Supporting information for

Ligand Dependent Switch from RXR Homo- to RXR-NURR1 Heterodimerization

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Table S1. Crystallographic statistics for RXRα complexes.

	Ligand **3**	Ligand **4**	Ligand **6**	Ligand **7**	Ligand **9**
Data collection					
Resolution (Å)	68.16-1.90 (1.94-1.90)	25.4-1.78 (1.82-1.78)	67.49-2.70 (2.83-2.70)	99.21-2.00 (2.0-2.05)	64.14-2.50 (2.50-2.60)
Space group	$P4_32_12$	$P3_221$	$P4_32_12$	$P2_12_12_1$	$P4_32_12$
Cell parameters (Å)	a=b=63.16, c=109.72	a=b=77.65, c=81.24	a=b=67.49, c=108.64	a=71.70, b=74.14, c=99.21	a=b=64.14, c=111.98
R_{merge}	0.079 (1.06)	0.12 (1.69)	0.155 (0.929)	0.12 (0.90)	0.17 (0.98)
Average $I/\sigma_{(I)}$[a]	22.1 (2.1)	13.1 (2.3)	14.0 (3.8)	13.1 (2.2)	12.0 (3.3)
$CC_{1/2}$ (%)	99.9 (51.0)	99.7 (84.2)	99.9 (86.2)	99.7 (65.5)	99.7 (78.8)
Completeness (%)[a]	99.9 (99.2)	99.6 (94.1)	100 (100)	99.9 (99.1)	100 (100)
Redundancy[a]	20.9 (9.8)	8.6 (4.7)	20.9 (21.2)	11.0 (7.3)	14.9 (15.9)
Refinement					
Number of protein/solvent/ligand atoms	1831/127/25	1861/335/21	1744/9/25	3728/489/52	1766/76/25
R_{work}/R_{free} (%)	19.7/24.9	14.8/17.7	20.0/25.3	17.1/22.9	19.3/24.5
Unique reflections used in refinement	21048	27456	7351	36389	8601
R.m.s. deviations from ideal values bond lengths (Å) / bond angles (°)	0.002 / 0.400	0.018/1.36	0.001/0.400	0.009/1.170	0.001/0.380
Average protein/solvent/ligand B-factor ($Å^2$)	47.1 / 48.3 / 35.7	15.0 / 32.9 / 9.84	62.4 / 46.5 / 54.5	32.8 / 42.4 / 24.5	47.6 / 41.4 / 46.7
Ramachandran favored (%)	98.2	98.7	98.1	98.2	97.7
Ramachandran allowed (%)	1.8	1.3	1.9	1.8	2.3
Ramachandran outliers (%)	0	0	0	0	0

[a] number in parentheses is for the highest resolution shell

[b] As reported by Aimless version 0.5.27

Figure S1. 1H NMR spectrum of *(E)*-methyl 3-(6-methoxy-[1,1':3',1''-terphenyl]-3-yl)acrylate (13)

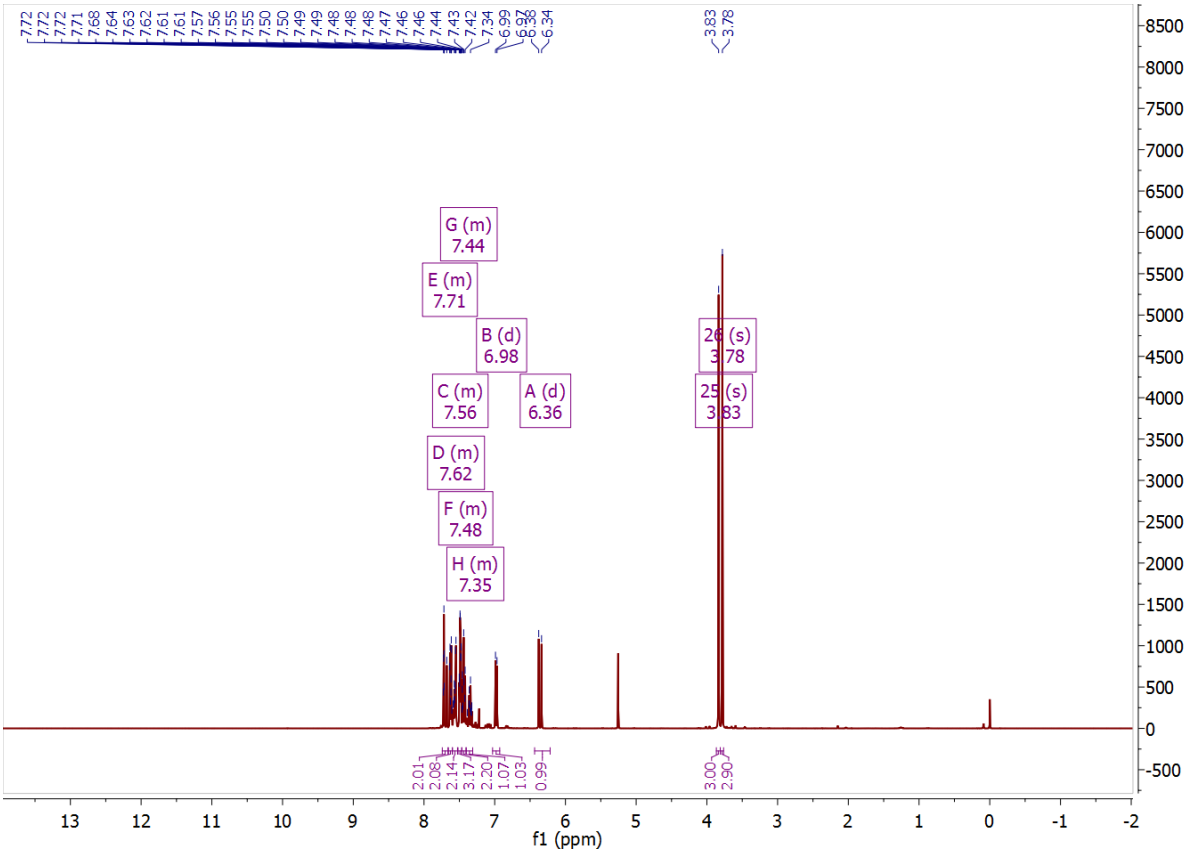


Figure S2. 13C NMR spectrum of *(E)*-methyl 3-(6-methoxy-[1,1':3',1''-terphenyl]-3-yl)acrylate (13)

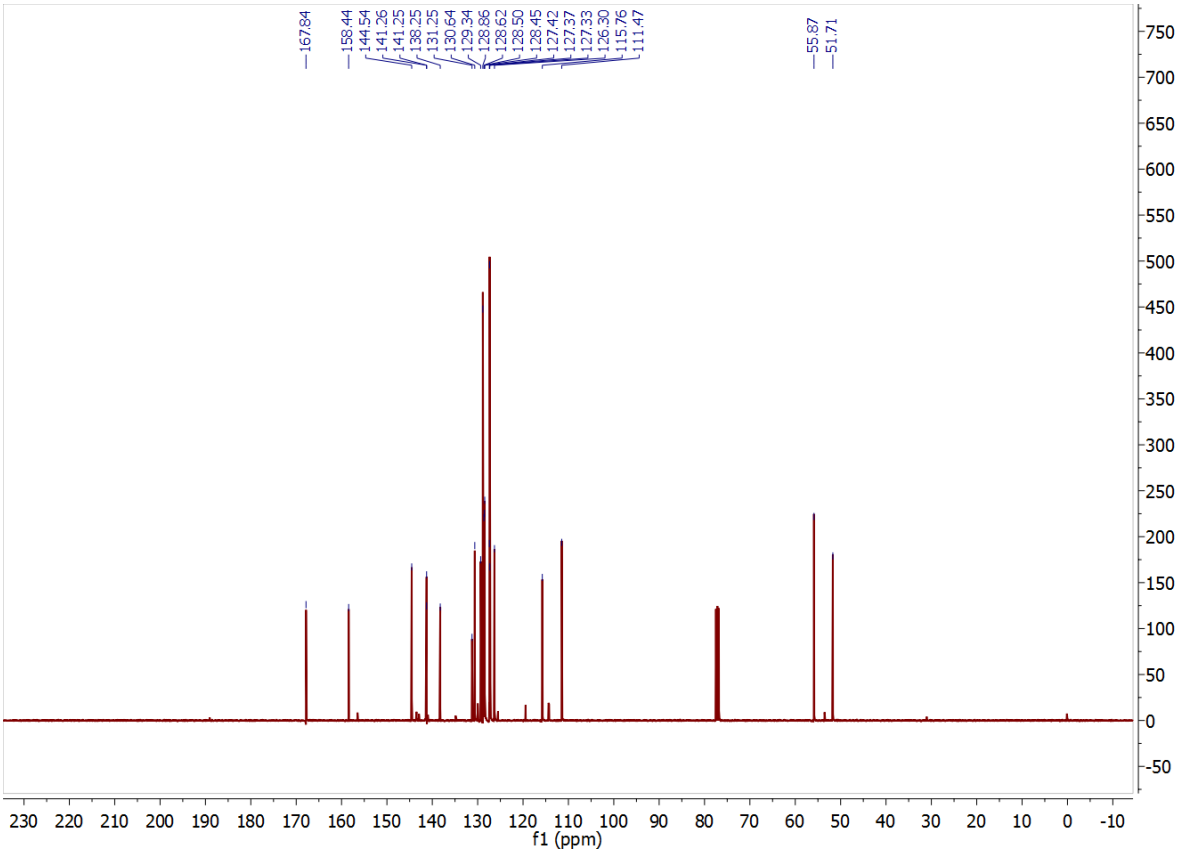


Figure S3. 1H NMR spectrum of *(E)*-3-(6-hydroxy-[1,1':3',1''-terphenyl]-3-yl)acrylic acid (2)

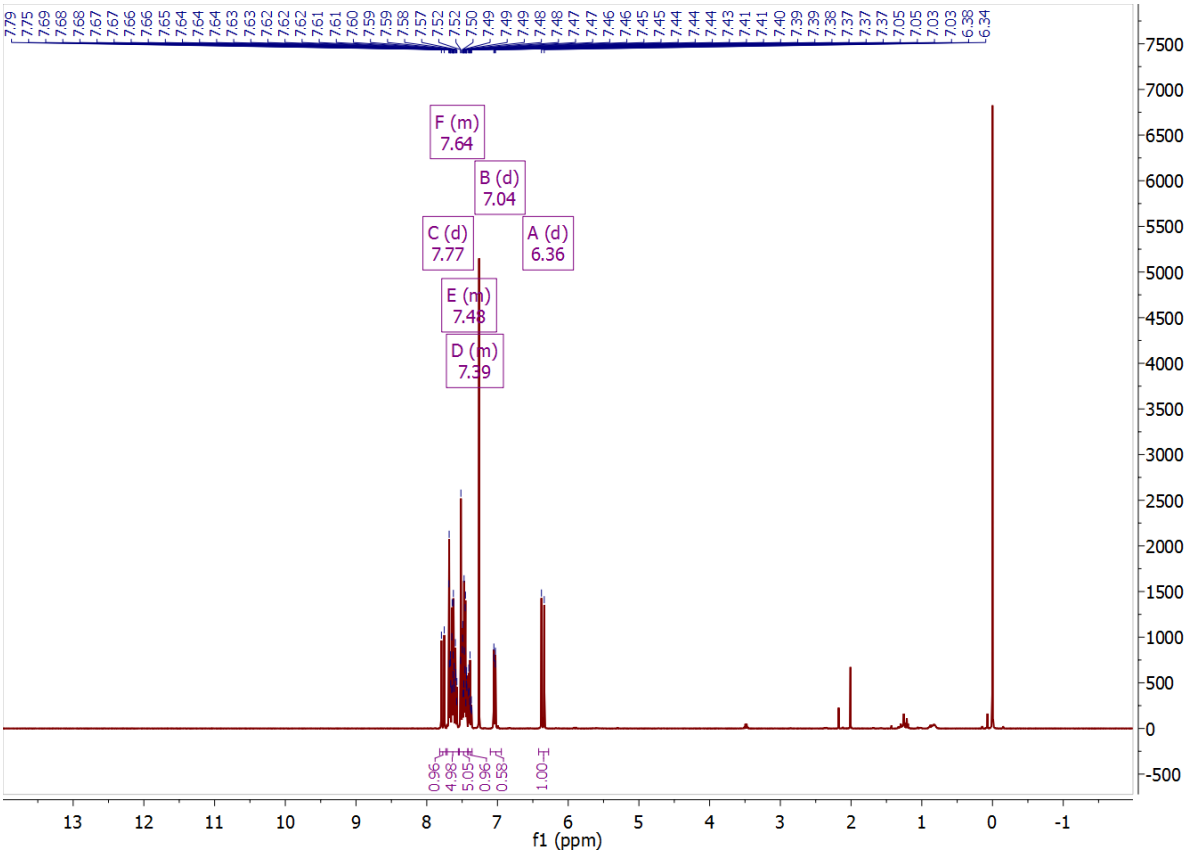


Figure S4. 13C NMR spectrum of *(E)*-3-(6-hydroxy-[1,1':3',1''-terphenyl]-3-yl)acrylic acid (2)

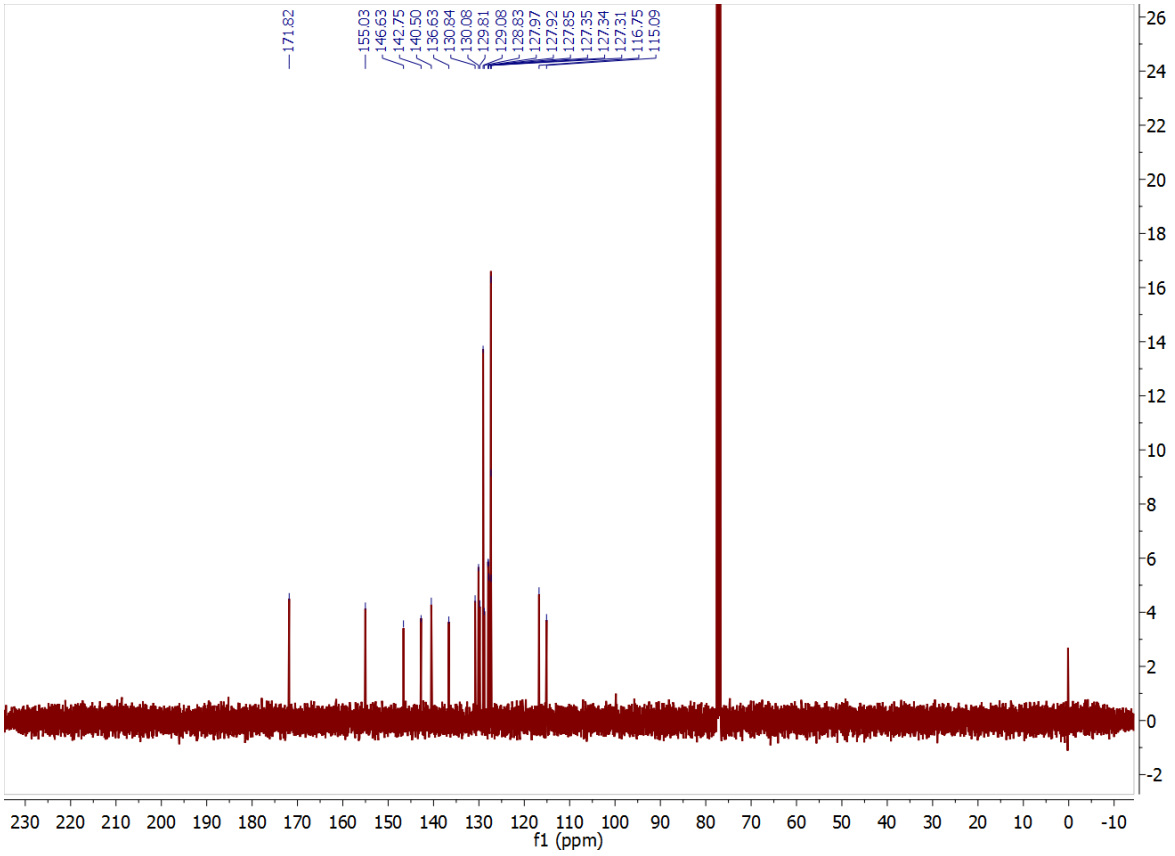


Figure S5. 1H NMR spectrum of *(E)*-methyl 3-(3'-benzyl-6-methoxy-[1,1'-biphenyl]-3-yl)acrylate (14)

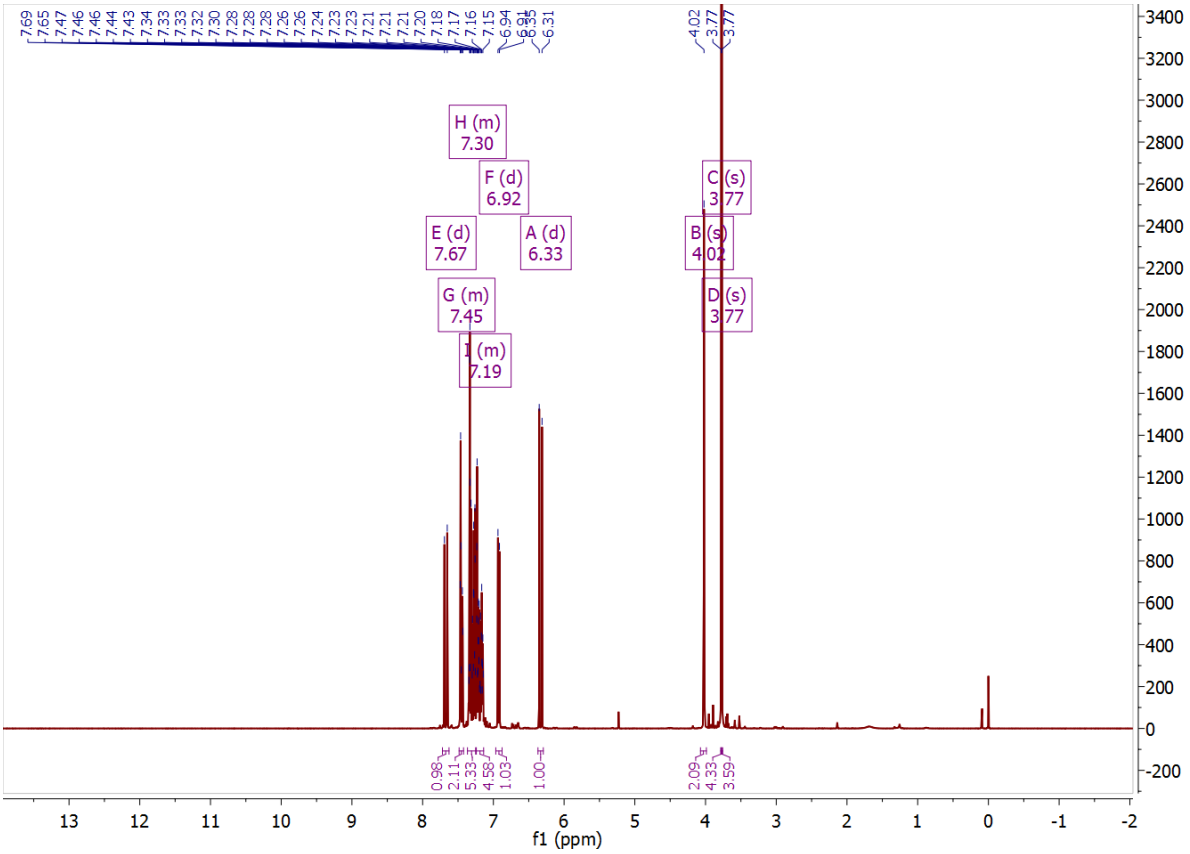


Figure S6. 13C NMR spectrum of *(E)*-methyl 3-(3'-benzyl-6-methoxy-[1,1'-biphenyl]-3-yl)acrylate (14)

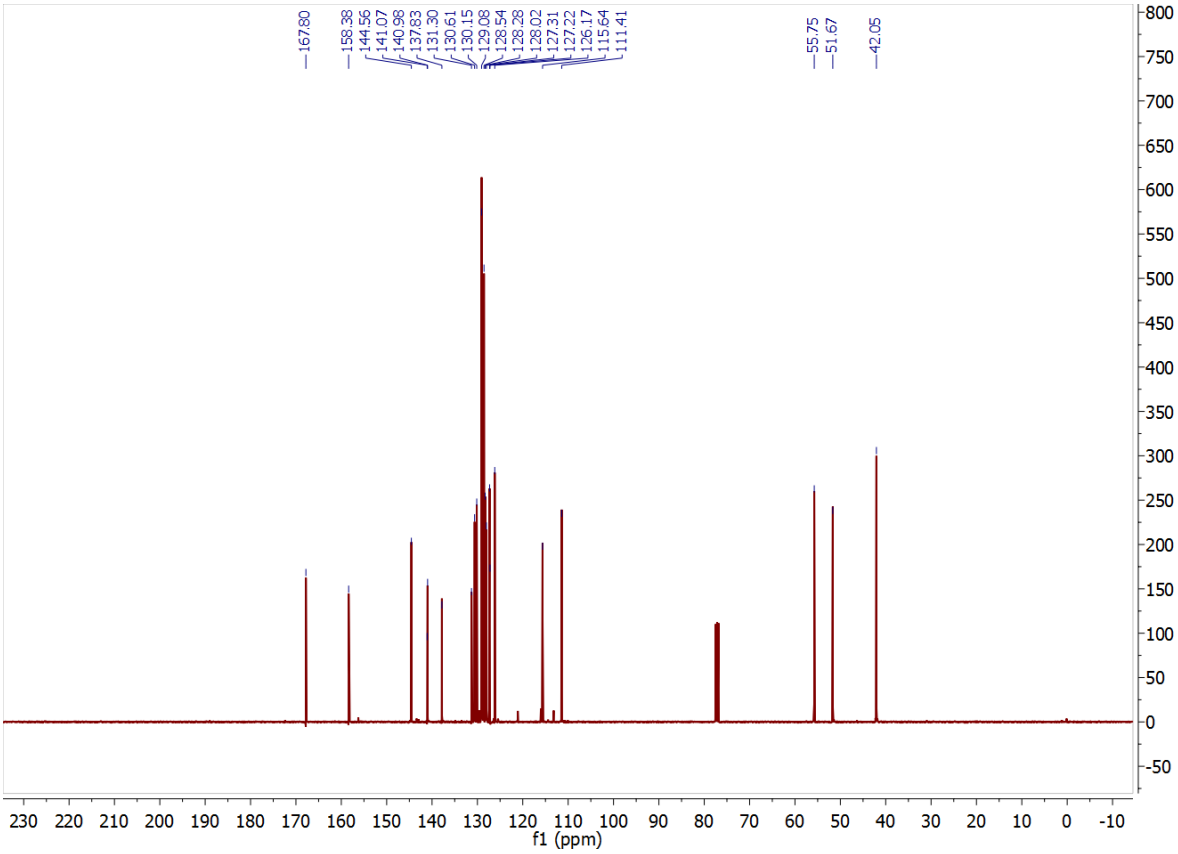


Figure S7. 1H NMR spectrum of *(E)*-3-(3'-benzyl-6-hydroxy-[1,1'-biphenyl]-3-yl)acrylic acid (3)

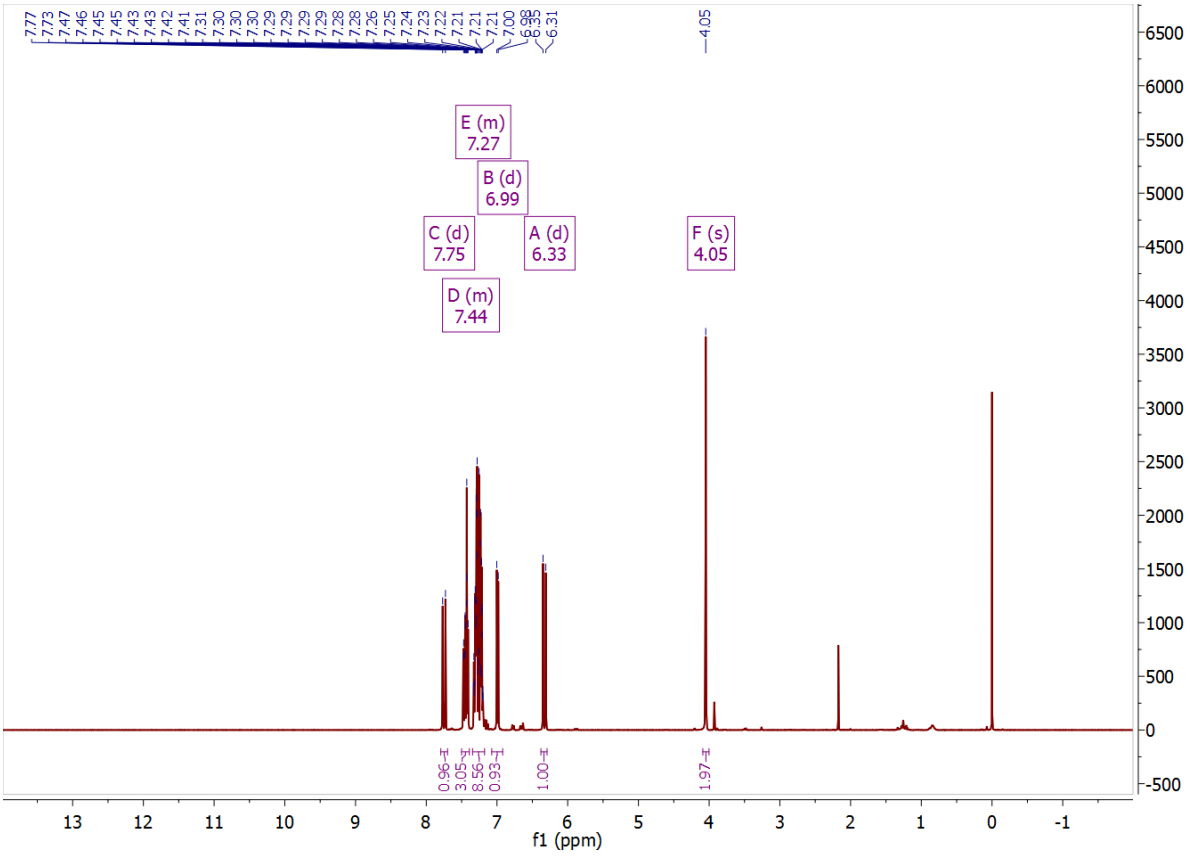


Figure S8. 13C NMR spectrum of *(E)*-3-(3'-benzyl-6-hydroxy-[1,1'-biphenyl]-3-yl)acrylic acid (3)

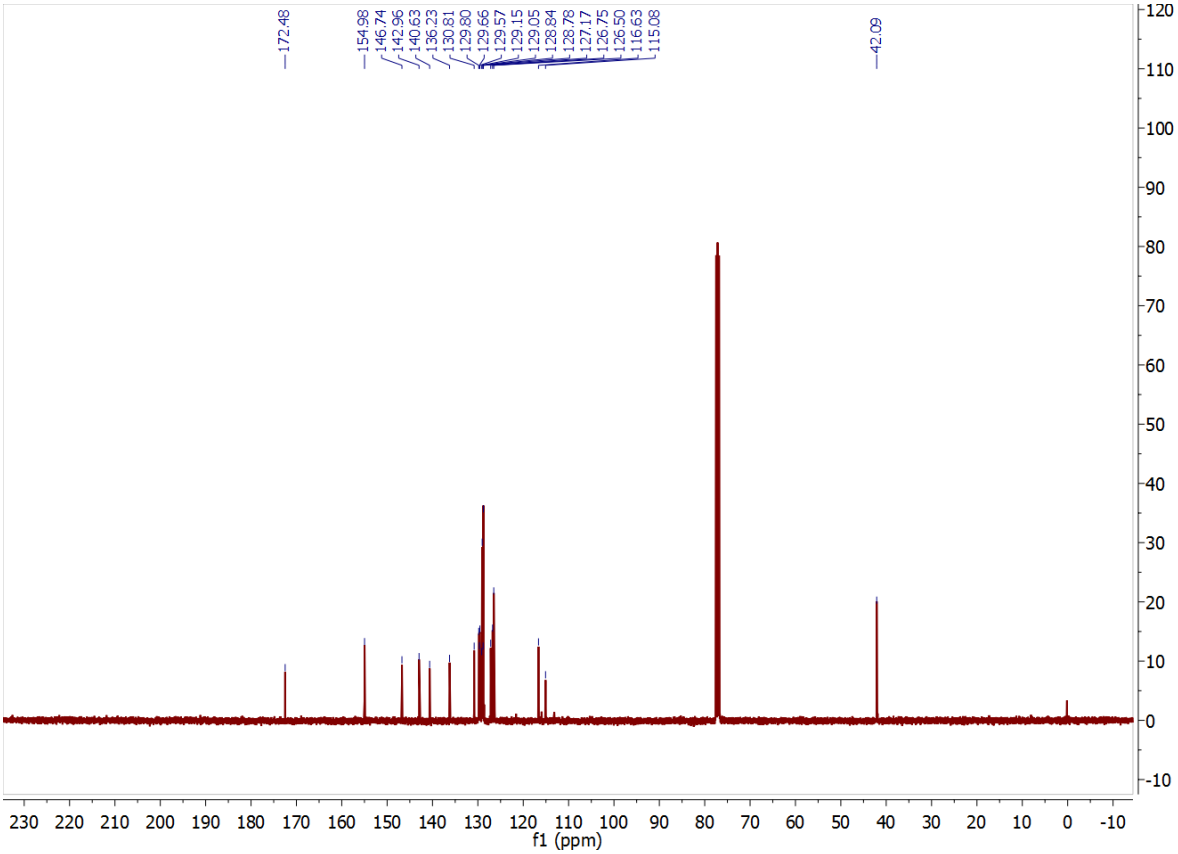


Figure S9. 1H NMR spectrum of *(E)*-methyl 3-(3'-isopropyl-6-methoxy-[1,1'-biphenyl]-3-yl)acrylate (15)

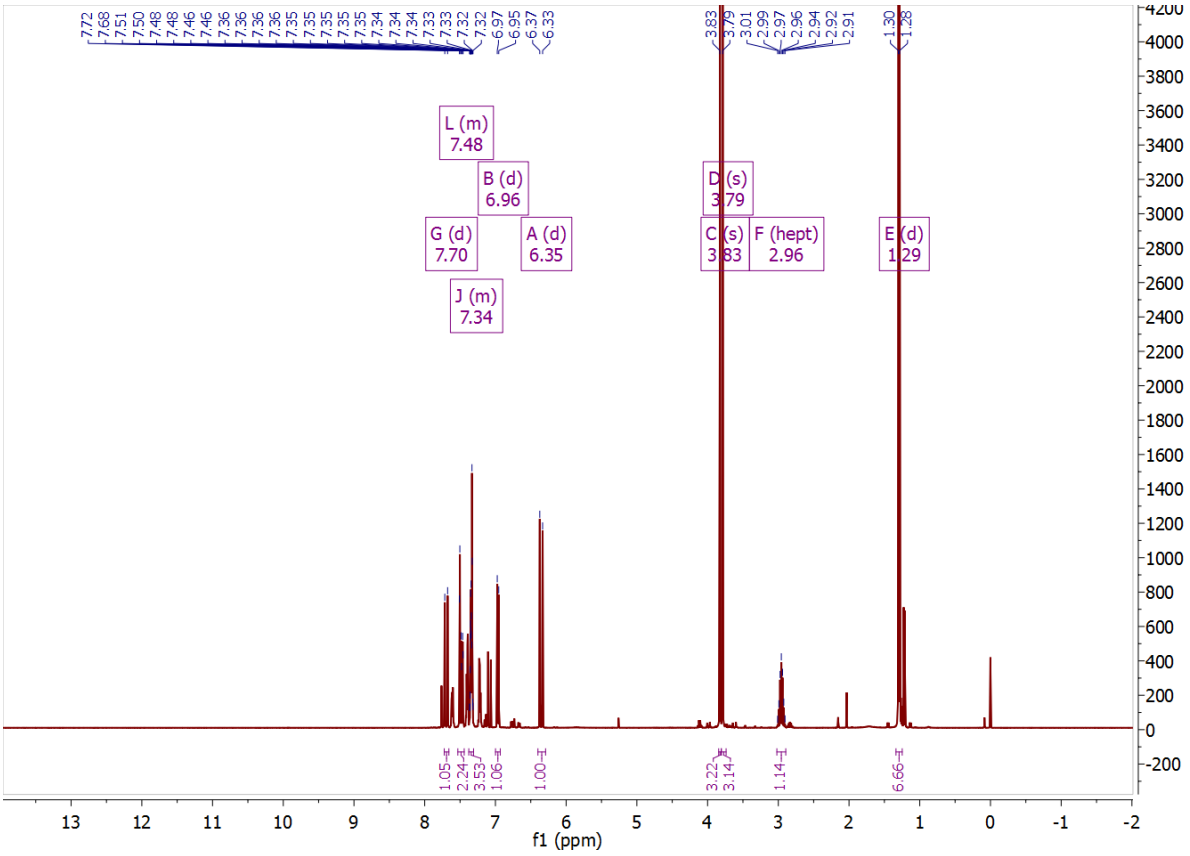


Figure S10. 13C NMR spectrum of *(E)*-methyl 3-(3'-isopropyl-6-methoxy-[1,1'-biphenyl]-3-yl)acrylate (15)

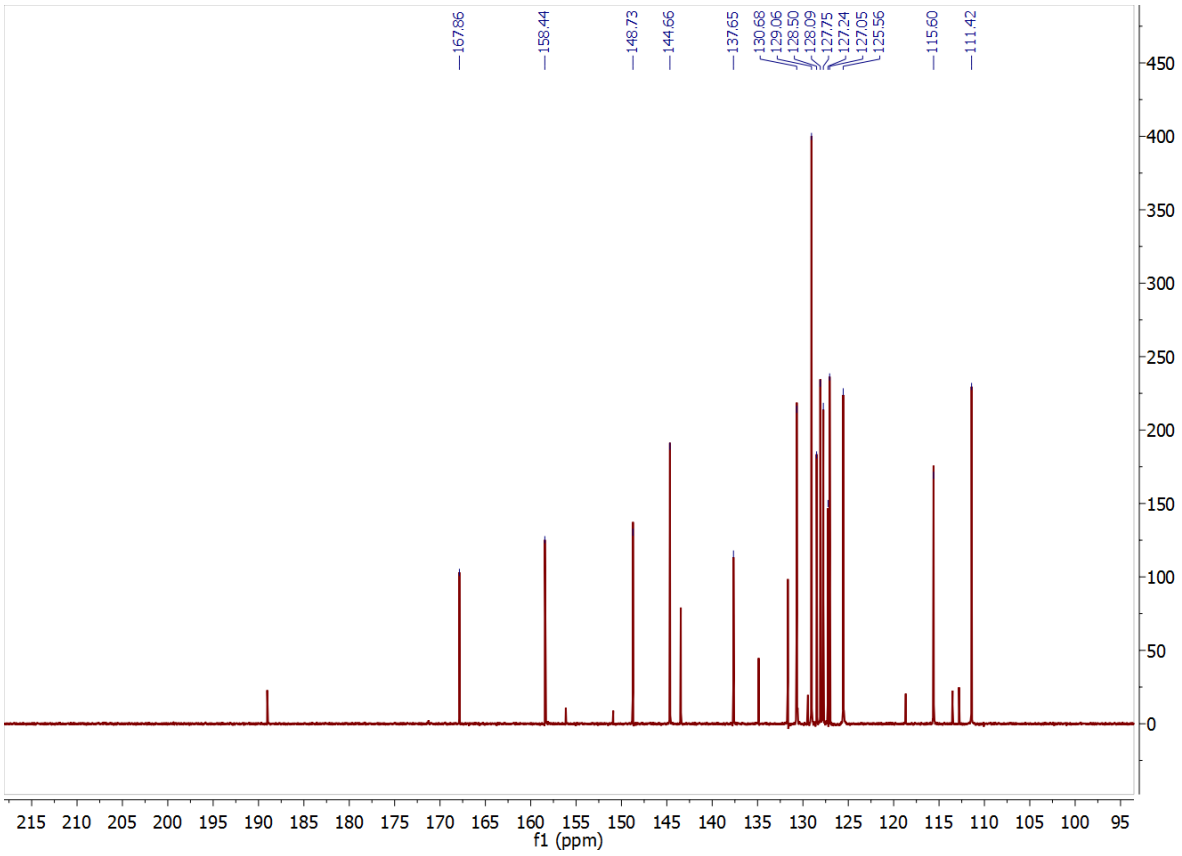


Figure S11. 1H NMR spectrum of *(E)*-3-(6-hydroxy-3'-isopropyl-[1,1'-biphenyl]-3-yl)acrylic acid (4)

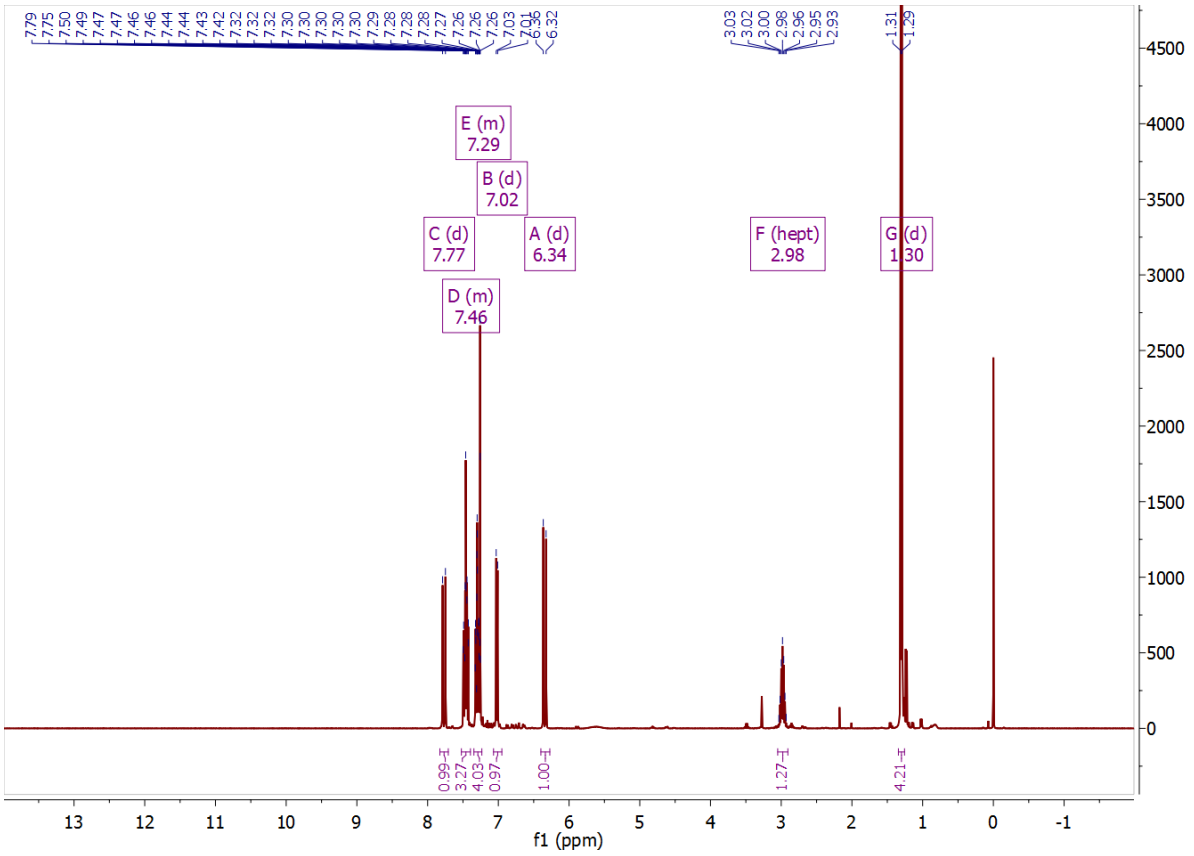


Figure S12. 13C NMR spectrum of *(E)*-3-(6-hydroxy-3'-isopropyl-[1,1'-biphenyl]-3-yl)acrylic acid (4)

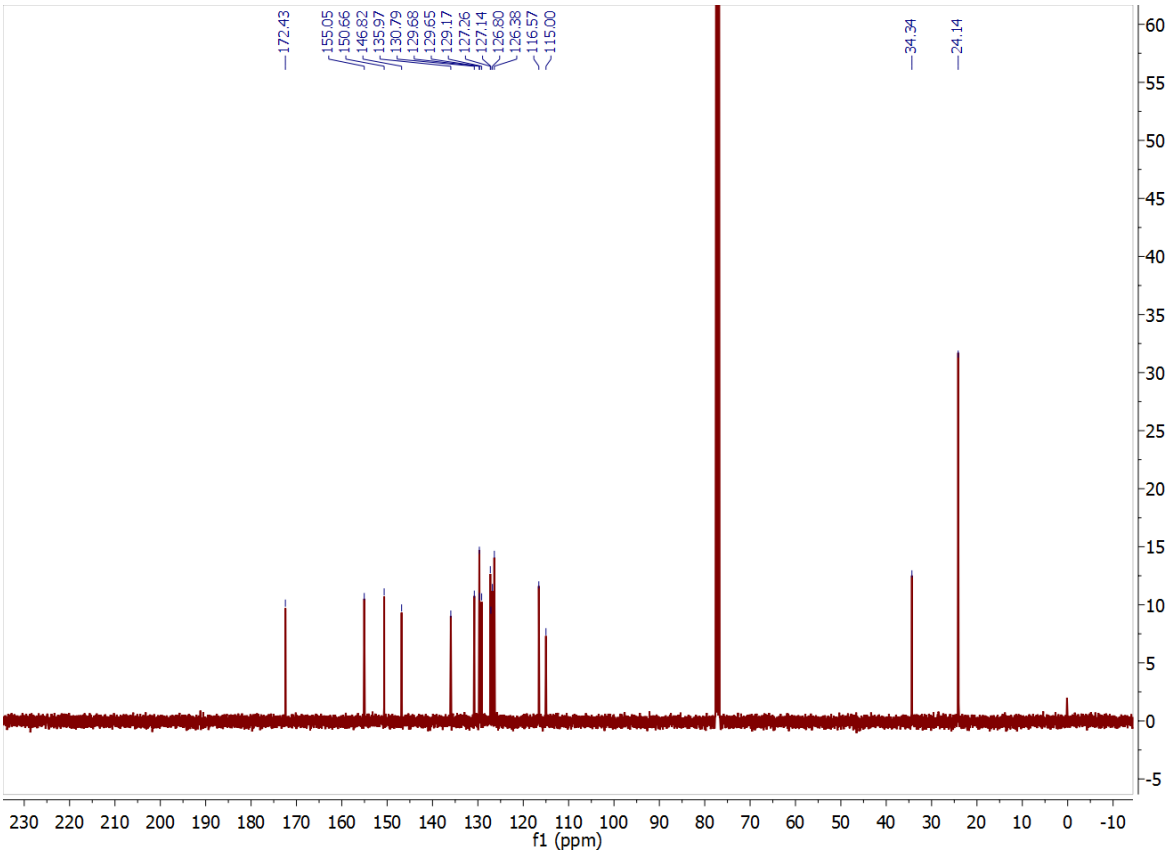


Figure S13. 1H NMR spectrum of 1-bromo-3-propylbenzene

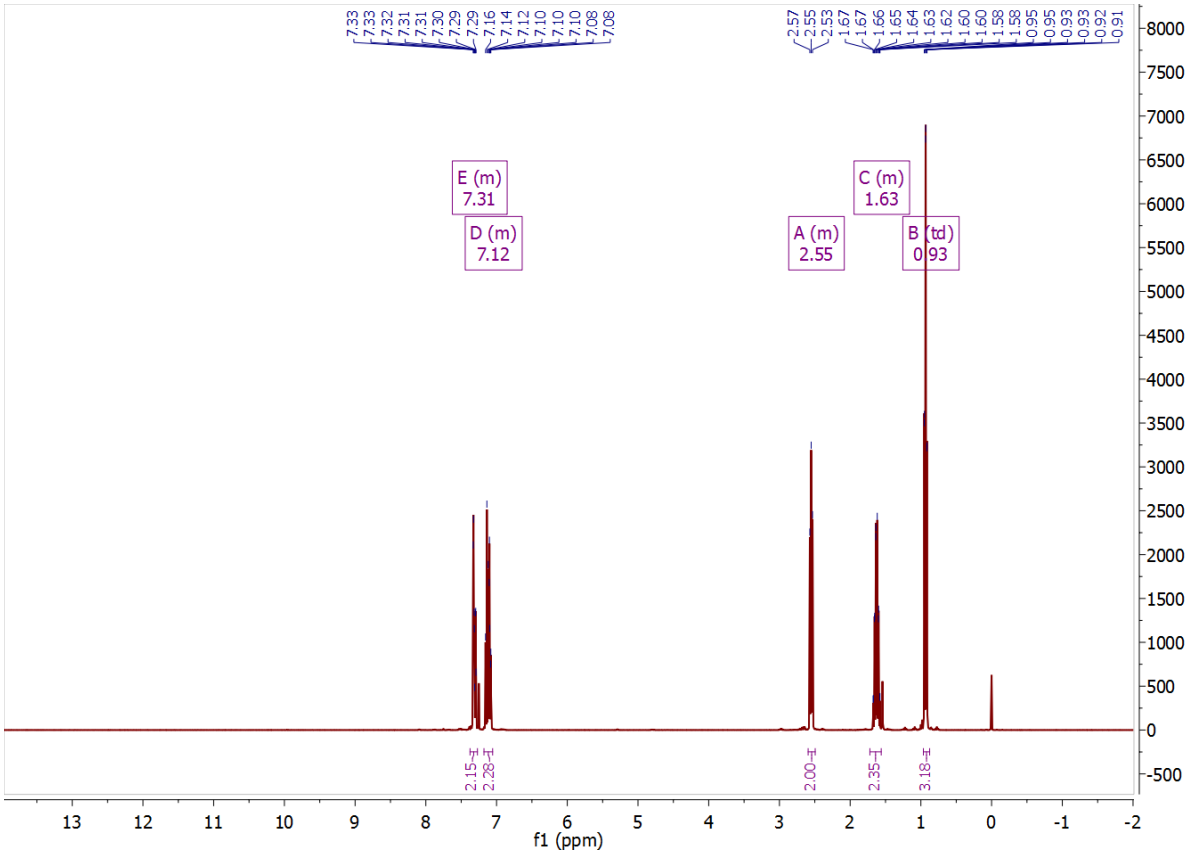


Figure S14. 13C NMR spectrum of 1-bromo-3-propylbenzene

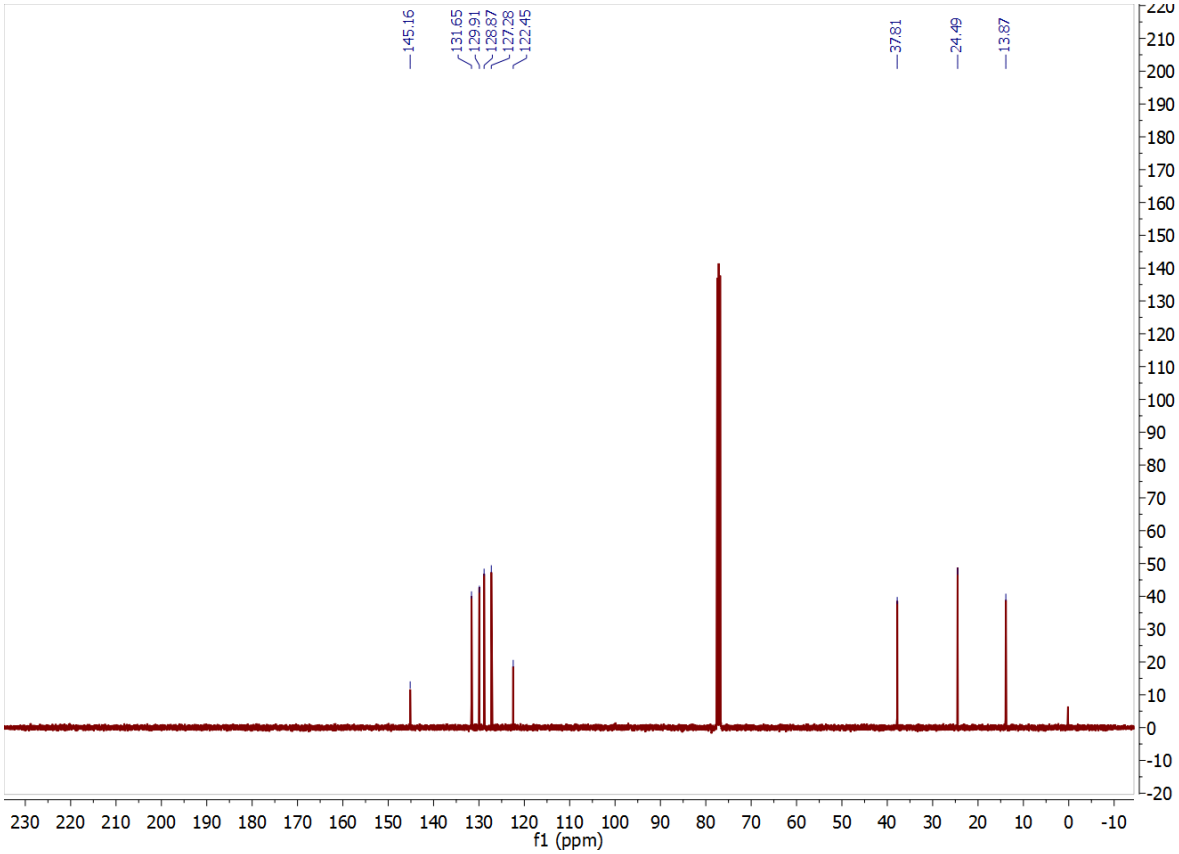


Figure S15. 1H NMR spectrum of *(E)*-methyl 3-(6-methoxy-3'-propyl-[1,1'-biphenyl]-3-yl)acrylate (16)

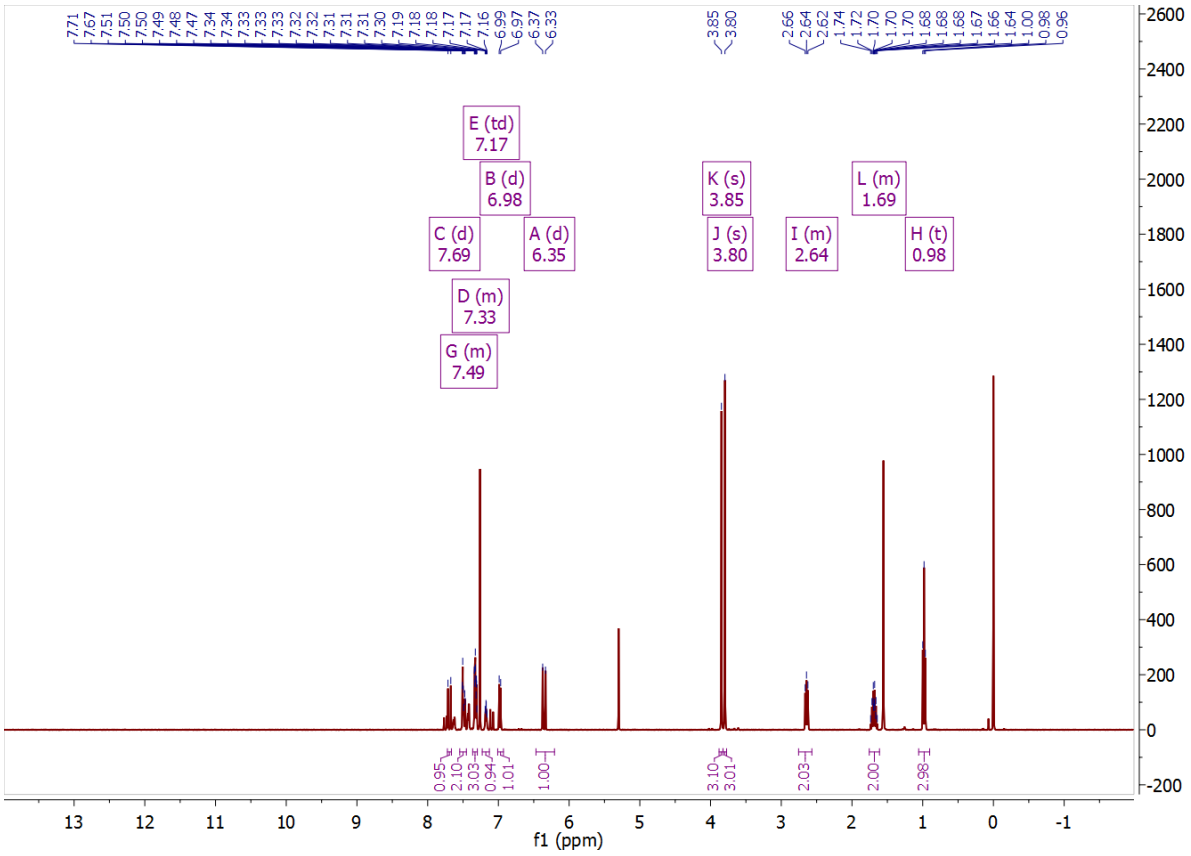


Figure S16. 13C NMR spectrum of *(E)*-methyl 3-(6-methoxy-3'-propyl-[1,1'-biphenyl]-3-yl)acrylate (16)

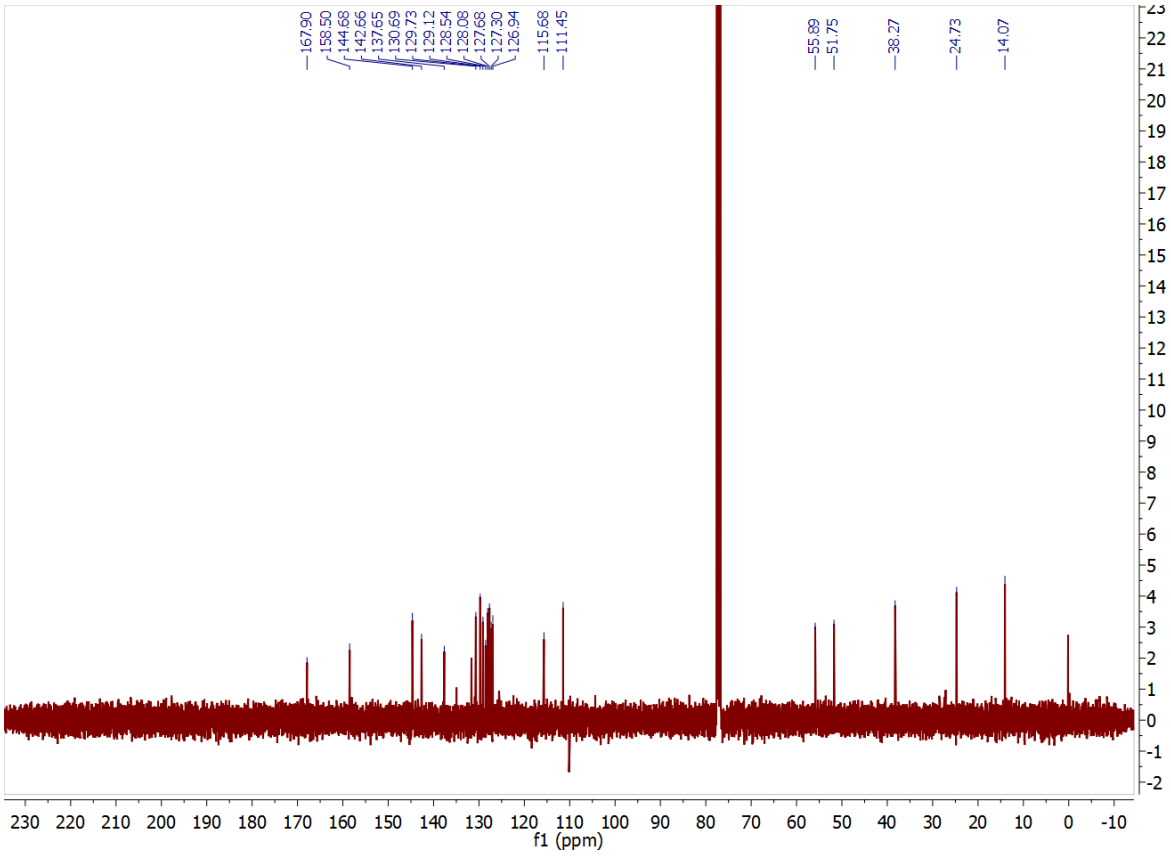


Figure S17. 1H NMR spectrum of *(E)*-3-(6-hydroxy-3'-propyl-[1,1'-biphenyl]-3-yl)acrylic acid (5)

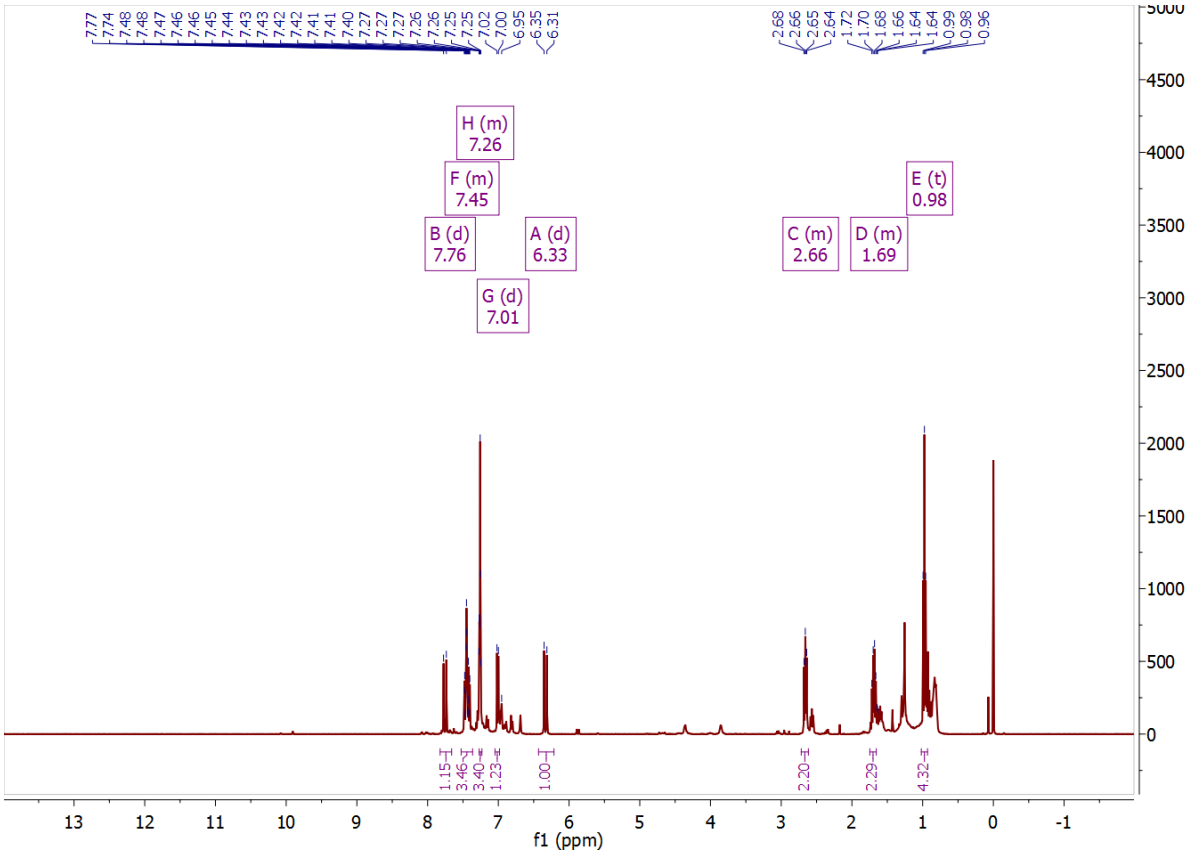


Figure S18. 13C NMR spectrum of *(E)*-3-(6-hydroxy-3'-propyl-[1,1'-biphenyl]-3-yl)acrylic acid (5)

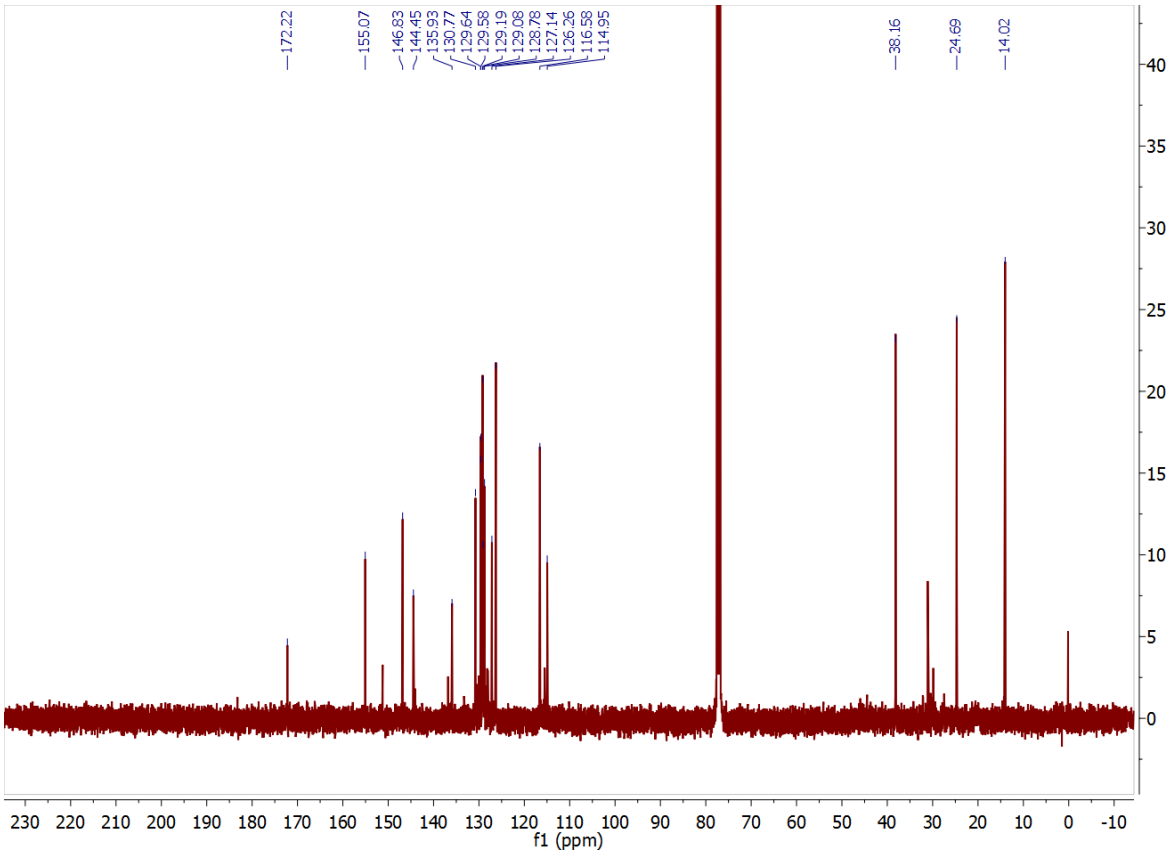


Figure S19. 1H NMR spectrum of 3-chloro-2-methyl-1,1'-biphenyl (19)

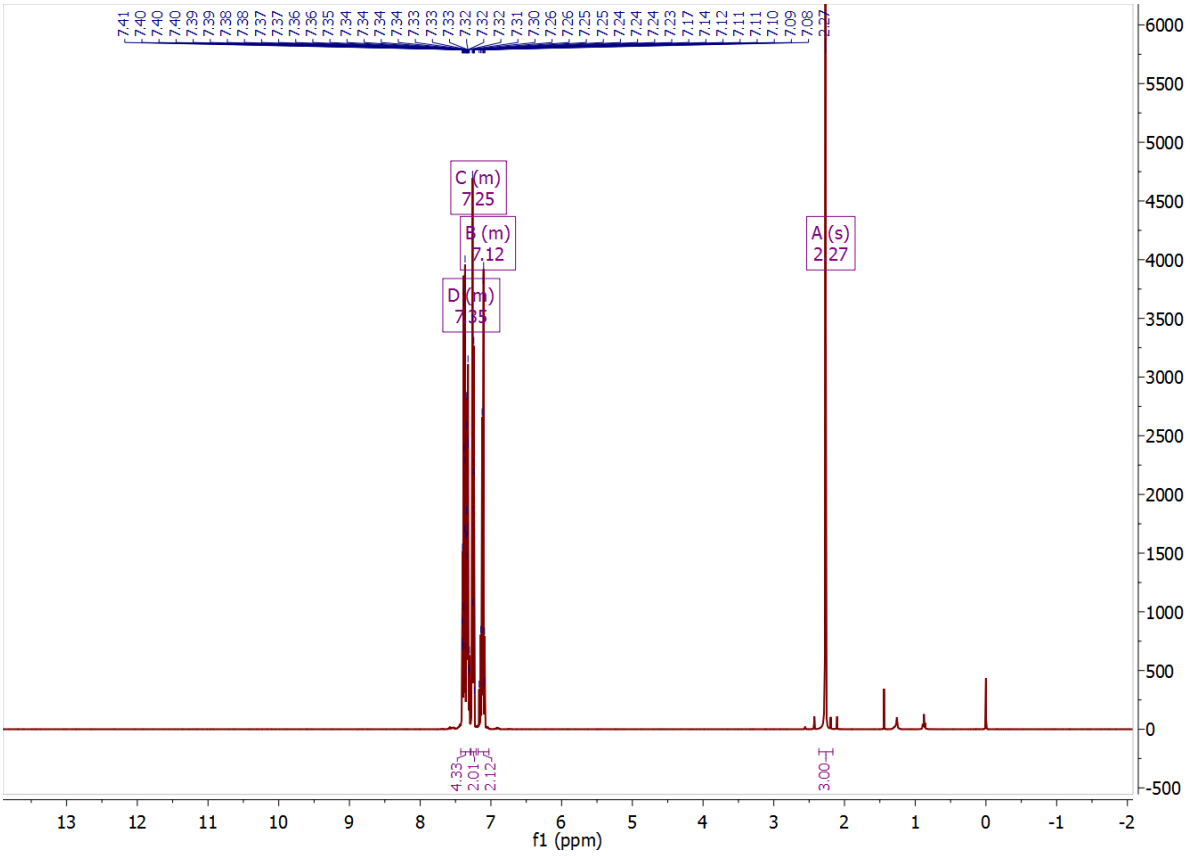


Figure S20. 13C NMR spectrum of 3-chloro-2-methyl-1,1'-biphenyl (19)

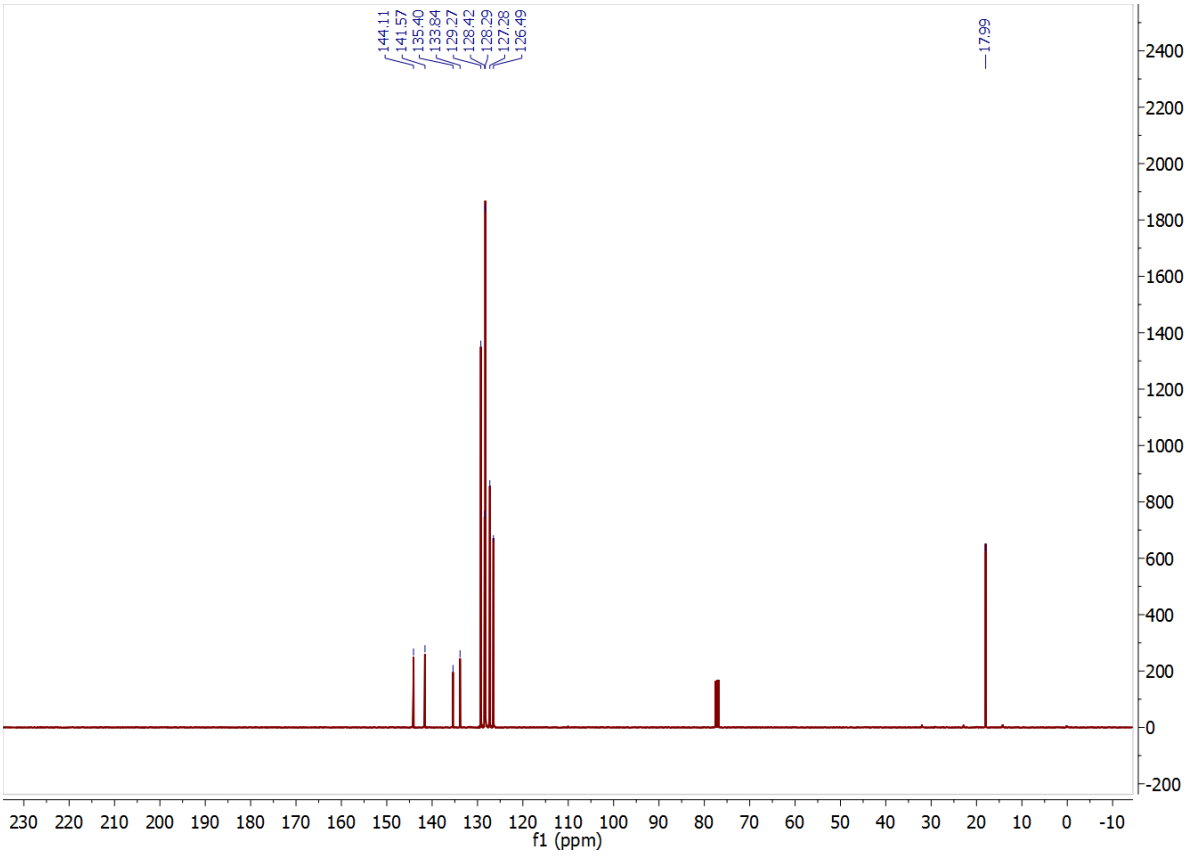


Figure S21. 1H NMR spectrum of *(E)*-methyl 3-(6-(methoxymethoxy)-2'-methyl-[1,1':3',1''-terphenyl]-3-yl)acrylate (21)

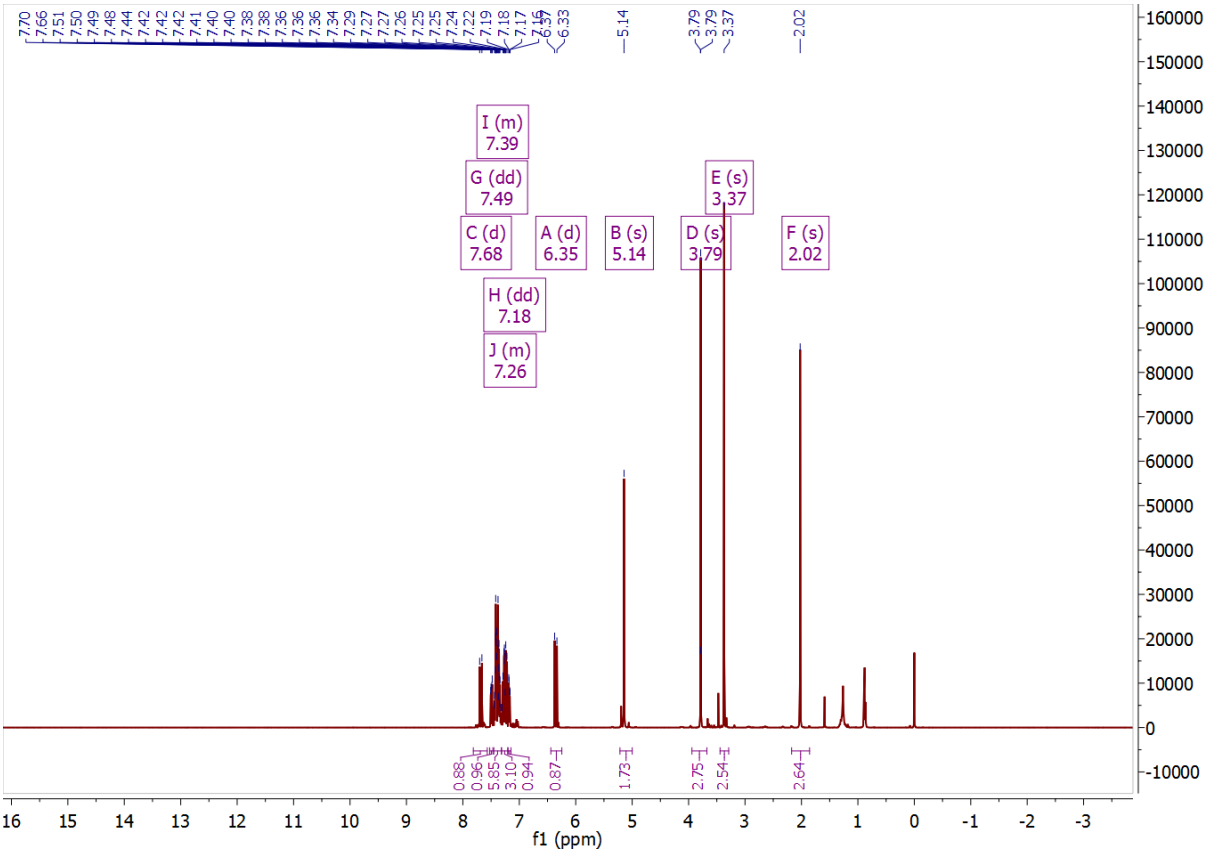


Figure S22. 13C NMR spectrum of *(E)*-methyl 3-(6-(methoxymethoxy)-2'-methyl-[1,1':3',1''-terphenyl]-3-yl)acrylate (21)

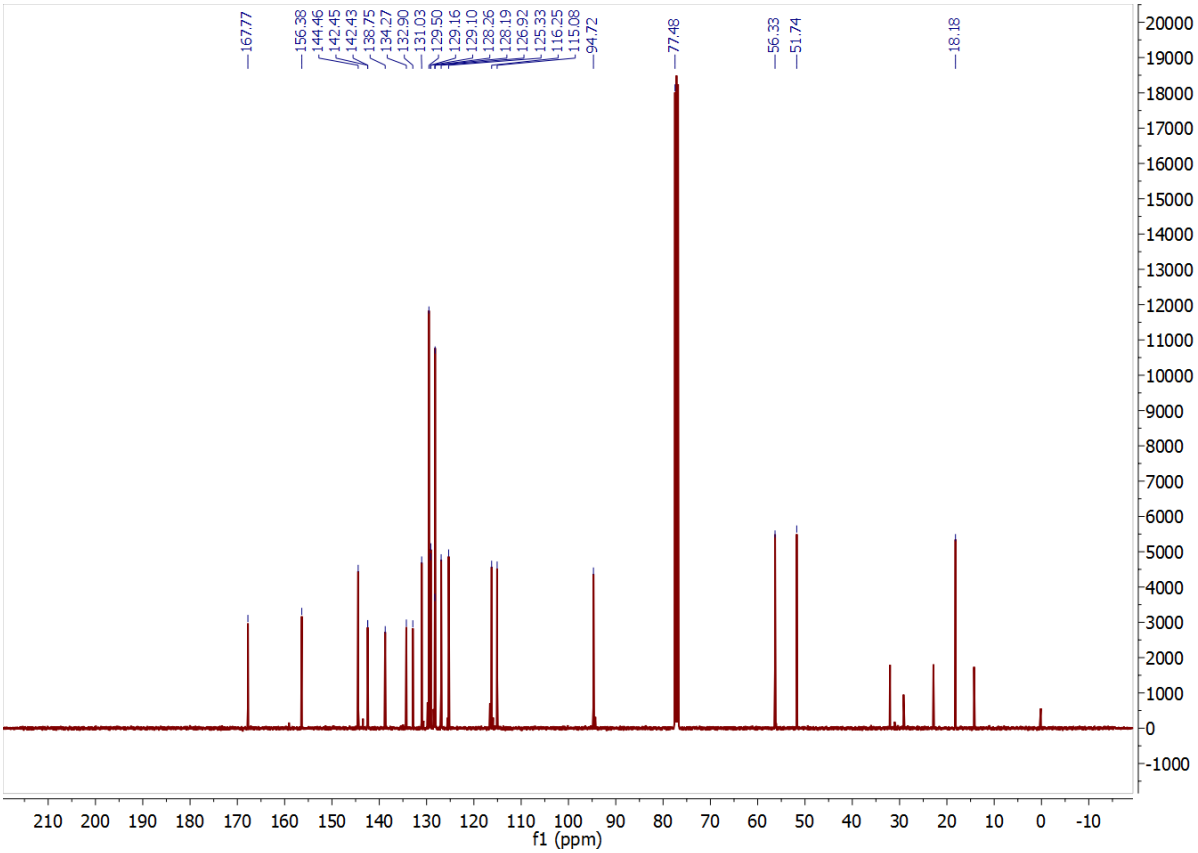


Figure S23. 1H NMR spectrum of *(E)*-3-(6-hydroxy-2'-methyl-[1,1':3',1''-terphenyl]-3-yl)acrylic acid (6)

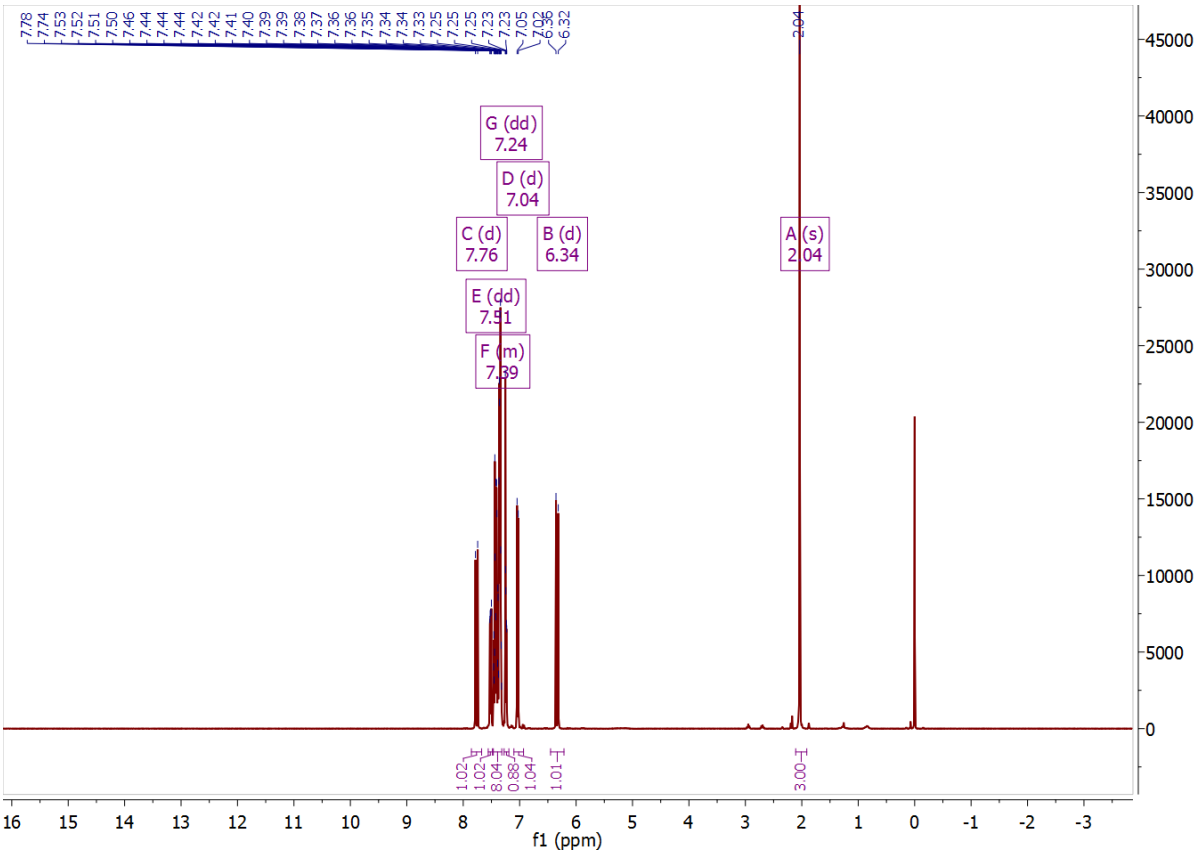


Figure S24. 13C NMR spectrum of *(E)*-3-(6-hydroxy-2'-methyl-[1,1':3',1''-terphenyl]-3-yl)acrylic acid (6)

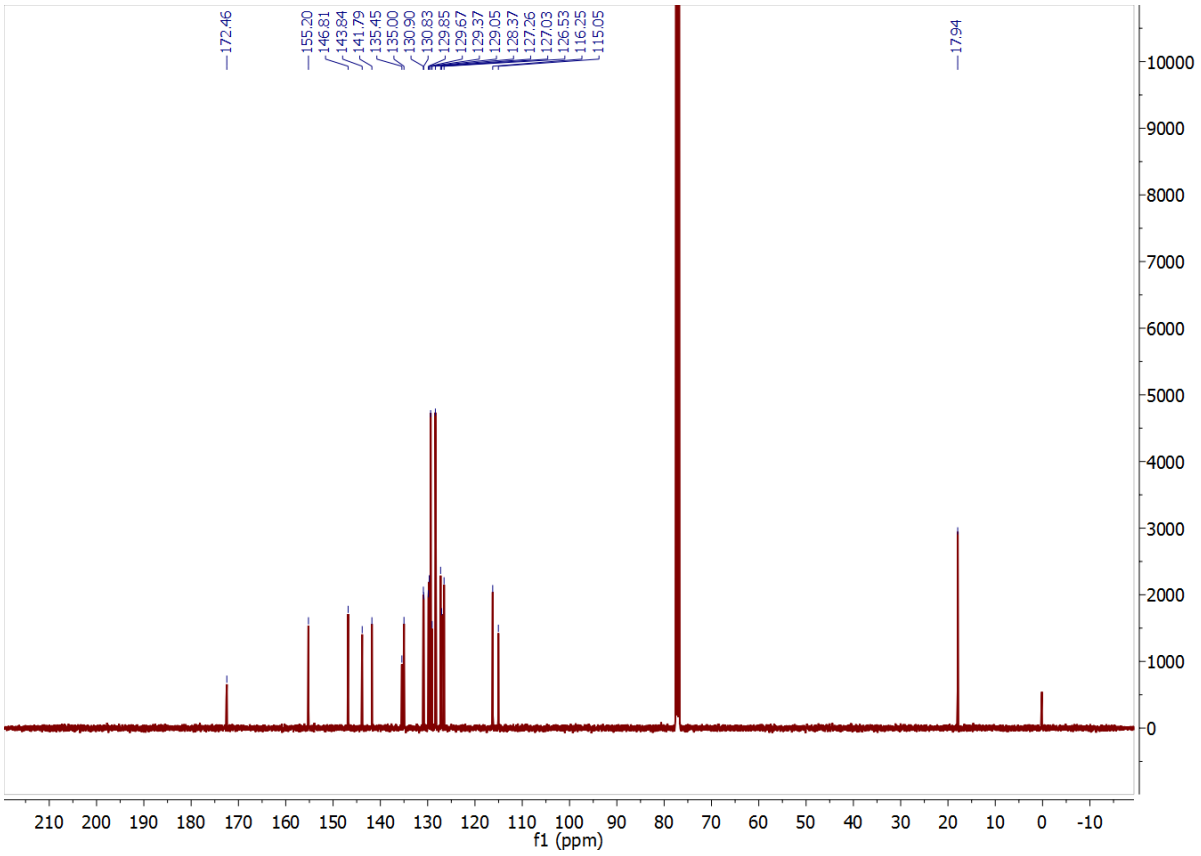


Figure S25. 1H NMR spectrum of 3-chloro-4-methyl-1,1'-biphenyl (20)

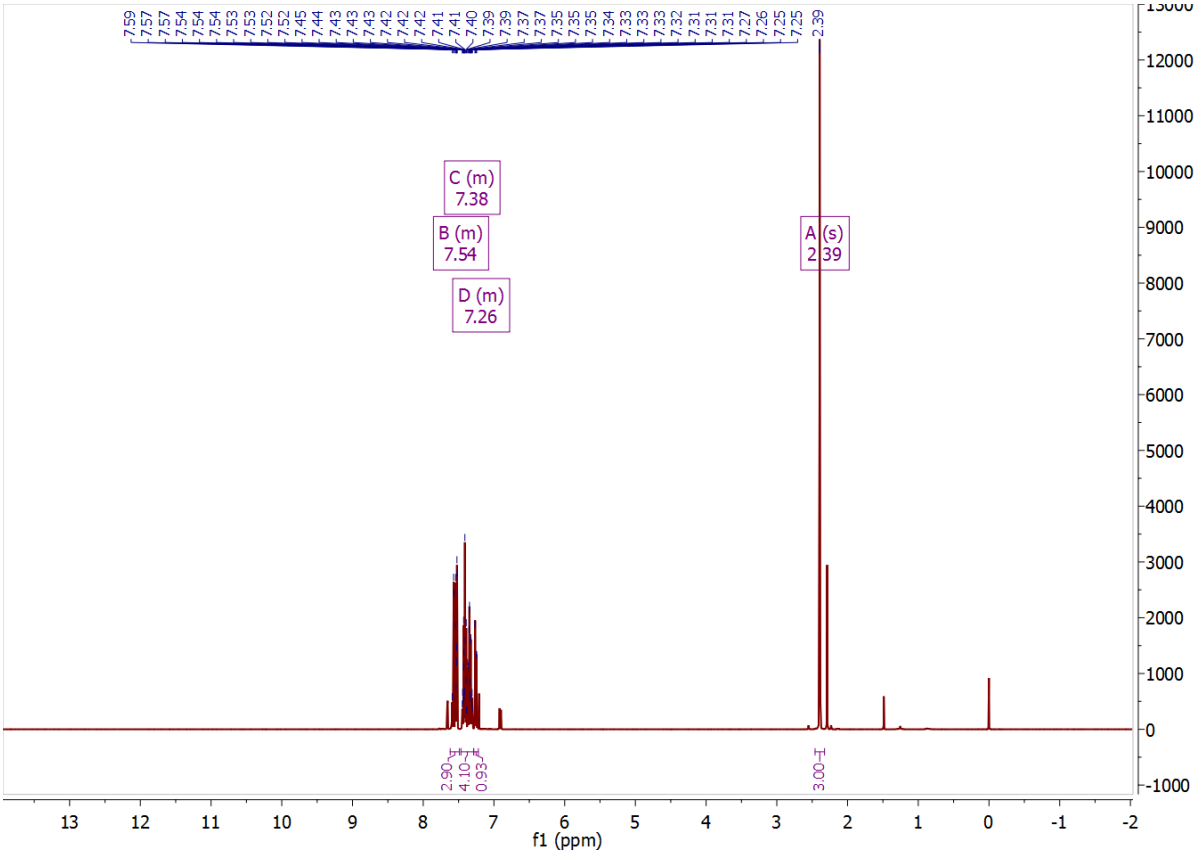


Figure S26. 13C NMR spectrum of 3-chloro-4-methyl-1,1'-biphenyl (20)

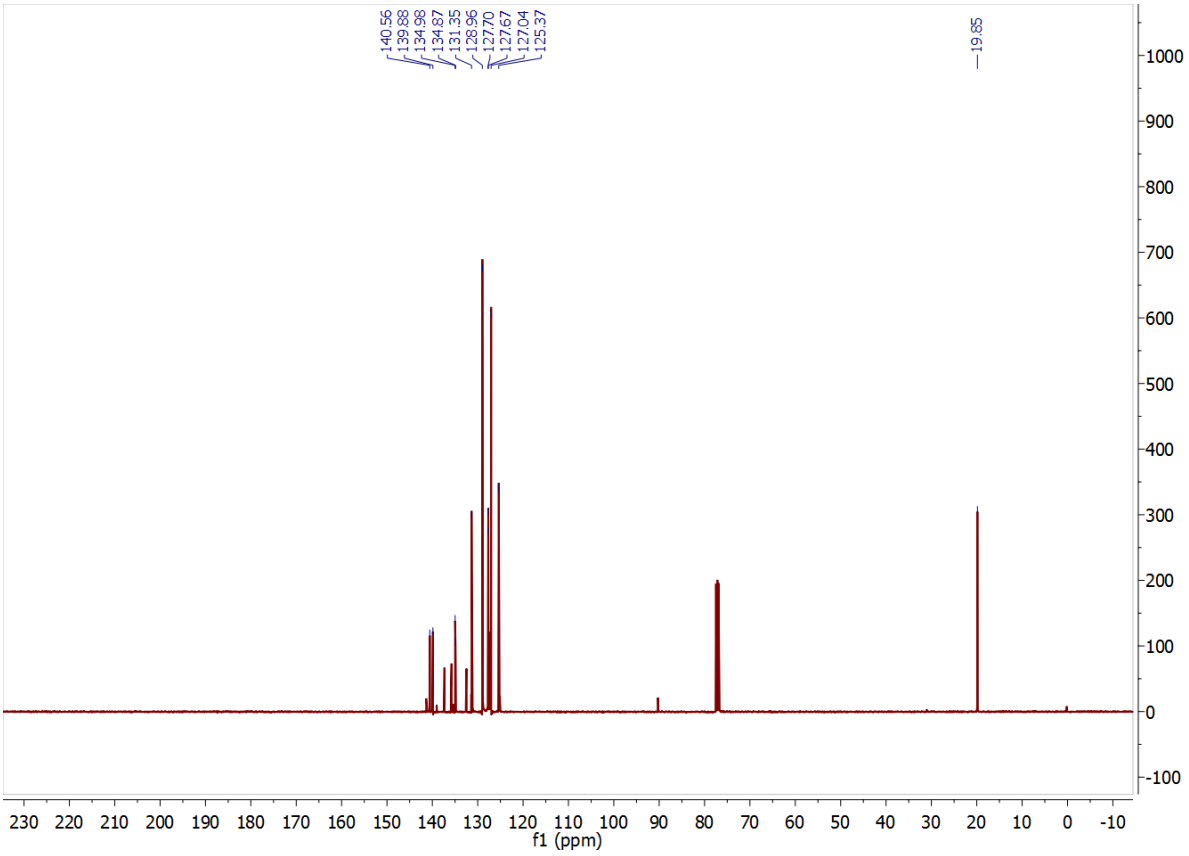


Figure S27. 1H NMR spectrum of *(E)*-methyl 3-(6-(methoxymethoxy)-6'-methyl-[1,1':3',1''-terphenyl]-3-yl)acrylate (22)

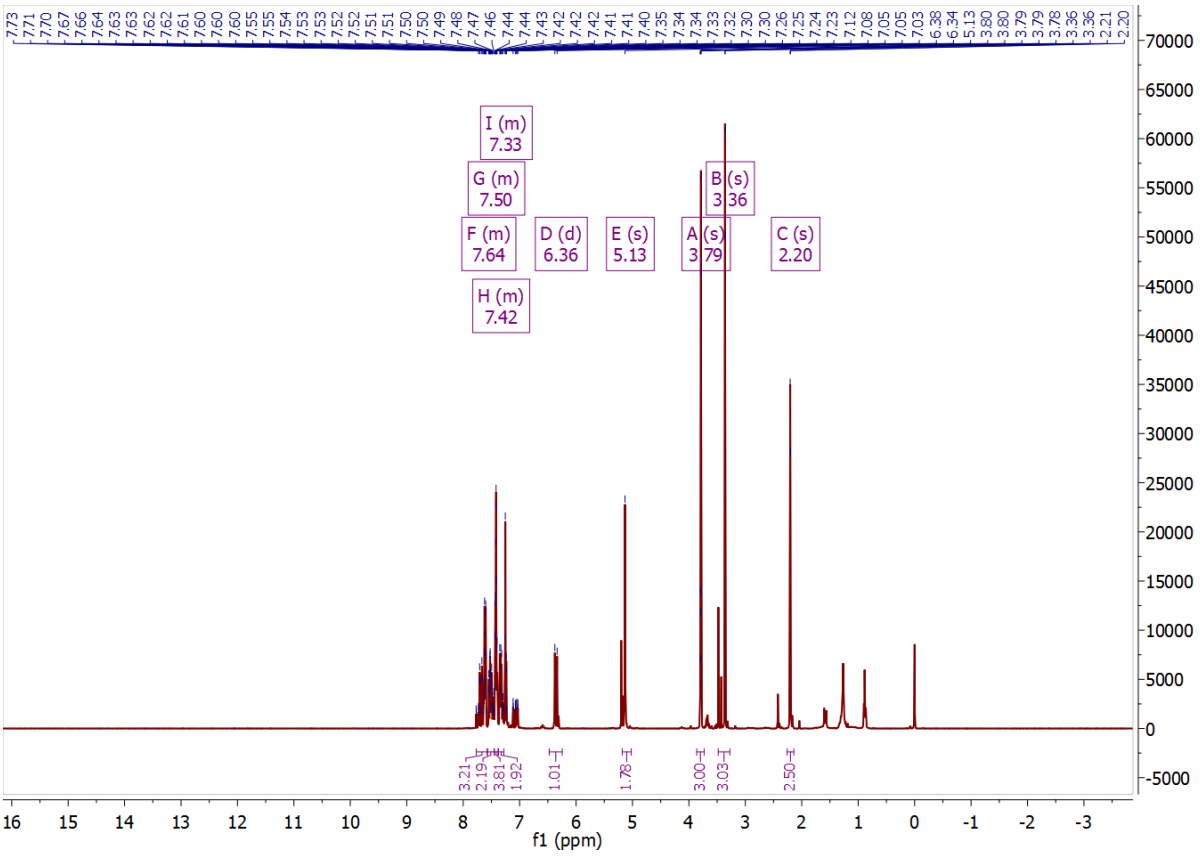


Figure S28. 13C NMR spectrum of *(E)*-methyl 3-(6-(methoxymethoxy)-6'-methyl-[1,1':3',1''-terphenyl]-3-yl)acrylate (22)

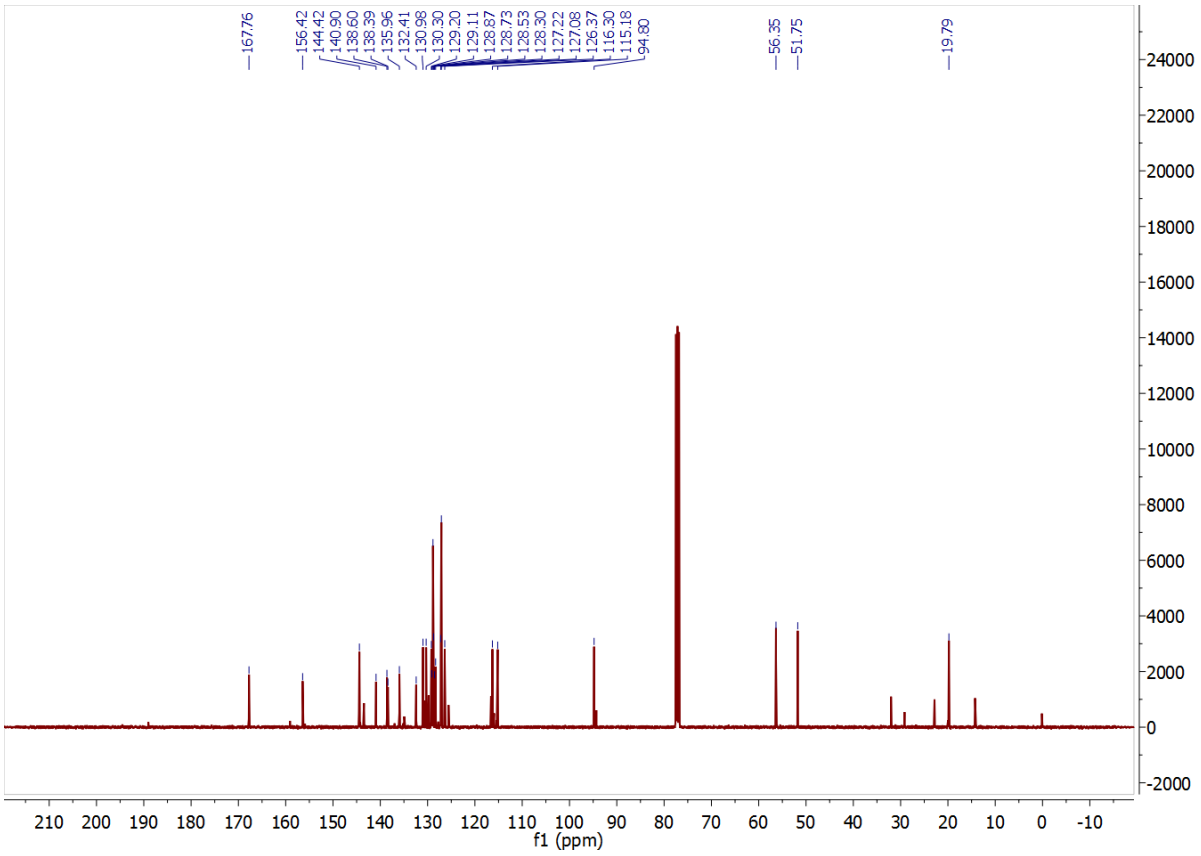


Figure S29. 1H NMR spectrum of *(E)*-3-(6-hydroxy-6'-methyl-[1,1':3',1''-terphenyl]-3-yl)acrylic acid (7)

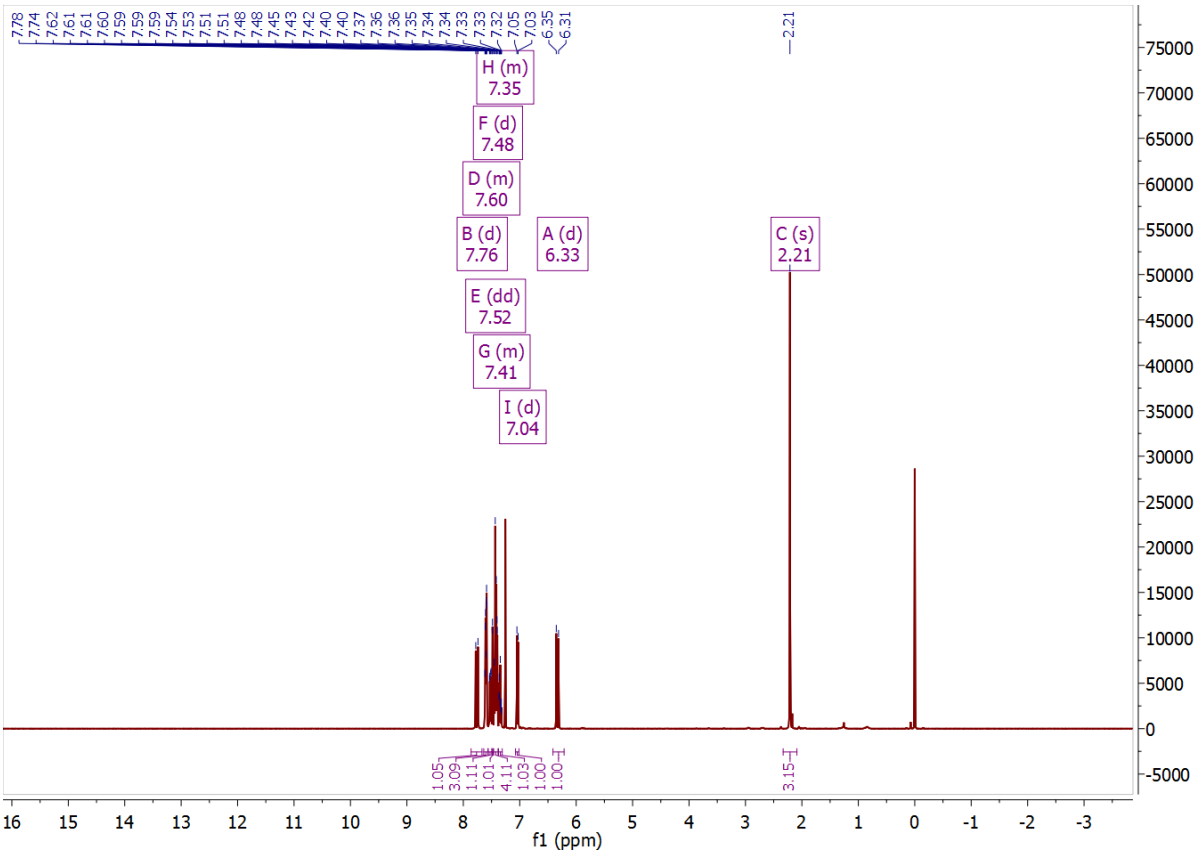


Figure S30. 13C NMR spectrum of *(E)*-3-(6-hydroxy-6'-methyl-[1,1':3',1''-terphenyl]-3-yl)acrylic acid (7)

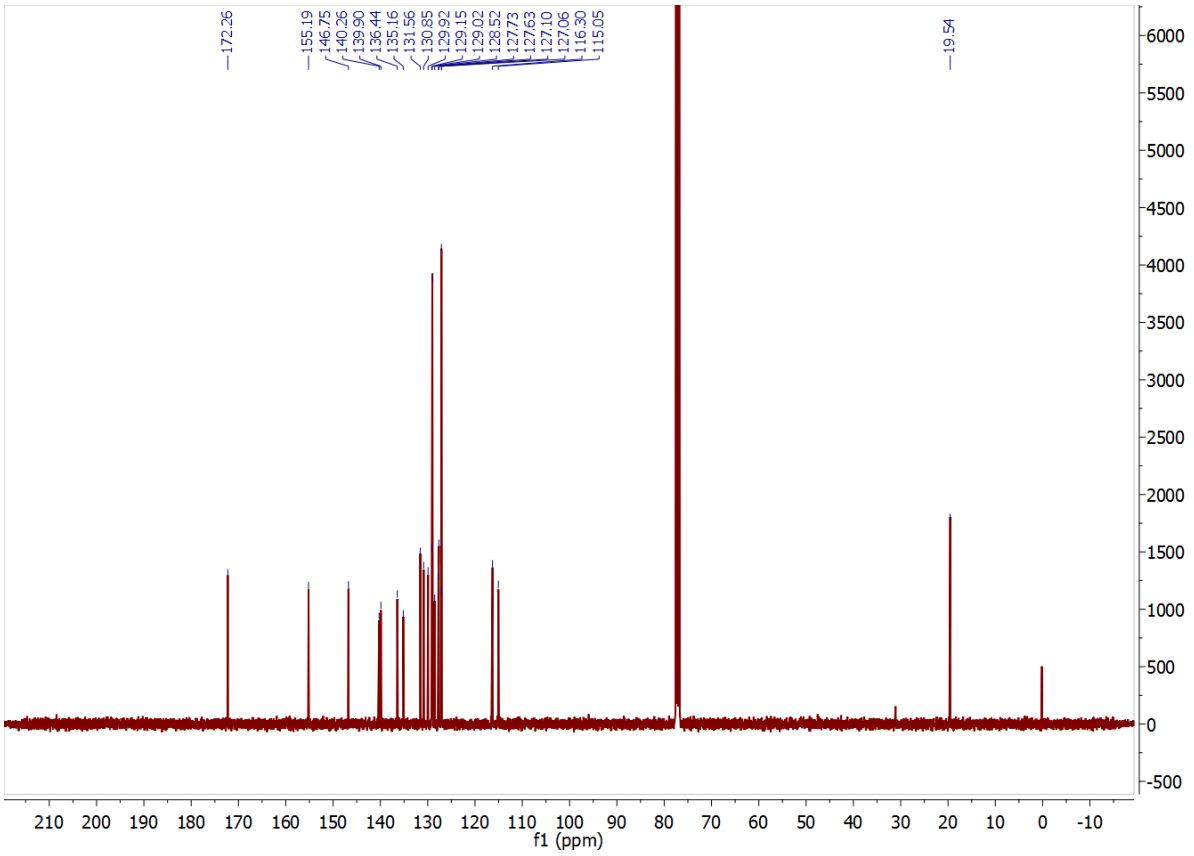


Figure S31. 1H NMR spectrum of *(E)*-methyl 3-(5'-allyl-6-(methoxymethoxy)-2'-propoxy-[1,1'-biphenyl]-3-yl)acrylate (25)

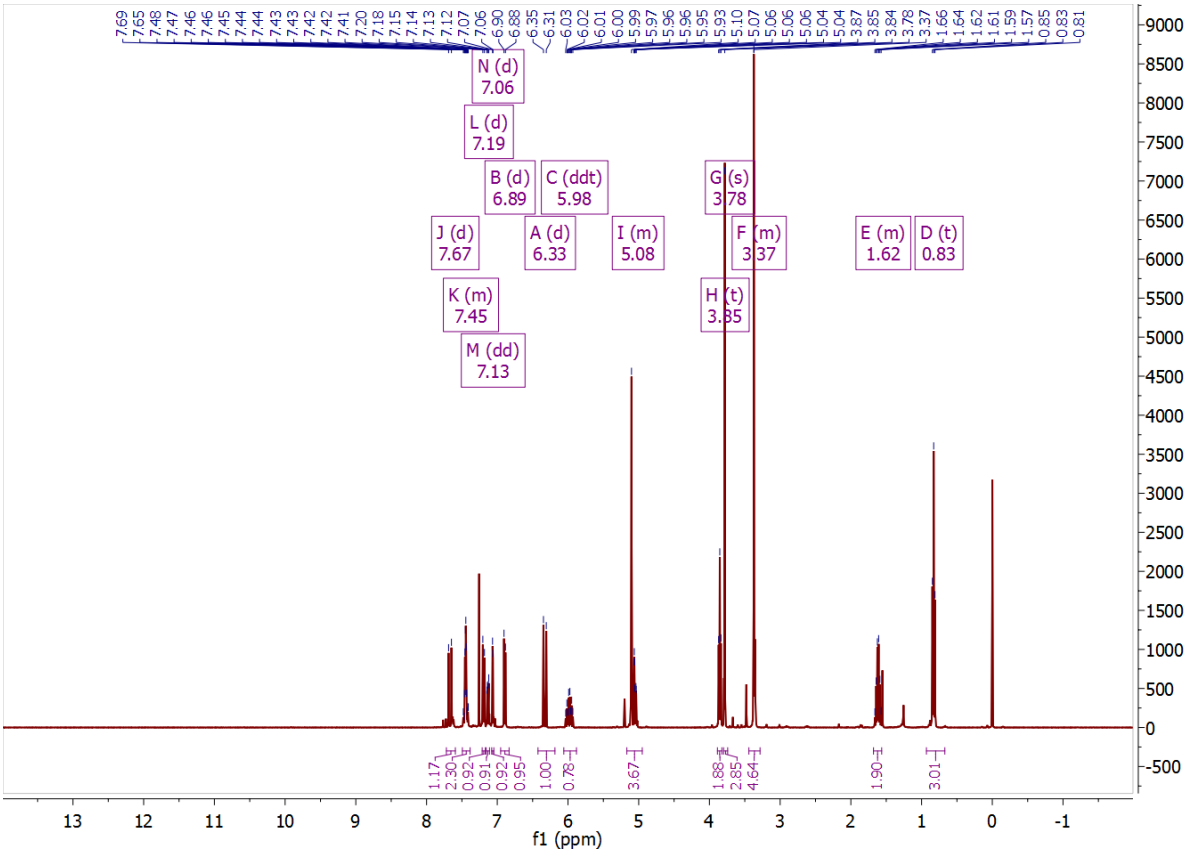


Figure S32. 13C NMR spectrum of *(E)*-methyl 3-(5'-allyl-6-(methoxymethoxy)-2'-propoxy-[1,1'-biphenyl]-3-yl)acrylate (25)

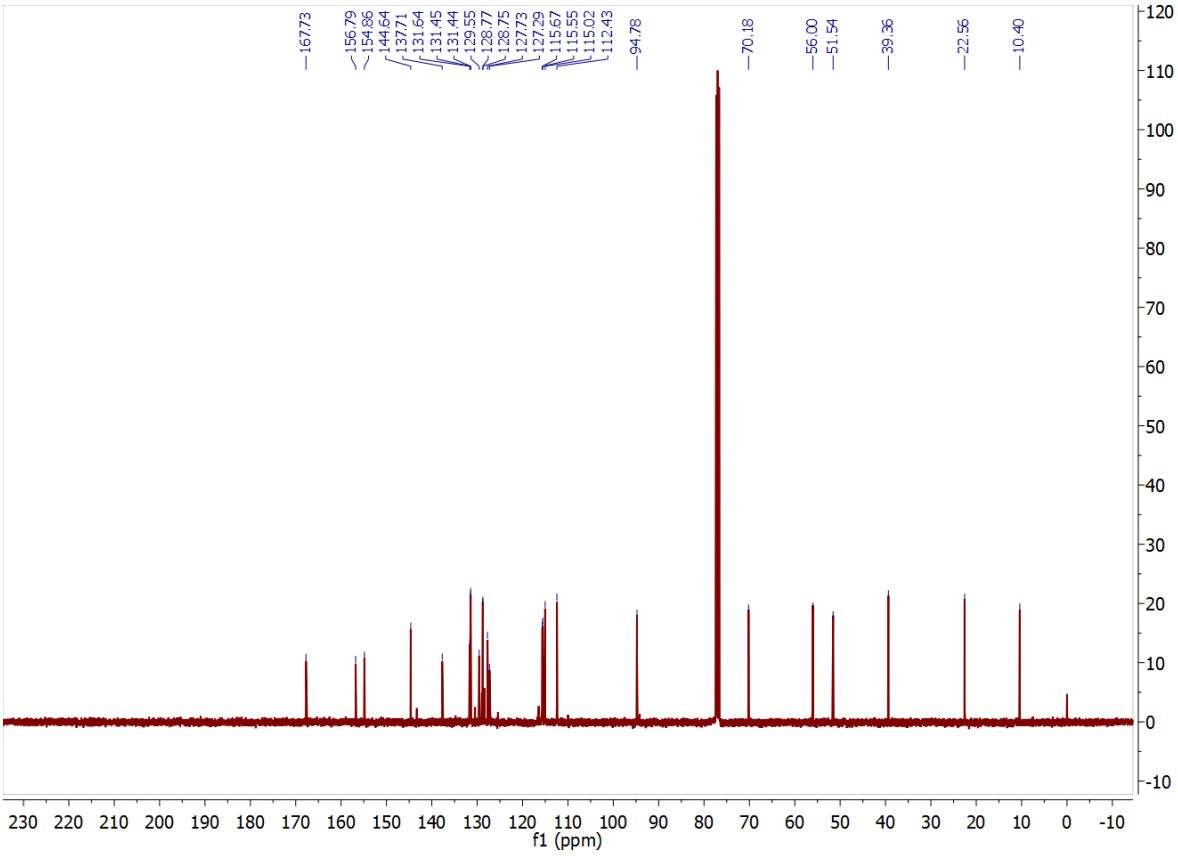


Figure S33. 1H NMR spectrum of *(E)*-3-(5'-allyl-6-hydroxy-2'-propoxy-[1,1'-biphenyl]-3-yl)acrylic acid (9)

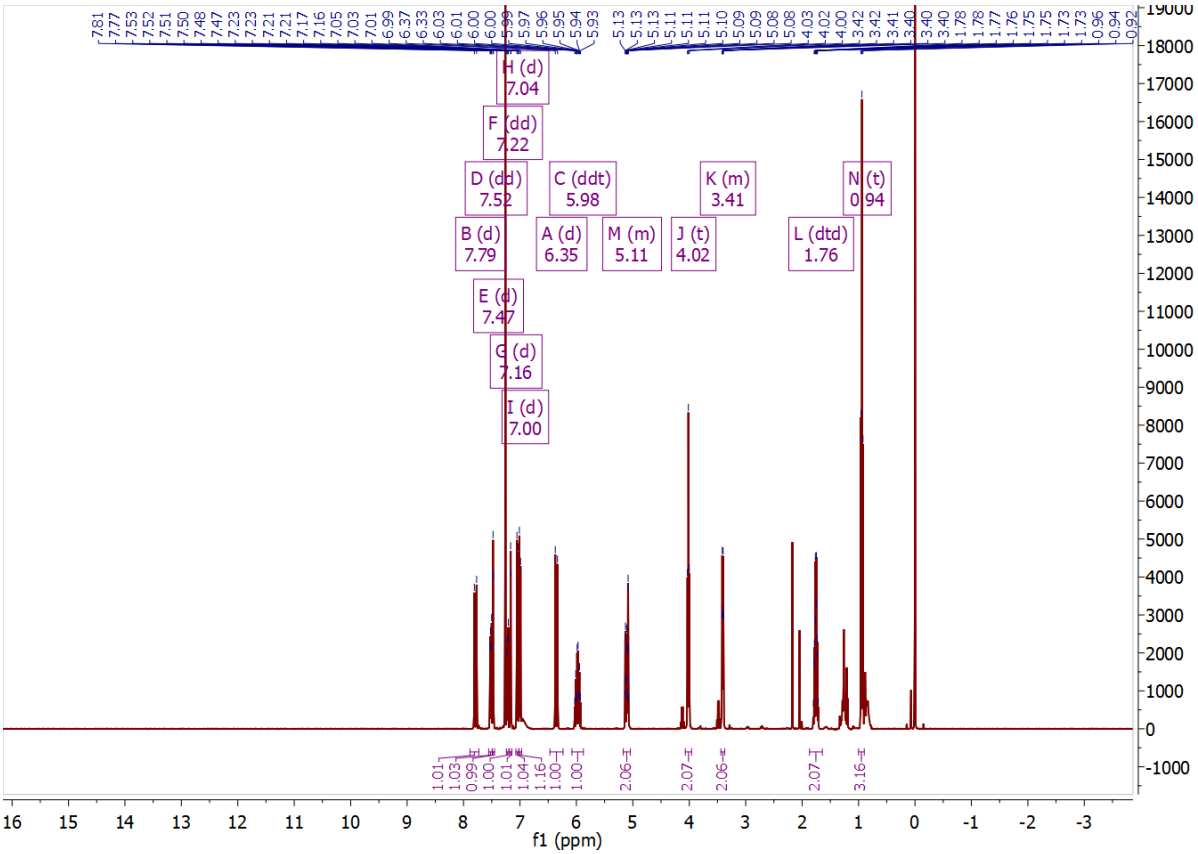


Figure S34. 13C NMR spectrum of *(E)*-3-(5'-allyl-6-hydroxy-2'-propoxy-[1,1'-biphenyl]-3-yl)acrylic acid (9)

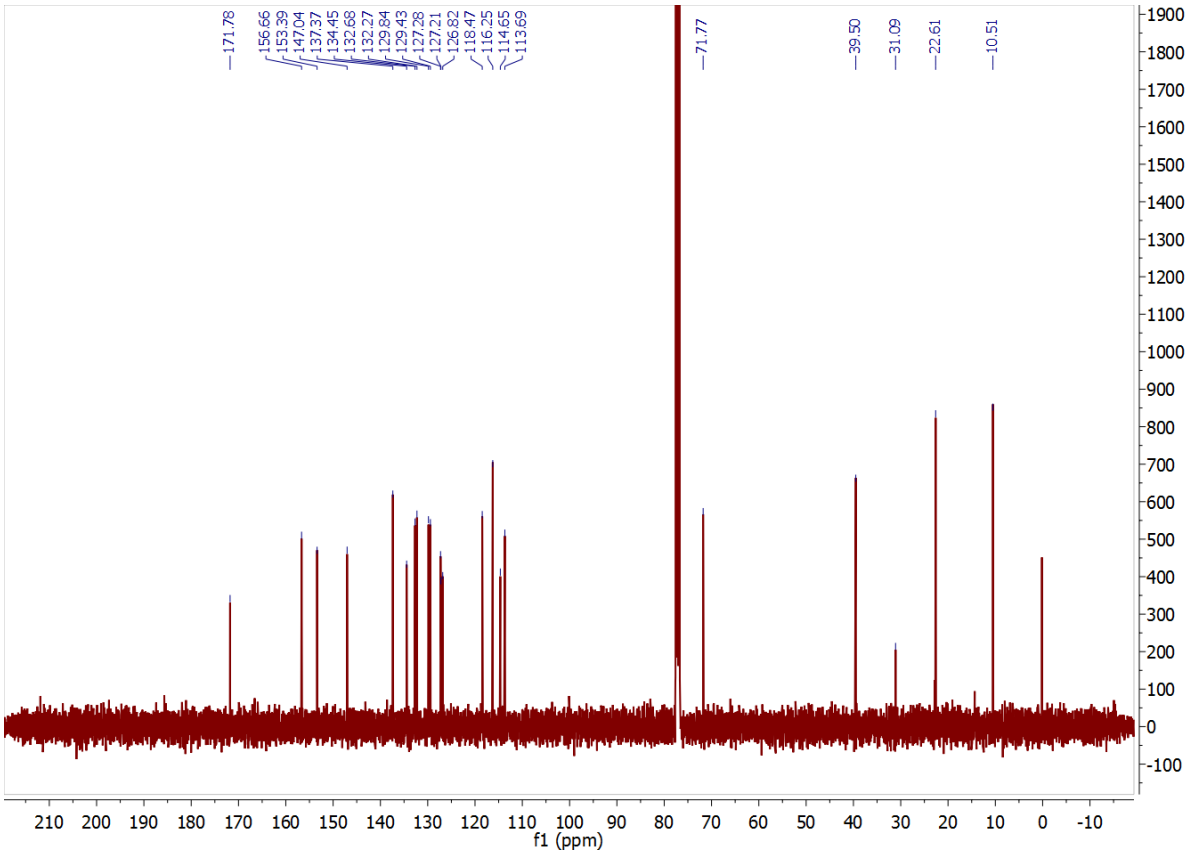


Figure S35. 1H NMR spectrum of *(E)*-methyl 3-(5'-allyl-2'-(hexyloxy)-6-(methoxymethoxy)-[1,1'-biphenyl]-3-yl)acrylate (26)

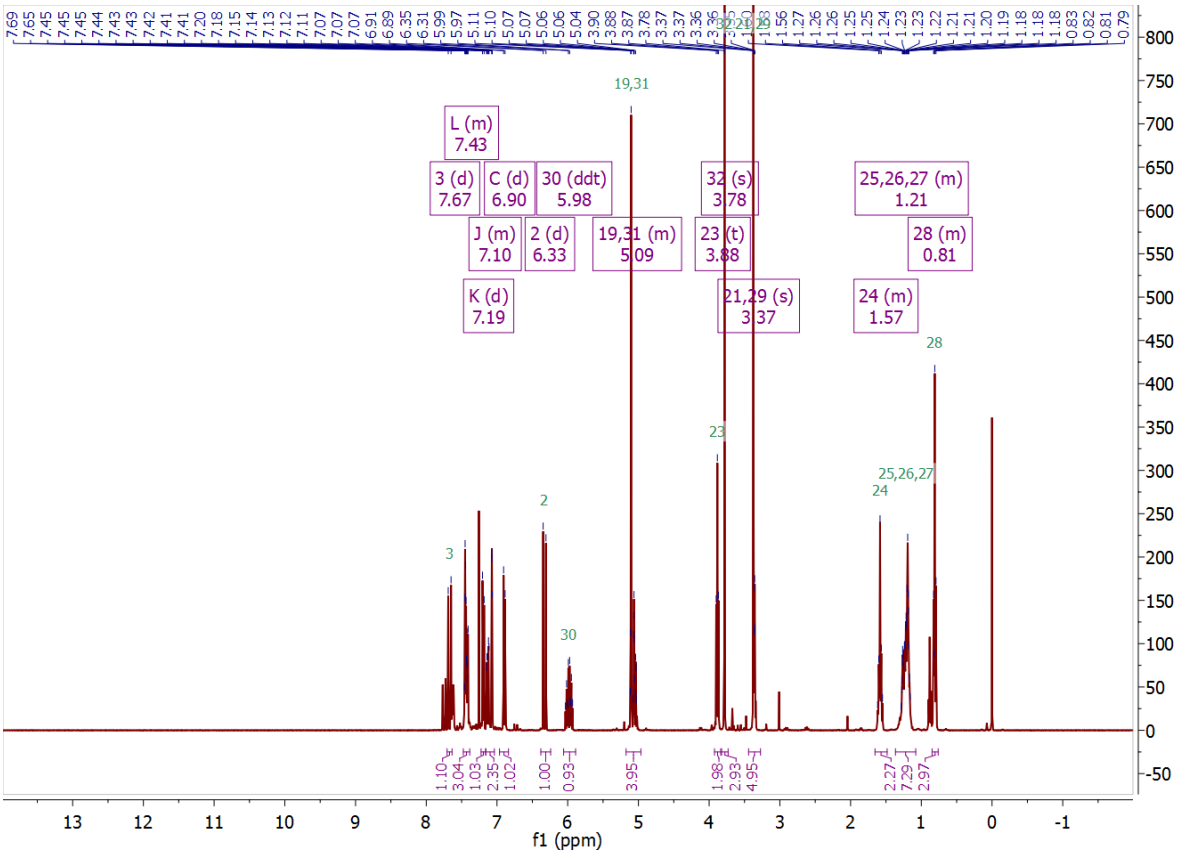


Figure S36. 13C NMR spectrum of *(E)*-methyl 3-(5'-allyl-2'-(hexyloxy)-6-(methoxymethoxy)-[1,1'-biphenyl]-3-yl)acrylate (26)

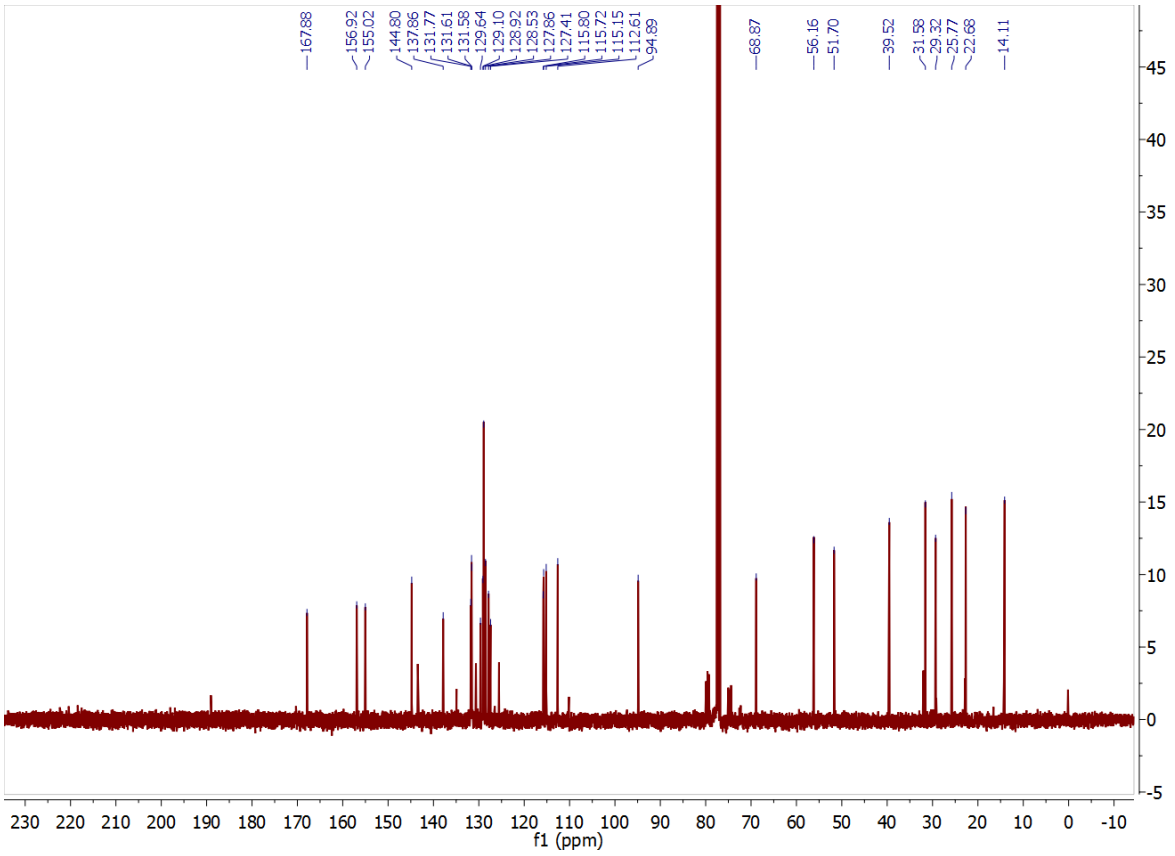


Figure S37. 1H NMR spectrum of *(E)*-3-(5'-allyl-2'-(hexyloxy)-6-hydroxy-[1,1'-biphenyl]-3-yl)acrylic acid (10)

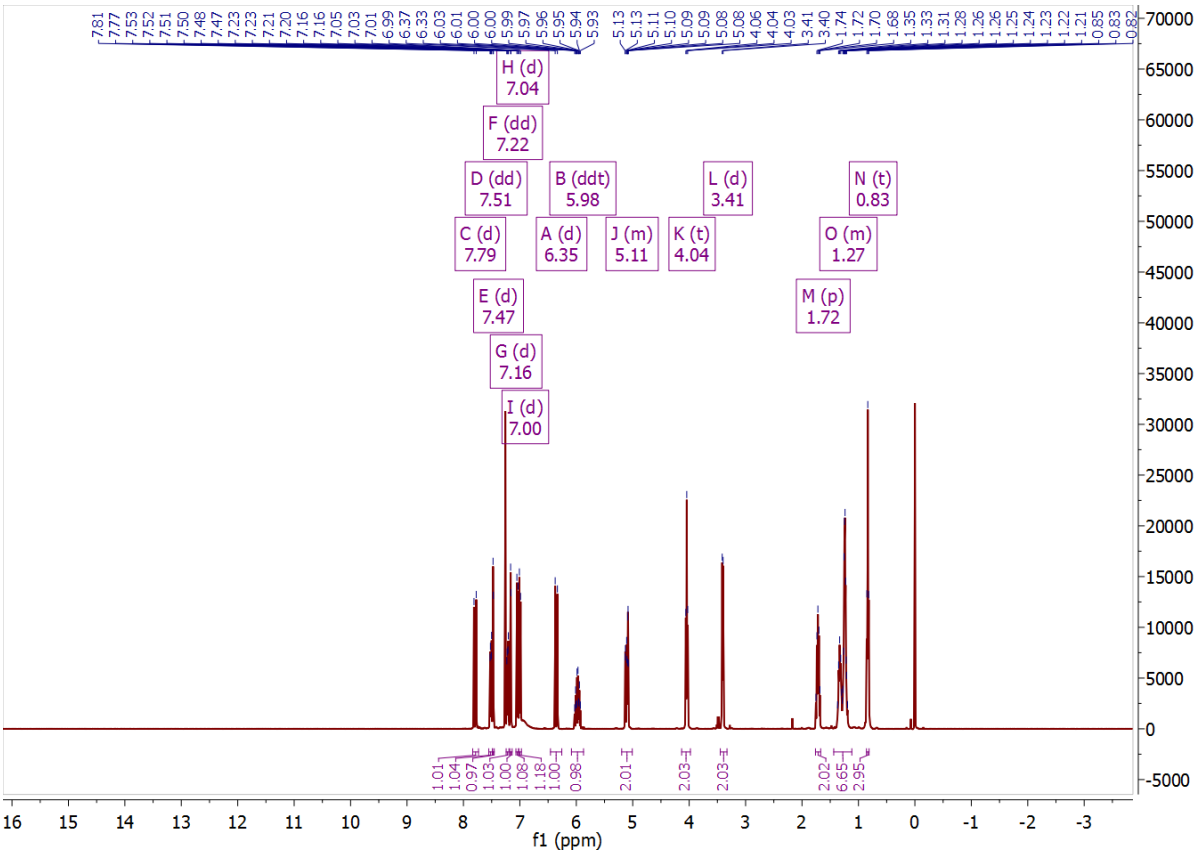


Figure S38. 13C NMR spectrum of *(E)*-3-(5'-allyl-2'-(hexyloxy)-6-hydroxy-[1,1'-biphenyl]-3-yl)acrylic acid (10)

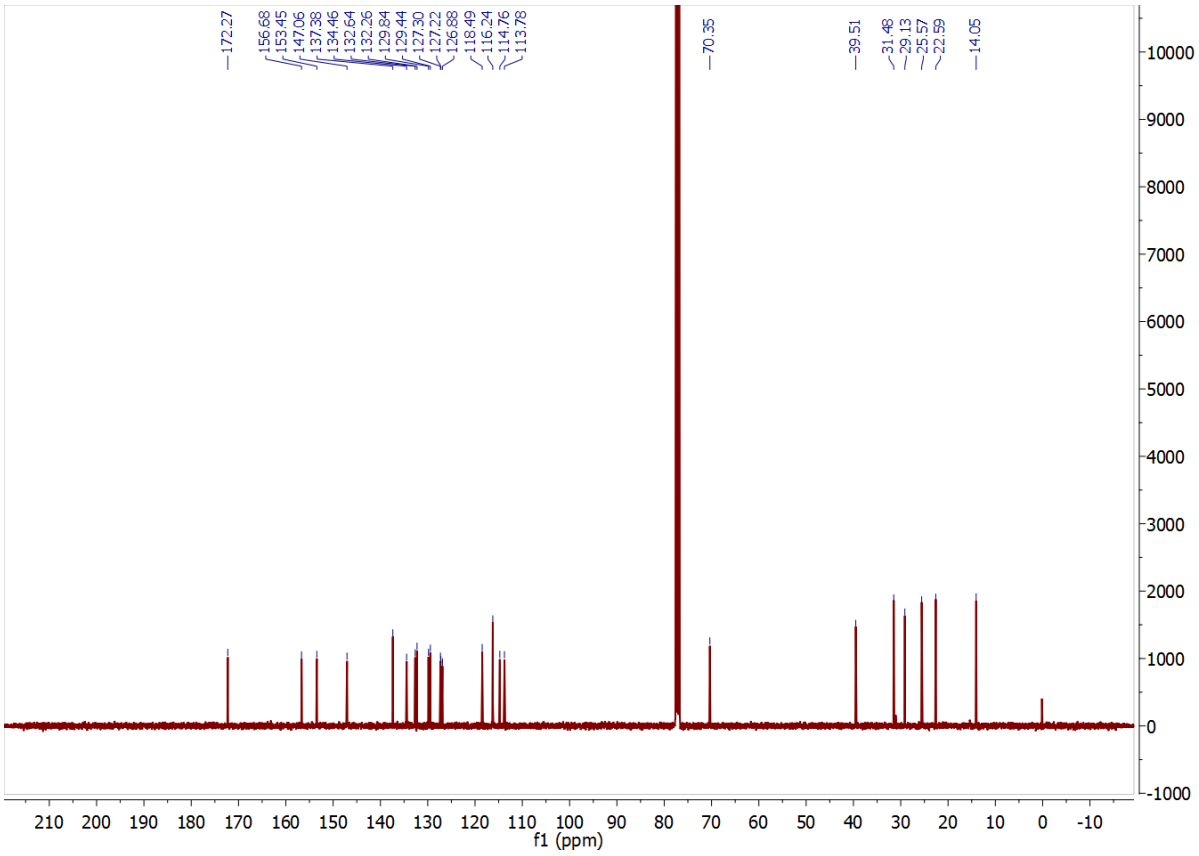


Figure S39. 1H NMR spectrum of 4-bromo-2-chloro-1-(methoxymethoxy)benzene

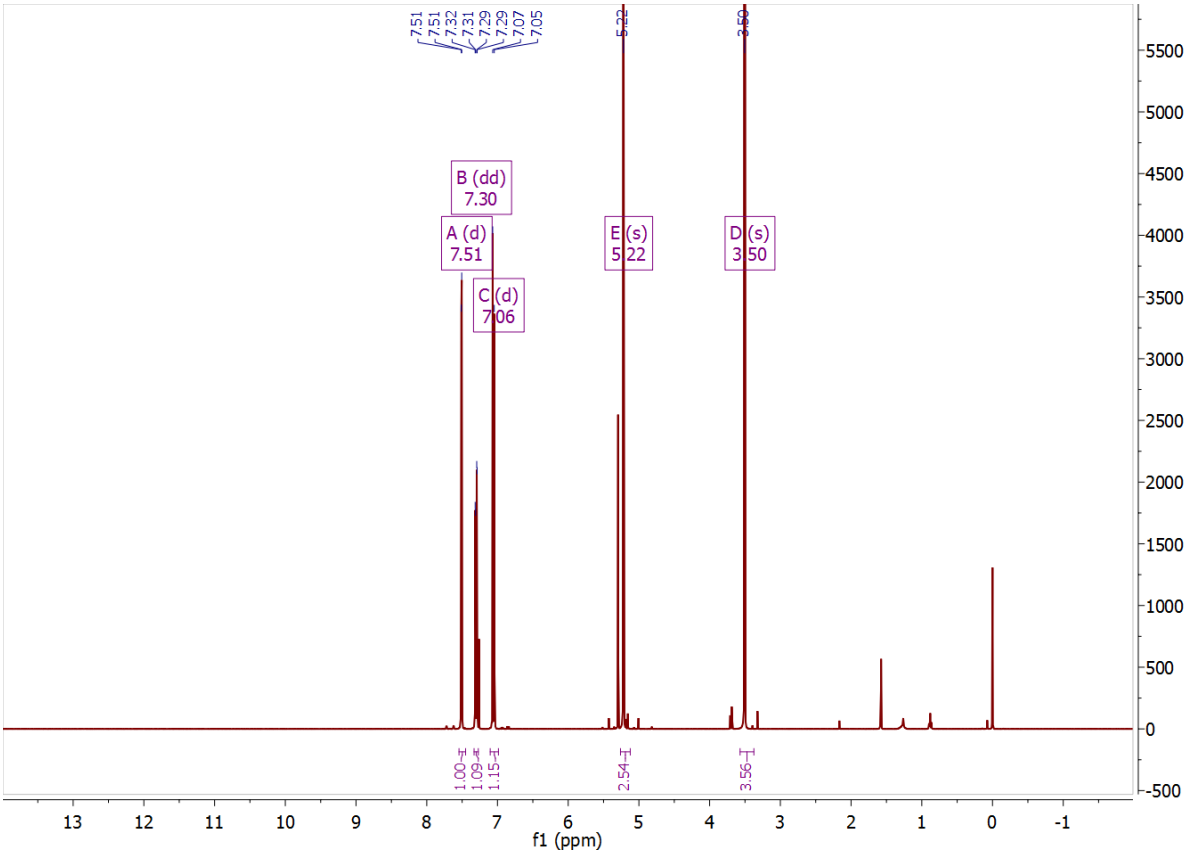


Figure S40. 13C NMR spectrum of 4-bromo-2-chloro-1-(methoxymethoxy)benzene

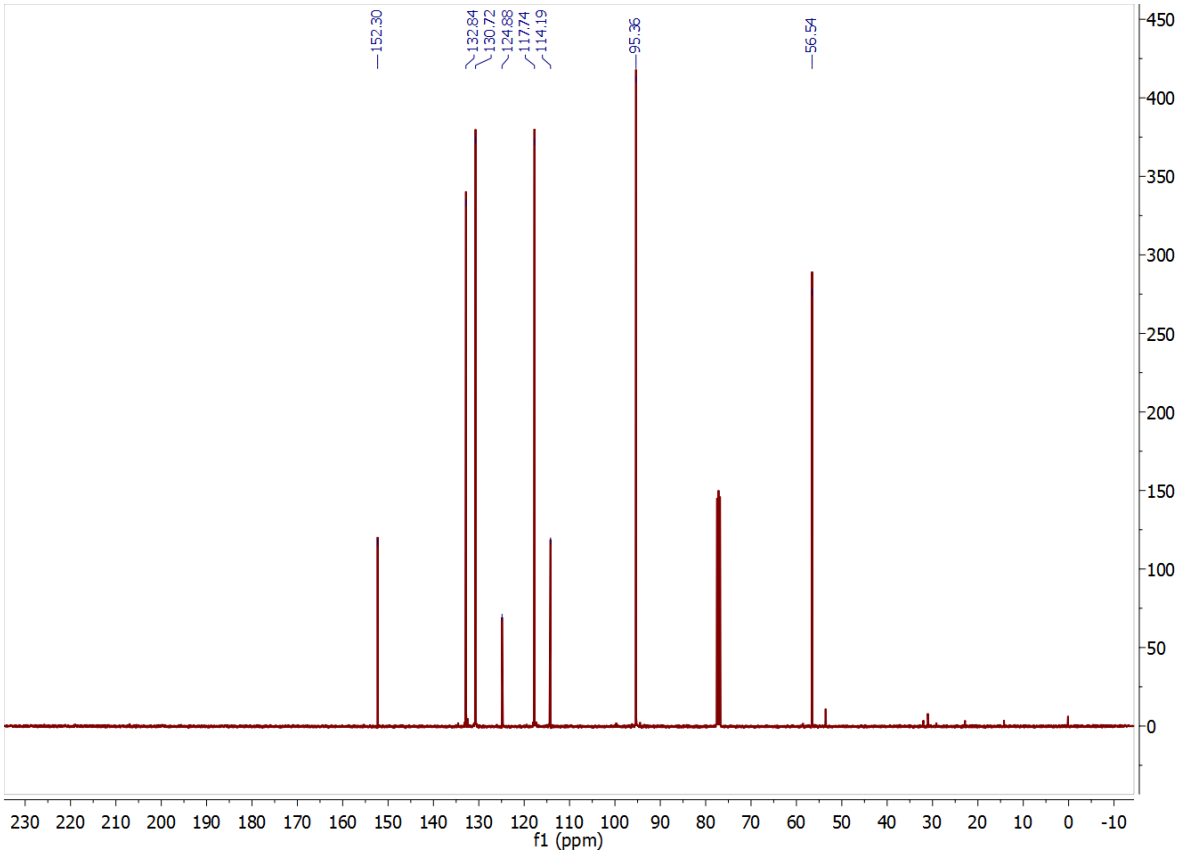


Figure S41. 1H NMR spectrum of *(E)*-methyl 3-(3-chloro-4-(methoxymethoxy)phenyl)acrylate (17)

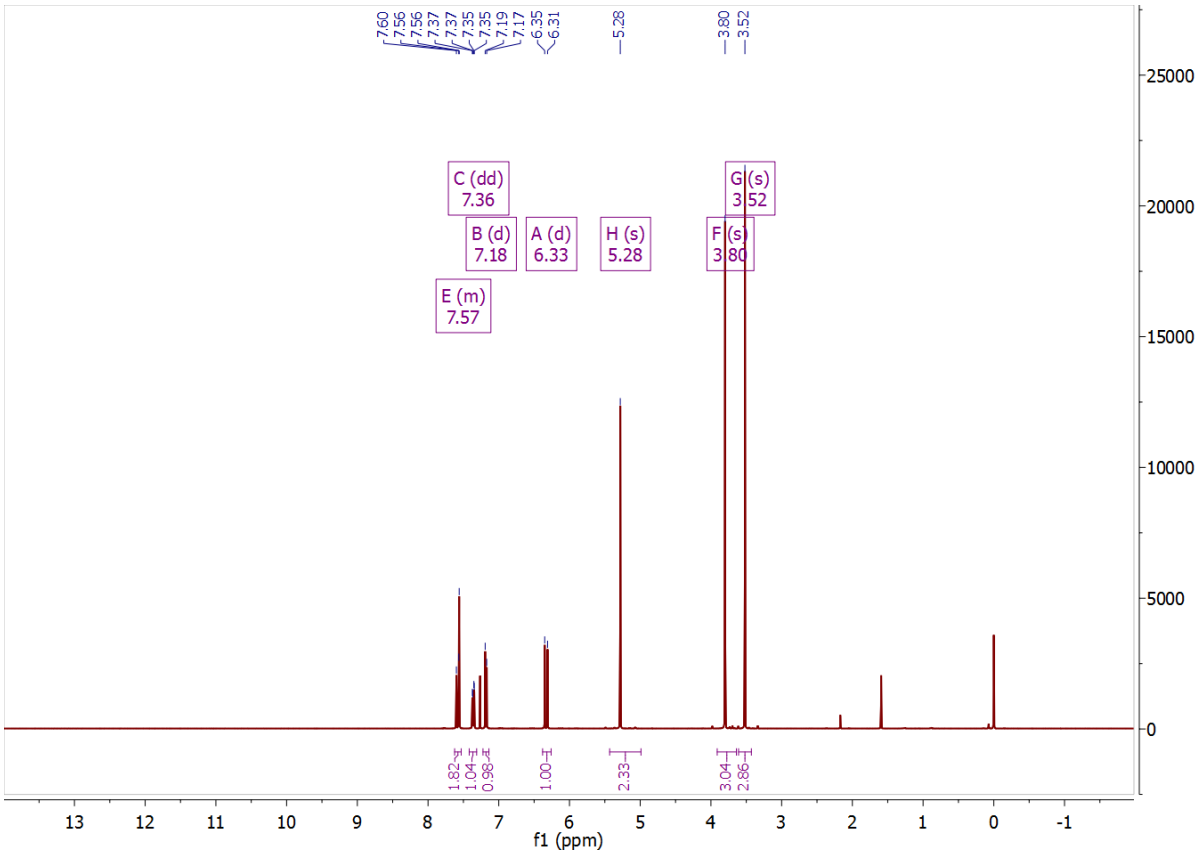


Figure S42. 13C NMR spectrum of *(E)*-methyl 3-(3-chloro-4-(methoxymethoxy)phenyl)acrylate (17)

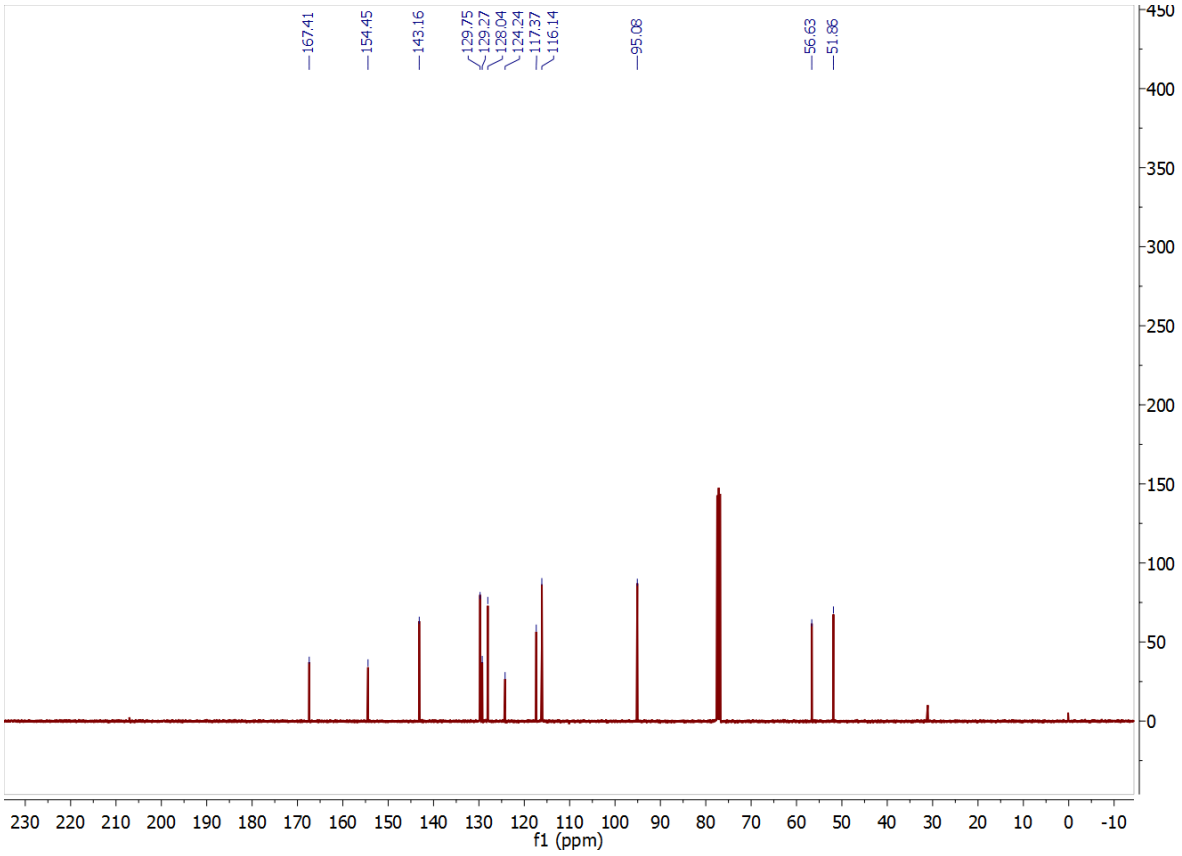


Figure S43. 1H NMR spectrum of *(E)*-methyl 3-(4-(methoxymethoxy)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)acrylate (18)

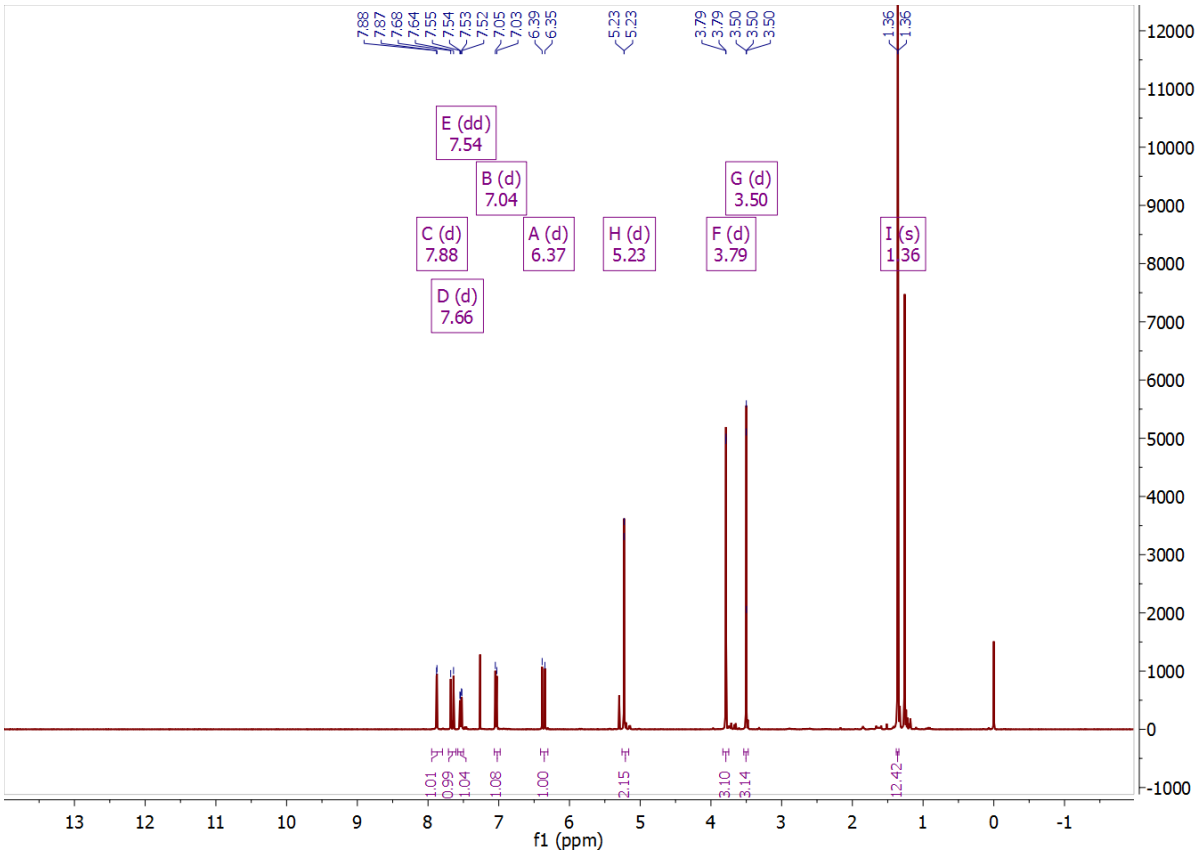


Figure S44. 13C NMR spectrum of *(E)*-methyl 3-(4-(methoxymethoxy)-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)phenyl)acrylate (18)

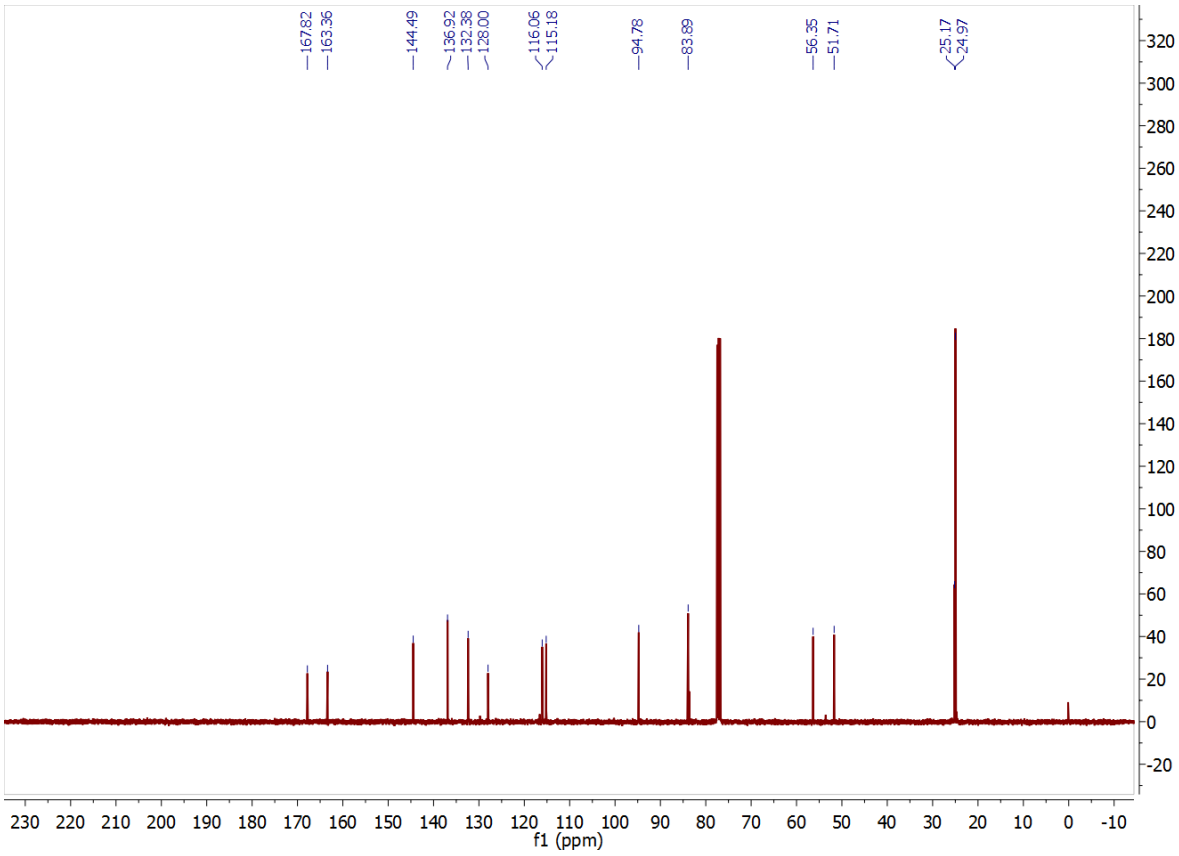


Figure S45. 1H NMR spectrum of 4-bromo-2-chloro-1-propoxybenzene

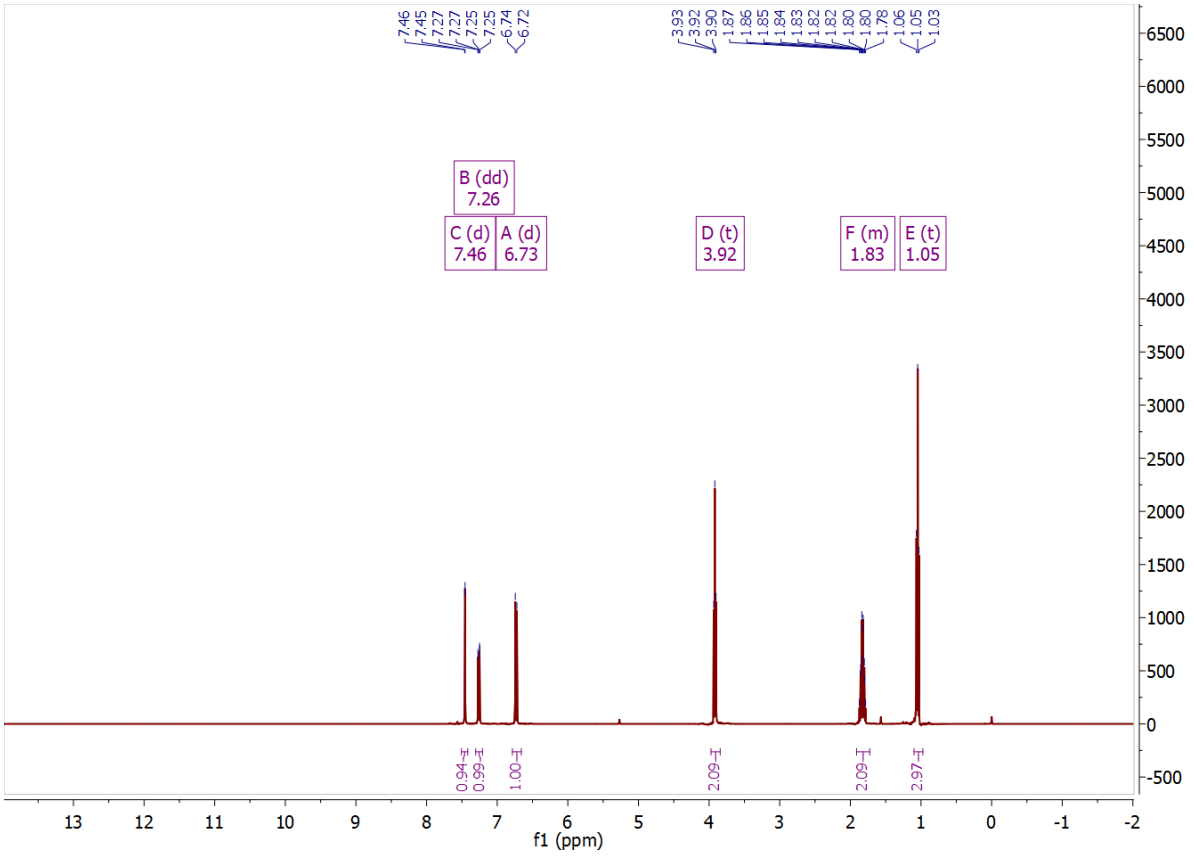


Figure S46. 13C NMR spectrum of 4-bromo-2-chloro-1-propoxybenzene

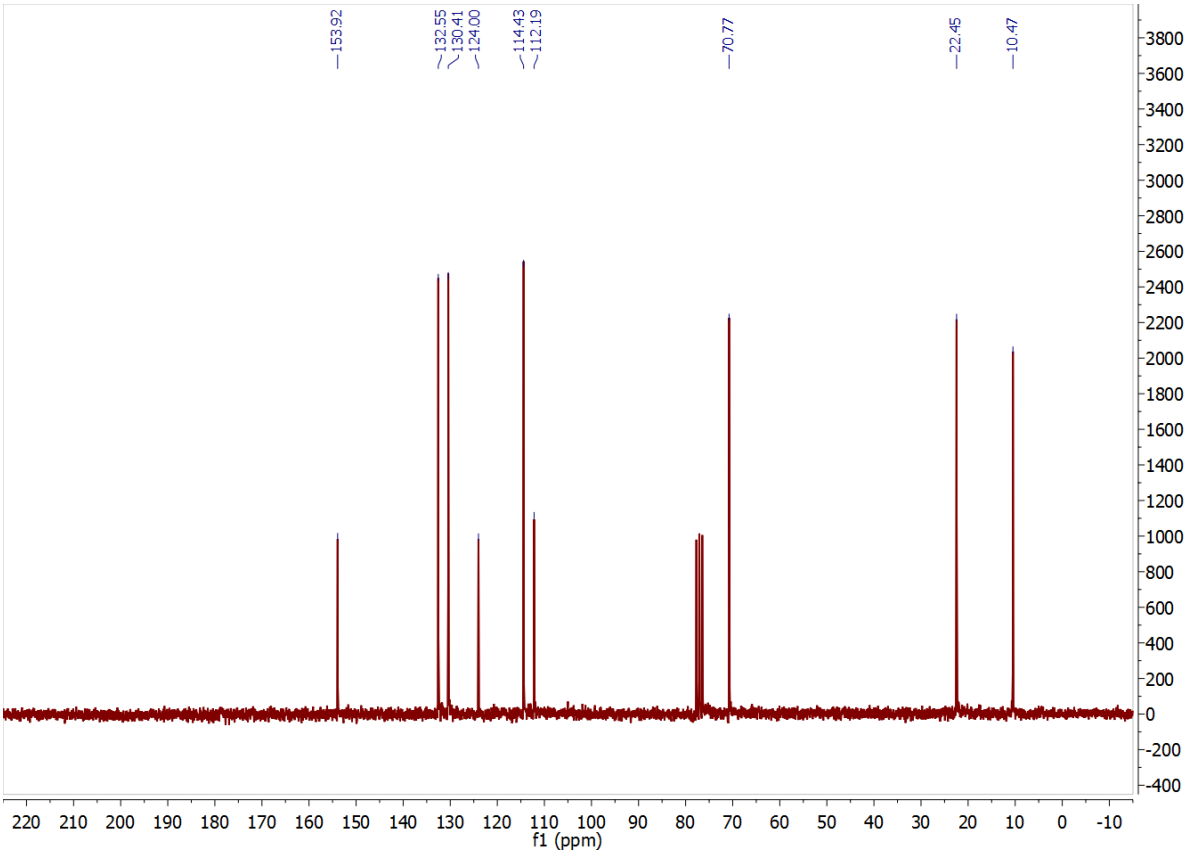


Figure S47. 1H NMR spectrum of 4-allyl-2-chloro-1-propoxybenzene (23)

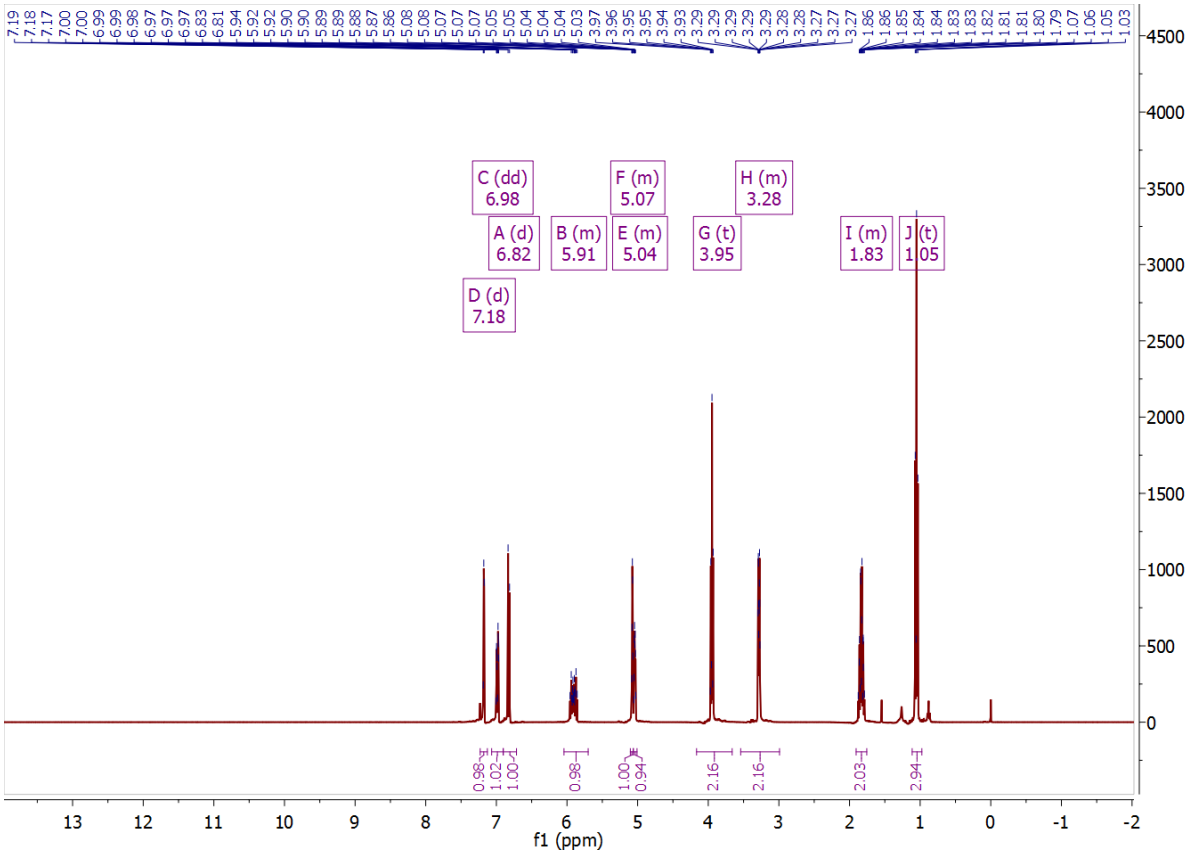


Figure S48. 13C NMR spectrum of 4-allyl-2-chloro-1-propoxybenzene (23)

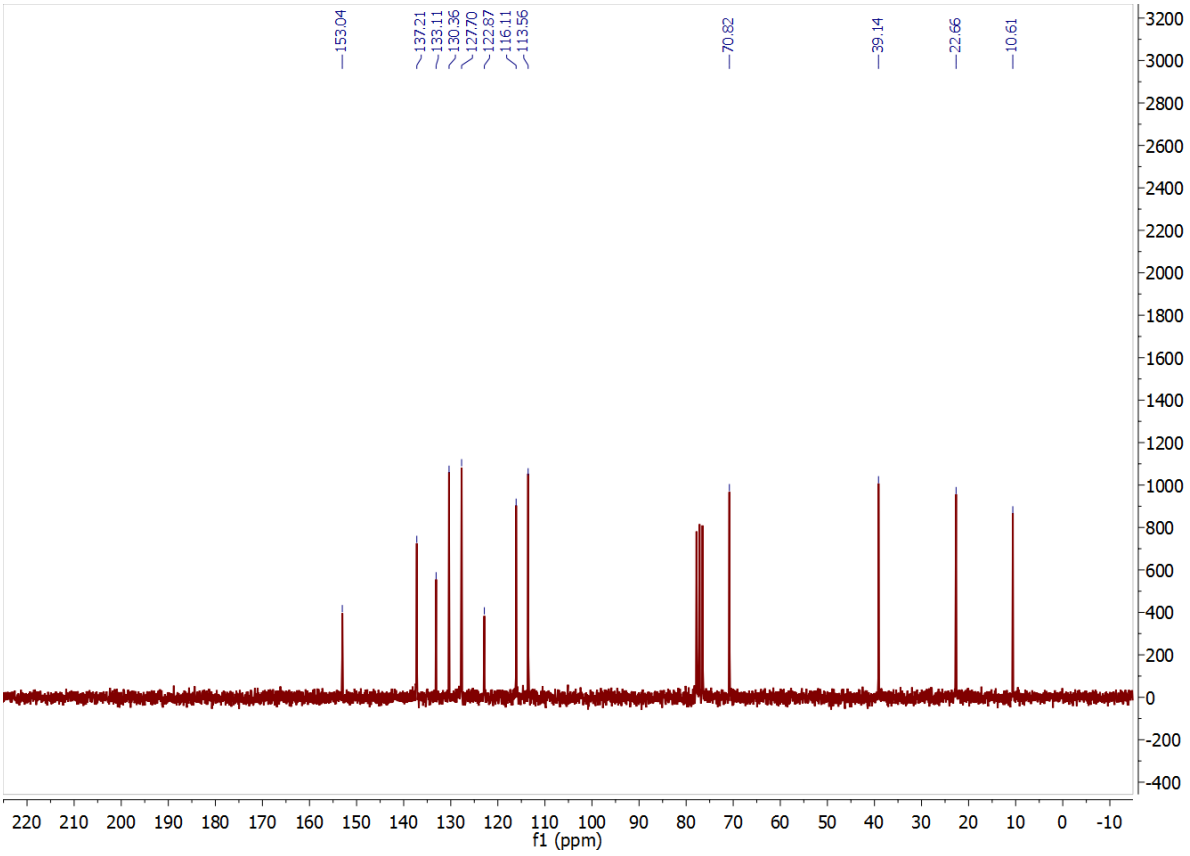


Figure S49. 1H NMR spectrum of 4-bromo-2-chloro-1-(hexyloxy)benzene

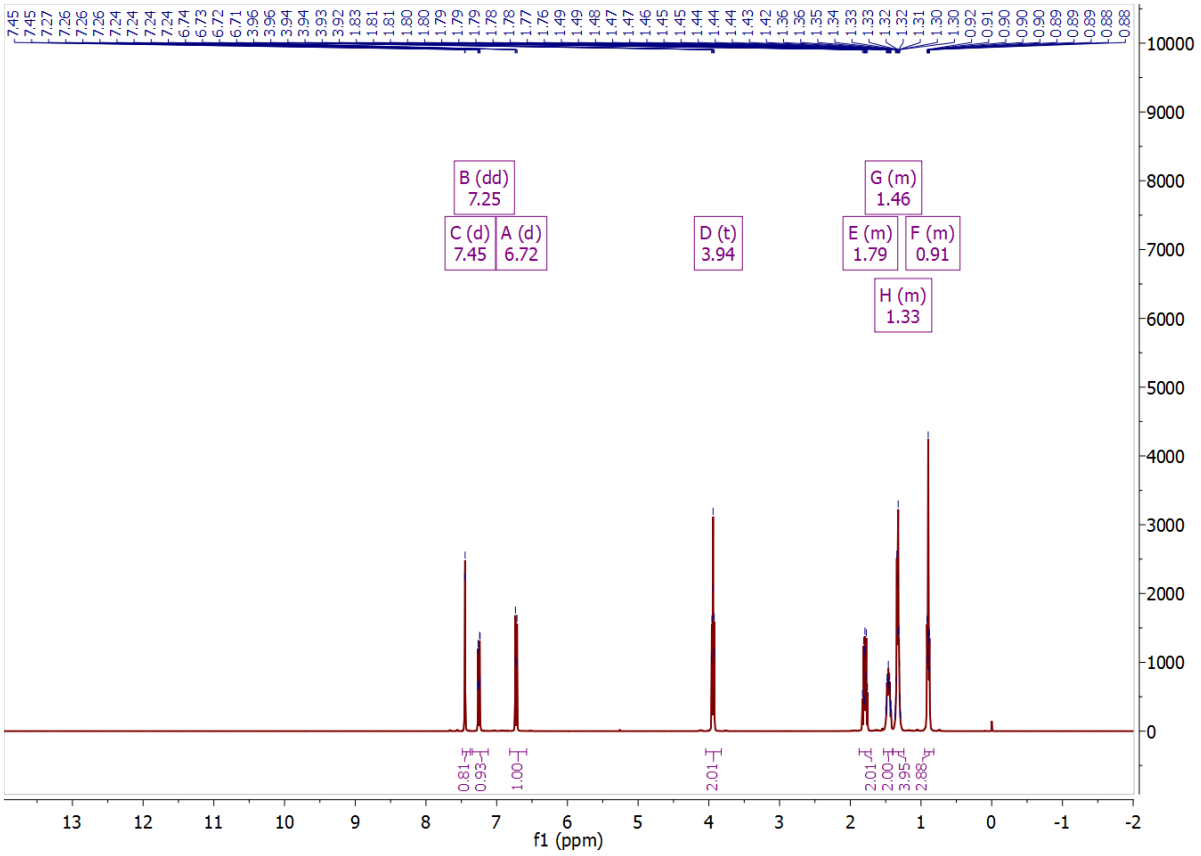


Figure S50. 13C NMR spectrum of 4-bromo-2-chloro-1-(hexyloxy)benzene

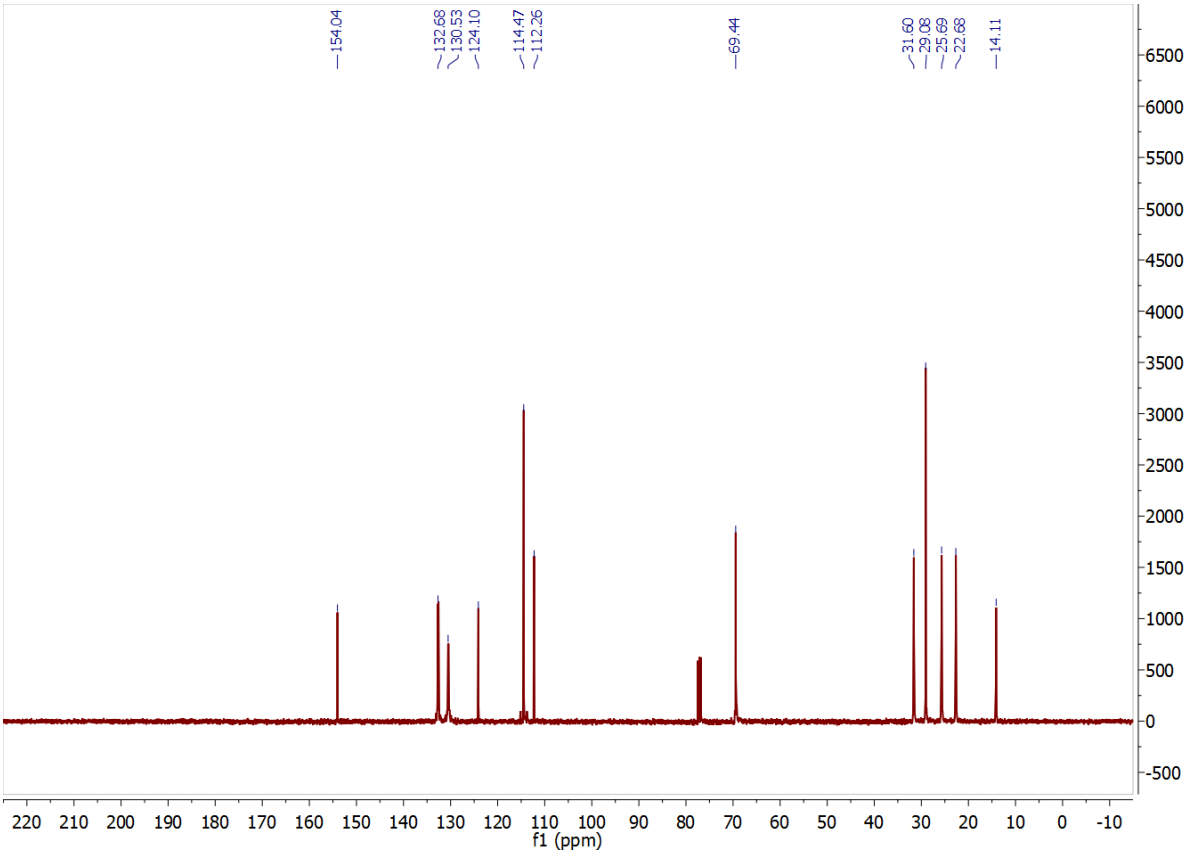


Figure S51. 1H NMR spectrum of 4-allyl-2-chloro-1-(hexyloxy)benzene (24)

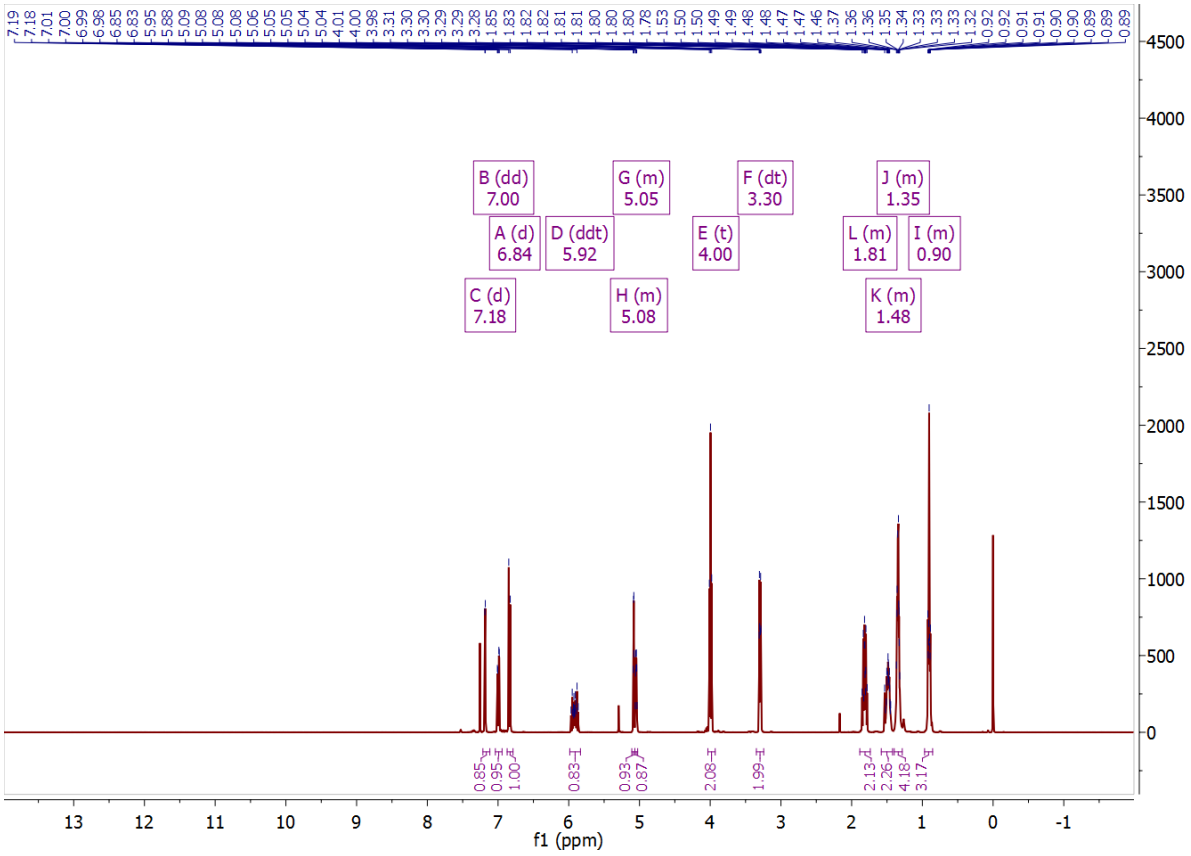


Figure S52. 13C NMR spectrum of 4-allyl-2-chloro-1-(hexyloxy)benzene (24)

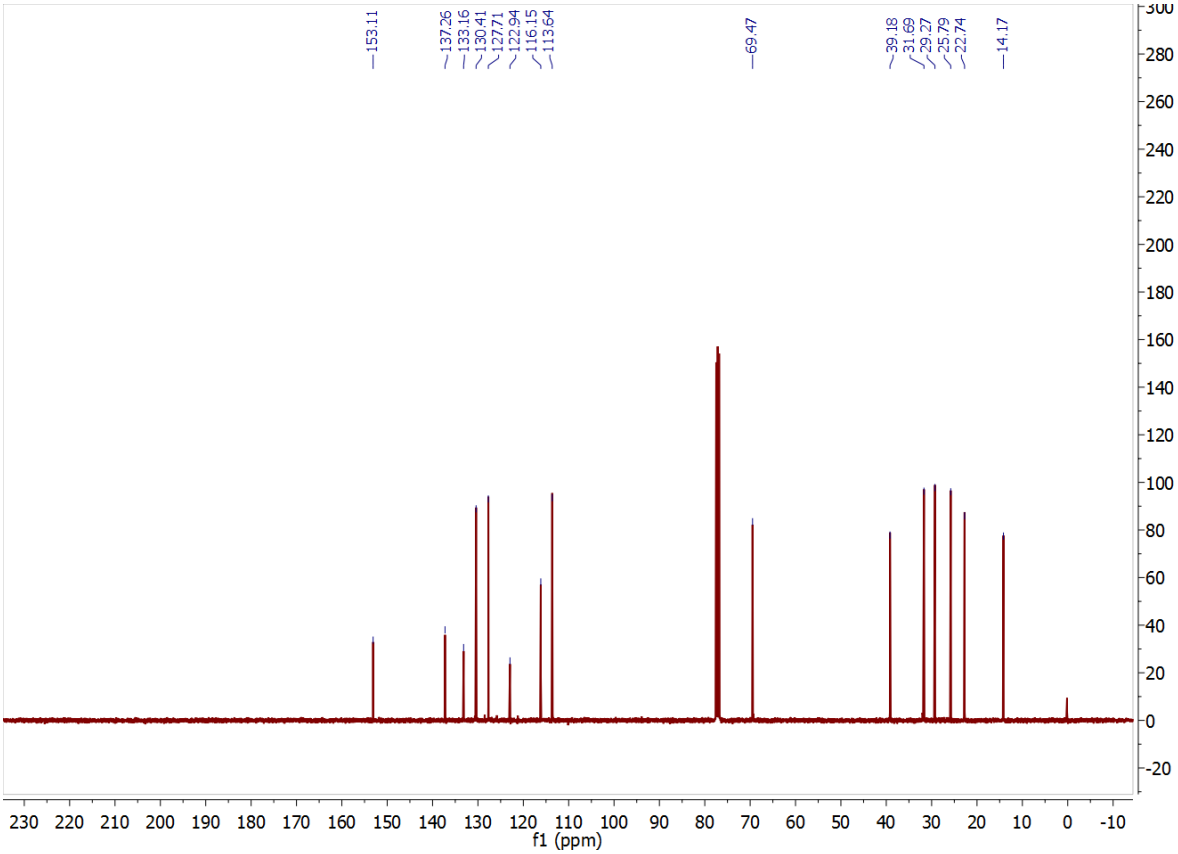


Figure S53. LC-MS data for *(E)*-3-(6-hydroxy-[1,1':3',1''-terphenyl]-3-yl)acrylic acid (2)

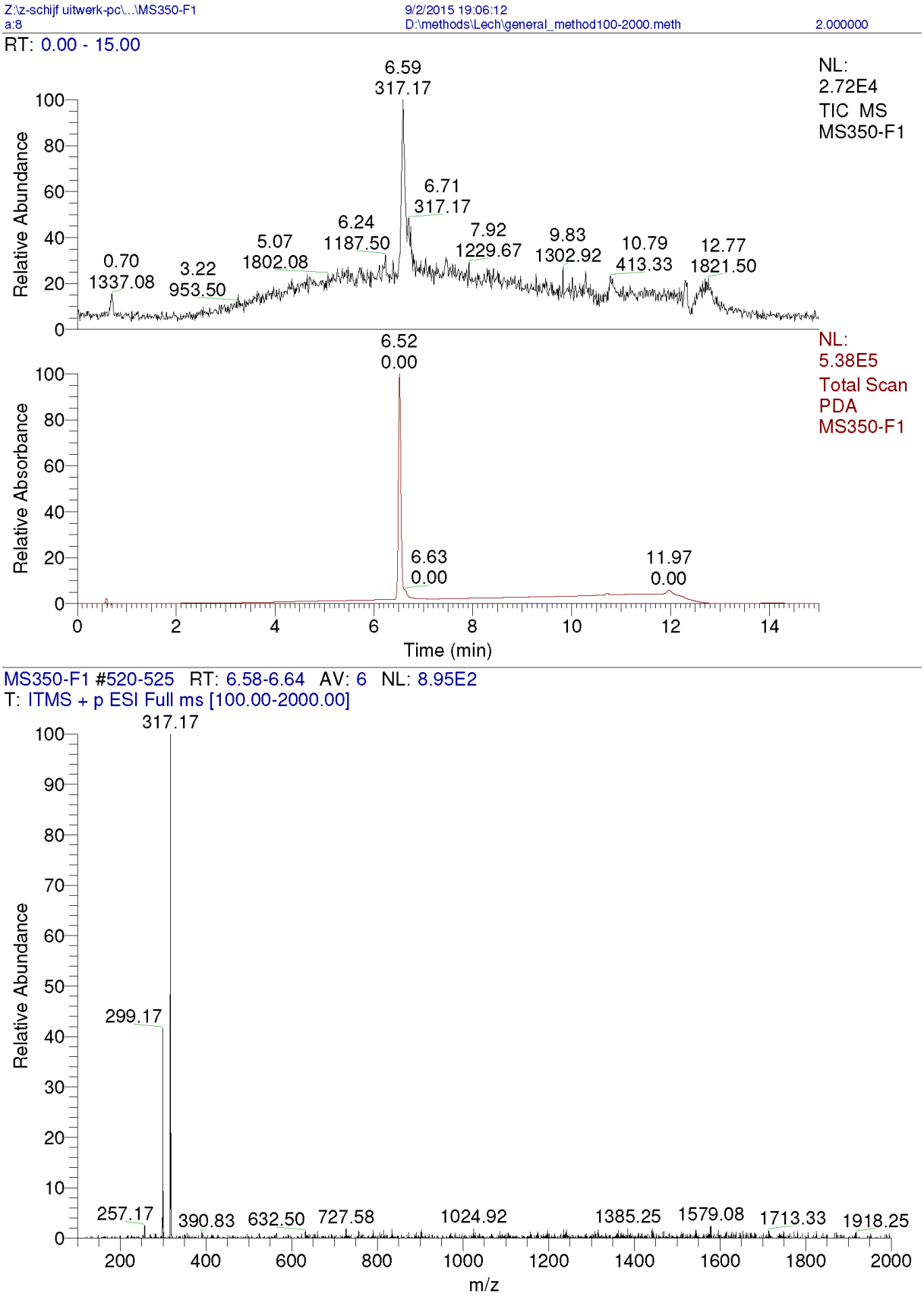


Figure S54. LC-MS data for *(E)*-3-(3'-benzyl-6-hydroxy-[1,1'-biphenyl]-3-yl)acrylic acid (3)

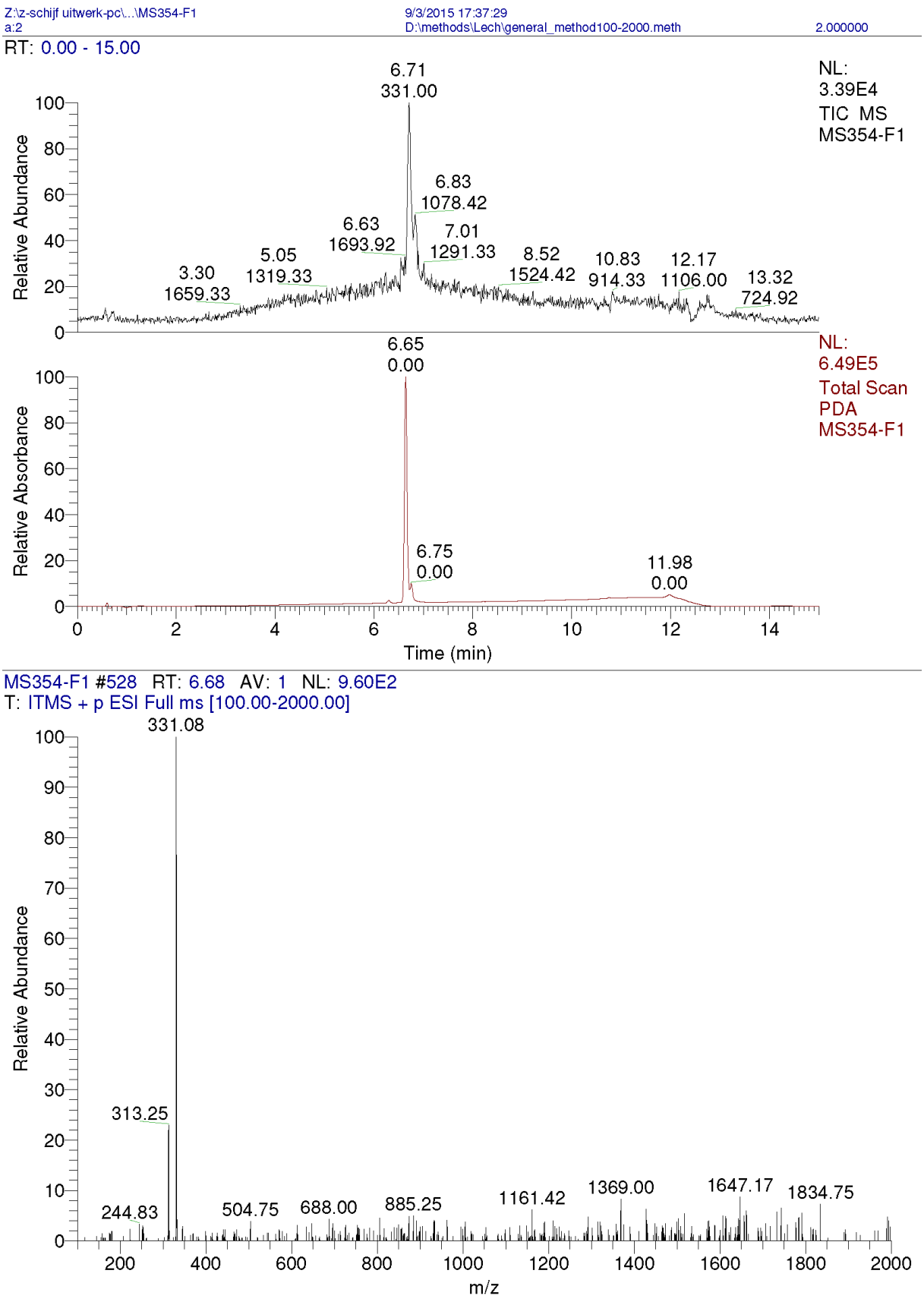


Figure S55. LC-MS data for *(E)*-3-(6-hydroxy-3'-isopropyl-[1,1'-biphenyl]-3-yl)acrylic acid (4)

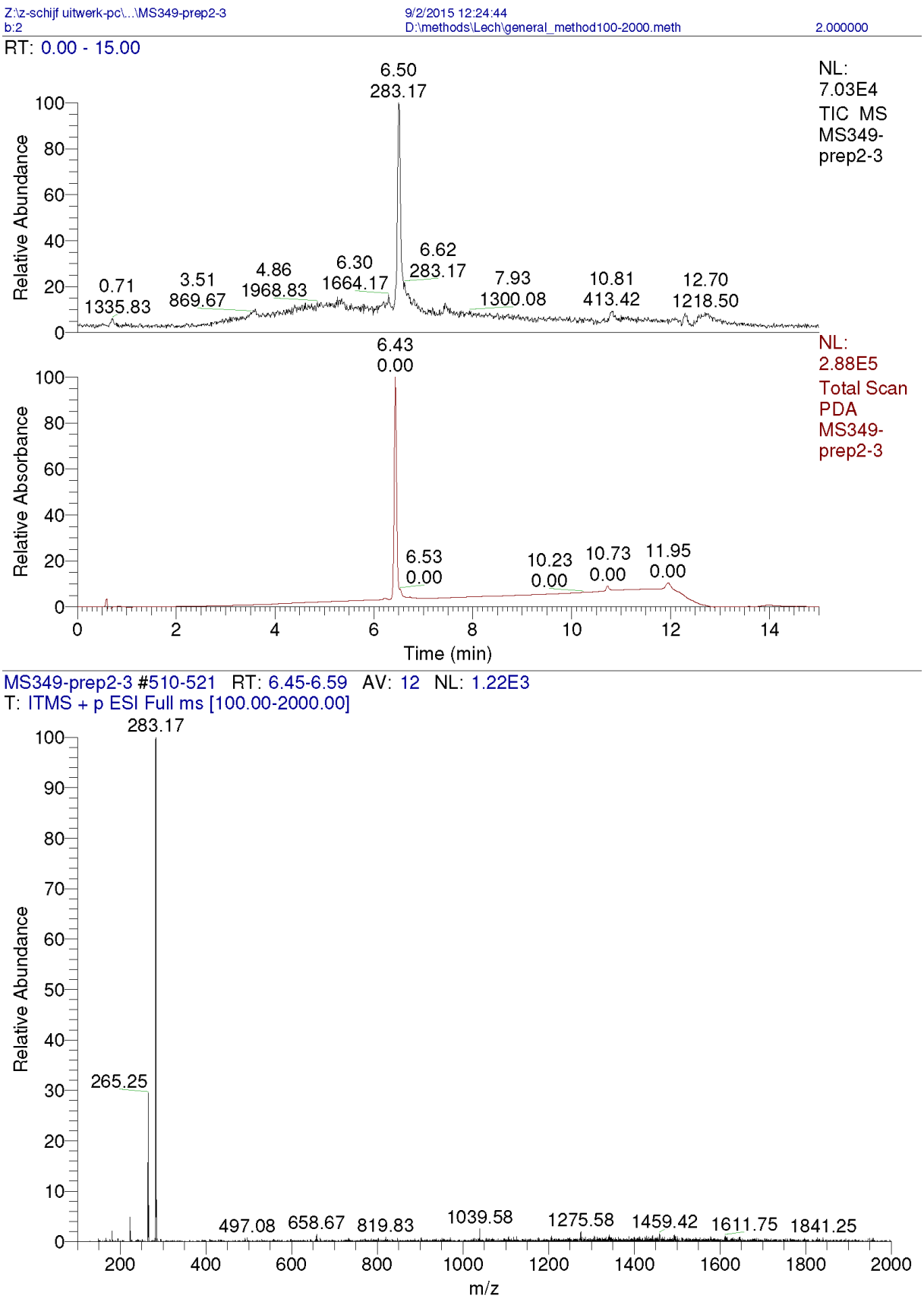


Figure S56. LC-MS data for *(E)*-3-(6-hydroxy-2'-methyl-[1,1':3',1''-terphenyl]-3-yl)acrylic acid (6)

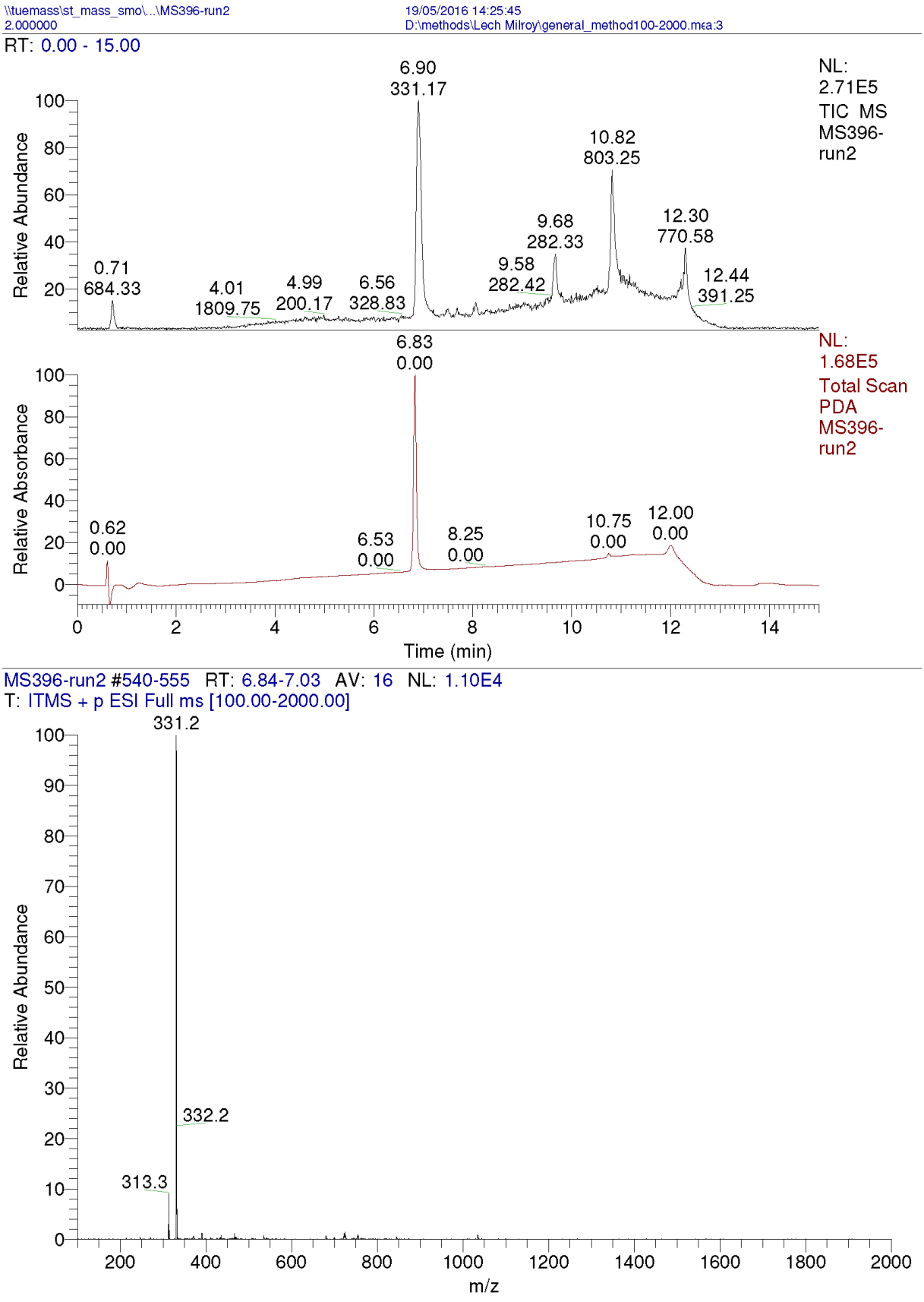


Figure S57. LC-MS data for *(E)*-3-(6-hydroxy-6'-methyl-[1,1':3',1''-terphenyl]-3-yl)acrylic acid (7)

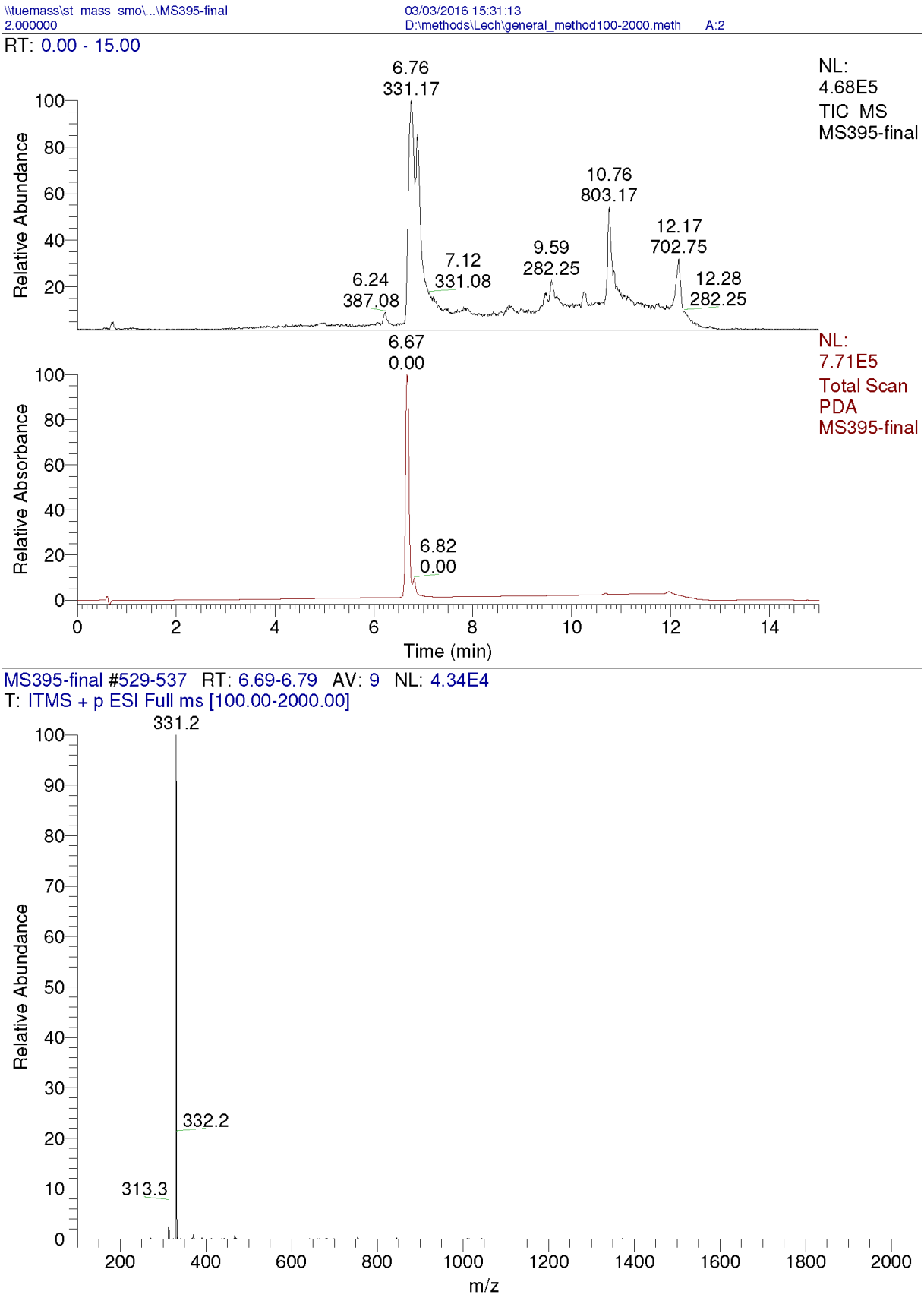


Figure S58. LC-MS data for *(E)*-3-(5'-allyl-6-hydroxy-2'-propoxy-[1,1'-biphenyl]-3-yl)acrylic acid (9)

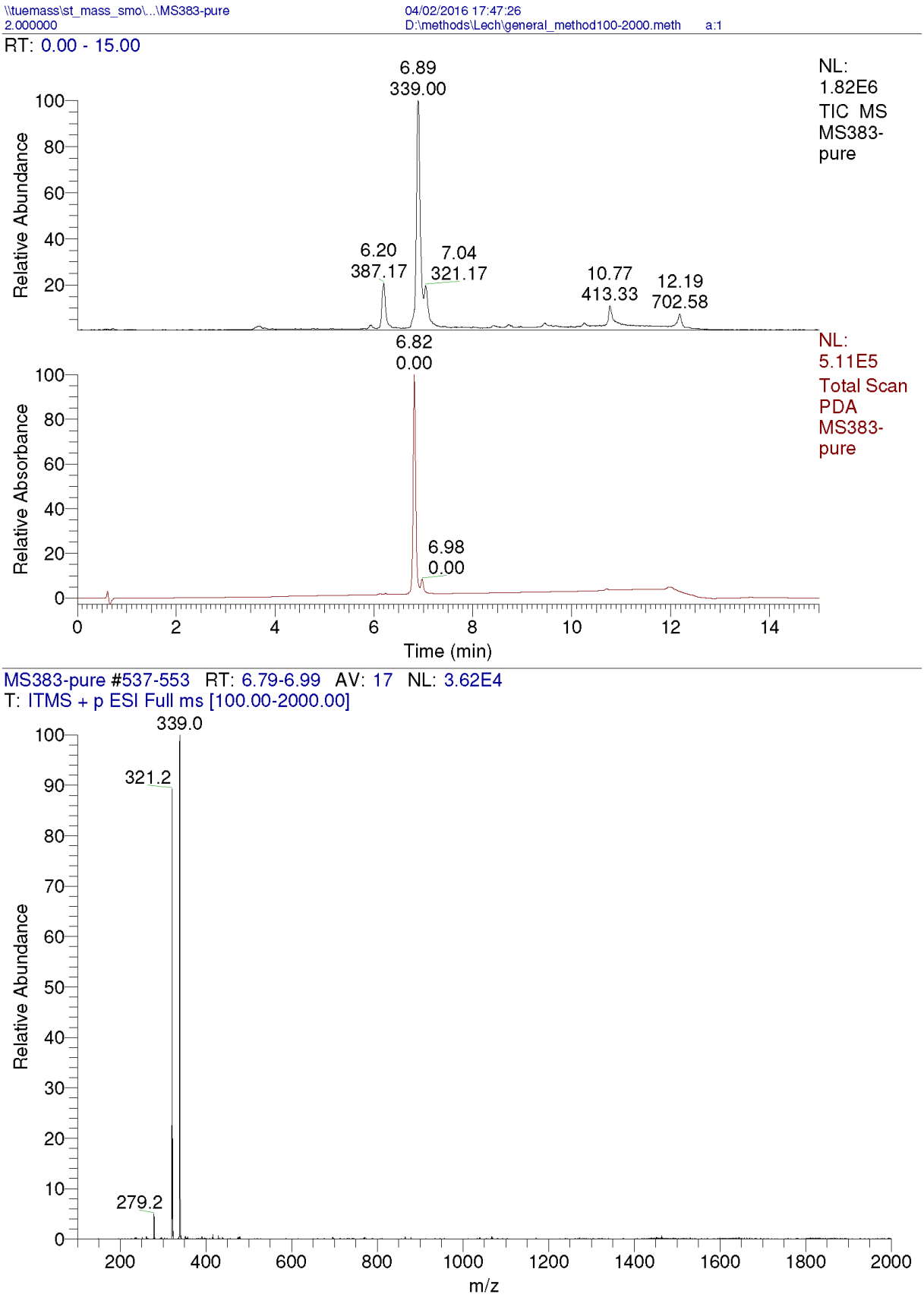
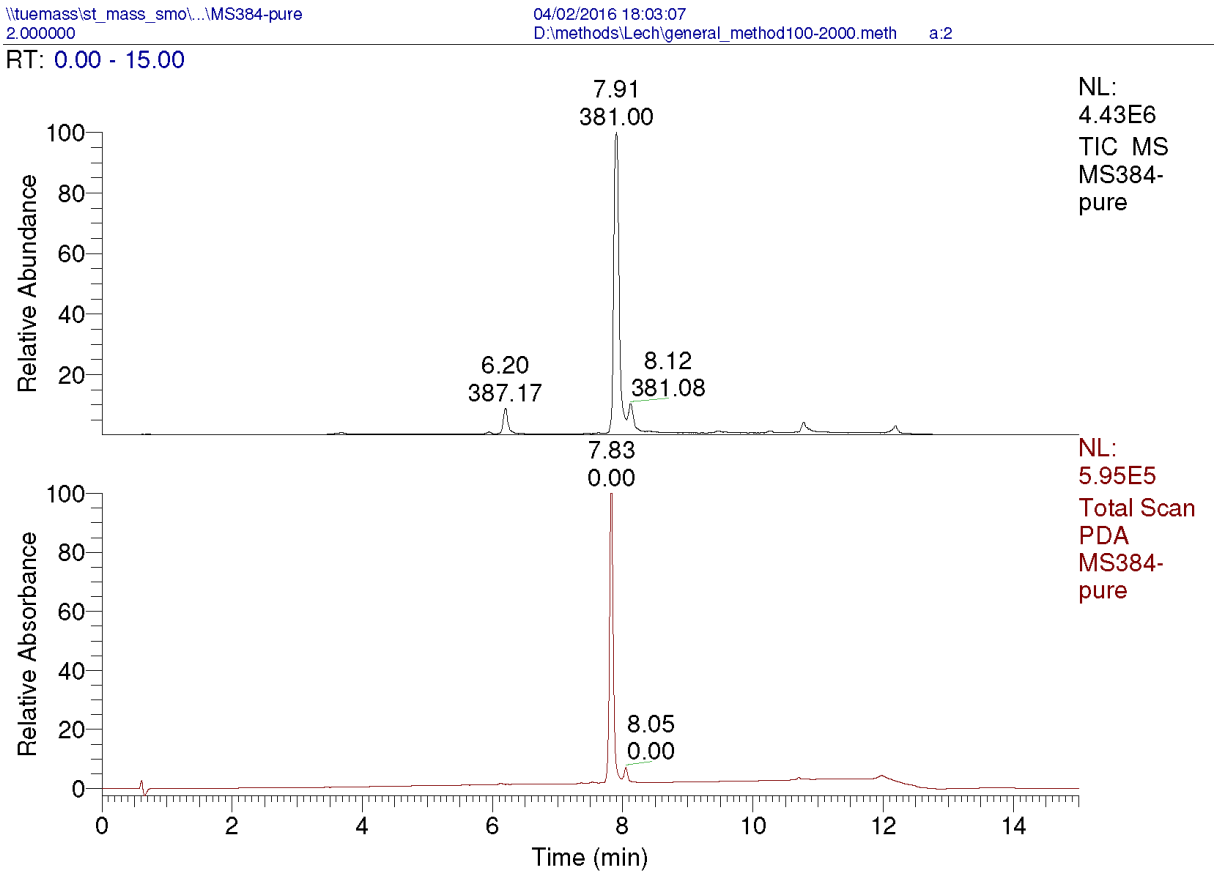


Figure S59. LC-MS data for *(E)*-3-(5'-allyl-2'-(hexyloxy)-6-hydroxy-[1,1'-biphenyl]-3-yl)acrylic acid (10)



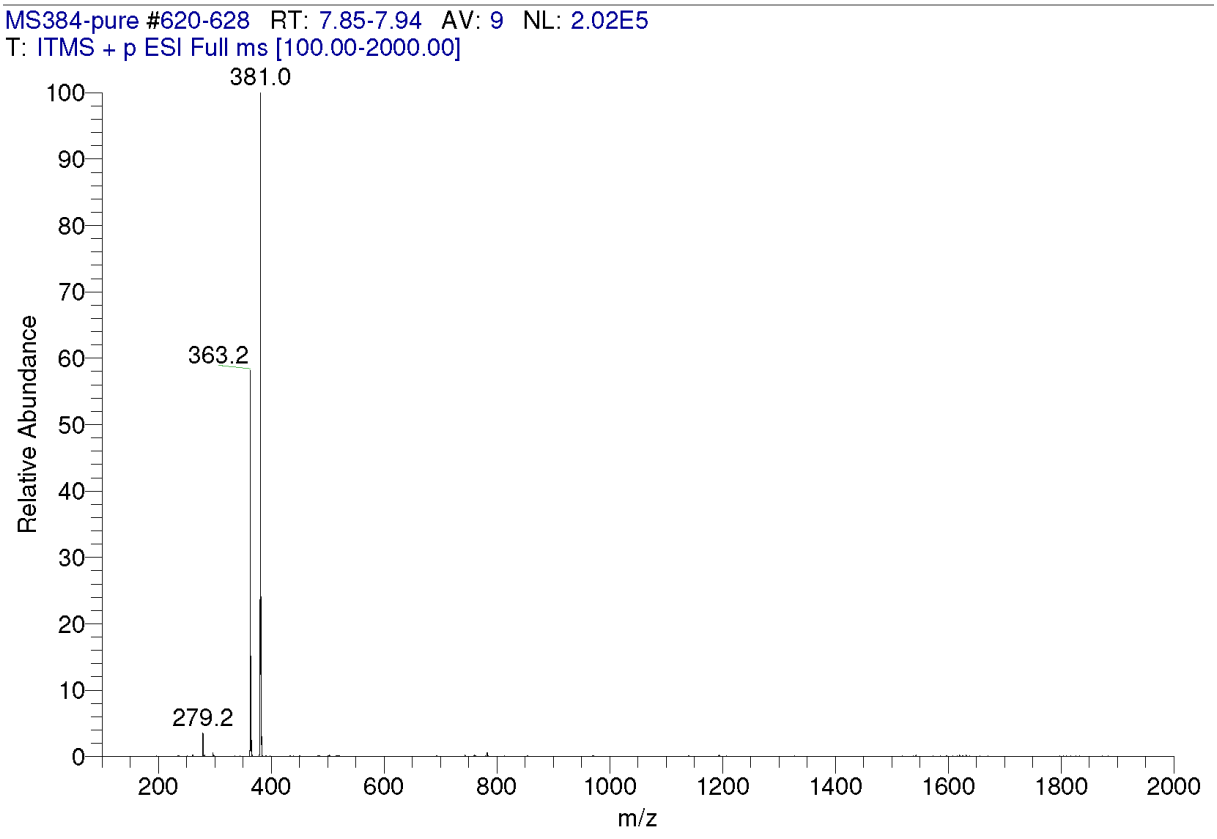
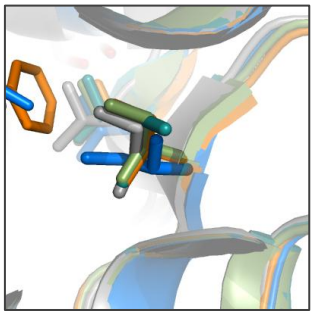


Figure S60. Overview of key side-chains displacements (in Å) in the helices 5-7 region of the ligand binding domain for ligands 1, 3, 4, 6, and 7.

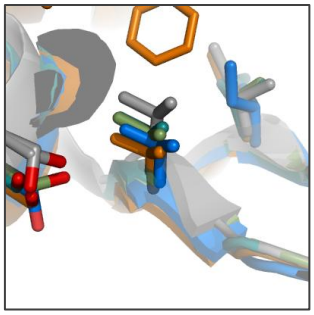
Ile 324

cpd	1	3	4	6	7
1	x	0.4	0.6	0.6	0.5
3	0.4	x	0.3	0.2	0.1
4	0.6	0.3	x	0.3	0.3
6	0.6	0.2	0.3	x	0.1
7	0.5	0.1	0.3	0.1	x



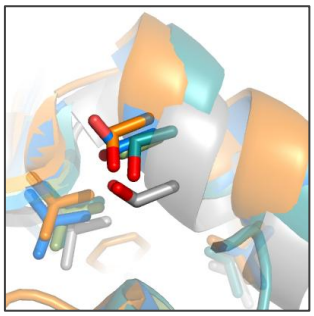
Val 332

cpd	1	3	4	6	7
1	x	0.7	1.2	0.7	0.8
3	0.7	x	1.6	0.7	0.7
4	1.2	1.6	x	1.0	1.0
6	0.7	0.7	1.0	x	0.1
7	0.8	0.7	1.0	0.1	x



Ser 336

cpd	1	3	4	6	7
1	x	0.7	2.2	0.3	0.7
3	0.7	x	2.8	0.8	1.1
4	2.2	2.8	x	2.0	2.2
6	0.3	0.8	2.0	x	0.6
7	0.7	1.1	2.2	0.6	x



Val 342

cpd	1	3	4	6	7
1	x	0.6	1.4	0.3	0.8
3	0.6	x	1.7	0.7	0.8
4	1.4	1.7	x	1.2	0.9
6	0.3	0.7	1.2	x	0.8
7	0.8	0.8	0.9	0.8	x

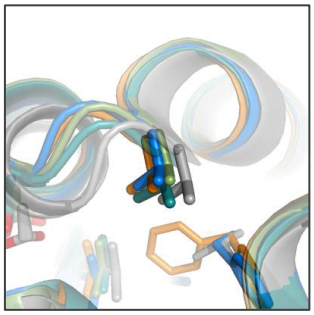


Figure S61. Overlay of the X-ray co-crystal structures of ligands 4 (grey) and 6 (green) bound to RXRα as zoom-in on the ligand binding pocket of RXRα.

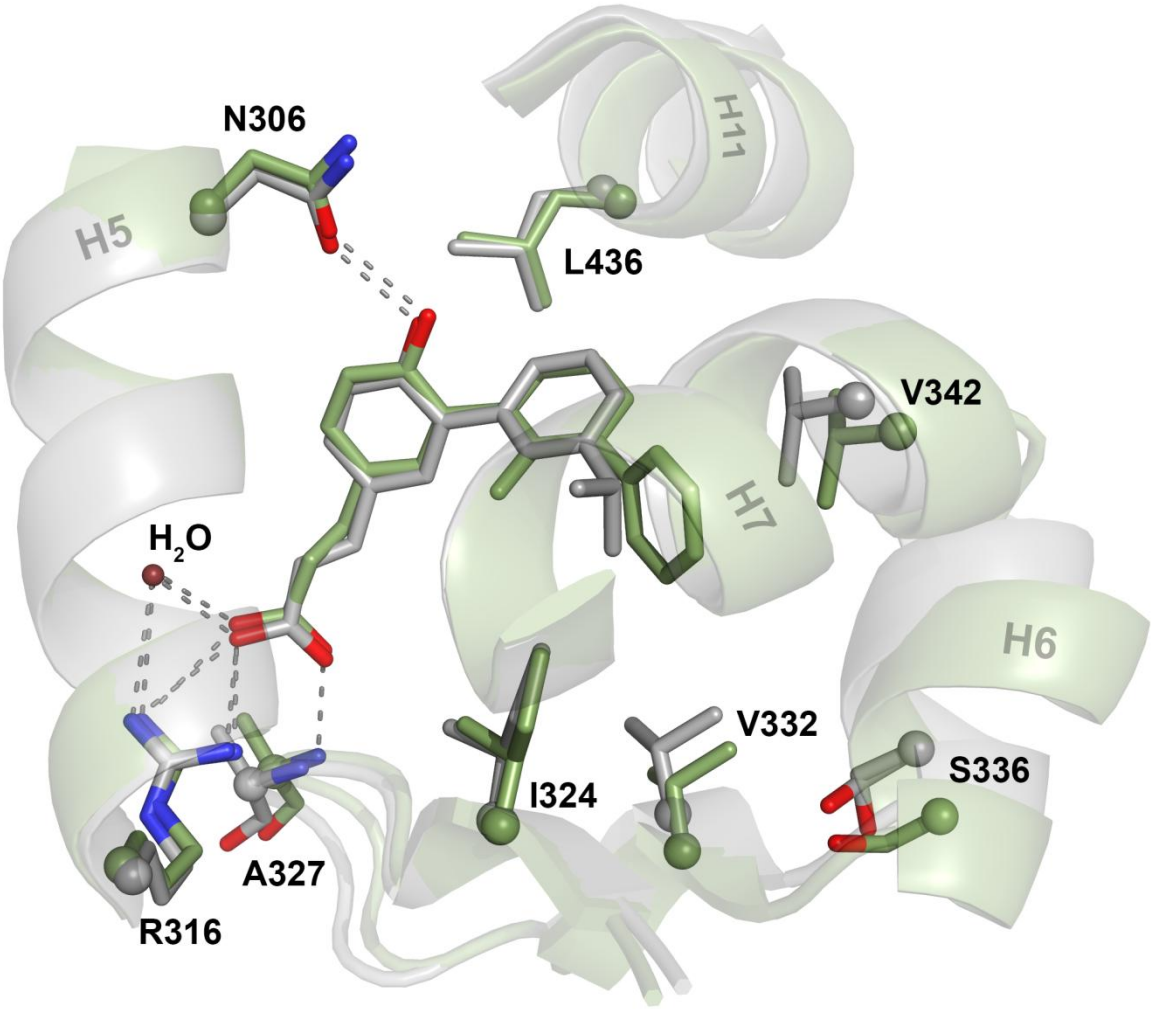


Figure S62. Overlay of the X-ray co-crystal structures of ligands 4 (grey) and 7 (blue) bound to RXRα as zoom-in on the ligand binding pocket of RXRα.