (1 mL) and the product extracted with EtOAc (1 mL). The organic layer was dried over $MgSO_4$, then injected to the chiral GC at the specified time interval to determine the enantiomeric excess and conversion. Filtration of the mixture through a small plug of silica gel in 1:1 hexane:EtOAc serves to remove residues of the catalyst before injection into the GC.

General procedure for asymmetric transfer hydrogenation of all substrates followed by ^{1}H NMR.

Catalyst (1 mol%) was added to an NMR tube, then dissolved in FA/TEA 5:2 complex (0.5 mL) by shaking the tube with cap and left for 20 min to form the active form of catalyst. C_6D_6 (0.1 mL) was added to lock the ^{1}H NMR. The ketone (0.5 mmol) was then added to the mixture and the cap replaced with a perforated cap to release the CO_2 generated during the reaction. NMR spectra were recorded at the intervals indicated.

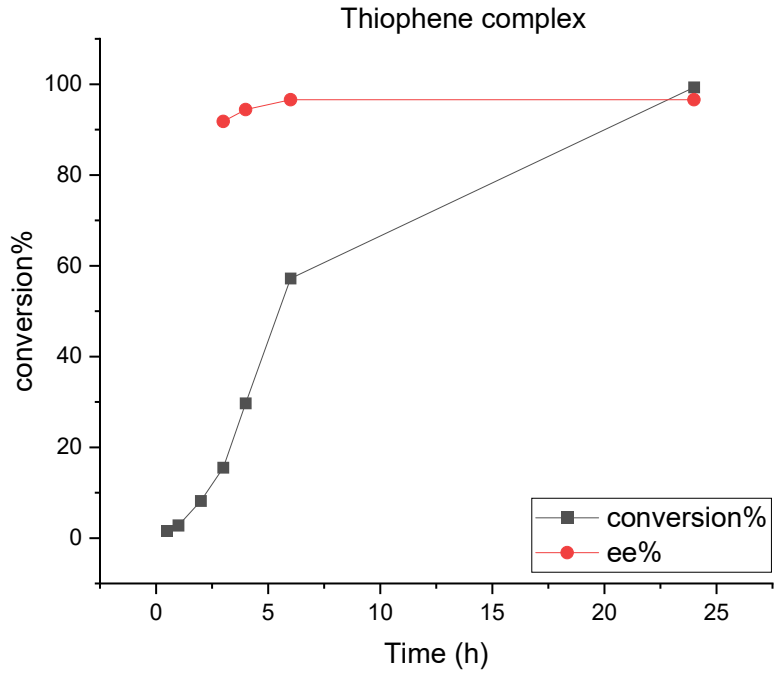
Optimization of acetophenone reduction in different conditions using thiophene complex (*S,S)*-12a as a model:

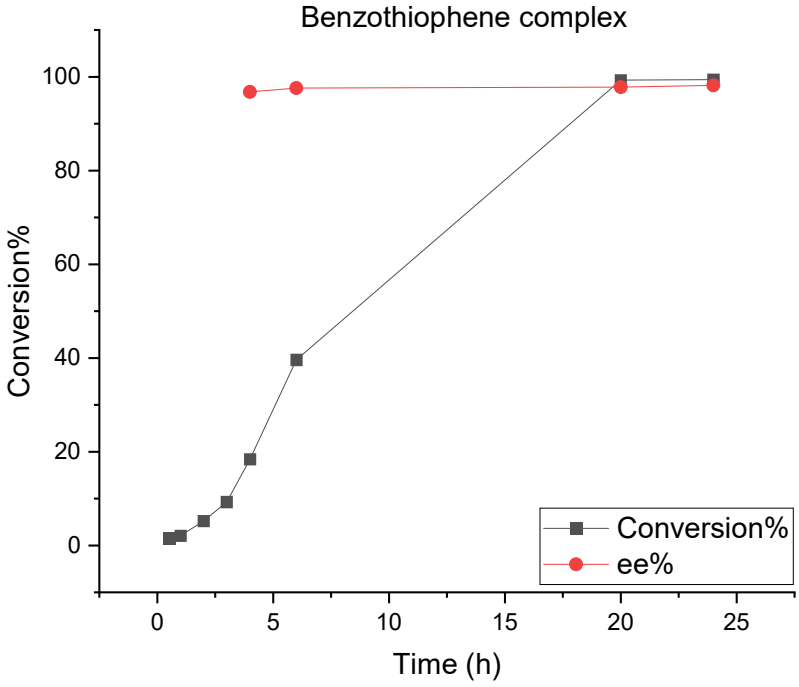
Cat.	Co-solvent	T	time	FA:TEA	Conv.* /%	Ee /%	Yield** /%	Configuration
(*S,S)*-**12a**	DCM	r.t	22h	5:2	99	97.8	66	***S***
(*S,S)*-**12a**	None	r.t	56h	5:2	97	96.6	60	***S***
(*S,S)*-**12a**	MeCN	r.t	61h	5:2	98	96.2	72	***S***
(*S,S)*-**12a**	MeOH	r.t	35h	5:2	99	96.6	76	***S***
(*S,S)*-**12a**	DCM	40 ºC	16h	5:2	99	96	63	***S***
(*S,S)*-**12a**	DCM	60 ºC	6h	5:2	97	91.2	42	***S***
(*S,S)*-**12a**	H_2O	r.t	56h	5:2	66	95.4	64	***S***
(*S,S)*-**12a**	DCM	r.t	26h	1.2:1	99	96.6	66	***S***
(*S,S)*-**12a**	DCM	r.t	26h	0.2:1	97	96.4	76	***S***
(*S,S)*-**1**	H_2O	40 ºC	69h	1.2:1	98	95	56	***S***
(*S,S)*-**1**	DCM	r.t	40h	5:2	97	96.8	40	***S***

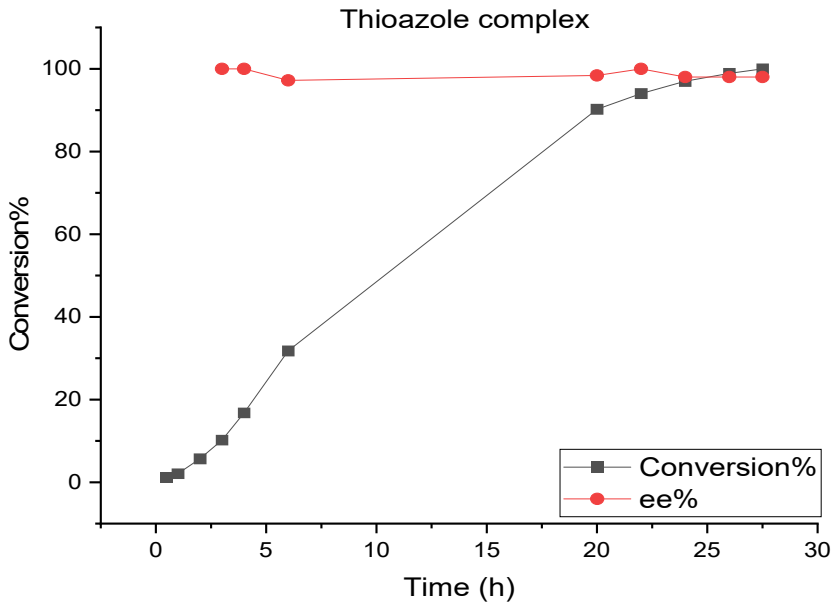
* GC conversion from sample. ** isolated yield at end of experiment.

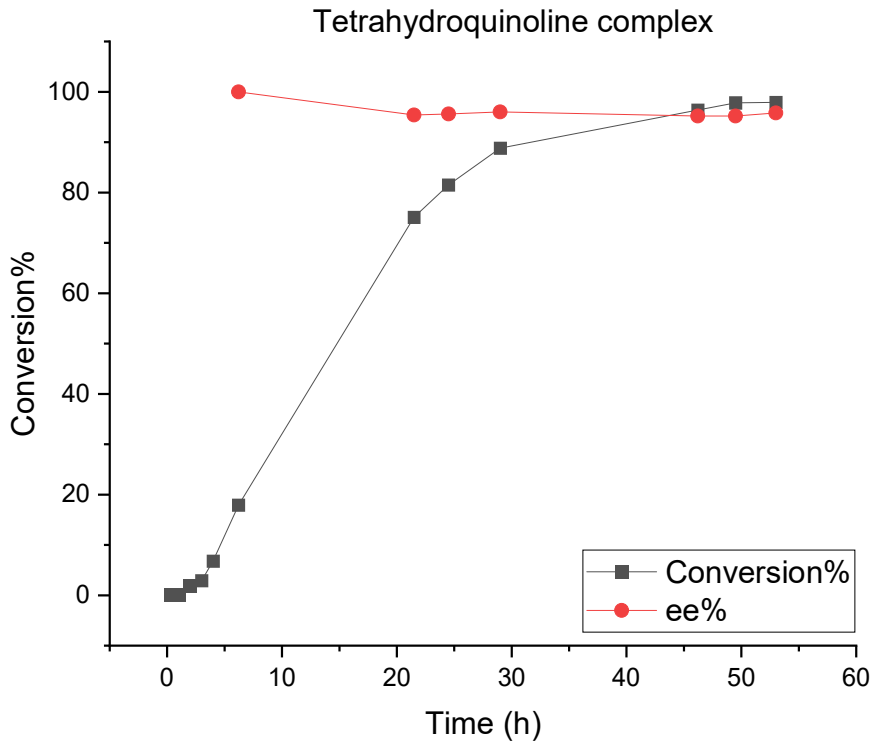
Comparative rate studies –chiral GC:

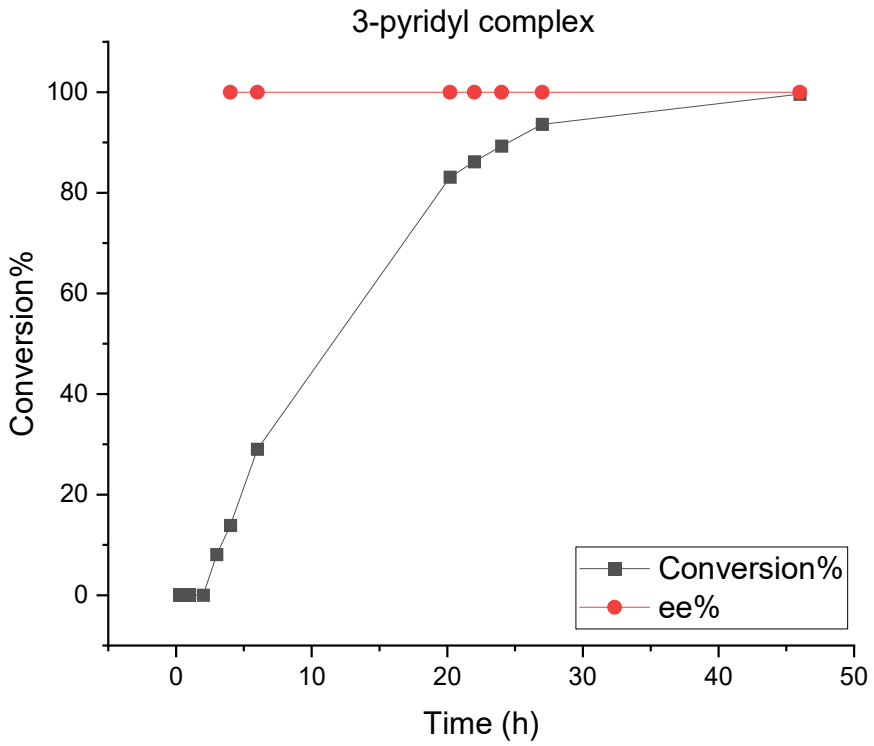
Shown below are the conversion and ee, as determined by Chiral GC for acetophenone reduction under the following conditions;1 mmole ketone, 1% catalyst, 0.5 mL FA:TEA, and 0.5 mL DCM, S=[1.0], followed by chiral GC. Ees are shown only for conversions above 10%, as they were difficult to measure accurately at low conversion. The Noyori catalyst is [(cymene)Ru(TsDPEN)Cl]:

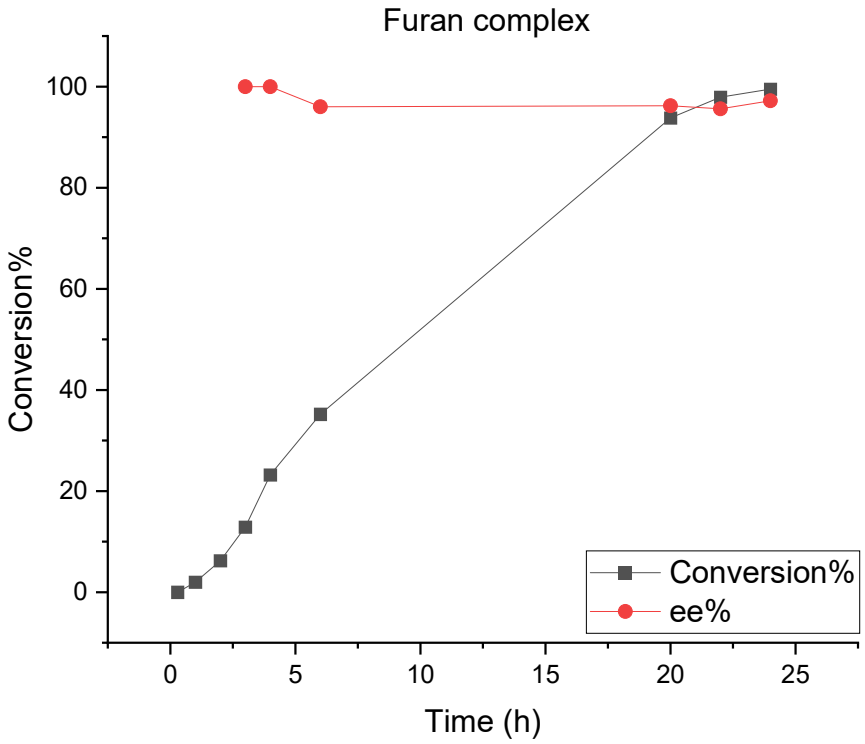


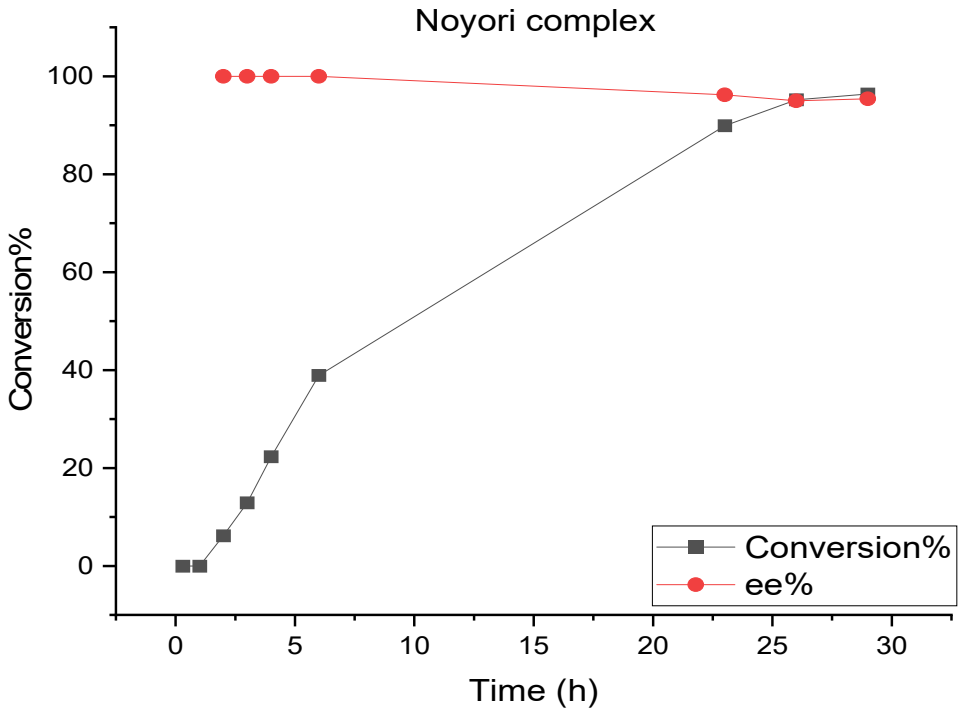



Thioazole complex
Conversion%
Time (h)
Conversion%
ee%
0
20
40
60
80
100
0
5
10
15
20
25
30


Tetrahydroquinoline complex
Conversion%
Time (h)
Conversion%
ee%
0
20
40
60
80
100
0
10
20
30
40
50
60

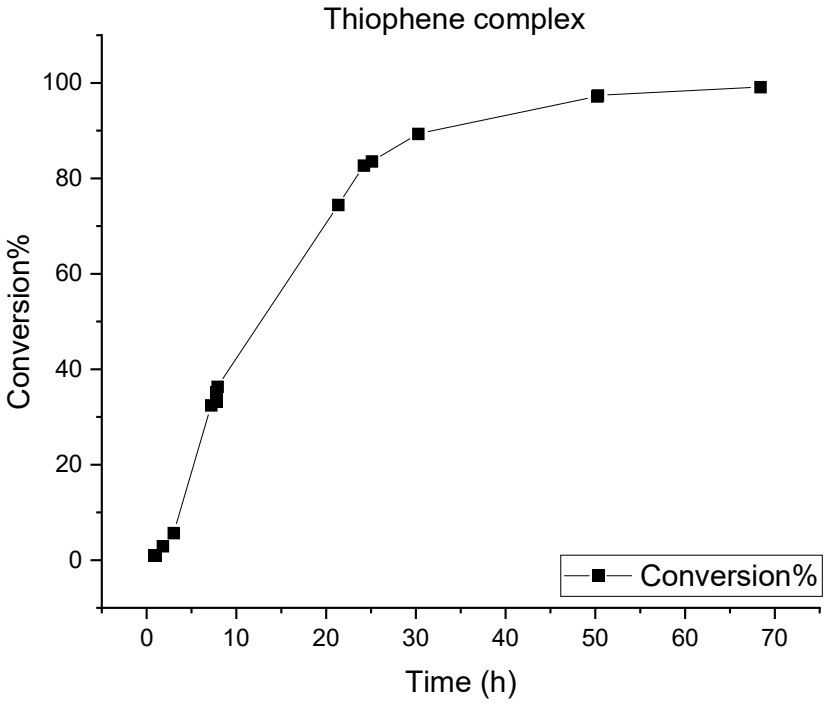

3-pyridyl complex
Conversion%
Time (h)
Conversion%
ee%
0
20
40
60
80
100
0
10
20
30
40
50

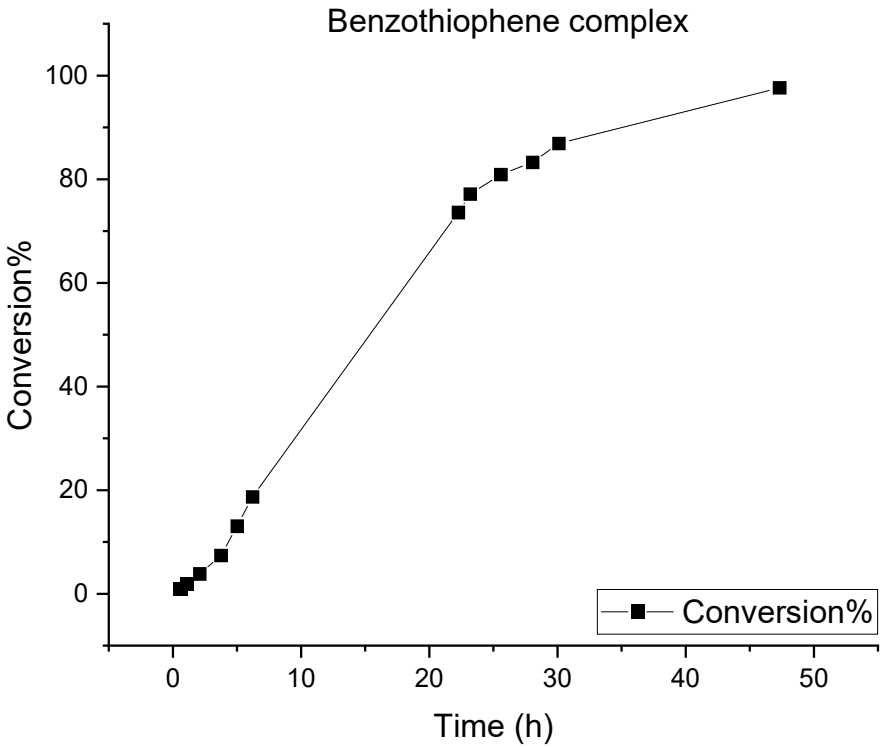

Furan complex
Conversion%
Time (h)
Conversion%
ee%
0
20
40
60
80
100
0
5
10
15
20
25

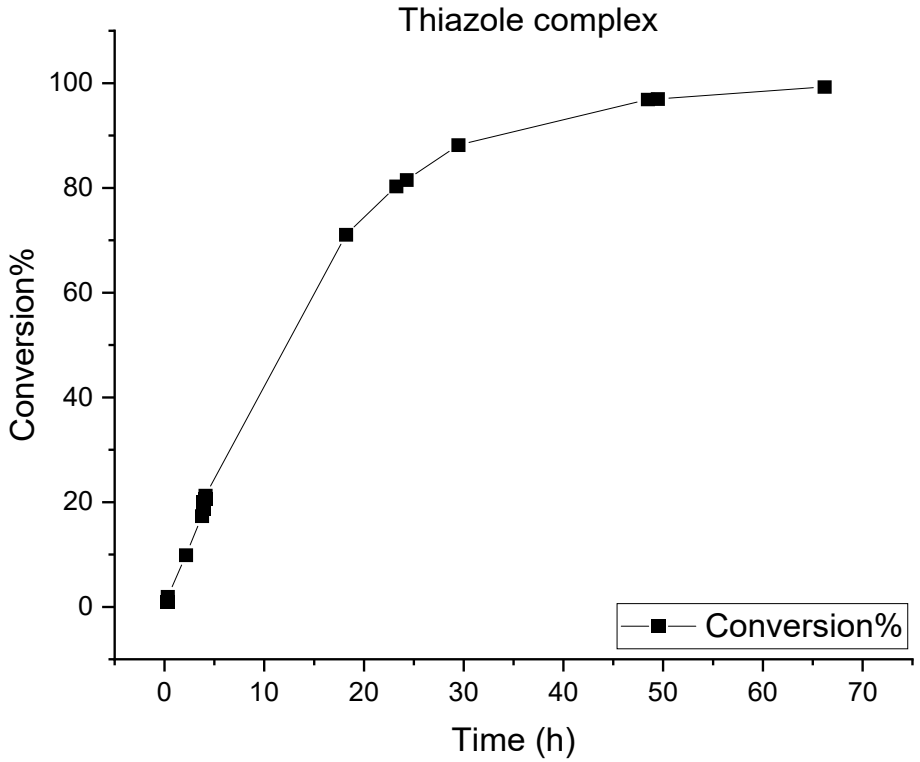

Noyori complex
Conversion%
Time (h)
Conversion%
ee%
0
20
40
60
80
100
0
5
10
15
20
25
30

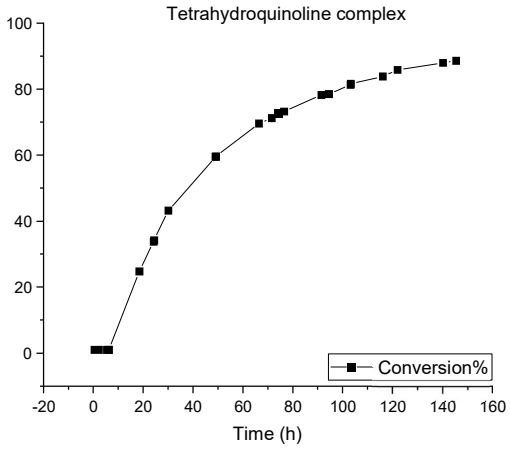
Comparative rate studies – ^{1}H NMR:

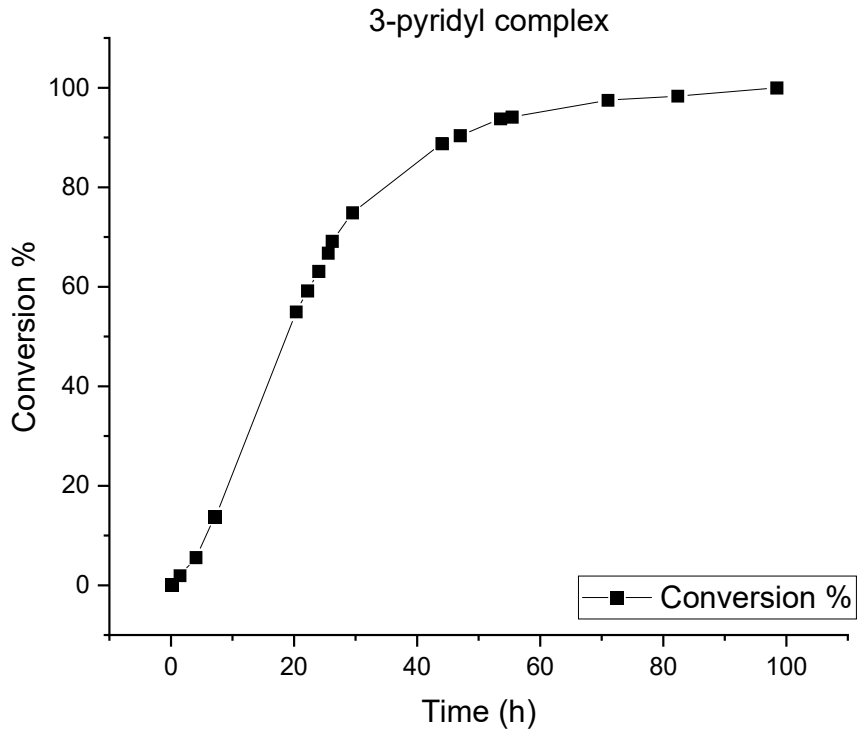
The conversion of acetophenone reduction is shown below. Conditions; 0.5 mmol ketone, 1% catalyst, 0.5 mL FA:TEA, S=[1], and 0.1 mL C_6D_6 to lock the ^{1}H NMR, followed by ^{1}H NMR (300 MHz):

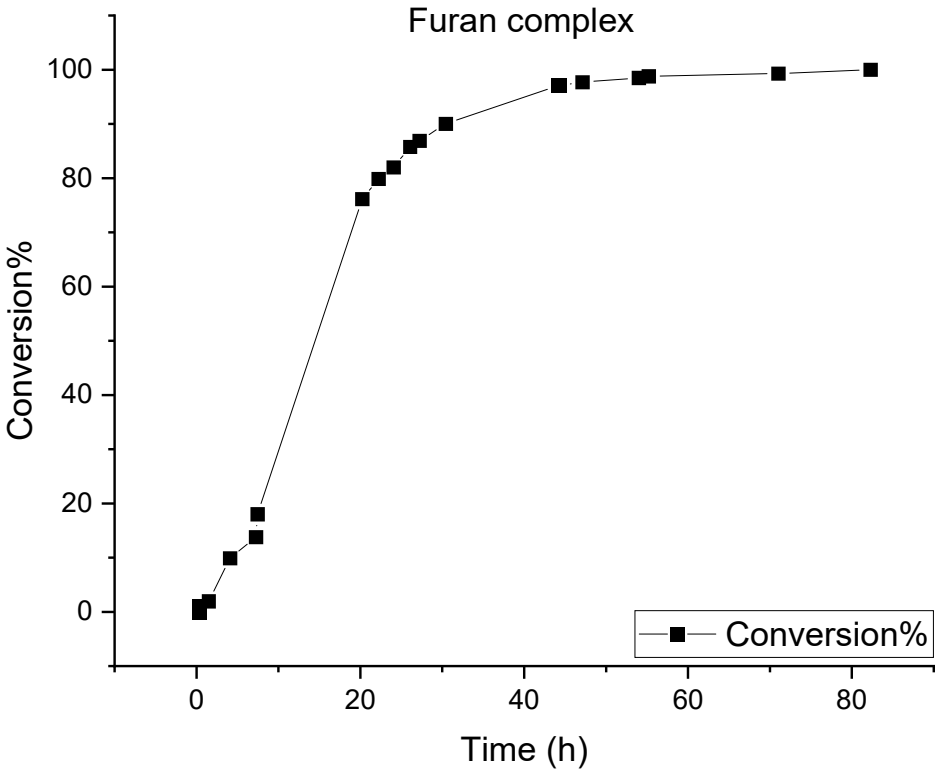


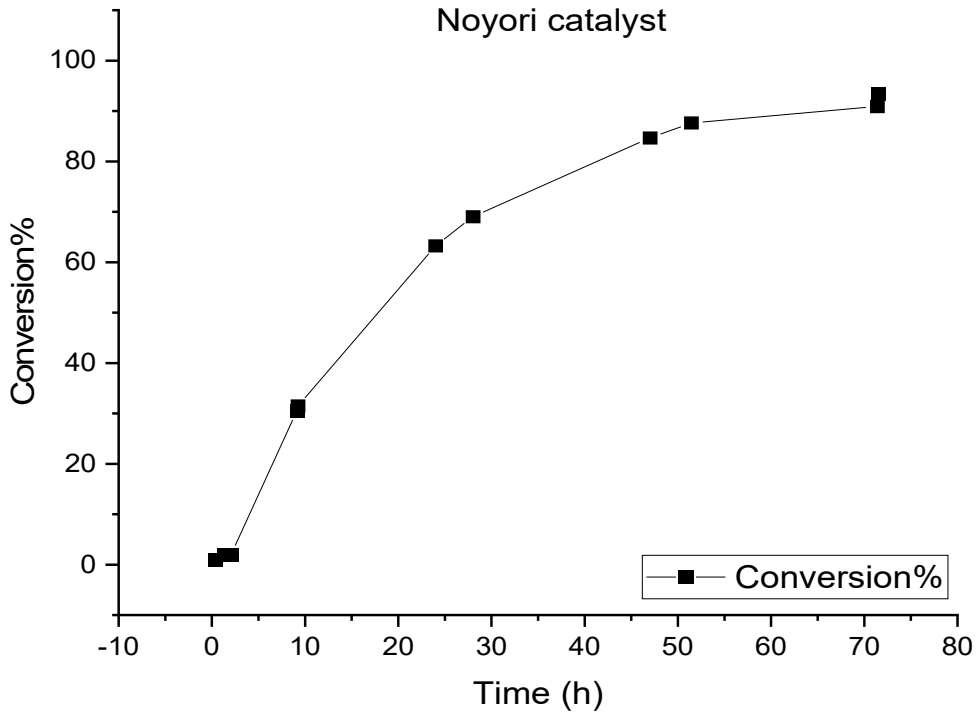



Thiazole complex
Conversion%
Time (h)
Conversion%
0
20
40
60
80
100
0
10
20
30
40
50
60
70


Tetrahydroquinoline complex
Time (h)
Conversion%
0
20
40
60
80
100
-20
0
20
40
60
80
100
120
140
160


3-pyridyl complex
Conversion %
Time (h)
Conversion %
0
20
40
60
80
100


Furan complex
Conversion%
Time (h)
Conversion%
0
20
40
60
80
100

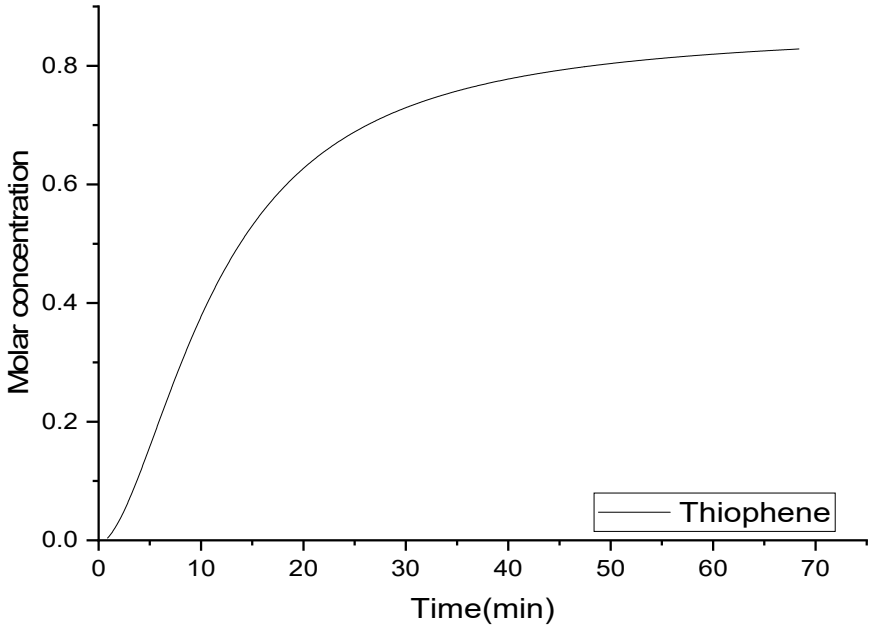

Noyori catalyst
Conversion%
Time (h)
Conversion%
100
80
60
40
20
0
-10
0
10
20
30
40
50
60
70
80

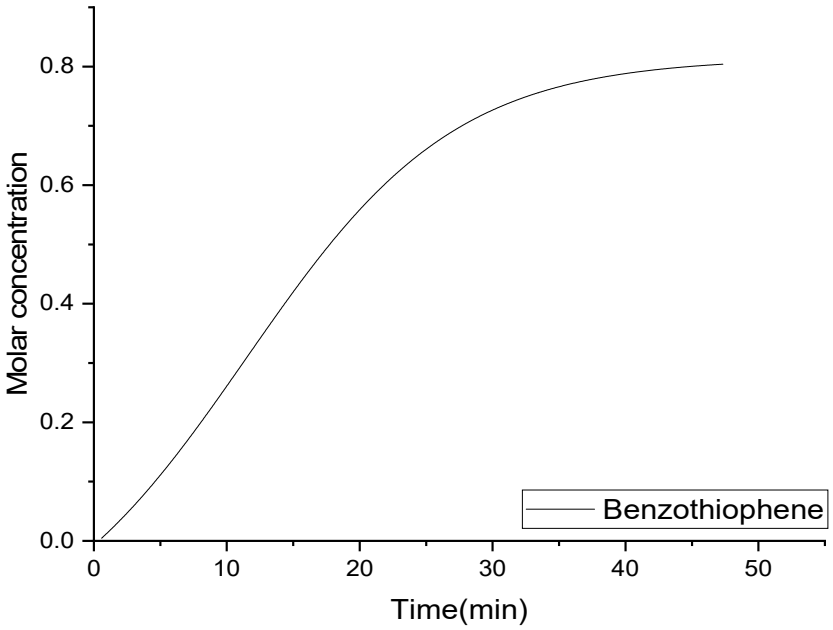
Comparison between the maximum rate of reaction of complexes.

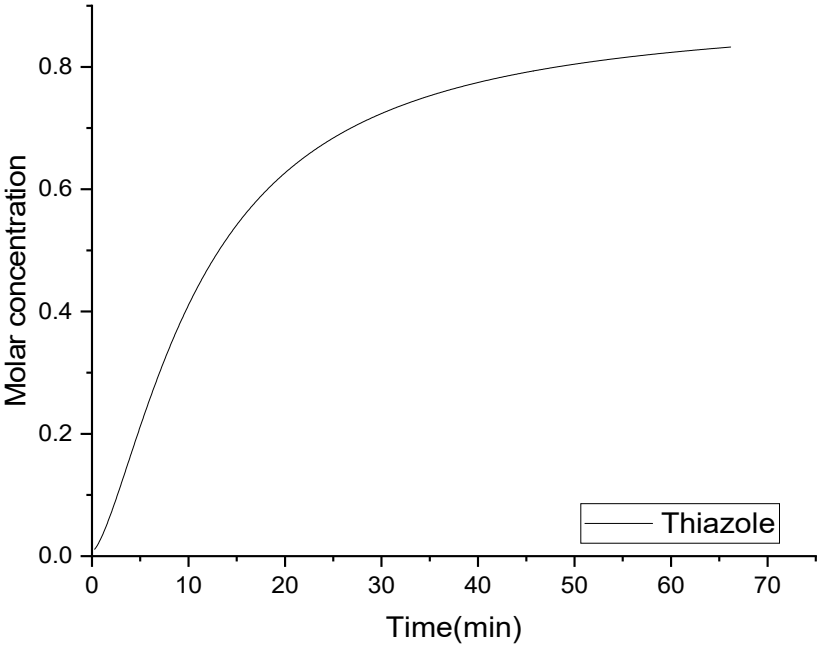
The data collected using ^{1}H NMR was processed in Origin software, the function used for non-linear fitting was the logistic function and the algorithm used to fit the data was Levenberg Marquardt. The R^2 for each data set was larger than 0.99, reflecting an excellent fit with the experimental data as shown below.

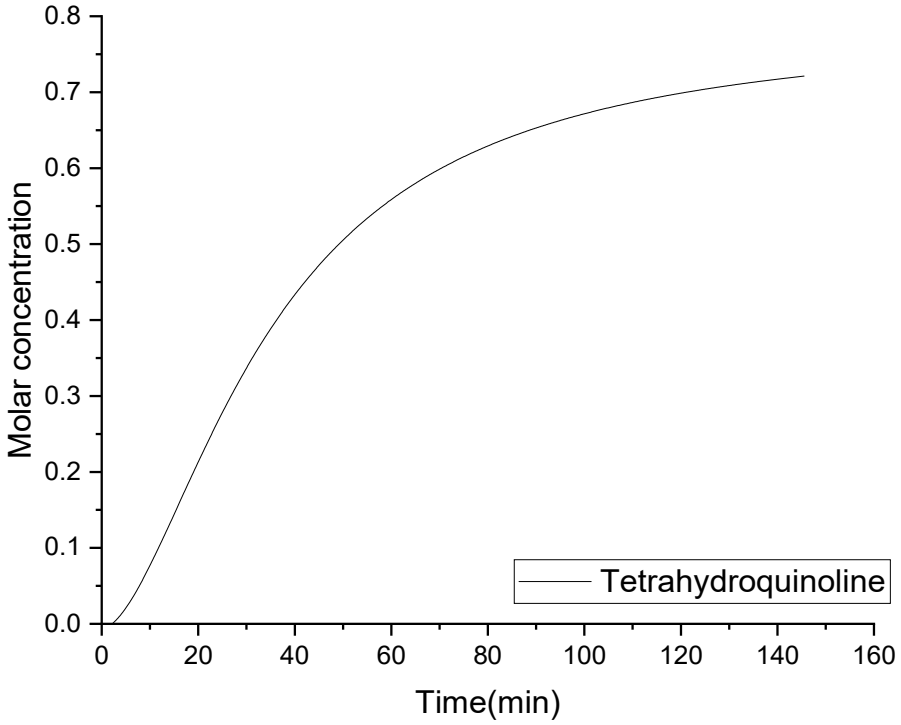
Complex	R-Square
Thiazole	0.99965
Thiophene	0.99893
Benzothiophene	0.99947
Tetrahydroquinoline	0.99773
Noyori	0.99904
3-Pyridyl	0.99969
Furan	0.99893

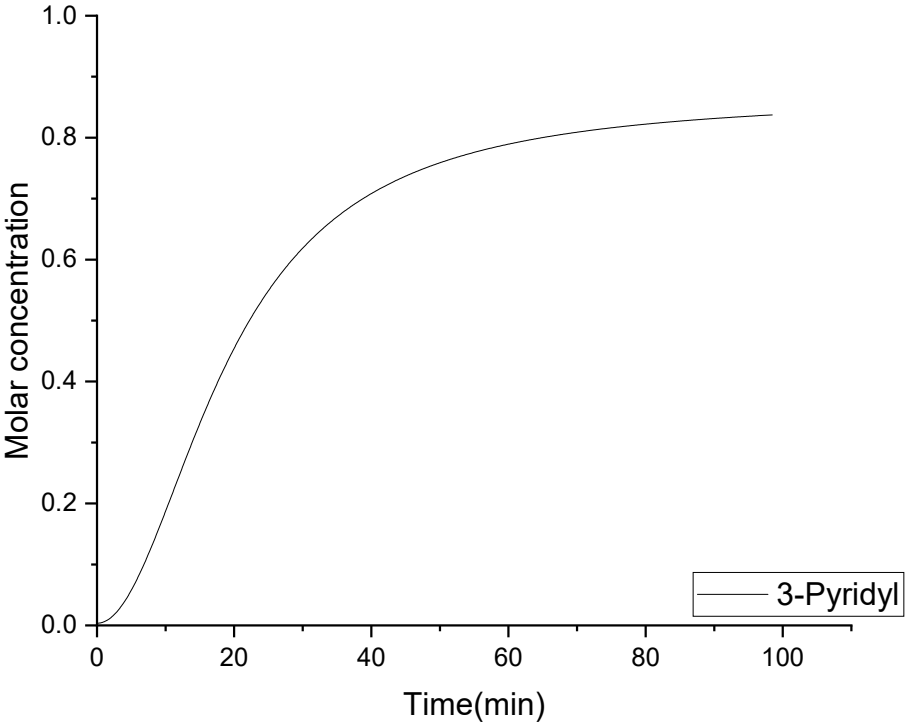
Fitted plots are shown below:




Molar concentration
0.0
0.2
0.4
0.6
0.8
0
10
20
30
40
50
Time(min)
Benzothiophene


Molar concentration
0.0
0.2
0.4
0.6
0.8
0
10
20
30
40
50
60
70
Time(min)
Thiazole


Molar concentration
0.0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0
20
40
60
80
100
120
140
160
Time(min)
Tetrahydroquinoline


Molar concentration
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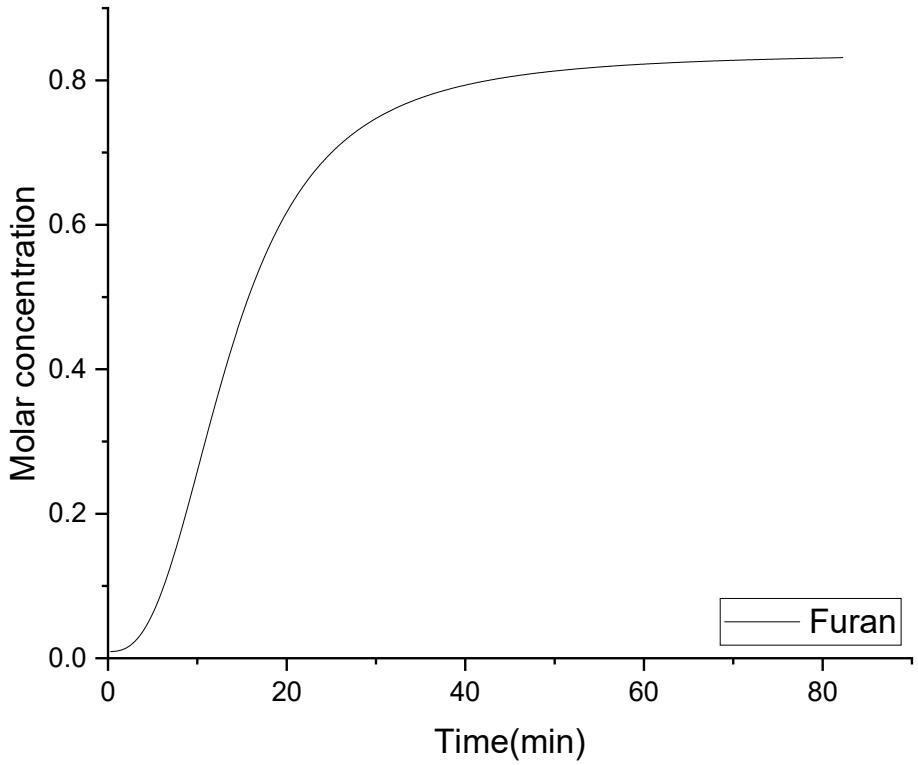
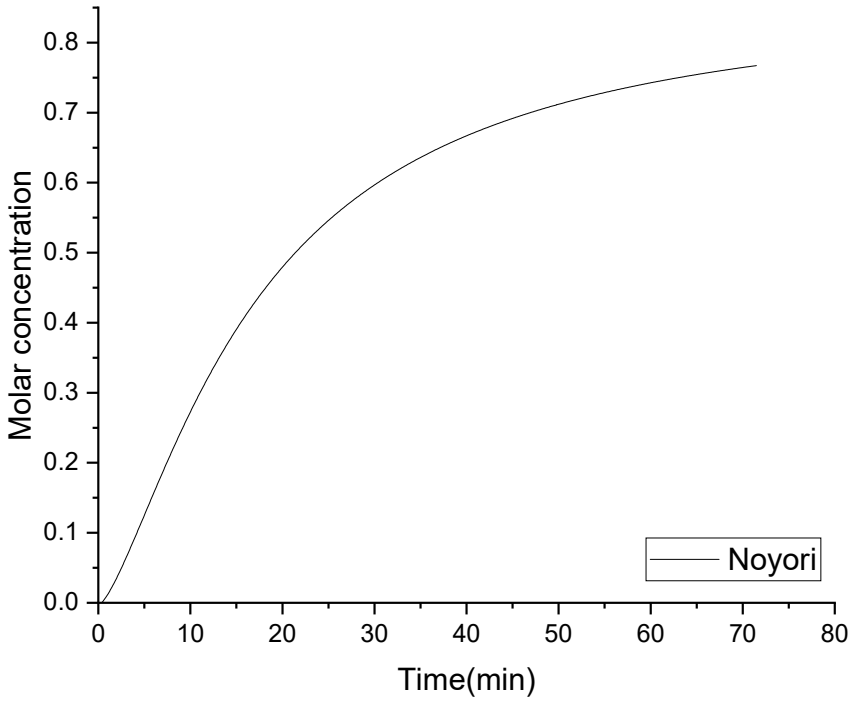
0.2
0.4
0.6
0.8
1.0
0
20
40
60
80
100
Time(min)
3-Pyridyl


Molar concentration
0.0
0.2
0.4
0.6
0.8
0
20
40
60
80
Time(min)
Furan


Molar concentration
0.0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0
10
20
30
40
50
60
70
80
Time(min)
Noyori

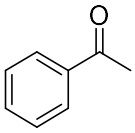
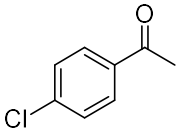
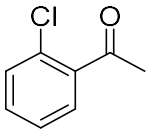
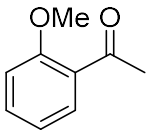
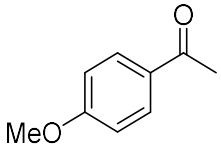
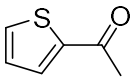
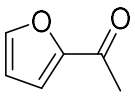
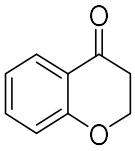
Maximum rate of reaction of each complex ([S] = 0.83 M).

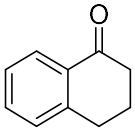
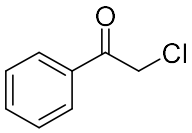
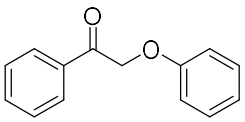
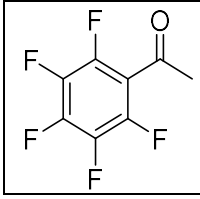
Complex	**Rate of reaction (mol min^{-1} L^{-1})**
Thiophene **12a**	0.03868 ± 2.21184E-4
Benzothiophene **12b**	0.03039 ± 5.96019E-5
Thiazole **12c**	0.03416 ± 2.50659E-4
Tetrahydroquinoline **12e**	0.01121 ± 5.50525E-5
3-Pyridyl **12f**	0.02532 ± 1.13979E-4
Furan **12g**	0.0403 ± 2.50407E-4
Noyori **1**	0.02278 ± 1.08426E-4

The reaction rate of the furan complex is faster than the Noyori one by a factor of 1.77, while the tetrahydroquinoline complex is slower by a factor of 0.5 than the Noyori catalyst.

Table of Results for ATH of ketones:

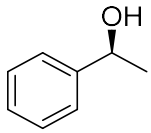
Conditions; 1 mmole ketone, 1% catalyst, 0.5 mL FA:TEA, and 0.5 mL DCM, S=[1].

Substrates	**(*S*,*S*)-Thiophene (12a)**	**(*R*,*R*)-Benzothiophene (12b)**	**(*R*,*R*)-Thioazole (12c)**	**(*S*,*S*)-Tetrahydroquinoline (12e)**	**(*R*,*R*)-3-pyridyl (12f)**	**(*S*,*S*)-Furan (12g)**
	97.8% ee (*S*) 100% Conv 66% yield 22h	>99% ee (*R*) 98% Conv 91% yield 22h	98.6% ee (*R*) 99% Conv 73% yield 27h	96.8% ee (*S*) 100% Conv 77% yield 49h	>99% ee (*R*) 98% Conv 88% yield 46h	96.6% ee (*S*) 99% Conv 91% yield 46h
	94% ee (*S*) 100% Conv 72% yield 40h	>99 % ee (*R*) 88% Conv 70% yield 26h	>99 % ee (*R*) 89% Conv 79% yield 26h	97.4% ee (*S*) 99% Conv 79% yield 91h	>99% ee (*R*) 99% Conv 92% yield 47h	91.2% ee (*S*) 99% Conv 93% yield 48h
	95.8% ee (*S*) 100% Conv 76% yield 48h	96.2% ee (*R*) 100% Conv 72% yield 21h	96.8 % ee (*R*) 100% Conv 72% yield 27h	87.4% ee (*S*) 100% Conv 80% yield 161h	97.2 % ee (*R*) 100% Conv 93% yield 165h	96.2 % ee (*S*) 100% Conv 88% yield 23h
	91.6 % ee (*S*) 99% Conv 64% yield 97h	92% ee (*R*) 99% Conv 71% yield 111h	96.4% ee (*R*) 100% Conv 73% yield 96h	89.4 % ee (*S*) 30% Conv 183h	95% ee (*R*) 99% Conv 81% yield 165h	91.2% ee (*S*) 98% Conv 70.6% yield 96h
	94.2% ee (*S*) 97% Conv 89% yield 167h	98.3 % ee (*R*) 98% Conv 91% yield 142h	96.7 % ee (*R*) 99% Conv 81% yield 142h	98.9% ee (*S*) 51% Conv 44% yield 167h	97.2 % ee (*R*) 98% Conv 95%yield 165h	93.6 % ee (*S*) 96% Conv 82% yield 187h
	97.6% ee (*S*) 99% Conv 46% yield 120h	>99% ee (*R*) 99% Conv 41% yield 120h	>99% ee (*R*) 99% Conv 59% yield 120h	97.6% ee (*S*) 97% Conv 65% yield 145h	>99% ee (*R*) 100% Conv 97% yield 165h	98.4% ee (*S*) 98% Conv 42% yield 96h
	99.4% ee (*S*) 93% Conv 70% yield 26h	>99% ee (*R*) 99% Conv 75% yield 26h	>99% ee (*R*) 99% Conv 72% yield 26h	99% ee (*S*) 99% Conv 85% yield 26h	>99% ee (*R*) 93% Conv 70% yield 22h	96.4% ee (*S*) 98% Conv 81% yield 23h
	99.1% ee (*S*) 98% Conv 97% yield 27h	>99% ee (*R*) 99% Conv 91% yield 27h	>99% ee (*R*) 99% Conv 93% yield 27h	99.3% ee (*S*) 100% Conv 90% yield 27h	>99% ee (*R*) 99% Conv 82% yield 22h	>99% ee (*S*) 99% Conv 98% yield 23h

	>99% ee (*S*) 99% Conv 71% yield 111h	92.8% ee (*R*) 99% Conv 82% yield 111h	>99% ee (*R*) 99% Conv 82% yield 160h	99% ee (*S*) 99% Conv 82% yield 160h	>99% ee (*R*) 99% Conv 88% yield 47h	99.6% ee (*S*) 99% Conv 87% yield 48h
	99.2% ee (*R*) 100% Conv 82% yield 15h	>98.9% ee (*S*) 100% Conv 74.6% yield 15h	>99% ee (*S*) 100% Conv 73% yield 15h	>99% ee (*R*) 100% Conv 86% yield 15h	98.4% ee (*S*) 100% Conv 93% yield 22h	95.8% ee (*R*) 100% Conv 88% yield 15h
	96.8% ee (*R*) 99% Conv 91% yield 23h	94.6% ee (*S*) 99% Conv 84% yield 23h	98.1% ee (*S*) 99% Conv 84% yield 23h	97.2% ee (*R*) 98% Conv 87% yield 23h	96.2% ee (*S*) 99% Conv 93% yield 22h	94.6% ee (*R*) 99% Conv 87% yield 23h
	8% ee (*R*) 100% Conv 68% yield 15h	20.2% ee (*S*) 100% Conv 69% yield 15h	33.8% ee (*S*) 100% Conv 74% yield 15h	9.8% ee (*R*) 100% Conv 78% yield 15h	35.2% ee (*S*) 100% Conv 82% yield 22h	1.2% ee (*R*) 100% Conv 76% yield 15h

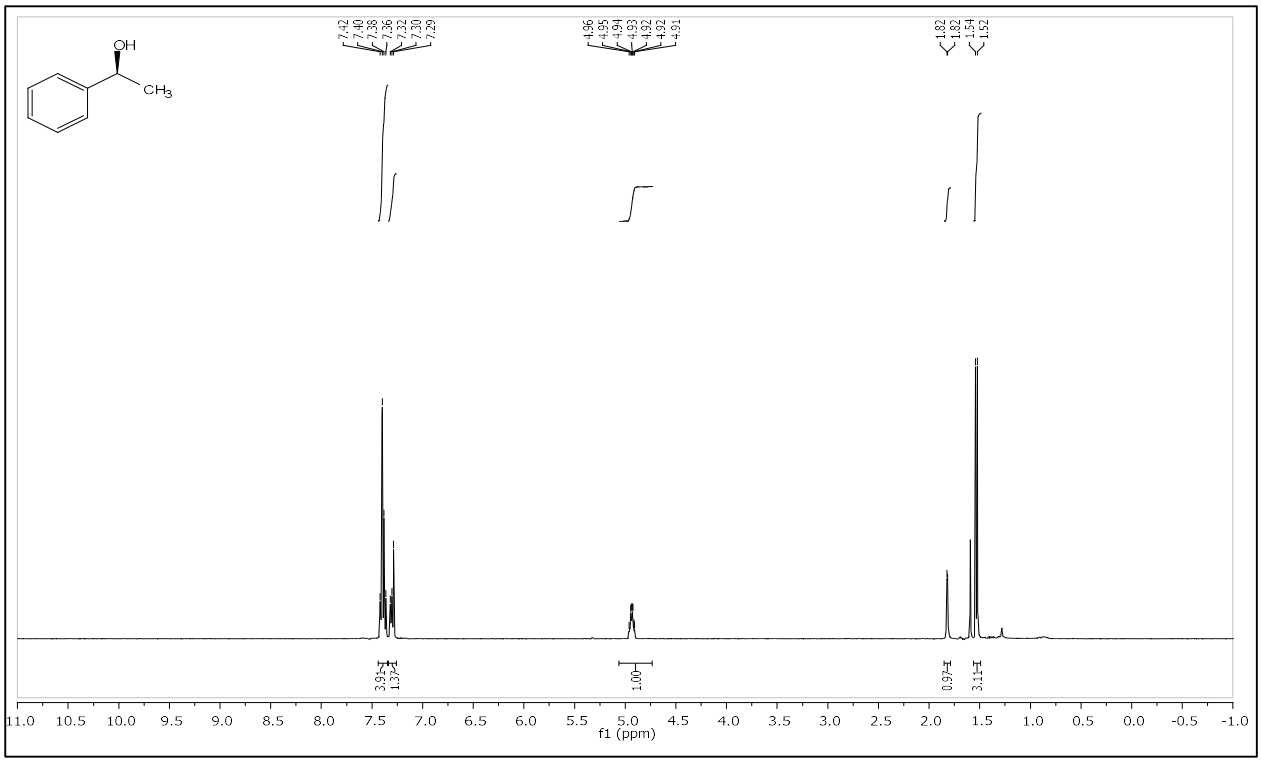
^{1}H NMR, ^{13}C NMR, HPLC, and GC spectra for tested substrates:

(*S*)-1-Phenylethanol (NK224).

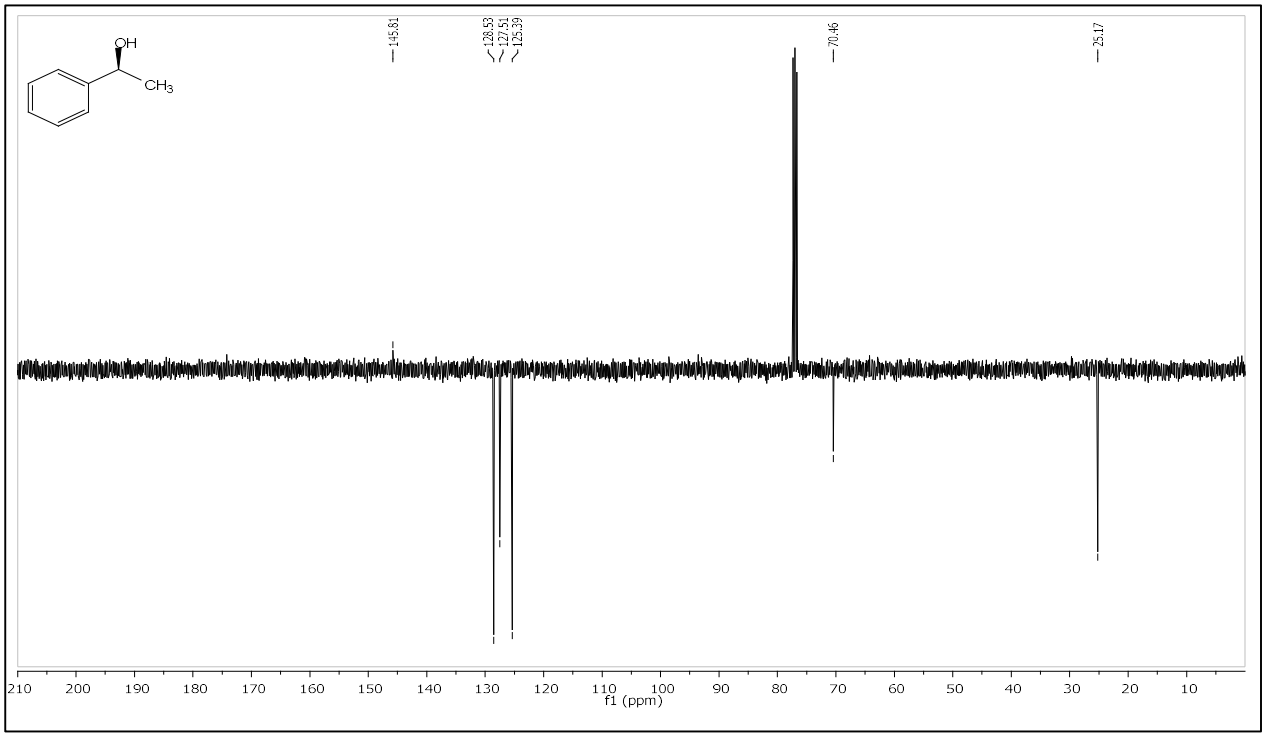


Acetophenone (120 mg, 1.00 mmol) and catalyst **(*S*,*S*)-12a** (6.30 mg, 0.01 mmol) were reacted following the general procedure to give (*S*)-1-phenylethanol as a colourless oil (79.1 mg, 65.9 mmol, 65.9%); δ_H (400 MHz, $CDCl_3$) 7.43 – 7.35 (4 H, m, ArH), 7.33 – 7.27 (1 H, m, ArH), 5.01 – 4.88 (1 H, m, CH), 1.82 (1 H, br. s, OH), 1.53 (3 H, d, *J* 6.5, CH_3).; δ_C (101 MHz, $CDCl_3$) 145.81 (C, Ar), 128.53 (CH, Ar), 127.51 (CH, Ar), 125.39 (CH, Ar), 70.46 (CH), 25.17 (CH_3).; $[\alpha]^{25}$ -22.8 (c 0.136 in $CHCl_3$) 97.8% ee (S) (lit.[2] $[\alpha]^{27}$ +54.9 (*c* 1.0 in $CHCl_3$) 96% ee. (*R*)); GC analysis (CHROMPACCYCLODEXTRIN-β-236M-19, 50 m × 0.25 mm × 0.25 μm, gas H_2, T = 110 °C, P = 15 psi, FID temp 250 °C, injector temp 220 °C, ketone 9.09 min., *R* isomer 14.30 min., *S* isomer 15.17min.).

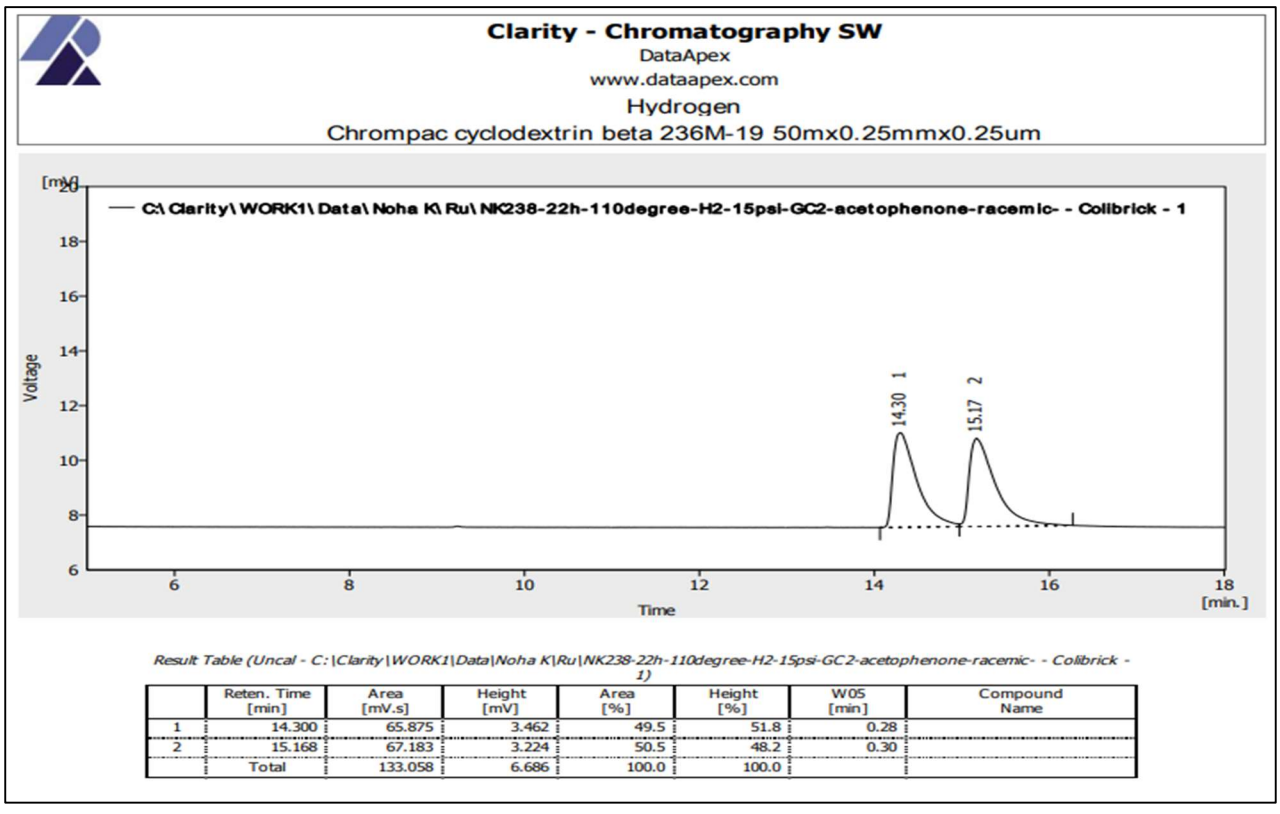
δ_H (400 MHz, $CDCl_3$)



δ_C (101 MHz, $CDCl_3$)



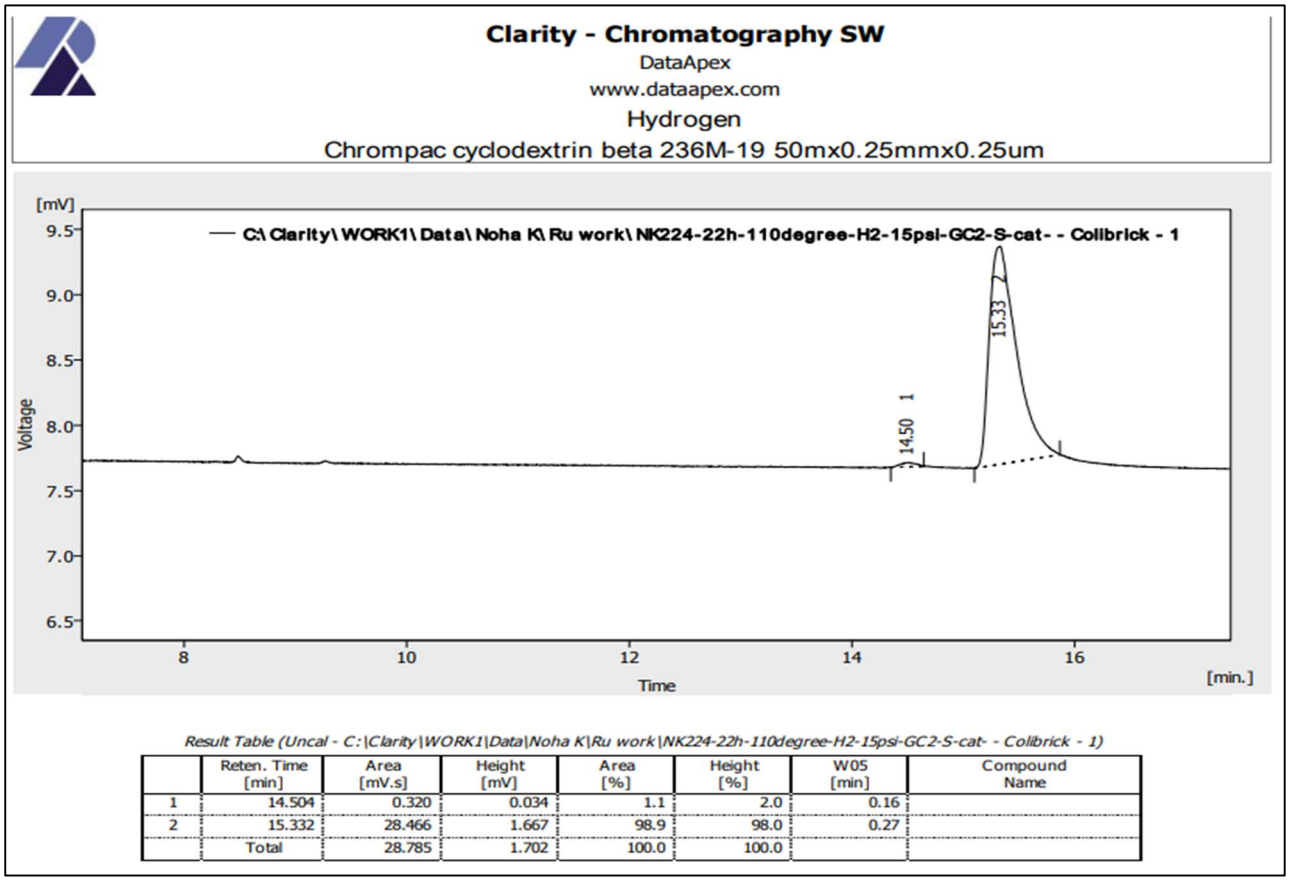
Chiral GC - racemic



Result Table (Uncal - C:\|Clarity\|WORK1\|Data\|Noha K\|Ru\|NK238-22h-110degree-H2-15psi-GC2-acetophenone-racemic- - Colibrick - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	14.300	65.875	3.462	49.5	51.8	0.28	
2	15.168	67.183	3.224	50.5	48.2	0.30	
	Total	133.058	6.686	100.0	100.0		

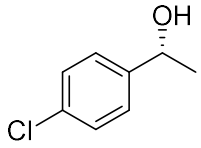
Chiral GC – asymmetric



Result Table (Uncal - C:\Clarity\WORK1\Data\Noha K\Ru work\NK224-22h-110degree-H2-15psi-GC2-S-cat- - Colibrick - 1)

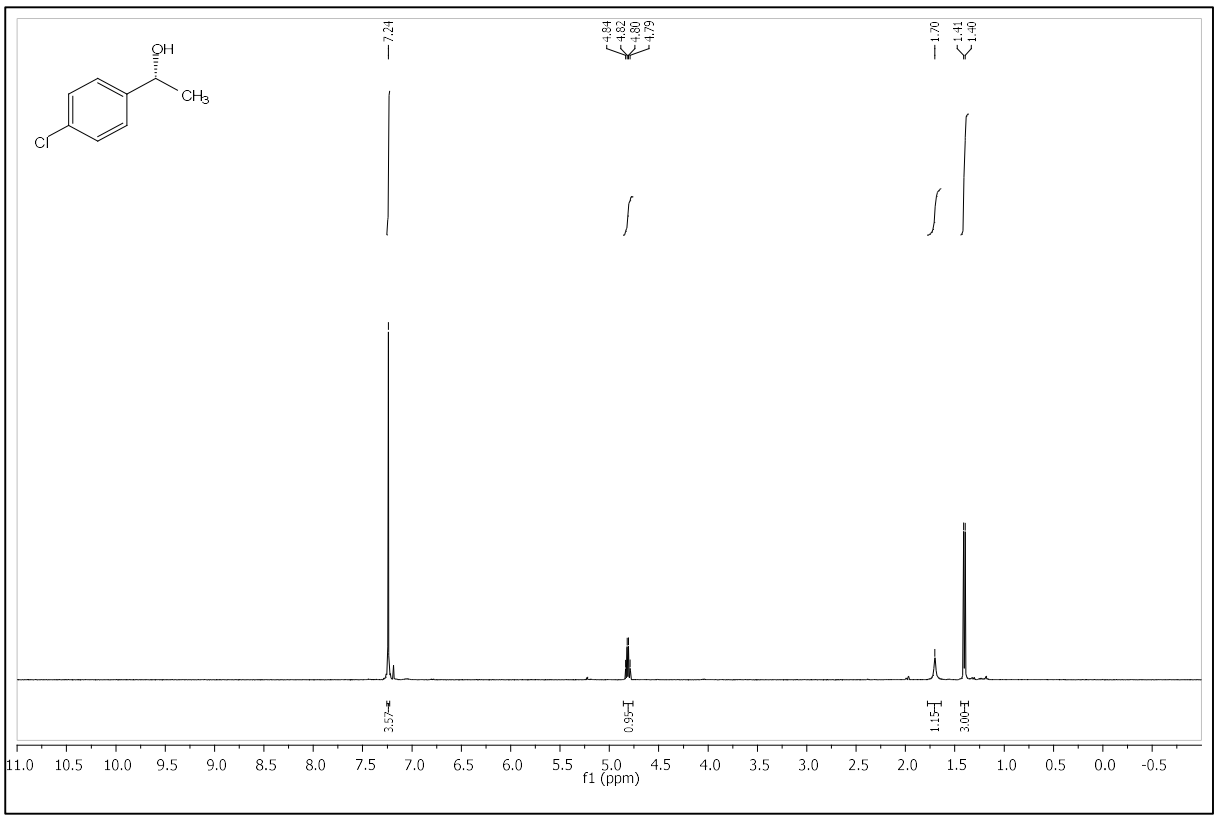
	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	14.504	0.320	0.034	1.1	2.0	0.16	
2	15.332	28.466	1.667	98.9	98.0	0.27	
	Total	28.785	1.702	100.0	100.0		

(*R*)-1-(4-Chlorophenyl)ethan-1-ol (NK271)

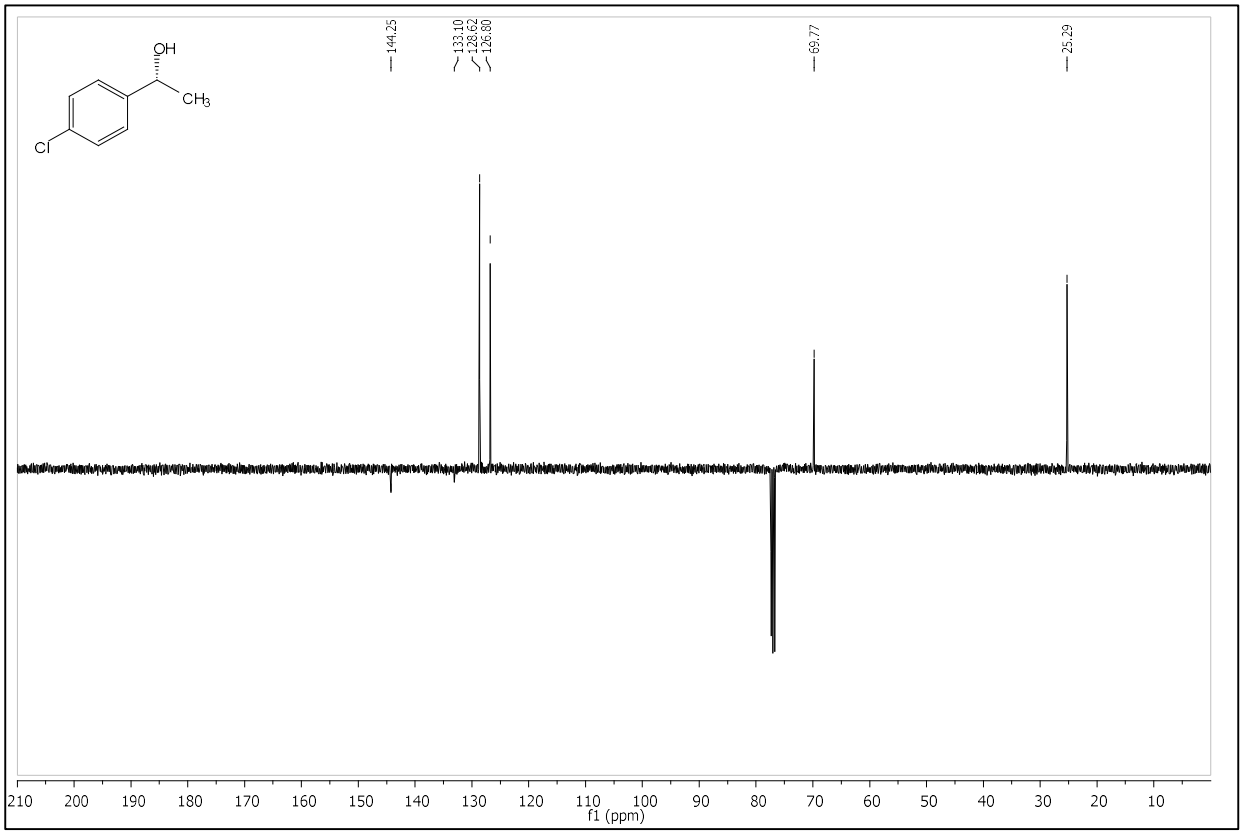


1-(4-Chlorophenyl)ethan-1-one (155 mg, 1.00 mmol) and catalyst **(*R,R*)-12b** (6.78 mg, 0.01 mmol) were reacted following the general procedure to give (*R*)-1-(4-chlorophenyl)ethan-1-ol as a yellow oil (109.4 mg, 69.9 mmol, 70%); δ_H (400 MHz, $CDCl_3$) 7.24-7.20 (4 H, m, ArH), 4.81 (1 H, q, *J* 6.5, CH), 1.70 (1 H, br. s, OH), 1.40 (3 H, d, *J* 6.5, CH_3); δ_C (101 MHz, $CDCl_3$) 144.25 (C Ar), 133.10 (C, Ar), 128.62 (CH, Ar), 126.80 (CH, Ar), 69.77 (CH), 25.29 (CH_3). $[\alpha]^{26}$ +42.5 (c 0.102 in $CHCl_3$) >99% ee (*R*) ((lit.[3] $[\alpha]^D$ = +51.7 (c = 0.23, $CHCl_3$), 94% ee (*R*)); GC analysis (CHROMPACCYCLODEXTRIN-β-236M-19, 50 m × 0.25 mm × 0.25 μm, gas H_2, T = 125 °C, P = 15 psi, FID temp 250 °C, injector temp 220 °C, ketone 13.8 min., *R* isomer 27.04 min., *S* isomer 29.26 min.)

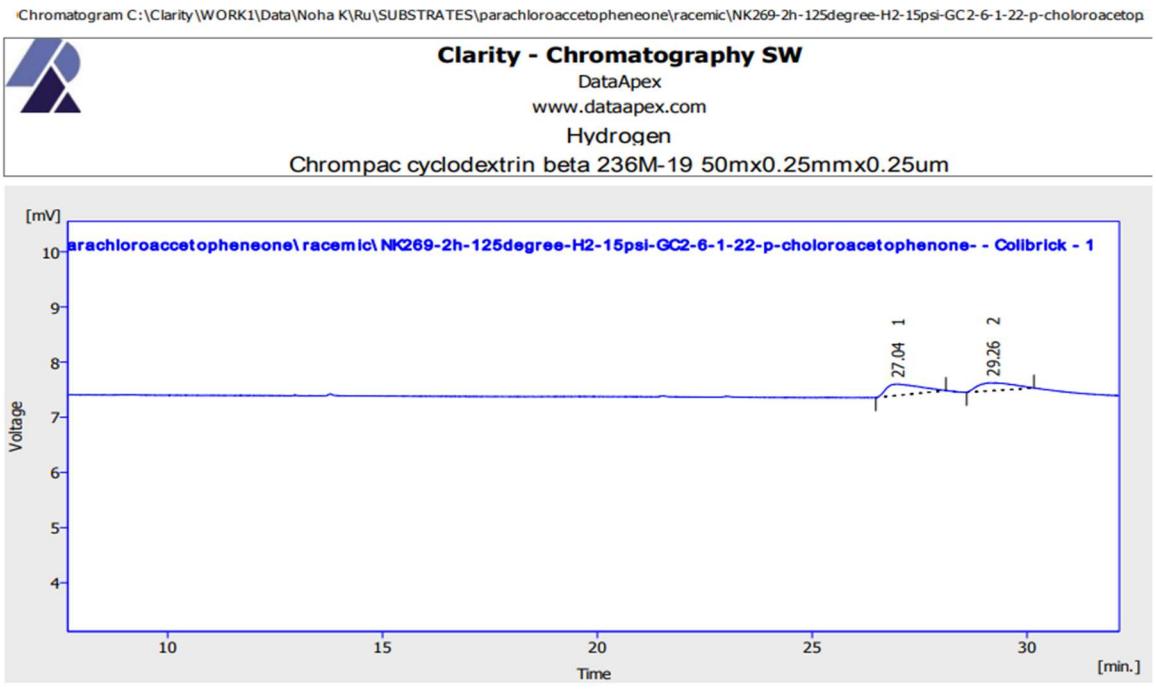
δ_H (400 MHz, $CDCl_3$)



δ_C (101 MHz, $CDCl_3$)



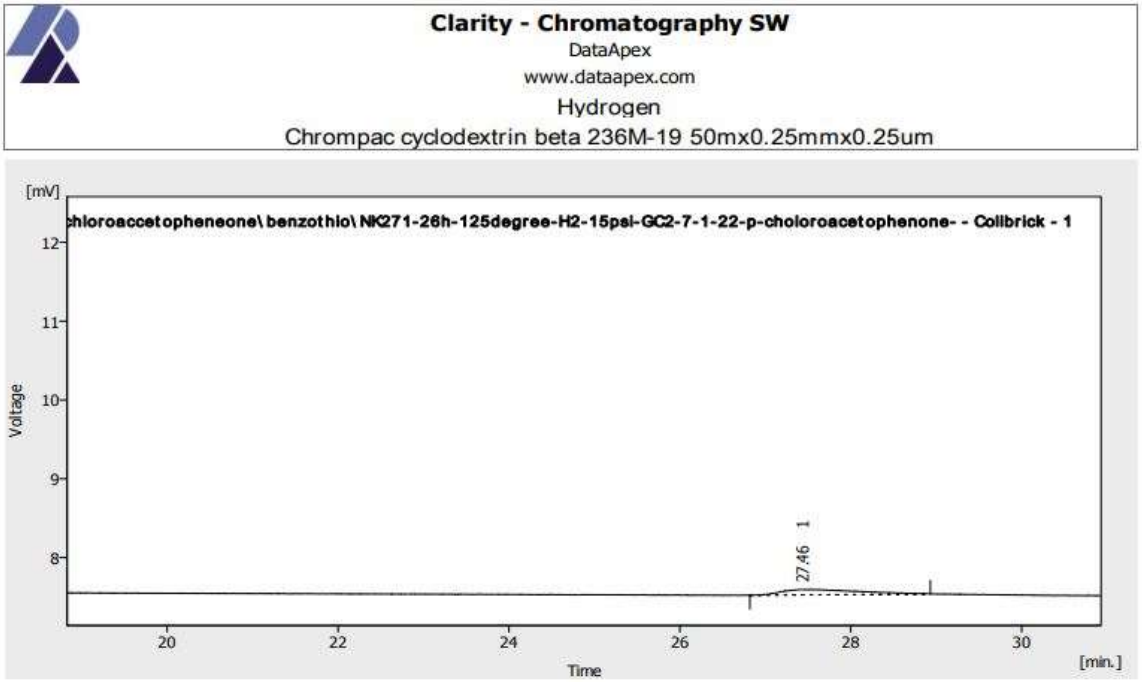
Chiral GC- racemic



Result Table (Uncal - C:\Clarity\WORK1\Data\Noha K\Ru\SUBSTRATES\parachloroaccetopheneone\racemic\NK269-2h-125degree-H2-15psi-GC2-6-1-22-p-choloroacetophenone- - Colibrick - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	27.036	10.804	0.202	57.2	58.9	1.26	
2	29.260	8.081	0.141	42.8	41.1	1.14	
	Total	18.886	0.343	100.0	100.0		

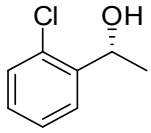
Chiral GC-asymmetric



Result Table (Uncal - C:\Clarity\WORK1\Data\Noha K\Ru\SUBSTRATES\parachloroaccetopheneone\benzothio\NK271-26h-125degree-H2-15psi-GC2-7-1-22-p-choloroacetophenone- - Colibrick - 1)

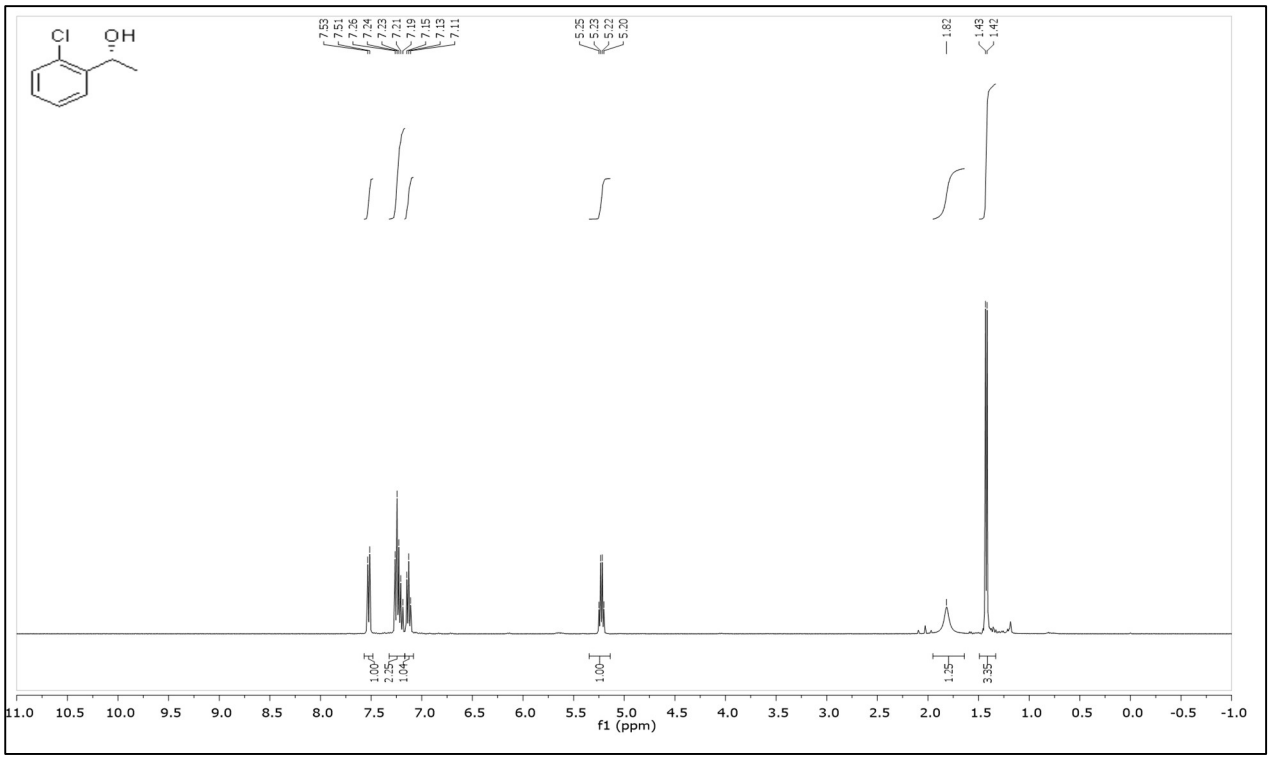
	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	27.456	4.435	0.071	100.0	100.0	1.11	
	Total	4.435	0.071	100.0	100.0		

(*R*)-1-(2-Chlorophenyl)ethan-1-ol (NK277)

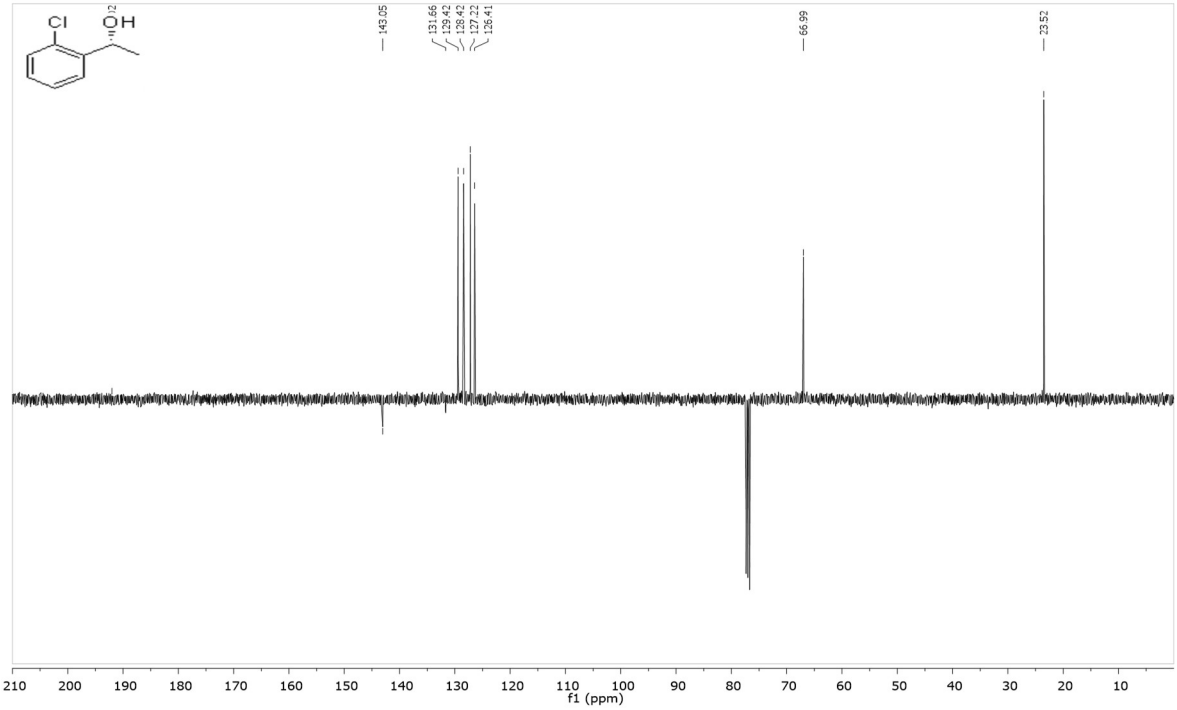


1-(2-Chlorophenyl)ethan-1-one (155 mg, 1.00 mmol) and catalyst **(*R*,*R*)-12c** (6.6 mg, 0.01 mmol) were reacted following the general procedure to give (*R*)-1-(2-chlorophenyl)ethan-1-ol as a yellow oil (113 mg, 0.722 mmol, 72%); δ_H (400 MHz, $CDCl_3$) 7.52 (1 H, d, *J* 7.7, ArH), 7.23 (2 H, m, ArH), 7.13 (1 H, t, *J* 7.6, ArH), 5.23 (1 H, q, *J* 6.4, CH), 1.82 (1 H, br. s, OH), 1.42 (3 H, d, *J* 6.4, CH_3); δ_C (101 MHz, $CDCl_3$) 143.05 (C), 131.66 (C), 129.42 (CH), 128.42 (CH), 127.22 (CH), 126.41 (CH), 66.99 (CH), 23.52 (CH_3); $[\alpha]^{25}$ +68.0 (c 0.122 in $CHCl_3$) 96.8% ee (*R*) (lit.[3] $[\alpha]^D$ = +64.8 (c = 0.42, $CHCl_3$), 88% ee (*R*)); GC analysis (CP-Chiralsil-Dex CB 25m x 0.25mm x 0.25um), gas He, T = 140 °C, P = 15 psi, FID temp 250 °C, injector temp 220 °C, ketone 2.300 min., *R* isomer 5.31 min., *S* isomer 6.31 min.).

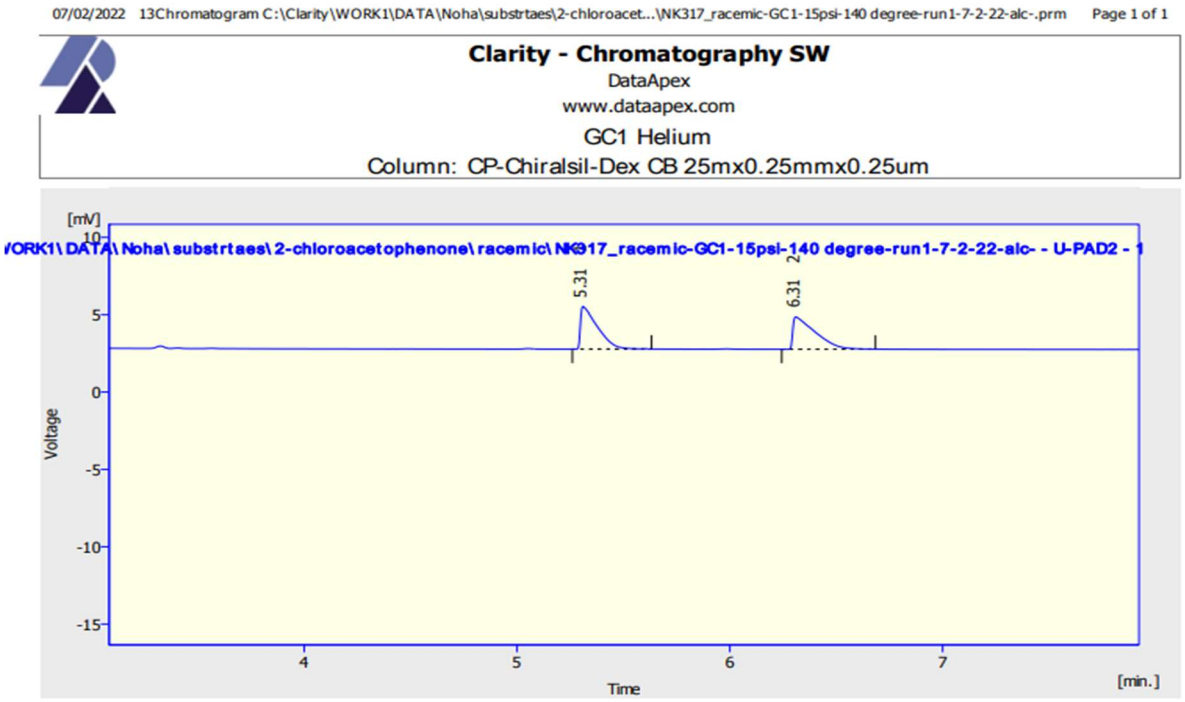
δ_H (400 MHz, $CDCl_3$)



δ_C (101 MHz, $CDCl_3$)



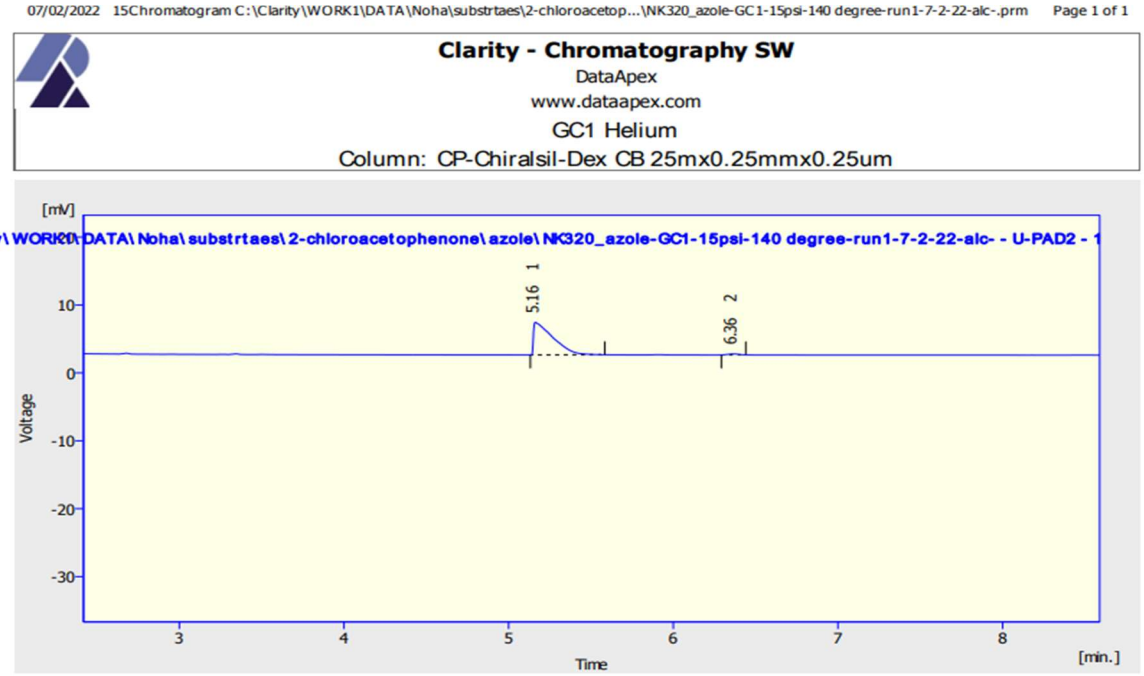
Chiral GC – racemic.



Result Table (Uncal - C:\Clarity\WORK1\DATA\Noha\substrtaes\2-chloroacetophenone\racemic\NK317_racemic-GC1-15psi-140 degree-run1-7-2-22-alc- - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	5.312	15.208	2.749	50.1	56.9	0.09	
2	6.312	15.175	2.085	49.9	43.1	0.12	
	Total	30.383	4.834	100.0	100.0		

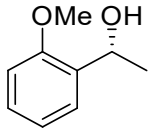
Chiral GC – asymmetric.



Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|Noha\|substrtaes\|2-chloroacetophenone\|azole\|NK320_azole-GC1-15psi-140 degree-run1-7-2-22-alc- - U-PAD2 - 1)

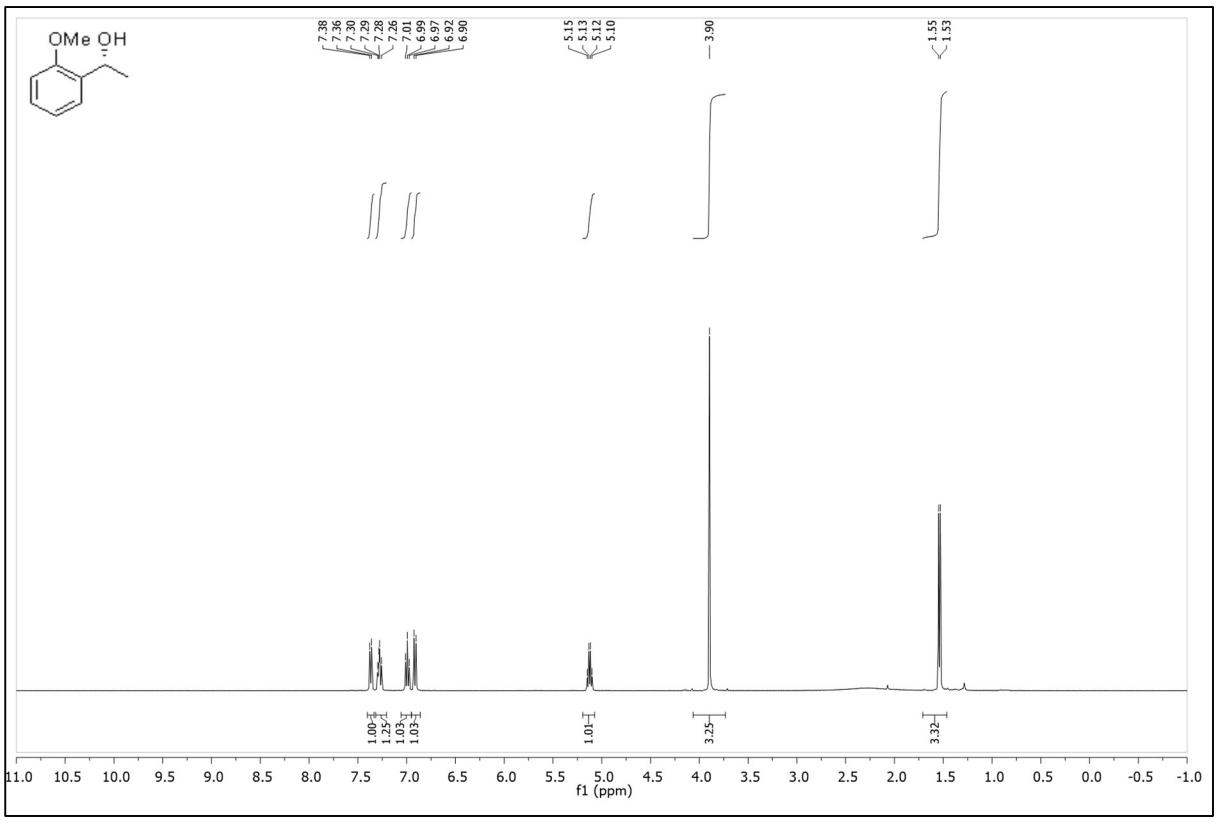
	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	5.164	39.252	4.802	98.4	97.1	0.13	
2	6.364	0.644	0.142	1.6	2.9	0.08	
	Total	39.896	4.944	100.0	100.0		

(*R*)-1-(2-Methoxyphenyl)ethan-1-ol (NK280)

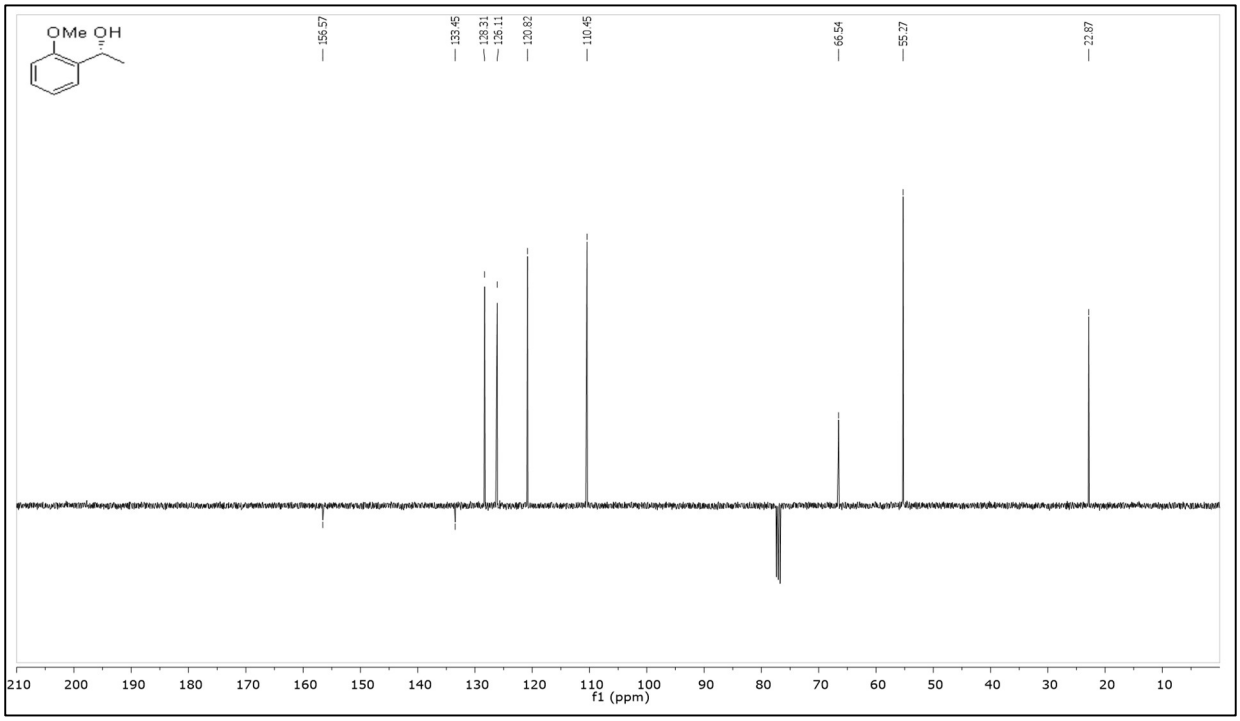


1-(2-Methoxyphenyl)ethan-1-one (150.2 mg, 1.00 mmol) and catalyst **(*R*,*R*)-12b** (6.8 mg, 0.01 mmol) were reacted following the general procedure to give (*R*)-1-(2-methoxyphenyl)ethan-1-ol as a yellow oil (108.6 mg, 0.714 mmol, 71.4%); δ_H (400 MHz, $CDCl_3$) 7.37 (1 H, d, *J* 7.5, ArH), 7.28 (1 H, m, ArH), 6.99 (1 H, t, *J* 7.5, ArH), 6.91 (1 H, d, *J* 8.2, ArH), 5.12 (1 H, q, *J* 6.5, CH), 3.90 (3 H, br. s, OCH_3), 1.54 (3 H, d, *J* 6.5, CH_3); δ_C (101 MHz, $CDCl_3$) 156.57 (C), 133.45 (C), 128.31 (CH), 126.11(CH), 120.82 (CH), 110.45 (CH), 66.54 (CH), 55.27 (OCH_3), 22.87 (CH_3); $[\alpha]^{25}$ +17.3 (c 0.084 in $CHCl_3$) 92% ee (*R*) (lit.[3] $[\alpha]^D$ = +16.4 (c = 0.39, $CHCl_3$), 87% ee (*R*)) ; GC analysis (CP-Chiralsil-Dex CB 25m x 0.25mm x 0.25um), gas He, T = 140 °C, P = 15 psi, FID temp 250 °C, injector temp 220 °C, ketone 3.20 min., *R* isomer 5.22 min., *S* isomer 4.90 min.).

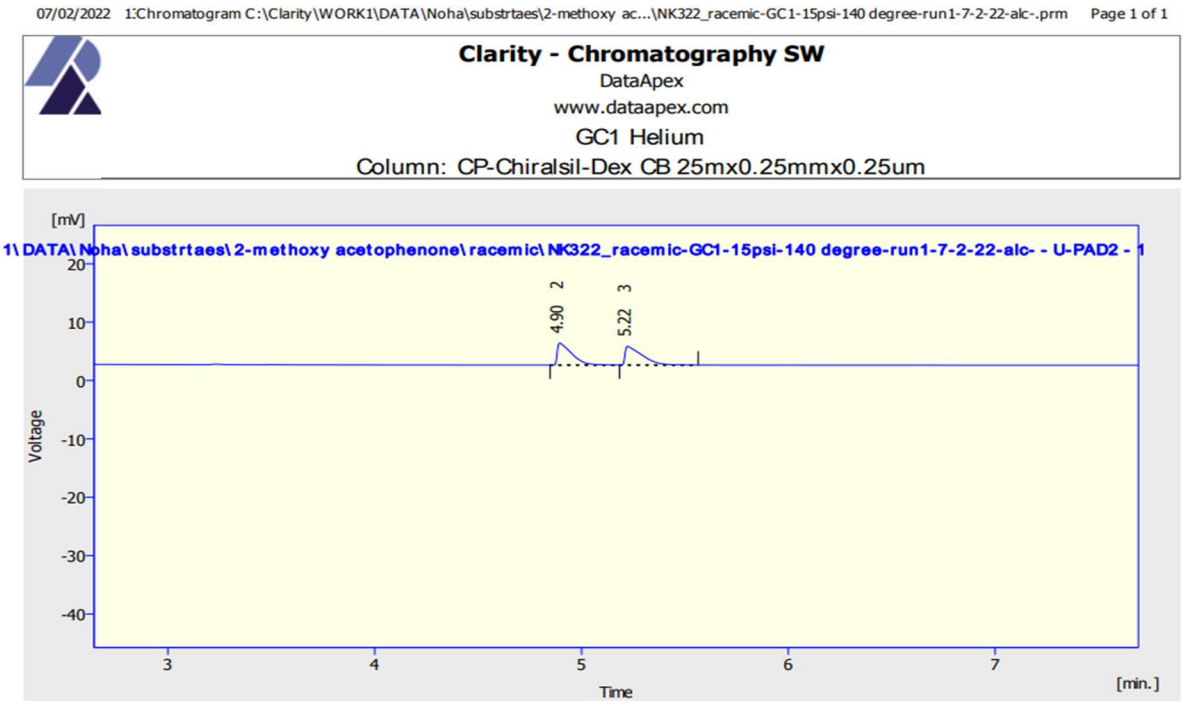
δ_H (400 MHz, $CDCl_3$)



δ_C (101 MHz, $CDCl_3$)



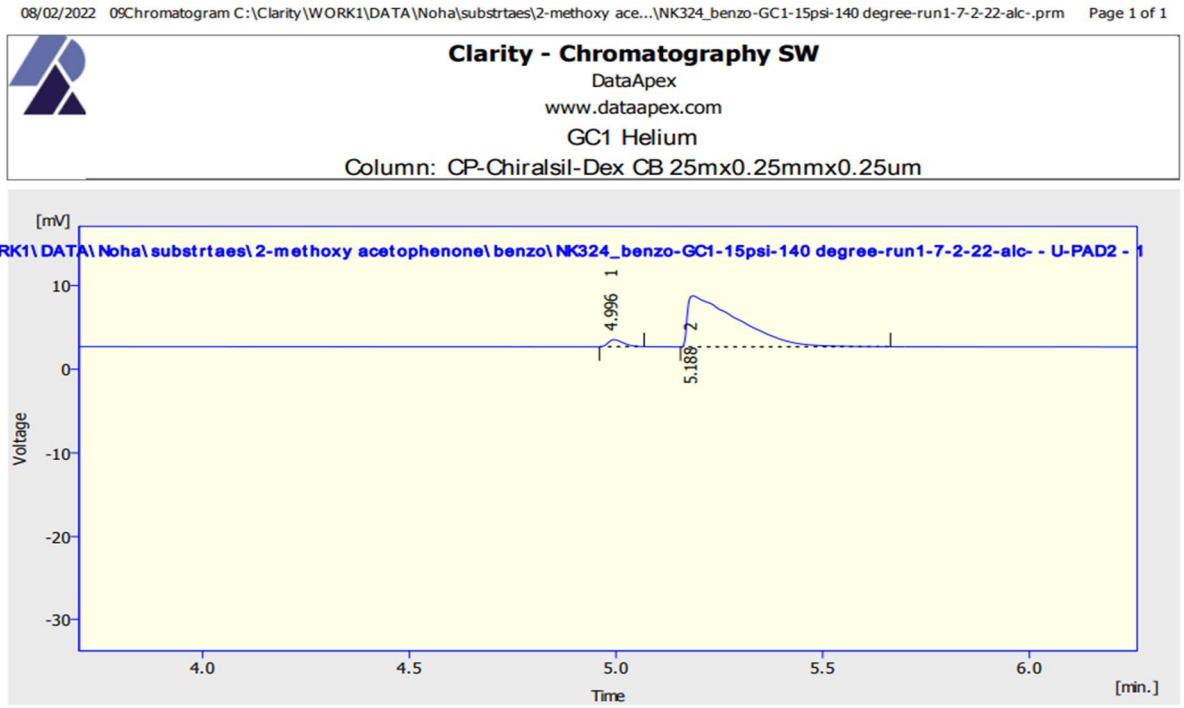
Chiral GC – racemic.



Result Table (Uncal - C:\Clarity\WORK1\DATA\Noha\substrtaes\2-methoxy acetophenone\racemic\NK322_racemic-GC1-15psi-140 degree-run1-7-2-22-alc- - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
2	4.896	18.226	3.758	50.0	54.0	0.08	
3	5.224	18.220	3.207	50.0	46.0	0.09	
	Total	36.446	6.965	100.0	100.0		

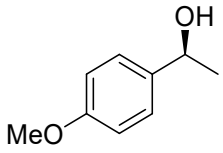
Chiral GC – asymmetric.



Result Table (Uncal - C:\Clarity\WORK1\DATA\Noha\substrtaes\2-methoxy acetophenone\benzo\NK324_benzo-GC1-15psi-140 degree-run1-7-2-22-alc- - U-PAD2 - 1)

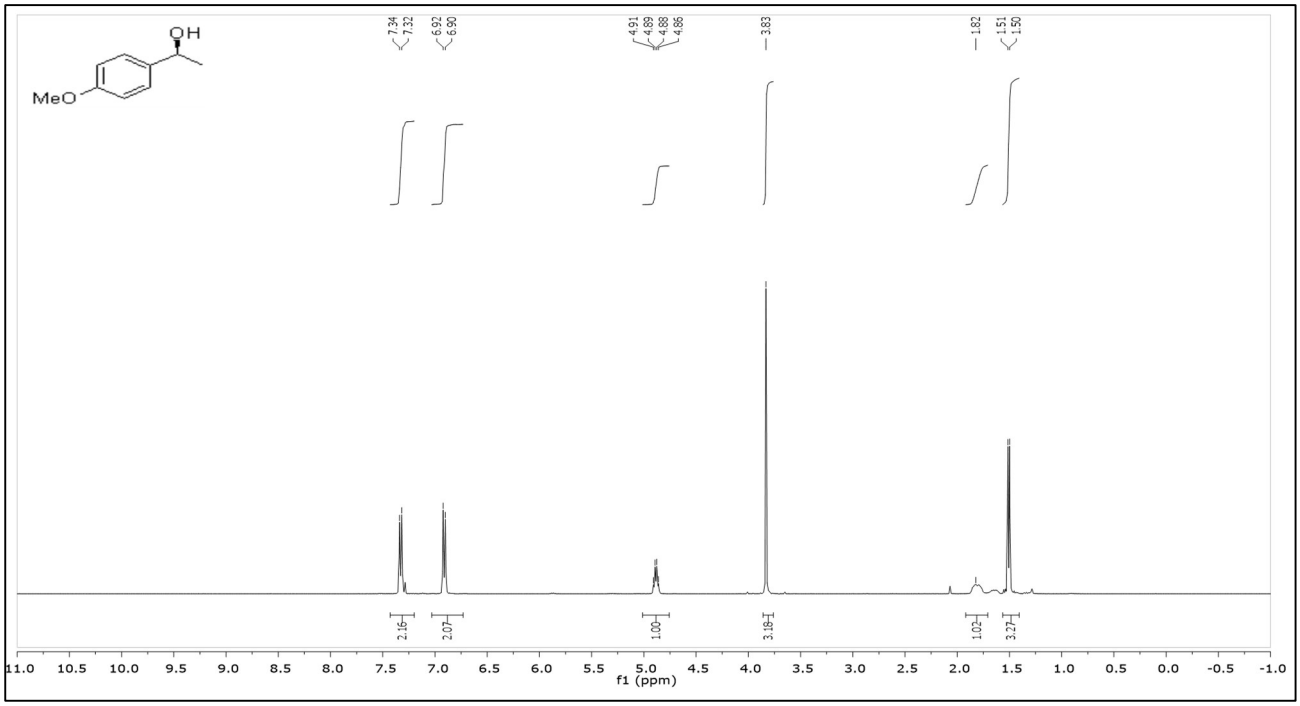
	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	4.996	2.133	0.852	4.0	12.3	0.04	
2	5.188	51.703	6.089	96.0	87.7	0.14	
	Total	53.837	6.940	100.0	100.0		

(*S*)-1-(4-Methoxyphenyl)ethan-1-ol (NK289)

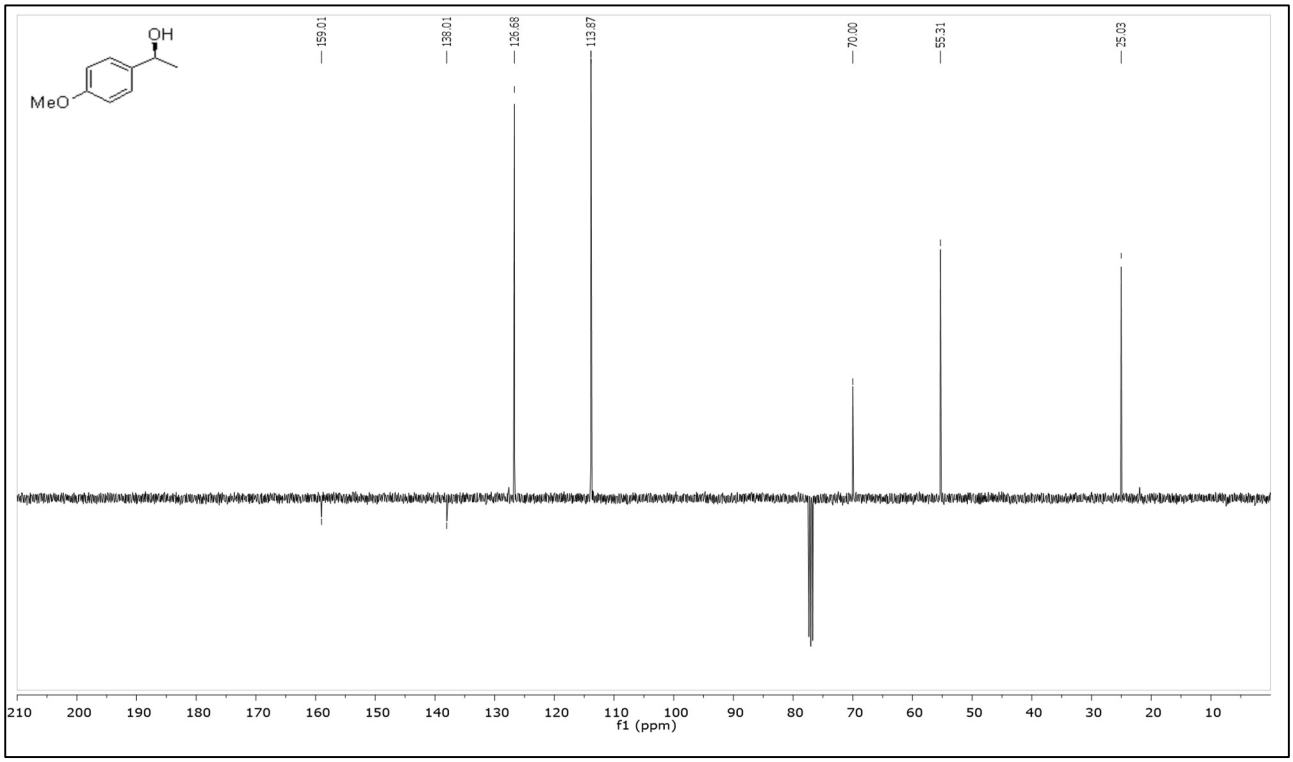


1-(4-methoxyphenyl)ethan-1-one (150.18 mg, 1.00 mmol) and catalyst **(*S*,*S*)-12a** (6.29 mg, 0.01 mmol) were reacted following the general procedure to give (*S*)-1-(4-methoxyphenyl)ethan-1-ol as a yellow oil (135.4 mg, 0.135 mmol, 89.1%); δ_H (400 MHz, $CDCl_3$) 7.33 (2 H, d, *J* 8.4, ArH), 6.91 (2 H, d, *J* 8.4, ArH), 4.88 (1 H, q, *J* 6.3, CH), 3.83 (3 H, s, OCH_3), 1.82 (1 H, br. s, OH), 1.51 (3 H, d, *J* 6.4, CH_3); δ_C (101 MHz, $CDCl_3$) 159.01 (C), 138.01 (C), 126.68 (CH), 113.87 (CH), 70.00 (CH), 55.31 (CH_3), 25.03 (CH_3); $[\alpha]^{25}$ -46.6 (c 0.092 in $CHCl_3$) 94.2% ee (*S*) (lit.[4] $[\alpha]^{30}$ +46.6 (c 1.0 in $CHCl_3$) 91.7% (*R*)) ; GC analysis (CP-Chiralsil-Dex CB 25m x 0.25mm x 0.25um), gas He, T = 120 °C, P = 15 psi, FID temp 250 °C, injector temp 220 °C, ketone 10.132 min., *R* isomer 13.57 min., *S* isomer 14.74).

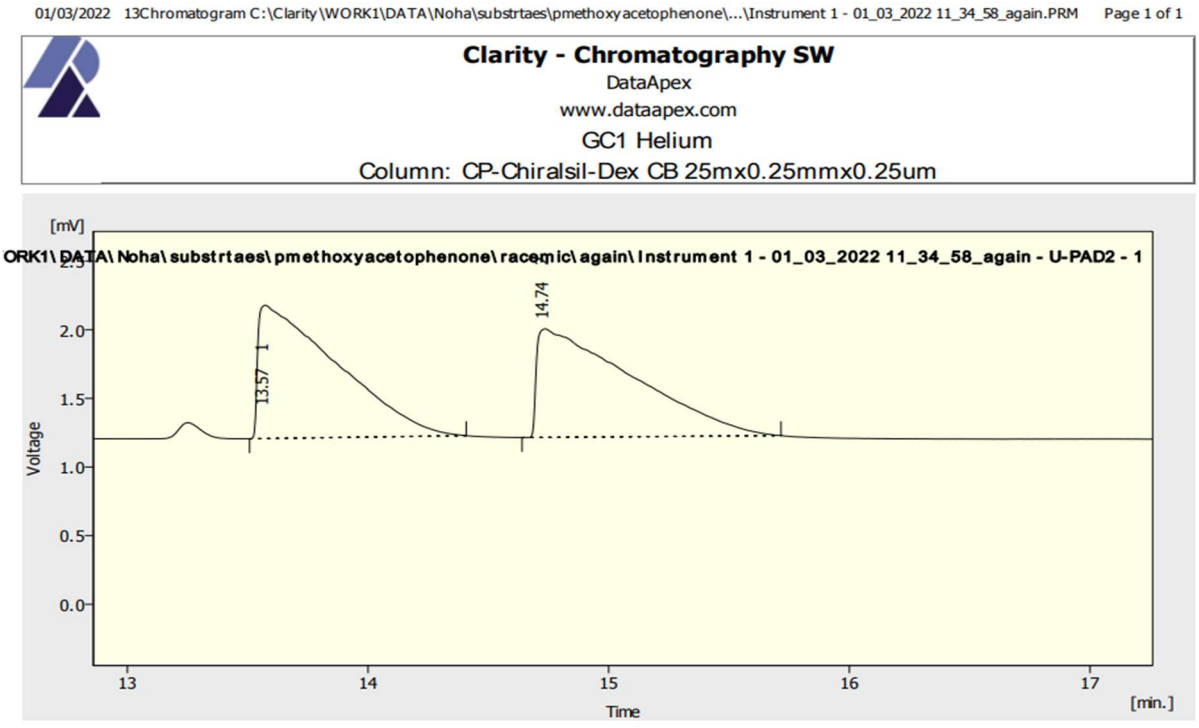
δ_H (400 MHz, $CDCl_3$)



δ_C (101 MHz, $CDCl_3$)



Chiral GC – racemic.



Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|Noha\|substrtaes\|pmethoxyacetophenone\|racemic\|again\|Instrument 1 - 01_03_2022 11_34_58_again - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	13.572	44.155	1.942	50.3	55.1	0.38	
2	14.736	43.604	1.581	49.7	44.9	0.46	
	Total	87.760	3.523	100.0	100.0		

Chiral GC – asymmetric.

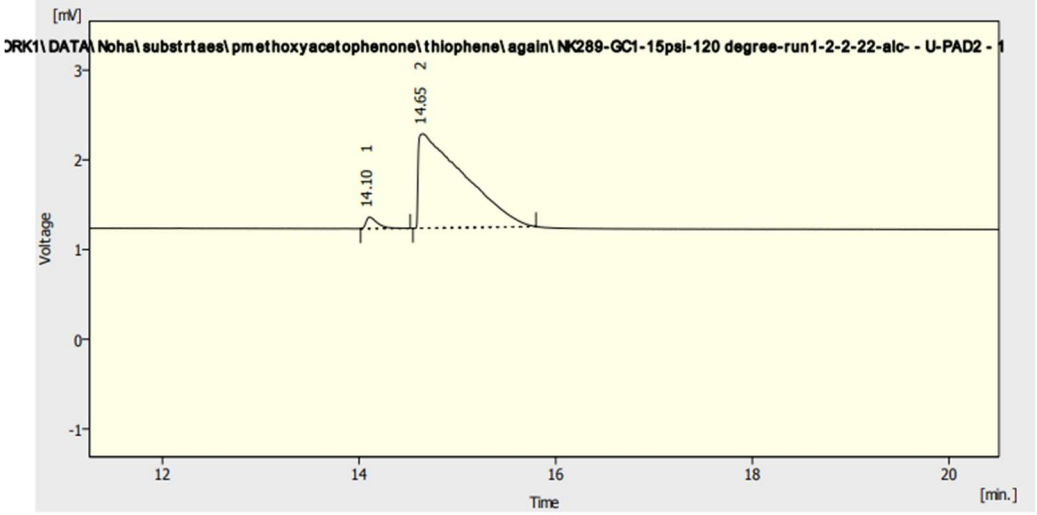
Clarity - Chromatography SW

DataApex

www.dataapex.com

GC1 Helium

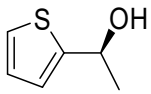
Column: CP-Chiralsil-Dex CB 25mx0.25mmx0.25um



Result Table (Uncal - C:\Clarity\WORK1\DATA\Noha\substrtaes\pmethoxyacetophenone\thiophene\again\NK289-GC1-15psi-120 degree-run1-2-2-22-alc- - U-PAD2 - 1)

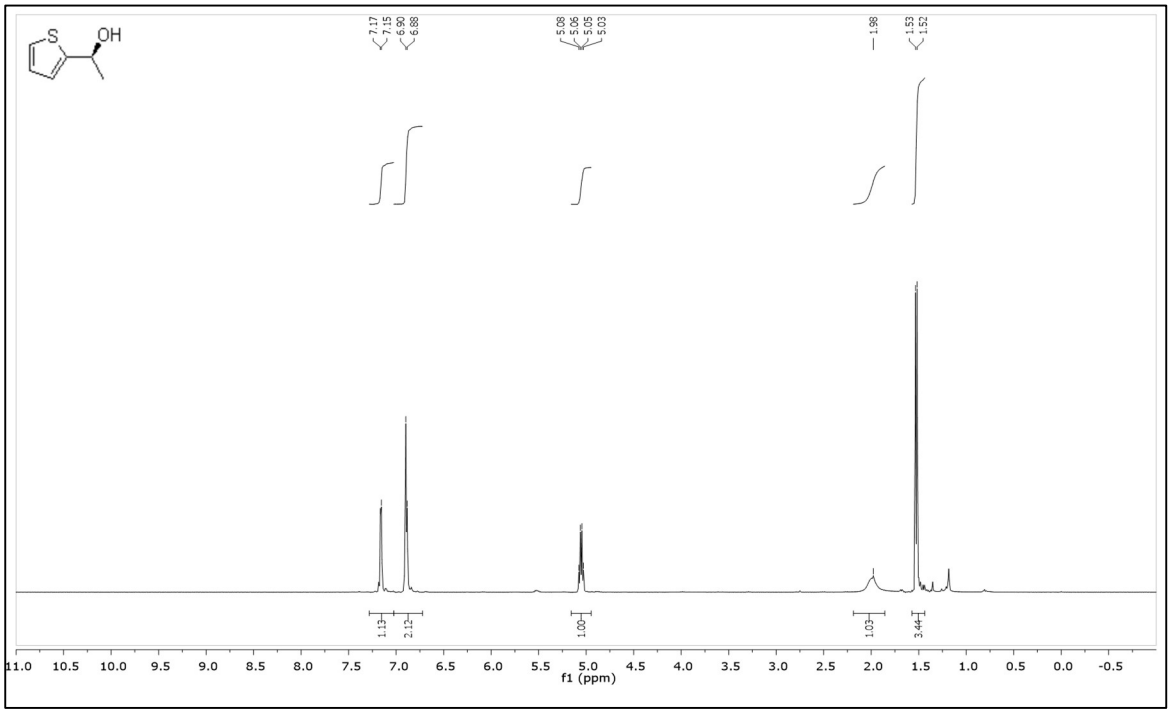
	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	14.104	2.048	0.257	2.9	10.9	0.12	
2	14.652	68.586	2.102	97.1	89.1	0.54	
	Total	70.634	2.359	100.0	100.0		

(*S*)-1-(Thiophen-2-yl)ethan-1-ol (NK297)

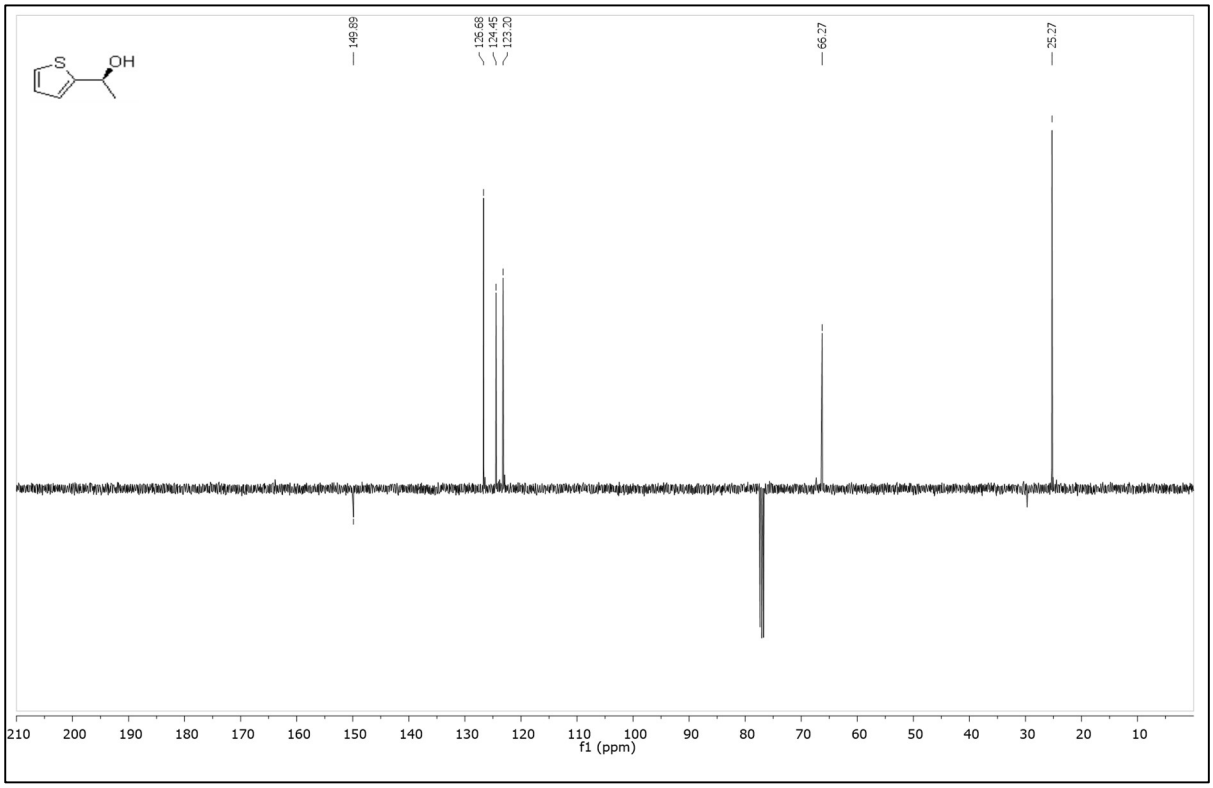


1-(Thiophen-2-yl)ethan-1-one (126.2 mg, 1.00 mmol) and catalyst **(*S*,*S*)-12a** (6.29 mg, 0.01 mmol) were reacted following the general procedure to give (*S*)-1-(thiophen-2-yl)ethan-1-ol as a yellow oil (58.7 mg, 0.459 mmol, 45.9%); δ_H (400 MHz, $CDCl_3$) 7.16 (1 H, d, *J* 4.8, ArH), 6.89 (2 H, m, ArH), 5.05 (1 H, q, *J* 6.4, CH), 1.98 (1 H, br. s, OH), 1.53 (3 H, d, *J* 6.4, CH_3); δ_C (101 MHz, $CDCl_3$) 149.89 (C), 126.68 (CH), 124.45 (CH), 123.20(CH), 66.27 (CH), 25.27 (CH_3). $[\alpha]^{25}$ -102.3 (c 0.128 in $CHCl_3$) 97.6% ee (*R*) (lit.[5] $[\alpha]^{23}$ = +21.7 (*c* 1.1, $CHCl_3$) 96% ee(*R*)); GC analysis (CP-Chiralsil-Dex CB 25m x 0.25mm x 0.25um), gas He, T = 115 °C, P = 120 kPa, FID temp 250 °C, injector temp 220 °C, ketone 2.56 min., *R* isomer 4.72 min., *S* isomer 5.15 min.).

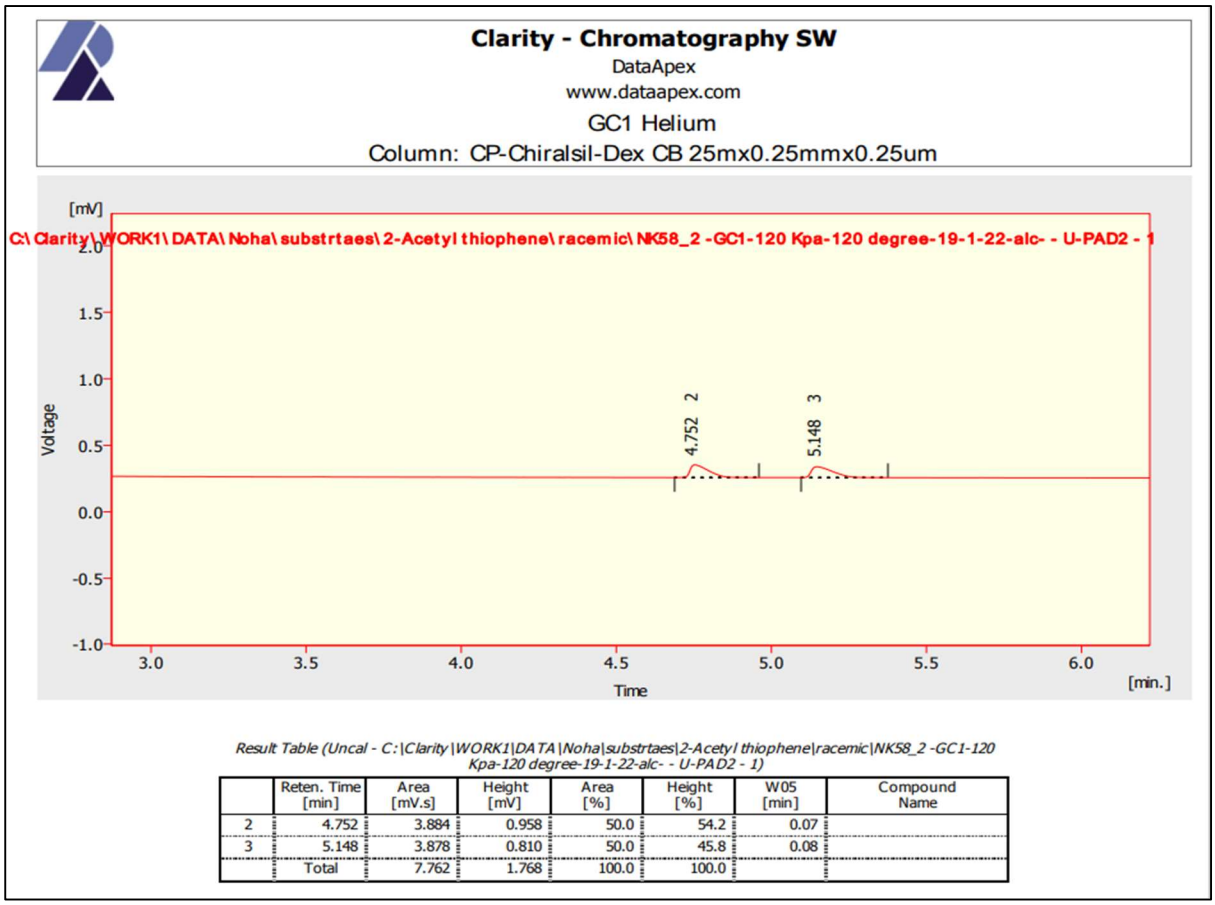
δ_H (400 MHz, $CDCl_3$)



δ_C (101 MHz, $CDCl_3$)



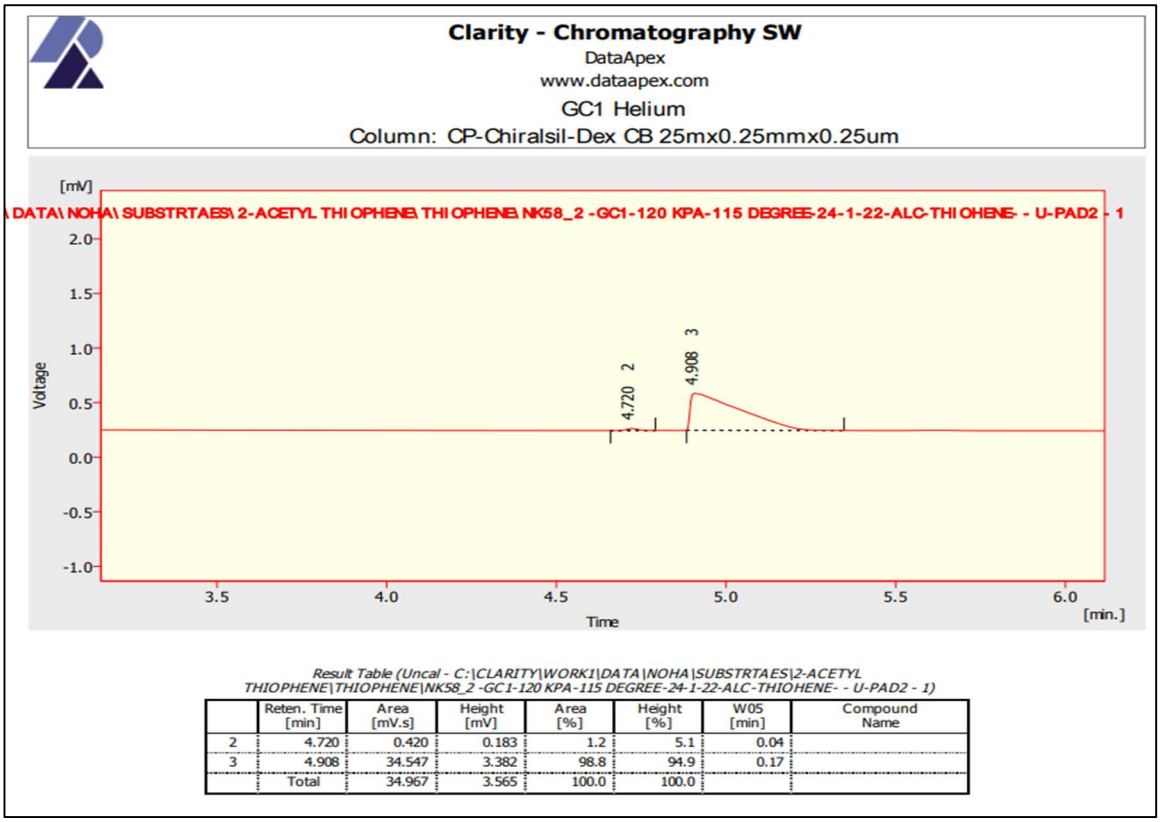
Chiral GC – racemic.



Result Table (Uncal - C:\Clarity\WORK1\DATA\Noha\substrtaes\2-Acetyl thiophene\racemic\NK58_2 -GC1-120 Kpa-120 degree-19-1-22-alc- - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
2	4.752	3.884	0.958	50.0	54.2	0.07	
3	5.148	3.878	0.810	50.0	45.8	0.08	
	Total	7.762	1.768	100.0	100.0		

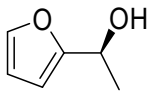
Chiral GC - asymmetric



Result Table (Uncal - C:\CLARITY\WORK1\DATA\NOHA\SUBSTRTAES\2-ACETYL THIOPHENE\THIOPHENE\NK58_2 -GC1-120 KPA-115 DEGREE-24-1-22-ALC-THIOHENE- - U-PAD2 - 1)

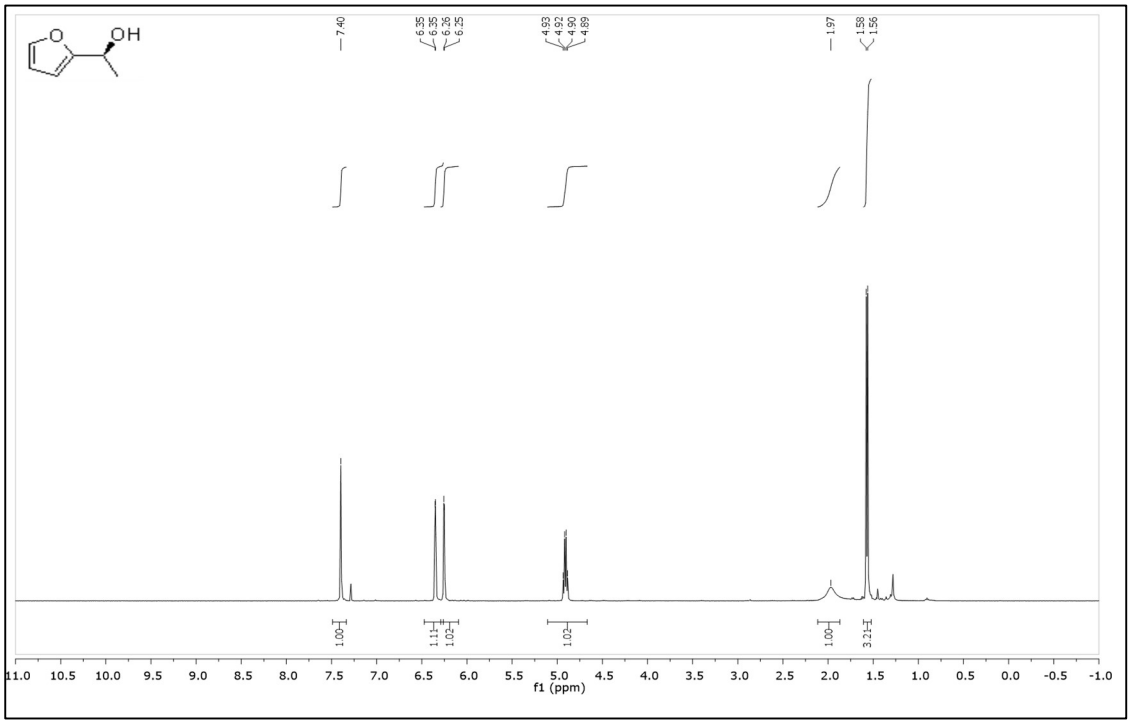
	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
2	4.720	0.420	0.183	1.2	5.1	0.04	
3	4.908	34.547	3.382	98.8	94.9	0.17	
	Total	34.967	3.565	100.0	100.0		

(*S*)-1-(Furan-2-yl)ethan-1-ol (NK351)

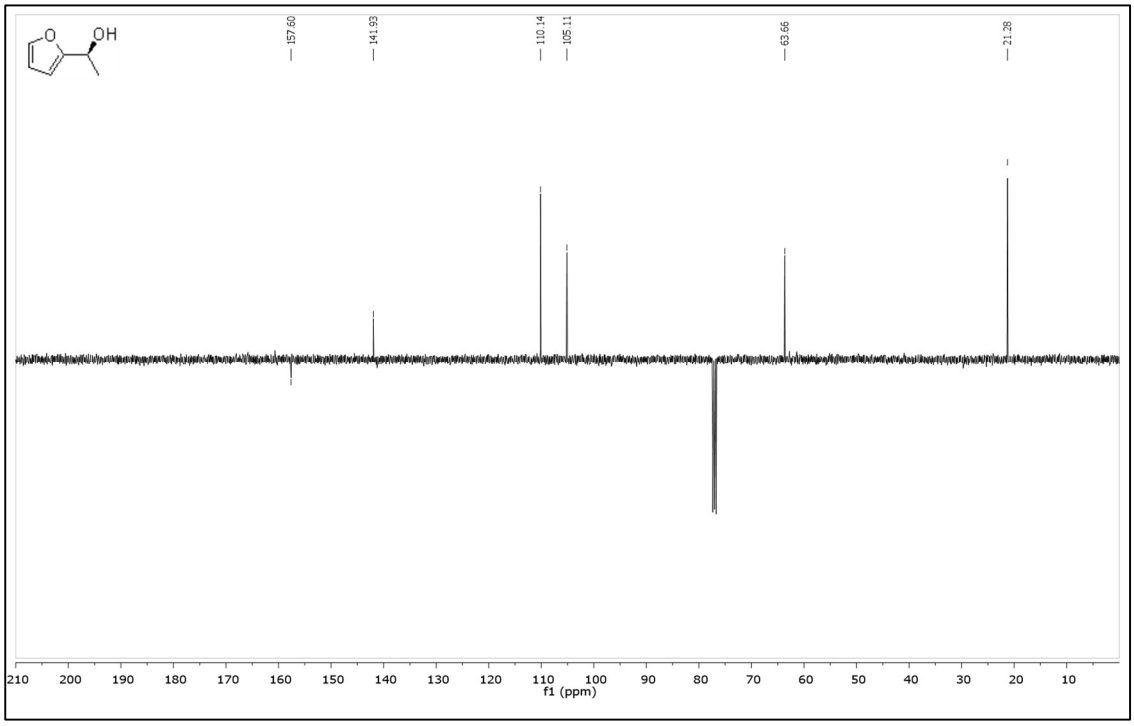


1-(Furan-2-yl)ethan-1-one (110.1 mg, 1.00 mmol) and catalyst **(*S*,*S*)-12g** (6.12 mg, 0.01 mmol) were reacted following the general procedure to give (*S*)-1-(furan-2-yl)ethan-1-ol as a yellow oil (90.5 mg, 0.808 mmol, 80.8%); δ_H (400 MHz, $CDCl_3$) 7.40 (1 H, s, ArH), 6.35 (1 H, br. S, ArH), 6.25 (1 H, d, *J* 2.7, ArH), 4.91 (1 H, q, *J* 6.5, CH), 1.97 (1 H, br. s, OH), 1.57 (3 H, d, *J* 6.6, CH_3); δ_C (101 MHz, $CDCl_3$) 157.60 (C), 141.93 (CH), 110.14 (CH), 105.11 (CH), 63.66 (CH), 21.28 (CH_3), $[\alpha]^{21}$ -42.0 (c 0.184 in $CHCl_3$) 96.4% ee (*S*) (lit.[3] $[\alpha]^D$ = +24.7 (c = 0.36, $CHCl_3$), 94% ee (*R*)); GC analysis (CP-Chiralsil-Dex CB 25m x 0.25mm x 0.25um), gas He, T = 90 °C, P = 120 kPa, FID temp 250 °C, injector temp 220 °C, ketone 2.06 min., *R* isomer 4.09 min., *S* isomer 4.28 min.).

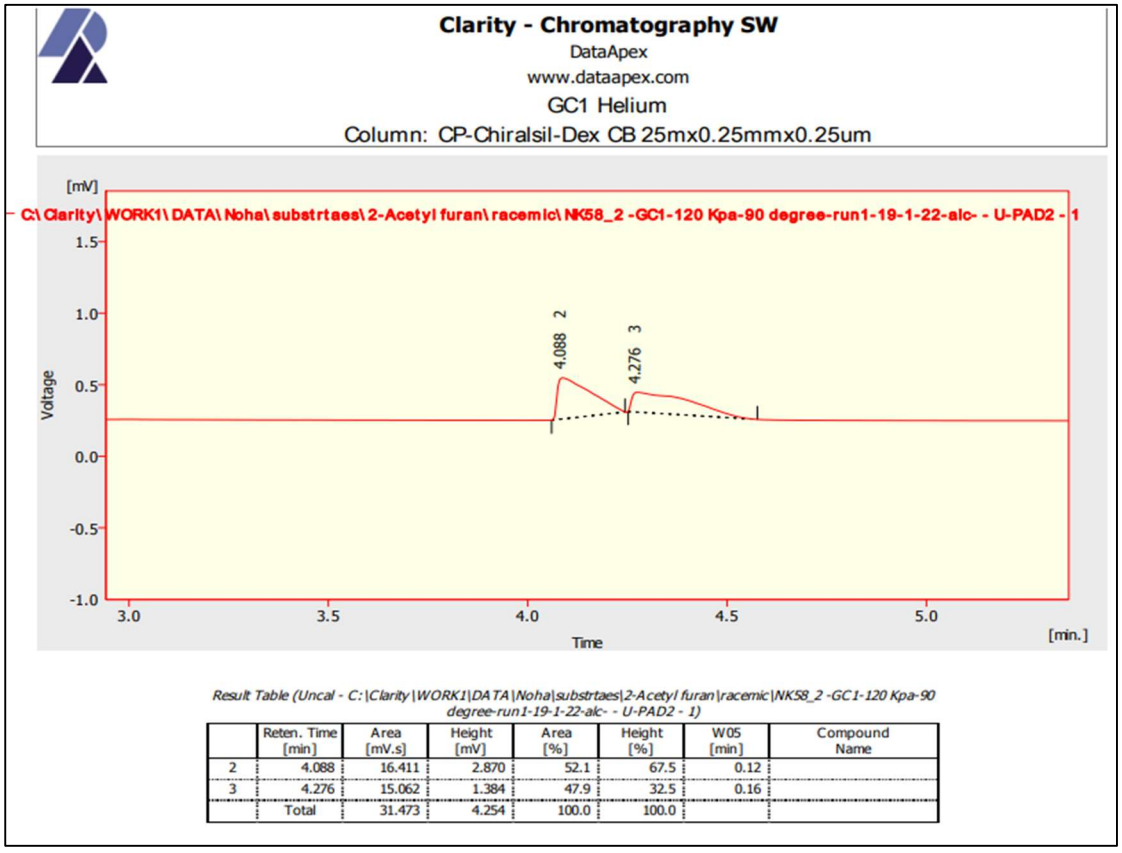
δ_H (400 MHz, $CDCl_3$)



δ_C (101 MHz, $CDCl_3$)



Chiral GC - racemic

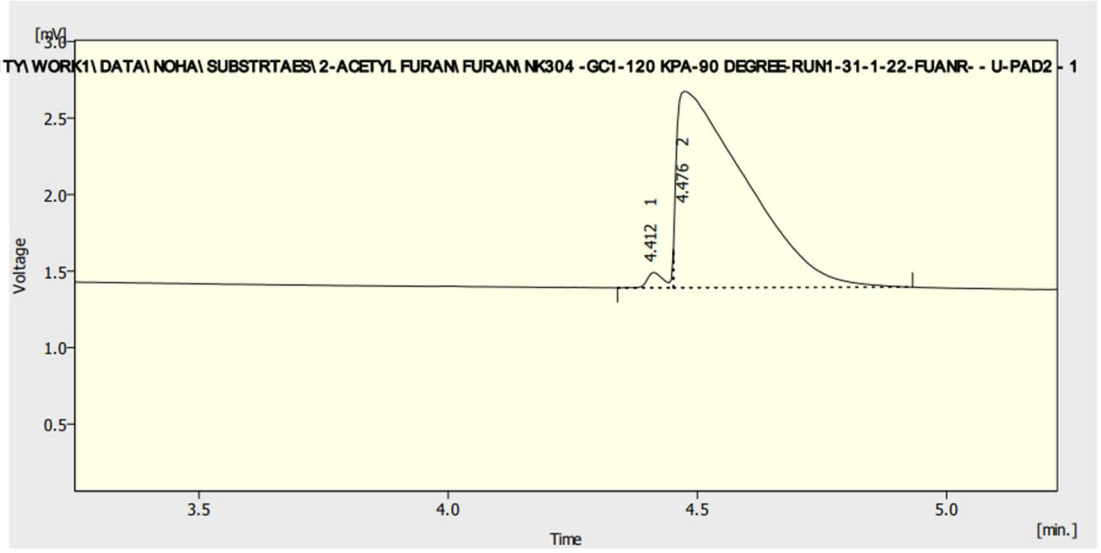


Result Table (Uncal - C:\Clarity\WORK1\DATA\Noha\substrtaes\2-Acetyl furan\racemic\NK58_2 -GC1-120 Kpa-90 degree-run1-19-1-22-alc- - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
2	4.088	16.411	2.870	52.1	67.5	0.12	
3	4.276	15.062	1.384	47.9	32.5	0.16	
	Total	31.473	4.254	100.0	100.0		

Chiral GC-asymmetric

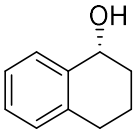
Clarity - Chromatography SW
DataApex
www.dataapex.com
GC1 Helium
Column: CP-Chiralsil-Dex CB 25mx0.25mmx0.25um



Result Table (Uncal - C:\CLARITY\WORK1\DATA\NOHA\SUBSTRTAES\2-ACETYL FURAN\FURAN\NK304 -GC1-120 KPA-90 DEGREE-RUN1-31-1-22-FUANR- - U-PAD2 - 1)

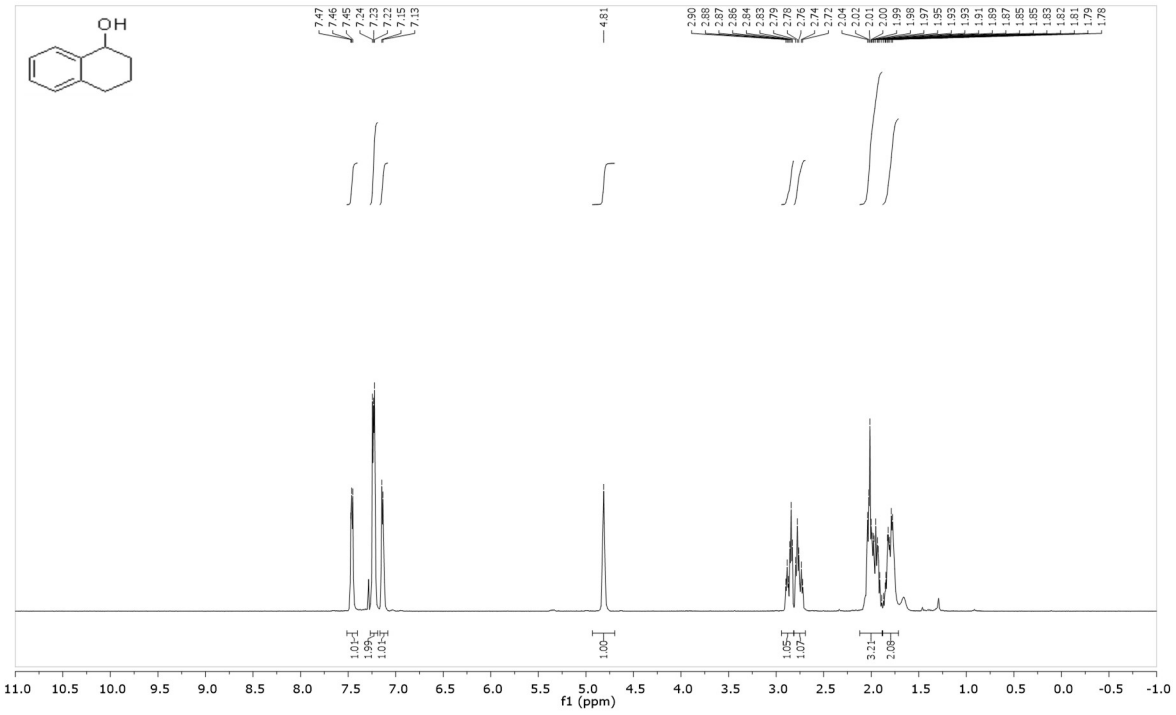
	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	4.412	0.453	0.198	1.8	7.2	0.04	
2	4.476	25.049	2.563	98.2	92.8	0.16	
	Total	25.502	2.761	100.0	100.0		

(*R*)-1,2,3,4-Tetrahydronaphthalen-1-ol (NK310)

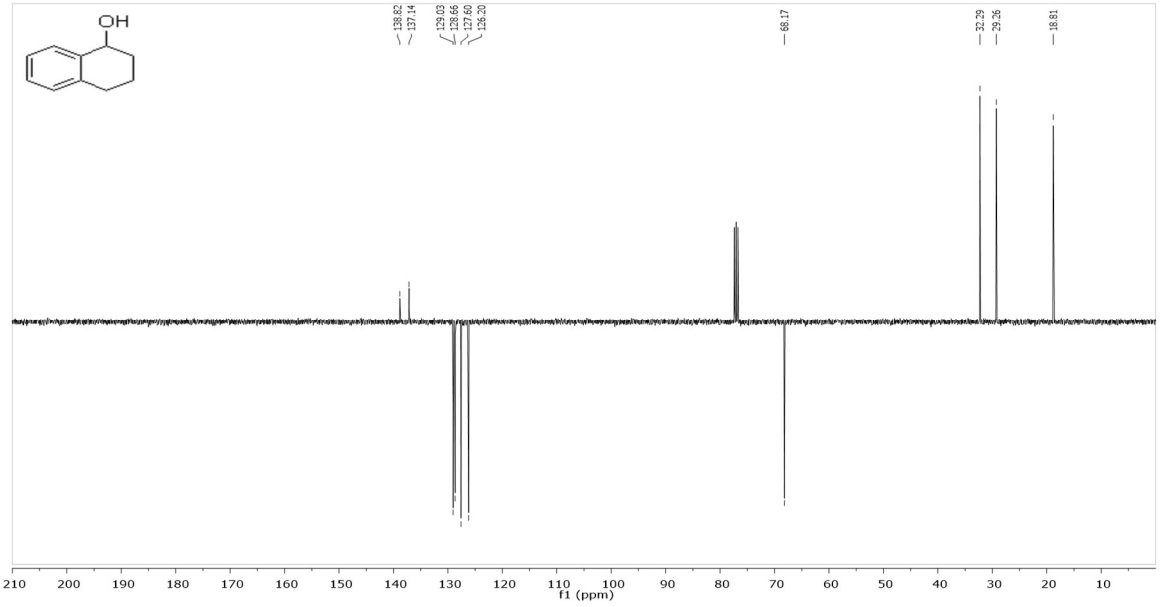


3,4-Dihydronaphthalen-1(2H)-one (146 mg, 1.00 mmol) and catalyst **(*R*,*R*)-12c** (6.6 mg, 0.01 mmol) were reacted following the general procedure to give (*R*)-1,2,3,4-tetrahydronaphthalen-1-ol as a orange oil (120.7 mg, 0.82 mmol, 82%); δ_H (400 MHz, $CDCl_3$) 7.53 – 7.40 (1 H, m, ArH), 7.28 – 7.19 (2 H, m, ArH), 7.14 (1 H, d, *J* 4.7, ArH), 4.81 (1 H, br. s, C*H*OH), 2.86-2.80 (1 H, m, CH_2), 2.80 – 2.69 (1 H, m, CH_2), 2.12 – 1.88 (3 H, m, CH_2+OH), 1.84-1.80 (2 H, m, CH_2); δ_C (101 MHz, $CDCl_3$) 138.82 (C), 137.14 (C), 129.03 (CH), 128.66 (CH), 127.60 (CH), 126.20 (CH), 68.17 (CH), 32.29 (CH_2), 29.26 (CH_2), 18.81 (CH_2); $[\alpha]^{23}$ -23.7 (c 0.05 in $CHCl_3$) >99% ee (*R*) (lit.[3] $[\alpha]^D$ = −34.4 (c = 0.57, $CHCl_3$), 99% ee (*R*)); HPLC analysis (Chiralcel OD-H, 250 × 4.6 mm column, hexane/2-propanol 98:02, 1 mL/min, 210 nm, Ketone: 7.33 min, R isomer: 15.12 min, S isomer: 13.19 min.

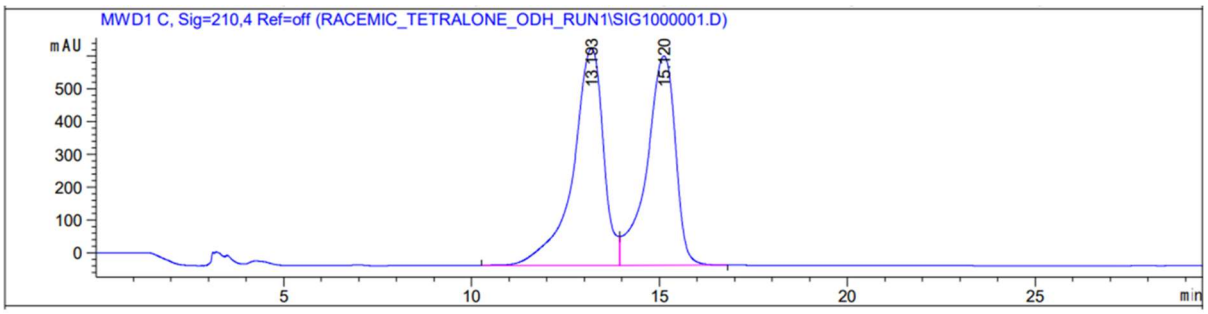
δ_H (400 MHz, $CDCl_3$)



δ_C (101 MHz, $CDCl_3$)

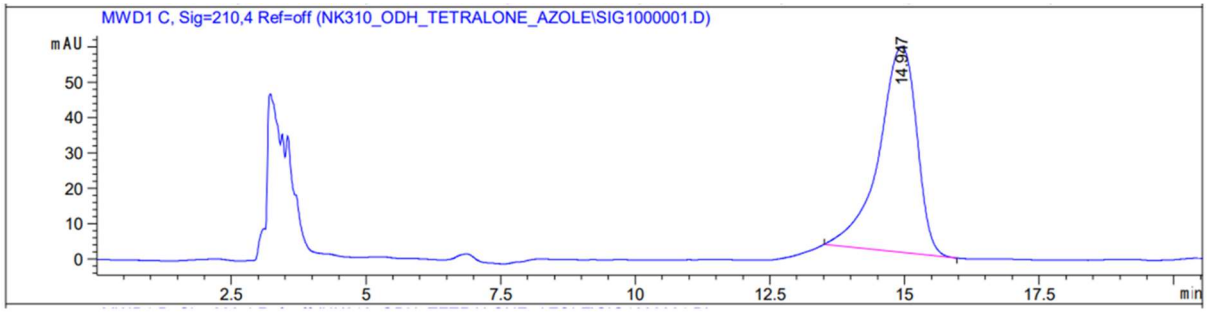


Chiral HPLC- racemic.



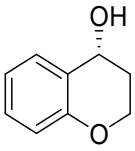
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.193	BV	0.8509	3.73828e4	661.91278	52.3397
2	15.120	VB	0.8140	3.40405e4	638.47064	47.6603
Totals :				7.14233e4	1300.38342	

Chiral HPLC- asymmetric.



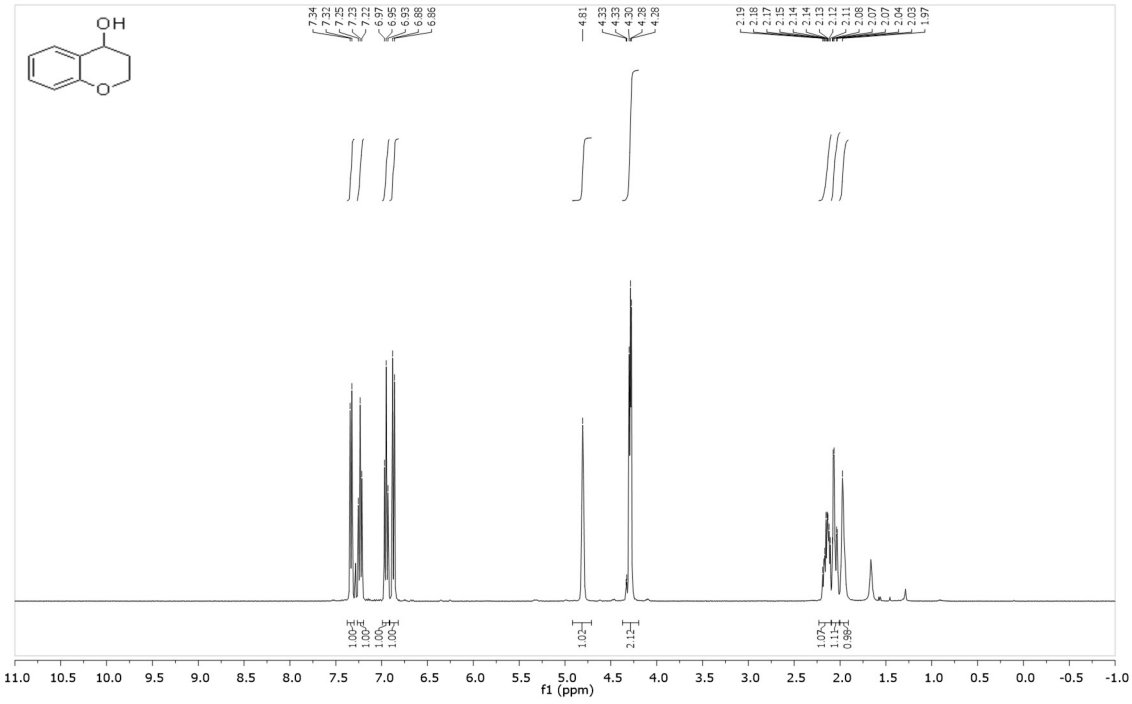
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	14.947	BB	0.7453	2842.52368	58.25013	100.0000
Totals :				2842.52368	58.25013	

(*R*)-Chroman-4-ol (NK315)

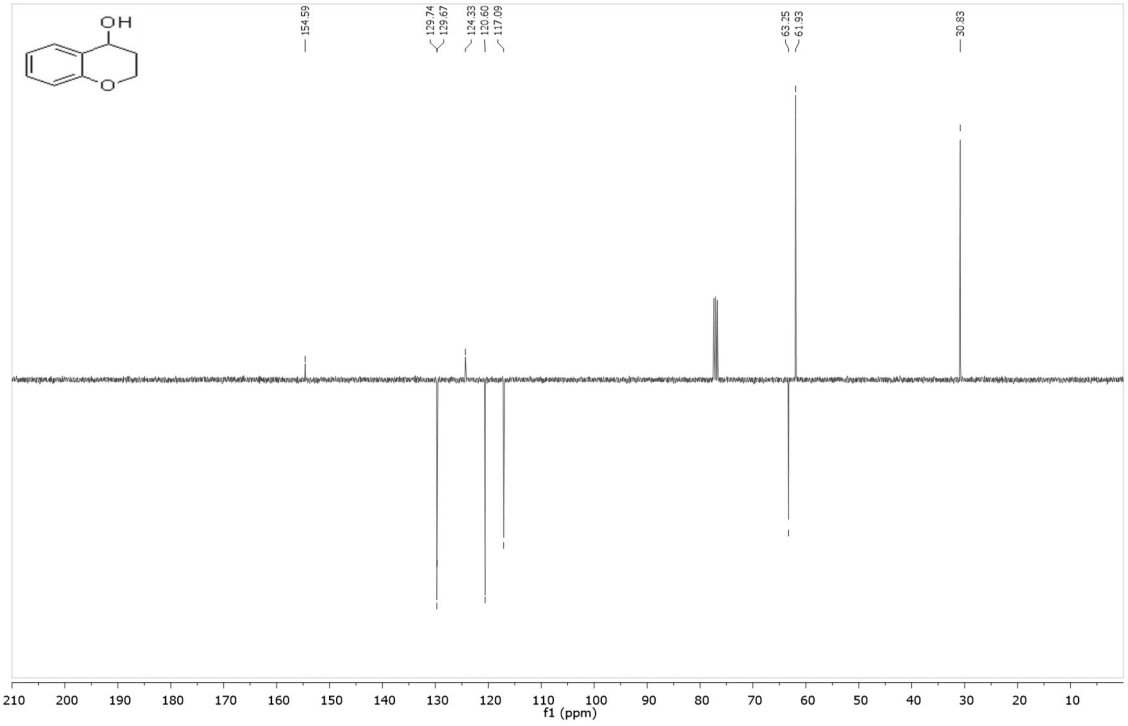


Chroman-4-one (148.2 mg, 1.00 mmol) and catalyst **(*R,R*)-12c** (6.6 mg, 0.01 mmol) were reacted following the general procedure to give (*R*)-chroman-4-ol as a white solid (139 mg, 0.93 mmol, 93%); δ_H (400 MHz, $CDCl_3$) 7.33 (1 H, d, *J* 7.6, ArH), 7.23 (1 H, t, *J* 7.7, ArH), 6.95 (1 H, t, *J* 7.4, ArH), 6.87 (1 H, d, *J* 8.2, ArH), 4.81 (1 H, s, CH), 4.35 – 4.16 (2 H, m, CH_2), 2.22 – 2.09 (1 H, m, CH), 2.09 – 2.01 (1 H, m, CH), 1.97 (1 H, s, OH); δ_C (101 MHz, $CDCl_3$) 154.59 (C), 129.74 (CH), 129.67 (CH), 124.33 (C), 120.60 (CH), 117.09 (CH), 63.25 (CH), 61.93 (CH_2), 30.83 (CH_2); $[\alpha]^{23}$ +88.3 (c 0.078 in $CHCl_3$) >99% ee (R) (lit.[3] $[\alpha]^D$ = +64.63 (c = 0.55, $CHCl_3$), 99% ee (*R*)); HPLC analysis (Chiralcel OD-H, 250 × 4.6 mm column, hexane/2-propanol 95:05, 1 mL/min, 210 nm, Ketone: 7.33 min, *R* isomer: 11.37 min, *S* isomer: 9.70 min.

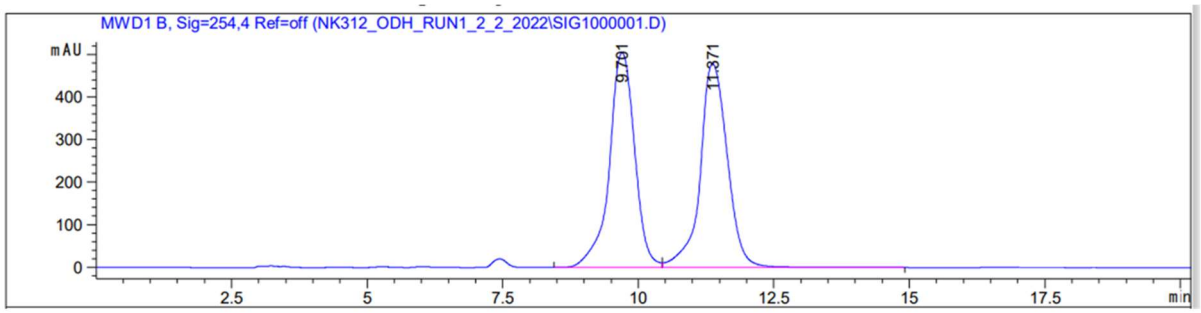
δ_H (400 MHz, $CDCl_3$)



δ_C (101 MHz, $CDCl_3$)

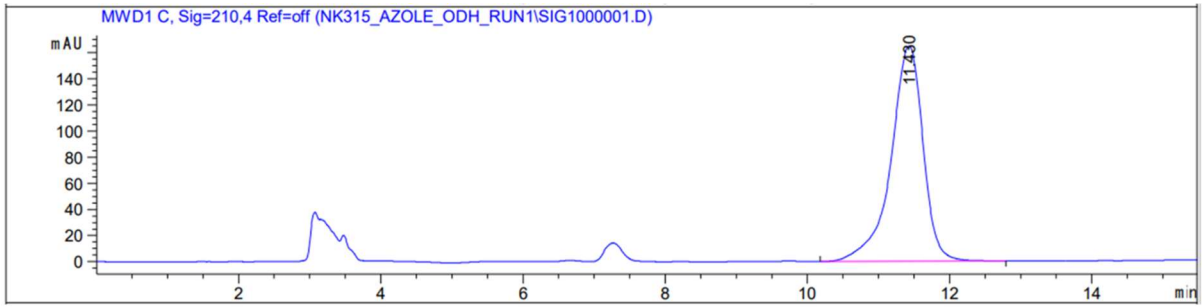


Chiral HPLC – racemic.



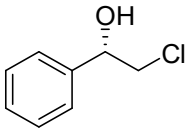
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.701	BV	0.7094	9.38682e4	2076.31812	48.8580
2	11.369	VB	0.7565	9.82564e4	2045.11304	51.1420
Totals :				1.92125e5	4121.43115	

Chiral HPLC -asymmetric.



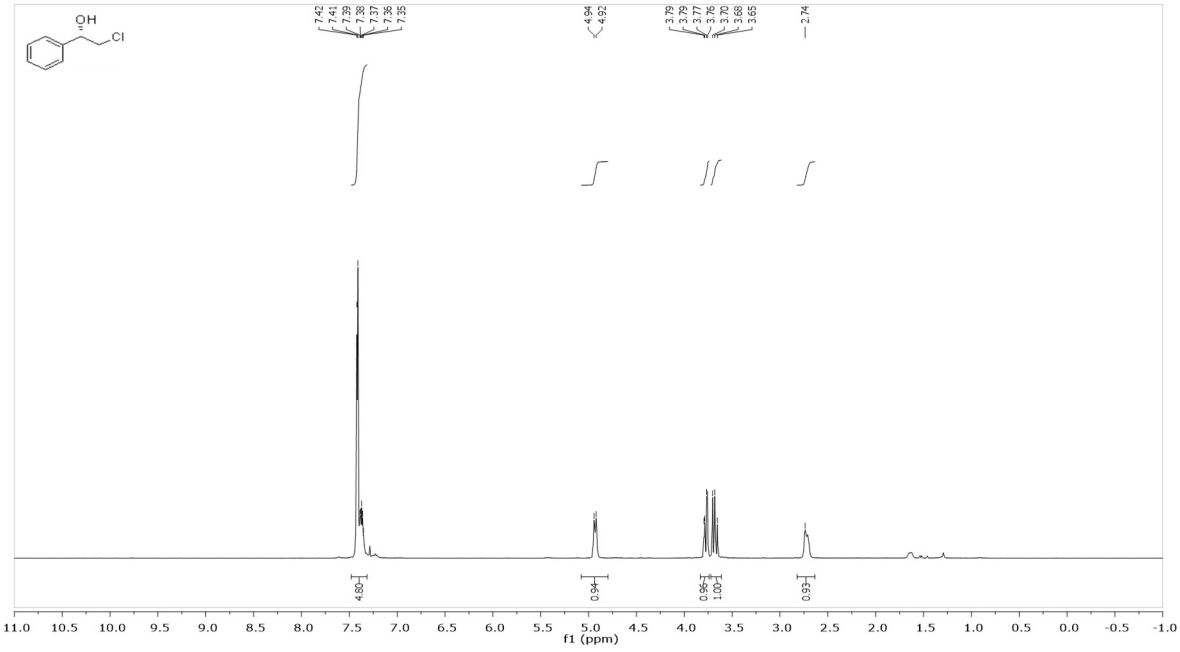
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.430	BB	0.4812	5181.16699	164.61308	100.0000
Totals :				5181.16699	164.61308	

(*R*)-2-Chloro-1-phenylethan-1-ol.(NK330)

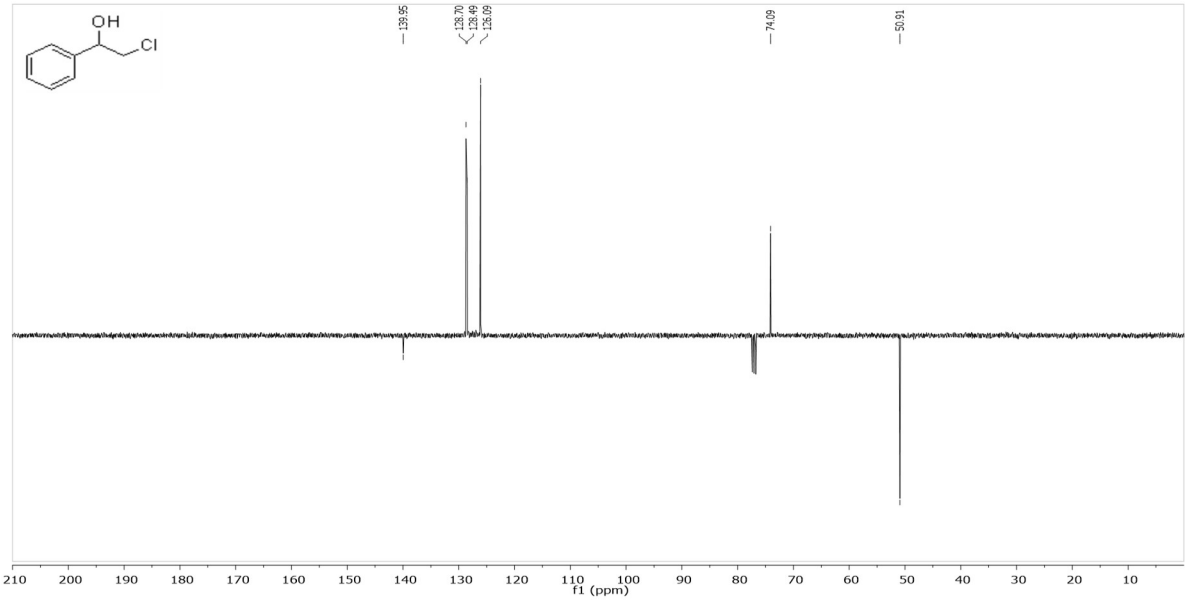


2-Chloro-1-phenylethan-1-one (154.6.1 mg, 1.00 mmol) and catalyst **(*R*,*R*)-12c** (6.6 mg, 0.01 mmol) were reacted following the general procedure to give (*R*)-2-chloro-1-phenylethan-1-ol as a colourless oil (114 mg, 0.73 mmol, 73%); δ_H (400 MHz, $CDCl_3$) 7.51 – 7.28 (5 H, m, ArH), 5.05 – 4.85 (1 H, m, CH), 3.75(1 H, dd, *J* 11.2, 3.3, CH_2), 3.68-3.62 (1 H, m, CH_2), 2.72 (1 H, br. s., OH); δ_C (101 MHz, $CDCl_3$) 139.95 (C), 128.70 (CH), 128.49 (CH), 126.09 (CH), 74.09 (CH), 50.91 (CH_2); $[\alpha]^{21}$ +58.04 (c 0.17 in $CHCl_3$) >99% ee (*S*) (lit.[3] $[\alpha]^{D}$ = +89.5 (c = 0.31, $CHCl_3$), 97% ee (*S*)), GC analysis (CP-Chiralsil-Dex CB 25m x 0.25mm x 0.25um), gas He, T = 140 °C, P = 15 psi, FID temp 250 °C, injector temp 220 °C, ketone 4.15 min., *S* isomer 6.54 min., *R* isomer 6.98 min.).

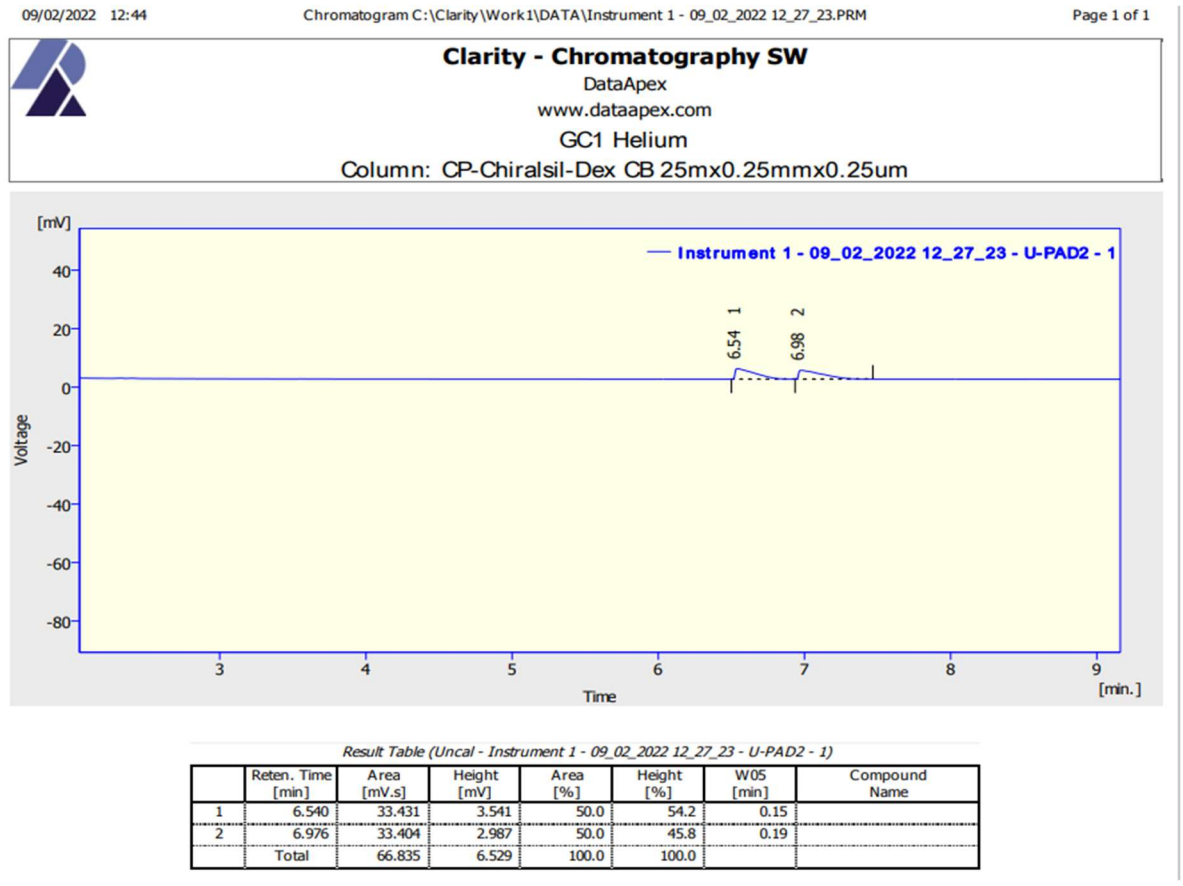
δ_H (400 MHz, $CDCl_3$)



δ_C (101 MHz, $CDCl_3$)



Chiral GC- racemic.

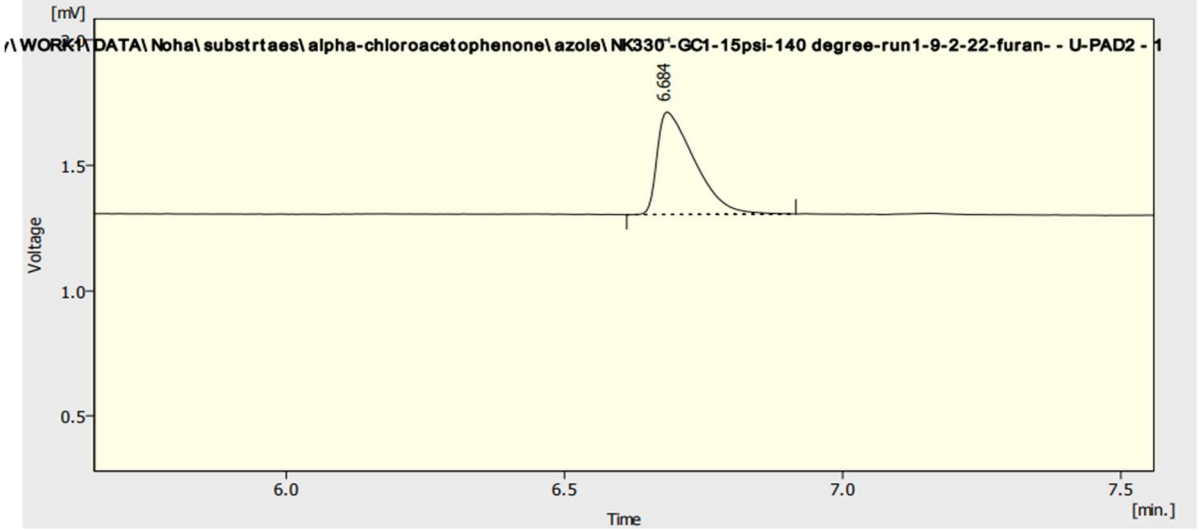


Result Table (Uncal - Instrument 1 - 09_02_2022 12_27_23 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	6.540	33.431	3.541	50.0	54.2	0.15	
2	6.976	33.404	2.987	50.0	45.8	0.19	
	Total	66.835	6.529	100.0	100.0		

Chiral GC – asymmetric.

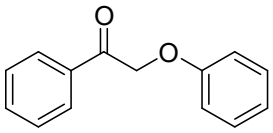
Clarity - Chromatography SW
DataApex
www.dataapex.com
GC1 Helium
Column: CP-Chiralsil-Dex CB 25mx0.25mmx0.25um



Result Table (Uncal - C:\Clarity\WORK1\DATA\Noha\substrtaes\alpha-chloroacetophenone\azole\NK330 -GC1-15psi-140 degree-run1-9-2-22-furan- - U-PAD2 - 1)

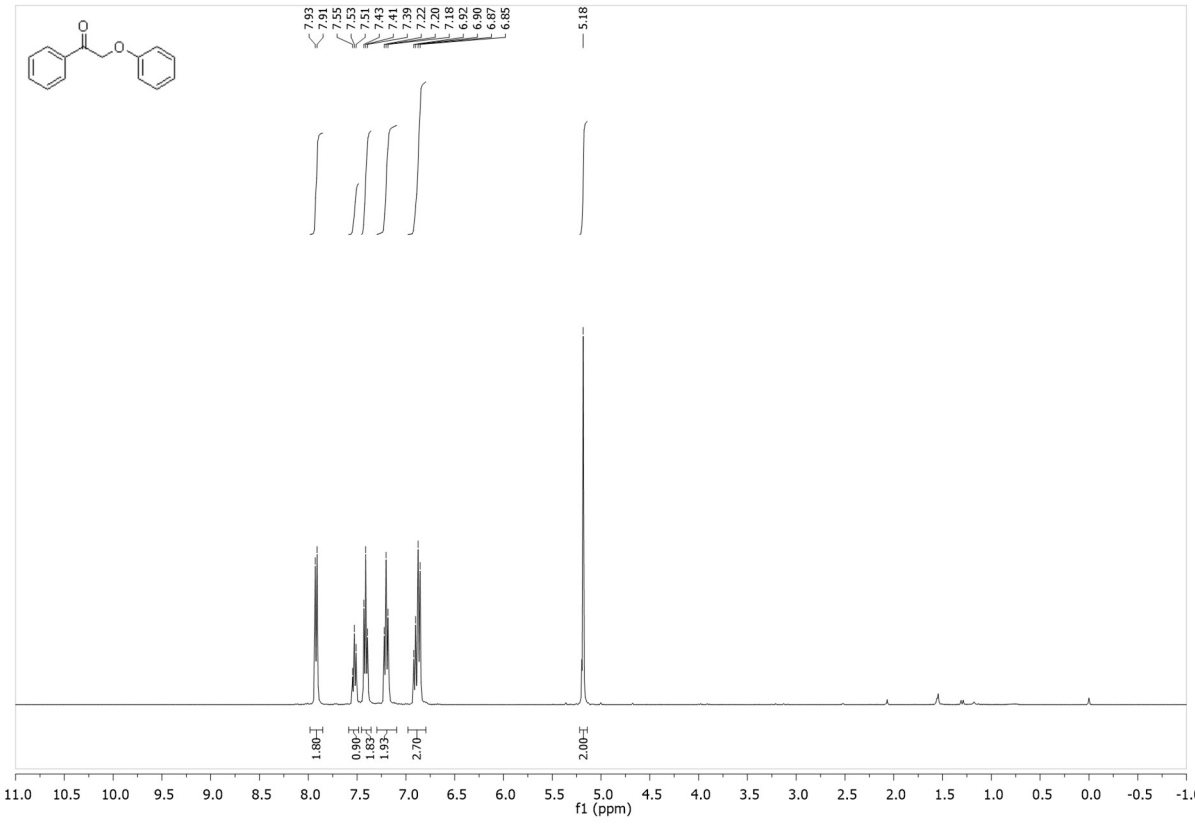
	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	6.684	3.815	0.817	100.0	100.0	0.08	
	Total	3.815	0.817	100.0	100.0		

2-Phenoxy-1-phenylethan-1-one (NK340)

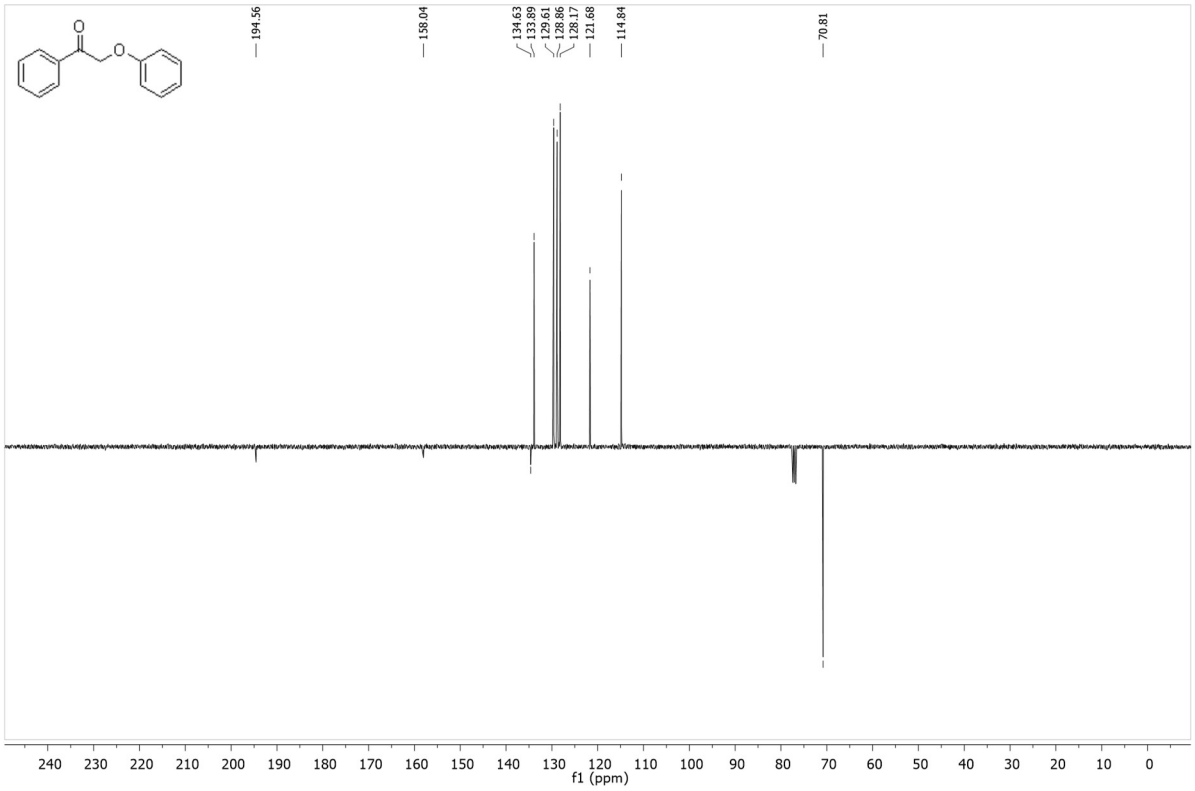


A 250 mL three neck round-bottom flask was charged with phenol (780 mg, 8.30 mmol) and K_2CO_3 (1.66 g, 1.19 mmol), suspended in acetone (70 mL) and left for 30 min at rt. 2-Bromoacetophenone (1.50 g, 7.50 mmol) was added to the mixture using a dropping funnel over 45 min, then the solution was refluxed for 4h. The solvent was then evaporated under vacuum and the residue was extracted using DCM (3 x 50 mL) from 2M NaOH (50 mL), then dried using dry $MgSO_4$. The crude product was recrystalized from petroleum ether to afford the desired product as a yellow solid (1.26 g, 5.94 mmol, 79%); δ_H (400 MHz, $CDCl_3$) 7.92 (2 H, d, *J* 7.7, ArH), 7.53 (1 H, t, *J* 7.3, ArH), 7.41 (2 H, t, *J* 7.6, ArH), 7.20 (2 H, t, *J* 7.7, ArH), 7.00 – 6.78 (3 H, m, ArH), 5.19 (2 H, br. s, CH_2); δ_C (101 MHz, $CDCl_3$) 194.56 (C), 158.04 (C), 134.63 (C), 133.89 (CH), 129.61 (CH), 128.86 (CH), 128.17 (CH), 121.68 (CH), 114.84 (CH), 70.81 (CH_2); MP = 78.2 ºC. The data matched that reported.[6]

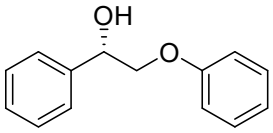
δ_H (400 MHz, $CDCl_3$)



δ_C (101 MHz, $CDCl_3$)

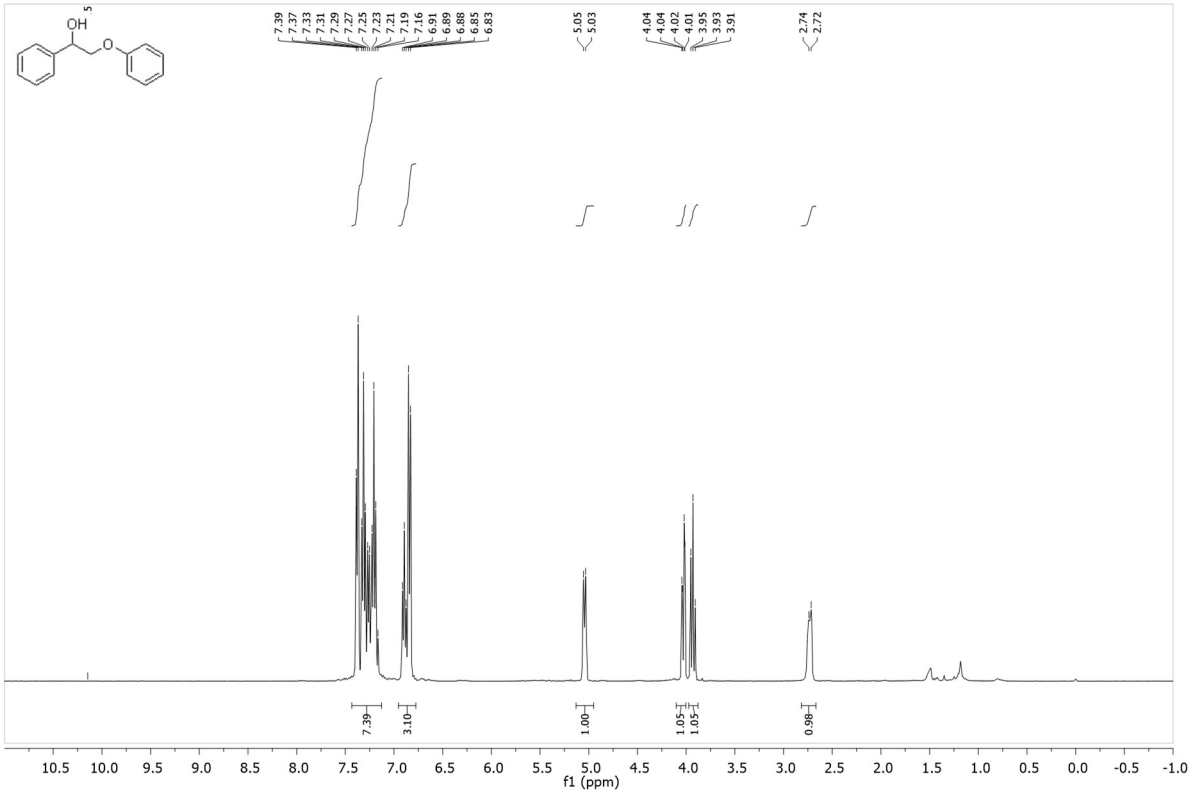


(*S*)-2-Methoxy-1-phenylethan-1-ol (NK344).

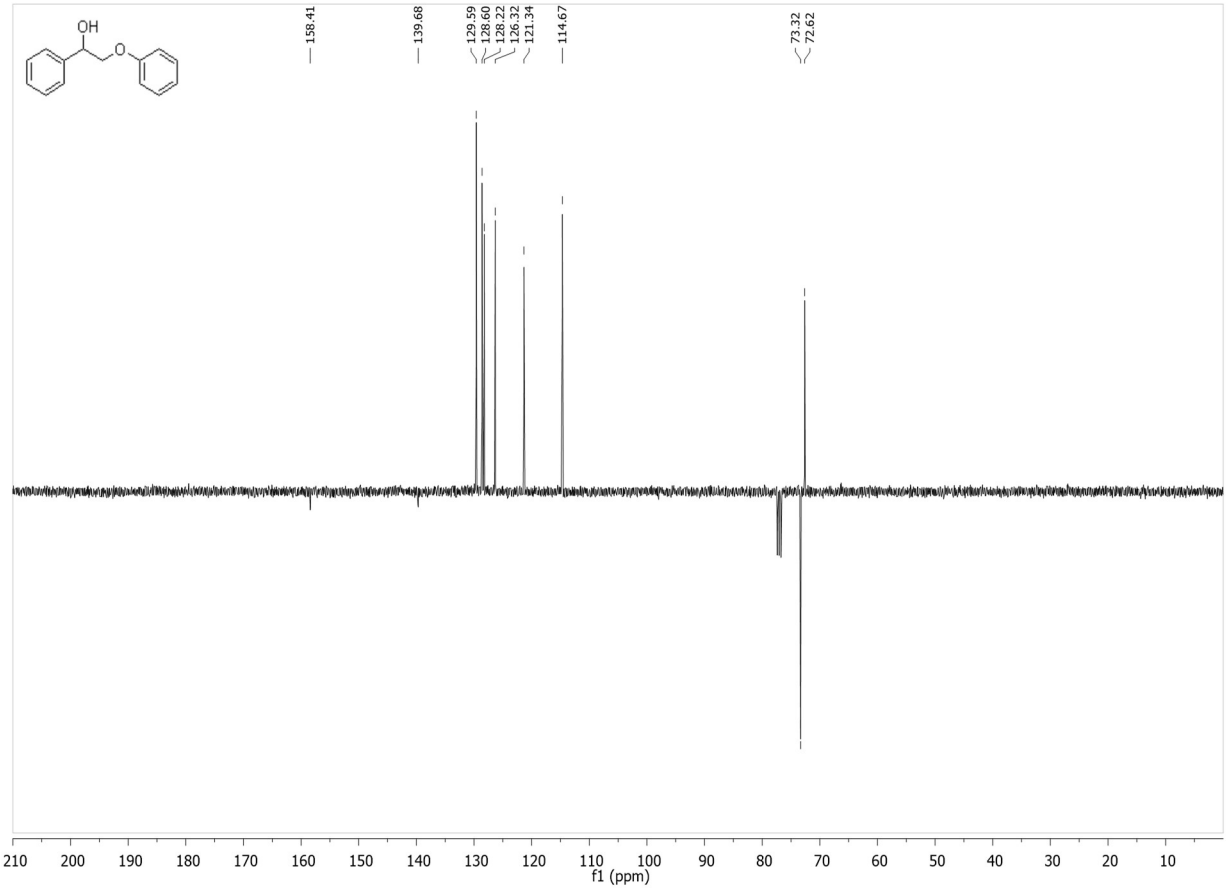


2-Methoxy-1-phenylethan-1-one (212.3 mg, 1.00 mmol) and catalyst **(*R*,*R*)-12f** (6.6 mg, 0.01 mmol) were reacted following the general procedure to give (*R*)- 2-methoxy-1-phenylethan-1-ol as a colourless oil (179 mg, 0.84 mmol, 84%); δ_H (400 MHz, $CDCl_3$) 7.47 – 7.12 (7 H, m, ArH), 6.94 – 6.78 (3 H, m, ArH), 5.04 (1 H, d, *J* 8.7, CH), 4.03-4.00 (1 H, m, CH_2), 3.93-3.90 (1 H, m, CH_2), 2.73 (1 H, d, *J* 8.8, OH); δ_C (101 MHz, $CDCl_3$) 158.41 (C), 139.68 (C), 129.59 (CH), 128.60 (CH), 128.22 (CH), 126.32 (CH), 121.34 (CH), 114.67 (CH), 73.32 (CH_2), 72.62 (CH); $[\alpha]^{21}$ +57.43 (c 0.184 in $CHCl_3$) 96.2% ee (*S*) (lit.[3] $[\alpha]^D$ = +56.6 (c = 0.35, $CHCl_3$), 93% ee (*S*)), HPLC analysis (Chiralcel OD-H, 250 × 4.6 mm column, hexane/2-propanol 93:07, 1 mL/min, 210 nm, Ketone: 15.22 min, *S* isomer: 26.55 min, *R* isomer: 16.19 min.

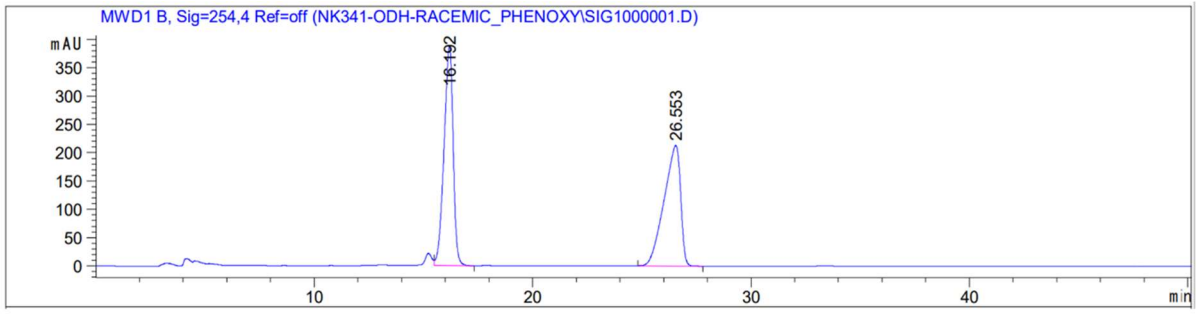
δ_H (400 MHz, $CDCl_3$)



δ_C (101 MHz, $CDCl_3$)

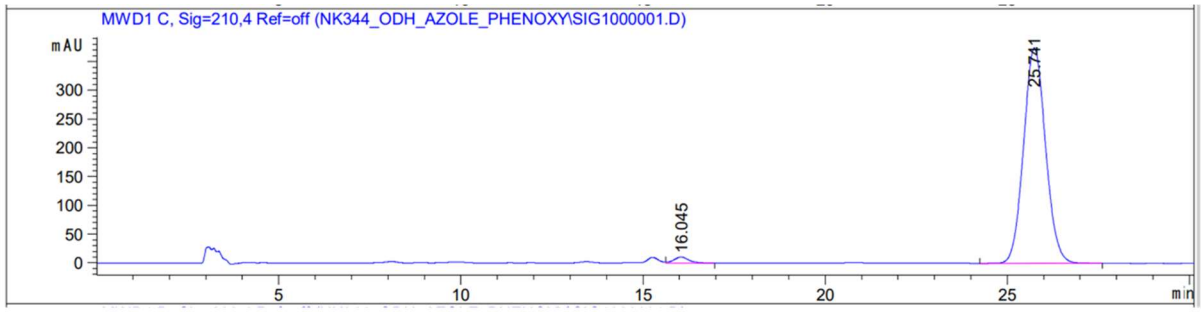


Chiral HPLC – racemic.



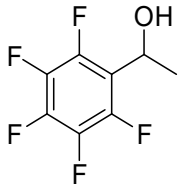
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.192	VB	0.4501	1.12928e4	387.38953	50.2552
2	26.553	BB	0.7873	1.11781e4	212.65256	49.7448
Totals :				2.24709e4	600.04208	

Chiral HPLC- asymmetric.



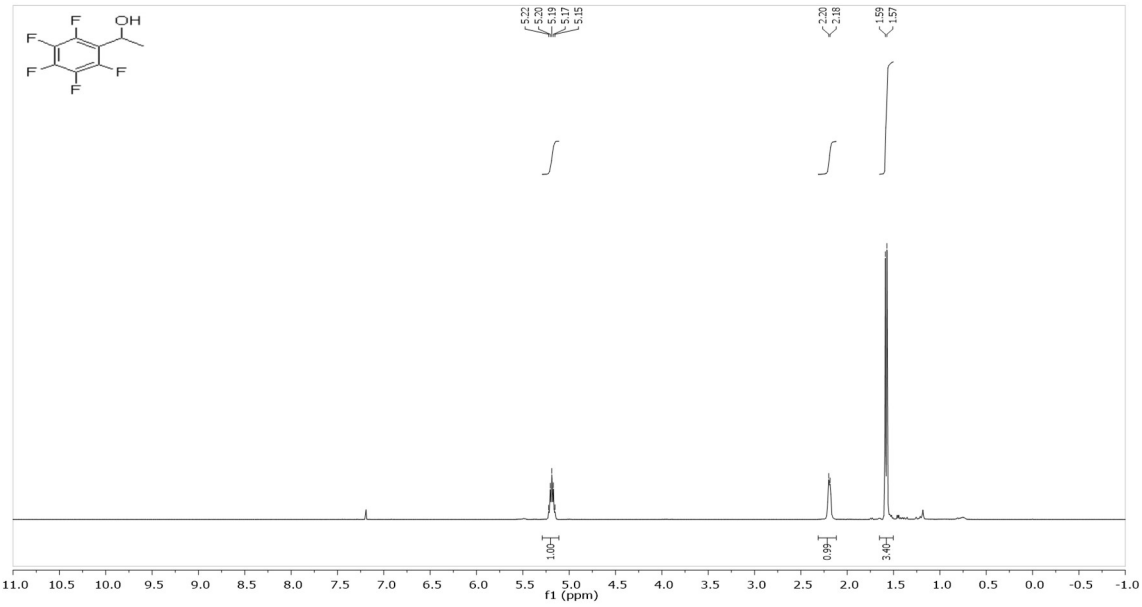
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.045	VB	0.4228	308.68591	10.75745	1.9245
2	25.741	BB	0.6520	1.57314e4	374.52927	98.0755
Totals :				1.60401e4	385.28672	

1-(Perfluorophenyl)ethan-1-ol (NK337)

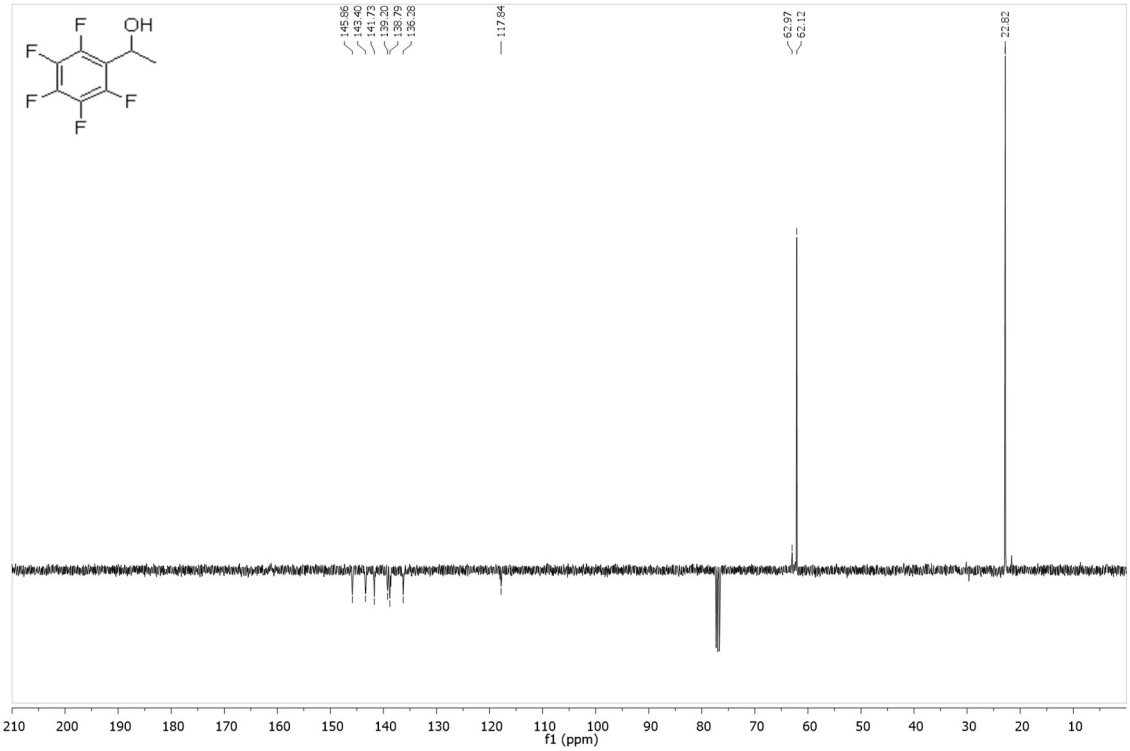


1-(Perfluorophenyl)ethan-1-one (210 mg, 1.00 mmol) and catalyst **(*S*,*S*)-12e** (6.8 mg, 0.01 mmol) were reacted following the general procedure to give 1-(perfluorophenyl)ethan-1-ol as a yellow oil (164 mg, 0.77 mmol, 78%). δ_H (400 MHz, $CDCl_3$) 5.29 – 5.10 (1 H, m, CH), 2.19 (1 H, br. S, OH), 1.58 (1 H, d, *J* 6.7, CH_3); δ_C (101 MHz, $CDCl_3$) 145.86 (C), 143.40 (C), 141.73 (C), 139.20 (C), 138.79 (C), 136.28 (C), 117.84 (C), 62.12 (CH), 22.82 (CH_3); δ_F (376 MHz, $CDCl_3$) -144.64, -144.66, -144.70, -144.72, -155.54, -155.60, -155.65, -161.90, -161.92, -161.96, -161.98, -162.01, -162.03, -162.04; $[\alpha]^{21}$ +0.96 (c 0.17 in $CHCl_3$) 9.8% ee (*R*) (lit.[7] $[\alpha]^D$ 25 -6.7 (c 0.1 in $CHCl_3$) 90.2 % ee (*S*)); GC analysis (CP-Chiralsil-Dex CB 25 m x 0.25 mm x 0.25 um), gas He, T = 80 °C, P = 15 psi, FID temp 250 °C, injector temp 220 °C, ketone 28.66 min., R isomer 19.30 min., *S* isomer 30.32 min.).

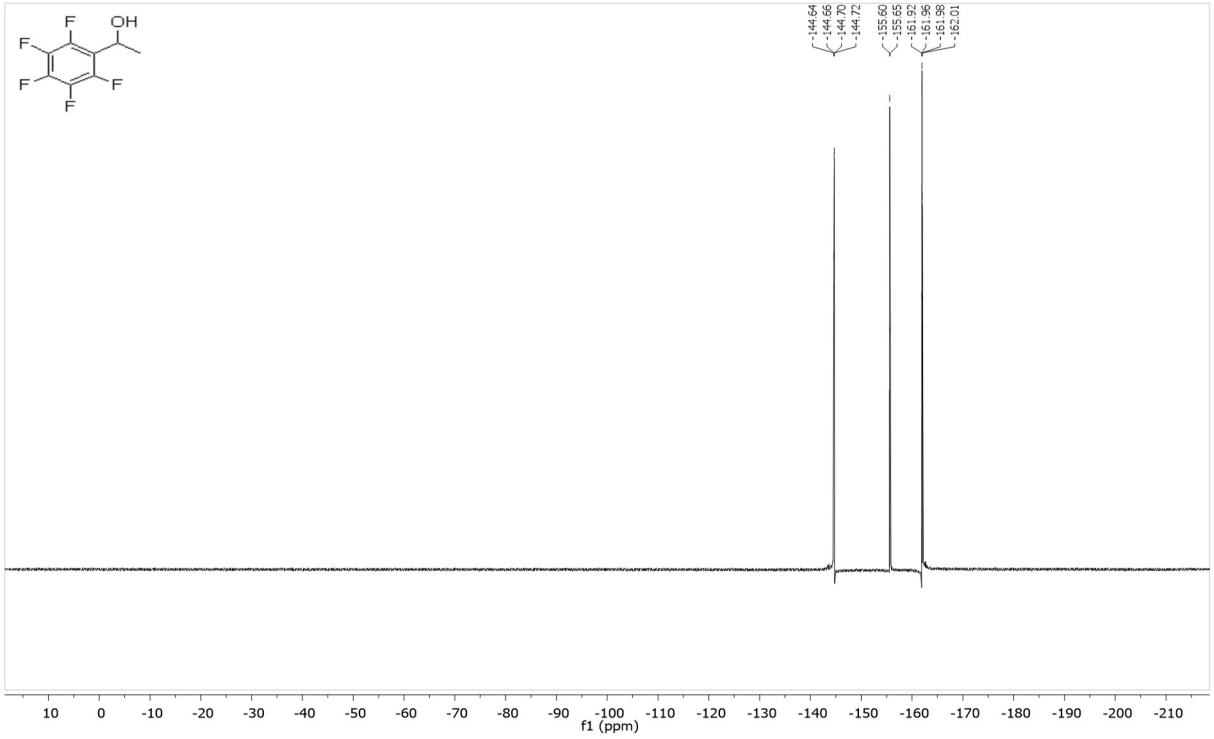
δ_H (400 MHz, $CDCl_3$)



δ_C (101 MHz, $CDCl_3$)

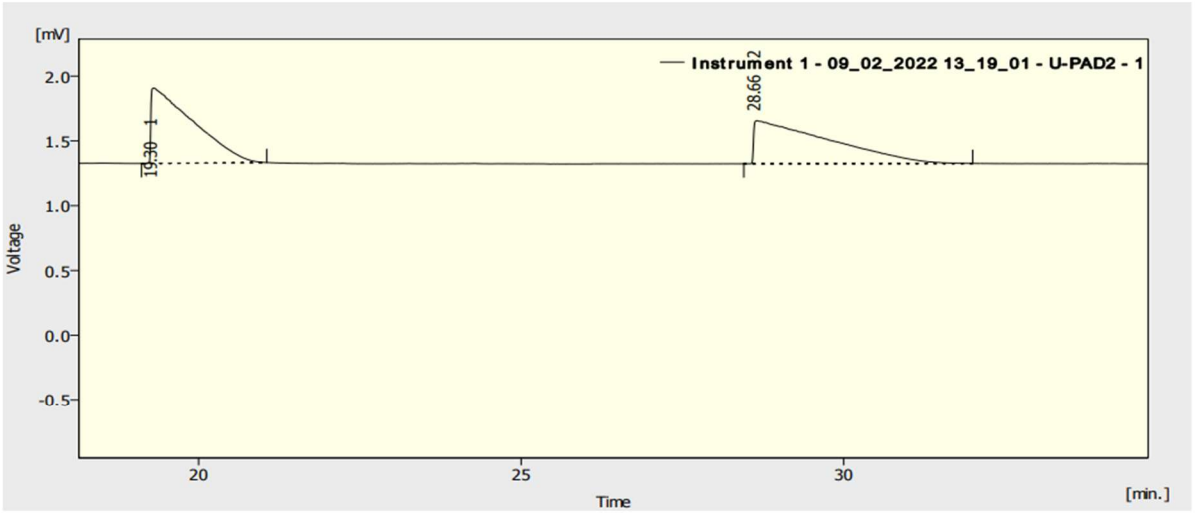


δ_F (376 MHz, $CDCl_3$



Chiral GC – racemic.

Clarity - Chromatography SW
DataApex
www.dataapex.com
GC1 Helium
Column: CP-Chiralsil-Dex CB 25mx0.25mmx0.25um

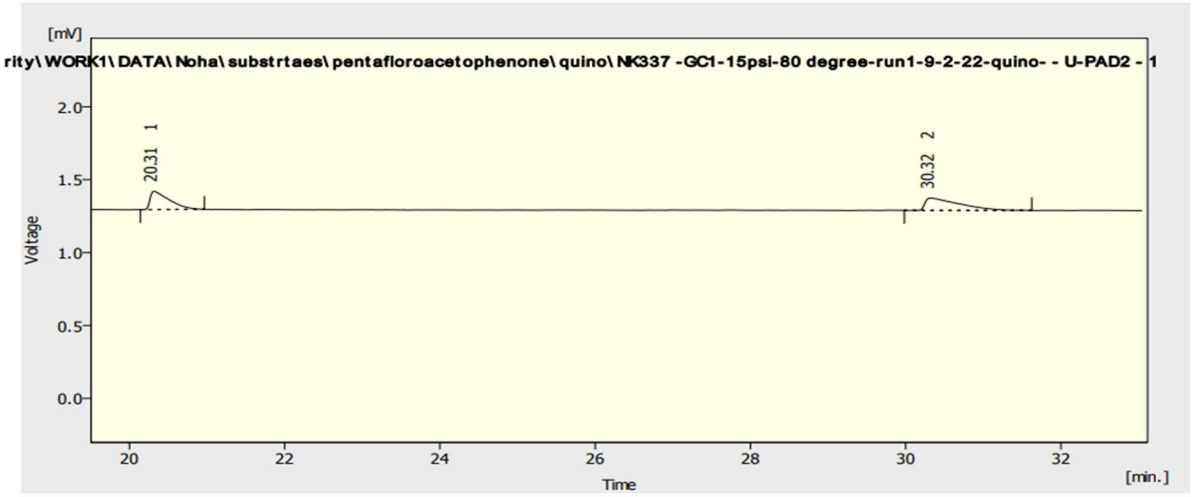


Result Table (Uncal - Instrument 1 - 09_02_2022 13_19_01 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	19.304	52.881	1.164	49.5	63.6	0.74	
2	28.656	54.001	0.667	50.5	36.4	1.32	
	Total	106.882	1.831	100.0	100.0		

Chiral GC – asymmetric.

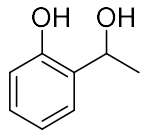
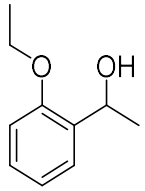
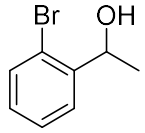
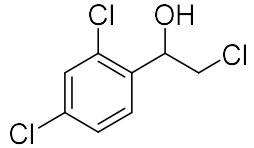
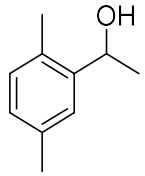
Clarity - Chromatography SW
DataApex
www.dataapex.com
GC1 Helium
Column: CP-Chiralsil-Dex CB 25mx0.25mmx0.25um



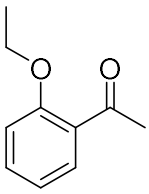
Result Table (Uncal - C:\Clarity\WORK1\DATA\Noha\substrtaes\pentafloroacetophenone\quino\NK337 -GC1-15psi-80 degree-run1-9-2-22-quino- - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	20.312	4.302	0.252	45.1	59.7	0.27	
2	30.320	5.240	0.170	54.9	40.3	0.48	
	Total	9.542	0.421	100.0	100.0		

Reduction of hindered *ortho*-substituted substrates using catalysts (*R,R*)-**12c** and **12f**.

Products	**(*R*,*R*)-Thioazole 12c**	**(*R*,*R*)-3-pyridyl 12f**	**(*S*,*S*)-1**
	98% ee (*R*) 95.3% conv 82% yield 118 h	92.4% ee (*R*) 99.5% conv 84% yield 118 h	-
	>99% ee (*R*) 100% conv 97% yield 118 h	>99% ee (*R*) 96% conv 94% yield 168 h	>99% ee (*S*) 57% conv 41% yield 158 h
	95.6% ee (*R*) 100% conv 85% yield 118 h	96.2% ee (*R*) 99.4% conv 87% yield 118 h	-
	88.6% ee (*R*) 99.4% conv 85% yield 118 h	90.6% ee (*R*) 100% conv 89% yield 118 h	-
	90.6% ee (*R*) 94% conv 87% yield 168 h	94.6% ee (*R*) 85.4% conv 71.3% yield 168 h	-

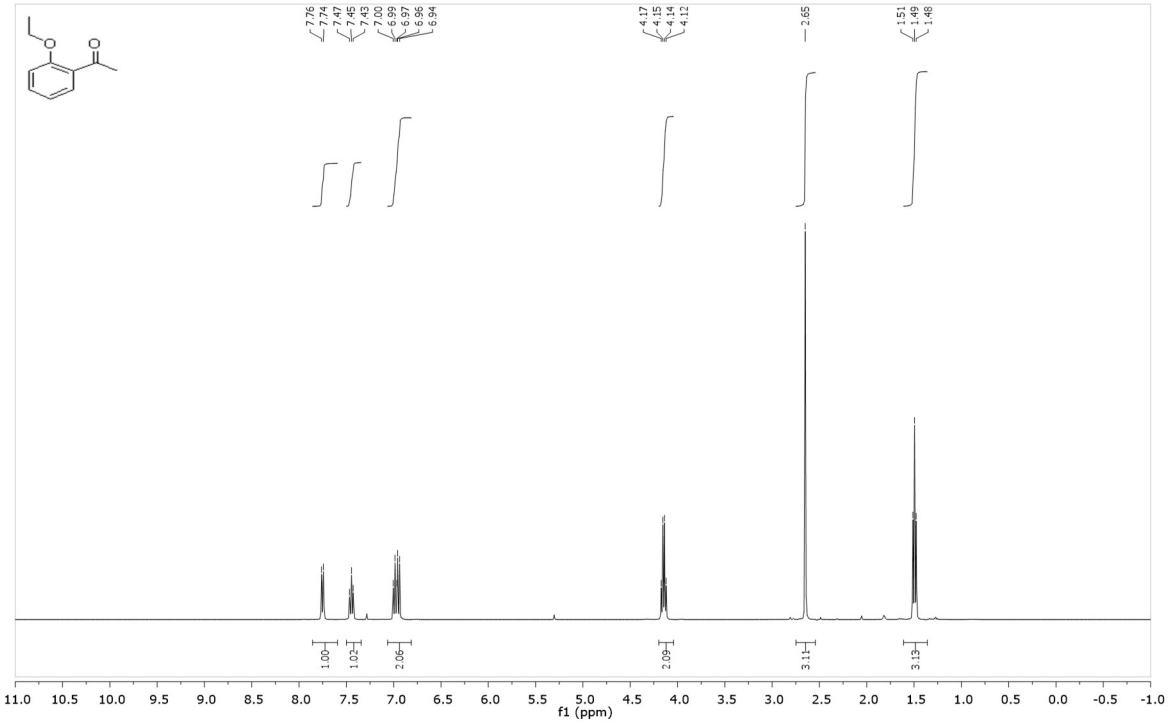
1-(2-Ethoxyphenyl)ethan-1-one (NK387).



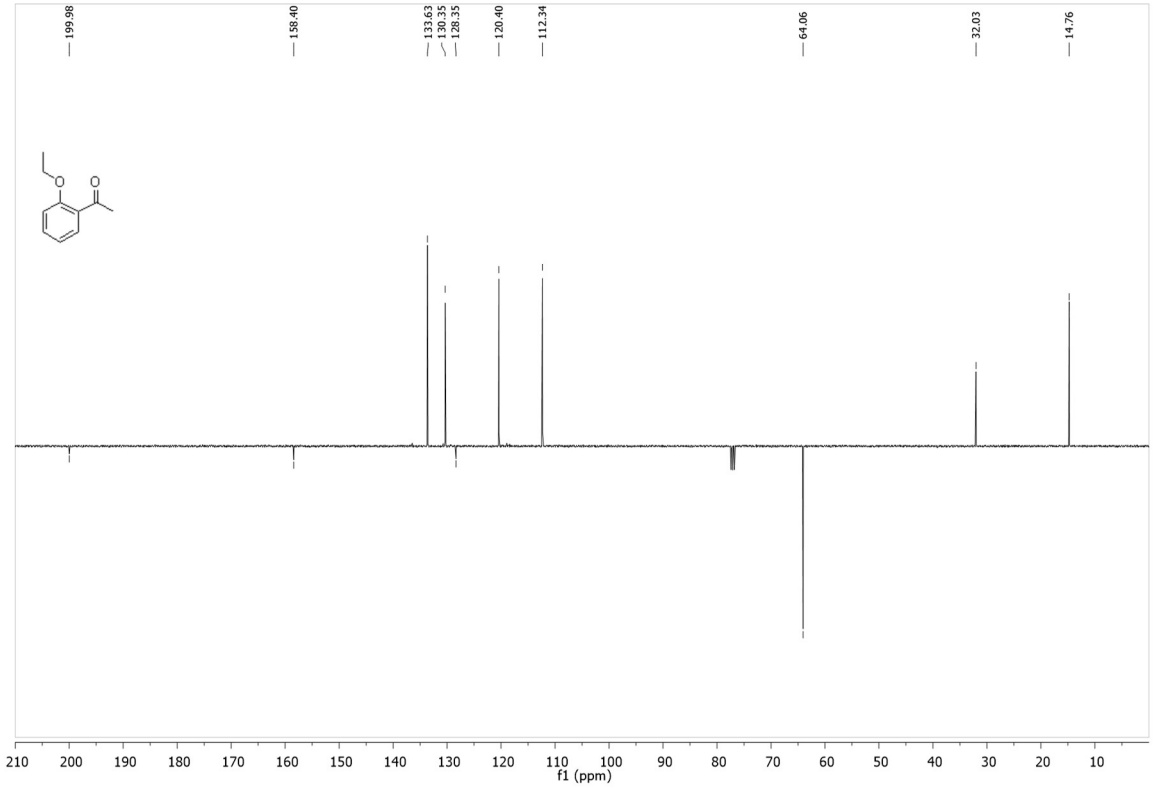
In 100 mL round bottomed flask, 1-(2-hydroxyphenyl)ethan-1-one (1.00 g, 7.35 mmol) and K_2CO_3 (1.31 g, 9.5 mmol) were added to DMF (20 mL). Bromoethane (2.5 mL, 3.67 g, 33.4 mmol) was added and the mixture heated to 50 ^oC until the ketone was consumed (ca. 2 days). The mixture was cooled to r.t and filtered to remove the K_2CO_3. The product was extracted using DCM (3 x 50 mL) after adding iced water (50 mL). The organic extracts were combined, dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. The crude product was purified by column chromatography (0 – 5% EtOAc in Pet. Ether) to give 1-(2-ethoxyphenyl)ethan-1-one as a white solid (1.10 g, 6.70 mmol, 91%); TLC: Rf ca 0.5 (20% EtOAc: 80% Pet. Ether), strong UV and $KMnO_4$; δ_H (400 MHz, $CDCl_3$) 7.75 (1 H, d, *J* 7.7, ArH), 7.45 (1 H, t, *J* 7.8, ArH), 7.07 – 6.84 (2 H, m, ArH), 4.15 (2 H, q, *J* 7.0, CH_2), 2.65 (3 H, s, CH_3), 1.49 (3 H, t, *J* 7.0, CH_3); δ_C (101 MHz, $CDCl_3$) 199.98 (C), 158.40 (C), 133.63

(CH), 130.35 (CH), 128.35 (C), 120.40 (CH), 112.34 (CH), 64.06 (CH_2), 32.03 (CH_3), 14.76 (CH_3). The data matched that reported.[8]

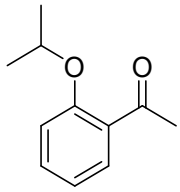
δ_H (400 MHz, $CDCl_3$).



δ_C (101 MHz, $CDCl_3$)

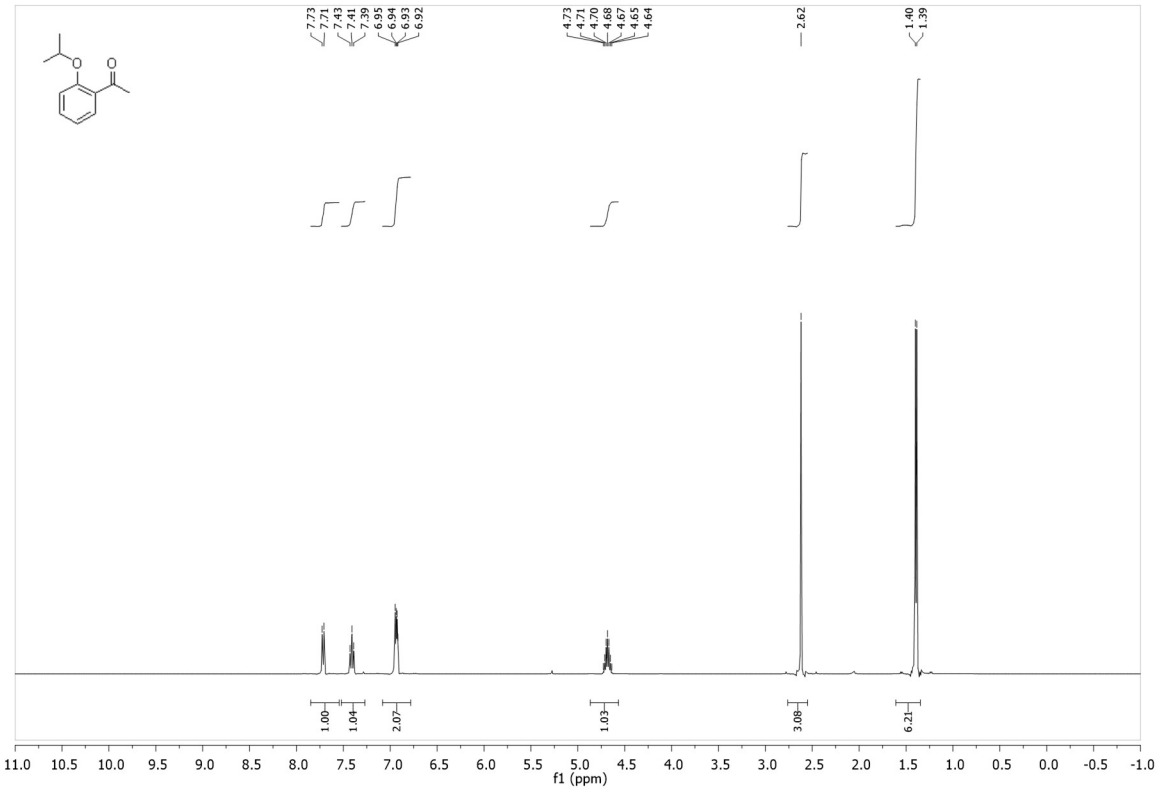


1-(2-Isopropoxyphenyl)ethan-1-one (NK388)

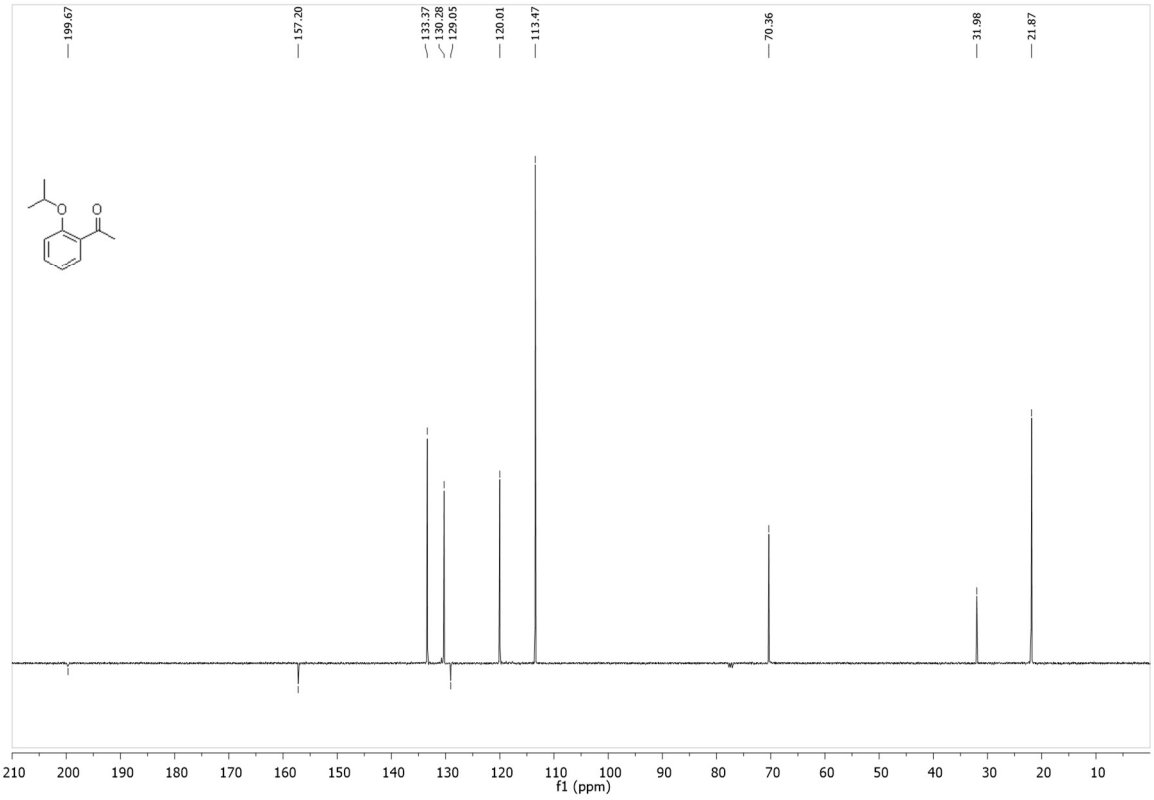


In a 100 mL round bottomed flask, 1-(2-hydroxyphenyl)ethan-1-one (1.00 g, 7.35 mmol) and K_2CO_3 (2.03 g, 14.7 mmol) were added to DMF (20 mL), then 2-bromopropane (1.4 mL, 1.83 g, 14.7 mmol) was added and the mixture heated to 70 ^oC until the ketone was consumed (3 days). The mixture was cooled to r.t and the K_2CO_3 was removed by filtration. The product was extracted using DCM (3 x 50 mL)after adding iced water (50 mL). The organic extracts were combined, dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. The crude product was purified by column chromatography (0 – 5% EtOAc in Pet. Ether) to give 1-(2-isopropoxyphenyl)ethan-1-one as a colourless oil (1.25g, 7.01 mmol, 95%); TLC: Rf ca 0.6 (20% EtOAc: Pet. Ether), strong UV and $KMnO_4$; δ_H (400 MHz, $CDCl_3$) 7.72 (1 H, d, *J* 7.9, ArH), 7.41 (1 H, t, *J* 7.8, ArH), 6.95-6.90 (2 H, m, ArH), 4.68 (1 H, hept, *J* 6.0, CH), 2.62 (3 H, s, CH_3), 1.39 (6 H, d, *J* 6.0, CH_3); δ_C (101 MHz, $CDCl_3$) 199.67 (C), 157.20 (C), 133.37 (CH), 130.28 (CH), 129.05 (C), 120.01 (CH), 113.47 (CH), 70.36 (CH), 31.98 (CH_3), 21.87 (CH_3). The data matched that reported.[9]

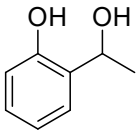
δ_H (400 MHz, $CDCl_3$)



δ_C (101 MHz, $CDCl_3$)

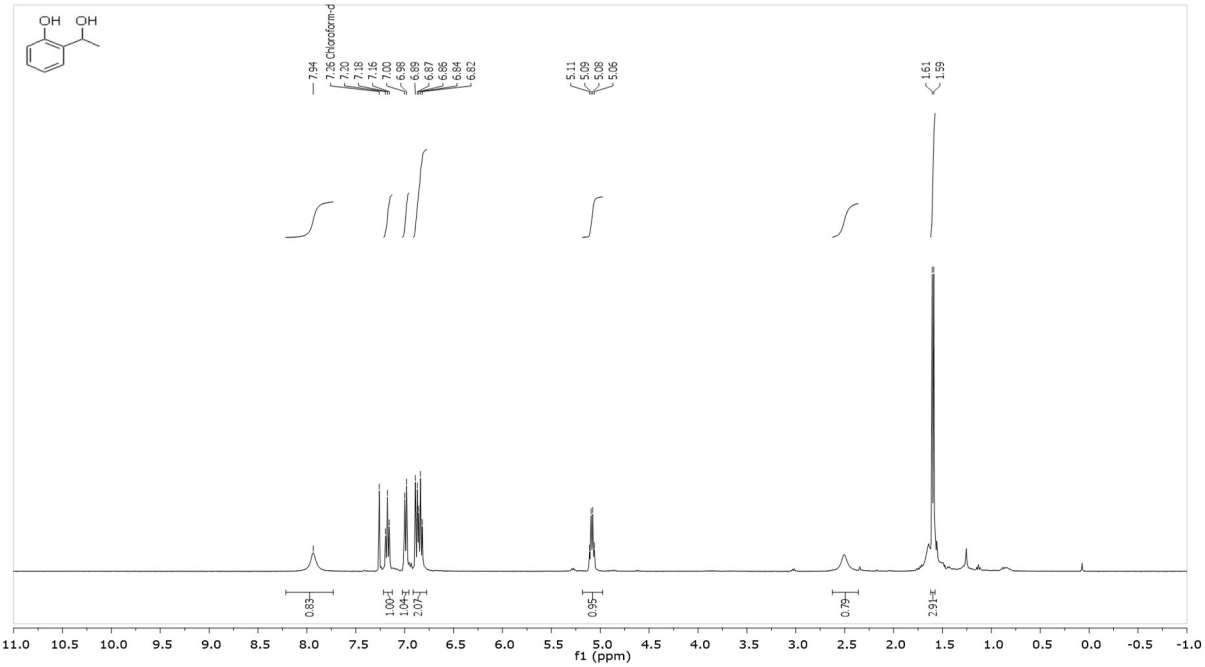


(*R*)-2-(1-Hydroxyethyl)phenol (NK408)

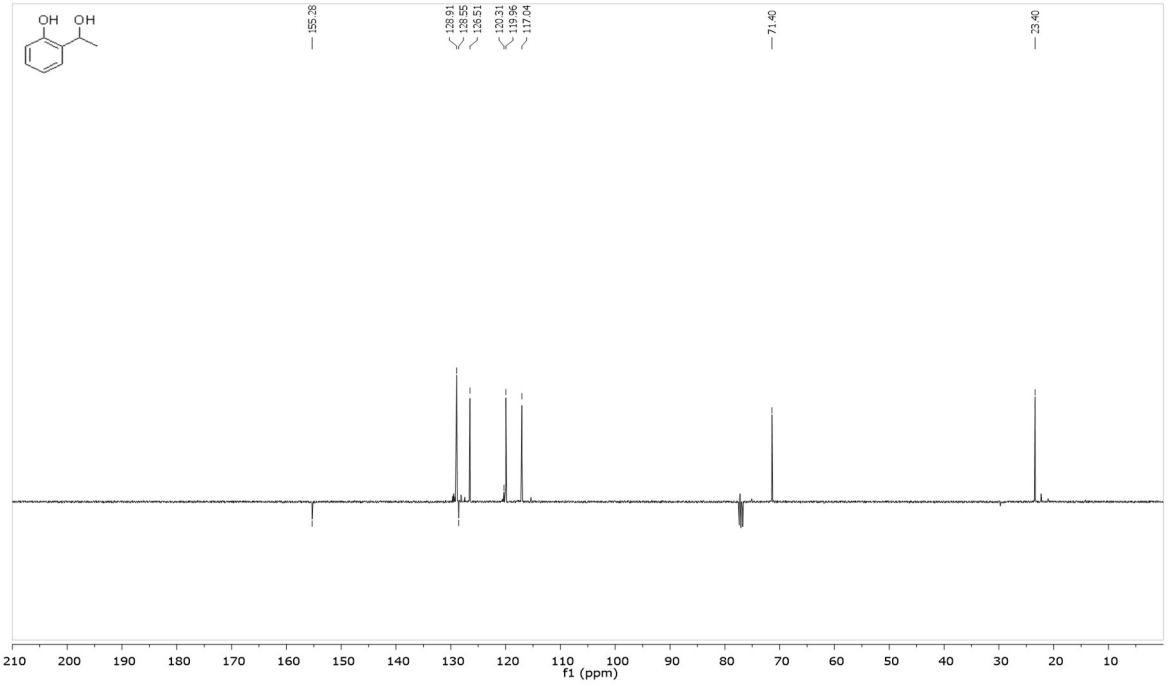


1-(2-Hydroxyphenyl)ethan-1-one (136 mg, 1.00 mmol) and catalyst **(*R,R*)-12f** (6.2 mg, 0.010 mmol) were reacted following the general procedure to give 2-(1-hydroxyethyl)phenol (116 mg, 0.84 mmol , 84%) as a colourless oil; δ_H (400 MHz, $CDCl_3$) 7.94 (1 H, s, ArOH), 7.18 (1 H, t, *J* 7.7, ArH), 6.99 (1 H, d, *J* 7.5, ArH), 6.92 – 6.81 (2 H, m, ArH), 5.09 (1 H, q, *J* 6.5, CH), 2.50 (1 H, br. s, OH), 1.60 (3 H, d, *J* 6.6, CH_3); δ_C (101 MHz, $CDCl_3$) 155.28 (C), 128.91 (CH), 128.55 (C), 126.51 (CH), 119.96 (CH), 117.04 (CH), 71.40 (CH), 23.40 (CH_3). $[\alpha]^{21}$ +32.4 (c 0.14 in $CHCl_3$) 92.4 % ee (*R*) (lit.[10] $[\alpha]^{32}$ +22.3 (0.65 c in CH_2Cl_2) – 98.8% ee (*R*); GC analysis (CP-Chiralsil-Dex CB 25m x 0.25mm x 0.25um), gas H_2, T = 140 °C, P = 15 psi, FID temp 250 °C, injector temp 220 °C, ketone 2.078 min., R isomer 11.53 min., S isomer 13.64 min.)

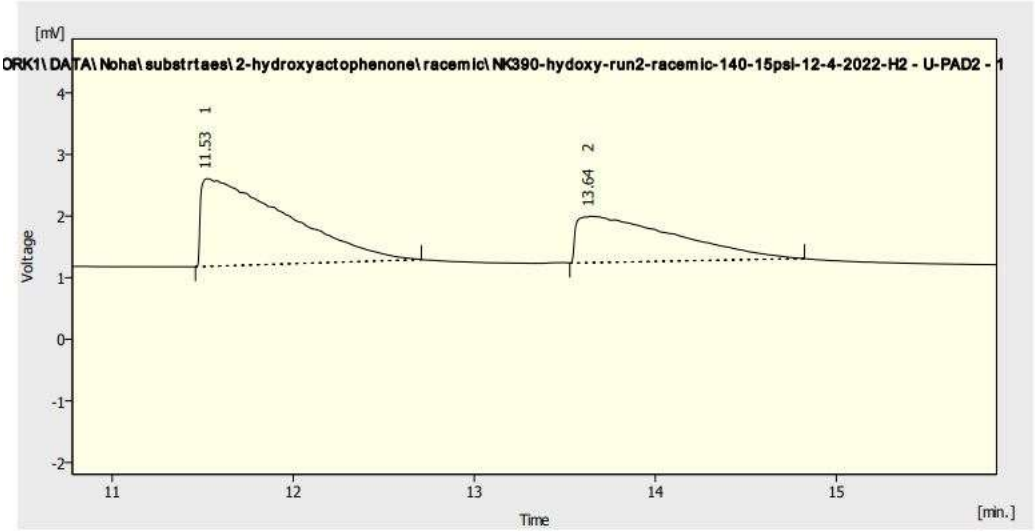
δ_H (400 MHz, $CDCl_3$)



δ_C (101 MHz, $CDCl_3$)



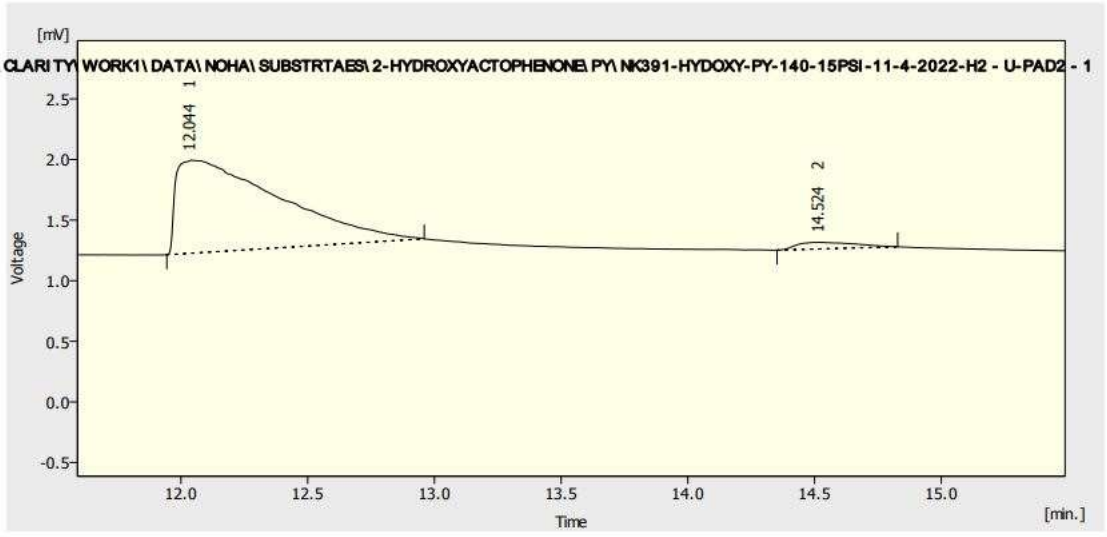
Chiral GC – racemic.



Result Table (Uncal - C:\Clarity\WORK1\DATA\Noha\substrtaes\2-hydroxyactophenone\racemic\NK390-hydoxy-run2-racemic-140-15 psi-12-4-2022-H2 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	11.528	94.083	2.847	62.3	65.4	0.57	
2	13.644	56.962	1.507	37.7	34.6	0.66	
	Total	151.045	4.354	100.0	100.0		

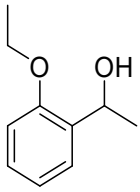
Chiral GC – asymmetric



Result Table (Uncal - C:\CLARITY\WORK1\DATA\NOHA\SUBSTRTAES\2-HYDROXYACTOPHENONE\PY\NK391-HYDOXY-PY-140-15PSI-11-4-2022-H2 - U-PAD2 - 1)

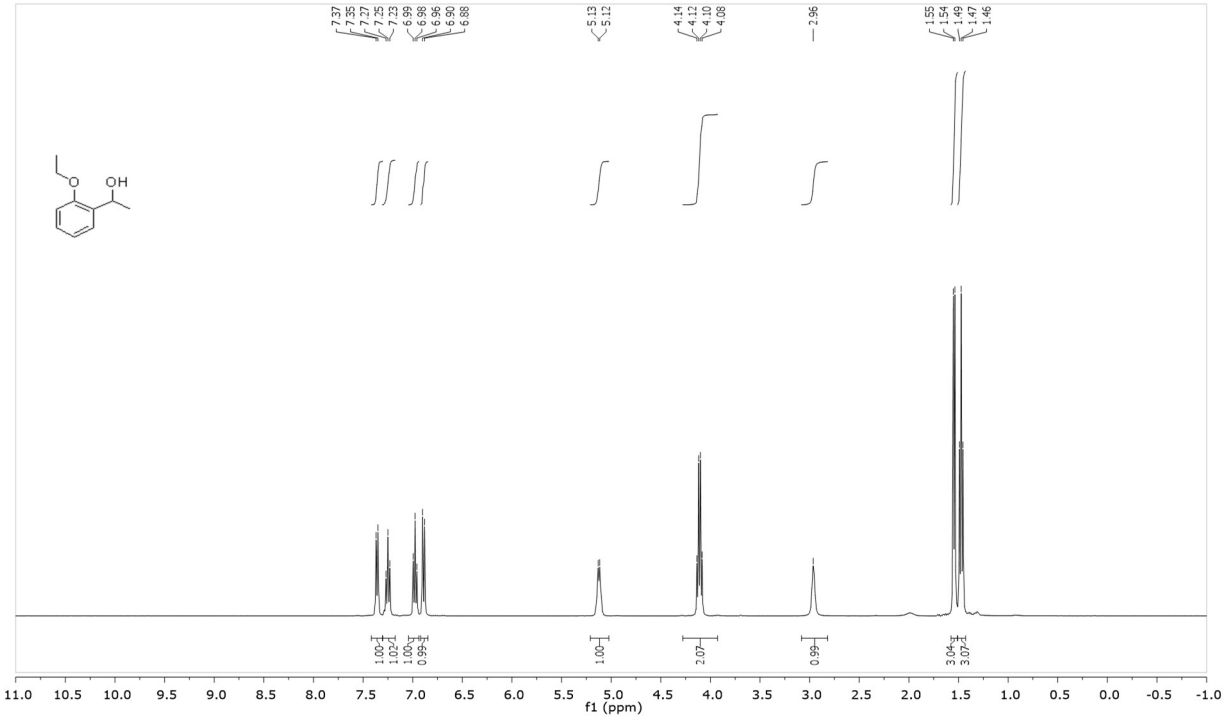
	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	12.044	43.295	1.536	96.2	93.3	0.50	
2	14.524	1.725	0.110	3.8	6.7	0.32	
	Total	45.020	1.646	100.0	100.0		

(*R*)-1-(2-Ethoxyphenyl)ethan-1-ol (NK395).

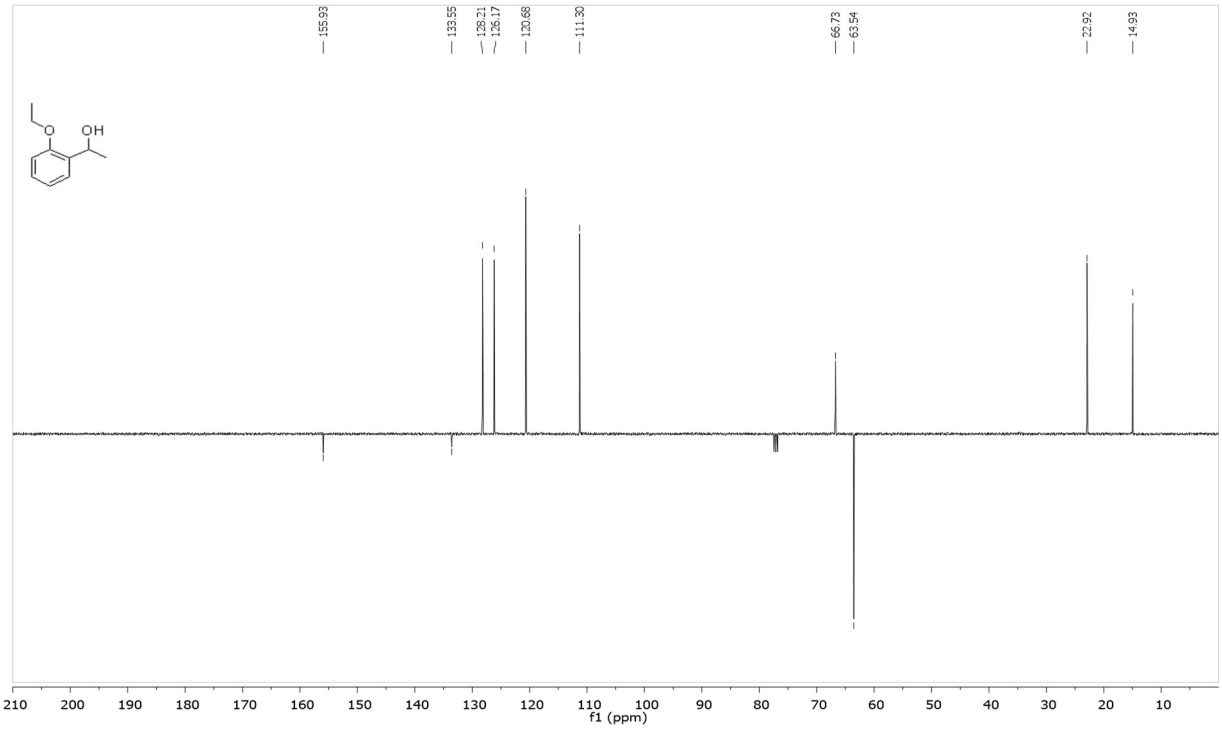


1-(2-Ethoxyphenyl)ethan-1-one (164 mg, 1.00 mmol) and catalyst **(*R,R*)-12c** (6.6 mg, 0.010 mmol) were reacted following the general procedure to give 1-(2-ethoxyphenyl)ethan-1-ol as a colourless oil (161 mg, 0.96 mmol, 96%); δ_H (400 MHz, $CDCl_3$) 7.36 (1 H, d, *J* 7.4, ArH), 7.28-7.23 (1 H, m, ArH), 6.98 (1 H, t, *J* 7.4, ArH), 6.89 (1 H, d, *J* 8.2, ArH), 5.12 (1 H, br.s, CH), 4.11 (2 H, q, *J* 6.9, CH_2), 2.96 (1 H, s, OH), 1.54 (3 H, d, *J* 6.5, CH_3), 1.47 (3 H, t, *J* 7.0, CH_3); δ_C (101 MHz, $CDCl_3$) 155.93 (C), 133.55 (C), 128.21 (CH), 126.17 (CH), 120.68 (CH), 111.30 (CH), 66.73 (CH), 63.54 (CH_2), 22.92 (CH_3), 14.93 (CH_3); $[\alpha]^{21}$ +32.5 (c 0.096 in $CHCl_3$) > 99% ee (*R*) (lit.[11] $[\alpha]\ ^{20}_D = -33.48$ (c = 0.233 in $CHCl_3$)- 93% ee (*S*); HPLC analysis (Chiralcel OJ , 250 × 4.6 mm column, hexane/2-propanol 99:01, 0.8 mL/min, 290 nm, Ketone: 8.28 min, *S* isomer: 11.04 min, *R* isomer: 12.85 min.

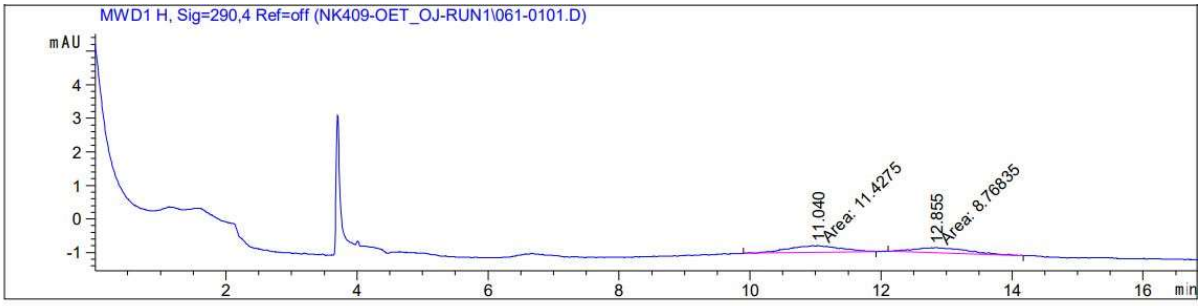
δ_H (400 MHz, $CDCl_3$)



δ_C (101 MHz, $CDCl_3$)



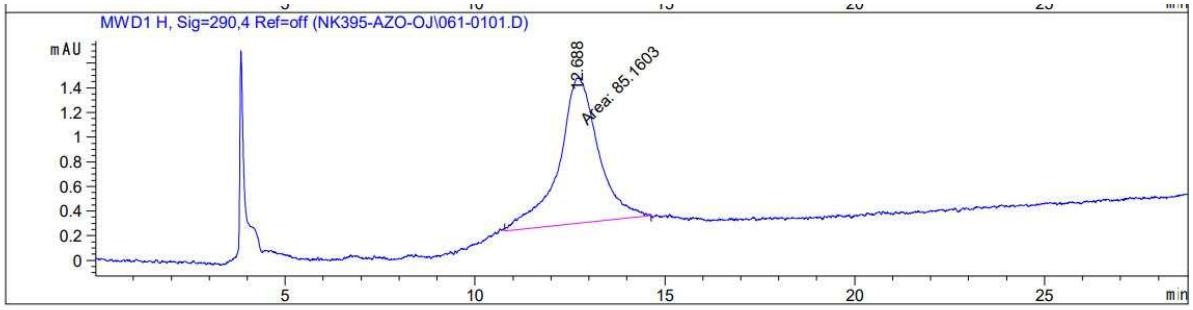
Chiral HPLC – racemic.



Signal 8: MWD1 H, Sig=290,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.040	MM	0.9372	11.42751	2.03213e-1	56.5834
2	12.855	MM	0.9290	8.76835	1.57304e-1	43.4166
Totals :				20.19586	3.60517e-1	

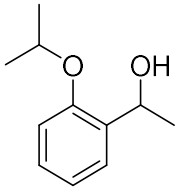
Chiral HPLC – asymmetric sample.



Signal 8: MWD1 H, Sig=290,4 Ref=off

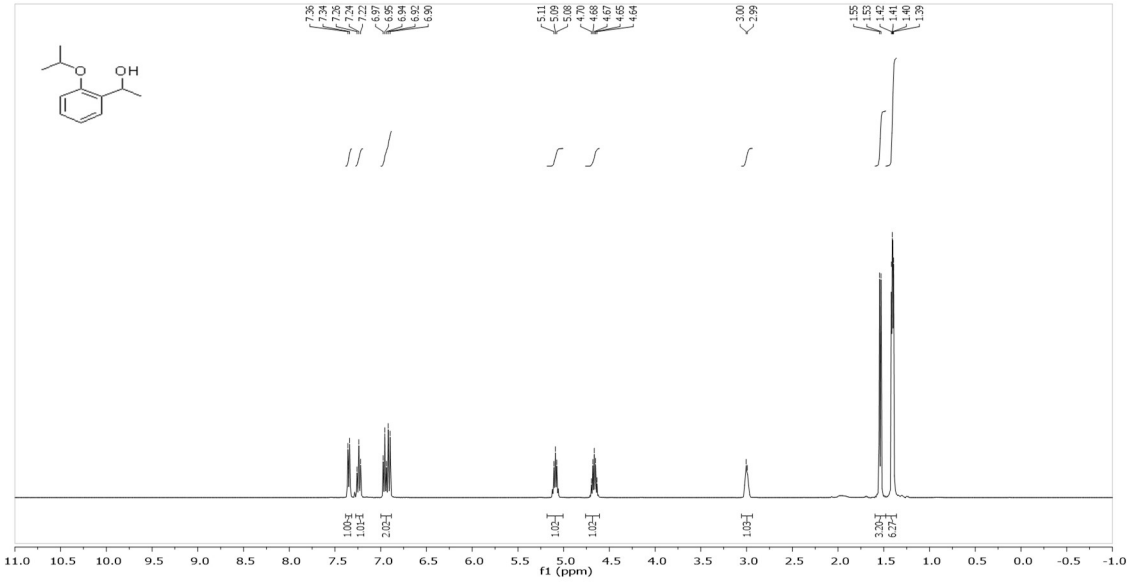
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.688	MM	1.2038	85.16027	1.17909	100.0000
Totals :				85.16027	1.17909	

(*R*)-1-(2-Isopropoxyphenyl)ethan-1-ol (NK398).

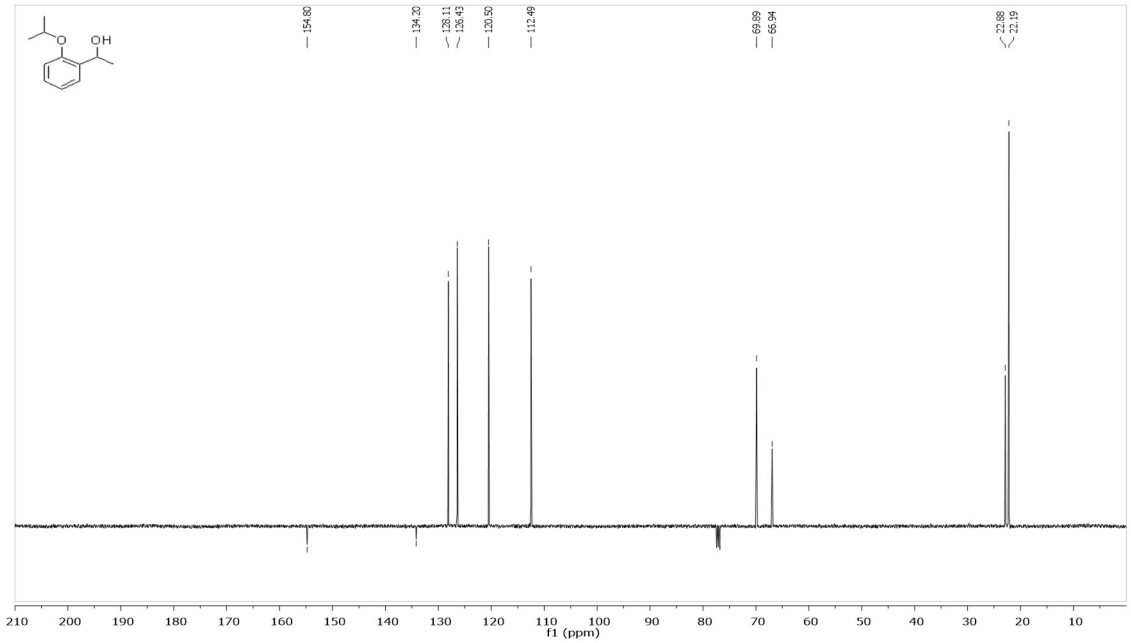


1-(2-Isopropoxyphenyl)ethan-1-one (178 mg, 1.00 mmol) and catalyst **(*R,R*)-10** (6.6 mg, 0.010 mmol) were reacted following the general procedure to give 1-(2-isopropoxyphenyl)ethan-1-ol as a colourless oil (97 mg, 0.78 mmol, 78%); δ_H (400 MHz, $CDCl_3$) 7.35 (1 H, d, *J* 7.5, ArH), 7.24 (1 H, t, *J* 7.8,ArH), 6.99 – 6.86 (2 H, m, ArH), 5.19 – 5.03 (1 H, m, CH), 4.67 (1 H, m, CH), 3.00 (1 H, br.s, OH), 1.54 (3 H, d, *J* 6.5, CH_3), 1.40 (6 H, m, CH_3); δ_C (101 MHz, $CDCl_3$) 154.80 (C), 134.20 (C), 128.11 (CH), 126.43 (CH), 120.50 (CH), 112.49 (CH), 69.89 (CH), 66.94 (CH), 22.88 (CH_3), 22.19 (CH_3); $[\alpha]^{21}$ +14.62 (c 0.122 in $CHCl_3$). The separation of enantiomers proved difficult and an ee could not be determined.

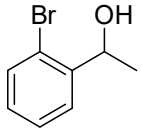
δ_H (400 MHz, $CDCl_3$)



δ_C (101 MHz, $CDCl_3$)

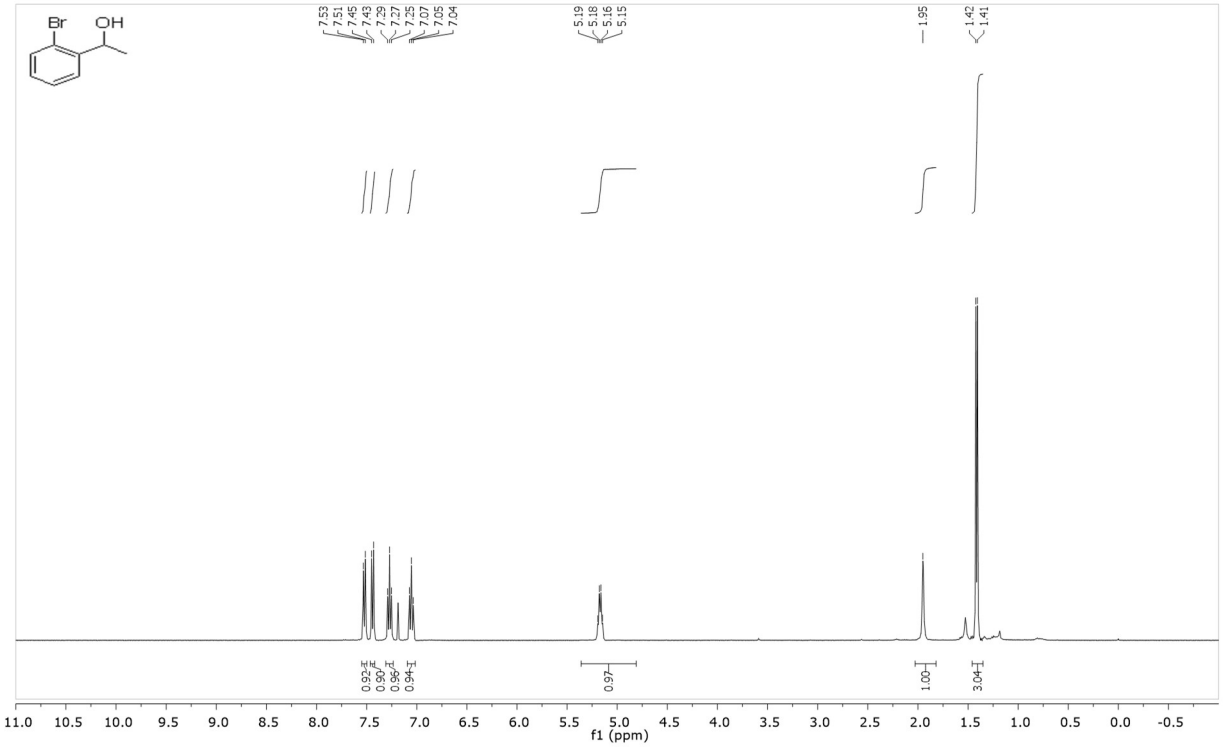


(*R*)-1-(2-Bromophenyl)ethan-1-ol (NK400)

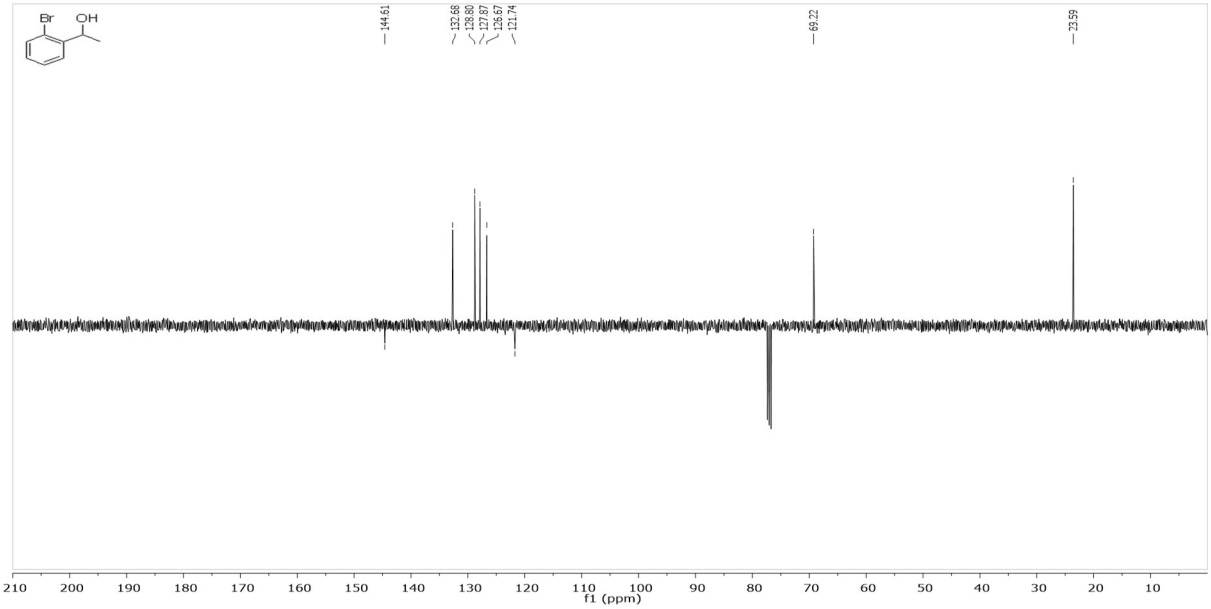


1-(2-bromophenyl)ethan-1-one (199 mg, 1.00 mmol) and catalyst **(*R,R*)-12f** (6.2 mg, 0.010 mmol) were reacted following the general procedure to give 1-(2-bromophenyl)ethan-1-ol as a white solid (175 mg, 0.87 mmol, 87%); δ_H (400 MHz, $CDCl_3$) 7.52 (1 H, d, *J* 7.8,ArH), 7.44 (1 H, d, *J* 8.0,ArH), 7.27 (1 H, t, *J* 7.5, ArH), 7.05 (1 H, t, *J* 7.6, ArH), 5.17 (1 H, q, *J* 6.0, CH), 1.95 (1 H, s, OH), 1.41 (3 H, d, *J* 6.4, CH_3); δ_C (101 MHz, $CDCl_3$) 144.61 (C), 132.68 (CH), 128.80 (CH), 127.87 (CH), 126.67 (CH), 121.74 (C), 69.22 (CH), 23.59 (CH_3); MP. 61.9 ºC; $[\alpha]^{21}$ +54.3 (c 0.194 in $CHCl_3$) 96.2% ee (*R*) (lit.[11] $[\alpha]\ ^{20}_D = -44.45$ (c = 0.432 in CHCl3)- 91% ee (*S*); GC analysis (CP-Chiralsil-Dex CB 25m x 0.25mm x 0.25um), gas H_2, T = 140 °C, P = 15 psi, FID temp 250 °C, injector temp 220 °C, ketone 3.11 min., R isomer 8.25 min., S isomer 10.79 min.)

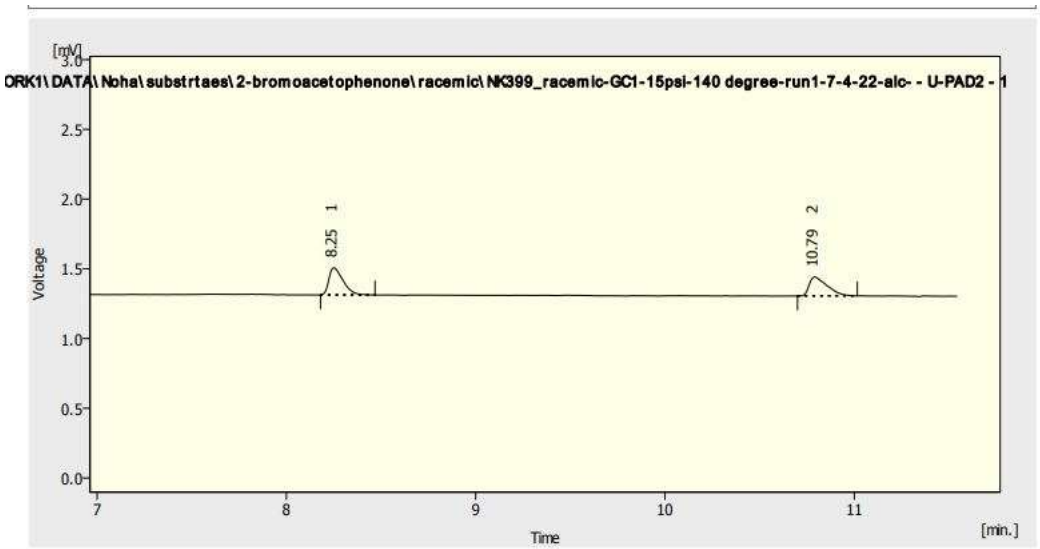
δ_H (400 MHz, $CDCl_3$)



δ_C (101 MHz, $CDCl_3$)



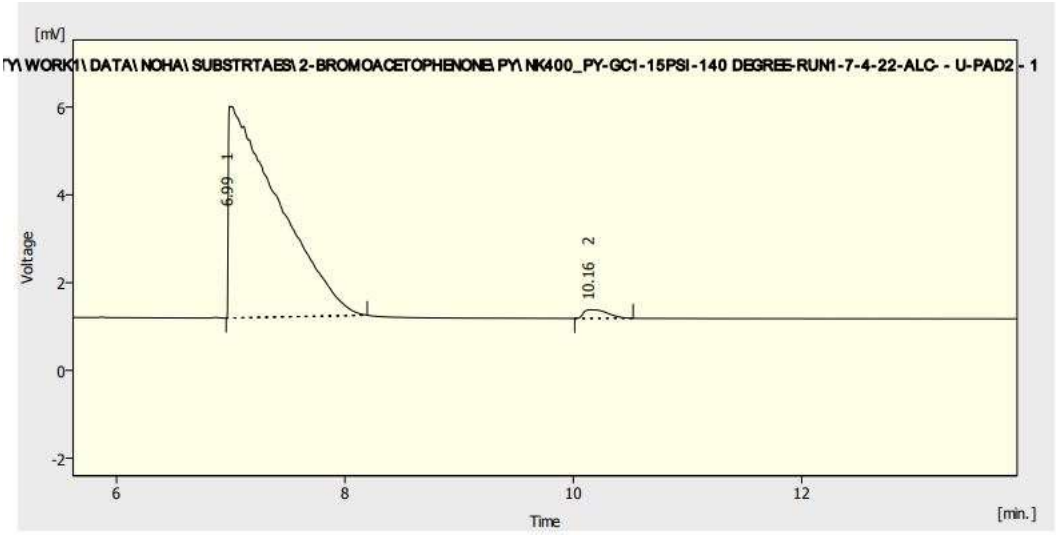
Chiral GC – racemic.



Result Table (Uncal - C:\Clarity\WORK1\DATA\Noha\substrtaes\2-bromoacetophenone\racemic\NK399_racemic-GC1-15psi-140 degree-run1-7-4-22-alc- - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	8.252	2.003	0.389	52.7	58.9	0.08	
2	10.792	1.800	0.272	47.3	41.1	0.11	
	Total	3.803	0.661	100.0	100.0		

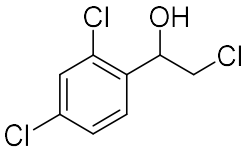
Chiral GC – asymmetric.



Result Table (Uncal - C:\CLARITY\WORK1\DATA\NOHA\SUBSTRTAES\2-BROMOACETOPHENONE\PY\NK400_PY-GC1-15PSI-140 DEGREE-RUN1-7-4-22-ALC- - U-PAD2 - 1)

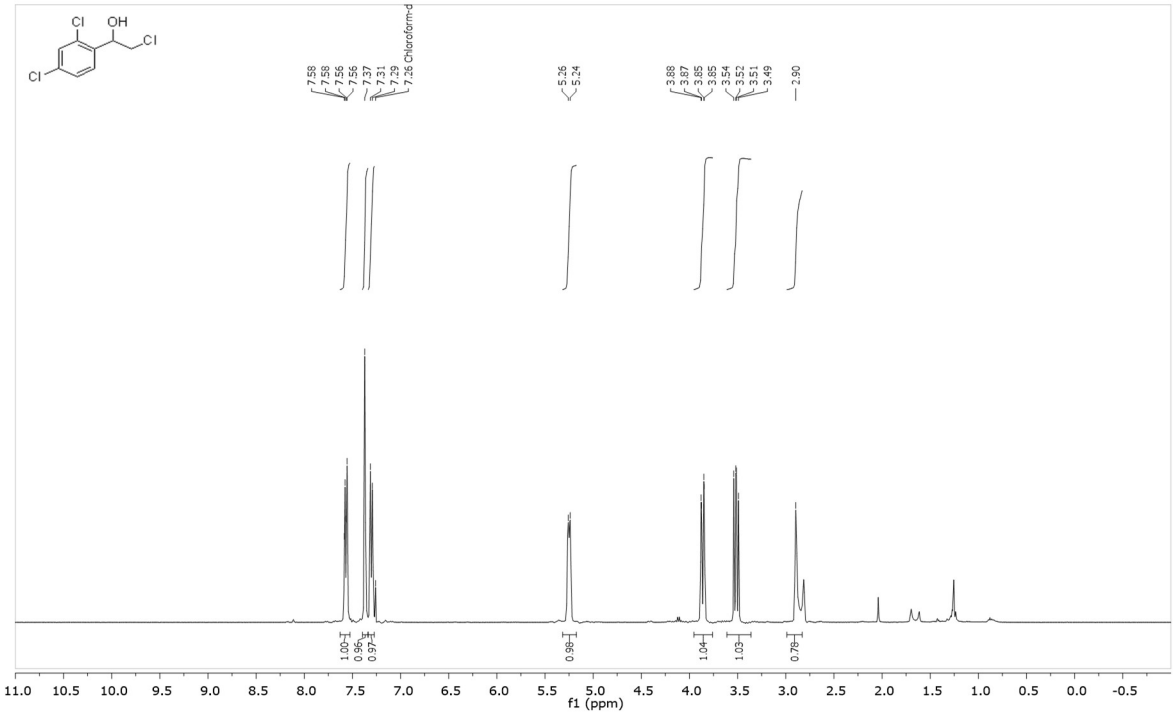
	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	6.992	294.955	9.662	98.1	96.1	0.48	
2	10.156	5.667	0.390	1.9	3.9	0.24	
	Total	300.621	10.052	100.0	100.0		

(*S*)-2-Chloro-1-(2,4-dichlorophenyl)ethan-1-ol (NK403).

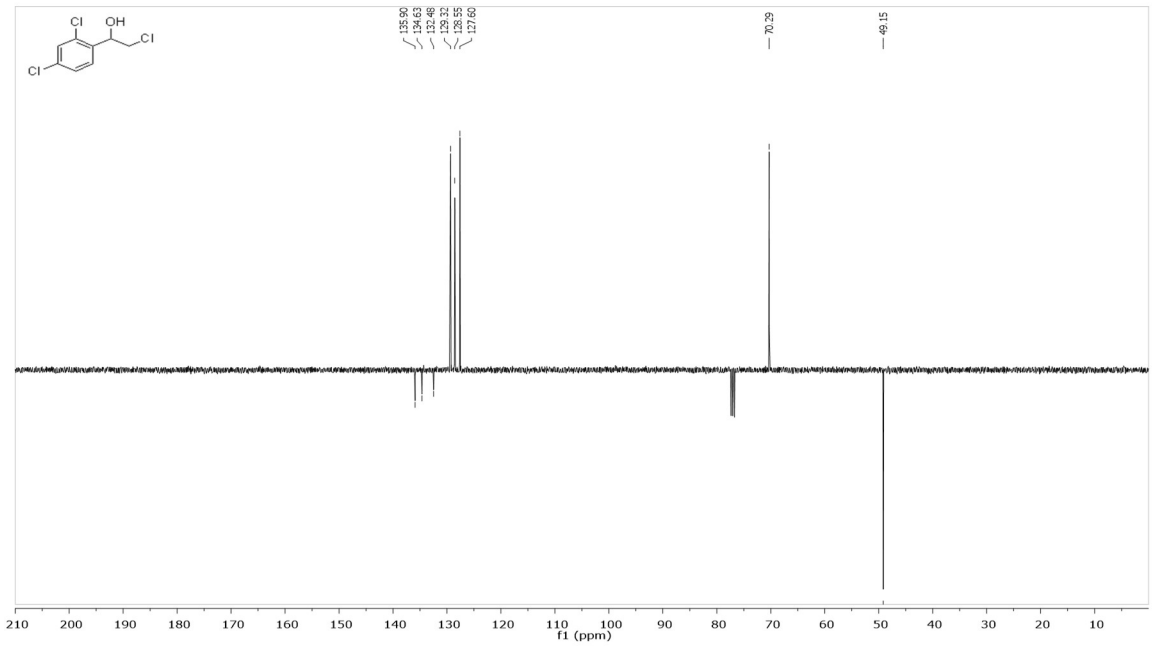


2-Chloro-1-(2,4-dichlorophenyl)ethan-1-one (224 mg, 1.00 mmol) and catalyst **(*R,R*)-12f** (6.2 mg, 0.010 mmol) were reacted following the general procedure to give 2-chloro-1-(2,4-dichlorophenyl)ethan-1-ol as a white solid (200 mg, 0.89 mmol, 89%); δ_H (400 MHz, $CDCl_3$) 7.57-7.55 (1 H, m, ArH), 7.37 (1 H, br.s, ArH), 7.30 (1 H, d, *J* 8.4, ArH), 5.25 (1 H, br. s, CH), 3.86 (1 H, dd, *J* 11.3, 1.6, CH_2), 3.52 (1 H, dd, *J* 11.2, 8.6, CH_2), 2.90 (1 H, s, OH); δ_C (101 MHz, $CDCl_3$) 135.90 (C), 134.63 (C), 132.48 (C), 129.32 (CH), 128.55 (CH), 127.60 (CH), 70.29 (CH), 49.15 (CH_2); MP. 62.8 ºC ; $[\alpha]^{21}$ +55.3 (c 0.12 in $CHCl_3$) 90.6% ee (*S*) (lit.[12] $[\alpha]^{20}$= +57.3 (c 2.50 in $CHCl_3$) - >99% ee (*S*), GC analysis (CP-Chiralsil-Dex CB 25 m x 0.25mm x 0.25um), gas H_2, T = 170 °C, P = 15 psi, FID temp 250 °C, injector temp 220 °C, ketone 3.62 min., S isomer 7.40 min., R isomer 8.18 min.)

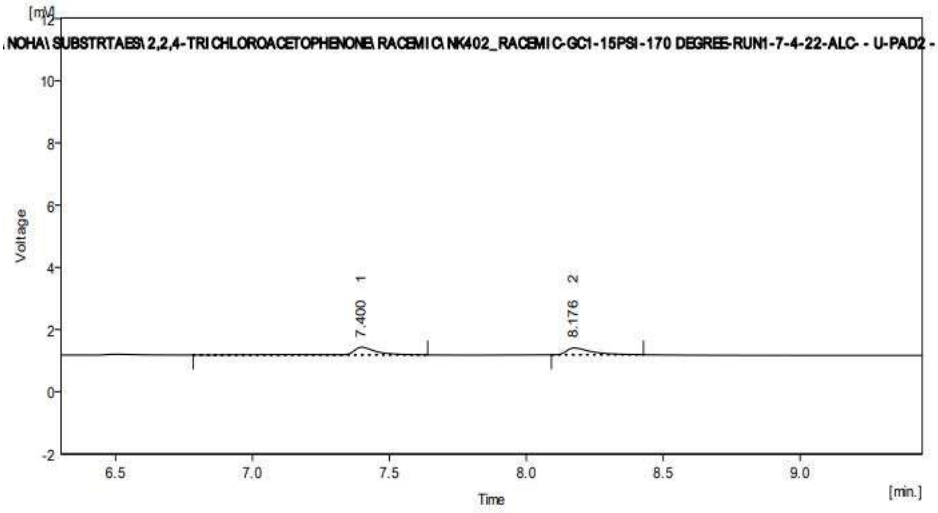
δ_H (400 MHz, $CDCl_3$)



δ_C (101 MHz, $CDCl_3$)



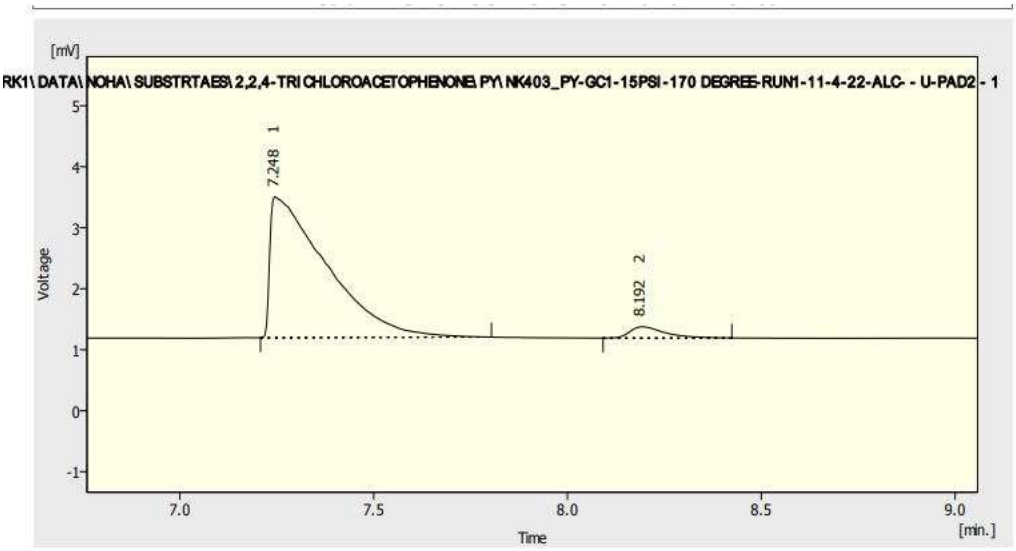
Chiral GC – racemic.



Result Table (Uncal - C:\CLARITY\WORK1\DATA\NOHA\SUBSTRTA

	Reten. Time [min]	Start Time [min]	End Time [min]	Start Value [mV]	End Value [mV]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]
1	7.400	6.784	7.640	2.360	2.367	3.196	0.499	53.3	53.1	0.08
2	8.176	8.092	8.428	2.374	2.378	2.797	0.441	46.7	46.9	0.09
	Total					5.994	0.940	100.0	100.0	

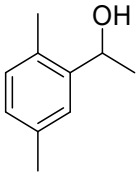
Chiral GC – asymmetric.



Result Table (Uncal - C:\CLARITY\WORK1\DATA\NOHA\SUBSTRTAES\2,2,4-TRICHLOROACETOPHENONE\PY\NK403_PY-GC1-15PSI -170 DEGREE-RUN1-11-4-22-ALC- - U-PAD2 - 1)

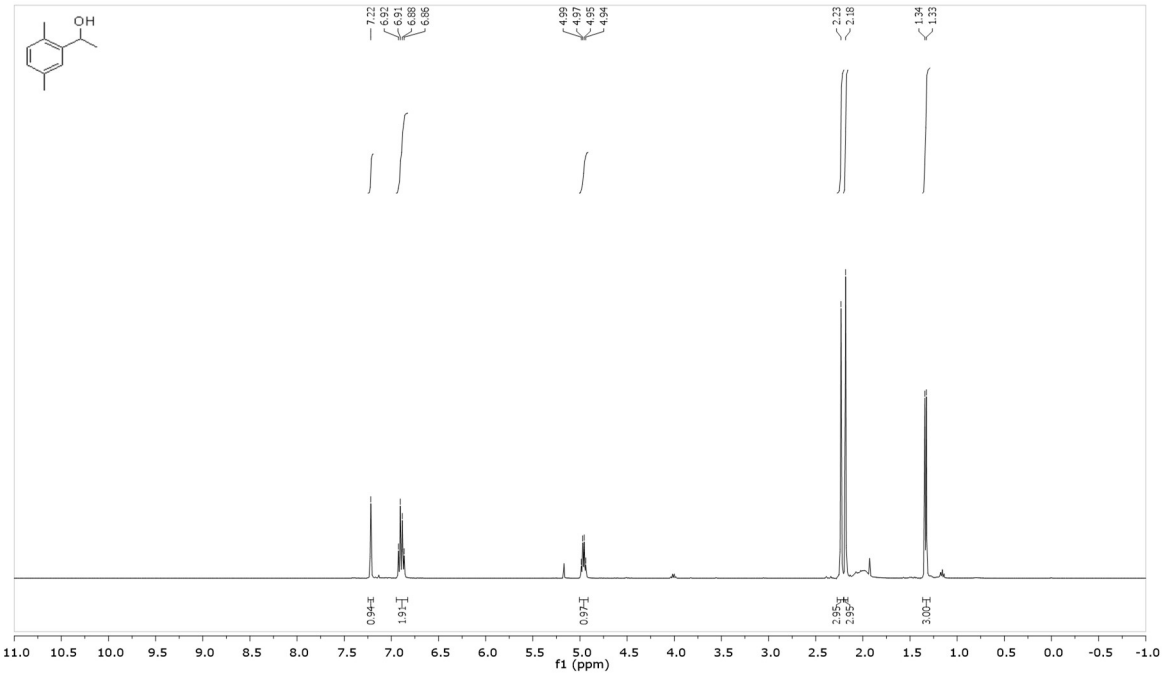
	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	7.248	46.727	4.613	95.3	92.6	0.16	
2	8.192	2.285	0.369	4.7	7.4	0.10	
	Total	49.012	4.982	100.0	100.0		

(*R*)-1-(2,5-Dimethylphenyl)ethan-1-ol (NK407).

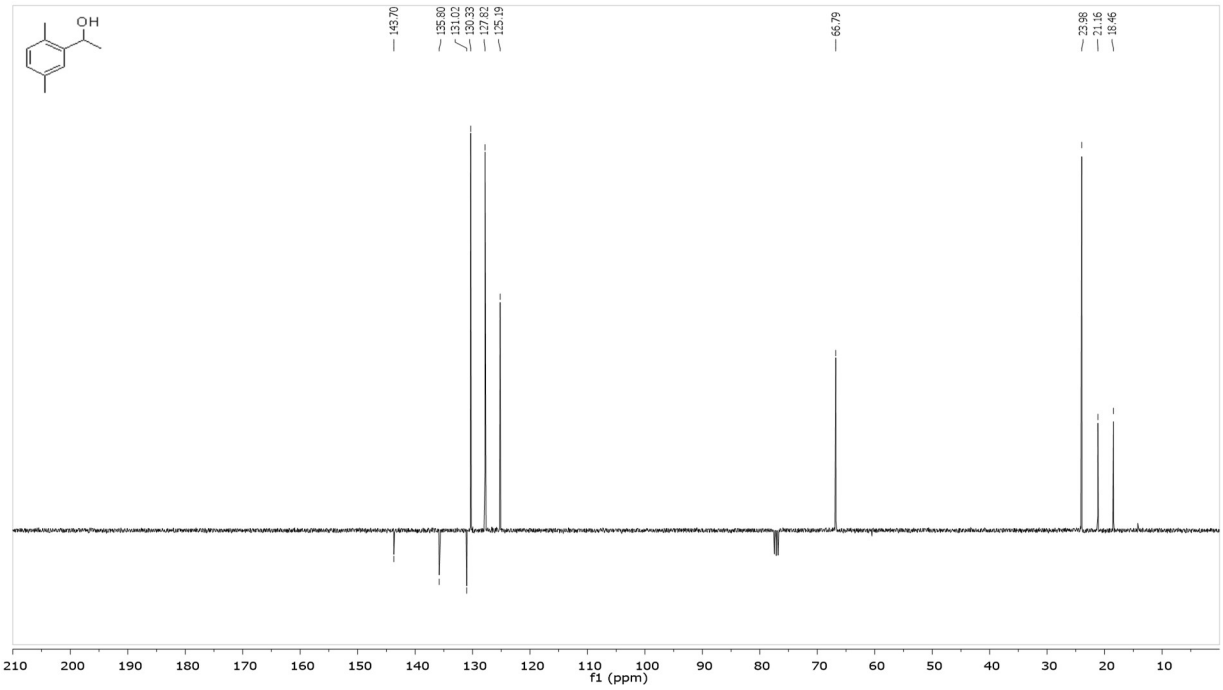


1-(2,5-Dimethylphenyl)ethan-1-one (148 mg, 1.00 mmol) and catalyst **(*R*,*R*)-12c** (6.6 mg, 0.010 mmol) were reacted following the general procedure to give 1-(2,5 dimethylphenyl)ethan-1-ol as a yellow oil (131 mg, 0.87mmol, 87%); δ_H (400 MHz, $CDCl_3$) 7.22 (1 H, s, ArH), 6.90-6.87 (2 H, m, ArH), 4.96 (1 H, q, *J* 6.4, CH), 2.23 (3 H, s, CH_3), 2.18 (3 H, s, CH_3), 1.33 (3 H, d, *J* 6.4, CH_3); δ_C (101 MHz, $CDCl_3$) 143.70 (C), 135.80 (C), 131.02 (C), 130.33 (CH), 127.82 (CH), 125.19 (CH), 66.79 (CH), 23.98 (CH_3), 21.16 (CH_3), 18.46 (CH_3). $[\alpha]^{21}$ +81.04 (c 0.08 in $CHCl_3$) 90.6% ee (*R*) (lit.[13] $[\alpha]^{18}$ +31.7 (c 1.01 in CH_2Cl_2) 62% ee (*R*), GC analysis (CP-Chiralsil-Dex CB 25m x 0.25mm x 0.25um), gas H_2, T = 140 °C, P = 15 psi, FID temp 250 °C, injector temp 220 °C, ketone 3.11 min., R isomer 4.68 min., S isomer 5.46 min.)

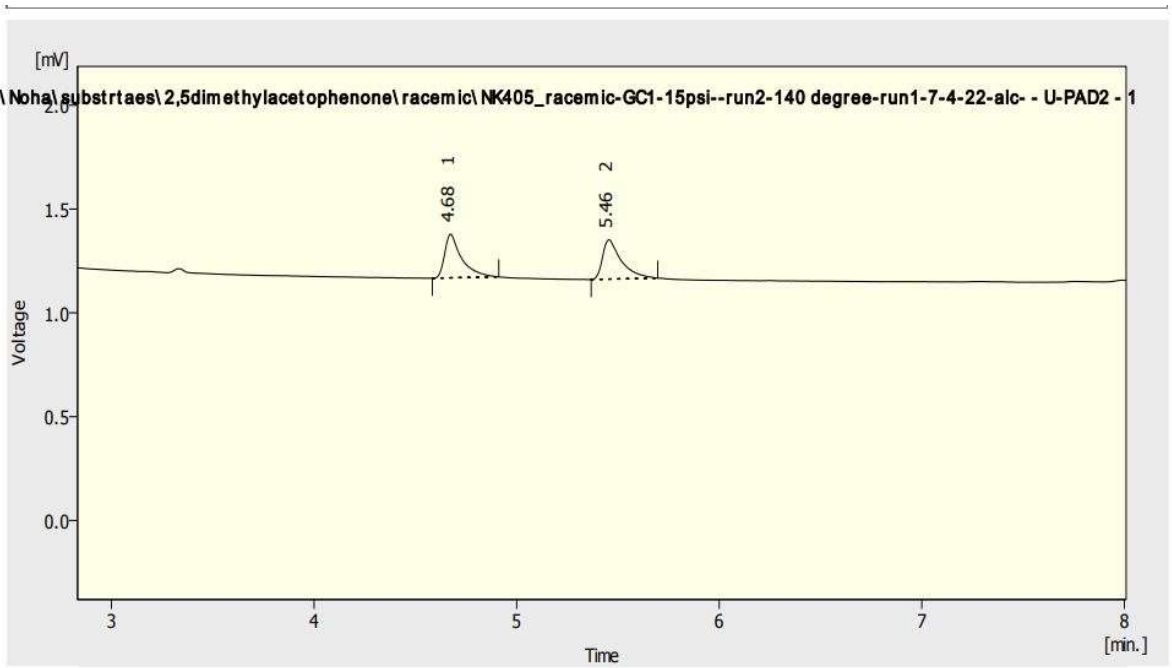
δ_H (400 MHz, $CDCl_3$)



δ_C (101 MHz, $CDCl_3$)



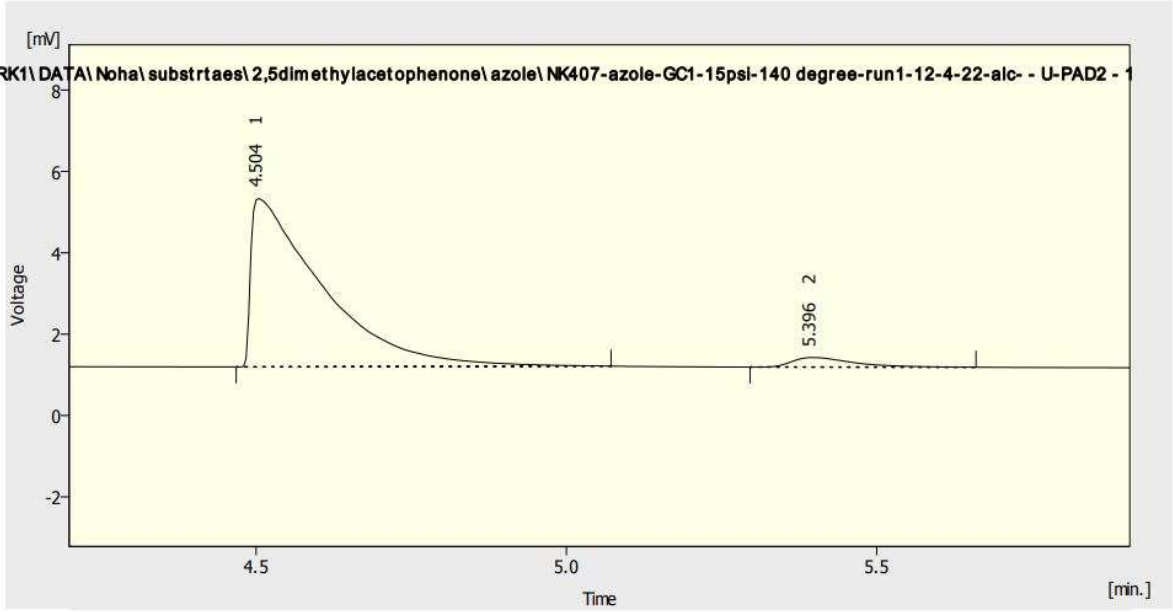
Chiral GC – racemic.



Result Table (Uncal - C:|Clarity|WORK1|DATA|Noha|substrtaes|2,5dimethylacetophenone|racemic|NK405_racemic-GC1-15psi--run2-140 degree-run1-7-4-22-alc- - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	4.676	2.438	0.421	50.1	52.4	0.08	
2	5.456	2.432	0.382	49.9	47.6	0.09	
	Total	4.870	0.802	100.0	100.0		

Chiral GC – asymmetric.



Result Table (Uncal - C:\Clarity\WORK1\DATA\Noha\substrtaes\2,5dimethylacetophenone\azole\NK407-azole-GC1-15psi-140 degree-run1-12-4-22-alc- - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	4.504	65.889	8.272	95.3	94.6	0.12	
2	5.396	3.217	0.470	4.7	5.4	0.11	
	Total	69.107	8.742	100.0	100.0		

In situ procedure has been performed using (*R*,*R*)-12f for acetophenone reduction:

To a Schlenk tube charged with $[RuCl_2(p\text{-cymene})]_2$ (3.1 mg, 5.0 x 10^{-3} mmol) and ligand **11f** (3.5 mg, 0.010 mmol) was added formic acid/triethylamine 5:2 complex (0.5 mL). After stirring for 30 min, acetophenone (120 mg, 1.00 mmol) was added and DCM (0.5 mL) was added and the reaction was stirred at rt. Upon completion, saturated $NaHCO_3$ (10 mL) was added and the product was extracted with EtOAc (3 x 10 mL). The organic extracts were combined, dried over $MgSO_4$, filtered and the solvent was removed under reduced pressure. The crude product was purified by column chromatography (0 – 50% EtOAc in Pet. Ether) to give (*R*)-1-phenylethanol as a colourless oil (100 mg, 0.823 mmol, 82%); >99% ee (*R*); GC analysis (CHROMPACCYCLODEXTRIN-β-236M-19, 50 m × 0.25 mm × 0.25 μm, gas H_2, T = 110 °C, P = 15 psi,FID temp 250 °C, injector temp 220 °C, ketone 9.09 min., *R* isomer 14.30 min., *S* isomer 15.17 min.).

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