Supporting Information

Design, Synthesis and Antifungal Activity of Novel Longifolene-Derived Diacylhydrazine Compounds

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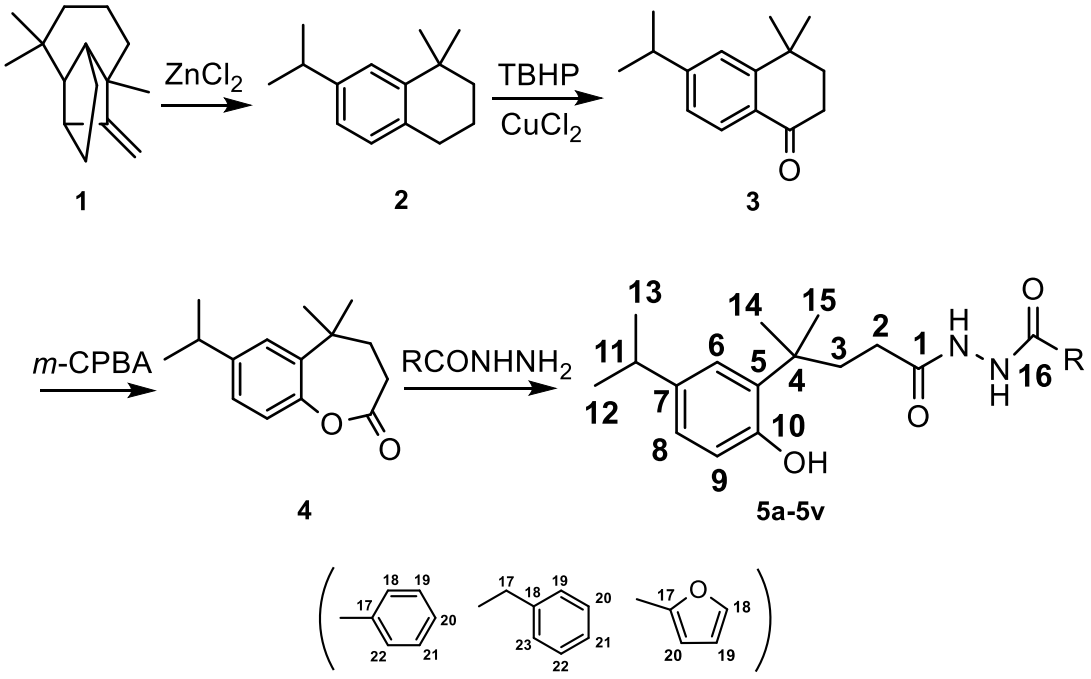


Scheme S1. Synthetic Route of the Longifolene-derived Diacylhydrazine Compounds

5a-**5v** (Table 1).

Table S1. The R Groups of the Compounds **5a**-**5v**.

compounds	R	compounds	R	compounds	R
5a	*o*-I Ph	**5i**	*o*-CF_3 Ph	**5q**	*p*-$C(CH_3)_3$ Ph
5b	2,4-OH Ph	**5j**	*o*-NO_2 Ph	**5r**	Ph
5c	*o*-OH Ph	**5k**	*o*-Cl Ph	**5s**	CH_3
5d	*p*-OCH_3 Ph	**5l**	*m*-Cl Ph	**5t**	CH_2 Ph
5e	*o*-Br Ph	**5m**	*p*-Cl Ph	**5u**	CH_2CN
5f	*p*-Br Ph	**5n**	*p*-CH_3 Ph	**5v**	α-furyl
5g	*p*-F Ph	**5o**	*o*-CH_3 Ph		
5h	*o*-F Ph	**5p**	*p*-CH_2OH Ph		

7-isopropyl-5,5-dimethyl-4,5-dihydrobenzo[b]oxepin-2(3H)-one (**4**). The product is obtained as a colorless oily liquid, yield 77.7%. FT-IR ν (cm^{-1}): 3036 (Ar-H), 2962, 2931, 2872 (C-H), 1769 (C=O), 1607, 1487 (Ar). ^{1}H NMR ($CDCl_3$, 600 MHz): δ 7.18 (d, J = 2.1 Hz, 1H), 7.13 (dd, J = 8.2, 2.1 Hz, 1H), 7.01 (d, J = 8.2 Hz, 1H), 2.92 (dt, J = 13.8, 6.9 Hz, 1H), 2.44 (t, J = 7.2 Hz, 2H), 2.07 (t, J = 7.2 Hz, 2H), 1.43 (s, 6H), 1.26 (d, J = 6.9 Hz, 6H). ^{13}C NMR ($CDCl_3$, 151 MHz): δ 172.46, 149.53, 146.33, 135.67, 125.60, 124.75, 120.62, 41.17, 36.08, 33.90, 30.82, 29.49, 24.12.

N'-(4-(2-hydroxy-5-isopropylphenyl)-4-methylpentanoyl)-2-iodobenzohydrazide (**5a**). The product is obtained as a white powder, yield 78.4%, mp 132.0-132.3℃. FT-IR ν (cm^{-1}): 3373 (N-H, O-H), 3012 (Ar-H), 2958, 2925, 2867 (C-H), 1692 (C=O), 1504, 1461, 1421, 1383 (Ar), 1249, 1211, 1128, 1078 (C-N). ^{1}H NMR (600 MHz, DMSO-d_6): δ 10.06 (s, 1H, -NH), 9.84 (s, 1H, -NH), 9.10 (s, 1H, -OH), 7.90 (d, J = 7.9 Hz, 1H, C_{19}-H), 7.47 (dd, J = 11.1, 4.0 Hz, 1H, C_{20}-H), 7.39 (dd, J = 7.5, 1.3 Hz,

1H, C_{22}-H), 7.20 (td, *J* = 7.7, 1.4 Hz, 1H, C_{21}-H), 6.96 (d, *J* = 1.7 Hz, 1H, C_6-H), 6.89 (dd, *J* = 8.1, 1.9 Hz, 1H, C_8-H), 6.70 (d, *J* = 8.1 Hz, 1H, C_9-H), 2.78 (dt, *J* = 13.6, 6.8 Hz, 1H,C_{11}-H), 2.11 (dd, *J* = 10.4, 6.6 Hz, 2H, C_2-H), 1.88 (dd, *J* = 10.4, 6.6 Hz, 2H, C_3-H), 1.34 (s, 6H, C_{14}-H, C_{15}-H), 1.17 (d, *J* = 6.9 Hz, 6H, C_{12}-H, C_{13}-H). ^{13}C NMR (151 MHz, DMSO-d_6): δ 172.30, 168.10, 154.12, 140.95, 139.89, 138.57, 132.96, 131.83, 129.15, 128.39, 125.88, 124.55, 116.38, 94.17, 37.60, 35.82, 33.33, 30.18, 28.11, 24.81. MS(ESI) *m/z*: 517.13 ($[M+Na]^+$). Anal. Calcd. For $C_{22}H_{27}IN_2O_3$: C, 53.45; H, 5.51; N, 5.67. Found: C, 53.47; H, 5.52; N, 5.67.

2,4-dihydroxy-N'-(4-(2-hydroxy-5-isopropylphenyl)-4-methylpentanoyl)benzohydrazide (**5b**). The product is obtained as a white powder, yield 76.5%, mp 184.4-184.6℃. FT-IR *v* (cm^{-1}): 3504, 3369, 3289 (N-H,O-H), 2960, 2924, 2869(C-H), 1668 (C=O), 1507, 1455, 1420, 1350 (Ar), 1246, 1222, 1176, 1082 (C-N). ^{1}H NMR (600 MHz, DMSO-d_6): δ 12.22 (s, 1H, -OH), 10.19 (s, 2H, -NH, -OH), 9.80 (s, 1H, -NH), 9.10 (s, 1H, -OH), 7.70 (d, *J* = 8.7 Hz, 1H, C_{22}-H), 6.95 (s, 1H, C_6-H), 6.89 (d, *J* = 7.9 Hz, 1H, C_8-H), 6.70 (d, *J* = 8.0 Hz, 1H, C_9-H), 6.32 (d, *J* = 10.0 Hz, 1H, C_{19}-H), 6.28 (s, 1H, C_{21}-H), 2.78 (dt, *J* = 13.4, 6.6 Hz, 1H, C_{11}-H), 2.16 – 2.06 (m, 2H, C_2-H), 1.93 – 1.83 (m, 2H, C_3-H), 1.34 (s, 6H, C_{14}-H, C_{15}-H), 1.17 (d, *J* = 6.8 Hz, 6H, C_{12}-H, C_{13}-H). ^{13}C NMR (151 MHz, DMSO-d_6): δ 172.31, 168.28, 163.04, 162.37, 154.12, 138.58, 132.89, 129.89, 125.89, 124.57, 116.35, 107.88, 106.01, 103.17, 37.60, 35.84, 33.32, 30.19, 28.12, 24.79. MS(ESI) *m/z*: 423.22 ($[M+Na]^+$). Anal. Calcd. For $C_{22}H_{28}N_2O_5$: C, 65.98; H, 7.05; N, 7.00; Found: C, 66.00; H, 7.07; N, 7.01.

2-hydroxy-N'-(4-(2-hydroxy-5-isopropylphenyl)-4-methylpentanoyl)benzohydra

zide (**5c**). The product is obtained as a white powder, yield 76.9%, mp 89.9-90.3℃. FT-IR ν (cm^{-1}): 3268 (N-H, O-H), 3041 (Ar-H), 2958, 2928, 2869 (C-H), 1682 (C=O), 1505, 1488, 1420, 1364 (Ar), 1303, 1242, 1210, 1081 (C-N). ^{1}H NMR (600 MHz, $CDCl_3$): δ 11.12 (s, 1H, -OH), 10.01 (d, J = 2.5 Hz, 1H, -NH), 8.60 (d, J = 1.9 Hz, 1H, -NH), 7.53 (dd, J = 8.0, 1.1 Hz, 1H, C_{22}-H), 7.28 – 7.25 (m, 1H, C_{20}-H), 6.98 (d, J = 1.9 Hz, 1H, C_6-H), 6.86 (dd, J = 8.1, 2.0 Hz, 1H, C_{19}-H), 6.81 (d, J = 8.2 Hz, 1H, C_8-H), 6.71 (t, J = 7.6 Hz, 1H, C_{21}-H), 6.62 (d, J = 8.1 Hz, 1H, C_9-H), 6.44 (s, 1H, -OH), 2.79 (dt, J = 13.8, 6.9 Hz, 1H, C_{11}-H), 2.30 – 2.21 (m, 2H, C_2-H), 2.02 – 1.96 (m, 2H, C_3-H), 1.32 (s, 6H, C_{14}-H, C_{15}-H), 1.18 (d, J = 6.9 Hz, 6H, C_{12}-H, C_{13}-H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 173.94, 167.37, 159.95, 152.31, 140.67, 134.81, 132.58, 127.09, 126.41, 124.84, 119.41, 118.03, 116.74, 112.74, 37.90, 36.12, 33.52, 31.09, 28.13, 24.29. MS(ESI) *m/z*: 407.20 ($[M+Na]^+$). Anal. Calcd. For $C_{22}H_{28}N_2O_4$: C, 68.73; H, 7.34; N, 7.29; Found: C, 68.74; H, 7.36; N, 7.27.

N'-(4-(2-hydroxy-5-isopropylphenyl)-4-methylpentanoyl)-4-methoxybenzohydr azide (**5d**). The product is obtained as a white powder, yield 76.5%, mp 93.7-94.0℃. FT-IR ν (cm^{-1}): 3378, 3265 (N-H, O-H), 3006 (Ar-H), 2958, 2931, 2869, 2842 (C-H), 1676 (C=O), 1504, 1462, 1419 (Ar), 1258, 1174, 1120, 1082, 1028 (C-N). ^{1}H NMR (600 MHz, DMSO-d_6): δ 10.05 (s, 1H, -NH), 9.63 (s, 1H, -NH), 9.09 (s, 1H, -OH), 7.84 (d, J = 8.8 Hz, 2H, C_{18}-H, C_{22}-H), 7.01 (d, J = 8.8 Hz, 2H, C_{19}-H, C_{21}-H), 6.96 (d, J = 1.8 Hz, 1H, C_6-H), 6.89 (dd, J = 8.1, 2.0 Hz, 1H, C_8-H), 6.71 (d, J = 8.1 Hz, 1H, C_9-H), 3.82 (s, 3H, C_{23}-H), 2.78 (dt, J = 13.7, 6.9 Hz, 1H, C_{11}-H), 2.11 (dd, J = 10.5, 6.5 Hz, 2H, C_2-H), 1.88 (dd, J = 10.5, 6.4 Hz, 2H, C_3-H), 1.34 (s, 6H, C_{14}-H, C_{15}-H),

1.17 (d, J = 6.9 Hz, 6H, C_{12}-H, C_{13}-H). ^{13}C NMR (151 MHz, DMSO-d_6): δ 172.66, 165.38, 162.35, 154.13, 138.56, 132.94, 129.73, 125.88, 125.17, 124.55, 116.36, 114.08, 55.83, 37.60, 35.89, 33.32, 30.28, 28.13, 24.80. MS(ESI) *m/z*: 421.23 ($[M+Na]^+$). Anal. Calcd. For $C_{23}H_{30}N_2O_4$: C, 69.32; H, 7.59; N, 7.03; Found: C, 69.36; H, 7.57; N, 7.04.

2-bromo-N'-(4-(2-hydroxy-5-isopropylphenyl)-4-methylpentanoyl)benzohydrazide (**5e**). The product is obtained as a white powder, yield 78.2%, mp 132.5-132.8℃. FT-IR v (cm^{-1}): 3295, 3187(N-H, O-H), 3009 (Ar-H), 2960, 2928, 2868 (C-H), 1693 (C=O), 1505, 1462, 1421 (Ar), 1291, 1223, 1129, 1078 (C-N) . ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.23 (s, 1H, -NH), 9.10 (s, 1H, -NH), 7.55 (d, J = 7.6 Hz, 1H, C_{22}-H), 7.46 (d, J = 7.0 Hz, 1H, C_{19}-H), 7.28 (d, J = 7.5 Hz, 2H, C_{20}-H, C_{21}-H), 6.99 (s, 1H, C_6-H), 6.88 (d, J = 8.0 Hz, 1H, C_8-H), 6.68 – 6.59 (m, 2H, C_9-H, -OH), 2.80 (dt, J = 13.8, 6.9 Hz, 1H, C_{11}-H), 2.27 – 2.20 (m, 2H, C_2-H), 1.99 (d, J = 7.2 Hz, 2H, C_3-H), 1.35 (s, 6H, C_{14}-H, C_{15}-H), 1.20 (d, J = 6.9 Hz, 6H, C_{12}-H, C_{13}-H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 171.81, 164.23, 152.46, 140.43, 134.23, 133.58, 132.72, 132.05, 129.97, 127.48, 126.32, 124.76, 120.03, 116.86, 37.88, 36.14, 33.53, 31.02, 28.22, 24.35. MS(ESI) *m/z*: 469.17 ($[M+Na]^+$). Anal. Calcd. For $C_{22}H_{27}BrN_2O_3$: C, 59.07; H, 6.08; N, 6.26; Found: C, 59.07; H, 6.04; N, 6.27.

4-bromo-N'-(4-(2-hydroxy-5-isopropylphenyl)-4-methylpentanoyl)benzohydrazide (**5f**). The product is obtained as a white powder, yield 77.6%, mp 100.5-100.7℃. FT-IR v (cm^{-1}): 3381, 3259 (N-H, O-H), 3033 (Ar-H), 2958, 2925, 2868 (C-H), 1688 (C=O), 1504, 1479, 1420 (Ar), 1298, 1251, 1218, 1080 (C-N). ^{1}H NMR (600 MHz,

$CDCl_3$): δ 9.86 (s, 1H, -NH), 8.97 (s, 1H, -NH), 7.54 (d, J = 8.4 Hz, 2H, C_{18}-H, C_{22}-H), 7.40 (d, J = 8.4 Hz, 2H, C_{19}-H, C_{21}-H), 6.96 (s, 1H, C_6-H), 6.87 – 6.82 (m, 2H, C_8-H, -OH), 6.60 (d, J = 8.1 Hz, 1H, C_9-H), 2.78 (dt, J = 13.8, 6.9 Hz, 1H, C_{11}-H), 2.23 – 2.17 (m, 2H, C_2-H), 1.95 – 1.90 (m, 2H, C_3-H), 1.29 (s, 6H, C_{14}-H, C_{15}-H), 1.18 (d, J = 6.9 Hz, 6H, C_{12}-H, C_{13}-H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 173.89, 164.81, 152.42, 140.41, 132.65, 131.82, 129.70, 128.92, 127.34, 126.33, 124.73, 116.68, 37.86, 36.37, 33.51, 31.11, 28.13, 24.33. MS(ESI) *m/z*: 469.15 ($[M+Na]^+$). Anal. Calcd. For $C_{22}H_{27}BrN_2O_3$: C, 59.07; H, 6.08; N, 6.26; Found: C, 59.07; H, 6.08; N, 6.29.

4-fluoro-N'-(4-(2-hydroxy-5-isopropylphenyl)-4-methylpentanoyl)benzohydrazide (**5g**). The product is obtained as a white powder, yield 76.3%, mp 86.0-86.3℃. FT-IR v (cm^{-1}): 3378, 3267 (N-H, O-H), 3024 (Ar-H), 2959, 2928, 2869 (C-H), 1688 (C=O), 1501, 1462, 1420 (Ar), 1238, 1160, 1082 (C-N). ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.86 (d, J = 3.0 Hz, 1H, -NH), 9.01 (d, J = 2.9 Hz, 1H, -NH), 7.71 (dd, J = 8.5, 5.3 Hz, 2H, C_{18}-H, C_{22}-H), 6.96 – 6.91 (m, 3H, C_{19}-H, C_{21}-H, -OH), 6.89 (s, 1H, C_6-H), 6.82 (dd, J = 8.1, 1.6 Hz, 1H, C_8-H), 6.60 (d, J = 8.1 Hz, 1H, C_9-H), 2.78 (dt, J = 13.8, 6.9 Hz, 1H, C_{11}-H), 2.23 - 2.17 (m, 2H, C_2-H), 1.95 – 1.89 (m, 2H, C_3-H), 1.28 (s, 6H, C_{14}-H, C_{15}-H), 1.18 (d, J = 6.9 Hz, 6H, C_{12}-H, C_{13}-H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 173.98, 166.02, 164.78, 164.33, 152.47, 140.38, 132.66, 129.91, 127.09, 126.30, 124.70, 116.69, 115.76, 115.61, 37.84, 36.38, 33.50, 31.10, 28.10, 24.30. MS(ESI) *m/z*: 409.22 ($[M+Na]^+$). Anal. Calcd. For $C_{22}H_{27}FN_2O_3$: C, 68.37; H, 7.04; N, 7.25; Found: C, 68.34; H, 7.04; N, 7.27.

2-fluoro-N'-(4-(2-hydroxy-5-isopropylphenyl)-4-methylpentanoyl)benzohydrazide (**5h**). The product is obtained as a white powder, yield 78.5%, mp 143.4-143.6℃. FT-IR ν (cm^{-1}): 3427, 3331, 3243 (N-H, O-H), 3047 (Ar-H), 2959, 2923, 2865 (C-H), 1686 (C=O), 1507, 1484, 1451, 1422 (Ar), 1317, 1263, 1214, 1087 (C-N). ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.72 (d, J = 3.5 Hz, 1H, -NH), 9.37 (dd, J = 11.9, 4.9 Hz, 1H, -NH), 7.91 (td, J = 7.7, 1.7 Hz, 1H, C_{22}-H), 7.53 – 7.46 (m, 1H, C_{19}-H), 7.25 – 7.19 (m, 1H, C_{20}-H), 7.13 (dd, J = 11.8, 8.3 Hz, 1H, C_{21}-H), 6.94 (d, J = 2.0 Hz, 1H, C_6-H), 6.68 (dd, J = 8.1, 2.0 Hz, 1H, C_8-H), 6.62 (d, J = 8.1 Hz, 1H, C_9-H), 6.49 (d, J = 8.3 Hz, 1H, -OH), 2.71 (dt, J = 13.8, 6.9 Hz, 1H, C_{11}-H), 2.32 – 2.24 (m, 2H, C_2-H), 2.03 – 1.97 (m, 2H, C_3-H), 1.35 (s, 6H, C_{14}-H, C_{15}-H), 1.12 (d, J = 6.9 Hz, 6H, C_{12}-H,C_{13}-H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 171.93, 161.37, 160.02, 159.71, 152.52, 140.05, 134.21, 132.65, 131.79, 126.19, 124.90, 124.54, 118.36, 116.50, 116.24, 116.08, 37.74, 36.04, 33.43, 30.86, 28.13, 24.25. MS(ESI) *m/z*: 409.22 ($[M+Na]^+$). Anal. Calcd. For $C_{22}H_{27}FN_2O_3$: C, 68.37; H, 7.04; N, 7.25; Found: C, 68.35; H, 7.04; N, 7.24.

N'-(4-(2-hydroxy-5-isopropylphenyl)-4-methylpentanoyl)-2-(trifluoromethyl)benzohydrazide (**5i**). The product is obtained as a white powder, yield 77.6%, mp 116.1-116.4℃. FT-IR ν (cm^{-1}): 3390, 3265 (N-H, O-H), 3036 (Ar-H), 2960, 2925, 2870 (C-H), 1697 (C=O), 1506, 1482, 1421 (Ar), 1315, 1174, 1131, 1034 (C-N). ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.14 (d, J = 3.5 Hz, 1H, -NH), 8.99 (d, J = 3.6 Hz, 1H, -NH), 7.68 (d, J = 7.3 Hz, 1H, C_{22}-H), 7.57 – 7.49 (m, 3H, C_{19}-H, C_{20}-H, C_{21}-H), 7.01 (d, J = 1.9 Hz, 1H, C_6-H), 6.90 (dd, J = 8.1, 1.9 Hz, 1H, C_8-H), 6.65 (d, J = 8.1 Hz,

2H, C_9-H, -OH), 2.83 (dt, *J* = 13.8, 6.9 Hz, 1H, C_{11}-H), 2.26 – 2.19 (m, 2H, C_2-H), 2.01 – 1.94 (m, 2H, C_3-H), 1.35 (s, 6H, C_{14}-H, C_{15}-H), 1.22 (d, *J* = 6.9 Hz, 6H, C_{12}-H, C_{13}-H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 172.33, 165.07, 152.50, 140.42, 132.67, 132.48 – 131.83, 130.67, 129.01, 128.19, 127.97, 126.58, 126.28, 124.74, 124.17, 122.35, 116.81, 37.83, 36.01, 33.52, 30.93, 29.71, 28.14, 24.31. MS(ESI) *m/z*: 459.21 ($[M+H]^+$). Anal. Calcd. For $C_{23}H_{27}F_3N_2O_3$: C, 63.29; H, 6.24; N, 6.42; Found: C, 63.26; H, 6.25; N, 6.44.

N'-(4-(2-hydroxy-5-isopropylphenyl)-4-methylpentanoyl)-2-nitrobenzohydrazide (**5j**). The product is obtained as a white powder, yield 77.9%, mp 161.4-161.7℃. FT-IR *v* (cm^{-1}): 3454 (N-H, O-H), 3024 (Ar-H), 2961, 2922, 2868 (C-H), 1661 (C=O), 1523, 1361 (-NO_2), 1503, 1469, 1423 (Ar), 1248, 1201, 1130, 1079 (C-N). ^{1}H NMR (600 MHz, DMSO-d_6): δ 10.42 (s, 1H, -NH), 9.97 (s, 1H, -NH), 9.10 (s, 1H, -OH), 8.08 – 8.05 (m, 1H, C_{19}-H), 7.83 (td, *J* = 7.6, 0.8 Hz, 1H, C_{20}-H), 7.74 (td, *J* = 8.1, 1.2 Hz, 1H, C_{21}-H), 7.66 (dd, *J* = 7.5, 1.0 Hz, 1H, C_{22}-H), 6.95 (d, *J* = 1.9 Hz, 1H, C_6-H), 6.89 (dd, *J* = 8.1, 2.0 Hz, 1H, C_8-H), 6.70 (d, *J* = 8.1 Hz, 1H, C_9-H), 2.78 (dt, *J* = 13.8, 6.9 Hz, 1H, C_{11}-H), 2.10 (dd, *J* = 10.4, 6.6 Hz, 2H, C_2-H), 1.89 (dd, *J* = 10.4, 6.6 Hz, 2H, C_3-H), 1.34 (s, 6H, C_{14}-H, C_{15}-H), 1.17 (d, *J* = 6.9 Hz, 6H, C_{12}-H, C_{13}-H). ^{13}C NMR (151 MHz, DMSO-d_6): δ 172.32, 164.77, 154.11, 147.67, 138.57, 134.11, 132.94, 131.82, 130.84, 129.95, 125.88, 124.70, 124.55, 116.37, 39.45 – 39.11, 37.60, 35.83, 33.32, 30.15, 28.08, 24.79. MS(ESI) *m/z*: 436.21 ($[M+Na]^+$). Anal. Calcd. For $C_{22}H_{27}N_3O_5$: C, 63.91; H, 6.58; N, 10.16; Found: C, 63.93; H, 6.55; N, 10.17.

2-chloro-N'-(4-(2-hydroxy-5-isopropylphenyl)-4-methylpentanoyl)benzohydrazi

de (**5k**). The product is obtained as a white powder, yield 75.7%, mp 109.5-109.7℃. FT-IR v (cm^{-1}): 3438, 3263 (N-H, O-H), 3032 (Ar-H), 2956, 2925, 2868 (C-H), 1706 (C=O), 1508, 1421, 1364 (Ar), 1293, 1251, 1208, 1081 (C-N). ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.49 (d, J = 8.4 Hz, 1H, -NH), 9.33 (d, J = 11.3 Hz, 1H, -NH), 7.56 (d, J = 7.7 Hz, 1H, C_{22}-H), 7.36 (q, J = 8.0 Hz, 2H, C_{19}-H, C_{20}-H), 7.27 – 7.23 (m, 1H, C_{21}-H), 7.00 (d, J = 1.9 Hz, 1H, C_6-H), 6.87 (dd, J = 8.1, 1.9 Hz, 1H, C_8-H), 6.73 (s, 1H, -OH), 6.67 (d, J = 8.1 Hz, 1H, C_9-H), 2.82 (dt, J = 13.8, 6.9 Hz, 1H, C_{11}-H), 2.26 (dd, J = 9.8, 6.8 Hz, 2H, C_2-H), 2.02 (dd, J = 9.8, 6.7 Hz, 2H, C_3-H), 1.36 (s, 6H, C_{14}-H, C_{15}-H), 1.21 (d, J = 6.9 Hz, 6H, C_{12}-H, C_{13}-H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 171.92, 163.26, 152.56, 140.27, 132.69, 132.07, 131.67, 131.48, 130.38, 126.98, 126.26, 124.72, 116.78, 37.83, 36.16, 33.52, 30.96, 28.19, 24.34. MS(ESI) *m/z*: 403.32 ($[M+H]^+$). Anal. Calcd. For $C_{22}H_{27}ClN_2O_3$: C, 65.58; H, 6.75; N, 6.95; Found: C, 65.57; H, 6.73; N, 6.96.

3-chloro-N'-(4-(2-hydroxy-5-isopropylphenyl)-4-methylpentanoyl)benzohydrazide (**5l**). The product is obtained as a white powder, yield: 77.5%, mp 153.0-153.2℃. FT-IR v (cm^{-1}): 3437, 3261 (N-H, O-H), 3033 (Ar-H), 2959, 2925, 2869 (C-H), 1706 (C=O), 1507, 1466, 1420 (Ar), 1293, 1253, 1217, 1081 (C-N). ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.99 (d, J = 3.4 Hz, 1H, -NH), 9.06 (d, J = 3.4 Hz, 1H, -NH), 7.68 (s, 1H, C18-H), 7.57 (d, J = 7.8 Hz, 1H, C22-H), 7.40 (dd, J = 8.0, 1.1 Hz, 1H, C20-H), 7.20 (t, J = 7.9 Hz, 1H, C21-H), 6.95 (d, J = 1.9 Hz, 1H, C6-H), 6.82 (dd, J = 8.1, 1.9 Hz, 1H, C8-H), 6.73 (s, 1H, -OH), 6.60 (d, J = 8.1 Hz, 1H, C9-H), 2.78 (dt, J = 13.8, 6.9 Hz, 1H, C11-H), 2.20 (dd, J = 9.8, 6.8 Hz, 2H, C2-H), 1.93 (dd, J = 9.7, 6.8 Hz, 2H,

C3-H), 1.28 (s, 6H, C14-H, C15-H), 1.18 (d, J = 6.9 Hz, 6H, C12-H, C13-H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 173.82, 164.30, 152.43, 140.38, 134.82, 132.63, 132.38, 129.87, 127.89, 126.30, 125.28, 124.72, 116.72, 37.85, 36.36, 33.50, 31.12, 28.13, 24.32. MS(ESI) *m/z*: 403.22 ($[M+H]^+$). Anal. Calcd. For $C_{22}H_{27}ClN_2O_3$: C, 65.58; H, 6.75; N, 6.95; Found: C, 65.55; H, 6.75; N, 6.96.

4-chloro-N'-(4-(2-hydroxy-5-isopropylphenyl)-4-methylpentanoyl)benzohydrazide (**5m**). The product is obtained as a white powder, yield 76.6%, mp 92.7-92.9℃. FT-IR v (cm^{-1}): 3372, 3256 (N-H, O-H), 3036 (Ar-H), 2958, 2925, 2868 (C-H), 1691 (C=O), 1505, 1482, 1420 (Ar), 1251, 1095, 1082 (C-N). ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.87 (s, 1H, -NH), 8.99 (s, 1H, -NH), 7.62 (d, J = 8.5 Hz, 2H, C_{18}-H, C_{22}-H), 7.24 (d, J = 8.5 Hz, 2H, C_{19}-H, C_{21}-H), 6.96 (d, J = 1.8 Hz, 1H, C_6-H), 6.87 (s, 1H, -OH), 6.83 (dd, J = 8.1, 1.9 Hz, 1H, C_8-H), 6.60 (d, J = 8.1 Hz, 1H, C_9-H), 2.78 (dt, J = 13.8, 6.9 Hz, 1H, C_{11}-H), 2.23 – 2.17 (m, 2H, C_2-H), 1.95 – 1.90 (m, 2H, C_3-H), 1.29 (s, 6H, C_{14}-H, C_{15}-H), 1.18 (d, J = 6.9 Hz, 6H, C_{12}-H, C_{13}-H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 173.90, 164.72, 152.43, 140.41, 138.77, 132.65, 129.25, 128.82, 126.32, 124.72, 116.68, 37.85, 36.37, 33.50, 31.11, 28.12, 24.31. MS(ESI) *m/z*: 425.20 ($[M+Na]^+$). Anal. Calcd. For $C_{22}H_{27}ClN_2O_3$: C, 65.58; H, 6.75; N, 6.95; Found: C, 65.57; H, 6.74; N, 6.95.

N'-(4-(2-hydroxy-5-isopropylphenyl)-4-methylpentanoyl)-4-methylbenzohydrazide (**5n**). The product is obtained as a white powder, yield 78.6%, mp 80.5-80.7℃. FT-IR v (cm^{-1}): 3385, 3244 (N-H, O-H), 3028 (Ar-H), 2956, 2925, 2867 (C-H), 1681 (C=O), 1505, 1480, 1419 (Ar), 1341, 1248, 1193, 1031, 1081 (C-N). ^{1}H NMR (600

MHz, $CDCl_3$): δ 9.63 (d, J = 3.6 Hz, 1H, -NH), 9.19 (d, J = 3.6 Hz, 1H,-NH), 7.61 (d, J = 8.1 Hz, 2H, C_{18}-H, C_{22}-H), 7.08 (d, J = 8.1 Hz, 2H, C_{19}-H, C_{21}-H), 7.06 (s, 1H, -OH), 6.94 (d, J = 1.8 Hz, 1H, C_6-H), 6.79 (dd, J = 8.1, 1.8 Hz, 1H, C_8-H), 6.62 (d, J = 8.1 Hz, 1H, C_9-H), 2.77 (dt, J = 13.8, 6.9 Hz, 1H, C_{11}-H), 2.32 (s, 3H, C_{23}-H), 2.23 – 2.18 (m, 2H, C_2-H), 1.94 – 1.88 (m, 2H, C_3-H), 1.28 (s, 6H, C_{14}-H, C_{15}-H), 1.17 (d, J = 6.9 Hz, 6H, C_{12}-H, C_{13}-H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 173.40, 165.62, 152.63, 142.88, 140.08, 132.73, 129.23, 128.24, 127.41, 126.21, 124.63, 116.77, 37.82, 36.37, 33.49, 31.10, 28.14, 24.31, 21.50. MS(ESI) *m/z*: 405.23 ($[M+Na]^+$). Anal. Calcd. For $C_{23}H_{30}N_2O_3$: C, 72.22; H, 7.91; N, 7.32; Found: C, 72.24; H, 7.92; N, 7.33.

N'-(4-(2-hydroxy-5-isopropylphenyl)-4-methylpentanoyl)-2-methylbenzohydrazide (**5o**). The product is obtained as a white powder, yield 78.4%, mp 127.5-127.8°C. FT-IR v (cm^{-1}): 3392, 3253 (N-H, O-H), 3047 (Ar-H), 2960, 2928, 2872 (C-H), 1678 (C=O), 1506, 1455, 1421 (Ar), 1316, 1261, 1212,1082 (C-N). ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.15 (s, 1H, -NH), 8.97 (s, 1H, -NH), 7.33 (d, J = 7.6 Hz, 1H, C_{22}-H), 7.29 (t, J = 7.5 Hz, 1H, C_{20}-H), 7.15 (d, J = 7.6 Hz, 1H, C_{19}-H), 7.09 (t, J = 7.5 Hz, 1H, C_{21}-H), 6.96 (s, 1H, C_6-H), 6.89 (s, 1H, -OH), 6.82 (d, J = 8.0 Hz, 1H, C_8-H), 6.59 (d, J = 8.0 Hz, 1H, C_9-H), 2.79 (dt, J = 13.7, 6.9 Hz, 1H, C_{11}-H), 2.32 (s, 3H, C_{23}-H), 2.22 – 2.17 (m, 2H, C_2-H), 1.98 – 1.89 (m, 2H, C_3-H), 1.31 (s, 6H, C_{14}-H, C_{15}-H), 1.18 (d, J = 6.9 Hz, 6H, C_{12}-H, C_{13}-H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 172.49, 167.41, 152.62, 140.23, 137.16, 132.74, 132.34, 131.19, 130.87, 127.49, 126.24, 125.74, 124.68, 116.77, 37.80, 36.14, 33.52, 31.01, 28.19, 24.34, 19.84. MS(ESI) *m/z*:

405.24 ($[M+Na]^+$). Anal. Calcd. For $C_{23}H_{30}N_2O_3$: C, 72.22; H, 7.91; N, 7.32; Found: C, 72.22; H, 7.92; N, 7.32.

N'-(4-(2-hydroxy-5-isopropylphenyl)-4-methylpentanoyl)-4-(hydroxymethyl)benzohydrazide (**5p**). The product is obtained as a white powder, yield 78.8%, mp 167.3-167.5℃. FT-IR ν (cm^{-1}): 3384, 3247 (N-H, O-H), 3107, 3033 (Ar-H), 2961, 2923, 2867 (C-H), 1698 (C=O), 1508, 1479, 1422, 1361 (Ar), 1253, 1212, 1082 (C-N). ^{1}H NMR (600 MHz, DMSO-d_6): δ 10.16 (s, 1H, -NH), 9.69 (s, 1H, -NH), 9.13 (s, 1H, -OH), 7.81 (d, J = 8.2 Hz, 2H, C_{18}-H, C_{22}-H), 7.41 (d, J = 8.1 Hz, 2H, C_{19}-H, C_{21}-H), 6.96 (d, J = 1.8 Hz, 1H, C_6-H), 6.89 (dd, J = 8.1, 1.9 Hz, 1H, C_8-H), 6.70 (d, J = 8.1 Hz, 1H, C_9-H), 5.37 (t, J = 5.7 Hz, 1H, -OH), 4.56 (d, J = 5.6 Hz, 2H, C_{23}-H), 2.78 (dt, J = 13.7, 6.9 Hz, 1H, C_{11}-H), 2.11 (dd, J = 10.4, 6.5 Hz, 2H, C_2-H), 1.88 (dd, J = 10.4, 6.5 Hz, 2H, C_3-H), 1.34 (s, 6H, C_{14}-H, C_{15}-H), 1.17 (d, J = 6.9 Hz, 6H, C_{12}-H, C_{13}-H). ^{13}C NMR (151 MHz, DMSO-d_6): δ 172.68, 165.86, 154.11, 146.90, 138.60, 132.95, 131.32, 127.72, 126.54, 125.89, 124.57, 116.36, 62.88, 37.59, 35.86, 33.31, 30.27, 28.11, 24.79. MS(ESI) *m/z*: 421.25 ($[M+Na]^+$). Anal. Calcd. For $C_{23}H_{30}N_2O_4$: C, 69.32; H, 7.59; N, 7.03; Found: C, 69.34; H, 7.57; N, 7.04.

4-(tert-butyl)-N'-(4-(2-hydroxy-5-isopropylphenyl)-4-methylpentanoyl)benzohydrazide (**5q**). The product is obtained as a white powder, yield: 76.8%, mp 97.7-97.9℃. FT-IR ν (cm^{-1}): 3372, 3258 (N-H, O-H), 3036 (Ar-H), 2961, 2931, 2908, 2869 (C-H), 1688 (C=O), 1505, 1420, 1364 (Ar), 1255, 1125, 1082 (C-N). ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.68 (d, J = 3.6 Hz, 1H, -NH), 9.19 (d, J = 3.6 Hz, 1H, -NH), 7.66 (d, J = 8.4 Hz, 2H, C_{18}-H, C_{22}-H), 7.30 (d, J = 8.4 Hz, 2H, C_{19}-H, C_{21}-H), 7.08 (s,

1H, -OH), 6.94 (d, *J* = 1.7 Hz, 1H, C_6-H), 6.78 (dd, *J* = 8.1, 1.8 Hz, 1H, C_8-H), 6.63 (d, *J* = 8.1 Hz, 1H, C_9-H), 2.76 (dt, *J* = 13.8, 6.9 Hz, 1H, C_{11}-H), 2.22 (dd, *J* = 9.8, 6.8 Hz, 2H, C_2-H), 1.94 – 1.88 (m, 2H, C_3-H), 1.28 (s, 6H, C_{14}-H, C_{15}-H), 1.27 (s, 9H, C_{24}-H, C_{25}-H, C_{26}-H), 1.16 (d, *J* = 6.9 Hz, 6H, C_{12}-H, C_{13}-H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 173.52, 165.52, 155.84, 152.64, 140.05, 132.72, 128.12, 127.26, 126.20, 125.52, 124.63, 116.78, 37.83, 36.38, 34.95, 33.49, 31.08, 28.17, 24.33. MS(ESI) *m/z*: 425.35 ($[M+H]^+$). Anal. Calcd. For $C_{26}H_{36}N_2O_3$: C, 73.55; H, 8.55; N, 6.60; Found: C, 73.52; H, 8.53; N, 6.61.

N'-(4-(2-hydroxy-5-isopropylphenyl)-4-methylpentanoyl)benzohydrazide (**5r**). The product is obtained as a white powder, yield 78.7%, mp 178.4-178.7℃. FT-IR *v* (cm^{-1}): 3381, 3318, 3244 (N-H, O-H), 3053, 3027 (Ar-H), 2959, 2928, 2868 (C-H), 1685 (C=O), 1508, 1485, 1420 (Ar), 1256, 1218, 1081 (C-N). ^{1}H NMR (600 MHz, DMSO-d_6): δ 10.21 (s, 1H, -NH), 9.71 (s, 1H, -NH), 9.10 (s, 1H, -OH), 7.85 (d, *J* = 7.7 Hz, 2H, C_{18}-H, C_{22}-H), 7.56 (t, *J* = 7.2 Hz, 1H, C_{20}-H), 7.48 (t, *J* = 7.5 Hz, 2H, C_{19}-H, C_{21}-H), 6.96 (s, 1H, C_6-H), 6.89 (d, *J* = 8.0 Hz, 1H, C_8-H), 6.71 (d, *J* = 8.1 Hz, 1H, C_9-H), 2.79 (dt, *J* = 13.7, 6.8 Hz, 1H, C_{11}-H), 2.12 (dd, *J* = 10.3, 6.5 Hz, 2H, C_2-H), 1.89 (dd, *J* = 10.4, 6.5 Hz, 2H, C_3-H), 1.35 (s, 6H, C_{14}-H, C_{15}-H), 1.17 (d, *J* = 6.9 Hz, 6H, C_{12}-H, C_{13}-H). ^{13}C NMR (151 MHz, DMSO-d_6): δ 172.63, 154.15, 138.58, 132.99, 132.18, 128.87, 127.85, 125.90, 124.57, 116.38, 37.61, 35.87, 33.33, 30.28, 28.14, 24.81. MS(ESI) *m/z*: 369.28 ($[M+H]^+$). Anal. Calcd. For $C_{22}H_{28}N_2O_3$: C, 71.71; H, 7.66; N, 7.60; Found: C, 71.74; H, 7.65; N, 7.62.

N'-acetyl-4-(2-hydroxy-5-isopropylphenyl)-4-methylpentanehydrazide (**5s**). The

product is obtained as a white powder, yield 77.7%, mp 130.7-131.0℃. FT-IR v (cm^{-1}): 3357, 3268 (N-H, O-H), 3039 (Ar-H), 2959, 2930, 2869 (C-H), 1692 (C=O), 1504, 1421, 1370 (Ar), 1253, 1220, 1081(C-N). ^{1}H NMR (600 MHz, DMSO-d_6): δ 9.60 (s, 1H, -NH), 9.51 (s, 1H, -NH), 9.09 (s, 1H, -OH), 6.93 (d, J = 2.0 Hz, 1H, C_6-H), 6.87 (dd, J = 8.1, 2.1 Hz, 1H, C_8-H), 6.69 (d, J = 8.1 Hz, 1H, C_9-H), 2.77 (dt, J = 13.7, 6.9 Hz, 1H, C_{11}-H), 2.11 – 2.01 (m, 2H, C_2-H), 1.81 (s, 3H, C_{17}-H), 1.79 (d, J = 8.4 Hz, 2H, C_3-H), 1.31 (s, 6H, C_{14}-H, C_{15}-H), 1.15 (d, J = 6.9 Hz, 6H, C_{12}-H, C_{13}-H). ^{13}C NMR (151 MHz, DMSO-d_6): δ 172.11, 168.49, 154.09, 138.55, 132.94, 125.85, 124.53, 116.34, 37.57, 35.83, 33.31, 30.08, 28.09, 24.78, 20.92. MS(ESI) *m/z*: 307.24 ($[M+H]^+$). Anal. Calcd. For $C_{17}H_{26}N_2O_3$: C, 66.64; H, 8.55; N, 9.14; Found: C, 66.66; H, 8.55; N, 9.17.

4-(2-hydroxy-5-isopropylphenyl)-4-methyl-N'-(2-phenylacetyl)pentanehydrazide (**5t**). The product is obtained as a white powder, yield 77.9%, mp 82.3-82.5℃. FT-IR v (cm^{-1}): 3398, 3262 (N-H, O-H), 3031 (Ar-H), 2958, 2925, 2868 (C-H), 1691 (C=O), 1508, 1458, 1420 (Ar), 1253, 1209, 1080 (C-N). ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.33 (s, 1H, -NH), 8.88 (d, J = 3.4 Hz, 1H, -NH), 7.21 (t, J = 7.2 Hz, 3H, C_{19}-H, C_{20}-H, C_{21}-H), 7.19 – 7.16 (m, 2H, C_{22}-H, C_{23}-H), 6.95 (d, J = 1.6 Hz, 1H, C_6-H), 6.82 (dd, J = 8.1, 1.8 Hz, 1H, C_8-H), 6.76 (s, 1H, -OH), 6.55 (d, J = 8.1 Hz, 1H, C_9-H), 3.46 (s, 2H, C_{17}-H), 2.78 (dt, J = 13.8, 6.9 Hz, 1H, C_{11}-H), 2.18 (dd, J = 9.7, 6.8 Hz, 2H, C_2-H), 1.88 – 1.84 (m, 2H, C_3-H), 1.31 (s, 6H, C_{14}-H, C_{15}-H), 1.18 (d, J = 6.9 Hz, 6H, C_{12}-H, C_{13}-H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 172.41, 168.96, 152.56, 140.26, 133.83, 132.67, 129.33, 128.77, 127.35, 126.30, 124.69, 116.70, 40.87, 37.81, 36.21,

33.52, 30.95, 28.19, 24.35. MS(ESI) *m/z*: 383.29 ($[M+H]^+$). Anal. Calcd. For $C_{23}H_{30}N_2O_3$: C, 72.22; H, 7.91; N, 7.32; Found: C, 72.24; H, 7.93; N, 7.34.

N'-(2-cyanoacetyl)-4-(2-hydroxy-5-isopropylphenyl)-4-methylpentanehydrazide (**5u**). The product is obtained as a white powder, yield 77.4%, mp 119.2-119.5℃. FT-IR *v* (cm^{-1}): 3509, 3429, 3306, 3270 (N-H, O-H), 3110, 3025 (Ar-H), 2962, 2922, 2867 (C-H), 2271 (C≡N), 1696 (C=O), 1505, 1421, 1363, 1349 (Ar), 1254, 1203, 1134, 1081 (C-N). ^{1}H NMR (600 MHz, DMSO-d_6): δ 10.08 (s, 1H, -NH), 9.80 (s, 1H, -NH), 9.09 (s, 1H, -OH), 6.93 (d, *J* = 1.9 Hz, 1H, C_6-H), 6.88 (dd, *J* = 8.1, 2.0 Hz, 1H, C_8-H), 6.69 (d, *J* = 8.1 Hz, 1H, C_9-H), 3.70 (s, 2H, C_{17}-H), 2.77 (dt, *J* = 13.8, 6.9 Hz, 1H, C_{11}-H), 2.11 – 2.02 (m, 2H, C_2-H), 1.82 (dd, *J* = 10.3, 6.6 Hz, 2H, C_3-H), 1.32 (s, 6H, C_{14}-H, C_{15}-H), 1.16 (d, *J* = 6.9 Hz, 6H, C_{12}-H, C_{13}-H); ^{13}C NMR (151 MHz, DMSO-d_6): δ 172.04, 161.67, 154.08, 138.57, 132.86, 125.86, 124.57, 116.35, 116.10, 37.58, 35.74, 33.30, 30.03, 28.08, 24.77, 24.14. MS(ESI) *m/z*: 354.19 ($[M+Na]^+$). Anal. Calcd. For $C_{18}H_{25}N_3O_3$: C, 65.23; H, 7.60; N, 12.68; Found: C, 65.25; H, 7.64; N, 12.67.

N'-(4-(2-hydroxy-5-isopropylphenyl)-4-methylpentanoyl)furan-2-carbohydrazide (**5v**). The product is obtained as a white powder, yield 77.2%, mp 150.0-150.3℃. FT-IR *v* (cm^{-1}): 3372, 3260 (N-H, O-H), 3036 (Ar-H), 2958, 2928, 2868 (C-H), 1688 (C=O), 1507, 1467, 1420 (Ar), 1295, 1253, 1220, 1080 (C-N). ^{1}H NMR (600 MHz, $CDCl_3$): δ 9.56 (s, 1H, -NH), 9.25 (s, 1H, -NH), 7.33 (s, 1H, -OH), 7.05 (d, *J* = 3.4 Hz, 1H, C_{18}-H), 7.02 (s, 1H, C_{20}-H), 6.93 (d, *J* = 1.4 Hz, 1H, C_6-H), 6.78 (dd, *J* = 8.0, 1.5 Hz, 1H, C_8-H), 6.64 (d, *J* = 8.1 Hz, 1H, C_9-H), 6.38 (dd, *J* = 3.2, 1.4 Hz, 1H, C_{19}-H),

2.76 (dt, *J* = 13.7, 6.9 Hz, 1H, C_{11}-H), 2.21 (dd, *J* = 10.0, 6.7 Hz, 2H, C_2-H), 1.92 (dd, *J* = 9.9, 6.8 Hz, 2H, C_3-H), 1.29 (s, 6H, C_{14}-H, C_{15}-H), 1.17 (d, *J* = 6.9 Hz, 6H, C_{12}-H, C_{13}-H). ^{13}C NMR (151 MHz, $CDCl_3$): δ 173.87, 156.71, 152.66, 145.30, 140.01, 132.67, 126.20, 124.50, 116.66, 116.17, 112.06, 37.78, 36.29, 33.48, 31.02, 28.10, 24.32. MS(ESI) *m/z*: 381.20 ($[M+Na]^+$). Anal. Calcd. For $C_{20}H_{26}N_2O_4$: C, 67.02; H, 7.31; N, 7.82; Found: C, 67.04; H, 7.30; N, 7.85.

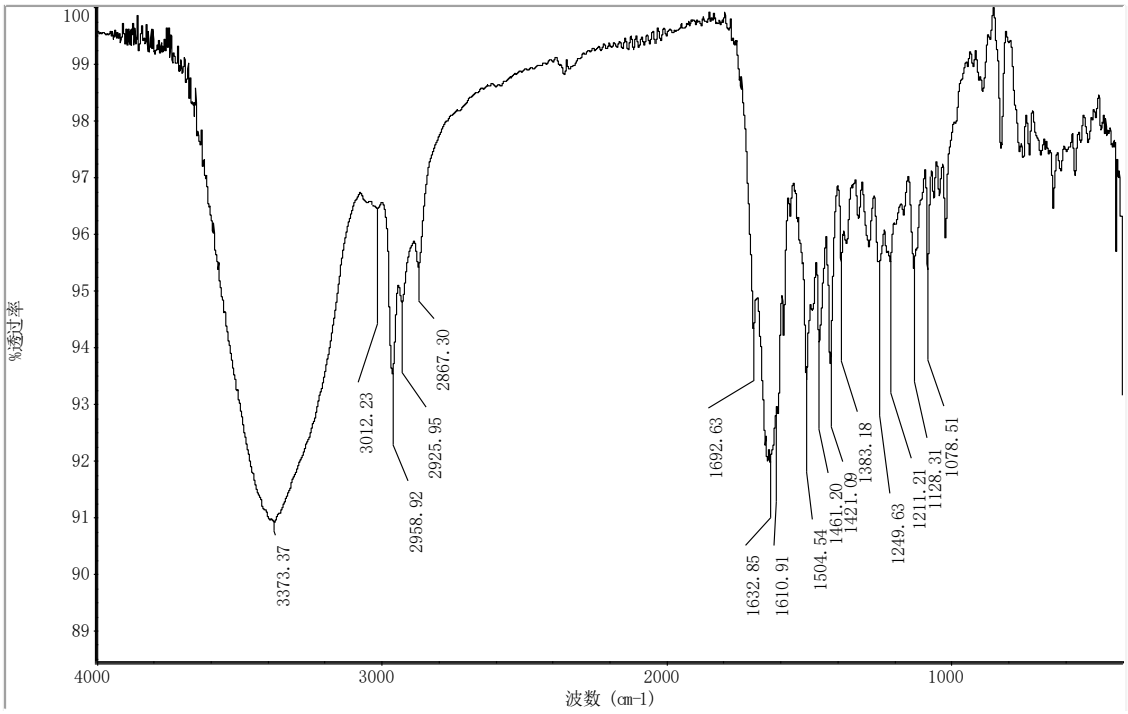


Figure S1. IR spectrum of **5a**

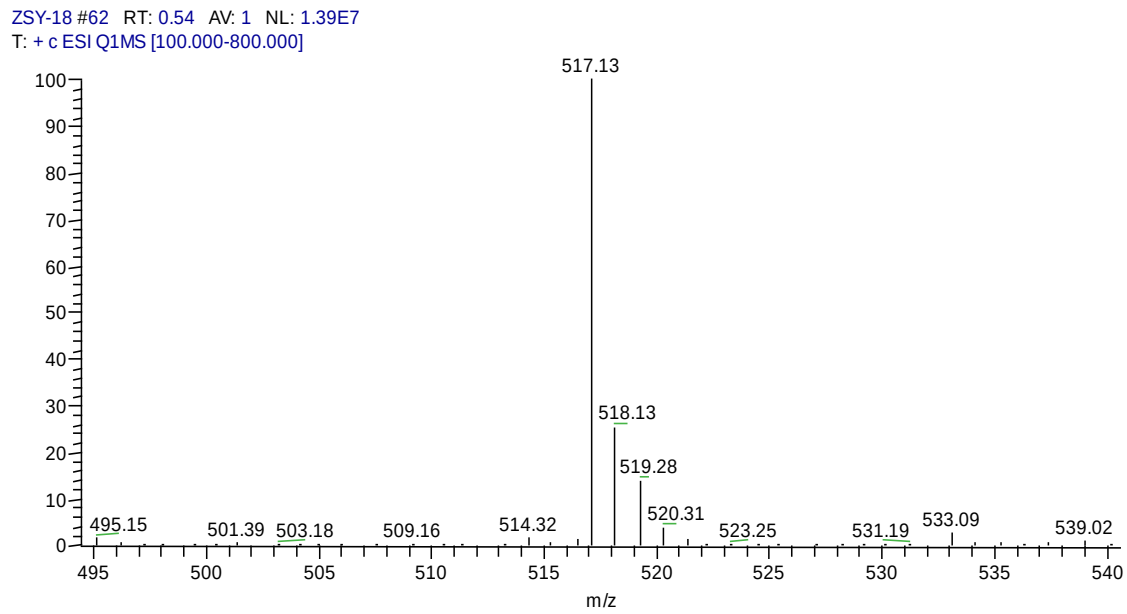


Figure S2. MS spectrum of **5a**

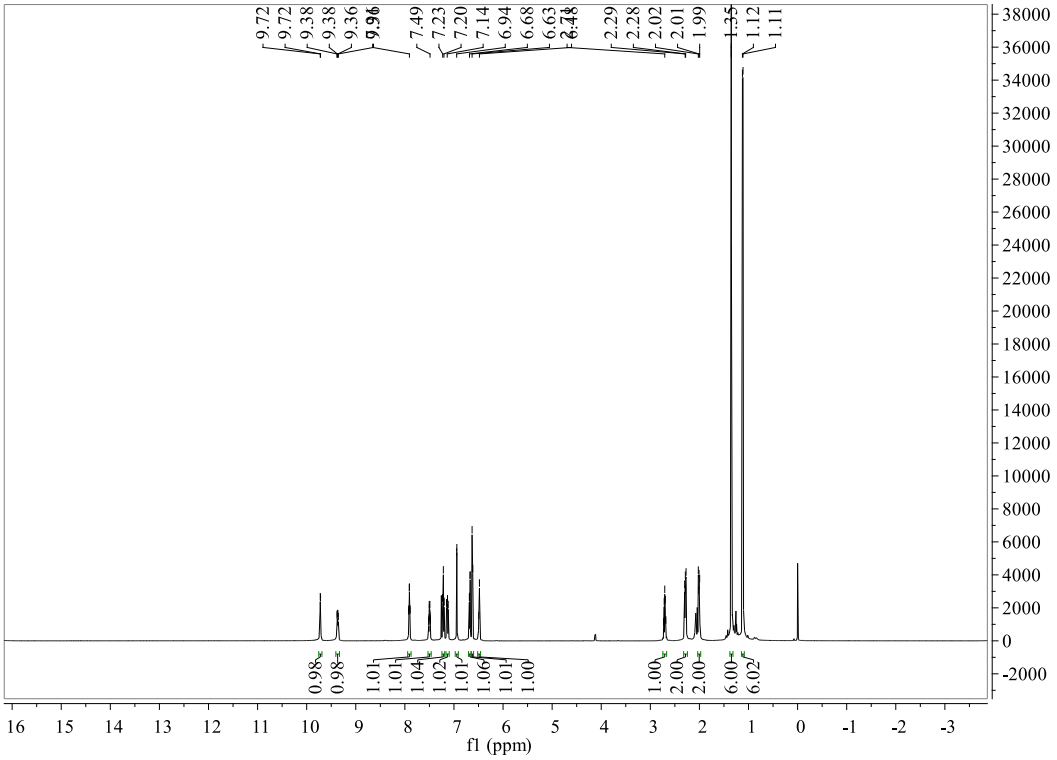


Figure S3. ^{1}H NMR spectrum of **5a**

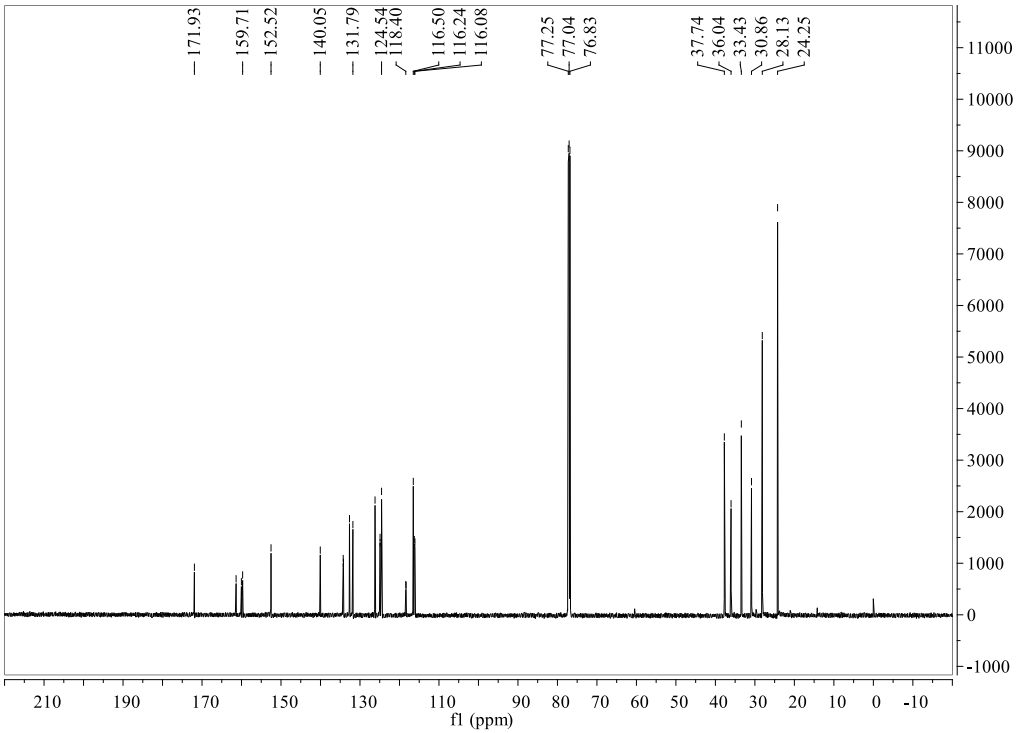


Figure S4. ^{13}C NMR spectrum of **5a**

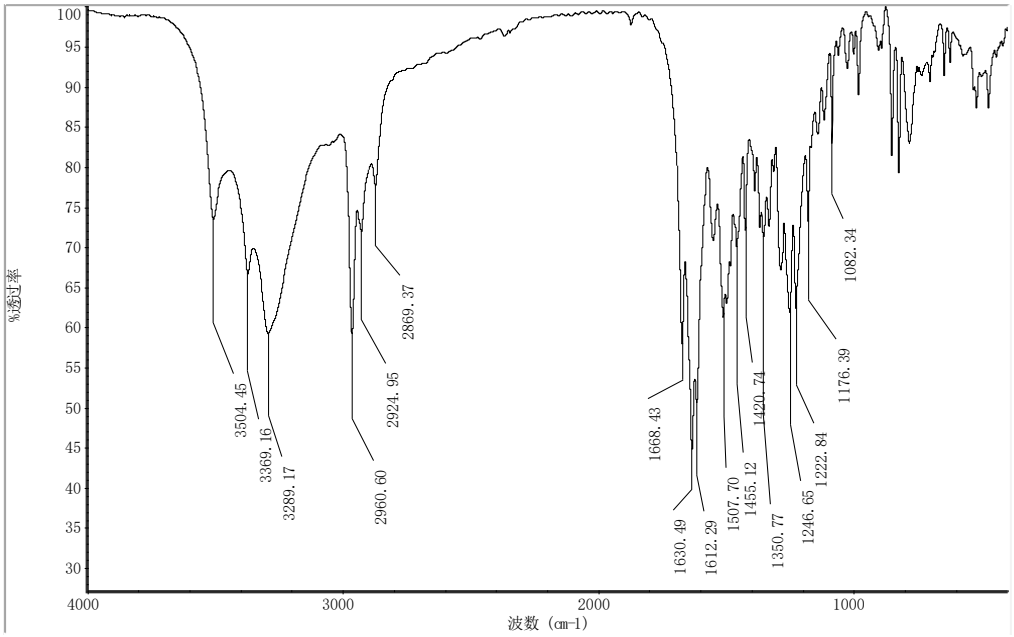


Figure S5. IR spectrum of **5b**

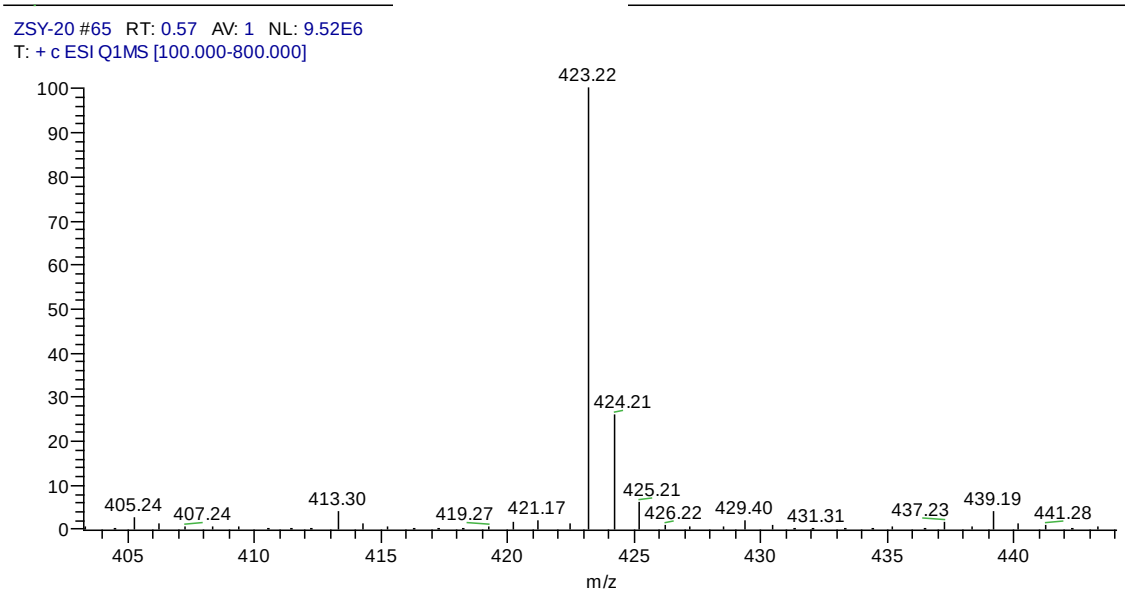


Figure S6. MS spectrum of **5b**

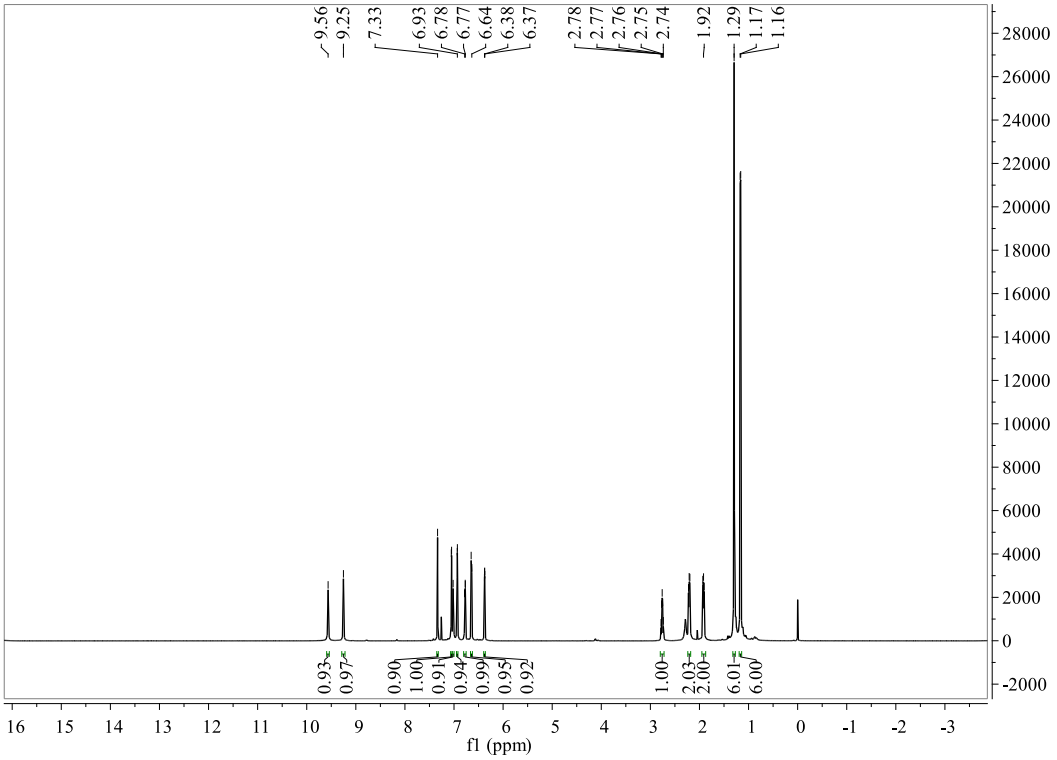


Figure S7. ^{1}H NMR spectrum of **5b**

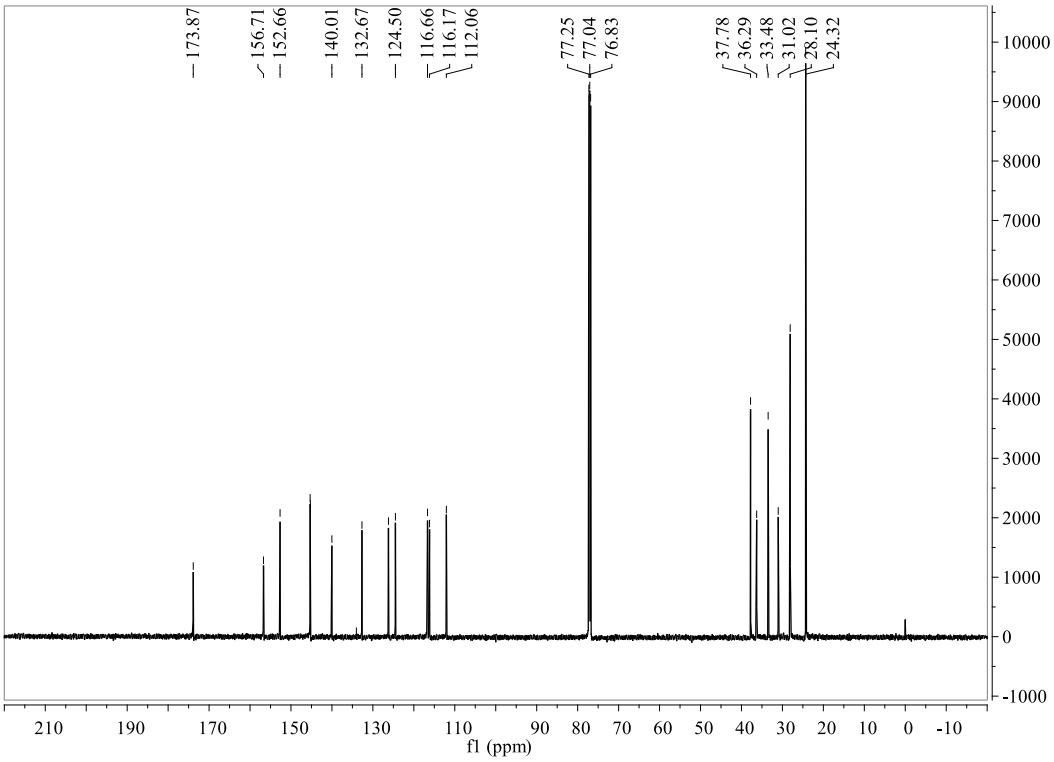


Figure S8. ^{13}C NMR spectrum of **5b**

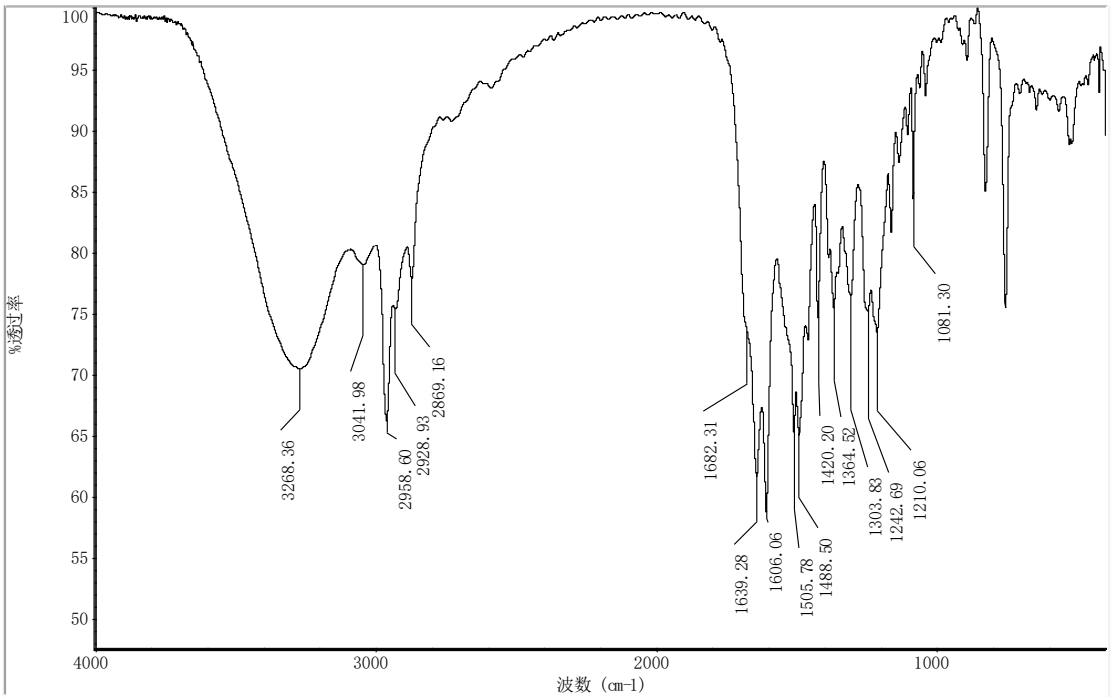


Figure S9. IR spectrum of **5c**

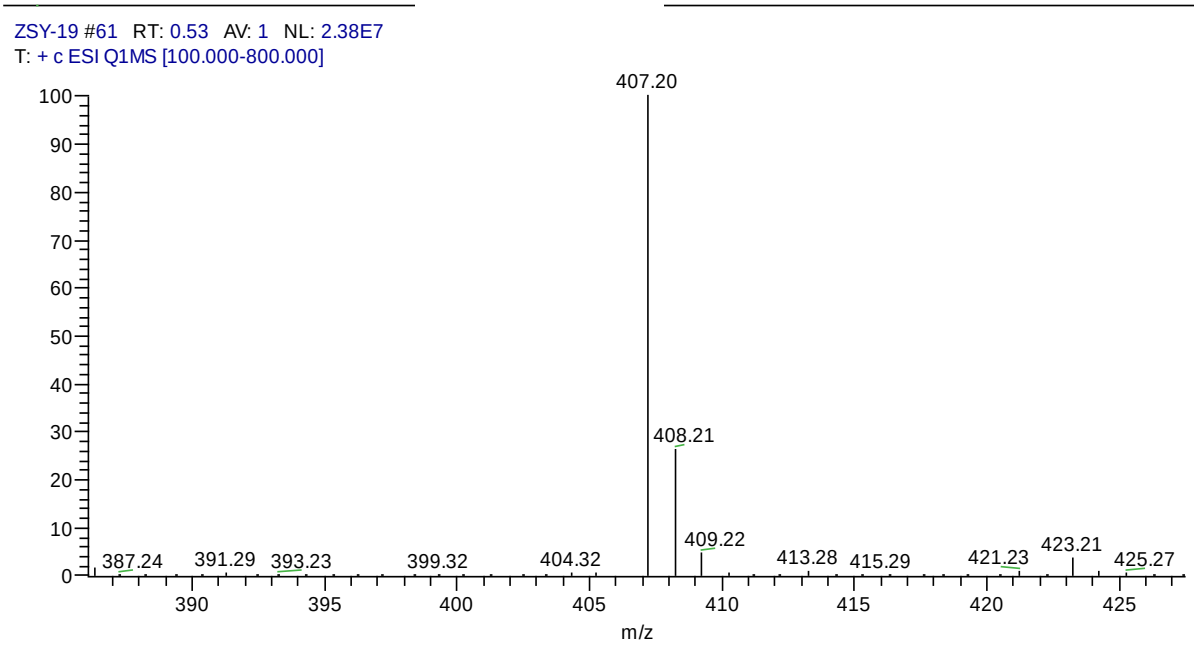


Figure S10. MS spectrum of **5c**

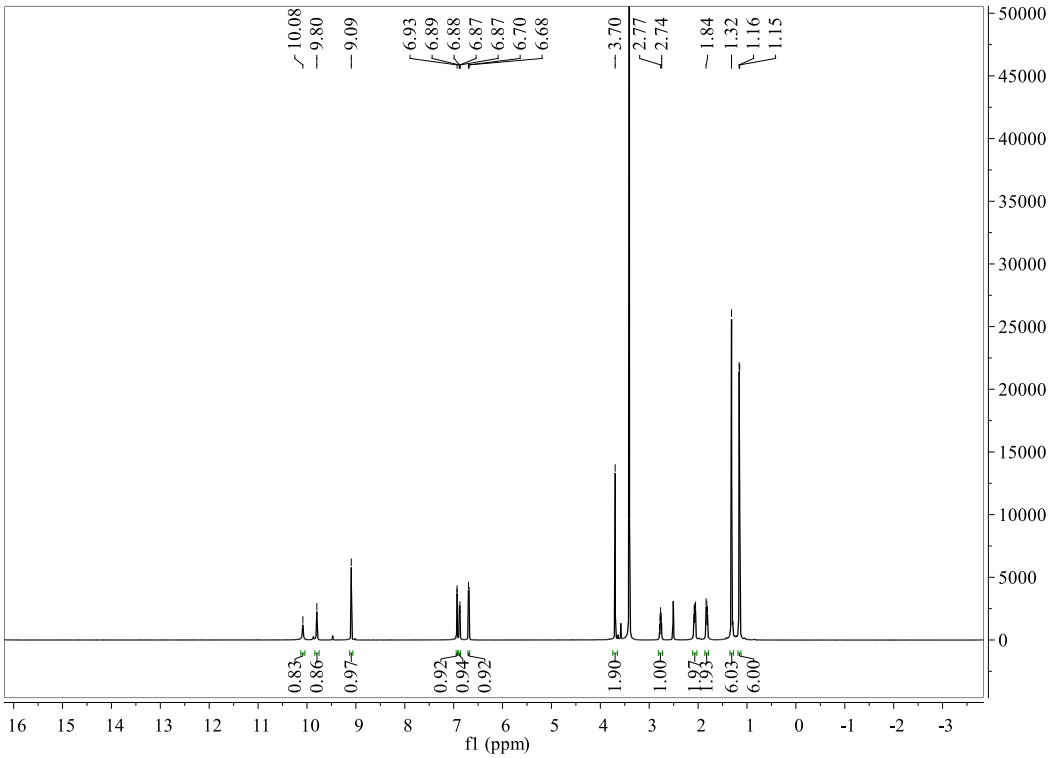


Figure S11. ^{1}H NMR spectrum of **5c**

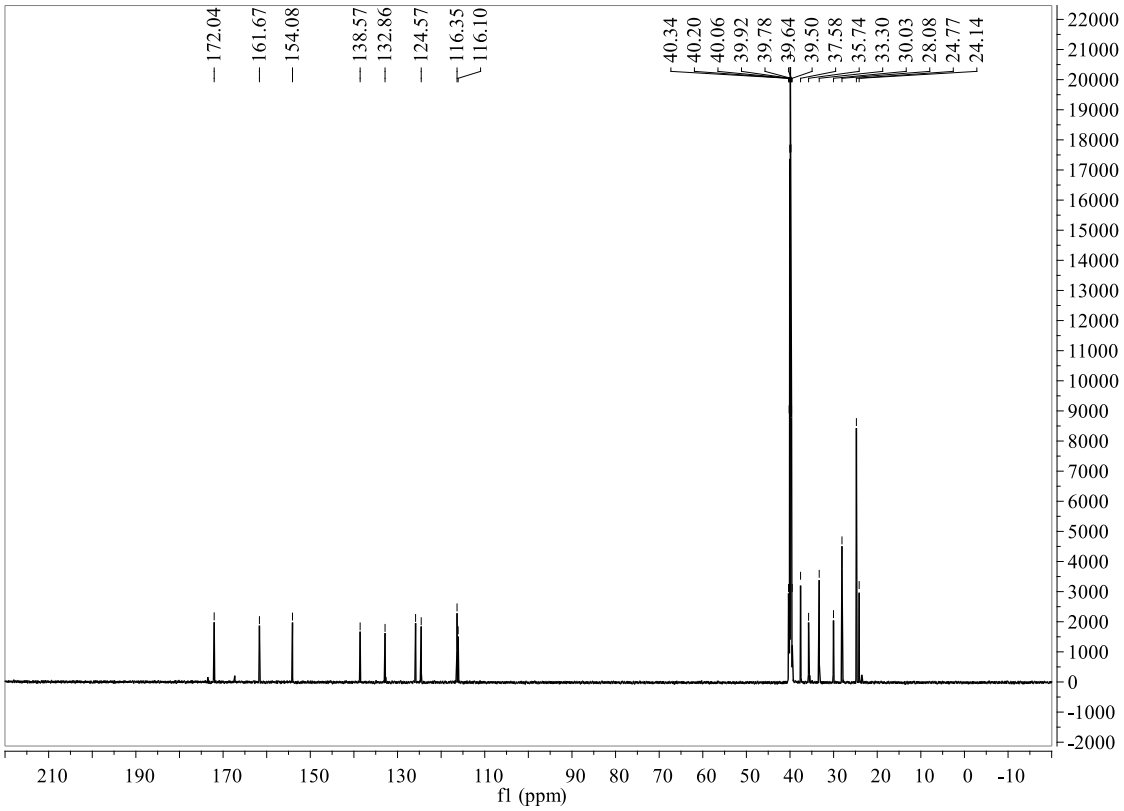


Figure S12. ^{13}C NMR spectrum of **5c**

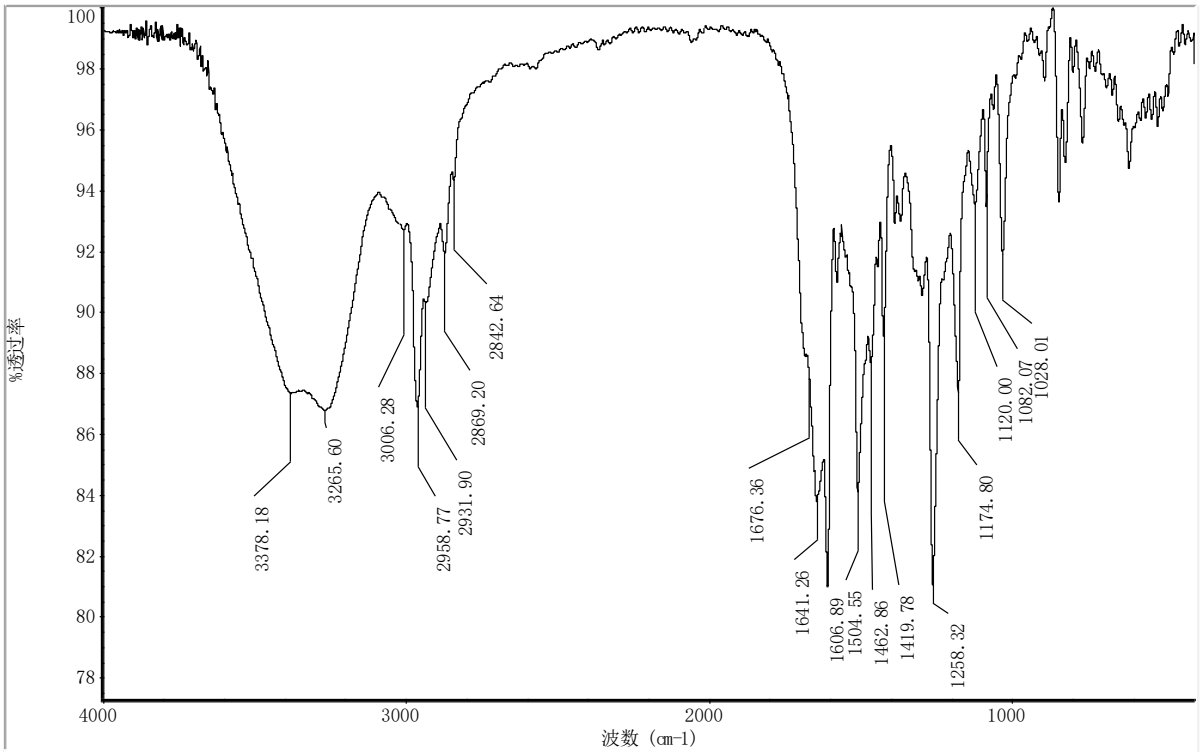


Figure S13. IR spectrum of **5d**

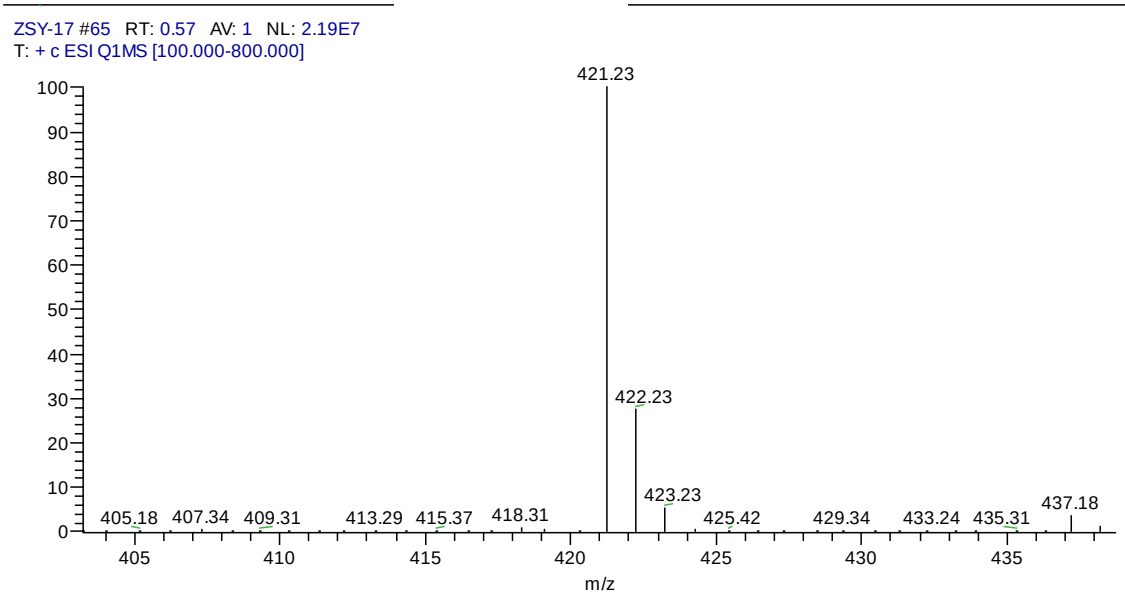


Figure S14. MS spectrum of **5d**

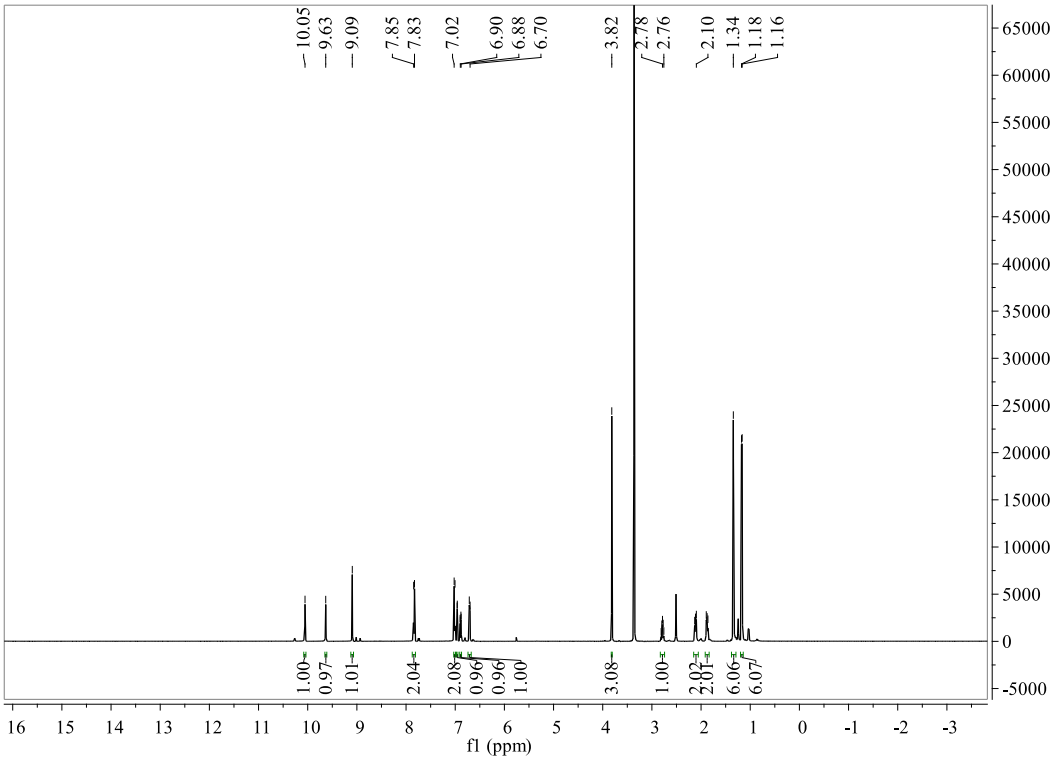


Figure S15. ^{1}H NMR spectrum of **5d**

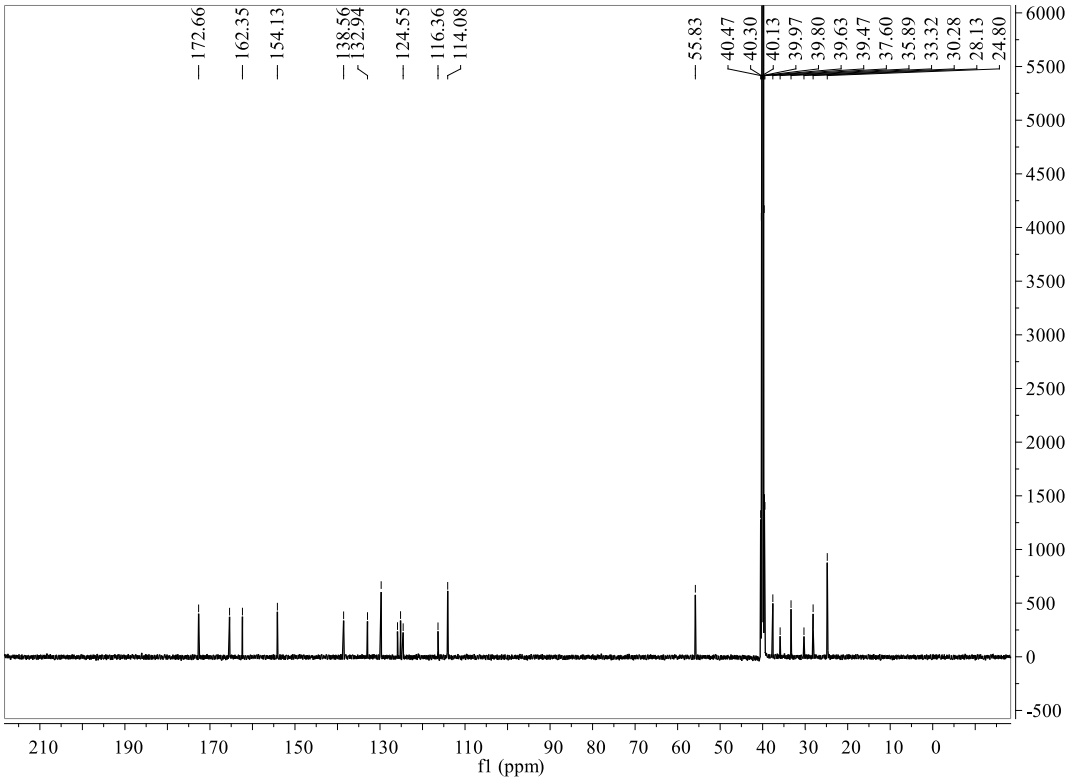


Figure S16. ^{13}C NMR spectrum of **5d**

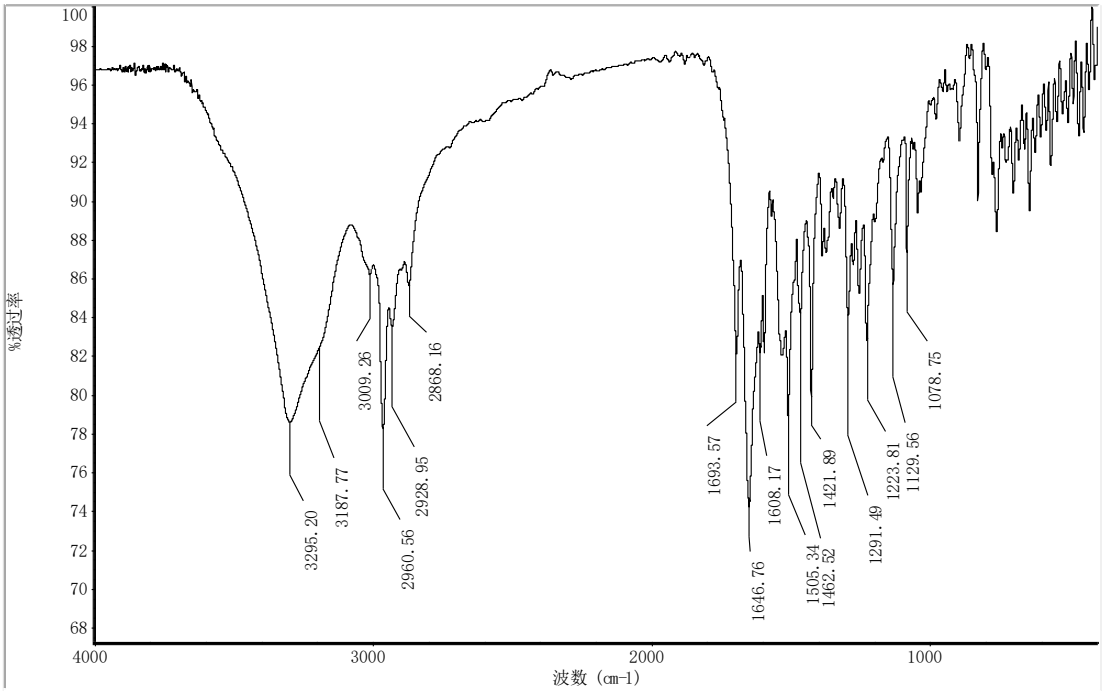


Figure S17. IR spectrum of **5e**

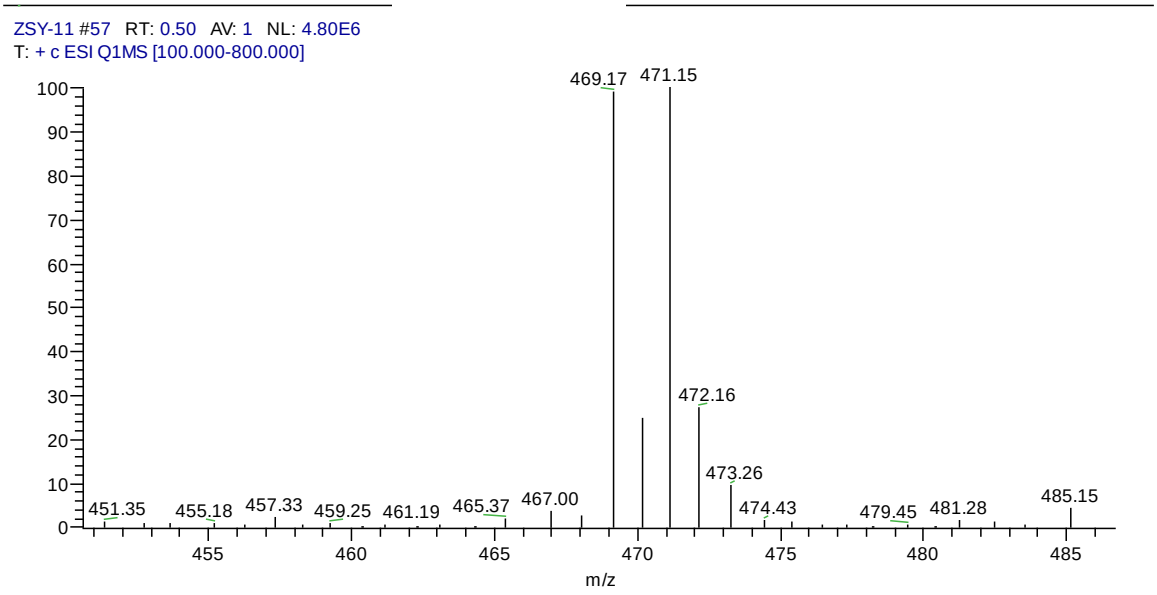


Figure S18. MS spectrum of **5e**

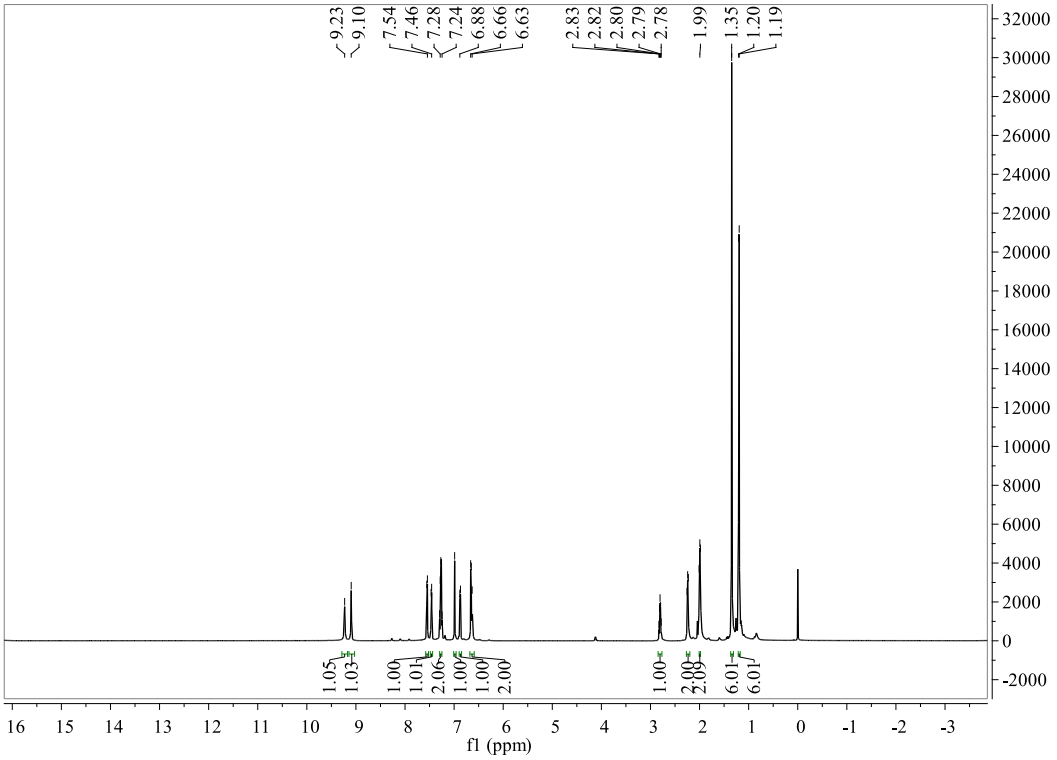


Figure S19. ^{1}H NMR spectrum of **5e**

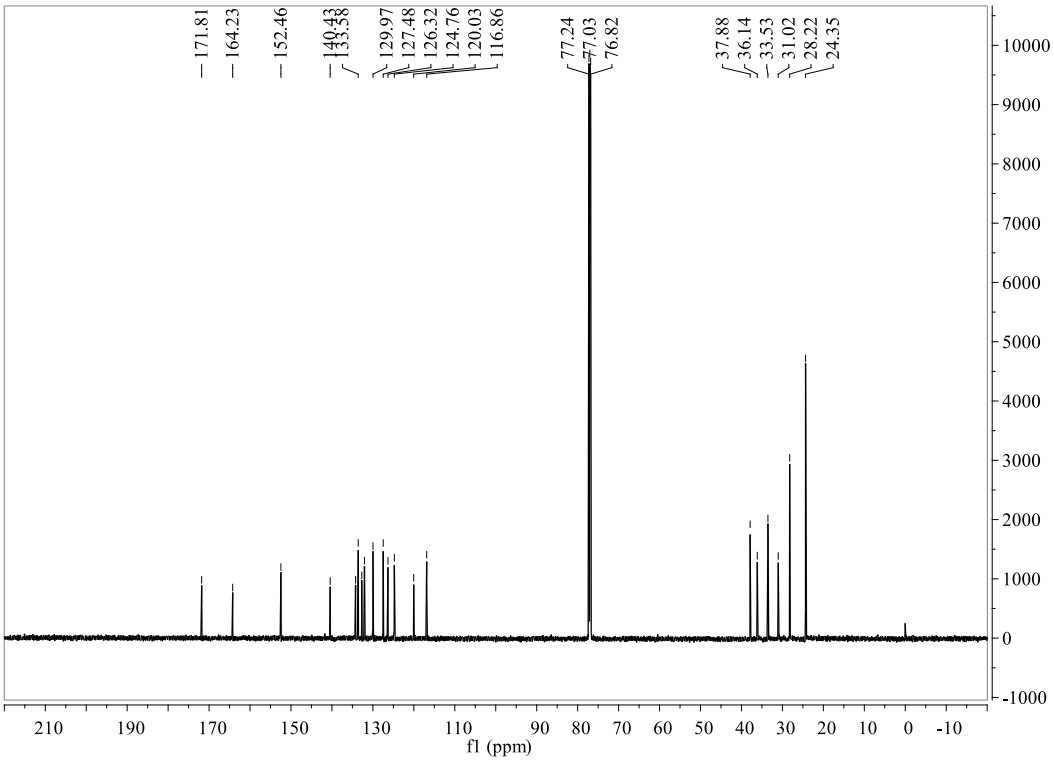


Figure S20. ^{13}C NMR spectrum of **5e**

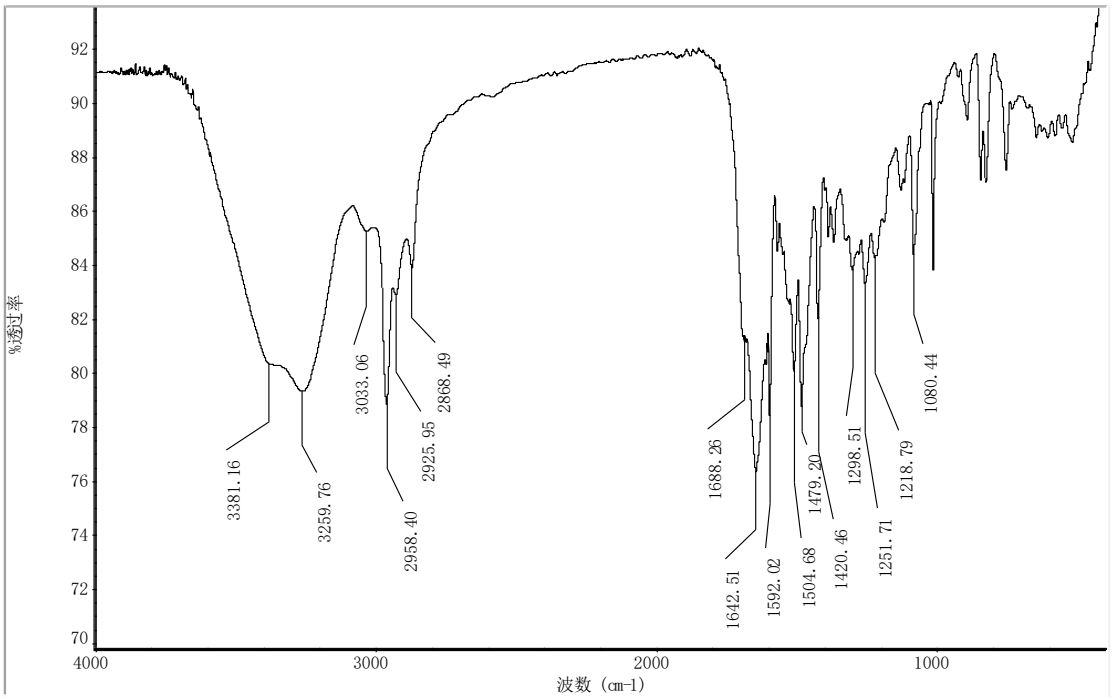


Figure S21. IR spectrum of **5f**

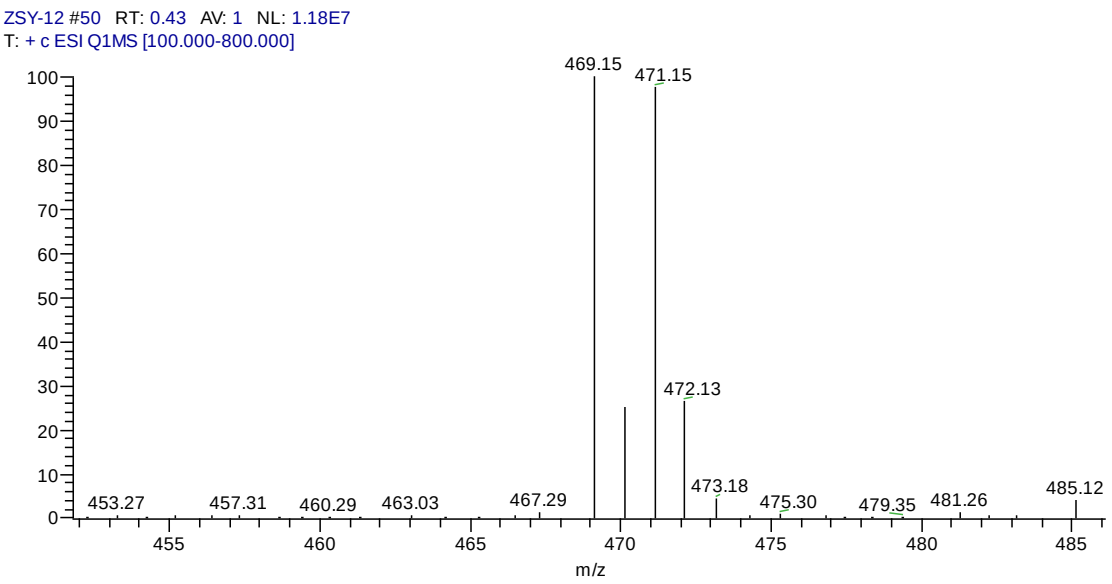


Figure S22. MS spectrum of **5f**

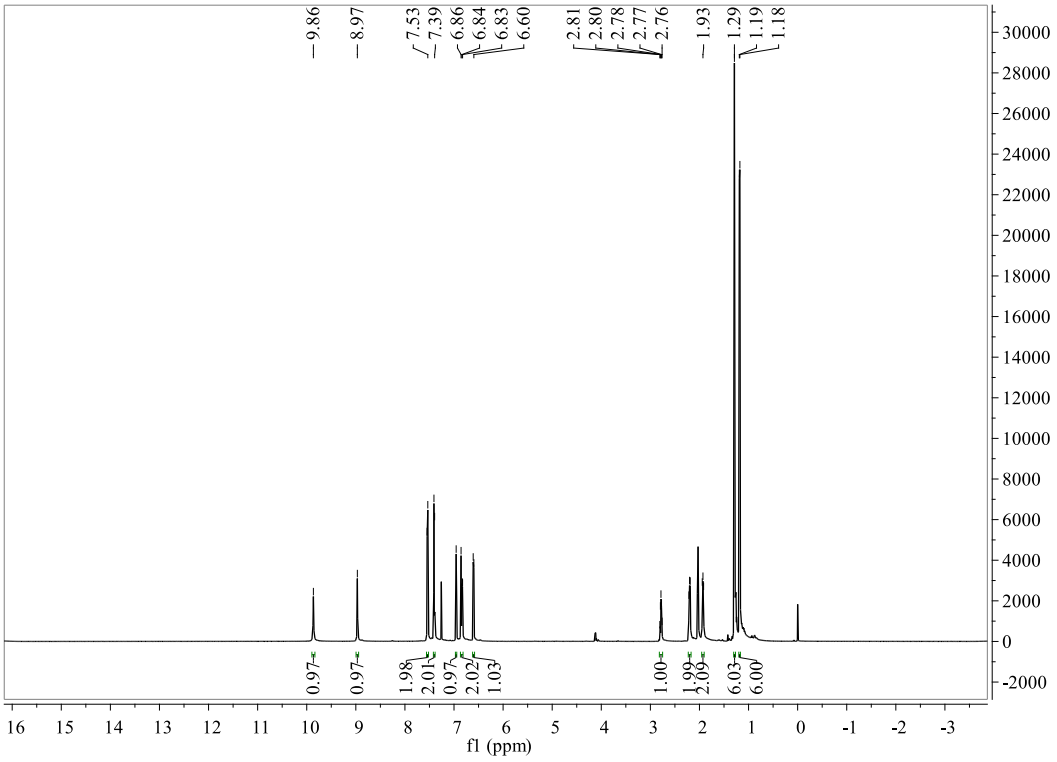


Figure S23. ^{1}H NMR spectrum of **5f**

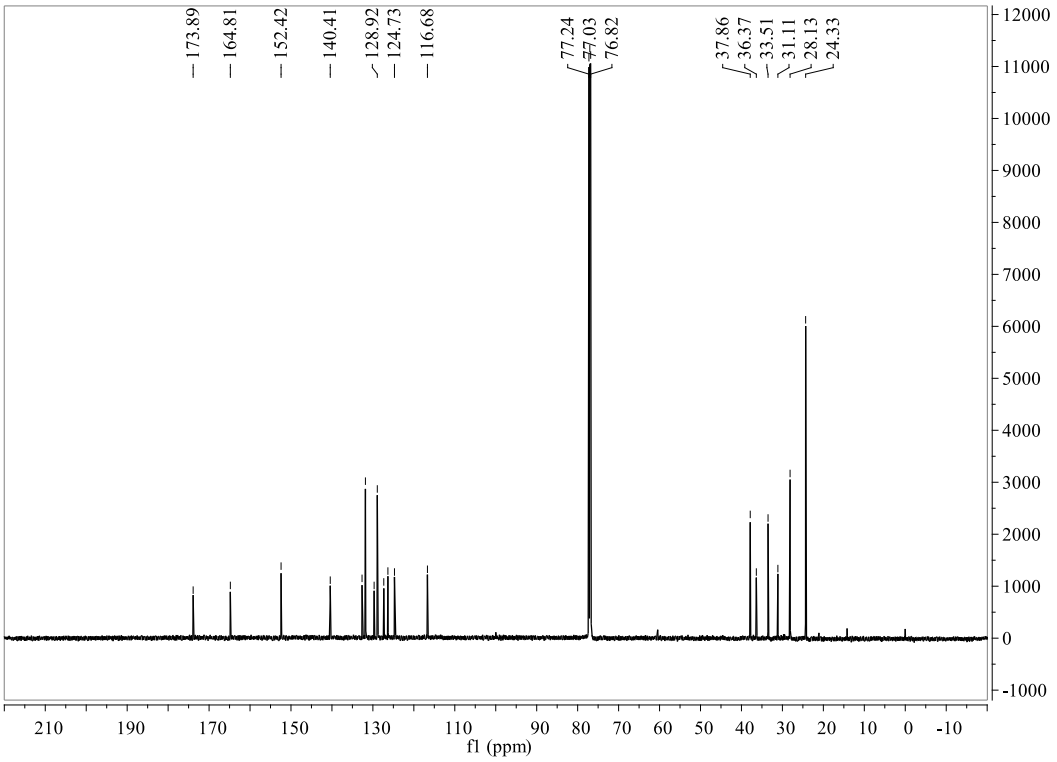


Figure S24. ^{13}C NMR spectrum of **5f**

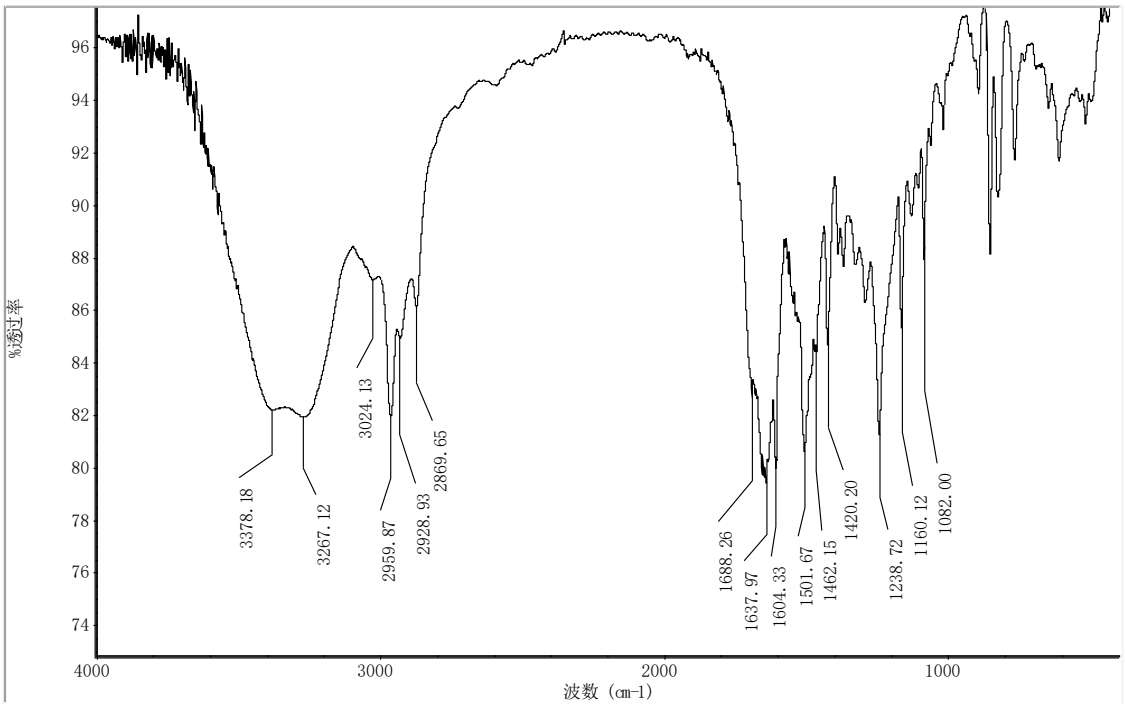


Figure S25. IR spectrum of **5g**

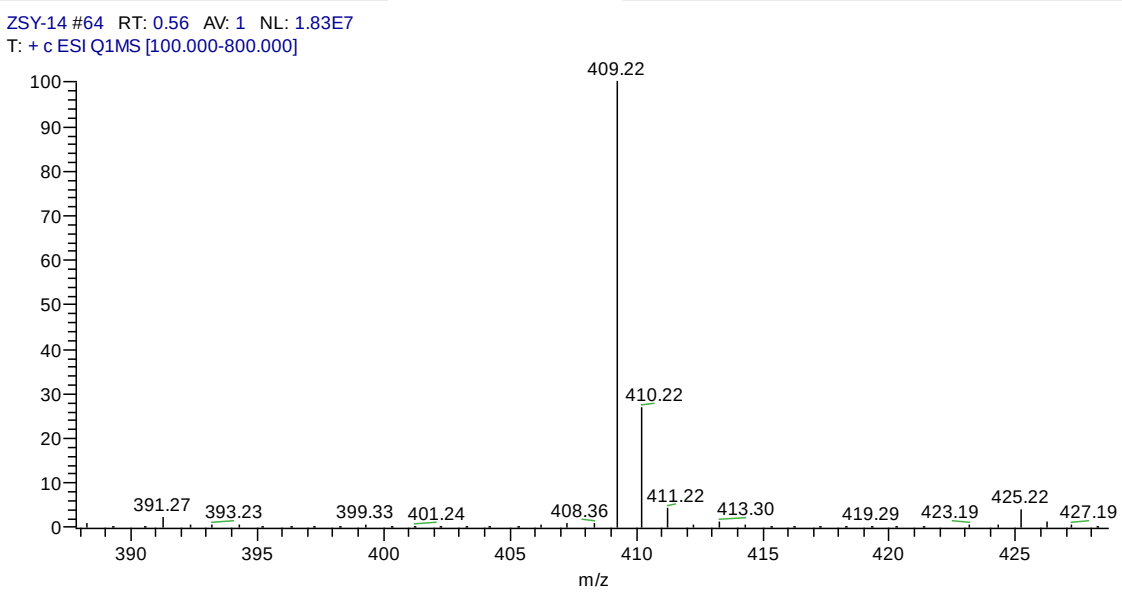


Figure S26. MS spectrum of **5g**

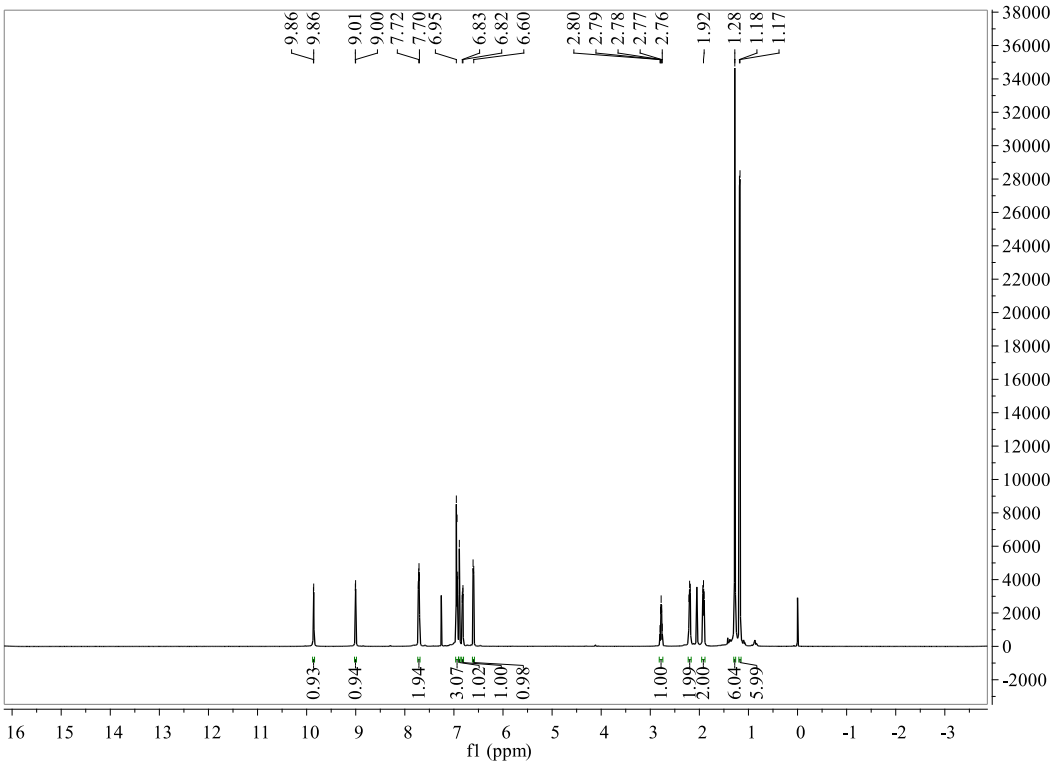


Figure S27. ^{1}H NMR spectrum of **5g**

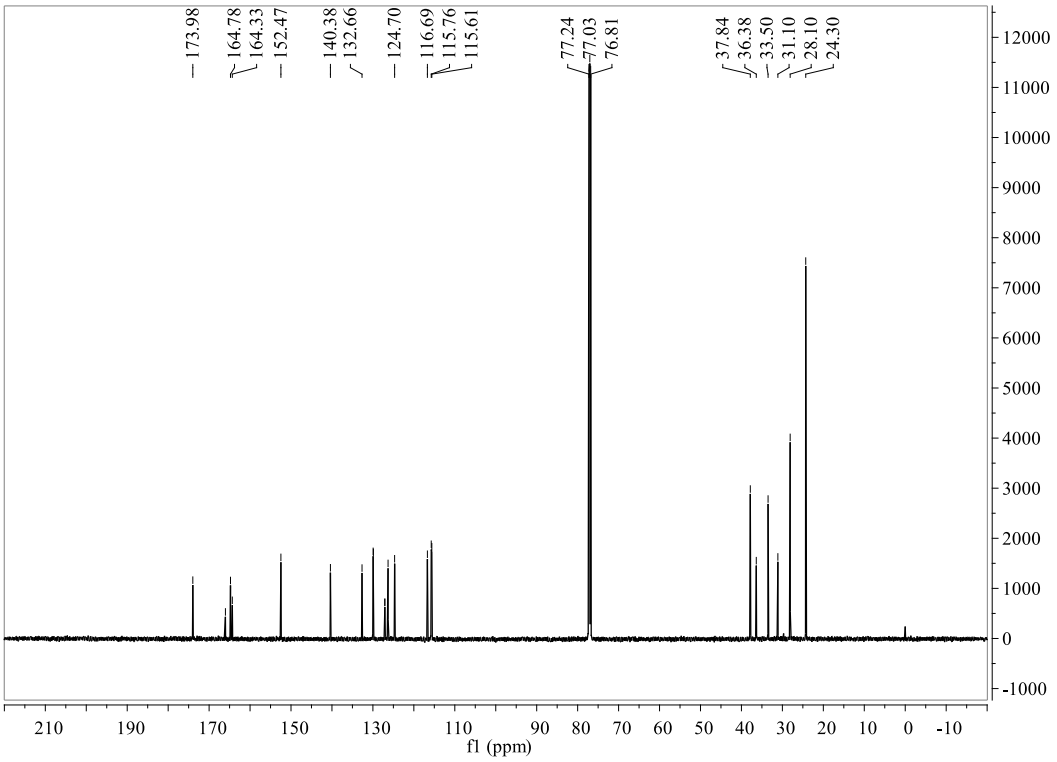


Figure S28. ^{13}C NMR spectrum of **5g**

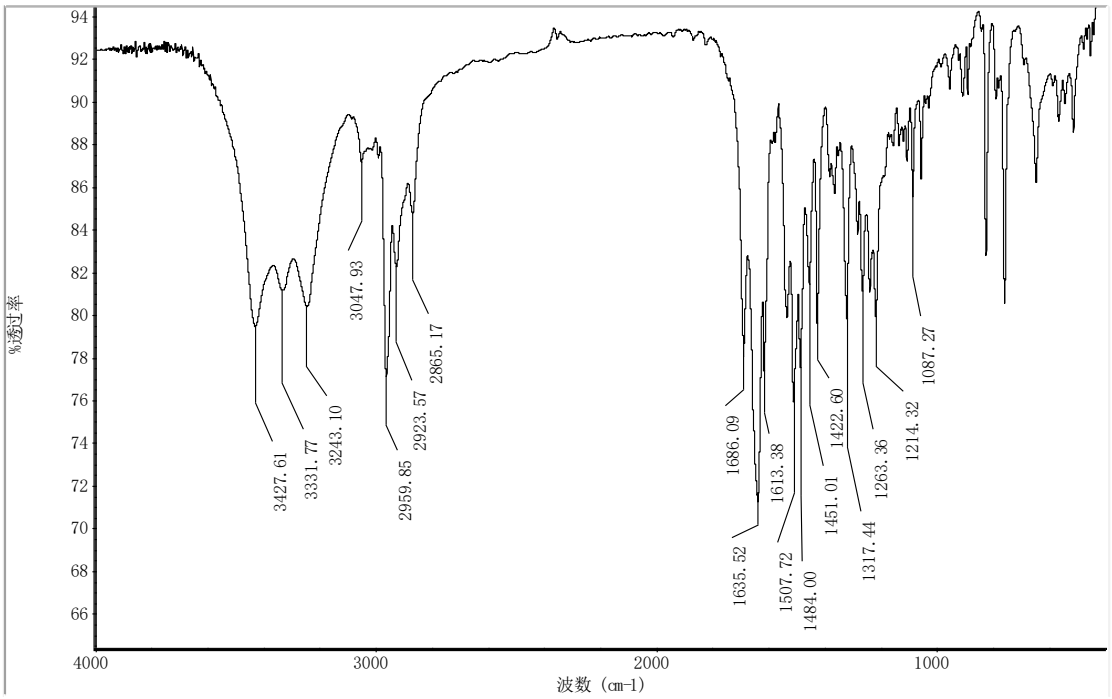


Figure S29. IR spectrum of **5h**

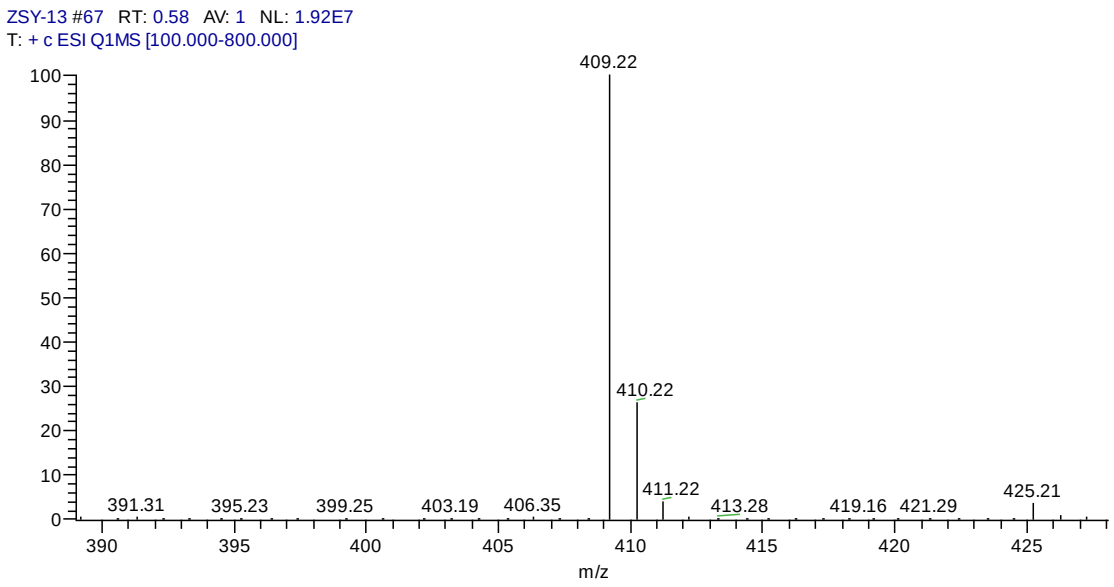


Figure S30. MS spectrum of **5h**

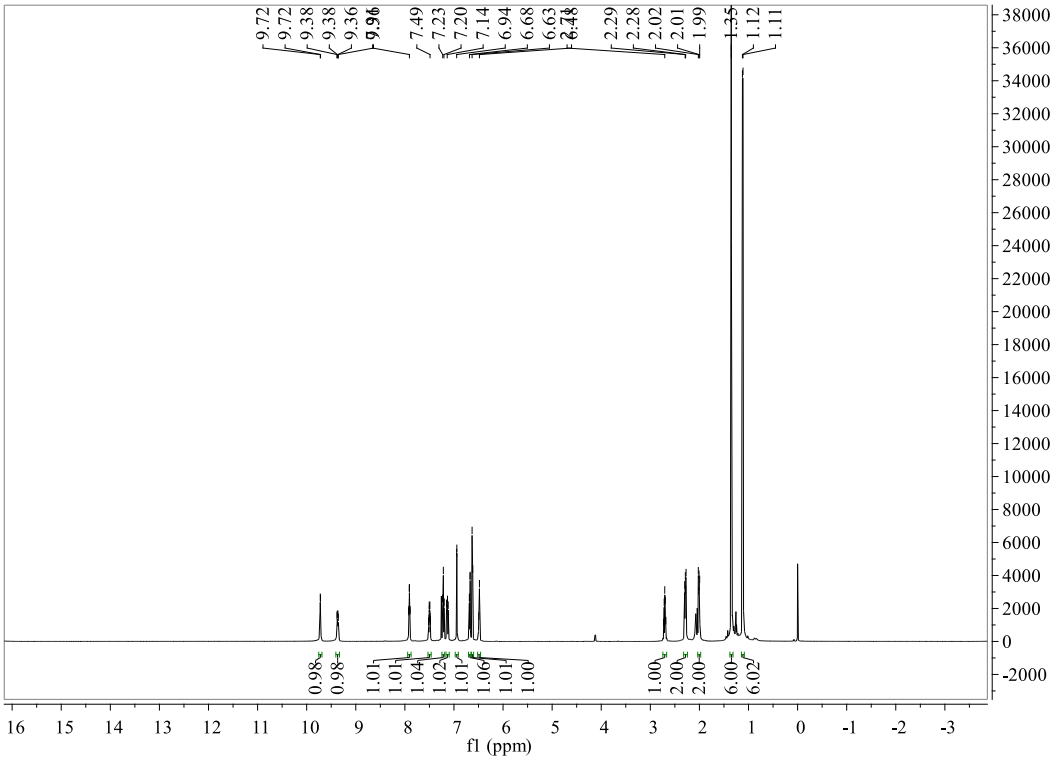


Figure S31. ^{1}H NMR spectrum of **5h**

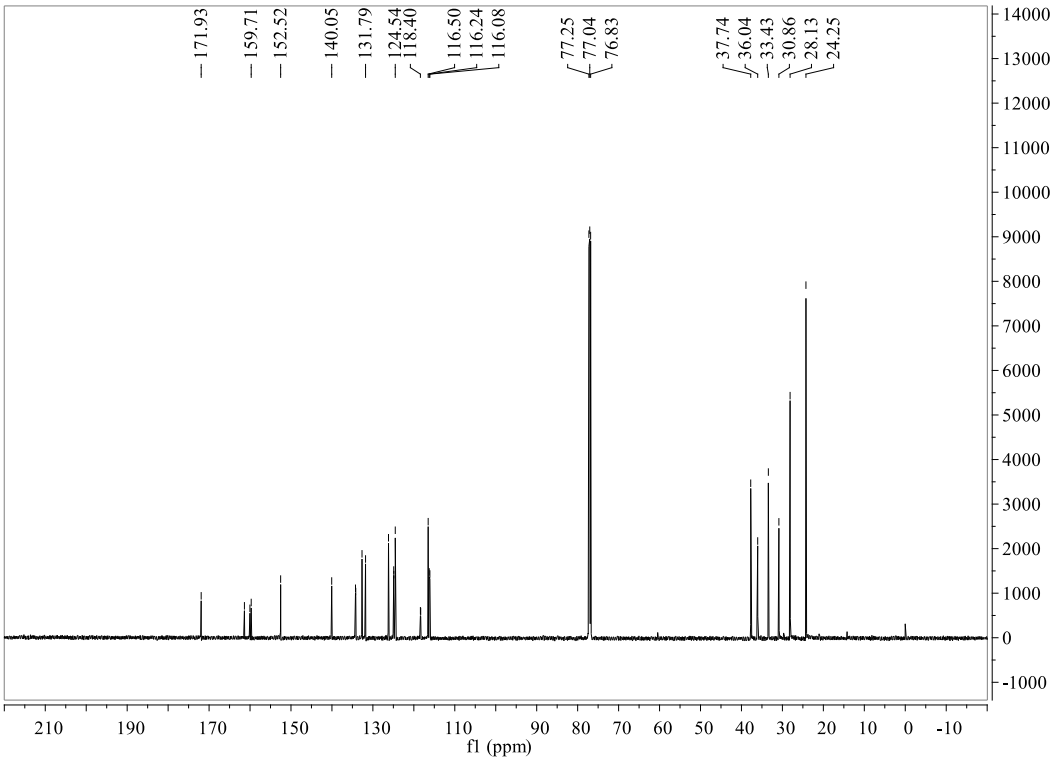


Figure S32. ^{13}C NMR spectrum of **5h**

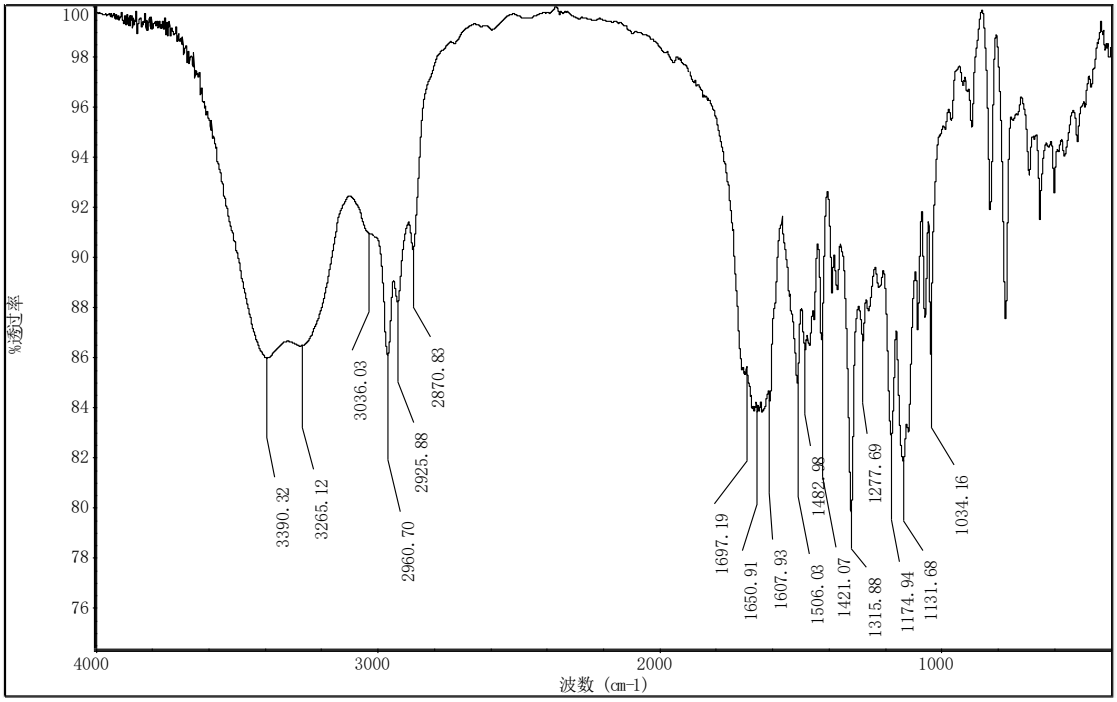


Figure S33. IR spectrum of **5i**

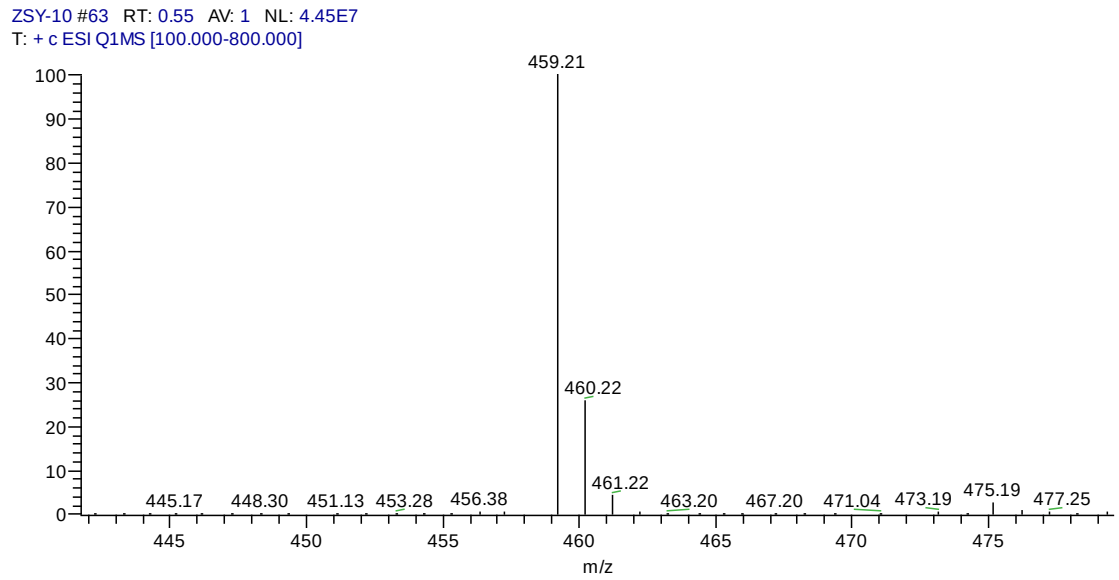


Figure S34. MS spectrum of **5i**

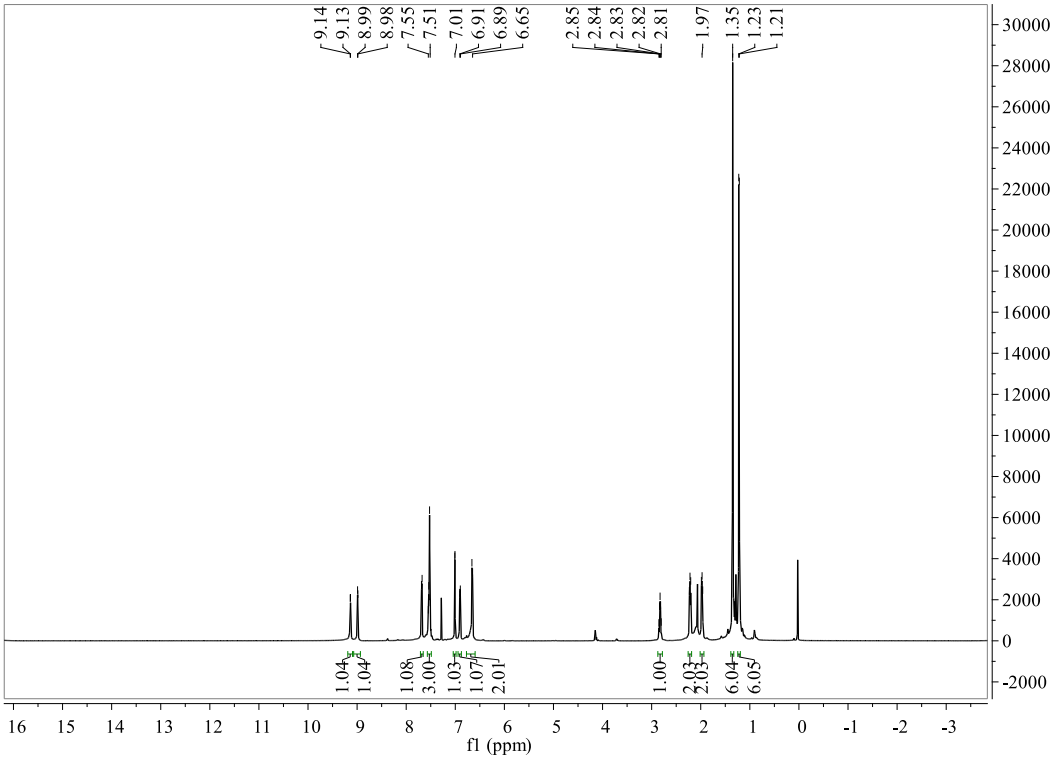


Figure S35. ^{1}H NMR spectrum of **5i**

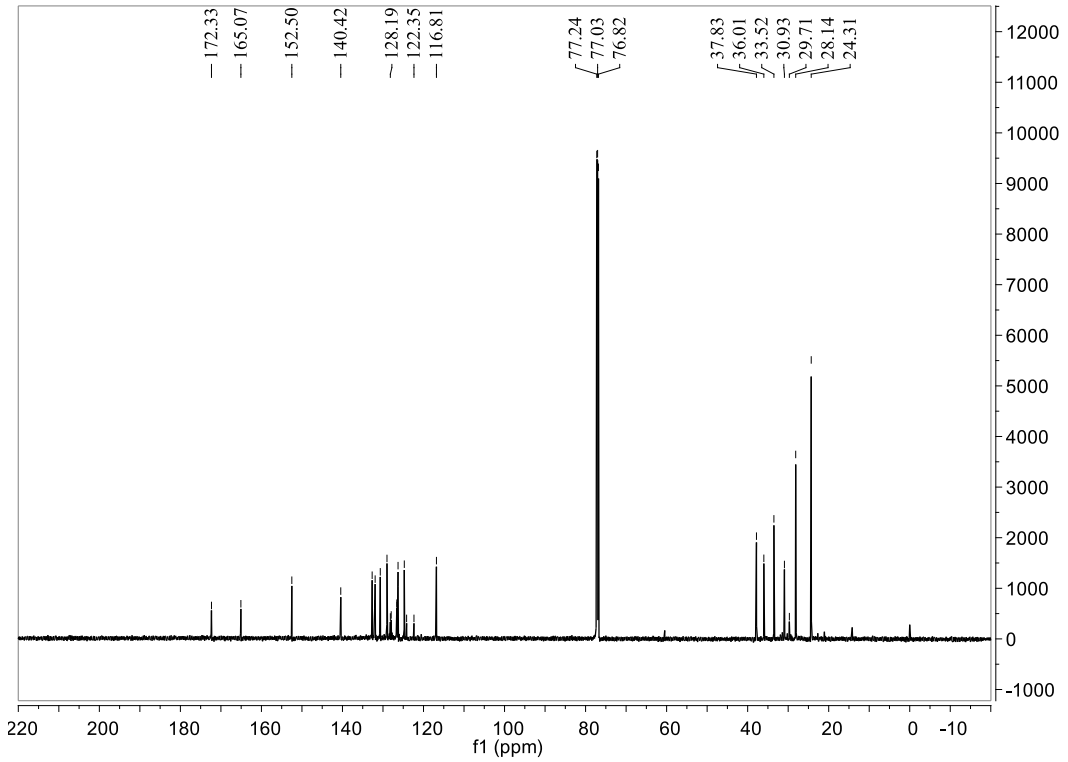


Figure S36. ^{13}C NMR spectrum of **5i**

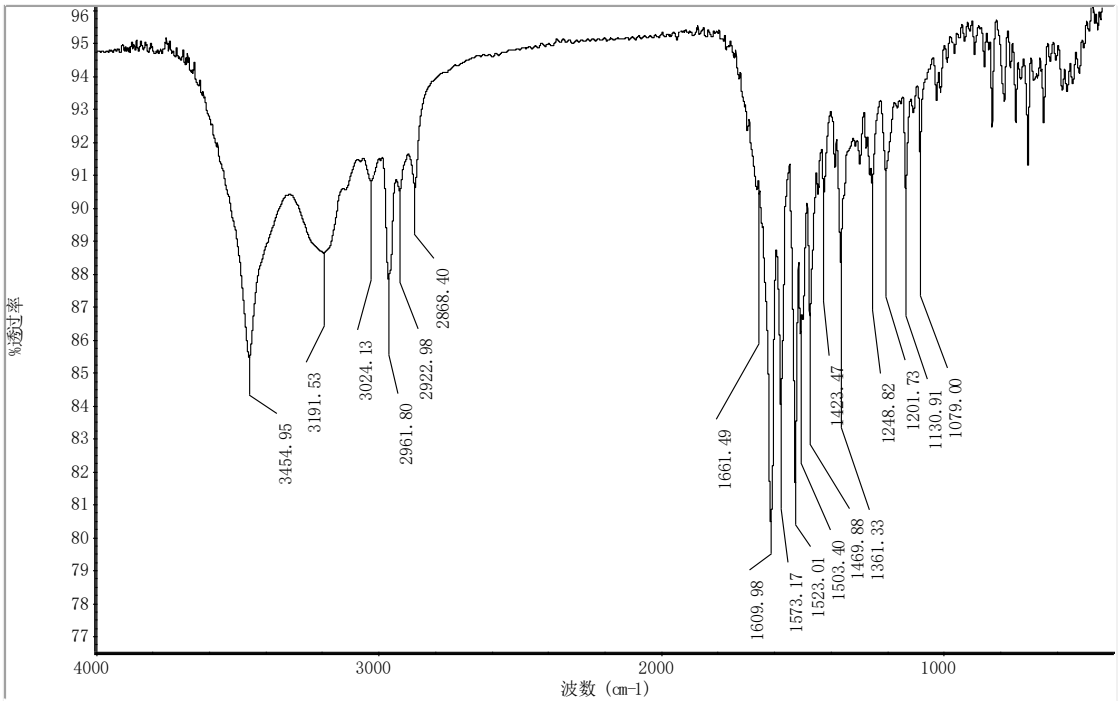


Figure S37. IR spectrum of **5j**

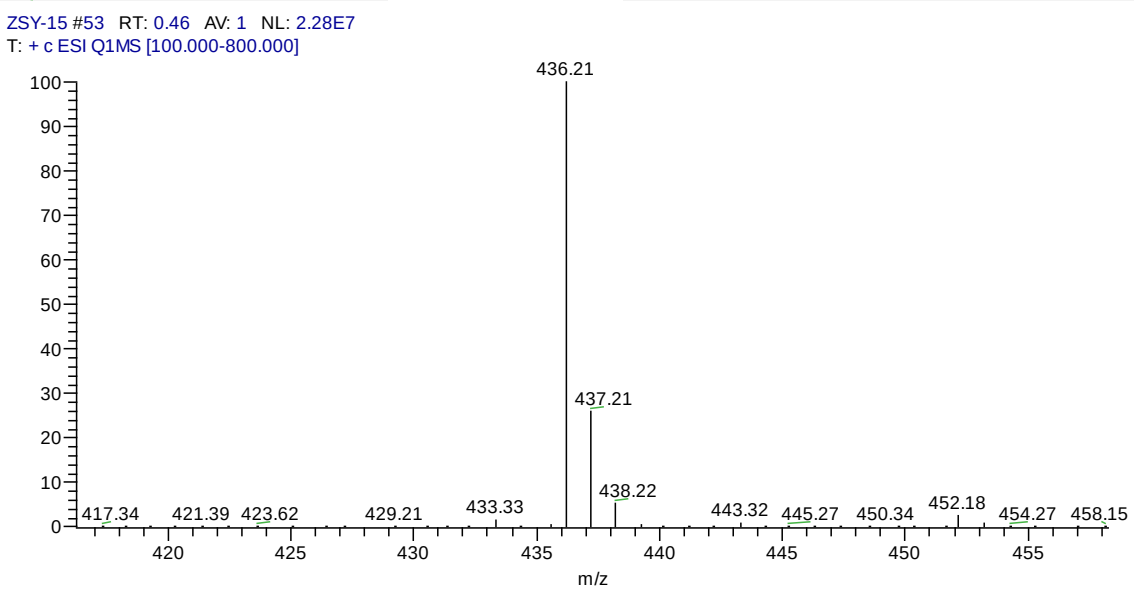


Figure S38. MS spectrum of **5j**

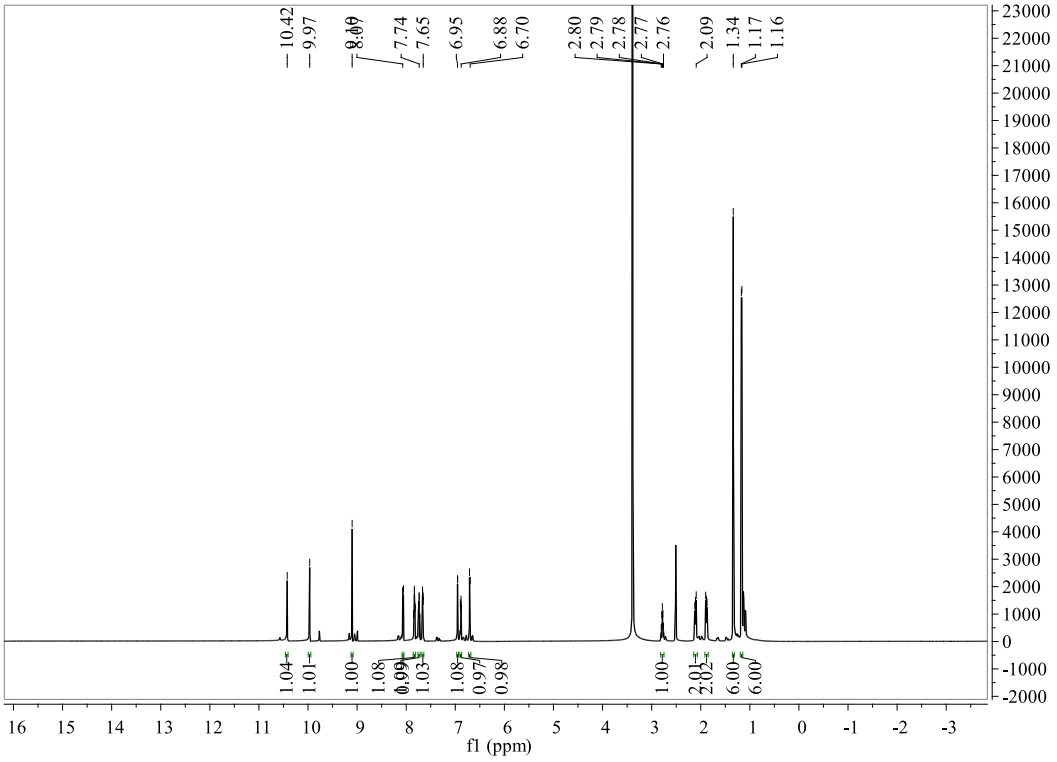


Figure S39. ^{1}H NMR spectrum of **5j**

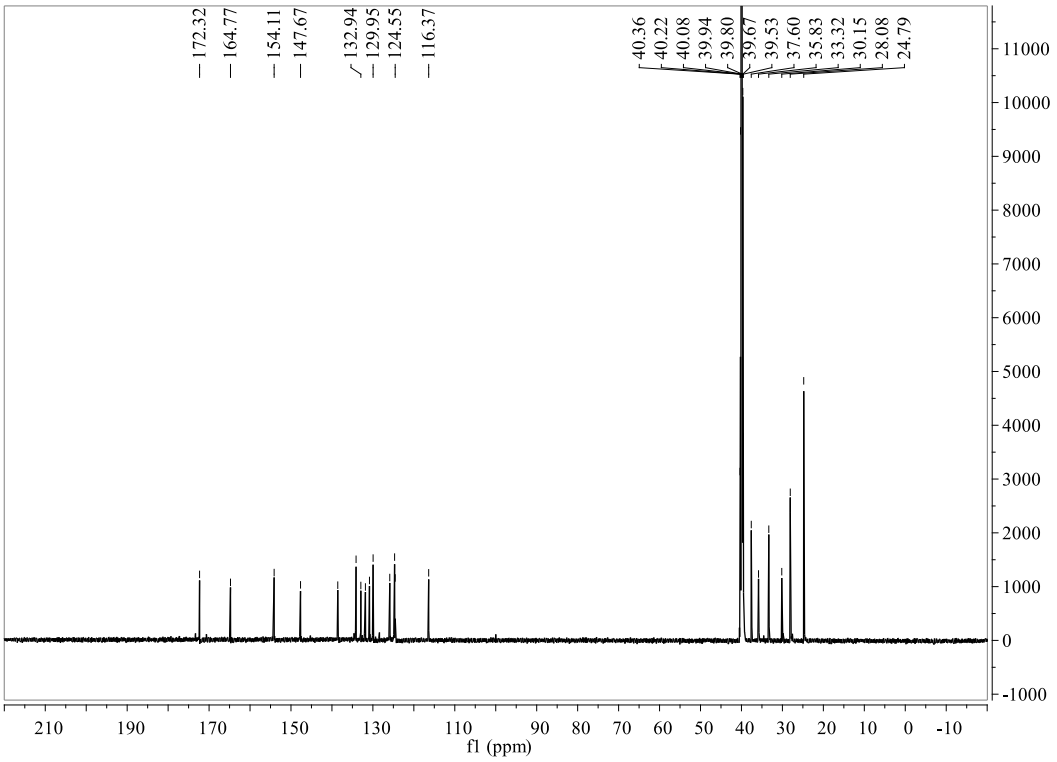


Figure S40. ^{13}C NMR spectrum of **5j**

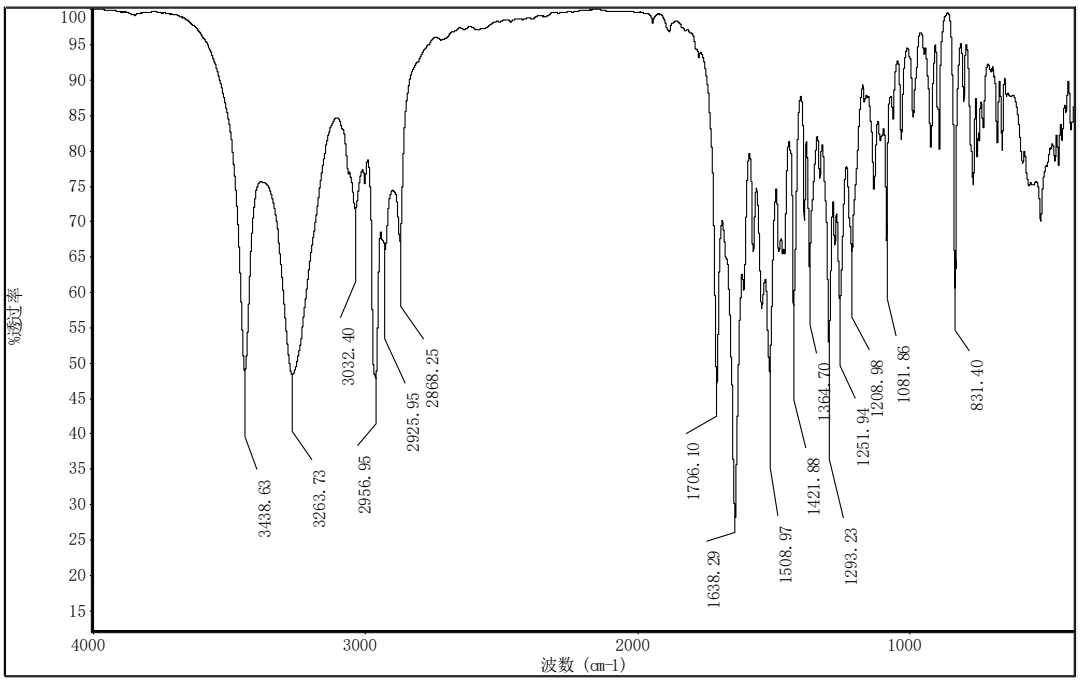


Figure S41. IR spectrum of **5k**

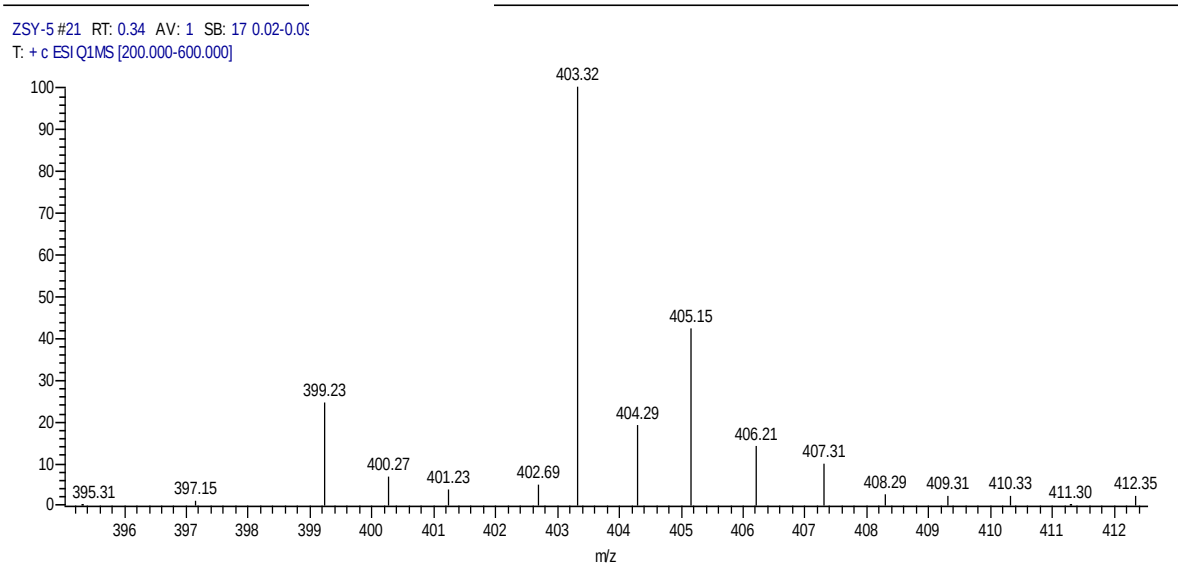


Figure S42. MS spectrum of **5k**

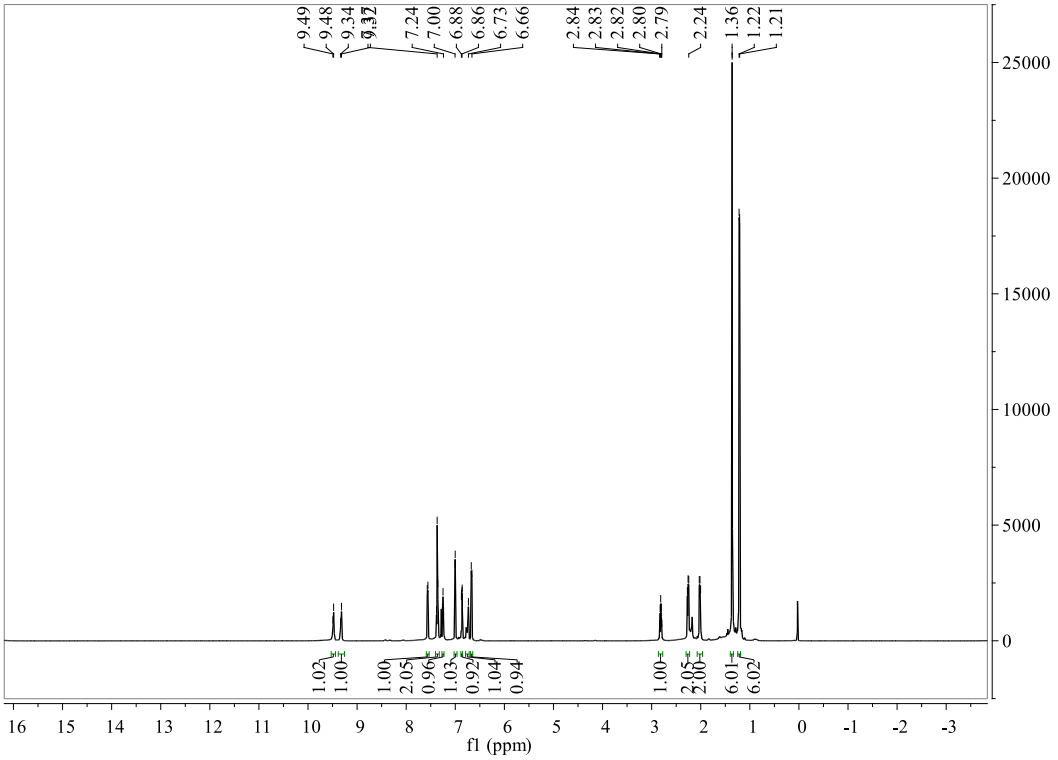


Figure S43. ^{1}H NMR spectrum of **5k**

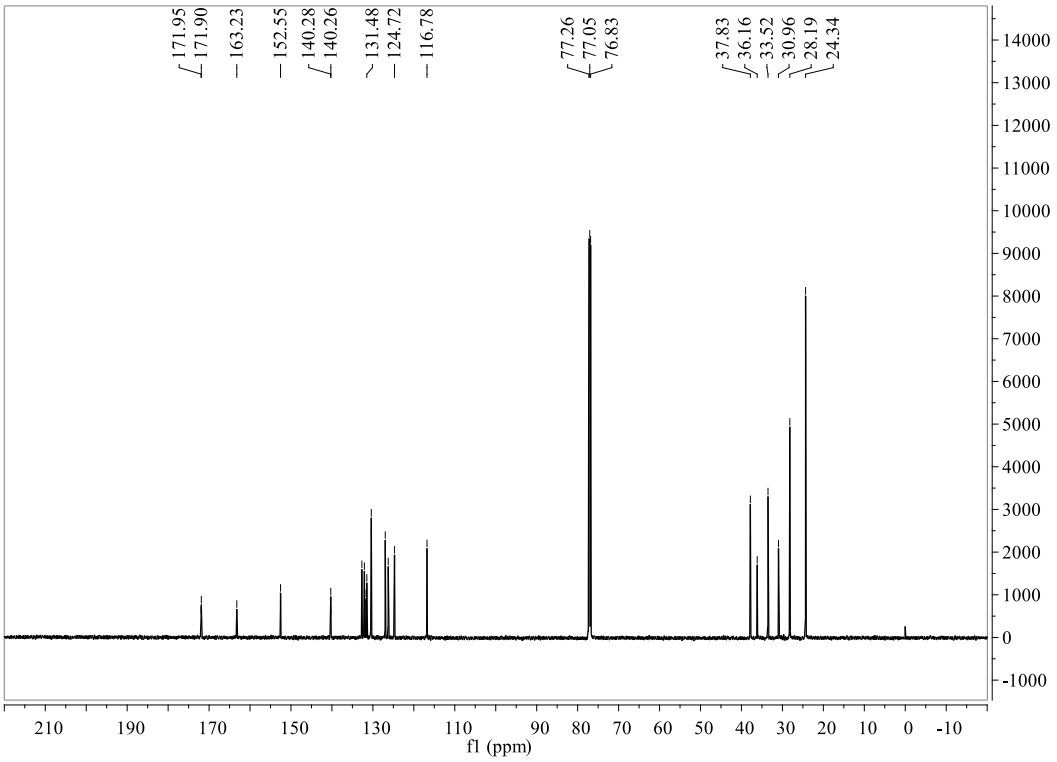


Figure S44. ^{13}C NMR spectrum of **5k**

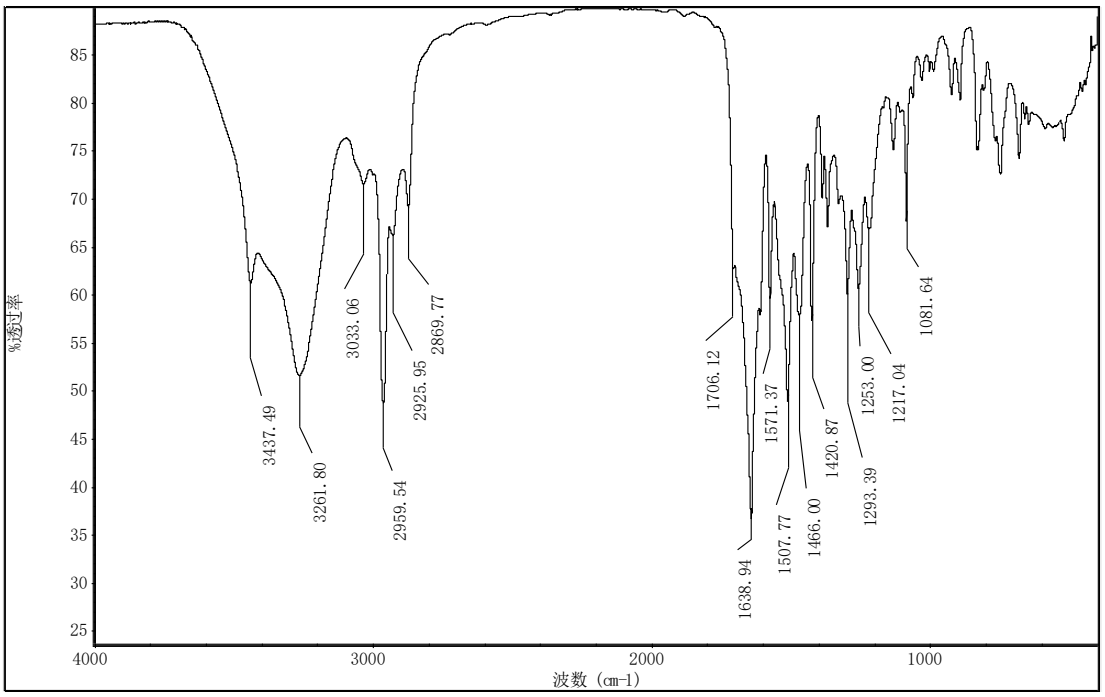


Figure S45. IR spectrum of **5l**

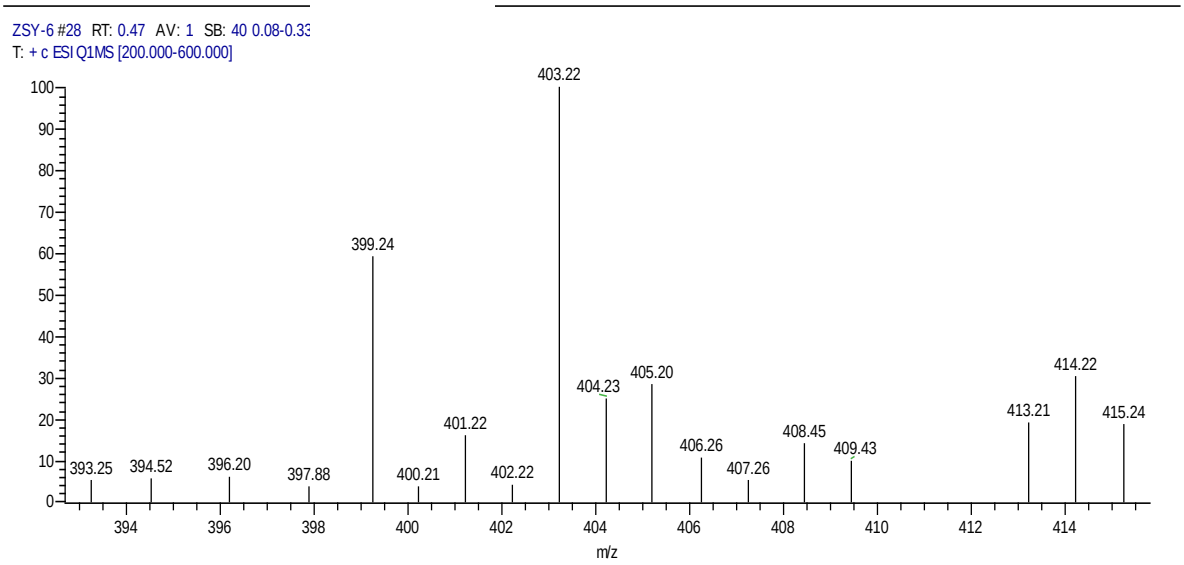


Figure S46. MS spectrum of **5l**

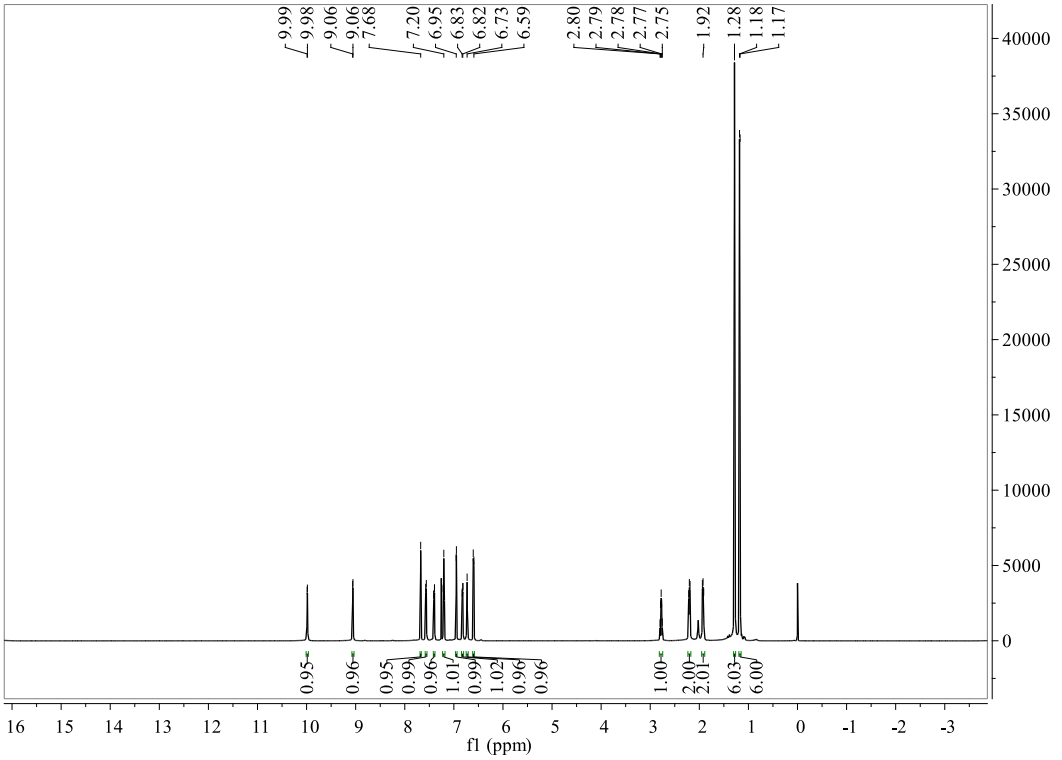


Figure S47. ^{1}H NMR spectrum of **5l**

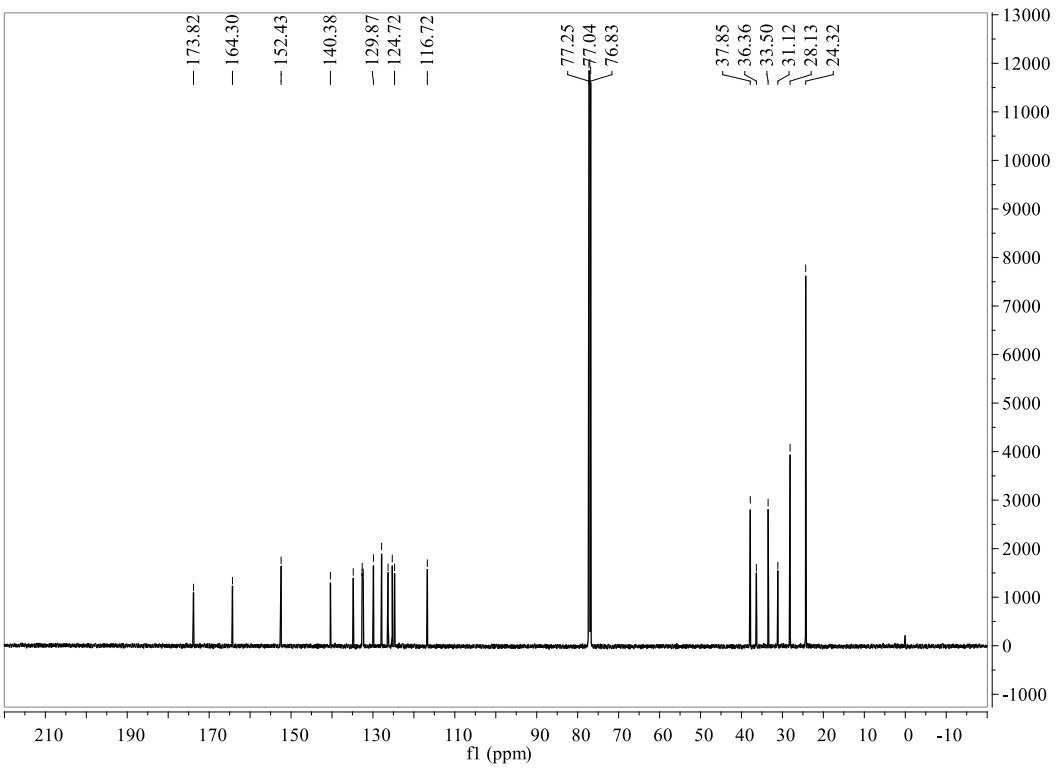


Figure S48. ^{13}C NMR spectrum of **5l**

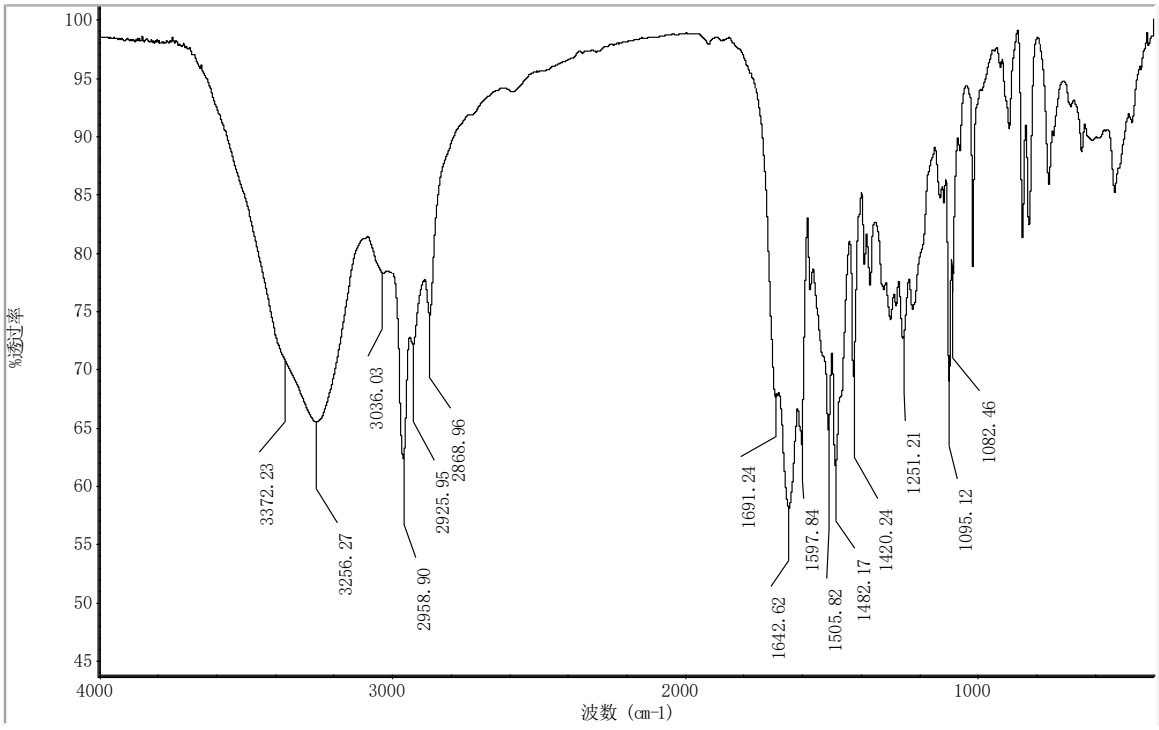


Figure S49. IR spectrum of **5m**

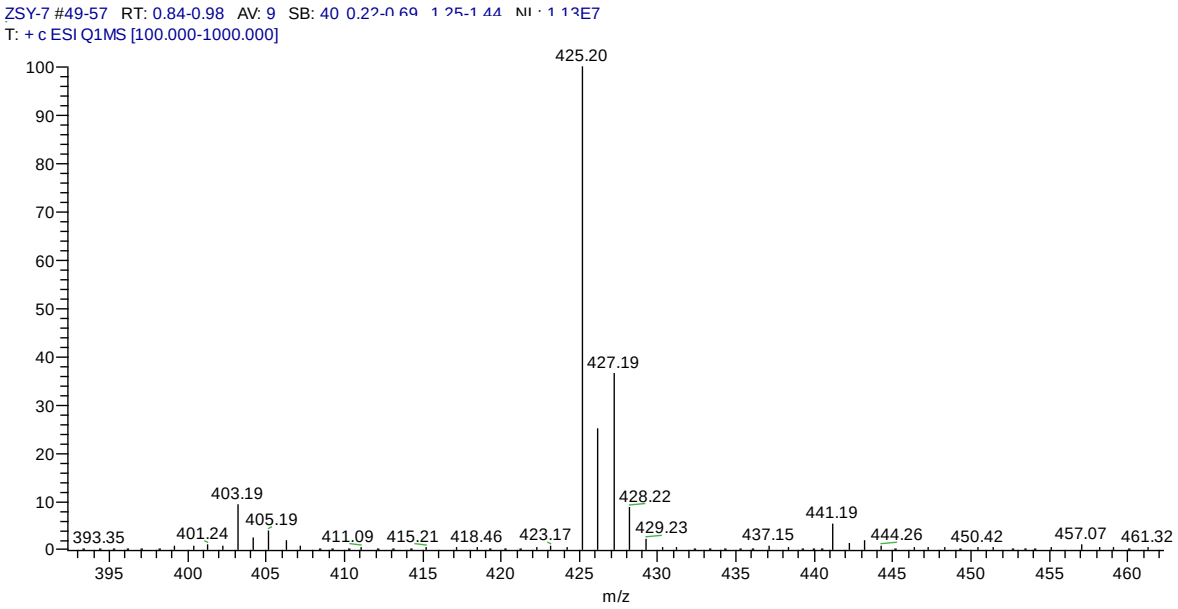


Figure S50. MS spectrum of **5m**

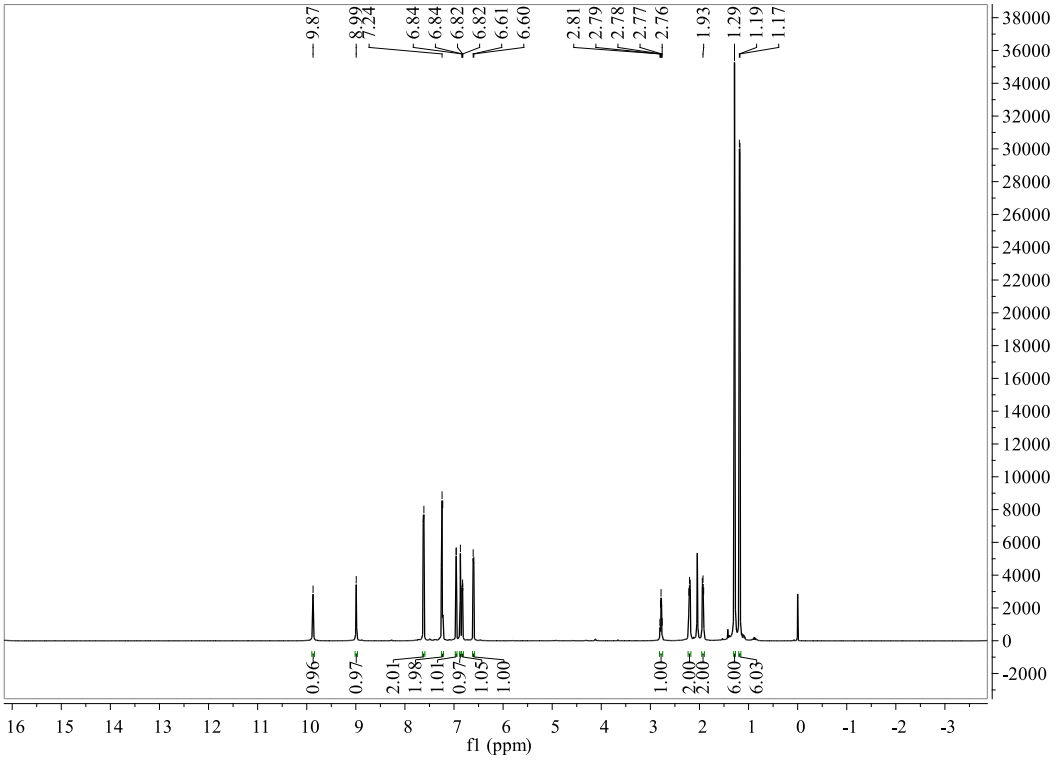


Figure S51. ^{1}H NMR spectrum of **5m**

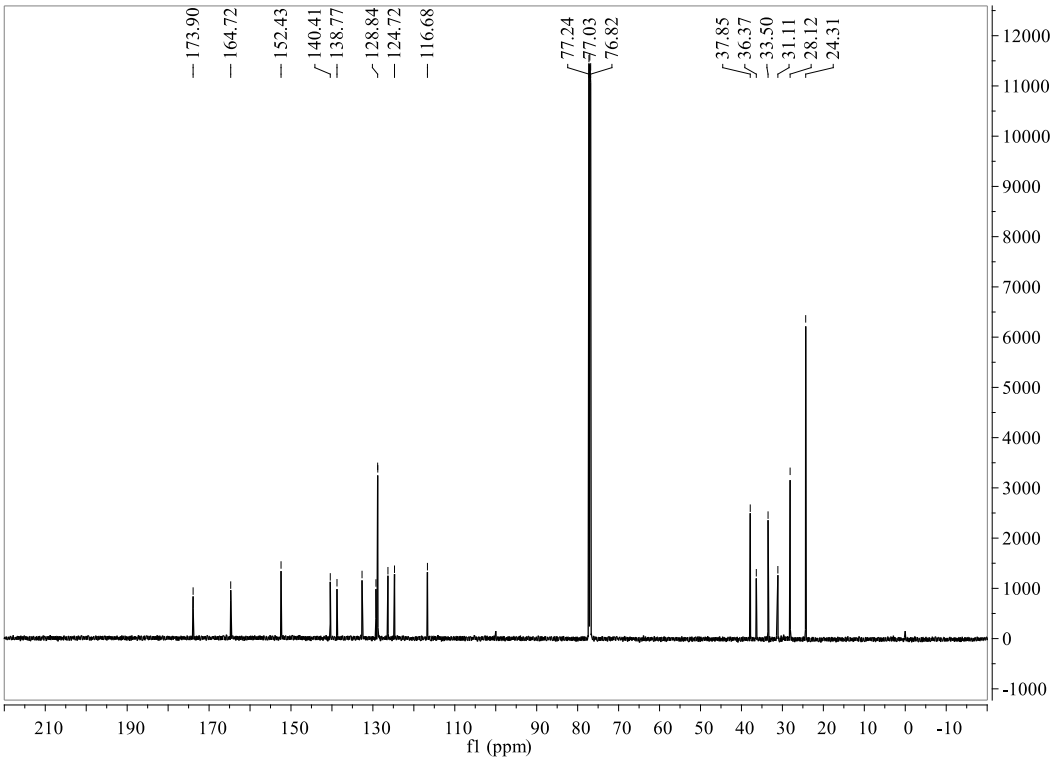


Figure S52. ^{13}C NMR spectrum of **5m**

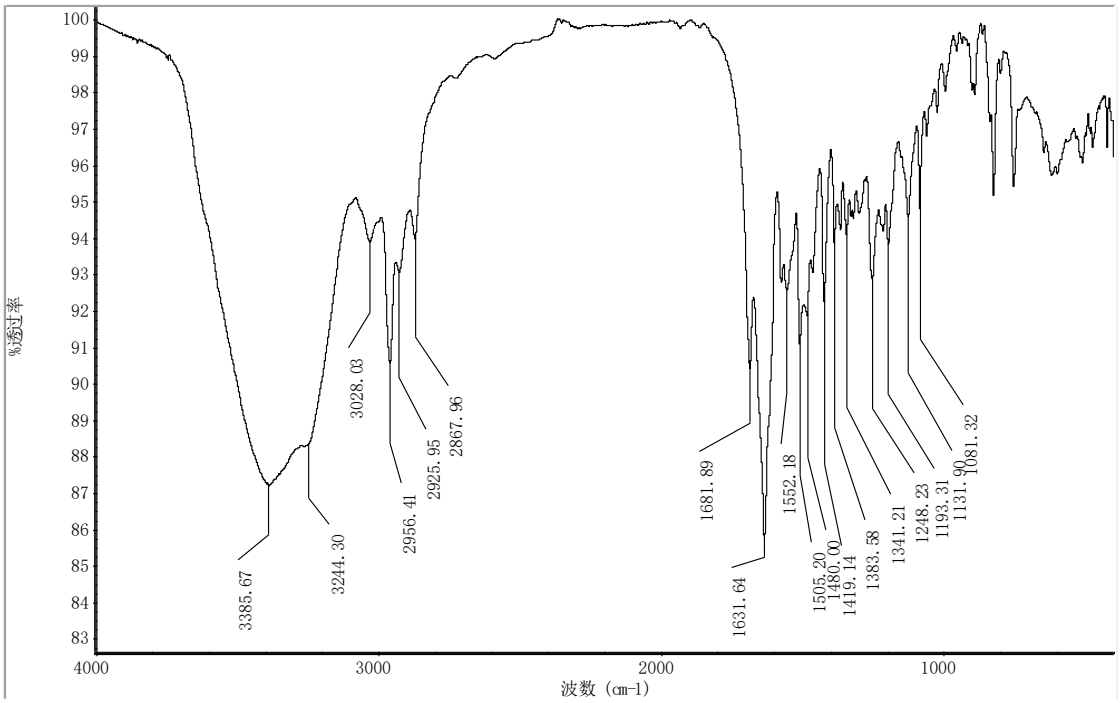


Figure S53. IR spectrum of **5n**

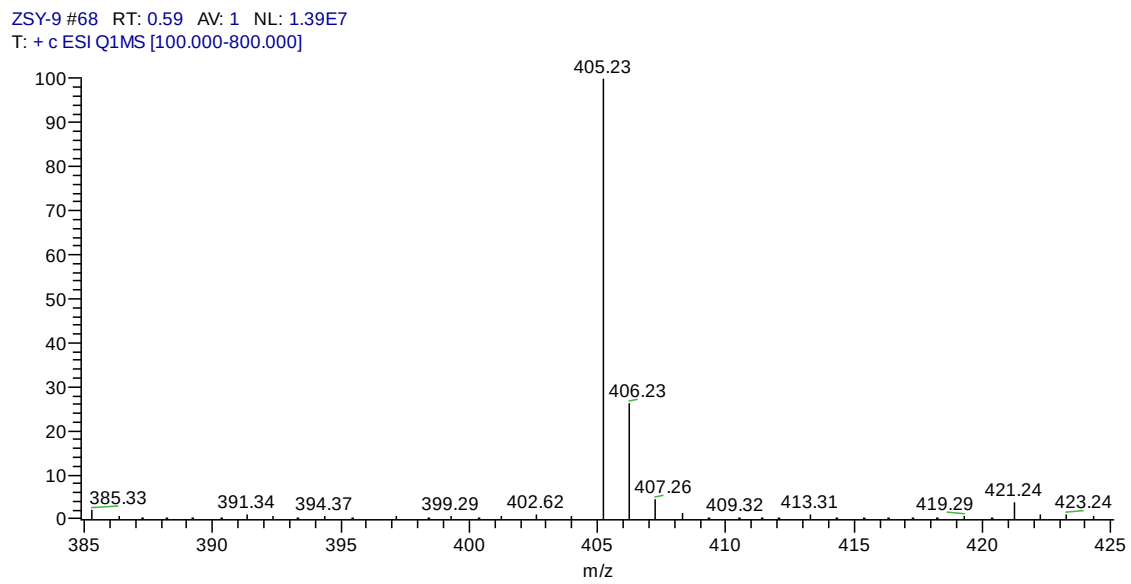


Figure S54. MS spectrum of **5n**

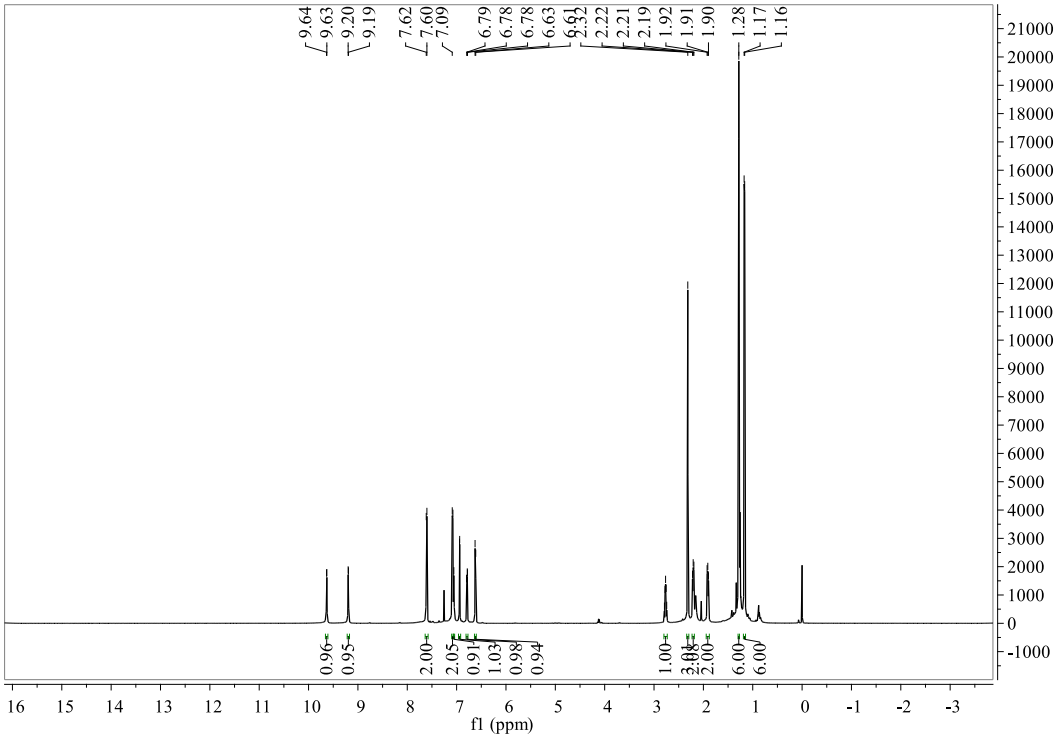


Figure S55. ^{1}H NMR spectrum of **5n**

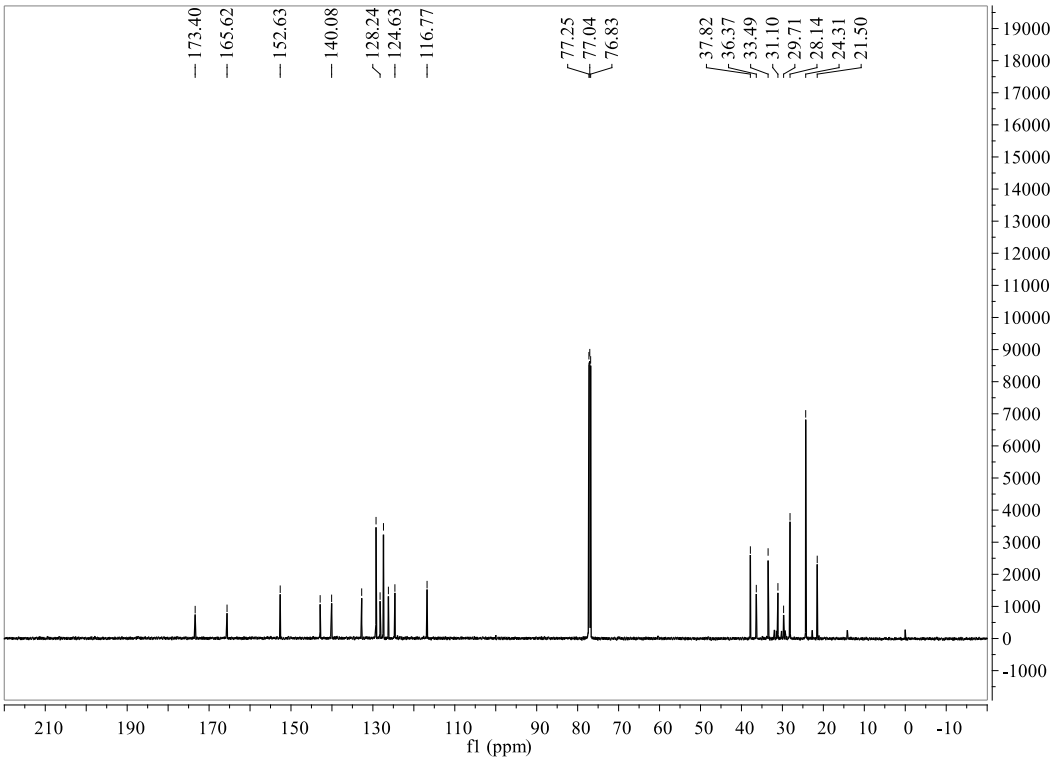


Figure S56. ^{13}C NMR spectrum of **5n**

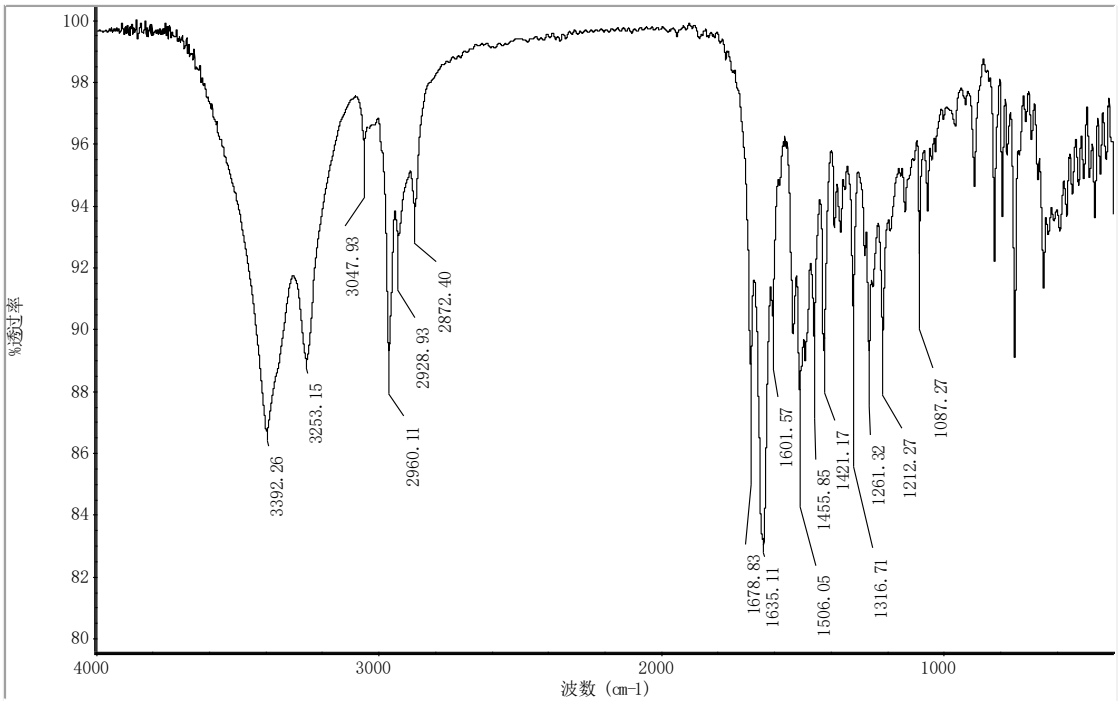


Figure S57. IR spectrum of **5o**

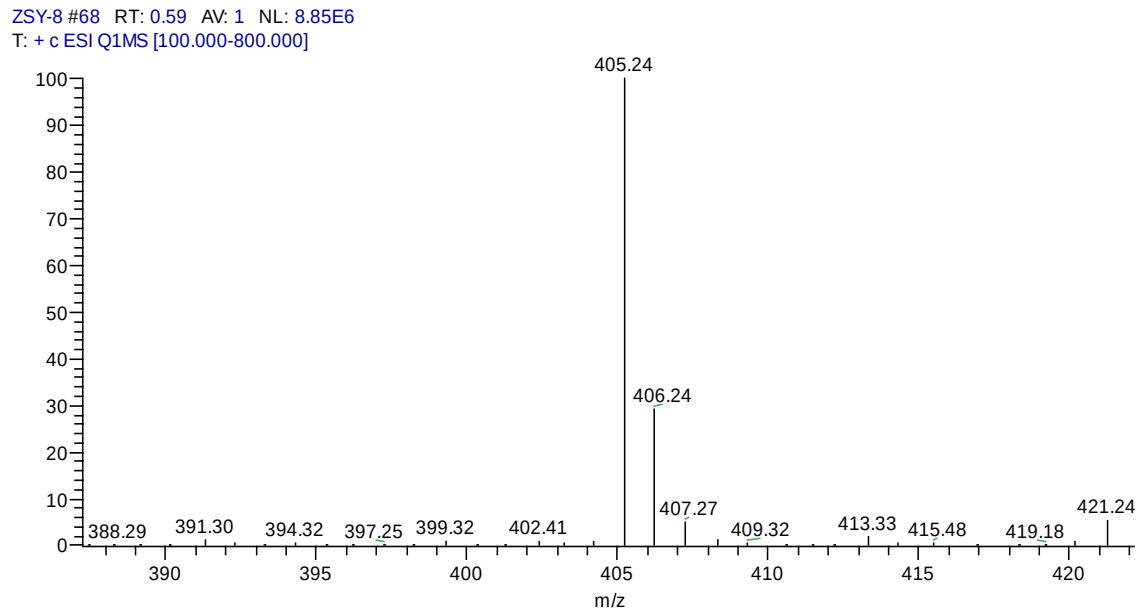


Figure S58. MS spectrum of **5o**

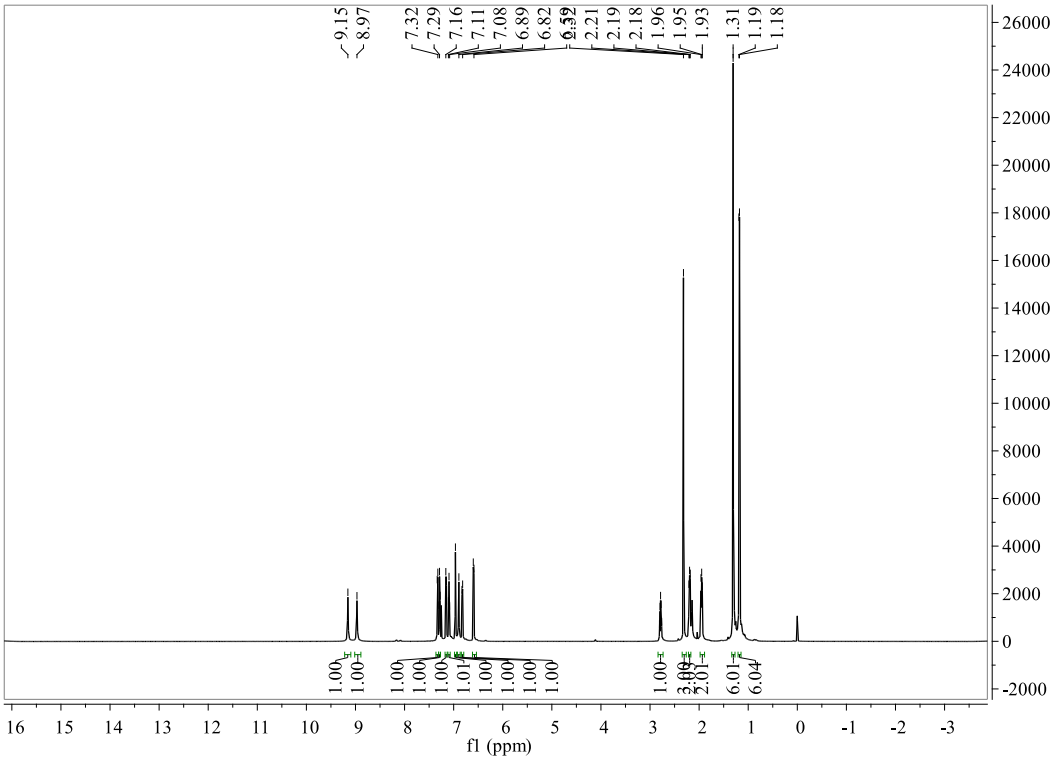


Figure S59. ^{1}H NMR spectrum of **5o**

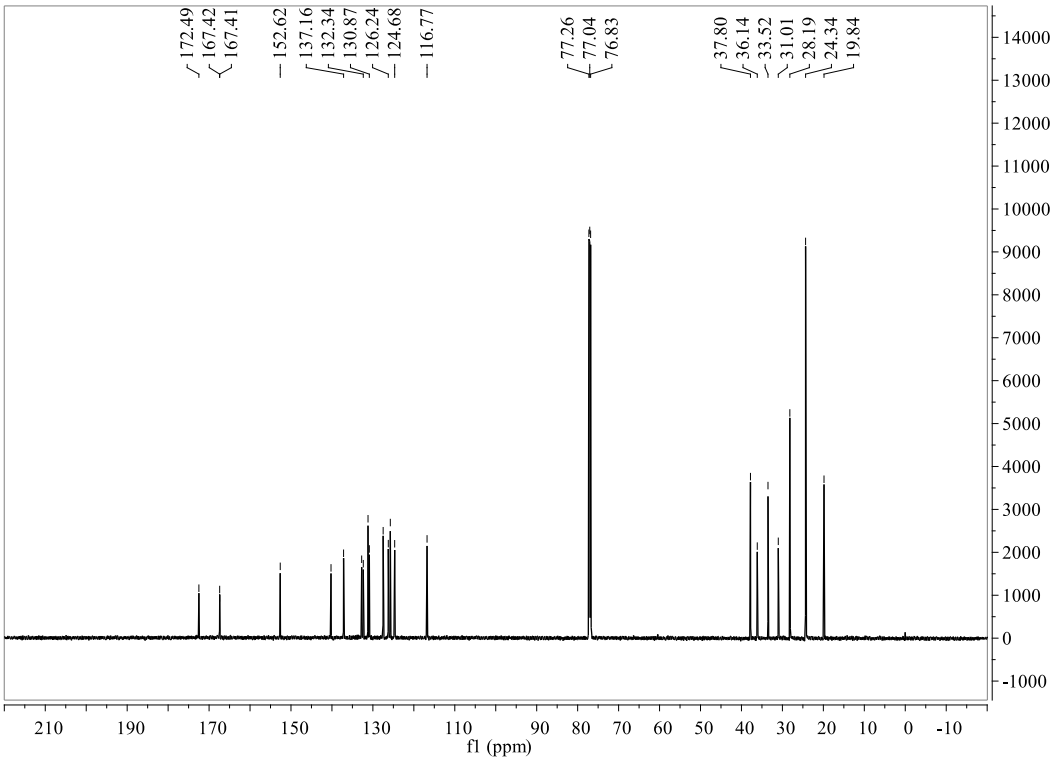


Figure S60. ^{13}C NMR spectrum of **5o**

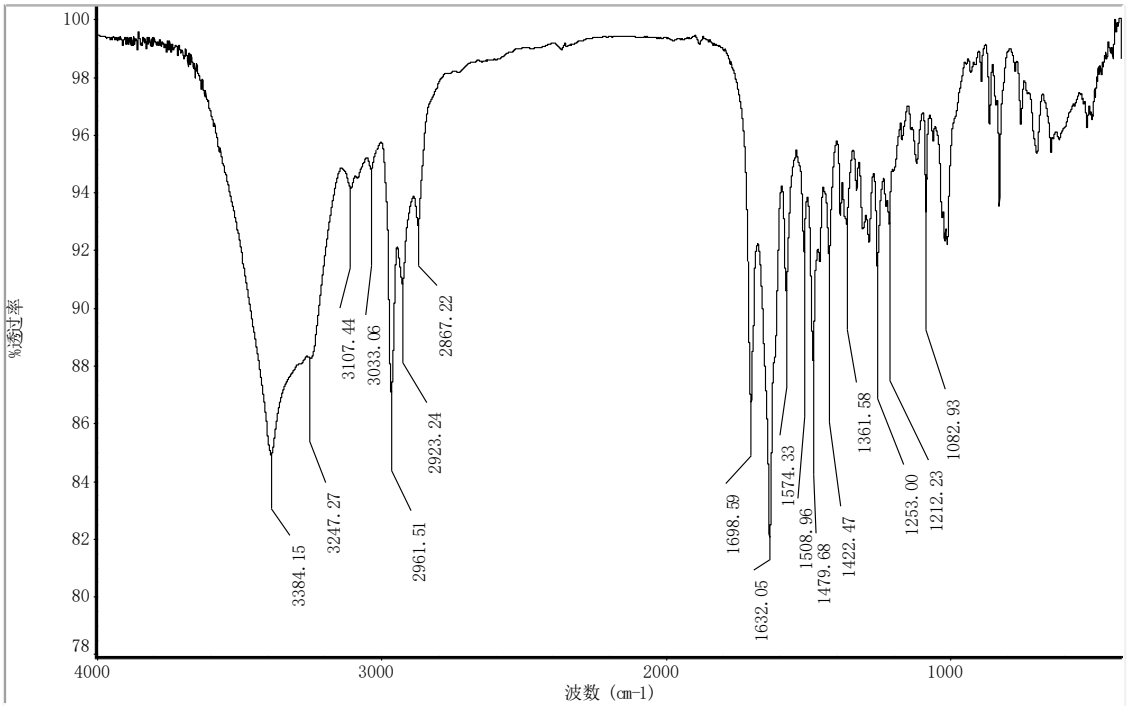


Figure S61. IR spectrum of **5p**

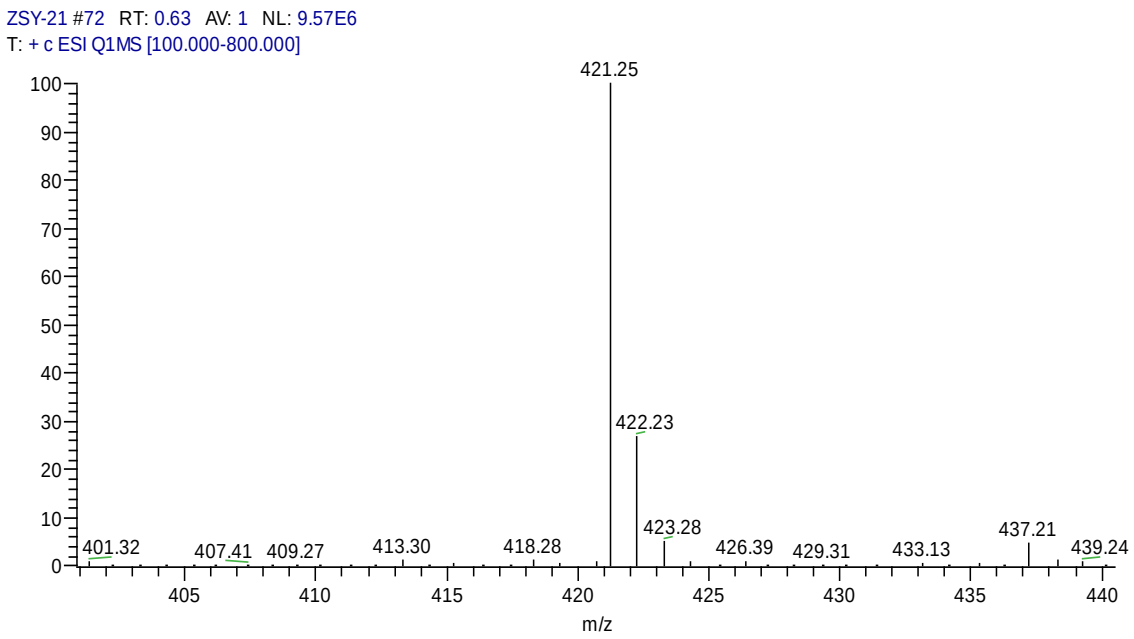


Figure S62. MS spectrum of **5p**

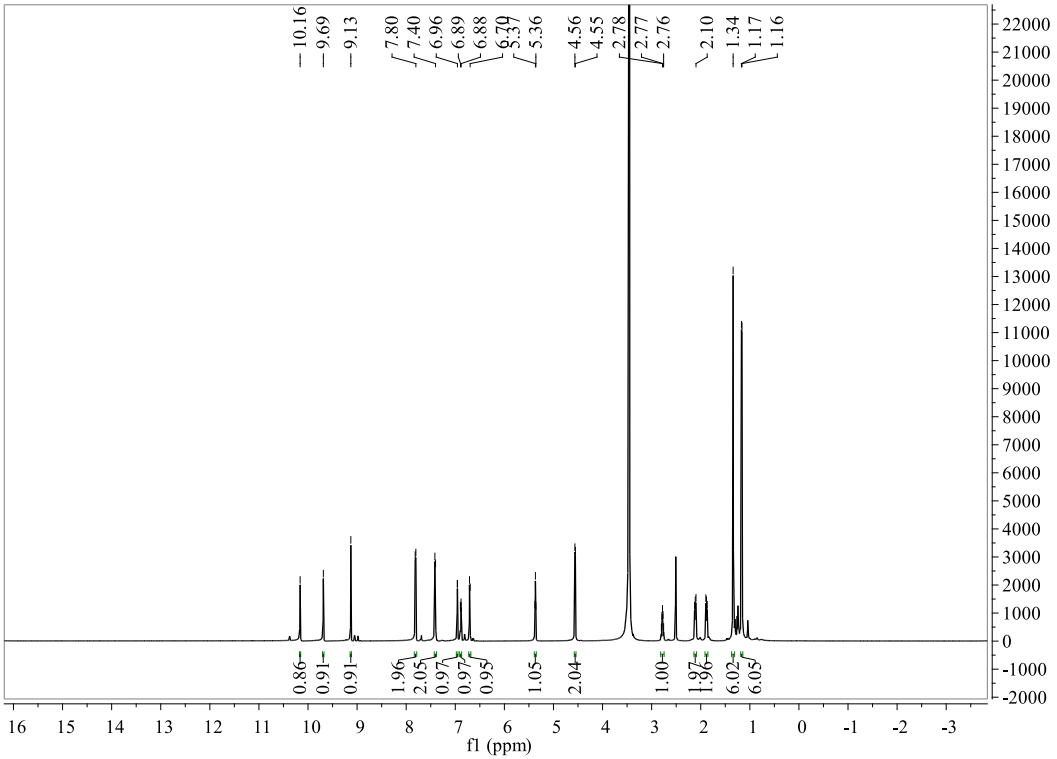


Figure S63. ^{1}H NMR spectrum of **5p**

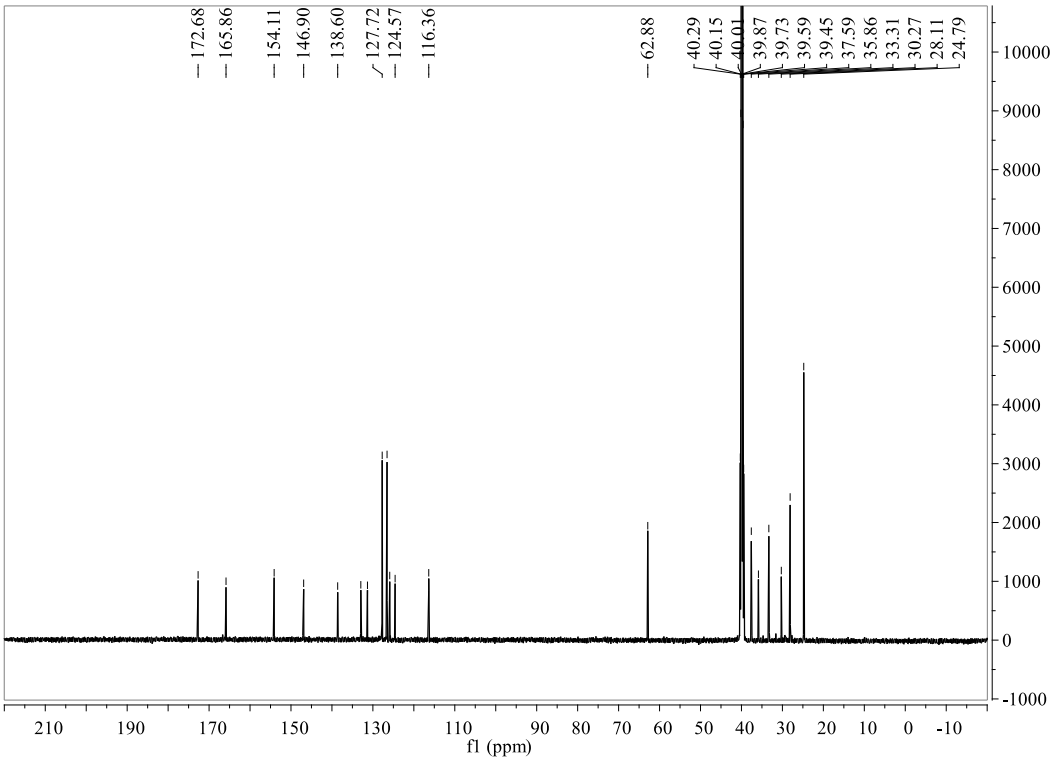


Figure S64. ^{13}C NMR spectrum of **5p**

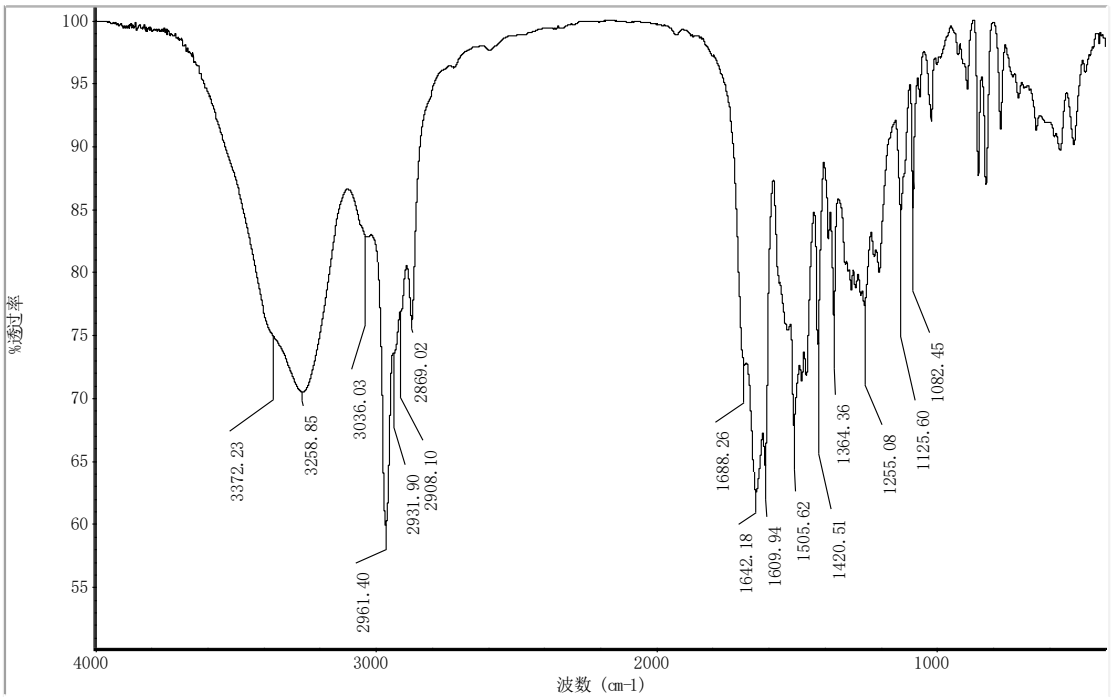


Figure S65. IR spectrum of **5q**

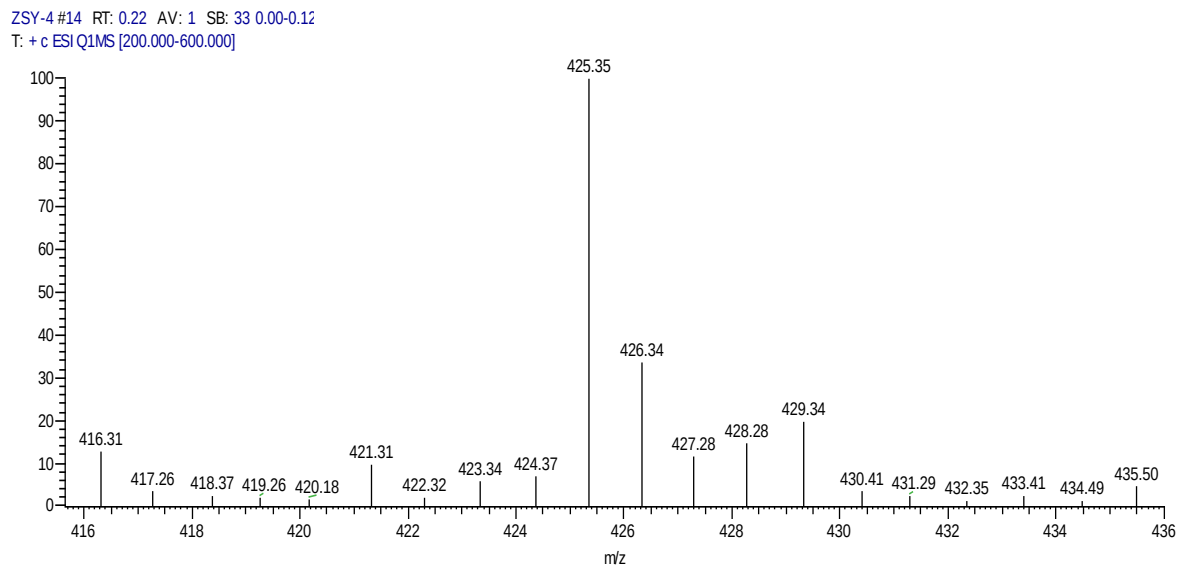


Figure S66. MS spectrum of **5q**

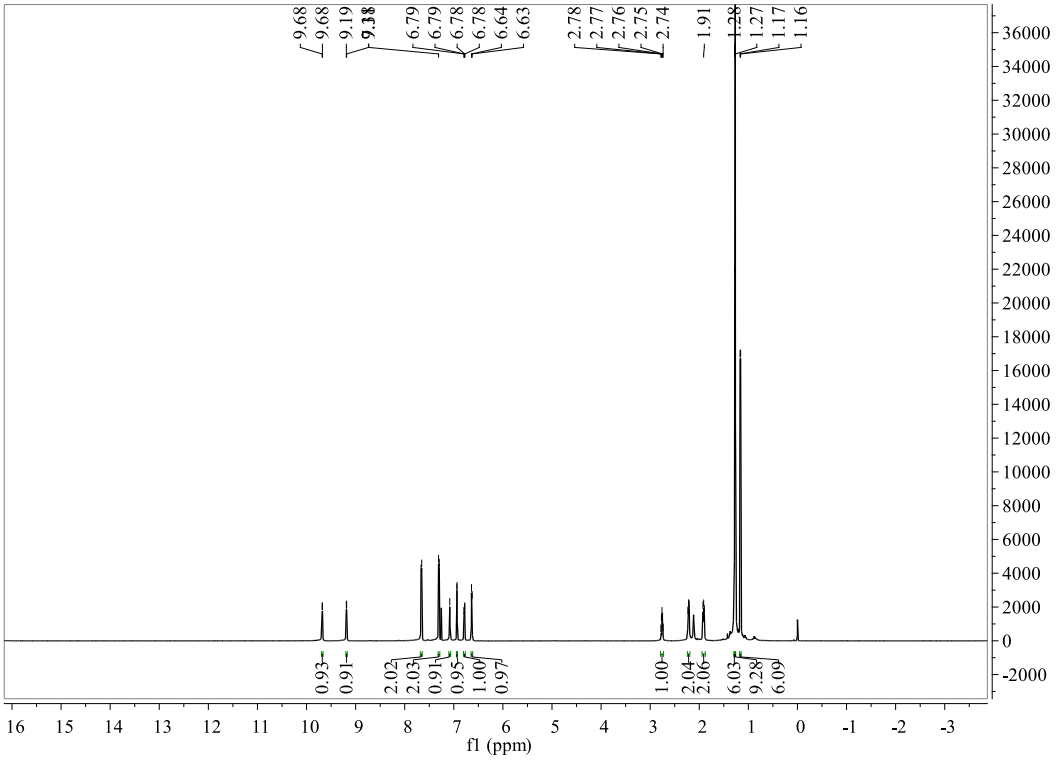


Figure S67. ^{1}H NMR spectrum of **5q**

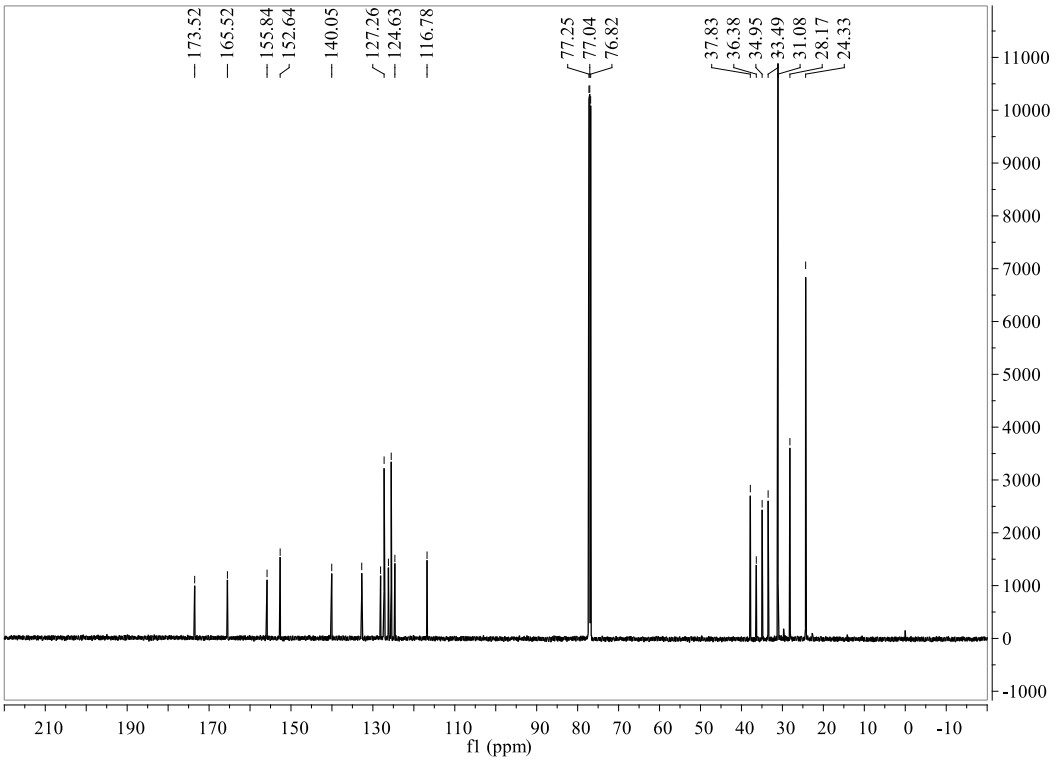


Figure S68. ^{13}C NMR spectrum of **5q**

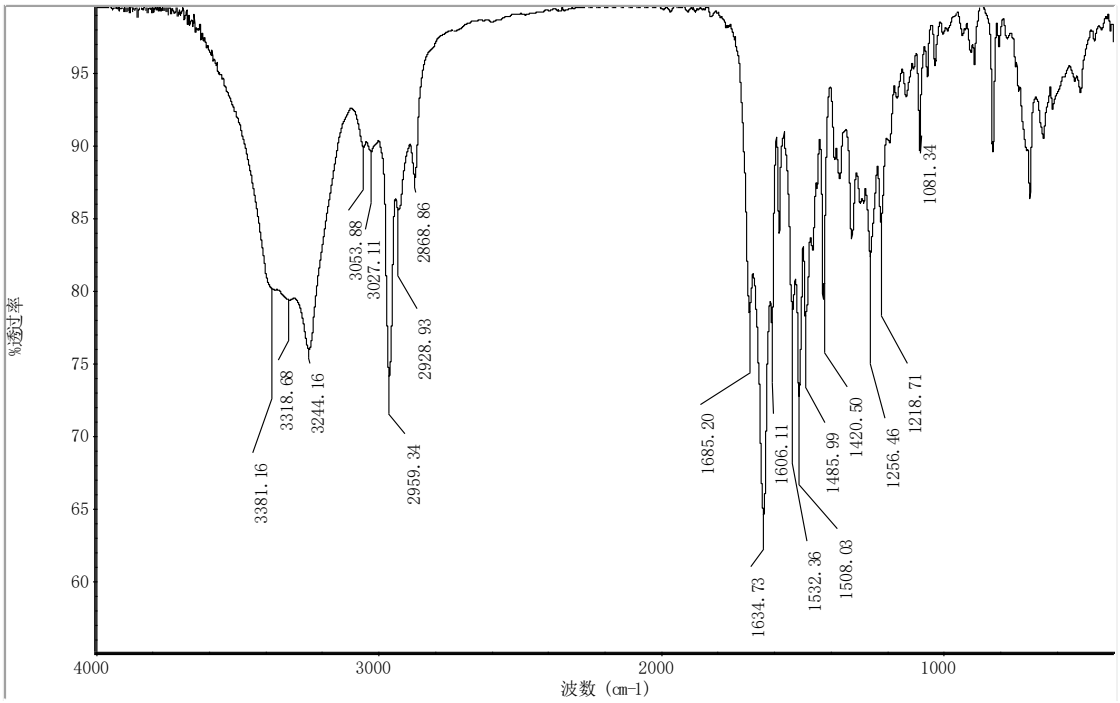


Figure S69. IR spectrum of **5r**

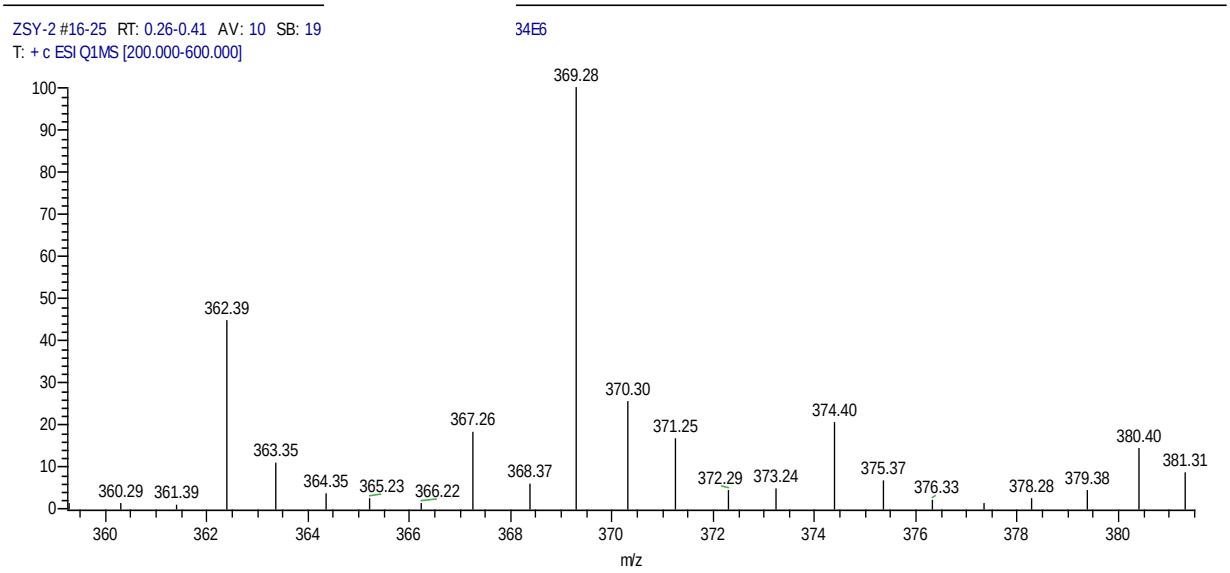


Figure S70. MS spectrum of **5r**

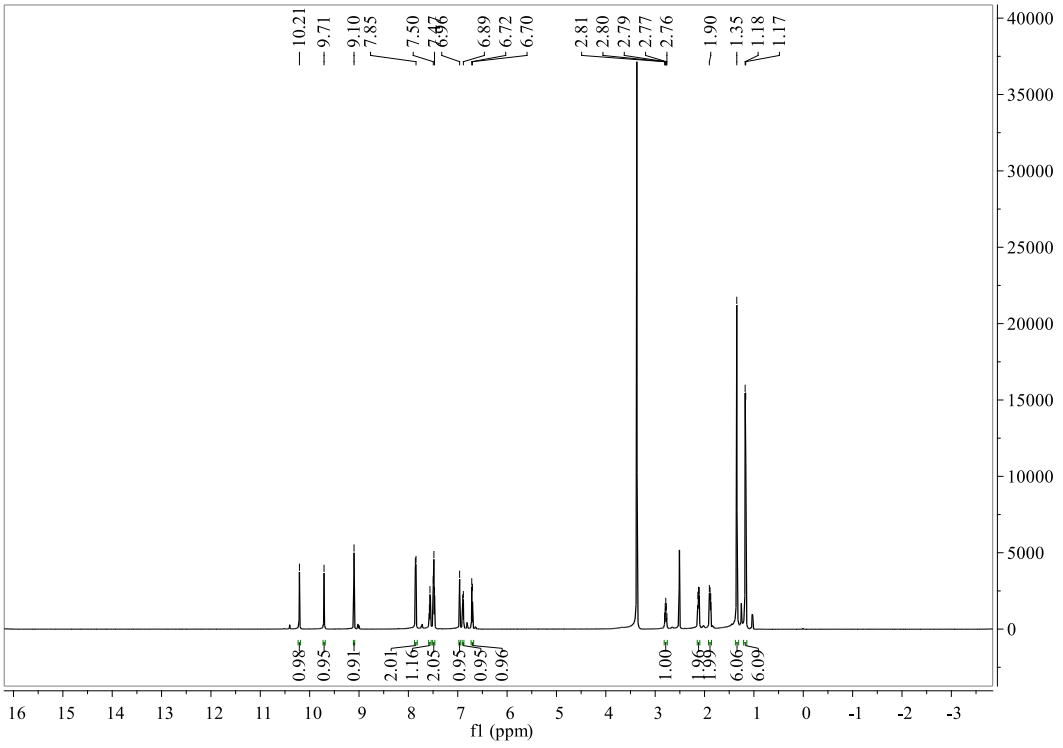


Figure S71. ^{1}H NMR spectrum of **5r**

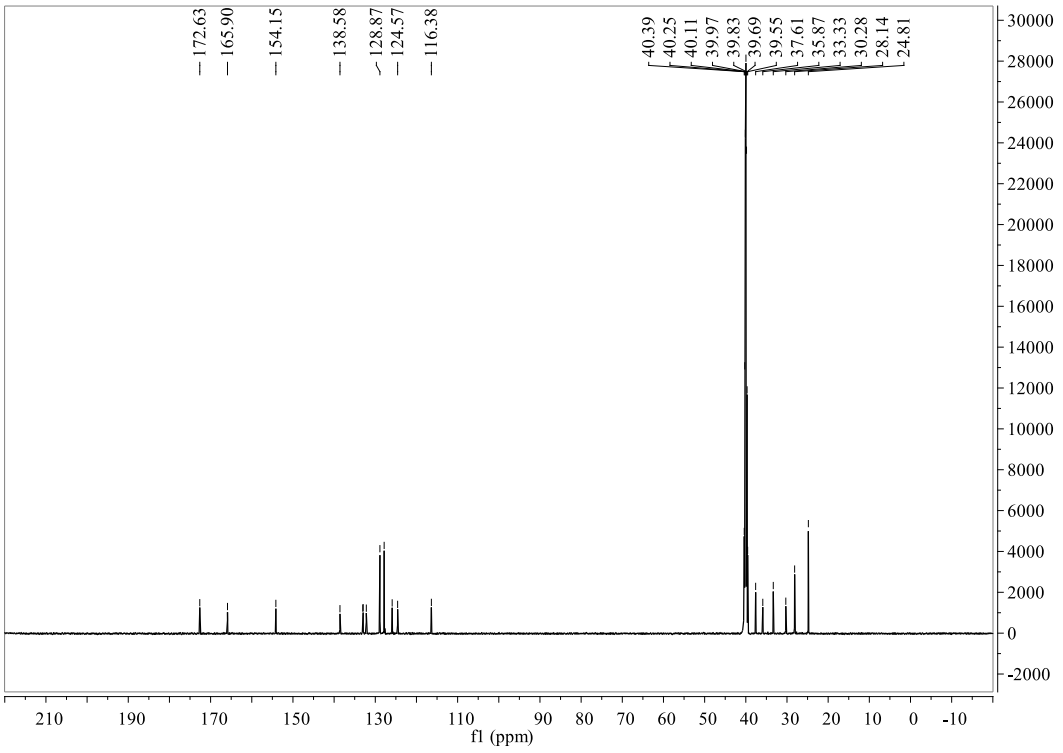


Figure S72. ^{13}C NMR spectrum of **5r**

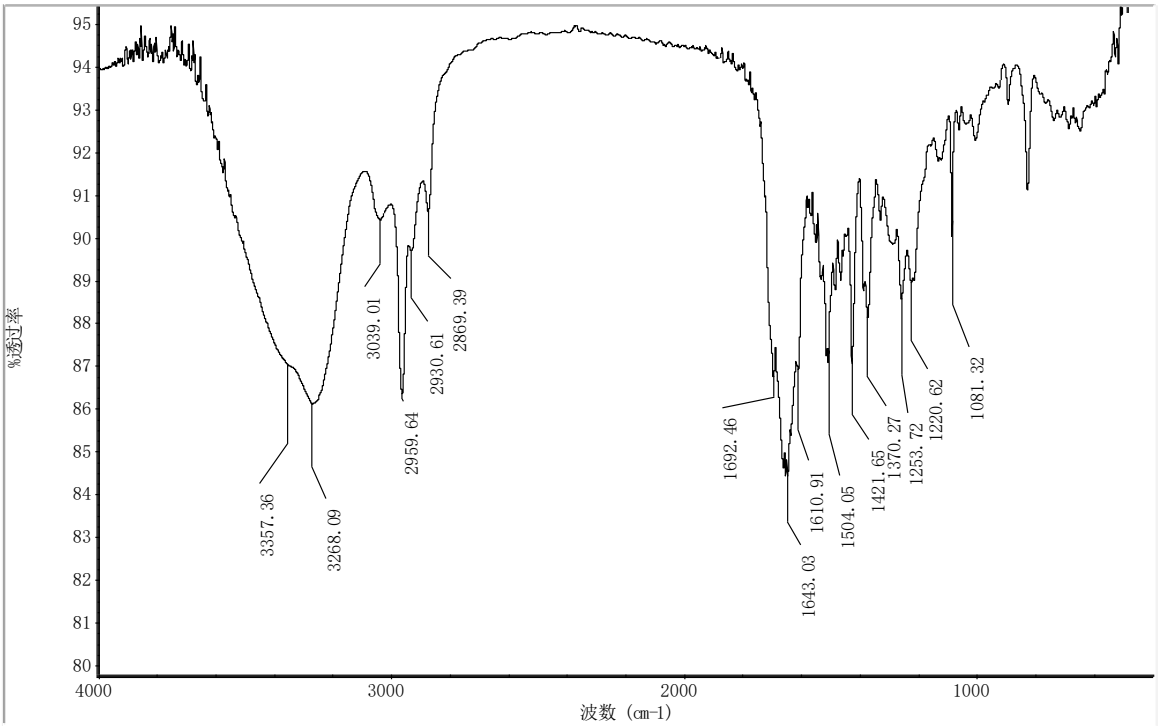


Figure S73. IR spectrum of **5s**

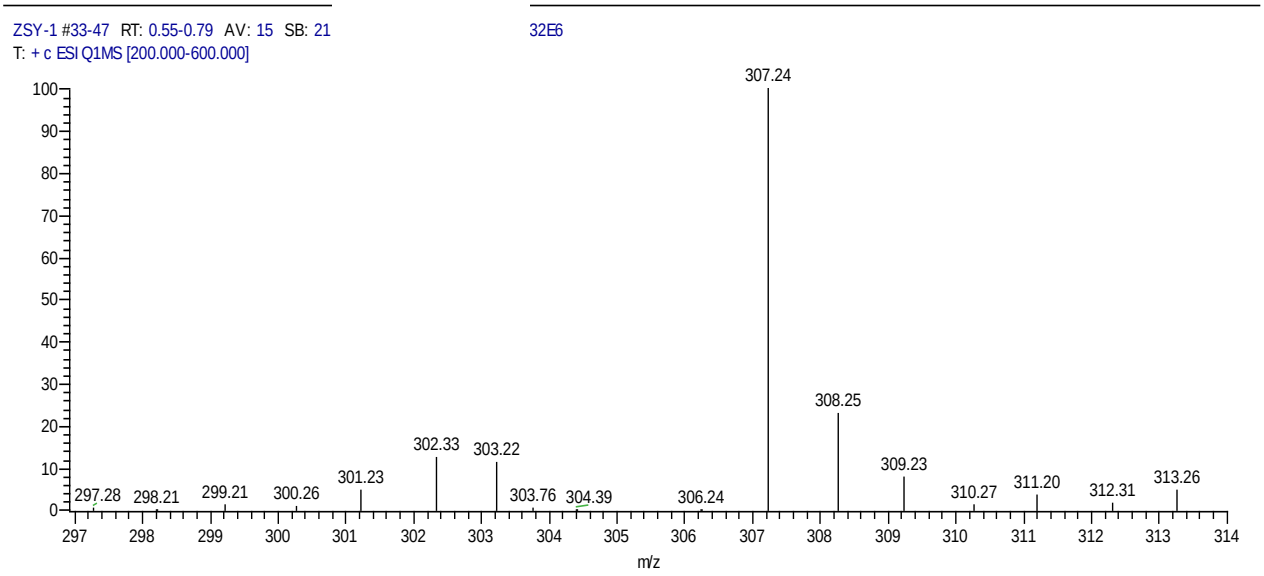


Figure S74. MS spectrum of **5s**

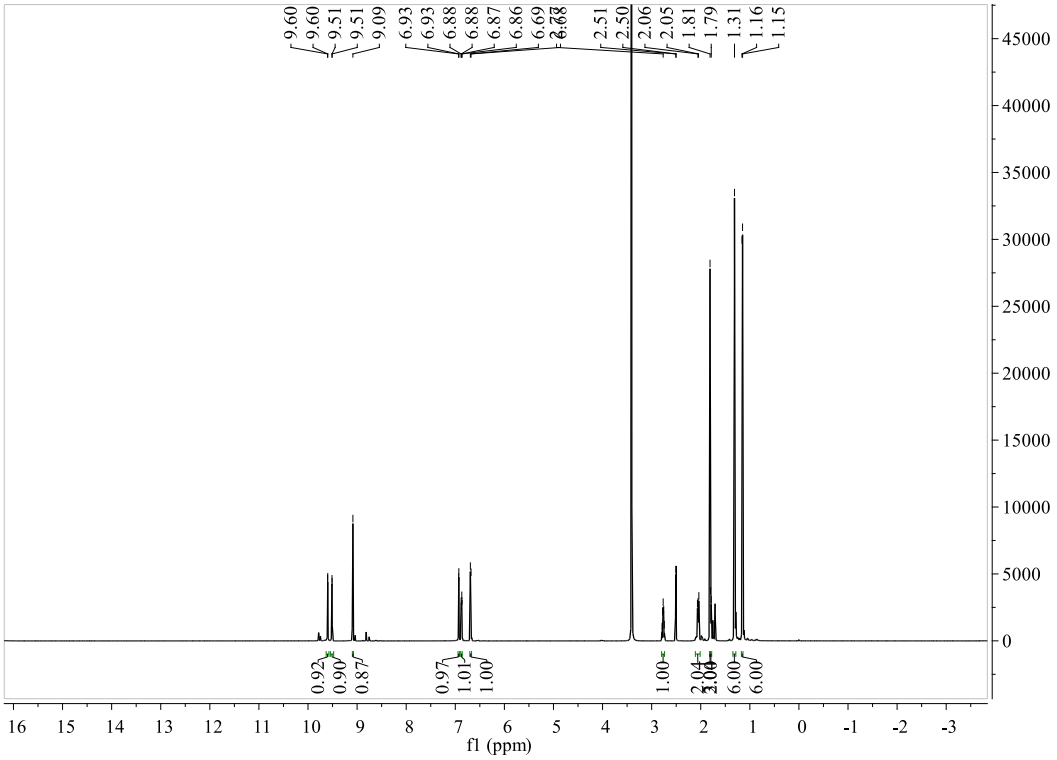


Figure S75. ^{1}H NMR spectrum of **5s**

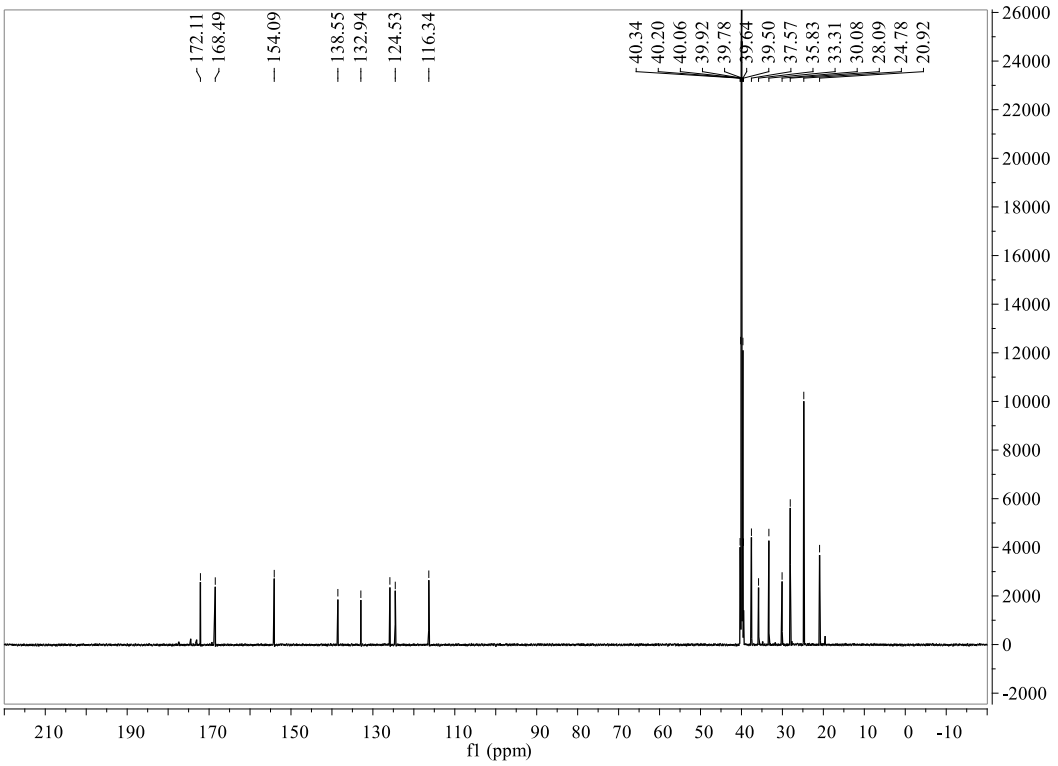


Figure S76. ^{13}C NMR spectrum of **5s**

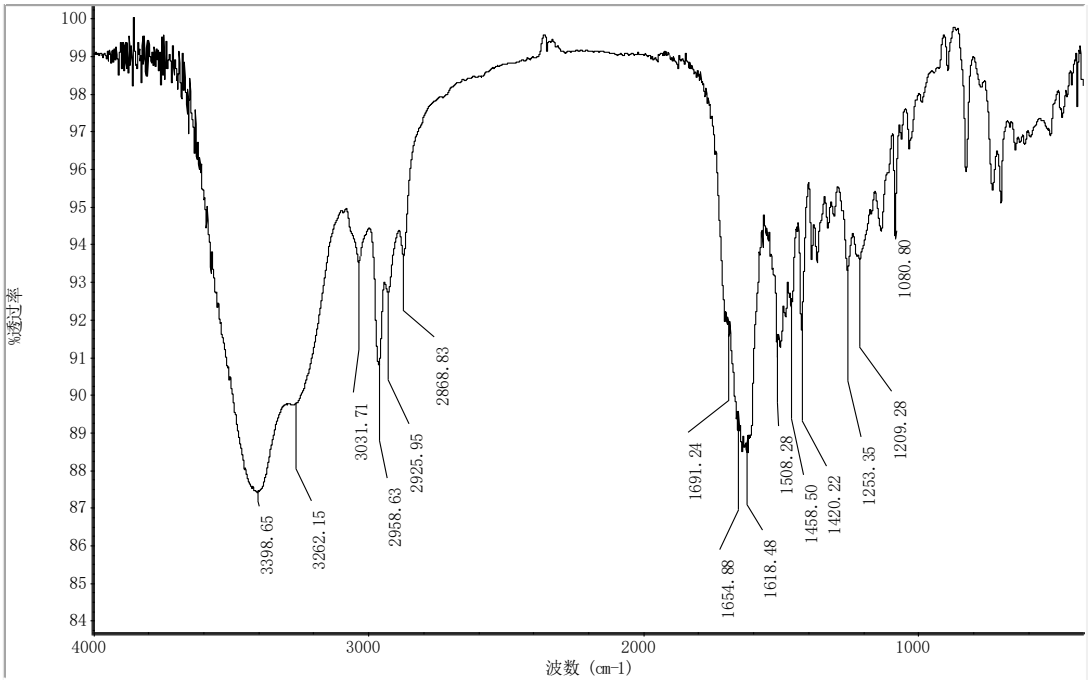


Figure S77. IR spectrum of **5t**

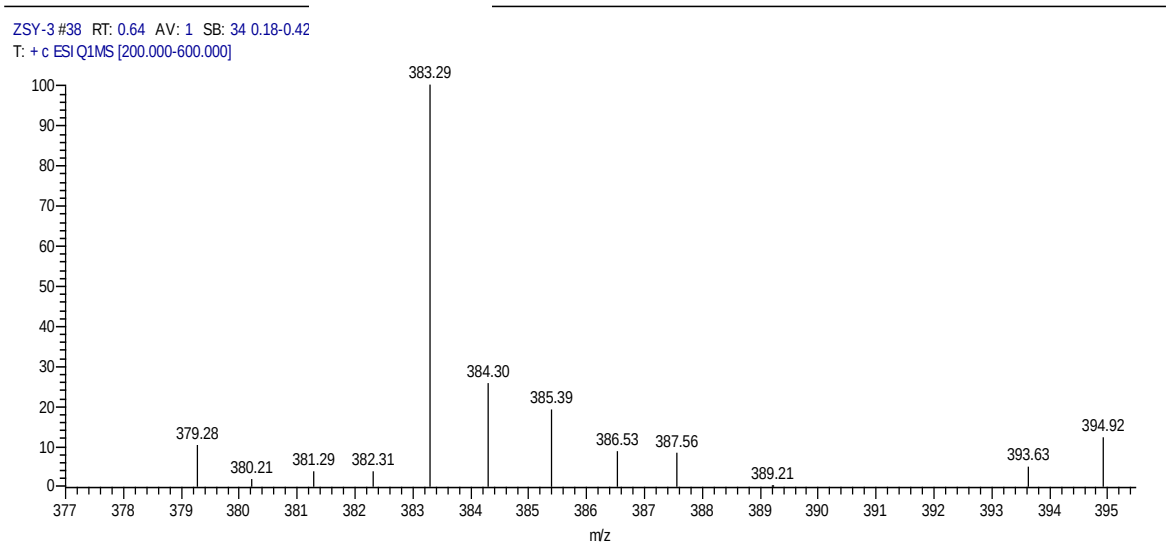


Figure S78. MS spectrum of **5t**

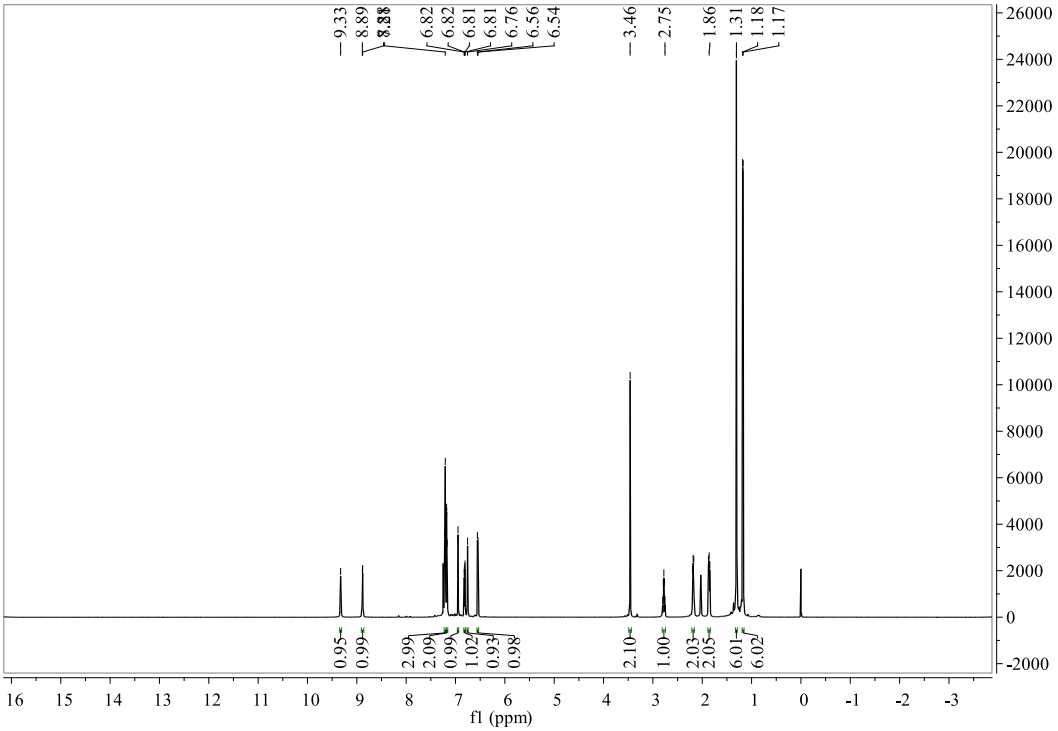


Figure S79. ^{1}H NMR spectrum of **5t**

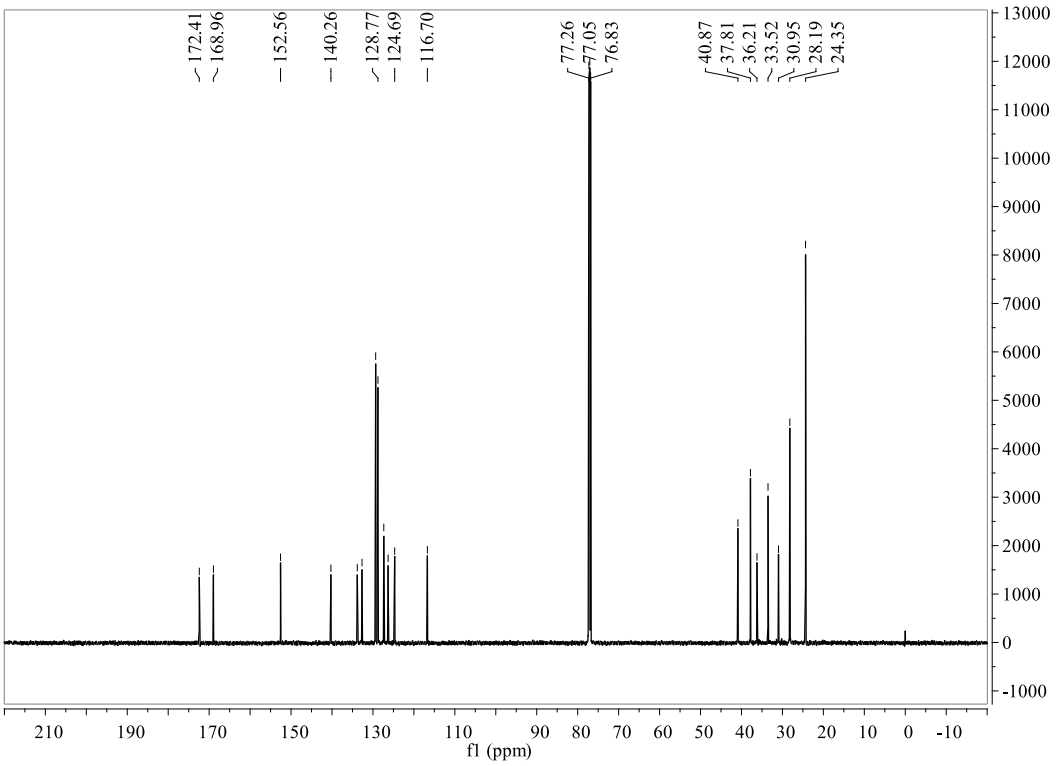


Figure S80. ^{13}C NMR spectrum of **5t**

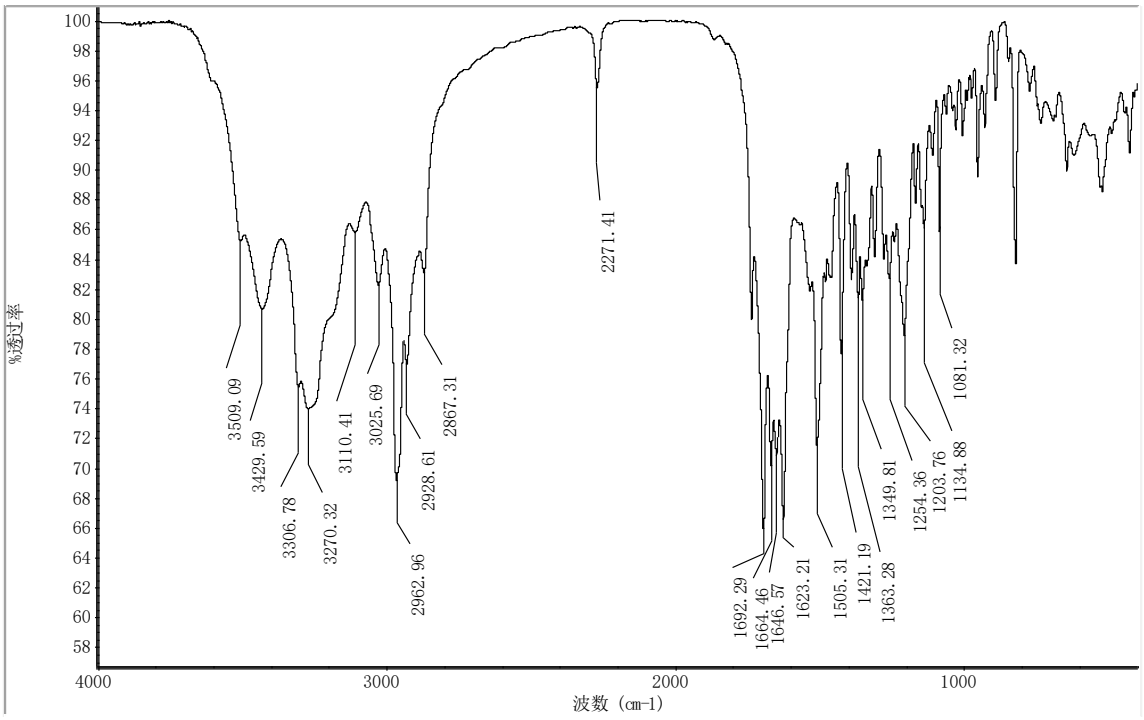


Figure S81. IR spectrum of **5u**

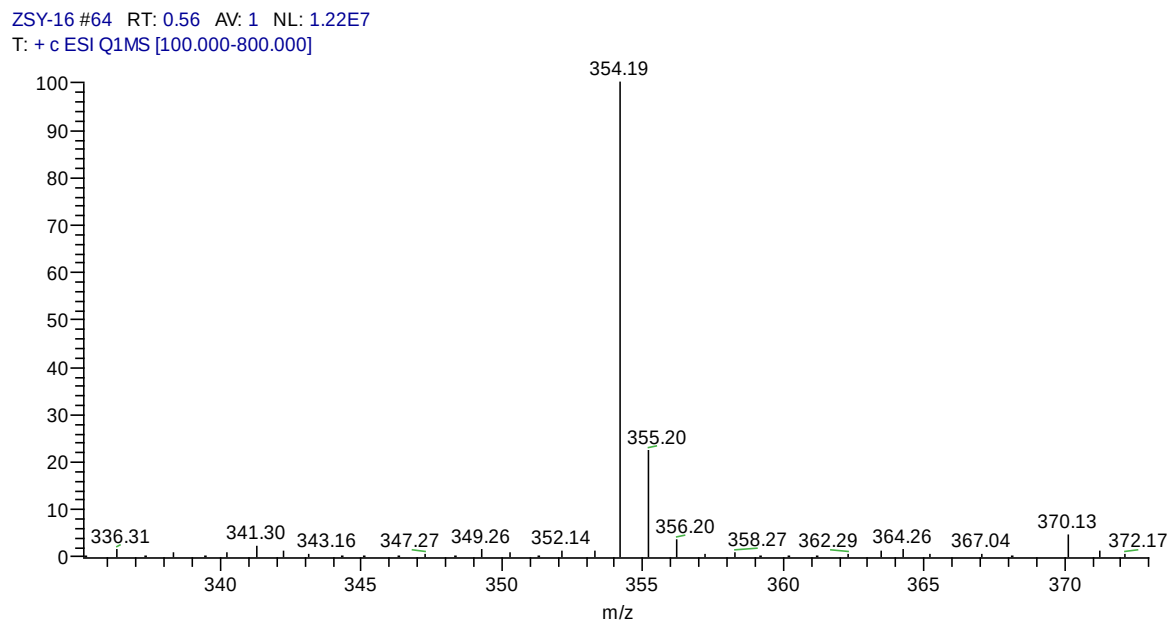


Figure S82. MS spectrum of **5u**

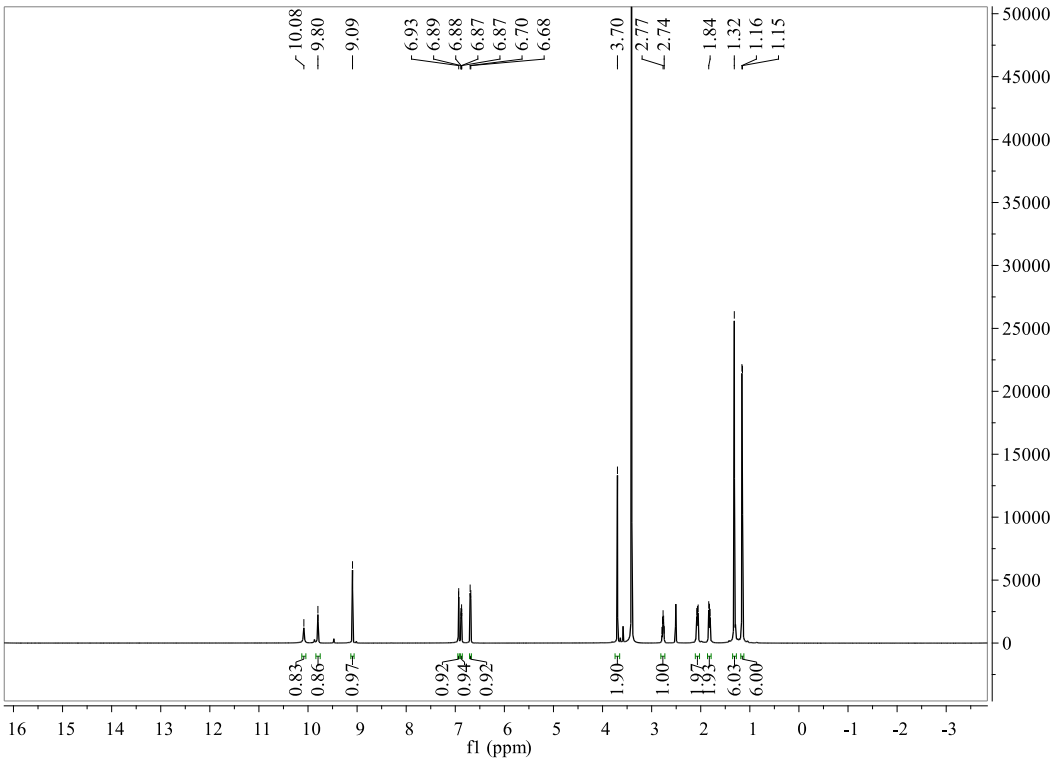


Figure S83. ^{1}H NMR spectrum of **5u**

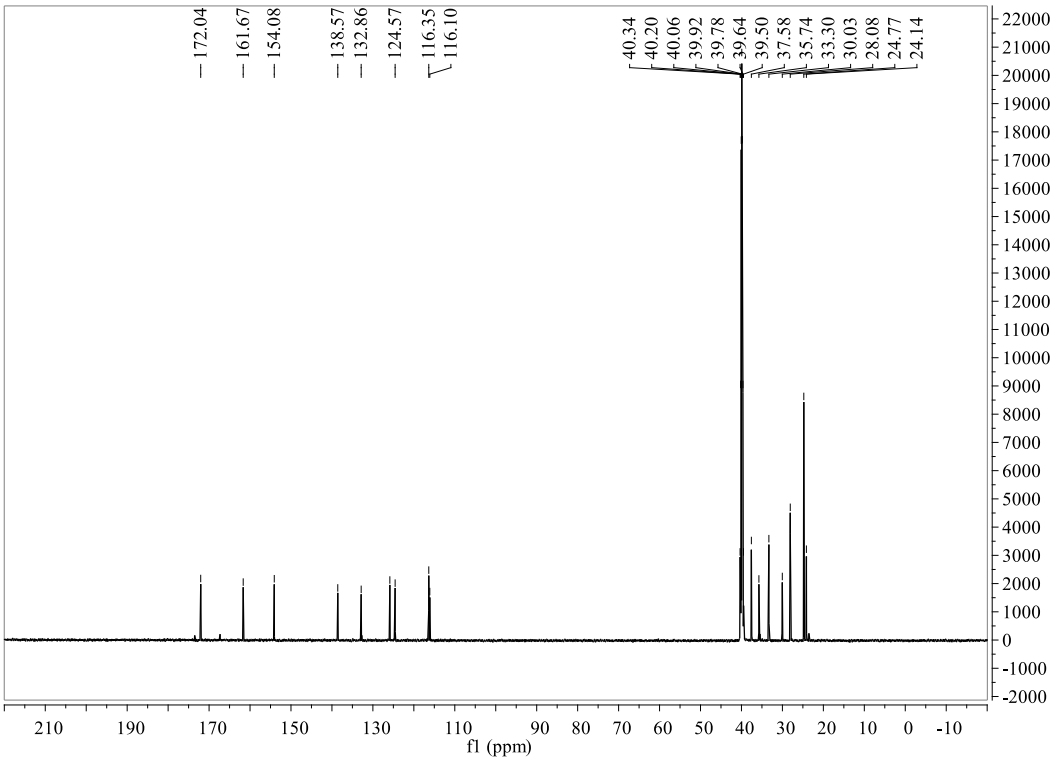


Figure S84. ^{13}C NMR spectrum of **5u**

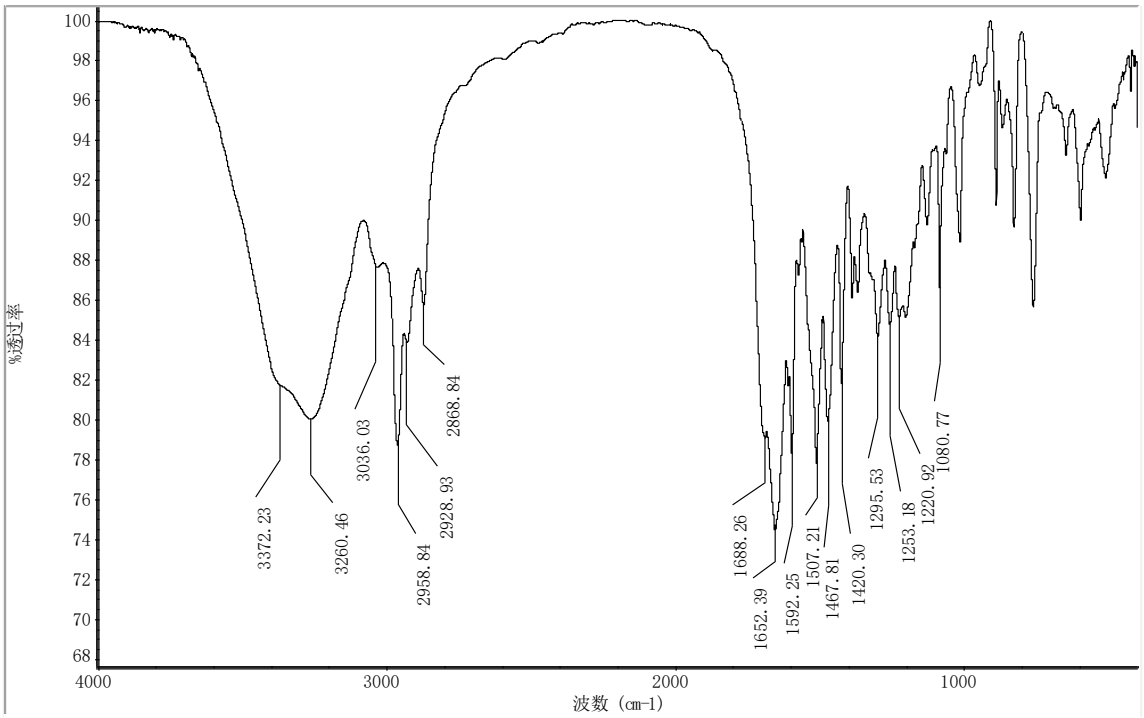


Figure S85. IR spectrum of **5v**

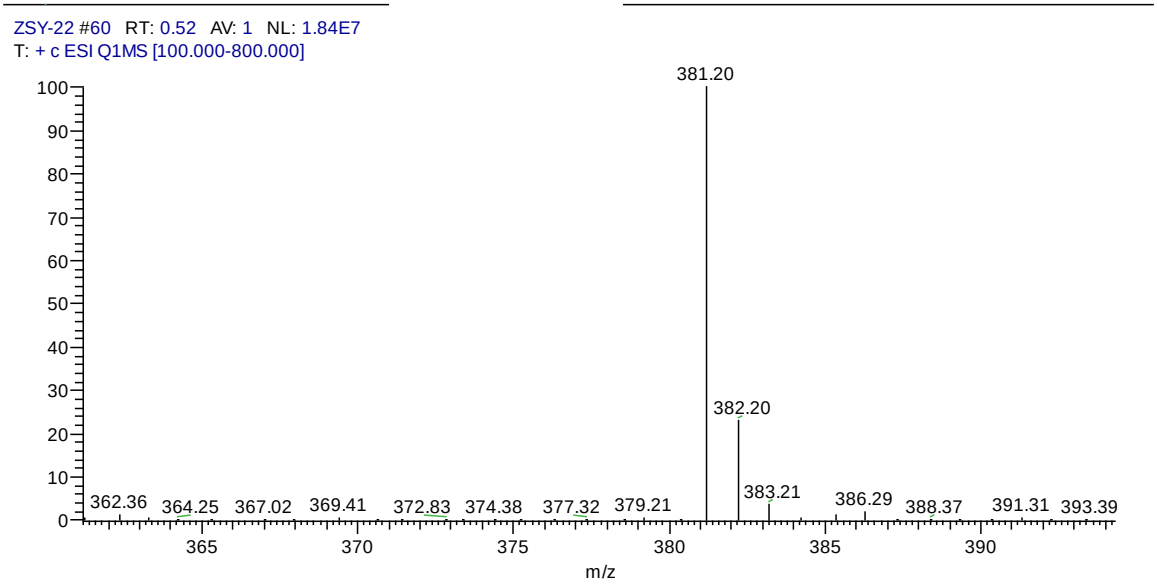


Figure S86. MS spectrum of **5v**

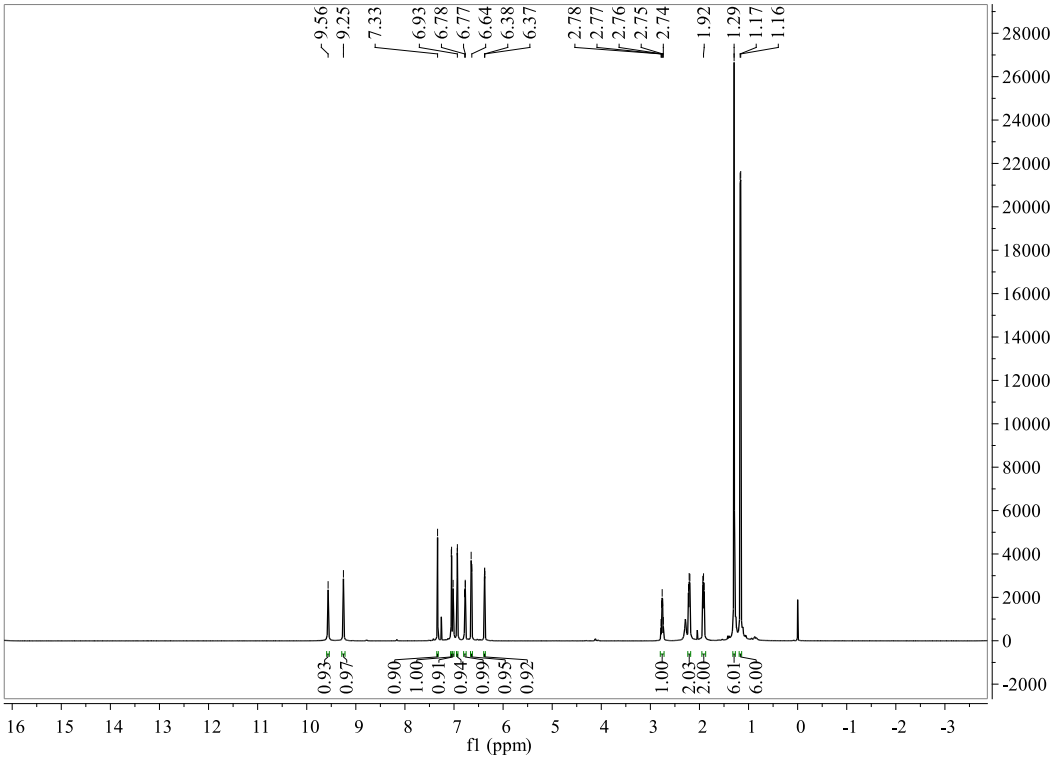


Figure S87. ^{1}H NMR spectrum of **5v**

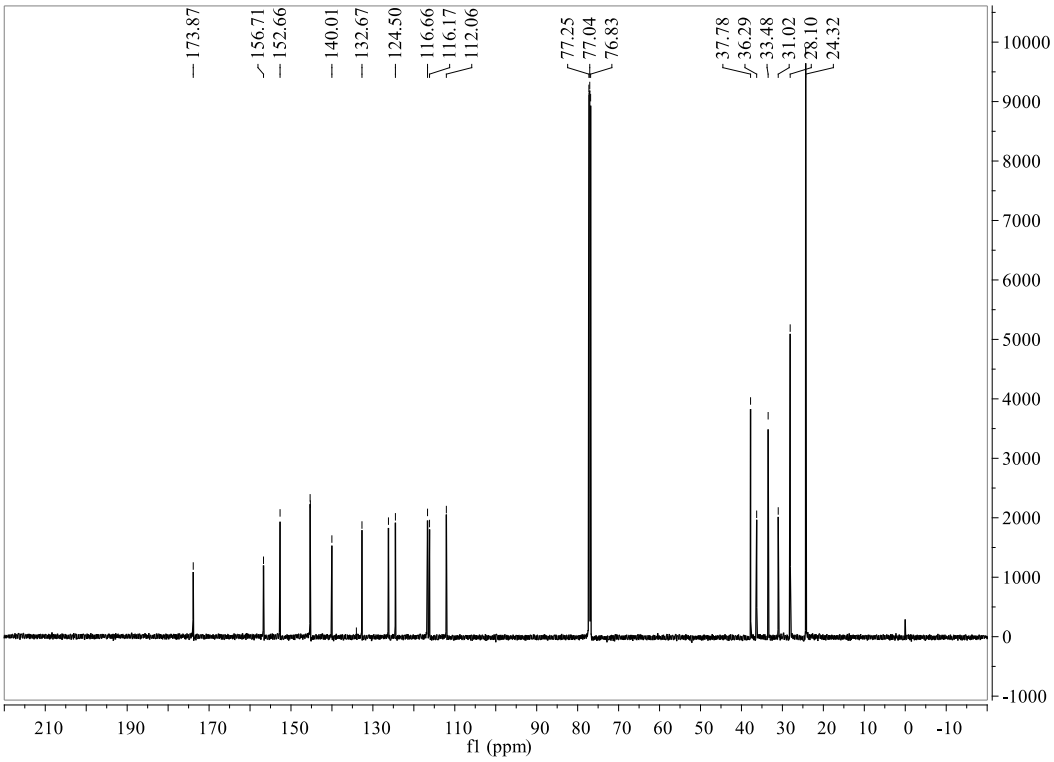


Figure S88. ^{13}C NMR spectrum of **5v**

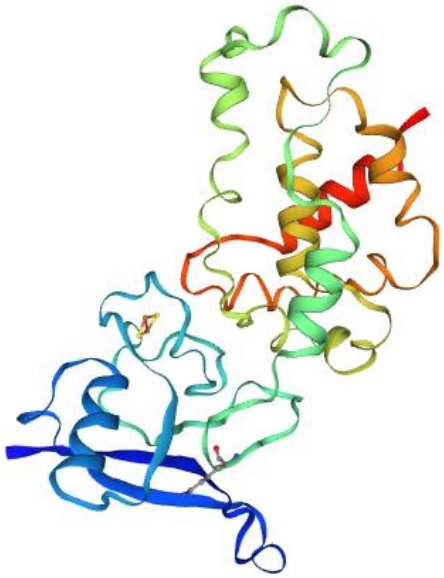


Figure S89. The 3D structure [UniProtKB AC P32420, homology modeling built using PDB ID: 2FBW.1.B (Avian respiratory complex II with carboxin bound) as a template]

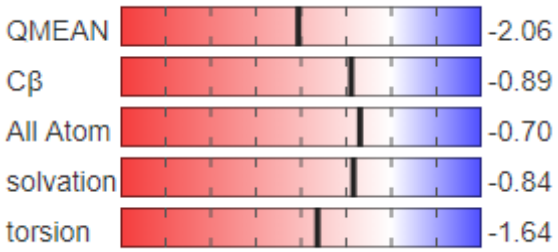
```
MODEL   PQHLKQFKIYRWNPDKPSEKPRLQSYTLDLNQTGPMVLDALIKIKNEIDPTLTFRRSCREGICGSCAMNI 118
2fbw.1.B TSRIKKFSIYRWDPDKPGDKPRMQTYEVDLNKCGPMVLDALIKIKNELDSTLTFRRSCREGICGSCAMNI  77

MODEL   DGVNTLACLCRIDK--QNDTKIYPLPHMYIVKDLVPDLTQFYKQYRSIEPFLKSNNTPSEG--EHLQSPE 184
2fbw.1.B AGGNTLACTKKIDPDLSKTTKIYPLPHMYVVKDLVPDLSNFYAQYKSIEPYLKKKDESKQGKEQYLQSIE 147

MODEL   ERRRLDGLYECILCACCSTSCPSYWWNQDEYLGPAVLMQAYRWMADSRDDFGEERRQKLENTFSLYRCHT 254
2fbw.1.B DRQKLDGLYECILCACCSTSCPSYWWNGDKYLGPAVLMQAYRWMIDSRDDYTEERLAQLQDPFSLYRCHT 217

MODEL   IMNCSRTCPKNLNPGKAIAQIKKDMAVGA                                         283
2fbw.1.B IMNCTRTCPKGLNPGKAIAEIKKMMATYK                                         246
```

Figure S90. The sequence alignments based on 2FBW.1.B succinate dehydrogenase Ip subunit. Sequence identity: 71.60%; Sequence similarity: 0.54



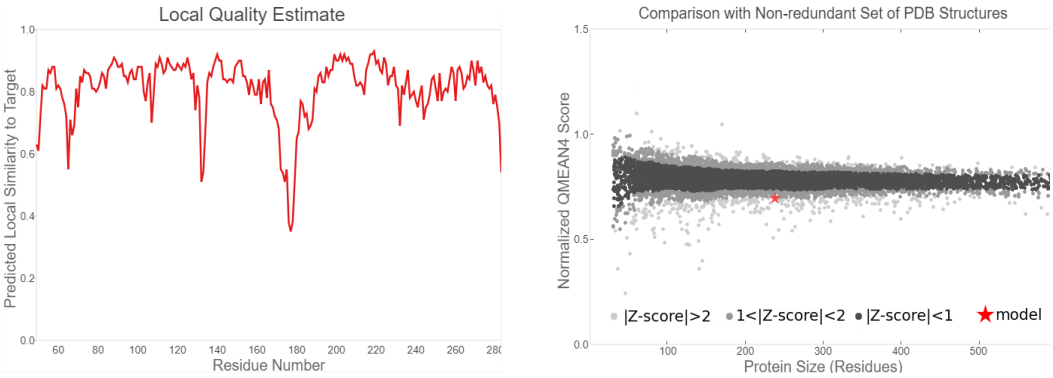
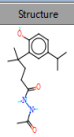
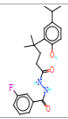
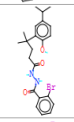
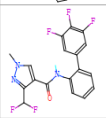


Figure S91. The model quality estimate of homology modeling

Table S2 The partial result of molecular docking-based virtual screening for the designed compounds in descending order by D score vs G score based on the 3D structure of the SDH.

Spreadsheet

		Name	Structure	1: Total_Score	2: Crash	3: Polar	4: FragIndex	5: FragRMSD	6: D_score	7: PMF_score	8: G_score	9: ChemScore	10: CSCORE
16	☐	001_000		5.4794	-2.0049	0.8662	-1	-1	-107.6427	-48.7248	-196.78	-23.1588	1
17	☐	011_000		6.8146	-2.3164	3.9597	-1	-1	-125.1245	-90.0153	-201.5325	-32.0772	4
18	☐	023_000		6.1093	-1.897	2.2898	-1	-1	-130.6059	-71.7492	-201.6225	-27.7335	2
19	☐	C2_1_000		5.9333	-1.6056	0.0007	-1	-1	-101.8321	-62.7131	-204.5075	-27.1954	1

Rows: (0/101) Data Columns: (2/10) | Visible Rows: 101 | Filtered Rows: 0 | Marked Rows: 0

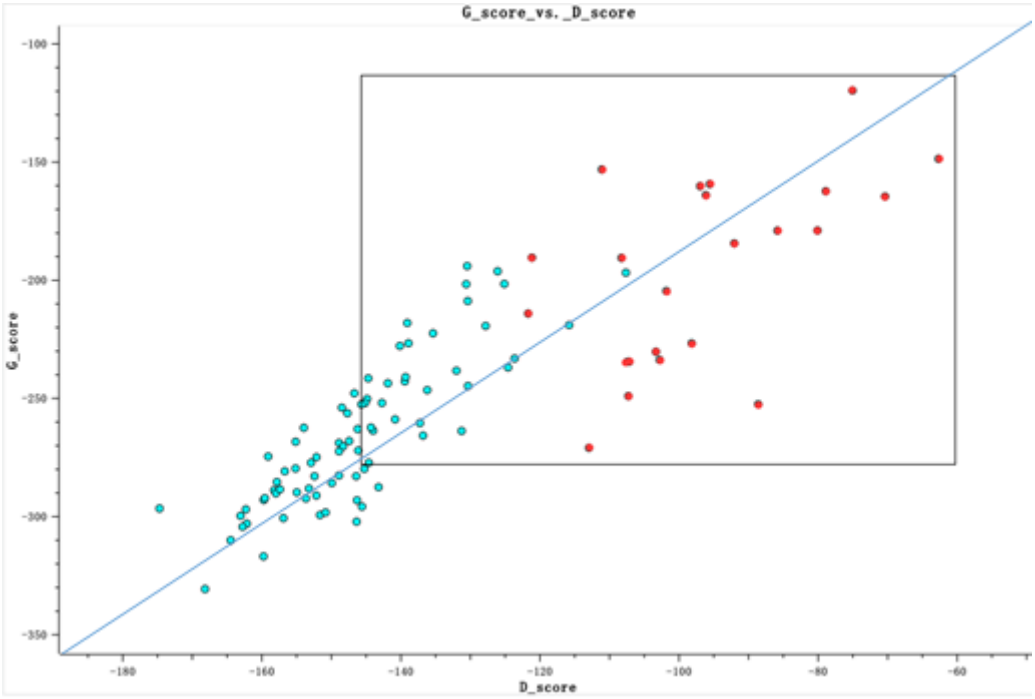


Figure S92. Scatter plot of D score vs G score (red spot: commercial SDHI fungicides; blue spot: designed compounds)