Exploring anticancer activity of structurally modified benzylphenoxyacetamide (BPA). I: Synthesis strategies and computational analyses of substituted BPA variants with high anti-glioblastoma potential.

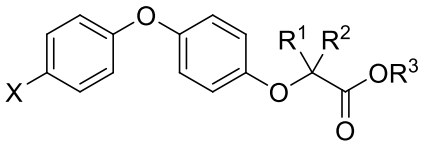
Joanna Stalinska[c,d], Lisa Houser[a], Monika Rak[c,d] , Susan Colley[c], Krzysztof Reiss[c*], and Branko S. Jursic[a,b*]

[a]Department of Chemistry, University of New Orleans, New Orleans, LA 70148, United States; [b]Stepharm llc., PO Box 24220, New Orleans, LA 70184, United States; [c]Neurological Cancer Research, Stanley S. Scott Cancer Center, Department of Medicine, LSU Health Sciences Center, New Orleans, LA 70112; [d]Department of Cell Biology, Faculty of Biochemistry, Biophysics and Biotechnology, Jagiellonian University, Cracow Poland.

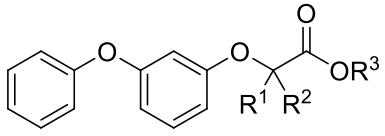
Supplementary Materials

Ester and Acid Structures

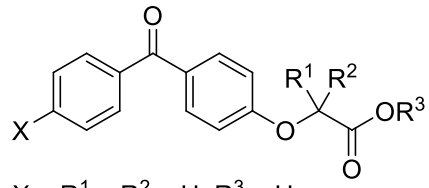
NMR and MS



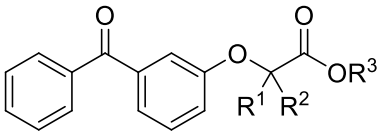
1a: X = R^1 = R^2 = H, R^3 = H
1b: X = R^1 = R^2 = H, R^3 = CH_2CH_3
1c: X = R^1 = H, R^2 = CH_3, R^3 = H
1d: X = H = R^1 = H, R^2 = CH_3, R^3 = CH_2CH_3
1e: X = H, R^1 = R^2 = CH_3, R^3 = H
1f: X = H, R^1 = R^2 = CH_3, R^3 = $CH(CH_3)_2$
1g: X = Cl, R^1 = R^2 = H, R^3 = H
1h: X = Cl, R^1 = R^2 = H, R^3 = CH_2CH_3
1i: X = Cl, R^1 = H, R^2 = CH_3, R^3 = H
1j: X = Cl, R^1 = H, R^2 = CH_3, R^3 = CH_2CH_3
1k: X = Cl, R^1 = R^2 = CH_3, R^3 = H
1l: X = Cl, R^1 = R^2 = CH_3, R^3 = $CH(CH_3)_2$



2a: R^1 = R^2 = R^3 = H
2b: R^1 = R^2 = H, R^3 = CH_2CH_3
2c: R^1 = H, R^2 = CH_3, R^3 = H
2d: R^1 = H, R^2 = CH_3, R^3 = CH_2CH_3
2e: R^1 = R^2 = CH_3, R^3 = H
2f: R^1 = R^2 = CH_3, R^3 = $CH(CH_3)_2$



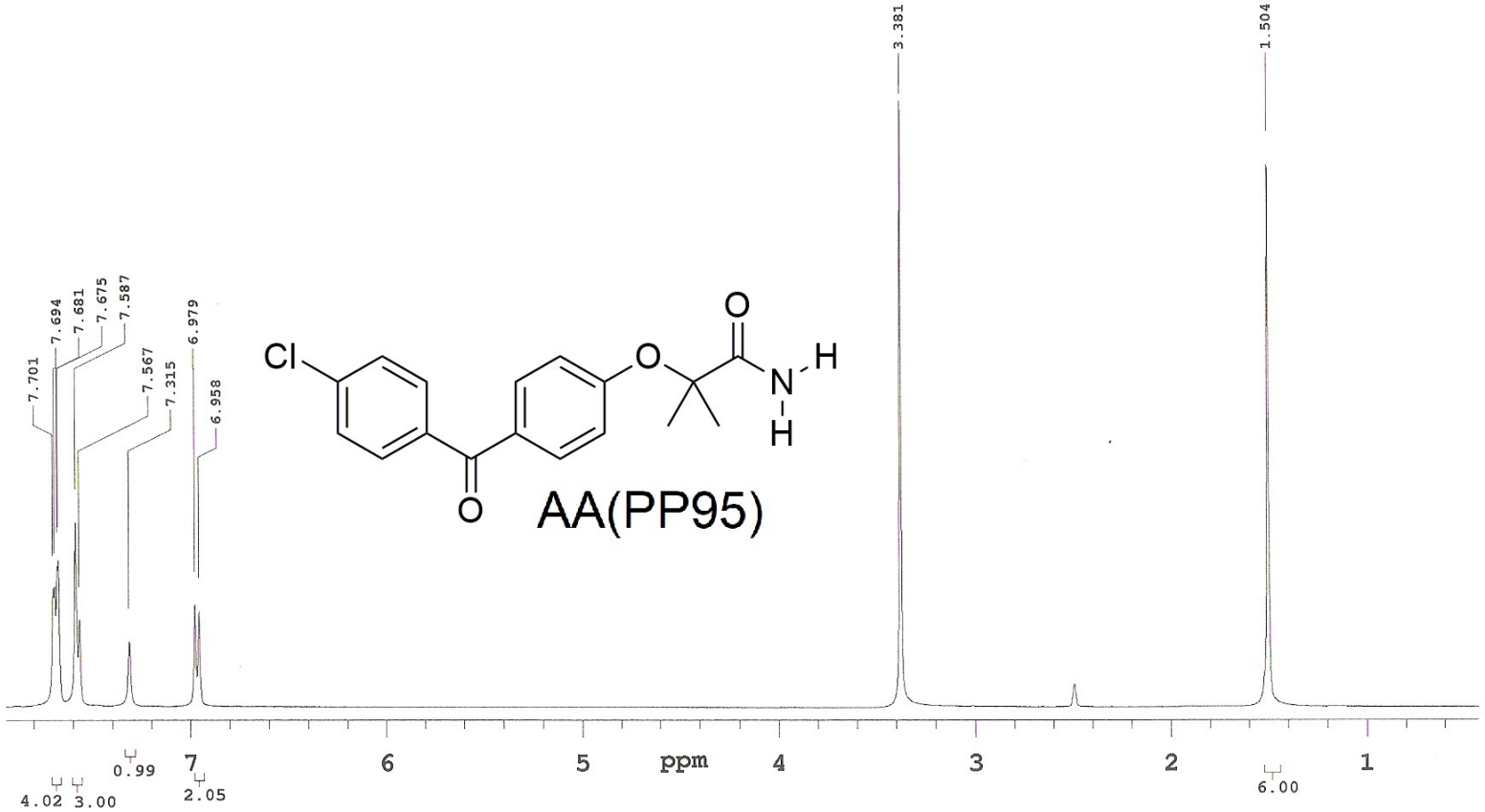
3a: X = R^1 = R^2 = H, R^3 = H
3b: X = R^1 = R^2 = H, R^3 = CH_2CH_3
3c: X = R^1 = H, R^2 = CH_3, R^3 = H
3d: X = H = R^1 = H, R^2 = CH_3, R^3 = CH_2CH_3
3e: X = H, R^1 = R^2 = CH_3, R^3 = H
3f: X = H, R^1 = R^2 = CH_3, R^3 = $CH(CH_3)_2$
3g: X = F, R^1 = R^2 = H, R^3 = H
3h: X = F, R^1 = R^2 = H, R^3 = CH_2CH_3
3i: X = F, R^1 = H, R^2 = CH_3, R^3 = H
3j: X = F, R^1 = H, R^2 = CH_3, R^3 = CH_2CH_3
3k: X = F, R^1 = R^2 = CH_3, R^3 = H
3l: X = F, R^1 = R^2 = CH_3, R^3 = $CH(CH_3)_2$
3m: X = Cl, R^1 = R^2 = H, R^3 = H
3n: X = Cl, R^1 = R^2 = H, R^3 = $CH(CH_3)_2$
3o: X = Cl, R^1 = H, R^2 = CH_3, R^3 = H
3p: X = Cl, R^1 = H, R^2 = CH_3, R^3 = CH_2CH_3
3r: X = Cl, R^1 = R^2 = CH_3, R^3 = H
3s: X = Cl, R^1 = R^2 = CH_3, R^3 = $CH(CH_3)_2$



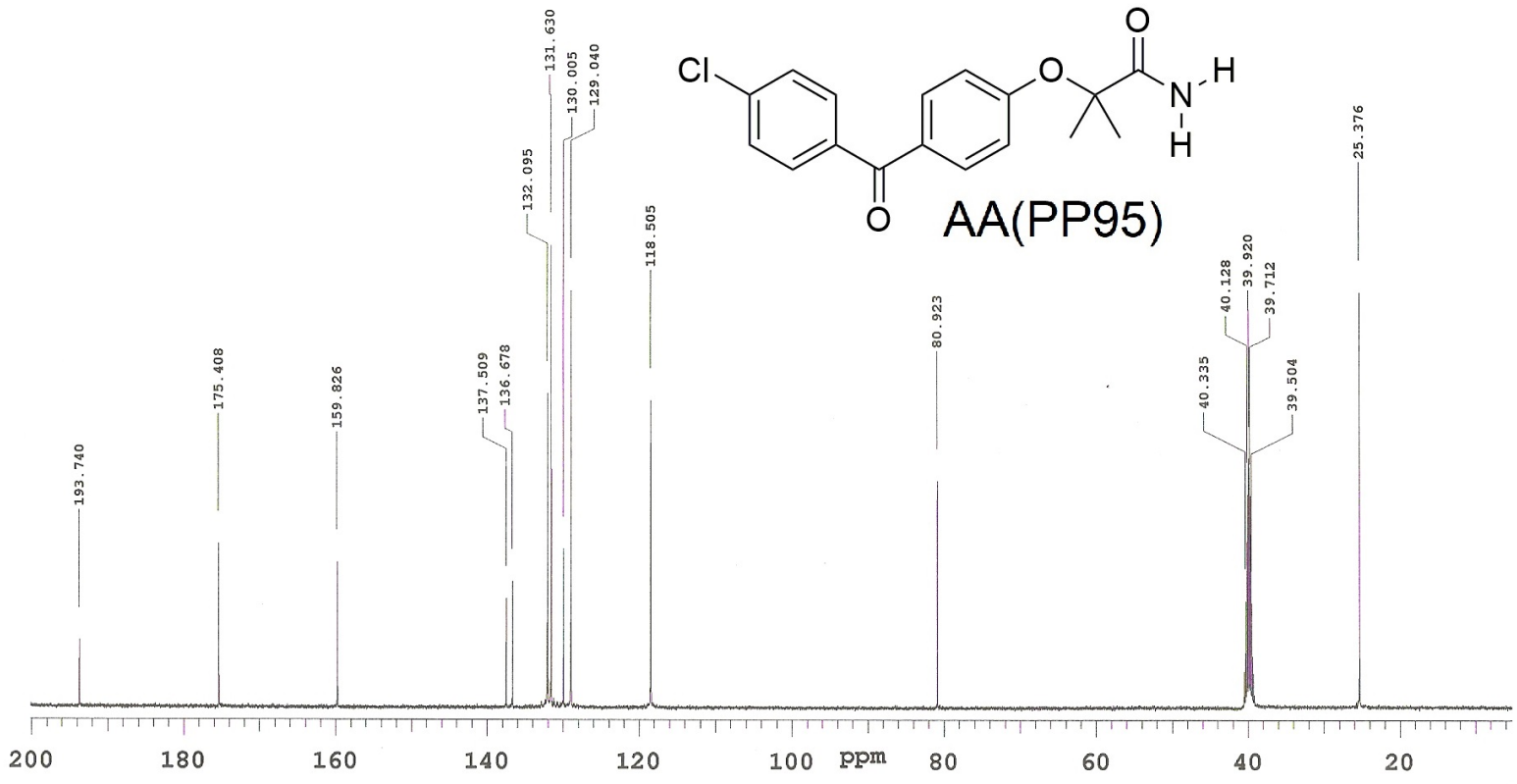
4a: R^1 = R^2 = R^3 = H
4b: R^1 = R^2 = H, R^3 = CH_2CH_3
4c: R^1 = CH_3, R^2 = H, R^3 = H
4d: R^1 = CH_3, R^2 = H, R^3 = $CH(CH_3)_2$
4e: R^1 = R^2 = CH_3, R^3 = H
4f: R^1 = R^2 = CH_3, R^3 = $CH(CH_3)_2$

Structures of synthesized ester and acids required for preparation of **BPA** derivatives

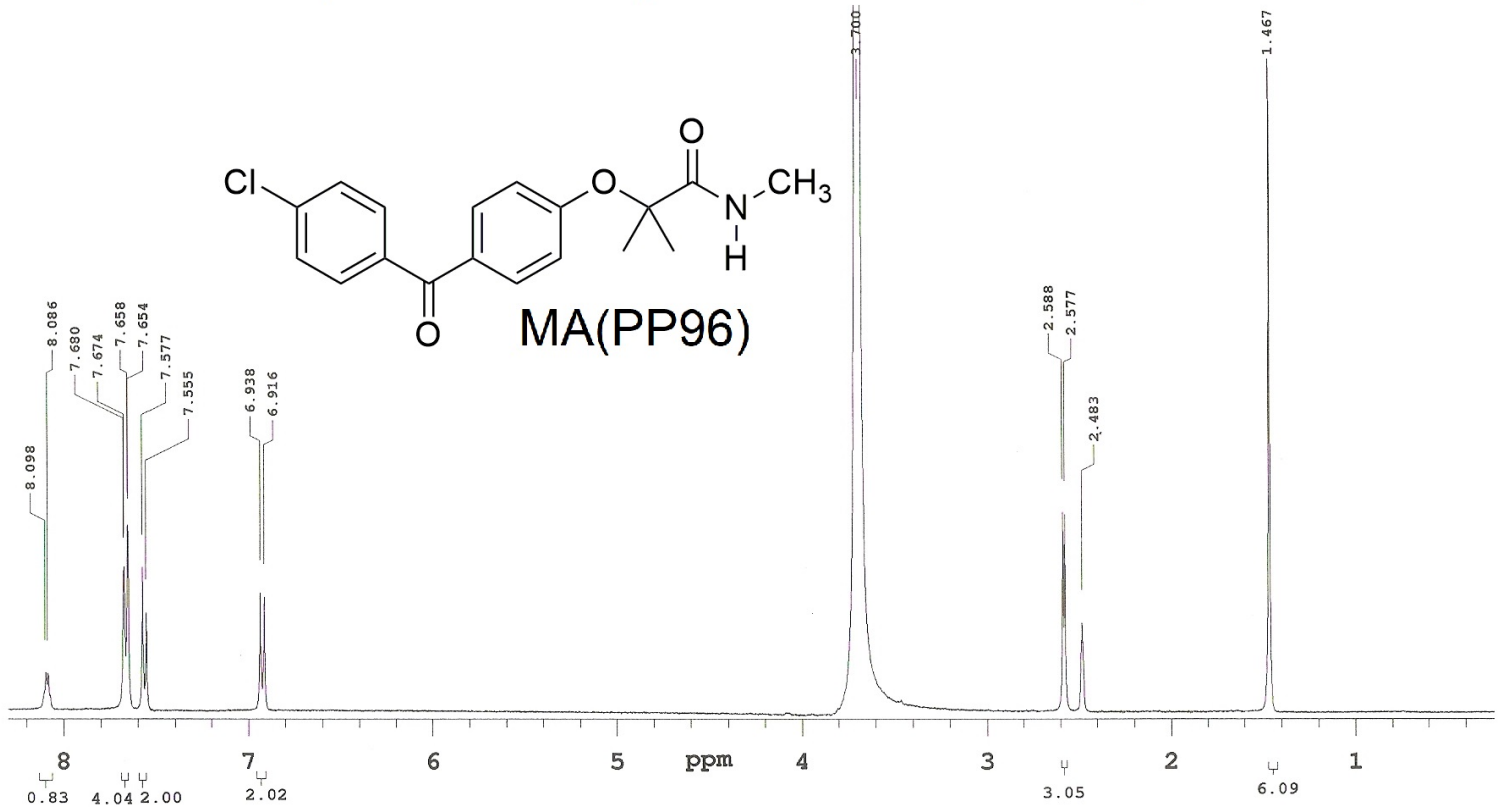
^{1}H-NMR (DMSO-d_6) Varian Mercury 400 Plus



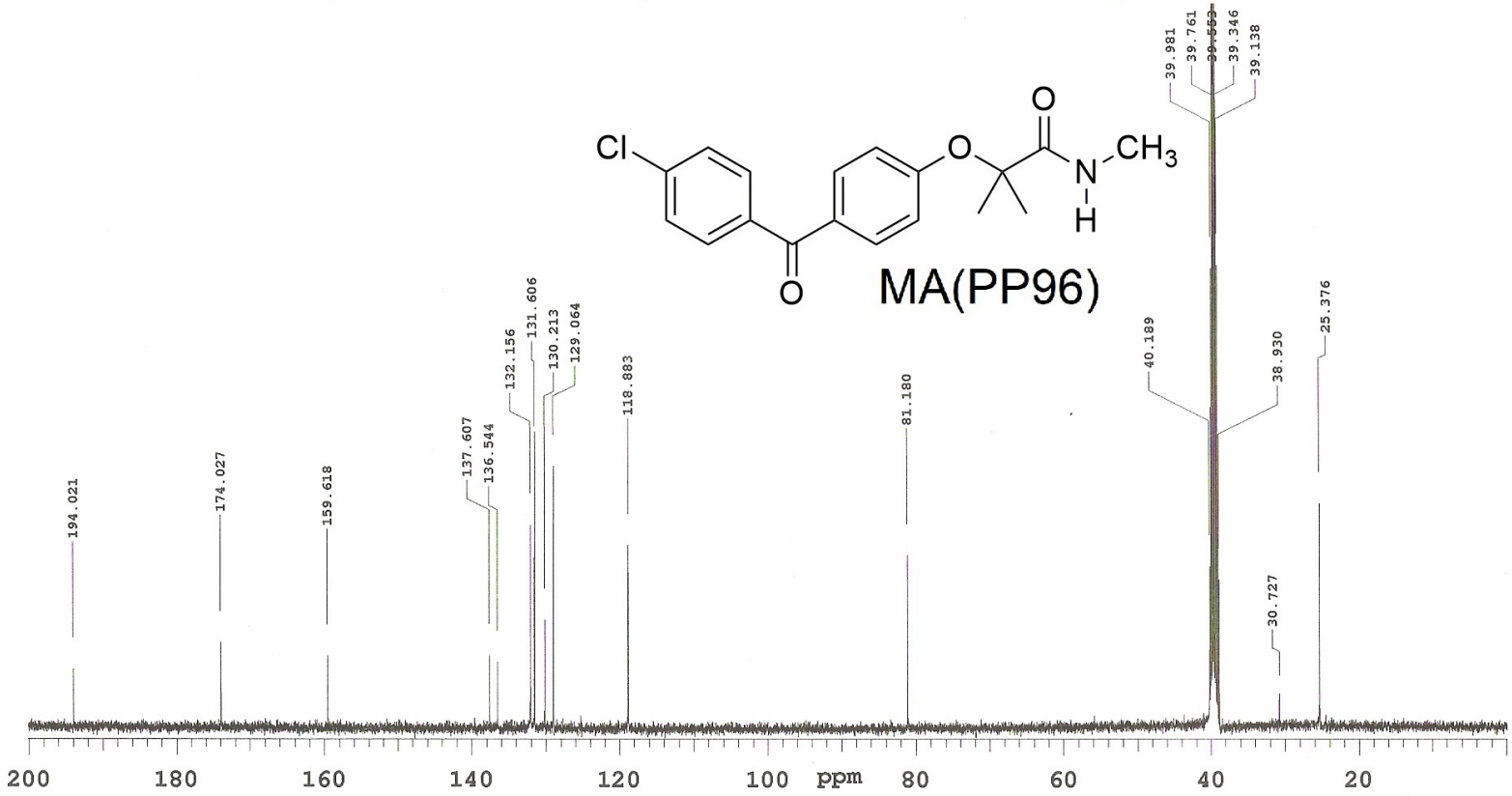
^{13}C-NMR (DMSO-d_6) Varian Mercury 400 Plus



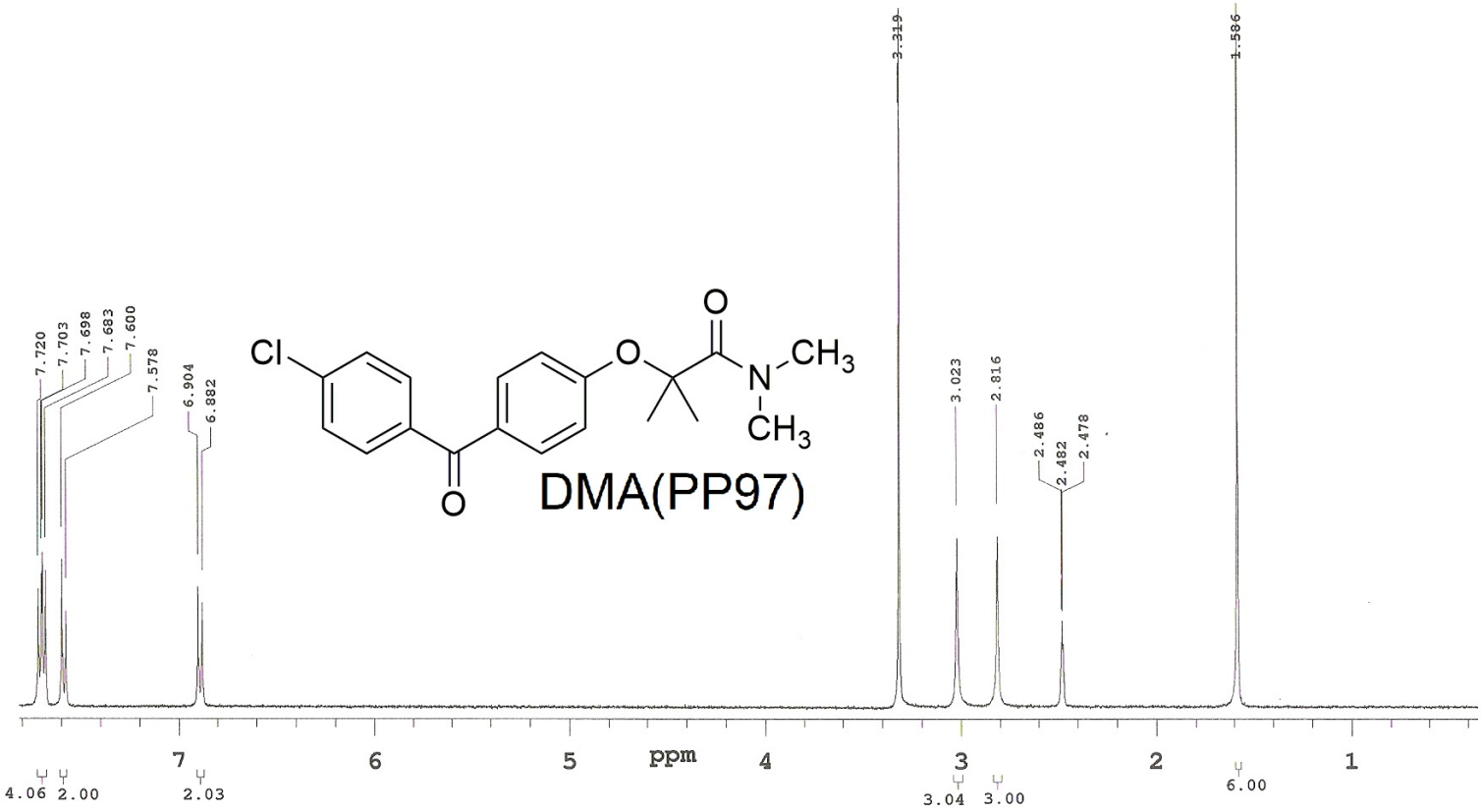
^{1}H-NMR (DMSO-d_6) Varian Mercury 400 Plus



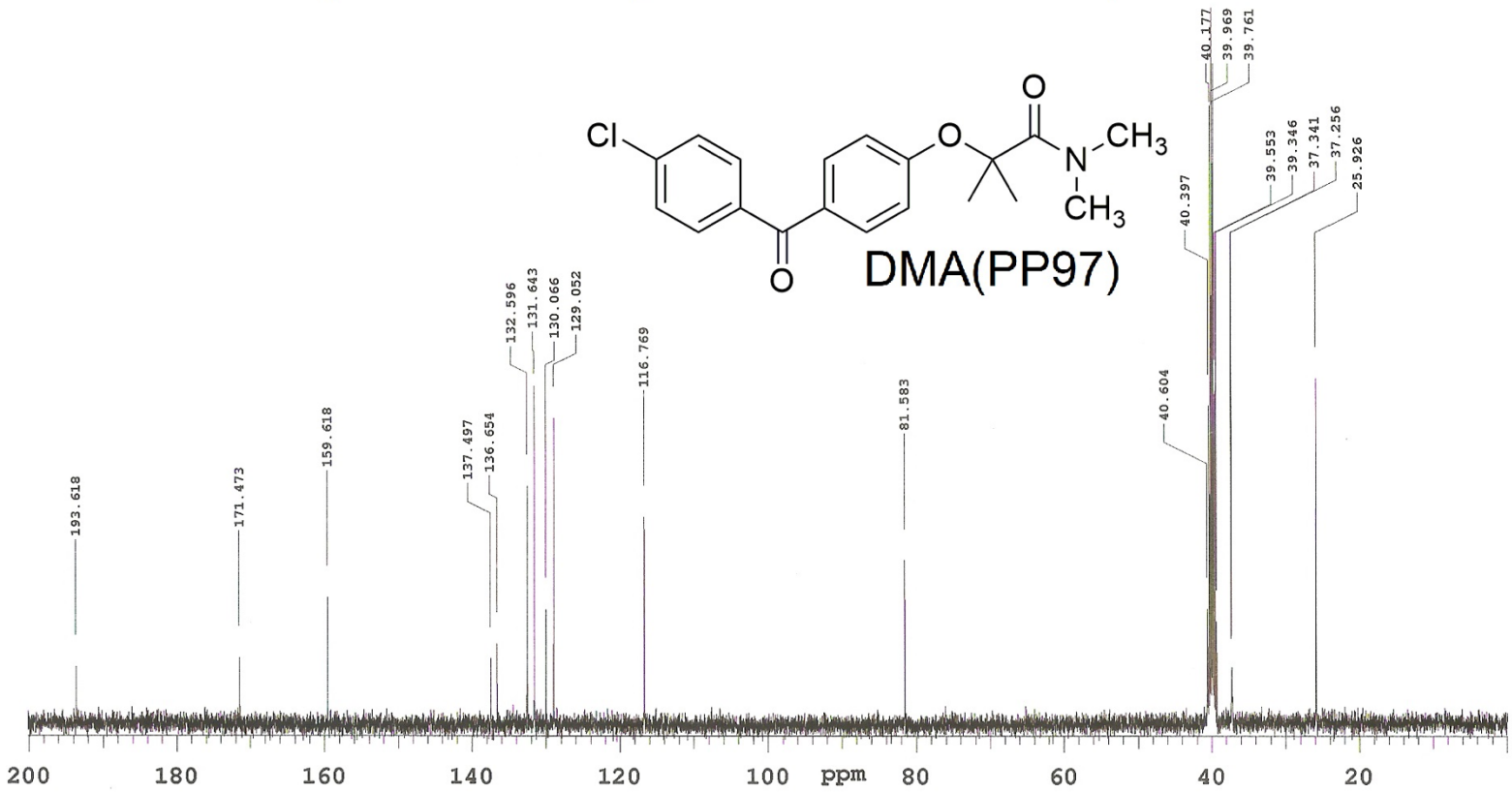
^{13}C-NMR (DMSO-d_6) Varian Mercury 400 Plus



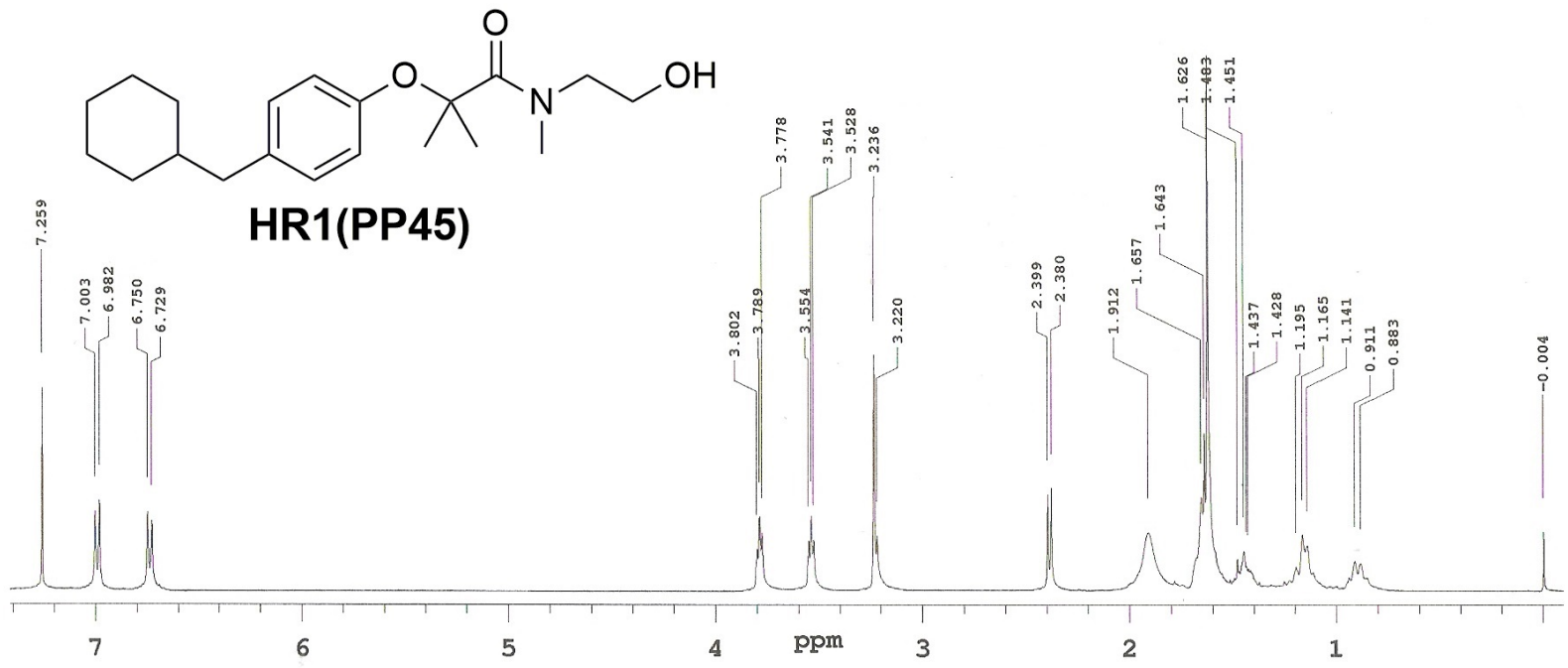
^{1}H-NMR (DMSO-d_6) Varian Mercury 400 Plus



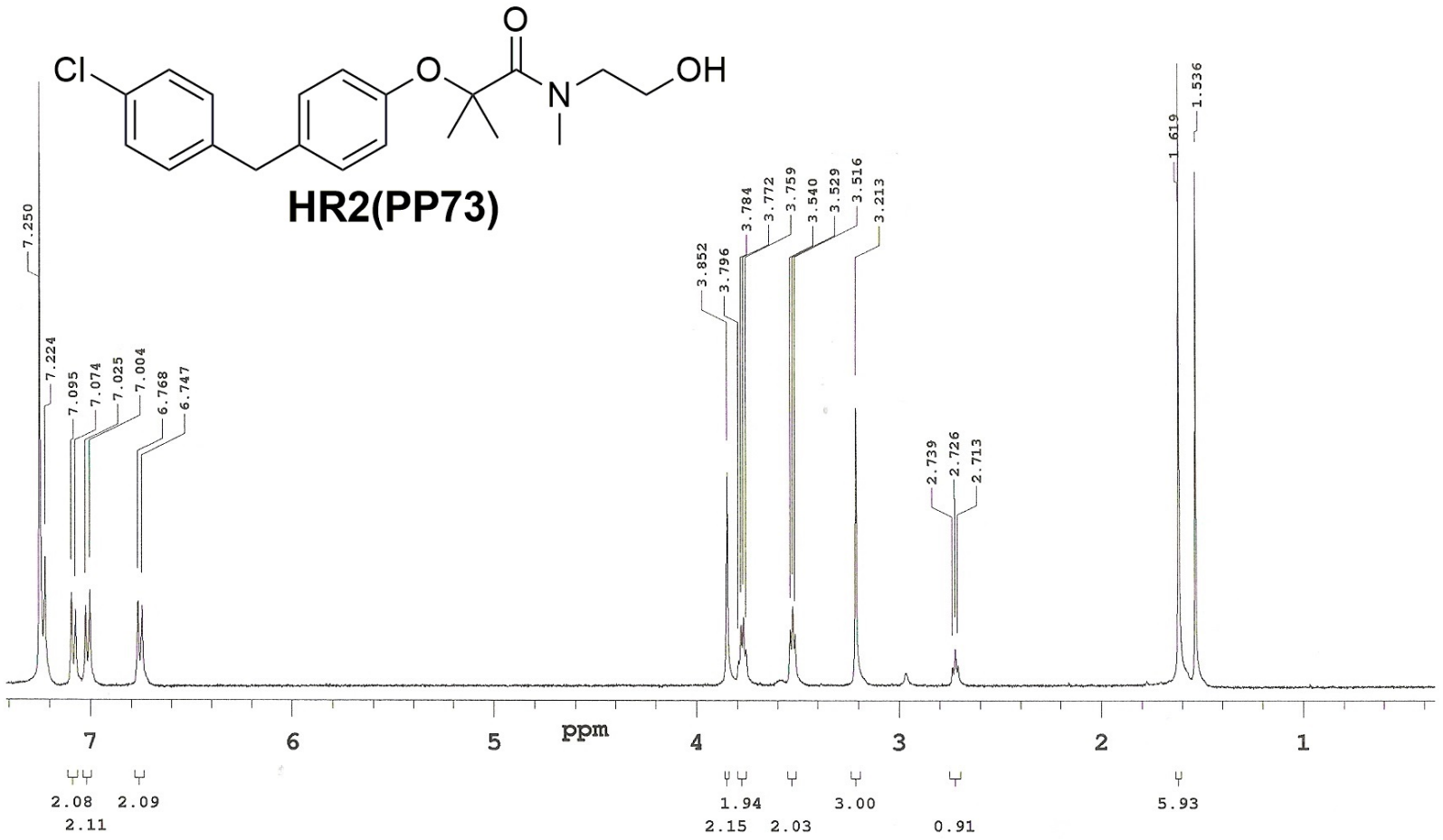
^{13}C-NMR (DMSO-d_6) Varian Mercury 400 Plus



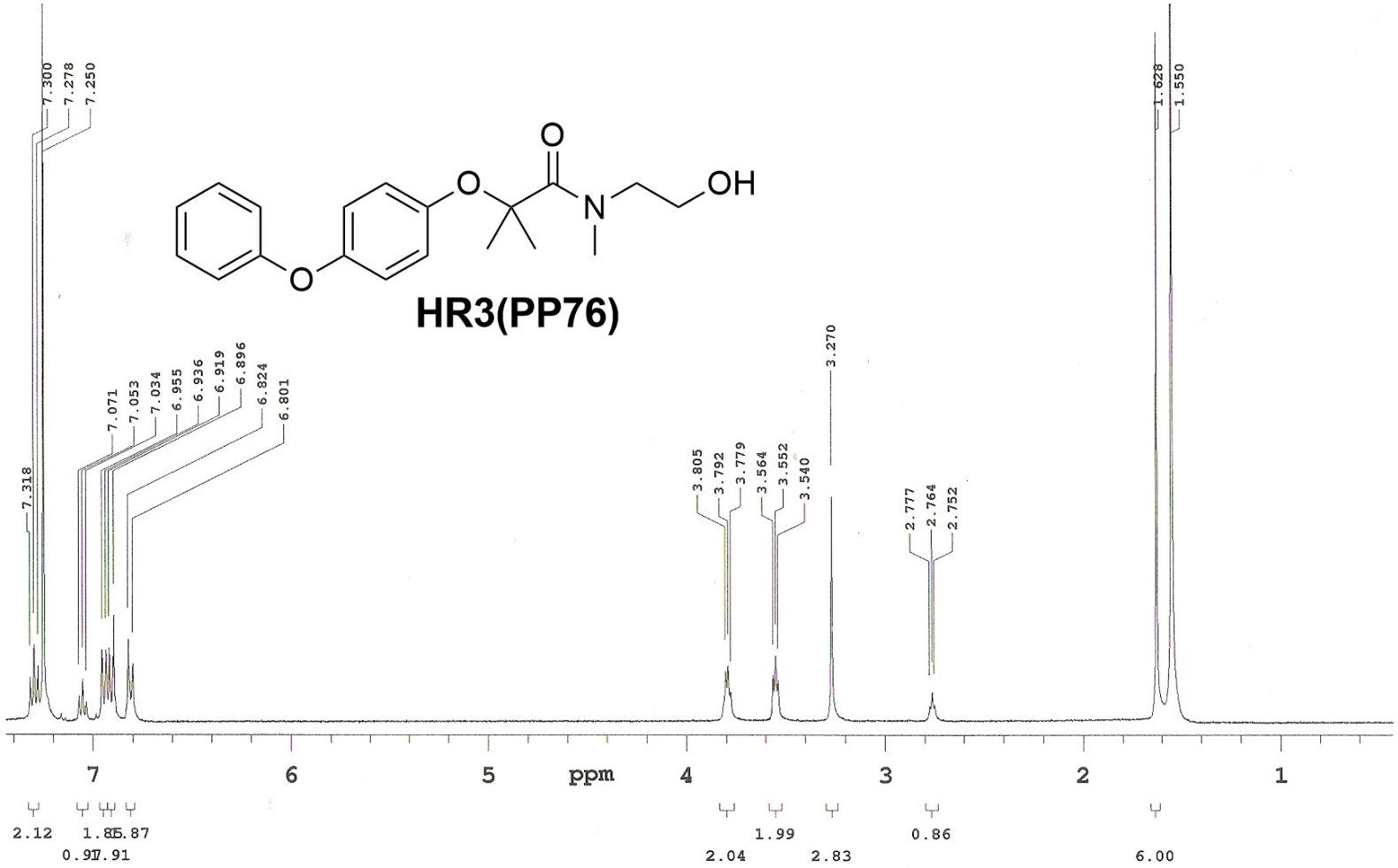
^{1}H-NMR ($CDCl_3$) Varian Mercury 400 Plus



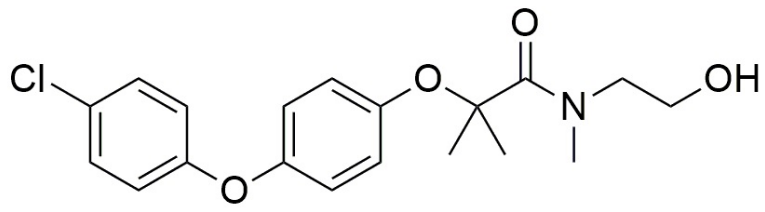
^{1}H-NMR ($CDCl_3$) Varian Mercury 400 Plus



^{1}H-NMR ($CDCl_3$) Varian Mercury 400 Plus

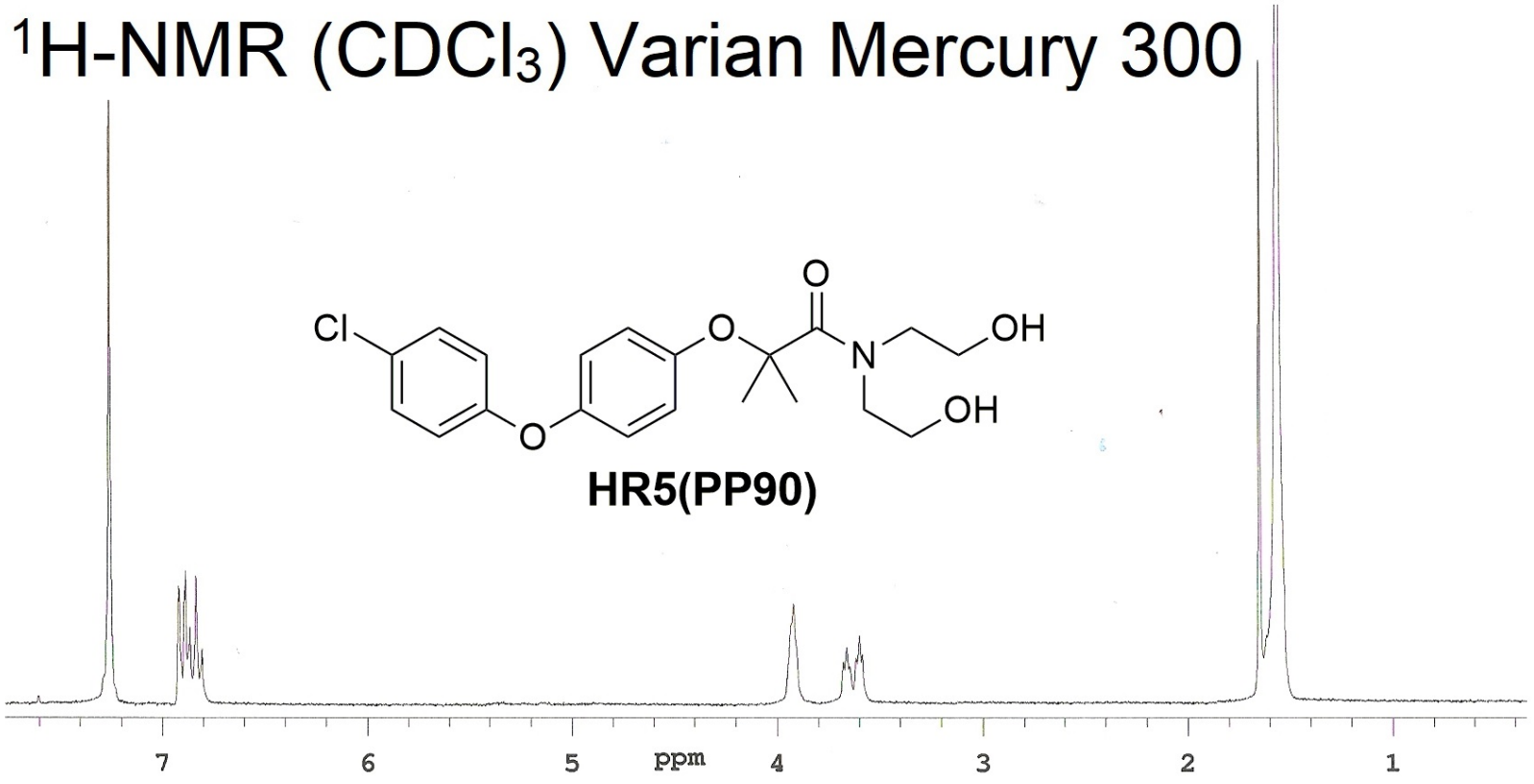


^{1}H-NMR ($CDCl_3$) Varian Mercury 300



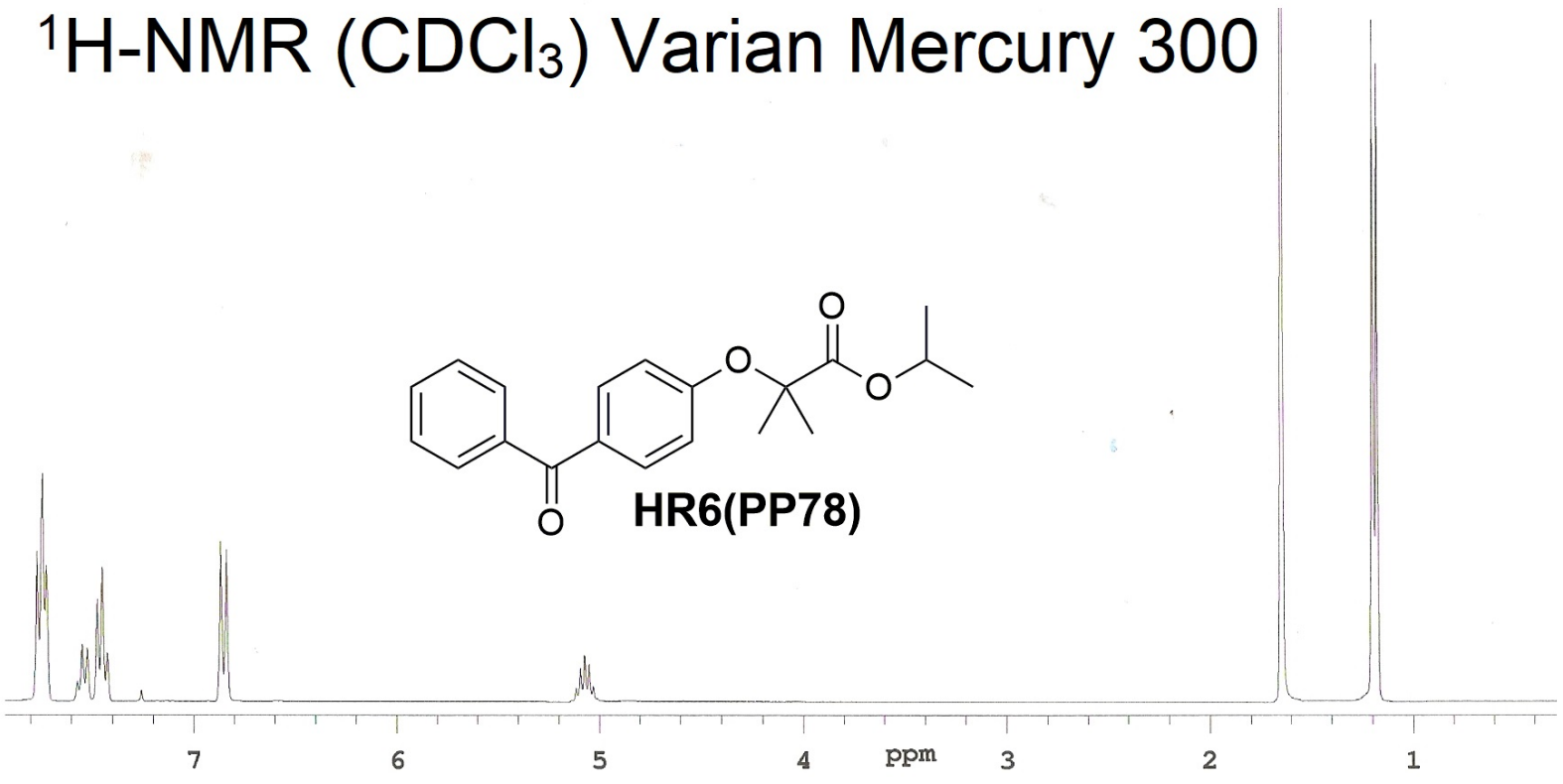
HR4(PP89)

^{1}H-NMR ($CDCl_3$) Varian Mercury 300



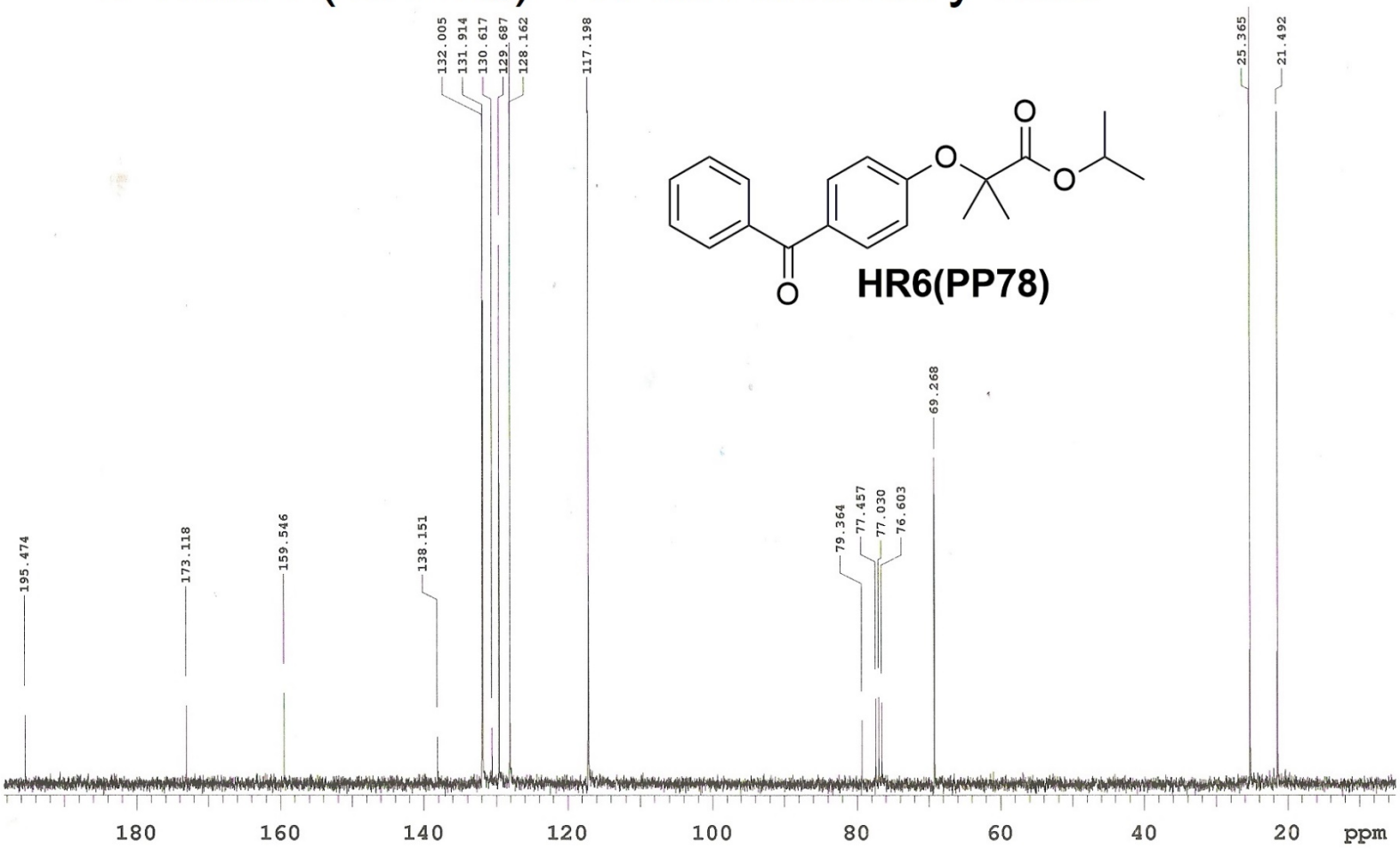
HR5(PP90)

^{1}H-NMR ($CDCl_3$) Varian Mercury 300

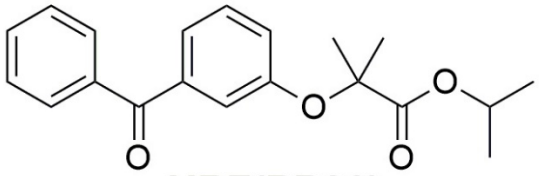


HR6(PP78)

^{13}C-NMR ($CDCl_3$) Varian Mercury 300

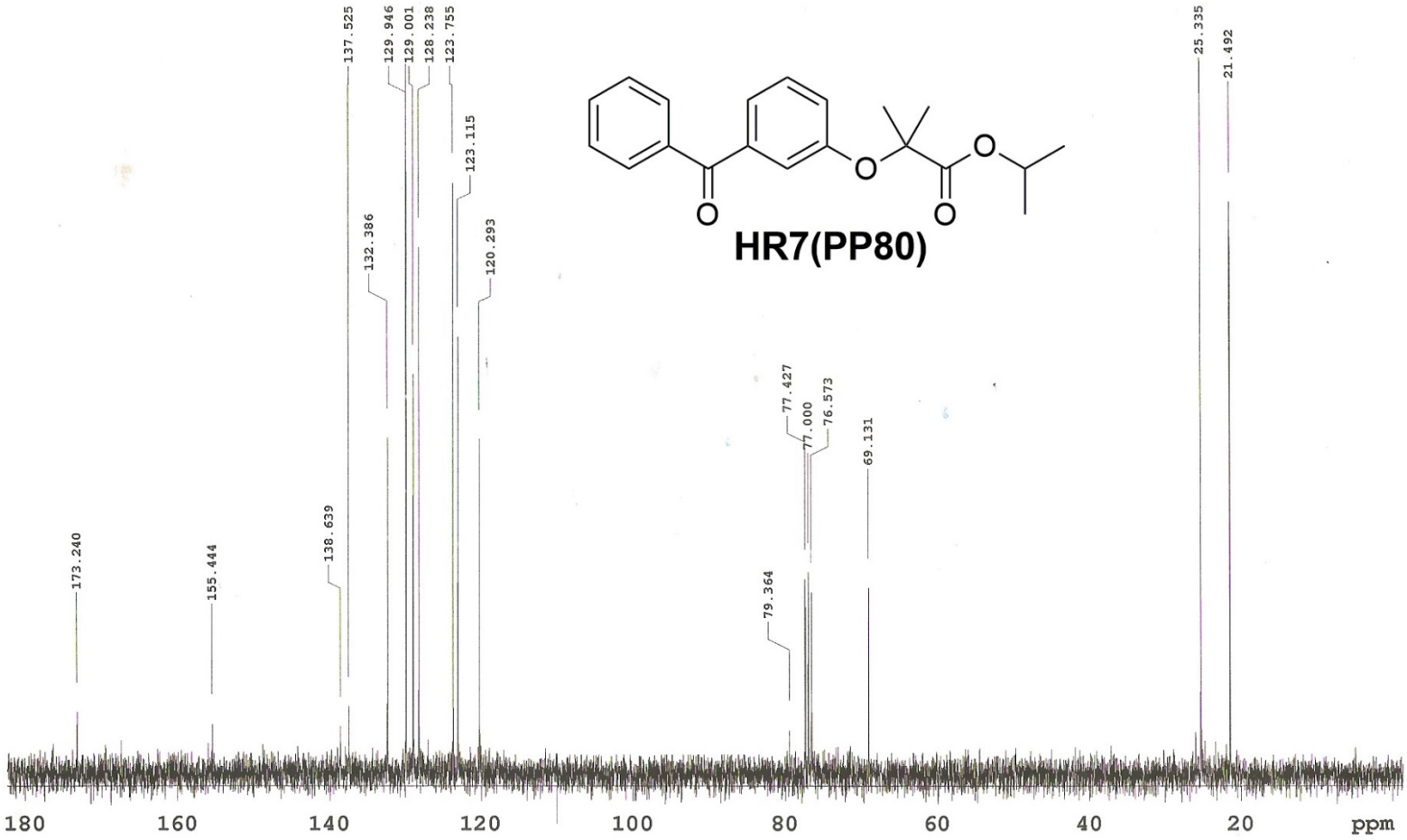


^{1}H-NMR ($CDCl_3$) Varian Mercury 300

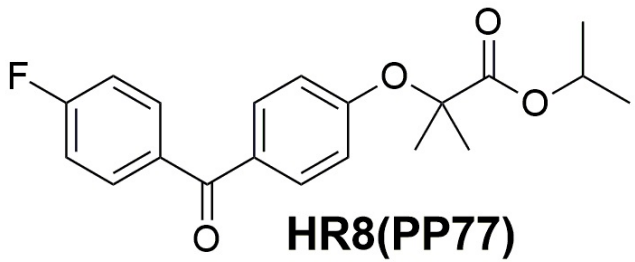


HR7(PP80)

^{13}C-NMR ($CDCl_3$) Varian Mercury 300

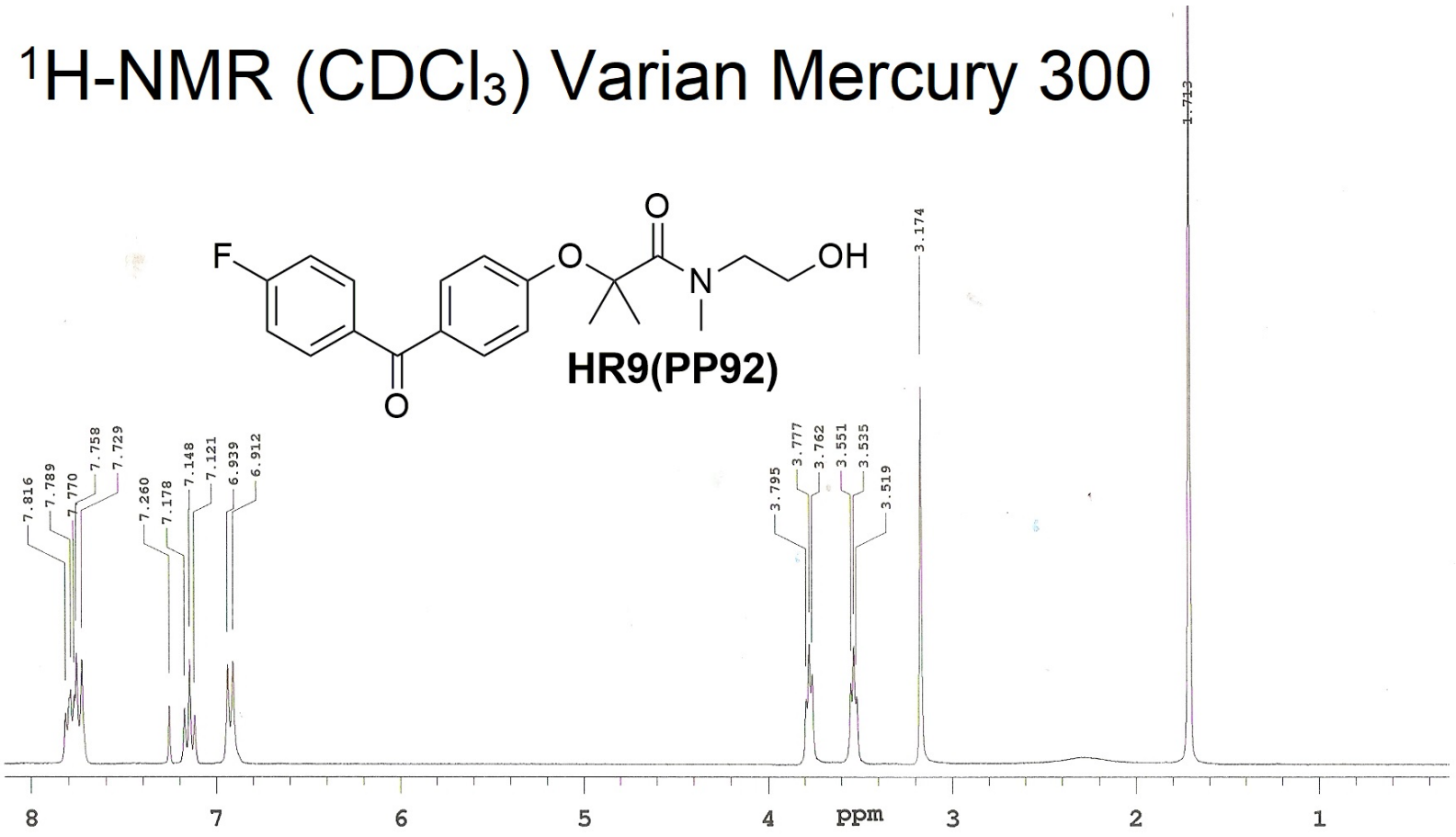


^{1}H-NMR ($CDCl_3$) Varian Mercury 300

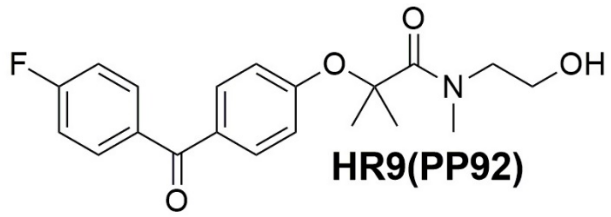


HR8(PP77)

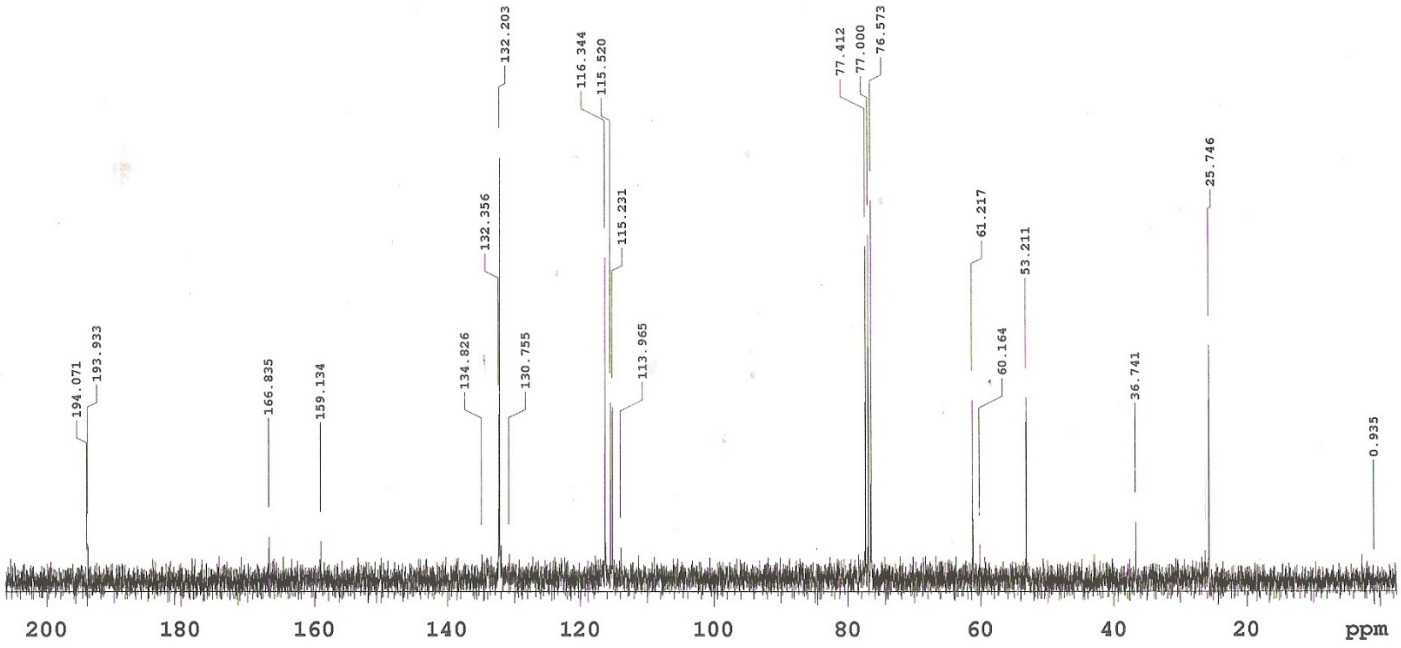
^{1}H-NMR ($CDCl_3$) Varian Mercury 300



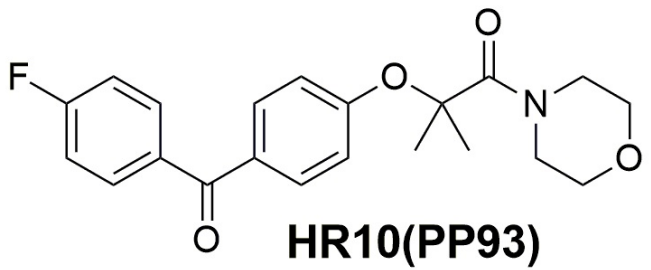
^{13}C-NMR ($CDCl_3$) Varian Mercury 300



HR9(PP92)

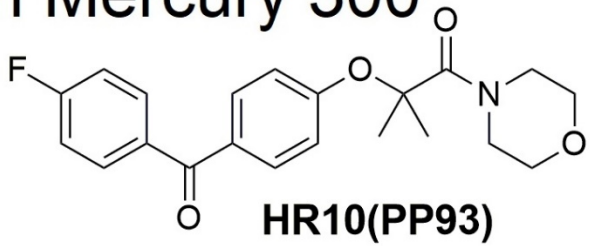


^{1}H-NMR ($CDCl_3$) Varian Mercury 300

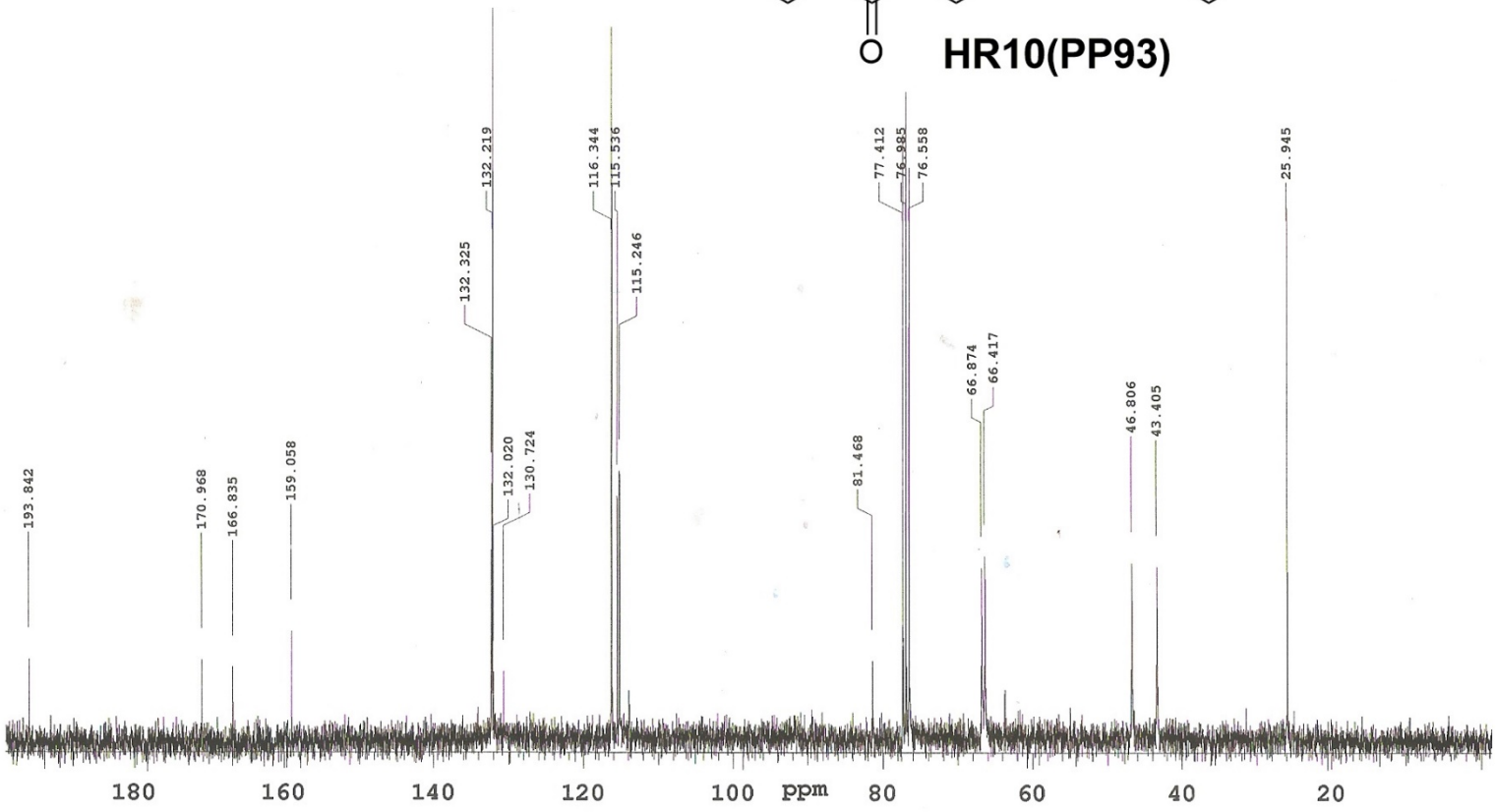


HR10(PP93)

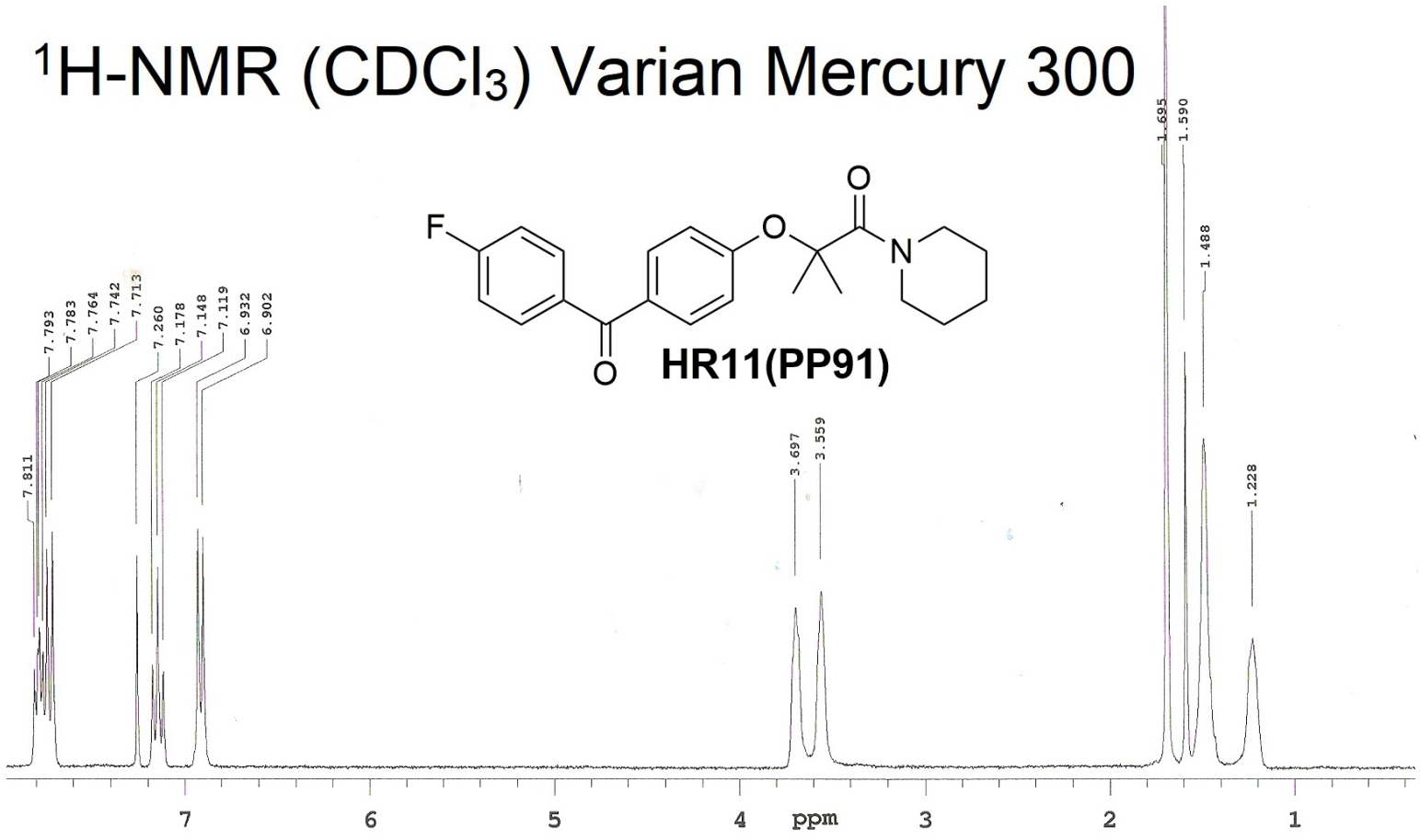
^{13}C-NMR ($CDCl_3$) Varian Mercury 300



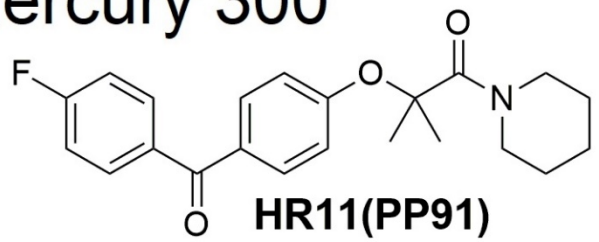
HR10(PP93)



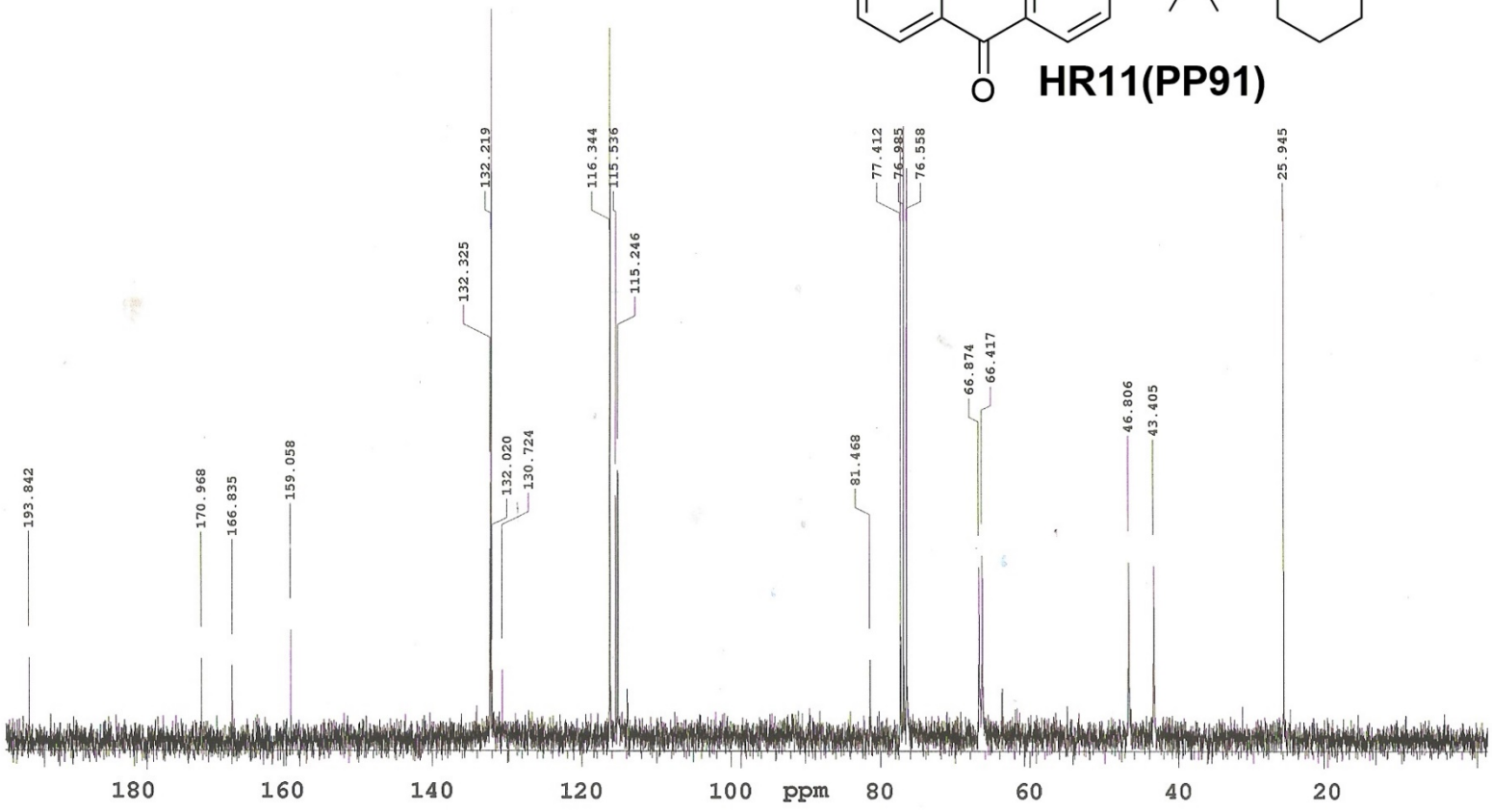
^{1}H-NMR ($CDCl_3$) Varian Mercury 300



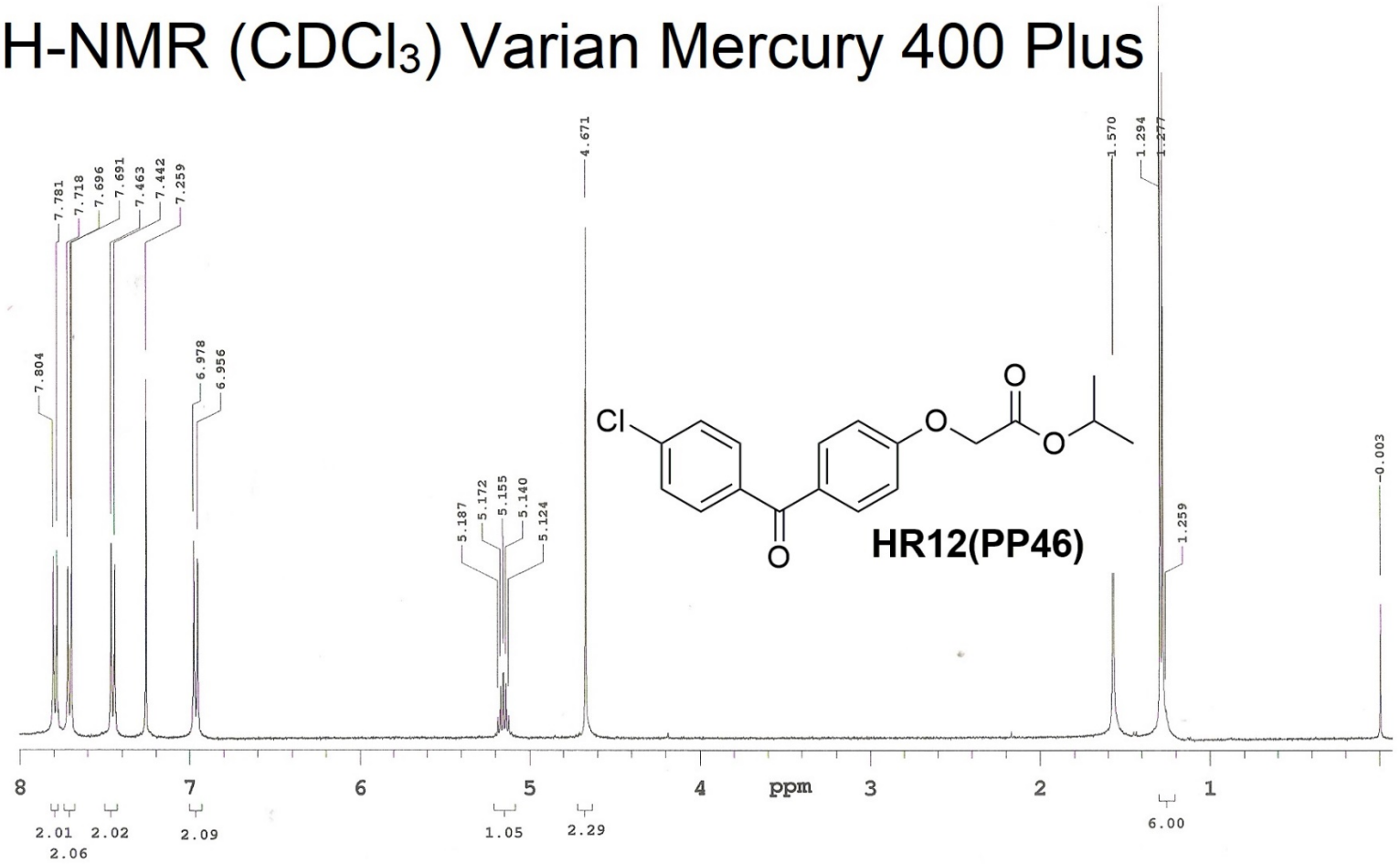
^{13}C-NMR ($CDCl_3$) Varian Mercury 300



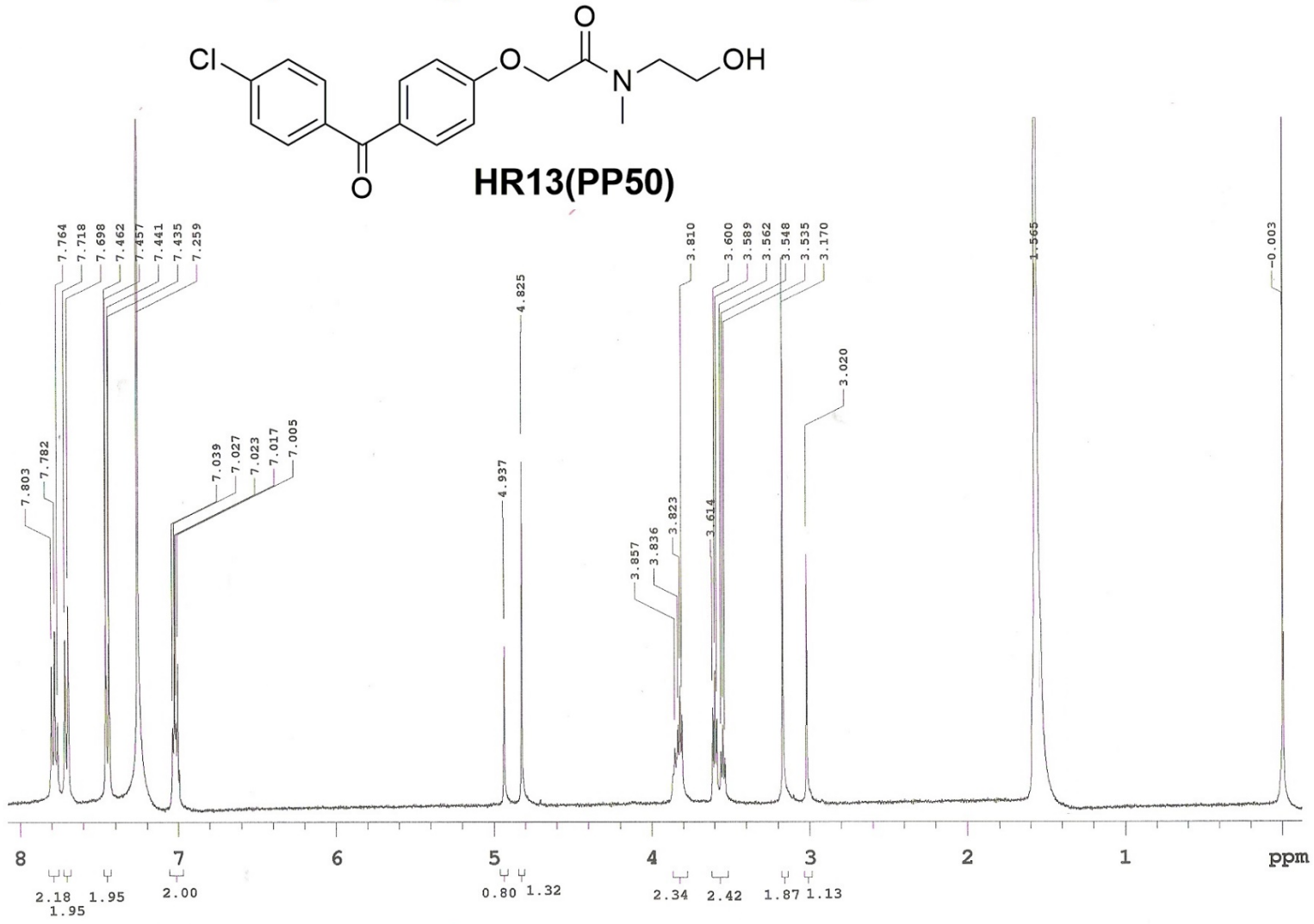
HR11(PP91)



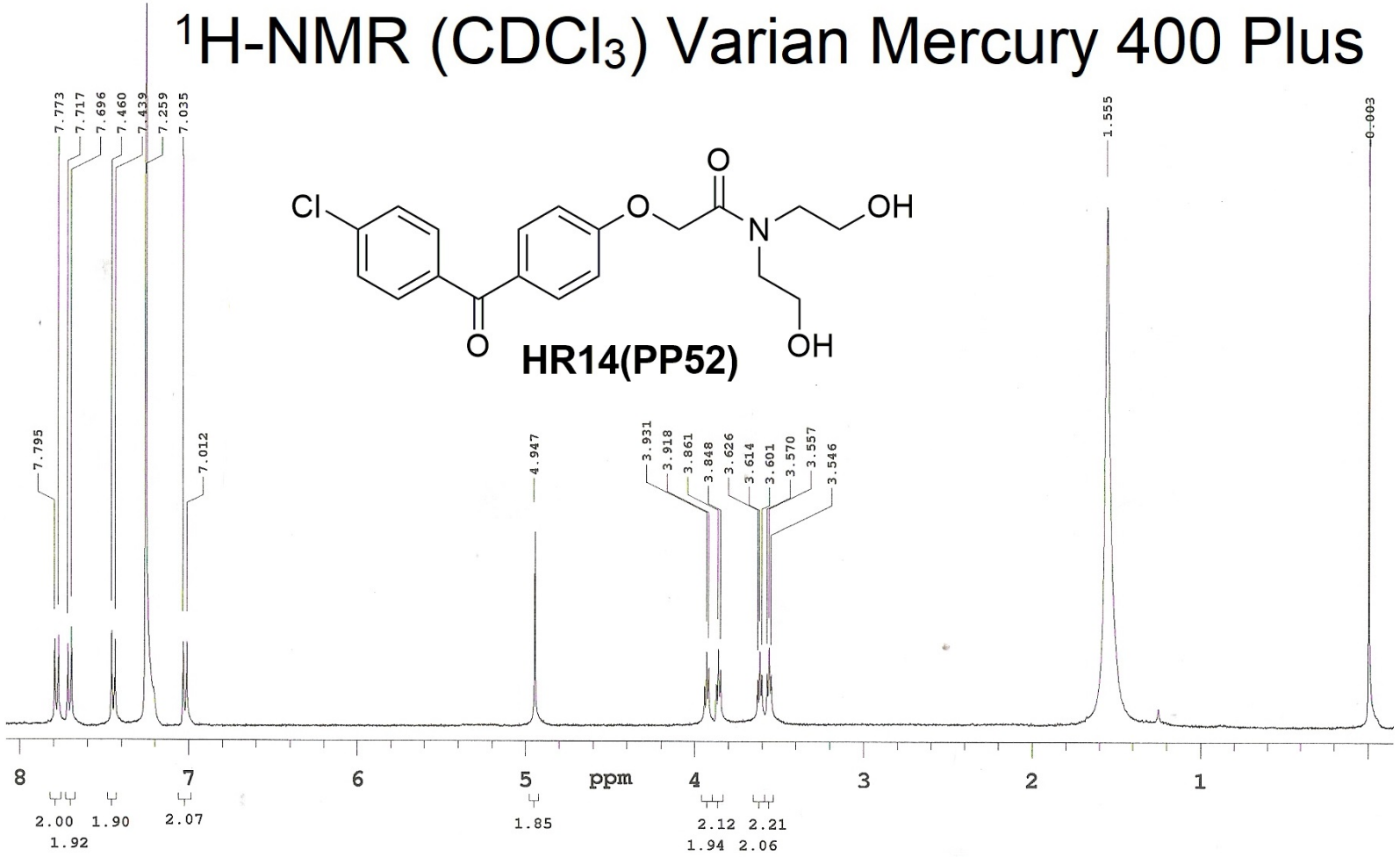
^{1}H-NMR ($CDCl_3$) Varian Mercury 400 Plus



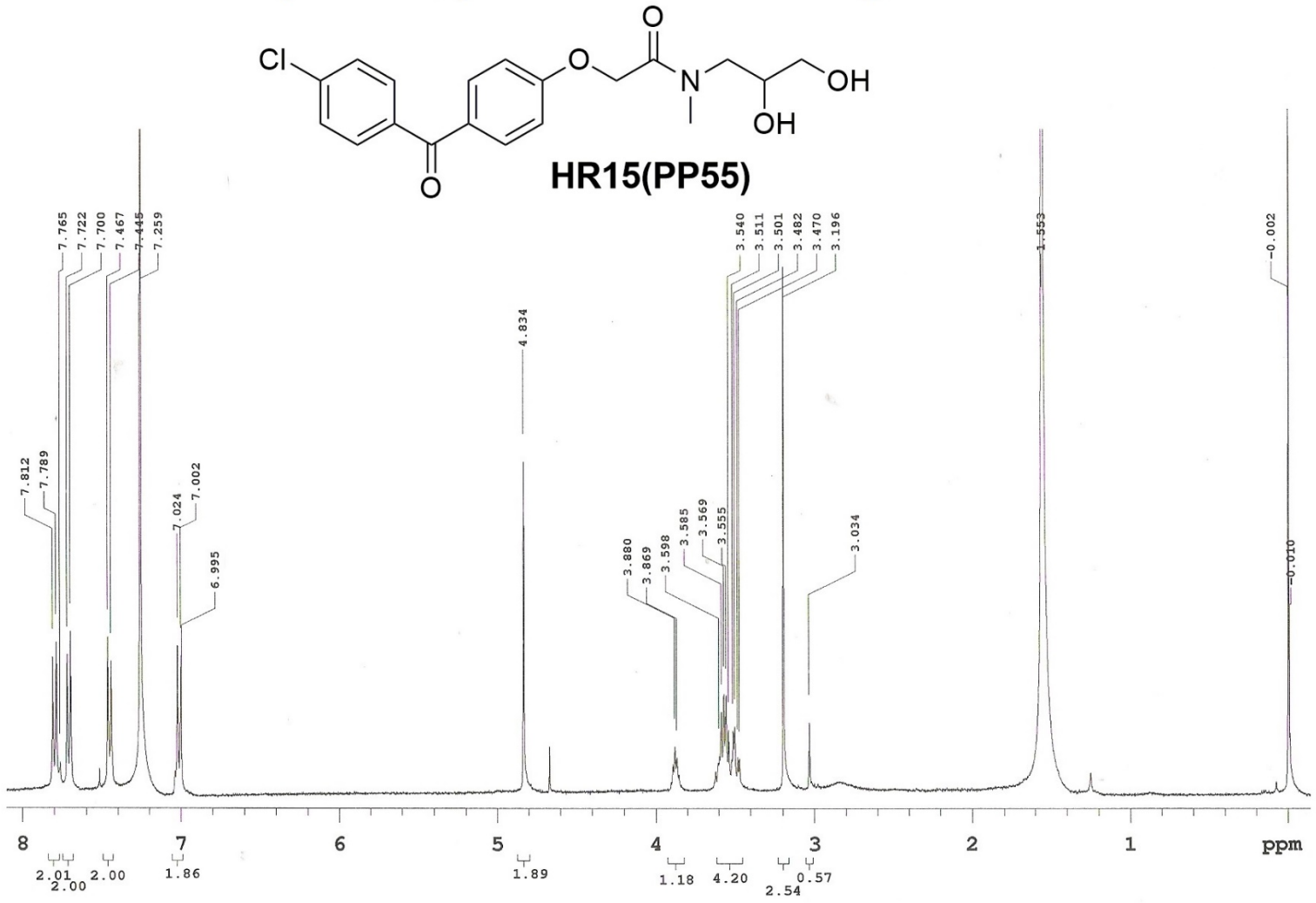
^{1}H-NMR ($CDCl_3$) Varian Mercury 400 Plus



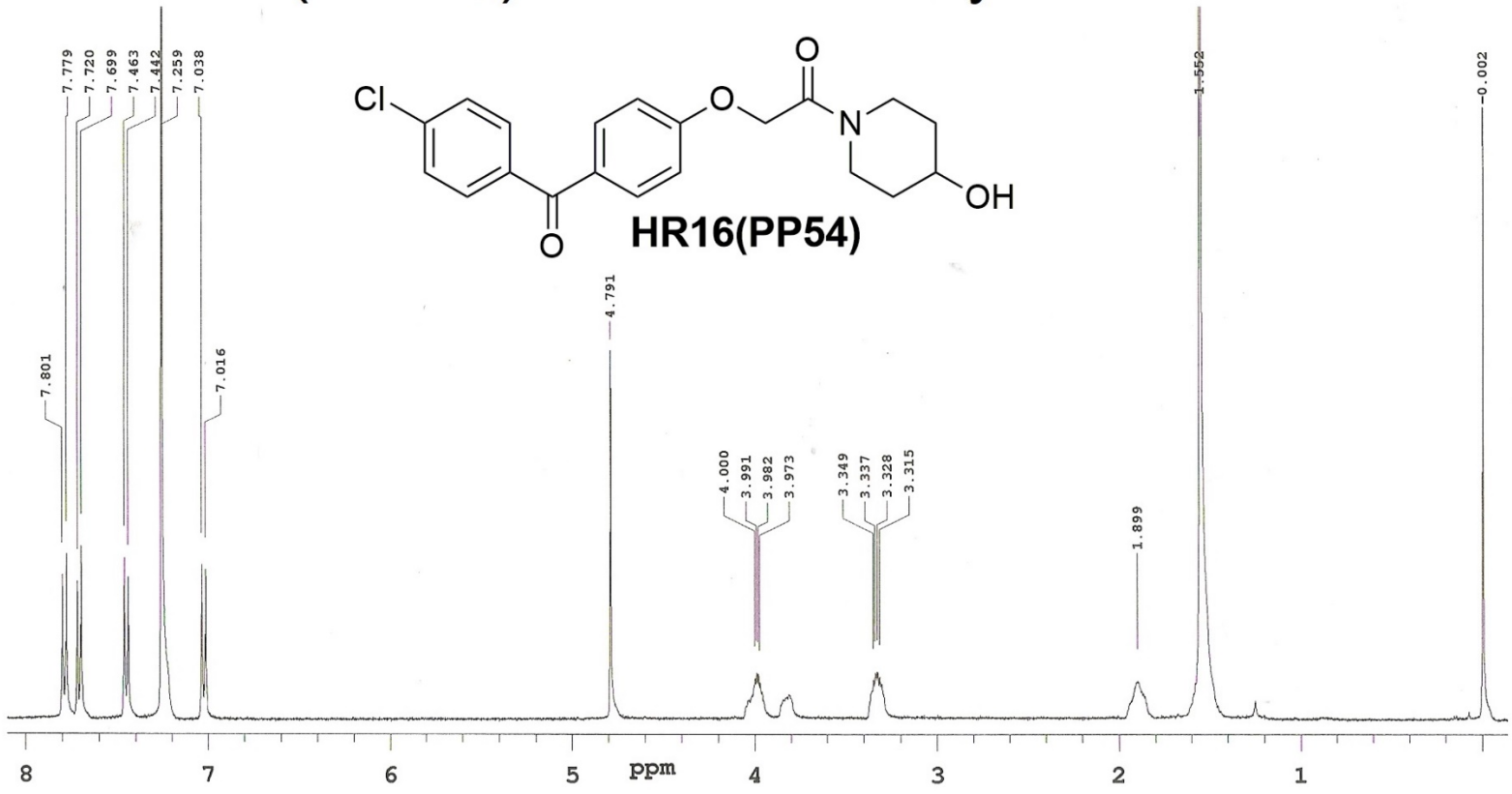
^{1}H-NMR ($CDCl_3$) Varian Mercury 400 Plus



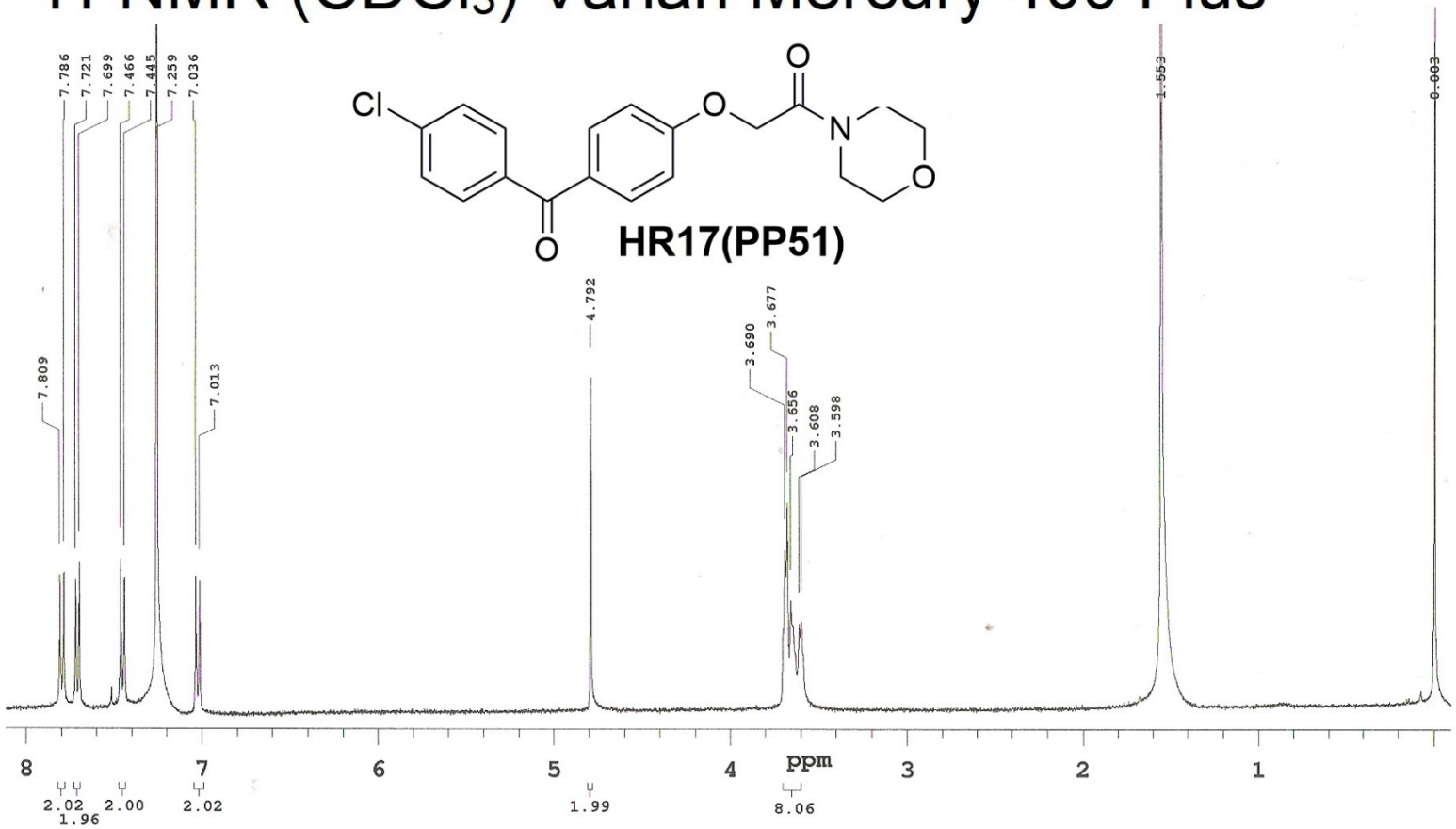
^{1}H-NMR ($CDCl_3$) Varian Mercury 400 Plus



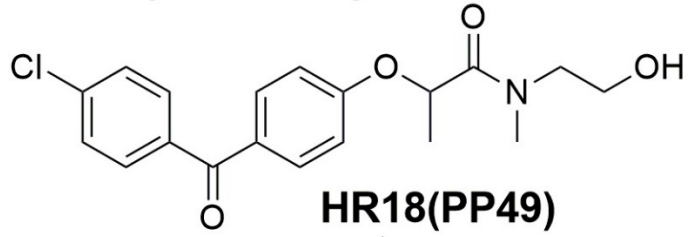
^{1}H-NMR ($CDCl_3$) Varian Mercury 400 Plus



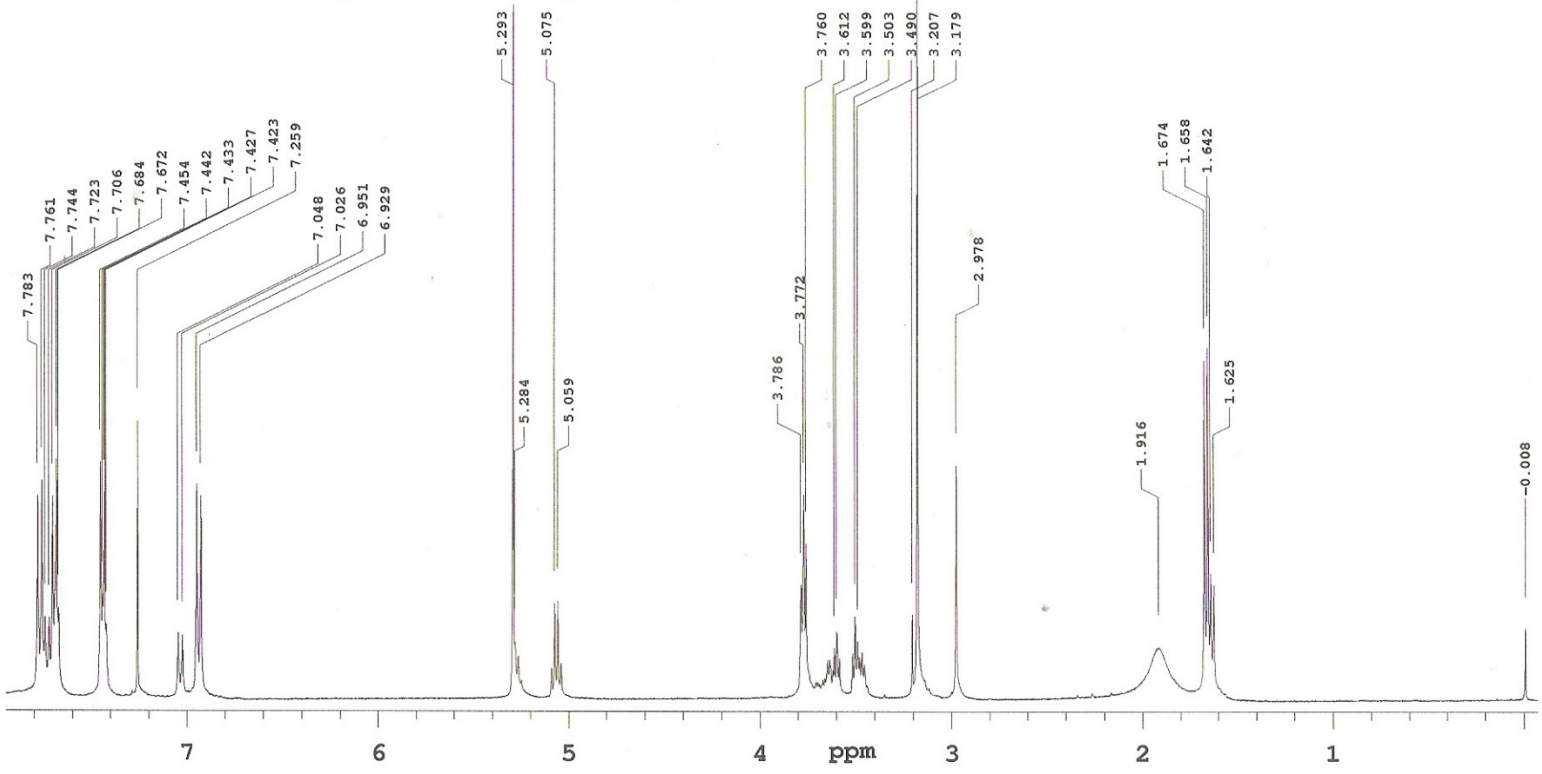
^{1}H-NMR ($CDCl_3$) Varian Mercury 400 Plus



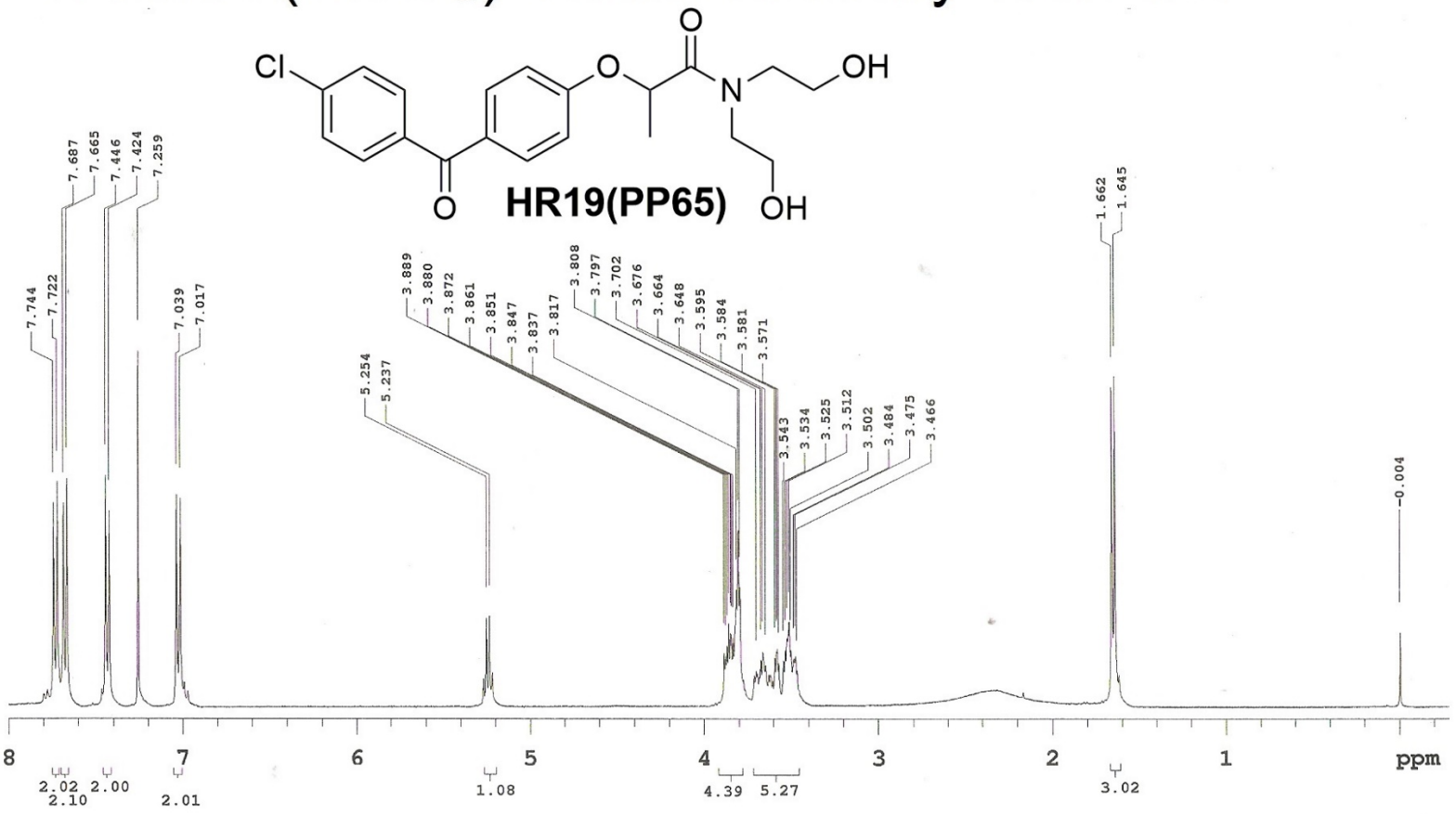
^{1}H-NMR ($CDCl_3$) Varian Mercury 400 Plus



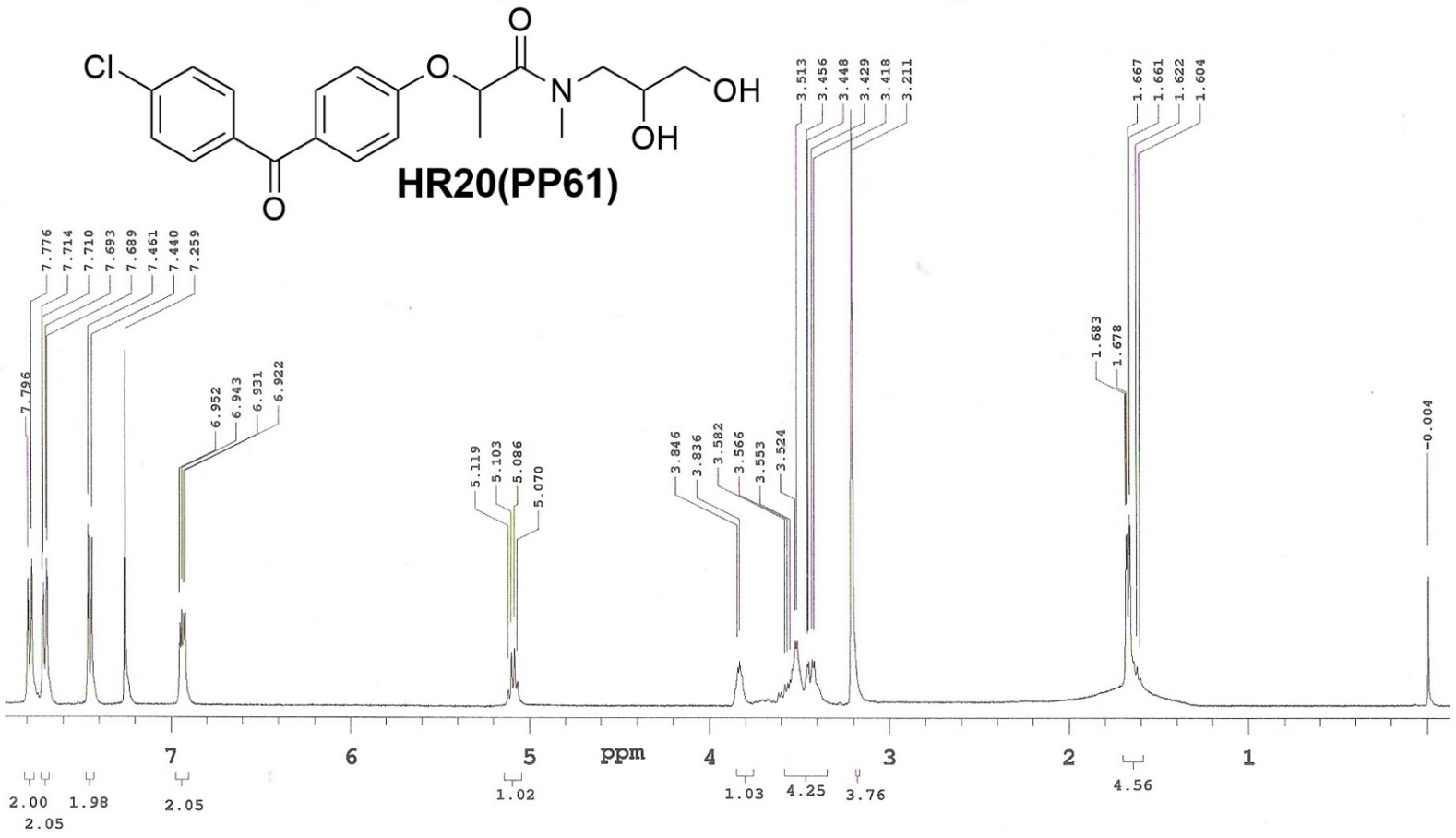
HR18(PP49)



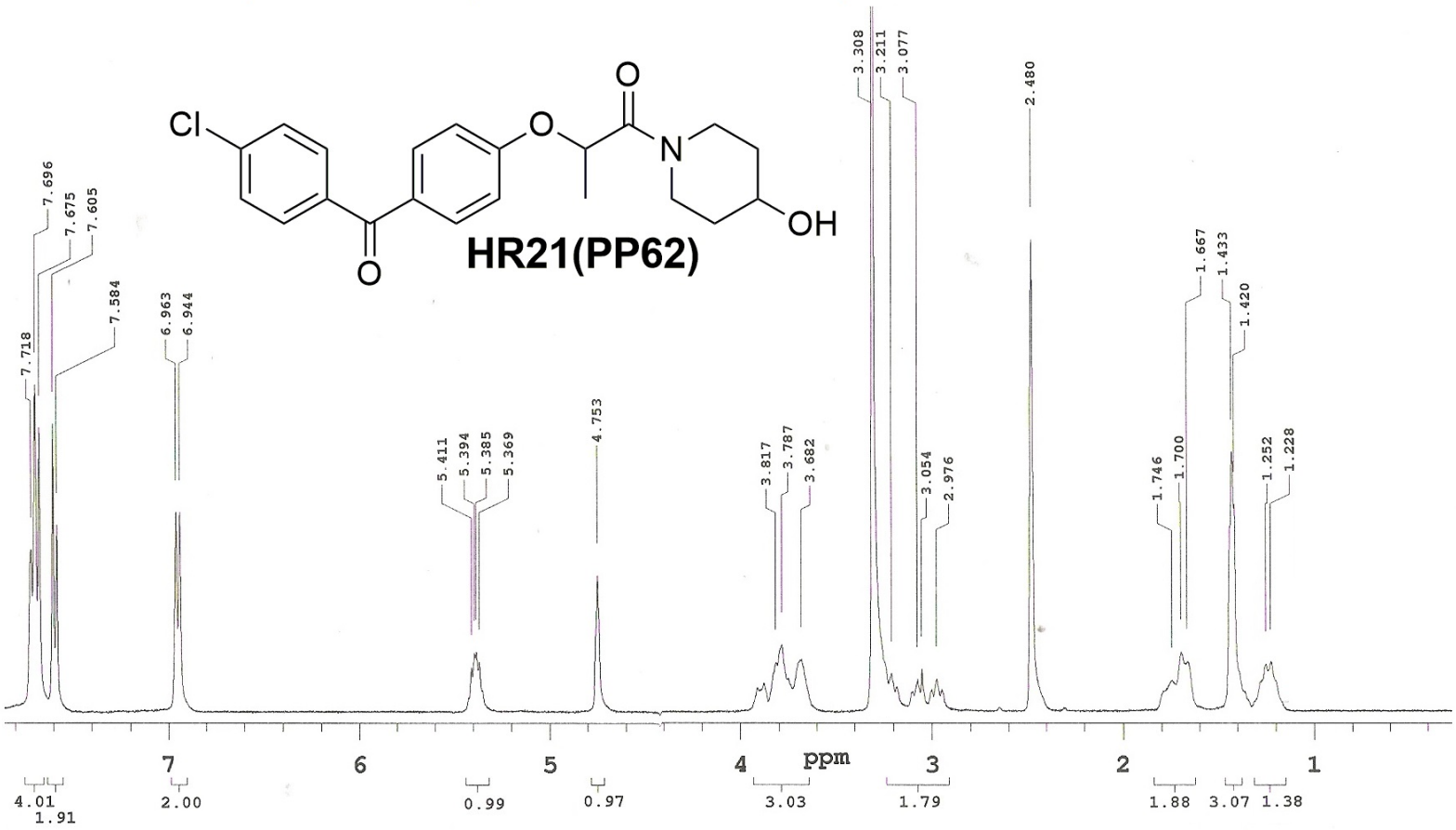
^{1}H-NMR ($CDCl_3$) Varian Mercury 400 Plus



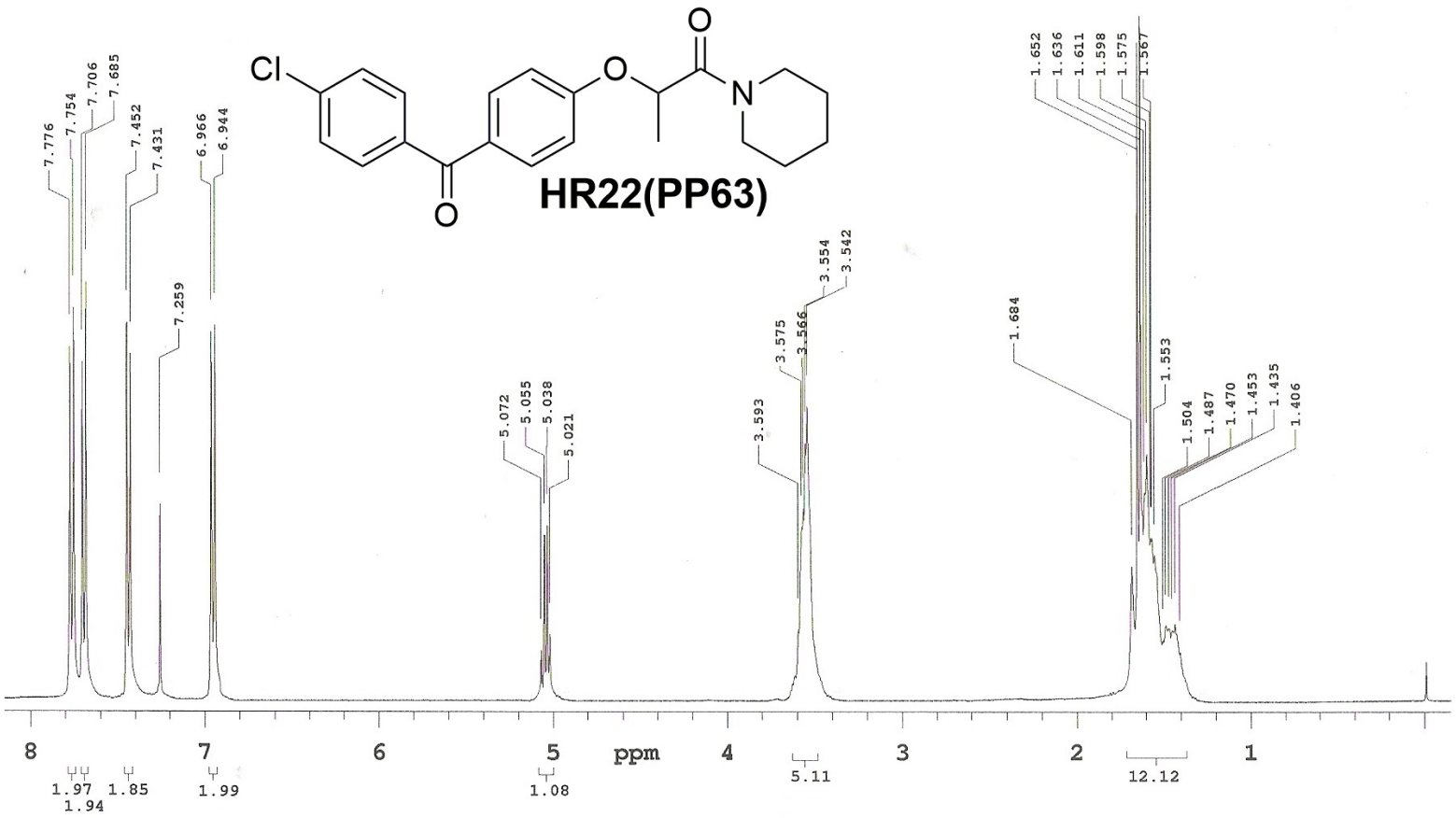
^{1}H-NMR ($CDCl_3$) Varian Mercury 400 Plus



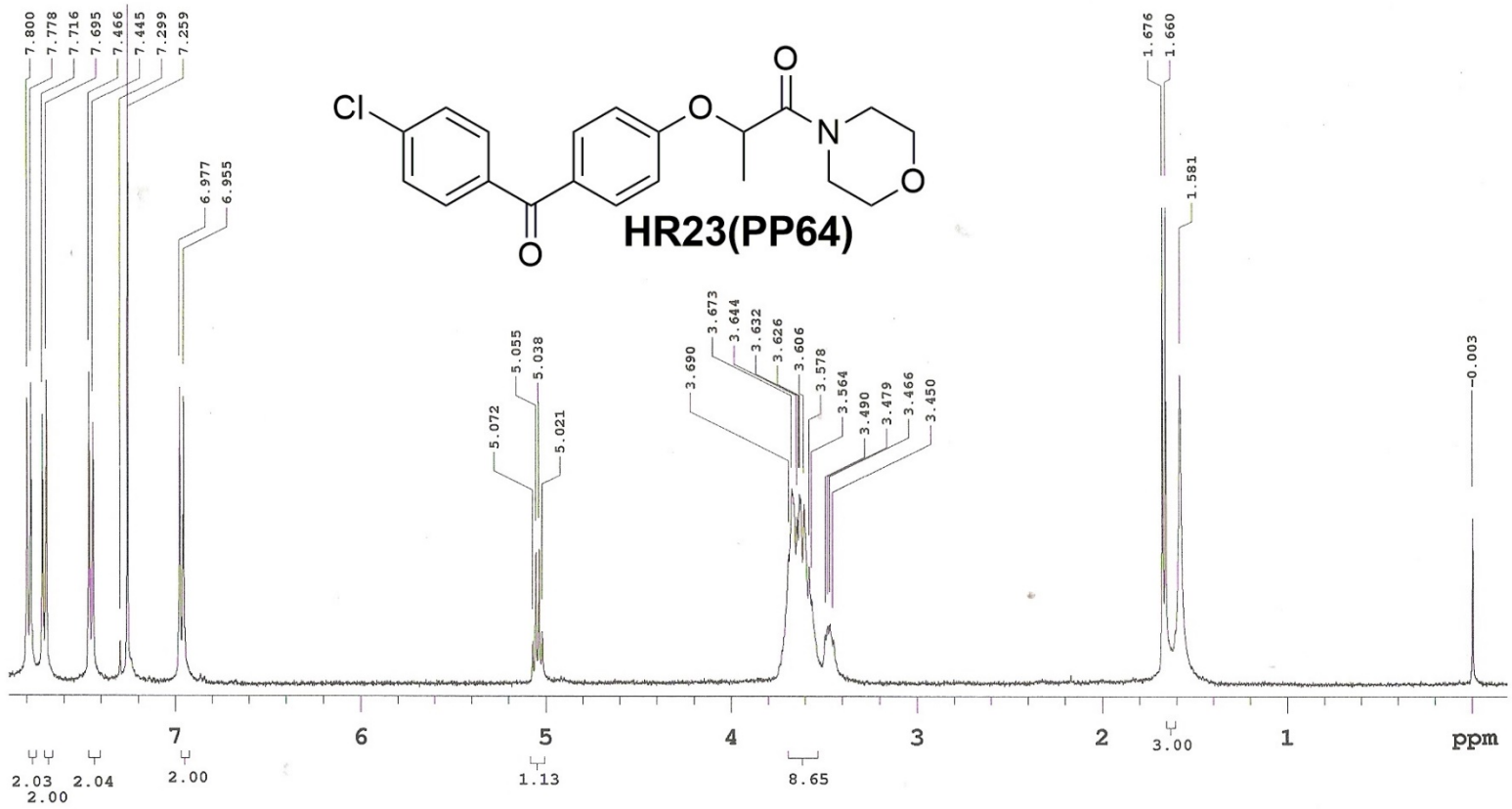
^{1}H-NMR (DMSO-d_6) Varian Mercury 400 Plus



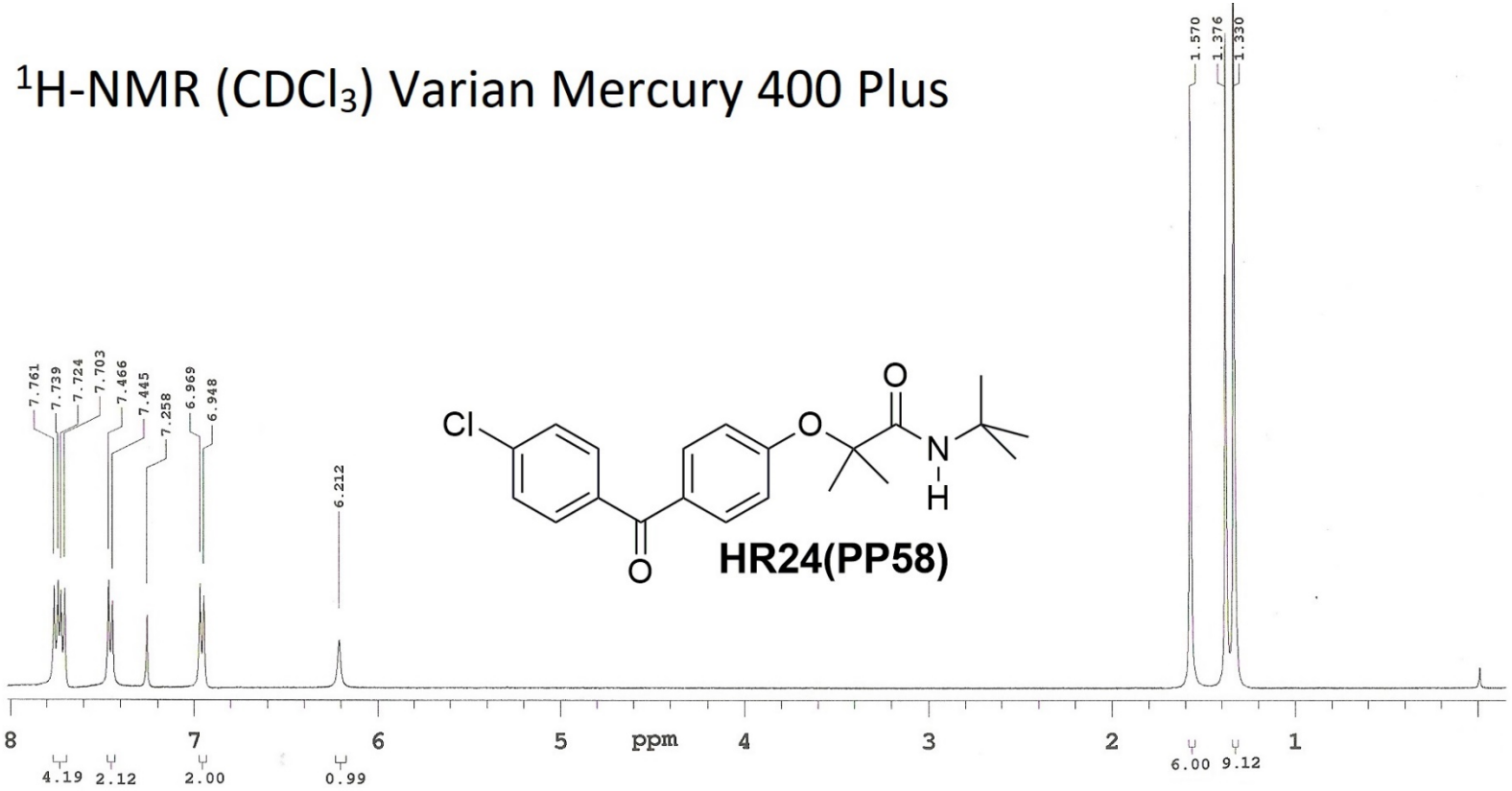
^{1}H-NMR ($CDCl_3$) Varian Mercury 400 Plus



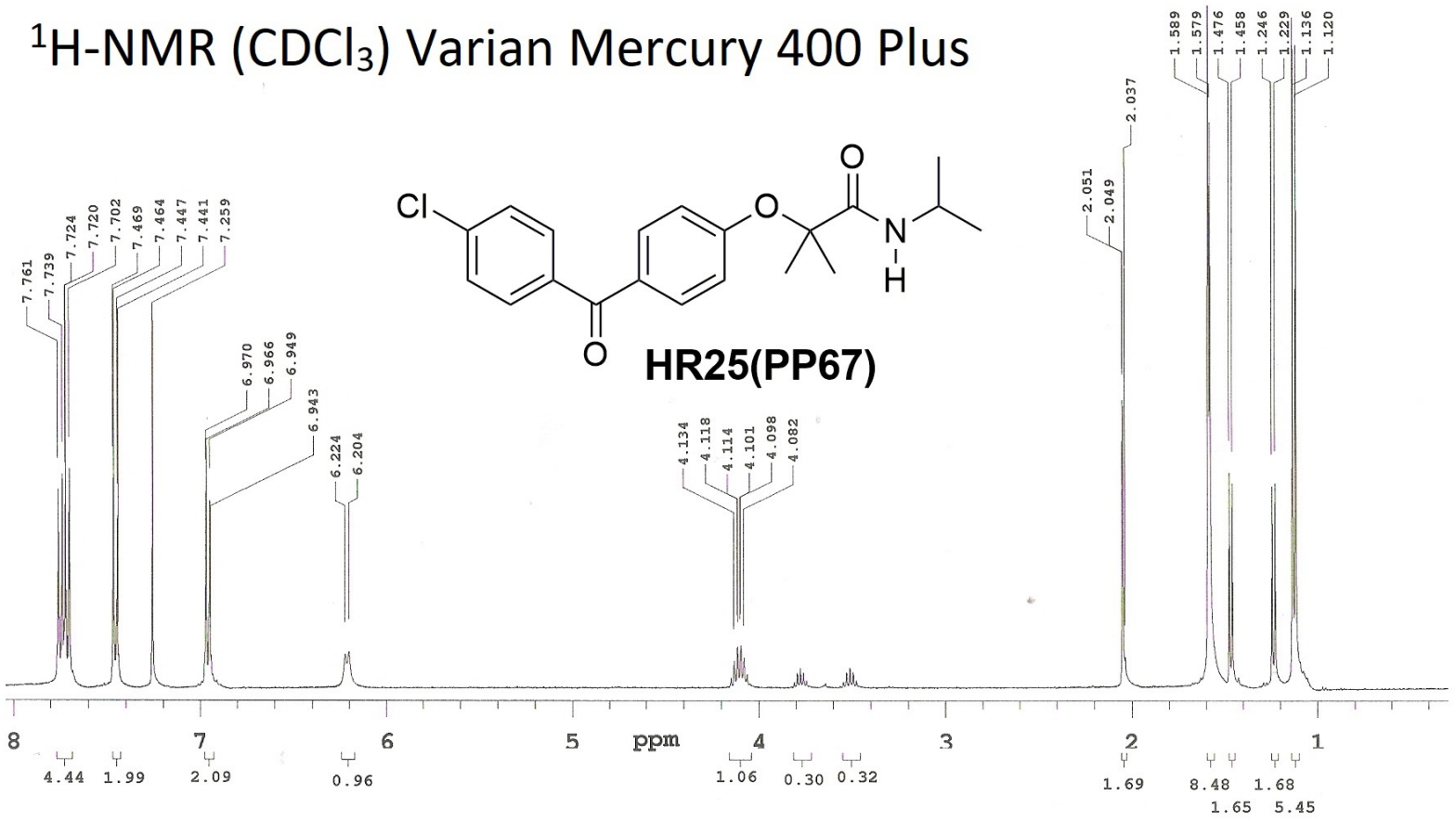
^{1}H-NMR ($CDCl_3$) Varian Mercury 400 Plus



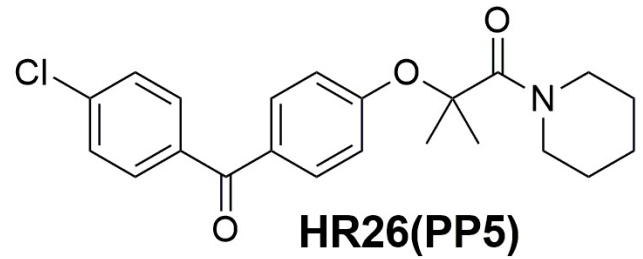
^{1}H-NMR ($CDCl_3$) Varian Mercury 400 Plus



^{1}H-NMR ($CDCl_3$) Varian Mercury 400 Plus

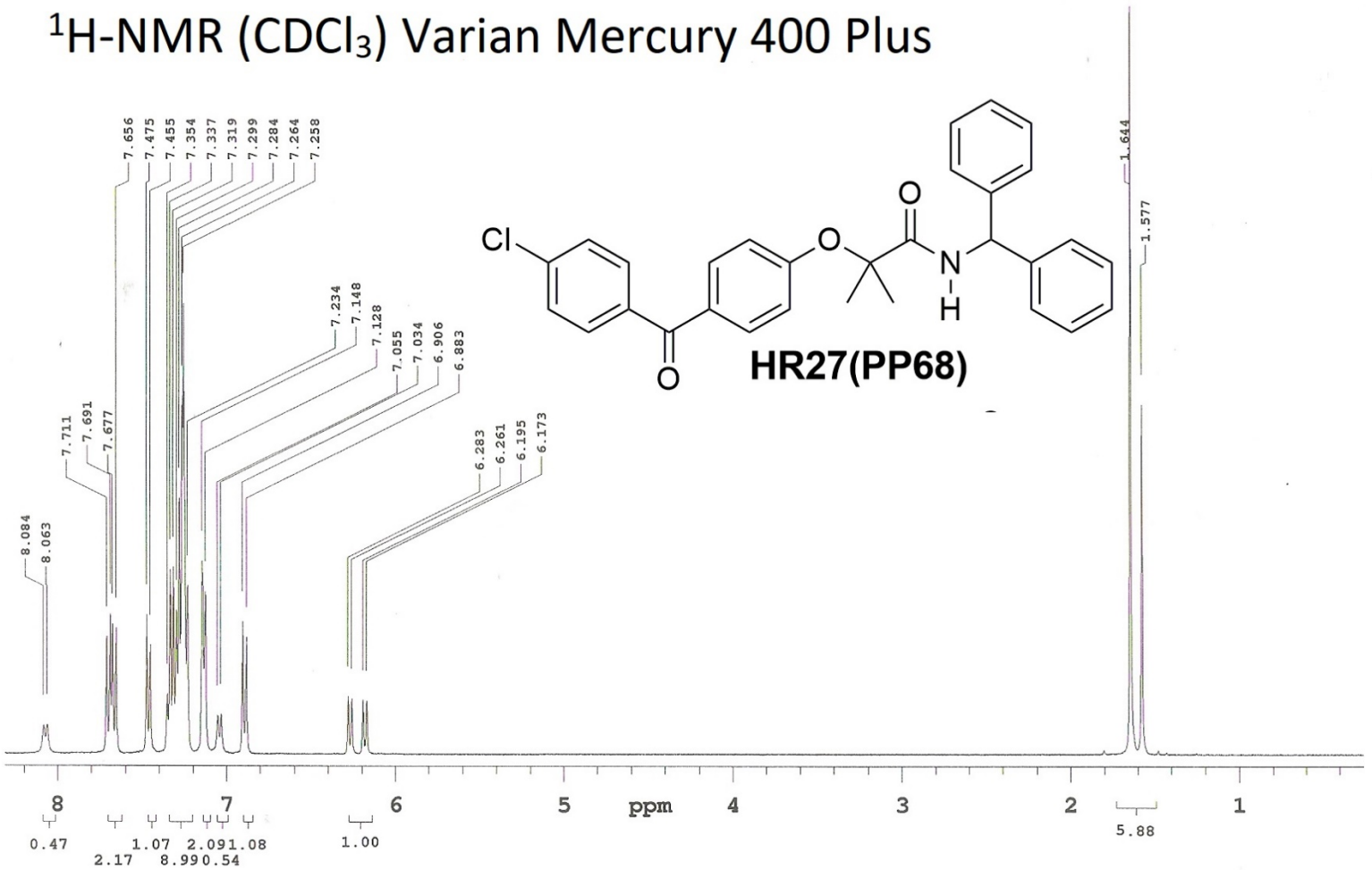


^{1}H-NMR ($CDCl_3$) Varian Mercury 400 Plus

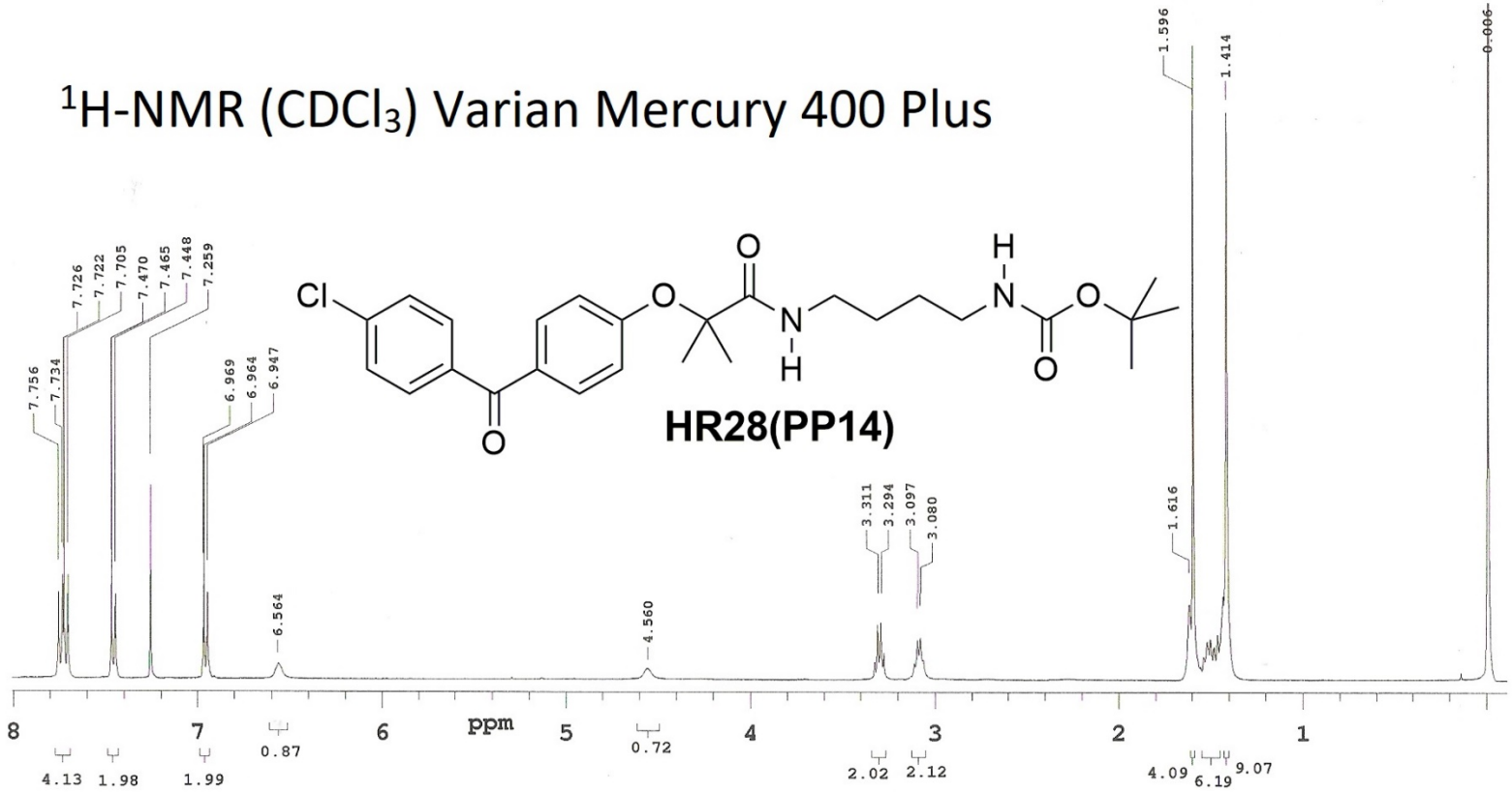


HR26(PP5)

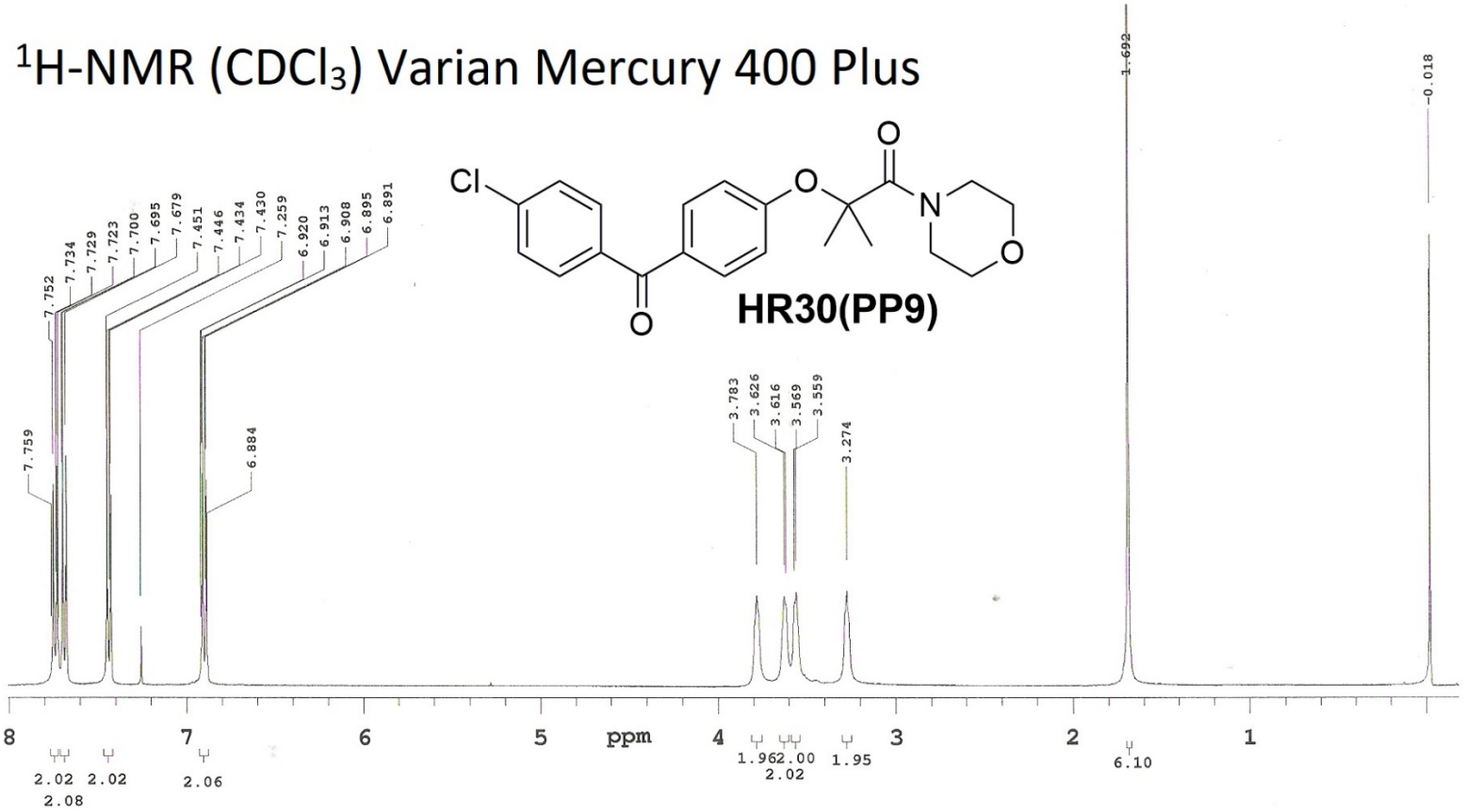
^{1}H-NMR ($CDCl_3$) Varian Mercury 400 Plus



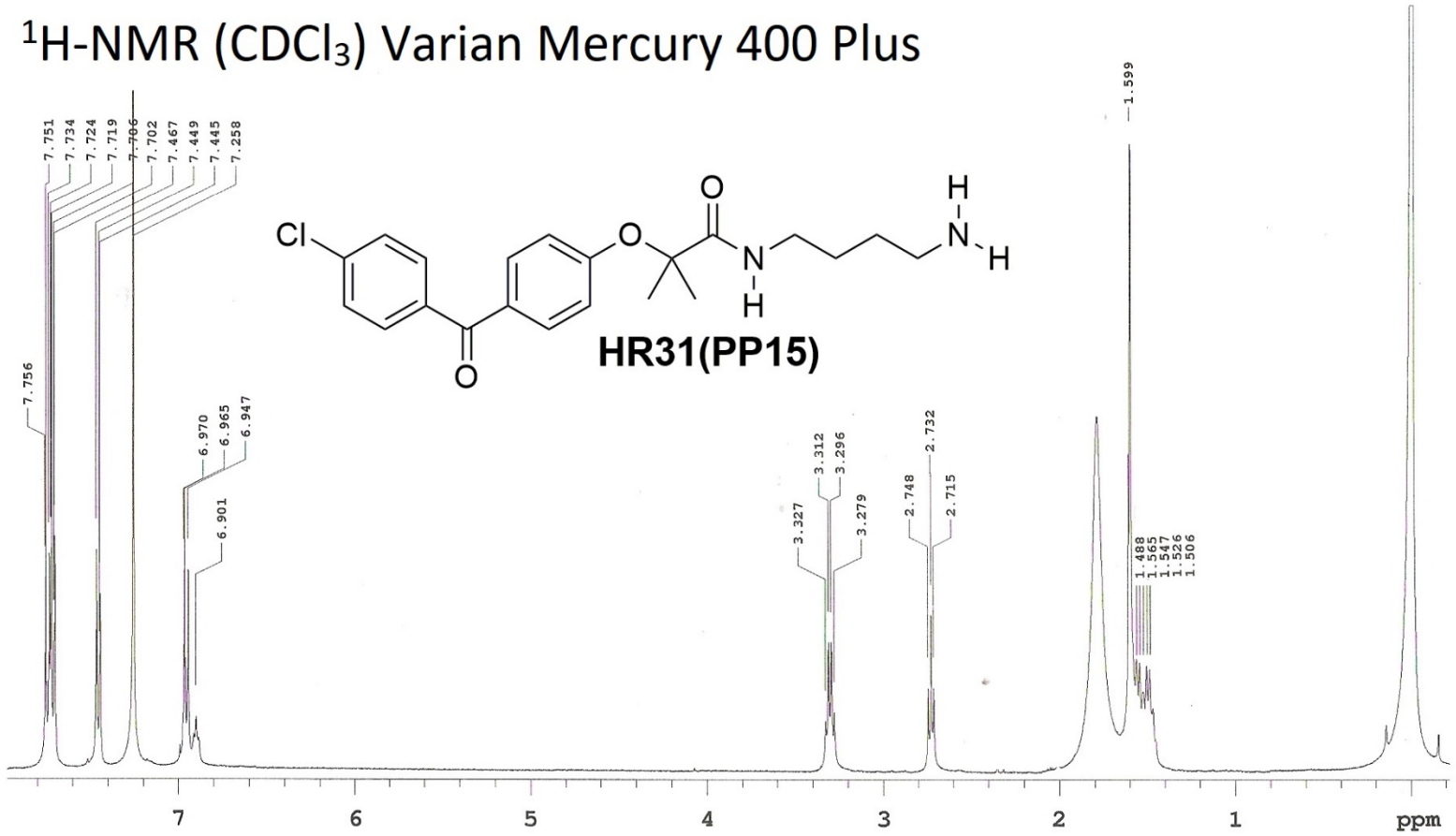
^{1}H-NMR ($CDCl_3$) Varian Mercury 400 Plus



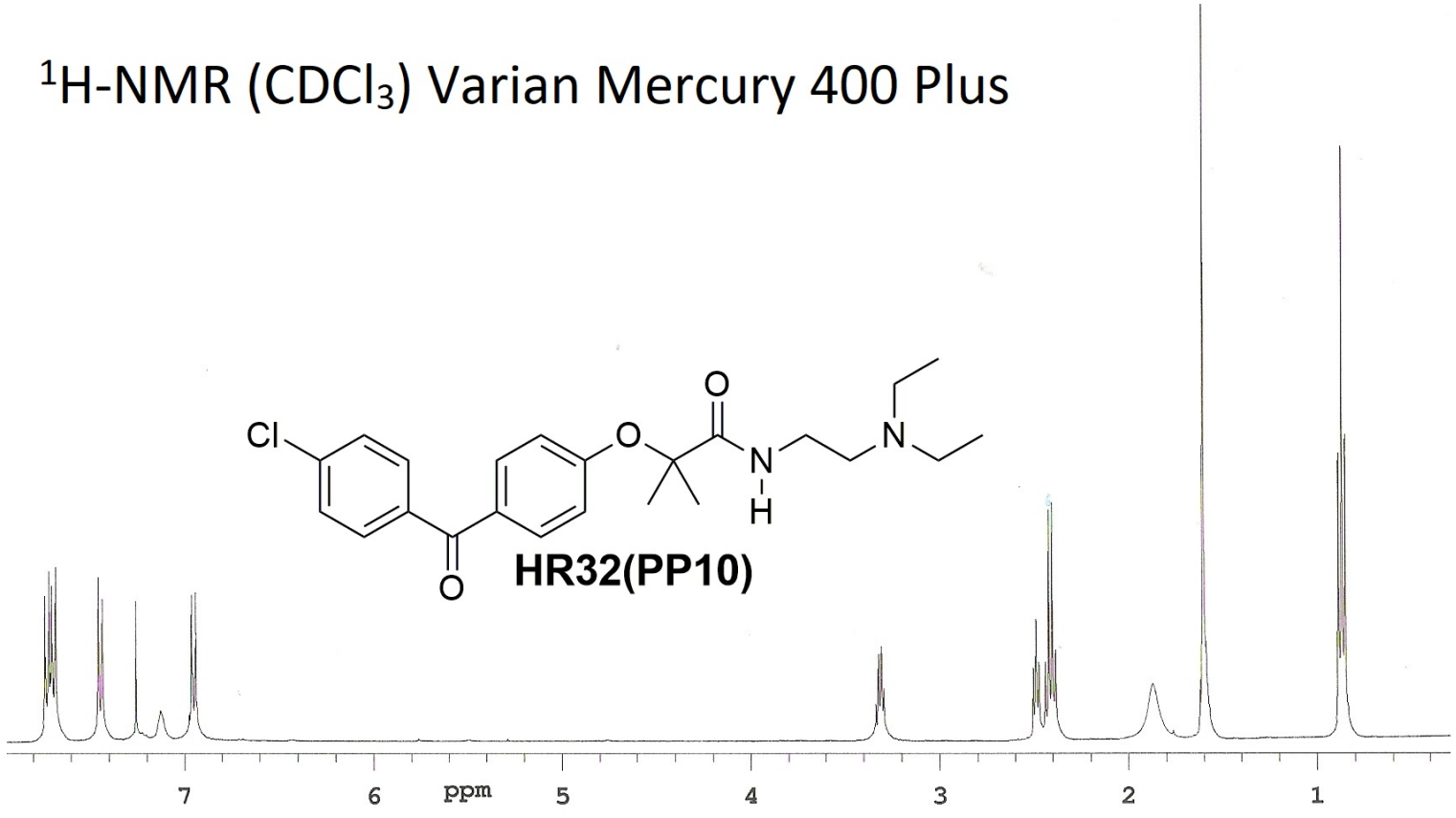
^{1}H-NMR ($CDCl_3$) Varian Mercury 400 Plus



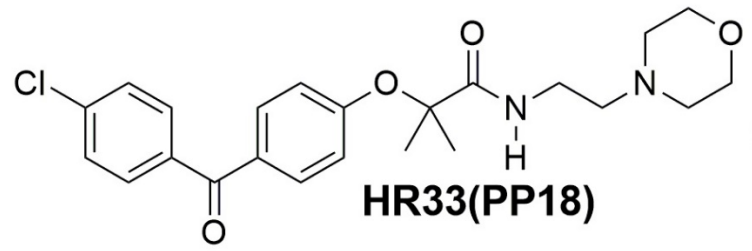
^{1}H-NMR ($CDCl_3$) Varian Mercury 400 Plus



^{1}H-NMR ($CDCl_3$) Varian Mercury 400 Plus

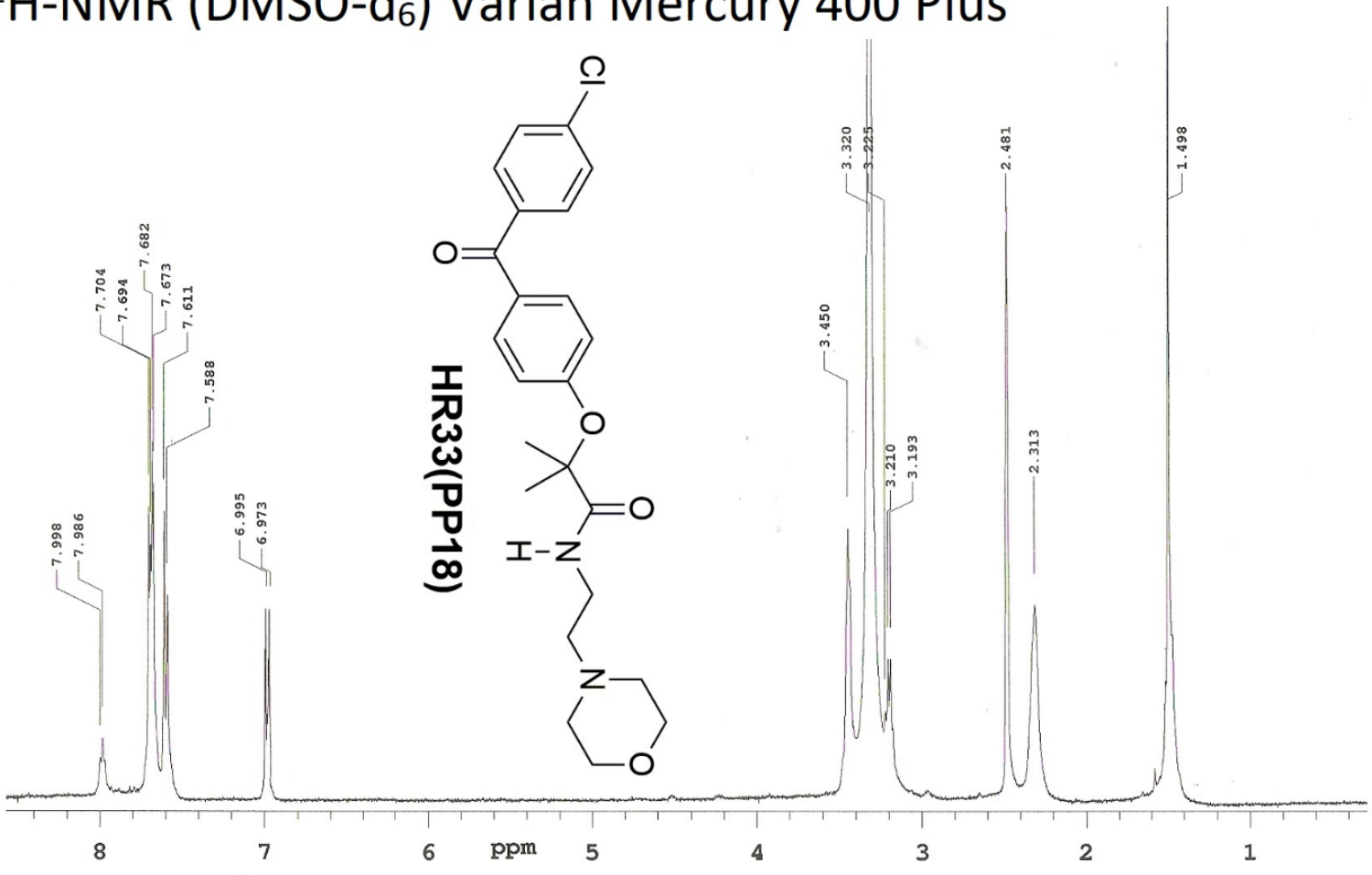


^{1}H-NMR ($CDCl_3$) Varian Mercury 400 Plus

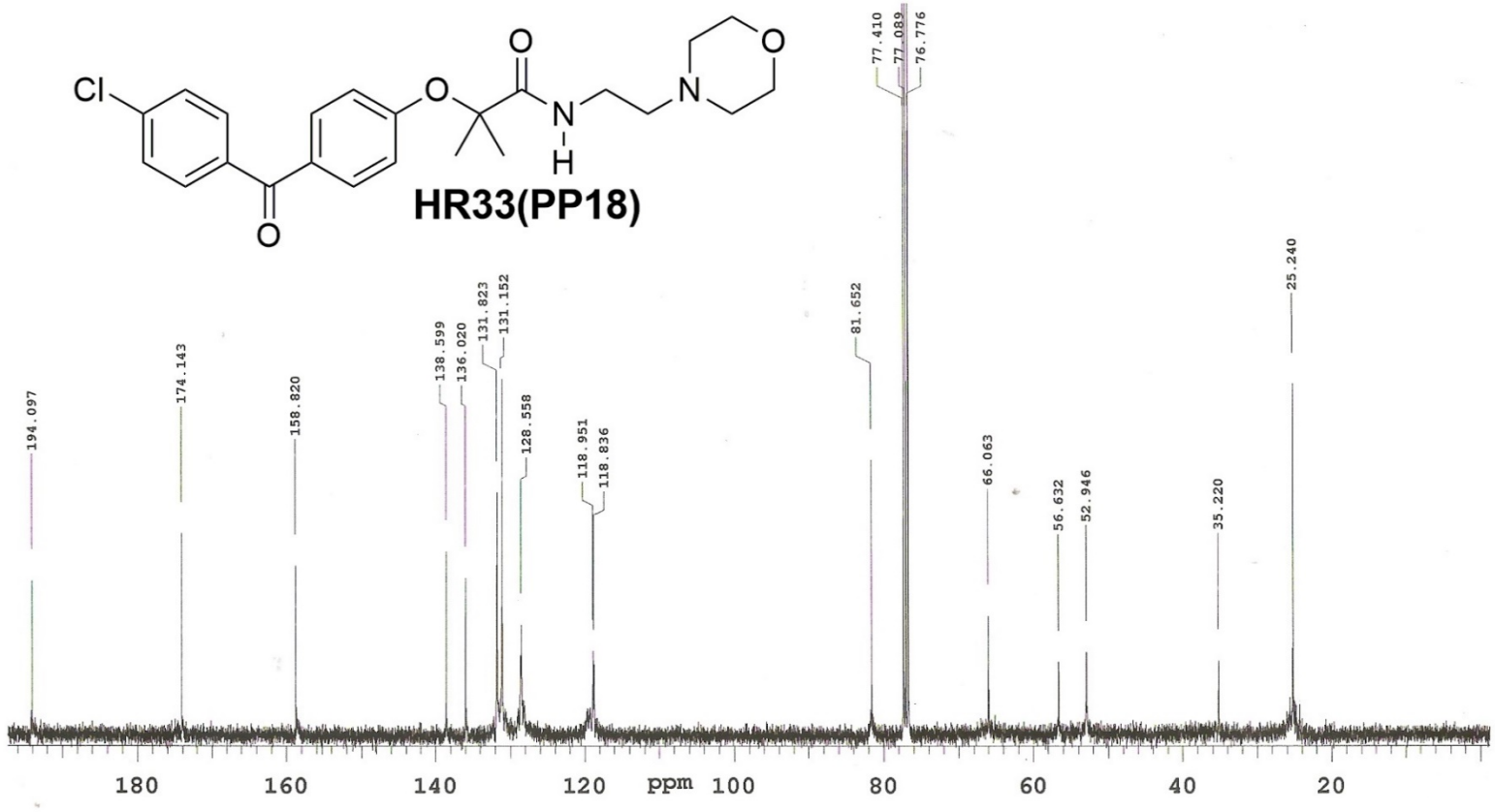


HR33(PP18)

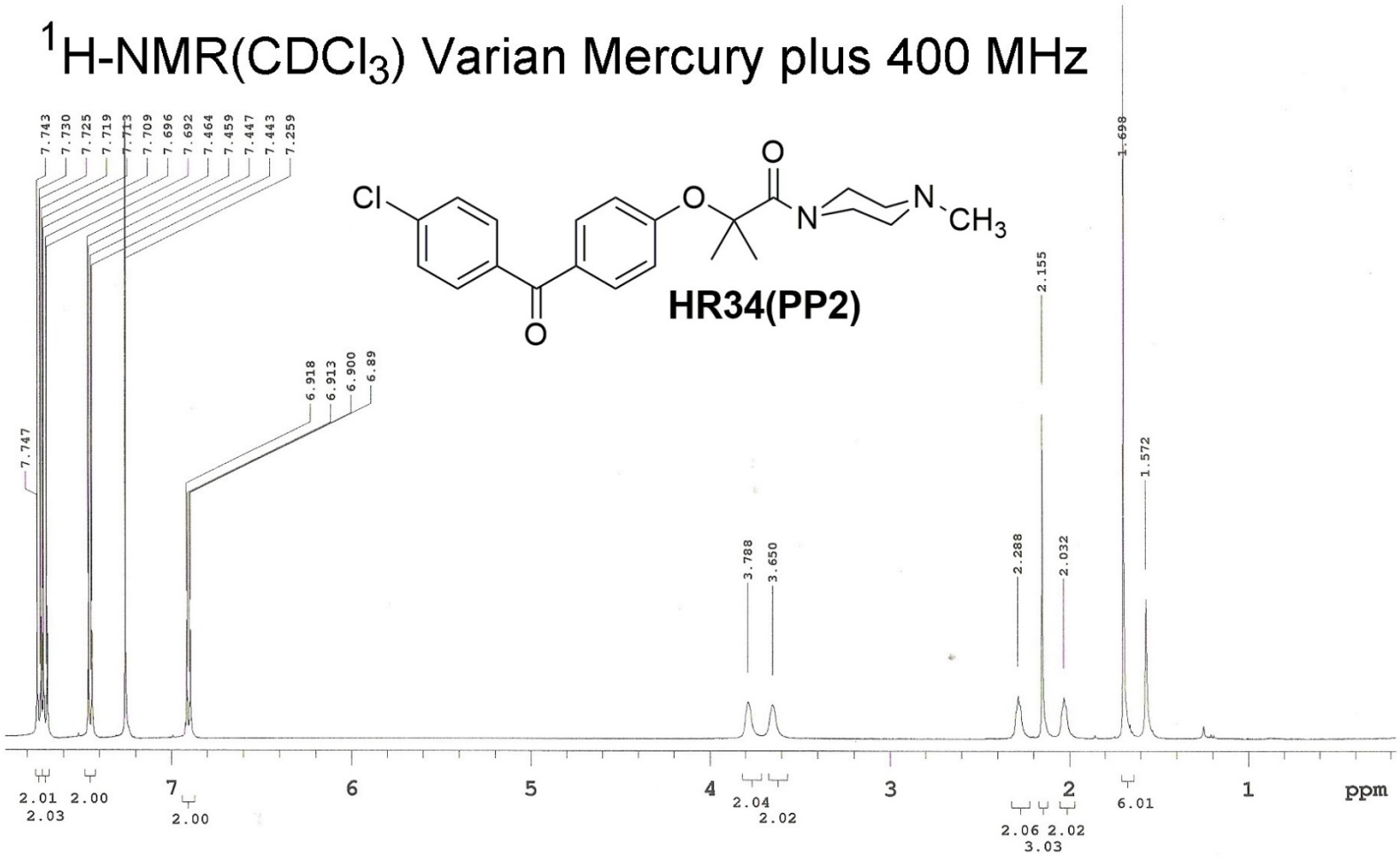
^{1}H-NMR (DMSO-d_6) Varian Mercury 400 Plus



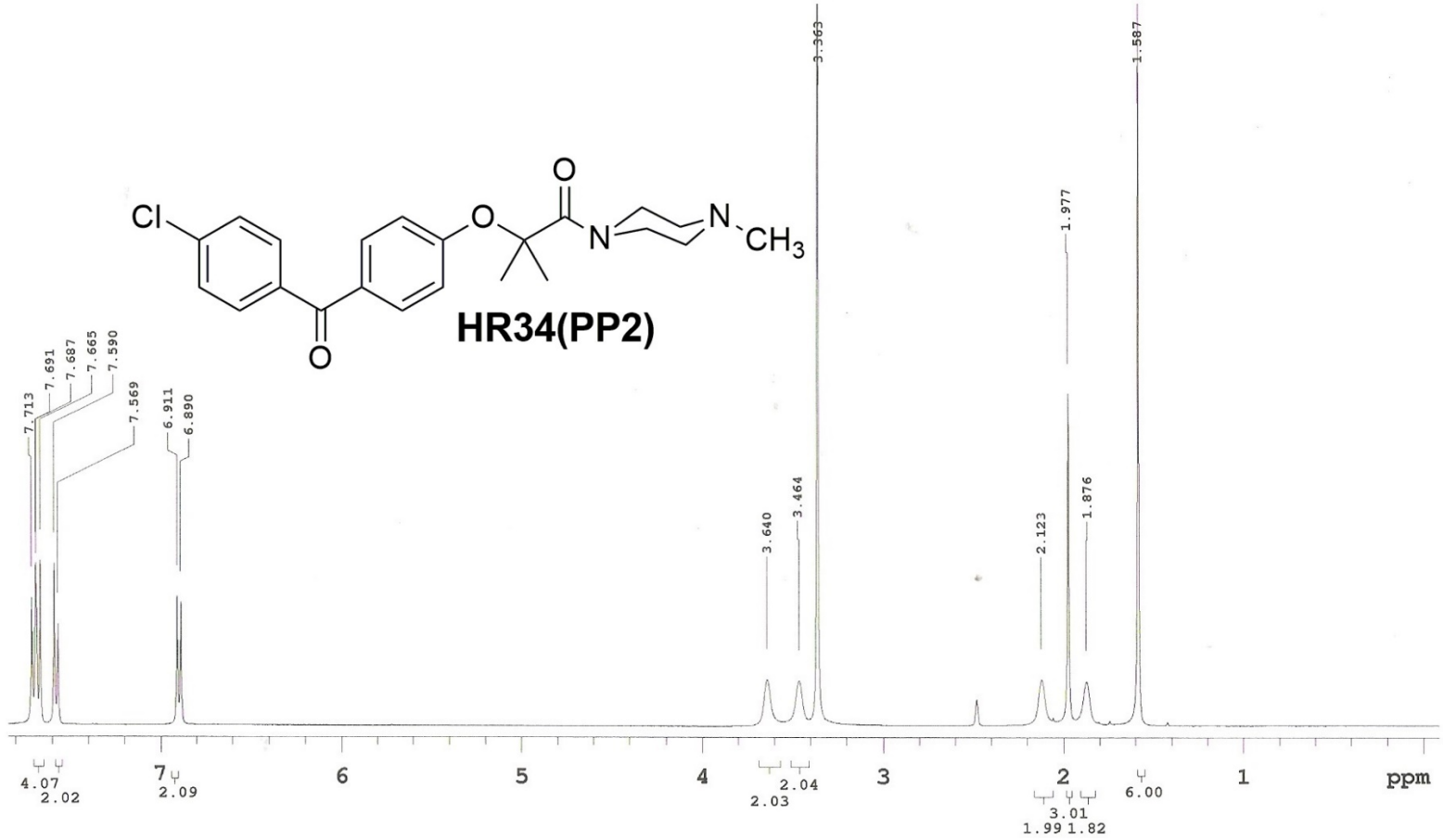
^{13}C-NMR ($CDCl_3$) Varian Mercury 400 Plus



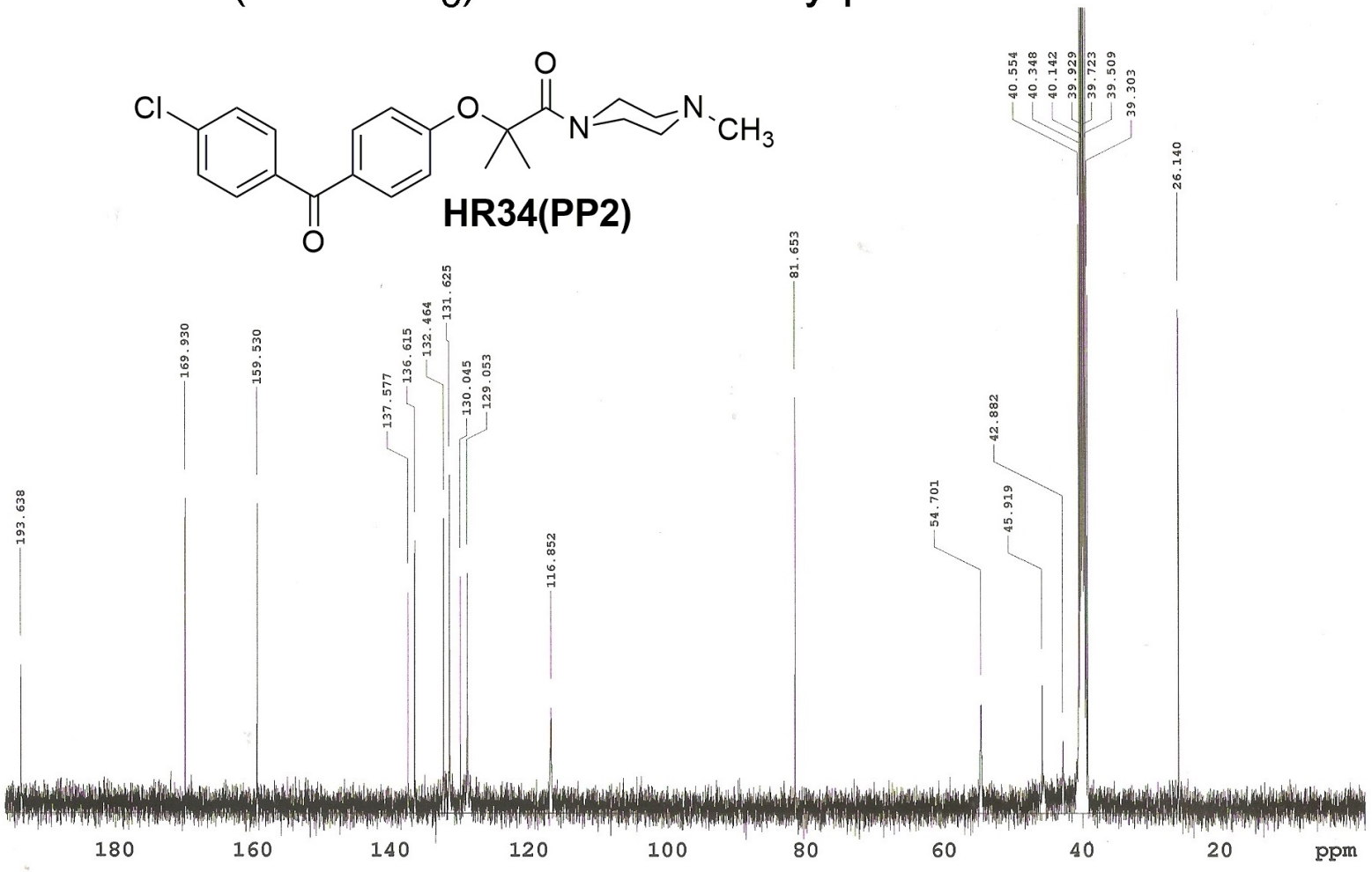
^{1}H-NMR($CDCl_3$) Varian Mercury plus 400 MHz



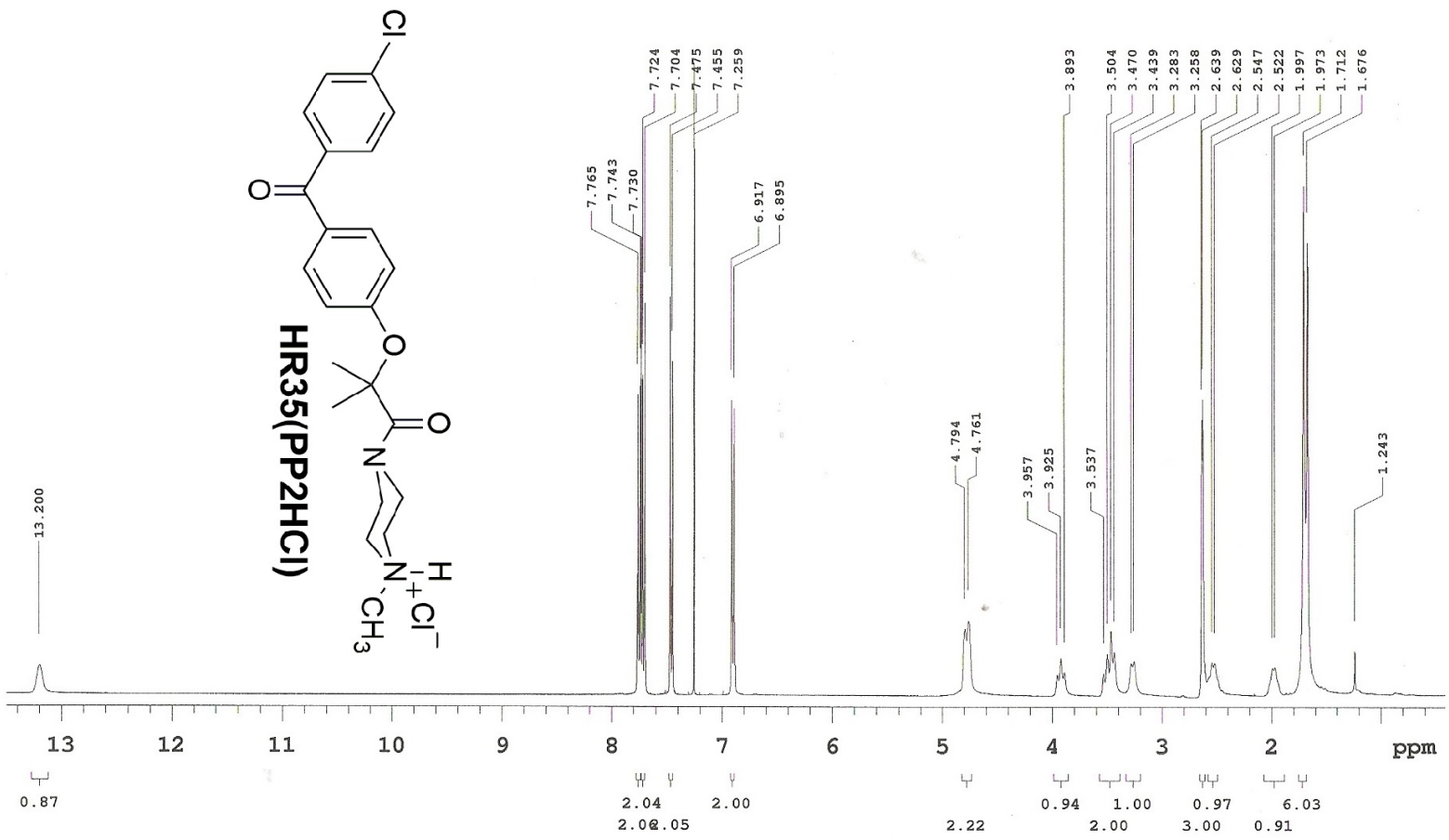
^{1}H-NMR(DMSO-d_6) Varian Mercury plus 400 MHz



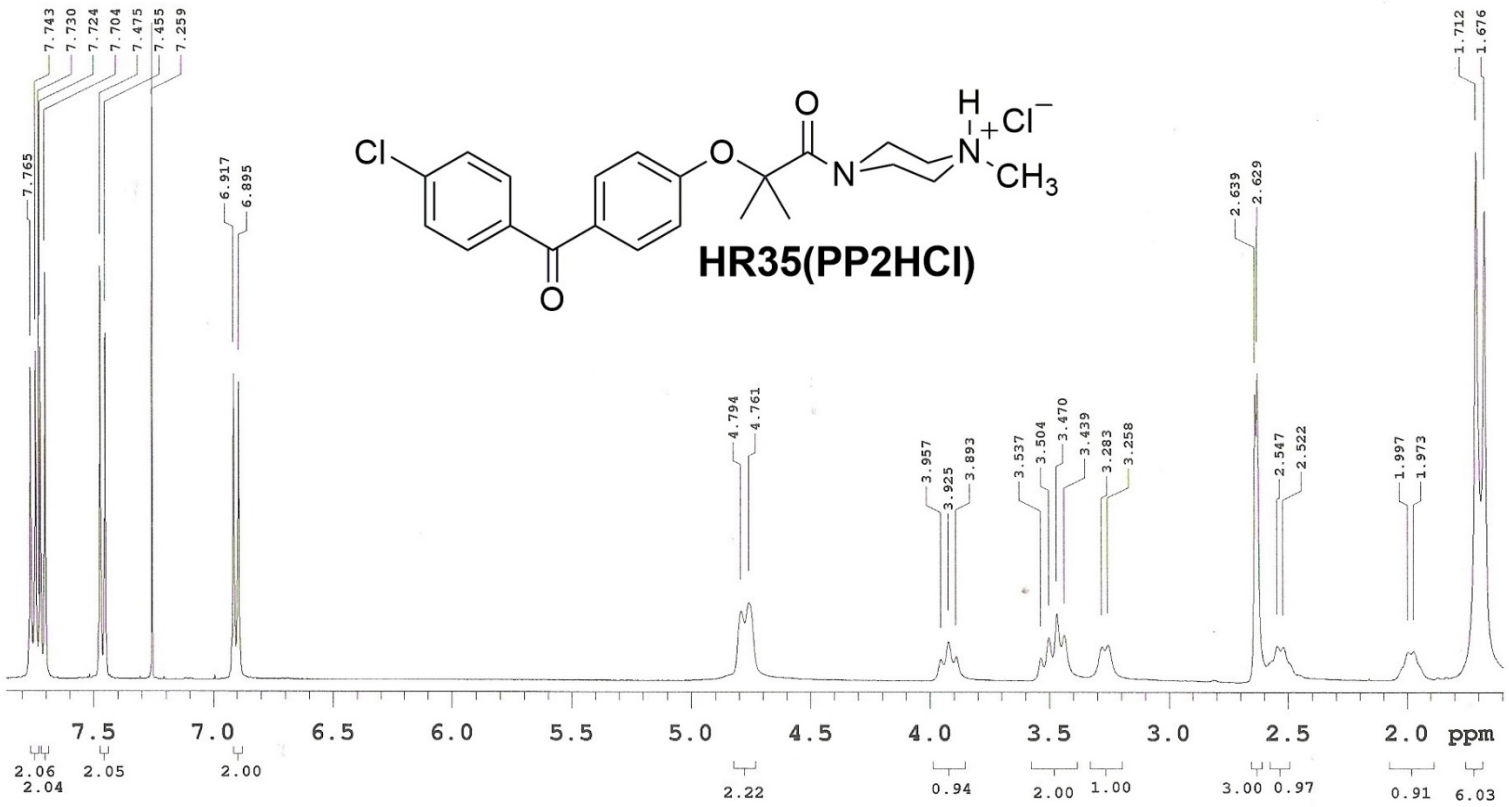
^{13}C-NMR(DMSO-d_6) Varian Mercury plus 400 MHz



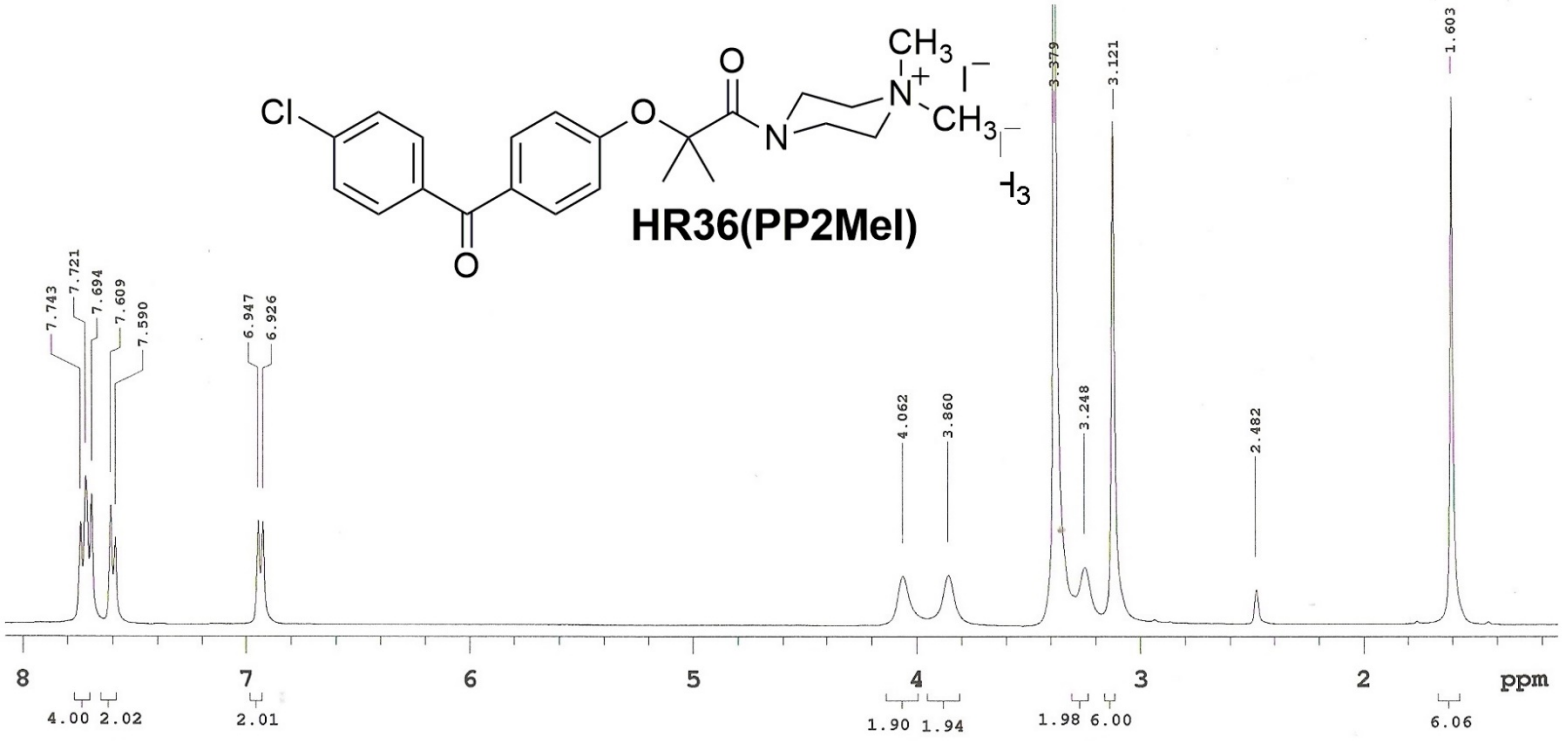
^{1}H-NMR($CDCl_3$) Varian Mercury plus 400 MHz



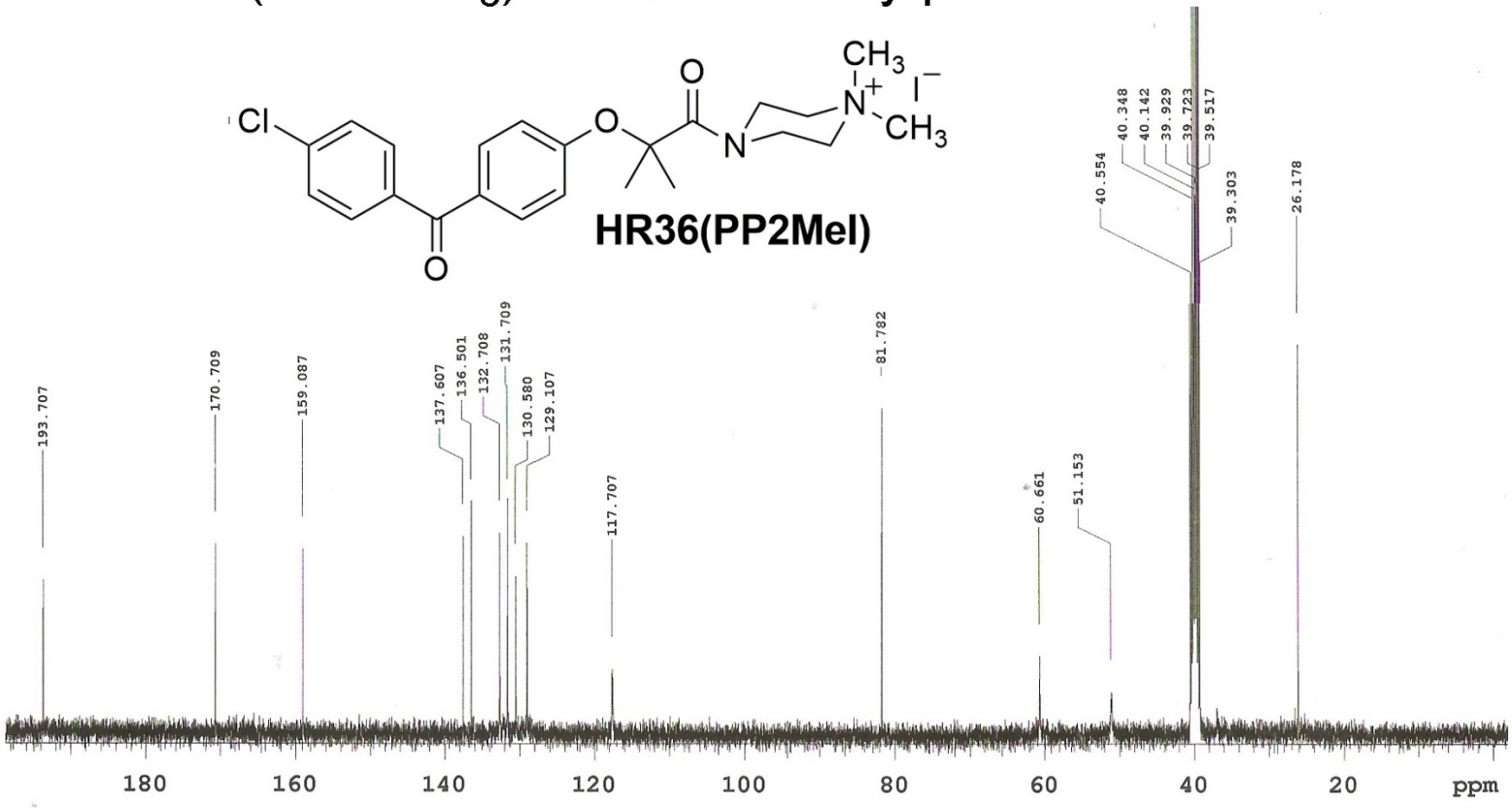
^{1}H-NMR($CDCl_3$) Varian Mercury plus 400 MHz



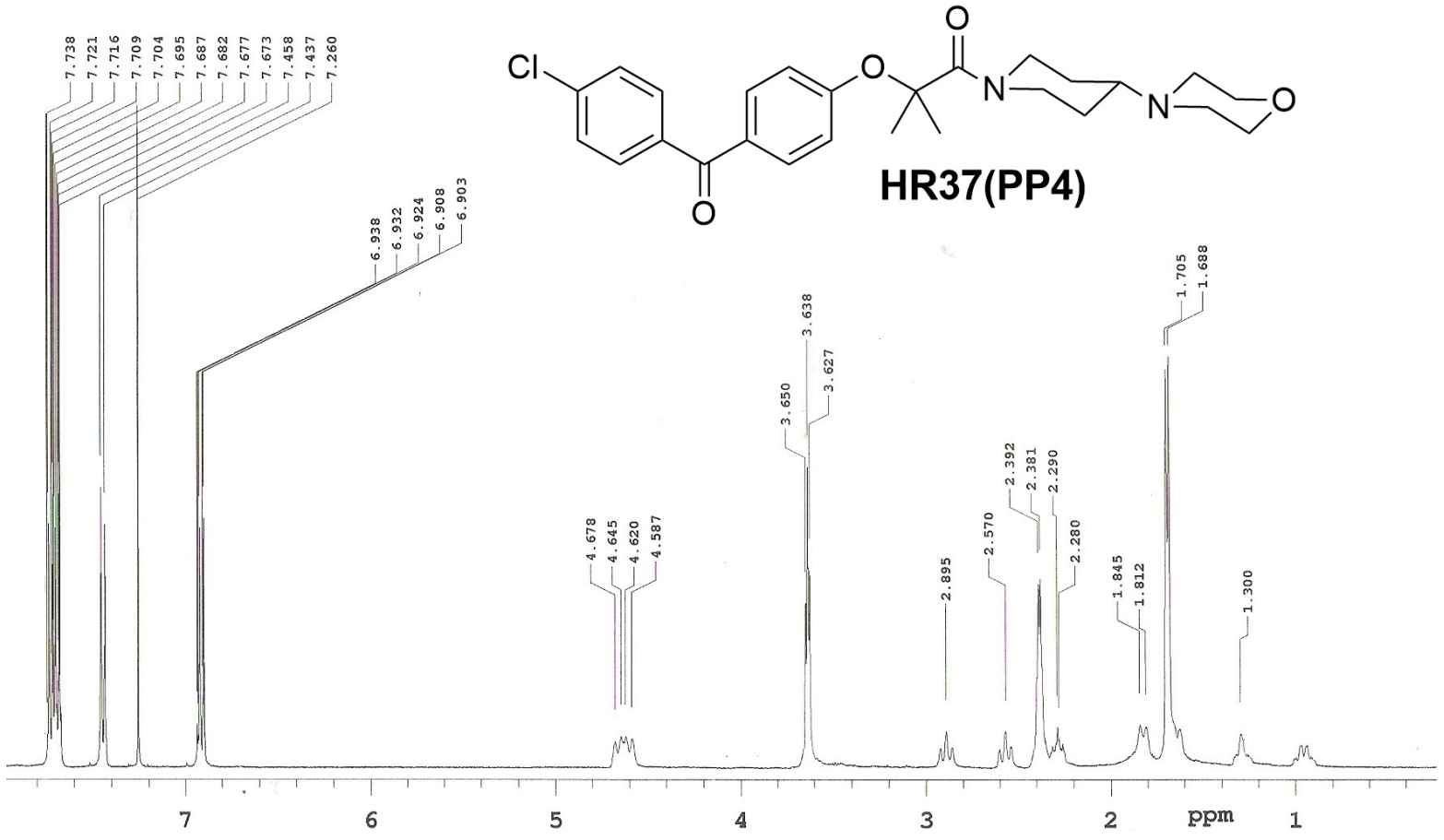
^{1}H-NMR(DMSO-d_6) Varian Mercury plus 400 MHz



^{13}C-NMR(DMSO-d_6) Varian Mercury plus 400 MHz

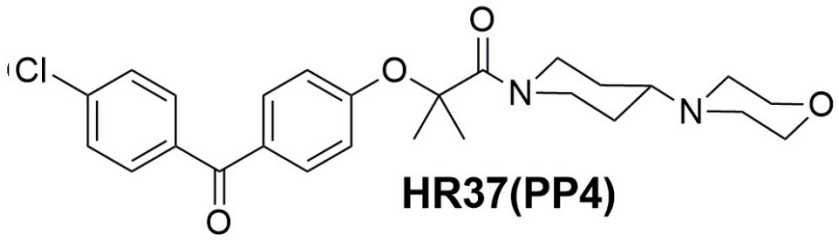


^{1}H-NMR($CDCl_3$) Varian Mercury plus 400 MHz

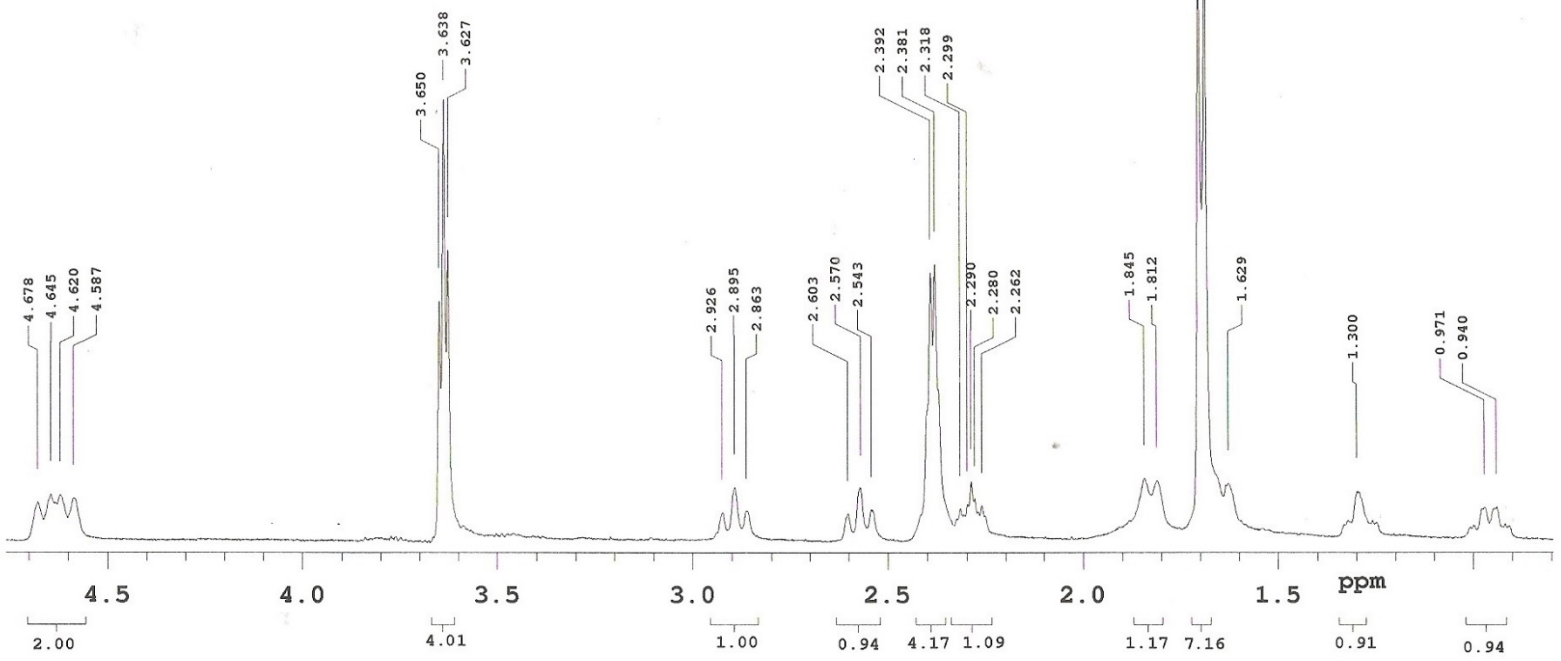


HR37(PP4)

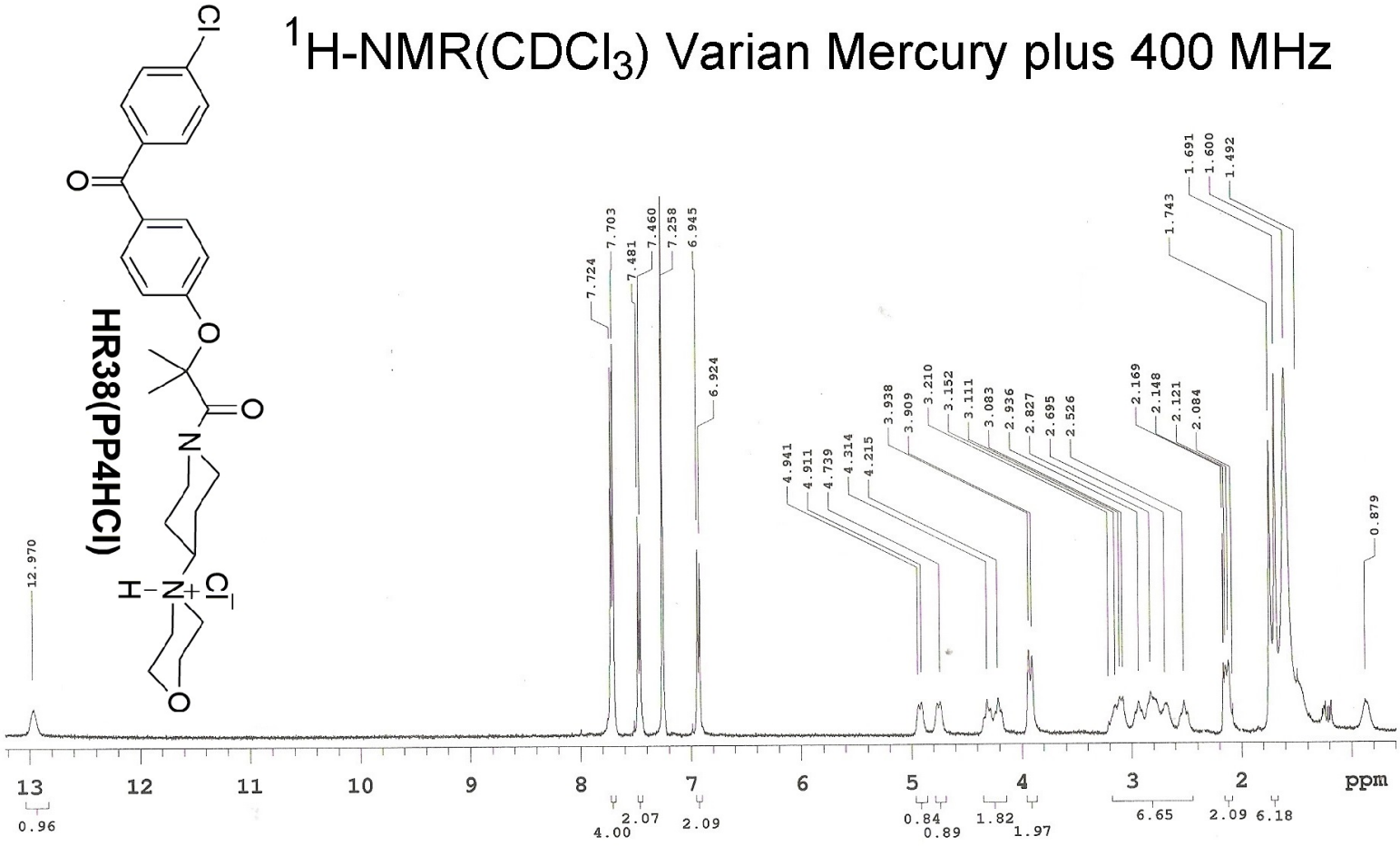
^{1}H-NMR($CDCl_3$) Varian Mercury plus 400 MHz



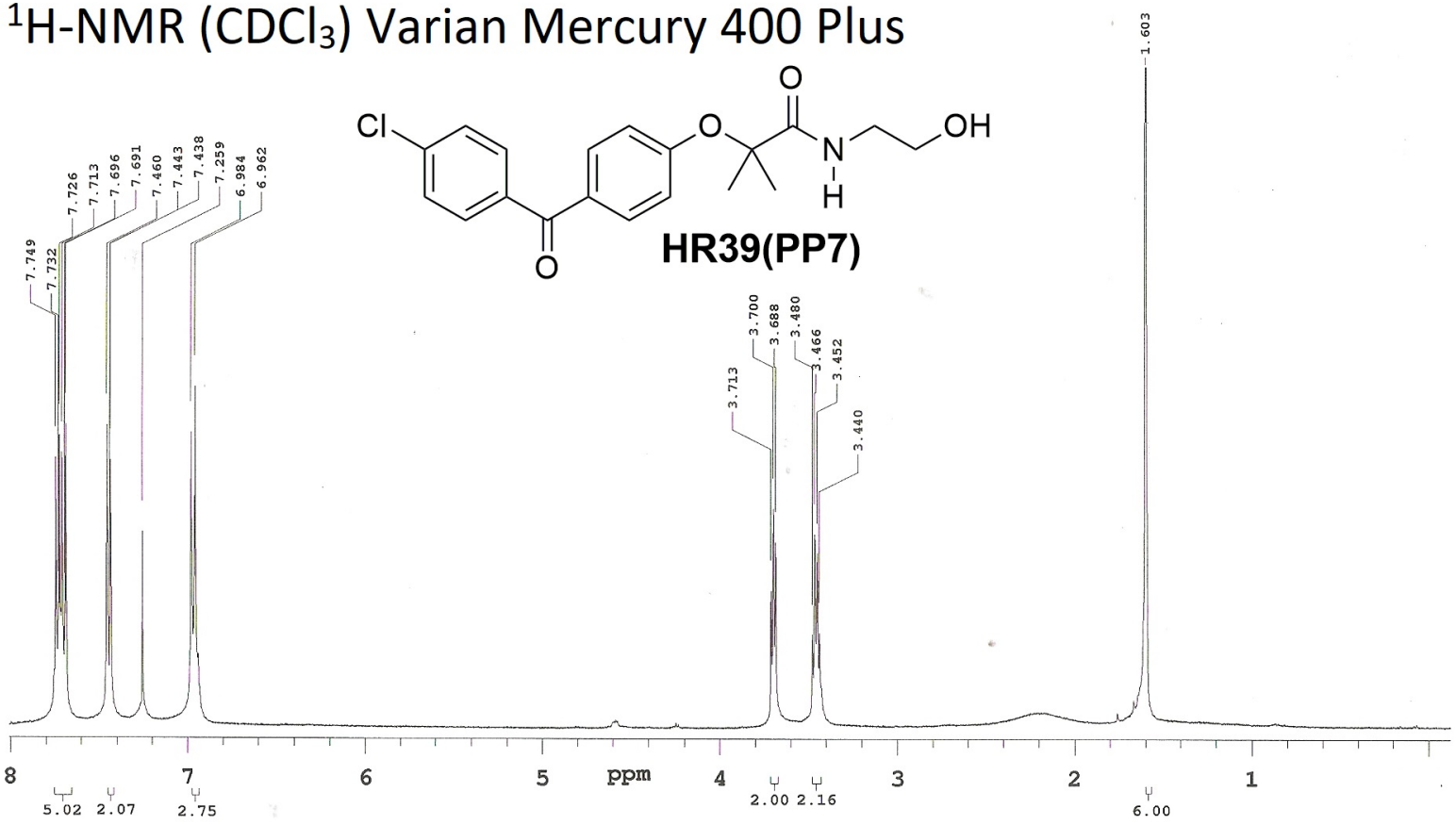
HR37(PP4)



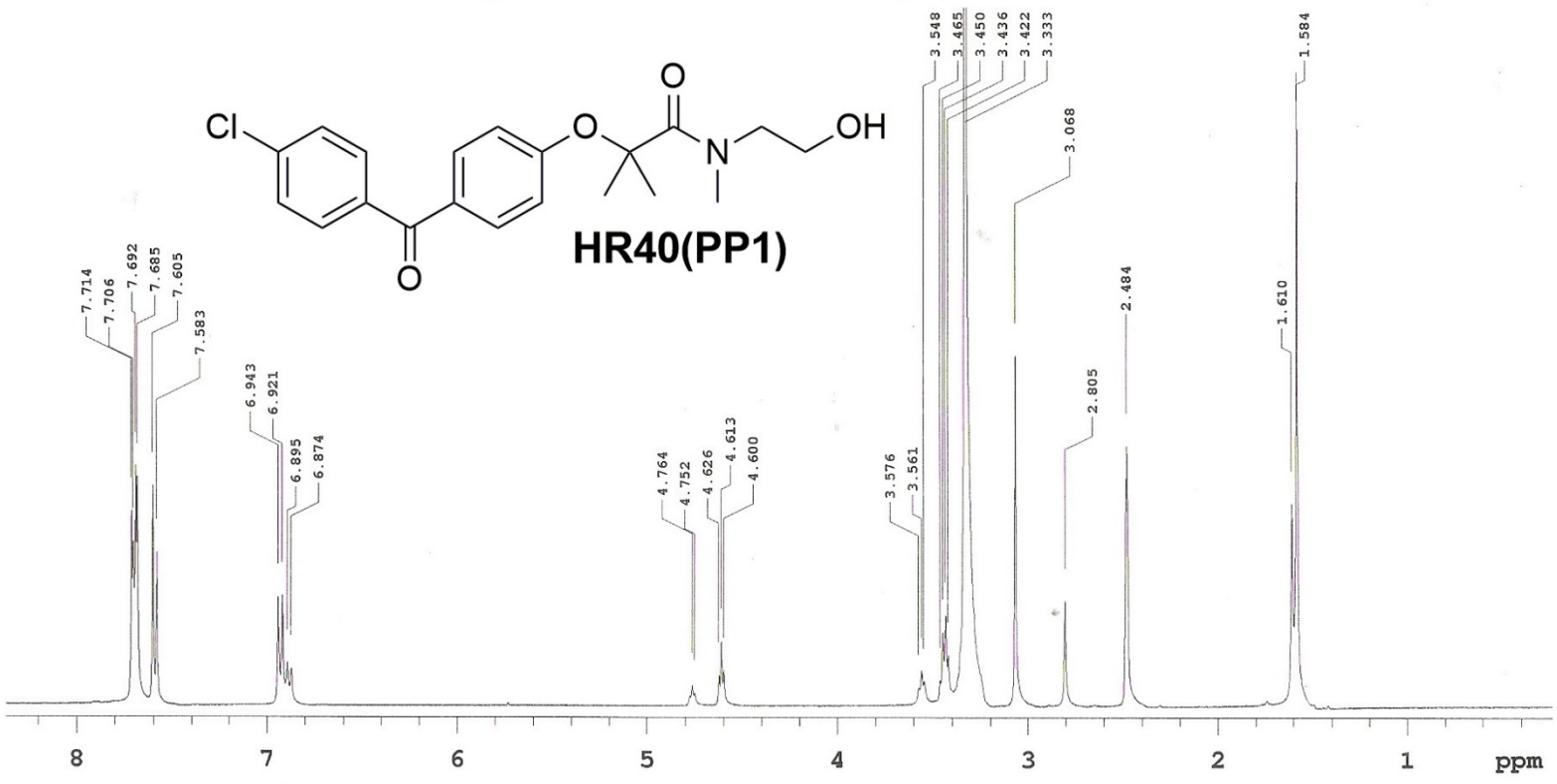
^{1}H-NMR($CDCl_3$) Varian Mercury plus 400 MHz



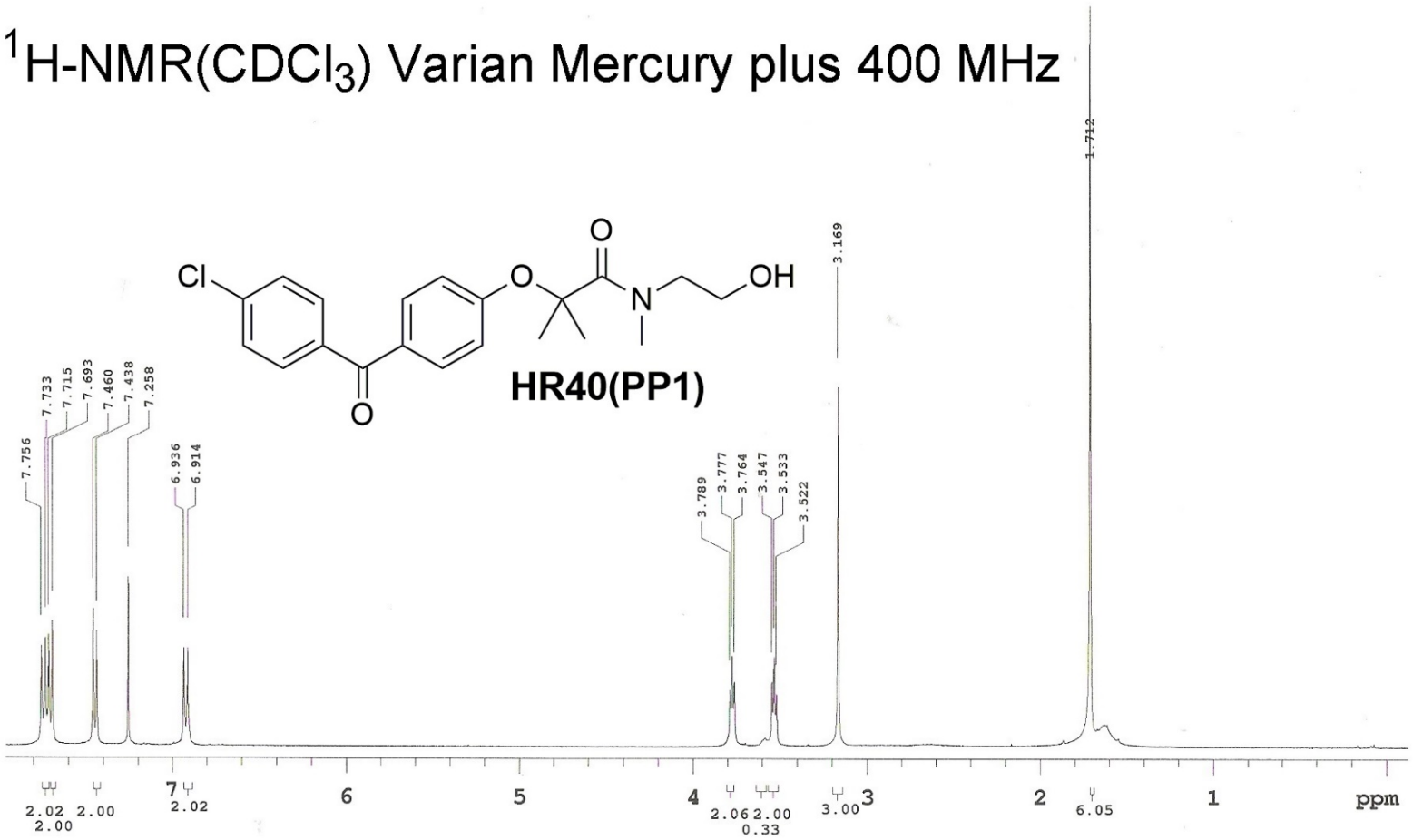
^{1}H-NMR ($CDCl_3$) Varian Mercury 400 Plus



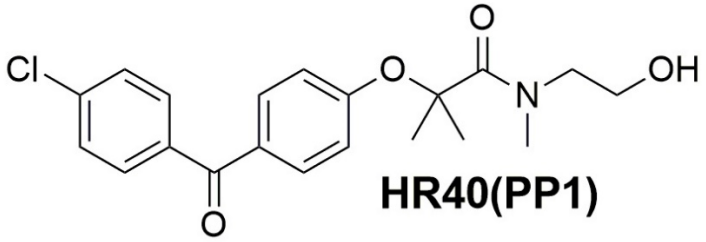
^{1}H-NMR(DMSO-d_6) Varian Mercury plus 400 MHz



^{1}H-NMR($CDCl_3$) Varian Mercury plus 400 MHz

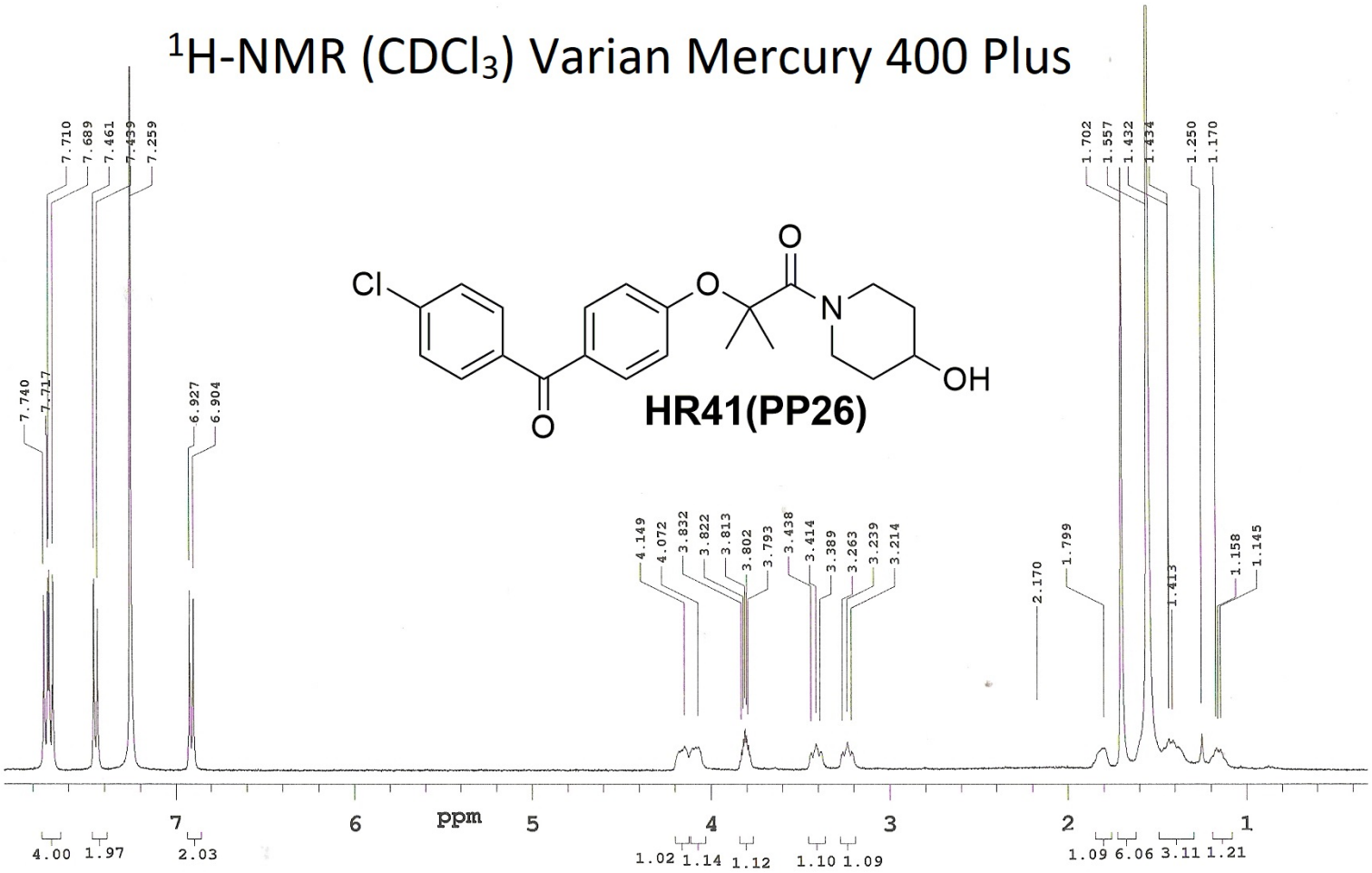


^{13}C-NMR($CDCl_3$) Varian Mercury plus 400 MHz

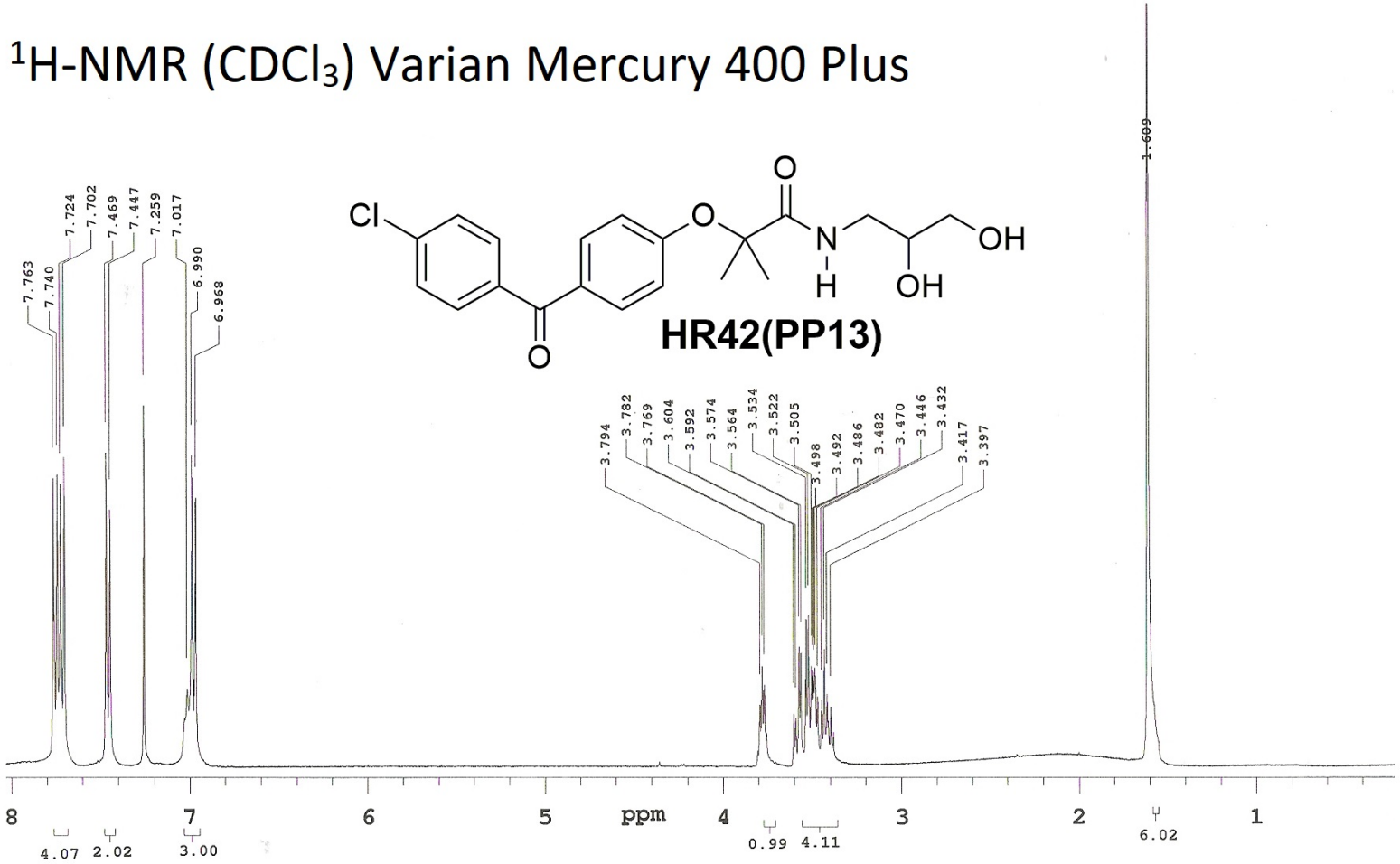


HR40(PP1)

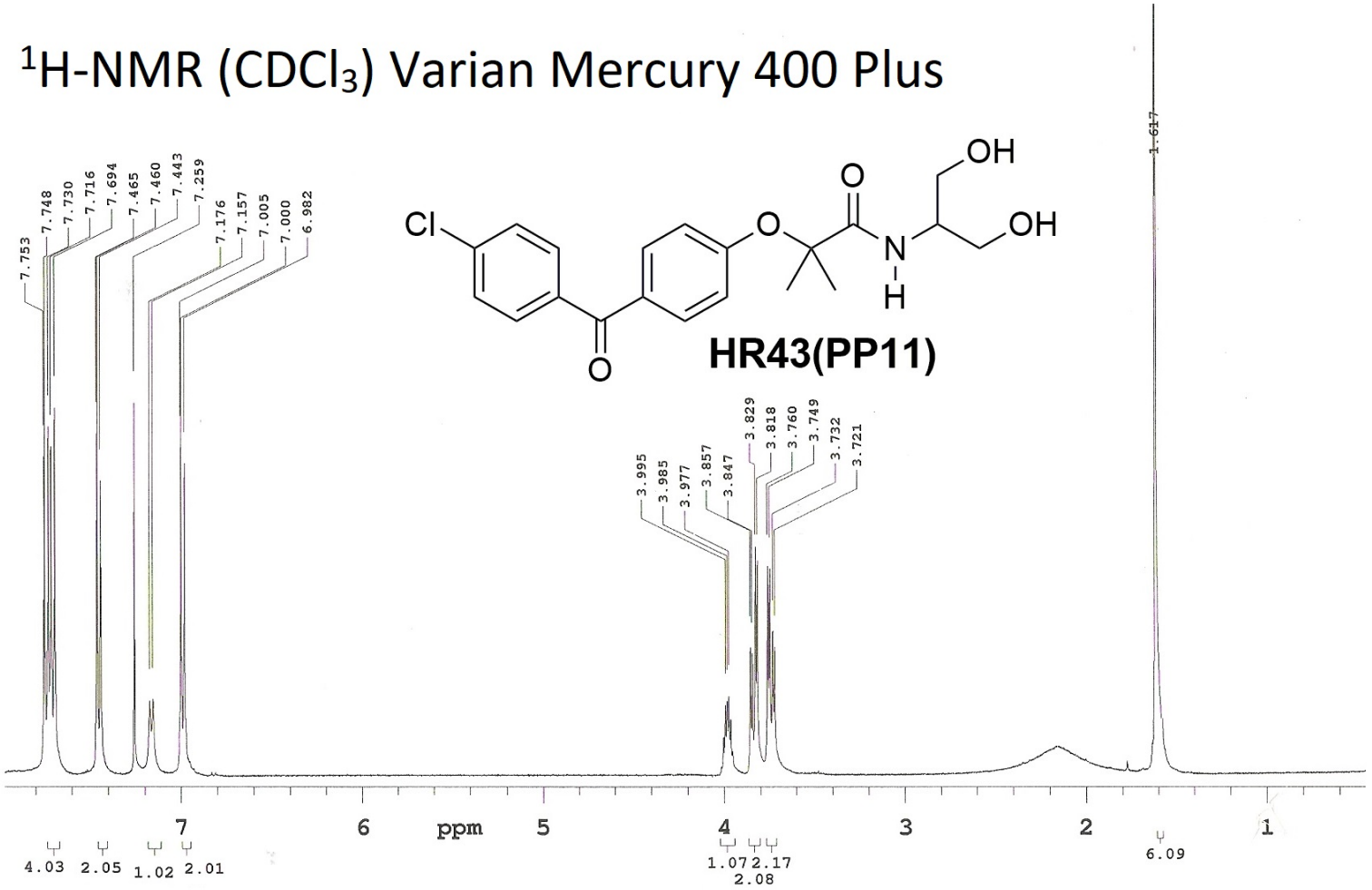
^{1}H-NMR ($CDCl_3$) Varian Mercury 400 Plus



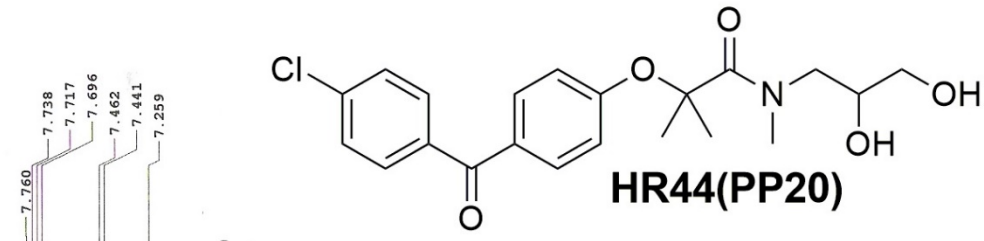
^{1}H-NMR ($CDCl_3$) Varian Mercury 400 Plus



^{1}H-NMR ($CDCl_3$) Varian Mercury 400 Plus

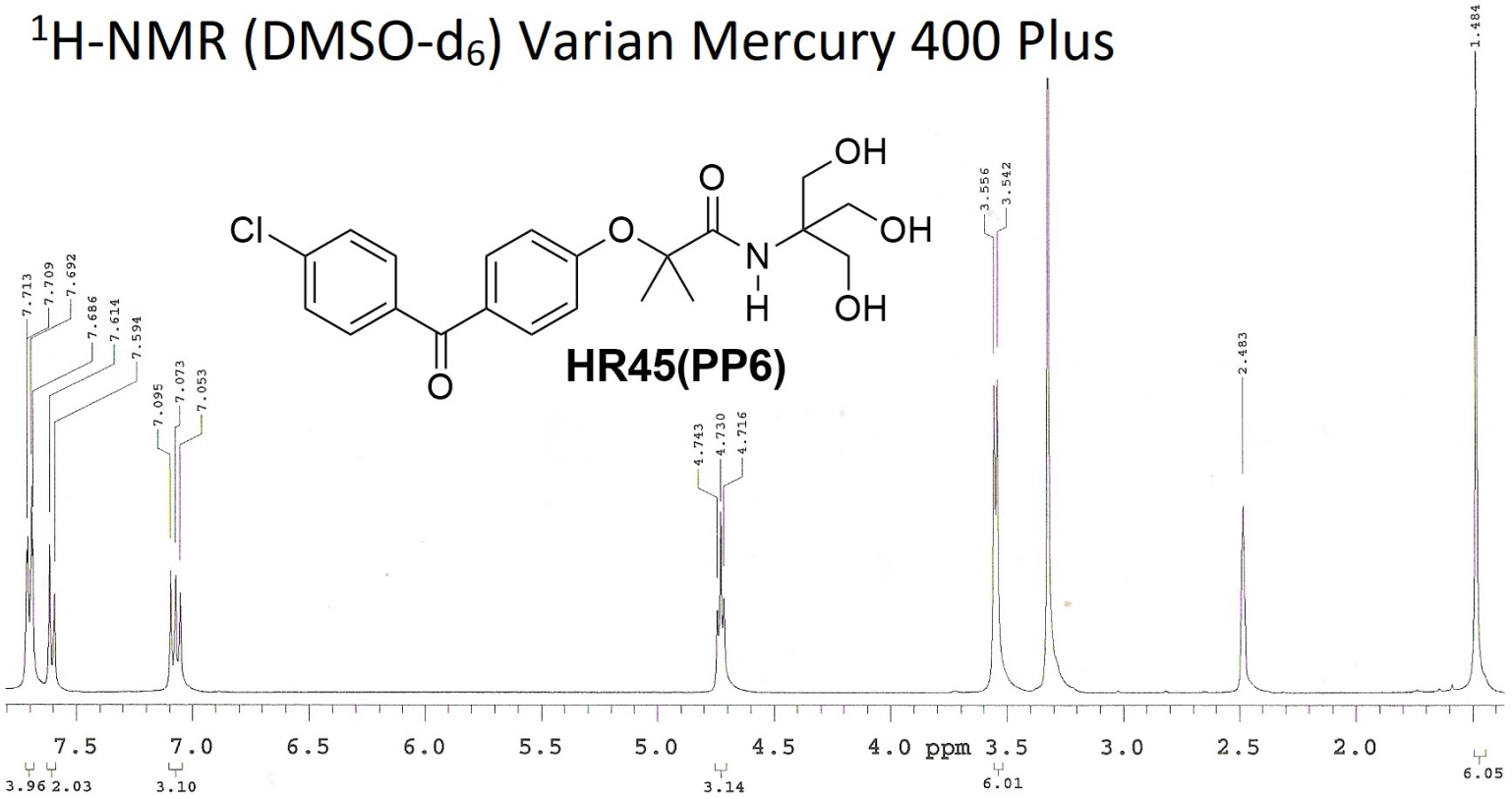


^{1}H-NMR ($CDCl_3$) Varian Mercury 400 Plus

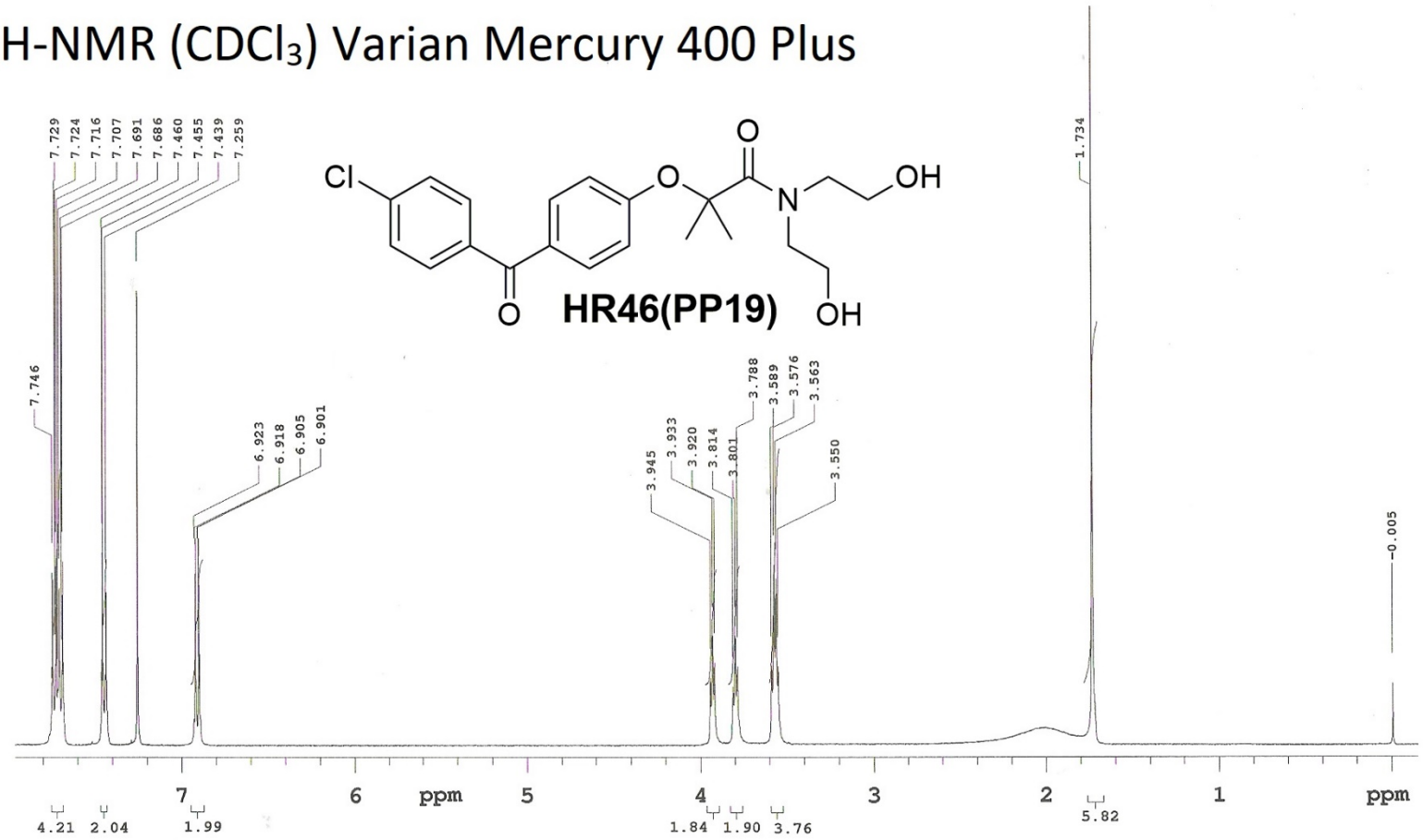


HR44(PP20)

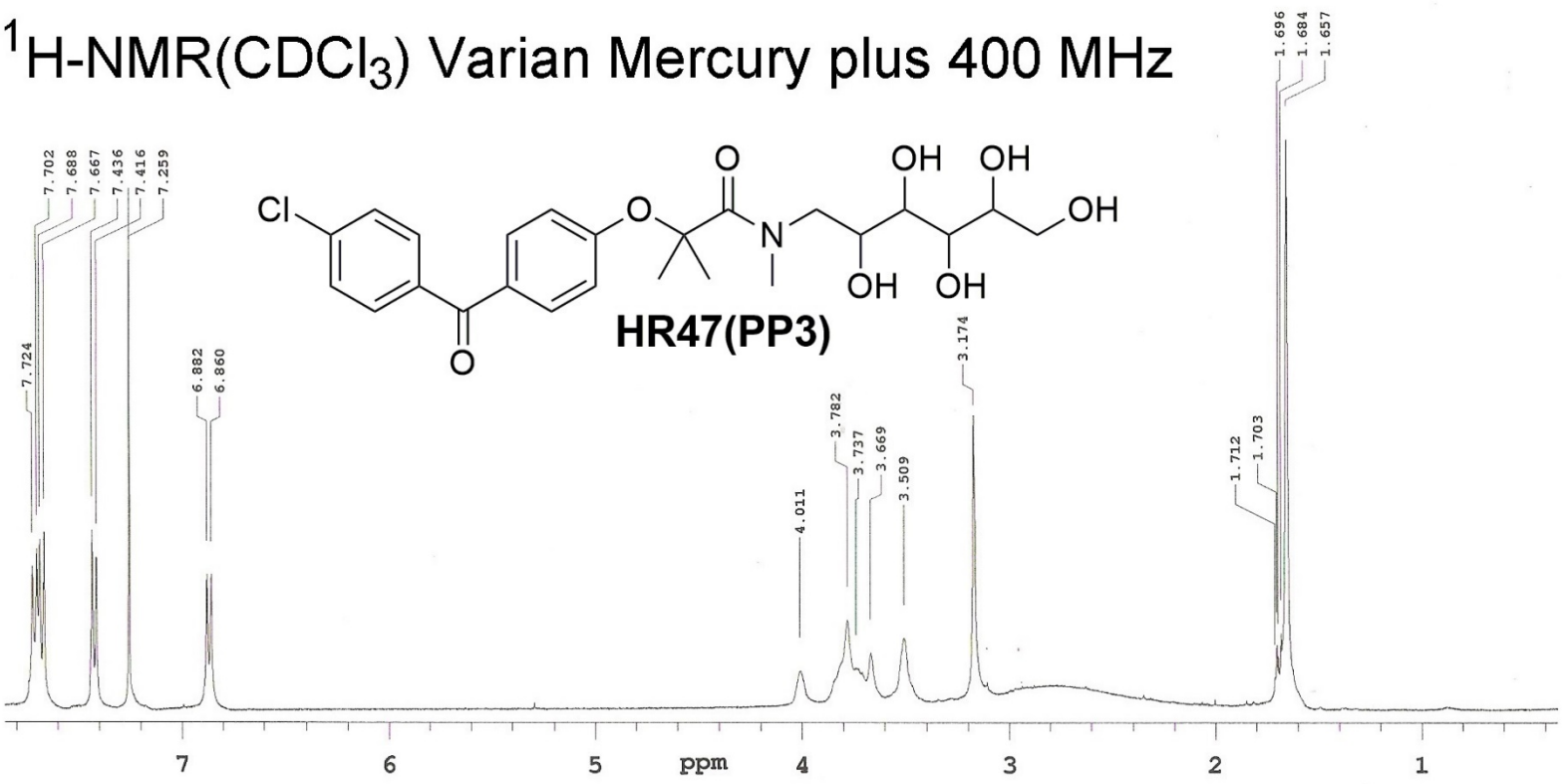
^{1}H-NMR (DMSO-d_6) Varian Mercury 400 Plus



^{1}H-NMR ($CDCl_3$) Varian Mercury 400 Plus



^{1}H-NMR($CDCl_3$) Varian Mercury plus 400 MHz

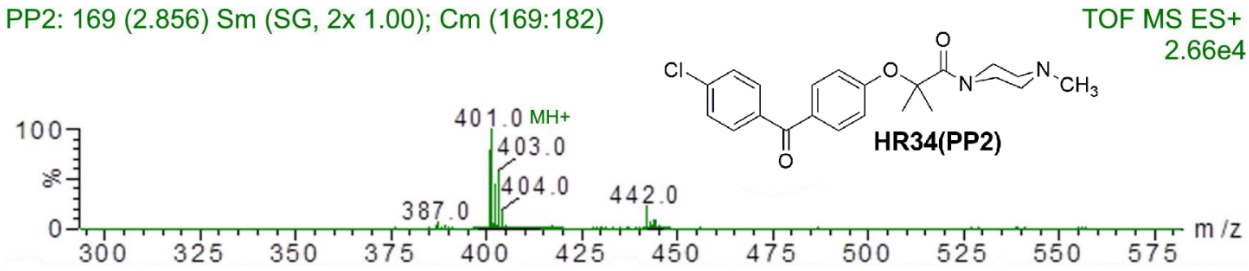


Electrospray Mass Spectra of Few Selected **HR** compounds

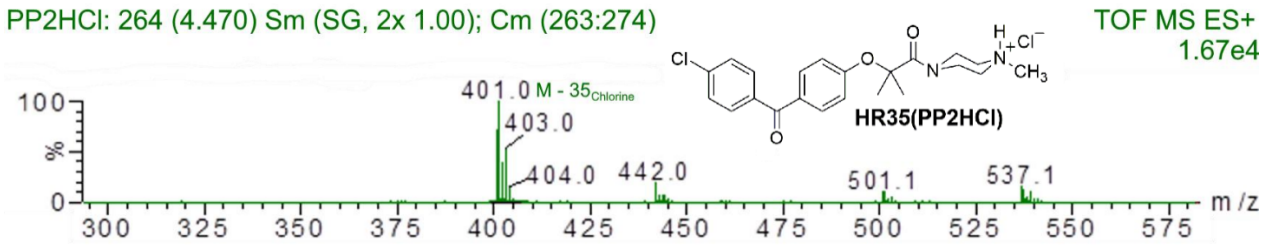
TOF MS ES$^+$ (5 µL loop injection, 100% MeCN, 0.2 ml/min)				
Sample	Monoisotopic Mass (M) (Da)	Observed Mass		Formula
HR34(PP2)	400	401	[M + H$^+$]	$C_{22}H_{25}Cl_2N_2O_3$
HR35(PP2HCl)	436	401	[M – Cl$^-$]	$C_{22}H_{26}Cl_2N_2O_3$
HR36(PP2MeI)	542	415	[M – I$^-$]	$C_{23}H_{28}ClIN_2O_3$
HR37(PP4)	470	471	[M + H$^+$]	$C_{26}H_{31}ClN_2O_4$
HR38(PP4HCl)	506	471	[M – Cl$^-$]	$C_{26}H_{32}Cl_2N_2O_4$
HR40(PP1)	375	376	[M + H$^+$]	$C_{20}H_{22}ClNO_4$
HR47(PP3)	495	496	[M + H$^+$]	$C_{24}H_{30}ClNO_8$

The MS was a Waters LCT Premier XE (that's a Tof MS) with an ESI source, scanning 100-2000 m/z with direct injections of 5 µl sample, using a 0.2 ml/min flow of acetonitrile

HR34(PP2)



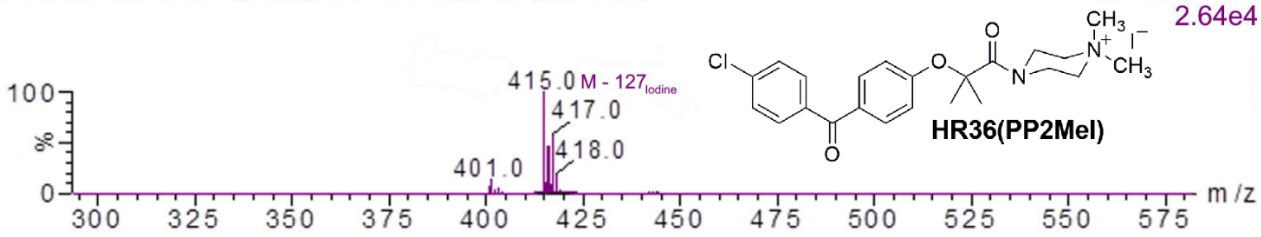
HR35(PP2HCl)



HR36(PP2MeI)

PP2MeI: 472 (8.005) Sm (SG, 2x 1.00); Cm (472:485)

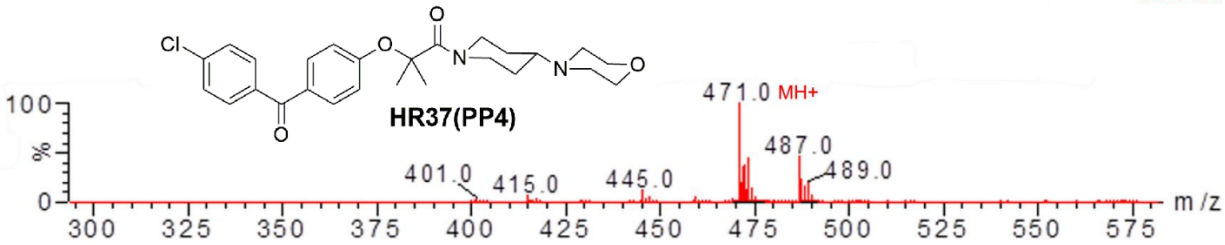
TOF MS ES+
2.64e4



HR37(PP4)

PP4: 1239 (21.040) Sm (SG, 2x 1.00) Cm (1233:1274)

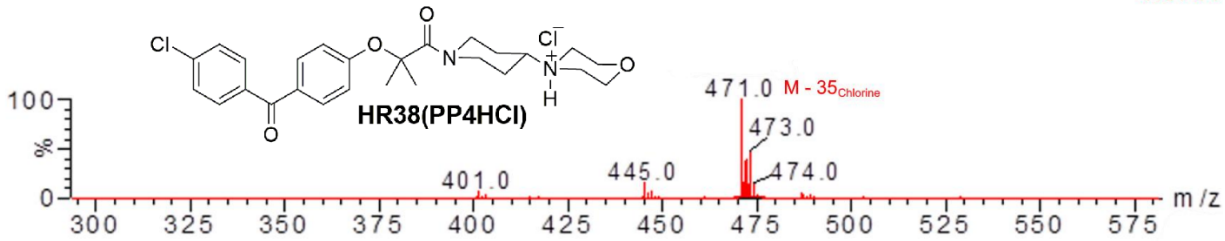
TOF MS ES+
3.47e4



HR38(PP4HCl)

PP4HCl: 1526 (25.918) Sm (SG, 2x 1.00); Cm (1524:1560)

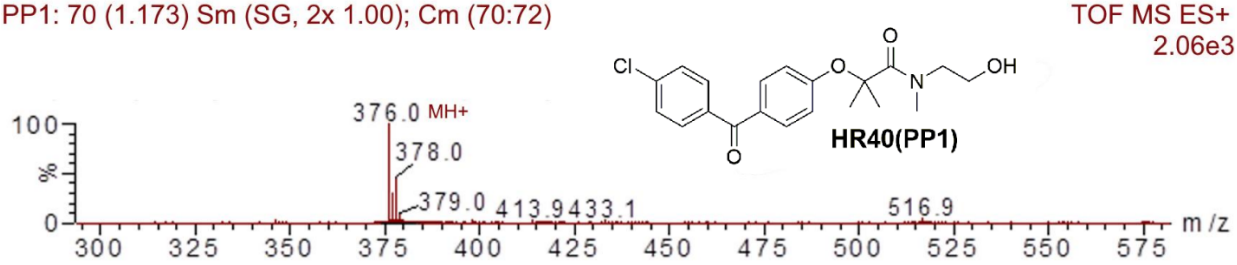
TOF MS ES+
3.67e4



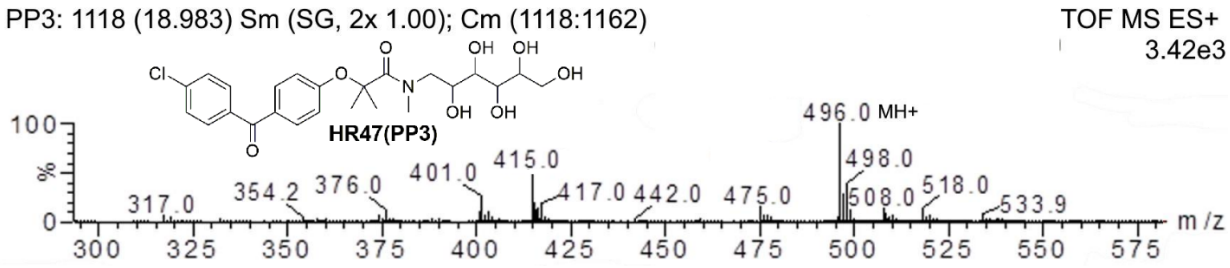
HR40(PP1)

PP1: 70 (1.173) Sm (SG, 2x 1.00); Cm (70:72)

TOF MS ES+
2.06e3



HR47(PP3)


PP3: 1118 (18.983) Sm (SG, 2x 1.00); Cm (1118:1162)
TOF MS ES+
3.42e3
HR47(PP3)
100
%
0
317.0
354.2
376.0
401.0
415.0
417.0
442.0
475.0
496.0 MH+
498.0
508.0
518.0
533.9
m/z
300
325
350
375
400
425
450
475
500
525
550
575