Supporting information

Asymmetric transfer hydrogenation (ATH) of *ortho*-hydroxyphenyl ketones; utilizing directing effects which optimize the asymmetric synthesis of challenging alcohols.

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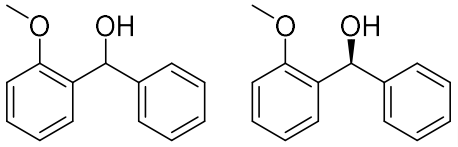
Index:

General procedures for the syntheses.

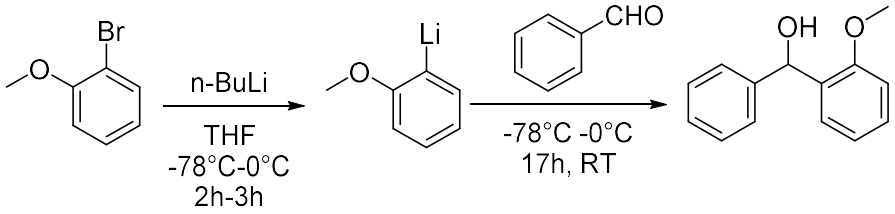
Solvents and reagents for the synthesis of complexes and catalytic reactions were degassed prior to use and all reactions were carried out under either a nitrogen or argon atmosphere. Reactions were monitored by TLC using aluminum backed silica gel 60 (F254) plates, visualized using UV 254 nm and phosphomolybdic acid (PMA), potassium permanganate or vanillin dips as appropriate. Flash column chromatography was carried out routinely using 60 micrometer silica gel. Reagents were used as received from commercial sources unless otherwise stated. 1H NMR spectra were recorded on a Bruker DPX (300, 400 or 500 MHz) spectrometer. Chemical shifts are reported in δ units, parts per million relative to the singlet at 7.26 ppm for chloroform and 0.00 ppm 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. GC analysis was performed using a Hewlett Packard 5890. Dry solvents were purchased and used as received. HPLC analyses on a Hewlett-Packard 1050 instrument. Optical rotations were measured on an AA-1000 polarimeter. The details of the X-ray instrument are given in the X-ray crystallography section. A description of the sample preparation (i.e., solvent and method for crystal growth) and crystal measurement are given for each of the four crystal structures of **8c**, **8e**, **8g**, and **C** (page S173-S174).

Synthesis and characterisation of reaction products 8a-8l.

2-Methoxyphenyl)(phenyl)methanol 8a.



Racemic: YZ193. Asymmetric: YZ198

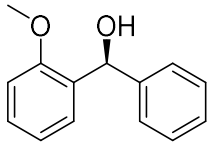


This compound has been reported and fully characterized: Li, K.; Hu, N.; Luo, R.; Yuan, W.; Tang, W.; *J. Org. Chem.;* 2013, **78**, 6350 – 6355.

To a solution of 2-bromoanisole (582 mg, 0.39 mL, 3.11 mmol) in THF (3 mL) at -78 °C was added a solution of n-butyllithium (1.13 mL, 2.5M in hexanes, 2.83 mmol). The reaction mixture was then stirred under a nitrogen atmosphere for 2-3 hours, after which benzaldehyde (300 mg, 2.83 mmol) was added dropwise. The reaction mixture was left stirring under the nitrogen atmosphere and allowed to warm to rt. The reaction was followed by TLC (9:1 hexane: EtOAc). The mixture was quenched by saturated NH_4Cl solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 × 20 mL), and the combined organic layers were dried ($MgSO_4$) and filtered. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-20% ethyl acetate in hexane to give (2-methoxyphenyl)(phenyl)methanol **8a** as a colorless oil (542.6 mg, 2.54 mmol, 90%). δ_H (400 MHz, $CDCl_3$) 7.39-7.21 (7H, m, ArOH), 6.95-6.87 (2H, m, ArH), 6.05 (1H, d, *J* = 4.0, Ar*CH*OH), 3.80 (3H, s, OCH_3), 3.01 (1H, s, ArCH*OH*) ppm; δ_C (100 MHz, $CDCl_3$) 156.8 (C), 143.3 (C), 132.0 (C), 128.8 (CH), 128.2 (CH), 127.9 (CH), 127.2 (CH), 126.6 (CH), 120.8 (CH), 110.8 (CH), 72.3 (CH), 55.4 (CH_3) ppm. Data matched that reported.

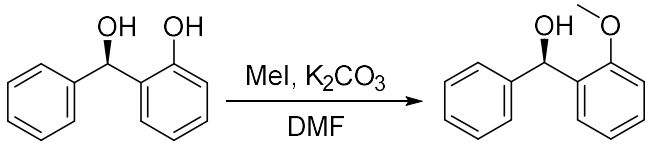
Enantiomeric excess and conversion were determined by HPLC analysis (Chiralcel ODH, 30 cm x 6mm column, hexane:iPrOH 95:5, 0.7 mL/min, T = 25°C) ketone 15.0 min, *R* isomer 33.9 min and *S* isomer 29.9 min.

ATH of (2- methoxyphenyl)(phenyl)methanone **7a** using (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst **2**.



Catalyst (*R,R*)-**2** (0.00187 mmol, 1 mol%) was added to FA: TEA (5:2 azeotropic mixture, 0.18 mL) at rt and the mixture was stirred under a nitrogen atmosphere for 10-15 minutes; after which a solution of (2- methoxyphenyl)(phenyl)methanone **7a** (40 mg, 0.187 mmol) in DCM (0.25 mL) was added. The reaction mixture was stirred under a nitrogen atmosphere, followed by TLC (9:1 hexane: EtOAc). After 168 hours, the reaction was quenched using saturated $NaHCO_3$ solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried ($MgSO_4$) and filtered. The solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-20% ethyl acetate in hexane to give (*S*)-(2-methoxyphenyl)(phenyl)methanol **8a** (28.1 mg, 0.13 mmol, 69.6%; (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst example). The reaction was also followed by HPLC (Chiralcel ODH, 30 cm x 6 mm column, hexane:iPrOH 95:5, 0.7 mL/min, T = 25°C); (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst: 81.4% conversion (HPLC calibration: 1:1 (2-methoxyphenyl)(phenyl)methanone : (2-methoxyphenyl)(phenyl)methanol gives 13.9:1 ratio of absorption at 254 nm); $[\alpha]_D^{24}$ -28.1 (c 1.405 in $CHCl_3$) 73.4% ee (*S*) (lit. $[\alpha]_D^{20}$ +16.3 (c 0.62 in $CHCl_3$) 84% ee (*R*)) Reference: Li, K.; Hu, N.; Luo, R.; Yuan, W.; Tang, W.; *J. Org. Chem.* **2013**, *78*, 6350 – 6355.

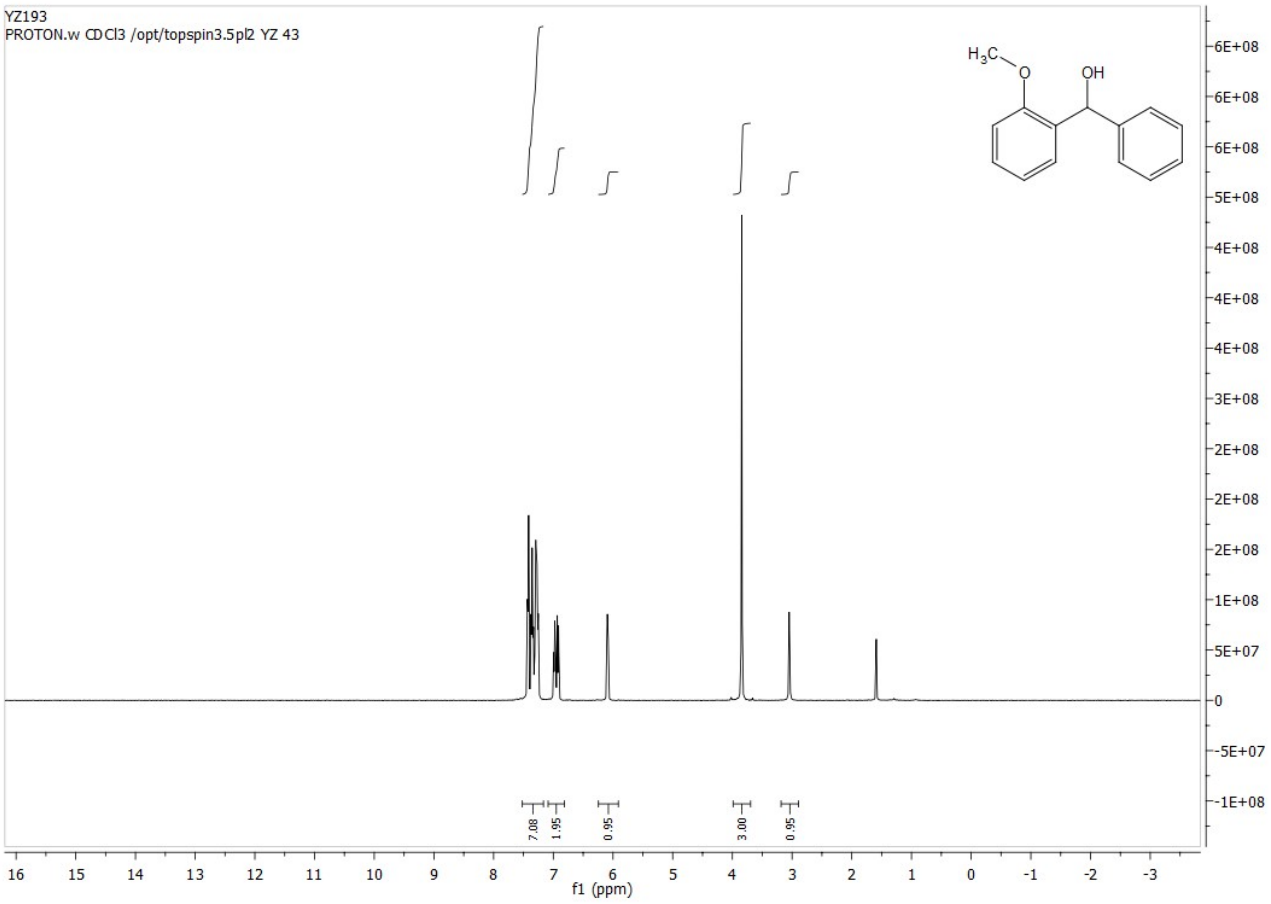
Formation of **8a** by methylation of **8b** (YZ219) to compare with ATH above (YZ198) to confirm configuration.



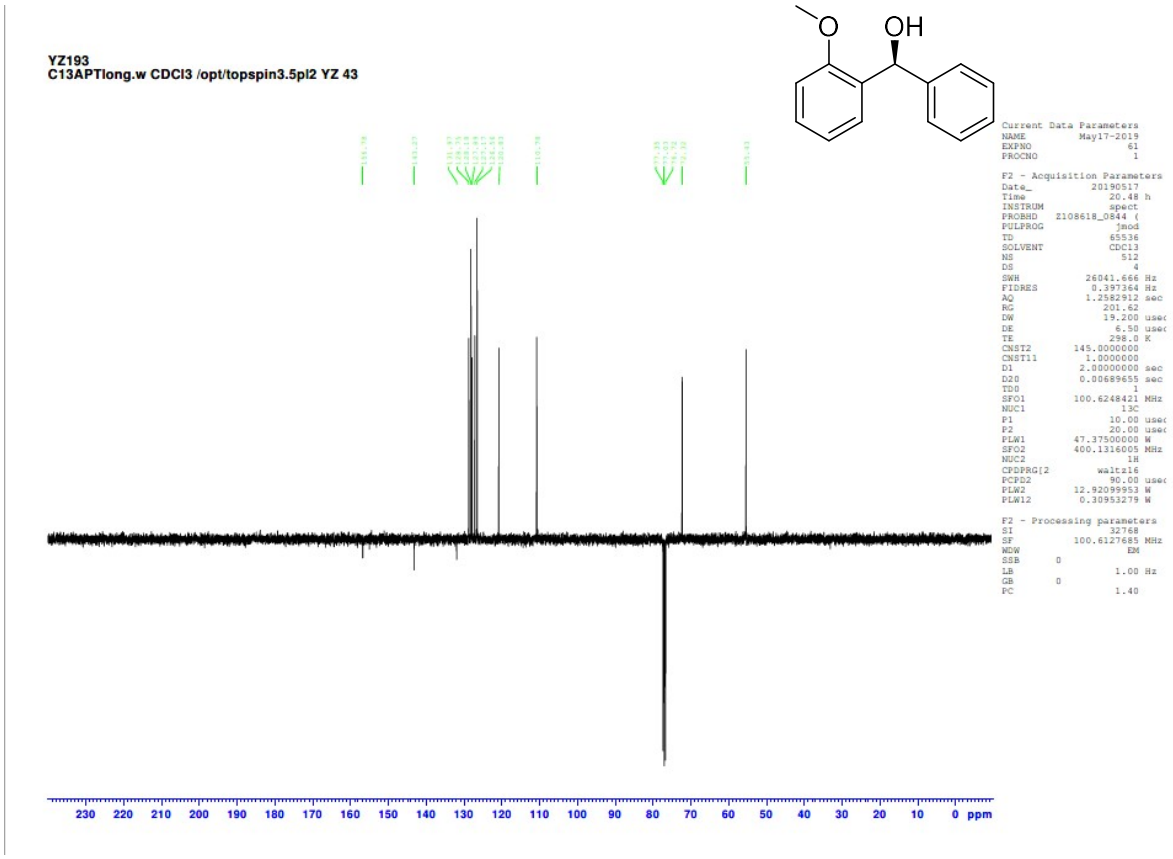
To a solution of asymmetric (*R*)-2-(hydroxy(phenyl)methyl)phenol **8b** (200 mg, 1.0 mmol) in DMF (10 mL) was added potassium carbonate (165.6 mg, 1.2 mmol) and iodomethane (156 mg, 1.0 mmol) at rt. The mixture was heated to 70 °C on a hot plate and stirred under a nitrogen atmosphere overnight. TLC (9:1 hexane: EtOAc) after this time indicated full conversion. Solvent was removed to give the crude product. The product was isolated via flash chromatography on

silica eluted with 0-20% ethyl acetate in hexane to give asymmetric (*R*)-(2-methoxyphenyl)(phenyl)methanol **8a** as a colorless oil (186.3 mg, 0.87 mmol, 87%). The reaction was also followed by HPLC analysis (Chiralcel ODH, 30 cm x 6mm column, hexane:iPrOH 95:5, 0.7 mL/min, T = 25°C): 77.4% ee (*R* configuration). It was shown that the product of ATH of **7b** using the same catalyst (YZ157- see below) was of *R* configuration by comparison with the HPLC of the ATH product formed from **7a** (YZ 198).

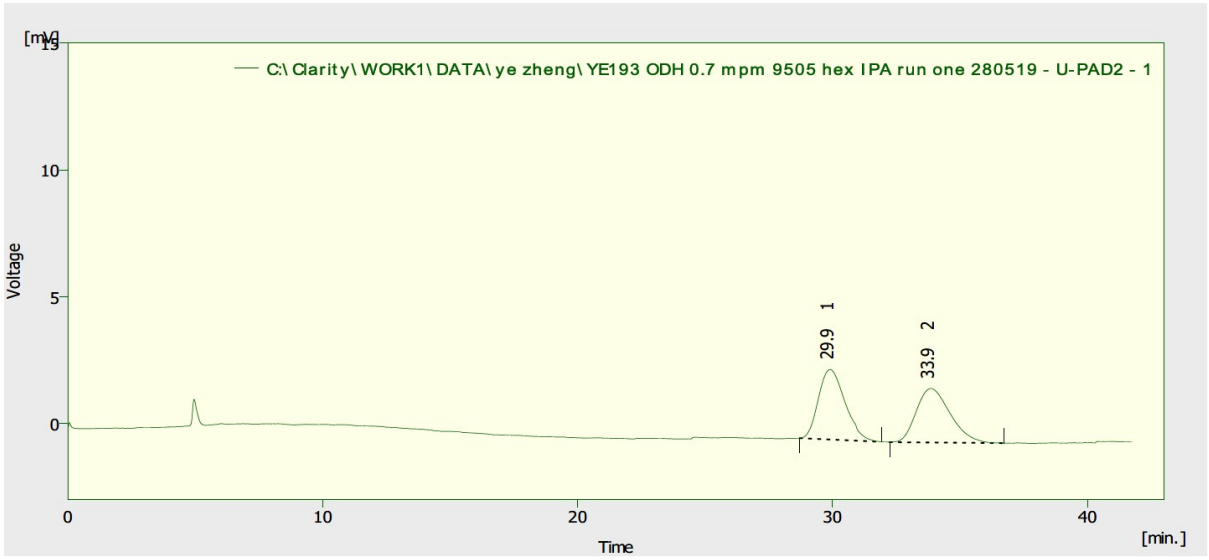
^{1}H NMR (400 MHz, $CDCl_3$) **of 8a**:



^{13}C NMR (100 MHz, $CDCl_3$) of **8a**:



HPLC of racemic (2-methoxyphenyl)(phenyl)methanol **8a:**

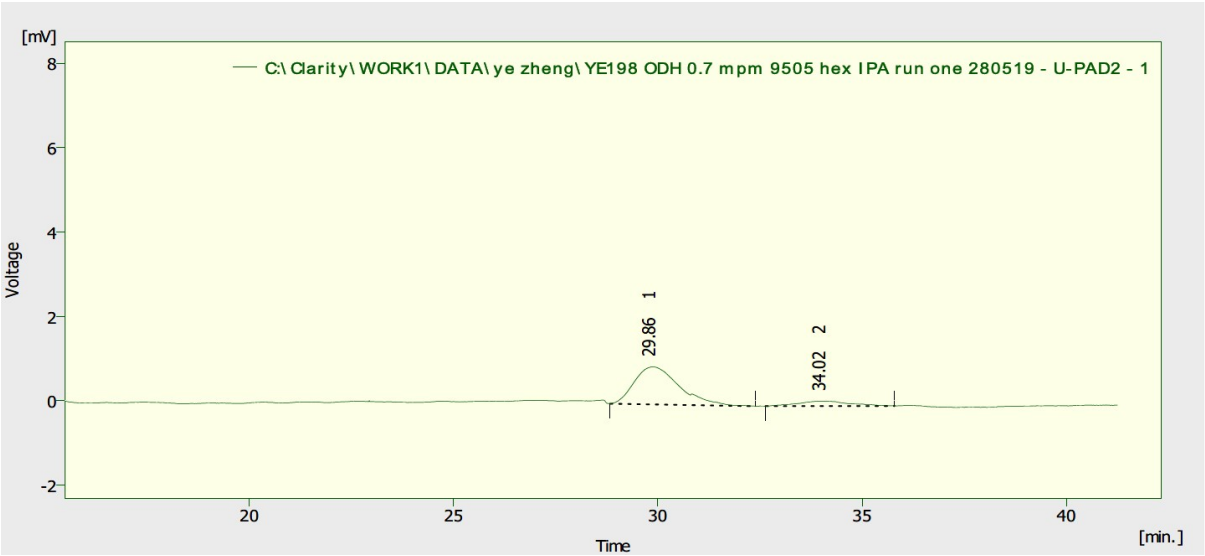


Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|ye zheng\|YE193 ODH 0.7 mpm 9505 hex IPA run one 280519 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	29.908	200.476	2.767	50.4	56.5	1.14	
2	33.852	197.017	2.133	49.6	43.5	1.44	
	Total	397.492	4.900	100.0	100.0		

HPLC of **8a** after ATH of (2-methoxyphenyl)(phenyl)methanone **7a**:

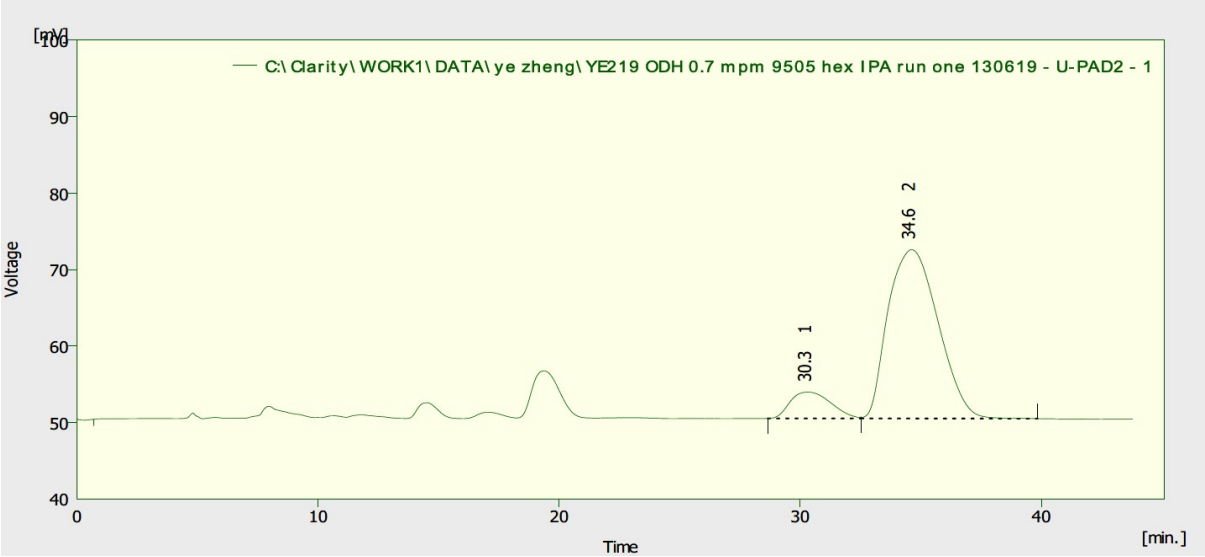
(*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst (after 168 hours, 81.4% conversion, 73.4% ee, *S* configuration).



Result Table (Uncal - C:|Clarity|WORK1|DATA|ye zheng|YE198 ODH 0.7 mpm 9505 hex IPA run one 280519 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	29.860	68.126	0.893	86.7	88.2	1.15	
2	34.020	10.495	0.119	13.3	11.8	1.21	
	Total	78.621	1.013	100.0	100.0		

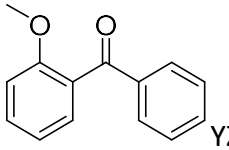
HPLC of **8a** after methylation of 2-(hydroxy(phenyl)methyl)phenol **8b** (YZ219, 77.4% ee, *R* configuration):



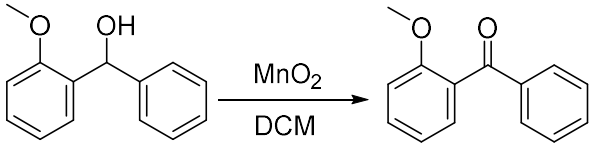
Result Table (Uncal - C:|Clarity|WORK1|DATA|ye zheng|YE219 ODH 0.7 mpm 9505 hex IPA run one 130619 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	30.316	405.456	3.448	11.3	13.5	1.94	
2	34.624	3185.586	22.093	88.7	86.5	2.38	
	Total	3591.042	25.541	100.0	100.0		

(2-Methoxyphenyl)(phenyl)methanone 7a.



YZ196

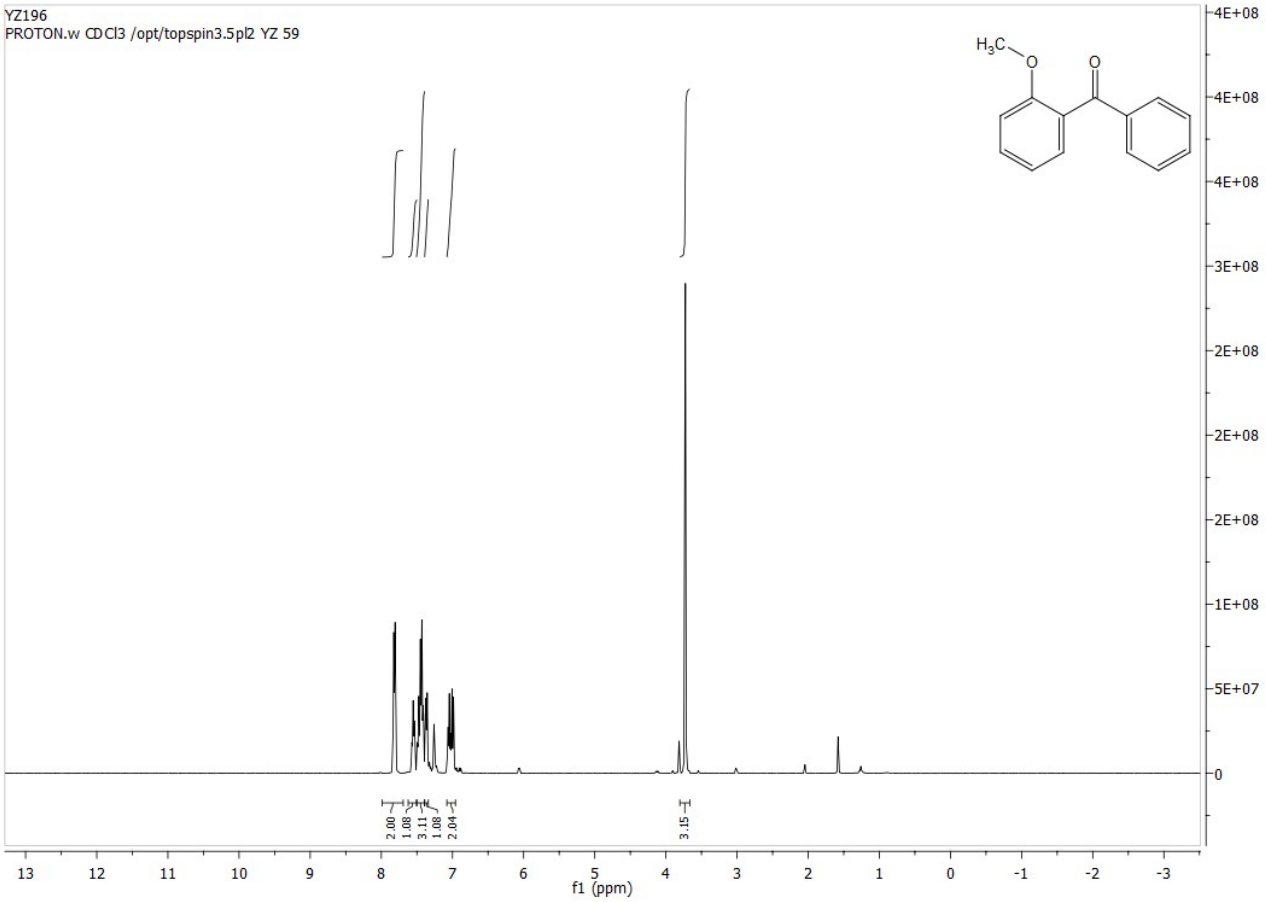


This compound has been reported and fully characterized.

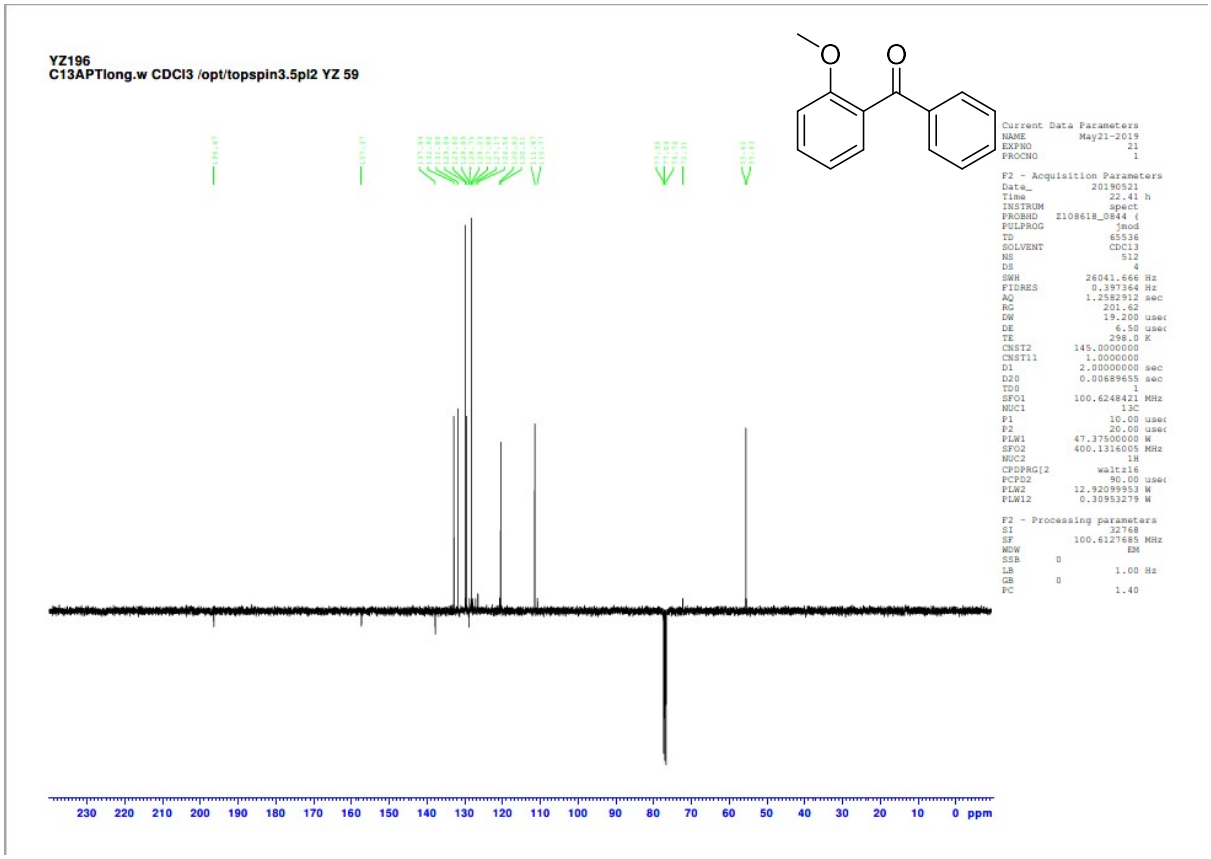
Reference: Forbes, Alaina M.; Meier, G. P.;, Jones-Mensah, E.; Magolan, J. *Eur. J. Org. Chem.;* **2016**, *2016*, 2983 – 2987.

To a solution of (2-methoxyphenyl)(phenyl)methanol **8a** (300 mg, 1.40 mmol) in DCM (10 mL) at rt was added manganese dioxide (1.8 g, 21 mmol). The reaction mixture was stirred under a nitrogen atmosphere overnight. TLC (9:1 hexane: EtOAc) after this time indicated full conversion. The solids were removed by gravity filtration and washed with DCM. The solvent was removed to give the product **7a** as a colorless oil (277.7 mg, 1.31 mmol, 93.5%). TLC: Rf ca 0.40 (9:1 hexane: EtOAc), strong UV and $KMnO_4$; δ_H (400 MHz, $CDCl_3$) 7.83 (2H, d, *J* = 7.2, ArH), 7.57-7.54 (1H, m, ArH), 7.49-7.41 (3H, m, ArH), 7.37 (1H, d, *J* = 7.2, ArH), 7.06-6.99 (2H, m, ArH), 3.73 (3H, s, OCH_3) ppm; δ_C (100 MHz, $CDCl_3$) 196.5 (C), 157.4 (C), 137.8 (C), 132.9 (CH), 131.9 (CH), 129.8 (CH), 129.6 (CH), 128.9 (C), 128.2 (CH), 120.5 (CH), 111.5 (CH), 55.5 (CH_3) ppm. Data matched that reported.

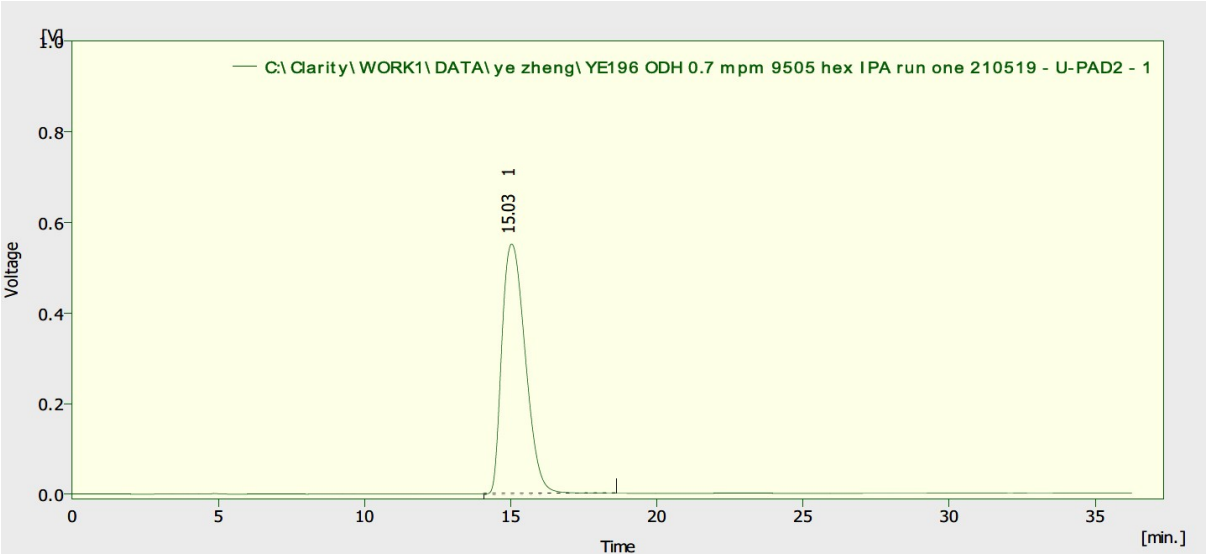
^{1}H NMR (400 MHz, $CDCl_3$) of **7a**:



^{13}C NMR (100 MHz, $CDCl_3$) of **7a**:



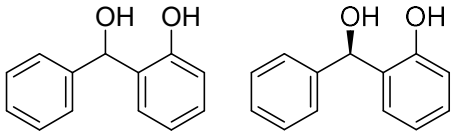
HPLC of (2-methoxyphenyl)(phenyl)methanone **7a**:

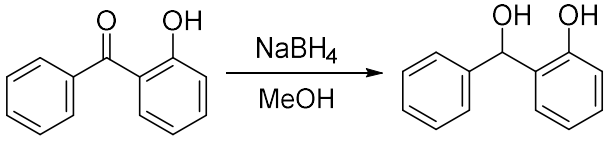


Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|ye zheng\|YE196 ODH 0.7 mpm 9505 hex IPA run one 210519 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	15.032	30733.762	551.660	100.0	100.0	0.89	
	Total	30733.762	551.660	100.0	100.0		

2-(Hydroxy(phenyl)methyl)phenol 8b.


racemic: YZ158, Asymmetric: YZ157



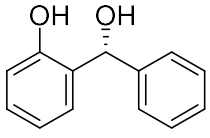
This compound has been reported and fully characterized.

Reference: Su, B.; Zhou, T. G.; Xu, P. L.; Shi, Z. J.; Hartwig, J. F.; *Angew. Chem. Int. Ed.* **2017**, *56*, 7205 – 7208. The starting material ketone is commercially available.

To a solution of 2-hydroxybenzophenone **7b** (80 mg, 0.40 mmol) in MeOH (2 mL) was added sodium borohydride (32 mg, 0.82 mmol). The reaction was stirred for 4 hours. TLC (1:1 hexane: EtOAc) after this time indicated full conversion. Distilled water (20 mL) was added, and the mixture was extracted with EtOAc (3 × 20ml), dried with $MgSO_4$, and the solvent was removed under vacuum to give 2-(hydroxy(phenyl)methyl)phenol **8b** as a colorless oil (65 mg, 0.33 mmol, 80%). TLC: Rf ca 0.20 (1:1 hexane: EtOAc), strong UV and $KMnO_4$; δ_H (400 MHz, $CDCl_3$) 7.94 (1H, s, ArH), 7.37-7.18 (5H, m, ArH), 6.91-6.80 (3H, m, ArH), 6.00 (1H, s, *CH*OH), 3.05 (1H, s, CH*OH*) ppm; δ_C (100 MHz, $CDCl_3$) 155.5 (C), 141.8 (C), 129.3 (CH), 128.8 (CH), 128.3 (CH), 126.9 (CH), 126.6 (C), 120.0 (CH), 117.3 (CH), 77.1 (CH) ppm. Data matched that reported.

Enantiomeric excess and conversion was determined by HPLC analysis (Chiralcel ODH, 30 cm x 6mm column, hexane:iPrOH 9:1, 1.0 mL/min, T = 25°C) ketone 5.4 min, *S* isomer 13.1 min and *R* isomer 20.2 min.

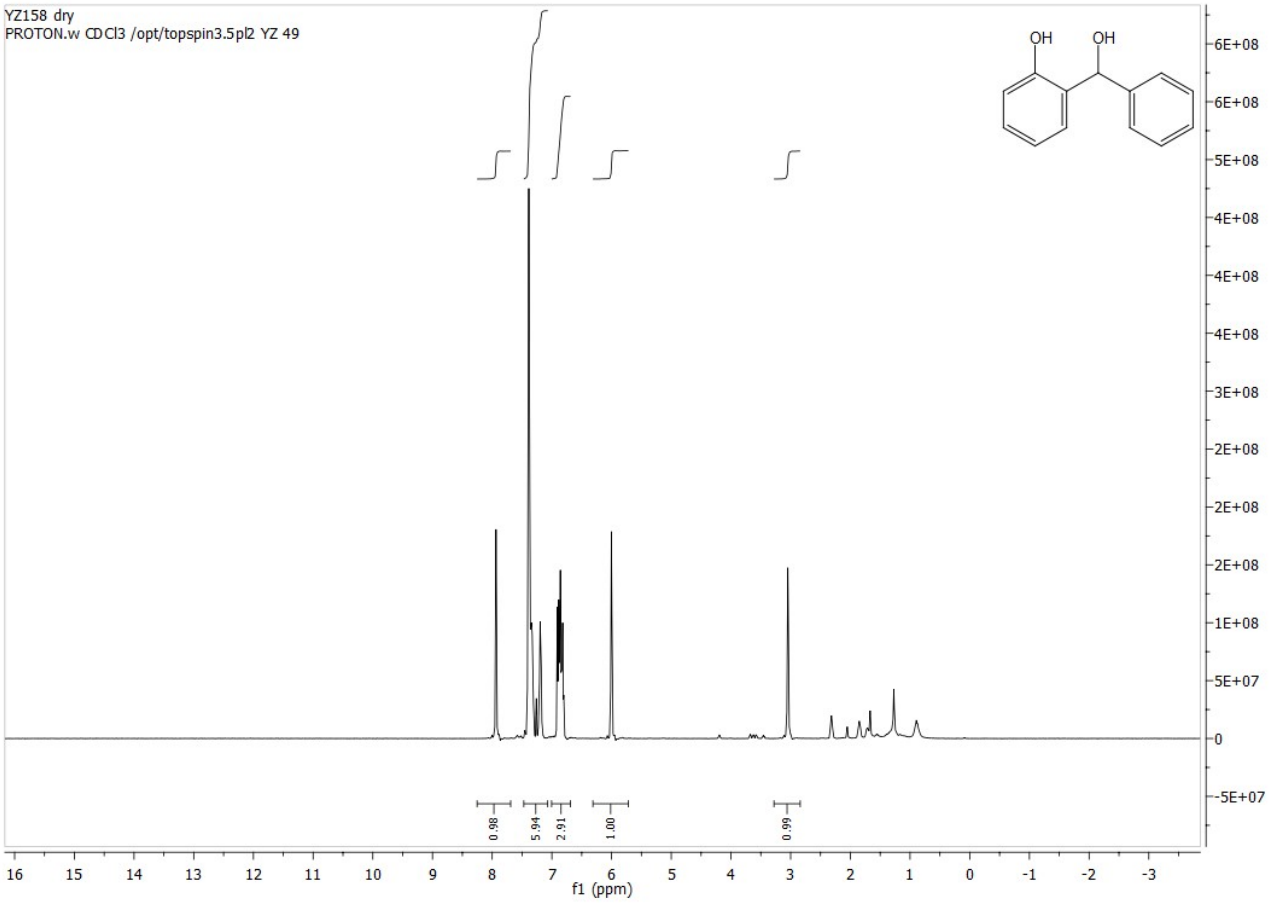
Reduction of **7b** to give (*R*)-**8b** using (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst **2** (YZ157).



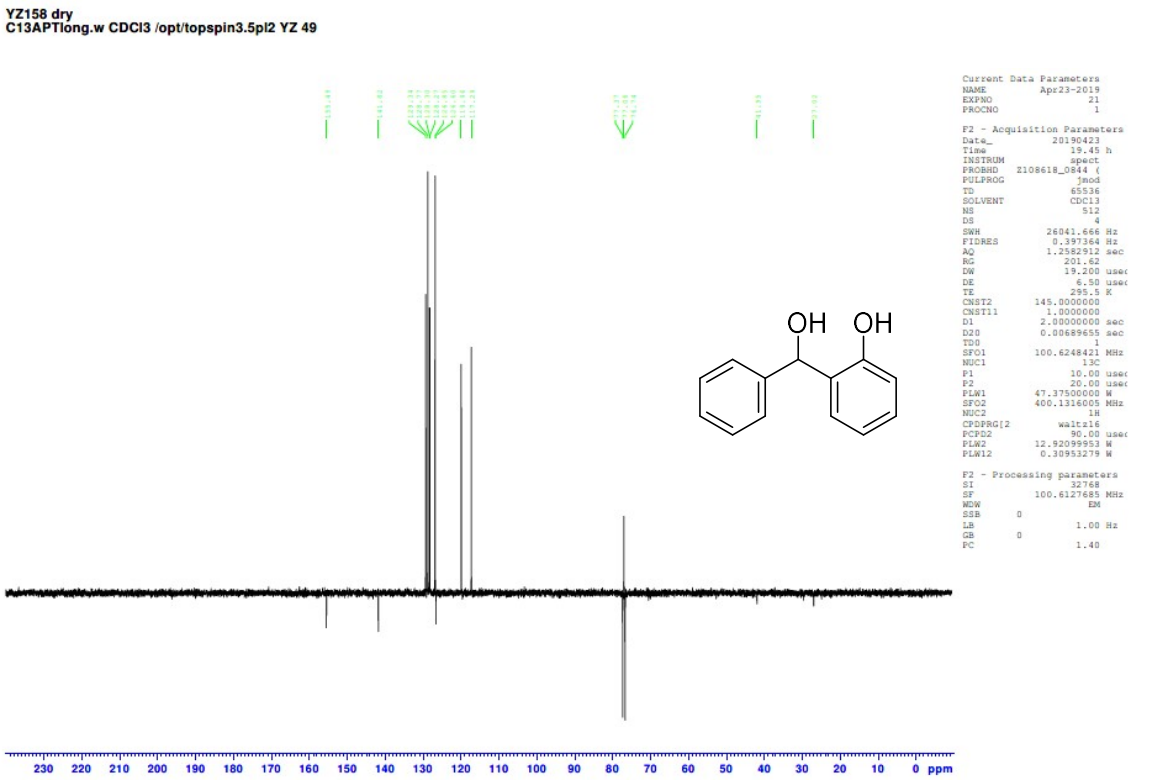
Catalyst (*R,R*)-**2** (0.0020 mmol, 1 mol%) was added to FA: TEA (5:2 azeotropic mixture, 0.18 mL) at rt and the mixture was stirred under a nitrogen atmosphere for 10-15 minutes; after which a solution of 2-hydroxybenzopenone **7b** (40 mg, 0.20 mmol) in DCM (0.25 mL) was added. The reaction mixture was stirrer under a nitrogen atmosphere, followed by TLC (1:1 hexane: ethyl acetate). After 72 hours, the reaction was quenched using saturated $NaHCO_3$ solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted

with EtOAc (3 x 20 mL) and the combined organic layers were dried ($MgSO_4$) and filtered. The solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 25-100% ethyl acetate in hexane to give (*R*)-2-(hydroxy(phenyl)methyl)phenol **8b** (32.6 mg, 0.16 mmol, 80.7%; (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst example). The reaction was also followed by HPLC analysis (Chiralcel ODH, 30 cm x 6mm column, hexane:iPrOH 9:1, 1.0 mL/min, T = 25°C); (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst: 100% conversion; $[\alpha]_D^{26}$ -4.38 (c 0.65 in MeCN) 80% ee (*R*) (lit. $[\alpha]_D^{20}$ -12.8 (c 1.2 in MeCN) 91% ee (*R*)) Reference: Su, B.; Zhou, T. G.; Xu, P. L.; Shi, Z. J.; Hartwig, J. F. *Angew. Chem. Int. Ed.* **2017**, *56*, 7205 – 7208.

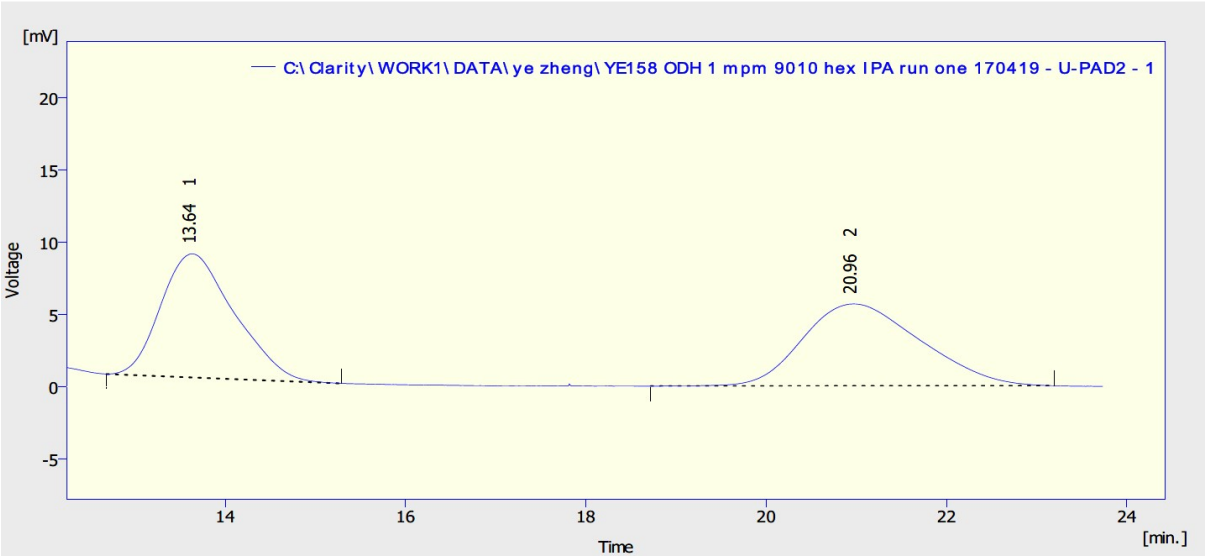
^1H NMR (400 MHz, $CDCl_3$) of **7b**:



^{13}C NMR (100 MHz, $CDCl_3$) of **7b**:



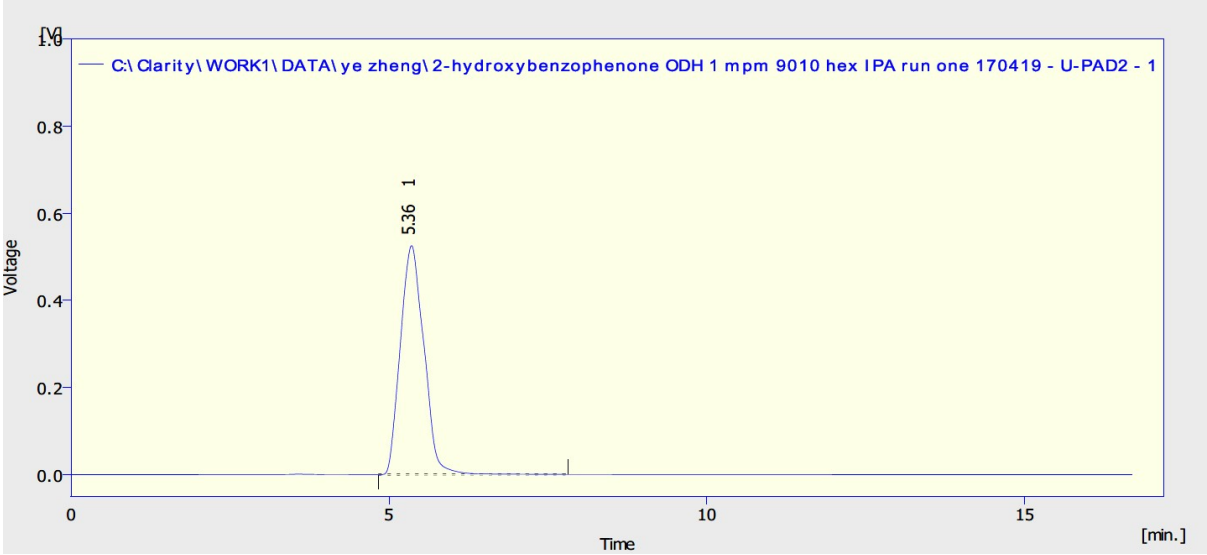
HPLC of racemic 2-(hydroxy(phenyl)methyl)phenol **7b**:



Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|ye zheng\|YE158 ODH 1 mpm 9010 hex IPA run one 170419 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	13.636	483.432	8.556	48.3	60.1	0.88	
2	20.964	516.640	5.681	51.7	39.9	1.45	
	Total	1000.072	14.237	100.0	100.0		

HPLC of 2-hydroxybenzophenone **7b**:

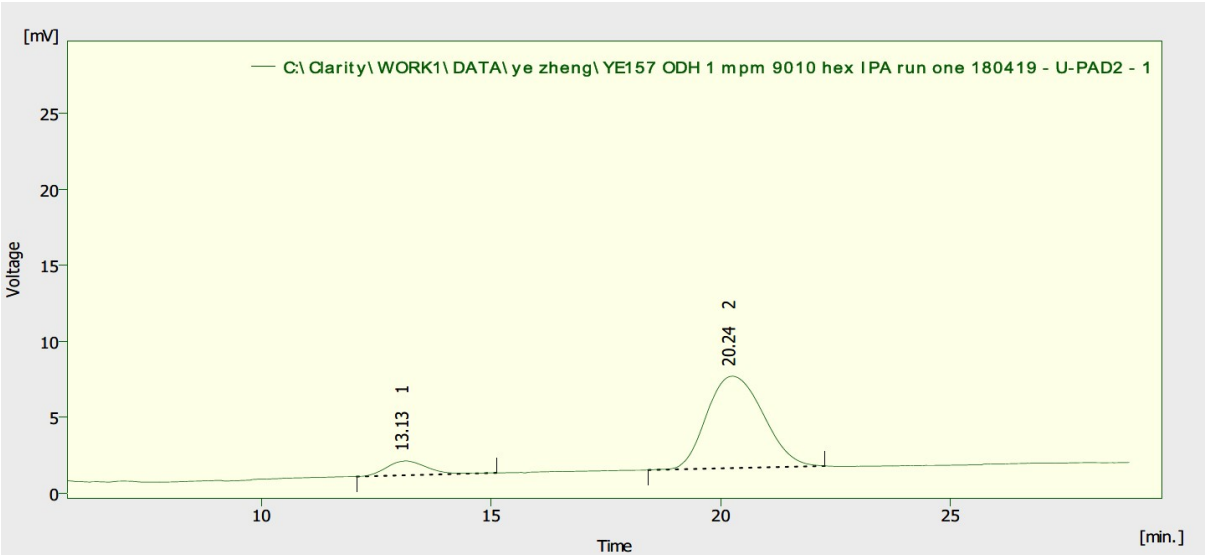


Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|ye zheng\|2-hydroxybenzophenone ODH 1 mpm 9010 hex IPA run one 170419 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	5.356	13543.315	526.167	100.0	100.0	0.42	
	Total	13543.315	526.167	100.0	100.0		

HPLC of **7a** after ATH of 2-hydroxybenzophenone **7b**:

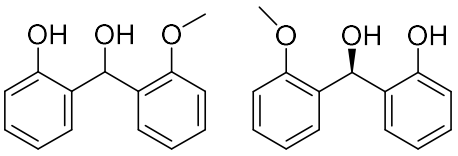
(*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst (after 72 hours, 100% conversion, 80% ee, *R* configuration)



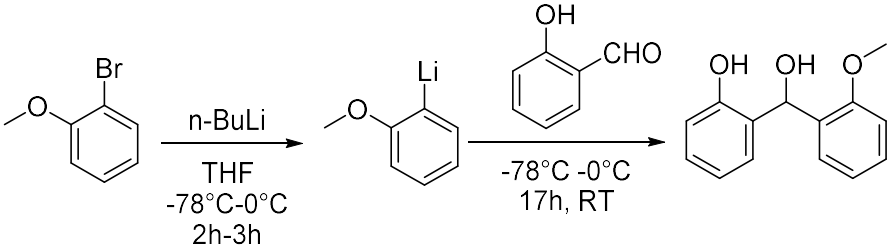
Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|ye zheng\|YE157 ODH 1 mpm 9010 hex IPA run one 180419 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	13.128	57.297	0.953	10.0	13.6	0.95	
2	20.244	517.299	6.050	90.0	86.4	1.38	
	Total	574.596	7.004	100.0	100.0		

2-(Hydroxy(2-methoxyphenyl)methyl)phenol 8c.



racemic: YZ161, YZ372**.**Asymmetric: YZ171, YZ377, YZ378, YZ379.



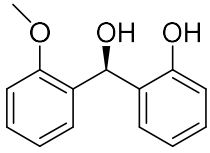
This compound has been reported and fully characterized.

Reference: Lai, Z.; Wang, Z.; Sun, J. *Org. Lett.* **2015**, *17*, 6058 – 6061.

To a solution of 2-bromoanisole (935 mg, 0.62 mL, 5.0 mmol) in THF (5 mL) at -78 °C was added dropwise a solution of n-butyllithium (2 mL, 2.5M in hexanes, 5.0 mmol). The reaction mixture was then stirred under a nitrogen atmosphere for 2-3 hours, after which salicylaldehyde (250 mg, 2.05mmol) was added dropwise. The reaction mixture was stirred under anitrogen atmosphere and allowed to warm to rt. The reaction was followed by TLC (4:1 hexane: EtOAc). The mixture was quenched by saturated NH_4Cl solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 × 20 mL), and the combined organic layers were dried ($MgSO_4$) and filtered. Solvent was removed to give the crude product **8c**. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give 2-(hydroxy(2-methoxyphenyl)methyl)phenol as a white solid (319 mg, 1.39 mmol, 67.7%). TLC: Rf ca 0.20 (4:1 hexane: EtOAc), strong UV and $KMnO_4$; δ_H (400 MHz, $CDCl_3$) 8.31 (1H, s, ArOH), 7.35-7.31 (1H, m, ArH), 7.26-7.22 (1H, m, ArH), 6.97-6.92 (4H, m, ArH), 6.81 (2H, s, ArH), 6.21 (1H, s, Ar*CH*OH), 4.09 (1H, s, ArCH*OH*), 3.91 (3H, s, OCH_3) ppm; δ_C (100 MHz, $CDCl_3$) 157.0 (C), 156.5 (C), 129.6 (CH), 129.3 (CH), 129.2 (C), 128.5 (CH), 128.0 (CH), 125.1 (C), 121.3 (CH), 119.7 (CH), 117.2 (CH), 110.8 (CH), 74.0 (CH), 55.6 (CH_3) ppm. Data matched that reported.

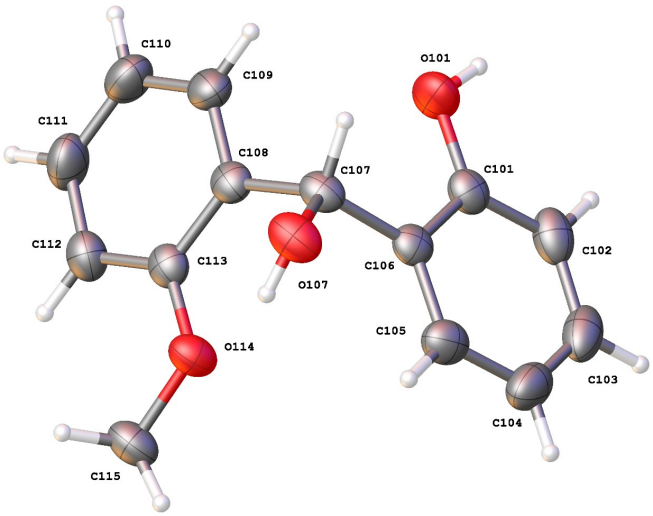
Enantiomeric excess and conversion determined by HPLC analysis (Chiralpak IC, 30 cm x 6mm column, hexane: iPrOH 9:1, 0.8 mL/min, T = 25°C) ketone 9.8 min, *R* isomer 20.5 min and *S* isomer 22.5 min ((*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst); or *R* isomer 22.1 min and *S* isomer 24.4 min ((*R,R*)-benzyl-tethered Ru(II)-TsDPEN catalyst, (*S,S*)-Noyori Ru(II)-TsDPEN catalyst and (*R,R*)-3C-tethered, 4-methoxy-Ru(II)-TsDPEN catalyst).

ATH of (2-hydroxyphenyl)(2-methoxyphenyl)methanone **7c**.



Catalyst (*R,R*)-**2** (0.00175 mmol, 1 mol%) was added to FA: TEA (5:2 azeotropic mixture, 0.18 mL) at rt and the mixture was stirred under a nitrogen atmosphere for 10-15 minutes; after which a solution of (2-hydroxyphenyl)(2-methoxyphenyl)methanone **7c** (40 mg, 0.175 mmol) in DCM (0.25 mL) was added. The reaction mixture was stirred under a nitrogen atmosphere, followed by TLC (4:1 hexane: EtOAc). After 72 hours, the reaction was quenched by saturated $NaHCO_3$ solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried ($MgSO_4$) and filtered. The solvent was removed to give the crude product **8c**. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give (*S*)-(2-hydroxyphenyl)(2-methoxyphenyl)methanol **8c** (29.1 mg, 0.13 mmol, 72%; (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst example). The reaction was also followed by HPLC analysis (Chiralpak IC, 30 cm x 6mm column, hexane:iPrOH 9:1, 0.8 mL/min, T = 25°C); (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst: 100% conversion; $[\alpha]_D^{25}$ -35.9 (c 1.0 in $CHCl_3$) 99.4% ee (*S*)

Crystal Structure of **8c**: *S* configuration CCDC 1978884 (local code yz7).
Unit Cell Parameters: a 10.53840(10) b 10.63310(10) c 20.91760(10) P212121



Crystal structure determination of [yz7]

Yz7 contains two crystallographically independent but chemically identical molecules in the asymmetric, there are eight molecules in the unit cell.

The OHs were located in a difference map and refined with distance restraints. The form H bonds tabulated below.

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

D-H	H...A	D...A	<(DHA)	
0.84	1.82	2.6295(17)	162.1	O101-H101...O207_$1
0.84	2.12	2.7533(17)	132.3	O107-H10A...O114
0.84	1.81	2.6518(16)	175.2	O201-H201...O107_$2
0.84	2.00	2.6820(18)	137.2	O207-H20A...O201

Symmetry operators used to generate symmetry related atoms discussed in the above contacts was

$1 1.5-X,1-Y,0.5+Z

$2 0.5-X,1-Y,-0.5+Z

The Flack parameter and related Hooft y parameter are small with a small error so we can be reasonably confident with the assignment of the handedness of the crystal measured

Hooft y: -0.00(3)

Flack x: -0.01(4)

Experimental

Single crystals of $C_{14}H_{14}O_3$ were grown from DCM/Hexane in a small vial at room temperature. 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 duel 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.

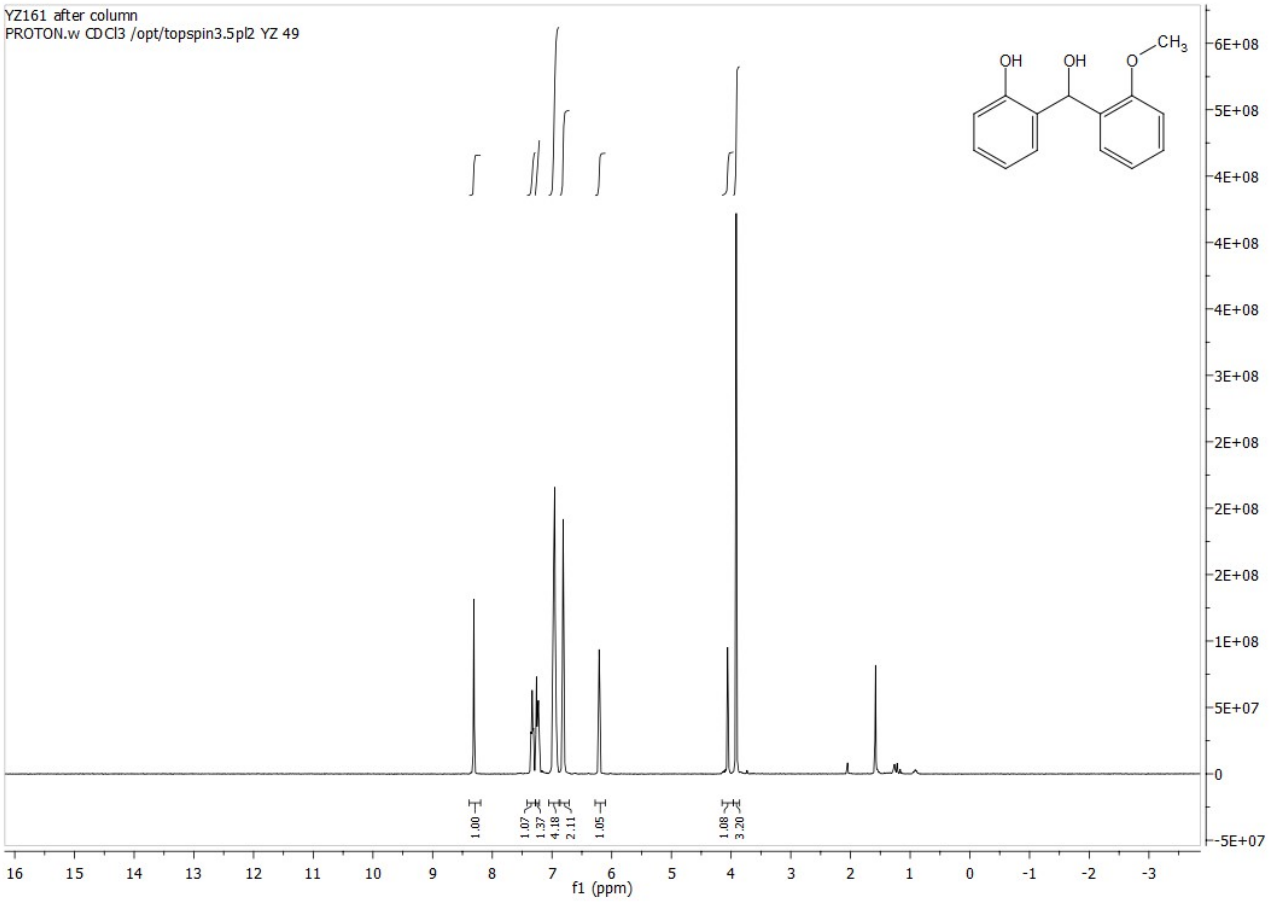
1. Dolomanov, O.V.; Bourhis, L.J.; Gildea, R.J, Howard, J.A.K. & Puschmann, H. (2009), J. Appl. Cryst. 42, 339-341.
2. Sheldrick, G.M. (2015). Acta Cryst. A71, 3-8.
3. Sheldrick, G.M. (2015). Acta Cryst. C71, 3-8.

Crystal Data for $C_{14}H_{14}O_3$ (M =230.25 g/mol): orthorhombic, space group $P2_12_12_1$ (no. 19), a = 10.53840(10) Å, b = 10.63310(10) Å, c = 20.91760(10) Å, V = 2343.94(3) Å^3, Z = 8, T = 150(2) K, μ(CuKα) = 0.744 mm^{-1}, *Dcalc* = 1.305 g/cm^3, 37252 reflections measured (8.454° ≤ 2Θ ≤ 147.264°), 4693 unique (R_{int} = 0.0255, R_{sigma} = 0.0111) which were used in all calculations. The final R_1 was 0.0280 (I > 2σ(I)) and wR_2 was 0.0781 (all data).

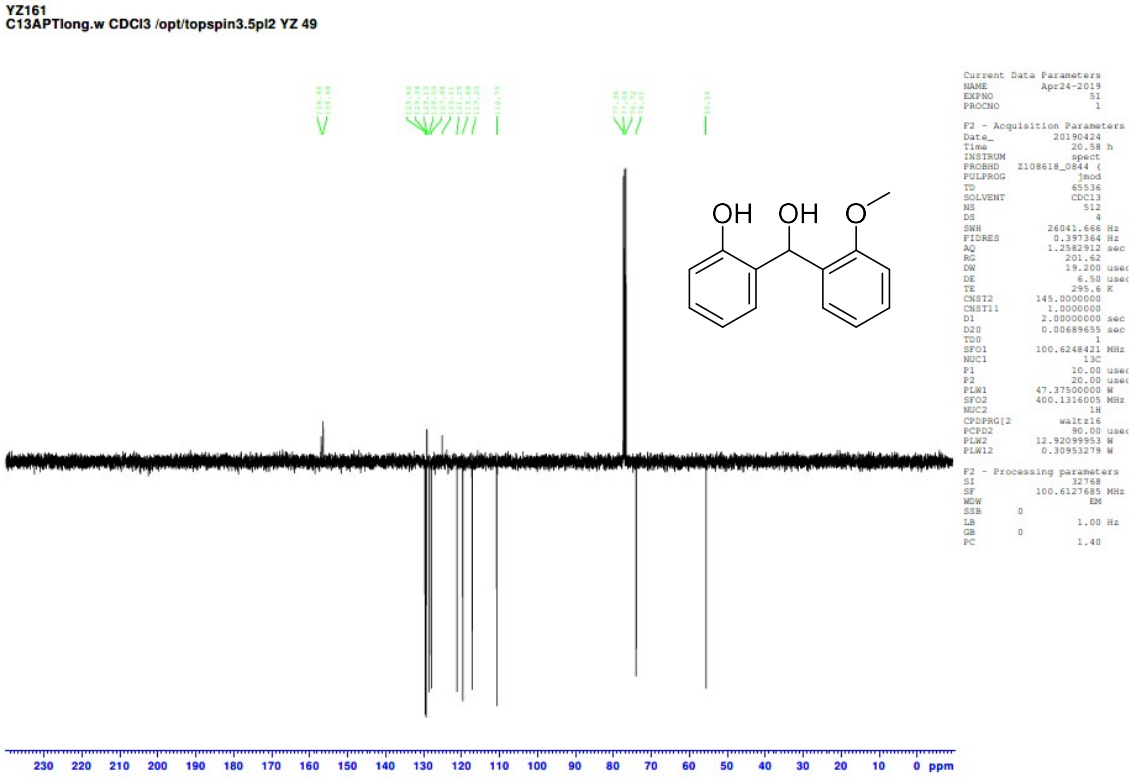
Table 1 Crystal data and structure refinement for yz7.

Identification code	yz7
Empirical formula	$C_{14}H_{14}O_3$
Formula weight	230.25
Temperature/K	150(2)
Crystal system	orthorhombic
Space group	$P2_12_12_1$
a/Å	10.53840(10)
b/Å	10.63310(10)
c/Å	20.91760(10)
α/°	90
β/°	90
γ/°	90
Volume/Å^3	2343.94(3)
Z	8
ρ_{calc}g/cm^3	1.305
μ/mm^{-1}	0.744
F(000)	976.0
Crystal size/mm^3	0.3 × 0.3 × 0.2 colourless block
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	8.454 to 147.264
Index ranges	-11 ≤ h ≤ 13, -13 ≤ k ≤ 13, -26 ≤ l ≤ 25
Reflections collected	37252
Independent reflections	4693 [R_{int} = 0.0255, R_{sigma} = 0.0111]
Data/restraints/parameters	4693/0/313
Goodness-of-fit on F^2	1.053
Final R indexes [I>=2σ (I)]	R_1 = 0.0280, wR_2 = 0.0778
Final R indexes [all data]	R_1 = 0.0282, wR_2 = 0.0781
Largest diff. peak/hole / e Å^{-3}	0.21/-0.15
Flack parameter	-0.01(4)

^{1}H NMR (400 MHz, $CDCl_3$) of **8c**:

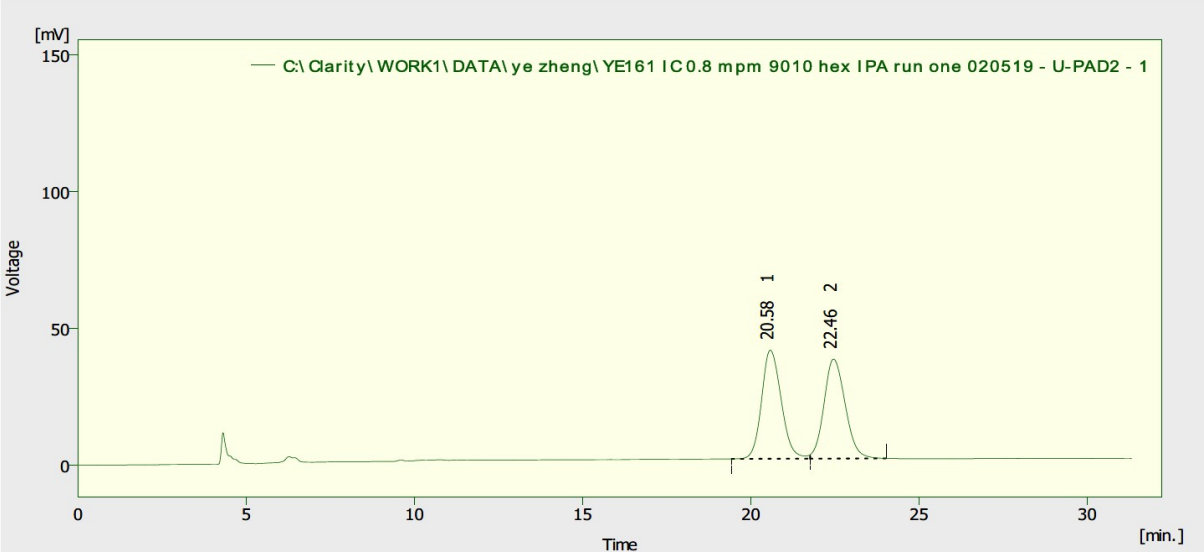


^{13}C NMR (100 MHz, $CDCl_3$) of **8c**:



HPLC of racemic 2-(hydroxy(2-methoxyphenyl)methyl)phenol **8c**:

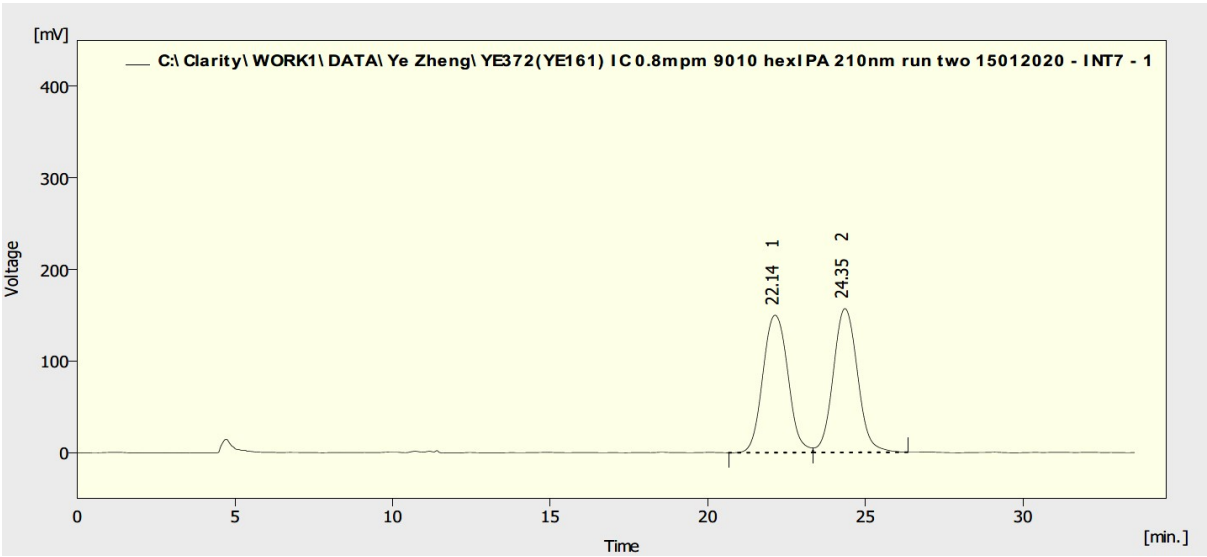
Standard for comparison with reduction using (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst: *R* isomer 20.5 min and *S* isomer 22.5 min.



Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|ye zheng\|YE161 IC 0.8 mpm 9010 hex IPA run one 020519 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	20.576	1616.757	39.756	50.3	52.2	0.62	
2	22.456	1597.039	36.440	49.7	47.8	0.68	
	Total	3213.796	76.196	100.0	100.0		

Standard of racement **8c** for comparison with reduction using (*R,R*)-benzyl-tethered Ru(II)-TsDPEN catalyst, (*S,S*)-Noyori Ru(II)-TsDPEN catalyst and (*R,R*)-3C-tethered, 4-methoxy-Ru(II)-TsDPEN catalyst: *R* isomer 22.1 min and *S* isomer 24.4 min.

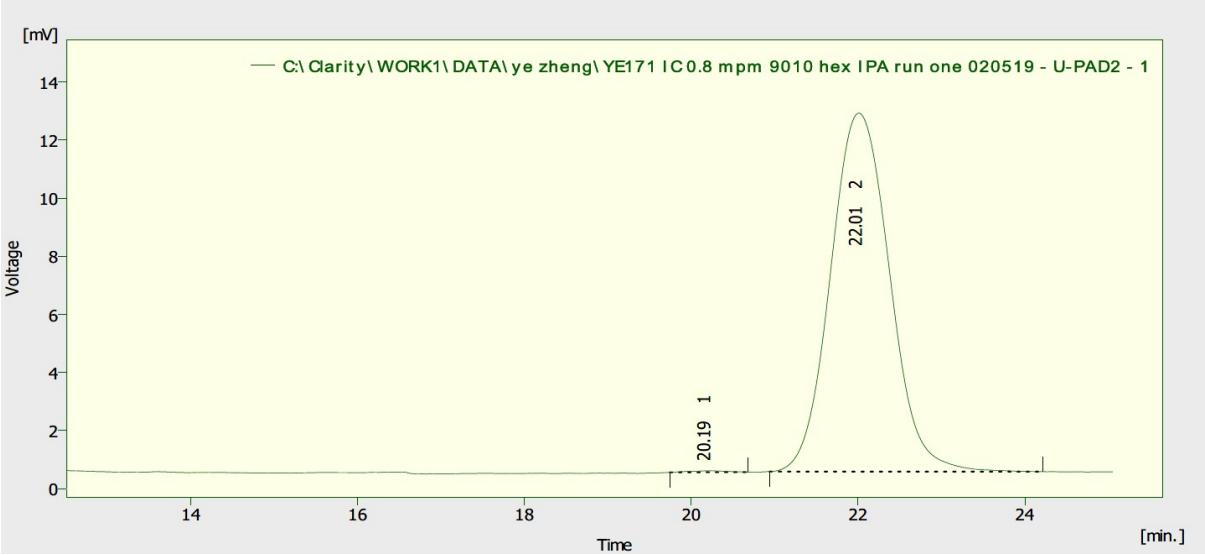


Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|Ye Zheng\|YE372(YE161) IC 0.8mpm 9010 hexIPA 210nm run two 15012020 - INT7 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	22.137	8318.831	150.063	49.7	48.9	0.88	
2	24.350	8435.403	157.068	50.3	51.1	0.83	
	Total	16754.233	307.132	100.0	100.0		

HPLC after ATH of 2-(hydroxy(2-methoxyphenyl)methyl)phenone **7c**:

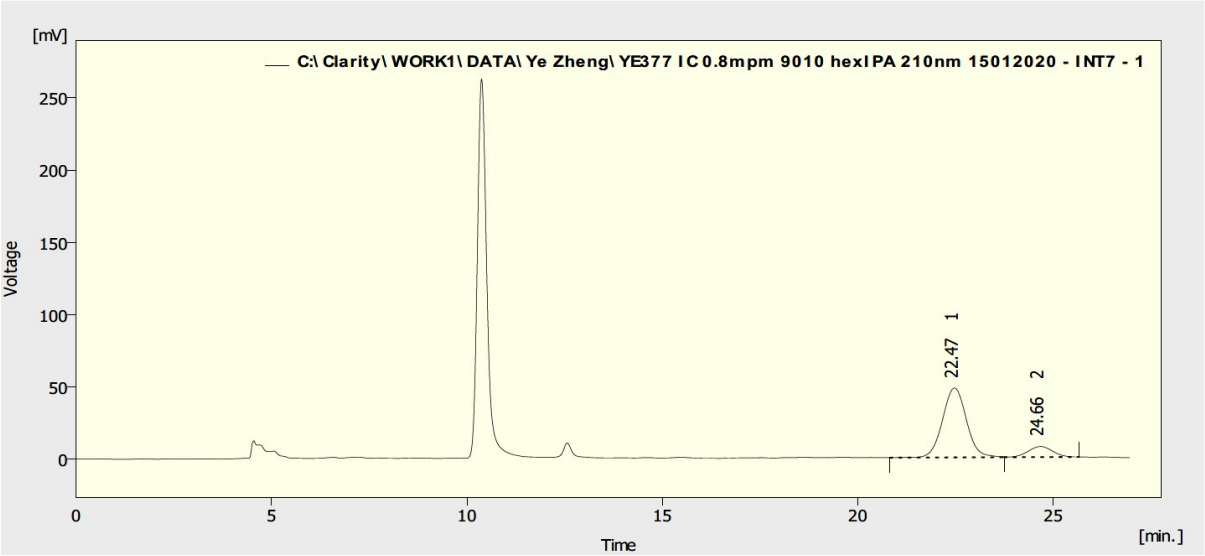
Using (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst **2** (after 72 hours, 100% conversion, 99.4% ee, *S* configuration).



Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|ye zheng\|YE171 IC 0.8 mpm 9010 hex IPA run one 020519 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	20.188	1.652	0.053	0.3	0.4	0.51	
2	22.008	607.332	12.349	99.7	99.6	0.77	
	Total	608.984	12.402	100.0	100.0		

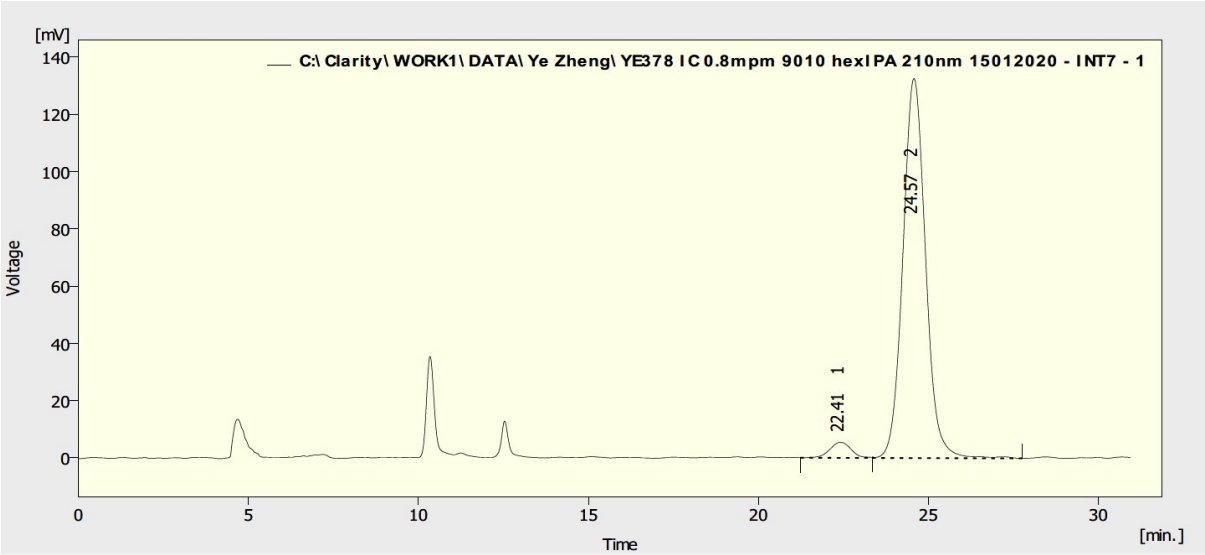
Using (*S,S*)-Noyori Ru(II)-TsDPEN catalyst **6** (after 168 hours, 48.6% conversion, 73% ee, *R* configuration).



Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|Ye Zheng\|YE377 IC 0.8mpm 9010 hexIPA 210nm 15012020 - INT7 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	22.473	2043.314	48.053	86.5	86.8	0.65	
2	24.663	318.082	7.330	13.5	13.2	0.68	
	Total	2361.396	55.382	100.0	100.0		

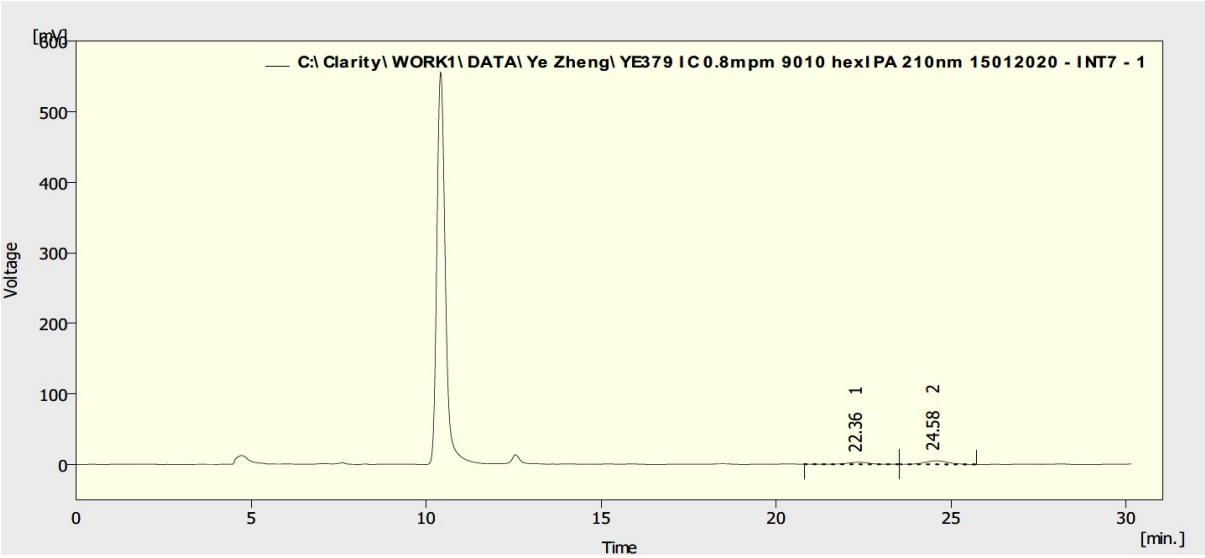
Using (*R,R*)-benzyl-tethered Ru(II)-TsDPEN catalyst **4** (after 168 hours, 84% conversion, 92.6% ee, *S* configuration).



Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|Ye Zheng\|YE378 IC 0.8mpm 9010 hexIPA 210nm 15012020 - INT7 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	22.410	238.978	5.452	3.7	3.9	0.67	
2	24.573	6144.449	132.639	96.3	96.1	0.71	
	Total	6383.426	138.092	100.0	100.0		

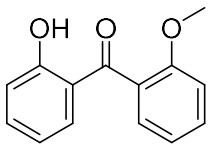
Using (*R,R*)-3C-tethered, 4-methoxy-Ru(II)-TsDPEN catalyst **5** (after 168 hours, 16% conversion, 30% ee, *S* configuration).



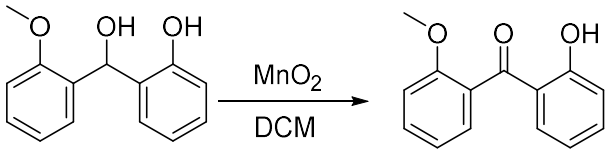
Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|Ye Zheng\|YE379 IC 0.8mpm 9010 hexIPA 210nm 15012020 - INT7 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	22.357	125.956	2.844	35.0	35.7	0.65	
2	24.577	233.426	5.113	65.0	64.3	0.70	
	Total	359.382	7.957	100.0	100.0		

2-Hydroxyphenyl)(2-methoxyphenyl)methanone 7c.



YZ164

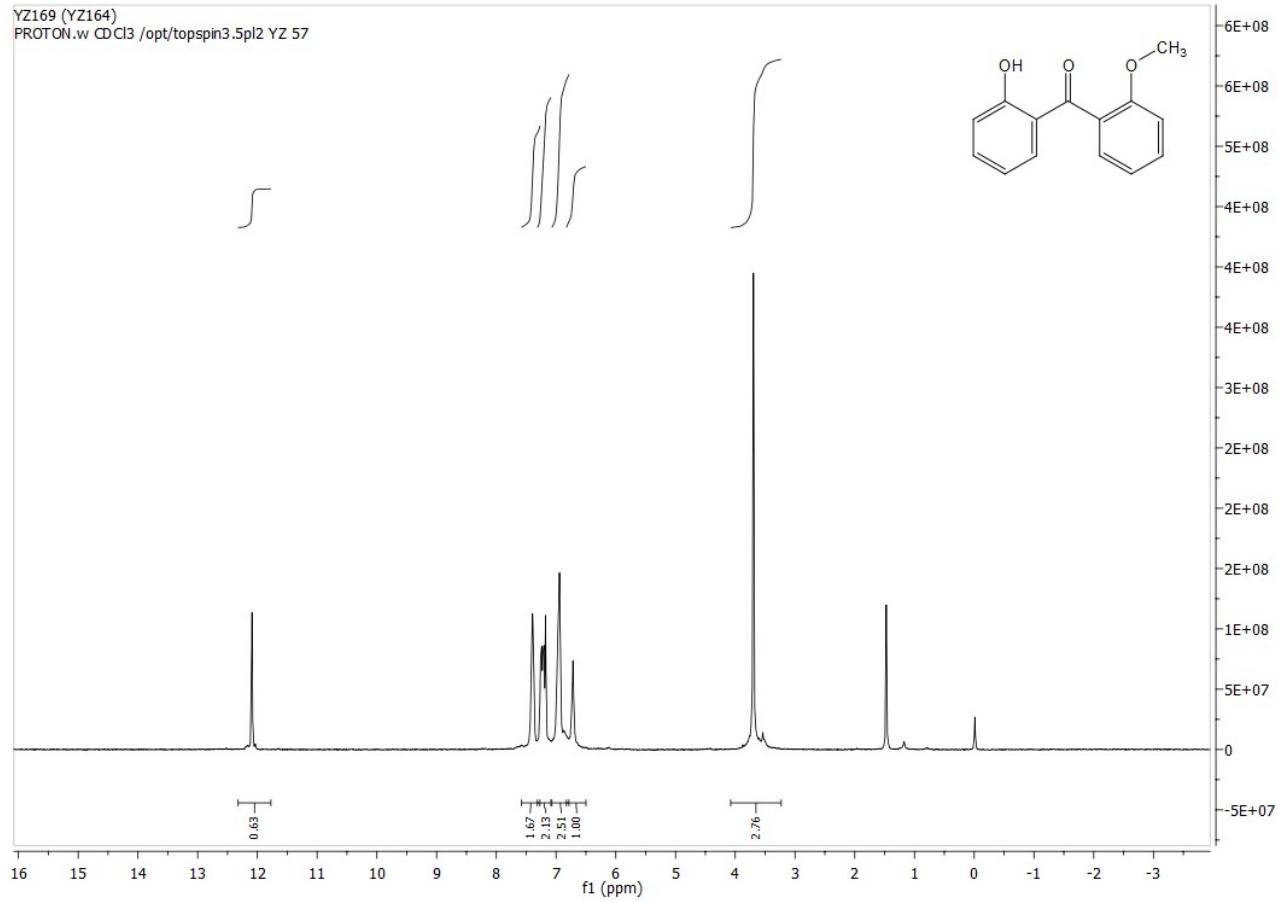


This compound has been reported and fully characterized.

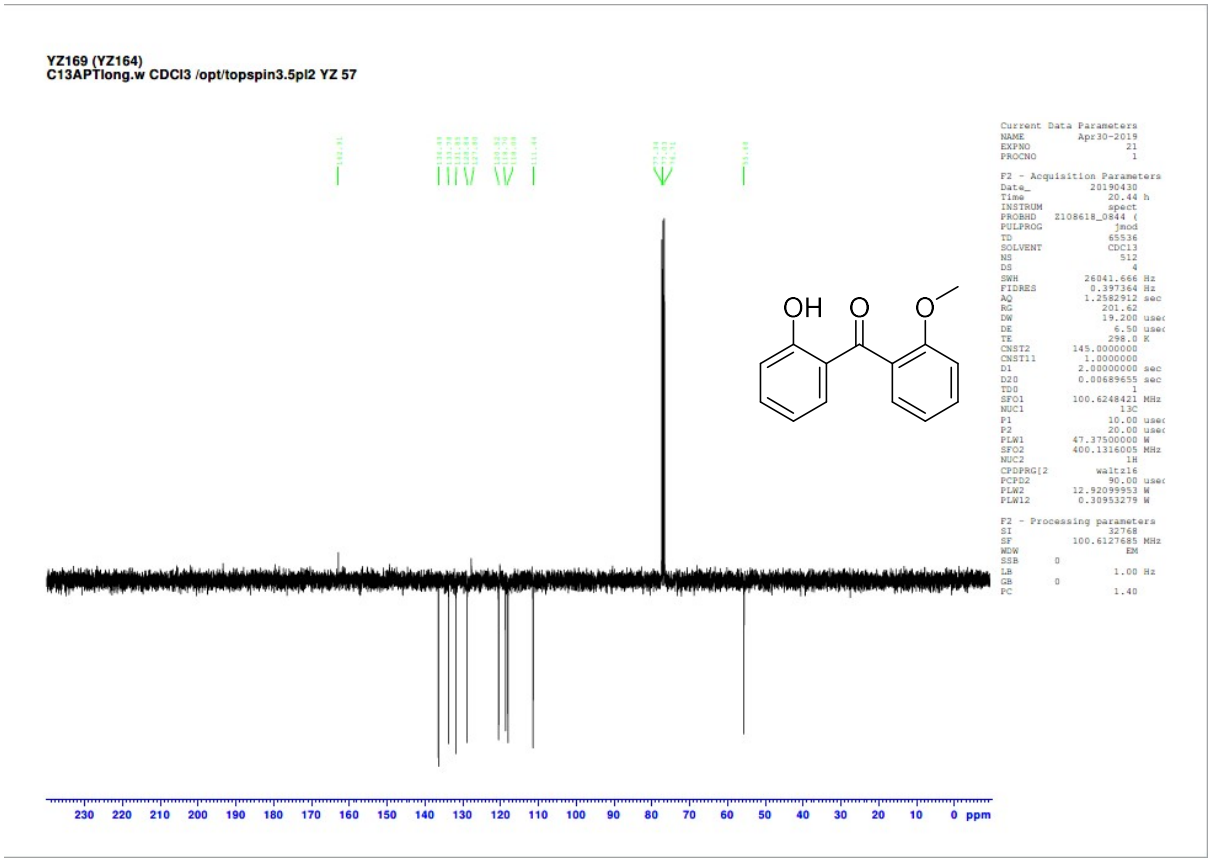
Reference: Johnson, M. M.; Naidoo, J. M.; Fernandes, M. A.; Mutlane, E. M.; van Otterlo, W. A.; de Koning, C. B. *J. Org. Chem.* **2019**, *84*, 150 – 160.

To a solution of 2-(hydroxy(2-methoxyphenyl)methyl)phenol **8c** (300 mg, 1.30 mmol) in DCM (10 mL) at rt was added manganese dioxide (1.7 g, 19.6 mmol). The reaction mixture was left to stir under a nitrogen atmosphere overnight. TLC (4:1 hexane: ethyl acetate) after this time indicated full conversion. The solids were removed by gravity filtration and the solid was washed with DCM. The combined solvent was removed to give the product **7c** as a brown oil (204 mg, 0.89 mmol, 68.6%). TLC: Rf ca 0.40 (4:1 hexane: EtOAc), strong UV and $KMnO_4$; δ_H (400 MHz, $CDCl_3$) 12.17 (1H, s, OH), 7.48-7.47 (2H, m, ArH), 7.34-7.26 (2H, m, ArH), 7.08-7.03 (3H, m, ArH), 6.82-6.78 (1H, m, ArH), 3.78 (3H, s, OCH_3) ppm; δ_C (100 MHz, $CDCl_3$) 162.9 (C), 136.5 (CH), 133.8 (CH), 131.9 (CH), 128.8 (CH), 127.8 (C), 120.5 (CH), 120.0 (C), 118.7 (CH), 118.1 (CH), 111.4 (CH), 55.7 (CH_3) ppm. Data matched that reported.

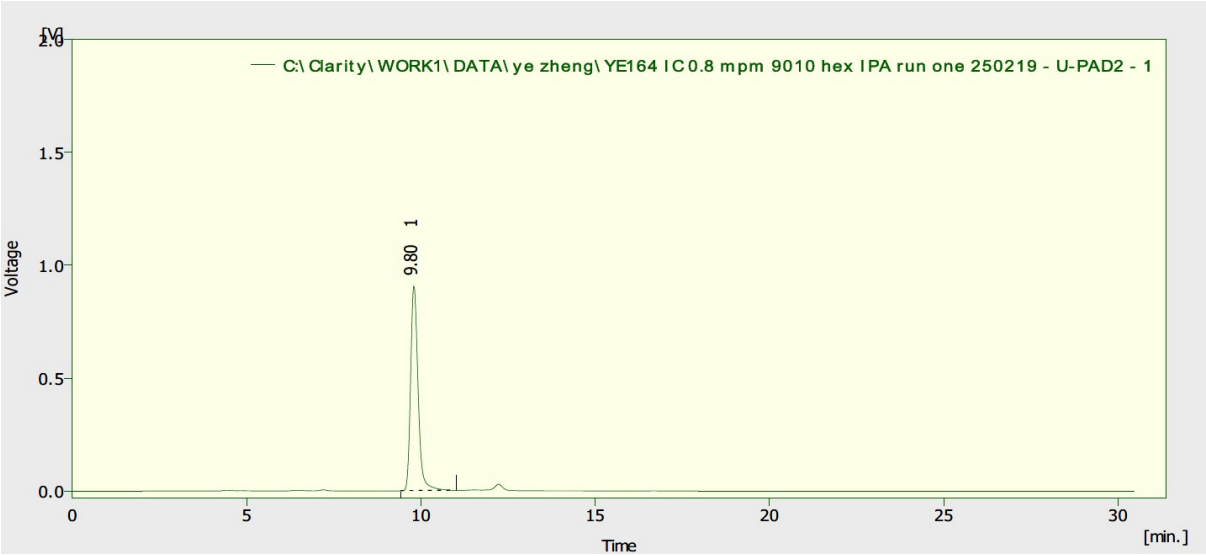
^{1}H NMR (400 MHz, $CDCl_3$) of **7c**:



^{13}C NMR (100 MHz, $CDCl_3$) of **7c**:



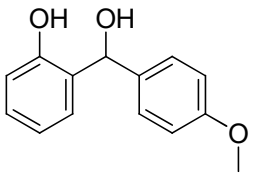
HPLC of (2-hydroxyphenyl)(2-methoxyphenyl)methanone **7c**:



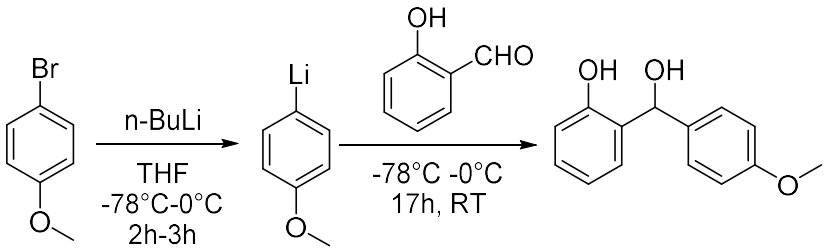
Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|ye zheng\|YE164 IC 0.8 mpm 9010 hex IPA run one 250219 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	9.800	13594.575	908.907	100.0	100.0	0.22	
	Total	13594.575	908.907	100.0	100.0		

2-(Hydroxy(4-methoxyphenyl)methyl)phenol 8d.



racemic: YZ207, Asymmetric: YZ213



This compound has been reported and fully characterized.

Reference: Lanzi, M.; Merad, J.; Boyarskaya, D. V.; Maestri, G.; Allain, C.; Masson, G.; *Org. Lett.* 2018, **20**, 5247-5250.

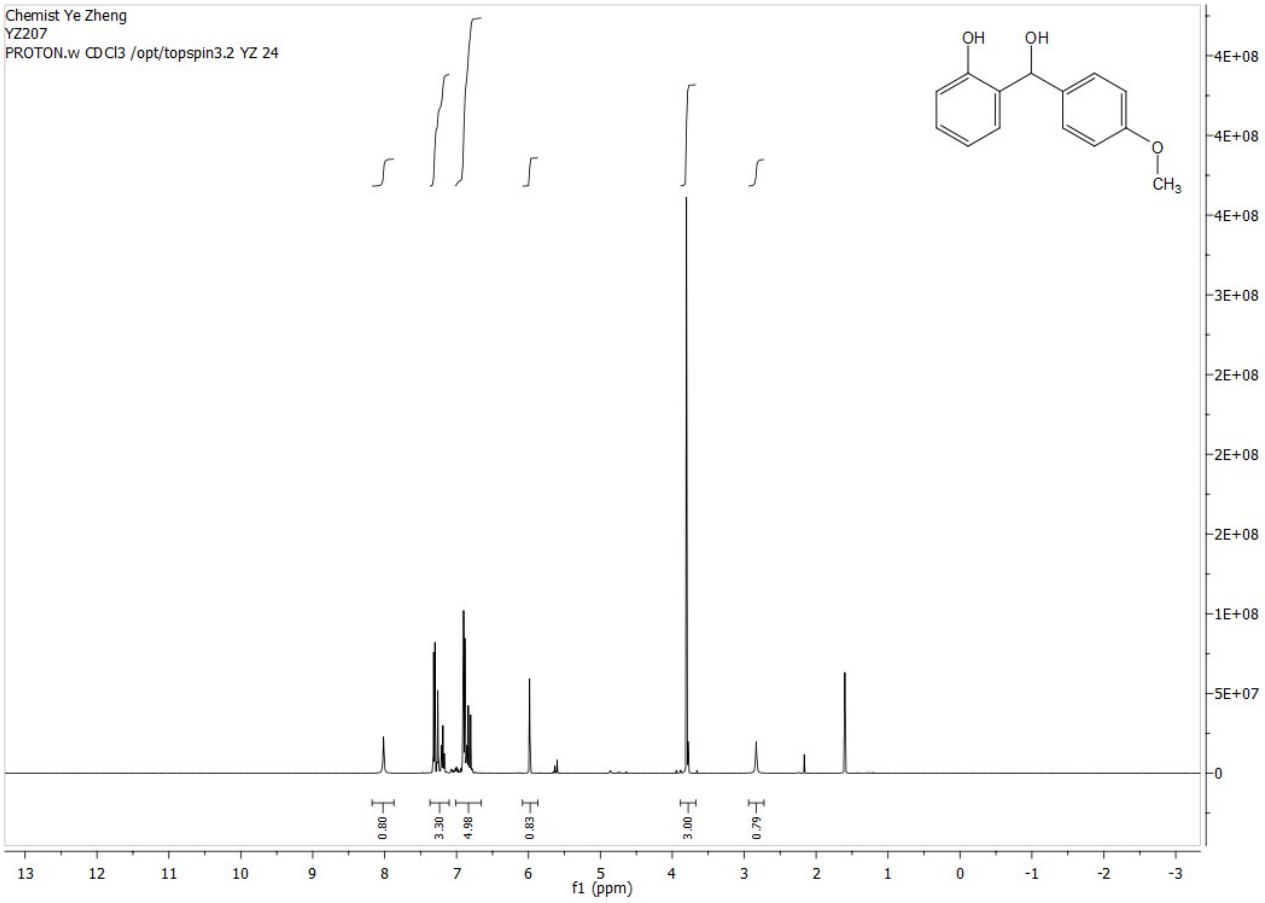
To a solution of 4-bromoanisole (935 mg, 0.62 mL, 5.0 mmol) in THF (5 mL) at -78 °C was added dropwise a solution of n-butyllithium (2.0 mL, 2.5M in hexanes, 5.0 mmol. The reaction mixture was then stirred under a nitrogen atmosphere for 2-3 hours, after which salicylaldehyde (305 mg, 2.50 mmol) was added dropwise. The reaction mixture was stirred under the nitrogen atmosphere and allowed to warm to rt. The reaction was followed by TLC (4:1 hexane: EtOAc). The mixture was quenched by saturated NH_4Cl solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 × 20 mL), and the combined organic layers were dried ($MgSO_4$) and filtered. The solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give 2-(hydroxy(4-methoxyphenyl)methyl)phenol **8d** as a yellow oil (450 mg, 1.96 mmol, 78%). TLC: Rf ca 0.20 (4:1 hexane: EtOAc), strong UV and $KMnO_4$; δ_H (500 MHz, $CDCl_3$) 8.02 (1H, s, ArOH), 7.32-7.17 (3H, m, ArH), 6.92-6.80 (5H, m, ArH), 5.98 (1H, s, Ar*CH*OH), 3.80 (3H, s, OCH_3), 2.83 (1H, s, ArCH*OH*) ppm; δ_C (125 MHz, $CDCl_3$) 159.6 (C), 155.6 (C), 134.1 (C), 129.7 (CH), 129.5 (CH), 129.2 (CH), 128.3 (CH), 119.9 (CH), 117.3 (CH), 114.1 (CH), 77.0 (CH), 55.3 (CH_3) ppm. Data matched that reported.

Enantiomeric excess and conversion determined by HPLC analysis (Chiralcel ODH, 30 cm x 6mm column, hexane:iPrOH 9:1, 1.0 mL/min, T = 25°C) ketone 6.4 min, *R* isomer and *S* isomer are 18.2 min and 22.5 min, configuration was assigned by analogy.

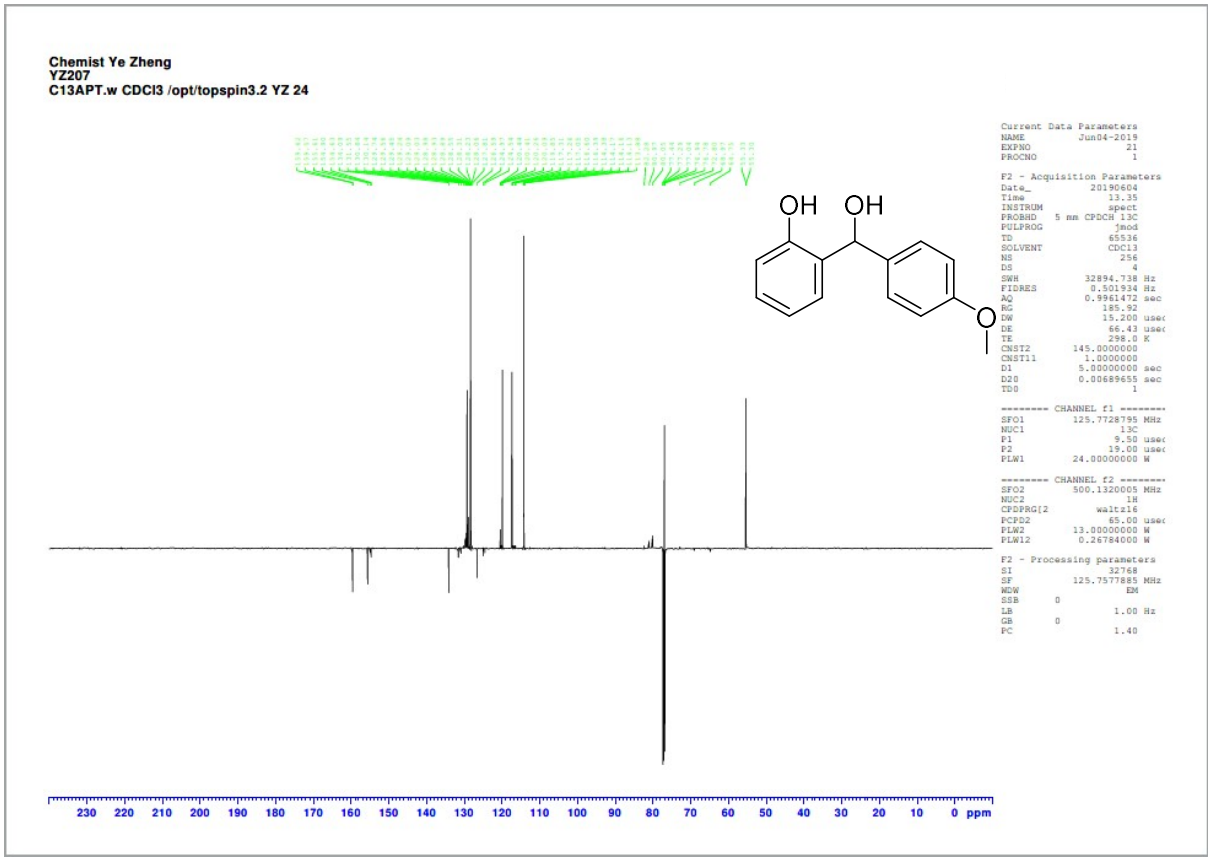
ATH of 2-(hydroxy(4-methoxyphenyl)methyl)phenome (YZ213).

Catalyst (*R,R*)-**2** (0.00175 mmol, 1 mol%) was added to FA: TEA (5:2 azeotropic mixture, 0.18 mL) at rt and the mixture was stirred under a nitrogen atmosphere for 10-15 minutes; after which a solution of 2-(hydroxy(4-methoxyphenyl)methyl)phenone **7d** (40 mg, 0.175 mmol) in DCM (0.25 mL) was added. The reaction mixture was stirred under a nitrogen atmosphere and followed by TLC (4:1 hexane: EtOAc). After 72 hours, the reaction was quenched using saturated $NaHCO_3$ solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried ($MgSO_4$) and filtered. The solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give2-(hydroxy(4-methoxyphenyl)methyl)phenol **8d** (8.4 mg, 0.037 mmol, 20.8%; (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst example). This reaction also followed by HPLC (Chiralcel ODH, 30 cm x 6 mm column, hexane:iPrOH 9:1, 1.0 mL/min, T = 25°C); (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst: 100% conversion; $[\alpha]_D^{25}$ -43.2 (c 0.614 in $CHCl_3$) 63.8% ee.

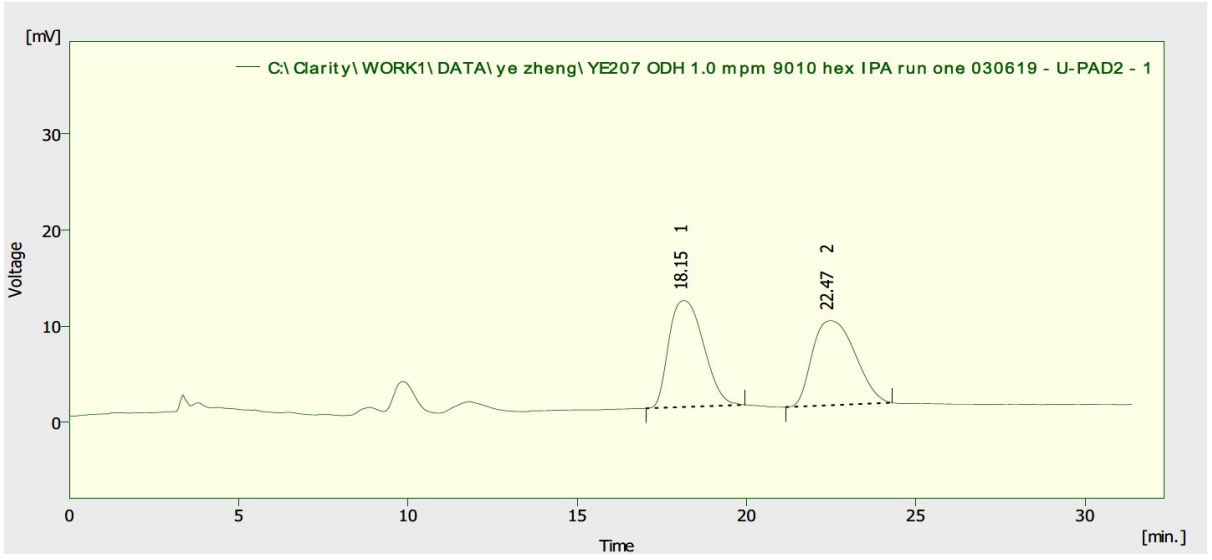
^1H NMR (500 MHz, $CDCl_3$) of **8d**:



^{13}C NMR (125 MHz, $CDCl_3$) of **8d**:



HPLC of racemic 2-(hydroxy(4-methoxyphenyl)methyl)phenol **8d**:

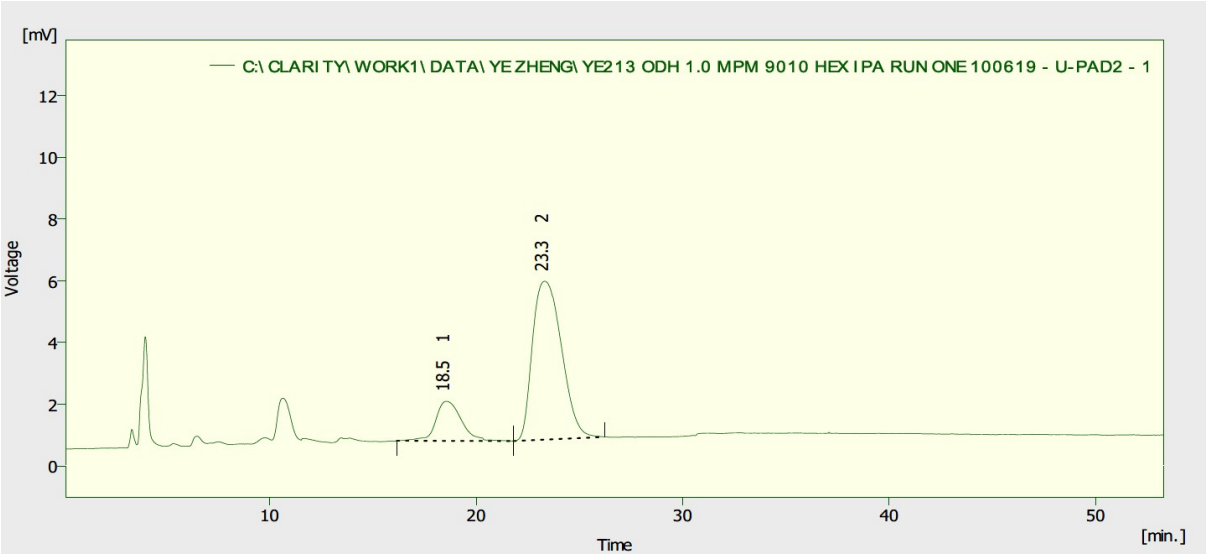


Result Table (Uncal - C:|Clarity|WORK1|DATA|ye zheng|YE207 ODH 1.0 mpm 9010 hex IPA run one 030619 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	18.148	790.371	11.076	50.5	55.7	1.16	
2	22.468	774.044	8.797	49.5	44.3	1.46	
	Total	1564.415	19.872	100.0	100.0		

HPLC of **8d** after ATH of 2-(hydroxy(4-methoxyphenyl)methyl)phenone **7d**:

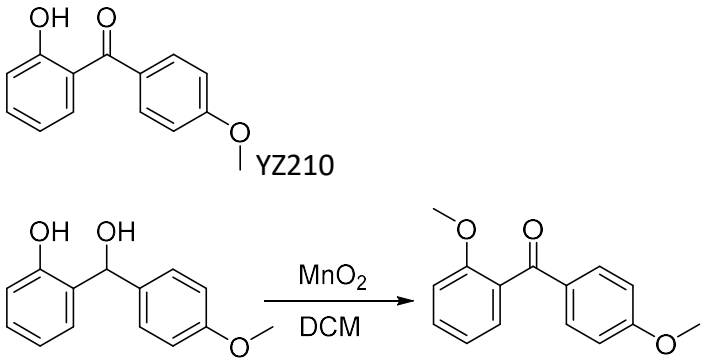
(*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst (after 72 hours, 100% conversion, 63.8% ee).



Result Table (Uncal - C:\CLARITY\WORK1\DATA\YE ZHENG\YE213 ODH 1.0 MPM 9010 HEX IPA RUN ONE 100619 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	18.540	111.256	1.285	18.1	20.0	1.28	
2	23.320	502.575	5.131	81.9	80.0	1.59	
	Total	613.831	6.416	100.0	100.0		

(2-Hydroxyphenyl)(4-methoxyphenyl)methanone 7d.

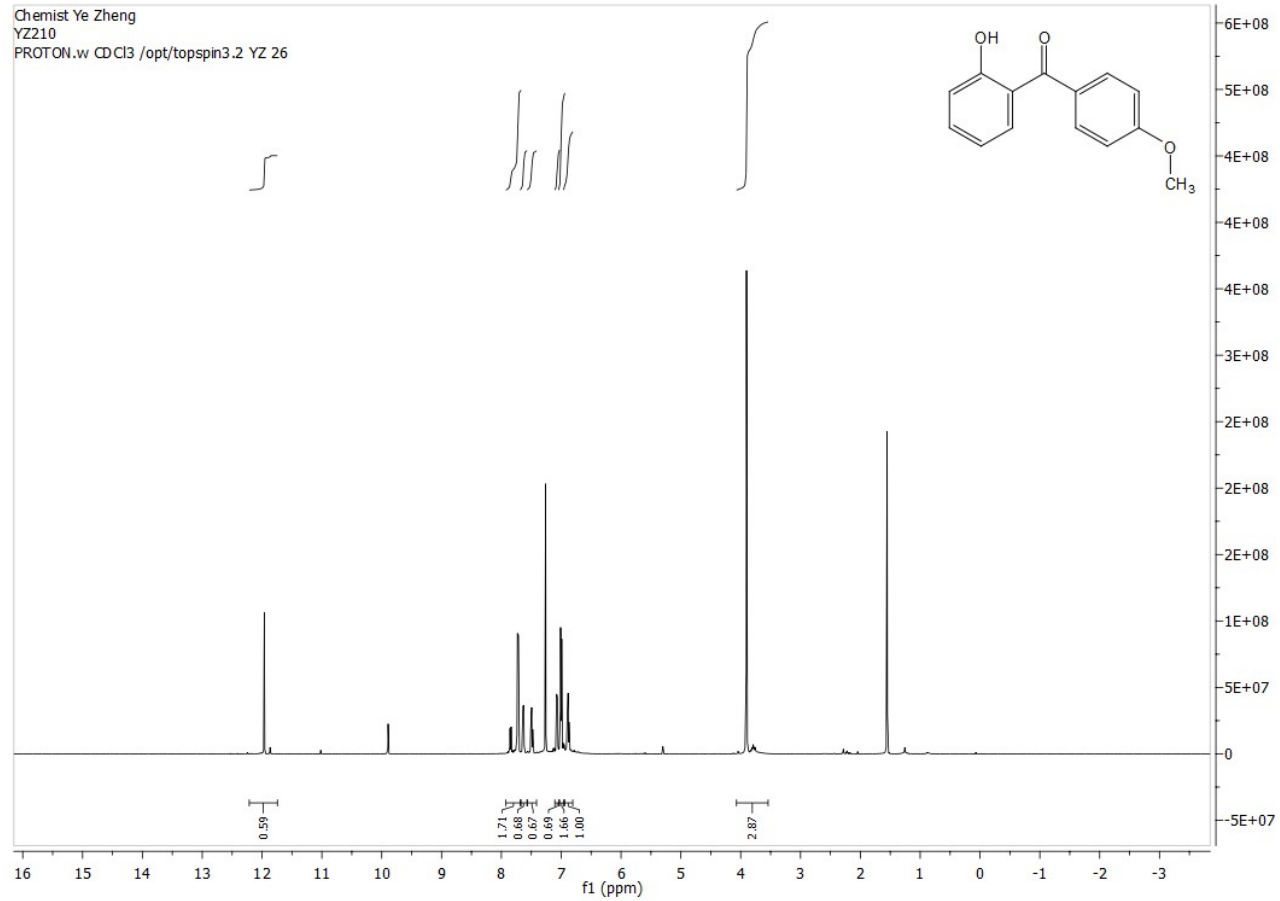


This compound has been reported and fully characterized.

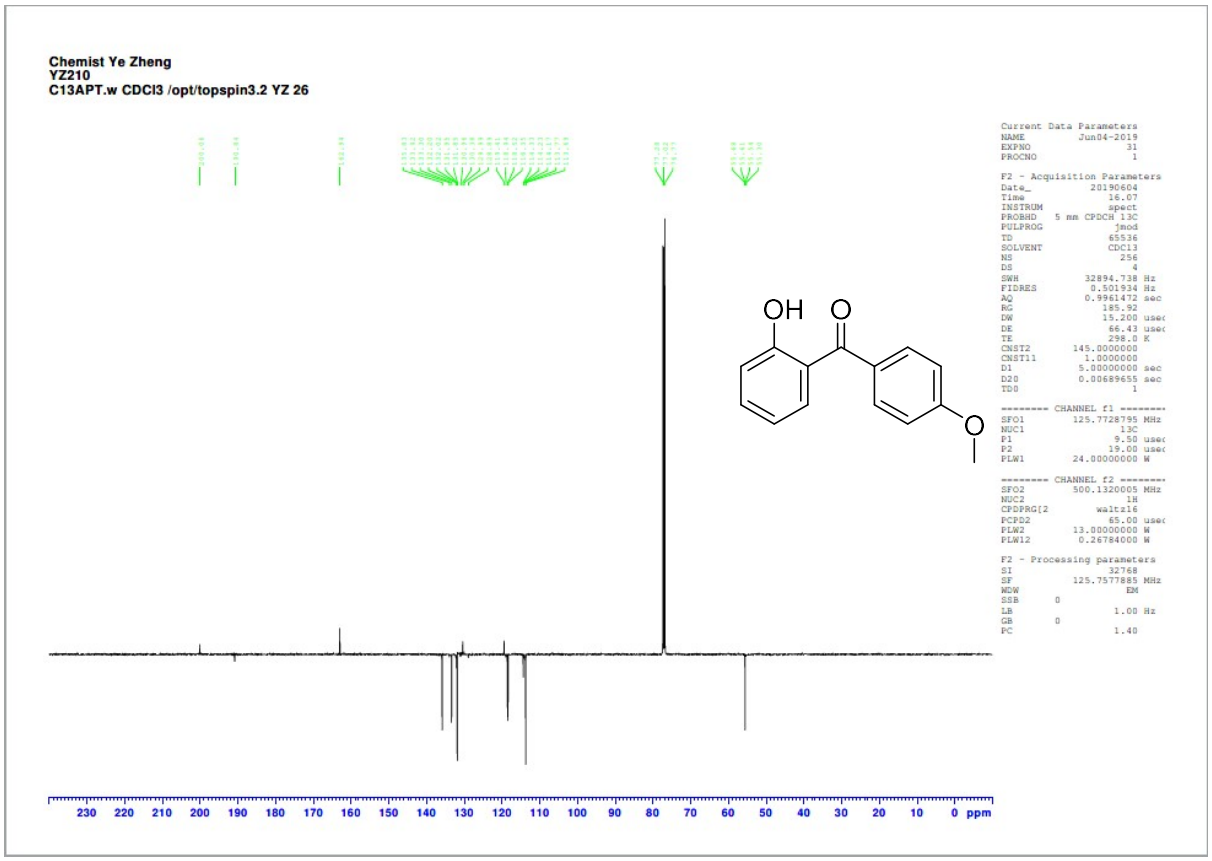
Reference: Serratore, N. A.; Anderson, C. B.; Frost, G. B.; Hoang, T. G.; Underwood, S. J.; Gemmel, P. M.; Hardy, M. A.; Douglas, C. J. *J. Am. Chem. Soc.* **2018**, *140*, 10025 – 10033.

To a solution of 2-(hydroxy(4-methoxyphenyl)methyl)phenol **8d** (360 mg, 1.57 mmol) in DCM (10 mL) at rt was added manganese dioxide (2.05 g, 23.6 mmol). The reaction mixture was left to stir under a nitrogen atmosphere overnight. TLC (4: 1 hexane: EtOAc) after this time indicated full conversion. The solids were removed by gravity filtration and the solids were washed with DCM. The combined solvent was removed to give the product as a brown oil (98.7 mg, 0.43 mmol, 28%). TLC: Rf ca 0.40 (4:1 hexane: EtOAc), strong UV and $KMnO_4$; δ_H (500 MHz, $CDCl_3$) 11.96 (1H, s, OH), 7.73 (2H, d, *J* = 8.5, ArH), 7.64 (1H, dd, *J* = 8.0, 1.0, ArH), 7.51-7.48 (1H, m, ArH), 7.08 (1H, d, *J* = 8.5, ArH), 7.02-6.99 (2H, m, ArH), 6.88 (1H, t, *J* = 8.0, ArH), 3.90 (3H, s, OCH_3) ppm; δ_C (125 MHz, $CDCl_3$) 200.1 (C), 162.9 (C), 135.8 (CH), 132.3 (CH), 131.9 (CH), 130.4 (C), 119.4 (C), 118.5 (CH), 118.3 (C), 114.3 (CH), 113.7 (CH), 55.5 (CH_3) ppm. Data matched that reported.

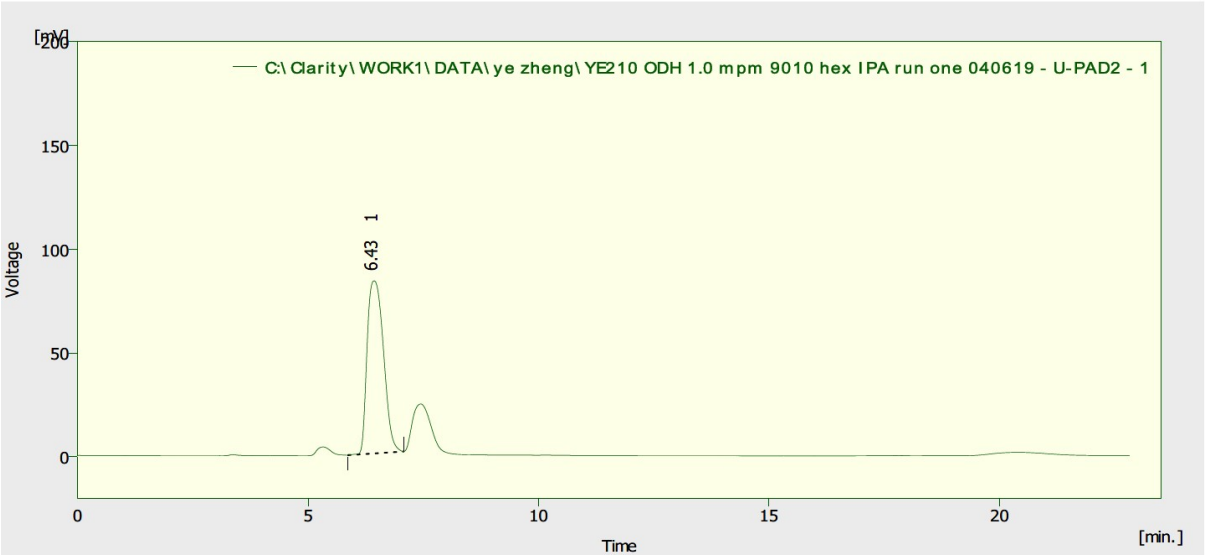
^{1}H NMR (500 MHz, $CDCl_3$) of **7d**:



^{13}C NMR (125 MHz, $CDCl_3$) of **7d**:



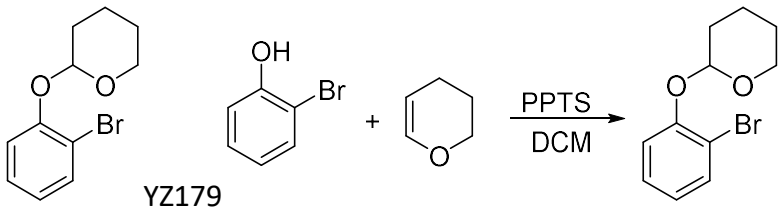
HPLC of (2-hydroxyphenyl)(4-methoxyphenyl)methanone **7d**:



Result Table (Uncal - C:\Clarity\WORK1\DATA\ye zheng\YE210 ODH 1.0 mpm 9010 hex IPA run one 040619 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	6.432	2053.339	83.264	100.0	100.0	0.41	
	Total	2053.339	83.264	100.0	100.0		

2-(Tetrahydropyran-2-yloxy)phenyl bromide.



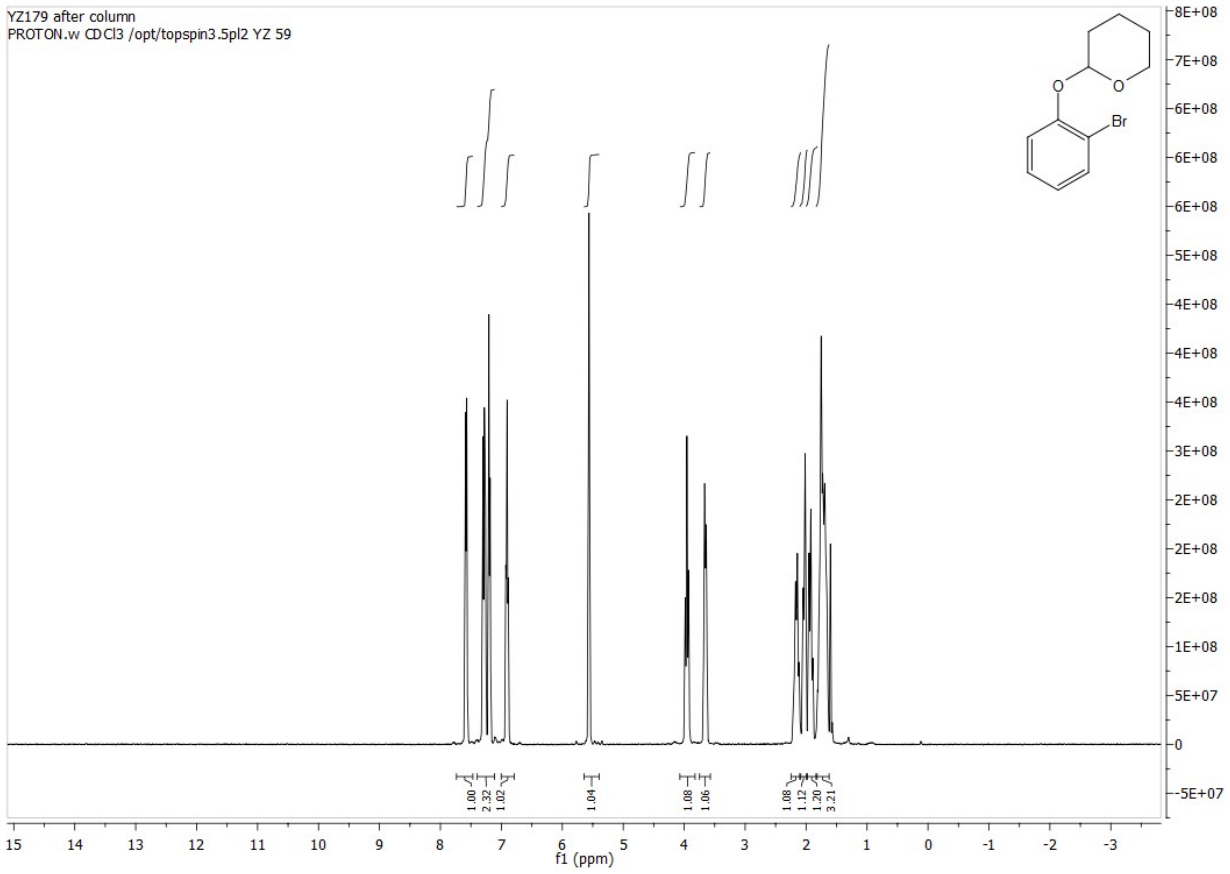
YZ179

This compound has been reported and fully characterized.

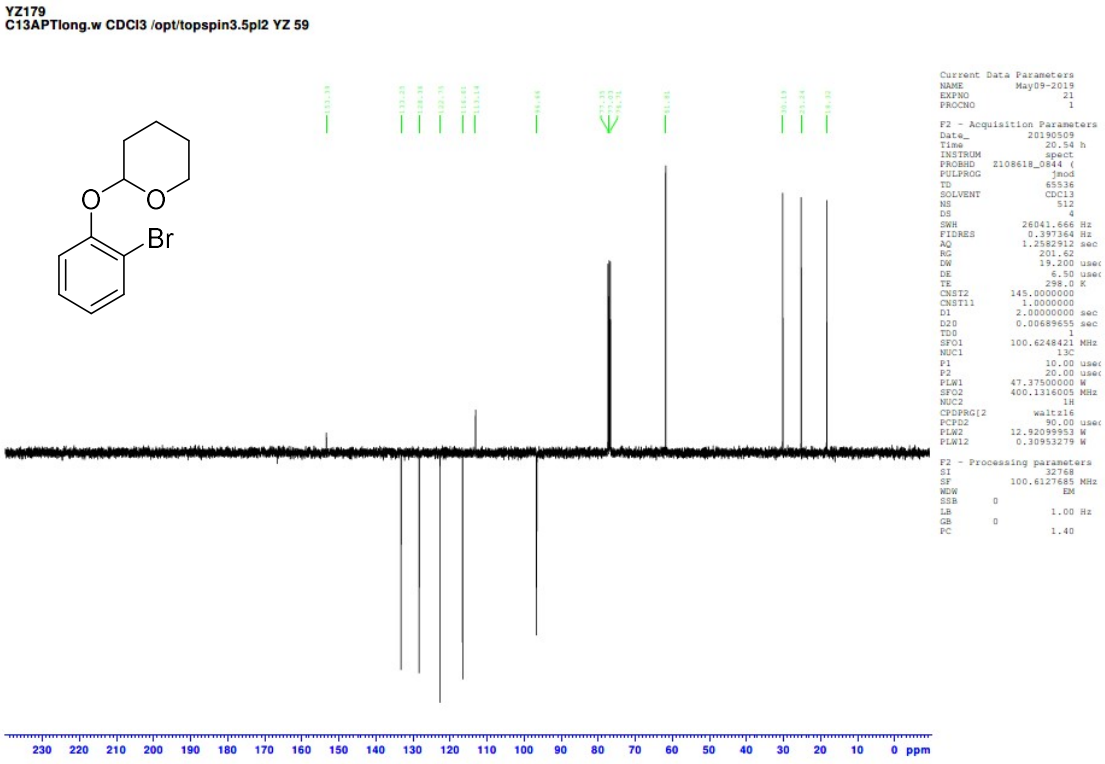
Reference: Dobele, M.; Wiehn, M. S.; Brase, S. *Angew. Chem. Int. Ed. Engl.* **2011**, *50*, 11533 – 11535.

To a solution of 2-bromophenol (300 mg, 1.73 mmo/) in DCM (6 mL) at rt was added dropwise 3, 4-dihydro-2H-pyran (291.5 mg, 3.47 mmol) and pyridinium p-toluenesulfonate (PPTS) (43.4 mg, 0.173 mmol). The reaction mixture was left stirring under the nitrogen atmosphere overnight. The reaction was followed by TLC (9:1 hexane: ethyl acetate). The mixture was quenched by distilled water (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 × 20 mL), and the combined organic layers were dried ($MgSO_4$) and filtered. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-20% ethyl acetate in hexane to give 2-(tetrahydropyran-2-yloxy)phenyl bromide as a colorless oil (380 mg, 1.48 mmol, 85.5%). TLC: Rf ca 0.90 (9:1 hexane: EtOAc), strong UV and $KMnO_4$; δ_H (400 MHz, $CDCl_3$) 7.59 (1H, t, *J* = 7.6, ArH), 7.30-7.18 (2H, m, ArH), 6.92-6.89 (1H, m, ArH), 5.56 (1H, s, O*CH*), 3.96 (1H, t, *J* = 11.0, O*CH*$_2$$CH_2$), 3.67 (1H, d, *J* = 11.0, O*CH*$_2$$CH_2$), 2.17-2.12 (1H, m, CH_2), 2.05-2.02 (1H, m, CH_2), 1.96-1.89 (1H, m, CH_2), 1.81-1.66 (3H, m, CH_2) ppm; δ_C (100 MHz, $CDCl_3$) 153.4 (C), 133.3 (CH), 128.4 (CH), 122.8 (CH), 116.6 (CH), 113.1 (CBr), 96.7 (CHO), 61.8 (CH_2O), 30.2 (CH_2), 25.2 (CH_2), 18.3 (CH_2) ppm. Data matched that reported.

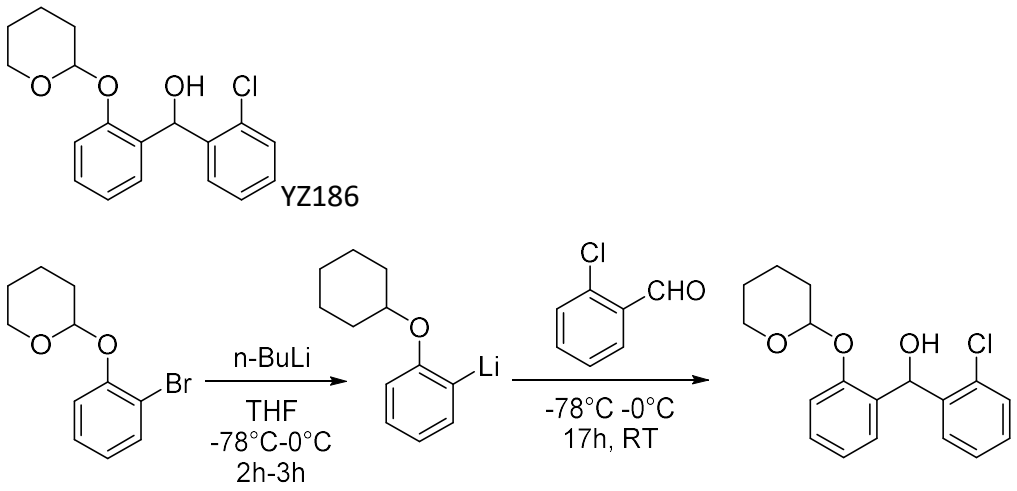
^{1}H NMR (400 MHz, $CDCl_3$) of 2-(Tetrahydropyran-2-yloxy)phenyl bromide:



^{13}C NMR (100 MHz, $CDCl_3$) of 2-(Tetrahydropyran-2-yloxy)phenyl bromide:



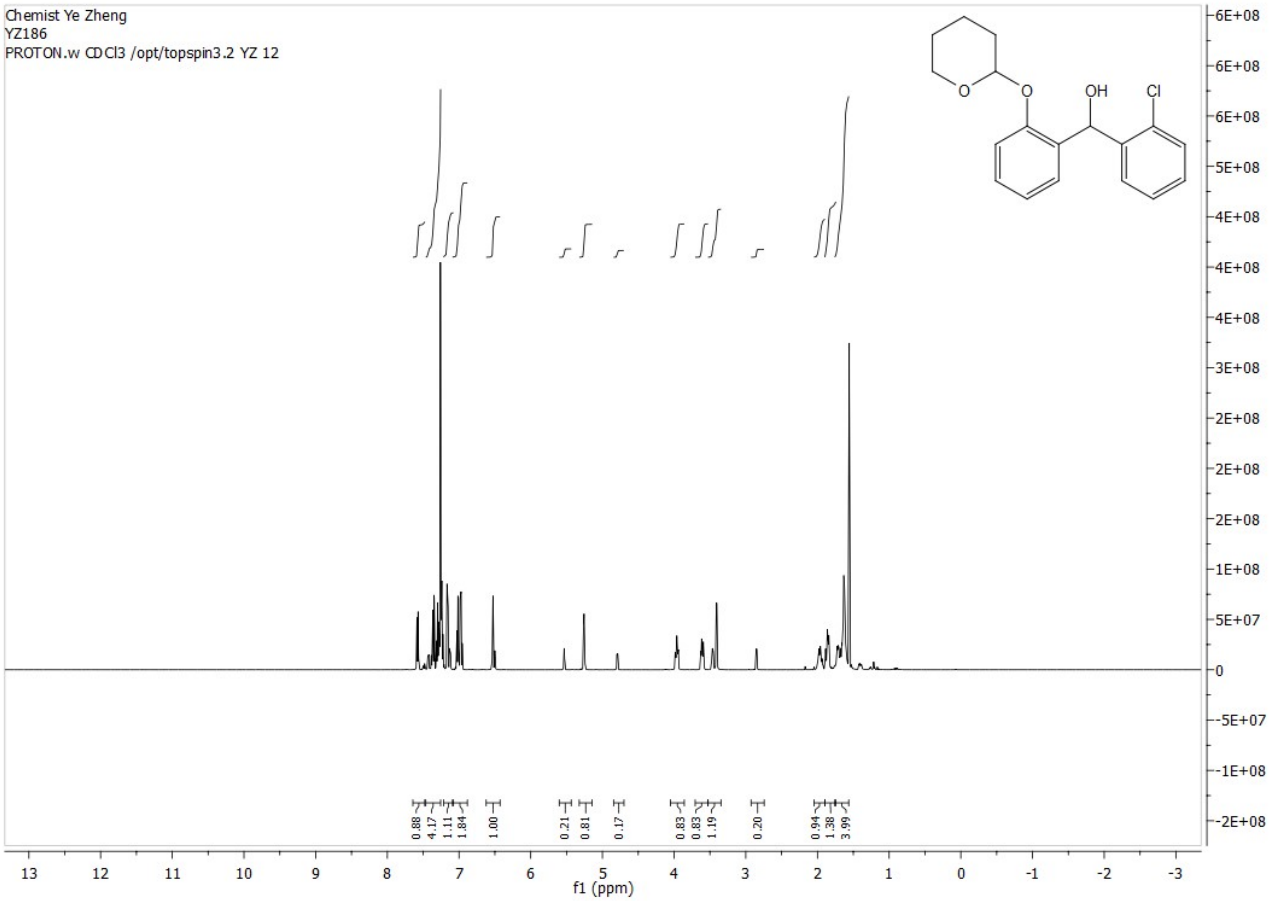
(2-Chlorophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol.



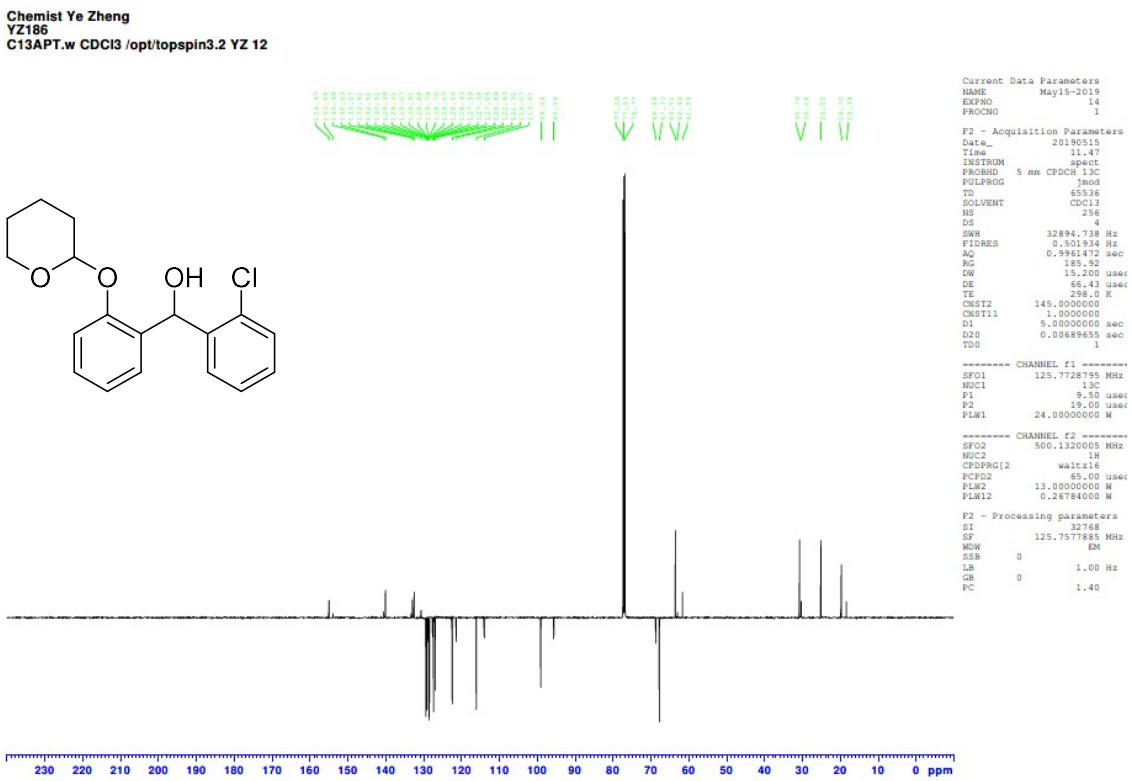
This compound is novel.

To a solution of 2-(2-bromophenoxy)tetrahydro-2H-pyran (339.7 mg, 1.33 mmol) THF (1.6 mL) at -78 °C was added dropwise a solution of n-butyllithium (0.48 mL, 2.5M in hexanes, 1.21 mmol). The reaction mixture was then stirred under a nitrogen atmosphere for 3 hours, after which 2-chlorobenzaldehyde (170 mg, 1.21 mmol) was added dropwise. The reaction mixture was left stirring under the nitrogen atmosphere and allowed to warm to rt. The reaction was followed by TLC (4:1 hexane: ethyl acetate). The mixture was quenched by saturated NH_4Cl solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 × 20 mL), and the combined organic layers were dried ($MgSO_4$) and filtered. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give (2-chlorophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol as a white solid (330 mg, 1.04 mmol, 85.7%). TLC: Rf ca 0.20 (4:1 hexane: EtOAc), strong UV and $KMnO_4$; Mp: 87 °C; HRMS: (found (ESI+): [M+Na]+, Calcd for $C_{18}H_{19}ClNaO_3$ 341.0911; Found 341.0915; 1.7 ppm error); ν_{max} 3435 (br), 2948, 1484, 1389, 1240, 1026, 750 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.59-7.57 (1H, m, ArH), 7.39-7.22 (4H, m, ArH), 7.17-7.12 (1H, m, ArH), 7.03-6.96 (2H, m, ArH), 6.53-6.50 (1H, m, Ar*CH*OH), 5.26-5.25 (1H, m, O*CH*), 3.96-3.94 (1H, m, O*CH*$_2$$CH_2$), 3.63-3.58 (1H, m, O*CH*$_2$$CH_2$), 3.47-3.40 (1H, m, ArCH*OH*), 1.99-1.95 (1H, m, CH_2), 1.89-1.84 (1H, m, CH_2), 1.73-1.60 (4H, m, CH_2) ppm; δ_C (125 MHz, $CDCl_3$) 155.0 (C), 140.0 (C), 132.5 (C), 129.3 (CH), 129.1 (CH), 128.6 (CH), 128.4 (CH), 127.4 (CH), 126.9 (CH), 122.4 (C), 121.3 (CH), 116.1 (CH), 99.0 (CH), 67.7 (CH), 63.5 (CH_2), 30.7 (CH_2), 25.0 (CH_2), 19.7 (CH_2) ppm; m/z (ES-API+) 341.2 (M^+ + 23, 100%).

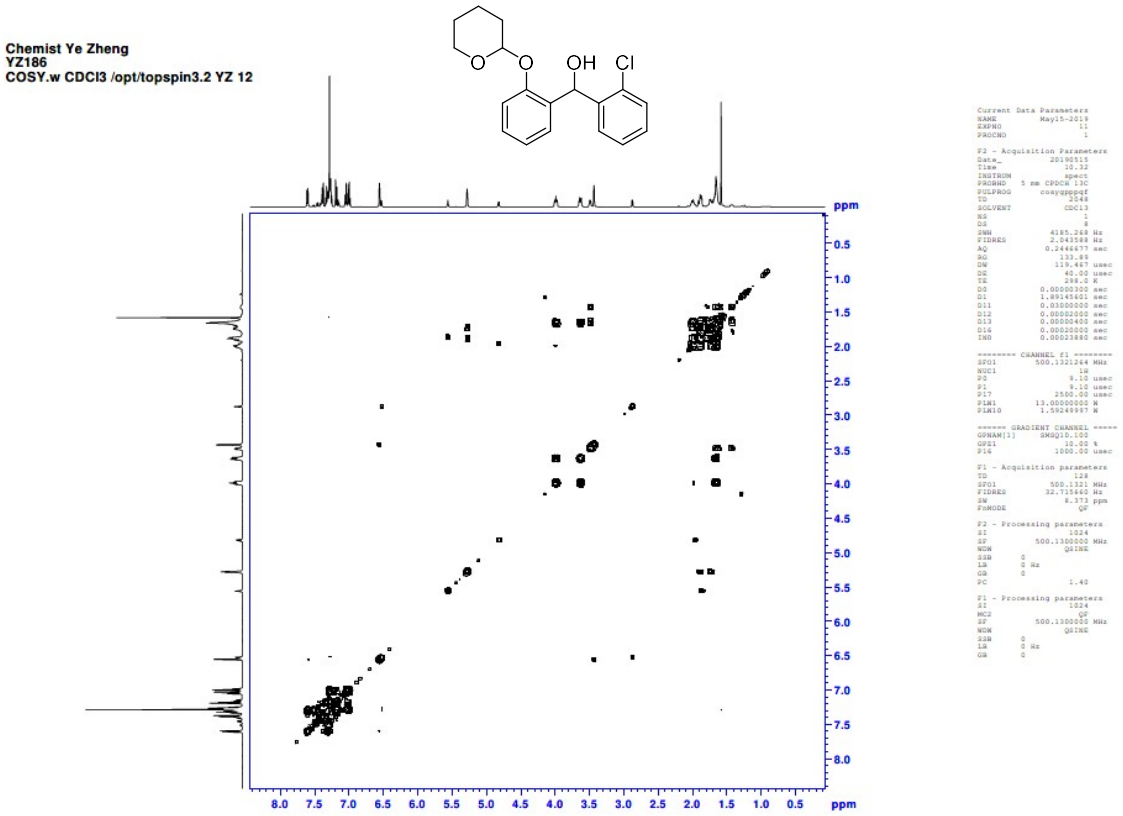
^{1}H NMR (500 MHz, $CDCl_3$) of (2-Chlorophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol:



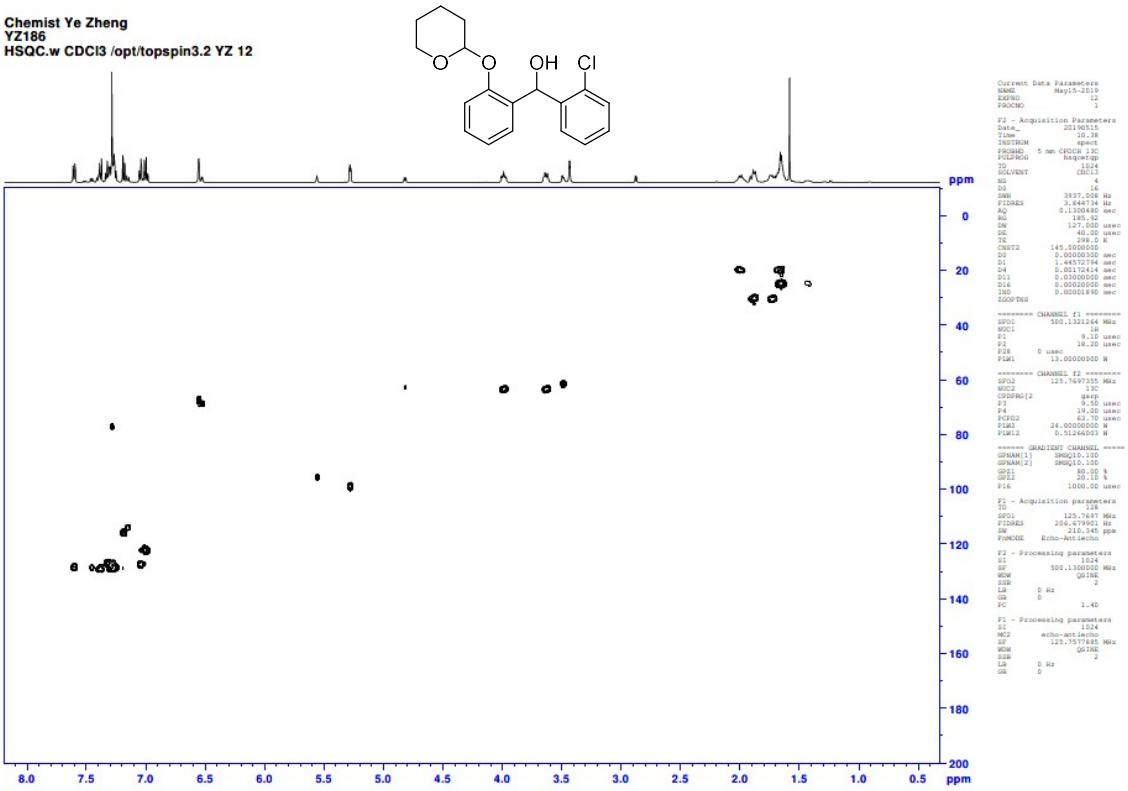
^{13}C NMR (125 MHz, $CDCl_3$) of (2-Chlorophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol:



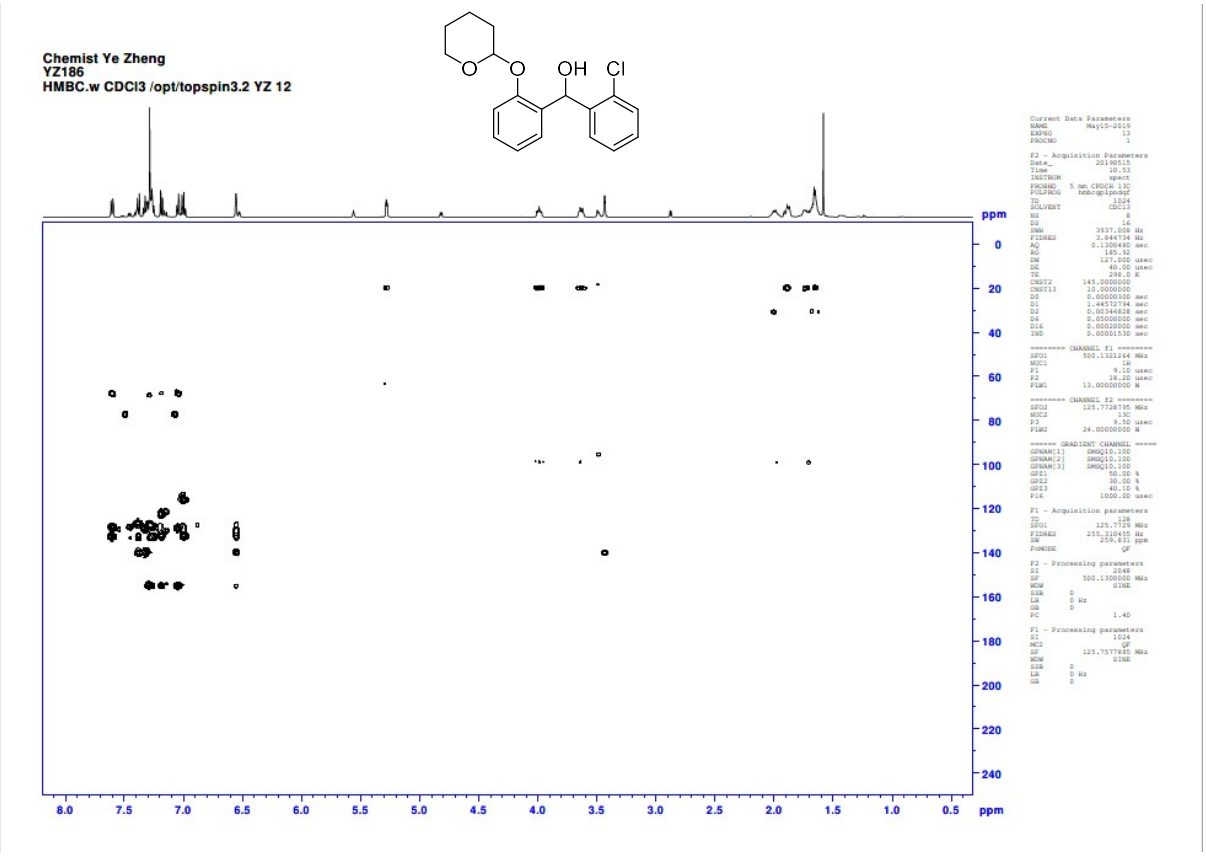
COSY (500 MHz, $CDCl_3$) of (2-Chlorophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol:



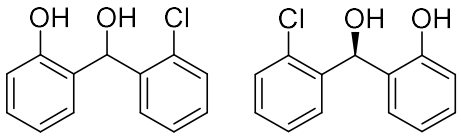
HSQC (500 MHz, $CDCl_3$) of of (2-Chlorophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol:



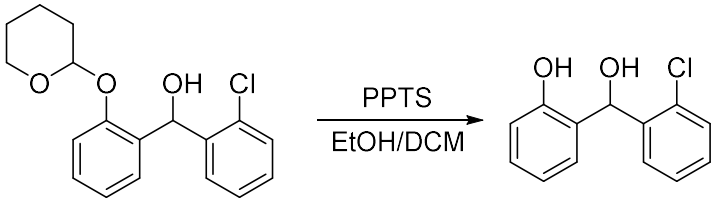
HMBC (500 MHz, $CDCl_3$) of (2-Chlorophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol:



2-((2-Chlorophenyl)(hydroxy)methyl)phenol 8e.



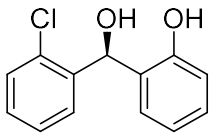
racemic: YZ191, Asymmetric: YZ199, YZ385, YZ386, YZ387.



This compound is novel.

To a solution of (2-chlorophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol (220 mg, 0.69 mmol) in EtOH (3.4 mL)/DCM (1.7mL) was added pyridinium *p*-Toluenesulfonate (PPTS) (26 mg, 0.10 mmol) at rt. The reaction mixture was left stirring under the nitrogen atmosphere and followed by TLC (4:1 hexane: EtOAc). Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-20% ethyl acetate in hexane to give 2-((2-chlorophenyl)(hydroxy)methyl)phenol **8e** as a colorless oil (120.2 mg, 0.51 mmol, 74%). TLC: Rf ca 0.20 (4:1 hexane: EtOAc), strong UV and $KMnO_4$; HRMS: (found (ESI+): [M+Na]+, Calcd for $C_{13}H_{11}ClNaO_2$ 257.0335; Found 257.0340; 1.7 ppm error); ν_{max} 3291 (br), 1587, 1488, 1234, 747 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.42-7.40 (1H, m, ArH), 7.33-7.19 (4H, m, ArH), 6.94 (1H, t, *J* = 8.5, ArH), 6.82-6.78 (2H, m, ArH), 6.43 (1H, s, Ar*CH*OH) ppm; δ_C (125 MHz, $CDCl_3$) 156.0 (C), 138.9 (C), 133.1 (C), 129.8 (CH), 129.7 (CH), 129.6 (CH), 129.2 (CH), 128.1 (CH), 127.5 (CH), 124.6 (C), 120.1 (CH), 117.4 (CH), 73.8 (CH) ppm; m/z (ES-API+) 257.1 (M^+ + 23, 100%).

Enantiomeric excess and conversion determined by HPLC analysis (Chiralpak IC, 30 cm x 6mm column, hexane:iPrOH 9:1, 0.5 mL/min, T = 25°C) ketone 11.6 min, *S* isomer 13.2 min, *R* isomer 16.9 min.



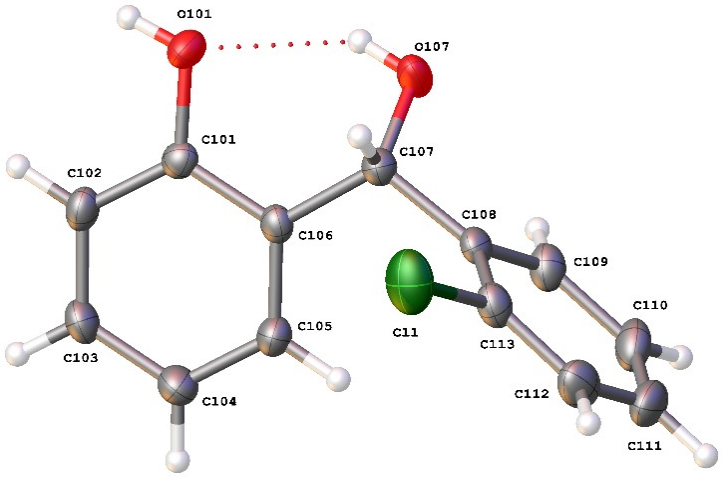
ATH of (2-chlorophenyl)(2-hydroxyphenyl)methanone) (YZ199, 385, 386, 387).

Catalyst (*R,R*)-**2** (0.0017 mmol, 1mol%) was added to FA: TEA (5:2 azeotropic mixture, 0.18 mL) at rt and the mixture was stirred under a nitrogen inert atmosphere for 10-15 minutes; after which a solution of (2-chlorophenyl)(2-hydroxyphenyl)methanone **7e** (40 mg, 0.17 mmol) in DCM (0.25 mL) was added. The reaction mixture was stirrer under a nitrogen atmosphere, followed by TLC (4:1

hexane: EtOAc). After 72 hours, the reaction was quenched using saturated $NaHCO_3$ solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried ($MgSO_4$) and filtered. The solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give 2-((2-chlorophenyl)(hydroxy)methyl)phenol **8e** (22.4 mg, 0.096 mmol, 55.5%); (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst example). The reaction was also followed by HPLC analysis (Chiralpak IC, 30 cm x 6 mm column, hexane:iPrOH 9:1, 0.5 mL/min, T = 25°C); (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst: 100% conversion; $[\alpha]_D^{31}$ -47.7 (c 0.448 in $CHCl_3$) 93% ee (*S*)

Crystal structure determination of 8e:

Crystal structure: *S* configuration. CCDC 1978885 (local code yz8).



The asymmetric unit contains two diphenylmethanols, there are four molecules in the unit cell. The OHs were located in a difference map but 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)	
0.84	1.87	2.7059(19)	174.8	O101-H101...O107_$1
0.84	1.84	2.571(2)	145.1	O201-H201...O207
0.84	2.17	2.782(2)	129.5	O107-H107...O101
0.84	2.03	2.846(2)	162.8	O207-H207...O201_$2

Symmetry operators used to generate symmetry equivalent atoms in above contacts were

$1 -0.5+X,1.5-Y,1-Z

$2 -0.5+X,0.5-Y,1-Z

The Flack parameter and related Hooft y parameter as a measure of the confidence we can have in the assignment of the handedness of the crystal measured were

Flack x: 0.006(3) Shelx 2018

Hooft y: -0.002(3) Olex 2

Which is small with a small error so we can be confident of the assignment of the handedness of the crystal measured.

Experimental

Single crystals of $C_{13}H_{11}ClO_2$ were grown from DCM/hexane in a small vial at room temperature. 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 duel 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.

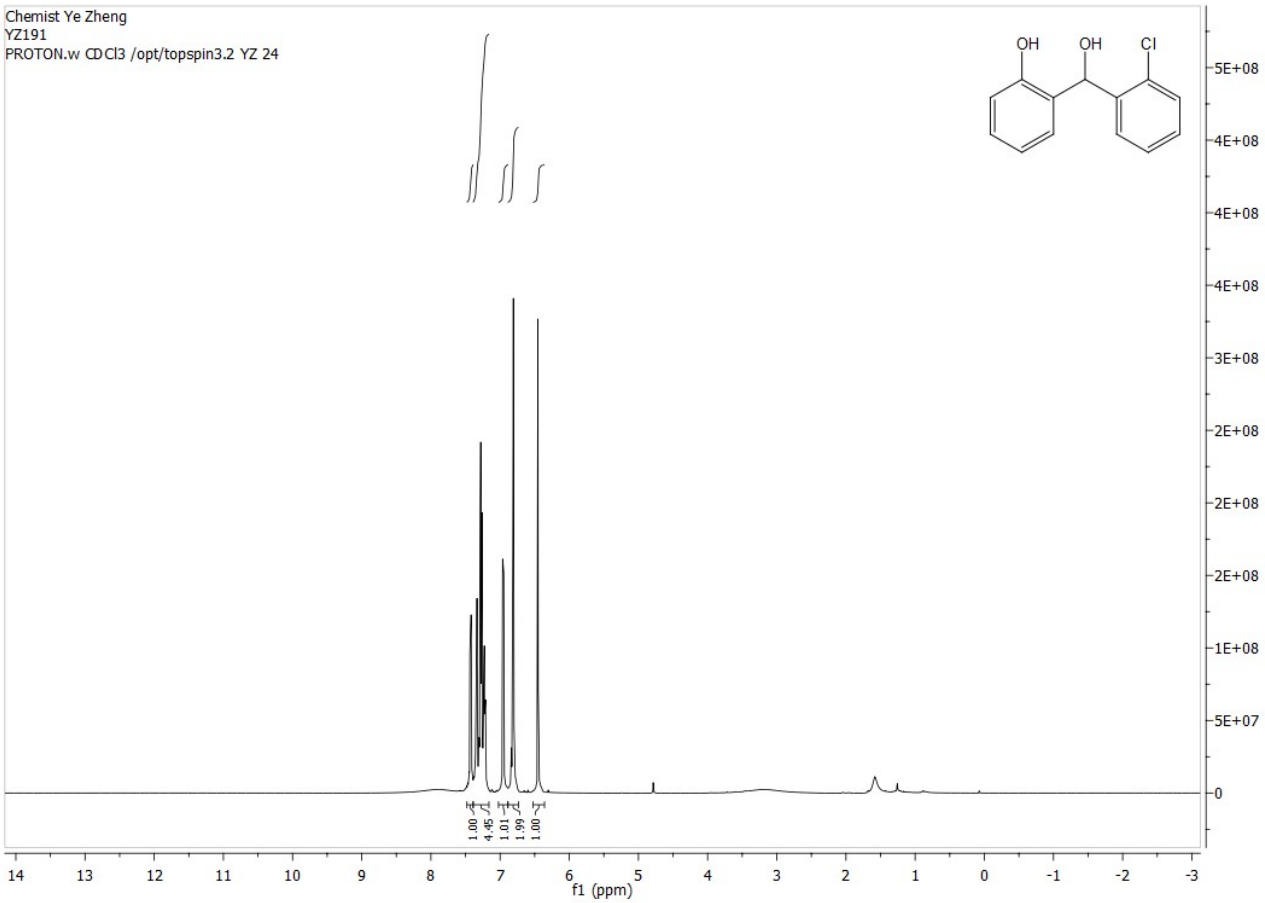
Crystal Data for $C_{13}H_{11}ClO_2$ (M =234.67 g/mol): orthorhombic, space group $P2_12_12_1$ (no. 19), a = 10.17811(5) Å, b = 11.15611(4) Å, c = 19.73742(9) Å, V = 2241.148(17) Å^3, Z = 8, T = 150(2) K, μ(CuKα) = 2.864 mm^{-1}, *Dcalc* = 1.391 g/cm^3, 34336 reflections measured (8.96° ≤ 2Θ ≤ 147.308°), 4512 unique (R_{int} = 0.0320, R_{sigma} = 0.0188) which were used in all calculations. The final R_1 was 0.0271 (I > 2σ(I)) and wR_2 was 0.0703 (all data).

Table 1 Crystal data and structure refinement for yz8.

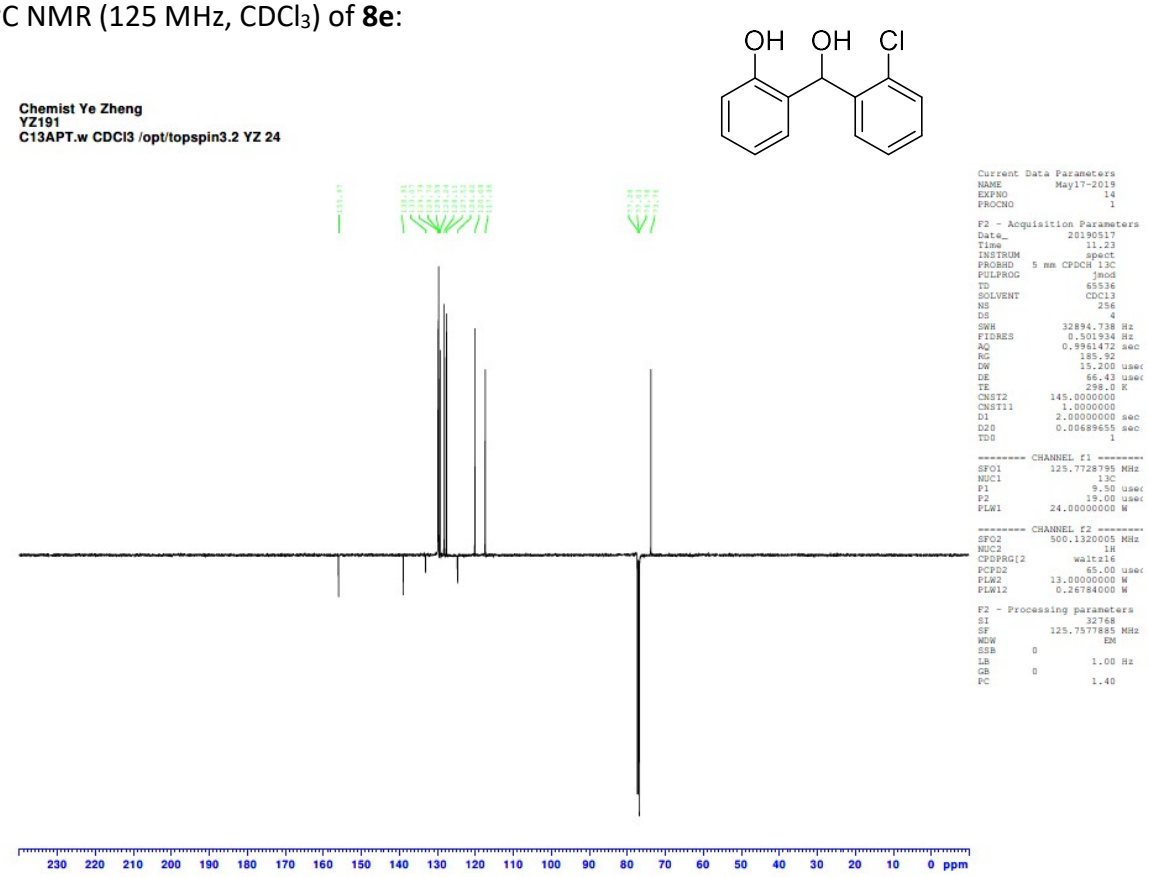
Identification code	yz8
Empirical formula	$C_{13}H_{11}ClO_2$
Formula weight	234.67
Temperature/K	150(2)
Crystal system	Orthorhombic
Space group	$P2_12_12_1$
a/Å	10.17811(5)
b/Å	11.15611(4)
c/Å	19.73742(9)
α/°	90

β/°	90
γ/°	90
Volume/Å^3	2241.148(17)
Z	8
ρ_{calc}g/cm^3	1.391
μ/mm^{-1}	2.864
F(000)	976.0
Crystal size/mm^3	0.2 × 0.18 × 0.16 colourless block
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	8.96 to 147.308
Index ranges	-12 ≤ h ≤ 10, -13 ≤ k ≤ 13, -24 ≤ l ≤ 24
Reflections collected	34336
Independent reflections	4512 [R_{int} = 0.0320, R_{sigma} = 0.0188]
Data/restraints/parameters	4512/0/293
Goodness-of-fit on F^2	1.046
Final R indexes [I>=2σ (I)]	R_1 = 0.0271, wR_2 = 0.0700
Final R indexes [all data]	R_1 = 0.0274, wR_2 = 0.0703
Largest diff. peak/hole / e Å^{-3}	0.27/-0.33
Flack parameter	0.006(3)

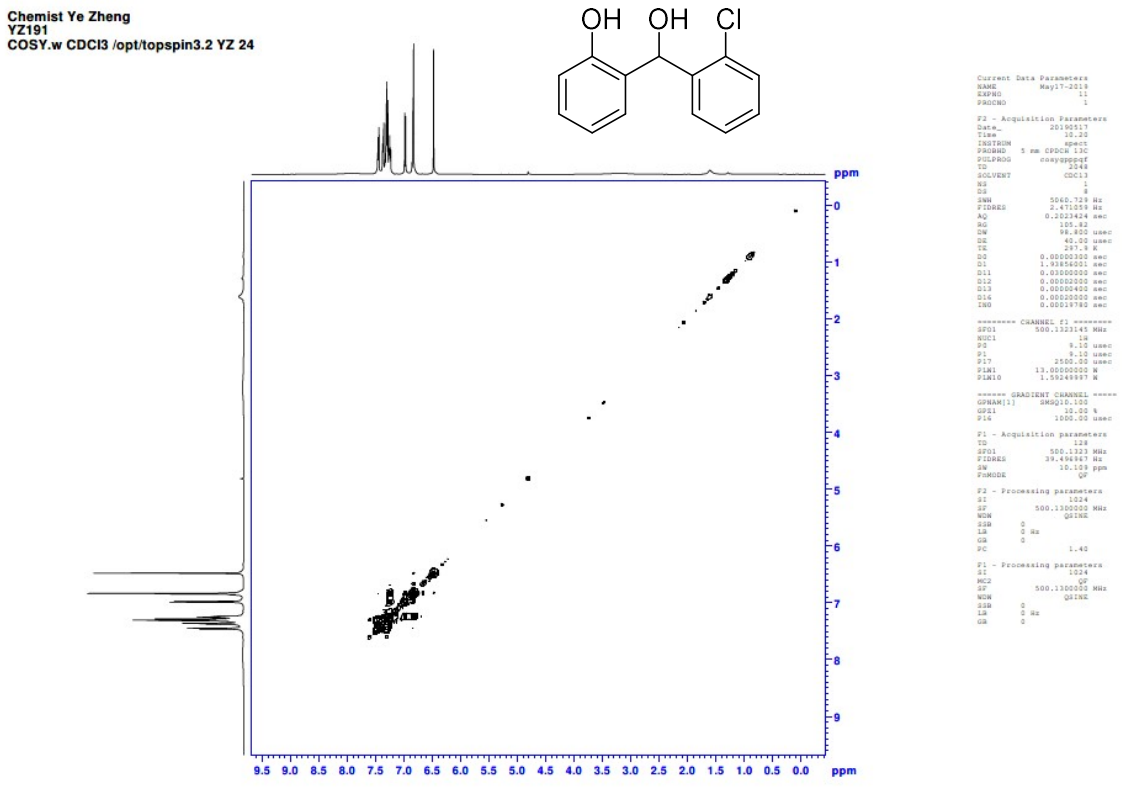
^{1}H NMR (500 MHz, $CDCl_3$) of **8e**:



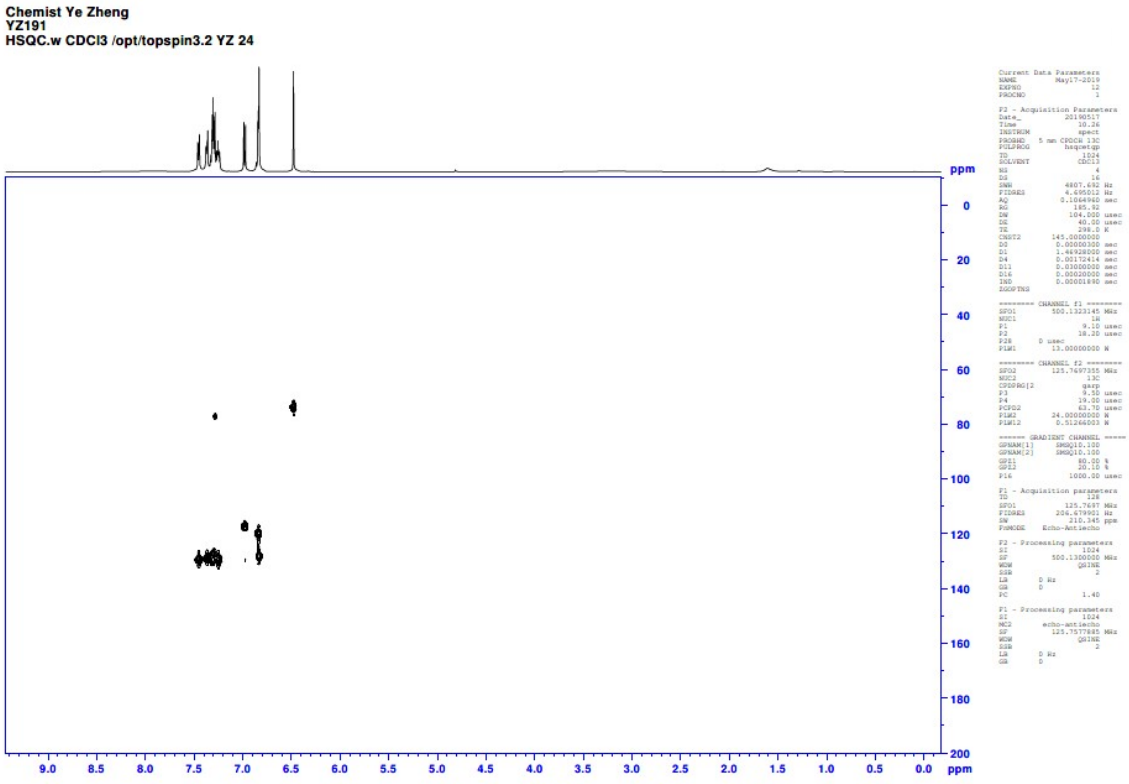
^{13}C NMR (125 MHz, $CDCl_3$) of **8e**:



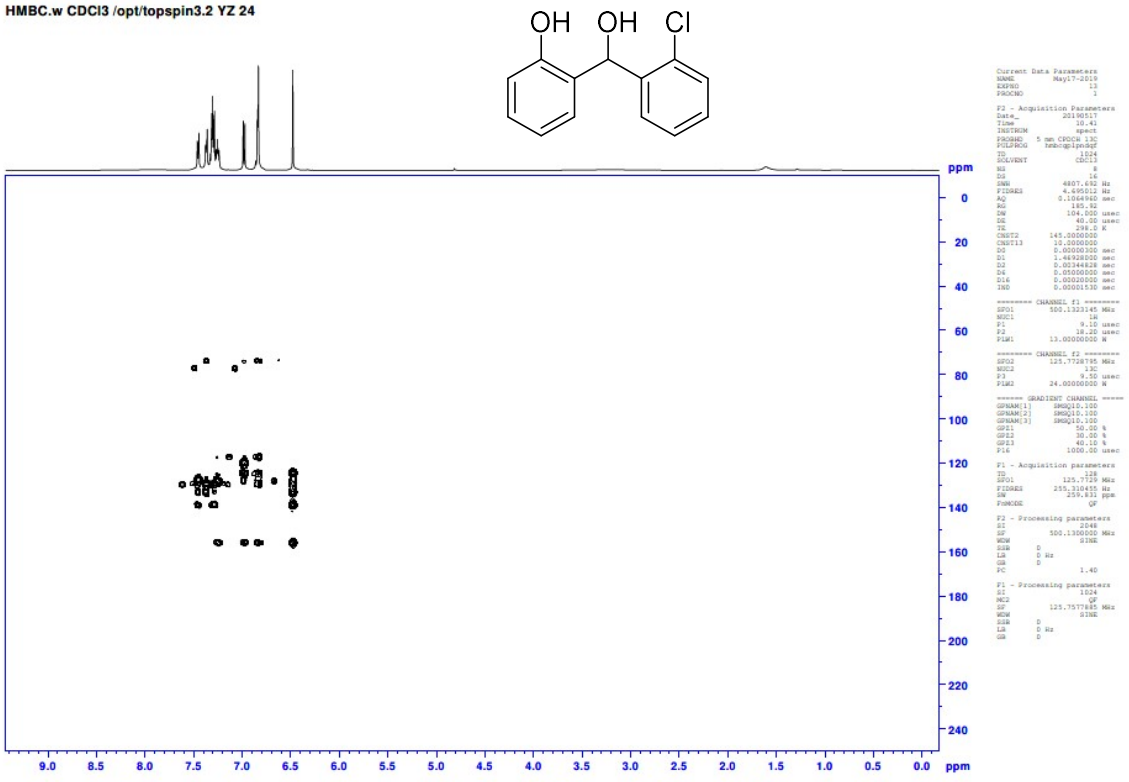
COSY (500 MHz, $CDCl_3$) of **8e**:



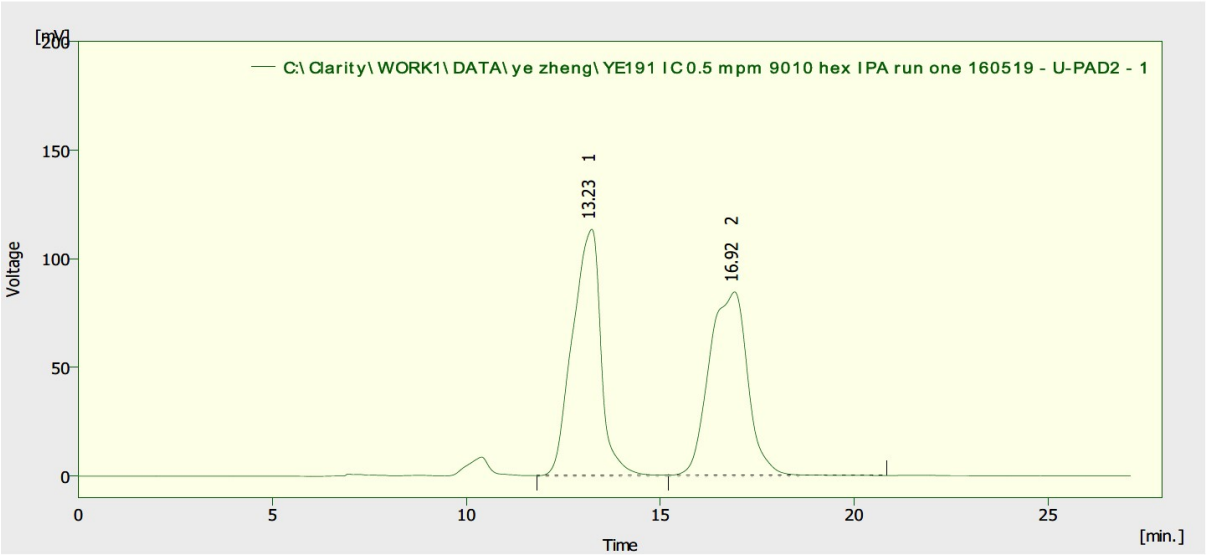
HSQC (500 MHz, $CDCl_3$) of **8e:**



HMBC (500 MHz, $CDCl_3$) of **8e**:



HPLC of racemic 2-((2-chlorophenyl)(hydroxy)methyl)phenol **8e**:

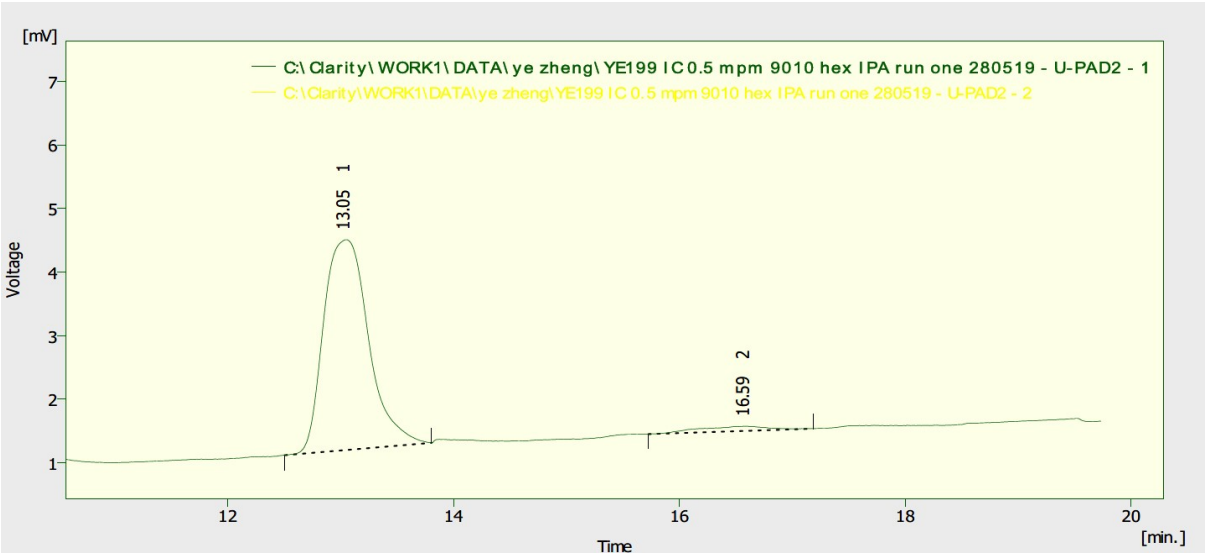


Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|ye zheng\|YE191 IC 0.5 mpm 9010 hex IPA run one 160519 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	13.232	5794.062	113.543	49.8	57.3	0.81	
2	16.916	5837.050	84.659	50.2	42.7	1.09	
	Total	11631.113	198.202	100.0	100.0		

HPLC of **8e** after ATH of (2-chlorophenyl)(2-hydroxyphenyl)methanone **7e**:

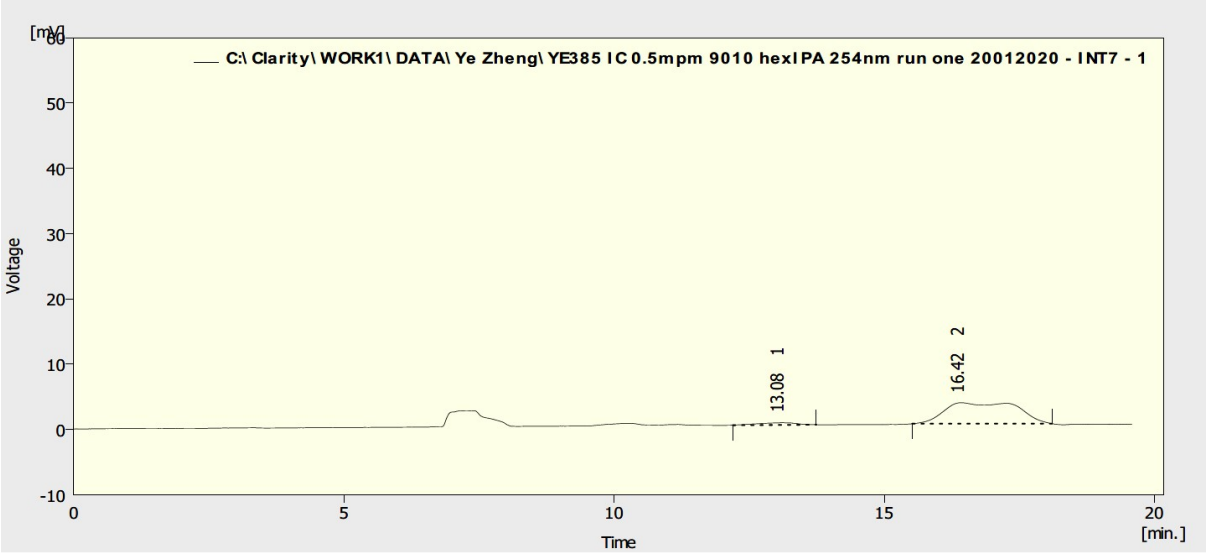
(*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst **2** (after 72 hours, 100% conversion, 93% ee, *S* configuration).



Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|ye zheng\|YE199 IC 0.5 mpm 9010 hex IPA run one 280519 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	13.048	91.588	3.310	96.5	97.8	0.43	
2	16.588	3.317	0.075	3.5	2.2	0.65	
	Total	94.905	3.385	100.0	100.0		

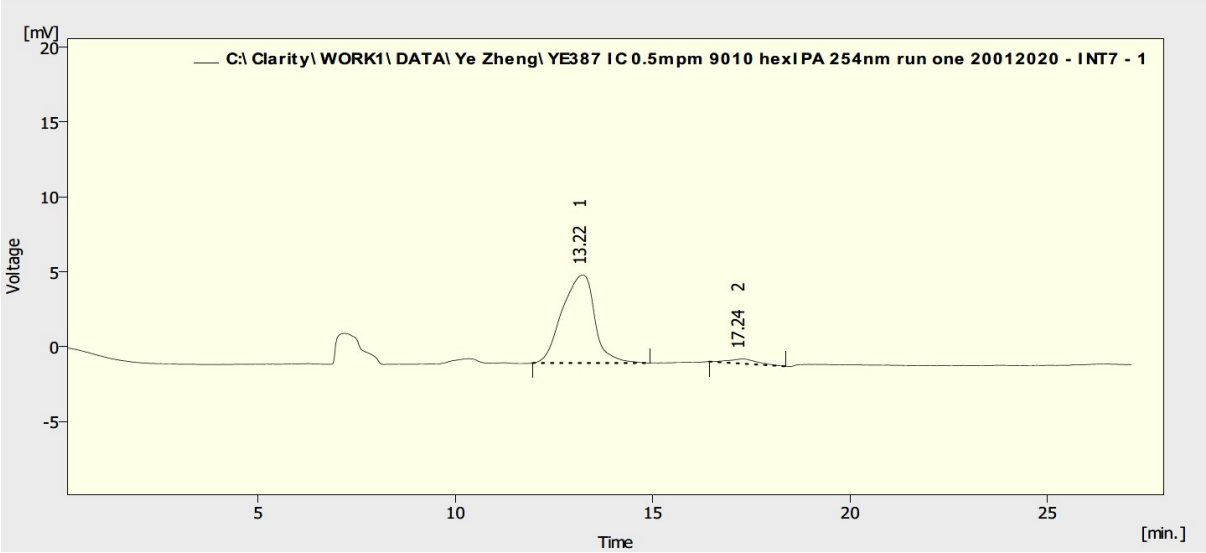
(*S,S*)-Noyori Ru(II)-TsDPEN catalyst **6** (after 168 hours, 100% conversion, 89.2% ee, *R* configuration).



Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|Ye Zheng\|YE385 IC 0.5mpm 9010 hexIPA 254nm run one 20012020 - INT7 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	13.080	17.206	0.335	5.4	9.4	0.82	
2	16.420	301.319	3.219	94.6	90.6	1.59	
	Total	318.524	3.554	100.0	100.0		

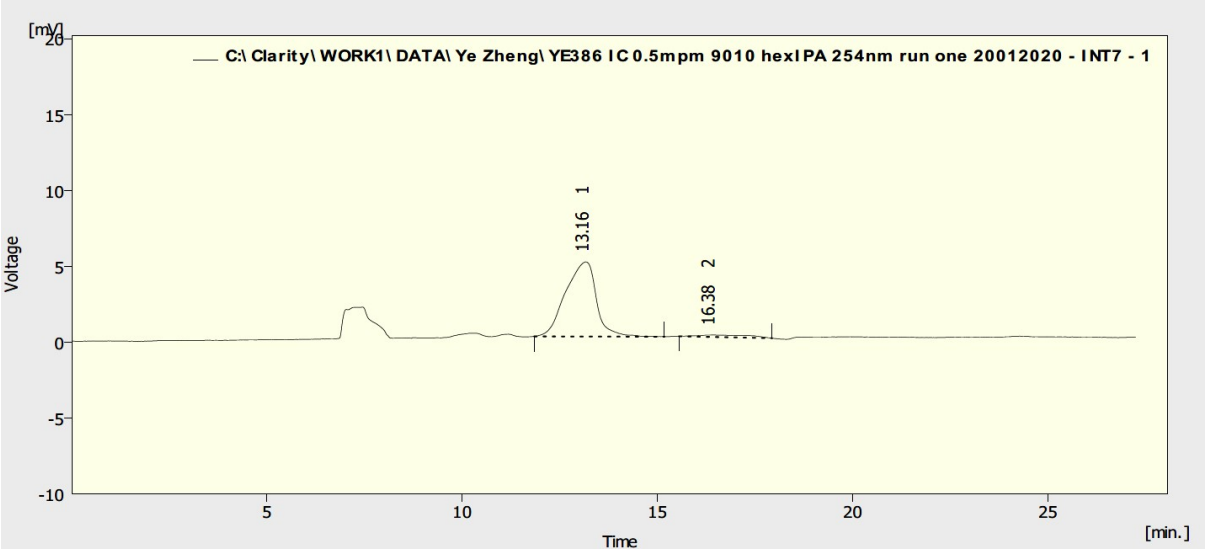
(*R,R*)-Benzyl-tethered Ru(II)-TsDPEN catalyst **4** (after 168 hours, 100% conversion, 91.2% ee, *S* configuration).



Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|Ye Zheng\|YE387 IC 0.5mpm 9010 hexIPA 254nm run one 20012020 - INT7 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	13.223	337.298	5.874	95.6	95.1	0.91	
2	17.237	15.666	0.305	4.4	4.9	0.99	
	Total	352.964	6.178	100.0	100.0		

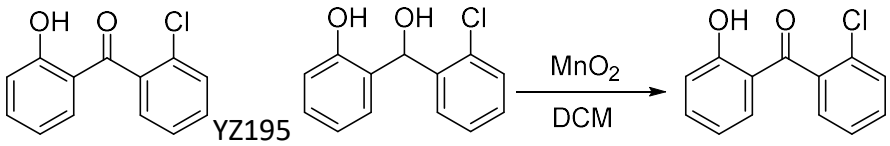
(*R,R*)-3C-Tethered, 4-methoxy-Ru(II)-TsDPEN catalyst **5** (after 168 hours, 100% conversion, 90.2% ee, *S* configuration).



Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|Ye Zheng\|YE386 IC 0.5mpm 9010 hexIPA 254nm run one 20012020 - INT7 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	13.157	269.812	4.922	95.1	97.3	0.88	
2	16.377	13.823	0.135	4.9	2.7	1.68	
	Total	283.635	5.057	100.0	100.0		

(2-Chlorophenyl)(2-hydroxyphenyl)methanone 7e.

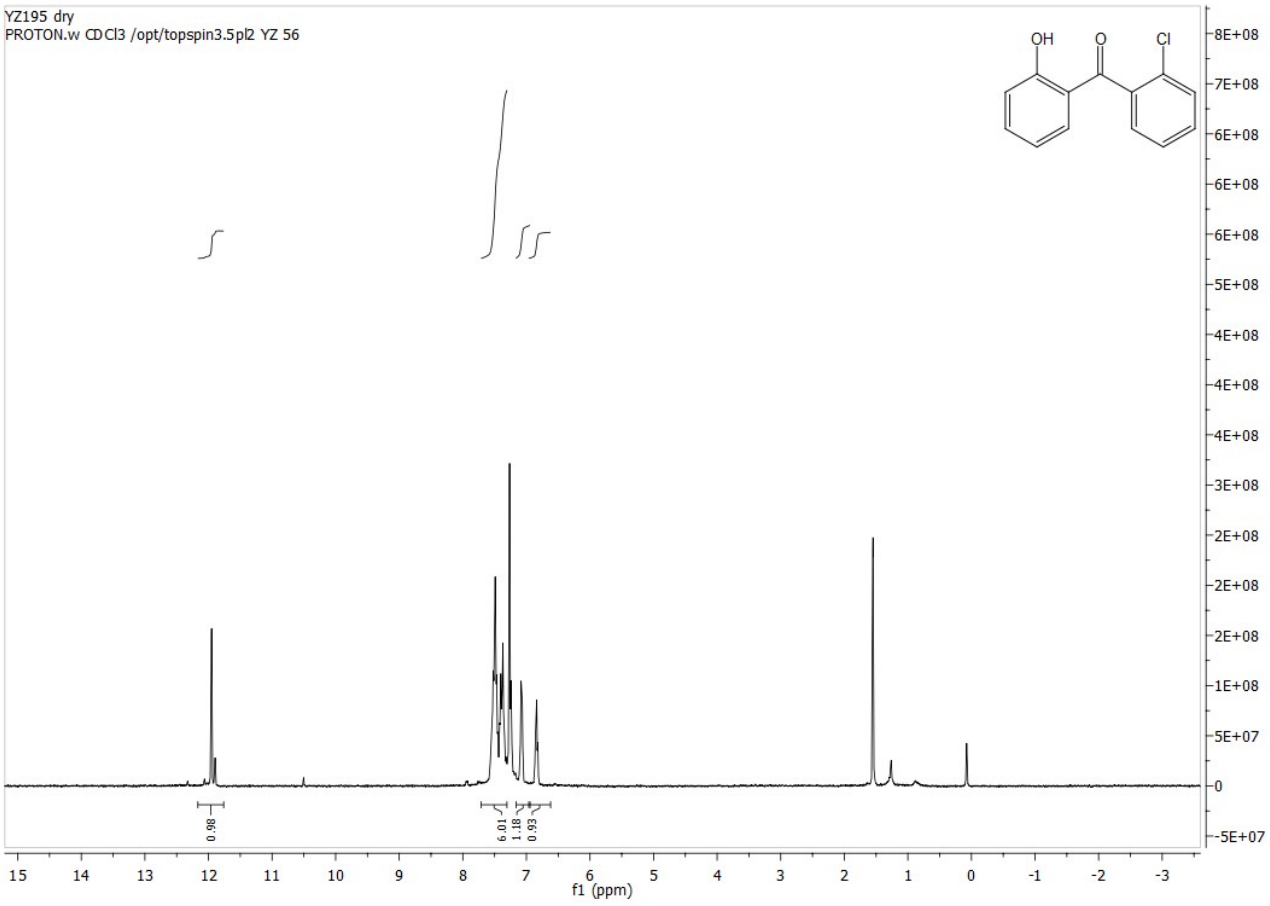


This compound has been reported and fully characterized.

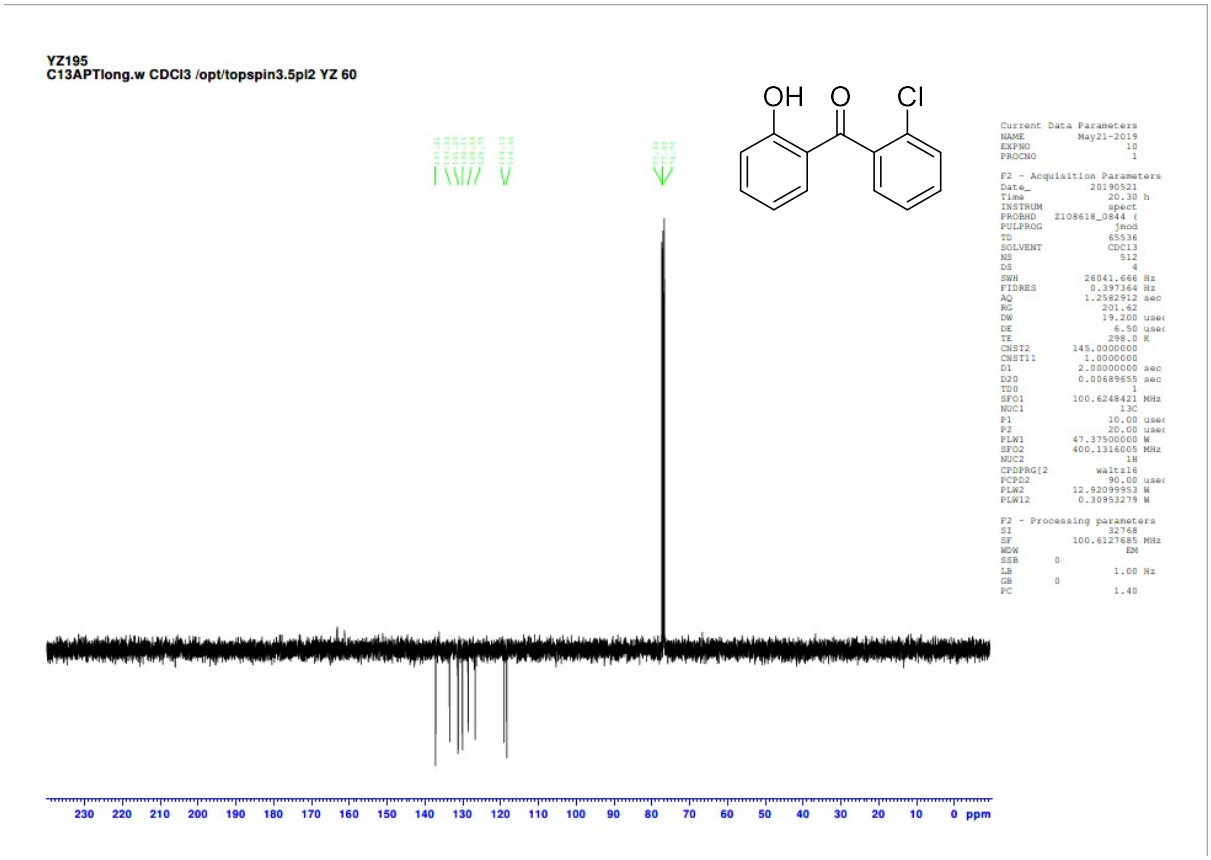
Reference: Shan, G.;Yang, X.; Ma, L.; Rao, Y.; *Angew. Chem. Int. Ed.* 2012, **51**, 13070 –13074.

To a solution of 2-((2-chlorophenyl)(hydroxy)methyl)phenol **8e** (120 mg, 0.51 mmol) in DCM (5 mL) at rt was added manganese dioxide (665 mg, 7.65 mmol). The reaction mixture was left to stir under a nitrogen atmosphere overnight. TLC (4:1 hexane: EtOAc) after this time indicated full conversion. The solids were removed by gravity filtration and washed with DCM. The combined solvent was removed to give the product **7e** as a colorless oil (40.1 mg, 0.17 mmol, 33.4%). TLC: Rf ca 0.40 (4:1 hexane: EtOAc), strong UV and $KMnO_4$; δ_H (400 MHz, $CDCl_3$) 11.95 (1H, s, OH), 7.54-7.29 (6H, m, ArH), 7.08 (1H, d, *J* = 8.4, ArH), 6.83 (1H, t, *J* = 8.0, ArH) ppm; δ_C (100 MHz, $CDCl_3$) 200.6 (C), 163.2 (C), 137.2 (CH), 136.2 (C), 133.5 (CH), 131.3 (CH), 131.0 (C), 130.1 (CH), 128.6 (CH), 126.8 (CH), 119.4 (C), 119.1 (CH), 118.4 (CH) ppm. Data matched that reported.

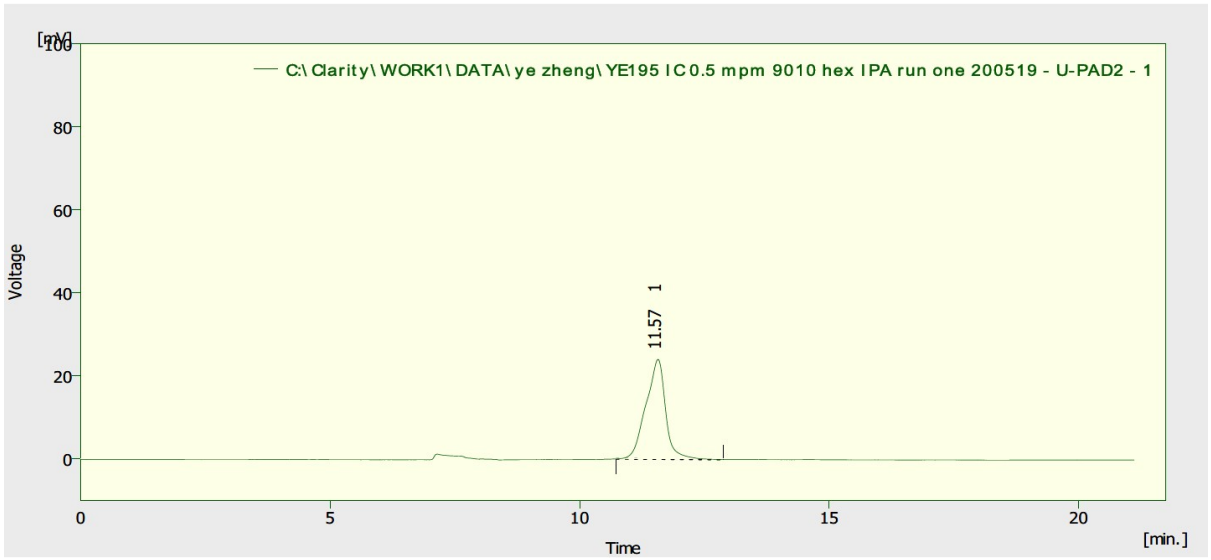
^{1}H NMR (400 MHz, $CDCl_3$) of **7e**:



^{13}C NMR (100 MHz, $CDCl_3$) of **7e**:



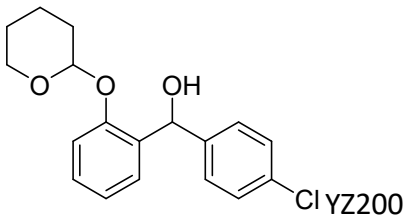
HPLC of (2-chlorophenyl)(2-methoxyphenyl)methanone **7e**:

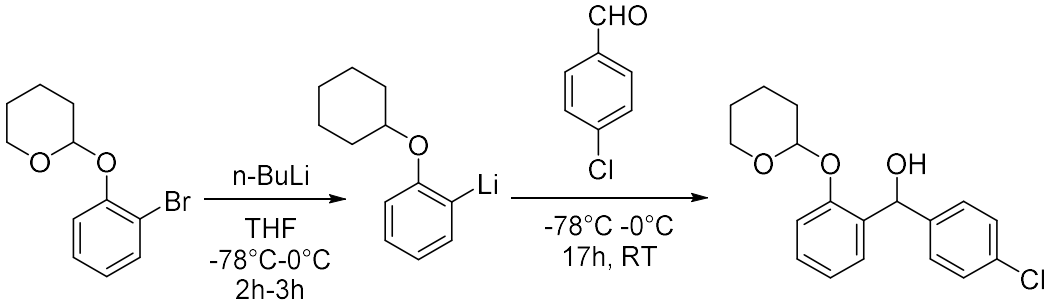


Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|ye zheng\|YE195 IC 0.5 mpm 9010 hex IPA run one 200519 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	11.568	656.531	24.056	100.0	100.0	0.43	
	Total	656.531	24.056	100.0	100.0		

(4-Chlorophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol.

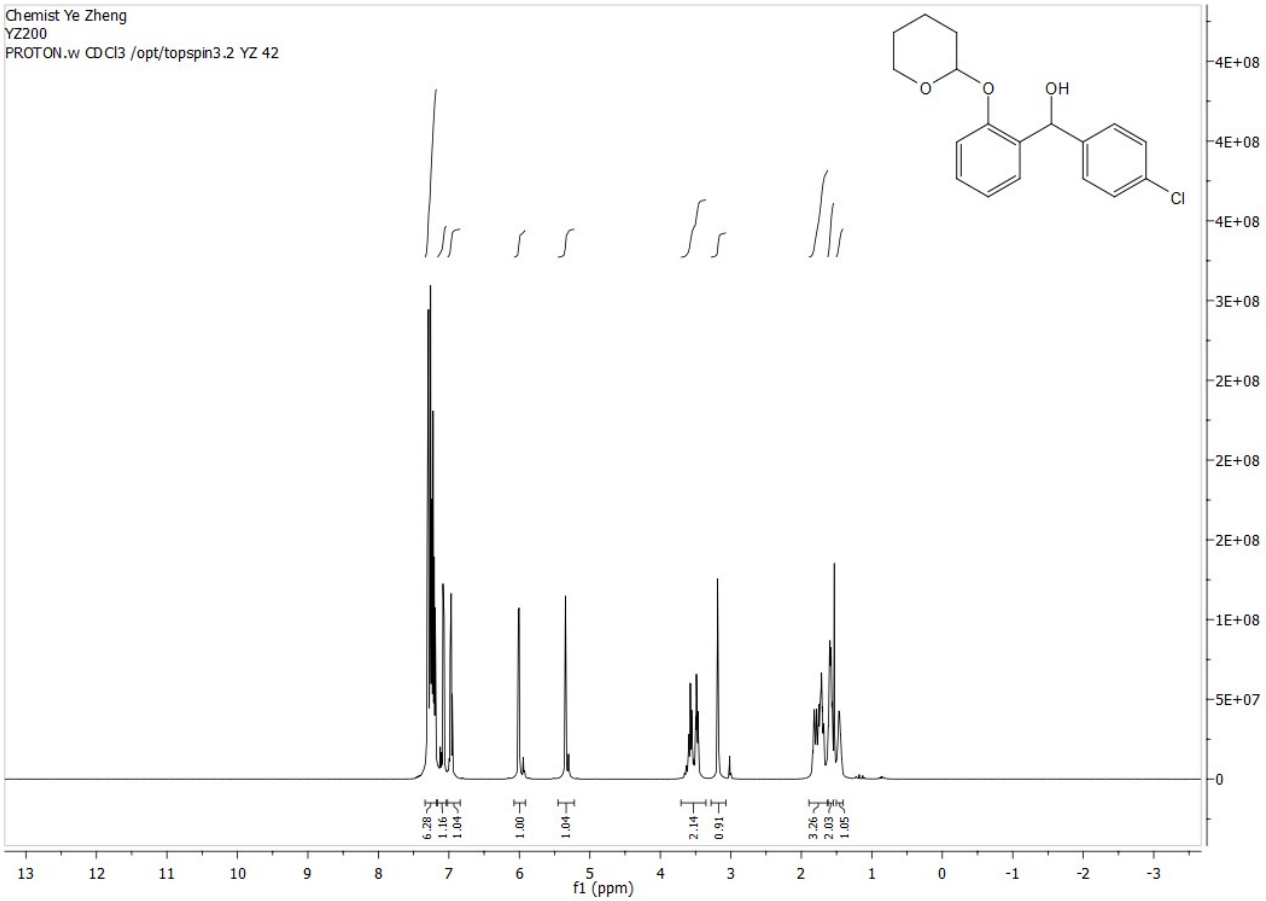




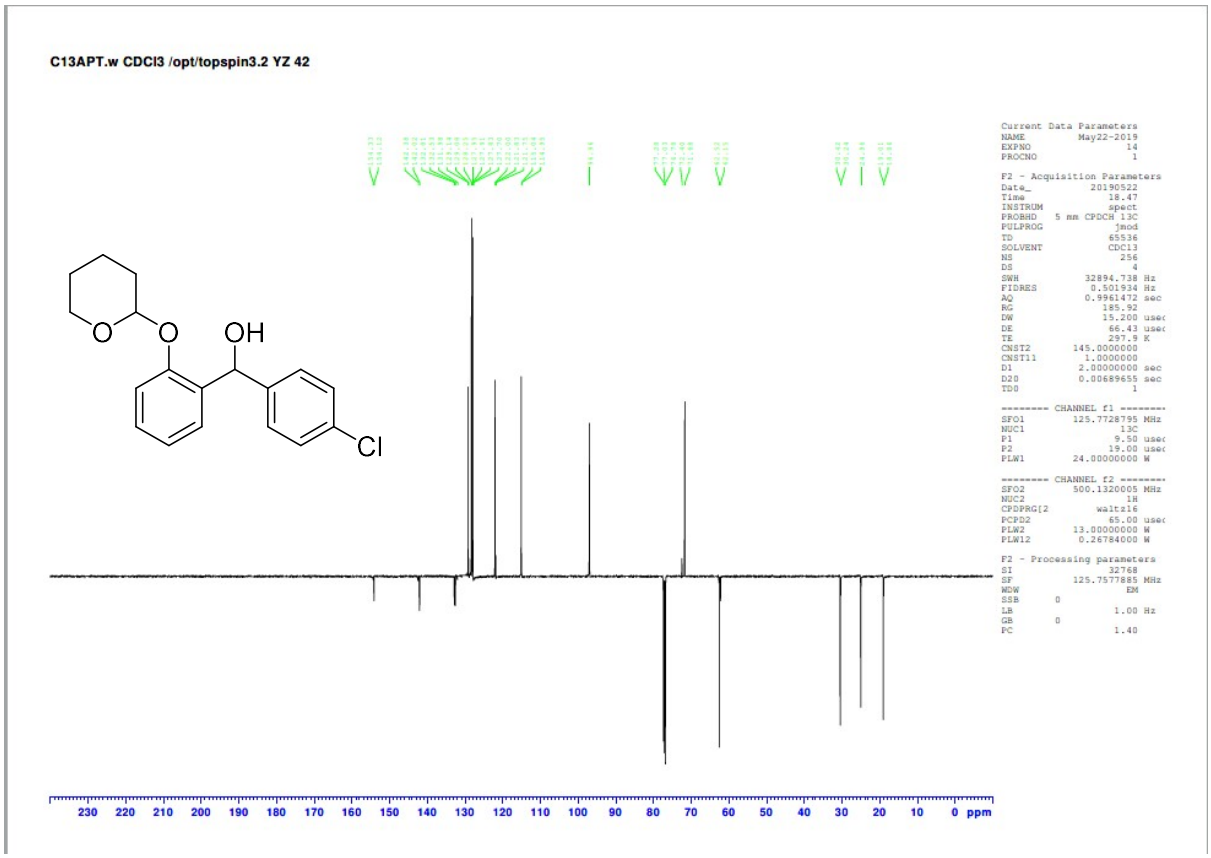
This compound is novel.

To a solution of 2-(2-bromophenoxy)tetrahydro-2H-pyran (431.9 mg, 1.69 mmol) THF) (2 mL at -78 °C was added a solution of n-butyllithium (0.61 mL, 2.5M in hexanes, 1.54 mmol). The reaction mixture was then stirred under a nitrogen atmosphere for 2-3 hours, after which 4-chlorobenzaldehyde (215.8 mg, 1.54 mmol) was added dropwise. The reaction mixture was left stirring under the nitrogen atmosphere and allowed to warm to rt. The reaction was followed by TLC (4:1 hexane: EtOAc). The mixture was quenched by saturated NH_4Cl solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 × 20 mL), and the combined organic layers were dried ($MgSO_4$) and filtered. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give (4-chlorophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol as a pale yellow solid (377 mg, 1.19 mmol, 77.2%). TLC: Rf ca 0.40 (4:1 hexane: EtOAc), strong UV and $KMnO_4$; Mp: 90 °C; HRMS: (found (ESI+): [M+Na]+, Calcd for $C_{18}H_{19}ClNaO_3$ 341.0903; Found 341.0899; -1.3 ppm error); ν_{max} 3422 (br), 2931, 1485, 1385, 1238, 1027, 755 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.31-7.20 (6H, m, ArH), 7.08 (1H, d, *J* = 8.0, ArH), 6.97 (1H, t, *J* = 7.5, ArH), 6.01 (1H, d, *J* = 5.5, Ar*CH*OH), 5.35 (1H, t, *J* = 3.5, O*CH*O), 3.63-3.46 (2H, m, O*CH*$_2$$CH_2$), 3.19 (1H, d, *J* = 5.5, ArCH*OH*), 1.83-1.68 (3H, m, CH_2), 1.63-1.55 (2H, m, CH_2), 1.48-1.43 (1H, m, CH_2) ppm; δ_C (125 MHz, $CDCl_3$) 154.1 (C), 142.0 (C), 132.5 (C), 129.1 (CH), 128.2 (CH), 128.0 (CH), 122.0 (C), 115.0 (CH), 97.0 (CH), 71.7 (CH), 62.5 (CH_2), 30.4 (CH_2), 25.0 (CH_2), 19.0 (CH_2) ppm; m/z (ES-API+) 341.2 (M^+ + 23, 100%).

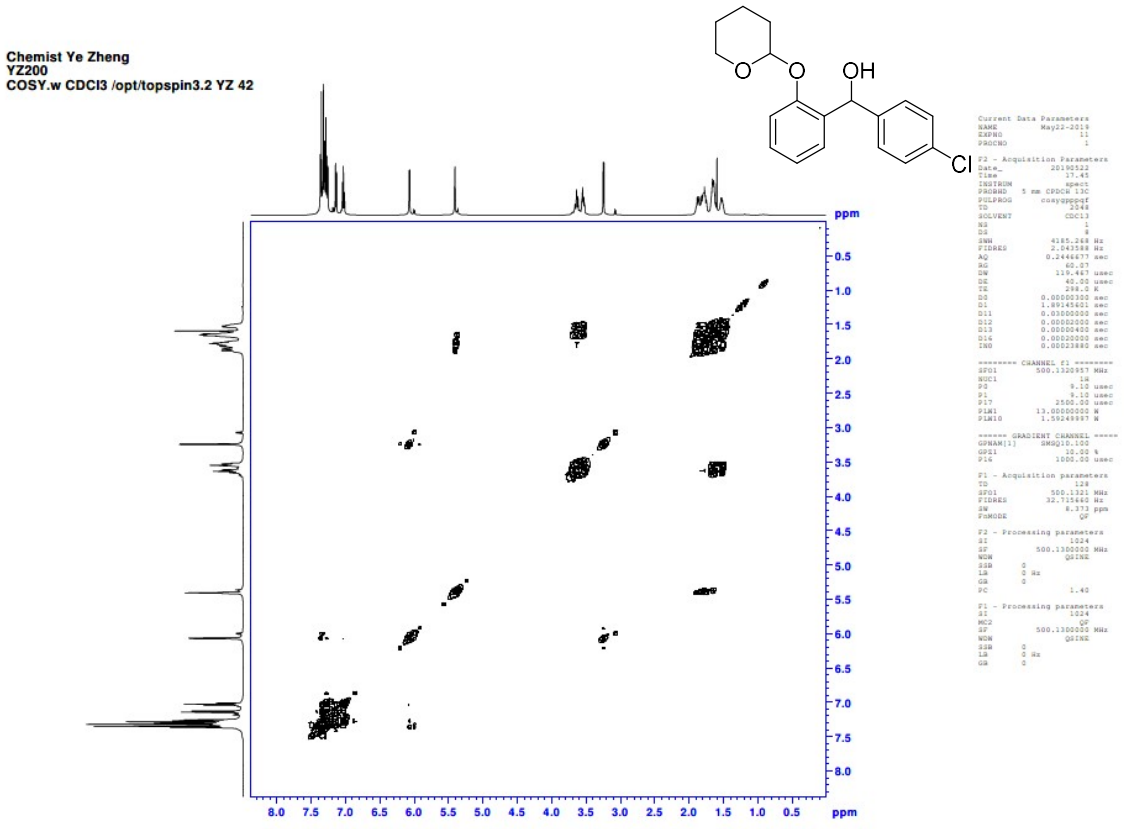
^{1}H NMR (500 MHz, $CDCl_3$) of (4-Chlorophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol:



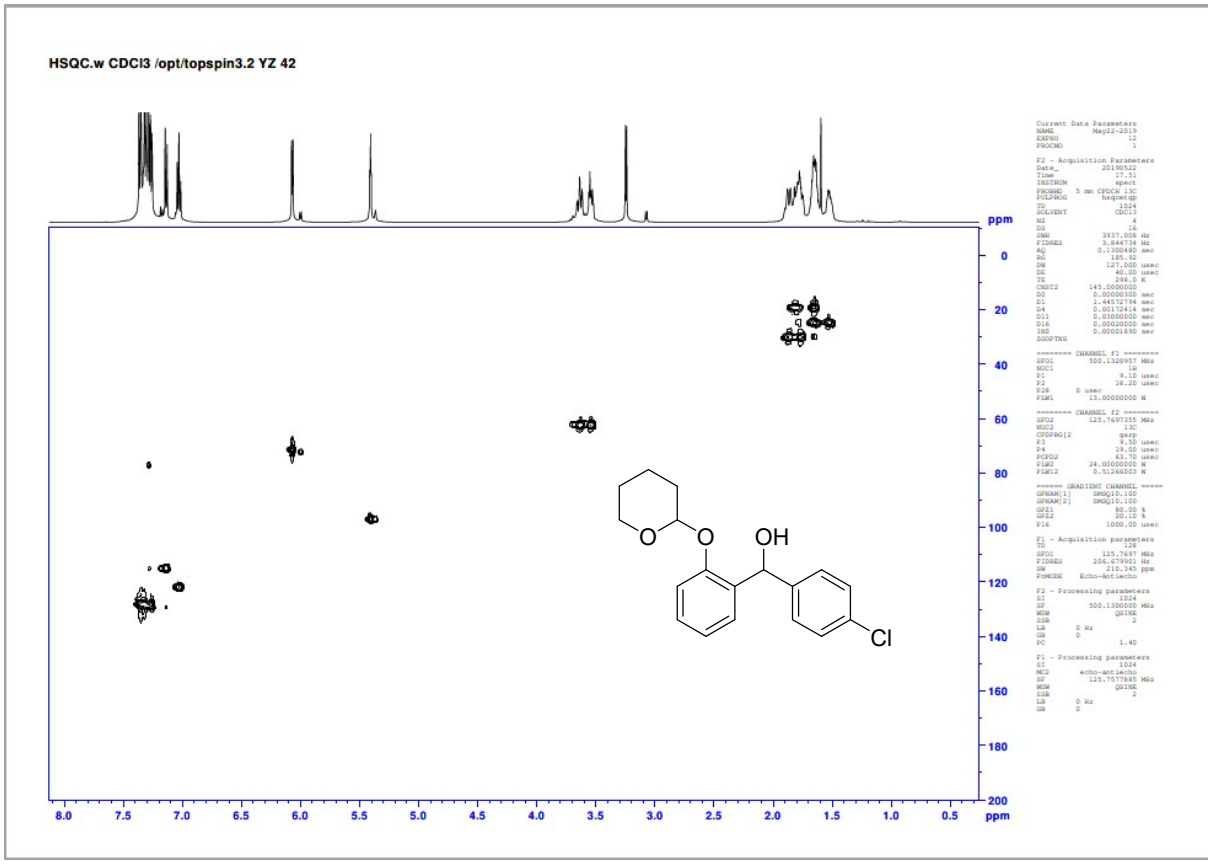
^{13}C NMR (125 MHz, $CDCl_3$) of (4-Chlorophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol:



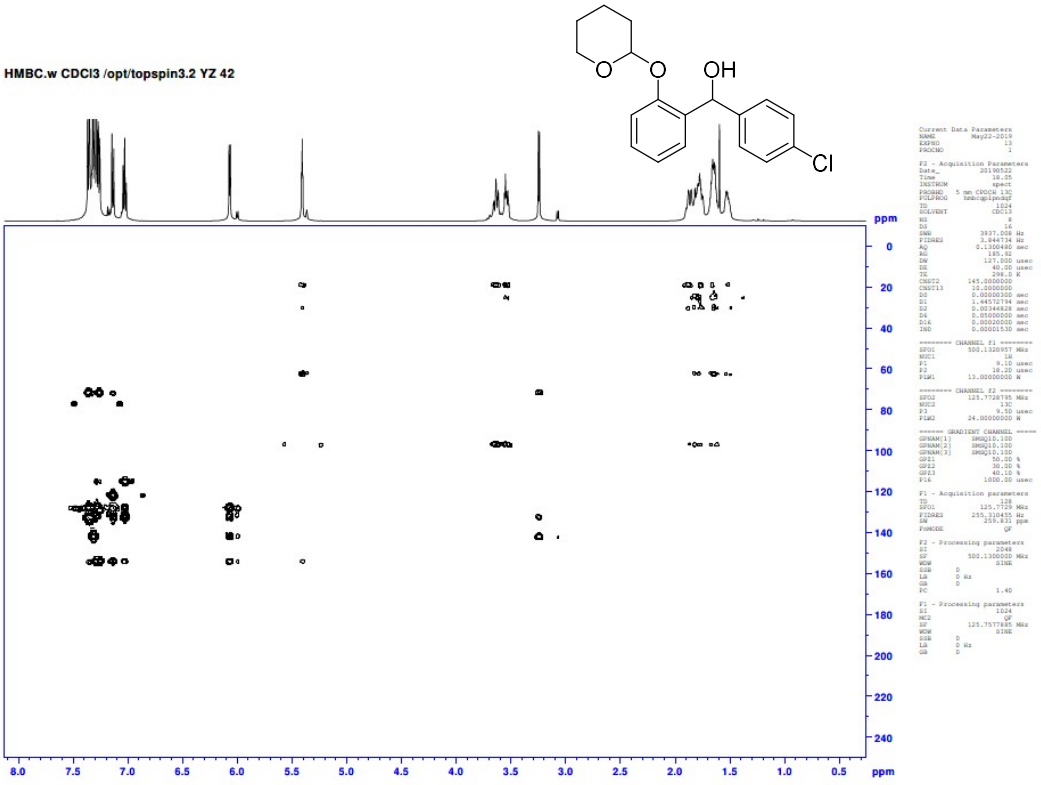
COSY (500 MHz, $CDCl_3$) of (4-Chlorophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol:



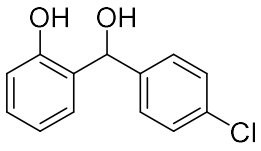
HSQC (500 MHz, $CDCl_3$) of (4-Chlorophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol:



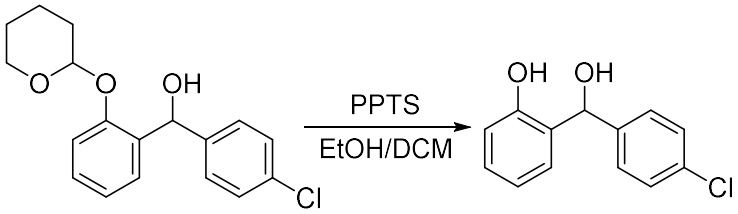
HMBC (500 MHz, $CDCl_3$) of (4-Chlorophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol:



2-((4-Chlorophenyl)(hydroxy)methyl)phenol 8f.



racemic: YZ203, Asymmetric: YZ208



This compound has been reported and fully characterized.

Reference: Lai, Z.; Wang, Z.; Sun, J. *Org. Lett.* **2015**, *17*, 6058 – 6061.

To a solution of (4-chlorophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol (375 mg, 1.18 mmol) in EtOH (5.9 mL)/DCM (3.0 mL) was added pyridinium *p*-toluenesulfonate (PPTS) (44.4 mg, 0.18 mmol) at rt. The reaction mixture was left to stir under a nitrogen atmosphere overnight. TLC (4:1 hexane: EtOAc) after this time indicated full conversion. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give 2-((4-chlorophenyl)(hydroxy)methyl)phenol **8f** as a colorless oil (120.1 mg, 0.51 mmol, 43.5%). TLC: Rf ca 0.20 (4:1 hexane: EtOAc), strong UV and $KMnO_4$; δ_H (400 MHz, $CDCl_3$) 7.51 (1H, s, ArOH), 7.33 (4H, s, ArH), 7.21 (1H, t, *J* = 7.2, ArH), 6.91-6.82 (3H, m, ArH), 6.00 (1H, s, Ar*CH*OH), 2.84 (1H, s, ArCH*OH*) ppm; δ_C (100 MHz, $CDCl_3$) 155.3 (C), 140.3 (C), 152.9 (C), 129.6 (CH), 128.9 (CH), 128.2 (CH), 126.7 (C), 120.1 (CH), 117.4 (CH), 76.2 (CH) ppm. Data matched that reported.

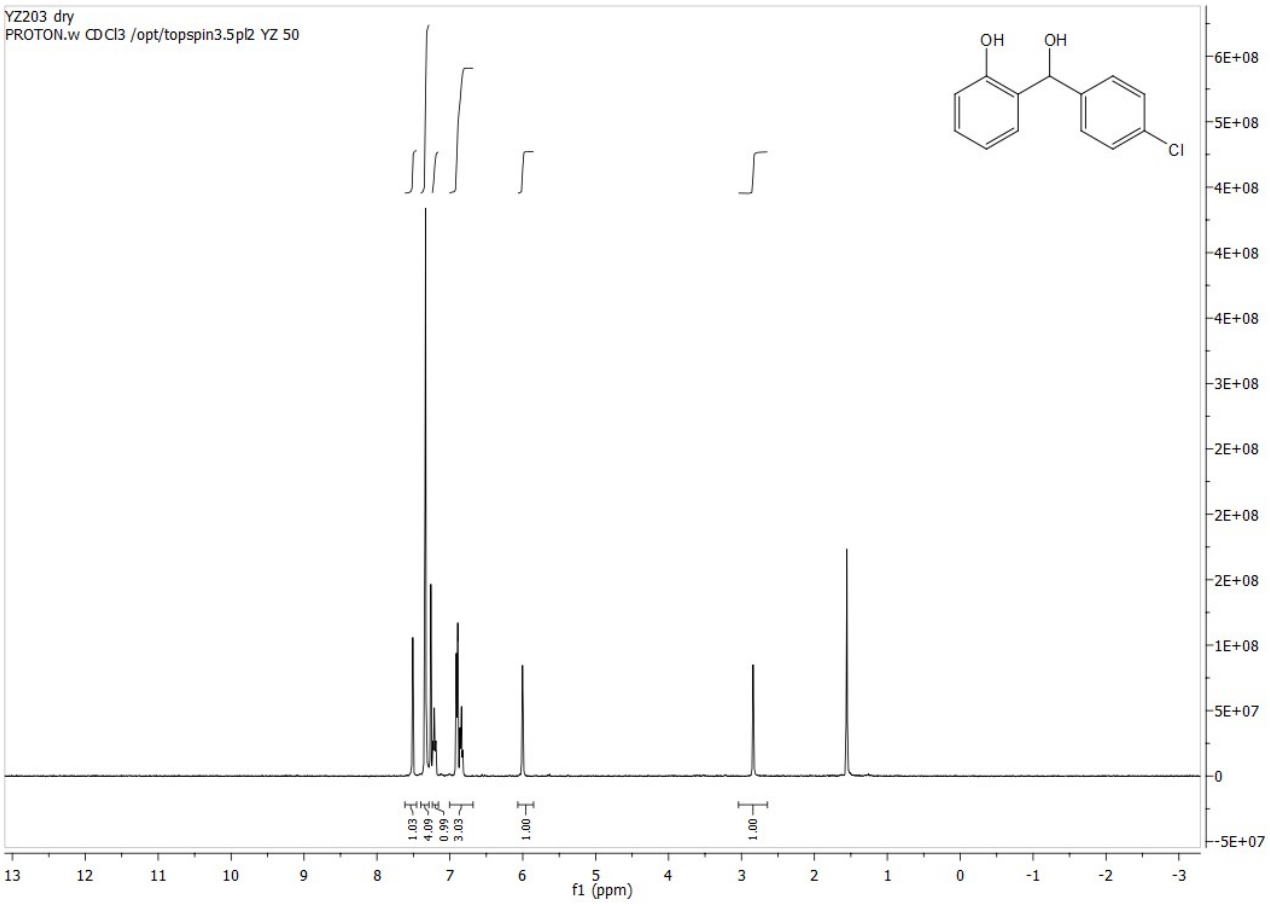
Enantiomeric excess and conversion determined by HPLC analysis (Chiralcel ODH, 30 cm x 6mm column, hexane:iPrOH 9:1, 1.0 mL/min, T = 25°C) ketone 5.4 min, *R* isomer and *S* isomer are 12.2 min and 13.8 min, configuration was assigned by analogy.

ATH of 2-((4-chlorophenyl)(hydroxy)methyl)phenol 7f (YZ208)

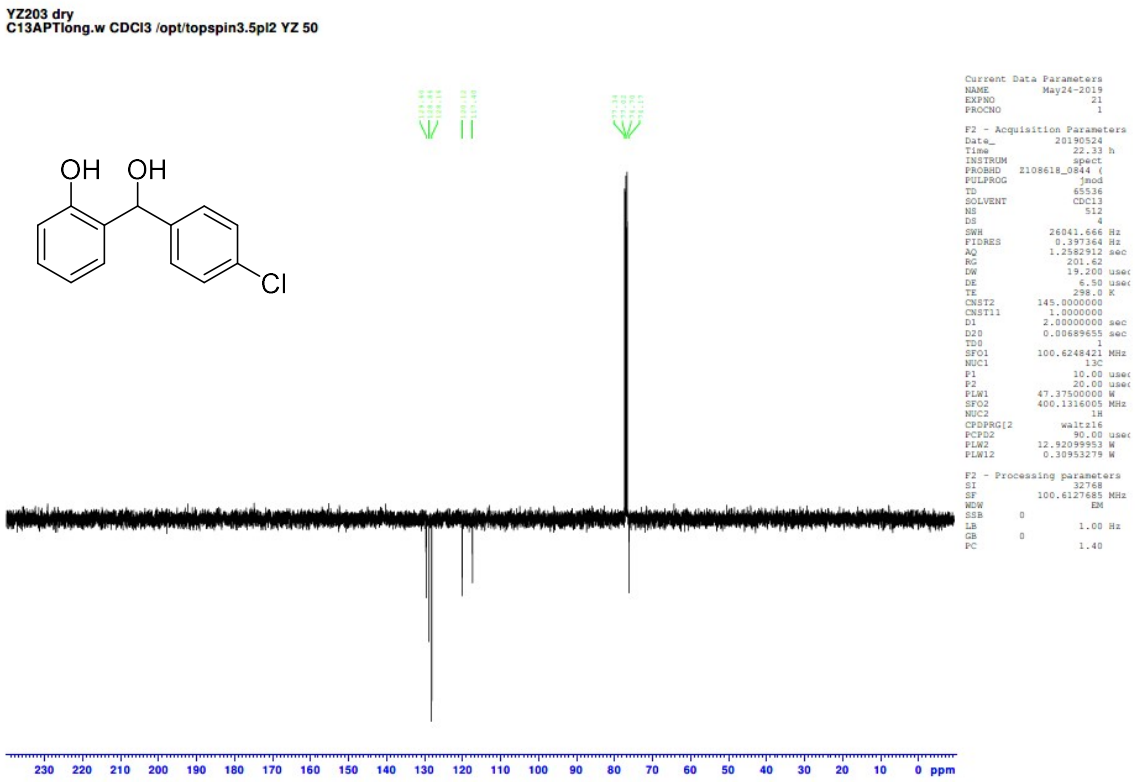
Catalyst (*R*<*R*)-**2** (0.0017 mmol, 1mol%) was added to FA: TEA (5:2 azeotropic mixture, 0.18 mL) at rt and stirred under a nitrogen atmosphere for 10-15 minutes; after which a solution of 2-((4-chlorophenyl)(hydroxy)methyl)phenone **7f** (40 mg, 0.17 mmol) in DCM (0.25 mL) was added. The reaction mixture was stirred under a nitrogen atmosphere, followed by TLC (4:1 hexane: EtOAc). After 72 hours, the reaction was quenched using saturated $NaHCO_3$ solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried ($MgSO_4$) and filtered. The solvent was

removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give 2-((4-chlorophenyl)(hydroxy)methyl)phenol **8f** (24.5 mg, 0.10 mmol, 60.7%; (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst example). The reaction was also followed by HPLC (Chiralcel ODH, 30 cm x 6mm column, hexane:iPrOH 9:1, 1.0 mL/min, T = 25°C); (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst: 100% conversion; $[\alpha]_D^{31}$ -40.3 (c 0.178 in $CHCl_3$) 89% ee.

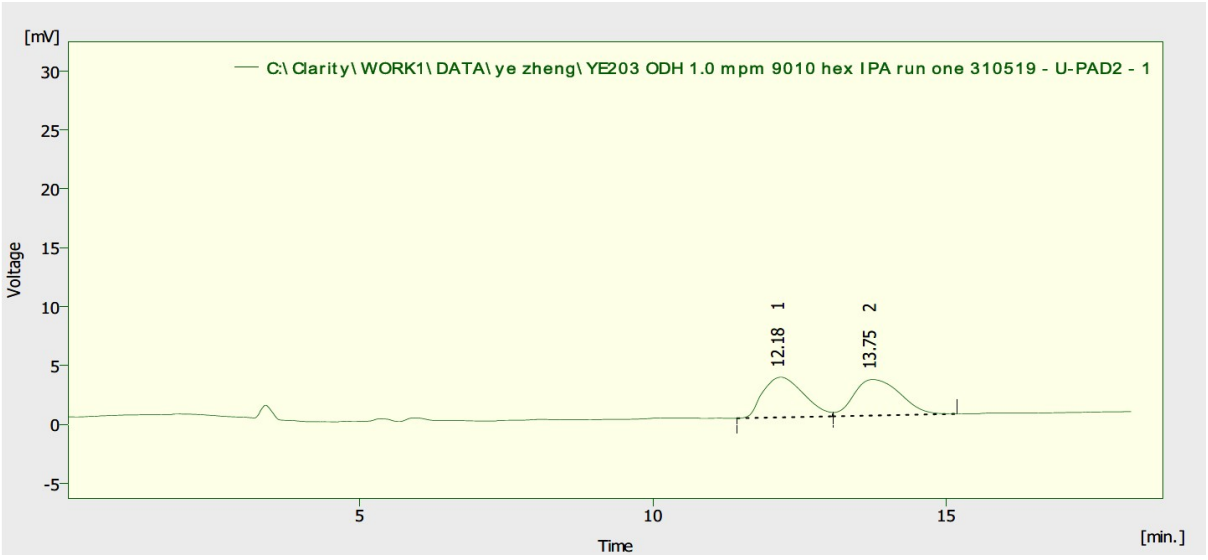
^{1}H NMR (400 MHz, $CDCl_3$) of **8f**:



^{13}C NMR (100 MHz, $CDCl_3$) of **8f**:



HPLC of racemic 2-((4-chlorophenyl)(hydroxy)methyl)phenol **8f**:

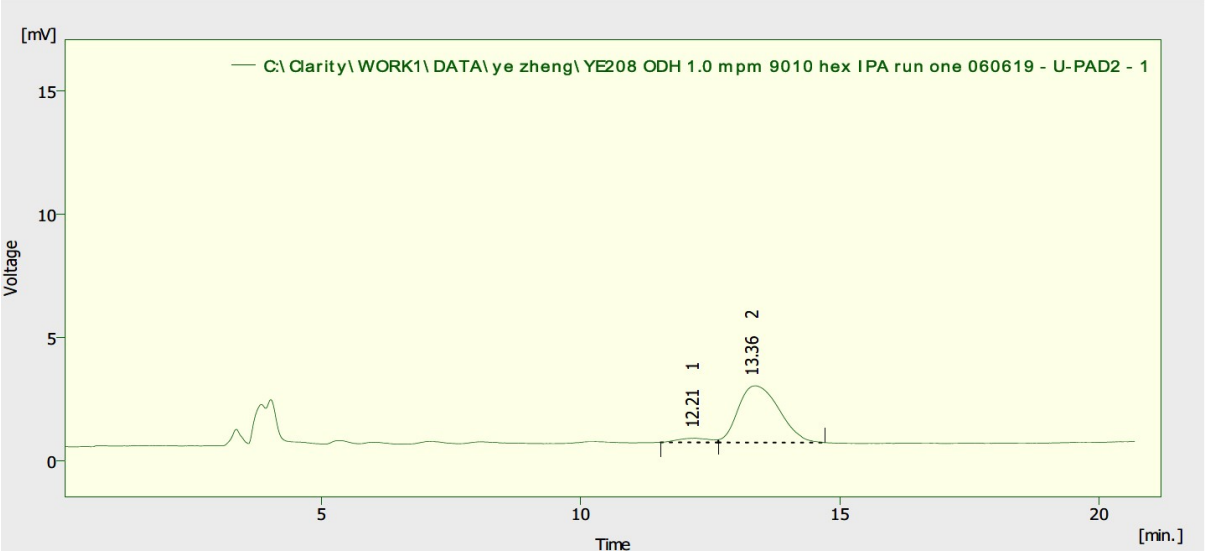


Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|ye zheng\|YE203 ODH 1.0 mpm 9010 hex IPA run one 310519 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	12.184	165.840	3.417	49.5	52.8	0.82	
2	13.748	168.922	3.061	50.5	47.2	0.90	
	Total	334.761	6.478	100.0	100.0		

HPLC of **8f** after ATH of 2-((4-chlorophenyl)(hydroxy)methyl)phenone **7f**:

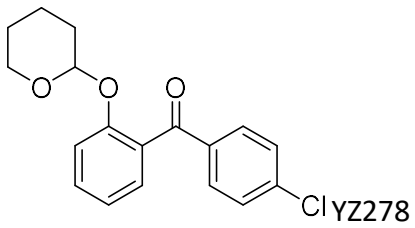
(*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst (after 72 hours, 100% conversion, 89% ee)

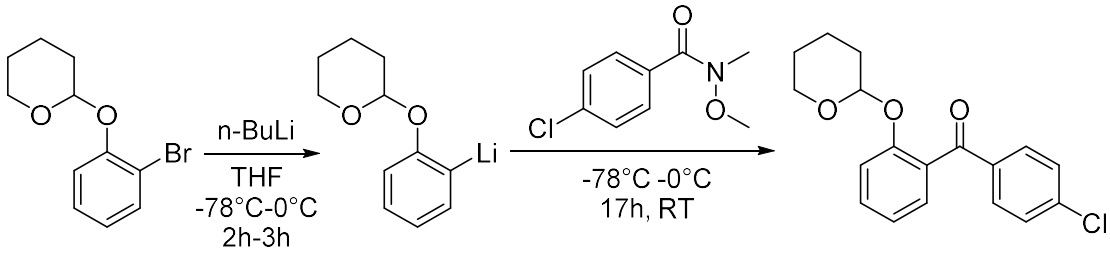


Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|ye zheng\|YE208 ODH 1.0 mpm 9010 hex IPA run one 060619 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	12.212	7.429	0.170	5.5	6.9	0.84	
2	13.364	126.686	2.305	94.5	93.1	0.89	
	Total	134.115	2.475	100.0	100.0		

(4-Chlorophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanone; via Weinreb reagent.

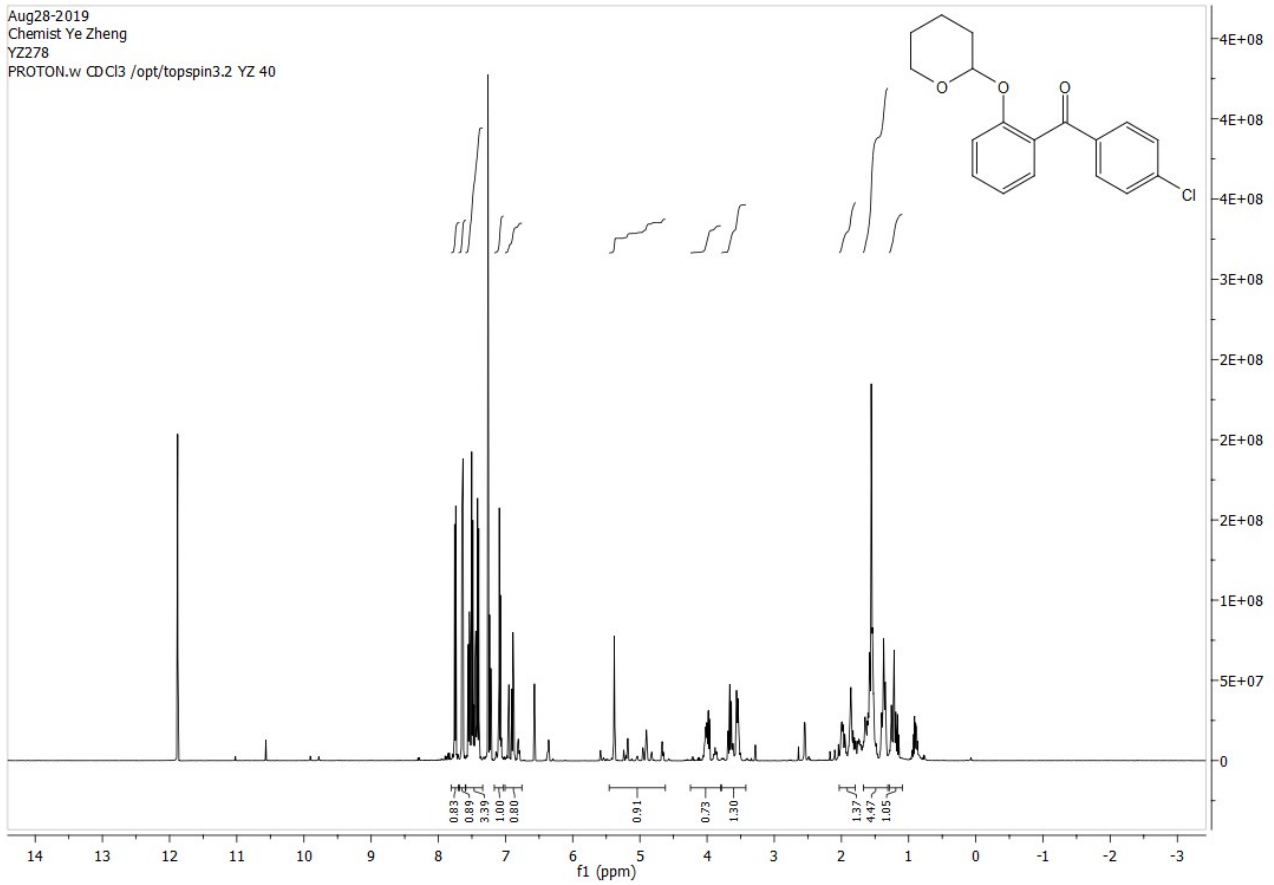




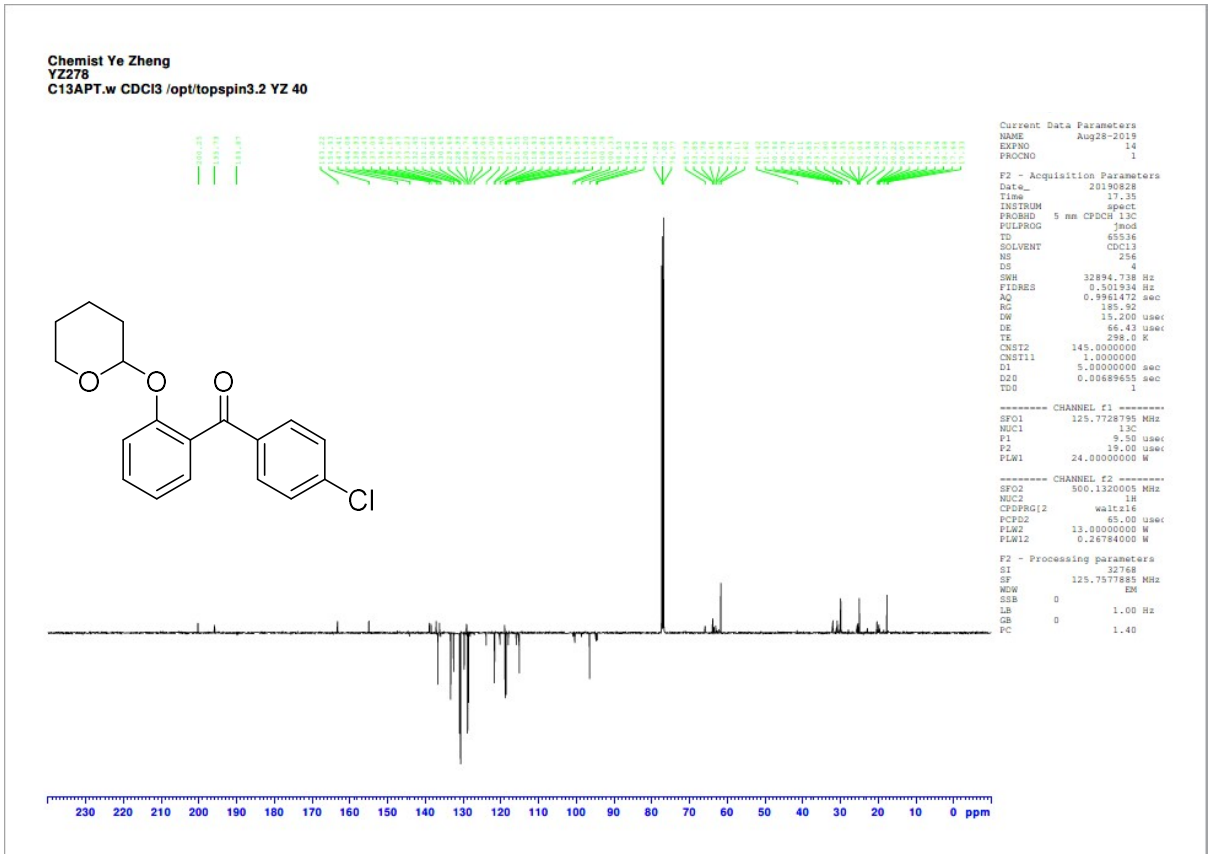
This compound is novel.

To a solution of 2-(2-bromophenoxy)tetrahydro-2H-pyran (210.9 mg, 0.824 mmol in THF (3 mL) at -78 °C was added a solution of n-butyllithium (0.30 mL, 2.5M in hexanes, 0.749 mmol). The reaction mixture was then stirred under a nitrogen atmosphere for 2-3 hours, after which 4-chloro-N-methoxy-N-methylbenzamide (149 mg, 0.749 mmol) was added dropwise. The reaction mixture was left stirring under the nitrogen atmosphere and allowed to warm to rt. The reaction was followed by TLC (4:1 hexane: EtOAc). The mixture was quenched by saturated NH_4Cl solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 × 20 mL), and the combined organic layers were dried ($MgSO_4$) and filtered. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give (4-chlorophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanone as a colorless oil (82.0 mg, 0.259 mmol, 34.7%). TLC: Rf ca 0.60 (4:1 hexane: EtOAc), strong UV and $KMnO_4$; HRMS: (found (ESI+): [M+Na]+, Calcd for $C_{18}H_{17}ClNaO_3$ 339.0756; Found 339.0758; 0.8 ppm error); ν_{max} 3069, 2943, 2872, 1661, 1596, 1585, 1481, 1449, 1258, 1200, 956 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.75 (1H, d, *J* = 8.6, ArH), 7.64 (1H, d, *J* = 8.6, ArH), 7.60-7.34 (3H, m, ArH), 7.17-7.03 (1H, m, ArH), 7.01-6.76 (1H, m, ArH), 5.46-4.62 (1H, m, OCH_2O), 4.25-3.80 (1H, m, OCH_2CH_2), 3.78-3.42 (1H, m, OCH_2CH_2), 2.03-1.79 (1H, m, CH_2), 1.67-1.31 (1H, m, CH_2), 1.29-1.09 (1H, m, CH_2) ppm; δ_C (125 MHz, $CDCl_3$) 154.9 (C), 138.9 (C), 137.1 (C), 136.6 (CH), 133.2 (CH), 130.7 (CH), 129.0 (C), 128.7 (CH), 121.6 (CH), 118.8 (CH), 118.9 (C), 115.1 (CH), 96.4 (CH), 61.6 (CH_2), 29.9 (CH_2), 24.9 (CH_2), 17.6 (CH_2) ppm; m/z (ES-API+) 339.2 (M^+ + 23, 100%).

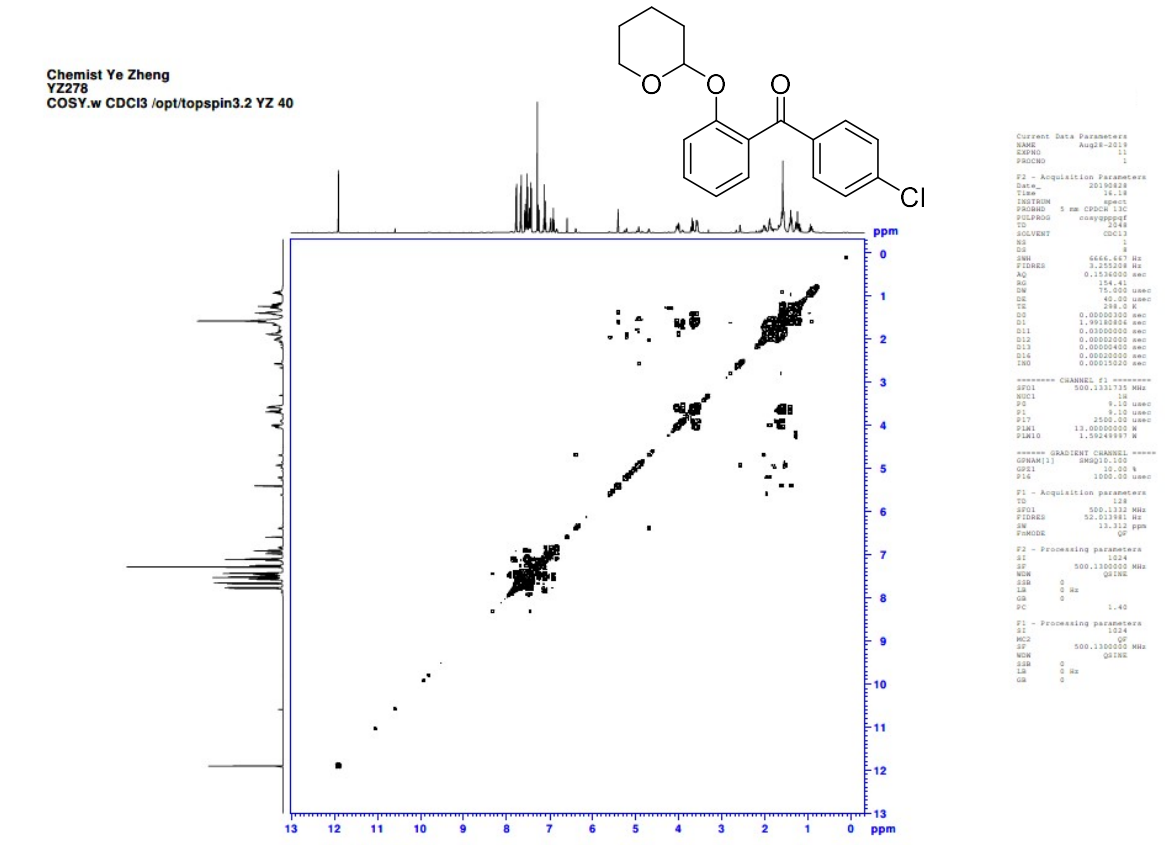
^{1}H NMR (500 MHz, $CDCl_3$) of (4-Chlorophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanone:



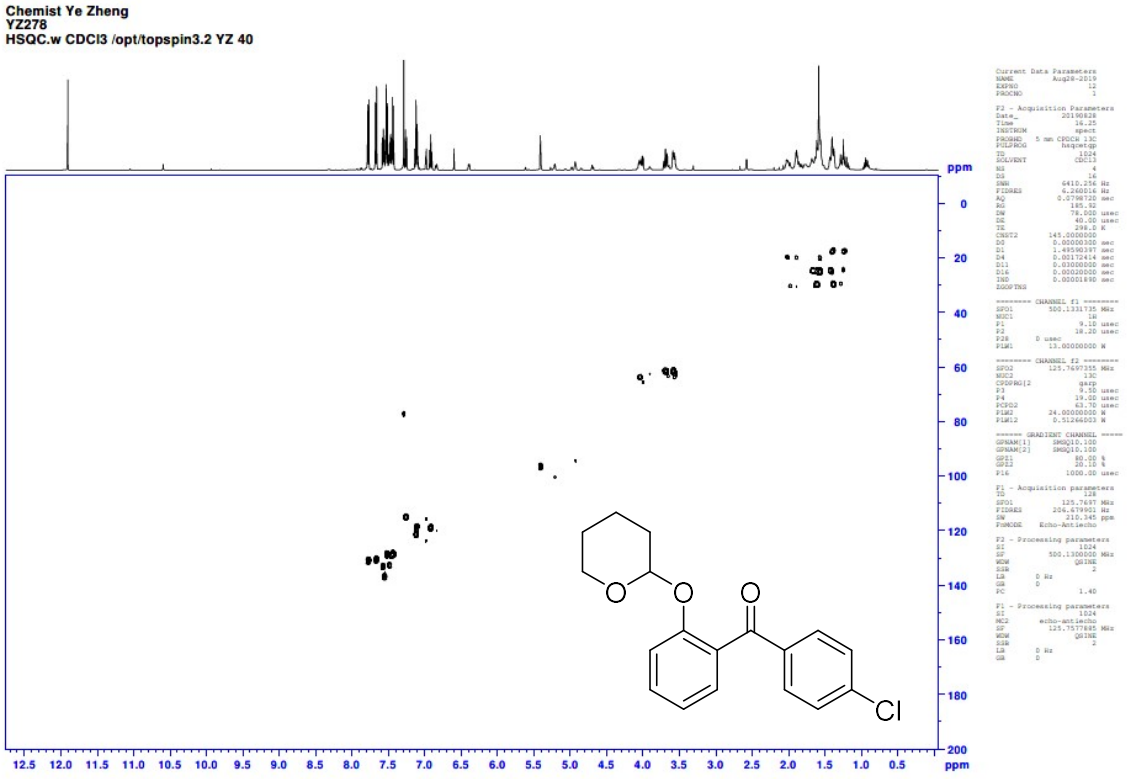
^{13}C NMR (125 MHz, $CDCl_3$) of (4-Chlorophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanone:



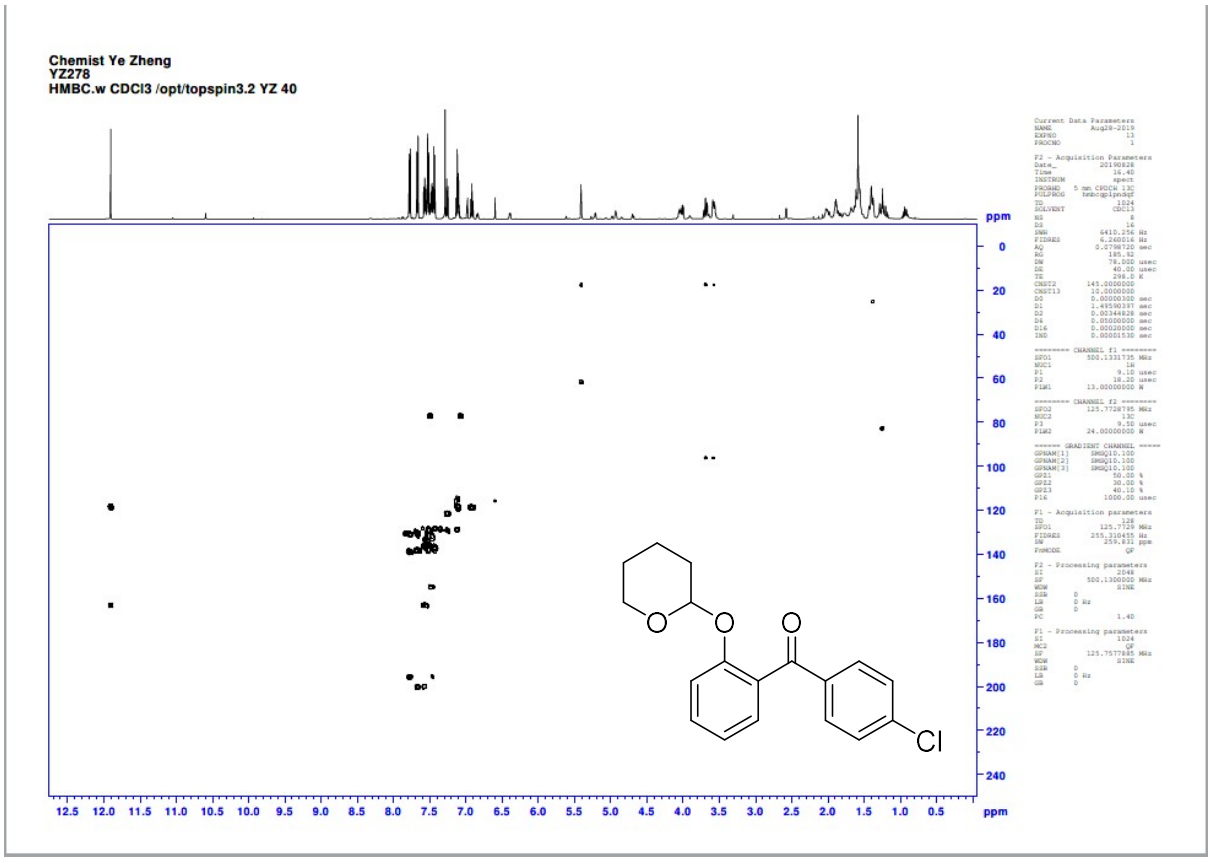
COSY (500 MHz, $CDCl_3$) of (4-Chlorophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanone:



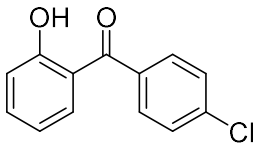
HSQC (500 MHz, $CDCl_3$) of (4-Chlorophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanone:



HMBC (500 MHz, $CDCl_3$) of (4-Chlorophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanone:

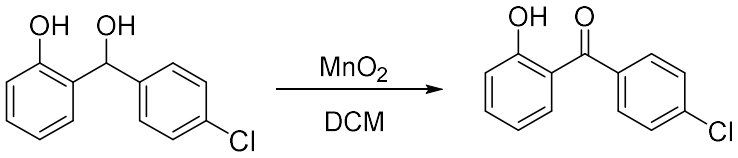


(4-Chlorophenyl)(2-hydroxyphenyl)methanone 7f.

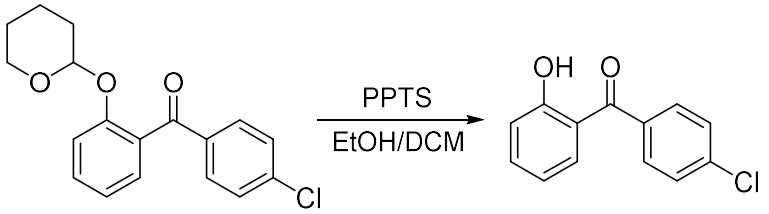


via oxidation; YZ205, from THP ether; YZ308

YZ205



YZ308



from Weinreb route.

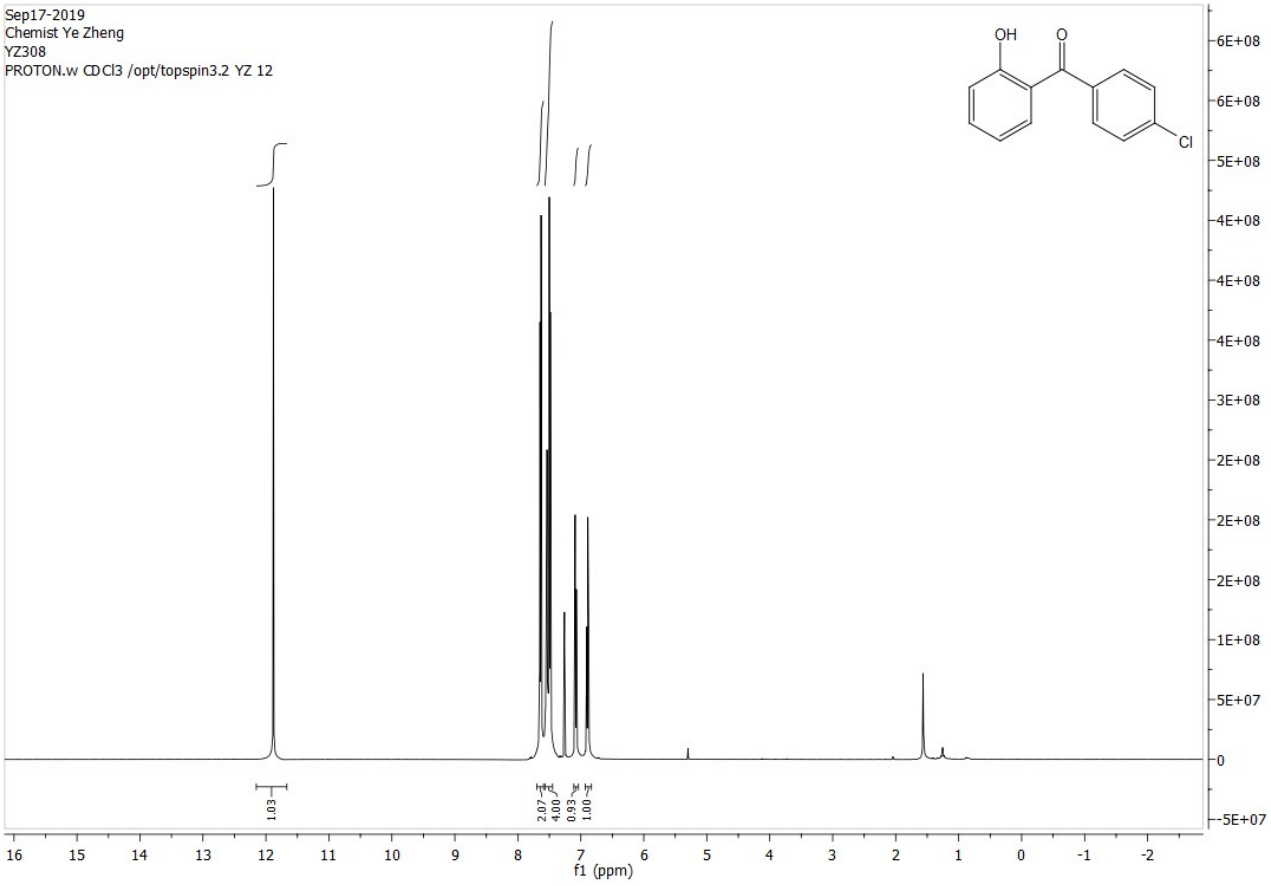
This compound has been reported and fully characterized.

Reference: Rao, Maddali L. N.; Ramakrishna, Boddu S. *Eur. J. Org. Chem.* **2017**, *2017*, 5080 – 5093.

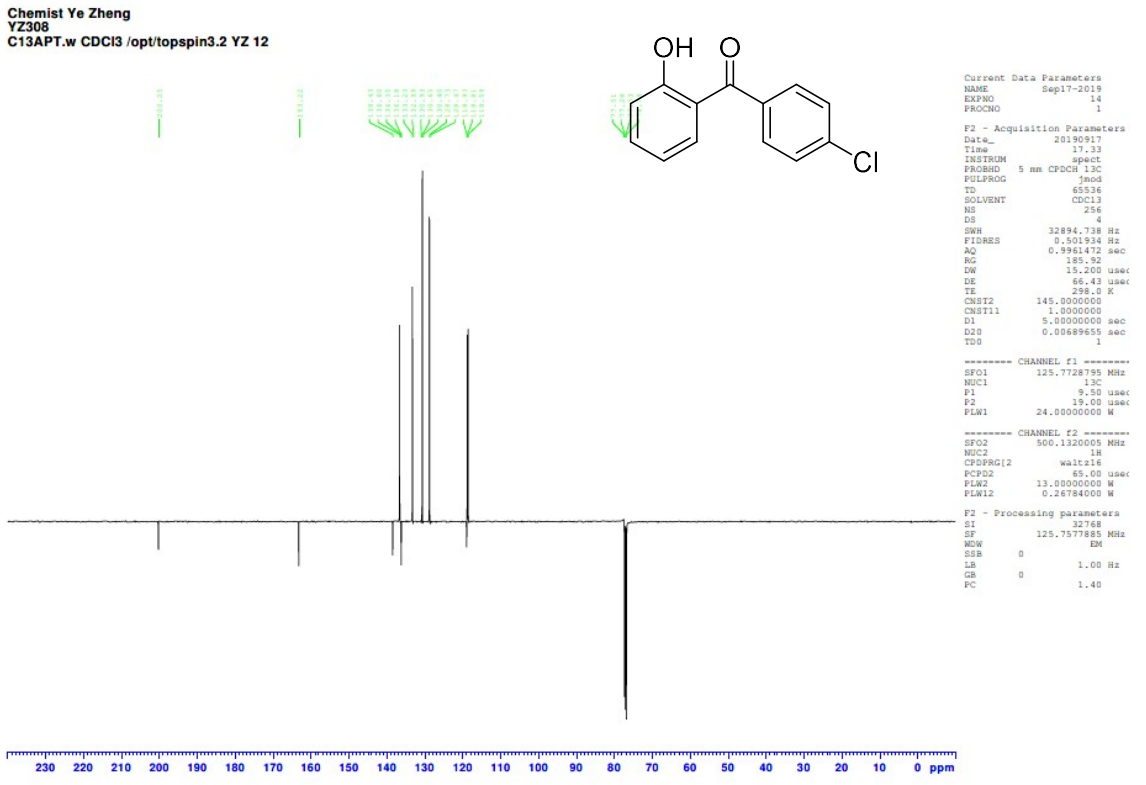
Via oxidation: To a solution of (4-chlorophenyl)(2-hydroxyphenyl)methanol (120 mg, 0.51 mmol) in DCM (5 mL) at rt was added manganese dioxide (665 mg, 7.65 mmol). The reaction mixture was left to stir under a nitrogen atmosphere overnight. TLC (4:1 hexane: EtOAc) after this time indicated full conversion. The solids were removed by gravity filtration and washed with DCM. The solvent was removed to give (4-chlorophenyl)(2-hydroxyphenyl)methanone **7f** as a yellow oil (55.8 mg, 0.24 mmol, 47%).

From Weinreb route: To a solution of (4-chlorophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanone (440.5 mg, 1.39 mmol) in EtOH (6.8 mL)/DCM (3.4mL) was added pyridinium *p*-toluenesulfonate (PPTS) (52.5 mg, 0.209 mmol) at rt. The reaction mixture was left to stir under a nitrogen atmosphere overnight. TLC (4:1 hexane: EtOAc) after this time indicated full conversion. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give (4-chlorophenyl)(2-hydroxyphenyl)methanone **7f** as a yellow oil (205.5 mg, 0.886 mmol, 63.5%). TLC: Rf ca 0.40 (4:1 hexane: EtOAc), strong UV and KMnO4; TLC: Rf ca 0.40 (4:1 hexane: EtOAc), strong UV and KMnO4; δ_H (500 MHz, $CDCl_3$) 11.88 (1H, s, OH), 7.64 (2H, d, *J* = 8.5, ArH), 7.57-7.45 (4H, m, ArH), 7.08 (1H, d, *J* = 8.3, ArH), 6.89 (1H, t, *J* = 7.9, ArH) ppm; δ_C (125 MHz, $CDCl_3$) 200.2 (C), 163.2 (C), 138.4 (C), 136.6 (CH), 136.2 (C), 133.2 (CH), 130.7 (CH), 128.7 (CH), 118.8 (CH), 118.9 (C), 118.6 (CH) ppm. Data matched that reported.

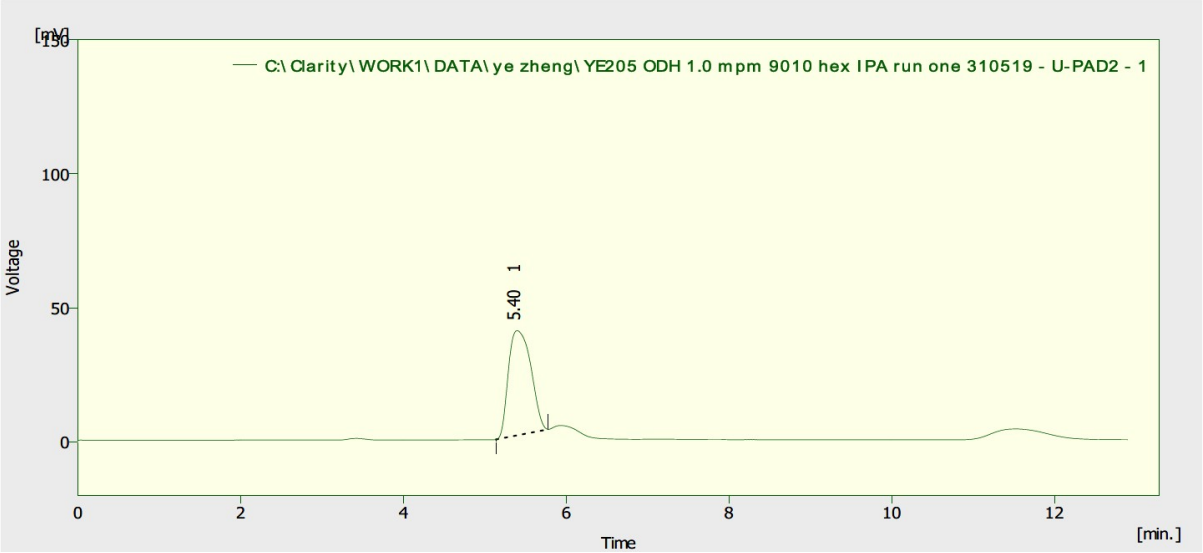
^{1}H NMR (500 MHz, $CDCl_3$)of **7f**:



^{13}C NMR (125 MHz, $CDCl_3$) of **7f**:



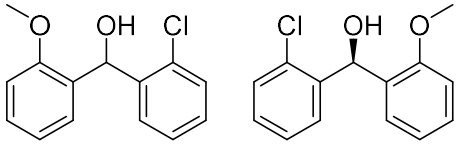
HPLC of (2-chlorophenyl)(2-methoxyphenyl)methanone **7f**:



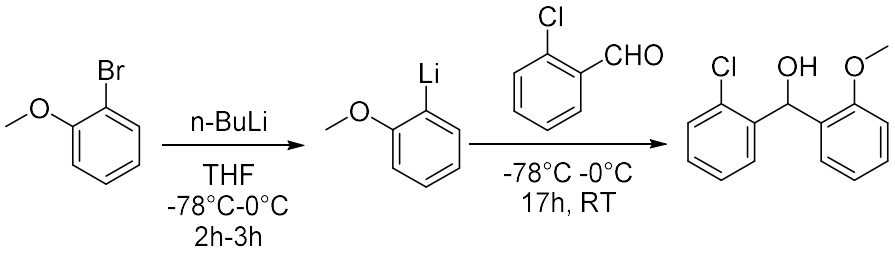
Result Table (Uncal - C:|Clarity|WORK1|DATA|ye zheng|YE205 ODH 1.0 mpm 9010 hex IPA run one 310519 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	5.396	748.355	39.138	100.0	100.0	0.33	
	Total	748.355	39.138	100.0	100.0		

(2-Chlorophenyl)(2-methoxyphenyl)methanol 8g.



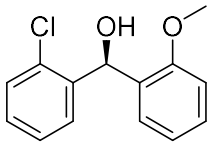
racemic: YZ162, Asymmetric: YZ172



This compound is novel.

To a solution of 2-bromoanisole (840 mg, 0.560 mL, 4.52 mmol) in THF (3.5 mL) at -78 °C was added dropwise a solution of n-butyllithium (1.8 mL, 2.5M in hexanes, 4.5 mmol). The reaction mixture was then stirred under a nitrogen atmosphere for 2-3 hours, after which 2-chlorobenzaldehyde (250 mg, 1.79 mmol) was added dropwise. The reaction mixture was left stirring under the nitrogen atmosphere and allowed to warm to rt. The reaction was followed by TLC (4:1 hexane: EtOAc). The mixture was quenched by saturated NH_4Cl solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 × 20 mL), and the combined organic layers were dried ($MgSO_4$) and filtered. The solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give (2-chlorophenyl)(2-methoxyphenyl)methanol **7g** as a colorless oil (300 mg, 1.21 mmol, 68%). TLC: Rf ca 0.20 (4:1 hexane: EtOAc), strong UV and $KMnO_4$; HRMS: (found (ESI+): [M+Na]+, Calcd for $C_{14}H_{13}ClNaO_2$ 271.0499; Found 271.0496; -1.1 ppm error); ν_{max} 3406 (br), 3065, 2937, 2836, 1600, 1489, 1239, 1023, 749 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.59 (1H, d, *J* = 7.5, ArH), 7.37-7.23 (4H, m, ArH), 6.98-6.88 (3H, m, ArH), 6.46 (1H, d, *J* = 4.0, Ar*CH*OH), 3.88 (3H, s, OCH_3), 3.10 (1H, d, *J* = 4.0, ArCH*OH*) ppm; δ_C (125 MHz, $CDCl_3$) 157.1 (C), 139.9 (C), 132.9 (C), 130.4 (C), 129.4 (CH), 129.1 (CH), 128.6 (CH), 128.5 (C), 127.8 (CH), 126.8 (CH), 120.7 (CH), 110.6 (CH), 68.6 (CH), 55.5 (CH_3) ppm; m/z (ES-API+) 271.2 (M^+ + 23, 100%).

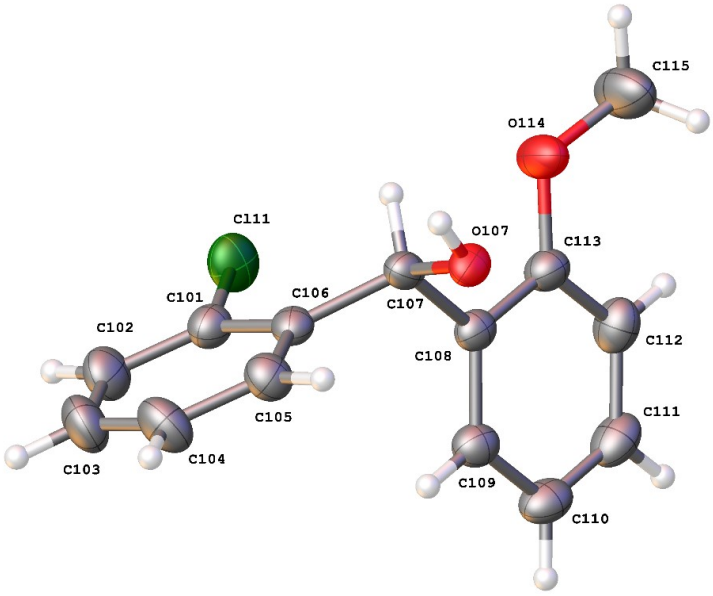
Enantiomeric excess and conversion determined by HPLC analysis (Chiralpak IC, 30 cm x 6mm column, hexane: iPrOH 95:5, 0.8 mL/min, T = 25°C) ketone 24.2 min, *R* isomer 15.8 min and *S* isomer 12.9 min.



ATH of (2-chlorophenyl)(2-methoxyphenyl)methanone 7g (YZ172)

Catalyst (*R,R*)-**2** (0.00162 mmol, 1 mol%) was added to the FA: TEA (5:2 azeotropic mixture, 0.18 mL) at rt and the mixture was stirred under a nitrogen atmosphere for 10-15 minutes; after which a solution of (2-chlorophenyl)(2-methoxyphenyl)methanone **7g** (40 mg, 0.162 mmol) in DCM (0.25 mL) was added.The reaction mixture was stirred under a nitrogen atmosphere, followed by TLC (4:1 hexane: EtOAc). After 168 hours, the reaction was quenched by saturated $NaHCO_3$ solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried ($MgSO_4$) and filtered. The solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give (2-chlorophenyl)(2-methoxyphenyl)methanol **8g** (35.1 mg, 0.141 mmol, 87%; (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst example). The reaction was also followed by HPLC analysis (Chiralpak IC, 30 cm x 6 mm column, hexane:iPrOH 95:5, 0.8 mL/min, T = 25°C); (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst: 98% conversion (HPLC calibration: 1:1 (2-chlorophenyl)(2-methoxyphenyl)methanone: (2-chlorophenyl)(2-methoxyphenyl)methanol gives 12.7:1 absorption at 254 nm); $[\alpha]_D^{25}$ -20.2 (c 0.875 in $CHCl_3$) 85.8% ee (*S*).

Crystal structure determination of 8g CCDC 1978883 [local code yz6]



The asymmetric unit contains five crystallographically independent but chemically identical molecules in the asymmetric unit of yz6, ten in the unit cell. The chlorobenzene ring of molecule Cl31-C317 was disordered over two closely related positions. The occupancy of the two components was linked to a free variable which refine to 78:22. The minor component was refined isotropically. An AFIX 66 restraint and several SIMU and RIGU restraints were used to give the thermal parameters of the minor disordered component sensible thermal parameters.
The OHs were located in a difference map but refined with positional restraints. They form short contacts tabulated below.

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

D-H	H...A	D...A	<(DHA)	
0.82	1.98	2.787(3)	167.7	O107-H10A...O507_$1
0.82	1.96	2.772(3)	172.5	O207-H20A...O307
0.82	1.93	2.747(3)	179.5	O307-H30A...O107
0.82	1.90	2.721(3)	173.0	O407-H40B...O207
0.82	1.88	2.700(3)	174.6	O507-H50A...O407

Symmetry elements used to generate symmetry equivalent atoms in above contacts $1 -1+X,+Y,+Z
The Flack parameter as a measure of the confidence we can have in the assignment of the refined stereochemistry is
Flack x: 0.002(5) Shelxl 2018
Hooft y: -0.005(6) Olex2
This is low with a low error so we can be confident in the assignment of the crystal measured (caution here as the all the crystals examined were twinned and the data is a little weak)

Note All crystals measured were rather poor and twinned. The data used here was from the main twin component of the best sample (strongest diffracting, least twinned) as no suitable twin refinement could be found.

Experimental

Single crystals of $C_{14}H_{13}ClO_2$ **[yz6]** were grown from DCM/hexane in a small vial at room temperature. 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 duel 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.

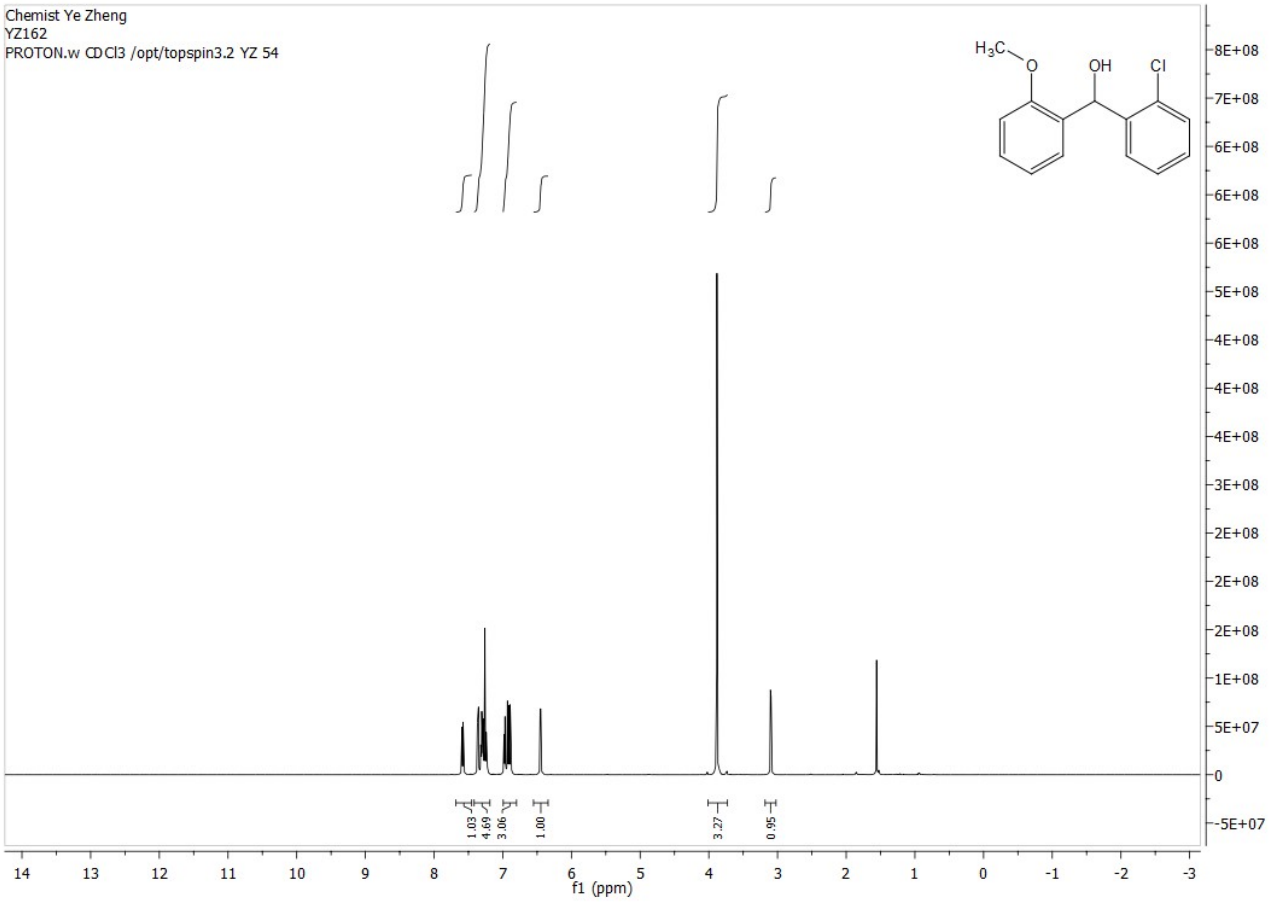
1. Dolomanov, O.V.; Bourhis, L.J.; Gildea, R.J, Howard, J.A.K. & Puschmann, H. (2009), J. Appl. Cryst. 42, 339-341.
2. Sheldrick, G.M. (2015). Acta Cryst. A71, 3-8.
3. Sheldrick, G.M. (2015). Acta Cryst. C71, 3-8.

Crystal Data for $C_{14}H_{13}ClO_2$ (M =248.69 g/mol): monoclinic, space group $P2_1$ (no. 4), a = 11.49164(17) Å, b = 21.8268(3) Å, c = 13.18932(16) Å, β = 108.4101(14)°, V = 3138.91(7) Å^3, Z = 10, T = 150(2) K, μ(CuKα) = 2.585 mm^{-1}, *Dcalc* = 1.316 g/cm^3, 56916 reflections measured (7.064° ≤ 2Θ ≤ 147.322°), 12126 unique (R_{int} = 0.0679, R_{sigma} = 0.0587) which were used in all calculations. The final R_1 was 0.0312 (I > 2σ(I)) and wR_2 was 0.0604 (all data).

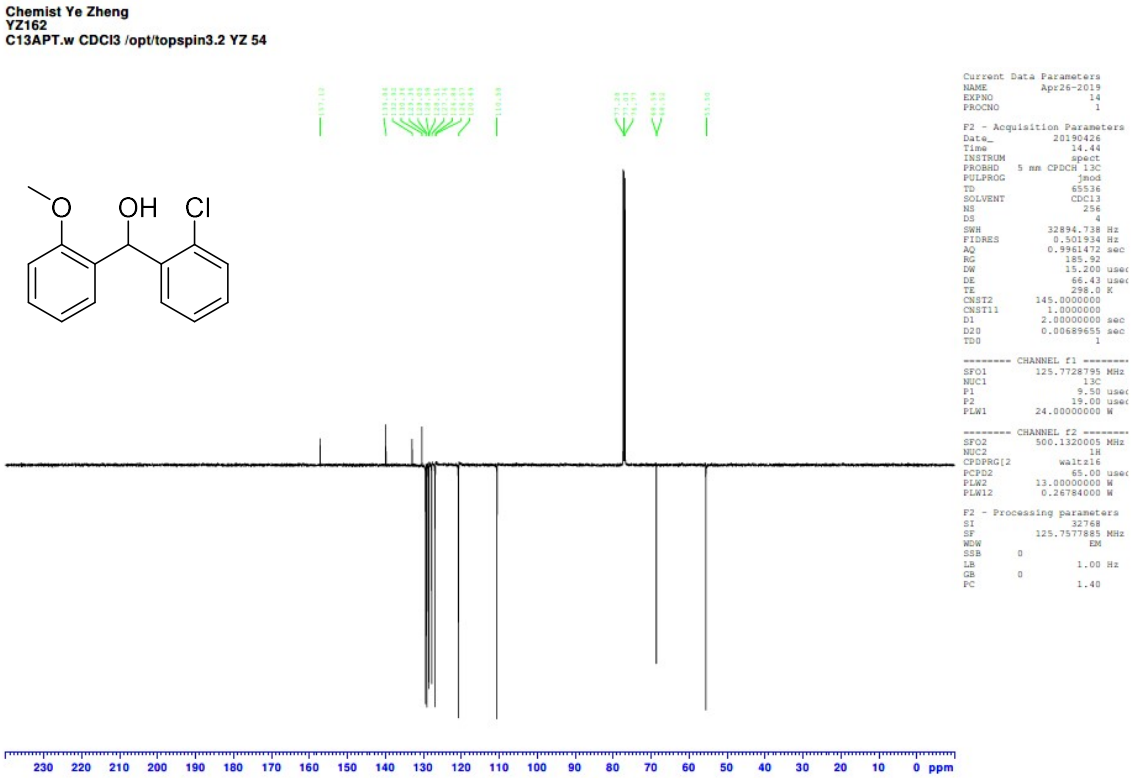
Table 1 Crystal data and structure refinement for yz6.

Identification code	yz6
Empirical formula	$C_{14}H_{13}ClO_2$
Formula weight	248.69
Temperature/K	150(2)
Crystal system	Monoclinic
Space group	$P2_1$
a/Å	11.49164(17)
b/Å	21.8268(3)
c/Å	13.18932(16)
α/°	90
β/°	108.4101(14)
γ/°	90
Volume/Å^3	3138.91(7)
Z	10
ρ_{calc}g/cm^3	1.316
μ/mm^{-1}	2.585
F(000)	1300.0
Crystal size/mm^3	0.2 × 0.04 × 0.03 colourless block
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	7.064 to 147.322
Index ranges	-12 ≤ h ≤ 14, -27 ≤ k ≤ 27, -16 ≤ l ≤ 16
Reflections collected	56916
Independent reflections	12126 [R_{int} = 0.0679, R_{sigma} = 0.0587]
Data/restraints/parameters	12126/50/793
Goodness-of-fit on F^2	0.883
Final R indexes [I>=2σ (I)]	R_1 = 0.0312, wR_2 = 0.0591
Final R indexes [all data]	R_1 = 0.0395, wR_2 = 0.0604
Largest diff. peak/hole / e Å^{-3}	0.16/-0.20
Flack parameter	0.002(5)

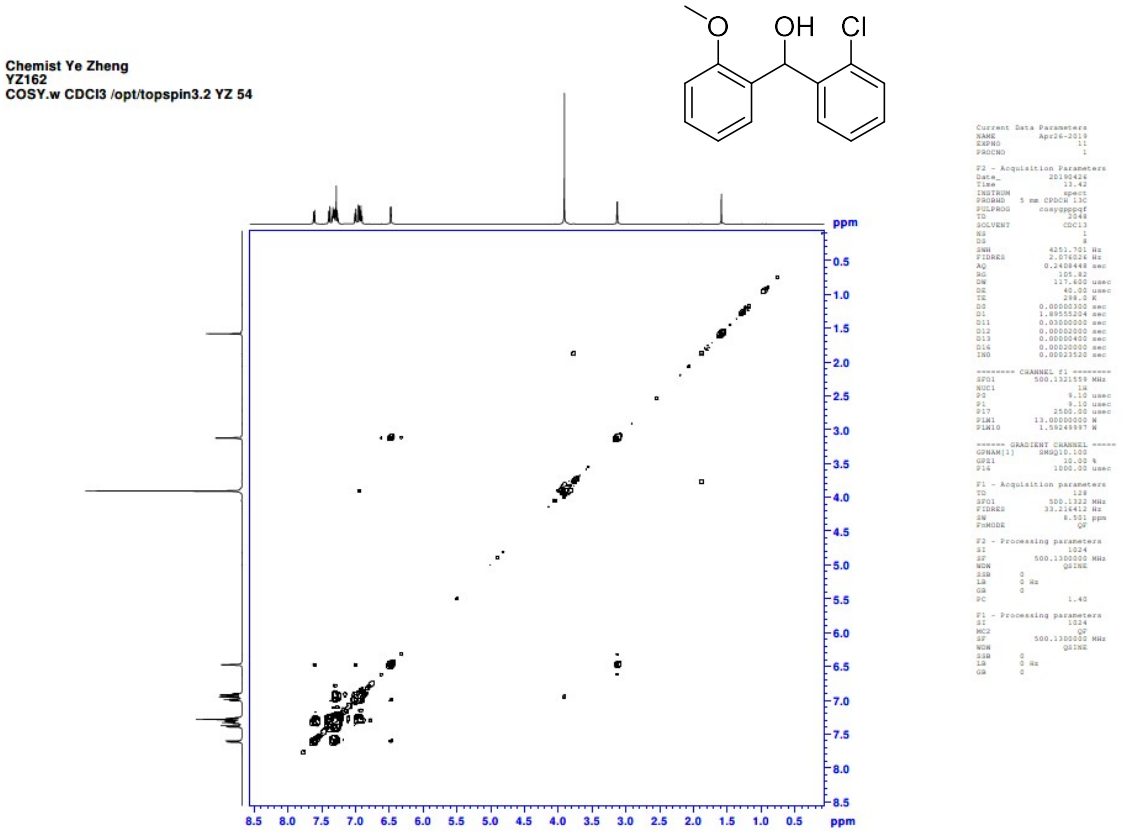
^{1}H NMR (500 MHz, $CDCl_3$) of **8g**:



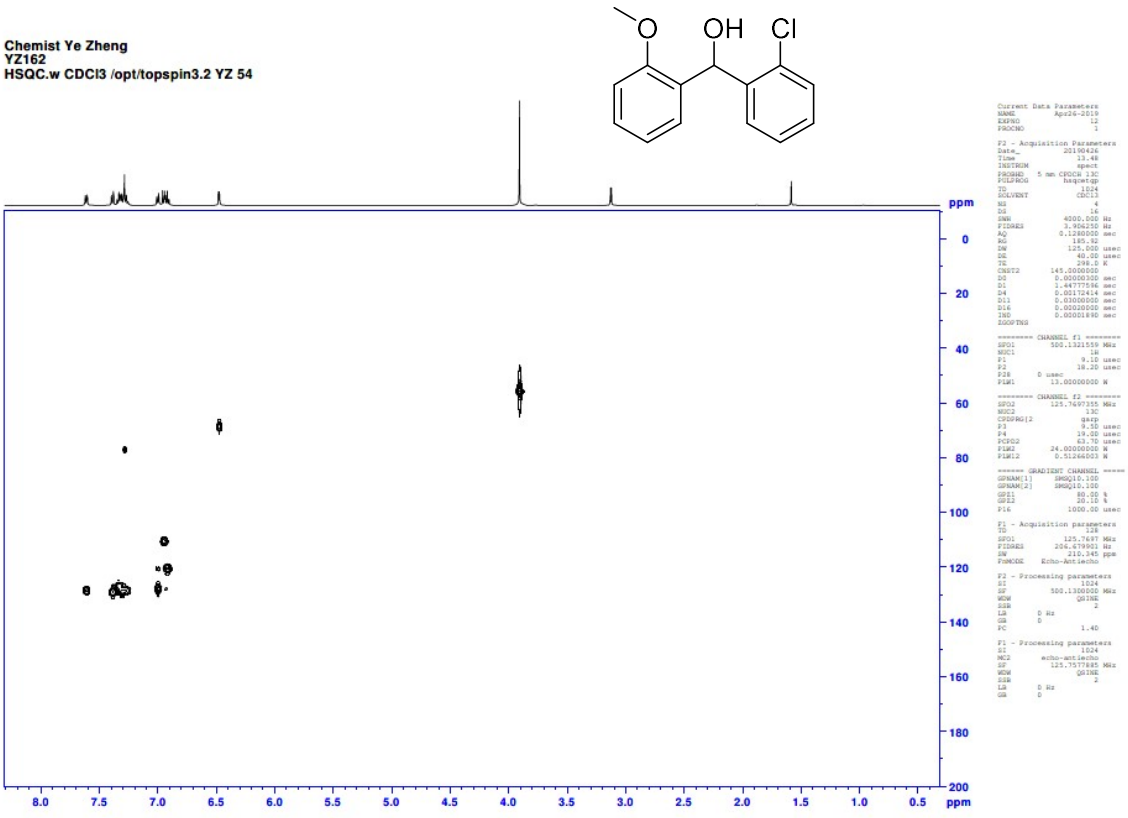
^{13}C NMR (125 MHz, $CDCl_3$) of **8g**:



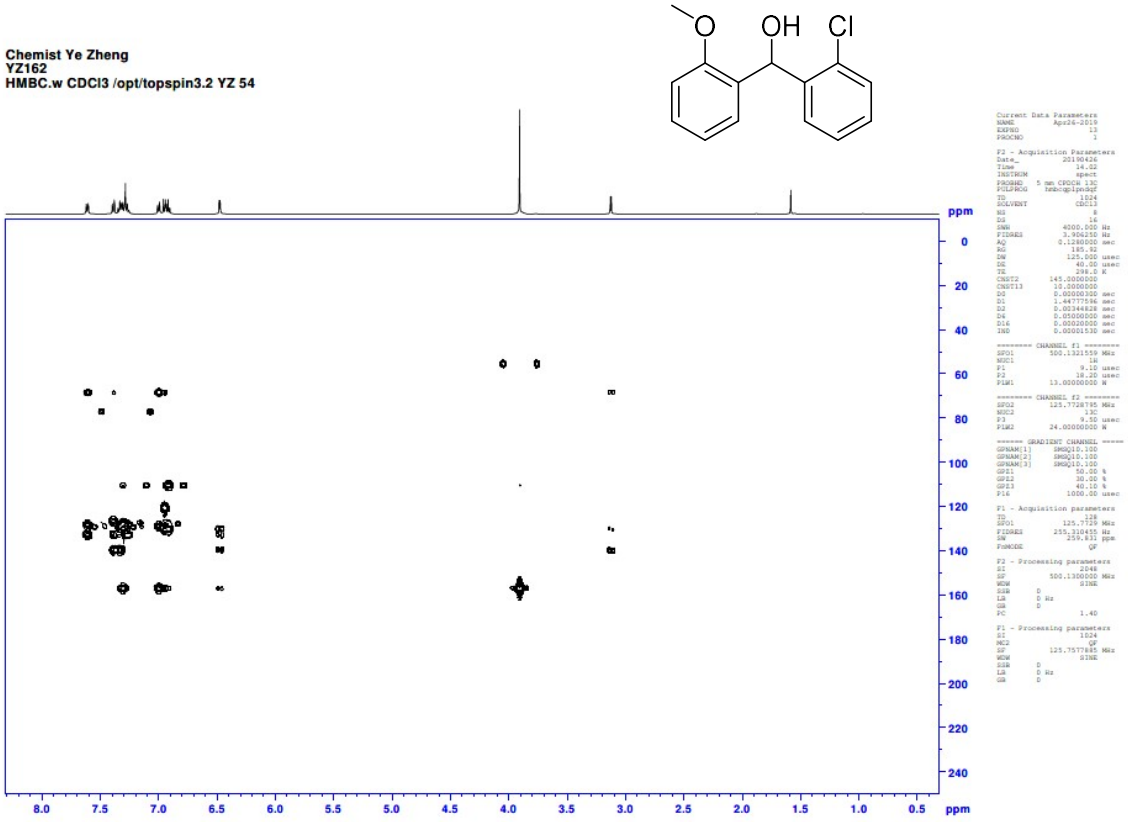
COSY (500 MHz, $CDCl_3$) of **8g**:



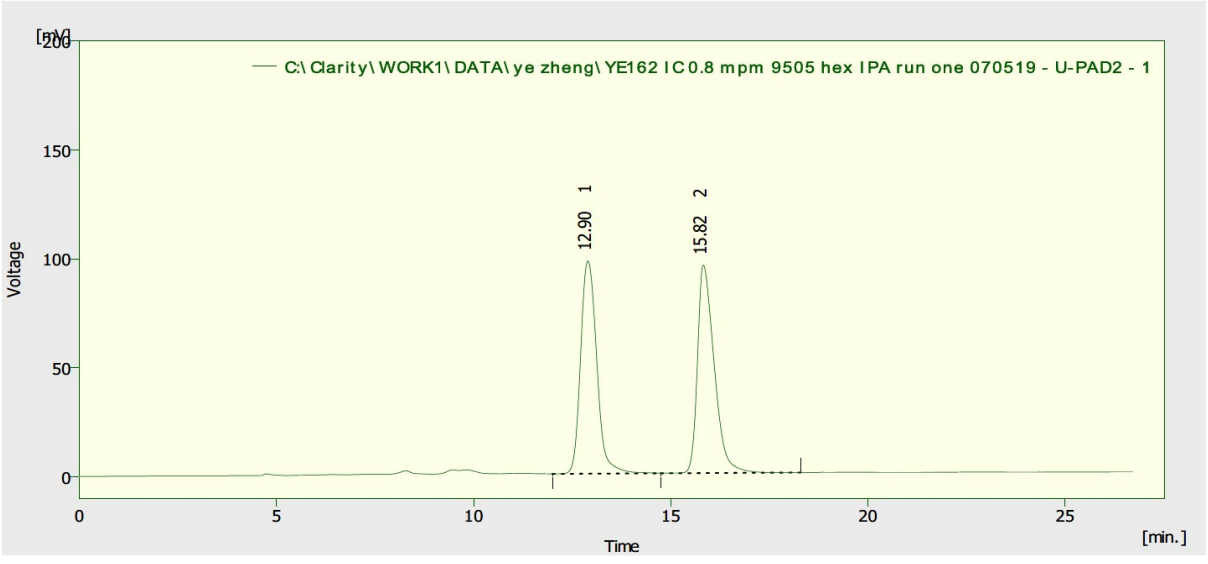
HSQC (500 MHz, $CDCl_3$) of **8g**:



HMBC (500 MHz, $CDCl_3$) of **8g**:



HPLC of racemic (2-chlorophenyl)(2-methoxyphenyl)methanol **8g**:

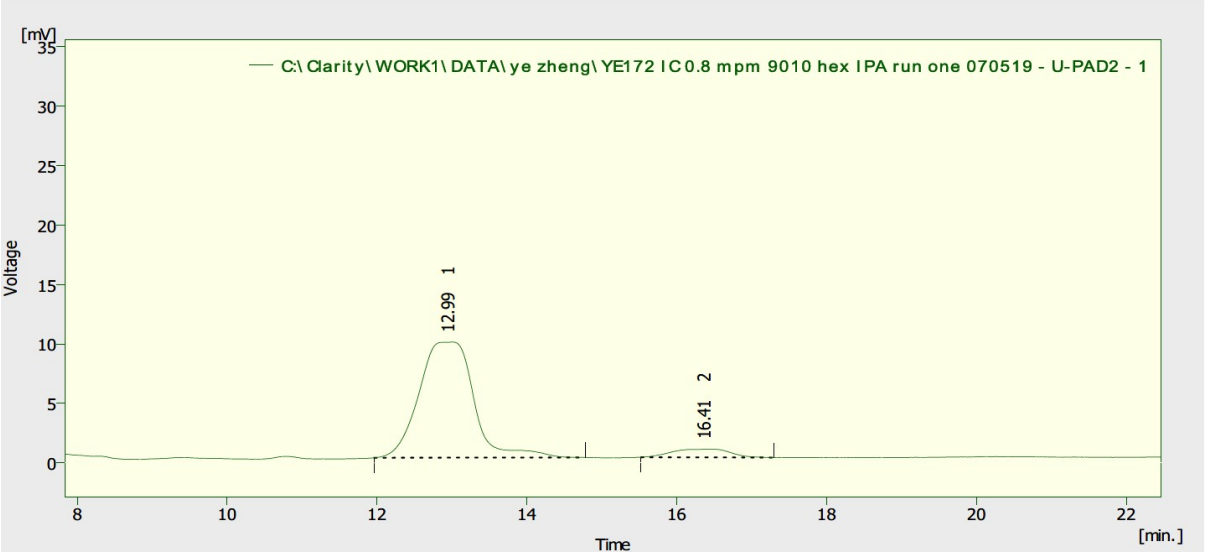


Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|ye zheng\|YE162 IC 0.8 mpm 9505 hex IPA run one 070519 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	12.896	2792.896	97.774	49.8	50.6	0.44	
2	15.824	2819.026	95.550	50.2	49.4	0.45	
	Total	5611.923	193.324	100.0	100.0		

HPLC of **8g** after ATH of (2-chlorophenyl)(2-methoxyphenyl)methanone **7g**:

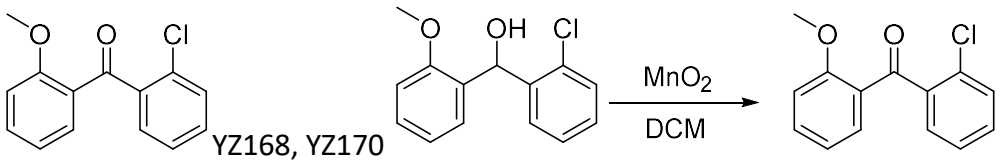
(*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst (after 168 hours, 98% conversion, 85.8% ee, *S* configuration)



Result Table (Uncal - C:|Clarity|WORK1|DATA|ye zheng|YE172 IC 0.8 mpm 9010 hex IPA run one 070519 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	12.992	493.602	9.733	92.9	93.4	0.76	
2	16.408	37.523	0.692	7.1	6.6	0.90	
	Total	531.125	10.425	100.0	100.0		

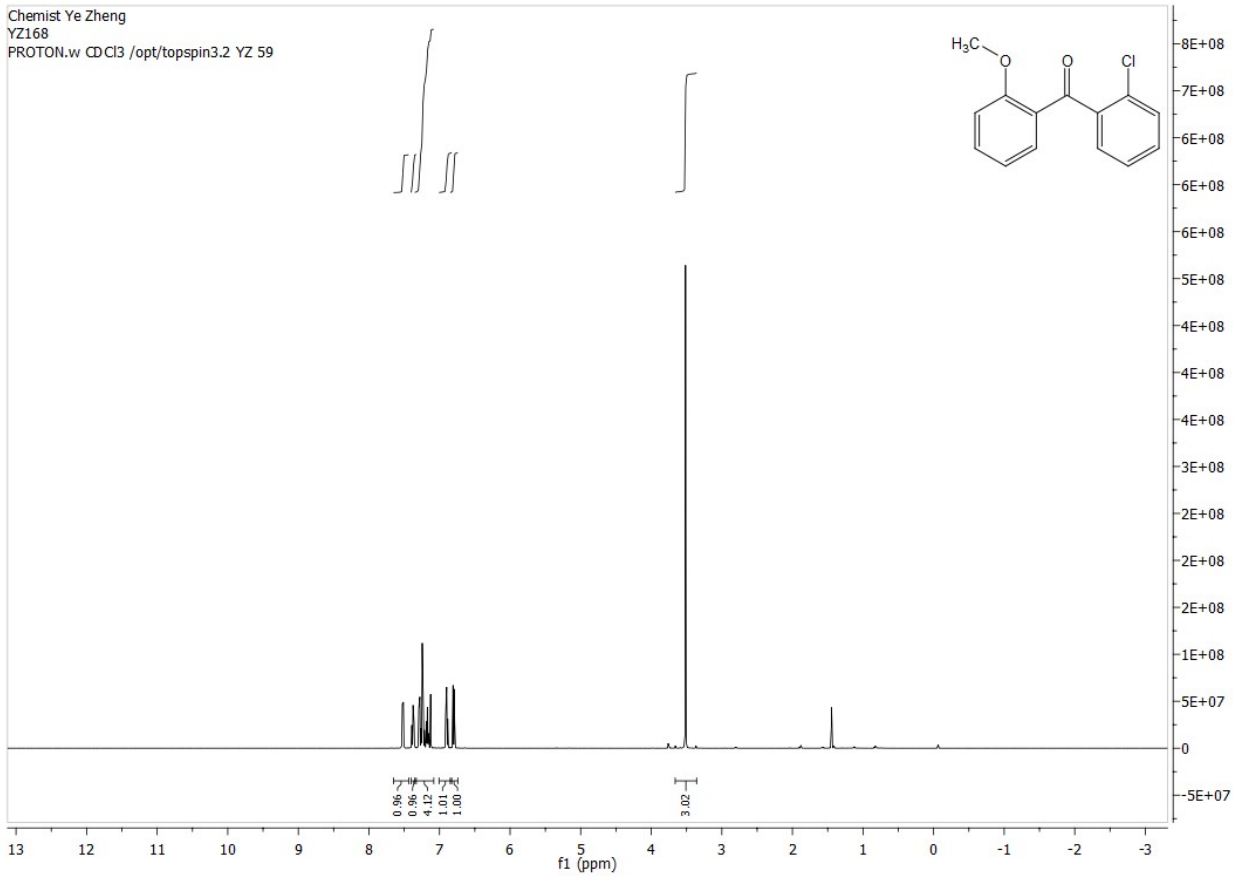
(2-Chlorophenyl)(2-methoxyphenyl)methanone 7g.



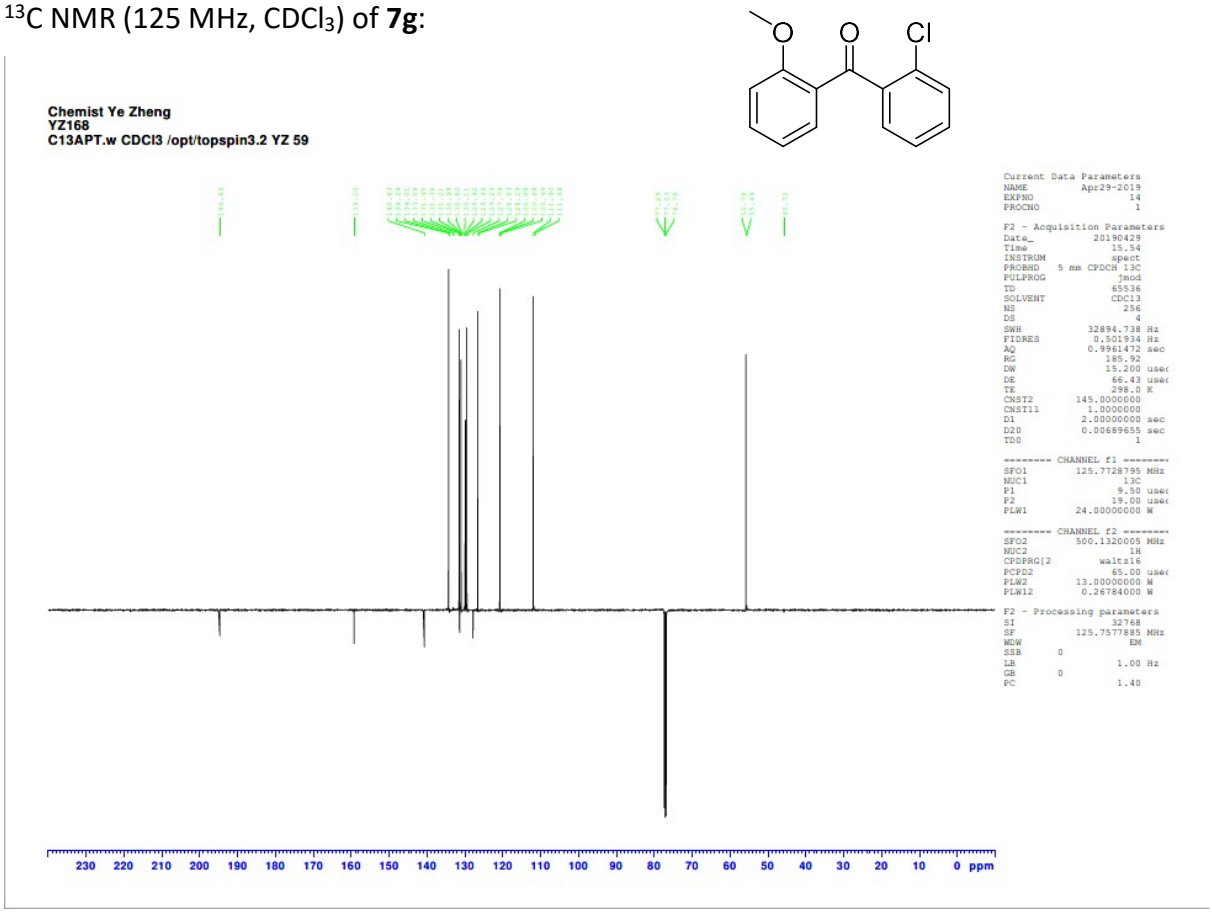
This compound is novel.

To a solution of (2-chlorophenyl)(2-methoxyphenyl)methanol **8g** (100 mg, 0.40 mmol) in DCM (3 mL) at rt was added manganese dioxide (521.4 mg, 6.0 mmol). The reaction mixture was left to stir under a nitrogen atmosphere overnight. TLC (4:1 hexane: ethyl acetate) after this time indicated full conversion. The solids were removed by gravity filtration and washed with DCM. The solvent was removed to give the product **7g** as a white solid (69 mg, 0.28 mmol, 69%). TLC: Rf ca 0.40 (4:1 hexane: EtOAc), strong UV and $KMnO_4$; HRMS: (found (ESI+): [M+Na]+, Calcd for $C_{14}H_{11}ClNaO_2$ 269.0342; Found 269.0340; -0.8 ppm error); ν_{max} 3067, 2995, 2940, 2838, 1643, 1591, 1482, 1434, 1307, 1250, 1153, 930, 770, 754 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.56 (1H, dd, *J* = 8.0, 1.5, ArH), 7.42-7.39 (1H, m, ArH), 7.32-7.15 (4H, m, ArH), 6.93 (1H, t, *J* = 7.5, ArH), 6.84 (1H, d, *J*= 8.5, ArH), 3.54 (3H, s, OCH_3) ppm; δ_C (125 MHz, $CDCl_3$) 194.7 (C), 159.2 (C), 140.6 (C), 134.2 (CH), 131.5 (CH), 131.4 (C), 131.0 (CH), 129.8 (CH), 129.5 (CH), 127.8 (C), 126.5 (CH), 120.7 (CH), 111.9 (CH), 55.8 (CH_3) ppm; m/z (ES-API+) 269.1 (M^+ + 23, 100%).

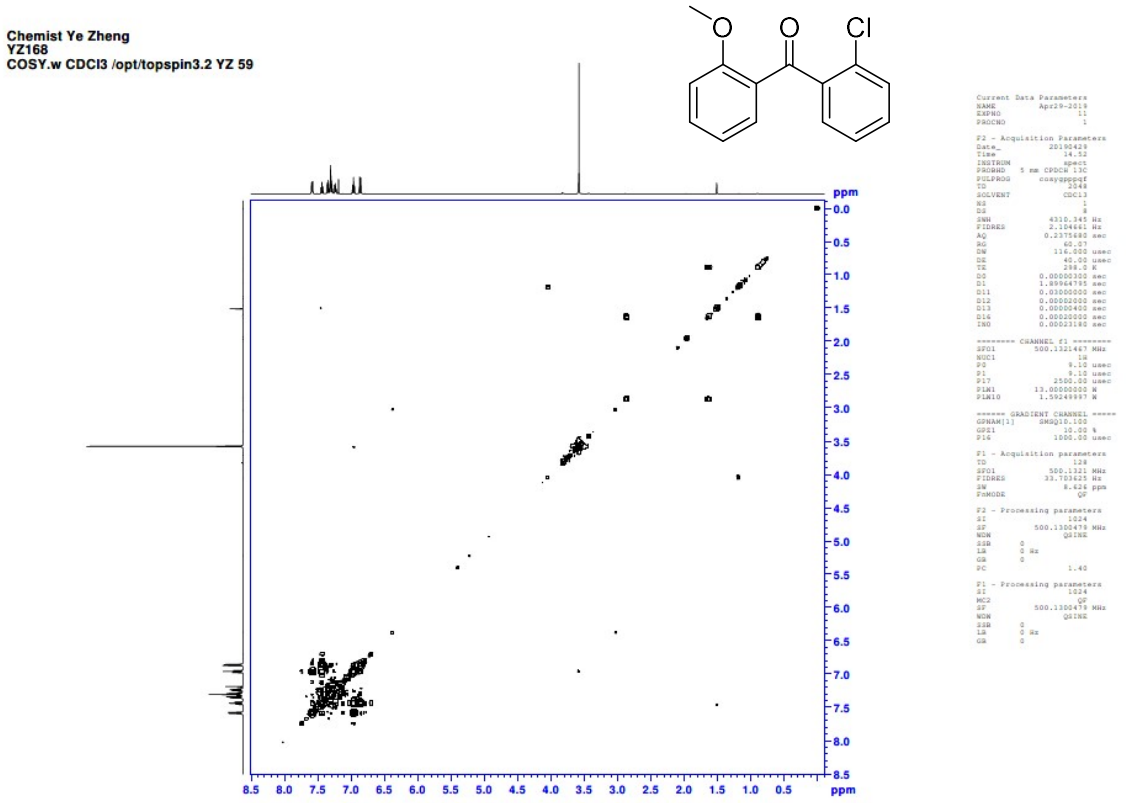
^{1}H NMR (500 MHz, $CDCl_3$) of **7g**:



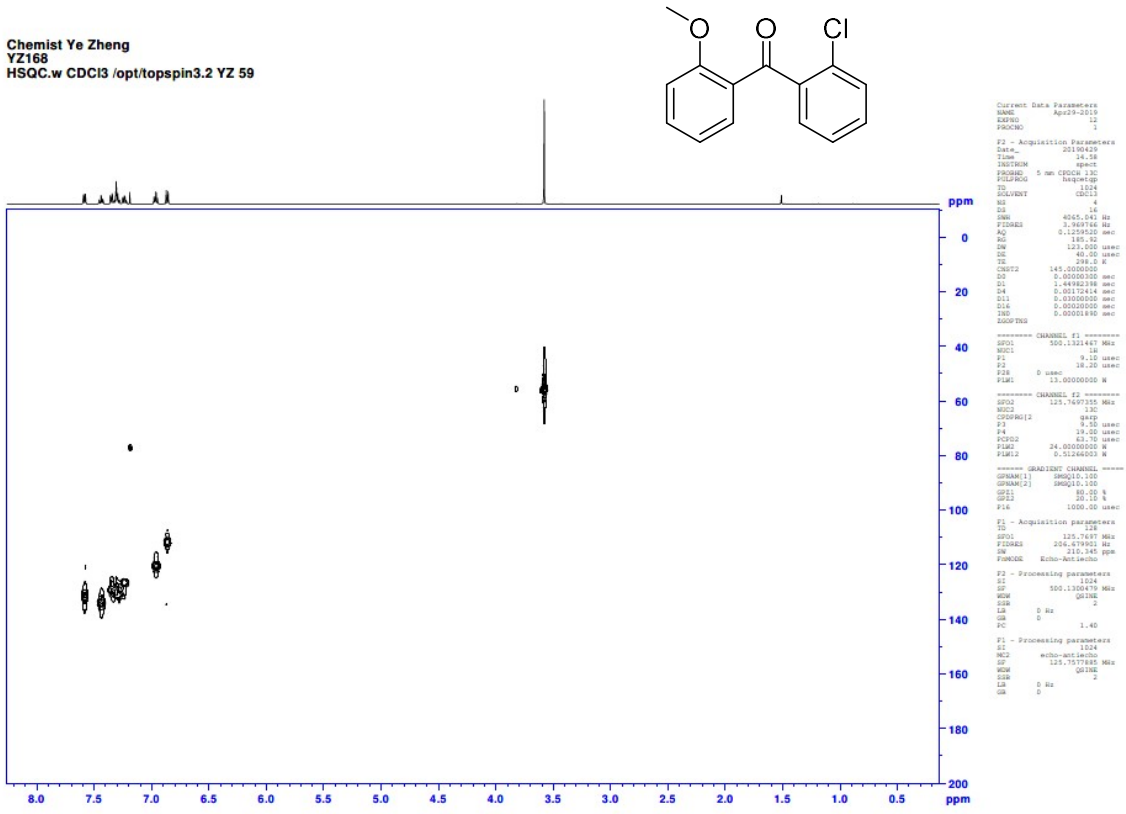
^{13}C NMR (125 MHz, $CDCl_3$) of **7g**:



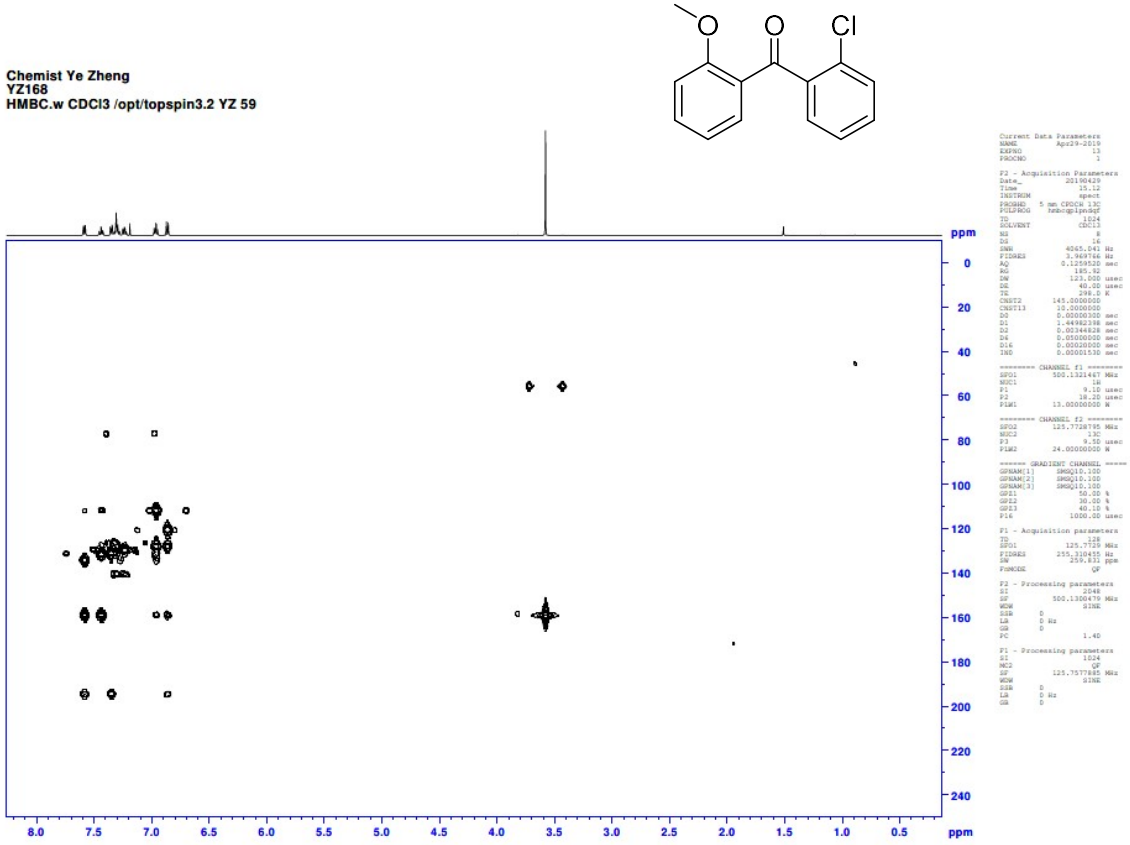
COSY (500 MHz, $CDCl_3$) of **7g:**



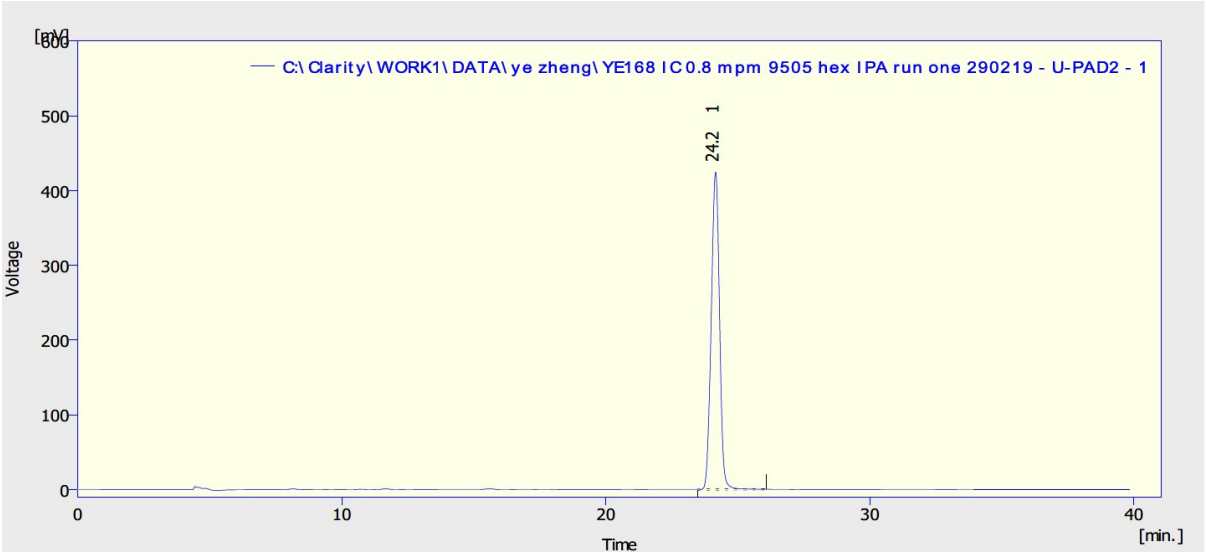
HSQC (500 MHz, $CDCl_3$) of **7g**:



HMBC (500 MHz, $CDCl_3$) of **7g**:



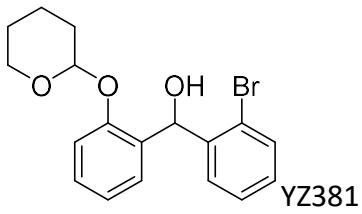
HPLC of (2-Chlorophenyl)(2-methoxyphenyl)methanone **7g**:



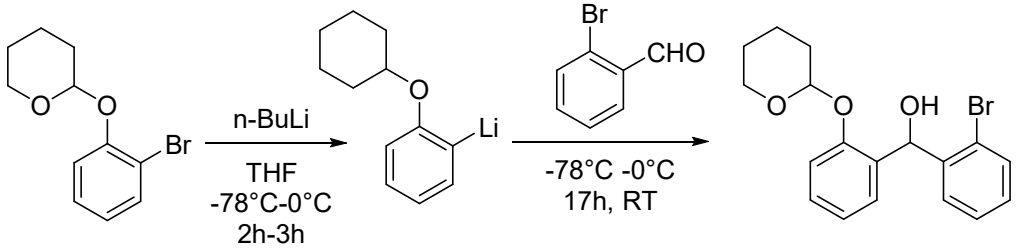
Result Table (Uncal - C:\Clarity\WORK1\DATA\ye zheng\YE168 IC 0.8 mpm 9505 hex IPA run one 290219 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	24.152	9270.682	425.084	100.0	100.0	0.34	
	Total	9270.682	425.084	100.0	100.0		

(2-Bromophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol.



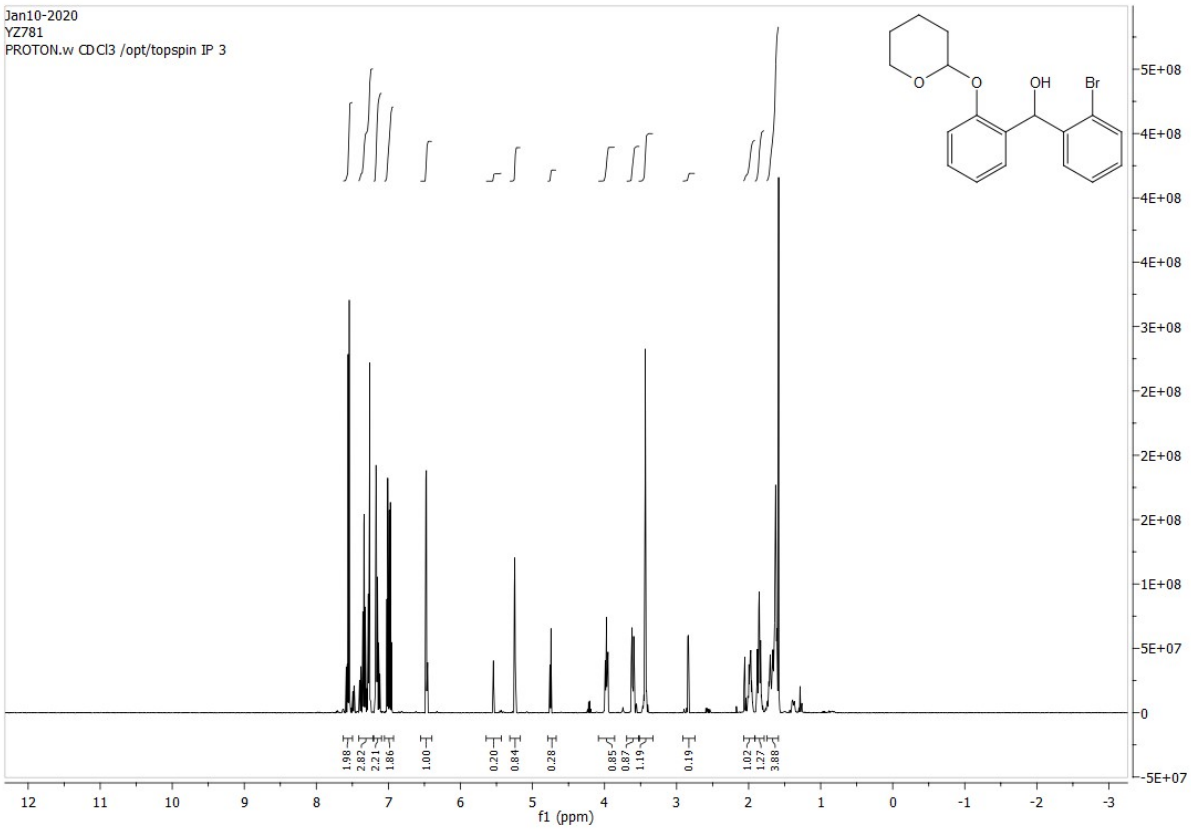
YZ381



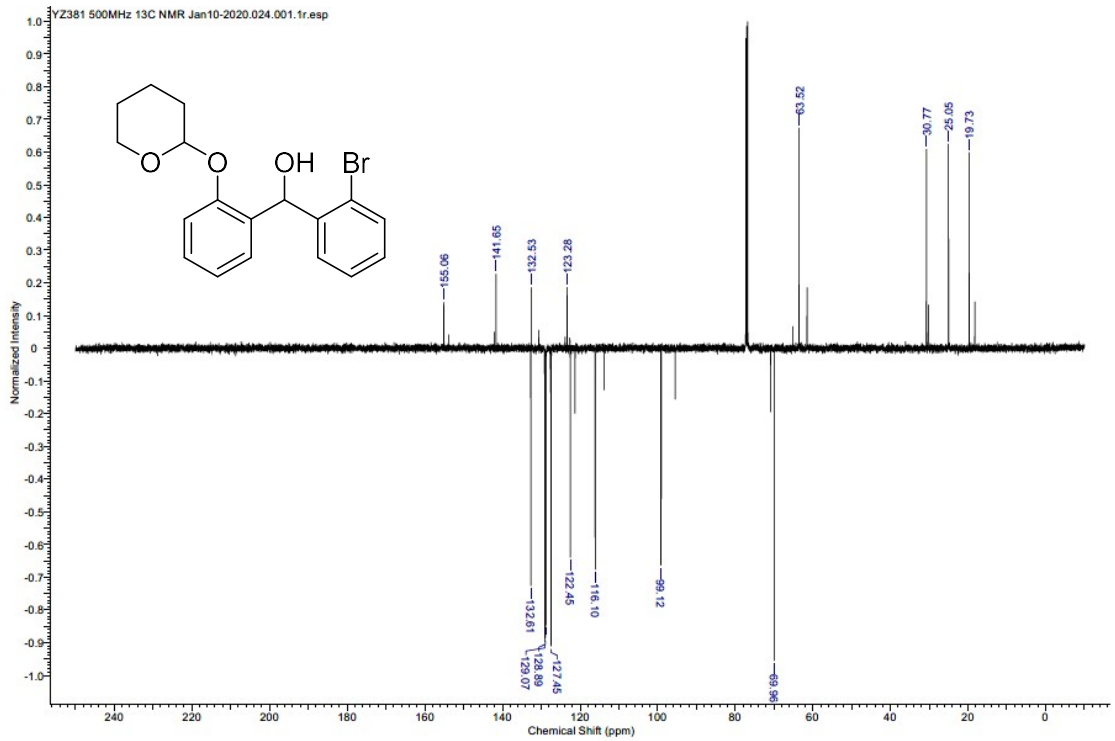
This compound is novel.

To a solution of 2-(2-bromophenoxy)tetrahydro-2H-pyran (2.58g, 10.1 mmol) THF (12 mL) at -78 °C was added dropwise a solution of n-butyllithium (3.67 mL, 2.5M in hexanes, 9.18 mmol). The reaction mixture was then stirred under a nitrogen atmosphere for 3 hours, after which 2-bromobenzaldehyde (1.70 g, 9.18 mmol) was added dropwise. The reaction mixture was left stirring under the nitrogen atmosphere and allowed to warm to rt. The reaction was followed by TLC (9:1 hexane: ethyl acetate). The mixture was quenched by saturated NH_4Cl solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 × 20 mL), and the combined organic layers were dried ($MgSO_4$) and filtered. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-20% ethyl acetate in hexane to give (2-bromophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol as a white solid (2.45 g, 6.77 mmol, 73.7%). TLC: Rf ca 0.30 (9:1 hexane: EtOAc), strong UV and $KMnO_4$; Mp: 104.2 °C; HRMS: (found (ESI+): [M+Na]+, Calcd for $C_{18}H_{19}{}^{79}BrNaO_3$ 385.0411; Found 385.0410; -0.3 ppm error); ν_{max} 3381 (br), 2947, 2927, 2860, 1483, 1384, 1229, 1020, 751 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.63-7.50 (2H, m, ArH), 7.41-7.21 (3H, m, ArH), 7.20-7.10 (2H, m, ArH), 7.05-6.93 (2H, m, ArH), 6.48-6.45 (1H, m, Ar*CH*OH), 5.25-5.24 (1H, m, O*CH*), 4.00-3.95 (1H, m, O*CH*$_2$CH$_2$), 3.69-3.52 (1H, m, O*CH*$_2$CH$_2$), 3.53-3.33 (1H, m, ArCH*OH*), 2.07-1.91 (1H, m, CH_2), 1.91-1.78 (1H, m, CH_2), 1.75-1.59 (4H, m, CH_2) ppm; δ_C (125 MHz, $CDCl_3$) 155.1 (C), 141.7 (C), 132.5 (C), 132.6 (CH), 129.1 (CH), 128.9 (CH), 128.7 (CH), 127.5 (CH), 127.4 (CH), 123.3 (C), 122.5 (CH), 116.1 (CH), 99.1 (CH), 70.0 (CH), 63.5 (CH_2), 30.8 (CH_2), 25.1 (CH_2), 19.7 (CH_2) ppm; m/z (ES-API+) 385.1 (M^+ + 23, 100%).

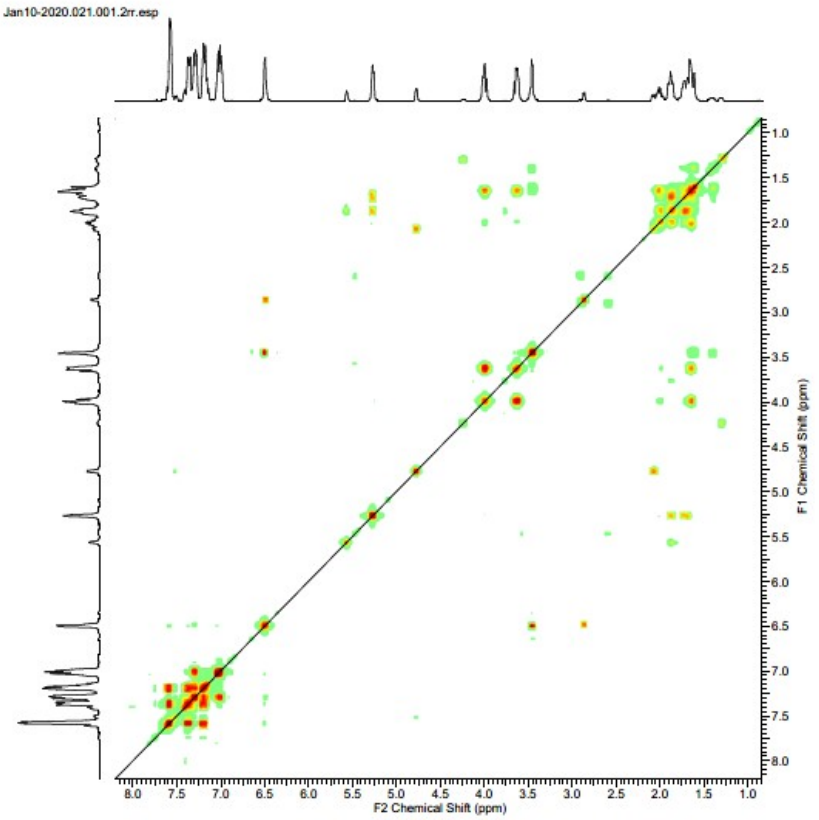
^{1}H NMR (500 MHz, $CDCl_3$) of (2-Bromophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol:

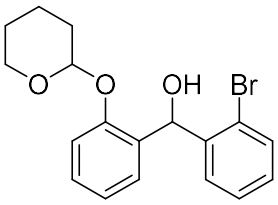


^{13}C NMR (125 MHz, $CDCl_3$) of (2-Bromophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol:

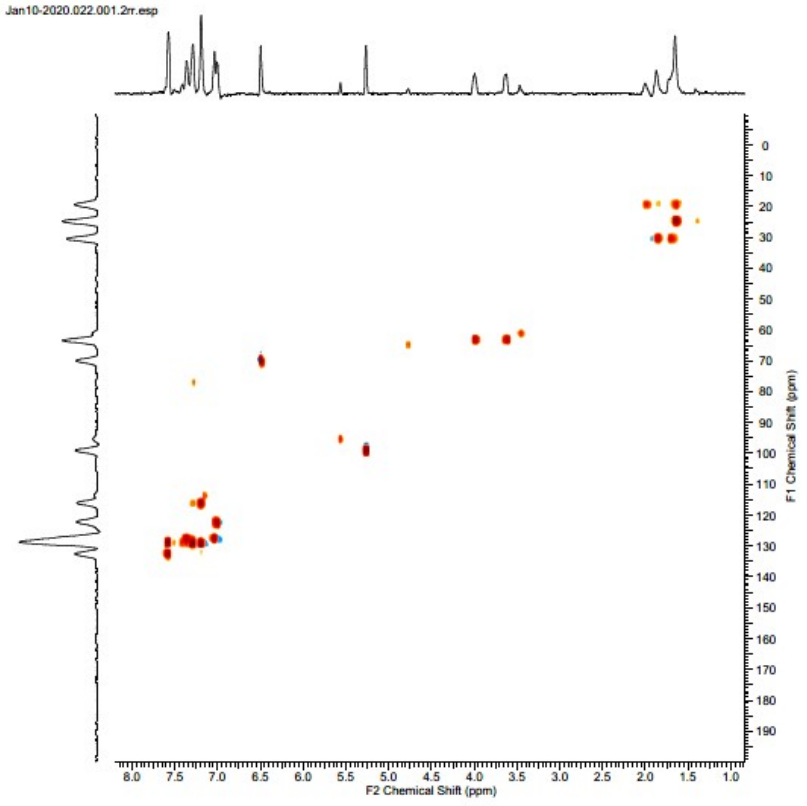


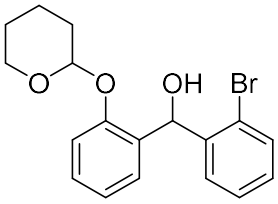
COSY (500 MHz, $CDCl_3$) of (2-Bromophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol:



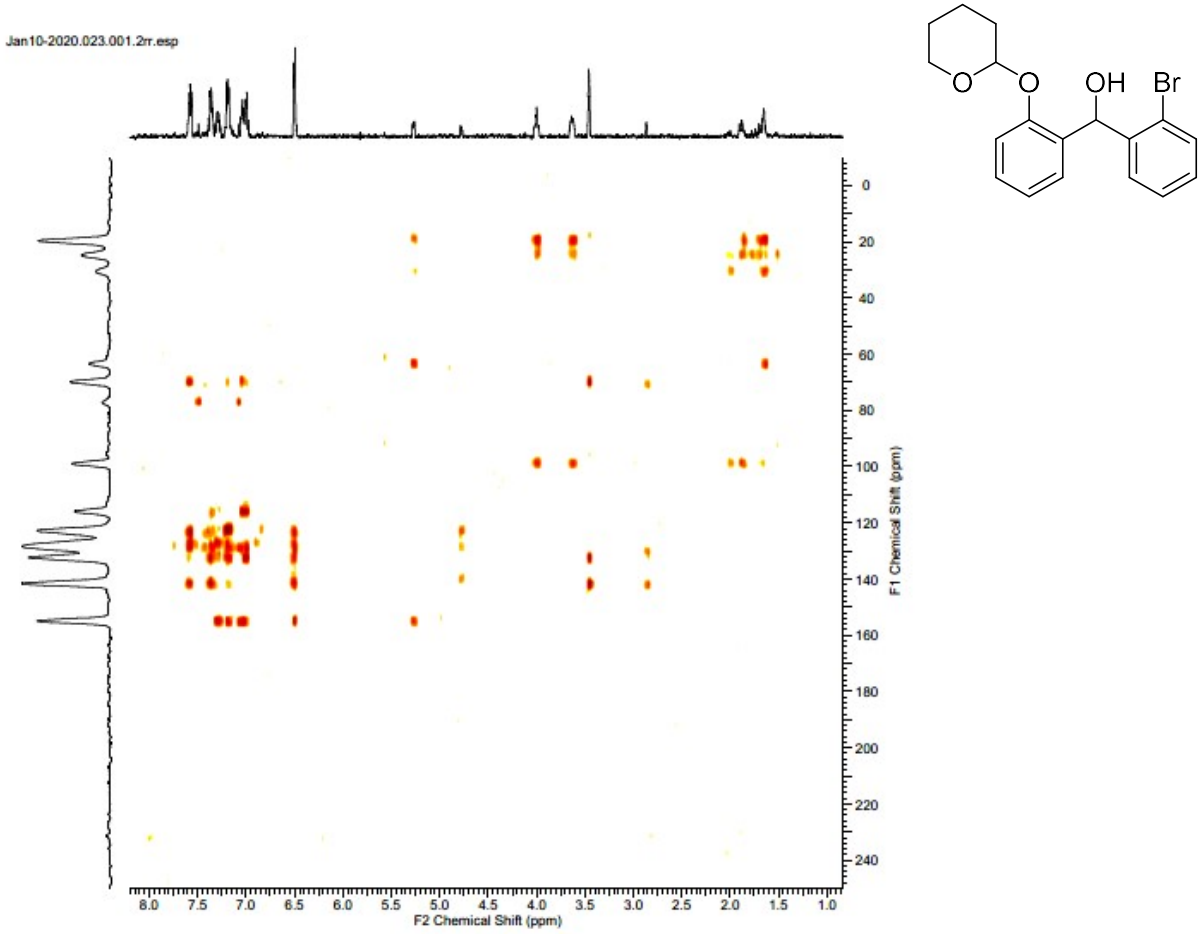


HSQC (500 MHz, $CDCl_3$) of (2-Bromophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol:

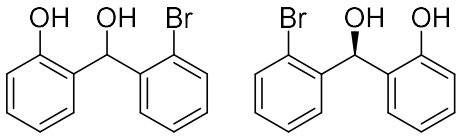




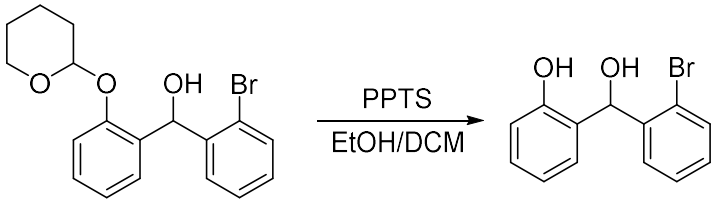
HMBC (500 MHz, $CDCl_3$) of (2-Bromophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol:



2-((2-Bromophenyl)(hydroxy)methyl)phenol 8h.



racemic: YZ383, Asymmetric: YZ390



This compound is novel.

To a solution of (2-bromophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol (2.45 g, 6.77 mmol) in EtOH (34 mL)/DCM (17.5 mL) was added pyridinium *p*-Toluenesulfonate (PPTS) (256 mg, 1.02 mmol) at rt. The reaction mixture was left stirring under the nitrogen atmosphere and followed by TLC (4:1 hexane: EtOAc). Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give 2-((2-Bromophenyl)(hydroxy)methyl)phenol **8h** as a colorless oil (1.27 g, 4.57 mmol, 67.5%). TLC: Rf ca 0.30 (4:1 hexane: EtOAc), strong UV and $KMnO_4$; HRMS: (found (ESI+): [M+Na]+, Calcd for $C_{13}H_{11}{}^{79}BrNaO_2$ 300.9834; Found 300.9835; 0.1 ppm error); ν_{max} 3229 (br), 1602, 1453, 1403, 1304, 1279, 1009, 711 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.95 (1H, m, ArH), 7.61 (1H, dd, *J* = 8.0, 1.0, ArH), 7.40-7.30 (2H, m, ArH), 7.24-7.19 (2H, m, ArH), 7.07-6.87 (1H, m, ArH), 6.91-6.63 (2H, m, ArH), 6.42 (1H, d, *J* = 3.7, Ar*CH*OH), 3.24 (1H, d, J = 3.8, ArCH*OH*) ppm; δ_C (125 MHz, $CDCl_3$) 156.0 (C), 140.6 (C), 133.1 (CH), 130.0 (CH), 129.6 (CH), 129.6 (CH), 128.2 (CH), 128.2 (CH), 124.9 (C), 123.3 (C), 120.1 (CH), 117.4 (CH), 75.8 (CH) ppm; m/z (ES-API+) 301.2 (M^+ + 23, 100%).

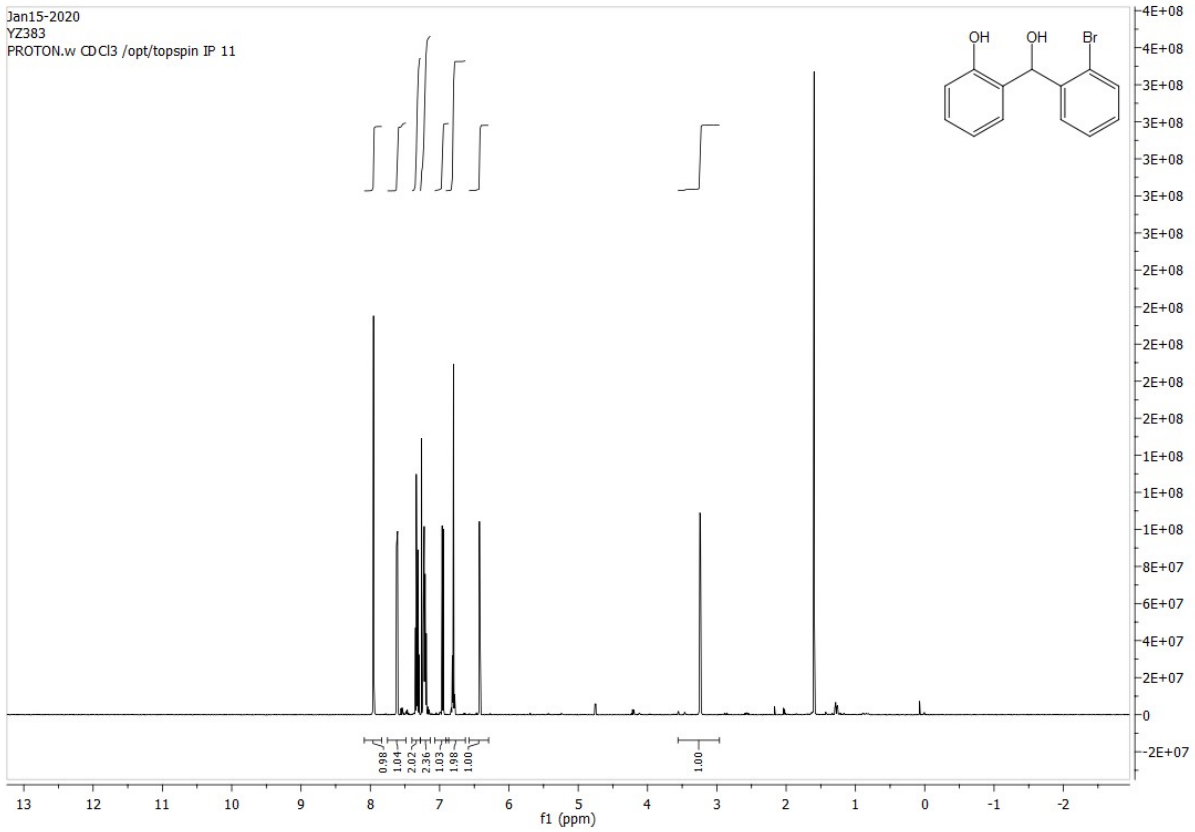
Enantiomeric excess and conversion determined by HPLC analysis (Chiralpak IG, 30 cm x 6mm column, hexane:iPrOH 9:1, 0.5 mL/min, T = 25°C) ketone 15.1 min, *R* isomer 17.9 min, *S* isomer 20.2 min.

ATH of (2-bromophenyl)(2-hydroxyphenyl)methanone (Y390, YZ394) **7h**:

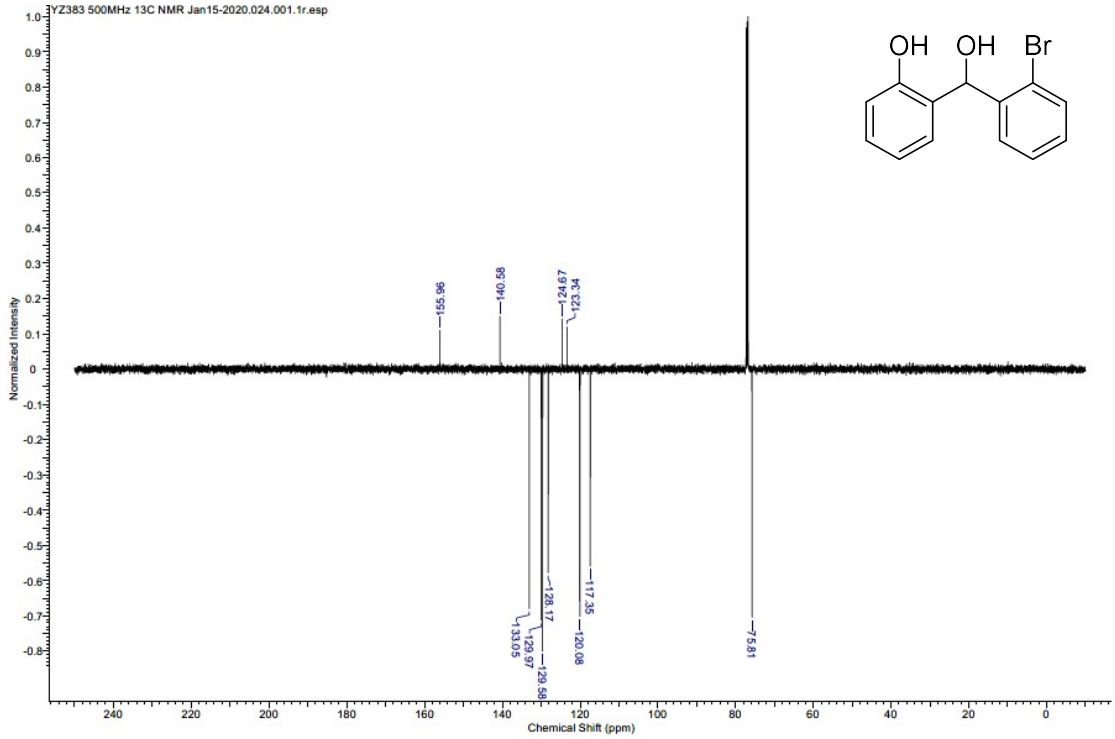
(*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst **2** (12.6 mg, 0.0203 mmol, 1 mol%) was added to FA: TEA (5:2 azeotropic mixture, 2.52 mL) at rt and the mixture was stirred under a nitrogen inert atmosphere for 10-15 minutes; after which a solution of (2-bromophenyl)(2-hydroxyphenyl)methanone (559.2 mg, 2.03 mmol) in DCM (3.97 mL) was added. The reaction mixture was stirrer under a nitrogen atmosphere, followed by TLC (4:1 hexane: EtOAc). After 72 hours, the reaction was quenched using saturated $NaHCO_3$ solution (20 mL). EtOAc (20 mL) was

added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried ($MgSO_4$) and filtered. The solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give 2-((2-chlorophenyl)(hydroxy)methyl)phenol **8h** (290 mg, 1.04 mmol, 51.5%). The reaction was also followed by HPLC analysis (Chiralpak IG, 30 cm x 6mm column, hexane:iPrOH 9:1, 0.5 mL/min, T = 25°C): 100% conversion; $[\alpha]_D^{24}$ -162.8 (c 0.390 in $CHCl_3$) 99% ee (*S*)

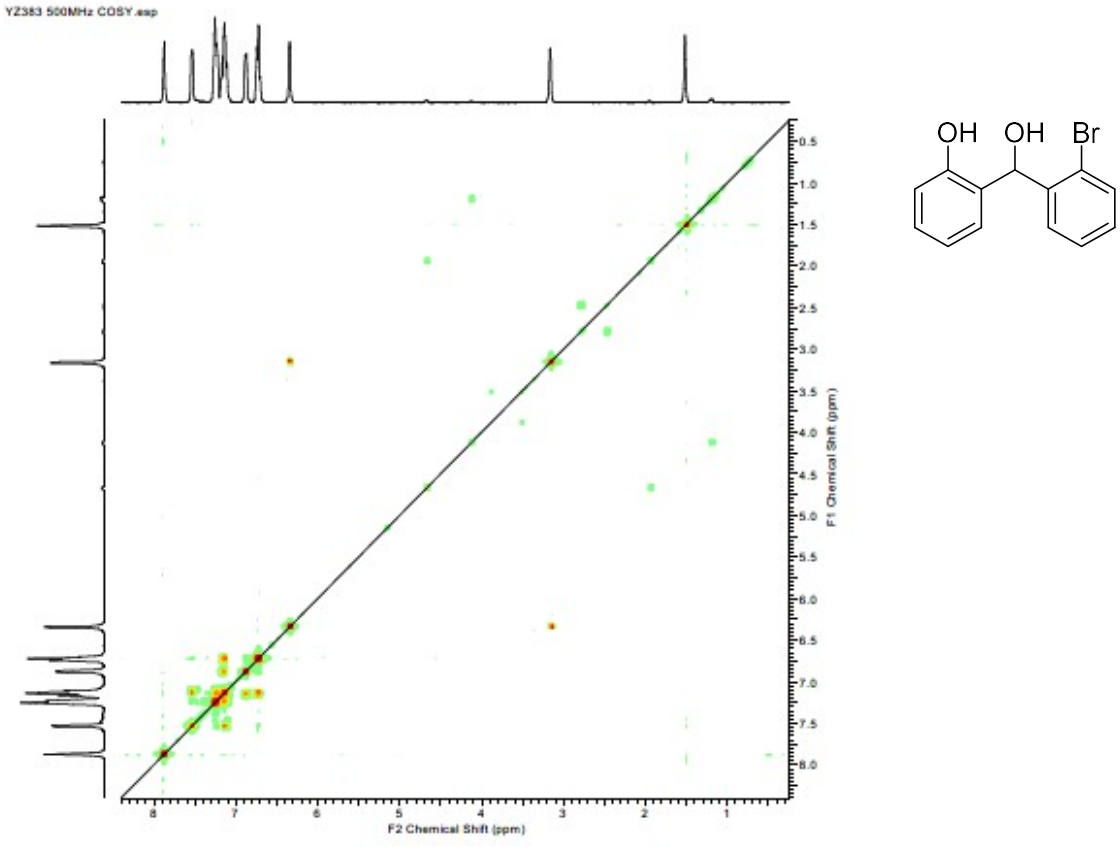
^{1}H NMR (500 MHz, $CDCl_3$) of **8h**:



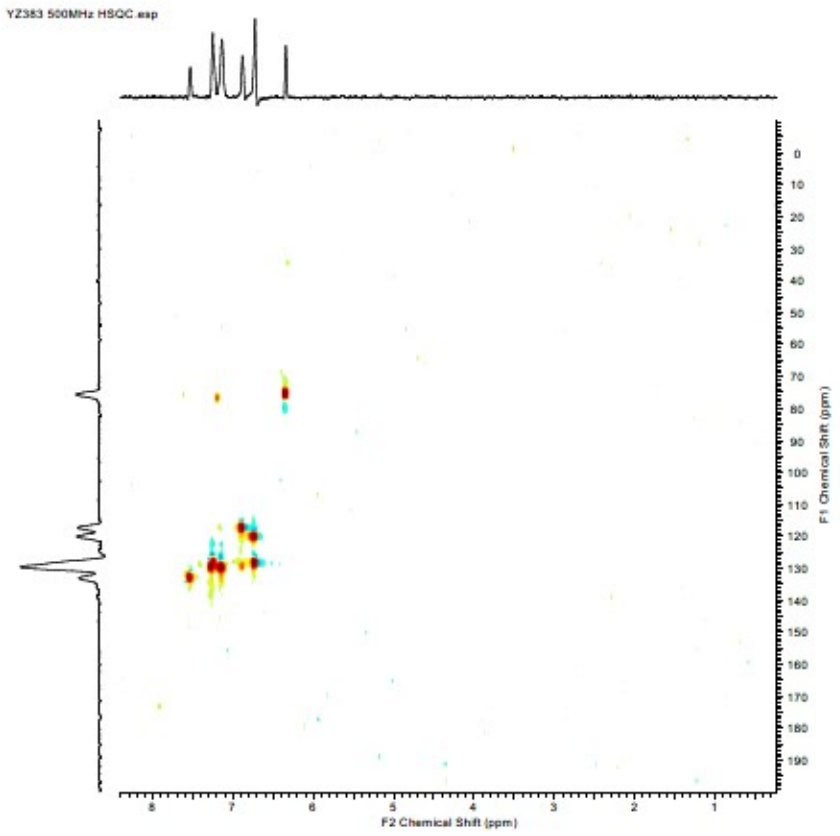
^{13}C NMR (125 MHz, $CDCl_3$) of **8h**:

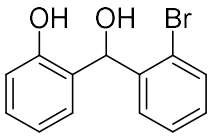


COSY (500 MHz, $CDCl_3$) of **8h:**

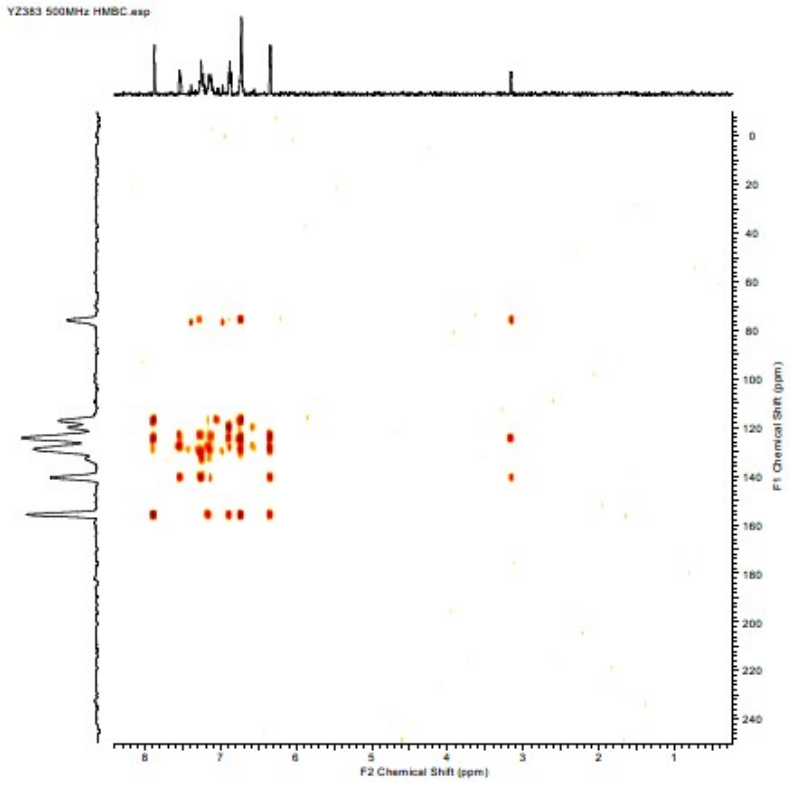


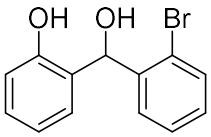
HSQC (500 MHz, $CDCl_3$) of **8h**:



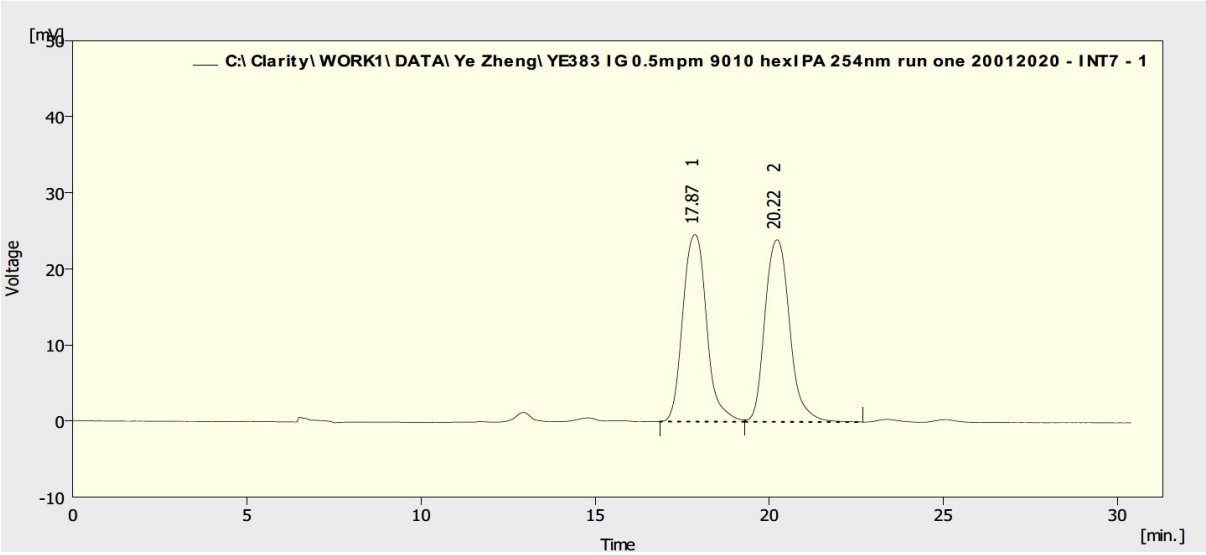


HMBC (500 MHz, $CDCl_3$) of **8h**:





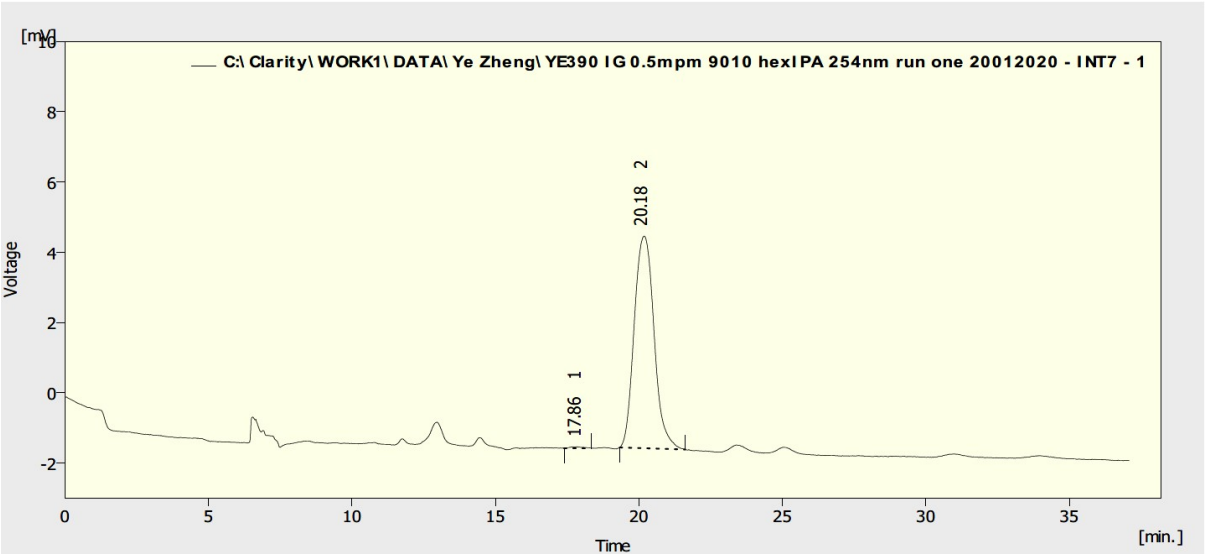
HPLC of racemic 2-((2-bromophenyl)(hydroxy)methyl)phenol **8h**:



Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|Ye Zheng\|YE383 IG 0.5mpm 9010 hexIPA 254nm run one 20012020 - INT7 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	17.870	1171.676	24.601	49.7	50.7	0.74	
2	20.223	1184.225	23.935	50.3	49.3	0.77	
	Total	2355.902	48.536	100.0	100.0		

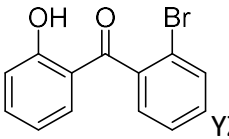
HPLC of **8h** after ATH of (2-bromophenyl)(2-hydroxyphenyl)methanone **7h**L (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst (after 72 hours, 100% conversion, 99% ee, *S* configuration)



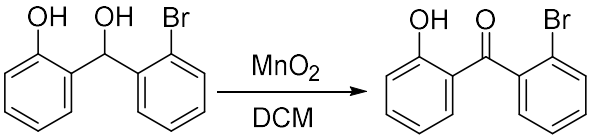
Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|Ye Zheng\|YE390 IG 0.5mpm 9010 hexIPA 254nm run one 20012020 - INT7 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	17.857	1.552	0.048	0.5	0.8	0.47	
2	20.183	290.238	6.041	99.5	99.2	0.75	
	Total	291.790	6.088	100.0	100.0		

2-Bromophenyl)(2-hydroxyphenyl)methanone 7h.



YZ388

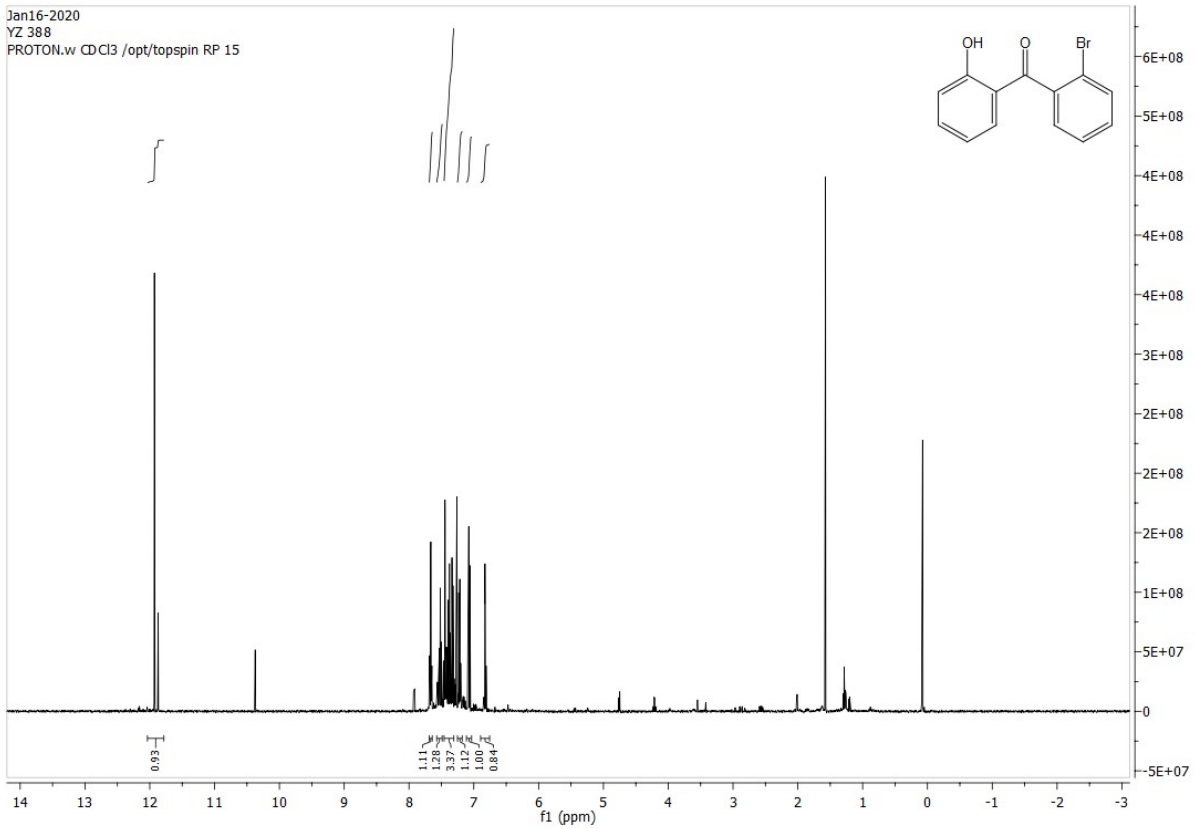


This compound has been reported but not fully characterized.

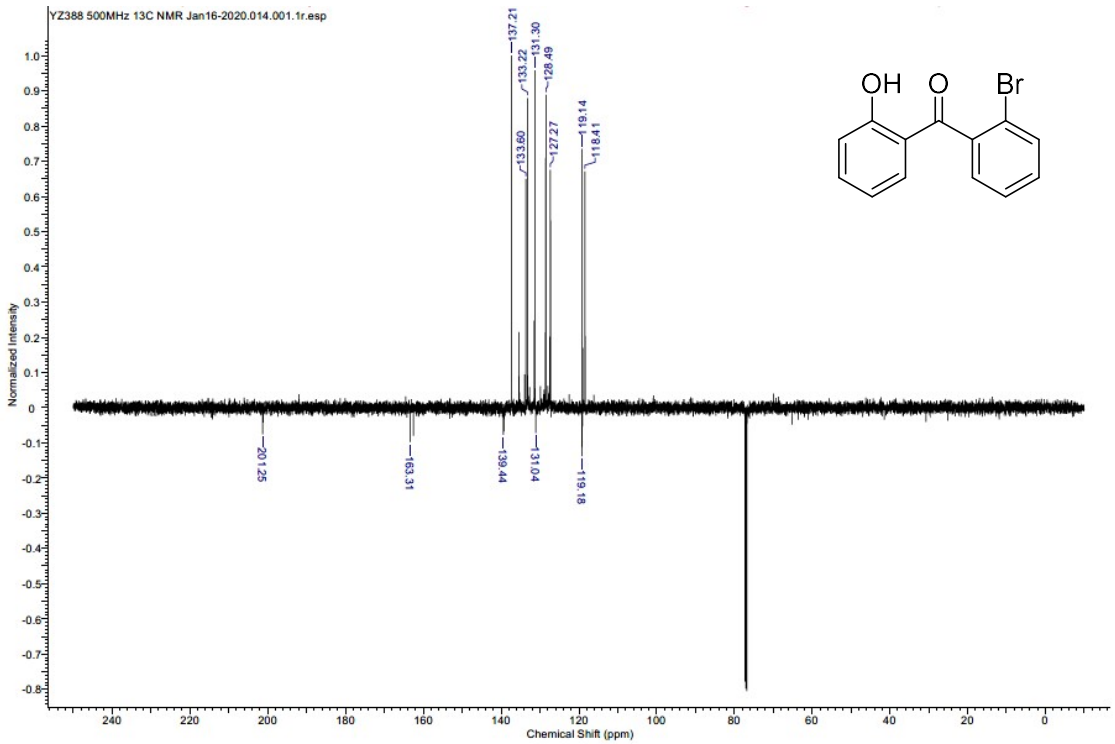
Reference: Li, J.; Liu, Z.; Wu, S.; Chen, Y. *Org. Lett.* **2019**, *21*, 2077-2080.

To a solution of 2-((2-bromophenyl)(hydroxy)methyl)phenol **8h** (1.53 g, 5.50 mmol) in DCM (55 mL) at rt was added manganese dioxide (7.17 g, 82.5 mmol). The reaction mixture was left to stir under a nitrogen atmosphere overnight. TLC (4:1 hexane: EtOAc) after this time indicated full conversion. The solids were removed by gravity filtration and washed with DCM. The combined solvent was removed to give the product **7h** as a brown oil (559.2 mg, 2.03 mmol, 36.8%). TLC: Rf ca 0.40 (4:1 hexane: EtOAc), strong UV and $KMnO_4$; HRMS: (found (ESI+): [M+Na]+, Calcd for $C_{13}H_9BrNaO_2$ 298.9682; Found 298.9678; -1.3 ppm error); ν_{max} 3229 (br), 3055, 2927, 1626, 1482, 1428, 1260, 1240, 752 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 11.93 (1H, s, OH), 7.68-7.65 (1H, m, ArH), 7.56-7.50 (1H, m, ArH), 7.46-7.32 (3H, m, ArH), 7.24-7.20 (1H, m, ArH), 7.09-7.06 (1H, m, ArH), 6.84-6.81 (1H, m, ArH) ppm; δ_C (125 MHz, $CDCl_3$) 201.3 (C), 163.3 (C), 139.4 (C), 137.2 (CH), 133.6 (CH), 133.2 (CH), 131.3 (CH), 131.0 (C), 128.5 (CH), 127.3 (CH), 119.2 (C), 119.1 (CH), 118.4 (CH) ppm; m/z (ES-API+) 299.0 (M^+ + 23, 100%). Data matched that reported.

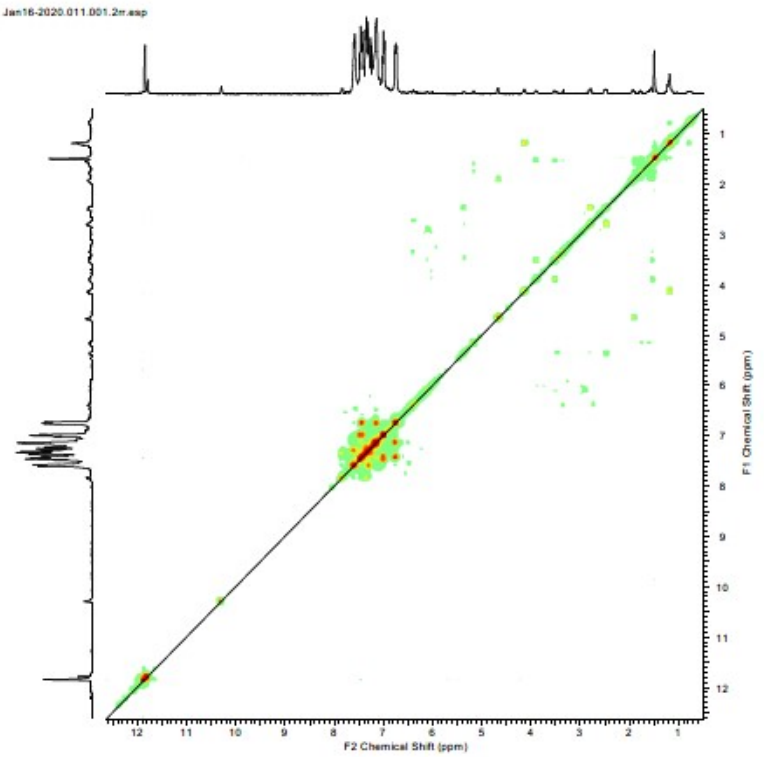
^{1}H NMR (500 MHz, $CDCl_3$) of **7h**:

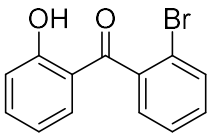


^{13}C NMR (125 MHz, $CDCl_3$) of **7h**:

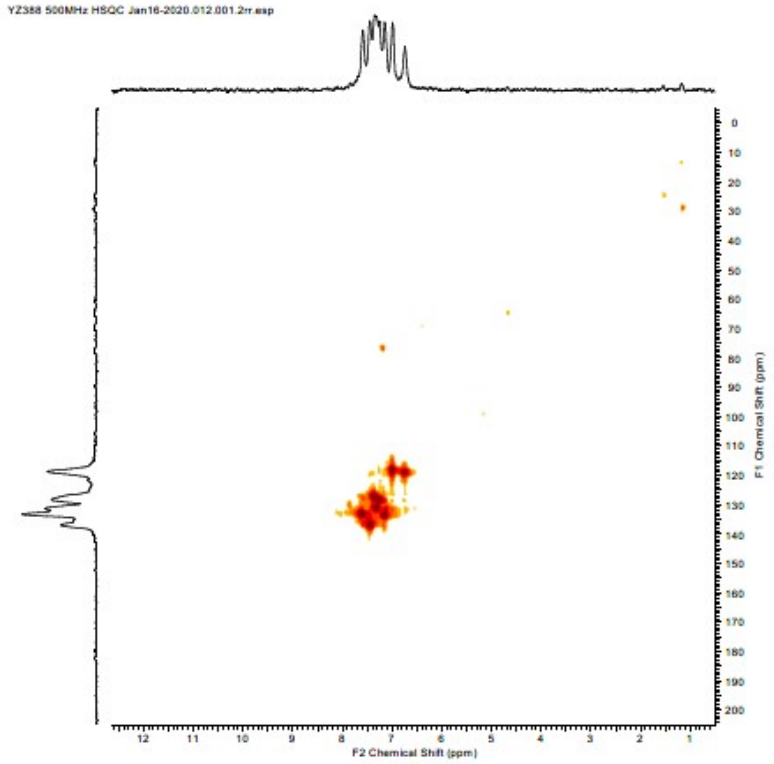


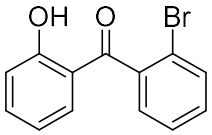
COSY (500 MHz, $CDCl_3$) of **7h**:



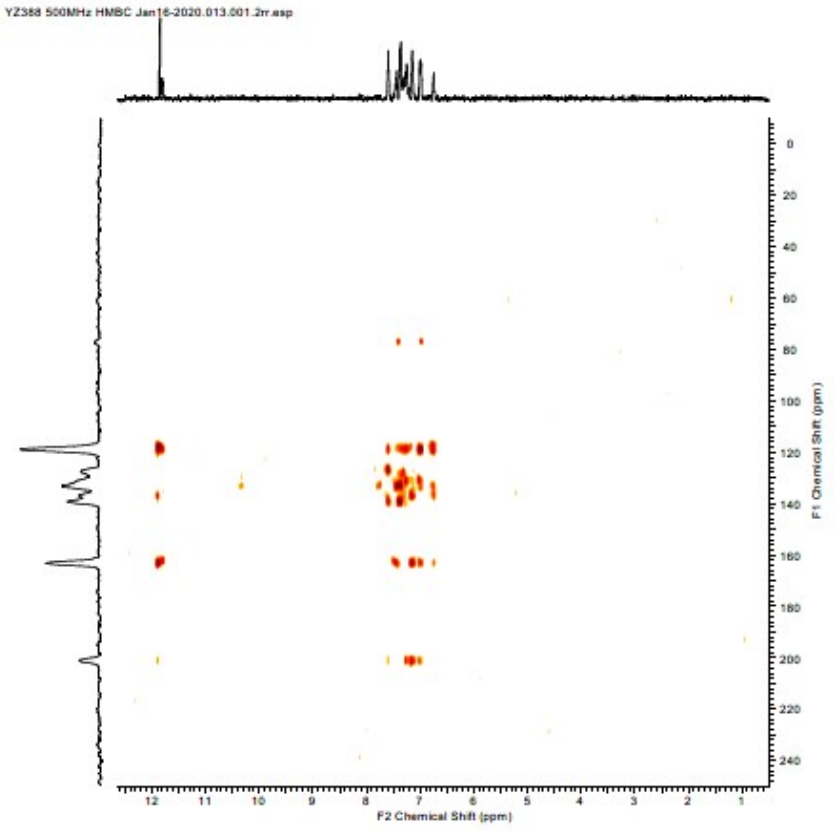


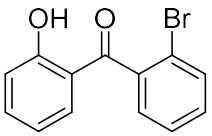
HSQC (500 MHz, $CDCl_3$) of **7h**:



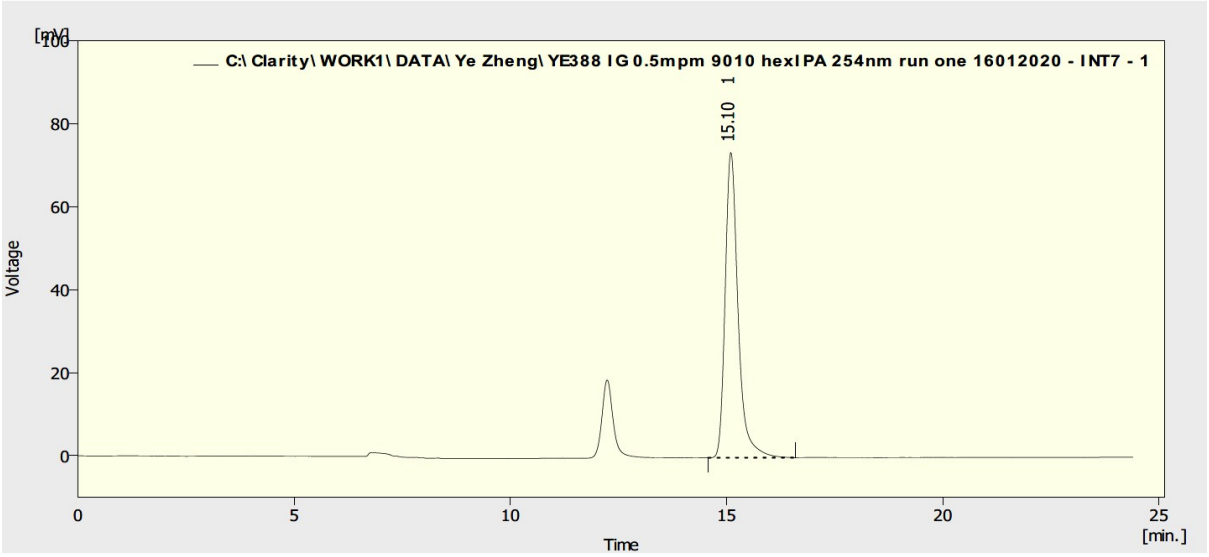


HMBC (500 MHz, $CDCl_3$) of **7h**:





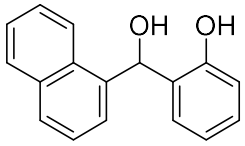
HPLC of (2-chlorophenyl)(2-methoxyphenyl)methanone **7h**



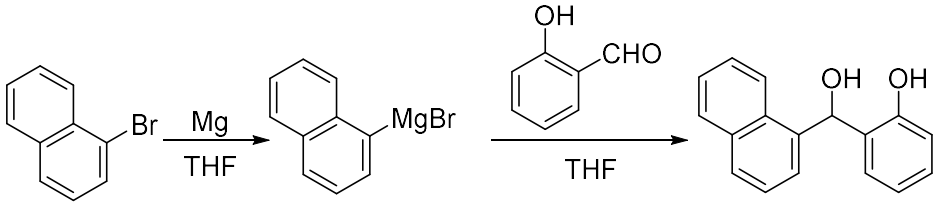
Result Table (Uncal - C:\Clarity\WORK1\DATA\Ye Zheng\YE388 IG 0.5mpm 9010 hexIPA 254nm run one 16012020 - INT7 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	15.100	1525.388	73.611	100.0	100.0	0.30	
	Total	1525.388	73.611	100.0	100.0		

2-(Hydroxy(naphthalen-1-yl)methyl)phenol 8i.



racemic: YZ253, Asymmetric: YZ258



This compound is novel.

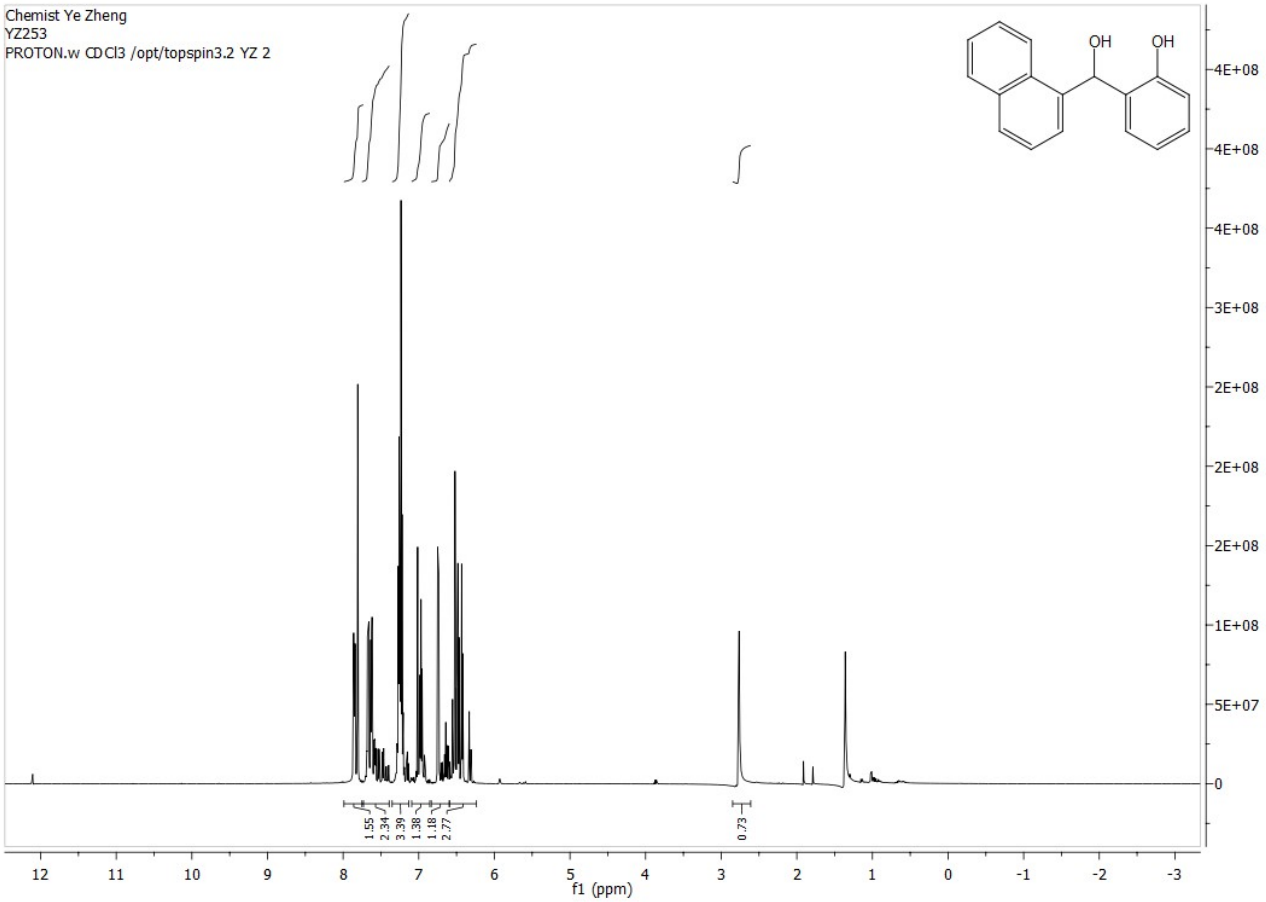
To a solution of 1-bromonaphthalene (849 mg, 4.10 mmol) in THF (4.3 mL) at rt was added magnesium (98.4 mg, 4.10 mmol). The reaction mixture was then stirred under a nitrogen atmosphere for 30 minutes and heated to reflux on a hot plate for 1 hour, after which a solution of salicylaldehyde (200 mg, 1.64 mmol) in THF (1.8 mL) was added dropwise at 0 °C. The reaction mixture was left stirring under the nitrogen atmosphere and allowed to warm to rt. The reaction was followed by TLC (9:1 hexane: EtOAc). The mixture was quenched by saturated NH_4Cl solution (20 mL). DCM (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with DCM (3 × 20 mL), and the combined organic layers were dried ($MgSO_4$) and filtered. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-20% ethyl acetate in hexane to give 2-(hydroxy(naphthalen-1-yl)methyl)phenol **8i** as a colorless oil (355 mg, 1.42 mmol, 86.6%). TLC: Rf ca 0.20 (9:1 hexane: EtOAc), strong UV and $KMnO_4$; HRMS: (found (ESI+): [M+Na]+, Calcd for $C_{17}H_{14}NaO_2$ 273.0886; Found 273.0886; 0.2 ppm error; ν_{max} 3518 (br), 3220, 1591, 1507, 1457, 1364, 1233, 1057, 980 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.89-7.83 (2H, m, ArH), 7.70-7.42 (2H, m, ArH), 7.31-7.16 (3H, m, ArH), 7.04-6.95 (1H, m, ArH), 6.78-6.63 (1H, m, ArH), 6.58-6.33 (3H, m, ArH + Ar*CH*OH), 2.79 (1H, s, ArCH*OH*) ppm; δ_C (125 MHz, $CDCl_3$) 155.9 (C), 136.6 (C), 134.1 (C), 130.9 (C), 129.5 (CH), 129.4 (CH), 129.0 (CH), 128.5 (CH), 126.6 (CH), 125.9 (CH), 125.9 (CH), 125.9 (C), 125.5 (CH), 124.1 (CH), 120.1 (CH), 117.2 (CH), 74.4 (CH) ppm; m/z (ES-API+) 273.4 (M^+ + 23, 100%).

Enantiomeric excess and conversion determined by HPLC analysis (Chiralcel ODH, 30 cm x 6mm column, hexane:iPrOH 90:10, 1.0 mL/min, T = 25°C) ketone 6.3 min, *R* and *S* isomer 19.5 min and 33.2 min, configuration was assigned by analogy.

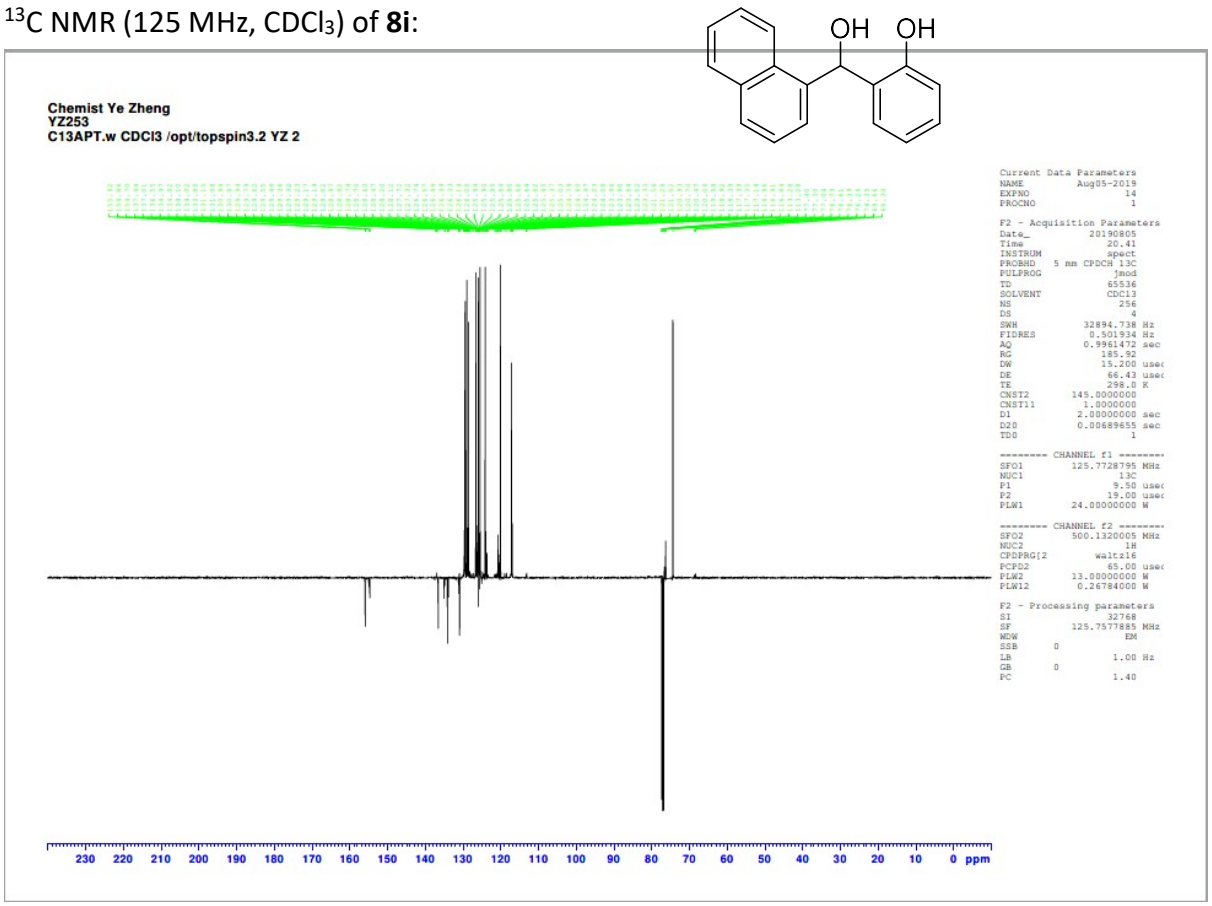
ATH of 2-(hydroxy(naphthalen-1-yl)methyl)phenone **7i** (YZ258).

Catalyst (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst **2** (0.99 mg, 0.00161 mmol, 1 mol%) was added to FA: TEA (5:2 azeotropic mixture, 0.18 mL) at rt and the mixture was stirred under a nitrogen atmosphere for 10-15 minutes; after which a solution of 2-(hydroxy(naphthalen-1-yl)methyl)phenone **7i** (40 mg, 0.161 mmol) in DCM (0.25 mL) was added. The reaction mixture was stirrer under a nitrogen atmosphere, followed by TLC (9:1 hexane: EtOAc). After 72 hours, the reaction was quenched using saturated $NaHCO_3$ solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried ($MgSO_4$) and filtered. The solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-20% ethyl acetate in hexane to 2-(hydroxy(naphthalen-1-yl)methyl)phenol (23 mg, 0.092 mmol, 57%; (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst example). The reaction was also followed by HPLC analysis (Chiralcel ODH, 30 cm x 6mm column, hexane:iPrOH 90:10, 1.0 mL/min, T = 25°C); (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst: 100% conversion; $[\alpha]_D^{25}$ -150 (c 0.115 in $CHCl_3$) 97.2% ee

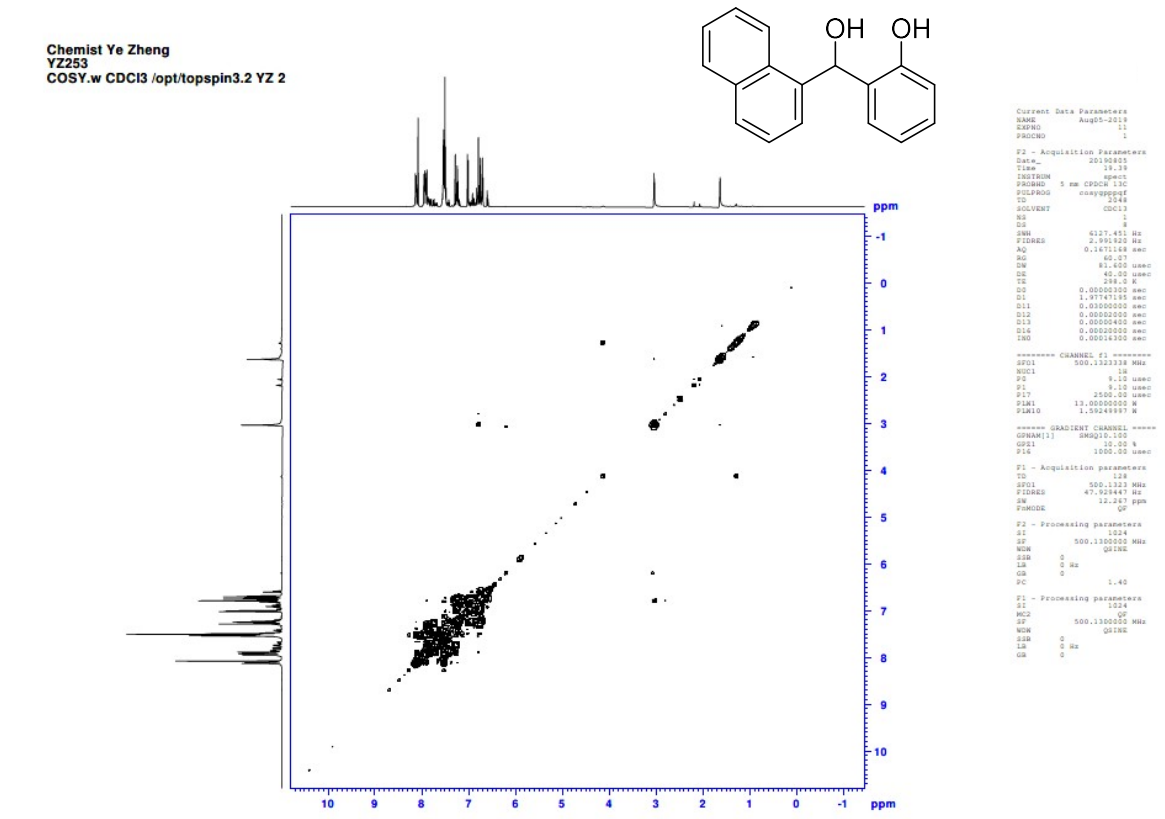
^1H NMR (500 MHz, $CDCl_3$) of **8i**:



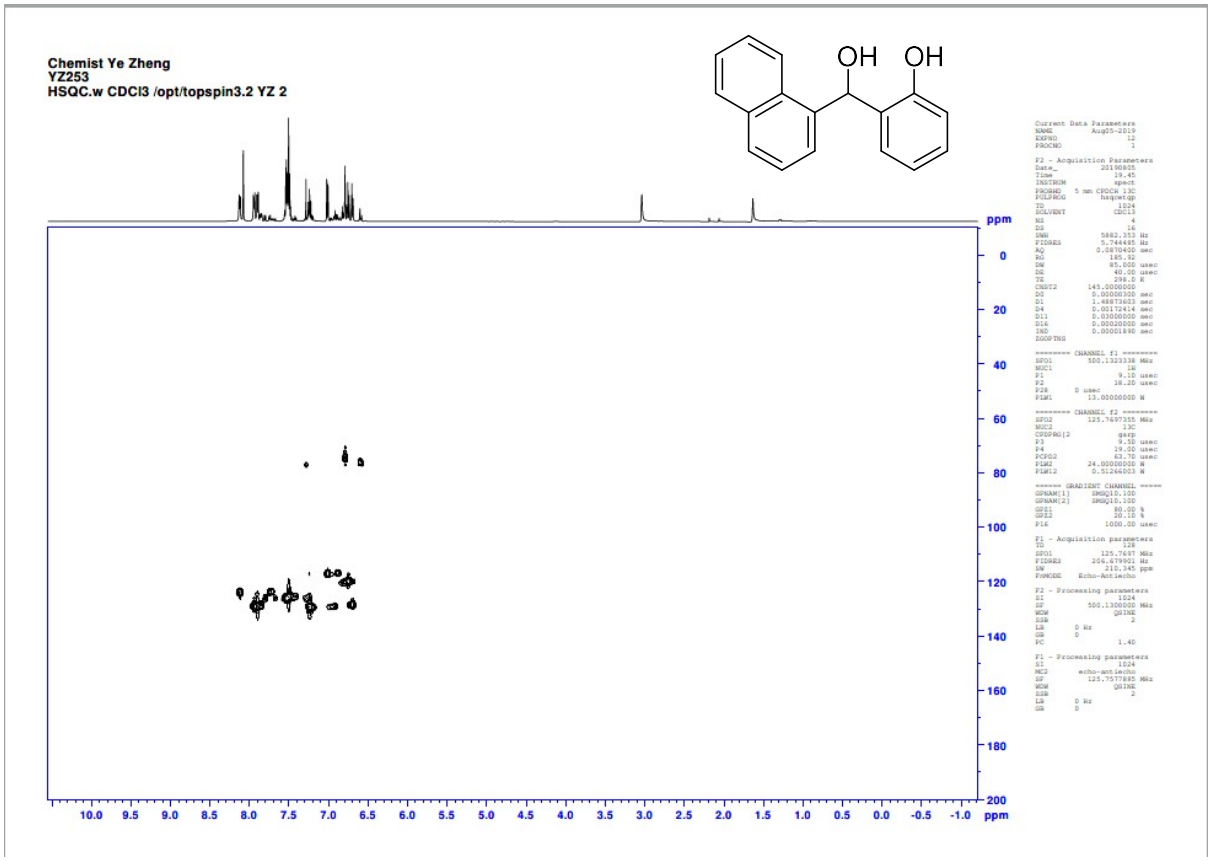
^{13}C NMR (125 MHz, $CDCl_3$) of **8i**:



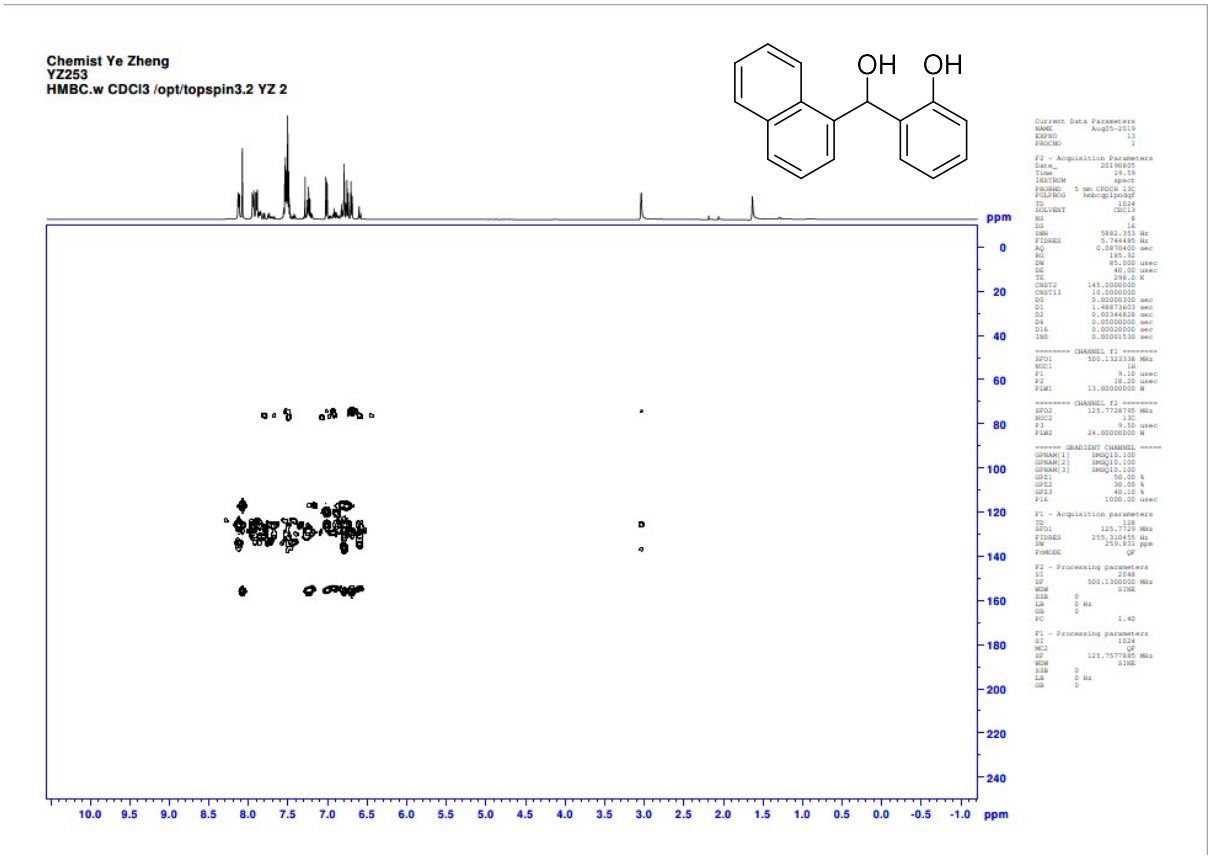
COSY (500 MHz, $CDCl_3$) of **8i**:



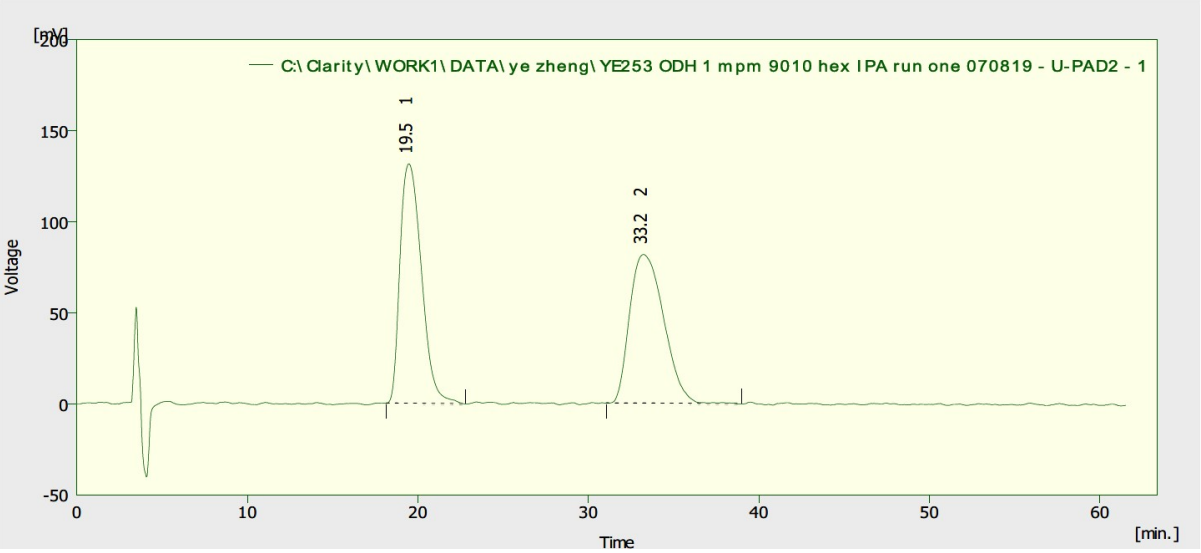
HSQC (500 MHz, $CDCl_3$) of **8i**:



HMBC (500 MHz, $CDCl_3$) of **8i**:



HPLC of racemic 2-(hydroxy(naphthalen-1-yl)methyl)phenol **8i**

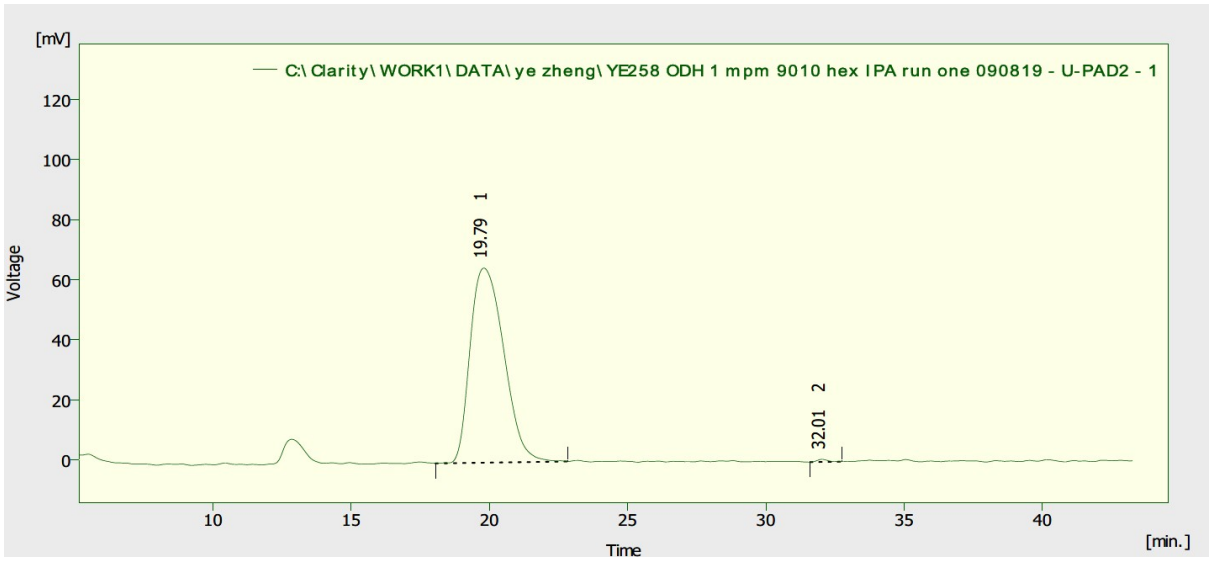


Result Table (Uncal - C:|Clarity|WORK1|DATA|ye zheng|YE253 ODH 1 mpm 9010 hex IPA run one 070819 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	19.480	11545.684	131.783	50.3	61.7	1.39	
2	33.240	11405.409	81.850	49.7	38.3	2.24	
	Total	22951.093	213.633	100.0	100.0		

HPLC of **8i** after ATH of 2-(hydroxy(naphthalen-1-yl)methyl)phenone **7i**:

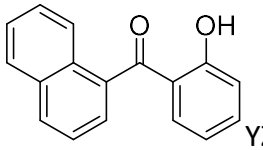
(*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst (after 72 hours, 100% conversion, 97.2% ee).



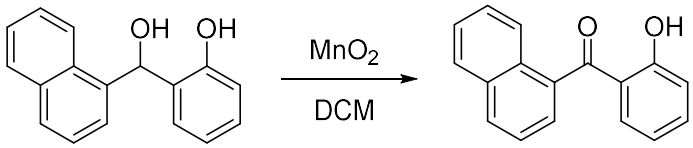
Result Table (Uncal - C:|Clarity|WORK1|DATA|ye zheng|YE258 ODH 1 mpm 9010 hex IPA run one 090819 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	19.792	5501.083	64.773	99.6	98.6	1.36	
2	32.012	23.732	0.896	0.4	1.4	0.41	
	Total	5524.815	65.669	100.0	100.0		

2-Hydroxyphenyl)(naphthalen-1-yl)methanone 7i.



YZ255

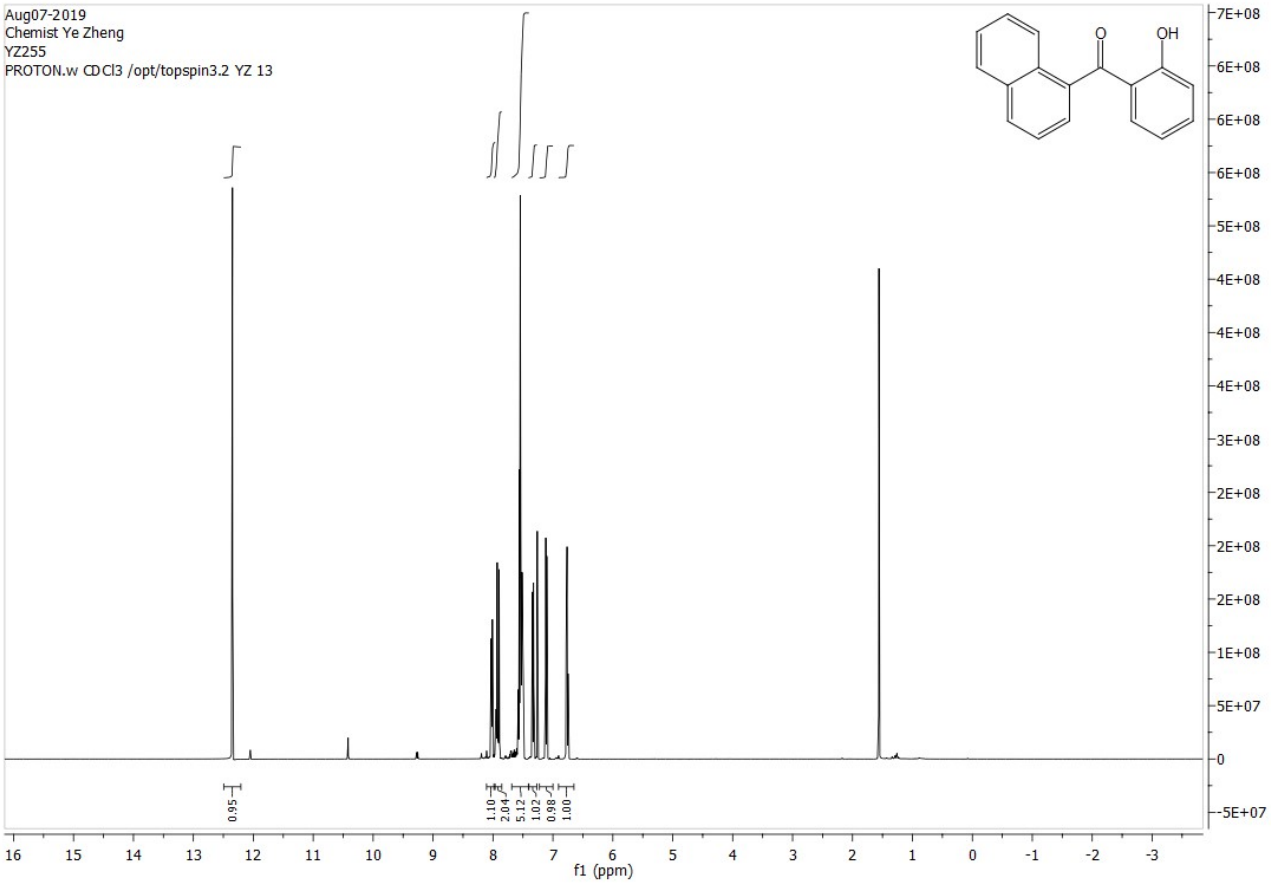


This compound has been reported and fully characterized.

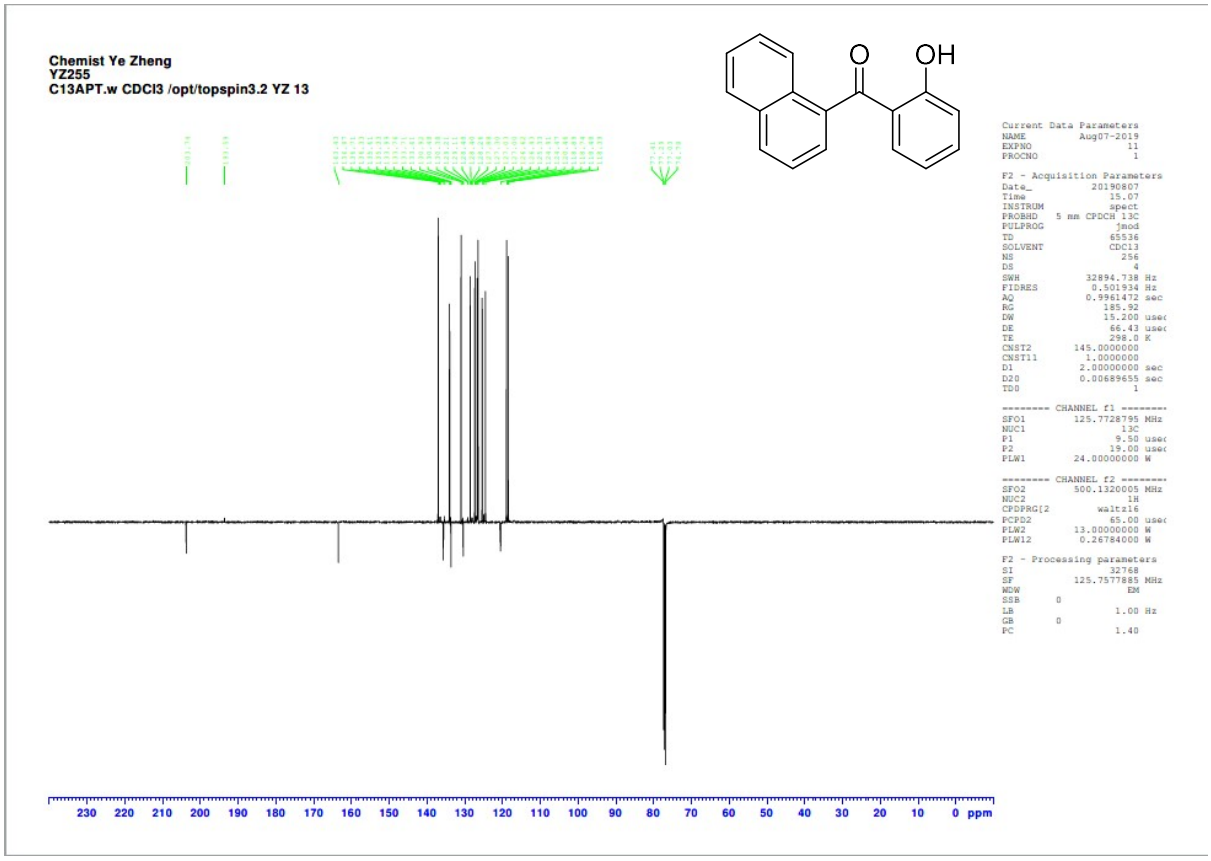
Reference: Rao, Maddali L. N.; Ramakrishna, Boddu S.; *Eur. J. Org. Chem*.; **2017**, 2017, 5080 - 5093

To a solution of 2-(hydroxy(naphthalen-1-yl)methyl)phenol **8i** (320.4 mg, 1.28 mmol) in DCM (10 mL) at rt was added manganese dioxide (1.67 g, 19.2 mmol). The reaction mixture was left to stir under a nitrogen atmosphere overnight. TLC (9:1 hexane: EtOAc) after this time indicated full conversion. The solids were removed by gravity filtration and wash with DCM. The combined solvent was removed to give the give the crude product. The product was isolated via flash chromatography on silica eluted with 0-20% ethyl acetate in hexane to give (2-hydroxyphenyl)(naphthalen-1-yl)methanone **7i** as a yellow oil (100.9 mg, 0.207 mmol, 31.7%). TLC: Rf ca 0.50 (9:1 hexane: EtOAc), strong UV and KMnO4; δ_H (500 MHz, CDCl3) 12.06 (1H, s, ArOH), 7.73 (1H, dd, *J* = 7.2, 1.9, ArH), 7.66-7.61 (2H, m, ArH), 7.29-7.21 (5H, m, ArH), 7.05-6.97 (1H, m, ArH), 6.82 (1H, d, *J* = 8.4, ArH), 6.48 (1H, t, *J* = 7.6, ArH) ppm; δ_C (125 MHz, CDCl3) 203.7 (C), 163.4 (C), 137.0 (CH), 135.6 (C), 134.0 (CH), 133.6 (C), 130.9 (CH), 130.4 (C), 128.5 (CH), 127.3 (CH), 126.6 (CH), 126.4 (CH), 125.3 (CH), 124.5 (CH), 120.5 (C), 118.9 (CH), 118.4 (CH) ppm.

^{1}H NMR (500 MHz, $CDCl_3$) of **7i**:



^{13}C NMR (125 MHz, $CDCl_3$) of **7i**:

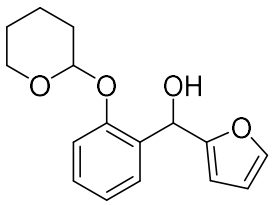


HPLC of (2-hydroxyphenyl)(naphthalen-1-yl)methanone **7i**:

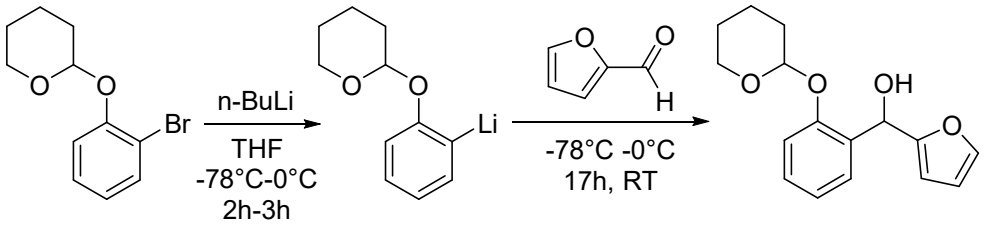
Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|ye zheng\|YE255 ODH 1 mpm 9010 hex IPA run two 070819 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	6.300	15262.191	456.296	100.0	100.0	0.48	
	Total	15262.191	456.296	100.0	100.0		

Furan-2-yl(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol 8j.



YZ261, Asymmetric: YZ289



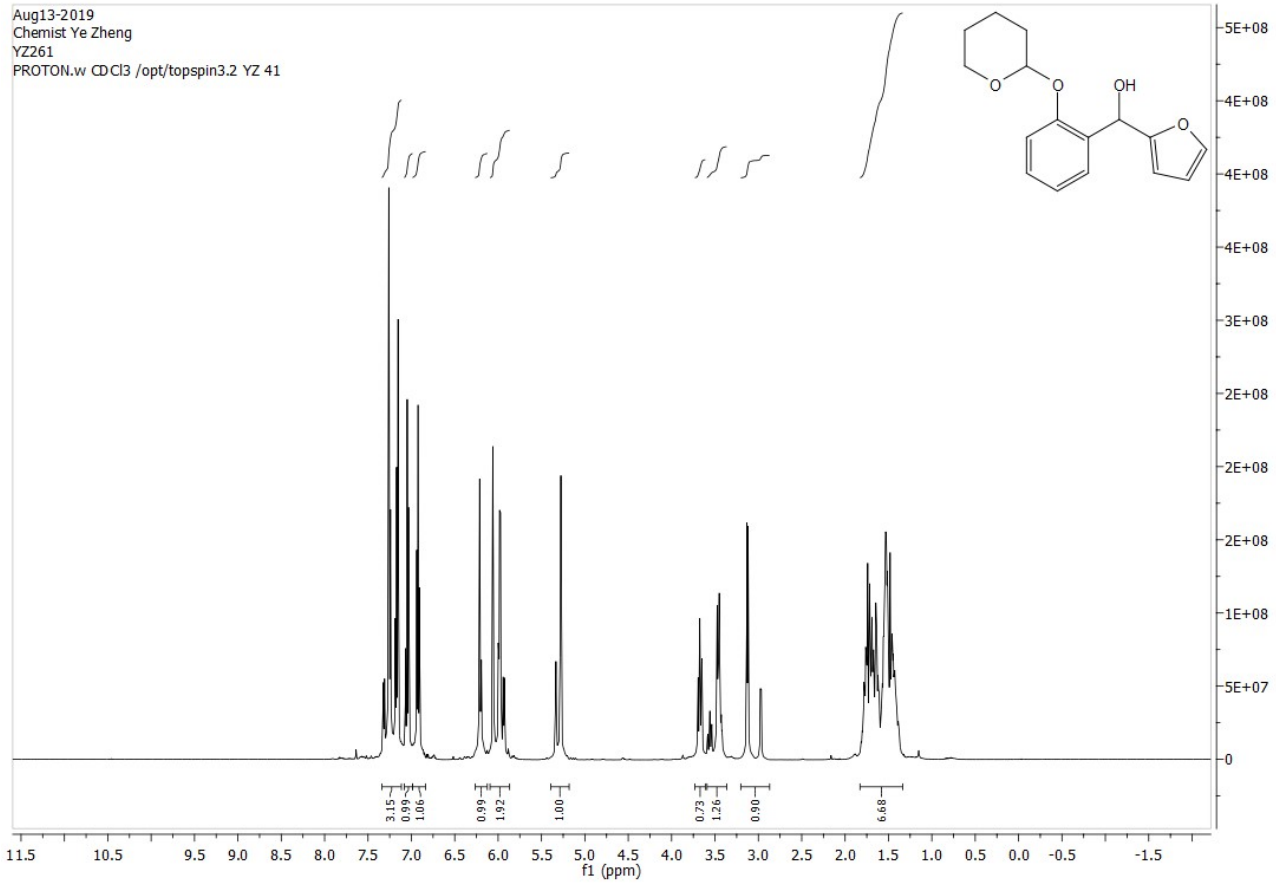
This compound is novel.

To a solution of 2-(2-bromophenoxy)tetrahydro-2H-pyran (591.4 mg, 2.31 mmol) in THF (3 mL) at -78 °C was added a solution of n-butyllithium (0.84 mL, 2.5M in hexanes, 2.10 mmol). The reaction mixture was then stirred under a nitrogen atmosphere for 2-3 hours, after which furfural (202 mg, 2.10 mmol) was added dropwise. The reaction mixture was left stirring under the nitrogen atmosphere and allowed to warm to rt. The reaction was followed by TLC (9:1 hexane: EtOAc). The mixture was quenched by saturated NH_4Cl solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 × 20 mL), and the combined organic layers were dried ($MgSO_4$) and filtered. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-20% ethyl acetate in hexane to give furan-2-yl(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol **8j** as a yellow oil (481.8 mg, 1.76 mmol, 84.4%). TLC: Rf ca 0.20 (9:1 hexane: EtOAc), strong UV and $KMnO_4$; HRMS: (found (ESI+): [M+Na]+, Calcd for $C_{16}H_{18}NaO_4$ 297.1094; Found 297.1097; 1.2 ppm error); ν_{max} 3422 (br), 3120, 2940, 2882, 1600, 1484, 1450, 1235, 1024, 960 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.34-7.12 (3H, m, ArH + C_4H_3O), 7.05 (1H, t, *J* = 8.8, ArH), 6.92 (1H, t, *J* = 7.5, ArH), 6.26-6.12 (1H, m, C_4H_3O), 6.06-5.93 (2H, m, C_4H_3O + Ar*CH*OH), 5.39-5.18 (1H, m, ArOCHO), 3.73-3.61 (1H, m, O*CH*$_2$CH$_2$), 3.59-3.36 (1H, m, O*CH*$_2$CH$_2$), 3.13-2.97 (1H, m, ArCH*OH*), 1.83-1.34 (6H, m, CH_2) ppm; δ_C (125 MHz, $CDCl_3$) 155.9 (C), 154.4 (C), 142.0 (CH), 130.2 (C), 129.2 (CH), 127.8 (CH), 122.0 (CH), 115.0 (CH), 110.2 (CH), 106.7 (CH), 97.0 (CH), 99.0 (CH), 62.3 (CH_2), 30.4 (CH_2), 25.1 (CH_2), 18.9 (CH_2) ppm; m/z (ES-API+) 297.2 (M^+ + 23, 100%).

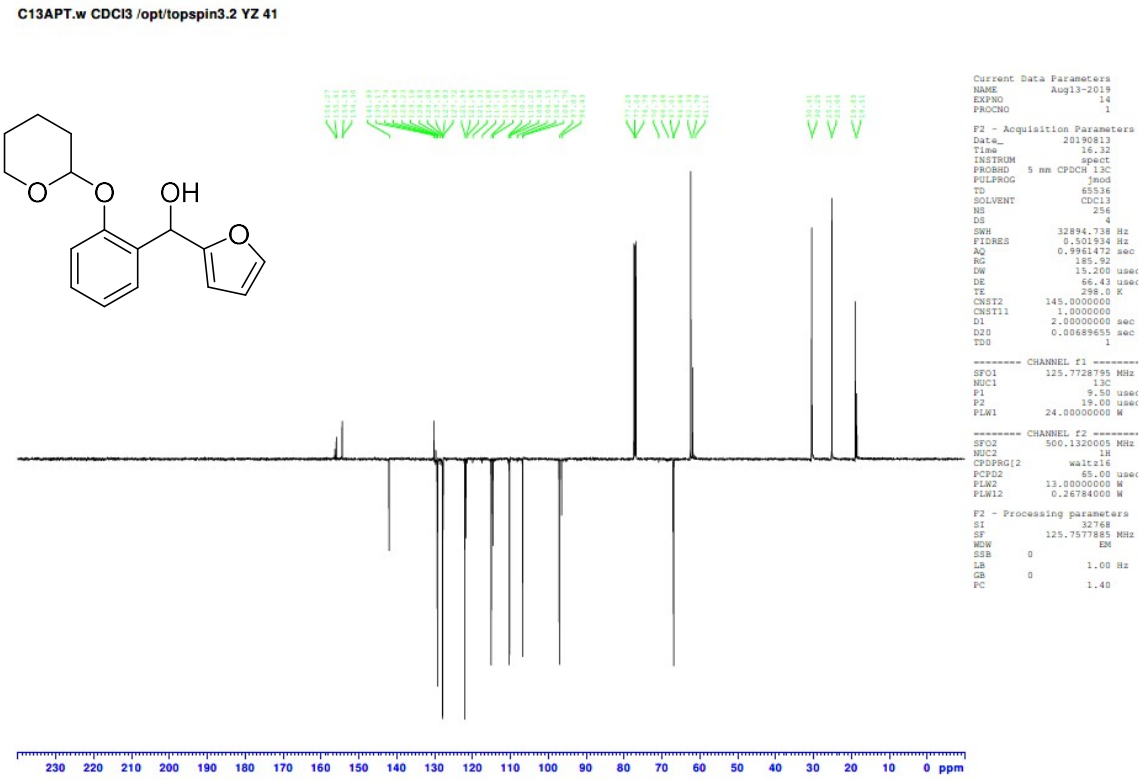
Enantiomeric excess and conversion determined by HPLC analysis (Chiralpak IA, 30 cm x 6mm column, hexane:iPrOH 95:5, 0.5 mL/min, T = 25°C) ketone 21.7 and 23.0 min, *R* and *S* isomer 30.8, 37.3 min and 33.9, 41.1 min, configuration was assigned by analogy.

Catalyst (*R.R*)-**2** (0.00147 mmol, 1mol%) was added to FA: TEA (5:2 azeotropic mixture, 0.18 mL) at rt and the mixture was stirred under a nitrogen inert atmosphere for 10-15 minutes; after which a solution of furan-2-yl(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanone (40 mg, 0.147 mmol) in DCM (0.25 mL) was added. The reaction mixture was stirrer under a nitrogen atmosphere, followed by TLC (9:1 hexane: ethyl acetate). After 72 hours, the reaction was quenched using saturated $NaHCO_3$ solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried ($MgSO_4$) and filtered. The solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-20% ethyl acetate in hexane to give furan-2-yl(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol **8j** (15.7 mg, 0.0573 mmol, 39%); (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst example). The reaction was also followed by HPLC analysis (Chiralpak IA, 30 cm x 6mm column, hexane:iPrOH 95:5, 0.5 mL/min, T = 25°C); (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst: 100% conversion; $[\alpha]_D^{23}$ -11.3 (c 0.785 in $CHCl_3$) 66.8% ee and 81.4% ee.

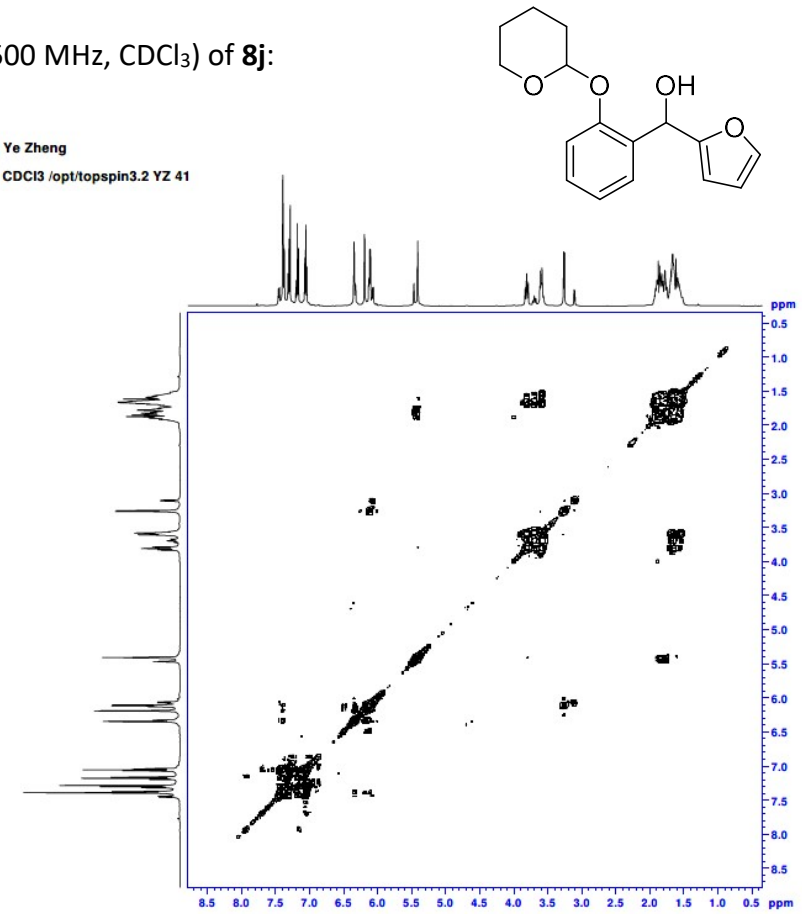
^1H NMR (500 MHz, $CDCl_3$) of **8j**:



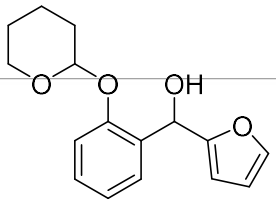
^{13}C NMR (125 MHz, $CDCl_3$) of **8j**:

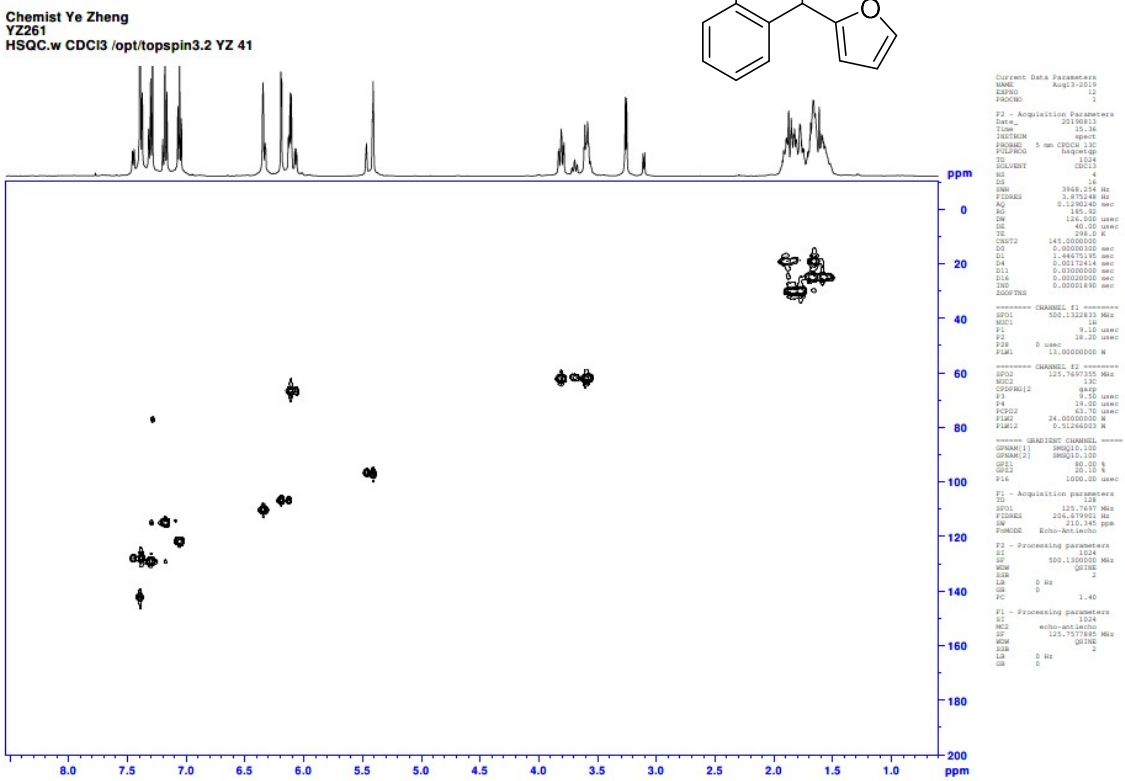


COSY (500 MHz, $CDCl_3$) of **8j**:

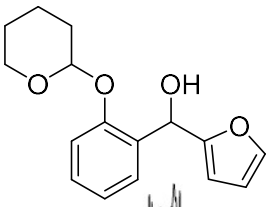


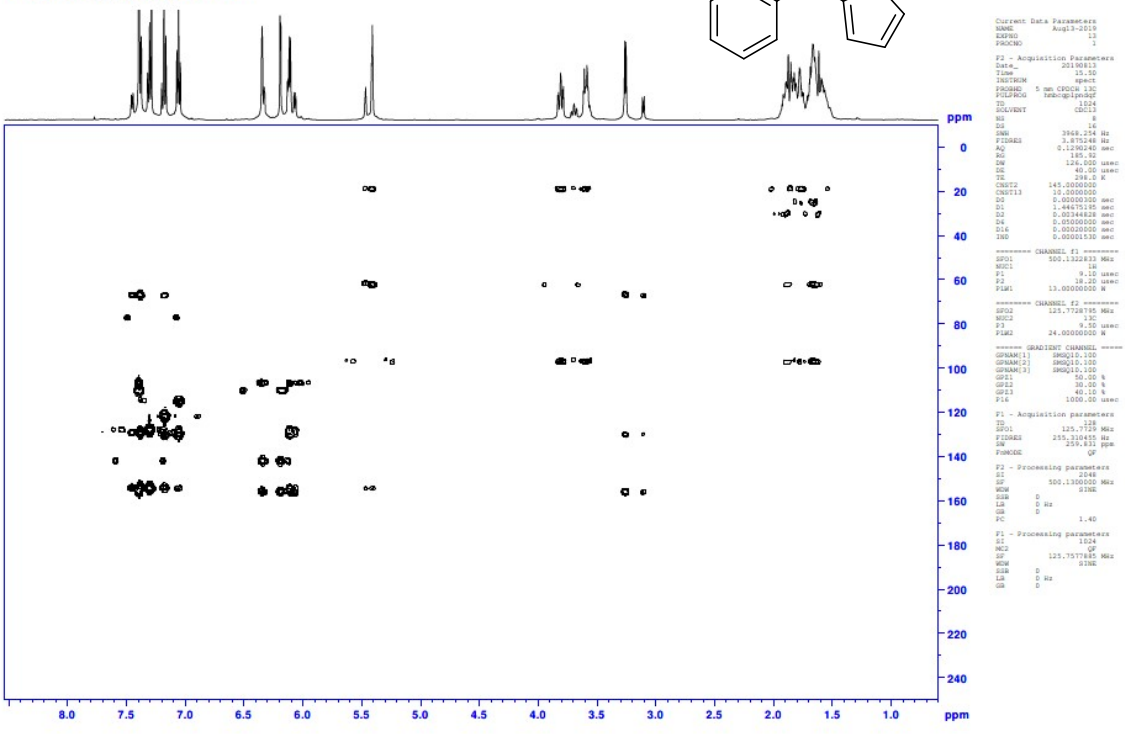
HSQC (500 MHz, $CDCl_3$) of **8j**:



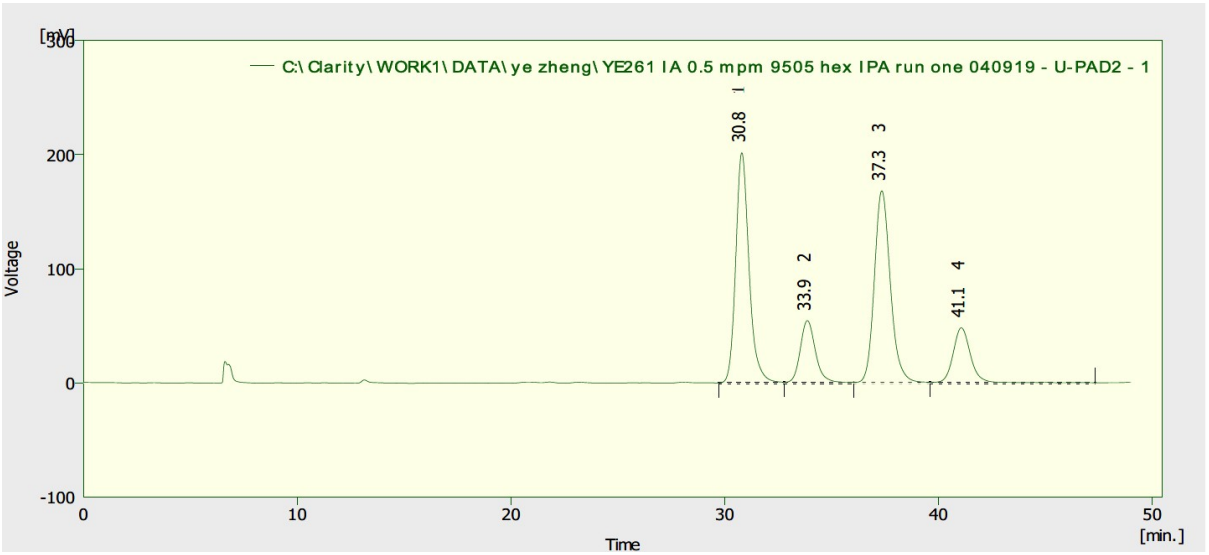


HMBC (500 MHz, $CDCl_3$) of **8j**:





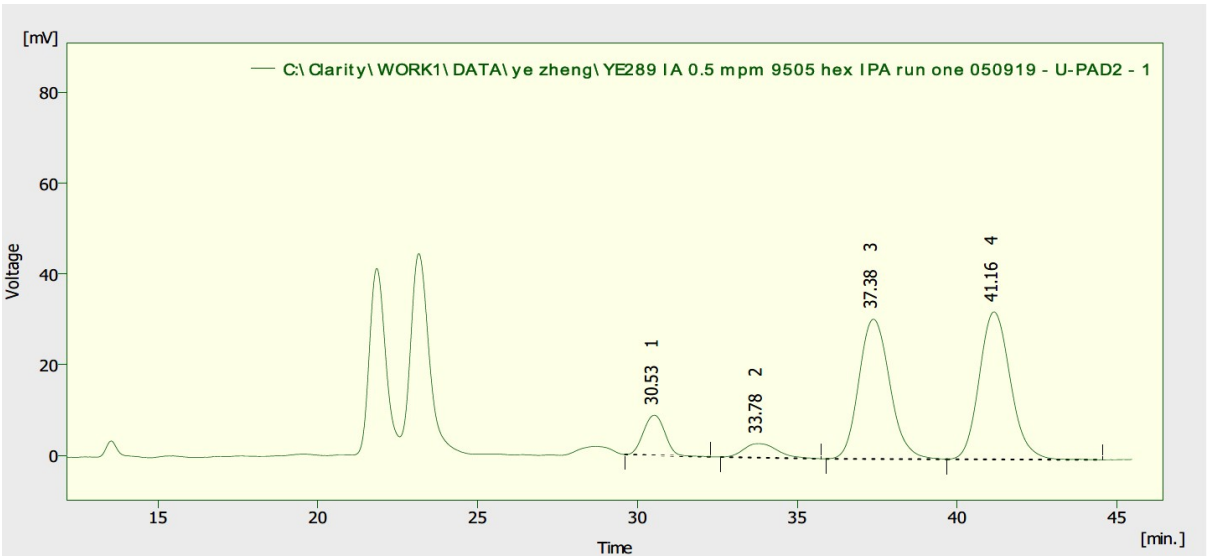
HPLC of racemic furan-2-yl(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol **8j**:



Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|ye zheng\|YE261 IA 0.5 mpm 9505 hex IPA run one 040919 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	30.796	8757.873	202.059	38.0	42.7	0.64	
2	33.864	2725.407	54.688	11.8	11.5	0.74	
3	37.344	8799.534	168.545	38.2	35.6	0.79	
4	41.064	2769.037	48.335	12.0	10.2	0.84	
	Total	23051.851	473.627	100.0	100.0		

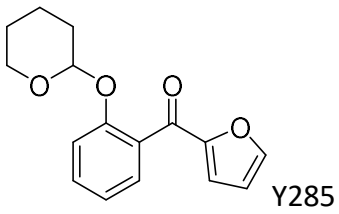
HPLC of **8j** after ATH of furan-2-yl(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanone **7j**: (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst (after 72 hours, 100% conversion, 66.8% ee and 81.4% ee).



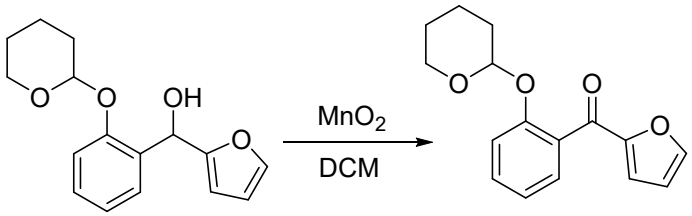
Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|ye zheng\|YE289 IA 0.5 mpm 9505 hex IPA run one 050919 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	30.528	414.047	8.850	8.4	11.8	0.75	
2	33.784	228.679	3.109	4.6	4.1	1.14	
3	37.380	2074.784	30.789	42.2	40.9	1.04	
4	41.156	2202.409	32.494	44.8	43.2	1.05	
	Total	4919.920	75.242	100.0	100.0		

Furan-2-yl(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanone 7j.



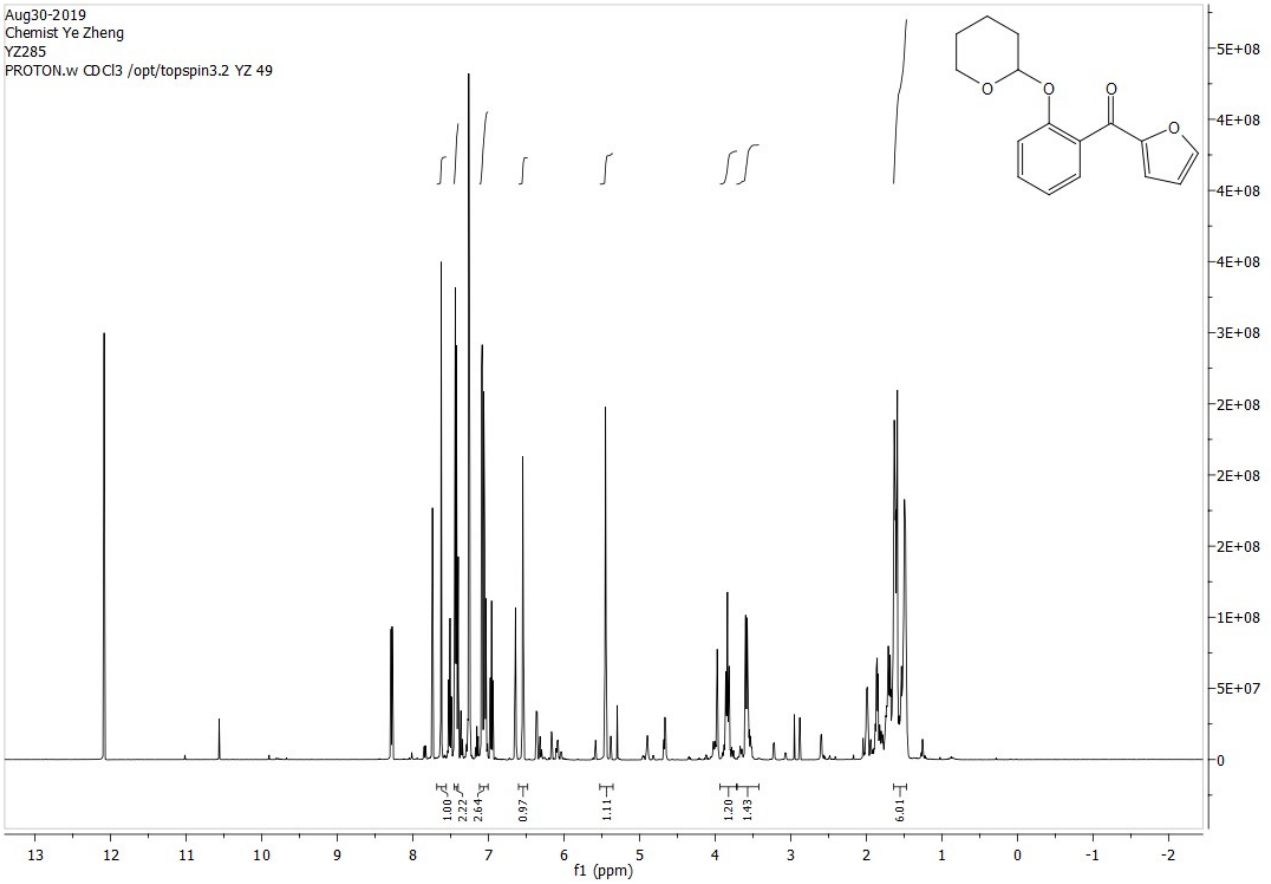
Y285



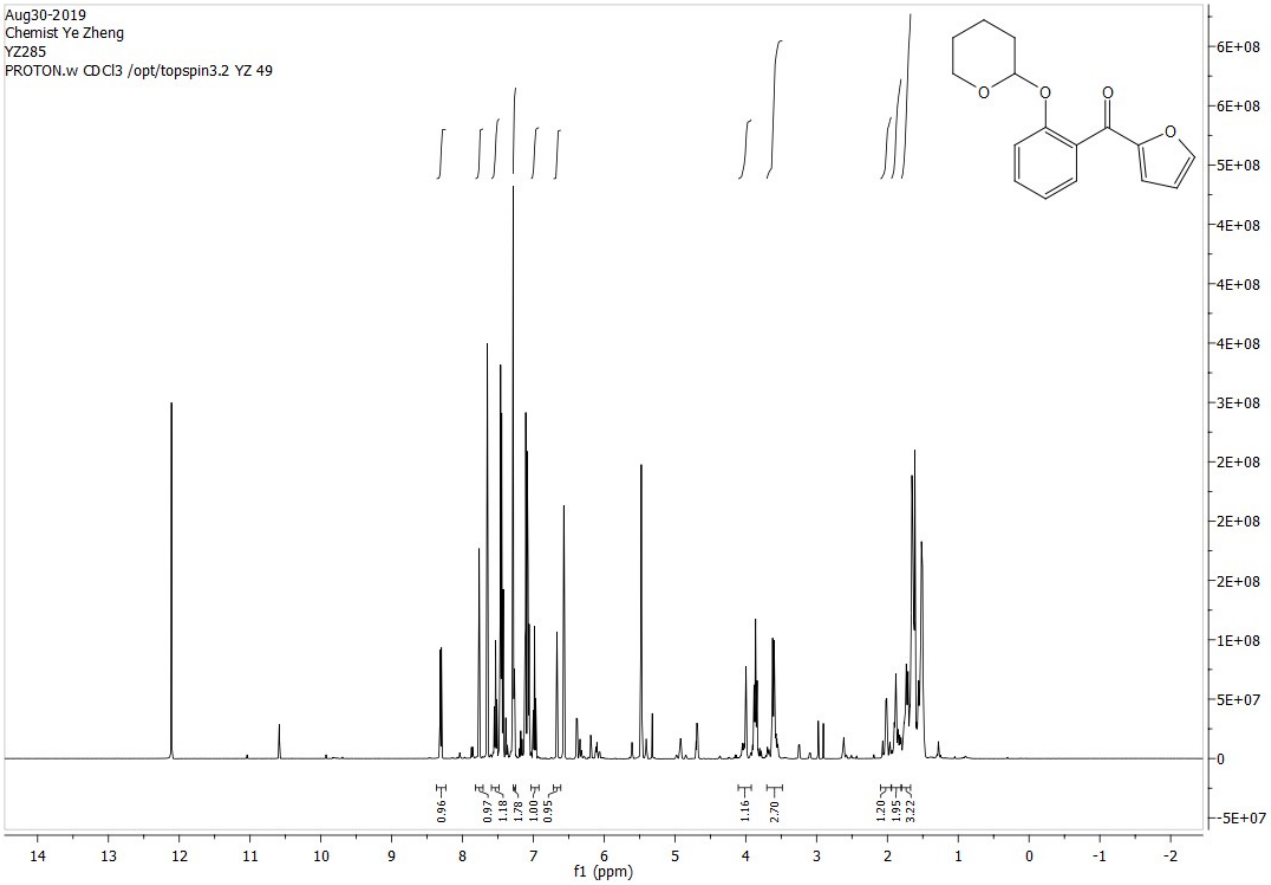
This compound is novel.

To a solution of furan-2-yl(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol **8j** (554 mg, 2.02 mmol) in DCM (20 mL) at rt was added manganese dioxide (2.63 g, 30.3 mmol). The reaction mixture was left to stir under a nitrogen atmosphere overnight. TLC (9:1 hexane: EtOAc) after this time indicated full conversion. The solids were removed by gravity filtration and wash with DCM. The solvent was removed to give furan-2-yl(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanone **7j**as a yellow solid (402.4 mg, 1.48 mmol, 73.1%). TLC: Rf ca 0.40 (9:1 hexane: EtOAc), strong UV and $KMnO_4$; Mp: 74 °C; HRMS: (found (ESI+): [M+Na]+, Calcd for $C_{16}H_{16}NaO_4$ 295.0939; Found 295.0941; 0.5 ppm error; ν_{max} 2944, 2885, 2849, 1642, 1595, 1460, 1304, 1235, 1115, 1016, 948 cm^{-1}; Major diastereomer: δ_H (500 MHz, $CDCl_3$) 7.62 (1H, s, ArH), 7.45-7.40 (2H, m, ArH), 7.12-7.01 (3H, m, ArH + C_4H_3O), 6.55-6.54 (1H, m, C_4H_3O), 5.45 (1H, s, OCHO), 3.94-3.71 (1H, m, O*CH*$_2$$CH_2$), 3.72-3.42 (1H, m, O*CH*$_2$$CH_2$), 1.64-1.47 (6H, m, CH_2) ppm; Minor diastereomer: δ_H (500 MHz, $CDCl_3$) 8.31 (1H, d, *J* = 9.4, ArH), 7.76 (1H, s, ArH), 7.53 (1H, t, *J* = 7.8, ArH), 7.27-7.26 (2H, m, ArH + C_4H_3O), 6.98 (1H, t, *J* = 7.6, C_4H_3O), 6.67-6.66 (1H, m, C_4H_3O), 4.11-3.92 (1H, m, OCHO), 3.70-3.48 (2H, m, O*CH*$_2$$CH_2$), 2.10-1.95 (1H, m, CH_2), 1.94-1.81 (2H, m, CH_2), 1.80-1.67 (3H, m, CH_2) ppm; Major diastereomer: δ_C (125 MHz, $CDCl_3$) 163.4 (C), 155.0 (C), 153.3 (C), 136.1 (CH), 132.2 (CH), 129.3 (CH), 128.9 (C), 121.3 (CH), 119.6 (CH), 115.6 (CH), 112.2 (CH), 96.7 (CH), 61.7 (CH_2), 30.0 (CH_2), 25.1 (CH_2), 18.0 (CH_2) ppm; Minor diastereomer: δ_C (125 MHz, $CDCl_3$) 163.4 (C), 155.0 (C), 153.3 (C), 136.1 (CH), 131.5 (CH), 129.3 (CH), 128.9 (C), 121.0 (CH), 119.0 (CH), 118.5 (CH), 112.5 (CH), 96.7 (CH), 61.7 (CH_2), 30.0 (CH_2), 25.1 (CH_2), 17.97 (CH_2) ppm; m/z (ES-API+) 295.2 (M^+ + 23, 100%).

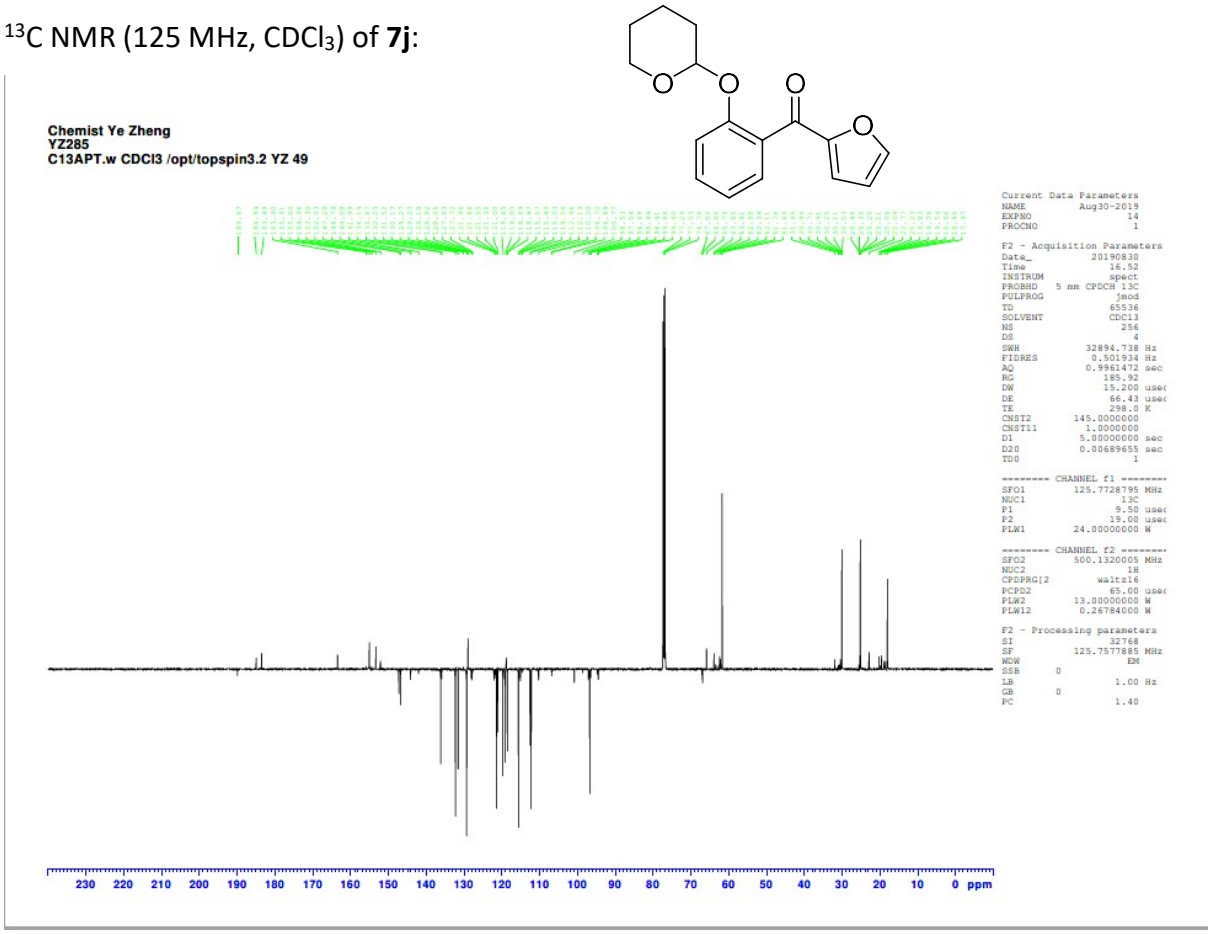
^{1}H NMR (500 MHz, $CDCl_3$) **7j** Major diastereomer:



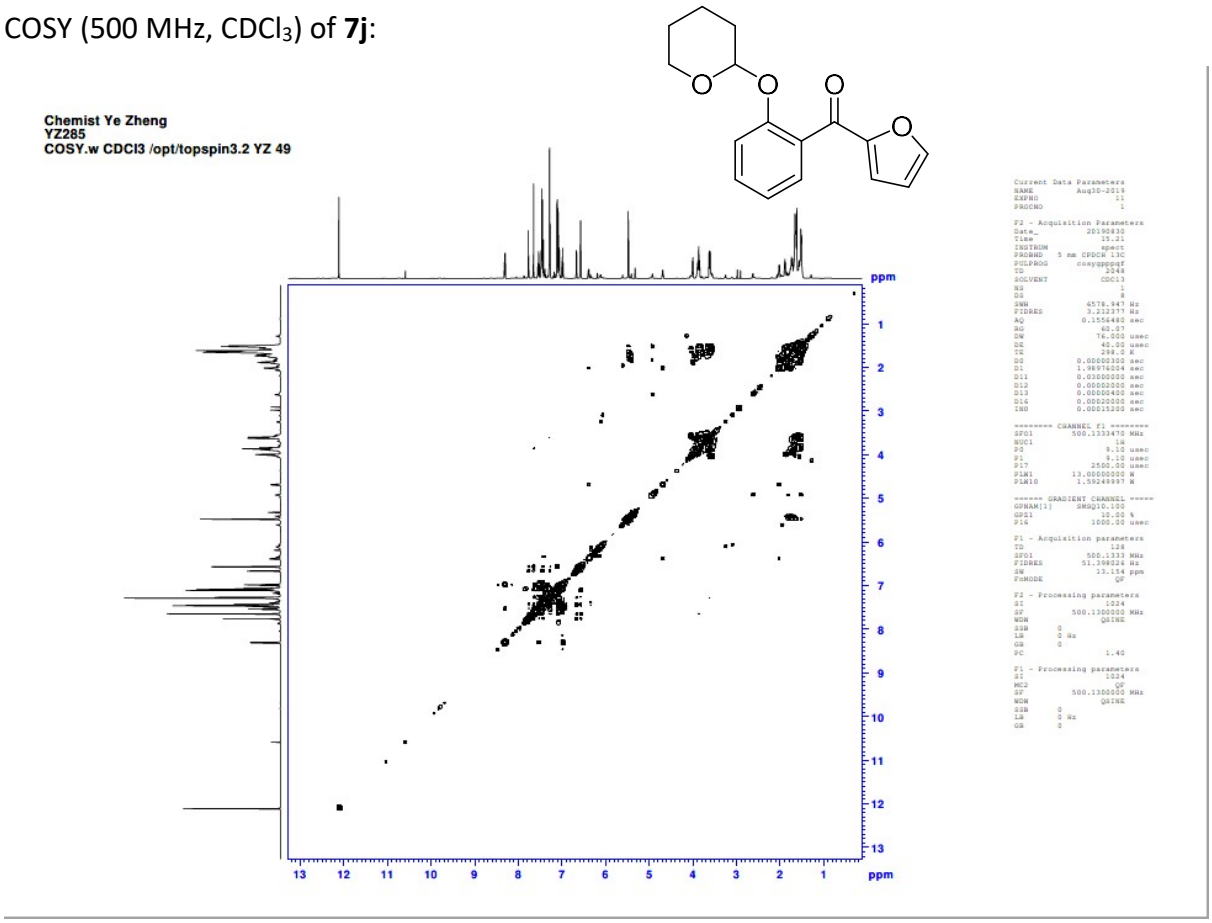
7j Minor diastereomer:



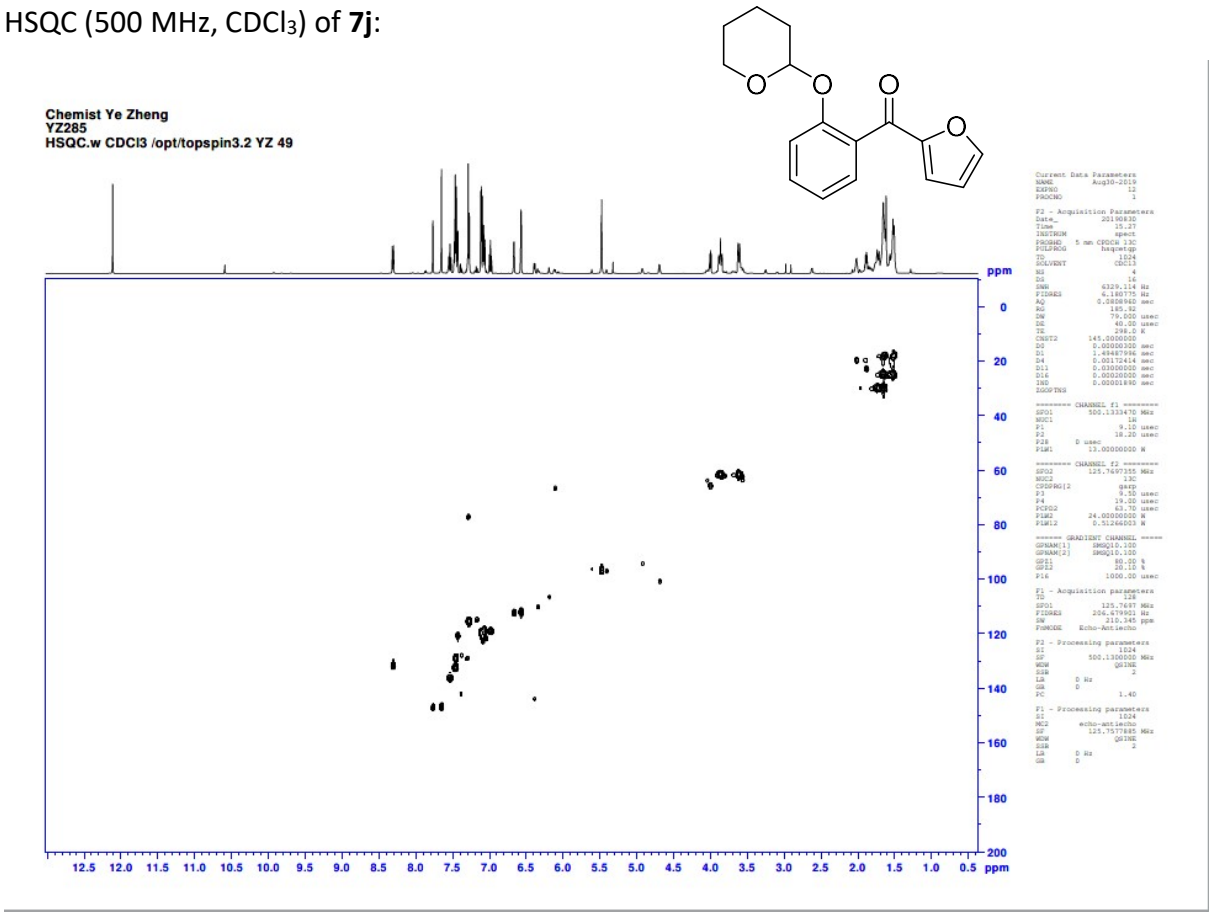
^{13}C NMR (125 MHz, $CDCl_3$) of **7j**:



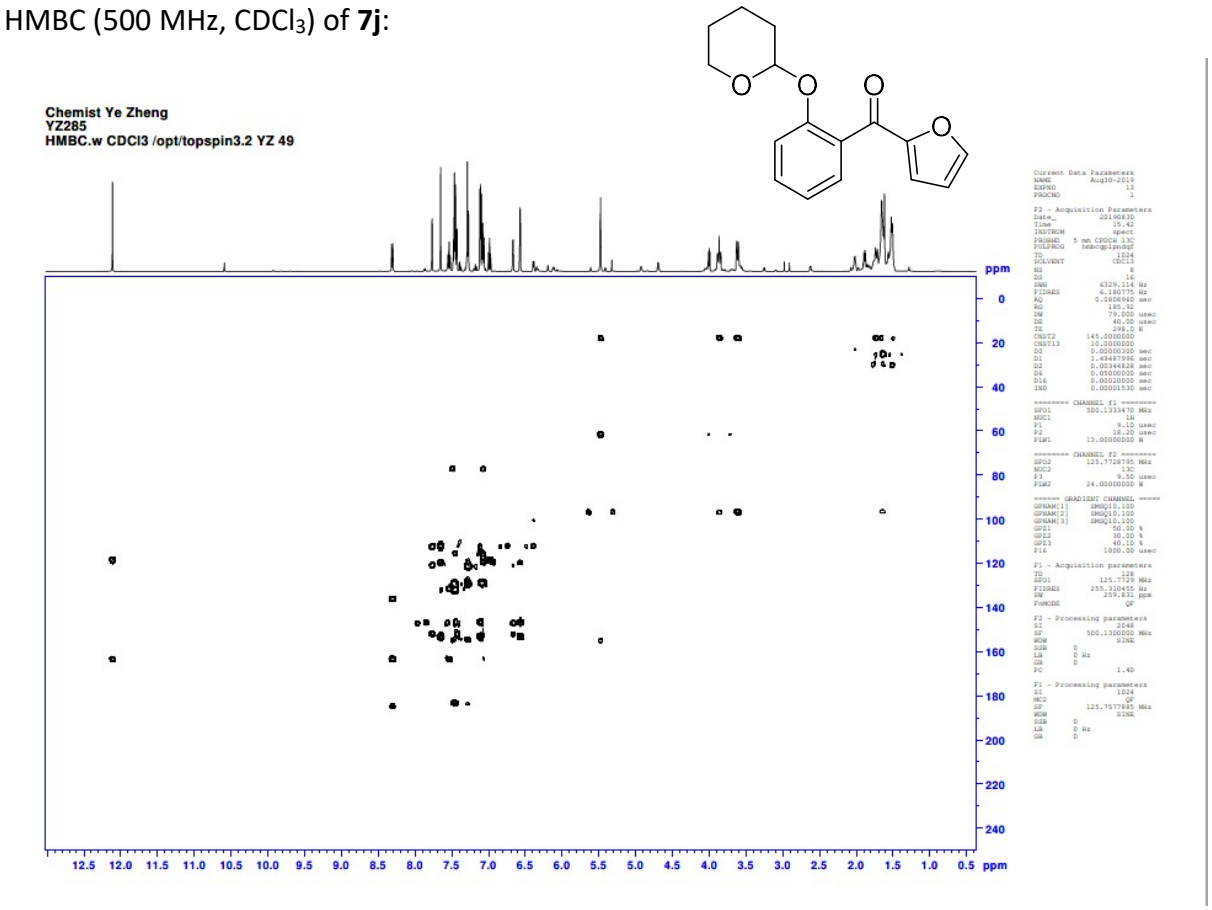
COSY (500 MHz, $CDCl_3$) of **7j**:



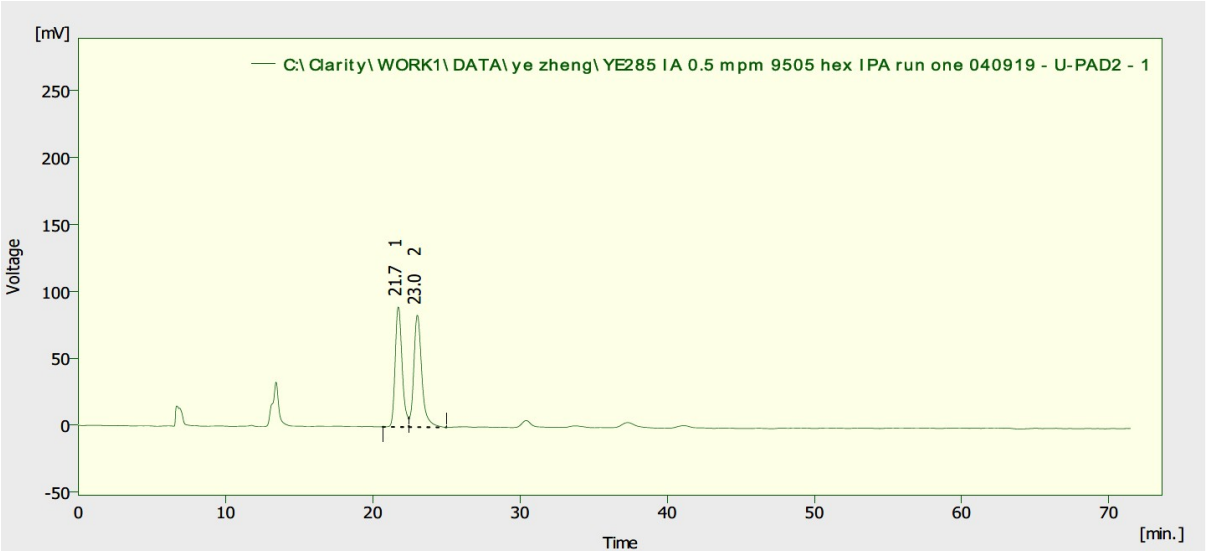
HSQC (500 MHz, $CDCl_3$) of **7j**:



HMBC (500 MHz, $CDCl_3$) of **7j**:



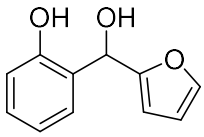
HPLC of furan-2-yl(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanone **7j**:



Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|ye zheng\|YE285 IA 0.5 mpm 9505 hex IPA run one 040919 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	21.728	2950.761	90.173	48.2	51.8	0.50	
2	23.020	3171.829	83.959	51.8	48.2	0.55	
	Total	6122.590	174.132	100.0	100.0		

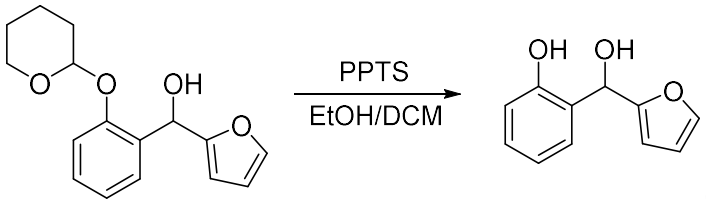
2-(Furan-2-yl(hydroxy)methyl)phenol 8k.



YZ266

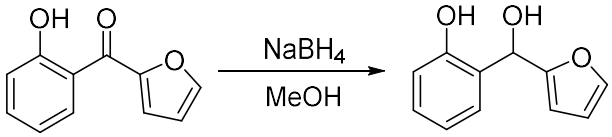
Asymmetric: YZ297

YZ266: attempt



compound decomposed

YZ293: attempt



sample partially decomposed.

This compound is novel.

YZ266: To a solution of furan-2-yl(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol (457 mg, 1.67 mmol) in EtOH (8.6 mL)/DCM (4.3 mL) was added pyridinium *p*-toluenesulfonate (PPTS) (62.8 mg, 0.25 mmol) at rt. The reaction mixture was left to stir under a nitrogen atmosphere overnight. TLC (4:1 hexane: EtOAc) after this time indicated full conversion. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane but NMR indicated the product had decomposed.

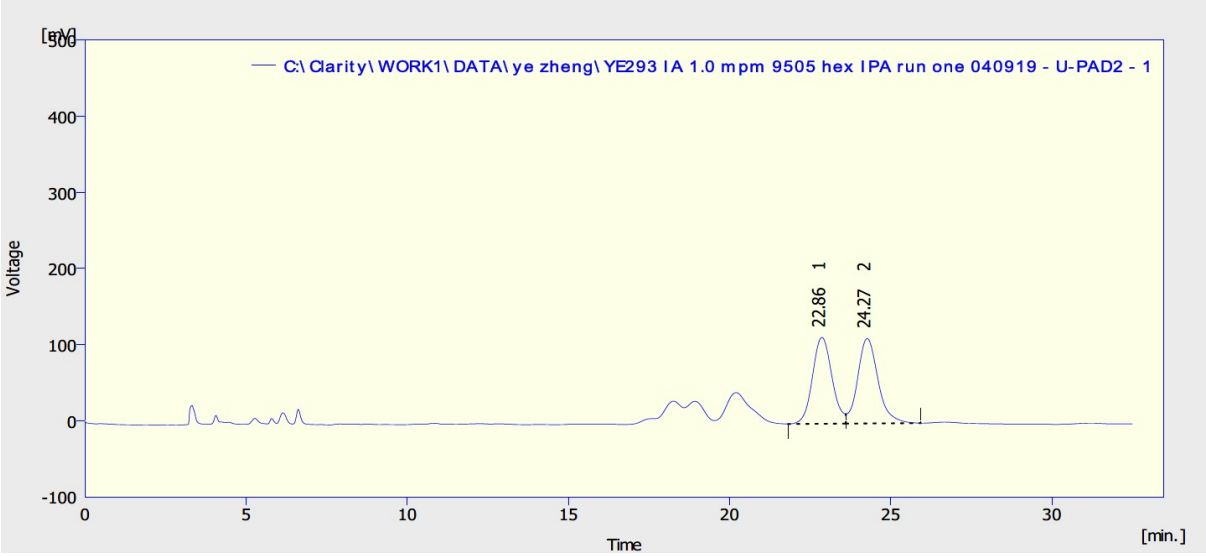
YZ293: To a solution of furan-2-yl(2-hydroxyphenyl)methanone (115.5 mg, 0.614 mmol) in MeOH (2.8 mL) was added sodium borohydride (46.7 mg, 1.228 mmol). The reaction was stirred for 4 hours. TLC (4:1 hexane: EtOAc) after this time indicated full conversion. Distilled water (20 mL) was added, and the mixture was extracted with EtOAc (3 × 20ml), dried with $MgSO_4$, filtered, and the solvent was removed under vacuum to give the product. NMR indicated the product was significantly decomposed but HPLC was obtained and showed two peaks sufficient for location of products.

Enantiomeric excess and conversion determined by HPLC analysis (Chiralpak IA, 30 cm x 6mm column, hexane:iPrOH 95:5, 1.0 mL/min, λ= 210 nm, T = 25°C) ketone 6.6 min, *R* and *S* isomers 22.7 min and 24.0 min, configuration was assigned by analogy.

ATH of furan-2-yl(2-hydroxyphenyl)methanone **7k**.

(*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst **2** (0.00213 mmol, 1mol%) was added to FA: TEA (5:2 azeotropic mixture, 0.18 mL) at rt and the mixture was stirred under a nitrogen inert atmosphere for 10-15 minutes; after which a solution of furan-2-yl(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanone **7k** (40 mg, 0.213 mmol) in DCM (0.25 mL) was added. The reaction mixture was stirrer under a nitrogen atmosphere, followed by TLC (4:1 hexane: ethyl acetate). After 168 hours, the reaction was quenched using saturated $NaHCO_3$ solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried ($MgSO_4$) and filtered. The solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-20% ethyl acetate in hexane but the product was decomposed. The reaction was also followed by HPLC analysis (Chiralpak IA, 30 cm x 6mm column, hexane:iPrOH 95:5, 1.0 mL/min, T = 25°C); (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst: 74.6% conversion and 0.8% ee

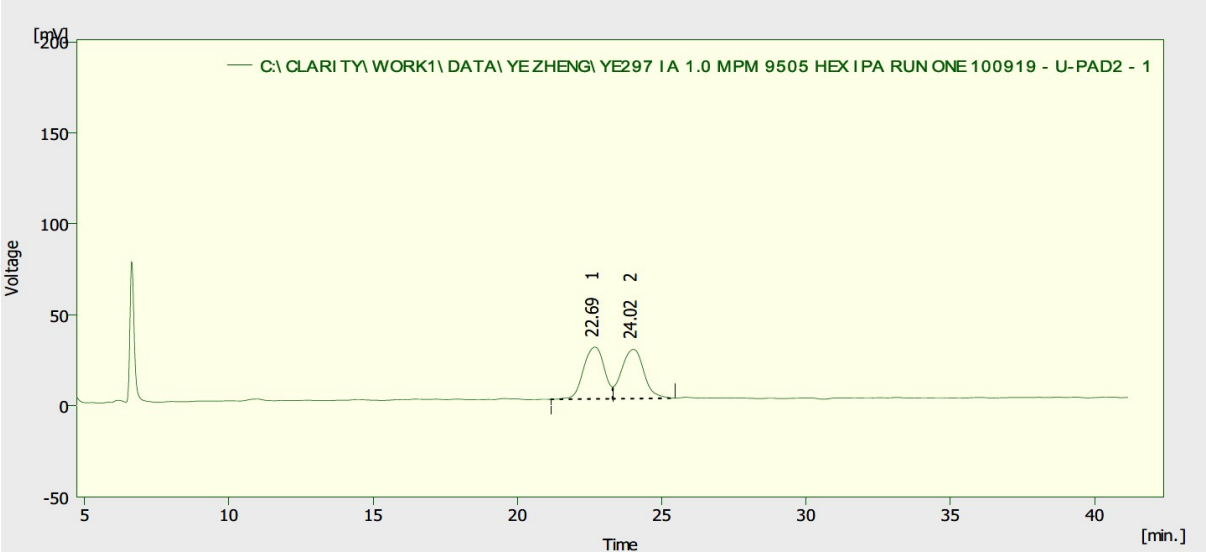
YZ293 (HPLC of racemic 2-(furan-2-yl(hydroxy)methyl)phenol) **8k**:



Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|ye zheng\|YE293 IA 1.0 mpm 9505 hex IPA run one 040919 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	22.864	4767.774	113.569	49.3	50.4	0.65	
2	24.268	4910.746	111.623	50.7	49.6	0.66	
	Total	9678.520	225.191	100.0	100.0		

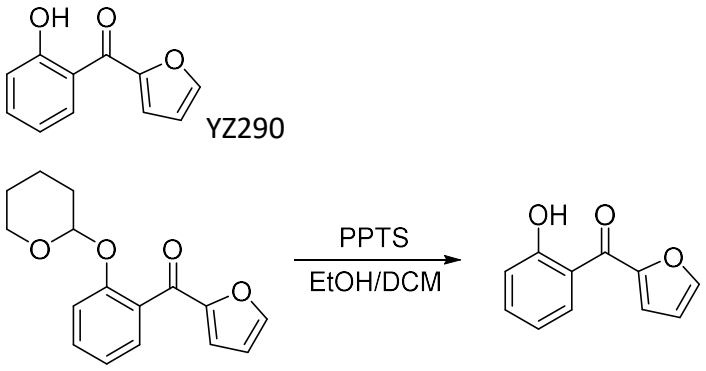
HPLC of **8k** after ATH of furan-2-yl(2-hydroxyphenyl)methanone **7k**, after 168 hours, 74.6% conversion, 0.8% ee).



Result Table (Uncal - C:|CLARITY|WORK1|DATA|YE ZHENG|YE297 IA 1.0 MPM 9505 HEX IPA RUN ONE 100919 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	22.688	1431.148	28.507	49.6	51.3	0.81	
2	24.016	1454.333	27.053	50.4	48.7	0.85	
	Total	2885.481	55.561	100.0	100.0		

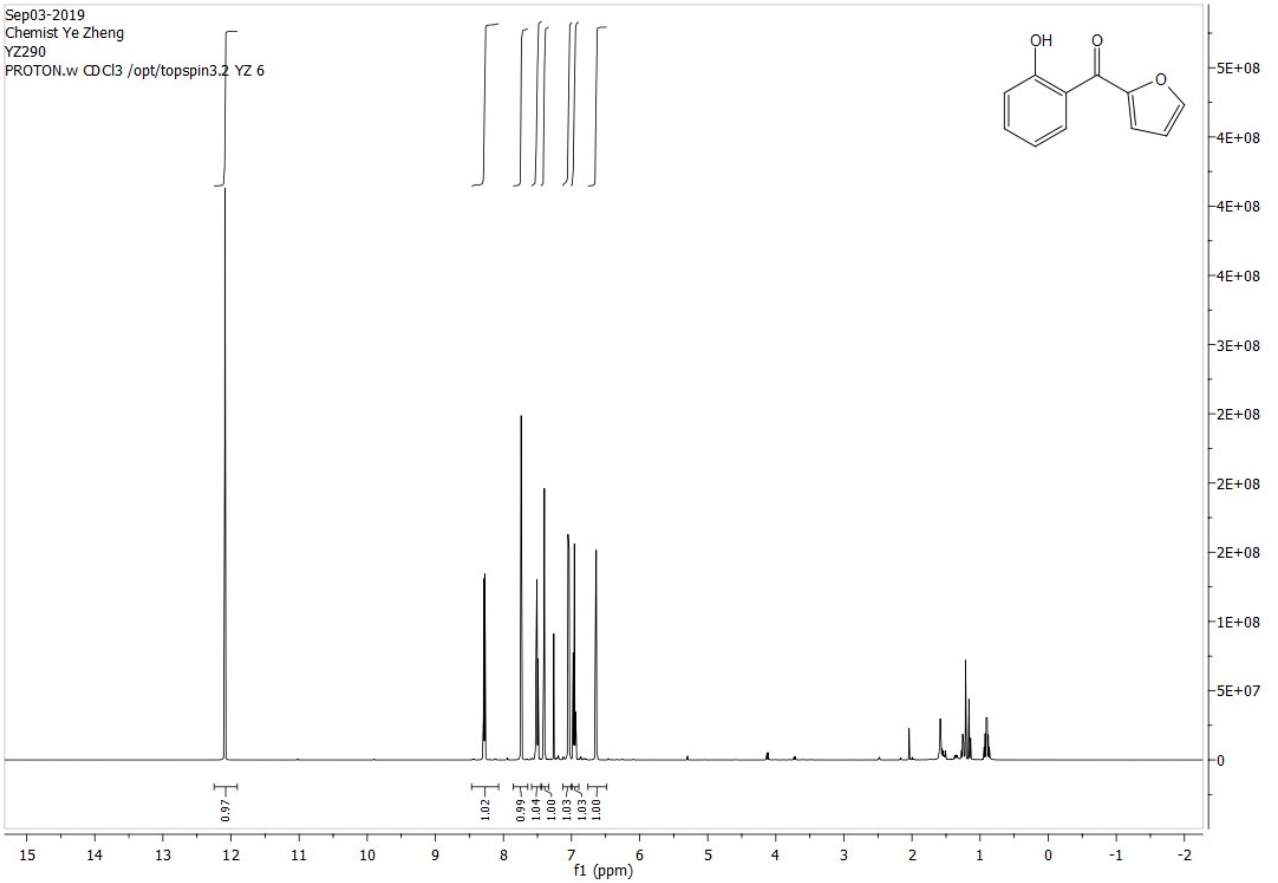
Furan-2-yl(2-hydroxyphenyl)methanone 7k.



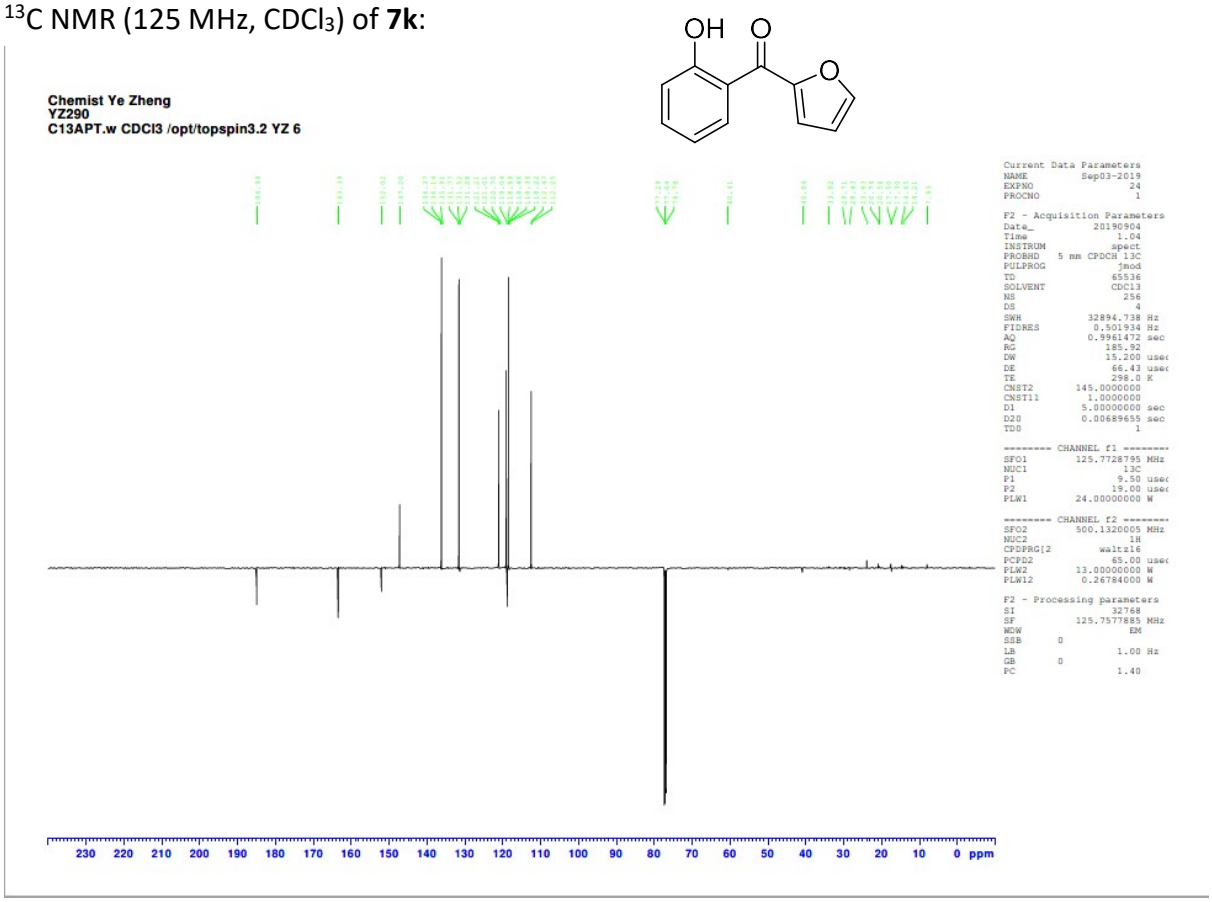
This compound is novel.

To a solution of furan-2-yl(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanone (350 mg, 1.29 mmol) in EtOH (6.5 mL)/DCM (3.25mL) was added Pyridinium *p*-Toluenesulfonate (PPTS) (48.7 mg, 0.194 mmol) at rt. The reaction mixture was left to stir under a nitrogen atmosphere overnight. TLC (9:1 hexane: EtOAc) after this time indicated full conversion. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-25% ethyl acetate in hexane to give furan-2-yl(2-hydroxyphenyl)methanone **7k** as a yellow oil (198.5 mg, 1.06 mmol, 82.1%). TLC: Rf ca 0.40 (9:1 hexane: EtOAc), strong UV and $KMnO_4$; HRMS: (found (ESI+): [M+Na]+, Calcd for $C_{11}H_8NaO_3$ 211.0362; Found 21.0366; 1.6 ppm error); ν_{max} 3135, 2961, 1621, 1587, 1558, 1459, 1220, 955, 750 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 12.09 (1H, s, OH), 8.28 (1H, d, *J* = 9.4, ArH), 7.74 (1H, s, ArH), 7.59-7.44 (1H, m, ArH), 7.40 (1H, d, *J* = 3.6, ArH), 7.04 (1H, d, *J* = 8.4, C_4H_3O), 6.96 (1H, t, *J* = 7.6, C_4H_3O), 6.64 (1H, dd, *J* = 3.5, 1.6, C_4H_3O) ppm; δ_C (125 MHz, $CDCl_3$) 184.9 (C), 163.4 (C), 152.0 (C), 147.2 (CH), 136.1 (CH), 131.5 (CH), 121.0 (CH), 119.0 (CH), 118.7 (C), 118.5 (CH), 112.5 (CH), 23.8 (CH) ppm; m/z (ES-API+) 211.1 (M^+ + 23, 100%).

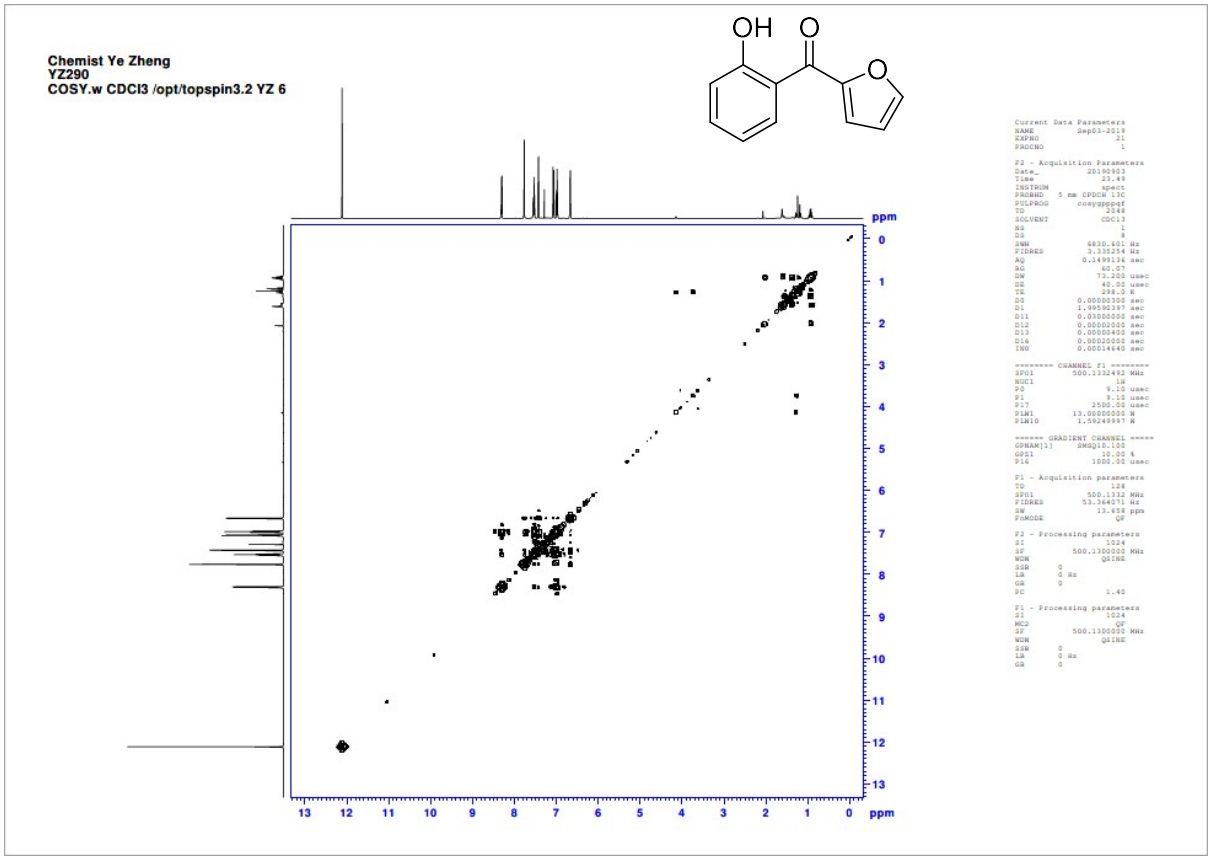
^{1}H NMR (500 MHz, $CDCl_3$) of **7k**:



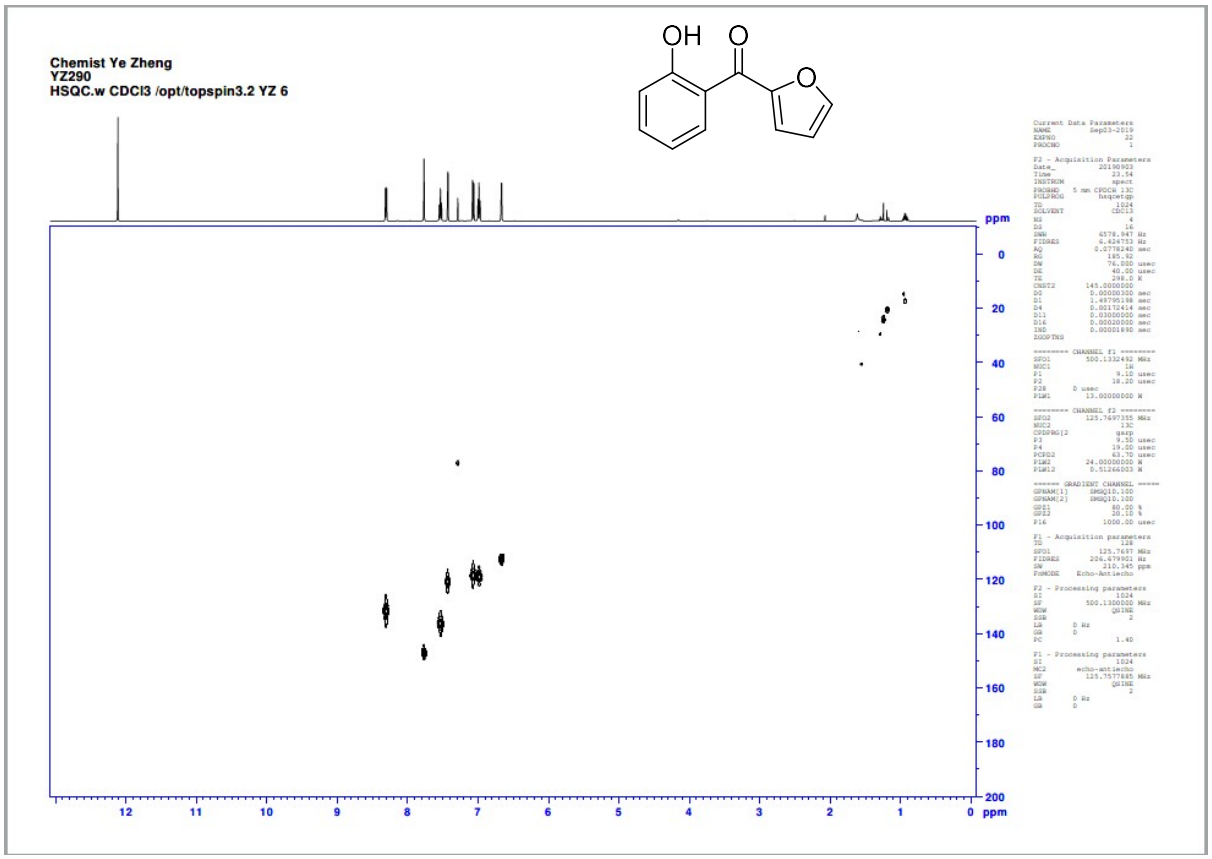
^{13}C NMR (125 MHz, $CDCl_3$) of **7k**:



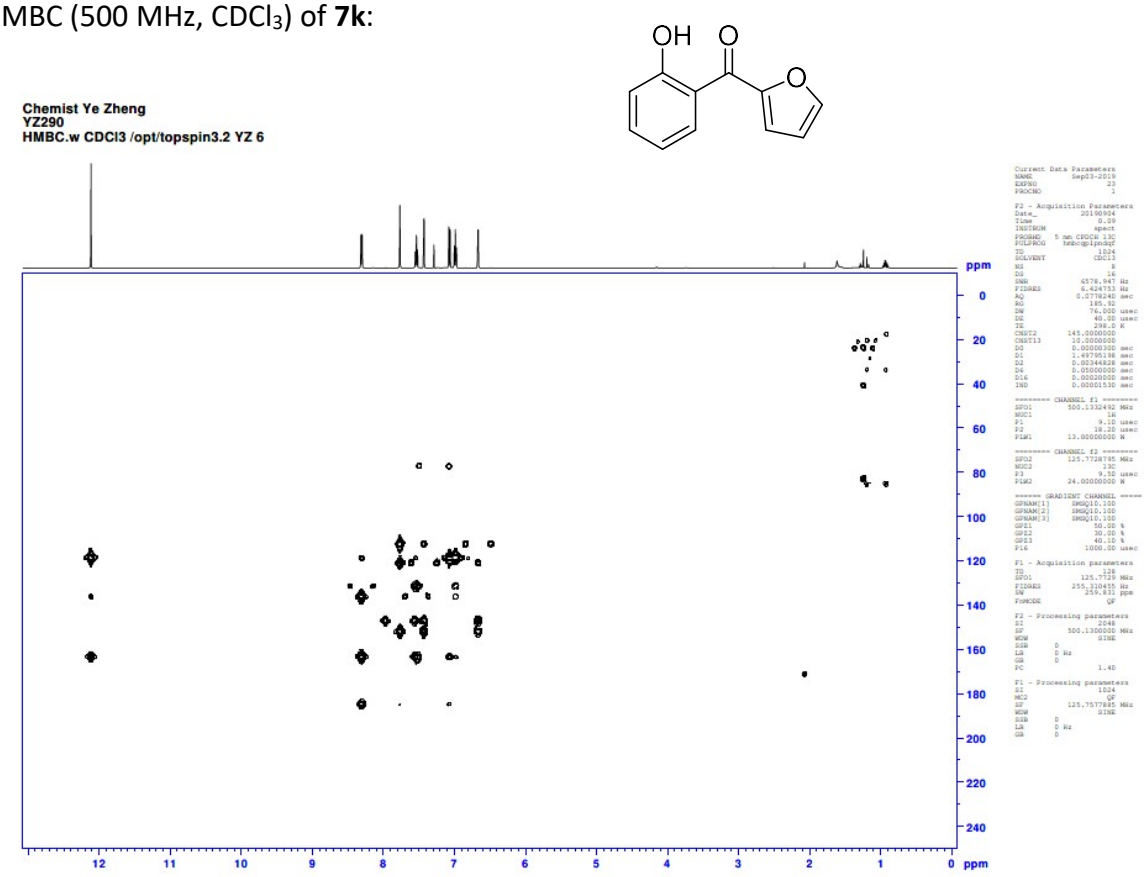
COSY (500 MHz, $CDCl_3$) of **7k**:



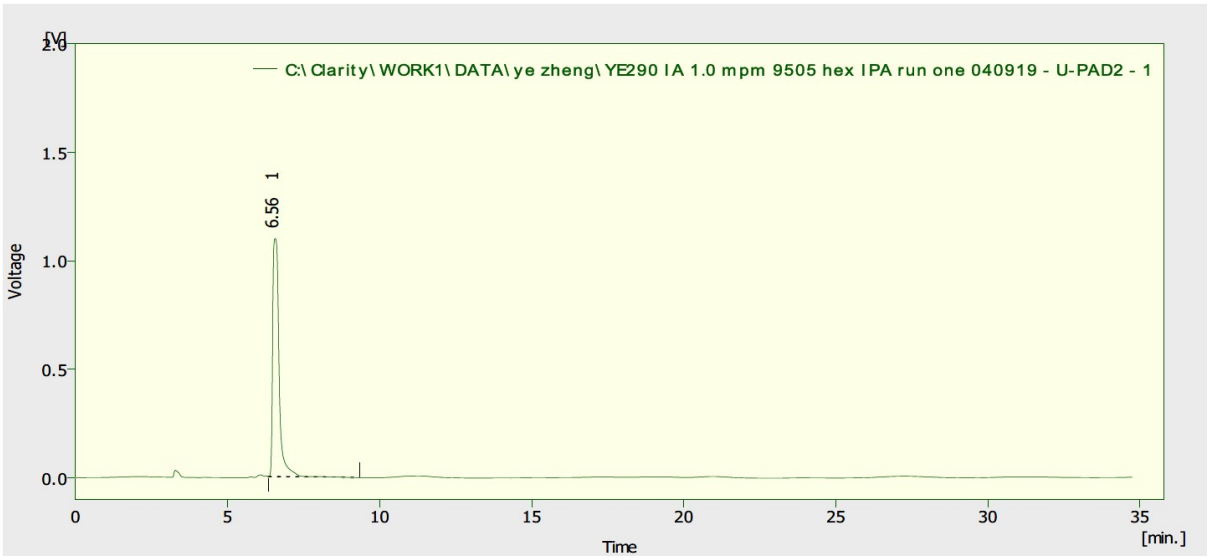
HSQC (500 MHz, $CDCl_3$) of **7k**:



HMBC (500 MHz, $CDCl_3$) of **7k**:



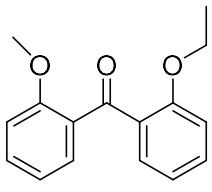
HPLC of furan-2-yl(2-hydroxyphenyl)methanone **7k**:



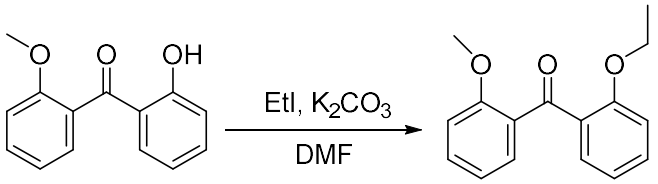
Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|ye zheng\|YE290 IA 1.0 mpm 9505 hex IPA run one 040919 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	6.564	16195.032	1099.608	100.0	100.0	0.21	
	Total	16195.032	1099.608	100.0	100.0		

(2-Ethoxyphenyl)(2-methoxyphenyl)methanone 7l.



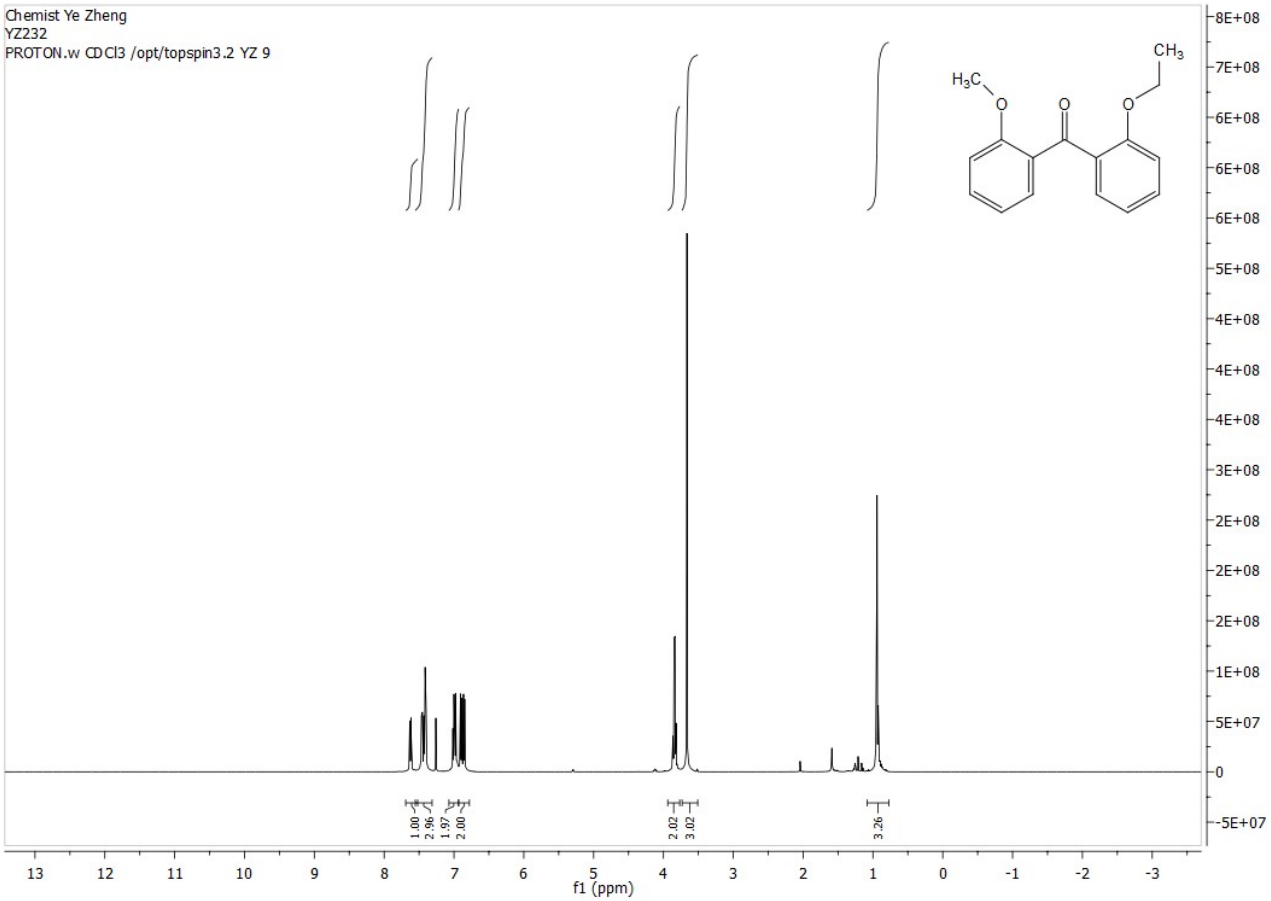
YZ232



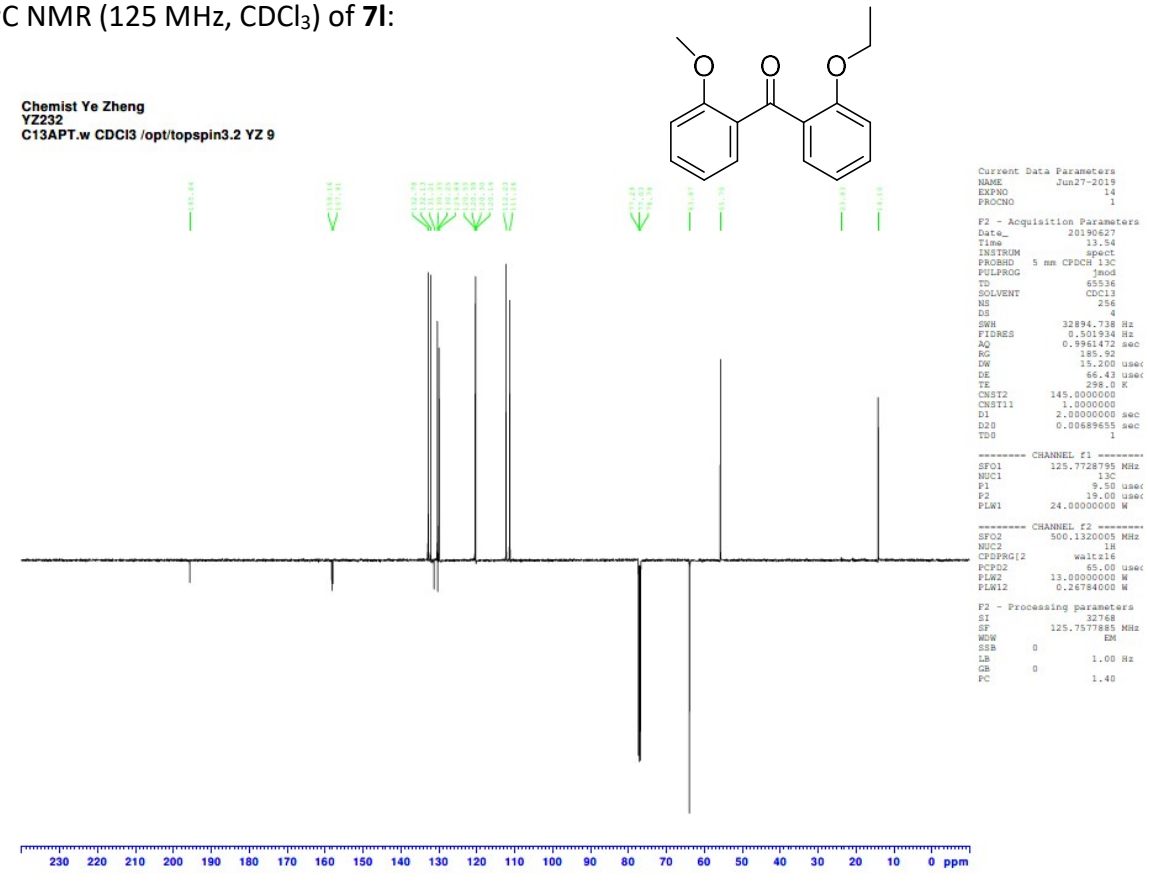
This compound is novel.

To a solution of (2-hydroxyphenyl)(2-methoxyphenyl)methanone **7c** (200 mg, 0.88 mmol) in DMF (8.8 mL) was added potassium carbonate (146 mg, 1.06 mmol) and iodomethane (137 mg, 0.88 mmol) at rt. The mixture was heated to 70 °C on a hot plate and stirred under a nitrogen atmosphere overnight. TLC (4:1 hexane: EtOAc) after this time indicated full conversion. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-20% ethyl acetate in hexane to give (2-ethoxyphenyl)(2-methoxyphenyl)methanone **7l** as a white solid (112.6 mg, 0.44 mmol, 50%). TLC: Rf ca 0.40 (4:1 hexane: EtOAc), strong UV and $KMnO_4$; HRMS: (found (ESI+): [M+Na]+, Calcd for $C_{16}H_{16}NaO_3$ 279.0989; Found 279.0992; 0.9 ppm error; ν_{max} 3073.83, 2980.82, 1650.68, 1596.45, 1484.84, 1307.50, 1247.35, 749.51 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.63-7.61 (1H, m, ArH), 7.47-7.40 (3H, m, ArH), 7.02-6.96 (2H, m, ArH), 6.91-6.85 (2H, m, ArH), 3.86-3.82 (2H, m, O*CH*$_2$$CH_3$), 3.66 (1H, s, OCH_3), 0.94 (3H, t, *J* = 7.0, OCH_2*CH*$_3$) ppm; δ_C (125 MHz, CDCl3) 195.6 (C), 158.2 (C), 157.9 (C), 132.8 (CH), 132.1 (CH), 131.2 (C), 130.4 (CH), 130.3 (C), 129.9 (CH), 120.4 (CH), 120.3 (CH), 112.2 (CH), 111.3 (CH), 63.9 (CH_2), 55.7 (CH_3), 14.1 (CH_3) ppm; m/z (ES-API+) 279.2 (M^+ + 23, 100%).
Enantiomeric excess and conversion determined by HPLC analysis (Chiralpak IC, 30 cm x 6mm column, hexane:iPrOH 9:1, 0.5 mL/min, T = 25°C) ketone 31.9 min, *R* isomer 18.5 min, *S* isomer 19.7 min.

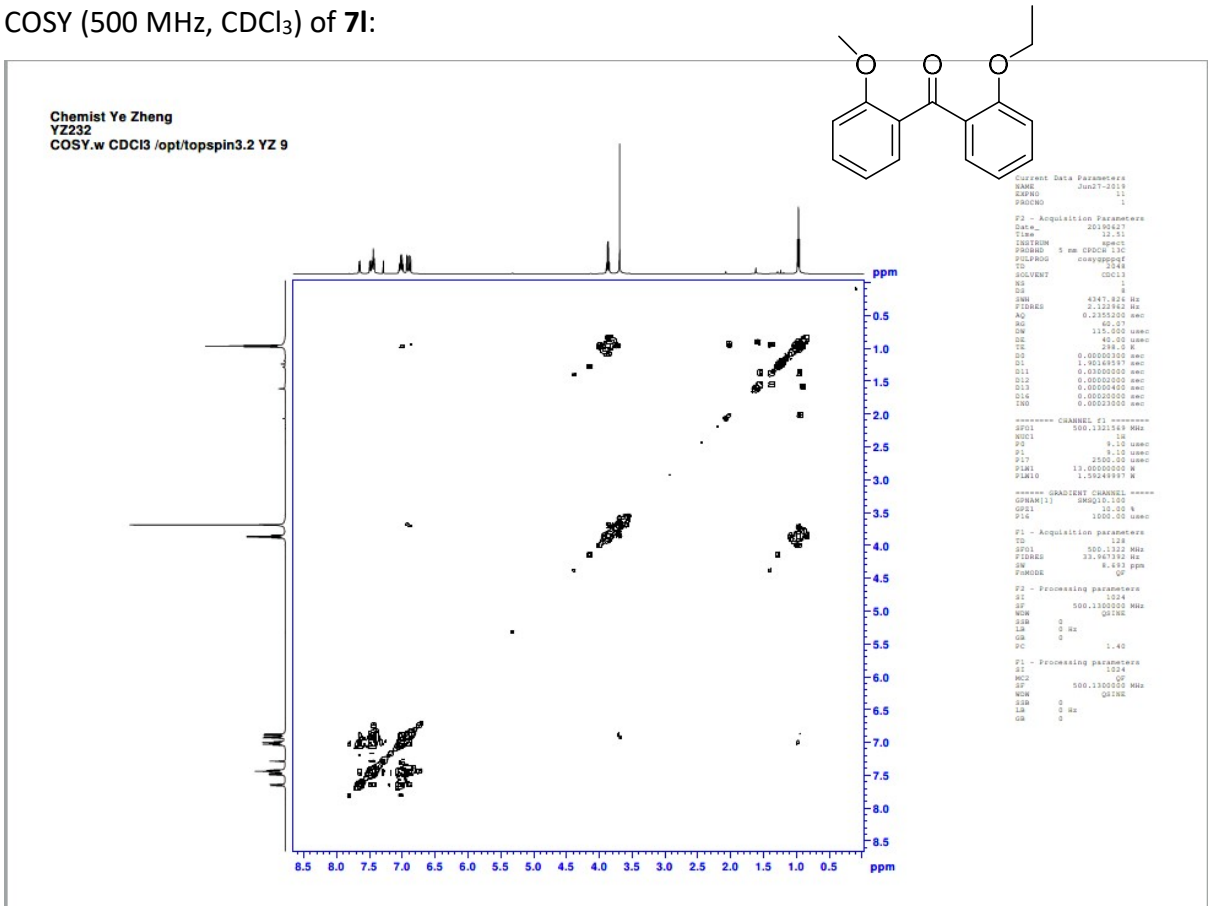
^{1}H NMR (500 MHz, $CDCl_3$) of **7l**:



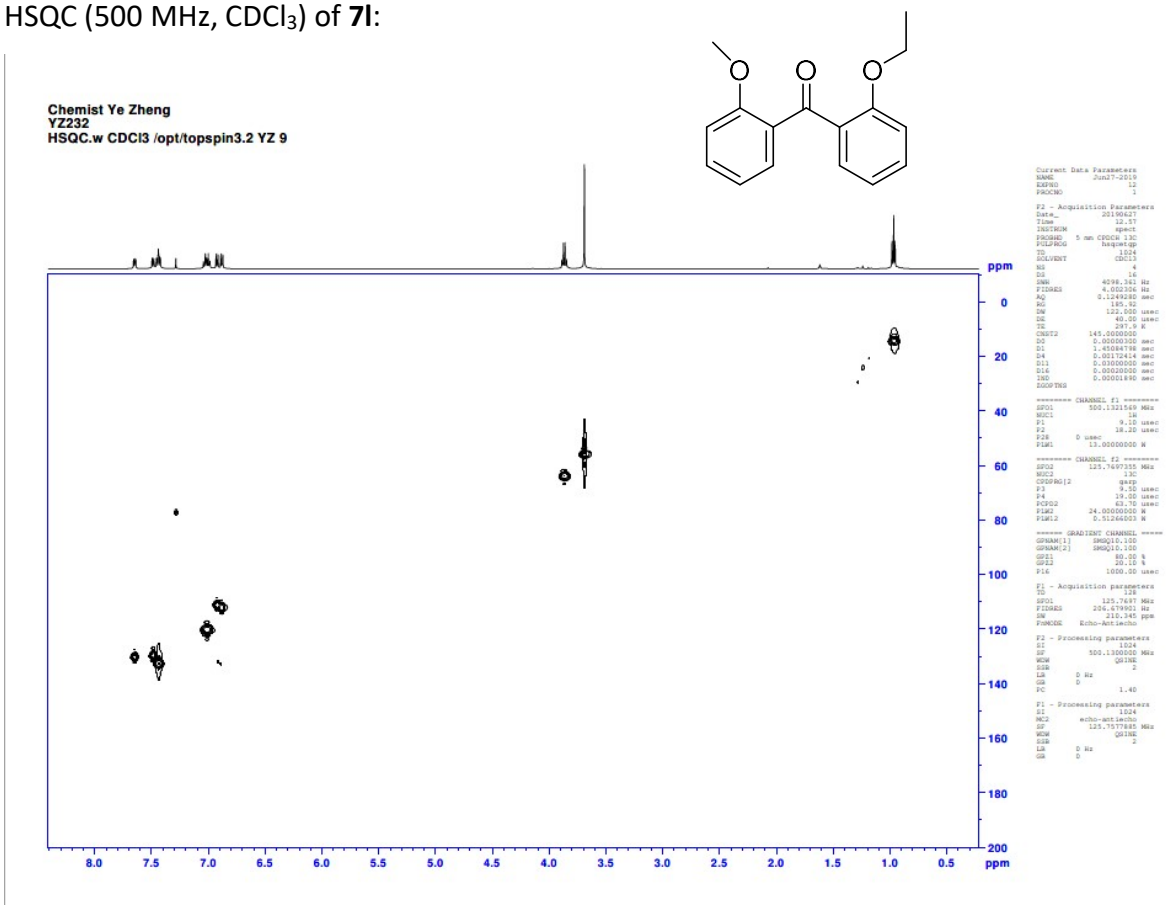
^{13}C NMR (125 MHz, $CDCl_3$) of **7l**:



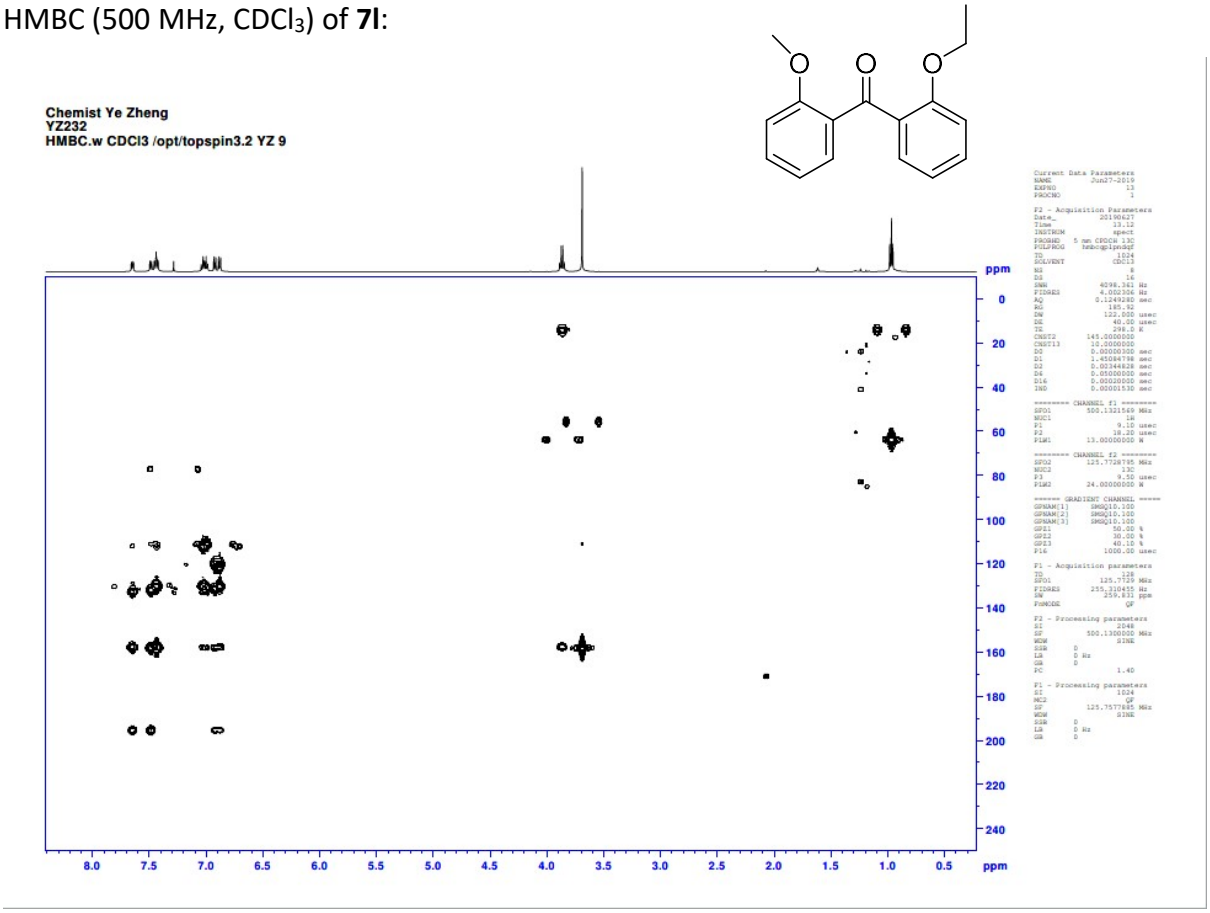
COSY (500 MHz, $CDCl_3$) of **7l**:



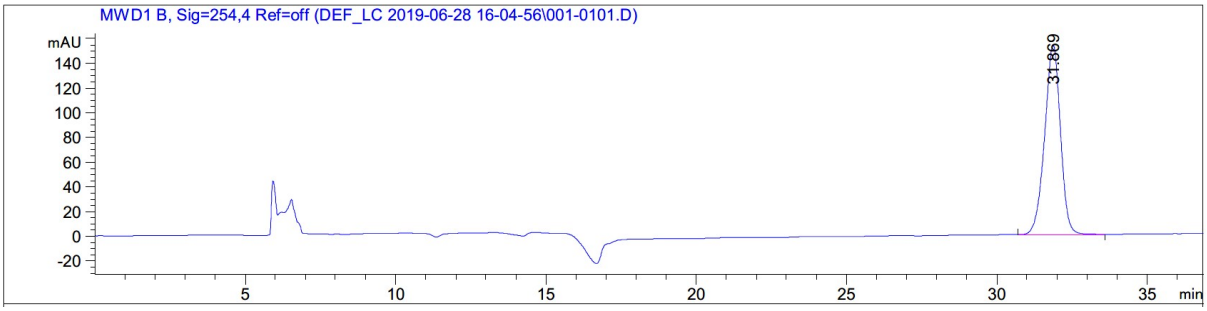
HSQC (500 MHz, $CDCl_3$) of **7l**:



HMBC (500 MHz, $CDCl_3$) of **7l**:



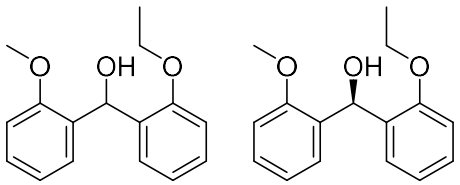
HPLC of (2-ethoxyphenyl)(2-methoxyphenyl)methanone **7l**:



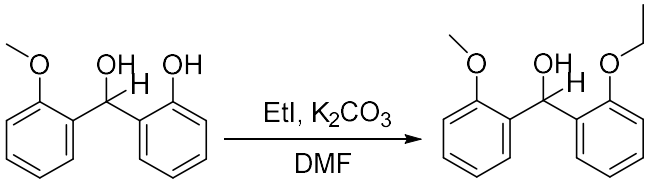
Signal 1: MWD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	31.869	BB	0.5559	5615.63525	153.83638	100.0000
Totals :				5615.63525	153.83638	

(2-Ethoxyphenyl)(2-methoxyphenyl)methanol 8l.



racemic: YZ225, Asymmetric: YZ236, YZ237, YZ384



This compound is novel.

To a solution of racemic 2-(hydroxyl-(2-methoxyphenyl)methyl)phenol **8c** (230 mg, 1.0 mmol) in DMF (10 mL) was added potassium carbonate (165.6 mg, 1.2 mmol) and iodoethane (156 mg, 1.0 mmol) at rt. The mixture was heated to 70 °C on a hot plate and stirred under a nitrogen atmosphere overnight. TLC (4:1 hexane: EtOAc) after this time indicated full conversion. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-20% ethyl acetate in hexane to give racemic (2-ethoxyphenyl)(2-methoxyphenyl)methanol **8l** as a colorless oil (69.6 mg, 0.27 mmol, 27%). TLC: Rf ca 0.30 (4:1 hexane: EtOAc), strong UV and $KMnO_4$; HRMS: (found (ESI+): [M+Na]+, Calcd for $C_{16}H_{18}NaO_3$ 281.1151; Found 281.1148; -1.1 ppm error; ν_{max} 3441 (br), 3034, 2977, 1600, 1488, 1237, 1026, 748 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.31 (1H, dd, *J* = 7.6, 1.6, ArH), 7.29-7.18 (3H, m, ArH), 7.06-6.76 (4H, m, ArH), 6.34 (1H, d, *J* = 5.7, Ar*CH*OH), 4.24-3.93 (2H, m, O*CH*$_2$$CH_3$), 3.82 (3H, s, OCH_3), 3.63 (1H, d, *J* = 5.8, ArCH*OH*), 1.38 (3H, t, *J* = 7.0, OCH_2*CH*$_3$) ppm; δ_C (125 MHz, $CDCl_3$) 156.8 (C), 156.2 (C), 131.3 (C), 131.1 (C), 128.4 (CH), 128.3 (CH), 128.0 (CH), 127.8 (CH), 120.5 (CH), 120.4 (CH), 111.4 (CH), 110.5 (CH), 67.8 (CH), 63.7 (CH_2), 55.4 (CH_3), 14.9 (CH_3) ppm; m/z (ES-API+) 281.2 (M^+ + 23, 100%).

Enantiomeric excess and conversion determined by HPLC analysis (Chiralpak IC, 30 cm x 6mm column, hexane:iPrOH 9:1, 0.5 mL/min, T = 25°C) ketone 31.9 min, *R* isomer 18.5 min, *S* isomer 19.7 min.

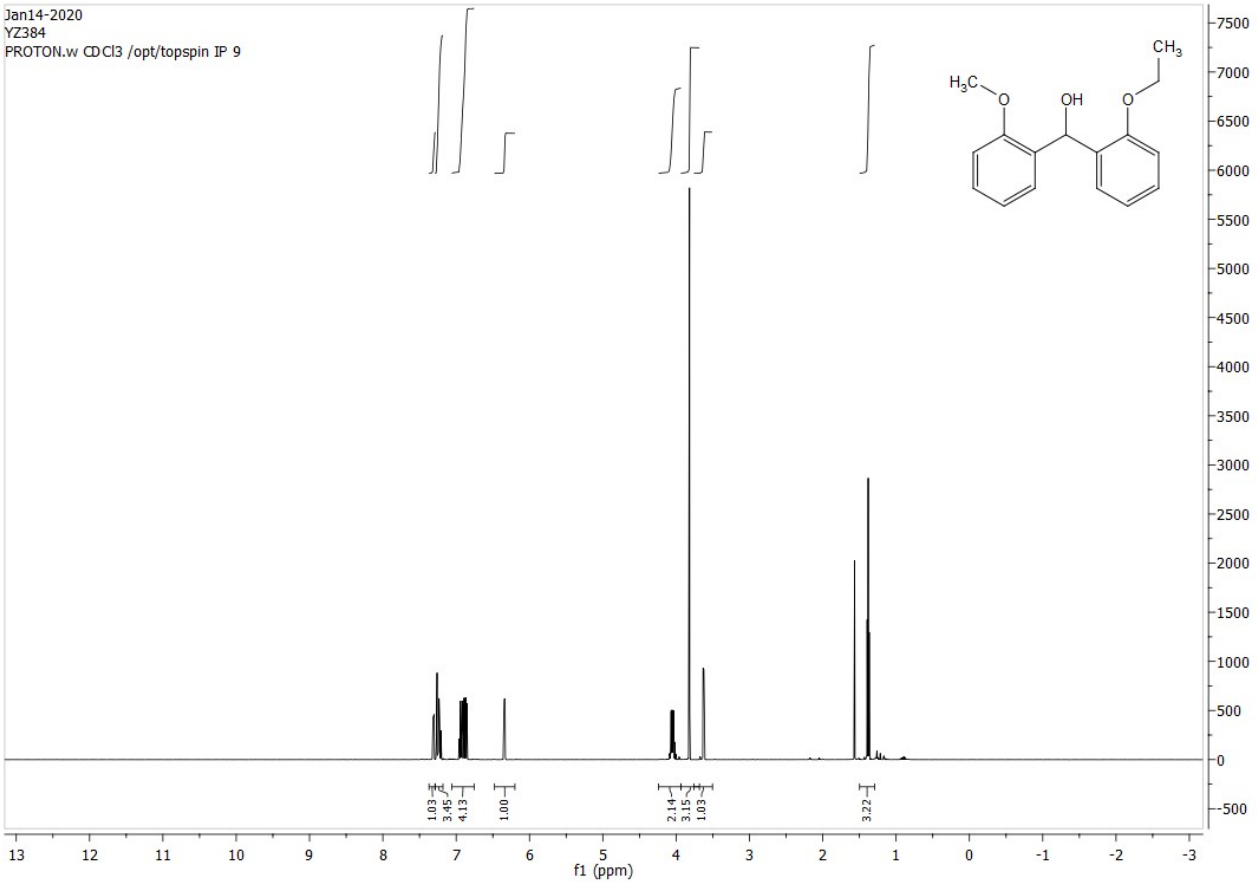
ATH of (2-ethoxyphenyl)(2-methoxyphenyl)methanone **7l** (YZ236).

Catalyst (*R,R*)-**2** (0.0020 mmol, 1 mol%) was added to FA: TEA (5:2 azeotropic mixture, 0.18 mL) at rt and the mixture was stirred under a nitrogen atmosphere for 10-15 minutes; after which a solution of (2-ethoxyphenyl)(2-methoxyphenyl)methanone **7l** (40 mg, 0.156 mmol) in DCM (0.25 mL) was added. The reaction mixture was stirrer under a nitrogen atmosphere, followed by TLC

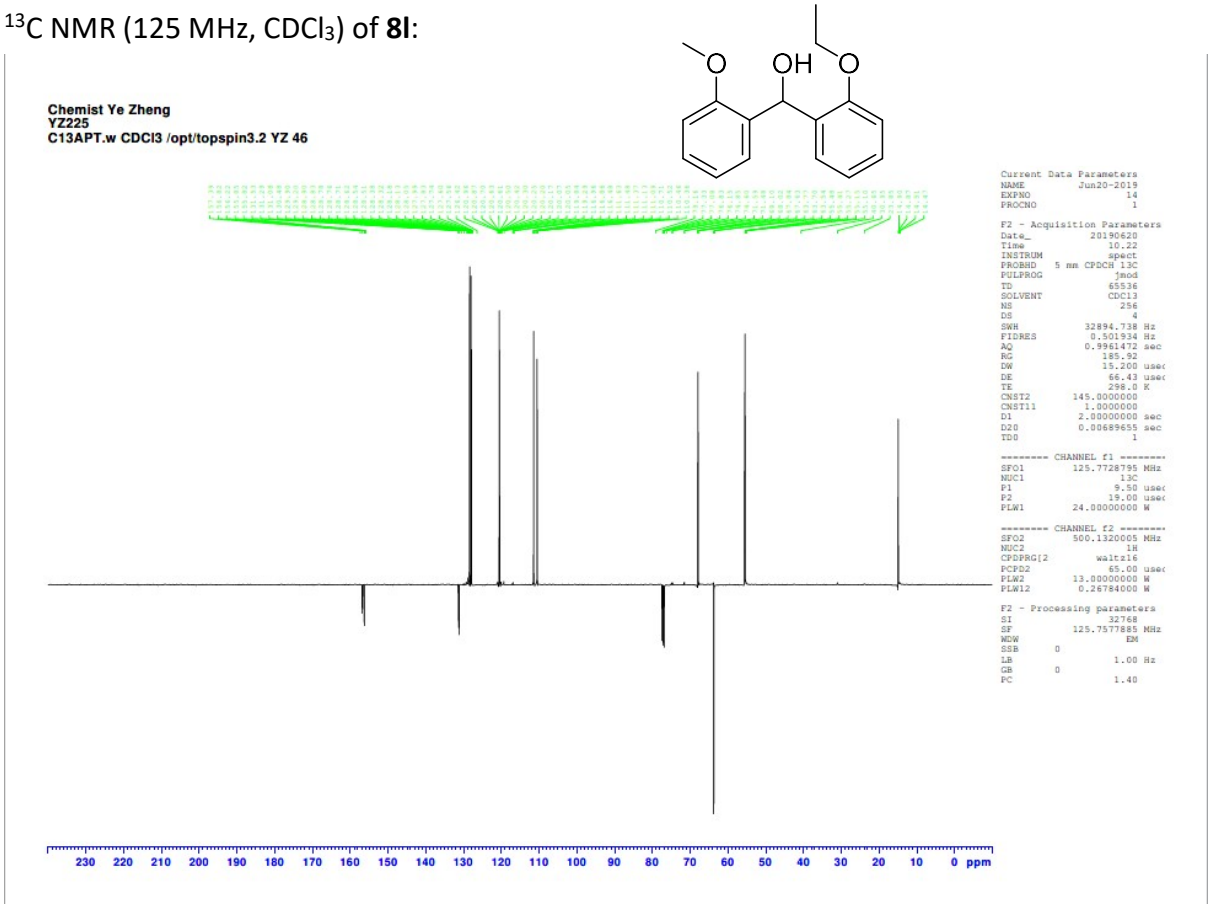
(4:1 hexane: ethyl acetate). After 168 hours, the reaction was quenched using saturated $NaHCO_3$ solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried ($MgSO_4$) and filtered. The solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 25-100% ethyl acetate in hexane to give 2-(hydroxy(phenyl)methyl)phenol **8l** (5.6 mg, 0.022 mmol, 13.9%; (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst example). The reaction was also followed by HPLC analysis (Chiralpak IC, 30 cm x 6mm column, hexane:iPrOH 9:1, 0.5 mL/min, T = 25°C); (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst: 52% conversion (HPLC calibration: 1:1 furan-2-yl(2-hydroxyphenyl)methanone : 2-(furan-2-yl(hydroxy)methyl)phenol gives 8.6:1 absorption at 254 nm) and 13.4% ee; *R* configuration.

Ethylation of **8c** (YZ237, 384): To a solution of asymmetric 2-(hydroxy(2-methoxyphenyl)methyl)phenol **8c** (92.7 mg, 0.403 mmol, 99.4% ee) in DMF (4.0 mL) was added potassium carbonate (66.8 mg, 0.484 mmol) and iodoethane (62.9 mg, 0.403 mmol) at rt. The mixture was stirred under a nitrogen atmosphere overnight. TLC (4:1 hexane: EtOAc) after this time indicated full conversion. The solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-20% ethyl acetate in hexane to give asymmetric (2-ethoxyphenyl)(2-methoxyphenyl)methanol **8l** as a colorless oil (59.7 mg, 0.231 mmol, 57.4%). $[\alpha]_D^{24}$ -10.3 (c 0.924 in $CHCl_3$) 97% ee (*R*).

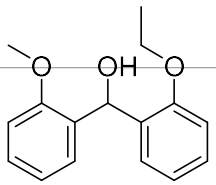
^{1}H NMR (500 MHz, $CDCl_3$) of **8l**:

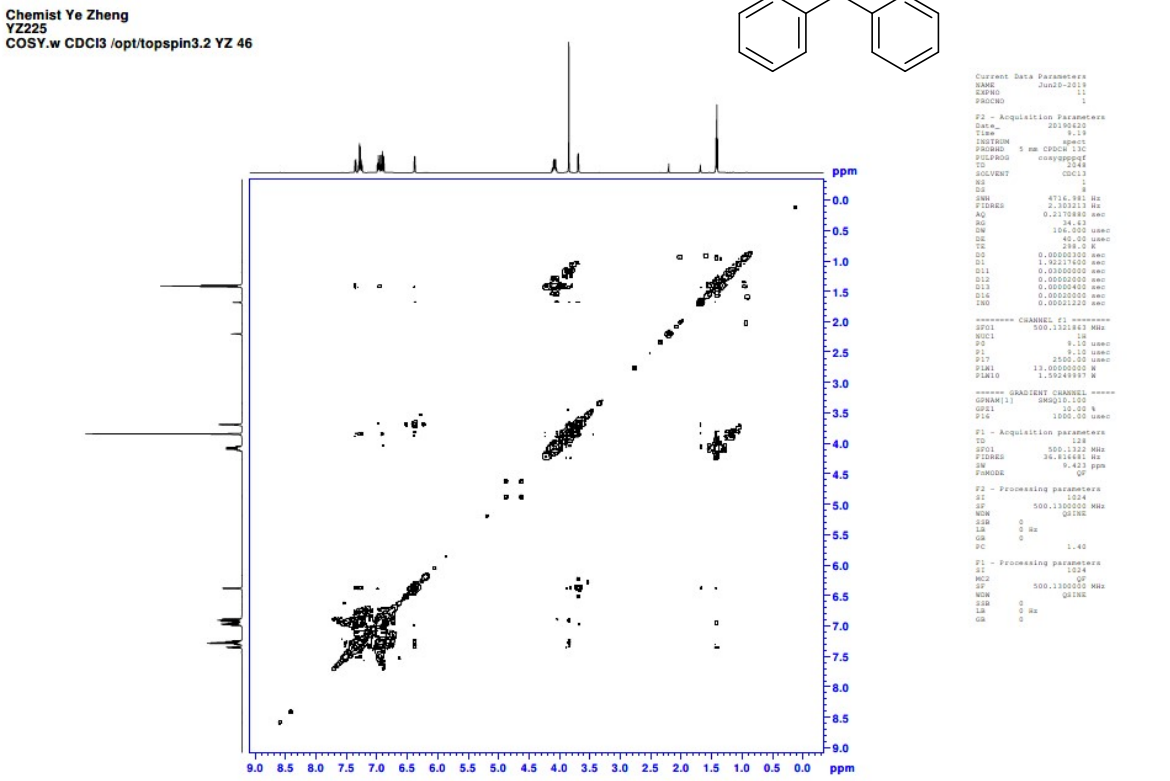


^{13}C NMR (125 MHz, $CDCl_3$) of **8l**:

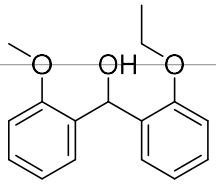


COSY (500 MHz, $CDCl_3$) of **8l**:

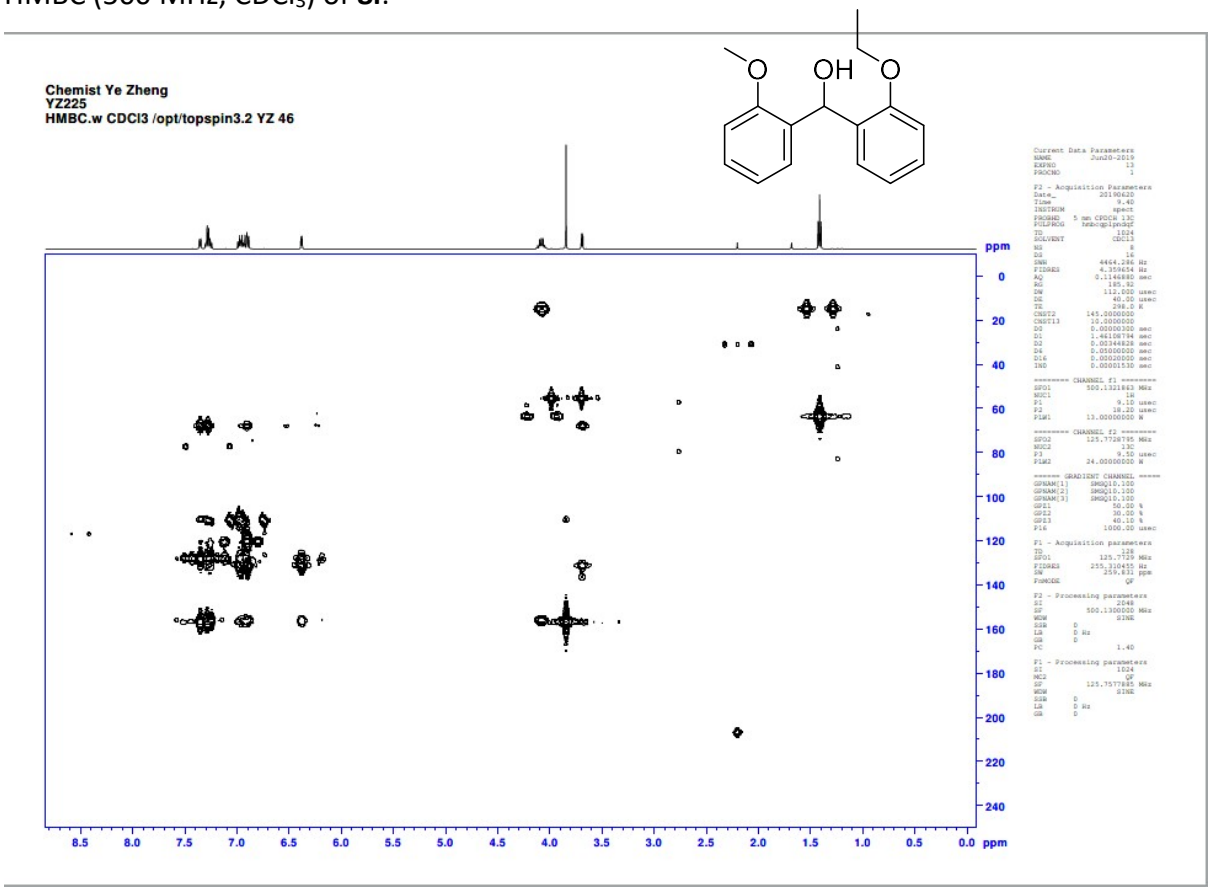




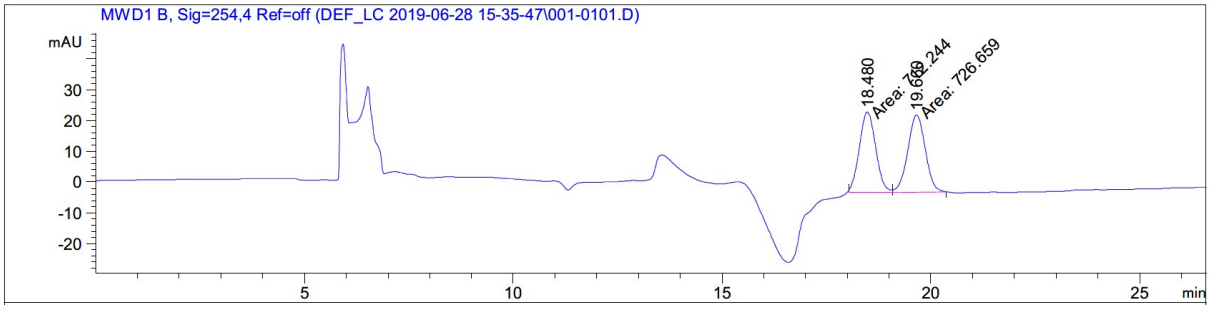
HSQC (500 MHz, $CDCl_3$) of **8l**:



HMBC (500 MHz, $CDCl_3$) of **8l**:



HPLC of racemic (2-ethoxyphenyl)(2-methoxyphenyl)methanol **8l**:

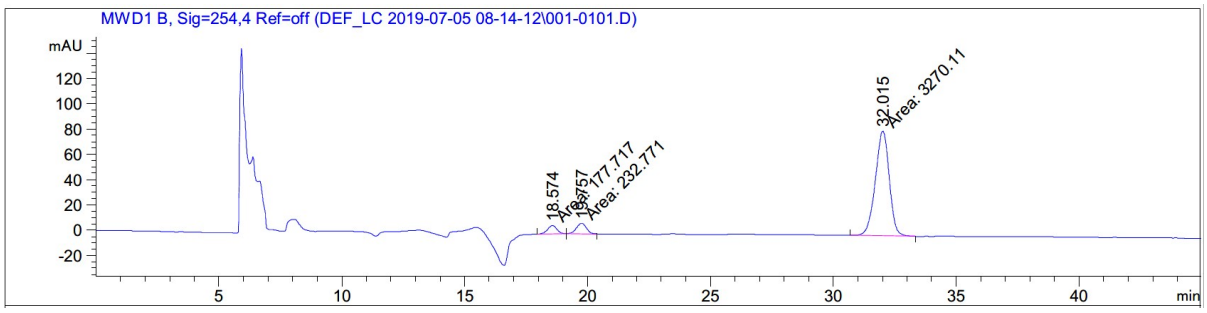


Signal 1: MWD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.480	MF	0.4541	712.24420	26.14005	49.4991
2	19.660	FM	0.4843	726.65863	25.00827	50.5009
Totals :				1438.90283	51.14832	

HPLC of **8l** after ATH of (2-ethoxyphenyl)(2-methoxyphenyl)methanone **7l**:

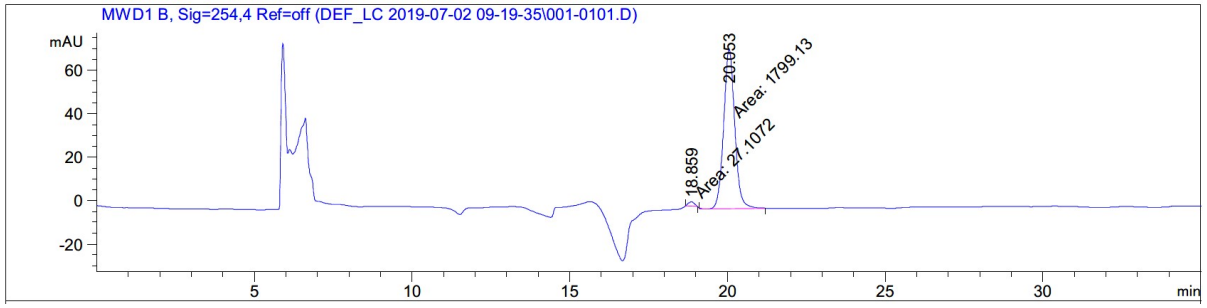
(*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst (after 168 hours, 52% conversion, 13.4% ee, *R* configuration).



Signal 1: MWD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.574	MM	0.4454	177.71739	6.64956	4.8285
2	19.757	MM	0.4684	232.77103	8.28239	6.3243
3	32.015	MM	0.6566	3270.11230	83.01182	88.8472
Totals :				3680.60072	97.94377	

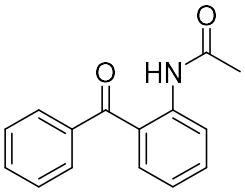
HPLC of **8l** (97% ee, *R* configuration) by ethylation of **8c** (YZ237).



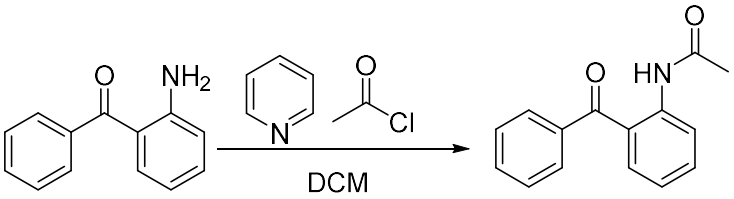
Signal 1: MWD1 B, Sig=254,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	18.859	MM	0.2281	27.10723	1.98048	1.4843
2	20.053	MM	0.4085	1799.13086	73.40620	98.5157
Totals :				1826.23808	75.38667	

N-(2-Benzoylphenyl)acetamide **7m.**



YZ222, YZ228

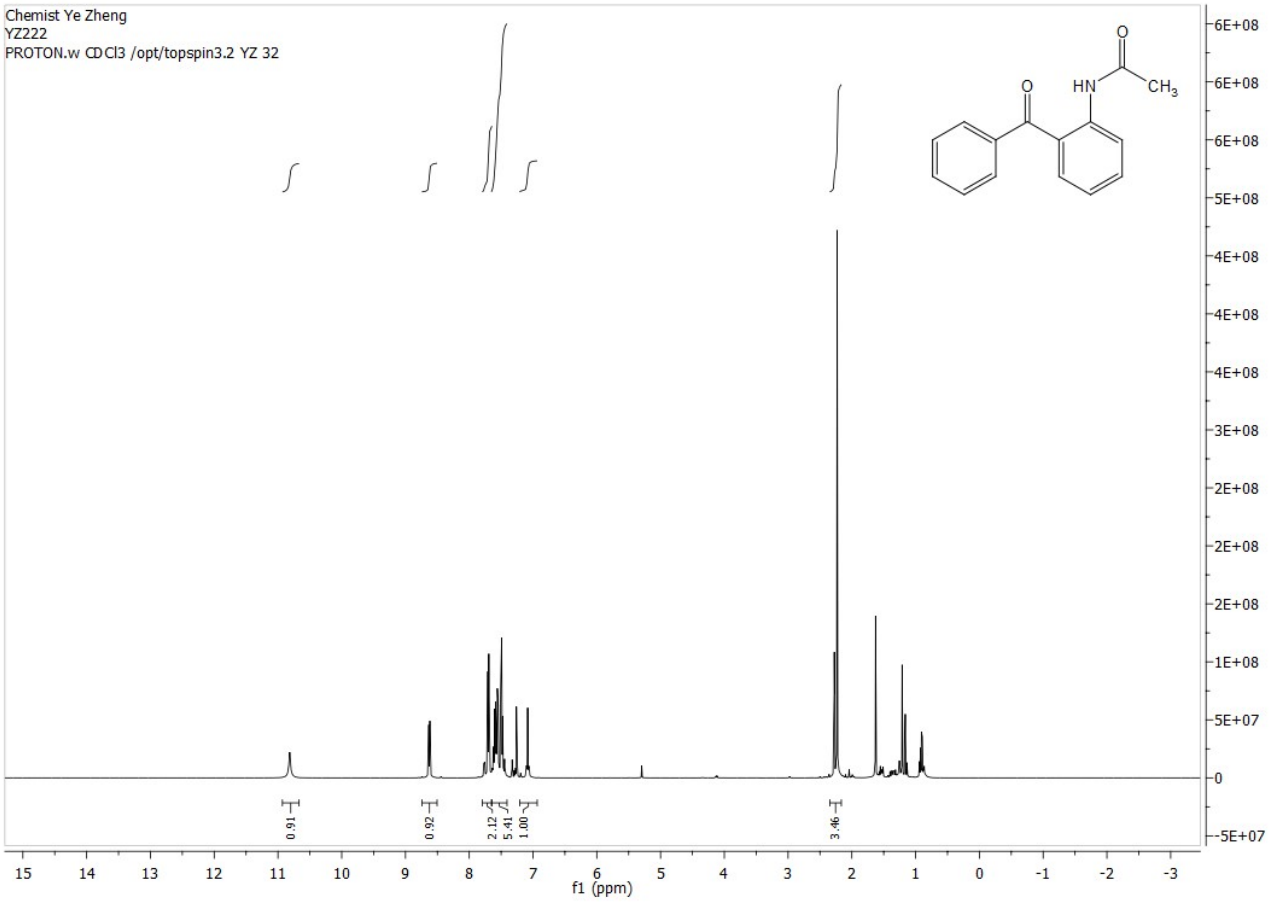


This compound has been reported and fully characterized.

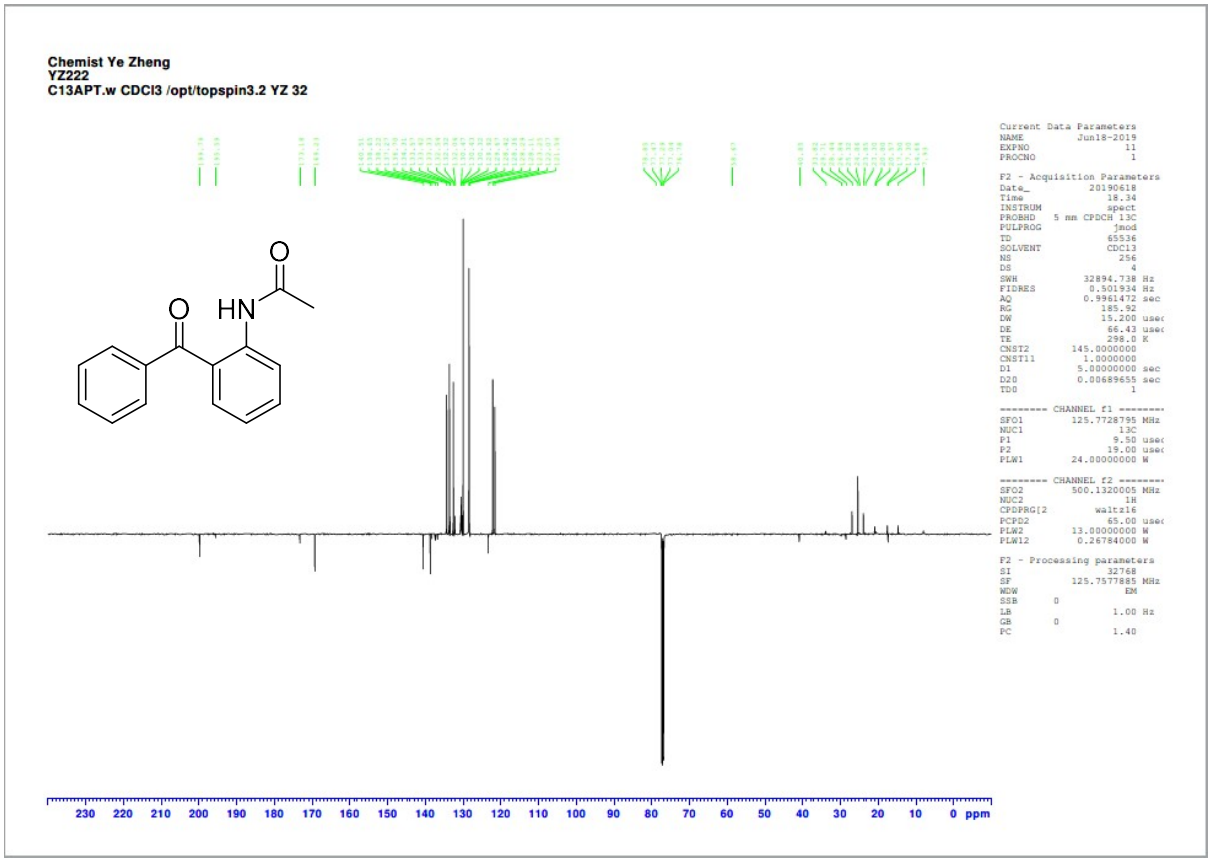
Reference: Wu, Y.; Li, B.; Mao, F.; Li, X.; Kwong, F. Y. *Org. Lett.* **2011**, *13*, 3258 – 3261.

To a solution of (2-aminophenyl)(phenyl)methanone **7s** (150 mg, 0.76 mmol) in DCM (3.8 mL) at 0°C was added pyridine (360 mg, 4.56 mmol) and acetyl chloride (71.6 mg, 0.91 mmol). The reaction mixture was left stirring under the nitrogen atmosphere and allowed to warm to rt. The reaction was followed by TLC (5:1 hexane: EtOAc). The mixture was quenched by 2M HCl solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 × 20 mL), and the combined organic layers were dried ($MgSO_4$) and filtered. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-40% ethyl acetate in hexane to give N-(2-benzoylphenyl)acetamide **7m** as a yellow oil (154.1 mg, 0.65 mmol, 85%). TLC: Rf ca 0.40 (5:1 hexane: EtOAc), strong UV and $KMnO_4$; δ_H (500 MHz, $CDCl_3$) 10.82 (1H, s, NH), 8.63 (1H, d, *J* = 8.4, ArH), 7.73 (2H, d, *J* = 7.3, ArH), 7.65-7.41 (5H, m, ArH), 7.08 (1H, t, *J* = 7.5, ArH), 2.23 (3H, s, CH_3) ppm; δ_C (125 MHz, $CDCl_3$) 199.8 (C), 169.2 (C), 140.5 (C), 134.3 (CH), 133.6 (CH), 132.5 (CH), 129.92 (CH), 128.4 (CH), 123.2 (C), 122.1 (CH), 121.5 (CH), 25.3 (CH_3) ppm. Data matched that reported.

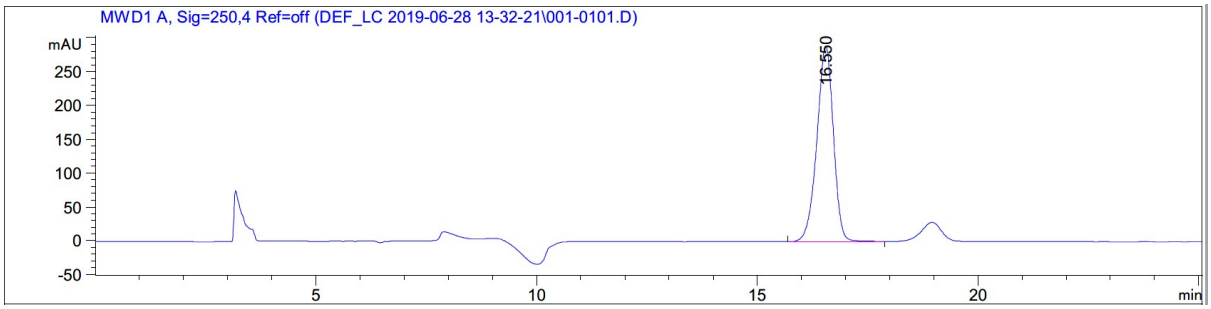
^{1}H NMR (500 MHz, $CDCl_3$) of **7m**:



^{13}C NMR (125 MHz, $CDCl_3$) of **7m**:



HPLC of N-(2-benzoylphenyl)acetamide **7m**:

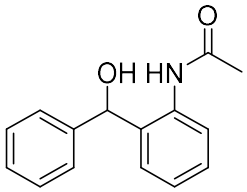


Signal 1: MWD1 A, Sig=250,4 Ref=off

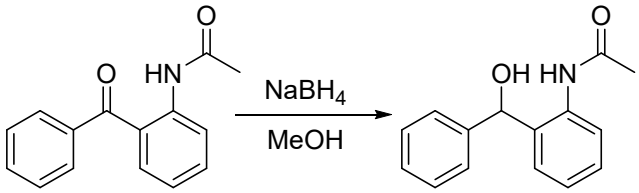
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	16.550	BB	0.3981	7533.63086	289.03574	100.0000
Totals :				7533.63086	289.03574	

Synthesis and characterisation of reaction products 8m-8s

N-(2-(hydroxy(phenyl)methyl)phenyl)acetamide 8m.



racemic: YZ224, Asymmetric: YZ230



This compound is novel.

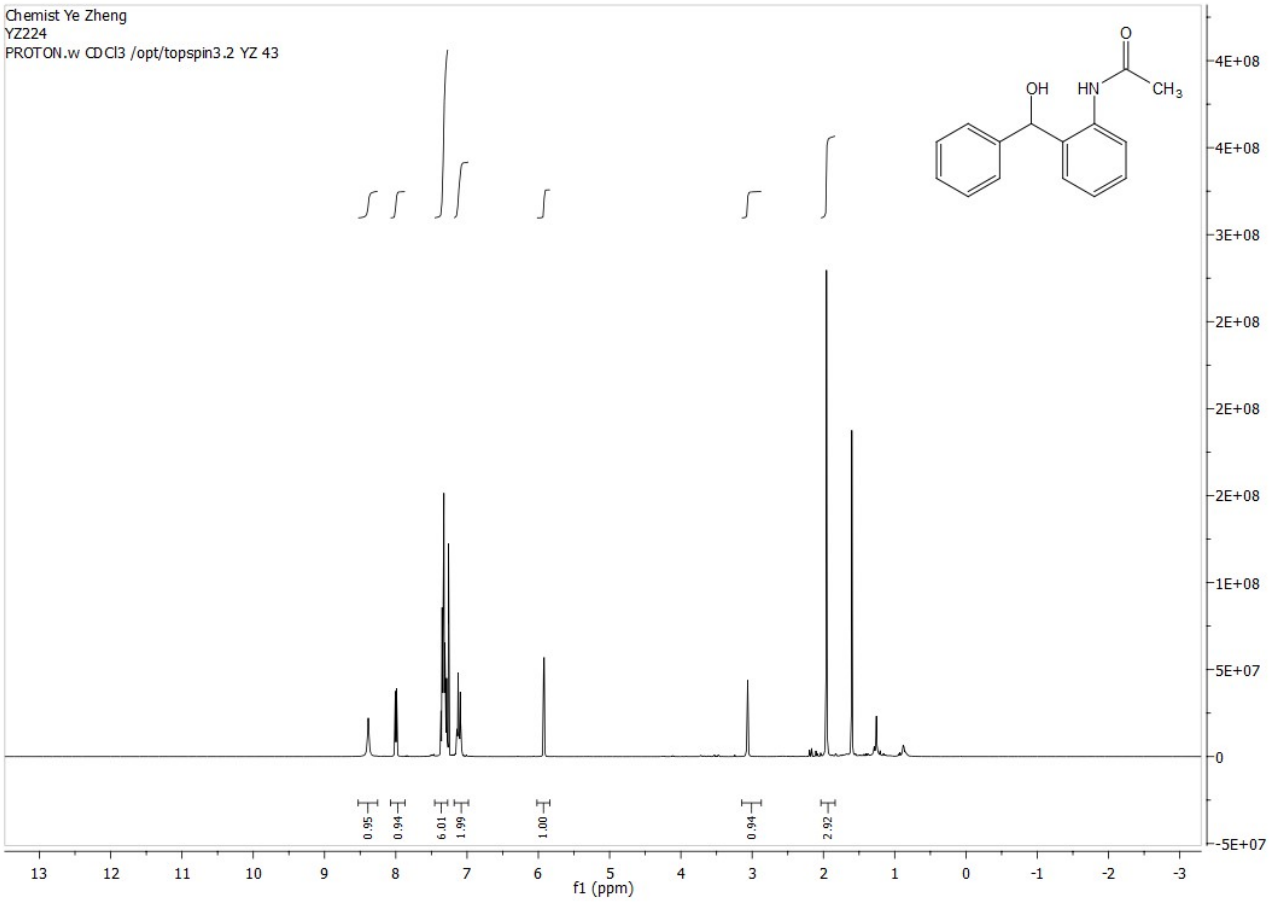
To a solution of (2-aminophenyl)(phenyl)methanone **7m** (100 mg, 0.42 mmol) in MeOH (3 mL) was added sodium borohydride (32 mg, 0.84 mmol). The reaction was stirred for 4 hours. TLC (9:1 hexane: EtOAc) after this time indicated full conversion. Distilled water (20 mL) was added, and the mixture was extracted with EtOAc (3 × 20ml), dried with $MgSO_4$, and the solvent was removed under vacuum to give crude product. The product was isolated via flash chromatography on silica eluted with 0-20% ethyl acetate in hexane to give (2-aminophenyl)(phenyl)methanol **8m** as a yellow oil (40.6 mg, 0.168 mmol, 40.3%). TLC: Rf ca 0.20 (9:1 hexane: EtOAc), strong UV and $KMnO_4$; HRMS: (found (ESI+): [M+Na]+, Calcd for $C_{15}H_{15}NNaO_2$ 264.0997; Found 264.0995; -0.9 ppm error; ν_{max} 3294 (br), 3061, 3029, 2927, 1664, 1587, 1522, 1493, 1303, 697 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 8.39 (1H, s, NH), 8.01 (1H, d, *J* = 8.0, ArH), 7.37-7.27 (6H, m, ArH), 7.14-7.08 (2H, m, ArH), 6.92 (1H, d, *J* = 3.0, Ar*CH*OH), 3.07 (1H, d, *J* = 3.0, OH), 1.96 (3H, s, CH_3) ppm; δ_C (125 MHz, $CDCl_3$) 168.6 (C), 141.3 (C), 136.6 (C), 132.3 (C), 129.0 (CH), 129.0 (CH), 128.7 (CH), 127.8 (CH), 126.0 (CH), 124.3 (CH), 113.6 (CH), 75.5 (CH), 29.7 (CH), 24.4 (CH_3) ppm; m/z (ES-API+) 264.2 (M^+ + 23, 100%). Enantiomeric excess and conversion determined by HPLC analysis (Chiralpak IC, 30 cm x 6mm column, hexane:iPrOH 9:1, 1.0 mL/min, T = 25°C) ketone 16.6 min, *R* and *S* isomers 22.4 min and 25.0 min, configuration was assigned by analogy.

(ATH of N-(2-benzoylphenyl)acetamide **7m** (YZ230).

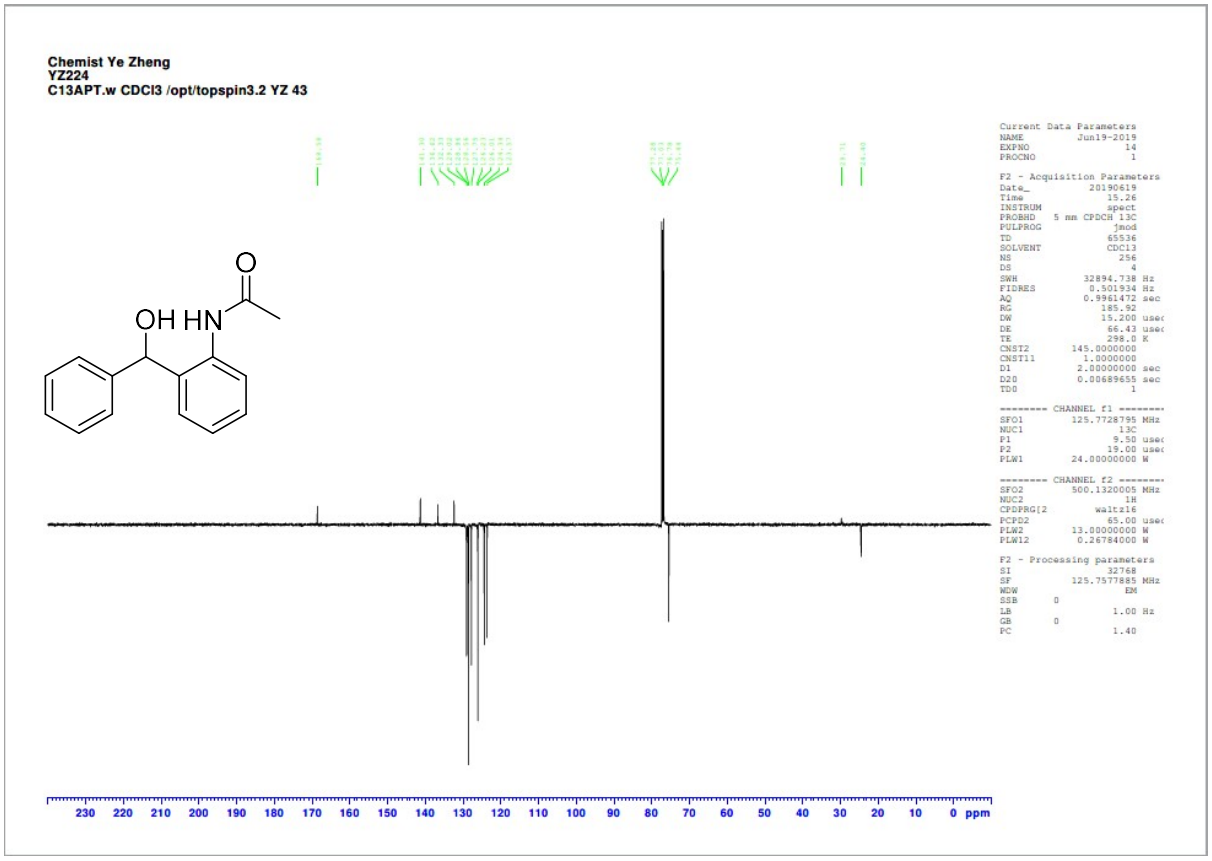
Catalyst (*R,R*)-**2** (0.0023 mmol, 1mol%) was added to the FA: TEA (5:2 azeotropic mixture, 0.18 mL) at rt and the mixture was stirred under a nitrogen atmosphere for 10-15 minutes; after which a solution of N-(2-benzoylphenyl)acetamide **7m** (40 mg, 0.167 mmol) in DCM (0.25 mL) was added. The reaction mixture was stirred under a nitrogen atmosphere, followed by TLC (9:1 hexane:

EtOAc). After 168 hours, the reaction was quenched using saturated $NaHCO_3$ solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried ($MgSO_4$) and filtered. The solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-20% ethyl acetate in hexane to give N-(2-(hydroxy(phenyl)methyl)phenyl)acetamide **8m** (24.6 mg, 0.102 mmol, 60.9%; (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst example). The reaction was also followed by HPLC (Chiralpak IC, 30 cm x 6mm column, hexane:iPrOH 9:1, 1.0 mL/min, T = 25°C); (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst: 95% conversion (HPLC calibration: 1:1 N-(2-benzoylphenyl)acetamide : N-(2-(hydroxy(phenyl)methyl)phenyl)acetamide gives 1.4:1 absorption at 254 nm); $[\alpha]_D^{24}$ -35.01 (c 0.692 in $CHCl_3$) 61.4% ee.

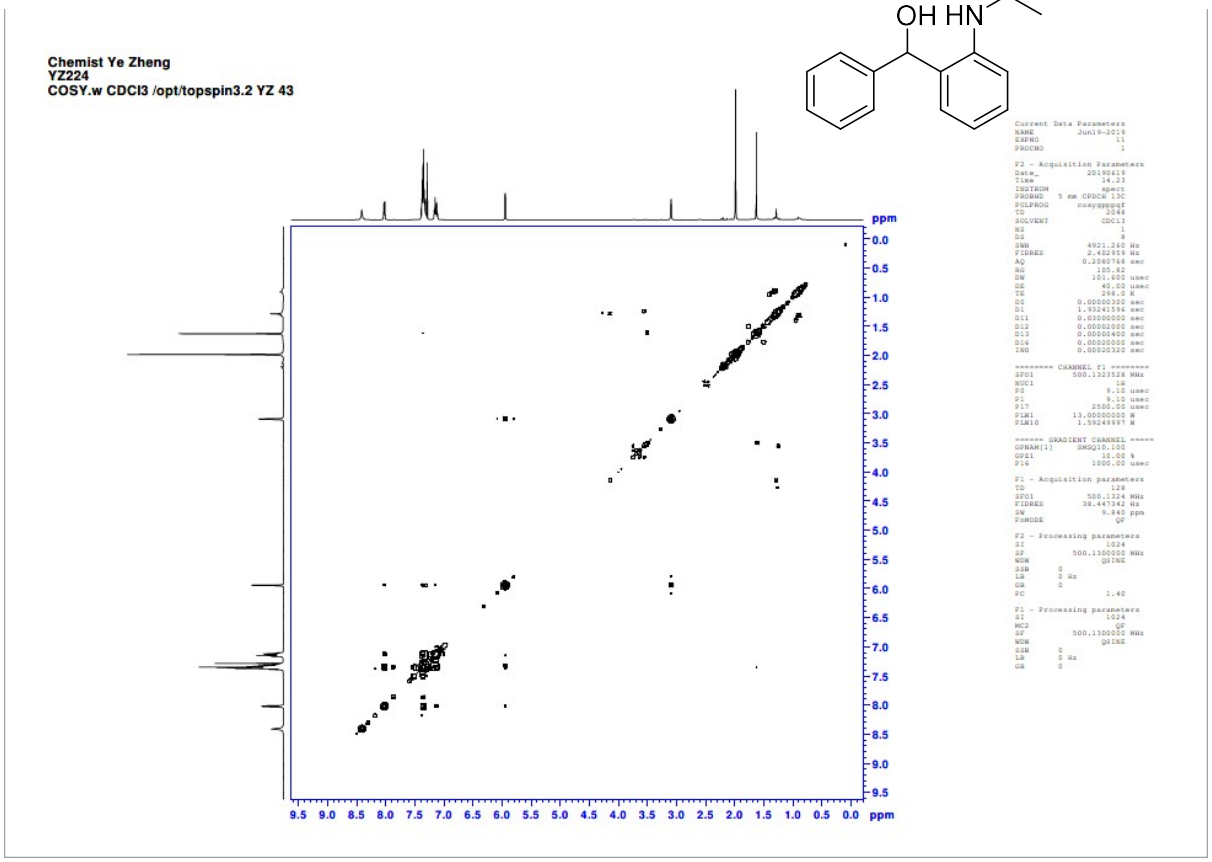
^1H NMR (500 MHz, $CDCl_3$) of **8m**:



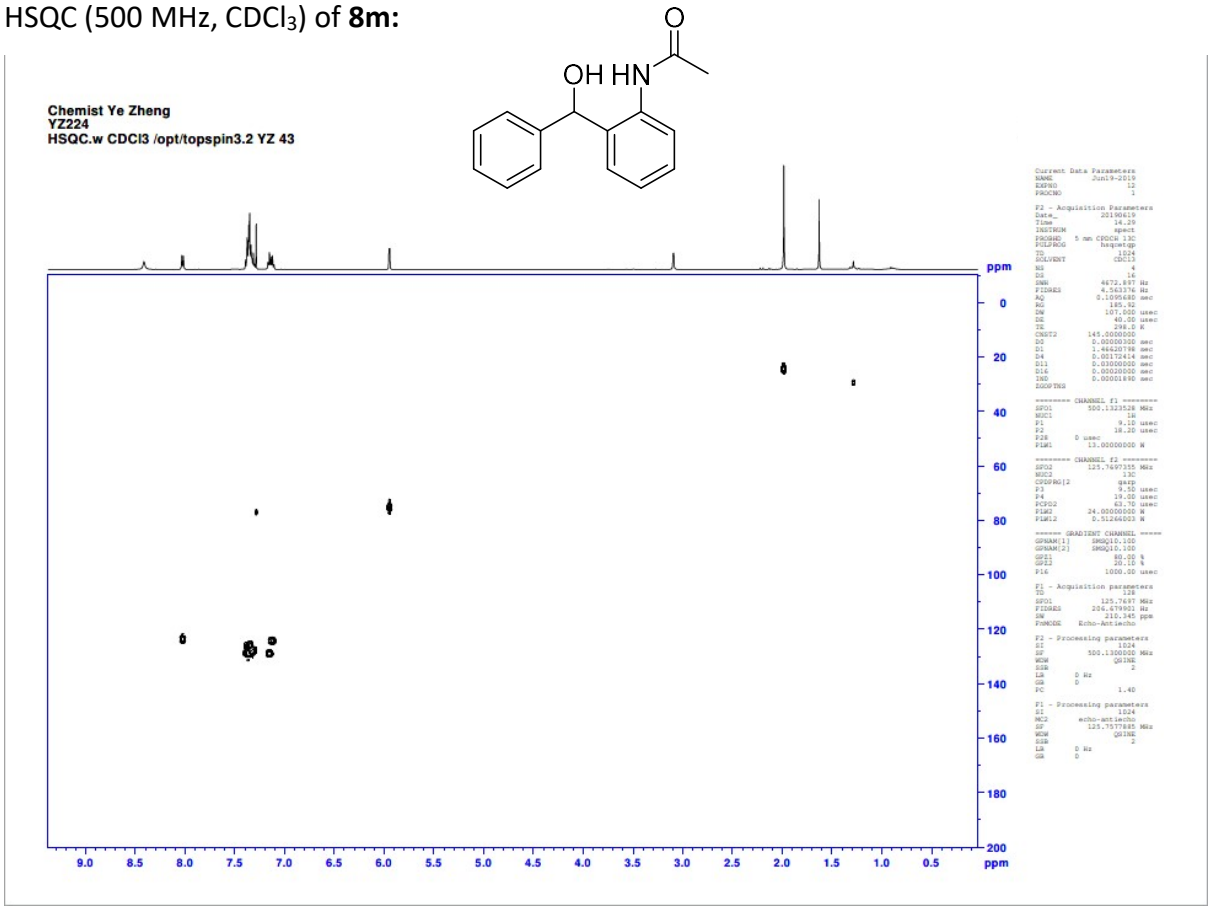
^{13}C NMR (125 MHz, $CDCl_3$) of **8m**:



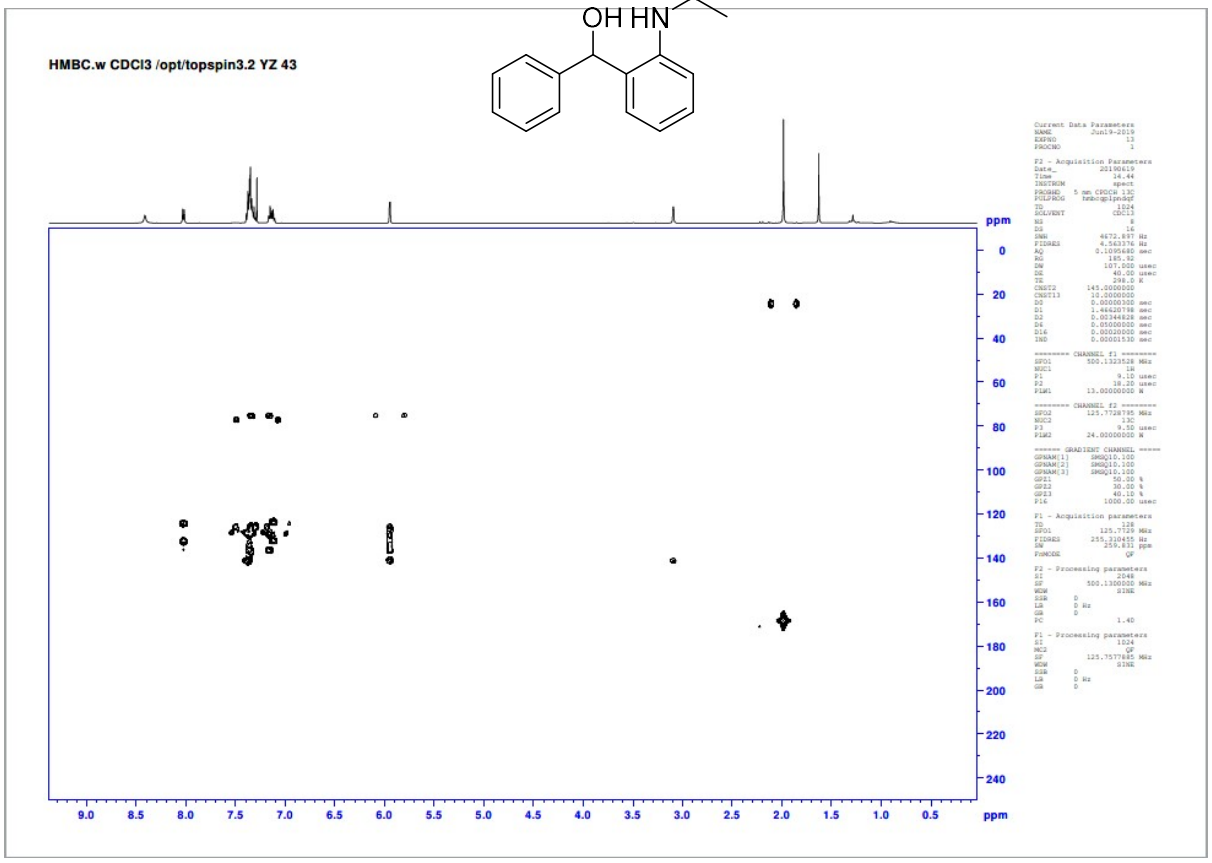
COSY (500 MHz, $CDCl_3$) of **8m**:



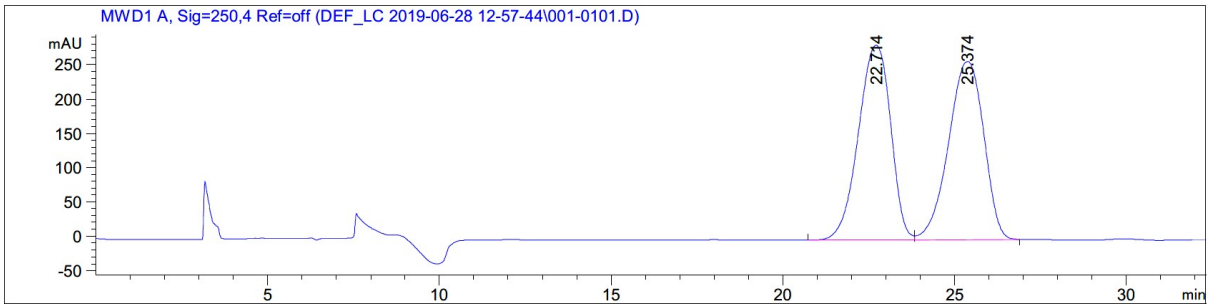
HSQC (500 MHz, $CDCl_3$) of **8m:**



HMBC (500 MHz, $CDCl_3$) of **8m**:



HPLC of racemic N-(2-(hydroxy(phenyl)methyl)phenyl)acetamide **8m**:

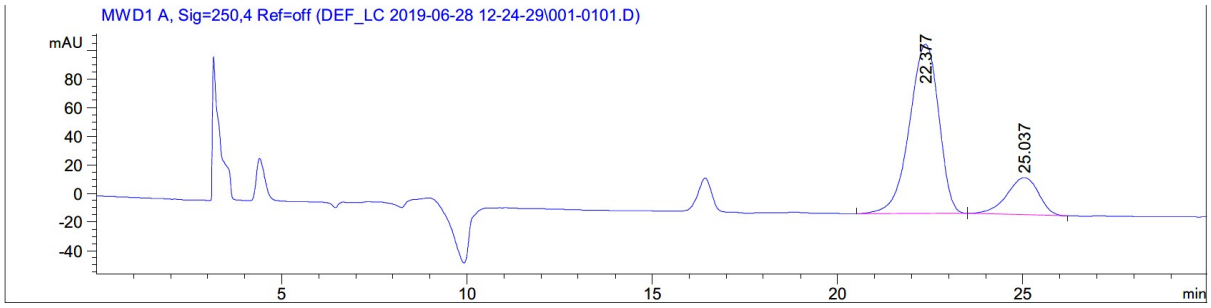


Signal 1: MWD1 A, Sig=250,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.714	BV	1.0417	1.85705e4	283.71063	50.0504
2	25.374	VB	1.1403	1.85331e4	259.78528	49.9496
Totals :				3.71036e4	543.49591	

HPLC of **8m** after ATH of N-(2-benzoylphenyl)acetamide **7m**:

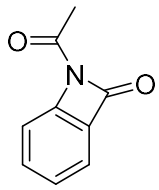
(*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst (after 168 hours, 95% conversion, 61.4% ee)



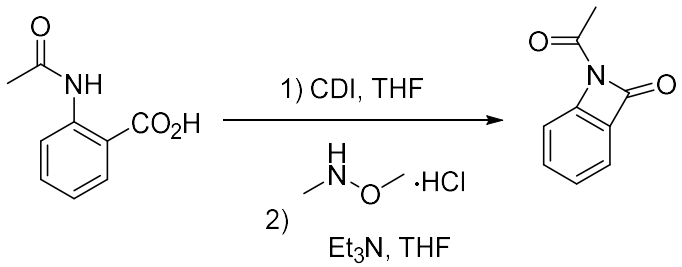
Signal 1: MWD1 A, Sig=250,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	22.377	BB	0.8732	6493.63965	118.14976	80.7207
2	25.037	BB	0.9190	1550.94214	25.95982	19.2793
Totals :				8044.58179	144.10958	

1-Acetylbenzo[b]azet-2(1H)-one.



YZ338

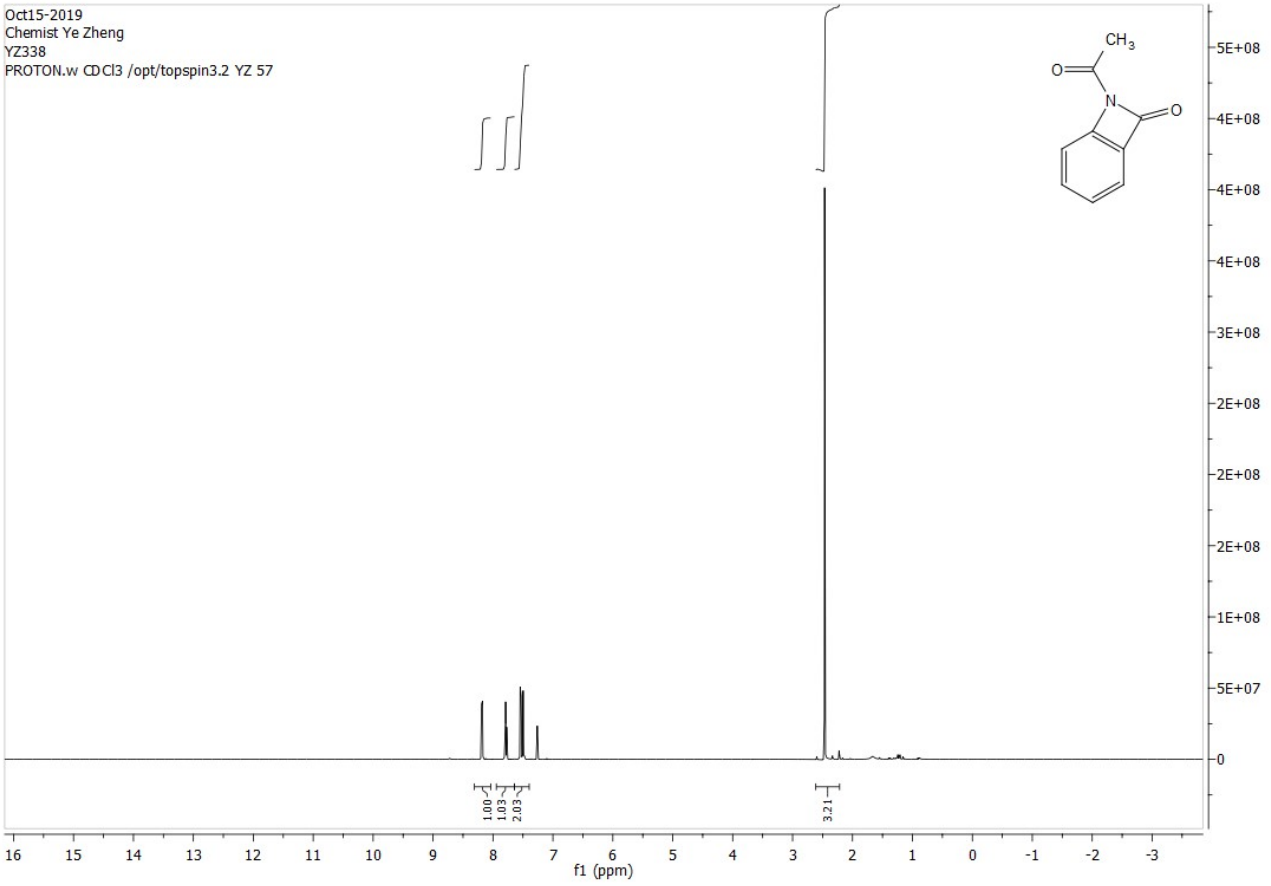


This compound has been reported but not fully characterized.

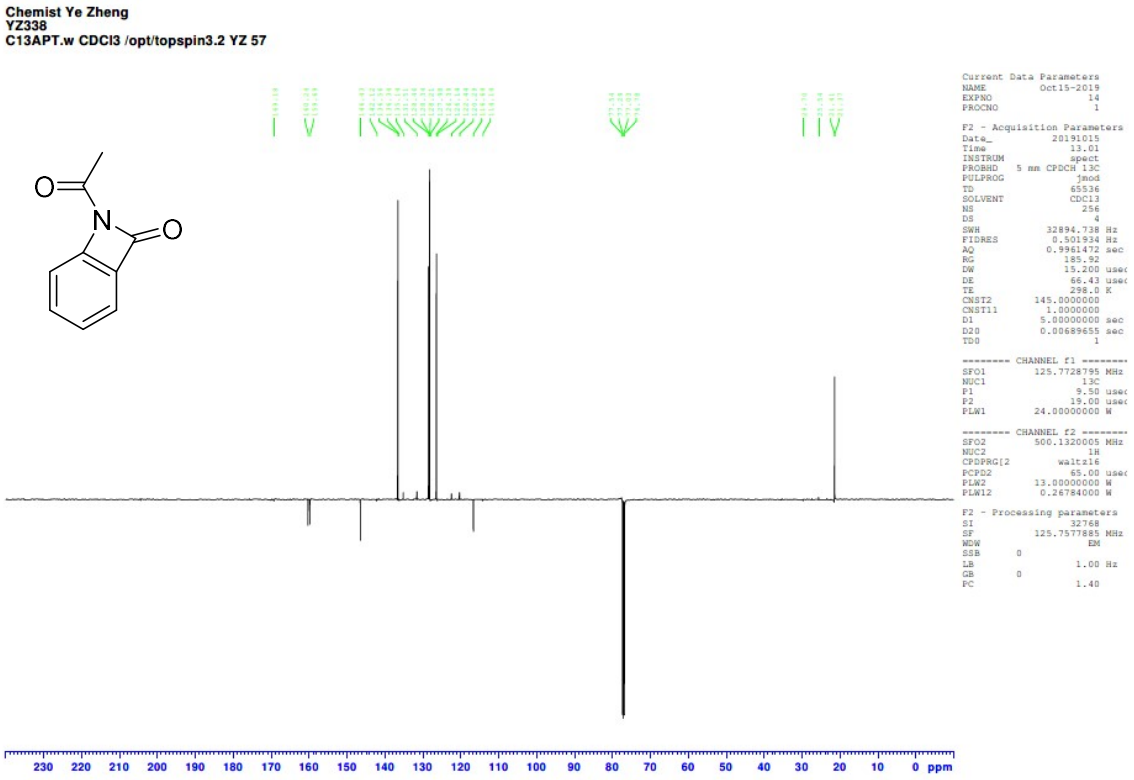
Reference: Ansary, I.; Das, A.; Sen G., Parth S.; Bandyopadhyay, A. K., *Synth. Commun.* **2017**, *47*, 1375 – 1386.

To a solution of 2-acetamidobenzoic acid (358 mg, 2.00 mmol) in THF (16 mL) at 0 °C was added CDI (324 mg, 2.00 mmol) and stirred under a nitrogen atmosphere for 2 hours. To a solution of *N, O*-dimethylhydroxylamine hydrochloride (195 mg, 2.00 mmol) in THF (4 mL) at rt was added triethylamine (202 mg, 2.00 mmol) and stirred under a nitrogen atmosphere for 2 hours. Then the two reaction mixture was combined and left to stir under a nitrogen atmosphere overnight. TLC (9:1 hexane: EtOAc) after this time indicated full conversion. The mixture was quenched by saturated $NaHCO_3$ solution (20 mL), EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 × 20 mL), and the combined organic layers were dried ($MgSO_4$) and filtered. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-20% ethyl acetate in hexane to give 1-acetylbenzo[b]azet-2(1H)-one as a white solid (138.5 mg, 0.860 mmol, 43%). TLC: Rf ca 0.20 (9:1 hexane: EtOAc), strong UV and $KMnO_4$; Mp: 173 °C; HRMS: (found (ESI+): [M+Na]+, Calcd for $C_9H_7NNaO_2$ 184.0371; Found 184.0369; -1.3 ppm error; ν_{max} 3070, 2930, 1778, 1752, 1643, 1604, 1470, 1264, 1051, 997, 960 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 8.18 (1H, d, *J* = 7.9, ArH), 7.79 (1H, t, *J* = 7.7, ArH), 7.64-7.40 (2H, m, ArH), 2.37 (3H, s, $COCH_3$) ppm; δ_C (125 MHz, $CDCl_3$) 160.2 (C), 159.7 (C), 146.4 (C), 136.6 (CH), 128.5 (CH), 128.2 (CH), 128.4 (CH), 116.6 (C), 21.4 (CH_3) ppm; m/z (ES-API+) did not show molecular ion.

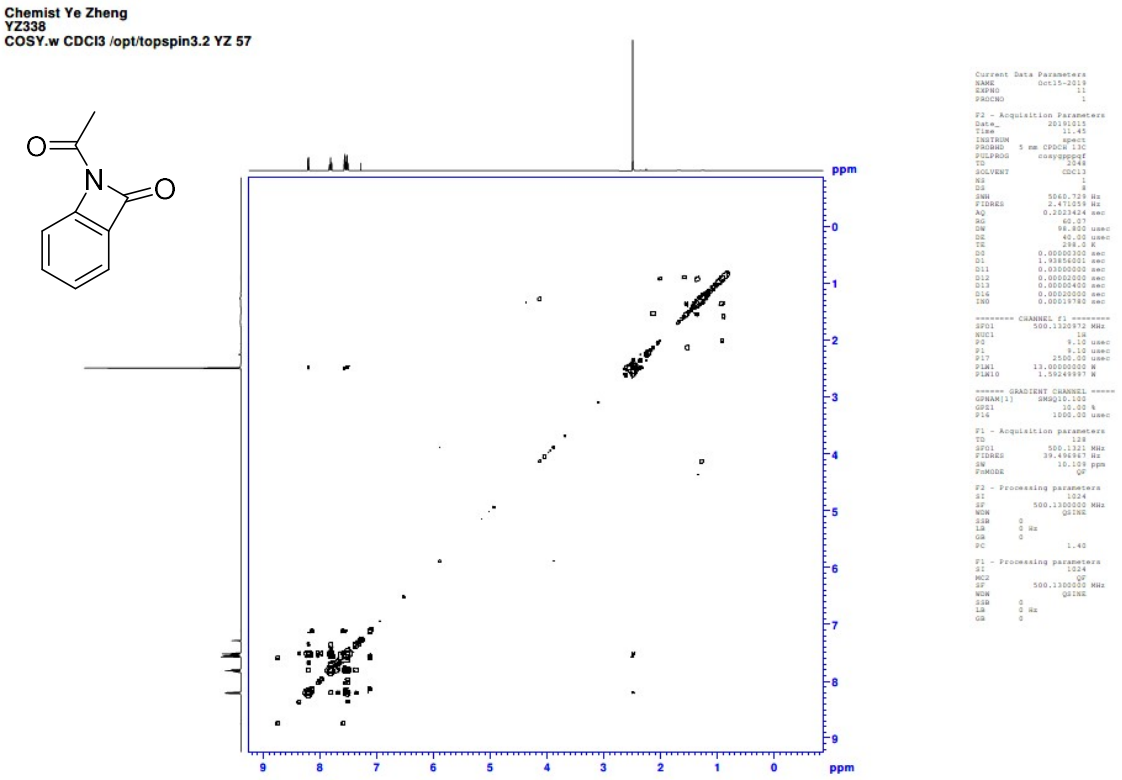
^{1}H NMR (500 MHz, $CDCl_3$) of 1-Acetylbenzo[b]azet-2(1H)-one:



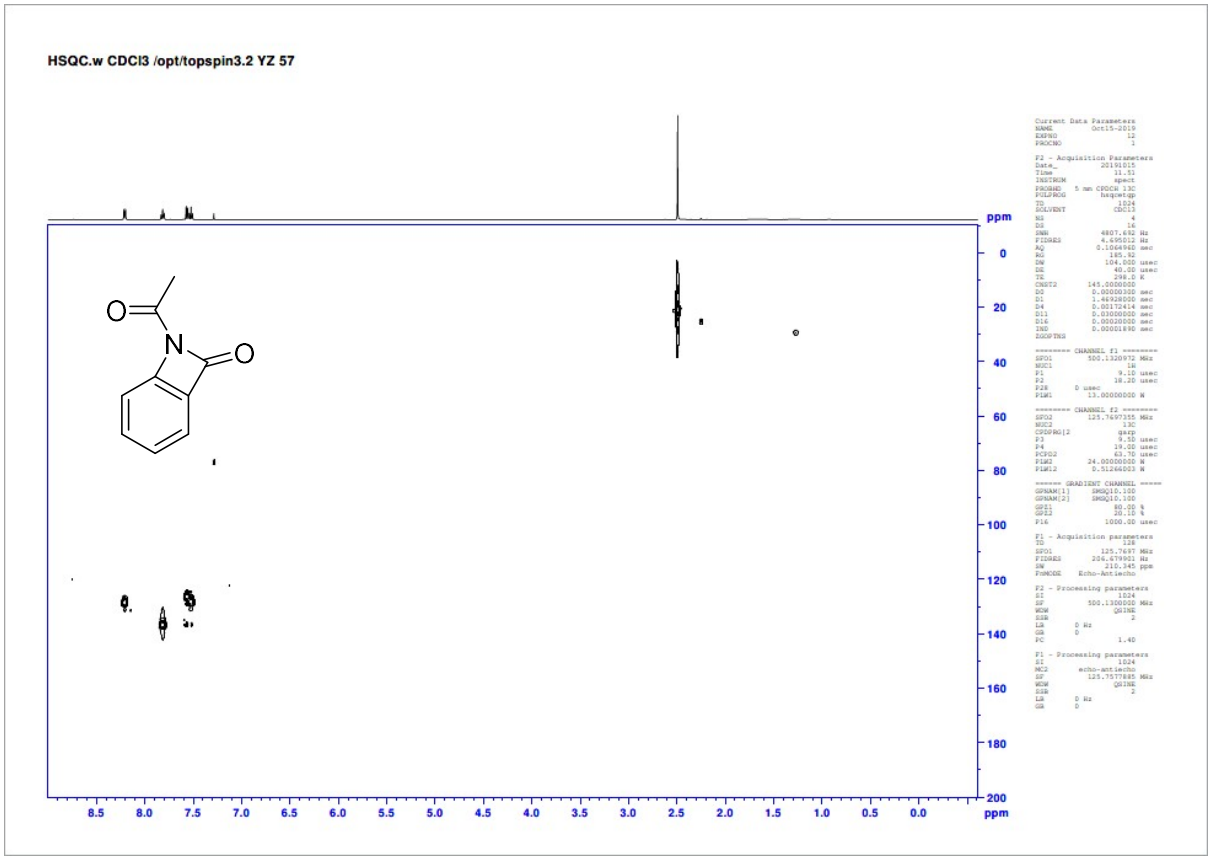
^{13}C NMR (125 MHz, $CDCl_3$) of 1-Acetylbenzo[b]azet-2(1H)-one:



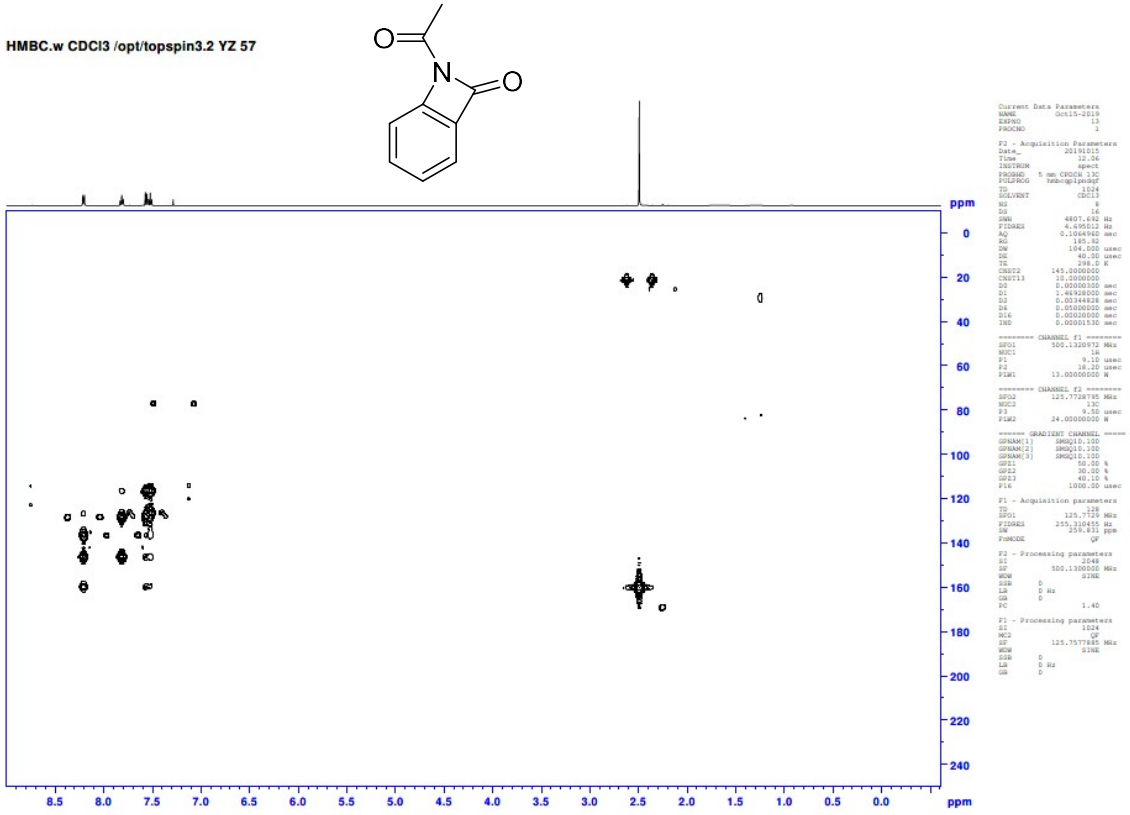
COSY (500 MHz, $CDCl_3$) of 1-Acetylbenzo[b]azet-2(1H)-one:



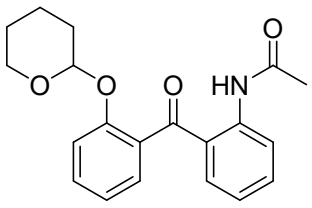
HSQC (500 MHz, $CDCl_3$) of 1-Acetylbenzo[b]azet-2(1H)-one:



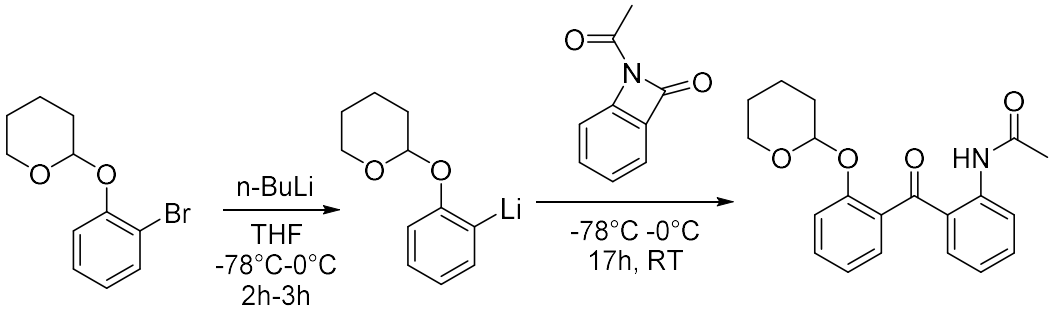
HMBC (500 MHz, $CDCl_3$) of 1-Acetylbenzo[b]azet-2(1H)-one:



N-(2-(2-((Tetrahydro-2H-pyran-2-yl)oxy)benzoyl)phenyl)acetamide.



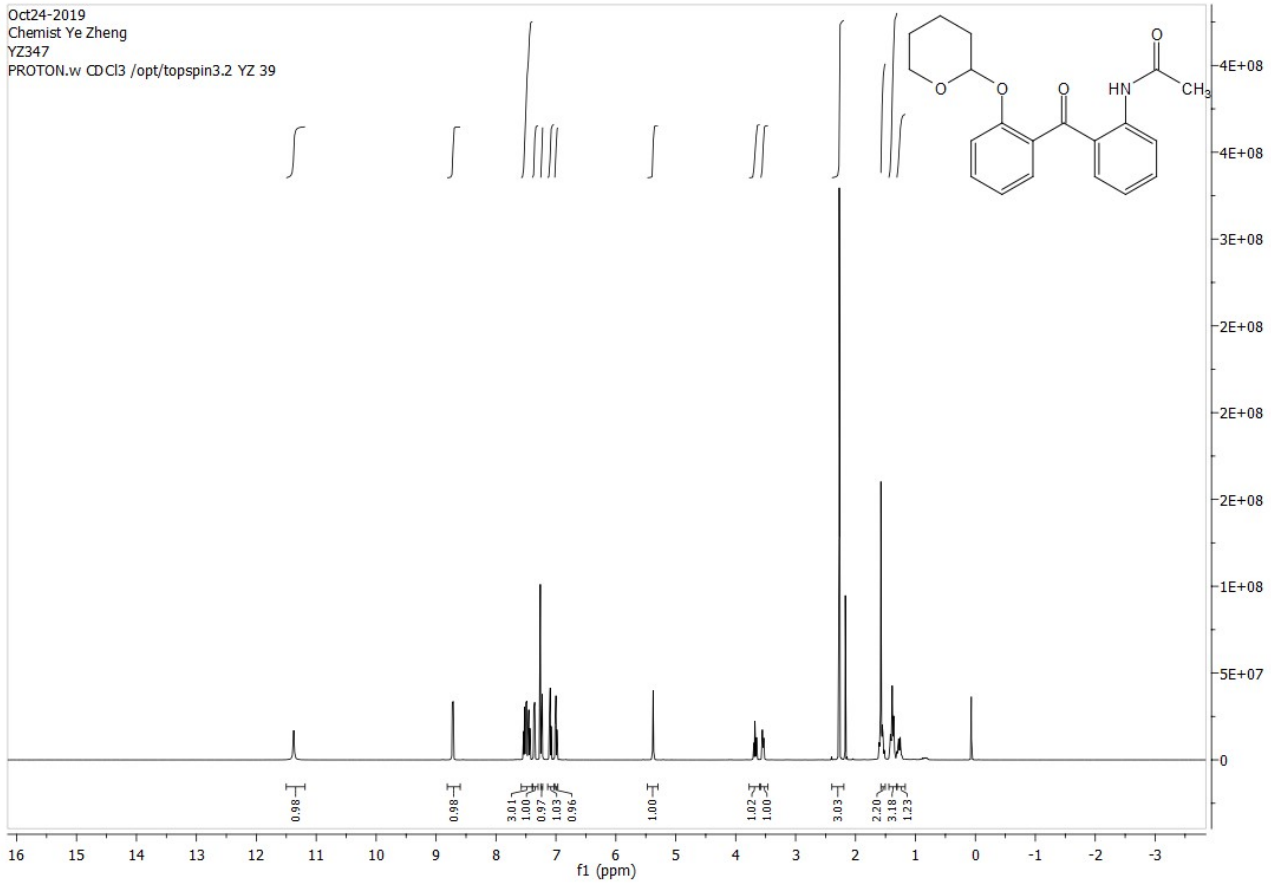
YZ347



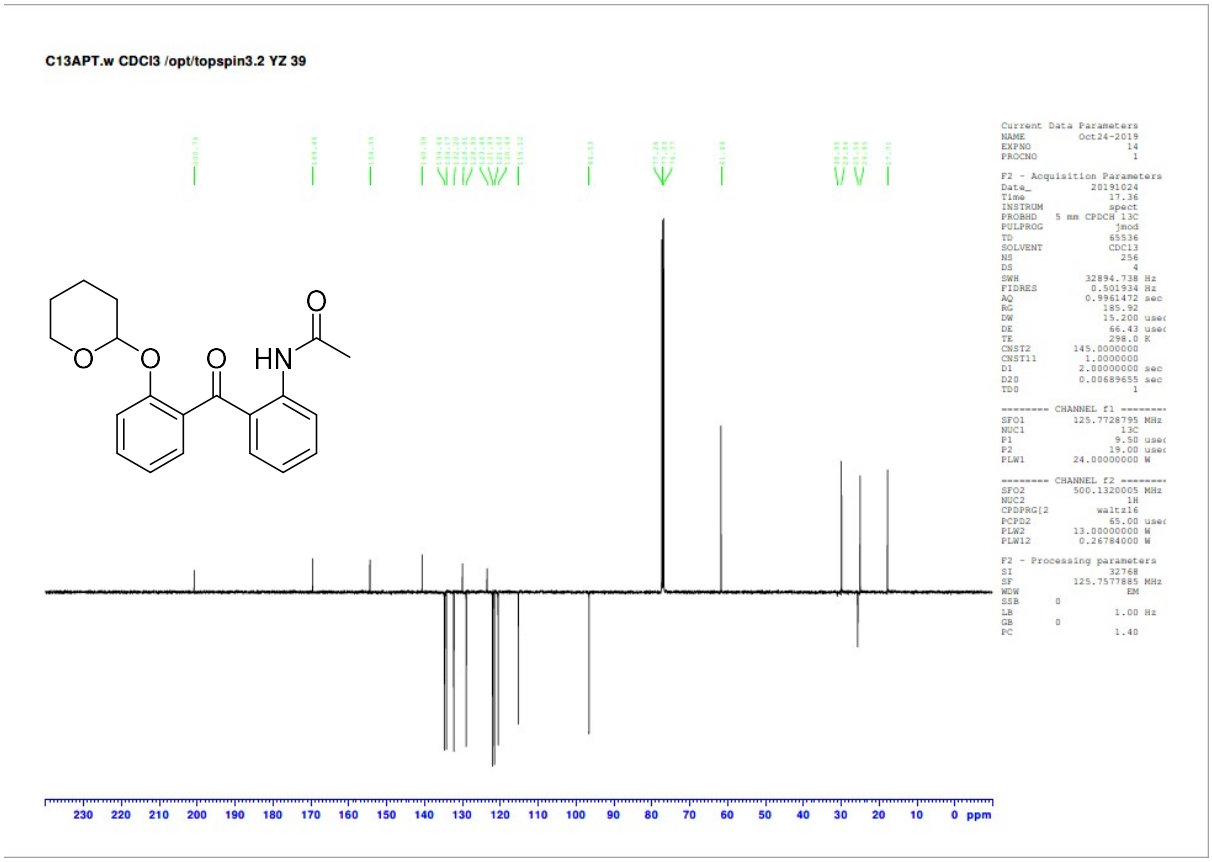
This compound is novel.

To a solution of 2-(2-bromophenoxy)tetrahydro-2H-pyran (270 mg, 1.05 mmol) in THF (2.1 mL) at -78 °C was added a solution of n-butyllithium (0.53 mL, 2.5M in hexanes, 1.05 mmol). The reaction mixture was then stirred under a nitrogen atmosphere for 2-3 hours, after which 1-acetylbenzo[b]azet-2(1H)-one (254.3 mg, 1.58 mmol) was added dropwise. The reaction mixture was left stirring under the nitrogen atmosphere and allowed to warm to rt. The reaction was followed by TLC (4:1 hexane: EtOAc). The mixture was quenched by saturated NH_4Cl solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 × 20 mL), and the combined organic layers were dried ($MgSO_4$) and filtered. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give N-(2-(2-((tetrahydro-2H-pyran-2-yl)oxy)benzoyl)phenyl)acetamide as a white solid (157.4 mg, 0.464 mmol, 44%). TLC: Rf ca 0.30 (4:1 hexane: EtOAc), strong UV and $KMnO_4$; Mp: 113 °C; HRMS: (found (ESI+): [M+Na]+, Calcd for $C_{20}H_{21}NNaO_4$ 362.1367; Found 362.1363; -1.2 ppm error); ν_{max} 2953, 2926, 2883, 1628, 1596, 1581, 1514, 1288, 1118, 956 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 11.38 (1H, s, NH), 8.72 (1H, d, *J* = 8.4, ArH), 7.58-7.39 (3H, m, ArH), 7.36 (1H, dd, *J* = 7.5, 1.5, ArH), 7.24 (1H, d, *J* = 8.4, ArH), 7.10 (1H, t, *J* = 7.4, ArH), 7.00 (1H, t, *J* = 7.6, ArH), 5.38 (1H, s, O*CH*O), 3.68 (1H, td, *J* = 11.2, 2.1, O*CH*$_2$CH$_2$), 3.54 (1H, d, *J* = 11.2, O*CH*$_2$CH$_2$), 2.27 (3H, s, $COCH_3$), 1.59-1.51 (2H, m, CH_2), 1.44-1.31 (3H, m, CH_2), 1.31-1.17 (1H, m, CH_2) ppm; δ_C (125 MHz, $CDCl_3$) 200.8 (C), 169.5 (C), 154.4 (C), 140.6 (C), 134.7 (CH), 134.2 (CH), 132.2 (CH), 129.9 (C), 128.9 (CH), 123.5 (C), 122.0 (CH), 121.5 (CH), 120.5 (CH), 115.1 (CH), 96.5 (CH), 61.7 (CH_2), 29.9 (CH_2), 25.6 (CH_3), 25.0 (CH_2), 17.7 (CH_2) ppm; m/z (ES-API+) 362.2 (M^+ + 23, 100%).

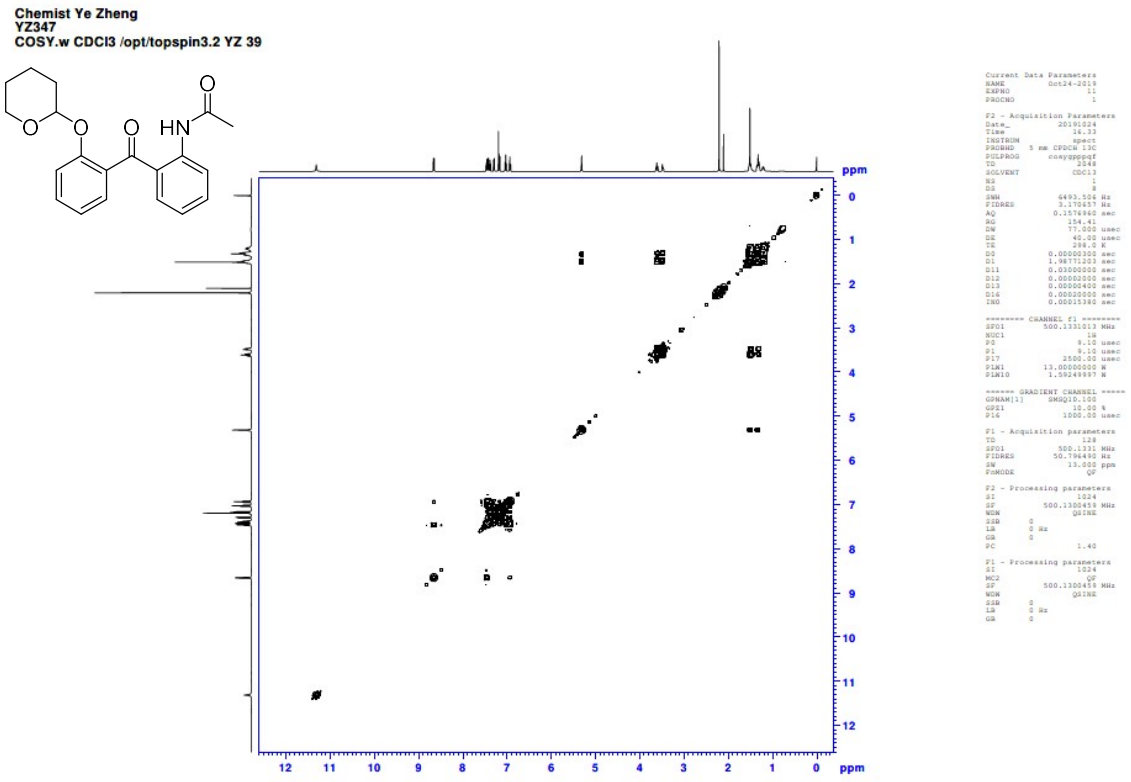
^{1}H NMR (500 MHz, $CDCl_3$) of N-(2-(2-((Tetrahydro-2H-pyran-2-yl)oxy)benzoyl)phenyl)acetamide:



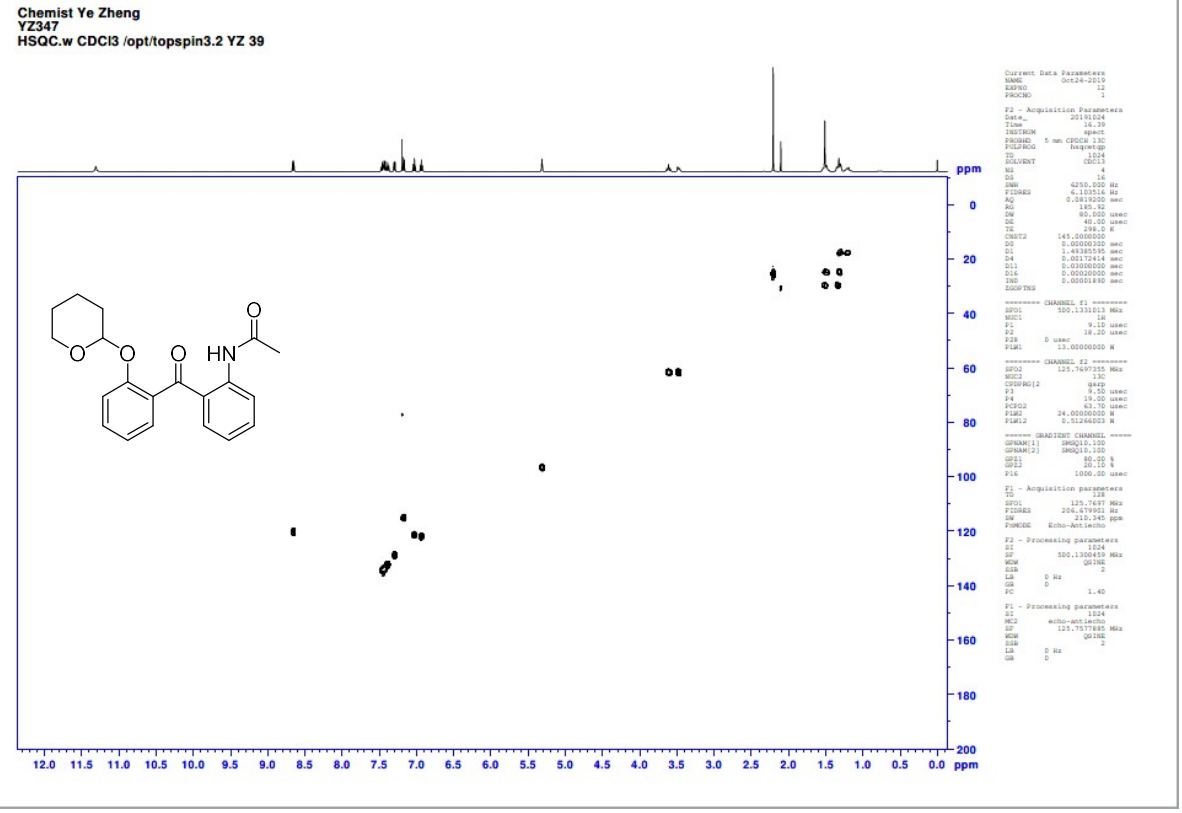
^{13}C NMR (125 MHz, $CDCl_3$) of N-(2-(2-((Tetrahydro-2H-pyran-2-yl)oxy)benzoyl)phenyl)acetamide:



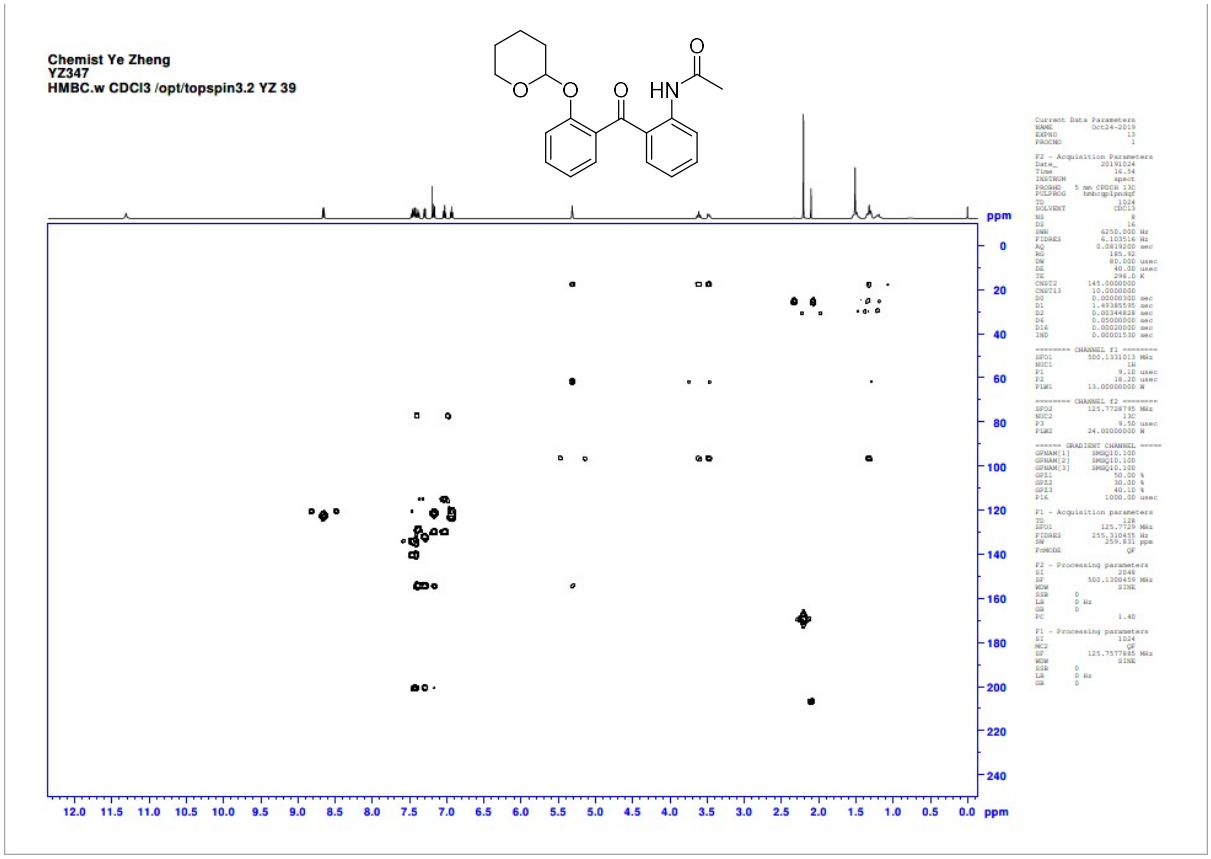
COSY (500 MHz, $CDCl_3$) of N-(2-(2-((Tetrahydro-2H-pyran-2-yl)oxy)benzoyl)phenyl)acetamide:



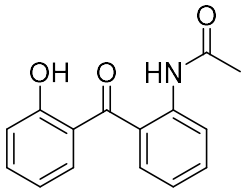
HSQC (500 MHz, $CDCl_3$) of N-(2-(2-((Tetrahydro-2H-pyran-2-yl)oxy)benzoyl)phenyl)acetamide:



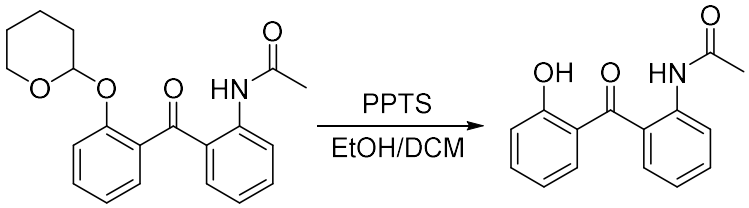
HMBC (500 MHz, $CDCl_3$) of N-(2-(2-((Tetrahydro-2H-pyran-2-yl)oxy)benzoyl)phenyl)acetamide:



N-(2-(2-Hydroxybenzoyl)phenyl)acetamide 7n.



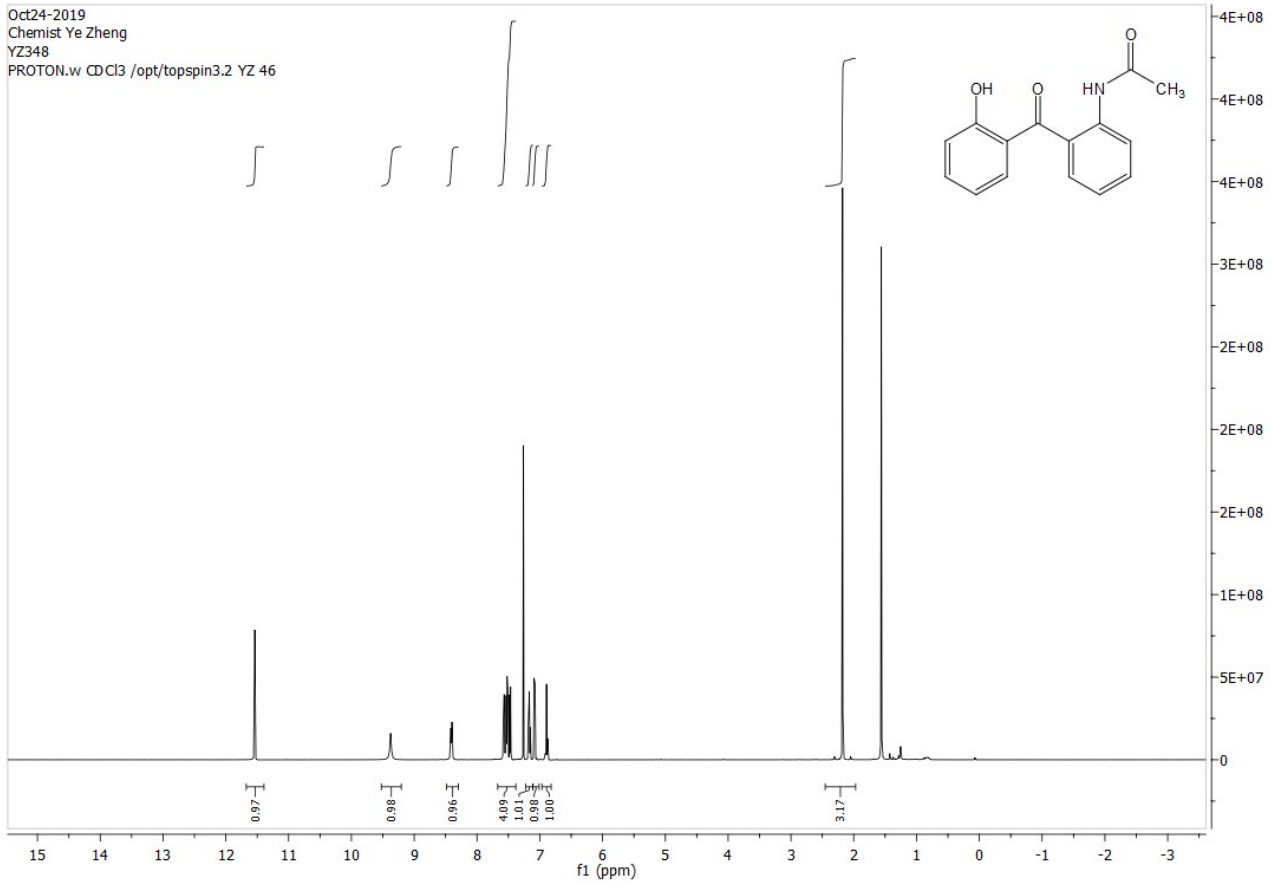
YZ348



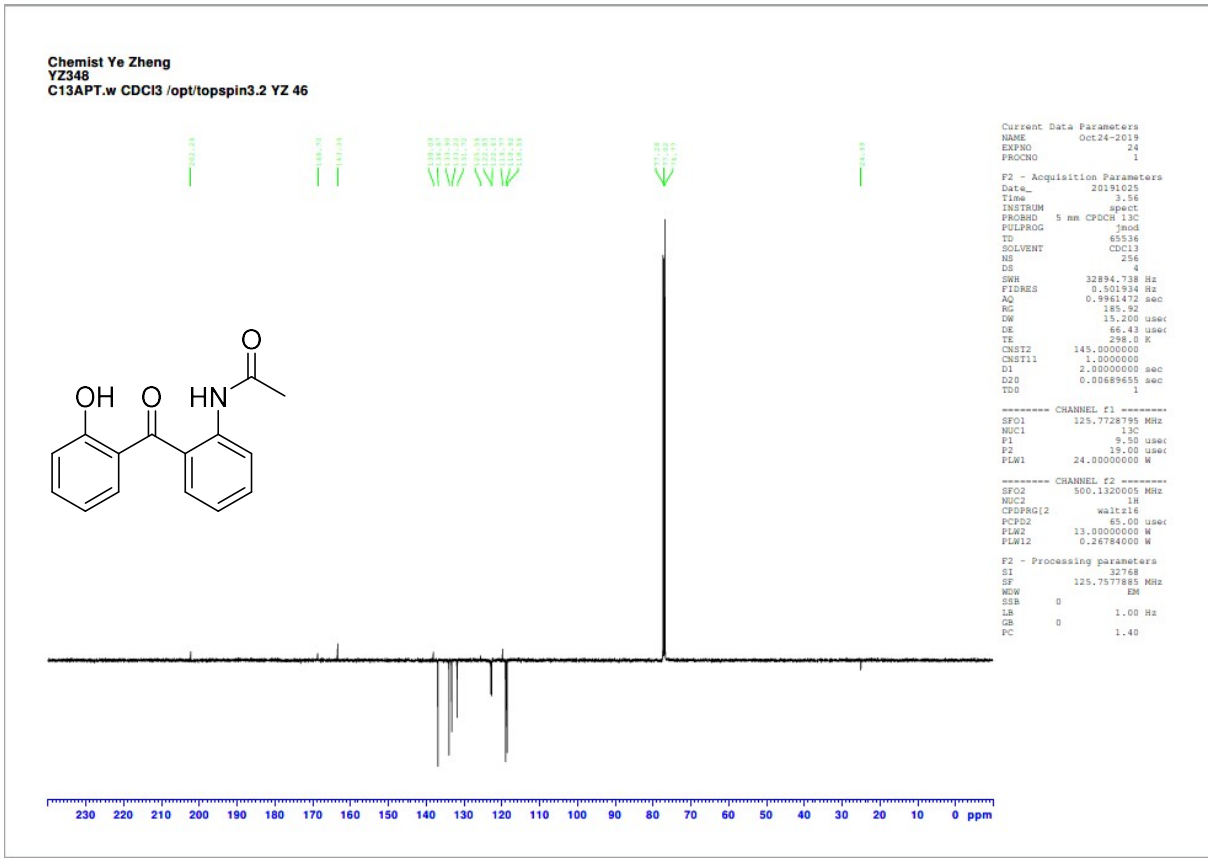
This compound is novel.

To a solution of N-(2-(2-((tetrahydro-2H-pyran-2-yl)oxy)benzoyl)phenyl)acetamide (151.5 mg, 0.450 mmol) in EtOH (2.28 mL)/DCM (1.14mL) was added pyridinium *p*-toluenesulfonate (PPTS) (16.9 mg, 0.0675 mmol) at rt. The reaction mixture was left to stir under a nitrogen atmosphere overnight. TLC (3:2 hexane: EtOAc) after this time indicated full conversion. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-80% ethyl acetate in hexane to give N-(2-(2-hydroxybenzoyl)phenyl)acetamide **7n** as a yellow solid (84.1 mg, 0.330 mmol, 73.8%). TLC: Rf ca 0.60 (3:2 hexane: EtOAc), strong UV and $KMnO_4$; Mp: 101 °C; HRMS: (found (ESI+): [M+Na]+, Calcd for $C_{15}H_{13}NNaO_3$ 278.0783; Found 278.0788; 1.5 ppm error; ν_{max} 3257 (br), 3050, 1665, 1623, 1604, 1578, 1515, 1481, 1443, 1292, 1283, 1118, 933 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 11.54, (1H, s, NH), 9.38 (1H, s, OH), 8.41 (1H, d, *J* = 8.3, ArH), 7.58-7.45 (4H, m, ArH), 7.17 (1H, t, *J*=7.6, ArH), 7.08 (1H, d, *J* = 8.3, ArH), 6.89 (1H, t, *J* = 7.6, ArH), 2.18 (1H, s, $COCH_3$) ppm; δ_C (125 MHz, $CDCl_3$) 202.3 (C), 168.7 (C), 163.3 (C), 138.1 (C), 136.9 (CH), 133.9 (CH), 133.2 (CH), 131 7 (CH), 125.6 (C), 122.9 (CH), 122.6 (CH), 119.8 (C), 118.9 (CH), 118.6 (CH), 25.0 (CH_3) ppm; m/z (ES-API+) 278.2 (M^+ + 23, 100%).

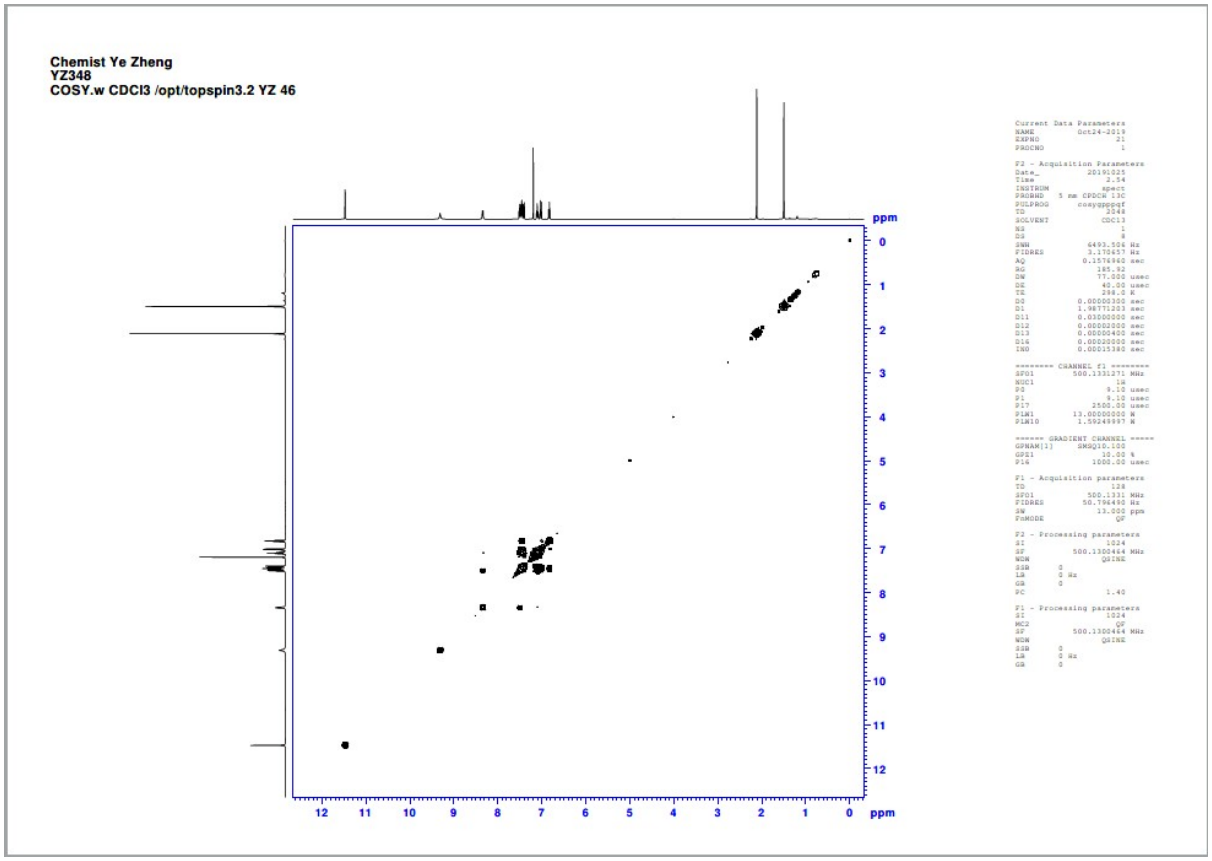
^{1}H NMR (500 MHz, $CDCl_3$) of **7n**:



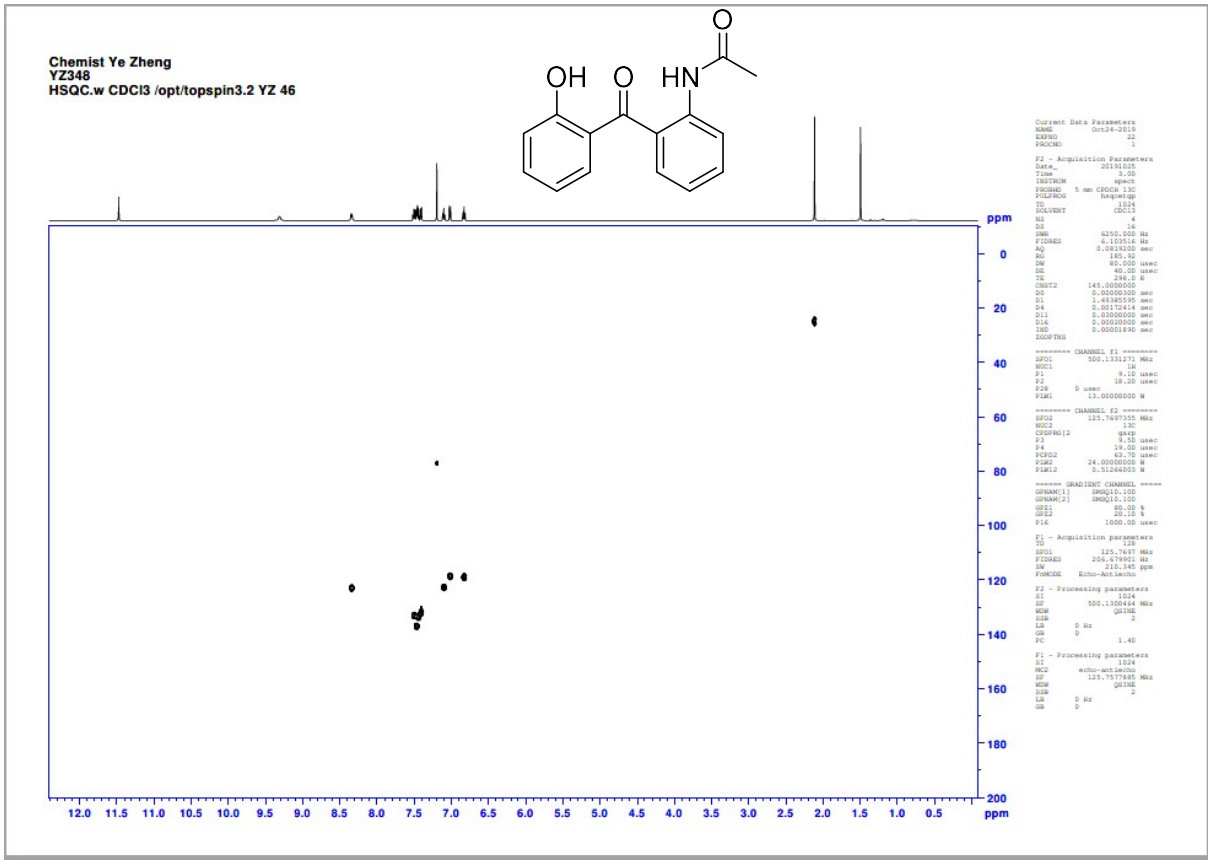
^{13}C NMR (125 MHz, $CDCl_3$) of **7n**:



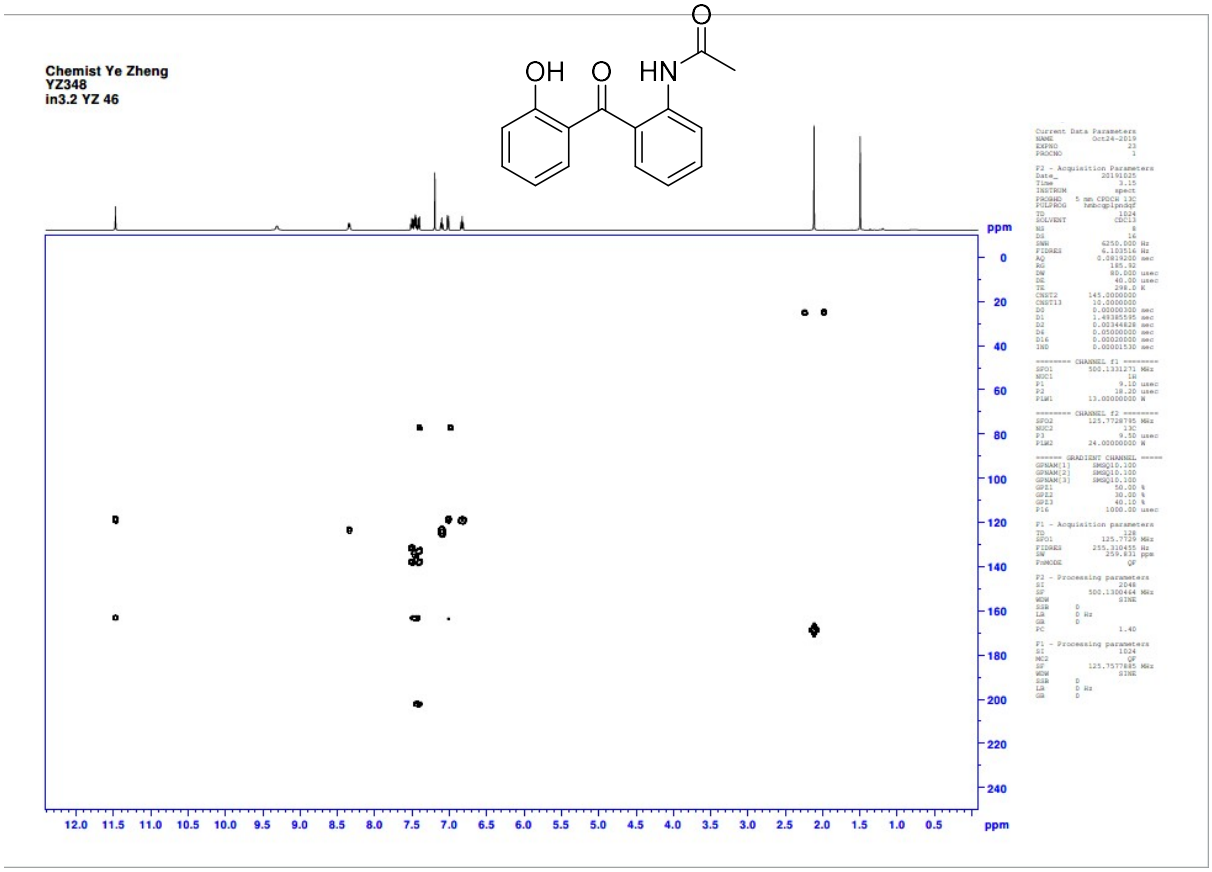
COSY (500 MHz, $CDCl_3$) of **7n**:



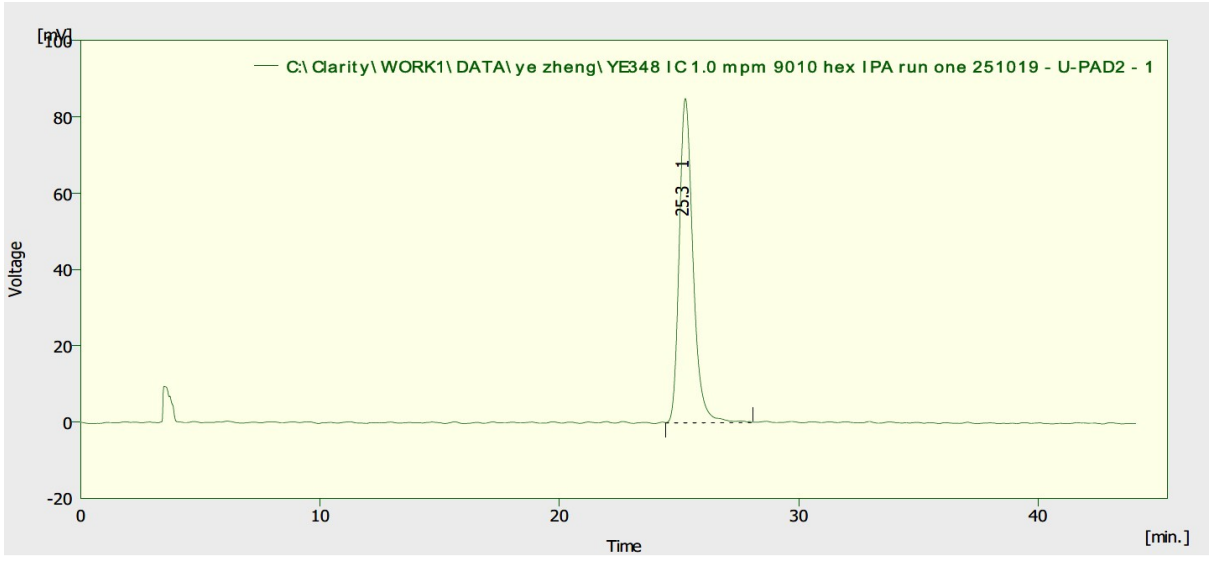
HSQC (500 MHz, $CDCl_3$) of **7n**:



HMBC (500 MHz, $CDCl_3$) of **7n**:



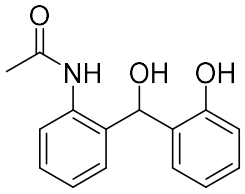
HPLC of N-(2-(2-hydroxybenzoyl)phenyl)acetamide **7n**:



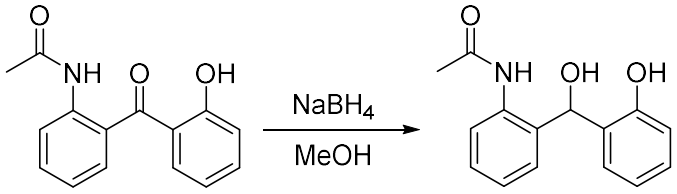
Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|ye zheng\|YE348 IC 1.0 mpm 9010 hex IPA run one 251019 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	25.260	3395.689	85.017	100.0	100.0	0.60	
	Total	3395.689	85.017	100.0	100.0		

N-(2-(Hydroxy(2-hydroxyphenyl)methyl)phenyl)acetamide 8n.



racemic: YZ349, Asymmetric: YZ359



This compound is novel.

To a solution of N-(2-(2-hydroxybenzoyl)phenyl)acetamide **7n** (84.1 mg, 0.330 mmol) in MeOH (2 mL) was added sodium borohydride (25.1 mg, 0.660 mmol). The reaction was stirred for 4 hours. TLC (1:1 hexane: EtOAc) after this time indicated full conversion. Distilled water (20 mL) was added, and the mixture was extracted with EtOAc (3 × 20ml), dried with $MgSO_4$, and the solvent was removed under vacuum to give crude product. The product was isolated via flash chromatography on silica eluted with 0-100% ethyl acetate in hexane to give N-(2-(hydroxy(2-hydroxyphenyl)methyl)phenyl)acetamide **8n** as a colorless oil (4.20 mg, 0.0163 mmol, 4.96%). TLC: Rf ca 0.20 (1:1 hexane: EtOAc), strong UV and $KMnO_4$; HRMS: (found (ESI+): [M+Na]+, Calcd for $C_{15}H_{15}NNaO_3$ 280.0945; Found 280.0944; -0.3 ppm error; ν_{max} 3236 (br), 3064, 2922, 2852, 1730, 1665, 1587, 1482, 1370, 1243, 1037, 966 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 8.36 (2H, d, *J* = 16.1, NH + Ar*OH*), 7.78 (1H, d, *J* = 8.0, ArH), 7.32 (1H, t, *J* = 8.3, ArH), 7.19-7.11 (3H, m, ArH), 6.90 (1H, d, *J* = 8.1, ArH), 6.83-6.67 (2H, m, ArH), 6.10 (1H, s, Ar*CH*OH), 4.73 (1H, s, ArCH*OH*) 2.01 (3H, s, $COCH_3$) ppm; δ_C (125 MHz, $CDCl_3$) 170.1 (C), 155.3 (C), 135.8 (C), 132.8 (C), 129.4 (CH), 129.2 (CH), 129.1 (CH), 127.9 (CH), 125.7 (CH), 125.2 (C), 124.3 (CH), 120.2 (CH), 116.9 (CH), 74.2 (CH), 24.1 (CH_3) ppm; m/z (ES-API+) 280.2 (M^+ + 23, 100%).

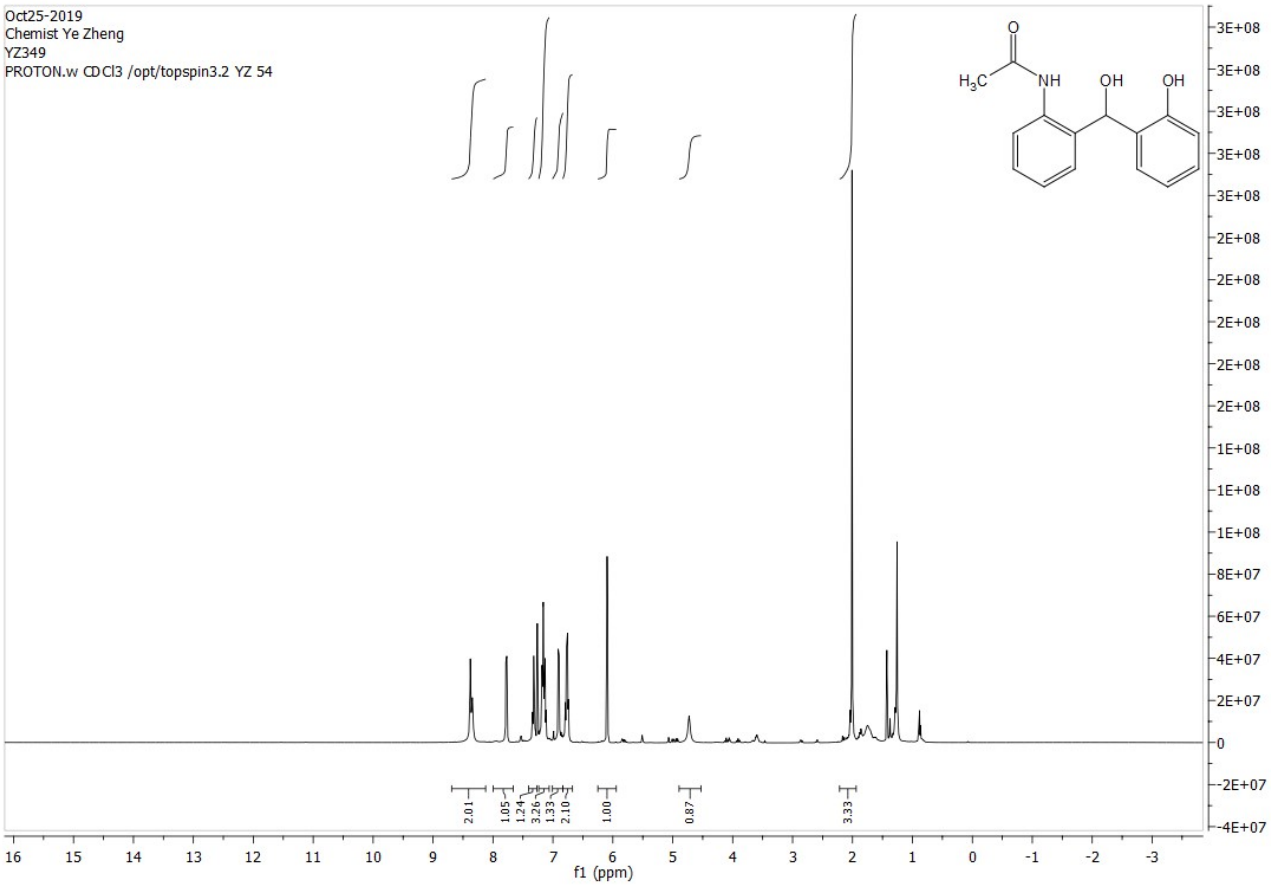
Enantiomeric excess and conversion determined by HPLC analysis (Chiralpak IC, 30 cm x 6mm column, hexane:iPrOH 90:10, 1.0 mL/min, T = 25°C) ketone 25.3 min, *R* and *S* isomer 33.9 min and 41.6 min, configuration was assigned by analogy.

ATH of N-(2-(2-hydroxybenzoyl)phenyl)acetamide **7n** (YZ359)

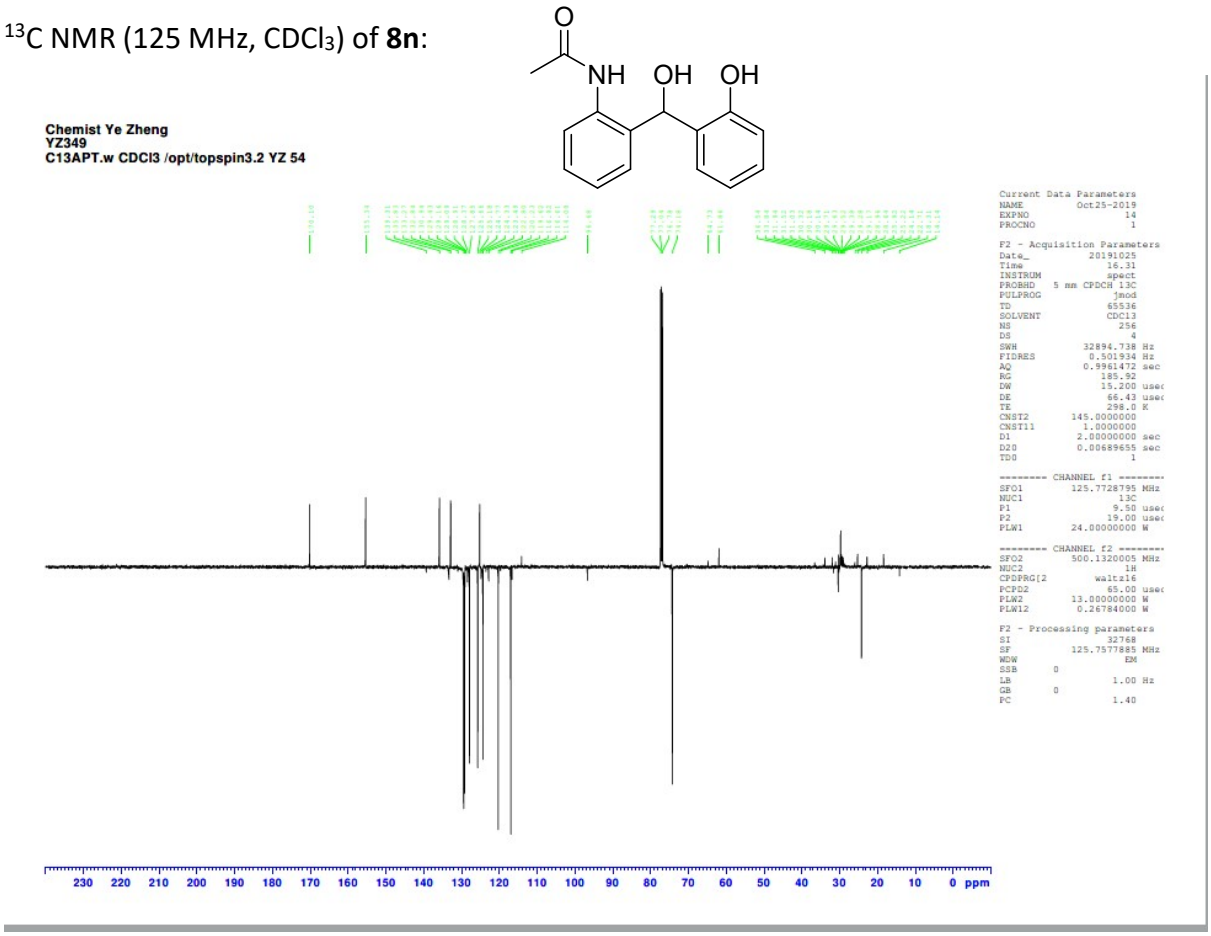
Catalyst (*R,R*)-**2** (0.00157 mmol, 1mol%) was added to FA: TEA (5:2 azeotropic mixture, 0.18 mL) at rt and the mixture was stirred under a nitrogen atmosphere for 10-15 minutes; after which a solution of N-(2-(2-hydroxybenzoyl)phenyl)acetamide **7n** (40 mg, 0.157 mmol) in DCM (0.25 mL)

was added. The reaction mixture was stirred under a nitrogen atmosphere, followed by TLC (1:1 hexane: EtOAc). After 72 hours, the reaction was quenched using saturated $NaHCO_3$ solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried ($MgSO_4$) and filtered. The solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-100% ethyl acetate in hexane to give N-(2-(hydroxy(2-hydroxyphenyl)methyl)phenyl)acetamide **8n** (30.3 mg, 0.118 mmol, 75.2%; (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst example). The reaction was also followed by HPLC analysis (Chiralpak IC, 30 cm x 6mm column, hexane:iPrOH 90:10, 1.0 mL/min, T = 25°C); (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst: 100% conversion; $[\alpha]_D^{24}$ -82 (c 0.995 in $CHCl_3$) 93.6% ee.

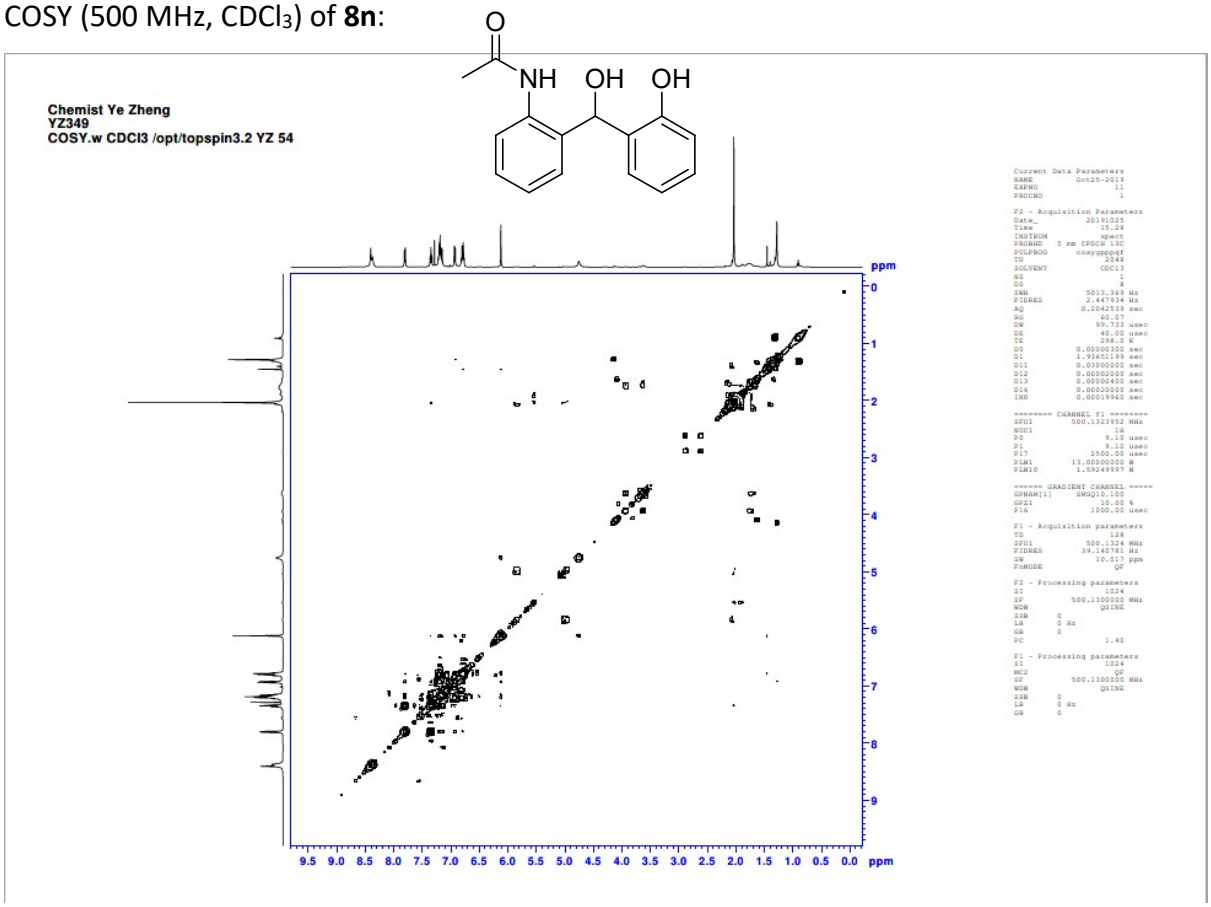
^{1}H NMR (500 MHz, $CDCl_3$) of **8n**:



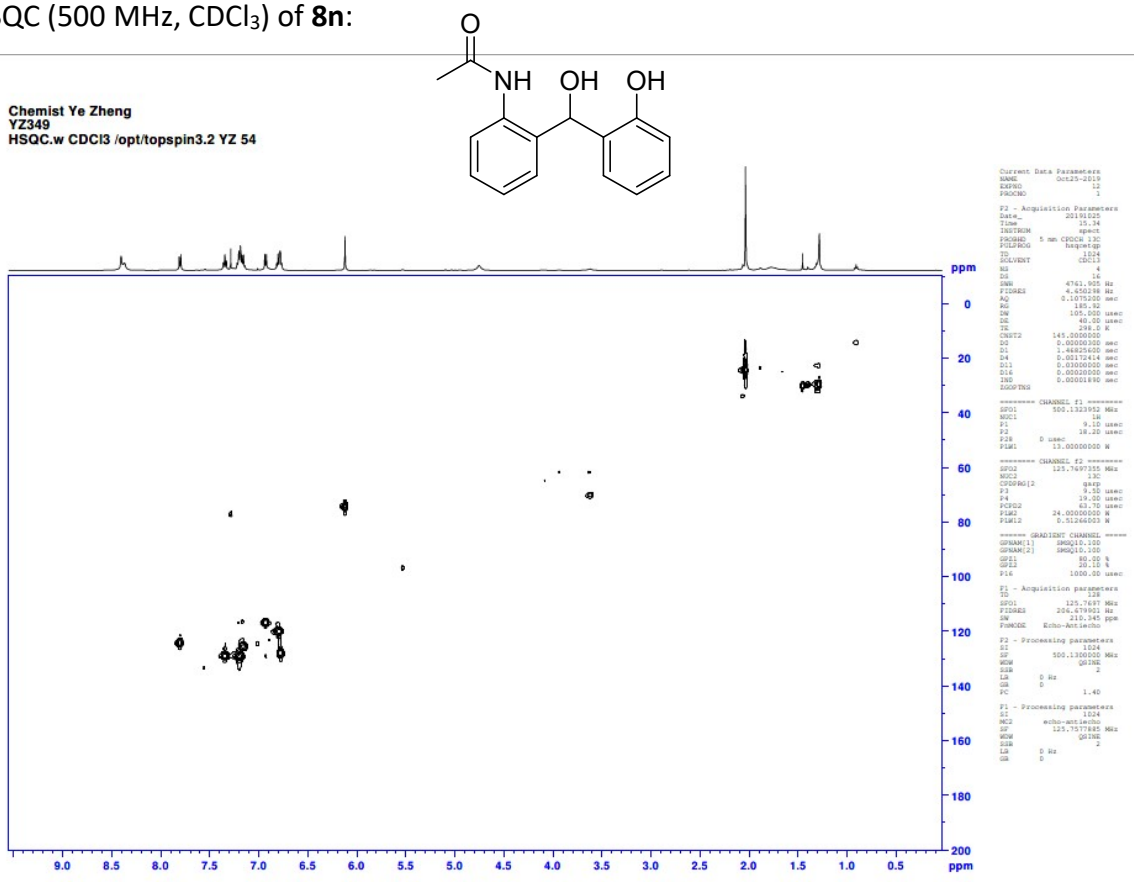
^{13}C NMR (125 MHz, $CDCl_3$) of **8n**:



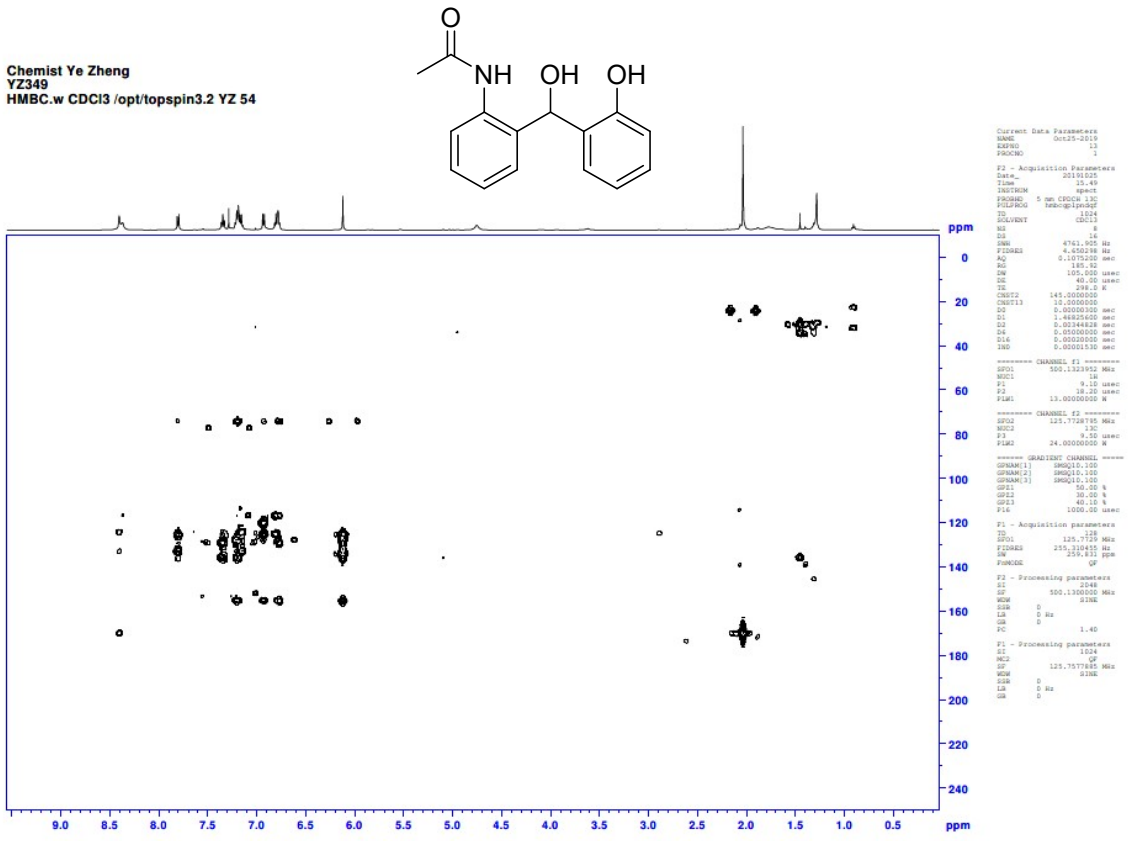
COSY (500 MHz, $CDCl_3$) of **8n**:



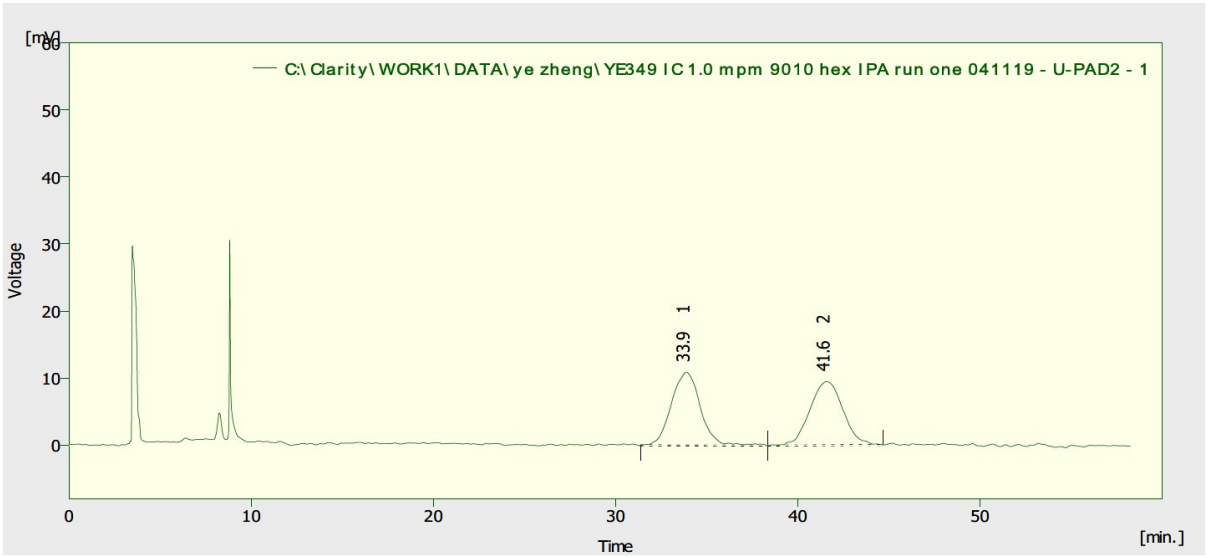
HSQC (500 MHz, $CDCl_3$) of **8n**:



HMBC (500 MHz, $CDCl_3$) of **8n**:



HPLC of racemic N-(2-(hydroxy(2-hydroxyphenyl)methyl)phenyl)acetamide **8n**:

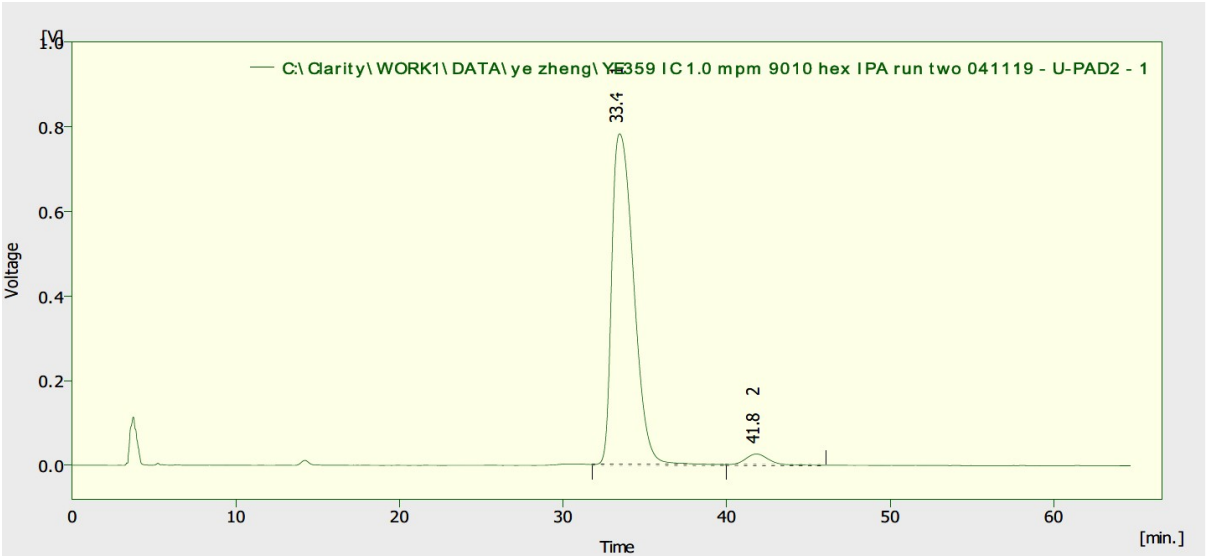


Result Table (Uncal - C:|Clarity|WORK1|DATA|ye zheng|YE349 IC 1.0 mpm 9010 hex IPA run one 041119 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	33.880	1220.458	10.949	50.3	53.5	1.69	
2	41.568	1206.307	9.527	49.7	46.5	1.98	
	Total	2426.765	20.476	100.0	100.0		

HPLC of **8n** after ATH of N-(2-(2-hydroxybenzoyl)phenyl)acetamide **7n**:

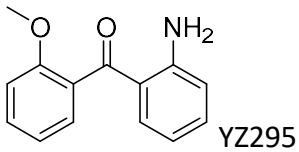
(*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst (after 72 hours, 100% conversion, 93.6% ee).



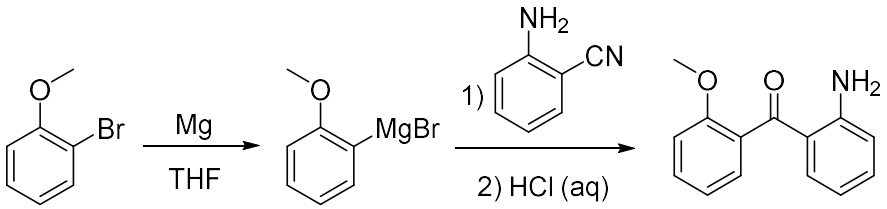
Result Table (Uncal - C:|Clarity|WORK1|DATA|ye zheng|YE359 IC 1.0 mpm 9010 hex IPA run two 041119 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	33.448	72740.205	782.705	96.5	96.8	1.46	
2	41.796	2616.851	26.264	3.5	3.2	1.50	
	Total	75357.056	808.969	100.0	100.0		

(2-Aminophenyl)(2-methoxyphenyl)methanone.



YZ295

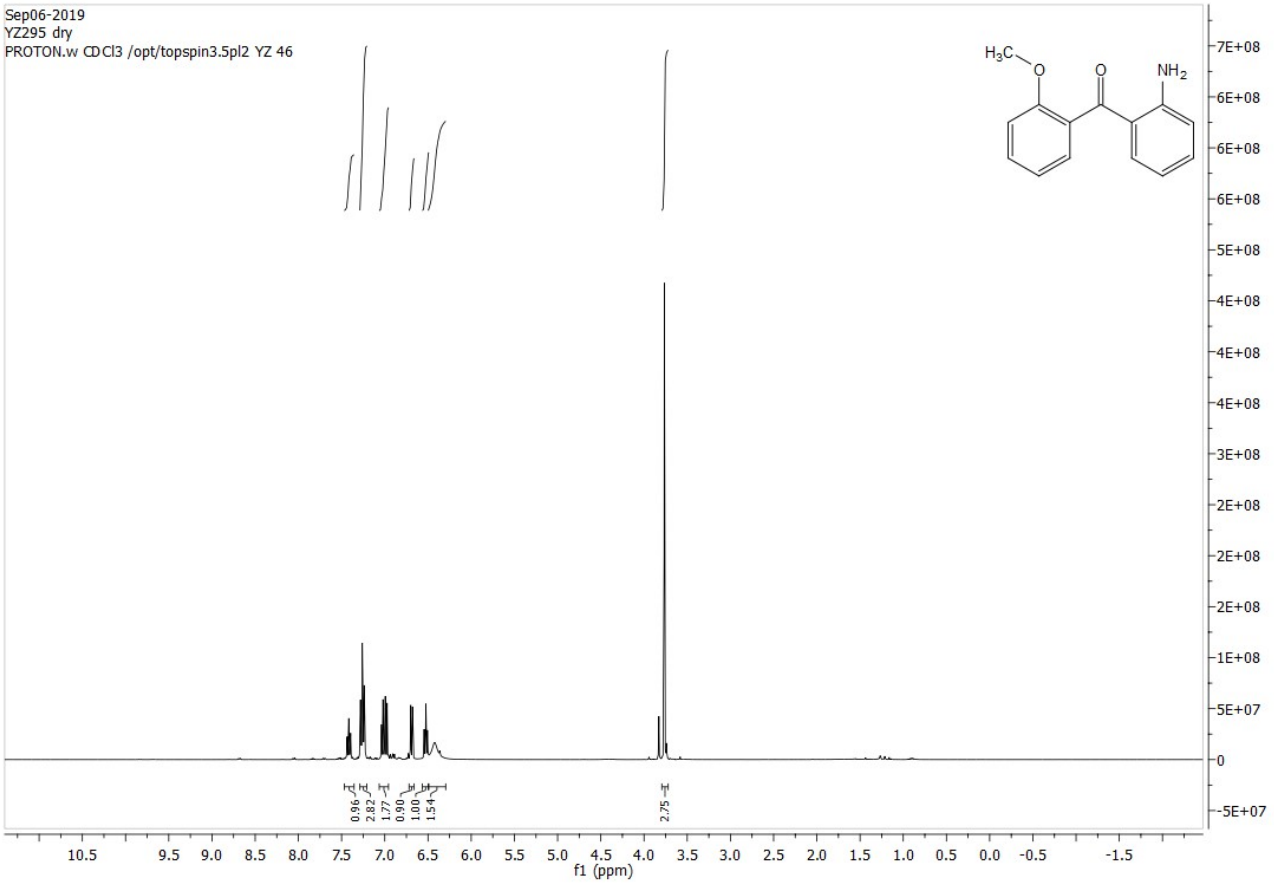


This compound has been reported and fully characterized.

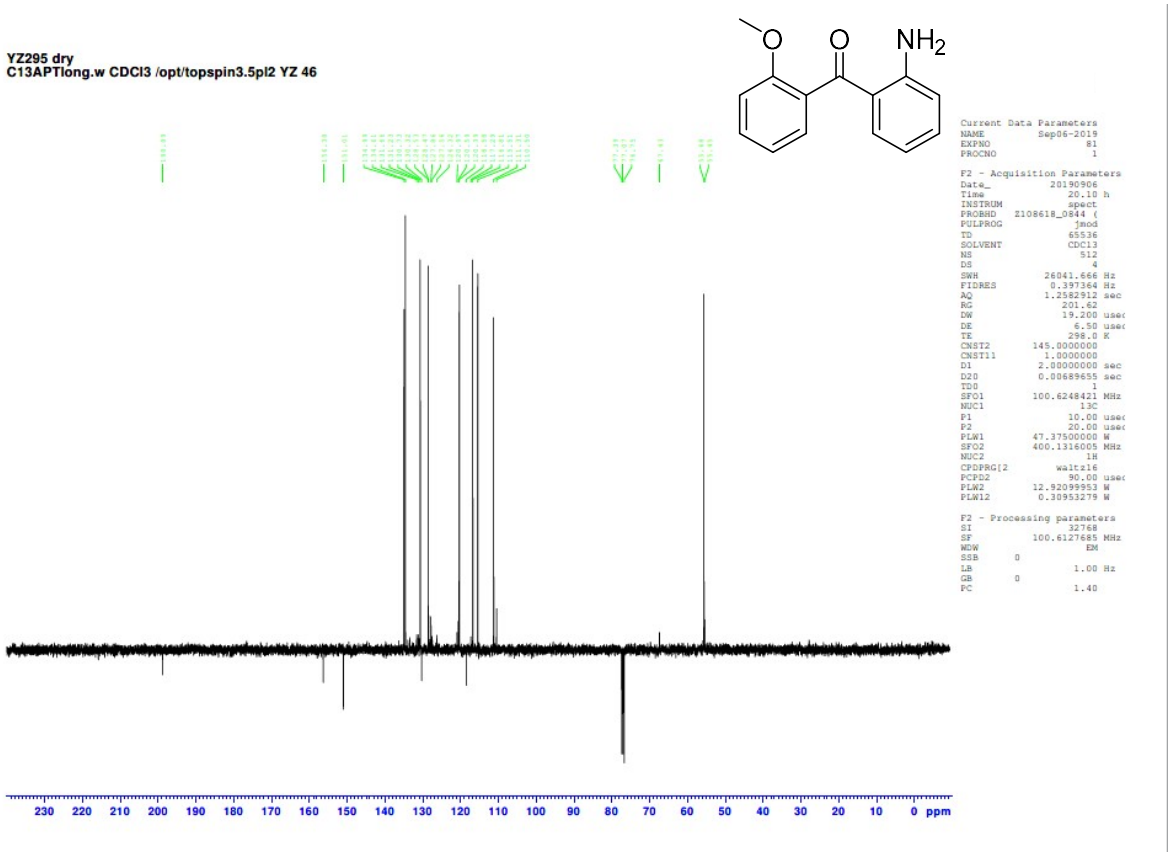
Reference: Caspers, L. D.; Finkbeiner, P.; Nachtsheim, B. J. *Chem.- Eur. J.* **2017**, *23*, 2748 – 2752.

To a solution of 2-bromoanisole (1.189 g, 6.36 mmol) in THF (6.36 mL) at rt was added magnesium (152.6 mg, 6.36 mmol). The reaction mixture was stirred under a nitrogen atmosphere at rt for 30 minutes and then heated to reflux on a hot plate for 1 hour. After cooling down to 0°C, a solution of 2-aminobenzonitrile (250 mg, 2.12 mmol) in THF (6.36 mL) was added dropwise and the reaction mixture was left stirring under the nitrogen atmosphere for 12 hours and allowed to warm to rt. After cooling down to 0°C, HCl solution (4.24 mL, 2.0 M, 8.48 mmol) was added dropwise and the mixture was stirred at rt for another 12 hours. The reaction was followed by TLC (4:1 hexane: EtOAc). The mixture was quenched by saturated $NaHCO_3$ solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 × 20 mL), and the combined organic layers were dried ($MgSO_4$) and filtered. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give (2-aminophenyl)(2-methoxyphenyl)methanone as a yellow solid (90.8 mg, 0.400 mmol, 19.5%). TLC: Rf ca 0.30 (4:1 hexane: EtOAc), strong UV and $KMnO_4$; δ_H (400 MHz, $CDCl_3$) 7.47-7.35 (1H, m, ArH), 7.29-7.21 (3H, m, ArH), 7.06-6.96 (2H, m, ArH), 6.69 (1H, d, *J* = 8.1, ArH), 6.52 (1H, t, *J* = 8.0, ArH), 6.42 (2H, s, NH_2), 3.76 (3H, s, OCH_3) ppm; δ_C (100 MHz, $CDCl_3$) 198.9 (C), 156.4 (C), 151.0 (C), 135.0 (CH), 134.6 (CH), 130.7 (CH), 130.3 (C), 128.5 (CH), 120.4 (CH), 118.6 (C), 116.8 (CH), 115.5 (CH), 111.3 (CH), 55.9 (CH_3). Data matched that reported. Enantiomeric excess and conversion determined by HPLC analysis (Chiralpak IC, 30 cm x 6mm column, hexane:iPrOH 90:10, 1.0 mL/min, T = 25°C) ketone 49.4 min, *R* and *S* isomer 30.5 min and 56.9 min, configuration is not known.

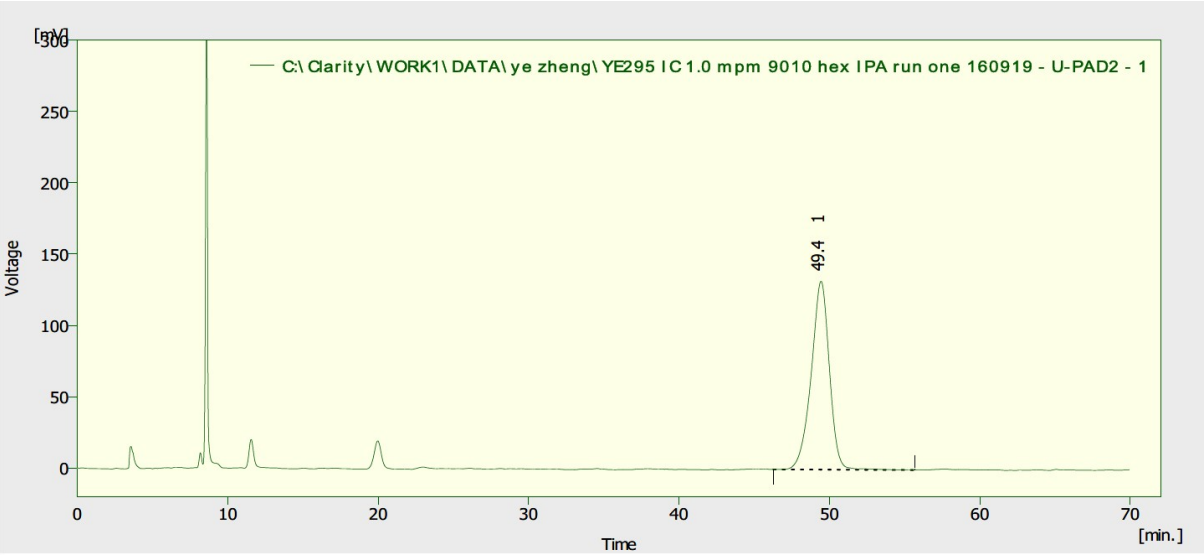
^{1}H NMR (400 MHz, $CDCl_3$) of (2-Aminophenyl)(2-methoxyphenyl)methanone:



^{13}C NMR (100 MHz, $CDCl_3$) of (2-Aminophenyl)(2-methoxyphenyl)methanone:



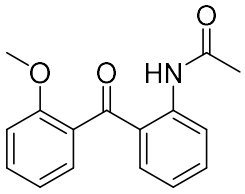
HPLC of (2-aminophenyl)(2-methoxyphenyl)methanone:



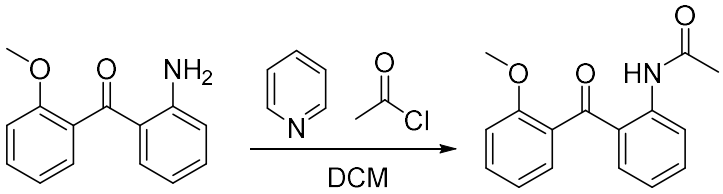
Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|ye zheng\|YE295 IC 1.0 mpm 9010 hex IPA run one 160919 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	49.436	11125.228	132.209	100.0	100.0	1.26	
	Total	11125.228	132.209	100.0	100.0		

N-(2-(2-Methoxybenzoyl)phenyl)acetamide 7o.



YZ314

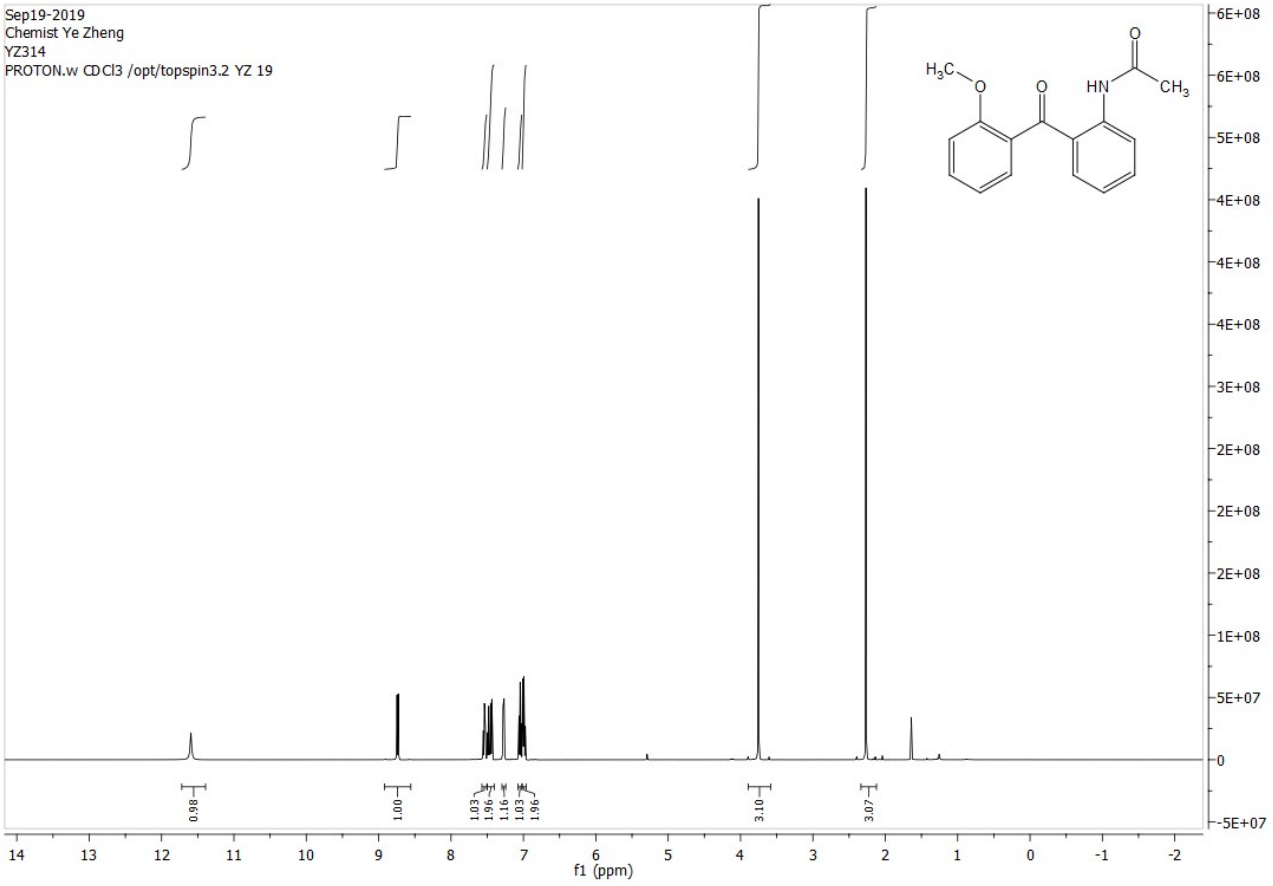


This compound has been reported and fully characterized.

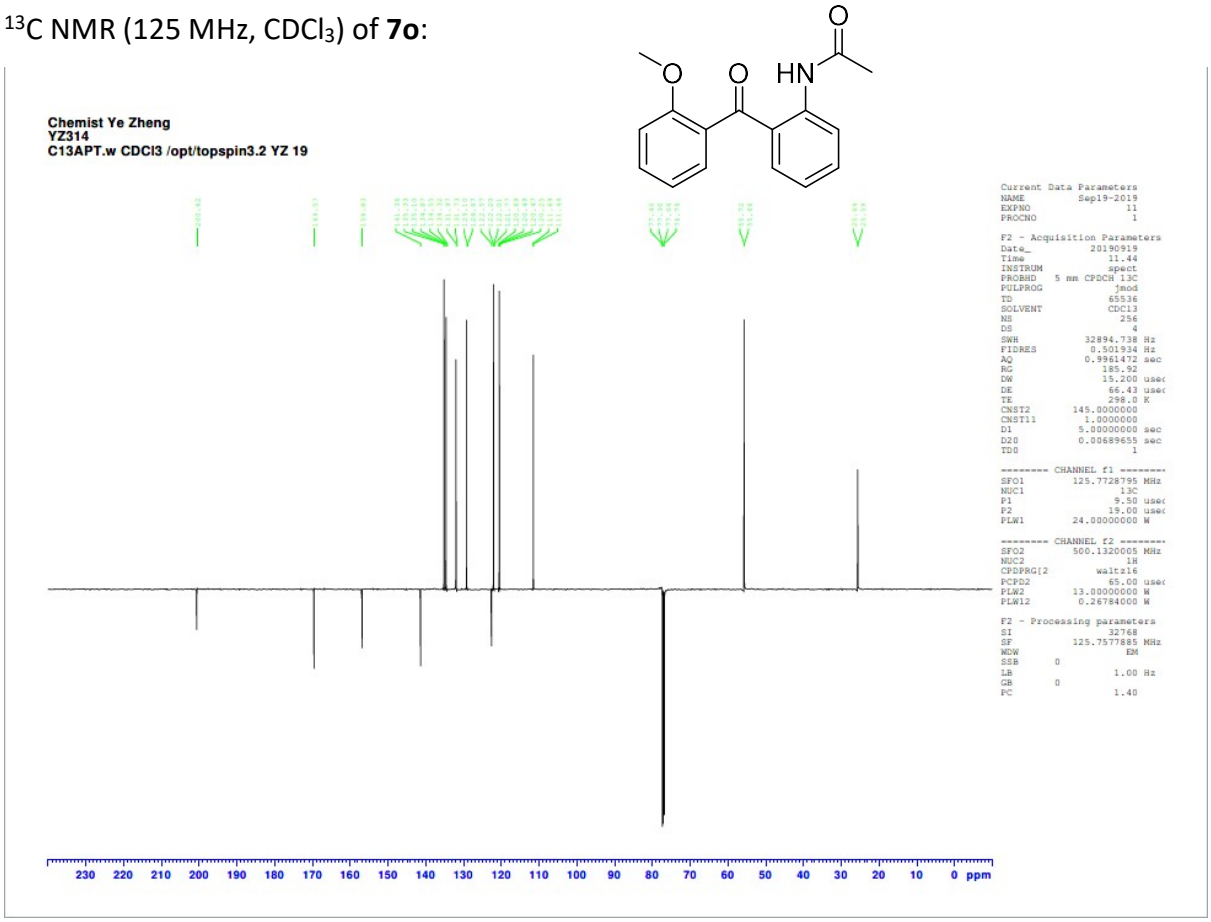
Reference: Wu, Y.; Choy, P. Y.; Mao, F.; Kwong, F. Y. *Chem. Commun.;* **2013**, *49*, 689 – 691.

To a solution of (2-aminophenyl)(2-methoxyphenyl)methanone (293.6 mg, 1.29 mmol) in DCM (6.5 mL) at 0°C was added pyridine (611.5 mg, 7.74 mmol) and acetyl chloride (121.8 mg, 1.55 mmol). The reaction mixture was left stirring under the nitrogen atmosphere and allowed to warm to rt. The reaction was followed by TLC (7:3 hexane: EtOAc). The mixture was quenched by 2M HCl solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 × 20 mL), and the combined organic layers were dried ($MgSO_4$) and filtered. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-60% ethyl acetate in hexane to give N-(2-(2-methoxybenzoyl)phenyl)acetamide **7o** as a white solid (229.6 mg, 0.854 mmol, 66%). TLC: Rf ca 0.40 (7:3 hexane: EtOAc), strong UV and $KMnO_4$; δ_H (500 MHz, $CDCl_3$) 11.59 (1H, s, NH), 8.74 (1H, d, *J* = 8.4, ArH), 7.57-7.51 (1H, m, ArH), 7.50-7.40 (2H, m, ArH), 7.30-7.24 (1H, m, ArH), 7.05 (1H, t, *J* = 7.4, ArH), 7.02-6.96 (2H, m, ArH), 3.75 (3H, s, OCH_3), 2.27 (3H, s, $COCH_3$) ppm; δ_C (125 MHz, $CDCl_3$) 200.6 (C), 196.6 (C), 158.8 (C), 141.4 (C), 135.1 (CH), 134.6 (CH), 132.0 (CH), 129.1 (CH), 122.6 (C), 122.0 (CH), 120.5 (CH), 120.5 (CH), 111.4 (CH), 55.7 (CH_3), 25.6 (CH_3) ppm. Data matched that reported.

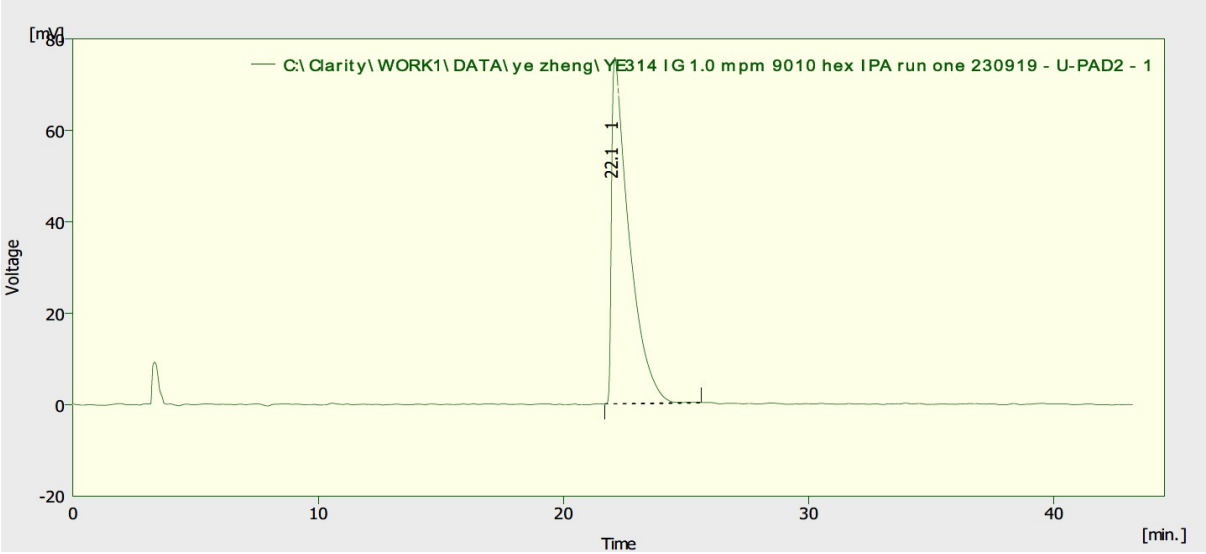
^{1}H NMR (500 MHz, $CDCl_3$) of **7o**:



^{13}C NMR (125 MHz, $CDCl_3$) of **7o**:



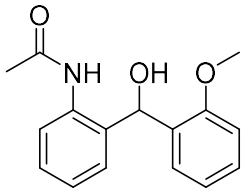
HPLC of N-(2-(2-methoxybenzoyl)phenyl)acetamide **7o**:



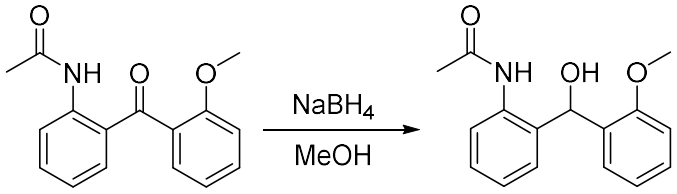
Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|ye zheng\|YE314 IG 1.0 mpm 9010 hex IPA run one 230919 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	22.092	3783.505	75.917	100.0	100.0	0.72	
	Total	3783.505	75.917	100.0	100.0		

N-(2-(Hydroxy(2-methoxyphenyl)methyl)phenyl)acetamide 8o.



racemic: YZ316, Asymmetric: YZ317



This compound is novel.

To a solution of N-(2-(2-methoxybenzoyl)phenyl)acetamide **7o** (139.6 mg, 0.519 mmol) in MeOH (3.7 mL) was added sodium borohydride (39.5 mg, 1.04 mmol). The reaction was stirred for 4 hours. TLC (3:2 hexane: EtOAc) after this time indicated full conversion. Distilled water (20 mL) was added, and the mixture was extracted with EtOAc (3 × 20ml), dried with $MgSO_4$, and the solvent was removed under vacuum to give crude product. The product was isolated via flash chromatography on silica eluted with 0-80% ethyl acetate in hexane to give N-(2-(Hydroxy(2-methoxyphenyl)methyl)phenyl)acetamide **8o** as a white solid (121.7 mg, 0.449 mmol, 86.5%). TLC: Rf ca 0.20 (3:2 hexane: EtOAc), strong UV and $KMnO_4$; Mp: 167.3 °C; HRMS: (found (ESI+): [M+Na]+, Calcd for $C_{16}H_{17}NNaO_3$ 294.1104; Found 294.1101; -1.2 ppm error; ν_{max} 3373, 1672, 1591, 1535, 1447, 1290, 1036, 1016, 784, 756 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 9.01 (1H, s, NH), 8.15 (1H, d, *J* = 8.0, ArH), 7.32 (2H, t, *J* = 7.7, ArH), 7.07-6.89 (5H, m, ArH), 6.09 (1H, d, *J* = 4.8, Ar*CH*OH), 3.90 (3H, s, OCH_3), 3.85 (1H, d, *J* =5.0, OH), 2.07 (3H, s, $COCH_3$) ppm; δ_C (125 MHz, $CDCl_3$) 168.4 (C), 156.9 (C), 137.3 (C), 130.1 (C), 129.4 (CH), 128.9 (C), 128.6 (CH), 128.2 (CH), 128.2 (CH), 124.0 (CH), 122.8 (CH), 121.3 (CH), 110.8 (CH), 72.8 (CH_3), 55.6 (CH_3) ppm; m/z (ES-API+) 294.2 (M^+ + 23, 100%).

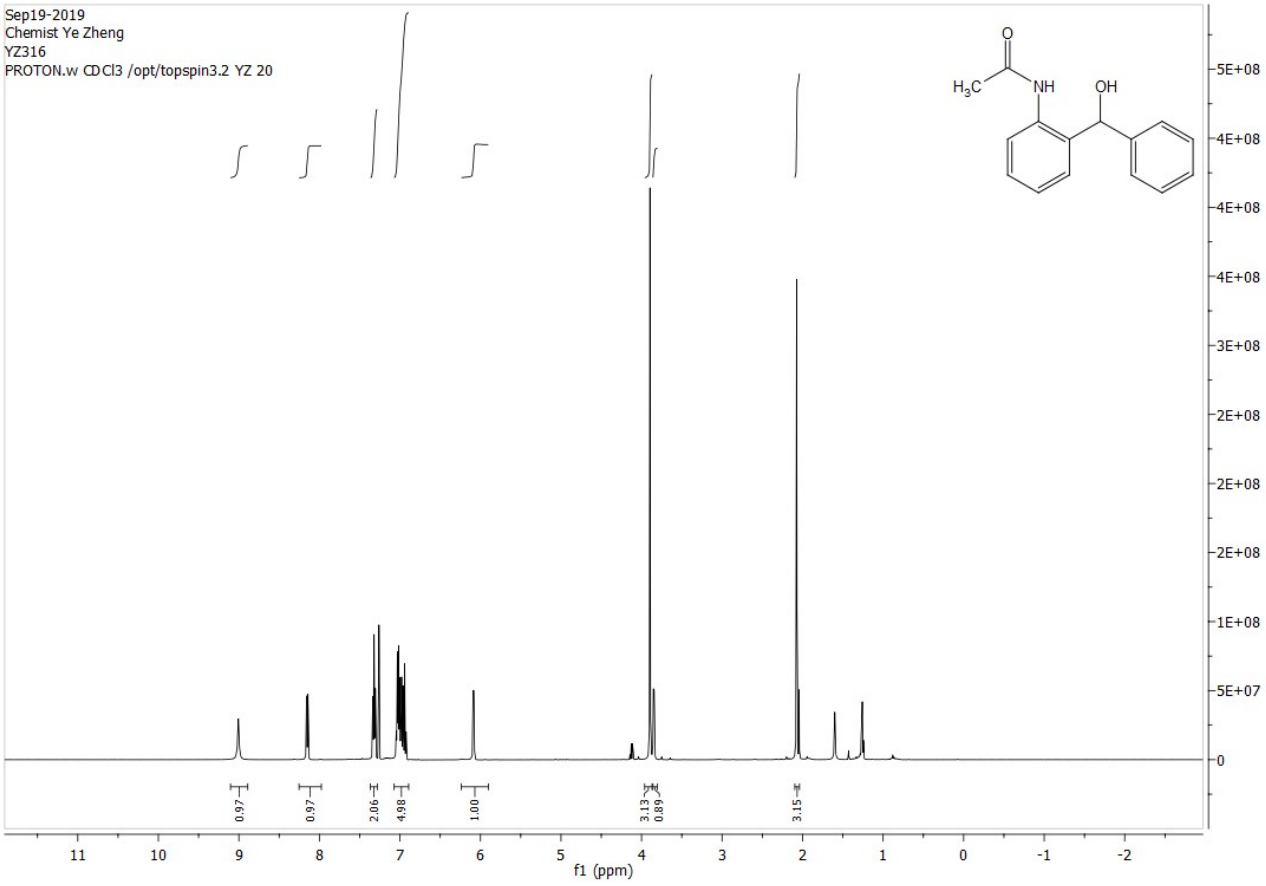
Enantiomeric excess and conversion determined by HPLC analysis (Chiralpak IG, 30 cm x 6mm column, hexane:iPrOH 9:1, 1.0 mL/min, T = 25°C) ketone 22.1 min, *R* and *S* isomers 40.4 min and 60.8 min, configuration was assigned by analogy.

ATH of N-(2-(2-methoxybenzoyl)phenyl)acetamide **7o** (YZ317).

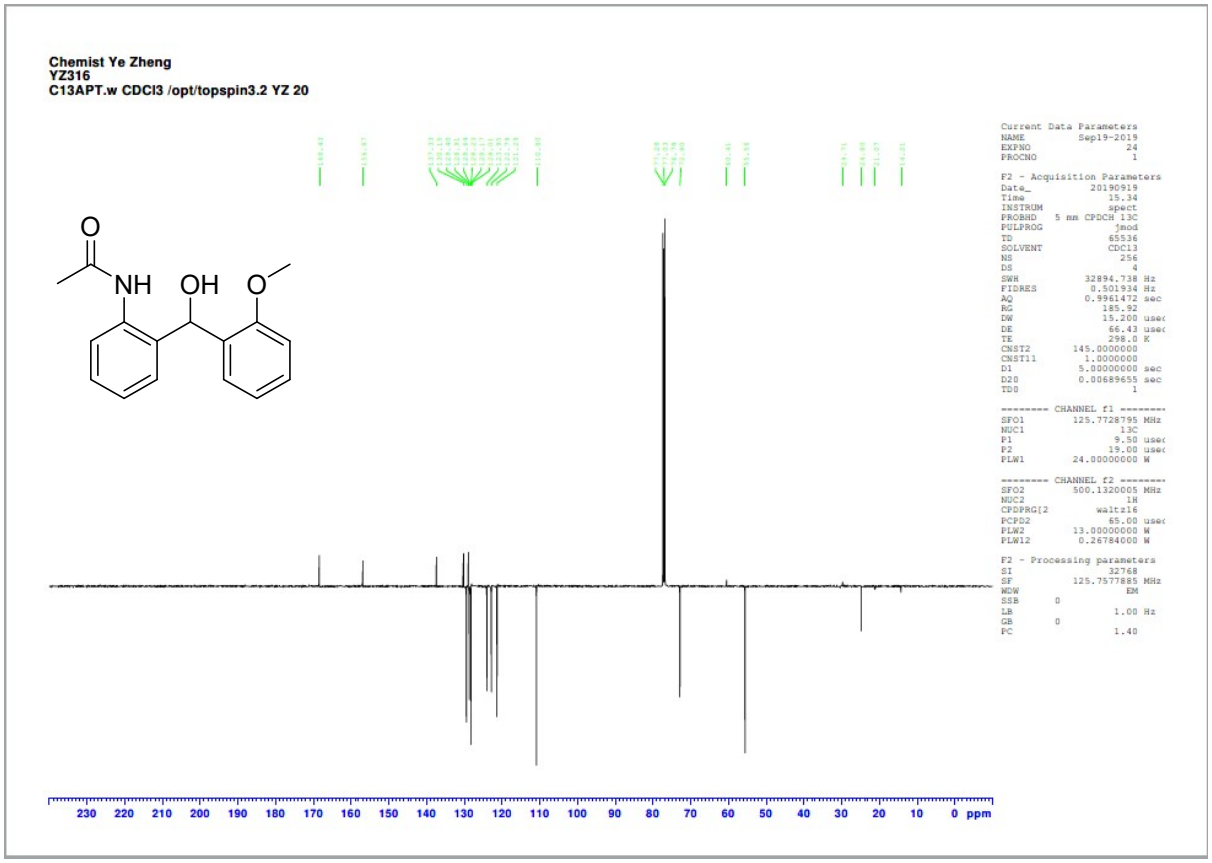
Catalyst (*R,R*)-**2** (0.00149 mmol, 1mol%) was added to the FA: TEA (5:2 azeotropic mixture, 0.18 mL) at rt and the mixture was stirred under a nitrogen atmosphere for 10-15 minutes; after which a solution of N-(2-(2-methoxybenzoyl)phenyl)acetamide **7o** (40 mg, 0.149 mmol) in DCM (0.25 mL)

was added. The reaction mixture was stirred under a nitrogen atmosphere, followed by TLC (3:2 hexane: EtOAc). After 168 hours, the reaction was quenched using saturated $NaHCO_3$ solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried ($MgSO_4$) and filtered. The solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-80% ethyl acetate in hexane to give N-(2-(hydroxy(2-methoxyphenyl)methyl)phenyl)acetamide **8o** (13.4 mg, 0.0494 mmol, 33.3%; (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst example). The reaction was also followed by HPLC analysis (Chiralpak IG, 30 cm x 6mm column, hexane:iPrOH 9:1, 1.0 mL/min, T = 25°C); (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst: 50% conversion; $[\alpha]_D^{26}$ +37.4 (c 0.0147 in $CHCl_3$) 59.4% ee. The conversion was established by NMR of the crude reduction mixture.

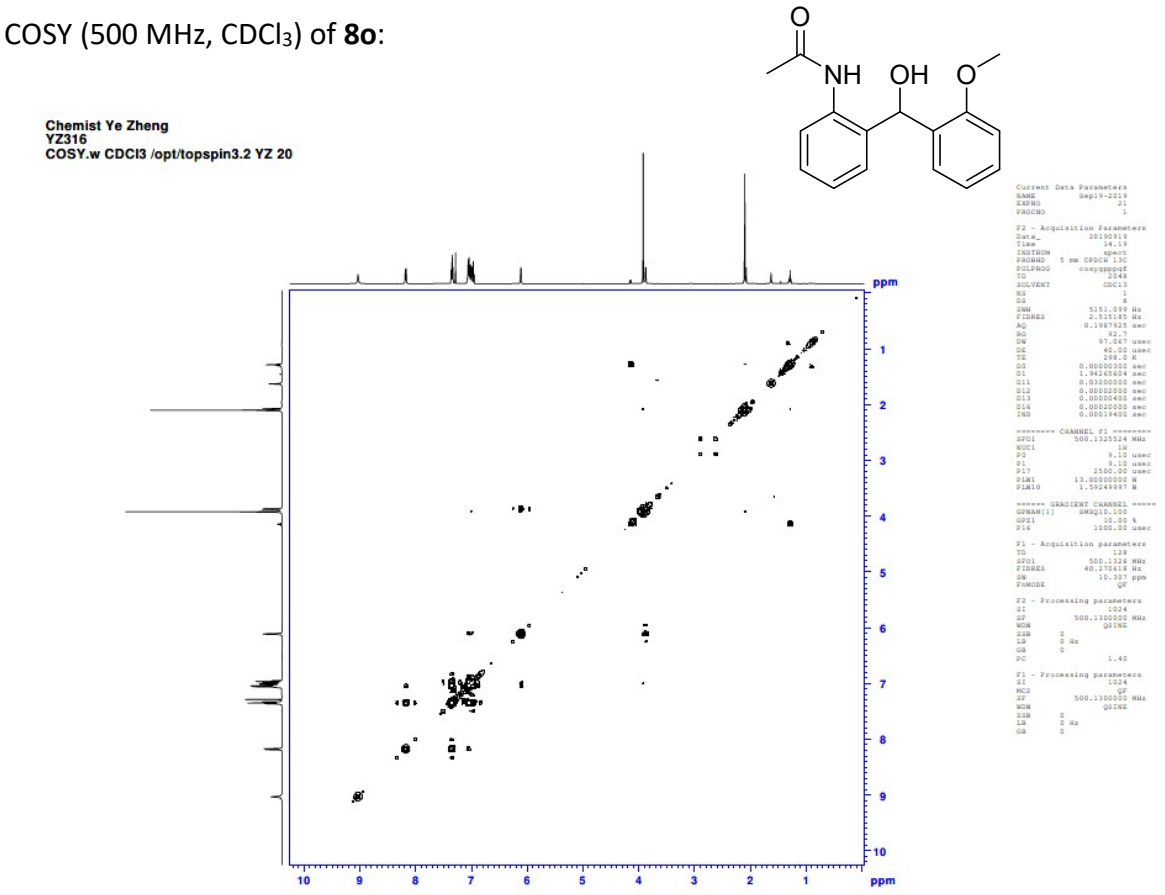
^1H NMR (500 MHz, $CDCl_3$) of **8o**:



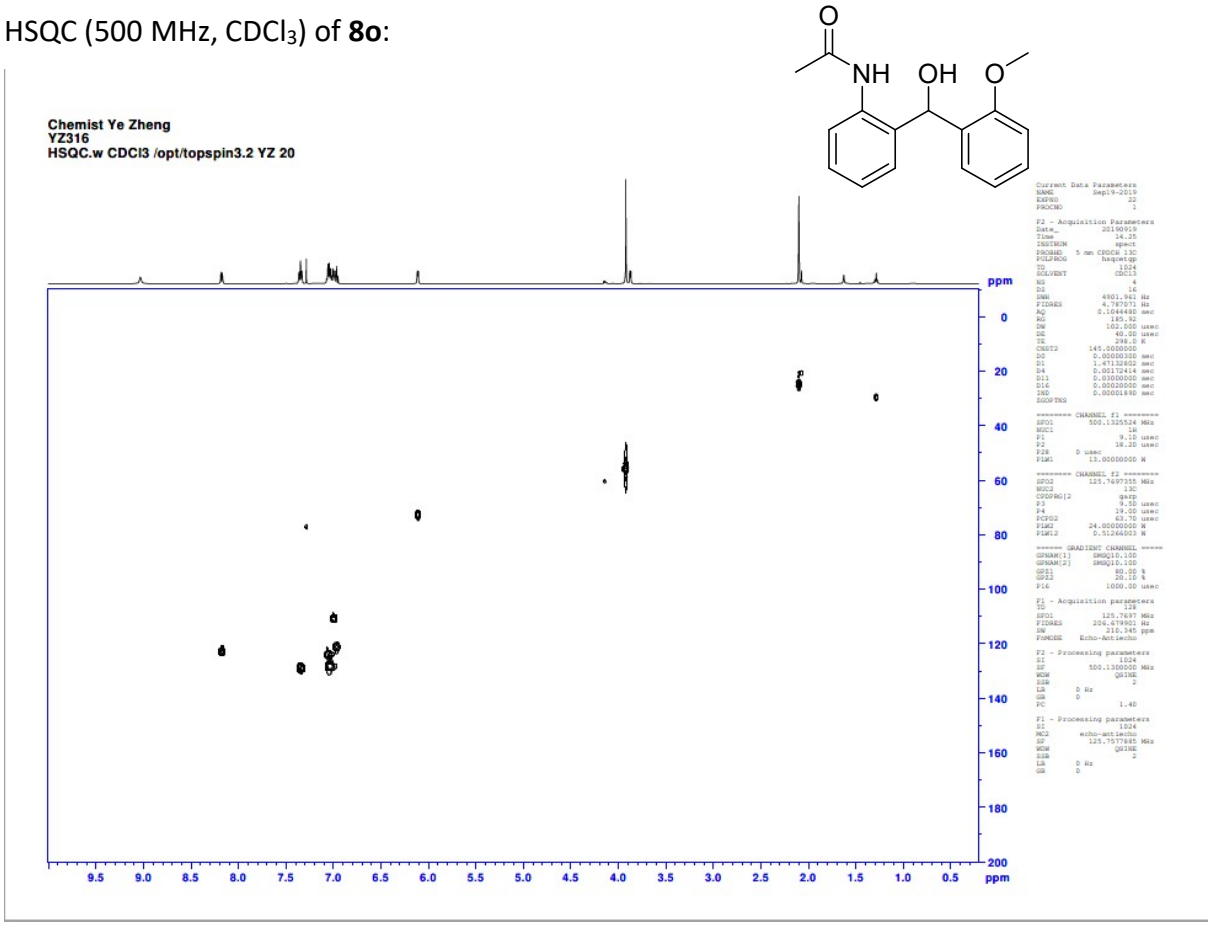
^{13}C NMR (125 MHz, $CDCl_3$) of **8o**:



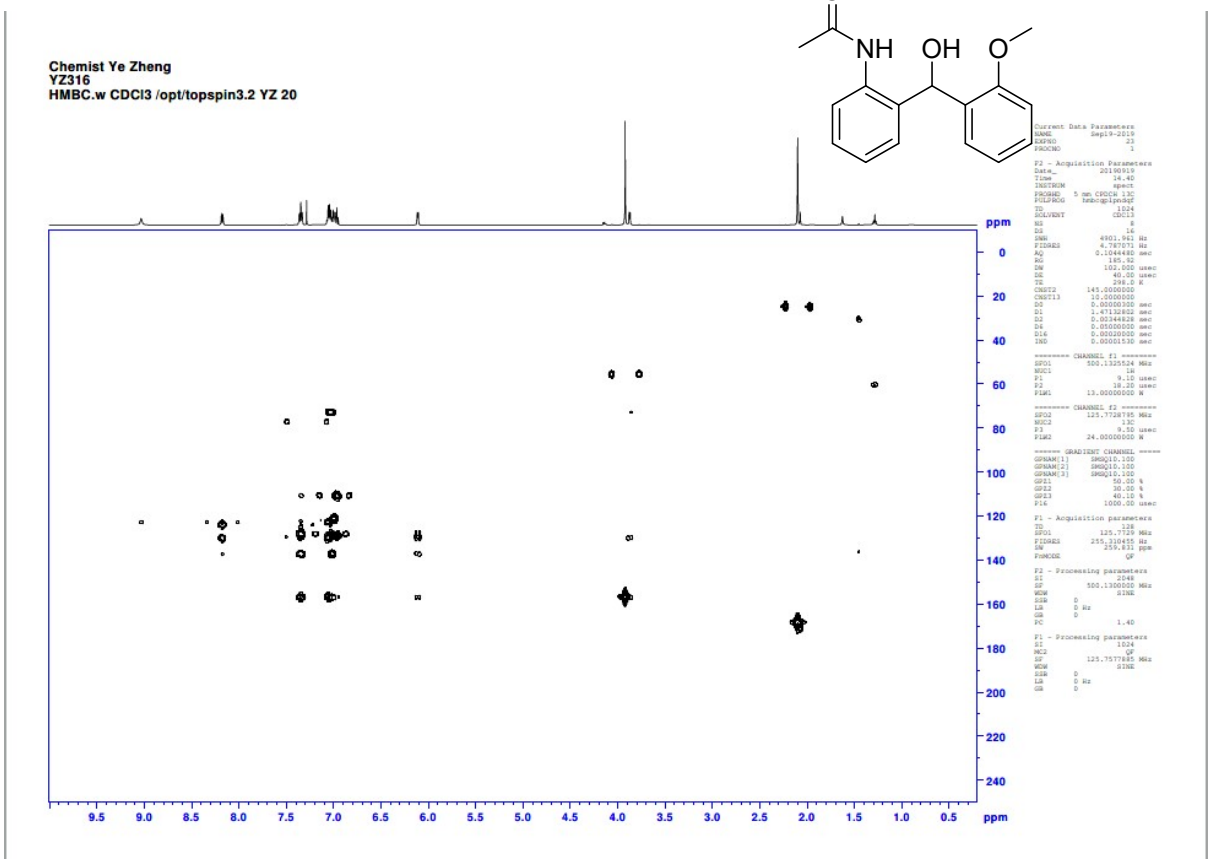
COSY (500 MHz, $CDCl_3$) of **8o**:



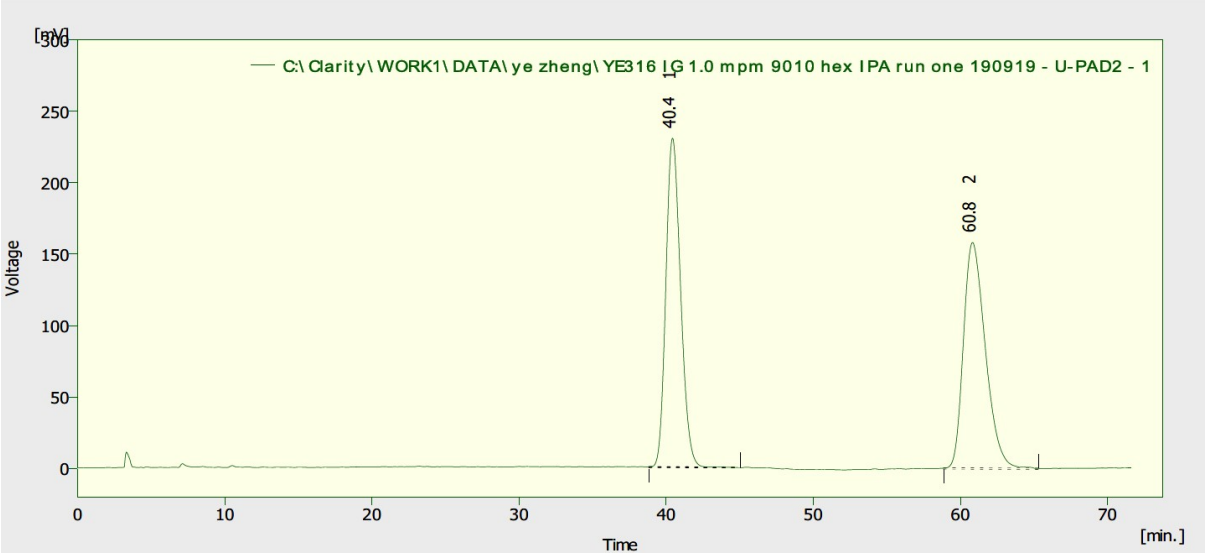
HSQC (500 MHz, $CDCl_3$) of **8o**:



HMBC (500 MHz, $CDCl_3$) of **8o**:



HPLC of racemic N-(2-(hydroxy(phenyl)methyl)phenyl)acetamide **8o**:

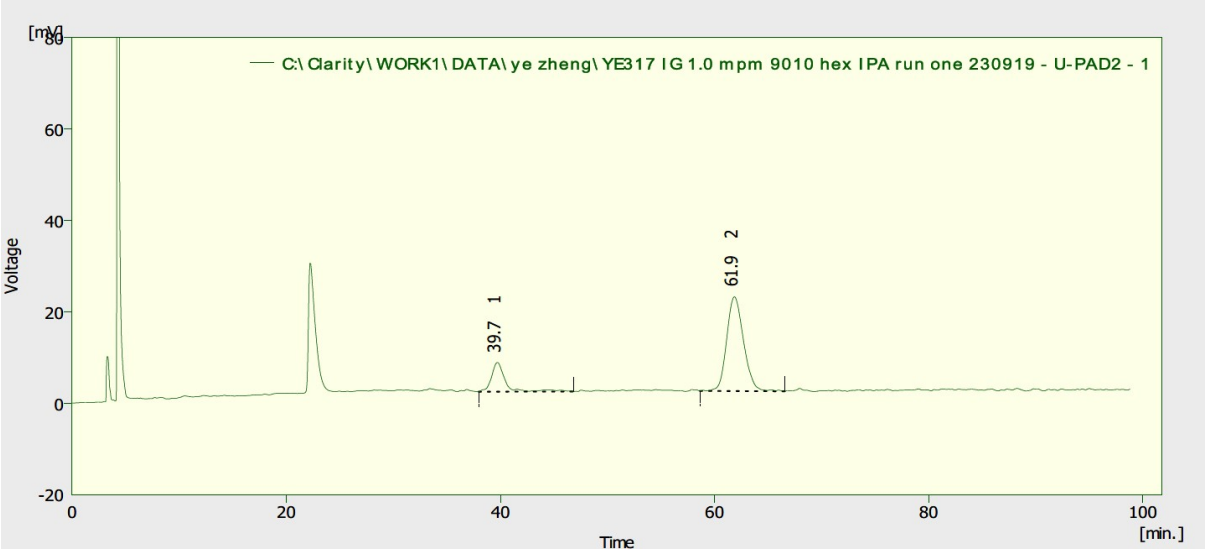


Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|ye zheng\|YE316 IG 1.0 mpm 9010 hex IPA run one 190919 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	40.432	16068.363	230.487	49.5	59.3	1.08	
2	60.824	16421.579	158.393	50.5	40.7	1.60	
	Total	32489.942	388.880	100.0	100.0		

HPLC of **8o** after ATH of N-(2-(2-methoxybenzoyl)phenyl)acetamide **7o**:

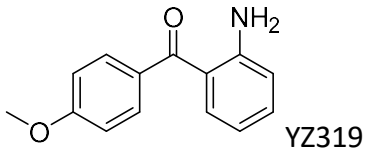
(*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst (after 168 hours, 50% conversion, 59.4% ee)



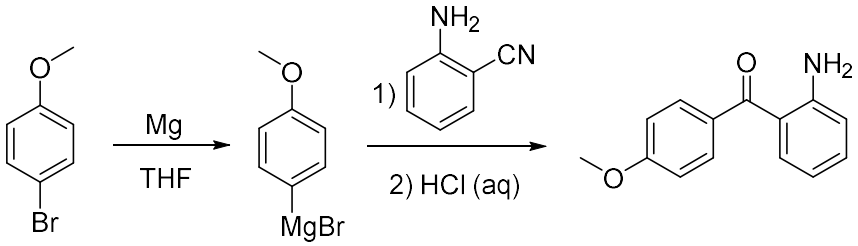
Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|ye zheng\|YE317 IG 1.0 mpm 9010 hex IPA run one 230919 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	39.704	579.105	6.406	20.3	23.7	1.17	
2	61.852	2272.845	20.658	79.7	76.3	1.68	
	Total	2851.949	27.064	100.0	100.0		

(2-Aminophenyl)(4-methoxyphenyl)methanone.



YZ319

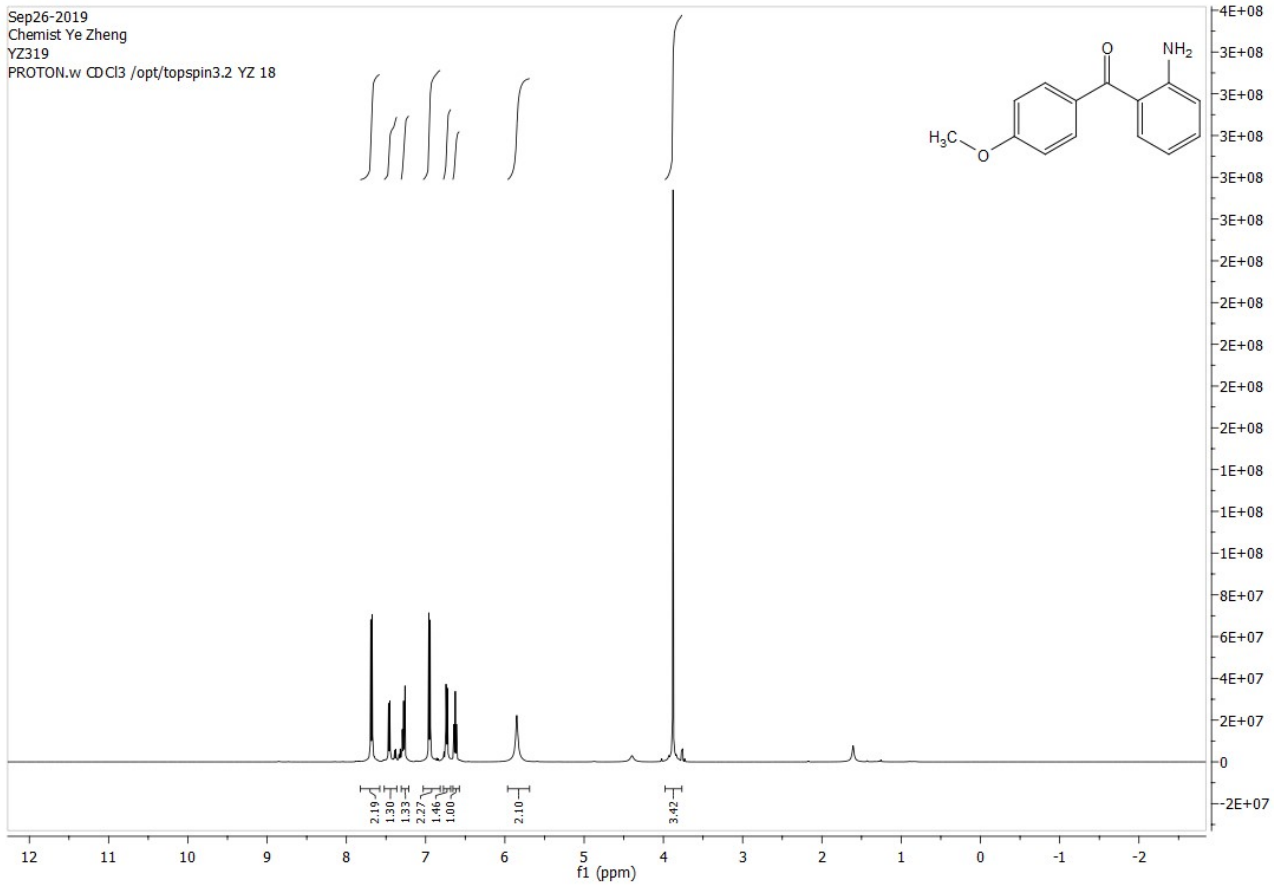


This compound has been reported and fully characterized.

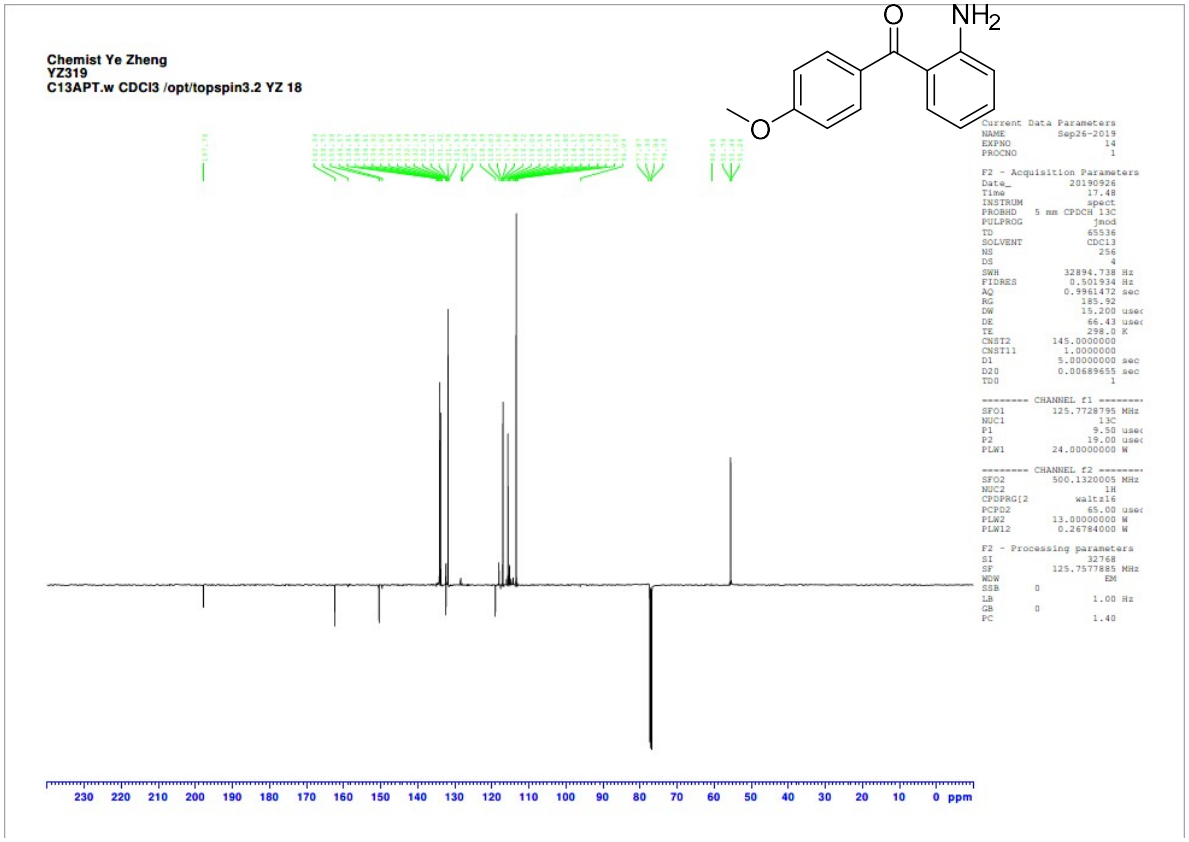
Reference: Caspers, L. D.; Finkbeiner, P.; Nachtsheim, B. J. *Chem.- Eur. J.* **2017**, *23*, 2748 – 2752.

To a solution of 4-bromoanisole (2.128 g, 12.3 mmol) in THF (12.3 mL) at rt was added magnesium (295.2 mg, 12.3 mmol). The reaction mixture was stirred under a nitrogen atmosphere at rt for 30 minutes and then heated to reflux on a hot plate for 1 hour. After cooling down to 0°C, a solution of 2-aminobenzonitrile (500 mg, 4.10 mmol) in THF (12.3 mL) was added dropwise and the reaction mixture was left stirring under the nitrogen atmosphere for 12 hours and allowed to warm to rt. After cooling down to 0°C, HCl solution (8.20 mL, 2.0 M, 16.4 mmol) was added dropwise and the mixture was stirred at rt for another 12 hours. The reaction was followed by TLC (4:1 hexane: EtOAc). The mixture was quenched by saturated $NaHCO_3$ solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 × 20 mL), and the combined organic layers were dried ($MgSO_4$) and filtered. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give (2-aminophenyl)(4-methoxyphenyl)methanone as a yellow solid (414 mg, 1.82 mmol, 44.5%). TLC: Rf ca 0.50 (4:1 hexane: EtOAc), strong UV and $KMnO_4$; δ_H (500 MHz, $CDCl_3$) 7.68 (2H, d, *J* = 8.8, ArH), 7.52-7.36 (1H, m, ArH), 7.31-7.21 (1H, m, ArH), 6.95 (2H, d, *J* = 8.8, ArH), 6.77-6.73 (1H, m, ArH), 6.63 (1H, t, *J* = 7.5, ArH), 5.85 (2H, s, NH_2), 3.88 (3H, s, OCH_3) ppm; δ_C (125 MHz, $CDCl_3$) 197.8 (C), 162.3 (C), 150.4 (C), 134.0 (CH), 133.7 (CH), 132.3 (C), 131.8 (CH), 119.0 (C), 117.0 (CH), 115.6 (CH), 113.4 (CH), 55.5 (CH_3). Data matched that reported.

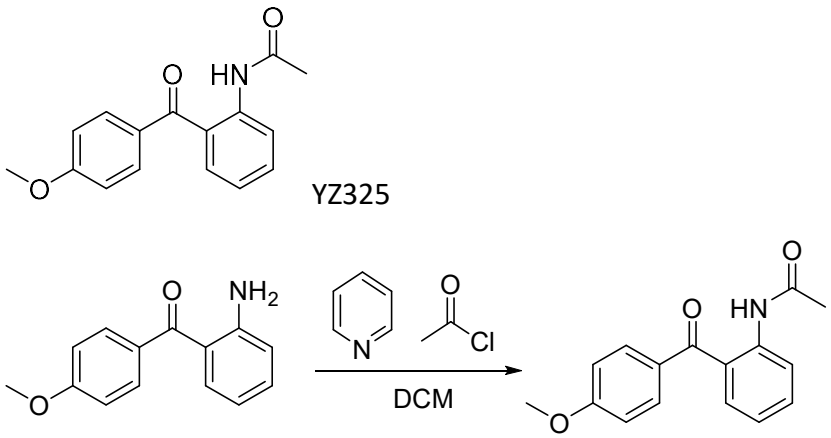
^{1}H NMR (500 MHz, $CDCl_3$) of (2-Aminophenyl)(4-methoxyphenyl)methanone:



^{13}C NMR (125 MHz, $CDCl_3$) of (2-Aminophenyl)(4-methoxyphenyl)methanone:



N-(2-(4-Methoxybenzoyl)phenyl)acetamide 7p.

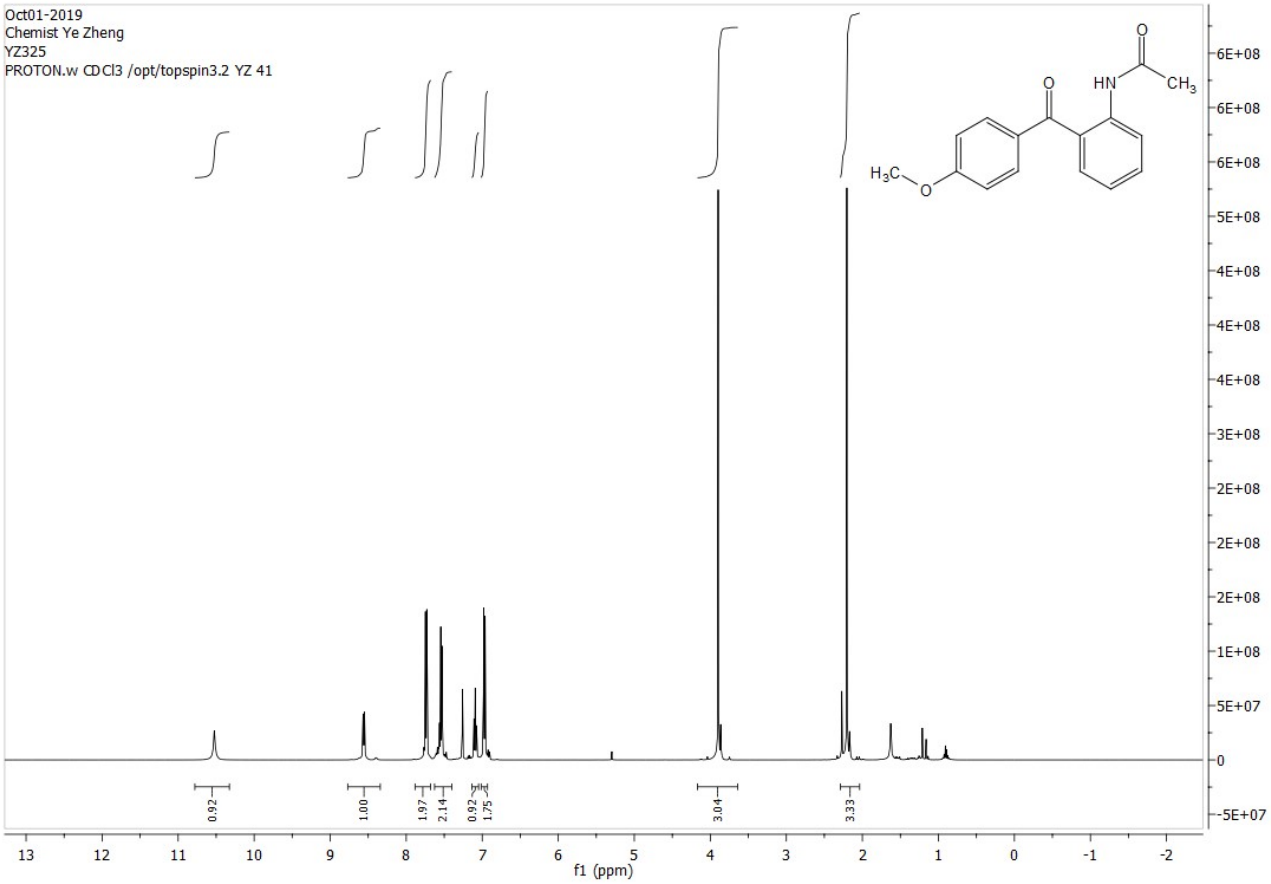


This compound has been reported and fully characterized.

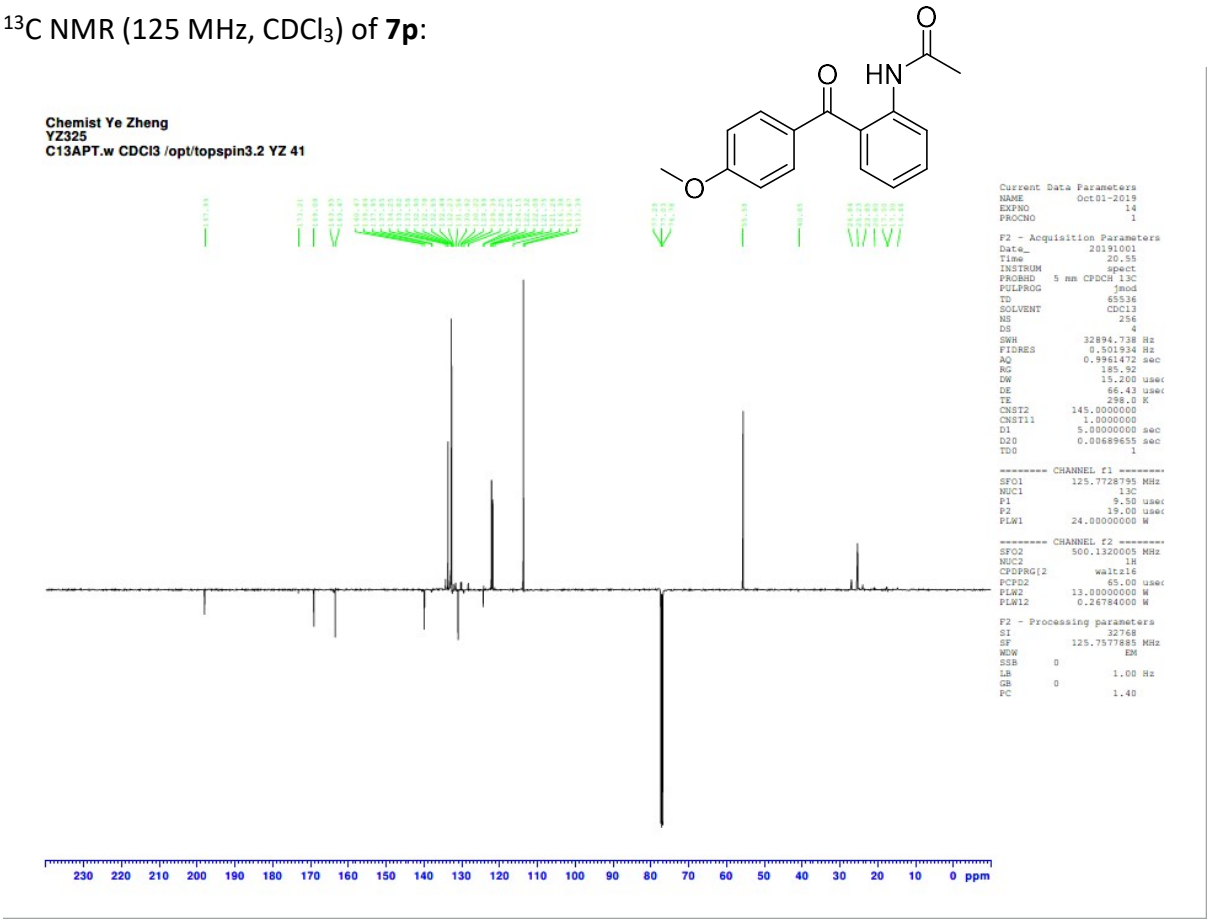
Reference: Wu, Y.; Choy, P. Y.; Mao, F.; Kwong, F. Y. *Chem. Commun.* **2013**, *49*, 689 – 691.

To a solution of (2-aminophenyl)(4-methoxyphenyl)methanone (476.8 mg, 2.10 mmol) in DCM (10.6 mL) at 0°C was added pyridine (995.4 mg, 12.6 mmol) and acetyl chloride (197.8 mg, 2.52 mmol). The reaction mixture was left stirring under the nitrogen atmosphere and allowed to warm to rt. The reaction was followed by TLC (7:3 hexane: EtOAc). The mixture was quenched by 2M HCl solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 × 20 mL), and the combined organic layers were dried ($MgSO_4$) and filtered. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-60% ethyl acetate in hexane to give N-(2-(4-methoxybenzoyl)phenyl)acetamide **7p** as a white solid (407 mg, 1.51 mmol, 72%). TLC: Rf ca 0.40 (7:3 hexane: EtOAc), strong UV and $KMnO_4$; δ_H (500 MHz, $CDCl_3$) 10.52 (1H, s, NH), 8.56 (1H, d, *J* = 8.2, ArH), 7.74 (2H, d, *J* = 8.8, ArH), 7.55 (2H, t, *J* = 8.0, ArH), 7.09 (1H, t, *J* = 7.6, ArH), 6.97 (2H, d, *J* = 8.8, ArH), 3.90 (3H, s, OCH_3), 2.20 (3H, s, $COCH_3$) ppm; δ_C (125 MHz, $CDCl_3$) 198.0 (C), 169.1 (C), 163.5 (C), 139.8 (C), 133.7 (CH), 132.8 (CH), 132.7 (CH), 130.9 (C), 124.3 (C), 122.1 (CH), 121.8 (CH), 1213.7 (CH), 55.6 (CH_3), 25.2 (CH_3) ppm. Data matched that reported.

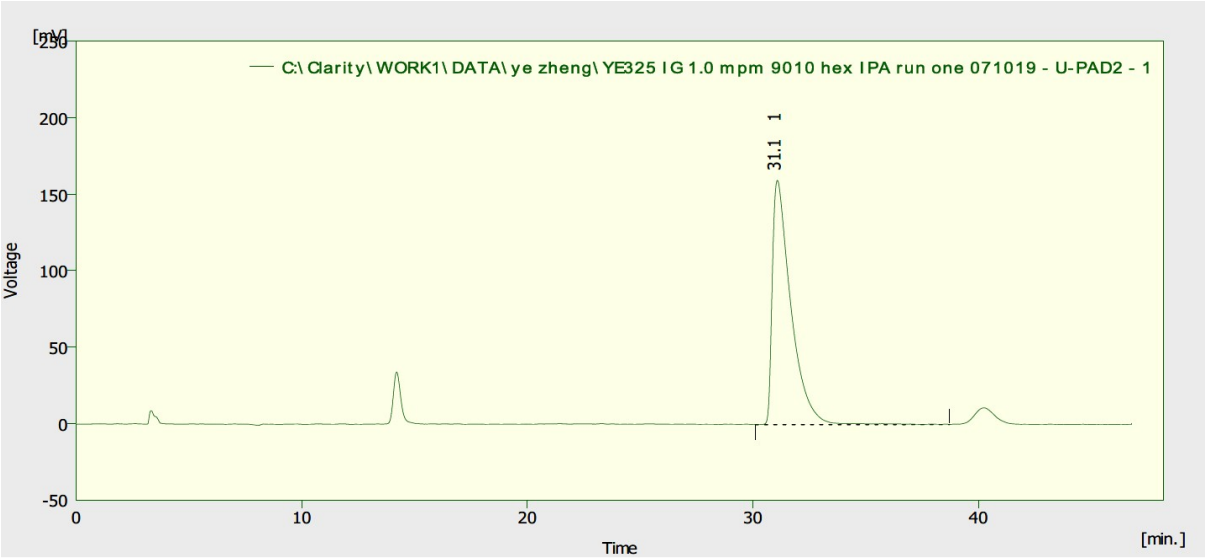
^{1}H NMR (500 MHz, $CDCl_3$) of **7p**:



^{13}C NMR (125 MHz, $CDCl_3$) of **7p**:



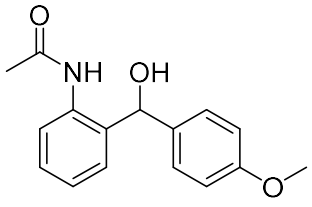
HPLC of N-(2-(2-methoxybenzoyl)phenyl)acetamide **7p:**



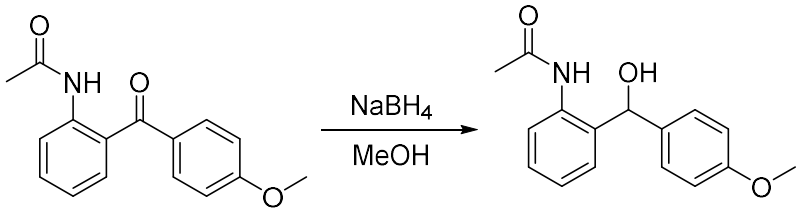
Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|ye zheng\|YE325 IG 1.0 mpm 9010 hex IPA run one 071019 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	31.088	9131.446	159.699	100.0	100.0	0.84	
	Total	9131.446	159.699	100.0	100.0		

N-(2-(Hydroxy(4-methoxyphenyl)methyl)phenyl)acetamide 8p.



racemic: YZ327, Asymmetric: YZ329.



This compound is novel.

To a solution of N-(2-(4-methoxybenzoyl)phenyl)acetamide (139.6 mg, 0.519 mmol) in MeOH (3.7 mL) was added sodium borohydride (39.5 mg, 1.04 mmol). The reaction was stirred for 4 hours. TLC (3:2 hexane: EtOAc) after this time indicated full conversion. Distilled water (20 mL) was added, and the mixture was extracted with EtOAc (3 × 20ml), dried with $MgSO_4$, and the solvent was removed under vacuum to give crude product. The product was isolated via flash chromatography on silica eluted with 0-80% ethyl acetate in hexane to give N-(2-(hydroxy(4-methoxyphenyl)methyl)phenyl)acetamide **8p** as a colorless oil (95.7 mg, 0.353 mmol, 68%). TLC: Rf ca 0.20 (3:2 hexane: EtOAc), strong UV and $KMnO_4$; HRMS: (found (ESI+): [M+Na]+, Calcd for $C_{16}H_{17}NNaO_3$ 294.1102; Found 294.1101; -0.4 ppm error; ν_{max} 3266 (br), 2998, 2959, 2836, 1633, 1610, 1509, 1368, 1244, 1029, 966 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 8.47 (1H, s, NH), 8.02 (1H, d, *J* = 8.1, ArH), 7.32 (1H, t, *J* = 8.4, ArH), 7.27-7.15 (2H, m, ArH), 7.14-7.02 (2H, m, ArH), 6.87 (2H, d, *J* = 8.7, ArH), 5.87 (1H, s, Ar*CH*OH), 3.80 (3H, s, OCH_3), 3.06 (1H, s, OH), 1.97 (3H, s, $COCH_3$) ppm; δ_C (125 MHz, $CDCl_3$) 168.6 (C), 159.2 (C), 136.6 (C), 134.2 (CH), 133.4 (C), 132.3 (C), 128.8 (CH), 128.7 (CH), 127.5 (CH), 124.2 (CH), 123.4 (CH), 114.0 (CH), 75.2 (CH), 55.3 (CH_3), 24.5 (CH_3) ppm; m/z (ES-API+) 294.2 (M^+ + 23, 100%).

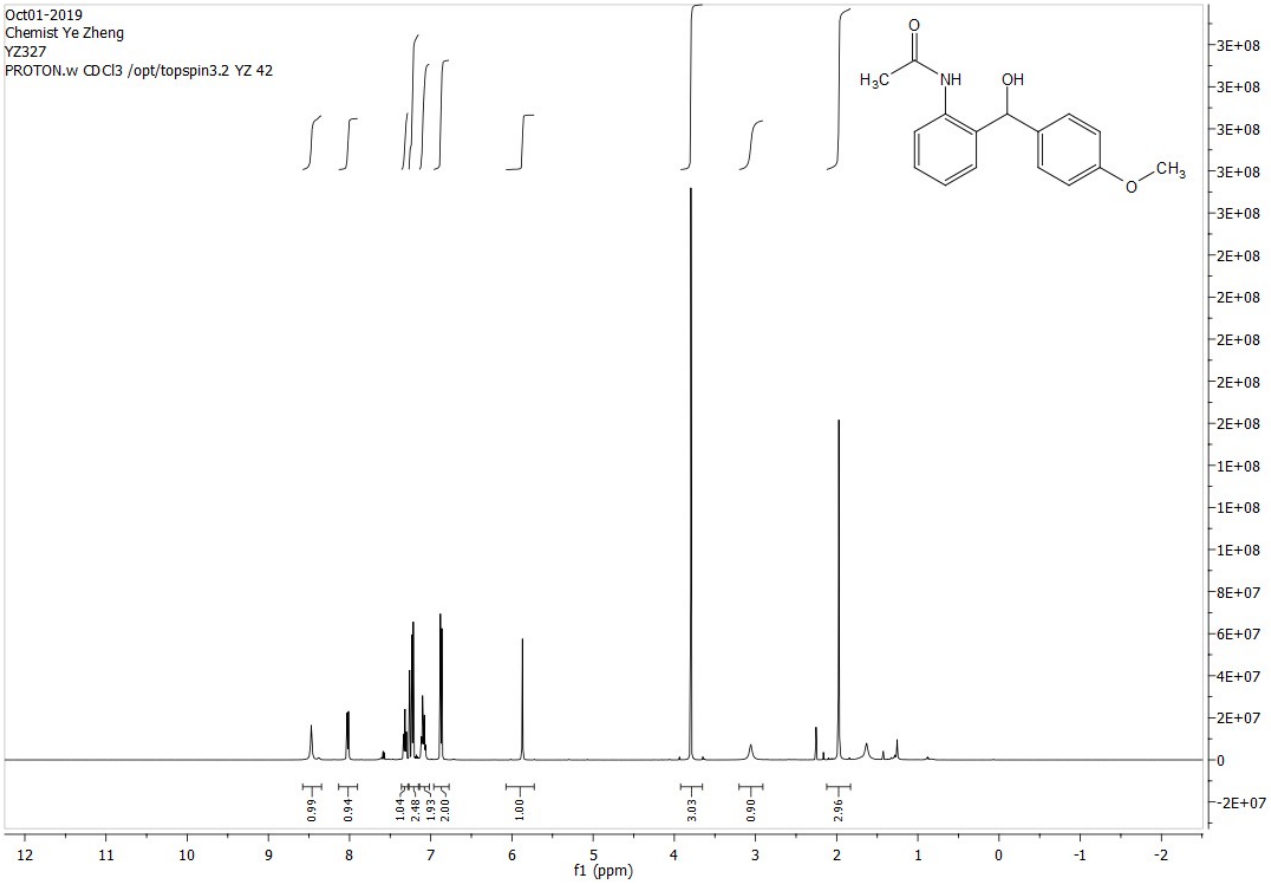
Enantiomeric excess and conversion determined by HPLC analysis (Chiralpak IG, 30 cm x 6mm column, hexane:iPrOH 9:1, 1.0 mL/min, T = 25°C) ketone 31.1 min, *R* and *S* isomers 39.4 min and 45.1 min, configuration was assigned by analogy.

ATH of N-(2-(4-methoxybenzoyl)phenyl)acetamide **7p** (YZ329).

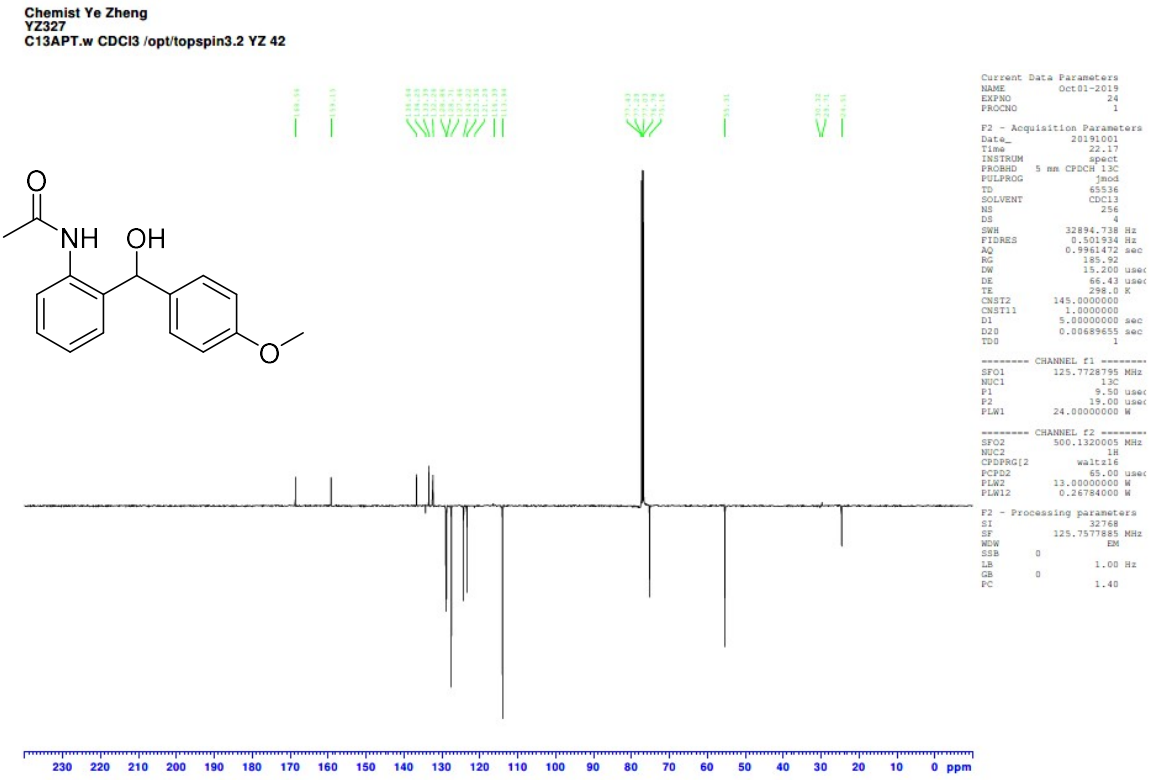
Catalyst (*R,R*)-**2** (0.00149 mmol, 1mol%) was added to the FA: TEA (5:2 azeotropic mixture, 0.18 mL) at rt and the mixture was stirred under a nitrogen atmosphere for 10-15 minutes; after which a solution of N-(2-(4-methoxybenzoyl)phenyl)acetamide **7p** (40 mg, 0.149 mmol) in DCM (0.25 mL)

was added. The reaction mixture was stirred under a nitrogen atmosphere, followed by TLC (3:2 hexane: EtOAc). After 168 hours, the reaction was quenched using saturated $NaHCO_3$ solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried ($MgSO_4$) and filtered. The solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-80% ethyl acetate in hexane to give N-(2-(hydroxy(4-methoxyphenyl)methyl)phenyl)acetamide (4.50 mg, 0.0166 mmol, 11.2%; (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst example). The reaction was also followed by HPLC analysis (Chiralpak IG, 30 cm x 6mm column, hexane:iPrOH 9:1, 1.0 mL/min, T = 25°C); (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst: 28.2% conversion; $[\alpha]_D^{24}$ -13.2 (c 0.0340 in $CHCl_3$) 53.6% ee. The conversion was established by NMR of the crude reduction mixture.

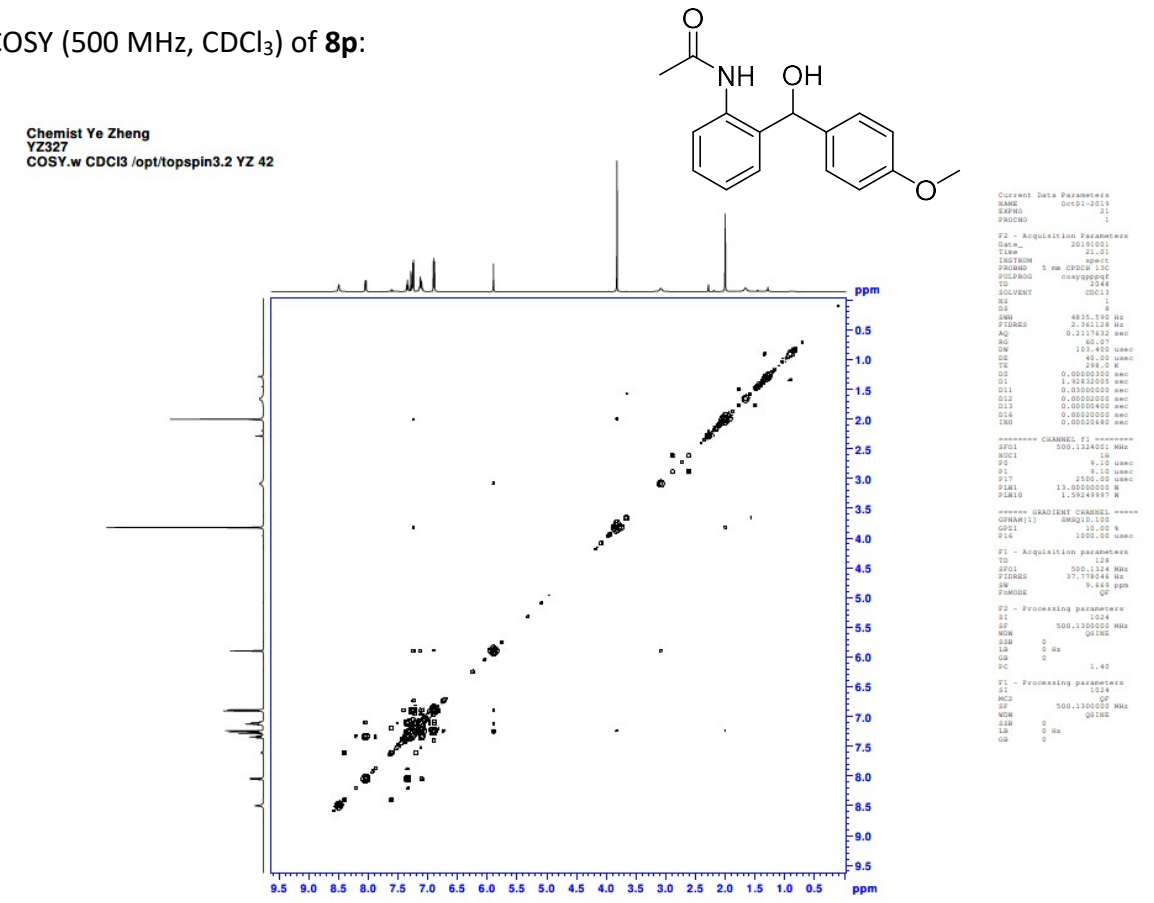
^{1}H NMR (500 MHz, $CDCl_3$) of **8p**:



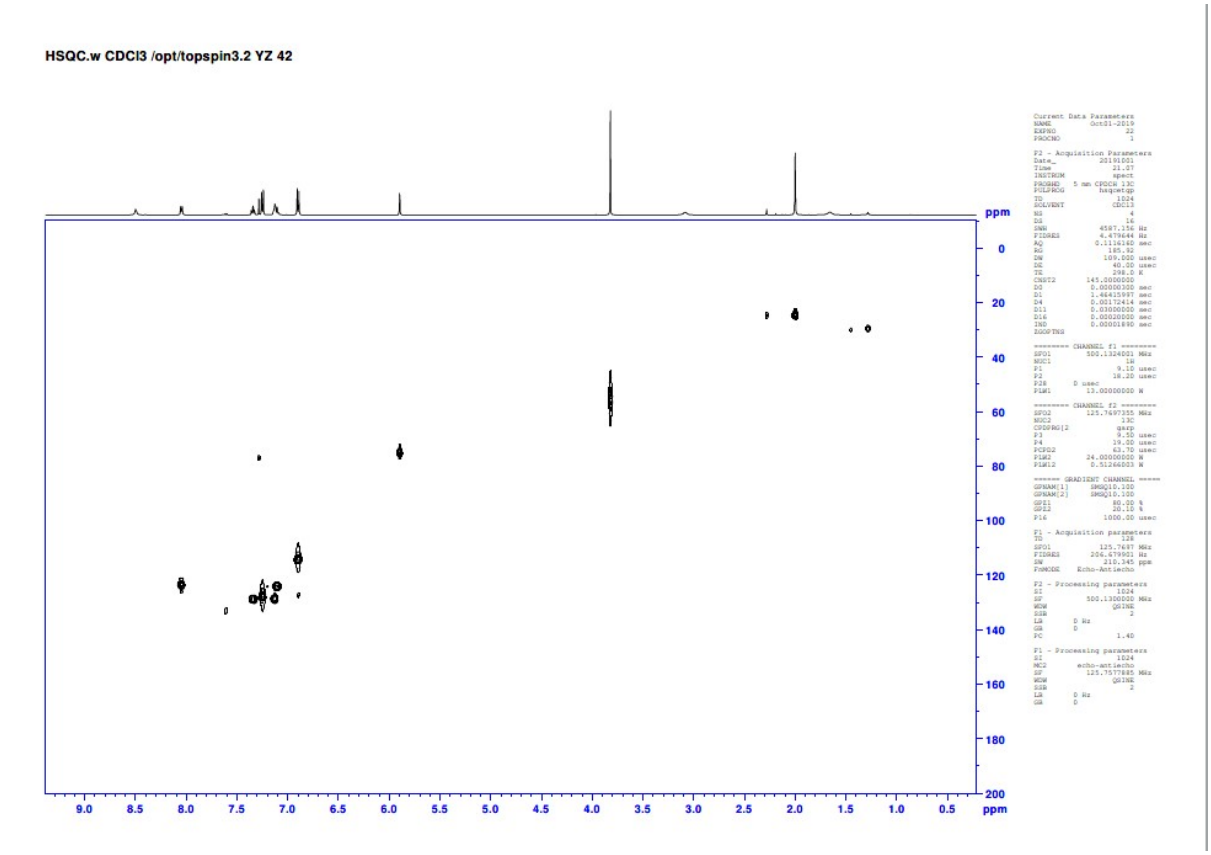
^{13}C NMR (125 MHz, $CDCl_3$) of **8p**:



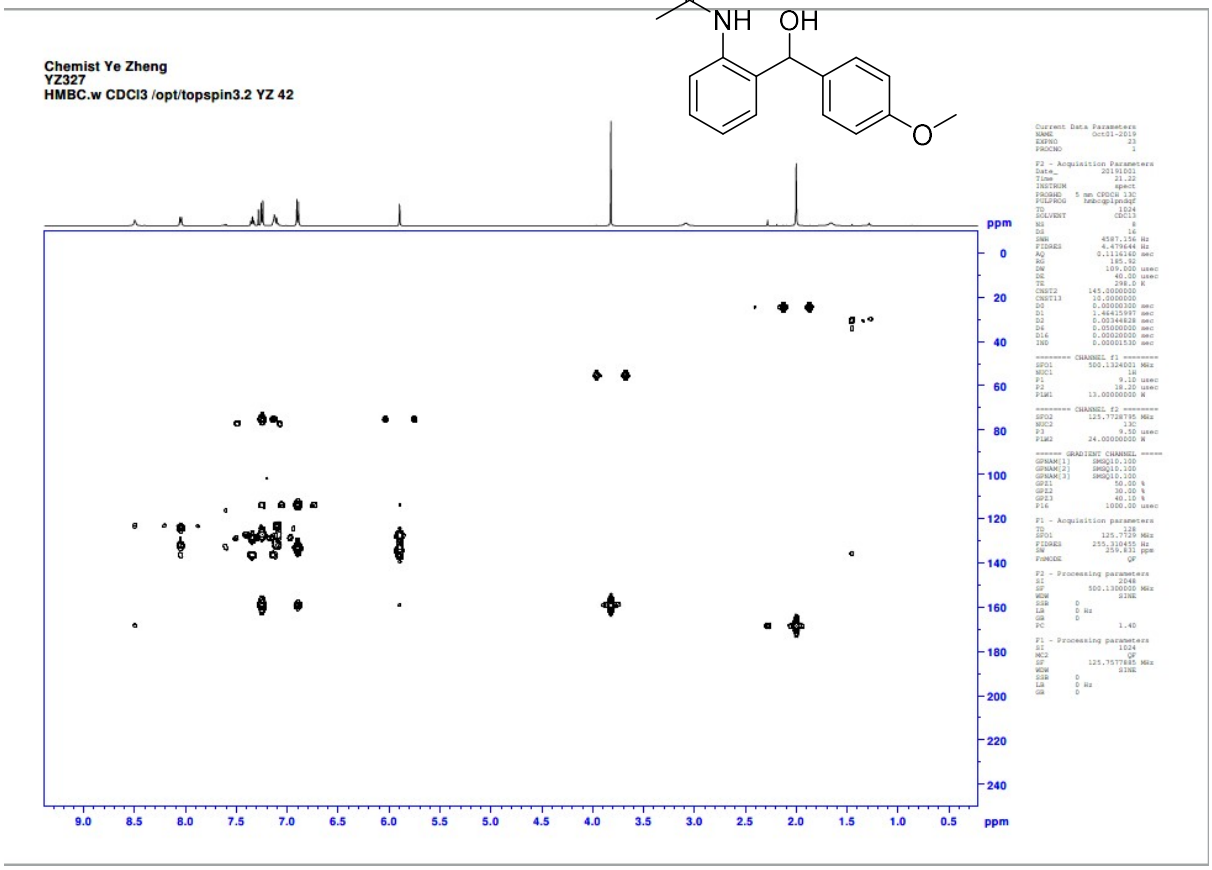
COSY (500 MHz, $CDCl_3$) of **8p**:



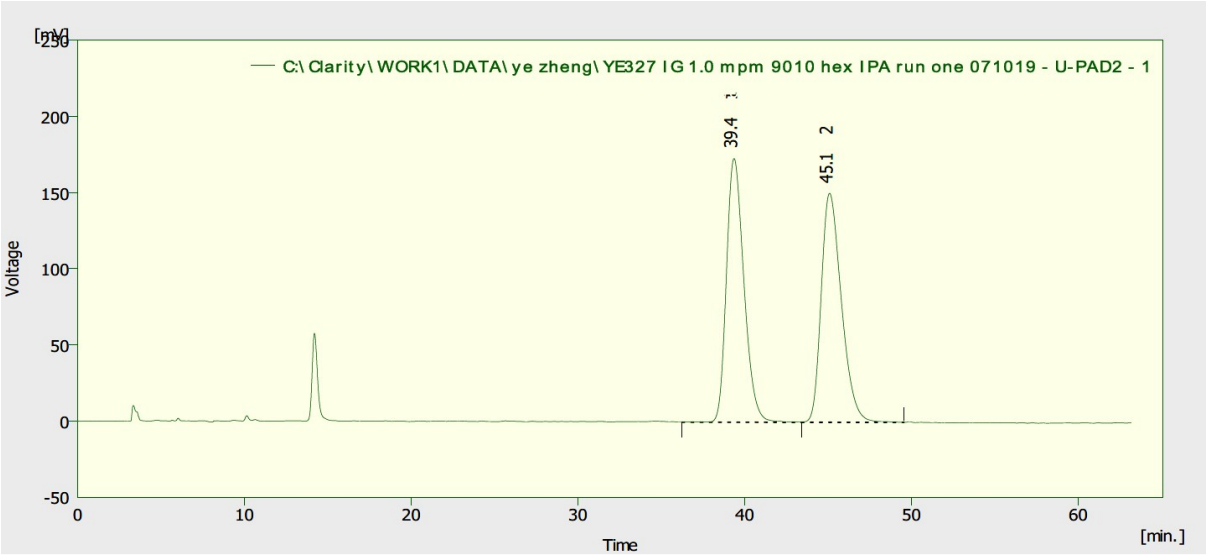
HSQC (500 MHz, $CDCl_3$) of **8p**:



HMBC (500 MHz, $CDCl_3$) of **8p**:



HPLC of racemic N-(2-(hydroxy(4-methoxyphenyl)methyl)phenyl)acetamide **8p**:

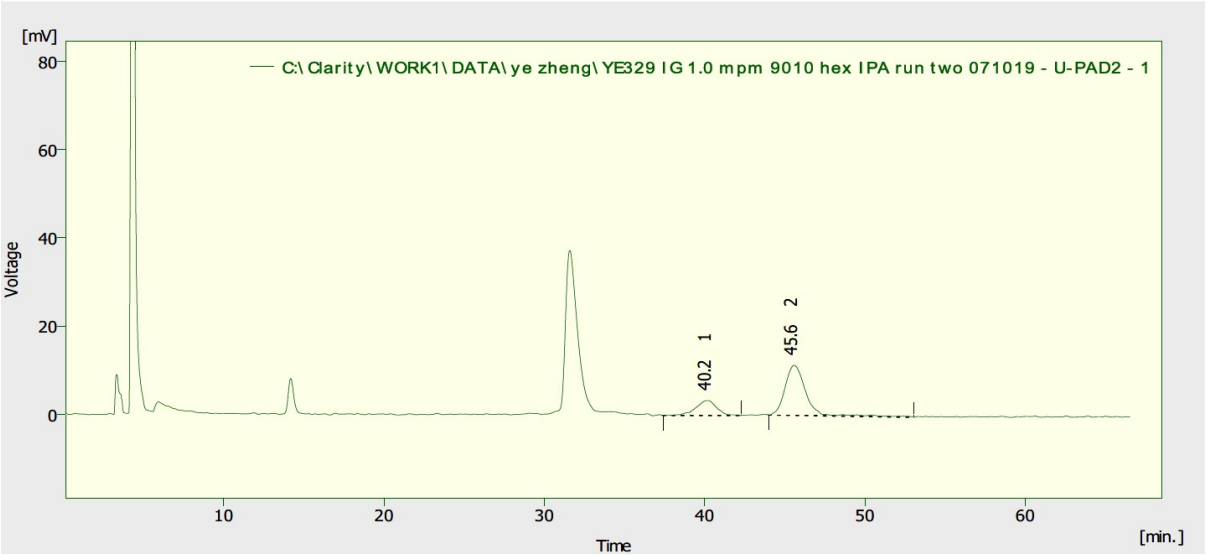


Result Table (Uncal - C:|Clarity|WORK1|DATA|ye zheng|YE327 IG 1.0 mpm 9010 hex IPA run one 071019 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	39.360	12646.139	173.261	50.0	53.5	1.13	
2	45.092	12654.068	150.439	50.0	46.5	1.30	
	Total	25300.207	323.700	100.0	100.0		

HPLC of **8p** after ATH of N-(2-(4-methoxybenzoyl)phenyl)acetamide **7p**:

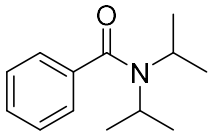
(*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst (after 168 hours, 28.2% conversion, 53.6% ee).



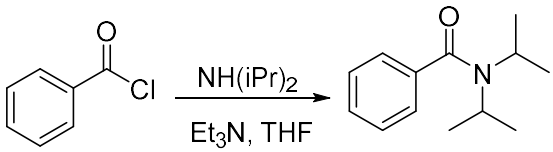
Result Table (Uncal - C:|Clarity|WORK1|DATA|ye zheng|YE329 IG 1.0 mpm 9010 hex IPA run two 071019 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	40.188	308.631	3.383	23.2	23.0	1.35	
2	45.572	1020.682	11.325	76.8	77.0	1.31	
	Total	1329.313	14.709	100.0	100.0		

N,N-Diisopropylbenzamide.



YZ209

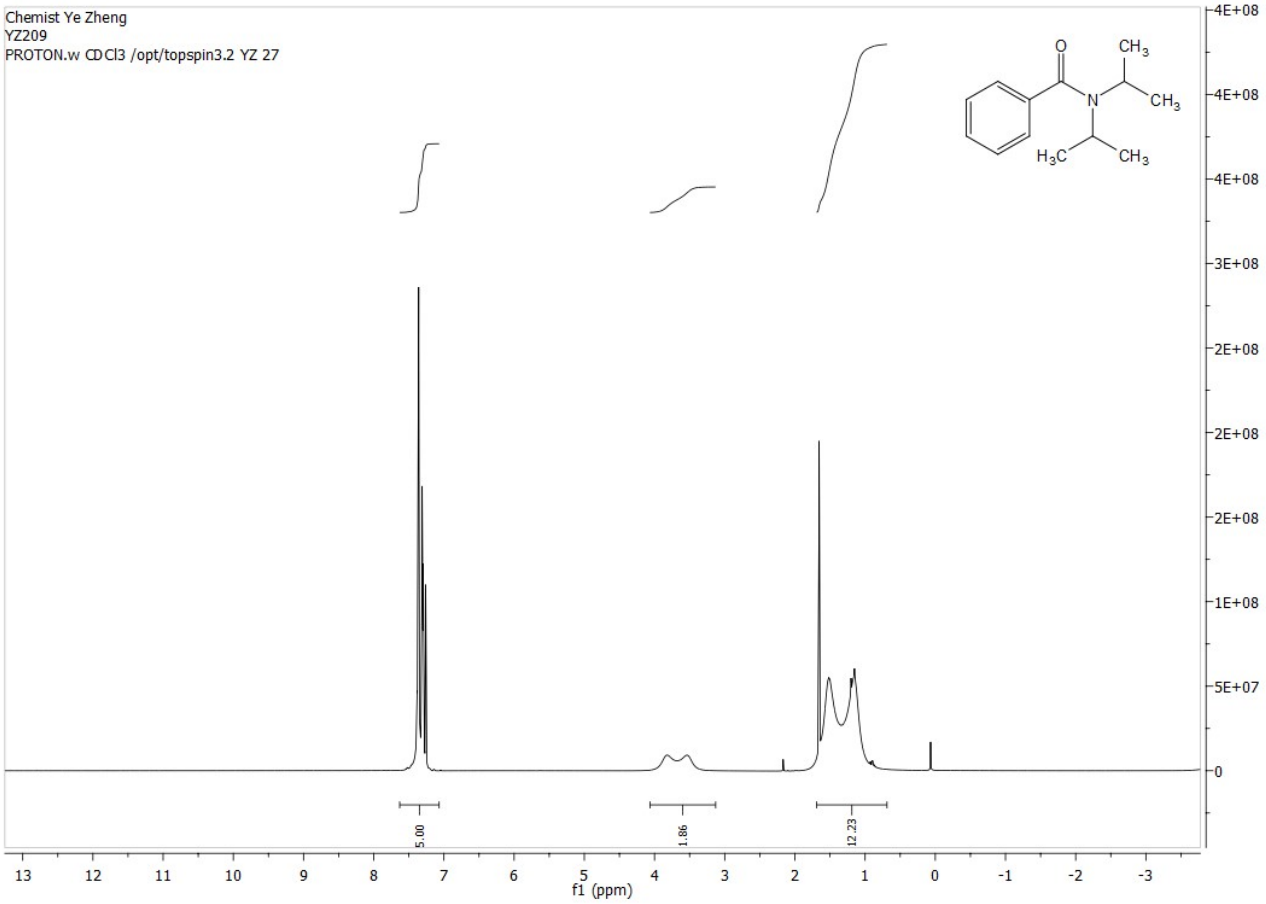


This compound has been reported and fully characterized.

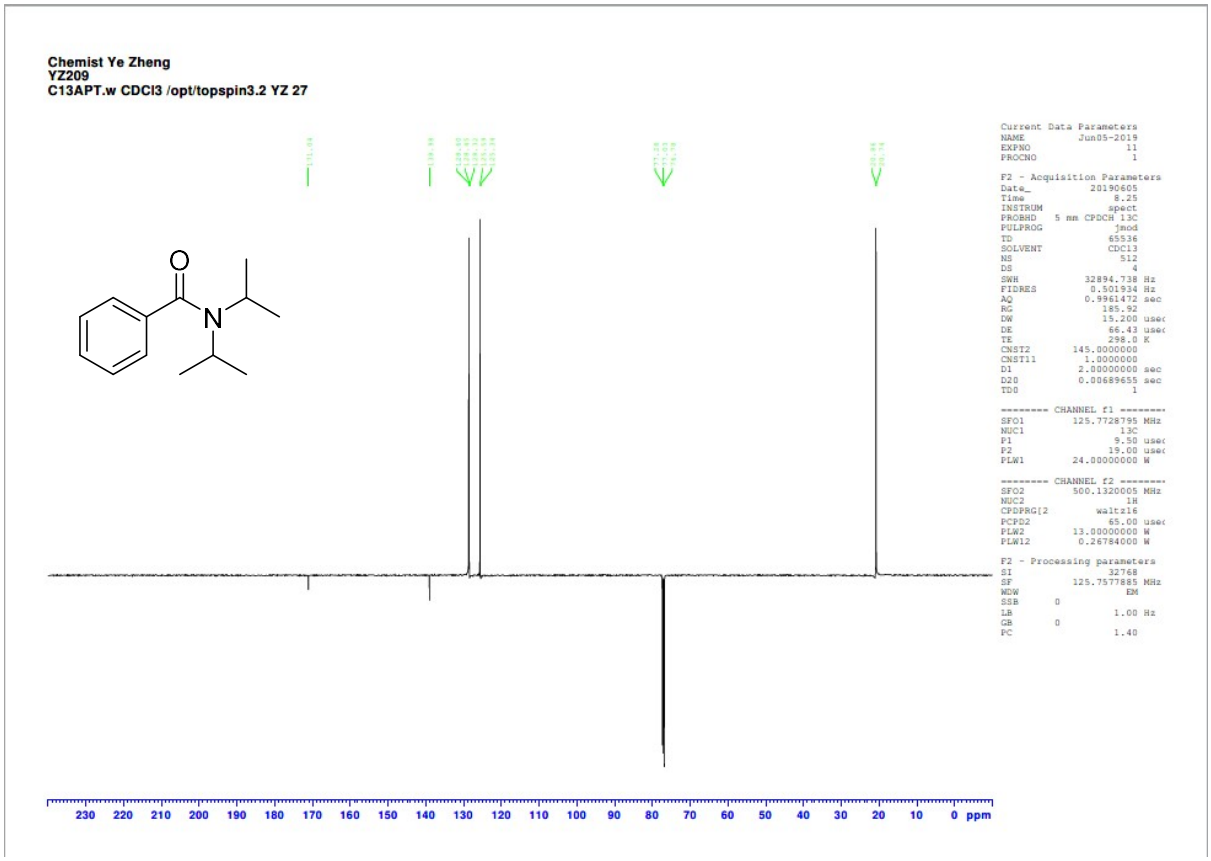
References: Laufer, R. S.; Dmitrienko, G. I.; *J. Am. Chem. Soc.* **2002**, *12*, 1854-1855.

To a solution of benzoyl chloride (421.5 mg, 3.0 mmo) in THF (10 mL) at 0 °C was added dropwise diisopropylamine (454.5 mg, 4.5 mmol) and Et3N (606 mg, 6.0 mmol). The reaction mixture was left stirring under the nitrogen atmosphere and allowed to warm to rt. The reaction was followed by TLC (4:1 hexane: EtOAc). The mixture was quenched by saturated NH_4Cl solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 × 20 mL), and the combined organic layers were washed with 1M HCl solution (2 ×20 mL), 1M Na_2CO_3 solution (20 mL) and brine (20 mL), dried ($MgSO_4$) and filtered. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give N,N-Diisopropylbenzamide as a white solid (552 mg, 2.69 mmol, 89.8%). TLC: Rf ca 0.40 (4:1 hexane: EtOAc), strong UV and $KMnO_4$; δ_H (500 MHz, CDCl3) 7.37-7.26 (5H, m, ArH), 3.83-3.53 (2H, m, NCH), 1.52-1.15 (12H, m, CH_3) ppm; δ_C (125 MHz, CDCl3) 171.0 (C), 139.0 (C), 128.6 (CH), 128.5 (CH), 125.6 (CH), 20.7 (CH_3) ppm. Data matched that reported.

^{1}H NMR (500 MHz, $CDCl_3$) of N,N-Diisopropylbenzamide:



^{13}C NMR (125 MHz, $CDCl_3$) of N,N-Diisopropylbenzamide:



Note on synthesis of **7q**.

Substrate **7q** was prepared by the addition of anion **A** to aldehyde **B**, followed by TBS removal and oxidation. An X-ray crystallographic structure of the initial adduct formed between **A** and **B** however revealed it to be the product **C** of TBS migration from the phenolic to the secondary alkyl hydroxyl group (Figure S1).

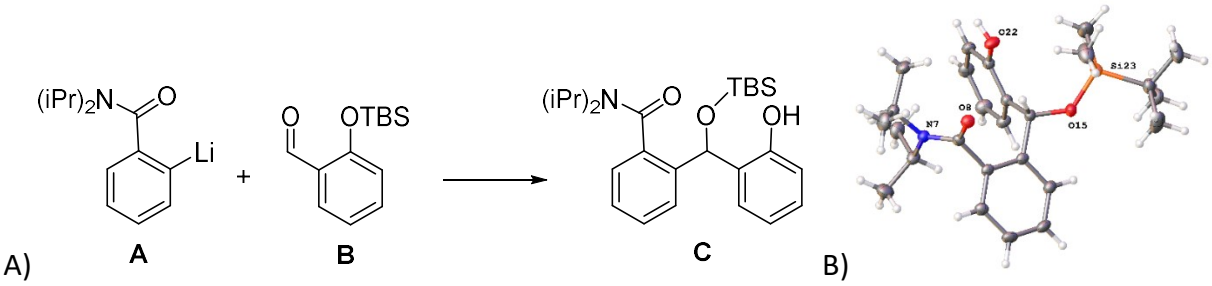
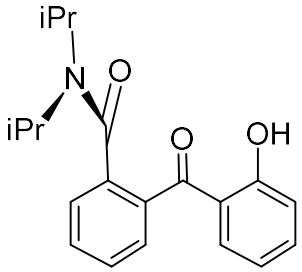


Figure S1. A). Formation of the precursor to **7q** results in TBS migration to form **C**. B). X-ray crystallographic structure of **C**.

Ketone **7q** and alcohol **8q** exhibited interesting rotameric properties, reflecting the likely out-of-plane conformation of the amide group, as evidenced by the peaks in their ^{1}H-NMR structures (Figure S2). Compound **7q** had two NCH resonances in the 1H-NMR spectrum (as did **7r**), reflecting the stereochemical non-equivalence of its isopropyl groups, whereas **8q** exhibited two major and two minor NCH peaks in the 1H-NMR spectrum, i.e. corresponding to the NCH of each isopropyl of the two diastereomers.

A. The iPr groups in **7p** are not equivalent hence two NCH resonances are observed:



B. Two diasteremers of **8p** may be formed, hence four NCH resonances are observed:

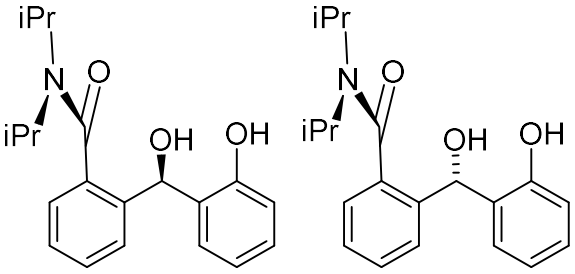
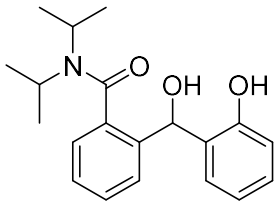


Figure S2. Diastereomers formed by **7q** and **8q**.

2-(Hydroxy(2-hydroxyphenyl)methyl)-N,N-diisopropylbenzamide 8q.



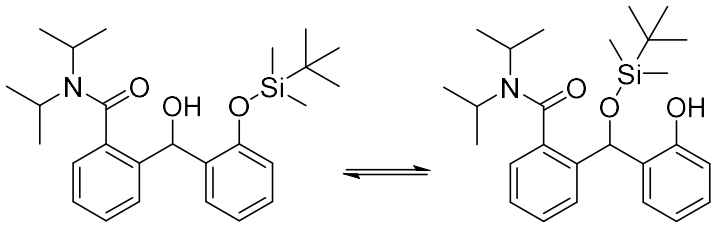
racemic: YZ249 Asymmetric: YZ251.

This compound is novel.

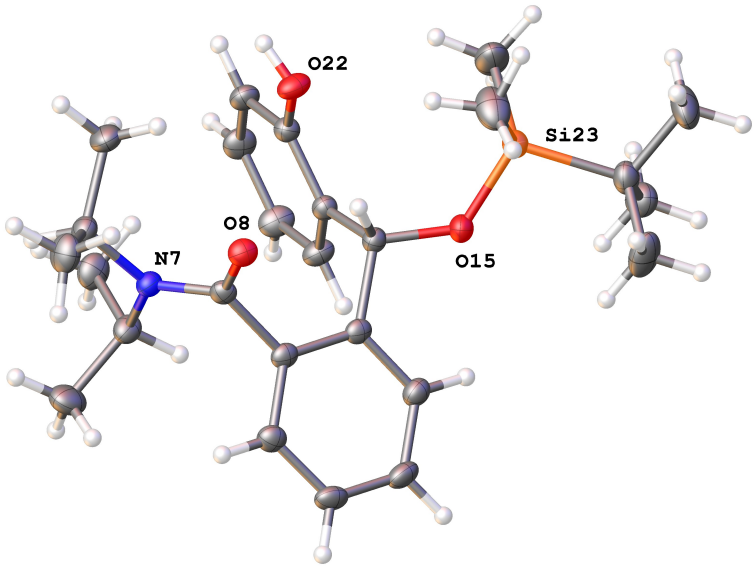
To a solution of N,N-diisopropylbenzamide (205 mg, 1.00 mmol) in THF (2 mL) at -78 °C was added dropwise a solution of n-butyllithium (0.400 mL, 2.5M in hexanes, 1.00 mmol). The reaction mixture was then stirred under a nitrogen atmosphere for 2-3 hours, after which 2-((*tert*-butyldimethylsilyl)oxy)benzaldehyde (354 mg, 1.50 mmol) was added dropwise. The reaction mixture was left stirring under the nitrogen atmosphere and allowed to warm to rt. The reaction was followed by TLC (4:1 hexane: EtOAc). The mixture was quenched by saturated NH_4Cl solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 × 20 mL), and the combined organic layers were dried ($MgSO_4$) and filtered. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give 2-((2-((*tert*-butyldimethylsilyl)oxy)phenyl)(hydroxy)methyl)-N,N-diisopropylbenzamide as a white solid (283.3 mg, 0.642 mmol, 64.2%). Then to a solution of 2-((2-((*tert*-butyldimethylsilyl)oxy)phenyl)(hydroxy)methyl)-N,N-diisopropylbenzamide (280 mg, 0.635 mmol) in THF (10 mL) was added a solution of *tetra*-n-butylammonium fluoride (TBAF) (0.95 mL, 1.0M in THF, 0.95 mmol) at rt. The reaction mixture was left stirring under the nitrogen atmosphere and followed by TLC (4:1 hexane: ethyl acetate). Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give 2-(hydroxy(2-hydroxyphenyl)methyl)-N,N-diisopropylbenzamide **8q** as a white solid (129 mg, 0.394 mmol, 62.1%). TLC: Rf ca 0.20 (4:1 hexane: EtOAc), strong UV and $KMnO_4$; HRMS: (found (ESI+): [M+Na]+, Calcd for $C_{20}H_{25}NNaO_3$ 350.1727; Found 350.1727; -0.1 ppm error); ν_{max} 3244 (br), 2969, 2932, 1589, 1485, 1454, 1370, 1345, 1232, 1030, 751 cm^{-1}; Major diastereomer: δ_H (500 MHz, $CDCl_3$) 8.97 (1H, s, ArOH), 7.31-7.20 (5H, m, ArH), 6.84-6.81 (3H, m, ArH), 5.97 (1H, s, Ar*CH*OH), 5.68 (1H, s, ArCH*OH*), 4.01-3.96 (1H, m, N[*CH*$(CH_3)_2]_2$), 3.64-3.59 (1H, m, N[*CH*$(CH_3)_2]_2$), 1.65-1.55 (7H, m, N[CH(*CH*$_3)_2]_2$), 1.31-1.13 (5H, m, N[CH(*CH*$_3)_2]_2$) ppm; Minor diastereomer: δ_H (500 MHz, $CDCl_3$) 9.86 (1H, s, ArOH), 7.43-7.38 (2H, m, ArH), 7.34-7.29 (2H, m, ArH), 7.09 (1H, t, *J* = 7.5, ArH), 7.04-7.03 (1H, m, ArH), 6.99 (1H, d, *J* = 8.2, ArH), 6.69 (1H, t, *J* = 7.5, ArH), 6.02 (1H, s,

Ar*C*HOH), 3.86-3.81 (3H, m, N[*C*H$(CH_3)_2]_2$), 1.19-1.14 (6H, m, N[*C*H$(CH_3)_2]_2$), 0.83-0.82 (3H, m, N[CH(CH_3)$_2]_2$ ppm; Major diastereomer: δ_C (125 MHz, $CDCl_3$) 172.1 (C), 157.2 (C), 140.0 (C), 137.3 (C), 129.6 (CH), 129.3 (CH), 128.7 (CH), 128.2 (CH), 126.6 (CH), 125.0 (CH), 123.3 (C), 119.5 (CH), 117.7 (CH), 75.7 (CH), 51.7 (CH), 46.5 (CH), 21.1 (CH_3), 20.8 (CH_3), 20.3 (CH_3), 20.1 (CH_3) ppm; Minor diastereomer: δ_C (125 MHz, $CDCl_3$) 172.1 (C), 156.6 (C), 140.6 (C), 136.2 (C), 131.1 (CH), 129.9 (CH), 128.8 (CH), 128.0 (CH), 127.8 (CH), 127.1 (C), 126.4 (CH), 119.3 (CH), 117.4 (CH), 75.8 (CH), 51.4 (CH), 46.6 (CH), 20.8 (CH_3), 20.6 (CH_3), 20.4 (CH_3), 19.9 (CH_3) ppm; m/z (ES-API+) 350.2 (M^+ + 23, 100%).

X-ray crystallographic structure of C (page S173, CCDC 1978886, local code yz9) revealed TBS migration from the phenolic to the secondary alkyl hydroxyl group to give **C**.



Unit Cell Parameters: a 12.84169(9) b 10.91697(5) c 18.56931(10) P21/n



solid state structure of yz9 with only key atoms labelled and thermal ellipsoids drawn at 50% probability level

Crystal structure determination of C [yz9]

The asymmetric unit contains the silyl ether, there are four molecules in the unit cell (two of each enantiomer)

The OH was located in a difference map but refined with distance constraints. It form an H bond with a neighbouring amide carbonyl tabulated below

D-H	H...A	D...A	<(DHA)	
0.84	1.87	2.7042(10)	171.1	O22-H22...O8_$1

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

Experimental

Single crystals of $C_{26}H_{39}NO_3Si$ **[yz9]** were grown from DCM/hexane in a small vial at room temperature. 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 duel 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 $C_{26}H_{39}NO_3Si$ (M =441.67 g/mol): monoclinic, space group $P2_1/n$ (no. 14), a = 12.84169(9) Å, b = 10.91697(5) Å, c = 18.56931(10) Å, β = 90.7611(5)°, V = 2603.05(3) Å^3, Z = 4, T = 150(2) K, μ(CuKα) = 0.986 mm^{-1}, *Dcalc* = 1.127 g/cm^3, 27378 reflections measured (8.32° ≤ 2Θ ≤ 147.258°), 5240 unique (R_{int} = 0.0250, R_{sigma} = 0.0270) which were used in all calculations. The final R_1 was 0.0329 (I > 2σ(I)) and wR_2 was 0.0864 (all data).

Table 1 Crystal data and structure refinement for yz9.

Identification code	yz9
Empirical formula	$C_{26}H_{39}NO_3Si$
Formula weight	441.67
Temperature/K	150(2)
Crystal system	monoclinic
Space group	$P2_1/n$
a/Å	12.84169(9)
b/Å	10.91697(5)
c/Å	18.56931(10)
α/°	90
β/°	90.7611(5)
γ/°	90
Volume/Å^3	2603.05(3)
Z	4

ρ_{calc}g/cm^3	1.127
μ/mm^{-1}	0.986
F(000)	960.0
Crystal size/mm^3	0.3 × 0.18 × 0.1 colourless block
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	8.32 to 147.258
Index ranges	-15 ≤ h ≤ 15, -11 ≤ k ≤ 13, -22 ≤ l ≤ 23
Reflections collected	27378
Independent reflections	5240 [R_{int} = 0.0250, R_{sigma} = 0.0270]
Data/restraints/parameters	5240/0/290
Goodness-of-fit on F^2	1.019
Final R indexes [I>=2σ (I)]	R_1 = 0.0329, wR_2 = 0.0848
Final R indexes [all data]	R_1 = 0.0387, wR_2 = 0.0864
Largest diff. peak/hole / e Å^{-3}	0.36/-0.40

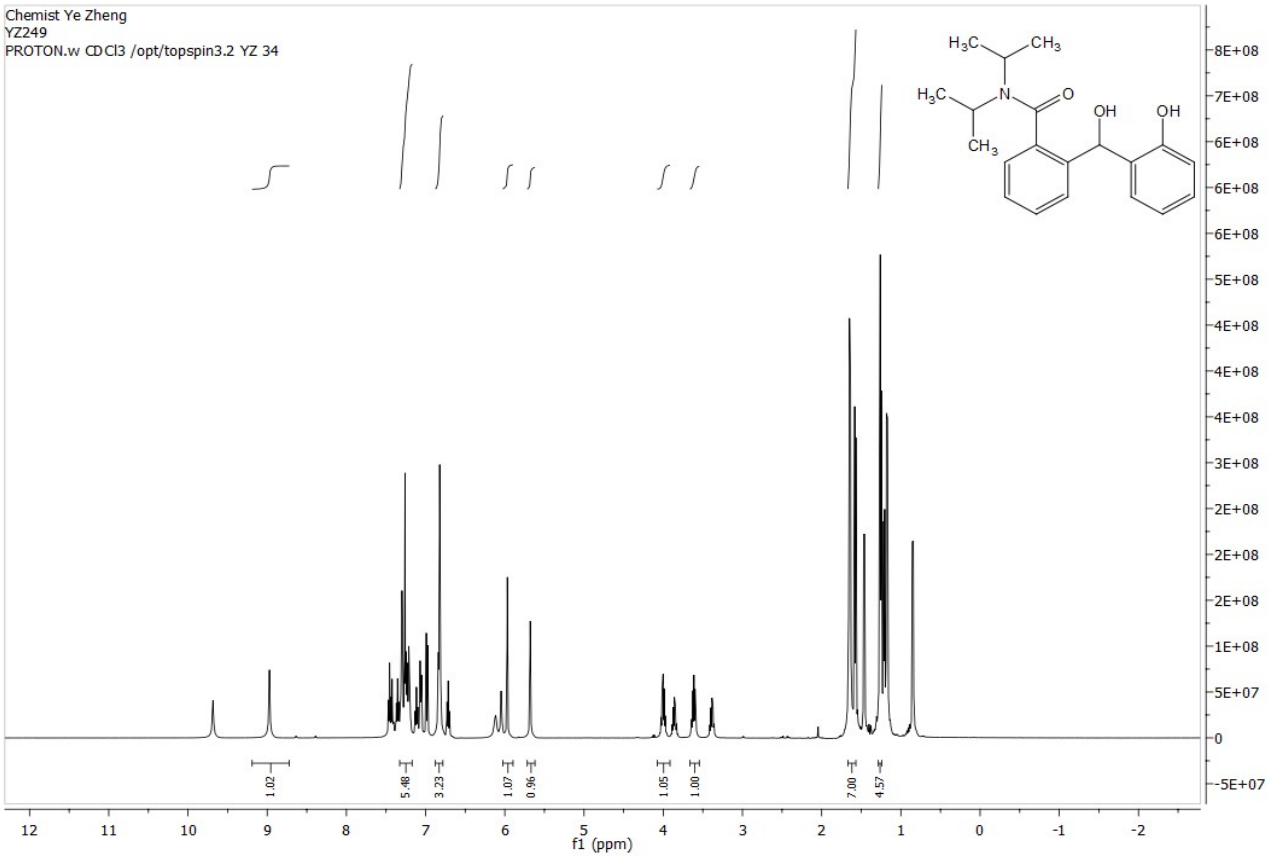
Enantiomeric excess and conversion were determined by HPLC analysis (Chiralpak IA, 30 cm x 6mm column, hexane:iPrOH 95:5, 0.5 mL/min, T = 25°C) ketone 23.9 min, *R* and *S* isomer 26.1 min and 29.3 min, configuration is not known.

ATH of **7q** using (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst **2** (YZ251).

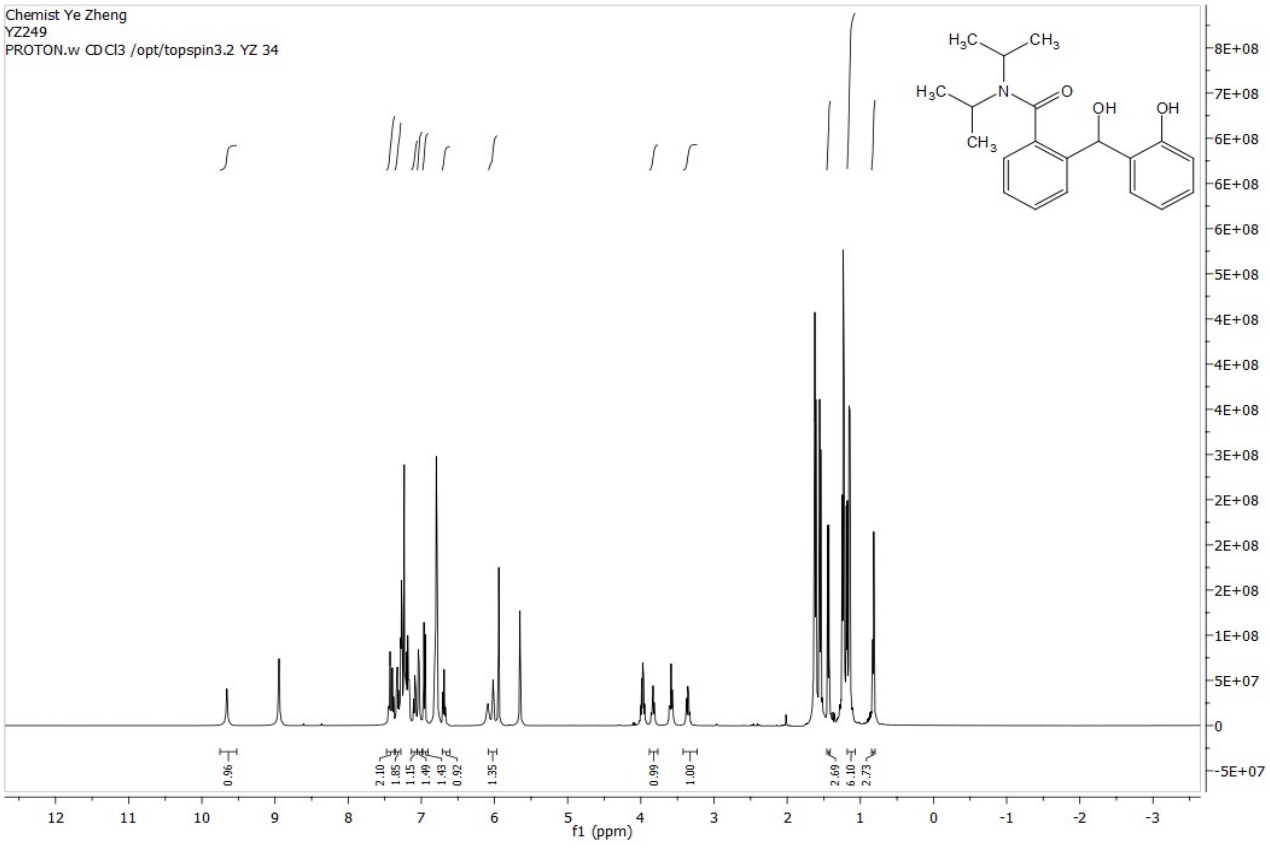
Catalyst (*R,R*)-**2** (0.00123 mmol, 1mol%) was added to FA: TEA (5:2 azeotropic mixture, 0.18 mL) at rt and the mixture was stirred under a nitrogen inert atmosphere for 10-15 minutes; after which a solution of 2-(2-hydroxybenzoyl)-N,N-diisopropylbenzamide **7q** (40 mg, 0.123 mmol) in DCM (0.25 mL) was added. The reaction mixture was stirrer under a nitrogen atmosphere, followed by TLC (4:1 hexane: ethyl acetate). After 72 hours, the reaction was quenched using saturated $NaHCO_3$ solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried ($MgSO_4$) and filtered. The solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give 2-(hydroxy(2-hydroxyphenyl)methyl)-N,N-diisopropylbenzamide **8q** (18.3 mg, 0.056 mmol, 45.5%; (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst example). The reaction was also followed by HPLC analysis (Chiralpak IA, 30 cm x 6mm column, hexane:iPrOH 95:5, 0.5 mL/min, T = 25°C); (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst: 100% conversion; $[\alpha]_D^{26}$ -57.5 (c 0.366 in $CHCl_3$) 86.8% ee

^{1}H NMR (500 MHz, $CDCl_3$) of **8q**:

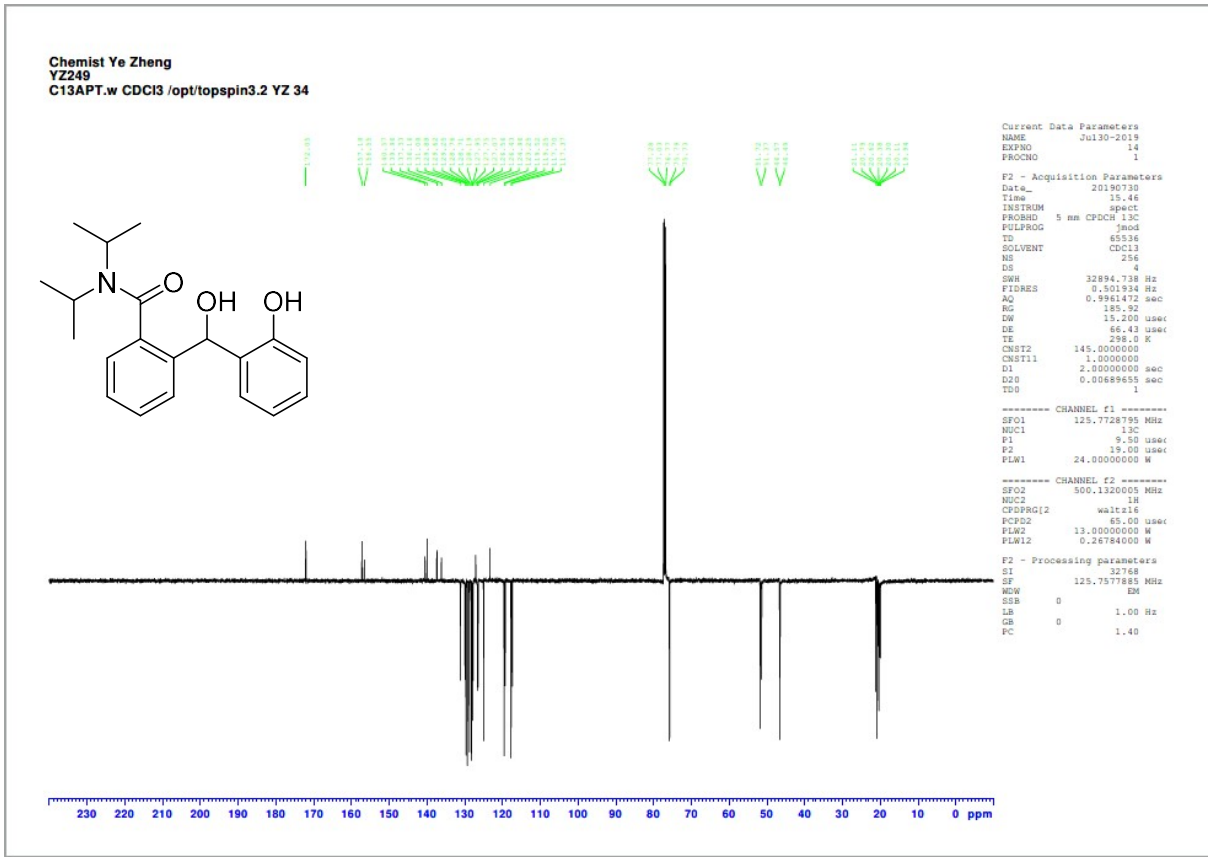
Major diastereomer:



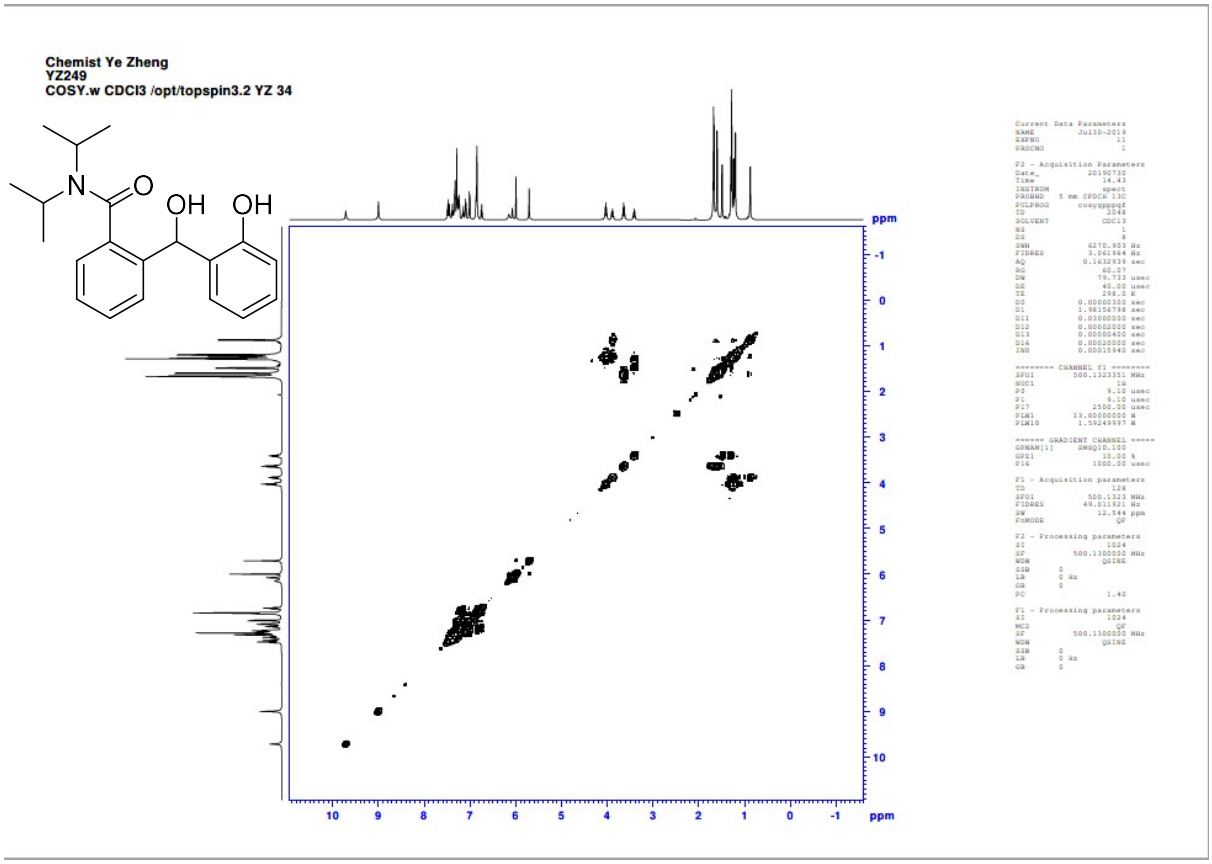
Minor diastereomer:



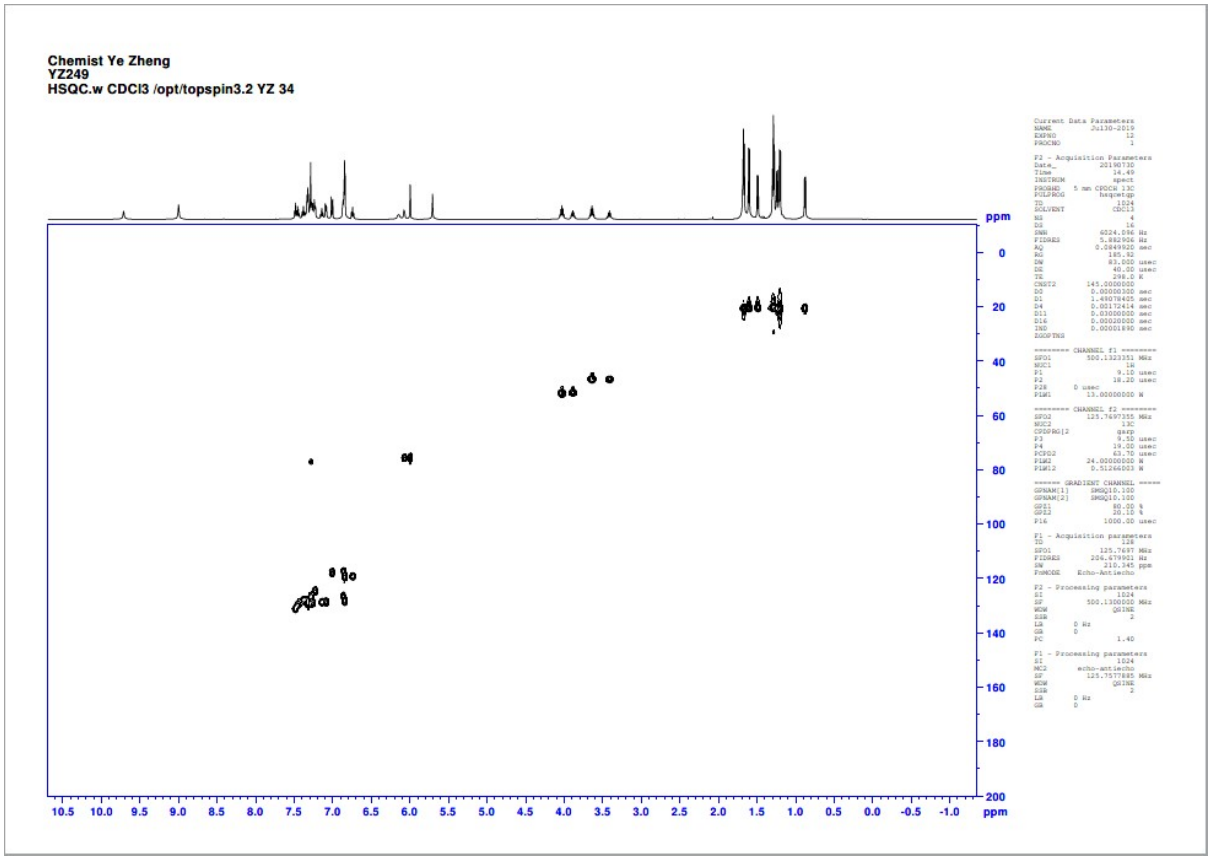
^{13}C NMR (125 MHz, $CDCl_3$) of **8q**:



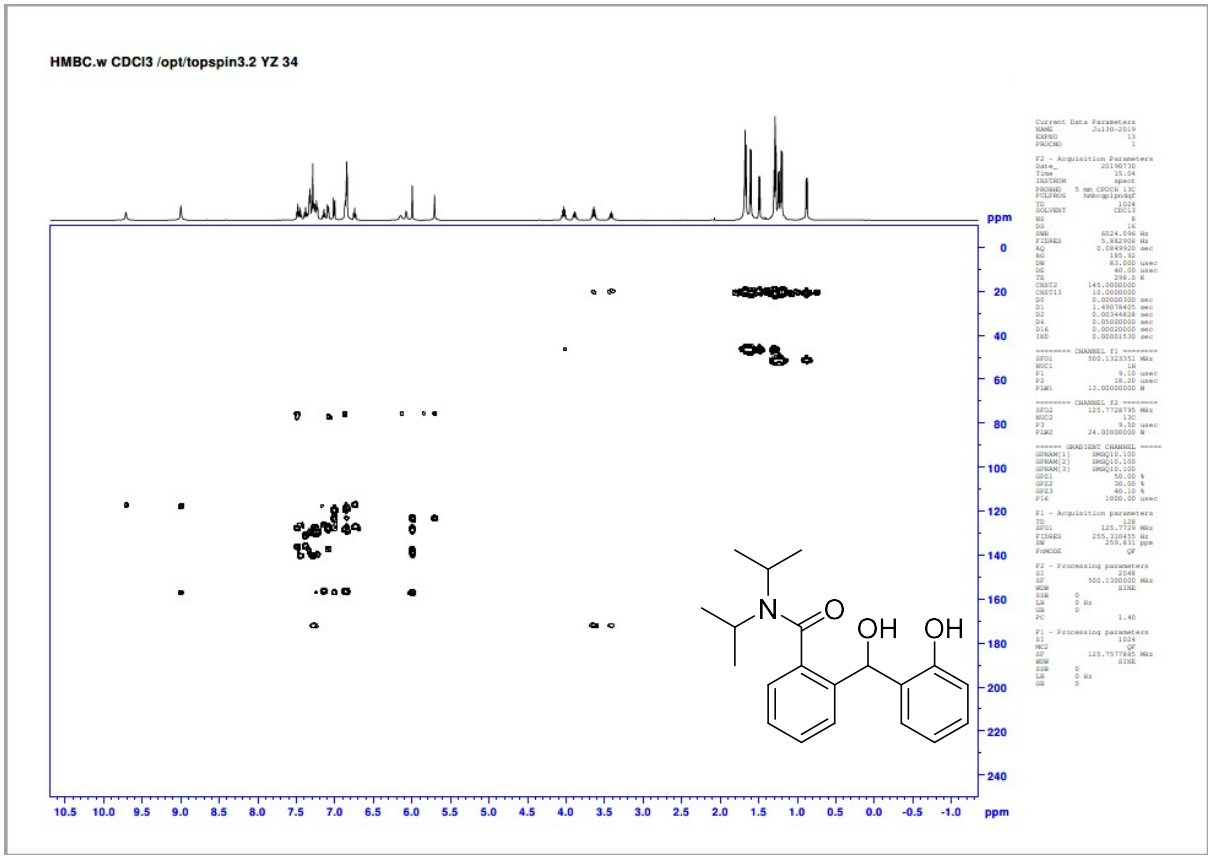
COSY (500 MHz, $CDCl_3$) of **8q**:



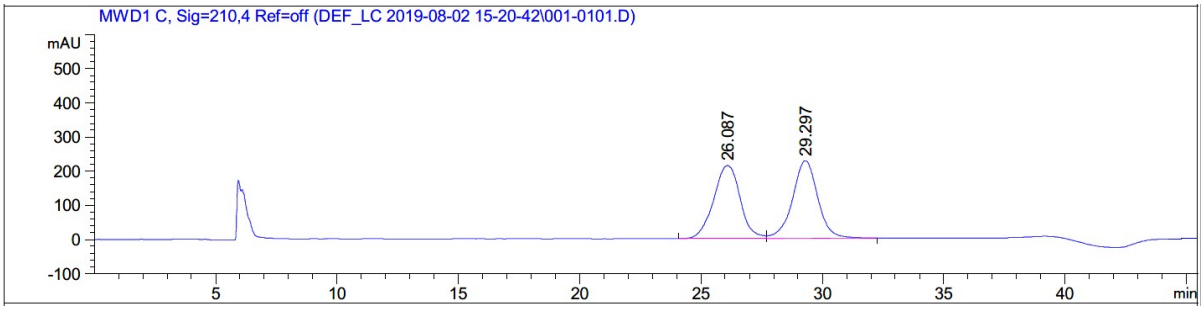
HSQC (500 MHz, $CDCl_3$) of **8q**:



HMBC (500 MHz, $CDCl_3$) of **8q**:



HPLC of racemic 2-(hydroxy(2-hydroxyphenyl)methyl)-N,N-diisopropylbenzamide **8q**:

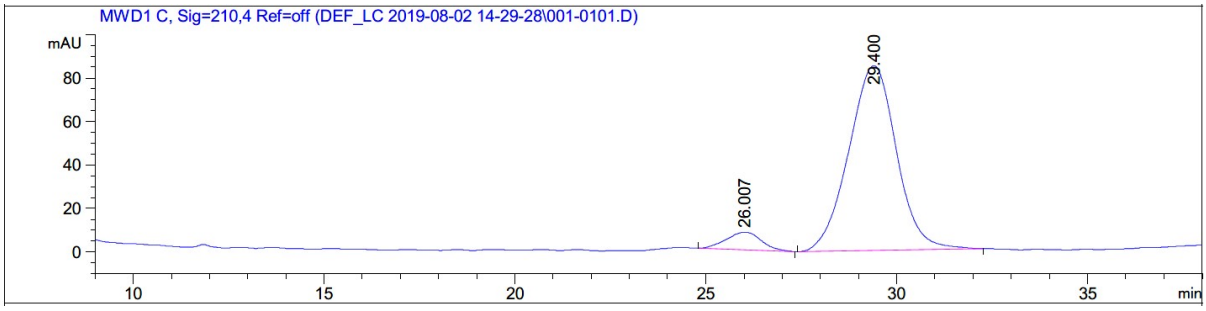


Signal 2: MWD1 C, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.087	BV	1.1738	1.61903e4	213.73332	49.7354
2	29.297	VB	1.0980	1.63626e4	226.71645	50.2646
Totals :				3.25530e4	440.44977	

HPLC of **8q** after ATH of 2-(2-hydroxybenzoyl)-N,N-diisopropylbenzamide **7q**:

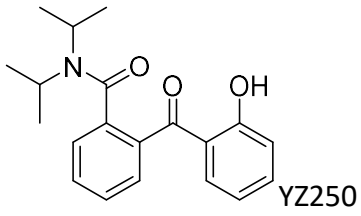
(*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst (after 72 hours, 100% conversion, 86.8% ee)



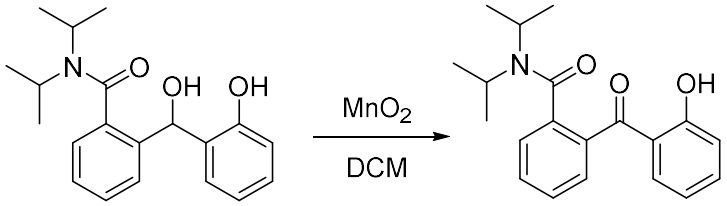
Signal 2: MWD1 C, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	26.007	BB	0.7920	522.53516	8.10658	6.6004
2	29.400	BB	1.3253	7394.24170	84.96331	93.3996
Totals :				7916.77686	93.06989	

2-(2-Hydroxybenzoyl)-N,N-diisopropylbenzamide 7q.



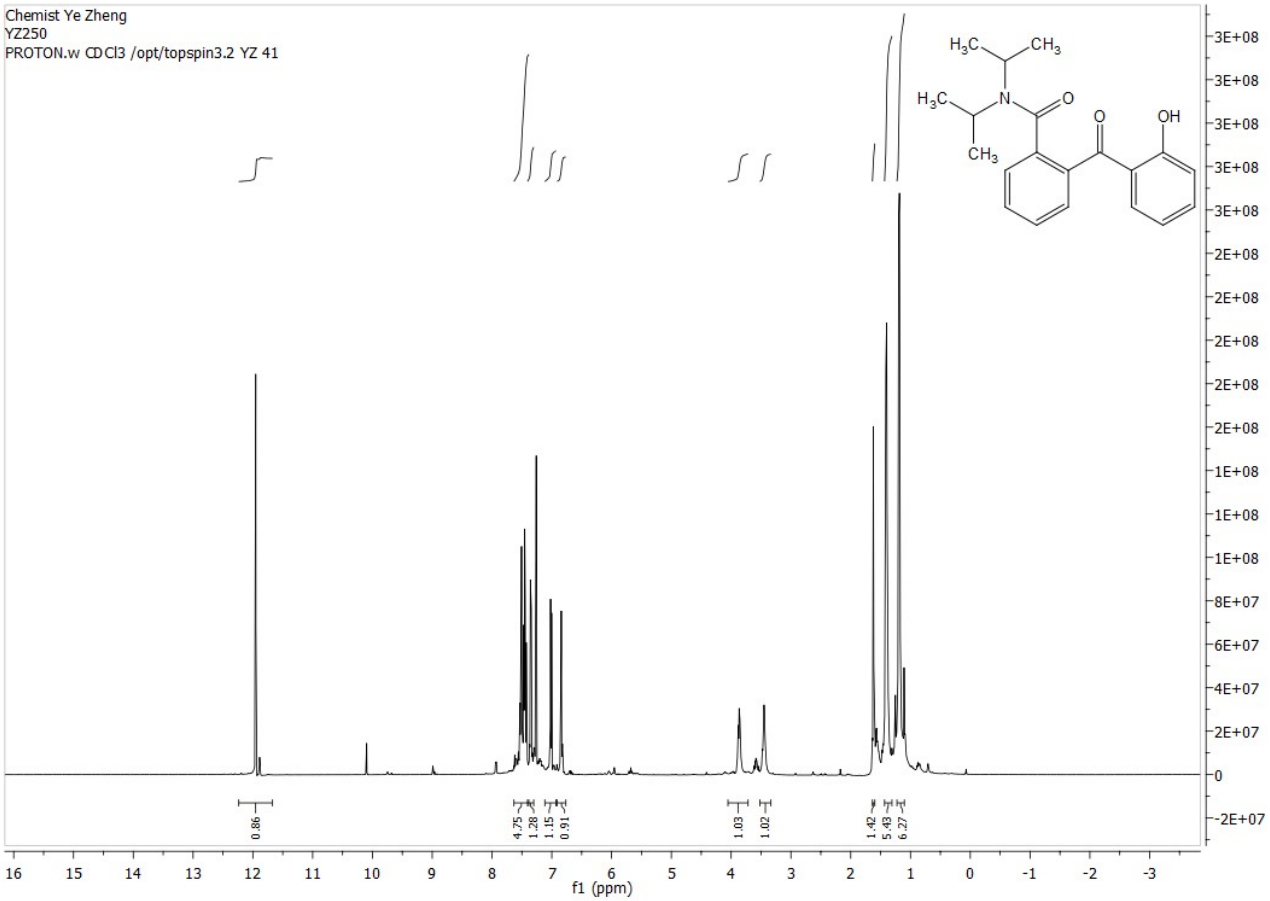
YZ250



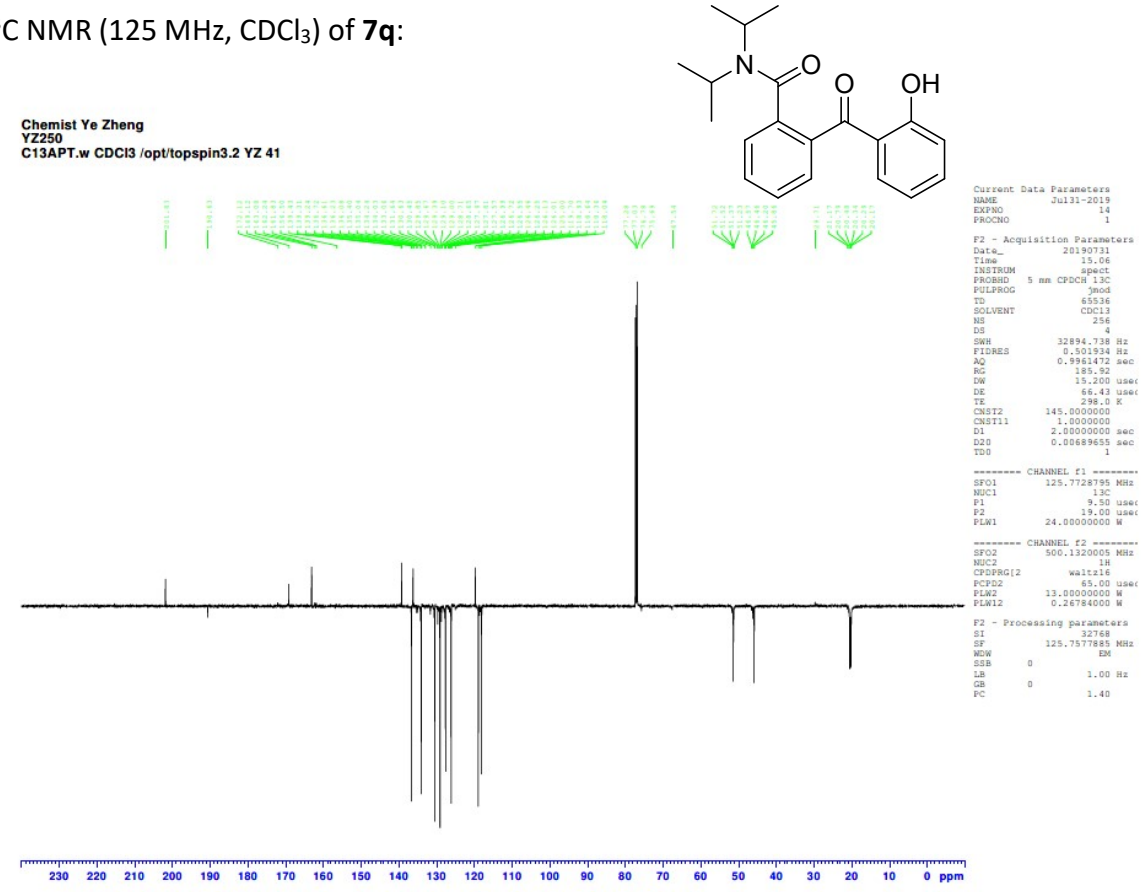
This compound is novel.

To a solution of 2-(hydroxy(2-hydroxyphenyl)methyl)-N,N-diisopropylbenzamide **8q** (119 mg, 0.36 mmol) in DCM (2.5 mL) at rt was added manganese dioxide (474 mg, 5.46 mmol). The reaction mixture was left to stir under a nitrogen atmosphere overnight. TLC (7:3 hexane: EtOAc) after this time indicated full conversion. The solids were removed by gravity filtration and wash with DCM. The combined solvent was removed to give the product **7q** as a yellow oil (56.2 mg, 0.173 mmol, 47.5%). TLC: Rf ca 0.40 (7:3 hexane: EtOAc), strong UV and $KMnO_4$; HRMS: (found (ESI+): [M+Na]+, Calcd for $C_{20}H_{23}NNaO_3$ 348.1561; Found 348.1570; 2.5 ppm error; ν_{max} 3052, 2971, 2933, 1624, 1485, 1445, 1370, 1340 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 11.95 (1H, s, ArOH), 7.52-7.43 (5H, m, ArH), 7.36 (1H, d, *J* = 7.5, ArH), 7.02 (1H, d, *J* = 8.3, ArH), 6.84 (1H, t, *J* = 7.5, ArH), 3.88-3.84 (1H, m, N[*CH*(CH_3)$_2$]$_2$), 3.48-3.42 (1H, m, N[*CH*(CH_3)$_2$]$_2$), 1.64-1.60 (1H, m, N[CH(*CH_3*)$_2$]$_2$), 1.41-1.40 (5H, m, N[CH(*CH_3*)$_2$]$_2$), 1.20-1.19 (6H, m, N[CH(*CH_3*)$_2$]$_2$) ppm; δ_C (125 MHz, $CDCl_3$) 201.8 (C), 169.1 (C), 163.1 (C), 129.2 (C), 136.6 (CH), 136.2 (C), 134.0 (CH), 130.5 (CH), 129.1 (CH), 127.6 (CH), 126.1 (CH), 119.7 (C), 118.9 (CH), 118.0 (CH), 51.4 (CH), 45.9 (CH), 20.5 (CH_3), 20.2 (CH_3) ppm; m/z (ES-API+) 348.3 (M^+ + 23, 100%).

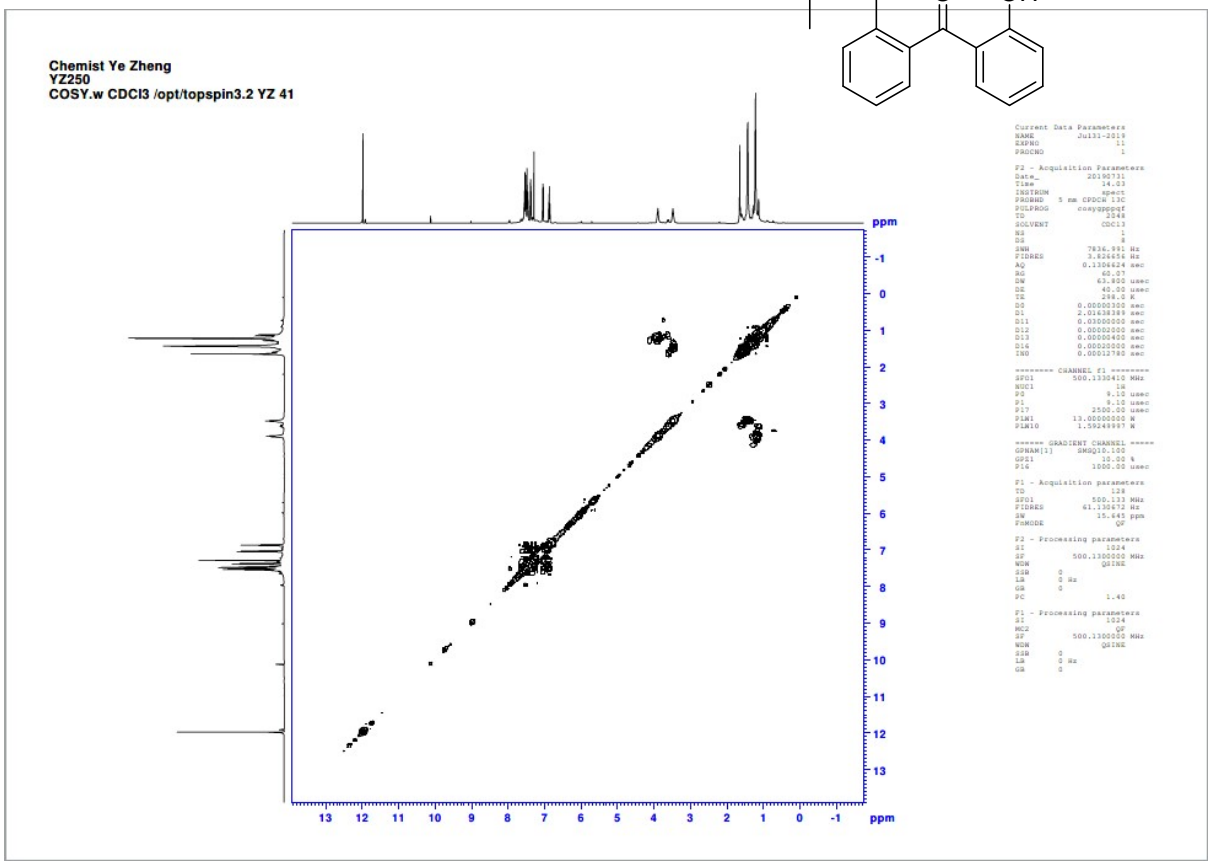
^{1}H NMR (500 MHz, $CDCl_3$) of **7q**:



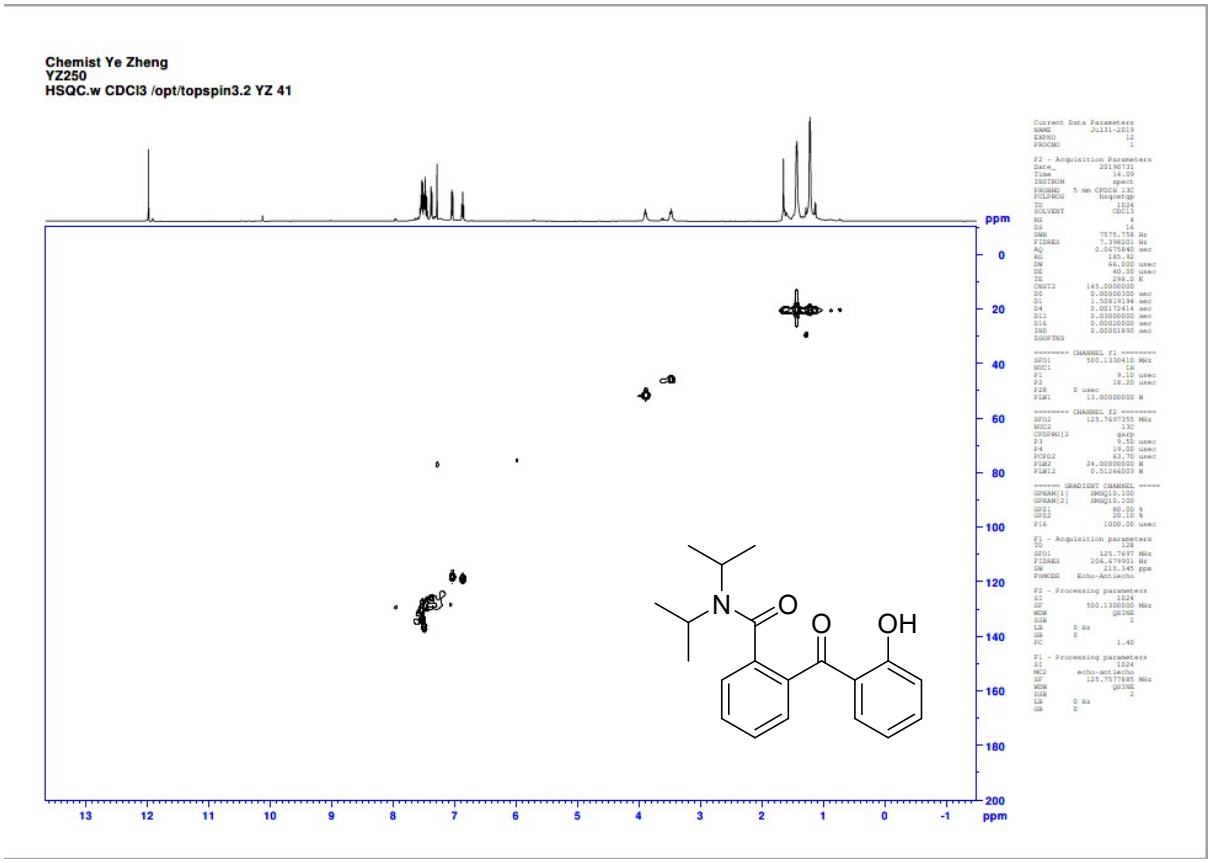
^{13}C NMR (125 MHz, $CDCl_3$) of **7q**:



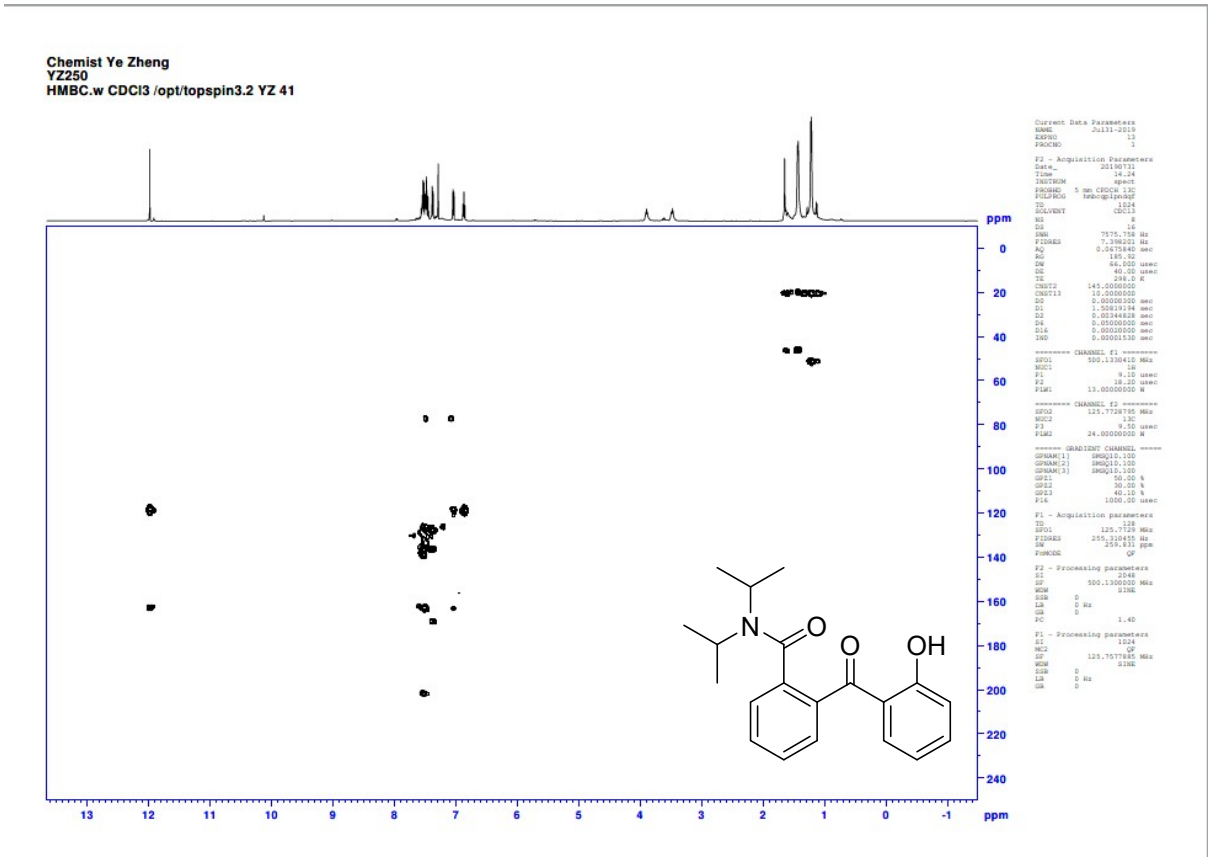
COSY (500 MHz, $CDCl_3$) of **7q**:



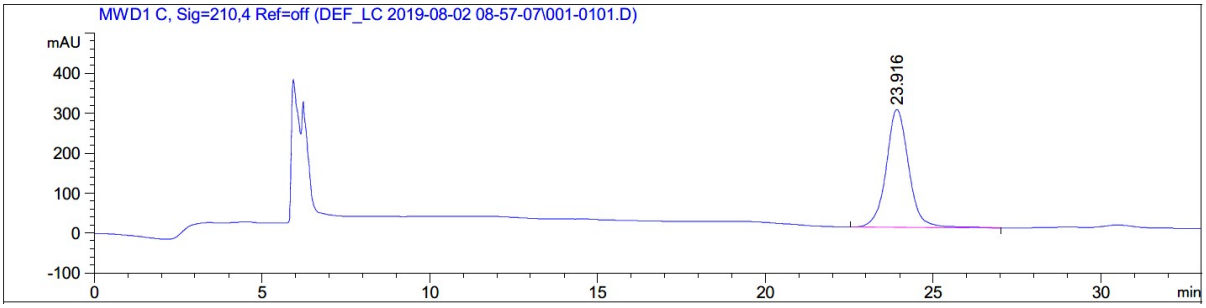
HSQC (500 MHz, $CDCl_3$) of **7q**:



HMBC (500 MHz, $CDCl_3$) of **7q**:



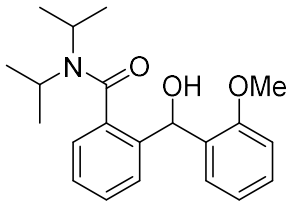
HPLC of 2-(2-hydroxybenzoyl)-N,N-diisopropylbenzamide **7q**:



Signal 2: MWD1 C, Sig=210,4 Ref=off

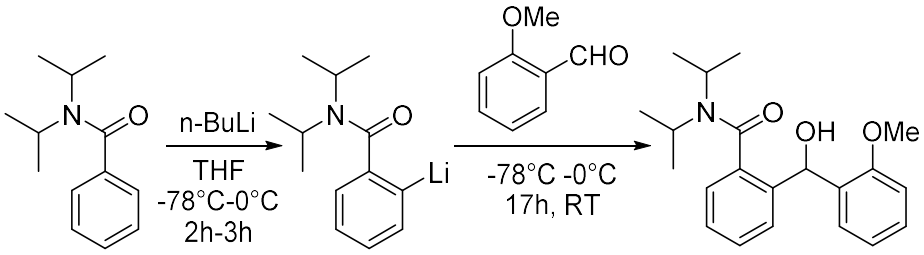
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	23.916	BB	0.7092	1.37298e4	294.90503	100.0000
Totals :				1.37298e4	294.90503	

2-(Hydroxy(2-methoxyphenyl)methyl)-N,N-diisopropylbenzamide 8r.

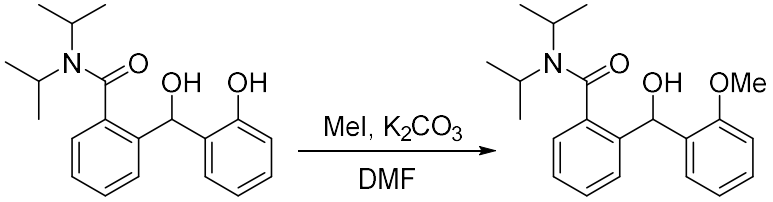


racemic: YZ216, YZ360 Asymmetric: YZ241, YZ363, YZ370.

YZ241



YZ363 and YZ370: methylation



This compound is novel.

YZ216 (racemic): To a solution of N,N-diisopropylbenzamide (200 mg, 0.976 mmol) in THF (2 mL) at -78 °C was added dropwise a solution of n-butyllithium (0.400 mL, 2.5M in hexanes, 0.976 mmol). The reaction mixture was then stirred under a nitrogen atmosphere for 2-3 hours, after which 2-methoxybenzaldehyde (199 mg, 1.46 mmol) was added dropwise. The reaction mixture was left stirring under the nitrogen atmosphere and allowed to warm to rt. The reaction was followed by TLC (4:1 hexane: EtOAc). The mixture was quenched by saturated NH_4Cl solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 × 20 mL), and the combined organic layers were dried ($MgSO_4$) and filtered. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give 2-(hydroxy(2-methoxyphenyl)methyl)-N,N-diisopropylbenzamide **8r** as a white solid (263 mg, 0.771 mmol, 79%). TLC: Rf ca 0.30 (4:1 hexane: EtOAc), strong UV and $KMnO_4$; Mp: 81 °C; HRMS: (found (ESI+): [M+Na]+, Calcd for $C_{21}H_{27}NNaO_3$ 364.1886; Found 364.1883; -0.8 ppm error; ν_{max} 3387 (br), 2968, 2872, 1595, 1463, 1442, 1371, 1237 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.77-7.57 (1H, m, ArH), 7.39-7.07 (5H, m, ArH), 6.96-6.75 (2H, m, ArH), 6.08 (1H, s, Ar*CH*OH), 4.52 (1H, s, ArCH*OH*), 4.02-3.97 (1H, m, N[*CH*$(CH_3)_2]_2$), 3.65 (1H, s, N[*CH*$(CH_3)_2]_2$), 3.61 (3H, s, OCH_3), 1.63-1.56 (4H, m, N[CH(*CH_3*$)_2]_2$), 1.49-1.44 (2H, m, N[CH(*CH_3*$)_2]_2$),

1.24-1.16 (5H, m, N[CH(CH_3)$_2$]$_2$), 1.06 (1H, d, *J* = 6.6, N[CH(CH_3)$_2$]$_2$) ppm; δ_C (125 MHz, $CDCl_3$) 172.0 (C), 155.9 (C), 142.0 (C), 137.9 (C), 131.6 (CH), 129.3 (C), 128.9 (CH), 128.3 (CH), 127.9 (CH), 127.0 (CH), 126.3 (CH), 124.5 (CH), 120.7 (CH), 110.0 (CH), 73.7 (CH), 68.0 (CH), 62.2 (CH_3), 55.1 (CH_3), 51.5 (CH_3), 46.2 (CH_3), 20.4 (CH_3) ppm; m/z (ES-API+) 263.1 (M^+ + 23, 100%).
Enantiomeric excess and conversion determined by HPLC analysis (Chiralpak IA, 30 cm x 6mm column, hexane:iPrOH 95:5, 0.5 mL/min, T = 25°C) ketone 39.2 min, *R* and *S* isomer 43.1 min and 46.1 min, configuration was assigned by analogy.

ATH of N,N-diisopropyl-2-(2-methoxybenzoyl)benzamide **7r** (YZ241)
(*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst (0.74 mg, 0.00168 mmol, 1 mol%) was added to FA: TEA (5:2 azeotropic mixture, 0.18 mL) at rt and the mixture was stirred under a nitrogen atmosphere for 10-15 minutes; after which a solution of N,N-diisopropyl-2-(2-methoxybenzoyl)benzamide **7r** (40 mg, 0.12 mmol) in DCM (0.25 mL) was added. The reaction mixture was stirrer under a nitrogen atmosphere, followed by TLC (4:1 hexane: EtOAc). After 168 hours, the reaction was quenched using saturated $NaHCO_3$ solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried ($MgSO_4$) and filtered. The solvent was removed to give the crude product. Crude NMR indicated there was only about 20% conversion. The reaction was also followed by HPLC analysis (Chiralpak IA, 30 cm x 6mm column, hexane:iPrOH 95:5, 0.5 mL/min, T = 25°C); (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst: 20% conversion and 11.9% ee.

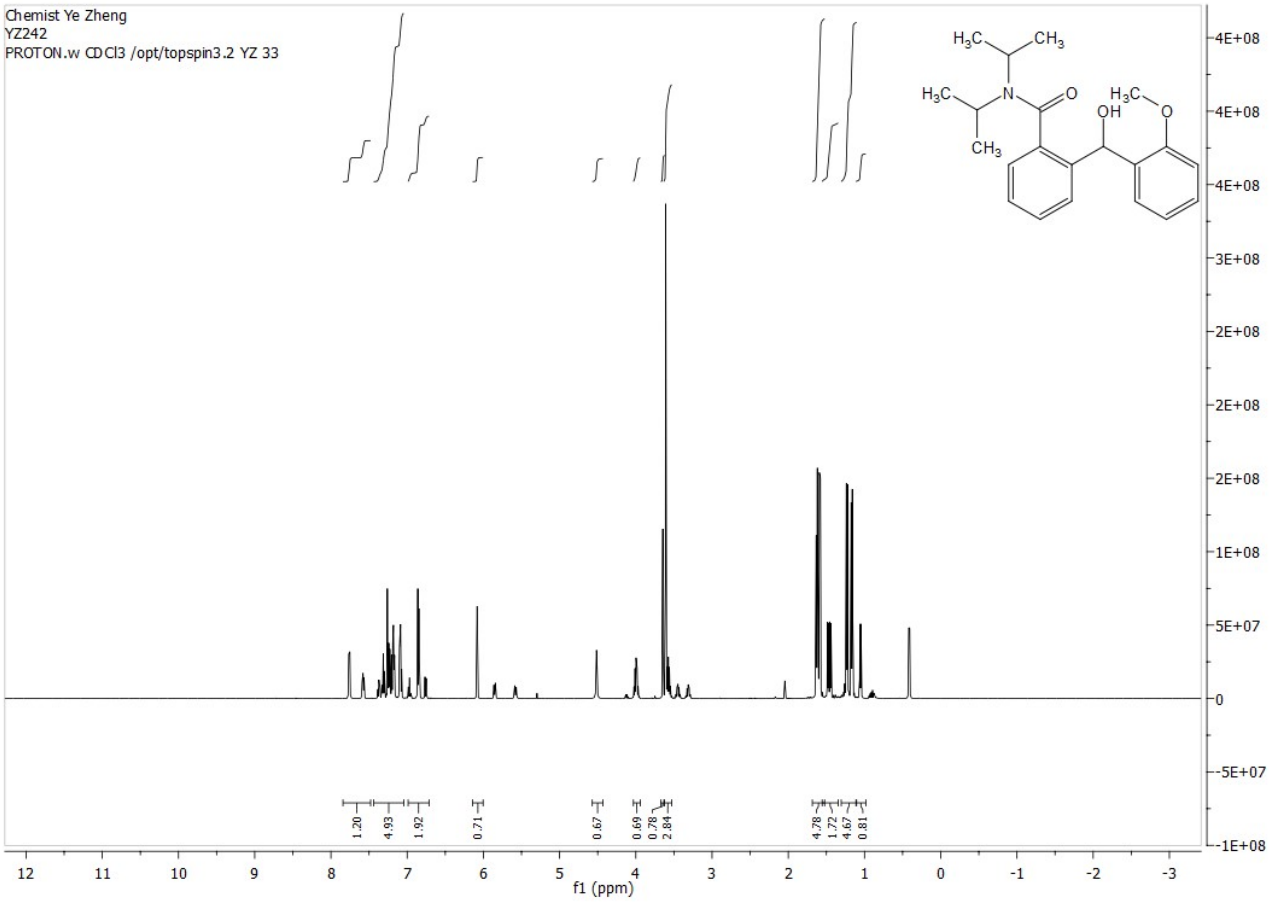
Racemic, by methylation (YZ360): To a solution of 2-(hydroxy(2-hydroxyphenyl)methyl)-N,N-diisopropylbenzamide **8q** (113.6 mg, 0.347 mmol) in DMF (3.5 mL) was added potassium carbonate (57.4 mg, 0.416 mmol) and iodomethane (49.3 mg, 0.347 mmol) at rt. The reaction mixture was left stirring under the nitrogen atmosphere overnight. TLC (4:1 hexane: EtOAc) after this time indicated full conversion. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give 2-(hydroxy(2-methoxyphenyl)methyl)-N,N-diisopropylbenzamide **8r** as a white solid (47.8 mg, 0.140 mmol, 40.3%). TLC: Rf ca 0.30 (4:1 hexane: EtOAc), strong UV and $KMnO_4$; Mp: 81 °C; HRMS: (found (ESI+): [M+Na]+, Calcd for $C_{21}H_{27}NNaO_3$ 364.1886; Found 364.1883; -0.8 ppm error; ν_{max} 3387 (br), 2968, 2872, 1595, 1463, 1442, 1371, 1237 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.77-7.57 (1H, m, ArH), 7.39-7.07 (5H, m, ArH), 6.96-6.75 (2H, m, ArH), 6.08 (1H, s, Ar*CH*OH), 4.52 (1H, s, ArCH*OH*), 4.02-3.97 (1H, m, N[*CH*(CH_3)$_2$]$_2$), 3.65 (1H, s, N[*CH*(CH_3)$_2$]$_2$), 3.61 (3H, s, OCH_3), 1.63-1.56 (4H, m,

N[CH(CH_3)$_2$]$_2$), 1.49-1.44 (2H, m, N[CH(CH_3)$_2$]$_2$), 1.24-1.16 (5H, m, N[CH(CH_3)$_2$]$_2$), 1.06 (1H, d, *J* = 6.6, N[CH(CH_3)$_2$]$_2$) ppm; δ_C (125 MHz, $CDCl_3$) 172.0 (C), 155.9 (C), 142.0 (C), 137.0 (C), 131.6 (CH), 129.3 (C), 128.9 (CH), 128.3 (CH), 127.9 (CH), 127.0 (CH), 126.3 (CH), 124.5 (CH), 120.7 (CH), 110.0 (CH), 73.7 (CH), 68.0 (CH), 62.2 (CH_3), 55.1 (CH_3), 51.5 (CH_3), 46.2 (CH_3), 20.4 (CH_3) ppm; m/z (ES-API+) 263.1 (M^+ + 23, 100%).

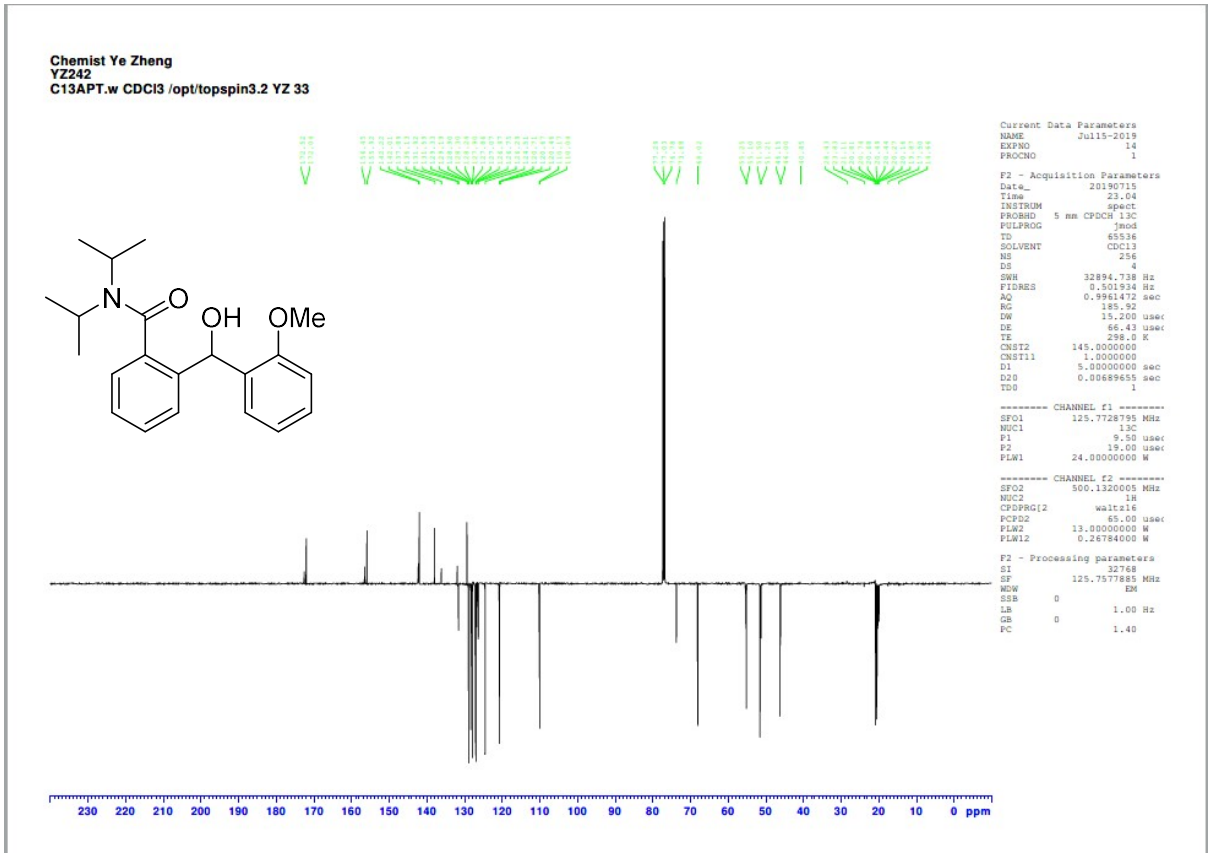
Racemic, by methylation (YZ360) and asymmetric, by methylation (YZ363,YZ370): Enantiomeric excess and conversion determined by HPLC analysis (Chiralpak IA, 30 cm x 6mm column, hexane:iPrOH 95:5, 0.5 mL/min, T = 25°C) ketone 39.2 min, *R* and *S* isomer 49.2 min and 53.8 min, configuration was assigned by analogy.

Asymmetric, by methylation (YZ363,YZ370): To a solution of 2-(hydroxy(2-hydroxyphenyl)methyl)-N,N-diisopropylbenzamide **8q** (69.4 mg, 0.212 mmol) in DMF (2 mL) was added potassium carbonate (35.1 mg, 0.254 mmol) and iodomethane (30.1 mg, 0.212 mmol) at rt. The reaction mixture was left stirring under the nitrogen atmosphere overnight. TLC (4:1 hexane: EtOAc) after this time indicated full conversion. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give 2-(hydroxy(2-methoxyphenyl)methyl)-N,N-diisopropylbenzamide **8r** as a white solid (48.8 mg, 0.143 mmol, 67.4%). (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst: $[\alpha]_D^{24}$ -110.9 (c 0.815 in $CHCl_3$) 86.8% ee

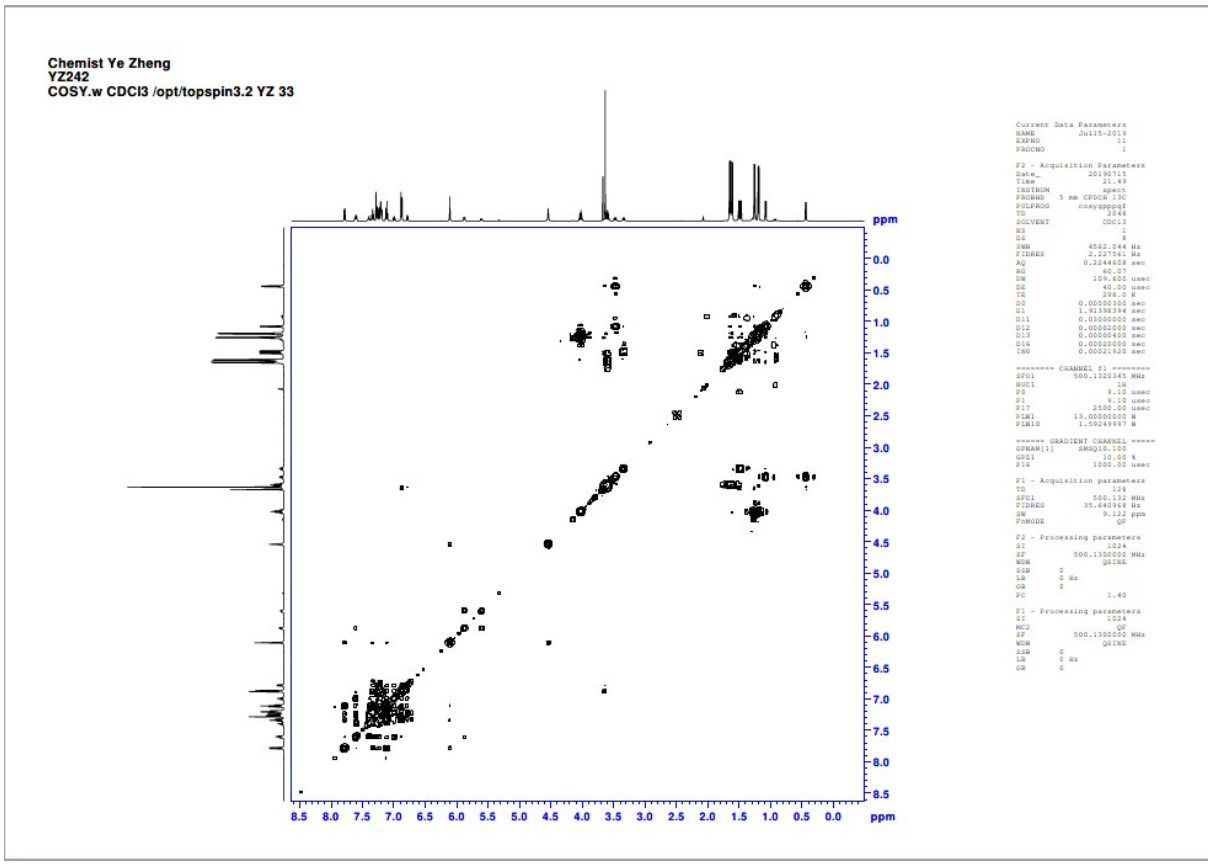
^{1}H NMR (500 MHz, $CDCl_3$) of **8r**:



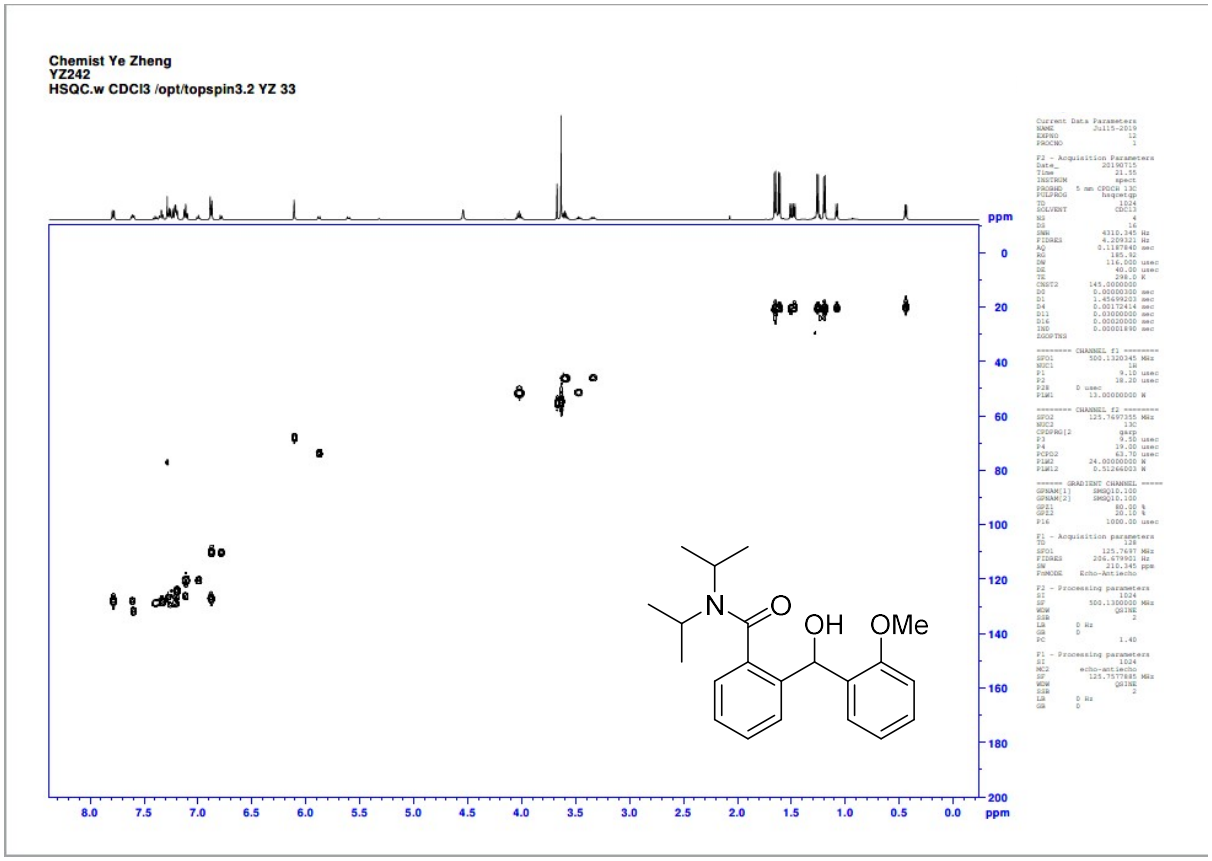
^{13}C NMR (125 MHz, $CDCl_3$) of **8r**:

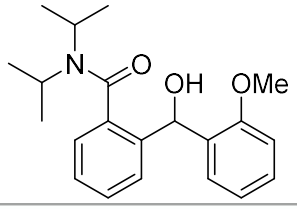


COSY (500 MHz, $CDCl_3$) of **8r**:

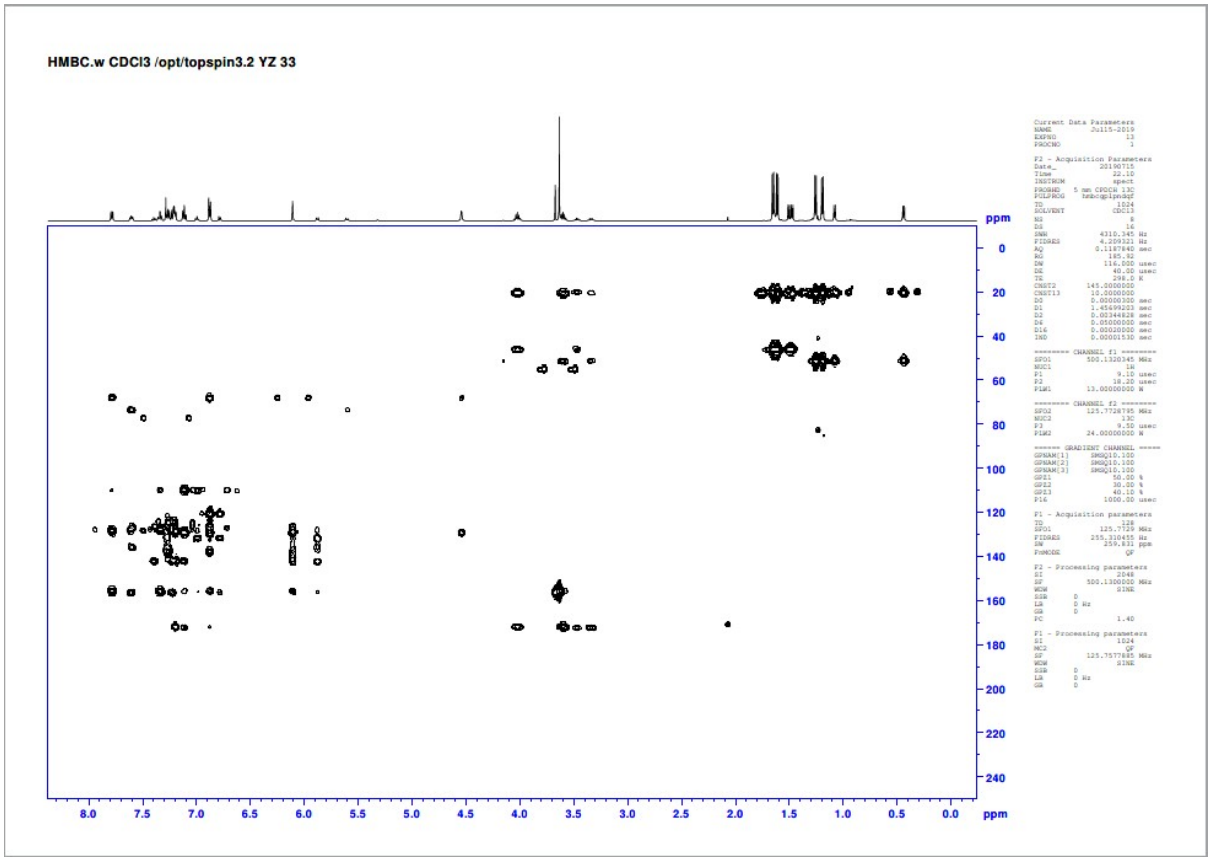


HSQC (500 MHz, $CDCl_3$) of **8r**:

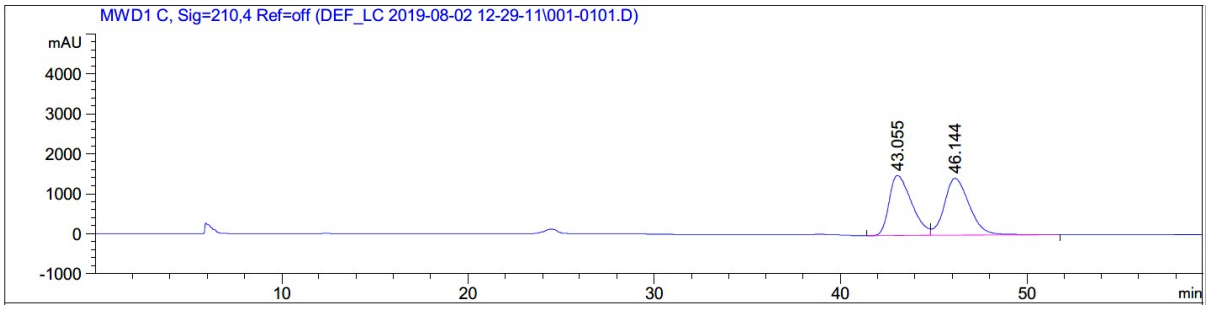




HMBC (500 MHz, $CDCl_3$) of **8r**:



HPLC of racemic 2-(hydroxy(2-methoxyphenyl)methyl)-N,N-diisopropylbenzamide **8r** (YZ216):

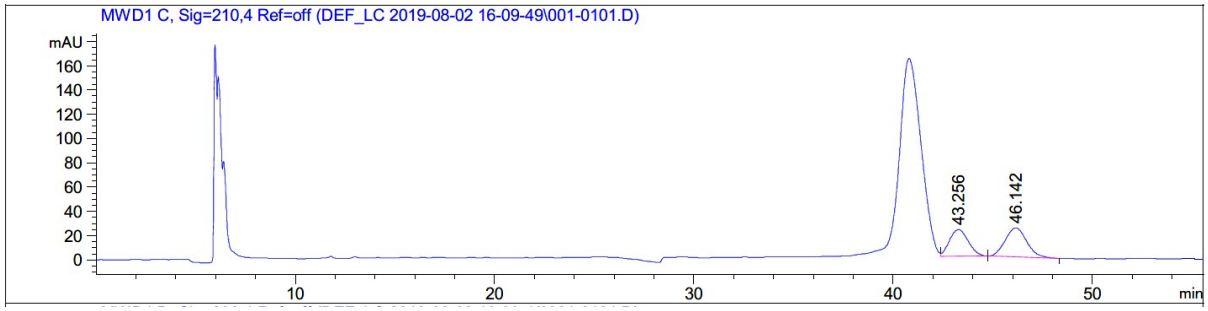


Signal 2: MWD1 C, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	43.055	BV	1.2857	1.26755e5	1506.44836	48.7608
2	46.144	VB	1.4211	1.33198e5	1426.87097	51.2392
Totals :				2.59953e5	2933.31934	

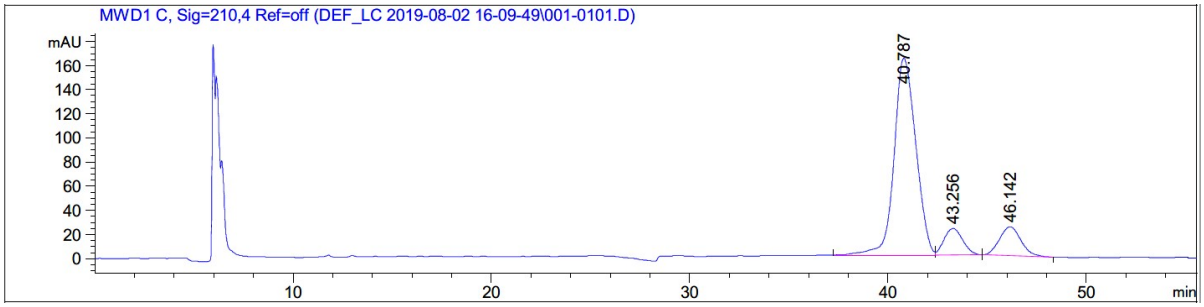
HPLC after ATH of N,N-diisopropyl-2-(2-methoxybenzoyl)benzamide **7r** (YZ241):

(*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst (after 168 hours, 20% conversion, 11.9% ee).



Signal 2: MWD1 C, Sig=210,4 Ref=off

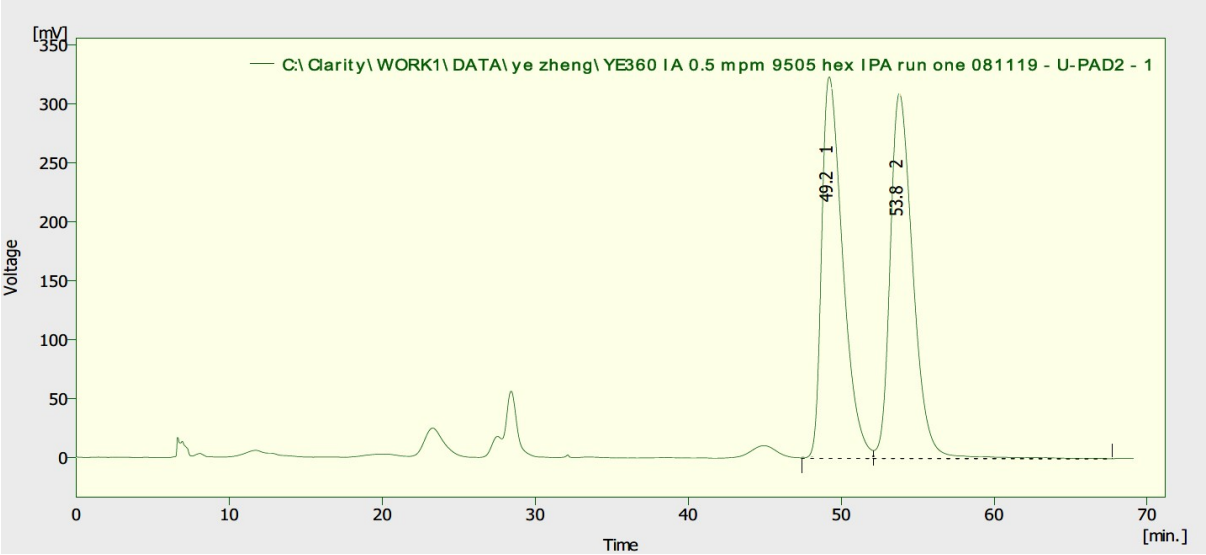
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	43.256	VB	0.9731	1429.45947	21.91137	44.0382
2	46.142	BB	1.0753	1816.49194	24.10279	55.9618
Totals :				3245.95142	46.01416	



Signal 2: MWD1 C, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	40.787	BV	1.1509	1.24247e4	163.06332	79.2864
2	43.256	VB	0.9731	1429.45947	21.91137	9.1219
3	46.142	BB	1.0753	1816.49194	24.10279	11.5917
Totals :				1.56706e4	209.07749	

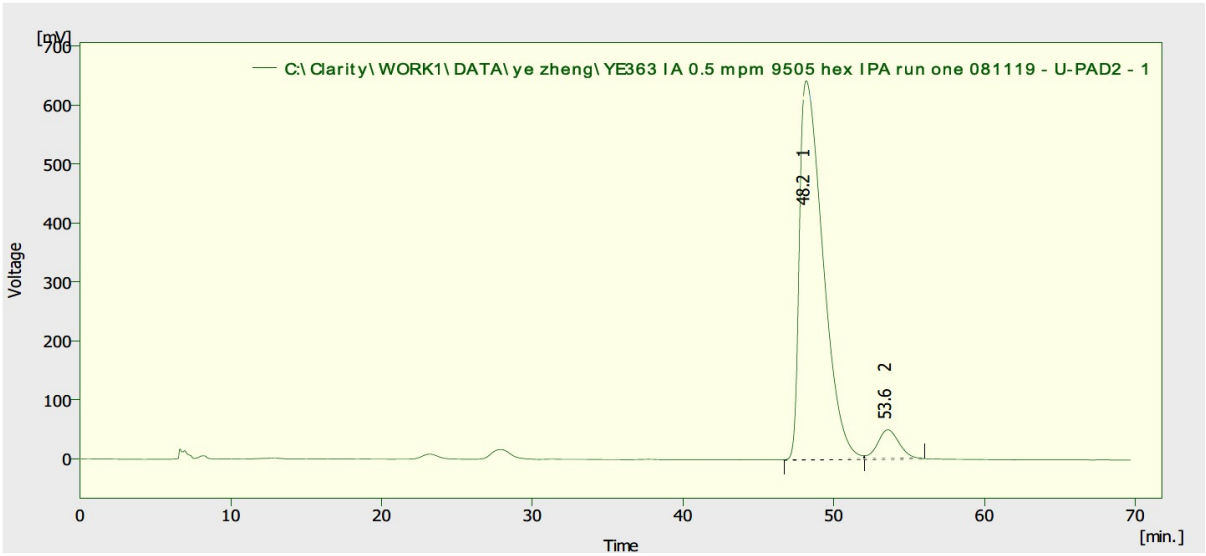
HPLC of racemic 2-(hydroxy(2-methoxyphenyl)methyl)-N,N-diisopropylbenzamide **8r** (after methylation of racemic 2-(hydroxy(2-hydroxyphenyl)methyl)-N,N-diisopropylbenzamide **8q**, YZ360).



Result Table (Uncal - C:|Clarity|WORK1|DATA|ye zheng|YE360 IA 0.5 mpm 9505 hex IPA run one 081119 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	49.220	30821.082	323.261	49.0	51.1	1.46	
2	53.804	32025.808	309.421	51.0	48.9	1.56	
	Total	62846.890	632.683	100.0	100.0		

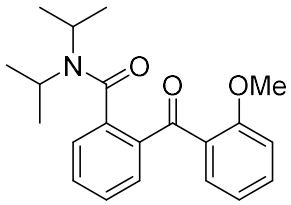
HPLC after methylation of asymmetric 2-(hydroxy(2-hydroxyphenyl)methyl)-N,N-diisopropylbenzamide **8c** (YZ363; (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst, 86.8% ee).



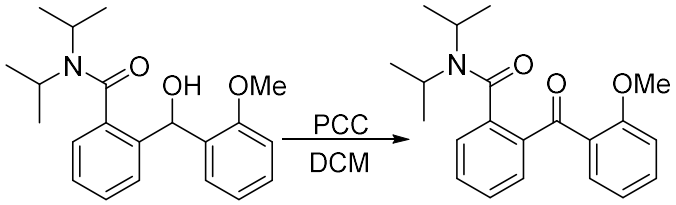
Result Table (Uncal - C:|Clarity|WORK1|DATA|ye zheng|YE363 IA 0.5 mpm 9505 hex IPA run one 081119 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	48.176	69546.612	642.788	93.4	92.8	1.68	
2	53.588	4942.470	49.636	6.6	7.2	1.53	
	Total	74489.081	692.424	100.0	100.0		

N,N-Diisopropyl-2-(2-methoxybenzoyl)benzamide 7r.



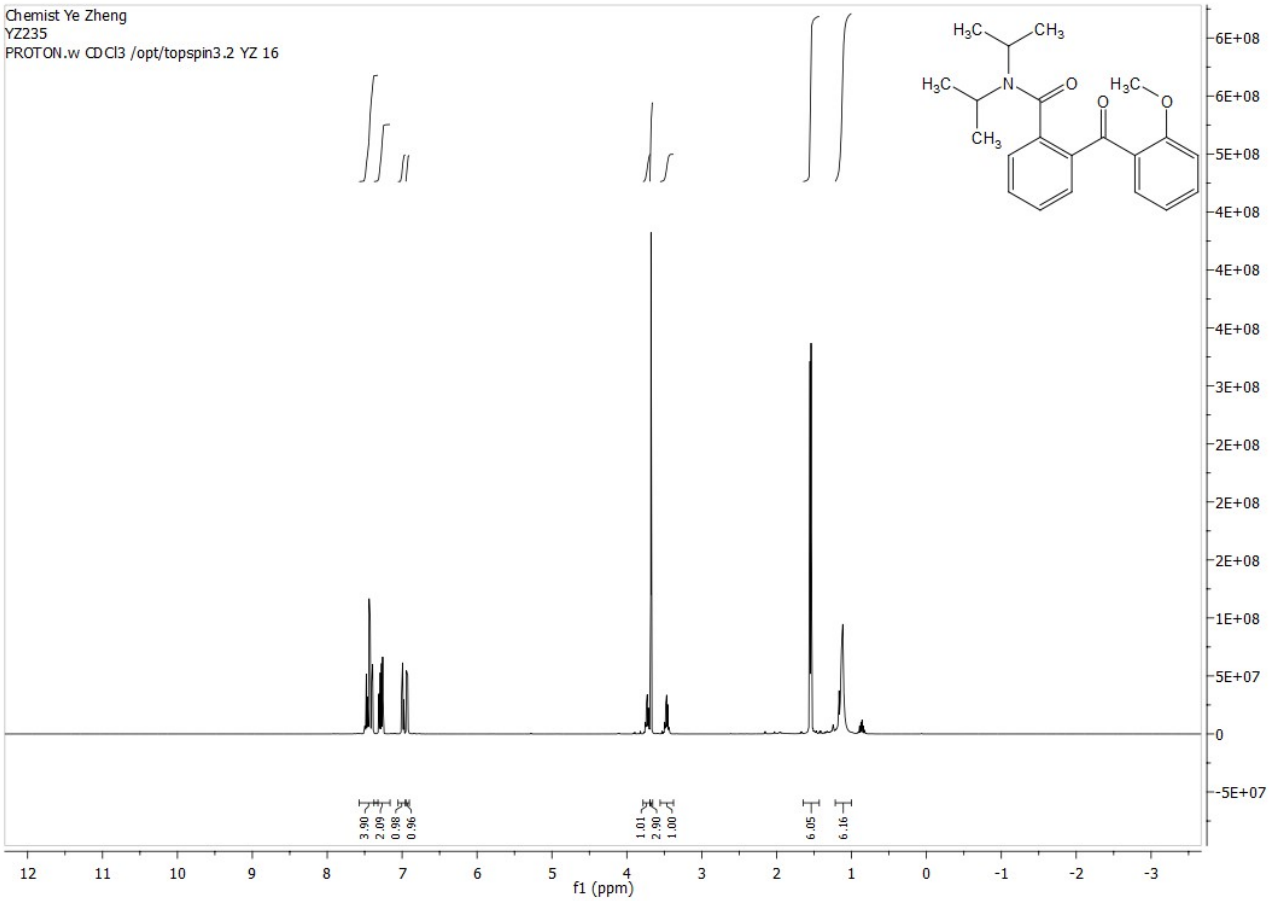
YZ235, YZ240



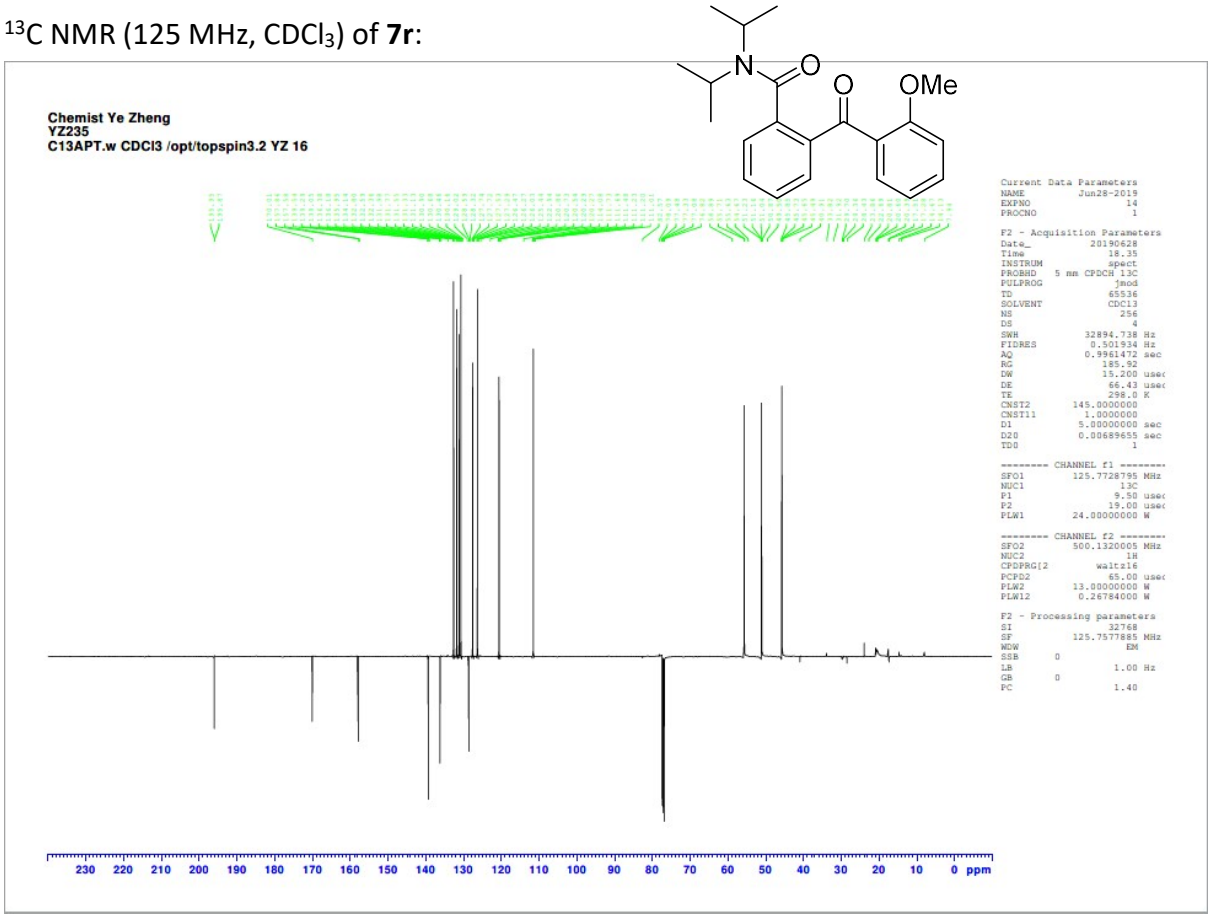
This compound is novel.

To a solution of 2-(hydroxy(2-methoxyphenyl)methyl)-N,N-diisopropylbenzamide **8r** (100 mg, 0.29 mmol) in DCM (1 mL) at rt was added pyridinium chlorochromate (95 mg, 0.44 mmol). The reaction mixture was left to stir under a nitrogen atmosphere overnight. TLC (4:1 hexane: EtOAc) after this time indicated full conversion. The solids were removed by gravity filtration and was washed with DCM. The combined solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give N,N-diisopropyl-2-(2-methoxybenzoyl)benzamide **8r** as a colorless oil (28,1 mg, 0.08 mmol, 28%). TLC: Rf ca 0.20 (4:1 hexane: EtOAc), strong UV and $KMnO_4$; HRMS: (found (ESI+): [M+Na]+, Calcd for $C_{21}H_{25}NNaO_3$ 362.1729; Found 362.1727; -0.6 ppm error; ν_{max} 2970, 2933, 1624, 1597, 1434, 1339, 1243 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.50-7.40 (4H, m, ArH), 7.31-7.26 (2H, m, ArH), 6.99 (1H, t, *J* = 7.4, ArH), 6.94 (1H, d, *J* = 8.7, ArH), 3.74-3.71 (1H, m, N[*CH*$(CH_3)_2]_2$), 3.68 (3H, s, OCH_3), 3.48-3.46 (1H, m, N[*CH*$(CH_3)_2]_2$), 1.55 (6H, d, *J*= 6.8, N[CH(*CH₃*$)_2]_2$), 1.17-1.10 (6H, m, N[CH(*CH₃*$)_2]_2$) ppm; δ_C (125 MHz, $CDCl_3$) 196.0 (C), 170.0 (C), 157.9 (C), 139.3 (C), 136.2 (C), 132.6 (CH), 131.8 (CH), 131.1 (CH), 130.7 (CH), 128.6 (C), 127.5 (CH), 126.3 (CH), 120.5 (CH), 111.5 (CH), 55.6 (CH), 51.0 (CH), 45.6 (CH_3), 23.9 (CH_3), 20.8 (CH_3), 20.4 (CH_3) ppm; m/z (ES-API+) 362.3 (M^+ + 23, 100%).

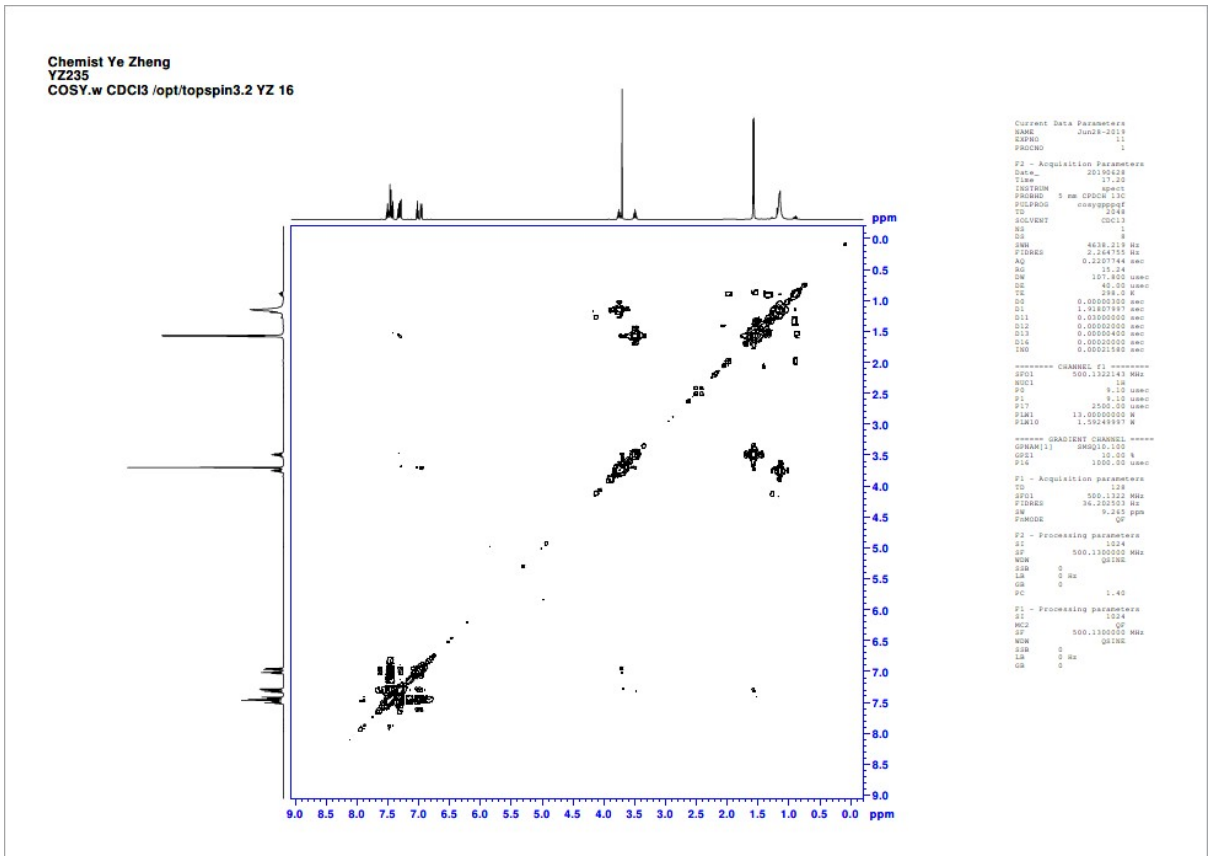
^{1}H NMR (500 MHz, $CDCl_3$) of **7r**:



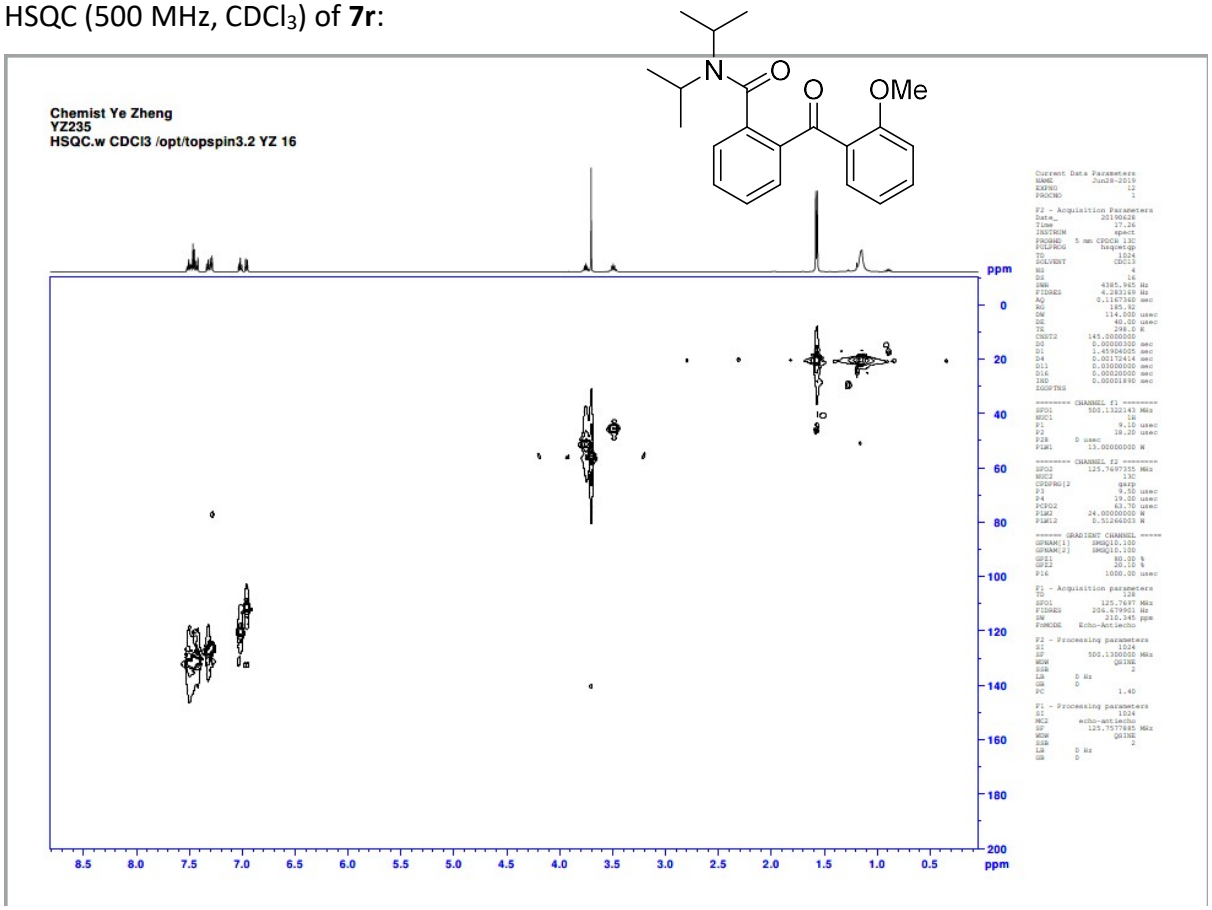
^{13}C NMR (125 MHz, $CDCl_3$) of **7r**:



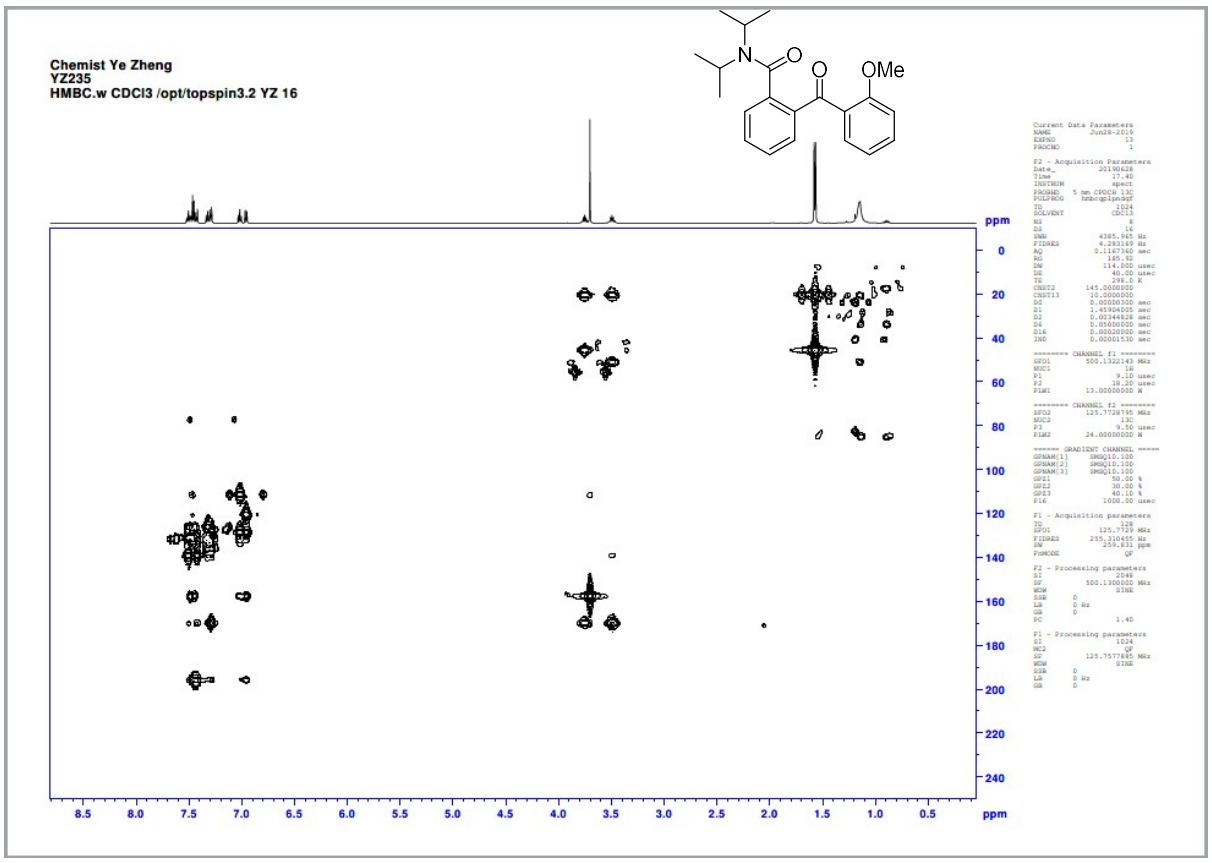
COSY (500 MHz, $CDCl_3$) of **7r**:



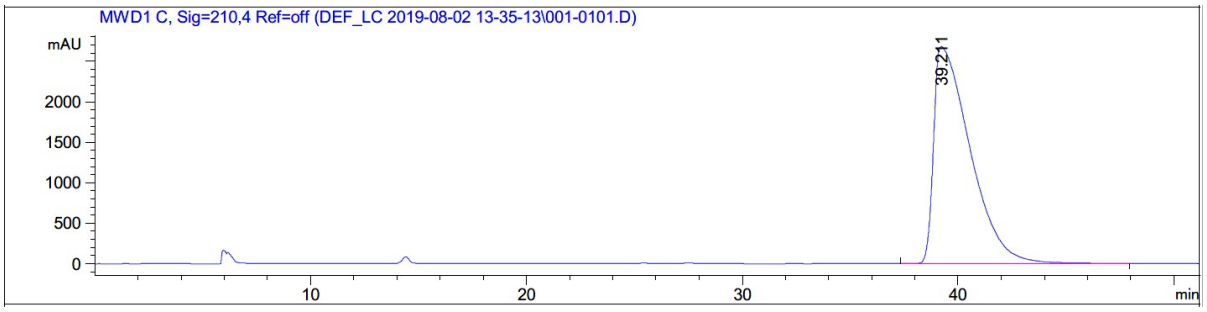
HSQC (500 MHz, $CDCl_3$) of **7r**:



HMBC (500 MHz, $CDCl_3$) of **7r**:



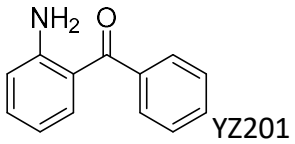
HPLC of N,N-diisopropyl-2-(2-methoxybenzoyl)benzamide **7r**:



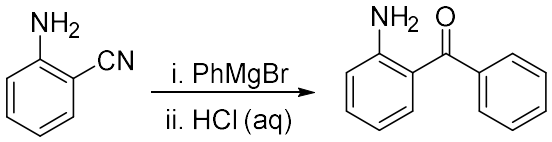
Signal 2: MWD1 C, Sig=210,4 Ref=off

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	39.211	BB	1.4847	3.14424e5	2680.12549	100.0000
Totals :				3.14424e5	2680.12549	

(2-Aminophenyl)(phenyl)methanone 7s.



YZ201

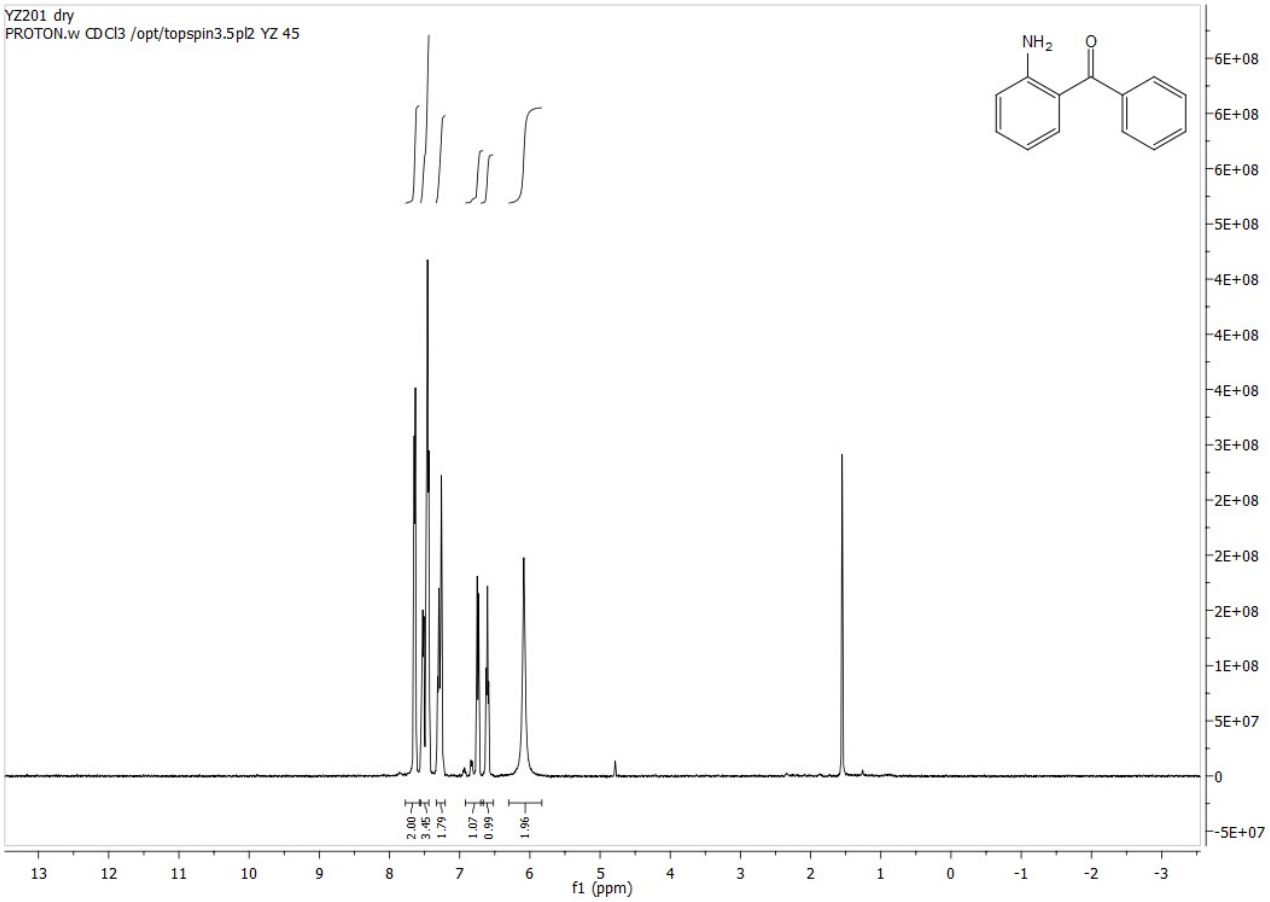


This compound has been reported and fully characterized.

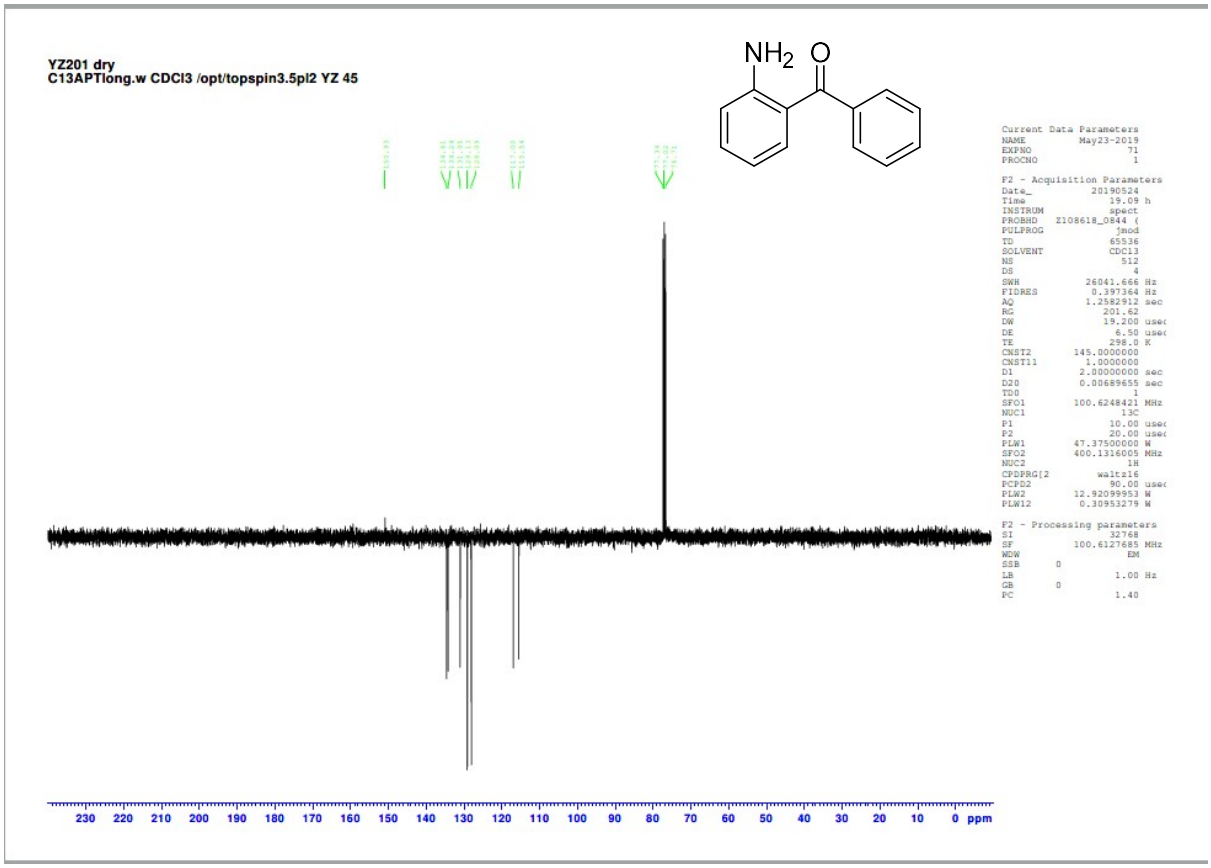
Reference: Basuli, S., Satyanarayana, G. *Eur. J. Org. Chem.* **2018**, *2018*, 957 – 970.

To a solution of 2-aminobenzonitrile (250 mg, 2.12 mmol) in THF (2.5 mL) was added phenyl magnesium bromide (2.12 mL, 3.0 M in diethyl ether, 6.36 mmol) dropwise at 0°C and the reaction was stirred under a nitrogen atmosphere for 12 hours and allowed to warm to rt. After cooling down to 0°C, HCl solution (6.36 mL, 2.0 M, 12.7 mmol) was added dropwise and the mixture was stirred at rt for another 12 hours. TLC (9:1 hexane: EtOAc) after this time indicated full conversion. The mixture was basified to pH = 9 with 10% NaOH solution and extracted with EtOAc (20 mL × 3). The combined organic layers were then washed with brine (20 mL) and dried ($MgSO_4$) and filtered. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-20% ethyl acetate in hexane to give (2-aminophenyl)(phenyl)methanone **7s** as a yellow solid (99.1 mg, 0.50 mmol, 23.8%). TLC: Rf ca 0.40 (9:1 hexane: EtOAc), strong UV and $KMnO_4$; δ_H (400 MHz, $CDCl_3$) 7.65 (2H, d, *J* = 6.0, ArH), 7.53-7.44 (3H, m, ArH), 7.31-7.26 (2H, m, ArH), 6.75 (1H, d, *J* = 8.4, ArH), 6.60 (1H, t, *J* = 7.6, ArH), 6.09 (2H, s, NH_2) ppm; δ_C (100 MHz, $CDCl_3$) 150.9 (C), 134.6 (CH), 134.3 (CH), 131.1 (CH), 129.1 (CH), 128.1 (CH), 117.0 (CH), 115.5 (CH). Data matched that reported.

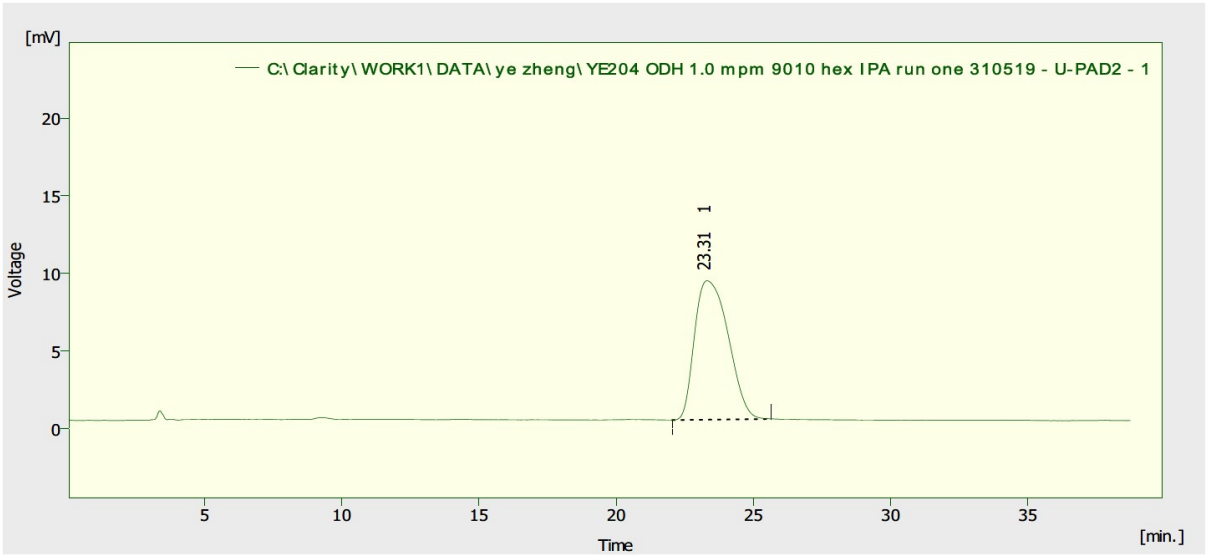
^{1}H NMR (400 MHz, $CDCl_3$) of **7s**:



^{13}C NMR (100 MHz, $CDCl_3$) of **7s**:



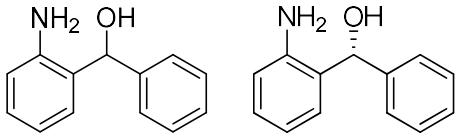
HPLC of (2-aminophenyl)(phenyl)methanone **7s**:

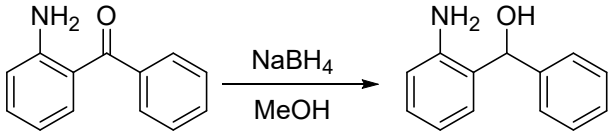


Result Table (Uncal - C:\Clarity\WORK1\DATA\ye zheng\YE204 ODH 1.0 mpm 9010 hex IPA run one 310519 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	23.308	765.688	8.958	100.0	100.0	1.41	
	Total	765.688	8.958	100.0	100.0		

(2-Aminophenyl)(phenyl)methanol **8s**.


racemic: YZ206. Asymmetric: YZ211

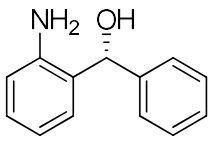


This compound has been reported and fully characterized.

Reference: Chen, J. H.; Chen, Z. C.; Zhao, H.; Zhang, T.; Wang, W. J.; Zou, Y.; Zhang, X. J.; Yan, M. *Org. Biomol. Chem.* **2016**, *14*, 4071-4076.

To a solution of (2-aminophenyl)(phenyl)methanone **7s** (100 mg, 0.51 mmol) in MeOH (3 mL) was added sodium borohydride (96.9 mg, 2.55 mmol). The reaction was stirred for 4 hours. TLC (9:1 hexane: EtOAc) after this time indicated full conversion. Distilled water (20 mL) was added, and the mixture was extracted with EtOAc (3 × 20 mL), dried with $MgSO_4$, and the solvent was removed under vacuum to give crude product. The product was isolated via flash chromatography on silica eluted with 0-20% ethyl acetate in hexane to give (2-aminophenyl)(phenyl)methanol **8s** as a yellow oil (40.6 mg, 0.20 mmol, 40.2%). TLC: Rf ca 0.30 (9:1 hexane: EtOAc), strong UV and $KMnO_4$; δ_H (500 MHz, $CDCl_3$) 7.41-7.30 (5H, m, ArH), 7.15-7.11 (1H, m, ArH), 7.05 (1H, d, *J* = 7.5, ArH), 6.77-6.74 (1H, m, ArH), 6.69 (1H, d, *J* = 8.0, ArH), 5.87 (1H, s, Ar*CH*OH), 3.97 (2H, s, NH_2), 2.61 (1H, s, ArCH*OH*) ppm; δ_C (125 MHz, $CDCl_3$) 144.9 (C), 141.9 (C), 129.0 (CH), 128.7 (CH), 128.5 (CH), 127.7 (CH), 127.5 (C), 126.6 (CH), 118.4 (CH), 117.0 (CH), 75.0 (CH) ppm. Data matched that reported.

Enantiomeric excess and conversion determined by HPLC analysis (Chiralcel ODH, 30 cm x 6mm column, hexane:iPrOH 9:1, 1.0 mL/min, T = 25°C) ketone 23.3 min, *R* isomer 36.0 min and *S* isomer 29.3 min.

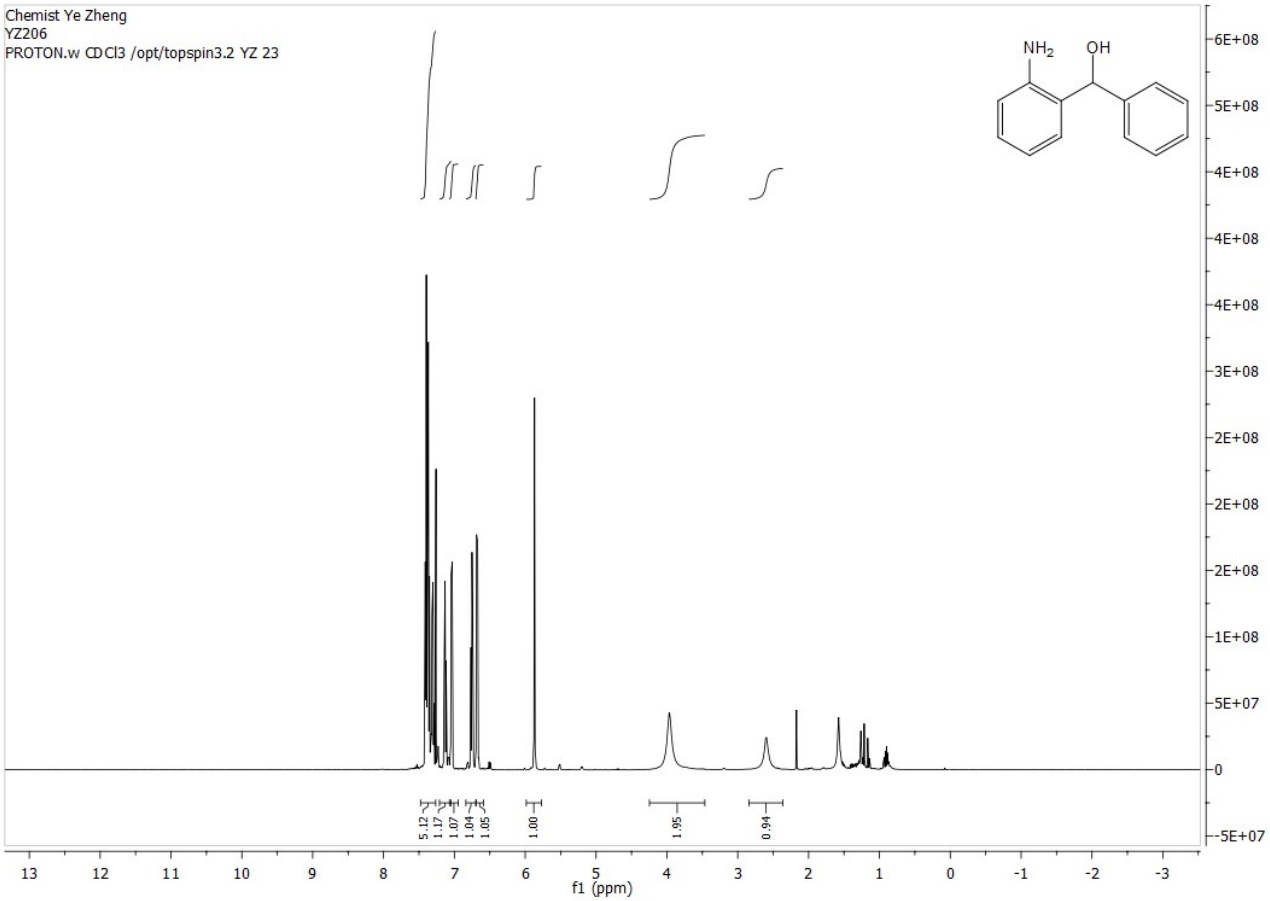


ATH of (2-aminophenyl)(phenyl)methanone **7s** (YZ221):

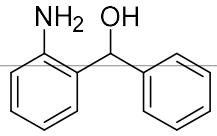
Catalyst (*R,R*)-**2** (0.0023 mmol, 1mol%) was added to the FA: TEA (5:2 azeotropic mixture, 0.18 mL) at rt and the mixture was stirred under a nitrogen atmosphere for 10-15 minutes; after which a solution of (2-aminophenyl)(phenyl)methanone **7s** (40 mg, 0.20 mmol) in DCM (0.25 mL) was added. The reaction mixture was stirrer under a nitrogen atmosphere, followed by TLC (9:1

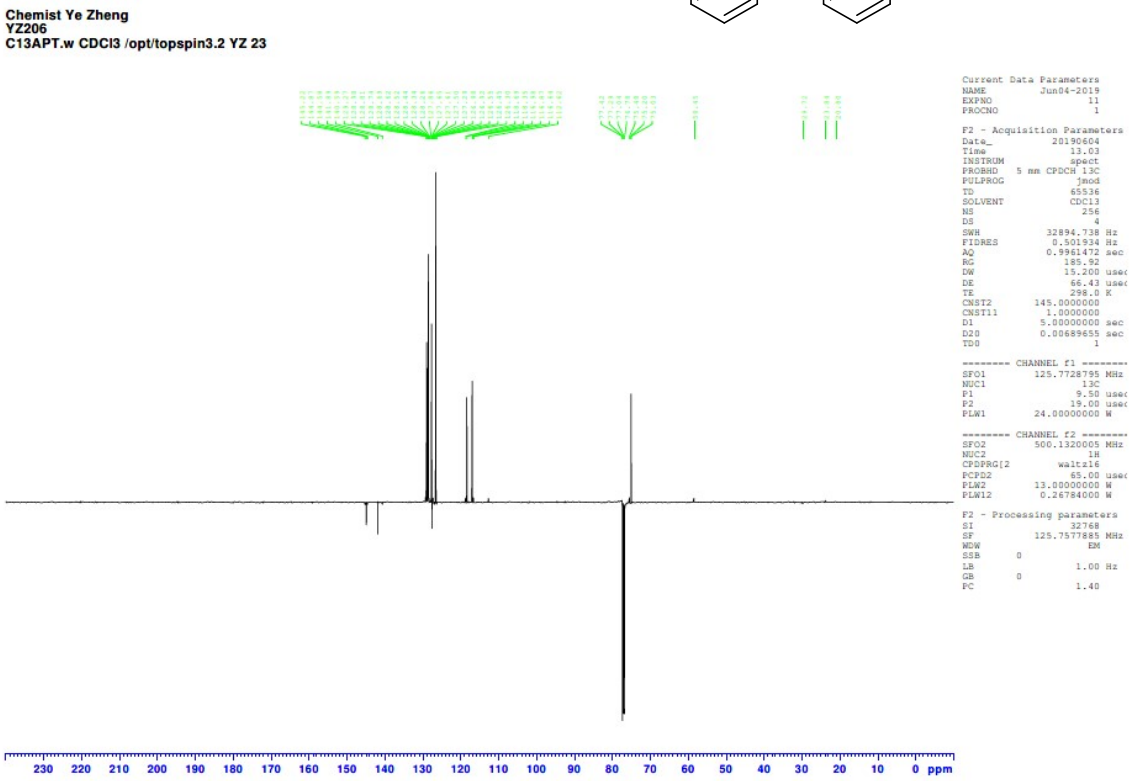
hexane: EtOAc). After 168 hours, the reaction was quenched using saturated $NaHCO_3$ solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried ($MgSO_4$) and filtered. The solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-20% ethyl acetate in hexane to give (2-aminophenyl)(phenyl)methanol **8s** (15.2 mg, 0.076 mmol, 37.6%; (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst example). The reaction was also followed by HPLC (Chiralcel ODH, 30 cm x 6 mm column, hexane:iPrOH 9:1, 1.0 mL/min, T = 25°C); (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst: 91% conversion (HPLC calibration: 1:1 (2-aminophenyl)(phenyl)methanone : (2-aminophenyl)(phenyl)methanol gives 6.04:1 absorption at 254 nm); $[\alpha]_D^{25}$ -13.6 (c 0.022 in MeOH) 46.2% ee (*R*) (lit. $[\alpha]_D^{20}$ +43.7 (c 1.0 in MeOH) 87% ee (*S*)) Reference: Mannam, S.; Sekar, G. *Tetrahedron: Asymmetry*, **2009**, *20*, 497-502.

^{1}H NMR (500 MHz, $CDCl_3$) of **8s**:

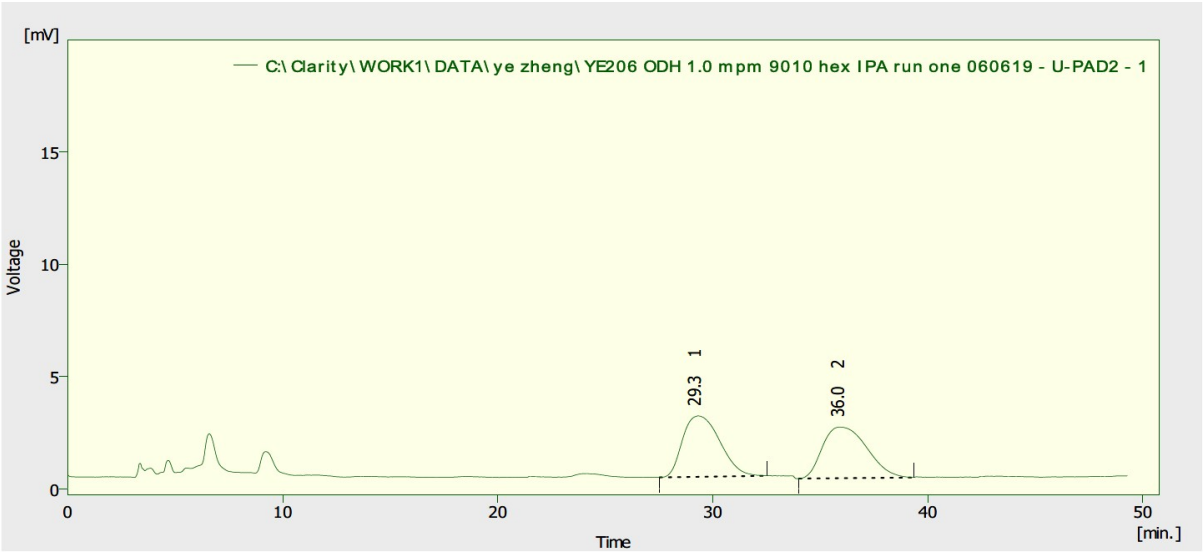


^{13}C NMR (125 MHz, $CDCl_3$) of **8s**:





HPLC of racemic (2-aminophenyl)(phenyl)methanol **8s**:

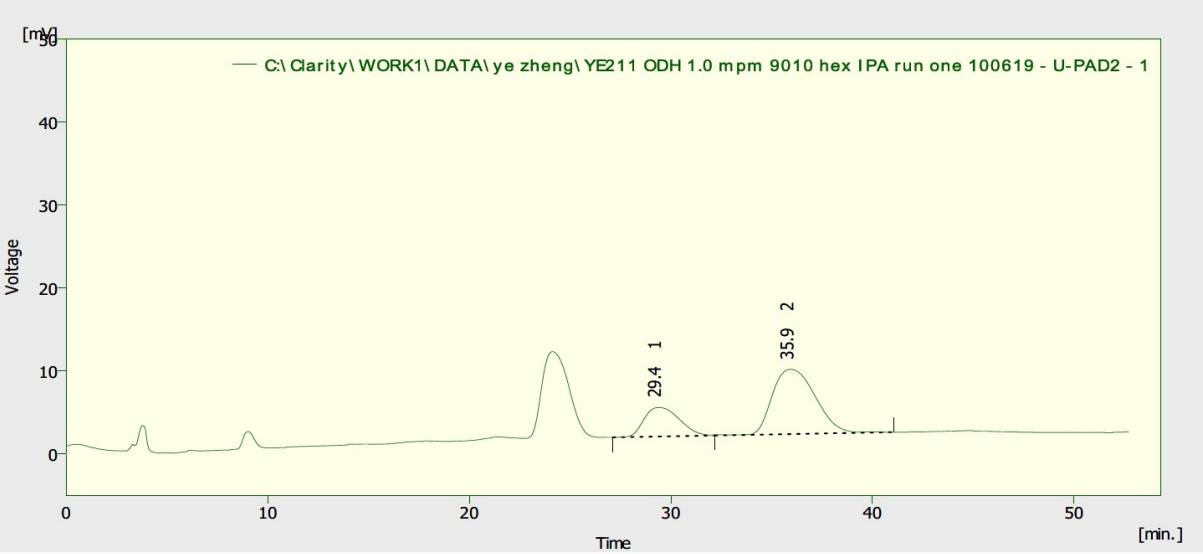


Result Table (Uncal - C:|Clarity|WORK1|DATA|ye zheng|YE206 ODH 1.0 mpm 9010 hex IPA run one 060619 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	29.292	327.220	2.714	50.0	54.3	1.96	
2	35.952	327.451	2.283	50.0	45.7	2.34	
	Total	654.671	4.996	100.0	100.0		

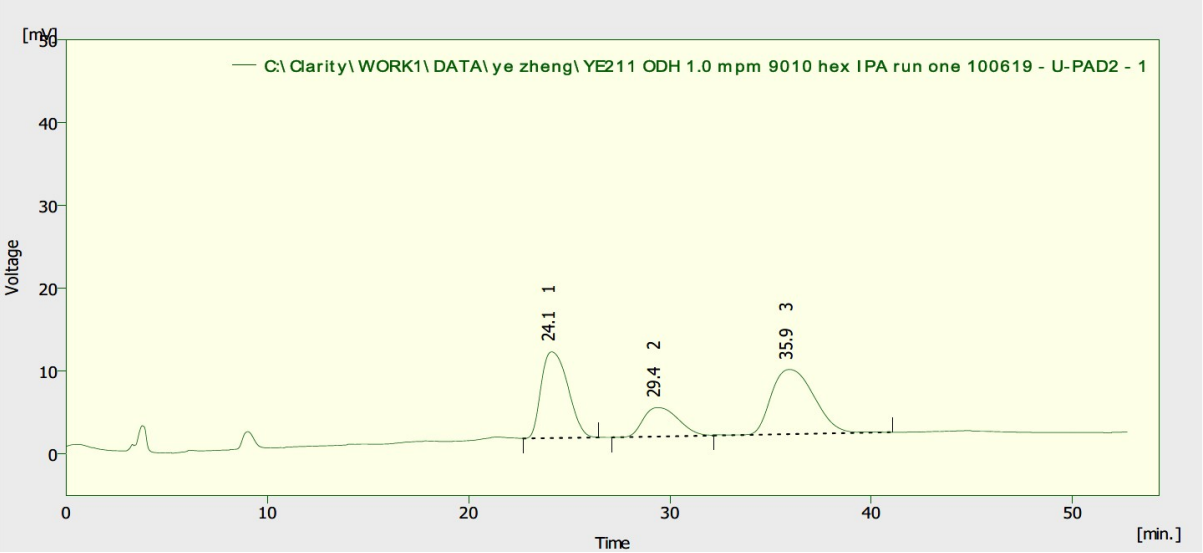
HPLC of **8s** after ATH of (2-aminophenyl)(phenyl)methanone **7s**:

(*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst (after 168 hours, 91% conversion, 46.2% ee, *R* configuration).



Result Table (Uncal - C:|Clarity|WORK1|DATA|ye zheng|YE211 ODH 1.0 mpm 9010 hex IPA run one 100619 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	29.356	425.624	3.508	26.9	31.0	1.98	
2	35.920	1157.409	7.813	73.1	69.0	2.39	
	Total	1583.032	11.321	100.0	100.0		



Result Table (Uncal - C:|Clarity|WORK1|DATA|ye zheng|YE211 ODH 1.0 mpm 9010 hex IPA run one 100619 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	24.120	962.672	10.423	37.8	47.9	1.51	
2	29.356	425.624	3.508	16.7	16.1	1.98	
3	35.920	1157.409	7.813	45.5	35.9	2.39	
	Total	2545.705	21.744	100.0	100.0		

Synthesis and characterisation of compounds 9-15.

Note on reaction not illustrated in paper: Imine **A** was prepared from 2'-hydroxyacetophenone in 93% yield and was converted to the racemic amine **B** using sodium borohydride (Figure S2). However in attempts at ATH with catalyst (*R,R*)-**2** using FA/TEA/DCM the hydrolysis of **B** was the major reaction. The alternative use of ammonium formate in DCM, at 70 °C (sealed tube) as reported by Mangion *et al*. (reference 10 in main paper) was used in order to avoid hydrolysis, but the major product was the dimer **C** rather than the desired amine **B**.

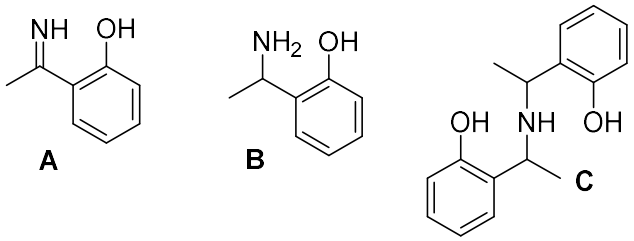
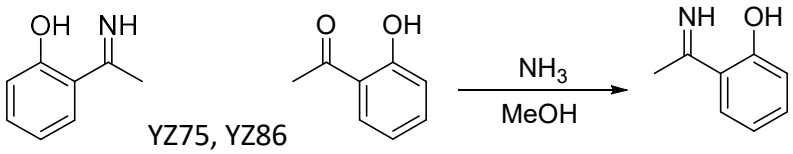


Figure S2. Attempted reduction of imine from 2'-hydroxyacetophenone.

2'-Hydroxyacetophenone imine A.

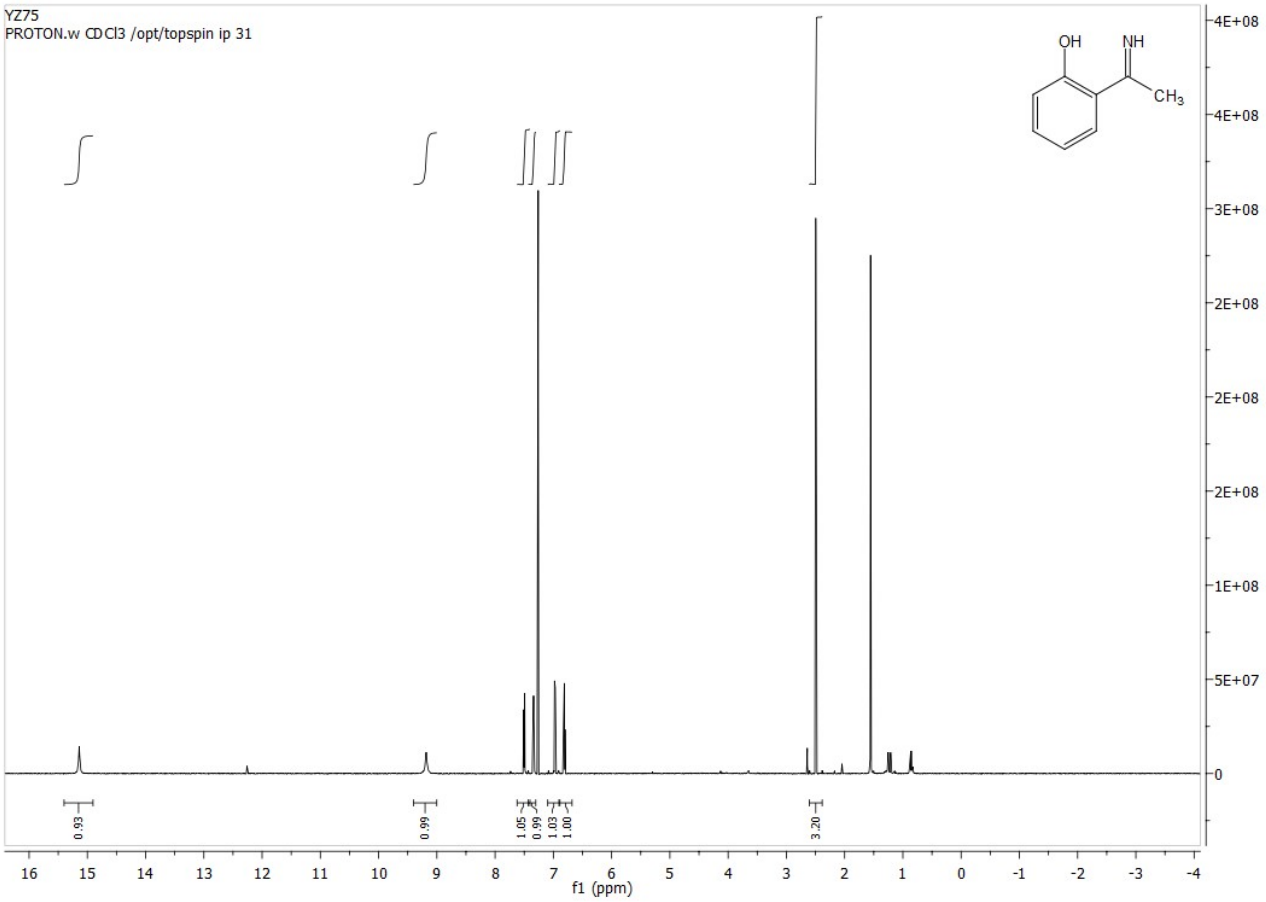


This compound has been reported and fully characterized.

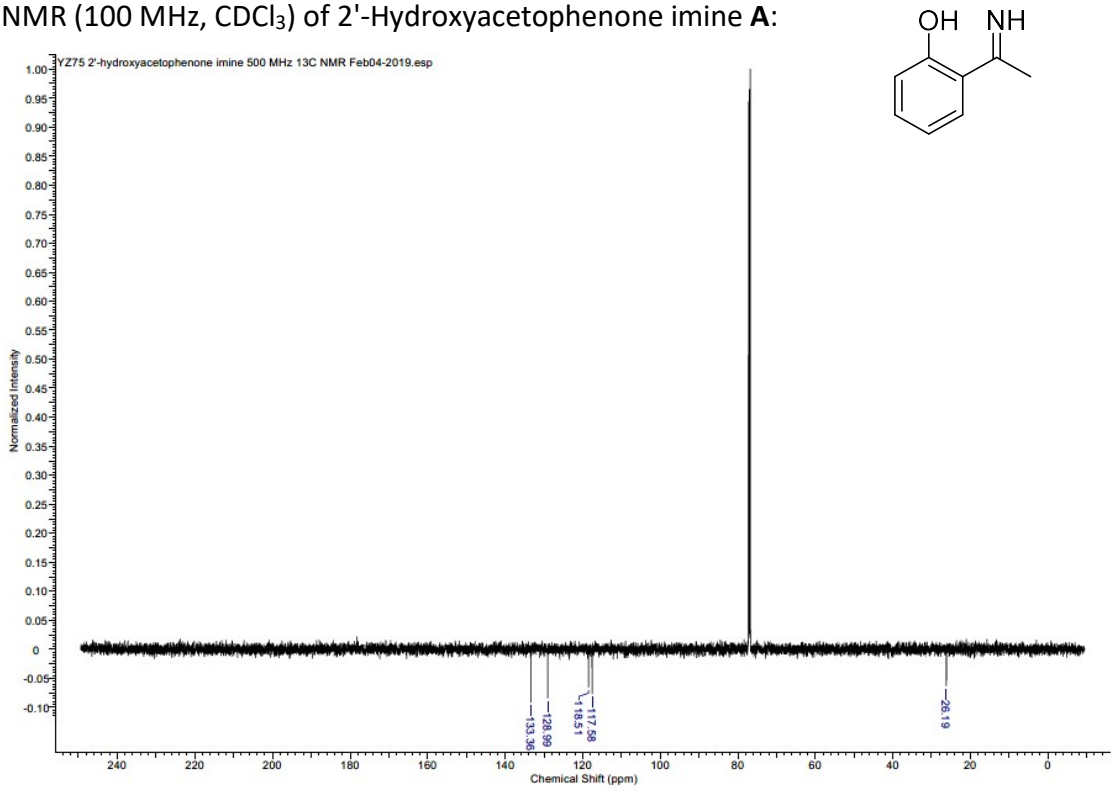
Reference: Taylor, N. J.; Emer, E.; Preshlock, S.; Schedler, M.; Tredwell, M.; Verhoog, S.; Mercier, J.; Genicot, C.; Gouverneur, V. *J. Am. Chem. Soc.* **2017**, *139*, 8267 – 8276.

2'-Hydroxyacetophenone (250 mg, 1.84 mmol) was dissolved in ammonia (1.32 mL, 7N in MeOH, 9.2 mmol) and the mixture was stirred under a nitrogen atmosphere overnight. TLC (1: 1 hexane: EtOAc) after this time indicated full conversion. The solvent was removed to give the product **A** as a yellow solid (231.2 mg, 1.71 mmol, 93%). TLC: Rf ca 0.20 (1:1 hexane: EtOAc), strong UV and $KMnO_4$; Mp: 140 °C; δ_H (500 MHz, $CDCl_3$) 15.14 (1H, s, ArOH), 9.18 (1H, s, NH), 7.50 (1H, dd, *J* = 8.0, 1.2, ArH), 7.43-7.30 (1H, m, ArH), 6.97 (1H, d, *J* = 8.2, ArH), 6.81 (1H, t, *J* = 7.5, ArH), 2.49 (3H, s, CH_3) ppm; δ_C (125 MHz, $CDCl_3$) 133.4 (CH), 129.0 (CH), 118.5 (C), 117.6 (CH), 26.2 (CH_3) ppm. Data matched that reported.

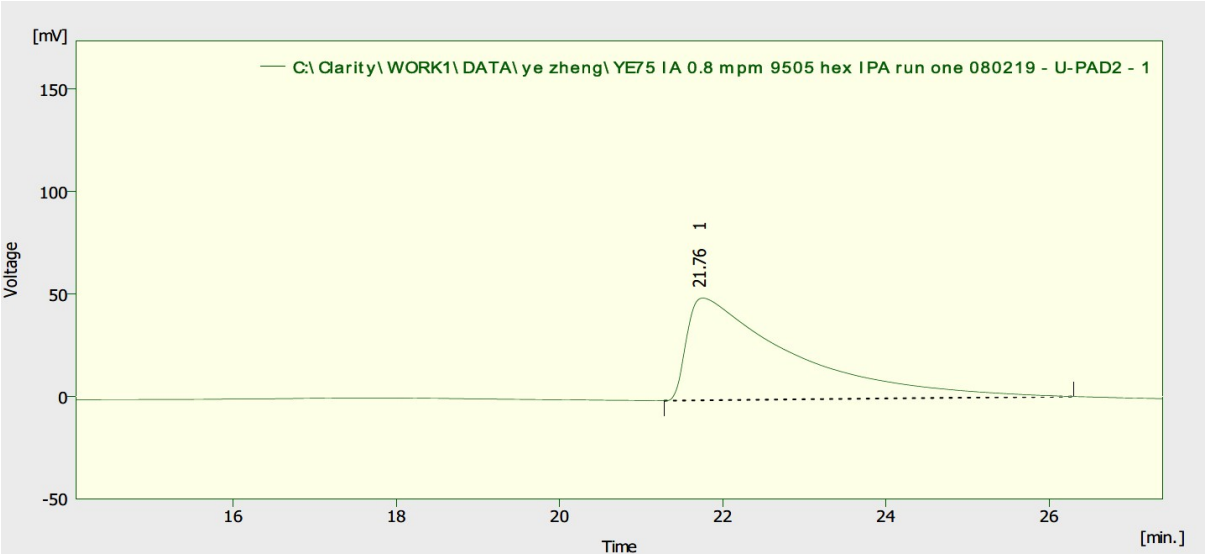
^{1}H NMR (500 MHz, $CDCl_3$) of 2'-Hydroxyacetophenone imine **A**:



^{13}C NMR (100 MHz, $CDCl_3$) of 2'-Hydroxyacetophenone imine **A**:



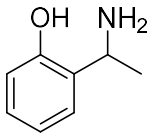
HPLC of 2'-hydroxyacetophenone imine **A**:



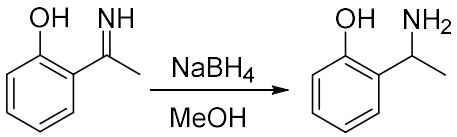
Result Table (Uncal - C:|Clarity|WORK1|DATA|ye zheng|YE75 IA 0.8 mpm 9505 hex IPA run one 080219 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	21.756	4445.826	49.935	100.0	100.0	1.22	
	Total	4445.826	49.935	100.0	100.0		

2-(1-Aminoethyl)phenol B.



racemic: YZ83. Asymmetric: YZ85, YZ97, YZ106



This compound has been reported and fully characterized.

Reference: Thanh B. N.; Hadjira B.; Qian W.; Francoise G.; *Org. Lett.* **2010**, *12*, 4705 – 4707.

To a solution of 2'-hydroxyacetophenone **A** (40 mg, 0.296 mmol) in MeOH (1 mL) was added sodium borohydride (22.5 mg, 0.592 mmol). The reaction was stirred for 4 hours. TLC (1: 1 hexane: EtOAc) after this time indicated full conversion. Distilled water (20 mL) was added, and the mixture was extracted with EtOAc (3 × 20ml), dried with $MgSO_4$, and the solvent was removed under vacuum to give 2-(1-aminoethyl)phenol **B** as a white solid (40.6 mg, 0.296 mmol, 88.9%). δ_H (400 MHz, $CDCl_3$) 7.20-7.13 (1H, m, ArH), 6.97 (1H, d, *J* = 7.3, ArH), 6.84 (1H, d, *J* = 8.3, ArH), 6.78 (1H, t, *J* = 7.2, ArH), 4.33 (1H, q, *J* = 6.8, *CH*NH_2), 1.48 (3H, d, *J* = 6.6, CH_3) ppm; δ_C (100 MHz, $CDCl_3$) 157.6 (C), 128.5 (CH), 128.1 (C), 127.2 (CH), 119.0 (CH), 117.2 (CH), 51.7 (CH), 23.9 (CH_3) ppm. Data matched that reported.

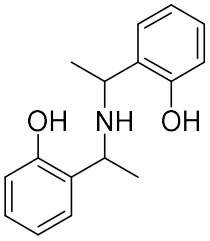
Enantiomeric excess and conversion determined by HPLC analysis (Chiralpak IA, 30 cm x 6mm column, hexane:iPrOH 95:5, 0.8 mL/min, T = 25°C) ketone 21.8 min, *R* and *S* isomers 13.1 min and 16.6 min, configuration is not known.

Attempt ATH in FA/TEA of 2'-Hydroxyacetophenone imine **A** (YZ85).

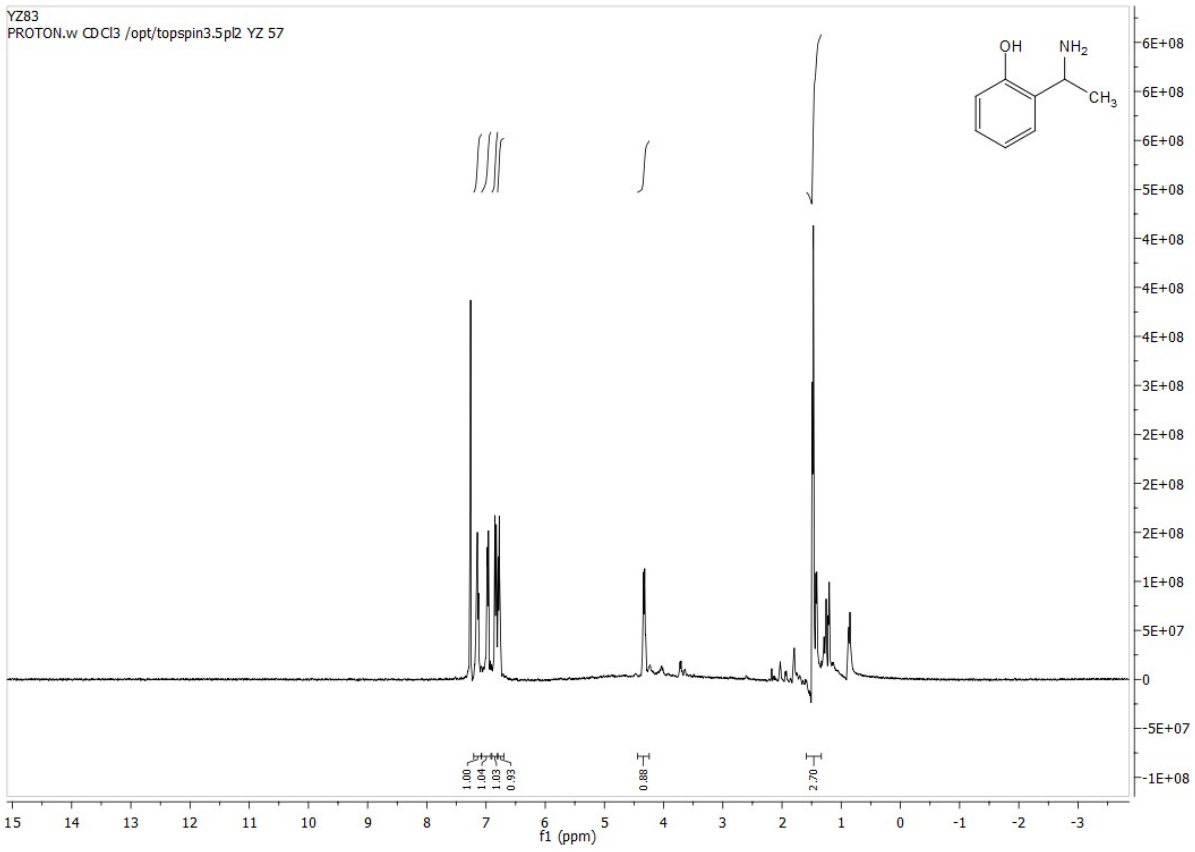
Catalyst (*R,R*)-**2** (0.00296 mmol, 1mol%) was added to FA: TEA (5:2 azeotropic mixture, 0.18 mL) at rt and the mixture was left to stir under a nitrogen inert atmosphere for 10-15 minutes; after which a solution of 2'-Hydroxyacetophenone imine **A**(40 mg, 0.296 mmol) in DCM (0.25 mL) was added. The reaction mixture was stirred under a nitrogen atmosphere overnight. The reaction was followed by TLC (19:1 DCM: MeOH). Then the reaction was quenched using saturated $NaHCO_3$ solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried ($MgSO_4$) and filtered. However, NMR indicated there is no product present. The starting material was hydrolysed.

Attempt ATH in water of **A** using (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst **2** and formation of **C** (YZ97 and YZ106).

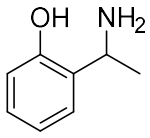
2'-Hydroxyacetophenone imine **A** (40 mg, 0.296 mmol), ammonium formate (74.6 mg, 1.184 mmol) and (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst (0.92 mg, 0.00148 mmol, 0.5 mol%) were added into a sealed tube and left to stir under a nitrogen atmosphere for 10 minutes. Dry DCM (1.5 mL) was degassed with nitrogen then added under nitrogen to the tube. The mixture was heated to 70 °C on a hot plate and stirred under a nitrogen atmosphere overnight. Then the reaction was quenched by saturated $NaHCO_3$ solution (20 mL). After which EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried (MgSO4) and filtered. NMR indicated there was no product present. m/z (ES-API+) 258.3 (M^+ + 1, 100%) indicated the product was the dimer **C**.

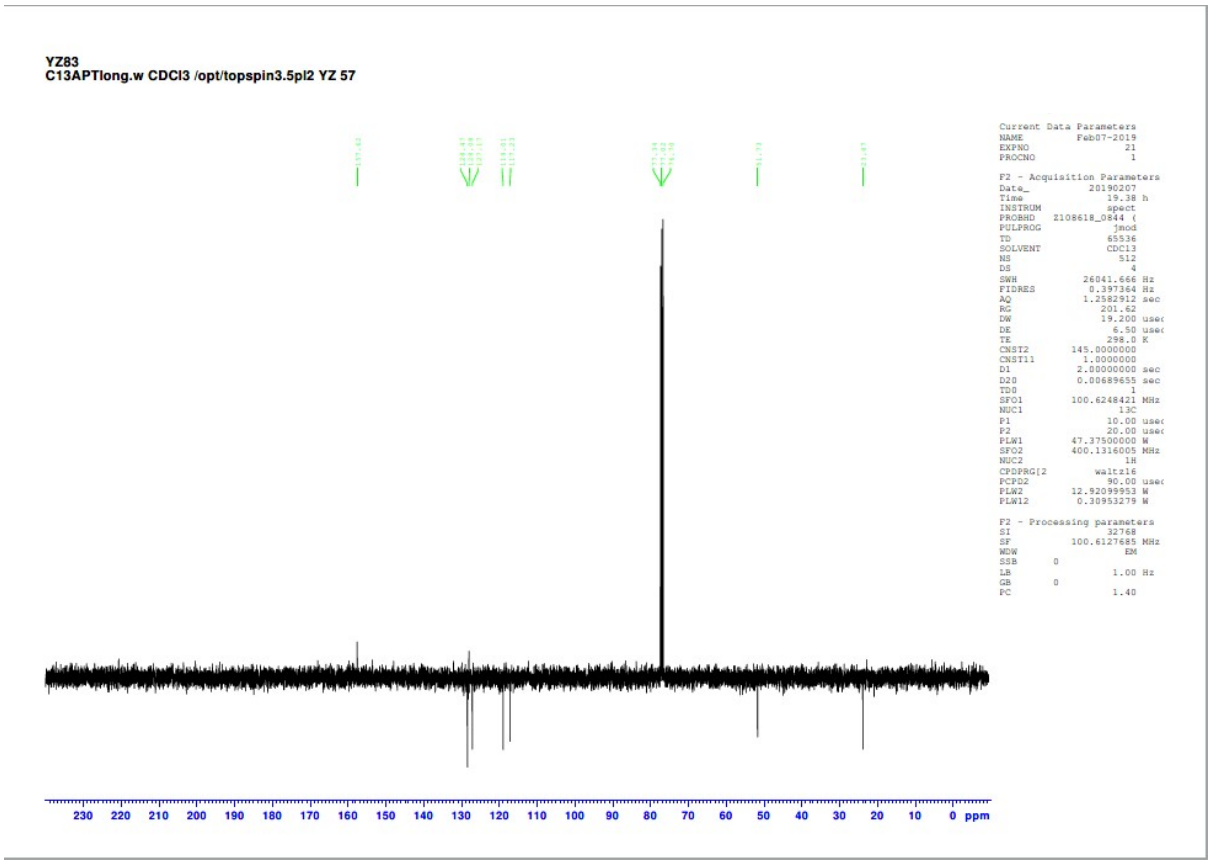


^{1}H NMR (400 MHz, $CDCl_3$) amine **B**:

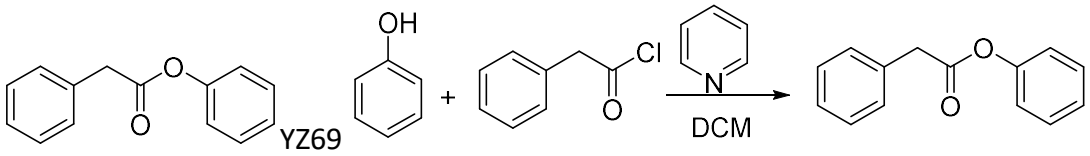


^{13}C NMR (100 MHz, $CDCl_3$) of amine **B**:





Phenyl 2-phenylacetate.



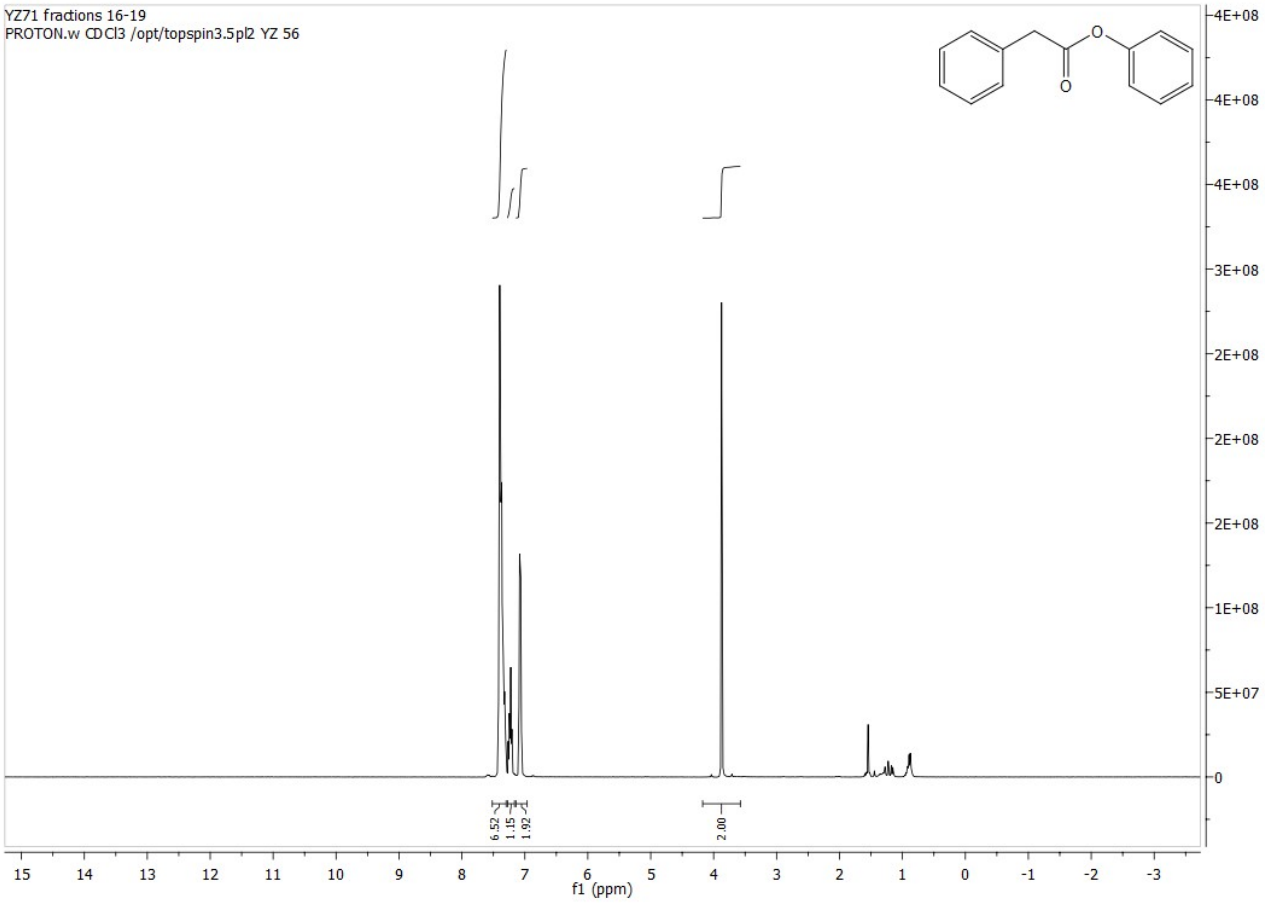
This compound has been reported and fully characterized.

Reference: Ackerman, L. K. G.; Martinez Alvarado, J. I.; Doyle, A. G.; *J. Am. Chem. Soc.* **2018**, *140*, 14059–14063.

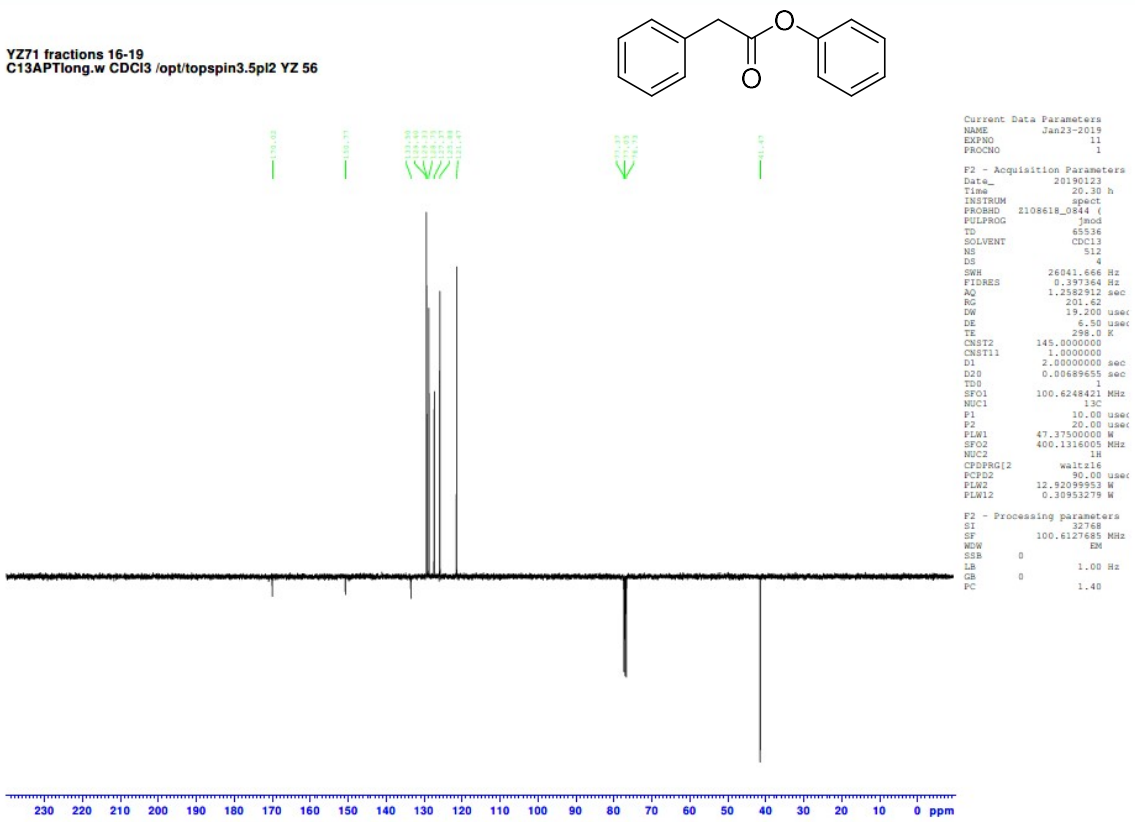
To a solution of phenol (227 mg, 2.42 mmol) and pyridine (190.8 mg, 2.415 mmol) in dry DCM (5 mL) was added dropwise 2-phenylacetyl chloride (250 mg, 1.61 mmol). The reaction mixture was stirred under a nitrogen atmosphere overnight. TLC (9:1 hexane: EtOAc) after this time indicated full conversion. After 17 hours, distilled water (20 mL) was added, and the mixture was extracted with EtOAc (3 × 20ml), dried with $MgSO_4$, and the solvent was removed under vacuum to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-20% ethyl acetate in hexane to give phenyl 2-phenylacetate as a white solid (308 mg, 1.45 mmol,

89.8%). TLC: Rf ca 0.50 (9:1 hexane: EtOAc), strong UV and $KMnO_4$; Mp: 43 °C; δ_H (400 MHz, $CDCl_3$) 7.40-7.32 (7H, m, ArH), 7.26-7.21 (1H, m, ArH), 7.08 (2H, d, *J* = 7.6, ArH), 3.87 (2H, s, CH_2) ppm; δ_C (100 MHz, $CDCl_3$) 170.0 (C), 150.8 (C), 133.5 (C), 129.4 (CH), 129.3 (CH), 128.8 (CH), 127.4 (CH), 125.9 (CH), 121.5 (CH), 41.5 (CH_2) ppm. Data matched that reported.

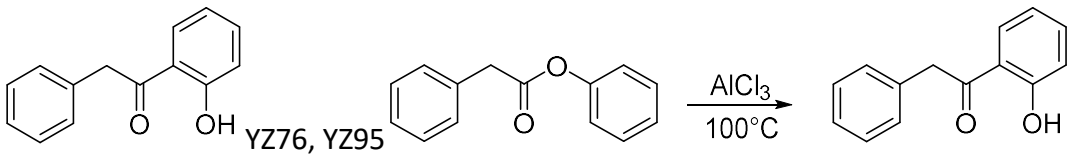
^{1}H NMR (400 MHz, $CDCl_3$) of phenyl 2-phenylacetate:



^{13}C NMR (100 MHz, $CDCl_3$) of phenyl 2-phenylacetate:



1-(2-Hydroxyphenyl)-2-phenylethan-1-one.

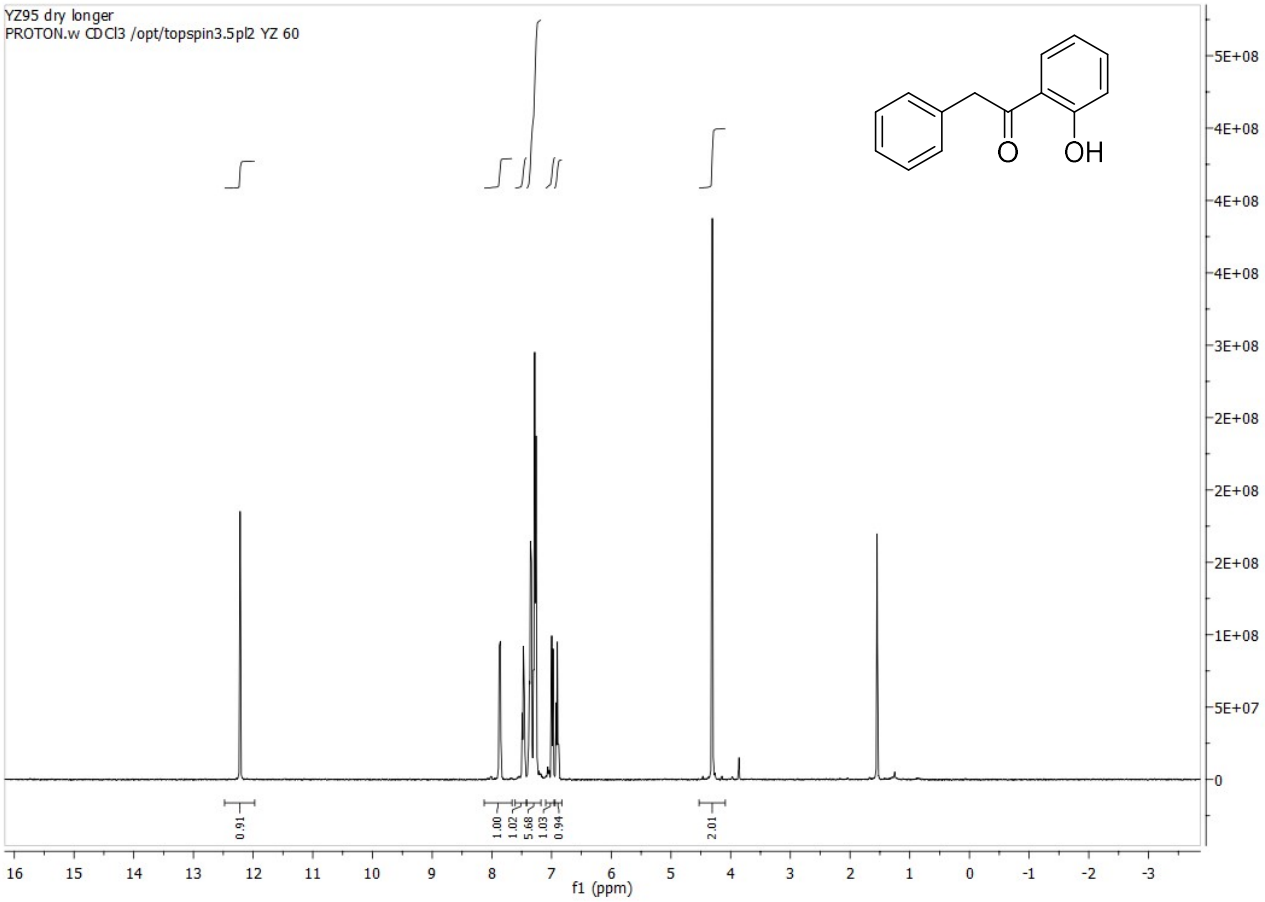


This compound has been reported and fully characterized.

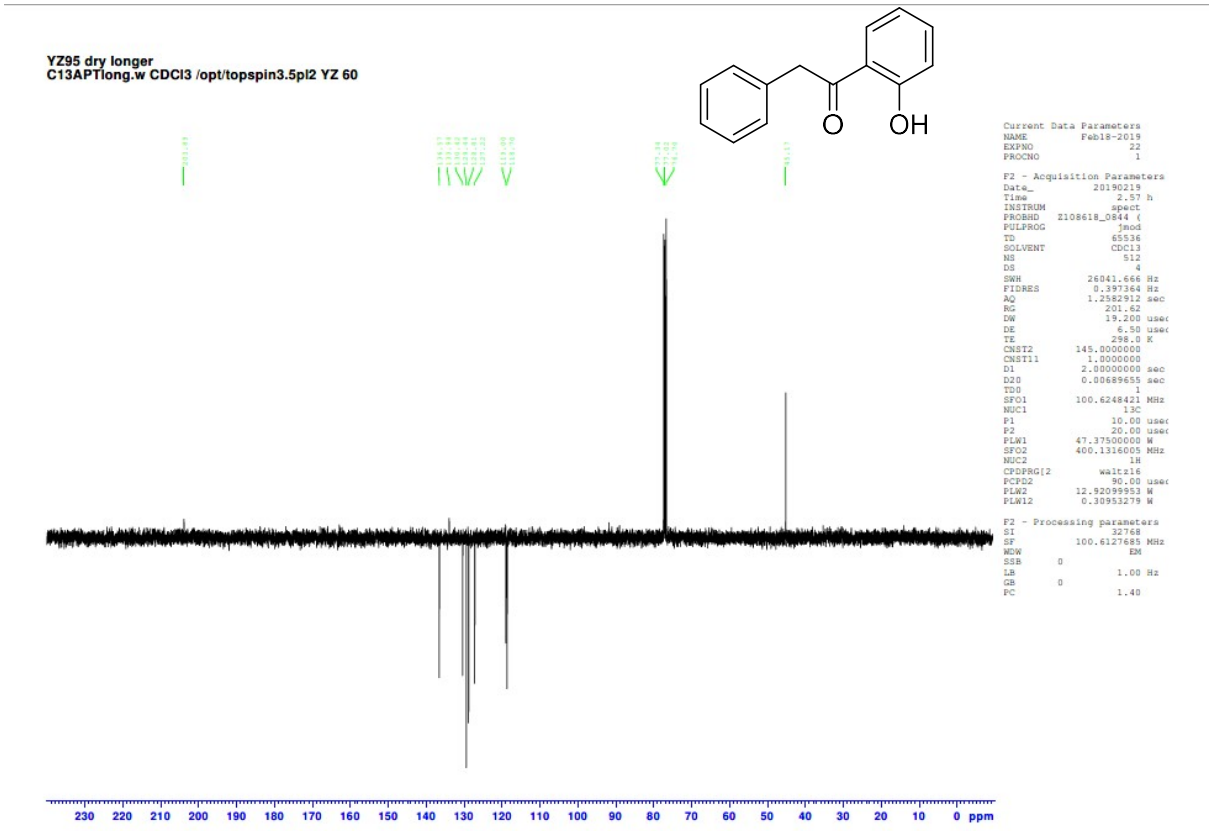
Reference: Majhi, B.; Kundu, D.; Ranu, B. C. *J. Org. Chem*. **2015**, *80*, 7739–7745.

Phenyl 2-phenylacetate (300 mg, 1.42 mmol) was mixed with aluminium chloride (378 mg, 2.84 mmol) and the mixture heated on a hot plate at 100° for 1.5 hr. Then the mixture was cooled in an ice bath and decomposed with 2M HCl solution. Chloroform was added and the organic layer was separated. The aqueous layer was extracted with $CHCl_3$ (3 × 20 mL). The combined organic layer was washed with water (3 × 20 mL), 2M NaOH solution (3 × 20 mL) and water (3 × 20 mL), successively, dried ($MgSO_4$) and filtered. Solvent was removed to give the crude product. The reaction was followed by TLC (9:1 hexane: ethyl acetate). The product was isolated via flash chromatography on silica eluted with 0-10% ethyl acetate in hexane to give 1-(2-hydroxyphenyl)-2-phenylethan-1-one as a white solid (153.2 mg, 0.72 mmol, 51.1%). TLC: Rf ca 0.40 (9:1 hexane: EtOAc), strong UV and $KMnO_4$; δ_H (400 MHz, $CDCl_3$) 12.22 (1H, s, OH), 7.88 (1H, d, *J* = 8.0, ArH), 7.47 (1H, t, *J* = 7.6, ArH), 7.37-7.26 (5H, m, ArH), 7.00 (1H, d, *J* = 8.4, ArH), 6.90 (1H, t, *J* = 7.6, ArH), 4.31 (2H, s, CH_2) ppm; δ_C (100 MHz, $CDCl_3$) 203.9 (C), 136.6 (CH), 133.9 (C), 130.4 (CH), 129.4 (CH), 128.8 (CH), 127.2 (CH), 119.0 (CH), 118.7 (CH), 45.2 (CH_2) ppm. Tha data matched that reported.

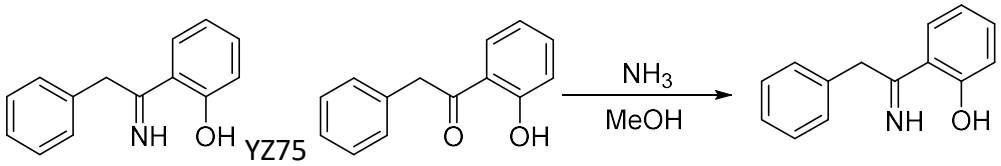
^{1}H NMR (400 MHz, $CDCl_3$) of 1-(2-hydroxyphenyl)-2-phenylethan-1-one:



^{13}C NMR (100 MHz, $CDCl_3$) of 1-(2-hydroxyphenyl)-2-phenylethan-1-one:



2-(1-Imino-2-phenylethyl)phenol **9**.

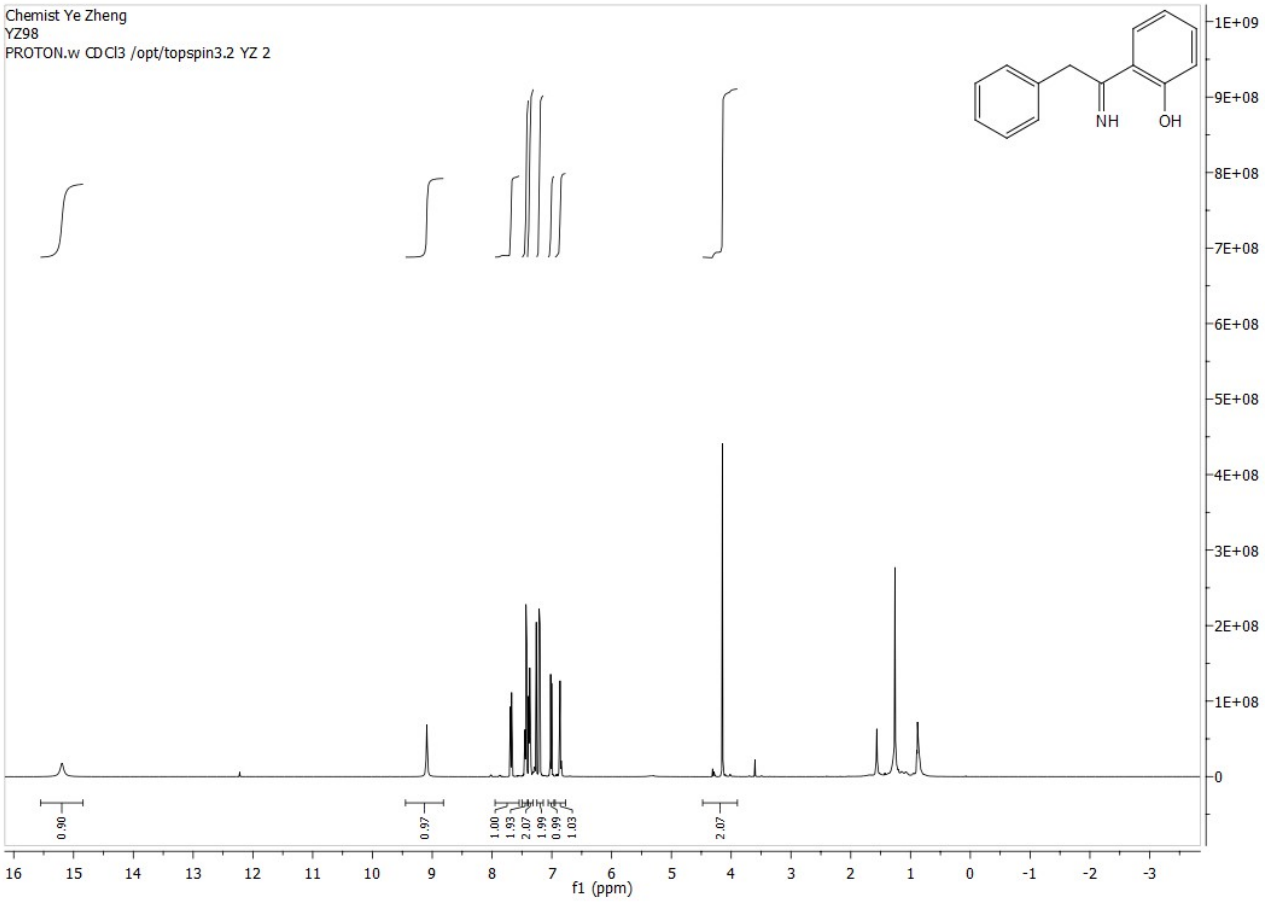


This compound has been reported but not fully characterized.

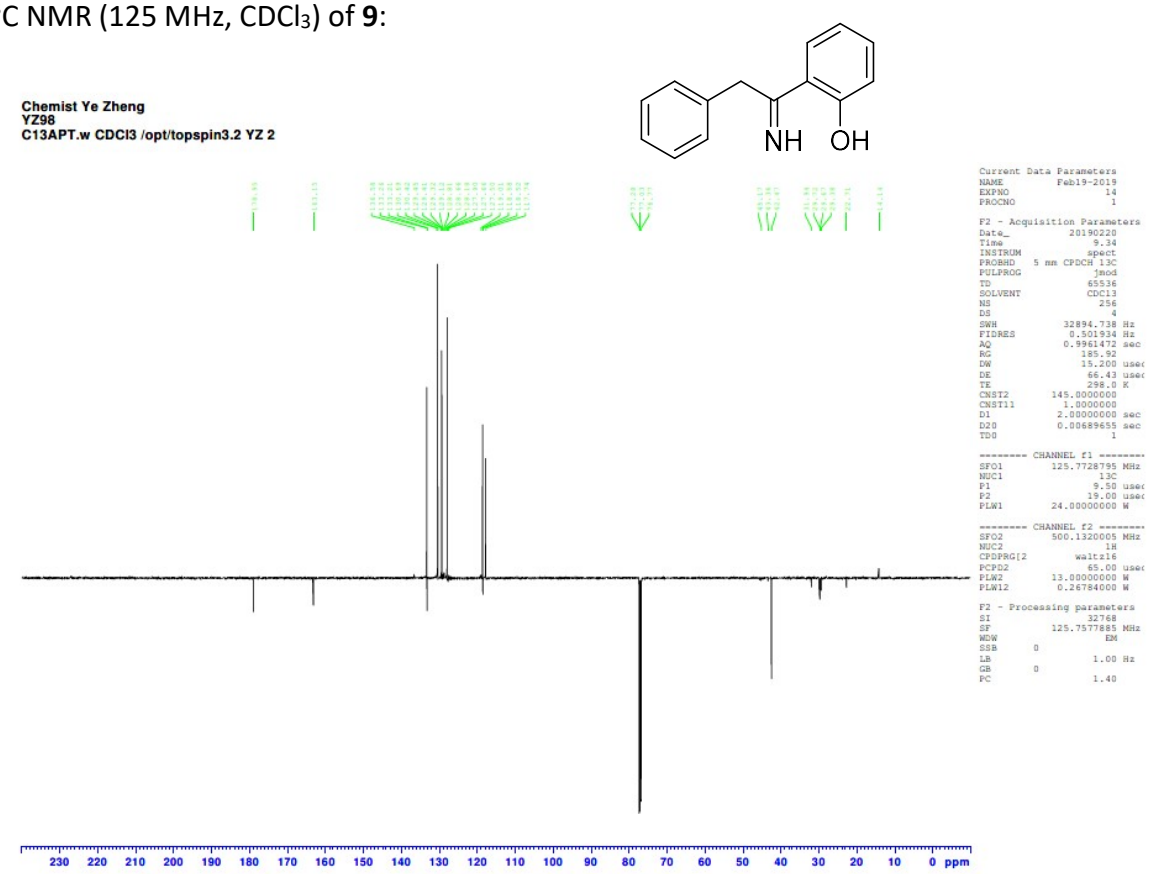
Reference: Mangion, I. K.; Chen, C.-Y.;Li, H.; Maligeres, P.; Christensen, Y. C. M.; Cohen, R.; Klapars, I. A.; Krska, S.; Nguyen, H.; Reamer, R. A.; Sherry, B. D.; Zavialov, I. *Org. Lett.* **2014**, *16*, 2310–2313.

1-(2-Hydroxyphenyl)-2-phenylethan-1-one (50 mg, 0.71 mmol) was dissolved in ammonia (1.72 mL, 7N in MeOH, 12.1 mmol) and the mixture was stirred under a nitrogen atmosphere overnight. The solvent was removed to give the product **9** as a yellow solid (104.8 mg, 0.50 mmol, 70.3%). TLC: Rf ca 0.30 (9:1 hexane: EtOAc), strong UV and $KMnO_4$; Mp: 97 °C; HRMS: (found (ESI+): [M+H]+, Calcd for $C_{14}H_{14}NO$ 212.1066; Found 212.1070; 1.9 ppm error); ν_{max} 3353, 2922, 2852, 1604,1518, 1473, 1251, 855, 740 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 15.19 (1H, s, OH), 9.10 (1H, s, NH), 7.69-7,67 (1H, m, ArH), 7.43 (2H, t, *J* = 7.3, ArH), 7.41-7.31 (2H, m, ArH), 7.21 (2H, d, *J* = 7.0, ArH), 7.02 (1H, d, *J* = 8.5, ArH), 6.86 (1H, t, *J* = 7.5, ArH), 4.15 (2H, s, CH_2) ppm; δ_C (125 MHz, $CDCl_3$) 179.0 (C), 163.2 (C), 133.3 (CH), 133.2 (C), 130.4 (CH), 129.4 (CH), 129.3 (CH), 127.9 (CH), 118.6 (CH), 118.5 (C), 117.7 (CH), 42.5 (CH_2) ppm; m/z (ES-API+) 212.2 (M^+ + 1, 100%).

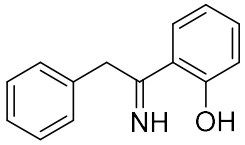
^{1}H NMR (500 MHz, $CDCl_3$) of **9**:

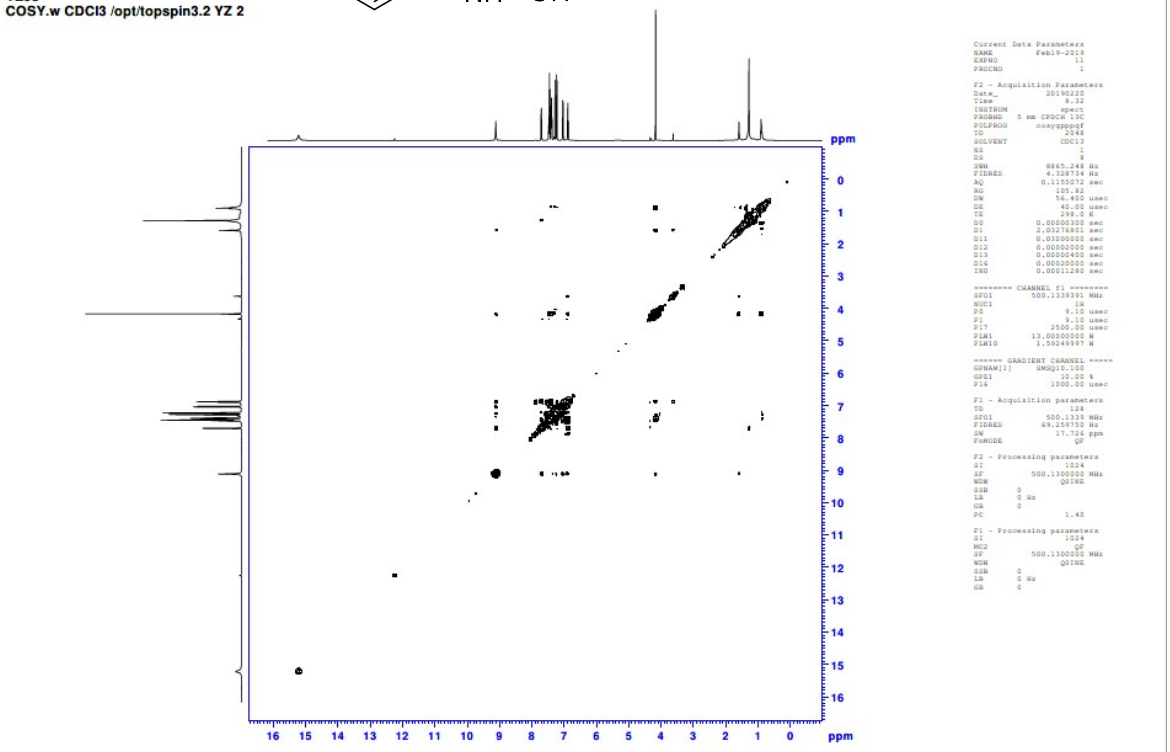


^{13}C NMR (125 MHz, $CDCl_3$) of **9**:

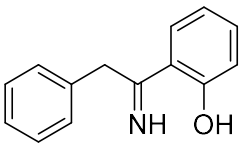


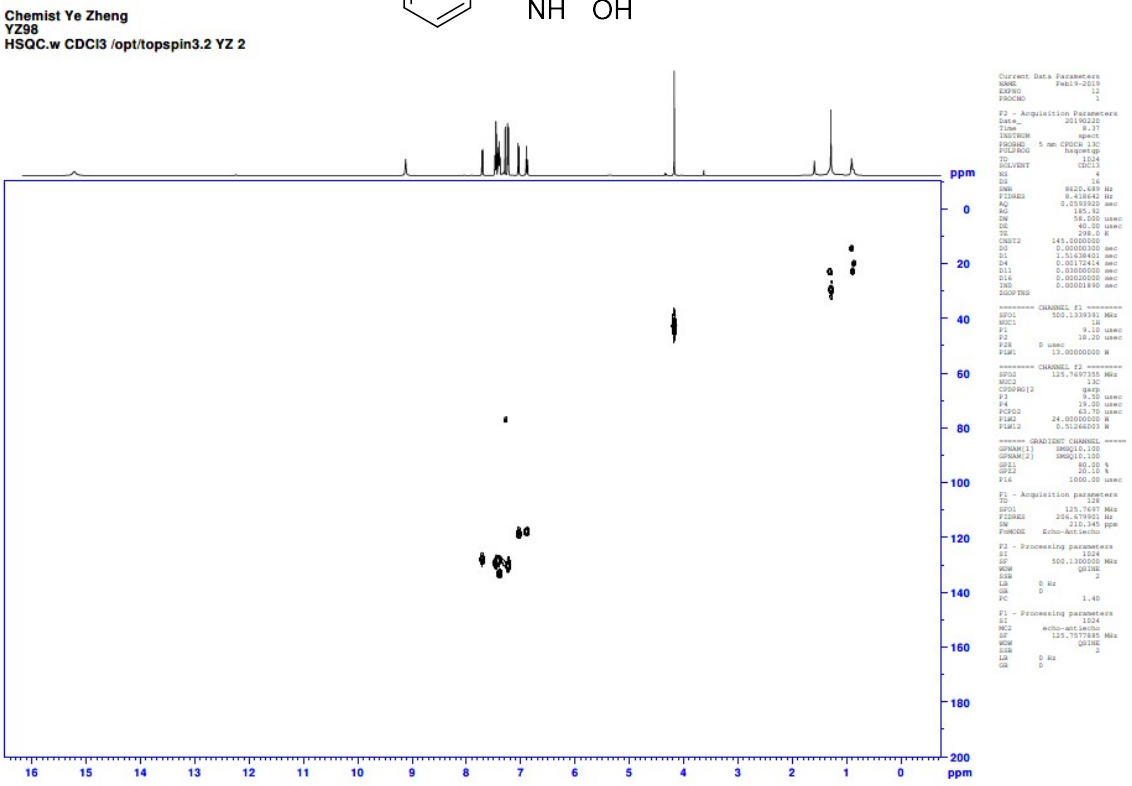
COSY (500 MHz, $CDCl_3$) of **9**:



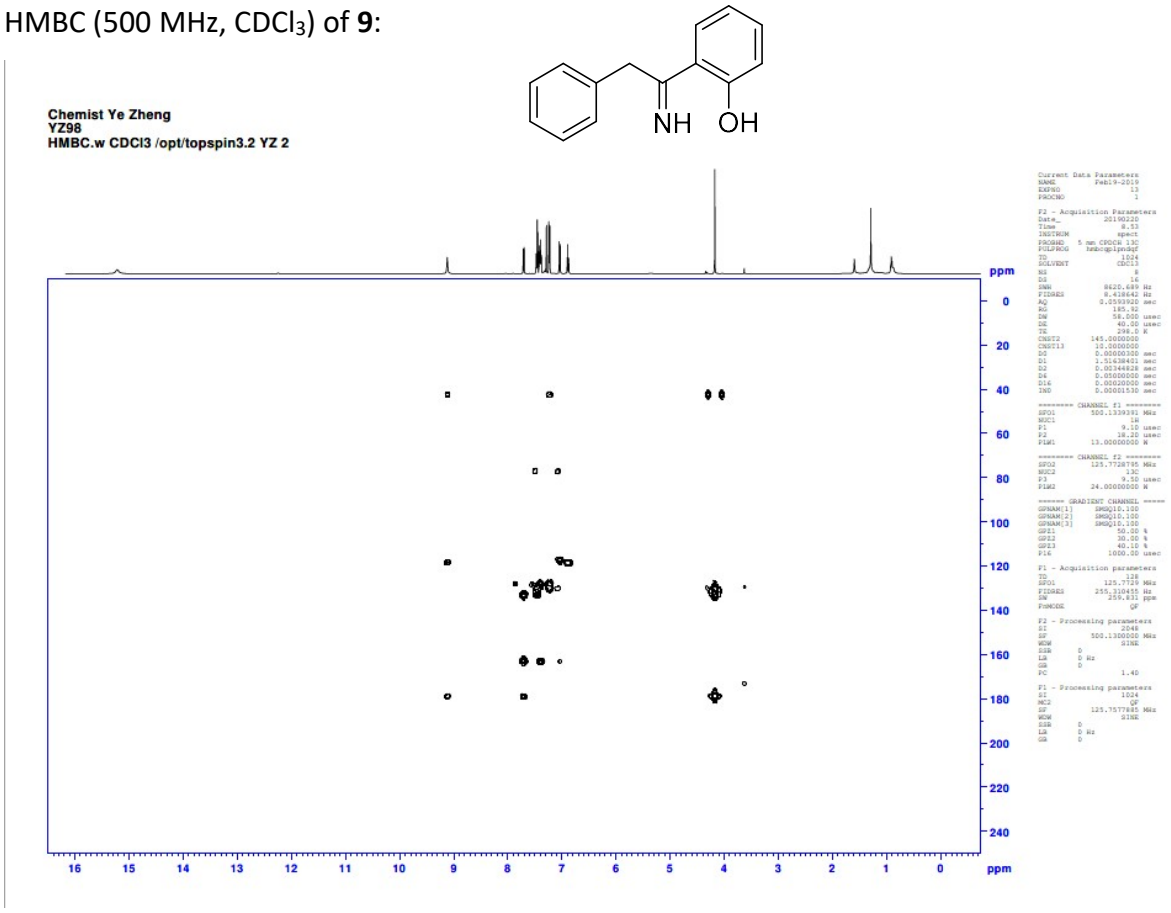


HSQC (500 MHz, $CDCl_3$) of **9**:

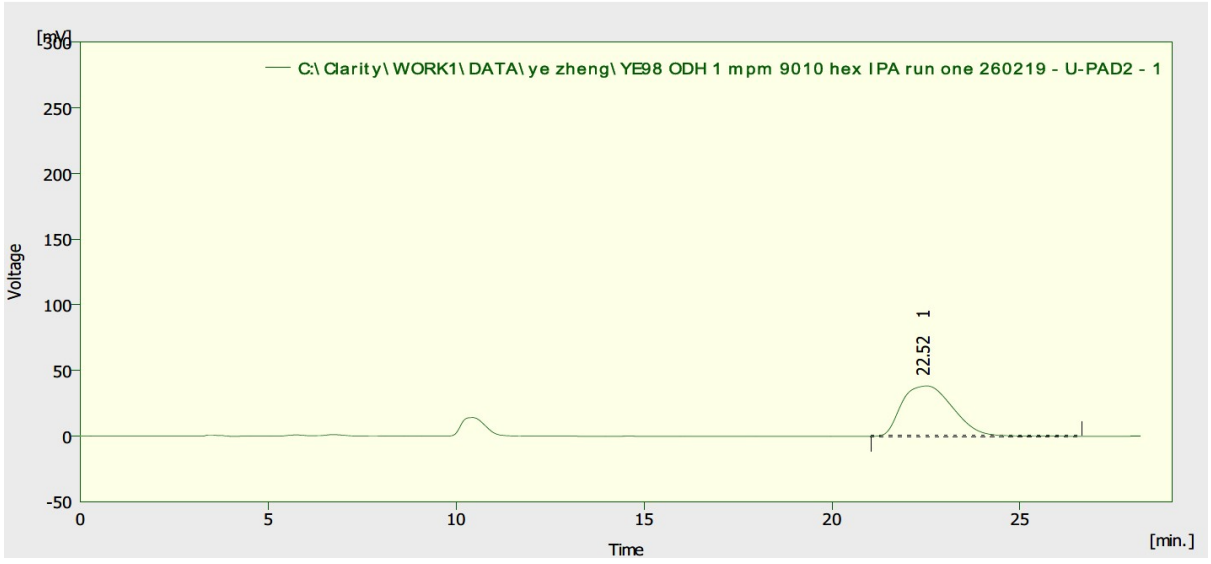




HMBC (500 MHz, $CDCl_3$) of **9**:



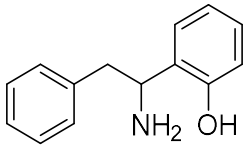
HPLC of 2-(1-imino-2-phenylethyl)phenol **9:**



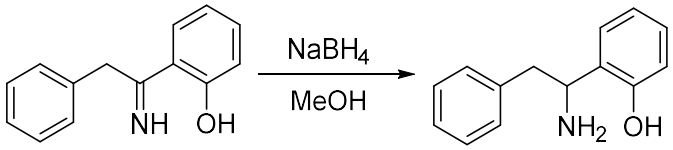
Result Table (Uncal - C:|Clarity|WORK1|DATA|ye zheng|YE98 ODH 1 mpm 9010 hex IPA run one 260219 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	22.516	3635.807	38.455	100.0	100.0	1.53	
	Total	3635.807	38.455	100.0	100.0		

1-(2-Aminophenyl)-2-phenylethan-1-ol 12.



racemic: YZ99. Asymmetric: YZ107, YZ114, YZ121, YZ123, YZ131



This compound is novel.

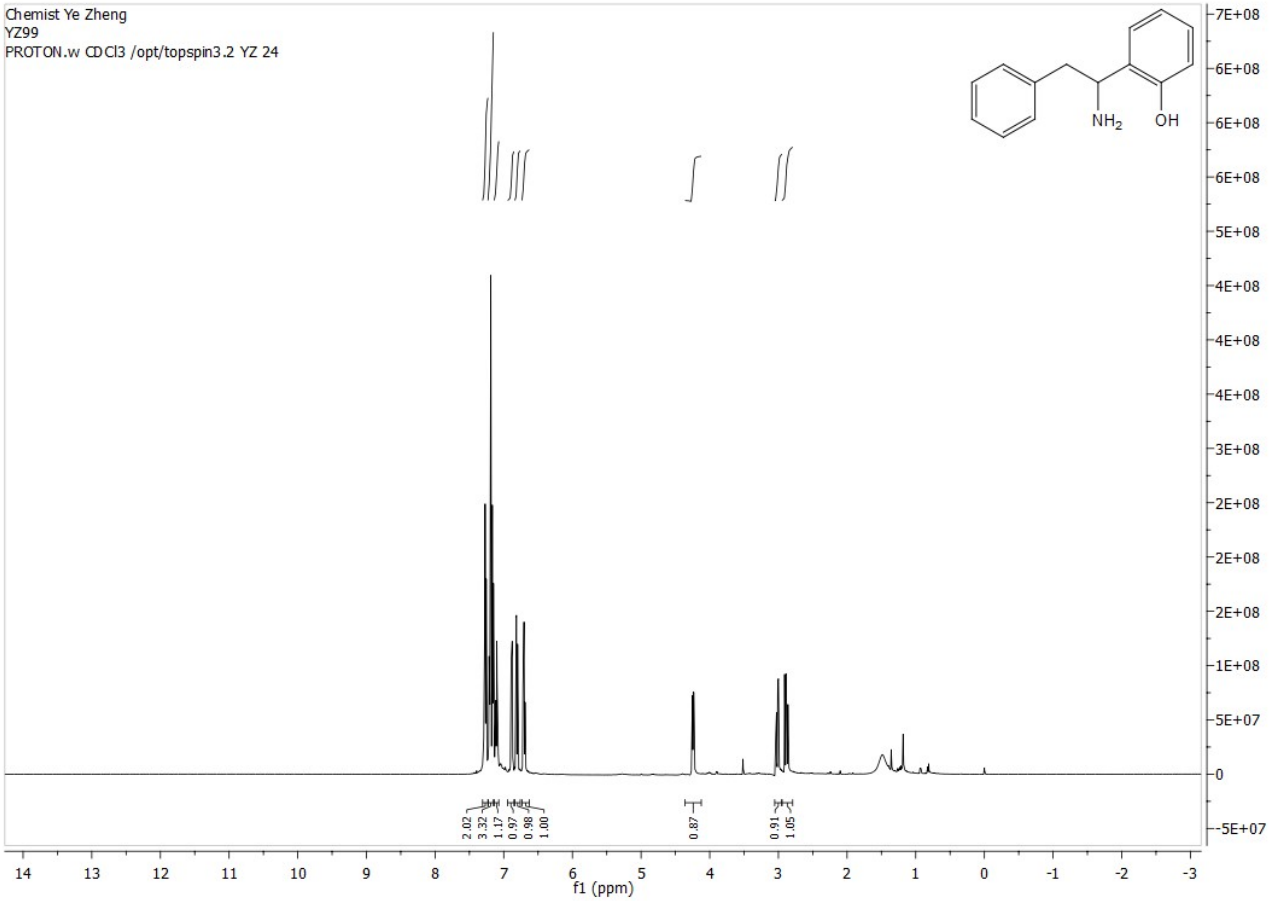
To a solution of 2-(1-imino-2-phenylethyl)phenol **9** (50 mg, 0.237 mmol) in MeOH (1 mL) was added sodium borohydride (18.1 mg, 0.474 mmol). The reaction was stirred for 4 hours. TLC (1:1 hexane: EtOAc) after this time indicated full conversion. Distilled water (20 mL) was added, and the mixture was extracted with EtOAc (3 × 20ml), dried with $MgSO_4$, and the solvent was removed under vacuum to give 1-(2-aminophenyl)-2-phenylethan-1-ol **12** as a yellow oil (39 mg, 0.18 mmol, 78%). TLC: Rf ca 0.20 (1:1 hexane: EtOAc), strong UV and $KMnO_4$; HRMS: (found (ESI+): [M+H]+, Calcd for $C_{14}H_{16}NO$ 214.1227; Found 214.1226; -0.2 ppm error); ν_{max} 3369, 3300, 3026, 2921, 1585, 1490, 1254, 1030, 751, 698 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.36 (2H, t, *J* = 7.5, ArH), 7.29-7.22 (3H, m, ArH), 7.19-7.16 (1H, m, ArH), 6.96 (1H, d, *J* = 7.0, ArH), 6.89 (1H, d, *J* = 8.5, ArH), 6.78 (1H, t, *J* = 7.5, ArH), 4.33 (1H, dd, *J* = 10.5, 5.0, *CH*NH_2), 3.11-3.07 (1H, m, CH_2), 2.98-2.93 (1H, m, CH_2) ppm; δ_C (125 MHz, $CDCl_3$) 157.7 (C), 138.0 (C), 129.3 (CH), 128.8 (CH), 128.7 (CH), 127.8 (CH), 126.9 (CH), 126.8 (C), 119.1 (CH), 117.4 (CH), 58.0 (CH), 43.2 (CH_2) ppm; m/z (ES-API+) 214.2 (M^+ + 1, 100%). Enantiomeric excess and conversion determined by HPLC analysis (Chiralcel ODH, 30 cm x 6mm column, hexane:iPrOH 9:1, 1.0 mL/min, T = 25°C) ketone 22.5 min, *R* isomer and *S* isomers 17.9 min and 20.5 min, configuration assigned by analogy with reported reduction.

ATH of 2-(1-imino-2-phenylethyl)phenol **9** (YZ107, 114.121.123.131).

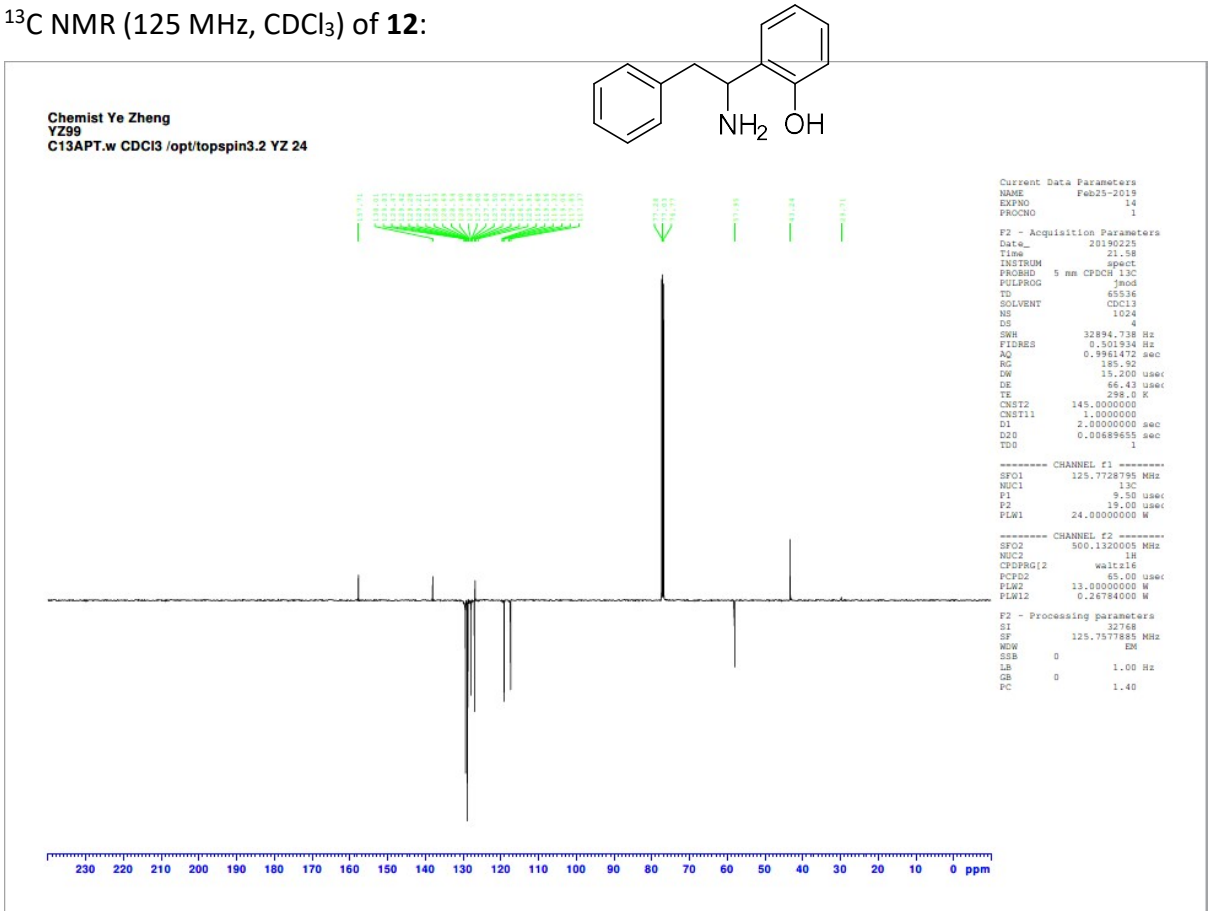
2-(1-Imino-2-phenylethyl)phenol **9** (40 mg, 0.19 mmol), ammonium formate (48 mg, 0.76 mmol) and catalyst (*R,R*)-**2** (0.00095 mmol, 0.5 mol%) were added into a sealed tube and stirred under a nitrogen atmosphere for 10 minutes. DCM (0.95 mL) was degassed with nitrogen then added under nitrogen to the tube. The mixture was heated to 70 °C on a hot plate and left to stir under nitrogen inert atmosphere overnight. Then the reaction quenched by saturated $NaHCO_3$ solution (20 mL), after which the EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried

($MgSO_4$) and filtered. The solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 50%-100% ethyl acetate in hexane to give 1-(2-aminophenyl)-2-phenylethan-1-ol **12** (18.7 mg, 0.088 mmol, 46%; (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst example). The reaction also by HPLC analysis (Chiralcel ODH, 30 cm x 6mm column, hexane:iPrOH 9:1, 1.0 mL/min, T = 25°C); (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst: 100% conversion; $[\alpha]_D^{24}$ -27.4 (c 0.0502 in $CHCl_3$) 84% ee; (*S,S*)-3C-tethered Ru(II)-TsDPEN catalyst: 100% conversion, 85% ee; (*S,S*)-Noyori Ru(II)-TsDPEN catalyst: 100% conversion, 31.8% ee; (*R,R*)-3C-tethered, 4-methoxy-Ru(II)-TsDPEN catalyst: 100% conversion, 92% ee; (*R,R*)-benzyl-tethered Ru(II)-TsDPEN catalyst: 100% conversion, 93.2% ee.

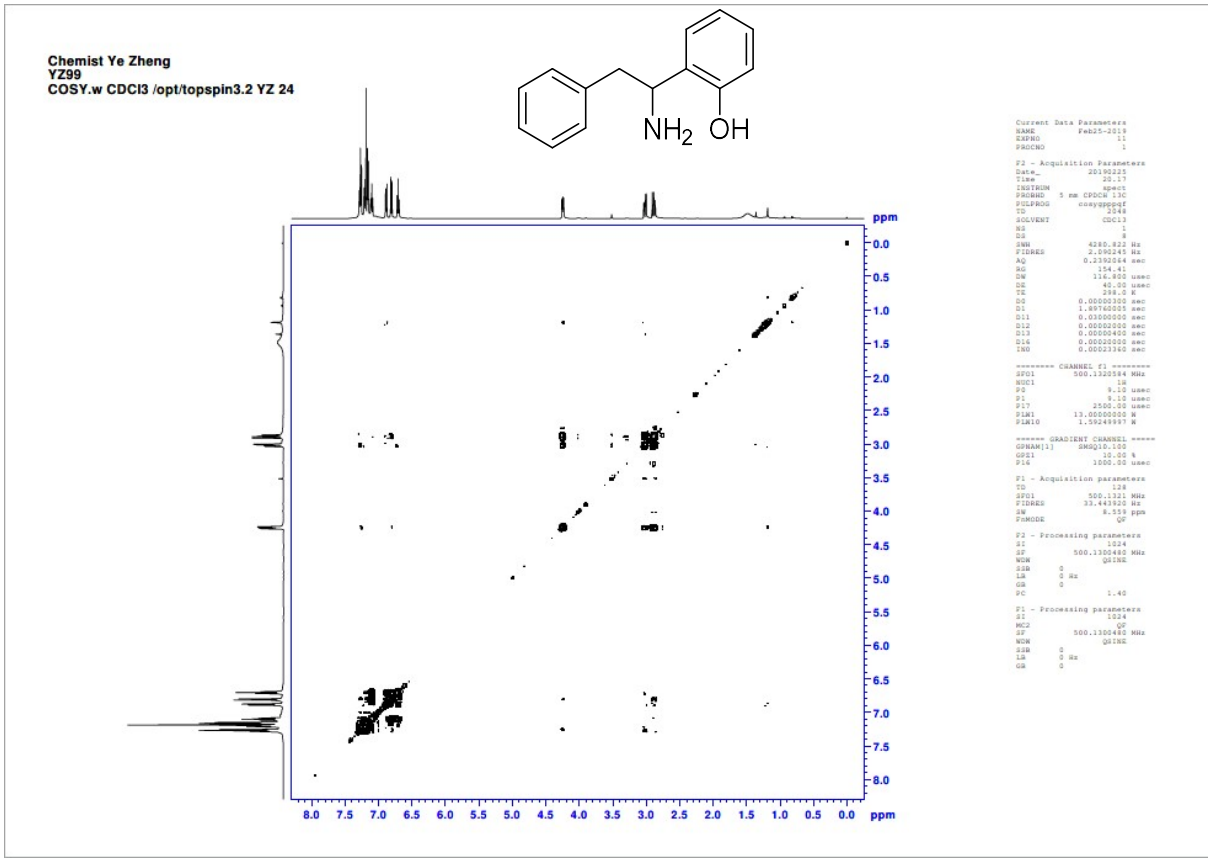
^1H NMR (500 MHz, $CDCl_3$) of **12**:



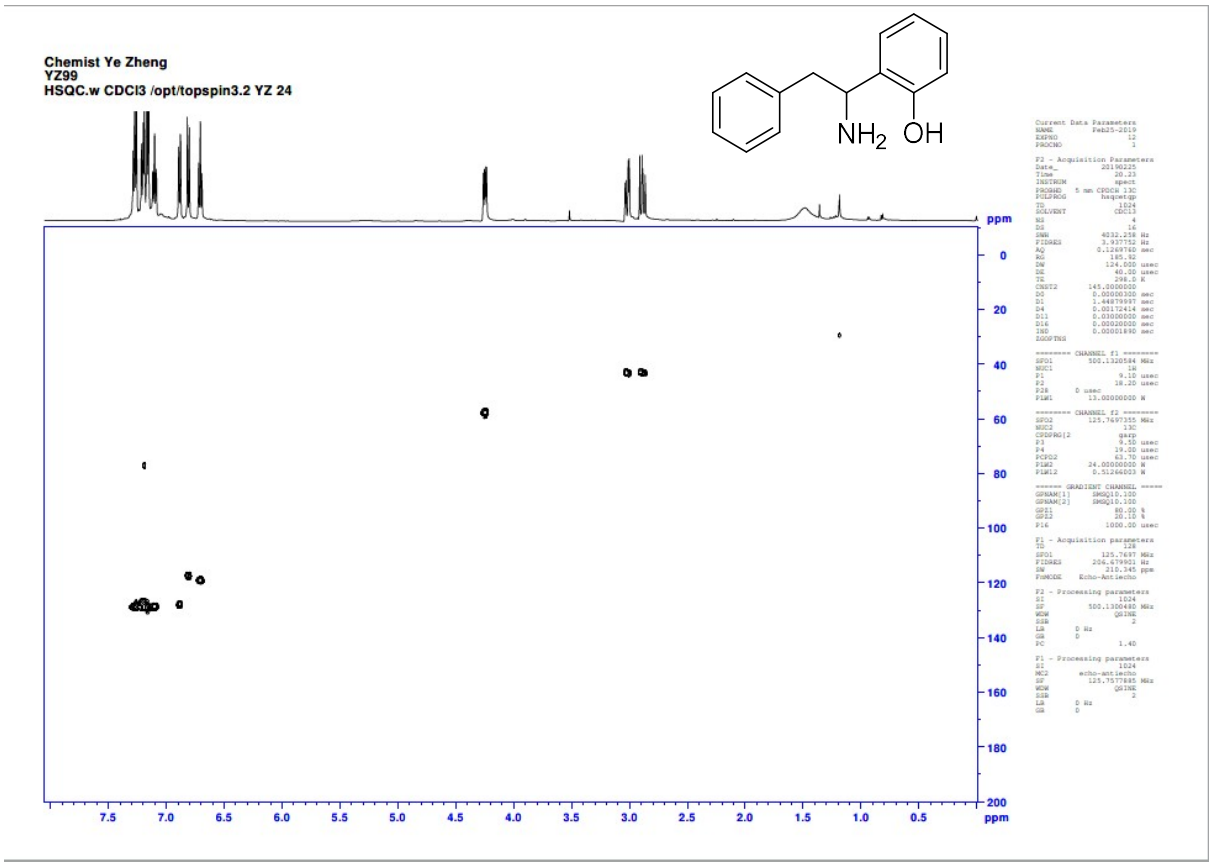
^{13}C NMR (125 MHz, $CDCl_3$) of **12**:



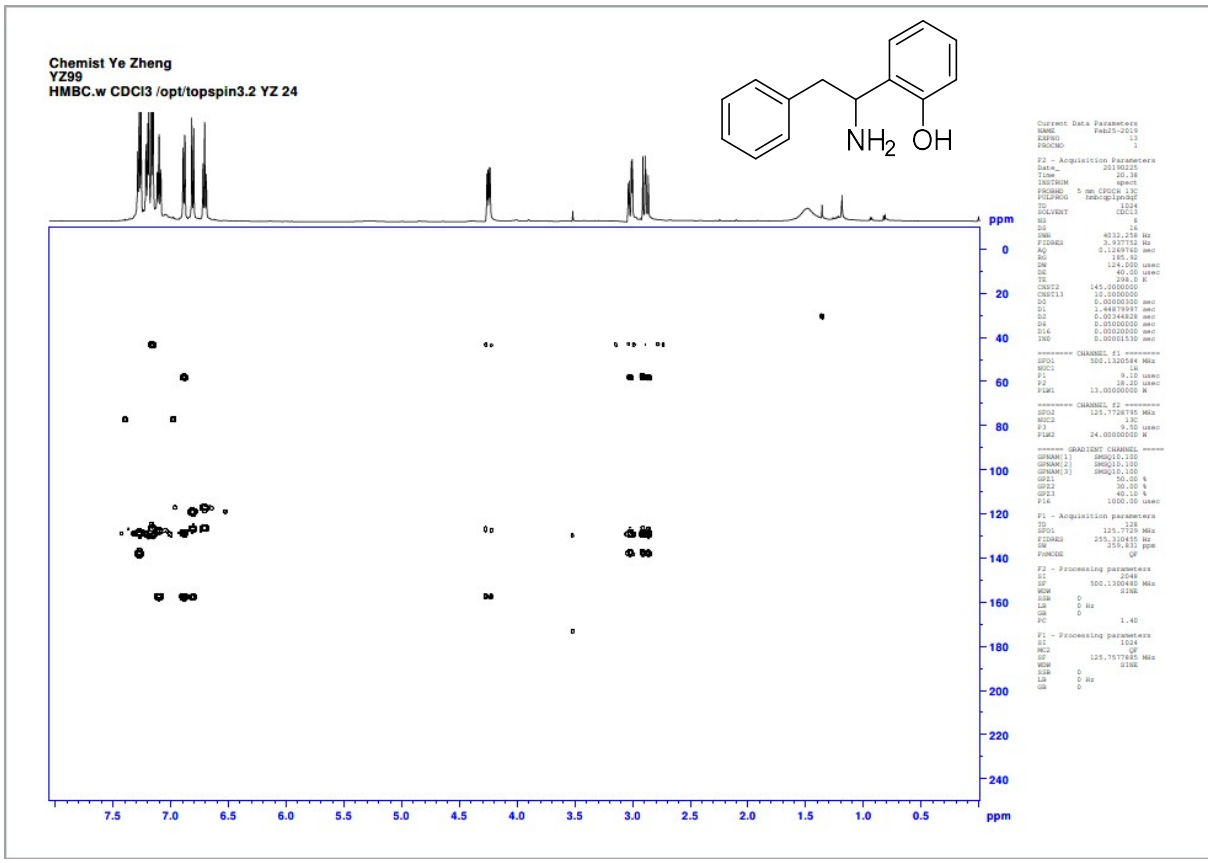
COSY (500 MHz, $CDCl_3$) of **12**:



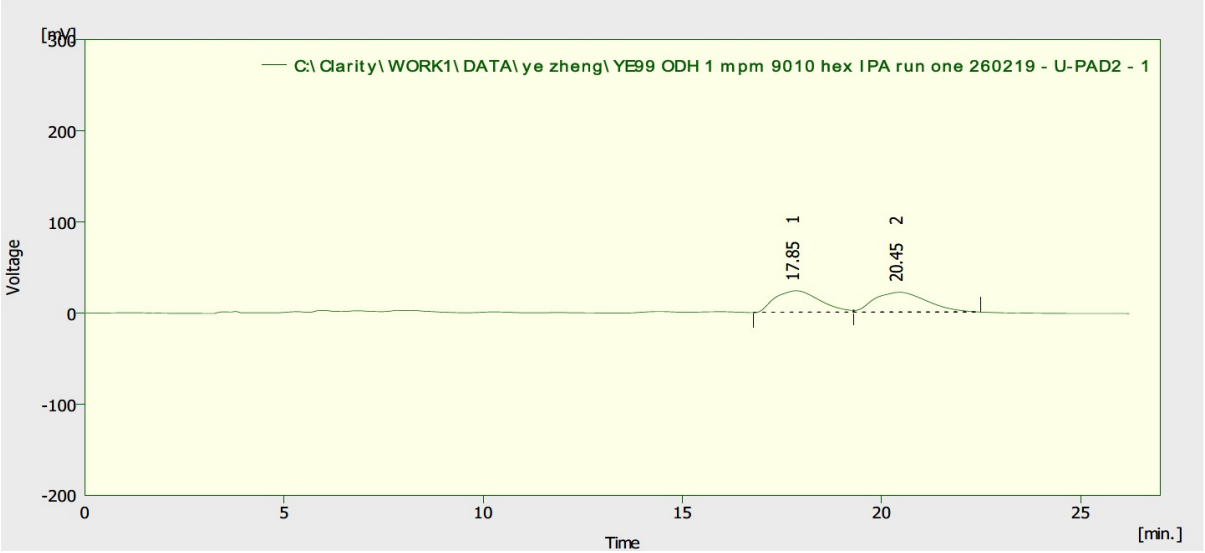
HSQC (500 MHz, $CDCl_3$) of **12**:



HMBC (500 MHz, $CDCl_3$) of **12**:



HPLC of racemic 1-(2-aminophenyl)-2-phenylethan-1-ol **12**:

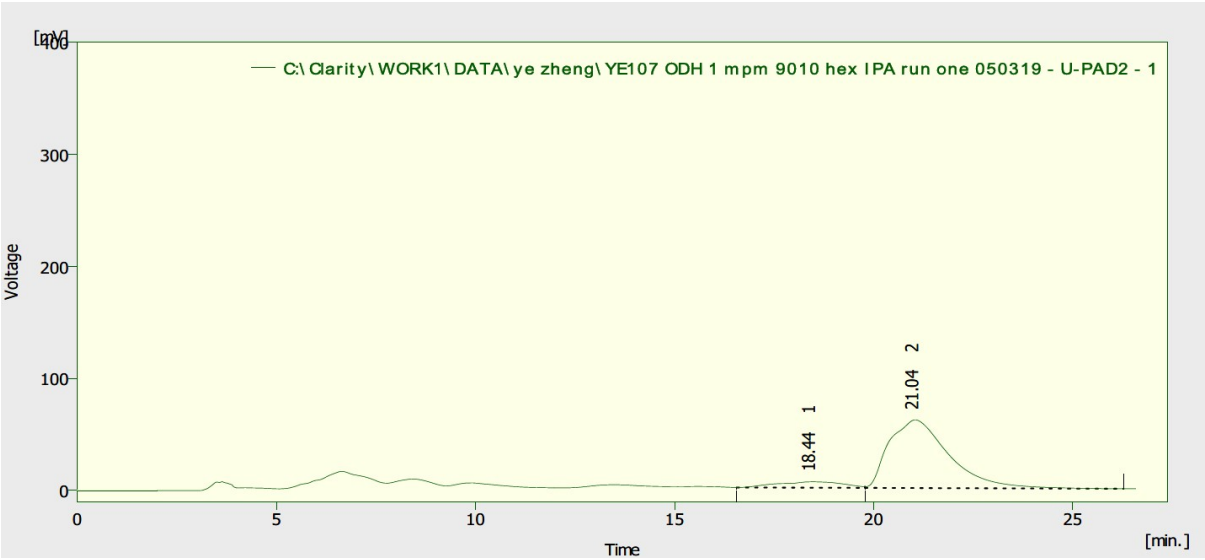


Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|ye zheng\|YE99 ODH 1 mpm 9010 hex IPA run one 260219 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	17.852	1898.239	24.011	48.2	52.2	1.31	
2	20.452	2038.906	21.975	51.8	47.8	1.52	
	Total	3937.145	45.986	100.0	100.0		

HPLC of **12** after ATH of 2-(1-imino-2-phenylethyl)phenol **9**:

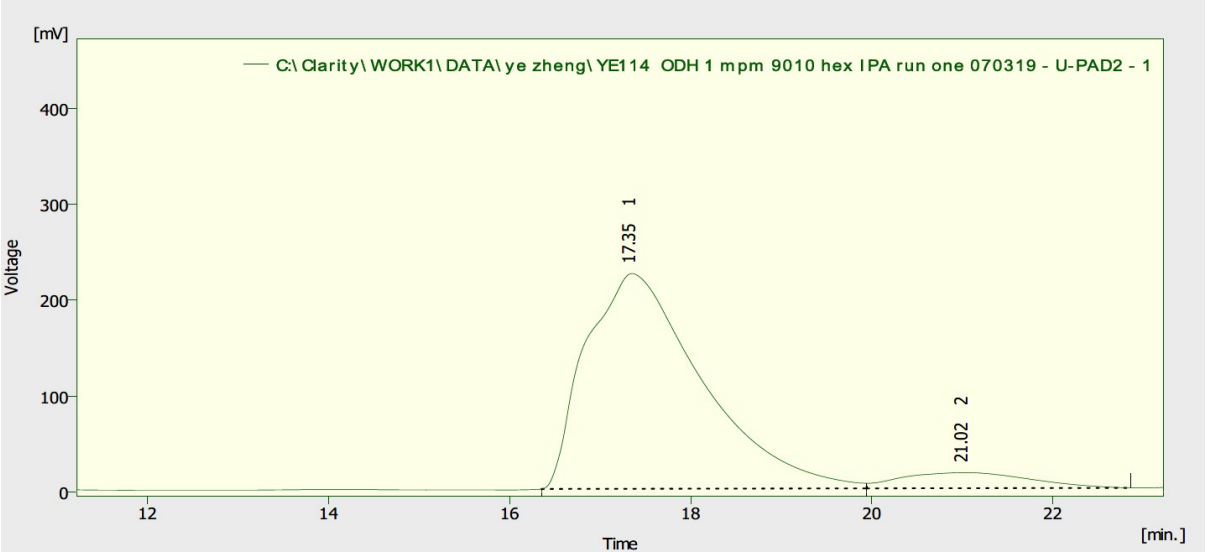
(*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst **2** (after 24 hours, 100% conversion, 84% ee).



Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|ye zheng\|YE107 ODH 1 mpm 9010 hex IPA run one 050319 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	18.444	613.254	5.300	8.8	8.0	2.10	
2	21.044	6360.846	60.928	91.2	92.0	1.64	
	Total	6974.099	66.227	100.0	100.0		

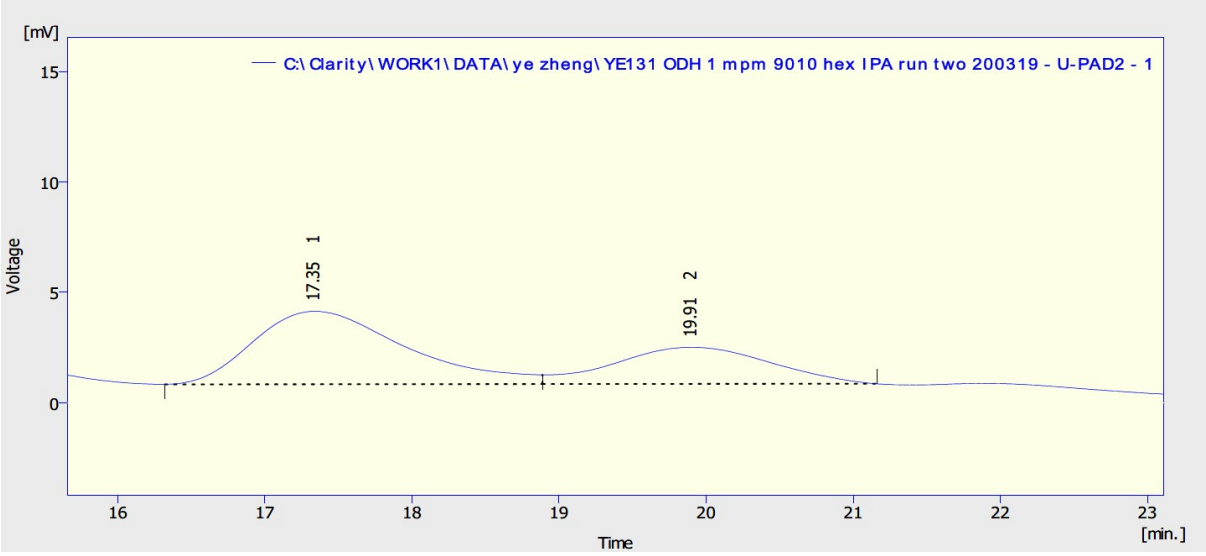
(*S,S*)-3C-tethered Ru(II)-TsDPEN catalyst **2** (after 24 hours, 100% conversion, 85% ee).



Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|ye zheng\|YE114 ODH 1 mpm 9010 hex IPA run one 070319 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	17.352	20045.097	224.345	92.5	93.2	1.43	
2	21.020	1617.738	16.334	7.5	6.8	1.67	
	Total	21662.835	240.678	100.0	100.0		

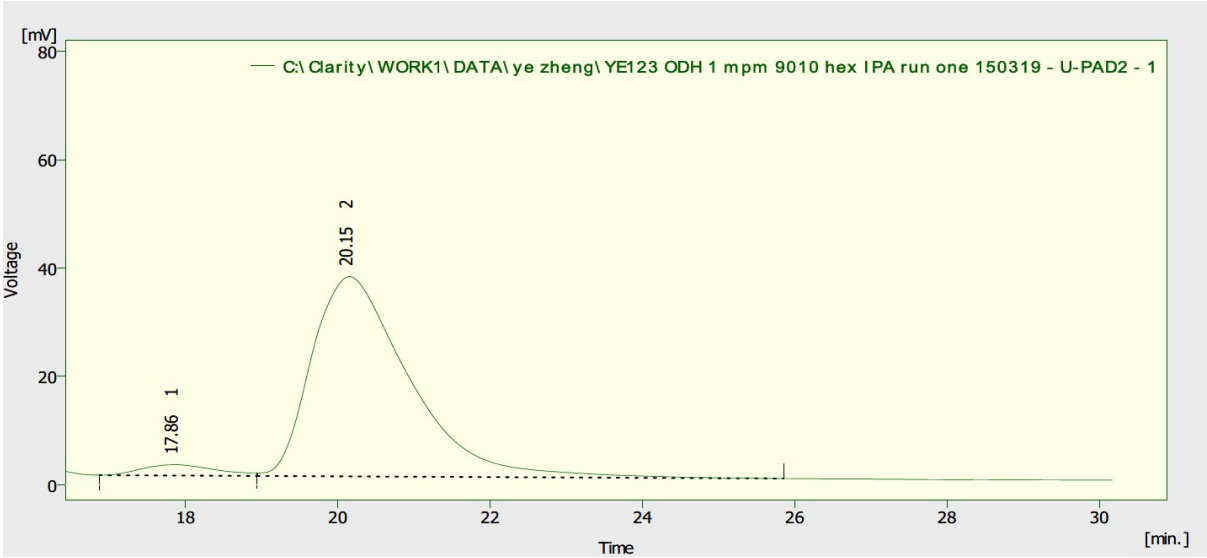
(*S,S*)-Noyori Ru(II)-TsDPEN catalyst **6** (after 24 hours, 100% conversion, 31.8% ee).



Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|ye zheng\|YE131 ODH 1 mpm 9010 hex IPA run two 200319 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	17.348	237.939	3.306	65.9	66.5	1.10	
2	19.912	123.247	1.664	34.1	33.5	1.18	
	Total	361.186	4.970	100.0	100.0		

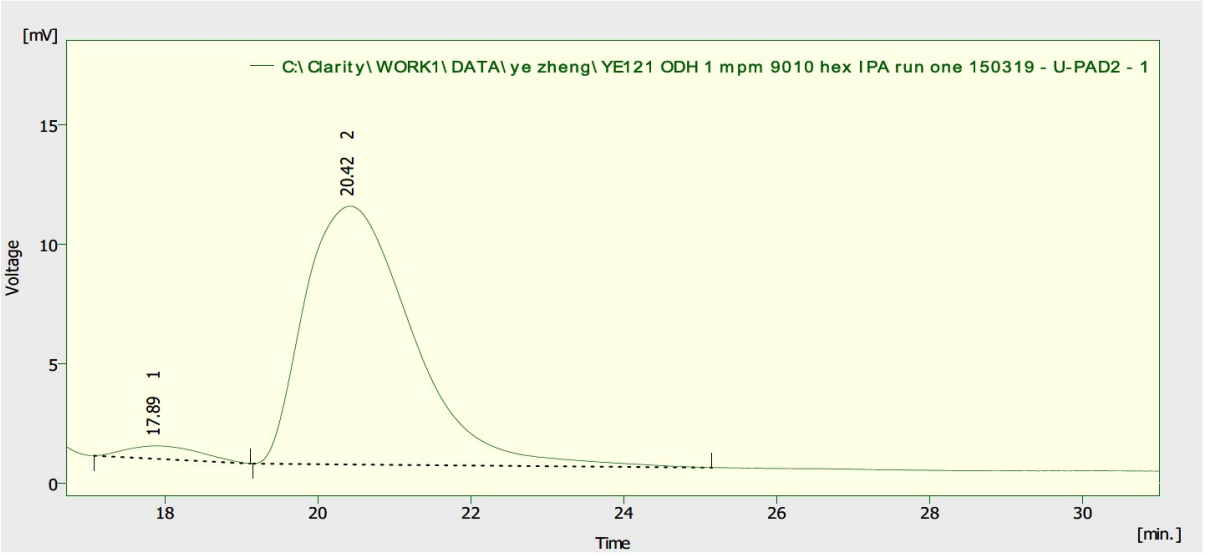
(*R,R*)-3C-tethered, 4-methoxy-Ru(II)-TsDPEN catalyst **5**(after 24 hours, 100% conversion, 92% ee).



Result Table (Uncal - C:|Clarity|WORK1|DATA|ye zheng|YE123 ODH 1 mpm 9010 hex IPA run one 150319 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	17.856	136.503	2.008	4.0	5.2	1.08	
2	20.152	3287.265	36.912	96.0	94.8	1.34	
	Total	3423.768	38.920	100.0	100.0		

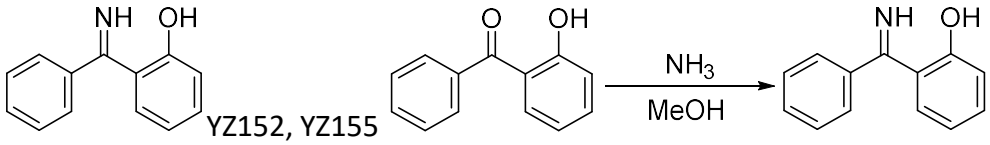
(*R,R*)-benzyl-tethered Ru(II)-TsDPEN catalyst **4** (after 24 hours, 100% conversion, 93.2% ee).



Result Table (Uncal - C:|Clarity|WORK1|DATA|ye zheng|YE121 ODH 1 mpm 9010 hex IPA run one 150319 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	17.888	37.218	0.543	3.4	4.8	1.12	
2	20.424	1059.625	10.811	96.6	95.2	1.52	
	Total	1096.843	11.355	100.0	100.0		

2-(Imino(phenyl)methyl)phenol 10.

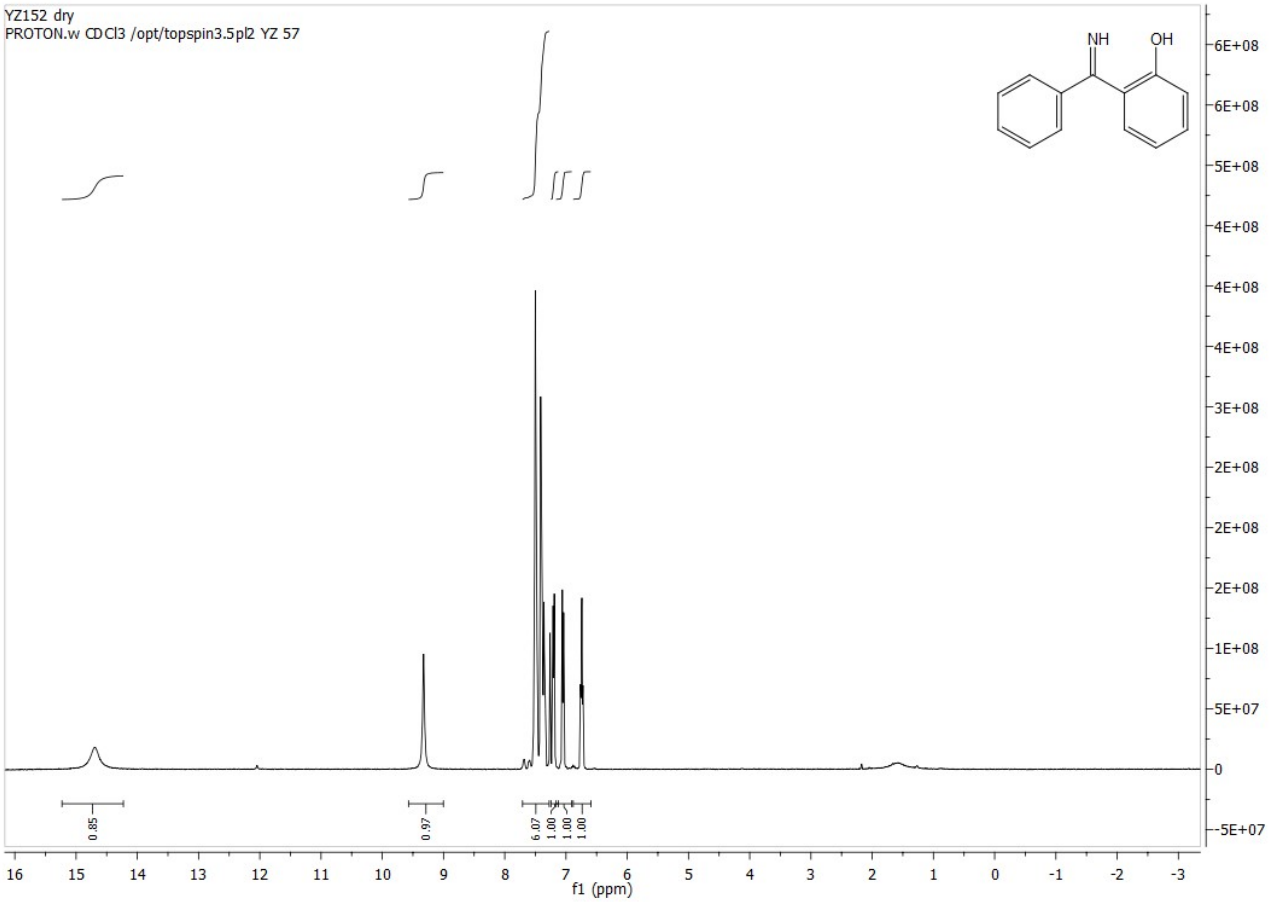


This compound has been reported and fully characterized.

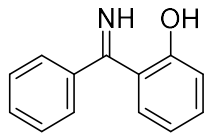
References: Choubane, H.; Garrido-Castro, A. F.; Alvarado, C.; Martin-Somer, A.; Guerrero-Corella, A.; Daaou, M.; Diaz-Tendero, S.; Carmen Maestro, M.; Fraile, A.; Aleman, J. *Chem. Commun.* **2018**, *54*, 3399 – 340.

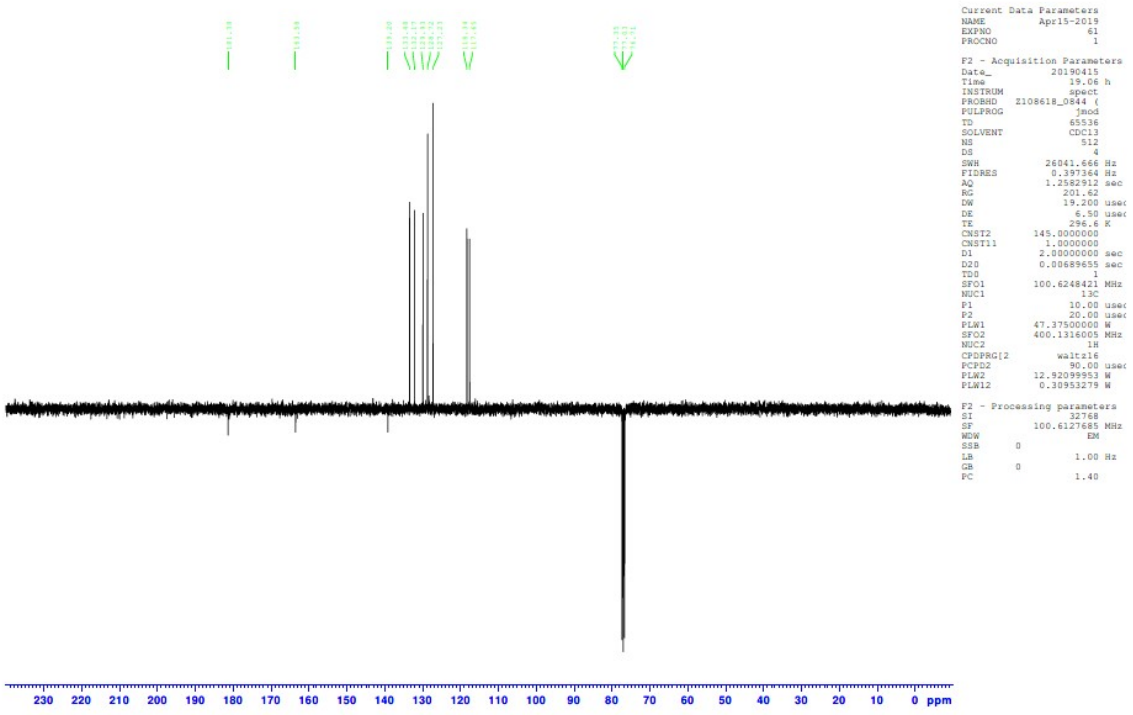
2-Hydroxybenzophenone (400 mg, 2.02 mmol) was dissolved in ammonia (1.45 mL, 7N in MeOH, 10.1 mmol) and the mixture was stirred under a nitrogen atmosphere overnight. Then the solvent was removed to give the product **10** as a yellow solid (279.6 mg, 1.42 mmol, 70%). TLC: Rf ca 0.40 (1:1 hexane: EtOAc), strong UV and $KMnO_4$; δ_H (400 MHz, $CDCl_3$) 12.04 (1H, s, OH), 9.33 (1H, s, NH), 7.50-7.34 (6H, m, ArH), 7.21 (1H, d, *J* = 7.6, ArH), 7.06 (1H, d, *J* = 8.4, ArH), 6.74 (1H, t, *J* = 7.2, ArH) ppm; δ_C (100 MHz, $CDCl_3$) 181.4 (C), 163.6 (C), 139.2 (C), 133.5 (CH), 132.2 (CH), 129.9 (CH), 128.7 (CH), 127.2 (CH), 118.4 (CH), 117.9 (CH) ppm; m/z (ES-API+) 198.2 (M^+ + 1, 100%). Data matched that reported.

^{1}H NMR (400 MHz, $CDCl_3$) of **10**:

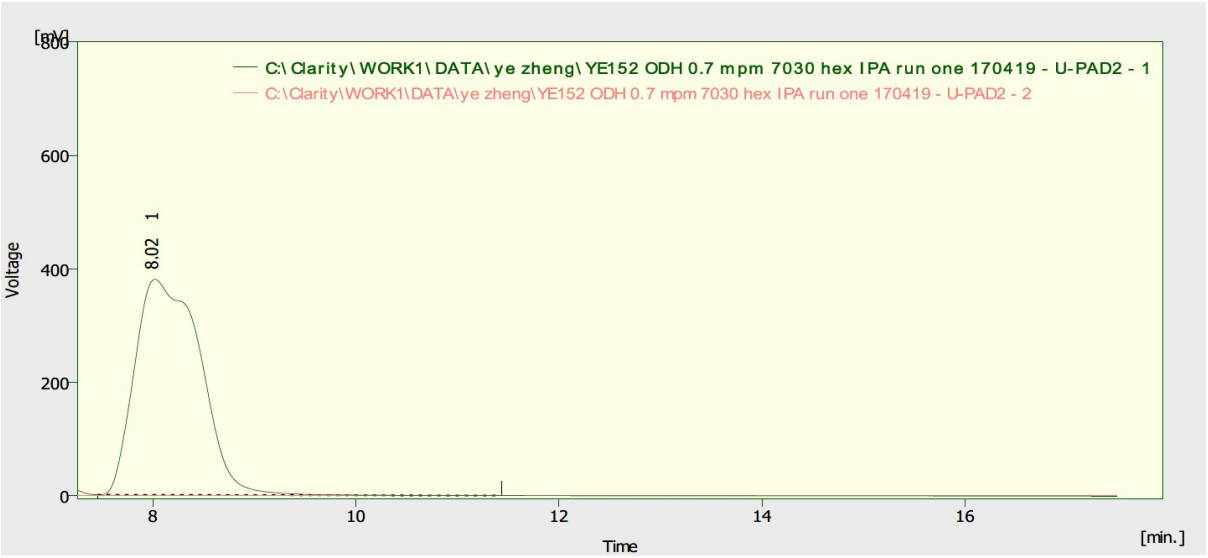


^{13}C NMR (400 MHz, $CDCl_3$) of **10**:





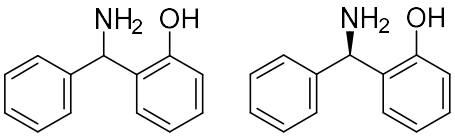
HPLC of 2-(imino(phenyl)methyl)phenol **10**:



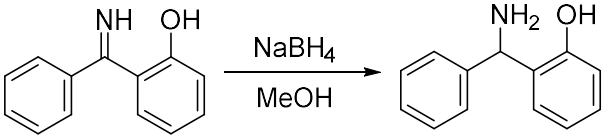
Result Table (Uncal - C:\Clarity\WORK1\DATA\ye zheng\YE152 ODH 0.7 mpm 7030 hex IPA run one 170419 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	8.020	17069.542	380.210	100.0	100.0	0.75	
	Total	17069.542	380.210	100.0	100.0		

2-(Amino(phenyl)methyl)phenol 13.



racemic:YZ153.Asymmetric: YZ154, YZ156, YZ159, YZ160, YZ163



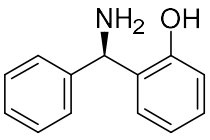
This compound has been reported and fully characterized.

References: Wang, Y.-Q.; Yu, C.-B.; Wang, D.-W.;Wang, X.-B.; Zhou, Y.-G. *Org. Lett*. **2018**, *10*, 2071-2074.

To a solution of 2-(imino(phenyl)methyl)phenol **10** (80 mg, 0.41 mmol) in MeOH (2 mL) was added sodium borohydride (32 mg, 0.82 mmol). The reaction was stirred for 4 hours. TLC (1:1 hexane: EtOAc) after this time indicated full conversion. Distilled water (20 mL) was added, and the mixture was extracted with EtOAc (3 × 20ml), dried with $MgSO_4$, and the solvent was removed under vacuum to give the 2-(amino(phenyl)methyl)phenol **13** as a white solid (60.1 mg, 0.30 mmol, 74.4%). TLC: Rf ca 0.20 (1:1 hexane: EtOAc), strong UV and $KMnO_4$; δ_H (400 MHz, $CDCl_3$) 7.38-7.26 (5H, m, ArH), 7.16 (1H, t, *J* = 7.0, ArH), 6.90 (1H, d, *J* = 8.0, ArH), 6.80-6.71 (2H, m, ArH), 5.32 (1H, s, *CH*NH_2) ppm; δ_C (100 MHz, $CDCl_3$) 157.9 (C), 143.2 (C), 129.0 (CH), 128.6 (CH), 127.8 (CH), 127.0 (CH), 126.3 (C), 119.1 (CH), 117.4 (CH), 60.0 (CH) ppm; m/z (ES-API+) 120.2 (M^+ + 1, 100%). Data matched that reported.

Enantiomeric excess and conversion determined by HPLC analysis (Chiralcel ODH, 30 cm x 6mm column, hexane:iPrOH 7:3, 0.7 mL/min, T = 25°C) ketone 8.02 min, *R* isomer 20.7 min and *S* isomer 13.5 min.

ATH of 2-(1-imino-2-phenylethyl)phenol (YZ154, 156, 159, 160, 163).



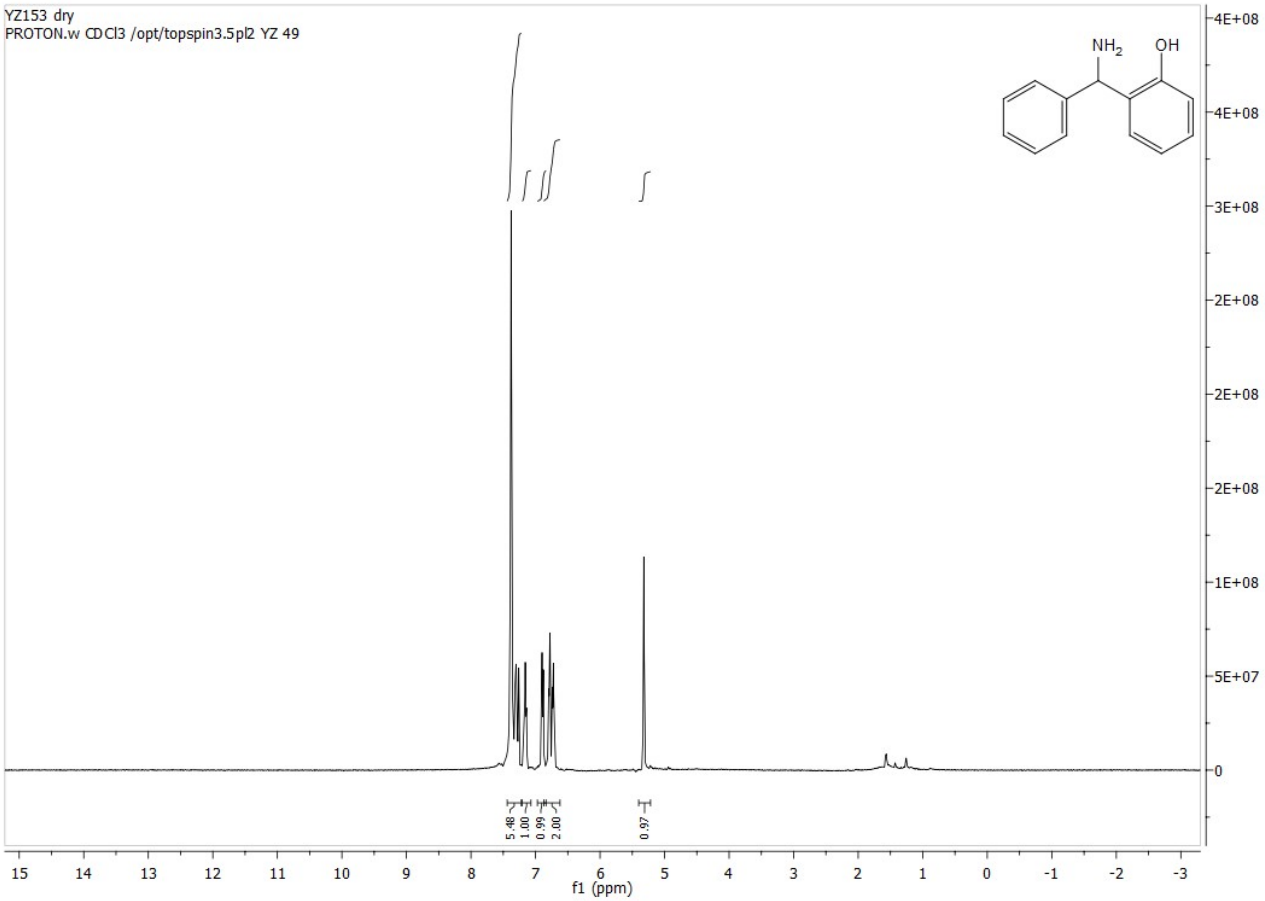
Attempted ATH of **10** using (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst **2** in FA/TEA (YZ154).

Catalyst (*R,R*)-**2** (0.002 mmol, 1 mol%) was added to FA: TEA (5:2 azeotropic mixture, 0.18 mL) at rt and the mixture was left to stir under a nitrogen inert atmosphere for 10-15 minutes; after which a solution of 2-(1-imino-2-phenylethyl)phenol **13** (40 mg, 0.20 mmol) in DCM (0.25 mL) was added. The reaction mixture was stirrer under a nitrogen atmosphere overnight. The reaction was

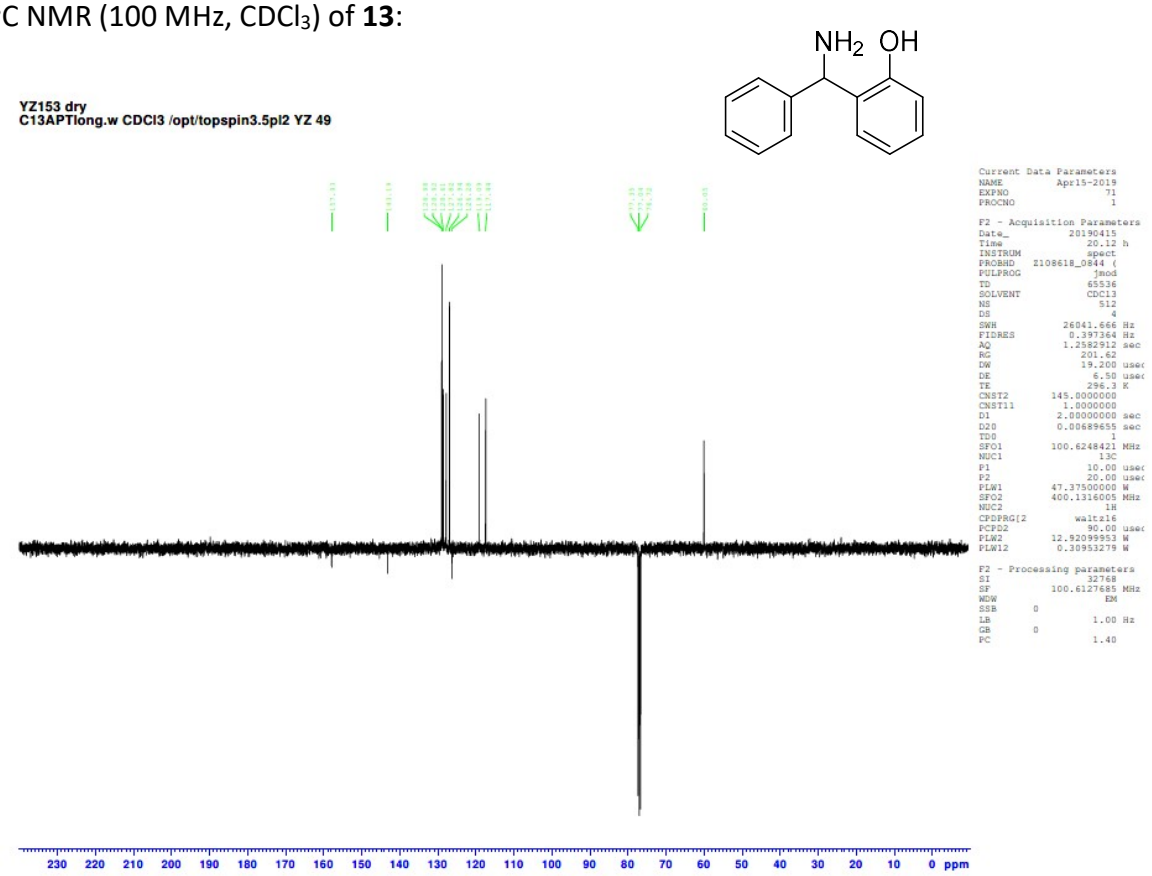
followed by TLC (1:1 hexane: EtOAc). Then the reaction was quenched using saturated $NaHCO_3$ solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried ($MgSO_4$) and filtered. However, NMR indicated there were both alcohol and imine present.

ATH of **13** using (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst **2** in water (YZ156, 159, 160, 163). 2-(1-Imino-2-phenylethyl)phenol **10** (40 mg, 0.20 mmol), ammonium formate (50.4 mg, 0.80 mmol) and catalyst (*R,R*)-**2** (0.0010 mmol, 0.5 mol%) were added into a sealed tube and left to stir under a nitrogen atmosphere for 10 minutes. DCM (1 mL) was degassed with nitrogen then added under nitrogen to the tube. The mixture was heated to 70 °C on a hot plate and stirred under a nitrogen atmosphere overnight. Then the reaction was quenched by saturated $NaHCO_3$ solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried ($MgSO_4$) and filtered. The solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 50%-100% ethyl acetate in hexane to give 2-(amino(phenyl)methyl)phenol **13** (8.3 mg, 0.042 mmol, 20.5%; (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst example). The reaction was also followed by HPLC analysis (Chiralcel ODH, 30 cm x 6mm column, hexane:iPrOH 7:3, 0.7 mL/min, T = 25°C); (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst: 100% conversion; $[\alpha]_D^{27}$ -2.41 (c 0.0415 in $CHCl_3$) 75.2% ee (*R*). Product is highly coloured. (lit. $[\alpha]_D^{24}$ +109.2 (c 0.60 in $CHCl_3$) 96% ee (*S*)) Reference: Wang, Y.-Q.; Yu, C.-B.; Wang, D.-W.;Wang, X.-B.; Zhou, Y.-G. *Org. Lett*. **2018**, *10*, 2071-2074; (*S,S*)-Noyori Ru(II)-TsDPEN catalyst: no conversion; (*R,R*)-3C-tethered, 4-methoxy-Ru(II)-TsDPEN catalyst: no conversion; (*R,R*)-benzyl-tethered Ru(II)-TsDPEN catalyst: no conversion.

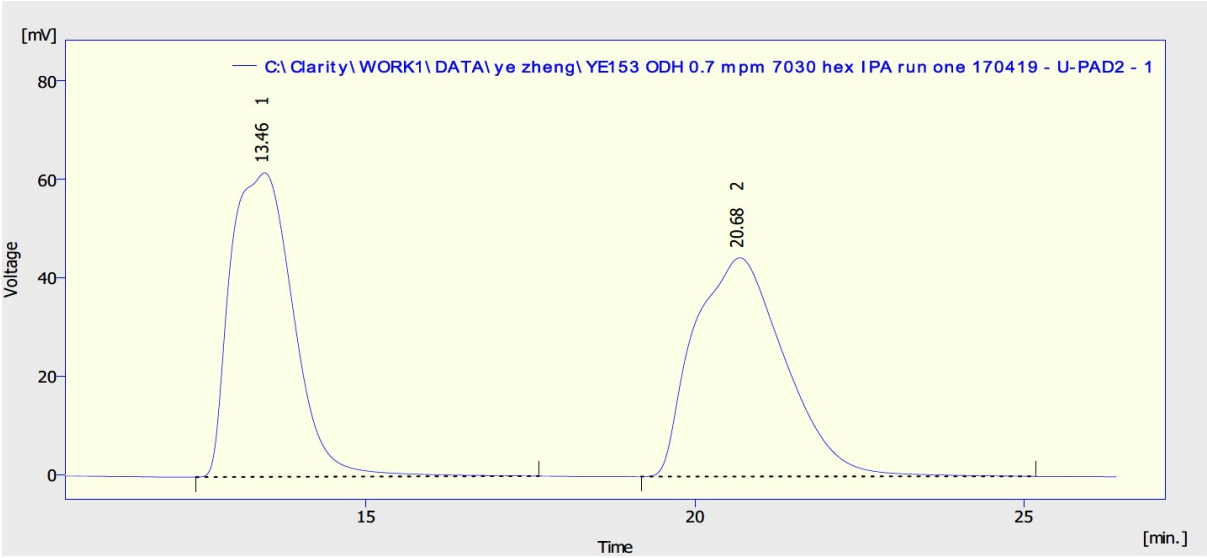
^{1}H NMR (400 MHz, $CDCl_3$) of **13**:



^{13}C NMR (100 MHz, $CDCl_3$) of **13**:



HPLC of racemic 2-(amino(phenyl)methyl)phenol **13**:

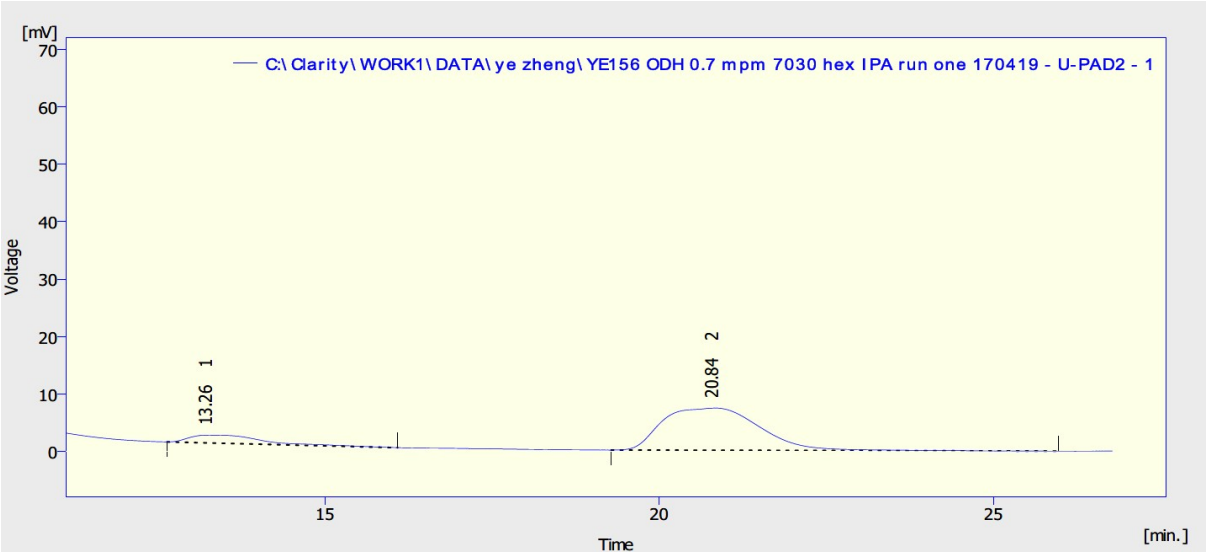


Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|ye zheng\|YE153 ODH 0.7 mpm 7030 hex IPA run one 170419 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	13.460	4103.709	61.776	49.0	58.2	1.07	
2	20.684	4268.682	44.446	51.0	41.8	1.60	
	Total	8372.392	106.221	100.0	100.0		

HPLC of **13** after ATH of 2-(1-imino-2-phenylethyl)phenol **10**:

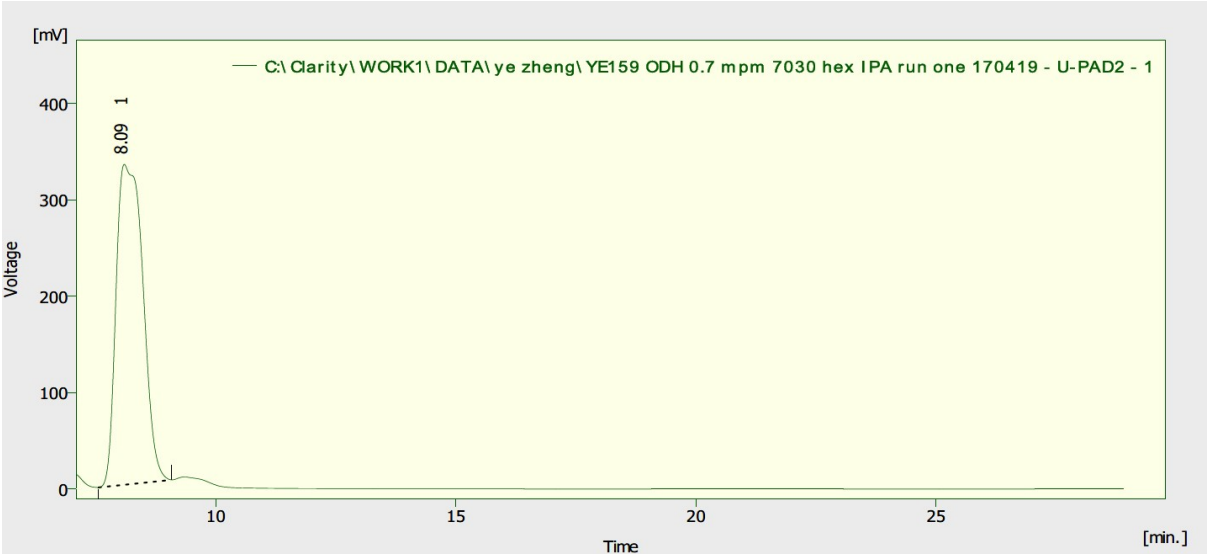
(*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst (after 24 hours, 100% conversion, 75.2% ee, *R* configuration)



Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|ye zheng\|YE156 ODH 0.7 mpm 7030 hex IPA run one 170419 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	13.260	105.950	1.371	12.4	15.7	1.04	
2	20.836	746.655	7.360	87.6	84.3	1.63	
	Total	852.606	8.731	100.0	100.0		

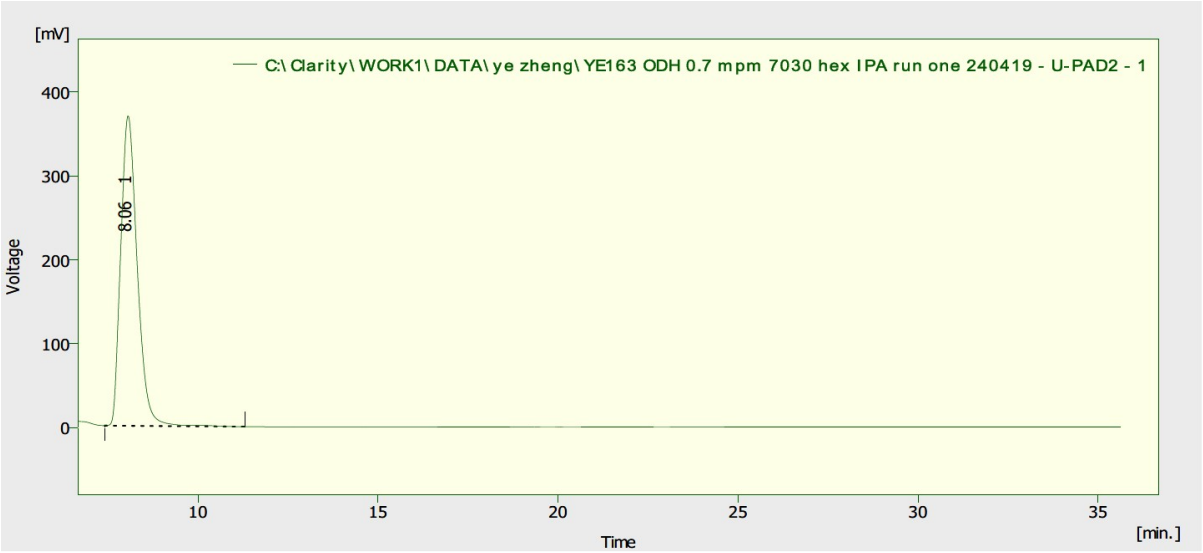
(*S,S*)-Noyori Ru(II)-TsDPEN catalyst (no conversion).



Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|ye zheng\|YE159 ODH 0.7 mpm 7030 hex IPA run one 170419 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	8.092	12853.829	332.535	100.0	100.0	0.64	
	Total	12853.829	332.535	100.0	100.0		

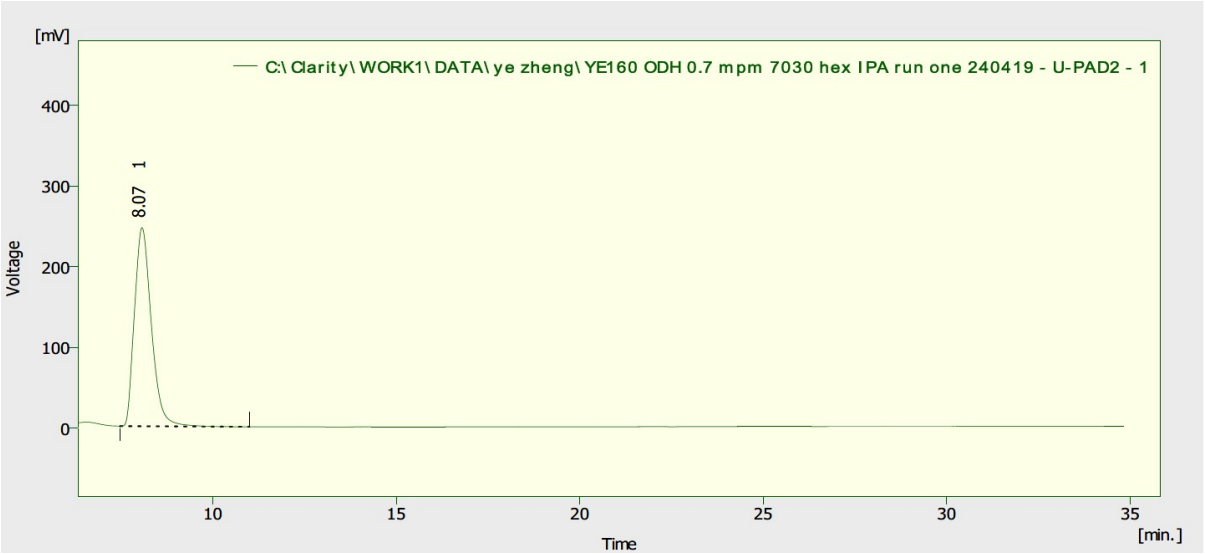
(*R,R*)-3C-tethered, 4-methoxy-Ru(II)-TsDPEN catalyst (no conversion).



Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|ye zheng\|YE163 ODH 0.7 mpm 7030 hex IPA run one 240419 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	8.060	11782.178	369.800	100.0	100.0	0.49	
	Total	11782.178	369.800	100.0	100.0		

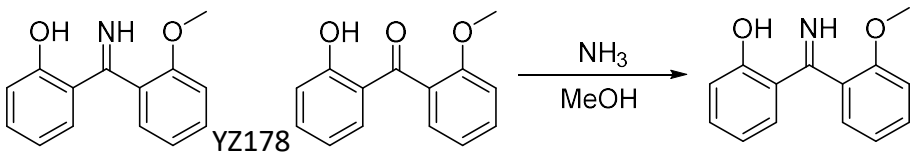
(*R,R*)-benzyl-tethered Ru(II)-TsDPEN catalyst (no conversion).



Result Table (Uncal - C:\Clarity\WORK1\DATA\ye zheng\YE160 ODH 0.7 mpm 7030 hex IPA run one 240419 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	8.072	7892.479	246.342	100.0	100.0	0.50	
	Total	7892.479	246.342	100.0	100.0		

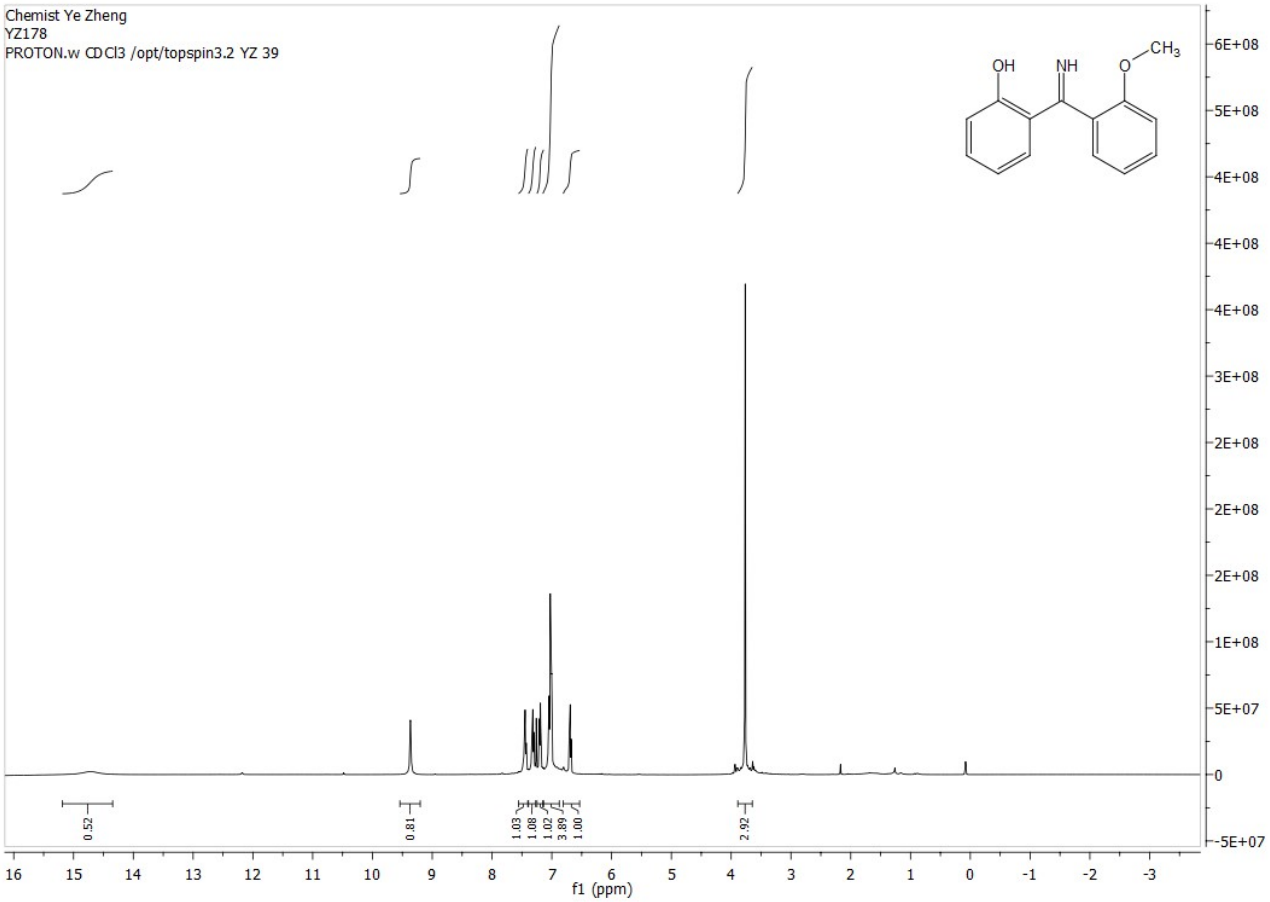
Compound name: 2-(Imino(2-methoxyphenyl)methyl)phenol **11**.



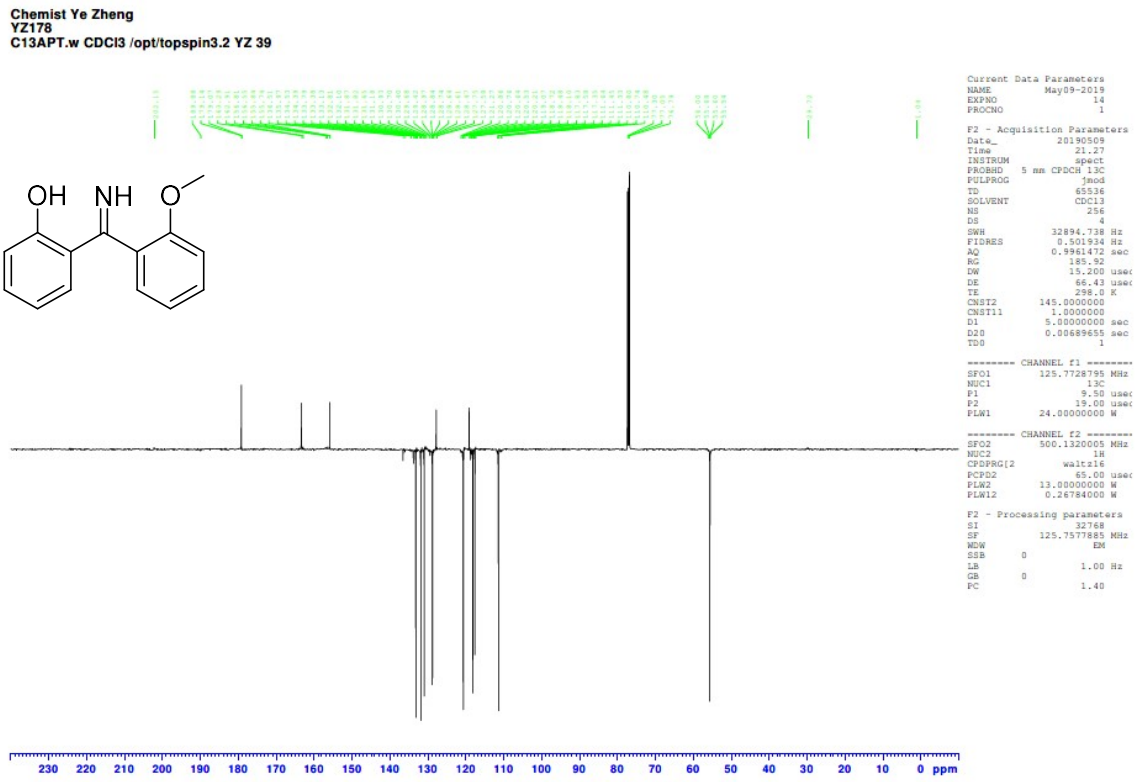
This compound is novel.

(2-Hydroxyphenyl)(2-methoxyphenyl)methanone (114 mg, 0.50 mmol) was dissolved in ammonia (1.2 mL, 7N in MeOH, 8.5 mmol) and the mixture was stirred under a nitrogen atmosphere overnight. The solvent was removed to give the product **11** as a brown solid (98.4 mg, 0.43 mmol, 86.7%). TLC: Rf ca 0.30 (4:1 hexane: EtOAc), strong UV and $KMnO_4$; Mp: 95 °C; HRMS: (found (ESI+): [M+Na]+, Calcd for $C_{14}H_{14}NO_2$ 228.1017; Found 228.1019; 0.1 ppm error); ν_{max} 2937, 2838, 1602, 1490, 1281, 1023, 902 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 14.70 (1H, s, OH), 9.37 (1H, s, NH), 7.45 (1H, t, *J* = 7.5, ArH), 7.32 (1H, t, *J* = 7.0, ArH), 7.21 (1H, d, *J* = 7.5, ArH), 7.06-7.00 (4H, m, ArH), 6.69 (1H, t, *J* = 7.5, ArH), 3.77 (3H, s, OCH_3) ppm; δ_C (125 MHz, $CDCl_3$) 179.1 (C), 163.3 (C), 155.8 (C), 133.1 (CH), 131.8 (CH), 130.9 (CH), 128.7 (CH), 127.8 (C), 120.6 (CH), 119.1 (C), 118.1 (CH), 117.6 (CH), 111.3 (CH), 55.6 (CH_3) ppm; m/z (ES-API+) 228.3 (M^+ + 1, 100%).

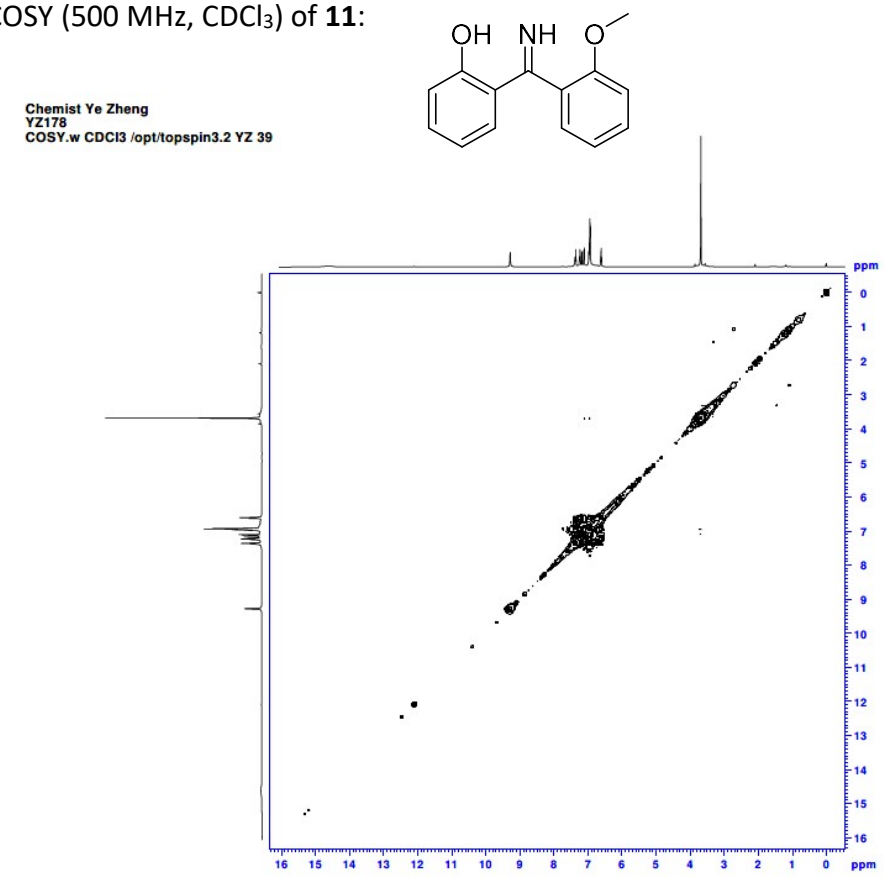
^{1}H NMR (500 MHz, $CDCl_3$) of **11**:



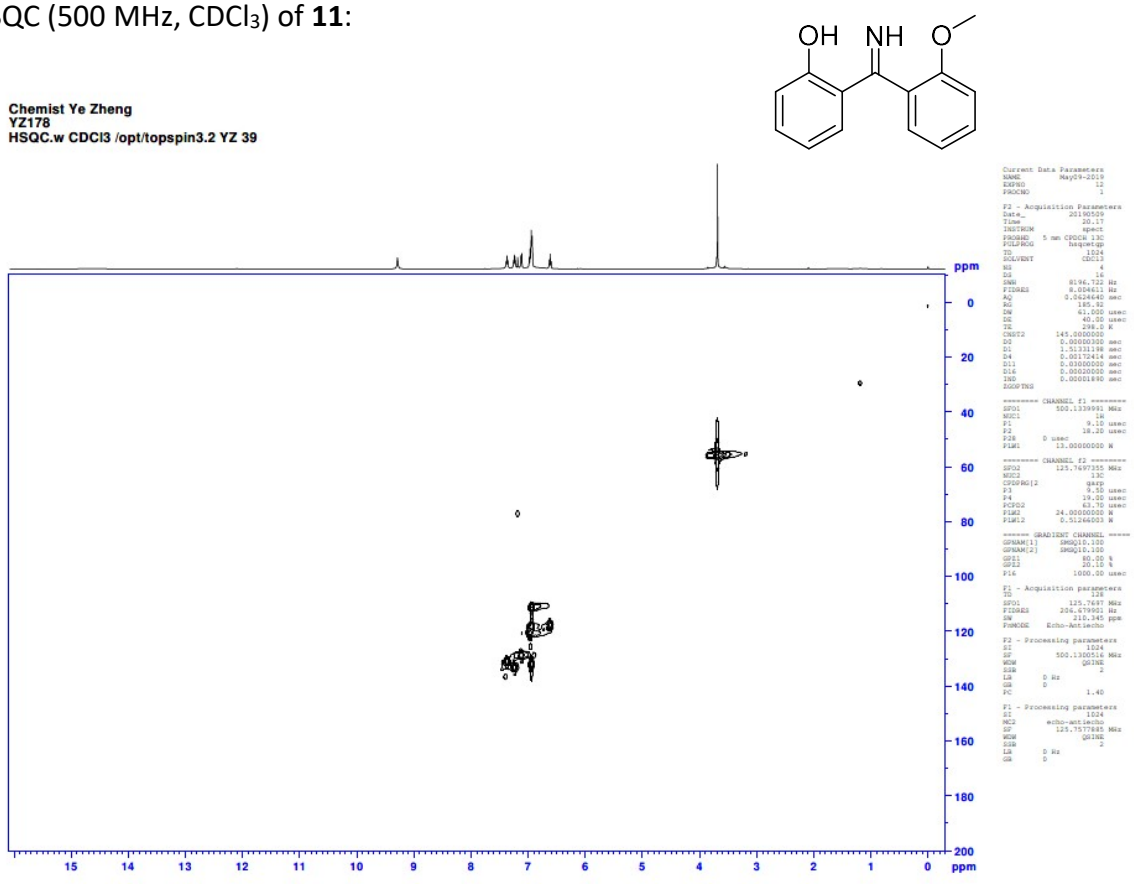
^{13}C NMR (125 MHz, $CDCl_3$) of **11**:



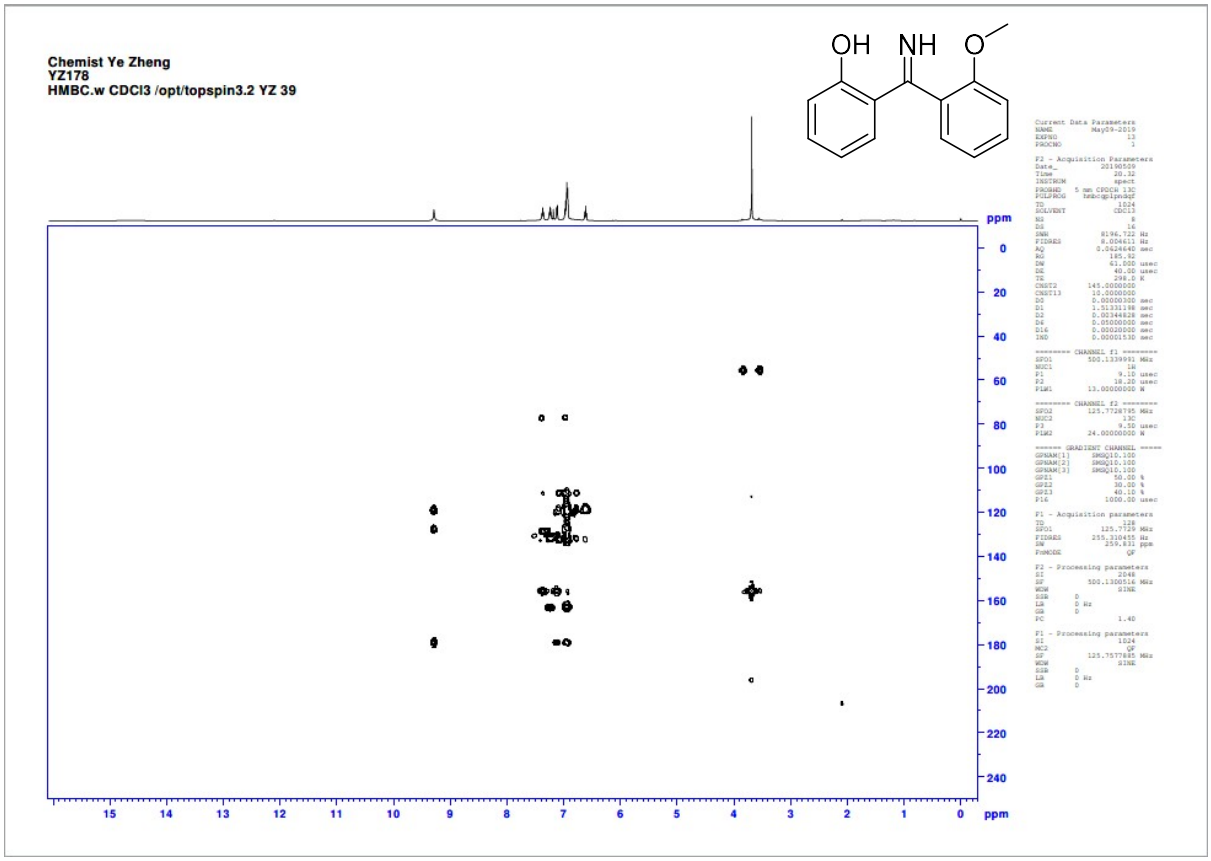
COSY (500 MHz, $CDCl_3$) of **11**:



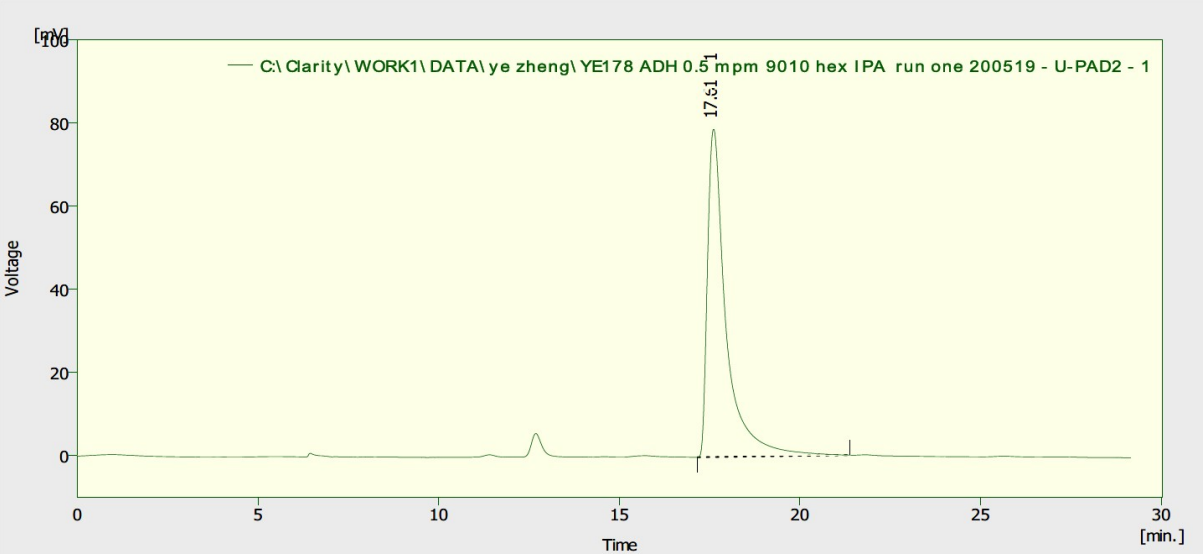
HSQC (500 MHz, $CDCl_3$) of **11**:



HMBC (500 MHz, $CDCl_3$) of **11**:



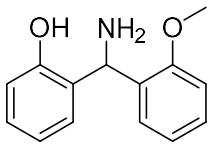
HPLC of 2-(imino(2-methoxyphenyl)methyl)phenol **11**:



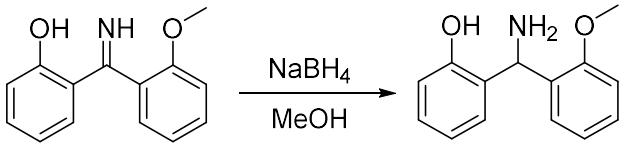
Result Table (Uncal - C:\Clarity\WORK1\DATA\ye zheng\YE178 ADH 0.5 mpm 9010 hex IPA run one 200519 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	17.608	2834.443	79.008	100.0	100.0	0.47	
	Total	2834.443	79.008	100.0	100.0		

2-(Amino(2-methoxyphenyl)methyl)phenol.



racemic: YZ184. Asymmetric: YZ192



This compound is novel.

Racemic: To a solution of 2-(imino(2-methoxyphenyl)methyl)phenol **11** (98 mg, 0.43 mmol) in MeOH (2 mL) was added sodium borohydride (33 mg, 0.86 mmol). The reaction was stirred for 4 hours. TLC (1:1 hexane: EtOAc) after this time indicated full conversion. Distilled water (20 mL) was added, and the mixture was extracted with EtOAc (3 × 20ml), dried with $MgSO_4$, and the solvent was removed under vacuum to give 2-(amino(2-methoxyphenyl)methyl)phenol as a brown oil (48 mg, 0.21 mmol, 48.5%). TLC: Rf ca 0.20 (1:1 hexane: EtOAc), strong UV and $KMnO_4$; HRMS: (found (ESI+): [M+Na]+, Calcd for $C_{14}H_{16}NO_2$ 230.1174; Found 230.1176; 0.8 ppm error); ν_{max} 3375, 2926, 2852, 1732, 1585, 1487, 1237, 1021, 748 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.31-7.28 (1H, m, ArH), 7.19-7.16 (1H, m, ArH), 7.09 (2H, d, *J* = 7.5, ArH), 6.95-6.90 (4H, m, ArH), 6.73-6.71 (2H, m, NH_2), 5.57 (1H, s, CH), 3.85 (3H, s, OCH_3) ppm; δ_C (125 MHz, $CDCl_3$) 158.5 (C), 157.0 (C), 130.3 (C), 129.0 (CH), 128.8 (CH), 128.8 (CH), 128.4 (CH), 125.6 (C), 121.0 (CH), 118.9 (CH), 117.2 (CH), 110.8 (CH), 55.4 (CH_3) ppm; m/z (ES-API+) 230.3 (M^+ + 1, 100%).

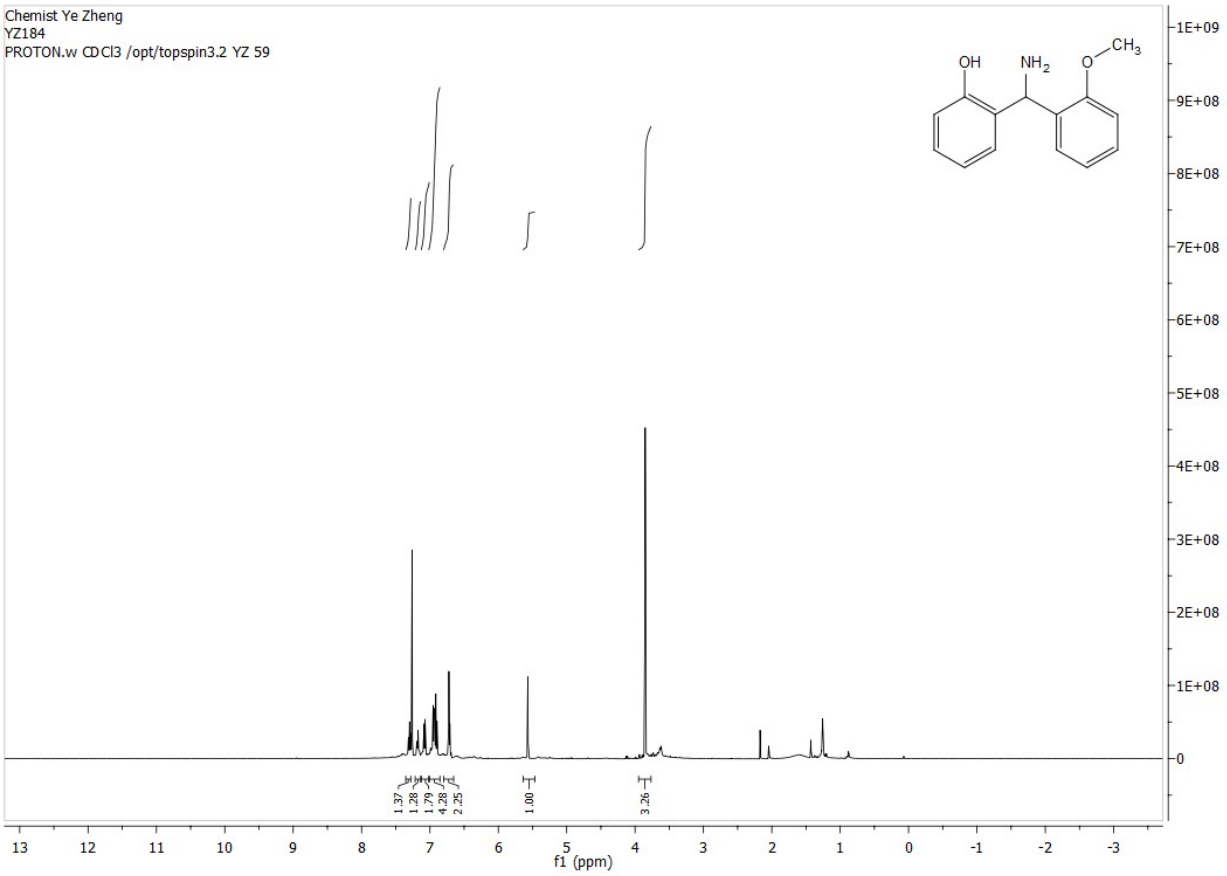
Enantiomeric excess and conversion determined by HPLC analysis (Chiralpak ADH, 30 cm x 6mm column, hexane: iPrOH 9:1, 0.5 mL/min, T = 25°C) imine 17.6 min, *R* and *S* isomers 18.4 min and 20.0 min, configuration is not known.

Attempted reduction of 2-(imino(2-methoxyphenyl)methyl)phenol **11** (YZ192).

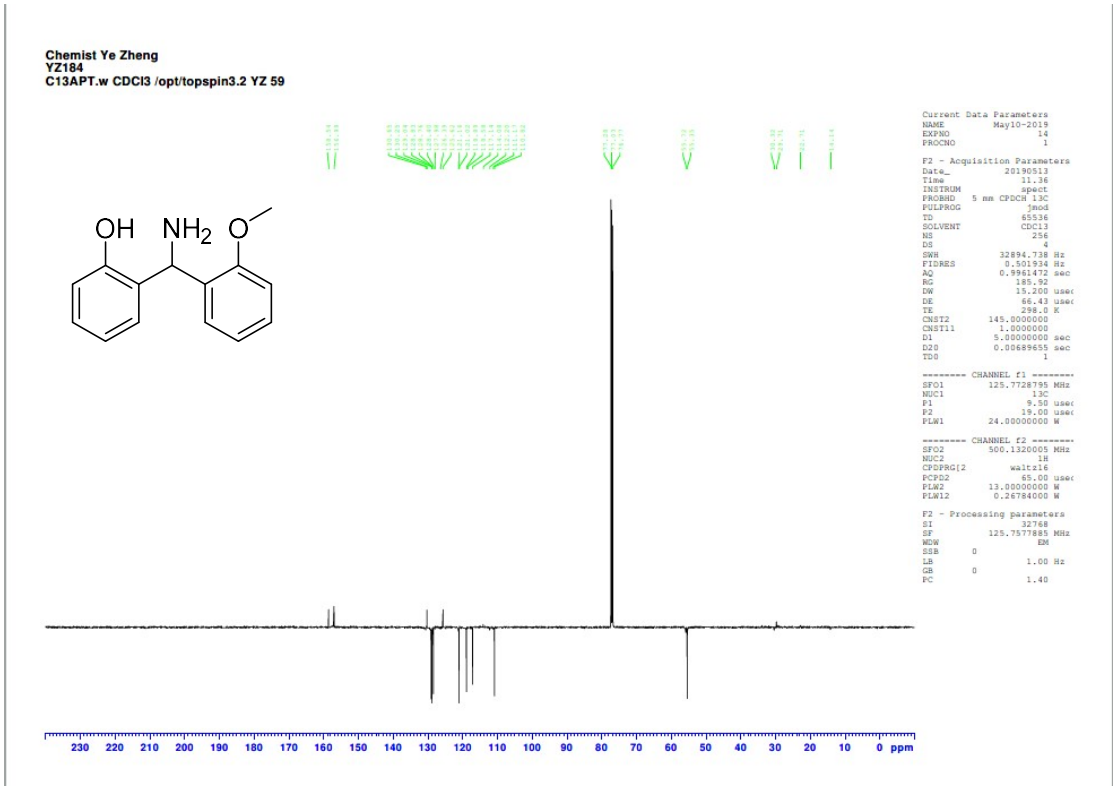
2-(Imino(2-methoxyphenyl)methyl)phenol **11** (40 mg, 0.176 mmol), ammonium formate (44.4 mg, 0.704 mmol) and catalyst (0.00088 mmol, 0.5 mol%) were added to a sealed tube and stirred under a nitrogen atmosphere for 10 minutes. DCM (0.88 mL) was degassed with nitrogen then added under nitrogen to the tube. The mixture was heated to 70 °C on a hot plate and stirred under a nitrogen atmosphere overnight. Then the reaction was quenched by saturated $NaHCO_3$ solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried ($MgSO_4$) and filtered. The solvent was removed. The reaction also followed by HPLC analysis (Chiralpak

ADH, 30 cm x 6mm column, hexane: iPrOH 9:1, 0.5 mL/min, T = 25°C). NMR and HPLC indicated no product present.

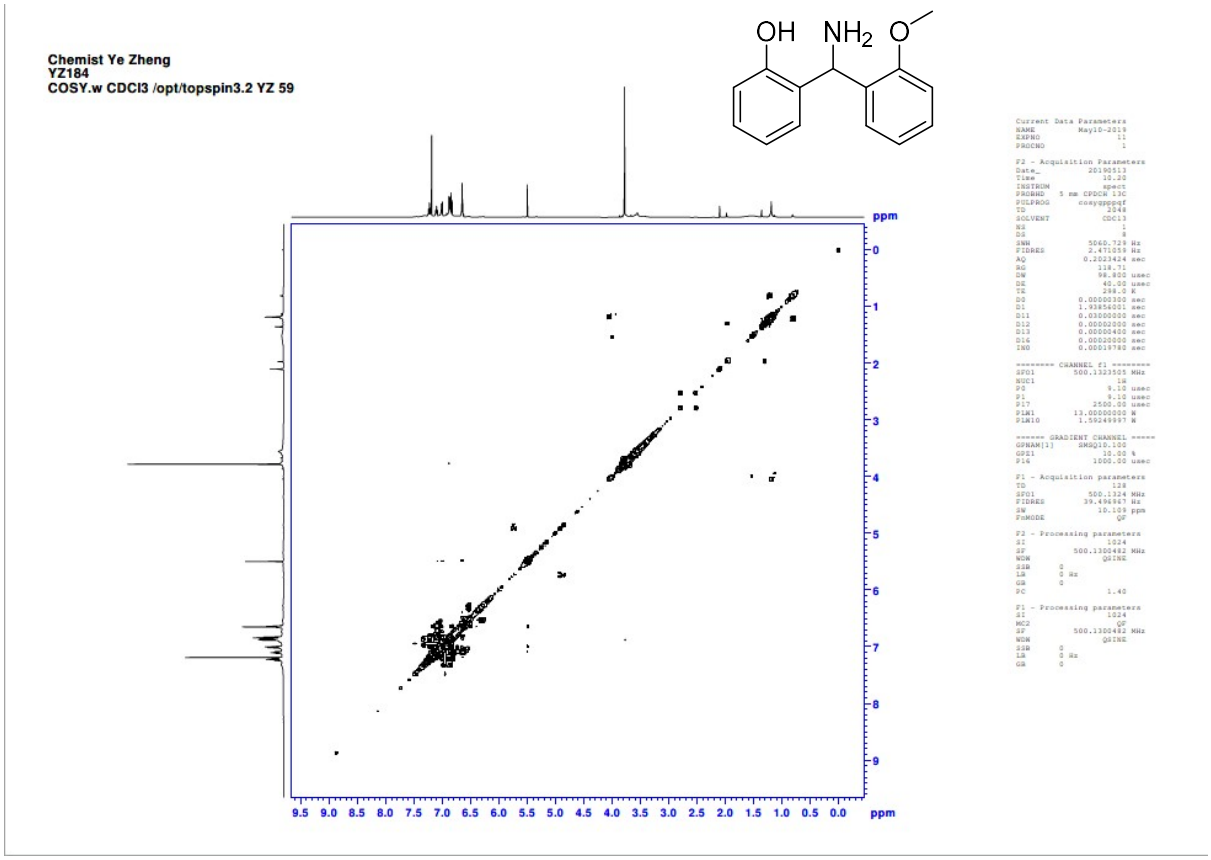
^{1}H NMR (500 MHz, $CDCl_3$) of 2-(Amino(2-methoxyphenyl)methyl)phenol:



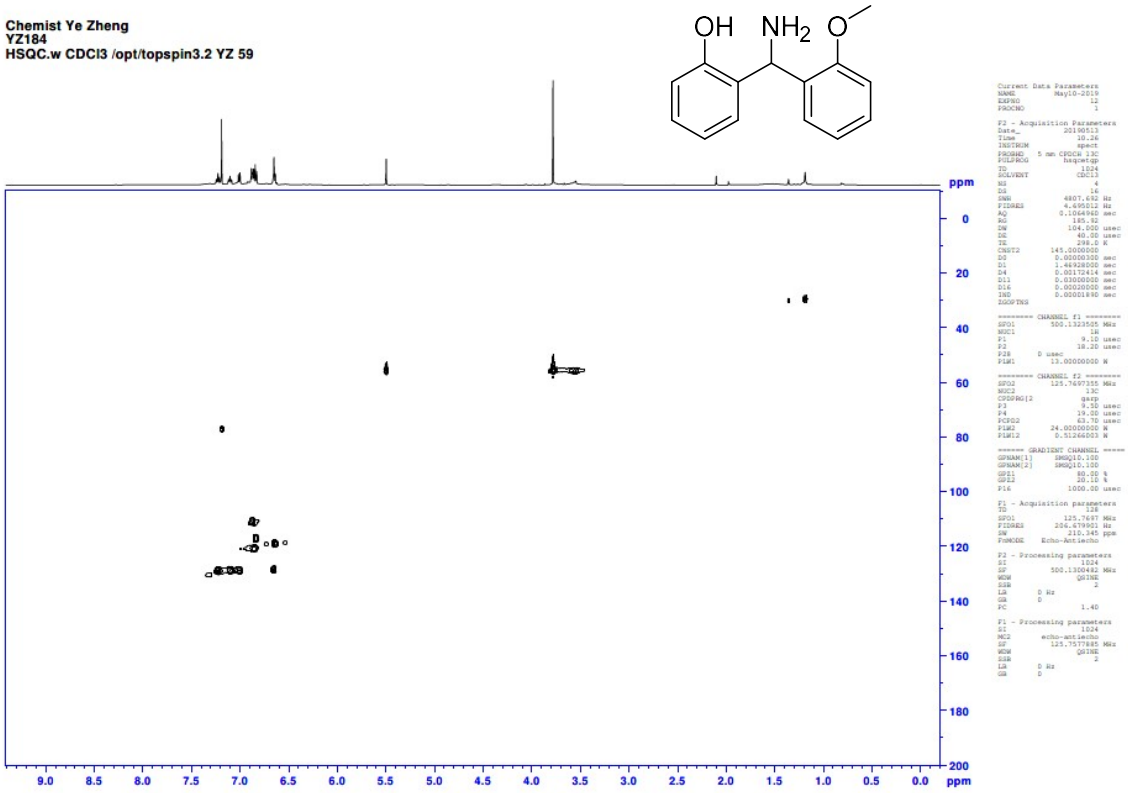
^{13}C NMR (125 MHz, $CDCl_3$) of 2-(Amino(2-methoxyphenyl)methyl)phenol:



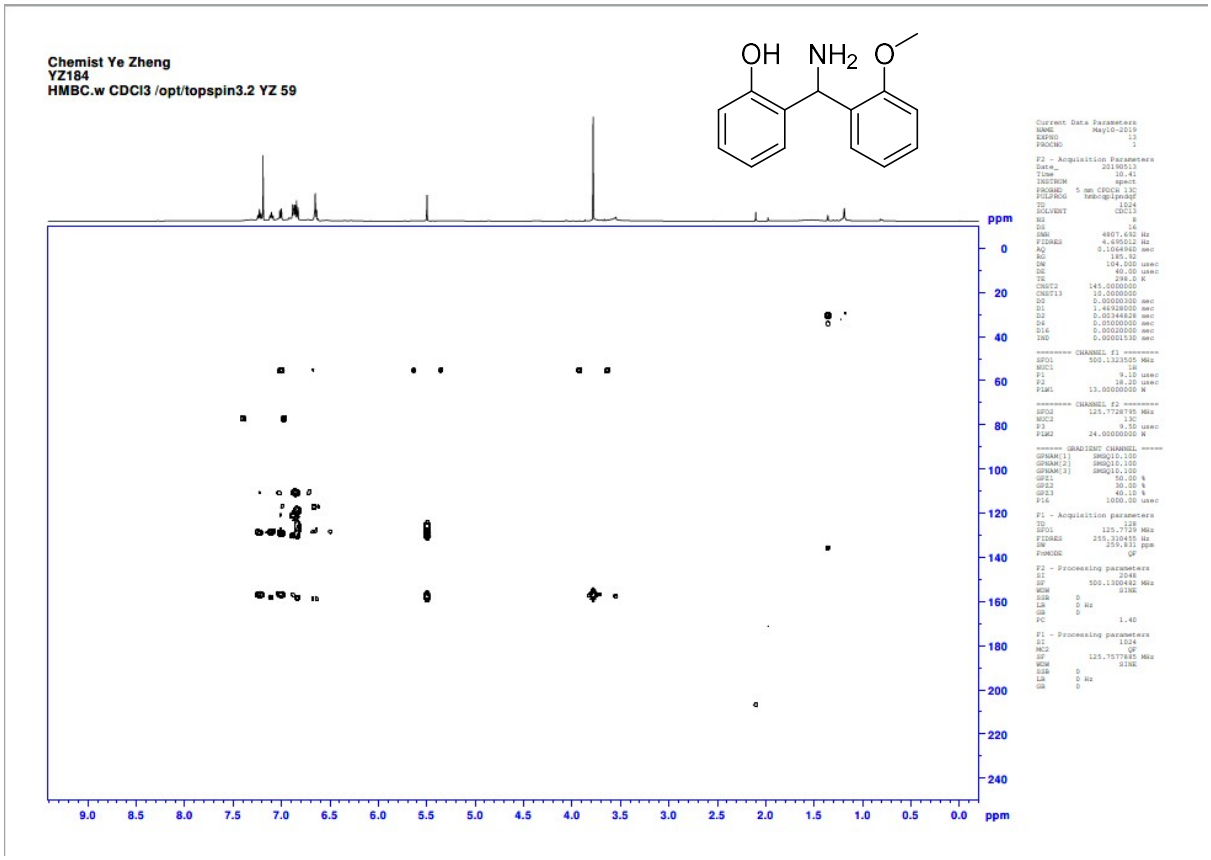
COSY (500 MHz, $CDCl_3$) of 2-(Amino(2-methoxyphenyl)methyl)phenol:



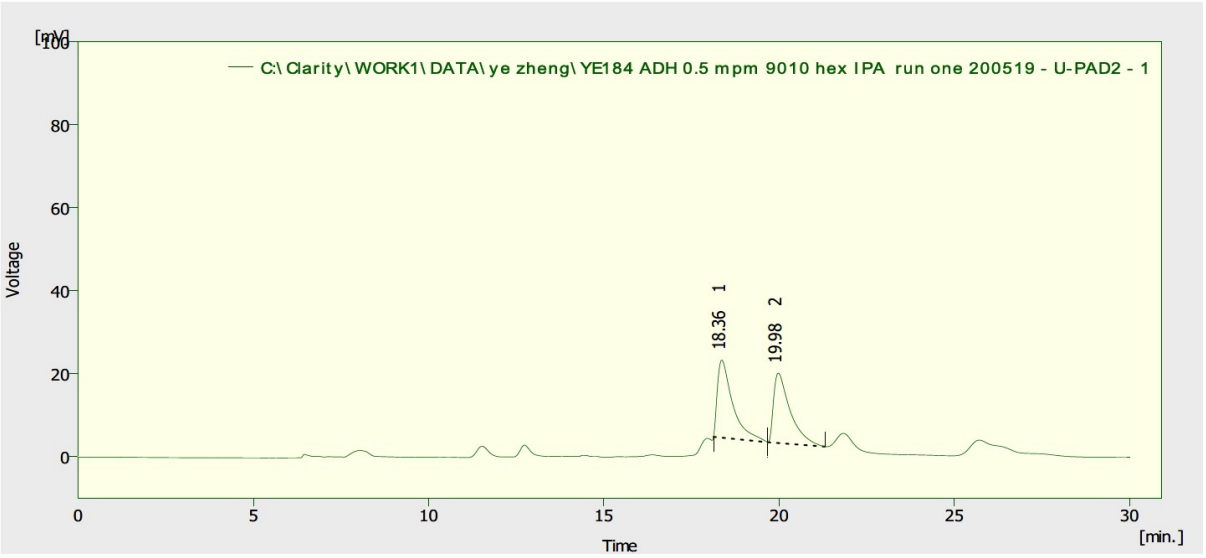
HSQC (500 MHz, $CDCl_3$) of 2-(Amino(2-methoxyphenyl)methyl)phenol:



HMBC (500 MHz, $CDCl_3$) of 2-(Amino(2-methoxyphenyl)methyl)phenol:



HPLC of racemic 2-(imino(2-methoxyphenyl)methyl)phenol of 2-(Amino(2-methoxyphenyl)methyl)phenol:

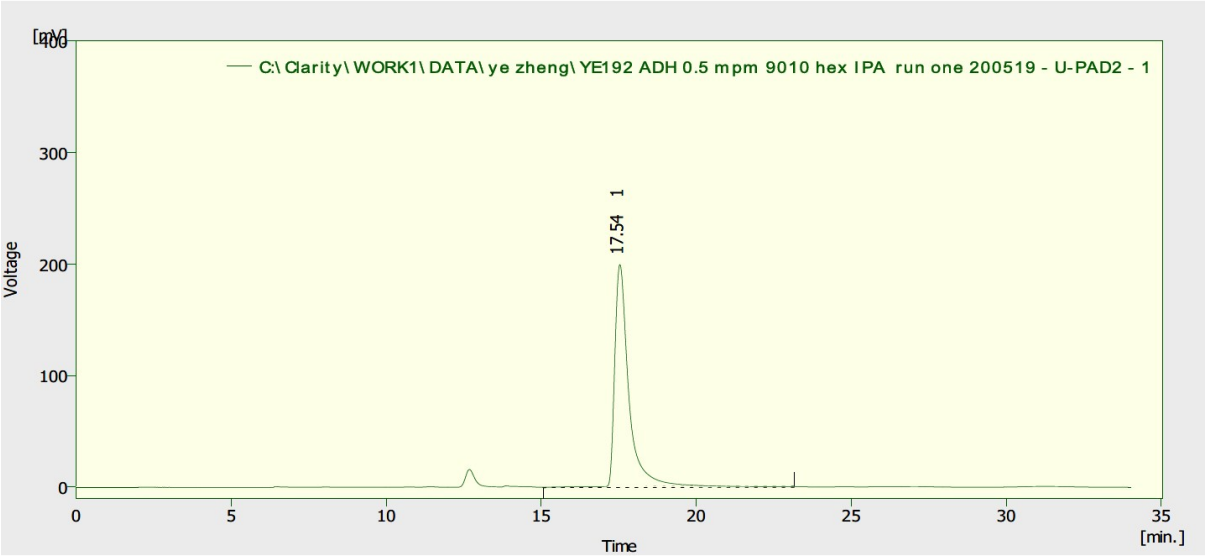


Result Table (Uncal - C:\Clarity\WORK1\DATA\ye zheng\YE184 ADH 0.5 mpm 9010 hex IPA run one 200519 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	18.364	568.918	18.736	50.6	52.6	0.42	
2	19.976	555.084	16.917	49.4	47.4	0.47	
	Total	1124.002	35.653	100.0	100.0		

HPLC after ATH of 2-(imino(2-methoxyphenyl)methyl)phenol:

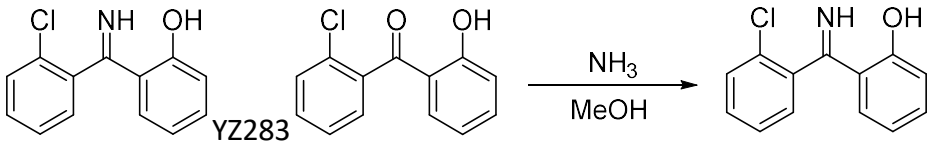
(*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst (no conversion).



Result Table (Uncal - C:|Clarity|WORK1|DATA|ye zheng|YE192 ADH 0.5 mpm 9010 hex IPA run one 200519 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	17.536	6429.441	199.823	100.0	100.0	0.43	
	Total	6429.441	199.823	100.0	100.0		

2-((2-Chlorophenyl)(imino)methyl)phenol.

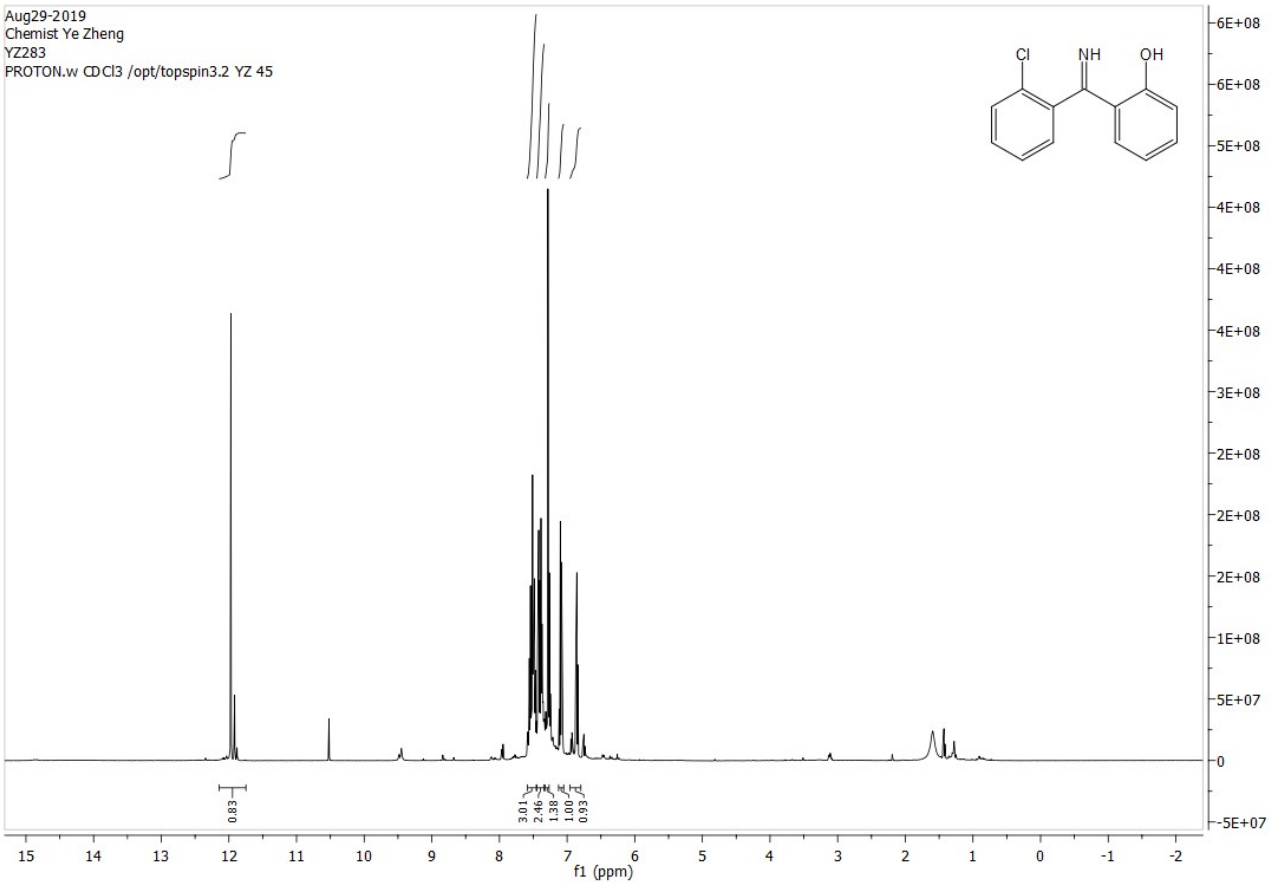


YZ283

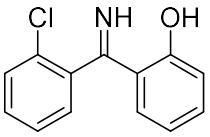
This compound is novel.

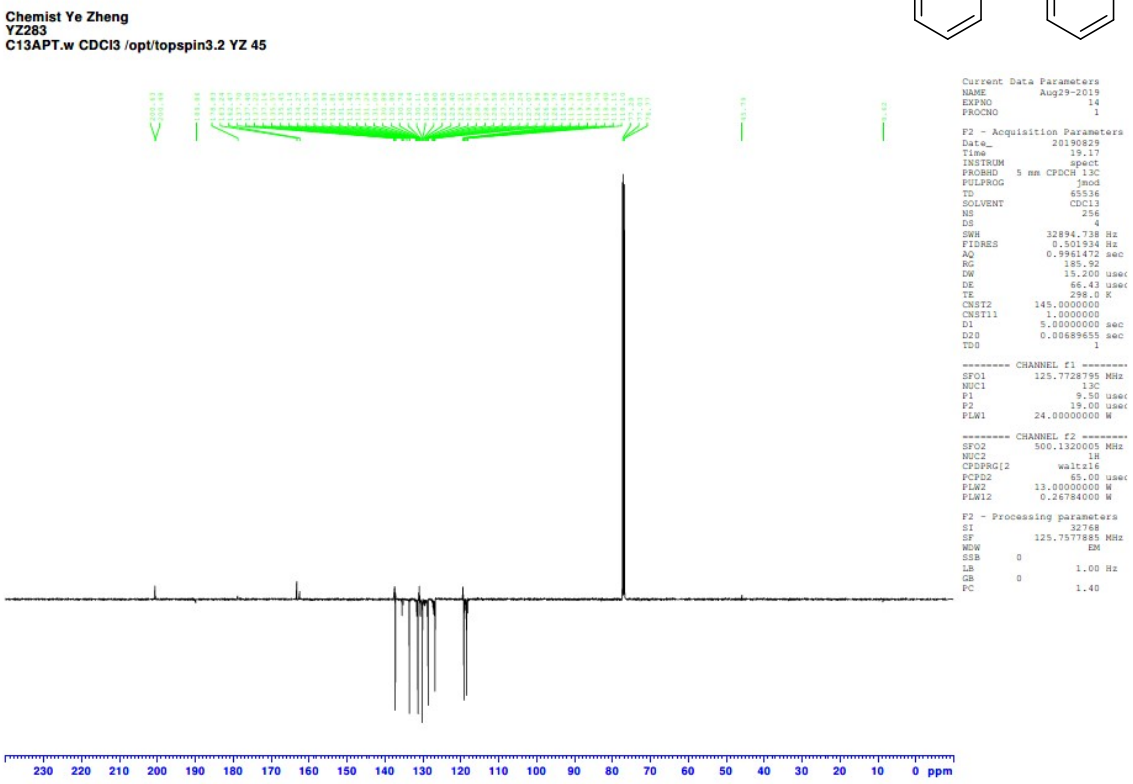
(2-Chlorophenyl)(2-hydroxyphenyl)methanone (156.4 mg, 0.674 mmol) was dissolved in ammonia (1.64 mL, 7N in MeOH, 11.46 mmol) and the mixture was stirred under a nitrogen atmosphere overnight. The solvent was removed to give the product as a brown oil (76.7 mg, 0.332 mmol, 49.3%). TLC: Rf ca 0.50 (4:1 hexane: EtOAc), strong UV and $KMnO_4$; HRMS: (found (ESI+): [M+H]+, Calcd for $C_{13}H_{11}ClNO$ 232.0522; Found 232.0524; 0.8 ppm error); ν_{max} 3061 (br), 1626, 1590, 1473, 1445, 1241, 935 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 11.97 (1H, s, OH), 7.45 (3H, m, ArH), 7.45-7.34 (2H, m, ArH), 7.32-7.28 (1H, m, ArH), 7.13-7.05 (1H, m, ArH), 6.94-6.74 (1H, m, ArH) ppm; δ_C (125 MHz, $CDCl_3$) 200.6 (C), 163.2 (C), 137.4 (C), 137.2 (CH), 133.5 (CH), 131.3 (CH), 130.9 (C), 130.1 (CH), 128.6 (CH), 126.8 (CH), 119.4 (C), 119.1 (CH), 118.4 (CH) ppm; m/z (ES-API+) 232.3 (M^+ + 1, 100%).

^1H NMR (500 MHz, $CDCl_3$) 2-((2-Chlorophenyl)(imino)methyl)phenol:

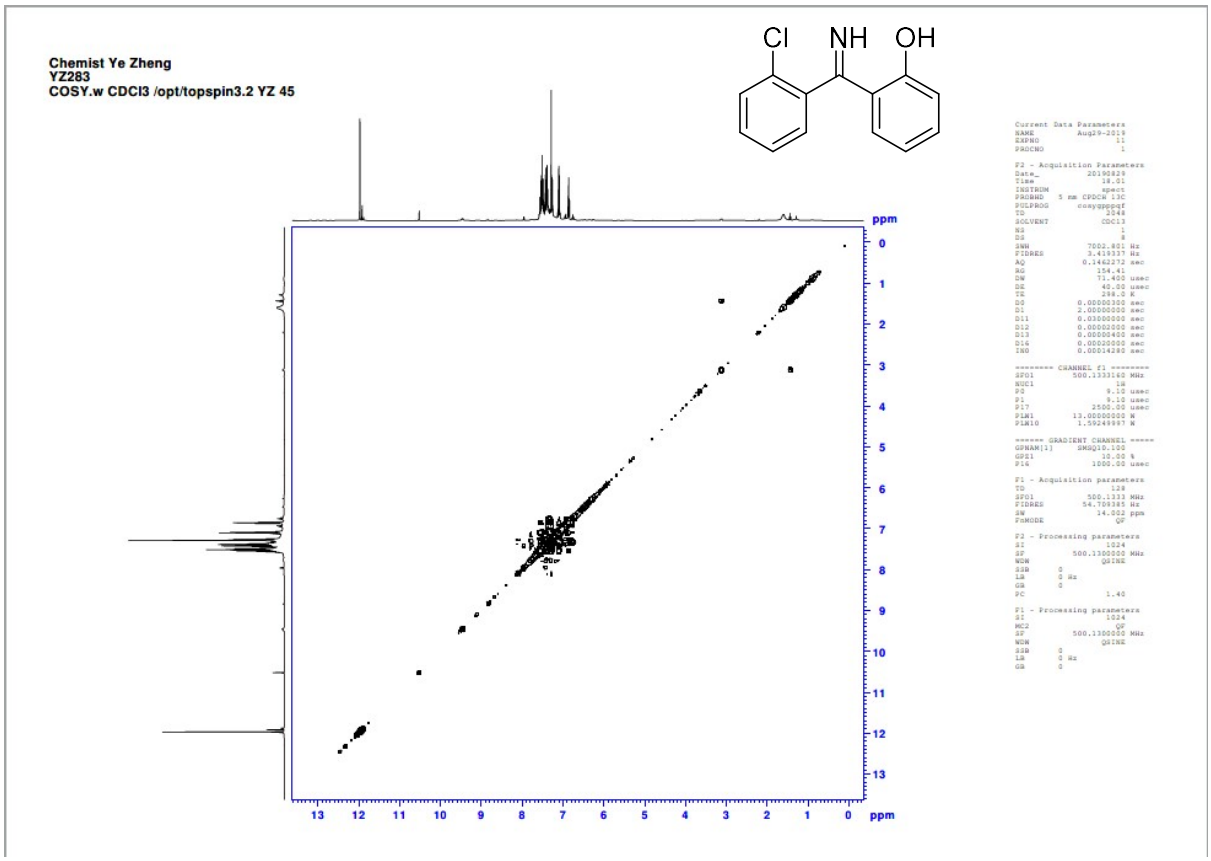


^{13}C NMR (125 MHz, $CDCl_3$) 2-((2-Chlorophenyl)(imino)methyl)phenol:

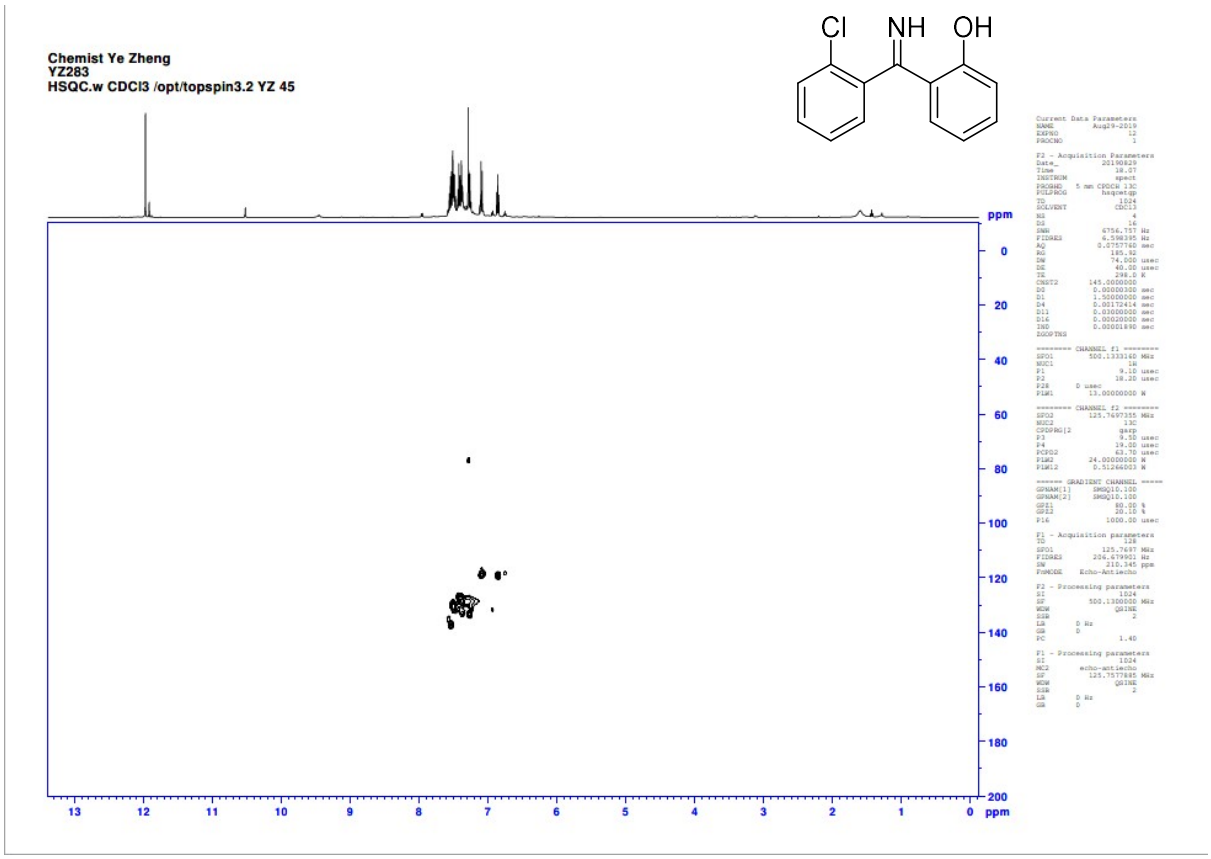




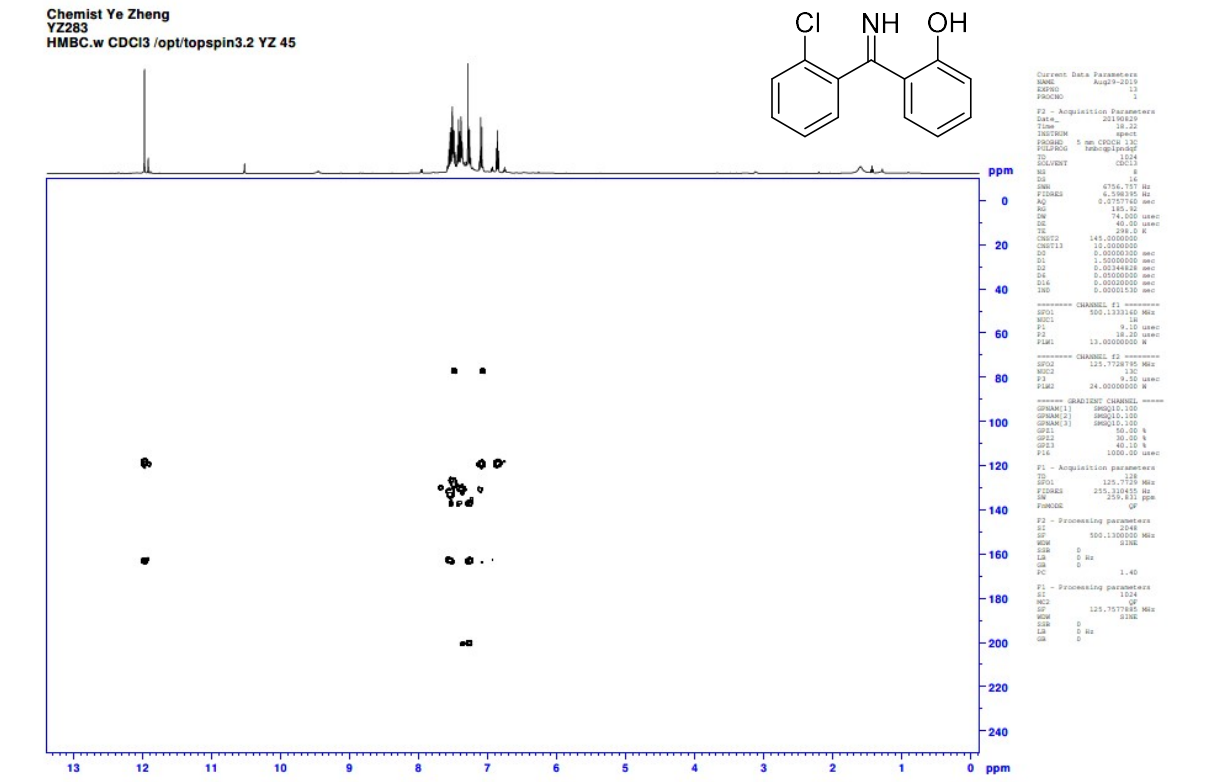
COSY (500 MHz, $CDCl_3$) 2-((2-Chlorophenyl)(imino)methyl)phenol:



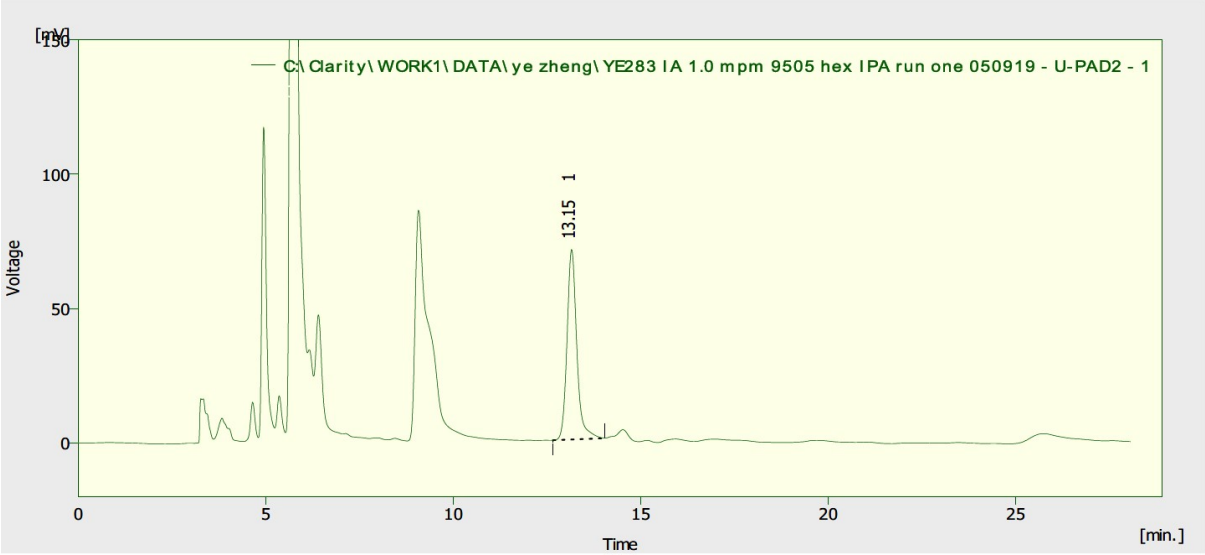
HSQC (500 MHz, $CDCl_3$) 2-((2-Chlorophenyl)(imino)methyl)phenol:



HMBC (500 MHz, $CDCl_3$) 2-((2-Chlorophenyl)(imino)methyl)phenol:



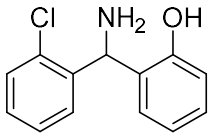
HPLC of 2-((2-chlorophenyl)(imino)methyl)phenol:



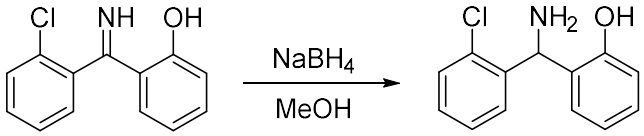
Result Table (Uncal - C:|Clarity|WORK1|DATA|ye zheng|YE283 IA 1.0 mpm 9505 hex IPA run one 050919 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	13.152	1284.430	70.817	100.0	100.0	0.26	
	Total	1284.430	70.817	100.0	100.0		

2-(Amino(2-chlorophenyl)methyl)phenol 14.



racemic: YZ292. Asymmetric: YZ315



This compound is novel.

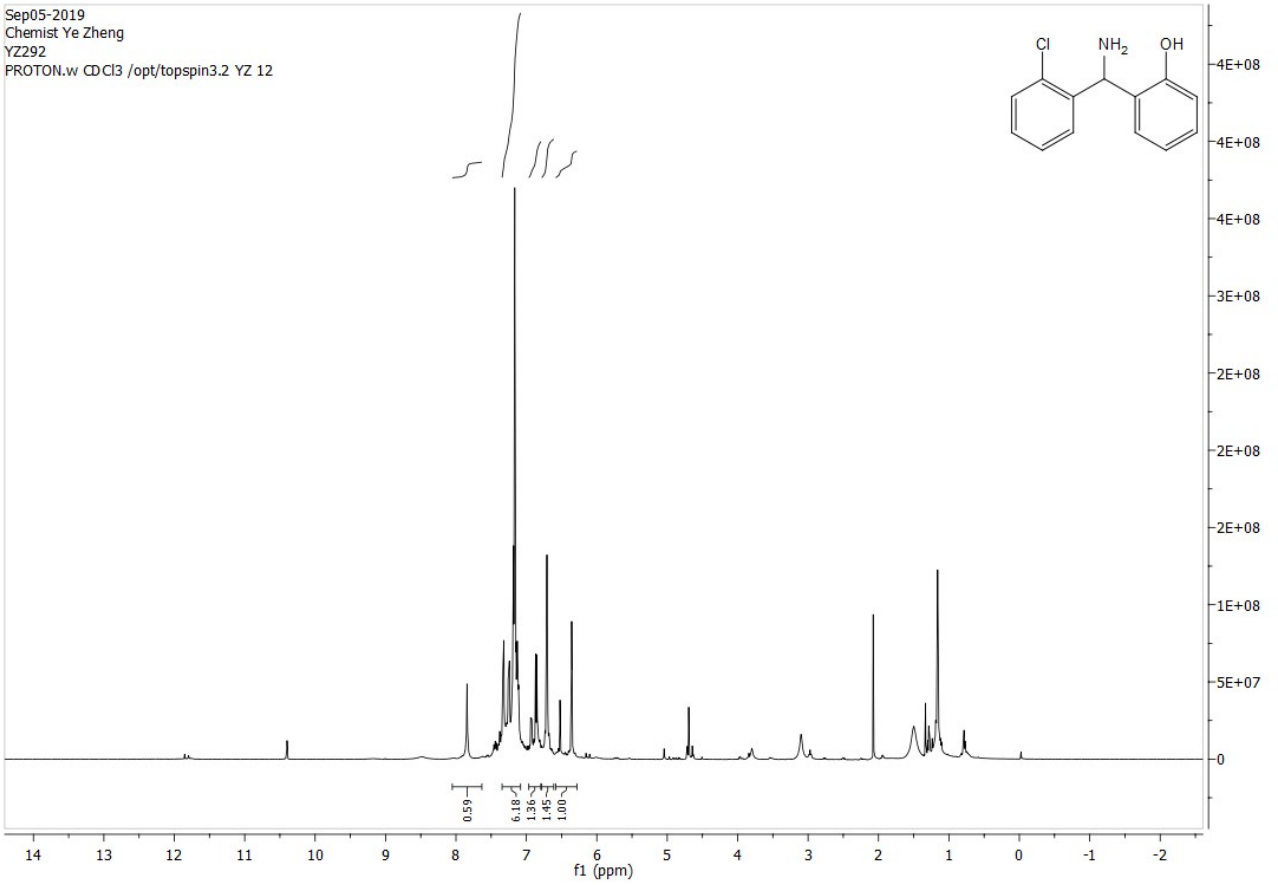
To a solution of 2-((2-chlorophenyl)(imino)methyl)phenol (70.8 mg, 0.306 mmol) in MeOH (1.4 mL) was added sodium borohydride (23.3 mg, 0.612 mmol). The reaction was stirred for 4 hours. TLC (4:1 hexane: EtOAc) after this time indicated full conversion. Distilled water (20 mL) was added, and the mixture was extracted with EtOAc (3 × 20ml), dried with $MgSO_4$, and the solvent was removed under vacuum to give 2-(amino(2-chlorophenyl)methyl)phenol **14** as a yellow oil (20.2 mg, 0.0867 mmol, 28.3%). TLC: Rf ca 0.40 (4:1 hexane: EtOAc), strong UV and KMnO4; HRMS: (found (ESI+): [M+H]+, Calcd for $C_{13}H_{13}ClNO$ 234.0674; Found 234.0680; 2.7 ppm error); ν_{max} 3060, 3039, 2955, 2924, 2844, 1592, 1242, 1009, 823 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.84 (1H, s, OH), 7.34-7.08 (6H, m, ArH), 6.94-6.83 (1H, m, ArH), 6.72-6.88 (1H, m, ArH), 6.52-6.36 (1H, m, CH) ppm; δ_C (125 MHz, $CDCl_3$) 156.0 (C), 149.9 (C), 133.1 (C), 130.0 (CH), 129.8 (CH), 129.7 (CH), 129.6 (CH), 129.2 (CH), 128.1 (CH), 127.5 (CH), 124.6 (C), 120.1 (CH), 117.6 (CH) ppm; m/z (ES-API+) 234.2 (M^+ + 1, 100%). Enantiomeric excess and conversion determined by HPLC analysis (Chiralpak IA, 30 cm x 6mm column, hexane: iPrOH 95:5, 1.0 mL/min, T = 25°C) imine 13.2 min, *R* and *S* isomers 19.6 min and 23.4 min, configuration was assigned by analogy.

ATH of 2-((2-chlorophenyl)(imino)methyl)phenol using (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst **2** (YZ315).

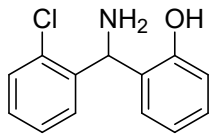
2-((2-Chlorophenyl)(imino)methyl)phenol (40 mg, 0.173 mmol), ammonium formate (44 mg, 0.692 mmol) and catalyst (*R,R*)-**2** (0.00085 mmol, 0.5 mol%) were added into a sealed tube and left to stir under a nitrogen atmosphere for 10 minutes. DCM (0.87 mL) was degassed with nitrogen then added under nitrogen to the tube. The mixture was heated to 70 °C on a hot plate and stirred under a nitrogen atmosphere overnight. Then the reaction was quenched by saturated $NaHCO_3$ solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried ($MgSO_4$) and filtered. Solvent was removed to give the product **14** (27.4 mg, 0.118 mmol, 67.9%). The

reaction also followed by HPLC analysis (Chiralpak IA, 30 cm x 6mm column, hexane: iPrOH 95:5, 1.0 mL/min, T = 25°C); (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst: 100% conversion; $[\alpha]_D^{27}$ -101 (c 0.048 in $CHCl_3$) 97.4% ee.

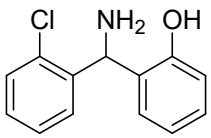
^1H NMR (500 MHz, $CDCl_3$) of **14b:**



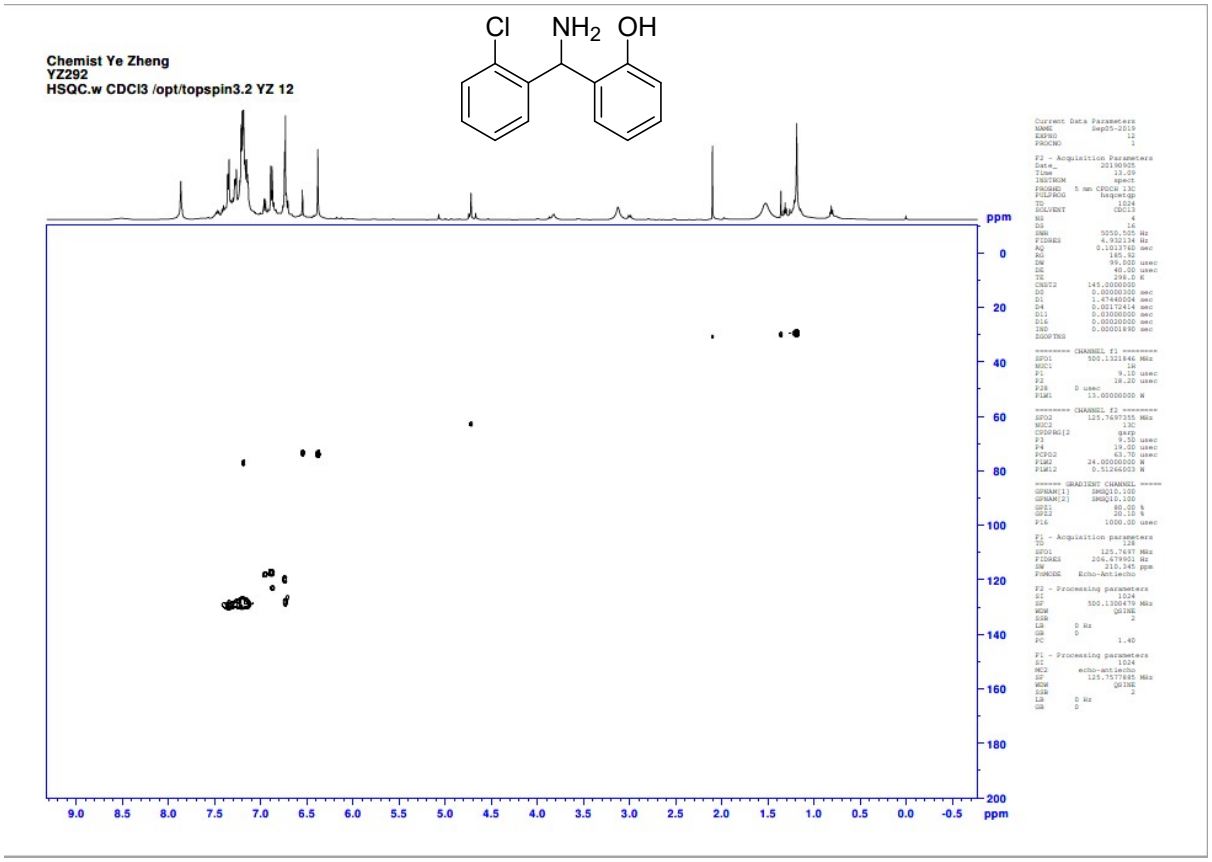
^{13}C NMR (125 MHz, $CDCl_3$) of **14**:



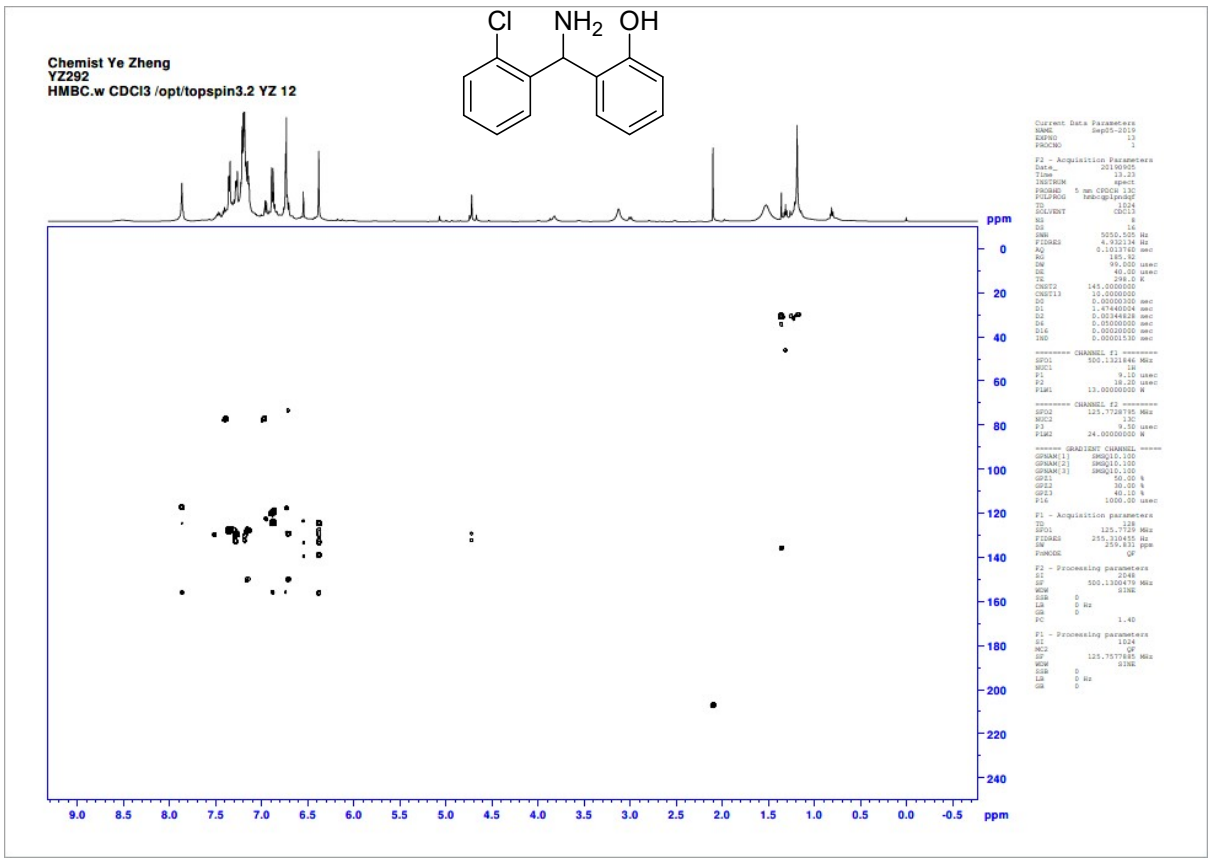
COSY (500 MHz, $CDCl_3$) of **14**:



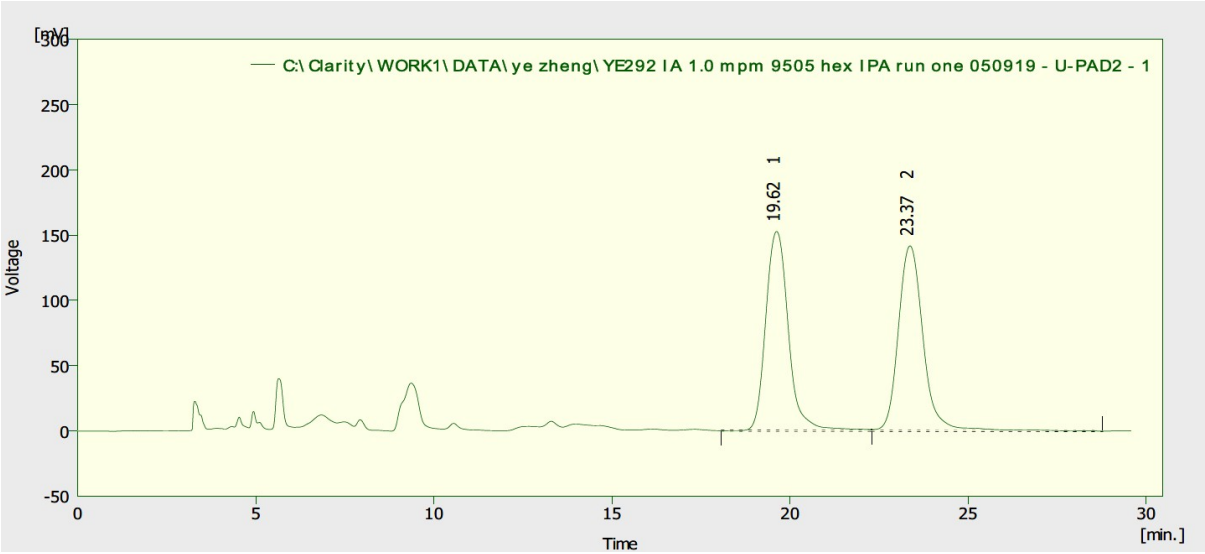
HSQC (500 MHz, $CDCl_3$) of **14**:



HMBC (500 MHz, $CDCl_3$) of **14**:



HPLC of racemic 2-(amino(2-chlorophenyl)methyl)phenol **14**:

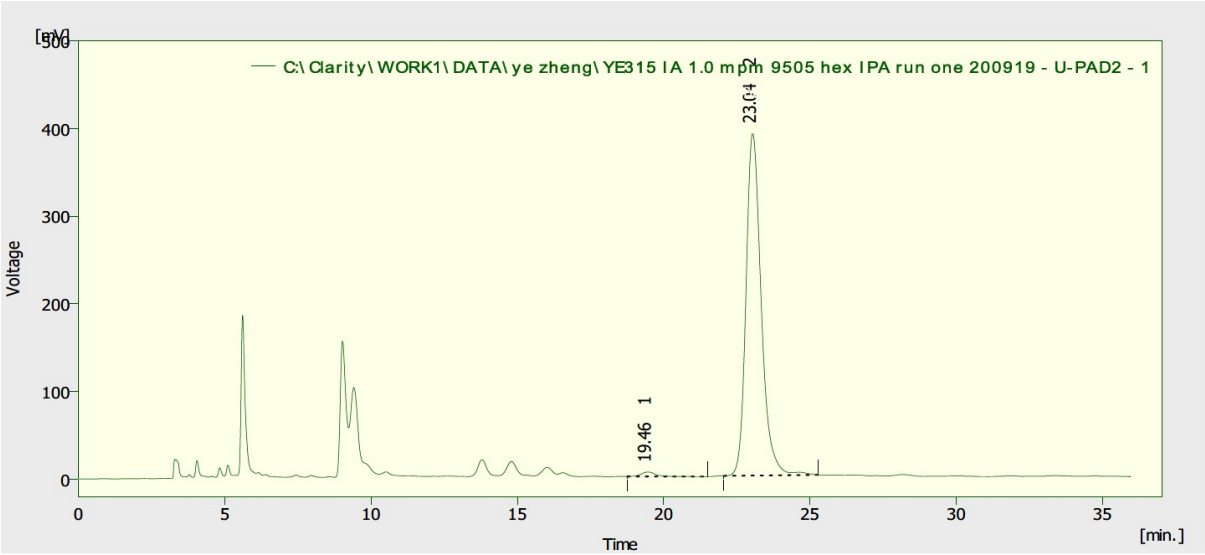


Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|ye zheng\|YE292 IA 1.0 mpm 9505 hex IPA run one 050919 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	19.620	6791.688	152.844	49.5	51.8	0.67	
2	23.368	6930.979	141.956	50.5	48.2	0.72	
	Total	13722.667	294.800	100.0	100.0		

HPLC of **14** after ATH of 2-(imino(2-methoxyphenyl)methyl)phenol:

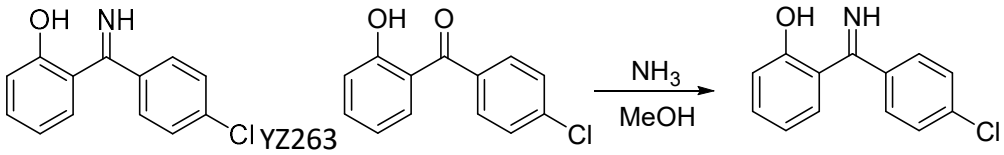
(*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst (after 24 hours, 100% conversion, 97.4% ee).



Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|ye zheng\|YE315 IA 1.0 mpm 9505 hex IPA run one 200919 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	19.456	179.424	5.132	1.3	1.3	0.50	
2	23.044	14132.321	390.713	98.7	98.7	0.54	
	Total	14311.746	395.845	100.0	100.0		

2-((4-Chlorophenyl)(imino)methyl)phenol.

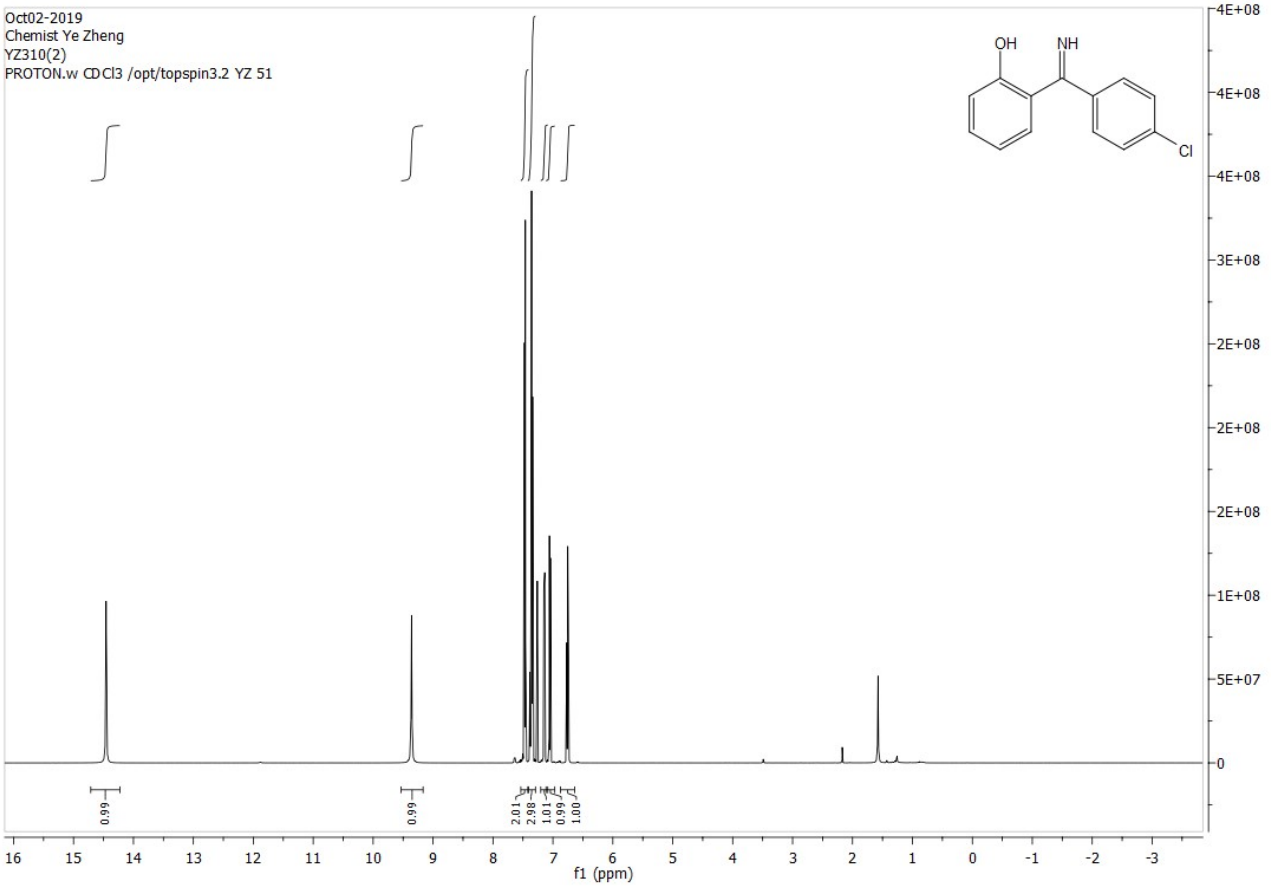


This compound has been reported and fully characterized.

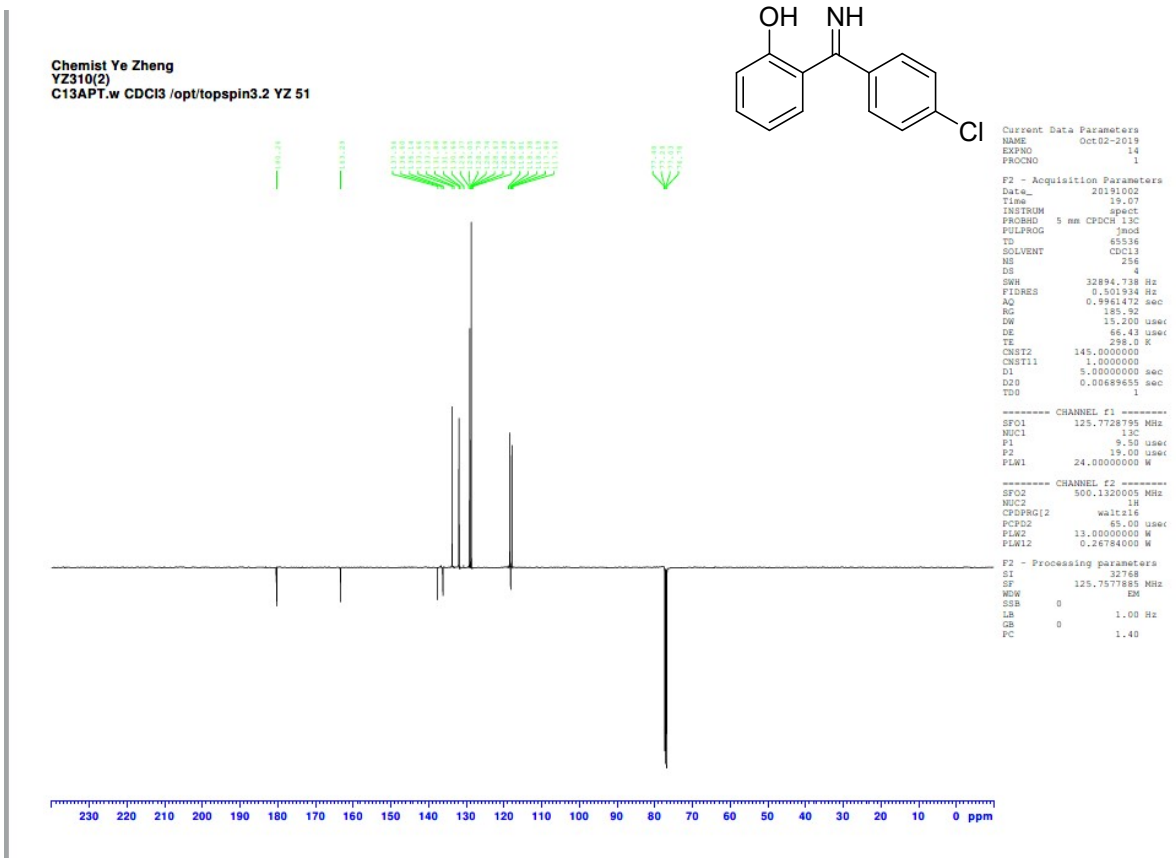
Reference: Nguyen, T. B.; Wang, Q.; Gueritte, F. *Chem.- Eur. J.* **2011**, *17*, 9576 – 9580.

(4-Chlorophenyl)(2-hydroxyphenyl)methanone (160 mg, 0.69 mmol) was dissolved in ammonia (1.68 mL, 7N in MeOH, 11.7 mmol) and the mixture was stirred under a nitrogen atmosphere overnight. The solvent was removed to give the product as a dark yellow oil (81.6 mg, 0.353 mmol, 51.2%). TLC: Rf ca 0.30 (4:1 hexane: EtOAc), strong UV and $KMnO_4$; δ_H (500 MHz, $CDCl_3$) 14.46 (1H, s, ArOH), 9.36 (1H, s, NH), 7.47 (2H, d, *J* = 8.4, ArH), 7.42-7.29 (3H, m, ArH), 7.14 (1H, dd, *J* = 8.0, 1.4, ArH), 7.05 (1H, t, *J* = 8.3, ArH), 6.75 (1H, t, *J* = 7.3, ArH) ppm; δ_C (125 MHz, $CDCl_3$) 180.3 (C), 163.3 (C), 137.6 (C), 136.1 (C), 133.7 (CH), 131.9 (CH), 129.1 (CH), 128.6 (CH), 118.4 (CH), 118.2 (C), 117.9 (CH) ppm. Data matched that reported.

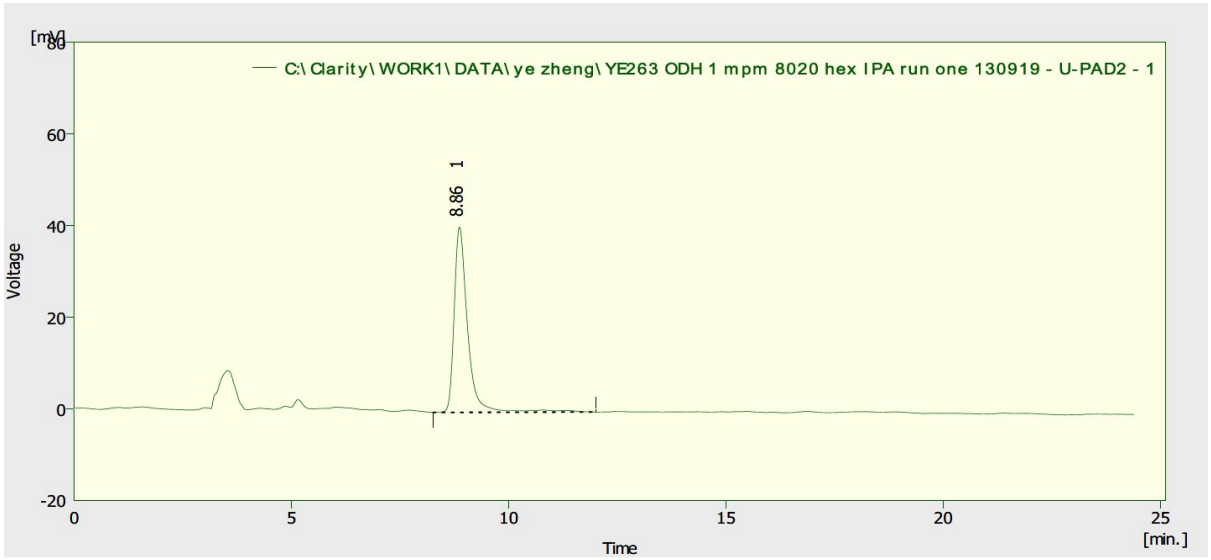
^{1}H NMR (500 MHz, $CDCl_3$) of 2-((4-Chlorophenyl)(imino)methyl)phenol.



^{13}C NMR (125 MHz, $CDCl_3$) of 2-((4-Chlorophenyl)(imino)methyl)phenol.



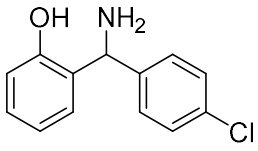
HPLC of 2-((4-chlorophenyl)(imino)methyl)phenol:

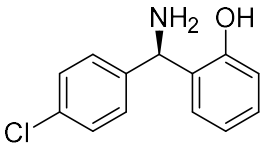


Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|ye zheng\|YE263 ODH 1 mpm 8020 hex IPA run one 130919 - U-PAD2 - 1)

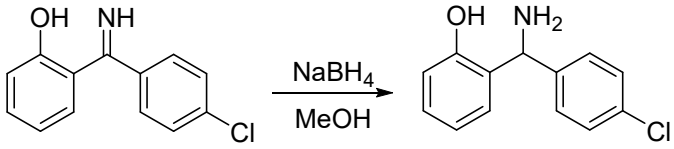
	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	8.864	880.094	40.502	100.0	100.0	0.30	
	Total	880.094	40.502	100.0	100.0		

2-(Amino(4-chlorophenyl)methyl)phenol 15.





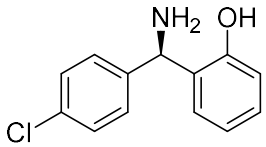
racemic: YZ265. Asymmetric: YZ312.



This compound has been reported and fully characterized.

Reference: Nguyen, T. B.; Wang, Q.; Gueritte, F. *Chem.- Eur. J.* **2011**, *17*, 9576 – 9580.

To a solution of 2-((4-chlorophenyl)(imino)methyl)phenol (81.6 mg, 0.353 mmol) in MeOH (1.6 mL) was added sodium borohydride (26.8 mg, 0.706 mmol). The reaction was stirred for 4 hours. TLC (99:1 DCM: MeOH) after this time indicated full conversion. Distilled water (20 mL) was added, and the mixture was extracted with EtOAc (3 × 20ml), dried with $MgSO_4$, and the solvent was removed under vacuum to give 2-(amino(4-chlorophenyl)methyl)phenol **15** as a yellow oil (74.7 mg, 0.321 mmol, 90.8%). TLC: Rf ca 0.20 (99:1 DCM: MeOH), strong UV and $KMnO_4$; δ_H (500 MHz, $CDCl_3$) 7.32 (4H, s, ArH), 7.19-7.11 (1H, m, ArH), 6.88 (1H, d, *J* = 8.0, ArH), 6.79-6.72 (2H, m, ArH), 5.30 (1H, s, Ar*CH*NH_2) ppm; δ_C (125 MHz, $CDCl_3$) 157.7 (C), 141.6 (C), 133.6 (C), 129.1 (CH), 128.4 (CH), 128.3 (CH), 125.8 (C), 119.3 (CH), 117. (CH), 59.5 (CH) ppm. Data matched that reported. Enantiomeric excess and conversion determined by HPLC analysis (Chiralcel ODH, 30 cm x 6mm column, hexane:iPrOH 80:20, 1.0 mL/min, T = 25°C) imine 8.86 min, *S* isomer 12.3 min and *R* isomer 15.3 min.

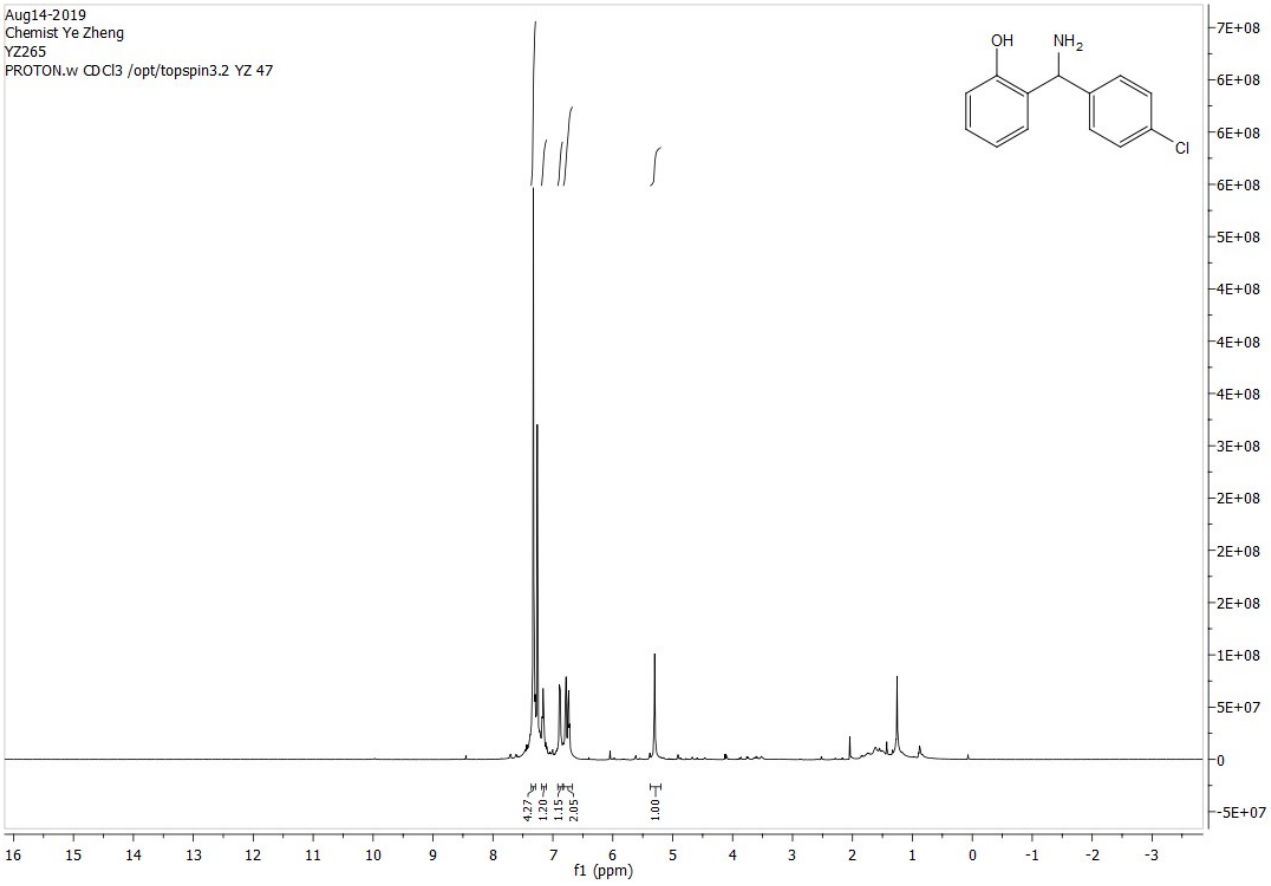


ATH of 2-((4-Chlorophenyl)(imino)methyl)phenol (YZ312) using (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst **2** (YZ312).

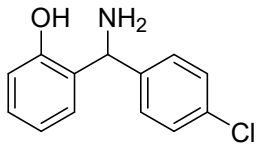
Ammonium formate (43.6 mg, 0.692 mmol) and (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst **2** (0.54 mg, 0.000865 mmol, 0.5 mol%) were added into a sealed tube and left to stir under a nitrogen atmosphere for 10 minutes. 2-((4-chlorophenyl)(imino)methyl)phenol (40 mg, 0.173 mmol) with DCM (0.87 mL) was degassed with nitrogen then added under nitrogen to the tube. The mixture was heated to 70 °C on a hot plate and stirred under a nitrogen atmosphere overnight. Then the reaction was quenched using saturated $NaHCO_3$ solution (20 mL). EtOAc (20 mL) was added and

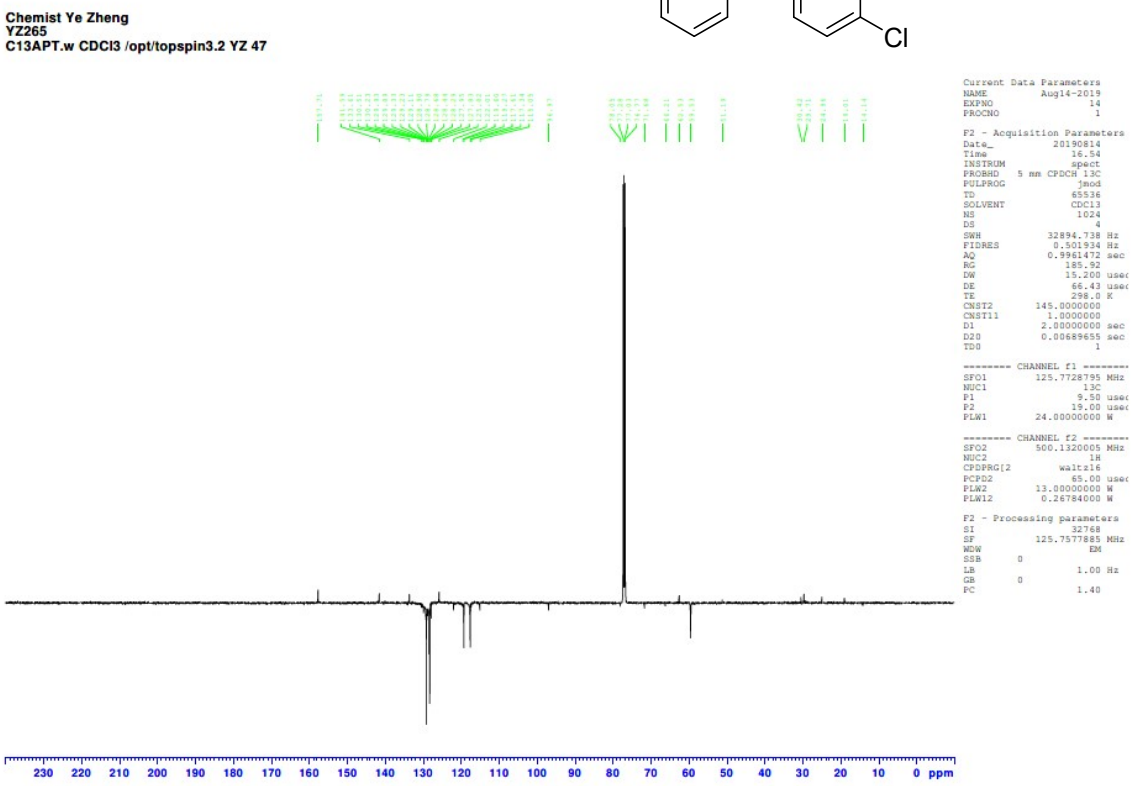
the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried ($MgSO_4$) and filtered. The solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to 2-(amino(4-chlorophenyl)methyl)phenol **15** (15.6 mg, 0.0670 mmol, 38.7%; (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst example). The reaction was also followed by HPLC analysis (Chiralcel ODH, 30 cm x 6mm column, hexane:iPrOH 80:20, 1.0 mL/min, T = 25°C); (*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst **2**: 78.7% conversion; $[\alpha]_D^{24}$ -20.4 (c 0.0147 in $CHCl_3$) 82.2% ee (*R*) (lit. $[\alpha]_D^{24}$ +99.1 (c 4.06 in $CHCl_3$) 93% ee (*S*)) Reference: Nguyen, T. B.; Wang, Q.; Gueritte, F. *Chem.- Eur. J*. **2011**, *17*, 9576 – 9580.

^1H NMR (500 MHz, $CDCl_3$) of **15**:

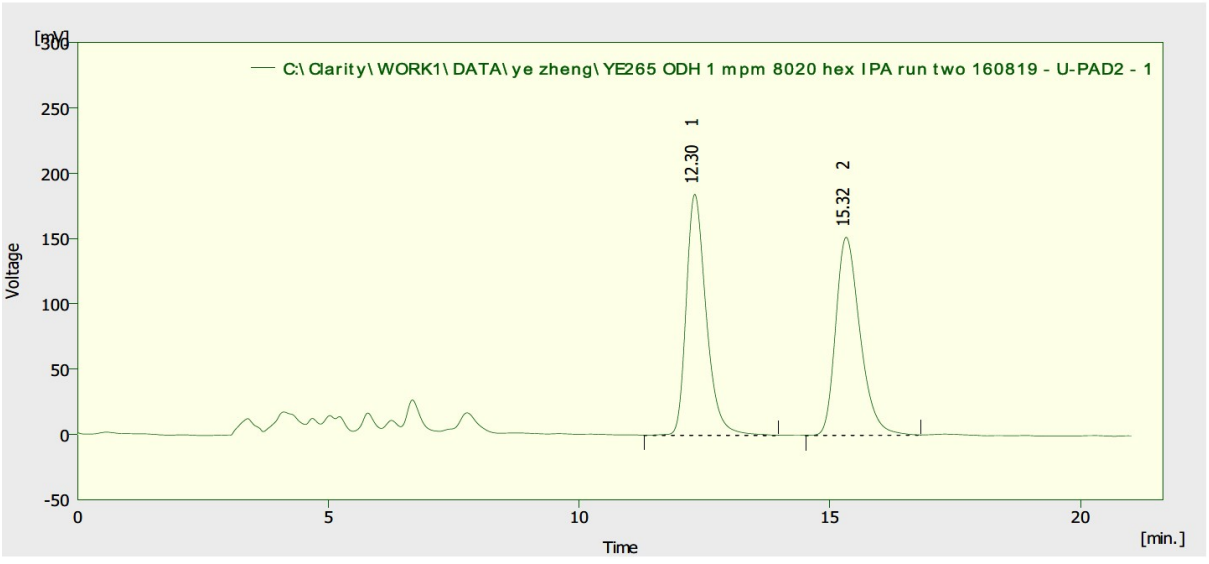


^{13}C NMR (125 MHz, $CDCl_3$) of **15**:





HPLC of racemic 2-(amino(4-chlorophenyl)methyl)phenol **15**:

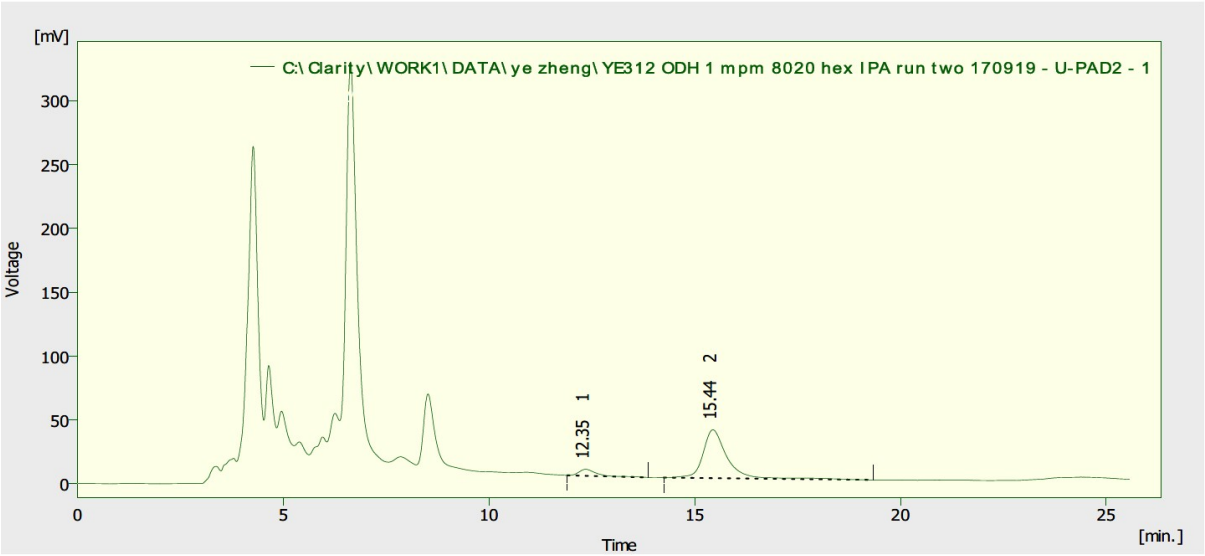


Result Table (Uncal - C:|Clarity|WORK1|DATA|ye zheng|YE265 ODH 1 mpm 8020 hex IPA run two 160819 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	12.304	5112.145	184.621	50.0	54.9	0.42	
2	15.324	5114.972	151.628	50.0	45.1	0.52	
	Total	10227.117	336.248	100.0	100.0		

HPLC after ATH of 2-((4-chlorophenyl)(imino)methyl)phenol:

(*R,R*)-3C-tethered Ru(II)-TsDPEN catalyst (after 24 hours, 78.7% conversion, 82.2% ee, *R* configuration).

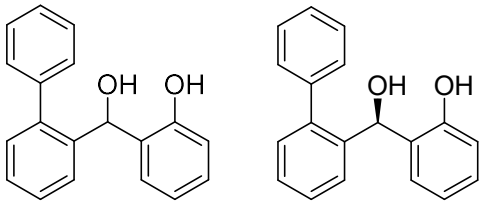


Result Table (Uncal - C:\Clarity\WORK1\DATA\ye zheng\YE312 ODH 1 mpm 8020 hex IPA run two 170919 - U-PAD2 - 1)

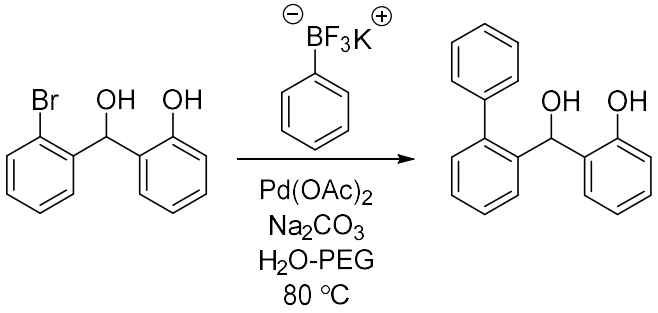
	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	12.348	152.312	5.152	8.9	12.0	0.41	
2	15.440	1561.333	37.915	91.1	88.0	0.55	
	Total	1713.645	43.066	100.0	100.0		

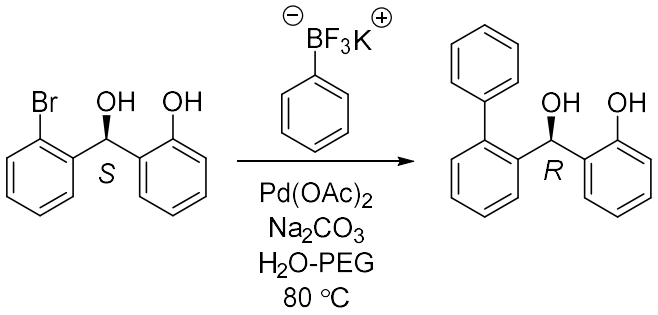
Synthesis and characterisation of reaction product 18.

2-([1,1'-Biphenyl]-2-yl(hydroxy)methyl)phenol 18.



racemic: YZ402, YZ406, Asymmetric: YZ418





This compound is novel.

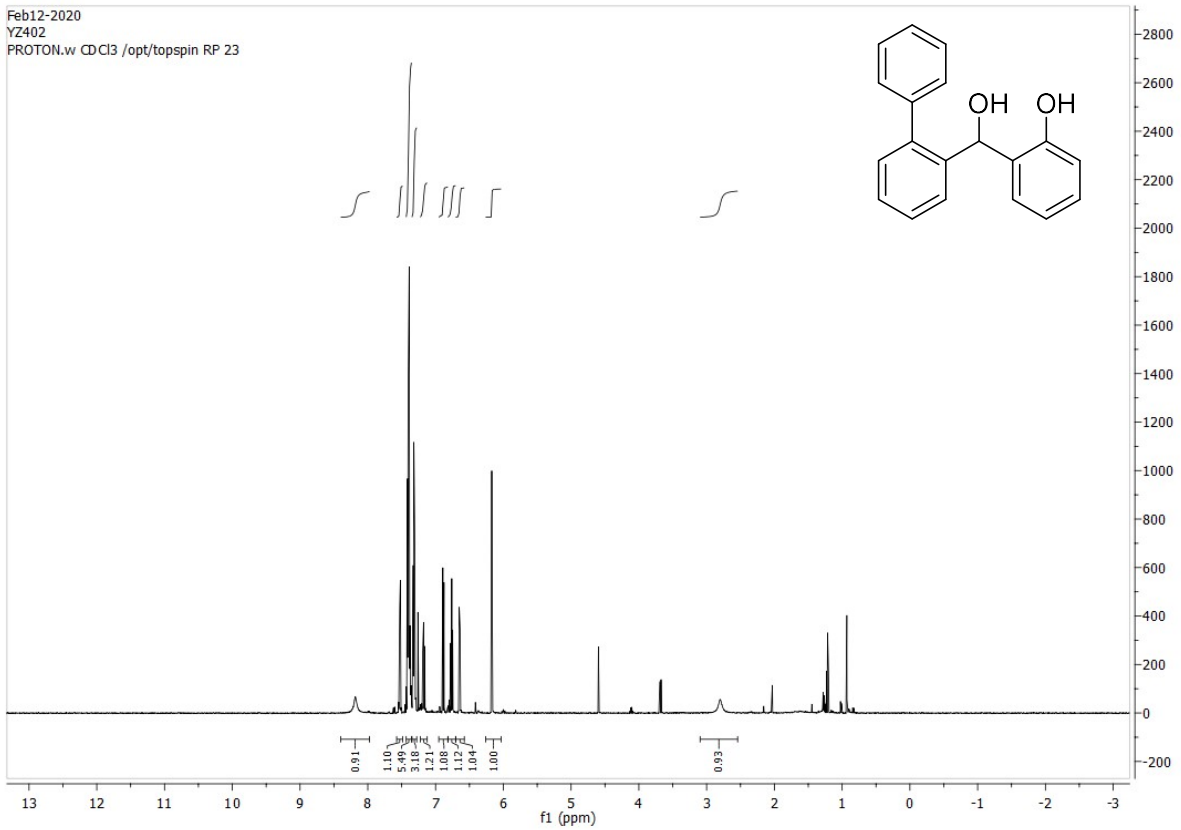
Racemic **18**: A round-bottom flask was charged with 2-((2-bromophenyl)(hydroxy)methyl)phenol **8h** (100 mg, 0.360 mmol), potassium phenyltrifluoroborate (79.5 mg, 0.720 mmol), sodium carbonate (76.3 mg, 0.720 mmol), $Pd(OAc)_2$ (1.62 mg, 0.00720 mmol) and H_2O-PEG (2.16:2.16 g). The reaction mixture was heated to 80 °C on a hot plate and left stirring under the nitrogen atmosphere overnight, followed by TLC (4:1 hexane: EtOAc). The mixture was quenched by distilled water (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 × 20 mL), and the combined organic layers were dried ($MgSO_4$) and filtered. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give 2-([1,1'-biphenyl]-2-yl(hydroxy)methyl)phenol **18** as a colorless oil (50.7 mg, 0.184 mmol, 51.1%). TLC: Rf ca 0.30 (4:1 hexane: EtOAc), strong UV and $KMnO_4$; HRMS: (found (ESI+): [M+Na]+, Calcd for $C_{19}H_{16}NaO_2$ 299.1044; Found 299.1043; -0.5 ppm error); ν_{max} 3298 (br), 3058, 3054, 1478, 1455, 1235, 994, 701 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 8.18 (1H, s, ArOH), 7.57-7.48 (1H, m, ArH), 7.43-7.36 (5H,

m, ArH), 7.35-7.28 (3H, m, ArH), 7.22-7.12 (1H, m, ArH), 6.89 (1H, dd, *J* = 8.1, 1.1, ArH), 6.76 (1H, td, *J* = 7.5, 1.2, ArH), 6.70-6.58 (1H, m, ArH), 6.17 (1H, s, Ar*CH*OH), 2.80 (1H, s, ArCH*OH*) ppm; δ_C (125 MHz, $CDCl_3$) 156.0 (C), 141.5 (C), 140.4 (C), 139.3 (C), 130.3 (CH), 129.3 (CH), 129.1 (CH), 128.5 (CH), 128.5 (CH), 128.3 (CH), 128.3 (CH), 128.2 (CH), 127.6 (CH), 126.6 (C), 119.8 (CH), 117.1 (CH), 73.2 (CH) ppm; m/z (ES-API+) 299.2 (M^+ + 23, 100%).

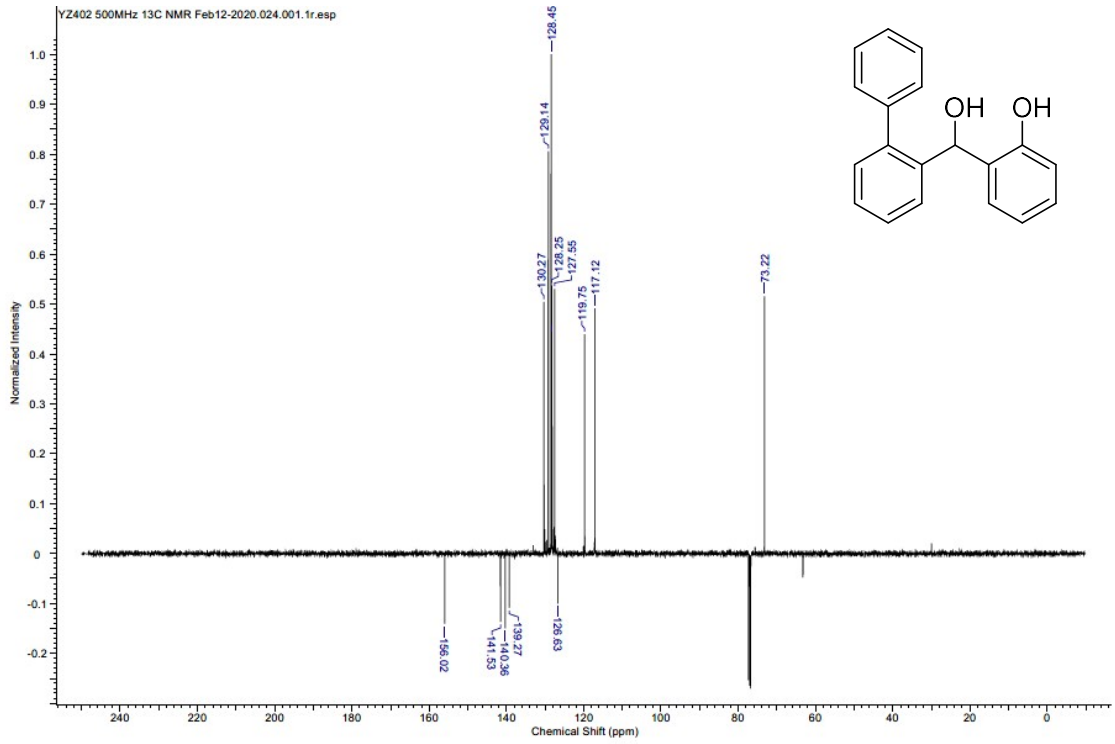
Enantiomeric excess and conversion determined by HPLC analysis (Chiralpak IC, 30 cm x 6mm column, hexane:iPrOH 95:5, 0.8 mL/min, T = 25°C) *R* isomer 16.4 min, *S* isomer 12.8 min.

Asymmetric 2-([1,1'-biphenyl]-2-yl(hydroxy)methyl)phenol **18** (YZ418): A round-bottom flask was charged with (*S*)-2-((2-bromophenyl)(hydroxy)methyl)phenol (286 mg, 1.03 mmol), potassium phenyltrifluoroborate (228 mg, 1.24 mmol), sodium carbonate (218 mg, 2.06 mmol), $Pd(OAc)_2$ (4.62 mg, 0.0206 mmol) and H_2O-PEG (6.18:6.18 g). The reaction mixture was heated to 80 °C on a hot plate and left stirring under the nitrogen atmosphere overnight, followed by TLC (4:1 hexane: EtOAc). The mixture was quenched by distilled water (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 × 20 mL), and the combined organic layers were dried ($MgSO_4$) and filtered. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give 2-([1,1'-biphenyl]-2-yl(hydroxy)methyl)phenol **18** as a colorless oil (147.6 mg, 0.535 mmol, 52%). HPLC analysis (Chiralpak IC, 30 cm x 6mm column, hexane:iPrOH 95:5, 0.8 mL/min, T = 25°C) indicated 96% ee (*R*).

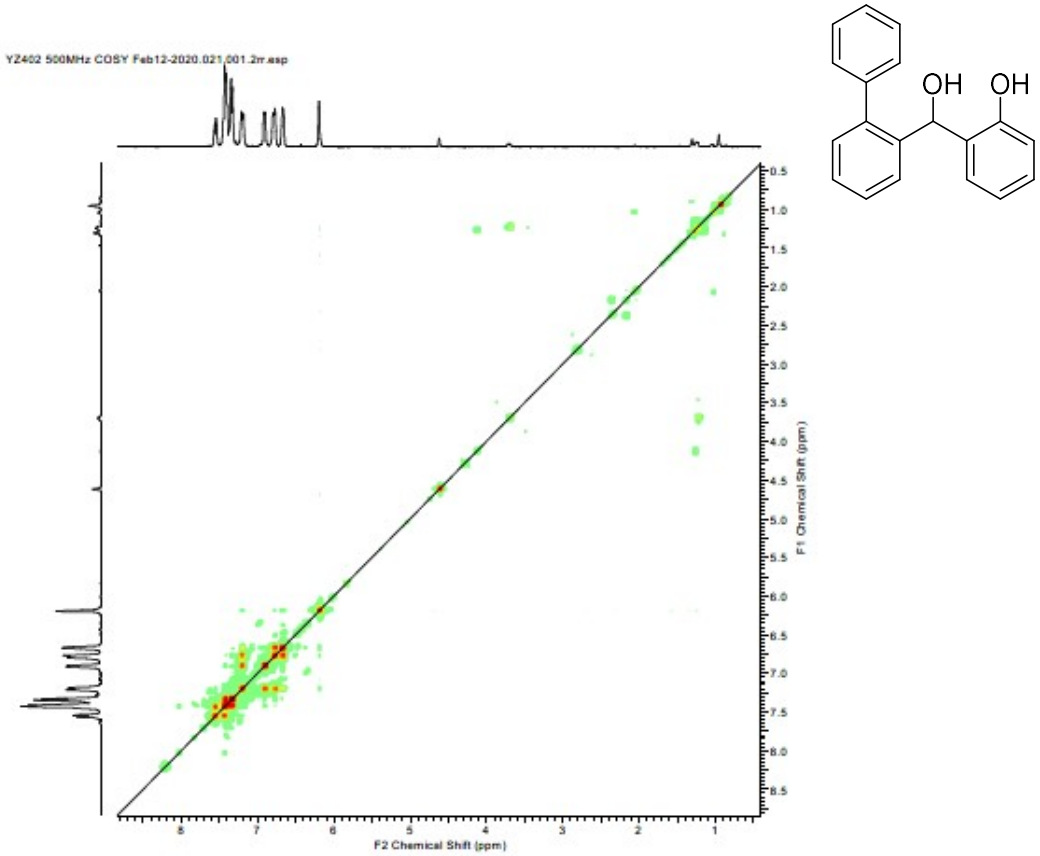
^{1}H NMR (500 MHz, $CDCl_3$) of **18**:



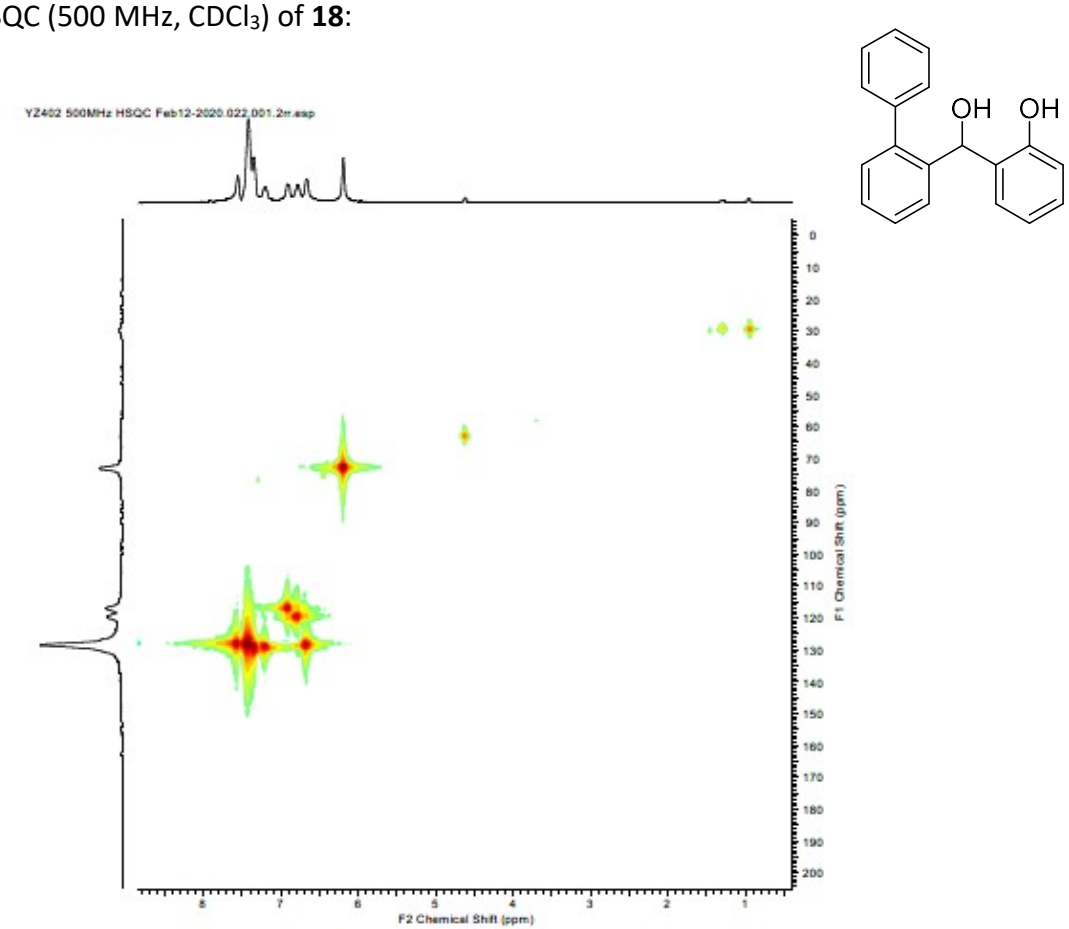
^{13}C NMR (125 MHz, $CDCl_3$) of **18**:



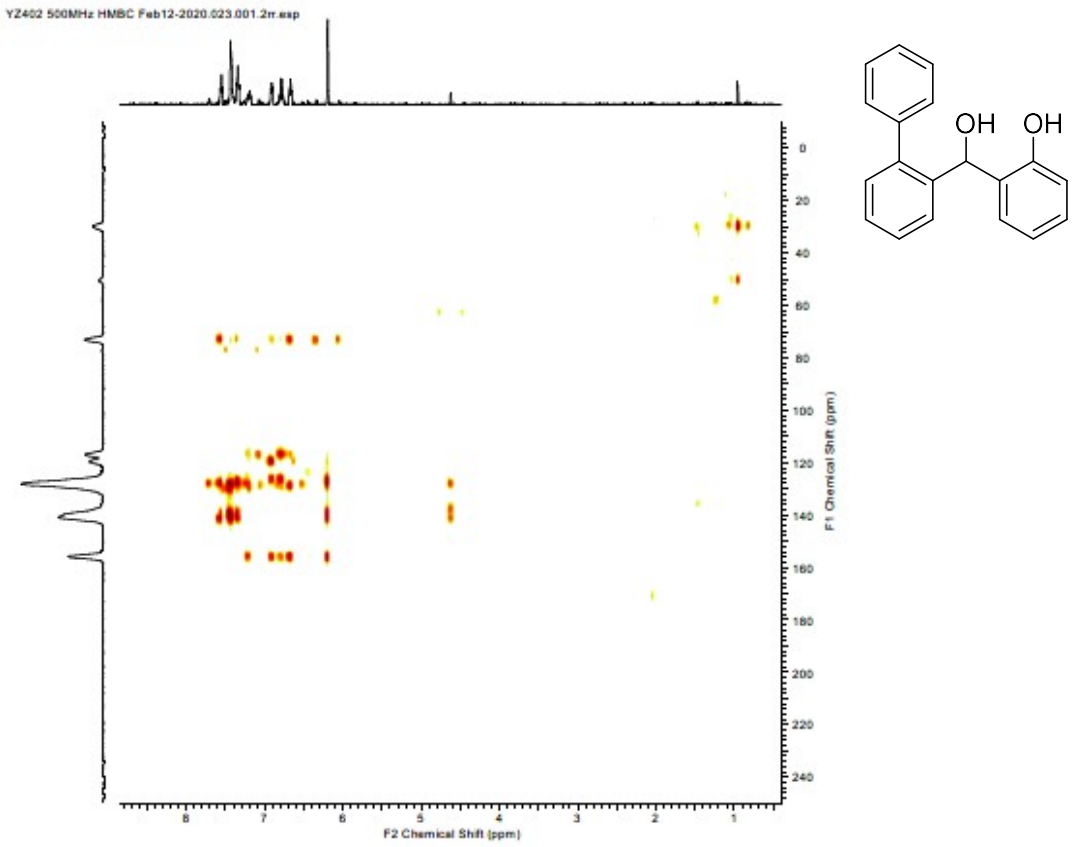
COSY (500 MHz, $CDCl_3$) of **18**:



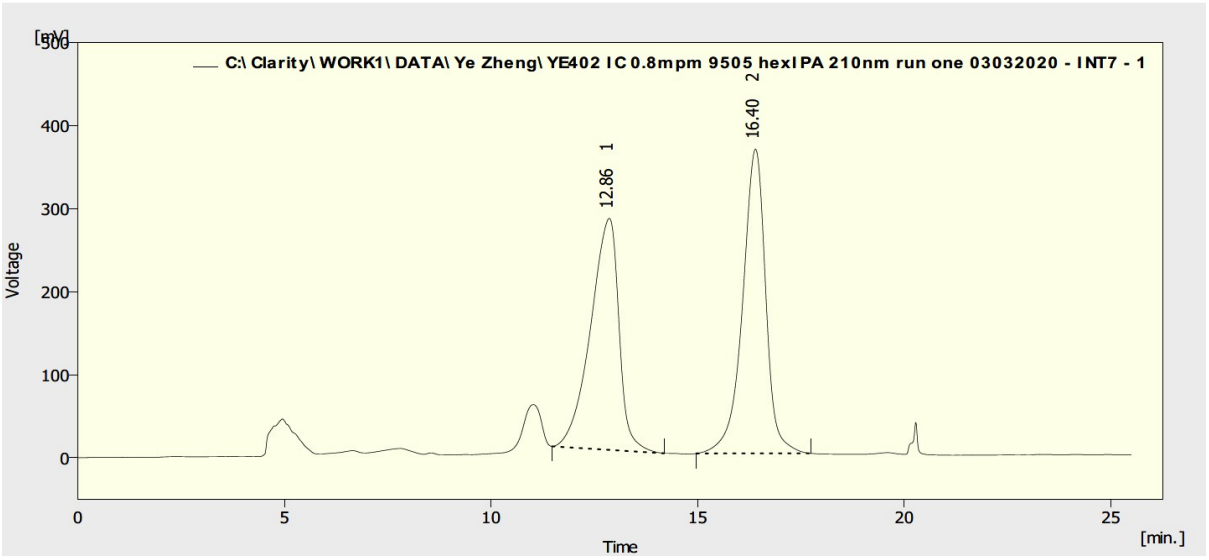
HSQC (500 MHz, $CDCl_3$) of **18**:



HMBC (500 MHz, $CDCl_3$) of **18**:



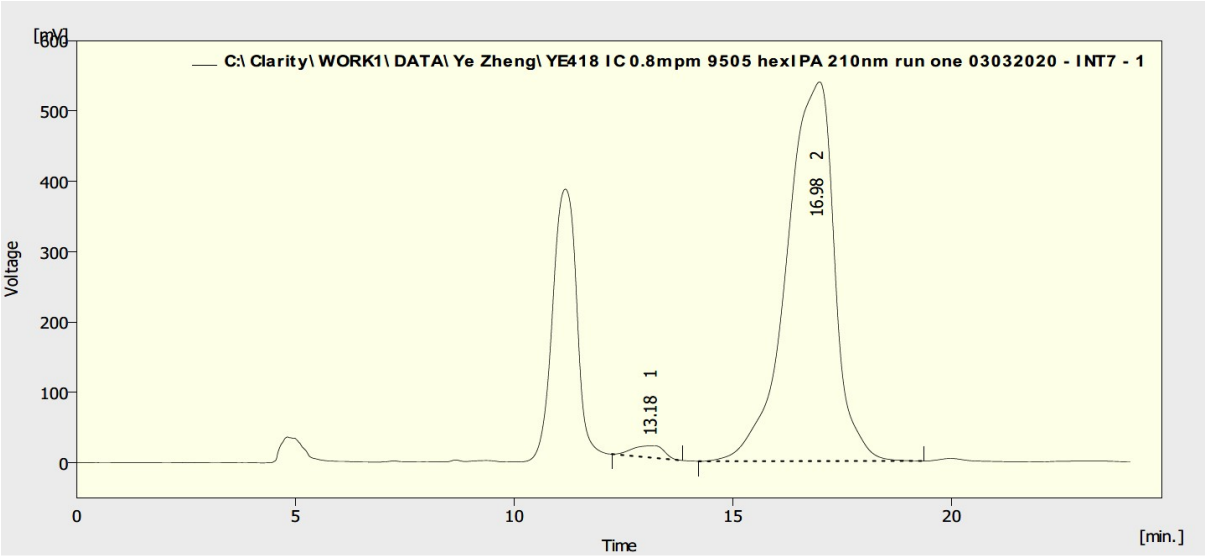
HPLC of racemic 2-([1,1'-biphenyl]-2-yl(hydroxy)methyl)phenol **18**:



Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|Ye Zheng\|YE402 IC 0.8mpm 9505 hexIPA 210nm run one 03032020 - INT7 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	12.860	13323.767	278.715	48.2	43.2	0.73	
2	16.397	14296.548	366.344	51.8	56.8	0.57	
	Total	27620.315	645.060	100.0	100.0		

HPLC of asymmetric 2-([1,1'-biphenyl]-2-yl(hydroxy)methyl)phenol (96% ee, *R* configuration) **18**:



Result Table (Uncal - C:\Clarity\WORK1\DATA\Ye Zheng\YE418 IC 0.8mpm 9505 hexIPA 210nm run one 03032020 - INT7 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	13.177	841.233	17.467	2.0	3.1	0.90	
2	16.983	41071.611	539.068	98.0	96.9	1.14	
	Total	41912.844	556.535	100.0	100.0		