Asymmetric Transfer Hydrogenation of 1,3- Alkoxy/Aryloxy Propanones Using Tethered Arene/Ru(II)/TsDPEN Complexes.

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Supporting information:

Additional Figures, Table and Schemes.

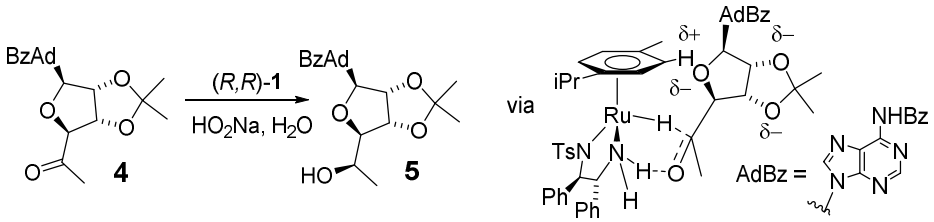


Figure S1; Catalyst-controlled diastereoselective reduction directed by multiple electrostatic alkoxide interactions with the η^6-arene. Reference: Bligh, C. M.; Anzalone, L.; Jung, Y. C.; Zhang, Y.; Nugent, W. A. *J. Org. Chem.* **2014**, *79*, 3238–3243.

Preparation of the ketones:

We prepared a series of ketone substrates (Scheme S1, Table S1) via the ring opening reactions of epoxides (which conveniently provided racemic samples for comparison) followed by an oxidation reaction. In some cases of ring-opening, the use of NaH in either the pure alcohol or a solution of it in an inert solvent gave good results. In other cases a catalysed ring-opening reaction was used with palladium dichloride acting as the catalyst along with TBAB and potassium carbonate in water (Seth, K.; Roy, S. R.; Pipaliya, B. V.; Chakraborti, A. K. *Chem. Commun.* **2013**, *49*, 5886-5888). In most cases the oxidation was achieved using a Swern oxidation but in the case of the chloro-substituted ketones, oxidation by PCC gave an improved result. The first series of substrates were designed to contain alkoxy groups opposed to para-substituted aryloxy groups (entries 1-11). A series of 2,6-dimethoxyphenoxy-containing substrates and ortho-tBocaminophenoxy substrates (entries 12-18) were also prepared in order to explore the effect of high levels of electron-density and sterically-hindered groups respectively. A final range of ortho-substituted aryloxy substrates, containing chloro, dimethylamino and alkoxy functionality were also prepared (entries 19-22).

Scheme S1; Preparation of ketone substrates.

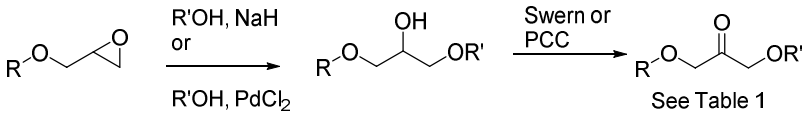
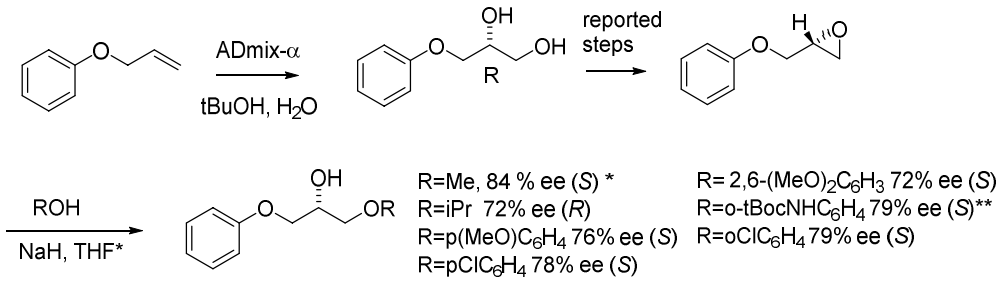


Table S1. Synthesis of ketones for asymmetric reduction studies.

Entry	R	R'	Epoxide opening Method	opening Yield/%	Oxidn method	Oxidn Yield/%	$\Delta\delta$ OCH_2 /ppm
1	Ph	Me	NaH	72	Swern	41	0.40
2	Ph	nBu	NaH	64	Swern	69	0.45
3	Ph	iPr	NaH	65	Swern	68	0.48
4	iPr	$p(MeO)C_6H_4$	$PdCl_2$	70	Swern	77	0.44
5	Ph	Di OMe ether	NaH	14	Swern	73	0.28
6	Ph	Allyl	NaH	100	Swern	67	0.41
7	$p(MeO)C_6H_4$	Allyl	NaH	58	Swern	32	0.36
8	Ph	$p(MeO)C_6H_4$	$PdCl_2$	46	Swern	48	0.04
9	Ph	$pClC_6H_4$	$PdCl_2$	61	PCC	39	0.06
10	Ph	$p\text{-}tBocNHC_6H_4$	$PdCl_2$	93	Swern	19	0.02
11	$p(MeO)C_6H_4$	$p\text{-}ClC_6H_4$	$PdCl_2$	75	PCC	23	0.09
12	iPr	$2,6\text{-}(MeO)_2C_6H_3$	$PdCl_2$	73	Swern	62	0.003
13	Ph	$2,6\text{-}(MeO)_2C_6H_3$	$PdCl_2$	36	Swern	63	0.51
14	$p(MeO)C_6H_4$	$2,6\text{-}(MeO)_2C_6H_3$	$PdCl_2$	57	Swern	62	0.47
15	iPr	$o\text{-}NHBocC_6H_4$	$PdCl_2$	84	Swern	84	0.74
16	Ph	$o\text{-}NHBocC_6H_4$	$PdCl_2$	91	Swern	76	0.28
17	$p(MeO)C_6H_4$	$o\text{-}NHBocC_6H_4$	$PdCl_2$	80	Swern	21	0.32
18	$2,6\text{-}(MeO)_2C_6H_3$	$o\text{-}NHBocC_6H_4$	$PdCl_2$	61	Swern	80	0.72
19	iPr	$o\text{-}ClC_6H_4$	$PdCl_2$	51	PCC	8	0.40
20	Ph	$o\text{-}ClC_6H_4$	$PdCl_2$	97	PCC	15	0.12
21	Ph	$o\text{-}(NMe_2)C_6H_4$	$PdCl_2$	38	Swern	42	0.03
22	Ph	$2,3\text{-}(MeO)_2C_6H_3$	$PdCl_2$	76	Swern	64	0.01
23	Ph	C_6F_5	$PdCl_2$	34	Swern	80	0.37
24	Ph	$p(CF_3)C_6H_4$	$PdCl_2$	40	Swern	81	0.15
25	Ph	$m(CF_3)C_6H_4$	$PdCl_2$	41	Swern	88	0.12
26	Ph	$o(CF_3)C_6H_4$	$PdCl_2$	27	Swern	82	0.17

Absolute configuration standards.

The absolute configuration of the OPh/OMe and OPh/OiPr reduction products were determined by comparison with authentic samples prepared following a published synthetic method by Sharpless *et al.* (Scheme S2; ADmix-α was used to prepare all except the OPh/OMe standard, for which ADmix-β was used). Full details are in the experimental section. References: 1) Wang, Z.-M.; Zhang, X.-L.; Sharpless, K. B. *Tetrahedron Lett.* **1993**, *14*, 2267-2270. 2) Kolb, H. C.; Sharpless, K. B. *Tetrahedron* **1992**, *48*, 10515-10530.



* For R=Me, the (*S*)-configuration alcohol was prepared using ADMix-β in the fist step.
** NHtBoc product prepared using $PdCl_2$ - catalysed ring opening.

Scheme S2. Synthesis of asymmetric standards for absolute configuration determination. Variations in the e.e.s of the products likely reflect some racemisation during the ring-opening.

Speculated 2,6-dimethoxyphenol resonance:

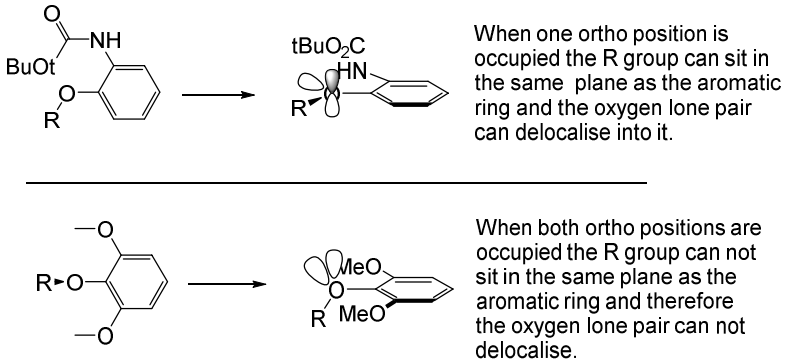


Figure S2. Two ortho-substituents reduce resonance into the adjacent aromatic ring.

Experimental Section.

General Experimental Methods

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, potassium permanganate or vanillin dips as appropriate. Flash column chromatography was carried out routinely on silica gel. Reagents were used as received from commercial sources unless otherwise stated. Dry solvents were purchased and used as received. ^{1}H NMR spectra were recorded on a Bruker DPX (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. Mass spectra for analysis of synthetic products were recorded on a Bruker Esquire2000 or a Bruker MicroTOF mass spectrometer. Coupling constants (J) are measured in Hertz. IR spectra were recorded on a Perkin-Elmer Spectrum One FT-IR Golden Gate. Melting points were recorded on a Stuart Scientific SMP 1 instrument and are uncorrected.

The general procedures below apply to the first two ketones and alcohols.

Ring opening of phenyl glycidyl ether

To alcohol (reagent and solvent in excess, 20 mL per 1 g of epoxide) sodium hydride (1.5 eq) was added and the mixture was stirred at room temperature for 30 minutes to allow deprotonation. Phenyl glycidyl ether (1 eq) was then added and allowed to react for at least 2 hours at room temperature. The reaction was quenched with ammonium chloride (10 mL per 1g of epoxide). Ethyl acetate (20 mL) and water (10 mL) were added to allow clear separation into two layers. The organic layer was extracted using ethyl acetate (3 x 10 mL) and water (10 mL) and was dried using sodium sulfate, filtered and concentrated *in vacuo* to give the alcohol.

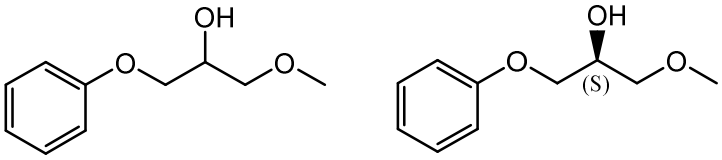
Swern oxidation

To oxalyl chloride (2 eq, 2 M solution in DCM) further DCM (20 mL per 1 g of alcohol) was added and the mixture cooled to -78°C. Dimethyl sulfoxide (4 eq) was dissolved in DCM (10 mL per 1 g of alcohol) and the mixture was stirred for 15 minutes. Reagent alcohol (1 eq) was added and the mixture was stirred for a further 15 minutes. Triethylamine (7 eq) was added and the solution was allowed to warm up to room temperature, and then stirred for at least another 30 minutes. The reaction was quenched with water (20 mL per 1 g of alcohol) and the organic layer was extracted with DCM (3 x 10 mL) and water (10 mL). The organic phase was dried using magnesium sulfate, filtered and concentrated *in vacuo* to give the ketone.

Reduction using catalyst (*R,R*)-2.

To solvent FA/TEA (1 mL per 200 mg of ketone, 2 M solution) catalyst [(*R,R*)Teth-TsDpen RuCl] (0.5 mol%) was added and stirred at room temperature for 20 minutes. Ketone (1 eq) was added and stirred for at least another 2 hours. Ethyl acetate (10 mL) was added to dissolve the product, which was then purified through silica with further ethyl acetate which removed any remaining FA/TEA. The product was concentrated *in vacuo* to give the alcohol.

1. 1-Methoxy-3-phenoxypropan-2-ol 4.



This compound has been reported and fully characterised.

Jungen, M.; Gais, H.-J. *Tetrahedron: Asymmetry*, **1999**, *10*, 3747-3758.

Ring opening method to produce 1-methoxy-3-phenoxypropan-2-ol: Phenyl glycidyl ether (1 g, 6.7 mmol, 1 eq), methanol (20 mL), sodium hydride (400 mg, 10 mmol, 1.5 eq) gave 1-methoxy-3-phenoxypropan-2-ol as a colourless oil (868 mg, 4.8 mmol, 71.5%).

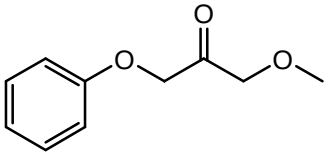
Reduction of 1-methoxy-3-phenoxypropan-2-one to produce (*S*) 1-methoxy-3-phenoxypropan-2-ol: 1-methoxy-3-phenoxypropan-2-one (90 mg, 0.5 mmol, 1 eq), FA/TEA (0.5 mL), [(*R*,*R*)Teth-TsDpen RuCl] (~2 mg, 0.5 mol%) after purification over silica gave alcohol (*S*) 1-methoxy-3-phenoxypropan-2-ol as a colourless oil (44 mg, 0.24 mmol, 48.4%).

$[\alpha]_D^{28}$ = -1.3° (c = 0.6, $CHCl_3$) 30.0% ee (S), lit.[1] $[\alpha]_D^{22}$ = -0.7° (c = 1.21, $CHCl_3$) 90% ee (S); ν_{max} = 3419, 2926, 2981, 1598, 1496, 1243, 1078, 752, 691 cm^{-1}; δ_H (300MHz, $CDCl_3$) 7.27 (2H, t, *J* 8.0, ArH) 6.95 (1H, t, *J* 7.6, ArH) 6.90 (2H, d, *J* 8.0, ArH) 4.20 – 4.10 (1H, m, *J* 4.9, CH) 4.05 – 3.95 (2H, m, *J* 5.4, CH_2) 3.55 (2H, sep, *J* 6.2, CH_2) 3.40 (1H, s, O-CH_3) 2.53 (1H, d, *J* 5.4, OH); δ_C (75MHz, $CDCl_3$) 164.6, 128.9, 120.5, 113.9, 72.9, 68.4, 58.7; m/z (ESI) 205.0 ($[M+Na]^+$, 100%).

1) Jungen, M.; Gais, H.-J. *Tetrahedron: Asymmetry*, **1999**, *10*, 3747-3758.

Enantiomeric excess determined by HPLC analysis (CHIRALPAK IA column, hexane 90:10 ^{i}PrOH, 1ml/min, T = 30°C, λ = 256 nm, *R* 7.98 min, *S* 9.44 min).

1. 1-Methoxy-3-phenoxypropan-2-one.



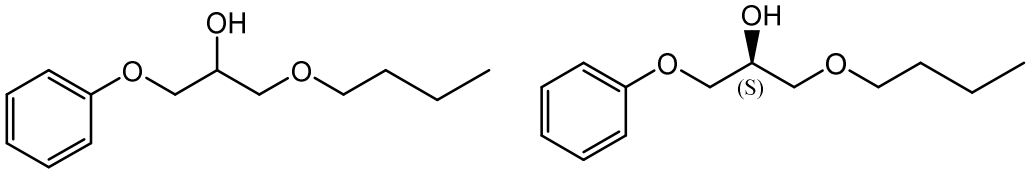
This compound has been reported but is not fully characterised.

Jeyakumar, K.; Chand, D. K. *Synthesis*, **2008**, 807-819.

Swern oxidation of 1-methoxy-3-phenoxypropan-2-ol to give 1-methoxy-3-phenoxypropan-2-one: 1-methoxy-3-phenoxypropan-2-ol (546 mg, 3 mmol, 1 eq), dimethyl sulfoxide (0.9 mL, 12 mmol, 4 eq), oxalyl chloride (3.5 mL, 6 mmol, 2 eq), triethylamine (3.5 mL, 21 mmol, 7 eq), DCM (30 mL) after recrystallization in boiling hexane gave 1-methoxy-3-phenoxypropan-2-one as a white solid (220 mg, 1.2 mmol, 40.7%).

MP = 51°C; (Found (ESI) $[M + Na]^+$ 203.0683, $C_{10}H_{12}NaO_3$ requires [M + Na] 203.0679); ν_{max} = 2944, 2894, 2819, 1731, 1450, 1246, 1083, 754, 687 cm^{-1}; δ_H (300MHz, $CDCl_3$) 7.29 (2H, t, *J* 8.1, ArH) 6.99 (1H, t, *J* 7.2, ArH) 6.88 (2H, d, *J* 8.6, ArH) 4.72 (2H, s, CH_2) 4.32 (2H, s, CH_2) 3.44 (3H, s, CH_3); δ_C (75MHz, $CDCl_3$) 164.7, 129.7, 121.9, 114.5, 76.2, 71.6, 59.6; m/z (ESI) 203.0 ($[M+Na]^+$, 24%).

2. 1-^{n}Butoxy-3-phenoxypropan-2-ol 5.



This compound has been reported but is not fully characterised.

Hofricht, G.; Hampel, H.; Liehn, H. D.; Ludwig, E. *ARZNEIMITTEL-FORSCHUNG/DRUG RESEARCH*, **1974**, *24*, 111.

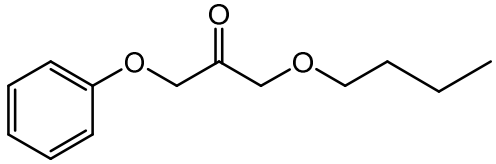
Ring opening method to 1-nbutoxy-3-phenoxypropan-2-ol: Phenyl glycidyl ether (1 g, 6.7 mmol, 1 eq), sodium hydride (400 mg, 5 mmol, 1.5 eq), ^{n}butan-1-ol (20ml) gave 1-nbutoxy-3-phenoxypropan-2-olas a colourless oil (950 mg, 4.2 mmol, 63.6%).

Reduction of 1-nbutoxy-3-phenoxypropan-2-one to produce (*S*) 1-nbutoxy-3-phenoxypropan-2-ol: 1-nbutoxy-3-phenoxypropan-2-one (100 mg, 0.45 mmol, 1 eq), FA/TEA (0.5 mL), catalyst [(*R,R*)Teth-TsDpen RuCl] (~2 mg, 0.5 mol%), purification through silica gave alcohol (*S*) 1-nbutoxy-3-phenoxypropan-2-ol as a colourless oil (30 mg, 0.13 mmol, 29.7%).

$[\alpha]_D^{28}$ = -0.8° (c = 0.5, $CHCl_3$) 40.7% ee (S); (Found (ESI) $[M + Na]^+$ 247.1305, $C_{13}H_{20}NaO_3$ requires [M + Na] 247.1305); ν_{max} 3422, 2957, 2931, 2869, 1599, 1495, 1242, 1112, 1041, 751, 690 cm^{-1}; δ_H (300MHz, $CDCl_3$) 7.27 (2H, t, *J* 8.0, ArH) 6.94 (1H, t, *J* 7.3, ArH) 6.90 (2H, d, *J* 7.8, ArH) 4.15 (1H, sex, *J* 5.0, CH) 4.06 – 3.96 (2H, m, *J* 5.4, CH_2) 3.63 – 3.51 (2H, m, *J* 5.0, CH_2) 3.48 (2H, t, *J* 6.8, O-CH_2-C_3H_7) 2.53 (1H, d, *J* 5.0, OH) 1.56 (2H, quin, *J* 8.4, OCH_2-CH_2-C_2H_5) 1.35 (2H, sex, *J* 8.0, OC_2H_4-CH_2-CH_3) 0.90 (3H, t, *J* 7.2, OC_3H_6-CH_3); δ_C (75MHz, $CDCl_3$) 129.6, 121.1, 114.6, 71.5, 69.1, 68.9, 31.7, 19.3, 13.9; m/z (ESI) 247.1 ($[M+Na)^+$, 100%).

Enantiomeric excess determined by HPLC analysis (CHIRALPAK IA column, hexane 98:2 ^{i}PrOH, 1ml/min, T = 30°C, λ = 256 nm, *R* 11.42 min, *S* 14.34 min).

2. 1-^{n}Butoxy-3-phenoxypropan-2-one.



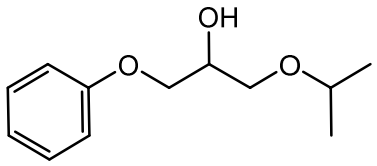
This compound is novel.

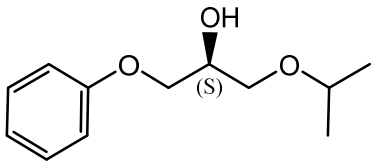
Swern oxidation of 1-nbutoxy-3-phenoxypropan-2-ol to 1-nbutoxy-3-phenoxypropan-2-one: 1-nbutoxy-3-phenoxypropan-2-ol (222 mg, 1 mmol, 1 eq), dimethyl sulfoxide (0.3 mL, 4 mmol, 4 eq), oxalyl chloride (1 mL, 2 mmol, 2 eq), triethylamine (1 mL, 2 mmol, 7 eq) DCM (20 mL), purification on silica column using gradient of ethyl acetate: pet ether gave 1-nbutoxy-3-phenoxypropan-2-one as a colourless oil (153 mg, 0.7 eq, 68.9%).

(Found (ESI) $[M + Na]^+$ 245.1140, $C_{13}H_{18}NaO_3$ requires [M + Na] 245.1148); ν_{max} = 2958, 2933, 2871, 1739, 1599, 1494, 1244, 1113, 751, 690 cm^{-1}; δ_H (300MHz, $CDCl_3$) 7.28 (2H, t, *J* 7.8, ArH) 6.98 (1H, t, *J* 7.5, ArH) 6.88 (2H, d, *J* 8.0, ArH) 4.76 (2H, s, CH_2) 4.31 (2H, s, CH_2) 3.51 (2H, t, *J* 6.6, O-CH_2-C_3H_7) 1.60 (2H, quin, *J* 7.9, OCH_2-CH_2-C_2H_5) 1.39 (2H, sex, *J* 7.4, OC_2H_4-CH_2-CH_3) 0.92 (3H, t, *J* 7.9, OC_3H_6-CH_3); δ_C (75MHz, $CDCl_3$) 129.0, 121.2, 113.9, 74.1, 71.3, 70.9, 30.9, 18.6, 13.3; m/z (ESI) 245.1 ($[M+Na]^+$, 66%).

From this point, individual experimental procedures are given.

3. 1-Isopropoxy-3-phenoxypropan-2-ol 6.





This compound is novel

Epoxide ring opening

To NaH, 60 % in oil, (79.2 mg, 1.98 mmol, 1.5 eq) isopropanol (4 mL) was added under nitrogen. The mixture was stirred for 30 min. Phenyl glycidyl ether (0.18 mL, 200 mg, 1.34 mmol, 1 eq) was then added dropwise. The mixture was then stirred at rt for 12 h. Water (4 mL) was added to quench the reaction mixture and the product was extracted using EtOAc (3 x 10 mL). The combined organic layers were dried over Na_2SO_4 and concentrated under vacuum. The resultant crude product was then purified by flash chromatography using a graduated EtOAc/hexane eluent (0 – 20% EtOAc in Hexane) to yield the pure product as a colourless oil (181.1 mg, 0.86 mmol, 65%).

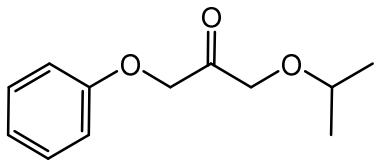
ATH using [(*R*,*R*)Teth-TsDpen RuCl]

To a 5:2 formic acid/trimethylamine azeotrope (0.5 mL), [(*R*,*R*)-Teth-TsDpen RuCl] (2.2 mg, 3.5 µmol, 0.75 mol %) was added and the mixture was stirred for 20 min. 1-Isopropoxy-3-phenoxypropan-2-one (108.5 mg, 0.52 mmol, 1 eq) was then added and the mixture was stirred for 12 h at rt. A saturated solution of $NaHCO_3$ (2 mL) and Et_2O were added to the stirring mixture. The organic layer was removed and the aqueous layer was further extracted with Et_2O. The combined organic layers were then dried over Na_2SO_4 and concentrated. The crude product was then purified through flash chromatography, removing traces of catalyst and yielding the product as a colourless oil (80.9 mg, 0.38 mmol, 80.2%).

$[\alpha]_D^{28}$ -2.0° (*c* 0.5 in $CDCl_3$) 39 % ee (S); (Found (ESI) $[M + Na]^+$ 233.1148, $C_{12}H_{18}NaO_3$ requires 233.1148); ν_{max} 3436, 2971, 2928, 2871, 1598, 1495, 1242 and 751 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.24 - 7.31 (2H, m, Ar**H**), 6.89 - 6.99 (3H, m, Ar**H**), 4.13 (1H, quin, *J* = 4.9 Hz, HOC**H**), 3.97 – 4.06(2H, m, ArOC**H₂**), 3.59 – 3.67 (2H, m, COHC**H₂**O), 3.51 – 3.58 (3H, m, C**H₂**OC**H**$(CH_3)_2$), 2.66 (1H, br. s, O**H**), 1.17 (6H, d, *J* = 6.1 Hz, (C**H₃**$)_2$); δ_C (100 MHz, $CDCl_3$) 158.60, 129.42, 120.98, 114.54, 72.30, 69.21, 68.91, 68.83 and 22.01; *m/z* (EI) 233 ($[M+Na]^+$.

Enantiomeric excess determined by HPLC analysis (Chiralpak IB, 0.46 cm ϕ x 25 cm, iPrOH:hexane 1:9, 1 mL/min, T = 30 °C, 254 nm) *R minor* isomer 6.2 min, *S major* isomer 9.6 min.

3. 1-Isopropoxy-3-phenoxypropan-2-one.



This compound is novel.

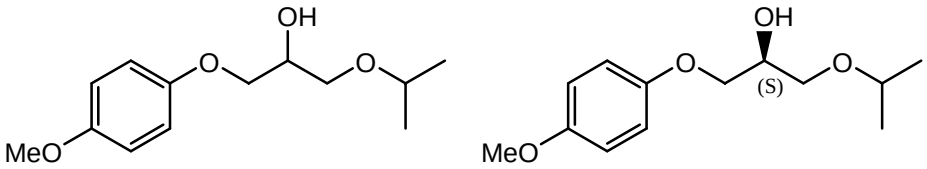
Swern Oxidation

A 2M solution of oxalyl chloride in DCM (1.9 mL, 3.8 mmol, 2 eq) was further diluted with DCM (10mL) and cooled to -78 °C. Anhydrous DMSO (593 mg, 0.54mL, 7.6 mmol, 4 eq) was then added dropwise and the mixture stirred for 20 min. The alcohol, 1-isopropoxy-3-phenoxypropan-2-ol (400 mg, 13.3 mmol, 1 eq), was then added and the mixture was stirred for another 20 min. TEA (1.34 g, 1.85 mL, 13.3 mmol, 7 eq) was then added dropwise and the mixture was stirred for 12 h. The reaction was then quenched with water (10 mL) and the product was extracted using DCM (3 x 5 mL). the combined organic layers were then dried over Na_2SO_4 and concentrated under vacuum to yield crude product, which was subsequently purified by flash column chromatography using a

graduated EtOAc/hexane eluent (0 – 20% EtOAc in Hexane) to yield pure ketone product as a colourless oil (271.1 mg, 1.30 mol, 68%).

ν_{max} 2972, 2929, 1738, 1598, 1494, 1244, 1099, 751 and 690 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.22 - 7.35 (2H, m, Ar***H***), 7.00 (1H, t, *J* = 7.3 Hz, Ar***H***), 6.90 (2H, d, *J* = 7.9 Hz, Ar***H***), 4.79 (2H, s, C***H₂***), 4.31 (2H, s, C***H₂***), 3.66 (1H, sept, *J* = 6.1 Hz, CH_3CHCH_3), 1.16 - 1.26 (6H, d, *J* = 6.2 Hz, $CH(CH_3)_2$); ^{13}C NMR (100 MHz, $CDCl_3$) 204.76, 157.72, 129.60, 121.71, 114.55, 72.97, 72.28, 71.53 and 21.76; *m/z* (ESI) 207.1 $[M-H]^-$.

4. 1-Isopropoxy-3-(4-methoxyphenoxy)propan-2-ol 7.



This compound is novel

Epoxide ring opening

A solution of $PdCl_2$ (7.6 mg, 43 µmol, 0.01 eq), TBAB (345 mg, 1.07 mmol, 0.25 eq) and K_2CO_3 (148 mg, 1.07 mmol, 0.25 eq) in H_2O (16 mL) was heated to 60 °C. To the mixture isopropyl glycidyl ether (500 mg, 4.31 mmol, 1 eq) and 4-methoxyphenol (587 mg, 4.74 mmol, 1 eq) were added and the mixture was stirred at 60 °C for 24 hrs. The product was then extracted using EtOAc (3 x 20 mL) and the combined organic layers were dried over Na_2SO_4 before being concentrated under vacuum. The crude product was then purified by flash column chromatography using a graduated eluent mixture of EtOAc in Hexane (0 - 25 %) to yield the pure product as a colourless oil (723 mg, 3.01 mmol, 70 %).

ATH using [(*R*,*R*)Teth-TsDpen RuCl]

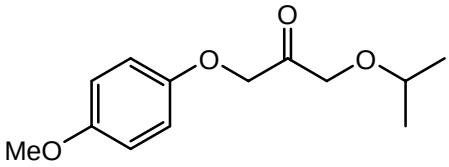
To a solution of [(*R*,*R*) Teth-TsDpen RuCl] (1.3 mg, 1 µmol, 0.005 eq) in 5:2 formic acid/triethylamine azeotrope (1.5 mL) the ketone, 1-isopropoxy-3-(4-methoxyphenoxy)propan-2-one (100 mg, 0.42 mmol, 1 eq), was added and the reaction was then stirred overnight. The reaction mixture was then diluted with Et_2O and quenched with $NaHCO_3$ until basic. The product was then extracted with Et_2O (3 x 5 mL) and the combined organic layers were dried over Na_2SO_4 before being concentrated under vacuum to give the crude product. The crude was then purified by flash column chromatography to yield the product as a colourless oil (58.8 mg, 0.25 mmol, 59 %).

$[\alpha]_D^{24}$ -0.604 (*c* 0.53 in $CDCl_3$) 27 % ee (*S*); (found (ESI): $[M+Na]^+$, 263.1257. $C_{13}H_{20}NaO_4$ requires 263.1254); ν_{max} 3442, 2971, 2931, 2871, 2834, 1506, 1461, 1227, 1036, 822 and 746 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 6.80 - 6.91 (4H, m, Ar***H***), 4.09 - 4.17 (1H, m, HOC***H***), 3.95 - 4.03 (2H, m, C***H₂***), 3.75 - 3.81 (3H, m, OC***H₃***), 3.52 - 3.69 (3H, m, C***H***+C***H₂***), 2.74 (1H, d, *J* = 4.7 Hz, O***H***), 1.19 (6H, d, *J* = 6.1 Hz,

($C\boldsymbol{H_3}$)$_2$); δ_C (126 MHz, $CDCl_3$) 154.0, 152.8, 115.6, 114.6, 72.3, 69.8, 69.3, 68.9, 55.7, 22.0; *m/z* (ESI)263 ([M+Na]$^+$, 80 %).

Enantiomeric excess determined by HPLC analysis (Chiralpak IB, 0.46 cm ϕ x 25 cm, iPrOH:hexane 1:9, 1 mL/min, T = 30 ^{o}C, 254 nm) *R minor* isomer 7.1 min, *S major* isomer 8.7 min.

4. 1-Isopropoxy-3-(4-methoxyphenoxy)propan-2-one.



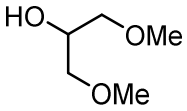
This compound is novel

Swern Oxidation

A 2M solution of oxalyl chloride in DCM (1.6 mL, 3.2 mmol, 2 eq) was further diluted with DCM (10 mL) and cooled to -78 ^{o}C. Anhydrous DMSO (499 mg, 0.45 mL, 6.4 mmol, 4 eq) was then added dropwise and the mixture stirred for 20 mins. The alcohol 1-isopropoxy-3-(4-methoxyphenoxy)propan-2-ol (400 mg, 1.6 mmol, 1 eq) was then added and the mixture was stirred for another 20 mins. TEA (1.13 g, 1.6 mL, 11 mmol, 7 eq) was then added dropwise and the mixture was stirred for 24 hrs. The reaction was then quenched with water (10 mL) and the product was extracted using DCM (3 x 20 mL). The combined organic layers were then dried over Na_2SO_4 and concentrated under vacuum to yield crude product, which was subsequently purified by flash column chromatography using a graduated eluent mixture of EtOAc in Hexane (0 - 20 %) to yield pure ketone product as a colourless oil (315 mg, 1.32 mmol, 77 %).

(found (ESI): [M-H]$^-$, 237.1129. $C_{13}H_{17}O_4$ requires 237.1132); ν_{max} 2972, 2932, 2835, 1737, 1505, 1231, 1215, 1101, 1032, 823 and 747 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 6.76 - 6.90 (4H, m, Ar***H***), 4.74 (2H, s, C$\boldsymbol{H_2}$), 4.30 (2H, s, C$\boldsymbol{H_2}$), 3.76 (3H, d, *J* = 0.3 Hz, OC$\boldsymbol{H_3}$), 3.65 (1H, spt, *J* = 6.0 Hz, C***H***), 1.21 (6H, d, *J* = 6.1 Hz, ($C\boldsymbol{H_3}$)$_2$); δ_C (126 MHz, $CDCl_3$) 205.1, 154.5, 152.0, 115.7, 114.7, 73.0, 72.5, 72.3, 55.7, 21.8; *m/z* (ESI) 237 ([M-H]$^-$, 100 %).

1,3-Dimethoxypropan-2-ol.

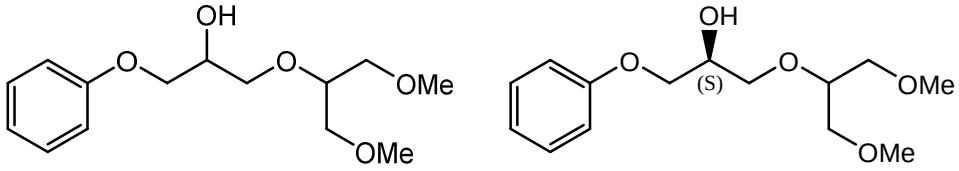


This compound is known and fully characterized.

García, J. I.; García-Marín, H.; Mayoral, J. A.; Pérez, P. *Green. Chem*, **2010**, *12*, 426-434.

To a round bottom flask which contained neat MeOH (5 mL), NaH 60 % in oil (956 mg, 24 mmol, 2.2 eq) was added in portions and stirred for 30 minutes at room temperature. Epichlorohydrin (1 g, 0.85 mL, 10.8 mmol, 1 eq) was then added and the mixture refluxed at 70 °C for 24 hrs. The mixture went from a colourless solution to cloudy white. Reaction was cooled to room temperature and water was added to quench the reaction. The remaining methanol was removed under vacuum and the crude product was extracted with EtOAc (3 x 25 mL). The combined organic layers were then dried over Na_2SO_4 and concentrated under vacuum. The crude product was then purified by flash column chromatography to yield the pure product as a colourless oil (783 mg, 6.64 mmol, 62%). ν_{max} 3422, 2984, 2925, 2892, 2821, 1644, 1452, 1329, 1227, 1102, 1079, 967 and 854 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 3.91 - 4.01 (1H, m, C***H***), 3.44 - 3.50 (3H, m, C***H₂***), 3.40 - 3.44 (2H, m, C***H₂***), 3.39 (6H, s, (C***H₃***)$_2$), 2.80 (1H, br. s., O***H***); δ_C (75 MHz, $CDCl_3$) 73.8, 69.2, 59.1; *m/z* (ESI) 143 ([M+Na]$^+$, 30 %).

5. 1-((1,3-Dimethoxypropan-2-yl)oxy)-3-phenoxypropan-2-ol 8.



This compound is novel

Epoxide ring opening

To a solution of 1,3-dimethoxypropan-2-ol (200 mg, 1.67 mmol, 1 eq) in THF (5 mL), NaH 60% in oil (80 mg, 2.00 mmol, 1.2 eq) was added and the mixture was stirred for 30 mins. Phenyl glycidyl ether (275 mg, 0.25 mL, 1.83 mmol, 1.1 eq) was then added to the stirring solution, and the mixture was refluxed at 70 °C for 2 hrs. The mixture was cooled to room temperature and the reaction was quenched with water. THF was then removed under vacuum and the product was extracted using Et_2O (3 x 30 mL). The combined organic extracts were then dried over Na_2SO_4 and concentrated under vacuum. The crude product was then purified by flash column chromatography using a graduated eluent mixture of EtOAc in Hexane (0 - 50 %) to yield the pure product as a colourless oil (65.3 mg, 0.24 mmol, 14 %).

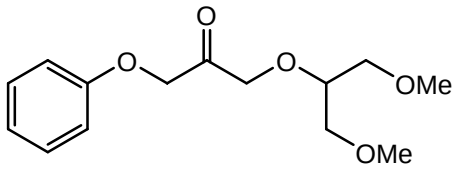
ATH using [(*R*,*R*)Teth-TsDpen RuCl]

To a solution of [(*R*,*R*) Teth-TsDpen RuCl] (1.7 mg, 1.5 µmol, 0.01 eq) in 5:2 formic acid/triethylamine azeotrope (0.5 mL) the ketone, 1-((1,3-dimethoxypropan-2-yl)oxy)-3-phenoxypropan-2-one (40 mg, 0.15 mmol, 1 eq), was added and the reaction was then stirred overnight. The reaction mixture was then diluted with Et_2O and quenched with a saturated solution of $NaHCO_3$ until basic. The product was then extracted with Et_2O (3 x 10 mL) and the combined organic layers were dried over Na_2SO_4

before being concentrated under vacuum to give the crude product. The crude was then purified by flash column chromatography to yield the product as a colourless oil (24 mg, 0.09 mmol, 59 %). $[\alpha]_D^{29}$ -1.7 ° (*c* 0.39 in $CDCl_3$) 46% ee (S); (found (ESI): $[M+Na]^+$, 293.1362. $C_{14}H_{22}NaO_5$ requires 293.1359); ν_{max} 3445, 3061, 2924, 2876, 1598, 1493, 1240, 1079, 1037, 751 and 690 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.27 (2H, t, *J* = 8.0 Hz, Ar***H***), 6.93 (3H, s, Ar***H***), 4.11 - 4.19 (1H, m, C***H***), 3.97 - 4.05 (2H, m, C***H₂***), 3.86 (1H, dd, *J* = 10.8 Hz, *J* = 3.7 Hz, CH_a***H_b***), 3.70 - 3.80 (3H, m, HOC***H***+CH_b***H_a***+O***H***), 3.42 - 3.49 (4H, m, (C***H₂***)$_2$), 3.37 (5H, s, (OC***H₃***)$_2$); δ_C (126 MHz, $CDCl_3$)158.7, 129.4, 120.9, 114.6, 79.2, 73.0, 72.9, 72.4, 69.4, 68.6, 59.3, 59.2; *m/z* (ESI) 293 ($[M+Na]^+$, 45 %).

Enantiomeric excess determined by HPLC analysis (Chiralpak IB, 0.46 cm ϕ x 25 cm, EtOAc:hexane 2:8, 1 mL/min, T = 30 °C, 254 nm) *R minor* isomer 12.6 min, *S major* isomer 16.5 min.

5. 1-((1,3-Dimethoxypropan-2-yl)oxy)-3-phenoxypropan-2-one.



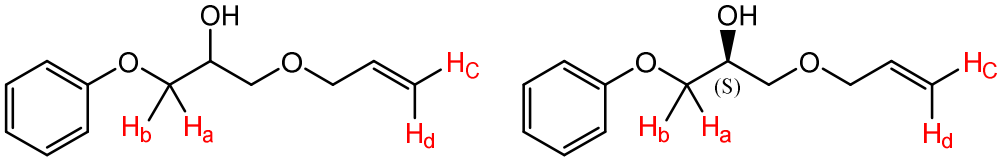
This compound is novel.

Swern oxidation

A 2M solution of oxalyl chloride in DCM (0.22 mL, 0.44 mmol, 2 eq) was further diluted with DCM (2.5 mL) and cooled to -78 °C. Anhydrous DMSO (68 mg, 0.06 mL, 0.88 mmol, 4 eq) was then added dropwise and the mixture stirred for 20 mins. The alcohol, 1-((1,3-dimethoxypropan-2-yl)oxy)-3-phenoxypropan-2-ol (60.5 mg, 0.22 mmol, 1 eq) was then added and the mixture was stirred for another 20 mins. TEA (155 mg, 0.22 mL, 1.54 mmol, 7 eq) was then added dropwise and the mixture was stirred for 12 hrs. The reaction was then quenched with water (10 mL) and the product was extracted using DCM (3 x 5 mL). The combined organic layers were then dried over Na_2SO_4 and concentrated under vacuum to yield crude product, which was subsequently purified by flash column chromatography using a graduated eluent mixture of EtOAc in Hexane (20 - 80 %) to yield pure ketone product as a colourless oil (43.1 mg, 0.16 mmol, 73 %).

(found(ESI): $[M+Na]^+$, 291.1202. $C_{14}H_{20}NaO_5$ requires 291.1203); ν_{max} 2893, 2814, 1738, 1598, 1494, 1244, 1100, 962, 752 and 690 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.27 - 7.34 (2H, m, Ar***H***), 6.99 (1H, t, *J* = 7.3 Hz, Ar***H***), 6.86 - 6.93 (2H, m, Ar***H***), 4.82 (2H, s, C***H₂***), 4.54 (2H, s, C***H₂***), 3.73 (1H, quin, *J* = 5.1 Hz, C***H***), 3.51 (4H, d, *J* = 5.0 Hz, (C***H₂***)$_2$), 3.33 - 3.37 (6H, m, (OC***H₃***)$_2$); δ_C (126 MHz, $CDCl_3$) 204.7, 157.8, 129.6, 121.7, 114.6, 79.2, 74.8, 73.1, 71.6, 59.2; *m/z* (ESI) 291 ($[M+Na]^+$, 65 %).

6. 1-(Allyloxy)-3-phenoxypropan-2-ol 9.



This compound is known and fully characterised.

Smith, T. C.; Li, H.; Clouthier, D. J. *J. Am. Chem. Soc*, **1999**, *121*, 6068-6087.

Epoxide ring opening

To allylic alcohol (2.26 mL, 33.3 mmol, 5 eq), sodium hydride (60% in oil, 399 mg, 9.99 mmol , 1.5 eq) was added and the mixture stirred for 30 minutes at room temperature. Phenyl glycidyl ether (0.90 mL, 6.66 mmol, 1 eq) was added and the reaction mixture was left stirring at room temperature overnight. Reaction completion was confirmed by TLC analysis. Saturated ammonium chloride solution (10 mL) was then used to quench the reaction. The product was then extracted from the biphasic mixture using ethyl acetate (30 mL) and washed with water (3 x 20 mL). The organic product was dried over magnesium sulphate and concentrated under vacuum and was isolated as a yellow oil (1.36 g, 6.60 mmol, 99.7 %).

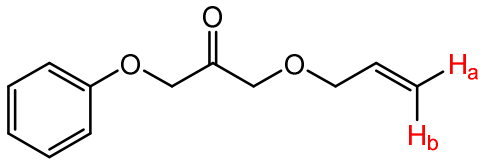
ATH using [(R,R)Teth-TsDpen RuCl]

1-(Allyloxy)-3-phenoxypropan-2-one (100 mg, 0.5 mmol, 1 eq) was added to a 10 mL RBF. To this, 5:2 formic acid/triethylamine azeoptrope (1.0 mL) was added, followed by the [(R,R)Teth-TsDpen RuCl] catalyst (3 mg, 24.3 µmol, 0.005 eq), and the reaction mixture was stirred at room temperature for 24 hrs. The reaction was diluted with Et_2O (2 mL) and quenched with saturated $NaHCO_3$ solution until basic. The product was then extracted using diethyl ether (3 x 20 mL) and the combined organic layers were dried over Na_2SO_4, before being concentrated under vacuum to yield the crude product. The crude product was then purified by flash column chromatography using hexane / ethyl acetate eluent (90:10 ratio) to give the pure product as a pale yellow oil (78.6 mg, 0.35 mmol, 70 %). $[\alpha]_D^{28}$ +27.3 ° (*c* 0.18 in MeOH) 37 % ee (*S*) (lit[1] $[\alpha]_D$ -3.0 ° (*c* 0.56 in MeOH) (*R*); ν_{max} 3436, 3068, 2924, 2868, 1597, 1494, 1241, 1078, 1040, 926 and 751 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.21 - 7.35 (2H, m, Ar***H***), 6.86 - 7.01 (3H, m, Ar***H***), 5.91 (1H, ddt, *J* = 17.3 Hz, 10.4 Hz, 5.7 Hz, ***H***CCH_cH_d), 5.29 (1H, dq, *J* = 17.2 Hz, 1.6 Hz, $HCCH_d$***H*****$_c$**), 5.20 (1H, dq, *J* = 10.4 Hz, 1.4 Hz, $HCCH_c$***H*****$_d$**), 4.13 - 4.25 (1H, m, HOC***H***), 3.98 - 4.09 (4H, m, H_2CCHC***H*****$_2$**), 3.65 (1H, dd, *J* = 9.6 Hz, 4.5 Hz, $PHOCH_b$***H*****$_a$**), 3.59 (1H, dd, *J* = 9.8 Hz, 5.8 Hz, $PhOCH_a$***H*****$_b$**), 2.61 (1H, d, *J* = 4.3 Hz, O***H***); δ_C (126 MHz, $CDCl_3$) 158.6, 134.4, 129.5, 121.1, 117.4, 114.6, 72.4, 71.0, 69.2, 68.9; *m/z* (ESI) 231 ($[M+Na]^+$, 35 %).

Enantiomeric excess determines by HPLC analysis (Chiralcel OD 0.46cm x 25cm, EtOH:Hexane 1:9, 1ml/min, 30 °C 210nm) *R minor* isomer 7.1 min, *S major* isomer 9.6 min.

1) Collington, E. W.; Finch, H.; Montana, J. G.; Taylor, R. J. K. *J. Chem. Soc. Perkin. Trans. 1,* **1990**, 1839-1846.

6. 1-(Allyloxy)-3-phenoxypropan-2-one.



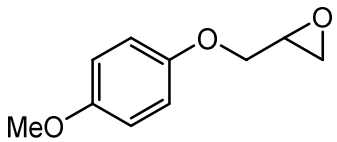
This compound is novel

Swern oxidation

To DCM (10ml), anhydrous oxalyl chloride (2.91 mL, 5.83 mmol, 2 eq) was added. This mixture was cooled to -78 °C . Anhydrous DMSO (0.83 mL, 913 mg, 11.7 mmol, 4 eq) was then added to the mixture and stirred for 20 minutes. A solution of 1-(allyloxy)-3-phenoxypropan-2-ol (598 mg, 2.90 mmol, 1 eq) in DCM (5 mL), was added to the reaction mixture, which was then left stirring for another 30 minutes. TEA (2.85 mL, 2.06 g 20.4 mmol, 7 eq) was added dropwise, and the reaction was left stirring overnight. Water (15 mL) was used to quench the reaction, and DCM (4 x 10 mL) was used to extract the product. The combined organic layers were then dried over sodium sulphate and concentrated under vacuum to give a dark yellow/brown oil as the crude product. The crude product was then purified by flash column chromatography with a gradient of EtOAc : Hexane to yield the product as a pale yellow oil (395.5 mg, 2.0 mmol, 66.6 %).

(found (ESI): $[M+Na]^+$, 229.0833. $C_{12}H_{14}NaO_3$ requires 229.0835); ν_{max} 3064, 2895, 1737, 1646, 1493, 1243, 1219, 1101, 927 and 751 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.27 - 7.34 (2H, m, Ar***H***), 7.01 (1H, t, *J* = 7.3 Hz, Ar***H***), 6.90 (2H, d, *J* = 7.8 Hz, Ar***H***), 5.92 (1H, ddt, *J* = 17.1 Hz, 10.5 Hz, 5.8 Hz, ***H***CCH_aH_b), 5.31 (1H, dd, *J* = 17.5 Hz, 1.5 Hz, $CHCH_b$***H_a***), 5.26 (1H, dd, *J* = 10.4 Hz, 1.1 Hz, $CHCH_a$***H_b***), 4.77 (2H, s, C***H_2***), 4.36 (2H, s, C***H_2***), 4.09 (2H, d, *J* = 5.8 Hz, CHC***H_2***); δ_C (126 MHz, $CDCl_3$) 204.3, 157.7, 133.6, 129.7, 121.9, 118.4, 114.6, 73.6, 72.6, 71.6; *m/z* (ESI) 229 ($[M+Na]^+$, 25 %).

2-((4-Methoxyphenoxy)methyl)oxirane.



This compound is known and fully characterized.

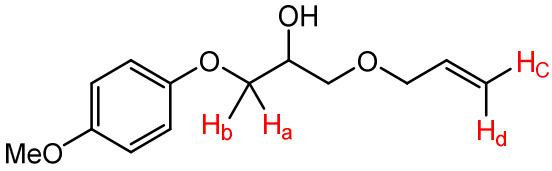
Byun , H.-S.;Sadlofsky, J. A.; Bittman, R. *J. Org. Chem*, **1998**, *63*, 2560-2563.

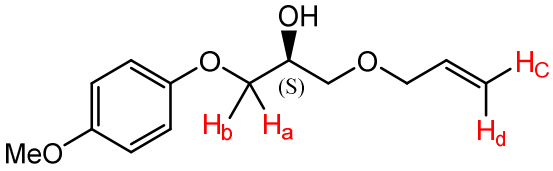
A solution of 4- methoxyphenol (520.9 mg, 4.2 mmol, 1 eq) and potassium carbonate (1.19 g, 8.4 mmol, 2 eq) in CH_3CN (10 mL) was heated under reflux at 70 °C. To the solution epichlorohydrin

(0.95 mL, 1.11 mg, 12. 1 mmol, 3 eq) was added and the mixture was stirred at 70 °C for 24 hrs. The reaction mixture was cooled to room temperature and the potassium carbonate removed by filtration. The resulting solution was then concentrated under vacuum to give the crude product, which was the purified by flash column chromatography using a graduated eluent mixture of EtOAc in Hexane (0 - 15 %) to give the pure product as a white solid (334 mg, 1.9 mmol, 46 %).

Mp 49.0 – 50.8 °C; ν_{max} 3017, 2956, 2932, 2878, 2836 1504, 1220, 1034, 822 and 733 cm $^{-1}$; δ_H (400 MHz, $CDCl_3$) 6.81 - 6.94 (4H, m, Ar***H***), 4.19 (1H, dd, *J* = 11.0 Hz, *J* = 3.2 Hz, OC***H***H), 3.94 (1H, dd, *J* = 11.1 Hz, *J* = 5.6 Hz, OCH***H***), 3.79 (3H, s, OC***H₃***), 3.32 - 3.40 (1H, m, CH_2C***H***O), 2.92 (1H, t, *J* = 4.5 Hz, CHOC***H***H), 2.77 (1H, dd, *J* = 5.0 Hz, *J* = 2.6 Hz, CHOCH***H***); δ_C (100 MHz, $CDCl_3$) 154.21, 152.68, 115.75, 114.67, 69.55, 55.71, 50.27 and 44.74; *m/z* (ESI) 203 ([M + Na]$^+$, 40 %) 242 ([M + Na + K]$^+$, 100 %).

7. 1-(Allyloxy)-3-(4-methoxyphenoxy)propan-2-ol 10.





This compound is novel

Epoxide ring opening

To allylic alcohol (0.94 mL, 13.9 mmol, 5 eq), sodium hydride (60% in oil, 166 mg, 4.16 mmol , 1.5 eq) was added and the mixture stirred for 30 minutes at room temperature 2-((4-methoxyphenoxy)methyl)oxirane (500 mg, 2.77 mmol, 1 eq) was added to the reaction mixture along with THF (2 mL), to aid solubility of the oxirane, and was stirred at room temperature overnight. Reaction completion was confirmed by TLC analysis. Water (10 mL) was then used to quench the reaction. The product was then extracted from the biphasic mixture using Et_2O (3 x 20 mL) The organic product was dried over magnesium sulphate and concentrated under vacuum and was isolated as a orange oil (382.4 mg, 1.60 mmol, 58 %).

ATH using [(R,R)Teth-TsDpen RuCl]

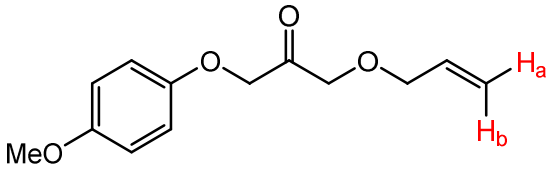
1-(Allyloxy)-3-(4-methoxyphenoxy)propan-2-one (100 mg, 0.42 mmol, 1 eq) was added to a 10ml RBF. To this, 5:2 formic acid/triethylamine azeotrope (1.0 mL) was added, followed by the [(R,R)Teth-TsDpen RuCl] catalyst (3.2 mg, 2.12 µmol, 0.005 eq), and the reaction mixture was stirred at room temperature for 24 hrs. The reaction was diluted with Et_2O (2 mL) and quenched with saturated $NaHCO_3$ solution until basic. The product was then extracted using diethyl ether (3 x 20 mL) and the combined organic layers were dried over Na_2SO_4, before being concentrated under vacuum to yield the crude product. The crude product was then purified by flash column

chromatography using hexane / ethyl acetate gradient eluent (up to 4:1)to give the pure product as a pale yellow oil (21.1 mg, 0.089 mmol, 21 %).

$[\alpha]_D^{31}$ +1.52 ° (*c* 0.475 in $CDCl_3$) 31 % ee (*S*); (found (ESI): [M+ Na]$^+$, 261.1097. $C_{13}H_{18}NaO_4$ requires 261.1097); ν_{max} 3426, 2928, 2868, 2834, 1506, 1460, 1228, 1040, 928, 823 and 747 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 6.79 - 6.91 (4H, m, Ar***H***), 5.85 - 5.96 (1H, m, ***H***CCH_cH_d), 5.29 (1H, dd, *J* = 17.2 Hz, 1.5 Hz, $HCCH_d$***H*$_c$**), 5.21 (1H, dd, *J* = 10.4 Hz, 1.2 Hz, $HCCH_c$***H*$_d$**), 4.16 (1H, s, HOC***H***), 4.05 (2H, d, *J* = 5.6 Hz, ***H*$_2$**$CCHCH_cH_d$), 3.95 - 4.02 (2H, m, C***H*$_2$**), 3.77 (3H, s, OC***H*$_3$**), 3.64 (1H, dd, *J* = 9.7 Hz, 4.5 Hz, CH_b***H*$_a$**), 3.59 (1H, dd, *J* = 9.7 Hz, 6.0 Hz, CH_a***H*$_b$**), 2.54 (1H, d, *J* = 4.7 Hz, O***H***); δ_C (126 MHz, $CDCl_3$) 154.1, 152.7, 134.4, 117.4, 115.6, 114.7, 72.4, 71.0, 69.7, 69.2, 55.7; *m/z* (ESI) 261 ([M+Na]$^+$, 10%).

Enantiomeric excess determined by HPLC analysis (Chiralcel OD 0.46cm x 25cm, EtOH:Hexane 1:9, 1mL/min, 30 °C 254nm) *R minor* isomer 8.2 min, *S major* isomer 9.5 min

7. 1-(Allyloxy)-3-(4-methoxyphenoxy)propan-2-one.

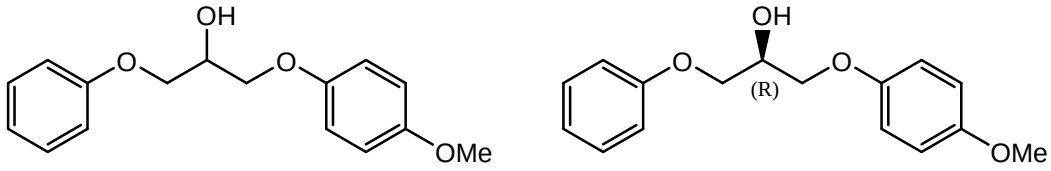


This compound is novel

To DCM (10 mL), 2 M oxalyl chloride (1.60 mL,X 3.21 mmol, 2 eq) was added. This mixture was cooled to -78 °C . Anhydrous DMSO (501 mg, 0.45 mL, 6.42 mmol, 4 eq) was then added to the mixture and stirred for 20 minutes. A solution of 1-(allyloxy)-3-(4-methoxyphenoxy)propan-2-ol (382 mg, 1.60 mmol, 1 eq) in DCM (5 mL), was added to the reaction mixture, which was then left stirring for another 30 minutes. TEA (1.20 g, 1.66 mL, 11.2 mmol, 7 eq) was added dropwise, and the reaction was left stirring overnight. Water (20 mL) was used to quench the reaction, and DCM (3 x 20 mL) was used to extract the product. The combined organic layers were then dried over sodium sulphate and concentrated under vacuum to give a dark yellow/brown oil as the crude product. The crude product was then purified by flash column chromatography with a gradient of EtOAc : Hexane to yield the product as a pale yellow oil (122 mg, 0.52 mmol, 32 %).

(found (ESI): [M+Na]$^+$ 259.0941. $C_{13}H_{16}NaO_4$ requires 259.0941); ν_{max} 3074, 2905, 2835, 1737, 1505, 1431, 1231, 1107, 1032, 824 and 748 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 6.84 (4H, s, Ar***H***), 5.83 - 5.96 (1H, m, ***H***CCH_aH_b), 5.31 (1H, dd, *J* = 17.2 Hz, 1.5 Hz, $HCCH_b$***H*$_a$**), 5.25 (1H, dd, *J* = 10.4 Hz, 1.1 Hz, $HCCH_a$***H*$_b$**), 4.71 (2H, s, C***H*$_2$**), 4.35 (2H, s, C***H*$_2$**), 4.08 (2H, d, *J* = 5.8 Hz, C***H*$_2$**$CHCH_aH_b$), 3.77 (3H, s, OC***H*$_3$**); δ_C (126 MHz, $CDCl_3$) 204.6, 154.6, 151.9, 133.6, 118.4, 115.7, 114.8, 73.6, 72.6, 72.5, 55.7; *m/z* (ESI) 235 ([M-H]$^-$, 95 %).

8. 1-(4-Methoxyphenoxy)-3-phenoxypropan-2-ol 11.



This compound has been reported and fully characterized.

Zvagulis, A.; Bonollo, S.; Lanari, D.; Pizzo, F.; Vaccaro, L. *Adv. Syth. Catal*, **2010**, *352*, 2489-2496.

Epoxide ring opening

To a solution of $PdCl_2$ (5 mg, 0.03 mmol, 0.01 eq), TBAB (257 mg, 0.80 mmol, 0.25 eq) and K_2CO_3 (110 mg, 0.8 mmol, 0.25 eq) in deionized H_2O (25 mL) at 60 ^oC phenyl glycidyl ether (500 mg, 3.34 mmol, 1 eq) and 4-methoxyphenol (455mg, 3.67 mmol, 1.1 eq) were added. The reaction mixture was then stirred for 3.5 h at 60 ^oC and a further 12 hrs at rt. EtOAc (3 x 15 mL) was added to extract the product from the aqueous solution. The organic layers were separated, combined, and dried over Na_2SO_4, before being concentrated under vacuum. The crude product was then purified by flash chromatography using a graduated eluent mixture of EtOAc in Hexane (0-20%) to yield the product as a white solid (419 mg, 1.53 mmol, 46%).

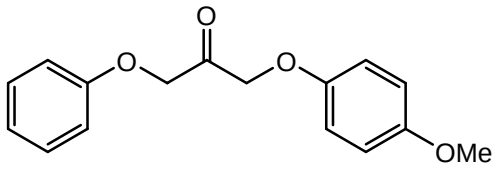
ATH using [(*R*,*R*)Teth-TsDpen RuCl]

A catalytic amount of [(*R*,*R*) Teth-TsDpen RuCl] (8.3 mg, 13.4 µmol, 0.005 eq) was measured and dissolved in of 5:2 formic acid/triethylamine azeotrope (0.3 mL). After stirring for 15 min the ketone, 1-(4-methoxyphenoxy)-3-phenoxypropan-2-one (75.5 mg, 0.28 mmol, 1 eq) was added and the reaction mixture was allowed to stir at rt for 12 h. A saturated solution of $NaHCO_3$ (5 mL) was then added dropwise to quench the reaction. Et_2O (3 x 5 mL) was then used to extract the product from the aqueous layer. The combined organic layers were then dried over Na_2SO_4 filtered and concentrated under vacuum to yield the crude product as a red oil. The crude product was then purified by flash chromatography using 30% EtOAc in hexane eluent. This yielded the product as a clear oil (61.7 mg, 0.225 mmol, 80.9%).

Mp 70.0 ^oC -70.8 ^oC; $[\alpha]_D^{25}$ +0.12 (*c* 6.3 in $CDCl_3$) 7% ee (*R*) ; ν_{Max} 3479, 3012, 2948, 1510, 1117 and 748 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.30 (2H, m, Ar**H**), 6.80 – 7.02 (7H, m, Ar**H**), 4.33 – 4.42 (1H, quin, *J*= 5.3 Hz, HOC**H**), 4.05 - 4.20 (4H, m, C**H₂**CHOHC**H₂**), 3.77 (3H, s, OC**H₃**), 2.63 (1H, d, *J* = 5.0 Hz, O**H**); δ_C (75 MHz, $CDCl_3$) 158.38, 154.15, 152.54, 129.53, 121.22, 115.53, 114.66, 114.52, 69.42, 68.84, 68.61 and 55.70; *m/z* (EI) 297 $[M+Na\}^+$.

Enantiomeric excess determined by HPLC analysis (Chiralpak IB, 0.46 cm ϕ x 25 cm, iPrOH:hexane 1:9, 1 mL/min, T = 30 ^oC, 254 nm) *S minor* isomer 21.5 min, *R major* isomer 24.9 min

8. 1-(4-Methoxyphenoxy)-3-phenoxypropan-2-one.



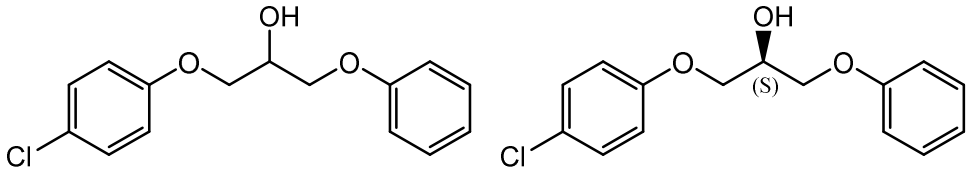
This compound is novel

Swern Oxidation

A 2M solution of oxalyl chloride in DCM (1.45 mL, 2.9 mmol, 2 eq) was further diluted with DCM (10ml) and cooled to -78 ^{o}C. Anhydrous DMSO (452.4 mg, 0.41 mL, 5.8 mmol, 4 eq) was then added dropwise and the mixture stirred for 20 min. The alcohol, 1-(4-methoxyphenoxy)-3-phenoxypropan-2-ol (400 mg, 1.45 mmol, 1 eq), was then added and the mixture was stirred for another 20 min. TEA (1.02 g, 1.41 mL, 10.15 mmol, 7 eq) was then added dropwise and the mixture was stirred for 12 h. the reaction was then quenched with water (10 mL) and the product was extracted using DCM (3 x 10 mL). the combined organic layers were then dried over Na_2SO_4 and concentrated under vacuum to yield crude product, which was subsequently purified by flash column chromatography using a graduated eluent mixture of EtOAc in Hexane (0-20%) to yield pure ketone product as a colourless oil (190 mg, 0.69 mmol, 48%).

(found(ESI): $[M+Na]^+$, 295.0938. $C_{16}H_{16}NaO_4$ requires 295.0941); ν_{max} 2904, 2834, 1740, 1597, 1504, 1430, 1214, 1108, 1030 and 750 cm^{-1};δ_H (400 MHz, $CDCl_3$) Shift = 7.26 - 7.33 (2H, m, Ar**H**), 7.00 (1H, t, J = 7.4 Hz, Ar**H**), 6.90 (2H, d, J = 8.1 Hz, Ar**H**), 6.80 - 6.88 (4H, m, Ar**H**), 4.86 (2H, s, C***H*₂***), 4.81 (2H, s, C***H*₂***), 3.76 (3H, s, OC***H*₃***); δ_C (100 MHz, $CDCl_3$) 202.92, 157.63, 154.71, 151.80, 129.75, 121.98, 115.76, 114.85, 114.62, 72.54, 71.62 and 55.71; *m/z* (ESI) 295 [M+Na] .

9. 1-(4-Chlorophenoxy)-3-phenoxypropan-2-ol, 12.



This compound is known and fully characterized.

Wu, X.; Li, X.; King, F.;Xiao, J. *Angew. Chem. Int. Ed*, **2005**, *44*, 3407-3434.

Epoxide ring opening

A solution of $PdCl_2$ (5.8 mg, 33 µmol, 0.01 eq), TBAB (267 mg, 0.83 mmol, 0.25 eq) and K_2CO_3 (115 mg, 0.83 mmol, 0.25 eq) in H_2O (12 mL) was heated to 60 ^{o}C. To the mixture phenyl glycidyl ether (500 mg, 3.3 mmol, 1 eq) and 4-chlorophenol (424 mg, 3.3 mmol, 1 eq) were added and the mixture was stirred at 60 ^{o}C for 24 hrs. The product was then extracted using EtOAc (3 x 20 mL) and the

combined organic layer were dried over Na_2SO_4 before being concentrated under vacuum. The crude product was then purified by flash column chromatography using a graduated eluent mixture of EtOAc in Hexane (0 - 10 %) to yield the pure product as a colourless oil (555.8 mg, 1.99 mmol, 60.5 %).

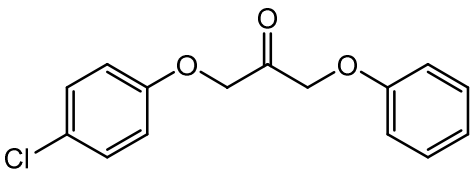
ATH using [(*R*,*R*)Teth-TsDpen RuCl]

To a solution of [(*R*,*R*) Teth-TsDpen RuCl] (0.8 mg, 1.36 µmol, 0.005 eq) in 5:2 formic acid/triethylamine azeotrope (1 mL) the ketone, 1-(4-chlorophenoxy)-3-phenoxypropan-2-one (75 mg, 0.27 mmol, 1 eq), was added and the reaction was then stirred overnight. The reaction mixture was then diluted with Et_2O and quenched with $NaHCO_3$ until basic. The product was then extracted with Et_2O (3 x 5 mL) and the combined organic layers were dried over Na_2SO_4 before being concentrated under vacuum to give the crude product. The crude was then purified by flash column chromatography to yield the product as a white solid (47.4 mg, 0.17 mmol, 63 %).

Mp 65.8 – 66.7 °C; $[\alpha]_D^{25}$ +1.27 ° (*c* 0.18 in $CDCl_3$) 5.2 % ee (S); ν_{max} 3508, 2947, 2928, 2873, 1588, 1487, 1441, 1230, 1011, 820, 756 and 674 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.30 (2H, t, *J* = 8.0 Hz, Ar***H***), 7.20 - 7.27 (2H, m, Ar***H***), 6.98 (1H, t, *J* = 7.4 Hz, Ar***H***), 6.90 - 6.96 (2H, m, Ar***H***), 6.82 - 6.89 (2H, m, Ar***H***), 4.38 (1H, sxt, *J* = 5.3 Hz, C***H***), 4.02 - 4.23 (4H, m, (C***H₂***)₂), 2.54 - 2.67 (1H, m, O***H***); δ_C (126 MHz, $CDCl_3$) 158.3, 157.0, 129.6, 129.4, 126.2, 121.3, 115.8, 114.5, 69.0, 68.7, 68.5; *m/z* (ESI) 301 ($[M + Na]^+$, 99 %), 303 ($[M + Na + 2]^+$, 35 %).

Enantiomeric excess determined by HPLC analysis (Chiralpak IB, 0.46 cm ϕ x 25 cm, iPrOH:hexane 1:9, 1 mL/min, T = 30 °C, 254 nm) *S major* isomer 10.9 min, *R minor* isomer 17.9 min.

9. 1-(4-Chlorophenoxy)-3-phenoxypropan-2-one.



This compound is has been reported but not fully characterised.

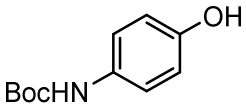
PCC oxidation

A stirred mixture of 1-(4-chlorophenoxy)-3-phenoxypropan-2-ol (300 mg, 1.07 mmol, 1 eq), sodium acetate (175.5 mg, 2.14 mmol, 2 eq) and silica (460 mg) in DCM (5.4 mL) was cooled to 0 °C. PCC (462 mg, 2.14 mmol, 2 eq) was then added in portions and the mixture was allowed to warm to room temperature overnight. The mixture had turned to a thick black tar and was subsequently filtered through silica which was washed with DCM (3 x 30 mL). DCM was then removed under vacuum to yield the crude product, which was then purified by flash column chromatography chromatography

using a graduated eluent mixture of EtOAc in Hexane (0 - 40 %) to yield the pure product as a colourless oil (114.5 mg, 0.41 mmol, 39 %).

(found (ESI): $[M-H]^-$, 275.0478. $C_{15}H_{12}{}^{35}ClO_3$ requires M, 275.0480); ν_{max} 3100, 3061, 3041, 2962, 2897, 1736, 1596, 1586, 1488, 1424, 1233, 1060, 822 and 748 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.29 - 7.39 (2H, m, Ar***H***), 7.22 - 7.29 (2H, m, Ar***H***), 7.03 (1H, t, *J* = 7.4 Hz, Ar***H***), 6.92 (2H, d, *J* = 7.8 Hz, Ar***H***), 6.78 - 6.87 (2H, m, Ar***H***), 4.90 (2H, s, C***H₂***), 4.84 (2H, s, C***H₂***); δ_C (126 MHz, $CDCl_3$) Shift = 202.1, 157.4, 156.2, 129.8, 129.6, 126.9, 122.1, 115.9, 114.5, 71.7, 71.7; *m/z* (ESI) 275 ($[M-H]^-$, 99 %), 277 ($[M-H+2]^-$, 35%).

tert-Butyl (4-hydroxyphenyl)carbamate.



This compound is known and fully characterized.

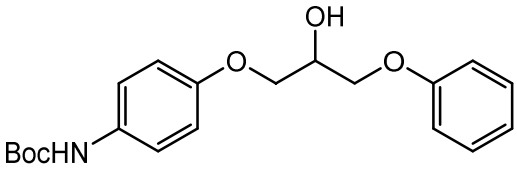
Clegg, N. J.; Paruthiyil, S.; Leitman, D.C.; Scanlan, T. S. *J. Med. Chem,* **2005**, *48*, 5989-6003.

Boc protection of amine

To a stirred solution of 4-aminophenol (1.01 g, 9.26 mmol, 1 eq) in THF (10 mL), di-tert-butyldicarbamate (2.2 g, 10.1 mmol, 1.1 eq) was added. The mixture was stirred for 12 hrs. stirring was stopped and THF was removed under vacuum to yield the product as a white solid (1.93 g, 9.21 mmol, 99.46 %) which was pure enough to continue reaction sequence.

ν_{max} 3359, 2977, 2935, 1695, 1513, 1227, 1160, 1057, 828, 627 and 515 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.13 - 7.23 (2H, m, Ar***H***), 6.71 - 6.78 (2H, m, Ar***H***), 6.34 (1H, br. s., N***H***), 5.12 (1H, s, O***H***), 1.52 (9H, s, 3 x C***H₃***); δ_H (100 MHz, $CDCl_3$) 151.9, 131.1, 121.3, 115.7, 28.4; *m/z* (ESI) 208.1 ($[M - H]^-$, 100 %).

10. *tert*-Butyl (4-(2-hydroxy-3-phenoxypropoxy)phenyl)carbamate 14.



This compound is novel.

Epoxide ring opening

A solution of $PdCl_2$ (16.3 mg, 6.1 µmol, 0.01 eq), TBAB (740.6 mg, 2.3 mmol, 0.25 eq) and K_2CO_3 (317.4 mg, 2.3 mmol, 0.25 eq) in water (50 mL) was heated to 60 °C. Phenyl glycidyl ether (1.36 ml, 1.5 2g, 10.2 mmol, 1.1 eq) and tert-butyl (4-hydroxyphenyl)carbamate (1.92 g, 9.23 mmol, 1 eq) were added and the mixture was stirred for 48 h. The mixture was cooled to rt and ethyl acetate (3 x

30 mL) was used to extract the product. The combined organic layers were then dried over Na_2SO_4 and concentrated under vacuum to yield the crude product as a black oil. The crude was then purified by flash column chromatography using a graduated eluent mixture of EtOAc in Hexane (0 - 100 %) to yield the pure product as a white solid (3.07 g, 8.54 mmol, 93.3 %).

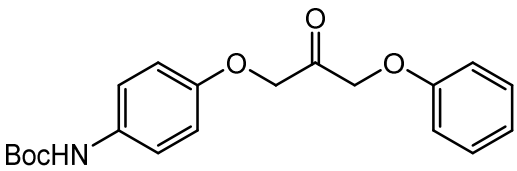
ATH using [(*R*,*R*)Teth-TsDpen RuCl]

To a stirring mixture of [(*R*,*R*) Teth-TsDpen RuCl] (1.2 mg, 1.5 µmol, 0.5 %) and 5:2 formic acid/triethylamine azeotrope (1 mL) was added *tert*-butyl (4-(2-hydroxy-3-phenoxypropoxy)phenyl)carbamate (87.4 mg, 0.24 mmol, 1 eq). The resulting mixture was stirred for 18 hrs. $NaHCO_3$ was added dropwise until the mixture was neutral and the product was extracted using Et_2O (3 x 5 mL). The combined organic layers were dried over Na_2SO_4 and concentrated under vacuum to yield the crude product, which was then then purified by flash column chromatography. The pure product was isolated as a white solid (63.2 mg, 0.18 mmol, 75%).

$[\alpha]_D^{29}$ + 2.196 (*c* 0.305 in $CDCl_3$); Mp 52.4 – 52.9 °C; (found (ESI): $[M-H]^-$, 358.1656. $C_{20}H_{24}NO_5^-$ requires 358.1660); ν_{max} 3366, 2980, 2934, 2876, 1696, 1598, 1518, 1229, 1161 and 751 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.26 - 7.34 (4H, m, Ar***H***), 6.92 - 7.02 (4H, m, Ar***H***), 6.88 (2H, d, *J* = 9.0 Hz, Ar***H***), 6.50 (1H, br. s., N***H***), 4.39 (1H, d, *J* = 5.0 Hz, HOC***H***), 4.09 - 4.20 (4H, m, 2 x C***H₂***), 2.83 (1H, d, *J* = 4.9 Hz, O***H***), 1.54 (9H, s, 3 x C***H₃***); δ_H (125 MHz, $CDCl_3$) 158.44, 154.50, 132.02, 129.58, 121.27, 115.01, 114.59, 70.41, 69.20, 68.83, 68.69, 63.67 and 28.40; *m/z* (ESI) 382.2 $[M + Na]^+$.

Enantiomeric excess determined by HPLC analysis (Chirelcel IB, 0.46 cm x 25 cm, EtOAc:Hexane 1:1, 1 ml/min, T = 30 °C) *S* isomer 5.6 min, *R* isomer 6.4 min.

10. *tert*-Butyl (4-(2-oxo-3-phenoxypropoxy)phenyl)carbamate.



This compound is novel.

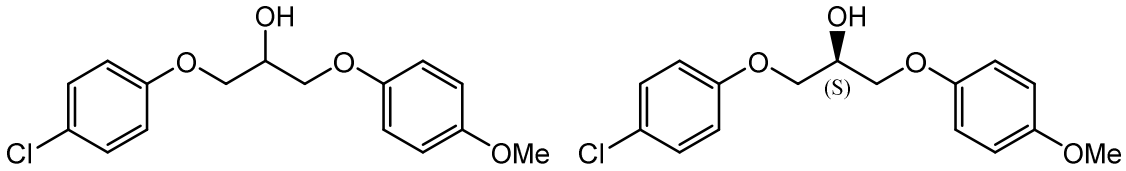
Swern oxidation

A 2M solution of oxalyl chloride in DCM (2.78 mL, 5.6 mmol, 2 eq) was further diluted with DCM (15 mL) and cooled to -78 °C. Anhydrous DMSO (867 mg, 0.78 mL, 11.1 mmol, 4 eq) was then added dropwise and the mixture stirred for 20 mins. The alcohol, tert-butyl (4-(2-hydroxy-3-phenoxypropoxy)phenyl)carbamate (959 mg, 2.7 mmol, 1 eq), was then added and the mixture was stirred for another 20 mins. TEA (1.96 g, 2.7 mL, 19.5 mmol, 7 eq) was then added dropwise and the mixture was stirred for 12 hrs. The reaction was then quenched with water (20 mL) and the product was extracted using DCM (3 x 15 mL). The combined organic layers were then dried over Na_2SO_4 and

concentrated under vacuum to yield crude product, which was subsequently purified by flash column chromatography using a graduated eluent mixture of EtOAc in Hexane (0 - 30 %) to yield the pure ketone product as a white solid (180.8 mg, 0.51 mmol, 18.9%).

Mp 92.8 – 97.9 °C; (found (ESI): $[M-H]^-$, 356.1507. $C_{20}H_{22}NO_5^-$ requires 356.1503); ν_{max} 3344, 2981, 2936, 2900, 1740, 1686, 1515, 1153, 1059, 823 and 753 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.27 - 7.35 (4H, m, Ar***H***), 6.99 - 7.04 (1H, m, Ar***H***), 6.92 (2H, d, *J* = 7.9 Hz, Ar***H***), 6.83 - 6.88 (2H, m, Ar***H***), 6.36 (1H, br. s., N***H***), 4.87 (2H, s, C***H₂***), 4.85 (2H, s, C***H₂***), 1.51 (9H, s, 3 x C***H₃***); δ_H (125 MHz, $CDCl_3$) 202.65, 157.55, 153.54, 132.69, 129.73, 122.00, 115.12, 114.57, 72.11, 71.60 and 28.33; *m/z* (ESI) 356.1 ($[M - H]^-$, 100 %).

11. 1-(4-Chlorophenoxy)-3-(4-methoxyphenoxy)propan-2-ol 13.



This compound is known and fully characterized.

Surendra, K.; Srilakshmi Krishnaveni , N.; Nageswar, Y. V. D.; Rama Rao, K. *J. Org. Chem,* **2003**, *68*, 4994-4995.

Epoxide ring opening

A solution of $PdCl_2$ (4.8 mg, 27 µmol, 0.01 eq), TBAB (219 mg, 0.68 mmol, 0.25 eq) and K_2CO_3 (94 mg, 0.68 mmol, 0.25 eq) in H_2O (12 mL) was heated to 60 °C. To the mixture 2-((4-methoxyphenoxy)methyl)oxirane (500 mg, 2.7 mmol, 1 eq) and 4-chlorophenol (346 mg, 2.7 mmol, 1 eq) were added and the mixture was stirred at 60 °C for 24 hrs. The product was then extracted using EtOAc (3 x 30 mL) and the combined organic layers were dried over Na_2SO_4 before being concentrated under vacuum. The crude product was then purified by flash column chromatography using a graduated eluent mixture of EtOAc in Hexane (0 - 40 %) to to yield the pure product as a white solid (623.3 mg, 2.02 mmol, 75 %).

ATH using [(*R*,*R*)Teth-TsDpen RuCl]

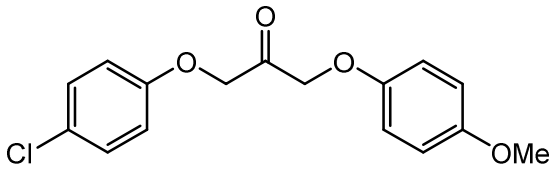
To a solution of [(*R*,*R*) Teth-TsDpen RuCl] (1.0 mg, 1.62 µmol, 0.005 eq) in 5:2 formic acid/triethylamine azeotrope (0.5 mL) the ketone, 1-(4-chlorophenoxy)-3-(4-methoxyphenoxy)propan-2-one (99.3 mg, 0.32 mmol, 1 eq), was added and the reaction was then stirred overnight. The reaction mixture was then diluted with Et_2O and quenched with $NaHCO_3$ until basic. The product was then extracted with Et_2O (3 x 10 mL) and the combined organic layers were dried over Na_2SO_4 before being concentrated under vacuum to give the crude product. The crude

was then purified by flash column chromatography to yield the product as a white solid (94.8 mg, 3.08 mmol, 95 %).

Mp 92.8 – 93.8 °C; $[\alpha]_D^{29}$ -1.13 ° (*c* 0.36 in $CDCl_3$) 12 % ee (S); δ_H (500 MHz, $CDCl_3$) 7.21 - 7.27 (2H, m, Ar***H***), 6.80 - 6.90 (6H, m, Ar***H***), 4.36 (1H, sxt, *J* = 5.3 Hz, C***H***), 4.05 - 4.16 (4H, m, ($C\boldsymbol{H_2}$)$_2$), 3.77 (3H, s, O$C\boldsymbol{H_3}$), 2.55 (1H, d, *J* = 5.3 Hz, O***H***); δ_C (125 MHz, $CDCl_3$) 157.1, 154.3, 152.5, 129.4, 126.2, 115.9, 115.6, 114.7, 69.4, 69.1, 68.9, 55.7; *m/z* (ESI) 331 ([M+Na]$^+$, 100%), 333 ([M+Na+2]$^+$, 30%).

Enantiomeric excess determined by HPLC analysis (Chiralpak IB, 0.46 cm ϕ x 25 cm, iPrOH:hexane 1:9, 1 mL/min, T = 30 °C, 254 nm) *S major* isomer 15.5 min, *R minor* isomer 20.7 min.

11. 1-(4-Chlorophenoxy)-3-(4-methoxyphenoxy)propan-2-one.



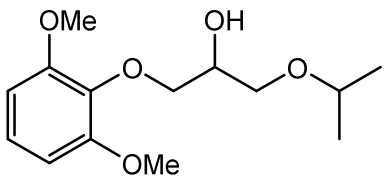
This compound is novel.

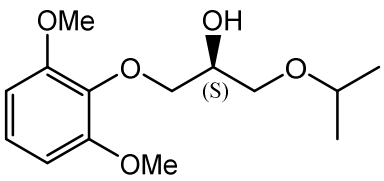
PCC oxidation

A stirred mixture of 1-(4-chlorophenoxy)-3-(4-methoxyphenoxy)propan-2-ol (500 mg, 1.62 mmol, 1 eq), sodium acetate (266 mg, 3.24 mmol, 2 eq) and silica (704 mg) in DCM (8.2 mL) was cooled to 0 °C. PCC (216 mg, 3.24 mmol, 2 eq) was then added in portions and the mixture was allowed to warm to room temperature overnight. The mixture had turned to a thick black tar and was subsequently filtered through silica which was washed with DCM (3 x 30 mL). DCM was then removed under vacuum to yield the crude product, which was then purified by flash column chromatography using a graduated eluent mixture of EtOAc in Hexane (0 - 15 %) to to yield the pure product as a white solid (114.2 mg, 0.37 mmol, 23 %).

Mp 69.7 – 73.3 °C; (found (ESI): [M+Na]$^+$ 329.550. $C_{16}H_{15}{}^{35}ClNaO_4$ requires 329.0551); ν_{max} 2892, 2836, 1736, 1490, 1237, 1167, 1184, 1032, 820 and 753 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.26 (2H, s, Ar***H***), 6.80 - 6.89 (6H, m, Ar***H***), 4.89 (2H, s, $C\boldsymbol{H_2}$), 4.79 (2H, s, $C\boldsymbol{H_2}$), 3.78 (3H, s, O$C\boldsymbol{H_3}$); δ_C (126 MHz, $CDCl_3$) 202.5, 156.2, 154.8, 151.7, 129.6, 126.9, 116.0, 115.7, 114.9, 72.6, 71.8, 55.7; *m/z* (ESI) 305 ([M-H]$^-$, 100%), 307 ([M-H+2]$^-$, 30 %).

12. 1-(2,6-Dimethoxyphenoxy)-3-isopropoxypropan-2-ol 15.





This compound is novel.

Epoxide ring opening

A solution of $PdCl_2$ (5.7 mg, 3.2 µmol, 0.01 eq), TBAB (261 mg, 0.81 mmol, 0.25 eq) and K_2CO_3 (112 mg, 0.81 mmol, 0.25 eq) in H_2O (12 mL) was heated to 60 °C. To the stirring mixture 2,6 dimethoxyphenol (500 mg, 3.24 mmol, 1 eq) and glycidyl isopropyl ether (415 mg, 3.57 mmol, 1.1 eq) were added. The mixture was stirred for 12 h before the organics were extracted with EtOAc (3 x 10 mL). The combined organic layers were dried over Na_2SO_4 and concentrated under vacuum to give a black oil. The crude product was then purified by flash column chromatography using a graduated eluent mixture of EtOAc in Hexane (0 - 50 %) to give a colourless oil (662 mg, 2.45 mmol, 73 %).

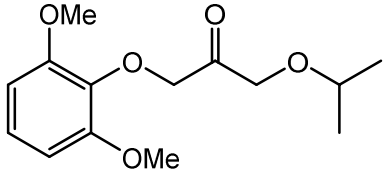
ATH using [(*R*,*R*)Teth-TsDpen RuCl]

The ketone, 1-(2,6-dimethoxyphenoxy)-3-isopropoxypropan-2-one (100 mg, 0.37 mmol, 1 eq) was added to a stirring mixture of [(*R*,*R*) Teth-TsDpen RuCl] (1.1 mg, 1.85 µmol, 0.005 eq) and 5:2 formic acid/triethylamine azeotrope (1 mL). The reaction mixture was then stirred overnight. The mixture was quenched with a saturated solution of $NaHCO_3$ until basic and the crude product was extracted with Et_2O (3 x 5 mL). Combined organics were then dried over Na_2SO_4 and concentrated under vacuum. The crude product was then purified by flash column chromatography to yield the pure product as a colourless oil (71 mg, 0.26 mmol, 71 %).

$[\alpha]_D^{31}$ +7.8 ° (c 0.405 in $CDCl_3$) 16% ee (S); (found (ESI): $[M+Na]^+$ 293.1360 $C_{14}H_{22}NaO_5$ requires 293.1359); ν_{max} 3498, 2969, 2938, 2838, 1596, 1477, 1295, 1252, 1106, 1010, 774 and 729 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.01 (1H, t, *J* = 8.4 Hz, Ar***H***), 6.59 (2H, d, *J* = 8.4 Hz, Ar***H***), 4.23 (1H, dd, *J* = 10.3 Hz, *J* = 2.8 Hz, C***H***H), 3.96 - 4.06 (1H, m, C***H***), 3.92 (1H, dd, ***J*** = 9.9 Hz, ***J*** = 7.6 Hz, CH***H***), 3.87 (6H, s, Ar(OC***H₃***)$_2$), 3.61 (1H, dt, *J* = 12.2 Hz, *J* = 6.1 Hz, HOC***H***), 3.53 (2H, d, *J* = 5.3 Hz, C***H₂***), 1.17 (6H, d, *J* = 6.1 Hz, (C***H₃***)***₂***); δ_C (75 MHz, $CDCl_3$) 153.3, 137.0, 123.9, 105.2, 76.1, 72.1, 69.6, 68.8, 56.1, 22.0; *m/z* (ESI) 293 ($[M + Na]^+$, 100 %), 271 ($[M + H]^+$, 4 %).

Enantiomeric excess determined by HPLC analysis (Chiralpak IB, 0.46 cm ϕ x 25 cm, iPrOH:hexane 1:9, 1 mL/min, T = 30 °C, 254 nm) *R minor* isomer 8.8 min, *S major* isomer 9.6 min.

12. 1-(2,6-Dimethoxyphenoxy)-3-isopropoxypropan-2-one.



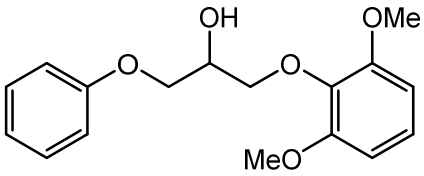
This compound is novel.

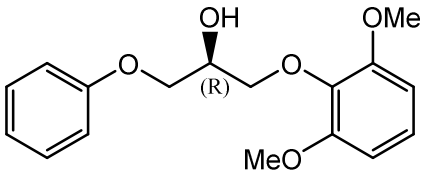
Swern oxidation

A 2M solution of oxalyl chloride in DCM (1.5 mL, 3.0 mmol, 2 eq) was further diluted with DCM (10 mL) and cooled to -78 °C. Anhydrous DMSO (464 mg, 0.42 mL, 5.9 mmol, 4 eq) was then added dropwise and the mixture stirred for 20 mins. The alcohol, 1-(2,6-dimethoxyphenoxy)-3-(4-methoxyphenoxy)propan-2-ol (500 mg, 1.49 mmol, 1 eq) was then added and the mixture was stirred for another 20 mins. TEA (1.05 g, 1.45 mL, 10.4 mmol, 7 eq) was then added dropwise and the mixture was stirred for 12 hrs. The reaction was then quenched with water (15 mL) and the product was extracted using DCM (3 x 20 mL). The combined organic layers were then dried over Na_2SO_4 and concentrated under vacuum to yield crude product, which was subsequently purified by flash column chromatography using a graduated eluent mixture of EtOAc in Hexane (0 - 50 %) to yield pure ketone product as a white solid (304.4 mg, 0.91 mmol, 62 %).

(found (ESI): M^+ + Na, 291.1203. $C_{14}H_{20}NaO_5$ requires 291.1203); ν_{max} 2970, 2939, 2838, 1736, 1597, 1477, 1253, 1105, 1034, 772 and 729 cm^{-1}; $_1$H NMR (400 MHz, $CDCl_3$) 7.01 (1H, t, *J* = 8.4 Hz, Ar***H***), 6.58 (2H, d, *J* = 8.4 Hz, Ar***H***), 4.63 (2H, s, C***H₂***), 4.63 (2H, s, C***H₂***), 3.84 (6H, s, Ar(OC***H₃***)$_2$), 1.23 (6H, d, *J* = 6.1 Hz, (C***H₃***)$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) 206.2, 152.9, 136.8, 124.1, 105.1, 77.3, 72.6, 72.0, 56.0, 21.8; *m/z* (ESI) 269 ([M + H]$^+$, 30 %), 291 ([M + Na]$^+$, 97 %).

13. 1-(2,6-Dimethoxyphenoxy)-3-phenoxypropan-2-ol 16.





This compound is novel

Epoxide ring opening

A solution of $PdCl_2$ (16.8 mg, 0.09 mmol, 0.03 eq), TBAB (271.4 mg, 0.84 mmol, 0.25 eq) and K_2CO_3 (116.4 mg, 0.84 mmol, 0.25 eq) in water was prepared and heated to 60 °C. Phenyl glycidyl ether (0.45 mL, 500 mg, 3.34 mmol, 1 eq) was then added to the stirring mixture along with 2,6 dimethoxy phenol (581.4 mg, 3.77 mmol, 1.1 eq). The reaction was then stirred for 3.5 h at 60 °C before being allowed to cool to rt and stirred for 12 h. The product was then extracted using EtOAc (3 x 20 mL). The combined organic layers were then dried over sodium sulphate and concentrated under vacuum to yield the black crude product, which was then purified by flash chromatography using a graduated eluent mixture of EtOAc in Hexane (0 - 50 %) to yield the product as a colourless oil (369.3 mg, 1.21 mmol, 36.2 %).

ATH using [(*R*,*R*)Teth-TsDpen RuCl]

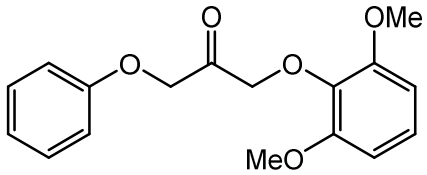
To a stirring solution of [(*R*,*R*) teth-TsDpen RuCl] (1.9 mg, 1.49 µmol, 0.5 %) in 5:2 formic acid/trimethylamine azeotrope (0.6 mL) was added 1-(2,6-dimethoxyphenoxy)-3-phenoxypropan-2-

one (76.8 mg, 0.25 mmol, 1 eq). The mixture was stirred at room temperature for 48 h. mixture was diluted with Et_2O (5mL) and a saturated solution of $NaHCO_3$ was added dropwise to neutralise the formic acid. The aqueous layer was extracted with Et_2O (3 x 5 mL) and the combined organic layers were dried over Na_2SO_4 before concentrating under vacuum to yield crude product. The product was then purified by flash column chromatography to yield the pure product as a colourless oil (35.6 mg, 0.12 mmol, 48%).

$[\alpha]_D^{23}$ -25.43 ^{o} (*c* 0.23 in $CDCl_3$) 42 % ee (R); (found (EI): $[M+Na]^+$, 327.1203. $C_{17}H_{20}NaO_5$ requires 327.1284); ν_{max} 3483, 2939, 2837, 1596, 1476, 1245, 1104, 1016, 753, 728 and 690 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.15 - 7.23 (1H, m, Ar***H***), 6.94 (1H, t, *J* = 8.4 Hz, Ar***H***), 6.81 - 6.90 (2H, m, Ar***H***), 6.51 (1H, d, *J* = 8.4 Hz, Ar***H***), 4.23 (1H, dd, *J* = 10.5 Hz, *J* = 3.2 Hz, C***H***H), 4.12 - 4.20 (1H, m, HOC***H***), 3.97 - 4.06 (3H, m, C***H₂***+CH***H***), 3.96 (1H, d, *J* = 4.0 Hz, O***H***), 3.78 (6H, s, 2 x OC***H₃***); δ_C (100 MHz, $CDCl_3$) 158.65, 153.14, 136.94, 129.31, 120.79, 114.48, 105.06, 75.70, 68.35 and 55.96; *m/z* (ESI) 327.1 $(M + Na)^+$, 95 %).

Enantiomeric excess determined by HPLC analysis (Chiralpak IB, 0.46 cm ϕ x 25 cm, iPrOH:hexane 1:9, 1 mL/min, T = 30 ^{o}C, 254 nm) *S minor* isomer 14.2 min, *R major* isomer 18.5 min.

13. 1-(2,6-Dimethoxyphenoxy)-3-phenoxypropan-2-one.



This compound is novel

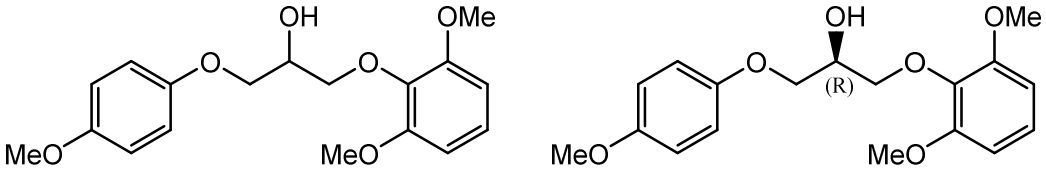
Swern Oxidation

A 2M solution of oxalyl chloride in DCM (0.66 mL, 1.32 mmol, 2 eq) was further diluted with DCM (5 mL) and cooled to -78 ^{o}C. Anhydrous DMSO (206 mg, 0.19 mL, 2.6 mmol, 4 eq) was then added dropwise and the mixture stirred for 20 min. The alcohol, 1-(2,6-dimethoxyphenoxy)-3-phenoxypropan-2-ol (198 mg, 0.65 mmol, 1 eq), was then added and the mixture was stirred for another 20 min. TEA (466 mg, 0.64 mL, 4.62 mmol, 7 eq) was then added dropwise and the mixture was stirred for 12 hrs. The reaction was then quenched with water (10 mL) and the product was extracted using DCM (3 x 10 mL). The combined organic layers were then dried over Na_2SO_4 and concentrated under vacuum to yield the crude product, which was subsequently purified by flash column chromatography using a 1:1 EtOAC:Hexane eluent to yield the pure ketone product as a colourless oil (123 mg, 0.41 mmol, 63%).

(found (ESI): $[M+Na]^+$, 325.1046. $C_{17}H_{18}NaO_5$ requires M, 325.1052); ν_{max} 3005, 2967, 2840, 1743, 1593, 1477, 1298, 1255, 1113, 1032 and 767 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.26 - 7.33 (2H, m, Ar***H***), 6.99

- 7.07 (1H, m, Ar***H***), 6.92 - 6.99 (3H, m, Ar***H***), 6.59 (2H, d, *J* = 8.4 Hz, Ar***H***), 5.22 (2H, s, C***H₂***), 4.71 (2H, s, C***H₂***), 3.83 (6H, s, 2 x OC***H₃***); δ_C (100 MHz, $CDCl_3$) 203.87, 157.94, 152.74, 136.69, 129.48, 124.26, 121.44, 114.65, 105.06, 77.36, 71.34 and 55.93; *m/z* (ESI) 325.1 ([M + Na]$^+$, 53%).

14. 1-(2,6-Dimethoxyphenoxy)-3-(4-methoxyphenoxy)propan-2-ol 17.



This compound is novel.

Epoxide ring opening

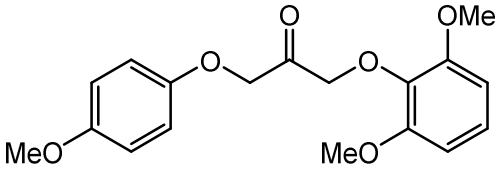
A solution of $PdCl_2$ (4.7 mg, 27 µmol, 0.01 %), TBAB (217 mg, 0.68 mmol, 0.25 eq) and K_2CO_3 (93.1 mg, 0.68 mmol, 0.25 eq) in H_2O (12 mL) was heated to 60 ^oC. To the solution 2-((4-methoxyphenoxy)methyl)oxirane (500 mg, 2.7 mmol, 1 eq) and 2,6 dimethoxyphenol (416 mg, 2.7 mmol, 1 eq) was added and the reaction was stirred for 12 h. The reaction mixture was allowed to cool to room temperature and the product was extracted with EtOAc (3 x 20 mL). The combined organic layers were then dried over Na_2SO_4 and concentrated under vacuum to yield the crude product as a black oil. The crude product was then purified by flash column chromatography using a graduated eluent mixture of EtOAc in Hexane (0 - 20 %) to yield the pure product as a colourless oil (524 mg, 1.57 mmol, 57 %).

ATH using [(*R*,*R*)Teth-TsDpen RuCl]

The ketone, 1-(2,6-dimethoxyphenoxy)-3-(4-methoxyphenoxy)propan-2-one (100 mg, 0.30 mmol, 1 eq), was added to a stirring mixture of [(*R*,*R*) TsDpen-teth RuCl] (0.93 mg, 1.5 µmol, 0.005 eq) in 5:2 formic acid/triethylamine azeotrope (1 mL). The mixture was stirred for 12 h before being quenched with a saturated solution of $NaHCO_3$, dropwise, until basic. The product was then extracted using Et_2O (3 x 5 ml), the combined organic layers were dried using Na_2SO_4 and concentrated under vacuum to yield a crude red oil. The crude product was then purified by flash column chromatography to yield the pure product as a colourless oil (60.4 mg, 0.18 mmol, 60 %). $[\alpha]_D^{31}$ -4.48 (c 0.91 in $CDCl_3$) 33 % ee (*R*); (found (ESI): $[M+Na]^+$, 357.1311. $C_{18}H_{22}NaO_6$ requires 357.1309); ν_{max} 3492, 2985, 2860, 1690, 1563, 1487, 1234, 1109 and 765 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.04 (1H, t, *J* = 8.4 Hz, Ar***H***), 6.80 - 6.91 (4H, m, Ar***H***), 6.61 (2H, d, *J* = 8.4 Hz, Ar***H***), 4.32 (1H, dd, *J* = 10.6 Hz, *J* = 3.1 Hz, C***H***H), 4.21 - 4.27 (1H, m, HOC***H***), 4.07 - 4.11 (1H, m, CH***H***), 4.06 (3H, d, *J* = 4.4 Hz, C***H₂*** + HCO***H***), 3.88 (6H, s, (OC***H₃***)2), 3.78 (3H, s, OC***H₃***); δ_C (126 MHz, $CDCl_3$) 154.0, 153.2, 153.0, 137.0, 124.1, 115.5, 114.6, 105.2, 75.9, 69.3, 69.0, 56.1 and 55.7; *m/z* 357 ([M + Na]$^+$, 100%), 335 ([M + H]$^+$, 10 %).

Enantiomeric excess determined by HPLC analysis (Chiralpak IB, 0.46 cm ϕ x 25 cm, iPrOH:hexane :9, 1 mL/min, T = 30 °C, 254 nm) *S minor* isomer 19.2 min, *R major* isomer 21.5 min.

14. 1-(2,6-Dimethoxyphenoxy)-3-(4-methoxyphenoxy)propan-2-one.



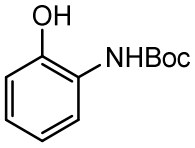
This compound is novel.

Swern oxidation

A 2M solution of oxalyl chloride in DCM (1.5 mL, 3.0 mmol, 2 eq) was further diluted with DCM (10 mL) and cooled to -78 °C. Anhydrous DMSO (464 mg, 0.42 mL, 5.9 mmol, 4 eq) was then added dropwise and the mixture stirred for 20 mins. The alcohol, 1-(2,6-dimethoxyphenoxy)-3-(4-methoxyphenoxy)propan-2-ol (500 mg, 1.49 mmol, 1 eq) was then added and the mixture was stirred for another 20 mins. TEA (1.05 g, 1.45 mL, 10.4 mmol, 7 eq) was then added dropwise and the mixture was stirred for 12 hrs. The reaction was then quenched with water (15 mL) and the product was extracted using DCM (3 x 20 mL). The combined organic layers were then dried over Na_2SO_4 and concentrated under vacuum to yield crude product, which was subsequently purified by flash column chromatography using a graduated eluent mixture of EtOAc in Hexane (0 - 40 %) to yield pure ketone product as a white solid (304.4 mg, 0.91 mmol, 62 %).

Mp 102.8 – 103.4 °C; (found (ESI): $[M+H]^+$, 355.1154. $C_{18}H_{20}NaO_6$ requires 355.1152); ν_{max} 3007, 2962, 2893, 2838, 1743, 1597, 1479, 1112, 1025, 822 and 713 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.05 (1H, t, *J* = 8.4 Hz, Ar***H***), 6.89 - 6.95 (2H, m, Ar***H***), 6.82 - 6.89 (2H, m, Ar***H***), 6.61 (2H, d, *J* = 8.4 Hz, Ar***H***), 5.19 (2H, s, C***H₂***), 4.72 (2H, s, C***H₂***), 3.86 (5H, s, (OC***H₃***)₂), 3.79 (3H, s, OC***H₃***); δ_C (126 MHz, CHLOROFORM-d) Shift = 204.3, 154.4, 152.8, 152.2, 136.7, 124.3, 115.8, 114.7, 105.1, 77.4, 72.3, 56.0 and 55.7; *m/z* (ESI) 331 ($[M - H]^-$, 100 %), 324.

tert-Butyl (2-hydroxyphenyl)carbamate.



This compound is known and fully characterized.

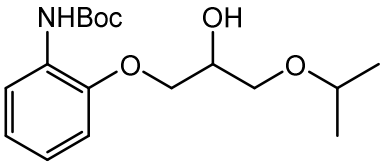
Varala, R.; Nuvula, S.; Adapa, S. R. *J. Org. Chem*, **2006**, *71*, 8283-8286

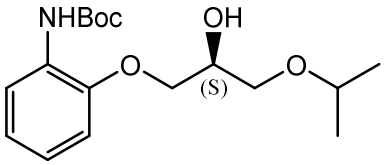
Boc protection of amine.

To a round bottom flask, 2-aminophenol (2.02g, 18.5 mmol, 1 eq) and di-tert-butyl dicarbamate (4.4 g, 20.1 mmol, 1.1 eq) was added and dissolved in anhydrous THF (20 mL). The mixture was stirred for 18 hours. The THF was then removed under vacuum to yield crude product which was then purified by flash column chromatography using a graduated eluent mixture of EtOAc in Hexane (0 - 20 %) to yield pure product as a white solid (3.65 g, 17.5 mmol, 95.6 %).

Mp 146.4 – 147.4 ^{o}C; ν_{max} 3425, 3289, 2984, 2968, 2932, 1688, 1612, 1519, 1453, 1224, 1146 and 748 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 8.13 (1H, br. s., N***H***), 7.01 - 7.11 (2H, m, Ar***H***), 6.94 - 6.98 (1H, m, Ar***H***), 6.81 - 6.88 (1H, m, Ar***H***), 6.66 (1H, br. s., O***H***), 1.53 (9H, s, 3 x C***H$_3$***);δ_C (75 MHz, $CDCl_3$) 147.48, 125.63, 125.53, 121.39, 120.74, 118.91, 82.10 and 28.23; *m/z* (ESI) 232.1 (M + Na]$^+$, 55%).

15. *tert*-Butyl (2-(2-hydroxy-3-isopropoxypropoxy)phenyl)carbamate 18.





This compound is novel.

Epoxide ring opening

A solution of $PdCl_2$ (4.2 mg, 23.9 µmol, 0.01 eq), TBAB (193 mg, 0.6 mmol, 0.25 eq) and K_2CO_3 (83 mg, 0.6 mmol, 0.25 eq) in H_2O (10 mL) was heated to 60 ^{o}C. To the mixture isopropyl glycidyl ether (305 mg, 2.63 mmol, 1.1 eq) and *tert*-butyl (2-hydroxyphenyl)carbamate (500 mg, 2.39 mmol, 1 eq) were added and the mixture was stirred at 60 ^{o}C for 24 h. The product was then extracted using EtOAc (3 x 20 mL) and the combined organic layer were dried over Na_2SO_4 before being concentrated under vacuum. The crude product was then purified by flash column chromatography using a graduated eluent mixture of EtOAc in Hexane (0 - 40 %) to yield the pure product as a colourless oil (653.6 mg, 2.01 mmol, 84 %).

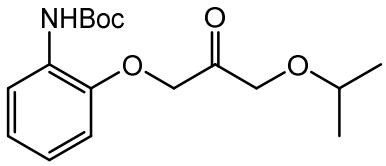
ATH using [(*R*,*R*)Teth-TsDpen RuCl]

To a solution of [(*R*,*R*) Teth-TsDpen RuCl] (0.9 mg, 1.6 µmol, 0.005 eq) in 5:2 formic acid/trimethylamine azeotrope (1 mL) the ketone, *tert*-butyl (2-(3-isopropoxy-2-oxopropoxy)phenyl)carbamate (100 mg, 0.31 mmol, 1 eq), was added and the reaction was then stirred overnight. The reaction mixture was then diluted with Et_2O and quenched with $NaHCO_3$ until basic. The product was then extracted with Et_2O (3 x 5 mL) and the combined organic layers were dried over Na_2SO_4 before being concentrated under vacuum to give the crude product. The crude was then purified by flash column chromatography to yield the product as a colourless oil (77 mg, 2.4 mmol, 76 %).

$[\alpha]_D^{31}$ +21.02 (*c* 0.205 in $CDCl_3$) 68 % ee (*S*); (found ESI: $[M+H]^+$,348.1789. $C_{17}H_{27}NNaO_5$ requires 348.1781); ν_{max} 3435, 2973, 2931, 2873, 1725, 1520, 1446, 1234, 1152, 1083, 1045 and 742 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 8.05 (1H, br. s., N***H***), 7.20 (1H, br. s., Ar***H***), 6.86 - 7.01 (3H, m, Ar***H***), 4.03 - 4.21 (3H, m, C***H₂*** + C***H***), 3.52 - 3.70 (3H, m, C***H₂*** + C***H***), 2.94 (1H, d, *J* = 4.9 Hz, CHO***H***), 1.54 (9H, s, (C***H₃***)$_3$), 1.20 (6H, d, *J* = 6.0 Hz, (C***H₃***)$_2$); δ_C (101 MHz, $CDCl_3$) 152.8, 146.8, 128.5, 122.4, 121.6, 118.7, 112.0, 72.3, 70.5, 69.0, 68.8, 28.3, 21.9; *m/z* (ESI) 348 $(M + Na]^+$, 100 %).

Enantiomeric excess determined by HPLC analysis (Chiralcel OD-H, 0.46 cm x 25 cm, iPrOH:Hexane 3:97, 1ml/min, 30 °C, 254 nm) *S major* isomer 17.5 min, *R minor* isomer 18.9 min.

15. *tert*-Butyl (2-(3-isopropoxy-2-oxopropoxy)phenyl)carbamate.



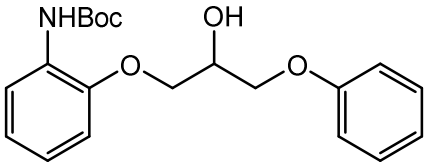
This compound is novel.

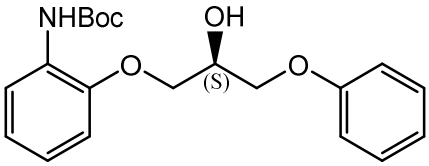
Swern oxidation

A 2M solution of oxalyl chloride in DCM (1.54 mL, 3.07 mmol, 2 eq) was further diluted with DCM (10 mL) and cooled to -78 °C. Anhydrous DMSO (479 mg, 0.44 mL, 6.15 mmol, 4 eq) was then added dropwise and the mixture stirred for 20 min. The alcohol *tert*-Butyl (2-(2-hydroxy-3-isopropoxypropoxy)phenyl)carbamate (500 mg, 1.54 mmol, 1 eq) was then added and the mixture was stirred for another 20 min. TEA (1.08 g, 1.5 mL, 10.8 mmol, 7 eq) was then added dropwise and the mixture was stirred for 24 h. Reaction was then quenched with water (10 mL) and the product was extracted using DCM (3 x 10 mL). Combined organic layers were then dried over Na_2SO_4 and concentrated under vacuum to yield crude product, which was subsequently purified by flash column chromatography using a graduated eluent mixture of EtOAc in Hexane (0 - 20 %) to yield pure ketone product as a white solid (420 mg, 1.3 mmol, 84 %).

(found (ESI): 346.1625. M^+ + Na, $C_{17}H_{25}NNaO_5$ requires 346.1625); ν_{max} 3431, 2976, 2932, 2252, 1723, 1603, 1522, 1452, 1237, 1203, 908 and 727 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) 8.11 (1H, br. s., N***H***), 7.43 (1H, br. s., Ar***H***), 6.98 - 7.04 (1H, m, Ar***H***), 6.95 (1H, td, *J* = 7.8 Hz, *J* = 1.6 Hz, Ar***H***), 6.77 (1H, dd, *J* = 8.1 Hz, *J* = 1.1 Hz, Ar***H***), 4.96 (2H, s, C***H₂***), 4.22 (2H, s, C***H₂***), 3.67 (1H, dt, *J* = 12.2 Hz, *J* = 6.1 Hz, C***H***), 1.55 (9H, s, (C***H₃***)$_3$), 1.24 (6H, d, *J* = 6.1 Hz, (C***H₃***)$_2$); ^{13}C NMR (126 MHz, $CDCl_3$) 204.7, 152.8, 146.3, 129.1, 122.5, 122.3, 118.9, 112.4, 73.2, 72.8, 72.5, 28.3, 21.8; *m/z* (ESI): 322 ($[M - H]^-$, 95 %),

16. *tert*-Butyl (2-(2-hydroxy-3-phenoxypropoxy)phenyl)carbamate 19.





This compound is novel.

Epoxide ring opening

A solution of $PdCl_2$ (4.2 mg, 2.4 µmol, 0.01 eq), TBAB (193 mg, 0.6 mmol, 0.25 eq) and K_2CO_3 (82.8 mg, 0.6 mmol, 0.25 eq) in water (25 mL) was heated to 60 °C. Phenyl glycidyl ether (396 mg, 0.36 mL, 2.64 mmol, 1.1 eq) and *tert*-butyl (2-hydroxyphenyl)carbamate (426 mg, 2.04 mmol, 1eq) were then added. The mixture was stirred at 60 °C for 12 h. The reaction was then cooled to room temperature before the crude product was extracted from the aqueous solution with EtOAc (3 x 15 mL). The combined organic layers were then dried over Na_2SO_4 and solvent was removed under vacuum to yield the crude product as a black oil. The crude product was then purified by flash column chromatography using a graduated eluent mixture of EtOAc in Hexane (0 - 50 %) to yield the pure product as a colourless oil (665.4 mg, 1.85 mmol, 90.9 %).

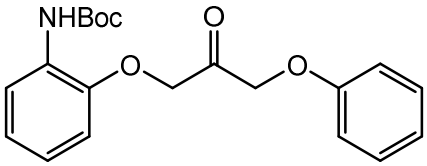
ATH using [(*R*,*R*)Teth-TsDpen RuCl]

To 5:2 formic acid/triethylamine azeotrope (2 mL) was added [(*R*,*R*) Teth-TsDpen RuCl] (2.1 mg, 3.4 µmol, 0.5 %). The mixture was allowed to stir for 20 min before addition of *tert*-butyl (2-(2-oxo-3-phenoxypropoxy)phenyl)carbamate (240 mg, 0.67 mmol, 1 eq), the mixture was then stirred for 48 h. A saturated solution of $NaHCO_3$ was added dropwise until the mixture was neutral. The product was then extracted from the aqueous layer using EtOAc (3 x 10 mL), and the combined organic layers were dried over Na_2SO_4 and concentrated under vacuum to yield the crude product. The crude product was purified by flash column chromatography to yield the pure product as a colourless oil (180.1 mg, 0.508 mmol, 75.8 %, 46 % ee).

$[\alpha]_D^{29}$ +2.2 (*c* 0.305 in $CDCl_3$) 46 % ee (*S*); (found (ESI): $[M-H]^-$, 358.1651. $C_{20}H_{24}NO_5$ requires 358.1660); ν_{max} 3432, 2978, 2932, 1722, 1599, 1520, 1447, 1234,1152 and 728 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 8.05 (1H, br. s., N***H***), 7.30 - 7.36 (2H, m, Ar***H***), 7.14 (1H, s, Ar***H***), 6.89 - 7.05 (6H, m, Ar***H***), 4.45 (1H, sxt, *J* = 5.2 Hz, HOC***H***), 4.10 - 4.30 (5H, m, 2 x C***H₂***), 2.95 (1H, d, *J* = 5.0 Hz, O***H***), 1.55 (9H, s, 3 x C***H₃***); δ_C (100 MHz, $CDCl_3$) 158.27, 152.88, 146.89, 129.56, 128.37, 122.72, 121.91, 121.39, 119.12, 114.52, 112.02, 70.23, 68.75, 68.68 and 28.33; *m/z* (ESI) 358.1 $[M-H]^-$, 100%).

Enantiomeric excess determined by HPLC analysis (Chirelcel IB, 0.46 cm x 25 cm, iPrOH:Hexane 1:9, 1 ml/min, T = 30 °C) *S major* isomer 11.9 min, *R minor* isomer 17.8 min.

16. *tert*-Butyl (2-(2-oxo-3-phenoxypropoxy)phenyl)carbamate.

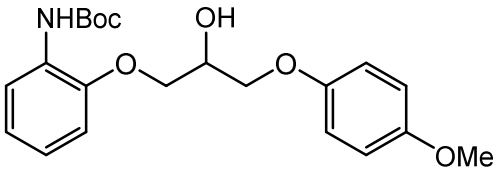


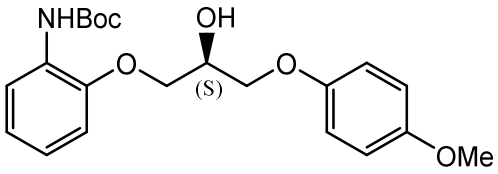
This compound is novel.

Swern oxidation

A 2M solution of oxalyl chloride in DCM (1.53 mL, 3.06 mmol, 2 eq) was further diluted with DCM (10 mL) and cooled to -78 ^{o}C. Anhydrous DMSO (477 mg, 0.44 mL, 6.12 mmol, 4 eq) was then added dropwise and the mixture stirred for 20 min. The alcohol, tert-butyl (2-(2-hydroxy-3-phenoxypropoxy)phenyl)carbamate (552 mg, 1.53 mmol, 1 eq), was then added and the mixture was stirred for another 20 min. TEA (1.08 mg, 1.49 mL, 10.71 mmol, 7 eq) was then added dropwise and the mixture was stirred for 12 h. The reaction was then quenched with water (20 mL) and the product was extracted using DCM (3 x 15 mL). The combined organic layers were then dried over Na_2SO_4 and concentrated under vacuum to yield crude product, which was subsequently purified by flash column chromatography using a graduated eluent mixture of EtOAc in Hexane (0 - 50 %) to yield the pure ketone product as a colourless oil (419 mg, 1.17 mmol, 76.3%).
(found(ESI): $[M+H]^+$, 358.1649. $C_{20}H_{24}NO_5$ requires 358.1654); ν_{max} 3427, 2978, 2931, 1722, 1599, 1521, 1479, 1236, 1047 and 745 cm^{-1}; δ_H(400 MHz, $CDCl_3$) 8.14 (1H, br. s., N***H***), 7.32 - 7.38 (2H, m, Ar***H***), 6.90 - 7.10 (6H, m, Ar***H***), 6.76 (1H, dd, *J* = 8.1 Hz, *J* = 1.3 Hz, Ar***H***), 5.06 (2H, s, C***H₂***), 4.78 (2H, s, C***H₂***), 1.56 (9H, s, 3 x C***H₃***); δ_C (100 MHz, $CDCl_3$) 202.48, 157.33, 152.75, 146.13, 129.82, 129.02, 122.67, 122.39, 122.25, 119.02, 114.42, 112.25, 72.58, 71.75 and 28.33; *m/z* (ESI) 356.1 ($[M - H]^-$, 10 %).

17. *tert*-Butyl (2-(2-hydroxy-3-(4-methoxyphenoxy)propoxy)phenyl)carbamate 20.





This compound is novel.

Epoxide ring opening

A stirred solution of $PdCl_2$ (2.7 mg, 15.3 µmol, 0.01 eq), TBAB (111 mg, 0.35 mmol, 0.25 eq) and K_2CO_3 (48.3 mg, 3,5 mmol, 0.25 eq) in H_2O (6 mL) was heated to 60 ^{o}C. 2-((4-Methoxyphenoxy)methyl)oxirane (212.3 mg, 1.18 mmol, 1 eq) was added along with *tert*-Butyl (2-hydroxyphenyl)carbamate (317.2 mg, 1.52 mmol, 1.3 mmol) and the reaction was stirred for 12 h. The mixture was cooled to room temperature and the product was extracted using EtOAc (3 x 10

mL). The combined organic layers were then dried over Na_2SO_4 and concentrated under vacuum to yield a crude black oil. The crude product was then purified by flash column chromatography using a graduated eluent mixture of EtOAc in Hexane (0 - 40 %) to yield the product as a colourless oil (369 mg, 0.94 mmol, 80 %).

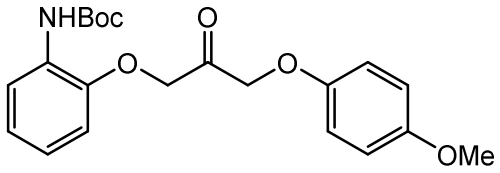
ATH using [(*R*,*R*)Teth-TsDpen RuCl]

A mixture of [(*R*,*R*)-TsDpen-teth RuCl] (0.5 mg, 0.82 µmol, 0.005 eq) and 5:2 formic acid/triethylamine azeotrope (0.5 mL) was stirred at room temperature. to the stirring mixture tert - butyl (2-(3-(4-methoxyphenoxy)-2-oxopropoxy)phenyl)carbamate (64 mg, 0.16 mmol, 1 eq) was added and the resulting mixture was stirred for 48 h. The reaction was then quenched with a saturated solution of $NaHCO_3$, dropwise until basic, and Et_2O (3 x 10 mL) was used to extract the product. The combined organic layers were dried over Na_2SO_4 and concentrated under vacuum to yield a crude product as a red oil, which was the purified by flash column chromatography to yield the product as a colourless oil (44.7 mg, 0.12 mmol, 72 %).

$[\alpha]_D^{31}$ +12.52 (*c* 0.19 in $CDCl_3$) 54 % ee (*S*); (found (ESI) $[M+Na]^+$, 412.1740. $C_{21}H_{27}NNaO_6$ requires 412.1731); ν_{max} 3433, 2977, 2933, 2833, 1723, 1601, 1506, 1227, 1152, 1024, 822 and 742 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 8.03 (1H, br. s., N***H***), 7.14 (1H, br. s., Ar***H***), 6.93 - 7.00 (2H, m, Ar***H***), 6.79 - 6.93 (5H, m, Ar***H***), 4.40 (1H, sxt, *J* = 5.1 Hz, HOC***H***), 4.16 - 4.25 (2H, m, C***H₂***), 4.07 - 4.11 (2H, m, C***H₂***), 3.77 (3H, s, OC***H₃***), 3.02 (1H, d, *J* = 5.10 Hz, O***H***), 1.52 (9H, s, 3 x C***H₃***); δ_C (100 MHz$CDCl_3$) 154.2, 152.9, 152.5, 146.9, 128.4, 122.7, 121.8, 119.0, 115.6, 114.7, 112.0, 80.4, 70.3, 69.6, 68.7, 55.7 and 28.3; *m/z* (ESI) 388 ($[M - H]^-$, 100 %).

Enantiomeric excess determined by HPLC analysis (Chiralpak IB, 0.46 cm ϕ x 25 cm, iPrOH:hexane 1:9, 1 mL/min, T = 30 °C, 254 nm) *S major* isomer 15.1 min, *R minor* isomer 17.3 min.

17. *tert*-Butyl (2-(3-(4-methoxyphenoxy)-2-oxopropoxy)phenyl)carbamate.



This compound is novel.

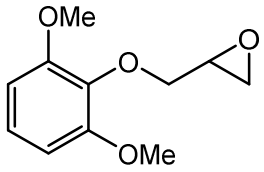
Swern oxidation

A 2M solution of oxalyl chloride in DCM (0.89 mL, 1.78 mmol, 2 eq) was further diluted with DCM (5 mL) and cooled to -78 °C. Anhydrous DMSO (273 mg, 0.25 mL, 3.5 mmol, 4 eq) was then added dropwise and the mixture stirred for 20 min. The alcohol, *tert*-butyl (2-(3-(4-methoxyphenoxy)-2-oxopropoxy)phenyl)carbamate (350 mg, 0.89 mmol, 1 eq), was then added and the mixture was stirred for another 20 min. TEA (629 mg, 0.86 mL, 6.23 mmol, 7 eq) was then added dropwise and

the mixture was stirred for 12 h. The reaction was then quenched with water (10 mL) and the product was extracted using DCM (3 x 10 mL). The combined organic layers were then dried over Na_2SO_4 and concentrated under vacuum to yield crude product, which was subsequently purified by flash column chromatography using a graduated eluent mixture of EtOAc in Hexane (0 - 40 %) to yield pure ketone product as a colourless oil (73.4 mg, 0.19 mmol, 21 %).

(found (ESI): $[M-H]^-$, 386.1607. $C_{21}H_{25}NO_6$ requires 386.1609); ν_{max} 3426, 2977, 2932, 2834, 1723, 1522, 1479, 1451, 1230, 1151, 1026, 824 and 744 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 8.13 (1H, d, *J* = 7.5 Hz, O***H***), 7.39 (1H, br. s., N***H***), 6.99 - 7.05 (1H, m, Ar***H***), 6.92 - 6.98 (1H, m, Ar***H***), 6.88 (4H, s, Ar***H***), 6.78 - 6.84 (1H, m, Ar***H***), 6.76 (1H, dd, *J* = 8.1 Hz, *J* = 1.1 Hz, Ar***H***), 5.05 (2H, s, C***H₂***), 4.73 (2H, s, C***H₂***), 3.80 (3H, s, O***CH₃***), 1.56 (9H, s, 3 x C***H₃***); δ_C(125 MHz, $CDCl_3$) 202.9, 154.8, 152.8, 151.5, 146.2, 129.1, 122.7, 122.4, 119.0, 115.5, 114.9, 112.3, 80.4, 72.7, 55.7 and 28.4; *m/z* (ESI) 386 ($[M - H]^-$, 50 %).

2-((2,6-Dimethoxyphenoxy)methyl)oxirane.



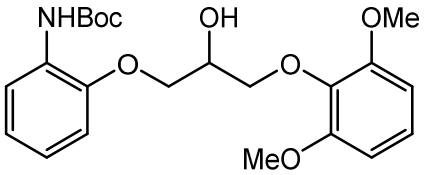
This compound is novel.

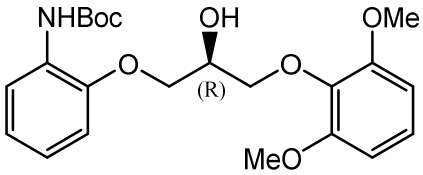
S_N2 reaction to form oxirane

A solution of 2,6 dimethoxyphenol (2.03, 13.2 mmol, 1 eq) and K_2CO_3 (3.67 g, 26.6 mmol, 2 eq) in CH_3CN (30 mL) was heated under reflux at 70 ^oC. To the solution epichlorohydrin (1.5 mL, 1.8 g, 19.5 mmol, 1.5 eq) was added and the mixture stirred for 48 hrs. The mixture was then filtered to remove K_2CO_3 and concentrated under vacuum to give the crude product, which was then purified by flash column chromatography using a graduated eluent mixture of EtOAc in Hexane (0 - 10 %) to yield the pure product as a colourless oil (1.84 g, 8.8 mmol, 68 %).

(found (ESI): $[M+Na]^+$, 233.0795. $C_{11}H_{14}NaO_4^+$ requires 233.0790); ν_{max} 3000, 2939, 2837, 1595, 1475, 1295, 1251, 1105, 1009 and 775 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.00 (1H, t, *J* = 8.4 Hz, Ar***H***), 6.58 (2H, d, *J* = 8.4 Hz, Ar***H***), 4.13 (1H, dd, *J* = 11.4 Hz, *J* = 4.0 Hz, OC***H***H), 4.00 (1H, dd, *J* = 11.4 Hz, *J* = 5.9 Hz, OCH***H***), 3.84 (6H, s, 2 x OC***H₃***), 3.35 - 3.40 (1H, m, C***H***OCHH), 2.81 (1H, t, *J* = 4.6 Hz, CHOC***H***H), 2.63 (1H, dd, *J* = 5.0 Hz, *J* = 2.6 Hz, CHOCH***H***); δ_C (125 MHz, $CDCl_3$) 153.50, 136.83, 124.01, 105.24, 74.14, 56.09, 50.52 and 44.75; *m/z* (ESI) 233 ($[M + Na]^+$, 15%), 249 ($[M + K]^+$, 12%), 217 (5%).

18. *tert*-Butyl (2-(3-(2,6-dimethoxyphenoxy)-2-hydroxypropoxy)phenyl)carbamate 21.





This compound is novel.

Epoxide ring opening

A solution of $PdCl_2$ (3.4 mg, 19 µmol, 0.01 eq), TBAB (154 mg, 0.48 mmol, 0.25 eq) and K_2CO_3 (66 mg, 0.48 mmol, 0.25 eq) in H_2O (8 mL) was heated to 60 °C. To the mixture 2-((2,6-dimethoxyphenoxy)methyl)oxirane (400 mg, 1.9 mmol, 1 eq) and tert-butyl (2-hydroxyphenyl)carbamate (397 mg, 1.9 mmol, 1 eq) were added and the mixture was stirred at 60 °C for 24 hrs. The product was then extracted using EtOAc (3 x 20 mL) and the combined organic layers were dried over Na_2SO_4 before being concentrated under vacuum. The crude product was then purified by flash column chromatography chromatography using a graduated eluent mixture of EtOAc in Hexane (0 - 30 %) to yield the pure product as a colourless oil (480.5 mg, 1.15 mmol, 60.5 %).

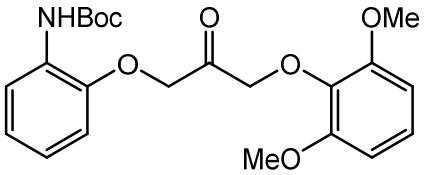
ATH using [(*R*,*R*)Teth-TsDpen RuCl]

To a solution of [(*R*,*R*) Teth-TsDpen RuCl] (1.5 mg, 24 µmol, 0.01 eq) in 5:2 formic acid/triethylamine azeotrope (0.5 mL) the ketone, tert-butyl (2-(3-(2,6-dimethoxyphenoxy)-2-oxopropoxy)phenyl)carbamate (100 mg, 0.24 mmol, 1 eq), was added and the reaction was then stirred overnight. The reaction mixture was then diluted with Et_2O and quenched with $NaHCO_3$ until basic. The product was then extracted with Et_2O (3 x 10 mL) and the combined organic layers were dried over Na_2SO_4 before being concentrated under vacuum to give the crude product. The crude was then purified by flash column chromatography to yield the product as a colourless oil (88.2 mg, 0.21 mmol, 87.5 %).

$[\alpha]_D^{28}$ -9.6 ° (*c* 0.15 in $CDCl_3$) 65 % ee (*R*); (found (ESI): $[M+H]^+$ 442.1832. $C_{22}H_{29}NNaO_7$ requires M, 442.1836); ν_{max} 3433, 2973, 2937, 2838, 1721, 1598, 1520, 1494, 1477, 1445, 1233, 1106 and 744 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 8.07 (1H, br. s, N***H***), 7.03 (1H, t, *J* = 8.5 Hz, Ar***H***), 6.79 - 6.99 (4H, m, Ar***H***), 6.60 (2H, d, *J* = 8.5 Hz, Ar***H***), 4.06 - 4.31 (6H, m, C***H₂***+C***H***+C***H₂***+O***H***), 3.87 (6H, s, (OC***H₃***)$_3$), 1.49 (9H, s, (C***H₃***)$_3$); δ_C (125 MHz, $CDCl_3$) 153.2, 146.9, 137.0, 129.6, 124.0, 122.31, 121.8, 118.5, 115.6, 114.8, 112.1, 105.1, 75.8, 70.2, 68.9, 56.1, 28.3; *m/z* (ESI) 442.2 ($[M+Na]^+$, 100 %).

Enantiomeric excess determined by HPLC analysis (Chiralpak IB, 0.46 cm ϕ x 25 cm, iPrOH:hexane 1:9, 1 mL/min, T = 30 °C, 254 nm) *R major* isomer 13.9 min, *S minor* isomer 15.2 min.

18. *tert*-Butyl (2-(3-(2,6-dimethoxyphenoxy)-2-oxopropoxy)phenyl)carbamate.



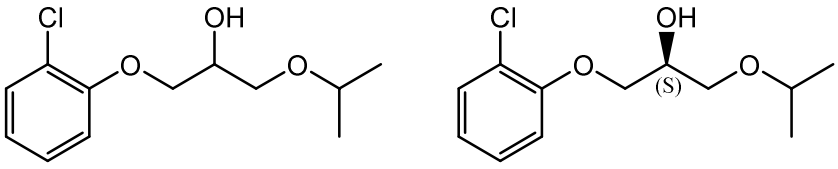
This compound is novel.

Swern oxidation

A 2M solution of oxalyl chloride in DCM (0.95 mL, 1.90 mmol, 2 eq) was further diluted with DCM (5 mL) and cooled to -78 °C. Anhydrous DMSO (296 mg, 0.27 mL, 3.8 mmol, 4 eq) was then added dropwise and the mixture stirred for 20 mins. The alcohol tert-butyl (2-(3-(2,6-dimethoxyphenoxy)-2-hydroxypropoxy)phenyl)carbamate (400 mg, 0.95 mmol, 1 eq) was then added and the mixture was stirred for another 20 mins. TEA (672 mg, 0.93 mL, 6.65 mmol, 7 eq) was then added dropwise and the mixture was stirred for 24 hrs. The reaction was then quenched with water (10 mL) and the product was extracted using DCM (3 x 30 mL). The combined organic layers were then dried over Na_2SO_4 and concentrated under vacuum to yield crude product, which was subsequently purified by flash column chromatography chromatography using a graduated eluent mixture of EtOAc in Hexane (0 - 10 %) to yield pure ketone product as a white solid (316 mg, 0.76 mmol, 80 %).

Mp = 94.7 – 98.1 °C; (found (ESI) $[M+Na]^+$, 440.1679. $C_{22}H_{27}NNaO_7$ requires 440.1680); ν_{max} 3423, 3005, 2981, 2918, 2837, 1739, 1724, 1597, 1476, 1449, 1236, 1153, 1105, 1028, 742 and 670 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 8.11 (1H, d, *J* = 7.2 Hz, O***H***), 7.56 (1H, br. s., N***H***), 7.04 (1H, t, *J* = 8.4 Hz, Ar***H***), 6.96 - 7.01 (1H, m, Ar***H***), 6.93 (1H, td, *J* = 7.7 Hz, *J* = 1.4 Hz, Ar***H***), 6.79 - 6.88 (2H, m, Ar***H***), 6.59 (2H, d, *J* = 8.4 Hz, Ar***H***), 5.35 (2H, s, C***H₂***), 4.63 (2H, s, C***H₂***), 3.82 (6H, s, (OC***H₃***)₂), 1.53 (9H, s, (C***H₃***)₃); δ_C (126 MHz, $CDCl_3$) 204.4, 152.9, 152.7, 146.6, 129.4, 124.5, 122.4, 122.2, 118.8, 115.7, 114.8, 112.9, 105.1, 77.7, 73.1, 56.0, 28.4; *m/z* 440.1 ($[M+Na]^+$, 10%).

19. 1-(2-Chlorophenoxy)-3-isopropoxypropan-2-ol 22.



This compound is reported but not fully characterized.

Epoxide ring opening.

A solution of $PdCl_2$ (6.8 mg, 39 µmol, 0.01 eq), TBAB (312 mg, 0.97 mmol, 0.25 eq) and K_2CO_3 (134 mg, 0.97 mmol, 0.25 eq) in H_2O (16 mL) was heated to 60 °C. To the mixture isopropyl glycidyl ether (451 mg, 3.89 mmol, 1 eq) and 2-chlorophenol (500 mg, 3.89 mmol, 1 eq) were added and the mixture was stirred at 60 °C for 24 hrs. The product was then extracted using EtOAc (3 x 30 mL) and

the combined organic layers were dried over Na_2SO_4 before being concentrated under vacuum. The crude product was then purified by flash column chromatography using a graduated eluent mixture of EtOAc in Hexane (0 - 20 %) to yield the pure product as a colourless oil (490.5 mg, 2.00 mmol, 51.4 %).

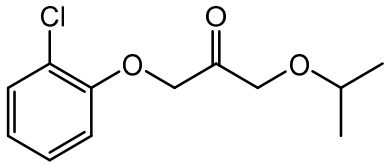
ATH using [(*R*,*R*)Teth-TsDpen RuCl]

To a solution of [(*R*,*R*) Teth-TsDpen RuCl] (0.6 mg, 1 μmol, 0.01 eq) in 5:2 formic acid/triethylamine azeotrope (0.5 ml) the ketone, 1-(2-chlorophenoxy)-3-isopropoxypropan-2-one (25 mg, 0.1 mmol, 1 eq), was added and the reaction was then stirred overnight. The reaction mixture was then diluted with Et_2O and quenched with $NaHCO_3$ until basic. The product was then extracted with Et_2O (3 x 5 mL) and the combined organic layers were dried over Na_2SO_4 before being concentrated under vacuum to give the crude product. The crude was then purified by flash column chromatography to yield the product as a colourless oil (22 mg, 0.09 mmol, 90 %).

$[\alpha]_D^{27}$ +1.83 ^{o} (*c* 0.175 in $CDCl_3$) 59 % ee (*S*); (found (ESI): $[M+Na]^+$, 267.0761. $C_{12}H_{17}{}^{35}ClNaO_3$ requires 267.0758); ν_{max} 3424, 2971, 2931, 2873, 1589, 1485, 1277, 1248, 1127, 1082 and 744 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.34 (1H, dd, *J* = 7.8 Hz, *J* = 1.6 Hz, Ar***H***), 7.14 - 7.23 (1H, m, Ar***H***), 6.84 - 6.99 (2H, m, Ar***H***), 4.16 (1H, sxt, *J* = 5.1 Hz, C***H***), 4.09 (1H, s, C$\boldsymbol{H_b}$), 4.07 (1H, d, *J* = 0.9 Hz, C$\boldsymbol{H_a}$), 3.55 - 3.73 (3H, m, C***H***+C$\boldsymbol{H_2}$), 2.97 (1H, d, *J* = 5.1 Hz, O***H***), 1.16 (6H, d, *J* = 6.2 Hz, (C$\boldsymbol{H_3}$)$_2$); δ_C (75 MHz, $CDCl_3$) 154.2, 130.2, 127.8, 123.0, 121.8, 113.8, 72.3, 70.1, 69.1, 68.7, 22.0; *m/z* (ESI) 267 ($[M+Na]^+$,100), 269 ($[M+Na+2]^+$, 30 %).

Enantiomeric excess determined by HPLC analysis (Chiralpak IB, 0.46 cm ϕ x 25 cm, iPrOH:hexane 1:9, 1 mL/min, T = 30 ^{o}C, 254 nm) *R minor* isomer 5.7 min, *S major* isomer 6.7 min.

19. 1-(2-Chlorophenoxy)-3-isopropoxypropan-2-one.



This compound has been reported but not fully characterized.

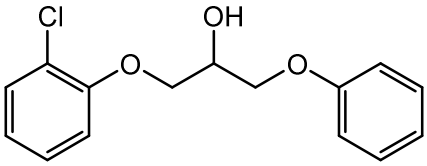
PCC oxidation

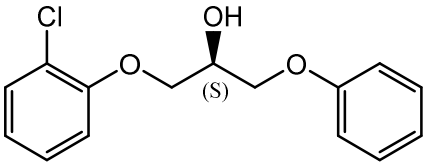
A stirring mixture 1-(2-chlorophenoxy)-3-isopropoxypropan-2-ol (450 mg, 1.85 mmol, 1 eq), sodium acetate (455 mg, 5.55 mmol, 3 eq) and silica (610 mg) in DCM (5 mL) was cooled to 0 ^{o}C. PCC (795mg, 3.68 mmol, 2 eq) was then added in portions and the mixture was allowed to warm to room temperature overnight. The mixture had turned to a thick black tar and was subsequently filtered through silica which was washed with DCM (3 x 30 mL). DCM was then removed under vacuum to yield the crude product, which was then purified by flash column chromatography using a geluent

mixture of EtOAc in Hexane (5 %) to yield the pure product as a white solid (8.2 mg, 0.15 mmol, 8.2 %).

(found(ESI): $[M+Na]^+$, 265.0602. $C_{12}H_{15}{}^{35}ClNaO_3$ requires 265.0602); ν_{max} 2972, 2928, 1739, 1588, 1482, 1447, 1468, 1280, 1250, 1069, 926 and 745 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.39 (1H, dd, *J* = 7.8 Hz, *J* = 1.6 Hz, Ar***H***), 7.16 - 7.25 (1H, m, Ar***H***), 6.96 (1H, td, *J* = 7.7 Hz, *J* = 1.4 Hz, Ar***H***), 6.82 (1H, dd, *J* = 8.3 Hz, *J* = 1.3 Hz, Ar***H***), 4.82 (2H, s, C***H₂***), 4.41 (2H, s, C***H₂***), 3.68 (1H, spt, *J* = 6.1 Hz, C***H***), 1.22 (5H, d, *J* = 6.0 Hz, (C***H₃***)₂); δ_C (126 MHz, $CDCl_3$) 204.2, 153.4, 130.6, 127.8, 123.2, 122.6, 113.7, 73.0, 72.6, 72.3, 21.8, *m/z* (ESI) 265 ($[M+Na]^+$, 50), 267 ($[M+Na+2]^+$, 12%).

20. 1-(2-Chlorophenoxy)-3-phenoxypropan-2-ol 23.





This compound is known and fully characterized.

García, J. I.; García-Marín, H.; Mayoral, J. A.; Pérez, P. *Green. Chem*, **2010**, *12*, 426-434.

Epoxide ring opening

A solution of $PdCl_2$ (5.8 mg, 33 µmol, 0.01 eq), TBAB (267 mg, 0.83 mmol, 0.25 eq) and K_2CO_3 (115 mg, 0.83 mmol, 0.25 eq) in H_2O (12 mL) was heated to 60 °C. To the mixture phenyl glycidyl ether (500 mg, 3.3 mmol, 1 eq) and 2-chlorophenol (424 mg, 3.3 mmol, 1 eq) were added and the mixture was stirred at 60 °C for 24 hrs. The product was then extracted using EtOAc (3 x 10 mL) and the combined organic layers were dried over Na_2SO_4 before being concentrated under vacuum. The crude product was then purified by flash column chromatography using a graduated eluent mixture of EtOAc in Hexane (0 - 20 %) to yield the pure product as a colourless oil (894.4 mg, 3.2 mmol, 97 %).

ATH using [(*R*,*R*)Teth-TsDpen RuCl]

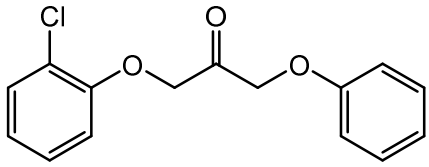
To a solution of [(*R*,*R*) Teth-TsDpen RuCl] (1.2 mg, 1.8 µmol, 0.01 eq) in 5:2 formic acid/triethylamine azeotrope (0.5 mL) the ketone, 1-(2-chlorophenoxy)-3-phenoxypropan-2-one (50 mg, 0.18 mmol, 1 eq), was added and the reaction was then stirred overnight. The reaction mixture was then diluted with Et_2O and quenched with $NaHCO_3$ until basic. The product was then extracted with Et_2O (3 x 10 ml) and the combined organic layers were dried over Na_2SO_4 before being concentrated under vacuum to give the crude product. The crude was then purified by flash column chromatography to yield the product as a colourless oil (28.8 mg, 0.1 mmol, 58 %).

$[\alpha]_D{}^{30}$ +13.57 (*c* 0.07 in $CDCl_3$) 21% ee (*S*); ν_{max} 3395, 3065, 2934, 2877, 1587, 1484, 1237,1061, 1038, 744 and 689 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.35 (1H, dd, *J* = 7.9 Hz, *J* = 1.4 Hz, Ar***H***), 7.24 - 7.32 (2H, m,

Ar***H***), 7.16 - 7.24 (1H, m, Ar***H***), 6.81 - 7.02 (5H, m, Ar***H***), 4.42 (1H, sxt, *J* = 5.3 Hz, HOC***H***), 4.11 - 4.26 (4H, m, HOCH(C***H₂***)$_2$), 2.82 (1H, d, *J* = 5.5 Hz, O***H***); δ_C (126 MHz, $CDCl_3$) 158.3, 153.9, 130.3, 129.5, 127.8, 123.1, 122.0, 121.2, 114.5, 113.8, 69.8, 68.6, 68.4; *m/z* (ESI) 301 ([M + Na]$^+$, 95 %), 302 ([M + 2 + Na]$^+$, 35 %).

Enantiomeric excess determined by HPLC analysis (Chiralpak IB, 0.46 cm ϕ x 25 cm, iPrOH:hexane 7:93, 1 mL/min, T = 30 ^{o}C, 254 nm) *S major* isomer 15.4 min, *R minor* isomer 24.0 min.

20. 1-(2-Chlorophenoxy)-3-phenoxypropan-2-one.



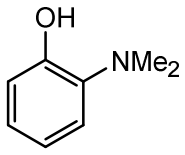
This compound is novel.

PCC oxidation

A stirring mixture of 1-(2-chlorophenoxy)-3-phenoxypropan-2-ol (400 mg, 1.44 mmol, 1 eq), sodium acetate (236 mg, 2.88 mmol, 2 eq) and silica (600 mg) in DCM (7.2 ml) was cooled to 0 ^{o}C. PCC (620 mg, 2.88 mmol, 2 eq) was then added in portions and the mixture was allowed to warm to room temperature overnight. The mixture had turned to a thick black tar and was subsequently filtered through silica which was washed with DCM (3 x 30 mL). DCM was then removed under vacuum to yield the crude product, which was then purified by flash column chromatography using a graduated eluent mixture of EtOAc in Hexane (0 - 10 %) to yield the pure product as a white solid (57.8 mg, 0.21 mmol, 14.6 %).

Mp 85.4 – 86.0 ^{o}C; (found (ESI): [M + Na]$^+$, 299.0445. $C_{15}H_{13}ClNaO_3$ requires 299.0445); ν_{max} 3091, 3064, 2897, 1740, 1588, 1481, 1447, 1360, 1296, 1282, 1237, 1168, 1068, 747 and 689 cm $^{-1}$; δ_H (500M Hz, $CDCl_3$) 7.42 (1H, dd, *J* = 7.9 Hz, J = 1.4 Hz, Ar***H***), 7.29 - 7.35 (2H, m, Ar***H***), 7.20 - 7.25 (1H, m, Ar***H***), 6.96 - 7.06 (2H, m, Ar***H***), 6.94 (2H, d, *J* = 7.9 Hz, Ar***H***), 6.80 - 6.87 (1H, m, Ar***H***), 5.02 (2H, s, C***H₂***), 4.90 (2H, s, C***H₂***); δ_C (126 MHz, $CDCl_3$) 201.9, 157.6, 153.2, 130.7, 129.7, 127.9, 123.3, 122.9, 122.0, 114.6, 113.7, 72.6, 71.6; *m/z* (ESI) 299 ([M + Na]$^+$, 10 %), 301 ([M + Na + 2]$^+$, 3 %).

2-(Dimethylamino)phenol.



This compound is known and fully characterized.

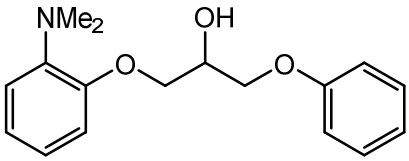
Lewis, R. S.; Wisthoff, M. F.; Grissmerson, J.; Chain, W. J. *Org. Lett,* **2014**, *16*, 3832-3835.

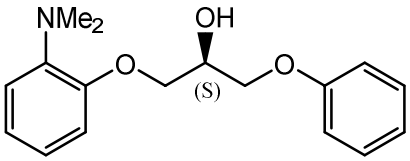
Dimethylation of amine

To a solution of 2-aminophenol (5 g, 45.8 mmol, 1 eq) and 37% formaldehyde, in H_2O (22.4 mL, 0.28 mol, 6 eq), in methanol (200 mL) at 0 °C, $NaCNBH_3$ (8.67 g, 0.14 mol, 3 eq) was added in portions. The reaction was followed by TLC and stirred until completion. Saturated NH_4Cl solution was added dropwise to the mixture to quench the reaction before the methanol was removed under vacuum. The product was extracted using Et_2O (3 x 70 mL) and the combined organic layers were dried over Na_2SO_4 and concentrated to yield the crude product which was purified by flash column chromatography using a graduated eluent mixture of EtOAc in Hexane (0 - 30 %) to give the pure product as a white solid (3.03 g, 22.07 mmol, 48%).

ν_{max} 3030, 2982, 2873,2837, 2800, 2730, 2600, 1589, 1512, 1222, 934 and 759 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.18 (1H, dd, *J* = 7.8 Hz, *J* = 1.2 Hz, Ar***H***), 7.07 (1H, t, *J* = 7.5 Hz, Ar***H***), 6.95 (1H, dd, *J* = 8.0 Hz, *J* = 1.1 Hz, Ar***H***), 6.87 (1H, t, *J* = 7.5 Hz, Ar***H***), 2.67 (6H, s, 2 x C***H₃***); δ_C (75 MHz, $CDCl_3$) 151.5, 140.5, 126.0, 120.7, 119.9, 114.0 and 45.1; *m/z* (ESI) 138.1 ($[M + H]^+$, 75 %).

21. (2-(Dimethylamino)phenoxy)-3-phenoxypropan-2-ol 24.





This compound is novel.

Epoxide ring opening

A solution of $PdCl_2$ (1.9 mg, 10.9 µmol, 0.01 eq), K_2CO_3 (37.3 mg, 0.27 mmol, 0.25 eq) and TBAB (86.9 mg, 0.27 mmol, 0.25 eq) in H_2O (4 ml) was stirred and heated to 60 °C. To the solution phenyl glycidyl ether (180 mg, 0.16 mL, 1.2 mmol, 1.1 eq) and 2-(dimethylamino)phenol (150 mg, 1.09 mmol, 1 eq) was added and the reaction was then stirred for 12 h. The mixture was allowed to cool to room temperature before EtOAc (3 x 10 mL) was used to extract the product. The combined organic layers were dried over Na_2SO_4 and concentrated under vacuum to yield the crude product as a black oil. The crude product was then purified by flash column chromatography using a graduated eluent mixture of EtOAc in Hexane (0 - 100 %) to yield the pure product as a colourless oil (188.2 mg, 0.41 mmol, 38 %).

ATH using [(*R*,*R*)Teth-TsDpen RuCl]

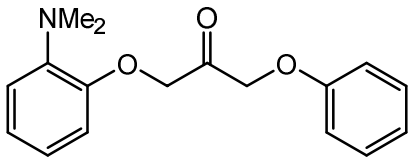
The ketone, 1-(2-(dimethylamino)phenoxy)-3-phenoxypropan-2-one (50 mg, 0.13 mmol, 1 eq), was added to a stirring mixture of [(*R*,*R*) TsDpen-teth RuCl] (0.4 mg, 0.65µmol, 0.005 eq) in 5:2 formic

acid/triethylamine azeotrope (0.5 mL). The mixture was stirred for 12 h before being quenched with a saturated solution of $NaHCO_3$, dropwise, until basic. The product was then extracted using Et_2O (3 x 10 mL), the combined organic layers were dried using Na_2SO_4 and concentrated under vacuum to yield a crude red oil. The crude product was then purified by flash column chromatography to yield the pure product as a colourless oil (20.8 mg, 0.07 mmol, 55.7 %).

$[\alpha]_D^{26}$ +1.28 (c 0.21 in $CDCl_3$) 7 % ee (*R*); (found (ESI): $[M+H]^+$, 288.1596. $C_{17}H_{22}NO_3$ requires 288.1594); ν_{max} 3345, 3062, 2937, 2870, 2832, 2786, 1597, 1495, 1234, 1039, 747 and 690 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.20 - 7.33 (2H, m, Ar***H***), 6.84 - 7.08 (7H, m, Ar***H***), 5.46 (1H, br. s., O***H***), 4.13 - 4.32 (3H, m, C***H₂*** + HOC***H***), 3.99 - 4.13 (2H, m, C***H₂***), 2.78 (6H, s, N(C***H₃***)$_2$); δ_C (100 MHz, $CDCl_3$) 158.6, 152.6, 144.3, 129.5, 124.0, 123.2, 121.0, 118.9, 118.2, 114.6, 74.5, 68.6, 68.3, 43.9; *m/z* (ESI) 288 ($[M + H]^+$, 100 %) and 310 ($[M + Na]^+$, 35 %).

Enantiomeric excess determined by HPLC analysis (Chiralpak IB, 0.46 cm ϕ x 25 cm, EtOH, 0.4 mL/min, T = 30 °C, 254 nm) *S major* isomer 10.9 min, *Rminor* isomer 12.0 min.

21. 1-(2-(Dimethylamino)phenoxy)-3-phenoxypropan-2-one.



This compound is novel.

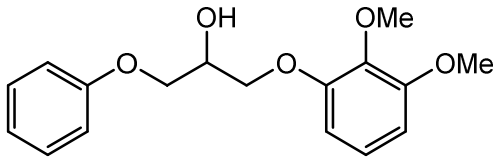
Swern oxidation

A 2M solution of oxalyl chloride in DCM (0.52 mL, 1.04 mmol, 2 eq) was further diluted with DCM (5 mL) and cooled to -78 °C. Anhydrous DMSO (162 mg, 0.15 mL, 2.08 mmol, 4 eq) was then added dropwise and the mixture stirred for 20 min. The alcohol, 1-(2-(dimethylamino)phenoxy)-3-phenoxypropan-2-ol (150 mg, 0.52 mmol, 1 eq) was then added and the mixture was stirred for another 20 min. TEA (369 mg, 0.50 mL, 3.64 mmol, 7 eq) was then added dropwise and the mixture was stirred for 12 h. The reaction was then quenched with water (10 mL) and the product was extracted using DCM (3 x 20 mL). The combined organic layers were then dried over Na_2SO_4 and concentrated under vacuum to yield crude product, which was subsequently purified by flash column chromatography using an eluent of 3:7 EtOAc to hexane ratio which yielded the pure ketone product as a colourless oil (61.4 mg, 0.22 mmol, 42.3 %).

(found (ESI): $[M+H]^+$, 286.1438. $C_{17}H_{20}NO_3$ requires 286.1438); ν_{max} 3062, 2941, 2865, 2830, 2781, 1740, 1596, 1494, 1237, 1113, 1050 and 746 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.30 - 7.37 (2H, m, Ar***H***), 6.98 - 7.06 (3H, m, Ar***H***), 6.91 - 6.98 (4H, m, Ar***H***), 6.79 (1H, d, *J* = 7.8 Hz, Ar***H***), 4.97 (2H, s, C***H₂***), 4.94 (2H,

s, C***H₂***), 2.85 (6H, s, N(C***H₃***)$_2$; δ_C (126 MHz, $CDCl_3$) 202.6, 157.5, 150.3, 143.0, 129.6, 122.6, 122.2, 121.8, 118.6, 114.5, 113.8, 72.1, 71.5 and 43.2; *m/z* (ESI) 318 (M^+ + 23, 100 %), 318 ($[M + H]^+$, 40 %).

22. 1-(2,3-Dimethoxyphenoxy)-3-phenoxypropan-2-ol 25.



This compound is novel

Epoxide ring opening

A solution of K_2CO_3 (110 mg, 0.79 mmol, 0.25 eq), TBAB (257.5 mg, 0.79 mmol, 0.25 eq) and $PdCl_2$ (5 mg, 0.03 mmol) in H_2O (25 mL) was heated to 60 °C and stirred. To the mixture 2,3 dimethoxyphenol (565 mg, 0.48 mL, 3.67 mmol, 1.1 eq) and phenyl glycidyl ether (500 mg 0.45 mL, 3.34 mmol, 1 eq) were added and the reaction mixture was allowed to stir overnight. Stirring was suspended and the mixture was allowed to cool to rt before EtOAc (3 x 15 mL) was added to extract the product. The combined organic layers were then dried over Na_2SO_4 and concentrated under vacuum to yield the crude product as a dark oil. The crude product was then purified by flash chromatography using a graduated EtOAc/hexane eluent (0 – 20% EtOAc in Hexane) to yield the pure product as a colourless oil (796.8 mg, 2.53 mmol, 75.8%).

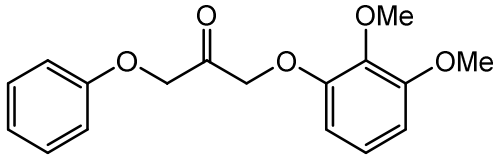
ATH using [(*R*,*R*)Teth-TsDpen RuCl]

[(*R*,*R*)Teth-TsDpen RuCl] (5.2 mg, 8.4 µmol, 0.05 eq) was added to a 5:2 formic acid/triethylamine azeotrope (0.3 mL) and the mixture was stirred for 30 min. The ketone (52.8 mg, 0.17 mmol, 1 eq) was then added and the mixture was stirred for 12 h. After this time stirring was suspended and $NaHCO_3$ saturated solution (5 mL) was added to neutralise the formic acid. The product was then extracted using Et_2O (3 x 5 mL), the combined organic layers were dried over Na_2SO_4 and concentrated under vacuum to yield the crude product as a dark red oil. The crude product was purified by flash chromatography to yield the product as a colourless oil (32.8 mg, 0.107 mmol, 63.5 %).

(found (EI): $[M+Na]^+$, 327.1203. $C_{17}H_{20}O_5Na$ requires 327.12084); ν_{max} 3420, 2937, 1596, 1493,1240, 1101 and 731 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 7.25 – 7.33 (2H, m, Ar**H**), 6.90 – 7.03 (4H, m, Ar**H**), 6.59 – 6.67 (2H, m, Ar**H**), 4.34 – 4.44 (1H, quin, J = 5.1 Hz, **H**COH), 4.14 – 4.25 (4H, m, C**H₂**CHOHC**H₂**), 3.86 (3H, s, OC**H₃**), 3.84 (3H, s, OC**H₃**), 3.01 (1H, d, J = 4.9 Hz, O**H**); δ_C (75 MHz, $CDCl_3$), 158.45, 153.70, 152.54, 129.50, 124.04, 123.84, 121.17, 114.53, 108.06, 106.19, 104.09, 70.96, 68.72, 61.00; *m/z* (EI) 327.1 $[M+Na]^+$.

Enantiomeric excess determined by HPLC analysis (Chiralpak IB, 0.46 cm ϕ x 25 cm, iPrOH:hexane 1:9, 1 mL/min, T = 30 °C, 254 nm) *R* isomer 16.6 min, *S* isomer 22.0 min.

22. 1-(2,3-Dimethoxyphenoxy)-3-phenoxypropan-2-one.



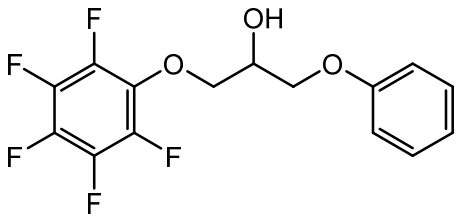
This compound is novel

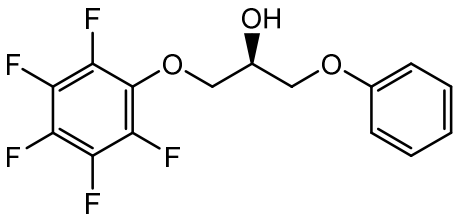
Swern Oxidation

A 2M solution of oxalyl chloride in DCM (1.31 mL, 2.6 mmol, 2 eq) was further diluted with DCM (20mL) and cooled to -78 °C. Anhydrous DMSO (410 mg, 0.37mL, 5.26 mmol, 4 eq) was then added dropwise and the mixture stirred for 20 min. The alcohol, 1-(2,3-dimethoxyphenoxy)-3-phenoxypropan-2-ol (385.5 mg, 1.26 mmol, 1 eq,) was then added and the mixture was stirred for another 20 min. TEA (930 mg, 1.28 mL, 9.21 mmol, 7 eq) was then added dropwise and the mixture was stirred for 12 h. The reaction was then quenched with water (10 mL) and the product was extracted using DCM (3 x 10 mL). The combined organic layers were then dried over Na_2SO_4 and concentrated under vacuum to yield the crude product, which was subsequently purified by flash column chromatography using a graduated EtOAc/hexane eluent (0 – 20% EtOAc in Hexane) to yield the pure ketone product as a white solid (199.1 mg, 0.66 mmol, 52%).

Mp 68.8 – 69.2 °C; (found (ESI): $[M+Na]^+$, 325.1046. $C_{17}H_{18}NaO_5$ requires 325.1052); ν_{max} 2941, 2890, 2832, 1735, 1600, 1495, 1473, 1421, 1247, 1115, 997 and 720 cm^{-1}; δ_H (400 MHz, $CDCl_3$) 7.27 - 7.34 (2H, m, Ar***H***), 6.88 - 7.04 (4H, m, Ar***H***), 6.65 (1H, dd, *J* = 8.4 Hz, *J* = 1.2 Hz, Ar***H***), 6.50 (1H, dd, *J* = 8.3 Hz, *J* = 1.2 Hz, Ar***H***), 4.93 (2H, s, C***H₂***), 4.92 (2H, s, C***H₂***), 3.90 (3H, s, OC***H₃***), 3.87 (3H, s, OC***H₃***); δ_C (100 MHz, $CDCl_3$) 129.71, 123.78, 121.91, 114.56, 107.74, 106.76, 73.30, 71.53, 61.01 and 56.10; *m/z* (ESI) 325 $[M+Na]^+$.

23. 1-(Pentafluorophenoxy)-3-phenoxypropan-2-ol 26.





This compound is novel

Epoxide ring opening

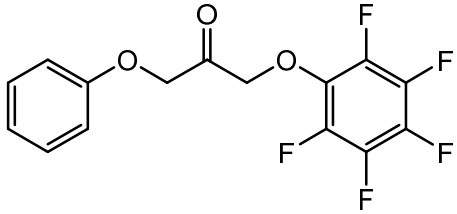
A solution of K_2CO_3 (167 mg, 1.67 mmol, 0.25 eq), TBAB (538 mg, 1.67 mmol, 0.25 eq) and $PdCl_2$ (12 mg, 0.067 mmol) in H_2O (25 mL) was heated to 60 ^oC and stirred. To the mixture pentafluorophenol (1.23 g, 6.67 mmol, 1.0 eq) and phenyl glycidyl ether (1.00 g, 6.67 mmol, 1.0 eq) were added and the reaction mixture was allowed to stir overnight. Stirring was suspended and the mixture was allowed to cool to rt before EtOAc (3 x 15 mL) was added to extract the product. The combined organic layers were then dried over Na_2SO_4 and concentrated under vacuum to yield the crude product as a colorless oil. The crude product was then purified by flash chromatography using a graduated EtOAc/hexane eluent (0 – 20% EtOAc in Hexane) to yield the pure product as a colorless oil (759 mg, 2.29 mmol, 34.2%).

ATH using [(*R*,*R*)Teth-TsDpen RuCl]

[(*R*,*R*)Teth-TsDpen RuCl] (1.0 mg, 1.6 µmol, 0.05 eq) was added to a 5:2 formic acid/triethylamine azeotrope (0.3 mL) and the mixture was stirred for 30 min. The ketone (107 mg, 0.322 mmol, 1.0 eq) was then added and the mixture was stirred for 12 h. After this time full conversion was observed and stirring was suspended and $NaHCO_3$ saturated solution (5 mL) was added to neutralise the formic acid. The product was then extracted using Et_2O (3 x 5 mL), the combined organic layers were dried over Na_2SO_4 and concentrated under vacuum to yield the crude product as a dark red oil. The crude product was purified by flash chromatography to yield the product as a colourless oil. (found (EI): $[M+Na]^+$, 357.0521. $C_{15}H_{11}F_5O_3Na$ requires 357.0521); ν_{max} 3409, 1599, 1512, 1242, 1031, 994, 754, 691 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.35 – 7.25 (2H, m, Ar**H**), 6.95 – 6.90 (1H, m, Ar**H**), 6.90 – 6.85 (2H, d, J = 11.8, Ar**H**), 4.35 – 4.25 (3H, m, C**H**$_2$C**H**OH), 4.12 (2H, d, J = 6 Hz, CH_2), 2.85 (1H, brs, O**H**); δ_C (125 MHz, $CDCl_3$), 158.26 (ipso of C_6F_5), 142.8-142.5 (m), 140.8-140.5 (m), 139.3-138.5 (m), 137.2-136.4 (m), 133.7-133.4 (m), 135.58 129.59, 121.75, 114.41, 69.12, 68.10; *m/z* (EI) 356.8 $[M+Na]^+$.

Enantiomeric excess (27% ee (*S*)) determined by HPLC analysis (Chiralpak IB, 0.46 cm ϕ x 25 cm, iPrOH:hexane 1:9, 1 mL/min, T = 30 ^oC, 254 nm) *S* isomer 8.46 min, *R* isomer 12.68 min. Absolute configuration established via preparation of a standard (TJB644).

23. 1-(Pentafluorophenoxy)-3-phenoxypropan-2-one.



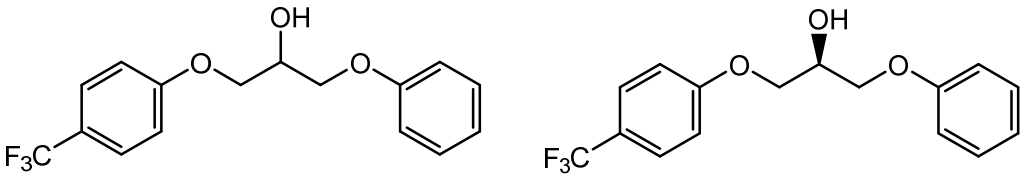
This compound is novel

Swern Oxidation

A 2M solution of oxalyl chloride in DCM (0.805 mL, 1.61 mmol, 2.0 eq) was further diluted with DCM (7.5 mL) and cooled to -78 °C. Anhydrous DMSO (252 mg, 3.22 mmol, 4.0 eq) was then added dropwise and the mixture stirred for 20 min. The alcohol, 1-(Pentafluorophenoxy)-3-phenoxypropan-2-ol (3268 mg, 0.806 mmol, 1.0 eq,) was then added and the mixture was stirred for another 20 min. TEA (571 mg, 5.64 mmol, 7.0 eq) was then added dropwise and the mixture was stirred for 12 h. The reaction was then quenched with water (10 mL) and the product was extracted using DCM (3 x 10 mL). The combined organic layers were then dried over Na_2SO_4 and concentrated under vacuum to yield the crude product, which was subsequently purified by flash column chromatography using a graduated EtOAc/hexane eluent (0 – 20% EtOAc in Hexane) to yield the pure ketone product as a waxy solid (212 mg, 0.642 mmol, 79.7%).

(found (ESI): $[M+Na]^+$, 355.0356. $C_{15}H_9F_5O_3Na$ requires 355.0364); ν_{max} 1745, 1598, 1512, 1243, 1048, 995, 754, 691 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.34 (2H, t, J = 9.0, ArH), 7.04 (1H, t, J = 9.0, ArH), 6.91 (2H, d, J = 9.0, ArH), 5.15 (2H, s, C***H₂***), 4.78 (2H, s, C***H₂***); δ_C (125 MHz, $CDCl_3$) 201.05, 157.24, 129.86, 122.29, 114.43, 76.19 (t, J = 4), 71.56, Positions of C atoms adjacent to F could not be determined due to multiple couplings; *m/z* (ESI) 355 $[M+Na]^+$.

24. 1-((4-Trifluoromethyl)phenoxy)-3-phenoxypropan-2-ol 27.



This compound is novel

Epoxide ring opening

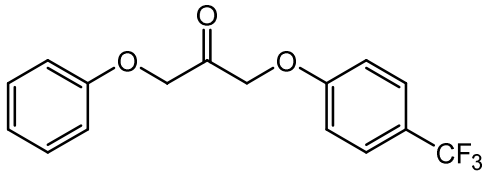
A solution of K_2CO_3 (167 mg, 1.67 mmol, 0.25 eq), TBAB (538 mg, 1.67 mmol, 0.25 eq) and $PdCl_2$ (12 mg, 0.067 mmol) in H_2O (25 mL) was heated to 60 °C and stirred. To the mixture 4-(trifluoromethyl)phenol (1.08 g, 6.67 mL, 1.0 eq) and phenyl glycidyl ether (1.00 g, 6.67 mmol, 1.0 eq) were added and the reaction mixture was allowed to stir overnight. Stirring was suspended and the mixture was allowed to cool to rt before EtOAc (3 x 15 mL) was added to extract the product. The combined organic layers were then dried over Na_2SO_4 and concentrated under vacuum to yield the crude product as a dark oil. The crude product was then purified by flash chromatography using a graduated EtOAc/hexane eluent (0 – 20% EtOAc in Hexane) to yield the pure product as a colourless oil (831 mg, 2.68 mmol, 40.2%).

ATH using [(*R*,*R*)Teth-TsDpen RuCl].

[(*R*,*R*)Teth-TsDpen RuCl] (1.0 mg, 1.6 µmol, 0.05 eq) was added to a 5:2 formic acid/triethylamine azeotrope (0.3 mL) and the mixture was stirred for 30 min. The ketone (99.8 mg, 0.322 mmol, 1.0 eq) was then added and the mixture was stirred for 12 h. After this time full conversion was observed and stirring was suspended and $NaHCO_3$ saturated solution (5 mL) was added to neutralise the formic acid. The product was then extracted using Et_2O (3 x 5 mL), the combined organic layers were dried over Na_2SO_4 and concentrated under vacuum to yield the crude product as a dark red oil. The crude product was purified by flash chromatography to yield the product as a colourless oil. (found (EI): $[M+Na]^+$, 335.0867. $C_{16}H_{15}F_3O_3Na$ requires 335.0865); ν_{max} 3412, 2934, 1613, 1518, 1324, 1239, 1108, 834, 753 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.55 (2H, d, J = 12.0 Hz, ArH), 7.30 (2H, t, J = 12.0 Hz, ArH), 7.04-6.95 (3H, m, ArH), 6.92 (2H, d, J = 12.0 Hz, ArH), 4.45-4.38 (1H, m, C**H**OH), 4.22-4.10 (4H, m, C**H₂**CHOHC**H₂**), 2.65 (1H, d, J = 6.0 Hz, OH); δ_C (125 MHz, $CDCl_3$), 160.87, 158.30, 129.63, 127.00 (q, J = 8.0 Hz), 124.4 (q, J = 275 Hz), 123.62 (q, J = 25 Hz), 121.46, 114.57, 68.95, 68.70, 68.48; *m/z* (EI) 334.8 $[M+Na]^+$.

Enantiomeric excess (10% ee (*S*)) determined by HPLC analysis (Chiralpak IB, 0.46 cm ϕ x 25 cm, iPrOH:hexane 1:9, 1 mL/min, T = 30 °C, 254 nm) *R* isomer 11.15 min, *S* isomer 21.75 min. Absolute configuration established via preparation of a standard (TJB648).

24. 1-((4-Trifluoromethyl)phenoxy)-3-phenoxypropan-2-one.



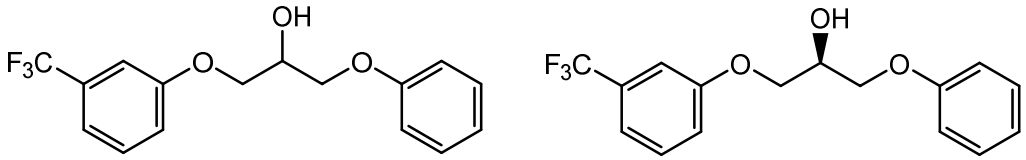
This compound is novel

Swern Oxidation

A 2M solution of oxalyl chloride in DCM (0.805 mL, 1.62 mmol, 2.0 eq) was further diluted with DCM (7.5 mL) and cooled to -78 °C. Anhydrous DMSO (252 mg, 3.33 mmol, 4.0 eq) was then added dropwise and the mixture stirred for 20 min. The alcohol, 1-(4-(trifluoromethyl)phenoxy)-3-phenoxypropan-2-ol (250 mg mg, 0.806 mmol, 1.0 eq,) was then added and the mixture was stirred for another 20 min. TEA (571 mg, 5.64 mmol, 7.0 eq) was then added dropwise and the mixture was stirred for 12 h. The reaction was then quenched with water (10 mL) and the product was extracted using DCM (3 x 10 mL). The combined organic layers were then dried over Na_2SO_4 and concentrated under vacuum to yield the crude product, which was subsequently purified by flash column chromatography using a graduated EtOAc/hexane eluent (0 – 20% EtOAc in Hexane) to yield the pure ketone product as a waxy solid (202 mg, 0.656 mmol, 81.5%).

(found (ESI): $[M+Na]^+$, 333.0704. $C_{16}H_{13}F_3O_3Na$ requires 333.0709); ν_{max} 1745, 1517, 1328, 907, 732 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.57 (2H, d, *J* = 12.0, ArH), 7.33 (2H, t, J = 11.5, ArH), 7.04 (1H, t, J = 12.0, ArH**)** 6.97 (2H, d, *J* = 12.0, ArH), 6.93 (1H, d, *J* = 12.0 Hz, ArH), 4.99 (2H, s, C**H₂**), 4.84 (2H, s, C**H₂**); δ_C (120 MHz, $CDCl_3$) 201.75, 159.99, 157.42, 129.87, 127.19 (q, J = 3.5), 124.16 (q, J = 33 Hz), 124.14 (q, J = 280), 114.66, 114.54, 71.75, 71.34; *m/z* (ESI) 311.8 $[M+H]^+$.

25. 1-((3-Trifluoromethyl)phenoxy)-3-phenoxypropan-2-ol 28.



This compound is novel

Epoxide ring opening

A solution of K_2CO_3 (167 mg, 1.67 mmol, 0.25 eq), TBAB (2538 mg, 1.67 mmol, 0.25 eq) and $PdCl_2$ (12 mg, 0.067 mmol) in H_2O (25 mL) was heated to 60 ^oC and stirred. To the mixture (3-trifluoromethyl)phenol (1.08 g, 6.67 mmol, 1.0 eq) and phenyl glycidyl ether (1.00 g, 6.67 mmol, 1.0 eq) were added and the reaction mixture was allowed to stir overnight. Stirring was suspended and the mixture was allowed to cool to rt before EtOAc (3 x 15 mL) was added to extract the product. The combined organic layers were then dried over Na_2SO_4 and concentrated under vacuum to yield the crude product as a dark oil. The crude product was then purified by flash chromatography using a graduated EtOAc/hexane eluent (0 – 20% EtOAc in Hexane) to yield the pure product as a white solid (839 mg, 2.71 mmol, 40.6%).

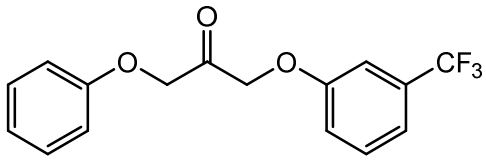
ATH using [(*R*,*R*)Teth-TsDpen RuCl].

[(*R*,*R*)Teth-TsDpen RuCl] (1.0 mg, 1.6 µmol, 0.05 eq) was added to a 5:2 formic acid/triethylamine azeotrope (0.3 mL) and the mixture was stirred for 30 min. The ketone (99.8 mg, 0.322 mmol, 1.0 eq) was then added and the mixture was stirred for 12 h. After this time full conversion was observed and stirring was suspended and $NaHCO_3$ saturated solution (5 mL) was added to neutralise the formic acid. The product was then extracted using Et_2O (3 x 5 mL), the combined organic layers were dried over Na_2SO_4 and concentrated under vacuum to yield the crude product as a dark red oil. The crude product was purified by flash chromatography to yield the product as a white solid. (found (EI): $[M+Na]^+$, 335.0866. $C_{16}H_{15}F_3O_3Na$ requires 335.0865); ν_{max} 3411, 2937, 1598, 1494, 1449, 1327, 1236, 1121, 1043, 751, 658 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.38 (1H, t, J = 12.0 Hz, ArH), 7.28 (2H, t, J = 12.0 Hz, ArH), 7.22 (1H, d, J = 14 Hz, ArH), 7.18 (1H, brs, ArH), 7.10-7.05 (2H, m, Arh), 6.98 (1H, t, J

= 12.0, ArH), 6.90 (2H, d, J = 14.0, ArH), 4.40-4.35 (1H, m, C**H**OH), 4.20-4.05 (4H, m, C**H₂**CHOHC**H₂**), 2.85 (1H, brs, O**H**); δ_C (125 MHz, $CDCl_3$), 158.61, 158.37, 131.90 (q, J = 32 Hz), 130.14, 129.56, 123.9 (q, J = 275 Hz), 121.45, 118.04, 117.98 (q, J = 6 Hz), 114.60, 111.50 (q, J = 3.5 Hz), 69.09, 68.74, 68.57 ; *m/z* (EI) 334.8 $[M+Na]^+$.

Enantiomeric excess (28% ee (*S*)) was determined by HPLC analysis (Chiralpak IB, 0.46 cm ϕ x 25 cm, iPrOH:hexane 1:9, 1 mL/min, T = 30 °C, 254 nm) *S* isomer 9.62 min, *R* isomer 16.10 min. Absolute configuration established via preparation of a standard (TJB647).

25. 1-((3-Trifluoromethyl)phenoxy)-3-phenoxypropan-2-one.



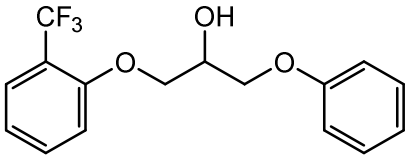
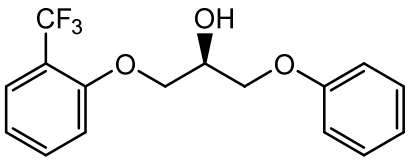
This compound is novel

Swern Oxidation

A 2M solution of oxalyl chloride in DCM (0.805 mL, 1.61 mmol, 2.0 eq) was further diluted with DCM (7.5 mL) and cooled to -78 °C. Anhydrous DMSO (252 mg, 3.22 mmol, 4.0 eq) was then added dropwise and the mixture stirred for 20 min. The alcohol, 1-((3-Trifluoromethyl)phenoxy)-3-phenoxypropan-2-ol (250 mg, 0.806 mmol, 1.0 eq,) was then added and the mixture was stirred for another 20 min. TEA (571 mg, 5.64 mmol, 7.0 eq) was then added dropwise and the mixture was stirred for 12 h. The reaction was then quenched with water (10 mL) and the product was extracted using DCM (3 x 10 mL). The combined organic layers were then dried over Na_2SO_4 and concentrated under vacuum to yield the crude product, which was subsequently purified by flash column chromatography using a graduated EtOAc/hexane eluent (0 – 20% EtOAc in Hexane) to yield the pure ketone product as a waxy solid (218 mg, 0.708 mmol, 87.9%).

(found (ESI): $[M+Na]^+$, 333.0705. $C_{16}H_{13}F_3O_3Na$ requires 333.0709); ν_{max} 3064, 2920, 1742, 1597, 1453, 1428, 1267, 1162, 1122, 1064, 1007, 754, 693 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.42 (1H, d, J = 9.0, ArH), 7.33 (2H, d, J = 9.0, ArH), 7.27 (1H, d, J = 9.0, ArH), 7.14 (1H, brs, ArH), 7.09-7.02 (2H, m, ArH), 6.93 (2H, d, J = 9.0, ArH), 4.97 (2H, s, C**H₂**), 4.85 (2H, s, C**H₂**); δ_C (125 MHz, $CDCl_3$) 201.80, 157.74, 157.45, 132.2 (q, J = 33), 130.30, 129.86, 123.7 (q, J = 260), 122.22, 118.71 (q, J = 4), 117.98, 114.53, 111.74 (q, J = 4), 71.74, 71.52; *m/z* (ESI) 311.8 $[M+H]^+$.

26. 1-((2-Trifluoromethyl)phenoxy)-3-phenoxypropan-2-ol 29.

This compound is novel

Epoxide ring opening

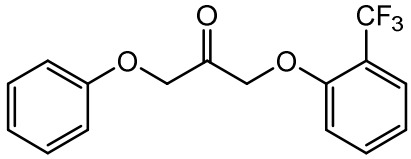
A solution of K_2CO_3 (213 mg, 1.54 mmol, 0.25 eq), TBAB (496 mg, 1.54 mmol, 0.25 eq) and $PdCl_2$ (11 mg, 0.062 mmol) in H_2O (25 mL) was heated to 60 ^oC and stirred. To the mixture (2-trifluoromethyl)phenol (1.00 mg, 6.17 mmol, 1.0 eq) and phenyl glycidyl ether (926 mg, 6.17 mmol, 1.0 eq) were added and the reaction mixture was allowed to stir overnight. Stirring was suspended and the mixture was allowed to cool to rt before EtOAc (3 x 15 mL) was added to extract the product. The combined organic layers were then dried over Na_2SO_4 and concentrated under vacuum to yield the crude product as a dark oil. The crude product was then purified by flash chromatography using a graduated EtOAc/hexane eluent (0 – 20% EtOAc in Hexane) to yield the pure product as a colourless oil (558 mg, 1.80 mmol, 27.0%).

ATH using [(*R*,*R*)Teth-TsDpen RuCl].

[(*R*,*R*)Teth-TsDpen RuCl] (1.0 mg, 1.6 µmol, 0.05 eq) was added to a 5:2 formic acid/triethylamine azeotrope (0.3 mL) and the mixture was stirred for 30 min. The ketone (99.8 mg, 0.322 mmol, 1.0 eq) was then added and the mixture was stirred for 12 h. After this time full conversion was observed and stirring was suspended and $NaHCO_3$ saturated solution (5 mL) was added to neutralise the formic acid. The product was then extracted using Et_2O (3 x 5 mL), the combined organic layers were dried over Na_2SO_4 and concentrated under vacuum to yield the crude product as a dark red oil. The crude product was purified by flash chromatography to yield the product as a colourless oil. (found (EI): $[M+Na]^+$, 335.0867. $C_{16}H_{15}F_3O_3Na$ requires 335.0865); ν_{max} 3389, 2936, 1608, 1496, 1459, 1321, 1242, 1058, 1037, 753 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.55 (1H, d, j = 10.0 Hz, ArH), 7.48 (1H, t, J= 10 Hz, ArH), 7.25-7.20 (2H, m, ArH), 7.05-6.85 (5H, m, ArH), 4.45-4.40 (1H, m, C**H**OH), 4.25-4.20 (2H, m, CH_2), 4.15-4.10 (2H, m, CH_2), 2.70 (1H, brs, OH); δ_C (125 MHz, $CDCl_3$), 161.77, 158.30, 136.10, 133.46, 129.60, 127.10 (q, J = 5.0 Hz), 123.70 (q, J = 275 Hz), 121.31, 120.70, 118.90 (q, J = 30 Hz), 114.55, 112.94, 69.27, 68.55, 68.25, ; *m/z* (EI) 334.8 $[M+Na]^+$.

Enantiomeric excess (50% ee (*S*)) determined by HPLC analysis (Chiralpak IB, 0.46 cm ϕ x 25 cm, iPrOH:hexane 1:9, 1 mL/min, T = 30 ^oC, 254 nm) *S* isomer 9.77 min, *R* isomer 17.99 min. Absolute configuration established via preparation of a standard (TJB646).

26. 1-((2-Trifluoromethyl)phenoxy)-3-phenoxypropan-2-one.



This compound is novel

Swern Oxidation

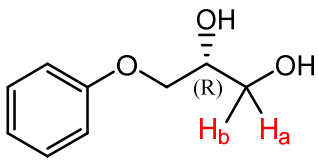
A 2M solution of oxalyl chloride in DCM (0.805 mL, 1.61 mmol, 2.0 eq) was further diluted with DCM (7.5 mL) and cooled to -78 °C. Anhydrous DMSO (252 mg, 3.22 mmol, 4.0 eq) was then added dropwise and the mixture stirred for 20 min. The alcohol, 1-((2-Trifluoromethyl)phenoxy)-3-phenoxypropan-2-ol (250 mg, 0.806 mmol, 1.0 eq,) was then added and the mixture was stirred for another 20 min. TEA (571 mg, 5.64 mmol, 7.0 eq) was then added dropwise and the mixture was stirred for 12 h. The reaction was then quenched with water (10 mL) and the product was extracted using DCM (3 x 10 mL). The combined organic layers were then dried over Na_2SO_4 and concentrated under vacuum to yield the crude product, which was subsequently purified by flash column chromatography using a graduated EtOAc/hexane eluent (0 – 20% EtOAc in Hexane) to yield the pure ketone product as a waxy solid (203 mg, 0.659 mmol, 81.9%.).

(found (ESI): $[M+Na]^+$, 333.0708. $C_{16}H_{15}F_3O_3Na$ requires 333.0709); ν_{max} 3072, 2904, 1745, 1591, 1494, 1321, 119, 755 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.64 (1H, d, J = 10.0, Ar**H**), 7.52 (1H, t, J = 10.0, Ar**H**), 7.32 (2H, t, J = 9.5, Ar**H**), 7.11 (1H, d, J = 10, Ar**H**), 7.02 (1H, d, J = 10, Ar**H**), 6.93 (2H, d, J = 10, Ar**H**), 6.88 (1H, d, J = 10, Ar**H**), 5.03 (2H, s, C**H₂**), 4.86 (2H, s, C**H₂**); δ_C (125 MHz, $CDCl_3$) 201.37, 157.60, 155.10, 133.56, 129.73, 127.53 (q, j = 5.5), 124.66 (q, J = 270), 121.91, 121.54, 119.20 (q, J = 31), 114.57, 112.54, 72.07, 71.37; *m/z* (ESI) 333 $[M+Na]^+$.

Formation of asymmetric standards.

For all except the OPh/OiPr combination, standards were prepared via the (*R*)-configuration diol, which is described below.

(*R*)-3-Phenoxypropane-1,2-diol.



This compound is known and fully characterized.

Babu, H. V.; Muralidharan, K. *Dalton. Trans*, **2013**, *42*, 1238-1248.

Sharpless Dihydroxylation

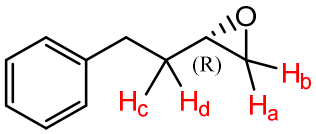
A solution of ADmix-α (1.4 g) in *t*-butanol (5 mL) and H_2O (5 mL) was stirred and cooled to 0 °C. To the solution allyl phenyl ether (0.137 mL, 134 mg, 1.00 mmol, 1 eq) was added and the mixture was stirred for 72 hrs, coming to room temperature. Na_2SO_3 (1.6 g) was added to the reaction mixture causing a separation of layers. The organic layer was removed and remaining organic material was extracted further with EtOAc (3 x 10 mL). The combined organic layers were washed with water (10 mL) and brine (10 mL), dried over Na_2SO_4 and concentrated to give the crude product. The crude product was then purified by flash column chromatography using an eluent mixture of 1:1 EtOAc and hexane to give the pure product as a white solid (109.8 mg, 0.65 mmol, 65 %).

Mp 54.3 – 55.5 °C; $[\alpha]_D^{28}$ -1.8 ° (*c* 0.415 in EtOH) 79.4 % ee (*R*) (lit. (*Tetrahedron Lett*. **1993**, *34*, 2267-2270)$[\alpha]_D$ +8.6 (*c* 1.1 in EtOH); ν_{max} 3445, 3266, 3060, 3039, 2932, 2896, 1599, 1586, 1496, 1489, 1465, 1456, 1238, 1045 and 755 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.27 - 7.37 (2H, m, Ar***H***), 6.98 (1H, t, *J* = 7.4 Hz, Ar***H***), 6.92 (2H, d, *J* = 7.9 Hz, ArH), 4.09 - 4.16 (1H, m, HOC***H***), 4.01 - 4.09 (2H, m, C***H₂***), 3.81 - 3.89 (1H, m, $OHCH_a\boldsymbol{H_b}$), 3.72 - 3.80 (1H, m, $HOCH_b\boldsymbol{H_a}$), 2.66 (1H, d, *J* = 4.7 Hz, O***H***), 2.09 (1H, t, *J* = 6.0 Hz, O***H***); δ_C(126 MHz, $CDCl_3$) 158.4, 129.6, 121.4, 114.5, 70.4, 69.1, 63.7; *m/z* 191 ($[M+Na]^+$, 35%).

Ref: Wang, Z.-M.; Zhang, X.-L.; Sharpless, K. B. *Tetrahedron Lett*. **1993**, *34*, 2267-2270

Enantiomeric excess determined by HPLC analysis (Chiralcel OD-H 0.46cm x 25cm, iPrOH:Hexane 2:8, 1mL/min, 30 °C 254nm) *R major* isomer 8.4 min, *S minor* isomer 14.2 min.

(*R*)-2-(Phenoxymethyl)oxirane.



This compound is known and fully characterized.

Kolb, H. C.; Sharpless, K. B. *Tetrahedron*, **1992**, *48*, 10515-10530

Epoxidation

Trimethoxy ortho acetate (518 mg, 0.55 mL, 4.32, 1.2 eq) was added to a solution of PPTS (9 mg, 36 µmol, 0.01 eq) and (*R*)-3-phenoxypropane-1,2-diol (600 mg, 3.6 mmol 1 eq) in DCM (5.4 mL) and the mixture was stirred for 30 mins. Volatiles were then removed under vacuum and the residue was then dissolved in DCM (5.4 mL). Acetyl bromide (531 mg, 0.32 mL, 4.32 mmol, 1.2 eq) was then added dropwise and the mixture was stirred for 1 hr before removing volatiles under vacuum to give an orange oil. The orange oil was then dissolved in MeOH (12 mL), before adding K_2CO_3 (646 mg, 4.68 mmol, 1.3 eq) and stirring for 24 hrs. The resultant mixture was poured onto saturated NH_4Cl solution (20 mL) and the product was extracted with DCM (3 x 20 mL). The combined organic layers were dried over Na_2SO_4 and concentrated under vacuum to give the crude product, which was then

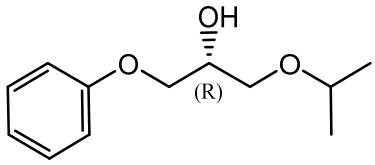
purified by column chromatography to yield pure product as a colourless oil (335 mg, 2.23 mmol, 62 %).

$[\alpha]_D^{35}$ -2.4 (*c* 0.235 in $CHCl_3$) 81 % ee (*R*) (lit.[1] $[\alpha]_D^{22}$ +3.48 (*c* 2.93 in $CHCl_3$); ν_{max} 3061, 3002, 2925, 2875, 1598, 1586, 1492, 1291, 1037 and 750 cm^{-1}; δ_H (500 MHz, $CDCl_3$) 7.26 - 7.34 (2H, m, Ar***H***), 6.97 (1H, t, *J* = 7.4 Hz, Ar***H***), 6.92 (2H, d, *J* = 7.8 Hz, Ar***H***), 4.21 (1H, dd, *J* = 11.0 Hz, *J* = 3.4 Hz, $PhOCH_d\boldsymbol{H_c}$), 3.97 (1H, dd, *J* = 11.1 Hz, *J* = 5.6 Hz, $PhOCH_c\boldsymbol{H_d}$), 3.36 (1H, ddt, *J* = 5.6 Hz, 3.9 Hz, 3.0 Hz, ***H***CO), 2.90 (1H, t, *J* = 4.6 Hz, $HCOCH_b\boldsymbol{H_a}$), 2.76 (1H, dd, *J* = 5.0 Hz, 2.7 Hz, $HCOCH_a\boldsymbol{H_b}$); δ_C(126 MHz, $CDCl_3$) 158.5, 129.5, 121.2, 114.6, 68.7, 50.2, 44.8; *m/z* (ESI) 173 ($[M+Na]^+$, 5%).

Enantiomeric excess determined by HPLC analysis (Chiralcel OD 0.46cm x 25cm, iPrOH:Hexane 17:83, 1mL/min, 30 °C 254nm) *R major* isomer 8.2 min, *S minor* isomer 11.8 mi

1) Fung Kei (Kathy) Cheung, Adam J. Clarke, Guy J. Clarkson, David J. Fox, Mark A. Graham, Changxue Lin, Adriana Lorente Crivillé and Martin Wills, *Dalton. Trans*, **2010**, *39*, 1395-1402.

(*R*)-1-Isopropoxy-3-phenoxypropan-2-ol 6.



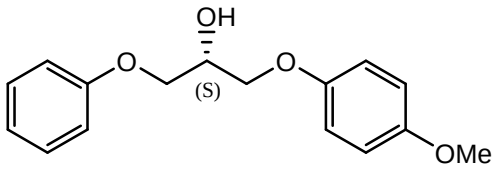
Asymmetric epoxide ring opening

To NaH, 60 % in oil, (7.9 mg, 1.7 mmol, 1.2 eq) isopropanol (0.5 mL) was added under nitrogen. The mixture was stirred for 30 mins. (*R*)-2-(phenoxymethyl)oxirane (20 mg, 1.4 mmol, 1 eq) was then added dropwise. The mixture was then stirred at room temperature for 24 hrs. Water (2 mL) was added to quench the reaction mixture and the product was extracted using EtOAc (3 x 10 mL). The combined organic layers were dried over sodium sulfate and concentrated under vacuum to yield product as a colourless oil (22.4 mg, 0.13 mmol, 92%).

$[\alpha]_D^{28}$ = +2.3 ° (*c* 0.3 in $CDCl_3$) 72 % ee (*R*)

Enantiomeric excess determined by HPLC analysis (Chiralpak IB, 0.46 cm ϕ x 25 cm, iPrOH:hexane 1:9, 1 mL/min, T = 30 °C, 254 nm) *R major* isomer 6.4 min, *S minor* isomer 9.8 min.

(*S*)-1-(4-Methoxyphenoxy)-3-phenoxypropan-2-ol 11.



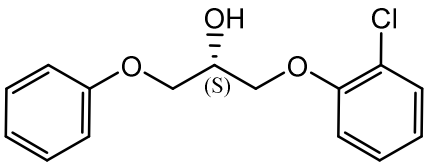
Asymmetric epoxide ring opening

To a solution of 4-methoxyphenol (84.4 mg, 0.68 mmol, 1 eq) in THF (2 mL), NaH 60 % in oil (32 mg, 0.82 mmol, 1.2 eq) was added and the mixture was stirred at room temperature for 30 mins. (*R*)-2-(phenoxymethyl)oxirane was then added to the mixture which was refluxed at 70 °C and stirred for 24 hrs. The mixture was then cooled to room temperature before being quenched with water (5 mL) and the organic product was then extracted using Et_2O (3 x 10 mL). The combined organic layers were dried over Na_2SO_4 and concentrated to give the product as a white solid (82 mg, 0.3 mmol, 44 %).

Mp 70.0 °C -70.8 °C; $[\alpha]_D^{27}$ -1.9 ° (*c* 0.26 in $CDCl_3$) 76.4 % ee (*S*)

Enantiomeric excess determined by HPLC analysis (Chiralpak IB, 0.46 cm ϕ x 25 cm, iPrOH:hexane 1:9, 1 mL/min, T = 30 oC, 254 nm) *S major* isomer 16.4 min, *R minor* isomer 19.7 min.

(*S*)-1-(2-Chlorophenoxy)-3-phenoxypropan-2-ol 23.



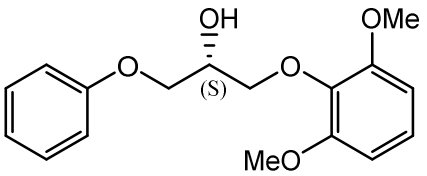
Asymmetric epoxide ring opening

To a solution of 2-chlorophenol (43 mg, 0.34 mmol, 1 eq) in THF (1 mL), NaH 60 % in oil (16 mg, 0.4 mmol, 1.2 eq) was added and the mixture was stirred at room temperature for 30 mins. (*R*)-2-(phenoxymethyl)oxirane was then added to the mixture which was refluxed at 70 °C and stirred for 24 hrs. The mixture was then cooled to room temperature before being quenched with water (5 mL) and the organic product was then extracted using Et_2O (3 x 10 mL). The combined organic layers were dried over Na_2SO_4 and concentrated to give the product as a colourless oil (53 mg, 0.20 mmol, 56 %).

$[\alpha]_D^{29}$ +10.2 ° (*c* 0.06 in $CDCl_3$) 79 % ee (*S*)

Enantiomeric excess determined by HPLC analysis (Chiralpak IB, 0.46 cm ϕ x 25 cm, iPrOH:hexane 7:93, 1 mL/min, T = 30 °C, 254 nm) *S major* isomer 14.9 min, *R minor* isomer 22.8 min.

(*S*)-1-(2,6-Dimethoxyphenoxy)-3-phenoxypropan-2-ol 16.



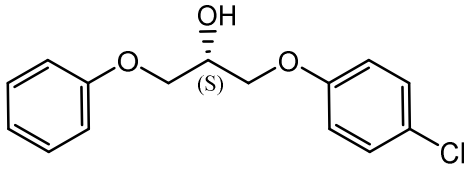
Asymmetric epoxide ring opening

A solution of $PdCl_2$ (0.6 mg, 3.4 µmol, 0.01 eq), TBAB (29 mg, 0.9 mmol, 0.25 eq) and K_2CO_3 (13 mg, 0.09 mmol, 0.25 eq) in water was made up and heated to 60 °C. (R)-2-(phenoxymethyl)oxirane (50 mg, 034 mmol, 1 eq) was then added to the stirring mixture along with 2,6 dimethoxy phenol (52.4 mg, 0.34 mmol, 1 eq). The reaction was then stirred for 24 hrs at 60 °C before being allowed to cool to room temperature. The product was then extracted using EtOAc (3 x 30 mL). The combined organic layers were then dried over sodium sulphate and concentrated under vacuum to yield the black crude product, which was then filtered through silica to yield the crude product (100.3 mg, 0.33 mmol, 97 %).

$[\alpha]_D^{25}$ +27.2 ° (*c* 0.18 in $CDCl_3$) 72 % ee (*S*)

Enantiomeric excess determined by HPLC analysis (Chiralpak IB, 0.46 cm ϕ x 25 cm, iPrOH:hexane 7:93, 1 mL/min, T = 30 °C, 254 nm) *S major* isomer 14.8 min, *R minor* isomer 19.3 min.

(*S*)-1-(4-Chlorophenoxy)-3-phenoxypropan-2-ol 12.



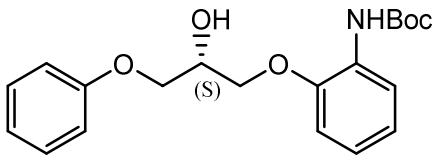
Asymmetric epoxide ring opening

To a solution of 4-chlorophenol (43 mg, 0.34 mmol, 1 eq) in THF (1 mL), NaH 60 % in oil (16 mg, 0.4 mmol, 1.2 eq) was added and the mixture was stirred at room temperature for 30 mins. (*R*)-2-(phenoxymethyl)oxirane was then added to the mixture which was refluxed at 70 °C and stirred for 24 hrs. The mixture was then cooled to room temperature before being quenched with water (5 mL) and the organic product was then extracted using Et_2O (3 x 10 mL). The combined organic layers were dried over Na_2SO_4 and concentrated to give the product as a colourless oil (62 mg, 0.22 mmol, 65 %).

$[\alpha]_D^{26}$ +17.5 ° (*c* 0.28 in $CDCl_3$) 78 % ee (*S*)

Enantiomeric excess determined by HPLC analysis (Chiralpak IB, 0.46 cm ϕ x 25 cm, iPrOH:hexane 7:93, 1 mL/min, T = 30 °C, 254 nm) S_{major} isomer 12.0 min, R_{minor} isomer 19.9 min.

tert-Butyl (S)-(2-(2-hydroxy-3-phenoxypropoxy)phenyl)carbamate 19.



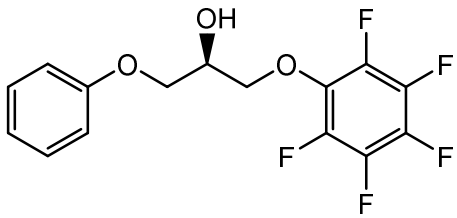
Asymmetric epoxide ring opening

To a solution of tert-butyl (2-hydroxyphenyl)carbamate (63 mg, 0.30 mmol, 1 eq) in THF (0.5 mL), NaH 60 % in oil (14 mg, 0.36 mmol, 1.2 eq) was added and the mixture was stirred at room temperature for 30 mins. (*R*)-2-(phenoxymethyl)oxirane (50 mg, 0.30 mmol, 1 eq) was then added to the mixture which was stirred for 24 hrs. The mixture was then quenched with water (10 mL) and the organic product was then extracted using Et_2O (3 x 15 mL). The combined organic layers were dried over Na_2SO_4 and concentrated to give the product as a colourless oil (78 mg, 0.22 mmol, 73 %). $[\alpha]_D^{29}$ +4.7 (*c* 0.33 in $CDCl_3$) 79.6 % (*S*)

Enantiomeric excess determined by HPLC analysis (Chiralpak IB, 0.46 cm ϕ x 25 cm, iPrOH:hexane 7:93, 1 mL/min, T = 30 °C, 254 nm) *S major* isomer 12.0 min, *R minor* isomer 18.0 min.

<u>The following compounds were prepared using (*S*)-2-(phenoxymethyl)oxirane:</u>

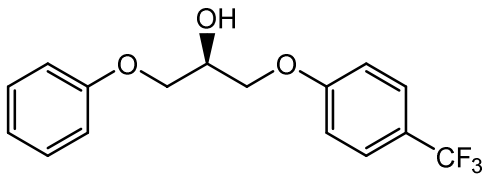
(*R*)-1-(Pentafluorophenoxy)-3-phenoxypropan-2-ol 26.



Asymmetric epoxide ring opening

A solution of $PdCl_2$ (1.0 mg, 6.7 µmol, 0.01 eq), TBAB (54 mg, 0.167 mmol, 0.25 eq) and K_2CO_3 (23 mg, 0.167 mmol, 0.25 eq) in water (2.5 mL) was made up and heated to 60 °C. (*S*)-2-(Phenoxymethyl)oxirane (90 mg, 0.67 mmol, 1.0 eq) was then added to the stirring mixture along with pentafluorophenol (122 mg, 0.67 mmol, 1.0 eq). The reaction was then stirred for 24 hrs at 60 °C before being allowed to cool to room temperature. The product was then extracted using EtOAc (3 x 30 mL). The combined organic layers were then dried over sodium sulphate and concentrated under vacuum before filteration through silica in hexane/EtOAc to yield the crude product which was analysed directly by HPLC. Enantiomeric excess (24%, *R*) was determined by HPLC analysis as previously described.

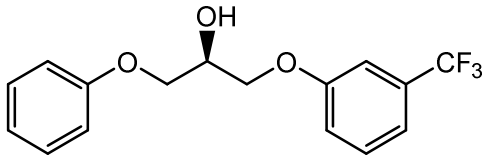
(*R*)-1-((4-Trifluoromethyl)phenoxy)-3-phenoxypropan-2-ol 27.



Asymmetric epoxide ring opening

A solution of $PdCl_2$ (1.0 mg, 6.7 µmol, 0.01 eq), TBAB (54 mg, 0.167 mmol, 0.25 eq) and K_2CO_3 (23 mg, 0.167 mmol, 0.25 eq) in water (2.5 mL) was made up and heated to 60 °C. (*S*)-2-(Phenoxymethyl)oxirane (90 mg, 0.67 mmol, 1.0 eq) was then added to the stirring mixture along with 4-trifluoromethylphenol (108 mg, 0.67 mmol, 1.0 eq). The reaction was then stirred for 24 hrs at 60 °C before being allowed to cool to room temperature. The product was then extracted using EtOAc (3 x 30 mL). The combined organic layers were then dried over sodium sulphate and concentrated under vacuum before filteration through silica in hexane/EtOAc to yield the crude product which was analysed directly by HPLC. Enantiomeric excess (80%, *R*) was determined by HPLC analysis as previously described.

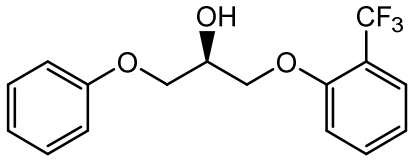
(*R*)-1-((3-Trifluoromethyl)phenoxy)-3-phenoxypropan-2-ol 28.



Asymmetric epoxide ring opening

A solution of $PdCl_2$ (1.0 mg, 6.7 µmol, 0.01 eq), TBAB (54 mg, 0.167 mmol, 0.25 eq) and K_2CO_3 (23 mg, 0.167 mmol, 0.25 eq) in water (2.5 mL) was made up and heated to 60 °C. (*S*)-2-(Phenoxymethyl)oxirane (90 mg, 0.67 mmol, 1.0 eq) was then added to the stirring mixture along with 3-trifluoromethylphenol (108 mg, 0.67 mmol, 1.0 eq). The reaction was then stirred for 24 hrs at 60 °C before being allowed to cool to room temperature. The product was then extracted using EtOAc (3 x 30 mL). The combined organic layers were then dried over sodium sulphate and concentrated under vacuum before filteration through silica in hexane/EtOAc to yield the crude product which was analysed directly by HPLC. Enantiomeric excess (70%, *R*) was determined by HPLC analysis as previously described.

(*R*)-1-((2-Trifluoromethyl)phenoxy)-3-phenoxypropan-2-ol 29.



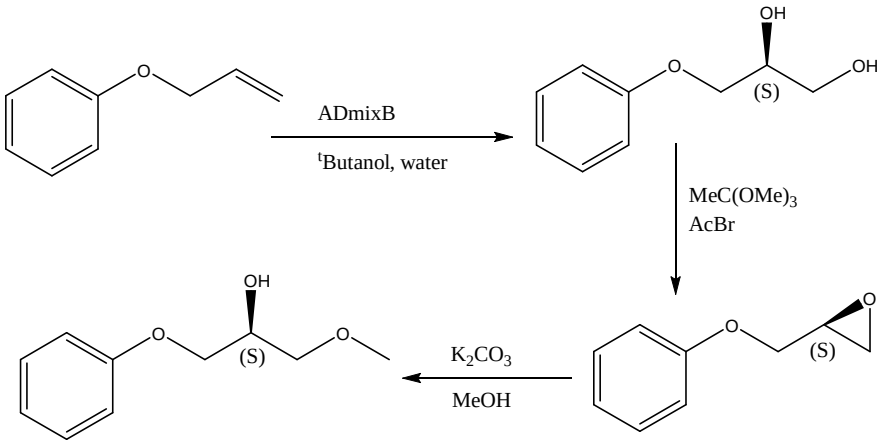
Asymmetric epoxide ring opening

A solution of $PdCl_2$ (1.0 mg, 6.7 µmol, 0.01 eq), TBAB (54 mg, 0.167 mmol, 0.25 eq) and K_2CO_3 (23 mg, 0.167 mmol, 0.25 eq) in water (2.5 mL) was made up and heated to 60 °C. (*S*)-2-(Phenoxymethyl)oxirane (90 mg, 0.67 mmol, 1.0 eq) was then added to the stirring mixture along with 3-trifluoromethylphenol (108 mg, 0.67 mmol, 1.0 eq). The reaction was then stirred for 24 hrs

at 60 °C before being allowed to cool to room temperature. The product was then extracted using EtOAc (3 x 30 mL). The combined organic layers were then dried over sodium sulphate and concentrated under vacuum before filteration through silica in hexane/EtOAc to yield the crude product which was analysed directly by HPLC. Enantiomeric excess (50%, *R*) was determined by HPLC analysis as previously described.

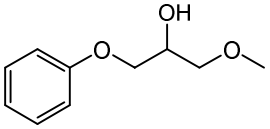
1-Methoxy-3-phenoxypropan-2-ol 4.

For this compound the route reported by Sharpless et al. was conducted with Admix-β and the same series of reactions as previously described to give a known standard of *S*-configuration alcohol of 84% e.e.

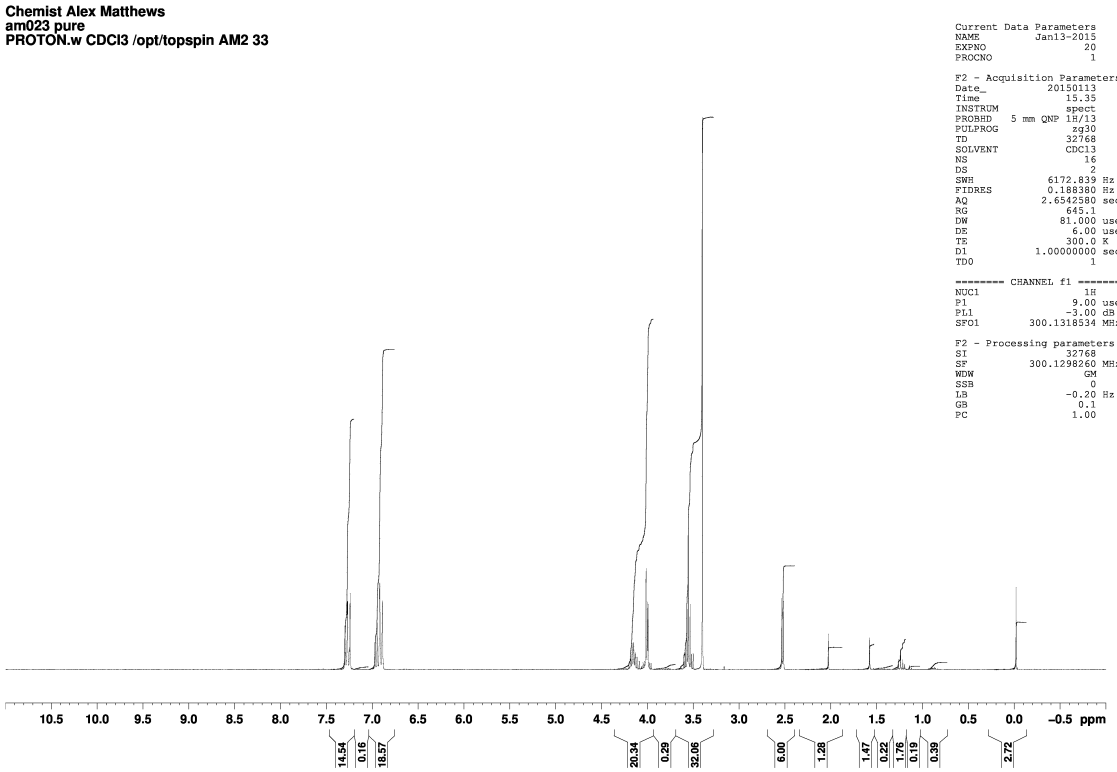


NMR Spectra and HPLC data for ee determination.

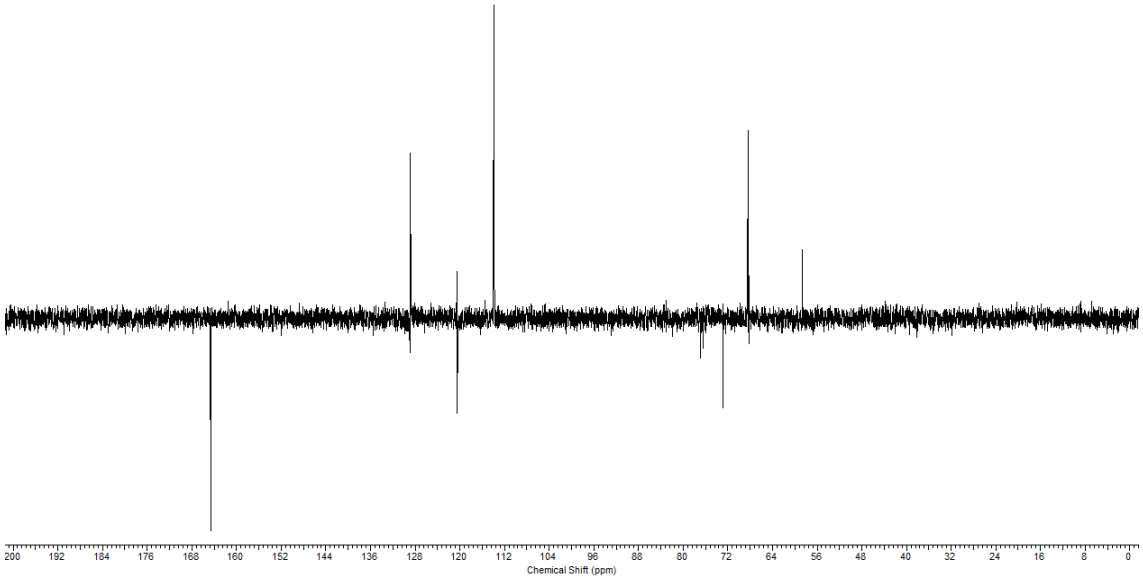
1-Methoxy-3-phenoxypropan-2-ol 4.



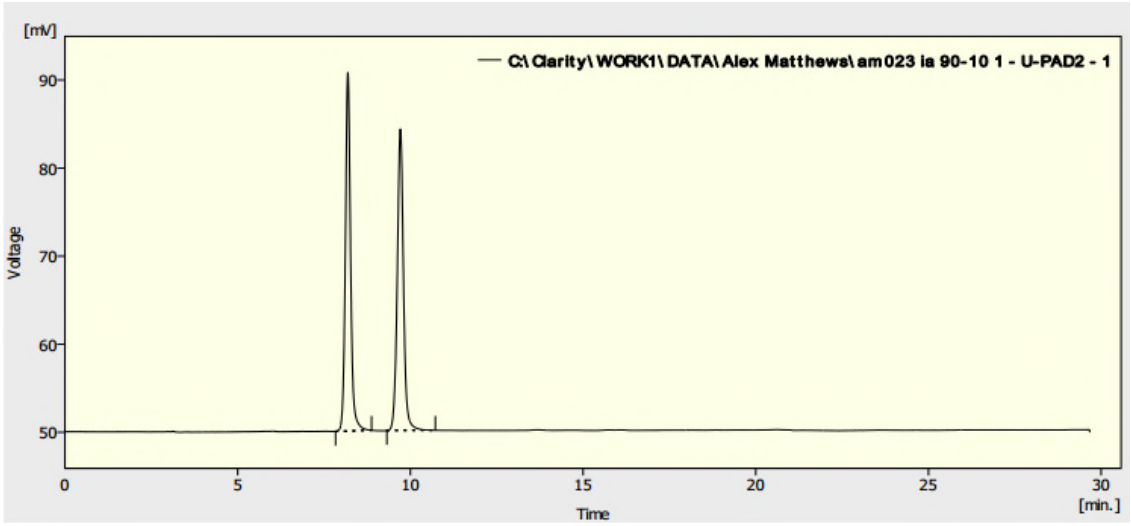
^{1}H NMR (300 MHz, $CDCl_3$).



^{13}C NMR (75 MHz, $CDCl_3$).



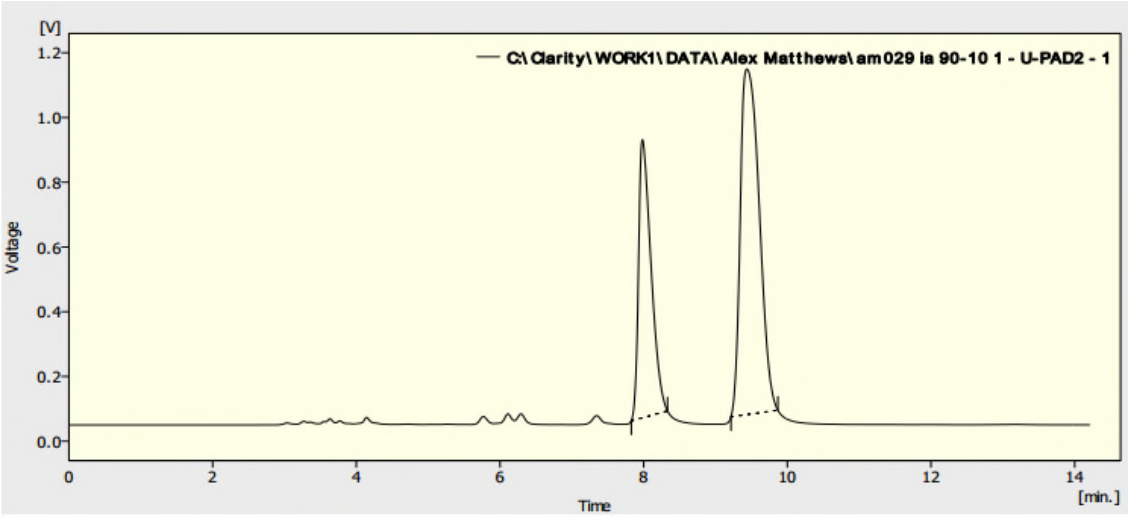
HPLC of racemic alcohol.



Result Table (Uncal - C:\Clarity\WORK1\DATA\Alex Matthews\am023 ia 90-10 1 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	8.192	425.682	40.714	49.9	54.3	0.16	
2	9.712	426.918	34.234	50.1	45.7	0.19	
	Total	852.600	74.948	100.0	100.0		

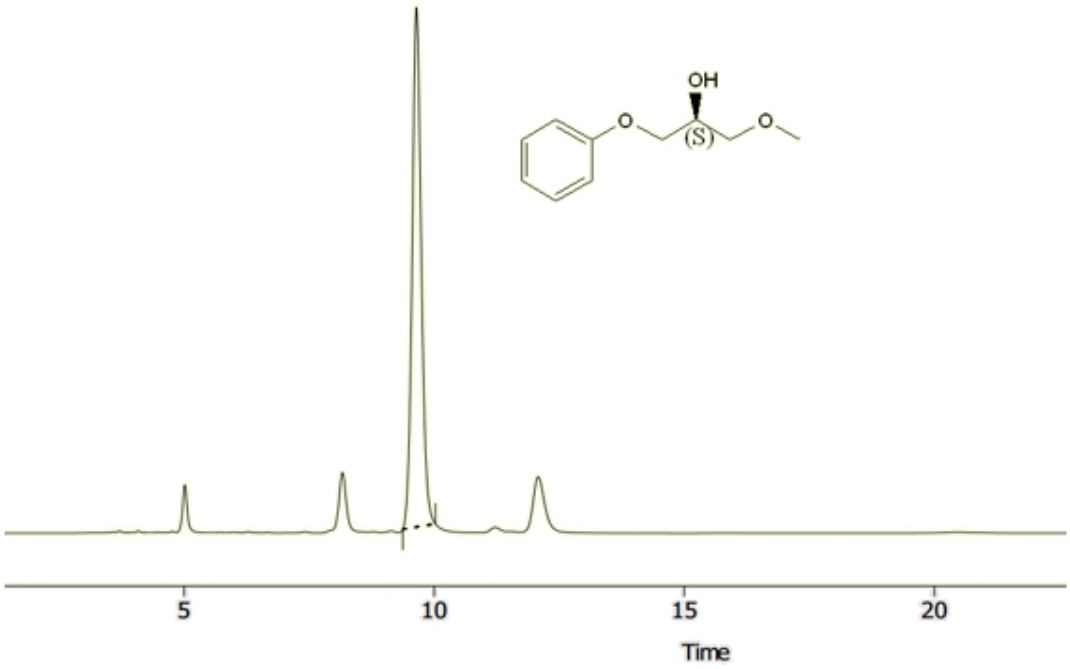
Asymmetric Alcohol.



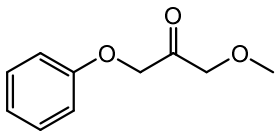
Result Table (Uncal - C:\Clarity\WORK1\DATA\Alex Matthews\am029 ia 90-10 1 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	7.984	10377.809	859.318	34.7	44.6	0.19	
2	9.436	19516.960	1067.420	65.3	55.4	0.30	
	Total	29894.769	1926.738	100.0	100.0		

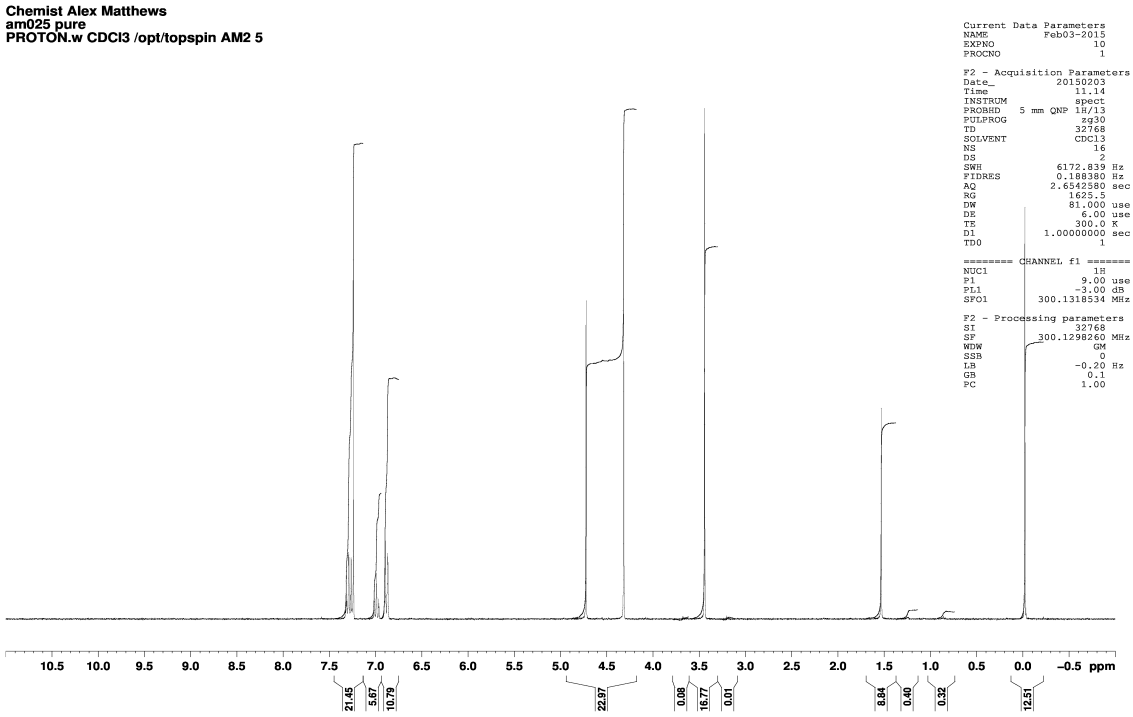
HPLC of known standard, S-configuration alcohol.



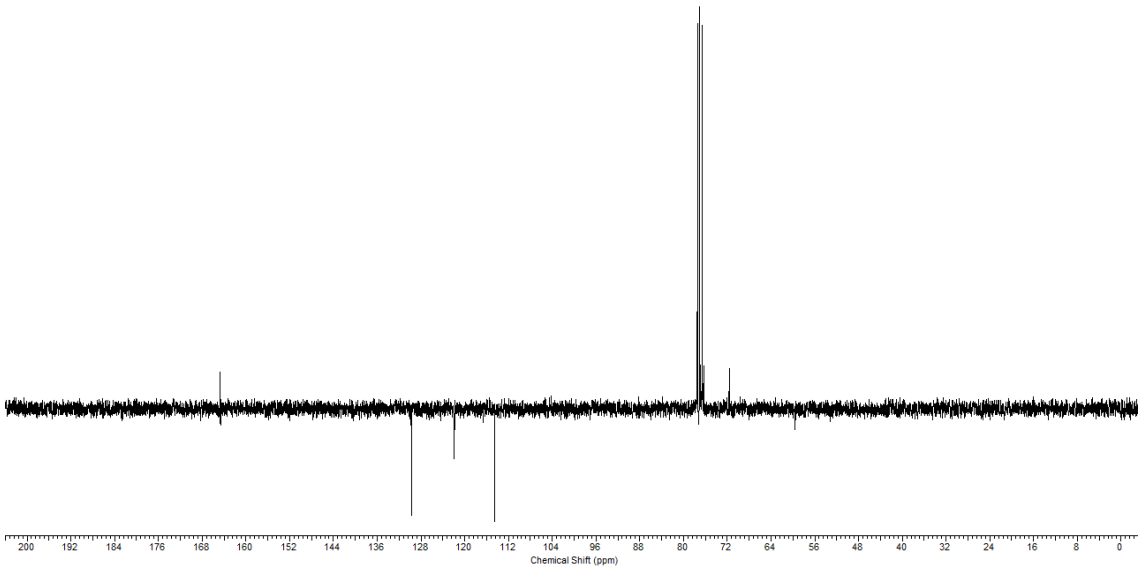
1-Methoxy-3-phenoxypropan-2-one.



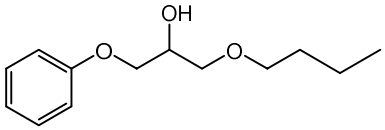
^{1}H NMR (300 MHz, $CDCl_3$).



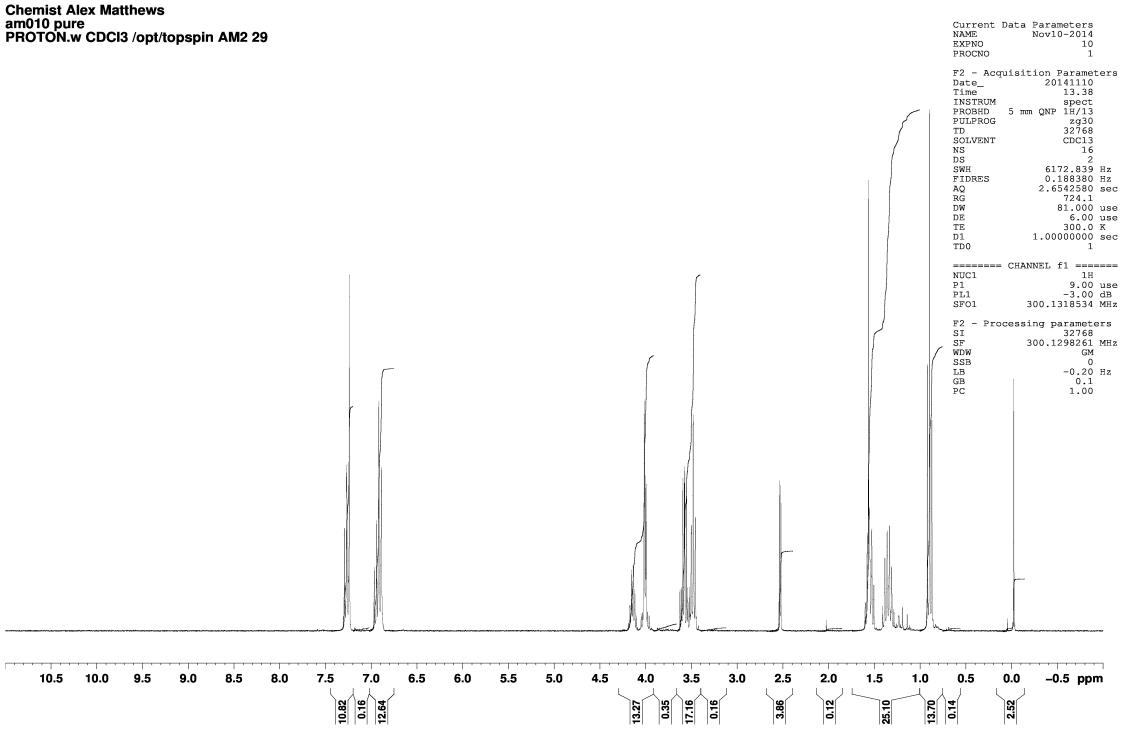
^{13}C NMR (75 MHz, $CDCl_3$).



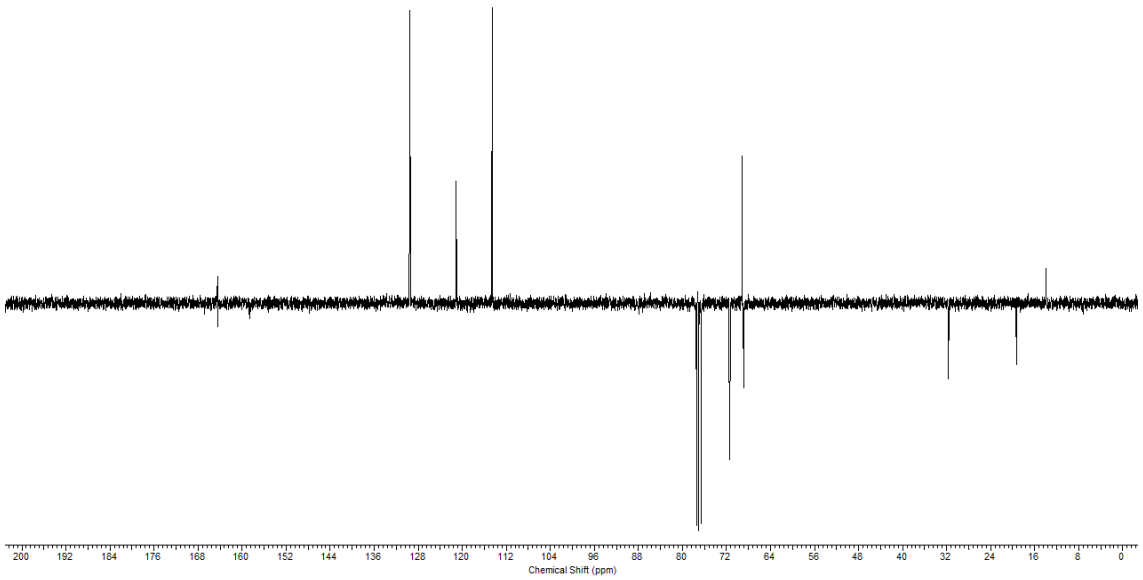
1-^{n}Butoxy-3-phenoxypropan-2-ol 5.



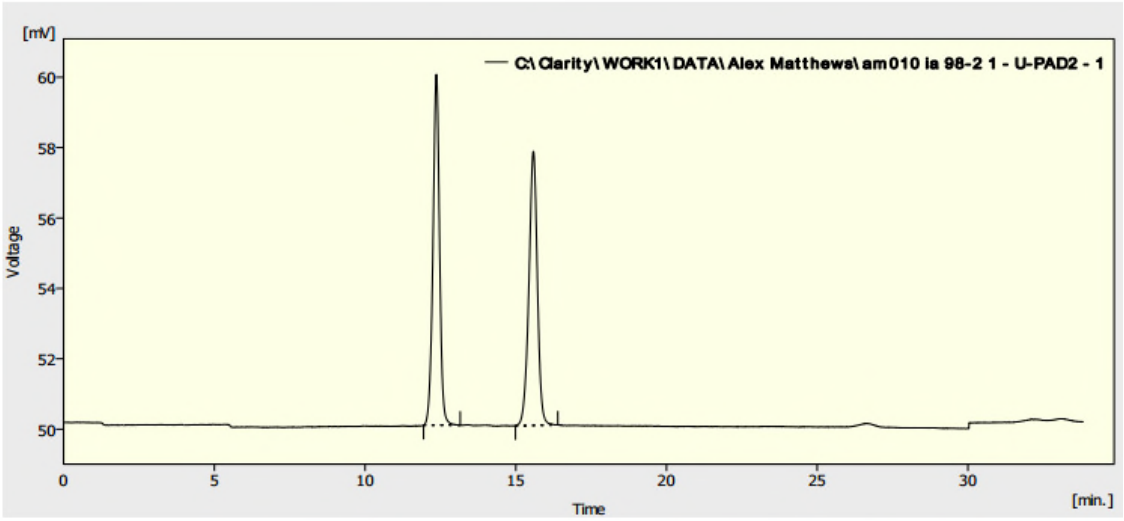
^{1}H NMR (300 MHz, $CDCl_3$).



^{13}C NMR (75 MHz, $CDCl_3$).



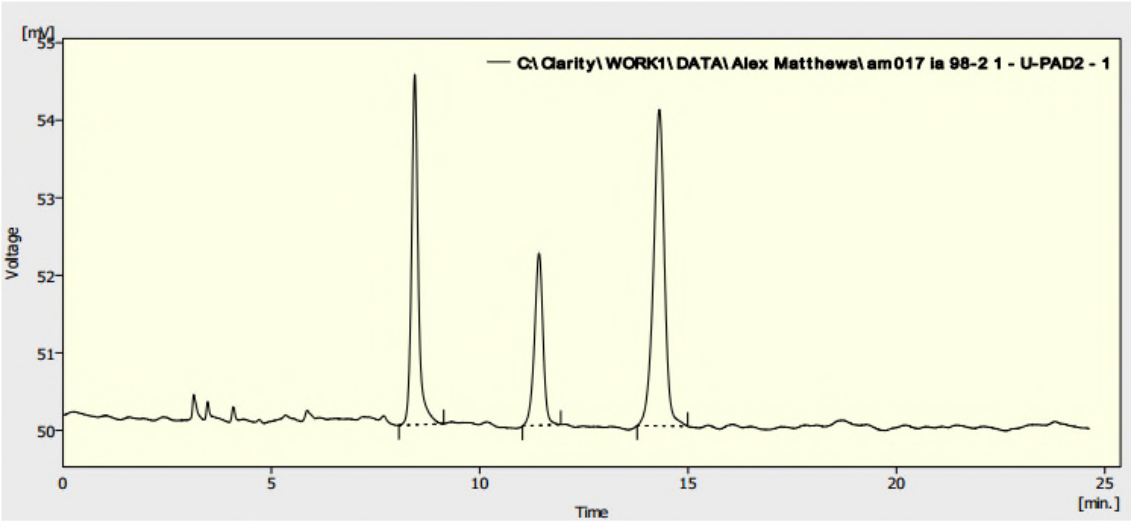
HPLC of Racemic alcohol.



Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|Alex Matthews\|am010 ia 98-2 1 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	12.364	151.463	9.971	49.9	56.1	0.23	
2	15.584	152.347	7.789	50.1	43.9	0.30	
	Total	303.810	17.760	100.0	100.0		

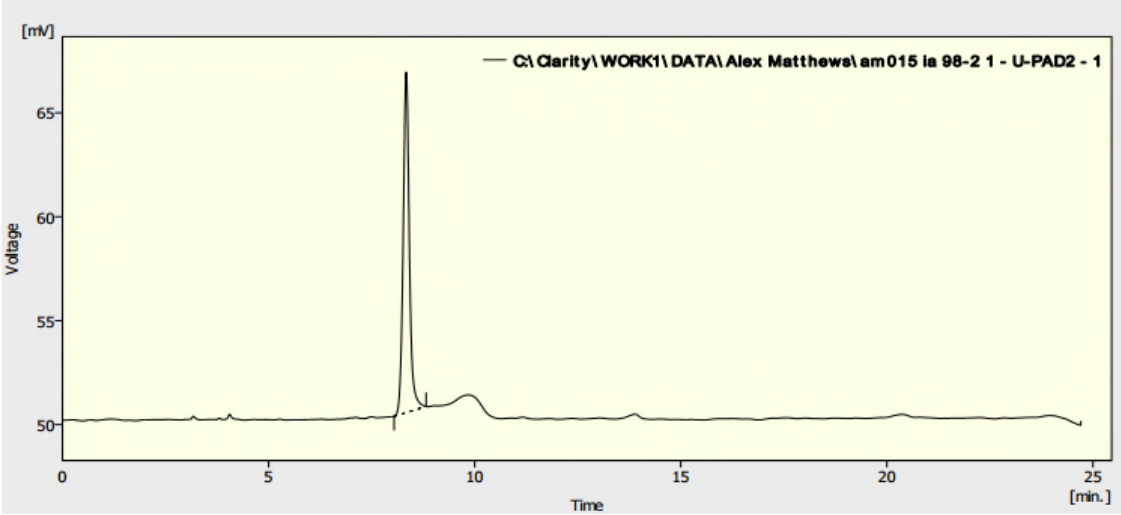
HPLC of Asymmetric Alcohol after ATH - not fully reduced (see following HPLC spectrum).



Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|Alex Matthews\|am017 ia 98-2 1 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	8.440	50.840	4.521	32.3	41.8	0.16	
2	11.424	31.620	2.221	20.1	20.5	0.21	
3	14.308	75.097	4.083	47.7	37.7	0.28	
	Total	157.557	10.824	100.0	100.0		

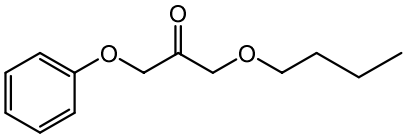
HPLC of Ketone – to confirm that 8.44 peak in HPLC above is ketone.



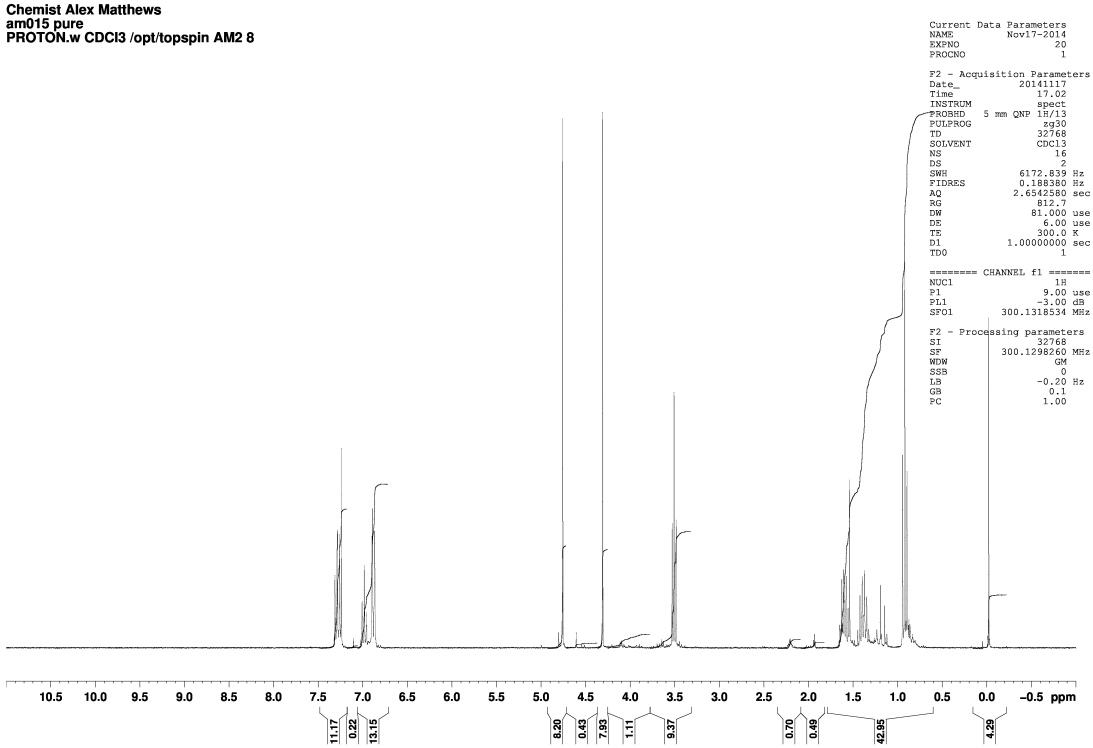
Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|Alex Matthews\|am015 ia 98-2 1 - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	8.336	171.247	16.382	100.0	100.0	0.16	
	Total	171.247	16.382	100.0	100.0		

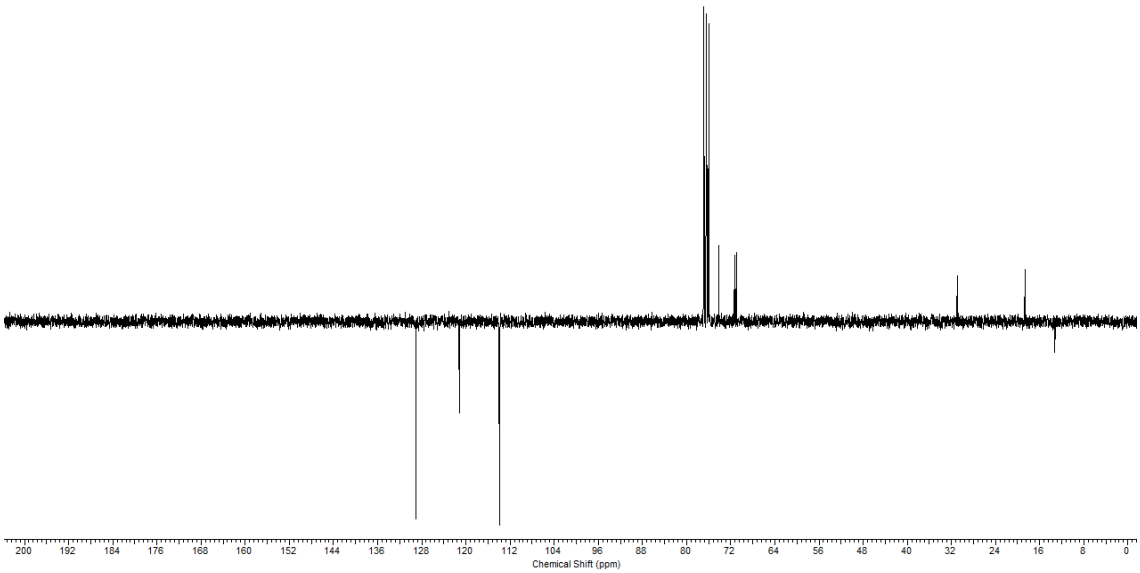
1-^{n}Butoxy-3-phenoxypropan-2-one.



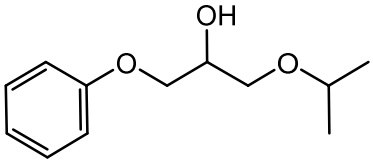
^{1}H NMR (300 MHz, $CDCl_3$).



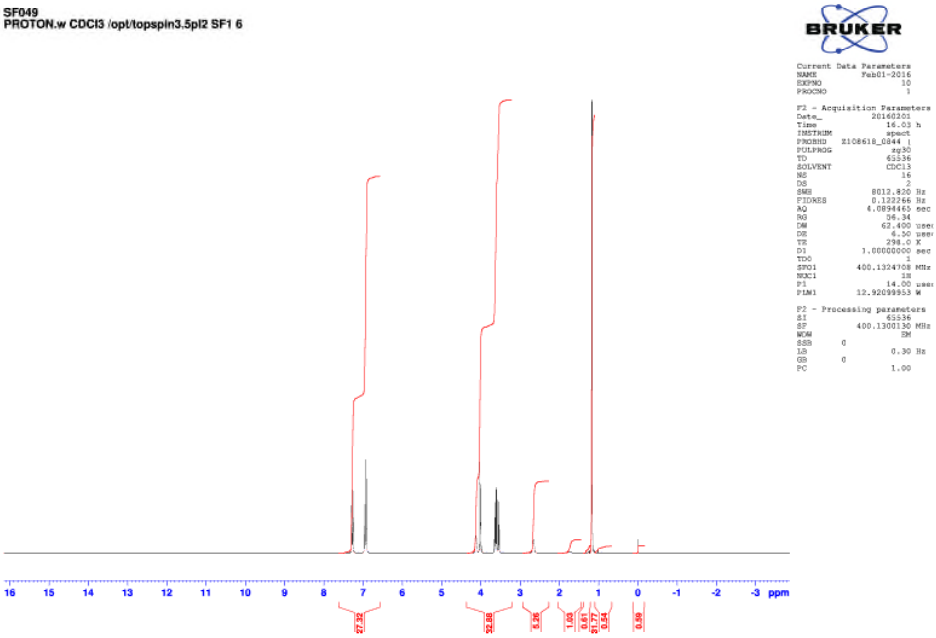
^{13}C NMR (75 MHz, $CDCl_3$).



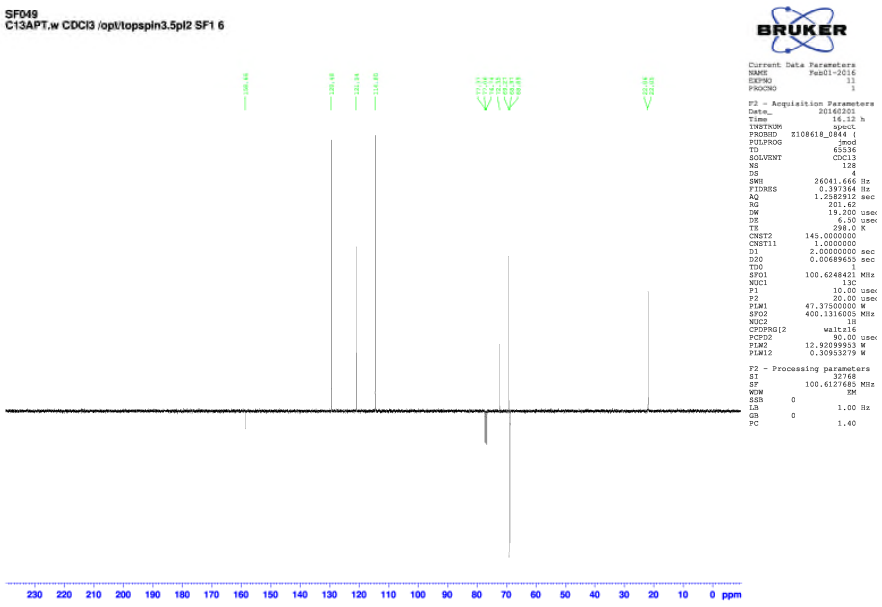
1-Isopropoxy-3-phenoxypropan-2-ol 6.



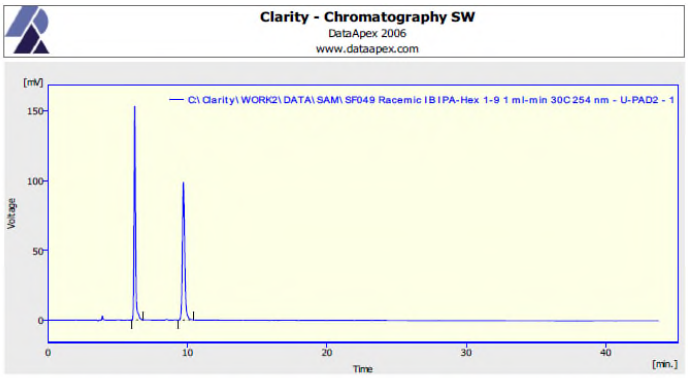
^{1}H NMR (400 MHz, $CDCl_3$).



^{13}C NMR (101 MHz, $CDCl_3$).



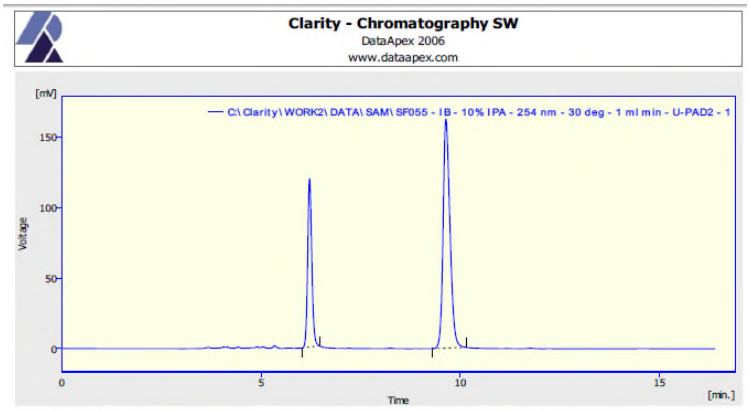
HPLC Racemic



Result Table (Uncal - C:|Clarity|WORK2|DATA|SAM|SF049 Racemic IB IPA-Hex 1-9 1 ml-min 30C 254 nm - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	6.220	1152.868	153.254	49.9	60.8	0.11	
2	9.708	1158.555	98.763	50.1	39.2	0.18	
	Total	2311.423	252.017	100.0	100.0		

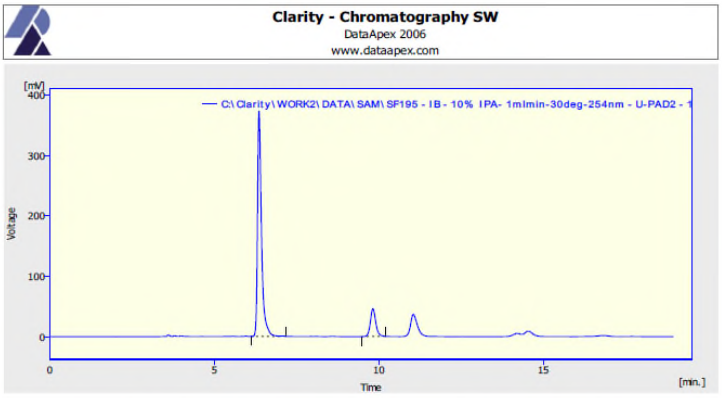
HPLC After ATH



Result Table (Uncal - C:|Clarity|WORK2|DATA|SAM|SF055 - IB - 10%IPA - 254 nm - 30 deg - 1 ml min - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	6.216	855.291	119.147	30.5	42.3	0.12	
2	9.640	1945.013	162.202	69.5	57.7	0.18	
	Total	2800.304	281.349	100.0	100.0		

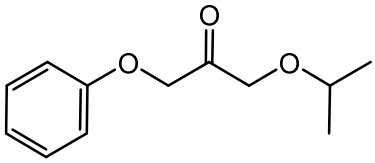
HPLC Asymmetric Standard



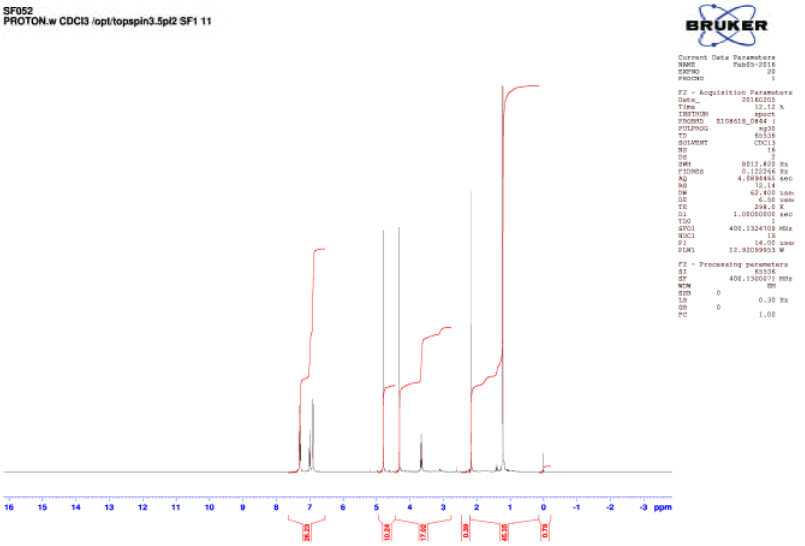
Result Table (Uncal - C:|Clarity|WORK2|DATA|SAM|SF195 - IB - 10% IPA- 1mlmin-30deg-254nm - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	6.360	3151.092	372.981	85.8	89.0	0.12	
2	9.820	523.507	45.997	14.2	11.0	0.17	
	Total	3674.598	418.978	100.0	100.0		

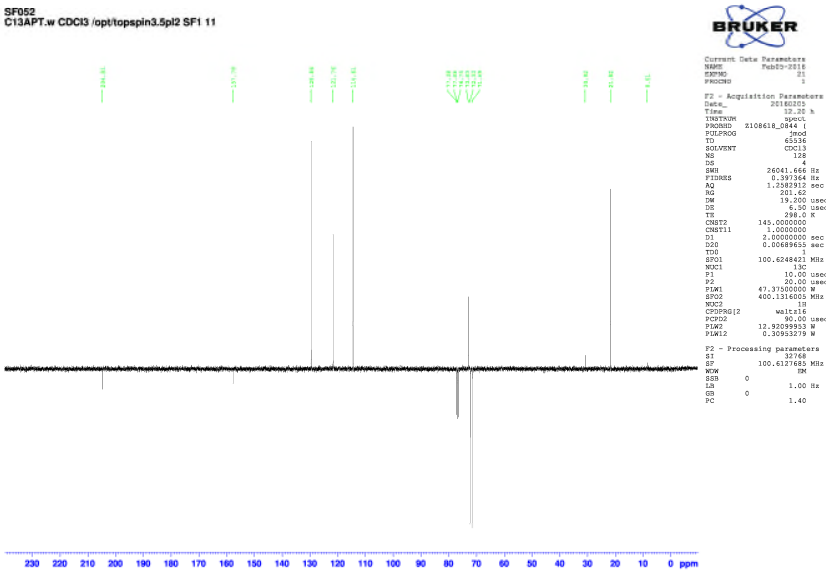
1-Isopropoxy-3-phenoxypropan-2-one.



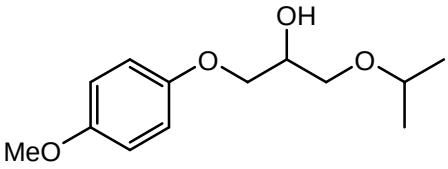
^{1}H NMR (400 MHz, $CDCl_3$).



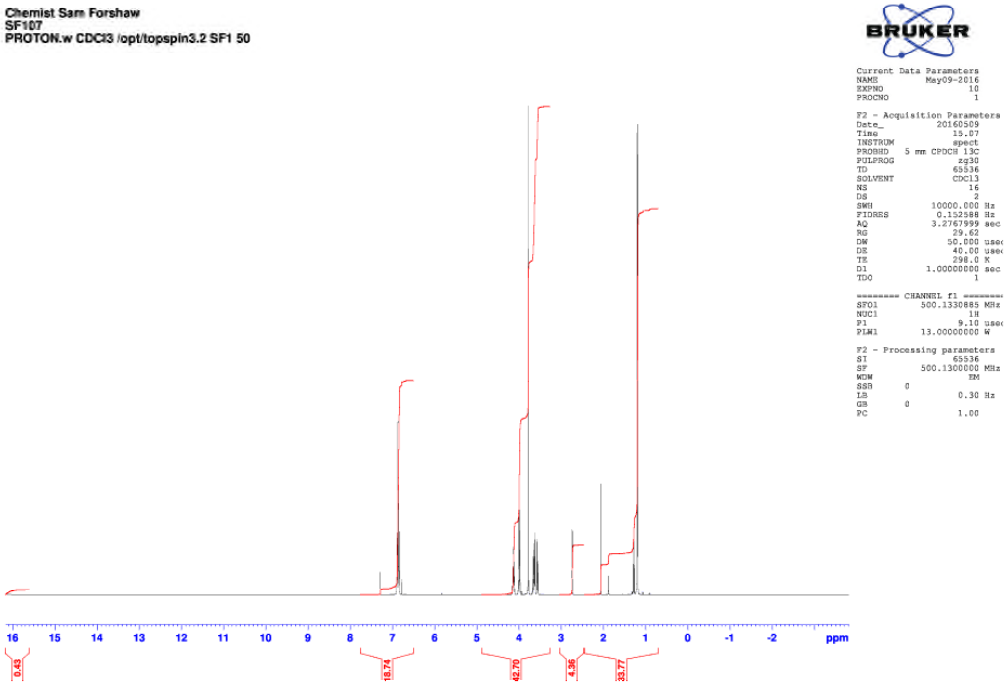
^{13}C NMR (101 MHz, $CDCl_3$).



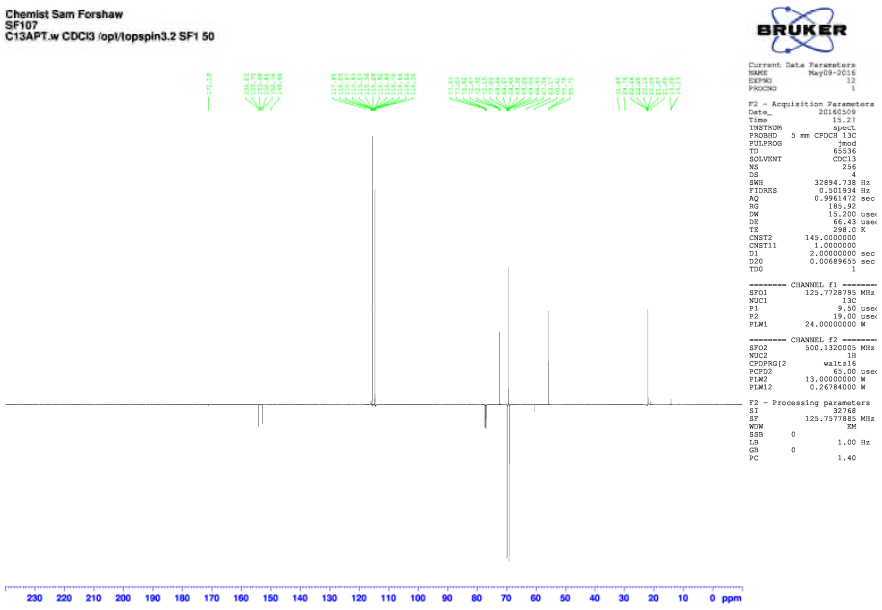
1-Isopropoxy-3-(4-methoxyphenoxy)propan-2-ol 7.



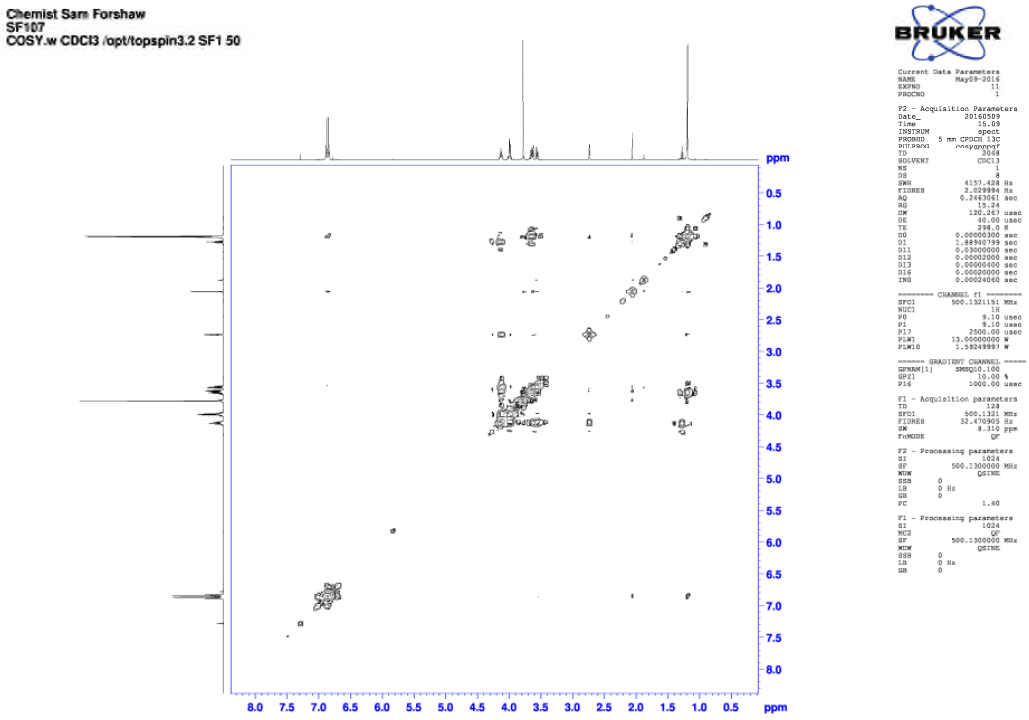
^{1}H NMR (500 MHz, $CDCl_3$).



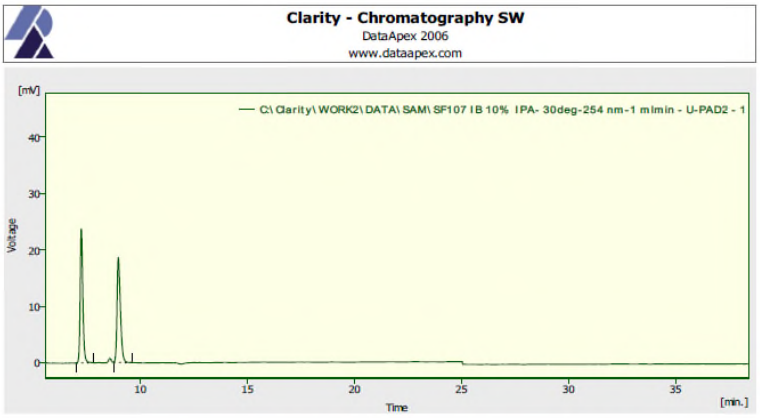
^{13}C NMR (125 MHz, $CDCl_3$).



COSY (500 MHz, $CDCl_3$)



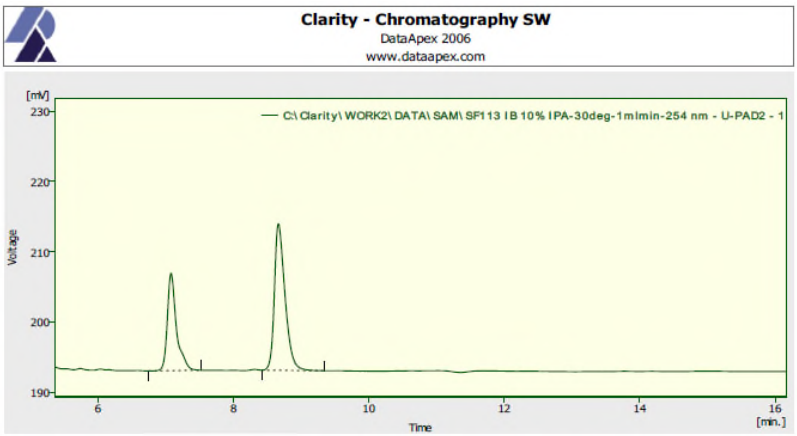
HPLC Racemic



Result Table (Uncal - C:\Clarity\WORK2\DATA\SAM\SF107 IB 10% IPA - 30deg-254 nm-1 mlmin - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	7.240	206.325	23.785	50.2	56.2	0.13	
2	8.968	204.589	18.551	49.8	43.8	0.17	
	Total	410.914	42.336	100.0	100.0		

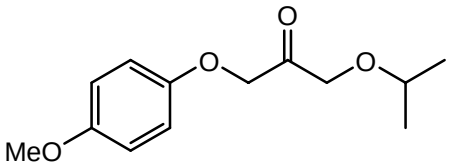
HPLC After ATH



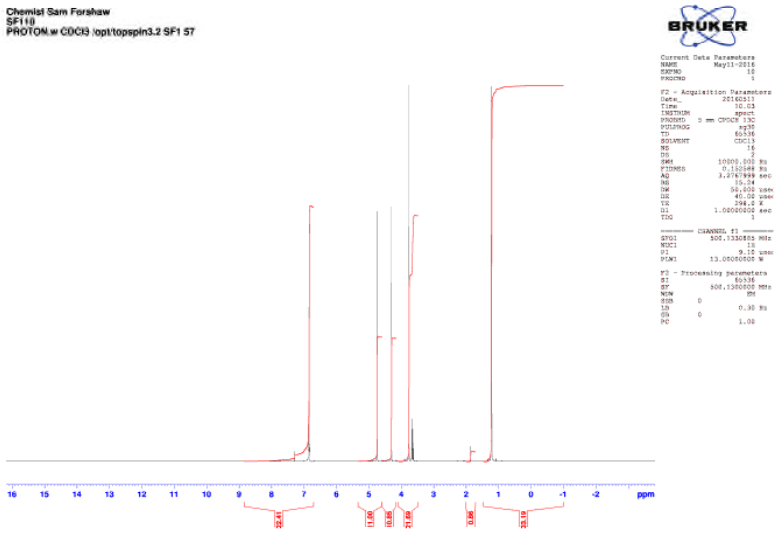
Result Table (Uncal - C:\Clarity\WORK2\DATA\SAM\SF113 IB 10%IPA-30deg-1mlmin-254 nm - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	7.080	130.068	13.842	36.4	39.9	0.13	
2	8.664	227.081	20.841	63.6	60.1	0.17	
	Total	357.148	34.684	100.0	100.0		

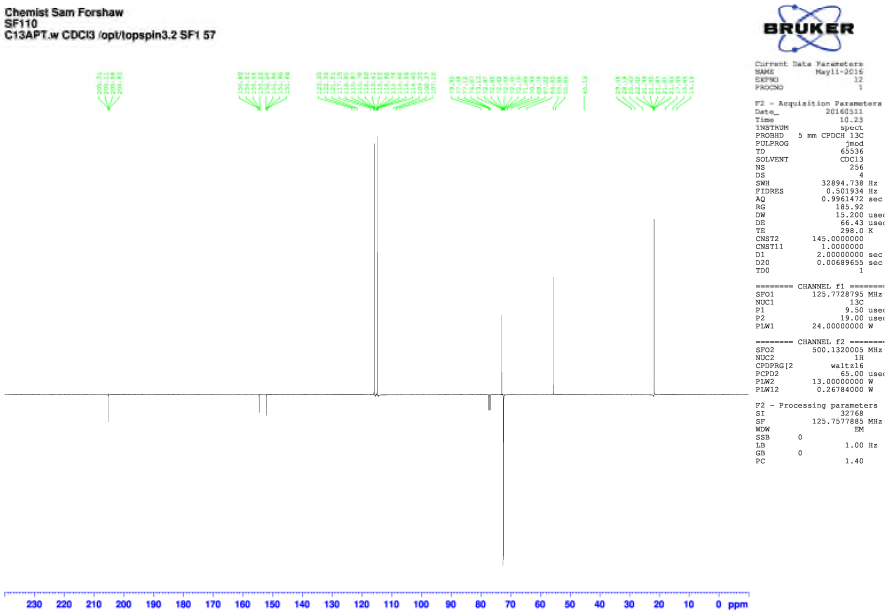
1-isopropoxy-3-(4-methoxyphenoxy)propan-2-one.



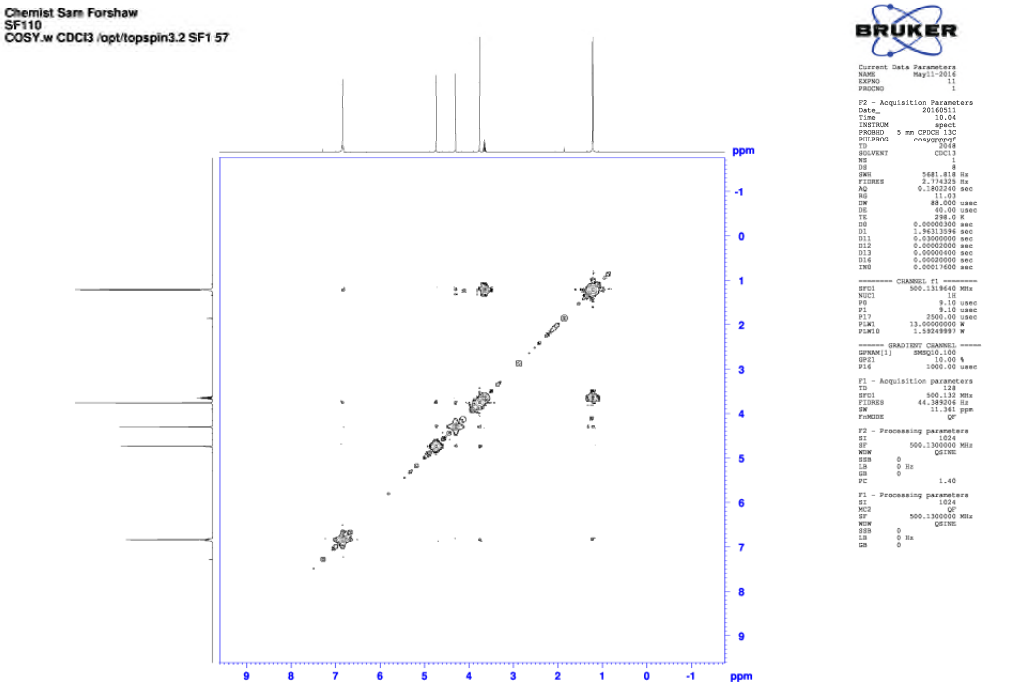
^{1}H NMR (500 MHz, $CDCl_3$)



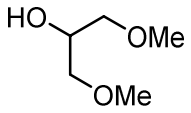
^{13}C NMR (125 MHz, $CDCl_3$)



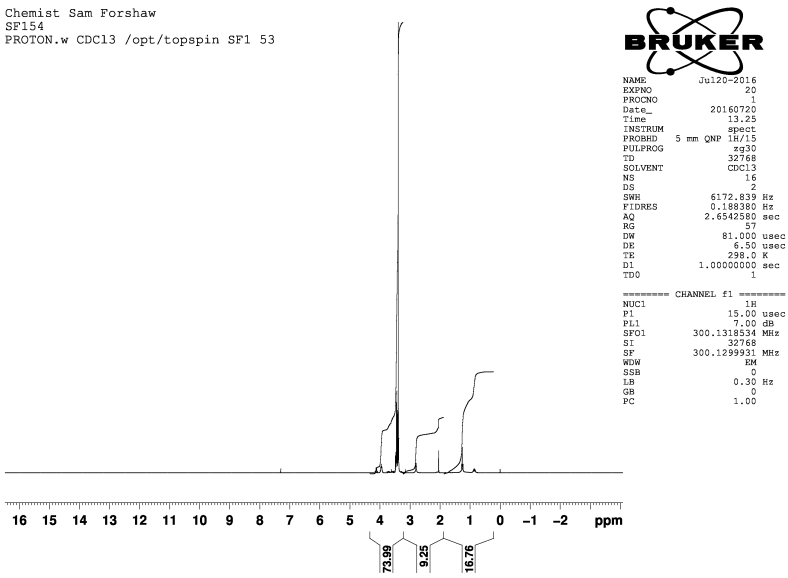
COSY (500 MHz, $CDCl_3$)



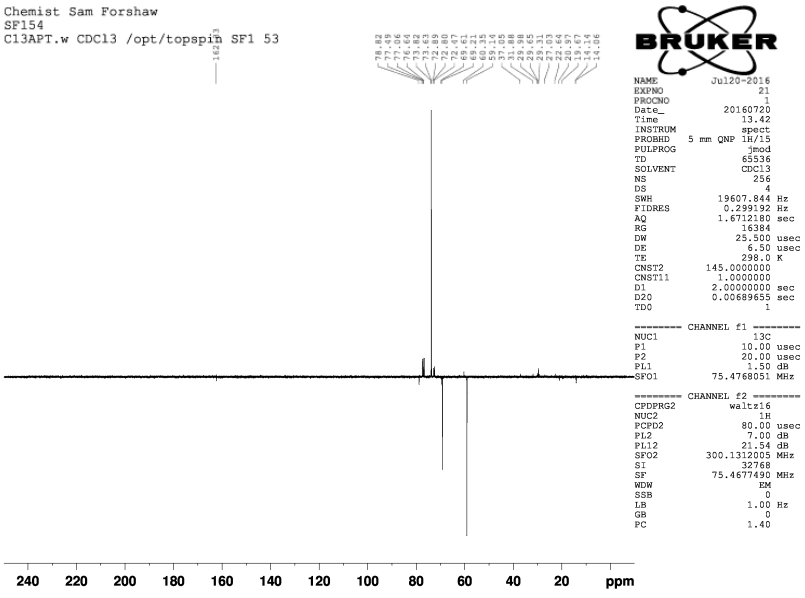
1,3-Dimethoxypropan-2-ol.



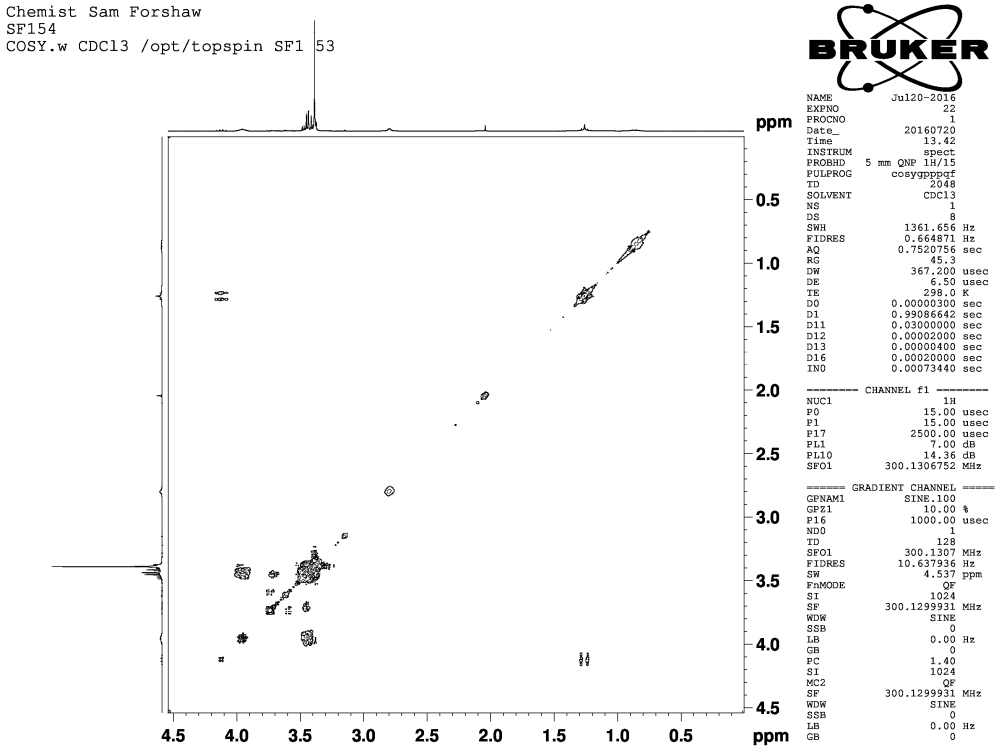
^{1}H NMR (300 MHz, $CDCl_3$)



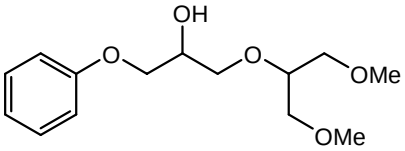
^{13}C NMR (75 MHz, $CDCl_3$)



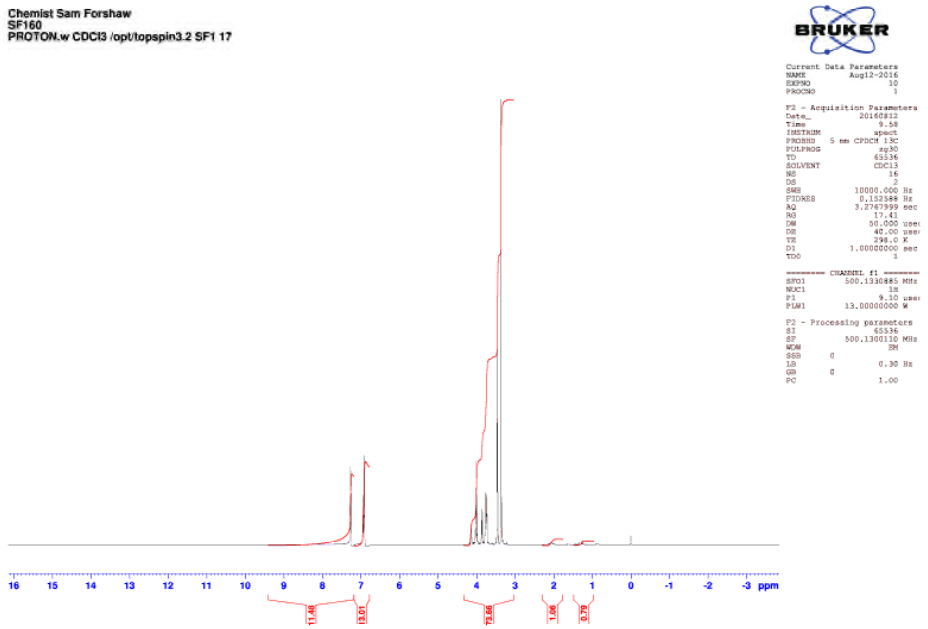
COSY (300 MHz, $CDCl_3$)



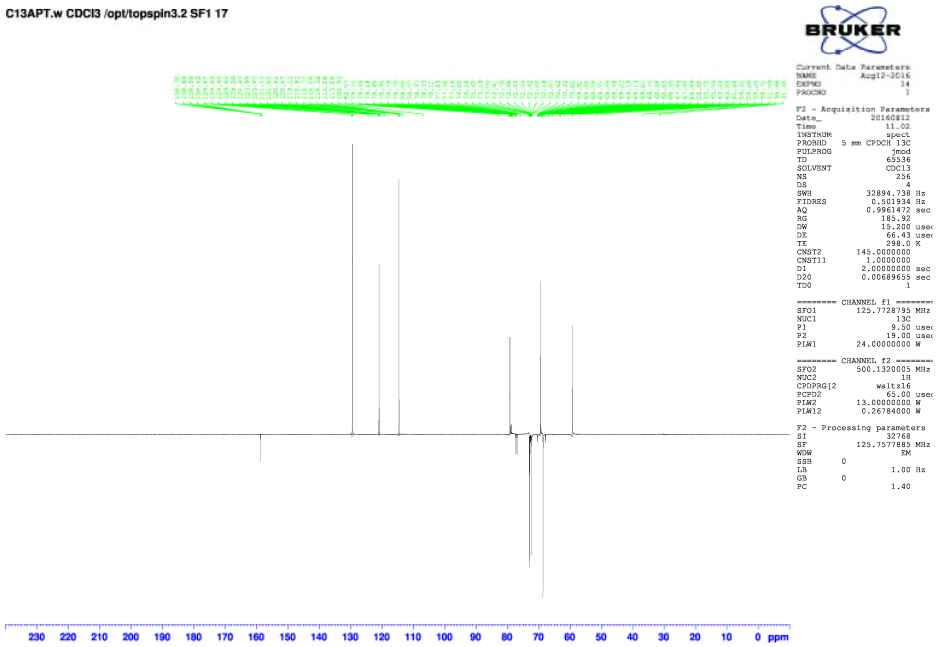
1-((1,3-Dimethoxypropan-2-yl)oxy)-3-phenoxypropan-2-ol 8.



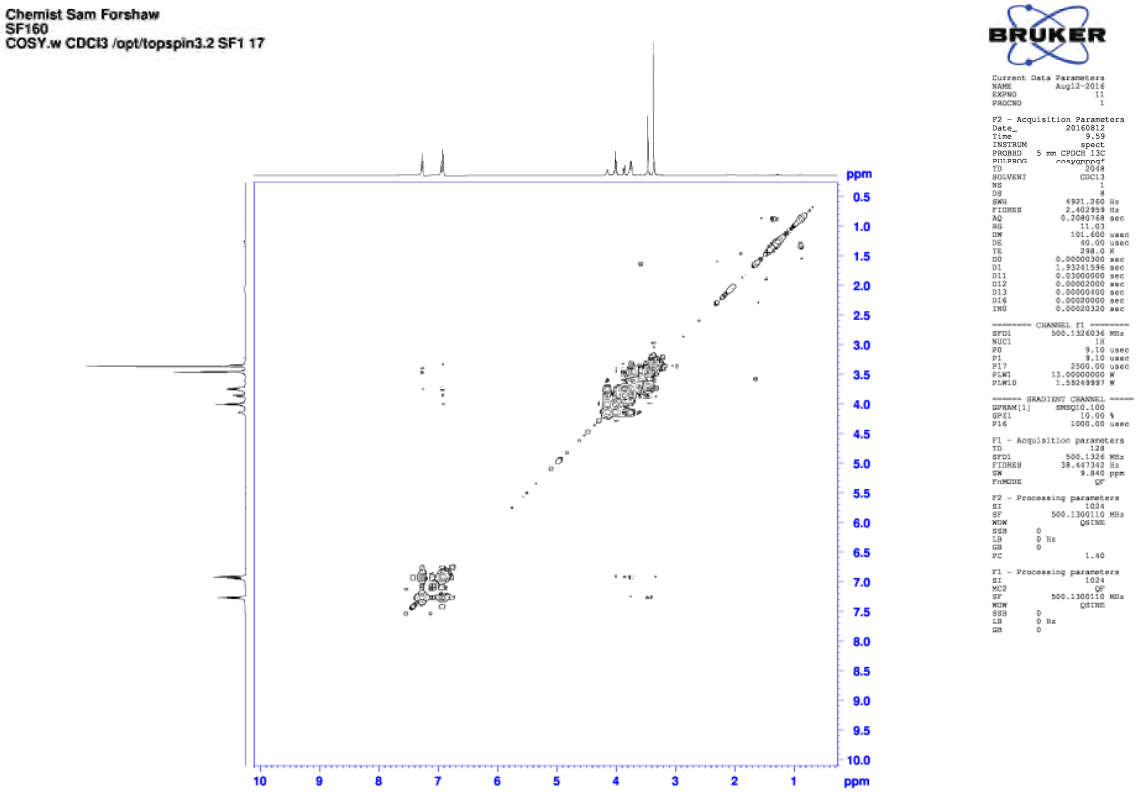
^{1}H NMR (500 MHz, $CDCl_3$)



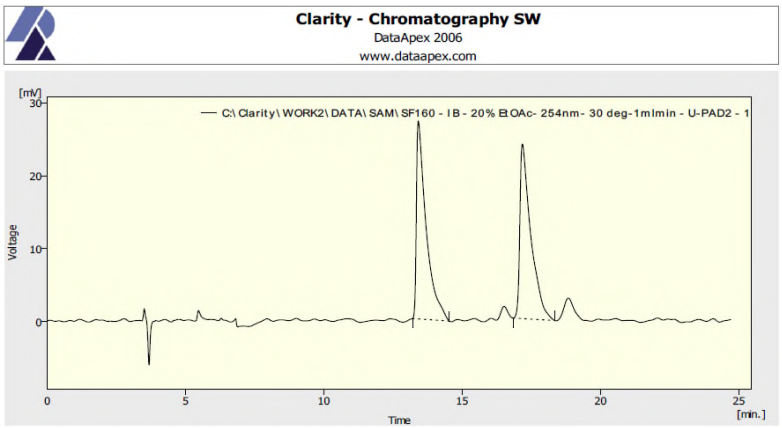
^{13}C NMR (125 MHz, $CDCl_3$)



COSY (500 MHz, $CDCl_3$)



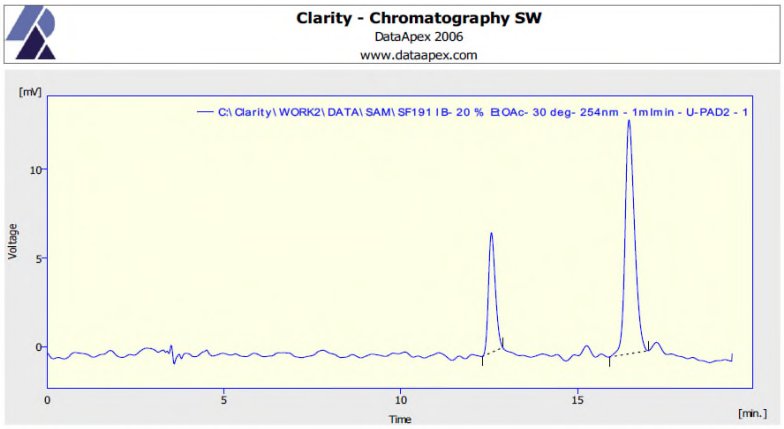
HPLC Racemic



Result Table (Uncal - C:\Clarity\WORK2\DATA\SAM\SF160 - IB - 20%EtOAc- 254nm- 30 deg-1mlmin - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	13.416	662.826	27.156	50.2	53.1	0.34	
2	17.176	657.939	23.957	49.8	46.9	0.39	
	Total	1320.765	51.114	100.0	100.0		

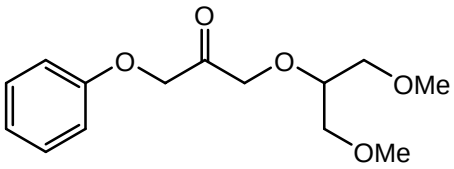
HPLC After ATH



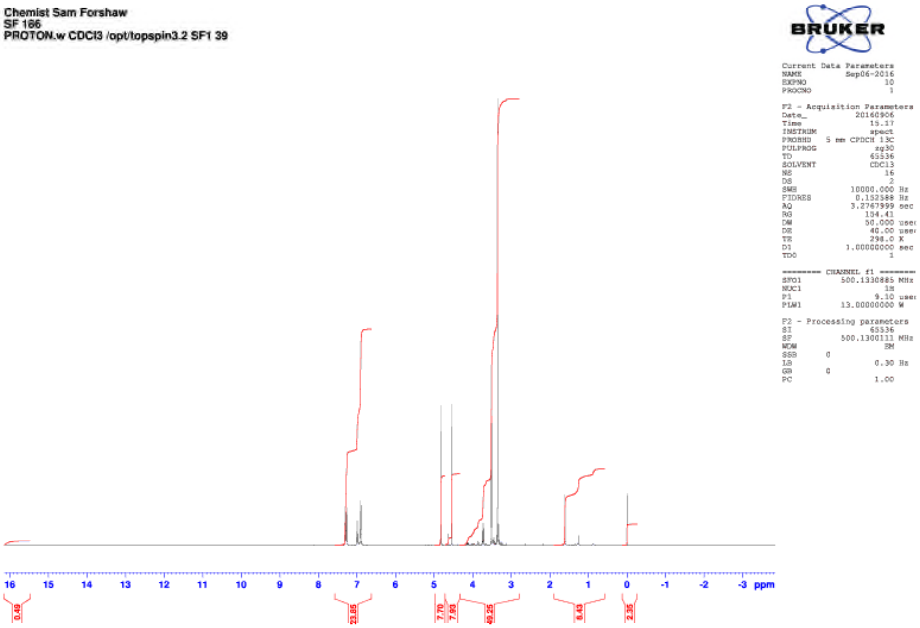
Result Table (Uncal - C:\Clarity\WORK2\DATA\SAM\SF191 IB- 20 % EtOAc- 30 deg- 254nm - 1mlmin - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	12.564	90.518	6.764	27.0	33.9	0.22	
2	16.452	245.281	13.203	73.0	66.1	0.29	
	Total	335.799	19.967	100.0	100.0		

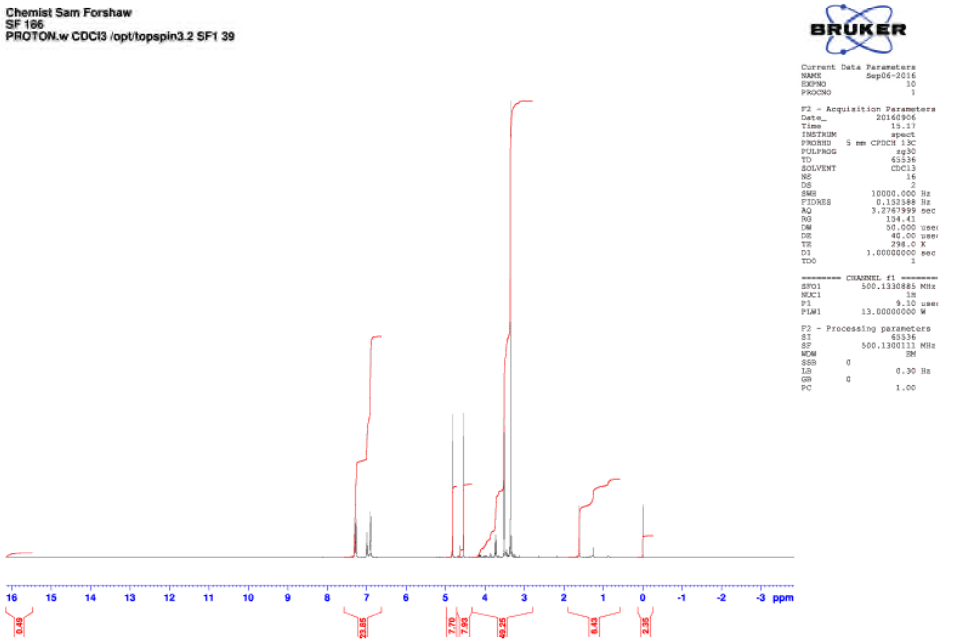
1-((1,3-Dimethoxypropan-2-yl)oxy)-3-phenoxypropan-2-one.



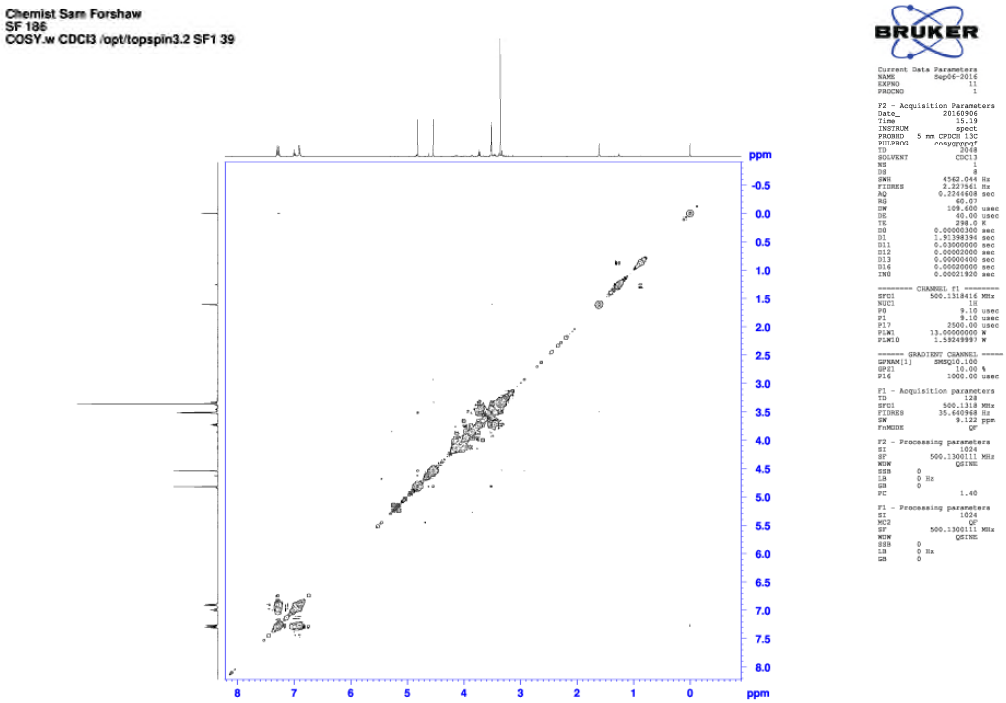
^{1}H NMR (500 MHz, $CDCl_3$)



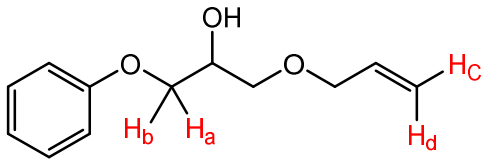
^{13}C NMR (125 MHz, $CDCl_3$)



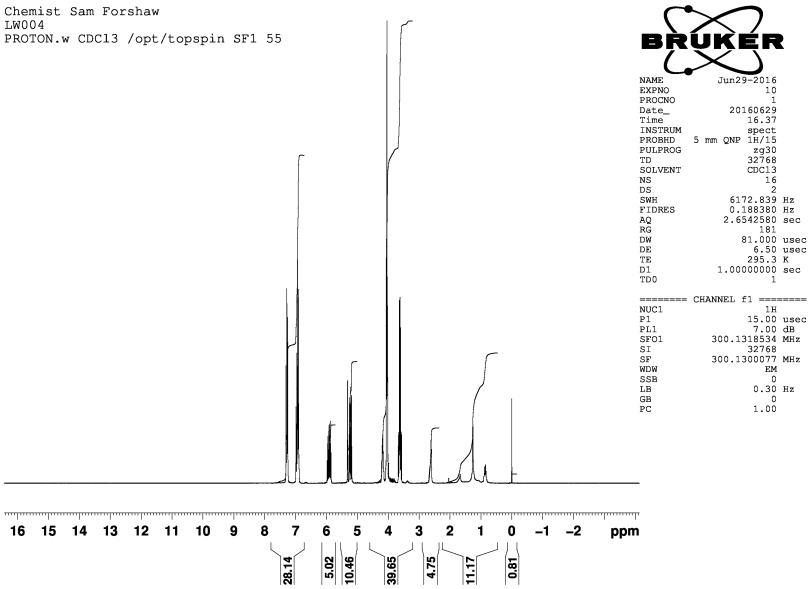
COSY (500 MHz, $CDCl_3$)



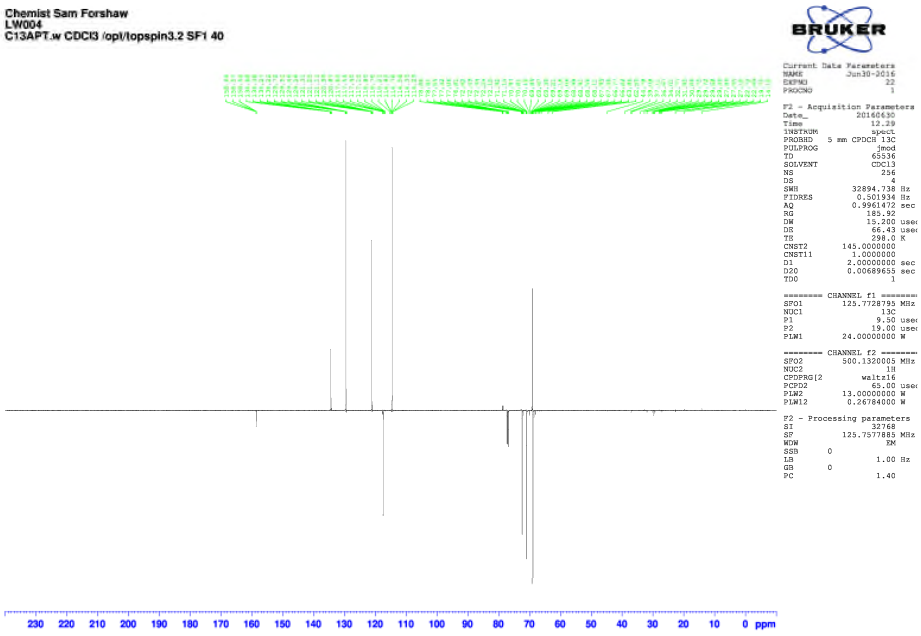
1-(Allyloxy)-3-phenoxypropan-2-ol 9.



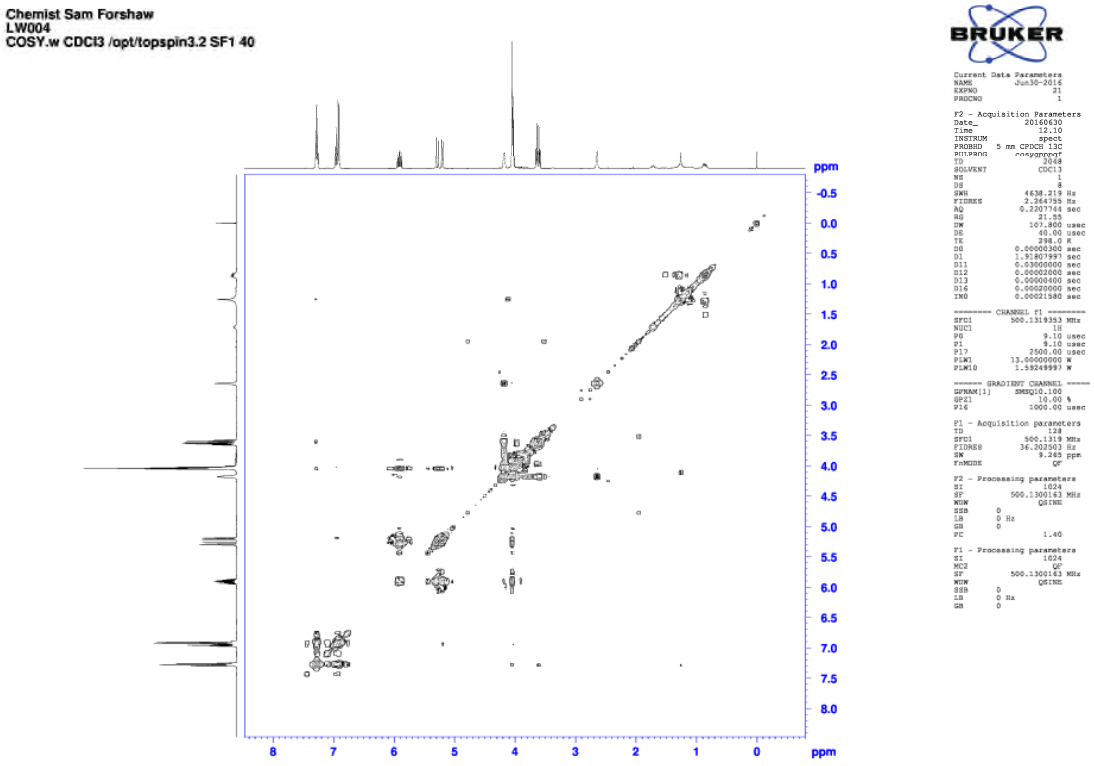
^{1}H NMR (300 MHz, $CDCl_3$)



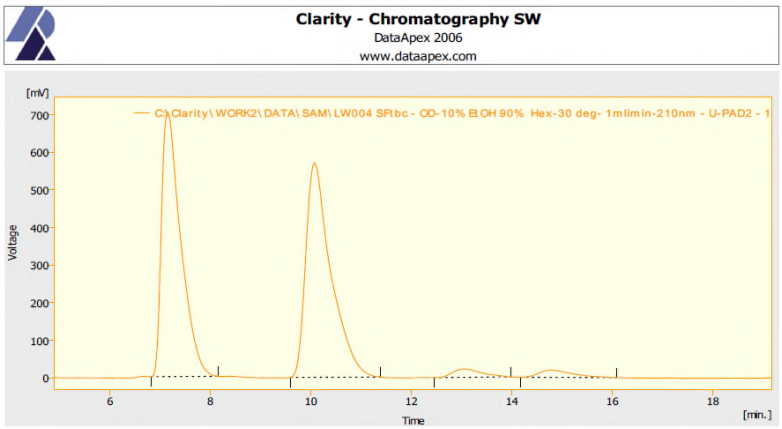
^{13}C NMR (500 MHz, $CDCl_3$)



COSY (500 MHz, CDCl3)



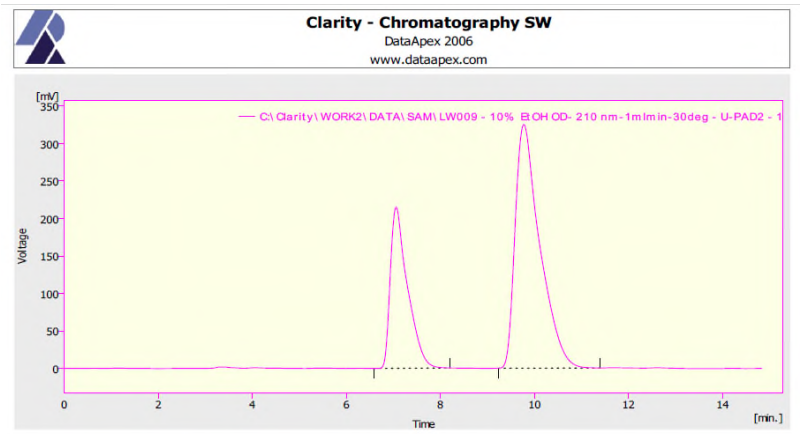
HPLC Racemic



Result Table (Uncal - C:\Clarity\WORK2\DATA\SAM\LW004 SFtbc - OD-10%EtOH 90% Hex-30 deg- 1mlimin-210nm - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	7.148	18773.931	703.962	46.5	53.5	0.41	
2	10.072	19776.009	570.325	49.0	43.3	0.50	
3	13.048	893.544	22.362	2.2	1.7	0.62	
4	14.780	906.006	19.361	2.2	1.5	0.71	
	Total	40349.490	1316.009	100.0	100.0		

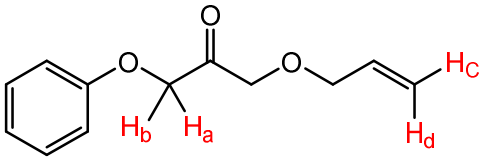
HPLC After ATH



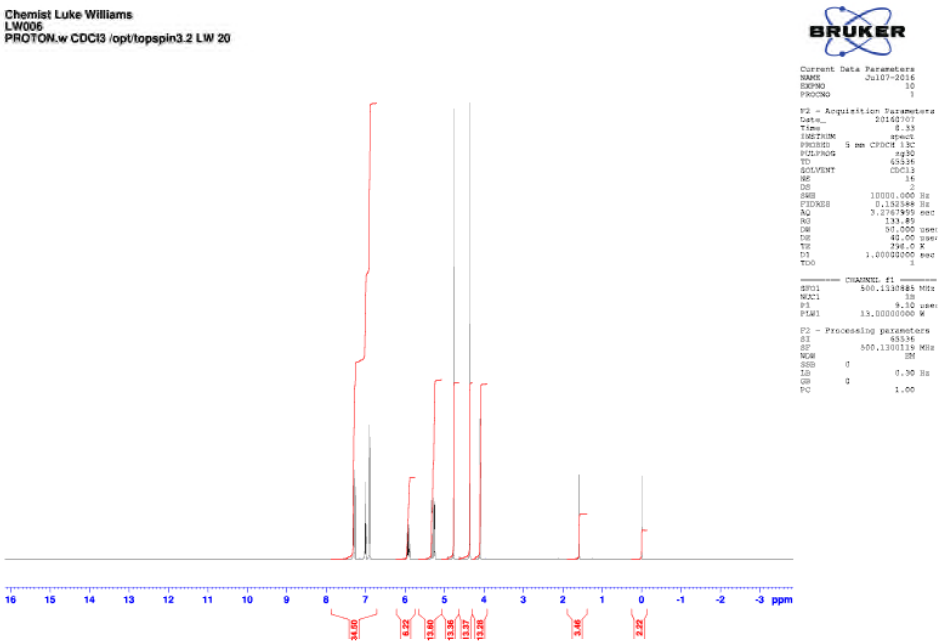
Result Table (Uncal - C:\Clarity\WORK2\DATA\SAM\LW009 - 10% EtOH OD- 210 nm-1mlmin-30deg - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	7.060	5461.597	215.003	31.6	39.8	0.39	
2	9.776	11842.275	325.321	68.4	60.2	0.55	
	Total	17303.872	540.324	100.0	100.0		

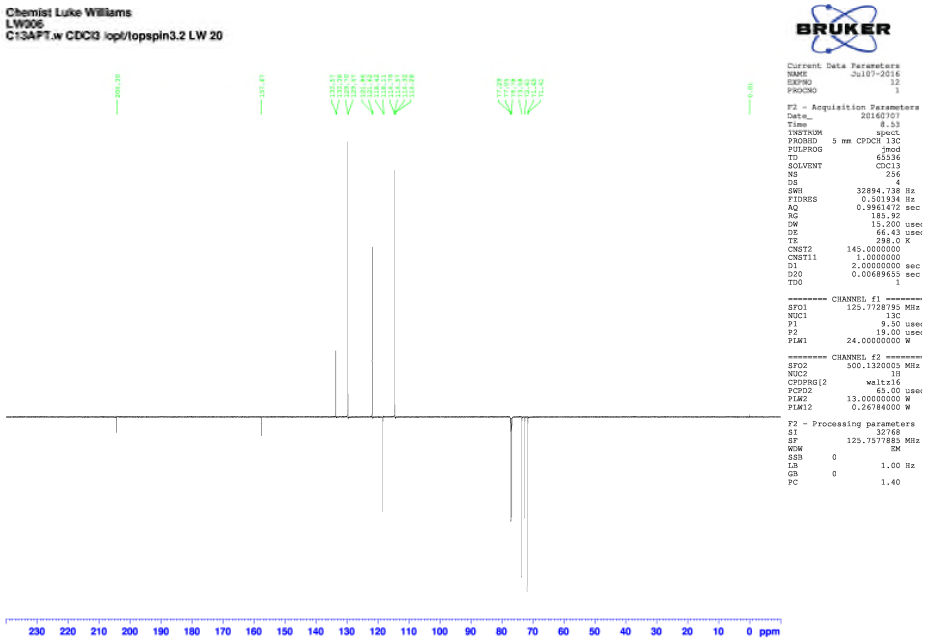
1-(Allyloxy)-3-phenoxypropan-2-one.



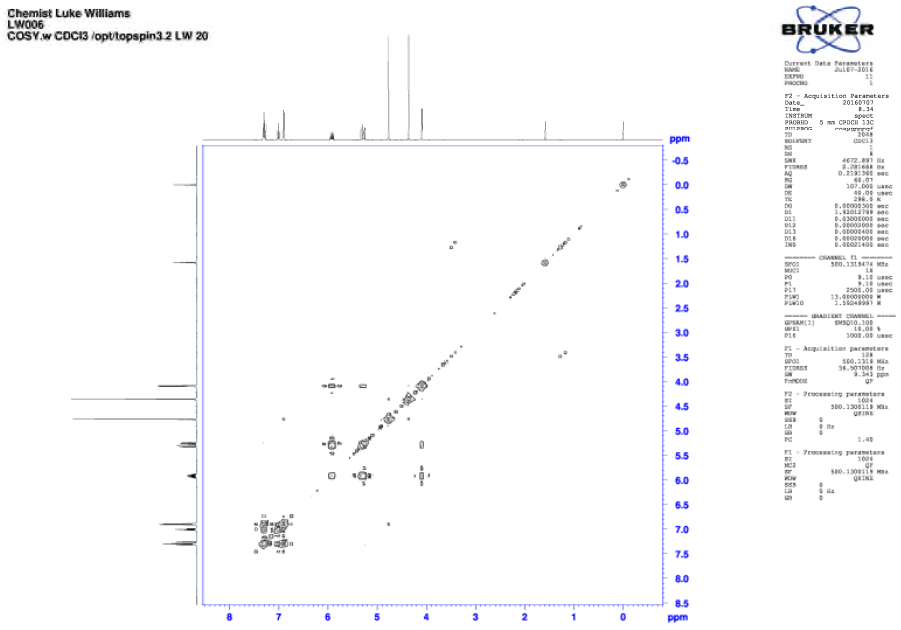
^{1}H NMR (500 MHz, $CDCl_3$)



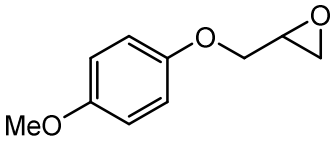
^{13}C NMR (125 MHz, $CDCl_3$)



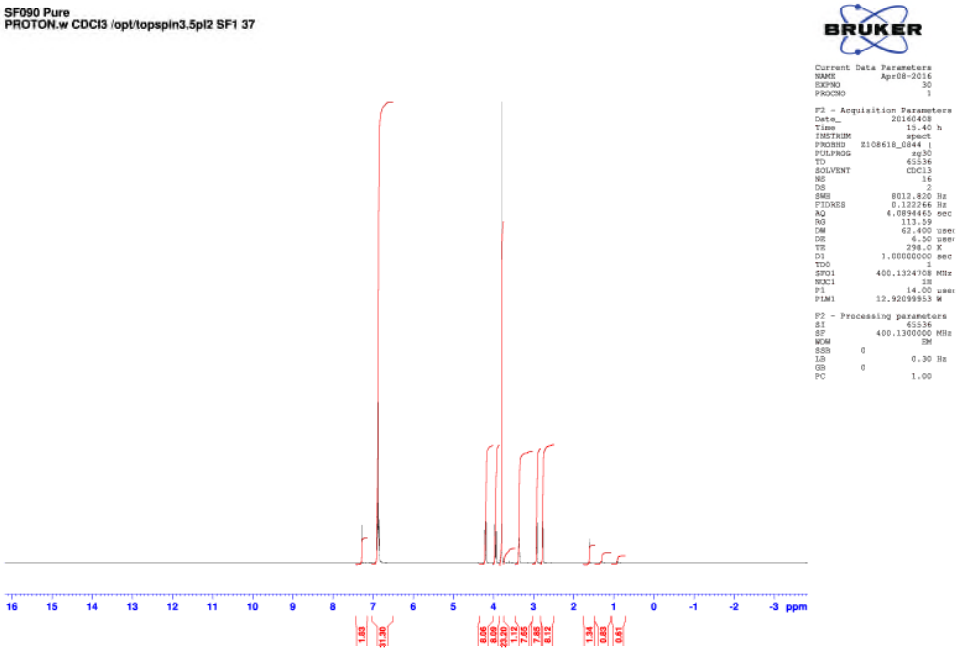
COSY (500 MHz, $CDCl_3$)



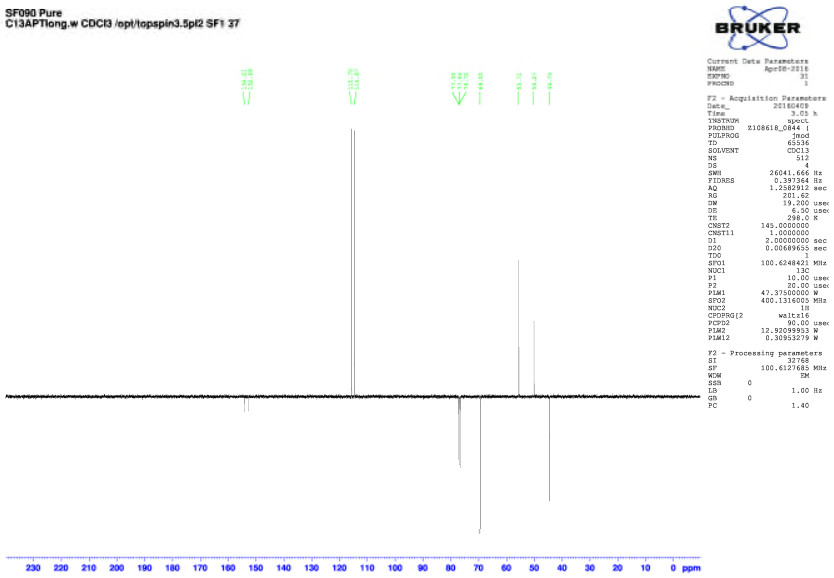
2-((4-Methoxyphenoxy)methyl)oxirane.



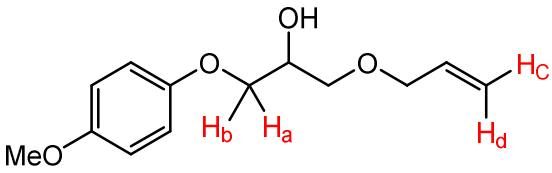
^{1}H NMR (400 MHz, $CDCl_3$)



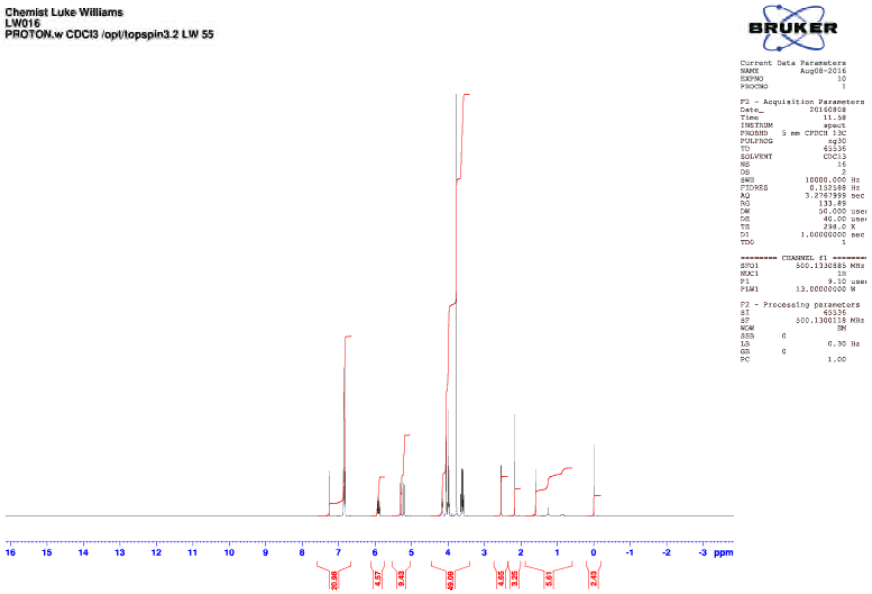
^{13}C NMR (100 MHz, $CDCl_3$)



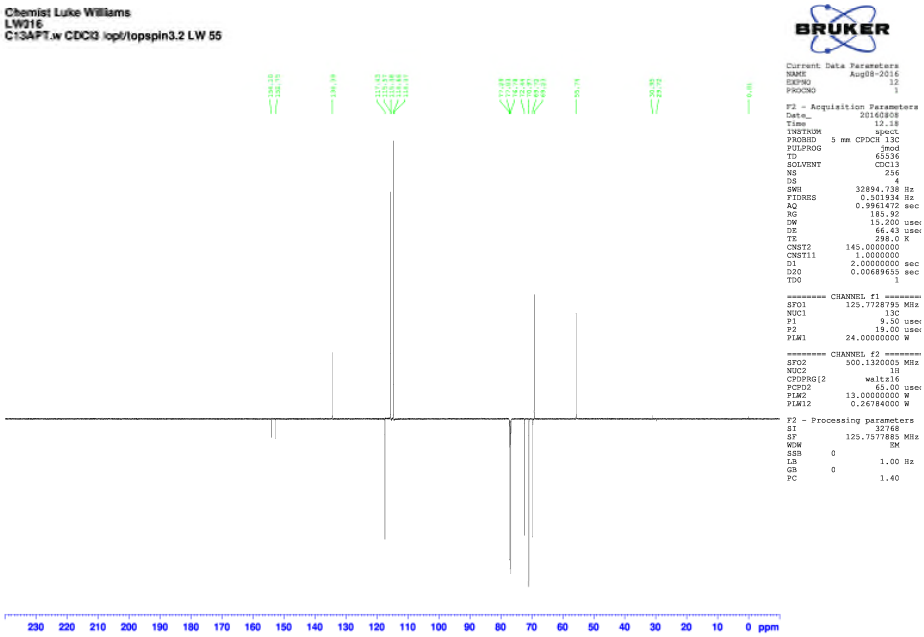
1-(Allyloxy)-3-(4-methoxyphenoxy)propan-2-ol 10.



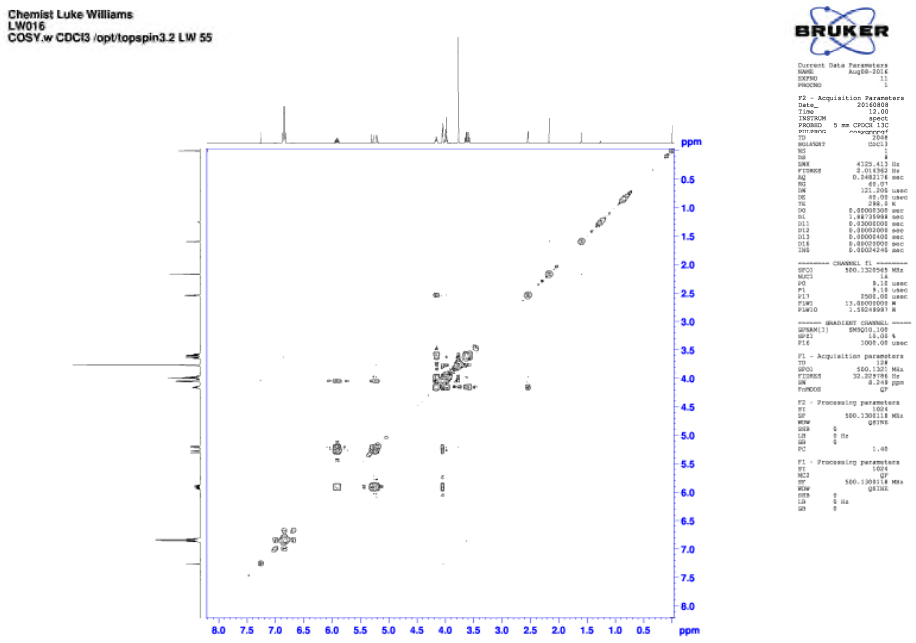
^{1}H NMR (500 MHz, $CDCl_3$)



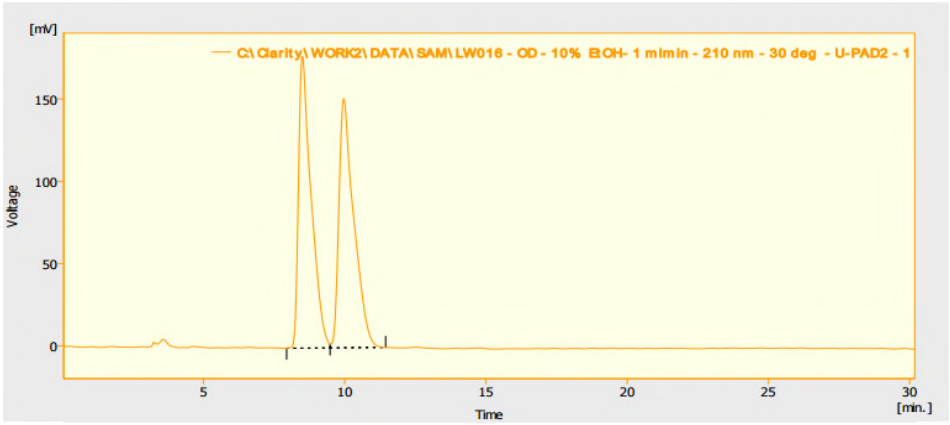
^{13}C NMR (125 MHz, $CDCl_3$)



COSY (500 MHz, $CDCl_3$)



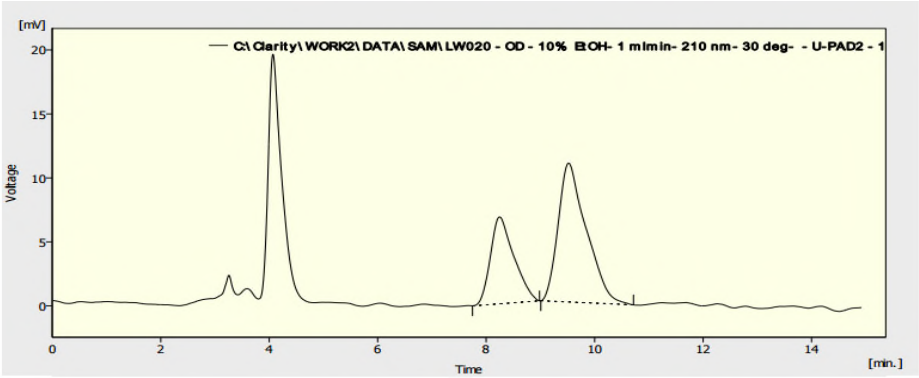
HPLC Racemic



Result Table (Uncal - C:\|Clarity\|WORK2\|DATA\|SAM\|LW016 - OD - 10% EtOH- 1 mlmin - 210 nm - 30 deg - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	8.504	5514.532	177.295	49.8	54.0	0.48	
2	9.968	5548.764	151.314	50.2	46.0	0.56	
	Total	11063.296	328.609	100.0	100.0		

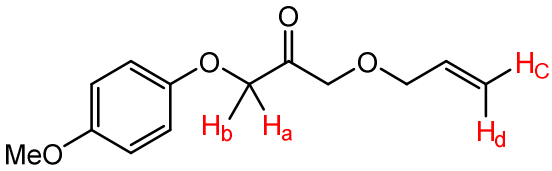
HPLC After ATH



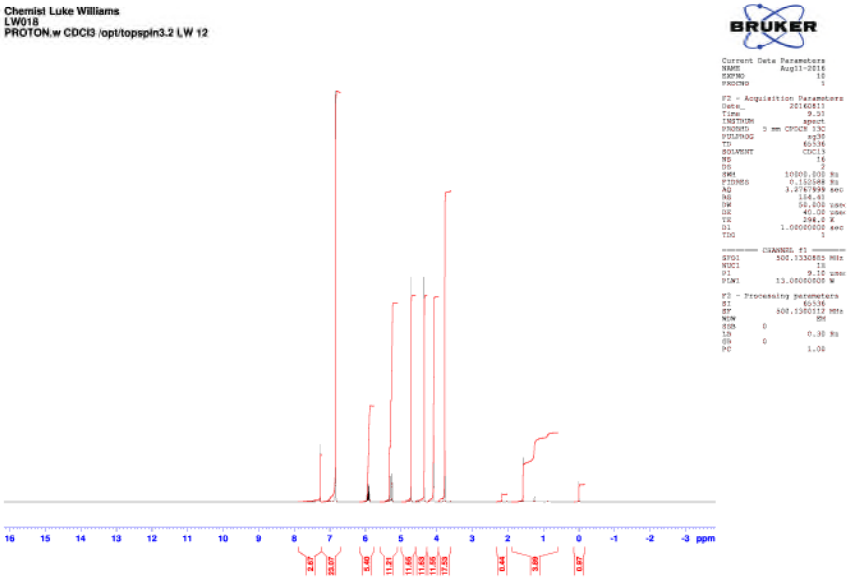
Result Table (Uncal - C:\Clarity\WORK2\DATA\SAM\LW020 - OD - 10% EtOH- 1 mlmin- 210 nm- 30 deg- - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	8.248	203.739	6.791	34.2	38.5	0.48	
2	9.528	392.200	10.851	65.8	61.5	0.56	
	Total	595.939	17.642	100.0	100.0		

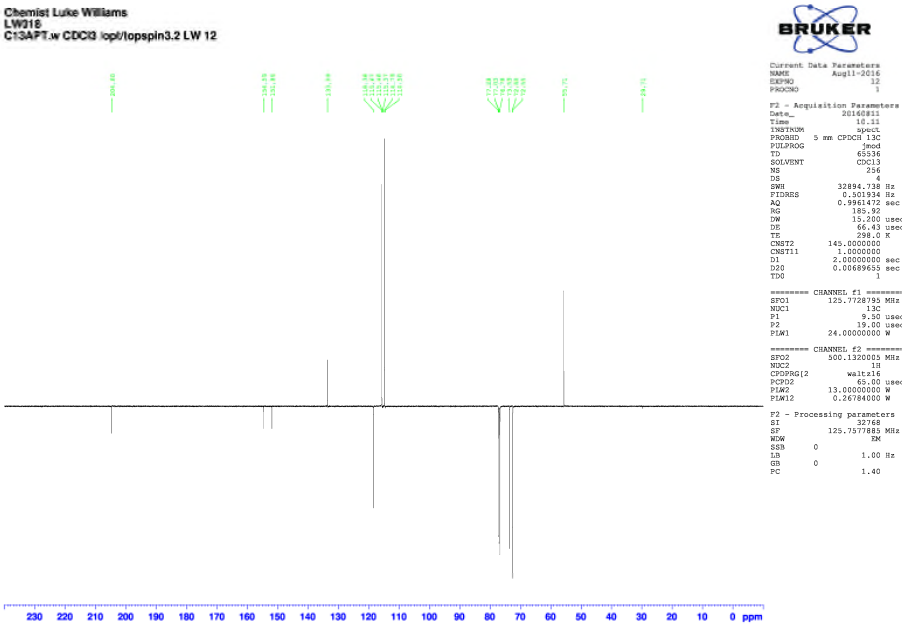
1-(Allyloxy)-3-(4-methoxyphenoxy)propan-2-one.



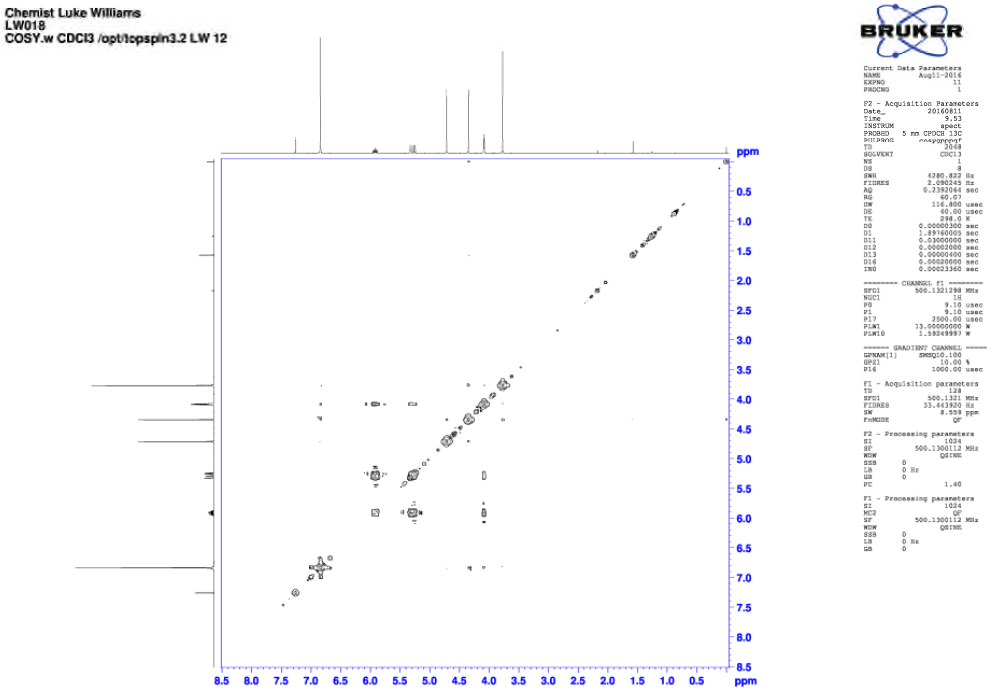
^{1}H NMR (500 MHz, $CDCl_3$)



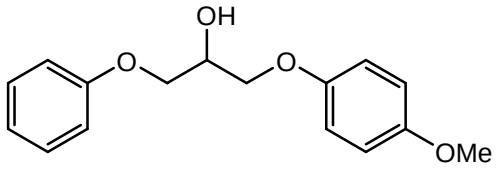
^{13}C NMR (125 MHz, $CDCl_3$)



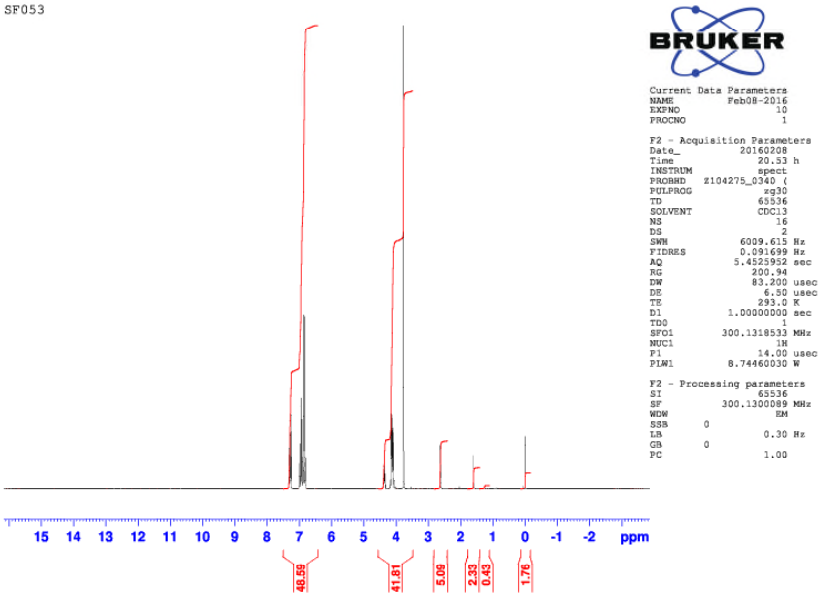
COSY (500 MHz, $CDCl_3$)



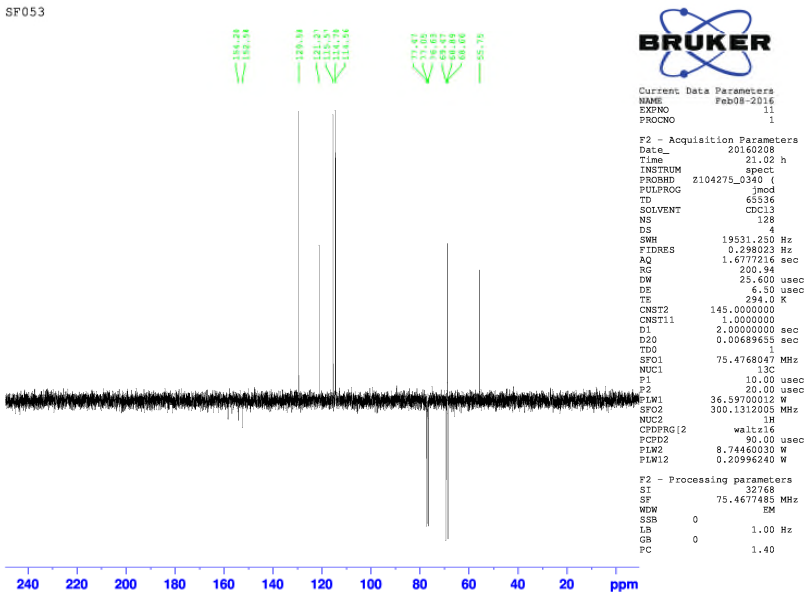
1-(4-Methoxyphenoxy)-3-phenoxypropan-2-ol 11.



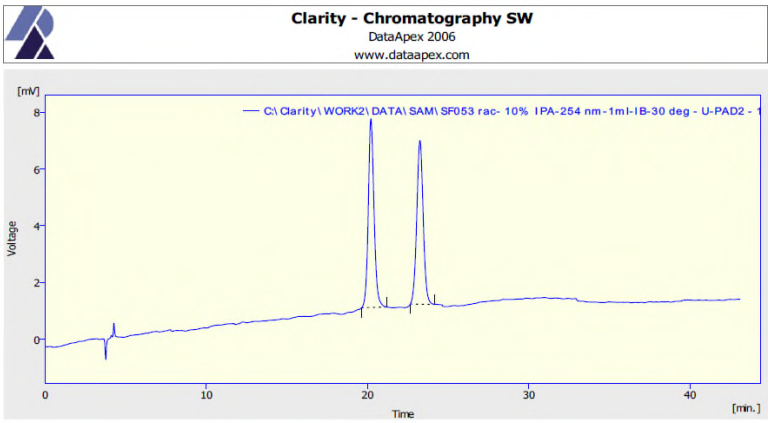
^{1}H NMR (300 MHz, $CDCl_3$)



^{13}C NMR (75 MHz, $CDCl_3$)



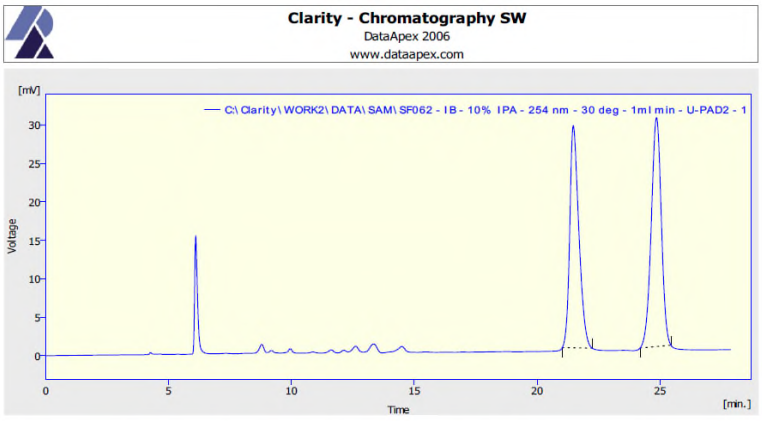
HPLC Racemic



Result Table (Uncal - C:\Clarity\WORK2\DATA\SAM\SF053 rac- 10% IPA-254 nm-1ml-IB-30 deg - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	20.204	164.525	6.648	50.7	53.6	0.37	
2	23.248	159.914	5.765	49.3	46.4	0.43	
	Total	324.439	12.412	100.0	100.0		

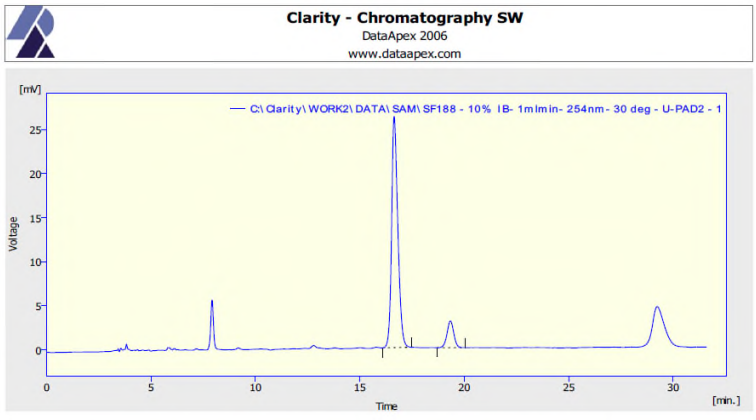
HPLC After ATH



Result Table (Uncal - C:\Clarity\WORK2\DATA\SAM\SF062 - IB - 10% IPA - 254 nm - 30 deg - 1ml min - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	21.472	741.565	28.876	46.8	49.3	0.39	
2	24.860	844.481	29.752	53.2	50.7	0.44	
	Total	1586.046	58.628	100.0	100.0		

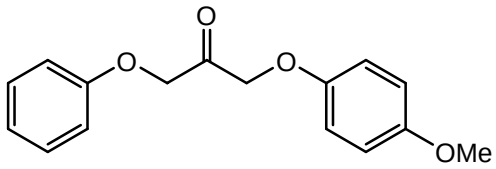
HPLC Asymmetric Standard



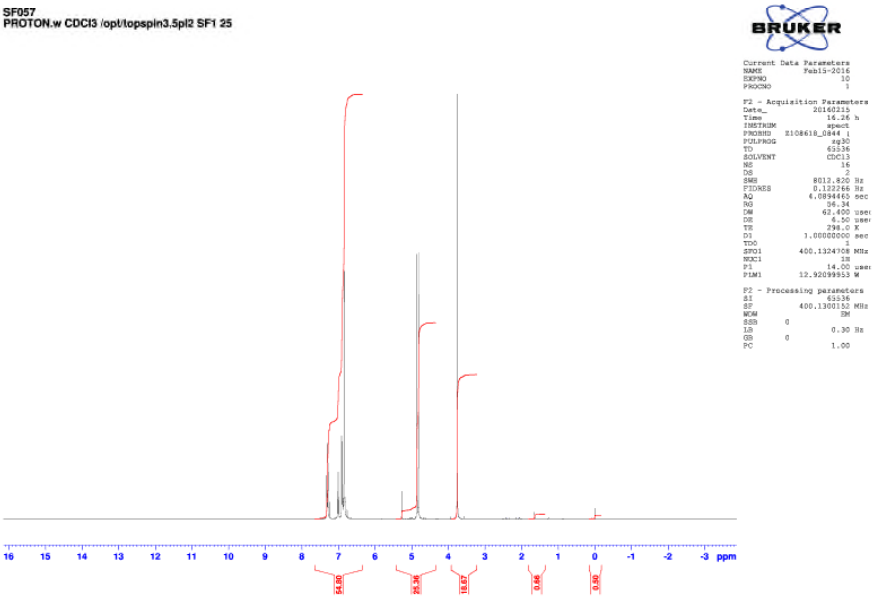
Result Table (Uncal - C:\Clarity\WORK2\DATA\SAM\SF188 - 10% IB- 1mlmin- 254nm- 30 deg - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	16.644	542.036	26.264	88.8	89.7	0.31	
2	19.336	68.085	3.030	11.2	10.3	0.35	
	Total	610.121	29.294	100.0	100.0		

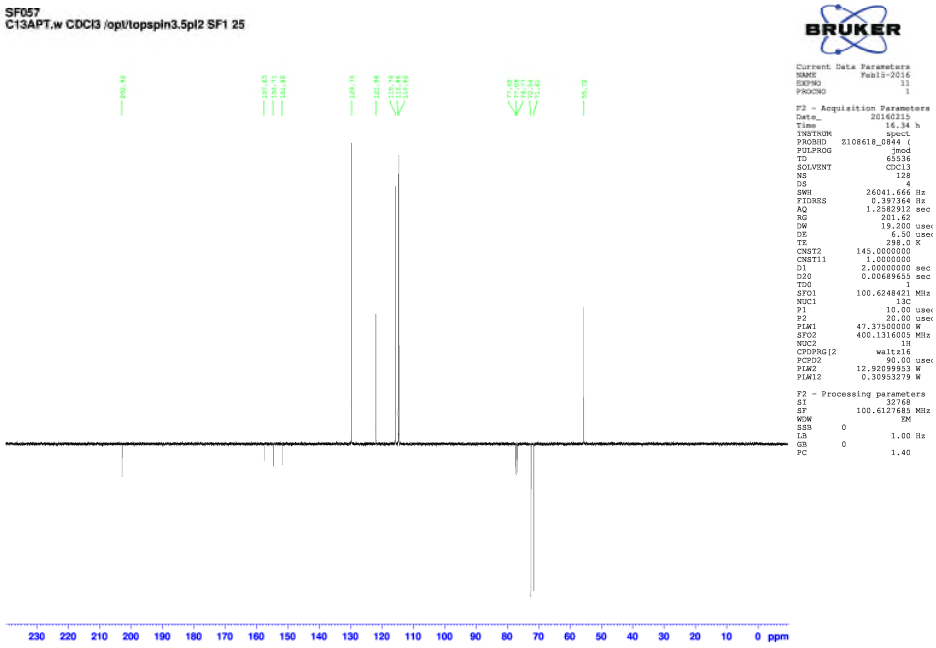
1-(4-Methoxyphenoxy)-3-phenoxypropan-2-one.



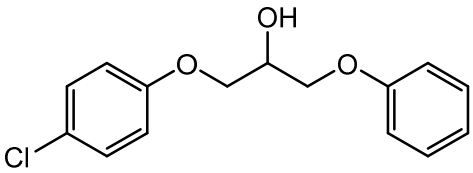
^{1}H NMR (400 MHz, $CDCl_3$)



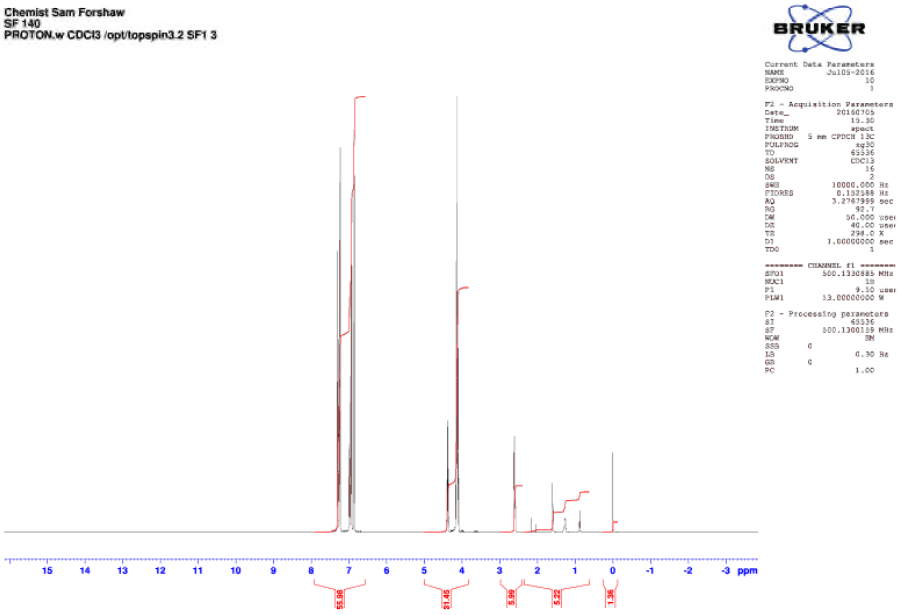
^{13}C NMR (100 MHz, $CDCl_3$)



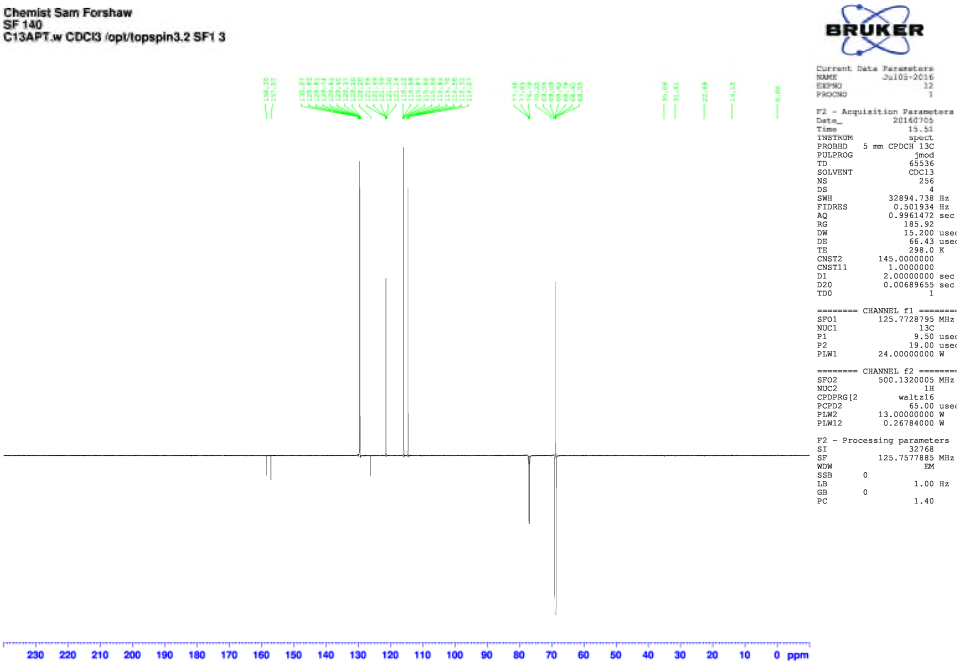
1-(4-Chlorophenoxy)-3-phenoxypropan-2-ol 12.



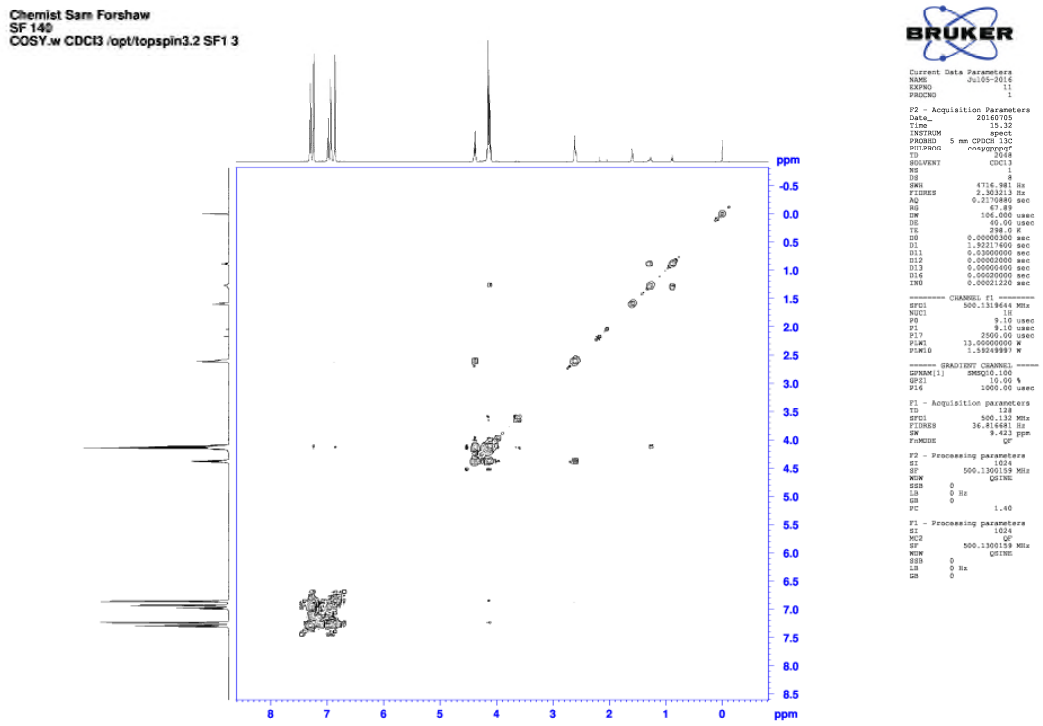
^{1}H NMR (500 MHz, $CDCl_3$)



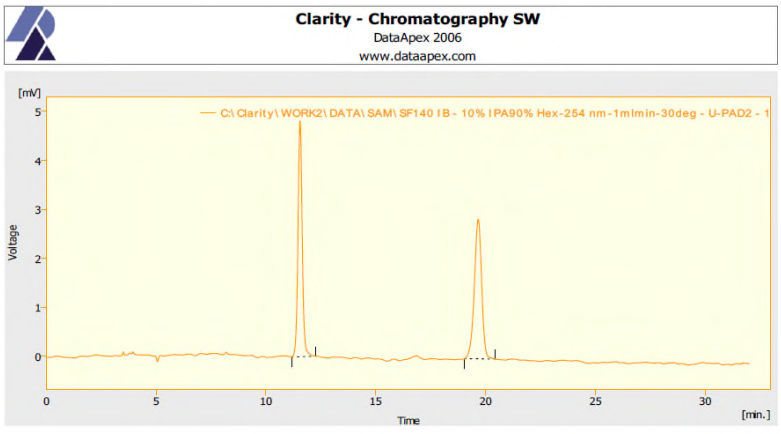
^{13}C NMR (125 MHz, $CDCl_3$)



COSY (500 MHz, $CDCl_3$)



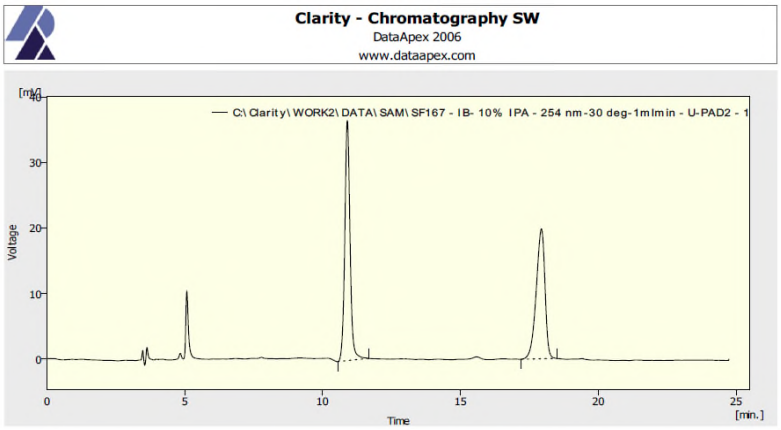
HPLC Racemic



Result Table (Uncal - C:\Clarity\WORK2\DATA\SAM\SF140 IB - 10%IPA90%Hex-254 nm-1mlmin-30deg - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	11.552	64.423	4.812	49.4	62.8	0.20	
2	19.664	65.877	2.855	50.6	37.2	0.35	
	Total	130.300	7.667	100.0	100.0		

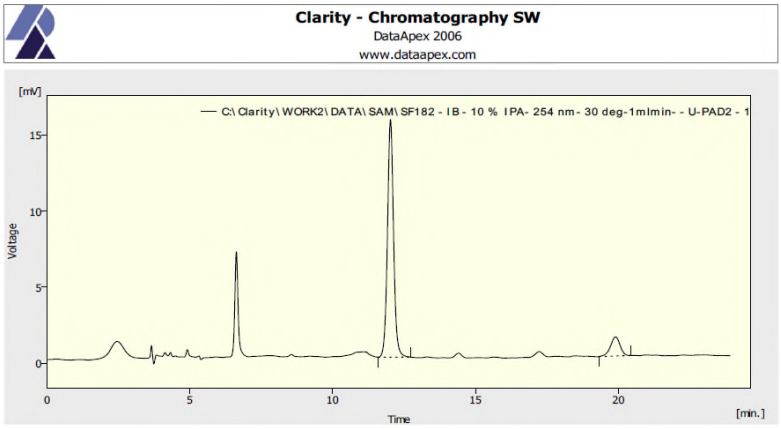
HPLC After ATH



Result Table (Uncal - C:\Clarity\WORK2\DATA\SAM\SF167 - IB- 10% IPA - 254 nm-30 deg-1mlmin - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	10.900	487.174	36.664	52.6	64.9	0.20	
2	17.940	438.615	19.829	47.4	35.1	0.34	
	Total	925.789	56.492	100.0	100.0		

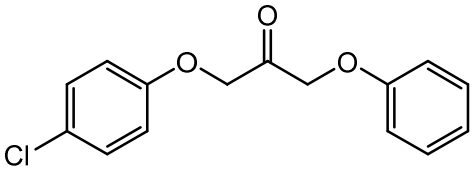
HPLC Asymmetric Standard



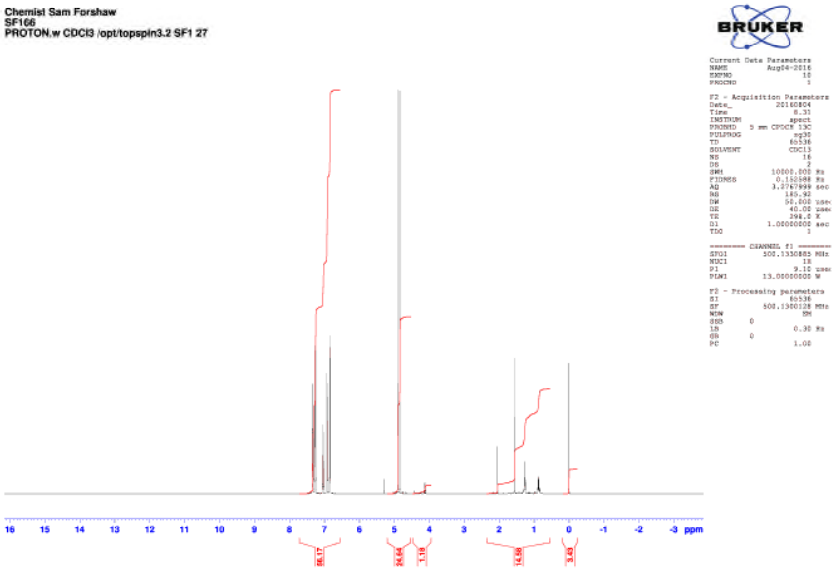
Result Table (Uncal - C:\Clarity\WORK2\DATA\SAM\SF182 - IB - 10 % IPA- 254 nm- 30 deg-1mlmin- - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	12.024	231.748	15.610	88.8	92.5	0.22	
2	19.904	29.201	1.261	11.2	7.5	0.36	
	Total	260.949	16.870	100.0	100.0		

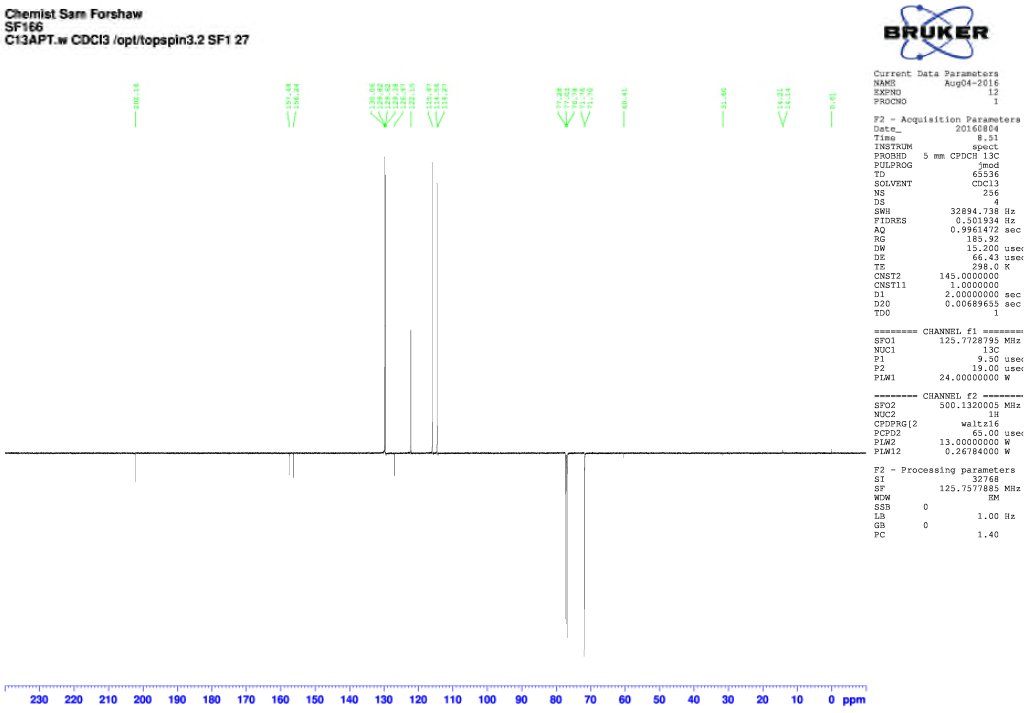
1-(4-Chlorophenoxy)-3-phenoxypropan-2-one.



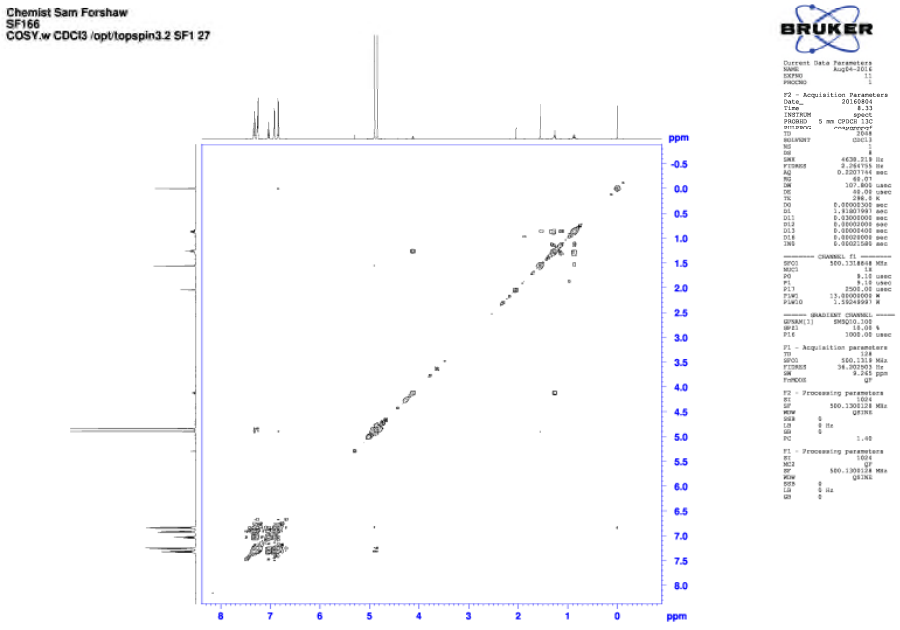
^{1}H NMR (500 MHz, $CDCl_3$)



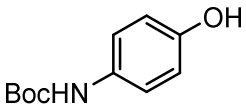
^{13}C NMR (125 MHz, $CDCl_3$)



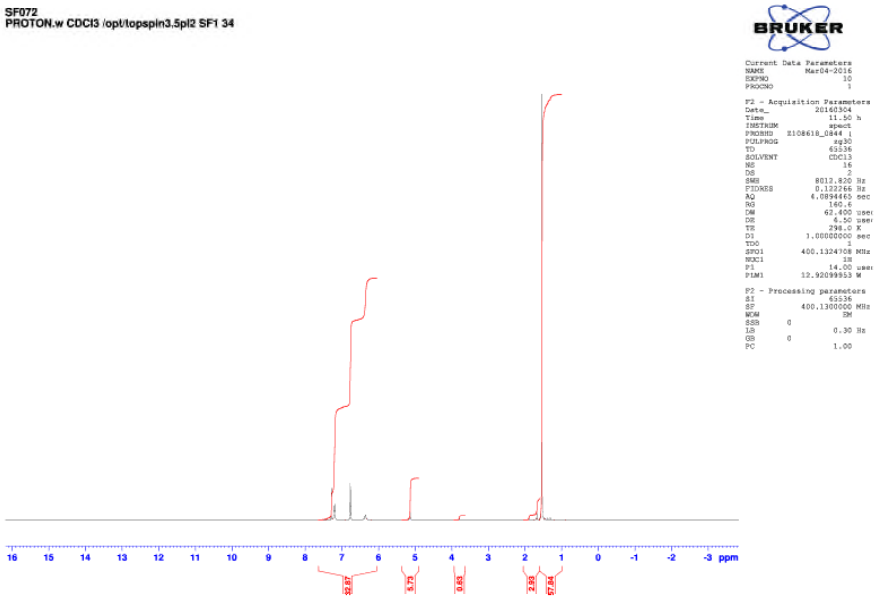
COSY (500 MHz, $CDCl_3$)



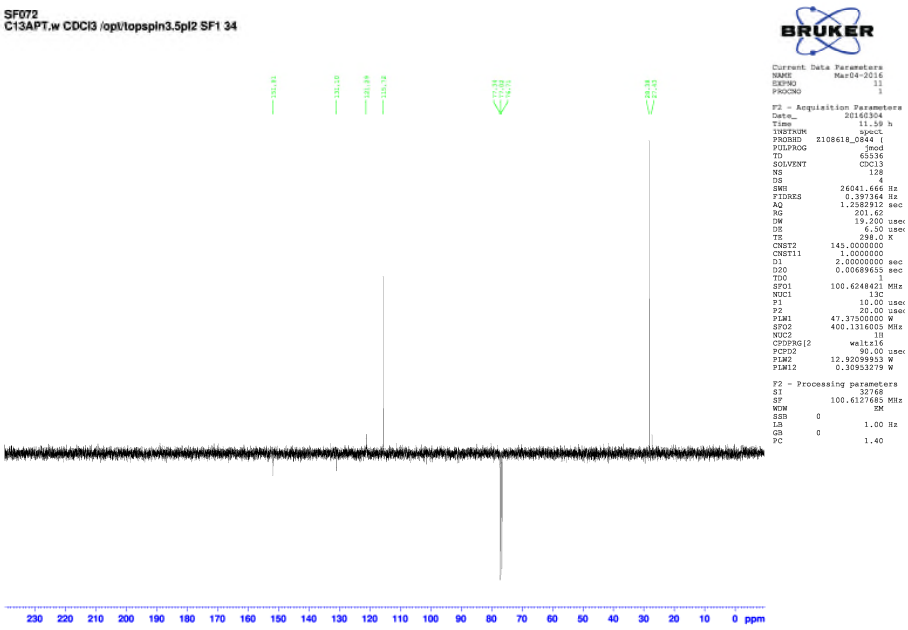
tert-Butyl (4-hydroxyphenyl)carbamate.



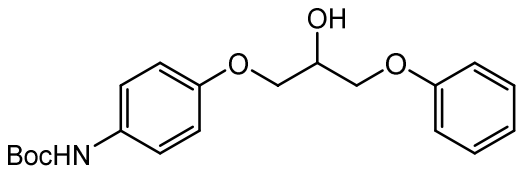
^{1}H NMR (400 MHz, $CDCl_3$)



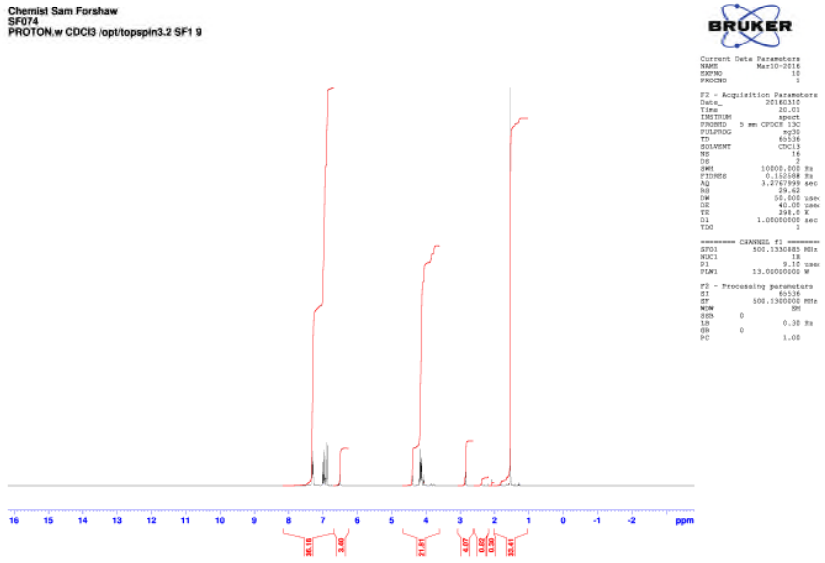
^{13}C NMR (100 MHz, $CDCl_3$)



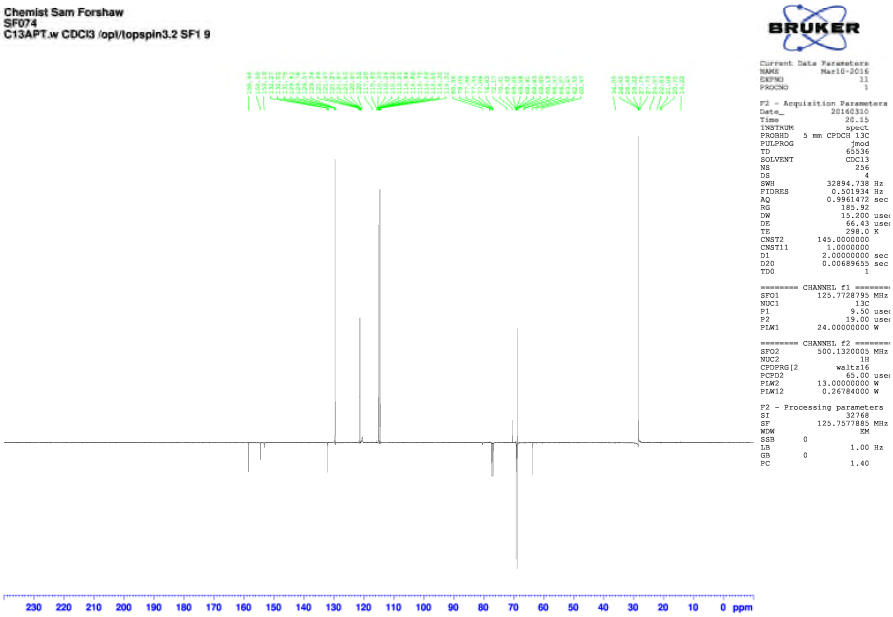
tert-Butyl (4-(2-hydroxy-3-phenoxypropoxy)phenyl)carbamate 14.



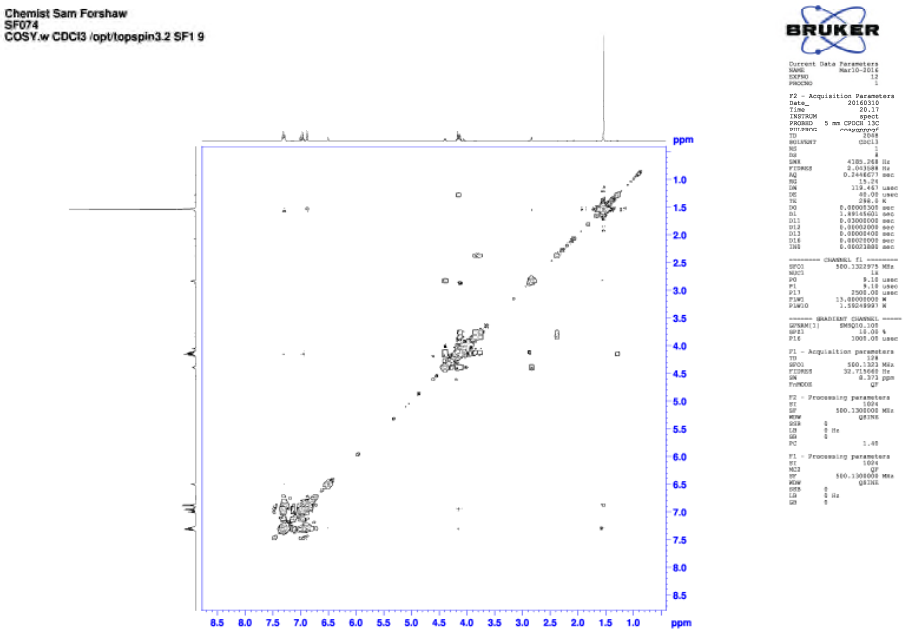
^{1}H NMR (500 MHz, $CDCl_3$)



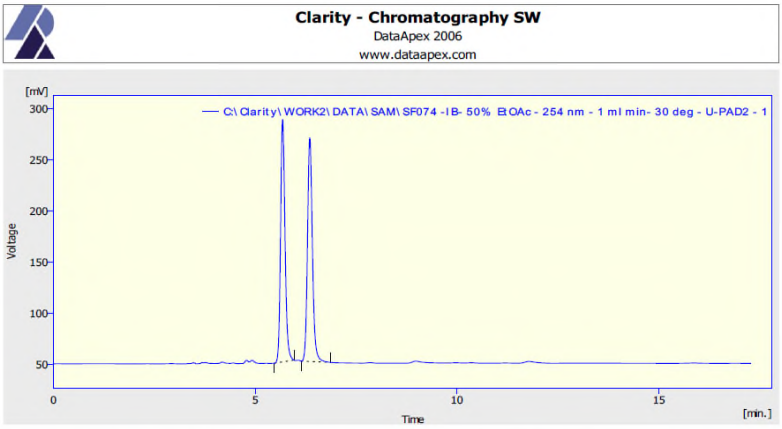
^{13}C NMR (125 MHz, $CDCl_3$)



COSY (500 MHz, $CDCl_3$)



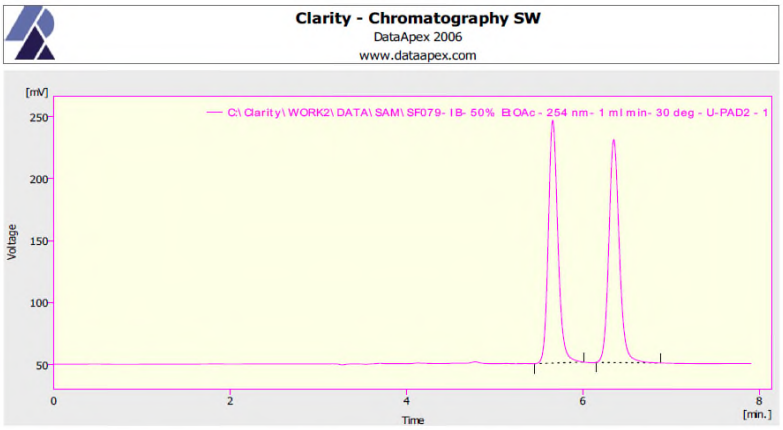
HPLC Racemic



Result Table (Uncal - C:\Clarity\WORK2\DATA\SAM\SF074 -IB- 50% EtOAc - 254 nm - 1 ml min- 30 deg - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	5.676	1816.745	236.887	49.5	52.0	0.12	
2	6.352	1853.741	218.613	50.5	48.0	0.13	
	Total	3670.486	455.501	100.0	100.0		

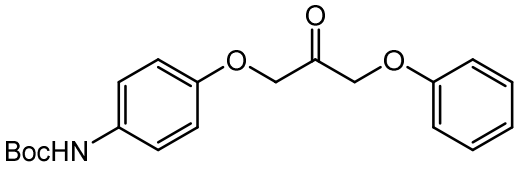
HPLC After ATH



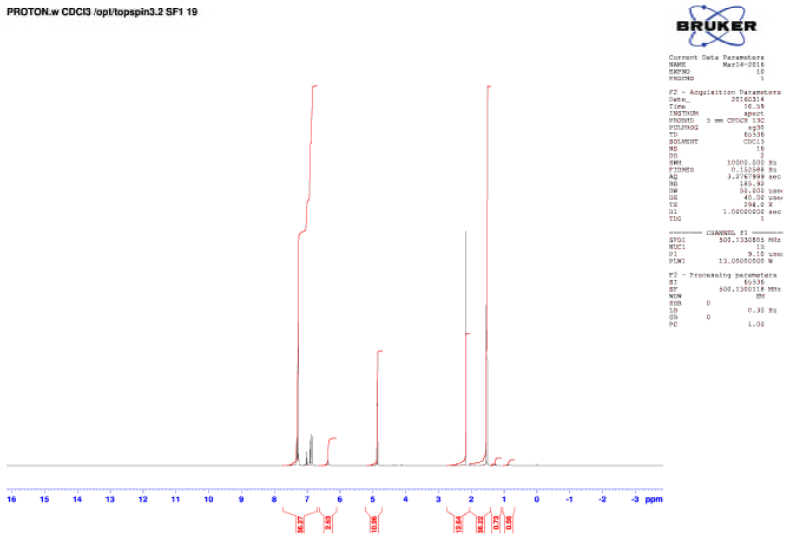
Result Table (Uncal - C:\Clarity\WORK2\DATA\SAM\SF079- IB- 50% EtOAc - 254 nm- 1 ml min- 30 deg - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	5.660	1477.916	195.985	49.8	52.1	0.12	
2	6.352	1491.098	180.149	50.2	47.9	0.13	
	Total	2969.013	376.134	100.0	100.0		

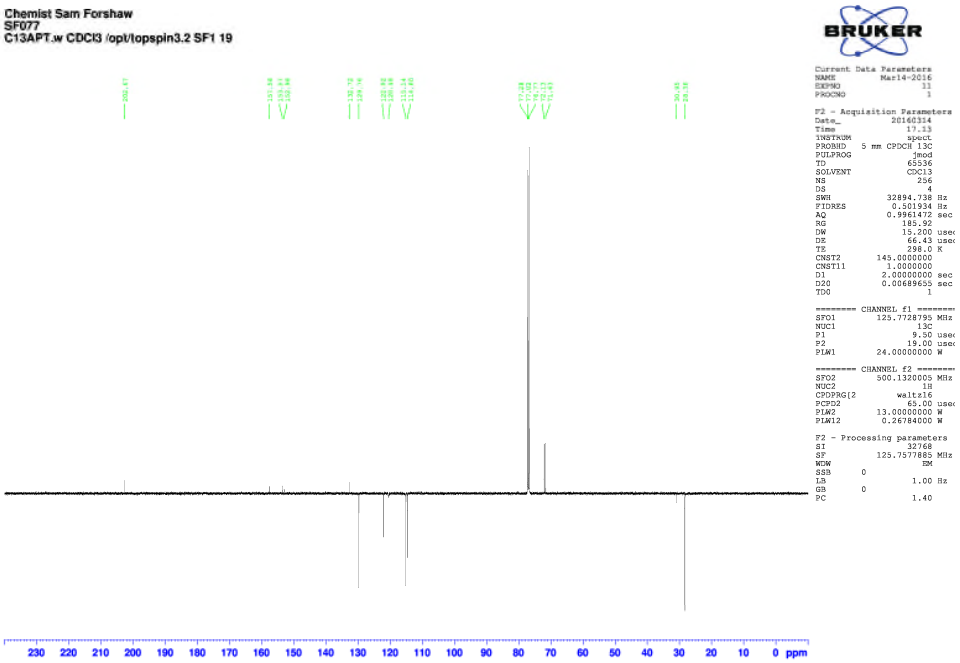
***tert*-Butyl (4-(2-oxo-3-phenoxypropoxy)phenyl)carbamate.**



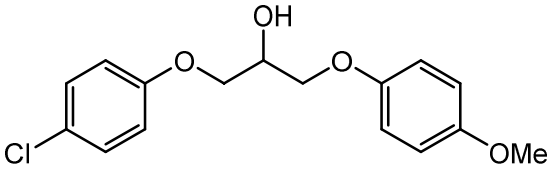
^{1}H NMR (500 MHz, $CDCl_3$)



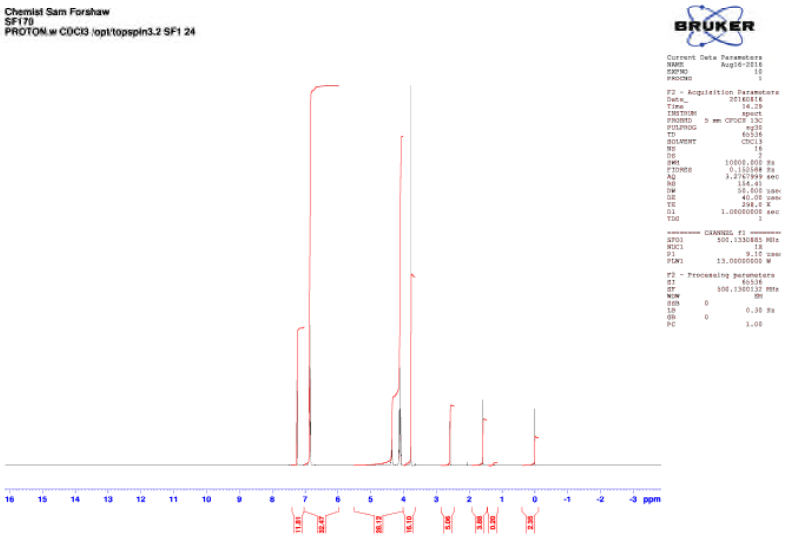
^{13}C NMR (125 MHz, $CDCl_3$)



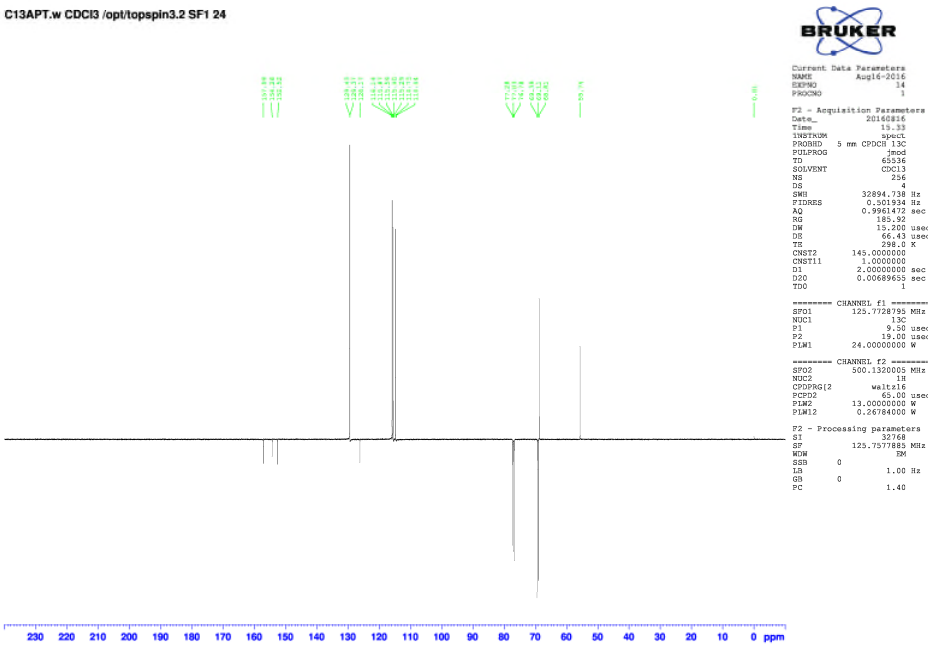
1-(4-Chlorophenoxy)-3-(4-methoxyphenoxy)propan-2-ol 13.



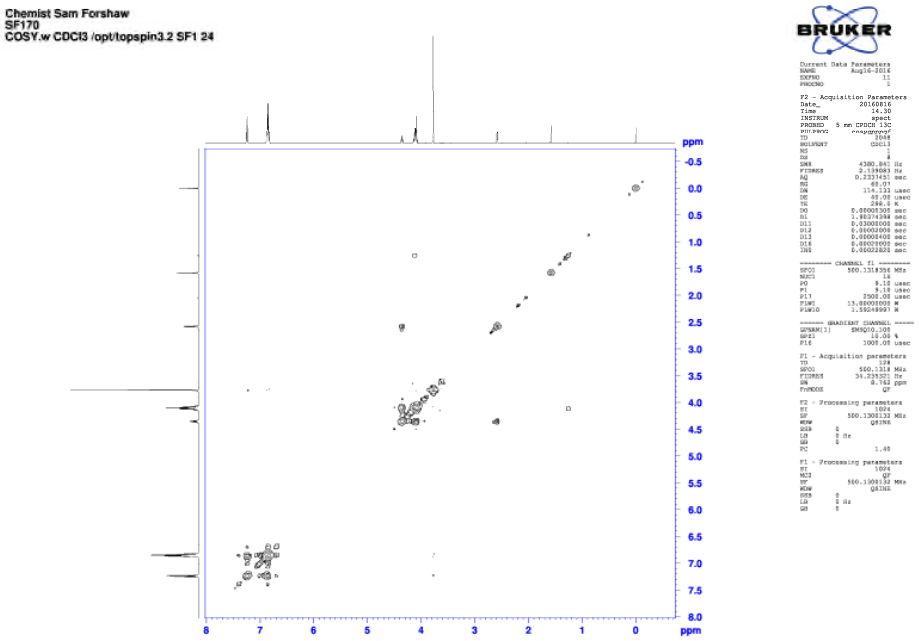
^{1}H NMR (500 MHz, $CDCl_3$)



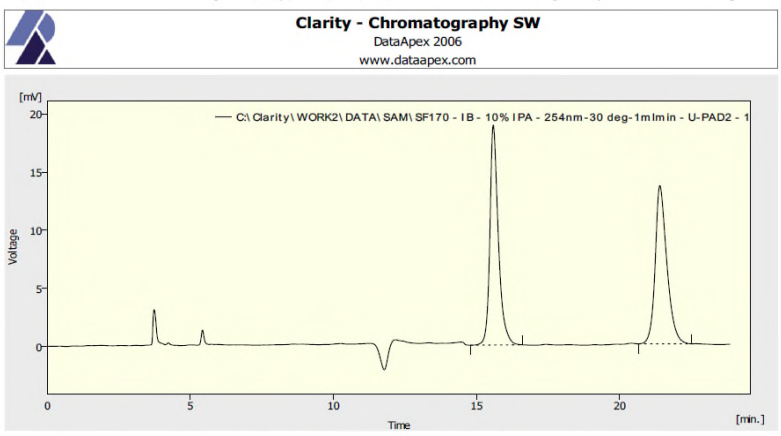
^{13}C NMR (125 MHz, $CDCl_3$)



COSY (500 MHz, $CDCl_3$)



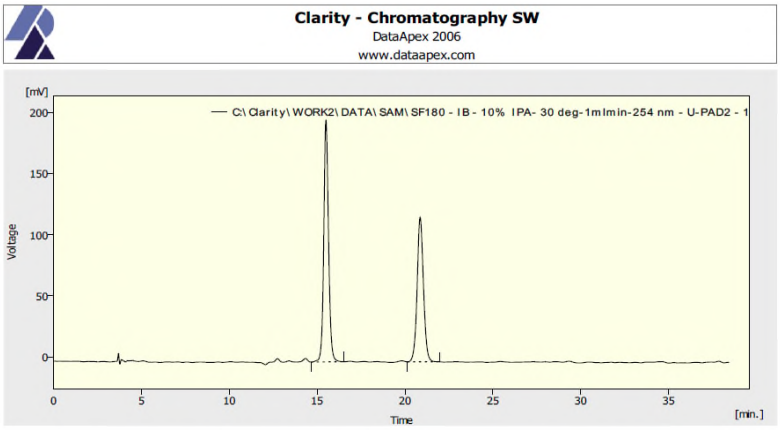
HPLC Racemic



Result Table (Uncal - C:\Clarity\WORK2\DATA\SAM\SF170 - IB - 10%IPA - 254nm-30 deg-1mlmin - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	15.584	389.735	18.886	50.3	58.2	0.30	
2	21.408	385.646	13.580	49.7	41.8	0.42	
	Total	775.380	32.466	100.0	100.0		

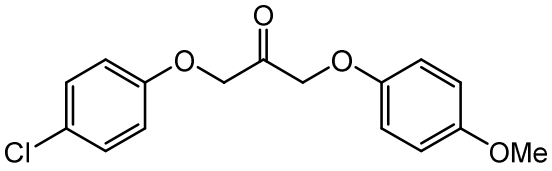
HPLC After ATH



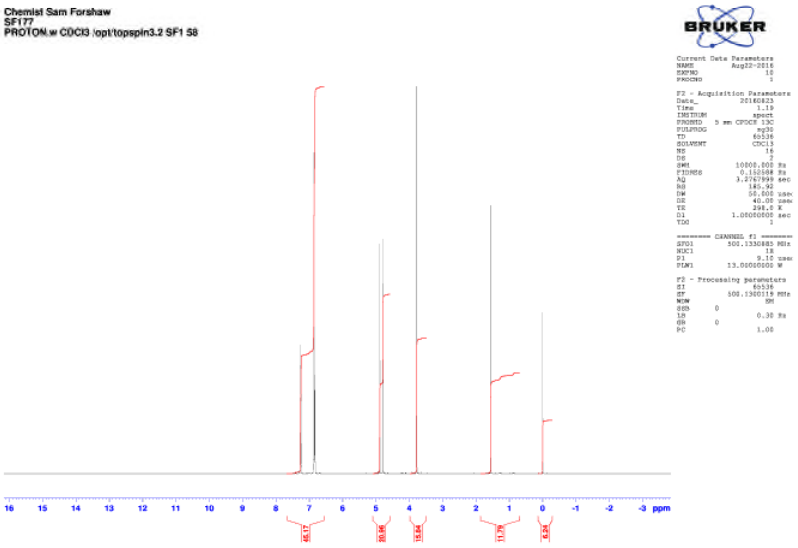
Result Table (Uncal - C:|Clarity|WORK2|DATA|SAM|SF180 - IB - 10% IPA - 30 deg-1mlmin-254 nm - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	15.504	3733.721	197.930	55.8	62.6	0.28	
2	20.860	2961.624	118.383	44.2	37.4	0.38	
	Total	6695.345	316.313	100.0	100.0		

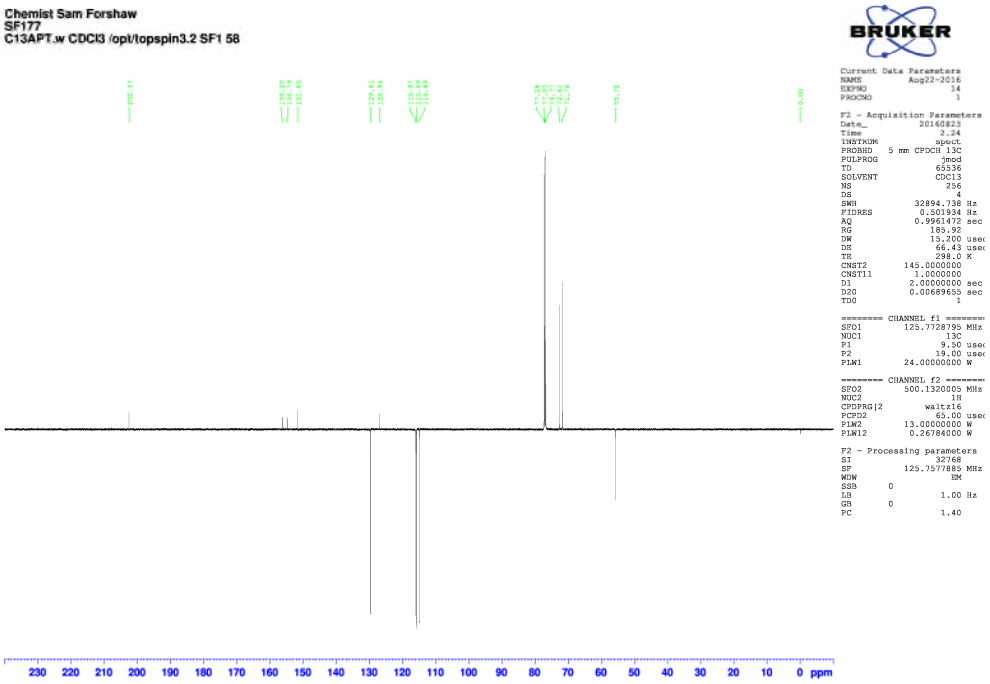
1-(4-Chlorophenoxy)-3-(4-methoxyphenoxy)propan-2-one.



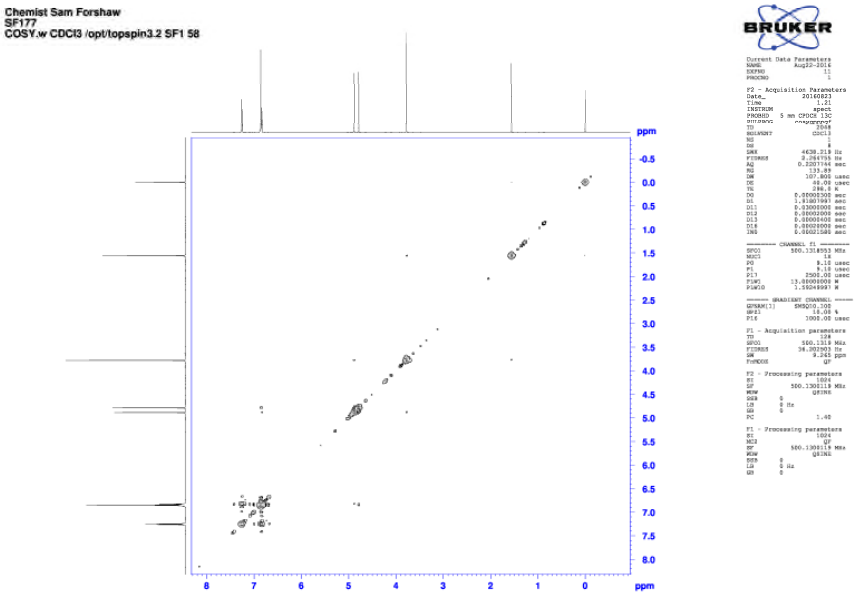
^{1}H NMR (500 MHz, $CDCl_3$)



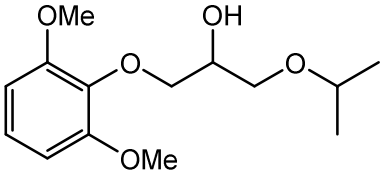
^{13}C NMR (125 MHz, $CDCl_3$)



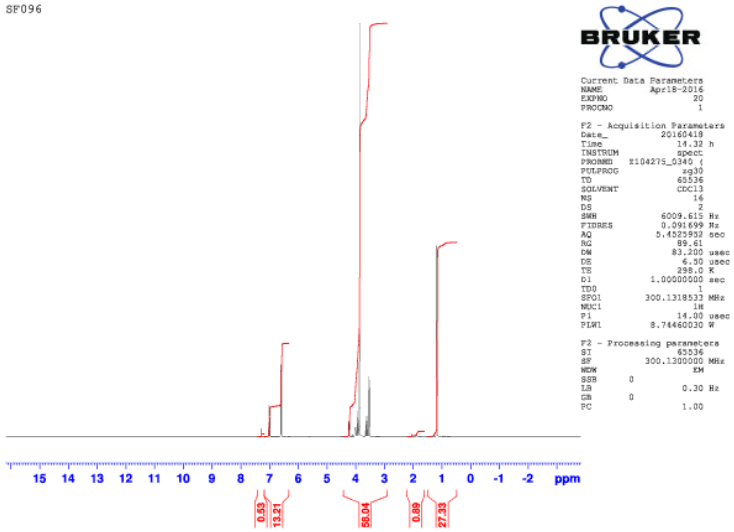
COSY (500 MHz, $CDCl_3$)



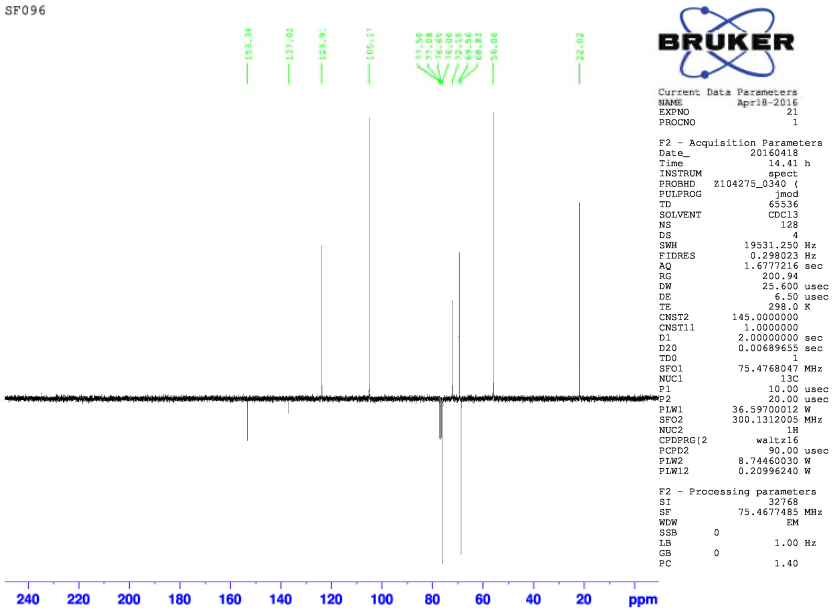
1-(2,6-Dimethoxyphenoxy)-3-isopropoxypropan-2-ol 15.



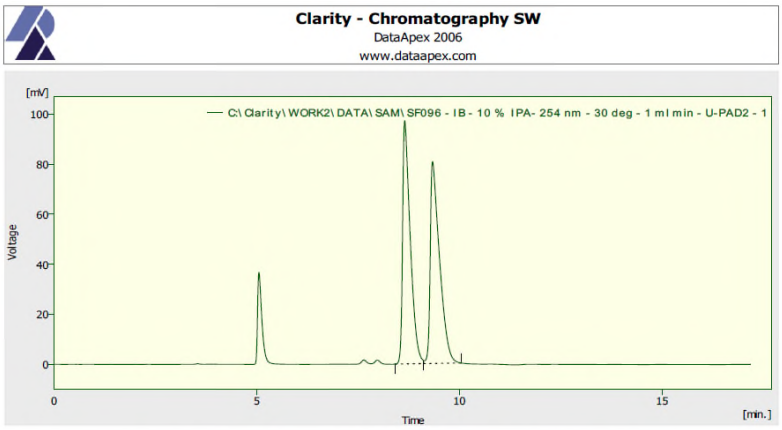
^{1}H NMR (300 MHz, $CDCl_3$)



^{13}C NMR (75 MHz, $CDCl_3$)



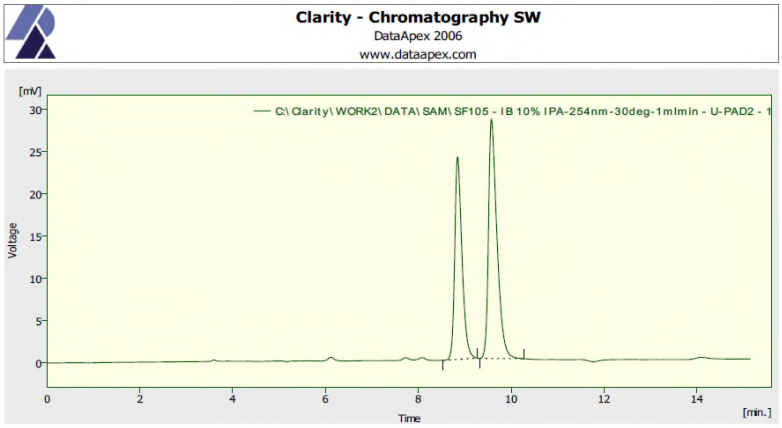
HPLC Racemic



Result Table (Uncal - C:\|Clarity\|WORK2\|DATA\|SAM\|SF096 - IB - 10 % IPA- 254 nm - 30 deg - 1 ml min - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	8.652	1275.300	97.310	49.7	54.6	0.20	
2	9.336	1288.205	80.755	50.3	45.4	0.24	
	Total	2563.505	178.064	100.0	100.0		

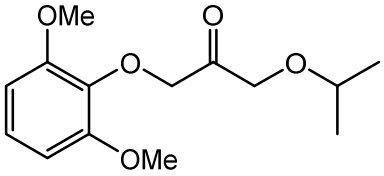
HPLC After ATH



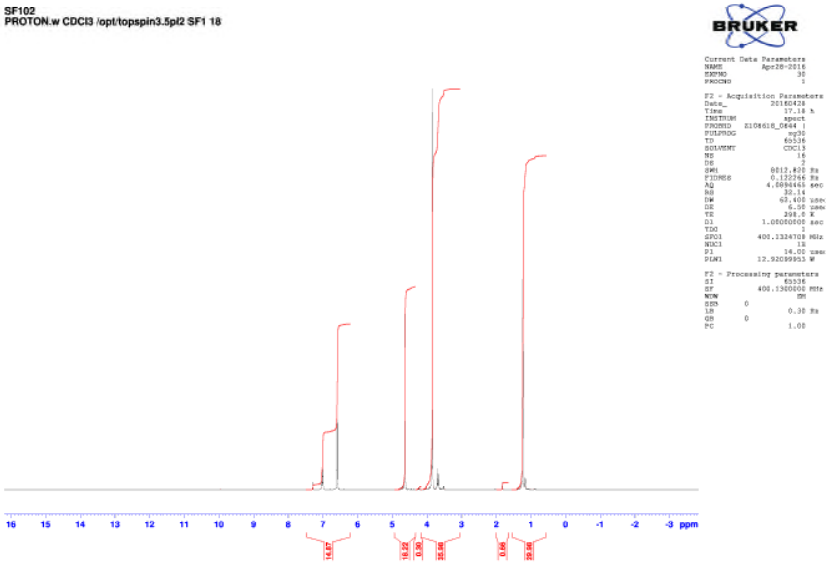
Result Table (Uncal - C:\|Clarity\|WORK2\|DATA\|SAM\|SF105 - IB 10%IPA-254nm-30deg-1mlmin - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	8.844	260.127	23.987	42.0	45.8	0.16	
2	9.576	359.286	28.343	58.0	54.2	0.20	
	Total	619.413	52.330	100.0	100.0		

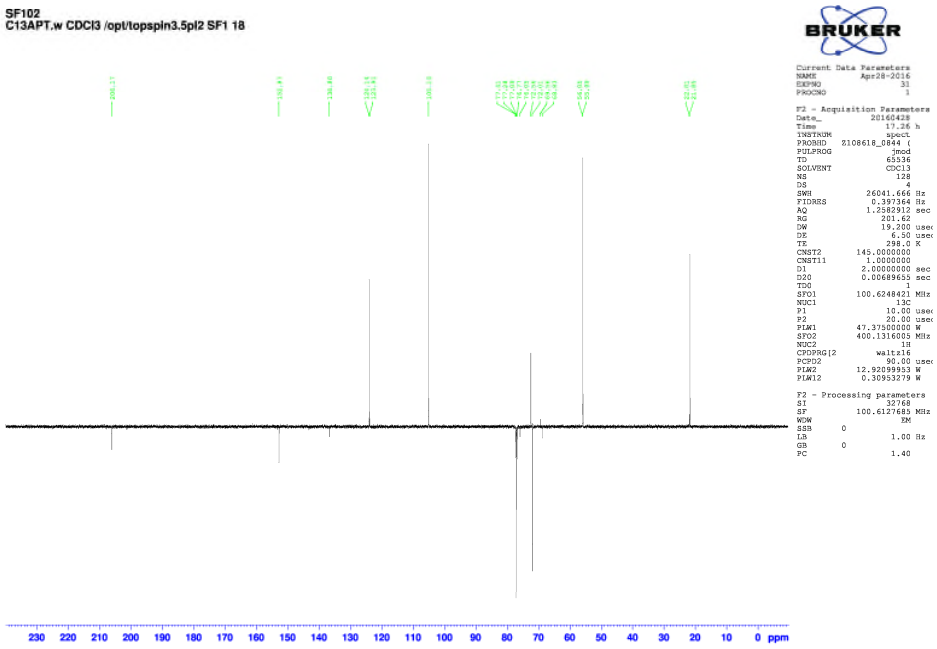
1-(2,6-Dimethoxyphenoxy)-3-isopropoxypropan-2-one.



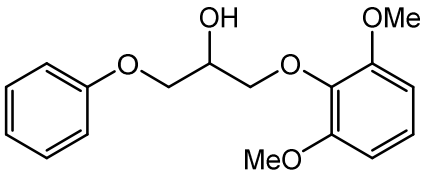
^{1}H NMR (400 MHz, $CDCl_3$)



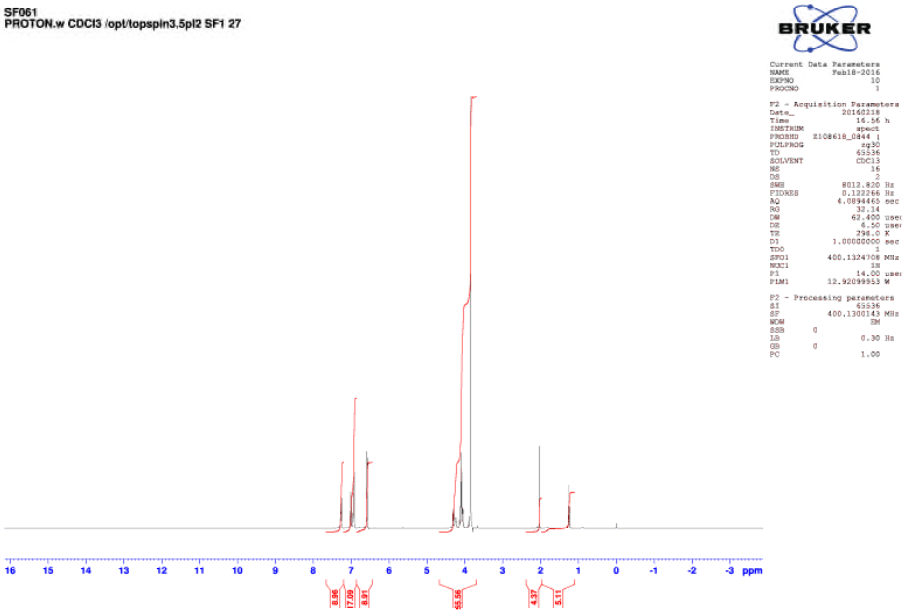
^{13}C NMR (100 MHz, $CDCl_3$)



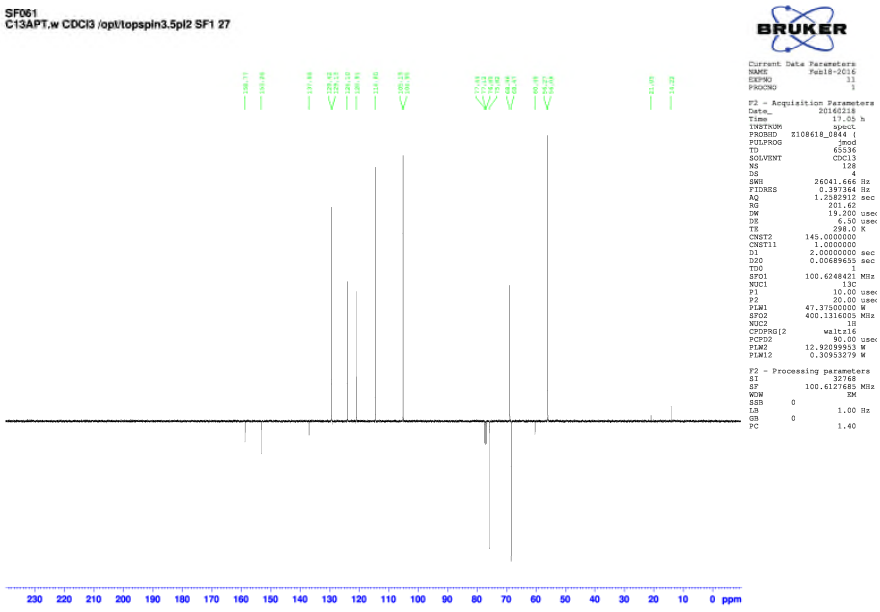
1-(2,6-Dimethoxyphenoxy)-3-phenoxypropan-2-ol 16.



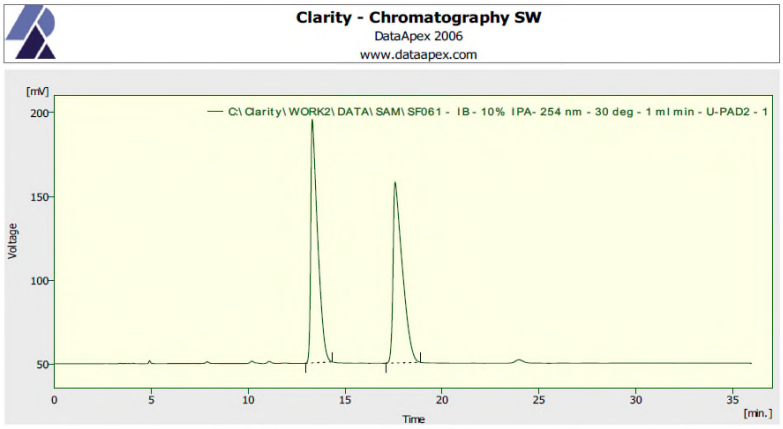
^{1}H NMR (400 MHz, $CDCl_3$)



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



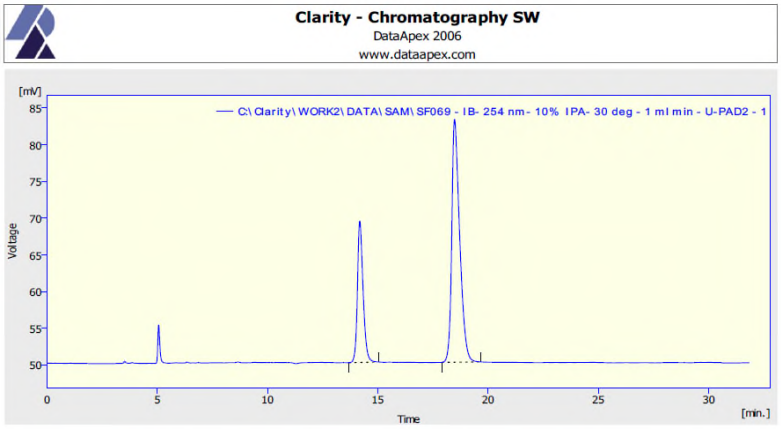
HPLC Racemic



Result Table (Uncal - C:\Clarity\WORK2\DATA\SAM\SF061 - IB - 10% IPA - 254 nm - 30 deg - 1 ml min - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	13.308	3582.881	145.160	49.8	57.4	0.38	
2	17.584	3607.495	107.799	50.2	42.6	0.51	
	Total	7190.377	252.959	100.0	100.0		

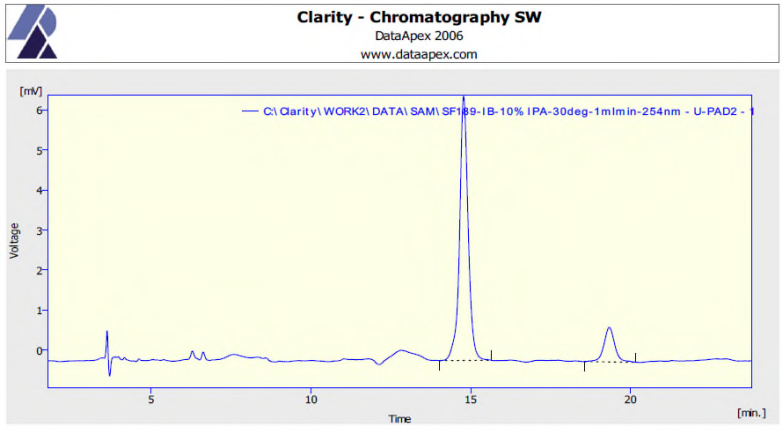
HPLC After ATH



Result Table (Uncal - C:\Clarity\WORK2\DATA\SAM\SF069 - IB - 254 nm - 10% IPA - 30 deg - 1 ml min - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	14.184	341.692	19.254	29.3	36.8	0.27	
2	18.480	825.255	33.061	70.7	63.2	0.38	
	Total	1166.948	52.315	100.0	100.0		

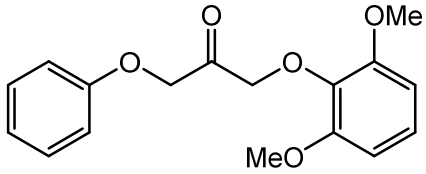
HPLC Asymmetric Standard



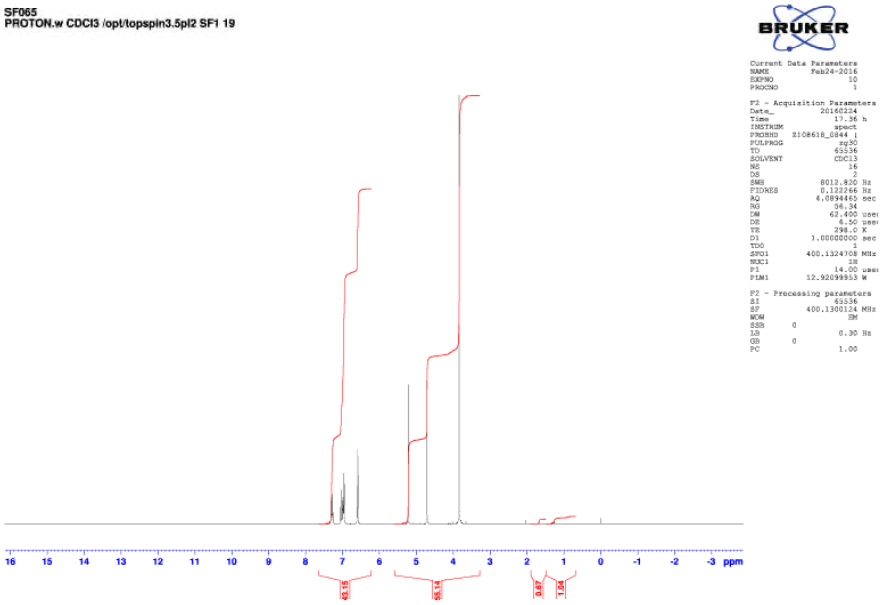
Result Table (Uncal - C:\Clarity\WORK2\DATA\SAM\SF189-IB-10%IPA-30deg-1mlmin-254nm - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	14.776	123.441	6.601	85.8	88.5	0.27	
2	19.340	20.457	0.862	14.2	11.5	0.35	
	Total	143.898	7.463	100.0	100.0		

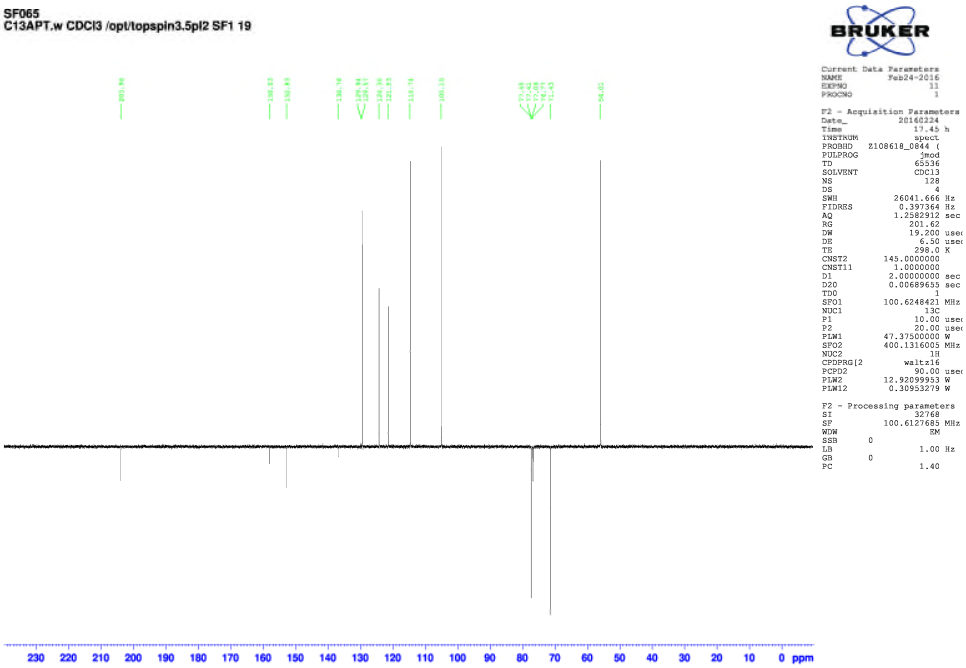
1-(2,6-Dimethoxyphenoxy)-3-phenoxypropan-2-one.



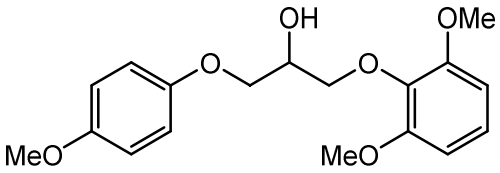
^{1}H NMR (400 MHz, $CDCl_3$)



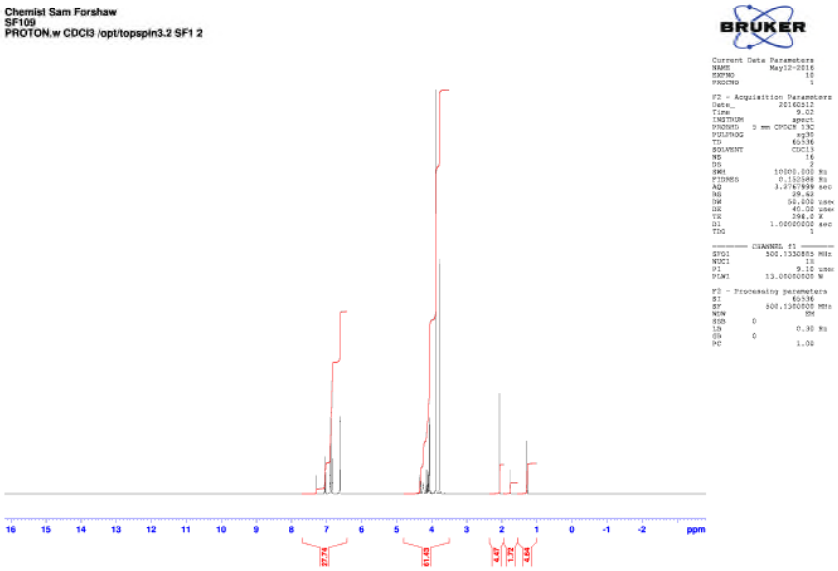
^{13}C NMR (100 MHz, $CDCl_3$)



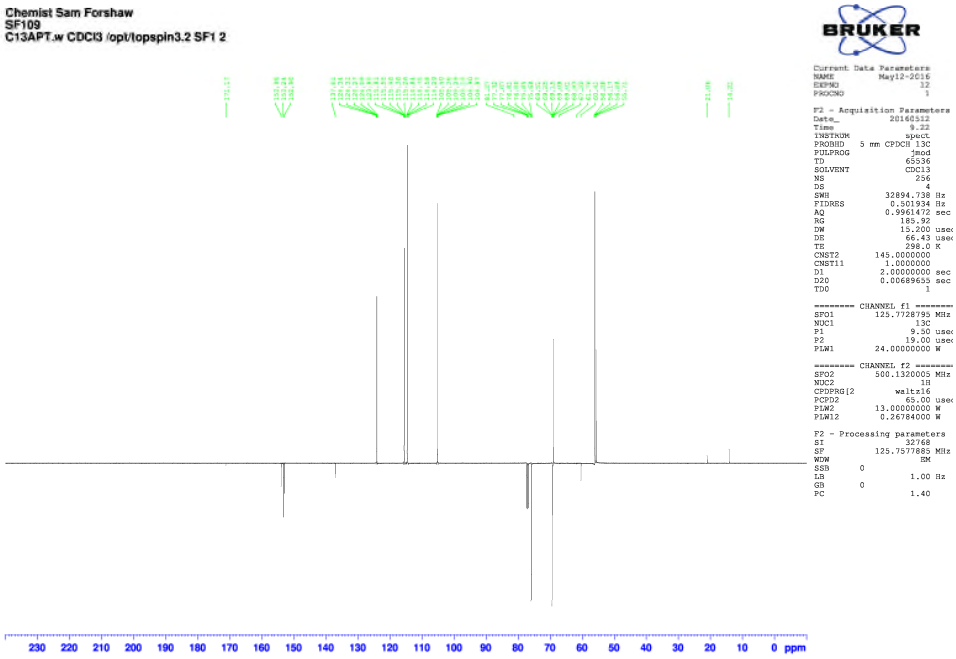
1-(2,6-Dimethoxyphenoxy)-3-(4-methoxyphenoxy)propan-2-ol 17.



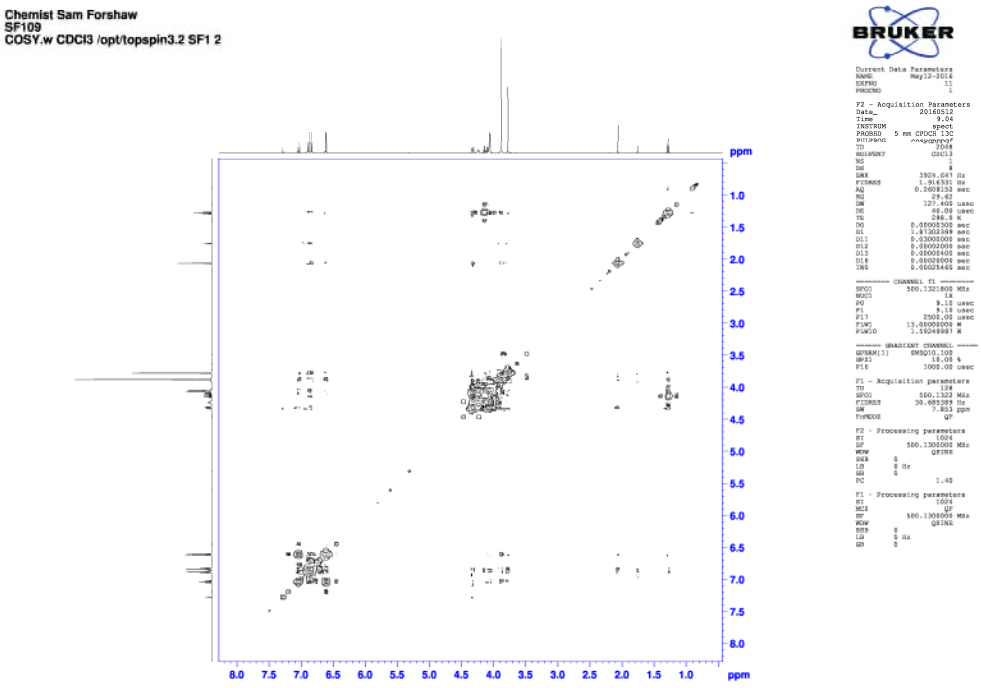
^{1}H NMR (500 MHz, $CDCl_3$)



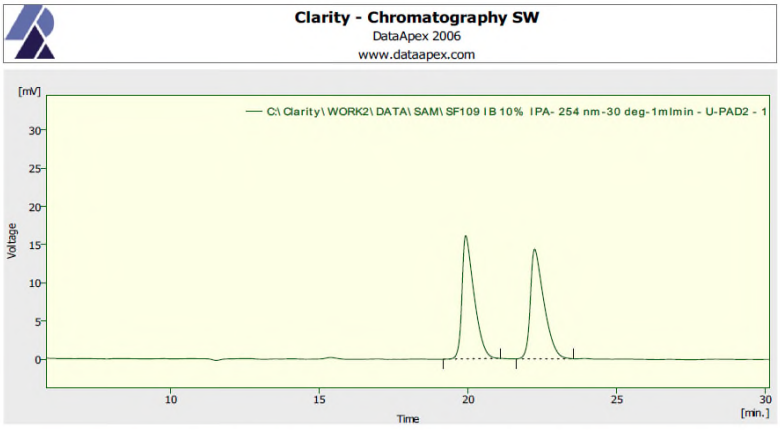
^{13}C NMR (125 MHz, $CDCl_3$)



COSY (500 MHz, $CDCl_3$)



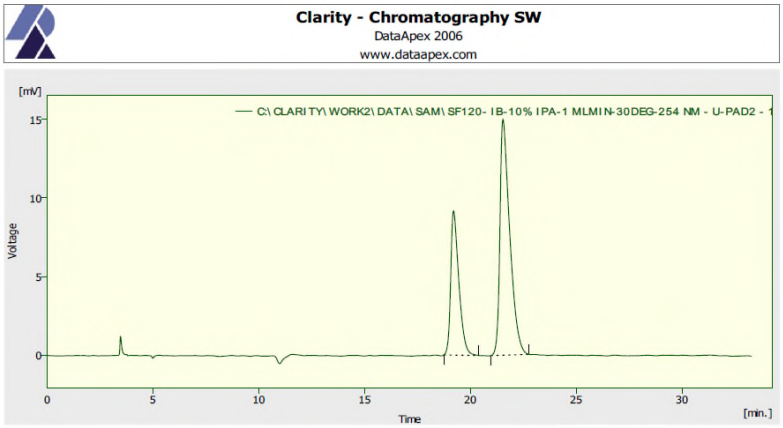
HPLC Racemic



Result Table (Uncal - C:\Clarity\WORK2\DATA\SAM\SF109 IB 10% IPA- 254 nm-30 deg-1mlmin - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	19.916	457.299	16.129	50.0	52.9	0.43	
2	22.236	457.581	14.357	50.0	47.1	0.48	
	Total	914.880	30.486	100.0	100.0		

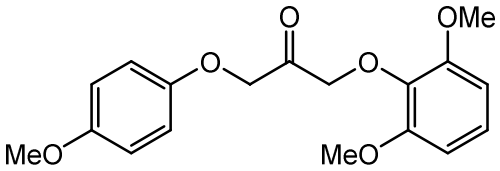
HPLC After ATH



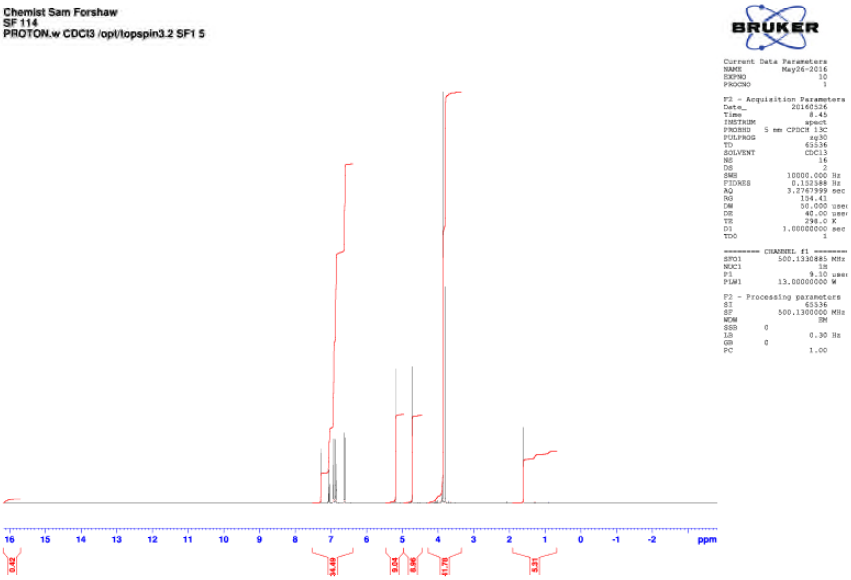
Result Table (Uncal - C:\CLARITY\WORK2\DATA\SAM\SF120- IB-10%IPA-1 MLMIN-30DEG-254 NM - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	19.208	244.174	9.167	33.5	37.9	0.40	
2	21.544	483.695	14.991	66.5	62.1	0.48	
	Total	727.869	24.159	100.0	100.0		

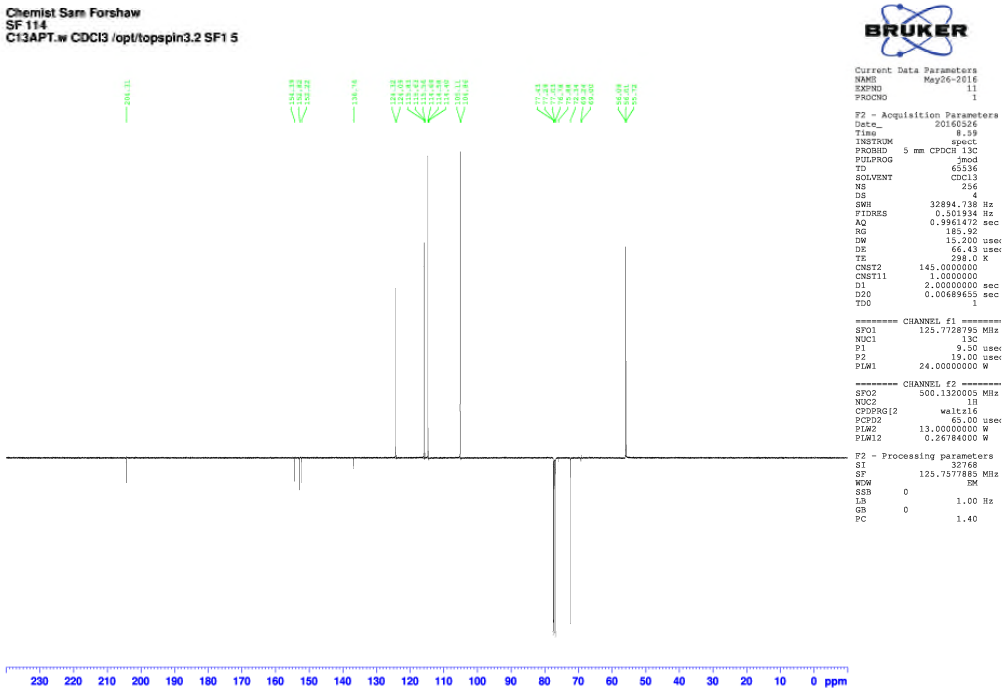
1-(2,6-Dimethoxyphenoxy)-3-(4-methoxyphenoxy)propan-2-one.



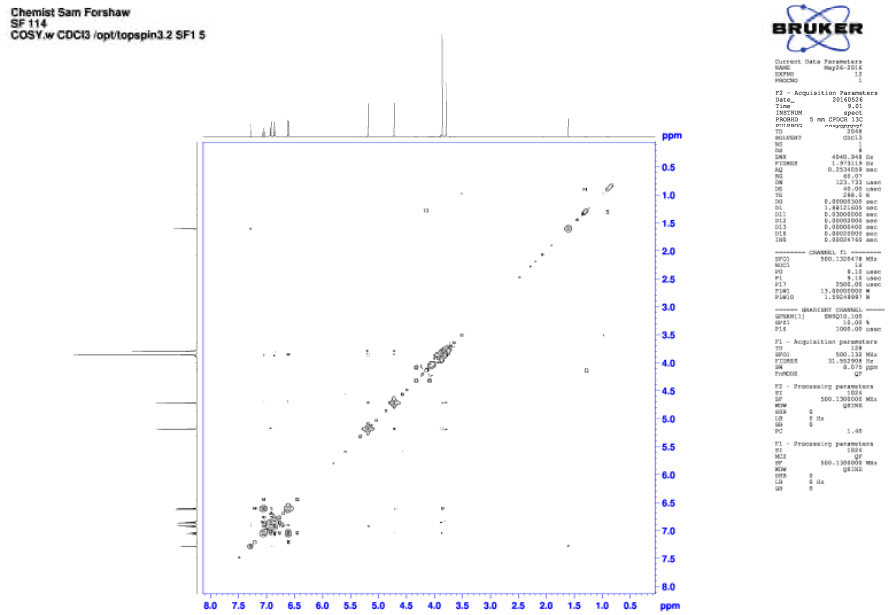
^{1}H NMR(500 MHz, $CDCl_3$)



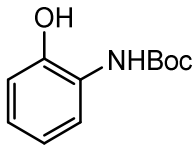
^{13}C NMR (125 MHz, $CDCl_3$)



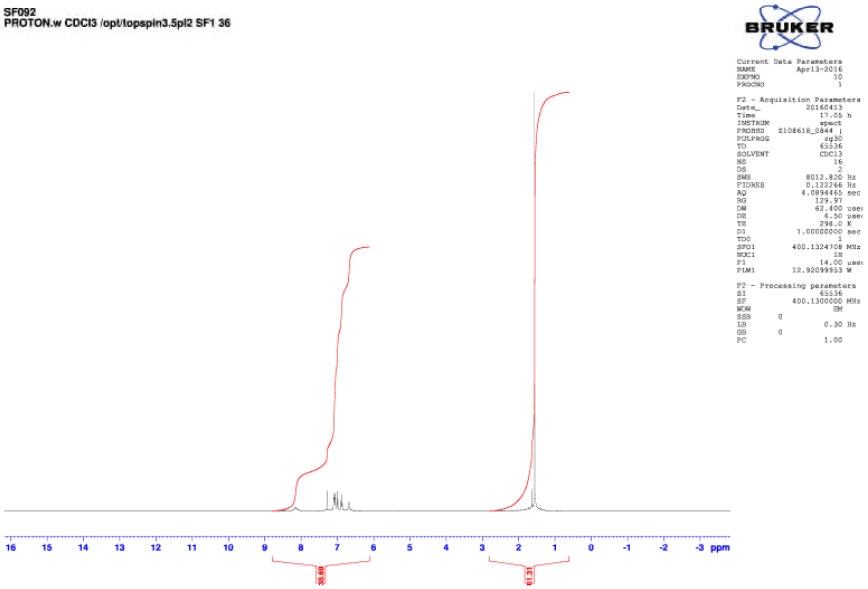
COSY (500 MHz, $CDCl_3$)



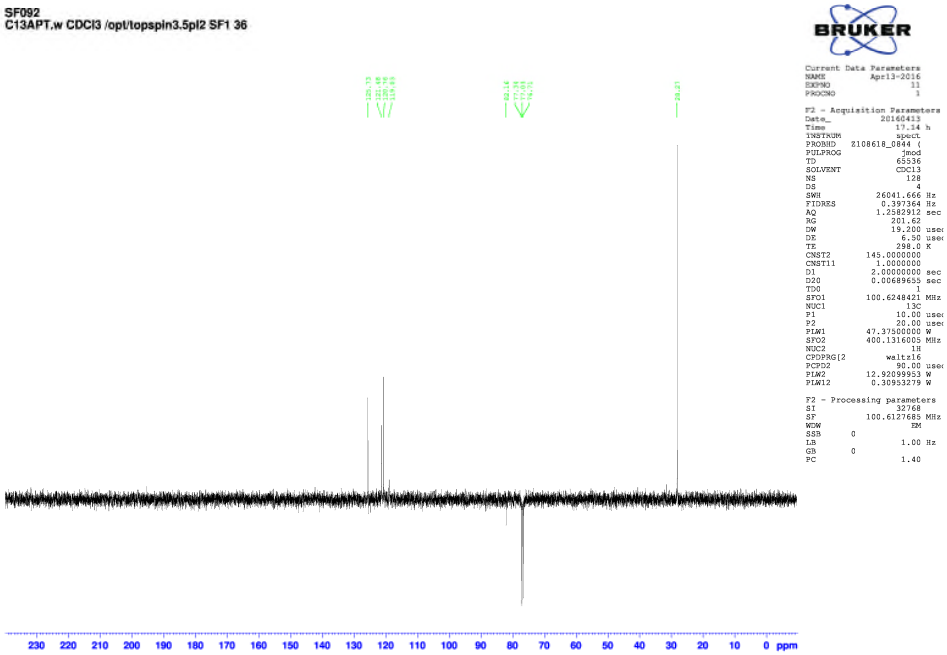
***tert*-Butyl (2-hydroxyphenyl)carbamate.**



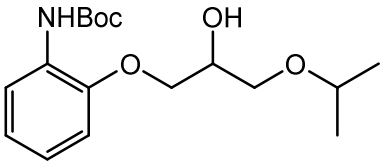
^{1}H NMR (400 MHz, $CDCl_3$)



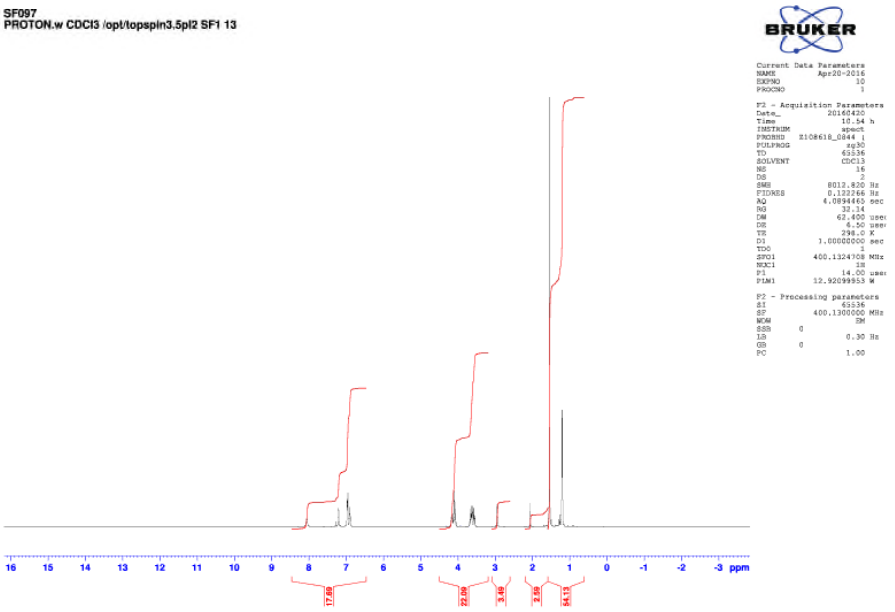
^{13}C NMR (100 MHz, $CDCl_3$)



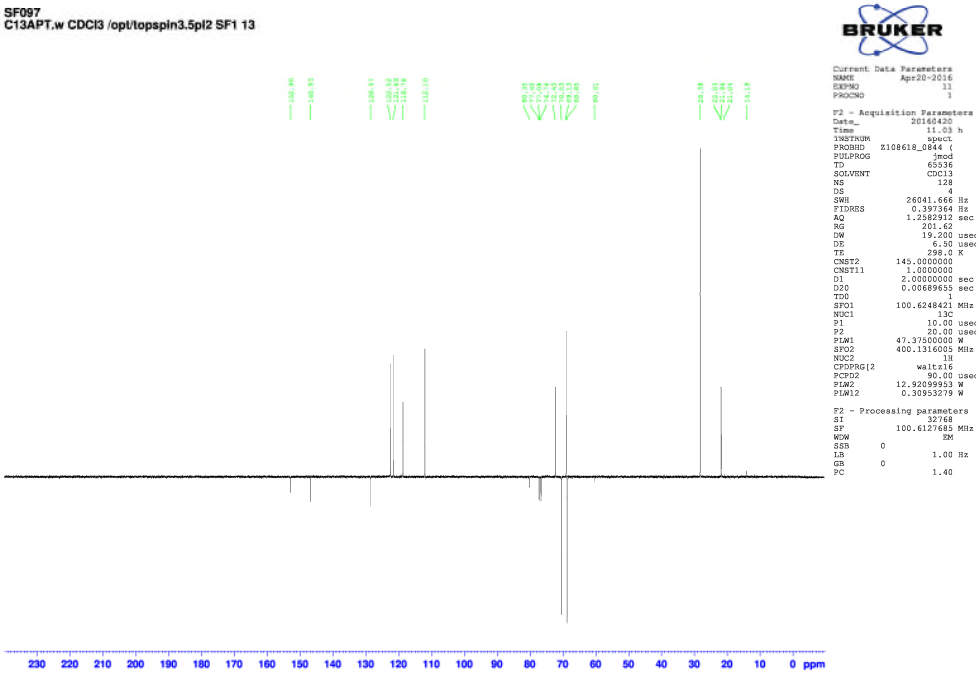
***tert*-Butyl (2-(2-hydroxy-3-isopropoxypropoxy)phenyl)carbamate 18.**



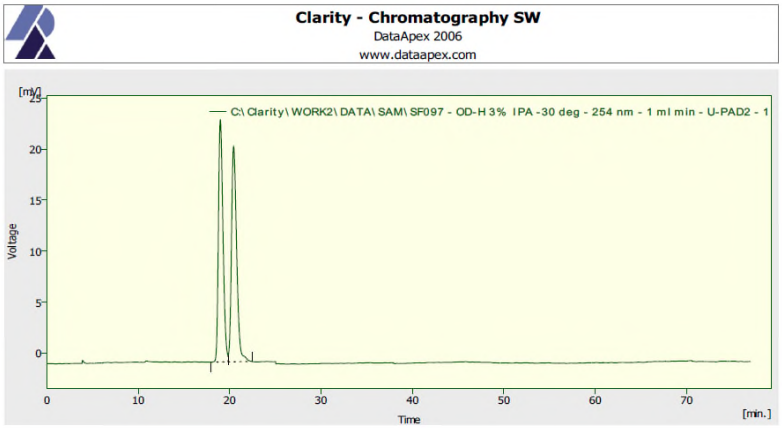
^{1}H NMR (400 MHz, $CDCl_3$)



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



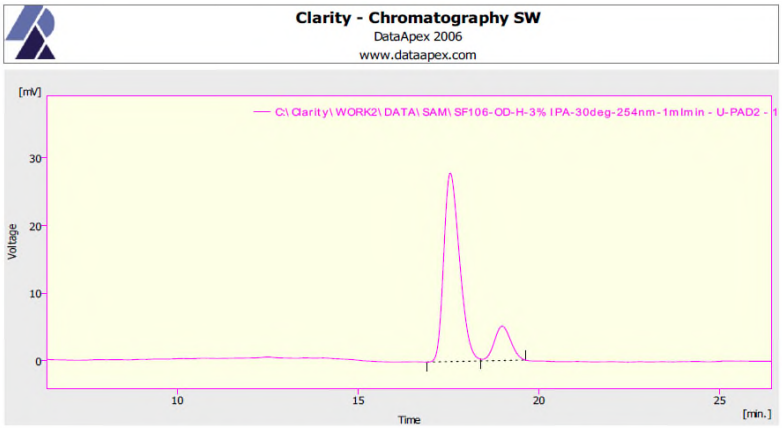
HPLC Racemic



Result Table (Uncal - C:\|Clarity\|WORK2\|DATA\|SAM\|SF097 - OD-H 3% IPA -30 deg - 254 nm - 1 ml min - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	18.988	822.275	23.758	49.6	52.9	0.54	
2	20.440	834.408	21.132	50.4	47.1	0.60	
	Total	1656.683	44.890	100.0	100.0		

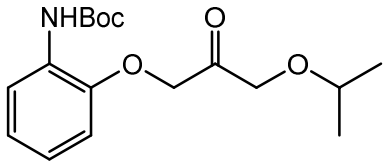
HPLC After ATH



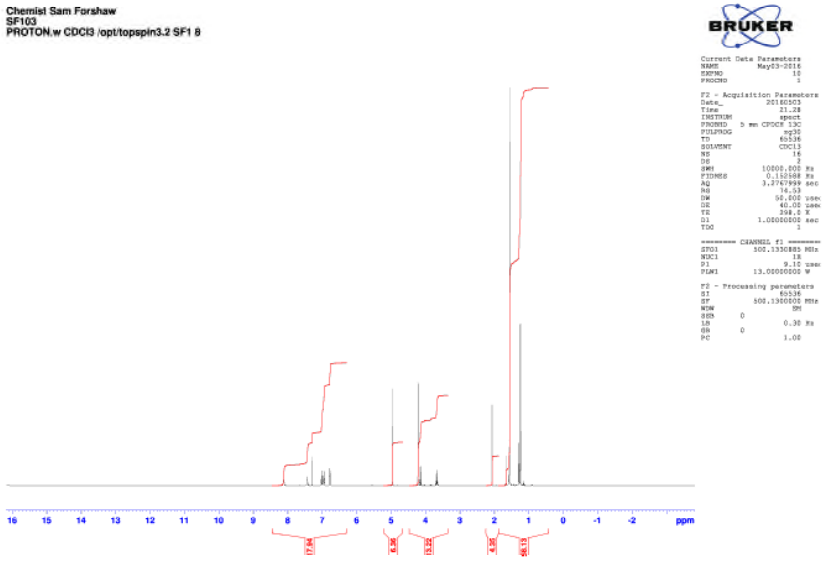
Result Table (Uncal - C:\|Clarity\|WORK2\|DATA\|SAM\|SF106-OD-H-3%IPA-30deg-254nm-1mlmin - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	17.548	847.091	27.849	84.0	84.6	0.48	
2	18.980	161.921	5.078	16.0	15.4	0.50	
	Total	1009.012	32.927	100.0	100.0		

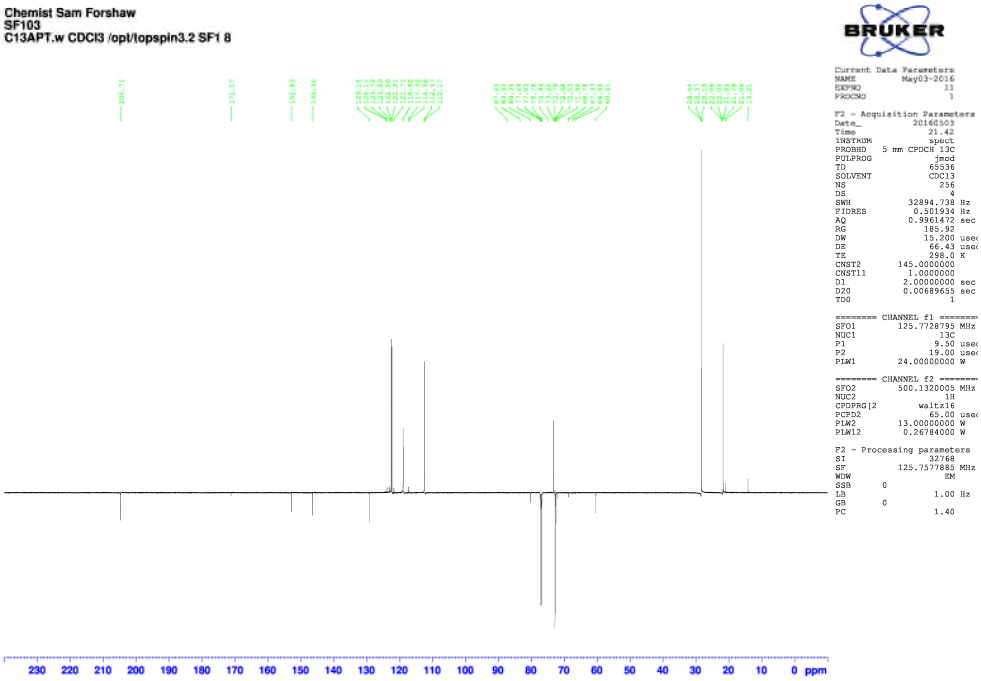
***tert*-Butyl (2-(3-isopropoxy-2-oxopropoxy)phenyl)carbamate.**



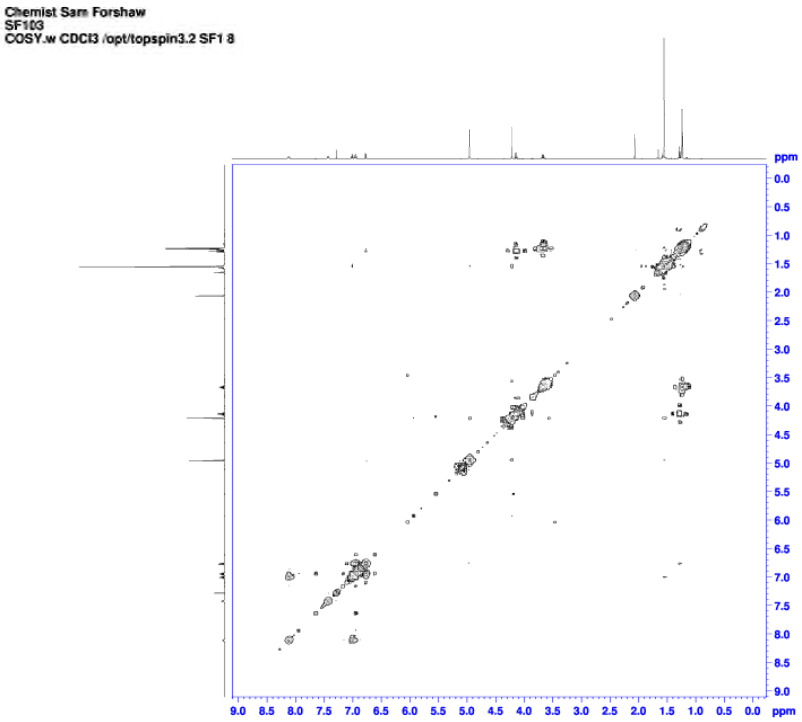
^{1}H NMR (500 MHz, $CDCl_3$)

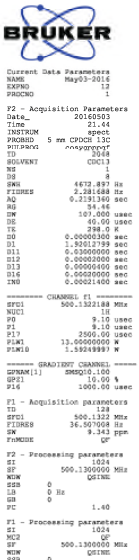


^{13}C NMR (125 MHz, $CDCl_3$)

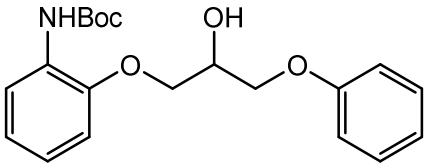


COSY (500 MHz, $CDCl_3$)

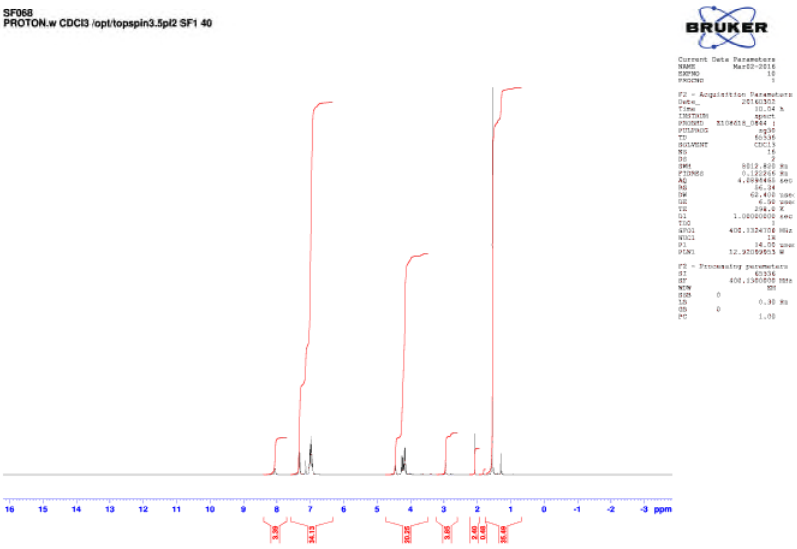




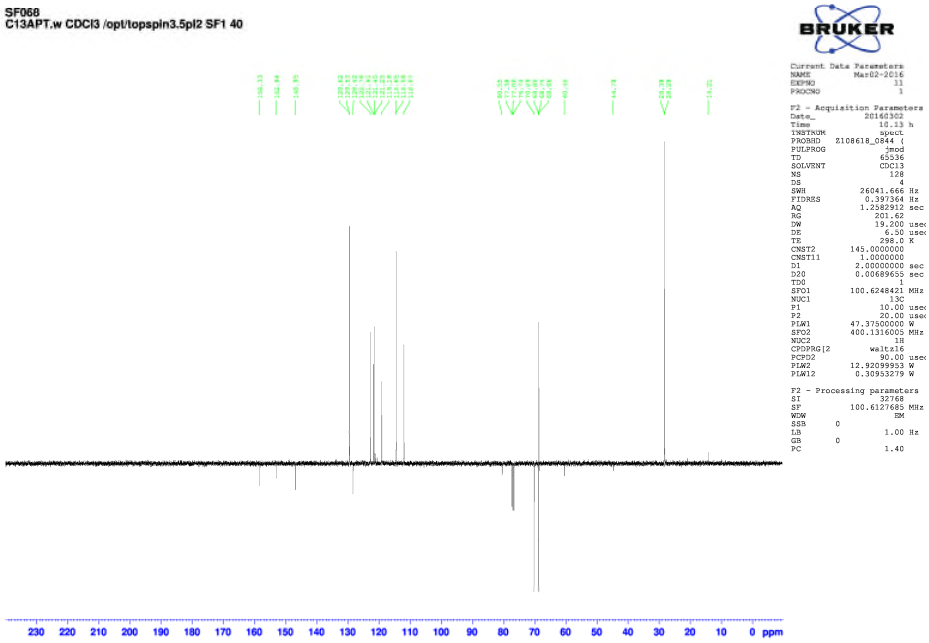
***tert*-Butyl (2-(2-hydroxy-3-phenoxypropoxy)phenyl)carbamate 19.**



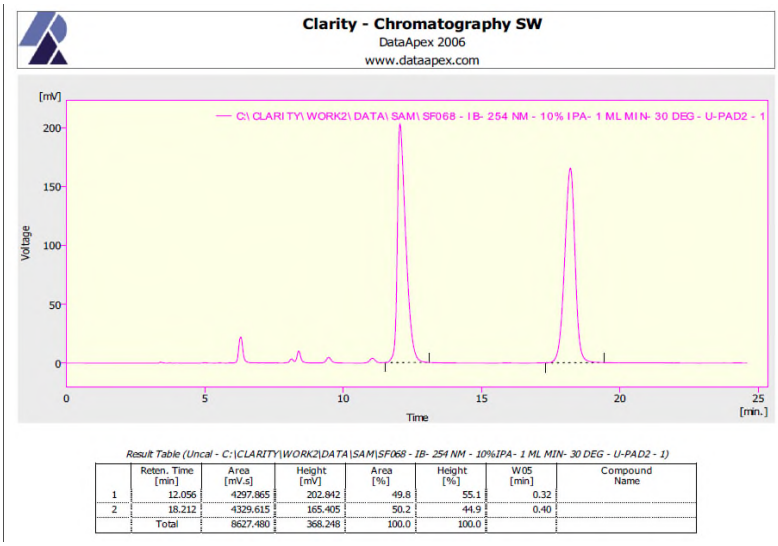
^{1}H NMR (400 MHz, $CDCl_3$)



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



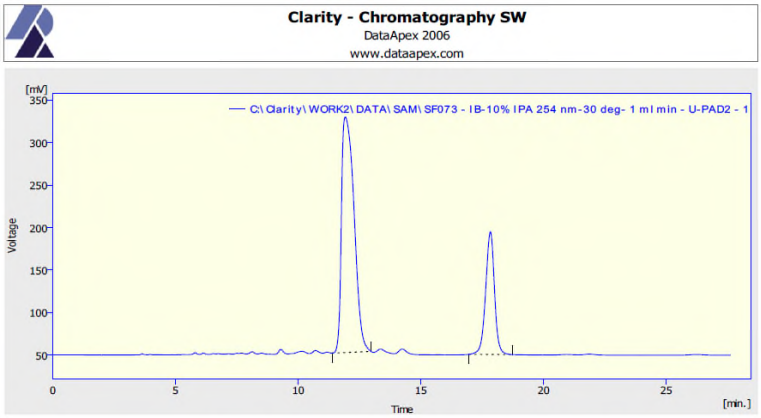
HPLC Racemic



Result Table (Uncal - C:\CLARITY\WORK2\DATA\SAM\SF068 - IB- 254 NM - 10%IPA- 1 ML MIN- 30 DEG - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	12.056	4297.865	202.842	49.8	55.1	0.32	
2	18.212	4329.615	165.405	50.2	44.9	0.40	
	Total	8627.480	368.248	100.0	100.0		

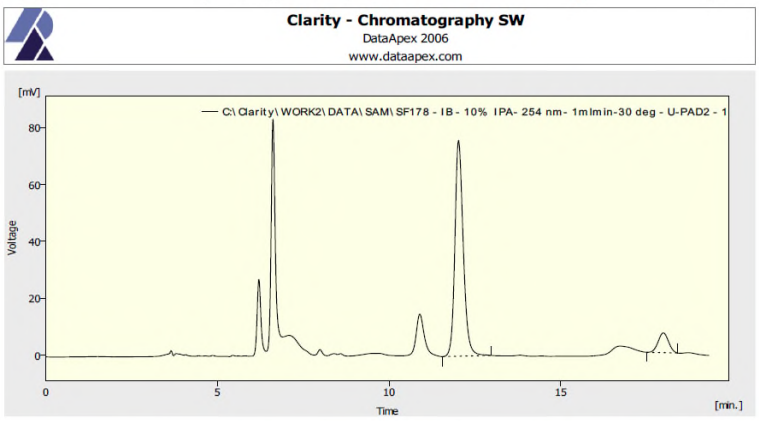
HPLC After ATH



Result Table (Uncal - C:\Clarity\WORK2\DATA\SAM\SF073 - IB-10%IPA 254 nm-30 deg- 1 ml min - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	11.920	9880.257	277.445	73.2	65.7	0.58	
2	17.832	3613.548	144.565	26.8	34.3	0.38	
	Total	13493.805	422.010	100.0	100.0		

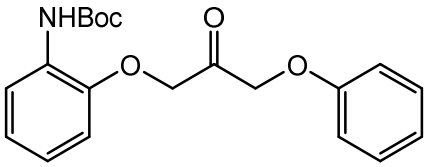
HPLC Asymmetric Standard



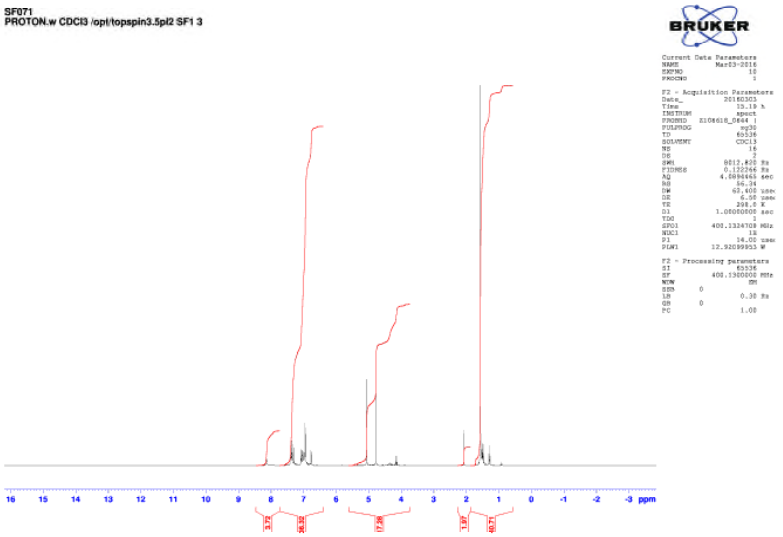
Result Table (Uncal - C:\Clarity\WORK2\DATA\SAM\SF178 - IB - 10% IPA- 254 nm- 1mlmin-30 deg - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	12.024	1285.014	75.829	89.8	91.6	0.26	
2	17.988	146.199	6.953	10.2	8.4	0.34	
	Total	1431.213	82.782	100.0	100.0		

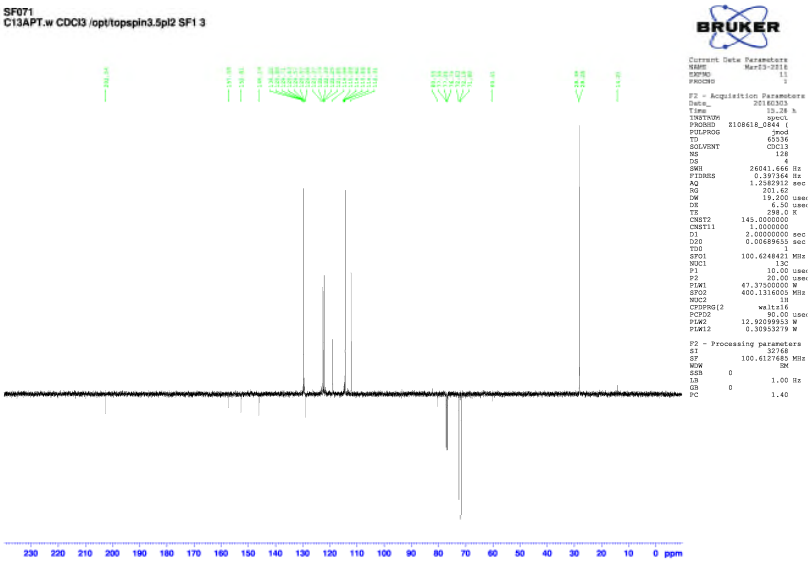
***tert*-Butyl (2-(2-oxo-3-phenoxypropoxy)phenyl)carbamate.**



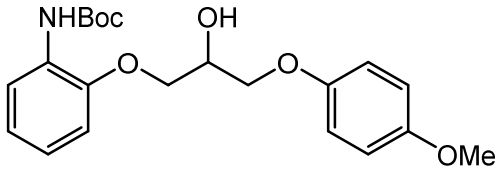
^{1}H NMR (400 MHz, $CDCl_3$)



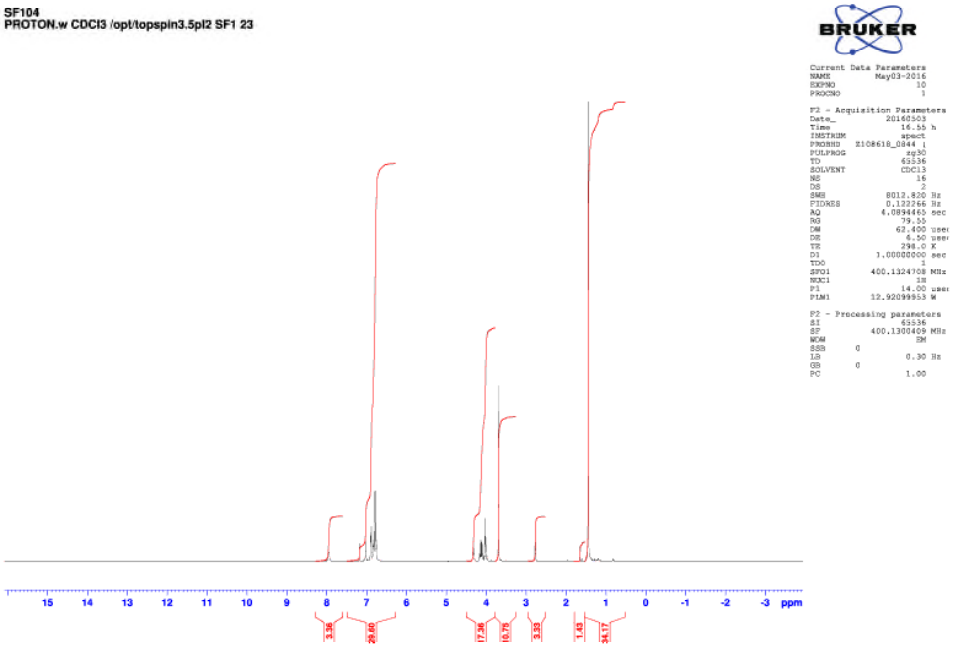
^{13}C NMR (100 MHz, $CDCl_3$)



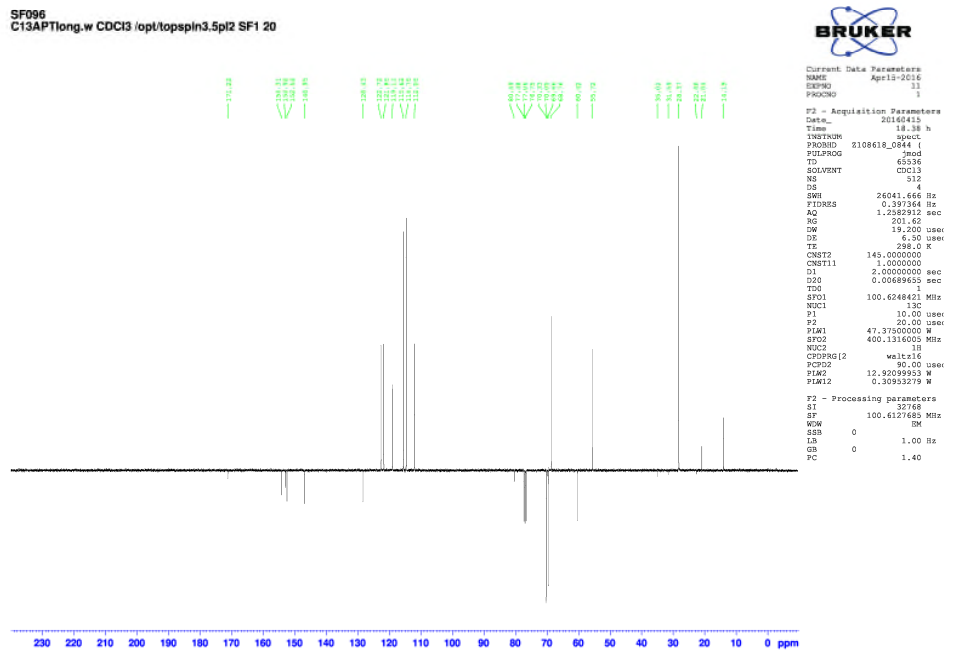
***tert*-Butyl (2-(2-hydroxy-3-(4-methoxyphenoxy)propoxy)phenyl)carbamate 20.**



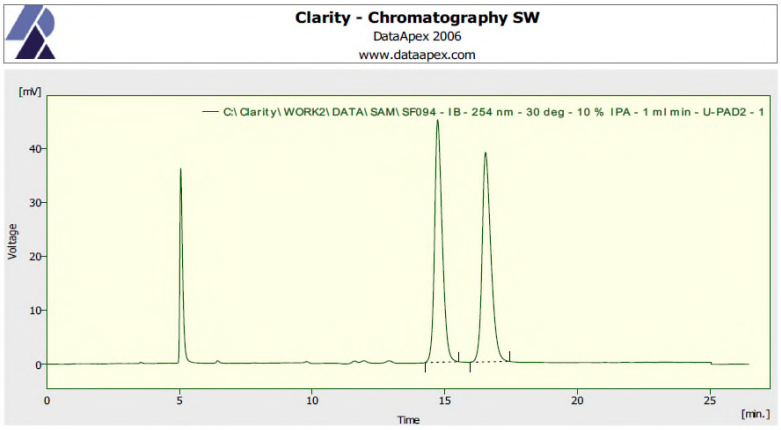
^{1}H NMR (400 MHz, $CDCl_3$)



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



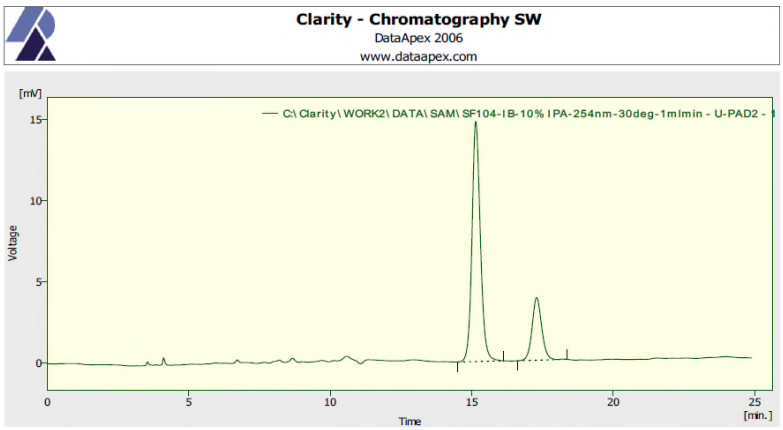
HPLC Racemic



Result Table (Uncal - C:\Clarity\WORK2\DATA\SAM\SF094 - IB - 254 nm - 30 deg - 10 % IPA - 1 ml min - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	14.736	897.702	44.959	50.0	53.7	0.30	
2	16.540	898.254	38.822	50.0	46.3	0.35	
	Total	1795.957	83.781	100.0	100.0		

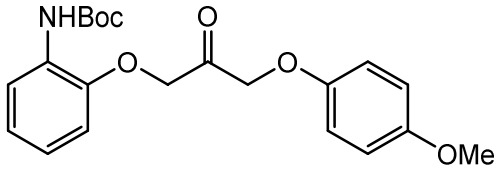
HPLC After ATH



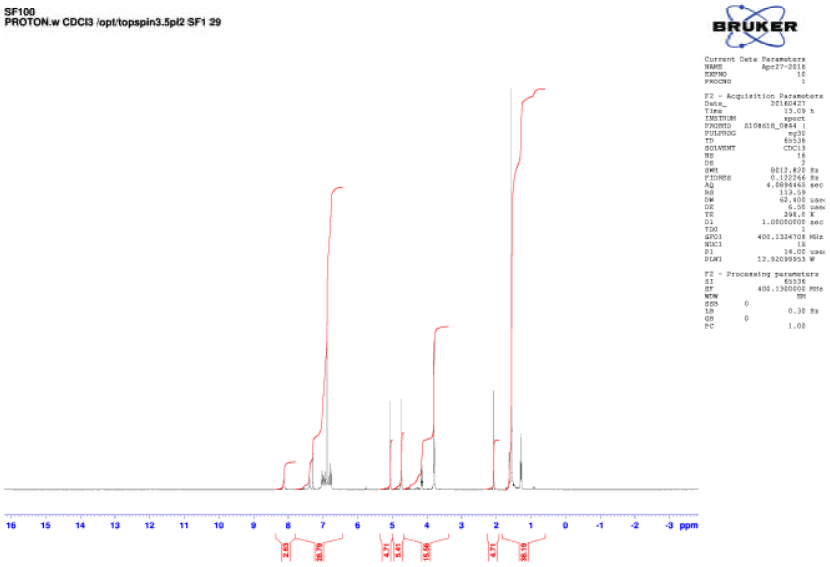
Result Table (Uncal - C:\Clarity\WORK2\DATA\SAM\SF104-IB-10%IPA-254nm-30deg-1mlmin - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	15.144	304.834	14.804	76.9	79.3	0.31	
2	17.292	91.345	3.862	23.1	20.7	0.36	
	Total	396.179	18.667	100.0	100.0		

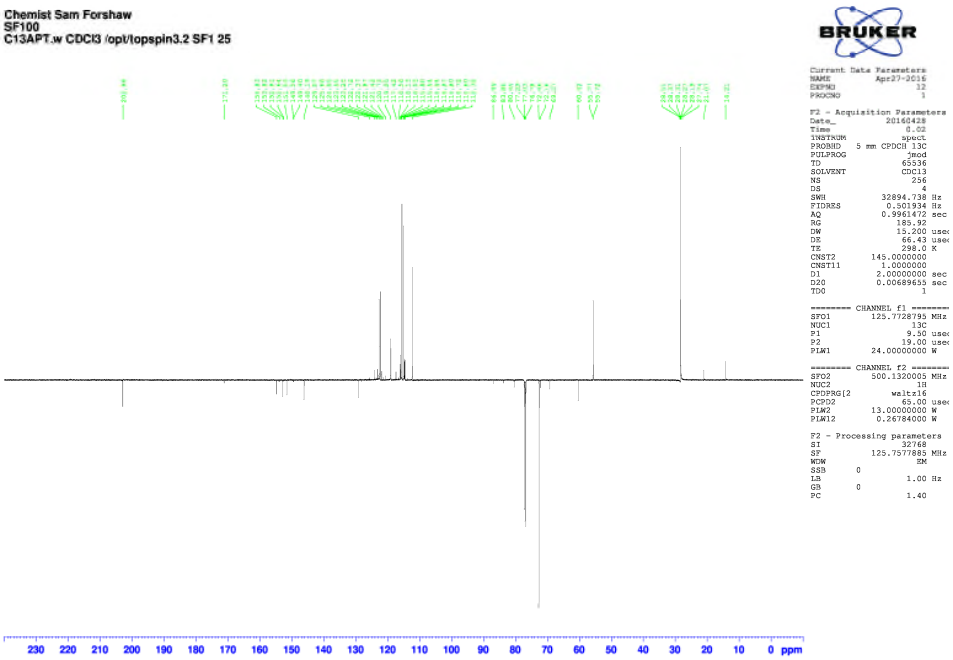
***tert*-Butyl (2-(3-(4-methoxyphenoxy)-2-oxopropoxy)phenyl)carbamate.**



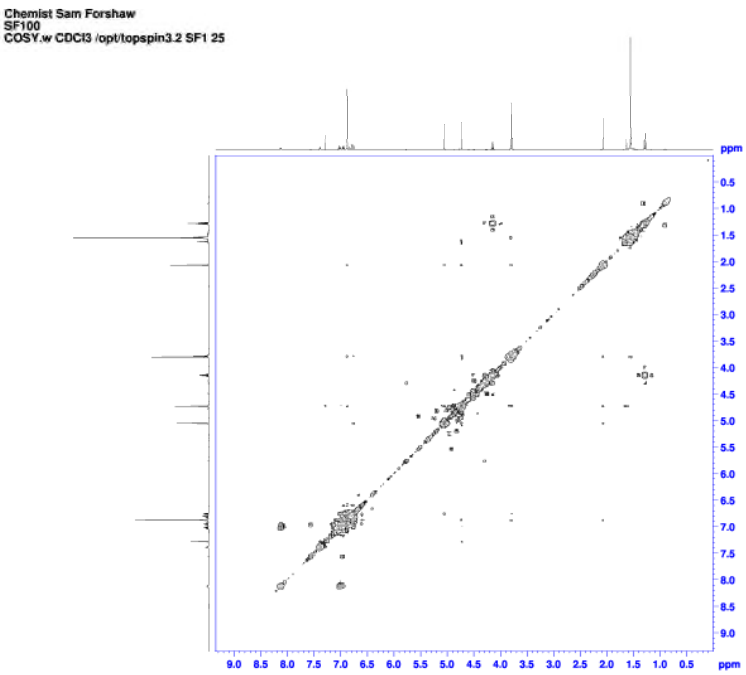
^{1}H NMR (400 MHz, $CDCl_3$)

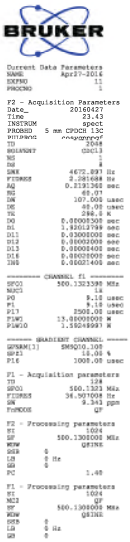


^{13}C NMR (125 MHz, $CDCl_3$)

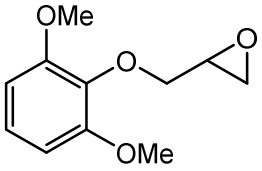


COSY (500 MHz, $CDCl_3$)

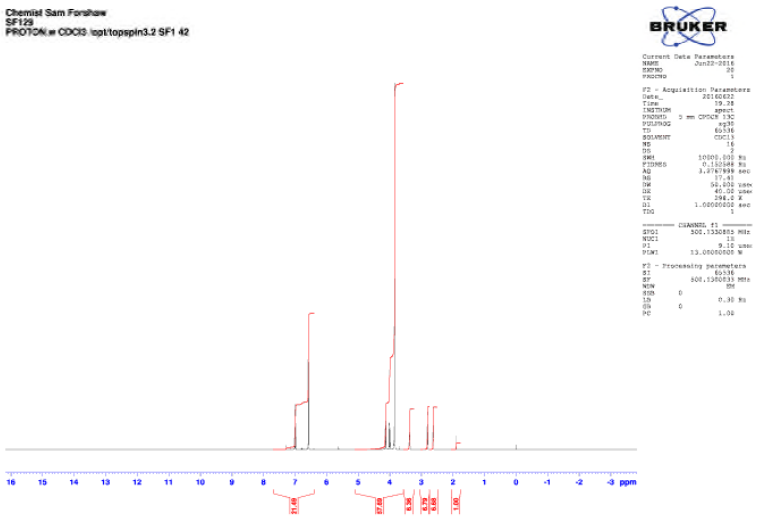




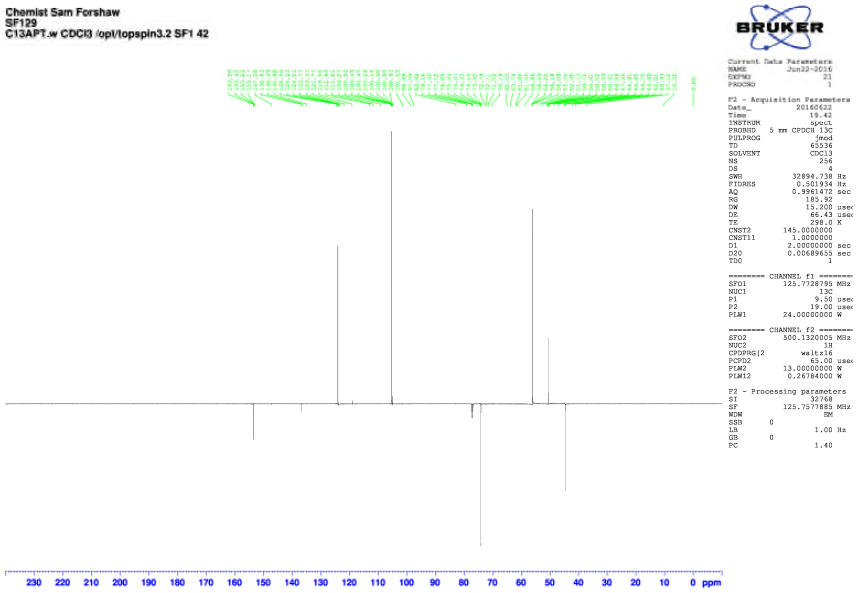
2-((2,6-Dimethoxyphenoxy)methyl)oxirane.



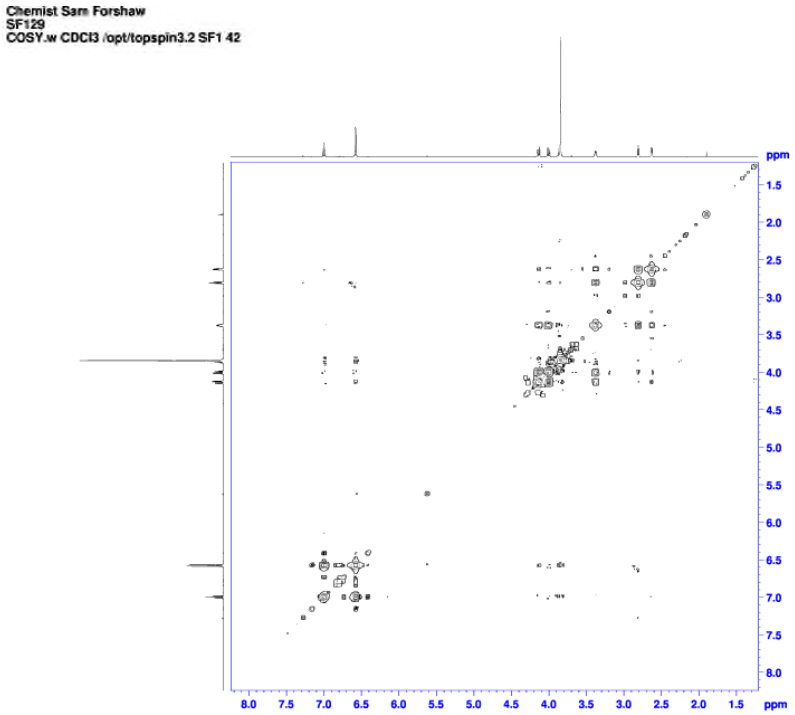
^{1}H NMR (500 MHz, $CDCl_3$)

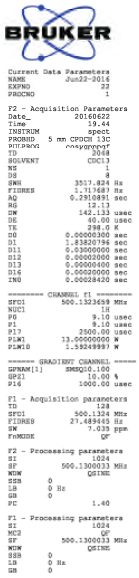


^{13}C NMR (125 MHz, $CDCl_3$)

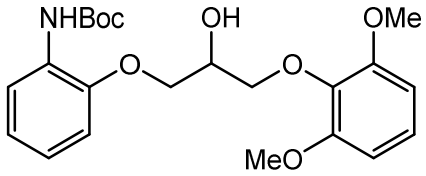


COSY(500 MHz, $CDCl_3$)

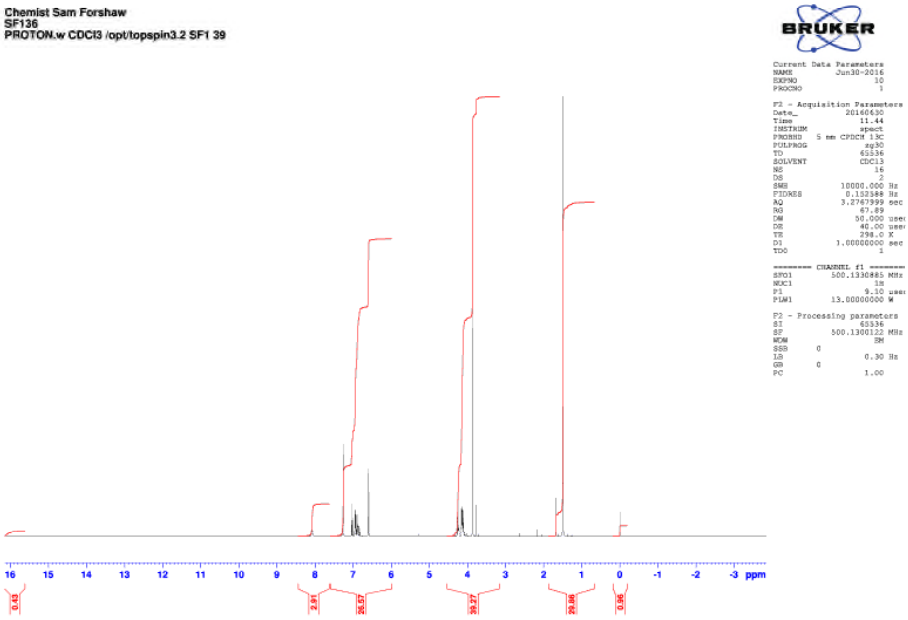




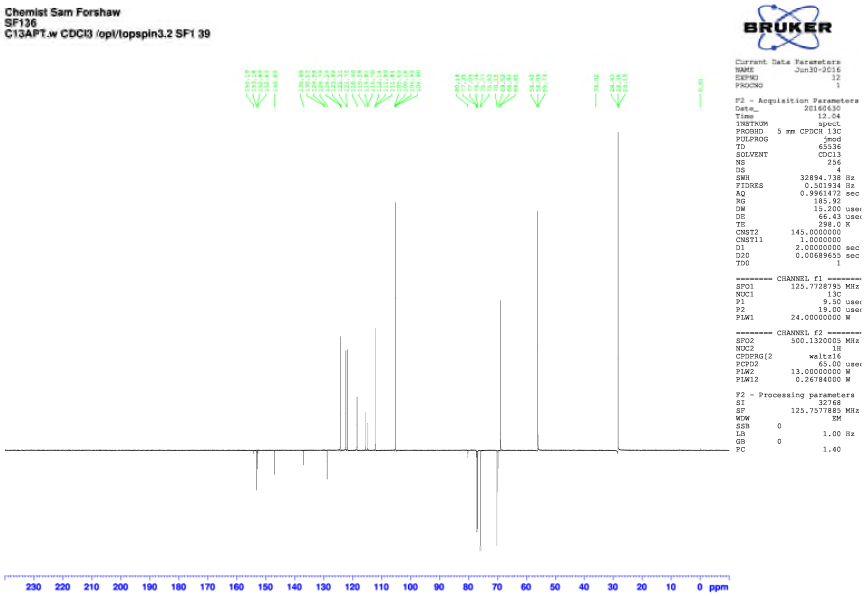
tert-Butyl (2-(3-(2,6-dimethoxyphenoxy)-2-hydroxypropoxy)phenyl)carbamate 21.



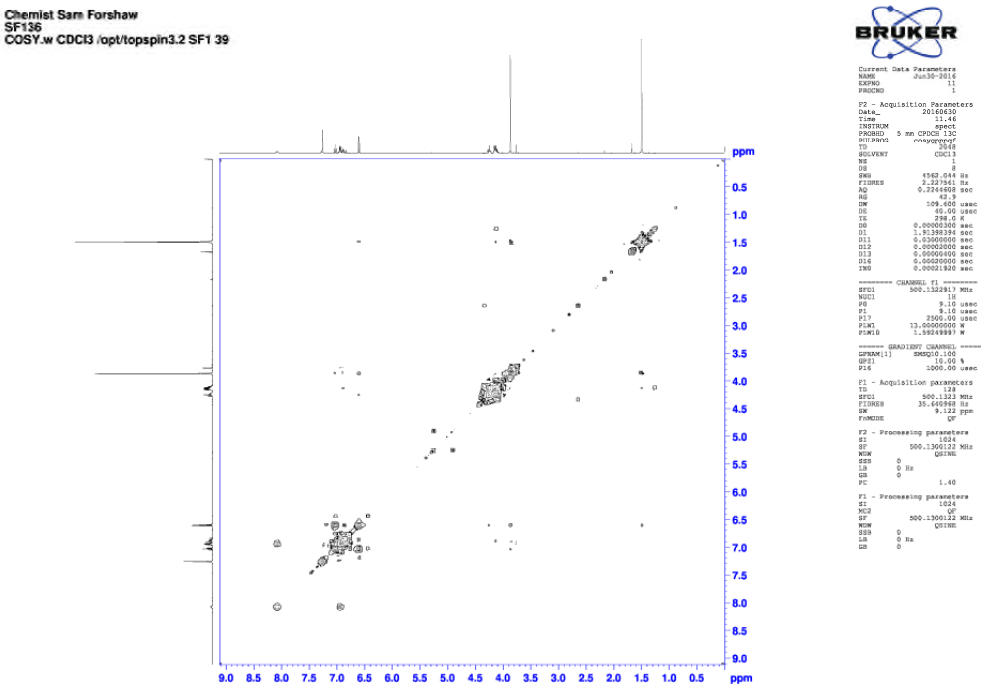
^{1}H NMR (500 MHz, $CDCl_3$)



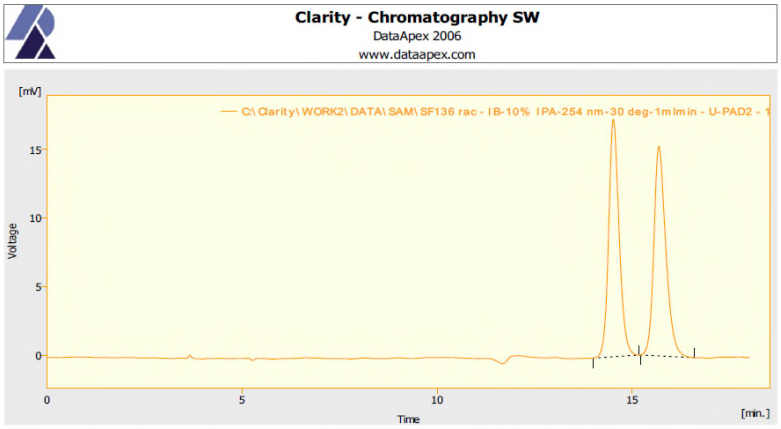
^{13}C NMR (125 MHz, $CDCl_3$)



COSY (500 MHz, $CDCl_3$)



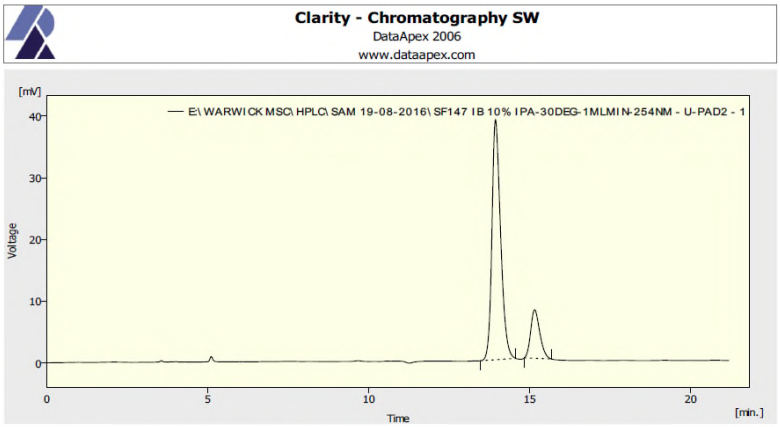
HPLC Racemic



Result Table (Uncal - C:\Clarity\WORK2\DATA\SAM\SF136 rac - IB-10% IPA-254 nm-30 deg-1mlmin - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	14.520	321.891	17.282	49.7	53.1	0.28	
2	15.684	325.906	15.273	50.3	46.9	0.32	
	Total	647.797	32.555	100.0	100.0		

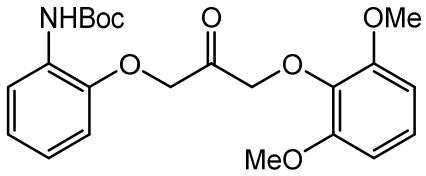
HPLC After ATH



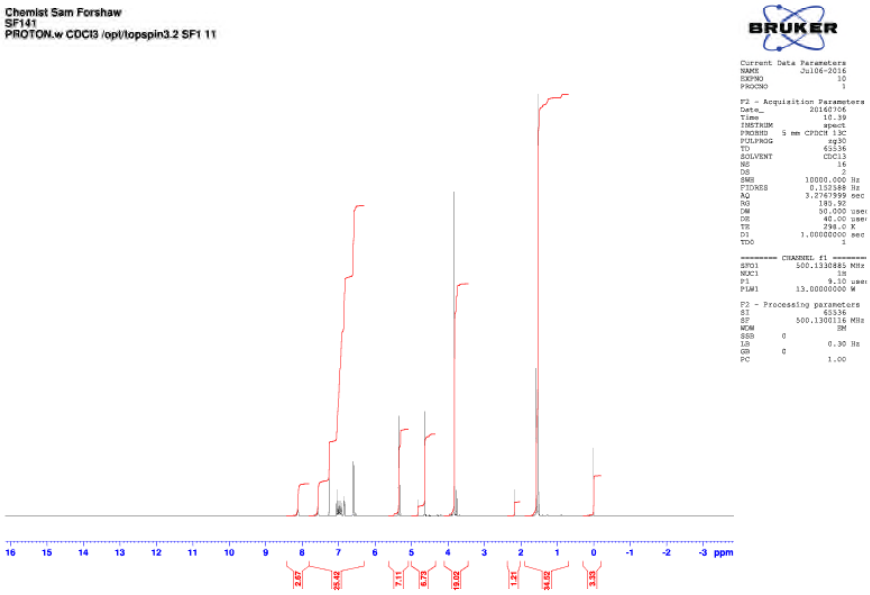
Result Table (Uncal - E:\WARWICK MSC\HPLC\SAM 19-08-2016\SF147 IB 10%IPA-30DEG-1MLMIN-254NM - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	13.936	729.819	38.945	82.5	83.2	0.28	
2	15.152	154.549	7.846	17.5	16.8	0.31	
	Total	884.368	46.791	100.0	100.0		

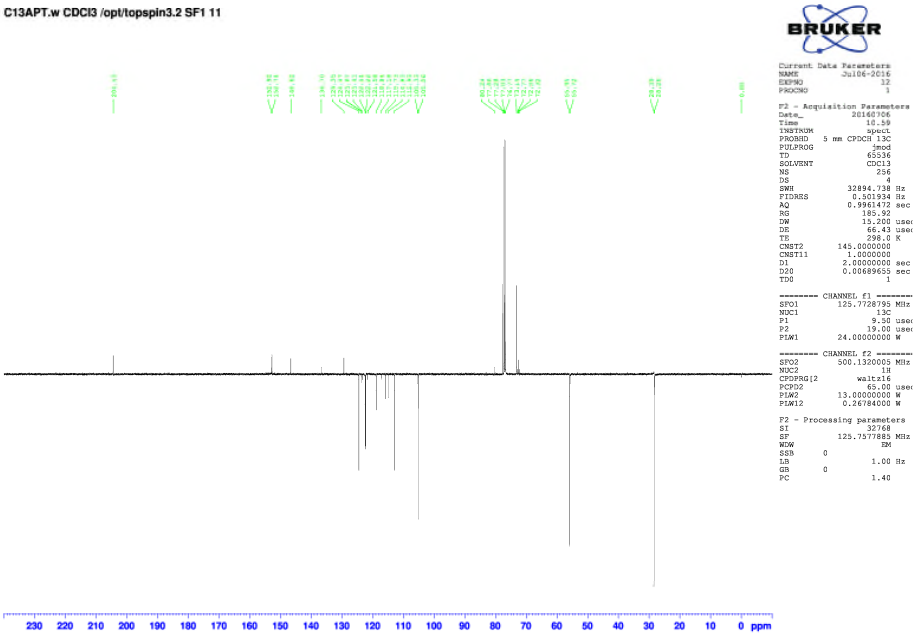
***tert*-Butyl (2-(3-(2,6-dimethoxyphenoxy)-2-oxopropoxy)phenyl)carbamate.**



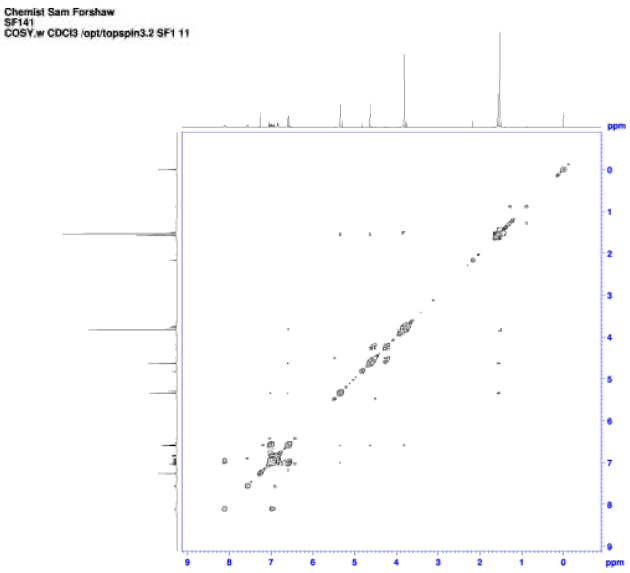
^{1}H NMR (500 MHz, $CDCl_3$)



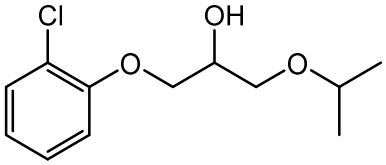
^{13}C NMR (125 MHz, $CDCl_3$)



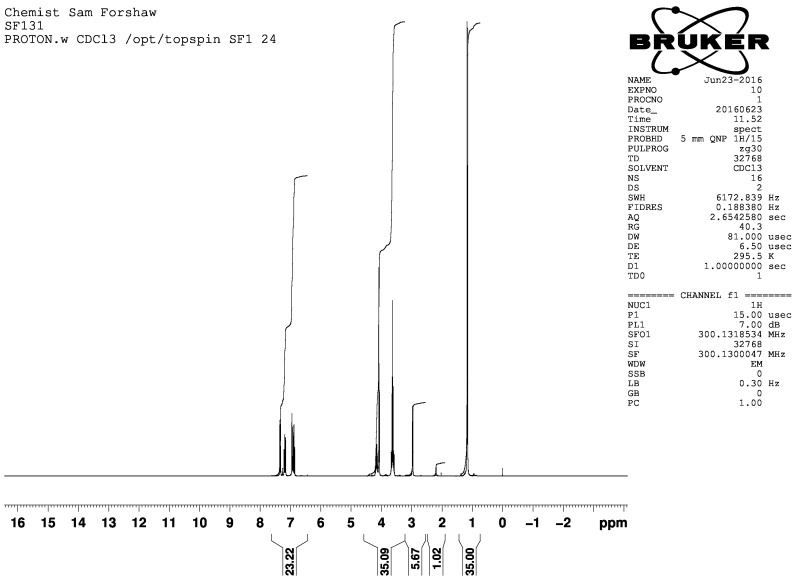
COSY (500 MHz, $CDCl_3$)



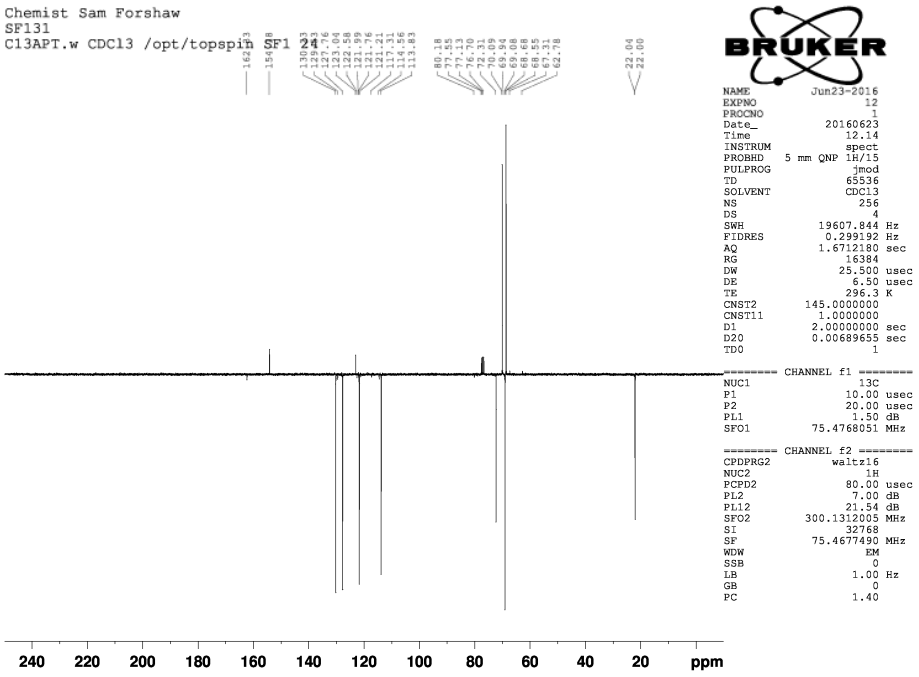
1-(2-Chlorophenoxy)-3-isopropoxypropan-2-ol 22.



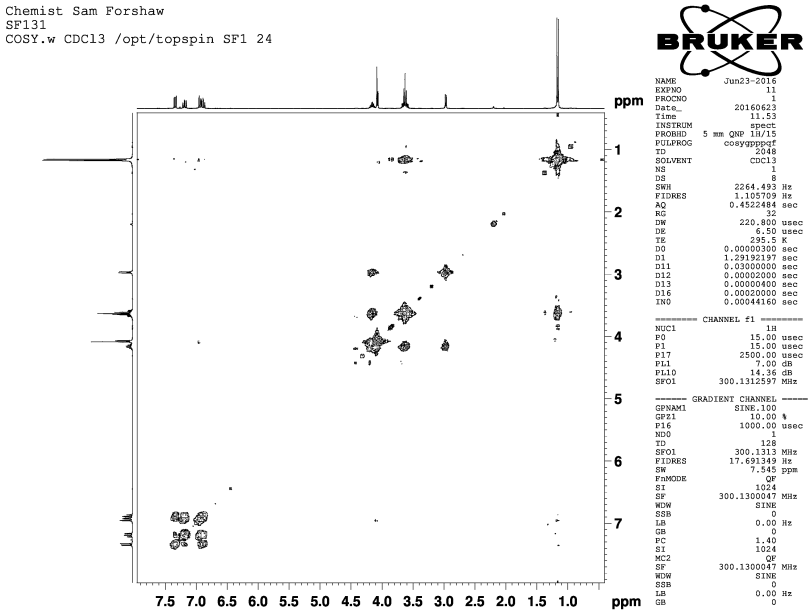
^{1}H NMR(300 MHz, $CDCl_3$)



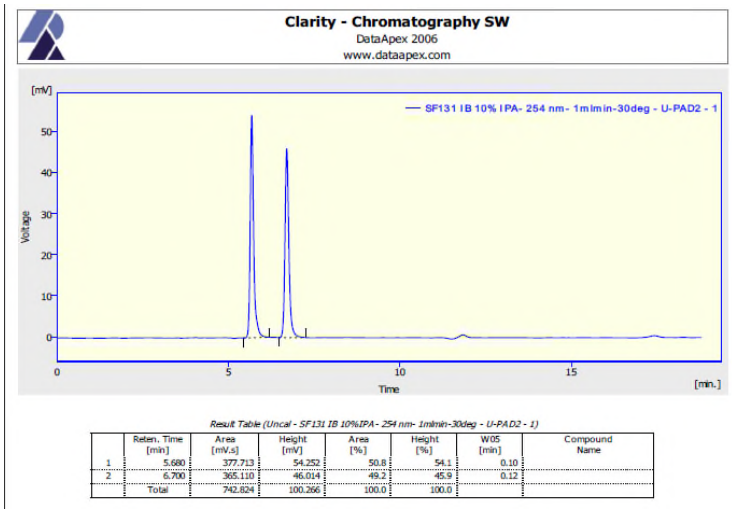
^{13}C NMR (75 MHz, $CDCl_3$)



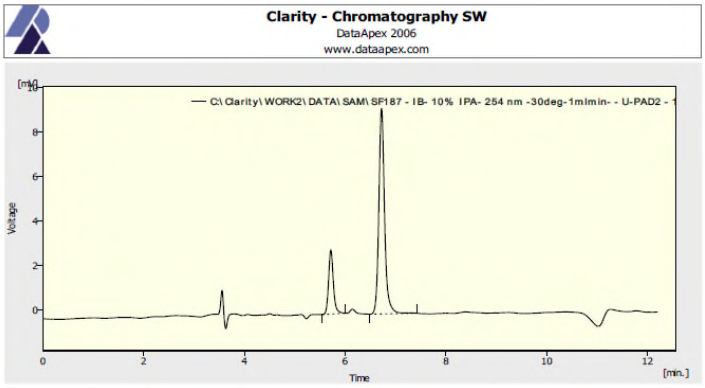
COSY (300 MHz, $CDCl_3$)



HPLC Racemic



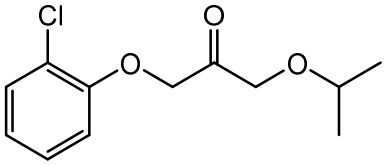
HPLC After ATH



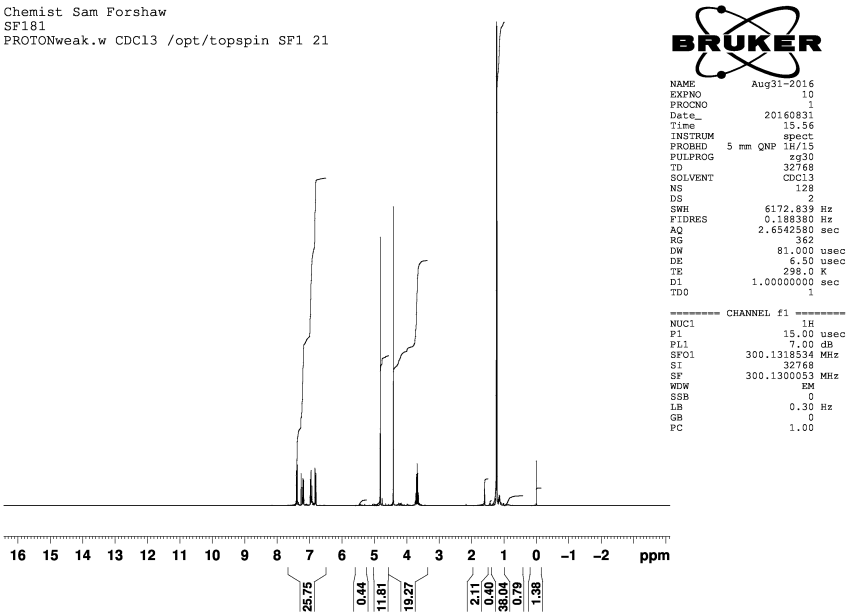
Result Table (Uncal - C:\Clarity\WORK2\DATA\SAM\SF187 - IB- 10% IPA- 254 nm -30deg-1mlmin- - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	5.716	19.035	2.890	20.6	23.8	0.10	
2	6.724	73.314	9.261	79.4	76.2	0.12	
	Total	92.349	12.152	100.0	100.0		

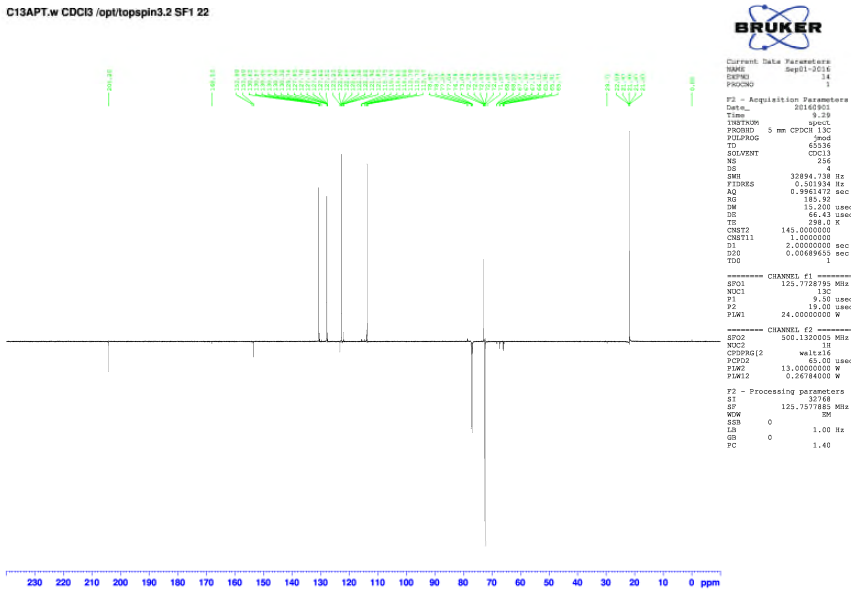
1-(2-Chlorophenoxy)-3-isopropoxypropan-2-one.



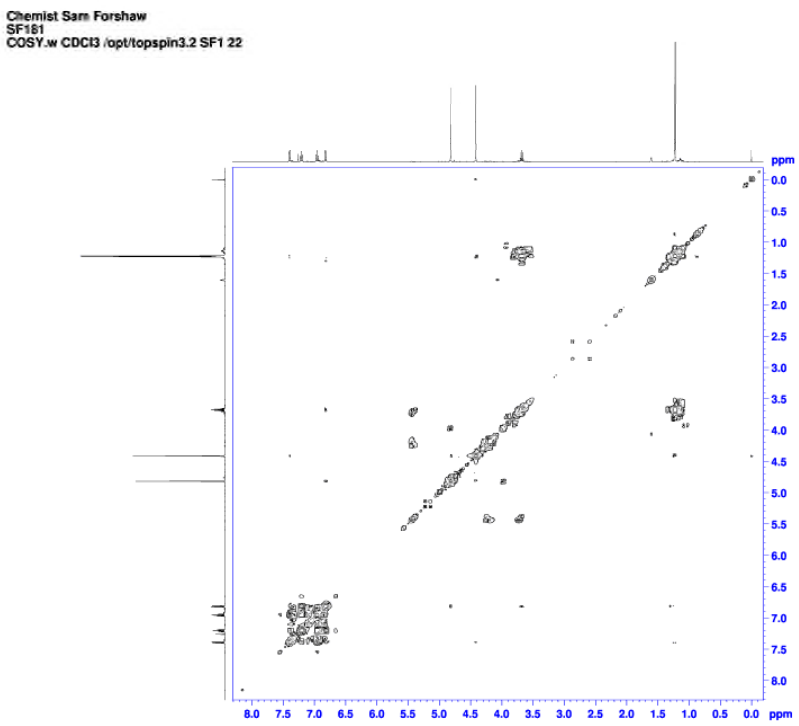
^{1}H NMR (300 MHz, $CDCl_3$)

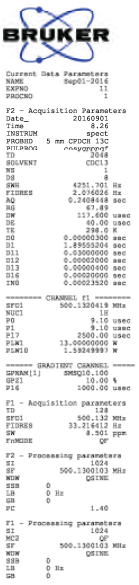


^{13}C NMR (125 MHz, $CDCl_3$)

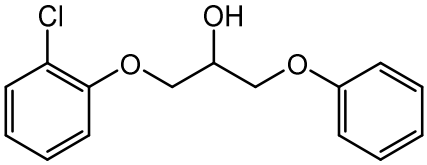


COSY (500 MHz, $CDCl_3$)

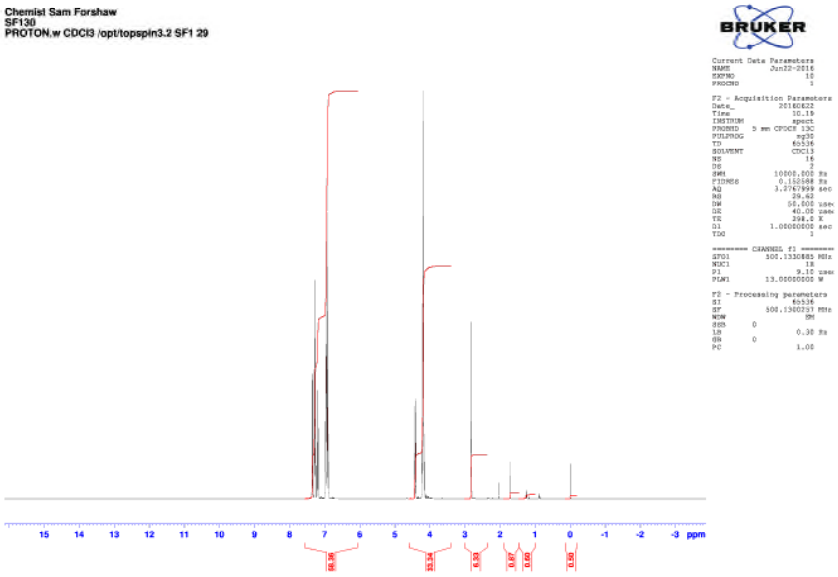




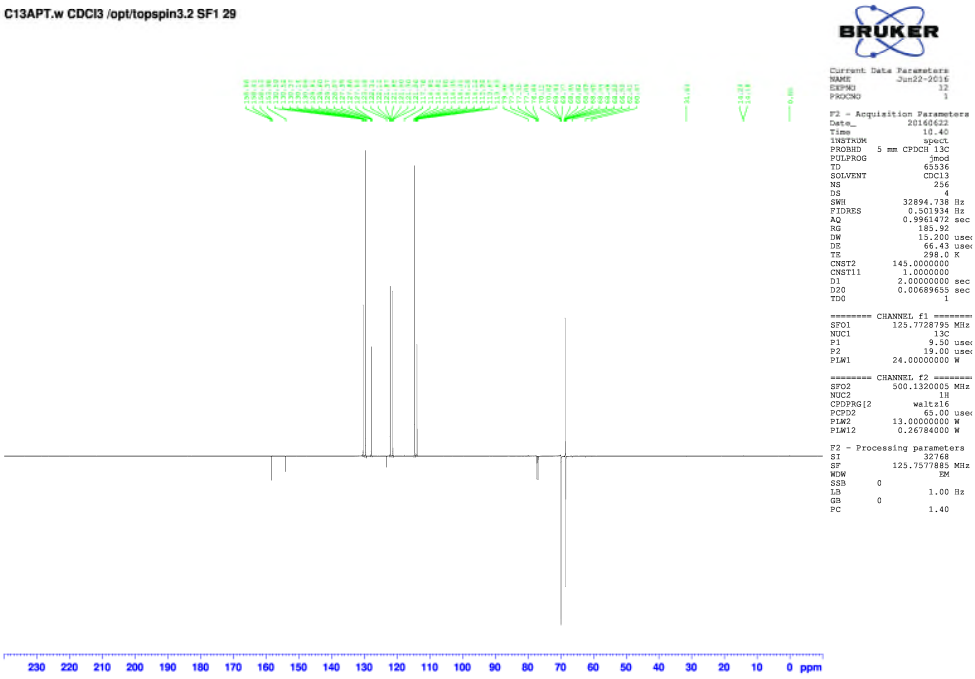
1-(2-Chlorophenoxy)-3-phenoxypropan-2-ol 23.



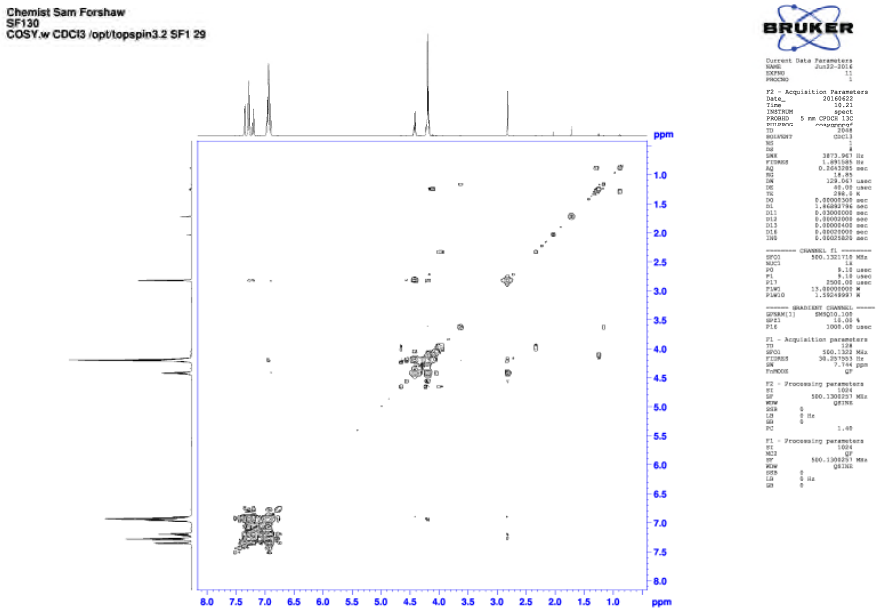
^{1}H NMR (500 MHz, $CDCl_3$)



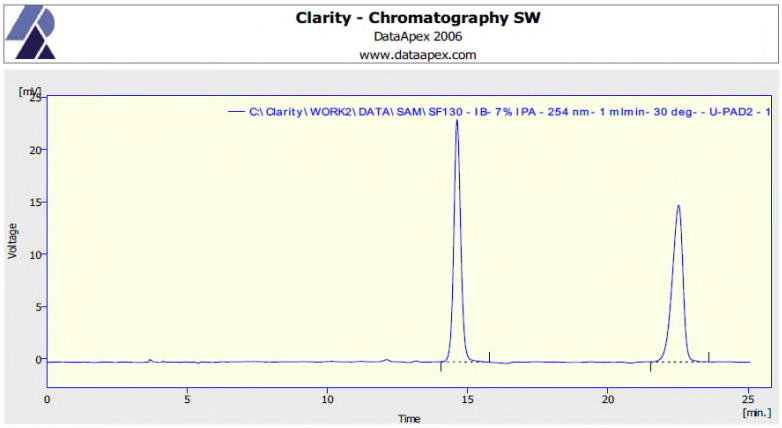
^{13}C NMR (125 MHz, $CDCl_3$)



COSY (500 MHz, $CDCl_3$)



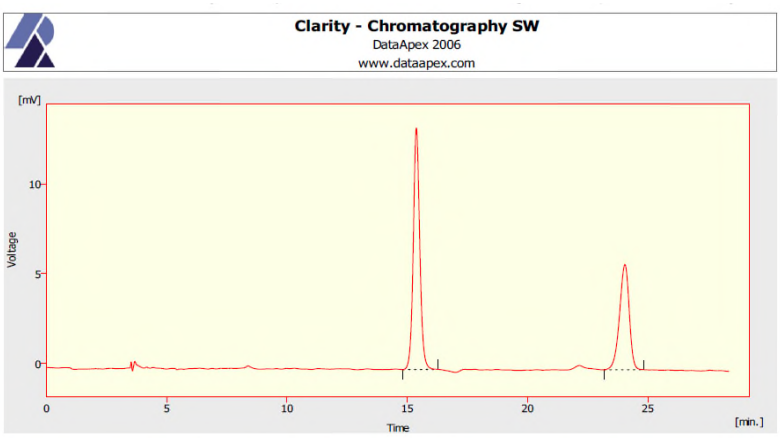
HPLC Racemic



Result Table (Uncal - C:\Clarity\WORK2\DATA\SAM\SF130 - IB- 7%IPA - 254 nm- 1 mlmin- 30 deg- - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	14.624	399.896	23.148	50.0	60.8	0.26	
2	22.520	399.752	14.951	50.0	39.2	0.41	
	Total	799.647	38.099	100.0	100.0		

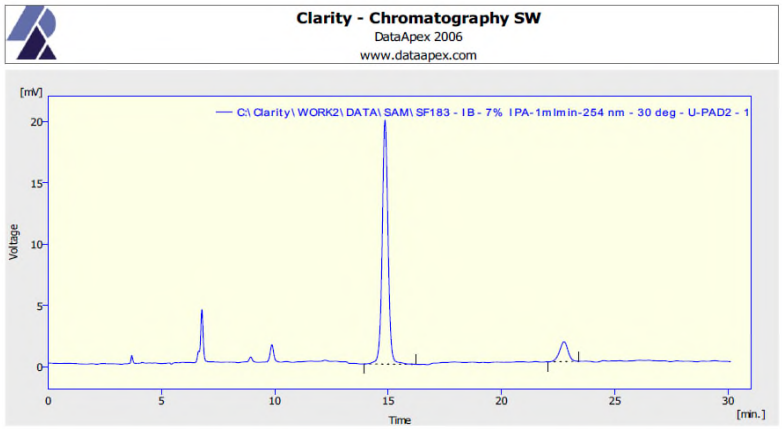
HPLC After ATH



Result Table (Uncal - C:\Clarity\WORK2\DATA\SAM\SF150 Run 2 IB-7%IPA-30deg-1mlmin-254nm- - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	15.380	251.863	13.435	60.5	69.6	0.28	
2	24.044	164.279	5.855	39.5	30.4	0.43	
	Total	416.142	19.289	100.0	100.0		

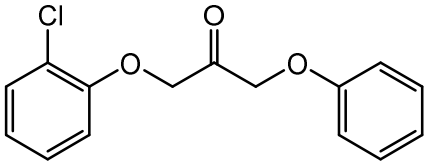
HPLC Asymmetric Standard



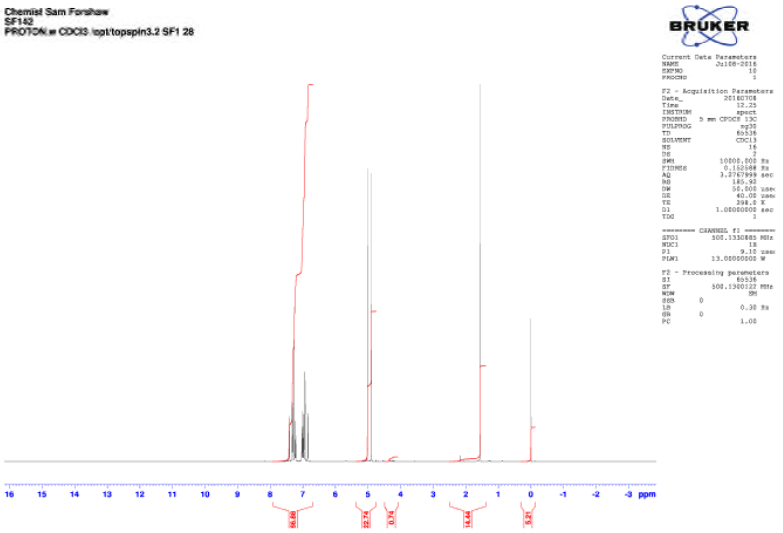
Result Table (Uncal - C:\Clarity\WORK2\DATA\SAM\SF183 - IB - 7% IPA-1mlmin-254 nm - 30 deg - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	14.860	357.264	19.894	89.5	92.5	0.27	
2	22.760	41.924	1.619	10.5	7.5	0.40	
	Total	399.188	21.513	100.0	100.0		

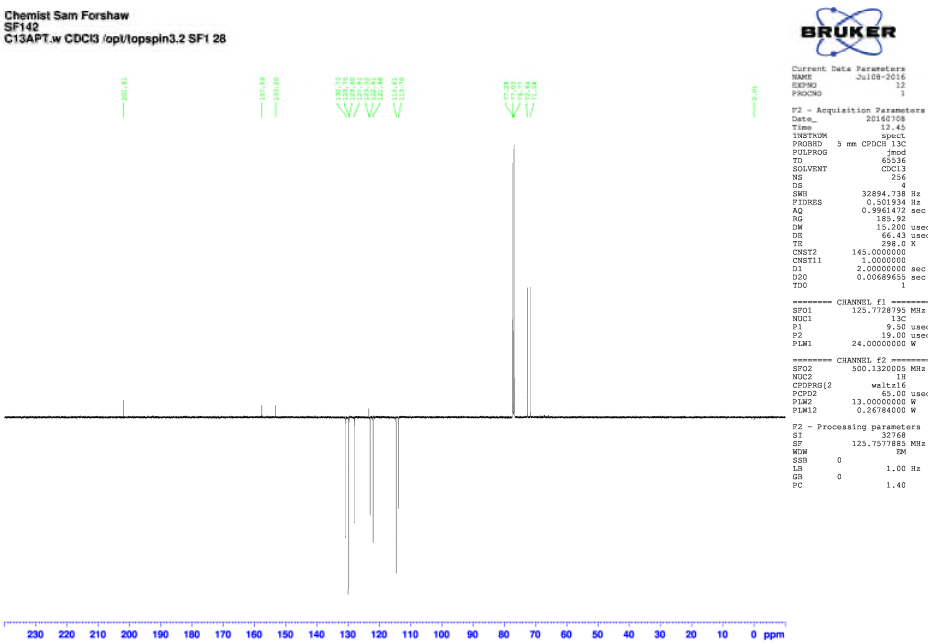
1-(2-Chlorophenoxy)-3-phenoxypropan-2-one.



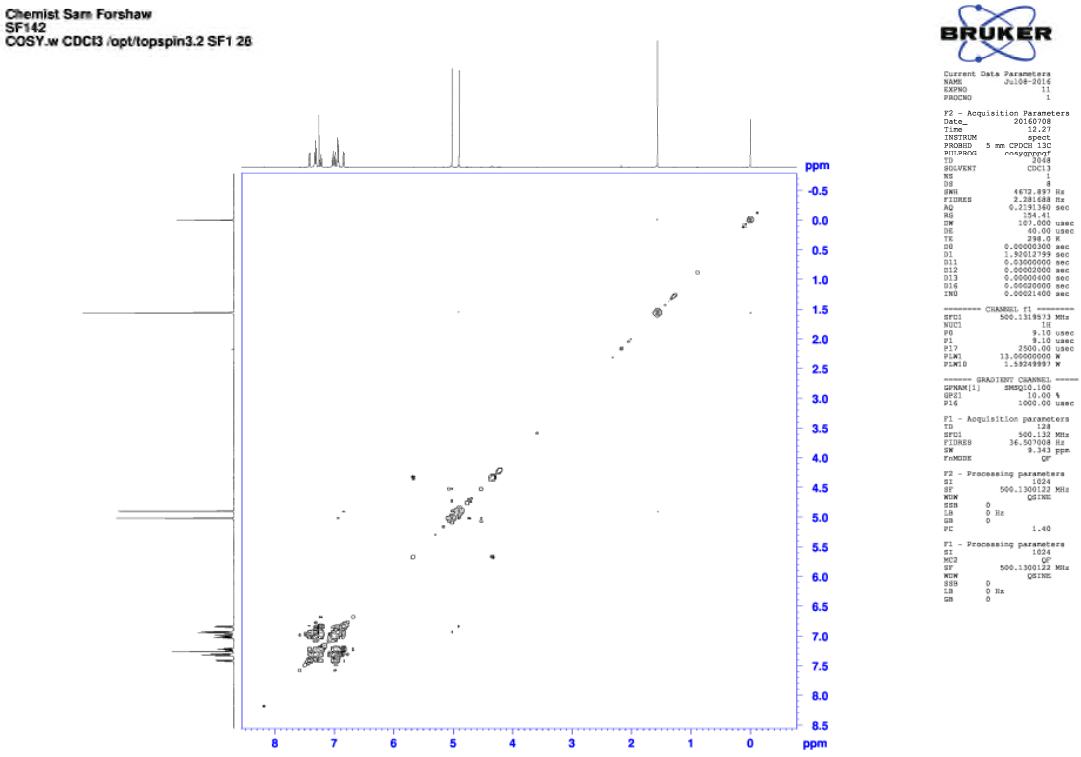
^{1}H NMR (500 MHz, $CDCl_3$)



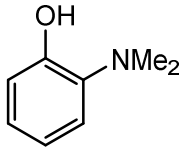
^{13}C NMR(125 MHz, $CDCl_3$)



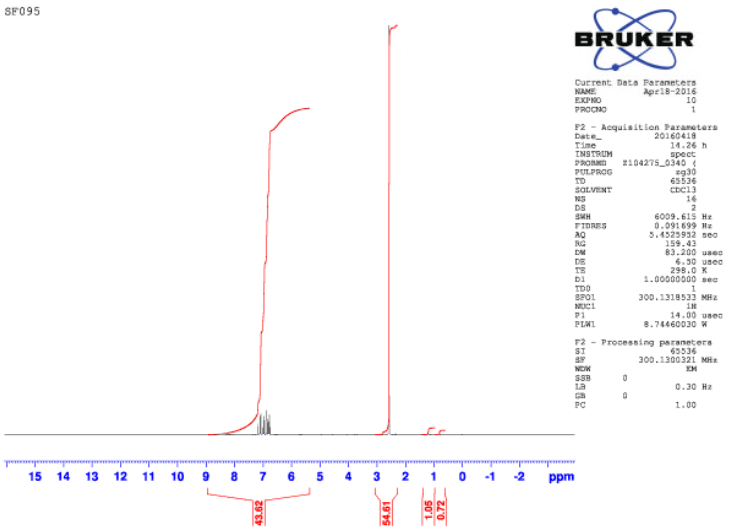
COSY (500 MHz, $CDCl_3$)



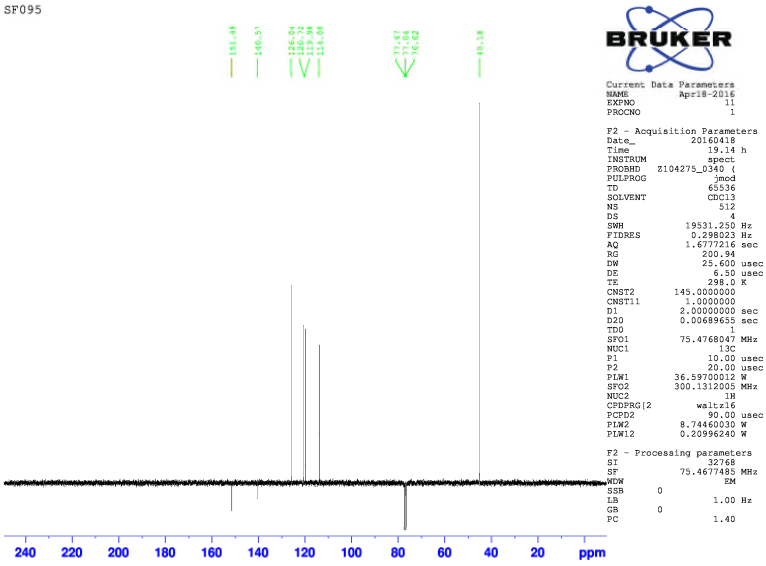
2-(Dimethylamino)phenol.



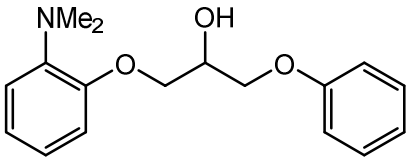
^{1}H NMR (300 MHz, $CDCl_3$)



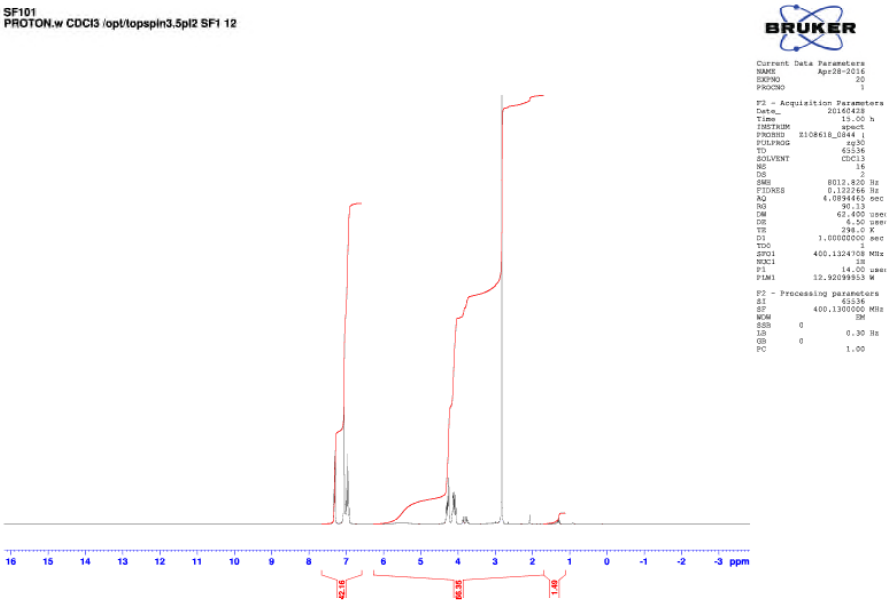
^{13}C NMR (75 MHz, $CDCl_3$)



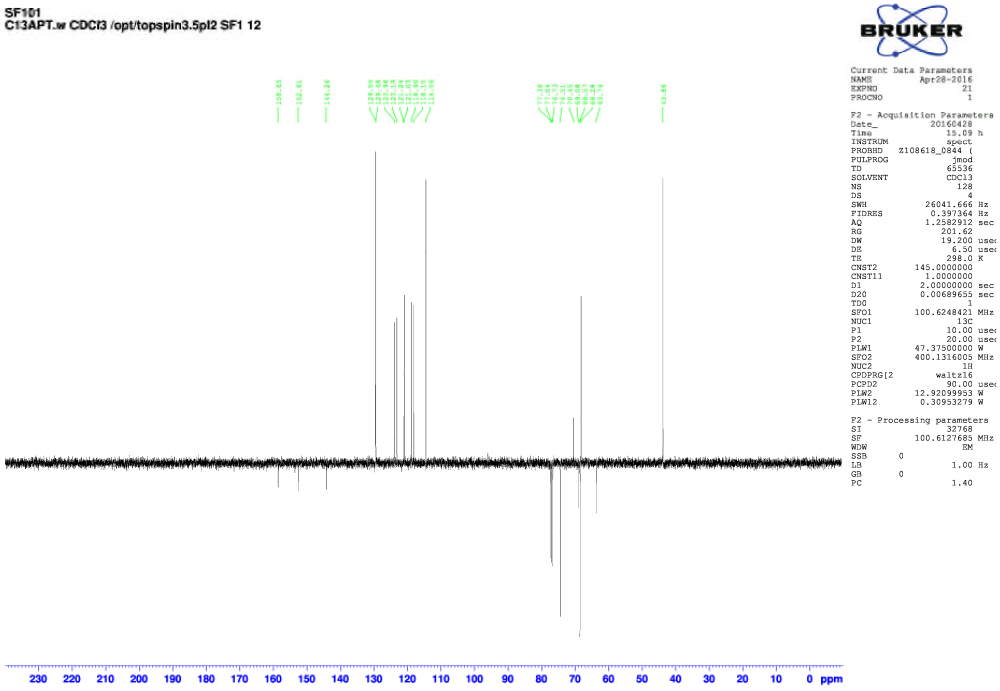
(2-(Dimethylamino)phenoxy)-3-phenoxypropan-2-ol 24.



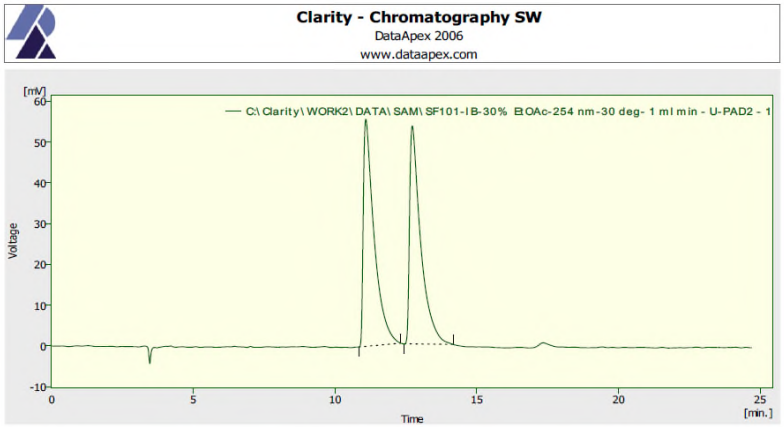
^{1}H NMR (400 MHz, $CDCl_3$)



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



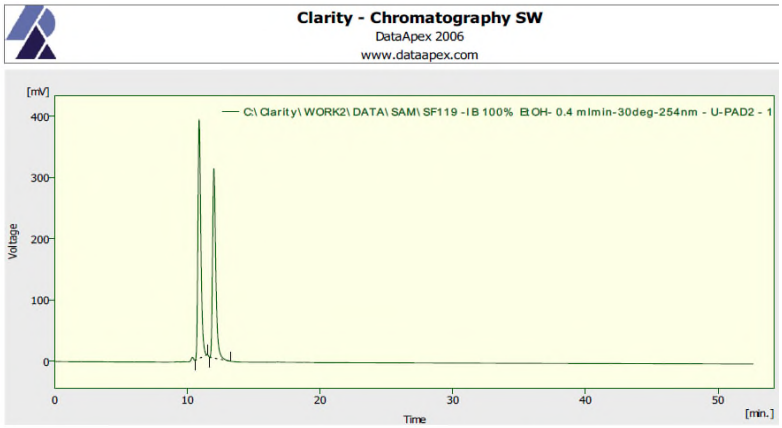
HPLC Racemic



Result Table (Uncal - C:\Clarity\WORK2\DATA\SAM\SF101-IB-30% EtOAc-254 nm-30 deg- 1 ml min - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	11.088	1477.524	55.667	50.4	51.0	0.38	
2	12.728	1451.939	53.435	49.6	49.0	0.38	
	Total	2929.463	109.102	100.0	100.0		

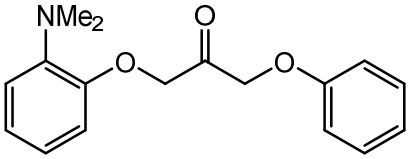
HPLC After ATH



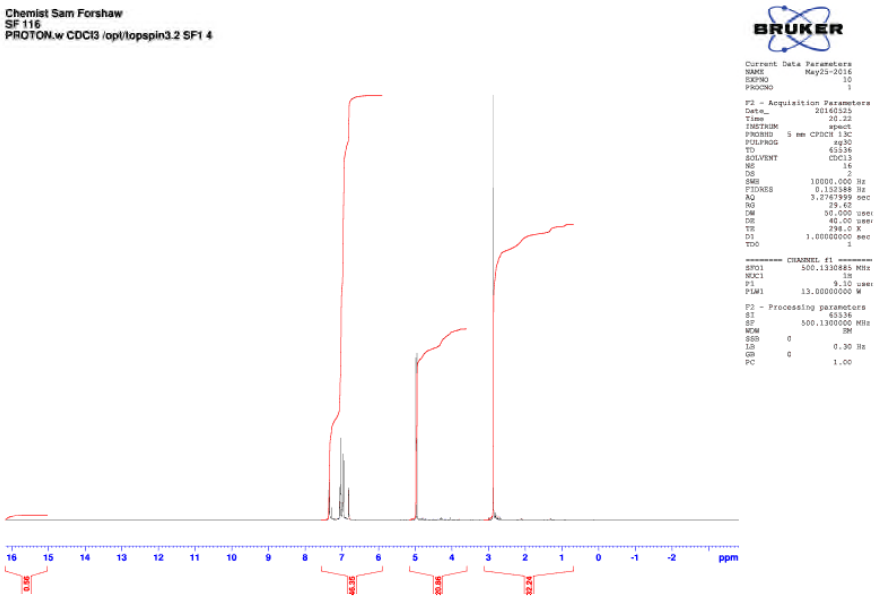
Result Table (Uncal - C:\Clarity\WORK2\DATA\SAM\SF119 -IB 100% EtOH- 0.4 mlmin-30deg-254nm - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	10.884	5975.683	389.688	53.4	55.8	0.24	
2	11.992	5213.757	309.110	46.6	44.2	0.25	
	Total	11189.440	698.798	100.0	100.0		

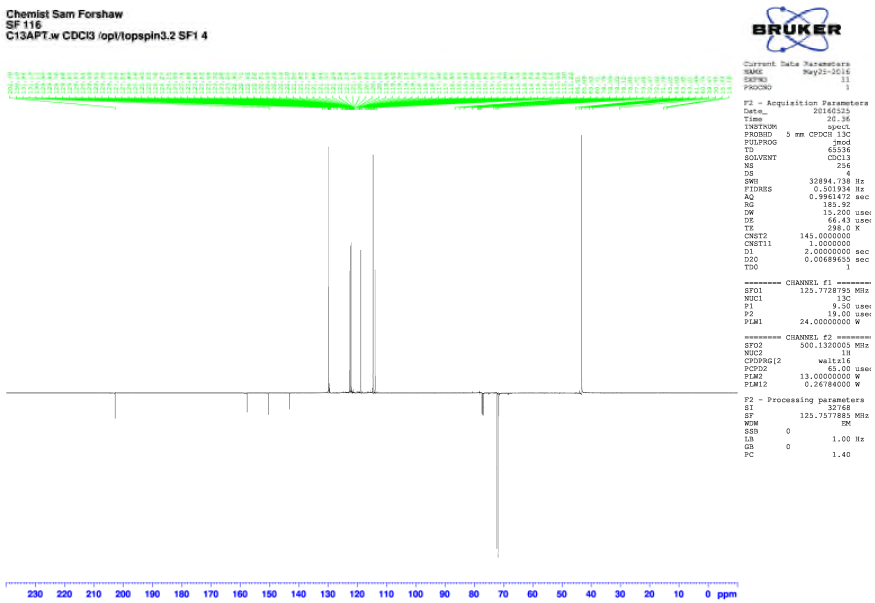
1-(2-(Dimethylamino)phenoxy)-3-phenoxypropan-2-one.



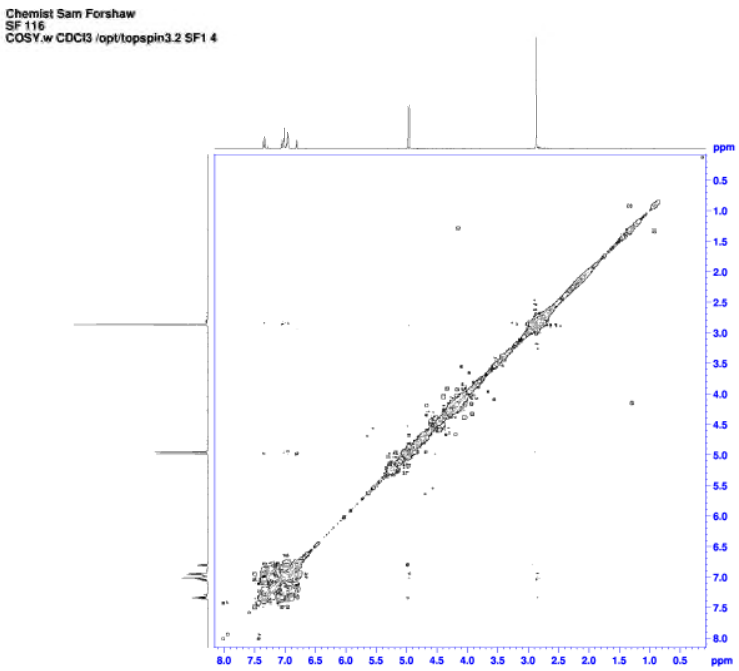
^{1}H NMR (500 MHz, $CDCl_3$)

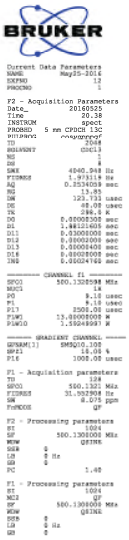


^{13}C NMR (125 MHz, $CDCl_3$)

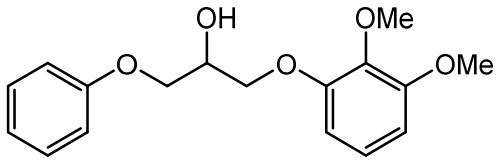


COSY (500 MHz, $CDCl_3$)

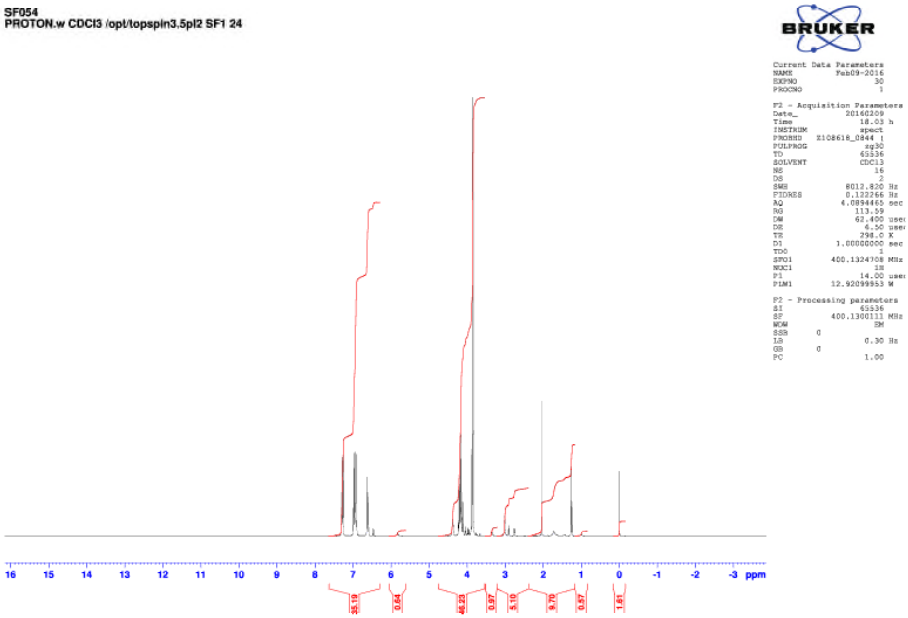




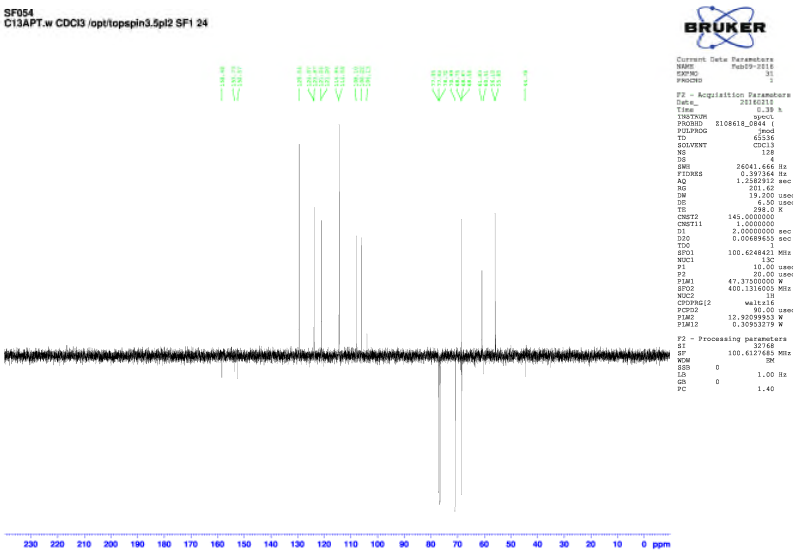
1-(2,3-Dimethoxyphenoxy)-3-phenoxypropan-2-ol 25.



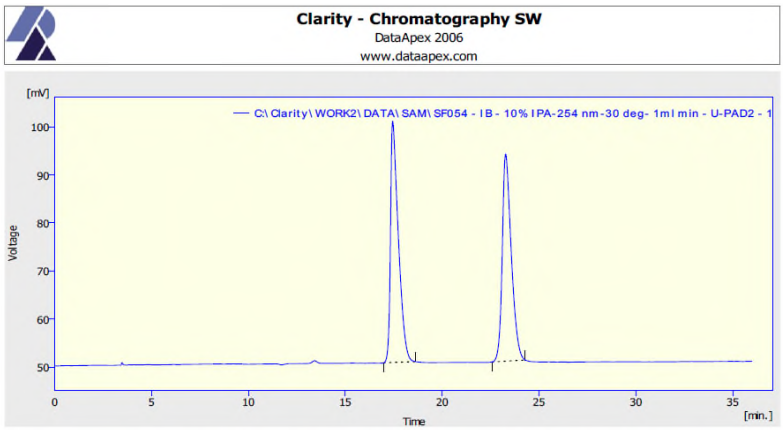
^{1}H NMR (400 MHz, $CDCl_3$)



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



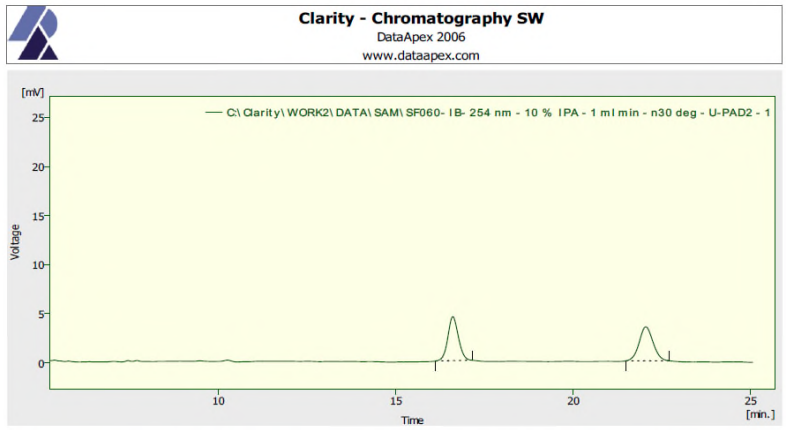
HPLC Racemic



Result Table (Uncal - C:\Clarity\WORK2\DATA\SAM\SF054 - IB - 10%IPA-254 nm-30 deg- 1ml min - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	17.448	1417.157	50.222	50.4	53.8	0.43	
2	23.280	1392.669	43.095	49.6	46.2	0.49	
	Total	2809.827	93.317	100.0	100.0		

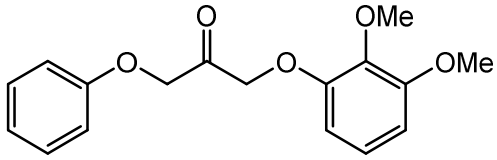
HPLC After ATH



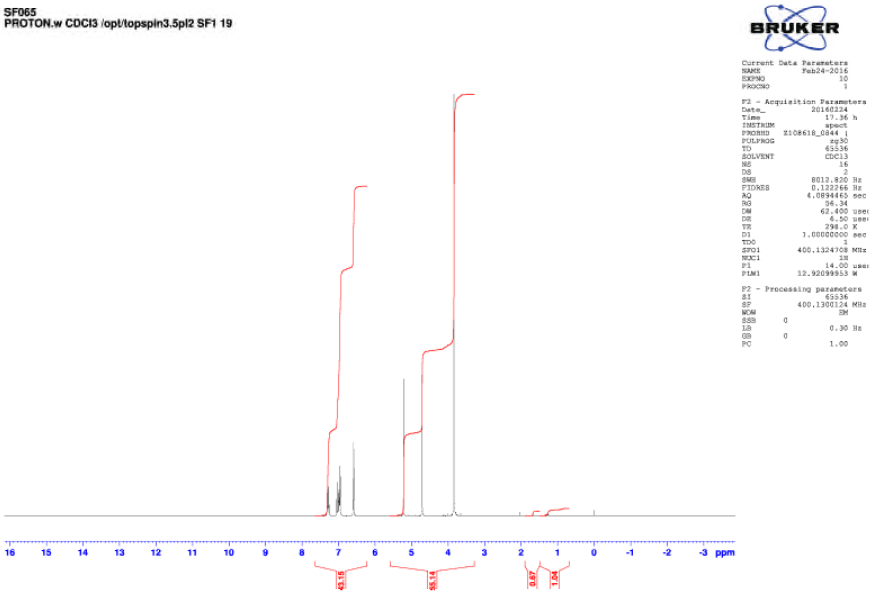
Result Table (Uncal - C:\Clarity\WORK2\DATA\SAM\SF060- IB- 254 nm - 10 % IPA - 1 ml min - n30 deg - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	16.604	92.494	4.476	49.5	56.4	0.32	
2	22.040	94.269	3.464	50.5	43.6	0.42	
	Total	186.763	7.940	100.0	100.0		

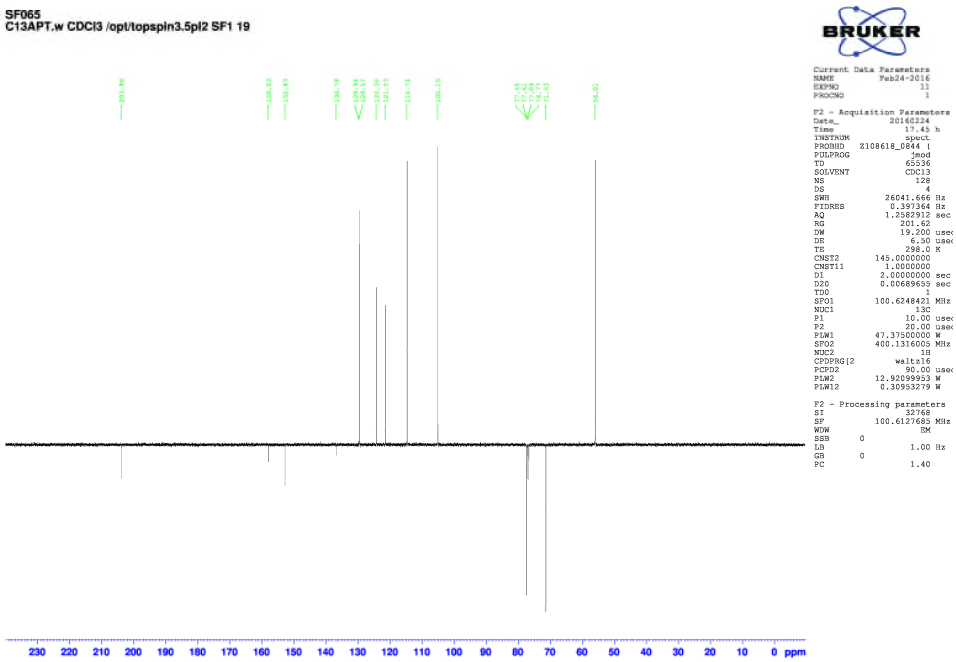
1-(2,3-Dimethoxyphenoxy)-3-phenoxypropan-2-one.



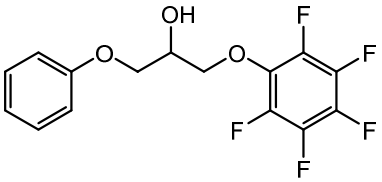
^{1}H NMR (400 MHz, $CDCl_3$)



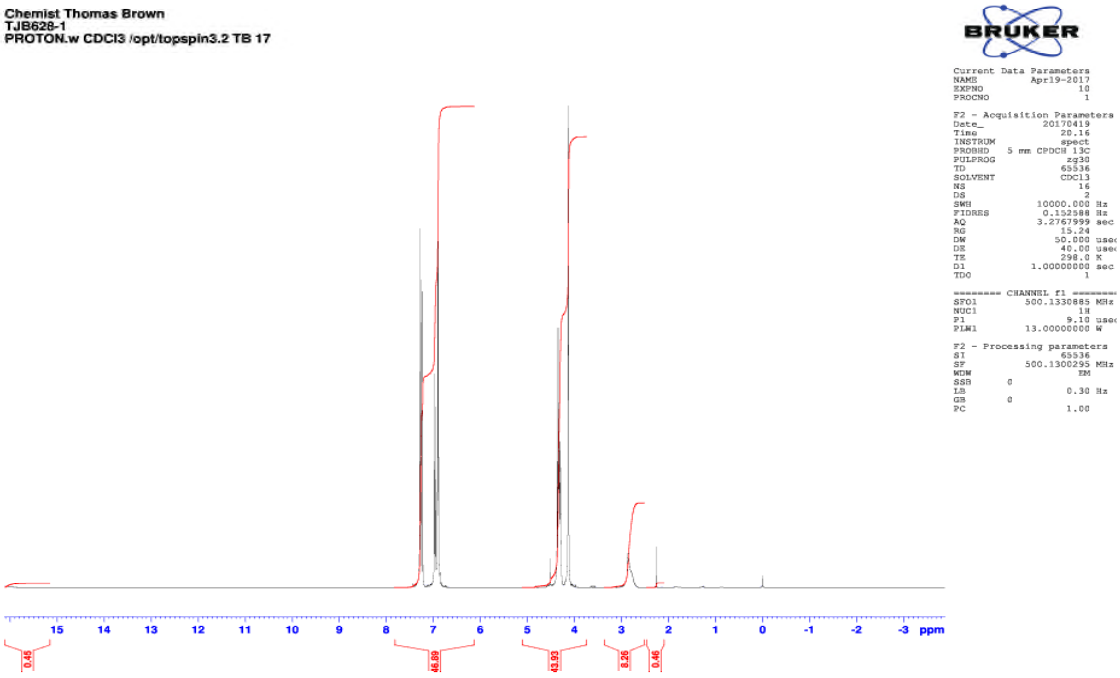
^{13}C NMR (100 MHz, $CDCl_3$)



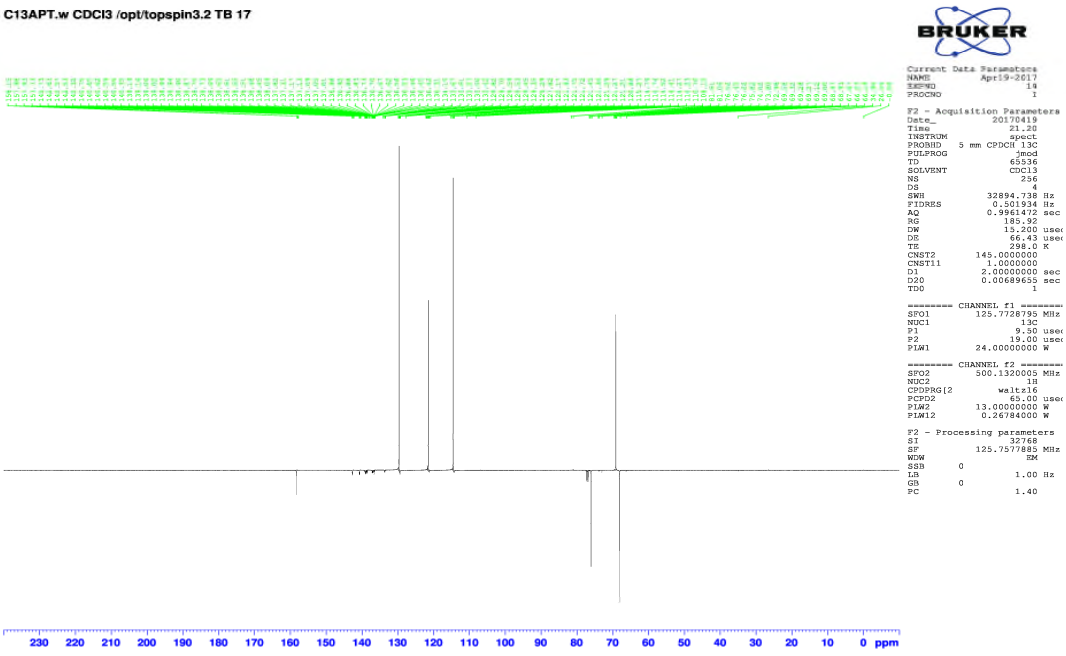
1-(Pentafluorophenoxy)-3-phenoxypropan-2-ol 26.



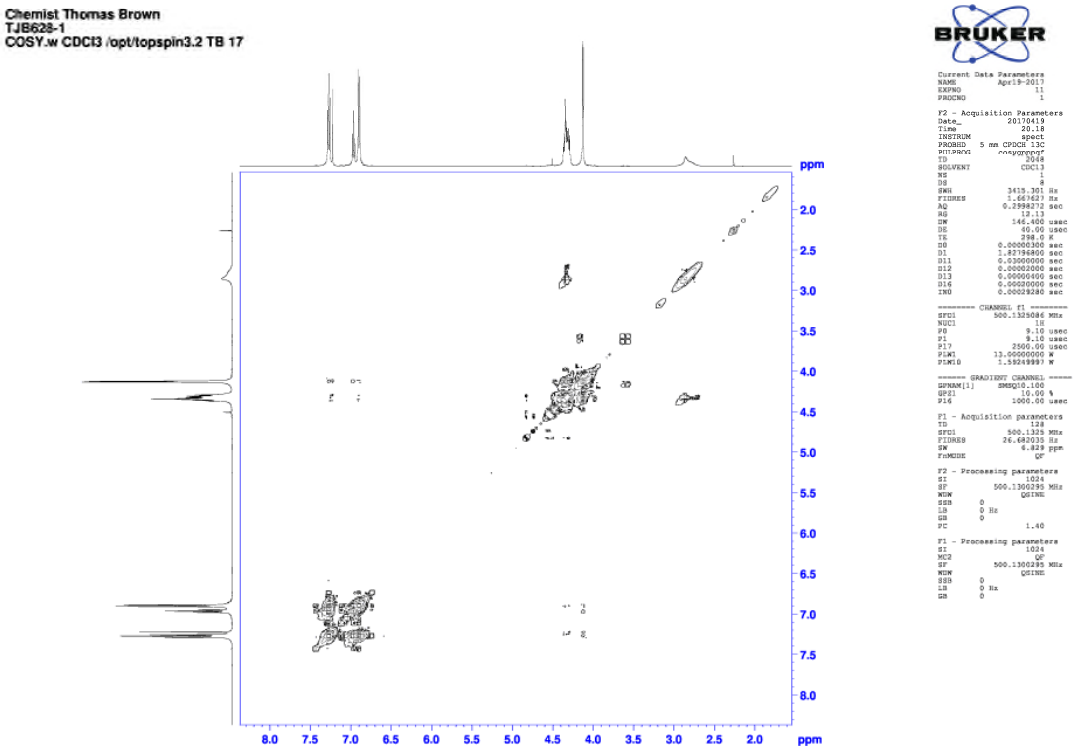
^{1}H NMR (500 MHz, $CDCl_3$)



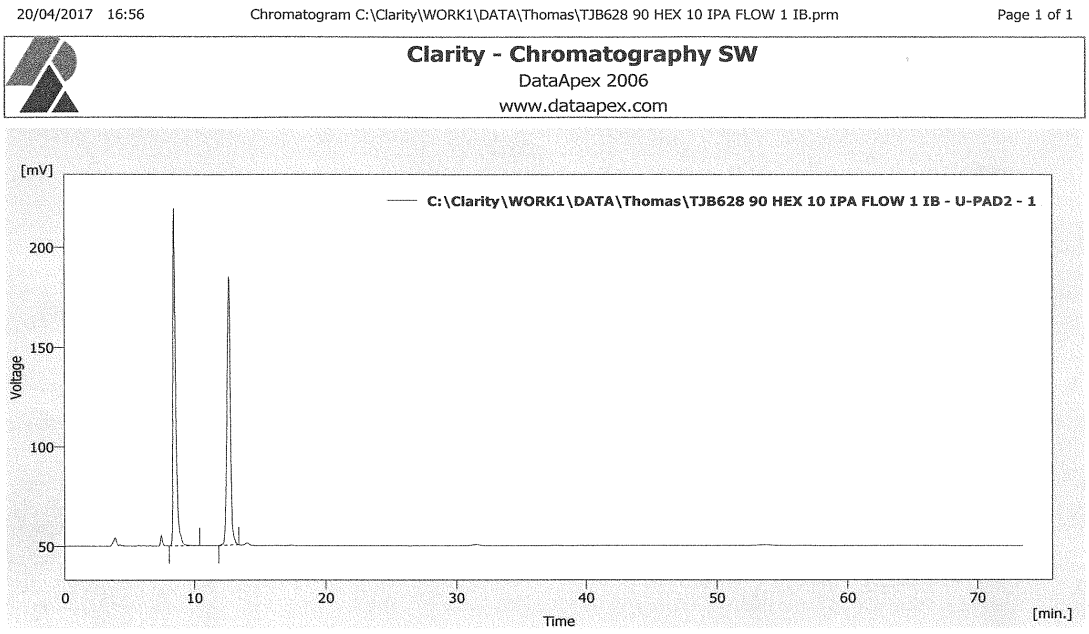
^{13}C NMR (125 MHz, $CDCl_3$)



COSY (500 MHz, $CDCl_3$)



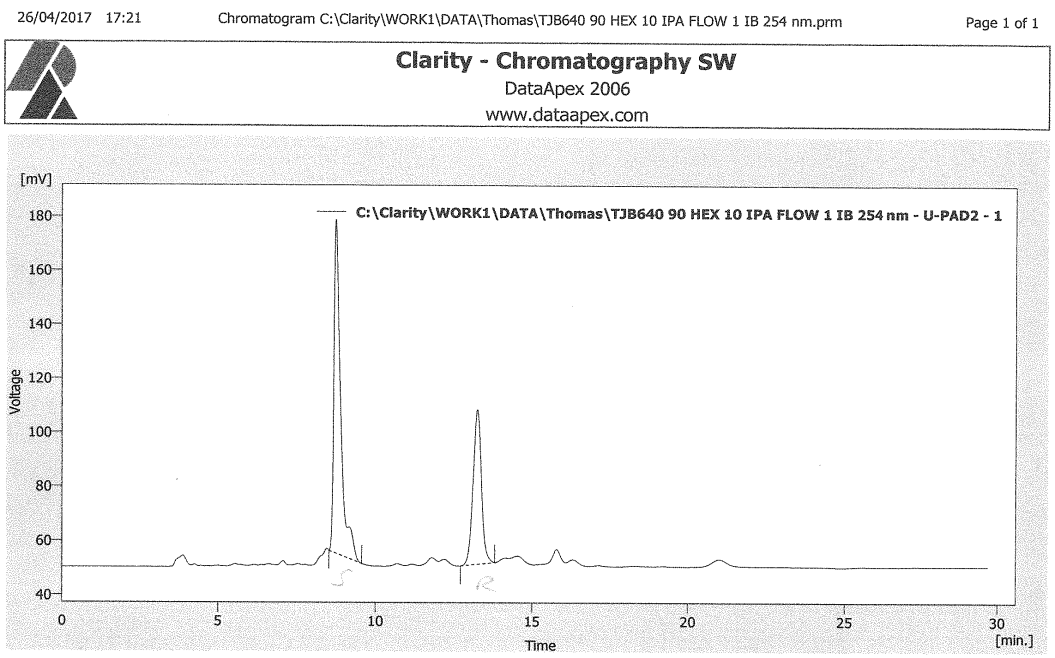
HPLC Racemic



Result Table (Uncal - C:\Clarity\WORK1\DATA\Thomas\TJB628 90 HEX 10 IPA FLOW 1 IB - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	8.464	2416.286	169.193	50.0	55.7	0.21	
2	12.676	2413.422	134.679	50.0	44.3	0.28	
	Total	4829.708	303.873	100.0	100.0		

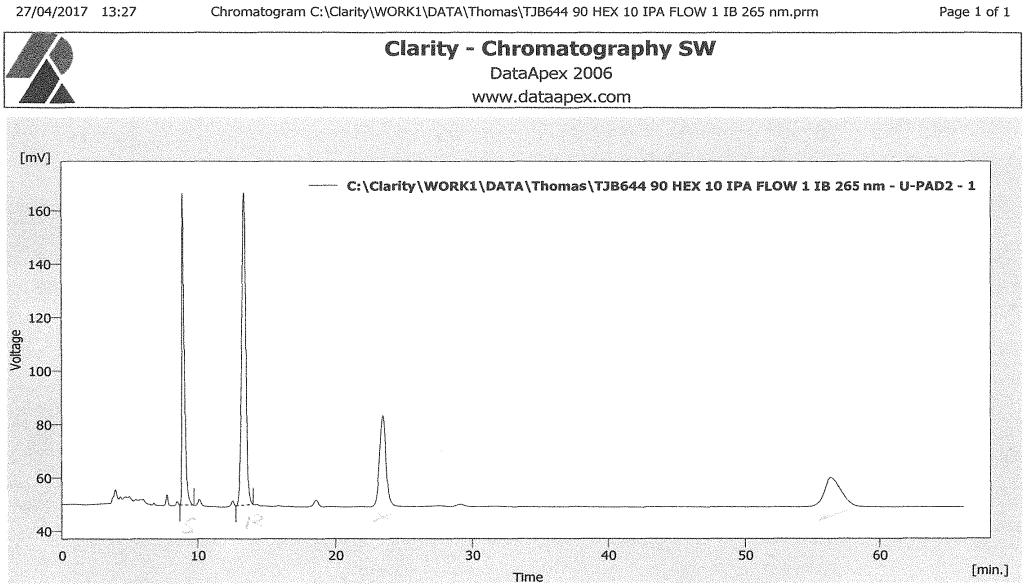
HPLC After ATH



Result Table (Uncal - C:\Clarity\WORK1\DATA\Thomas\TJB640 90 HEX 10 IPA FLOW 1 IB 254 nm - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	8.732	1856.357	123.355	63.5	68.3	0.21	
2	13.244	1067.743	57.204	36.5	31.7	0.28	
	Total	2924.099	180.559	100.0	100.0		

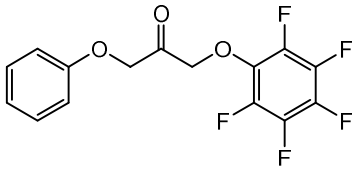
HPLC asymmetric standard.



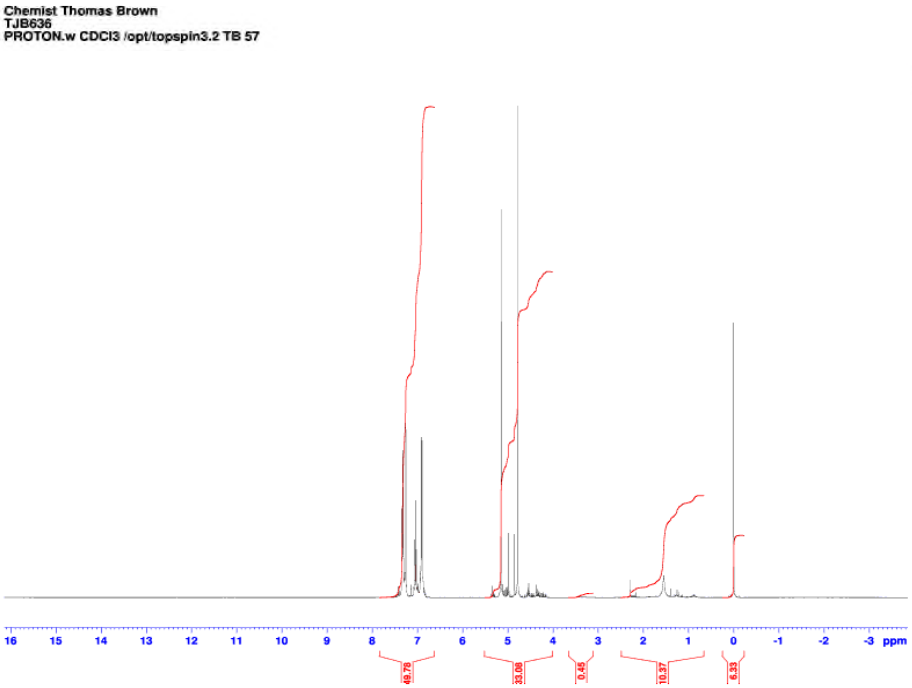
Result Table (Uncal - C:\Clarity\WORK1\DATA\Thomas\TJB644 90 HEX 10 IPA FLOW 1 IB 265 nm - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	8.904	1529.567	116.680	38.1	49.9	0.20	
2	13.392	2483.558	116.940	61.9	50.1	0.34	
	Total	4013.126	233.620	100.0	100.0		

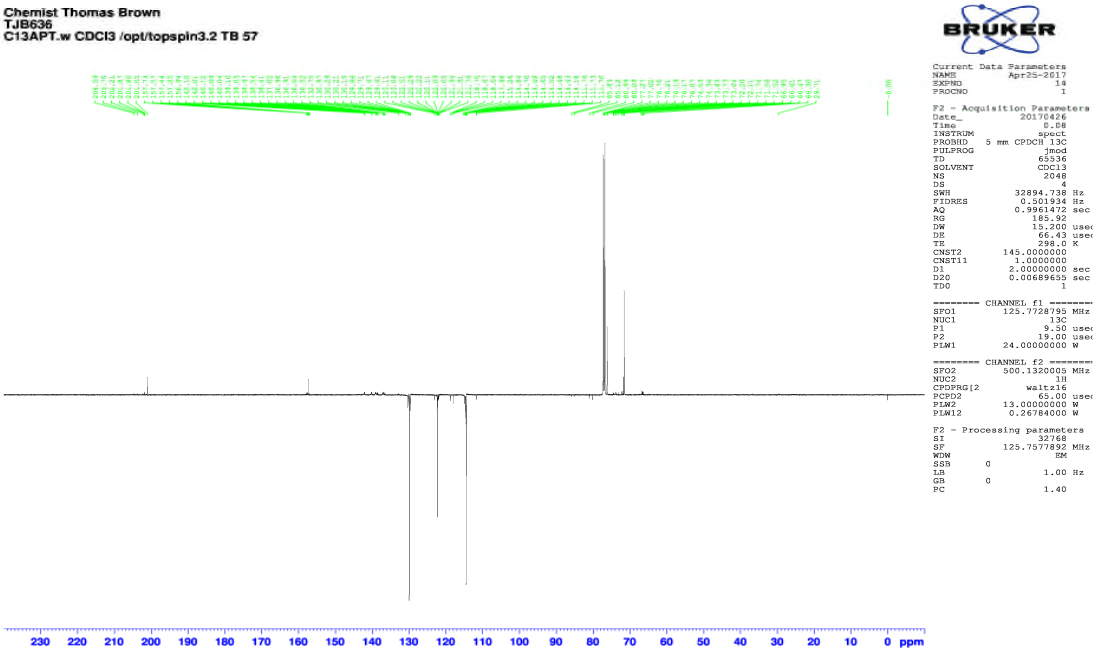
1-(Pentafluoromethylphenoxy)-3-phenoxypropan-2-one.



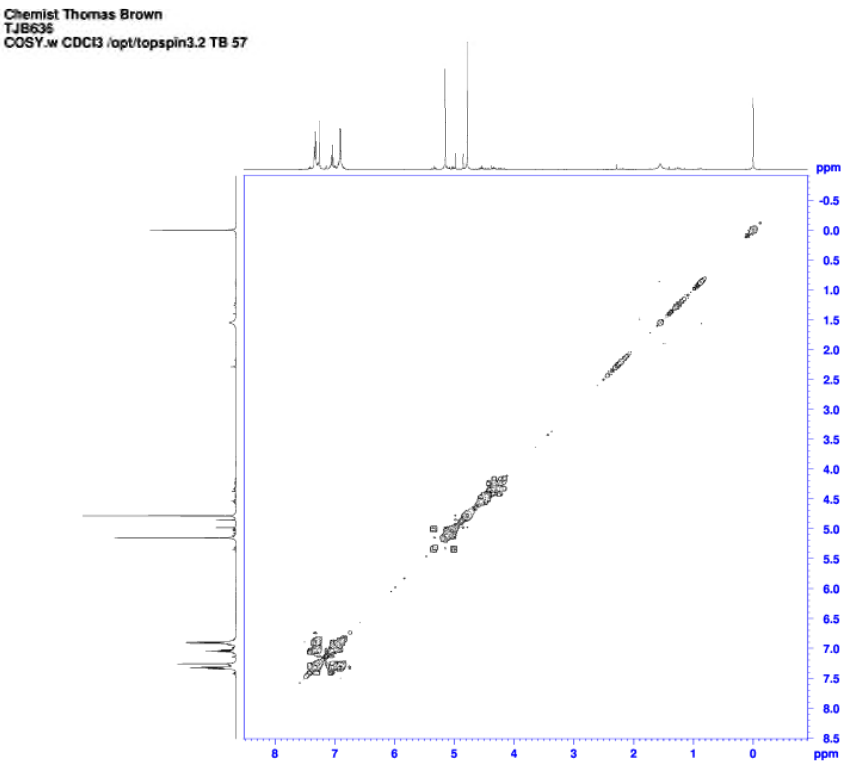
^{1}H NMR (500 MHz, $CDCl_3$)

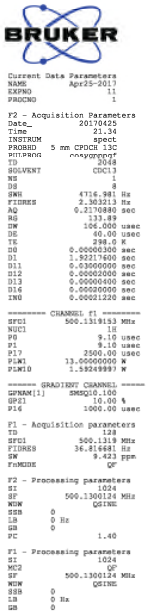


^{13}C NMR (125 MHz, $CDCl_3$)

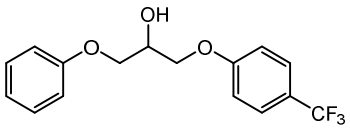


COSY (500 MHz, $CDCl_3$)

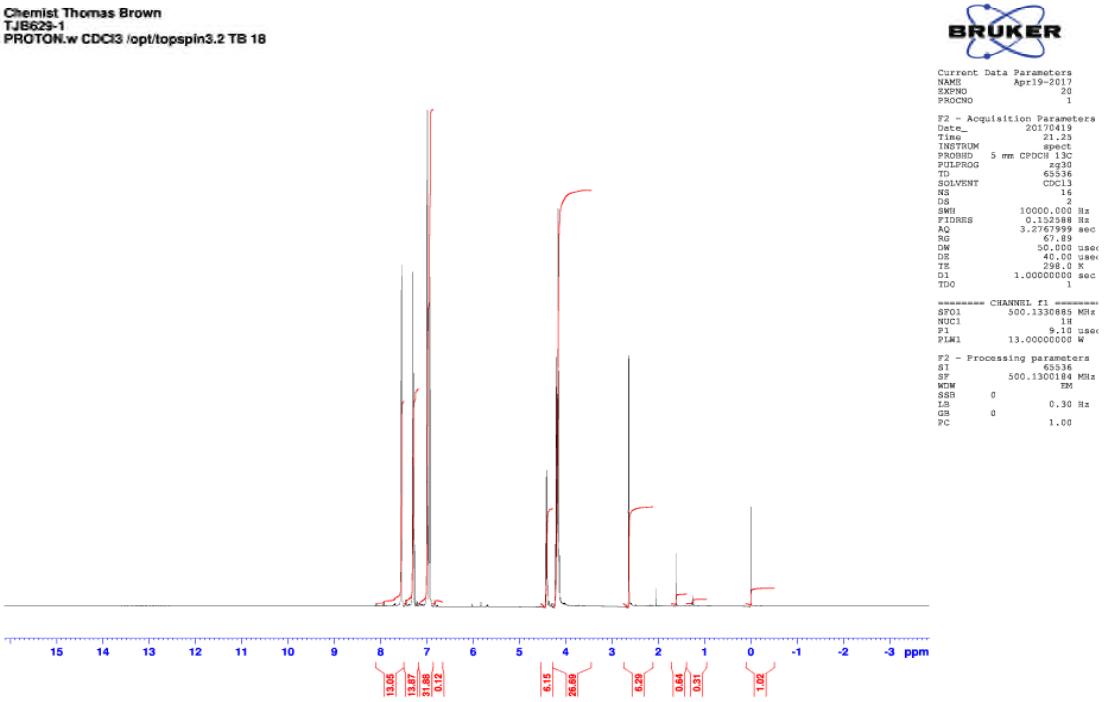




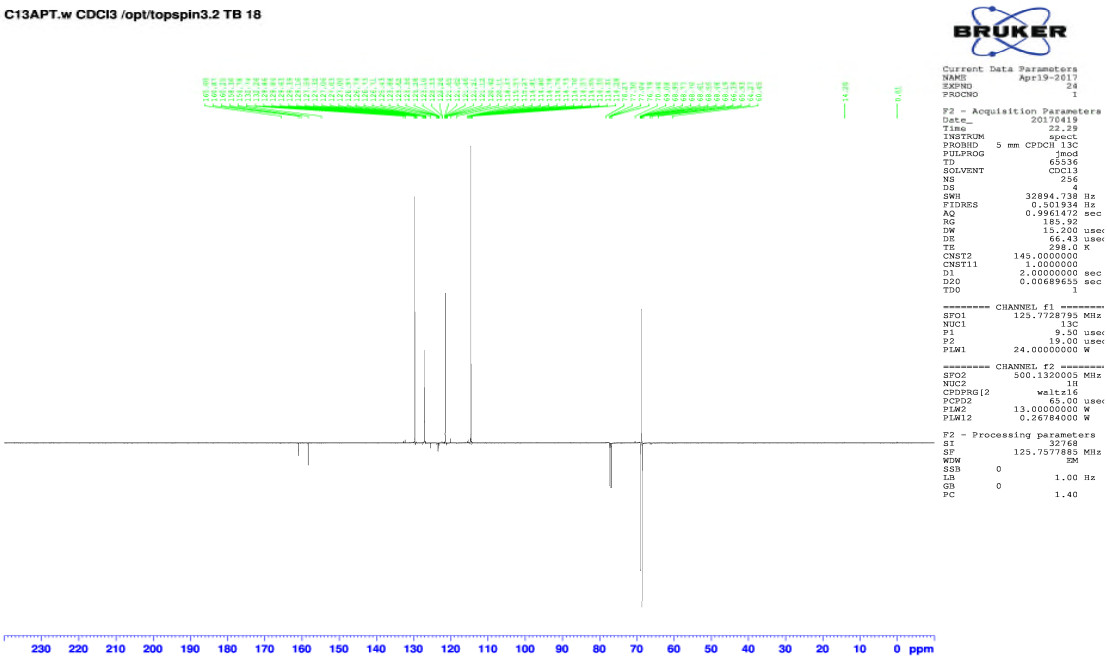
1-((4-Trifluoromethyl)phenoxy)-3-phenoxypropan-2-ol 27.



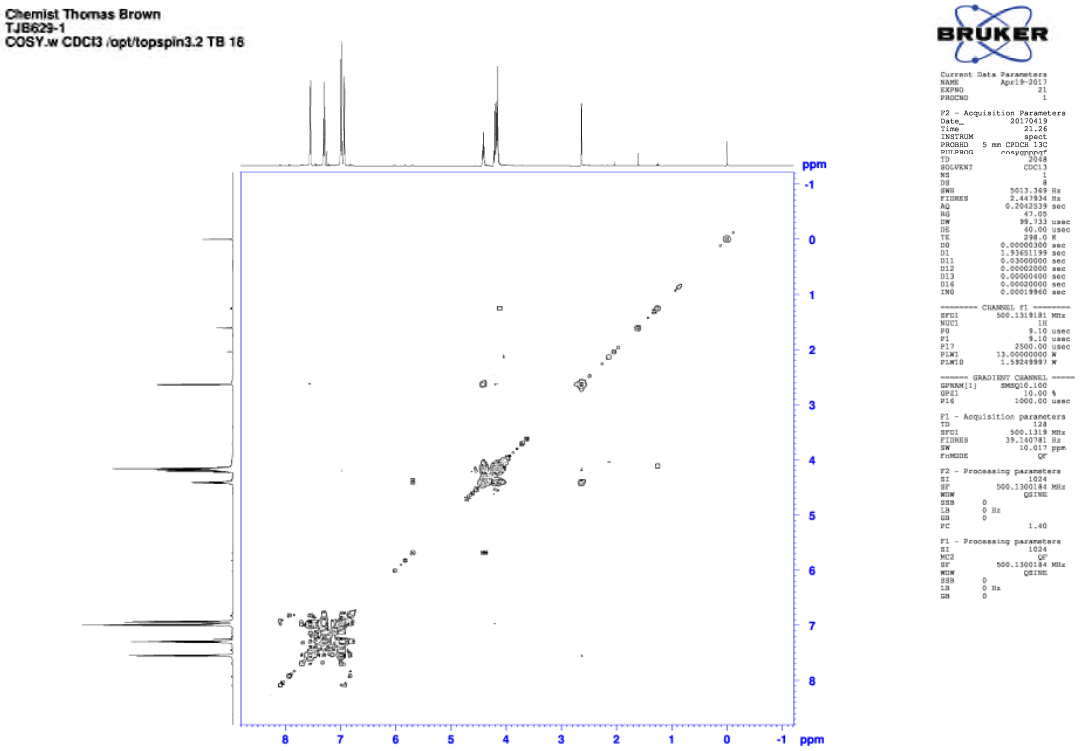
^{1}H NMR (500 MHz, $CDCl_3$)



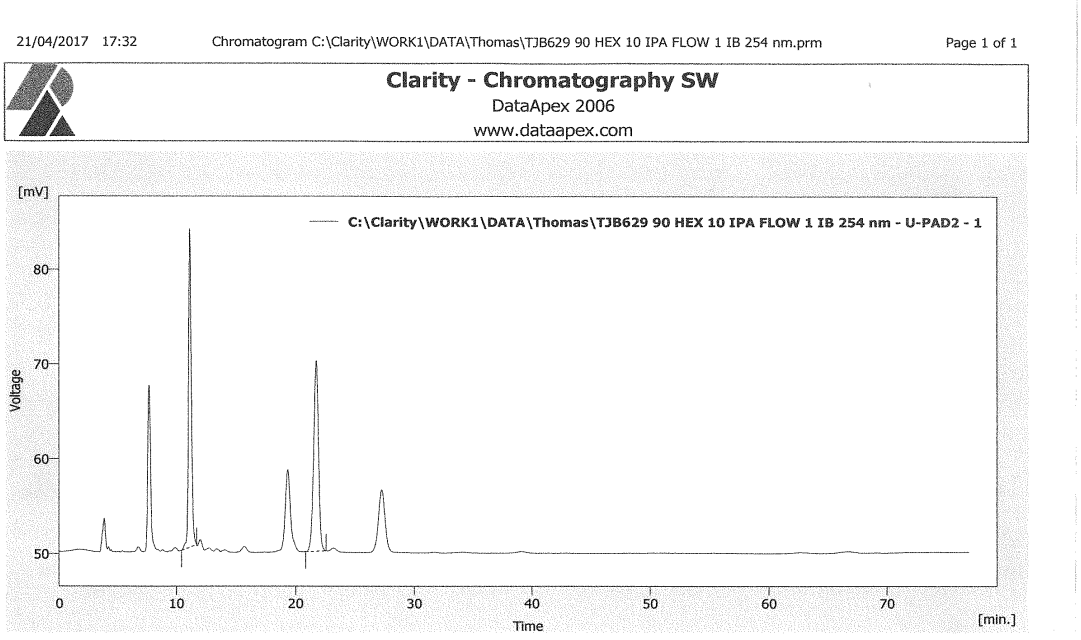
^{13}C NMR (125 MHz, $CDCl_3$)



COSY (500 MHz, $CDCl_3$)



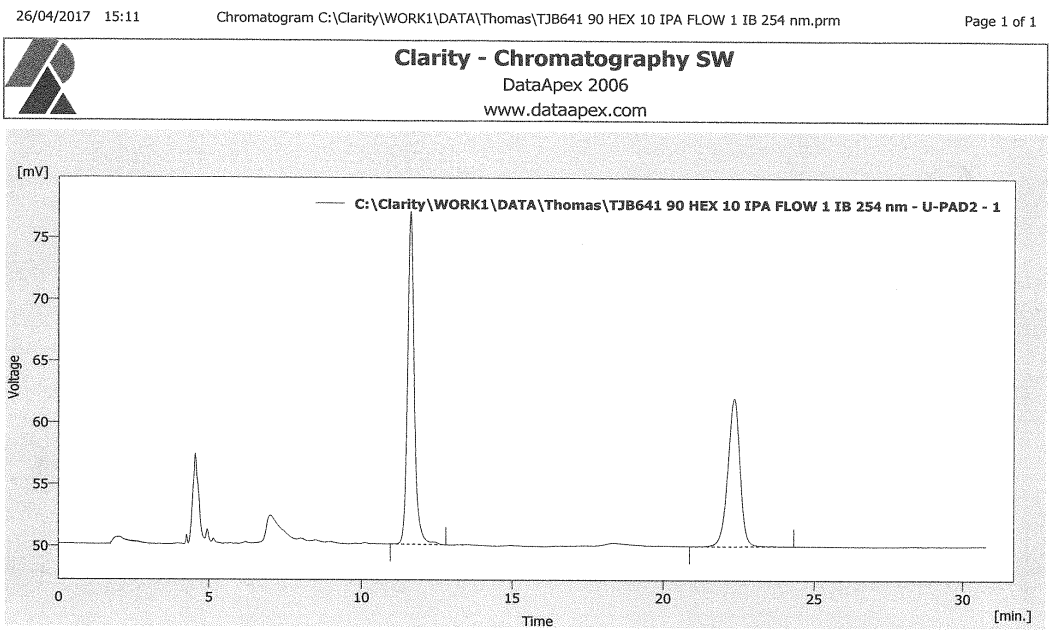
HPLC Racemic



Result Table (Uncal - C:\Clarity\WORK1\DATA\Thomas\TJB629 90 HEX 10 IPA FLOW 1 IB 254 nm - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	11.148	559.652	33.588	49.4	62.5	0.25	
2	21.748	572.520	20.127	50.6	37.5	0.44	
	Total	1132.172	53.716	100.0	100.0		

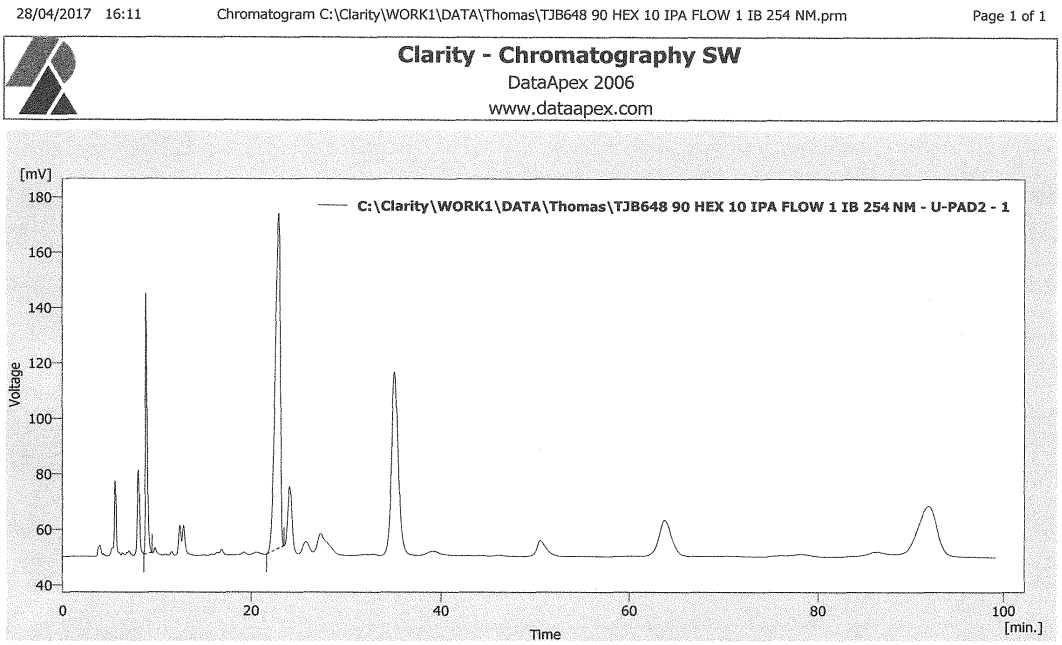
HPLC After ATH



Result Table (Uncal - C:\Clarity\WORK1\DATA\Thomas\TJB641 90 HEX 10 IPA FLOW 1 IB 254 nm - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	11.608	419.352	26.982	55.5	69.3	0.22	
2	22.344	335.697	11.973	44.5	30.7	0.42	
	Total	755.049	38.955	100.0	100.0		

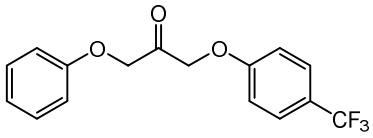
HPLC asymmetric standard.



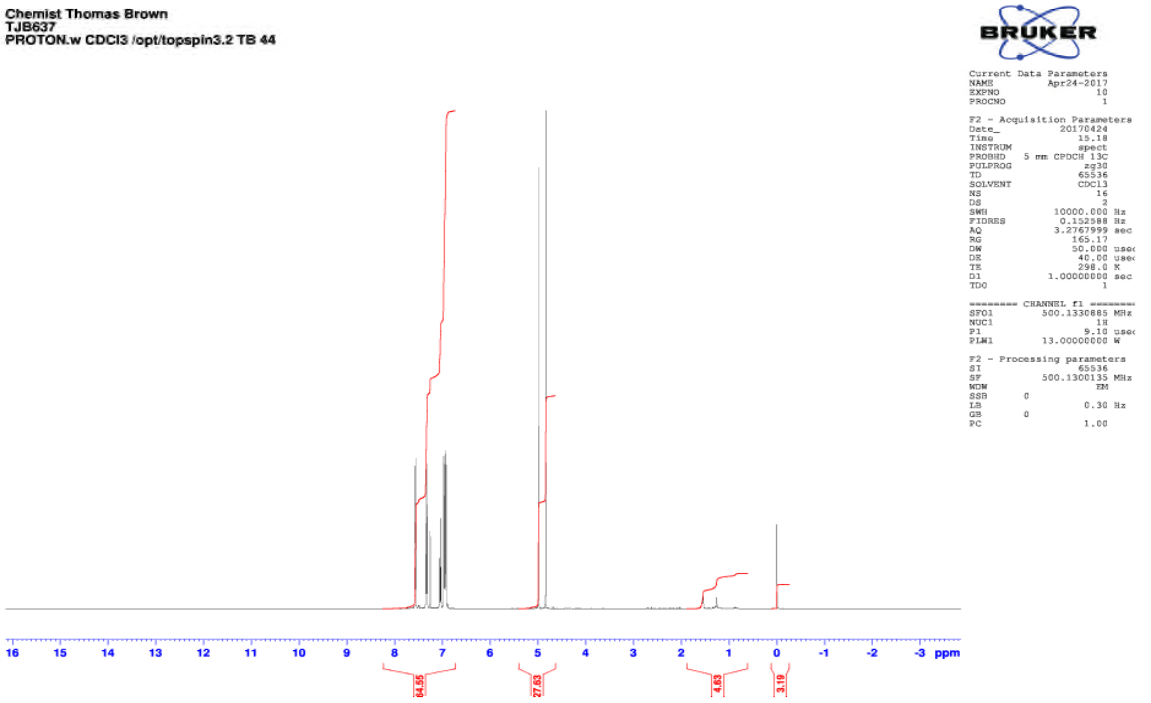
Result Table (Uncal - C:\Clarity\WORK1\DATA\Thomas\TJB648 90 HEX 10 IPA FLOW 1 IB 254 NM - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	8.880	1154.684	93.929	20.5	43.7	0.18	
2	22.932	4490.156	120.806	79.5	56.3	0.60	
	Total	5644.840	214.735	100.0	100.0		

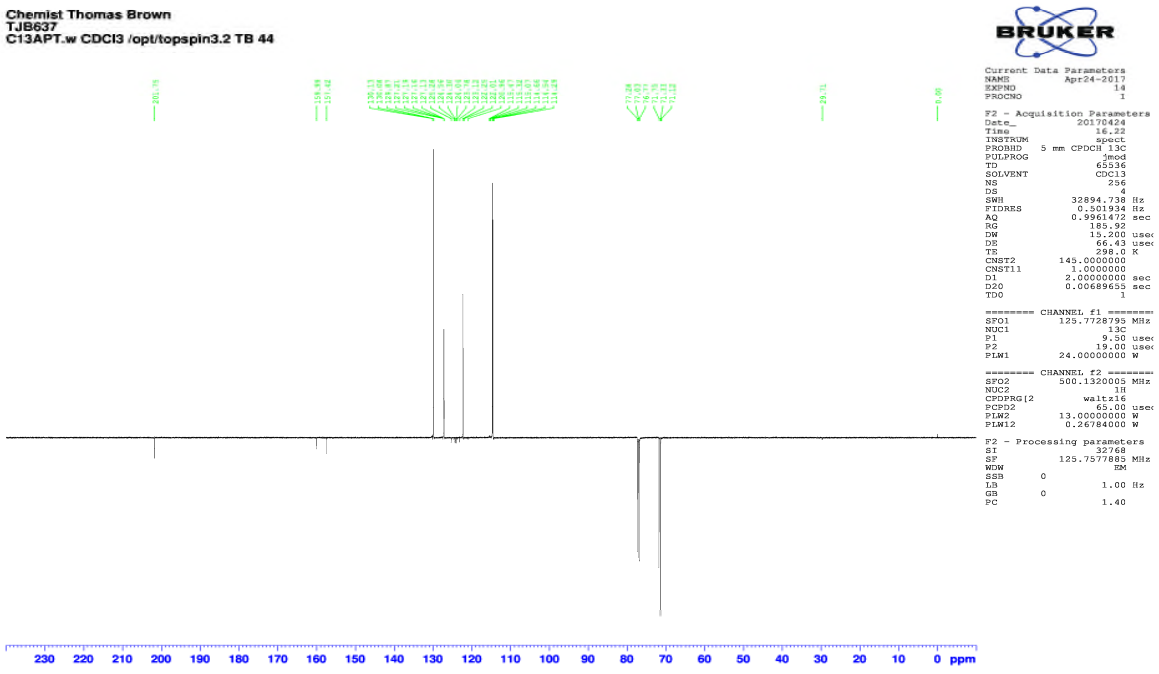
1-((4-Trifluoromethyl)phenoxy)-3-phenoxypropan-2-one.



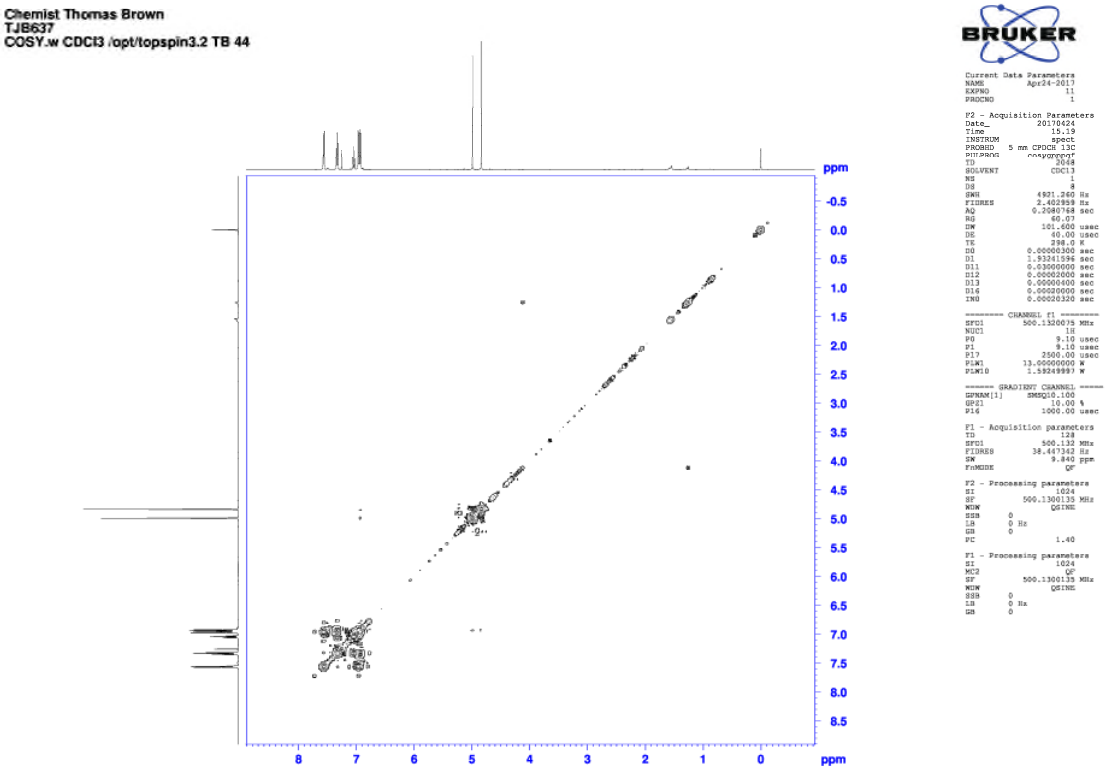
^{1}H NMR (500 MHz, $CDCl_3$)



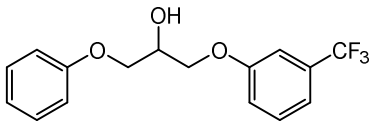
^{13}C NMR (125 MHz, $CDCl_3$)



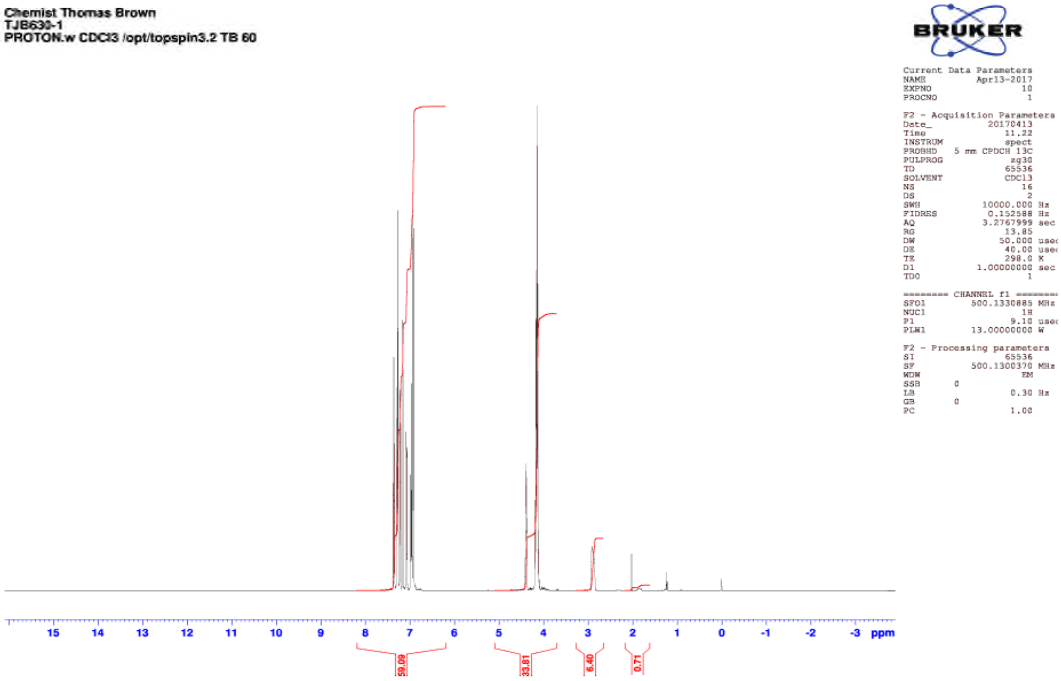
COSY (500 MHz, $CDCl_3$)



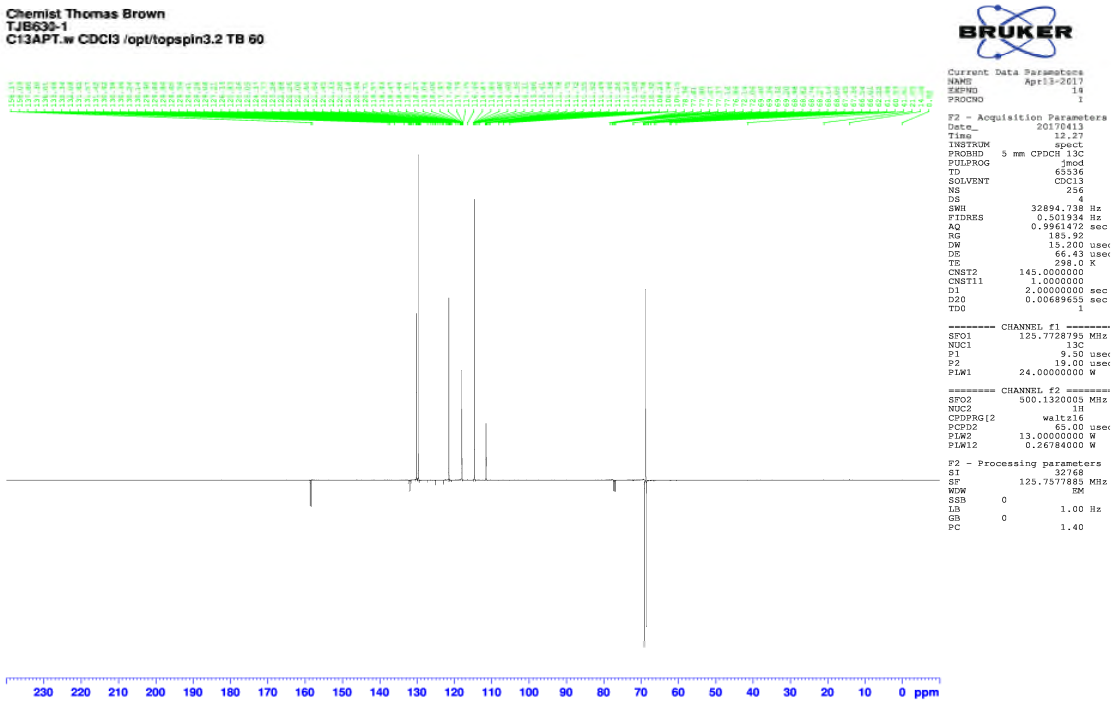
1-((3-Trifluoromethyl)phenoxy)-3-phenoxypropan-2-ol 28.



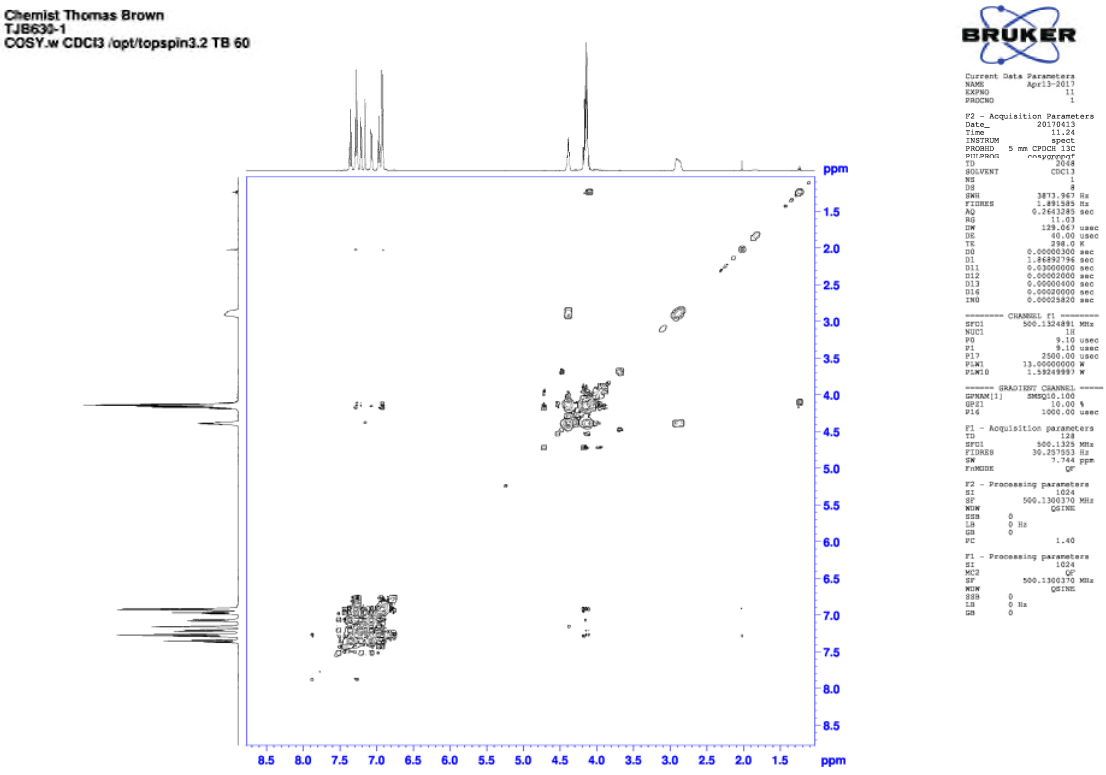
^{1}H NMR (500 MHz, $CDCl_3$)



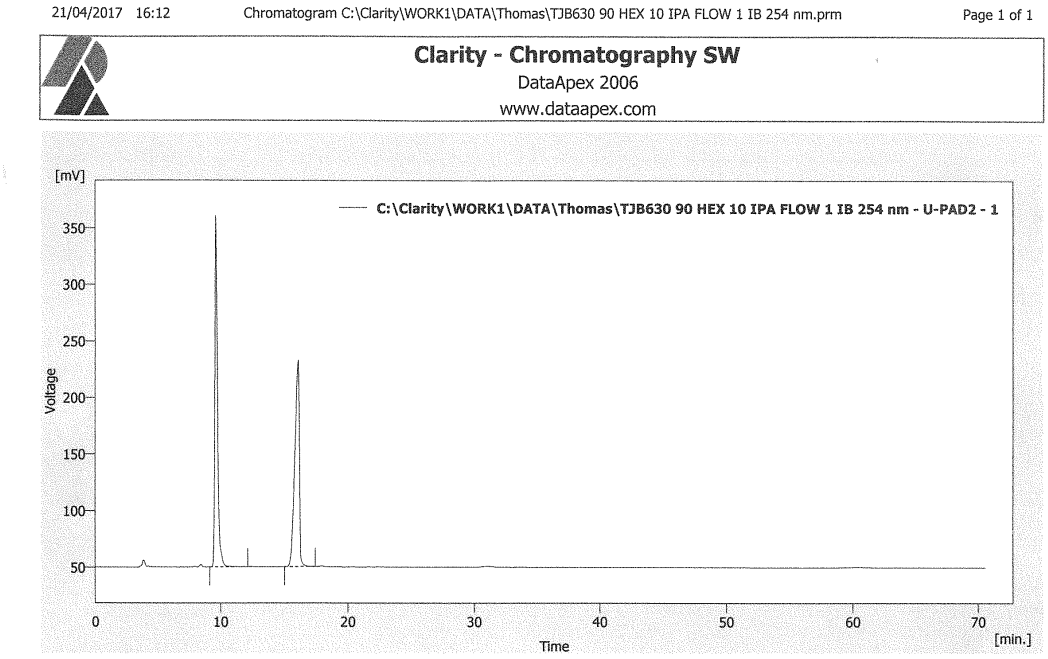
^{13}C NMR (125 MHz, $CDCl_3$)



COSY (500 MHz, $CDCl_3$)



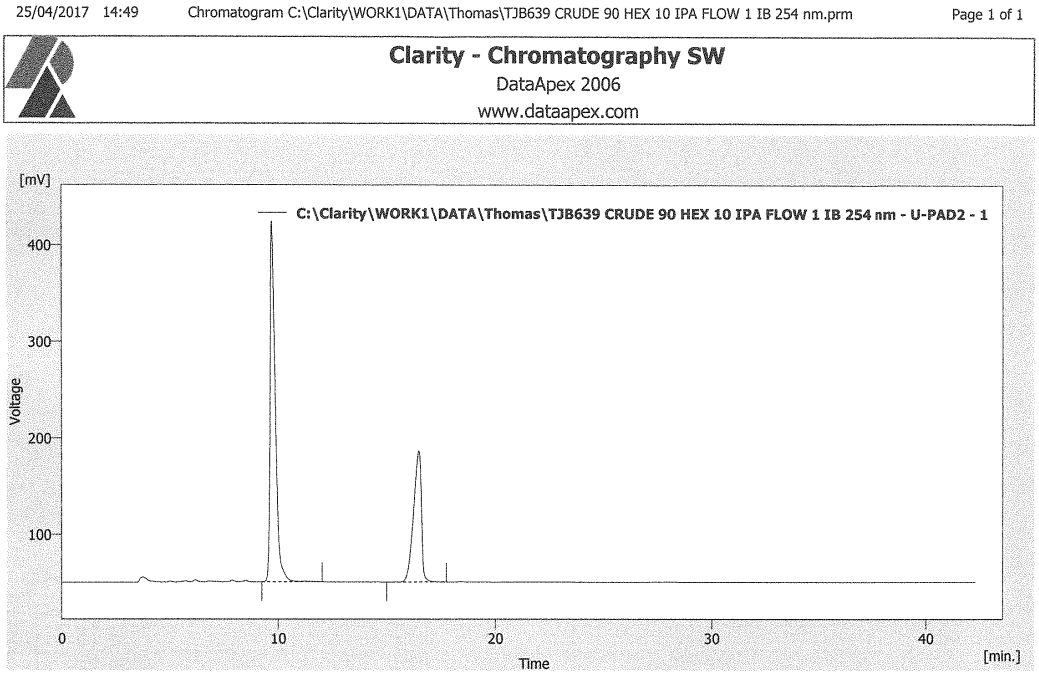
HPLC Racemic



Result Table (Uncal - C:|Clarity|WORK1|DATA|Thomas|TJB630 90 HEX 10 IPA FLOW 1 IB 254 nm - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	9.624	4570.341	310.605	50.0	63.0	0.22	
2	16.096	4568.289	182.605	50.0	37.0	0.39	
	Total	9138.630	493.210	100.0	100.0		

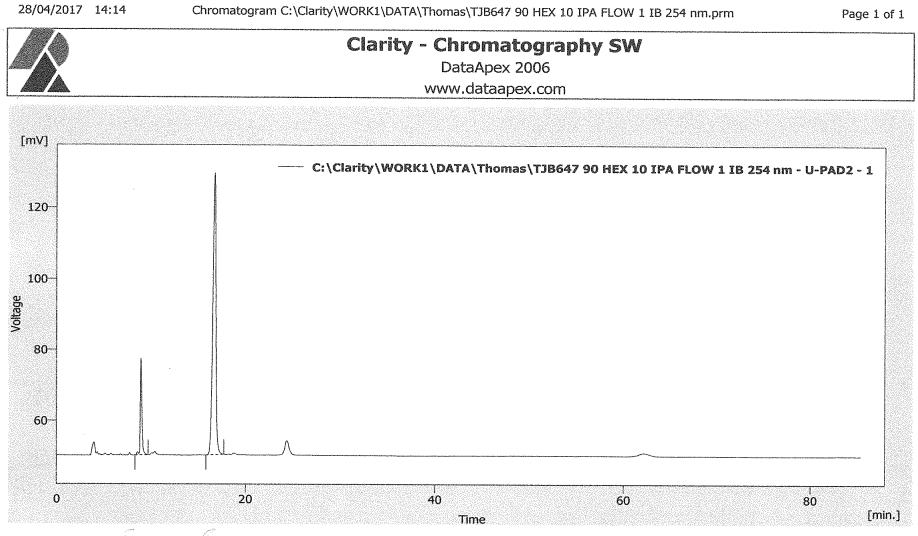
HPLC After ATH



Result Table (Uncal - C:|Clarity|WORK1|DATA|Thomas|TJB639 CRUDE 90 HEX 10 IPA FLOW 1 IB 254 nm - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	9.704	6147.101	373.987	64.1	73.3	0.24	
2	16.456	3448.233	136.212	35.9	26.7	0.40	
	Total	9595.334	510.199	100.0	100.0		

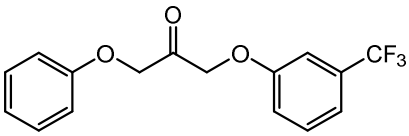
HPLC asymmetric standard.



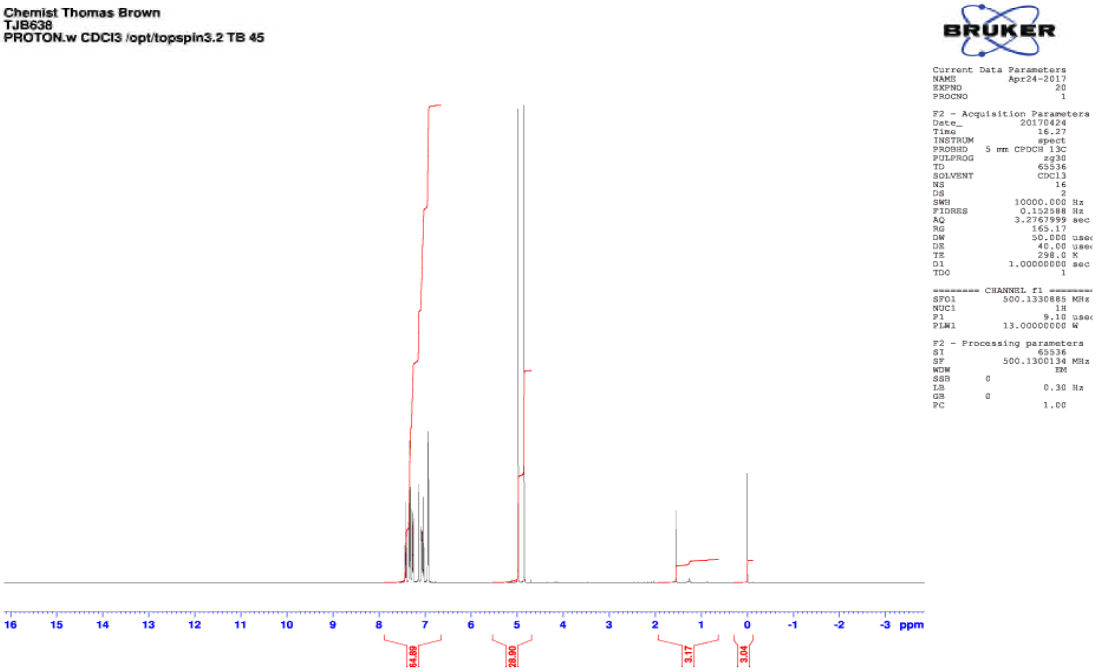
Result Table (Uncal - C:|Clarity|WORK1|DATA|Thomas|TJB647 90 HEX 10 IPA FLOW 1 IB 254 nm - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	8.984	317.816	27.216	14.9	25.6	0.16	
2	16.760	1817.317	79.197	85.1	74.4	0.35	
	Total	2135.133	106.414	100.0	100.0		

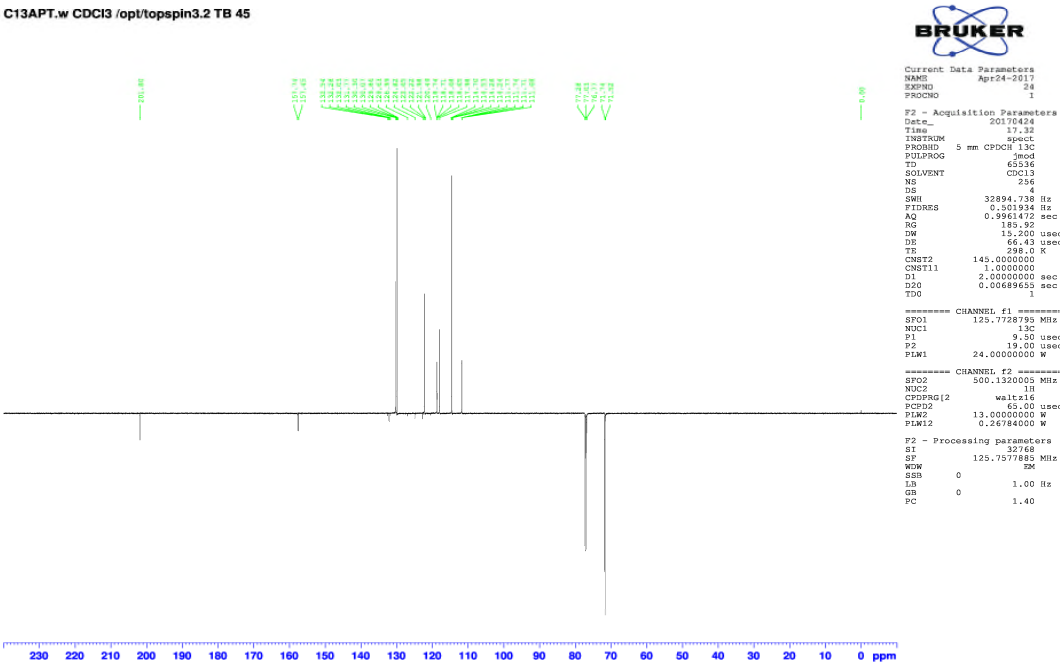
1-((3-Trifluoromethyl)phenoxy)-3-phenoxypropan-2-one.



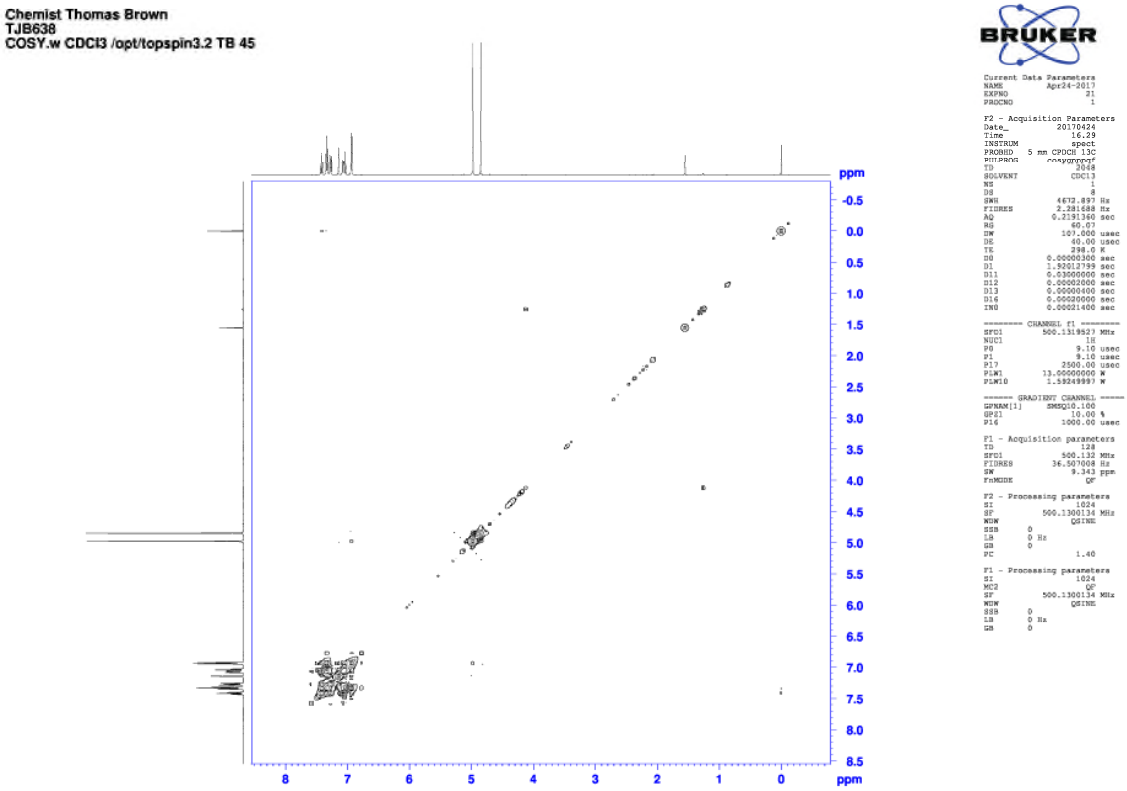
^{1}H NMR (500 MHz, $CDCl_3$)



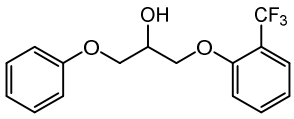
^{13}C NMR (125 MHz, $CDCl_3$)



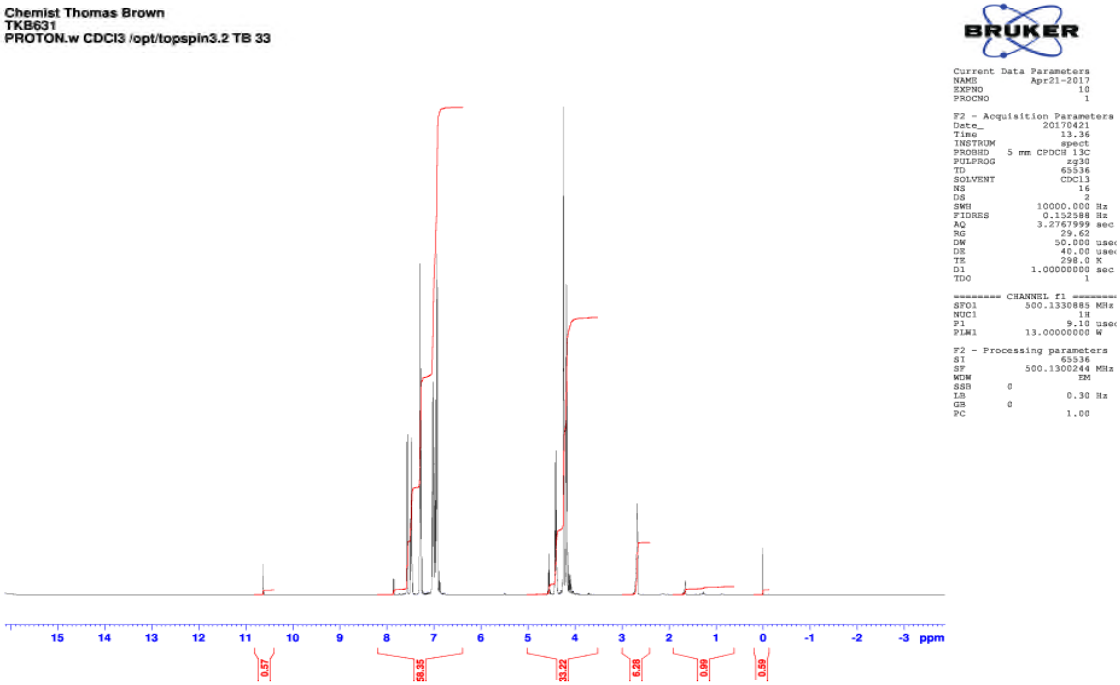
COSY (500 MHz, $CDCl_3$)



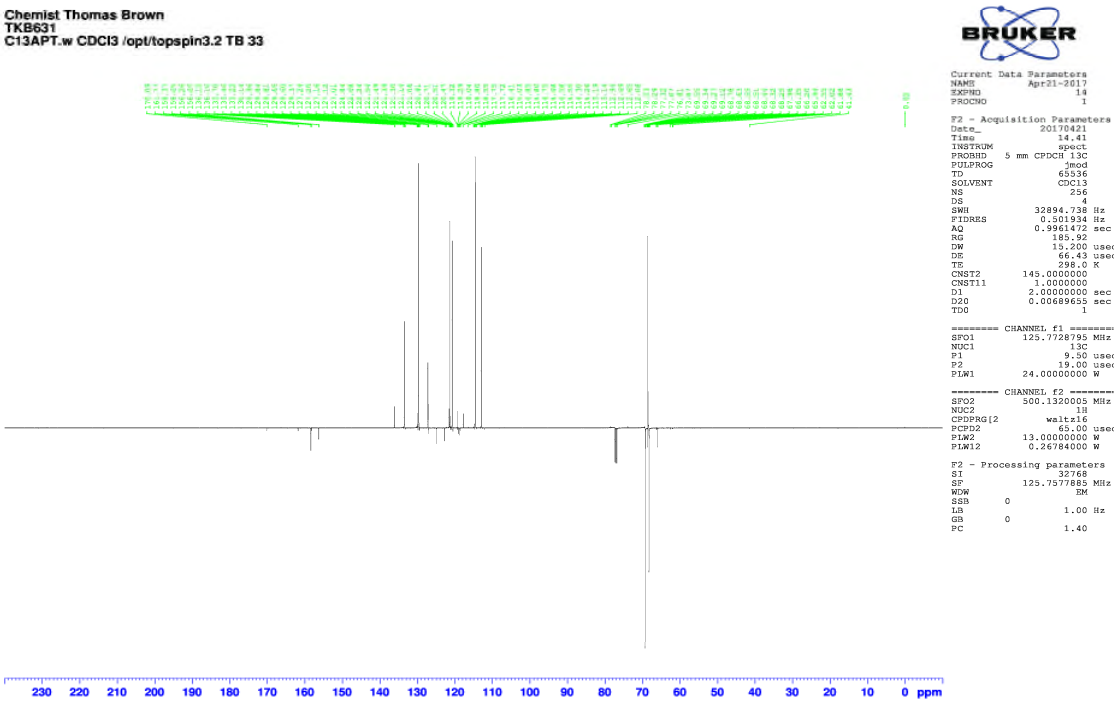
(*R*)-1-((2-Trifluoromethyl)phenoxy)-3-phenoxypropan-2-ol 29.



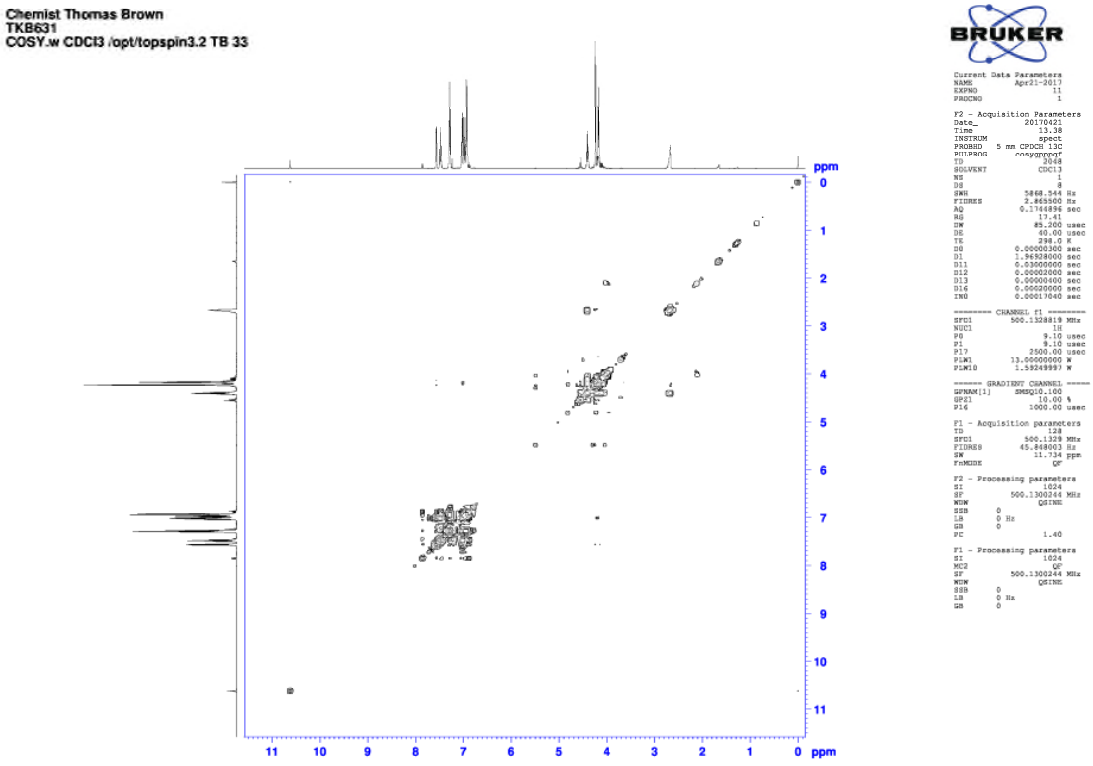
^{1}H NMR (500 MHz, $CDCl_3$)



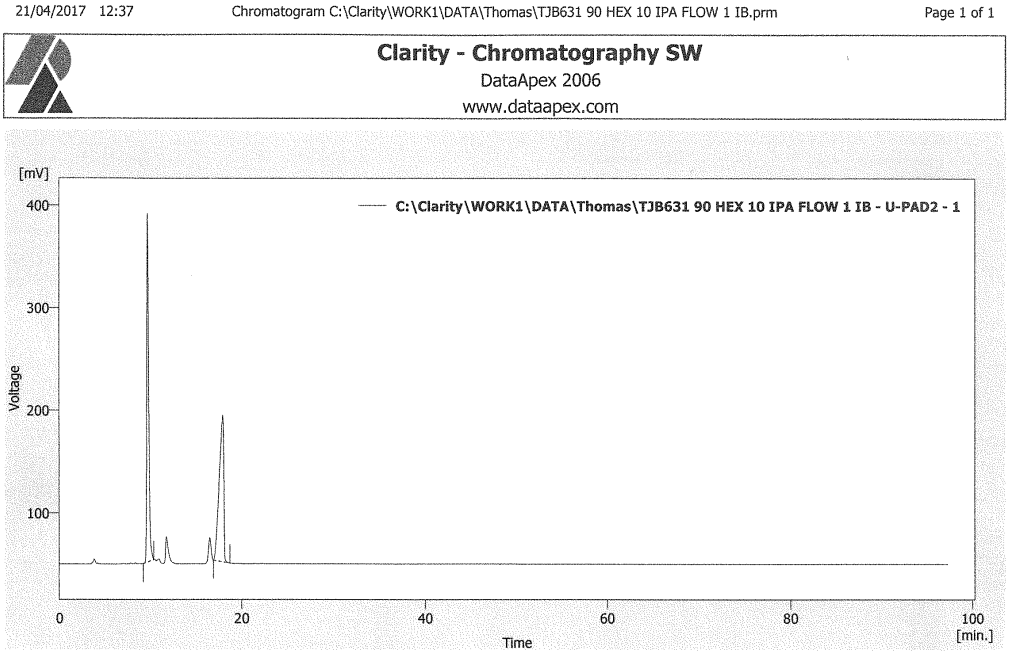
^{13}C NMR (125 MHz, $CDCl_3$)



COSY (500 MHz, $CDCl_3$)



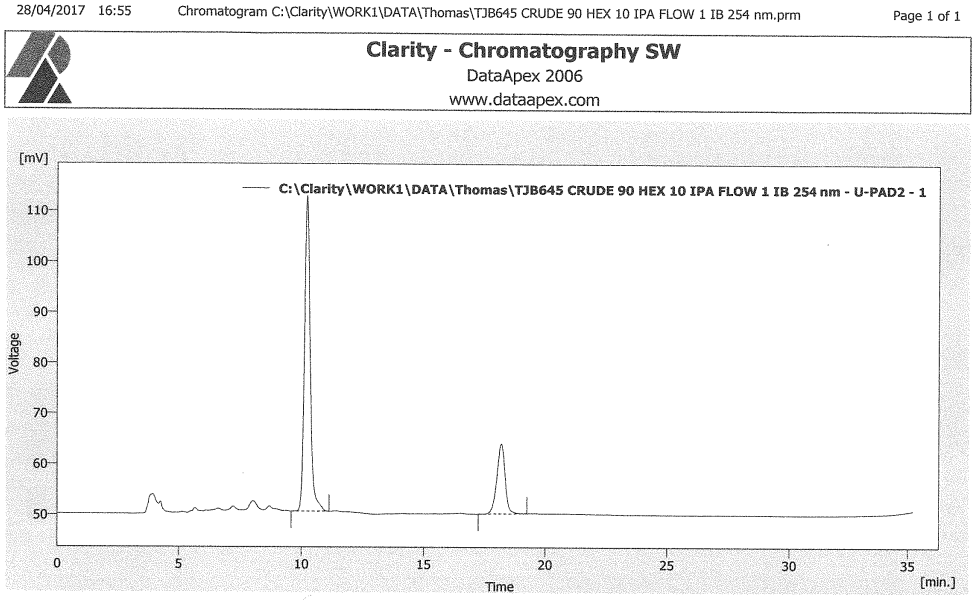
HPLC Racemic



Result Table (Uncal - C:\|Clarity\|WORK1\|DATA\|Thomas\|TJB631 90 HEX 10 IPA FLOW 1 IB - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	9.772	4930.967	340.012	49.8	70.4	0.22	
2	17.992	4970.418	142.830	50.2	29.6	0.57	
	Total	9901.385	482.842	100.0	100.0		

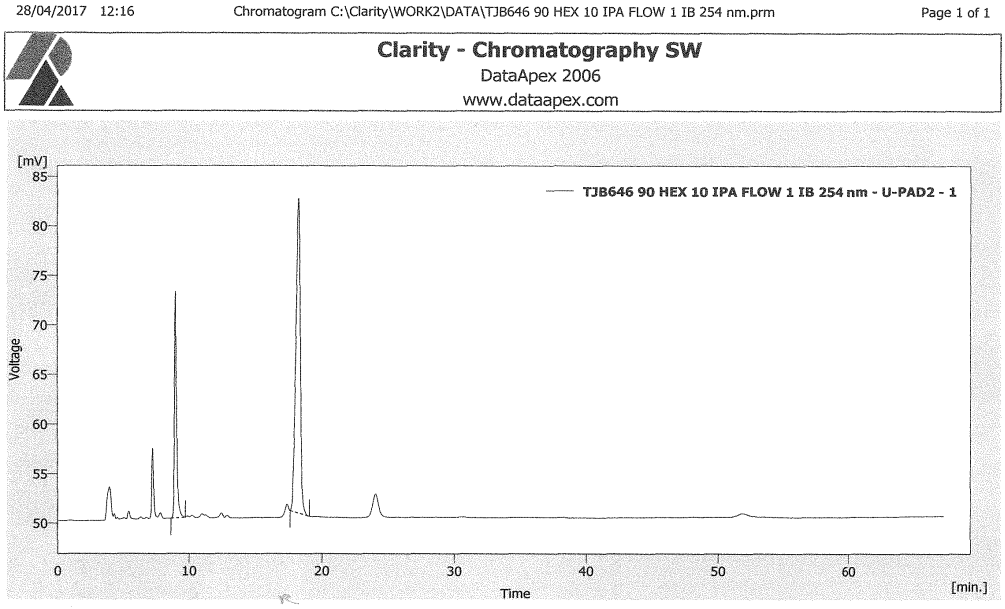
HPLC After ATH



Result Table (Uncal - C:\Clarity\WORK1\DATA\Thomas\TJB645 CRUDE 90 HEX 10 IPA FLOW 1 IB 254 nm - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	10.212	1022.875	62.364	75.7	81.9	0.25	
2	18.196	328.303	13.818	24.3	18.1	0.36	
	Total	1351.178	76.181	100.0	100.0		

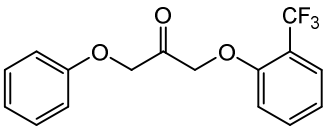
HPLC asymmetric standard.



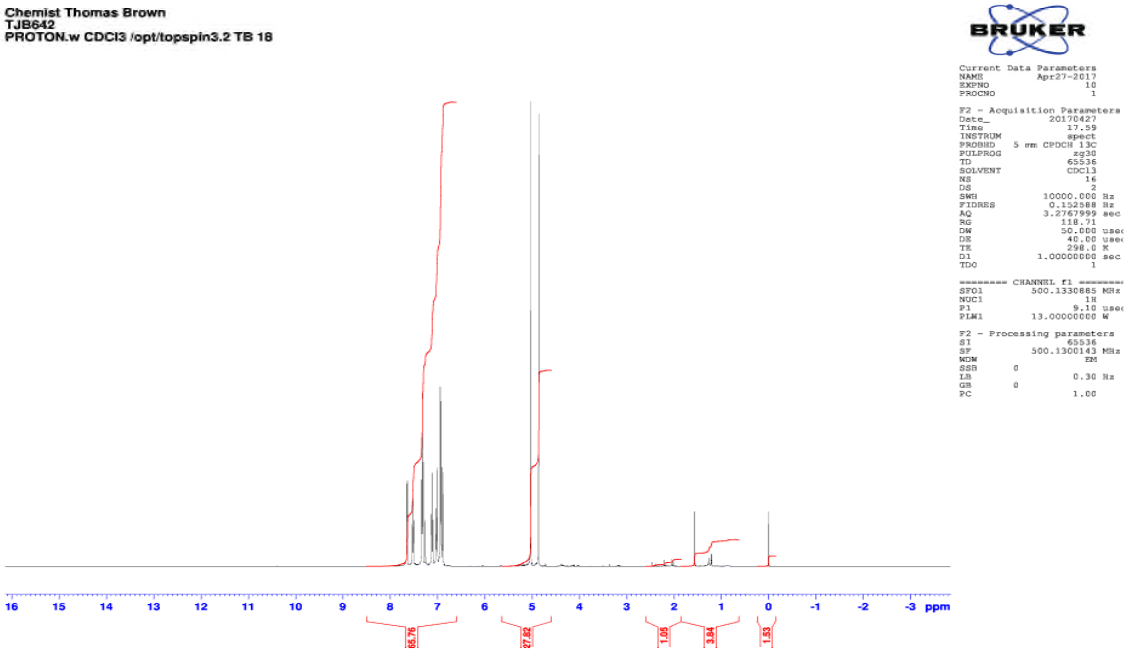
Result Table (Uncal - TJB646 90 HEX 10 IPA FLOW 1 IB 254 nm - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	8.968	257.354	22.866	25.6	41.8	0.16	
2	18.232	748.800	31.799	74.4	58.2	0.37	
	Total	1006.153	54.665	100.0	100.0		

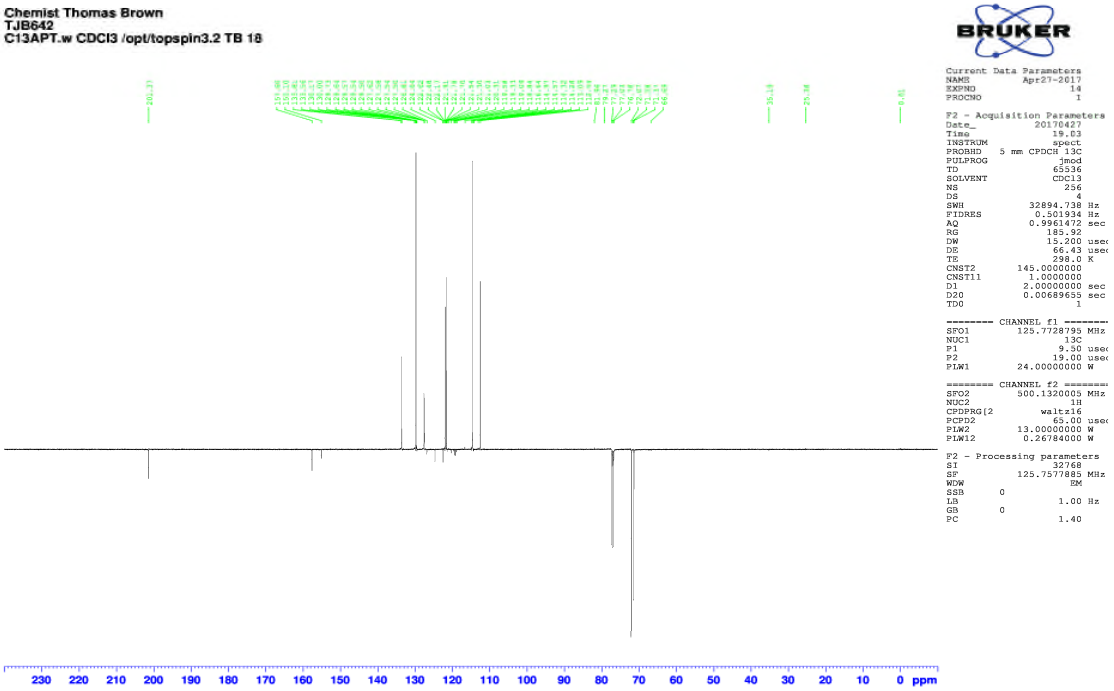
1-((2-Trifluoromethyl)phenoxy)-3-phenoxypropan-2-one.



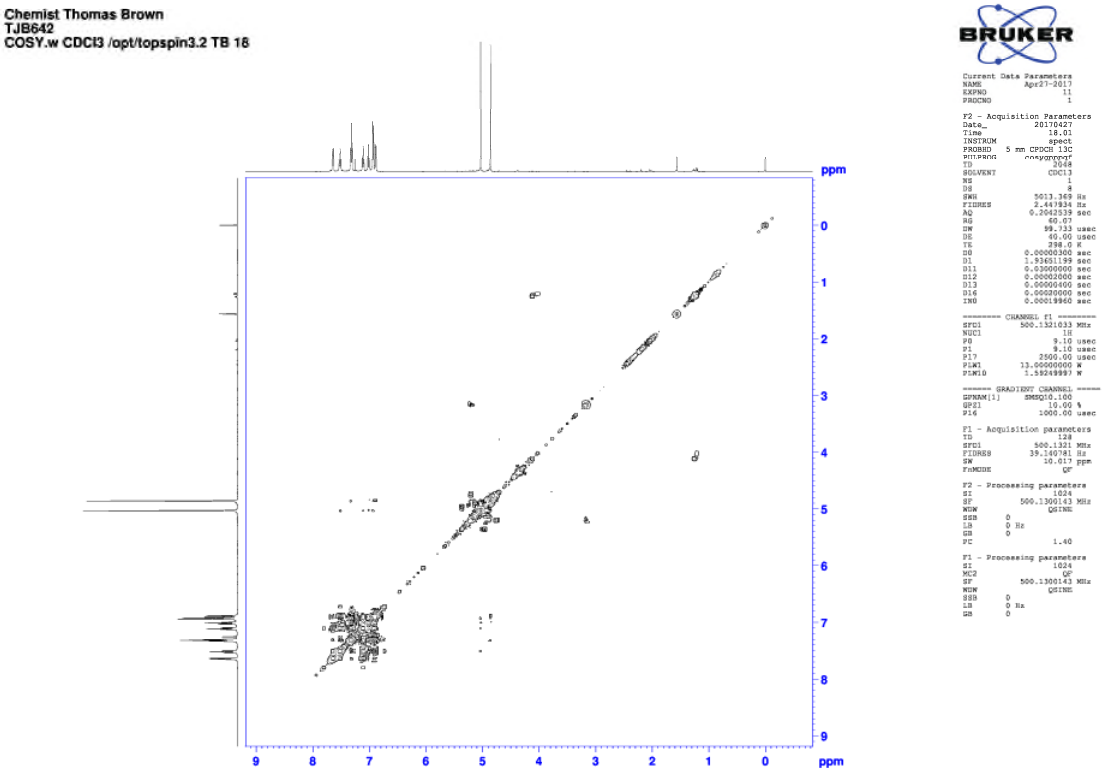
^{1}H NMR (500 MHz, $CDCl_3$)



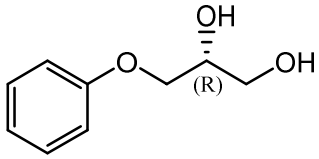
^{13}C NMR (125 MHz, $CDCl_3$)



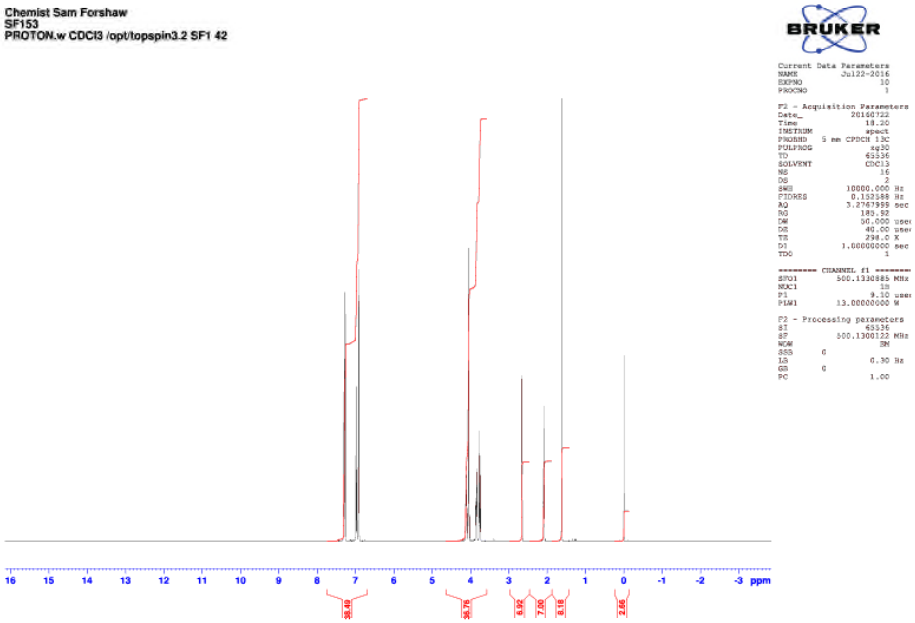
COSY (500 MHz, $CDCl_3$)



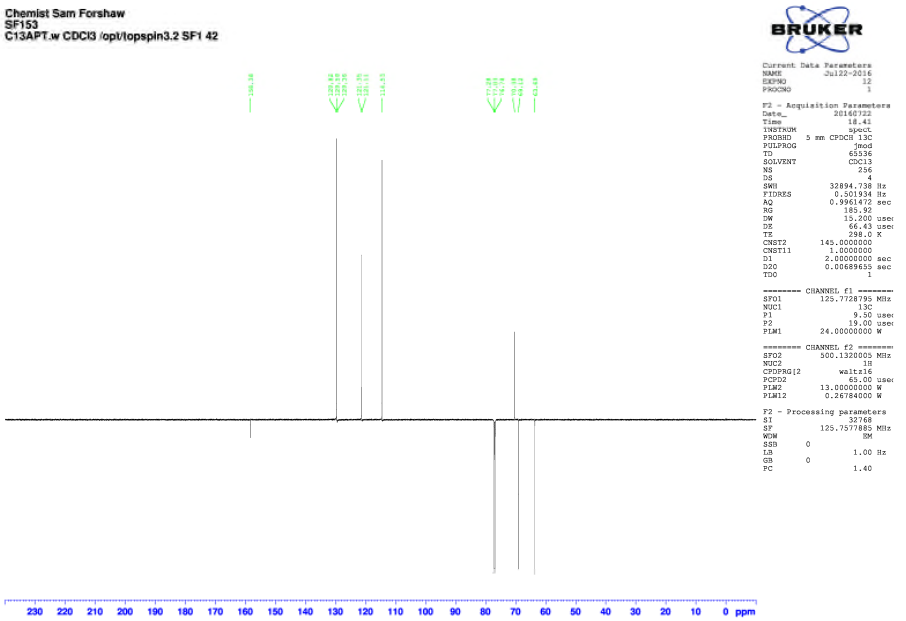
(*R*)-3-Phenoxypropane-1,2-diol.



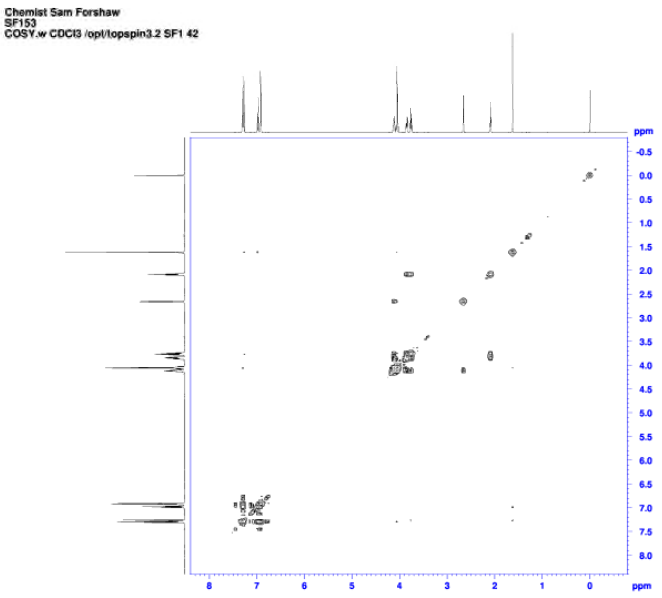
^{1}H NMR (500 MHz, $CDCl_3$)

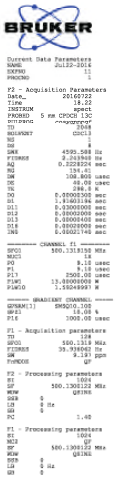


^{13}C NMR (125 MHz, $CDCl_3$)

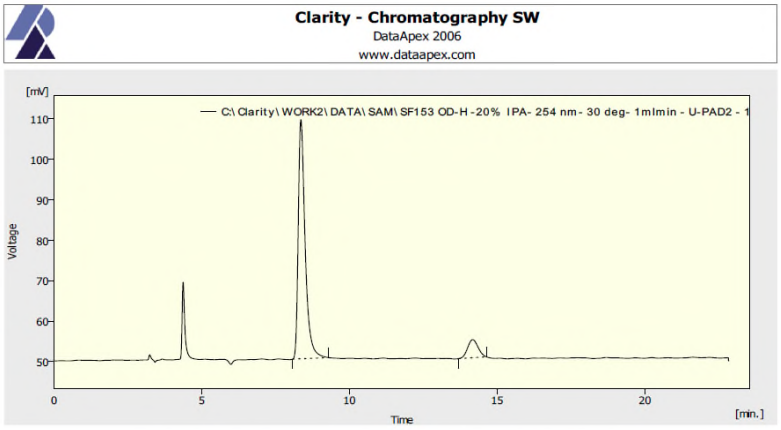


COSY (500 MHz, $CDCl_3$)





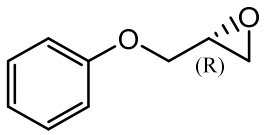
HPLC



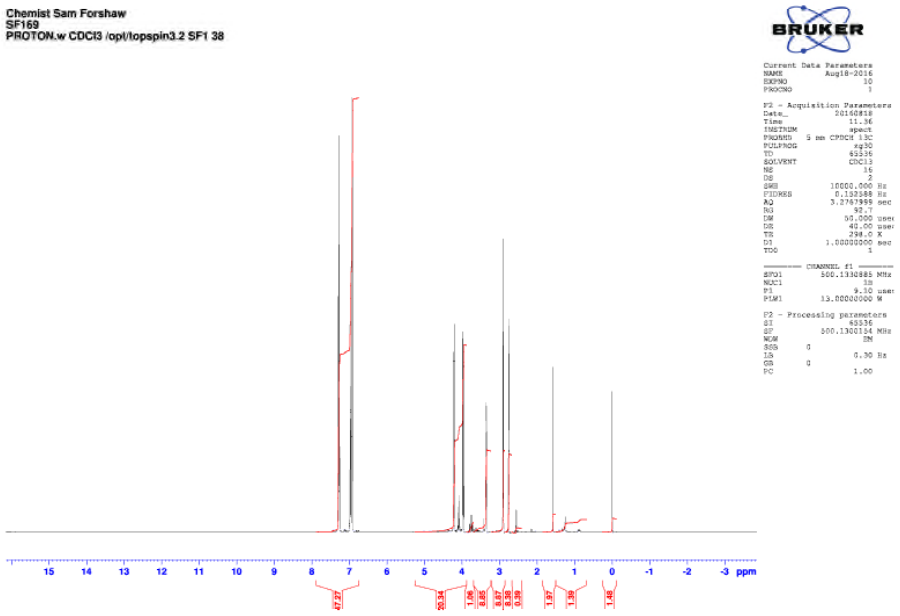
Result Table (Uncal - C:\Clarity\WORK2\DATA\SAM\SF153 OD-H -20% IPA- 254 nm- 30 deg- 1mlmin - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	8.356	956.601	59.105	89.7	93.0	0.24	
2	14.168	109.568	4.477	10.3	7.0	0.40	
	Total	1066.169	63.582	100.0	100.0		

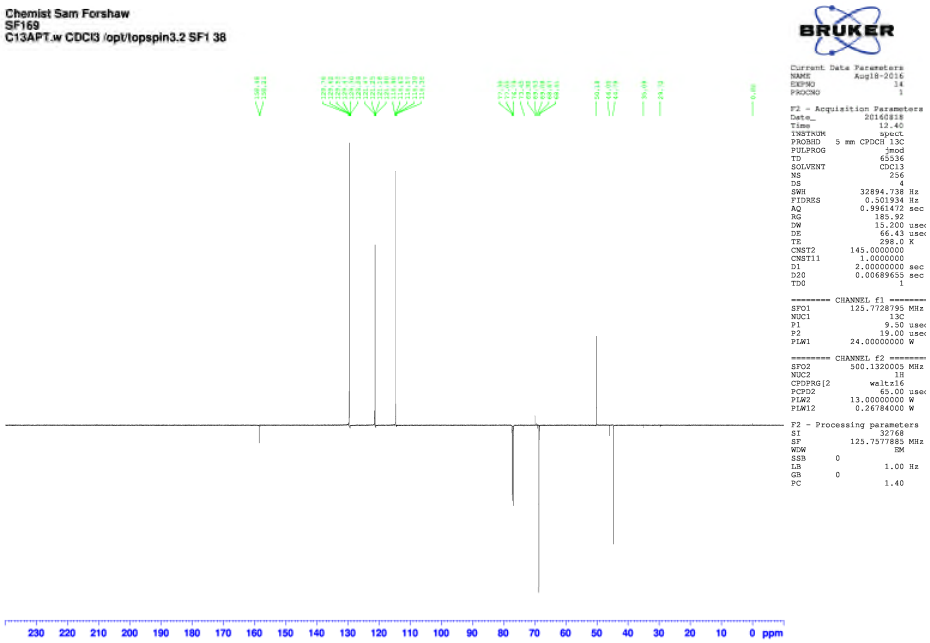
(*R*)-2-(phenoxymethyl)oxirane.



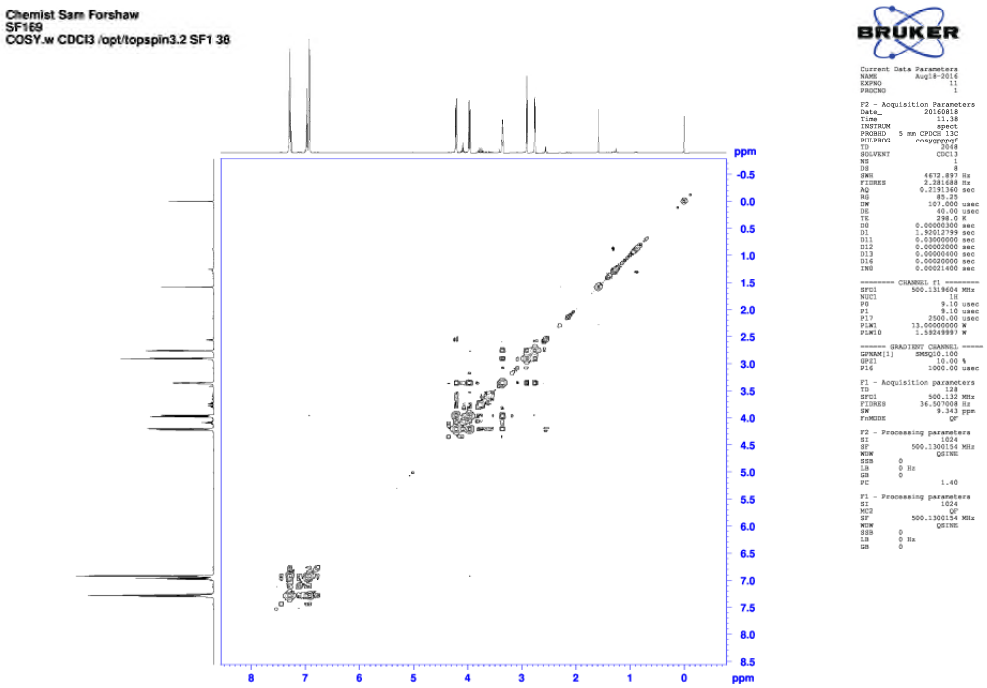
^{1}H NMR (500 MHz, $CDCl_3$)



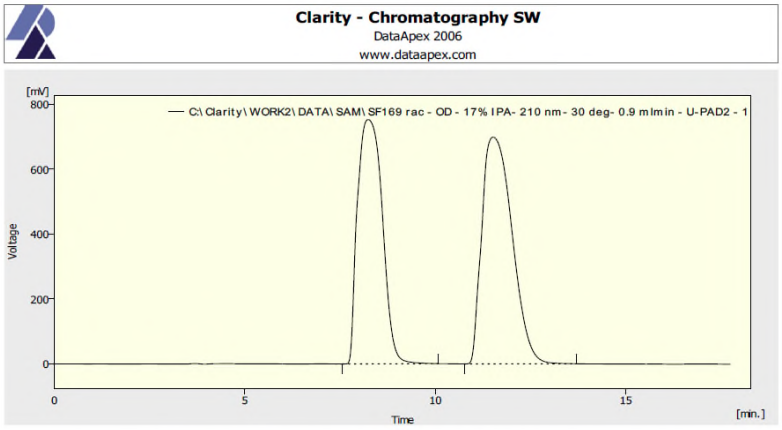
^{13}C NMR (125 MHz, $CDCl_3$)



COSY(500 MHz, $CDCl_3$)



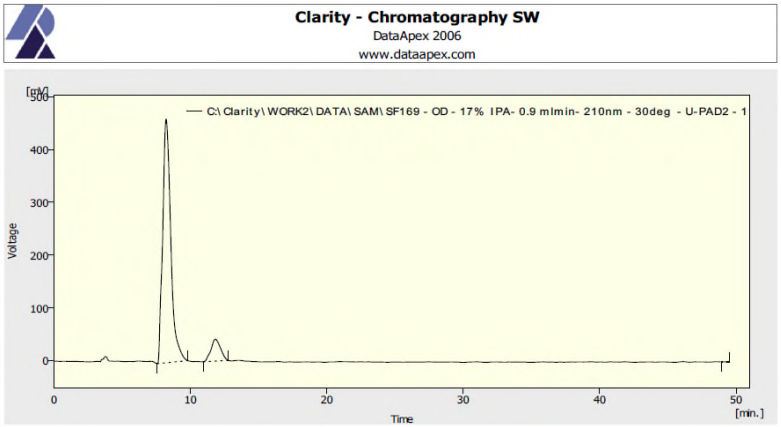
HPLC Racemic



Result Table (Uncal - C:\Clarity\WORK2\DATA\SAM\SF169 rac - OD - 17%IPA- 210 nm- 30 deg- 0.9 mlmin - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	8.228	34076.902	753.341	46.9	51.9	0.76	
2	11.520	38564.229	699.201	53.1	48.1	0.89	
	Total	72641.131	1452.542	100.0	100.0		

HPLC Asymmetric



Result Table (Uncal - C:\Clarity\WORK2\DATA\SAM\SF169 - OD - 17% IPA- 0.9 mlmin- 210nm - 30deg - U-PAD2 - 1)

	Reten. Time [min]	Area [mV.s]	Height [mV]	Area [%]	Height [%]	W05 [min]	Compound Name
1	8.220	19129.843	461.356	90.4	91.7	0.61	
2	11.828	2031.819	41.529	9.6	8.3	0.78	
3	49.224	5.341	0.278	0.0	0.1	0.33	
	Total	21167.002	503.162	100.0	100.0		