

Supplementary Material

Exploring synthetic dihydrobenzofuran and benzofuran neolignans as antiprotozoal agents against *Trypanosoma cruzi*

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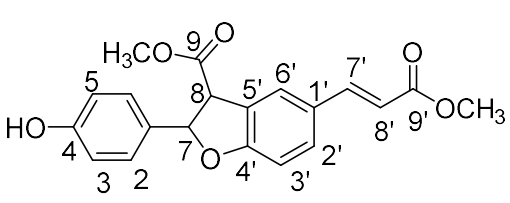
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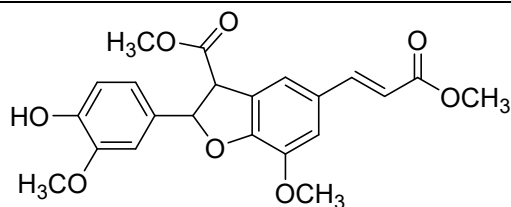
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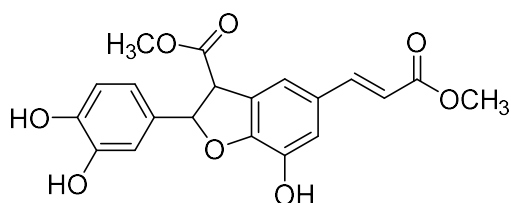
Table S1. ¹H (400 MHz) and ¹³C NMR (100 MHz) data of compounds 1-20.

Compound 1

(±)- <i>trans</i> -dehydrodicoumarate dimethyl ester (1). Yellow powder, m.p. 105-107 °C, 36% yield. NMR ¹ H (400 MHz, <i>Acetone-d</i> ₆ , S1): δ 3.73 (3H, s, H10'), 3.81 (3H, s, H10), 4.40 (1H, d, <i>J</i> _{8,7} = 7.3 Hz, H8), 6.03 (1H, d, <i>J</i> _{7,8} = 7.3 Hz, H7), 6.41 (1H, d, <i>J</i> _{8,7'} = 16.0 Hz, H8'), 6.87 (2H, dd, <i>J</i> _{3,5} = 1.8 Hz, <i>J</i> _{3,2} = 6.8 Hz, H3=H5), 6.91 (1H, d, <i>J</i> _{3',2'} = 8.2 Hz, H3'), 7.28 (2H, dd, <i>J</i> _{2,6} = 1.8 Hz, <i>J</i> _{2',3'} = 6.8 Hz, H2=H6), 7.60 (1H, dd, <i>J</i> _{2',6'} = 1.5 Hz, <i>J</i> _{2',3'} = 8.1 Hz, H2'), 7.65 (1H, d, <i>J</i> _{7',8'} = 16.0 Hz, H7'), 7.72 (1H, bs, H6'). ¹³ C (100 MHz, <i>Acetone-d</i> ₆ , S2): δ 52.0, 53.4, 56.0, 88.2, 111.2, 116.5, 116.9, 126.5, 126.9, 128.9, 128.9, 128.9, 131.3, 132.1, 145.5, 159.1, 162.6, 168.2, 172.0.
Compound 2



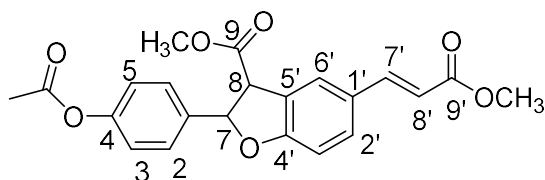
(±)-*trans*-dehydrodiferulate dimethyl ester (2). Yellow oil, 43% yield. NMR ^1H (400 MHz, *Acetone-d*₆, **S3**): δ 3.73 (3H, s, H10) , 3.81 (3H, s, H10') , 3.84 (3H, s, H11) , 3.92 (3H, s, H11') , 4.47 (1H, d, $J_{3,2}$ = 8.1 Hz, H8) , 6.04 (1H, d, $J_{2,3}$ = 8.1 Hz, H7) , 6.44 (1H, d, $J_{9,8}$ = 16.1 Hz, H8') , 6.84 (1H, d, $J_{5',6'}$ =8.1 Hz, H5) , 6.92 (1H, dd, $J_{6',5'}=8.1$ Hz, $J_{6',2'}=1.7$ Hz, H6) , 7.10 (1H, d, $J_{2',6'}=1.7$ Hz, H2) , 7.29 (1H, sl , H7') , 7.33 (1H, sl , H6') , 7.63 (1H, d, $J_{8,9}$ = 16.1 Hz, H7'). ^{13}C (100 MHz, *Acetone-d*₆, **S4**): δ 52.0, 53.5; 56.4, 56.8; 56.9 ; 88.8 ; 111.2, 113.9 , 116.3 , 116.7 , 119.4 , 120.7 , 127.8 , 129.9 , 132.5 , 145.9 , 146.3 , 148.5 , 149.0 , 151.5 , 168.2 , 172.1.

Compound 3



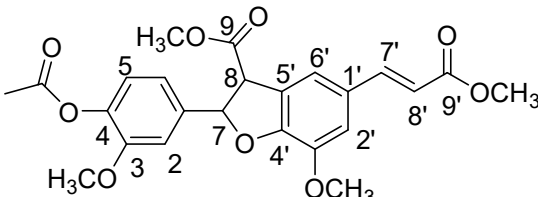
(±)-*trans*-dehydrodicafeoate dimethyl ester (3). Yellow oil, 12% yield. NMR ^1H (400 MHz, *Acetone-d*₆, **S5**): δ 3.73 (3H, s, H10'); 3.81 (3H, s, H10); 4.37 (1H, d, J = 7.3 Hz, H8); 5.98 (1H, d, J = 7.3 Hz, H7); 6.35 (1H, d, J = 16.1 Hz; H8'); 6.80 (1H, dd, J = 1.6 Hz; 8.2 Hz; H6); 6.85 (1H, d, J = 8.2 Hz; H5); 6.90 (1H, d, J = 1.6 Hz; H2); 7.15 (1H, s, H6'); 7.21 (1H, s, H2'); 7.58 (1H, d, J = 16.1 Hz; H7'); 8.04 (3-OH); 8.07 (3'-OH); 8.50 (4-OH). ^{13}C (100 MHz, *Acetone-d*₆, **S6**): δ 51.7; 53.1; 56.5; 88.1; 114.1; 116.2; 116.3; 117.6; 117.9; 118.9; 127.6; 129.6; 132.9; 142.8; 145.6; 146.3; 146.6; 150.3; 167.9; 171.8.

Compound 4



(±)-4-O-acetyl-*trans*-dehydrodicoumarate dimethyl ester (4). Yellow powder, m.p. 103-105 °C, 82% yield. NMR ^1H (400 MHz, *Acetone-d*₆, **S7**): δ 2.26 (3H, s, H12) , 3.73 (3H, s, H10') , 3.83 (3H, s, H10) , 4.44 (1H, d, $J_{8,7}$ = 7.2 Hz, H8) , 6.15 (1H, d, $J_{7,8}$ = 7.2 Hz, H7) , 6.42 (1H, d, $J_{8',7'}$ = 15.9 Hz, H8') , 6.97 (1H, d, $J_{3',2'}$ = 8.4 Hz) , 7.16 (2H, dd, $J_{3,5}$ = 1.9 Hz; $J_{3,2}$ = 6.7 Hz, H3=H5) , 7.49 (2H, dd, $J_{2,6}$ = 1.7 Hz; $J_{2,3}$ = 6.7 Hz, H2=H6) , 7.63 (1H, dd, $J_{2',6'}$ = 1.7 Hz; $J_{2',3'}$ = 8.3 Hz, H2') , 7.65 (1H,

Compound 5



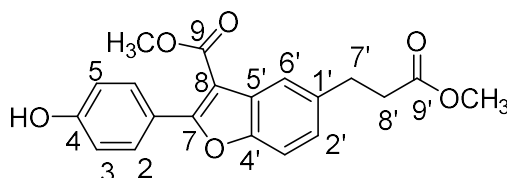
(±)-4-O-acetyl-trans-dehydrodiferulate dimethyl ester (5). Brown oil, 96% yield. NMR ^1H (400 MHz, *Acetone-d*₆, **S9**): δ 2.24 (3H, s, H12) , 3.73 (3H, s, H10') , 3.82 (3H, s, H10) , 3.83 (3H, s, H12) , 3.94 (3H, s, H11') , 4.50 (1H, d, $J_{8,7} = 7.5$ Hz, H8) , 6.14 (1H, d, $J_{7,8} = 7.5$ Hz, H7) , 6.45 (1H, d, $J_{8',7'} = 16.0$ Hz, H8') , 7.03 (1H, d, $J_{5,6} = 8.2$, H5) , 7.09 (1H, dd, $J_{6,5} = 8.2$ Hz; $J_{6,2} = 1.7$, H6) , 7.25 (1H, d, $J_{2,6} = 1.7$ Hz, H2) , 7.31 (1H, sl, H6') , 7.35 (1H, sl, H2') , 7.63 (1H, d, $J_{7',8'} = 16.0$ Hz, H7').

^{13}C (100 MHz, *Acetone-d*₆, **S10**): δ 21.0 , 52.1 , 53.7 , 56.7 , 56.9 , 57.2 , 88.2 , 111.9 , 114.3 , 117.1 , 119.6 , 124.5 , 127.7 , 130.3 , 140.3 , 141.7 , 145.9 , 146.5 , 151.5 , 153.2 , 168.3 , 169.5 , 172.1.

(±)-7,8-dehydro-*trans*-dehydrodicoumarate dimethyl ester (7). Orange powder, m. p. 204–206 °C, 74% yield. NMR ¹H (400 MHz, *Acetone-d*₆, **S13**): δ 3.77 (3H, s, H10'), 3.96 (3H, s, H10),

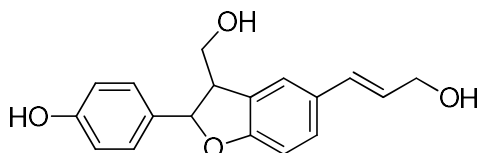
6.57 (1H, d, $J = 15.9$ Hz, H8'), 7.00 (2H, d, $J = 8.8$ Hz, H2=H6), 7.62 (1H, d, $J_{3',2'} = 8.6$ Hz), 7.74 (1H, dd, $J_{2',3'} = 8.6$ Hz, $J_{2',6'} = 1.6$) Hz, 7.82 (1H, d, $J = 15.9$ Hz, H7'), 8.03 (2H, d, $J = 8.8$ Hz, H3=H5), 8.29 (1H, d, $J = 1.6$ Hz, H6'), 9.14 (1H, s, OH). ^{13}C (100 MHz, *Acetone-d*₆, **S14**): δ 51.8 , 52.0 , 112.5 , 116.0 , 118.1 , 121.3 , 123.8 , 125.9 , 129.0 , 131.0 , 131.7 , 132.3 , 133.4 , 145.6 , 155.3 , 160.8 , 166.6 , 167.6.

Compound 8



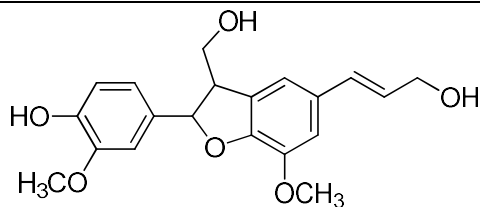
(±)-7,8-dehydro-7',8'-dihydro-trans-dehydrodicoumarate dimethyl ester (8). Yellow oil, 94% yield. NMR ^1H (400 MHz, *Acetone-d*₆, **S15**): δ 2.69 (2H, t, $J = 7.7$ Hz, H8'), 3.05 (2H, t, $J = 7.7$ Hz, H7'), 3.63 (3H, s, H10'), 3.91 (3H, s, H10), 6.99 (2H, d, $J = 8.8$ Hz, H2 = H6), 7.27 (1H, dd, $J = 1.6$ and 8.3 Hz, H2'), 7.49 (1H, d, $J = 8.3$ Hz, H3'), 7.90 (1H, d, $J = 1.6$ Hz, H6'), 7.98 (2H, d, $J = 8.8$ Hz, H2 = H6). ^{13}C (100 MHz, *Acetone-d*₆, **S16**): δ 31.7 , 36.8 , 51.7 , 51.8 , 107.9 , 111.6 , 115.9 , 121.8 , 122.7 , 126.5 , 128.4 , 132.1 , 137.7 , 153.1 , 160.5 , 162.2 , 165.0 , 173.5.

Compound 9



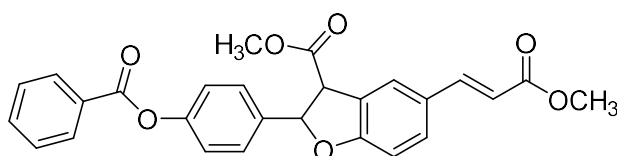
(±)-trans-dehydrodicoumarate-diol (9). White powder, m.p. 139-140°C, 62% yield. NMR ^1H (400 MHz, *Acetone-d*₆, **S17**): δ 3.49 (1H, q, $J=6.0$, H8); 3.85 (2H, m, H9); 3.85 (OH, m, H9); 4.20 (2H, m, H9'); 4.20 (OH, M, H9'); 5.55 (1H, d, $J=6.0$ Hz, H7); 6.22 (1H, dt, $J=15.8$ and 5.6 Hz, H7'); 6.55 (1H, d, $J= 15.8$ Hz, H7'); 6.74 (1H, d, $J=8.3$ Hz, H3'); 6.82 (2H, d, $J=8.5$ Hz, H2=H6); 7.22 (1H, d, $J=8.3$ Hz, H2'); 7.24 (2H, d, $J=8.5$ Hz, H2=H6); 7.39 (1H, s, H6'); 8.40 (1H, s, OH). ^{13}C (100 MHz, *Acetone-d*₆, **S18**): δ 54.5; 63.5; 64.9; 88.1; 109.7; 116.0; 116.1; 123.5; 128.1; 128.1; 128.1; 128.2; 129.6; 130.4; 131.1; 134.1; 158.1; 160.6.

Compound 10



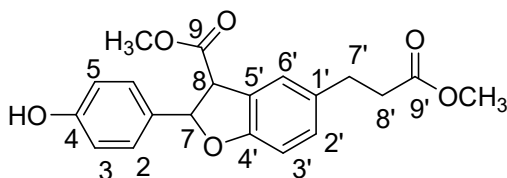
(±)-*trans*-dehydrodiferuloate-diol (10). Brown oil, 60% yield. NMR ^1H (400 MHz, *Acetone-d*₆, **S19**): δ 3.54 (1H, ddd, J =6.8, 5.5, and 3.9 Hz, H8); 3.82 (3H, s, H10); 3.84 (1H, t, J =5.5 Hz, H9b); 3.86 (3H, s, H10'); 3.88 (1H, t, J =5.5 Hz, H9a); 4.20 (2H, d, J =5.5 Hz, H9'); 5.57 (1H, d, J =6.8 Hz, H7); 6.24 (1H, dt, J =15.8 and 5.5; H8'); 6.53 (1H, d, J =15.8 Hz, H7'); 6.81 (1H, d, J =8.1 Hz, H5); 6.89 (1H, dd, J =2.1 and 8.1 Hz, H5); 6.95 (1H, s, H2'); 6.98 (1H, s, H6'); 7.04 (1H, d, J =2.1 Hz, H2). ^{13}C (100 MHz, *Acetone-d*₆, **S20**): δ 54.9; 56.5; 56.6; 63.5; 64.7; 88.7; 110.8; 112.1; 115.9; 116.3; 119.7; 128.6; 130.6; 130.7; 132.1; 134.6; 145.3; 147.5; 148.6; 149.2.

Compound 11



(±)-4-O-benzoyl-*trans*-dehydrodicoumarate dimethyl ester (11) White powder, m.p. 109–111 °C, 95% yield. NMR ^1H (400 MHz, CDCl_3 , **S21**): δ 3.82 (3H, s, H10'), 3.82 (3H, s, H10), 3.87 (3H, s, H11), 3.95 (3H, s, H11'), 4.38 (1H, d, $J_{8,7} = 8.0$ Hz, H8), 6.23 (1H, d, $J_{7,8} = 8.0$ Hz, H7), 6.34 (1H, d, $J_{8,7'} = 15.9$ Hz, H8'), 7.05 (1H, d, $J_{5,6} = 8.1$ Hz, H5), 7.07 (2H, m, H2=H2'), 7.16 (1H, d, $J_{6,5} = 8.1$ Hz, H6), 7.22 (1H, sl, H6'), 7.51 (3H, m, H15, H16, H17), 7.62 (2H, m, H14, H18), 7.67 (1H, d, $J_{7,8'} = 15.9$ Hz, H7'). ^{13}C (100 MHz, CDCl_3 , **S22**): 51.5, 52.7, 54.8, 54.9, 86.6, 110.1, 115.2, 115.7, 115.9, 116.1, 124.9, 125.2, 127.1, 127.3, 127.7, 128.3, 129.9, 130.0, 130.6, 130.8, 133.1, 141.5, 144.5, 145.5, 157.2, 161.1, 167.7, 169.5, 170.8.

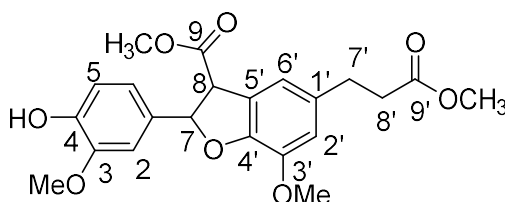
Compound 12



(±)-7',8'-dihydro-*trans*-dehydrodicoumarate dimethyl ester (12). White powder, m. p. 108–110 °C, 95% yield. NMR ^1H (400 MHz, *Acetone-d*₆, **S23**): δ 2.59 (2H, dt, $J = 7.8$ and 2.9 Hz, H7'), 2.86 (2H, d, $J = 7.8$ Hz, H8'), 3.61 (3H, s, H10'), 3.79 (3H, s, H10), 4.29 (1H, d, $J = 7.8$ Hz, H8), 5.95 (1H, d, $J = 7.8$ Hz, H7), 6.75 (1H, d, $J = 8.0$ Hz, H3'), 6.85 (2H, d, $J = 8.6$, H2 = H6), 7.12 (1H, dd, J

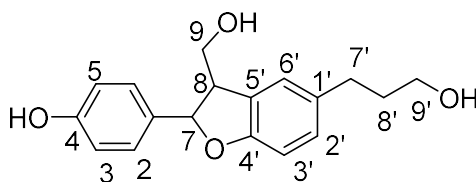
= 8.0 and 2.9 Hz, H2'), 7.23 (1H, s, H6'), 7.27 (2H, d, J = 8.6 Hz, H3 = H5), 8.52 (1H, s, OH). ^{13}C (100 MHz, *Acetone-d*₆, **S24**): δ 31.4, 36.7, 51.7, 52.9, 56.4, 87.0, 110.2, 116.4, 125.7, 126.0, 128.4, 130.4, 132.6, 134.4, 158.6, 158.9, 172.1, 173.5

Compound 13



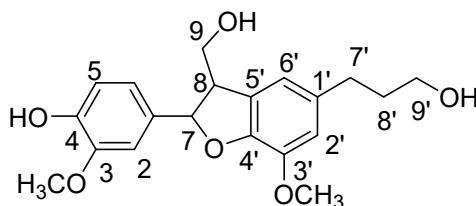
(±)-7',8'-dihydro-*trans*-dehydrodiferulate dimethyl ester (13). m.p. 118-120 °C, white powder, 88% yield. NMR ^1H (400 MHz, *Acetone-d*₆, **S25**): δ 2.59 (2H, dt, J = 7.8 and 2.6 Hz, H7'), 2.85 (2H, d, J = 7.8 Hz, H8'), 3.62 (3H, s, H10'), 3.78 (3H, s, H10), 3.83 (6H, s, H11 = H11'), 4.35 (1H, d, J = 8.3 Hz, H8), 5.94 (1H, d, J = 8.3 Hz), 6.83 (1H, d, J = 8.3 Hz, H5), 6.84 (2H, m, H2' = H6'), 6.89 (1H, dd, J = 8.3 and 1.8 Hz, H6), 7.07 (1H, d, $J_{2,6}$ = 1.8 Hz, H2). ^{13}C (100 MHz, *Acetone-d*₆, **S26**): δ 31.5, 36.7, 51.7, 52.9, 56.5, 56.6, 56.7, 87.6, 110.8, 114.8, 115.9, 117.5, 120.1, 126.8, 132.7, 134.0, 135.4, 145.4, 147.5, 147.9, 148.7, 172.1, 173.6.

Compound 14



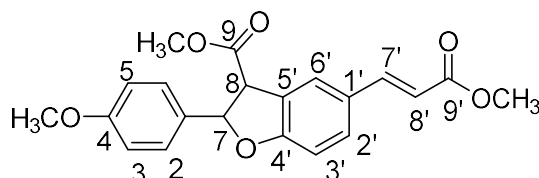
(±)-7',8'-dihydro-*trans*-dehydrocoumarate-9,9'-diol (14). White powder, m.p. 120-121°C, 59% yield. IR NMR ^1H (400 MHz, *Acetone-d*₆, **S51**): δ 1.78 (2H, dddd, J = 5.5, 6.6, 7.3, and 9.3 Hz, H8'); 2.62 (2H, dd, J = 6.6 and 9.3 Hz, H7'); 3.46 (1H, dt, J = 6.0 and 6.5 Hz, H8); 3.57 (2H, t, J = 6.5 Hz, H9); 3.79 (1H, dd, J = 10.7 and 7.3 Hz, H9a'); 3.86 (1H, dd, J = 10.7 and 7.3 Hz, H9b'); 5.51 (1H, d, J = 6.0 Hz, H7); 6.70 (1H, d, J = 8.1 Hz, H3'); 6.82 (2H, d, J = 8.6 Hz, H2=H6); 7.00 (1H, dd, J = 1.1 Hz; 8.1, H2'); 7.13 (1H, d, J = 1.1 Hz, H6'); 7.23 (2H, d, J = 8.6 Hz, H3=H5). ^{13}C (100 MHz, *Acetone-d*₆, **S52**): δ 32.7; 36.3; 55.1; 62.2; 65.3, 88.0, 109.7, 116.4, 116.4, 126.0, 128.3, 128.3, 129.2, 129.5, 134.7, 135.5, 158.3, 159.4.

Compound 15



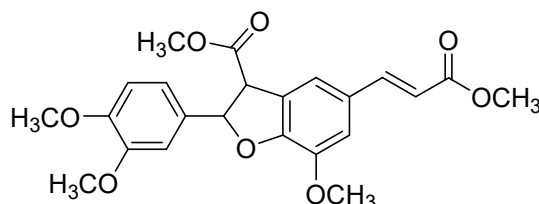
(±)-7',8'-dihydro-*trans*-dehydrodiferulate-9,9'-diol (15). Colorless oil, 52% yield. NMR ^1H (400 MHz, *Acetone-d*₆, **S29**): δ 1.79 (2H, dt, J = 6.5 and 6.0 Hz, H8'); 2.62 (2H, t, J =6.5 Hz, H7'); 3.51 (1H, t, J = 6.5 Hz, H8); 3.65 (2H; t, J =6.5 Hz, H9'); 3.80 (2H, dd, J = 10.8 and 6.0 Hz; H9b); 3.82 (3H, s, H10'); 3.84 (3H, s, H10); 3.87 (2H, dd, J =10.8 and 6.0 Hz; H9a); 5.53 (7H, d, J =6.7 Hz, H7); 6.72 (1H, bs, H2'); 6.75 (1H; bs, H6'); 6.81 (1H, d, J =8.0 Hz, H5); 6.89 (1H, dd, J =8.0 and 1.8 Hz, H6); 7.04 (1H, d, J =1.8 Hz, H2). ^{13}C (100 MHz, *Acetone-d*₆, **S30**): δ 33.3; 36.5; 54.2; 56.9; 57.1; 62.4; 65.3; 88.8; 111.1; 114.64; 116.2; 118.2; 120.1; 130.6; 136.9; 145.5; 147.6; 148.9.

Compound 16



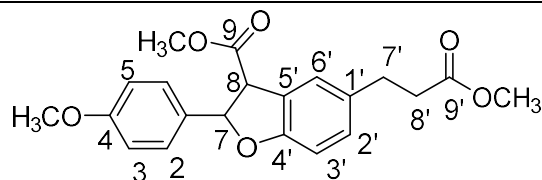
(±)-4-O-methyl-*trans*-dehydrodicoumarate dimethyl ester (16). Yellow oil, 22% yield. NMR ^1H (400 MHz, *Acetone-d*₆, **S31**): δ 3.73 (3H, s, H10'), 3.80 (3H, s, H10), 3.83 (3H, s, H11), 4.40 (1H, d, $J_{8,7}$ = 7.8 Hz, H8), 6.07 (1H, d, $J_{7,8}$ = 7.2 Hz, H7), 6.42 (1H, d, $J_{8',7'}$ = 16.0 Hz, H8'), 6.92 (1H, d, $J_{3',2'}$ = 8.3 Hz, H3'), 6.96 (2H, dd, $J_{3,5}$ = 2.0 Hz, $J_{3,2}$ = 6.7 Hz, H3=H5), 7.38 (2H, dd, $J_{2,6}$ = 2.0 Hz, $J_{2',3'}$ = 6.7 Hz, H2=H6), 7.61 (1H, dd, $J_{2',6'}$ = 1.8 Hz, $J_{2',3'}$ = 8.3 Hz, H2'), 7.66 (1H, d, $J_{7',8'}$ = 16.0 Hz, H7'), 7.72 (1H, d, $J_{6',2'}$ = 1.8 Hz, H6'). ^{13}C (100 MHz, *Acetone-d*₆, **S32**): δ 51.7 , 53.1 , 57.7 , 60.6 , 87.6 , 110.9 , 115.0 , 115.0 , 116.2 , 126.2 , 126.8 , 128.5, 128.5 , 128.9 , 131.8 , 133.1 , 145.2 , 161.1 , 162.2 , 167.8 , 171.7.

Compound 17



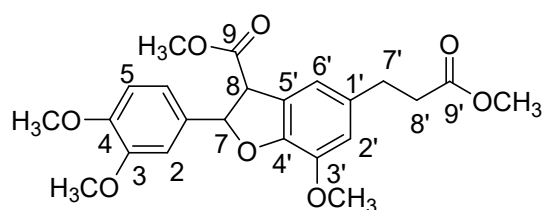
(±)-4-O-methyl-*trans*-dehydrodiferulate dimethyl ester (17). White powder, m.p. 96-98 °C, 18% yield. NMR ^1H (400 MHz, *Acetone-d*₆, **S33**): δ 3.73 (3H, s, H10') , 3.80, (3H, s, H10) , 3.81 (3H, s, H11), 3.81 (3H, s, H12), 3.93 (3H, s, H11'), 4.47 (1H, d, $J_{8,7}$ = 7.8 Hz, H8) , 6.06 (1H, d, $J_{7,8}$ = 7.8 Hz, H7) , 6.44 (1H, d, $J_{8',7'}$ = 15.9 Hz, H8'), 6.95 (1H, d, $J_{5,6}$ = 8.3 Hz, H5) , 6.99 (1H, dd, $J_{6,5}$ = 8.3 Hz, $J_{6,2}$ = 1.8 Hz, H6), 7.09 (1H, d, $J_{2,6}$ = 1.8 Hz, H2), 7.29 (1H, sl, H6'), 7.34 (1H, sl, H2') , 7.63 (1H, d, $J_{7',8'}$ = 15.9 Hz, H7'). ^{13}C (100 MHz, *Acetone-d*₆, **S34**): 51.6, 53.0, 56.0, 56.1, 56.2, 56.5, 88.2, 110.9, 112.6, 113.5, 116.3, 119.0, 119.7, 127.3, 129.5, 133.1, 145.4, 145.9, 150.6, 150.8, 151.0, 167.8, 171.6.

Compound 18



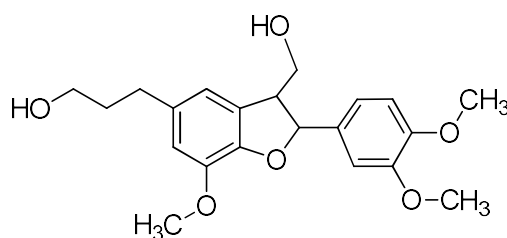
(±)-4-O-methyl-*trans*-dihydrodicoumarate dimethyl ester (18). Yellow oil, 90% yield. NMR ^1H (400 MHz, CDCl_3 , **S35**): δ 2.61 (2H, t, $J_{7,8'} = 7.6$ Hz, H7') , 2.92 (2H, t, $J_{8',7'} = 7.6$ Hz, H8') , 3.69 (3H, s, H10') , 3.81 (3H, s, H10) , 3.83 (3H, s, H11) , 4.26 (1H, d, $J_{8,7} = 7.8$ Hz, H7) , 6.03 (1H, d, $J_{8,7} = 7.8$ Hz, H8) , 6.82 (1H, d, $J_{3',2'} = 8.3$ Hz, H3') , 6.90 (2H, d, $J_{3=5, 2=6} = 8.6$ Hz, H2=H6) , 7.07 (1H, dd, $J_{2',3'} = 8.1$ Hz, $J_{6',2'} = 1.6$, H2') , 7.18 (1H, d, $J_{6',2'} = 1.6$ Hz, H6') , 7.33 (2H, d, $J_{2=6, 3=5} = 8.6$ Hz, H3=H5). ^{13}C (100 MHz, CDCl_3 , **S36**): δ 30.8, 36.5, 51.9, 55.6, 56.0, 86.1, 110.0, 114.5, 124.5, 125.2, 127.6, 129.8, 132.9, 133.5, 158.2, 160.1, 171.7, 173.7.

Compound 19



(±)-7',8'-dihydro-4-O-methyl-*trans*-dehydrodiferulate dimethyl ester (19). White powder, m.p. 108-110 °C, 91% yield. NMR ^1H (400 MHz, *Acetone- d_6* , **S37**): δ 2.59 (2H, t, $J_{7',8'} = 7.8$ Hz, H7') , 2.85 (2H, d, $J_{8',7'} = 7.8$ Hz, H8') , 3.62 (3H, s, H10') , 3.78 (3H, s, H10), 3.80 (3H, s, H11'), 3.80 (3H, s, H11), 3.84 (1H, s, H8), 4.35 (1H, d, $J_{7,8} = 8.3$ Hz), 5.94 (1H, d, $J_{8,7} = 8.3$ Hz), 6.84 (1H, s, H6'), 6.84, (1H, s, H2'), 6.93 (1H, dd, $J_{5,6} = 8.3$ Hz, $J_{5,2} = 1.8$ Hz), 6.99 (1H, d, $J_{8,7} = 1.8$ Hz). ^{13}C (100 MHz, *Acetone- d_6* , **S38**): δ 31.4 , 36.6 , 52.8 , 56.1 , 56.4 , 56.6 , 87.3 , 110.8 , 112.6 , 114.4 , 117.4 , 119.5 , 126.6 , 133.7 , 135.4 , 145.3 , 147.3 , 150.6 , 150.6 , 172.0 , 173.5.

Compound 20



3-[2-(3,4-Dimethoxyphenyl)-3-hydroxymethyl-7-methoxy-2,3-dihydro-1-benzofuran-5-yl]propan-1-ol (18). Colorless oil, 49% yield. NMR ^1H (500 MHz, CDCl_3 , **S39**): δ 1.89 (2H, dt, $J_{8',7'}=6.5$ Hz, $J_{8',9'}=6.4$ Hz, H8'), 2.68 (2H, t, $J_{7',8'}=6.5$ Hz, H7'), 3.62, (1H, m, H8), 3.70 (2H, t, $J_{9',8'}=6.4$ Hz, H9'), 3.86 (3H, s, H10), 3.87 (3H, s, H11), 3.89 (3H, s, H10'), 3.95 (2H, m, H9), 5.57 (1H, d, $J_{7,8} = 7.4$ Hz, H7), 6.69 (2H, bs, H2'=H6'), 6.85 (1H, d, $J_{6,5} = 8.8$ Hz, H6), 6.96 (1H, bs, H2), 6.97 (1H,

d, $J_{5,6} = 8.8$ Hz, H5). ^{13}C (100 MHz, CDCl_3 , **S40**): δ 32.0, 34.6, 53.8, 56.0, 56.0, 56.1, 62.3, 64.1, 87.8, 109.6, 111.3, 112.8, 116.1, 118.7, 127.8, 133.9, 144.3, 146.7, 149.3, 194.1.

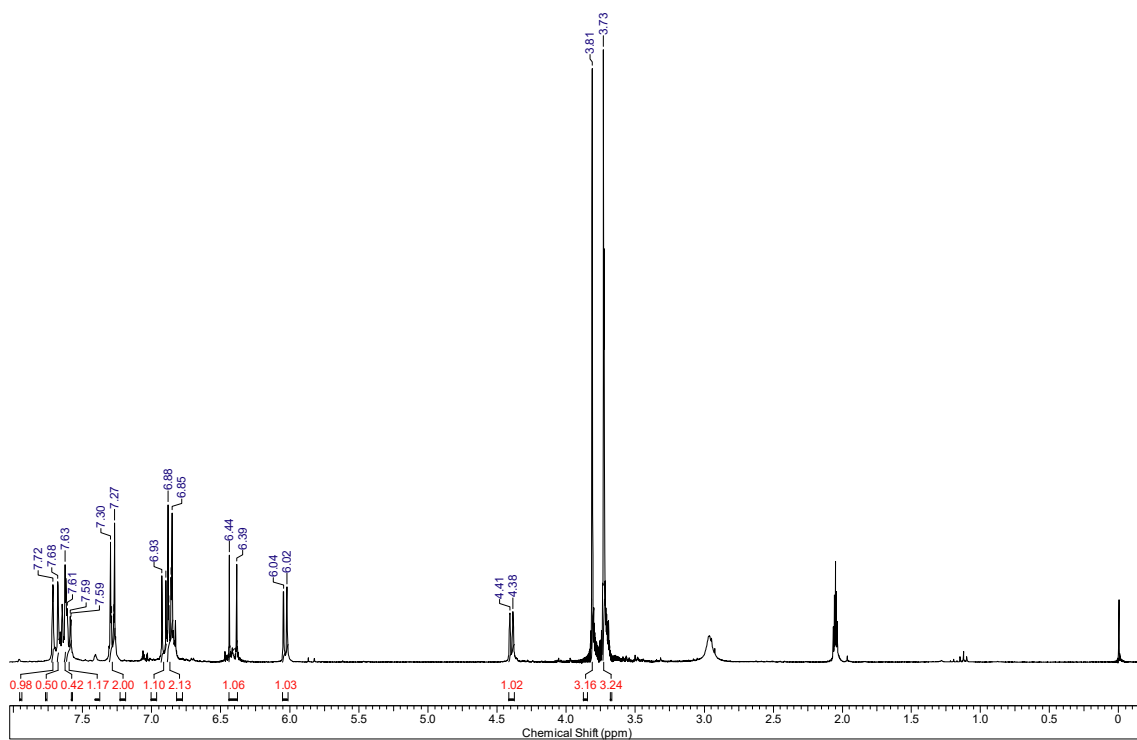


Figure S1. ¹H NMR spectra of compound **1** (Acetone-*d*₆, 400 MHz, TMS).

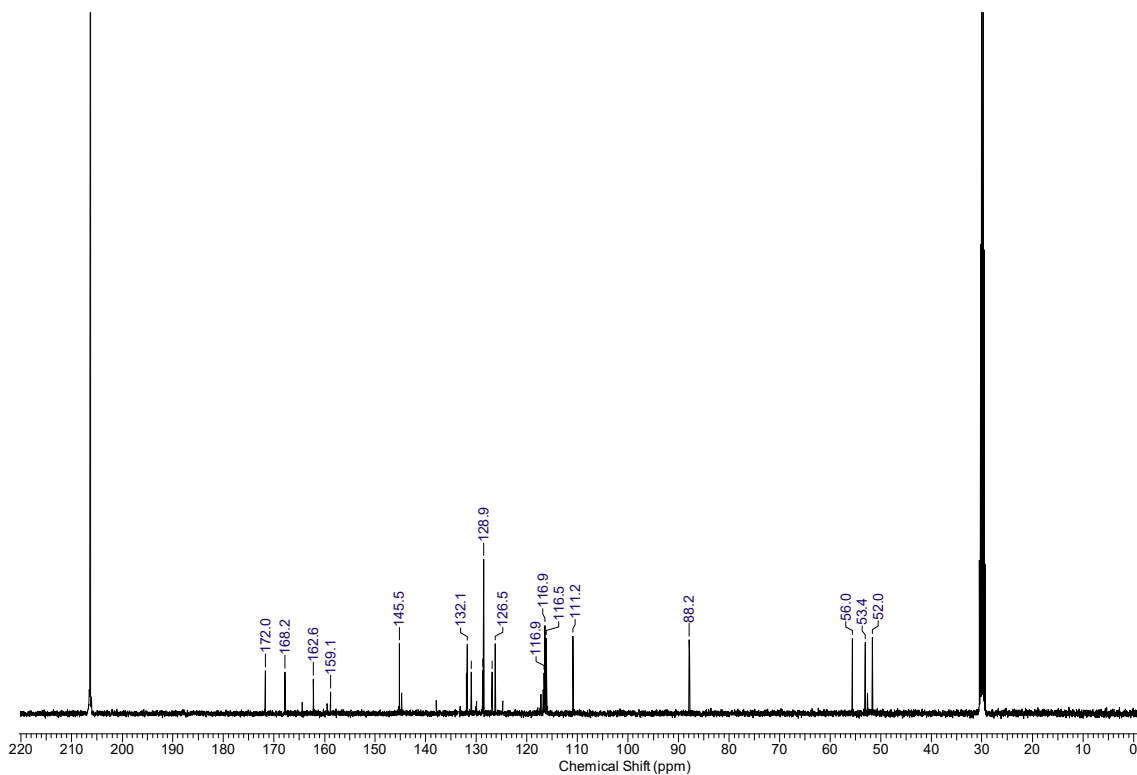


Figure S2. ¹³C NMR spectra of compound **1** (Acetone-*d*₆, 400 MHz, TMS).

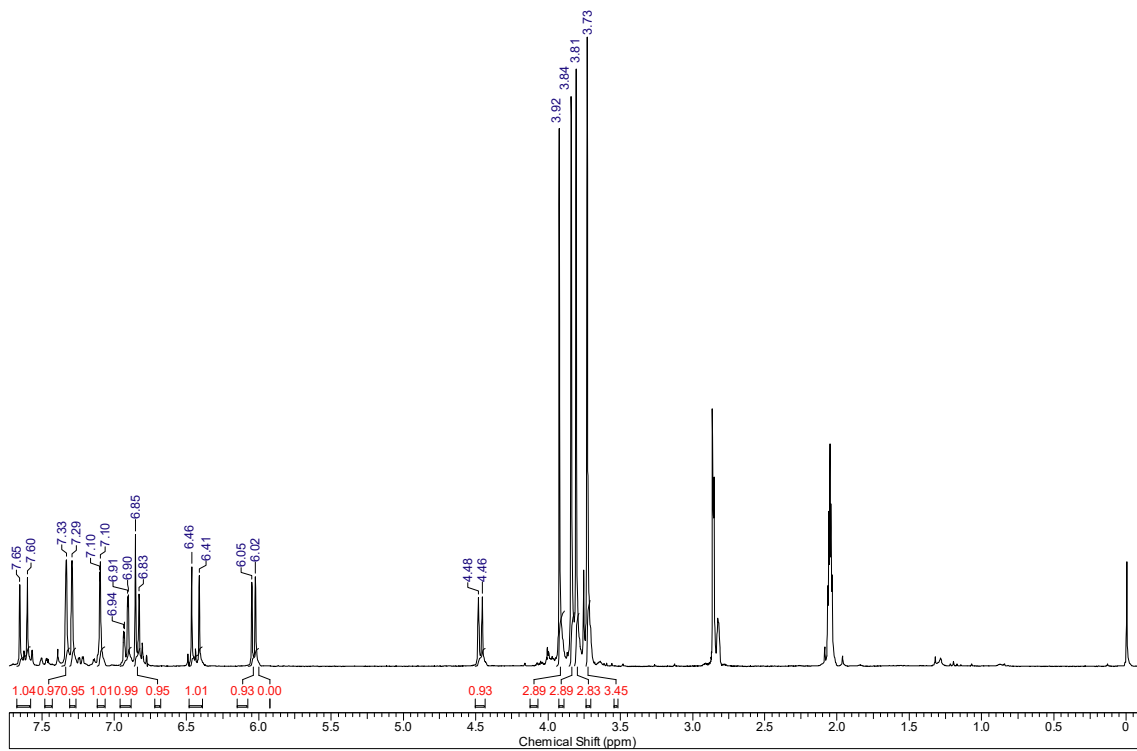


Figure S3. ¹H NMR spectra of compound **2** (Acetone-*d*₆, 400 MHz, TMS).

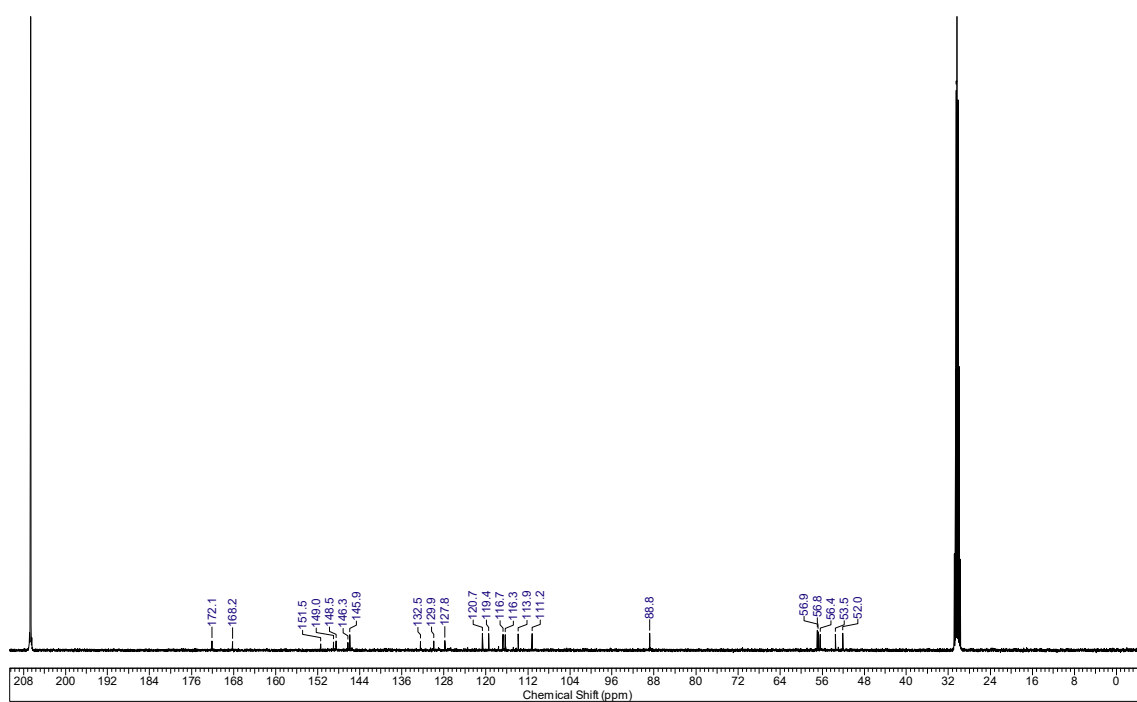


Figure S4. ¹³C NMR spectra of compound **2** (Acetone-*d*₆, 400 MHz, TMS).

hd_n13_168.001.001.1r.esp

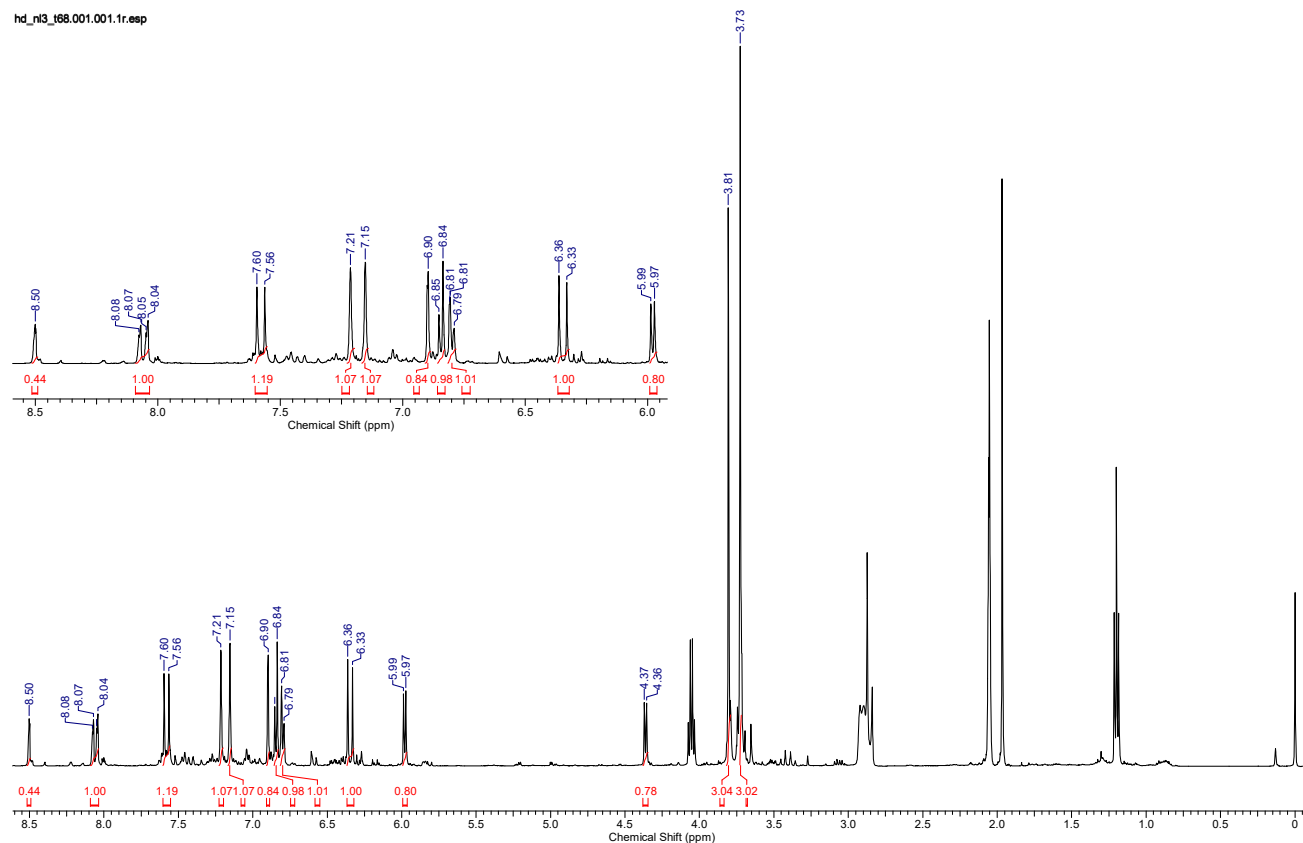


Figure S5. ^1H NMR spectra of compound **3** ($\text{Acetone-}d_6$, 400 MHz, TMS).

hd_n13_168.015.001.1r.esp

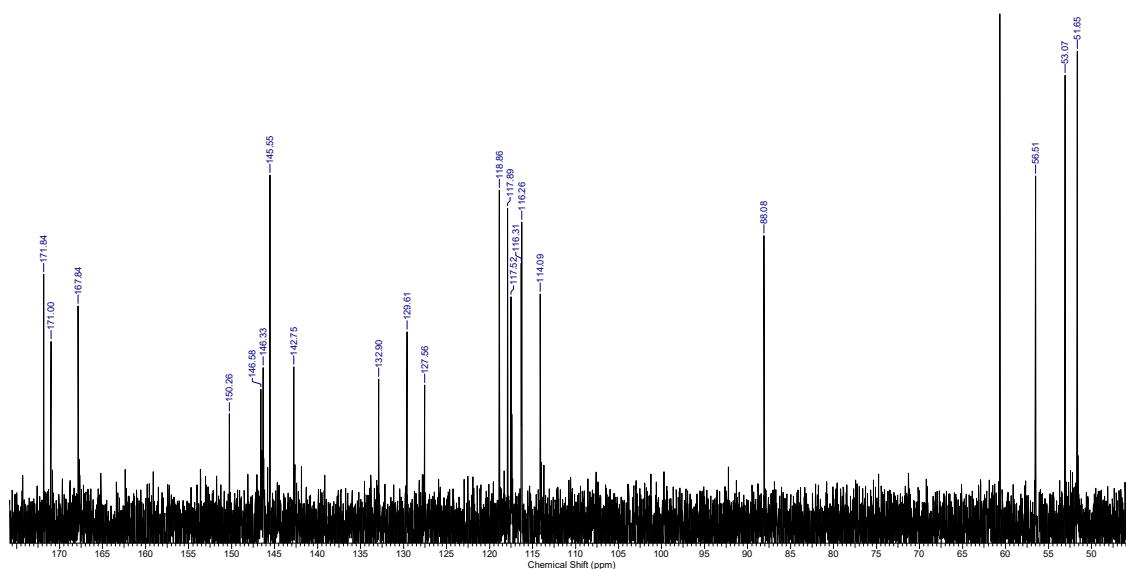


Figure S6. ^{13}C NMR spectra of compound **3** ($\text{Acetone-}d_6$, 400 MHz, TMS).

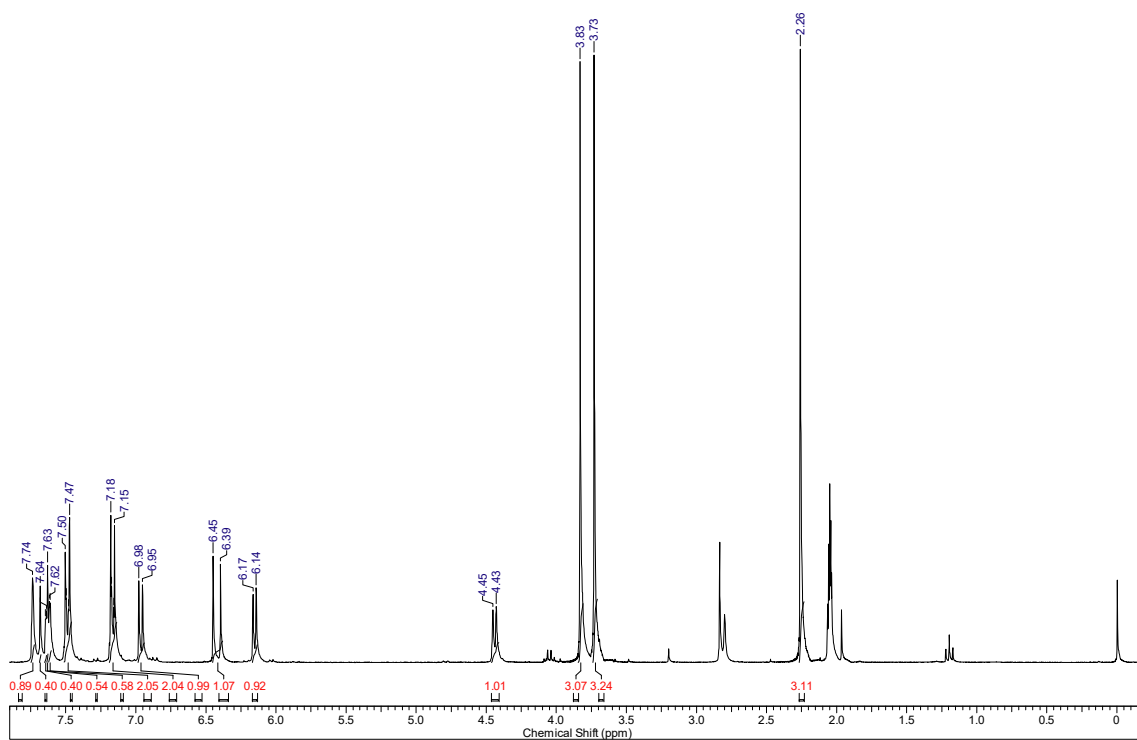


Figure S7. ¹H NMR spectra of compound **4** (Acetone-*d*₆, 400 MHz, TMS).

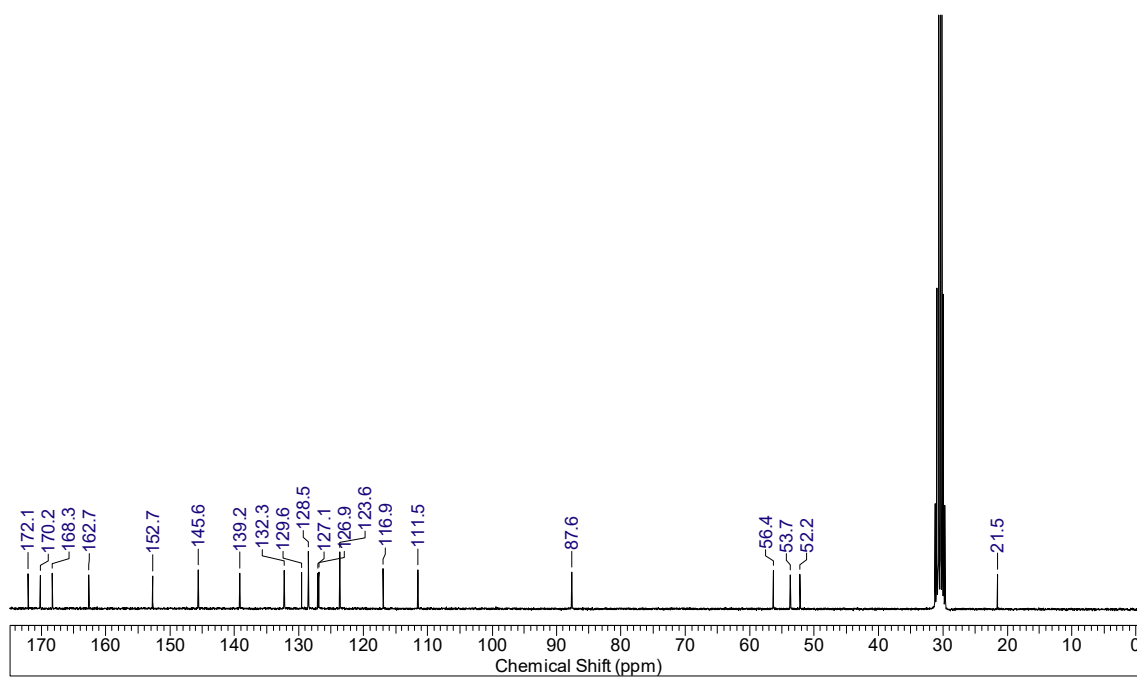
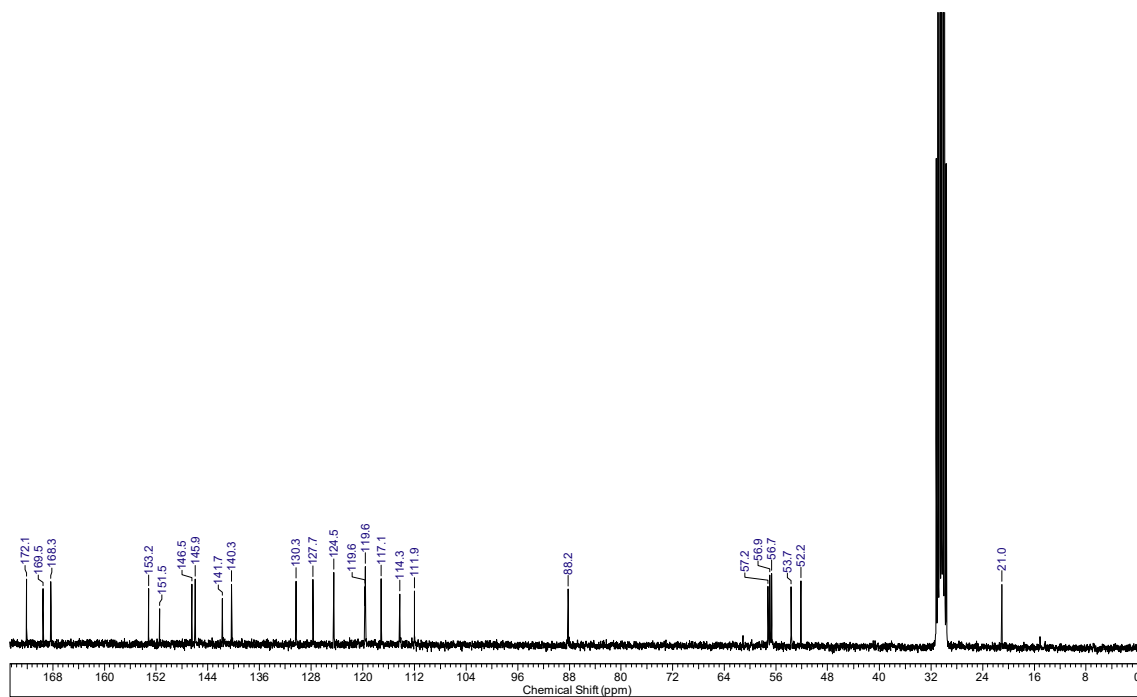
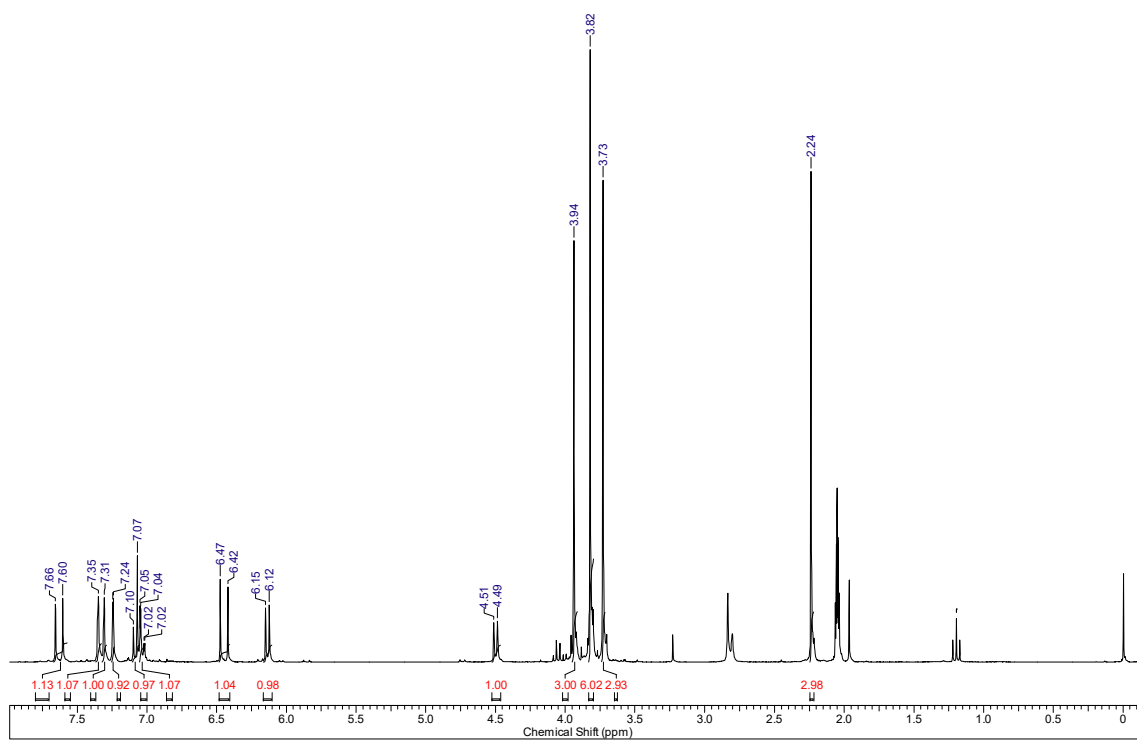


Figure S8. ¹³C NMR spectra of compound **4** (Acetone-*d*₆, 400 MHz, TMS).



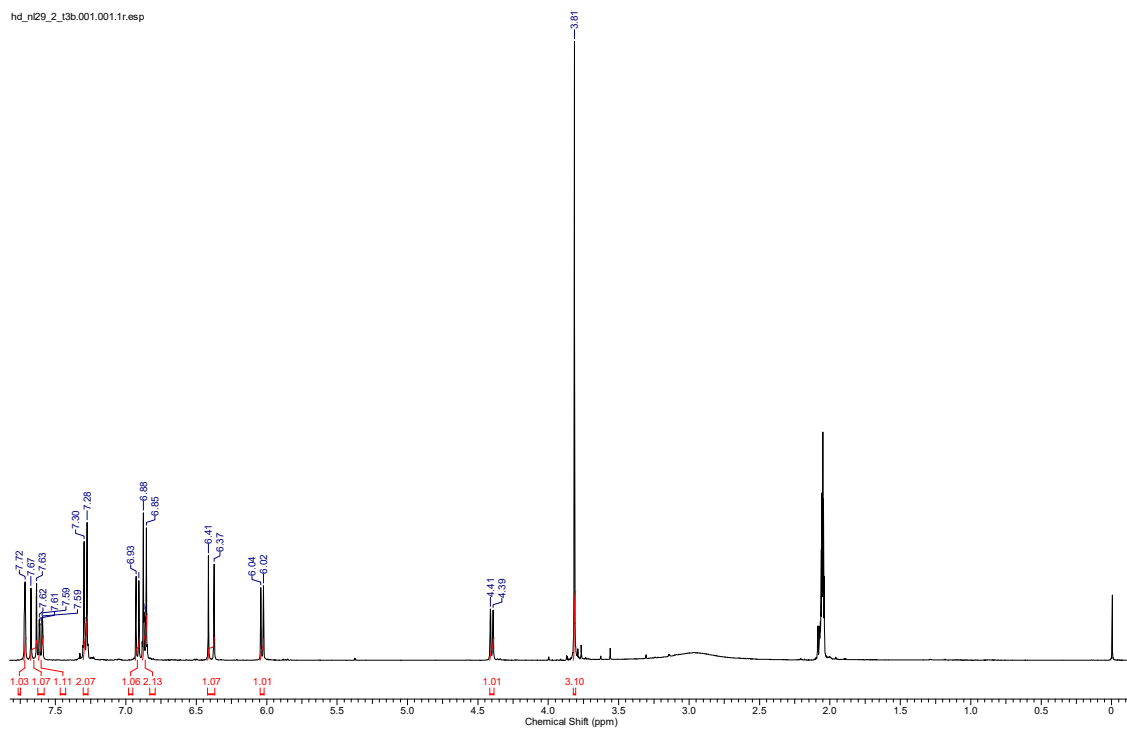
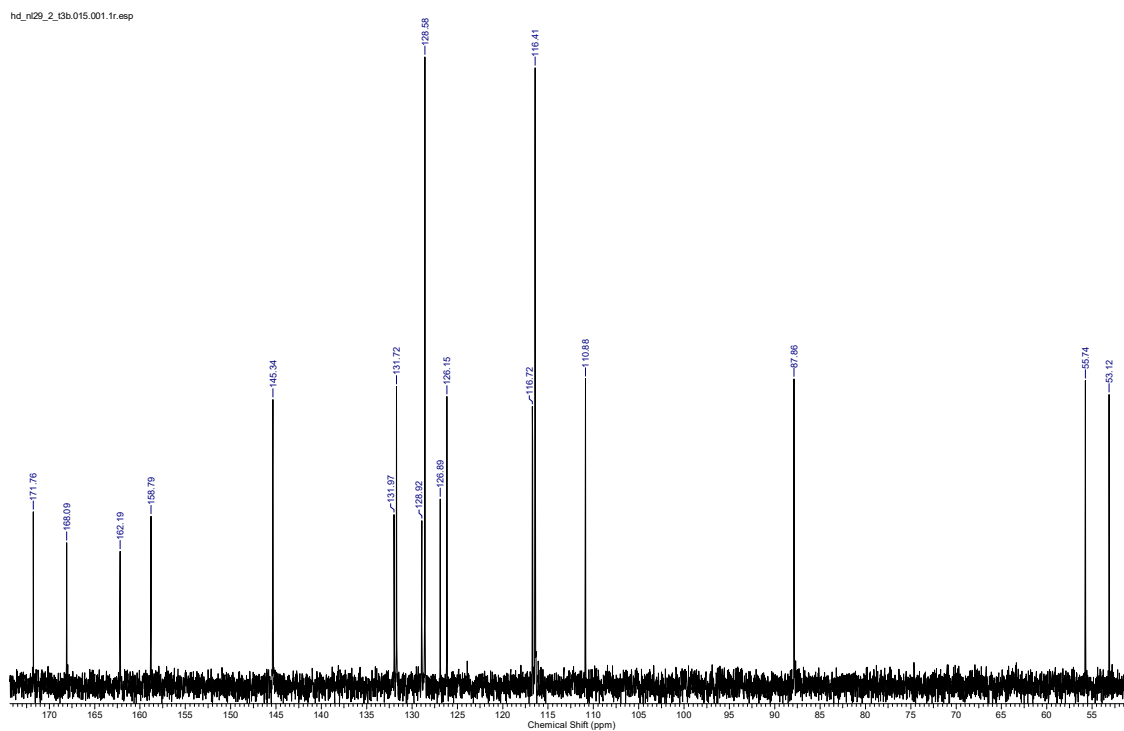
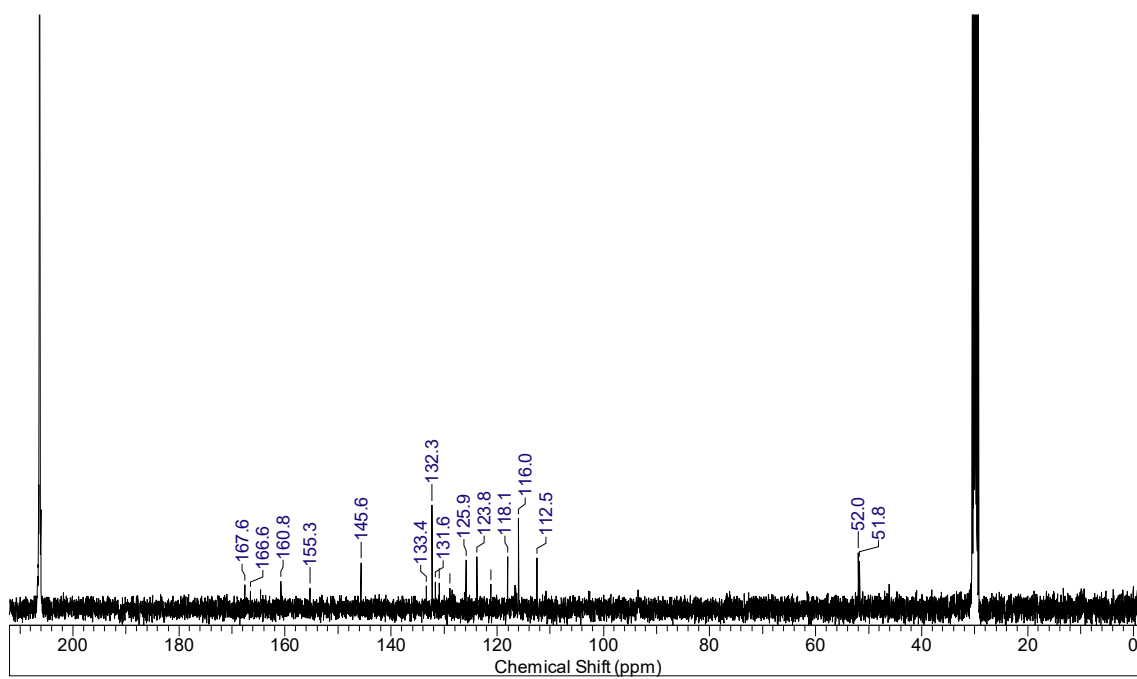
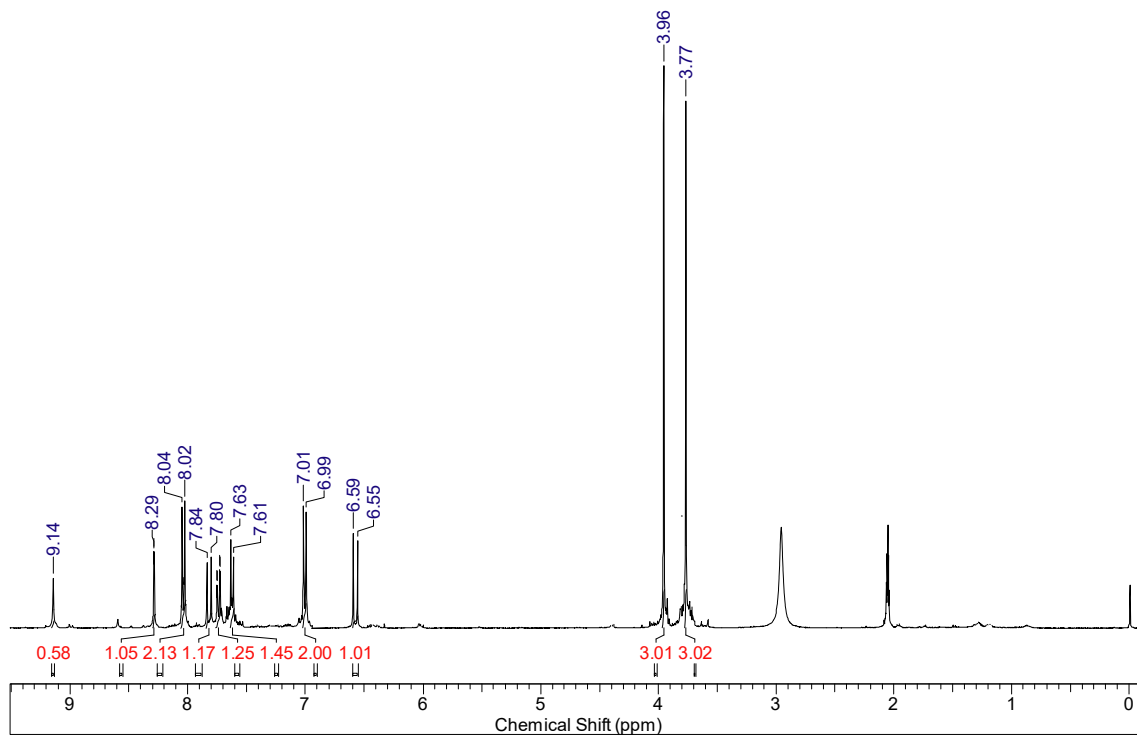


Figure S11. ¹H NMR spectra of compound **6** (Acetone-*d*₆, 400 MHz, TMS).



Figure

Figure S12. ¹³C NMR spectra of compound **6** (Acetone-*d*₆, 400 MHz, TMS).



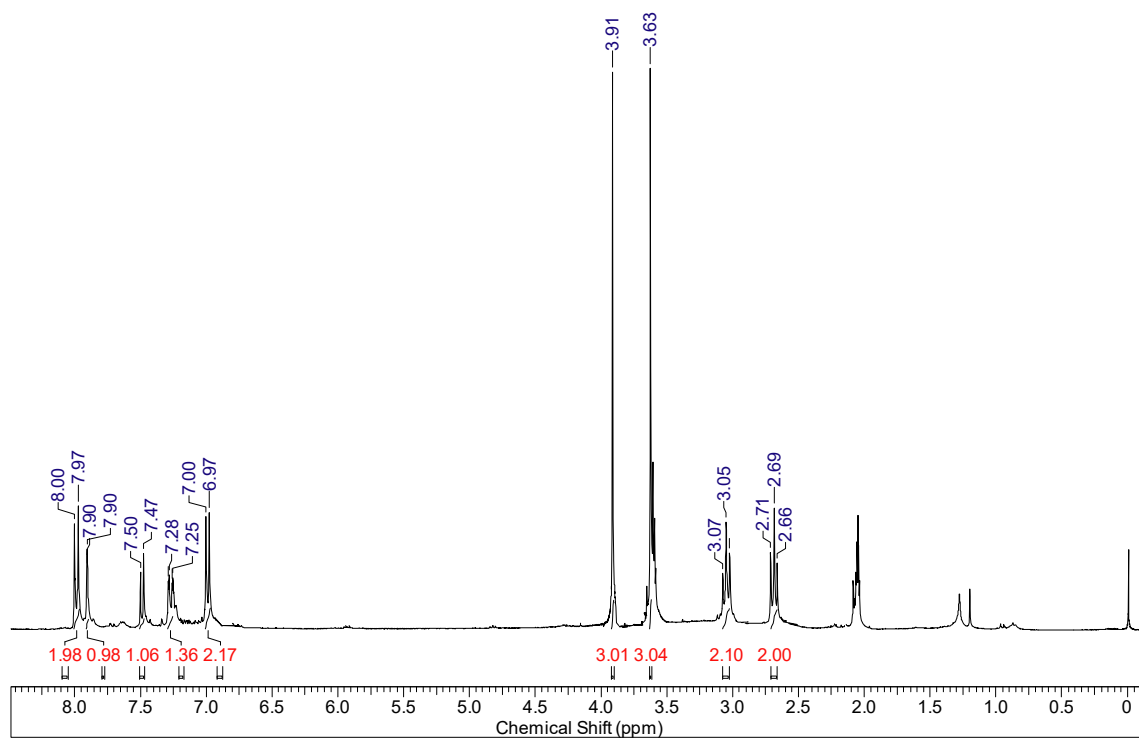


Figure S15 ¹H NMR spectra of compound **8** (Acetone-*d*₆, 400 MHz, TMS).

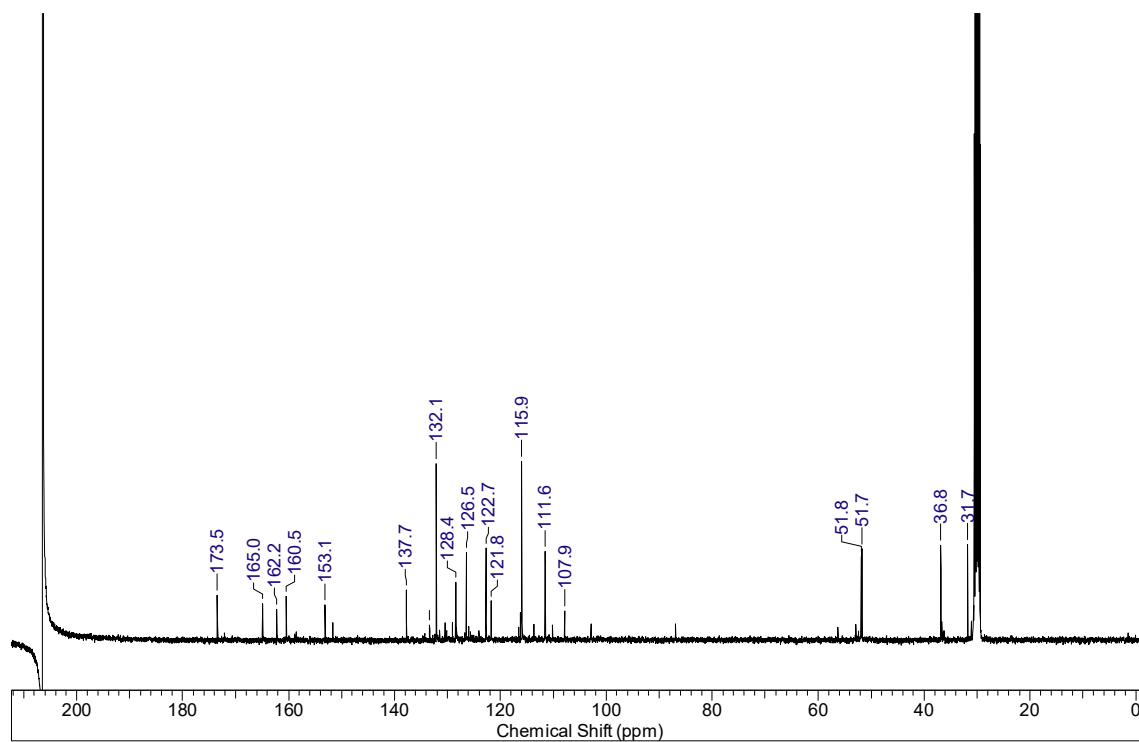


Figure S16. ¹³C NMR spectra of compound **8** (Acetone-*d*₆, 400 MHz, TMS).

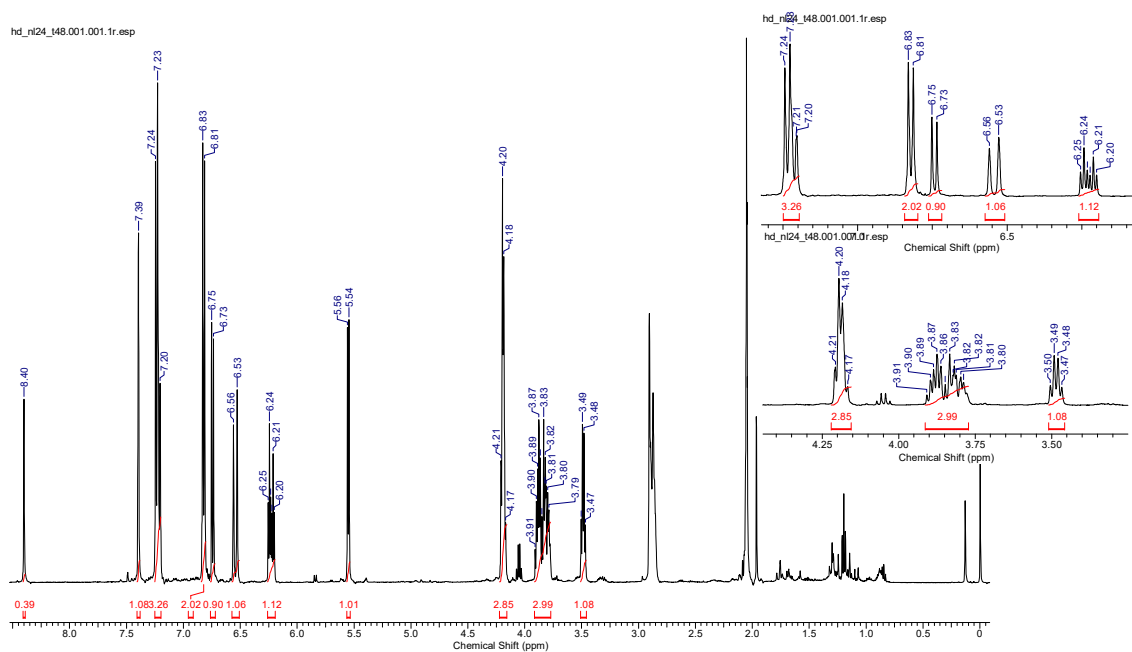


Figure S17. ^1H NMR spectra of compound **9** ($\text{Acetone-}d_6$, 400 MHz, TMS).

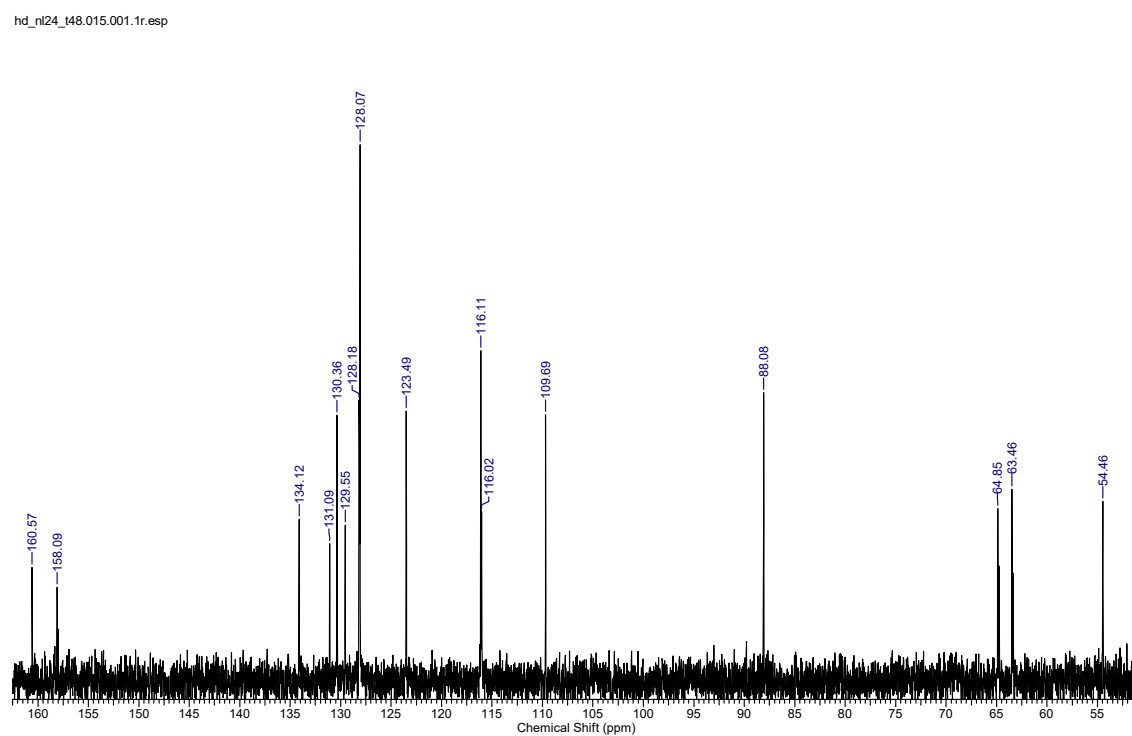


Figure S18. ^{13}C NMR spectra of compound **9** ($\text{Acetone-}d_6$, 400 MHz, TMS).

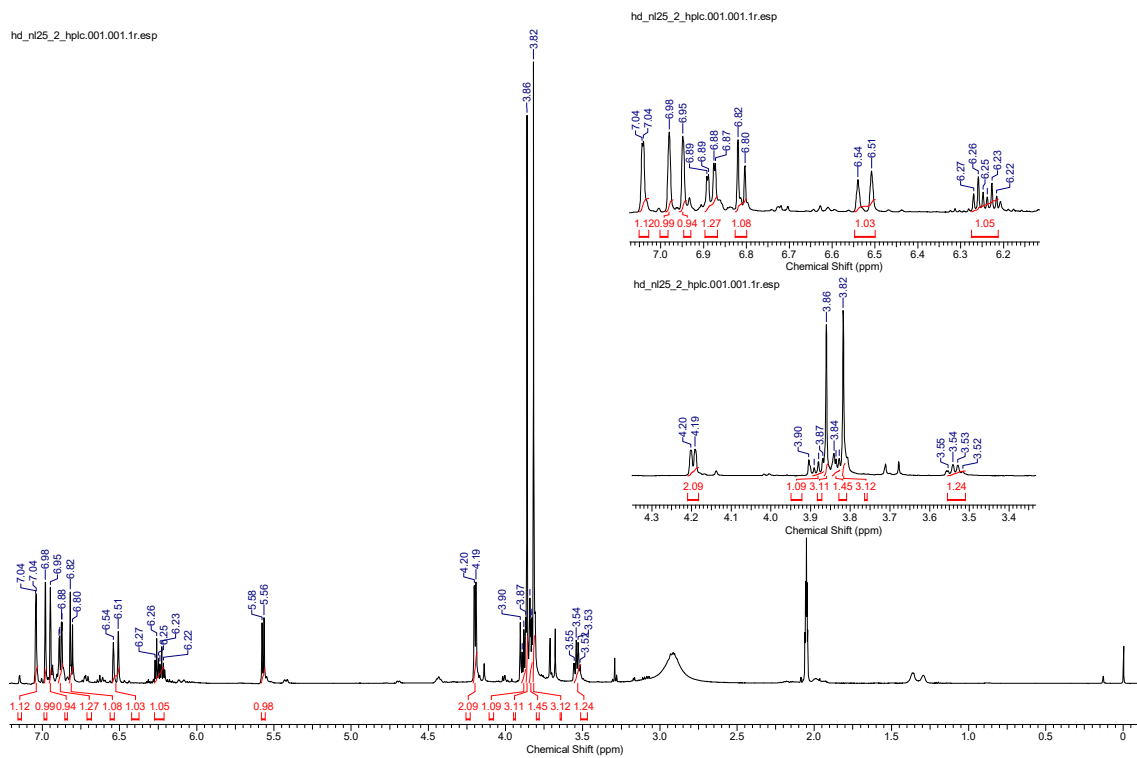


Figure S19. ^1H NMR spectra of compound **10** ($\text{Acetone-}d_6$, 400 MHz, TMS).

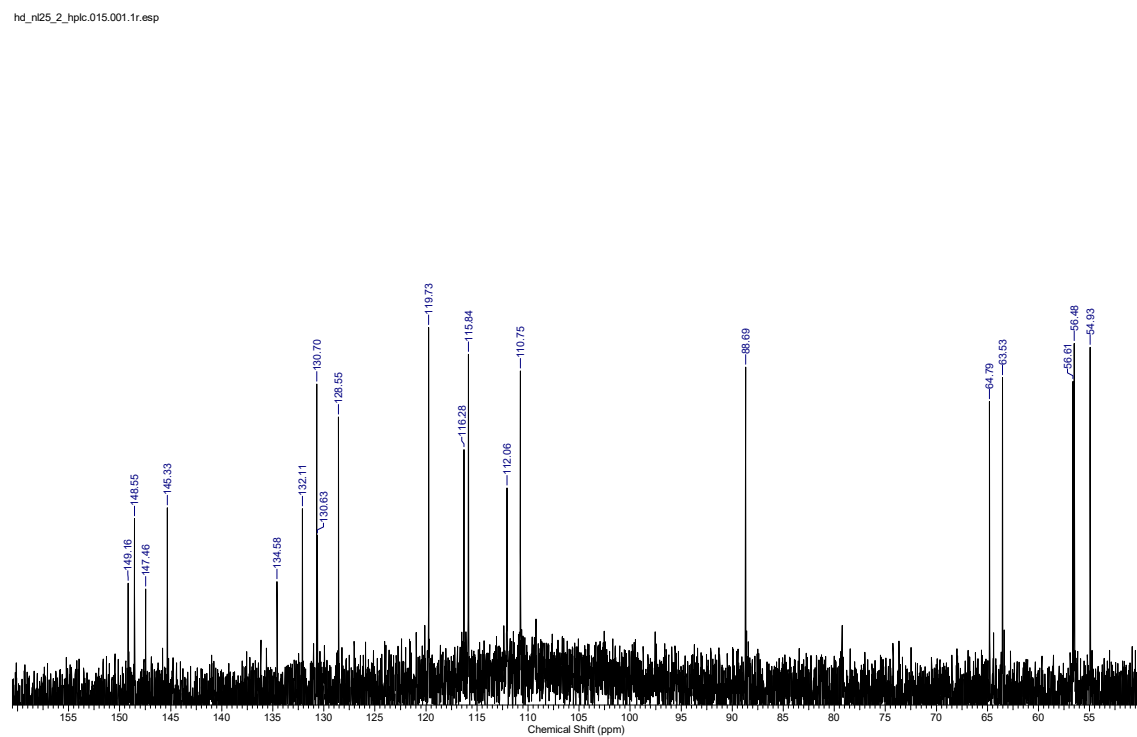
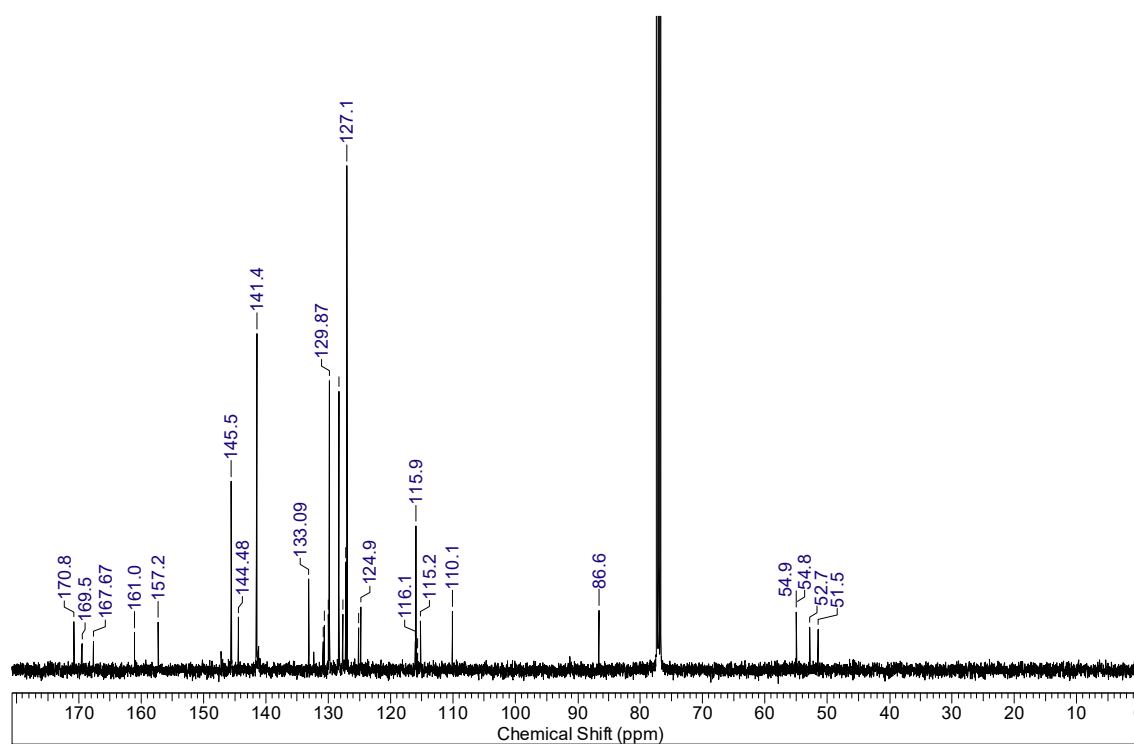
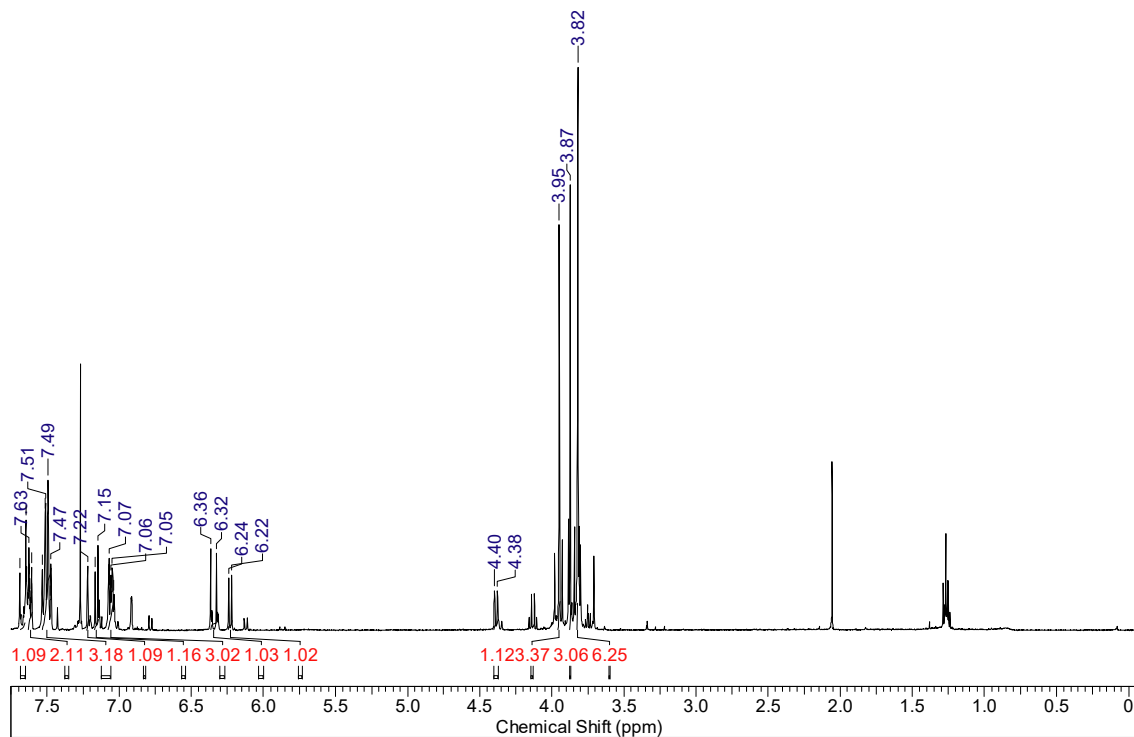
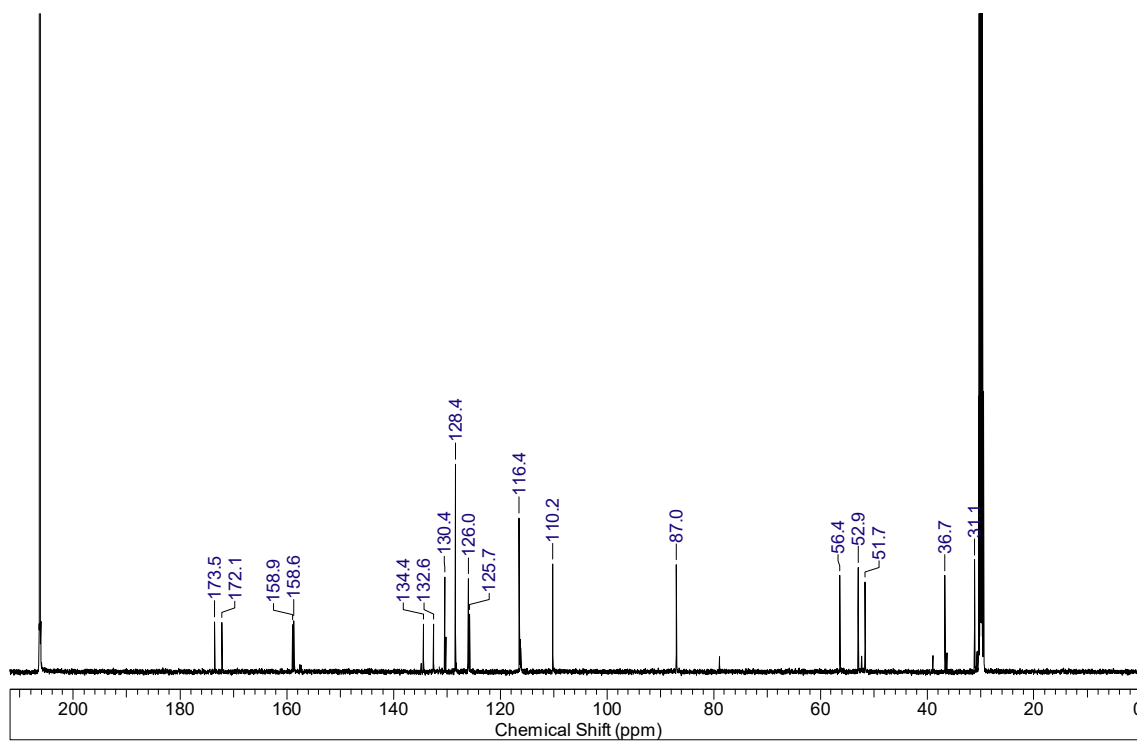
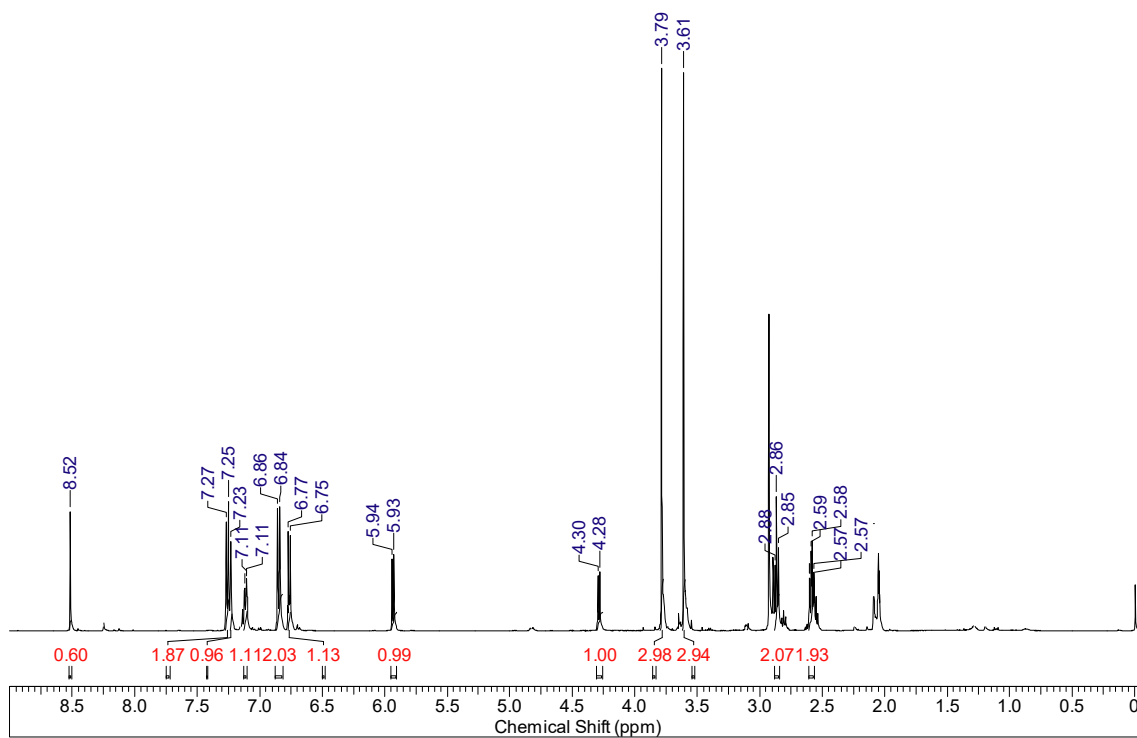
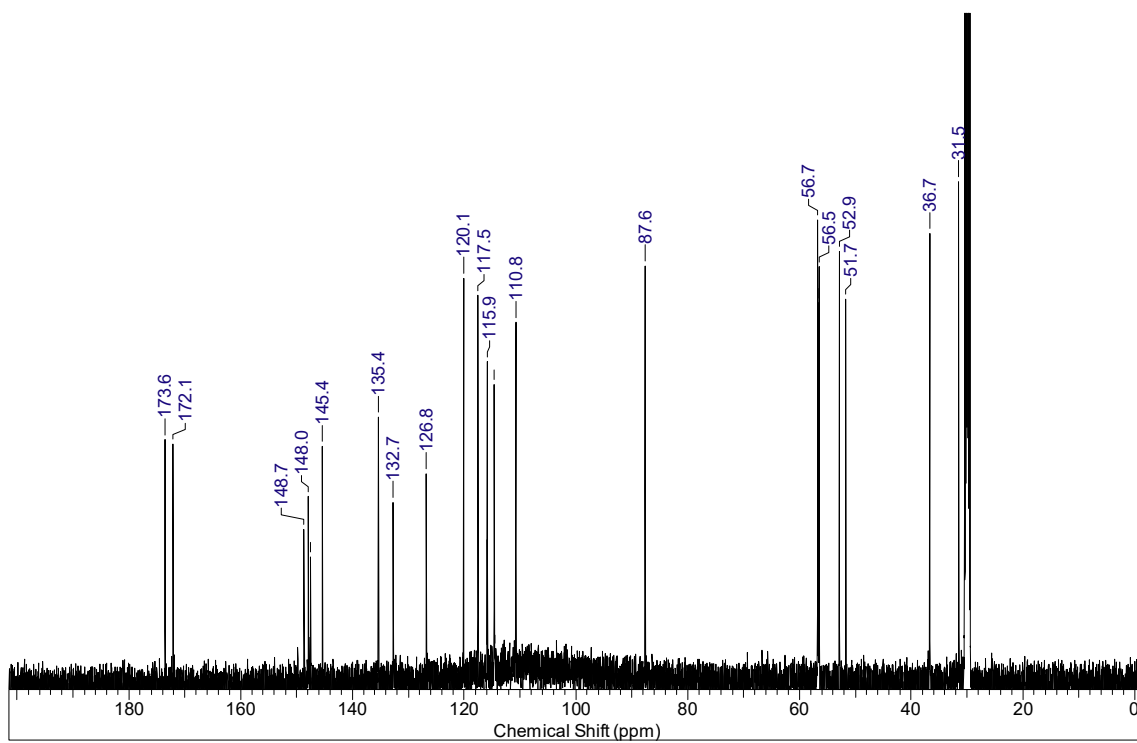
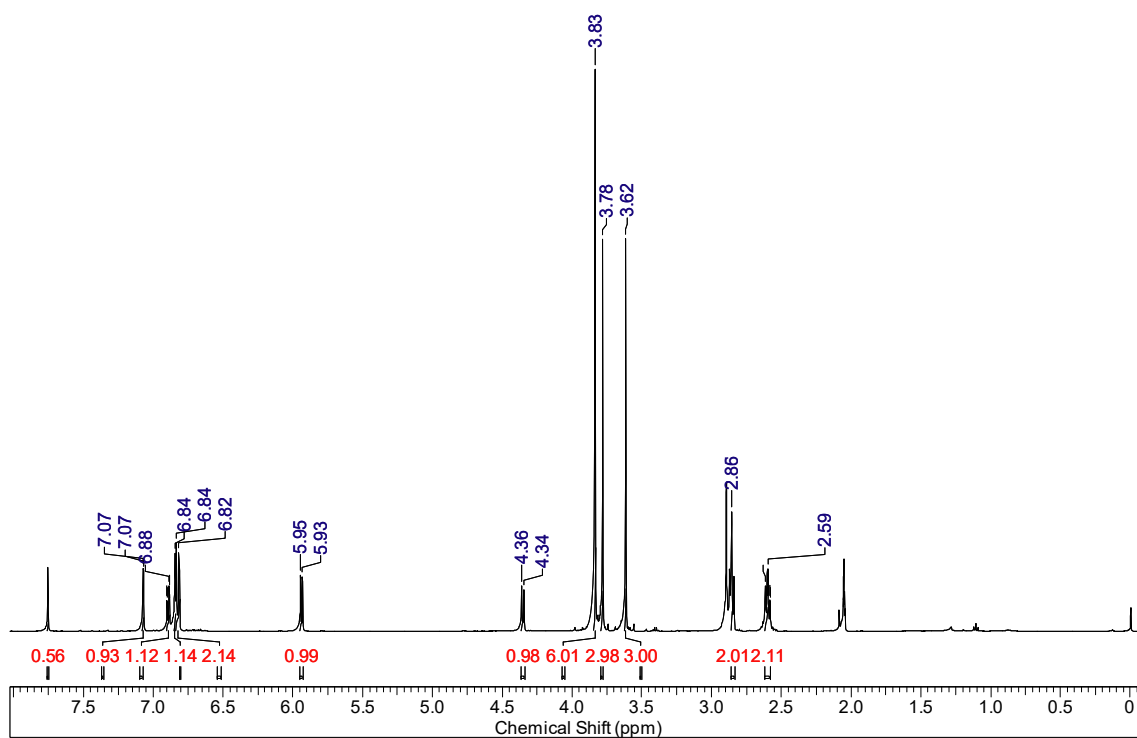


Figure S20. ^{13}C NMR spectra of compound **10** ($\text{Acetone-}d_6$, 400 MHz, TMS).







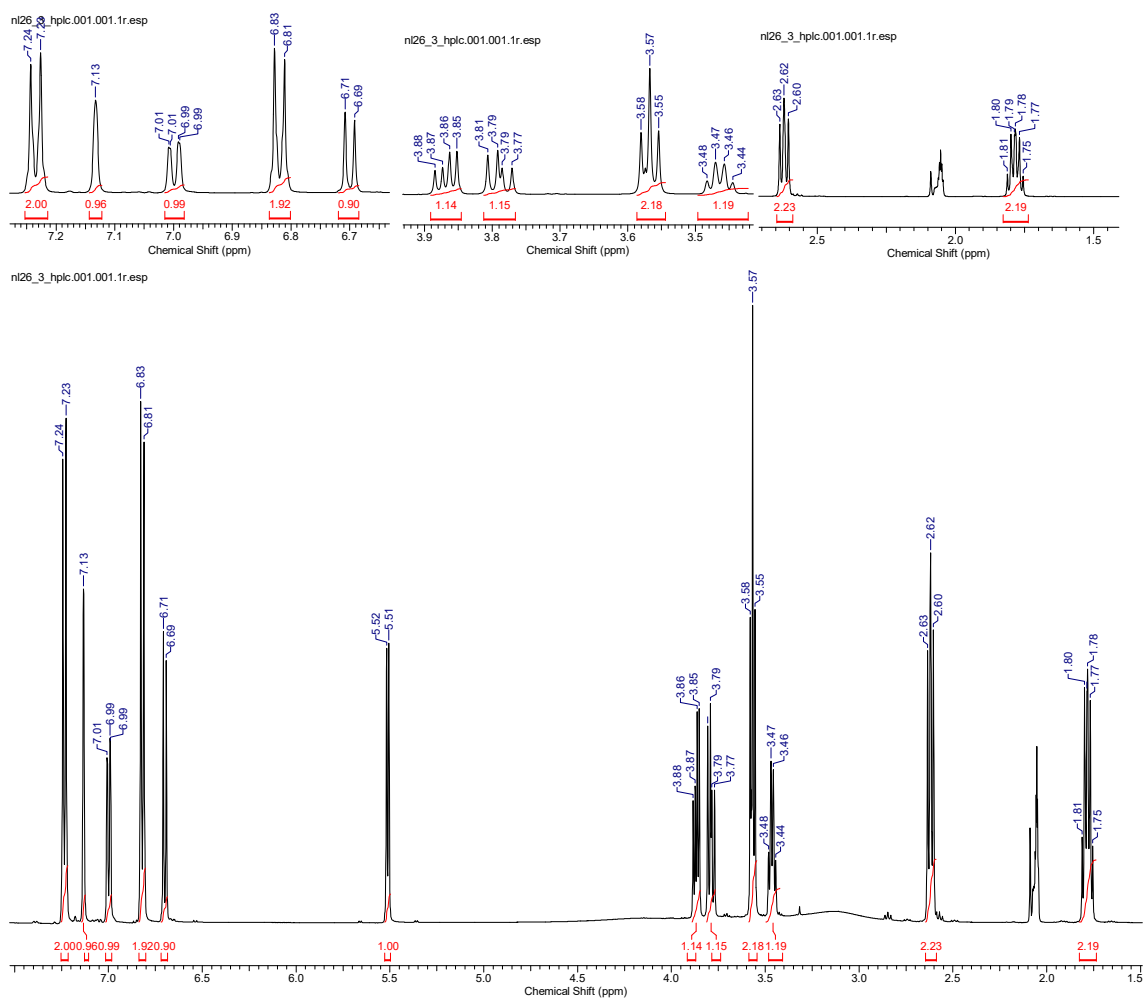


Figure S27. ^1H NMR spectra of compound **14** (Acetone- d_6 , 400 MHz, TMS).

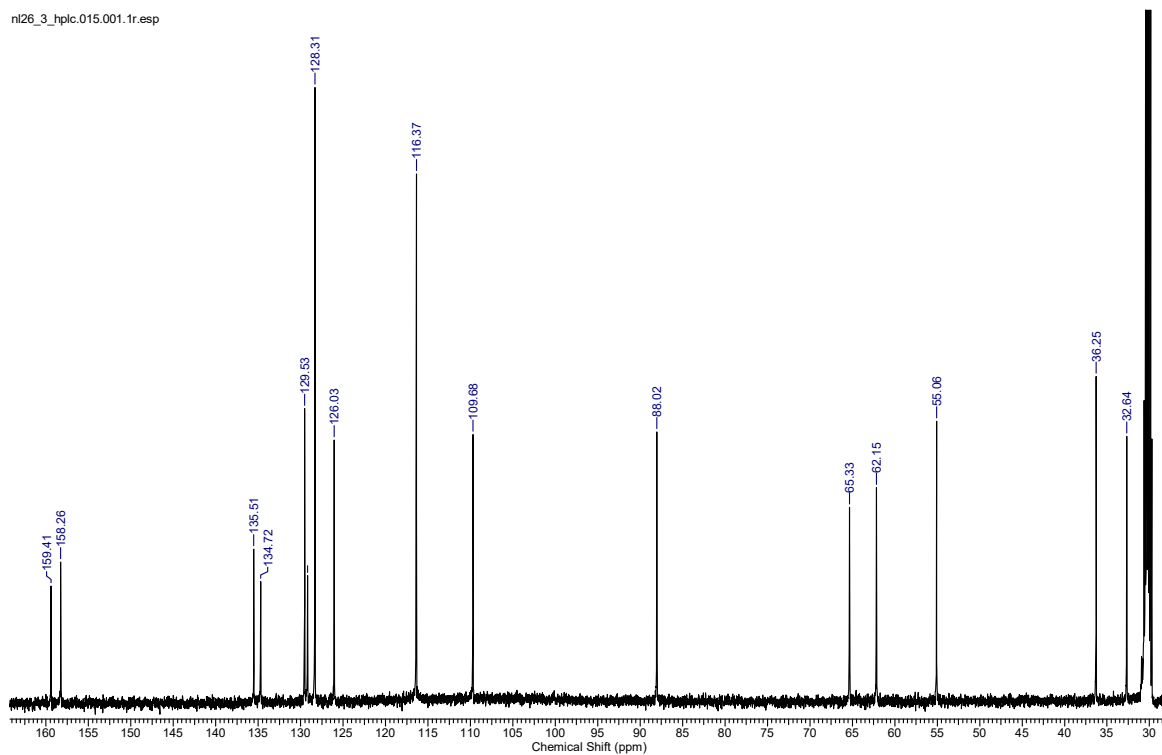


Figure S28. ^{13}C NMR spectra of compound **14** (Acetone- d_6 , 400 MHz, TMS).

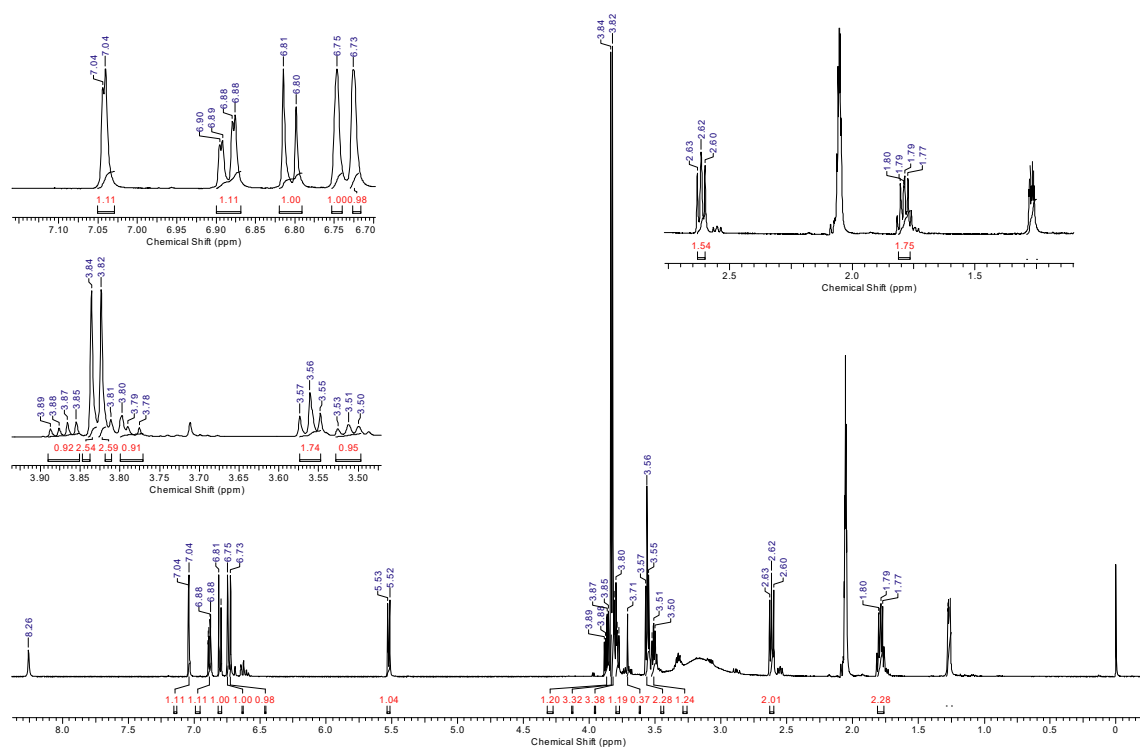


Figure S29. ^1H NMR spectra of compound **15** ($\text{Acetone-}d_6$, 400 MHz, TMS).

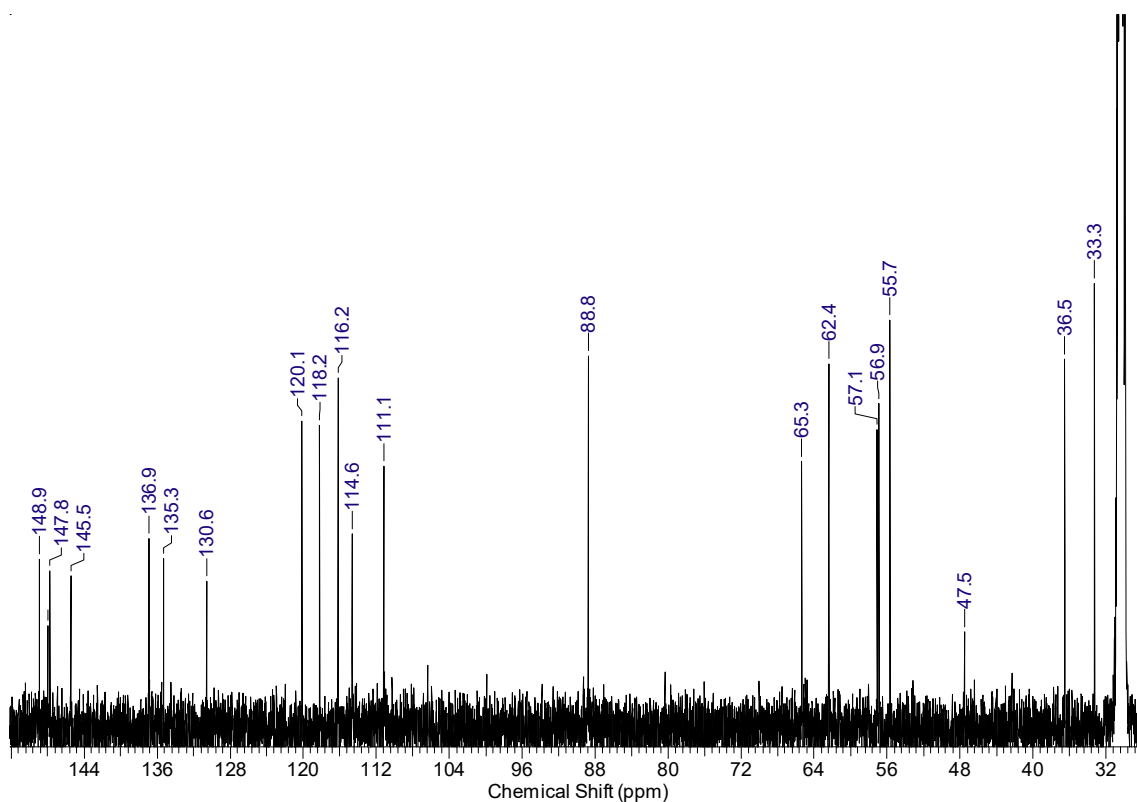


Figure S30. ^{13}C NMR spectra of compound **15** ($\text{Acetone-}d_6$, 400 MHz, TMS).

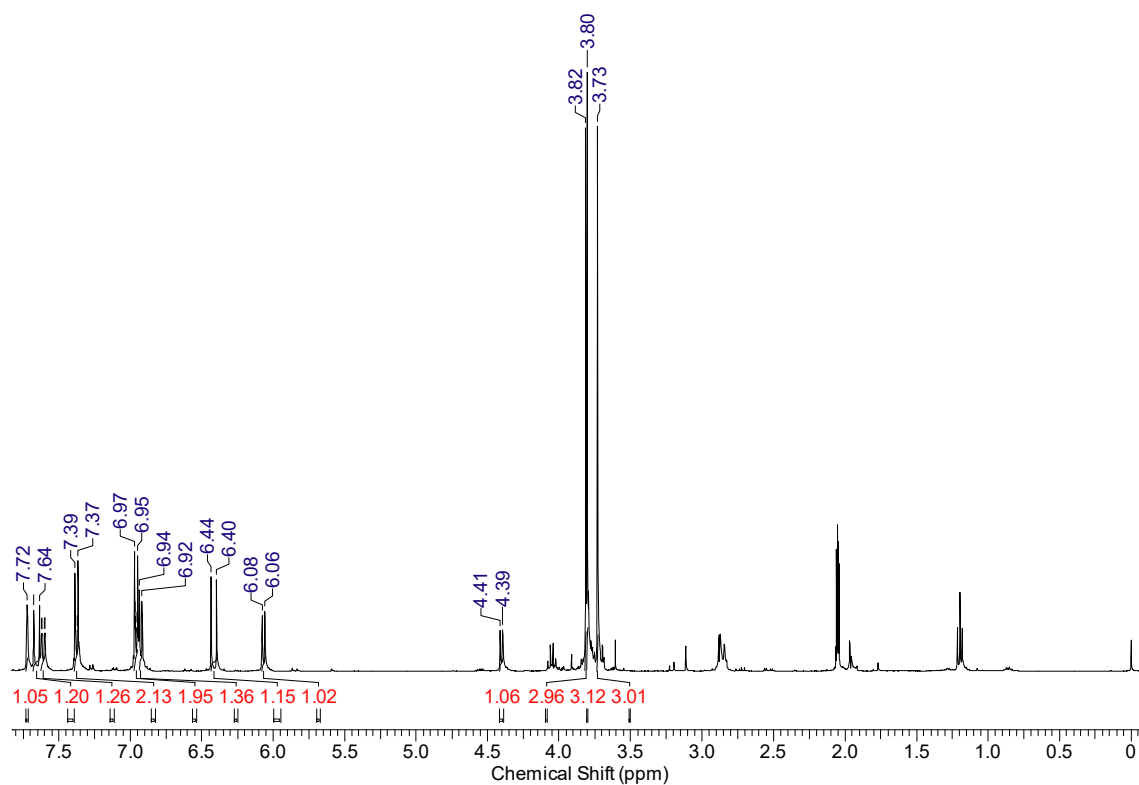


Figure S31. ¹H NMR spectra of compound **16** (Acetone-*d*₆, 400 MHz, TMS).

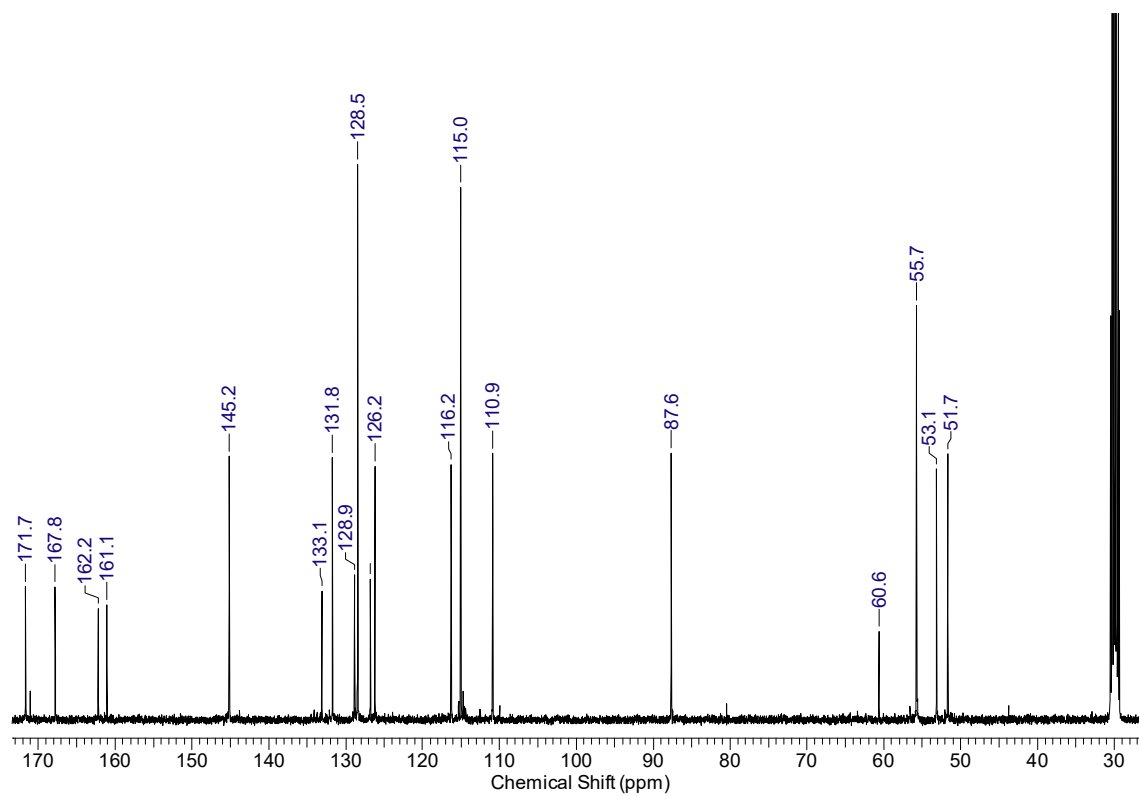


Figure S32. ¹³C NMR spectra of compound **16** (Acetone-*d*₆, 400 MHz, TMS).

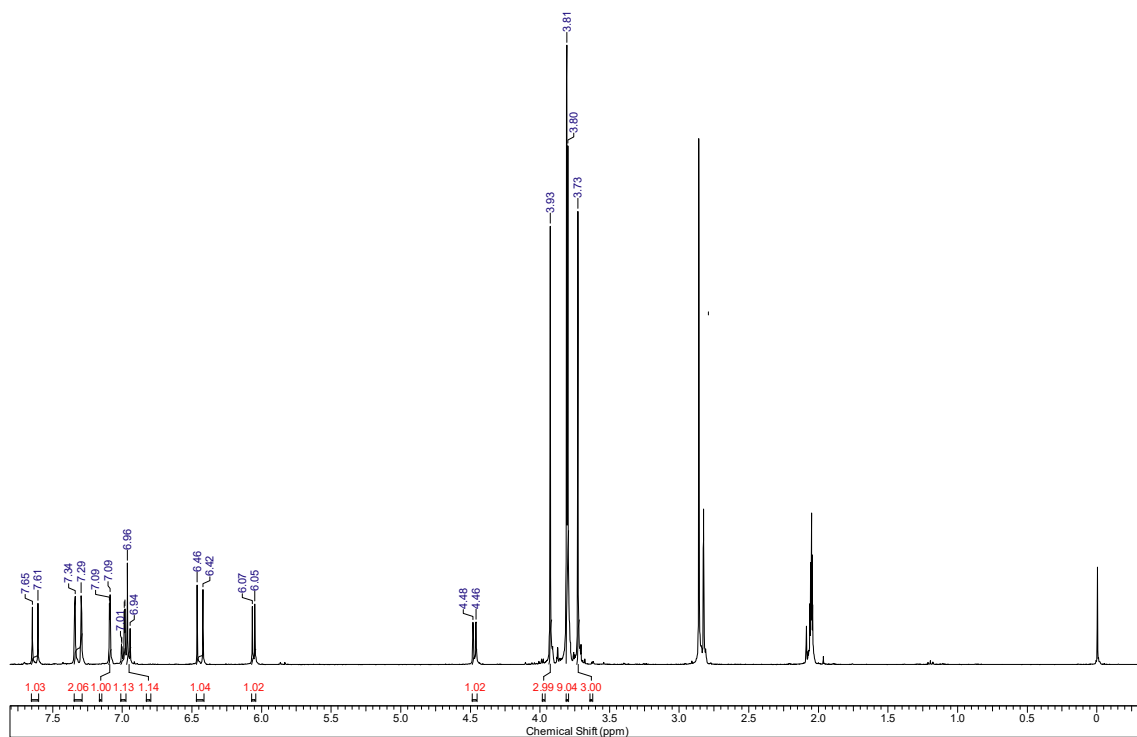


Figure S33. ^1H NMR spectra of compound **17** (*Acetone-d₆*, 400 MHz, TMS).

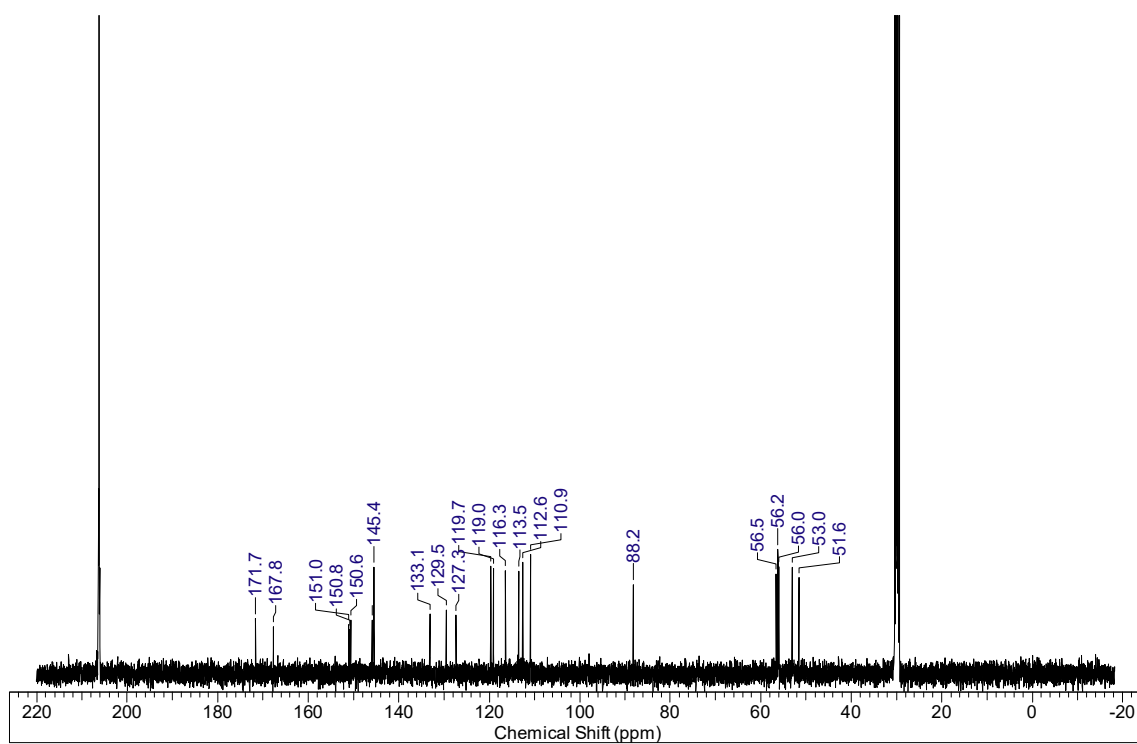


Figure S34. ^{13}C NMR spectra of compound **17** (*Acetone-d₆*, 400 MHz, TMS).

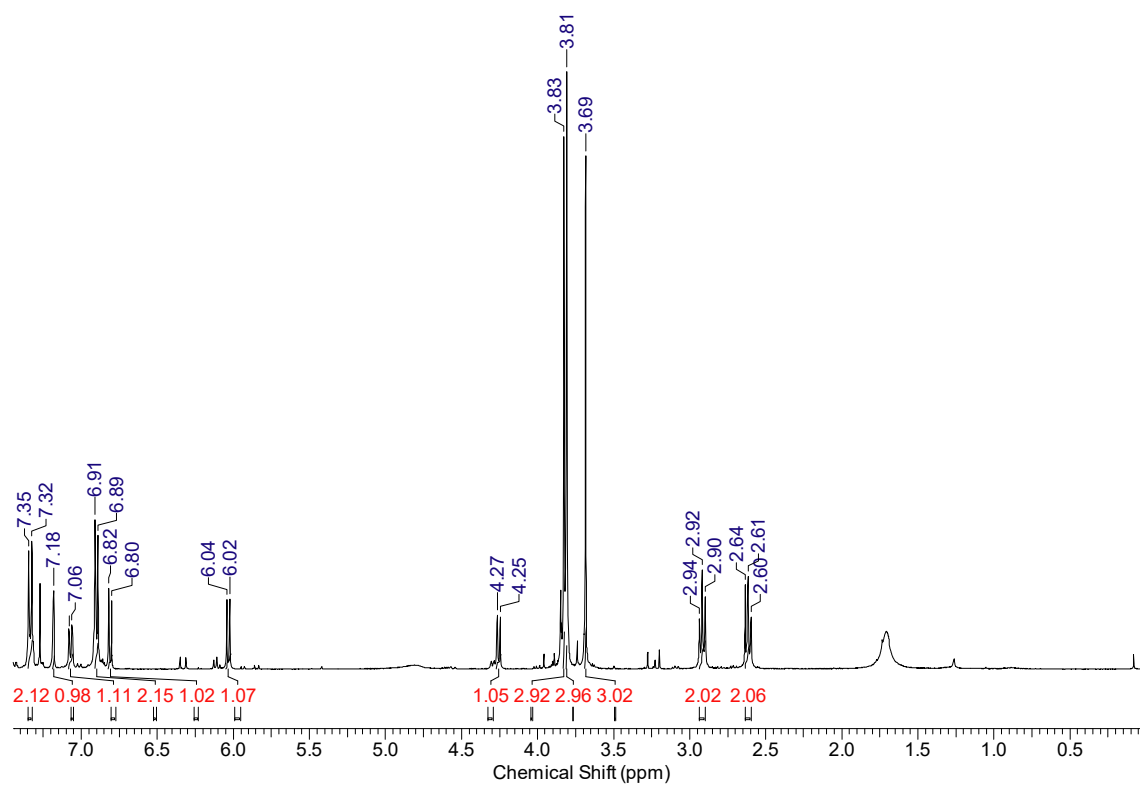


Figure S35. ¹H NMR spectra of compound **18** (CDCl₃, 400 MHz, TMS).

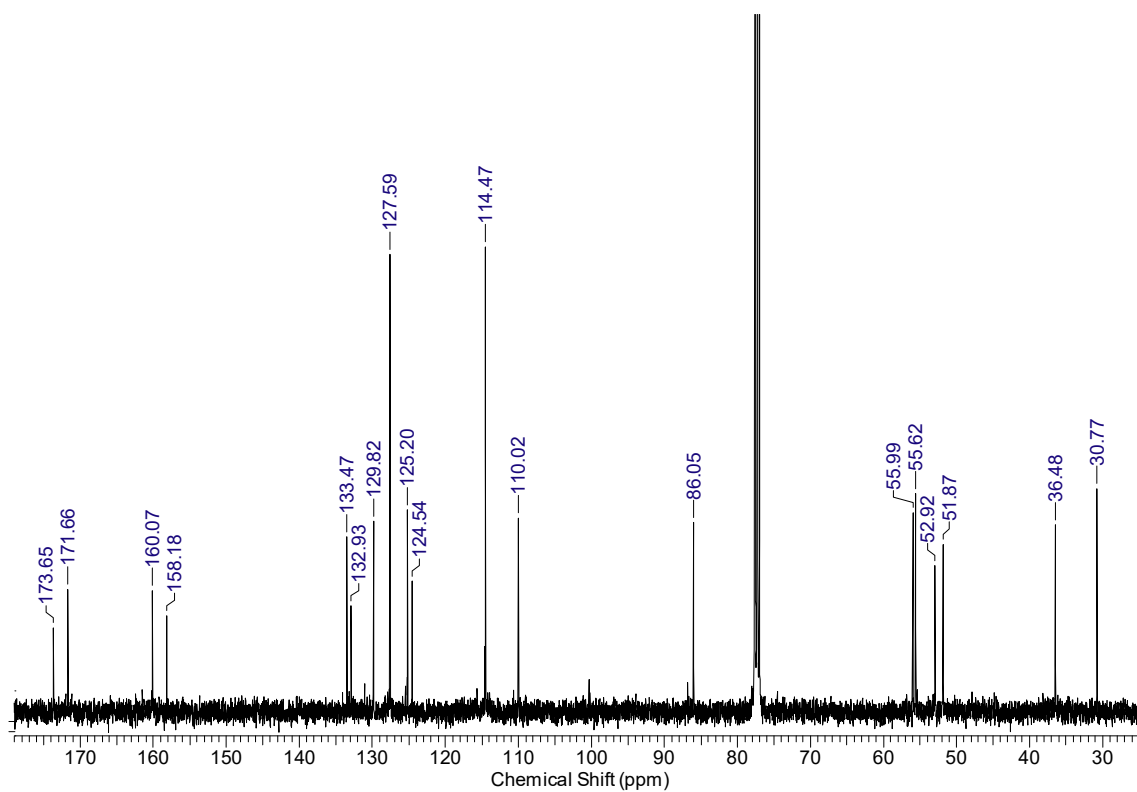


Figure S36. ¹³C NMR spectra of compound **18** (CDCl₃, 400 MHz, TMS).

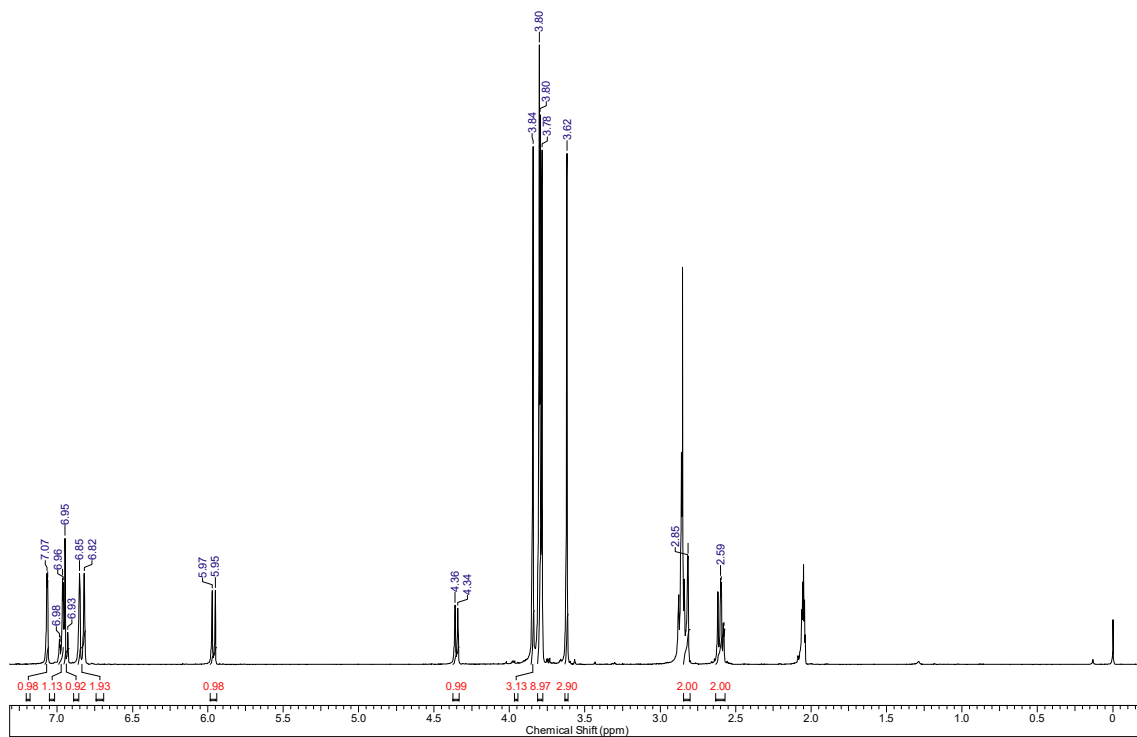


Figure S37. ¹H NMR spectra of compound **19** (Acetone-*d*₆, 400 MHz, TMS).

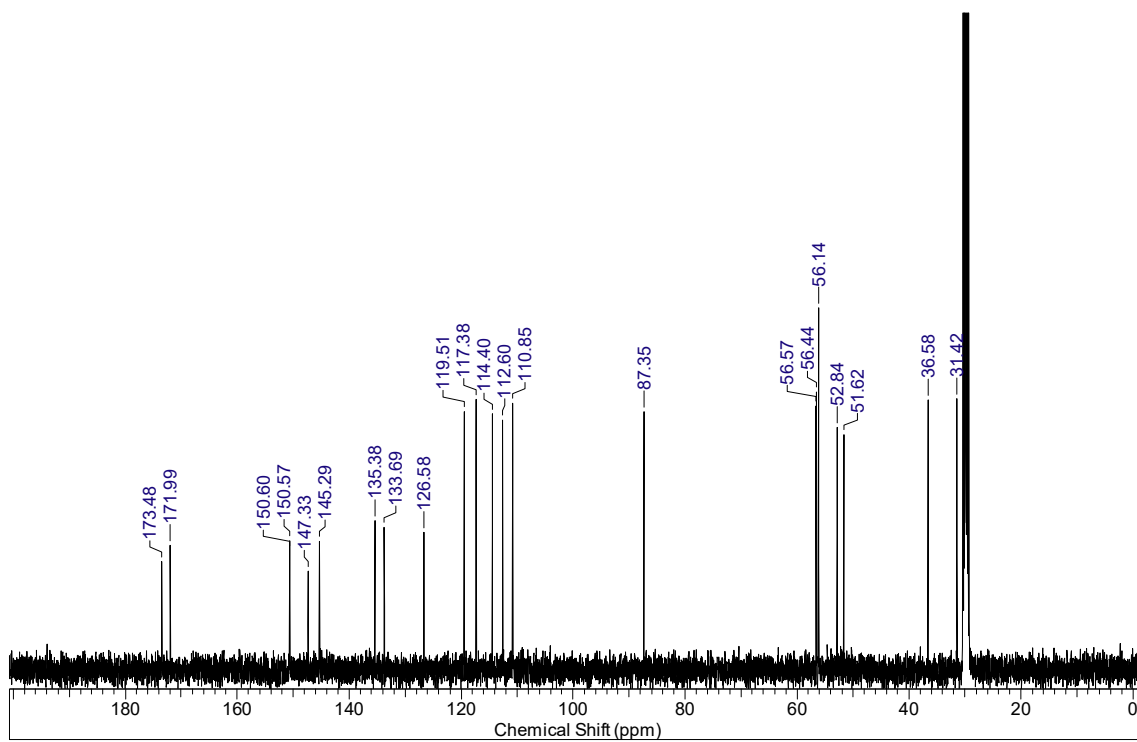
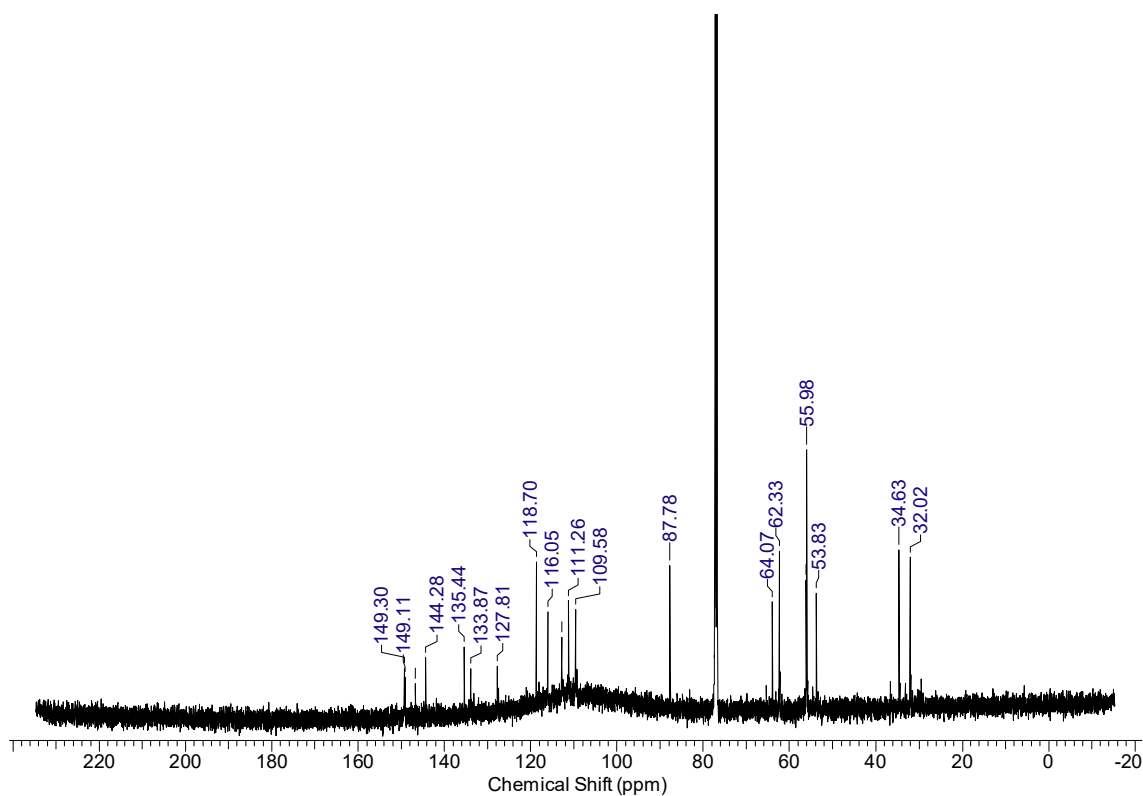
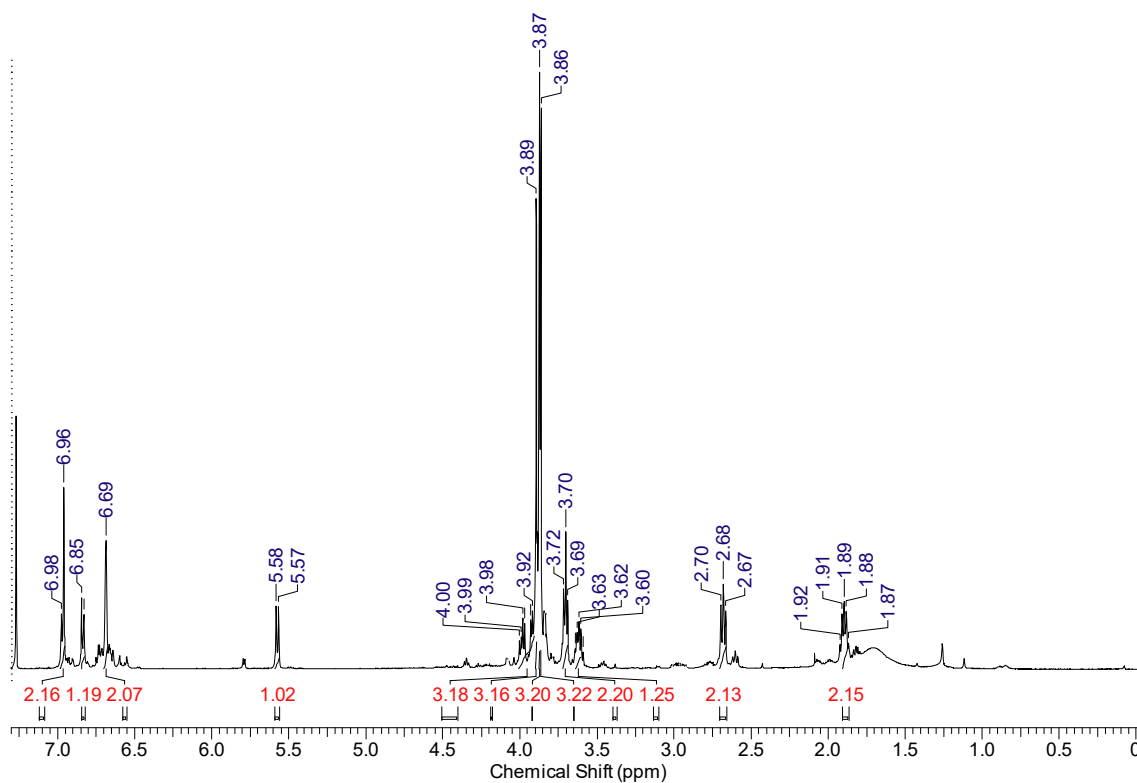


Figure S38. ¹³C NMR spectra of compound **19** (Acetone-*d*₆, 400 MHz, TMS).



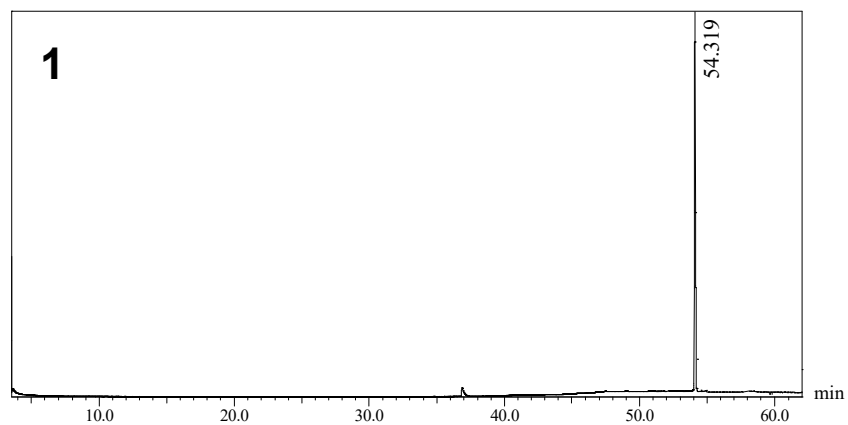


Figure S41. GC-FID chromatogram of compound **1**.

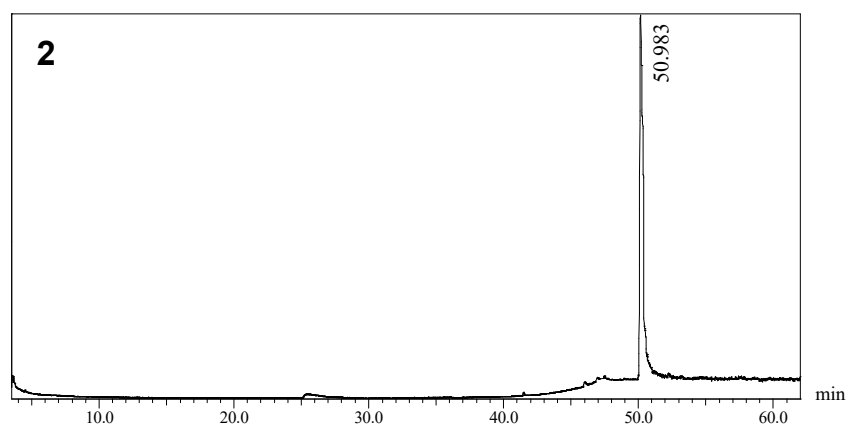


Figure S42. GC-FID chromatogram of compound **2**.

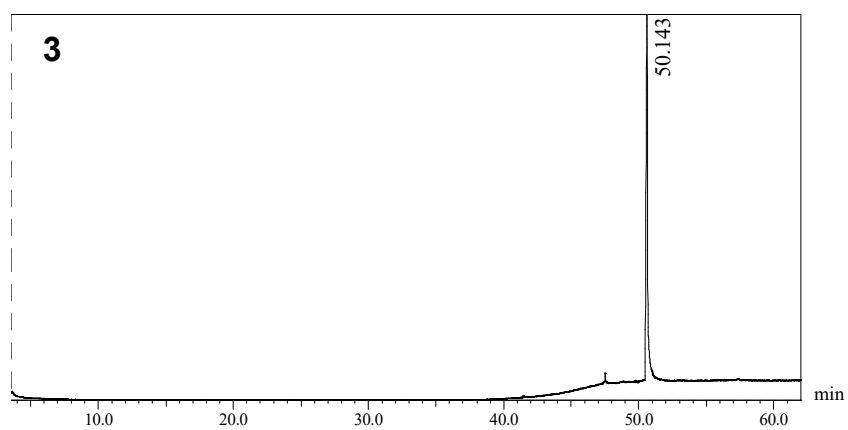


Figure S43. GC-FID chromatogram of compound **3**.

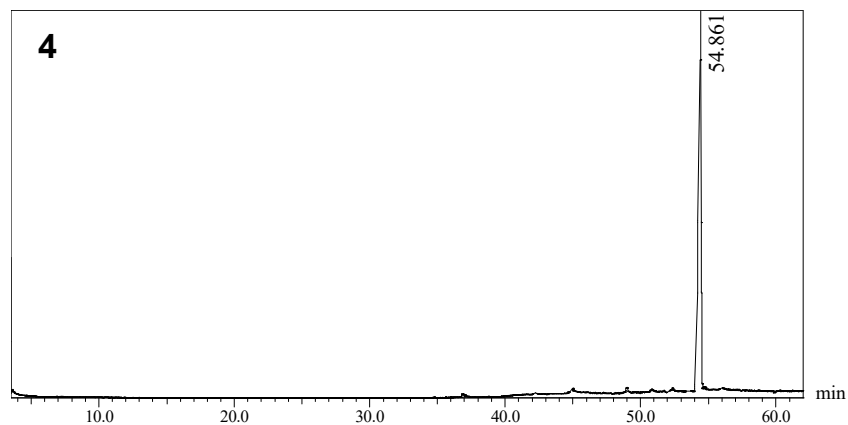


Figure S44. GC-FID chromatogram of compound **4**.

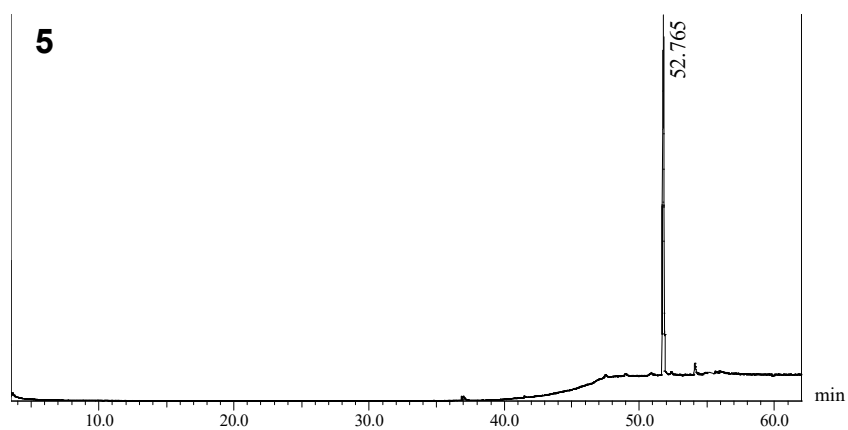


Figure S45. GC-FID chromatogram of compound **5**.

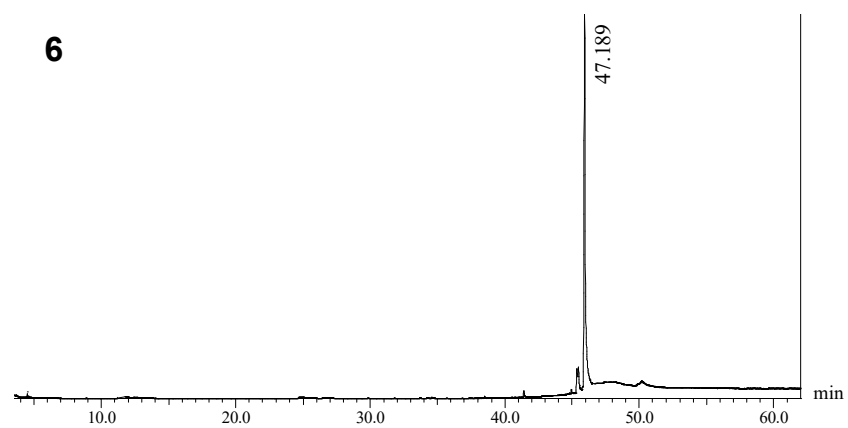


Figure S46. GC-FID chromatogram of compound **6**.

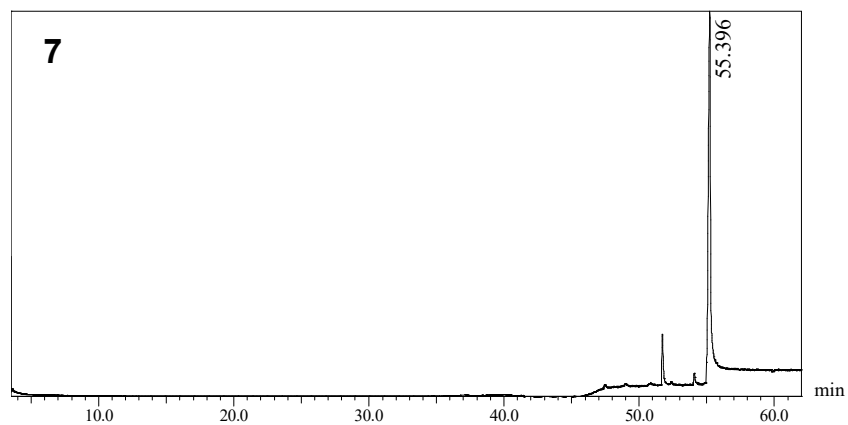


Figure S47. GC-FID chromatogram of compound **7**.

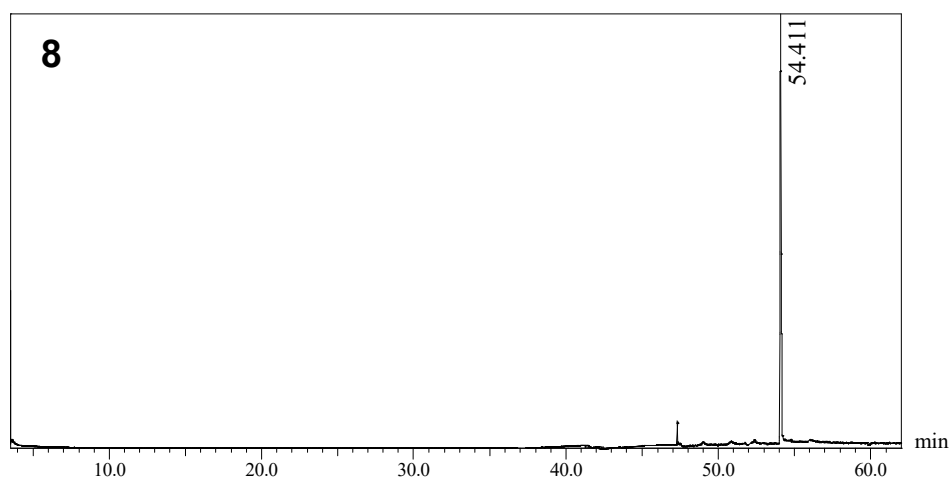


Figure S48. GC-FID chromatogram of compound **8**.

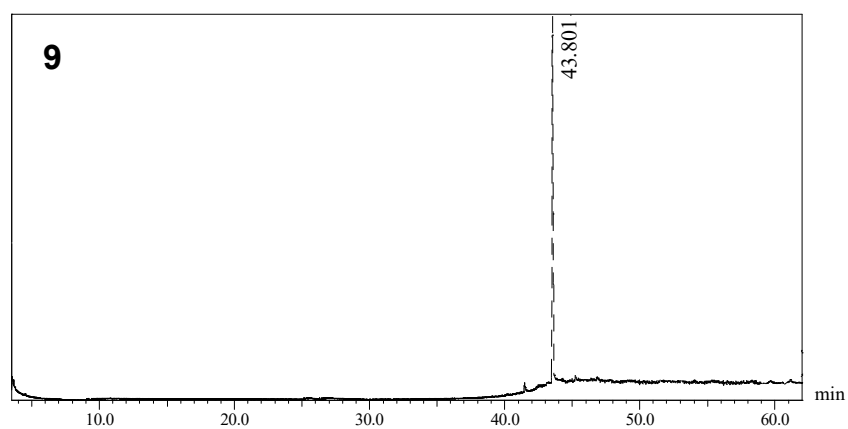


Figure S49. GC-FID chromatogram of compound **9**.

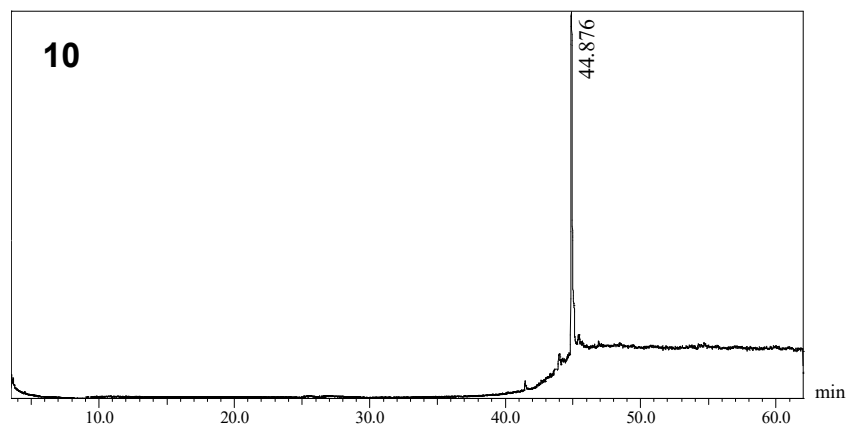


Figure S50. GC-FID chromatogram of compound **10**.

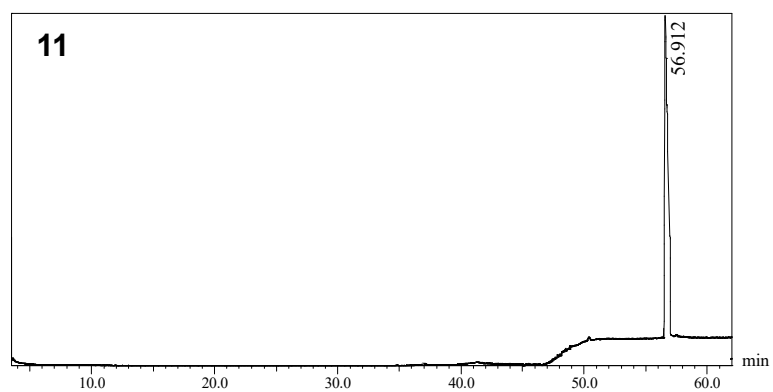


Figure S51. GC-FID chromatogram of compound **11**.

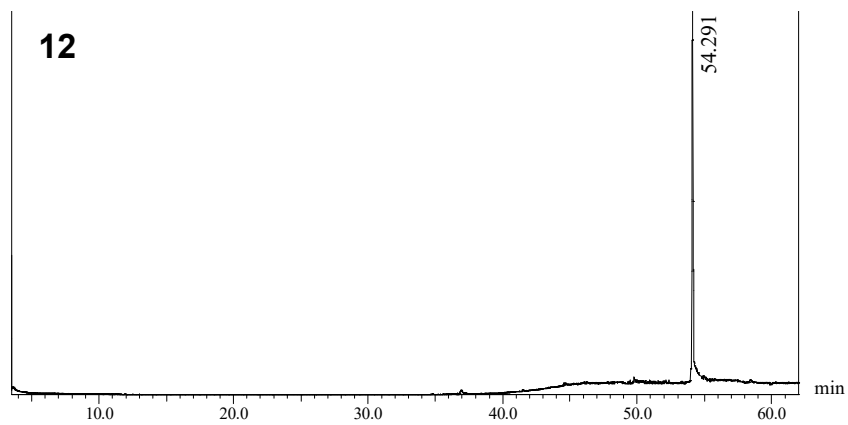


Figure S52. GC-FID chromatogram of compound **12**.

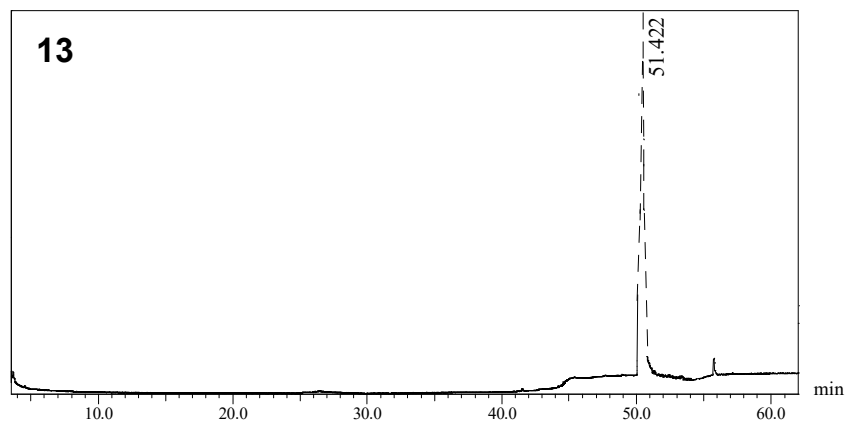


Figure S53. GC-FID chromatogram of compound **13**.

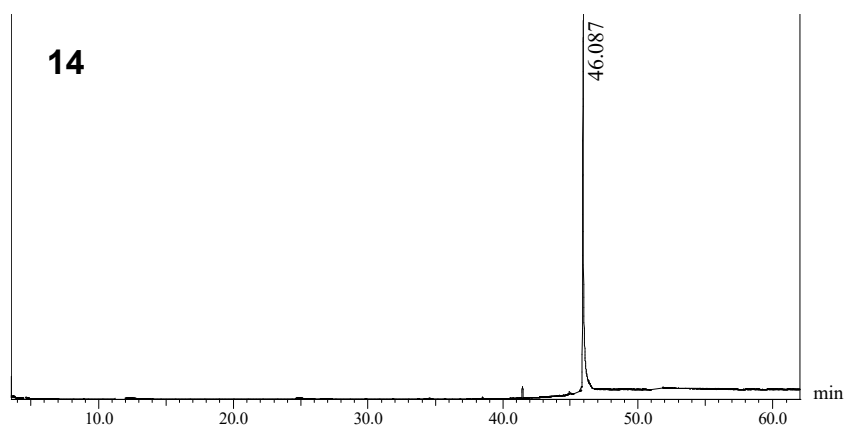


Figure S54. GC-FID chromatogram of compound **14**.

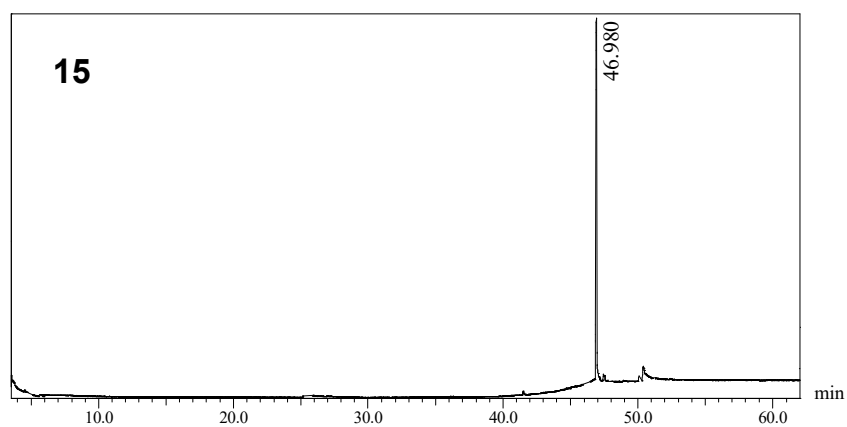


Figure S55. GC-FID chromatogram of compound **15**.

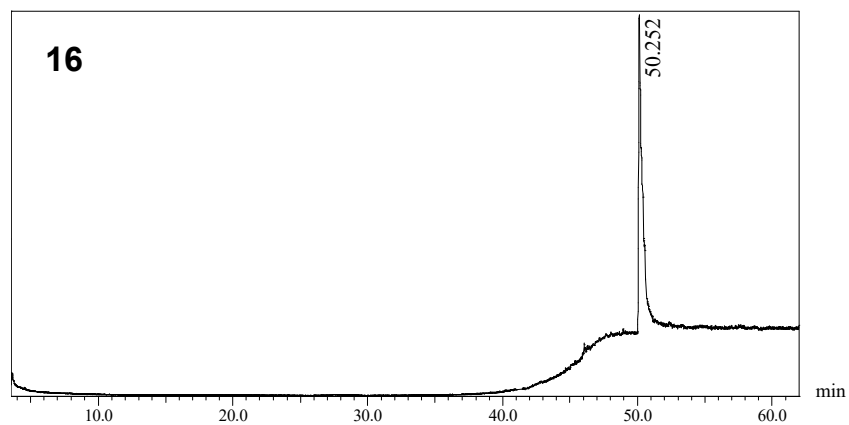


Figure S56. GC-FID chromatogram of compound **16**.

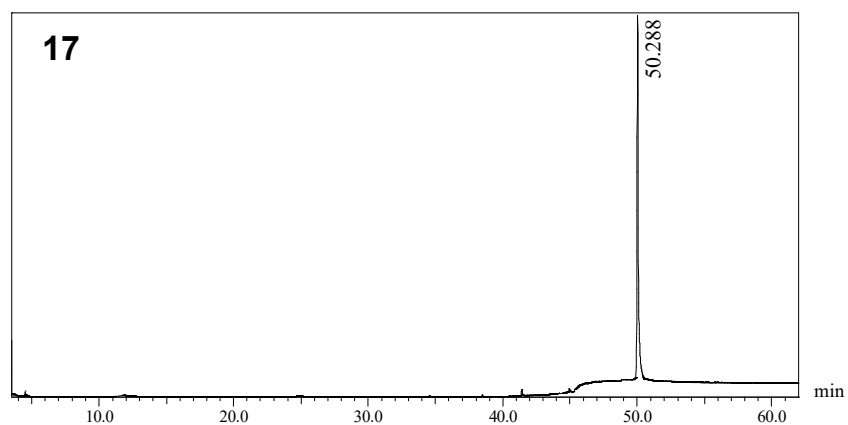


Figure S57. GC-FID chromatogram of compound **17**.

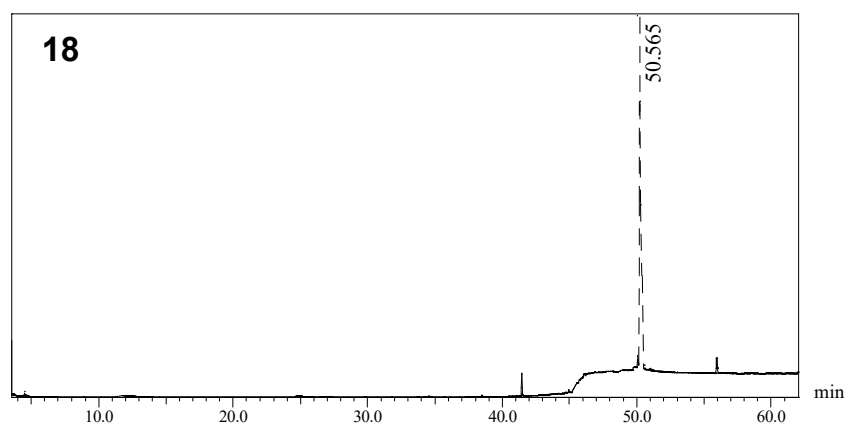


Figure S58. GC-FID chromatogram of compound **18**.

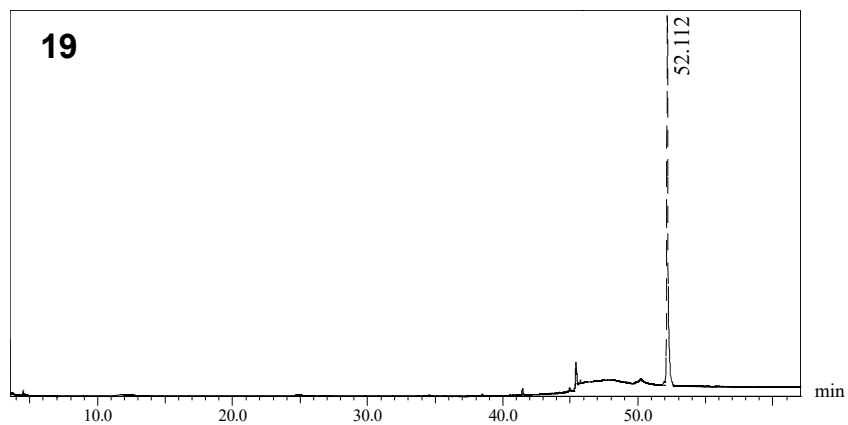


Figure S59. GC-FID chromatogram of compound **19**.

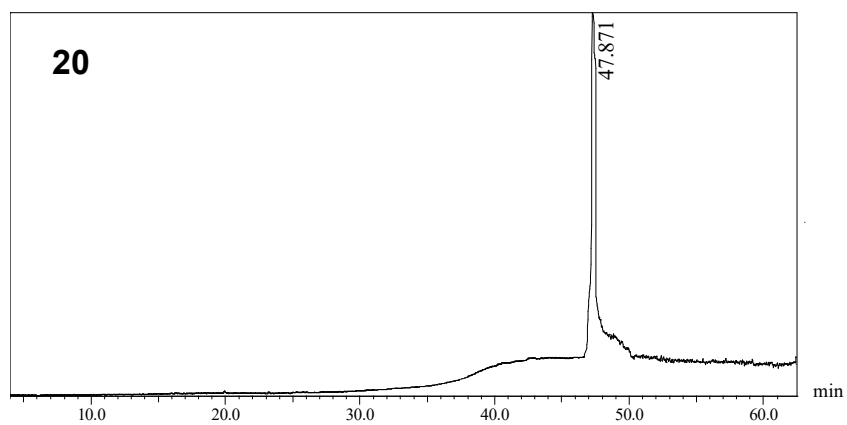


Figure S60. GC-FID chromatogram of compound **20**.

Experimental Information

Compounds **1-20** were identified on the basis of their nuclear magnetic resonance (NMR) data. The ^1H and ^{13}C NMR analysis of compounds **1-5** were achieved in a spectrometer Bruker DRX-400, operating in 400 MHz for ^1H and 100 MHz for ^{13}C . The samples were dissolved in *Acetone- d_6* (99.8 atom % D, Sigma-Aldrich), or CDCl_3 (99.8 atom % D, Sigma-Aldrich) with TMS (0.01%) as internal standard. The chemical shifts (δ) were expressed in parts per million (ppm) relative the residual solvent peak, and the multiplicity of signals was deduced according to the signals obtained in the spectrum. The coupling constants (J , Hz) were calculated in comparison to the same signal peaks, as well as the relative integral, from which was deduced the number of hydrogens.

Gas chromatography with flame ionization detection (GC-FID) analyses was performed on a GC-2010 Plus (Shimadzu Corp, Kyoto, Japan) system. Compounds **1-20** were dissolved in ethyl acetate and injected with the aid of an OAC-20s autosampler. The injector temperature was set at 250 °C. Nitrogen (N_2 , 99.999 %) was used as carrier gas. An Rtx-5 (30 m x 0.25 mm x 0.25 μm) capillary column (Restek Co., Bellefonte, PA, USA) was used. The column temperature was programmed to increase from 70 °C to 290 °C at 3 °C/min, then kept at 290 °C for 15 min. The purity of compounds **1-20** was estimated based on the relative peak area in the GC-FID chromatogram.