

Synthesis and antibiofilm activity of 1,2,3-triazole-pyridine hybrids against methicillin-resistant *Staphylococcus aureus* (MRSA)

Tamer El Malah,^{a*} Hanan A. Soliman,^a Bahaa A. Hemdan,^b Randa E. Abdel Mageid,^a and Hany F. Nour^{a*}

^aPhotochemistry Department, Chemical Industries Research Division, National Research Centre, 33 El Buhouth Street, P.O. Box 12622, Cairo, Egypt.

^bWater Pollution Research Department, Environmental Research Division, National Research Centre, 33 El Buhouth Street, P.O. Box 12622 Cairo, Egypt.

*Corresponding authors: tmara_nrc3000@yahoo.com (Tamer El Malah), hany.nour@daad-alumni.de (Hany F. Nour).

Supporting Information

Figure S1. ^1H NMR spectrum of compound 3 (400 MHz, CDCl_3 , 25 °C).....	4
Figure S2. ^{13}C NMR spectrum of of compound 3 (100 MHz, CDCl_3 , 25 °C).....	4
Figure S3. ^1H NMR spectrum of compound 4 (400 MHz, CDCl_3 , 25 °C).....	5
Figure S4. ^{13}C NMR spectrum of of compound 4 (100 MHz, CDCl_3 , 25 °C).....	5
Figure S5. ^1H NMR spectrum of compound 11 (400 MHz, CDCl_3 , 25 °C).....	6
Figure S6. ^{13}C NMR spectrum of of compound 11 (100 MHz, CDCl_3 , 25 °C).....	6
Figure S7. ^1H NMR spectrum of compound 12 (400 MHz, CDCl_3 , 25 °C).....	7
Figure S8. ^{13}C NMR spectrum of of compound 12 (100 MHz, CDCl_3 , 25 °C).....	7
Figure S9. ^1H NMR spectrum of compound 13 (400 MHz, CDCl_3 , 25 °C).....	8
Figure S10. ^{13}C NMR spectrum of of compound 13 (100 MHz, CDCl_3 , 25 °C).....	8
Figure S11. ^1H NMR spectrum of compound 14 (400 MHz, CDCl_3 , 25 °C).....	9
Figure S12. ^{13}C NMR spectrum of of compound 14 (100 MHz, CDCl_3 , 25 °C).....	9
Figure S13. ^1H NMR spectrum of compound 15 (400 MHz, CDCl_3 , 25 °C).....	10
Figure S14. ^{13}C NMR spectrum of of compound 15 (100 MHz, CDCl_3 , 25 °C).....	10
Figure S15. ^1H NMR spectrum of compound 16 (400 MHz, CDCl_3 , 25 °C).....	11
Figure S16. ^{13}C NMR spectrum of of compound 16 (100 MHz, CDCl_3 , 25 °C).....	11
Figure S17. ^1H NMR spectrum of compound 17 (400 MHz, CDCl_3 , 25 °C).....	12
Figure S18. ^{13}C NMR spectrum of of compound 17 (100 MHz, CDCl_3 , 25 °C).....	12
Figure S19. ^1H NMR spectrum of compound 18 (400 MHz, CDCl_3 , 25 °C).....	13
Figure S20. ^{13}C NMR spectrum of of compound 18 (100 MHz, CDCl_3 , 25 °C).....	13
Figure S21. ^1H NMR spectrum of compound 19 (400 MHz, CDCl_3 , 25 °C).....	14
Figure S22. ^{13}C NMR spectrum of of compound 19 (100 MHz, CDCl_3 , 25 °C).....	14
Figure S23. ^1H NMR spectrum of compound 20 (400 MHz, CDCl_3 , 25 °C).....	15
Figure S24. ^{13}C NMR spectrum of of compound 20 (100 MHz, CDCl_3 , 25 °C).....	15
Figure S25. ^1H NMR spectrum of compound 21 (400 MHz, CDCl_3 , 25 °C).....	16
Figure S26. ^{13}C NMR spectrum of of compound 21 (100 MHz, CDCl_3 , 25 °C).....	16
Figure S27. ^1H NMR spectrum of compound 22 (400 MHz, CDCl_3 , 25 °C).....	17
Figure S28. ^{13}C NMR spectrum of of compound 22 (100 MHz, CDCl_3 , 25 °C).....	17
Figure S29. 2D NOESY spectrum of compound 4 (400 MHz, CDCl_3 , 25 °C).....	18

Figure S30. 2D COSY spectrum of compound 4 (400 MHz, CDCl ₃ , 25 °C).....	18
Figure S31. 2D HSQC spectrum of compound 4 (400 MHz, CDCl ₃ , 25 °C).....	19
Figure S32. 2D HMBC spectrum of compound 4 (400 MHz, CDCl ₃ , 25 °C).....	19
Figure S33. 2D COSY spectrum of compound 19 (400 MHz, CDCl ₃ , 25 °C).....	20
Figure S34. 2D HSQC spectrum of compound 19 (400 MHz, CDCl ₃ , 25 °C).....	20
Figure S35. 2D HMBC spectrum of compound 19 (400 MHz, CDCl ₃ , 25 °C).....	21
Figure S36. FT-IR spectrum of compound 3	21
Figure S37. FT-IR spectrum of compound 4	22
Figure S38. FT-IR spectrum of compound 11	22
Figure S39. FT-IR spectrum of compound 12	23
Figure S40. FT-IR spectrum of compound 13	23
Figure S41. FT-IR spectrum of compound 14	24
Figure S42. FT-IR spectrum of compound 15	24
Figure S43. FT-IR spectrum of compound 16	25
Figure S44. FT-IR spectrum of compound 17	25
Figure S45. FT-IR spectrum of compound 18	26
Figure S46. FT-IR spectrum of compound 19	26
Figure S47. FT-IR spectrum of compound 20	27
Figure S48. FT-IR spectrum of compound 21	27
Figure S49. FT-IR spectrum of compound 22	28
Figure S50. Normalised absorbance (%) of compounds 11-22 against planktonic and sessile MRSA....	29
Table S1. 2D NMR correlations measured for compound 4	30
Table S2. 2D NMR correlations measured for compound 19	30
Table S1. Microtox effective concentration levels of toxicity.....	30

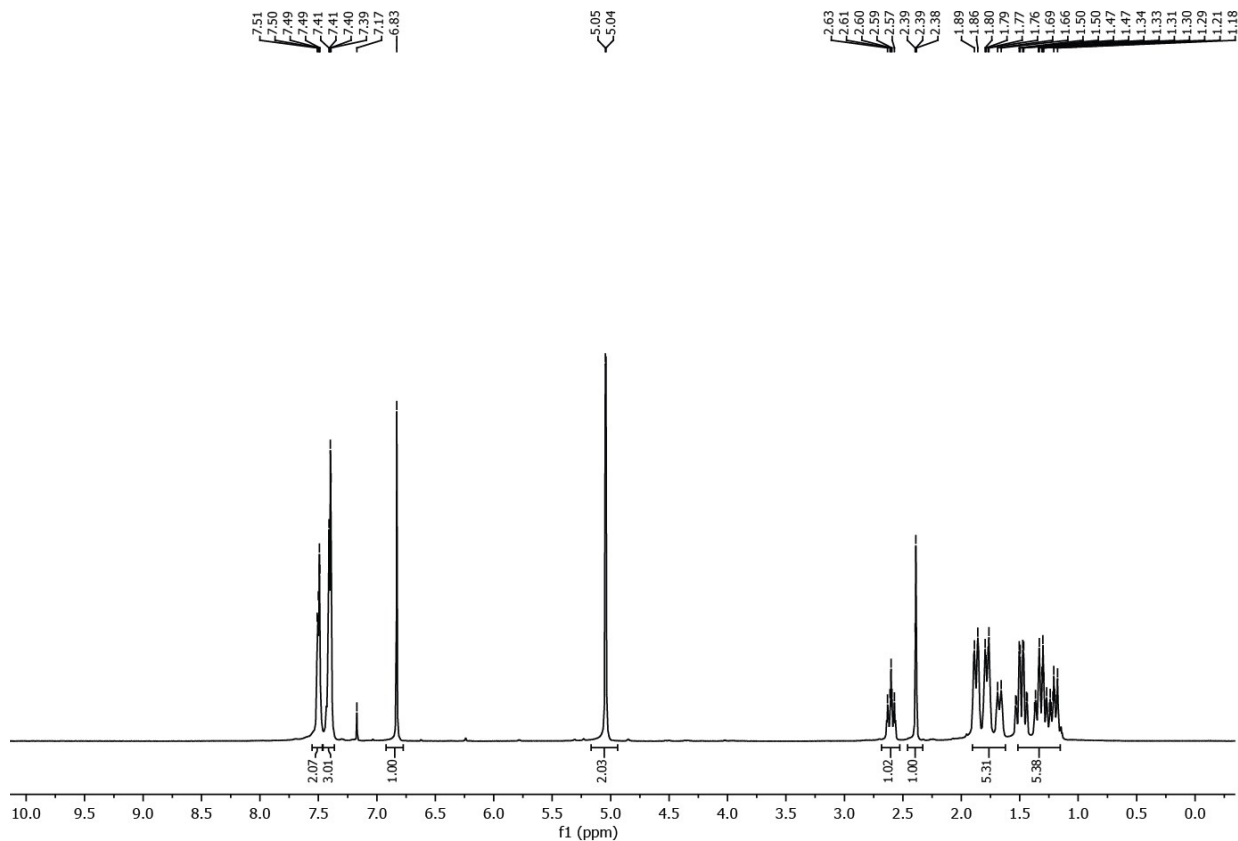


Figure S1. ^1H NMR spectrum of compound **3** (400 MHz, CDCl_3 , 25 $^\circ\text{C}$).

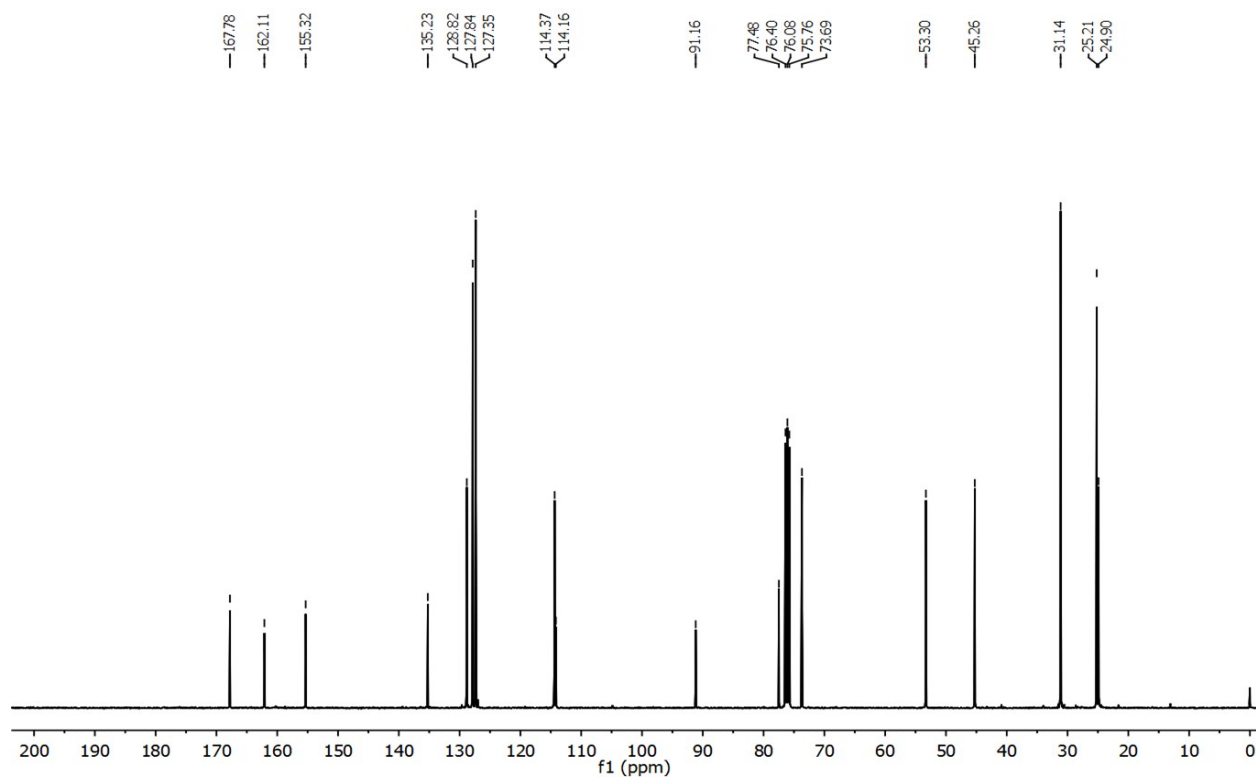


Figure S2. ^{13}C NMR spectrum of compound **3** (100 MHz, CDCl_3 , 25 $^\circ\text{C}$).

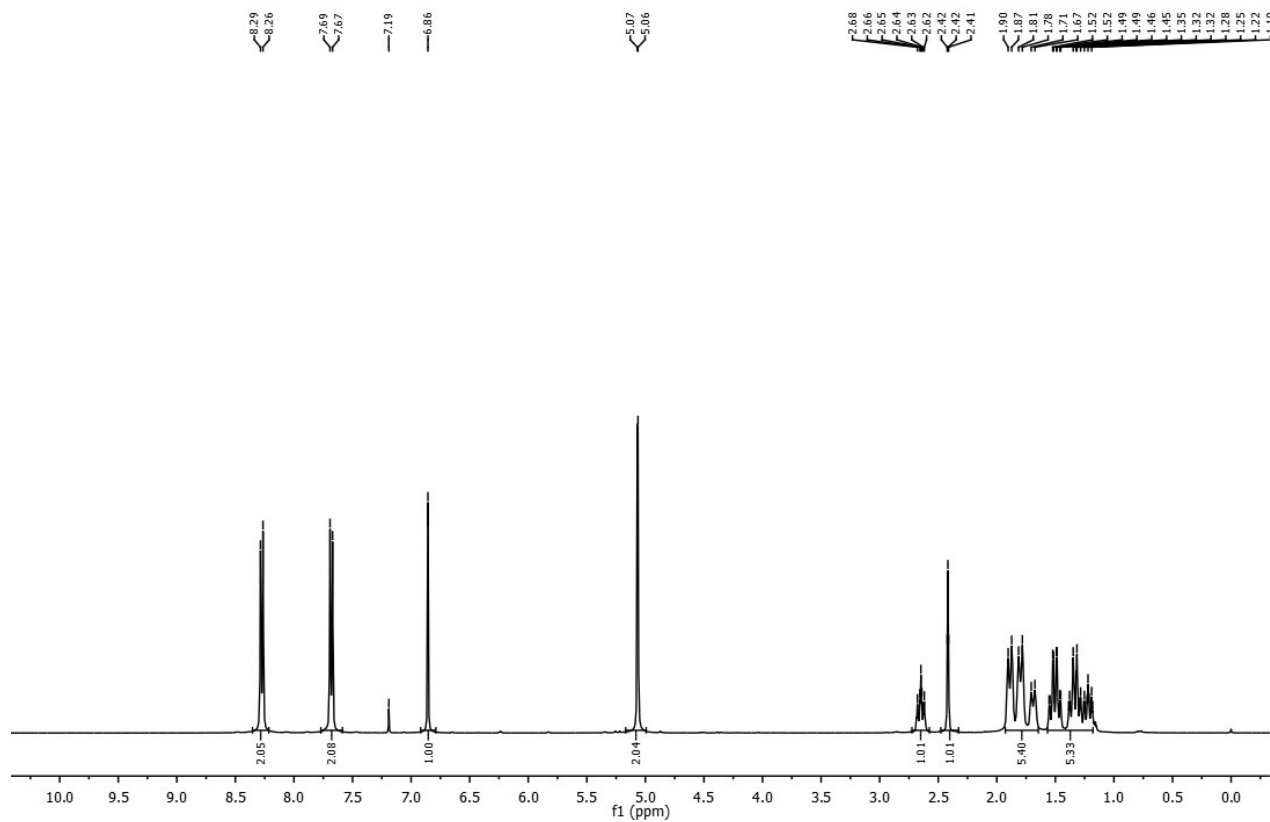


Figure S3. ^1H NMR spectrum of compound **4** (400 MHz, CDCl_3 , 25 $^\circ\text{C}$).

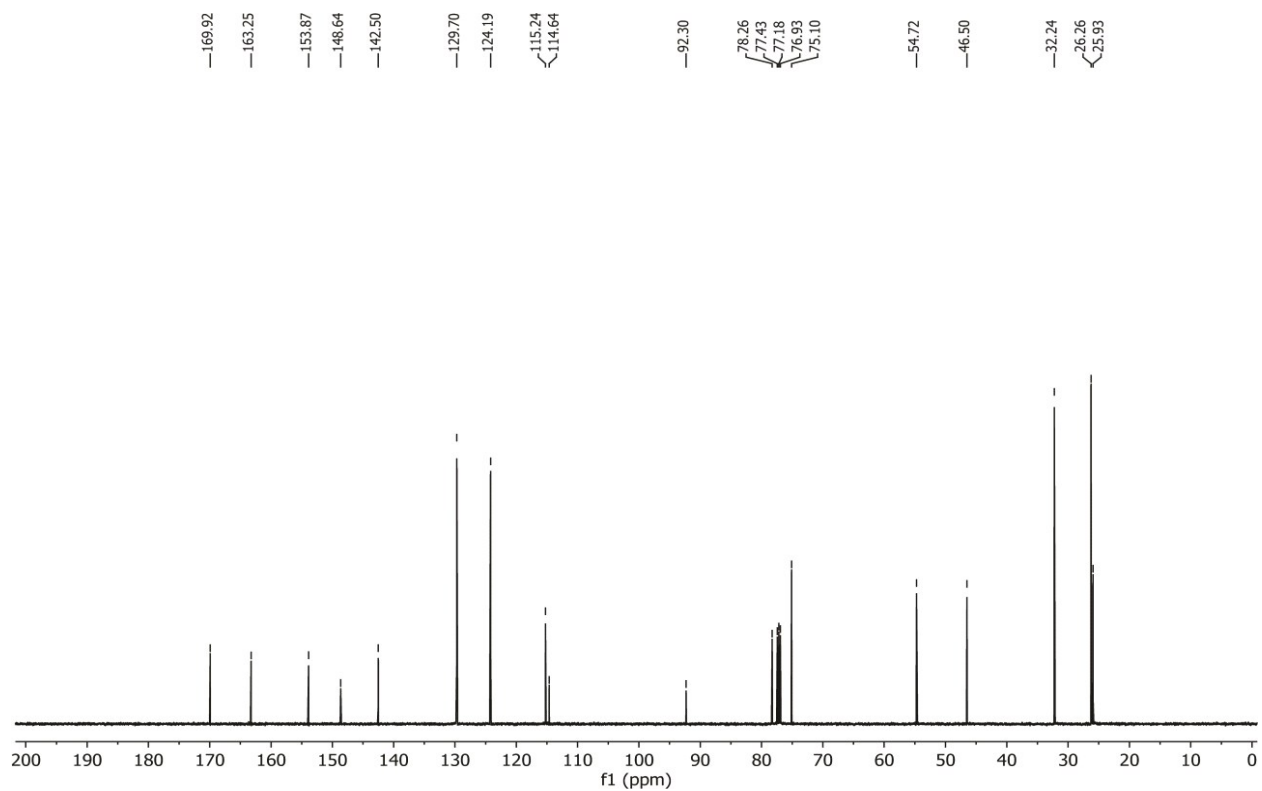


Figure S4. ^{13}C NMR spectrum of compound **4** (100 MHz, CDCl_3 , 25 $^\circ\text{C}$).

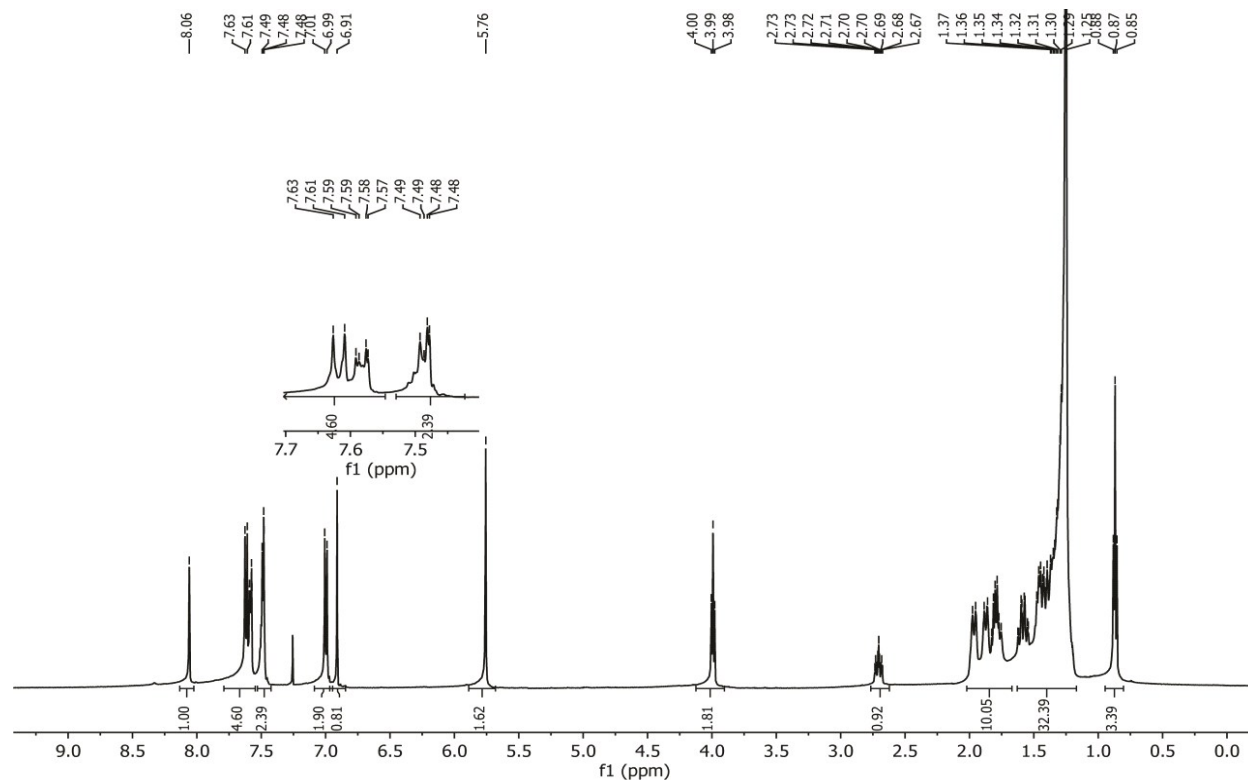


Figure S5. ^1H NMR spectrum of compound **11** (400 MHz, CDCl_3 , 25 °C).

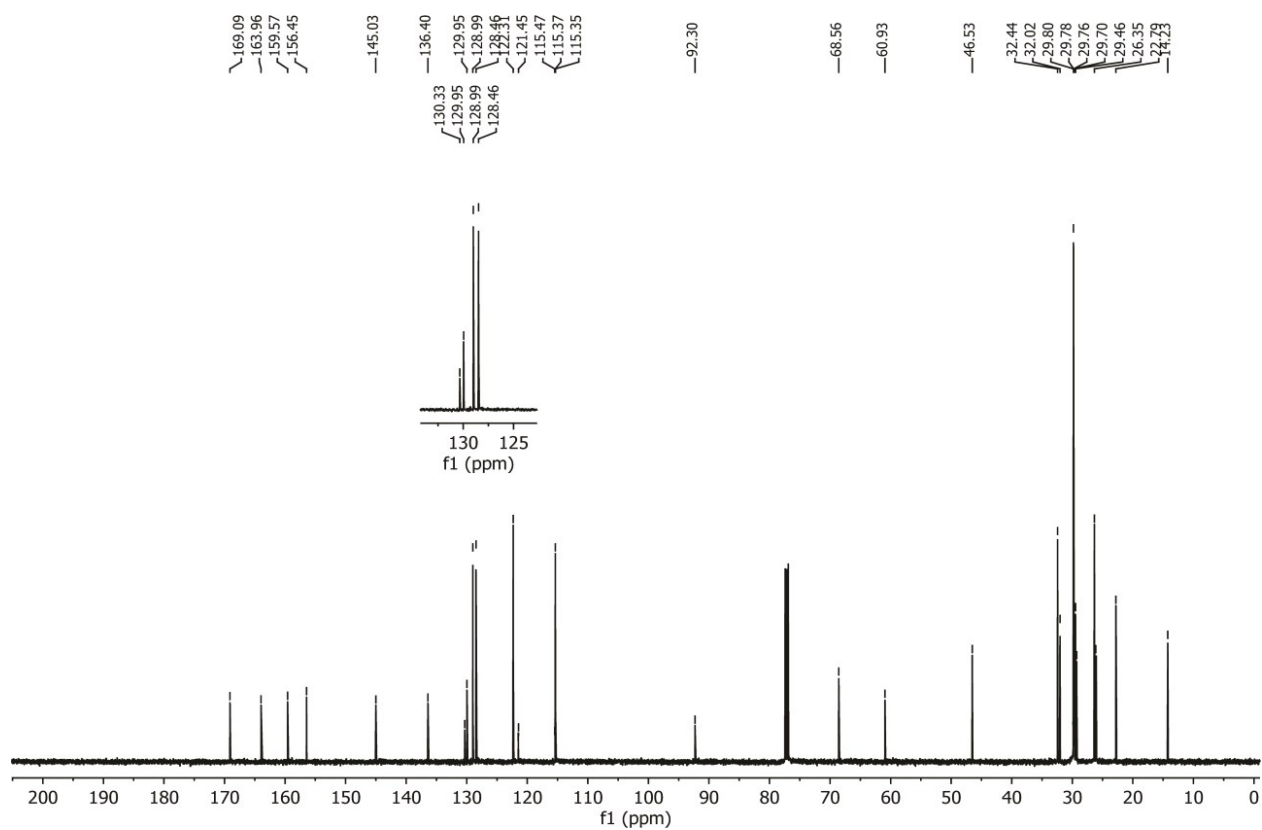


Figure S6. ^{13}C NMR spectrum of of compound **11** (100 MHz, CDCl_3 , 25 °C).

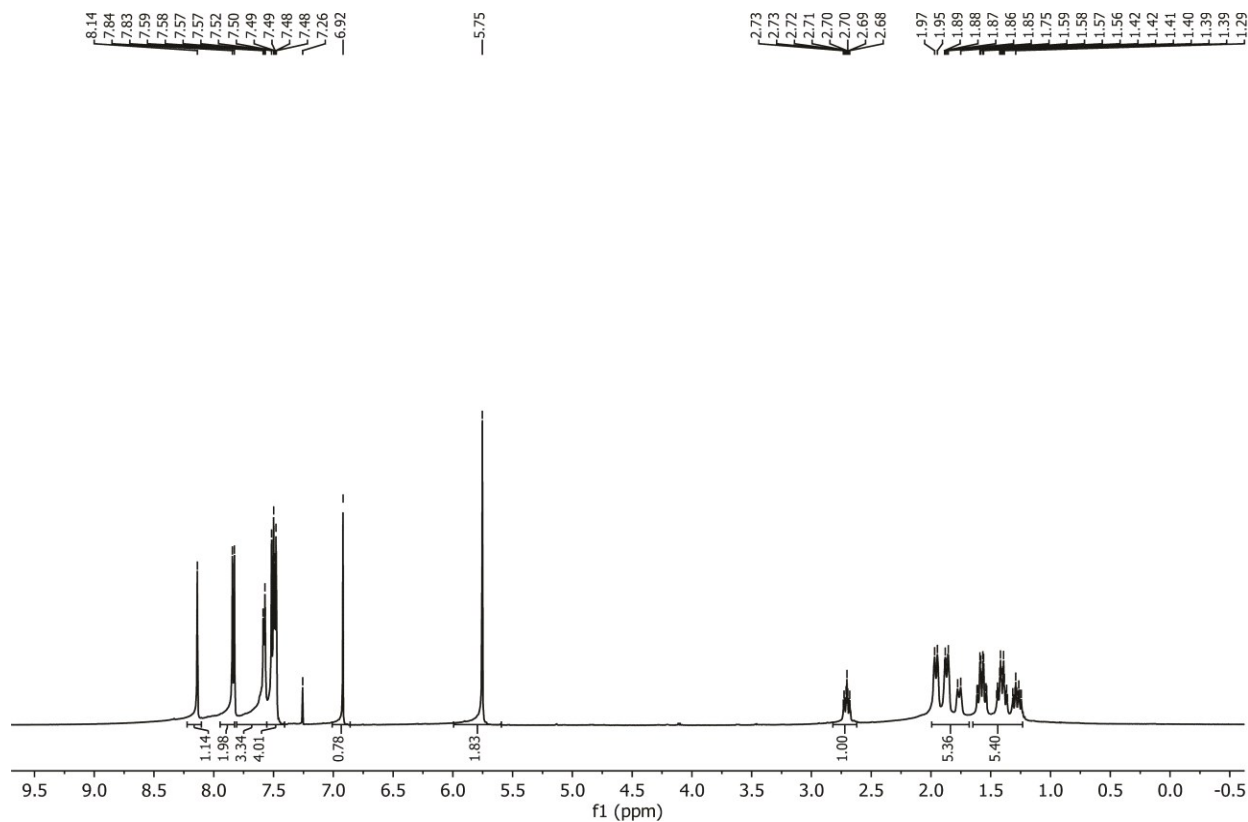


Figure S9. ^1H NMR spectrum of compound **13** (400 MHz, CDCl_3 , 25 $^\circ\text{C}$).

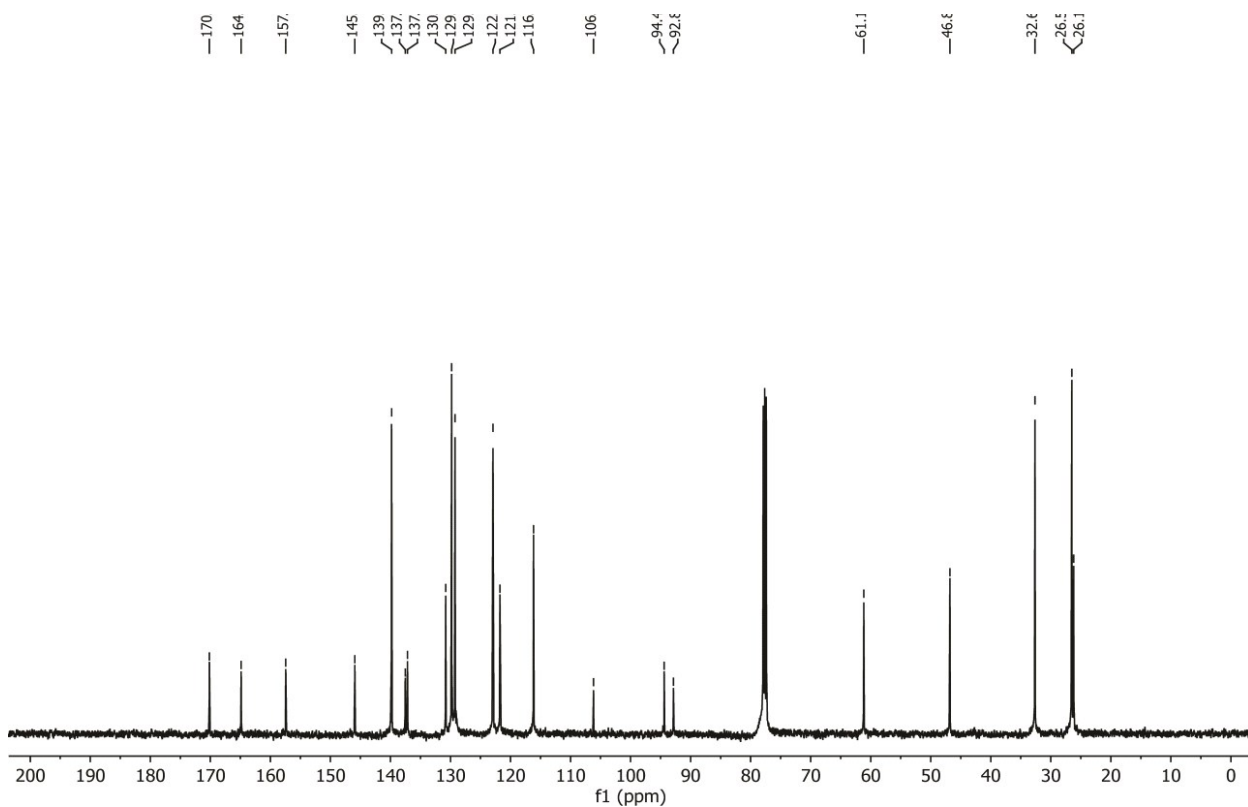


Figure S10. ^{13}C NMR spectrum of of compound **13** (100 MHz, CDCl_3 , 25 $^\circ\text{C}$).

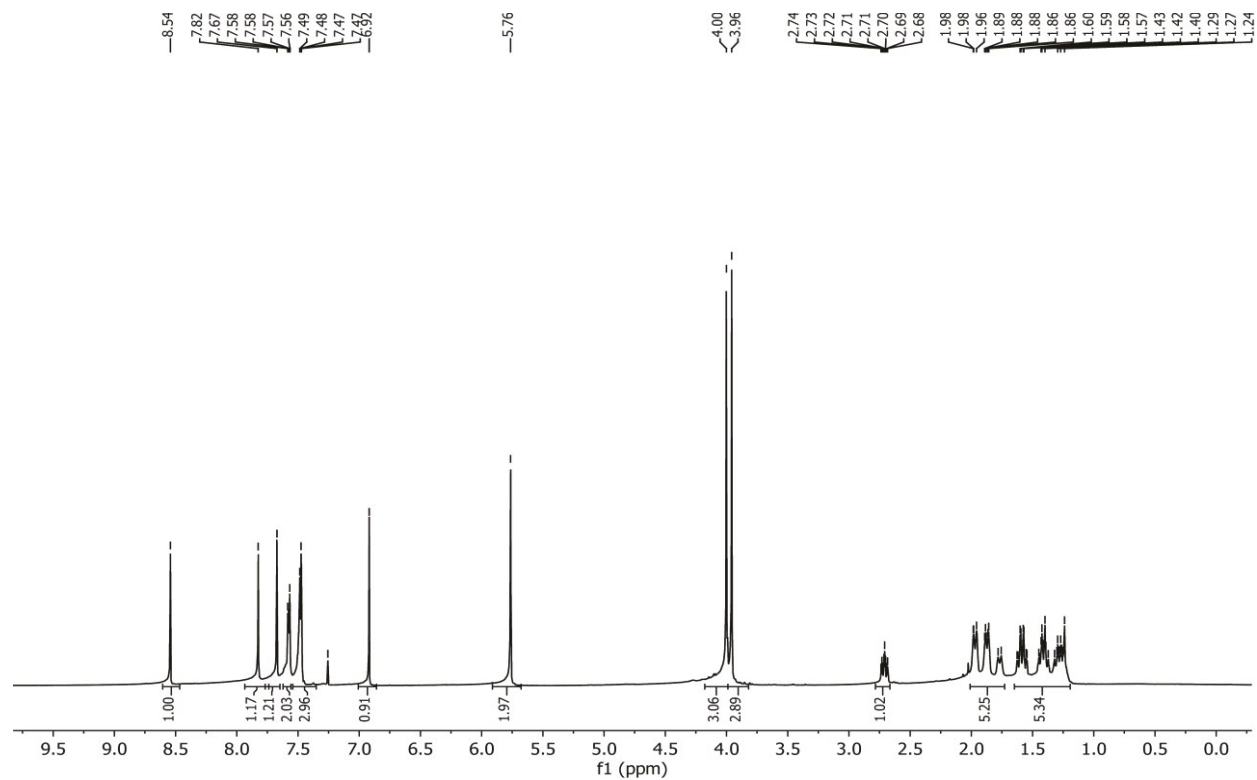


Figure S11. ^1H NMR spectrum of compound **14** (400 MHz, CDCl_3 , 25 $^\circ\text{C}$).

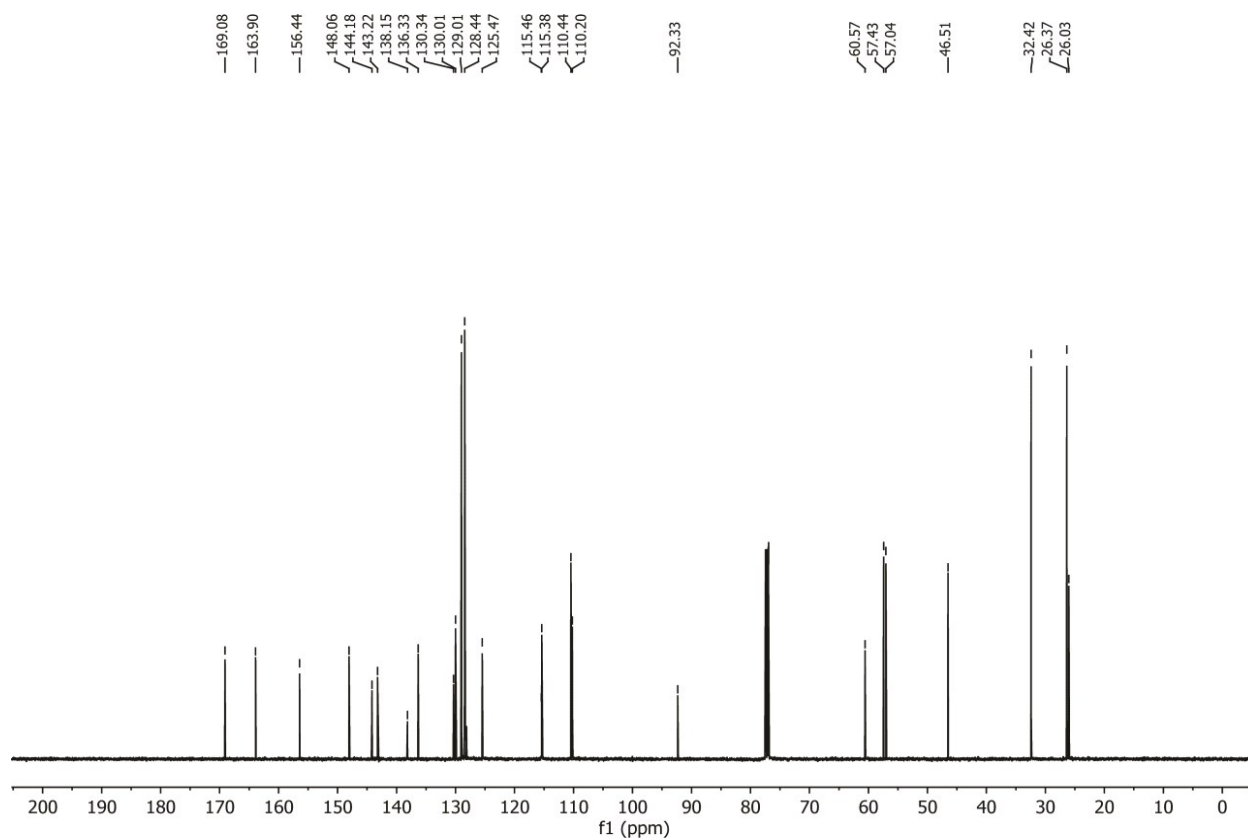


Figure S12. ^{13}C NMR spectrum of of compound **14** (100 MHz, CDCl_3 , 25 $^\circ\text{C}$).

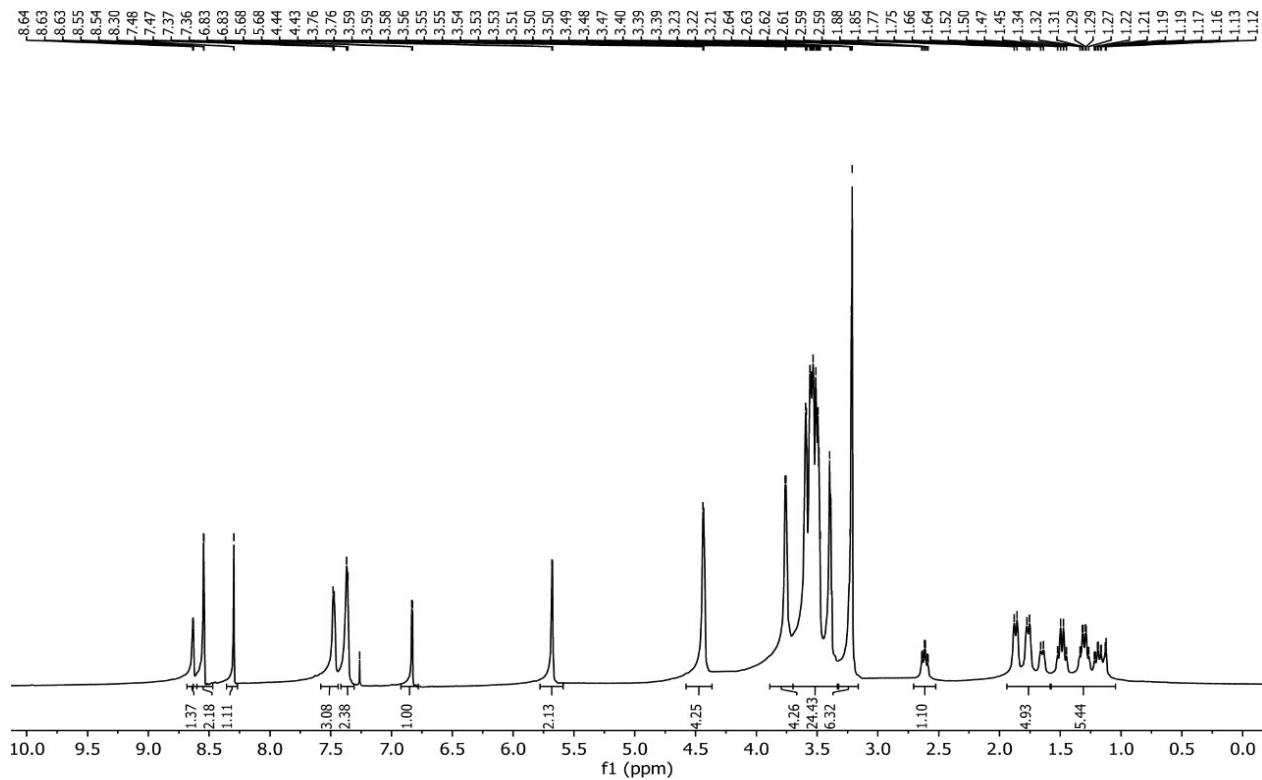


Figure S13. ^1H NMR spectrum of compound **15** (400 MHz, CDCl_3 , 25 $^\circ\text{C}$).

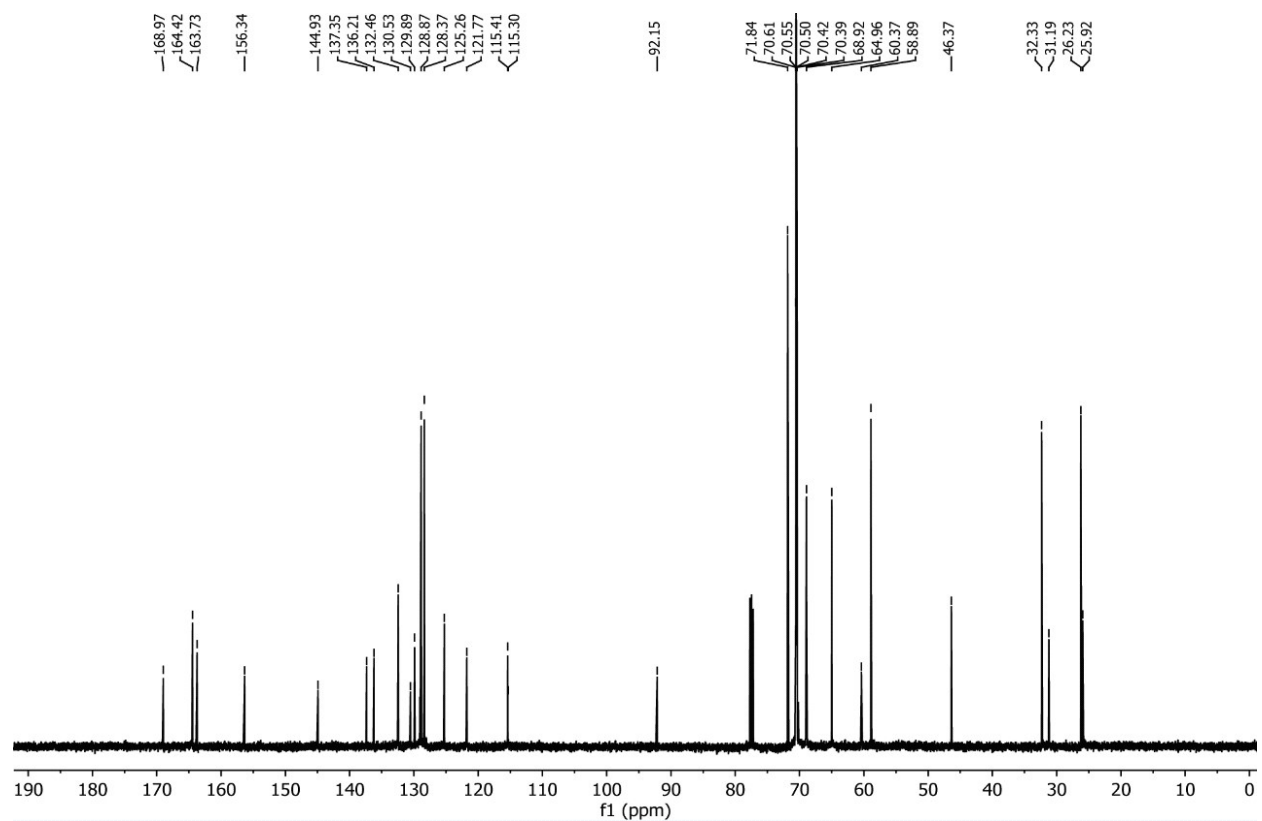


Figure S14. ^{13}C NMR spectrum of compound **15** (100 MHz, CDCl_3 , 25 $^\circ\text{C}$).

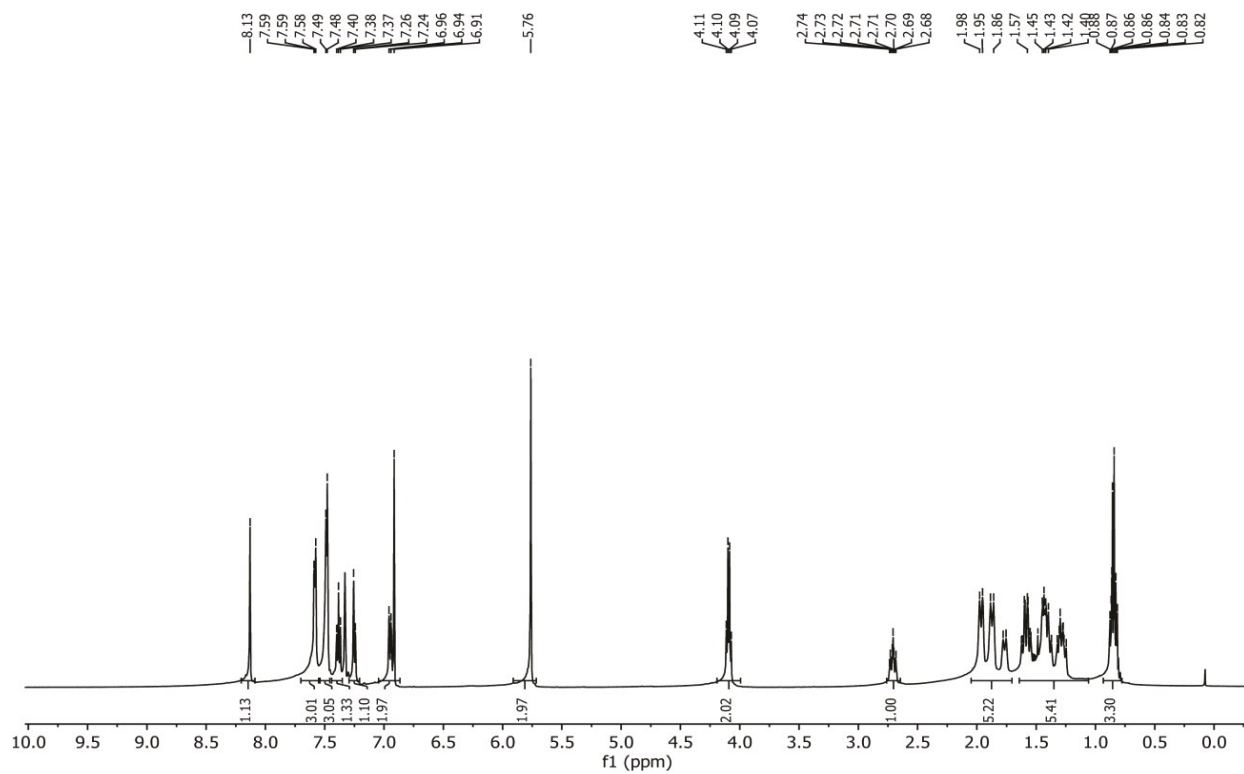


Figure S15. ^1H NMR spectrum of compound **16** (400 MHz, CDCl_3 , 25 $^\circ\text{C}$).

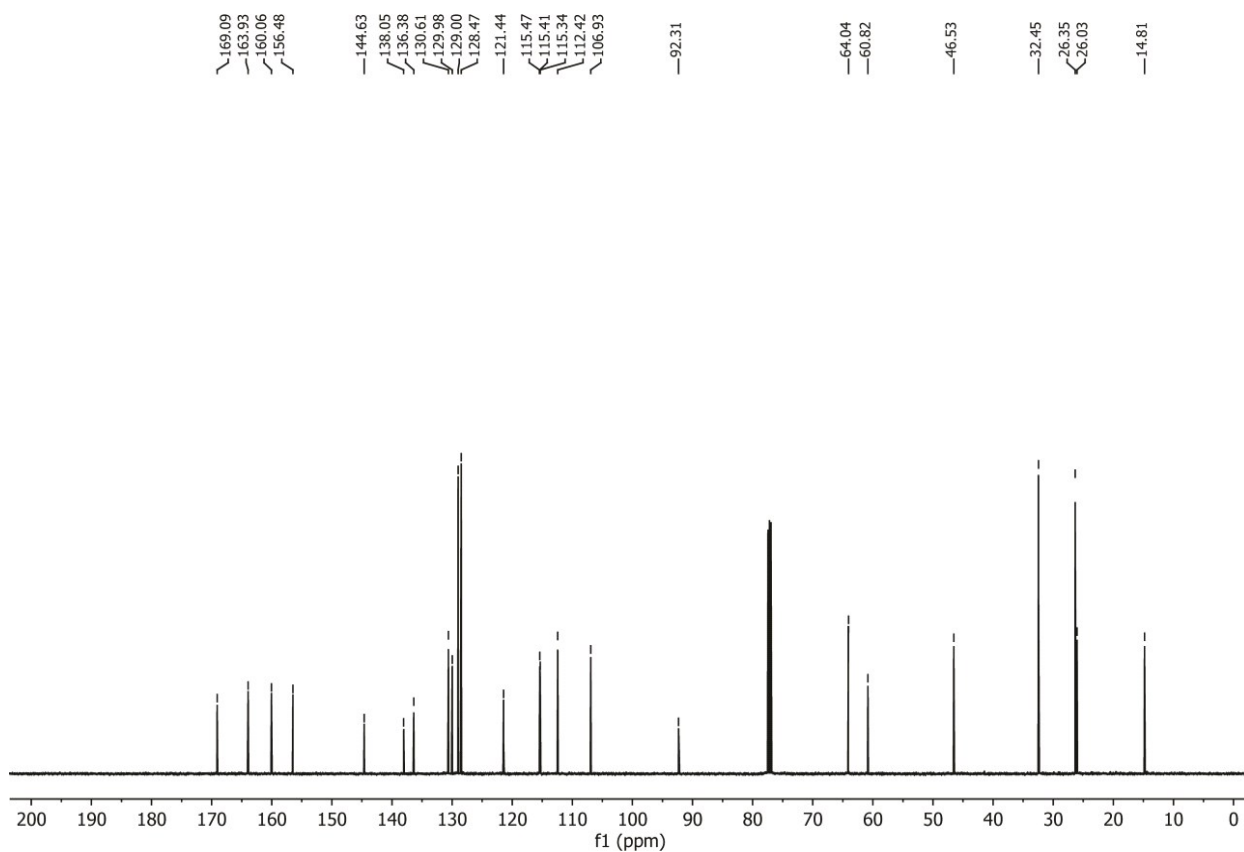


Figure S16. ^{13}C NMR spectrum of of compound **16** (100 MHz, CDCl_3 , 25 $^\circ\text{C}$).

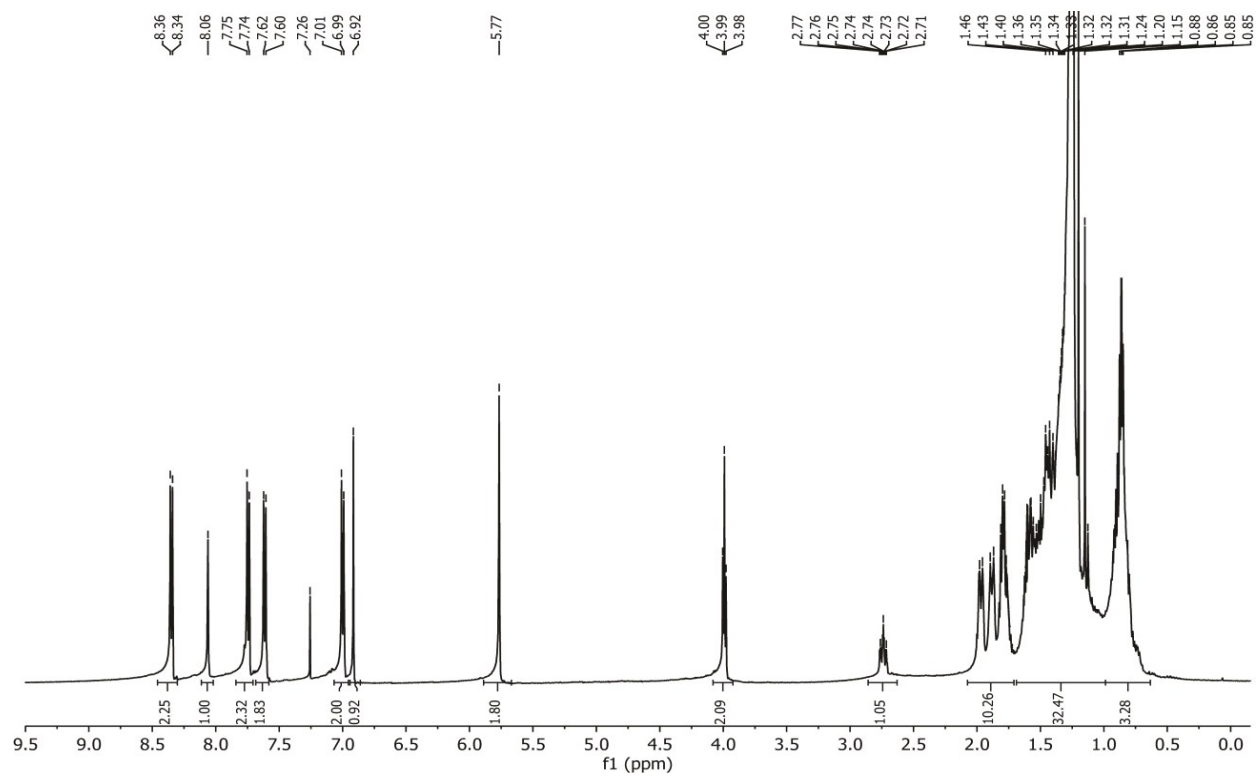


Figure S17. ^1H NMR spectrum of compound **17** (400 MHz, CDCl_3 , 25 $^\circ\text{C}$).

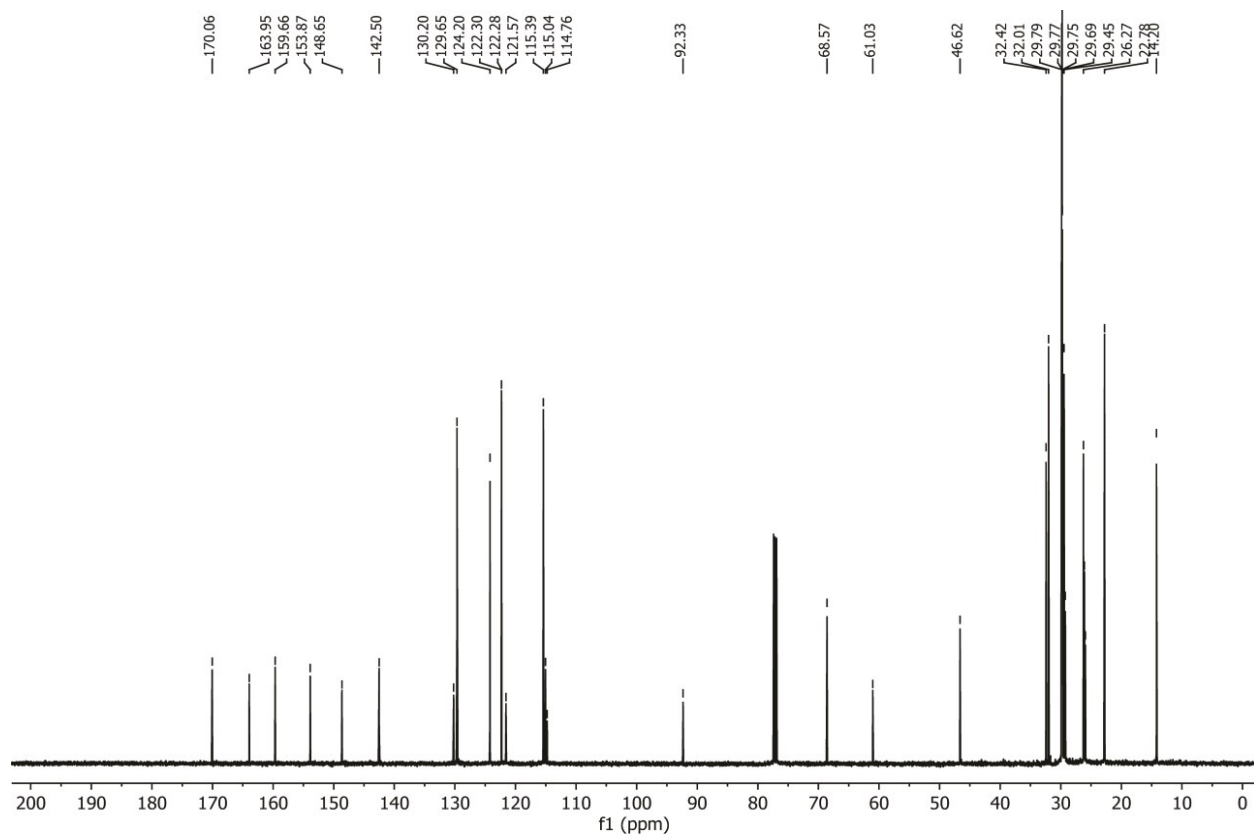


Figure S18. ^{13}C NMR spectrum of of compound **17** (100 MHz, CDCl_3 , 25 $^\circ\text{C}$).

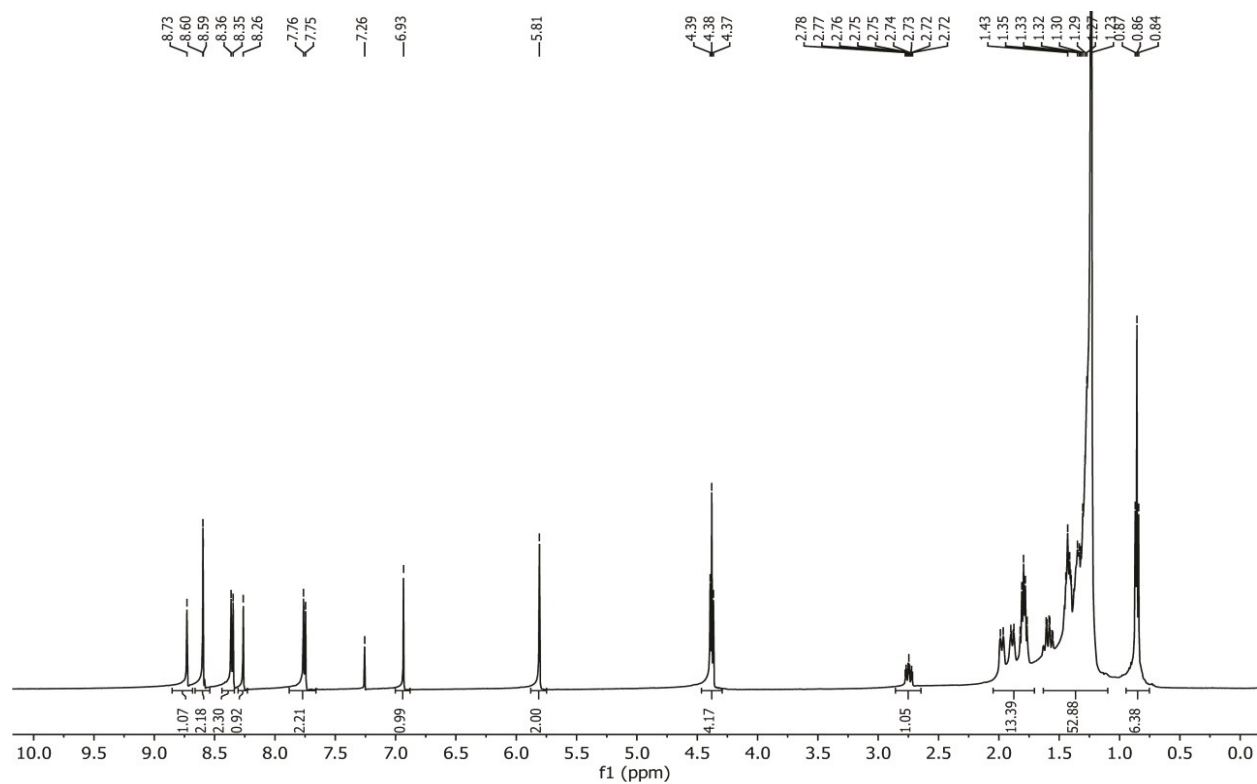


Figure S19. ^1H NMR spectrum of compound **18** (400 MHz, CDCl_3 , 25 $^\circ\text{C}$).

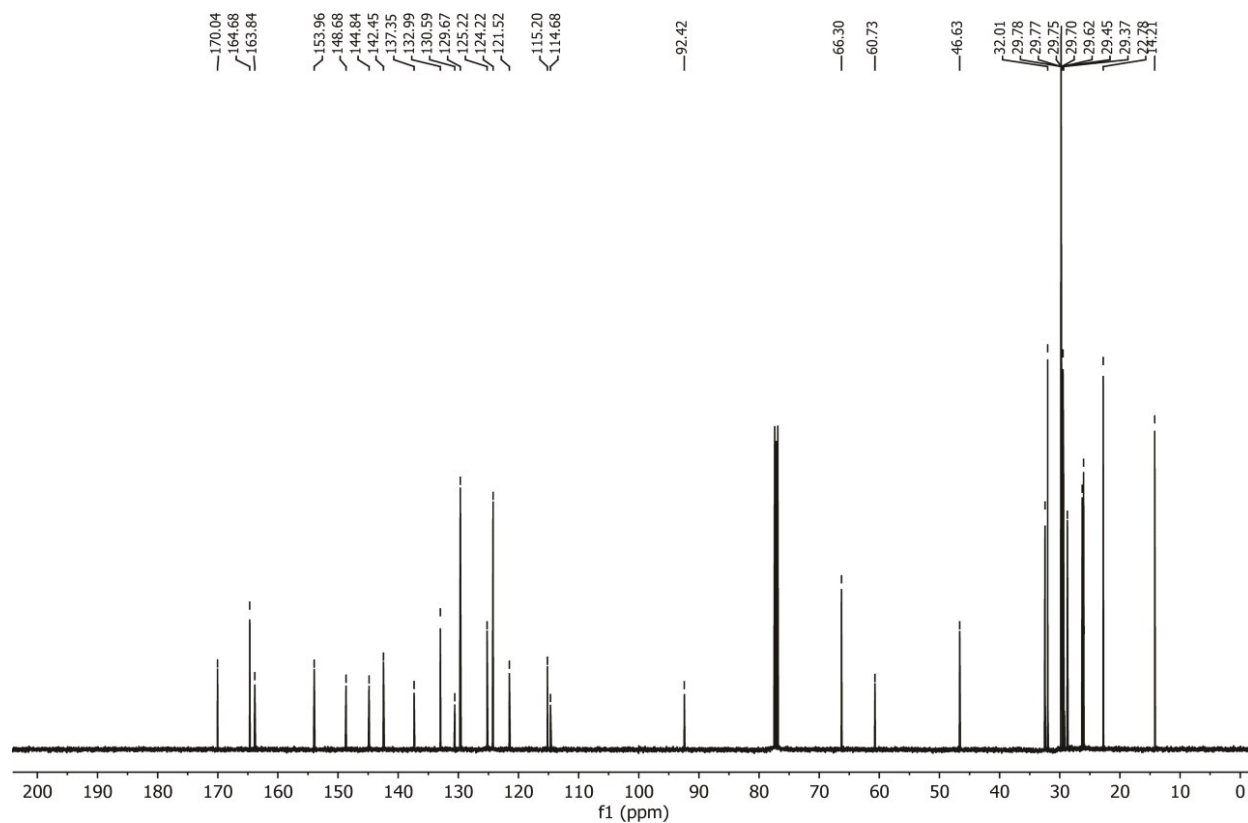


Figure S20. ^{13}C NMR spectrum of of compound **18** (100 MHz, CDCl_3 , 25 $^\circ\text{C}$).

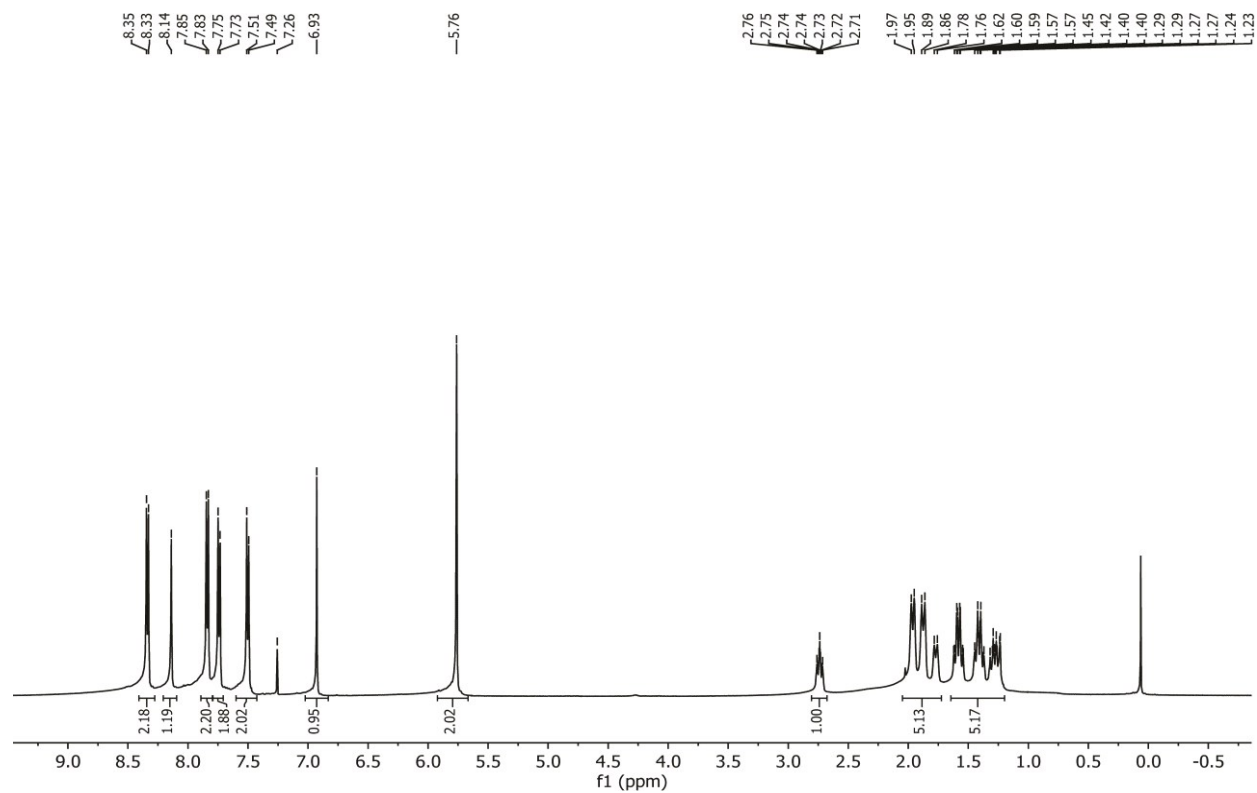


Figure S21. ^1H NMR spectrum of compound **19** (400 MHz, CDCl_3 , 25 $^\circ\text{C}$).

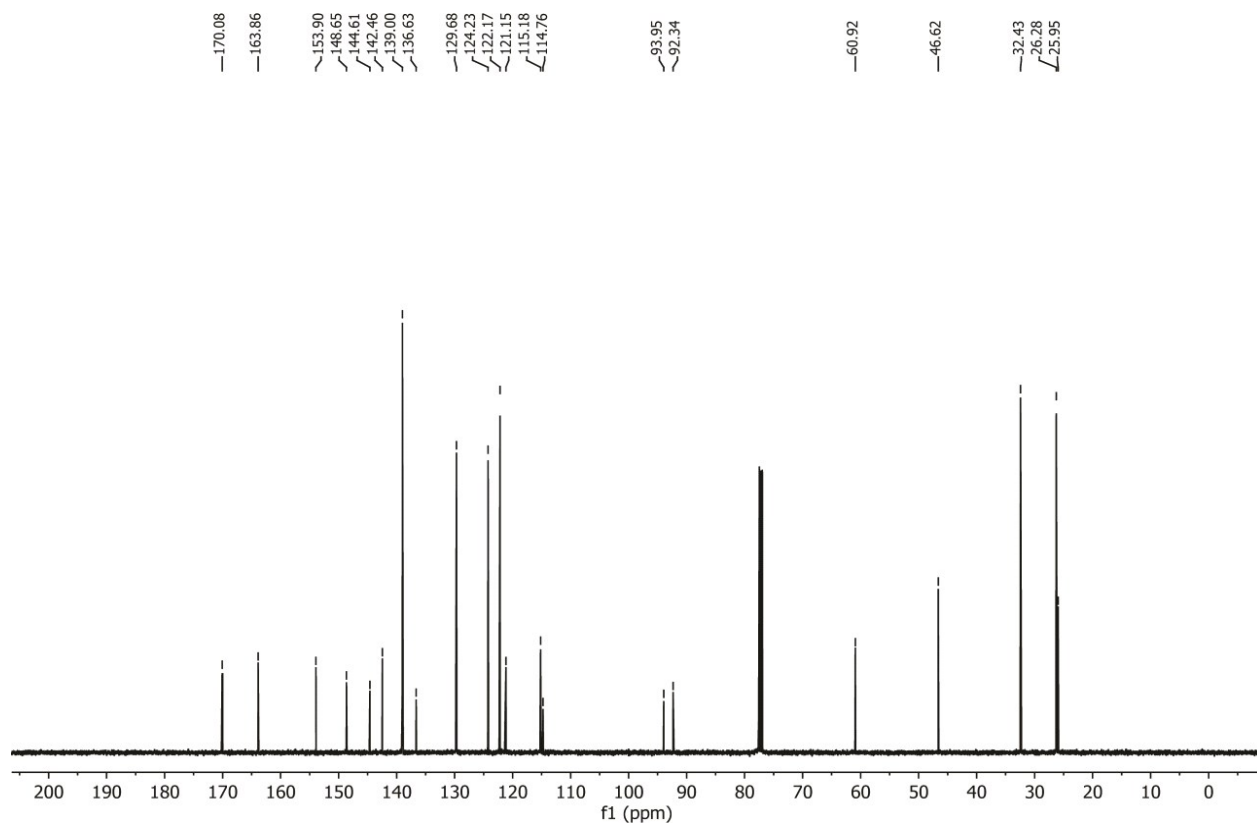


Figure S22. ^{13}C NMR spectrum of of compound **19** (100 MHz, CDCl_3 , 25 $^\circ\text{C}$).

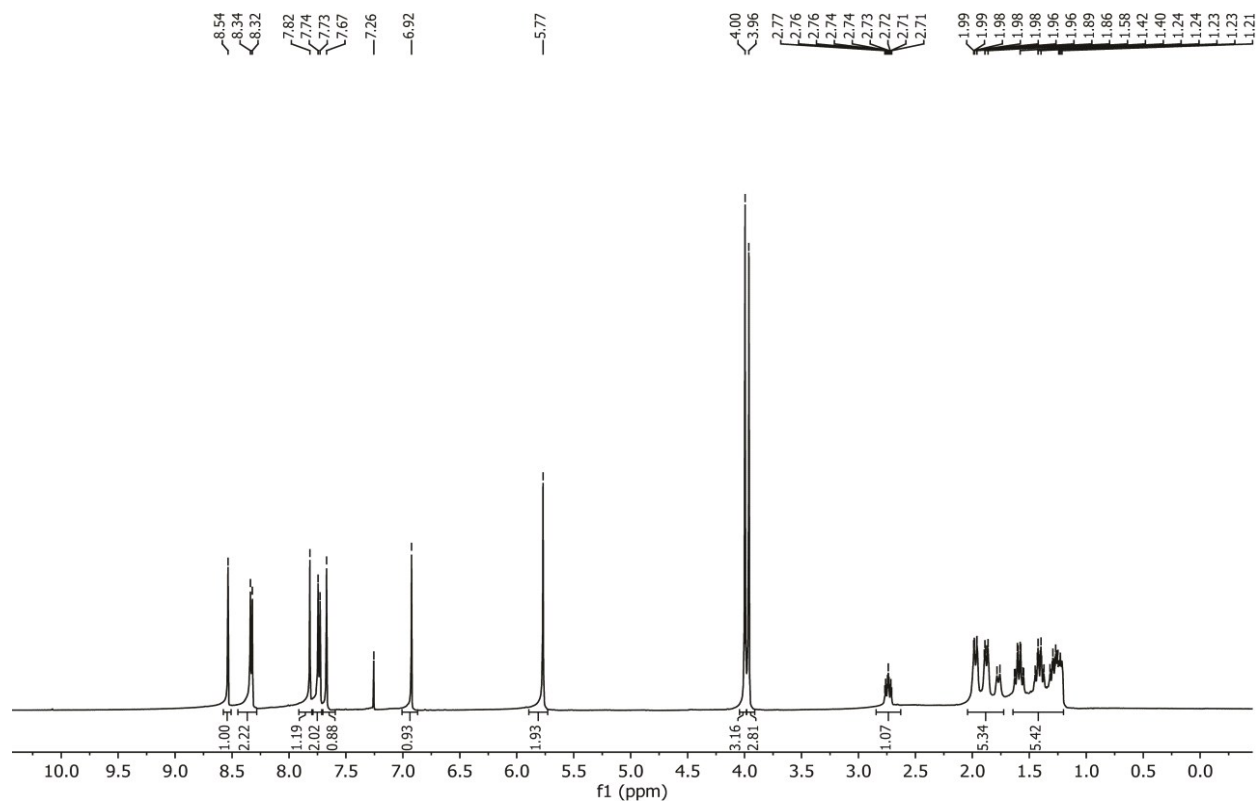


Figure S23. ^1H NMR spectrum of compound **20** (400 MHz, CDCl_3 , 25 $^\circ\text{C}$).

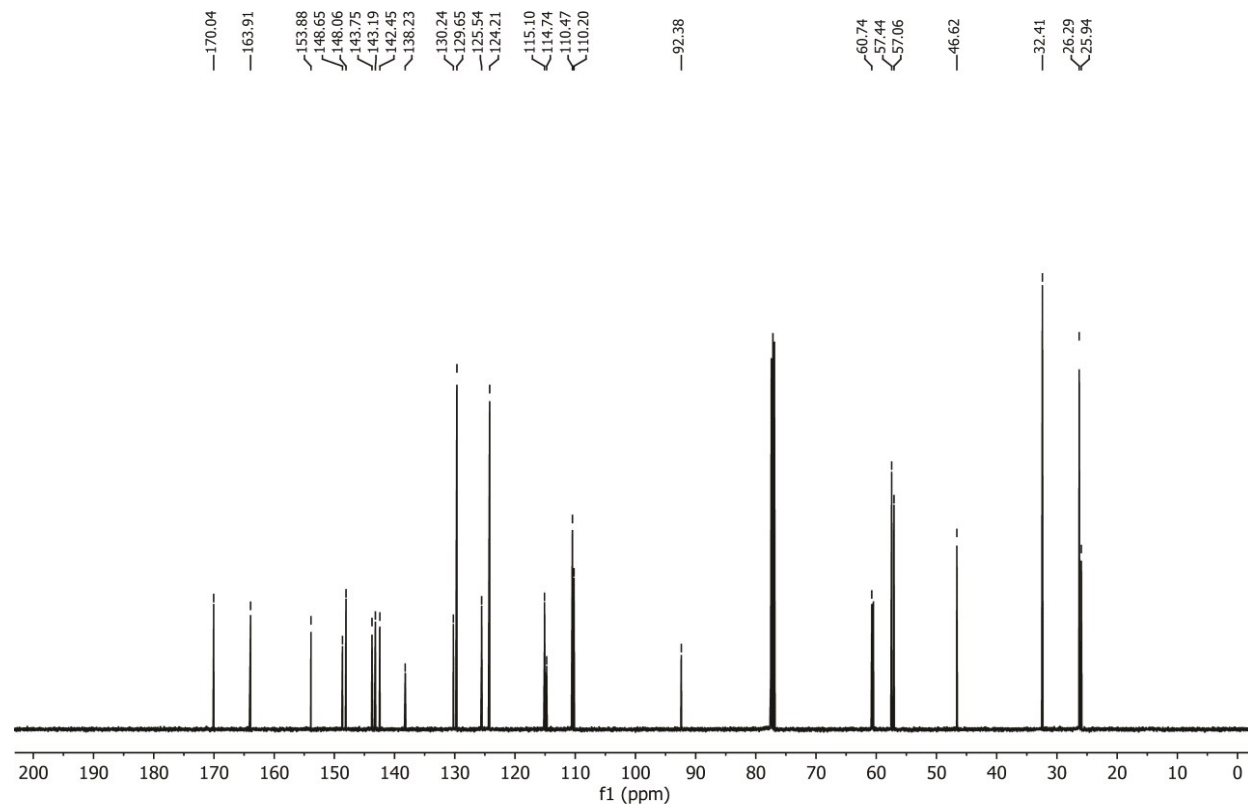


Figure S24. ^{13}C NMR spectrum of of compound **20** (100 MHz, CDCl_3 , 25 $^\circ\text{C}$).

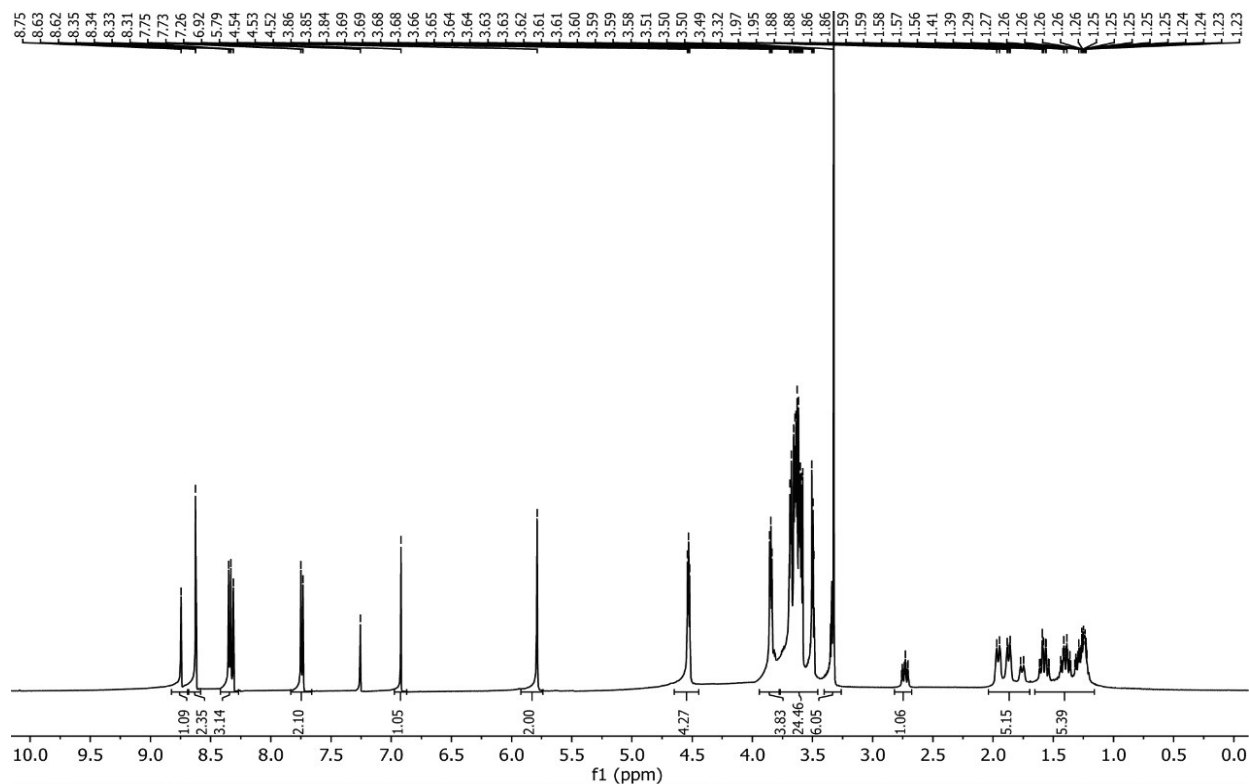


Figure S25. ^1H NMR spectrum of compound **21** (400 MHz, CDCl_3 , 25 $^\circ\text{C}$).

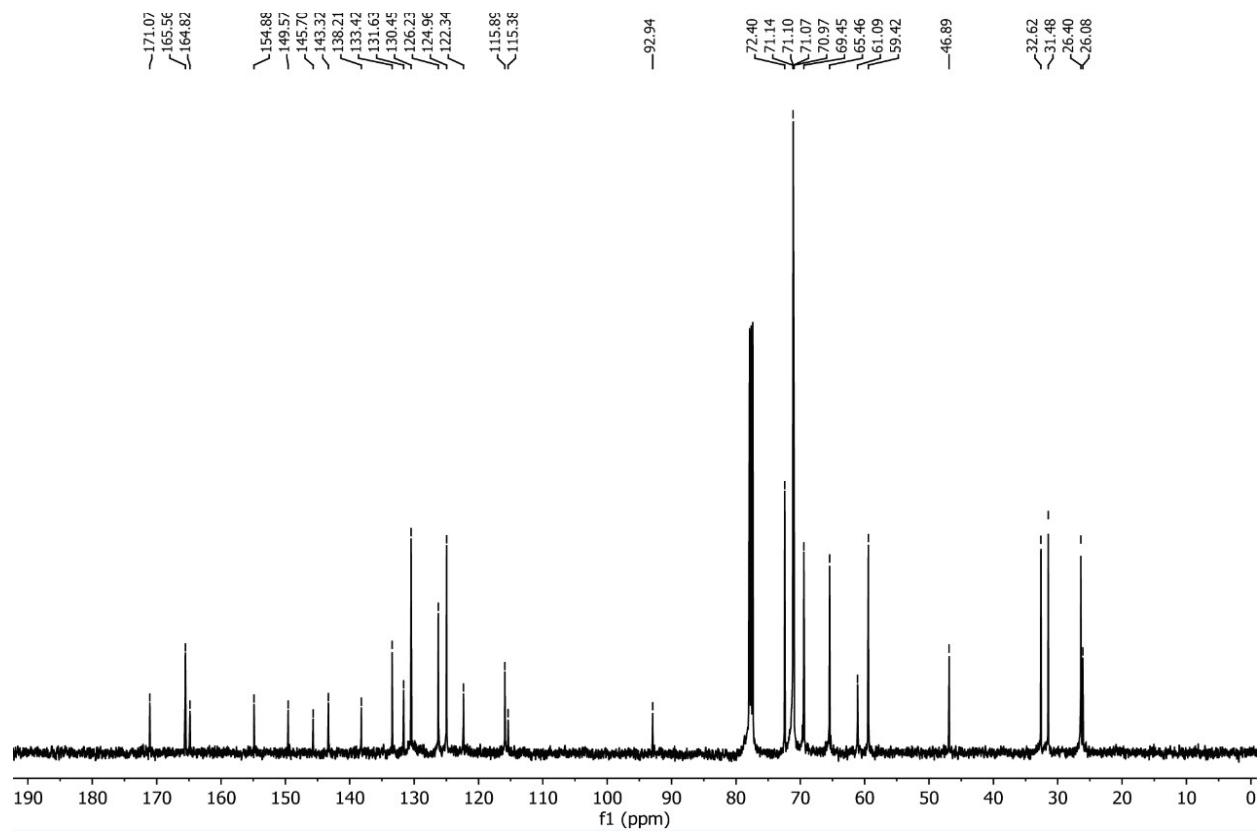


Figure S26. ^{13}C NMR spectrum of of compound **21** (100 MHz, CDCl_3 , 25 $^\circ\text{C}$).

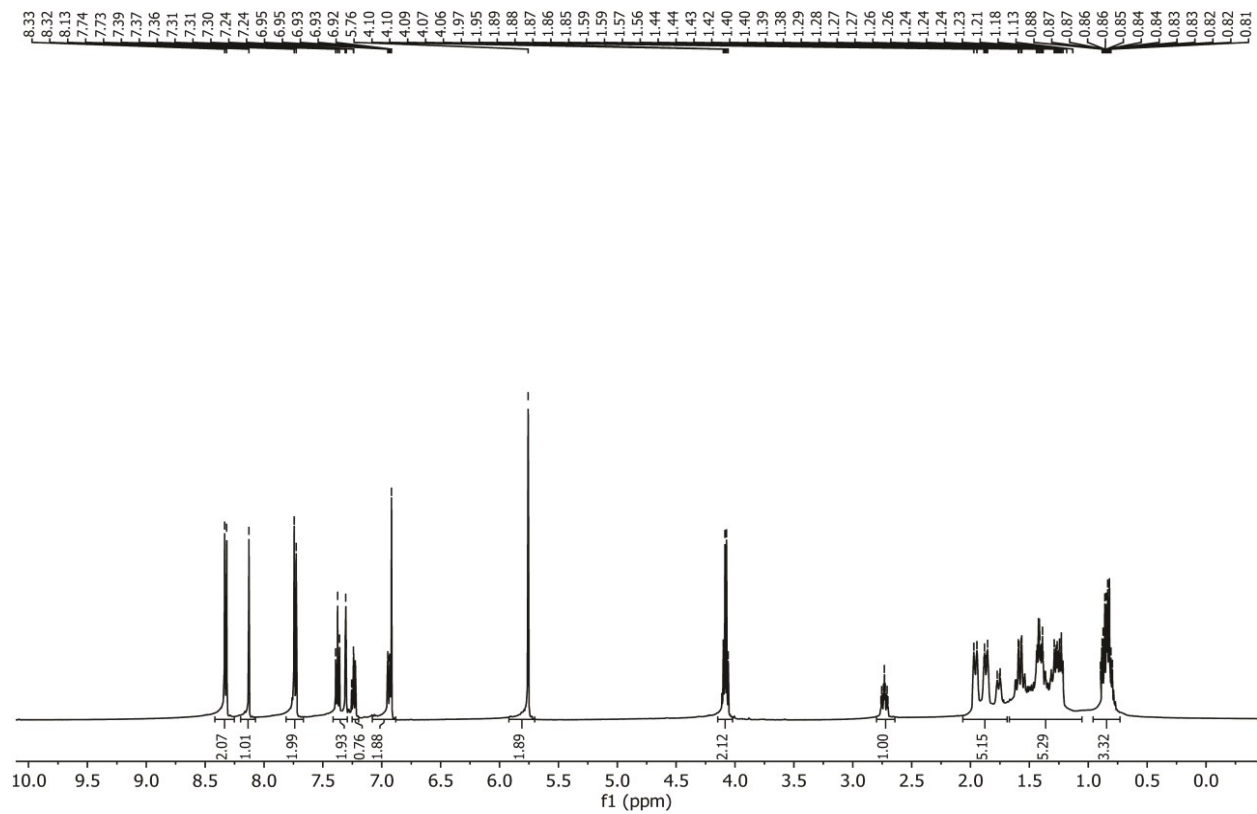


Figure S27. ^1H NMR spectrum of compound **22** (400 MHz, CDCl_3 , 25 $^\circ\text{C}$).

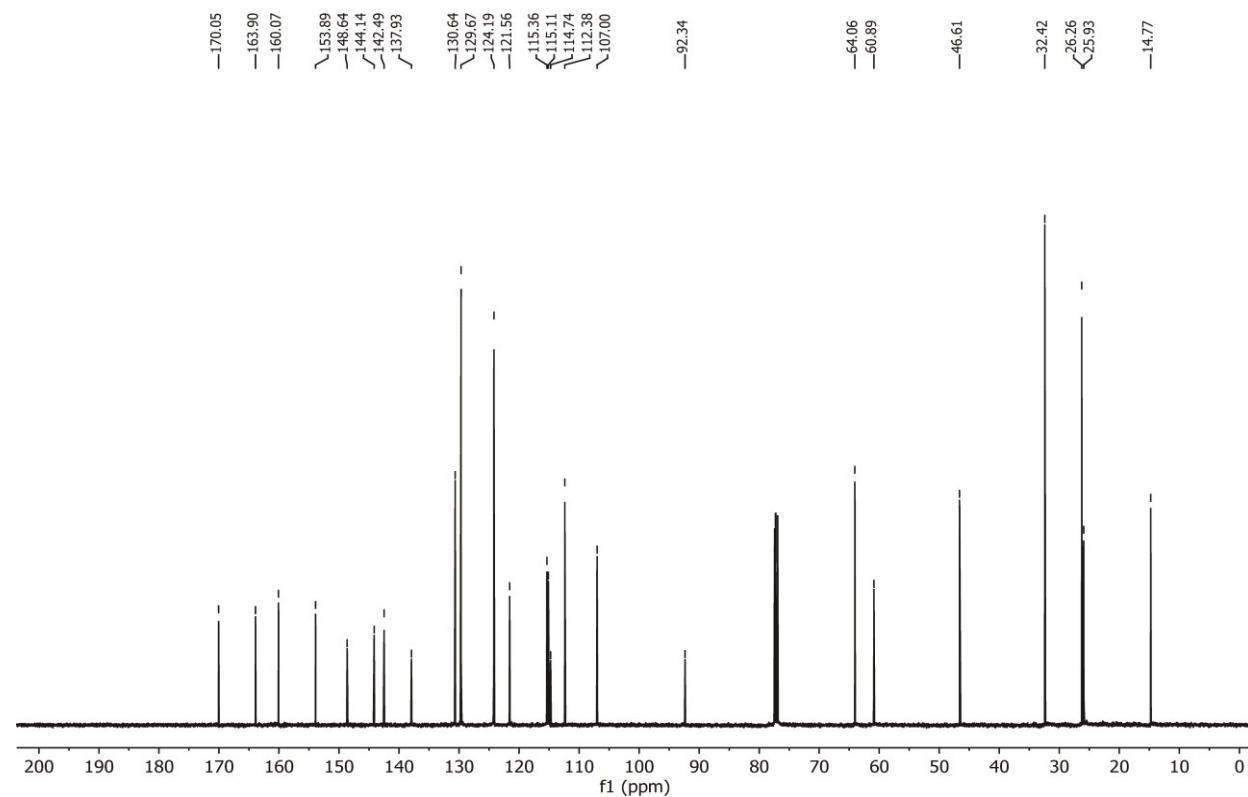


Figure S28. ^{13}C NMR spectrum of compound **22** (100 MHz, CDCl_3 , 25 $^\circ\text{C}$).

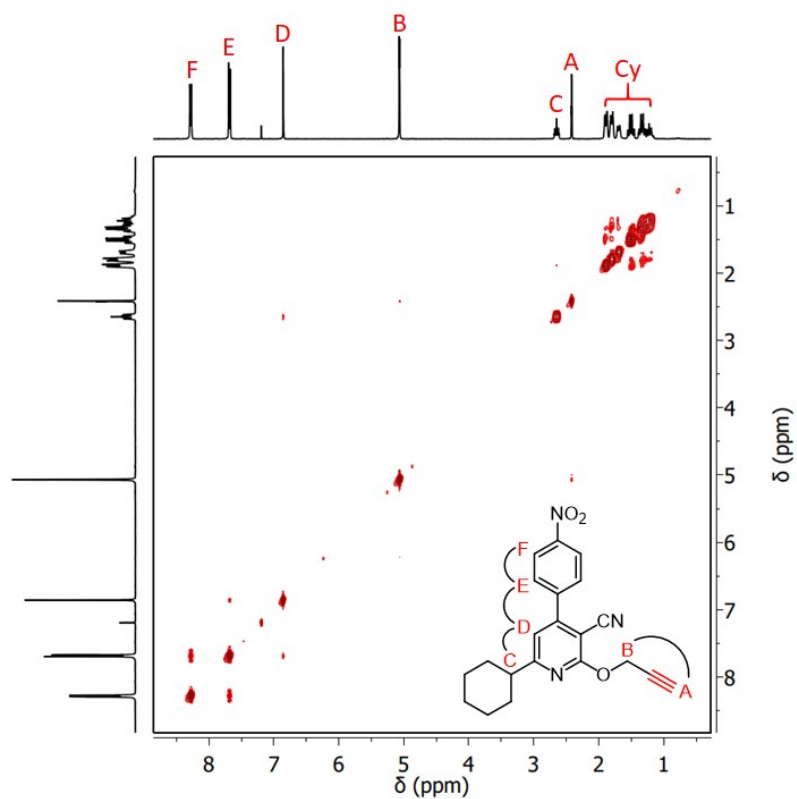


Figure S29. 2D NOESY spectrum of compound **4** (400 MHz, CDCl₃, 25 °C).

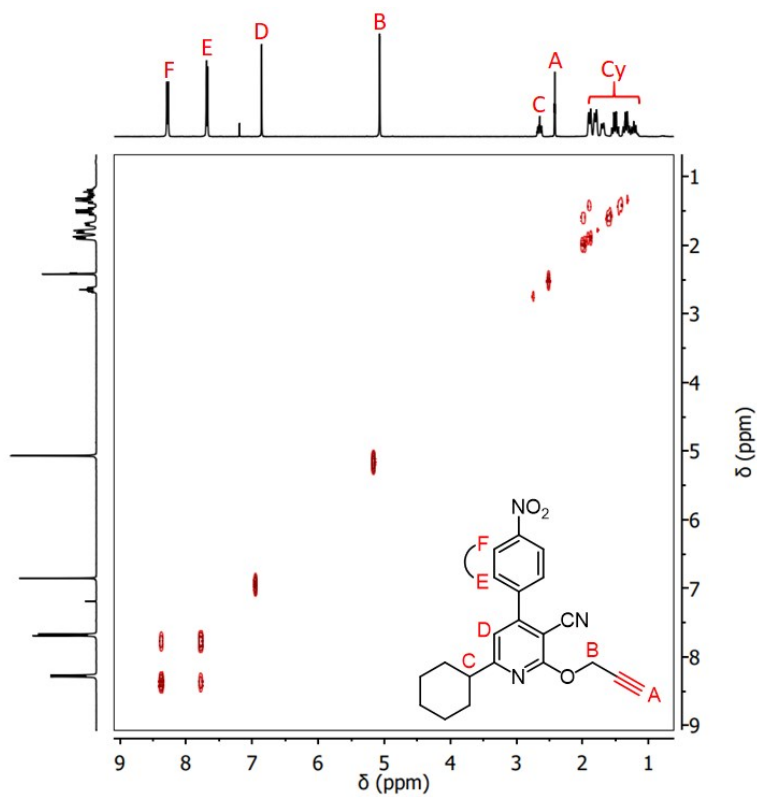


Figure S30. 2D COSY spectrum of compound **4** (400 MHz, CDCl₃, 25 °C).

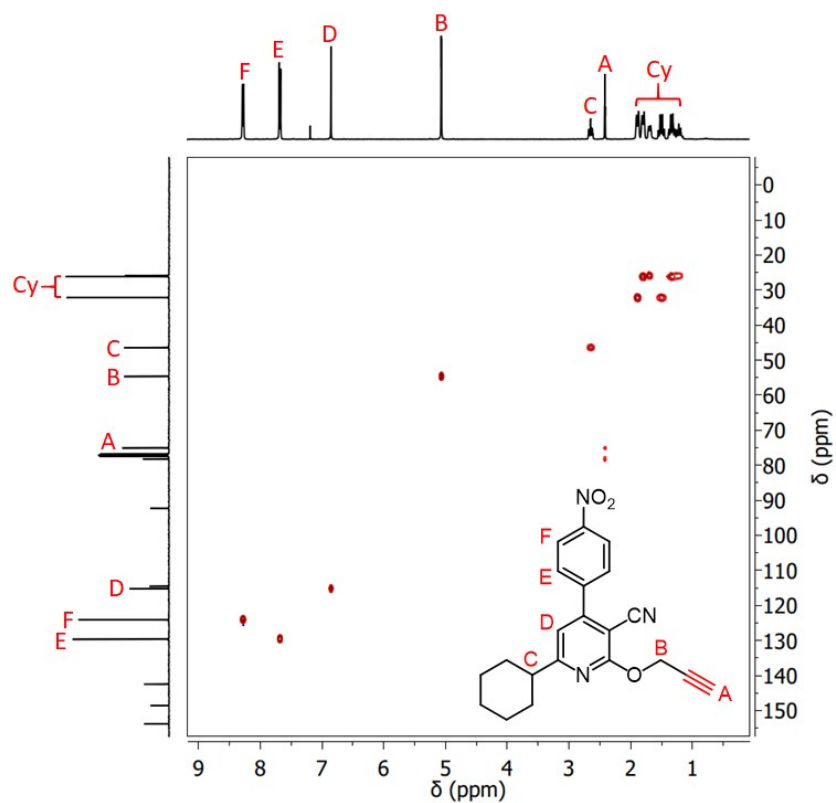


Figure S31. 2D HSQC spectrum of compound **4** (400 MHz, CDCl₃, 25 °C).

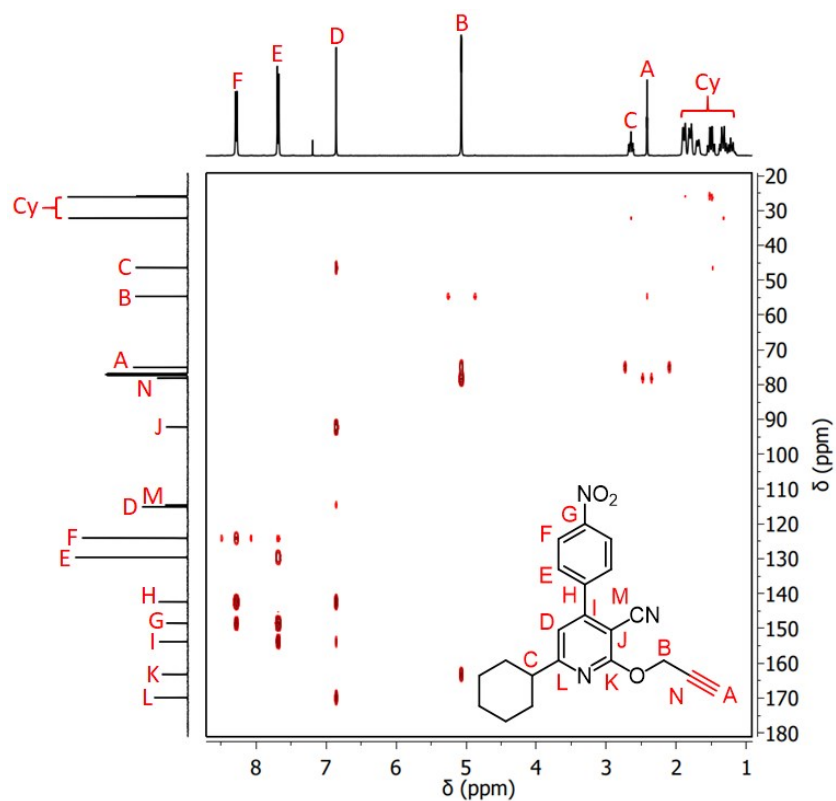


Figure S32. 2D HMBC spectrum of compound **4** (400 MHz, CDCl₃, 25 °C).

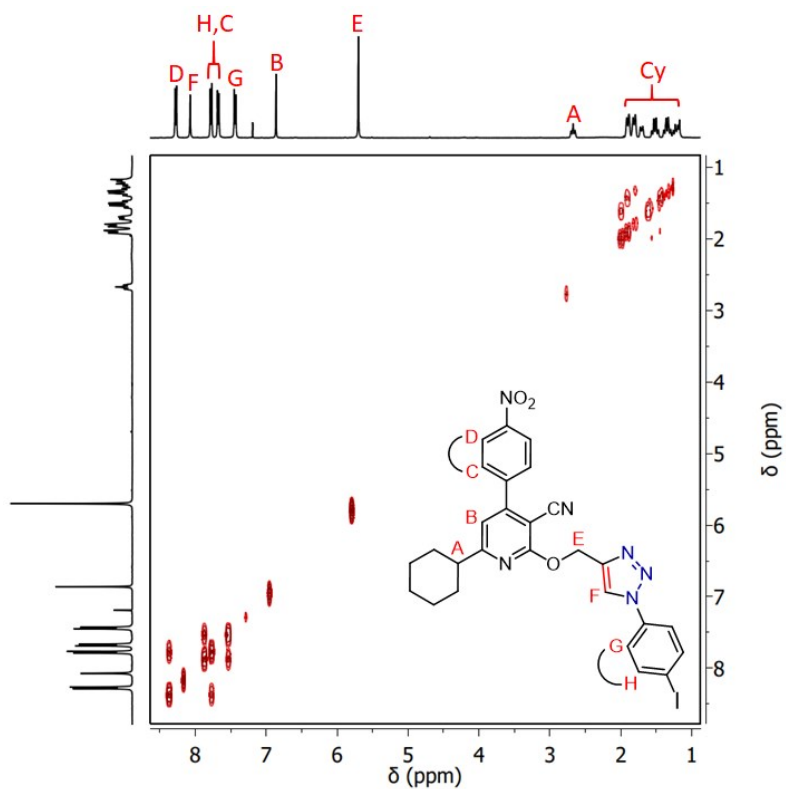


Figure S33. 2D COSY spectrum of compound **19** (400 MHz, CDCl_3 , 25 °C).

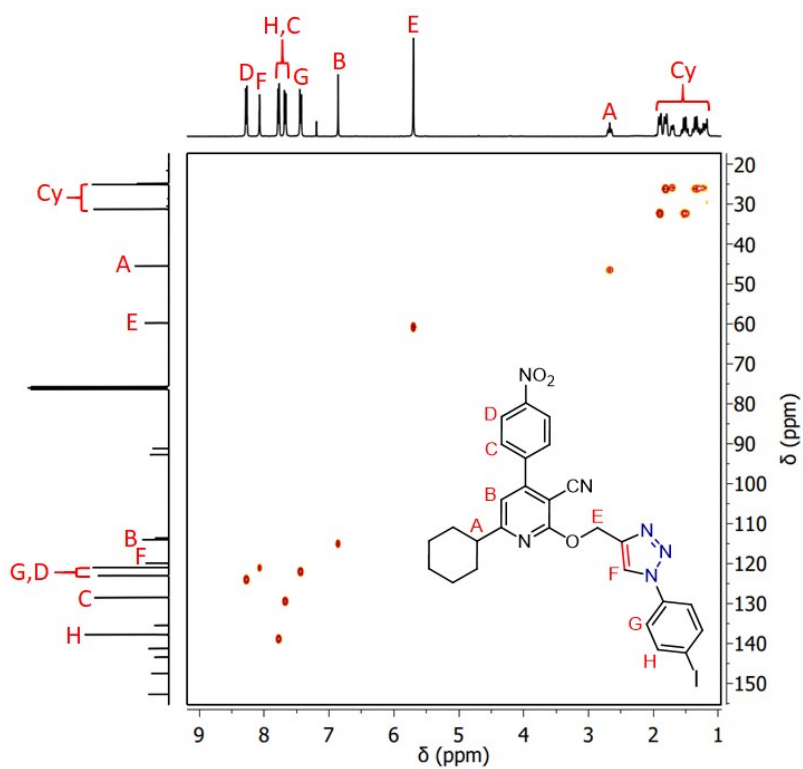


Figure S34. 2D HSQC spectrum of compound **19** (400 MHz, CDCl_3 , 25 °C).

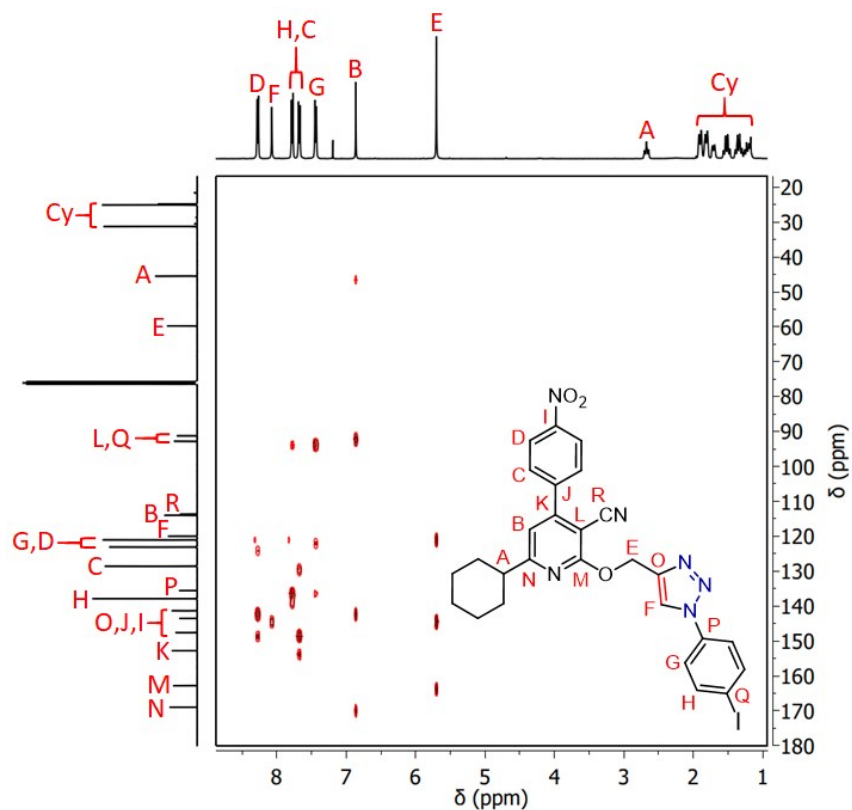
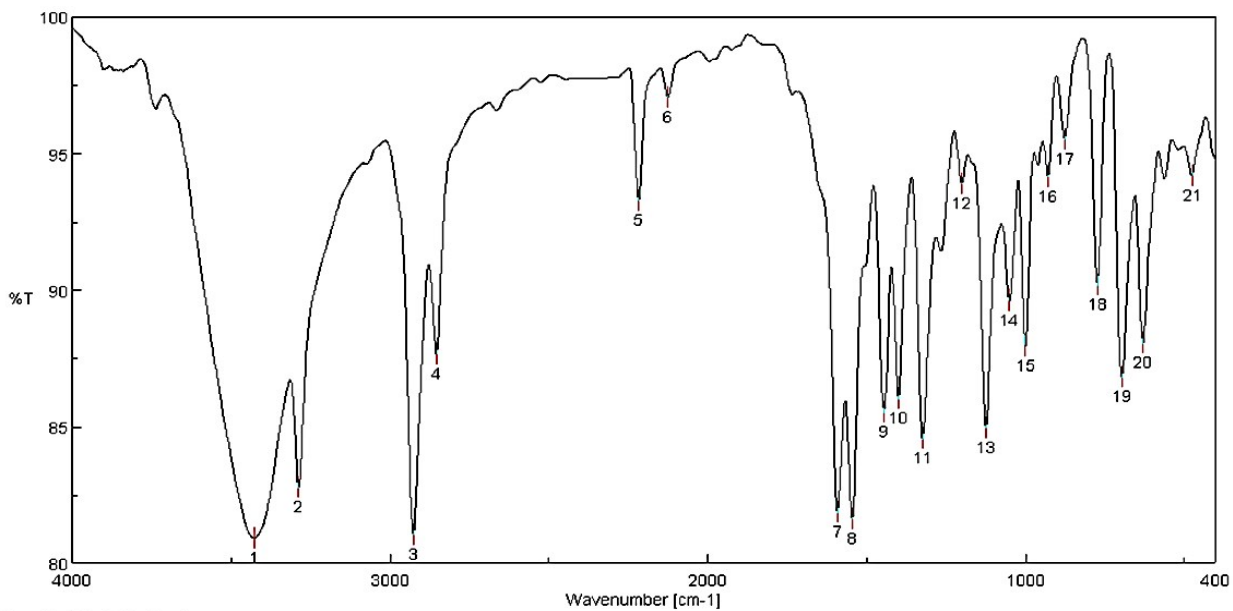


Figure S35. 2D HMBC spectrum of compound **19** (400 MHz, CDCl₃, 25 °C).



[Result of Peak Picking]

No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity
1	3427.85	80.93296	2	3287.07	82.76914	3	2926.45	81.05722	4	2854.13	87.66630
5	2217.74	93.28491	6	2125.17	97.08290	7	1591.95	81.87131	8	1544.7	81.62906
9	1445.39	85.52872	10	1400.07	86.03419	11	1323.89	64.56620	12	1200.47	93.91700
13	1124.3	84.95769	14	1050.05	89.63757	15	999.91	87.96706	16	929.521	94.16153
17	875.524	95.54895	18	773.315	90.19632	19	696.177	86.82561	20	630.609	88.06243
21	475.367	94.21258									

Figure S36. FT-IR spectrum of compound **3**.

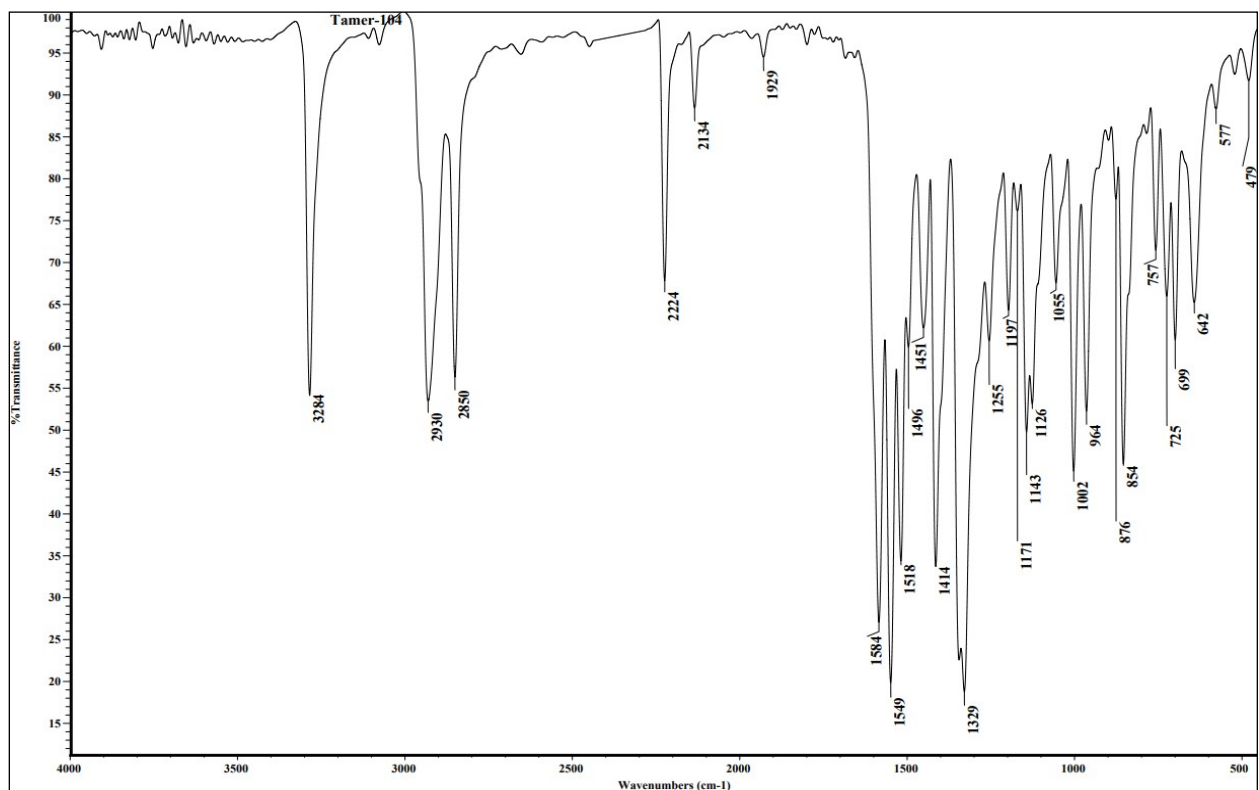
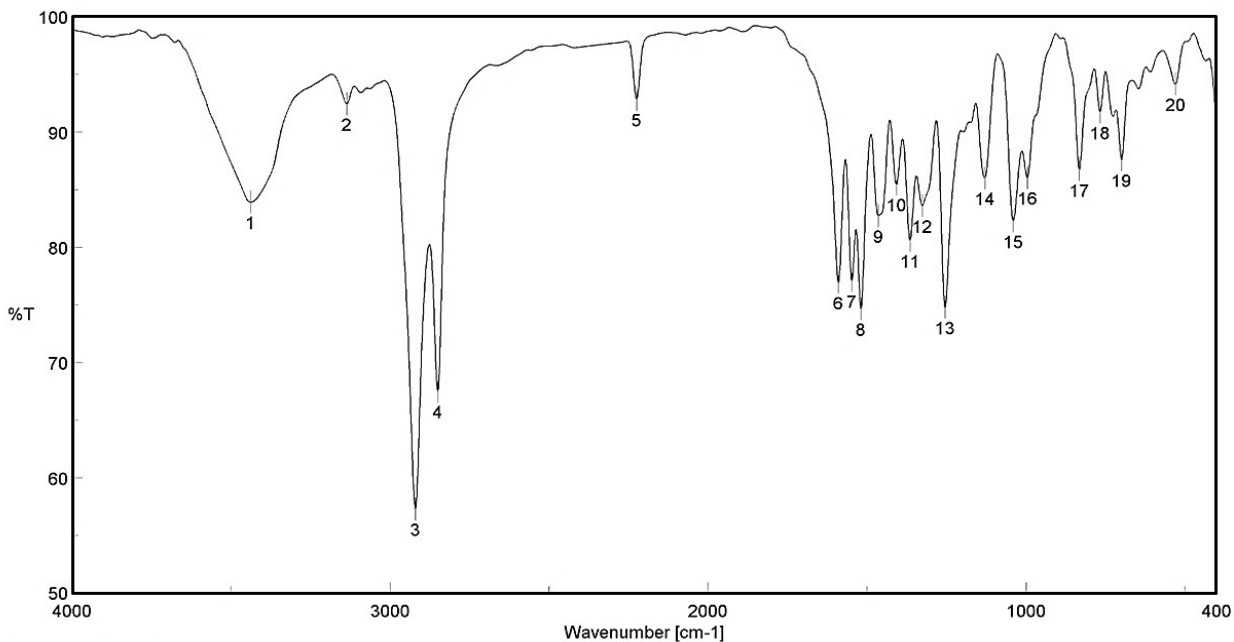


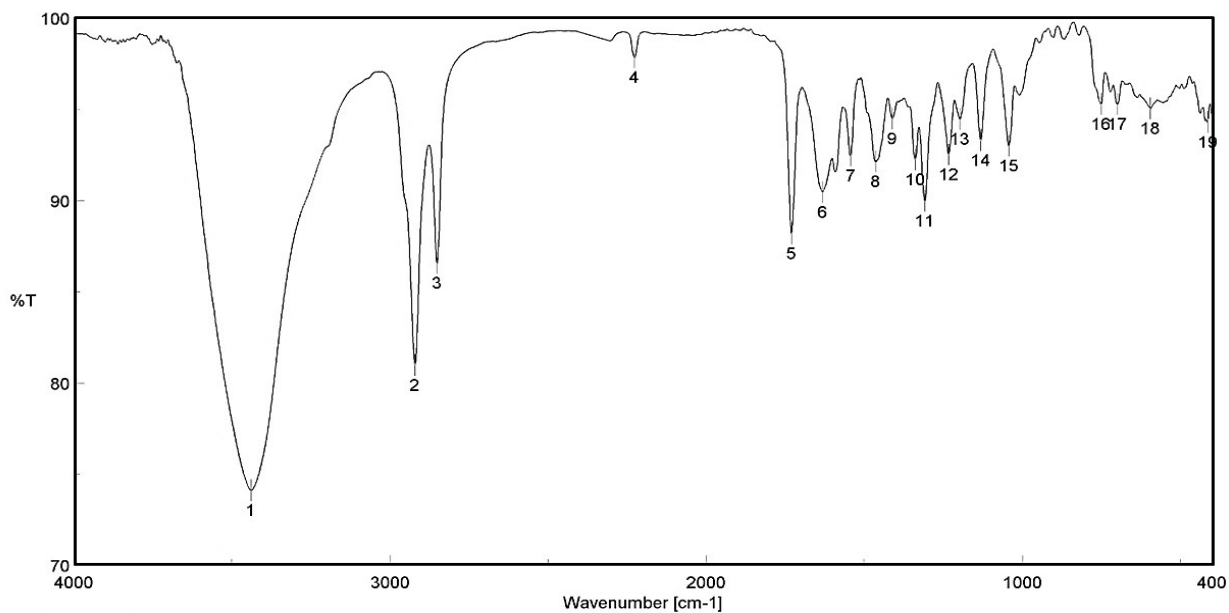
Figure S37. FT-IR spectrum of compound 4.



[Result of Peak Picking]

No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity
1	3438.46	83.89680	2	3135.69	92.41866	3	2919.7	57.26437	4	2849.31	67.48486
5	2224.49	92.82957	6	1590.02	76.92682	7	1547.59	77.08612	8	1518.67	74.63217
9	1463.71	82.71739	10	1406.82	85.43319	11	1364.39	80.57937	12	1325.82	83.59454
13	1254.47	74.76842	14	1129.12	85.99150	15	1039.44	82.26630	16	995.089	86.00856
17	832.133	86.72309	18	766.566	91.72246	19	699.069	87.58270	20	529.364	94.14059

Figure S38. FT-IR spectrum of compound 11.



[Result of Peak Picking]

No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity	No.	Position	Intensity
1	3439.42	74.10635	2	2920.66	80.97165	3	2851.24	86.56443	4	2226.42	97.84769
5	1729.83	88.19122	6	1631.48	90.46043	7	1542.77	92.45591	8	1463.71	92.12446
9	1411.64	94.48469	10	1338.36	92.25015	11	1308.46	89.97881	12	1233.25	92.51637
13	1197.58	94.46706	14	1131.05	93.29150	15	1042.34	92.99705	16	750.174	95.27834
17	699.069	95.28536	18	594.932	95.04222	19	413.656	94.28137			

Figure S39. FT-IR spectrum of compound 12.

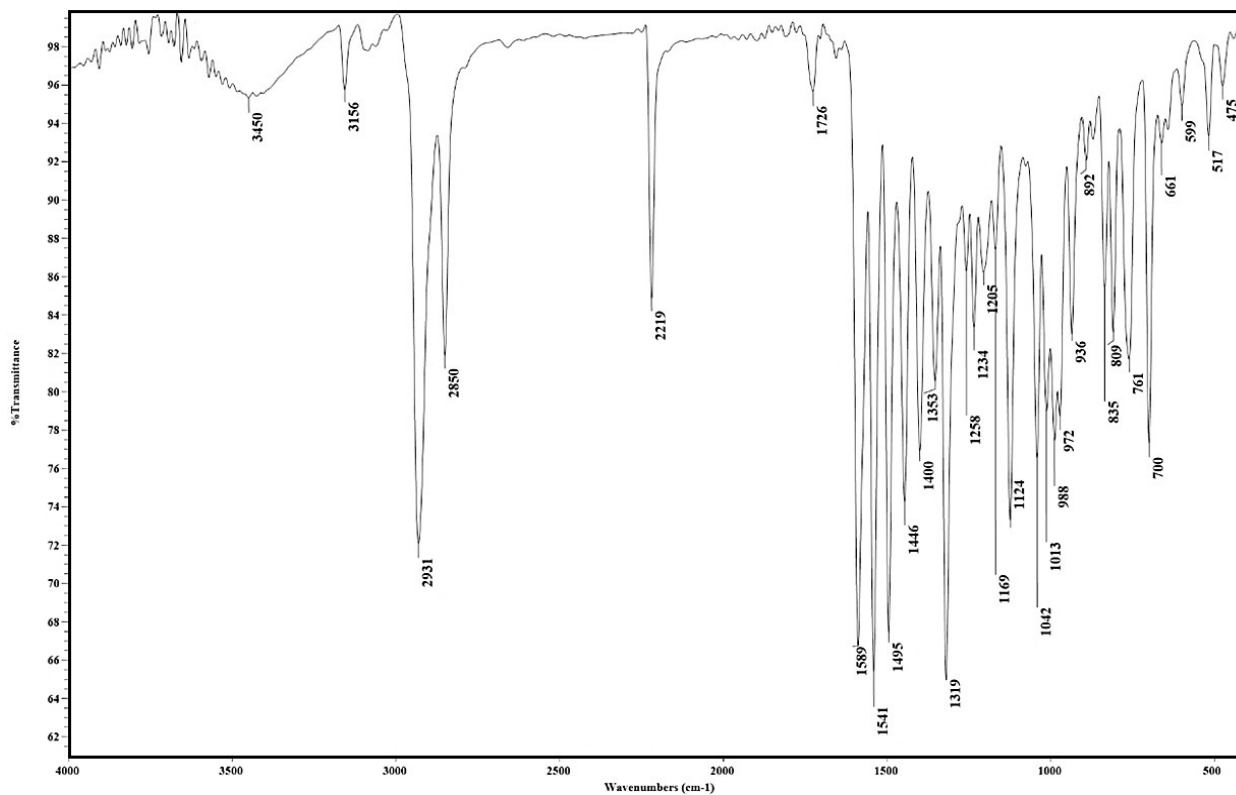


Figure S40. FT-IR spectrum of compound 13.

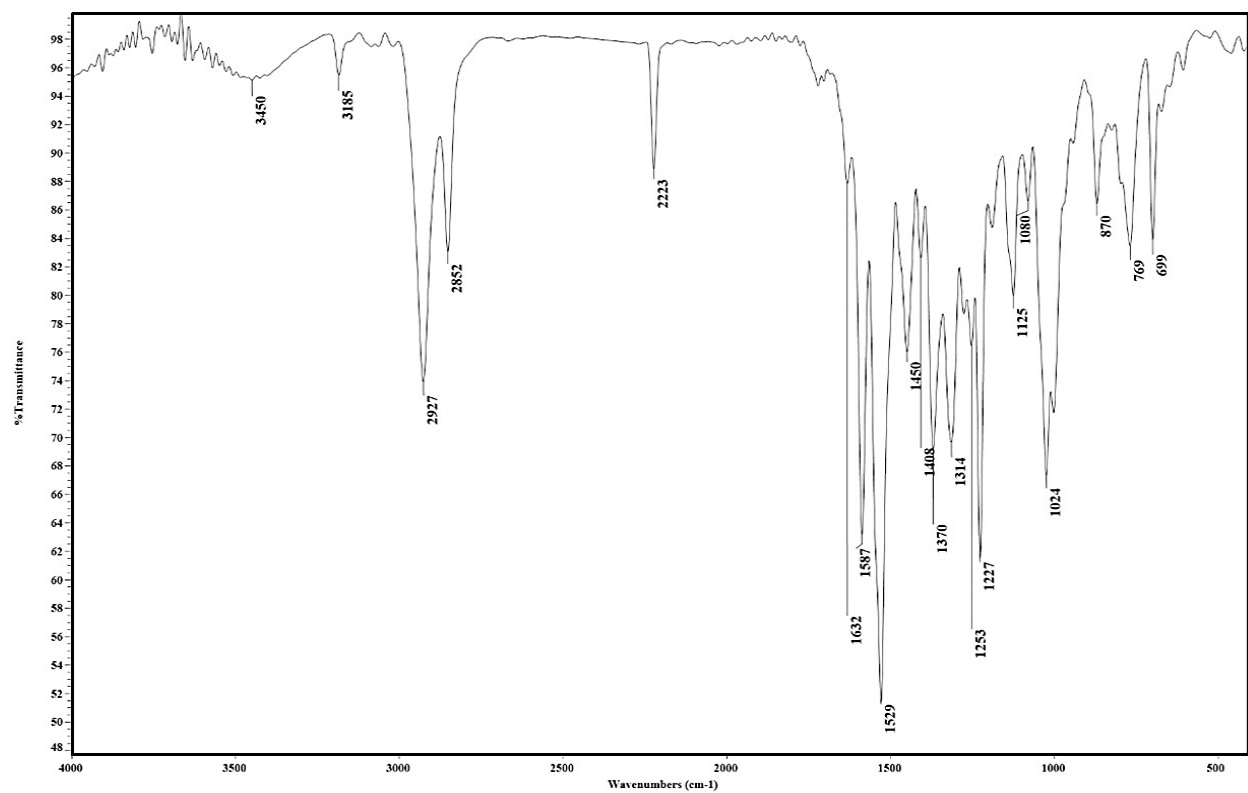


Figure S41. FT-IR spectrum of compound 14.

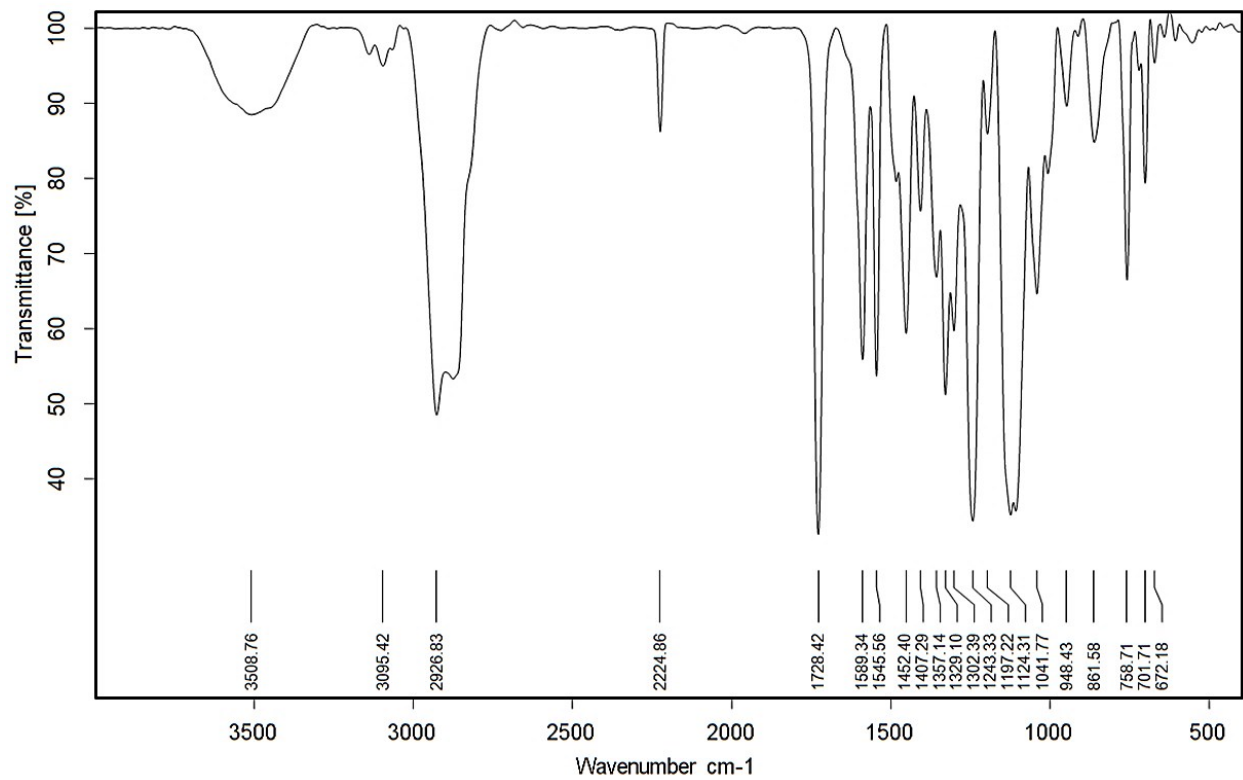


Figure S42. FT-IR spectrum of compound 15.

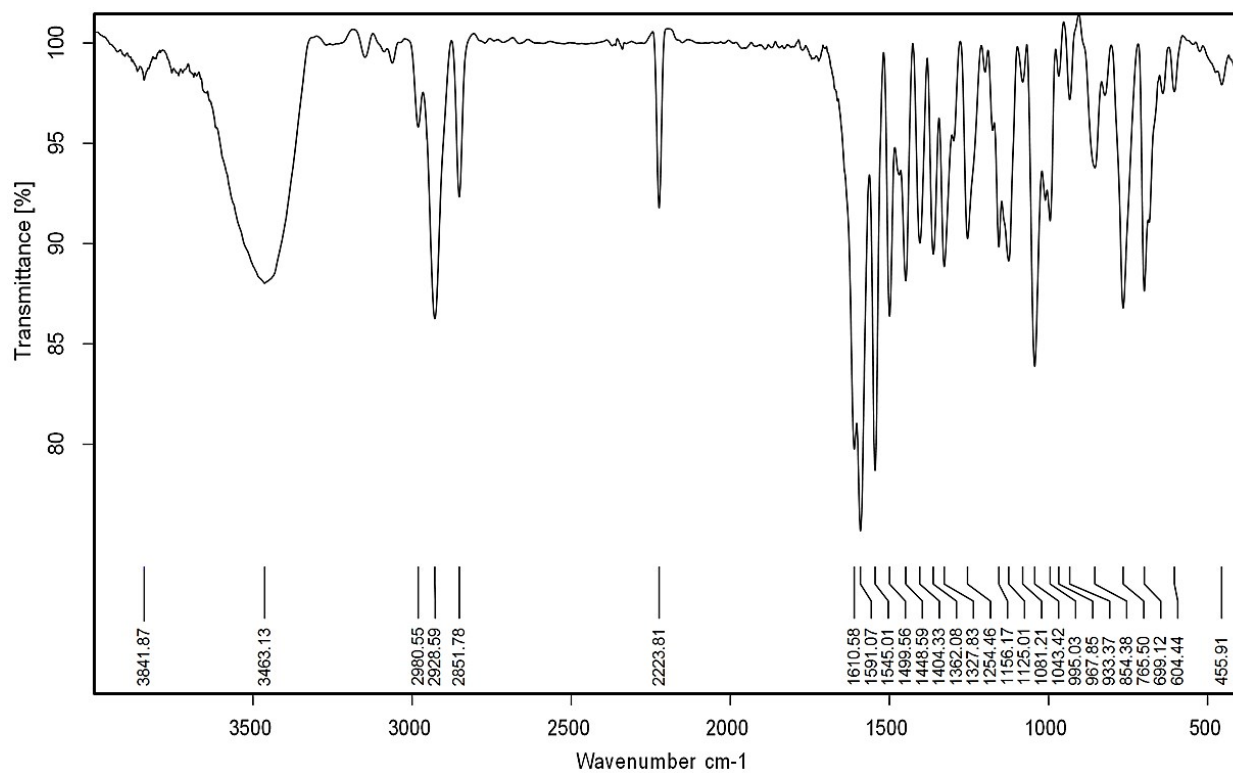


Figure S43. FT-IR spectrum of compound 16.

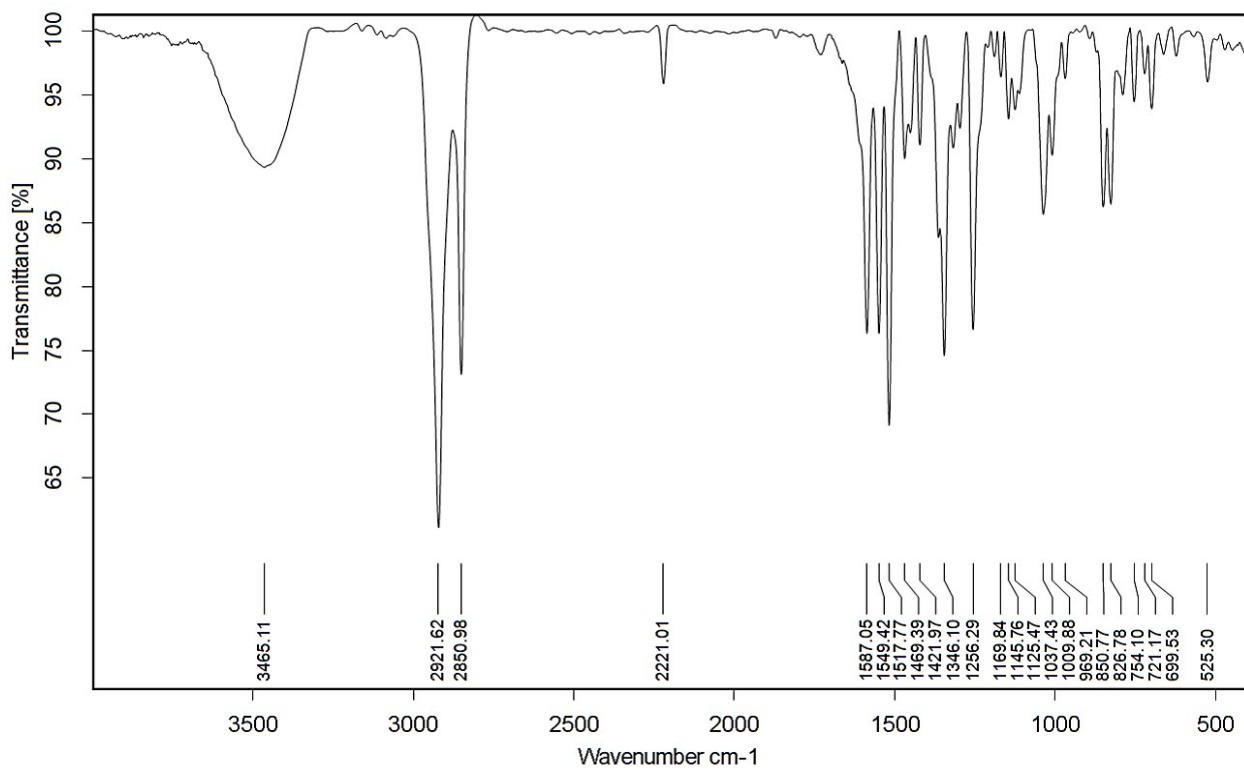


Figure S44. FT-IR spectrum of compound 17.

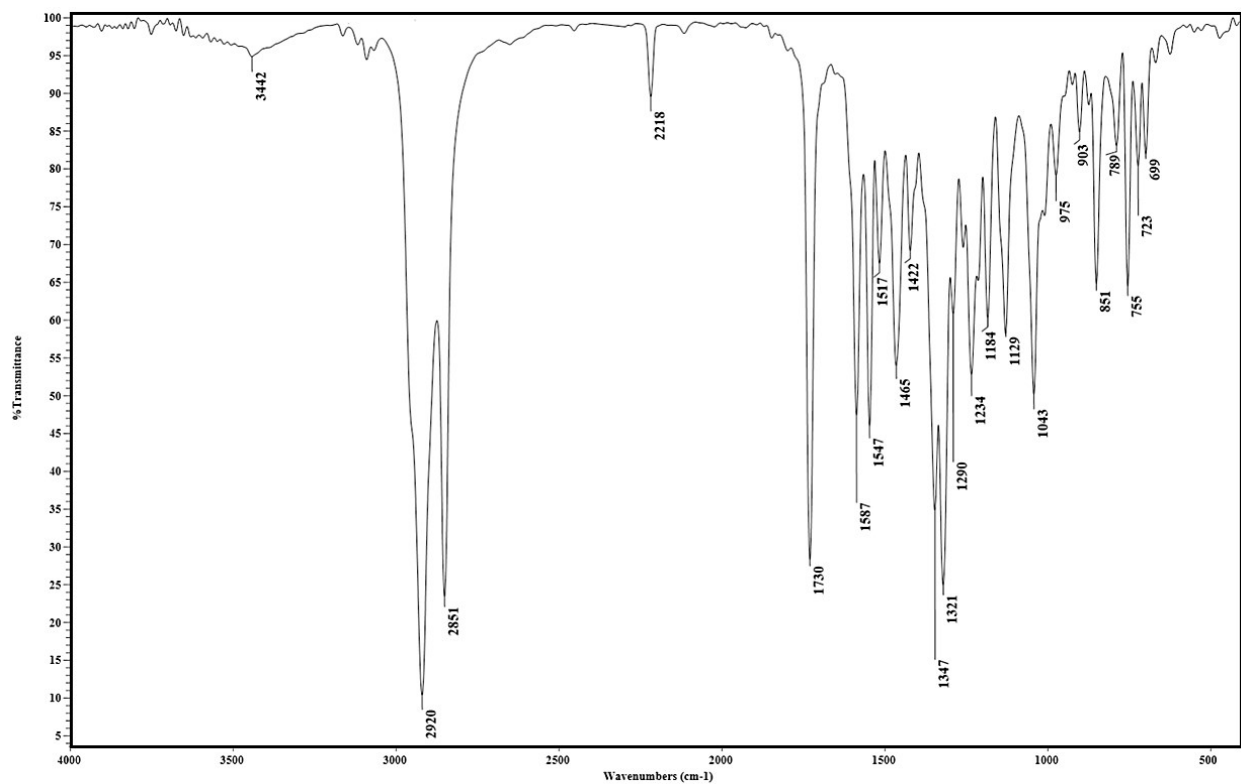


Figure S45. FT-IR spectrum of compound 18.

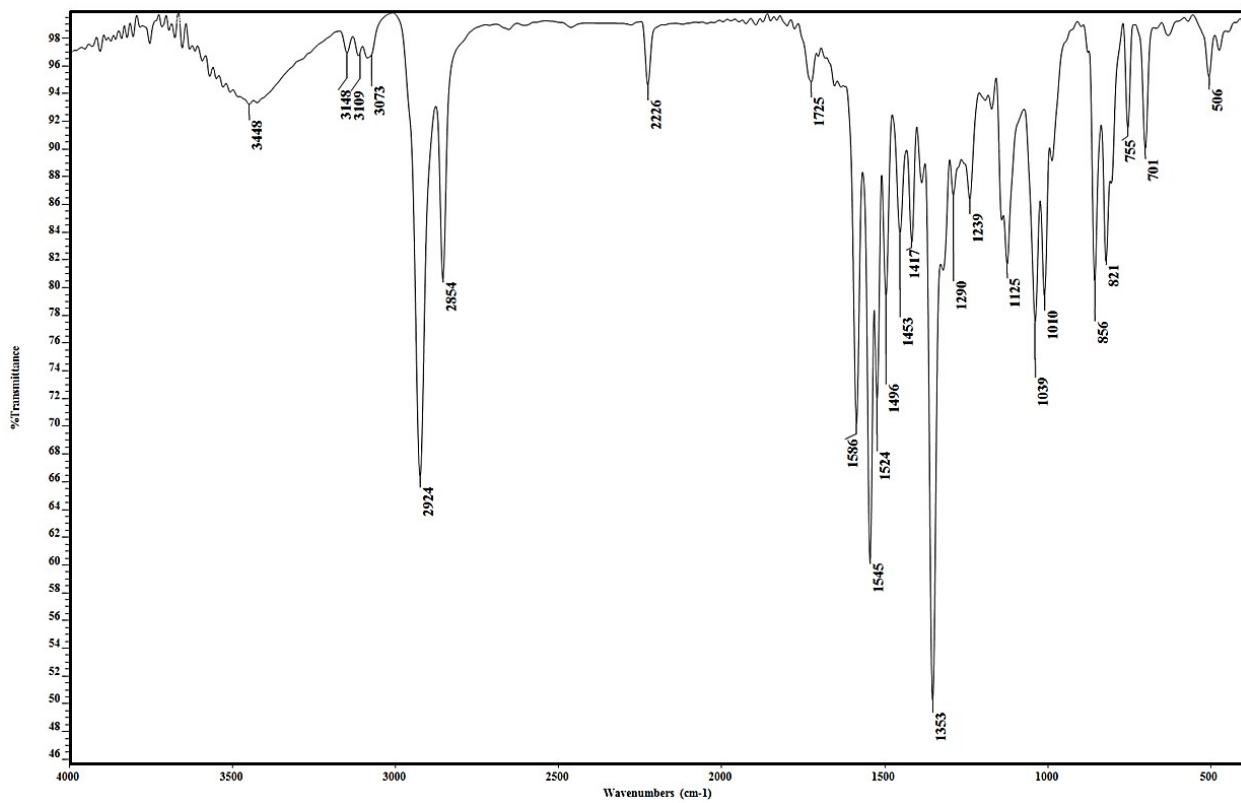


Figure S46. FT-IR spectrum of compound 19.

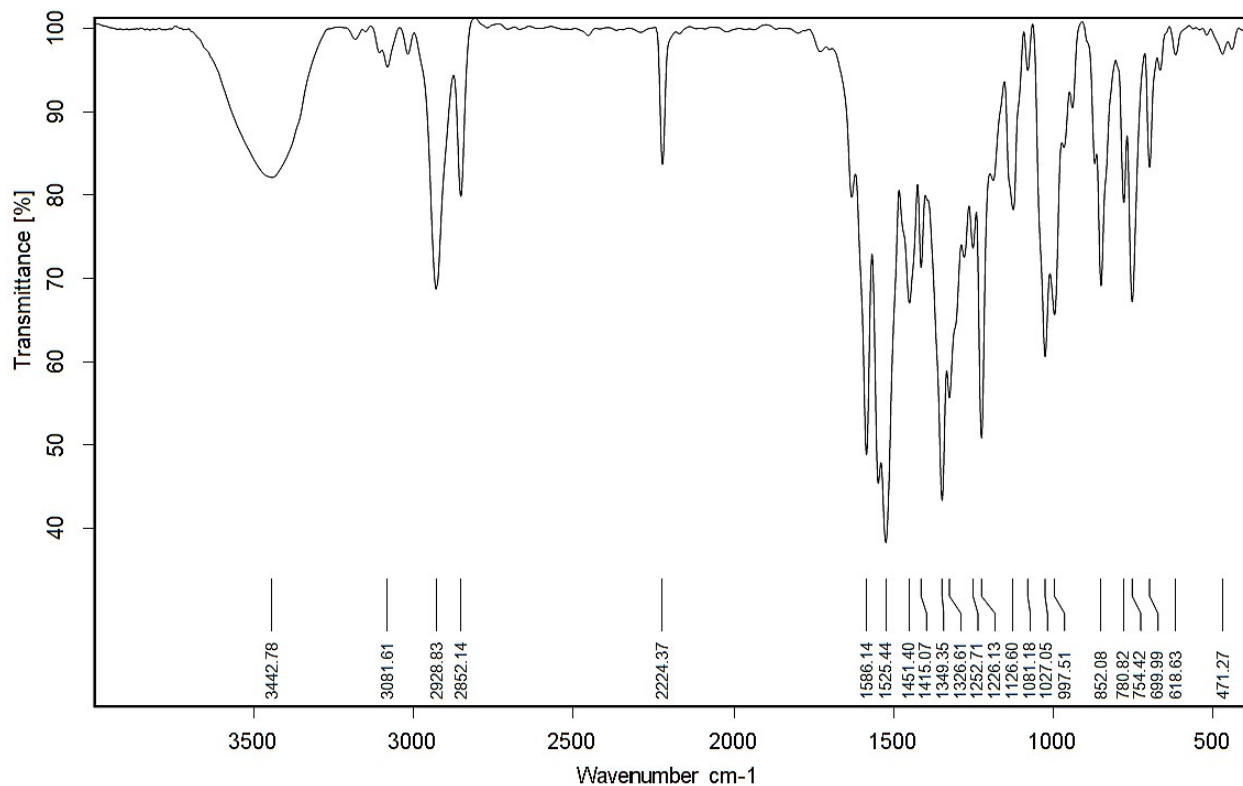


Figure S47. FT-IR spectrum of compound 20.

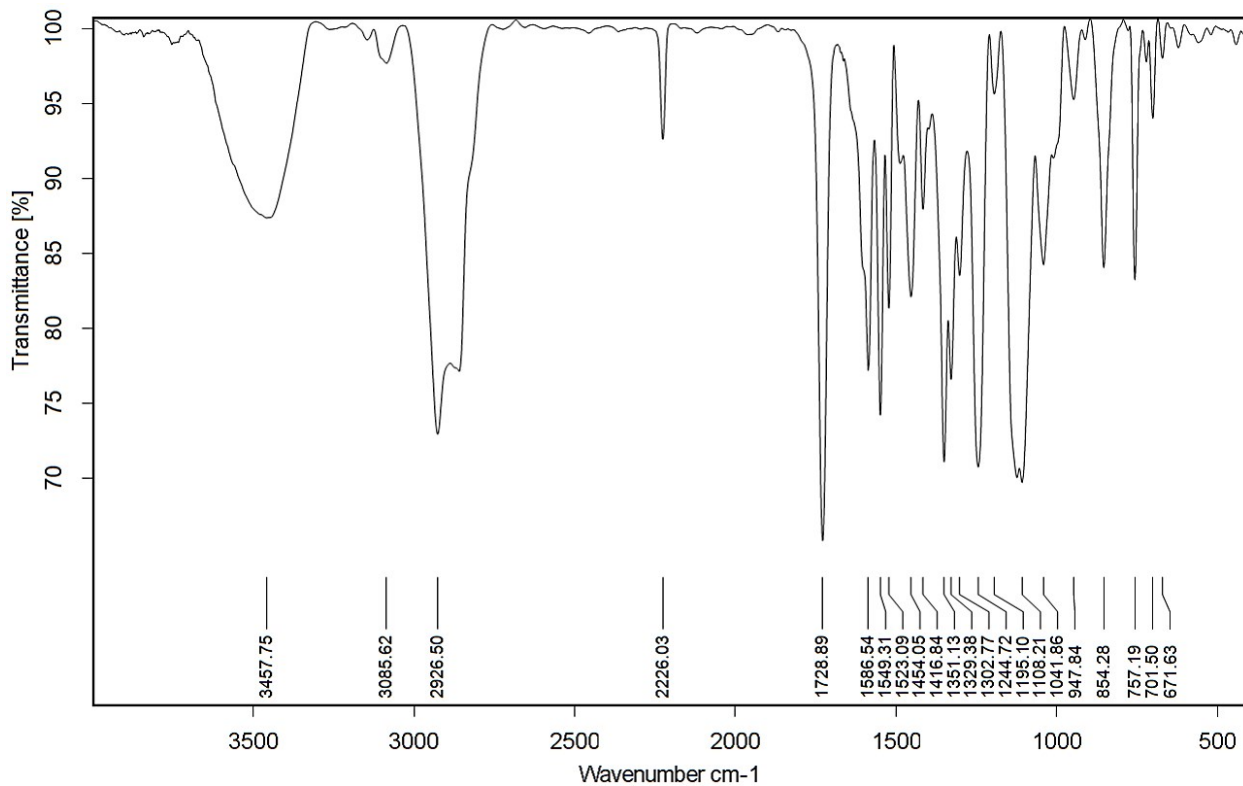


Figure S48. FT-IR spectrum of compound 21.

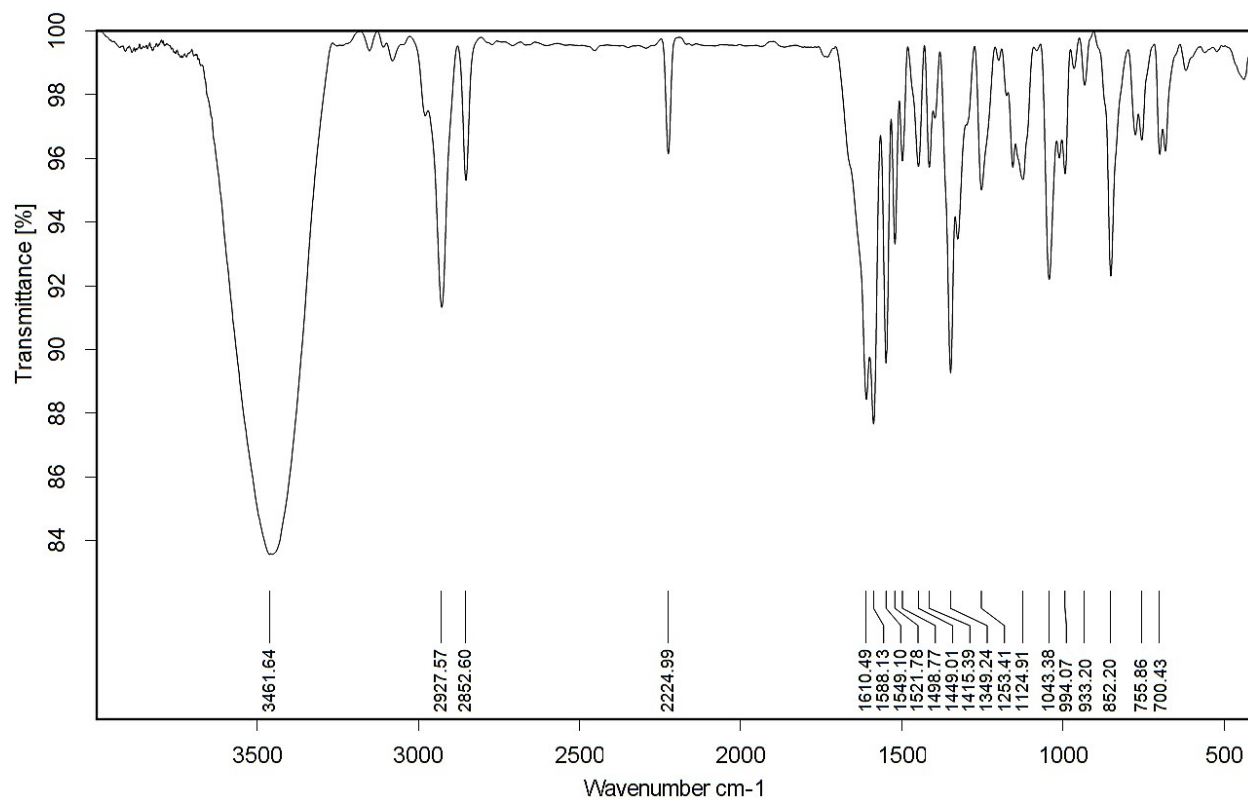


Figure S49. FT-IR spectrum of compound **22**.

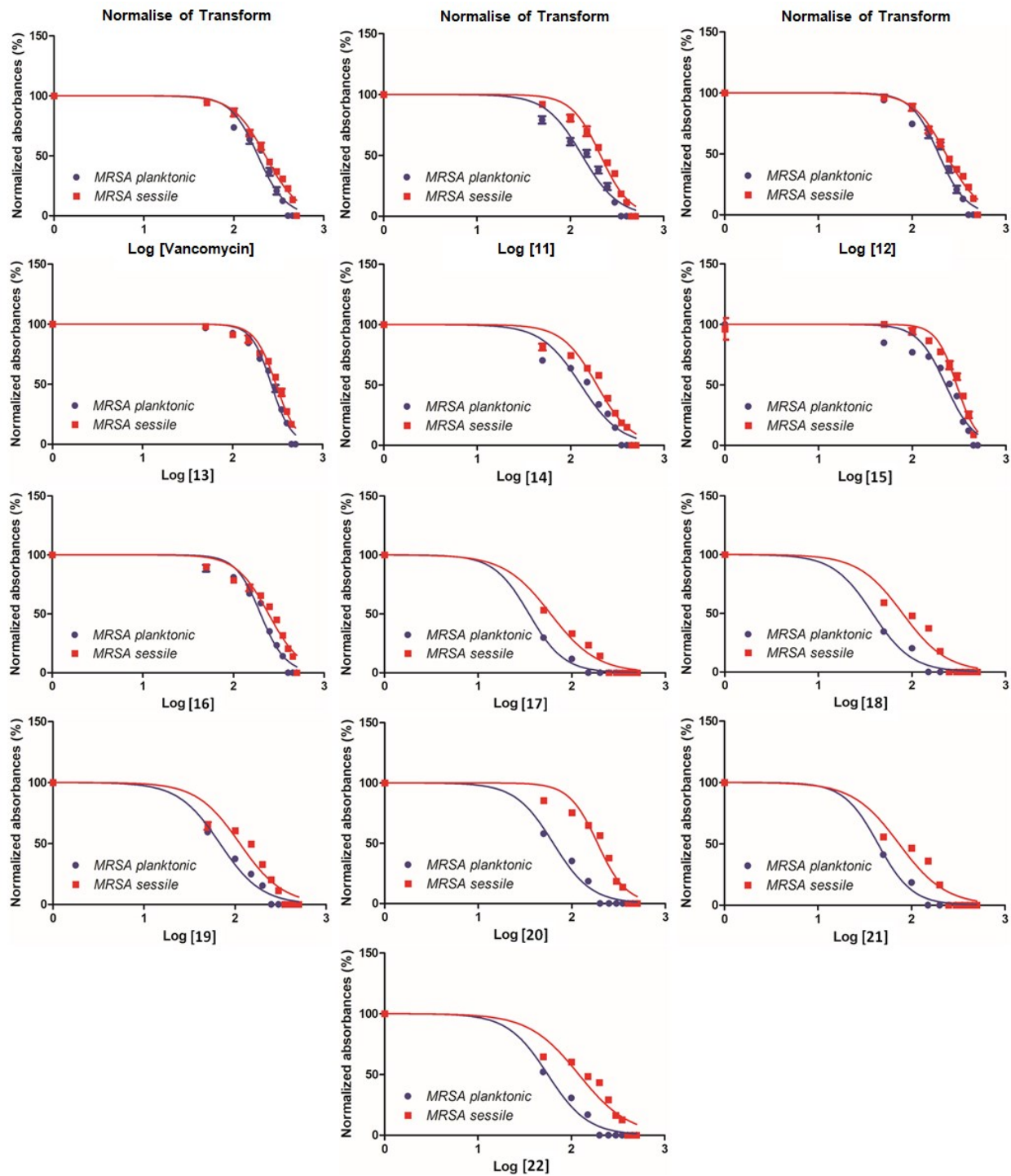


Figure S50. Normalised absorbance (%) of compounds 11-22 against planktonic and sessile MRSA.

Table S1. 2D NMR correlations measured for compound **4**

Spectra	Correlations
¹ H- ¹ H NOESY	H ^A -H ^B , H ^C -H ^D , H ^D -H ^E , H ^E -H ^F
¹ H- ¹ H COSY	H ^E -H ^F
HMBC	H ^B -C ^A (³ J), H ^B -C ^N (² J), H ^B -C ^K (³ J), H ^D -C ^C (³ J), H ^D -C ^J (³ J), H ^D -C ^H (³ J), H ^D -C ^I (² J), H ^D -C ^L (² J), H ^E -C ^F (² J), H ^E -C ^G (³ J), H ^E -C ^I (³ J), H ^F -C ^H (³ J), H ^F -C ^G (² J)
HSQC	H ^C -C ^C , H ^B -C ^B , H ^D -C ^D , H ^E -C ^E , H ^F -C ^F

Table S2. 2D NMR correlations measured for compound **19**

Spectra	Correlations
¹ H- ¹ H NOESY	H ^A -H ^B , H ^B -H ^C , H ^C -H ^D , H ^F -H ^G , H ^G -H ^H
¹ H- ¹ H COSY	H ^C -H ^D , H ^G -H ^H
HMBC	H ^E -C ^F (³ J), H ^E -C ^O (² J), H ^E -C ^M (³ J), H ^B -C ^A (³ J), H ^B -C ^L (³ J), H ^B -C ^J (³ J), H ^B -C ^N (² J), H ^G -C ^Q (³ J), H ^G -C ^H (² J), H ^C -C ^I (³ J), H ^C -C ^K (³ J), H ^H -C ^Q (² J), H ^H -C ^P (³ J), H ^F -C ^O (² J), H ^D -C ^J (³ J), H ^D -C ^I (² J)
HSQC	H ^A -C ^A , H ^E -C ^E , H ^B -C ^B , H ^G -C ^G , H ^C -C ^C , H ^H -C ^H , H ^F -C ^F , H ^D -C ^D

Table S3. Microtox effective concentration levels of toxicity

EC ₅₀ % degree	Toxicity level
0-19	Extremely toxic
20-39	Very toxic
40-59	Toxic
60-79	Moderately toxic
80-99	Light toxic
≥100	Nontoxic