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New thieno[2,3-*b*]pyridine-fused [1,2,4]triazolo[4,3-*a*]pyrimidinone hybrids as potential MRSA and VRE inhibitors

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Contents

1. Experimental

1.1. Materials

All solvents were acquired from commercial sources and used as received unless otherwise stated. All other chemicals were acquired from Merck or Aldrich and used without further purification. The melting points were measured on a Stuart melting point apparatus and are uncorrected. IR spectra were recorded on a Smart iTR, which is an ultra-high-performance, versatile Attenuated Total Reflectance (ATR) sampling accessory on the Nicolet iS10 FT-IR spectrometer. NMR spectra were recorded on Bruker Avance III 400 MHz spectrophotometer (400 MHz for ^{1}H and 100 MHz for ^{13}C) using TMS as an internal standard and DMSO-d_6 as solvent and chemical shifts were expressed as δ ppm units. Elemental analyses were carried out on a EuroVector instrument C, H, N, S analyzer EA3000 Series.

1.2. The procedures and spectral data

General procedure for synthesis of 2-thioxo-2,3-dihydropyridothieno[3,2-*d*]pyrimidin-4(1*H*)-ones 2.

A mixture thieno[2,3-*b*]pyridine-2-carboxamide **1a,b** (5 mmol) and carbon disulfide (7 ml) in pyridine (15 ml) was heated at reflux for 12 h. The solvent was evaporated to its half volume and cooled. The product was collected by filtration, washed with cold ethanol, dried and recrystallized from the proper solvent.

9-(Thiophen-2-yl)-2-thioxo-7-(*p*-tolyl)-2,3-dihydropyrido[3',2':4,5]thieno-[3,2-*d*]pyrimidin-4(1*H*)-one (2a).

Yellow solid (dioxane, 78%); m.p. above 300 ºC; IR (υ cm^{-1}): 3410, 3325 (2 NH), 1663 (CO); ^{1}H-NMR (DMSO-d_6): δ 2.40 (s, 3H, *p*-CH_3), 7.32 (t, *J* = 4.4 Hz, 1H, thiophene-H4), 7.36 (d, *J* = 8.4 Hz, 2H, Ar-H's), 7.90 (s, 1H, pyridine-H), 7.96-7.99 (m, 2H, thiophene-H3 and thiophene-H5), 8.19 (d, *J* = 8.4 Hz, 2H, Ar-H's), 10.80 (s, 1H, NH), 12.93 (s, 1H, NH); ^{13}C-NMR (DMSO-d_6): δ 21.4 (*p*-*C*H_3), 111.3, 116.3, 122.4, 127.5, 128.0, 128.6, 129.3, 129.8, 134.2, 136.3, 139.6, 140.7, 142.4, 154.3, 157.7, 163.8, 175.1; Anal. calcd. for $C_{20}H_{13}N_3OS_3$ (407.5): C, 58.95; H, 3.22; N, 10.31; found: C, 59.22; H, 3.04; N, 10.06%.

7-(4-Methoxyphenyl)-9-(thiophen-2-yl)-2-thioxo-2,3-dihydropyrido[3',2':4,5]thieno[3,2-*d*]pyrimidin-4(1*H*)-one (2b).

Yellow solid (DMF / ethanol mixture, 82%); m.p. above 300 ºC; IR (υ cm^{-1}): 3413, 3322 (2 NH), 1660 (CO); ^{1}H-NMR (DMSO-d_6): δ 3.85 (s, 3H, *p*-OCH_3), 7.09 (d, *J* = 8.8 Hz, 2H, Ar-H's), 7.32 (t, *J* = 4.4 Hz, 1H, thiophene-H4), 7.88 (s, 1H, pyridine-H), 7.97 (d, *J* = 2.4 Hz, 1H, thiophene-H5), 8.00 (d, *J* = 4.4 Hz, 1H, thiophene-H3), 8.27 (d, *J* = 8.8 Hz, 2H, Ar-H's), 10.77 (s, 1H, NH), 12.84 (s, 1H, NH); ^{13}C-NMR (DMSO-d_6): δ 55.7 (*p*-O*C*H_3), 111.7, 114.6, 116.5, 122.7, 128.2, 128.4, 128.6, 129.9, 130.2, 136.4, 139.3, 141.8, 154.6, 157.2, 159.4, 163.4, 174.9; Anal. calcd. for $C_{20}H_{13}N_3O_2S_3$ (423.5): C, 56.72; H, 3.09; N, 9.92; found: C, 56.95; H, 3.24; N, 9.65%.

General procedure for synthesis of pyridothieno[3,2-*d*]pyrimidin-4(3*H*)-ones 3 and 3'.

A mixture of thieno[2,3-*b*]pyridine-2-carboxamide **1a,b** (5 mmol) and formic acid or acetic anhydride (25 ml) was heated at reflux for 4 h. The solvent was evaporated to its half volume and cooled. The solid products were collected by filtration, washed with cold ethanol, dried and then recrystallized from the proper solvent.

9-(Thiophen-2-yl)-7-(*p*-tolyl)pyrido[3',2':4,5]thieno[3,2-*d*]pyrimidin-4(3*H*)-one (3a).

Colorless solid (glacial acetic acid, 74%); m.p. above 300 ºC; IR (υ cm^{-1}): 3325 (NH), 1653 (CO); ^{1}H-NMR (DMSO-d_6): δ 2.39 (s, 3H, *p*-CH_3), 7.31 (t, *J* = 4.4 Hz, 1H, thiophene-H4), 7.35 (d, *J* = 8.4 Hz, 2H, Ar-H's), 7.89 (s, 1H, pyridine-H), 7.94 (d, *J* = 2.4 Hz, 1H, thiophene-H5), 7.97 (d, *J* = 4.4 Hz, 1H, thiophene-H3), 8.12 (s, 1H, pyrimidine-H2), 8.17 (d, *J* = 8.4 Hz, 2H, Ar-H's), 12.78 (s, 1H, NH); ^{13}C-NMR (DMSO-d_6): δ 21.4 (*p*-*C*H_3), 110.5, 116.7, 127.6, 127.9, 128.2, 128.9, 129.5, 130.0, 134.5, 136.9, 141.1, 142.9, 147.1, 151.0, 155.7, 157.1, 164.6; Anal. calcd. for $C_{20}H_{13}N_3OS_2$ (375.4): C, 63.98; H, 3.49; N, 11.19; found: C, 64.14; H, 3.36; N, 10.92%.

7-(4-Methoxyphenyl)-9-(thiophen-2-yl)pyrido[3',2':4,5]thieno[3,2-*d*]pyrimidin-4(3*H*)-one (3b).

Colorless solid (glacial acetic acid, 70%); m.p. above 300 ^{o}C; IR (υ cm^{-1}): 3327 (NH), 1665 (CO); ^{1}H-NMR (DMSO-d_6): δ 3.84 (s, 3H, *p*-OCH$_3$), 7.09 (d, *J* = 8.8 Hz, 2H, Ar-H's), 7.34 (t, *J* = 4.4 Hz, 1H, thiophene-H4), 7.90 (s, 1H, pyridine-H), 7.94 (d, *J* = 2.4 Hz, 1H, thiophene-H5), 7.97 (d, *J* = 4.4 Hz, 1H, thiophene-H3), 8.13 (s, 1H, pyrimidine-H2), 8.26 (d, *J* = 8.8 Hz, 2H, Ar-H's), 12.69 (s, 1H, NH); ^{13}C-NMR (DMSO-d_6): δ 55.7 (*p*-O*C*H$_3$), 110.7, 114.9, 116.6, 127.2, 128.3, 128.5, 128.8, 129.9, 130.2, 136.4, 142.6, 146.5, 150.8, 155.3, 156.9, 159.2, 164.4; Anal. calcd. for $C_{20}H_{13}N_3O_2S_2$ (391.4): C, 61.36; H, 3.35; N, 10.73; found: C, 61.55; H, 3.28; N, 10.59%.

2-Methyl-9-(thiophen-2-yl)-7-(*p*-tolyl)pyrido[3',2':4,5]thieno[3,2-*d*]pyrimidin-4(3*H*)-one (3'a).

Colorless solid (DMF / ethanol mixture, 84%); m.p. above 300 ^{o}C; IR (υ cm^{-1}): 3322 (NH), 1659 (CO); ^{1}H-NMR (DMSO-d_6): δ 2.22 (s, 3H, CH$_3$), 2.39 (s, 3H, *p*-CH$_3$), 7.31 (t, *J* = 4.4 Hz, 1H, thiophene-H4), 7.35 (d, *J* = 8.4 Hz, 2H, Ar-H's), 7.87 (s, 1H, pyridine-H), 7.94 (d, *J* = 2.4 Hz, 1H, thiophene-H5), 7.99 (d, *J* = 4.4 Hz, 1H, thiophene-H3), 8.16 (d, *J* = 8.4 Hz, 2H, Ar-H's), 12.63 (s, 1H, NH); ^{13}C-NMR (DMSO-d_6): δ 21.4 (*p*-*C*H$_3$), 24.6 (*C*H$_3$), 110.2, 117.2, 126.9, 127.8, 128.3, 129.0, 129.4, 129.8, 134.3, 136.7, 140.7, 142.5, 151.3, 154.6, 155.2, 156.8, 164.2; Anal. calcd. for $C_{21}H_{15}N_3OS_2$ (389.4): C, 64.76; H, 3.88; N, 10.79; found: C, 64.98; H, 4.09; N, 10.51%.

7-(4-Methoxyphenyl)-2-methyl-9-(thiophen-2-yl)pyrido[3',2':4,5]thieno[3,2-*d*]pyrimidin-4(3*H*)-one (3'b).

Colorless solid (dioxane, 77%); m.p. above 300 ^{o}C; IR (υ cm^{-1}): 3320 (NH), 1652 (CO); ^{1}H-NMR (DMSO-d_6): δ 2.24 (s, 3H, CH$_3$), 3.85 (s, 3H, *p*-OCH$_3$), 7.08 (d, *J* = 8.8 Hz, 2H, Ar-H's), 7.34 (t, *J* = 4.4 Hz, 1H, thiophene-H4), 7.89 (s, 1H, pyridine-H), 7.94 (d, *J* = 2.4 Hz, 1H, thiophene-H5), 7.98 (d, *J* = 4.4 Hz, 1H, thiophene-H3), 8.26 (d, *J* = 8.8 Hz, 2H, Ar-H's), 12.74 (s, 1H, NH); ^{13}C-NMR (DMSO-d_6): δ 24.5 (*C*H$_3$), 55.8 (*p*-O*C*H$_3$), 110.3, 114.7, 117.4, 126.8, 128.2, 128.6, 129.1, 129.7, 130.3, 136.2, 142.1, 151.0, 154.4, 155.3, 156.9, 159.6, 164.4; Anal. calcd. for $C_{21}H_{15}N_3O_2S_2$ (405.4): C, 62.20; H, 3.73; N, 10.36; found: C, 62.05; H, 3.87; N, 10.17%.

General procedure for synthesis of pyridothieno[3,2-*d*][1,2,4]triazolo[4,3-*a*]pyrimidines 6 and 7.

A mixture of each of 2-thioxopyrimidin-4(3*H*)-one **2a,b** (5 mmol) and the appropriate hydrazonyl chlorides **4a-d** or **5a-d** (5 mmol) in the presence of triethylamine (0.5 ml) in dioxane (25 ml) was heated at reflux for 8 h. The solvent was evaporated to its half volume and cooled. The solid products were collected by filtration, washed with cold ethanol, dried and then recrystallized from the proper solvent.

3-Acetyl-1-phenyl-10-(thiophen-2-yl)-8-(*p*-tolyl)pyrido[3',2':4,5]-thieno[3,2-*d*][1,2,4]triazolo[4,3-*a*]pyrimidin-5(1*H*)-one (6a).

Yellow solid (DMF, 88%); m.p. 283-286 ºC; IR (υ cm^{-1}): 1717, 1674 (CO); ^{1}H-NMR (DMSO-d_6): δ 2.41 (s, 3H, *p*-CH_3), 2.74 (s, 3H, $COCH_3$), 7.27 (t, *J* = 7.6 Hz, 1H, Ar-H), 7.32 (t, *J* = 4.4 Hz, 1H, thiophene-H4), 7.36 (d, *J* = 8.4 Hz, 2H, Ar-H's), 7.42 (t, *J* = 7.6 Hz, 2H, Ar-H's), 7.55 (d, *J* = 7.6 Hz, 2H, Ar-H's), 7.84 (s, 1H, pyridine-H), 7.93 (d, *J* = 2.4 Hz, 1H, thiophene-H5), 7.96 (d, *J* = 4.4 Hz, 1H, thiophene-H3), 8.16 (d, *J* = 8.4 Hz, 2H, Ar-H's); ^{13}C-NMR (DMSO-d_6): δ 21.4 (*p*-*C*H_3), 27.4 (CO*C*H_3), 116.7, 120.9, 122.2, 124.3, 126.6, 127.7, 128.5, 128.9, 129.2, 129.4, 129.9, 134.2, 136.8, 138.1, 139.4, 143.2, 147.6, 151.8, 153.5, 153.7, 157.3, 165.6, 194.0 (*C*OCH$_3$); Anal. calcd. for $C_{29}H_{19}N_5O_2S_2$ (533.6): C, 65.27; H, 3.59; N, 13.12; found: C, 65.48; H, 3.32; N, 12.87%.

3-Acetyl-1-(4-chlorophenyl)-10-(thiophen-2-yl)-8-(*p*-tolyl)pyrido[3',2':4,5]-thieno[3,2-*d*][1,2,4]triazolo[4,3-*a*]pyrimidin-5(1*H*)-one (6b).

Yellow solid (DMF, 82%); m.p. above 300 ºC; IR (υ cm^{-1}): 1715, 1669 (CO); ^{1}H-NMR (DMSO-d_6): δ 2.39 (s, 3H, *p*-CH_3), 2.73 (s, 3H, $COCH_3$), 7.31 (t, *J* = 4.4 Hz, 1H, thiophene-H4), 7.36 (d, *J* = 8.4 Hz, 2H, Ar-H's), 7.42 (d, *J* = 8 Hz, 2H, Ar-H's), 7.83 (s, 1H, pyridine-H), 7.92 (d, *J* = 2.4 Hz, 1H, thiophene-H5), 7.97 (d, *J* = 4.4 Hz, 1H, thiophene-H3), 8.08 (d, *J* = 8 Hz, 2H, Ar-H's), 8.17 (d, *J* = 8.4 Hz, 2H, Ar-H's); ^{13}C-NMR (DMSO-d_6): δ 21.5 (*p*-*C*H_3), 27.4 (CO*C*H_3), 116.5, 120.8, 123.4, 124.4, 127.6, 128.5, 128.9, 129.3, 129.4, 129.8, 131.4, 134.6, 136.8, 137.0, 139.4, 143.1, 146.8, 151.3, 152.8, 153.5, 157.2, 164.7, 193.9 (*C*OCH$_3$); Anal. calcd. for $C_{29}H_{18}ClN_5O_2S_2$ (568.0): C, 61.32; H, 3.19; N, 12.33; found: C, 61.48; H, 3.08; N, 12.17%.

3-Acetyl-10-(thiophen-2-yl)-1,8-di-(*p*-tolyl)pyrido[3',2':4,5]-thieno[3,2-*d*][1,2,4]triazolo[4,3-*a*]pyrimidin-5(1*H*)-one (6c).

Yellow solid (DMF / ethanol mixture, 83%); m.p. 278 ºC; IR (υ cm^{-1}): 1713, 1670 (CO); ^{1}H-NMR (DMSO-d_6): δ 2.36 (s, 3H, *p*-CH_3), 2.42 (s, 3H, *p*-CH_3), 2.75 (s, 3H, $COCH_3$), 7.31 (t, *J* = 4.4 Hz, 1H, thiophene-H4), 7.36 (d, *J* = 8.4 Hz, 2H, Ar-H's), 7.49 (d, *J* = 8 Hz, 2H, Ar-H's), 7.84 (s, 1H, pyridine-H), 7.95 (d, *J* = 2.4 Hz, 1H, thiophene-H5), 8.00 (d, *J* = 4.4 Hz, 1H, thiophene-H3), 8.07 (d, *J* = 8 Hz, 2H, Ar-H's), 8.17 (d, *J* = 8.4 Hz, 2H, Ar-H's); ^{13}C-NMR (DMSO-d_6): δ 21.2, 21.4 (*p*-*C*H_3), 27.5 (CO*C*H_3), 116.4, 119.2, 120.6, 124.1, 127.5, 128.3, 128.7, 129.3, 129.7, 129.9, 133.6, 134.3, 136.5, 137.2, 139.8, 143.4, 147.2, 151.6, 153.2, 153.4, 157.4, 165.2, 193.8 (*C*OCH_3); Anal. calcd. for $C_{30}H_{21}N_5O_2S_2$ (547.6): C, 65.80; H, 3.87; N, 12.79; found: C, 65.94; H, 3.99; N, 12.60%.

3-Acetyl-1-(4-methoxyphenyl)-10-(thiophen-2-yl)-8-(*p*-tolyl)pyrido[3',2':4,5]-thieno[3,2-*d*][1,2,4]triazolo[4,3-*a*]pyrimidin-5(1*H*)-one (6d).

Yellow solid (DMF / ethanol mixture, 80%); m.p. 290 ºC; IR (υ cm^{-1}): 1716, 1672 (CO); ^{1}H-NMR (DMSO-d_6): δ 2.40 (s, 3H, *p*-CH_3), 2.74 (s, 3H, $COCH_3$), 3.82 (s, 3H, *p*-OCH_3), 7.10 (d, *J* = 8 Hz, 2H, Ar-H's), 7.32 (t, *J* = 4.4 Hz, 1H, thiophene-H4), 7.37 (d, *J* = 8.4 Hz, 2H, Ar-H's), 7.84 (s, 1H, pyridine-H), 7.95 (d, *J* = 2.4 Hz, 1H, thiophene-H5), 7.98-8.01 (m, 3H, thiophene-H3 and 2 Ar-H's), 8.16 (d, *J* = 8.4 Hz, 2H, Ar-H's); ^{13}C-NMR (DMSO-d_6): δ 21.5 (*p*-*C*H_3), 27.4 (CO*C*H_3), 55.3 (*p*-O*C*H_3), 114.2, 115.7, 121.0, 121.6, 122.8, 127.6, 128.0, 128.5, 129.4, 129.9, 133.3, 134.5, 136.7, 140.2, 142.9, 149.4, 151.8, 154.0, 155.6, 155.9, 159.9, 165.2, 193.7 (*C*OCH_3); Anal. calcd. for $C_{30}H_{21}N_5O_3S_2$ (563.6): C, 63.93; H, 3.76; N, 12.43; found: C, 64.20; H, 3.98; N, 12.19%.

3-Acetyl-8-(4-methoxyphenyl)-1-phenyl-10-(thiophen-2-yl)pyrido[3',2':4,5]-thieno[3,2-*d*][1,2,4]triazolo[4,3-*a*]pyrimidin-5(1*H*)-one (6e).

Yellow solid (DMF / ethanol mixture, 84%); m.p. 292 ºC; IR (υ cm^{-1}): 1720, 1676 (CO); ^{1}H-NMR (DMSO-d_6): δ 2.75 (s, 3H, $COCH_3$), 3.84 (s, 3H, *p*-OCH_3), 7.08 (d, *J* = 8.8 Hz, 2H, Ar-H's), 7.26 (t, *J* = 7.6 Hz, 1H, Ar-H), 7.34 (t, *J* = 4.4 Hz, 1H, thiophene-H4), 7.44 (t, *J* = 7.6 Hz, 2H, Ar-H's), 7.57 (d, *J* = 7.6 Hz, 2H, Ar-H's), 7.82 (s, 1H, pyridine-H), 7.95 (d, *J* = 2.4 Hz, 1H, thiophene-H5), 7.98 (d, *J* = 4.4 Hz, 1H, thiophene-H3), 8.25 (d, *J* = 8.8 Hz, 2H, Ar-H's); ^{13}C-NMR (DMSO-d_6): δ 27.5 (CO*C*H_3), 55.8 (*p*-O*C*H_3), 114.8, 116.5, 120.8, 122.4, 124.4, 126.7, 128.6, 128.8, 129.0, 129.1, 129.7, 130.2, 136.4, 138.0, 142.9, 147.4, 151.6, 153.4, 153.8, 157.4, 159.4, 165.3, 193.9 (*C*OCH_3); Anal. calcd. for $C_{29}H_{19}N_5O_3S_2$ (549.6): C, 63.37; H, 3.48; N, 12.74; found: C, 63.19; H, 3.56; N, 12.86%.

3-Acetyl-1-(4-chlorophenyl)-8-(4-methoxyphenyl)-10-(thiophen-2-yl)-pyrido[3',2':4,5]thieno[3,2-*d*][1,2,4]triazolo[4,3-*a*]pyrimidin-5(1*H*)-one (6f).

Yellow solid (DMF, 87%); m.p. above 300 ^{o}C; IR (υ cm^{-1}): 1716, 1662 (CO); ^{1}H-NMR (DMSO-d_6): δ 2.74 (s, 3H, $COCH_3$), 3.84 (s, 3H, *p*-OCH_3), 7.09 (d, *J* = 8.8 Hz, 2H, Ar-H's), 7.32 (t, *J* = 4.4 Hz, 1H, thiophene-H4), 7.44 (d, *J* = 8 Hz, 2H, Ar-H's), 7.85 (s, 1H, pyridine-H), 7.96 (d, *J* = 2.4 Hz, 1H, thiophene-H5), 7.99 (d, *J* = 4.4 Hz, 1H, thiophene-H3), 8.10 (d, *J* = 8 Hz, 2H, Ar-H's), 8.24 (d, *J* = 8.8 Hz, 2H, Ar-H's); ^{13}C-NMR (DMSO-d_6): δ 27.5 ($CO\mathit{C}H_3$), 55.7 (*p*-$O\mathit{C}H_3$), 114.8, 116.4, 120.6, 123.3, 124.7, 128.4, 128.5, 128.8, 129.1, 129.6, 130.2, 131.2, 136.3, 137.1, 142.7, 146.4, 151.6, 153.1, 153.6, 157.4, 159.7, 164.9, 193.8 ($\mathit{C}OCH_3$); Anal. calcd. for $C_{29}H_{18}ClN_5O_3S_2$ (584.0): C, 59.64; H, 3.11; N, 11.99; found: C, 59.51; H, 2.99; N, 12.08%.

3-Acetyl-8-(4-methoxyphenyl)-10-(thiophen-2-yl)-1-(*p*-tolyl)pyrido[3',2':4,5]-thieno[3,2-*d*][1,2,4]triazolo[4,3-*a*]pyrimidin-5(1*H*)-one (6g).

Yellow solid (DMF, 85%); m.p. 292-293 ^{o}C; IR (υ cm^{-1}): 1718, 1677 (CO); ^{1}H-NMR (DMSO-d_6): δ 2.35 (s, 3H, *p*-CH_3), 2.77 (s, 3H, $COCH_3$), 3.85 (s, 3H, *p*-OCH_3), 7.10 (d, *J* = 8.8 Hz, 2H, Ar-H's), 7.32 (t, *J* = 4.4 Hz, 1H, thiophene-H4), 7.47 (d, *J* = 8 Hz, 2H, Ar-H's), 7.86 (s, 1H, pyridine-H), 7.93 (d, *J* = 2.4 Hz, 1H, thiophene-H5), 7.95 (d, *J* = 4.4 Hz, 1H, thiophene-H3), 8.05 (d, *J* = 8 Hz, 2H, Ar-H's), 8.24 (d, *J* = 8.8 Hz, 2H, Ar-H's); ^{13}C-NMR (DMSO-d_6): δ 21.2 (*p*-$\mathit{C}H_3$), 27.4 ($CO\mathit{C}H_3$), 55.7 (*p*-$O\mathit{C}H_3$), 114.5, 116.8, 119.0, 120.4, 123.8, 128.1, 128.4, 128.6, 129.4, 129.6, 130.0, 133.8, 136.1, 137.0, 142.9, 146.8, 151.2, 152.6, 153.2, 156.8, 159.3, 164.8, 194.0 ($\mathit{C}OCH_3$); Anal. calcd. for $C_{30}H_{21}N_5O_3S_2$ (563.6): C, 63.93; H, 3.76; N, 12.43; found: C, 64.11; H, 3.63; N, 12.57%.

3-Acetyl-1,8-bis(4-methoxyphenyl)-10-(thiophen-2-yl)pyrido[3',2':4,5]-thieno[3,2-*d*][1,2,4]triazolo[4,3-*a*]pyrimidin-5(1*H*)-one (6h).

Yellow solid (DMF, 86%); m.p. 290 ^{o}C; IR (υ cm^{-1}): 1714, 1674 (CO); ^{1}H-NMR (DMSO-d_6): δ 2.77 (s, 3H, $COCH_3$), 3.82 (s, 3H, *p*-OCH_3), 3.85 (s, 3H, *p*-OCH_3), 7.08-7.11 (m, 4H, Ar-H's), 7.34 (t, *J* = 4.4 Hz, 1H, thiophene-H4), 7.81 (s, 1H, pyridine-H), 7.92 (d, *J* = 2.4 Hz, 1H, thiophene-H5), 7.94-7.97 (m, 3H, thiophene-H3 and 2 Ar-H's), 8.24 (d, *J* = 8.8 Hz, 2H, Ar-H's); ^{13}C-NMR (DMSO-d_6): δ 27.4 ($CO\mathit{C}H_3$), 55.3 (*p*-$O\mathit{C}H_3$), 55.8 (*p*-$O\mathit{C}H_3$), 114.3, 114.5, 115.6, 120.8, 121.8, 122.2, 128.3, 128.6, 128.8, 130.0, 130.2, 133.0, 136.4, 142.4, 148.6, 151.3, 154.4, 155.2, 155.5, 159.5, 159.8, 164.7, 193.9 ($\mathit{C}OCH_3$); Anal. calcd. for $C_{30}H_{21}N_5O_4S_2$ (579.6): C, 62.16; H, 3.65; N, 12.08; found: C, 61.95; H, 3.83; N, 11.89%.

Ethyl 5-oxo-1-phenyl-10-(thiophen-2-yl)-8-(*p*-tolyl)-1,5-dihydropyrido[3',2':4,5]-thieno[3,2-*d*][1,2,4]triazolo[4,3-*a*]pyrimidine-3-carboxylate (7a).

Yellow solid (DMF, 83%); m.p. 292 ºC; IR (υ cm^{-1}): 1744, 1679 (CO); ^{1}H-NMR (DMSO-d_6): δ 1.36 (t, *J* = 7.2 Hz, 3H, OC*H*$_3$CH$_2$), 2.39 (s, 3H, *p*-CH$_3$), 4.39 (q, *J* = 7.2 Hz, 2H, OCH$_3$C*H*$_2$), 7.25 (t, *J* = 7.6 Hz, 1H, Ar-H), 7.31 (t, *J* = 4.4 Hz, 1H, thiophene-H4), 7.35 (d, *J* = 8.4 Hz, 2H, Ar-H's), 7.43 (t, *J* = 7.6 Hz, 2H, Ar-H's), 7.57 (d, *J* = 7.6 Hz, 2H, Ar-H's), 7.81 (s, 1H, pyridine-H), 7.91 (d, *J* = 2.4 Hz, 1H, thiophene-H5), 7.94 (d, *J* = 4.4 Hz, 1H, thiophene-H3), 8.15 (d, *J* = 8.4 Hz, 2H, Ar-H's); ^{13}C-NMR (DMSO-d_6): δ 14.9 (O*C*H$_3$CH$_2$), 21.4 (*p*-*C*H$_3$), 60.7 (OCH$_3$*C*H$_2$), 117.0, 120.7, 122.4, 124.5, 126.6, 127.6, 128.3, 128.8, 129.0, 129.6, 129.9, 134.3, 136.5, 138.0, 139.1, 142.9, 147.4, 151.6, 153.6, 153.9, 157.4, 162.9, 164.6 (*C*OO); Anal. calcd. for $C_{30}H_{21}N_5O_3S_2$ (563.6): C, 63.93; H, 3.76; N, 12.43; found: C, 64.12; H, 3.92; N, 12.33%.

Ethyl 1-(4-chlorophenyl)-5-oxo-10-(thiophen-2-yl)-8-(*p*-tolyl)-1,5-dihydropyrido-[3',2':4,5]thieno[3,2-*d*][1,2,4]triazolo[4,3-*a*]pyrimidine-3-carboxylate (7b).

Yellow solid (DMF / ethanol mixture, 84%); m.p. above 300 ºC; IR (υ cm^{-1}): 1747, 1672 (CO); ^{1}H-NMR (DMSO-d_6): δ 1.35 (t, *J* = 7.2 Hz, 3H, OC*H*$_3$CH$_2$), 2.40 (s, 3H, *p*-CH$_3$), 4.37 (q, *J* = 7.2 Hz, 2H, OCH$_3$C*H*$_2$), 7.32 (t, *J* = 4.4 Hz, 1H, thiophene-H4), 7.35 (d, *J* = 8.4 Hz, 2H, Ar-H's), 7.44 (d, *J* = 8 Hz, 2H, Ar-H's), 7.86 (s, 1H, pyridine-H), 7.93 (d, *J* = 2.4 Hz, 1H, thiophene-H5), 7.98 (d, *J* = 4.4 Hz, 1H, thiophene-H3), 8.10 (d, *J* = 8 Hz, 2H, Ar-H's), 8.16 (d, *J* = 8.4 Hz, 2H, Ar-H's); ^{13}C-NMR (DMSO-d_6): δ 14.8 (O*C*H$_3$CH$_2$), 21.5 (*p*-*C*H$_3$), 60.8 (OCH$_3$*C*H$_2$), 116.3, 120.4, 123.1, 124.7, 127.4, 128.4, 128.8, 129.4, 129.6, 129.9, 131.2, 134.3, 136.4, 136.9, 139.3, 142.8, 146.6, 150.9, 152.9, 153.2, 156.9, 162.8, 164.5 (*C*OO); Anal. calcd. for $C_{30}H_{20}ClN_5O_3S_2$ (598.0): C, 60.25; H, 3.37; N, 11.71; found: C, 60.09; H, 3.52; N, 11.84%.

Ethyl 5-oxo-10-(thiophen-2-yl)-1,8-di-(*p*-tolyl)-1,5-dihydropyrido-[3',2':4,5]thieno[3,2-*d*][1,2,4]triazolo[4,3-*a*]pyrimidine-3-carboxylate (7c).

Yellow solid (DMF / ethanol mixture, 87%); m.p. 288-290 ºC; IR (υ cm^{-1}): 1740, 1679 (CO); ^{1}H-NMR (DMSO-d_6): δ 1.35 (t, *J* = 7.2 Hz, 3H, OC*H*$_3$CH$_2$), 2.34 (s, 3H, *p*-CH$_3$), 2.40 (s, 3H, *p*-CH$_3$), 4.38 (q, *J* = 7.2 Hz, 2H, OCH$_3$C*H*$_2$), 7.32 (t, *J* = 4.4 Hz, 1H, thiophene-H4), 7.36 (d, *J* = 8.4 Hz, 2H, Ar-H's), 7.48 (d, *J* = 8 Hz, 2H, Ar-H's), 7.80 (s, 1H, pyridine-H), 7.92 (d, *J* = 2.4 Hz, 1H, thiophene-H5), 7.98 (d, *J* = 4.4 Hz, 1H, thiophene-H3), 8.09 (d, *J* = 8 Hz, 2H, Ar-H's), 8.18 (d, *J* = 8.4 Hz, 2H, Ar-H's); ^{13}C-NMR (DMSO-d_6): δ 14.8 (O*C*H$_3$CH$_2$), 21.3, 21.5 (*p*-*C*H$_3$), 60.7 (OCH$_3$*C*H$_2$), 117.4, 118.9, 120.3, 123.9, 127.7, 128.5, 128.9, 129.4, 129.8, 130.0, 133.3, 134.2, 136.3, 136.9, 139.4, 143.0, 146.9, 151.4, 152.9, 153.6, 157.2, 163.2,

164.9 (*C*OO); Anal. calcd. for $C_{31}H_{23}N_5O_3S_2$ (577.6): C, 64.45; H, 4.01; N, 12.12; found: C, 64.29; H, 3.87; N, 12.03%.

Ethyl 1-(4-methoxyphenyl)-5-oxo-10-(thiophen-2-yl)-8-(*p*-tolyl)-1,5-dihydropyrido-[3',2':4,5]thieno[3,2-*d*][1,2,4]triazolo[4,3-*a*]pyrimidine-3-carboxylate (7d).

Yellow solid (DMF, 84%); m.p. 294 ^oC; IR (υ cm^{-1}): 1744, 1677 (CO); ^{1}H-NMR (DMSO-d_6): δ 1.36 (t, *J* = 7.2 Hz, 3H, OC*H*$_3$CH$_2$), 2.41 (s, 3H, *p*-CH$_3$), 3.81 (s, 3H, *p*-OCH$_3$), 4.37 (q, *J* = 7.2 Hz, 2H, OCH$_3$C*H*$_2$), 7.08 (d, *J* = 8 Hz, 2H, Ar-H's), 7.33 (t, *J* = 4.4 Hz, 1H, thiophene-H4), 7.37 (d, *J* = 8.4 Hz, 2H, Ar-H's), 7.79 (s, 1H, pyridine-H), 7.91 (d, *J* = 2.4 Hz, 1H, thiophene-H5), 7.93-7.96 (m, 3H, thiophene-H3 and 2 Ar-H's), 8.15 (d, *J* = 8.4 Hz, 2H, Ar-H's); ^{13}C-NMR (DMSO-d_6): δ 14.9 (OC*H*$_3$CH$_2$), 21.4 (*p*-C*H*$_3$), 55.3 (*p*-OC*H*$_3$), 60.8 (OCH$_3$C*H*$_2$), 114.3, 115.9, 120.8, 121.3, 122.6, 127.4, 128.3, 128.7, 129.6, 129.8, 133.2, 134.8, 136.4, 140.0, 143.2, 149.8, 151.6, 154.3, 155.8, 156.2, 159.7, 162.9, 164.8 (*C*OO); Anal. calcd. for $C_{31}H_{23}N_5O_4S_2$ (593.6): C, 62.72; H, 3.91; N, 11.80; found: C, 62.97; H, 3.67; N, 12.03%.

Ethyl 8-(4-methoxyphenyl)-5-oxo-1-phenyl-10-(thiophen-2-yl)-1,5-dihydropyrido-[3',2':4,5]thieno[3,2-*d*][1,2,4]triazolo[4,3-*a*]pyrimidine-3-carboxylate (7e).

Yellow solid (DMF / ethanol mixture, 85%); m.p. above 30 ^oC; IR (υ cm^{-1}): 1743, 1677 (CO); ^{1}H-NMR (DMSO-d_6): δ 1.39 (t, *J* = 7.2 Hz, 3H, OC*H*$_3$CH$_2$), 3.86 (s, 3H, *p*-OCH$_3$), 4.40 (q, *J* = 7.2 Hz, 2H, OCH$_3$C*H*$_2$), 7.11 (d, *J* = 8.8 Hz, 2H, Ar-H's), 7.27 (t, *J* = 7.6 Hz, 1H, Ar-H), 7.34 (t, *J* = 4.4 Hz, 1H, thiophene-H4), 7.43 (t, *J* = 7.6 Hz, 2H, Ar-H's), 7.55 (d, *J* = 7.6 Hz, 2H, Ar-H's), 7.83 (s, 1H, pyridine-H), 7.94 (d, *J* = 2.4 Hz, 1H, thiophene-H5), 7.99 (d, *J* = 4.4 Hz, 1H, thiophene-H3), 8.27 (d, *J* = 8.8 Hz, 2H, Ar-H's); ^{13}C-NMR (DMSO-d_6): δ 14.8 (OC*H*$_3$CH$_2$), 55.8 (*p*-OC*H*$_3$), 60.6 (OCH$_3$C*H*$_2$), 114.6, 117.2, 120.1, 121.9, 124.8, 126.8, 128.2, 128.6, 128.9, 129.2, 129.7, 130.3, 136.2, 137.7, 142.4, 146.9, 151.8, 153.4, 154.1, 157.1, 159.5, 162.6, 164.8 (*C*OO); Anal. calcd. for $C_{30}H_{21}N_5O_4S_2$ (579.6): C, 62.16; H, 3.65; N, 12.08; found: C, 62.02; H, 3.78; N, 11.92%.

Ethyl 1-(4-chlorophenyl)-8-(4-methoxyphenyl)-5-oxo-10-(thiophen-2-yl)-1,5-dihydro-pyrido[3',2':4,5]thieno[3,2-*d*][1,2,4]triazolo[4,3-*a*]pyrimidine-3-carboxylate (7f).

Yellow solid (DMF, 87%); m.p. above 300 ^oC; IR (υ cm^{-1}): 1746, 1664 (CO); ^{1}H-NMR (DMSO-d_6): δ 1.39 (t, *J* = 7.2 Hz, 3H, OC*H*$_3$CH$_2$), 3.85 (s, 3H, *p*-OCH$_3$), 4.39 (q, *J* = 7.2 Hz, 2H, OCH$_3$C*H*$_2$), 7.09 (d, *J* = 8.8 Hz, 2H, Ar-H's), 7.30 (t, *J* = 4.4 Hz, 1H, thiophene-H4), 7.43 (d, *J* = 8 Hz, 2H, Ar-H's), 7.83 (s, 1H, pyridine-H), 7.93 (d, *J* = 2.4 Hz, 1H, thiophene-H5), 7.97 (d, *J* = 4.4 Hz, 1H, thiophene-H3), 8.09 (d, *J* = 8 Hz, 2H, Ar-H's), 8.25 (d, *J* = 8.8

Hz, 2H, Ar-H's); ^{13}C-NMR (DMSO-d_6): δ 14.9 (O*C*H$_3$CH$_2$), 55.7 (*p*-O*C*H$_3$), 60.7 (OCH$_3$*C*H$_2$), 114.5, 117.3, 119.9, 122.7, 124.5, 128.2, 128.5, 128.9, 129.4, 129.6, 130.0, 131.3, 136.1, 136.7, 142.6, 146.3, 150.6, 152.8, 153.6, 156.8, 159.4, 163.2, 164.7 (*C*OO); Anal. calcd. for $C_{30}H_{20}ClN_5O_4S_2$ (614.0): C, 58.68; H, 3.28; N, 11.40; found: C, 58.74; H, 3.17; N, 11.25%.

Ethyl 8-(4-methoxyphenyl)-5-oxo-10-(thiophen-2-yl)-1-(*p*-tolyl)-1,5-dihydropyrido-[3',2':4,5]thieno[3,2-*d*][1,2,4]triazolo[4,3-*a*]pyrimidine-3-carboxylate (7g).

Yellow solid (DMF / ethanol mixture, 80%); m.p. 288-291 ºC; IR (υ cm^{-1}): 1748, 1672 (CO); ^{1}H-NMR (DMSO-d_6): δ 1.36 (t, *J* = 7.2 Hz, 3H, OC*H*$_3$CH$_2$), 2.32 (s, 3H, *p*-CH$_3$), 3.85 (s, 3H, *p*-OCH$_3$), 4.37 (q, *J* = 7.2 Hz, 2H, OCH$_3$C*H*$_2$), 7.10 (d, *J* = 8.8 Hz, 2H, Ar-H's), 7.33 (t, *J* = 4.4 Hz, 1H, thiophene-H4), 7.49 (d, *J* = 8 Hz, 2H, Ar-H's), 7.84 (s, 1H, pyridine-H), 7.95 (d, *J* = 2.4 Hz, 1H, thiophene-H5), 7.99 (d, *J* = 4.4 Hz, 1H, thiophene-H3), 8.08 (d, *J* = 8 Hz, 2H, Ar-H's), 8.24 (d, *J* = 8.8 Hz, 2H, Ar-H's); ^{13}C-NMR (DMSO-d_6): δ 14.7 (O*C*H$_3$CH$_2$), 21.3 (*p*-*C*H$_3$), 55.8 (*p*-O*C*H$_3$), 60.8 (OCH$_3$*C*H$_2$), 114.6, 117.7, 118.8, 120.6, 123.6, 128.2, 128.4, 128.6, 129.6, 130.0, 130.2, 133.6, 135.9, 136.3, 142.5, 146.6, 150.8, 152.4, 153.2, 156.6, 159.6, 163.4, 164.7 (*C*OO); Anal. calcd. for $C_{31}H_{23}N_5O_4S_2$ (593.6): C, 62.72; H, 3.91; N, 11.80; found: C, 62.90; H, 4.12; N, 11.57%.

Ethyl 1,8-bis(4-methoxyphenyl)-5-oxo-10-(thiophen-2-yl)-1,5-dihydropyrido-[3',2':4,5]thieno[3,2-*d*][1,2,4]triazolo[4,3-*a*]pyrimidine-3-carboxylate (7h).

Yellow solid (DMF, 83%); m.p. above 300 ºC; IR (υ cm^{-1}): 1746, 1675 (CO); ^{1}H-NMR (DMSO-d_6): δ 1.38 (t, *J* = 7.2 Hz, 3H, OC*H*$_3$CH$_2$), 3.81 (s, 3H, *p*-OCH$_3$), 3.86 (s, 3H, *p*-OCH$_3$), 4.39 (q, *J* = 7.2 Hz, 2H, OCH$_3$C*H*$_2$), 7.07-7.10 (m, 4H, Ar-H's), 7.32 (t, *J* = 4.4 Hz, 1H, thiophene-H4), 7.84 (s, 1H, pyridine-H), 7.94 (d, *J* = 2.4 Hz, 1H, thiophene-H5), 7.96-7.99 (m, 3H, thiophene-H3 and 2 Ar-H's), 8.24 (d, *J* = 8.8 Hz, 2H, Ar-H's); ^{13}C-NMR (DMSO-d_6): δ 14.8 (O*C*H$_3$CH$_2$), 55.3 (*p*-O*C*H$_3$), 55.8 (*p*-O*C*H$_3$), 60.6 (OCH$_3$*C*H$_2$), 114.1, 114.4, 115.6, 120.4, 121.7, 122.2, 128.1, 128.4, 128.6, 129.6, 130.1, 132.8, 135.8, 142.7, 149.3, 151.7, 153.9, 155.4, 155.8, 159.2, 159.9, 163.2, 164.6 (*C*OO); Anal. calcd. for $C_{31}H_{23}N_5O_5S_2$ (609.6): C, 61.07; H, 3.80; N, 11.49; found: C, 60.80; H, 4.03; N, 11.77%.

1.3. Minimum inhibitory concentration (MIC) determination.

The inhibitory activities against *Staphylococcus aureus* (ATCC:6538), *Enterococcus faecalis* (ATCC:29212), *Escherichia coli* (ATCC:9637), *Klebsiella pneumonia* (ATCC:10031) ATCC:33591 MRSA, ATCC:43300 MRSA, and ATCC:51299 VRE and ATCC:51575 VRE strains were estimated. MIC values were determined using microbroth serial dilution method [S1,S2] in a sterile 96-well microtiter plate after overnight incubation of tested bacteria at 37°C. This assay was performed in triplicates for consistency in accordance with guidelines provided by CLSI (2012) [S3]. Ciprofloxacin (100 µg susceptibility disc) and Linezolid (30 µg susceptibility disc) were used as standard drugs. The concentration of the tested hybrids as well as Ciprofloxacin used in the study ranged from 250 to 0.9 µg ml^{-1}. The sterile Muller-Hinton broth (MHB) was enriched with 2% NaCl before the tested antimicrobial agents were inserted into the well at concentration gradient in a serial dilution. Then the diluted bacterial suspension at final inoculum of 10^6 CFU/ml was added. The tested compound in MHB was used as negative control to ensure medium sterility, while the inoculum in MHB served as positive control to ensure the adequacy of the broth for bacterial growth. To facilitate the observation of the growth of bacteria in each well, 20 µl of 2,3,5-triphenyltetrazolium chloride (TTC) at 2 mg ml^{-1} was added into each well.

1.4. Minimum bactericidal concentration (MBC) determination.

The tested hybrids were screened against each of *Staphylococcus aureus* (ATCC:6538), *Enterococcus faecalis* (ATCC:29212), *Escherichia coli* (ATCC:9637), *Klebsiella pneumonia* (ATCC:10031) ATCC:33591 MRSA, ATCC:43300 MRSA, and ATCC:51299 VRE and ATCC:51575 VRE strains to estimate their MBC values [S4]. Each of the tested strains was cultured in sterile broth medium for 24 h at 37 ºC. The assay was performed in 2 ml microcentrifuge tubes with concentrations ranging from 250 to 0.9 µg ml^{-1} of the tested derivatives. To each concentration of the tested derivatives, 0.1 mL of the cultured bacterial strain was added and then, allowed to incubate for 24 h at 37 ºC. 10 µl sample was collected post incubation and seeded onto the agar plates and left to incubate for 24 h at 37 ºC. All the results were carried out in duplicate and the average values were determined.

2. References

[S1] A. E. M. Mekky and S. M. H. Sanad, *Bioorg. Chem.*, 2020, **102**, 104094.

[S2] H. Mohammad, P. N. Reddy, D. Monteleone, A. S. Mayhoub, M. Cushman and M. N. Seleem, *Eur. J. Med. Chem.*, 2015, **94**, 306.

[S3] CLSI. 2012. Methods for dilution antimicrobial susceptibility tests for bacteria that grow aerobically-7th edition. Approved standard M07-A9, Clinical and Laboratory Standards Institute Wayne, PA.

[S4] A. Kamal, A. Rahim, S. Riyaz, Y. Poornachandra, M. Balakrishna, C. G. Kumar, S. M. Hussaini, B. Sridhar and P. K. Machiraju, *Org. Biomol. Chem.*, 2015, **13**, 1347.

3. ^{1}H and ^{13}C NMR copies of new hybrids (Figures S1-S44)

Figure S1. ^{1}H-NMR of compound 2a

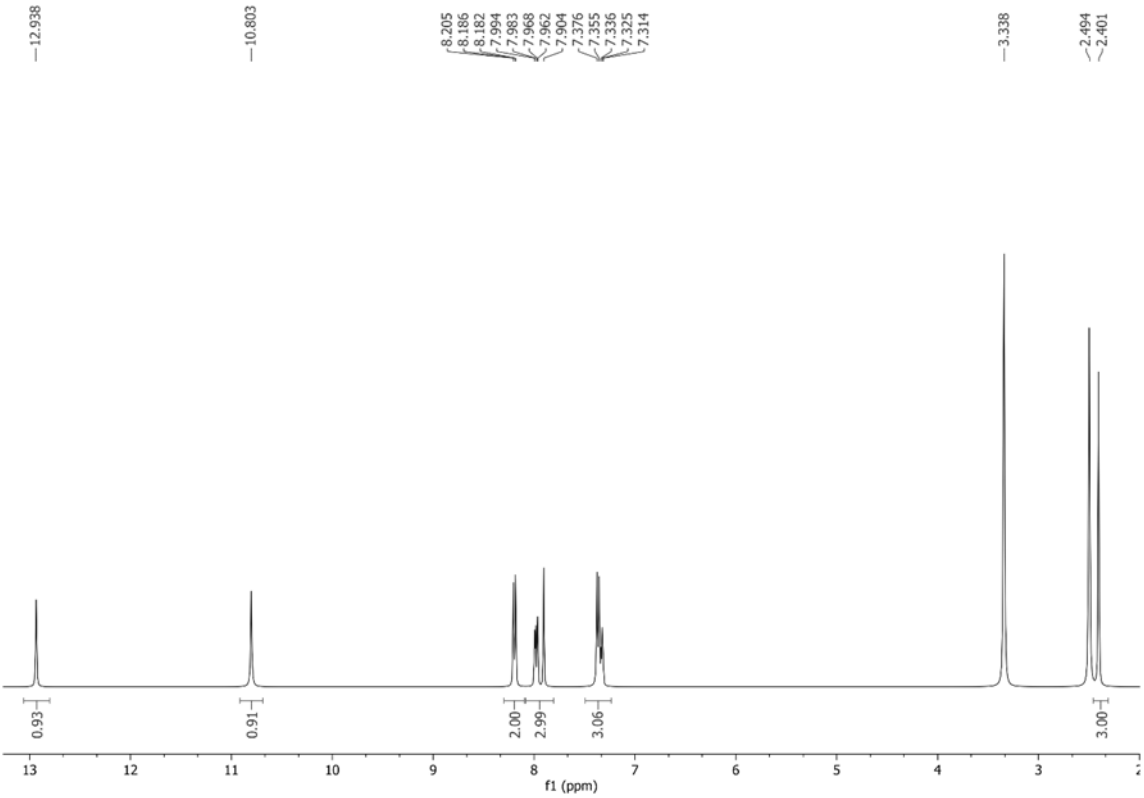

Figure S2. ^{13}C-NMR of compound 2a

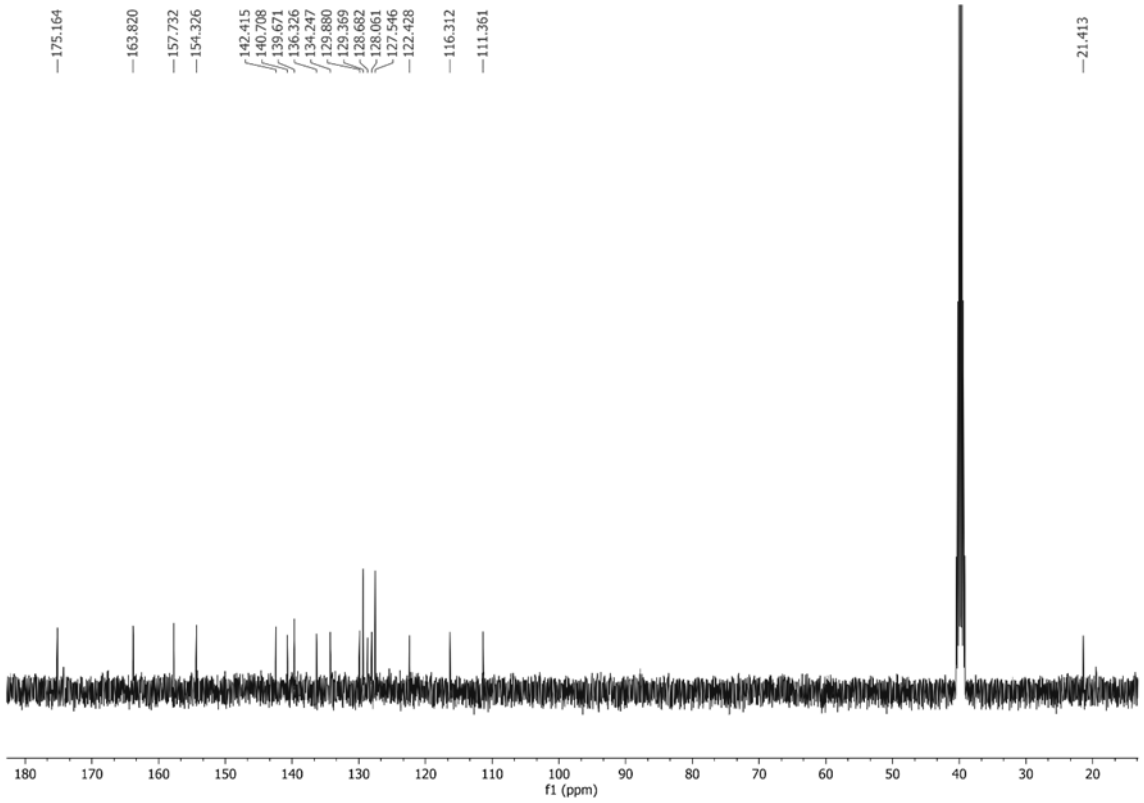

Figure S3. ^{1}H-NMR of compound 2b

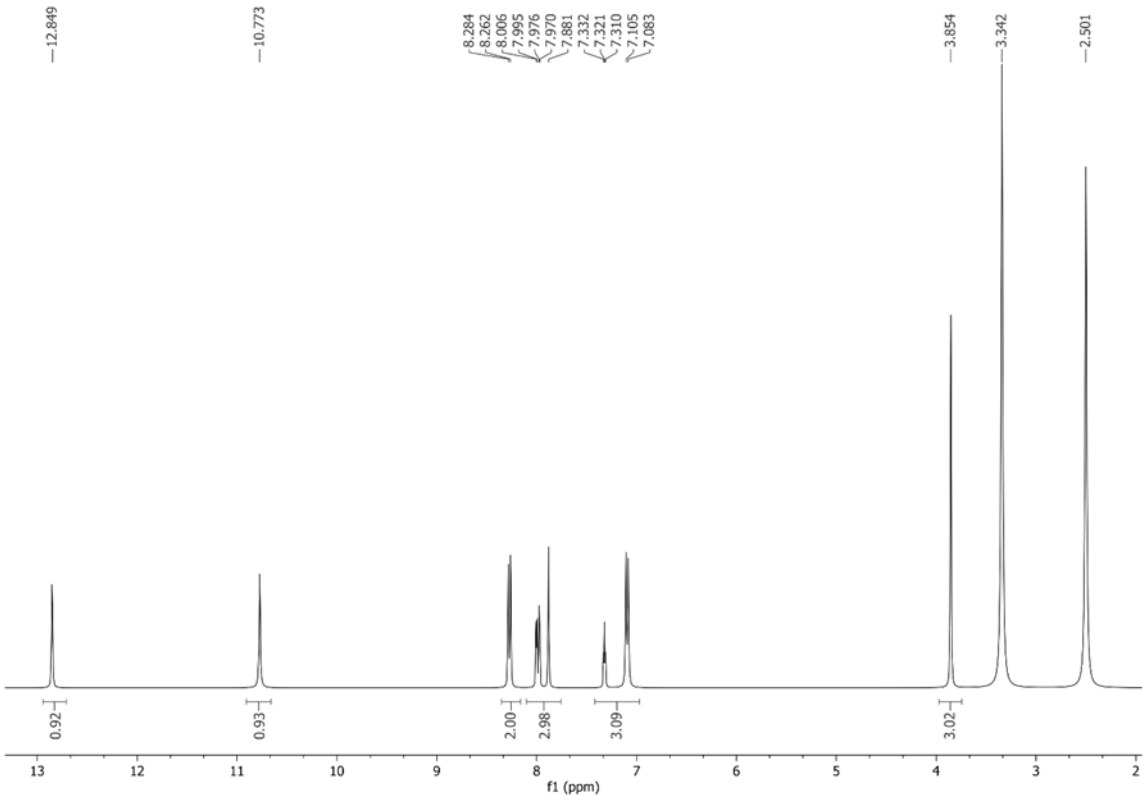

Figure S4. ^{13}C-NMR of compound 2b

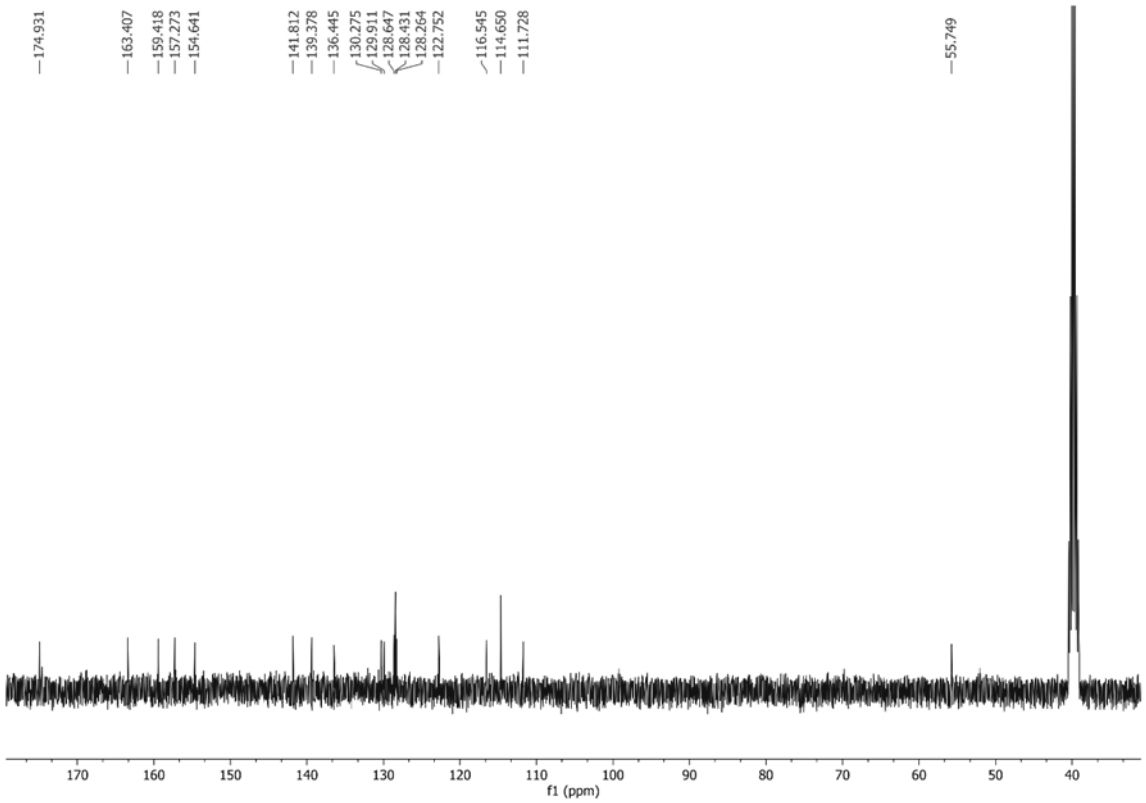

Figure S5. ^{1}H-NMR of compound 3a

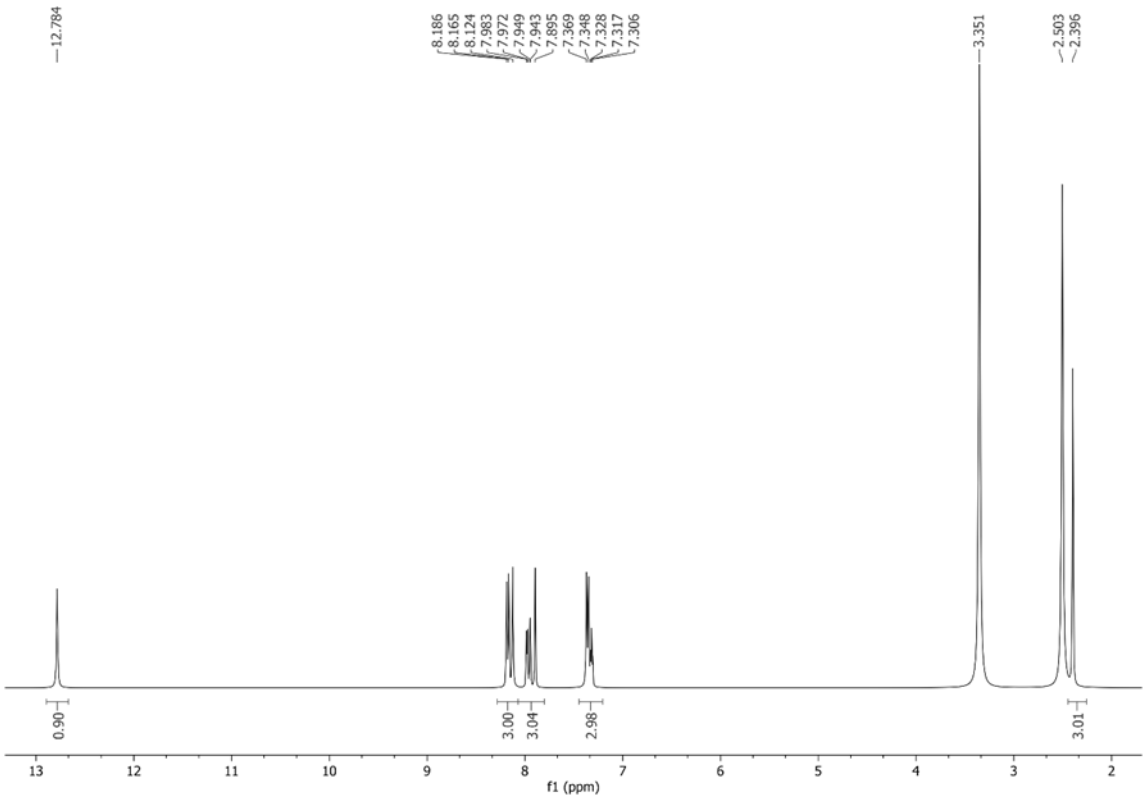

Figure S6. ^{13}C-NMR of compound 3a

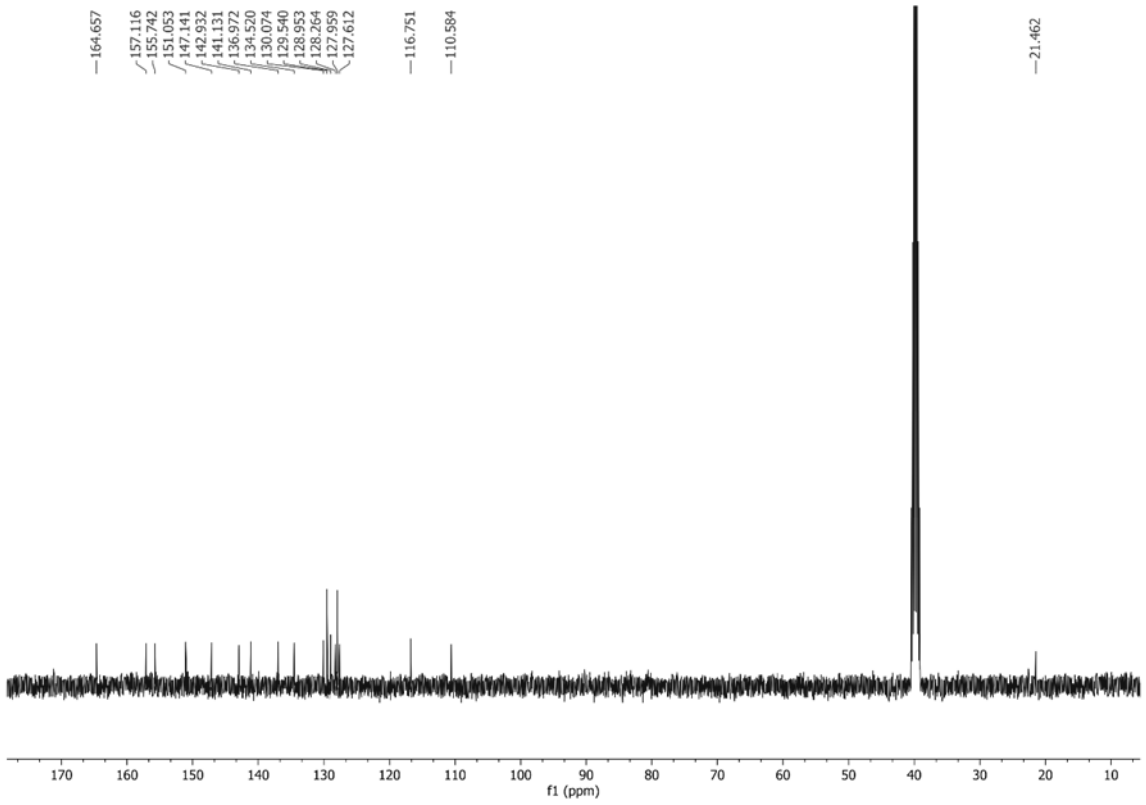

Figure S7. ^{1}H-NMR of compound 3b

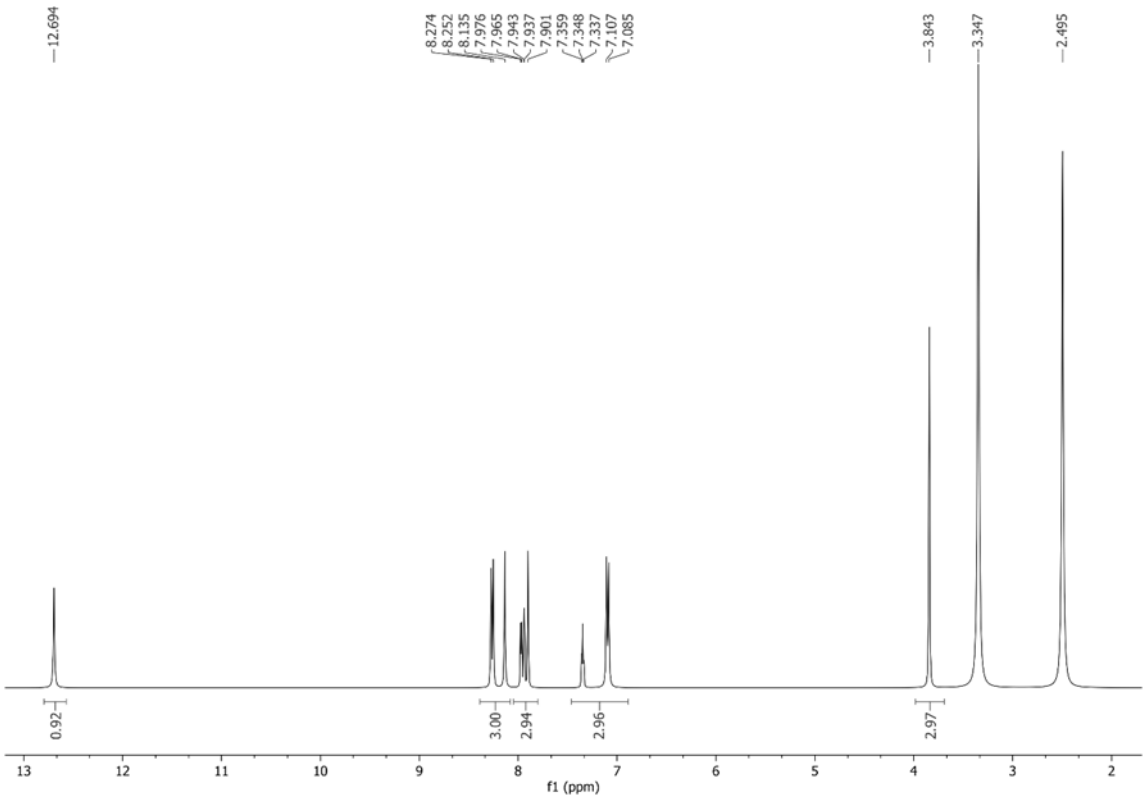

Figure S8. ^{13}C-NMR of compound 3b

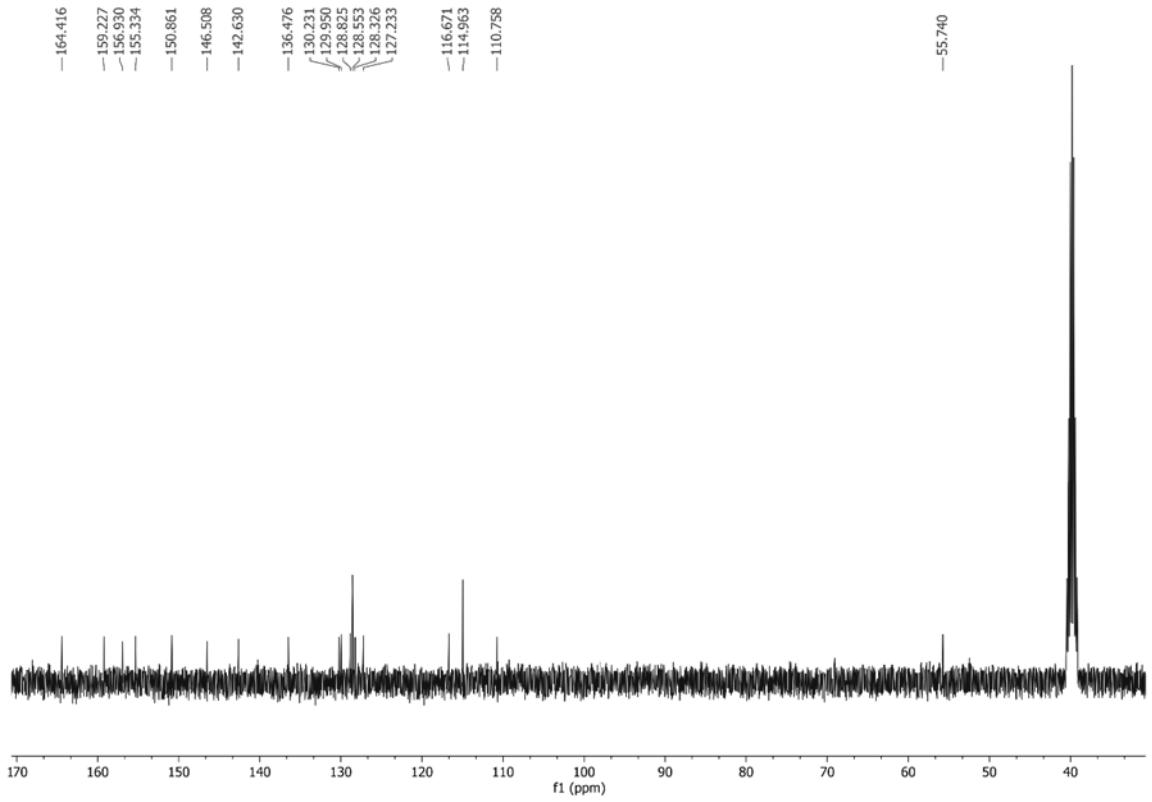

Figure S9. ^{1}H-NMR of compound 3'a

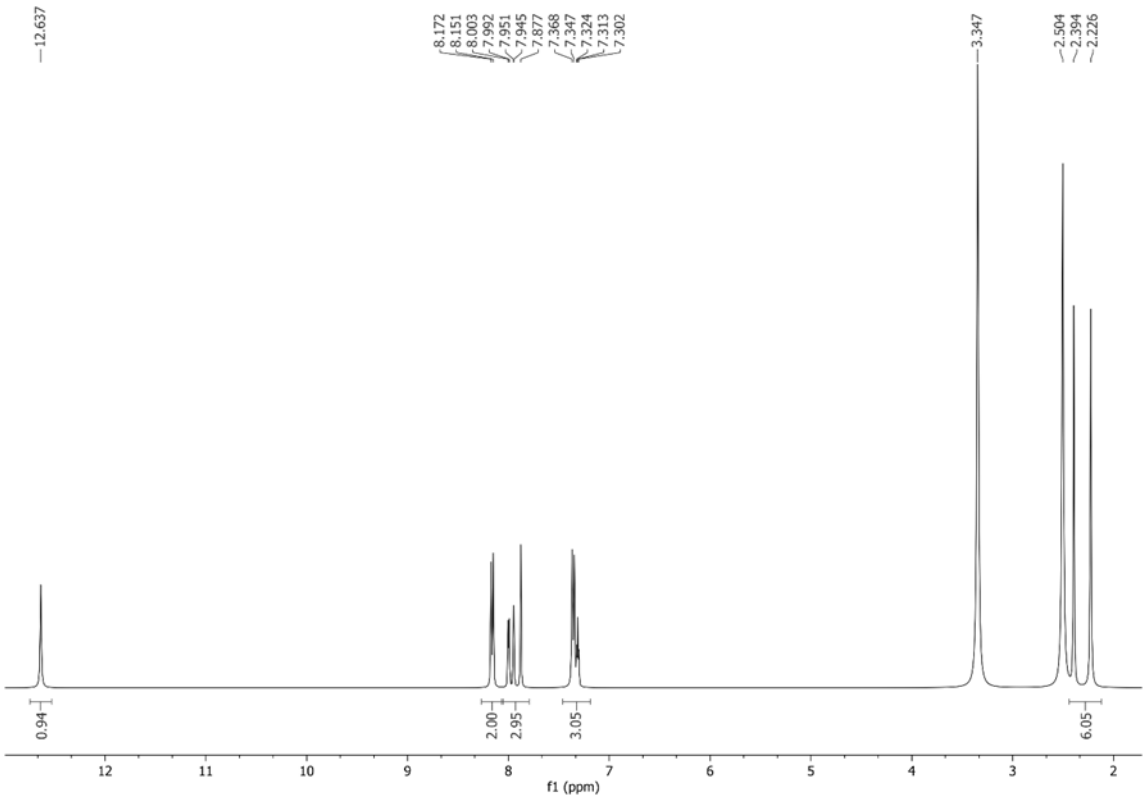

Figure S10. ^{13}C-NMR of compound 3'a

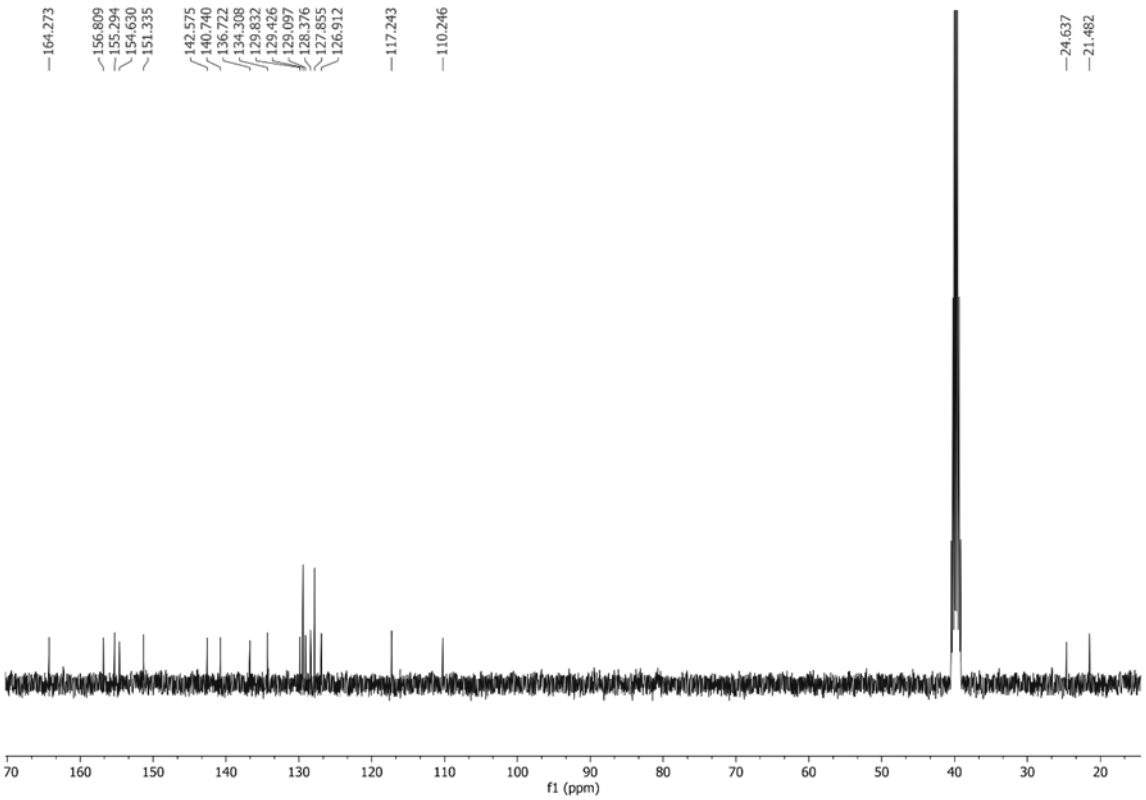

Figure S11. ^{1}H-NMR of compound 3'b

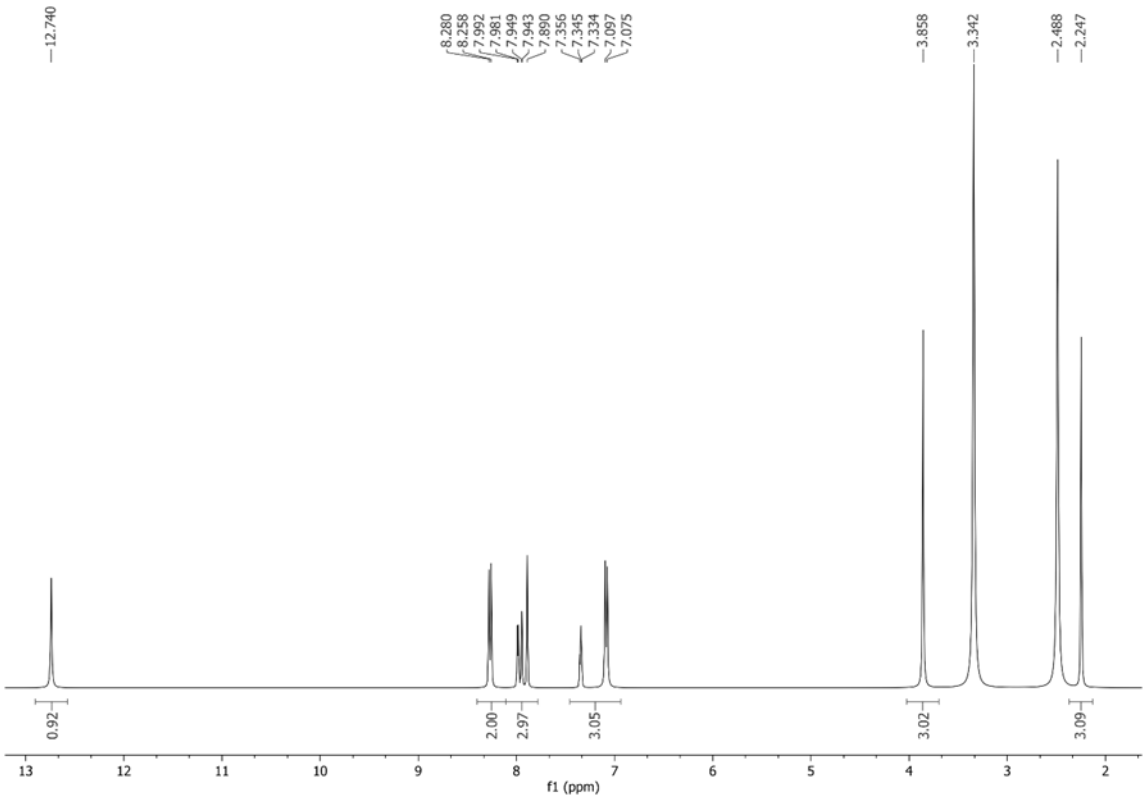

Figure S12. ^{13}C-NMR of compound 3'b

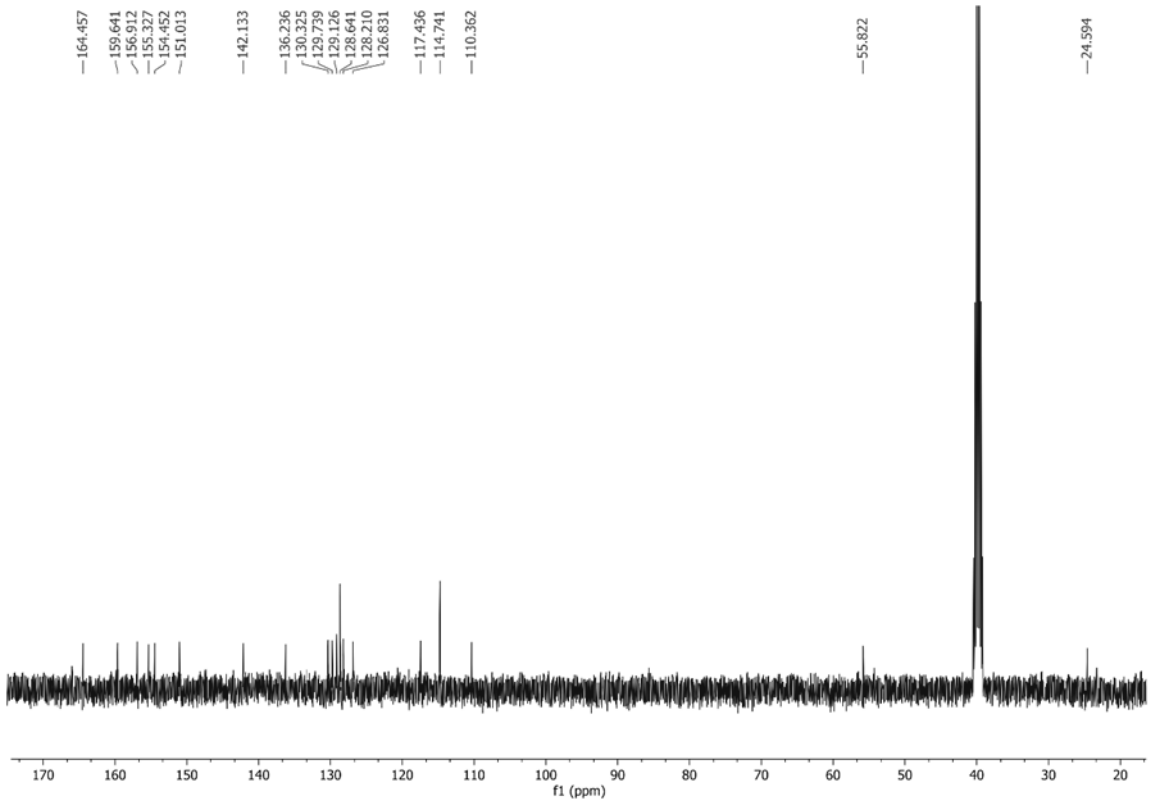

Figure S13. ^{1}H-NMR of compound 6a

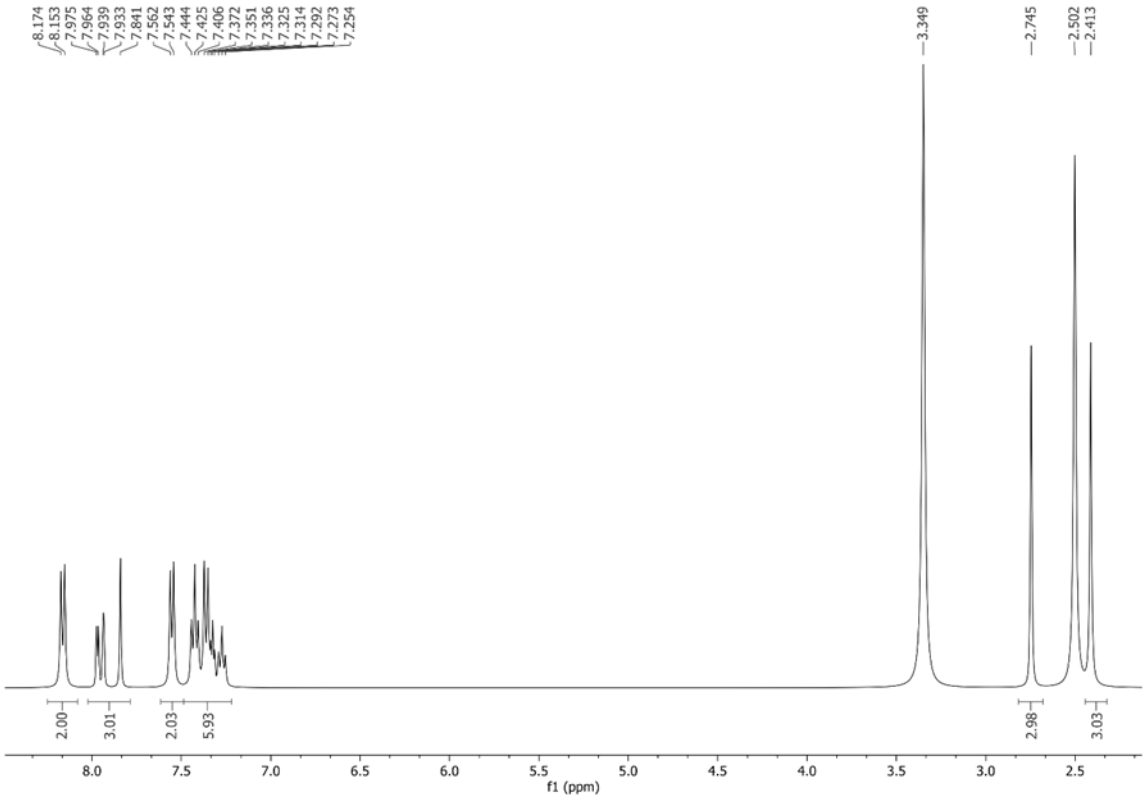

Figure S14. ^{13}C-NMR of compound 6a

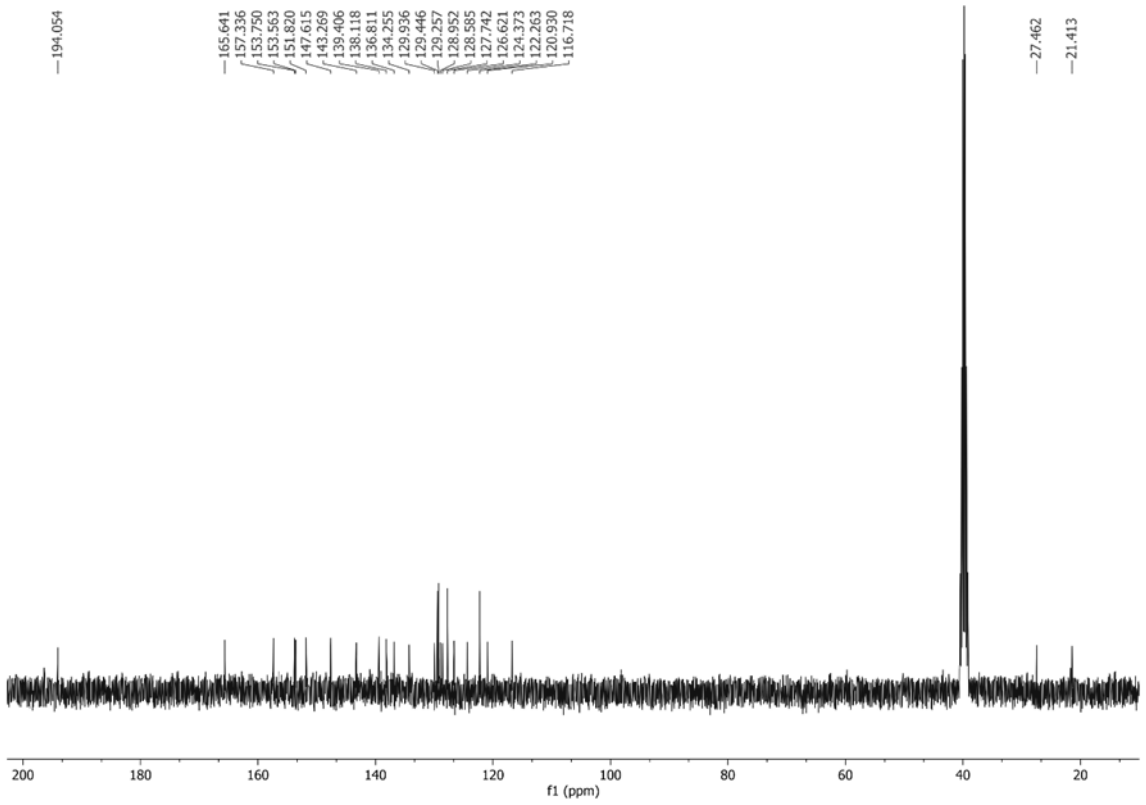

Figure S15. ^{1}H-NMR of compound 6b

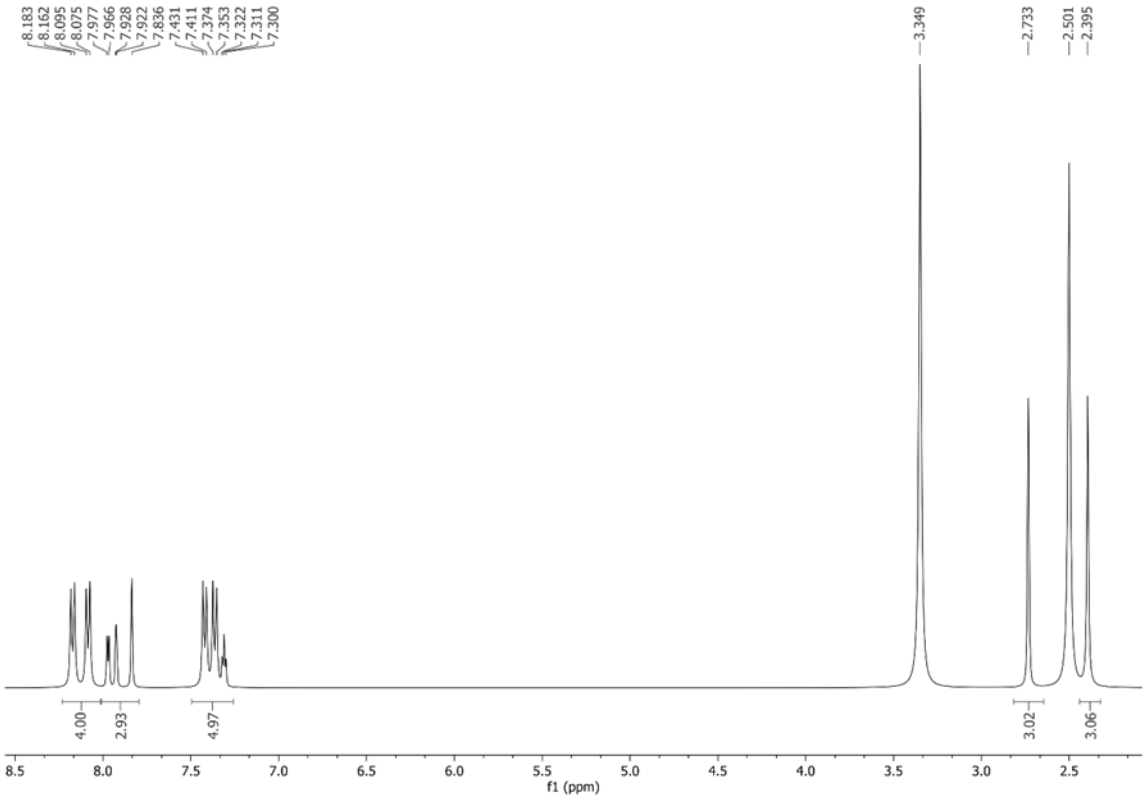

Figure S16. ^{13}C-NMR of compound 6b

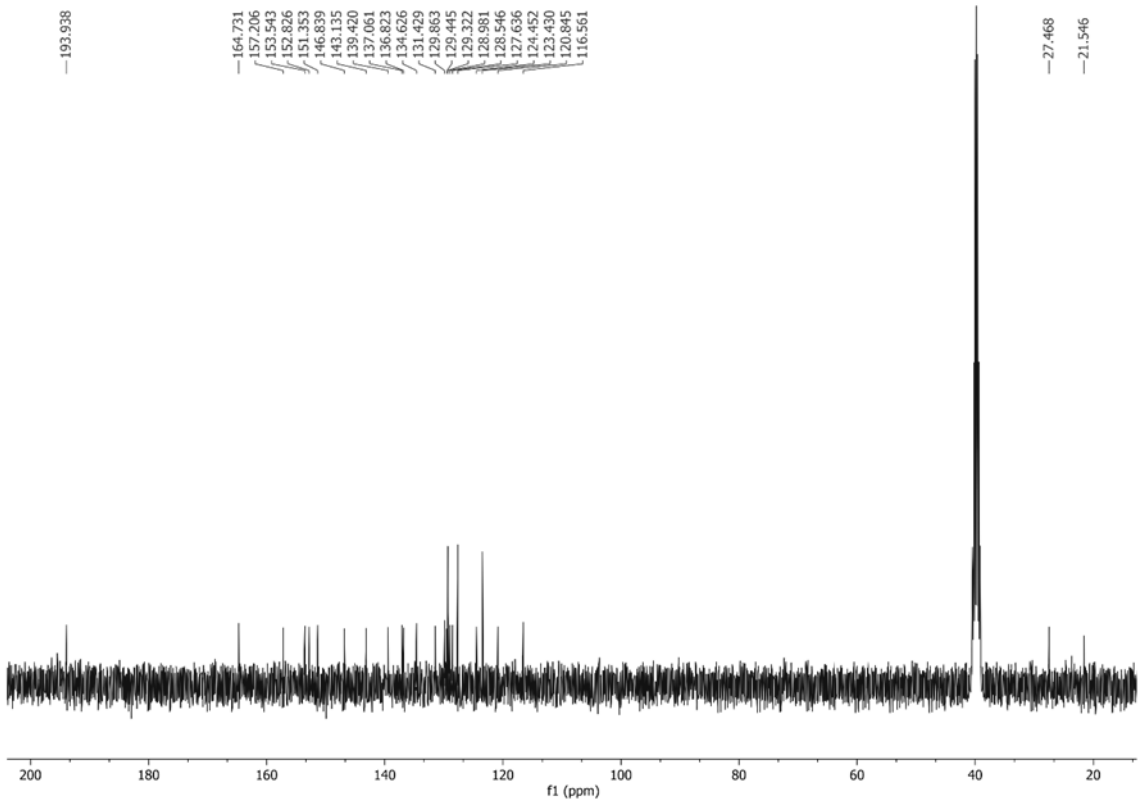

Figure S17. ^{1}H-NMR of compound 6c

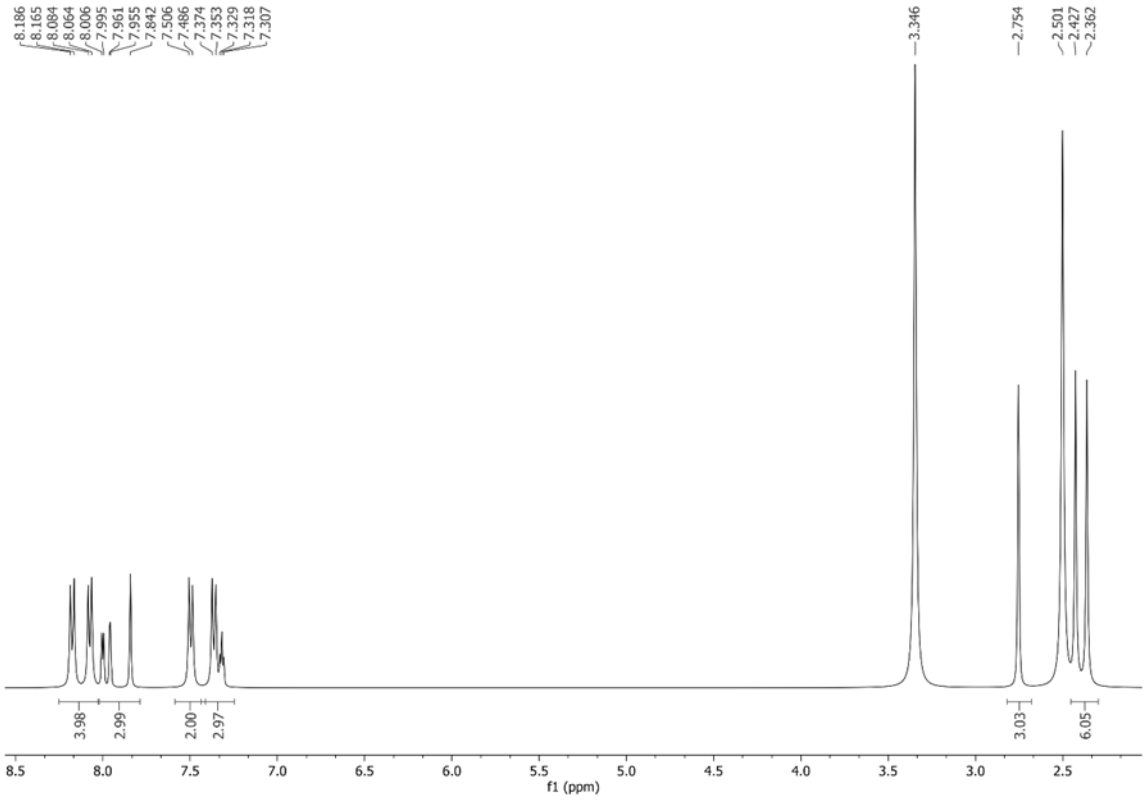

Figure S18. ^{13}C-NMR of compound 6c

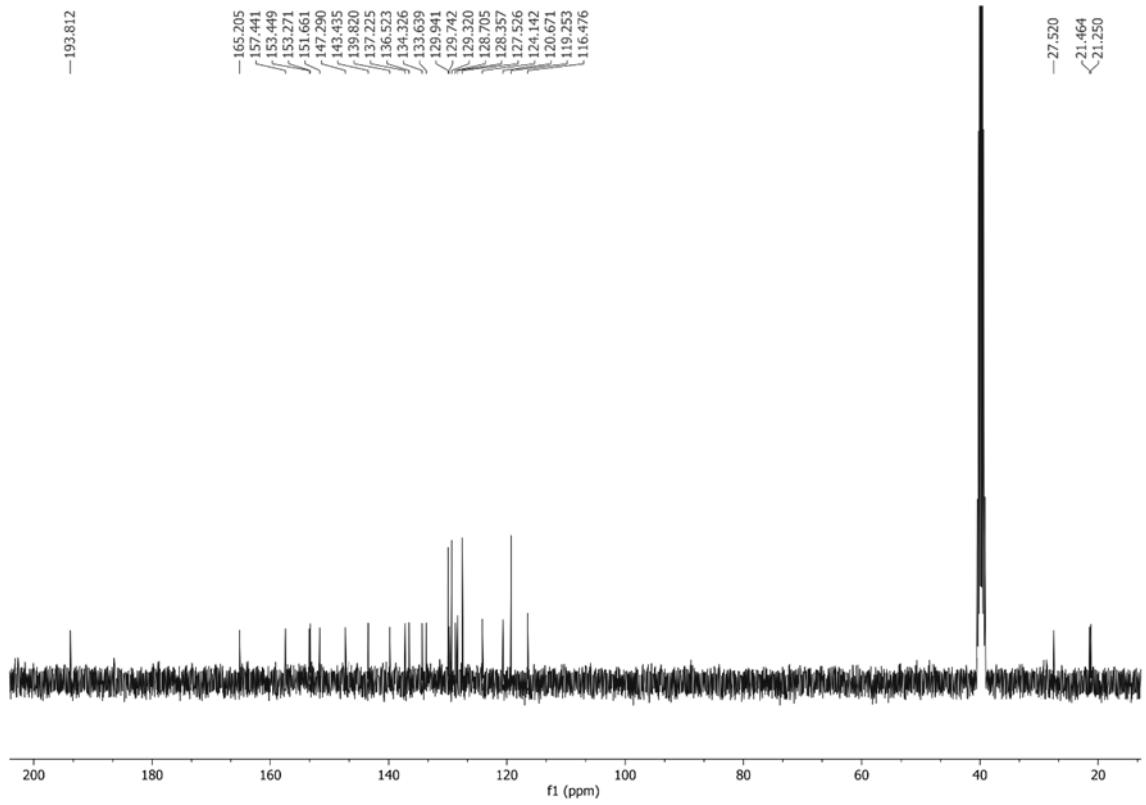

Figure S19. ^{1}H-NMR of compound 6d

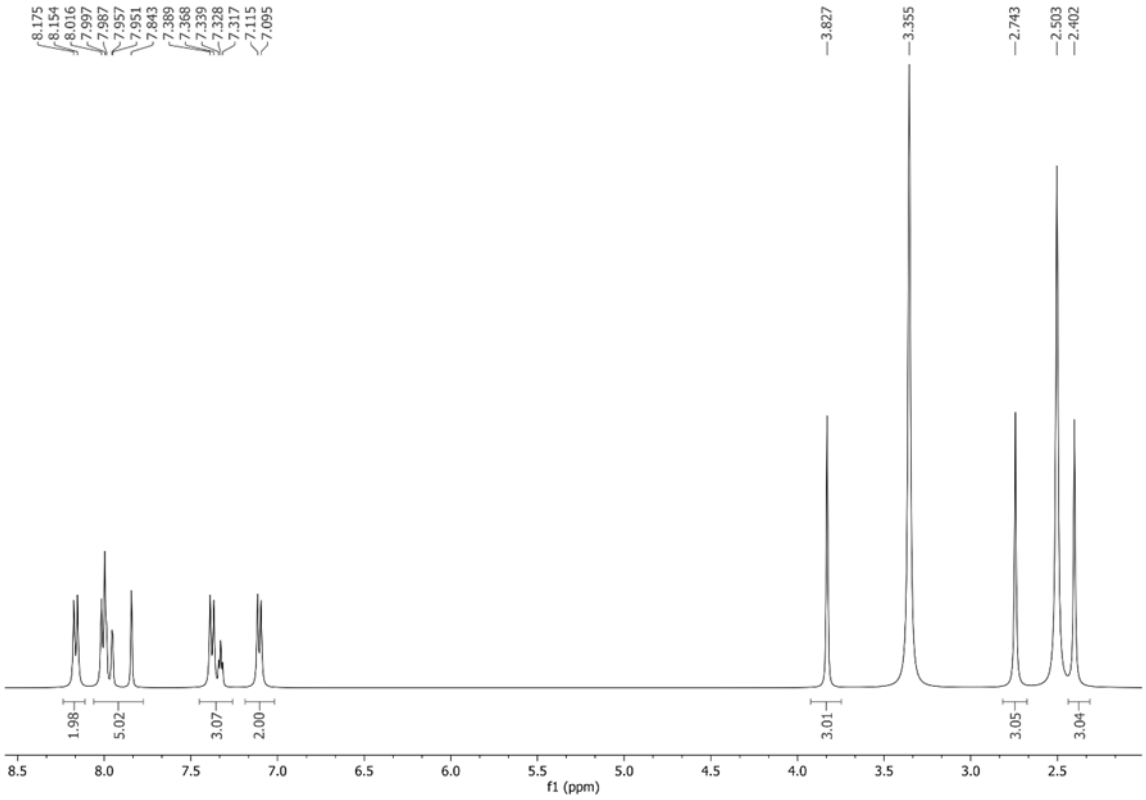

Figure S20. ^{13}C-NMR of compound 6d

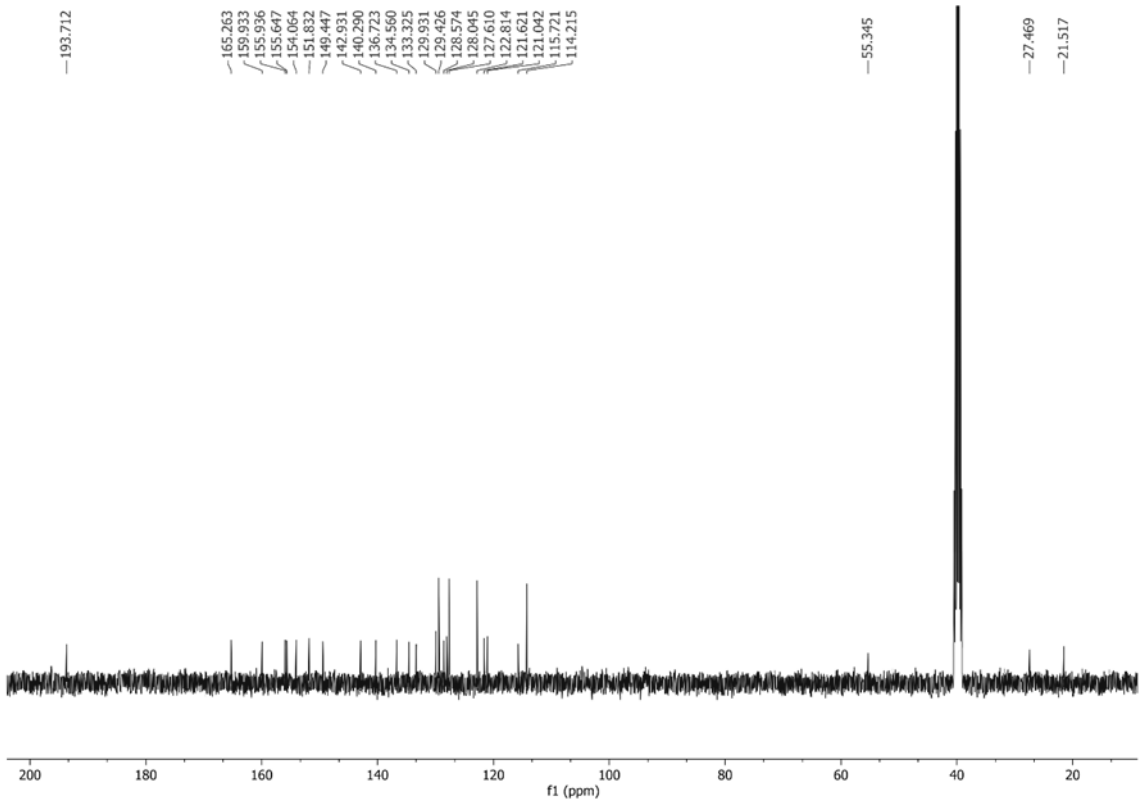

Figure S21. ^{1}H-NMR of compound 6e

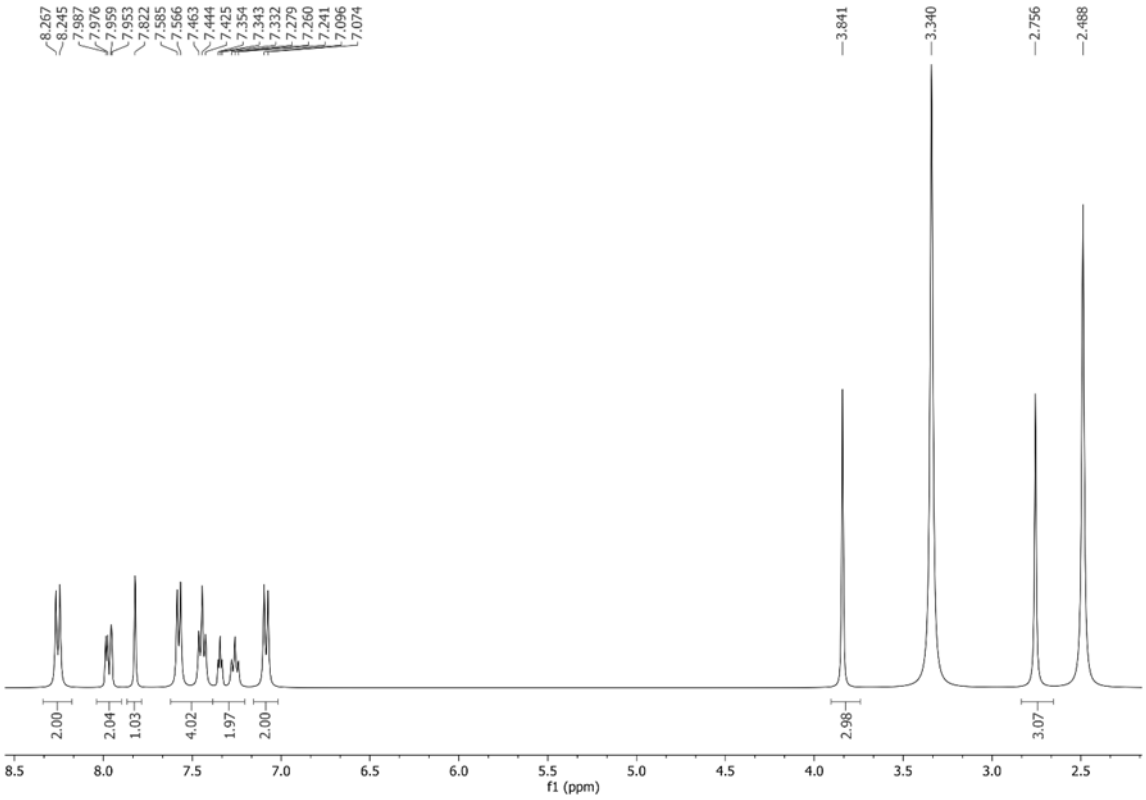

Figure S22. ^{13}C-NMR of compound 6e

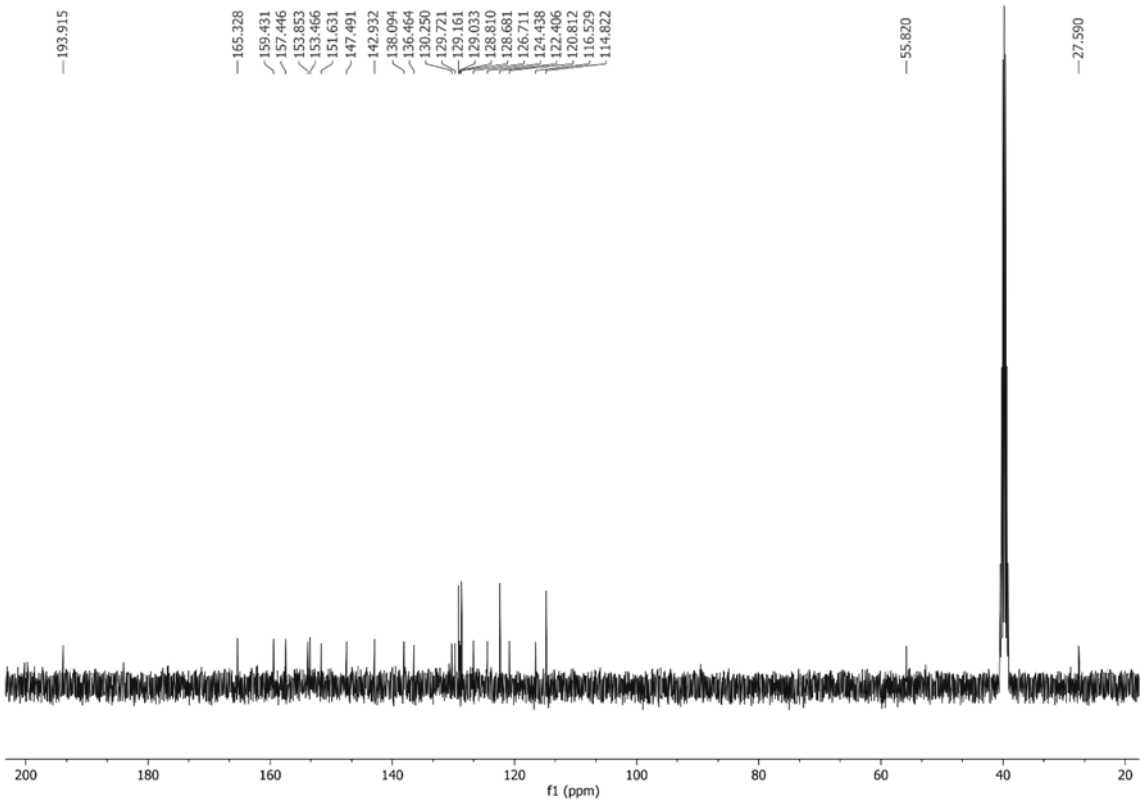

Figure S23. ^{1}H-NMR of compound 6f

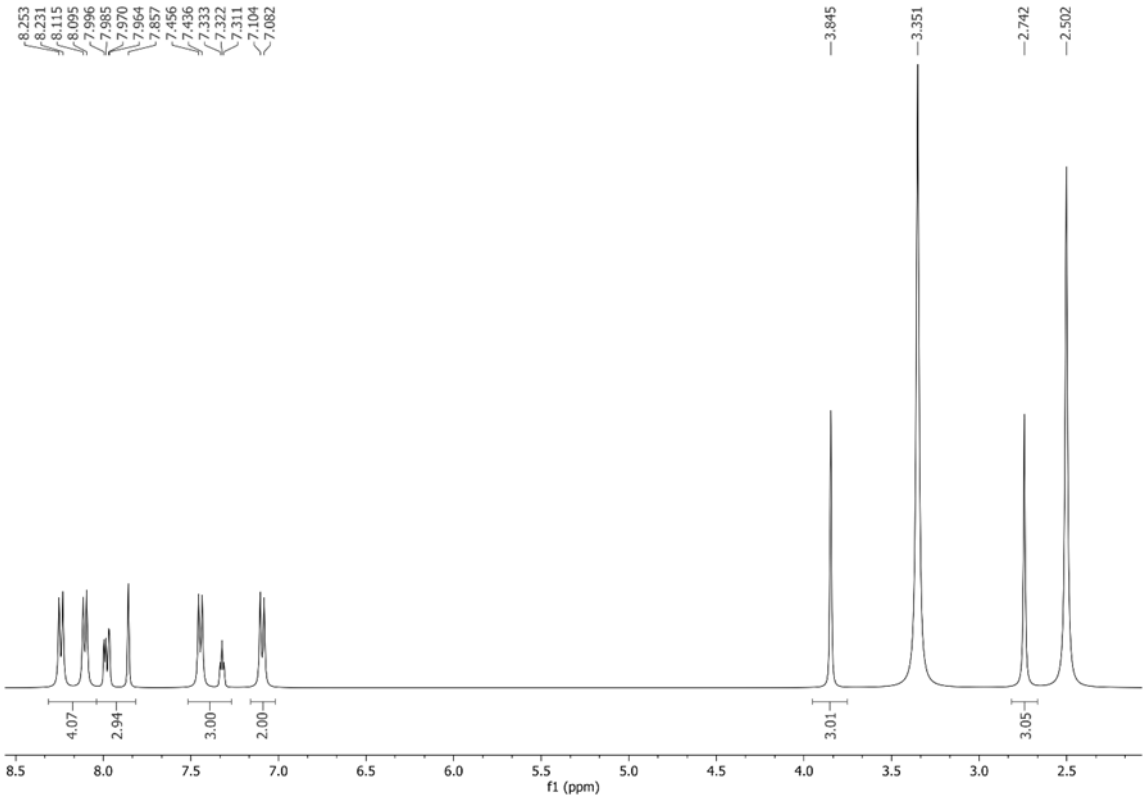

Figure S24. ^{13}C-NMR of compound 6f

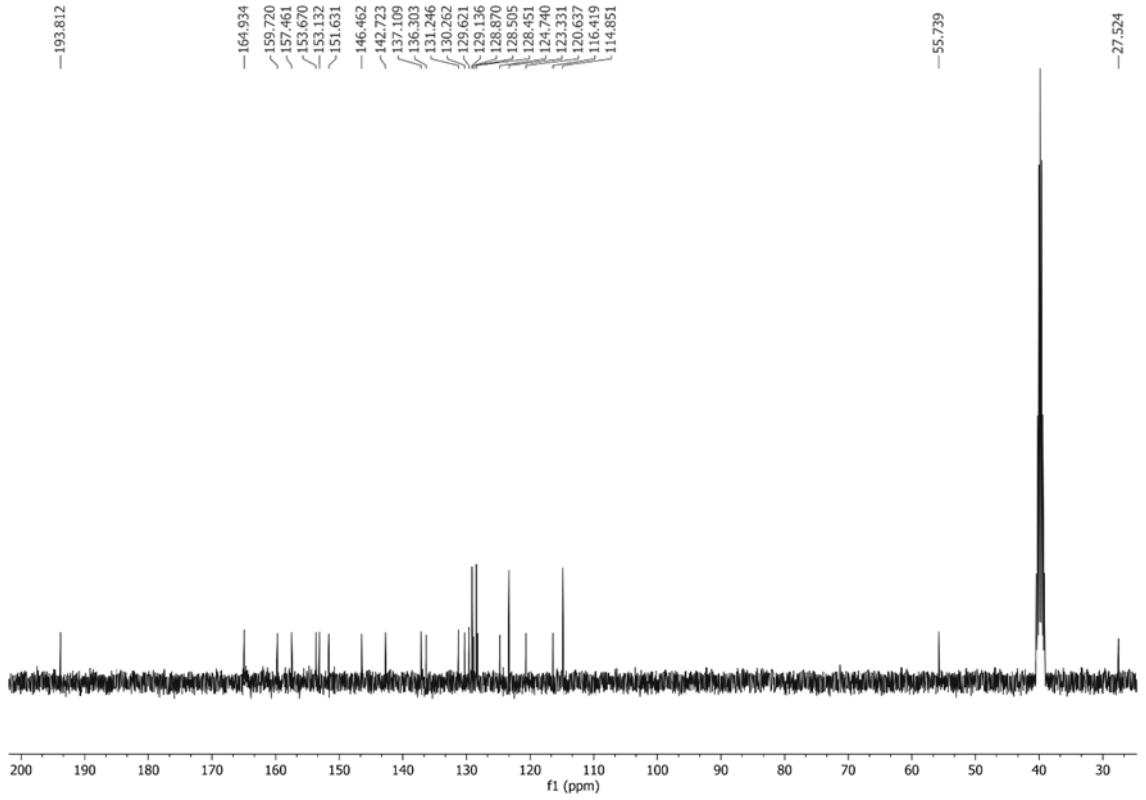

Figure S25. ^{1}H-NMR of compound 6g

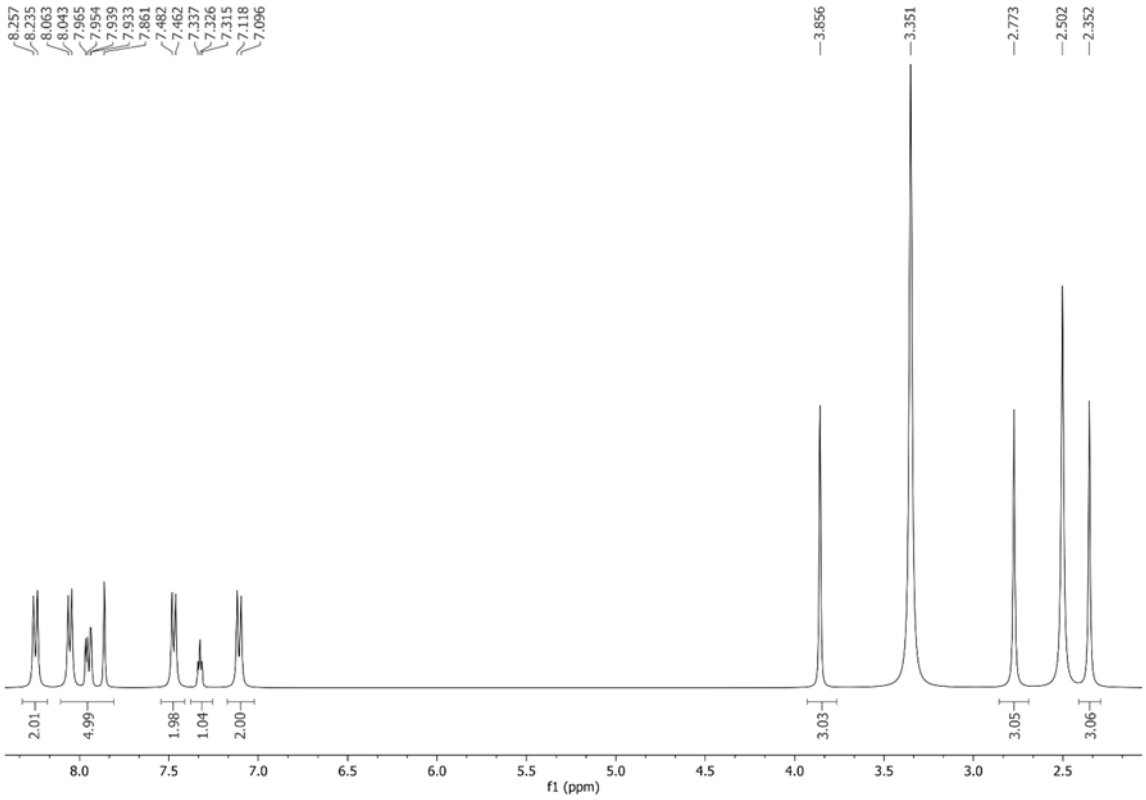

Figure S26. ^{13}C-NMR of compound 6g

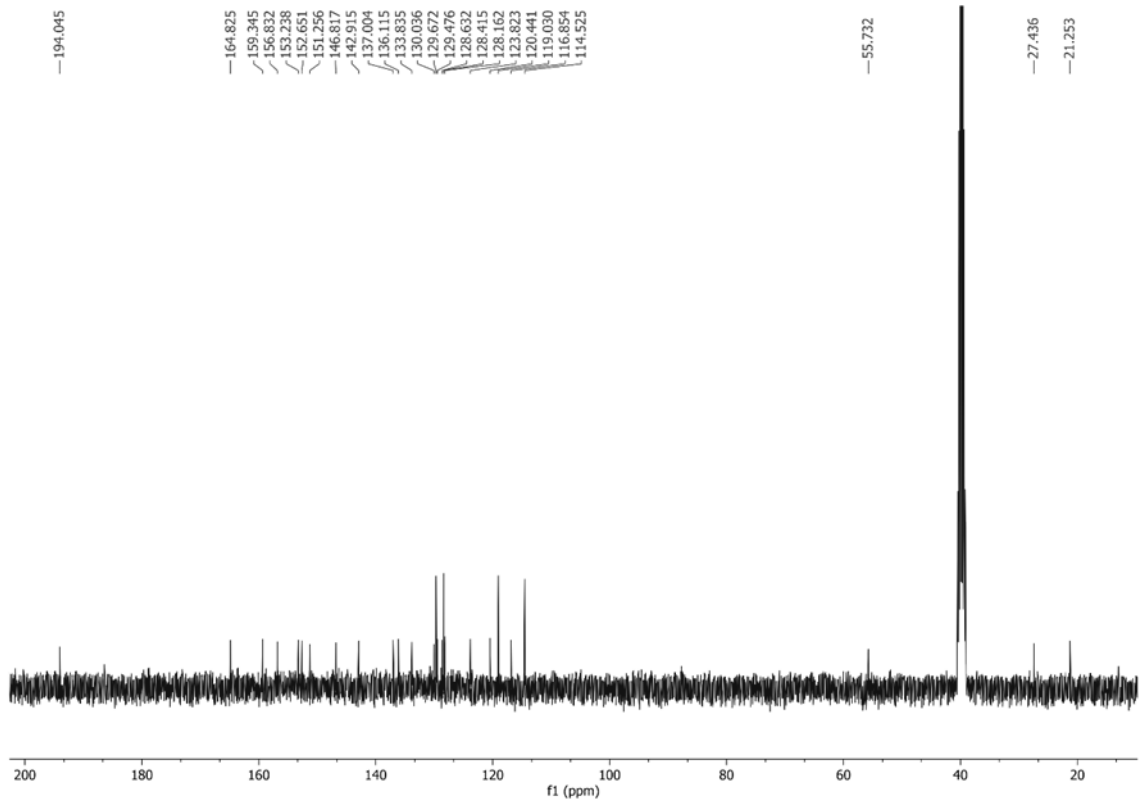

Figure S27. ^{1}H-NMR of compound 6h

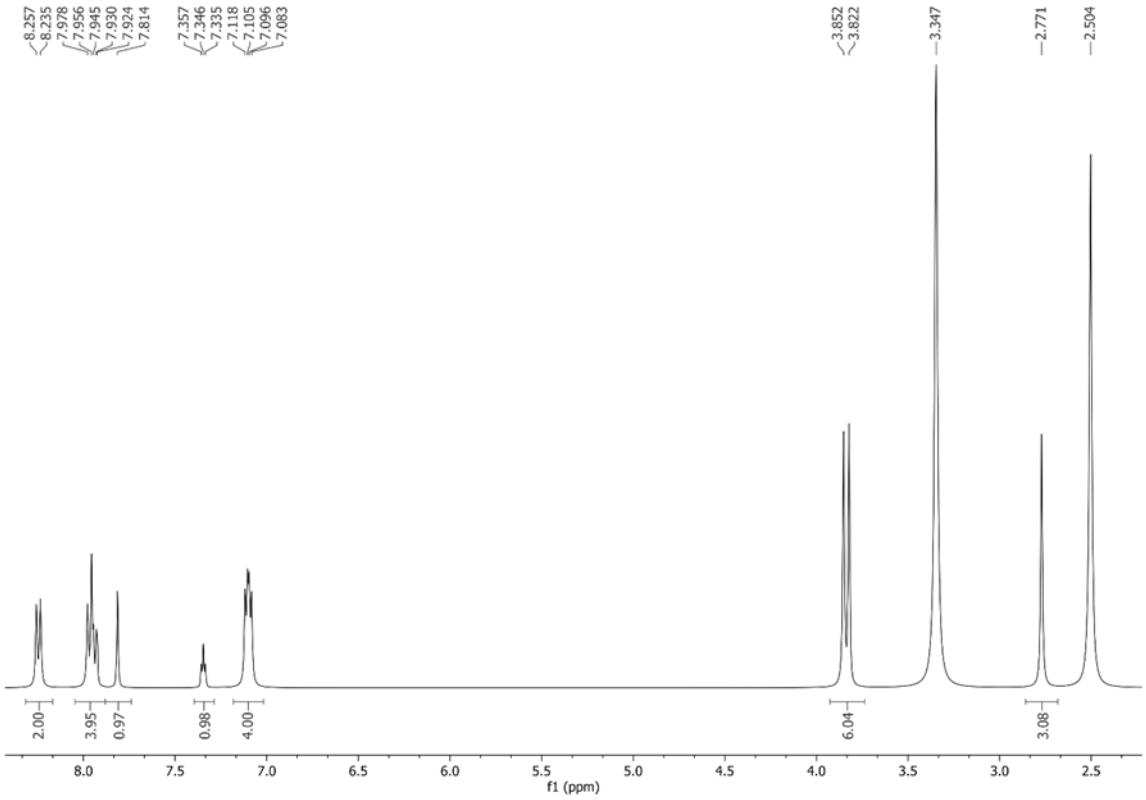

Figure S28. ^{13}C-NMR of compound 6h

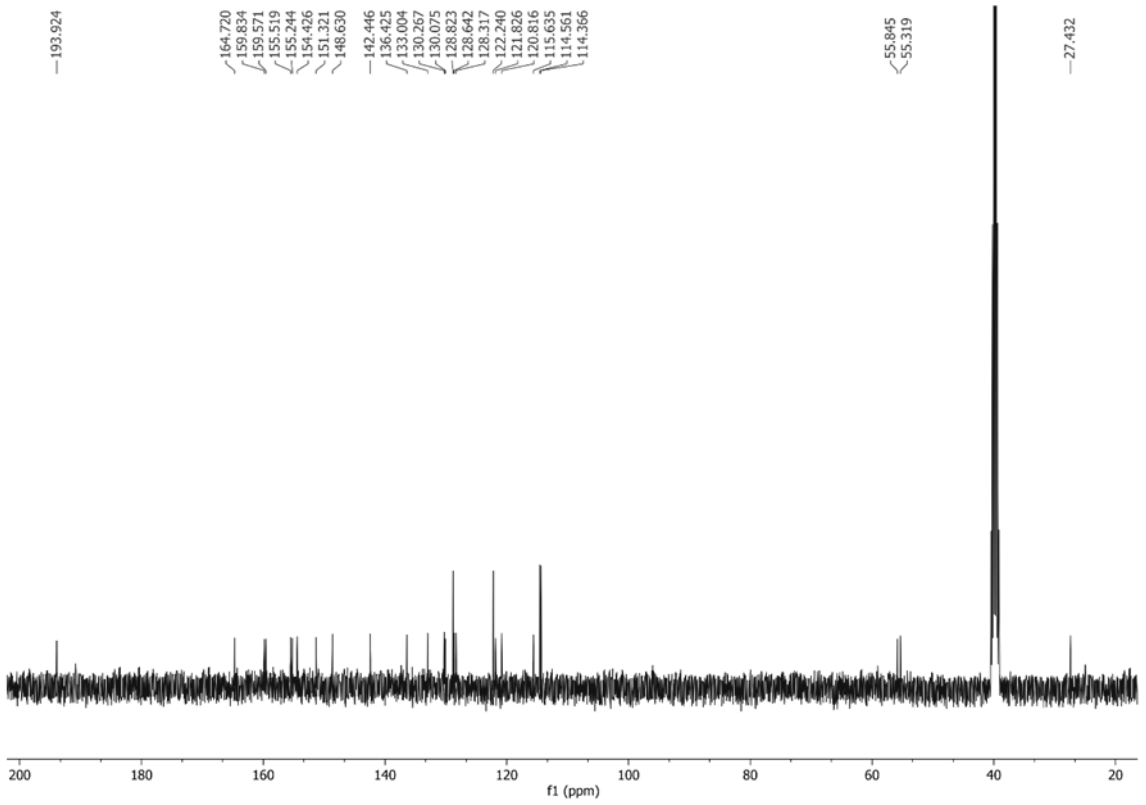

Figure S29. ^{1}H-NMR of compound 7a

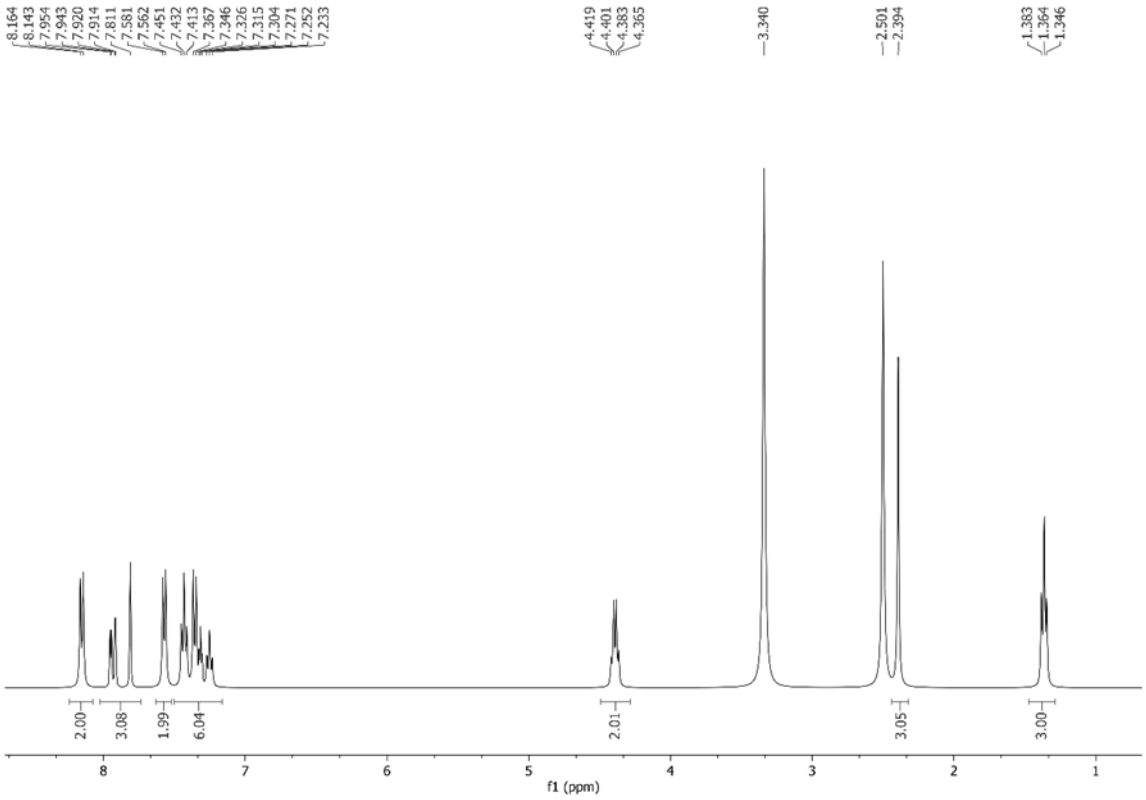

Figure S30. ^{13}C-NMR of compound 7a

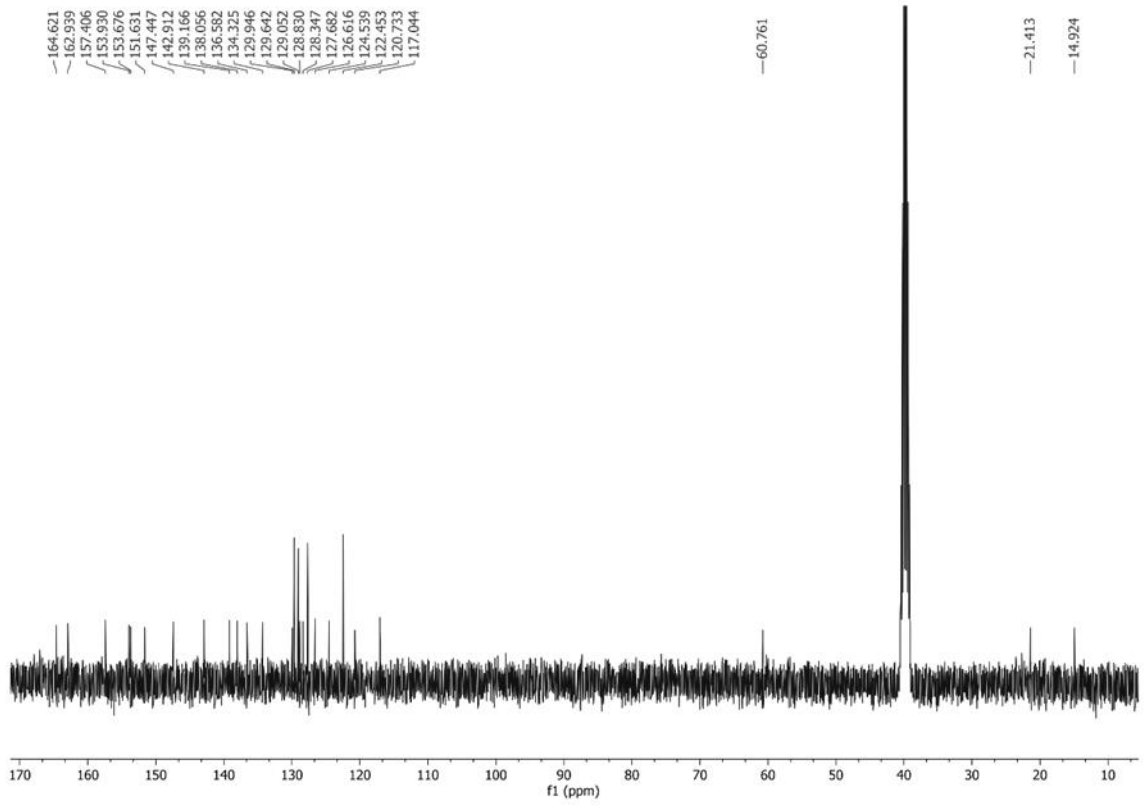

Figure S31. ^{1}H-NMR of compound 7b

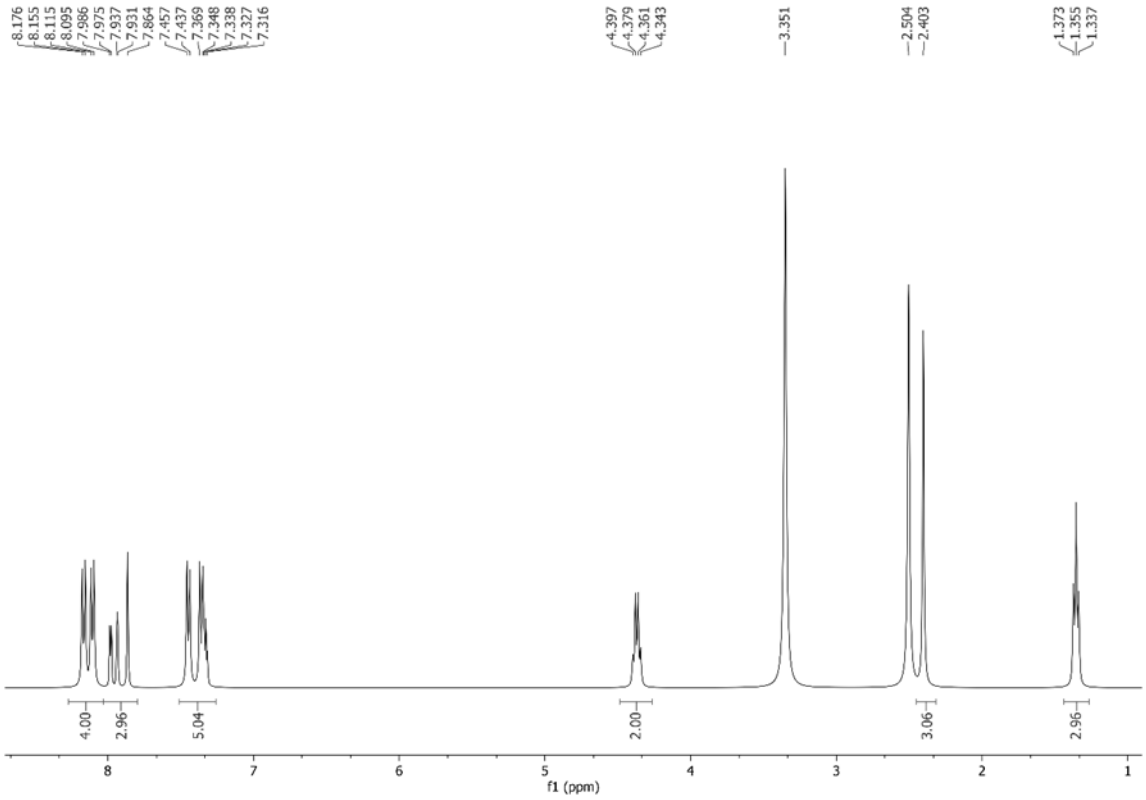

Figure S32. ^{13}C-NMR of compound 7b

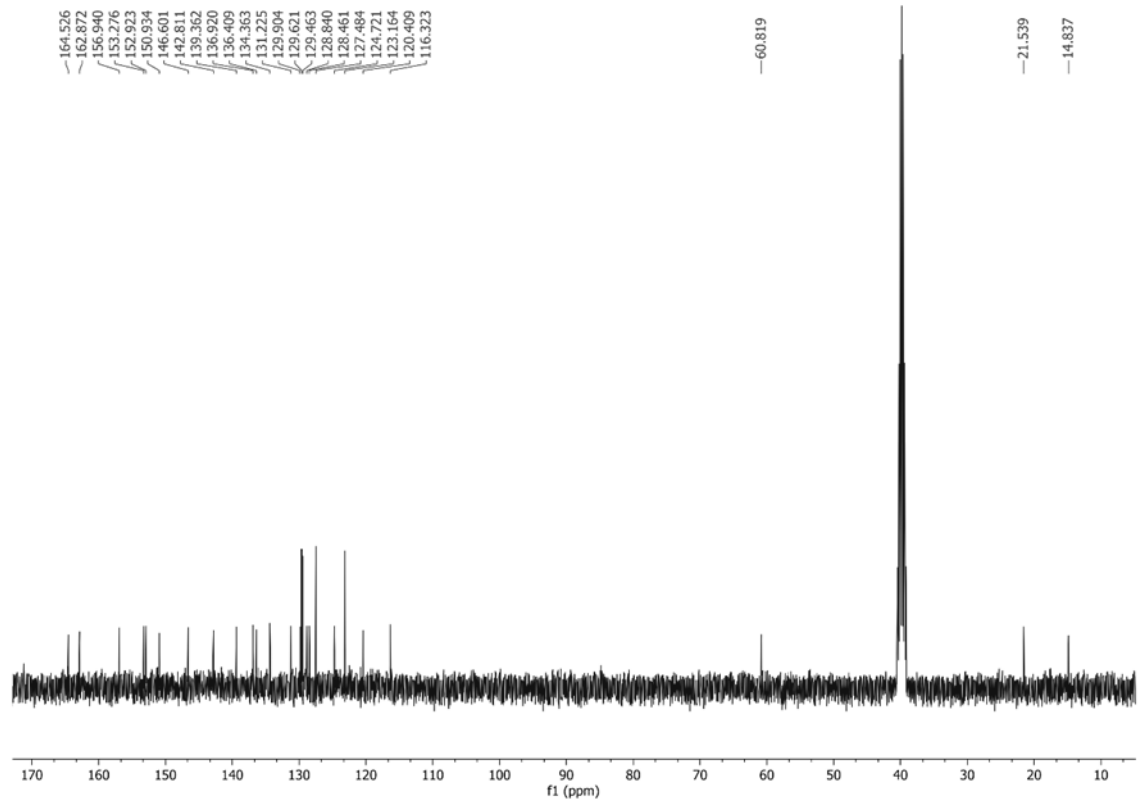

Figure S33. ^{1}H-NMR of compound 7c

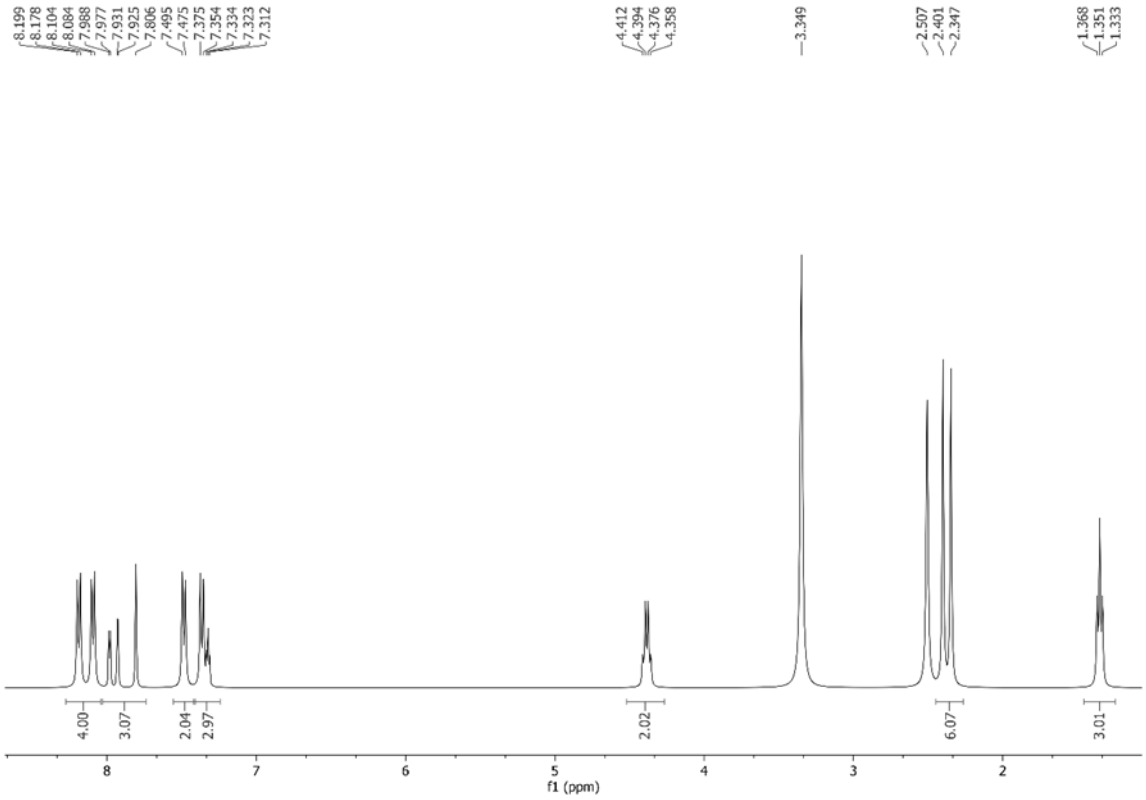

Figure S34. ^{13}C-NMR of compound 7c

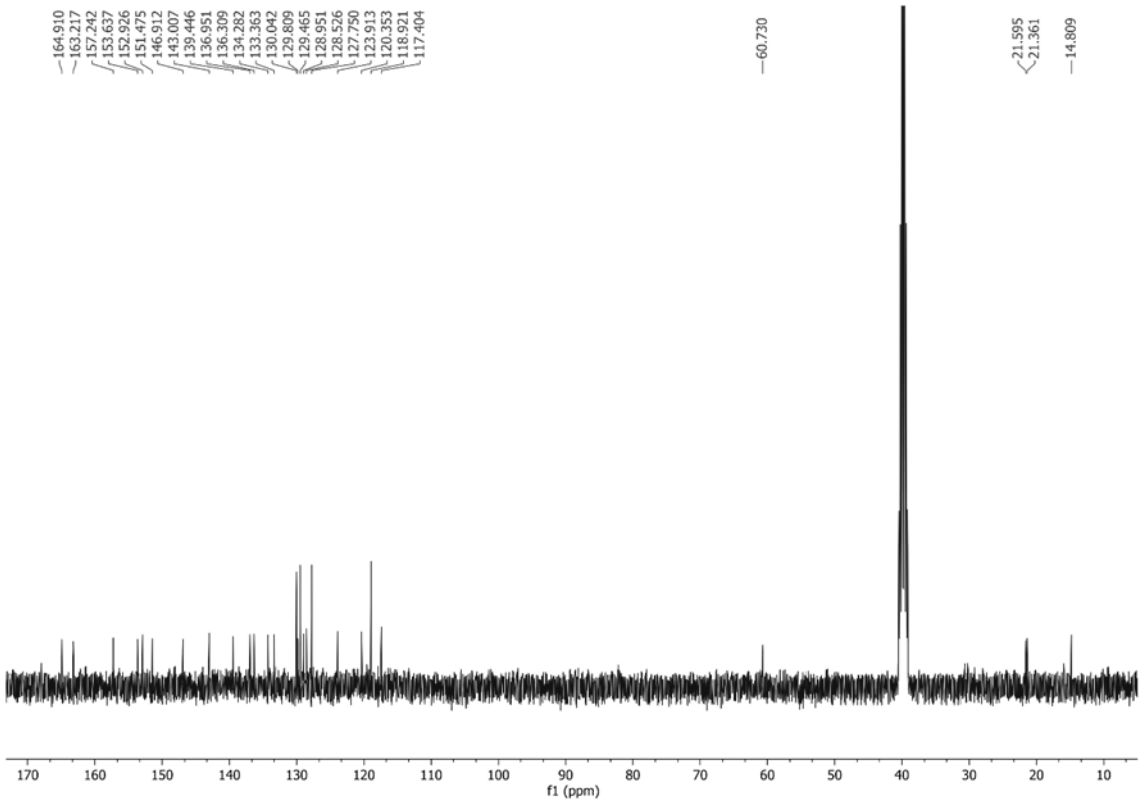

Figure S35. ^{1}H-NMR of compound 7d

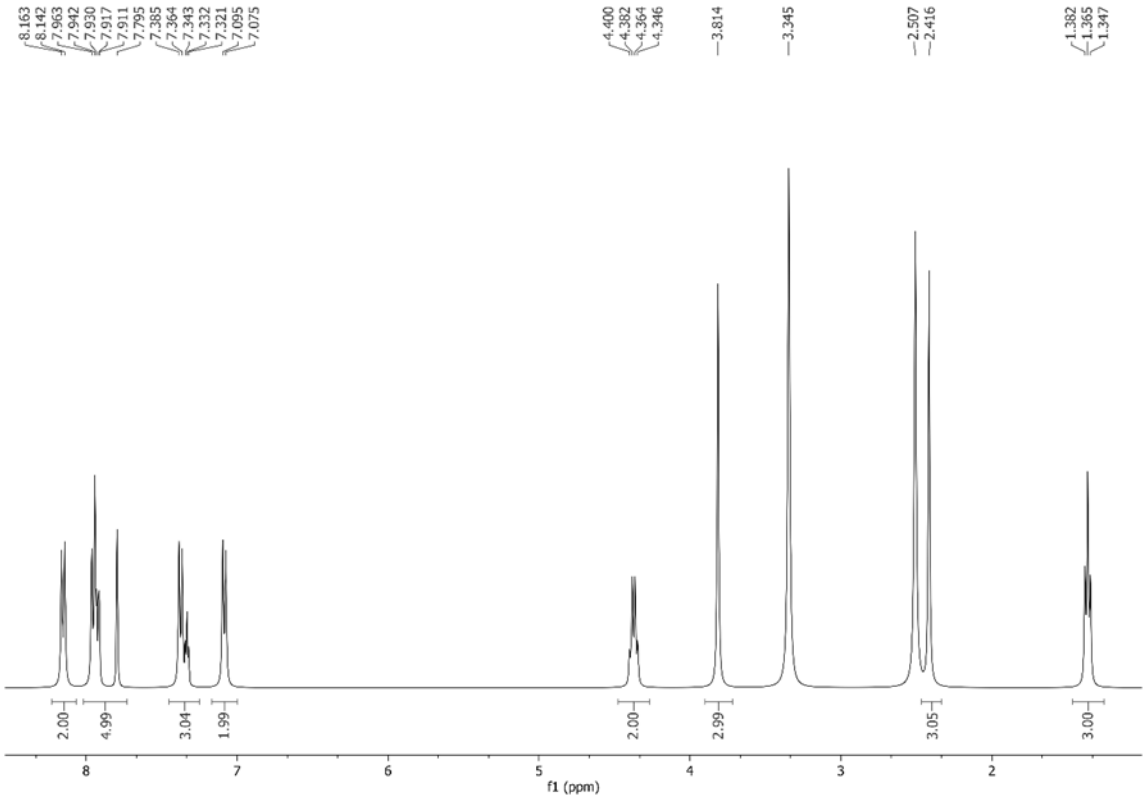

Figure S36. ^{13}C-NMR of compound 7d

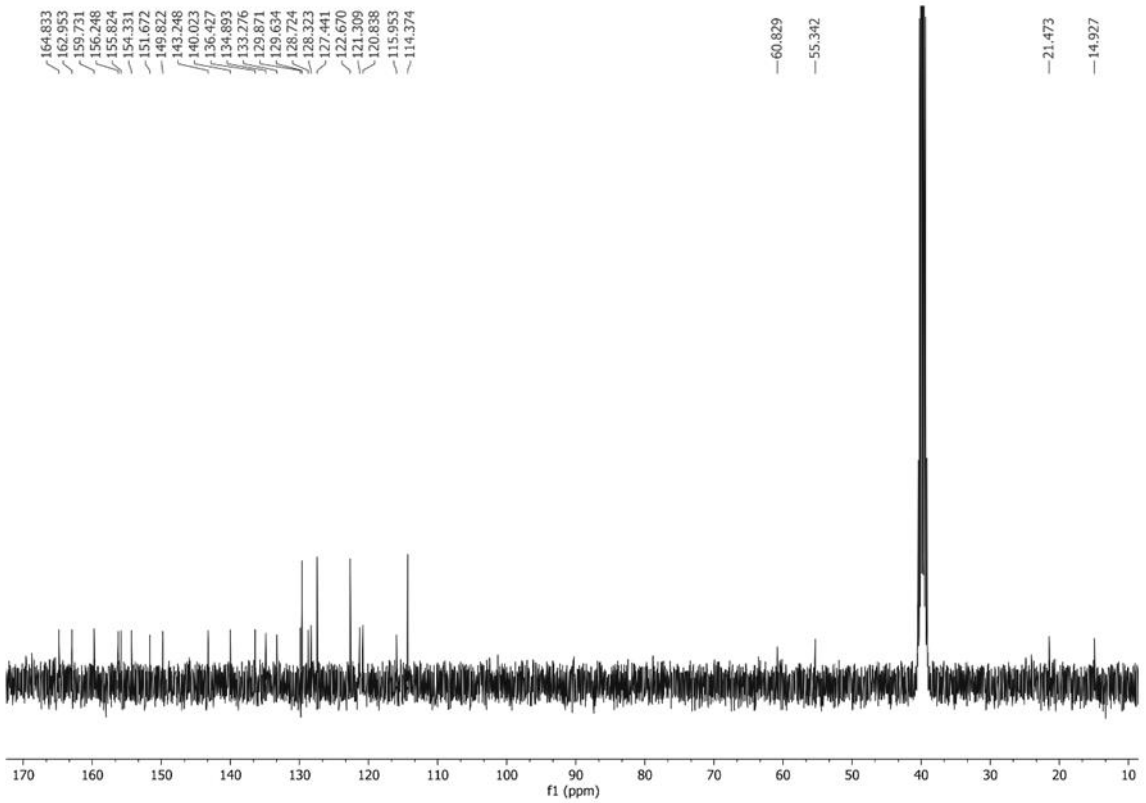

Figure S37. ^{1}H-NMR of compound 7e

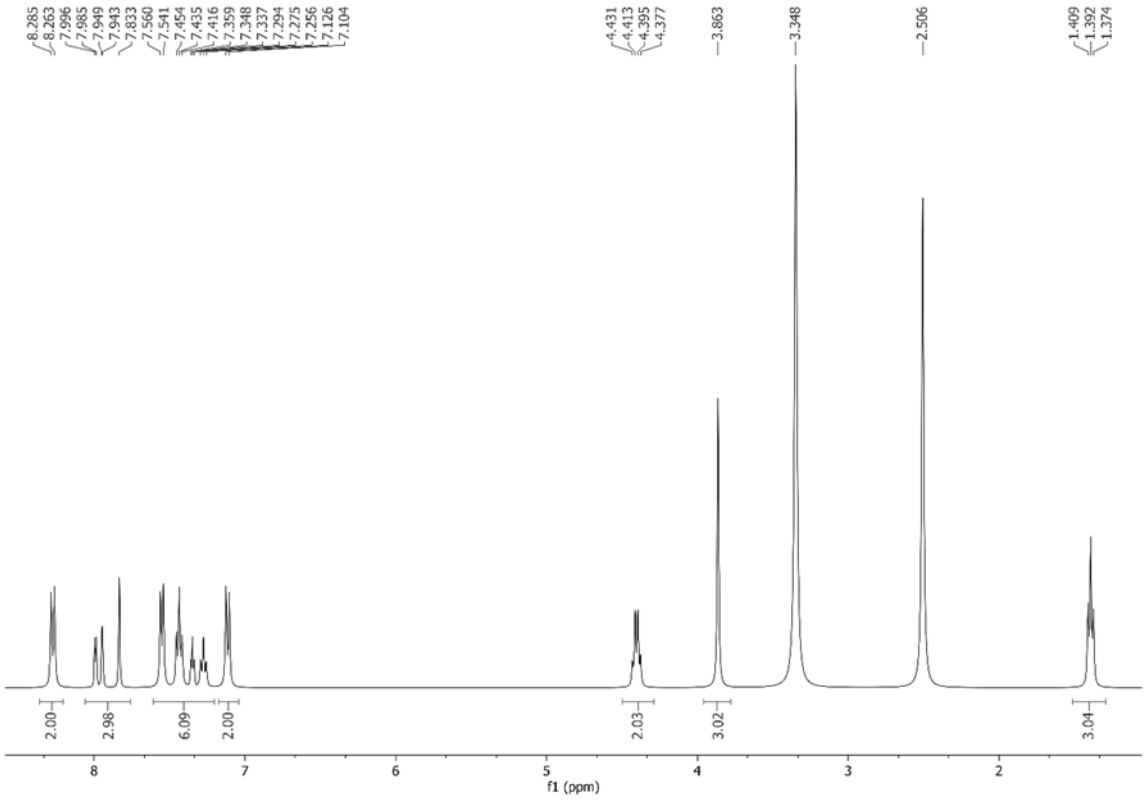

Figure S38. ^{13}C-NMR of compound 7e

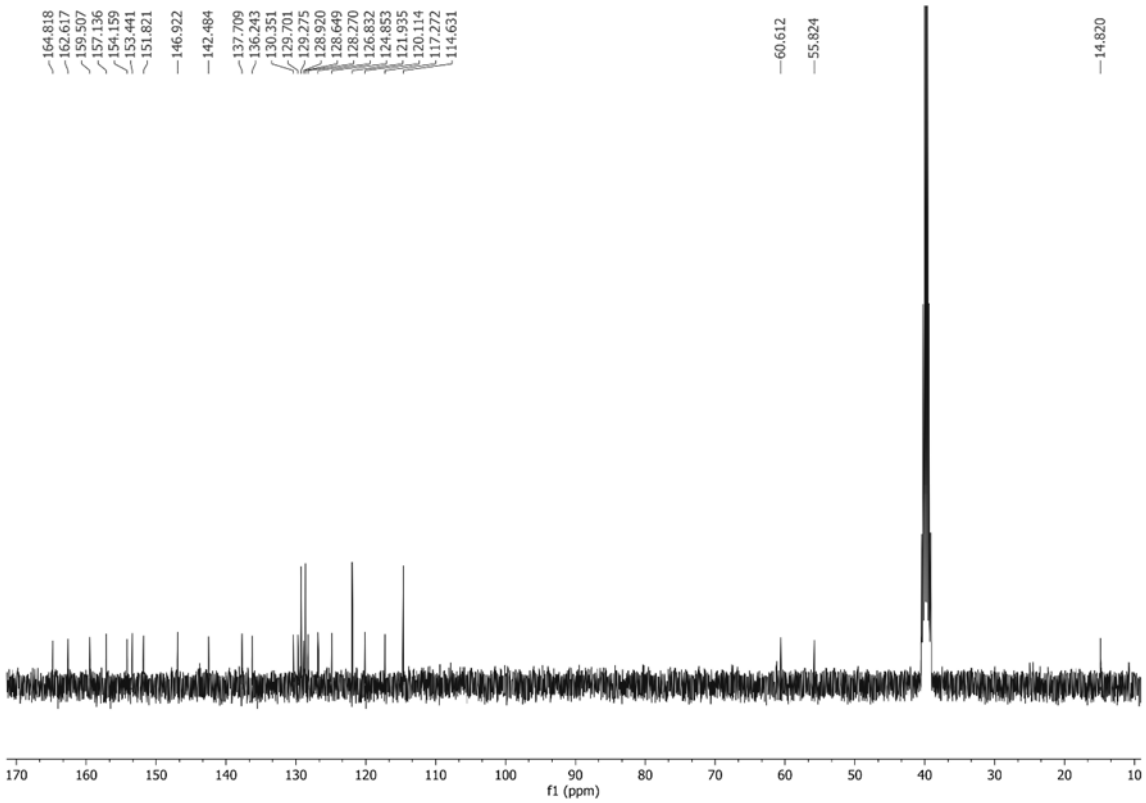

Figure S39. ^{1}H-NMR of compound 7f

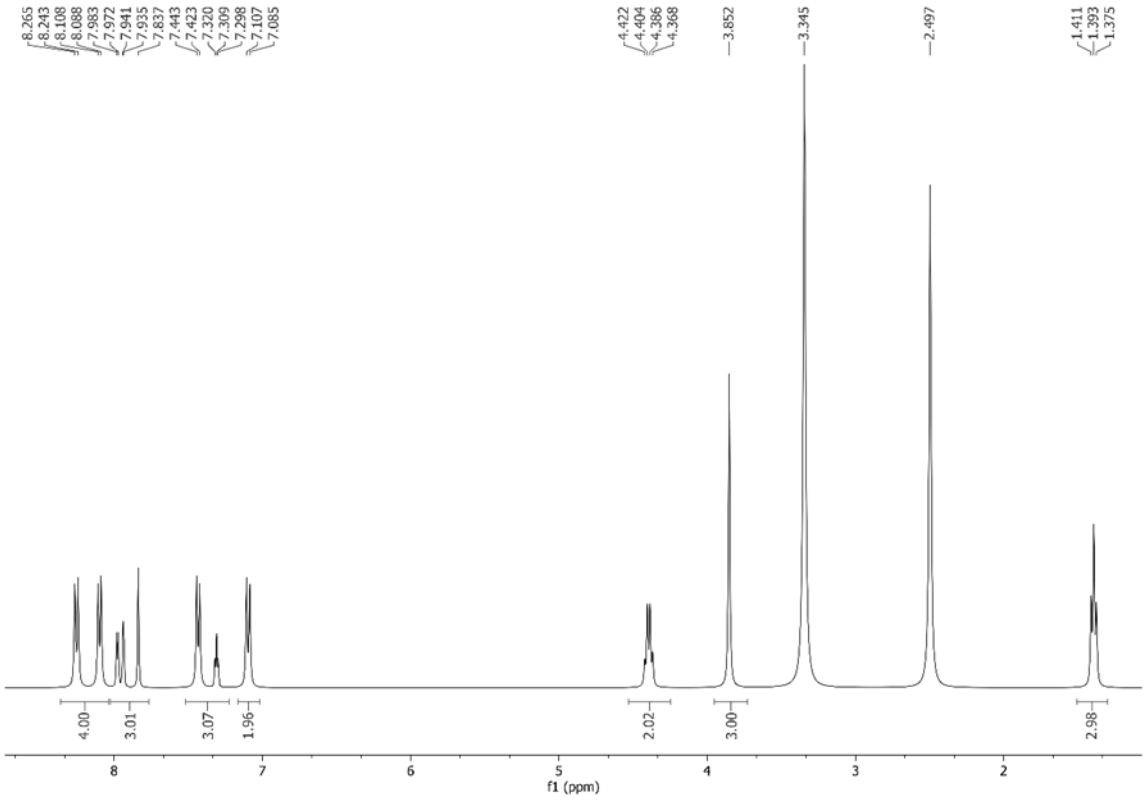

Figure S40. ^{13}C-NMR of compound 7f

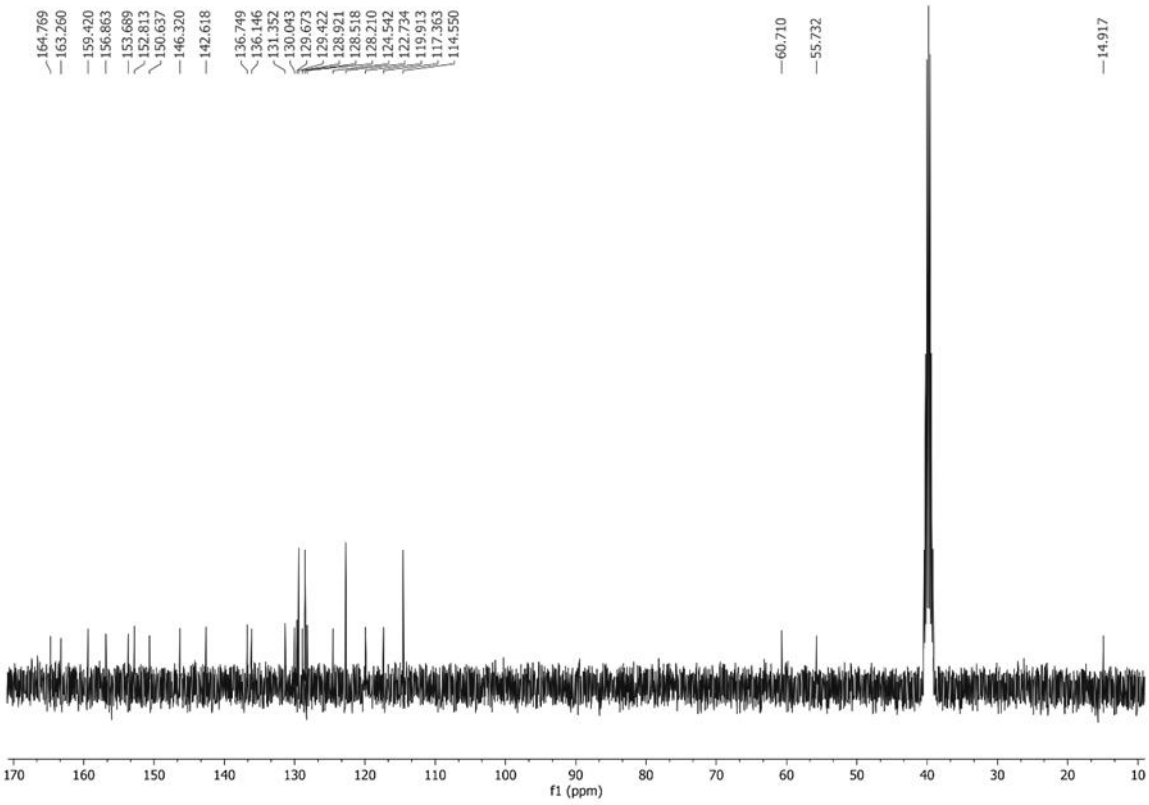

Figure S41. ^{1}H-NMR of compound 7g

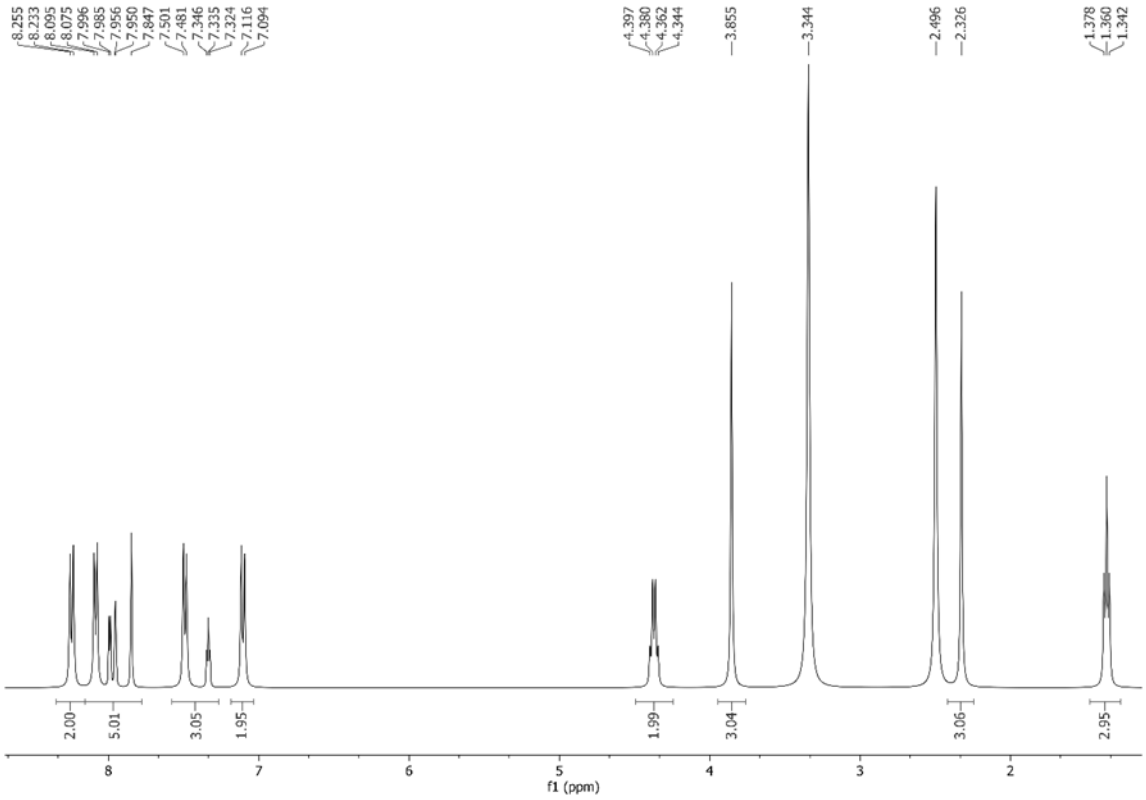

Figure S42. ^{13}C-NMR of compound 7g

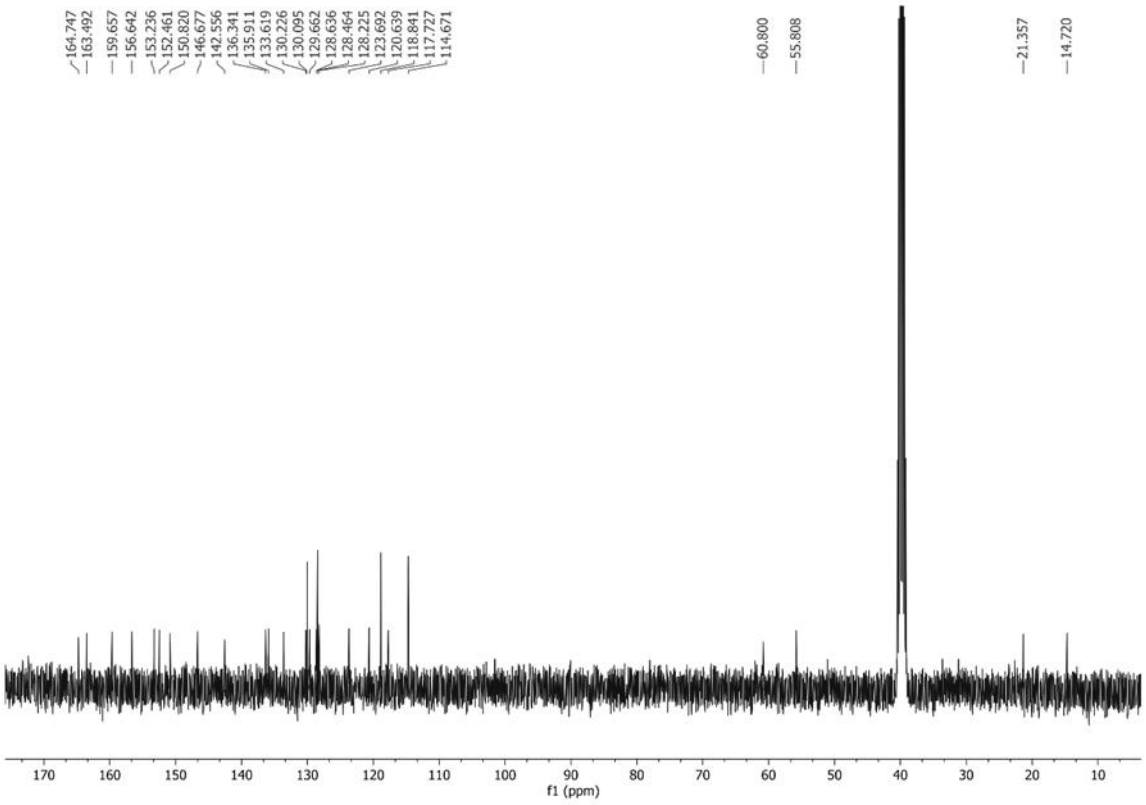

Figure S43. ^{1}H-NMR of compound 7h

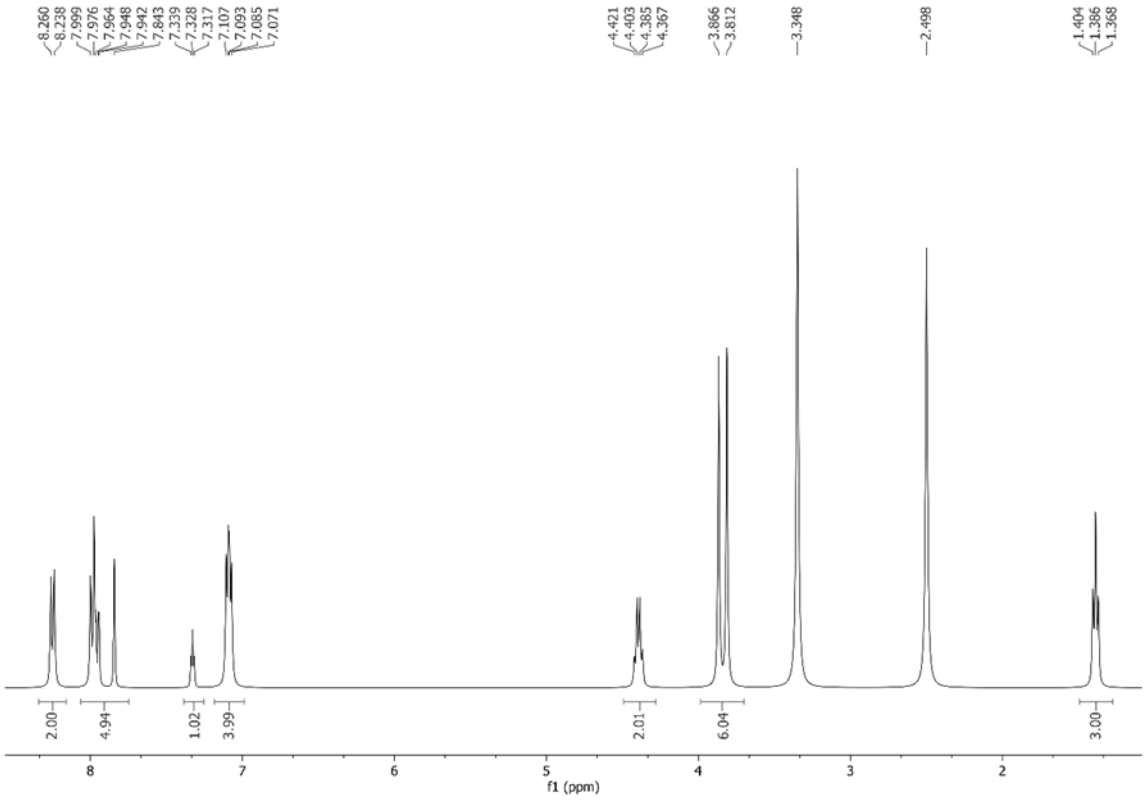

Figure S44. ^{13}C-NMR of compound 7h