Supporting Information

Synergistic Dual Activation Catalysis by Palladium Nanoparticles for Epoxide Ring Opening with Phenols

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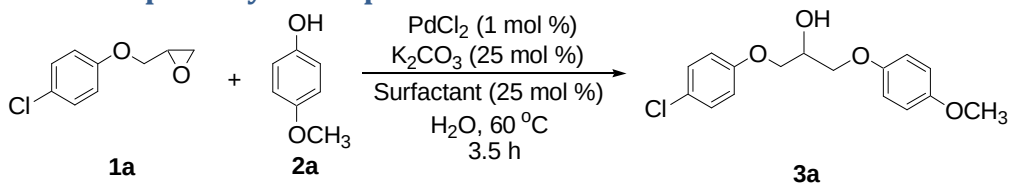
Table of Contents

Table A. The effect of various surfactants as stabilizer of the in situ formed Pd nanoparticles for phenolysis of epoxide.[a]

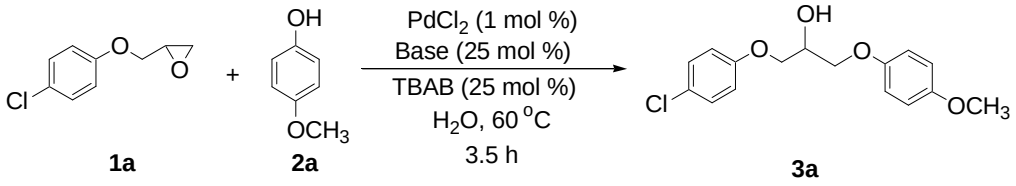


1a **2a** **3a**

Entry	Surfactant	Yield (%)[b]
1	None	0
2	SDS	0
3	SDOSS	0
4	TBAF	51
5	TBAF	0[c]
6	TBACl	55
7	TBAB	74
8	TBAI	62
9	CTAB	53
10	TMAOH	31
11	TMAOH	36[d]
12	Triton X 100	27
13	Tween 40	16
14	Span 80	0
15	PEG 400	29
16	PEG 600	31
17	PEG 1000	22
18	PEG 2000	12
19	PEG 4600	15
20	PEG 8000	17
21	PEG 10000	23

[a]The epoxide (2 mmol) was treated with the phenol (2 mmol, 1 equiv) in the presence of $PdCl_2$ (1 mol%), K_2CO_3 (25 mol%), and the surfactant (25 mol%) in water (8 mL). [b]The isolated yield of **3a**. [c]KF (25 mol%) was used instead of K_2CO_3. [d]TMAOH (50 mol%) was used instead of K_2CO_3.

Table B. The effect of the base on the phenolysis of epoxide catalysed by the in situ formed Pd nanoparticles.[a]



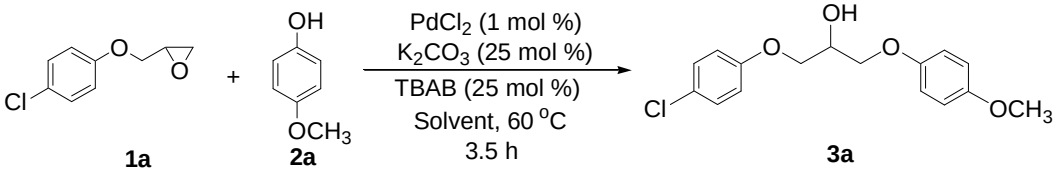
1a **2a** **3a**

Entry	Base	Yield (%)[b]
1	Li_2CO_3	63
2	Na_2CO_3	64
3	K_2CO_3	74
4	Cs_2CO_3	70
5	KOH	59

6	LiOH	56
7	$KHCO_3$	57
8	KBr	41
9	KI	38

[a]The epoxide (2 mmol) was treated with the phenol (2 mmol, 1 equiv) in the presence of $PdCl_2$ (1 mol%), base (25 mol%), and TBAB (25 mol%) in water (8 mL). [b]The isolated yield of **3a**.

Table C. The effect of the solvent on the phenolysis of epoxide catalysed by the in situ formed Pd nanoparticles.[a]

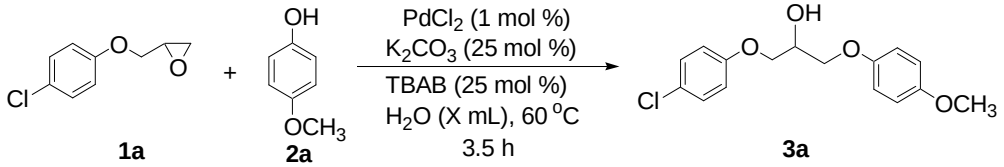


1a **2a** **3a**

Entry	Solvent	Yield (%)[b]
1	Hexane	0
2	Toluene	0
3	THF	0
4	Dioxane	0
5	CH_3CN	0
6	DCE	0
7	Nitromethane	0
8	PEG 400	22
9	PEG 400	25[c]
10	H_2O	74

[a]The epoxide (2 mmol) was treated with the phenol (2 mmol, 1 equiv) in the presence of $PdCl_2$ (1 mol%), K_2CO_3 (25 mol%), and TBAB (25 mol%) in 8 mL of solvents. [b]The isolated yield of **3a**. [c]No TBAB was used.

Table D. The effect of the amount of water on the phenolysis of epoxide catalysed by the in situ formed Pd nanoparticles.[a]



1a **2a** **3a**

Entry	X	Yield (%)[b]
1	None	27
2	2	63
3	4	74
4	6	73
5	8	77

6	10	73

[a]The epoxide (1 mmol) was treated with the phenol (1 mmol, 1 equiv) in the presence of $PdCl_2$ (1 mol%), K_2CO_3 (25 mol%), and TBAB (25 mol%) in varying amount of water. [b]The isolated yield of **3a**.

Figure 1. The UV absorption of the mixture of $PdCl_2$ (1 mol %), K_2CO_3 (25 mol %) and TBAB (25 mol %) in water (4 mL).

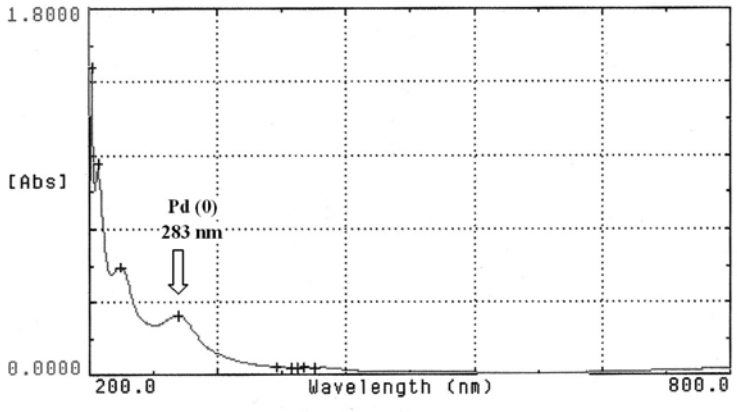


Figure 2. (A) TEM image of Pd Nanoparticles in the reaction mixture of $PdCl_2$ (1 mol %), K_2CO_3 (25 mol %) and TBAB (25 mol %) in water (4 mL), (B) Image of single particles, (C) HRTEM image of a single particle, (D) FFT view of area of C.

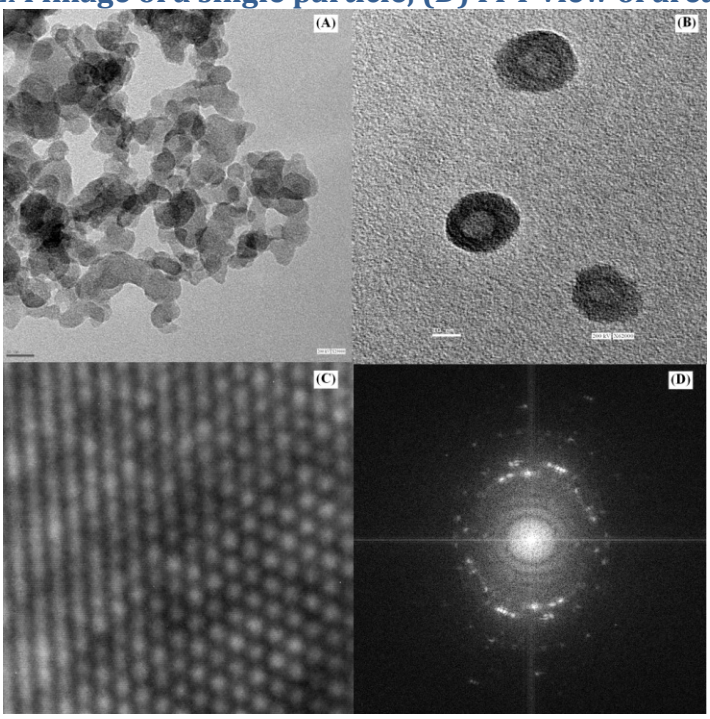
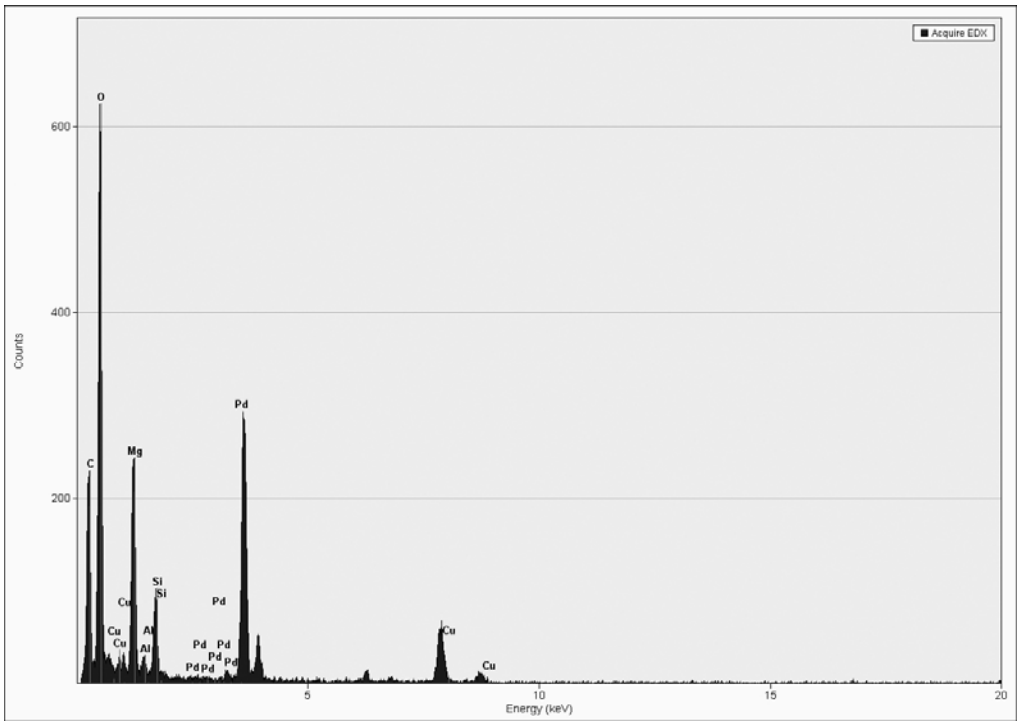


Figure 3. Energy dispersive X-ray spectra of Pd nanoparticles on Cu grid.



Discussion on the Mechanism and Experimental Evidences:

Synergistic Dual Activation Catalysis and the Role of Water:

The assistance by water in promoting the reaction is substantiated by the distinct advantage in using water as the reaction medium compared to the organic solvents based on the results under table C. The proposed 'dual activation' role of water through the hydrogen-bonded structure is based on literature reports on understanding the role of water in promoting organic reactions.

The rate enhancement of organic reaction in water has been of contemporary interest. Various factors such as enforced hydrophobic interactions, high cohesive energy density of water and hydrogen bonding (HB) effect have been invoked [S. Mellouli, L. Bousekkine, A. B. Theberge and W. T. S. Huck, *Angew. Chem. Int. Ed.*, 2012, **51**, 7981] and the HB effect appears to have gained popularity [Jung, Y. and R. A. Marcus, *J. Am. Chem. Soc.*, 2007, **129**, 5492; Y. Zheng and J. Zhang, *ChemPhysChem*, 2010, **11**, 65].

The reported works [Jung, Y. and R. A. Marcus, *J. Am. Chem. Soc.*, 2007, **129**, 5492; Y. Zheng and J. Zhang, *ChemPhysChem*, 2010, **11**, 65; E. Vohringer-Martinez, B. Hansmann, H. Hernandez, J. S. Francisco, J. Troe and B. Abel, *Science*, 2007, **315**, 497; I. Viotijevic and T. F. Jamison, *Science*, 2007, **317**, 1189] depicted hydrogen-bonded species during water-catalysis. Specifically the following articles are related to epoxide ring opening reactions in water [D. N. Kommi, D. Kumar, K. Seth and A. K. Chakraborti, *Org. Lett.*, 2013, **15**, 1158; D. N. Kommi, D. Kumar and A. K. Chakraborti, *Green Chem.*, 2013, **15**, 756; Y. Zheng and J. Zhang, *ChemPhysChem* 2010, *11*, 65. I. Viotijevic and T. F. Jamison, *Science*, 2007, **317**, 1189].

The HB-assisted dual activation role of water has also been invoked for other organic reactions [D. N. Kommi, P. S. Jadhavar, D. Kumar and A. K. Chakraborti, *Green Chem.*, 2013, **15**, 798; D. N. Kommi, D. Kumar, R. Bansal, R. Chebolu and A. K. Chakraborti, *Green Chem.*, 2012, **14**, 3329; S. V. Chankeshwara and A. K. Chakraborti, *Org. Lett.*, 2006, **8**, 3259; G. L. Khatik, R. Kumar and A. K. Chakraborti, *Org. Lett.*, 2006, **8**, 2433; A. K. Chakraborti, S. Rudrawar, K. B. Jadhav, G. Kaur and S. V. Chankeshwara, *Green Chem.*, 2007, **9**, 1335].

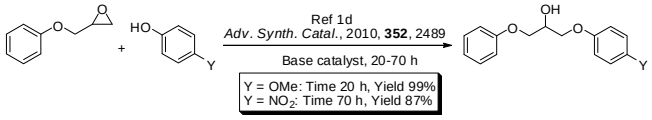
The proposed interaction of the Pd and the aromatic ring has been invoked based on the existing literature reports on cation-π interaction [A. Kumar, S. Mandal, S. P. Mathew, P. R. Selvakannan, A. B. Mandale, R. V. Chaudhari and M. Sastry, *Langmuir*, 2002, **18**, 6478 and the references cited therein] except the fact that in the present case it would involve anion- π interaction [as the metal centre after coordinating with the epoxide oxygen lone pair of electrons mimics the 'Pd-ate' species]

Role of Hydrogen Bond *vs* p*K*a of the Phenol on the Mechanistic Course of the Reaction:

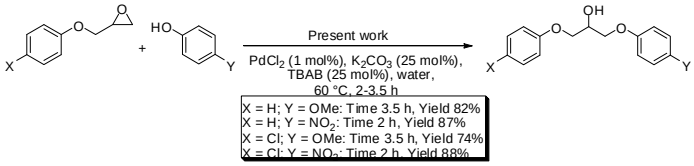
It might be thought that the reaction can be pKa driven. However, the results of entries 4, 6, and 14 (table 1) suggest that the efficiency of the reaction is not dependent upon the generation of the phenolate anion (although 1 equiv of K_2CO_3 has been used) (and hence not pKa driven). Had it been the case that the reaction is influenced by the pKa values then

certainly the phenol (bearing electron withdrawing substituent) with lower pKa would first undergo reaction with the base to form the corresponding phenolate as the effective nucleophile. However, in such cases the phenol bearing electron withdroawing substituent would be less reactive as the corresponding phenolate anion is less nucleophilic. This is amply reflected by literatrue reports wherein the reaction got to be pKa driven. Perhaps it is due to the inability of the 4-nitrophenolate anion to undergo epoxide ring opening reaction that the literature reports [1 (a) B. Das, M. Krishnaiah, P. Thirupathi and K. Laxminarayana, *Tetrahedron Lett.*, 2007, **48**, 4263; 1 (c) K. Surendra, N. S. Krishnaveni, Y. V. D. Nageswar and K. Rama Rao, *J. Org. Chem.*, 2003, **68**, 4994] do not have the example of 4-nitrophenol (or other electron deficient phenol) for epoxide phenolysis.

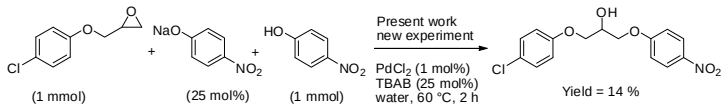
In the recent report on base-catalysed reaction for phenolysis of epoxide [1 (d) A. Zvagulis, S. Bonollo, D. Lanari, F. Pizzo and L. Vaccaro, *Adv. Synth. Catal.*, 2010, **352**, 2489] phenol with electron withdrawing substituent requires much longer time and afforded lesser yield than phenol bearing electron releasing group (pl see the following examples).



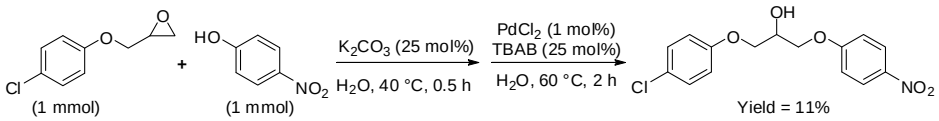
On the contrary, in the present work the epoxide phenolysis with phenol bearing electron withdrawing susbtitutent takes shorter reaction time and provide better yield than that of the phenol with electron donating group (exemplified in the following examples).



Under the present study there appears to be little scope for formation of the phenolate anion as the primary role of the base (K_2CO_3) used in catalytic amount (25 mol%) is as the reductant [B. G. Ershov, E. Janata, M. Michaelis and A. Henglein, *J. Phys. Chem.*, 1991, **95**, 8996; R. E. Huie, C. L. Clifton and P. Neta, *Radiat. Phys. Chem.*, 1991, **38**, 477] to form the Pd nanoparticle (PdNP) by reduction of the pre-catalyst $PdCl_2/Pd(OAc)_2$ and is expected to be consumed before the phenols is added to the reaction mixture. Once the base is consumed to form the phenolate anion there would be no scope for formation of the PdNP and hence no effective epoxide phenolysis should take place. To prove this, the epoxide phenolysis of 4-chlorophenyl glycidyl ether **1a** with 4-nitrophenol was performed in the presence of sodium salt of 4-nitrophenol (25 mol%) instead of (K_2CO_3) that resulted in 14% yield (the unreacted starting epoxide remained intact and was recovered) of the desired product.

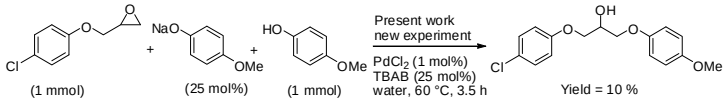


Further, in a separate experiment the epoxide phenolysis of 4-chlorophenyl glycidyl ether **1a** with 4-nitrophenol was performed by addition of K_2CO_3 (25 mol%) to the equimolar mixture of 4-chlorophenyl glycidyl ether **1a** and 4-nitrophenol in water at 40 °C followed by (after 30 min) the addition of $PdCl_2$ (1 mol%) and TBAB (25 mol%) at 60 °C that resulted 11% yield of the desired product after 2 h.

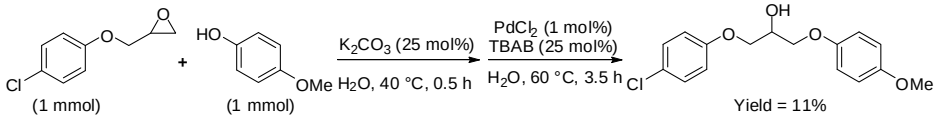


Similarly the following experiments were performed for the reaction of 4-chlorophenyl glycidyl ether **1a** and 4-methoxyphenol:

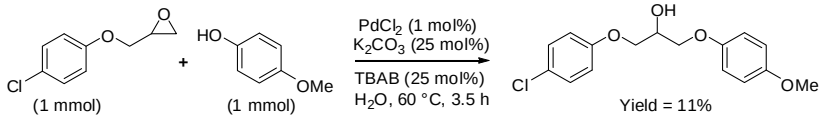
The epoxide phenolysis of 4-chlorophenyl glycidyl ether **1a** with 4-methoxyphenol was performed in the presence of sodium salt of 4-methoxyphenol (25 mol%) instead of (K_2CO_3) that resulted in 10% yield (the unreacted starting epoxide remained intact and was recovered) of the desired product.



Further, in a separate experiment K_2CO_3 (25 mol%) was added to the equimolar mixture of 4-chlorophenyl glycidyl ether **1a** and 4-methoxyphenol in water at 40 °C followed by (after 30 min) the addition of $PdCl_2$ (1 mol%) and TBAB (25 mol%) at 60 °C that resulted 11% yield of the desired product after 3.5 h.



Mixing 4-chlorophenyl glycidyl ether **1a** (1 mmol), 4-methoxyphenol (1 mmol), K_2CO_3 (25 mol%), $PdCl_2$ (1 mol%), and TBAB (25 mol%) at a time and subjecting the reaction to proceed for 3. 5 h at 60 °C that resulted 11% yield of the desired product.



These clearly demonstrate that the outcome of the reaction under the present study is not driven by the pKa values of the phenol.

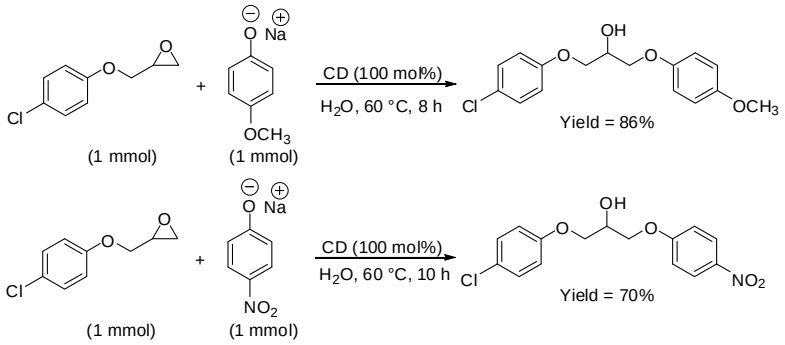
Evidences for the Role of Hydrogen Bond:

The involvement of the HB assisted assembly **I** for the 'synergistic dual activation catalysis' was demonstrated by the facts that when MeOH, EtOH, and $PhCH_2OH$ were separately used as the reactant instead of a phenol during the reaction of 4-chlorophenyl glycidyl ether **1a** follwoing the protocol of the present study no product arising out of epoxide ring opening by these alcoholic substrates was formed and the starting epoxide

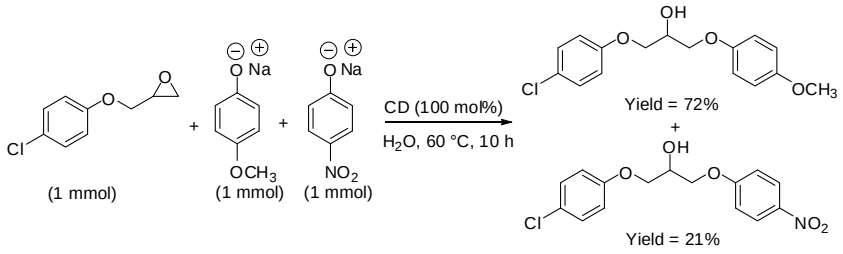
remained unchanged and was recovered. Due to the inferior HB donor ability of the alcohol compared to that of a phenol the corresponding hydrogen-bonded species **I** (Scheme 2) are not formed during the reaction with alcohols. To further demonstrate the role of HB involving the substrates, and the significance of the 'synergistic dual activation catalysis' the following intermolecular competition studies were performed involving an electron rich phenol and an electron deficient phenol.

Under the condition that is expected to have influence of the pKa values of the phenols and hence be driven by the nucleophilicity of the phenolate anion.

Thus, the following experiments were performed according to the reported procedure [1 (c) K. Surendra, N. S. Krishnaveni, Y. V. D. Nageswar and K. Rama Rao, *J. Org. Chem.*, 2003, **68**, 4994]:

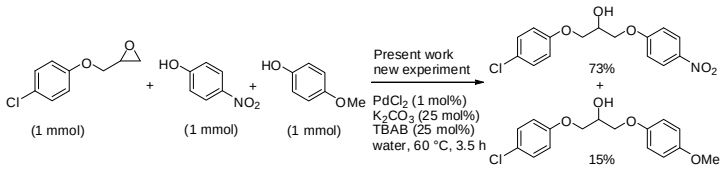


The longer reaction time and lesser yield obtained with the phenol containing the electron withdrawing substituent provides clear evidence that the p*K*a driven reaction will be dependent on the nucleophilicity of the phenolate anion. In competitive environment selectivity is in favour of the less acidic phenol as depicted below and this corresponds with the relative nucleophilicity.

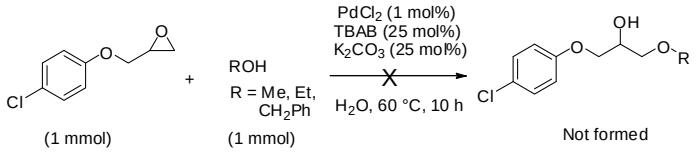


Under the condition of the present study:

During intermolecular competition between a phenol containing electron withdrawing group and a phenol having electron releasing group selective reaction takes place with the less nucleophilic phenol. Thus, 83:17 selectivity in favour of the product from the reaction of 4-chlorophenyl glycidyl ether **1a** with 4-nitrophenol during intermolecular competition involving 4-methoxyphenol provide the necessary evidence for HB bond formation as 4-nitrophenol is a better HB donor compared to 4-methoxyphenol.



The involvement of the HB assisted assembly **I** for the 'synergistic dual activation catalysis' was demonstrated by the facts that when MeOH, EtOH, and $PhCH_2OH$ were separately used as the reactant instead of a phenol during the reaction of 4-chlorophenyl glycidyl ether **1a** following the protocol of the present study no product arising out of epoxide ring opening by these alcoholic substrates was formed and the starting epoxide remained unchanged and was recovered. Due to the inferior HB donor ability of the alcohol compared to that of a phenol the corresponding hydrogen-bonded species **I** (Scheme 2) are not formed during the reaction with alcohols.



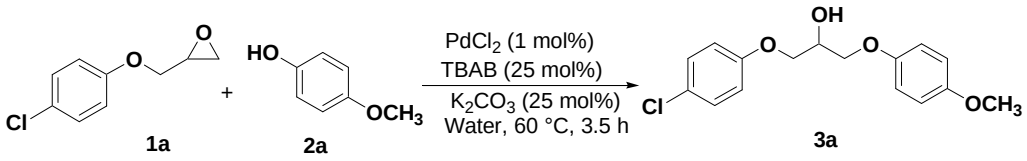
The role of HB involving the substrates, and the significance of the 'synergistic dual activation catalysis' is further justified by the 83:17 selectivity in favour of the product from the reaction of 4-chlorophenyl glycidyl ether **1a** with 4-nitrophenol during intermolecular competition involving 4-methoxyphenol provide the necessary evidence for HB bond formation as 4-nitrophenol is a better HB donor compared to 4-methoxyphenol.

General Information:

The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker Advance 400 MHz NMR spectrometer in $CDCl_3$ with residual undeuterated solvent ($CDCl_3$: 7.26/77.0) using Me_4Si as an internal standard. Chemical shifts (δ) are given in ppm and *J* values are given in Hz. The IR spectra were recorded either on KBr pellets (for solids) or neat (for liquids) on a Nicolet Impact 410 FTIR spectrometer. The UV spectra was recorded on a Beckman DU 7400 Spectrophotometer and the GCMS spectra were recorded on a Thermo Fischer GCMS-MS Focus GC instrument. Melting points were measured with Gupta scientific, India melting point apparatus. Open column chromatography, thin layer chromatography (TLC) was performed on Silica gel [CDH silica gel 60-120 mesh, F254 and Merck® silica gel respectively]. Evaporation of solvents was performed at reduced pressure, using a Bűchi rotary evaporator. All chemicals were purchased from Aldrich, Lancaster and Fluka Chemicals and used as received. All the TEM images are taken on carbon coated Cu grids in FEI-TECHNAI-G^2-F20 instrument equipped with EDX facility.

Experimental Procedure:

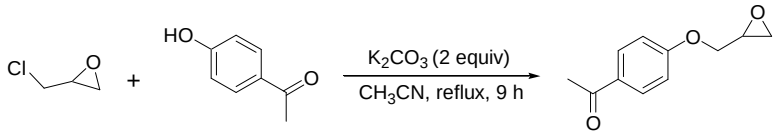
Typical procedure for epoxide ring opening using in-situ generated Pd nanoparticles (Table 2, Entry 2):



To a magnetically stirred solution of tetrabutylammonium bromide (TBAB) (0.161 g, 0.5 mmol, 25 mol %), $PdCl_2$ (0.003 g, 0.02 mmol, 1 mol %) and K_2CO_3 (0.069 g, 0.5 mmol, 25 mol %) in H_2O (8 mL) were added 4-chlorophenyl glycidyl ether **1a** (0.369 g, 2 mmol) and 4-methoxy phenol **2a** (0.248 g, 2 mmol, 1 equiv) at 60 °C. Upon completion of the reaction (3.5 h, monitored by TLC), the reaction mixture was diluted with ethyl acetate (2 X 5 mL) and the ethyl acetate layer was separated from the aqueous layer. The combined ethyl acetate layer was dried over anhydrous Na_2SO_4; then the ethyl acetate was evaporated to dryness under vacuum. The residual was purified by column chromatography (60-120 mesh silica-gel) using hexane/EtOAc solvent system to afford the 1-(4-chloro-phenoxy)-3-(4-methoxy-phenoxy)-propan-2-ol **3a** as off white solid, (0.457 g, 74%). IR (KBr) ν_{max}: 3435, 2929, 1508, 822 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm): 2.65 (d, 1H, J = 5.2 Hz, D_2O exchangeable), 3.78 (s, 3H), 4.07 – 4.16 (m, 4H), 4.32 – 4.38 (m, 1H), 6.84 – 6.91 (m, 2H), 7.25 – 7.27 (m, 2H); MS (ESI) m/z: 308.2 (M^+).

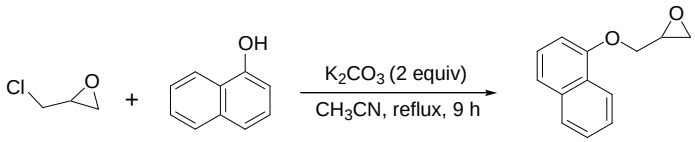
An aliquot portion (3 μL) of the reaction mixture of $PdCl_2$ (1 mol %), TBAB (25 mol %) and K_2CO_3 (25 mol %) was withdrawn after 15 min and kept on carbon coated Cu grid after dilution. The grid was air dried and was subjected to TEM analyses.

Typical procedure for the preparation of 1-(4-oxiranylmethoxy-phenyl)-ethanone (starting epoxide for Table 2, entry 9):



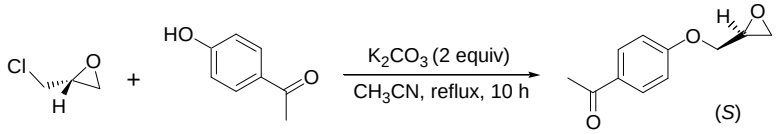
To a magnetically stirred solution of K_2CO_3 (1.380 g, 10 mmol, 2 equiv) and 4-hydroxyacetophenone (0.680 g, 5 mmol, 1 equiv) in anhydrous CH_3CN (10 mL) was added epichlorohydrin (0.462 g, 5 mmol, 0.39 mL, 1 equiv) and the mixture was stirred magnetically at 70 ^oC. After completion of the reaction (9 h, monitored by TLC), the reaction mixture was cooled to rt, filtered and the solvent was evaporated to dryness under vacuum. The residual was purified by column chromatography (60-120 mesh silica-gel) using hexane/EtOAc solvent system to afford the 1-(4-oxiranylmethoxy-phenyl)-ethanone as colorless oil, (0.759 g, 79%). IR (Neat) ν_{max}: 2929, 1760, 1663, 1259 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm): 2.55 (s, 3H), 2.77 (dd, 1H, J = 2.6 Hz, 4.8 Hz), 2.92 (t, 1H, J = 4.7 Hz), 3.35 – 3.39 (m, 1H), 3.99 (dd, 1H, J = 5.8 Hz, 11.0 Hz), 4.32 (dd, 1H, J = 2.9 Hz, 11.0 Hz), 6.94 – 6.97 (m, 2H), 7.91 – 7.94 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm): 26.4, 44.6, 49.9, 68.8, 114.3, 130.6, 162.3, 196.9; HRMS (ESI) $[M + Na]^+$ = 215.0693; Calculated = 215.0684.

Typical procedure for the preparation of 2-(naphthalen-1-yloxymethyl)-oxirane (starting epoxide for Table 2, entry 26):



To a magnetically stirred solution of K_2CO_3 (1.380 g, 10 mmol, 2 equiv) and 1-naphthol (0.721 g, 5 mmol, 1 equiv) in anhydrous CH_3CN (10 mL) was added epichlorohydrin (0.462 g, 5 mmol, 0.39 mL, 1 equiv) and the mixture was stirred magnetically at 70 ^oC. After completion of the reaction (9 h, monitored by TLC), the reaction mixture was cooled to rt, filtered and the solvent was evaporated to dryness under vacuum. The residual was purified by column chromatography (60-120 mesh silica-gel) using hexane/EtOAc solvent system to afford the 2-(naphthalen-1-yloxymethyl)-oxirane as light red semi-solid, (0.761 g, 76%). IR (KBr) ν_{max}: 2922, 1639, 1570, 1571 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm): 2.80 – 2.82 (m, 1H), 2.90 – 2.94 (m, 1H), 3.44 – 3.47 (m, 1H), 4.06 – 4.11 (m, 1H), 4.33 – 4.36 (m, 1H), 6.75 – 6.77 (m, 1H), 7.33 – 7.42 (m, 1H), 7.44 – 7.50 (m, 3H), 7.77 – 7.79 (m, 1H), 8.28 – 8.30 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm): 44.8, 50.4, 68.9, 105.1, 108.6, 120.9, 122.1, 125.4, 125.8, 126.6, 127.5, 134.6, 154.2; HRMS (ESI) $[M + Na]^+$ = 223.0740; Calculated = 223.0735.

Typical procedure for the preparation of (*S*) 1-(4-oxiranylmethoxy-phenyl)-ethanone (Starting epoxide of entries 10 & 11, footnotes C & d, Table 2):

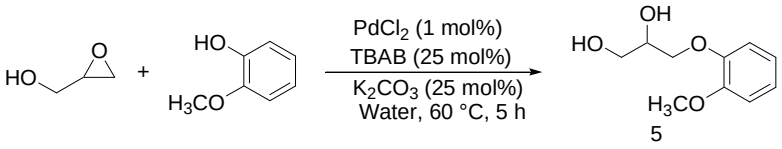


To a magnetically stirred solution of K_2CO_3 (1.380 g, 10 mmol, 2 equiv) and 4-hydroxy acetophenone (0.680 g, 5 mmol, 1 equiv) in anhydrous CH_3CN (10 mL) was added (*R*) epichlorohydrin (0.462 g, 5 mmol, 0.39 mL, 1 equiv) and the mixture was stirred magnetically at 70 ^oC. After completion of the reaction (10 h, monitored by TLC), the reaction mixture was cooled to rt, filtered and the solvent was evaporated to dryness under vacuum. The residual was purified by column chromatography (60-120 mesh silica-gel) using hexane/EtOAc solvent system to afford the (*S*) 1-(4-oxiranylmethoxy-phenyl)-ethanone as colorless oil, (0.711 g, 74%). IR (Neat) ν_{max}: 2926, 1759, 1673, 1600, 1258 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm): 2.56 (s, 3H), 2.78 – 2.79 (m, 1H), 2.92 – 2.94 (m, 1H), 3.37 – 3.38 (m, 1H), 3.98 – 4.02 (m, 1H), 4.31 – 4.34 (m, 1H), 6.96 (d, 2H, *J* = 7.4 Hz), 7.94 (m, 2H, *J* = 7.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm): 26.4, 44.6, 49.9, 68.8, 114.3, 130.6, 130.7, 162.3, 196.9; HRMS (ESI) $[M + Na]^+$ = 215.0687; Calculated = 215.0684. [ee = 80.06%]

HPLC Data:- Solvent- (IPA : Hexane)

Peak	Ret. Time	Area %
1	35.508	90.031
2	38.283	9.969

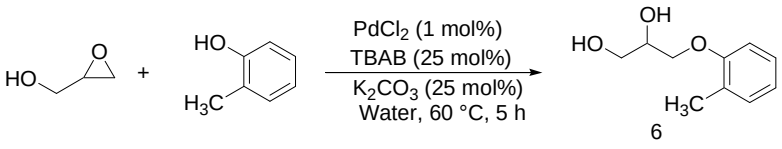
Typical procedure for the preparation of guaifenesin (Compound 5, Scheme 1):



5

To a magnetically stirred solution of tetrabutylammonium bromide (TBAB) (0.161 g, 0.5 mmol, 25 mol %), $PdCl_2$ (0.003 g, 0.02 mmol, 1 mol %) and K_2CO_3 (0.069 g, 0.5 mmol, 25 mol %) in H_2O (8 mL) were added glycidol **8** (0.148 g, 2 mmol) and 2-methoxy phenol (0.248 g, 2 mmol, 1 equiv) at 60 °C. Upon completion of the reaction (5 h, monitored by TLC), the reaction mixture was diluted with ethyl acetate (2 X 5 mL) and the ethyl acetate layer was separated from the aqueous layer. The combined ethyl acetate layer was dried over anhydrous Na_2SO_4; then the ethyl acetate was evaporated to dryness under vacuum. The residual was purified by column chromatography (60-120 mesh silica-gel) using hexane/EtOAc solvent system to afford the guaifenesin **5** as off white solid, (0.218 g, 55%). IR (KBr) ν_{max}: 3434, 2923, 1456, 1259, 749 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm): 3.76 – 3.82 (m, 2H), 3.86 (s, 3H), 4.04 – 4.09 (m, 2H), 4.14 – 4.17 (m, 1H), 6.89 – 7.00 (m, 4H); MS (ESI) *m*/*z*: 198.5 (M^+).

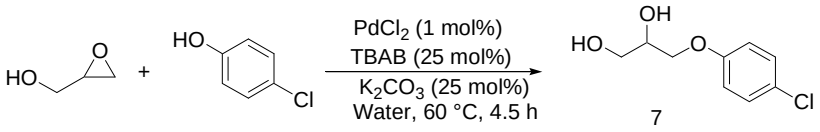
Typical procedure for the preparation of mefenesin (Compound 6, Scheme 1):



6

To a magnetically stirred solution of tetrabutylammonium bromide (TBAB) (0.161 g, 0.5 mmol, 25 mol %), $PdCl_2$ (0.003 g, 0.02 mmol, 1 mol %) and K_2CO_3 (0.069 g, 0.5 mmol, 25 mol %) in H_2O (8 mL) were added glycidol **8** (0.148 g, 2 mmol) and 2-methyl phenol (0.216 g, 2 mmol, 1 equiv) at 60 °C. Upon completion of the reaction (5 h, monitored by TLC), the reaction mixture was diluted with ethyl acetate (2 X 5 mL) and the ethyl acetate layer was separated from the aqueous layer. The combined ethyl acetate layer was dried over anhydrous Na_2SO_4; then the ethyl acetate was evaporated to dryness under vacuum. The residual was purified by column chromatography (60-120 mesh silica-gel) using hexane/EtOAc solvent system to afford the mefenesin **6** as off white solid, (0.240 g, 66%). IR (Neat) ν_{max}: 3399, 2924, 1754, 1601, 1457, 1246, 750 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm): 2.22 (s, 3H), 3.74 – 3.78 (m, 1H), 3.83 – 3.87 (m, 1H), 4.02 – 4.03 (m, 2H), 4.10 – 4.13 (m, 1H), 6.79 – 6.82 (m, 1H), 6.86 – 6.90 (m, 1H), 7.13 – 7.16 (m, 2H); MS (ESI) *m*/*z*: 182.6 (M^+).

Typical procedure for the preparation of chlorofenesin (Compound 7, Scheme 1):



To a magnetically stirred solution of tetrabutylammonium bromide (TBAB) (0.161 g, 0.5 mmol, 25 mol %), $PdCl_2$ (0.003 g, 0.02 mmol, 1 mol %) and K_2CO_3 (0.069 g, 0.5 mmol, 25 mol %) in H_2O (8 mL) were added glycidol **8** (0.148 g, 2 mmol) and 4-chloro phenol (0.256 g, 2 mmol, 1 equiv) at 60 °C. Upon completion of the reaction (4.5 h, monitored by TLC), the reaction mixture was diluted with ethyl acetate (2 X 5 mL) and the ethyl acetate layer was separated from the aqueous layer. The combined ethyl acetate layer was dried over anhydrous Na_2SO_4; then the ethyl acetate was evaporated to dryness under vacuum. The residual was purified by column chromatography (60-120 mesh silica-gel) using hexane/EtOAc solvent system to afford the chlorofenesin **7** as off white solid, (0.279 g, 69%). IR (KBr) ν_{max}: 3394, 2926, 1758, 1603, 1454, 1243, 752 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm): 2.44 (bs, 2H, D_2O exchangeable), 3.73 (dd, 1H, J = 5.6 Hz, 11.5 Hz), 3.83 (dd, 1H, J = 3.7 Hz, 11.5 Hz), 3.98 – 4.00 (m, 2H), 4.08 – 4.13 (m, 1H), 6.81 – 6.85 (m, 2H), 7.21 – 7.25 (m, 2H); MS (ESI) *m*/*z*: 202.9 (M^+).

Characterization of the Compounds:

1-(4-Chloro-phenoxy)-3-phenoxy-propan-2-ol (Table 2, entry 1):- Off white solid; IR (KBr) ν_{max}: 3429, 2932, 1593, 1492, 1241 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm): 2.68 (d, 1H, J = 5.2 Hz, D_2O exchangeable), 4.09 – 4.14 (m, 4H), 4.35 – 4.38 (m, 1H), 6.83 – 6.86 (m, 2H), 6.91 – 6.94 (m, 2H), 6.95 – 6.99 (m, 1H), 7.21 – 7.24 (m, 2H), 7.27 – 7.31 (m, 2H); MS (ESI) *m*/*z*: 278.9 (M^+).

1-(4-Chloro-phenoxy)-3-(4-methoxy-phenoxy)-propan-2-ol (Table 2, entry 2):- Off white solid; IR (KBr) ν_{max}: 3435, 2929, 1508, 822 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm): 2.65 (d, 1H, J = 5.2 Hz, D_2O exchangeable), 3.78 (s, 3H), 4.07 – 4.16 (m, 4H), 4.32 – 4.38 (m, 1H), 6.84 – 6.91 (m, 6H), 7.25 – 7.27 (m, 2H); MS (ESI) *m*/*z*: 308.2 (M^+).

1-(4-Bromo-phenoxy)-3-(4-chloro-phenoxy)-propan-2-ol (Table 2, entry 3):- Off white solid; mp: 66 °C; IR (KBr) ν_{max}: 3435, 2929, 1637, 1489, 1239 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm): 2.63 (d, 1H, J = 4.6 Hz, D_2O exchangeable), 4.09 – 4.16 (m, 4H), 4.34 – 4.40 (m, 1H), 6.80 – 6.89 (m, 4H), 7.24 – 7.27 (m, 2H), 7.38 – 7.42 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm): 68.6, 68.9, 69.0, 113.6, 115.9, 116.4, 126.3, 129.4, 132.4, 157.0, 157.5; HRMS (ESI) $[M + Na]^+$ = 378.9717; Calculated = 378.9713.

4-[3-(4-Chloro-phenoxy)-2-hydroxy-propoxy]-benzaldehyde (Table 2, entry 4):- Off white solid; mp: 90 °C; IR (KBr) ν_{max}: 3443, 2930, 1702, 1605, 1241 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm): 2.75 (bs, 1H, D_2O exchangeable), 4.11 – 4.18 (m, 2H), 4.20 – 4.27 (m, 2H), 4.43 – 4.45 (m, 1H), 6.86 (d, 2H, J = 8.7 Hz), 7.04 (d, 2H, J = 8.3 Hz), 7.24 (d, 2H, J = 8.7 Hz), 7.84 (d, 2H, J = 8.3 Hz), 9.89 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm): 68.5, 68.9, 69.0, 114.8,

115.8, 126.3, 129.5, 130.4, 132.1, 156.9, 163.3, 190.8; HRMS (ESI) $[M + Na]^+$ = 329.0560; Calculated = 329.0557.

1-{4-[3-(4-Chloro-phenoxy)-2-hydroxy-propoxy]-phenyl}-ethanone (Table 2, entry 5):- Off white solid; mp: 99 ^oC; IR (KBr) ν_{max}: 3398, 2924, 1727, 1599, 1459, 1260, 750 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm): 2.55 (s, 3H), 4.12 – 4.17 (m, 2H), 4.19 – 4.22 (m, 2H), 4.39 – 4.41 (m, 1H), 6.84 – 6.87 (m, 2H), 6.94 – 6.98 (m, 2H), 7.22 – 7.27 (m, 2H), 7.91 – 7.95 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm): 26.4, 68.6, 68.8, 68.9, 114.2, 115.8, 126.3, 129.5, 129.6, 130.7, 157.0, 162.2, 196.9; HRMS (ESI) $[M + Na]^+$ = 343.0713; Calculated = 343.0713.

4-[3-(4-Chloro-phenoxy)-2-hydroxy-propoxy]-benzoic acid methyl ester (Table 2, entry 6):- Off white solid; mp: 87 ^oC; IR (KBr) ν_{max}: 3131, 2355, 1712, 1256, 752 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm): 2.74 (bs, 1H, D_2O exchangeable), 3.88 (s, 3H), 4.09 – 4.23 (m, 4H), 4.38 – 4.41 (m, 1H), 6.86 (d, 2H, *J* = 7.9 Hz), 6.94 (d, 2H, *J* = 8.3 Hz), 7.22 – 7.26 (m, 2H), 7.99 (d, 2H, *J* = 8.4 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm): 52.0, 68.6, 68.8, 68.9, 114.1, 115.8, 123.2, 126.3, 129.4, 131.7, 157.0, 162.1, 166.8; HRMS (ESI) $[M + Na]^+$ = 359.0667; Calculated = 359.0662.

4-[3-(4-Chloro-phenoxy)-2-hydroxy-propoxy]-benzonitrile (Table 2, entry 7):- White solid; mp: 120 ^oC; IR (KBr) ν_{max}: 3435, 2929, 2223, 1726, 1280 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm): 2.61 (bs, 1H, D_2O exchangeable), 4.08 – 4.16 (m, 2H), 4.18 – 4.23 (m, 2H), 4.38 – 4.43 (m, 1H), 6.84 – 6.88 (m, 2H), 6.97 – 7.01 (m, 2H), 7.24 – 7.27 (m, 2H), 7.57 – 7.60 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm): 68.5, 68.8, 69.0, 104.7, 115.3, 115.8, 119.0, 126.4, 129.5, 134.1, 156.9, 161.6; HRMS (ESI) $[M + Na]^+$ = 326.0561; Calculated = 326.0560.

1-(4-Chloro-phenoxy)-3-(4-nitro-phenoxy)-propan-2-ol (Table 2, entry 8):- Off white solid; mp: 132 ^oC; IR (KBr) ν_{max}: 3435, 2927, 1635, 1492 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm): 2.59 (d, 1H, *J* = 4.9 Hz, D_2O exchangeable), 4.12 – 4.19 (m, 2H), 4.22 – 4.29 (m, 2H), 4.41 – 4.46 (m, 1H), 6.87 – 6.91 (m, 2H), 7.02 – 7.04 (m, 2H), 7.27 – 7.29 (m, 2H), 8.23 – 8.25 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm): 68.5, 68.8, 69.4, 114.6, 115.7, 126.0, 126.5, 129.5, 142.0, 156.8, 163.3; HRMS (ESI) $[M + Na]^+$ = 346.0462; Calculated = 346.0458.

1-[4-(2-Hydroxy-3-phenoxy-propoxy)-phenyl]-ethanone (Table 2, entry 9 & entry 18):- Off white semi-solid; IR (KBr) ν_{max}: 3411, 2918, 1709, 1668, 1599, 1259 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm): 2.56 (s, 3H), 3.11 (bs, 1H, D_2O exchangeable), 4.16 – 4.19 (m, 2H), 4.20 – 4.26 (m, 2H), 4.41 – 4.43 (m, 1H), 6.93 – 7.00 (m, 5H), 7.27 – 7.32 (m, 2H), 7.92 – 7.94 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm): 26.4, 68.5, 68.6, 69.0, 114.3, 114.5, 121.4, 129.6, 130.6, 130.7, 158.3, 162.4, 197.1; HRMS (ESI) $[M + Na]^+$ = 309.1109; Calculated = 309.1103.

1-{4-[2-Hydroxy-3-(4-methoxy-phenoxy)-propoxy]-phenyl}-ethanone (Table 2, entry 10):- Yellow liquid; IR (Neat) ν_{max}: 3436, 2956, 1726, 1274 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm): 2.52 (s, 3H), 3.29 (bs, 1H, D_2O exchangeable), 3.74 (s, 3H), 4.06 – 4.13 (m, 2H), 4.15 – 4.23 (m, 2H), 4.38 (q, 1H, *J* = 5.1 Hz), 6.80 – 6.87 (m, 4H), 6.93 (d, 2H, *J* = 8.7 Hz), 7.89 (d, 2H, *J* = 8.7 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm): 26.3, 55.7, 68.7, 69.1, 69.5, 114.3, 114.7, 115.6, 130.6, 152.6, 154.2, 162.4, 197.0; HRMS (ESI) $[M + Na]^+$ = 339.1213; Calculated = 339.1208.

1-{4-[2-Hydroxy-3-(4-nitro-phenoxy)-propoxy]-phenyl}-ethanone (Table 2, entry 11):- Light yellow solid; mp: 117 ^{o}C; IR (KBr) ν_{max}: 3433, 2924, 1727, 1594, 1257 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 2.57 (s, 3H), 2.77 (bs, 1H, D_2O exchangeable), 4.22 – 4.32 (m, 4H), 4.44 – 4.45 (m, 1H), 6.96 – 7.04 (m, 4H), 7.93 – 7.97 (m, 2H), 8.19 – 8.23 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm): 26.4, 68.4, 68.6, 69.4, 114.2, 114.6, 126.0, 130.7, 131.0, 142.0, 162.1, 163.3, 196.8; HRMS (ESI) $[M + Na]^+$ = 354.0959; Calculated = 354.0954.

1-{4-[3-(4-Acetyl-phenoxy)-2-hydroxy-propoxy]-phenyl}-ethanone (Table 2, entry 12):- Off white solid; mp: 100 ^{o}C; IR (KBr) ν_{max}: 3413, 2924, 1723, 1599, 1260, 750 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 2.55 (s, 6H), 4.21 – 4.28 (m, 4H), 4.43 – 4.49 (m, 1H), 6.95 – 6.98 (m, 4H), 7.91 – 7.94 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm): 26.4, 68.4, 68.8, 114.2, 130.6, 130.7, 162.3, 197.0; HRMS (ESI) $[M + Na]^+$ = 351.1212; Calculated = 351.1208.

1,3-Diphenoxy-propan-2-ol (Table 2, entry 13):- White solid; IR (KBr) ν_{max}: 3414, 2919, 1665, 1599, 1259 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 2.71 (d, 1H, J = 4.9 Hz, D_2O exchangeable), 4.15 – 4.22 (m, 4H), 4.40 – 4.45 (m, 1H), 6.96 – 7.02 (m, 6H), 7.30 – 7.35 (m, 4H); MS (ESI) m/z: 244.5 (M^+).

1-(4-Methoxy-phenoxy)-3-phenoxy-propan-2-ol (Table 2, entry 14):- Off white solid; IR (KBr) ν_{max}: 3436, 2939, 1586, 1230 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 2.71 (d, 1H, J = 5.1 Hz, D_2O exchangeable), 3.76 (s, 3H), 4.06 – 4.17 (m, 4H), 4.33 – 4.38 (m, 1H), 6.81 – 6.89 (m, 4H), 6.91 – 6.99 (m, 3H), 7.26 – 7.31 (m, 2H); MS (ESI) m/z: 274.6 (M^+).

1-(2-Methoxy-phenoxy)-3-phenoxy-propan-2-ol (Table 2, entry 15):- Light yellow liquid; IR (Neat) ν_{max}: 3435, 2843, 1639, 1016 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 3.71 (s, 3H), 4.04 – 4.14 (m, 5H), 4.30 – 4.33 (m, 1H), 6.78 – 6.91 (m, 7H), 7.20 (t, 2H, J = 7.8 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm): 55.9, 68.8, 71.0, 112.1, 114.6, 114.7, 121.1, 121.2, 122.0, 129.6, 148.3, 149.7, 158.8; HRMS (ESI) $[M + Na]^+$ = 297.1107; Calculated = 297.1103.

4-(2-Hydroxy-3-phenoxy-propoxy)-benzaldehyde (Table 2, entry 16):- Off white solid; mp: 91 ^{o}C; IR (KBr) ν_{max}: 3436, 2925, 1686, 1599, 1243 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 2.64 (bs, 1H, D_2O exchangeable), 4.14 – 4.21 (m, 2H), 4.22 – 4.30 (m, 2H), 4.40 – 4.47 (m, 1H), 6.93 – 6.96 (m, 2H), 6.97 – 7.01 (m, 1H), 7.04 – 7.06 (m, 2H), 7.29 – 7.33 (m, 2H), 7.84 – 7.86 (m, 2H), 9.90 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm): 68.4, 68.6, 69.0, 114.5, 114.8, 121.5, 129.6, 130.4, 132.1, 158.2, 163.4, 190.8; HRMS (ESI) $[M + Na]^+$ = 295.0948; Calculated = 295.0946.

2-(2-Hydroxy-3-phenoxy-propoxy)-benzaldehyde (Table 2, entry 17):- Light yellow liquid; IR (Neat) ν_{max}: 3435, 2846, 2099, 1635, 1239, 751 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 3.60 (bs, 1H, D_2O exchangeable), 4.15 – 4.19 (m, 2H), 4.22 – 4.30 (m, 2H), 4.44 (q, 1H, J = 5.2 Hz), 6. 87 – 7.05 (m, 5H), 7.24 – 7.29 (m, 2H), 7.50 – 7.53 (m, 1H), 7.77 – 7.79 (m, 1H), 10.40 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm): 68.5, 68.6, 69.7, 112.9, 114.6, 121.3, 121.4, 125.0, 129.6, 136.1, 158.3, 160.7, 190.0; HRMS (ESI) $[M + Na]^+$ = 295.0949; Calculated = 295.0946.

1-[2-(2-Hydroxy-3-phenoxy-propoxy)-phenyl]-ethanone (Table 2, entry 19):- Light yellow liquid; IR (Neat) ν_{max}: 3433, 2927, 1653, 1635, 1449, 751 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ

(ppm): 2.59 (s, 3H), 3.70 (bs, 1H, D_2O exchangeable), 4.11 – 4.14 (m, 2H), 4.22 – 4.29 (m, 2H), 4.39 – 4.42 (m, 1H), 6.90 – 6.92 (m, 2H), 6.96 – 7.01 (m, 3H), 7.25 – 7.29 (m, 2H), 7.41 – 7.45 (m, 1H), 7.68 – 7.70 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm): 31.4, 68.5, 68.6, 70.2, 113.4, 114.5, 121.1, 121.3, 128.3, 129.6, 130.5, 133.9, 157.9, 158.4, 200.0; HRMS (ESI) $[M + Na]^+$ = 309.1108; Calculated = 309.1103.

4-(2-Hydroxy-3-phenoxy-propoxy)-benzoic acid methyl ester (Table 2, entry 20):- Off white semi-solid; IR (KBr) ν_{max}: 3411, 2919, 1710, 1669, 1599, 1259 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm): 3.23 (bs, 1H, D_2O exchangeable), 3.87 (s, 3H), 4.12 – 4.24 (m, 4H), 4.42 (bs, 1H), 6.93 – 7.00 (m, 5H), 7.27 – 7.32 (m, 2H), 7.98 – 8.00 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm): 52.0, 68.6, 68.6, 69.0, 114.2, 114.6, 121.3, 123.0, 129.6, 131.7, 158.4, 162.3, 166.9; HRMS (ESI) $[M + Na]^+$ = 325.1057; Calculated = 325.1052.

1-(4-Nitro-phenoxy)-3-phenoxy-propan-2-ol (Table 2, entry 21):- Off white solid; mp: 78 ^oC; IR (KBr) ν_{max}: 3436, 2929, 1634, 1491 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm): 2.63 (bs, 1H, D_2O exchangeable), 4.17 – 4.21 (m, 2H), 4.24 – 4.32 (m, 2H), 4.44 – 4.47 (m, 1H), 6.94 – 6.97 (m, 2H), 7.00 – 7.04 (m, 3H), 7.31 – 7.35 (m, 2H), 8.22 – 8.24 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm): 68.3, 68.6, 69.4, 114.5, 114.6, 121.5, 126.0, 129.6, 141.9, 158.2, 163.4. HRMS (ESI) $[M + Na]^+$ = 312.0852; Calculated = 312.0848.

1-(Naphthalen-1-yloxy)-3-phenoxy-propan-2-ol (Table 2, entry 22):- Light reddish liquid; IR (Neat) ν_{max}: 3430, 2951, 1645, 1401, 1016 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm): 3.58 (bs, 1H, D_2O exchangeable), 4.30 – 4.40 (m, 4H), 4.66 – 4.67 (m, 1H), 6.90 – 6.92 (m, 1H), 7.11 – 7.19 (m, 3H), 7.44 – 7.54 (m, 3H), 7.63 – 7.67 (m, 3H), 7.97 – 7.99 (m, 1H), 8.49 – 8.50 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm): 68.6, 68.7, 104.8, 114.3, 120.5, 121.0, 121.6, 125.1, 125.2, 125.6, 126.2, 127.3, 129.3, 134.2, 153.8, 158.2; HRMS (ESI) $[M + Na]^+$ = 317.1156; Calculated = 317.1154.

1-(Naphthalen-2-yloxy)-3-phenoxy-propan-2-ol (Table 2, entry 23):- Off white solid; mp: 44 ^oC; IR (Neat) ν_{max}: 3400, 2953, 1629, 1599, 1403, 1259, 1018 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm): 3.22 (bs, 1H, D_2O exchangeable), 4.19 – 4.26 (m, 2H), 4.27 – 4.35 (m, 2H), 4.50 – 4.54 (m, 1H), 7.02 – 7.08 (m, 3H), 7.23 – 7.27 (m, 2H), 7.34 – 7.39 (m, 2H), 7.41 – 7.45 (m, 1H), 7.50 – 7.54 (m, 1H), 7.78 – 7.85 (m, 3H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm): 68.8, 68.9, 69.0, 107.0, 114.7, 118.8, 121.4, 124.0, 126.6, 127.0, 127.8, 129.3, 129.6, 129.7, 134.6, 156.5, 158.5; HRMS (ESI) $[M + Na]^+$ = 317.1159; Calculated = 317.1154.

1-tert-Butoxy-3-(4-methoxy-phenoxy)-propan-2-ol (Table 2, entry 24):- Yellow liquid; IR (Neat) ν_{max}: 3695, 2965, 1507, 1275 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm): 1.20 (s, 9H), 2.81 (bs, 1H, D_2O exchangeable), 3.48 (dd, 1H, J = 5.9 Hz, 9.1 Hz), 3.54 (dd, 1H, J = 4.7 Hz, 9.1 Hz), 3.75 (s, 3H), 3.94 – 3.98 (m, 2H), 4.04 – 4.07 (m, 1H), 6.80 – 6.83 (m, 2H), 6.84 – 6.87 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm): 27.5, 55.7, 62.6, 69.4, 69.7, 73.3, 114.6, 115.5, 152.9, 153.9; HRMS (ESI) $[M + Na]^+$ = 277.1419; Calculated = 277.1416.

1-(Furan-2-ylmethoxy)-3-(4-methoxy-phenoxy)-propan-2-ol (Table 2, entry 25):- Yellow liquid; IR (Neat) ν_{max}: 3430, 2923, 1513, 1460 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ (ppm): 2.64 (bs, 1H, D_2O exchangeable), 3.60 (dd, 1H, J = 6.0 Hz, 9.7 Hz), 3.66 (dd, 1H, J = 4.5 Hz, 9.7 Hz),

3.76 (s, 3H), 3.92 – 3.99 (m, 2H), 4.10 – 4.15 (m, 1H), 4.52 (s, 2H), 6.33 – 6.35 (m, 2H), 6.80 – 6.86 (m, 4H), 7.40 – 7.41 (m, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm): 55.7, 65.2, 69.2, 69.6, 70.8, 109.6, 110.3, 114.6, 115.6, 143.0, 151.4, 152.7, 154.1; HRMS (ESI) $[M + Na]^+$ = 301.1057; Calculated = 301.1052.

1,3-Bis-(naphthalen-1-yloxy)-propan-2-ol (Table 2, entry 26):- Light pink liquid; IR (Neat) ν_{max}: 3434, 2927, 1580, 1274, 750 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 3.35 (bs, 1H, D_2O exchangeable), 4.39 – 4.45 (m, 4H), 4.71 – 4.75 (m, 1H), 6.89 – 6.91 (m, 2H), 7.45 – 7.49 (m, 2H), 7.57 – 7.63 (m, 6H), 7.91 – 7.93 (m, 2H), 8.42 – 8.44 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm): 69.2, 69.3, 105.2, 121.0, 121.9, 125.6, 125.6, 126.0, 126.7, 127.8, 134.7, 154.2; HRMS (ESI) $[M + Na]^+$ = 367.1313; Calculated = 367.1310.

1-(4-Methoxy-phenoxy)-2-methyl-propan-2-ol (Table 2, entry 27):- Off white solid; mp: 57 ^{o}C; IR (KBr) ν_{max}: 3433, 2930, 1725, 1273 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 1.32 (s, 6H), 2.44 (bs, 1H, D_2O exchangeable), 3.73 (s, 2H), 3.76 (s, 3H), 6.81 – 6.86 (m, 4H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm): 26.1, 55.7, 70.1, 76.8, 114.7, 115.6, 153.0, 154.1; HRMS (ESI) $[M + Na]^+$ = 219.1001; Calculated = 219.0997.

2-(4-Methoxy-phenoxy)-2-phenyl-ethanol (Table 3, entry 1):- White solid; IR (KBr) ν_{max}: 3409, 2925, 2362, 1508, 1228 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 2.35 (dd, 1H, J = 3.8 Hz, 9.6 Hz, D_2O exchangeable), 3.70 (s, 3H), 3.76 – 3.82 (m, 1H), 3.86 – 3.92 (m, 1H), 5.16 (dd, 1H, J = 3.6 Hz, 8.3 Hz), 6.71 – 6.75 (m, 2H), 6.78 – 6.82 (m, 2H), 7.26 – 7.32 (m, 2H), 7.32 – 7.37 (m, 3H); MS (ESI) m/z: 267.7 (M^+).

2-(4-Bromo-phenoxy)-2-phenyl-ethanol (Table 3, entry 2):- Off white solid; mp: 97 ^{o}C; IR (KBr) ν_{max}: 3435, 2916, 2360, 1588, 1488, 1236, 1039 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 2.27 (bs, 1H, D_2O exchangeable), 3.78 – 3.83 (m, 1H), 3.89 – 3.94 (m, 1H), 5.21 (dd, 1H, J = 3.6 Hz, 8.2 Hz), 6.72 – 6.76 (m, 2H), 7.26 – 7.30 (m, 2H), 7.31 – 7.37 (m, 5H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm): 67.5, 81.5, 113.5, 117.7, 126.3, 128.4, 128.9, 132.3, 137.2, 156.8; HRMS (ESI) $[M + Na]^+$ = 314.9999; Calculated = 314.9997.

4-(2-Hydroxy-1-phenyl-ethoxy)-benzonitrile (Table 3, entry 3):- Off white solid; mp: 98 ^{o}C; IR (KBr) ν_{max}: 3443, 2924, 2224, 1604, 1460, 1259, 750 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 2.47 (bs, 1H, D_2O exchangeable), 3.82 – 3.85 (m, 1H), 3.94 – 3.99 (m, 1H), 5.31 (dd, 1H, J = 3.5 Hz, 8.0 Hz), 6.89 – 6.93 (m, 2H), 7.29 – 7.38 (m, 5H), 7.44 – 7.48 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm): 67.2, 81.6, 104.3, 116.6, 119.0, 126.2, 128.7, 129.0, 133.9, 136.5, 161.1; HRMS (ESI) $[M + Na]^+$ = 262.0849; Calculated = 262.0844.

2-(4-Nitro-phenoxy)-2-phenyl-ethanol (Table 3, entry 4):- Yellow liquid; IR (Neat) ν_{max}: 3434, 2923, 1459, 1260, 750 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 3.89 (dd, 1H, J = 3.5 Hz, 12.2 Hz), 4.02 (dd, 1H, J = 8.0 Hz, 12.2 Hz), 5.38 (dd, 1H, J = 3.5 Hz, 8.0 Hz), 6.92 – 6.96 (m, 2H), 7.31 – 7.40 (m, 5H), 8.07 – 8.14 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm): 67.2, 82.0, 115.8, 125.8, 126.2, 128.8, 129.1, 136.2, 141.7, 162.8; HRMS (ESI) $[M + Na]^+$ = 282.0746; Calculated = 282.0742.

(S) 1-{4-[2-Hydroxy-3-(4-methoxy-phenoxy)-propoxy]-phenyl}-ethanone (entry 10, footnote c, Table 2):- Light red liquid; IR (Neat) ν_{max}: 3438, 2929, 1726, 1508, 1260 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 2.53 (s, 3H), 3.21 (bs, 1H, D_2O exchangeable), 3.75 (s, 3H), 4.06 –

4.12 (m, 2H), 4.13 – 4.23 (m, 2H), 4.39 (q, 1H, *J* = 5.2 Hz), 6.80 – 6.87 (m, 4H), 6.94 (d, 2H, *J* = 8.8 Hz), 7.90 (d, 2H, *J* = 8.8 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm): 26.3, 55.7, 68.7, 69.1, 69.4, 114.3, 114.7, 115.6, 130.6, 152.5, 154.2, 162.4, 197.0; HRMS (ESI) $[M + Na]^+$ = 339.1213; Calculated = 339.1208. [ee = 76.85%].

HPLC Data:- Solvent- (IPA : Hexane)

Peak	Ret. Time	Area %
1	17.100	88.425
2	26.150	11.575

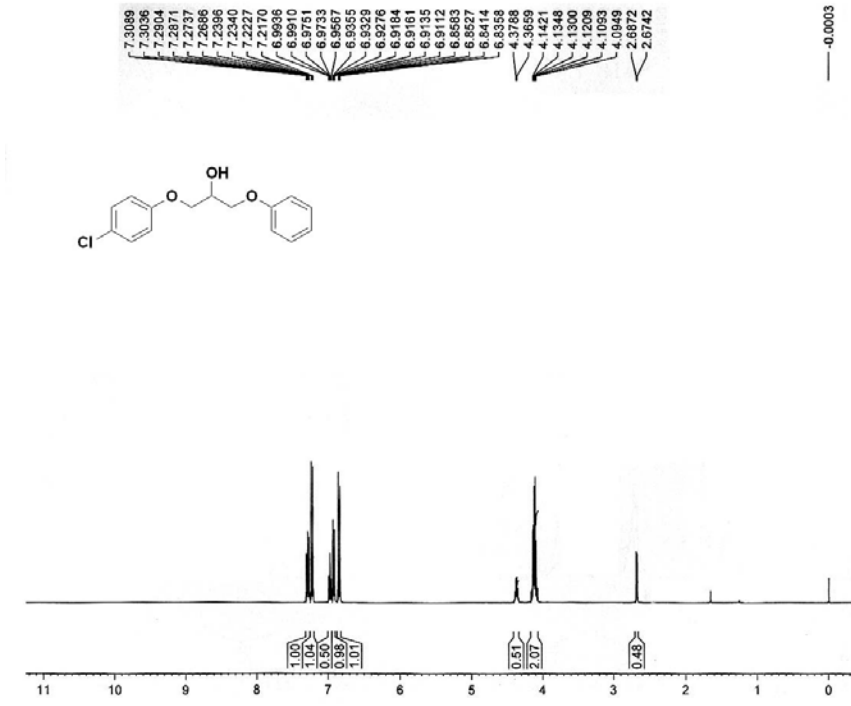
(S) 1-{4-[2-Hydroxy-3-(4-nitro-phenoxy)-propoxy]-phenyl}-ethanone (entry 11, footnote d, Table 2):- Light yellow solid; mp: 118 ^{o}C; IR (KBr) ν_{max}: 3443, 2929, 1725, 1594, 1262 cm^{-1}; ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 2.57 (s, 3H), 2.78 (bs, 1H, D_2O exchangeable), 4.22 – 4.32 (m, 4H), 4.49 (q, 1H, *J* = 5.0 Hz), 6.94 – 7.04 (m, 4H), 7.93 – 7.97 (m, 2H), 8.19 – 8.23 (m, 2H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm): 26.3, 68.4, 68.7, 69.4, 114.2, 114.6, 126.0, 130.7, 131.0, 142.0, 162.1, 163.1, 196.8; HRMS (ESI) $[M + Na]^+$ = 354.0957; Calculated = 354.0954. [ee = 82.79%]

HPLC Data:- Solvent- (IPA : Hexane)

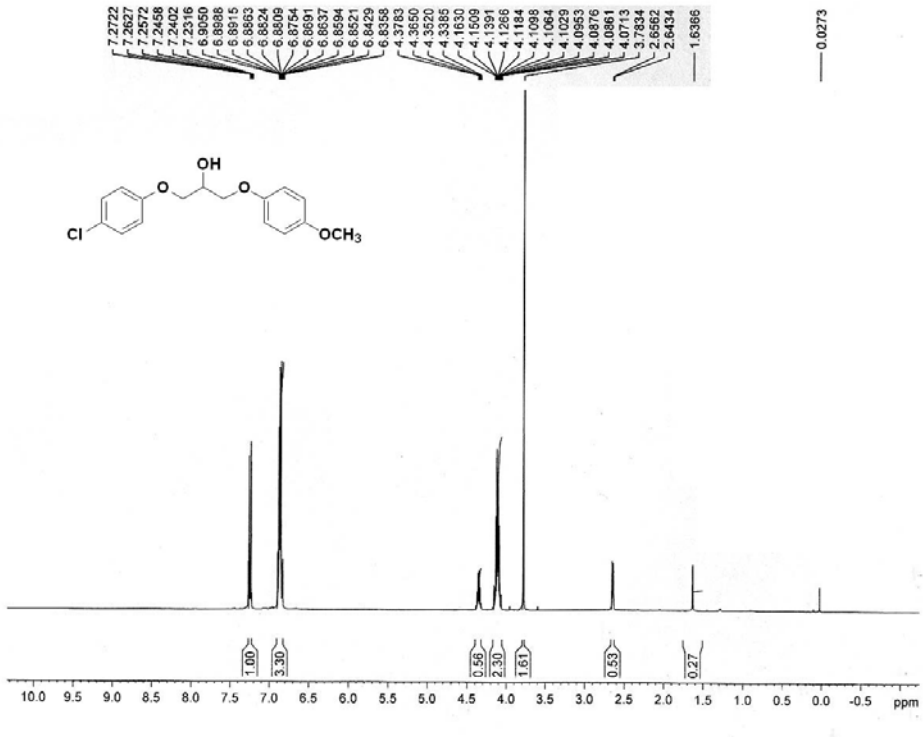
Peak	Ret. Time	Area %
1	34.675	8.606
2	36.667	91.394

Scanned NMR Spectra

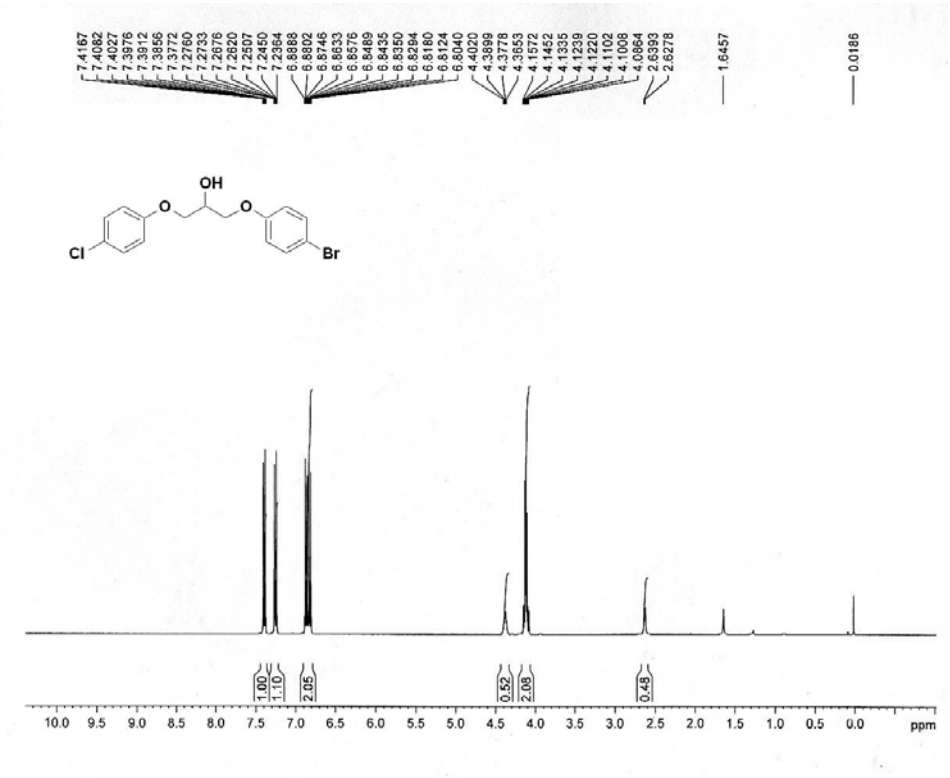
^{1}H NMR of 1-(4-Chloro-phenoxy)-3-phenoxy-propan-2-ol (Table 2, entry 1)



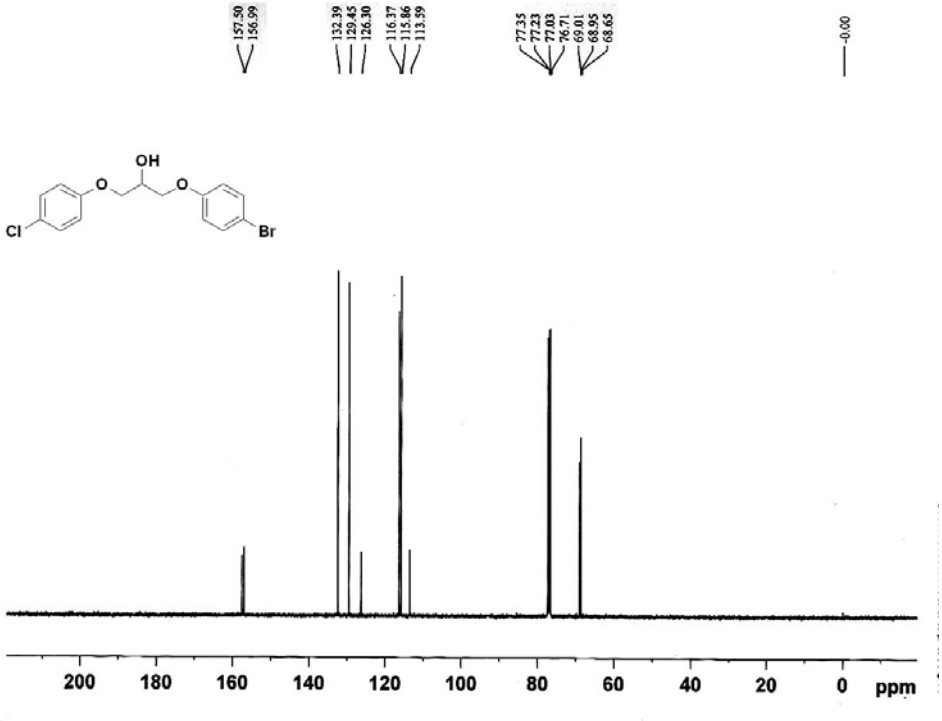
^{1}H NMR of 1-(4-Chloro-phenoxy)-3-(4-methoxy-phenoxy)-propan-2-ol (Table 2, entry 2)



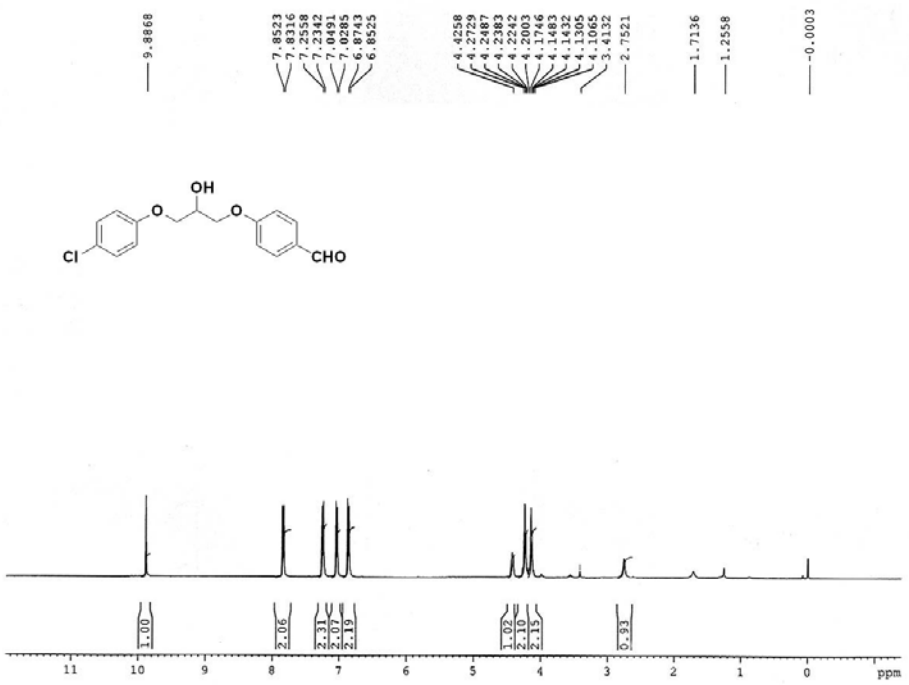
^{1}H NMR of 1-(4-Bromo-phenoxy)-3-(4-chloro-phenoxy)-propan-2-ol (Table 2, entry 3)



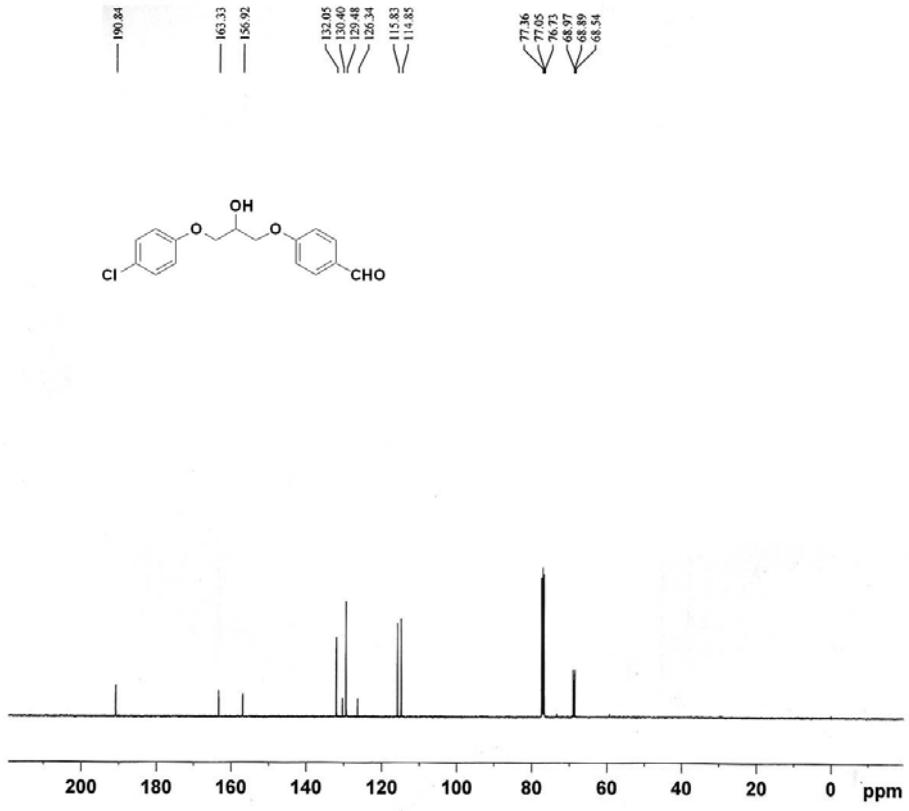
^{13}C NMR of 1-(4-Bromo-phenoxy)-3-(4-chloro-phenoxy)-propan-2-ol (Table 2, entry 3)



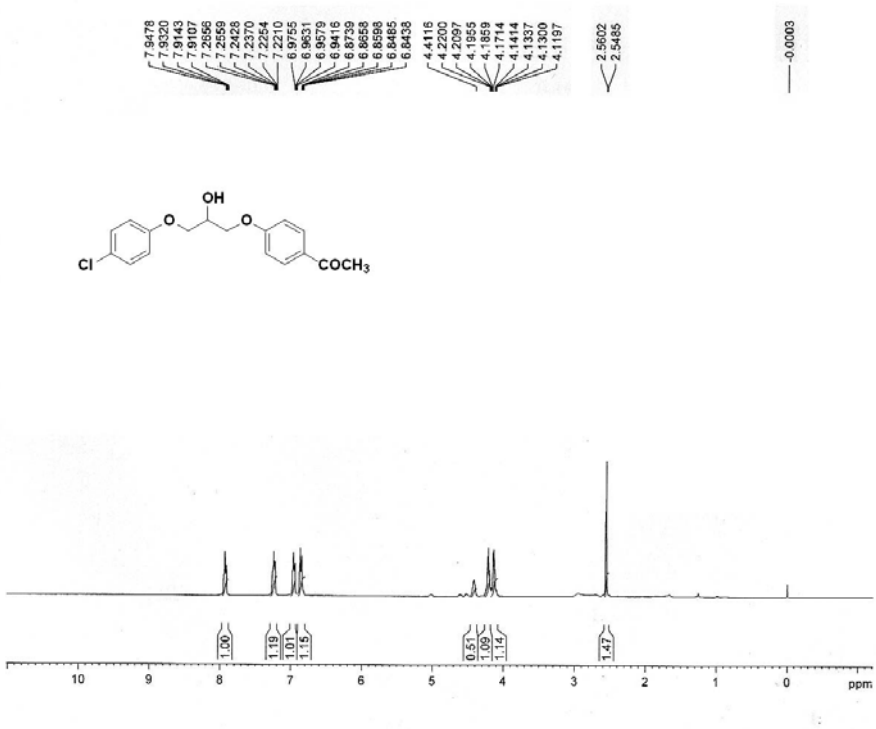
^{1}H NMR of 4-[3-(4-Chloro-phenoxy)-2-hydroxy-propoxy]-benzaldehyde (Table 2, entry 4)



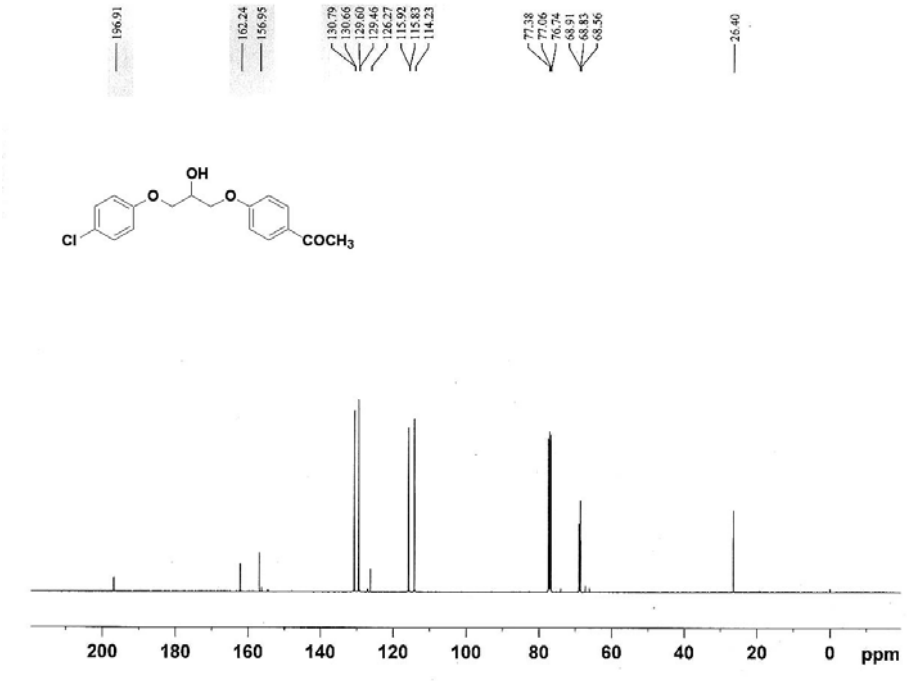
^{13}C NMR of 4-[3-(4-Chloro-phenoxy)-2-hydroxy-propoxy]-benzaldehyde (Table 2, entry 4)



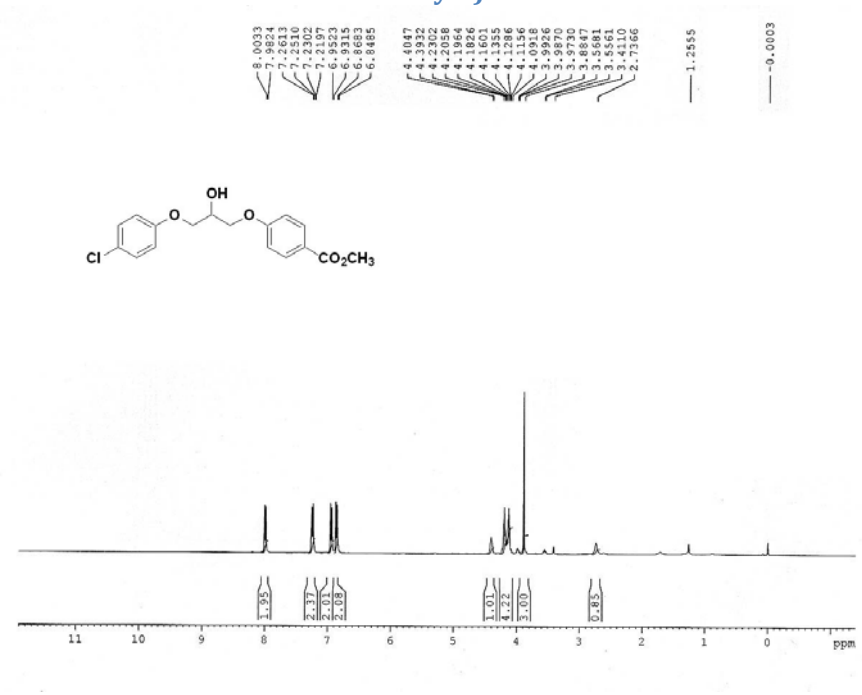
^{1}H NMR of 1-{4-[3-(4-Chloro-phenoxy)-2-hydroxy-propoxy]-phenyl}-ethanone (Table 2, entry 5)



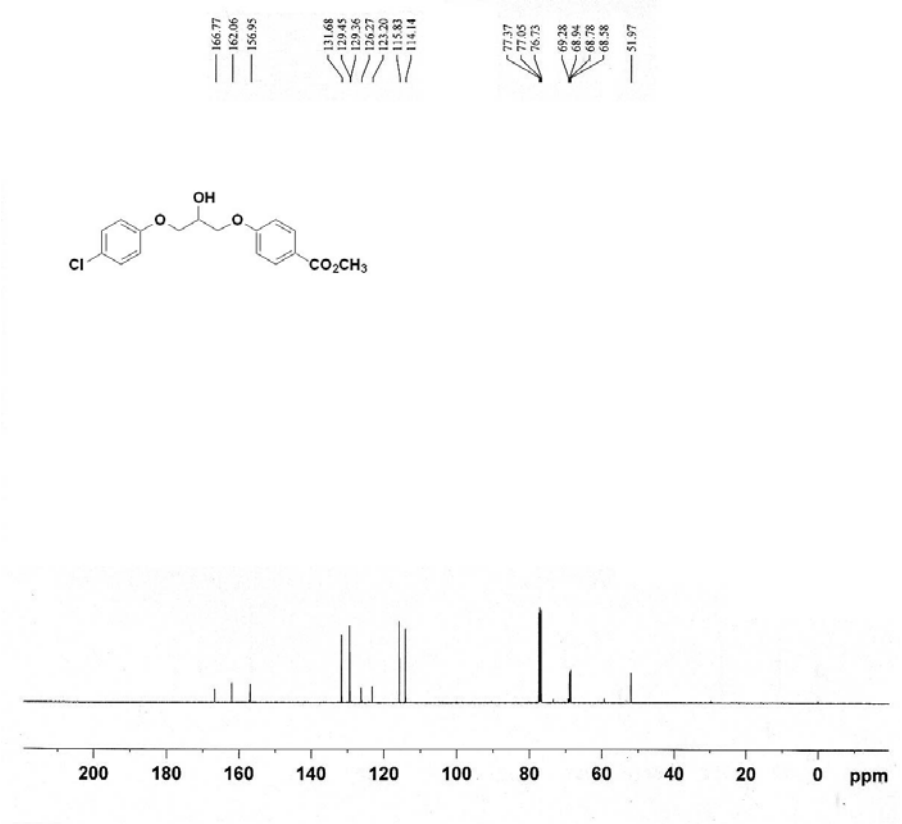
^{13}C NMR of 1-{4-[3-(4-Chloro-phenoxy)-2-hydroxy-propoxy]-phenyl}-ethanone (Table 2, entry 5)



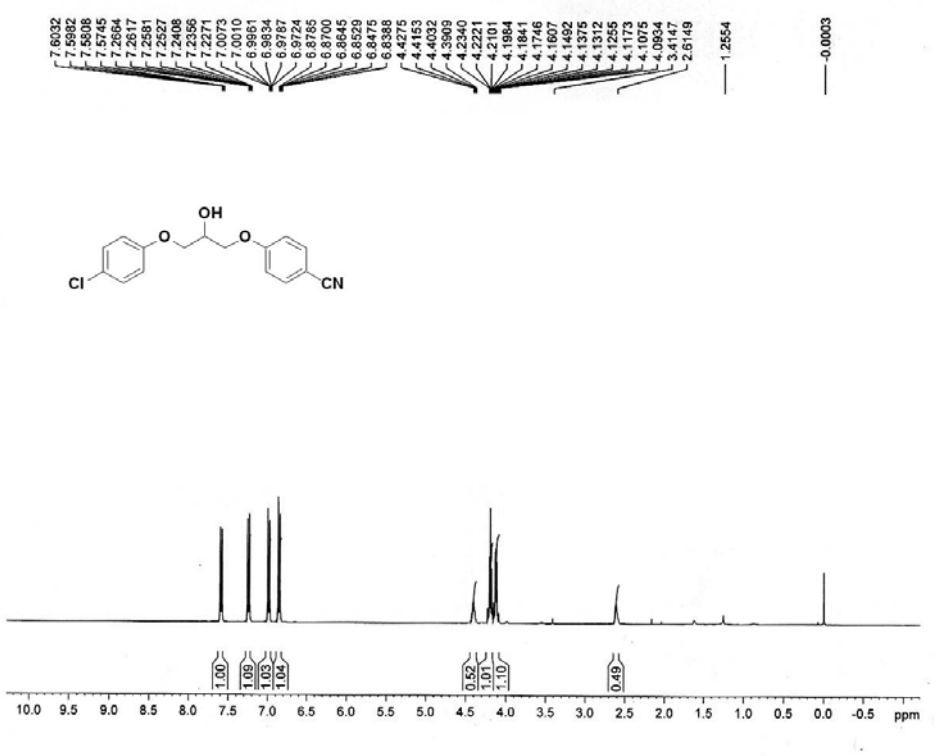
^{1}H NMR of 4-[3-(4-Chloro-phenoxy)-2-hydroxy-propoxy]-benzoic acid methyl ester (Table 2, entry 6)



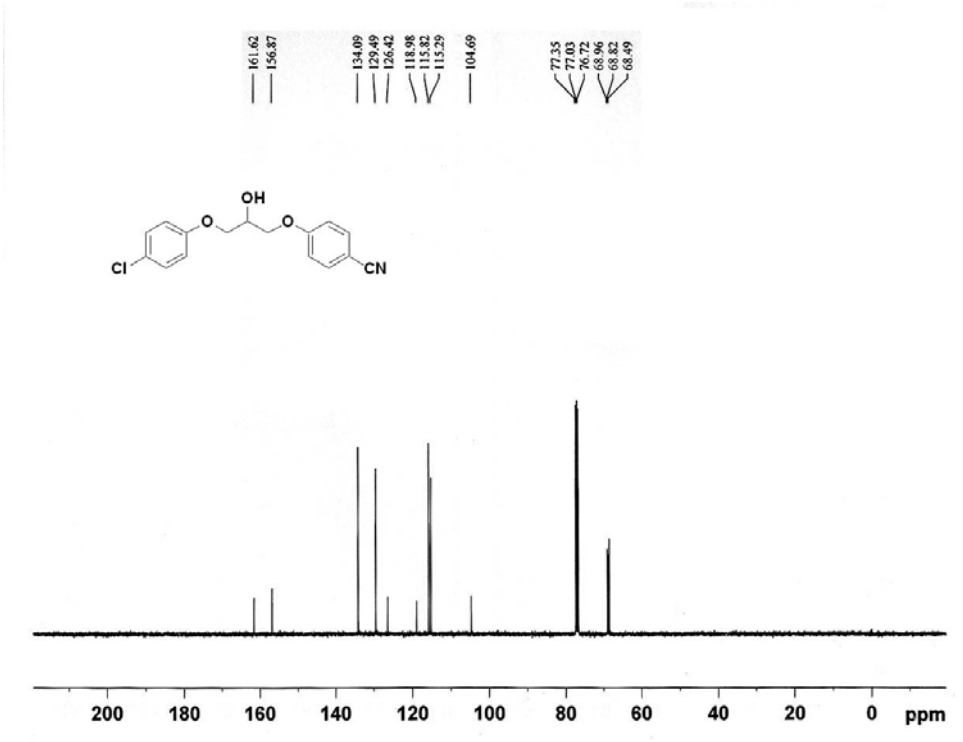
^{13}C NMR of 4-[3-(4-Chloro-phenoxy)-2-hydroxy-propoxy]-benzoic acid methyl ester (Table 2, entry 6)



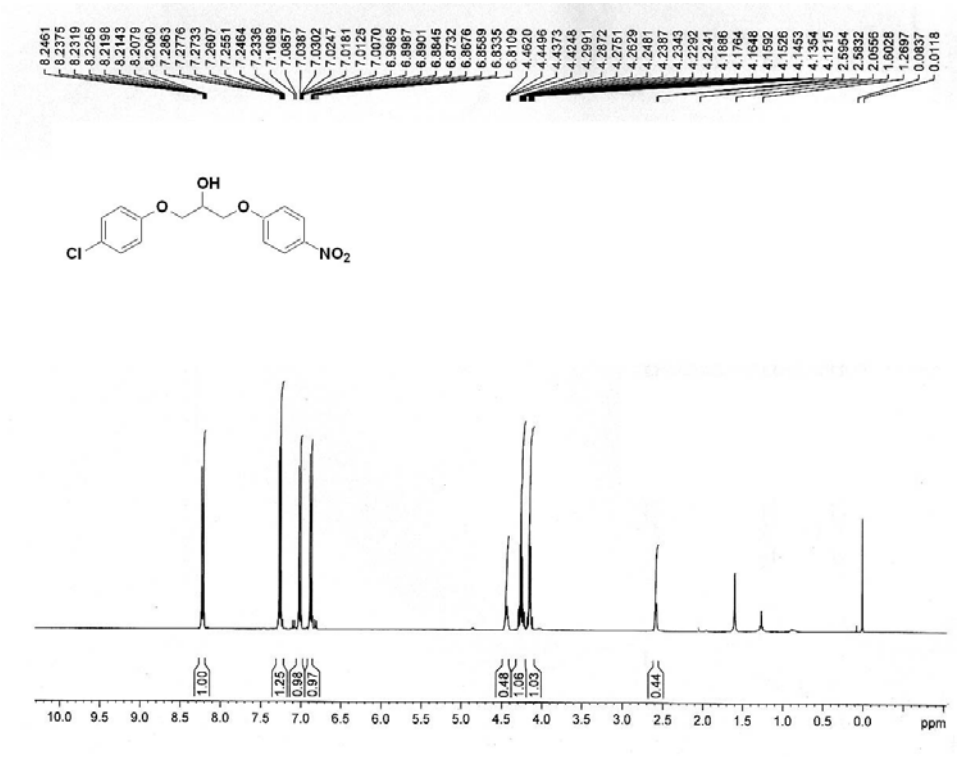
^{1}H NMR of 4-[3-(4-Chloro-phenoxy)-2-hydroxy-propoxy]-benzonitrile (Table 2, entry 7)



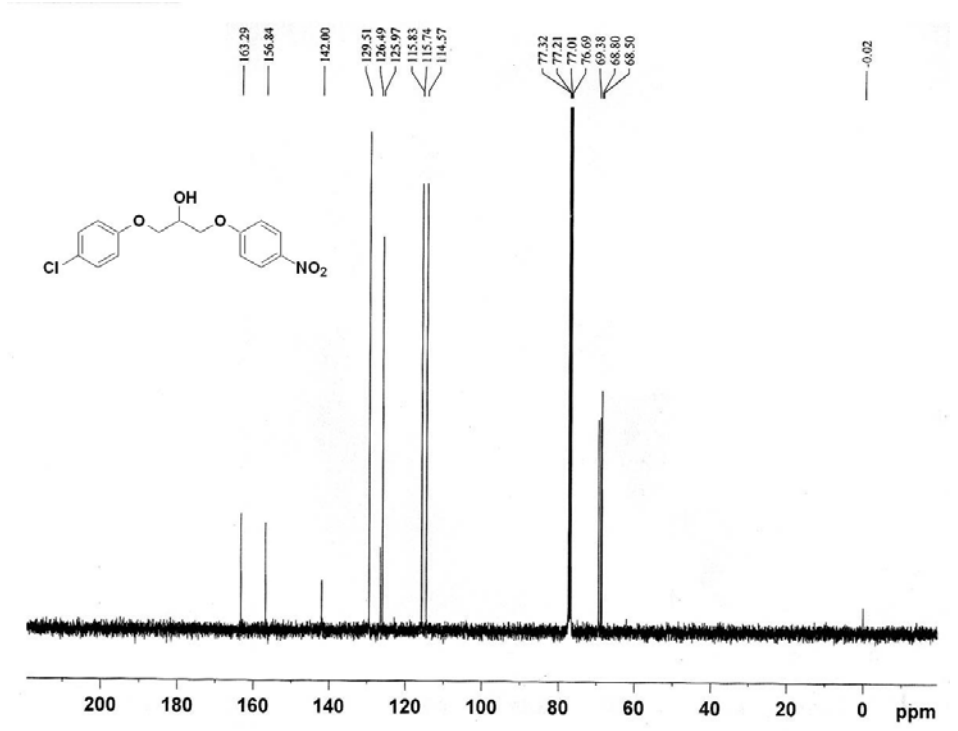
^{13}C NMR of 4-[3-(4-Chloro-phenoxy)-2-hydroxy-propoxy]-benzonitrile (Table 2, entry 7)



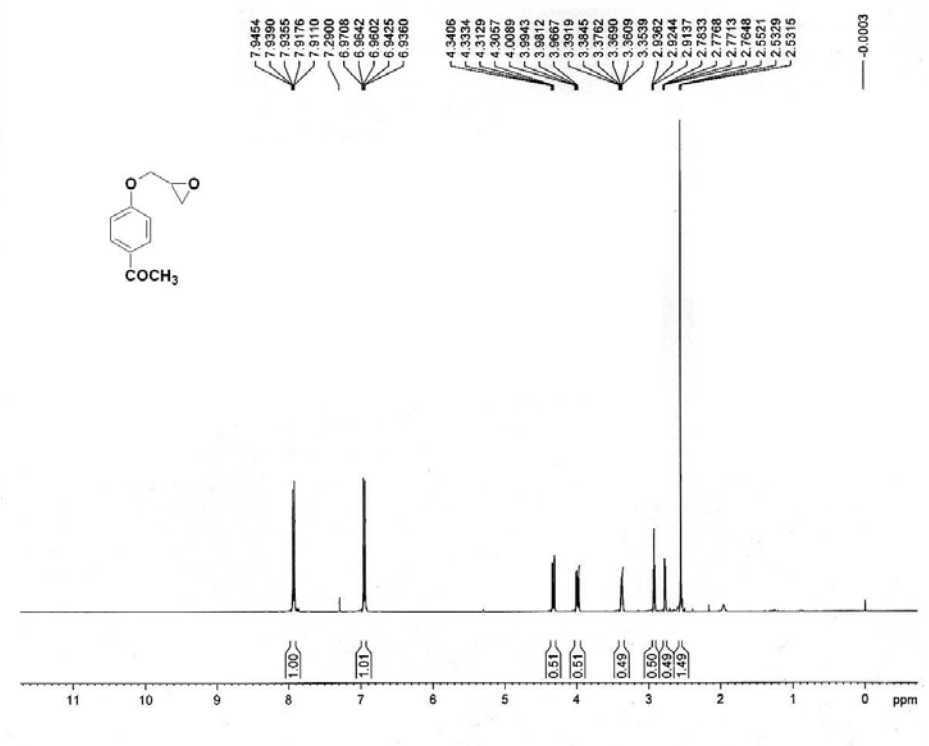
^{1}H NMR of 1-(4-Chloro-phenoxy)-3-(4-nitro-phenoxy)-propan-2-ol (Table 2, entry 8)



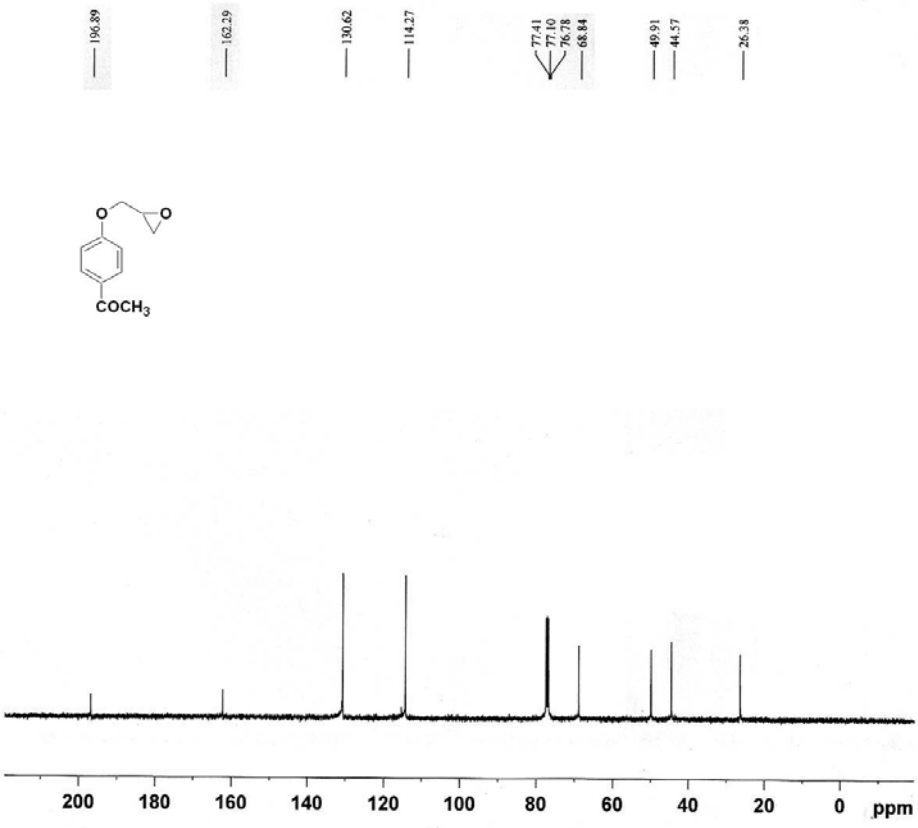
^{13}C NMR of 1-(4-Chloro-phenoxy)-3-(4-nitro-phenoxy)-propan-2-ol (Table 2, entry 8)



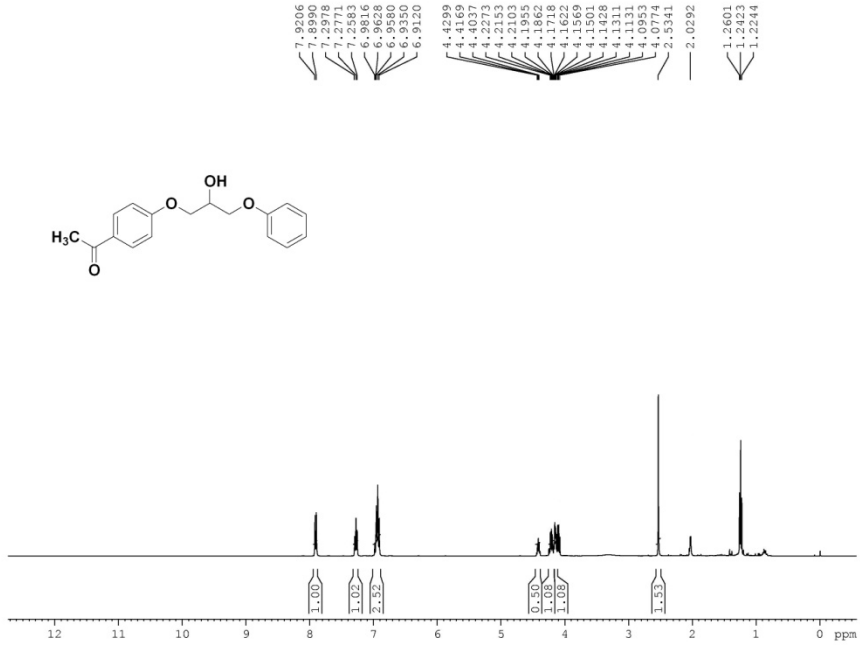
^{1}H NMR of 1-(4-Oxiranyl-phenyl)-ethanone (Starting epoxide of Table 2, entries 9 – 12)



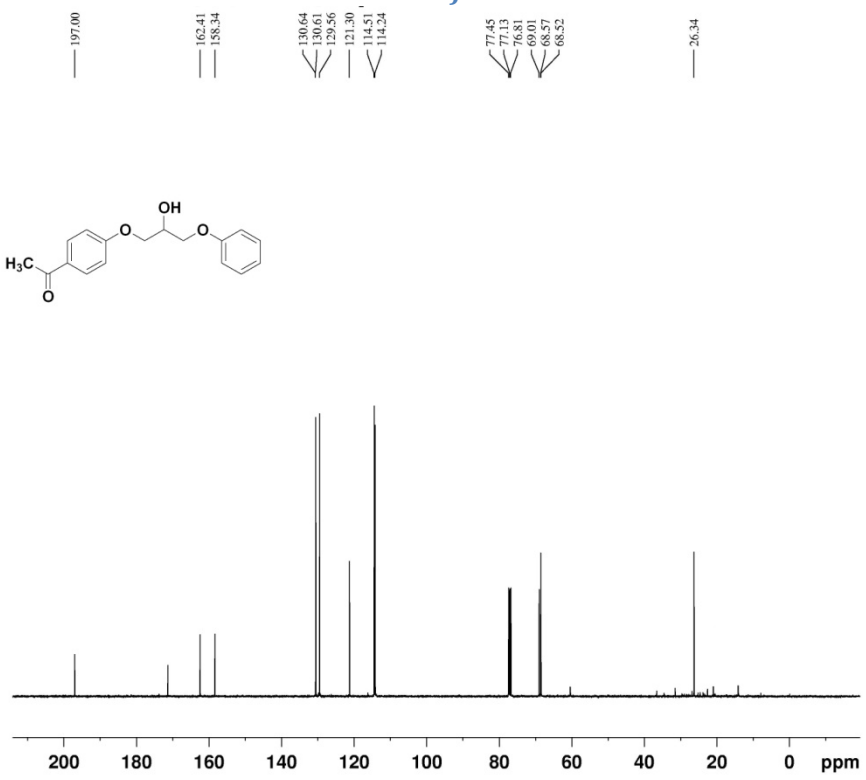
^{13}C NMR of 1-(4-Oxiranyl-phenyl)-ethanone (Starting epoxide of Table 2, entries 9 – 12)



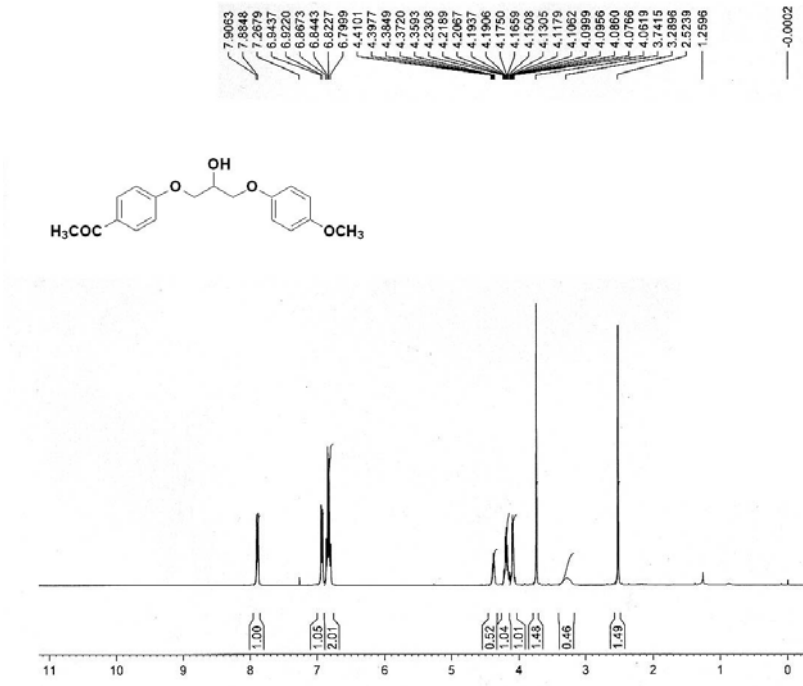
^{1}H NMR of 1-[4-(2-Hydroxy-3-phenoxy-propoxy)-phenyl]-ethanone (Table 2, entry 9 & entry 18)



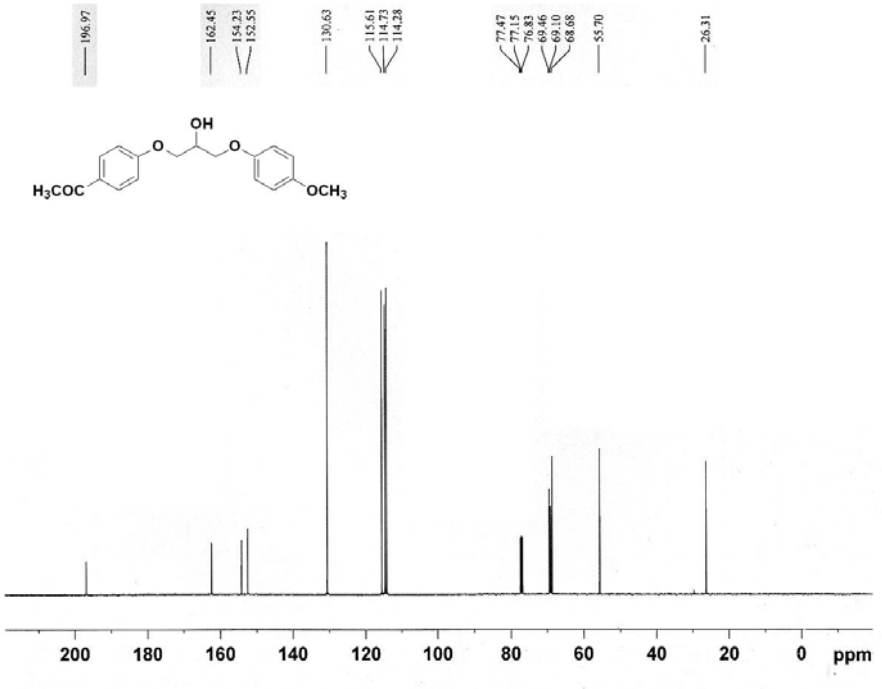
^{13}C NMR of 1-[4-(2-Hydroxy-3-phenoxy-propoxy)-phenyl]-ethanone (Table 2, entry 9 & entry 18)



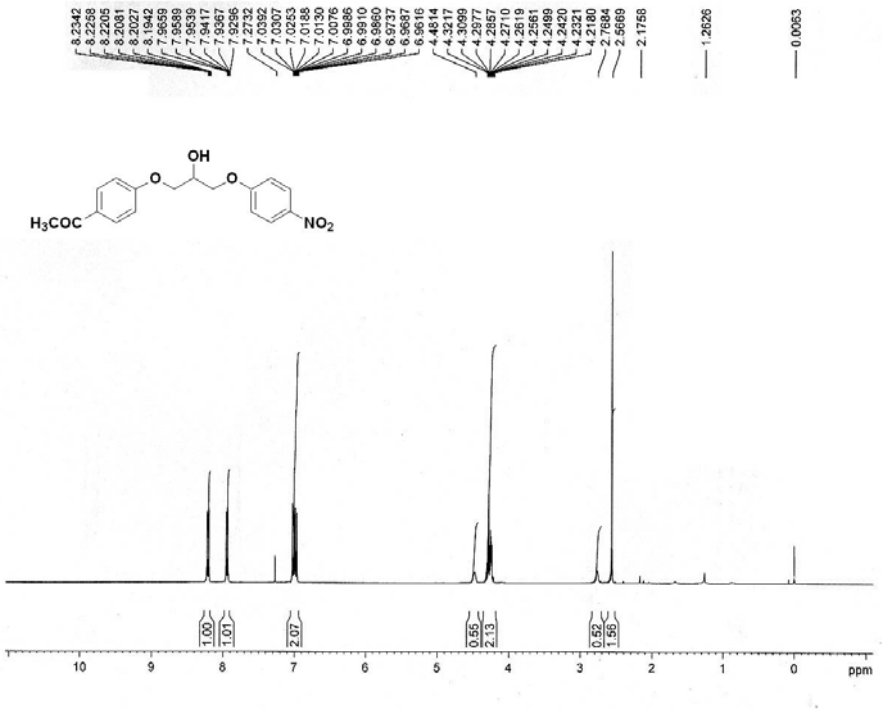
^{1}H NMR of 1-{4-[2-Hydroxy-3-(4-methoxy-phenoxy)-propoxy]-phenyl}-ethanone (Table 2, entry 10)



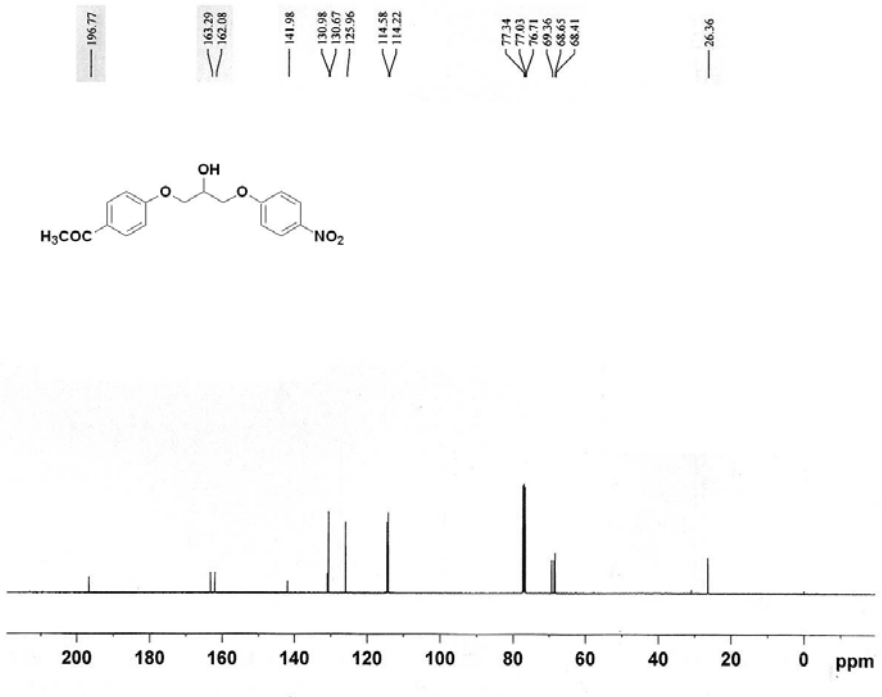
^{13}C NMR of 1-{4-[2-Hydroxy-3-(4-methoxy-phenoxy)-propoxy]-phenyl}-ethanone (Table 2, entry 10)



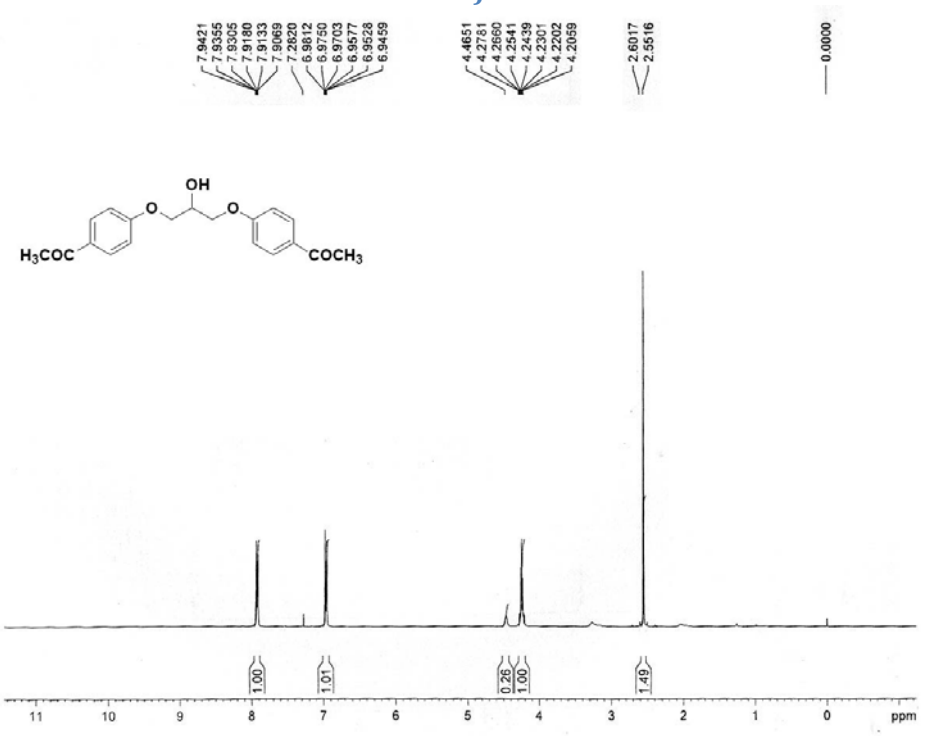
^{1}H NMR of 1-{4-[2-Hydroxy-3-(4-nitro-phenoxy)-propoxy]-phenyl}-ethanone (Table 2, entry 11)



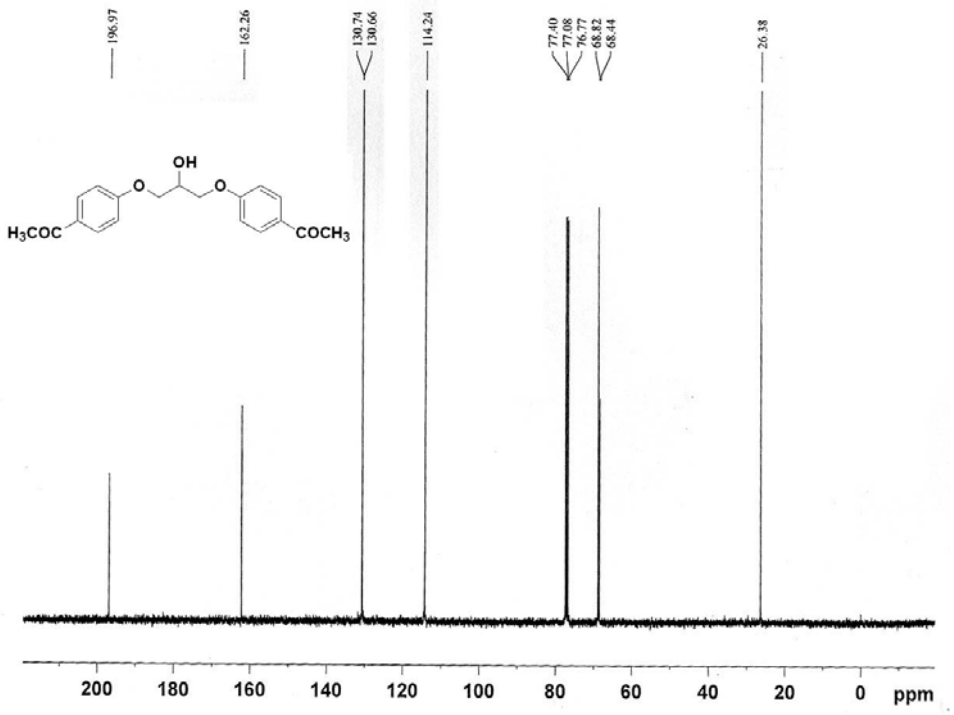
^{13}C NMR of 1-{4-[2-Hydroxy-3-(4-nitro-phenoxy)-propoxy]-phenyl}-ethanone (Table 2, entry 11)



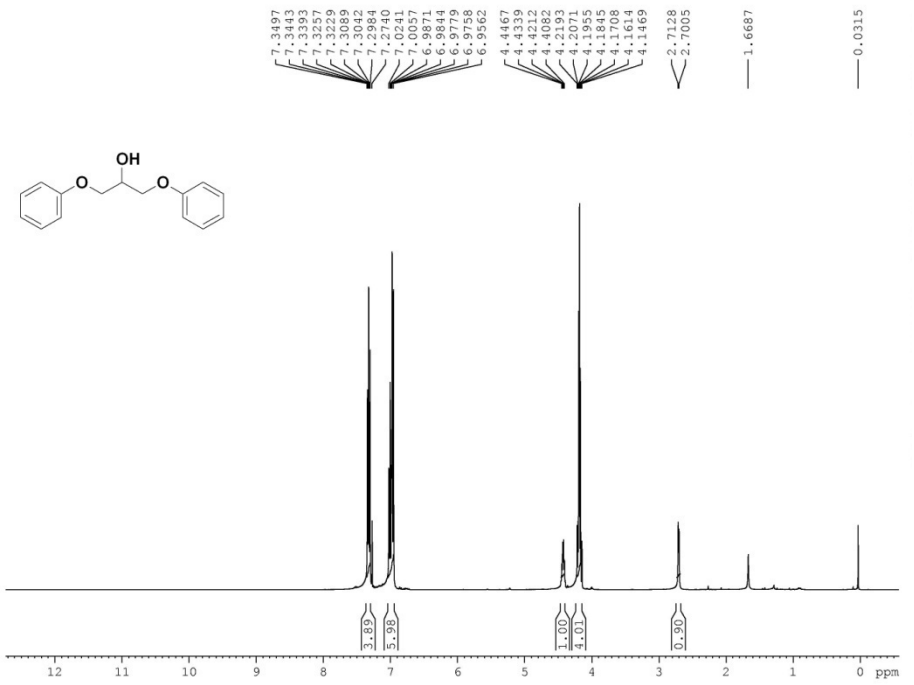
^{1}H NMR of 1-{4-[3-(4-Acetyl-phenoxy)-2-hydroxy-propoxy]-phenyl}-ethanone (Table 2, entry 12)



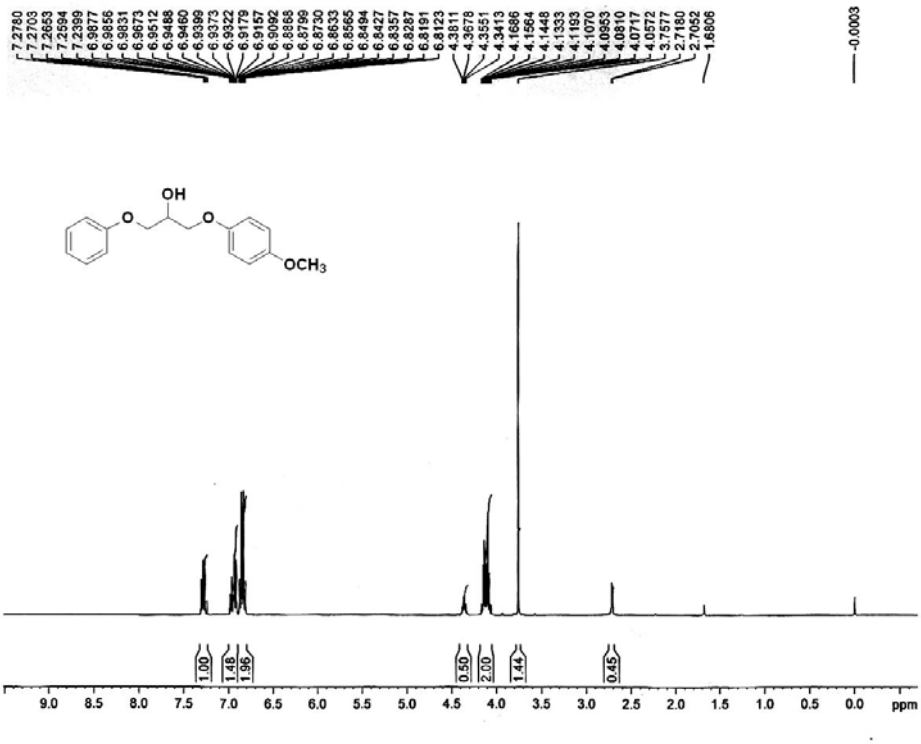
^{13}C NMR of 1-{4-[3-(4-Acetyl-phenoxy)-2-hydroxy-propoxy]-phenyl}-ethanone (Table 2, entry 12)



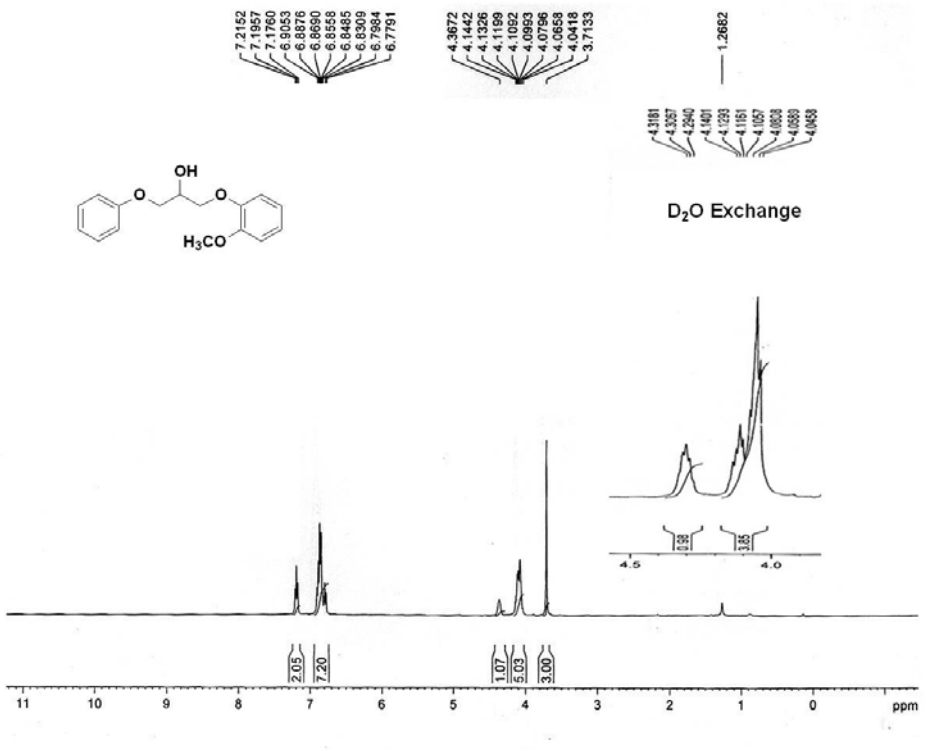
^{1}H NMR of 1,3-Diphenoxy-propan-2-ol (Table 2, entry 13)



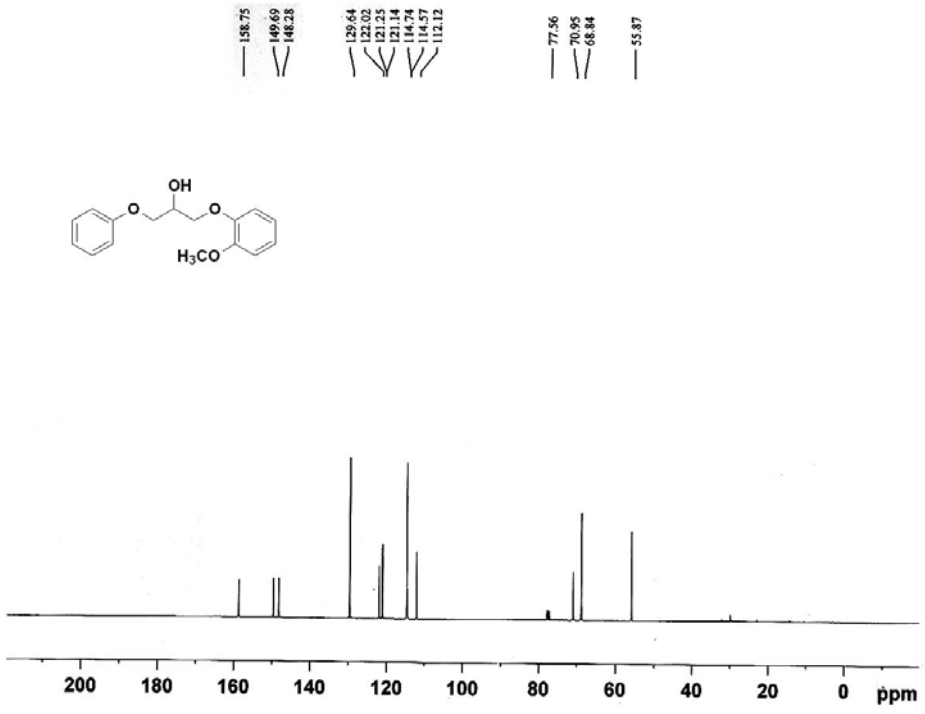
^{1}H NMR of 1-(4-Methoxy-phenoxy)-3-phenoxy-propan-2-ol (Table 2, entry 14)



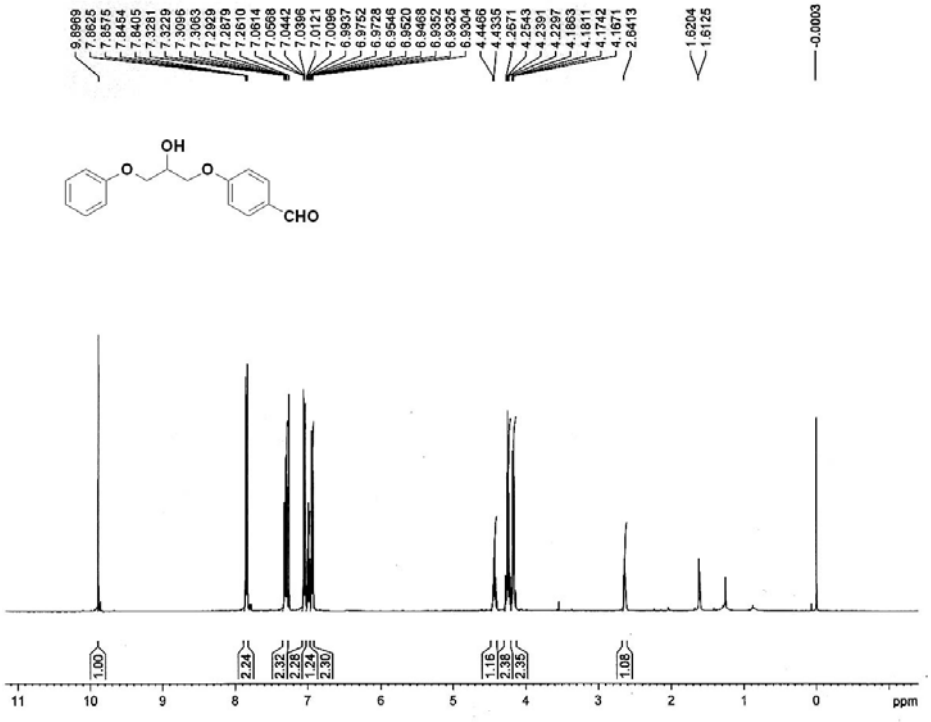
^{1}H NMR of 1-(2-Methoxy-phenoxy)-3-phenoxy-propan-2-ol (Table 2, entry 15)



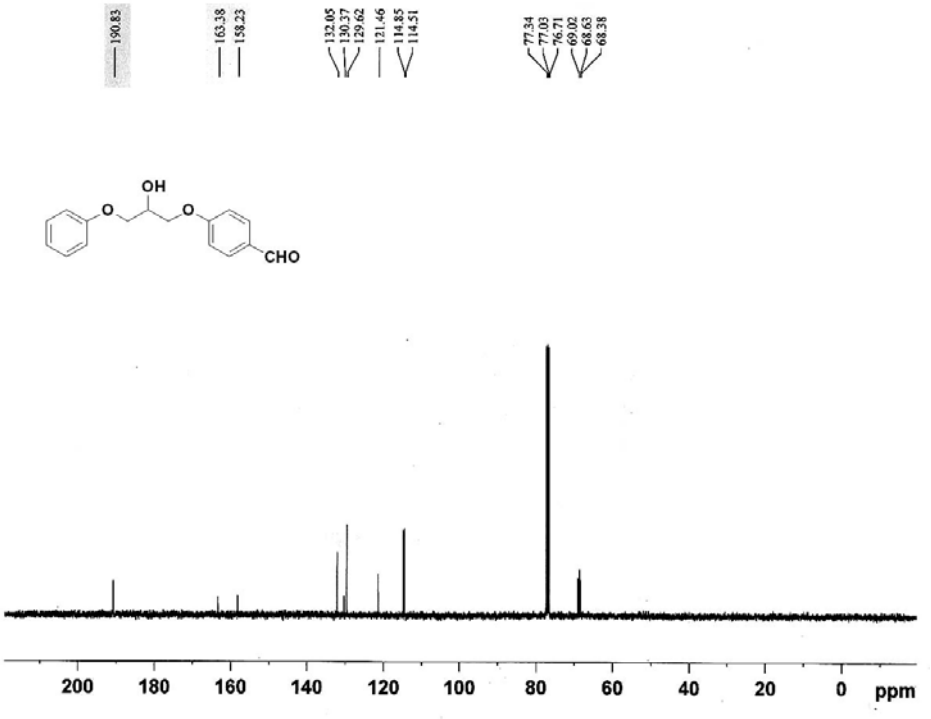
^{13}C NMR of 1-(2-Methoxy-phenoxy)-3-phenoxy-propan-2-ol (Table 2, entry 15)



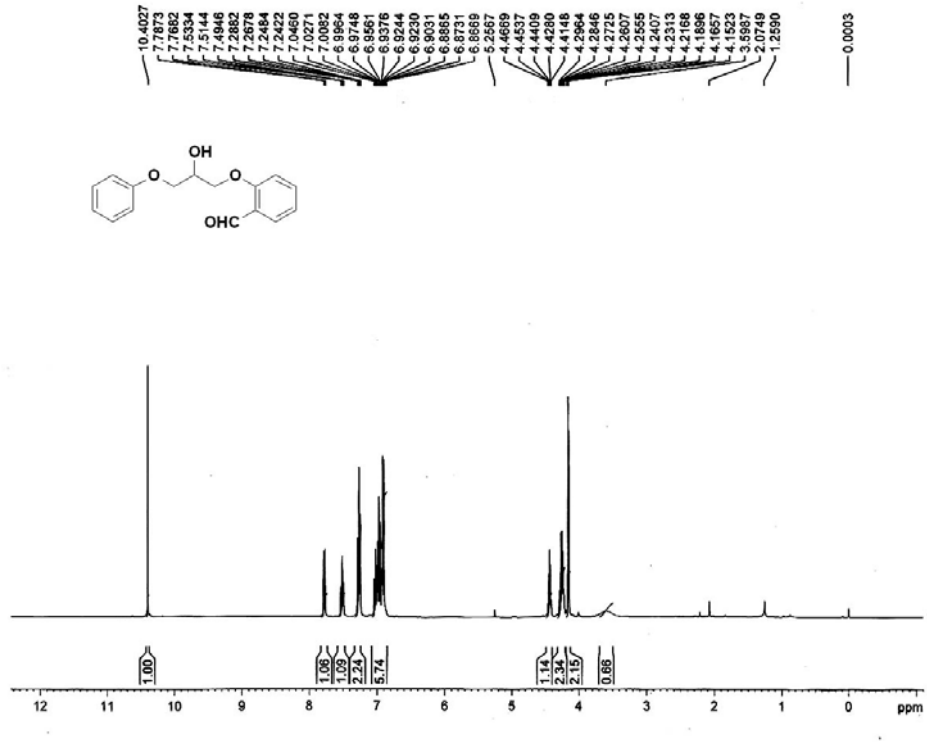
^{1}H NMR of 4-(2-Hydroxy-3-phenoxy-propoxy)-benzaldehyde (Table 2, entry 16)



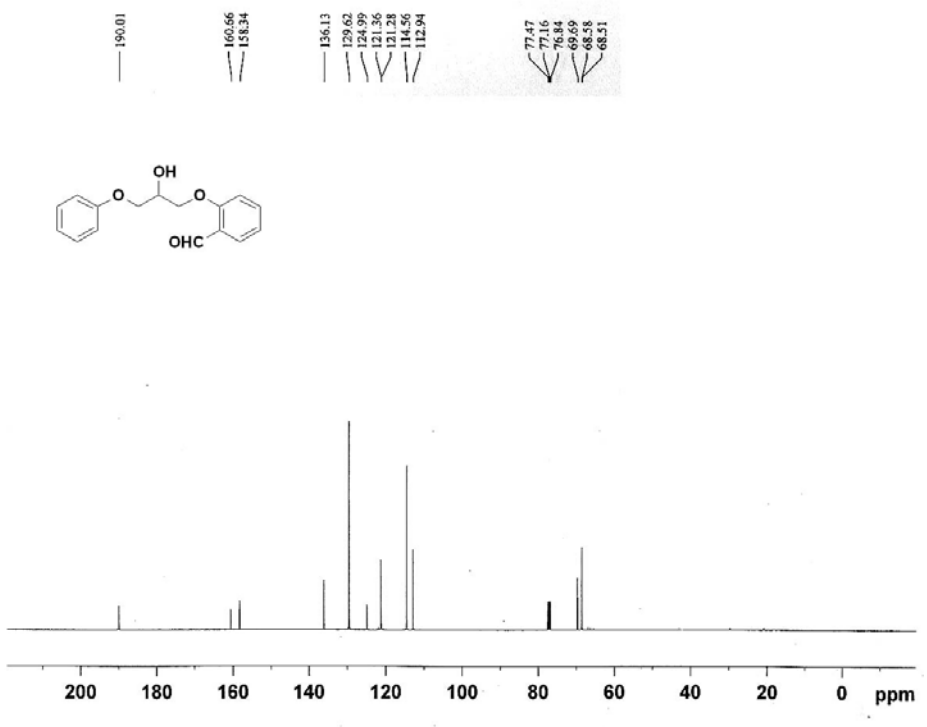
^{13}C NMR of 4-(2-Hydroxy-3-phenoxy-propoxy)-benzaldehyde (Table 2, entry 16)



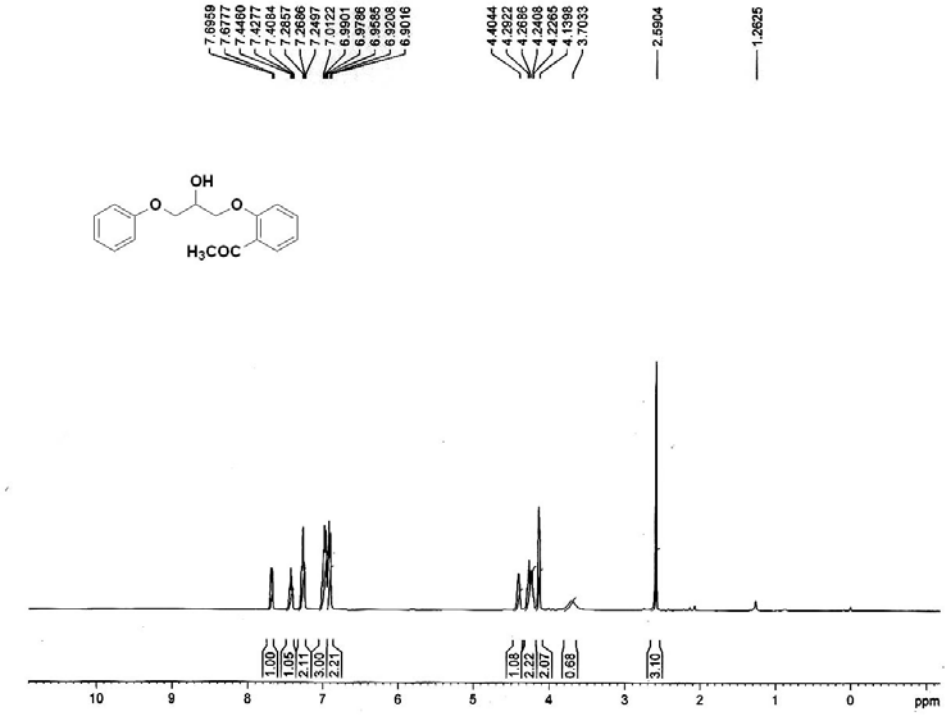
^{1}H NMR of 2-(2-Hydroxy-3-phenoxy-propoxy)-benzaldehyde (Table 2, entry 17)



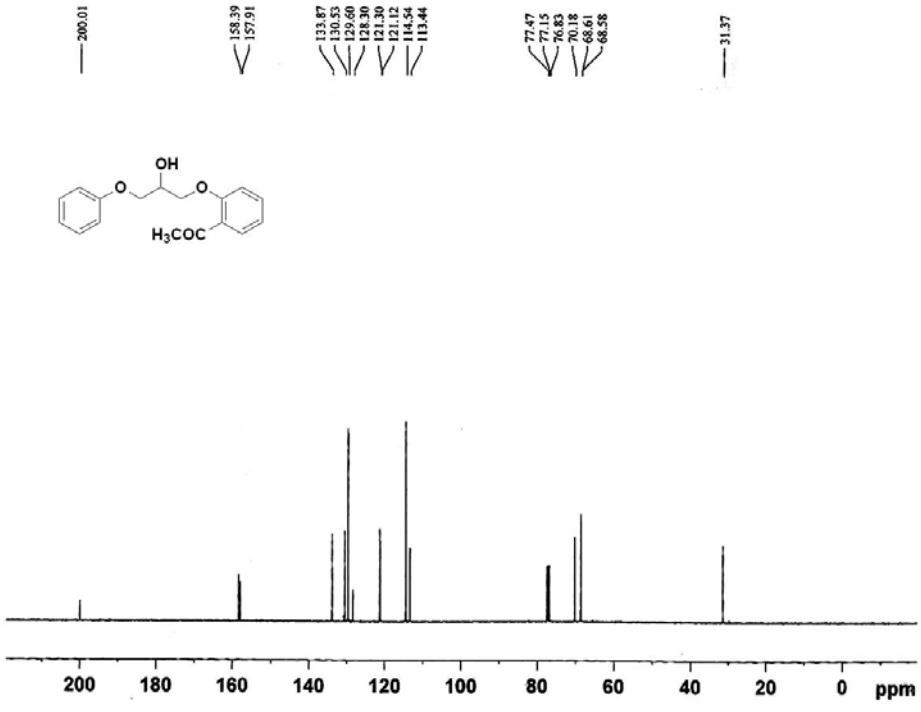
^{13}C NMR of 2-(2-Hydroxy-3-phenoxy-propoxy)-benzaldehyde (Table 2, entry 17)



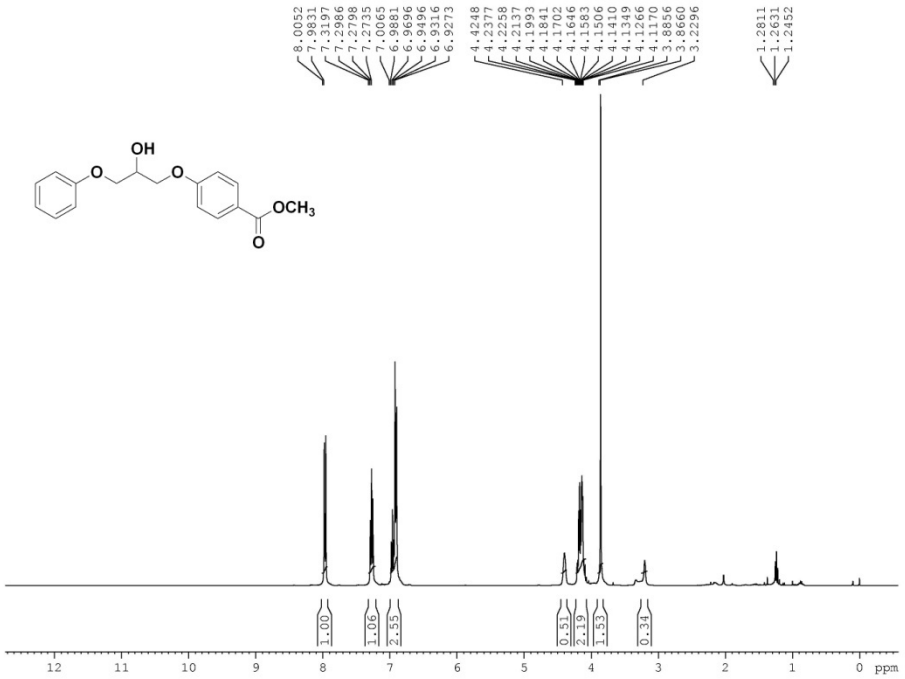
^{1}H NMR of 1-[2-(2-Hydroxy-3-phenoxy-propoxy)-phenyl]-ethanone (Table 2, entry 19)



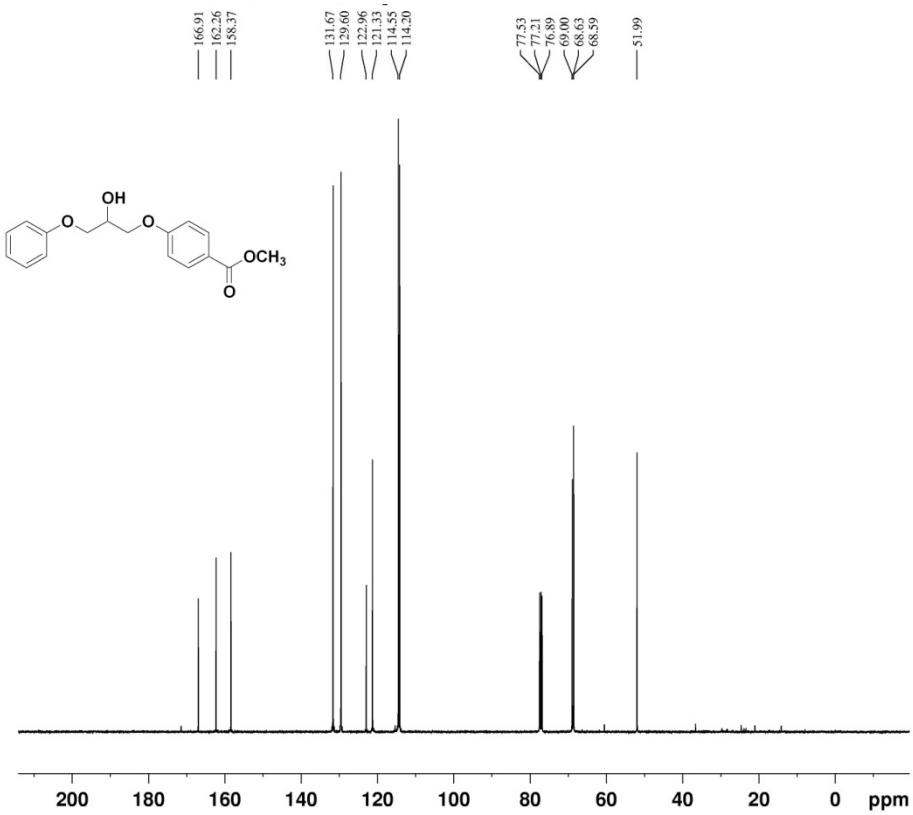
^{13}C NMR of 1-[2-(2-Hydroxy-3-phenoxy-propoxy)-phenyl]-ethanone (Table 2, entry 19)



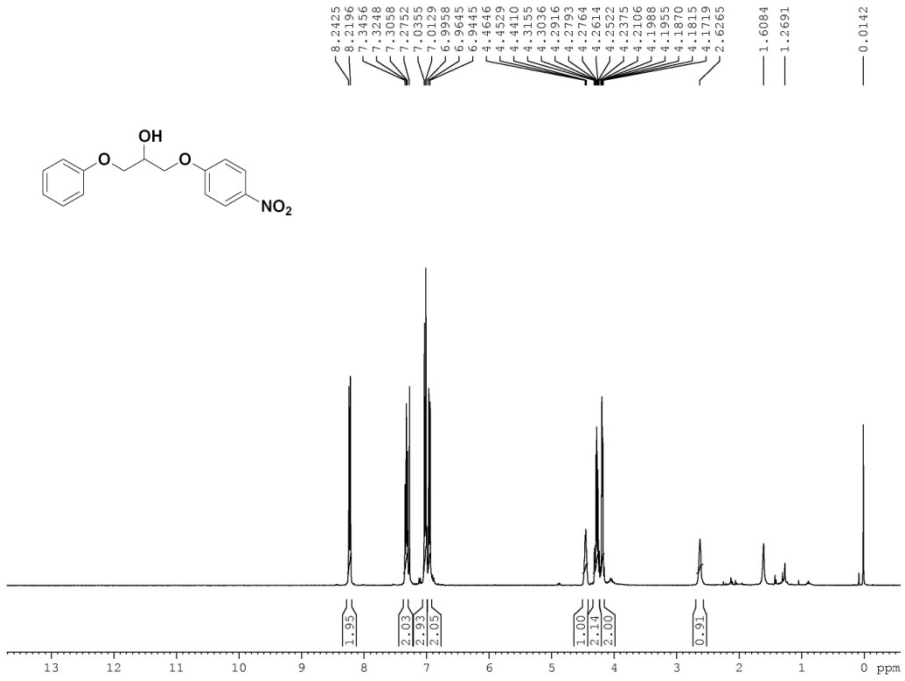
^{1}H NMR of 4-(2-Hydroxy-3-phenoxy-propoxy)-benzoic acid methyl ester (Table 2, entry 20)



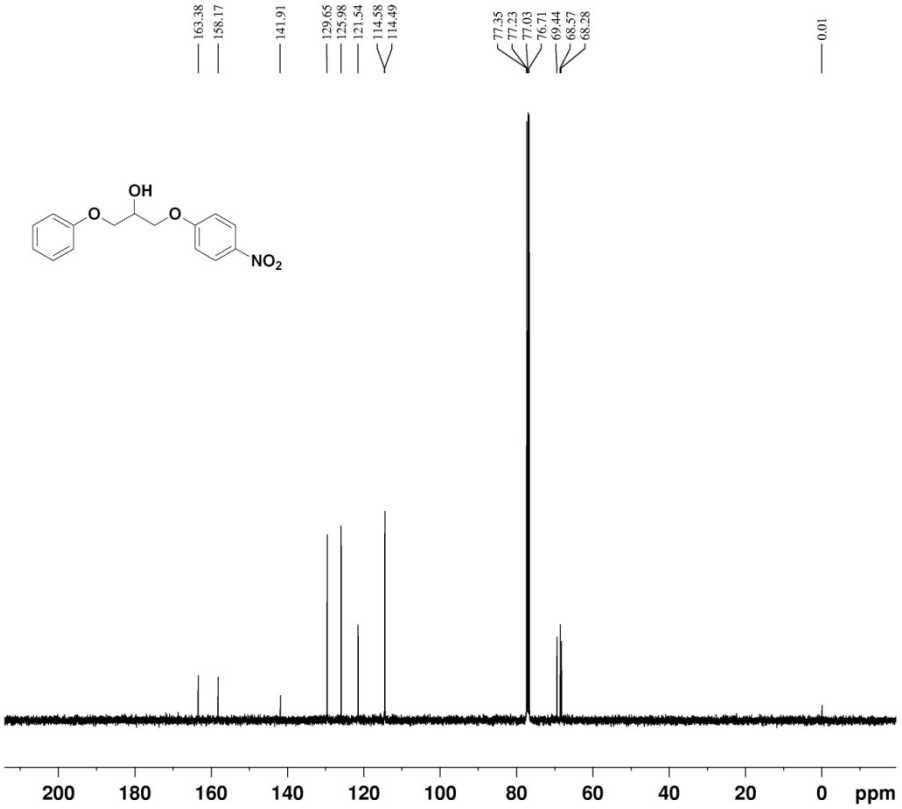
^{13}C NMR of 4-(2-Hydroxy-3-phenoxy-propoxy)-benzoic acid methyl ester (Table 2, entry 20)



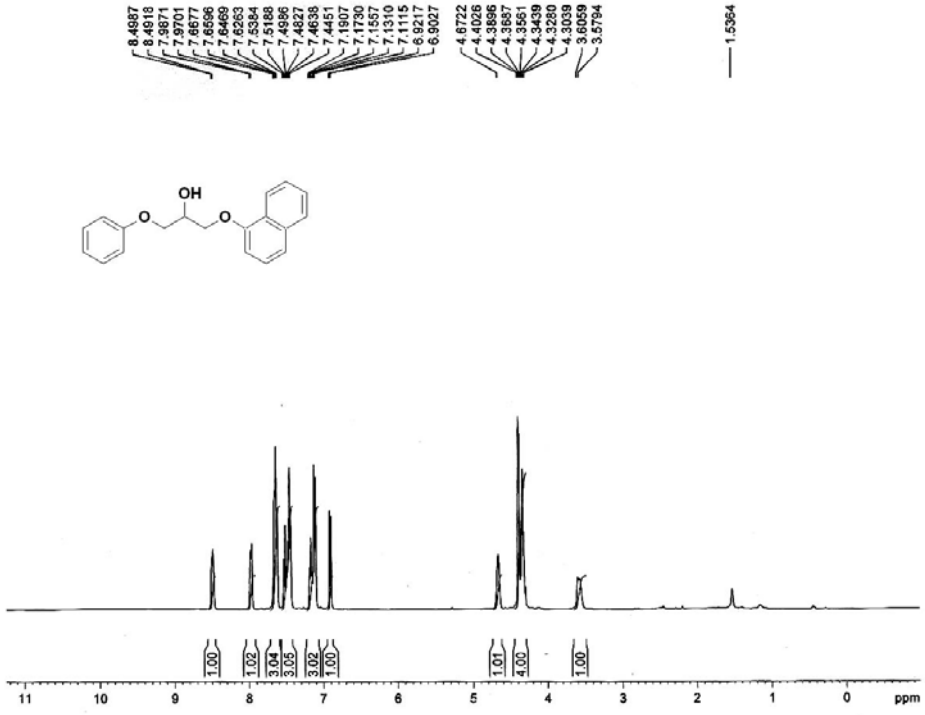
^{1}H NMR of 1-(4-Nitro-phenoxy)-3-phenoxy-propan-2-ol (Table 2, entry 21)



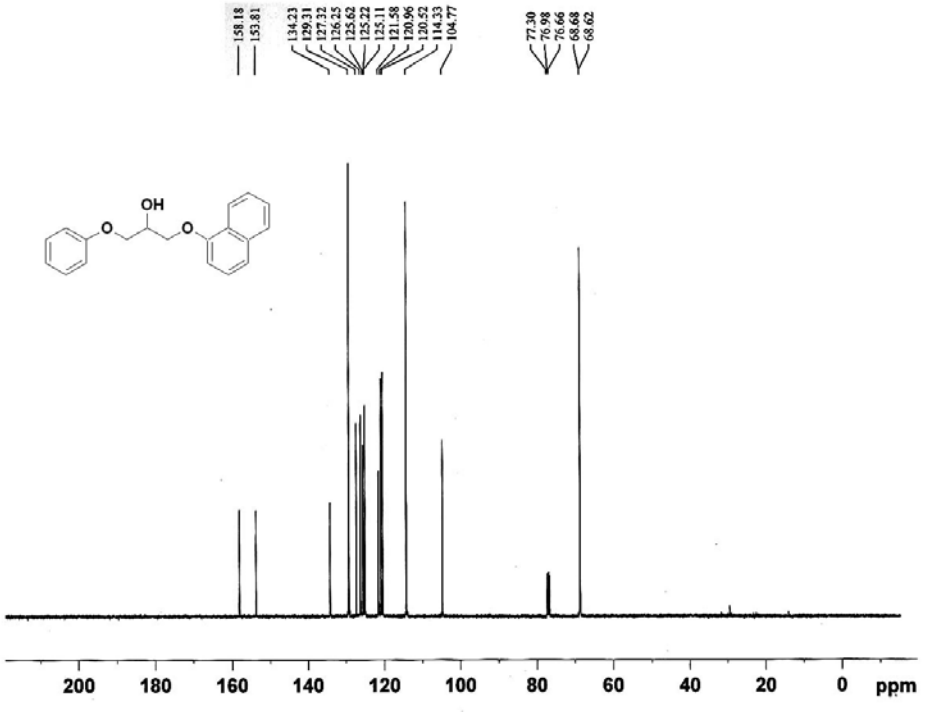
^{13}C NMR of 1-(4-Nitro-phenoxy)-3-phenoxy-propan-2-ol (Table 2, entry 21)



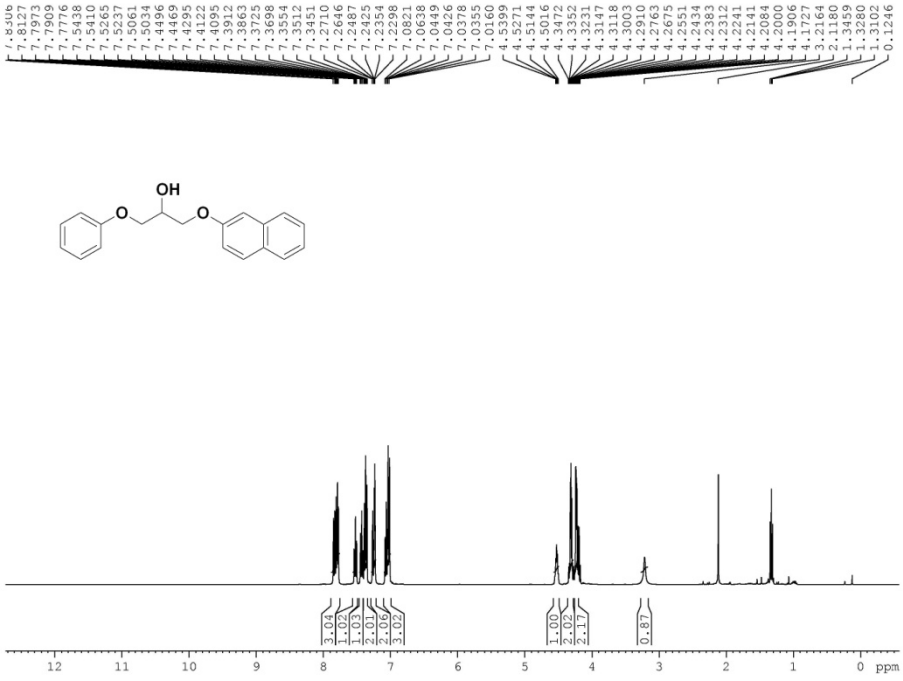
^{1}H NMR of 1-(Naphthalen-1-yloxy)-3-phenoxy-propan-2-ol (Table 2, entry 22)



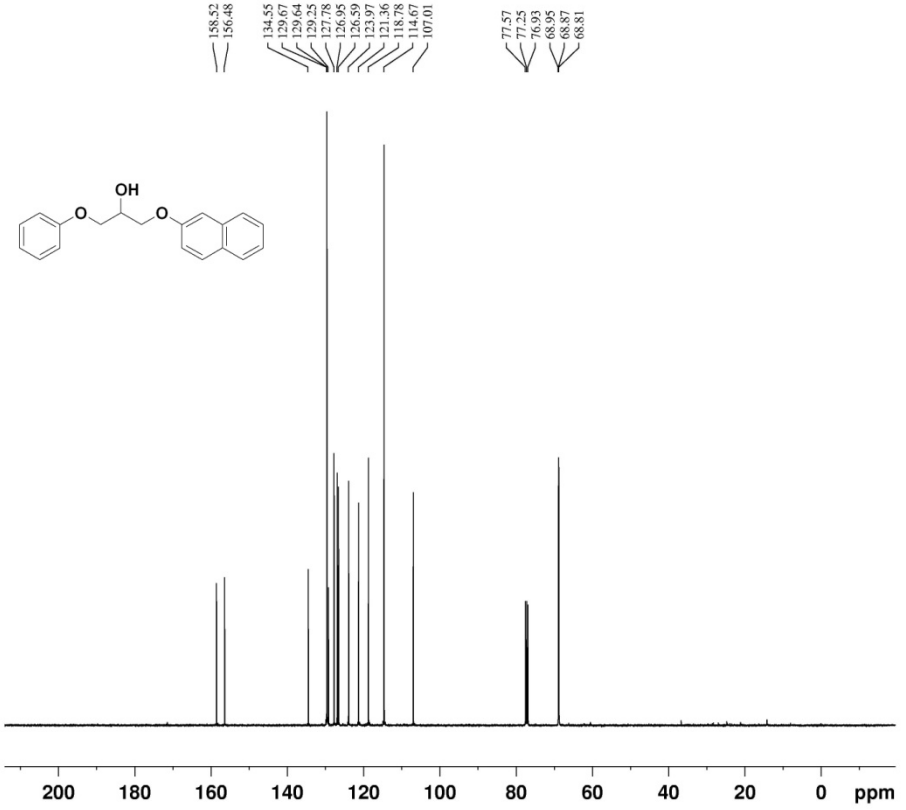
^{13}C NMR of 1-(Naphthalen-1-yloxy)-3-phenoxy-propan-2-ol (Table 2, entry 22)



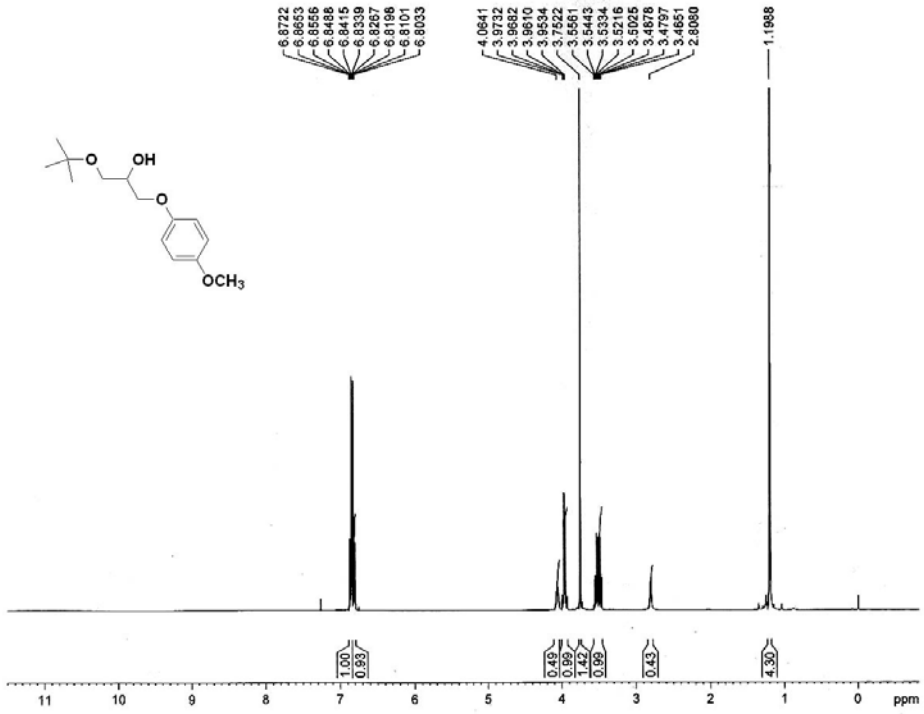
^{1}H NMR of 1-(Naphthalen-2-yloxy)-3-phenoxy-propan-2-ol (Table 2, entry 23)



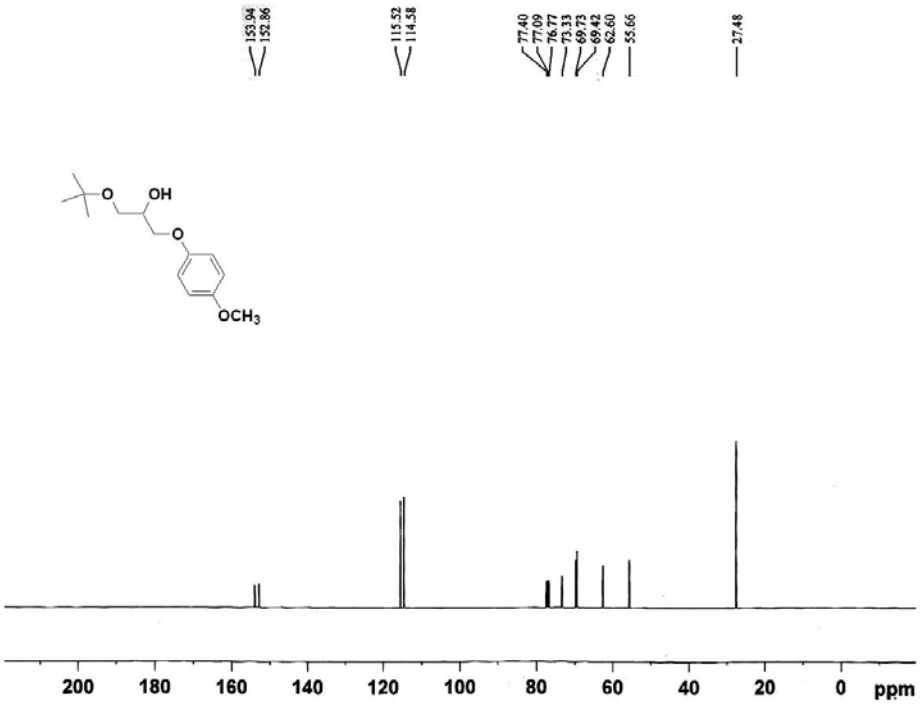
^{13}C NMR of 1-(Naphthalen-2-yloxy)-3-phenoxy-propan-2-ol (Table 2, entry 23)



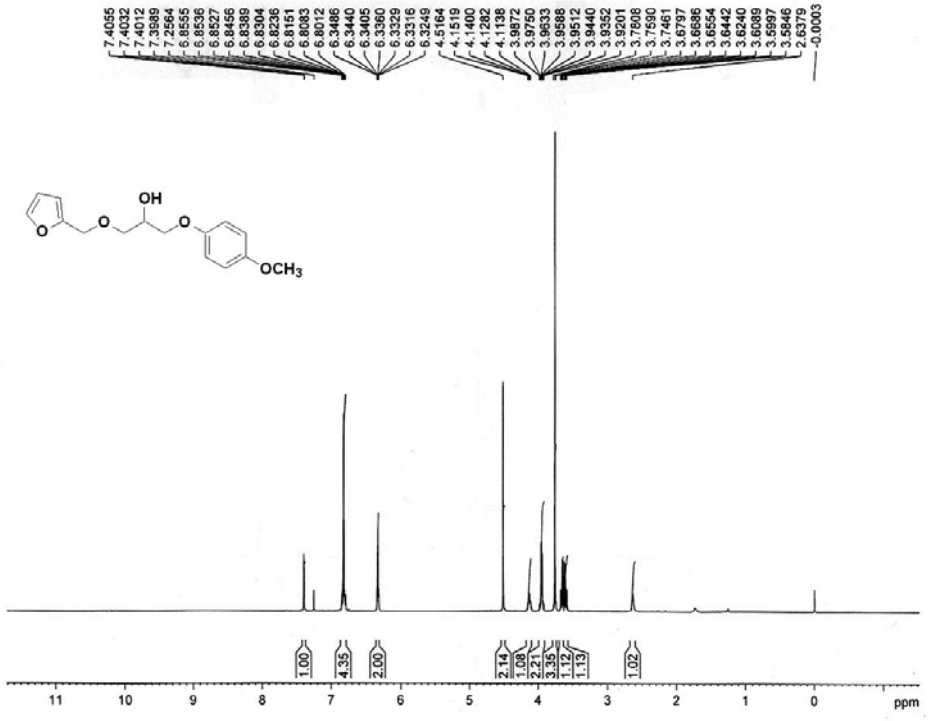
^{1}H NMR of 1-*tert*-Butoxy-3-(4-methoxy-phenoxy)-propan-2-ol (Table 2, entry 24)



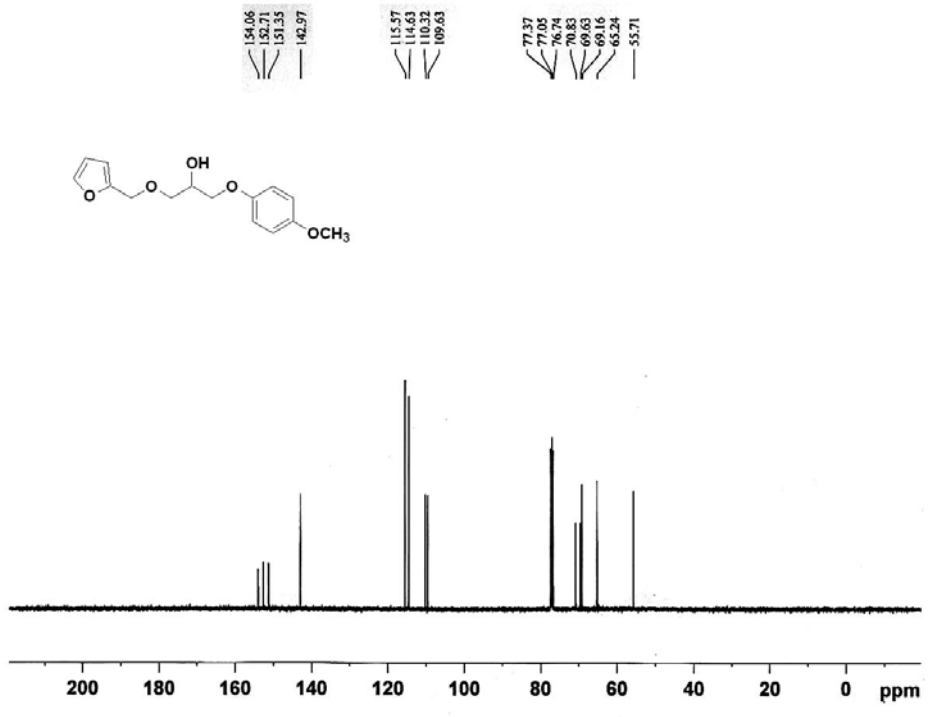
^{13}C NMR of 1-*tert*-Butoxy-3-(4-methoxy-phenoxy)-propan-2-ol (Table 2, entry 24)



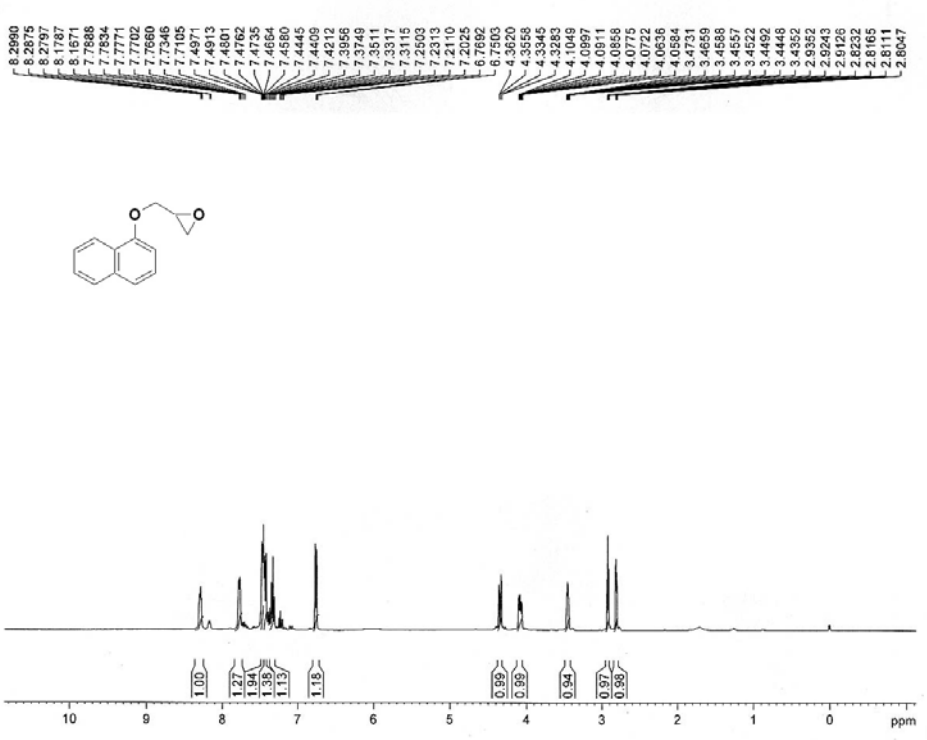
^{1}H NMR of 1-(Furan-2-ylmethoxy)-3-(4-methoxy-phenoxy)-propan-2-ol (Table 2, entry 25)



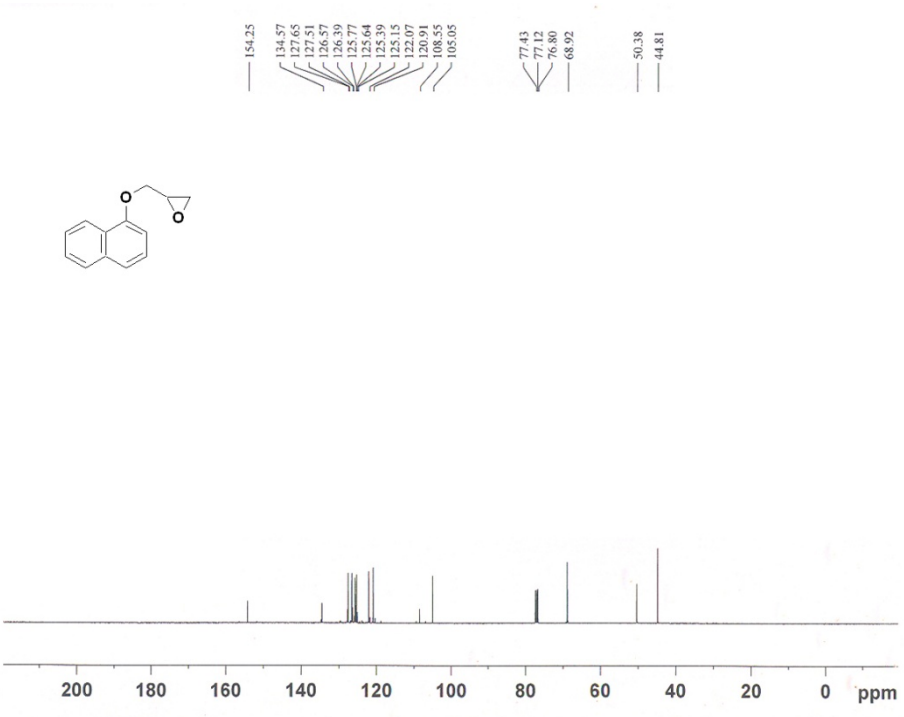
^{13}C NMR of 1-(Furan-2-ylmethoxy)-3-(4-methoxy-phenoxy)-propan-2-ol (Table 2, entry 25)



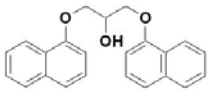
^{1}H NMR of 2-(Naphthalen-1-yloxymethyl)-oxirane (Starting epoxide of Table 2, entry 26)

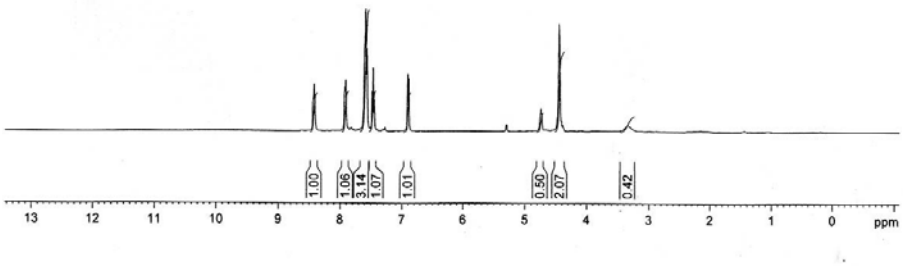


^{13}C NMR of 2-(Naphthalen-1-yloxymethyl)-oxirane (Starting epoxide of Table 2, entry 26)

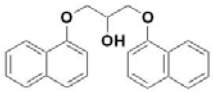


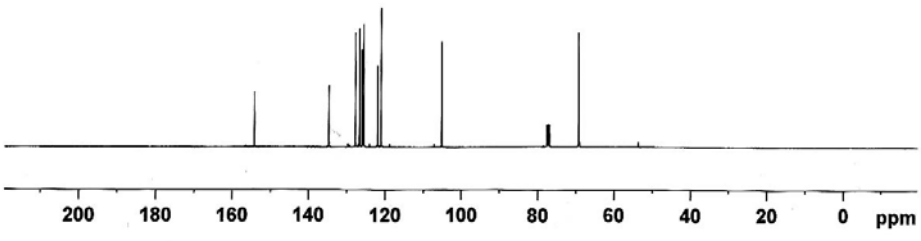
^{1}H NMR of 1,3-Bis-(naphthalen-1-yloxy)-propan-2-ol (Table 2, entry 26)



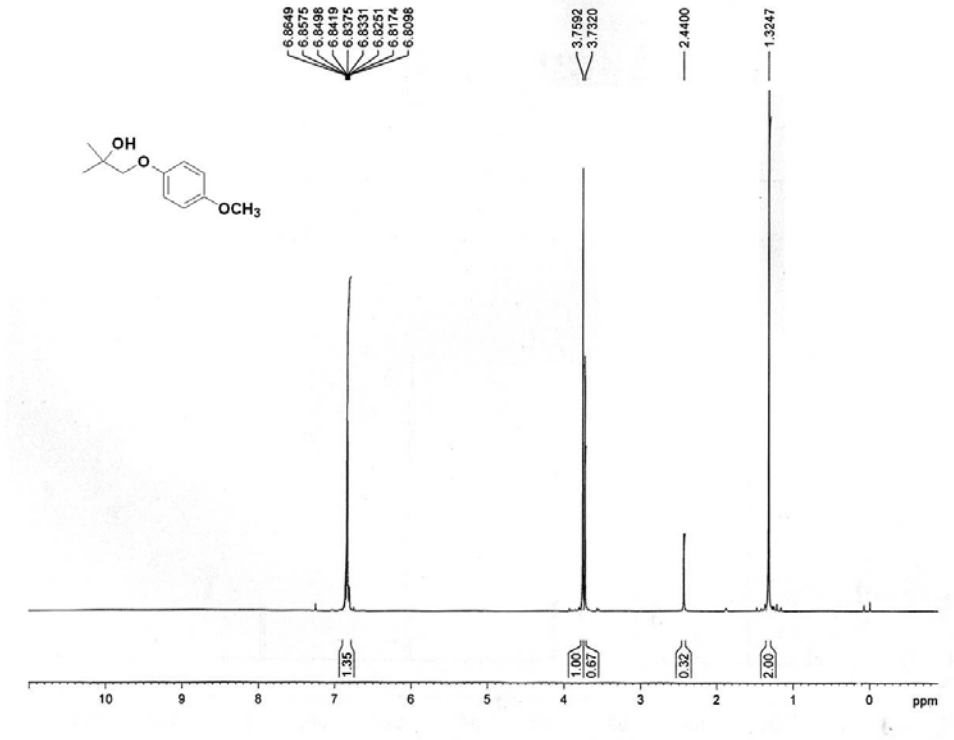


^{13}C NMR of 1,3-Bis-(naphthalen-1-yloxy)-propan-2-ol (Table 2, entry 26)

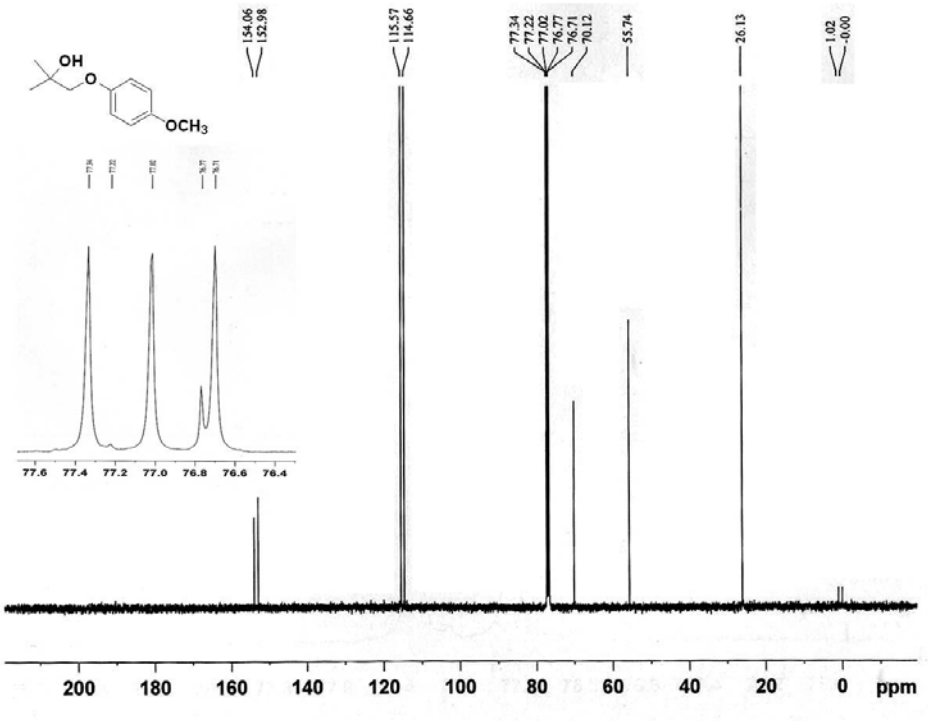




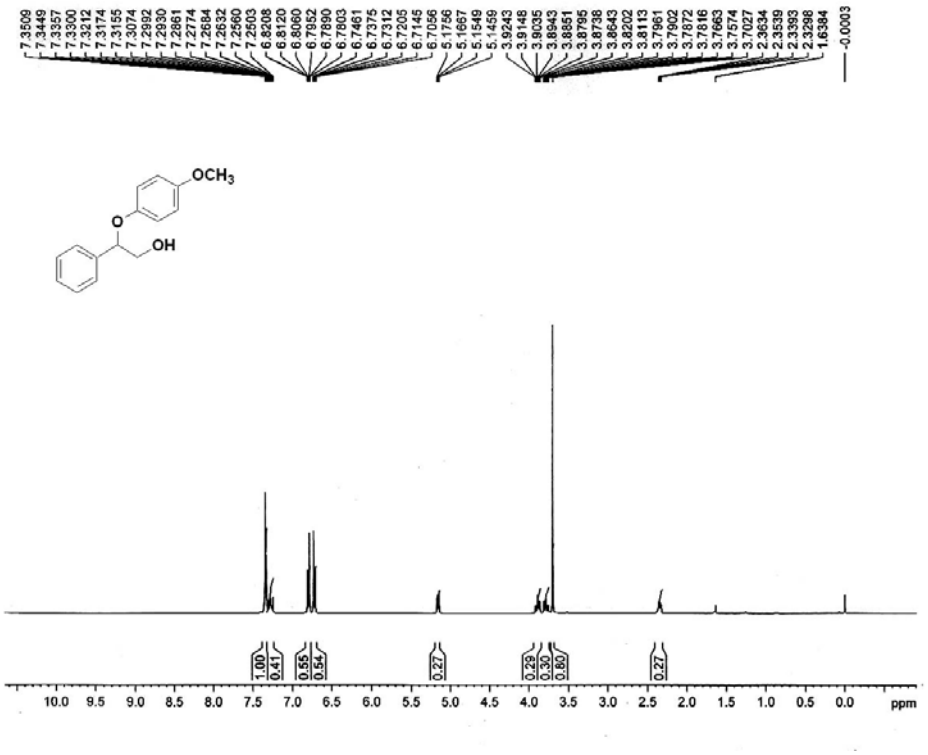
^{1}H NMR of 1-(4-Methoxy-phenoxy)-2-methyl-propan-2-ol (Table 2, entry 27)



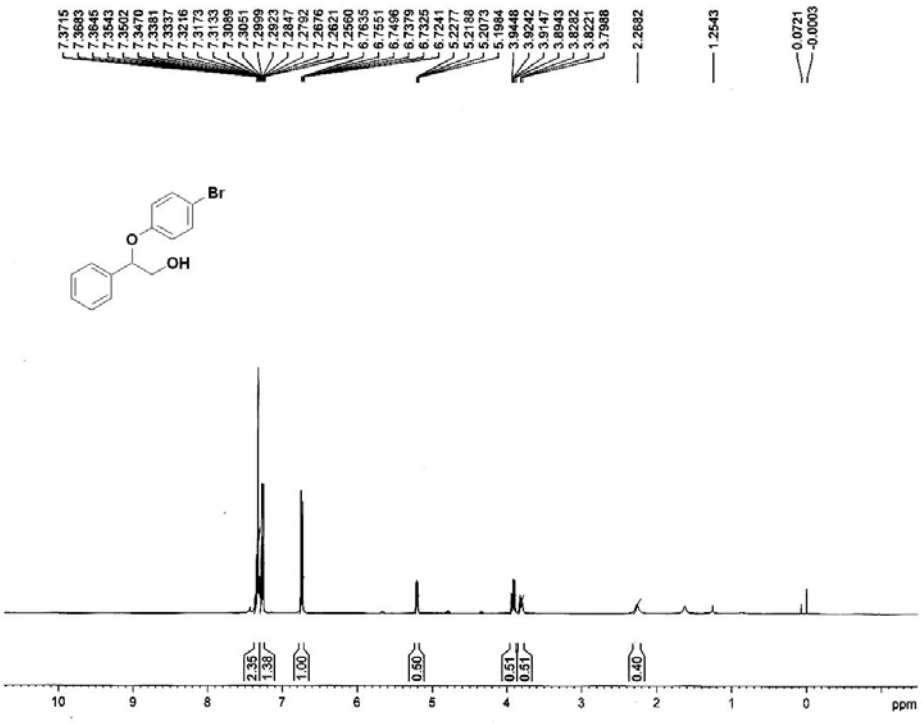
^{13}C NMR of 1-(4-Methoxy-phenoxy)-2-methyl-propan-2-ol (Table 2, entry 27)



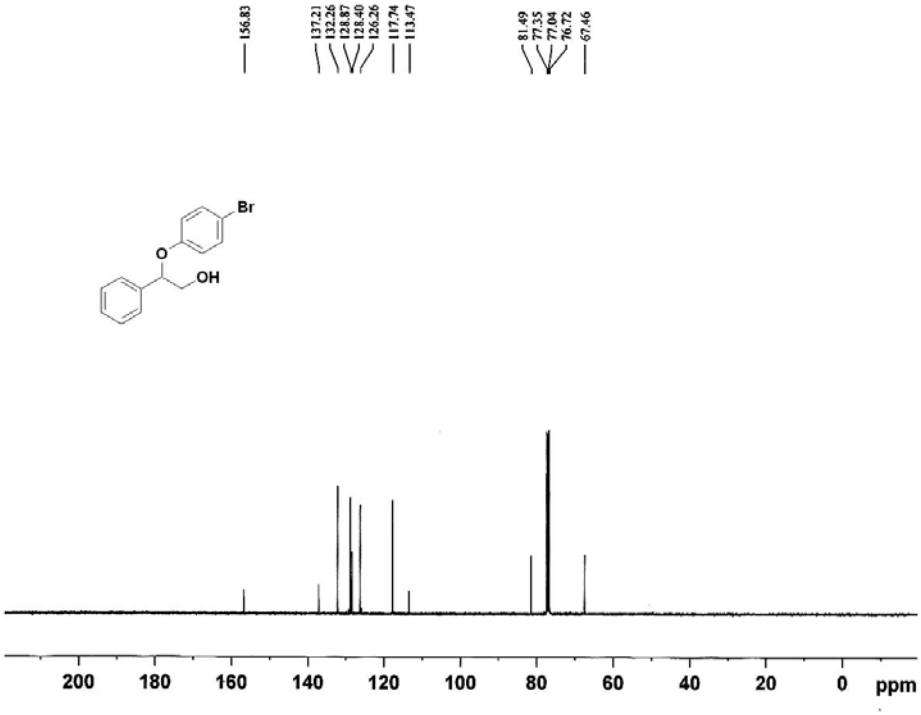
^{1}H NMR of 2-(4-Methoxy-phenoxy)-2-phenyl-ethanol (Table 3, entry 1)



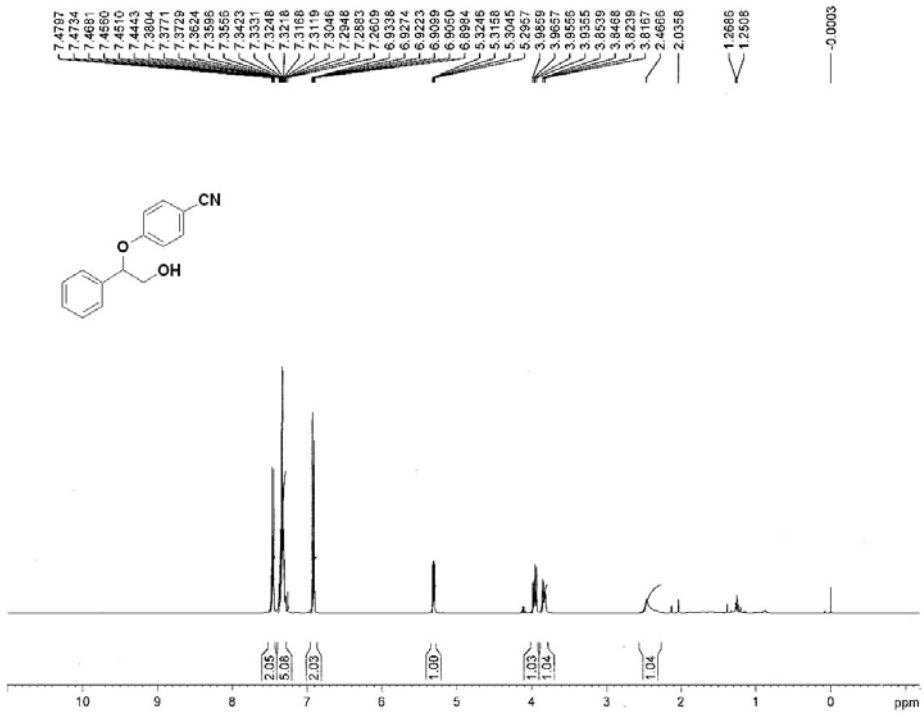
^{1}H NMR of 2-(4-Bromo-phenoxy)-2-phenyl-ethanol (Table 3, entry 2)



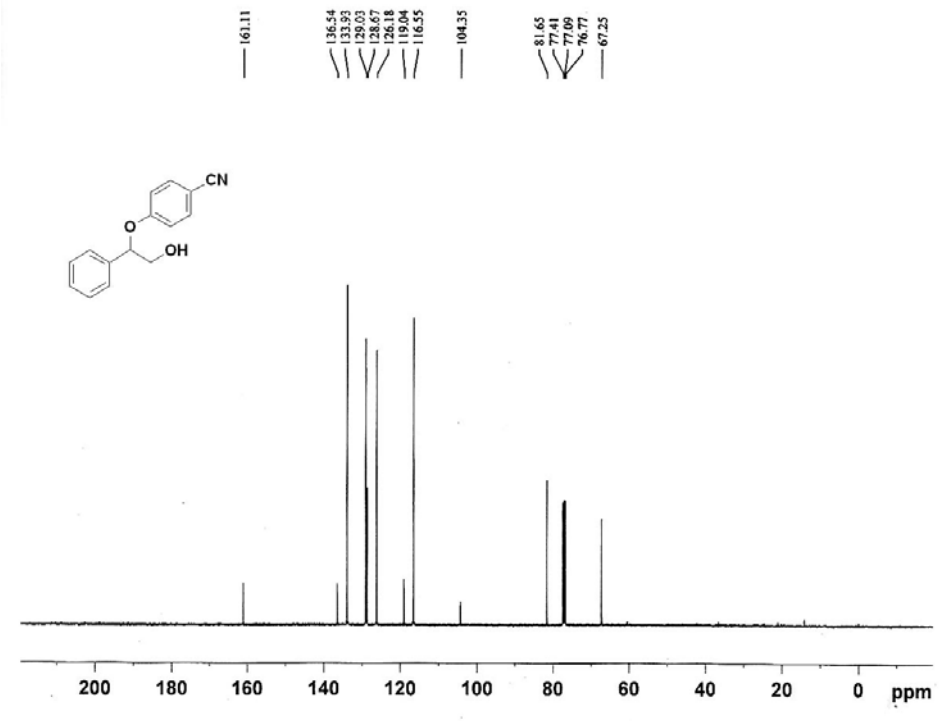
^{13}C NMR of 2-(4-Bromo-phenoxy)-2-phenyl-ethanol (Table 3, entry 2)



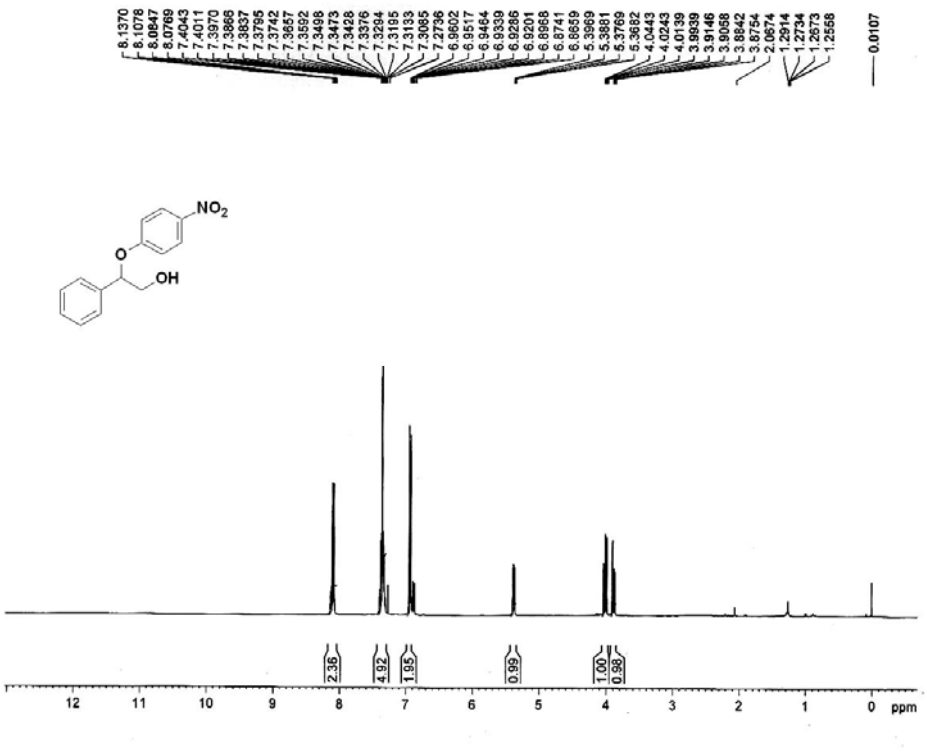
^{1}H NMR of 4-(2-Hydroxy-1-phenyl-ethoxy)-benzonitrile (Table 3, entry 3)



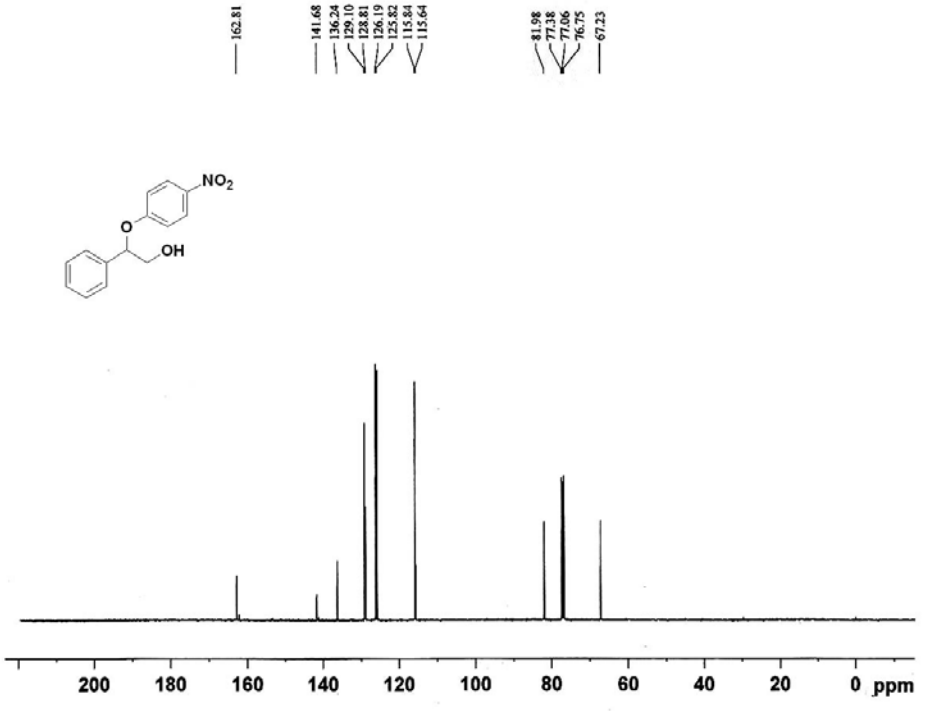
^{13}C NMR of 4-(2-Hydroxy-1-phenyl-ethoxy)-benzonitrile (Table 3, entry 3)



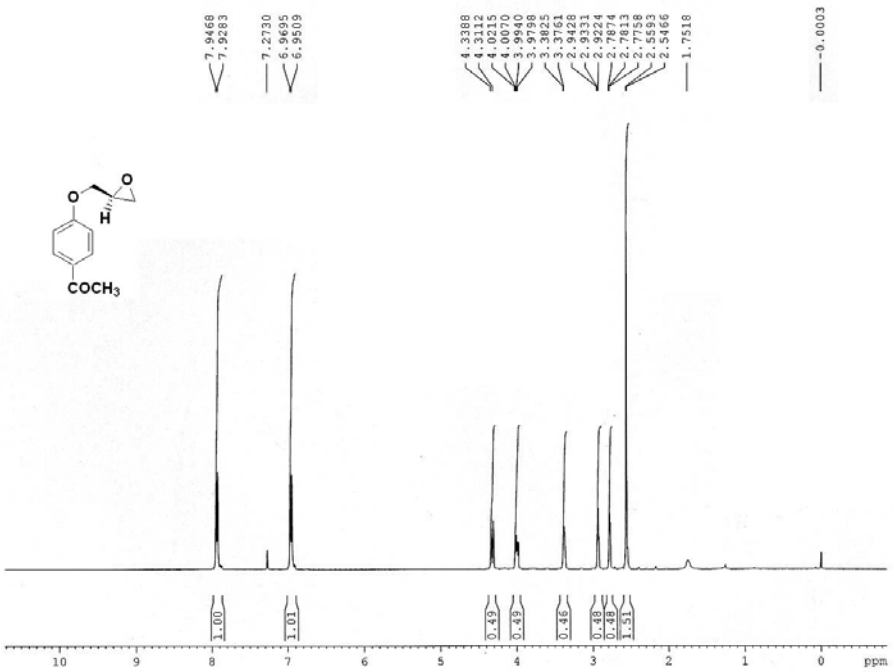
^{1}H NMR of 2-(4-Nitro-phenoxy)-2-phenyl-ethanol (Table 3, entry 4)



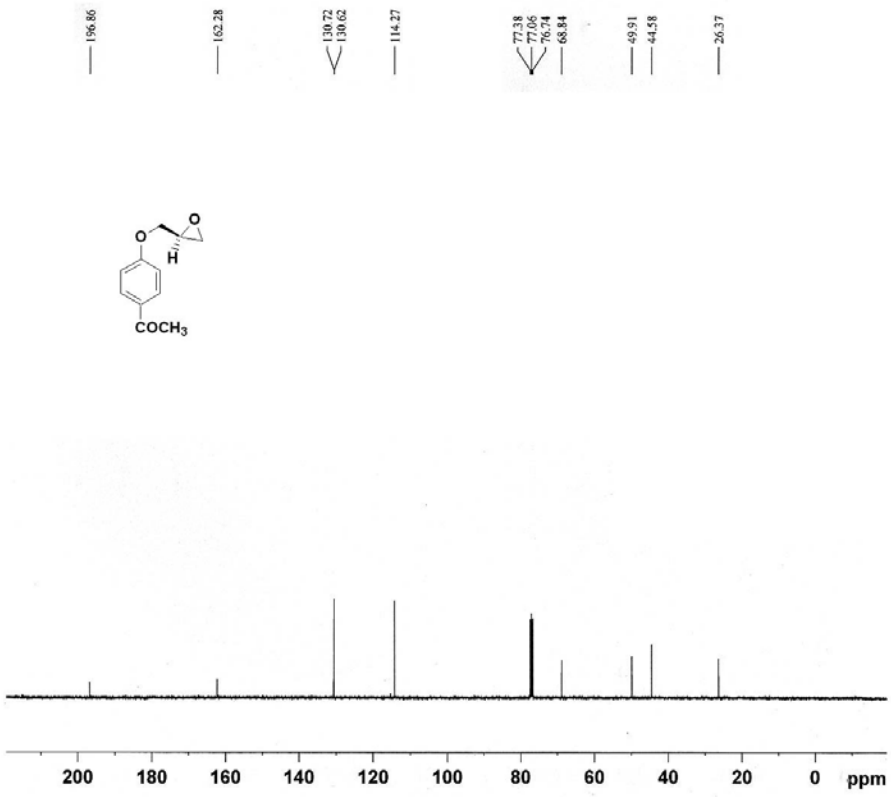
^{13}C NMR of 2-(4-Nitro-phenoxy)-2-phenyl-ethanol (Table 3, entry 4)



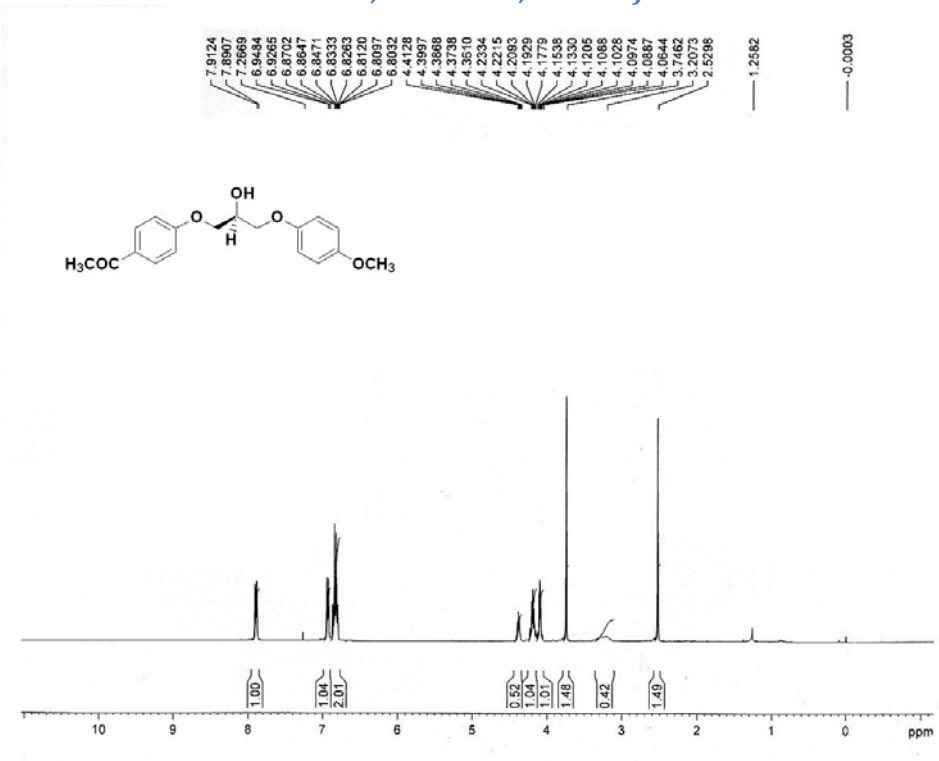
^{1}H NMR of (*S*) 1-(4-oxiranylmethoxy-phenyl)-ethanone (starting epoxide of entries 10 & 11, footnotes c & d, Table 2)



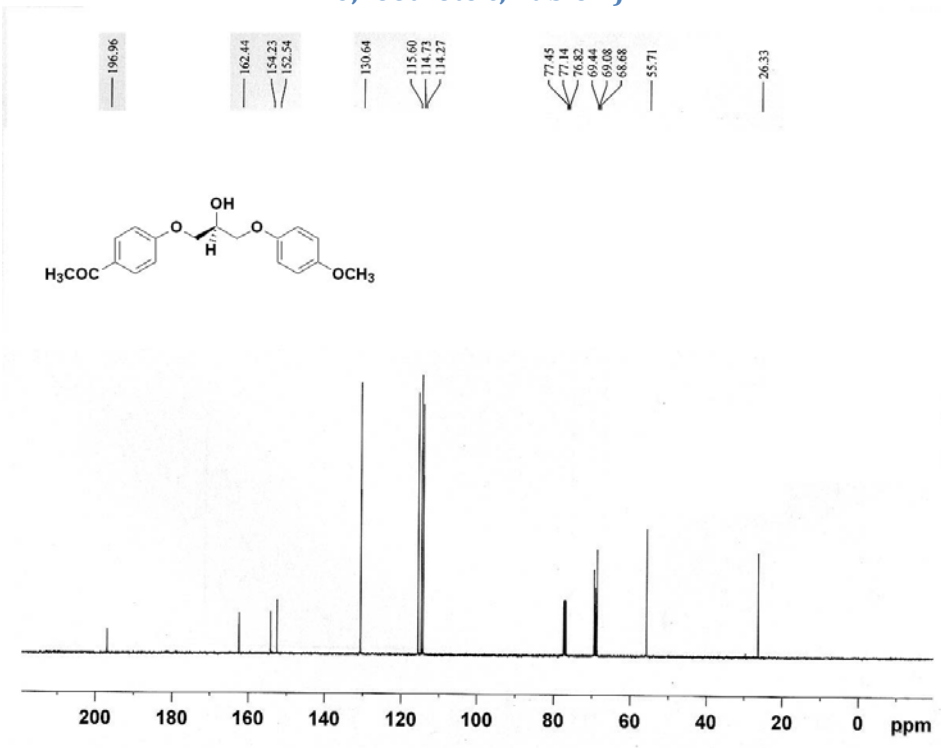
^{13}C NMR of (*S*) 1-(4-oxiranylmethoxy-phenyl)-ethanone (starting epoxide of entries 10 & 11, footnotes c & d, Table 2)



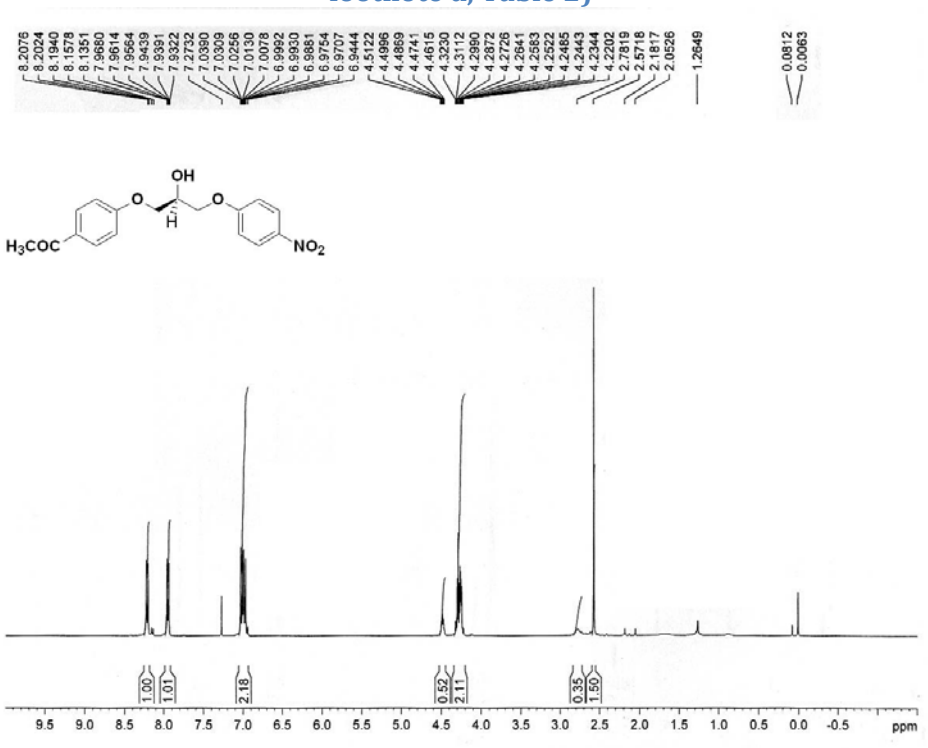
^{1}H NMR of (*S*) 1-{4-[2-Hydroxy-3-(4-methoxy-phenoxy)-propoxy]-phenyl}-ethanone (entry 10, footnote c, Table 2)



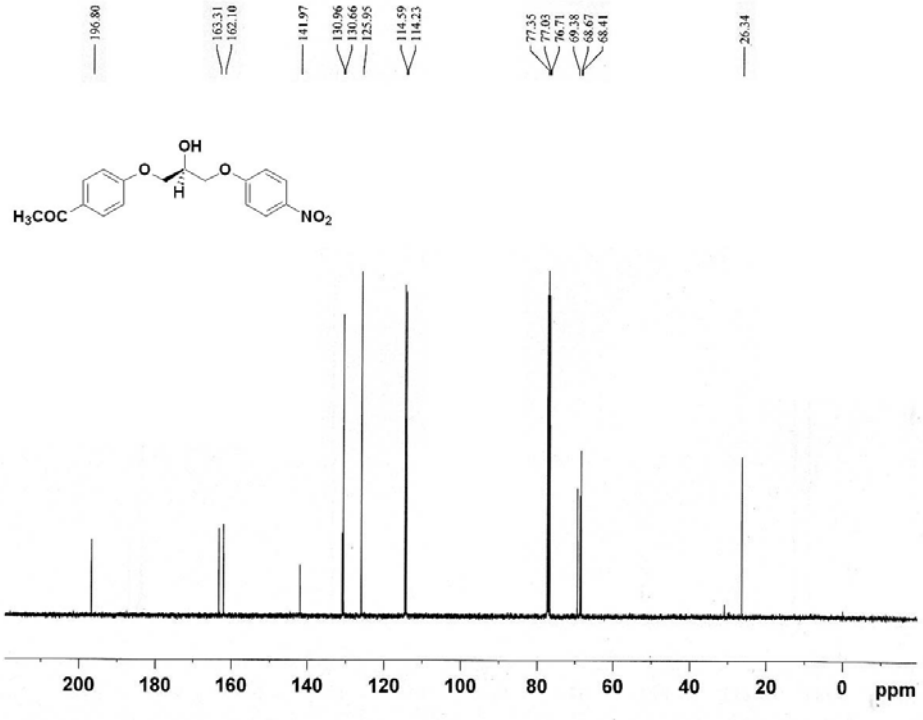
^{13}C NMR of (*S*) 1-{4-[2-Hydroxy-3-(4-methoxy-phenoxy)-propoxy]-phenyl}-ethanone (entry 10, footnote c, Table 2)



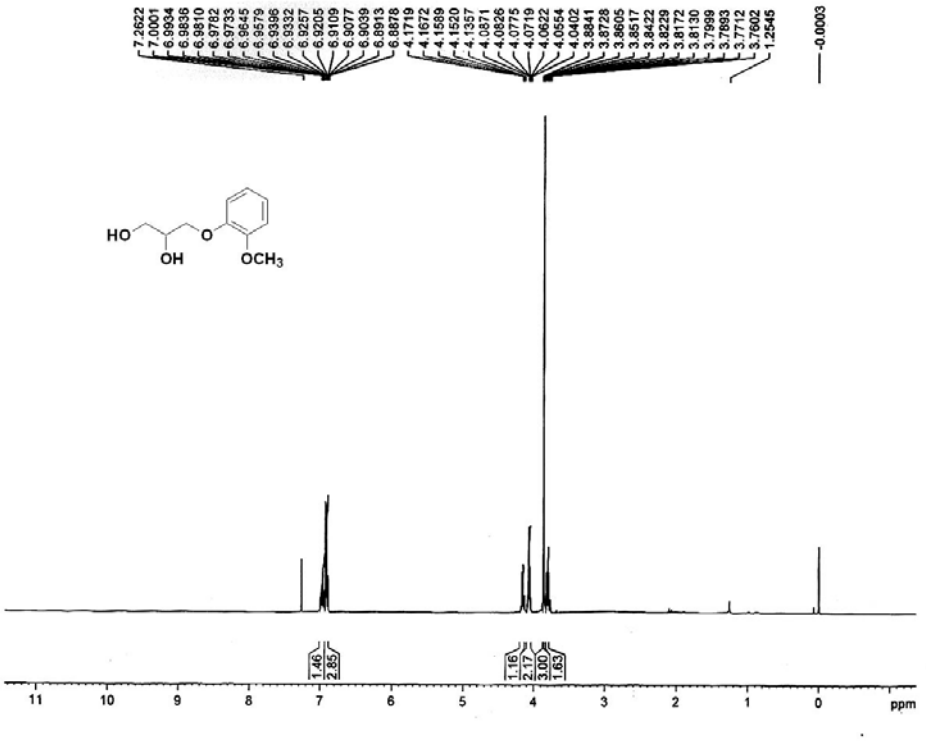
^{1}H NMR of (*S*) 1-{4-[2-Hydroxy-3-(4-nitro-phenoxy)-propoxy]-phenyl}-ethanone (entry 11, footnote d, Table 2)



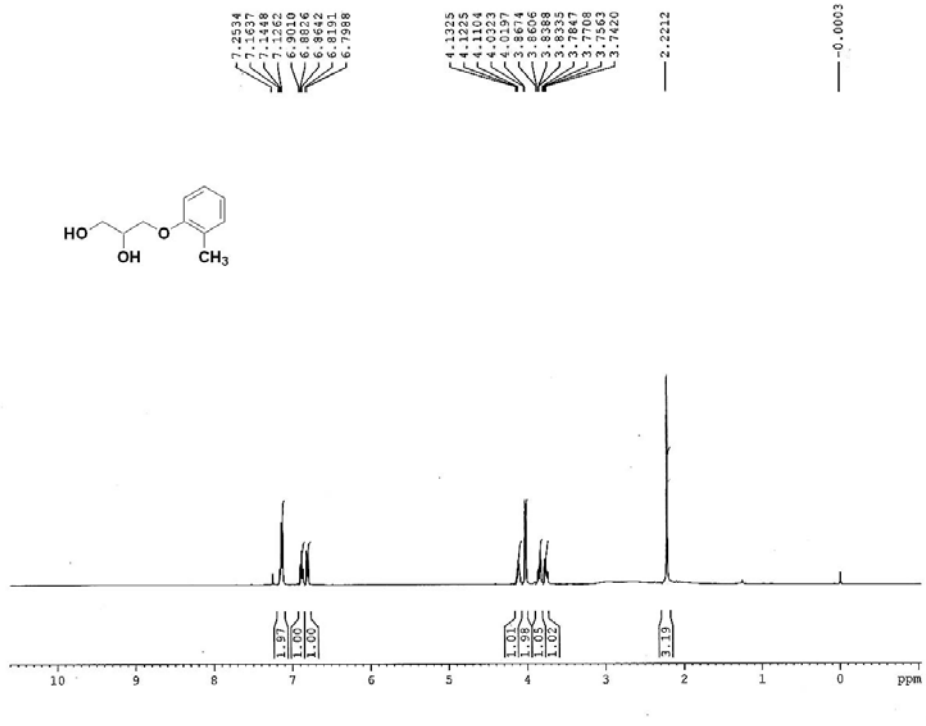
^{13}C NMR of (*S*) 1-{4-[2-Hydroxy-3-(4-nitro-phenoxy)-propoxy]-phenyl}-ethanone (entry 11, footnote d, Table 2)



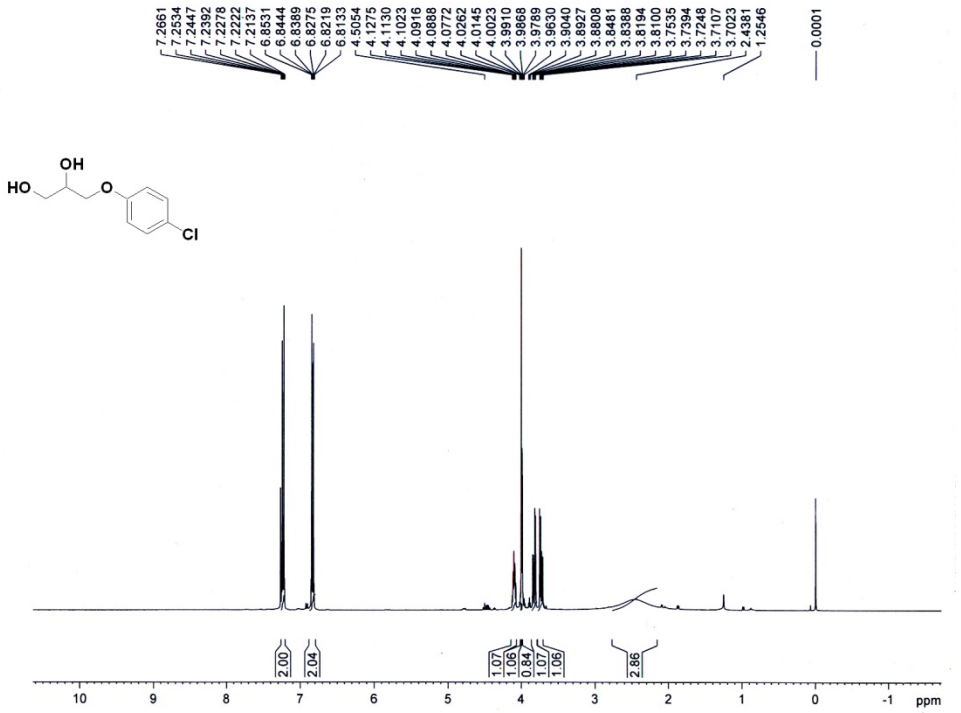
^{1}H NMR of 3-(2-Methoxy-phenoxy)-propane-1,2-diol (Scheme 1, compound 5)



^{1}H NMR of 3-o-Tolyloxy-propane-1,2-diol (Scheme 1, compound 6)

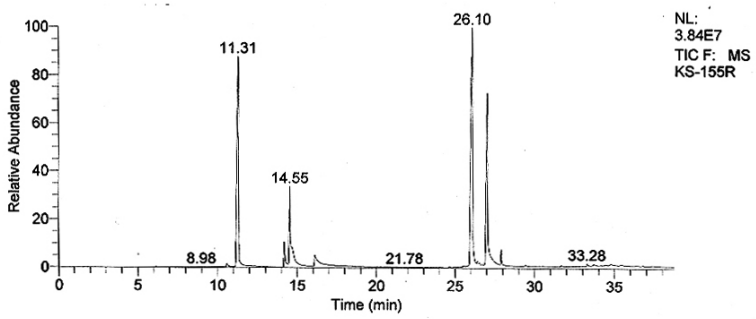


^{1}H NMR of 3-(4-Chloro-phenoxy)-propane-1,2-diol (Scheme 1, compound 7)

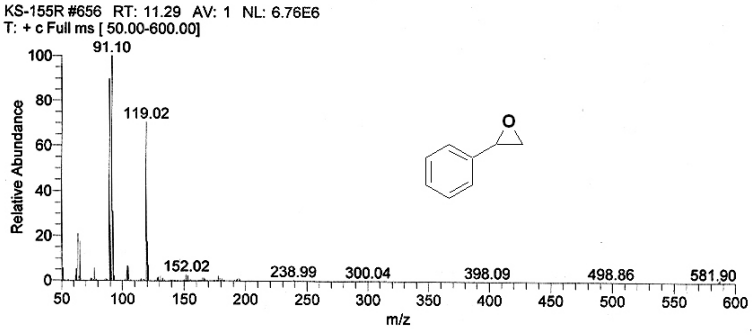


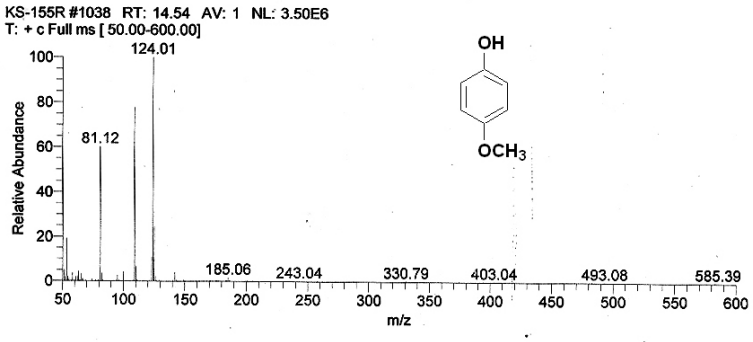
Scanned GCMS Spectra

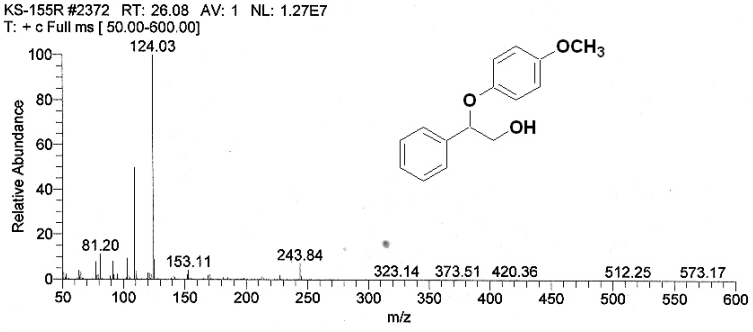
GCMS Spectra of Table 3, entry 1

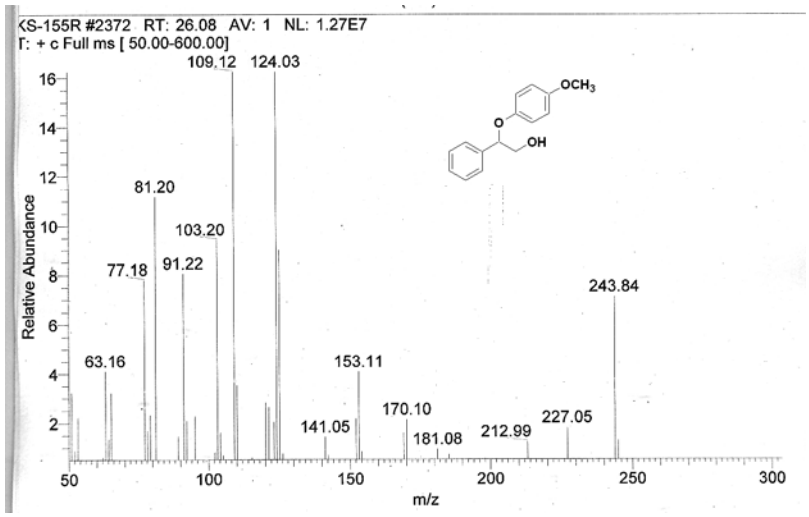


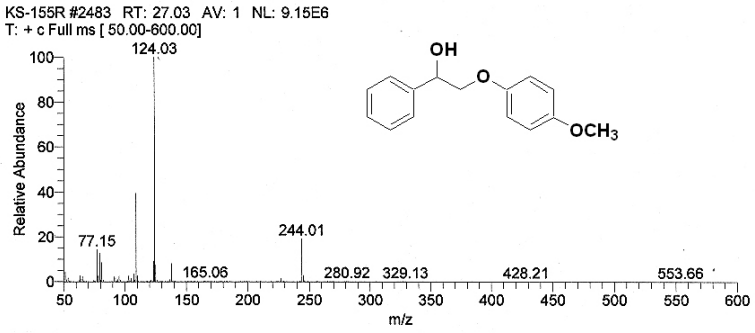
RT	Area %	Peak Area	Peak Height
11.29	29.71	231776326	29156483
14.54	9.79	76364617	9851443
26.08	39.08	304828960	33402425
27.03	21.42	167113924	22551651

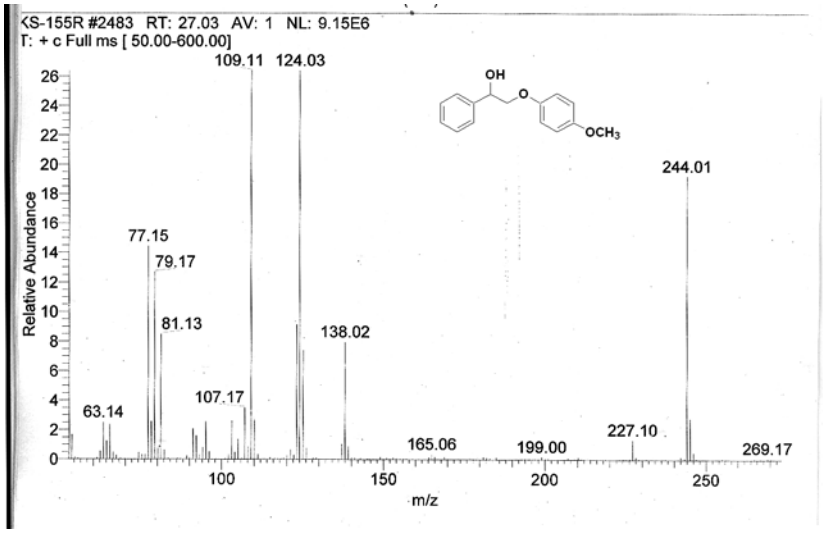




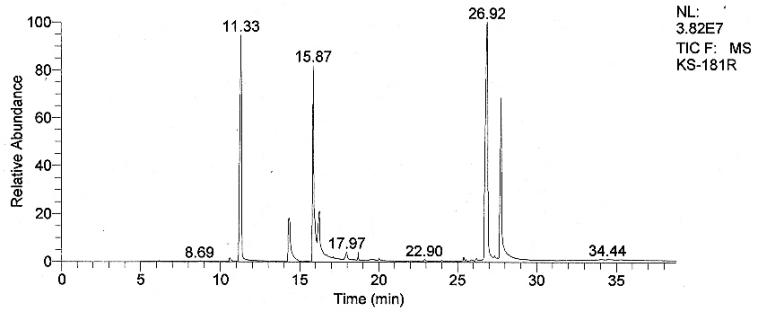



KS-155R #2372 RT: 26.08 AV: 1 NL: 1.27E7
T: + c Full ms [50.00-600.00]
109.12
124.03
81.20
103.20
77.18
91.22
63.16
153.11
170.10
141.05
181.08
212.99
227.05
243.84
OCH3
O
OH
Relative Abundance
m/z

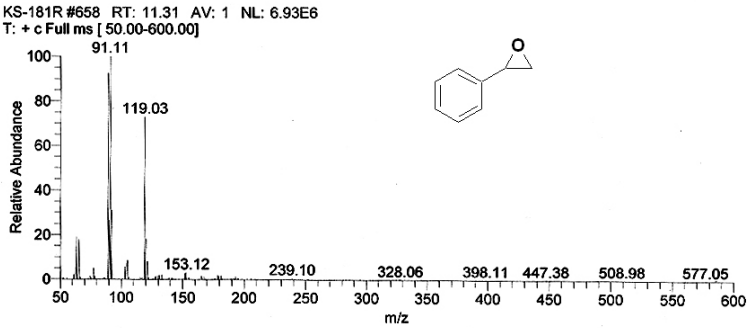

KS-155R #2483 RT: 27.03 AV: 1 NL: 9.15E6
T: + c Full ms [50.00-600.00]
124.03
77.15
244.01
165.06
280.92
329.13
428.21
553.66
OH
O
OCH3
Relative Abundance
m/z

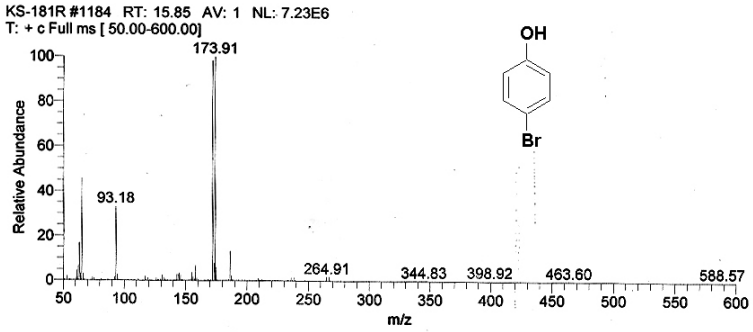

KS-155R #2483 RT: 27.03 AV: 1 NL: 9.15E6
T: + c Full ms [50.00-600.00]
109.11
124.03
77.15
79.17
81.13
138.02
107.17
63.14
165.06
199.00
227.10
244.01
269.17
OH
O
OCH3
Relative Abundance
m/z

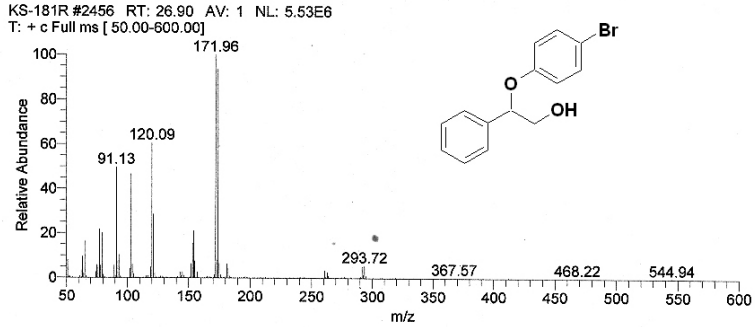
GCMS Spectra of Table 3, entry 2

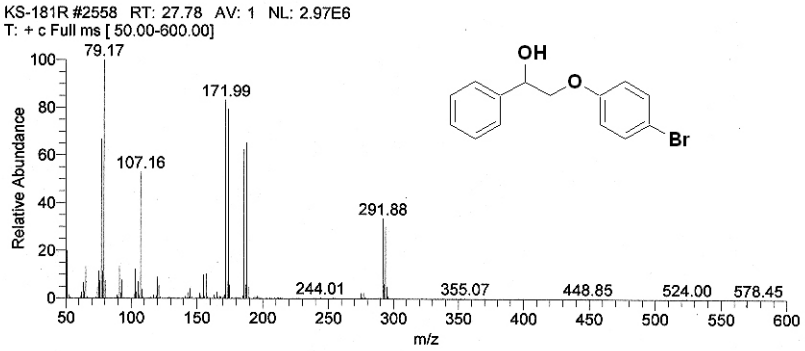


RT	Area %	Peak Area	Peak Height
11.31	26.69	273144589	31557795
15.85	21.15	216415800	26733060
26.90	36.18	370272360	34084877
27.78	15.98	163574412	21352255

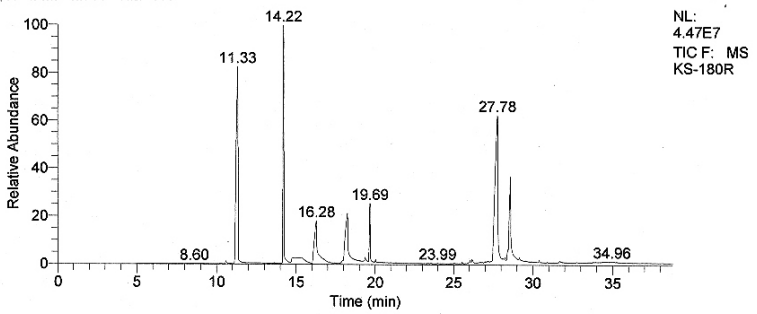




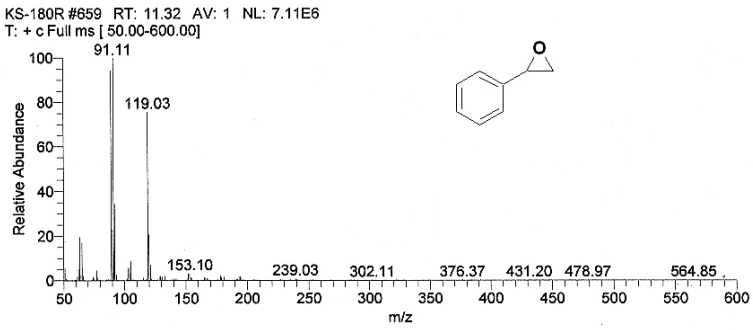


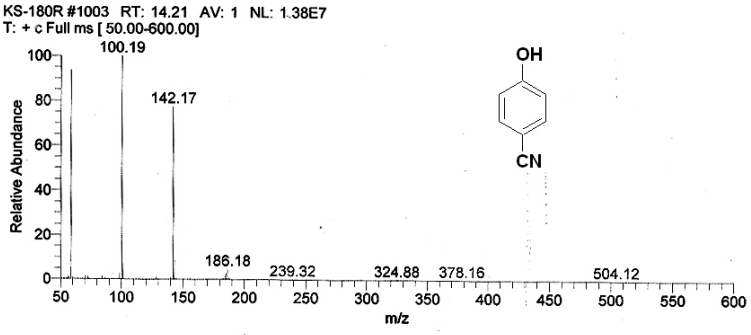


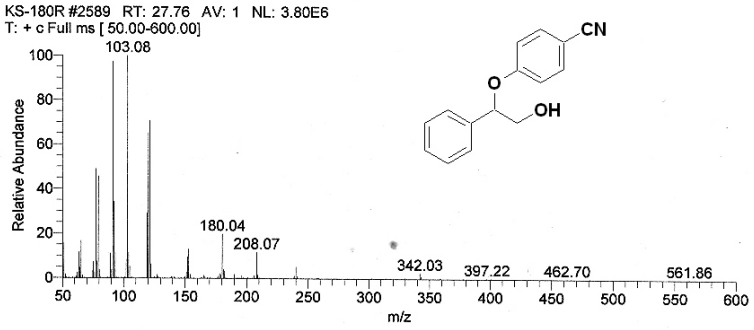
GCMS Spectra of Table 3, entry 3

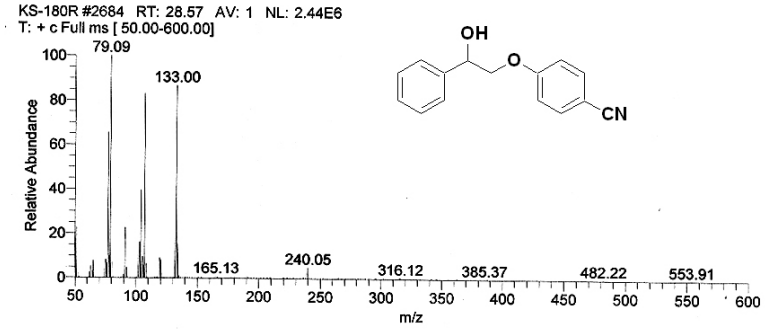


RT	Area %	Peak Area	Peak Height
11.32	33.41	286932148	32603681
14.21	19.66	168848298	33559116
27.76	34.70	298053748	23907764
28.57	12.24	105102498	12860287

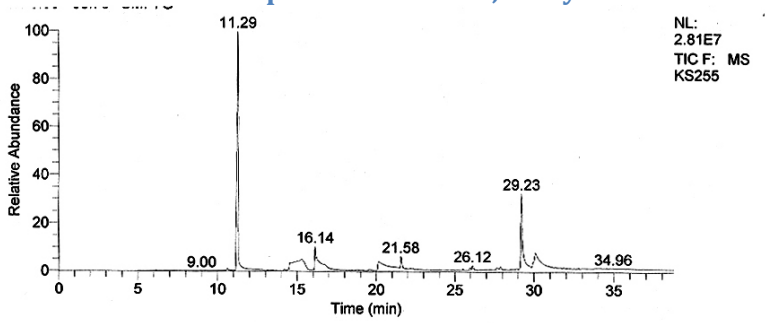




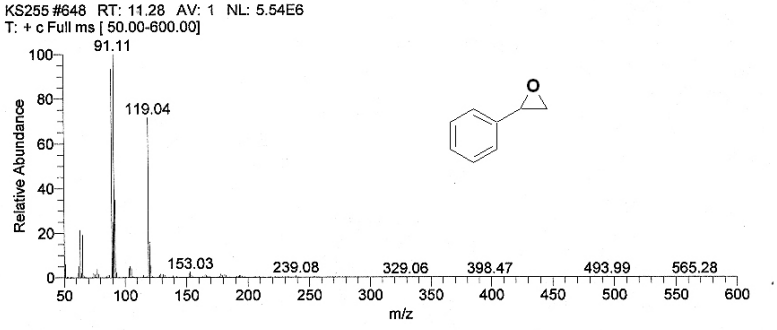


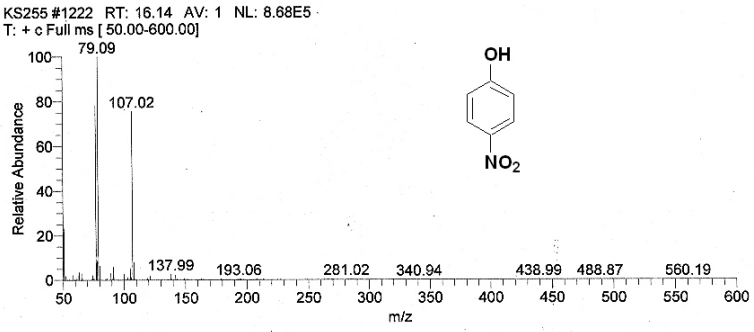


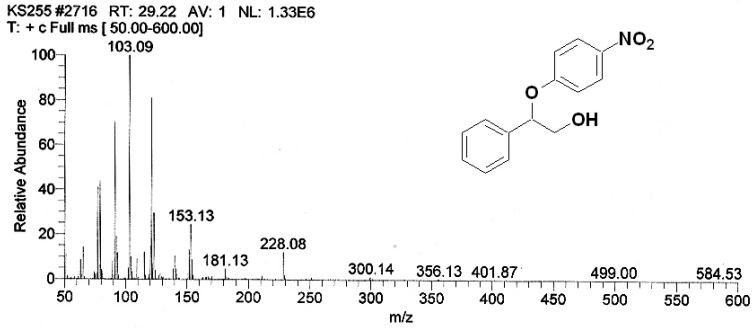
GCMS Spectra of Table 3, entry 4

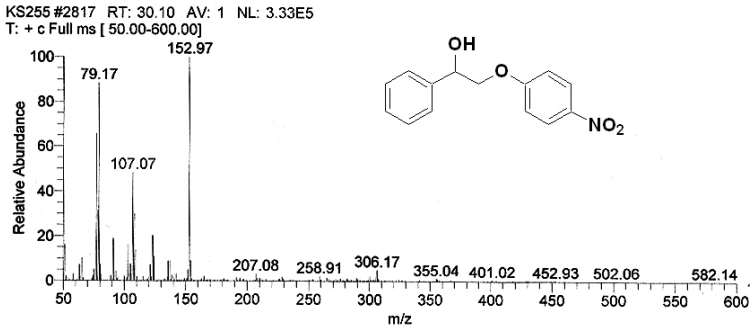


RT	Area %	Peak Area	Peak Height
11.28	70.81	151333017	22712354
16.14	5.47	11682136	1879644
29.22	17.87	38198534	6440850
30.10	5.85	12507484	1057476




KS255 #1222 RT: 16.14 AV: 1 NL: 8.68E5
T: + c Full ms [50.00-600.00]
Relative Abundance
m/z
79.09
107.02
137.99
193.06
281.02
340.94
438.99
488.87
560.19
OH
NO2


KS255 #2716 RT: 29.22 AV: 1 NL: 1.33E6
T: + c Full ms [50.00-600.00]
Relative Abundance
m/z
103.09
153.13
181.13
228.08
300.14
356.13
401.87
499.00
584.53
NO2
O
OH


KS255 #2817 RT: 30.10 AV: 1 NL: 3.33E5
T: + c Full ms [50.00-600.00]
Relative Abundance
m/z
152.97
79.17
107.07
207.08
258.91
306.17
355.04
401.02
452.93
502.06
582.14
OH
O
NO2

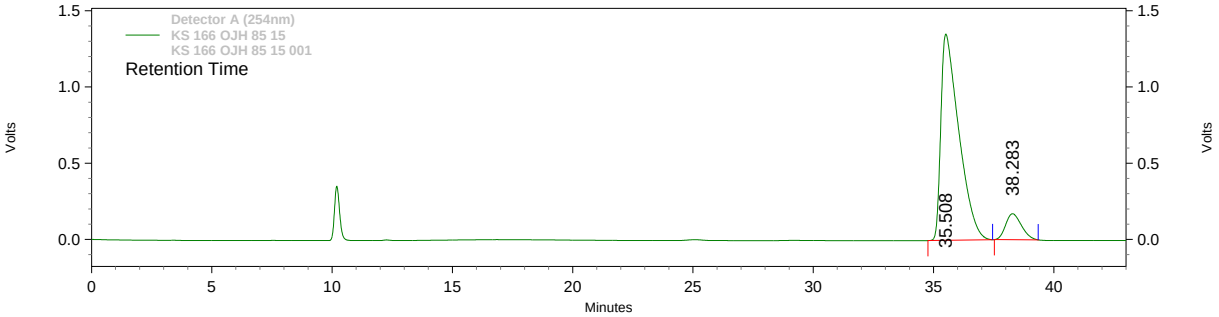
Scanned HPLC Spectra to Determine Enantiomeric Purity

HPLC of (*S*) 1-(4-Oxiranylmethoxy-phenyl)-ethanone (starting epoxide of entries 10 & 11, footnotes c & d, Table 2)

Shimadzu CLASS-VP V6.14 SP1 *Area % Report*

Method Name: D:\CLASSVP\DATA\HPLC Method

Data Name: D:\CLASSVP\DATA\19.11.12\KS 166 OJH 85 15 001
User: System
Acquired: 11/21/2012 10:50:50 PM



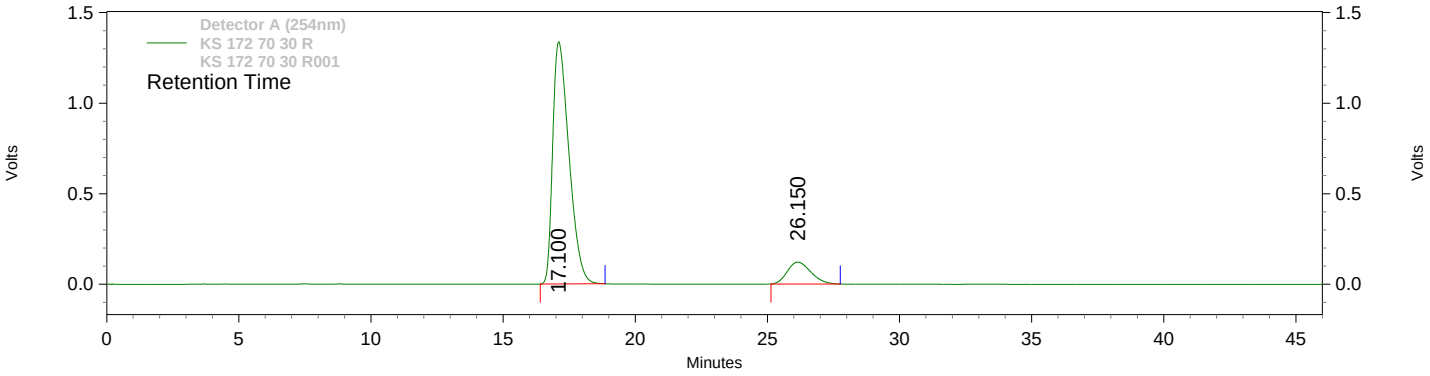
Detector A (254 nm)

Pk #	Retention Time	Area	Area %
1	35.508	70202079	90.031
2	38.283	7773693	9.969
Totals		77975772	100.000

HPLC of (*S*) 1-{4-[2-Hydroxy-3-(4-methoxy-phenoxy)-propoxy]-phenyl}-ethanone (entry 10, footnote c, Table 2)

Shimadzu CLASS-VP V6.14 SP1 ***Area % Report***

Method Name: D:\CLASSVP\DATA\HPLC Method
Data Name: D:\CLASSVP\DATA\19.11.12\KS 172 70 30 R001
User: System
Acquired: 11/20/2012 4:41:32 PM



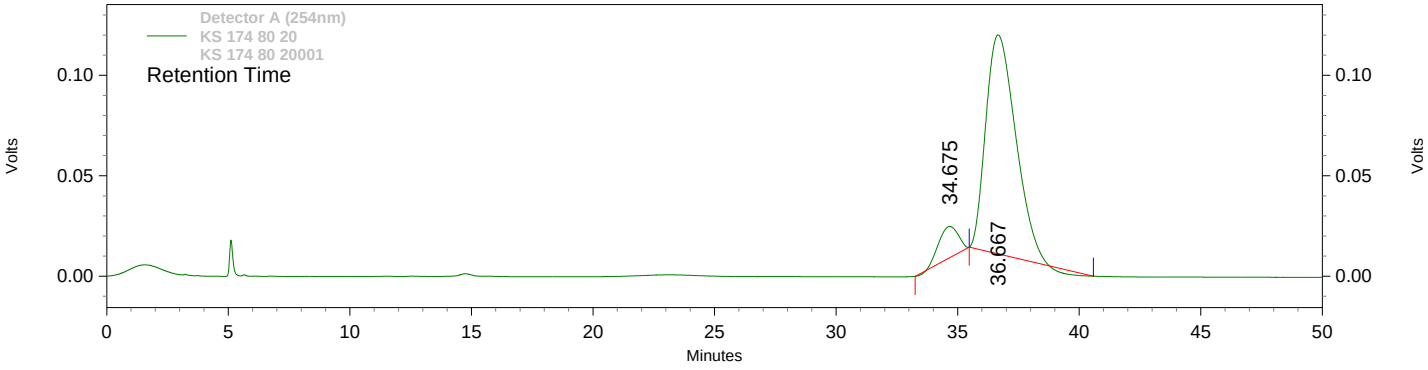
Detector A (254 nm)

Pk #	Retention Time	Area	Area %
1	17.100	57210130	88.425
2	26.150	7489238	11.575
Totals		64699368	100.000

HPLC of (*S*) 1-{4-[2-Hydroxy-3-(4-nitro-phenoxy)-propoxy]-phenyl}-ethanone (entry 11, footnote d, Table 2)

Shimadzu CLASS-VP V6.14 SP1 ***Area % Report***

Method Name: **D:\CLASSVP\DATA\HPLC Method**
Data Name: **D:\CLASSVP\DATA\19.11.12\KS 174 80 20001**
User: **System**
Acquired: **11/21/2012 11:01:23 AM**



Detector A (254nm)

Pk #	Retention Time	Area	Area %
1	34.675	870104	8.606
2	36.667	9240263	91.394
Totals		10110367	100.000

Typical procedure for the recovery and recyclability of Pd nanoparticles catalytic system for the epoxide (1a) opening with phenol (2a):- Upon completion of the reaction (3.5 h, monitored by TLC) between epoxide **1a** and phenol **2a**, the reaction mixture was diluted with ethyl acetate (2 X 5 mL) and the ethyl acetate layer was separated from the aqueous layer. Then into the aqueous layer that contains the Pd nanoparticles, were added **1a** (2 mmol) and **2a** (2 mmol, 1equiv) to carry out further reaction to give **3a**. The process was repeated for five consecutive times.

Table E. Reusability of Pd nanoparticle system.[a]

Entry	No. of Runs	Yield (%)[b]
1	1st reuse	72
2	2nd reuse	71
3	3rd reuse	69
4	4th reuse	66
5	5th reuse	60

[a]The epoxide **1a** (2 mmol) was treated with phenol **2a** (2 mmol, 1 equiv) with recovered catalytic system for each cycle in water (8 mL) at 60 °C. [b]The isolated yield of **3a**.

Figure 4. TEM image of self-assembled Pd nanoparticles in the reaction mixture after 5th cycle.