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Electronic Supplementary Information (ESI) for:

Development of highly active anti-*Pneumocystis* benzamidines: Insight into the influence of selected substituents on the *in vitro* activity

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Characterization of newly reported compounds and details of synthetic procedures

Bis[4-(*N*,*N*'-dimethylamidino)benzyl]piperazine tetrahydrochloride (2). Following the general procedure, pure white solid was obtained with 84% yield; MP = 317.0–318.0 °C (decomp.). ^{1}H NMR (299.87 MHz, D_2O) δ in ppm: 2.96 (s; 6H; H-11, H-11'), 3.09 (s; 6H; H-12, H-12'), 3.57 (br s; 8H; H-9, H-10, H-9', H-10'), 4.49 (br s; 4H; H-8, H-8', 7.69–7.77 (m; 8H; H-2, H-3, H-5, H-6, H-2', H-3', H-5', H-6'). ^{13}C NMR (75.40 MHz, D_2O) δ in ppm: 28.5 (C-11, C-11'), 31.4 (C-12, C-12'), 48.5 (C-9, C-10, C-9', C-10'), 59.7 (C-8, C-8'), 129.0 (C-3, C-5, C-3', C-5'), 129.5 (C-4, C-4'), 132.0 (C-2, C-6, C-2', C-6'), 132.2 (C-1, C-1'), 164.6 (C-7, C-7'). ^{1}H NMR (299.87 MHz, DMSO-d_6) δ in ppm: 2.81–2.82 (d; *J* = 4.8 Hz; 6H; H-11, H-11'), 2.98–2.99 (d; *J* = 4.8 Hz; 6H; H-12, H-12'), 3.72 (br s; 10H; H-9, H-10, H-9', H-10', 2 × NH), 4.32 (br s; 4H; H-8, H-8'), 7.64–7.67 (pd; *J* = 7.2 Hz; 4H; H-2, H-6, H-2', H-6'), 7.81 (br s; 4H; H-3, H-5, H-3', H-5'), 9.34–9.36 (m; 2H; 2 × NH), 9.73–9.75 (m; 2H; 2 × NH). Element. Anal. $C_{24}H_{36}N_6 \times 4HCl \times 3H_2O$ (606.46 g/mol) calcd. (%): C = 47.52, H = 7.26, N = 13.86, Cl = 23.43; found (%): C = 47.65, H = 7.29, N = 13.88, Cl = 23.04.

Bis[4-(*N*-propylamidino)benzyl]piperazine tetrahydrochloride (3). After the general procedure, after column chromatography (CH_2Cl_2/MeOH/AcOH/H_2O – 70/20/5/5), a white solid was obtained with 53% yield; MP = 300.0–300.5 °C (decomp.). ^{1}H NMR (299.87 MHz, D_2O) δ in ppm: 0.89–0.93 (t; *J* = 7.1 Hz; 6H; H-13, H-13'), 1.60–1.72 (sx; *J* = 7.1 Hz; 4H; H-12, H-12'), 3.16 (br s; 8H; H-9, H-10, H-9', H-10'), 3.31–3.36 (t; *J* = 7.1 Hz; 4H; H-11, H-11'), 4.13 (br s; 4H; H-8, H-8'), 7.54–7.57 (pd; *J* = 7.8 Hz; 4H; H-2, H-6, H-2', H-6'), 7.67–7.69 (pd; *J* = 7.8 Hz; 4H; H-3, H-5, H-3', H-5'). ^{13}C NMR (75.40 MHz, D_2O) δ in ppm: 12.3 (C-13, C-13'), 22.2 (C-12, C-12'), 46.4 (C-11, C-11'), 51.4 (C-9, C-10, C-9', C-10'), 61.7 (C-8, C-8'), 130.1 (C-3, C-5, C-3', C-5'), 131.8 (C-4, C-4'), 133.2 (C-2, C-6, C-2', C-6'), 137.8 (C-1, C-1'), 165.5 (C-7, C-7'). ^{1}H NMR (299.87 MHz, DMSO-d_6) δ in ppm: 0.93–0.98 (t; *J* = 7.2 Hz; 6H; H-13, H-13'), 1.56–1.72 (sx; *J* = 7.2 Hz; 4H; H-12, H-12'), 3.34–3.43 (m; 12H; 8H; H-9, H-10, H-11, H-9', H-10', H-11'), 4.42 (br s; 4H; H-8, H-8'), 7.55 (br s; 4H; H-2, H-6, H-2', H-6'), 7.79 (br s; 4H; H-3, H-5, H-3', H-5'), 9.10 (br s; 2H; 2 × NH), 9.48 (br s; 2H; 2 × NH–C_3H_7), 9.82 (br s; 2H; 2 × NH). Element. Anal. $C_{26}H_{38}N_6 \times 4HCl \times 4H_2O$ (652.53 g/mol) calcd. (%): C = 47.85, H = 7.67, N = 12.88, Cl = 21.78; found (%): C = 47.49, H = 7.42, N = 12.73, Cl = 21.56.

Bis[4-(*N*-butylamidino)benzyl]piperazine tetrahydrochloride (4). Following the general procedure, after crystallization from 96% EtOH with few drops of water, a white crystals were obtained with 46% yield; MP = 295.0–296.5 °C (decomp.). ^{1}H NMR (299.87 MHz, D_2O) δ in ppm: 0.96–1.01 (t; *J* = 7.5 Hz; 6H; H-14, H-14'), 1.42–1.54 (sx; *J* = 7.5 Hz; 4H; H-13, H-13'), 1.72–1.79 (p; *J* = 7.5 Hz; 4H; H-12, H-12'), 3.48–3.53 (m; 12H; H-9, H-10, H-11, H-9', H-10', H-11'), 4.45 (br s; 4H; H-8, H-8'), 7.70–7.73 (pd; *J* = 8.1 Hz; 4H; H-2, H-6, H-2', H-6'), 7.82–7.84 (pd; *J* = 8.1 Hz; 4H; H-3, H-5, H-3', H-5'). ^{13}C NMR (75.40 MHz, D_2O) δ in ppm: 12.8 (C-14, C-14'), 19.4 (C-13, C-13'), 28.8 (C-12, C-12'), 42.8 (C-11, C-11'), 48.6 (C-9, C-10, C-9', C-10'), 59.6 (C-8, C-8'), 128.6 (C-3, C-5, C-3', C-5'), 130.8 (C-4, C-4'), 131.9 (C-2, C-6, C-2', C-6'), 133.2 (C-1, C-1'), 163.5 (C-7, C-7'). ^{1}H NMR (299.87 MHz, DMSO-d_6) δ in ppm: 0.90–0.95 (t; *J* = 7.2 Hz; 6H; H-14, H-14'), 1.32–1.45 (sx; *J* = 7.2 Hz; 4H; H-13, H-13'), 1.58–1.67 (p; *J* = 7.2 Hz; 4H; H-12, H-12'), 3.20 (br s; 8H; H-9, H-10, H-9', H-10'), 3.37–3.41 (q; *J* = 6.6 Hz; 4H; H-11, H-11'), 4.01 (br s; 4H; H-8, H-8'), 7.81 (br s; 8H; H-2, H-3, H-5, H-6, H-2', H-3', H-5', H-6'), 9.11 (br s; 2H; 2 × NH), 9.51 (br s; 2H; 2 × NH–C_4H_9), 9.84 (br s; 2H; 2 × NH). Element. Anal. $C_{28}H_{42}N_6 \times 4HCl \times H_2O$ (626.53 g/mol) calcd. (%): C = 53.67, H = 7.67, N = 13.42, Cl = 22.68; found (%): C = 53.66, H = 7.69, N = 13.38, Cl = 22.36.

Bis[4-(*N*-pentylamidino)benzyl]piperazine tetrahydrochloride (5). After the general procedure, after column chromatography (CH_2Cl_2/MeOH/AcOH/H_2O – 70/20/5/5), a light beige powder was obtained with yield 23%; MP = 279.5–280.5 °C (decomp.). ^{1}H NMR (299.87 MHz, D_2O) δ in ppm: 0.91–0.96 (t; *J* = 6.9 Hz; 6H; H-15, H-15'), 1.37–1.47 (m; 8H; H-13, H-14, H-13', H-14'), 1.74–1.84 (p; *J* = 6.9 Hz; 4H; H-12, H-12'), 3.48–3.52 (m; 12H; H-9, H-10, H-11, H-9', H-10', H-11'), 4.46 (br s; 4H; H-8, H-8'), 7.71–7.73 (pd; *J* = 7.8 Hz; 4H; H-2, H-6, H-2', H-6'), 7.82–7.84 (pd; *J* = 7.8 Hz; 4H; H-3, H-5, H-3', H-5'). ^{13}C NMR (75.40 MHz, D_2O) δ in ppm: 13.1 (C-15, C-15'), 21.6 (C-14, C-14'), 26.4 (C-13, C-13'), 28.2 (C-12, C-12'), 43.0 (C-11, C-11'), 48.7 (C-9, C-10, C-9', C-10'), 59.6 (C-8, C-8'), 128.5 (C-3, C-5, C-3', C-5'), 130.7 (C-4, C-4'), 131.8 (C-2, C-6, C-2', C-6'), 133.5 (C-1, C-1'), 163.5 (C-7, C-7'). ^{1}H NMR (299.87 MHz, DMSO-d_6) δ in ppm: 0.87–0.92 (t; *J* = 6.9 Hz; 6H; H-15, H-15'), 1.28–1.39 (m; 8H; H-13, H-14, H-13', H-14'), 1.60–1.69 (p; *J* = 6.9 Hz; 4H; H-12, H-12'), 3.29 (br s; 8H; H-9, H-10, H-9', H-10'), 3.38–3.44 (q; *J* = 6.6 Hz; 4H;

H-11, H-11'), 4.29 (br s; 4H; H-8, H-8'), 7.83 (br s; 8H; H-2, H-3, H-5, H-6, H-2', H-3', H-5', H-6'), 9.16 (br s; 2H; 2 × NH), 9.54 (br s; 2H; 2 × NH–C_5H_{11}), 9.89 (br s; 2H; 2 NH). Element. Anal. $C_{30}H_{46}N_6$ × 4HCl × 1.5H_2O (663.59 g/mol) calcd. (%): C = 54.30, H = 7.99, N = 12.67, Cl = 21.42; found (%): C = 54.24, H = 7.79, N = 12.73, Cl = 21.15.

2,2'-Oxybis{*N*-[4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl]acetamide} (6a). White powder; yield 100%; MP = 234.5–236.0 °C. ^{1}H NMR (299.87 MHz, DMSO-d_6) δ in ppm: 2.65 (s; 6H; 2 × CH_3), 4.33 (s; 4H; H-8, H-8'), 7.85–7.88 (pd; *J* = 8.7 Hz; 4H; H-2, H-6, H-2', H-6'), 7.96–7.99 (pd; *J* = 8.7 Hz; 4H; H-3, H-5, H-3', H-5'), 10.33 (s; 2H; 2 × NH–CO). ^{13}C NMR (75.40 MHz, DMSO-d_6) δ in ppm: 12.0 (2 × CH_3), 70.8 (C-8, C-8'), 119.8 (C-2, C-6, C-2', C-6'), 121.3 (C-4, C-4'), 127.7 (C-3, C-5, C-3', C-5'), 141.1 (C-1, C-1'), 167.2 (C-7, C-7'), 168.5 (2 × C=O), 177.2 (2 × C–CH_3).

2,2'-Oxybis[*N*-(4-amidinophenyl)acetamide] dihydrochloride (6). Off white solid; yield 73%; MP > 360 °C. ^{1}H NMR (299.87 MHz, DMSO-d_6) δ in ppm: 4.35 (s; 4H; H-8, H-8'), 7.84–7.87 (pd; *J* = 9.0 Hz; 4H; H-3, H-5, H-3', H-5'), 7.93–7.96 (pd; *J* = 9.0 Hz; 4H; H-2, H-6, H-2', H-6'), 9.07 (br s; 4H; 4 × NH), 9.31 (br s; 4H; 4 × NH), 10.74 (s; 2H; 2 × NH–CO). ^{13}C NMR (75.40 MHz, DMSO-d_6) δ in ppm: 70.8 (C-8, C-8'), 119.1 (C-2, C-6, C-2', C-6'), 122.2 (C-4, C-4'), 129.2 (C-3, C-5, C-3', C-5'), 143.4 (C-1, C-1'), 164.8 (C-7, C-7'), 168.9 (2 × C=O). Element. Anal. $C_{18}H_{20}N_6O_3$ × 2HCl × 0.5H_2O (450.32 g/mol) calcd. (%): C = 48.00, H = 5.11, N = 18.67, Cl = 15.78; found (%): C = 48.19, H = 5.32, N = 18.25, Cl = 15.59.

2,2'-Sulfanediylbis{*N*-[4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl]acetamide} (7a). White powder; yield 93%; MP = 226.5–228.0 °C. ^{1}H NMR (299.87 MHz, DMSO-d_6) δ in ppm: 2.64 (s; 6H 2 × CH_3), 3.55 (s; 4H; H-8, H-8'), 7.74–7.77 (pd; *J* = 8.7 Hz; 4H; H-2, H-6, H-2', H-6'), 7.92–7.94 (pd; *J* = 8.7 Hz; 4H; H-3, H-5, H-3', H-5'), 10.42 (s; 2H 2 × NH–CO). ^{13}C NMR (75.40 MHz, DMSO-d_6) δ in ppm: 12.0 (2 × CH_3), 36.1 (C-8, C-8'), 119.3 (C-2, C-6, C-2', C-6'), 121.0 (C-4, C-4'), 127.7 (C-3, C-5, C-3', C-5'), 141.6 (C-1, C-1'), 167.2 (C-7, C-7'), 167.9 (2 × C=O), 177.1 (2 × C–CH_3).

2,2'-Sulfanediylbis[*N*-(4-amidinophenyl)acetamide] dihydrochloride (7). Light beige powder; yield 79%; MP > 360 °C. ^{1}H NMR (299.87 MHz, DMSO-d_6) δ in ppm: 3.60 (s; 4H; H-8, H-8'), 7.82 (s; 8H; H-2, H-3, H-5, H-6, H-2', H-3', H-5', H-6'), 8.96 (br s; 4H; 4 × NH), 9.25 (br s; 4H; 4 × NH), 10.84 (s; 2H; 2 × NH–CO). ^{13}C NMR (75.40 MHz, DMSO-d_6) δ in ppm: 36.1 (C-8, C-8'), 118.6 (C-2, C-6, C-2', C-6'), 121.8 (C-4, C-4'), 129.2 (C-3, C-5, C-3', C-5'), 144.0 (C-1, C-1'), 164.7 (C-7, C-7'), 168.4 (2 × C=O). Element. Anal. $C_{18}H_{20}N_6O_2S$ × 2HCl × H_2O (475.39 g/mol) calcd. (%): C = 45.47, H = 5.05, N = 17.68, S = 6.74, Cl = 14.95; found (%): C = 45.67, H = 5.03, N = 18.01, S = 6.99, Cl = 14.92.

***N*^{1},*N*^{4}-Dimethyl-*N*^{1},*N*^{4}-bis[4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl]butanediamide (8a).** Beige powder; yield 83%; MP = 199.5–200.5 °C. ^{1}H NMR (299.87 MHz, DMSO-d_6) δ in ppm: 2.36 (br s; 4H; H-8, H-8'), 2.68 (s; 6H; 2 × H_3C–C), 3.20 (s; 6H; 2 × H_3C–N), 7.51–7.54 (pd; *J* = 8.4 Hz; 4H; H-2, H-6, H-2', H-6'), 8.03–8.06 (pd; *J* = 8.4 Hz; 4H; H-3, H-5, H-3', H-5'). ^{13}C NMR (75.40 MHz, DMSO-d_6) δ in ppm: 12.0 (2 × H_3C–C), 29.2 (C-8, C-8'), 36.7 (2 × H_3C–N), 124.9 (C-4, C-4'), 127.9 (C-2, C-6, C-2', C-6'), 128.0 (C-3, C-5, C-3', C-5'), 146.4 (C-1, C-1'), 167.0 (C-7, C-7'), 170.8 (2 × C=O), 177.6 (2 × C-CH_3).

***N*^{1},*N*^{4}-Dimethyl-*N*^{1},*N*^{4}-bis(4-amidinophenyl)butanediamide dihydrochloride (8).** Light beige powder; yield 81%; MP = 255.0–256.0 °C (decomp.). ^{1}H NMR (299.87 MHz, DMSO-d_6) δ in ppm: 2.42 (s; 4H; H-8, H-8'), 3.22 (s; 6H; 2 × H_3C–N), 7.60–7.62 (pd; *J* = 8.4 Hz; 4H; H-2, H-6, H-2', H-6'), 7.91–7.94 (pd; *J* = 8.4 Hz; 4H; H-3, H-5, H-3', H-5'), 9.28 (br s; 4H; 4 × NH), 9.47 (br s; 4H; 4 × NH). ^{13}C NMR (75.40 MHz, DMSO-d_6) δ in ppm: 29.7 (C-8, C-8'), 37.2 (2 × H_3C–N), 126.7 (C-4, C-4'), 127.7 (C-2, C-6, C-2', C-6'), 129.8 (C-3, C-5, C-3', C-5'), 148.9 (C-1, C-1'), 165.4 (C-7, C-7'), 171.3 (2 × C=O). Element. Anal. $C_{20}H_{24}N_6O_2$ × 2HCl × 0.5H_2O (462.38 g/mol) calcd. (%): C = 51.95, H = 5.84, N = 18.18, Cl = 15.37; found (%): C = 51.61, H = 6.18, N = 18.31, Cl = 15.14.

***N*^{1},*N*^{5}-Dimethyl-*N*^{1},*N*^{5}-bis[4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl]pentanediamide (9a).** Off white powder; yield 94%; MP = 175.5–176.5 °C. ^{1}H NMR (299.87 MHz, DMSO-d_6) δ in ppm: 1.63–1.72 (p; *J* = 6.9 Hz; 2H; H-9), 2.10 (br s; 4H; H-8, H-8'), 2.67 (s; 6H; 2 × H_3C–C), 3.17 (s; 6H; 2 × H_3C–N), 7.42–7.45 (pd; *J* = 8.4 Hz; 4H; H-2, H-6, H-2', H-6'), 7.98–8.01 (pd; *J* = 8.4 Hz; 4H; H-3, H-5', H-3', H-5'). ^{13}C NMR (75.40 MHz, DMSO-d_6) δ in ppm: 12.0 (2 × H_3C–C), 20.8 (C-9), 32.7 (C-8, C-8'), 36.7 (2 × H_3C–N), 124.6 (C-4, C-4'), 127.8 (C-2, C-6, C-2', C-6'), 128.0 (C-3, C-5, C-3', C-5'), 146.4 (C-1, C-1'), 167.0 (C-7, C-7'), 171.2 (2 × C=O), 177.5 (2 × H_3C–C).

***N*^{1},*N*^{5}-Dimethyl-*N*^{1},*N*^{5}-bis(4-amidinophenyl)pentanediamide dihydrochloride (9).** White powder; yield 86%; MP = 212.0–215.0 °C (decomp.). ^{1}H NMR (299.87 MHz, DMSO-d_6) δ in ppm: 1.66–1.75 (p; *J* = 7.2 Hz; 2H; H-9), 2.20 (br s; 4H; H-8, H-8'), 3.21 (s; 6H; 2 × H_3C–N), 7.54–7.57 (pd; *J* = 8.6 Hz; 4H; H-2, H-6, H-2', H-6'), 7.90–7.93 (pd; *J* = 8.6 Hz; 4H; H-3, H-5, H-3', H-5'), 9.27 (br s; 4H; 4 × NH), 9.45 (br s; 4H; 4 × NH). ^{13}C NMR (75.40 MHz, DMSO-d_6) δ in ppm: 20.4 (C-9), 32.8 (C-8, C-8), 36.8 (2 × H_3C–N), 125.9 (C-4, C-4'), 127.1 (C-2, C-6, C-2', C-6'), 129.3 (C-3, C-5, C-3', C-5'), 148.5 (C-1, C-1'), 164.8 (C-7, C-7'), 171.3 (2 × C=O). Element. Anal. $C_{21}H_{26}N_6O_2$ × 2HCl × 1.5H_2O (494.42 g/mol) calcd. (%): C = 51.01, H = 6.28, N = 17.00, Cl = 14.37; found (%): C = 50.73; H = 6.29, N = 16.59, Cl = 14.63.

***N*^{1},*N*^{6}-Dimethyl-*N*^{1},*N*^{6}-bis[4-(5-methyl-1,2,4-oxadiazol-3-yl)phenyl]hexanediamide (10a).** Off white powder; yield 99%; MP = 143.5–145.5 °C. ^{1}H NMR (299.87 MHz, DMSO-d_6) δ in ppm: 1.39 (br s; 4H; H-9, H-9'), 2.04 (br s; 4H; H-8, H-8'), 2.68 (s; 6H; 2 × H_3C–C), 3.18 (s; 6H; 2 × H_3C–N), 7.44–7.46 (pd; *J* = 8.4 Hz; 4H; H-2, H-6, H-2', H-6'), 7.99–8.02 (pd; *J* = 8.4 Hz; 4H; H-3, H-5, H-3', H-5'). ^{13}C NMR (75.40 MHz, DMSO-d_6) δ in ppm: 12.0 (2 × H_3C–C), 24.2 (C-9, C-9'), 33.0 (C-8, C-8'), 36.7 (2 × H_3C–N), 124.8 (C-4, C-4'), 127.8 (C-2, C-6, C-2', C-6'), 128.0 (C-3, C-5, C-3', C-5'), 146.5 (C-1, C-1'), 167.00 (C-7, C-7'), 171.3 (2 × C=O), 177.5 (2 × H_3C–C).

***N*^{1},*N*^{6}-Dimethyl-*N*^{1},*N*^{6}-bis(4-amidinophenyl)hexanediamide dihydrochloride (10).** White powder; yield 88%; MP = 233.5–235.5 °C (decomp.). ^{1}H NMR (299.87 MHz, DMSO-d_6) δ in ppm: 1.40 (br s; 4H; H-9, H-9'), 2.15 (br s; 4H; H-8, H-8'), 3.21 (s; 6H; 2 × H_3C–N), 7.55–7.58 (pd; *J* = 8.6 Hz; 4H; H-2, H-6, H-2', H-6'), 7.87–7.90 (pd; *J* = 8.6 Hz; 4H; H-3, H-5, H-3', H-5'), 9.18 (br s; 4H; 4 × NH), 9.41 (br s; 4H; 4 × NH). ^{13}C NMR (75.40 MHz, DMSO-d_6) δ in ppm: 24.3 (C-9, C-9'), 33.3 (C-8, C-8'), 36.7 (2 × H_3C–N), 125.8 (C-4, C-4'), 127.1 (C-2, C-6, C-2', C-6'), 128.6 (C-3, C-5, C-3', C-5'), 147.5 (C-1, C-1'), 164.7 (C-7, C-7'), 171.3 (2 × C=O). Element. Anal. $C_{22}H_{28}N_6O_2$ × 2HCl (481.42 g/mol) calcd. (%): C = 54.89, H = 6.24, N = 17.46, Cl = 14.76; found (%): C = 54.74, H = 5.96, N = 17.40, Cl = 14.67.

Preparation of substrates for synthesis of bisbenzonitriles 11a–21a.

4-chlorobenzonitrile **11aS1** as intermediate to synthesis bisbenzonitrile **11a** was based on a previously published paper[28], and prepared as follows: 4-chlorobenzaldehyde 100 mmol (14.06 g) was refluxed for 1 h together with hydroxylamine hydrochloride 115 mmol (7.89 g), anhydrous sodium acetate (15 g) and pure formic acid (100 ml). The reaction was protected from atmospheric moisture. Then the cooled reaction mixture was poured into ice-water (1000 ml). The precipitated solid was filtered off, washed with water and dried to give white crystals; yield 85%; MP. 92.0–93.5 °C.[29]

4-Chloro-3-nitrobenzonitrile **15aS1** as intermediate to synthesis of bisbenzonitrile **15a** was obtained as follows: 4-chlorobenzonitrile 50 mmol (6.88 g) was slowly added in small amounts to cold (0 °C) stirred solution of concentrated sulfuric acid (50 ml) and potassium nitrate 100 mmol (11.01 g). After adding whole 4-chlorobenzonitrile the reaction mixture was stirred at 3–5 °C for 3 h and the poured into ice-water (500 ml). Precipitated solid was filtered off, washed with water and dried. After crystallization (EtOH/H_2O – 1/1) yellow solid of **15aS1** was obtained; yield 72%; MP. 98.5–100.0 °C.[30] ^{1}H NMR (299.87 MHz, DMSO-d_6) δ in ppm: 8.02–8.05 (d; *J* = 8.4 Hz; 1H; H-6), 8.19–8.23 (dd; J_1 = 2.1 Hz, J_2 = 8.4 Hz; 1H; H-5), 8.70–8.71 (d; *J*=2.1 Hz; 1H; H-3). ^{13}C NMR (75.40 MHz, DMSO-d_6) δ in ppm: 111.5 (C-4), 116.3 (C-7), 129.6 (C-6), 130.2 (C-1), 133.0 (C-5), 137.2 (C-3), 147.8 (C-2).

N,*N*-Bis(2-chloroethyl)benzenesulfonamide **19aS1** as intermediate to synthesis of bisbenzonitrile **19a** was based on the previously published synthesis[31], using an appropriate benzenesulfonyl chloride.

N,N-Bis(2-chloroethyl)-*N*-ethylamine hydrochloride **21aS1** as intermediate to synthesis of bisbenzonitrile **21a** was synthesized from *N*-ethyldiethanolamine 5 mmol (0.66 g) and thionyl chloride 20 mmol (2.38 g) that were refluxed while stirring together with $CHCl_3$ (15 ml) for 3 hours and then evaporated to give solid; yield 92%.[32]

1,5-Bis(4-cyanophenylthio)-3-oxapentane (11a). 4-chlorobenzonitrile 30 mmol (4.12 g) and bis(2-mercaptoethyl)ether 15 mmol (2.08 g) was stirred at 115.0–120.0 °C for 2 h together with anhydrous K_2CO_3 45 mmol (6.25 g) and *N*-methylpyrrolidone 20 ml, then cooled to room temperature and poured into cold water (150 ml). The precipitated solid was filtered off and dried. After crystallization with a small amount of ethanol, a white solid of **11a** was obtained; yield 82%; MP. 81.0–83.0 °C. ^{1}H NMR (299.87 MHz, DMSO-d_6) δ in ppm: 3.25 (t; *J*=6.3 Hz; 4H; H-8, H-8'), 3.67 (t; *J* = 6.3 Hz; 4H; H-9, H-9'), 7.45–7.48 (m; 4H; H-2, H-6, H-2', H-6'), 7.69–7.73 (m; 4H; H-3, H-5, H-3', H-5'). ^{13}C NMR (75.40 MHz, DMSO-d_6) δ in ppm: 30.7 (C-8, C-8'), 68.4 (C-9, C-9'), 107.0 (C-4, C-4'), 118.8 (C-7, C-7'), 126.7 (C-2, C-6, C-2', C-6'), 132.4 (C-3, C-5, C-3', C-5'), 144.4 (C-1, C-1').

1,5-Bis(4-amidinophenylthio)-3-oxapentane dihydrochloride (11). After the general procedure, the solvent was evaporated under the reduced pressure. The solid residue was additionally dried for 3 h at 100 °C to furnish the pure colourless crystals of **11**; yield 52%; MP: 266.0–269.0 °C (decomp.). ^{1}H NMR (299.87 MHz, DMSO-d_6) δ in ppm: 3.29 (t; *J* = 6.3 Hz; 4H; H-8, H-8'), 3.69 (t; *J* = 6.3 Hz; 4H; H-9, H-9'), 7.52 (d; *J* = 4.2 Hz; 4H; H-2, H-6, H-2', H-6'), 7.84 (d; *J* = 4.2 Hz; 4H; H-3, H-5, H-3', H-5'), 9.29 (br s; 4H; 4 × NH), 9.47 (br s; 4H; 4 × NH). ^{13}C NMR (75.40 MHz, DMSO-d_6) δ in ppm: 30.7 (C-8, C-8'), 68.5 (C-9, C-9'), 123.8 (C-4, C-4'), 126.2 (C-2, C-6, C-2', C-6'), 128.5 (C-3, C-5,C-3', C-5'), 144.7 (C-1, C-1'), 164.8 (C-7, C-7'). Element. Anal. $C_{18}H_{22}N_4OS_2$ × 2HCl (447.44 g/mol) calcd. (%): C = 48.32, H = 5.41, N = 12.52, S = 14.33; found (%): C = 48.16, H = 5.62, N = 12.49, S = 14.01.

1,5-Bis[4-(4,5-dihydro-2-imidazolyl)phenylthio]-3-oxapentane dihydrochloride (12). The crude imidate obtained from 5 mmol (1.70 g) of **11a** was suspended in 25 ml of anhydrous ethanol, then 1,2-ethanediamine 10 mmol (0.60 g) was added and the whole mixture was stirred in a vessel protected from moisture for 24 h at ambient temperature. After that the reaction mixture was refluxed for 3 h. The solvent was evaporated under vacuum. The semisolid residue was triturated with 20 ml of 2% aq. solution of NaOH to give a white microcrystalline solid of free amidine. The solid was filtered off, thoroughly washed with water, and dried under vacuum over anhydrous $CaCl_2$. The dry amidine was suspended in 6 ml of anhydrous ethanol, 1 ml of the saturated solution of HCl in ethanol was added, and the whole mixture was refluxed for several minutes. The solvent was evaporated under the reduced pressure. The solid residue was dried for 3 h at 100 °C to furnish the pure colourless crystals of **12**; yield 62%; MP: 278–282 °C (decomp.). ^{1}H NMR (299.87 MHz, DMSO-d_6) δ in ppm: 3.30 (t; *J* = 6.3 Hz; 4H; H-8, H-8'), 3.70 (t; *J* = 6.3 Hz; 4H; H-9, H-9'), 3.97 (s; 8H; H-10, H-11, H-10', H-11'), 7.54 (d; *J* = 8.7 Hz; 4H; H-2, H-6, H-2', H-6'), 8.03 (d; *J* = 8.7 Hz; 4H; H-3, H-5, H-3', H-5'), 10.85 (br s; 4H; 2 × NH). ^{13}C NMR (75.40 MHz, DMSO-d_6) δ in ppm: 30.6 (C-8, C-8'), 44.1 (C-10, C-11, C-10', C-11'), 68.4 (C-9, C-9'), 118.0 (C-4, C-4'), 126.2 (C-2, C-6, C-2', C-6'), 129.0 (C-3, C-5, C-3', C-5'), 146.0 (C-1, C-1'), 164.0 (C-7, C-7'). Element. Anal. $C_{22}H_{26}N_4OS_2$ × 2HCl (499.52 g/mol) calcd. (%): C = 52.90, H = 5.65, N = 11.22, S = 12.84; found (%): C = 52.69, H = 5.73, N = 12.28, S = 12.60.

1,5-Bis(4-cyano-2-nitrophenoxy)-3-oxapentane (13a). 1,5-Bis(4-cyanophenoxy)-3-oxapentane[33] 20 mmol (6.28 g) was dissolved in trifluoroacetic acid 75 ml and the solution of concentrated nitric acid 11 ml in acetic anhydride 17 ml was dropped into the dissolved 1,5-bis(4-cyanophenoxy)-3-oxapentane. The reaction was protected from atmospheric moisture and stirred at 45 °C for 24 h, and then diluted with ice-water 700 ml to obtain a cream solid crude product. After column chromatography (CH_2Cl_2/MeOH – 98/2) a pale yellow solid of pure **13a** was obtained; yield 60%; MP. 173.0–174.0 °C. ^{1}H NMR (299.87 MHz, DMSO-d_6) δ in ppm: 3.84 (t; *J* = 4.5 Hz; 4H; H-9, H-9'), 4.40 (t; *J* = 4.5 Hz; 4H; H-8, H-8'), 7.54 (d; *J* = 4.2 Hz; 2H; H-6, H-6'), 8.07–8.11 (m; 2H; H-5, H-5'), 8.44 (d; *J* = 2.1 Hz; 2H; H-3, H-3'). ^{13}C NMR (75.40 MHz, DMSO-d_6) δ in ppm: 68.6 (C-9, C-9'), 69.9 (C-8, C-8'), 103.0 (C-4, C-4'), 116.4 (C-6, C-6'), 117.2 (C-7, C-7'), 129.2 (C-3, C-3'), 138.0 (C-5, C-5'), 139.5 (C-2, C-2'), 154.3 (C-1.C-1').

1,5-Bis(4-amidino-2-nitrophenoxy)-3-oxapentane dihydrochloride (13). After the general procedure, the solid residue was filtered off, washed with ethanol and dried. The crude product was suspended in acetone (25 ml) and intensively stirred under reflux for 10 minutes, then cooled to RT, filtered off and dried to give a pale yellow solid of **13**; yield 41%; MP. 237.0–238.5 °C (decomp.). ^{1}H NMR (299.87 MHz, DMSO-d_6) δ in ppm: 3.88 (t; *J* = 4.2 Hz; 4H; H-9, H-9'), 4.44 (t; *J* = 4.2 Hz; 4H; H-8, H-8'), 7.62 (d; *J* = 4.5 Hz; 2H; H-6, H-6'), 8.16 (dd; J_1 = 2.1 Hz, J_2 = 8.4 Hz; 2H; H-5, H-5'), 8.45 (d; *J* = 2.1 Hz; 2H; H-3, H-3'), 9.31 (br s; 4H; 4 × NH), 9.54 (br s; 4H; 4 × NH). ^{13}C NMR (75.40 MHz, DMSO-d_6) δ in ppm: 68.6 (C-9,C-9'), 69.9 (C-8, C-8'), 115.6 (C-6,C-6'), 119.6 (C-4, C-4'), 125.5 (C-3, C-3'), 134.2 (C-5, C-5'), 138.9 (C-2, C-2'), 154.9 (C-1, C-1'), 163.3 (C-7, C-7'). Element. Anal. $C_{18}H_{20}N_6O_7$ × 2HCl (505.31 g/mol) calcd. (%): C = 42.78, H = 4.39, N = 16.63; found (%): C = 42.63, H = 4.51, N = 16.72.

1,5-Bis(2-amino-4-cyanophenoxy)-3-oxapentane (14a). 1,5-Bis(4-cyano-2-nitrophenoxy)-3-oxapentane **13a** 4 mmol (1.6 g) together with ethanol 30 ml, ethyl acetate 20 ml and Pd/C (10% Pd, 25% w/w) 0.15 g were reacted for 24 h under 2 atm. of hydrogen while stirring. Then ethyl acetate 40 ml was added and the catalyst was filtered off followed by evaporation of the solvent to yield a brown solid of crude product. After crystallization from ethanol, a light-brown solid of pure **14a** was obtained; yield 78%; MP. 143.5–144°C. ^{1}H NMR (299.87 MHz, DMSO-d_6) δ in ppm: 3.87 (t; *J* = 4.5 Hz; 4H; H-9, H-9'), 4.18 (t; *J* = 4.5 Hz; 4H; H-8, H-8'), 5.16 (s; 4H; 2 × NH_2), 6.92 (br s; 2H; H-3, H-3'), 6.95 (br s; 4H; H-5, H-6, H-5', H-6'). ^{13}C NMR (75.40 MHz, DMSO-d_6) δ in ppm: 68.0 (C-8, C-8'), 68.9 (C-9, C-9'), 103.0 (C-4, C-4'), 112.0 (C-6, C-6'), 115.2 (C-3, C-3'), 119.9 (C-7, C-7'), 120.9 (C-5, C-5'), 138.9 (C-2, C-2'), 148.9 (C-1, C-1').

1,5-Bis(4-amidino-2-aminophenoxy)-3-oxapentane tetrahydrochloride (14). Following the general procedure, the solid residue was filtered off, washed with ethanol and dried. The crude product was suspended in acetone (25 ml) and intensively stirred under reflux for 10 minutes, then cooled to RT, filtered off and dried to give a light-brown solid of **14**; yield 33%; MP = 219.0–222.0 °C. ^{1}H NMR (299.87 MHz, DMSO-d_6) δ in ppm: 3.93 (t; *J* = 4.1 Hz; 4H; H-9, H-9'), 4.29 (t; *J* = 4.1 Hz; 4H; H-8, H-8'), approx. 4.60 (very br s; 6H; 2 × NH_2 × HCl), 7.20–7.23 (m; 2H; H-3, H-3'), 7.40–7.43 (m ; 4H; H-5, H-6, H-5', H-6'), 9.07 (br s; 4H; 4 × NH), 9.26 (br s; 4H; 4 × NH_2). ^{13}C NMR (75.40 MHz, DMSO-d_6) δ in ppm: 68.7 (C-8, C-8'), 68.9 (C-9, C-9'), 112.4 (C-3, C-3'), 117.4 (C-5, C-5'), 120.4 (C-4, C-4'), 122.6 (C-6, C-6'), 130.8 (C-2, C-2'), 152.4 (C-1, C-1'), 165.3 (C-7, C-7'). Element. Anal. $C_{18}H_{24}N_6O_3$ × 4HCl × H_2O (536.29 g/mol) calcd. (%): C = 40.31, H = 5.64, N = 15.67, Cl = 26.44; found (%): C = 40.51, H = 5.69, N = 15.43, Cl = 26.02.

1,5-Bis[(4-cyano-2-nitrophenyl)amino]-3-oxapentane (15a). 4-chloro-3-nitrobenzonitrile (**15aS1**) 10 mmol (1.83 g), 3-oxa-1,5-pentanediamine dihydrochloride 5 mmol (0.88 g), K_2CO_3 30 mmol (4.14 g) and DMSO 15 ml were stirred together at 125 °C for 3 h and the poured into water (150 ml). The precipitated solid was filtered off and dried, and crystallization from ethanol with hot filtering was performed. After column chromatography yellow solid of **15a** was obtained; yield 46%; MP = 187.0–188.0 °C. ^{1}H NMR (299.87 MHz, $CDCl_3$) δ in ppm: 3.50–3.56 (q; *J* = 2.2 Hz; 4H; H-8, H-8'), 3.78 (t; *J* = 5.1 Hz; 4H; H-9, H-9'), 6.85–6.89 (d; *J* = 9.3 Hz; 2H; H-6, H-6'), 7.52–7.56 (m; 2H; H-5, H-5'), 8.44–8.45 (*J* = 2.1 Hz; 2H; H-3, H-3'), 8.53 (br s; 2H; 2 × NH). ^{13}C NMR (75.40 MHz, $CDCl_3$) δ in ppm: 43.0 (C-8, C-8'), 69.2 (C-9, C-9'), 98.8 (C-4,C-4'), 114.9 (C-6, C-6'), 118.1 (C-7, C-7'), 131.9 (C-1, C-1'), 132.4 (C-5, C-5'), 137.9 (C-3, C-3'), 147.3 (C-2, C-2').

1,5-Bis[(4-amidino-2-nitrophenyl)amino]-3-oxapentane dihydrochloride (15). After the general procedure, a yellow solid of **15** was filtered off and dried. To improve efficiency, the remaining solution was evaporated and the resultant solid was refluxed with a small amount of ethanol (4–5 ml) for 15 minutes and after cooling, the precipitated solid was filtered off. A yellow solid of **15** was obtained; yield 73%; MP = 286.0–287.5 °C. ^{1}H NMR (299.87 MHz, DMSO-d_6) δ in ppm: 3.59–3.68 (m; 4H; H-8, H-8'), 3.74–3.76 (m; 4H; H-9, H-9'), 7.27–7.31 (d; *J* = 9.3 Hz; 2H; H-6, H-6'), 7.94–7.99 (dd; J_1 = 2.1, J_2 = 9.3 Hz; 2H; H-5, H-5'), 8.62 (t; *J* = 5.1 Hz; 2H; 2 × NH), 8.70–8.71 (d; *J* = 2.4 Hz; 2H; H-3, H-3'), 9.03 (br s; 4H; 4 × NH), 9.33 (br s; 4H; 4 × NH). ^{13}C NMR (75.40 MHz, DMSO-d_6) δ in ppm: 42.3 (C-8, C-8'), 68.3 (C-9, C-9'), 113.1 (C-6, C-6'), 115.2 (C-4, C-4'), 127.9 (C-5, C-5'), 130.5 (C-3, C-3'), 134.5 (C-2, C-2'), 147.7 (C-1, C-1'), 163.2 (C-7, C-7'). Element. Anal. $C_{18}H_{22}N_8O_5$ × 2HCl (503.35 g/mol) calcd. (%): C = 42.95, H = 4.81, N = 22.26; found (%): C = 42.82, H = 4.91, N = 22.03.

1,5-Bis[(2-amino-4-cyanophenyl)amino]-3-oxapentane (16a). 1,5-Bis[(4-cyano-2-nitrophenyl)amino]-3-oxapentane (**15a**) 2.5 mmol (1.0 g) together with EtOH 20 ml, ethyl acetate 40 ml and 0.1 g of Pd/C (10% Pd, 25% w/w) were reduced for 24 h under 2 atm. of hydrogen while stirring, then the mixture was diluted with 200 ml of acetone and catalyst was filtered off, and the resulting solution was evaporated to give a grey-green solid. After crystallization from propanol, a grey solid of **16a** was obtained; yield 72%; MP = 198.5–200.0 °C. ^{1}H NMR (299.87 MHz, DMSO-d_6) δ in ppm: 3.28–3.35 (m; 4H; H-8, H-8'), 3.64 (t;

J = 5.7 Hz; 4H; H-9, H-9'), 4.96 (br s; 4H; 2 × NH_2) , 5.38 (t; *J* = 5.4 Hz; 2H; 2 × NH), 6.48–6.51 (d; *J* = 8.1 Hz; 2H; H-6, H-6'), 6.78–6.79 (d; *J* = 2.1 Hz; 2H; H-3, H-3'), 6.90–6.93 (dd; J_1 = 1.6 Hz, J_2 = 8.2 Hz; 2H; H-5, H-5'). ^{13}C NMR (75.40 MHz, DMSO-d_6) δ in ppm: 42.6 (C-8, C-8'), 68.5 (C-9, C-9'), 96.7 (C-4, C-4'), 108.6 (C-6, C-6'), 115.0 (C-3, C-3'), 121.0 (C-7, C-7'), 122.8 (C-5, C-5'), 135.2 (C-2, C-2'), 139.9 (C-1, C-1').

1,5-Bis[(4-amidino-2-aminophenyl)amino]-3-oxapentane tetrahydrochloride (16). After the general procedure, a grey solid of **16**, filtered off and dried under reduced pressure over $CaCl_2$ for 5 hours (it was not dried at higher temperature because the solid changed colour) was obtained; Yield 57%; MP = 224.0–226.0 °C. ^{1}H NMR (299.87 MHz, DMSO-d_6) δ in ppm: 3.39–3.41 (d; *J* = 4.8 Hz; 4H; H-8, H-8'), 3.72 (t; *J* = 4.8 Hz; 4H; H-9, H-9'), approx. 5.00 (very br s; 8H; 2 × NH, 2 × NH_2 × HCl); 6.80–6.83 (d; *J* = 8.4 Hz; 2H; H-6, H-6'), 7.39 (s; 2H; H-3, H-3'), 7.44–7.47 (d; *J* = 8.7 Hz; 2H; H-5, H-5'), 8.70 (br s; 4H; 4 × NH), 8.98 (br s; 4H; 4 × NH_2). ^{13}C NMR (75.40 MHz, DMSO-d_6) δ in ppm: 42.9 (C-8, C-8'), 68.3 (C-9, C-9'), 111.0 (C-4, C-4'), 114.1 (C-6, C-6'), 120.3 (C-3, C-3'), 122.2 (C-5, C-5'), 127.8 (C-2, C-2'), 145.6 (C-1, C-1'), 164.6 (C-7, C-7'). Element. Anal. $C_{18}H_{26}N_8O$ × 4HCl × $3H_2O$ (570.35 g/mol) calcd. (%): C = 37.91, H = 6.36, N = 19.65, Cl = 24.86; found (%): C = 38.22, H = 6.45, N = 19.28, Cl = 24.49.

1,5-Bis(4-cyano-2,6-dimethylphenoxy)pentane (17a). 4-Hydroxy-3,5-dimethylbenzonitrile 6 mmol (0.88 g) and 1,5-dibromopentane 3 mmol (0.69 g) was stirred at 120 °C for 1 h together with K_2CO_3 12 mmol (1.66 g) and *N*-methylpyrrolidone 10 ml, then poured into cold water (100 ml). The precipitated solid was filtered off and dried. After column chromatography, a white solid of **17a** was obtained; yield 92%; MP = 118.0–120.0 °C. ^{1}H NMR (299.87 MHz, DMSO-d_6) δ in ppm: 1.66–1.74 (m; 2H; CH_2), 1.79–1.88 (m; 4H; H-9, H-9'), 2.25 (s; 12H; 4 × CH_3), 3.84 (t; *J* = 6.0 Hz; 4H; H-8, H-8'), 7.54 (s; 4H; H-3, H-5, H-3', H-5'). ^{13}C NMR (75.40 MHz, DMSO-d_6) δ in ppm: 15.7 (4 × CH_3), 22.2 (CH_2), 29.6 (C-9, C-9'), 71.9 (C-8, C-8'), 106.1 (C-4, C-4'), 118.9 (C-7, C-7'), 132.5 (C-2, C-6, C-2', C-6'), 132.7 (C-3, C-5, C-3', C-5'), 159.7 (C-1, C-1').

1,5-Bis(4-amidino-2,6-dimethylphenoxy)pentane dihydrochloride (17). After the general procedure, the solid was filtered off and dried. A white solid of **17** was obtained; yield 77%; MP = 276.0–278.0 °C. ^{1}H NMR (299.87 MHz, DMSO-d_6) δ in ppm: 1.70–1.77 (m; 2H; CH_2), 1.81–1.91 (m; 4H; H-9, H-9'), 2.30 (s; 12H; 4 × CH_3), 3.86 (t; *J* = 6.0 Hz; 4H; H-8, H-8'), 7.58 (s; 4H; H-3, H-5, H-3', H-5'), 9.00 (br s; 4H; 4 × NH), 9.21 (br s; 4H; 4 × NH). ^{13}C NMR (75.40 MHz, DMSO-d_6) δ in ppm: 16.0 (4 × CH_3), 22.2 (CH_2), 29.6 (C-9, C-9'), 71.9 (C-8, C-8'), 122.8 (C-4, C-4'), 128.8 (C-2, C-6, C-2',C-6'), 131.4 (C-3, C-5, C-3', C-5'), 160.1 (C-1, C-1'), 165.1 (C-7, C-7'). Element. Anal. $C_{23}H_{32}N_4O_2$ × 2HCl (469.45 g/mol) calcd. (%): C = 58.85, H = 7.30, N = 11.93; found (%): C = 58.93, H = 7.19, N = 11.72.

1,5-Bis(4-cyano-2,6-dimethylphenoxy)-3-oxapentane (18a). 4-Hydroxy-3,5-dimethylbenzonitrile 6 mmol (0.88 g) and bis-2-chloroethyl ether 3 mmol (0.43 g) were stirred at 120 °C for 2 h together with K_2CO_3 12 mmol (1.66 g) and *N*-methylpyrrolidone 10 ml, then poured into cold water (100 ml). The precipitated solid was filtered off and dried. After column chromatography, a white solid of **18a** was obtained; yield 86%; MP = 155.0–156.5 °C. ^{1}H NMR (299.87 MHz, DMSO-d_6) δ in ppm: 2.22 (s; 12H; 4 × CH_3), 3.77–3.80 (m; 4H; H-8, H-8'), 3.97–4.00 (m; 4H; H-9, H-9'), 7.52 (s; 4H; H-3, H-5, H-3', H-5'). ^{13}C NMR (75.40 MHz, DMSO-d_6) δ in ppm: 15.7 (4 × CH_3), 69.8 (C-8, C-8'), 71.6 (C-9, C-9'), 106.1 (C-4, C-4'), 118.9 (C-7, C-7'), 132.6 (C-2, C-3, C-5, C-6, C-2', C-3', C-5', C-6'), 159.5 (C-1, C-1').

1,5-Bis(4-amidino-2,6-dimethylphenoxy)-3-oxapentane dihydrochloride (18). After the general procedure, the resultant solid was filtered off and dried at 95 °C for 2 h. A white solid of **18** was obtained; yield 68%; MP = 300.0–301.0 °C. ^{1}H NMR (299.87 MHz, DMSO-d_6) δ in ppm: 2.50 (s; 12H; 4 × CH_3), 4.00–4.03 (m; 4H; H-8, H-8'), 4.18–4.21 (m; 4H; H-9, H-9'), 7.78 (s; 4H; H-3, H-5, H-3', H-5'), 9.29 (br s; 4H; 4 × NH), 9.44 (br s; 4H; 4 × NH). ^{13}C NMR (75.40 MHz, DMSO-d_6) δ in ppm: 16.0 (4 × CH_3), 69.8 (C-8, C-8'), 71.6 (C-9, C-9'), 122.9 (C-4, C-4'), 128.7 (C-2, C-6, C-2', C-6'), 131.5 (C-3, C-5, C-3', C-5'). 160.0 (C-1, C-1'), 165.1 (C-7, C-7'). Element. Anal. $C_{22}H_{30}N_4O_3$ × 2HCl × $0.5H_2O$ (480 g/mol) calcd. (%): C = 54.95, H = 6.24, N = 11.65; found (%): C = 55.00, H = 6.63, N = 11.66.

***N*,*N*-Bis[2-(4-cyano-2,6-dimethylphenoxy)ethyl]benzenesulfonamide (19a).** 3,5-Dimethyl-4-hydroxybenzonitrile 6 mmol (0.88 g) and *N*,*N*-bis(2-chloroethyl)benzenesulfonamide (**19aS1**) 3 mmol (0.85 g) were stirred at 130 °C for 8 hours together with K_2CO_3 12 mmol (1.66 g) and *N*-methylpyrrolidone (10 ml), and then poured into ice-water (100 ml). The solid was isolated by extraction with CH_2Cl_2 (3 × 50 ml). After column chromatography, a yellow oil was obtained and then dry Et_2O was added and kept at 6 °C to give a yellow crystal solid of **19a**; yield 34%; MP = 110.5–113.0 °C. ^{1}H NMR (299.87 MHz, DMSO-d_6) δ in ppm: 2.15 (s; 12H; 4 × CH_3), 3.71 (t; *J* = 5.7 Hz; 4H; H-9, H-9'), 3.95 (t; *J* = 5.7 Hz; 4H; H-8, H-8'), 7.50 (s; 4H; H-2, H-6, H-2', H-6'), 7.58–7.64 (m; 2H; H-3", H-5"), 7.66–7.72 (m; 1H; H-4"), 7.88–7.92 (m; 2H; H-2", H-6"). ^{13}C NMR (75.40 MHz, DMSO-d_6) δ in ppm: 15.6 (4 × CH_3), 48.5 (C-9, C-9'), 70.6 (C-8, C-8'), 106.4 (C-1, C-1'), 118.8 (C-7, C-7'), 127.0 (C-2", C-6"), 129.4 (C-3", C-5"), 132.2 (C-3, C-5, C-3', C-5'), 132.7 (C-2, C-6, C-2' C-6'), 133.1 (C-4"), 139.0 (C-1"), 159.1 (C-1, C-1').

***N*,*N*-Bis[2-(4-amidino-2,6-dimethylphenoxy)ethyl]beznenesulfonamide dihydrochloride (19).** After the general procedure, resultant solution was evaporated to give a cream solid of **19**. The solid was dried *in vacuo* over $CaCl_2$. Note: it could not be dried at higher temperature, because its colour changed over 70 °C; yield 60%; MP = 196.0–200.0 °C. ^{1}H NMR (299.87 MHz, DMSO-d_6) δ in ppm: 2.22 (s; 12H; 4 × CH_3), 3.76 (t; *J* = 5.4 Hz; 4H; H-9, H-9'), 3.99 (t; *J* = 5.4 Hz; 4H; H-8, H-8'), 7.56 (s; 4H; H-2, H-6, H-2', H-6'), 7.60–7.65 (m; 2H; H-3" H-5"), 7.68–7.73 (m; 1H; H-4"), 7.90–7.92 (m; 2H; H-2", H-6"), 9.04 (br s; 4H; 4 × NH), 9.22

(br s; 4H; 4 × NH). ^{13}C NMR (75.40 MHz, DMSO-d_6) δ in ppm: 16.3 (4 × CH_3), 49.1 (C-9, C-9'), 71.0 (C-8, C-8'), 123.6 (C-1, C-1'), 127.4 (C-3, C-5, C-3', C-5'), 129.2 (C-2", C-6"), 129.9 (C-3", C-5"), 131.7 (C-2, C-6, C-2', C-6'), 133.5 (C-4"), 139.5 (C-1"), 160.0 (C-4, C-4'), 165.4 (C-7, C-7'). The large amount of water molecules in crystal structure of **19** was confirmed also in ^{1}H NMR – strong signal at 3.35 ppm (water from DMSO together with water of crystallization). Element. Anal. $C_{28}H_{35}N_5O_4S$ × 2HCl × 10H_2O (790 g/mol) calcd. (%): C = 42.53, H = 7.27, N = 8.86, S = 4.05; found (%): C = 42.57, H = 7.22, N = 8.88, S = 4.06.

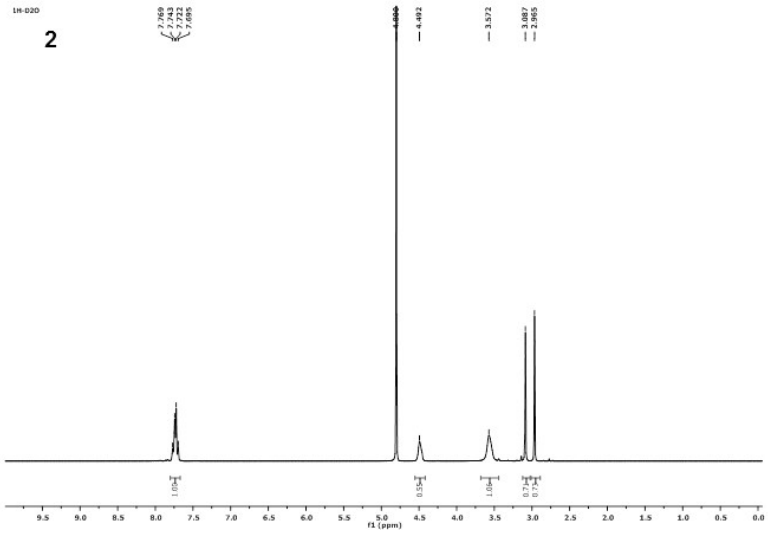
1,5-Bis(2-bromo-4-cyano-6-methoxyphenoxy)pentane (20a). 3-Bromo-4-hydroxy-5-methoxybenzonitrile 5 mmol (1.06 g) and 1,5-dibromopentane 2.5 mmol (0.57 g) were stirred at 130 °C for 3 hours together with K_2CO_3 10 mmol (1.38 g) and *N*-methylpyrrolidone (10 ml), then poured into ice-water (200 ml). The precipitated solid was filtered off and washed with water. After column chromatography (CH_2Cl_2), a white solid of **20a** was obtained; yield 92%; MP = 133.5–135.0 °C. ^{1}H NMR (299.87 MHz, DMSO-d_6) δ in ppm: 1.64 (p; *J* = 6.6 Hz; 2H; CH_2), 1.77 (p; *J* = 6.6 Hz; 4H; H-9, H-9'), 3.87 (s; 6H; 2 × OCH_3), 4.05 (t; *J* = 6.6 Hz; 4H; H-8, H-8'), 7.60 (d; *J* = 1.5 Hz; 2H; H-5, H-5'), 7.76 (d; *J* = 1.5 Hz; 2H; H-3, H-3'). ^{13}C NMR (75.40 MHz, DMSO-d_6) δ in ppm: 24.8 (CH_2), 29.1 (C-9, C-9'), 56.7 (2 × OCH_3), 73.0 (C-8, C-8'), 107.5 (C-4, C-4'), 116.2 (C-5, C-5'), 117.3 (C-7, C-7'), 117.5 (C-2, C-2'), 128.5 (C-3, C-3'), 149.2 (C-6, C-6'), 153.5 (C-1, C-1').

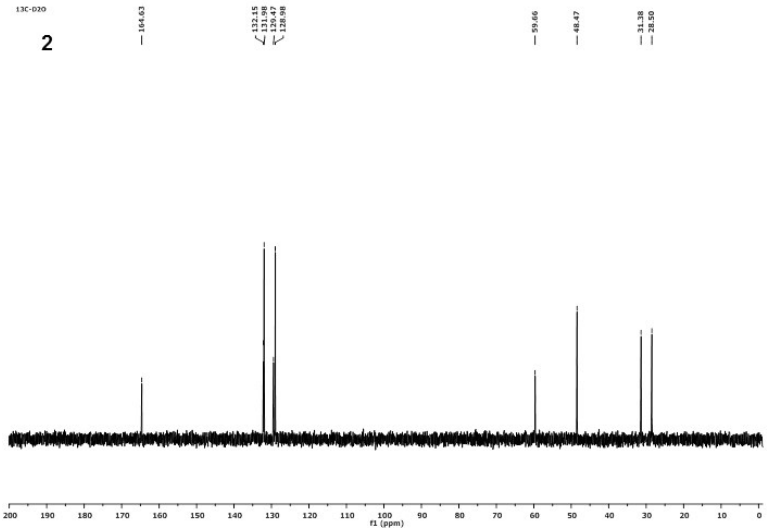
1,5-Bis(4-amidino-2-bromo-6-methoxyphenoxy)pentane dihydrochloride (20). After the general procedure, a white solid of **20** was filtered off and dried *in vacuo* over $CaCl_2$; yield 89%; MP = 246.0–247.5 °C. ^{1}H NMR (299.87 MHz, DMSO-d_6) δ in ppm: 1.66–1.69 (m; 2H; CH_2), 1.77–1.81 (p; *J* = 6.0 Hz; 4H; H-9, H-9'), 3.93 (s; 6H; 2 × OCH_3), 4.08 (t; *J* = 6.0; 4H; H-8, H-8'), 7.62 (d; 2H; H-5, H-5'), 7.75 (d; 2H; H-3, H-3'), 9.29 (br s; 4H; 4 × NH), 9.50 (br s; 4H; 4 × NH). ^{13}C NMR (75.40 MHz, DMSO-d_6) δ in ppm: 21.8 (CH_2), 29.2 (C-9, C-9'), 56.6 (2 × OCH_3), 72.9 (C-8, C-8'), 112.7 (C-5, C-5'), 116.9 (C-2, C-2'), 124.1 (C-3, C-3'), 124.3 (C-4, C-4'), 149.1 (C-6, C-6'), 153.1 (C-1, C-1'), 163.7 (C-7, C-7'). Element. Anal. $C_{21}H_{26}N_4O_4Br_2$ × 2HCl × 3H_2O (685.25 g/mol) calcd. (%): C = 36.81, H = 5.00, N = 8.18; found (%): C = 36.49, H = 4.67, N = 7.92.

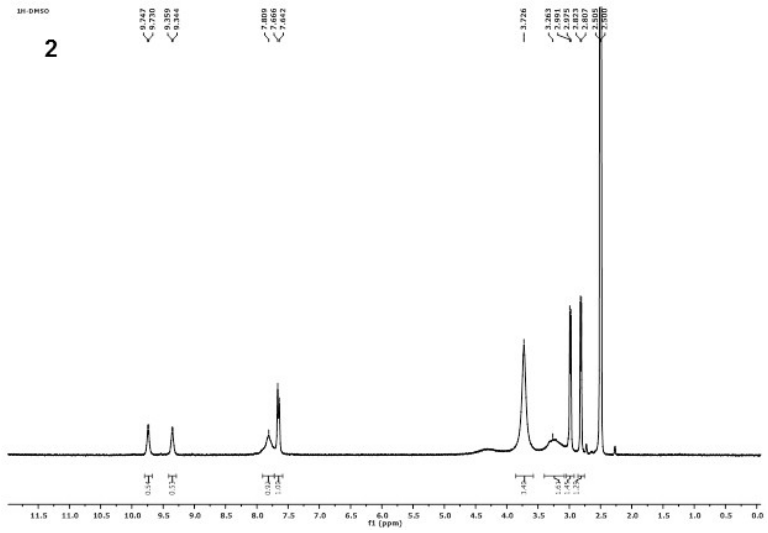
***N*-Ethyl-1,5-bis(4-cyanophenoxy)-3-azapentane (21a).** *N*,*N*-bis(2-chloroethyl)-*N*-ethylamine hydrochloride (**21aS1**) 5 mmol (1.03 g), 4-hydoxybenzonitrile 10 mmol (1.19 g), K_2CO_3 25 mmol (3.46 g) and *N*-methylpyrrolidone (15 ml) were stirred together at 130 °C for 6 hours and then poured into ice-water (200 ml) to give brown solid. After column chromatography, a yellowish oil was obtained and diluted in acetone (15 ml). The resultant solution was poured into water and kept at 4 °C. The precipitated solid was filtered off and dried to give a light-yellow solid of **21a**; yield 79%; MP = 48.5–50.0 °C. ^{1}H NMR (299.87 MHz, DMSO-d_6) δ in ppm: 0.99 (t; *J* = 7.0 Hz; 3H; CH_3), 2.66 (q; *J* = 7.0 Hz; 2H; CH_2), 2.91 (t; *J* = 6.0 Hz; 4H; H-9, H-9'), 4.12 (t; *J* = 6.0 Hz; 4H; H-8, H-8'), 7.08 (pd; *J* = 8.7 Hz 4H; H-2, H-6, H-2', H-6'), 7.74 (pd; *J* = 8.7 Hz; 4H; H-3, H-5, H-3', H-5'). ^{13}C NMR (75.40 MHz, DMSO-d_6) δ in ppm: 11.9 (CH_3), 48.2 (CH_2), 52.1 (C-9, C-9'), 67.0 (C-8, C-8'); 102.7 (C-4, C-4'), 115.5 (C-2, C-6, C-2', C-6'), 119.1 (C-7, C-7'), 134.1 (C-3, C-5, C-3', C-5'), 162.0 (C-1, C-1').

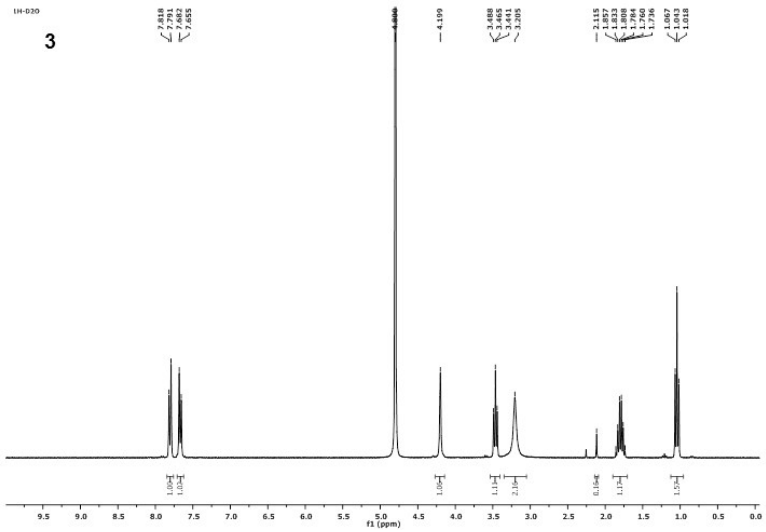
***N*-Ethyl-1,5-bis(4-amidinophenoxy)-3-azapentane trihydrochloride (21).** After the general procedure, the resultant solid **21** was filtered off. After crystallization from absolute ethanol, an almost white solid of **21** was obtained and dried at 100 °C; yield 63%; MP = 243.0–244.5 °C (decomp.). ^{1}H NMR (299.87 MHz, DMSO-d_6) δ in ppm: 1.34 (t; *J* = 7.0 Hz; 3H; CH_3), 3.33–3.37 (m; 2H; CH_2), 3.67–3.70 (m; 4H; H-9. H-9'), 4.59–4.62 (m; 4H; H-8, H-8'), , 7.21 (pd; 4H; H-2, H-6, H-2', H-6'), 7.92 (pd; 4H; *J* = 8.7 Hz; H-3, H-5, H-3', H-5'), 9.13 (br s; 4H; 4 × NH), 9.34 (br s; 4H; 4 × NH), 11.49 (br s; 1H; NEt × HCl). ^{13}C NMR (75.40 MHz, DMSO-d_6) δ in ppm: 8.5 (CH_3), 48.8 (CH_2), 50.9 (C-9, C-9'), 62.8 (C-8, C-8'); 115.0 (C-2, C-6, C-2', C-6'), 120.2 (C-4, C-4'), 130.2 (C-3, C-5, C-3', C-5'), 161.8 (C-1, C-1'), 164.6 (C-7, C-7'). Element. Anal. $C_{20}H_{27}N_5O_2$ × 3HCl (478.85 g/mol) calcd. (%): C = 50.17, H = 6.31, N = 14.63; found (%): C = 50.29, H = 6.18, N = 14.29.

^{1}H and ^{13}C NMR spectra for compounds 2–21





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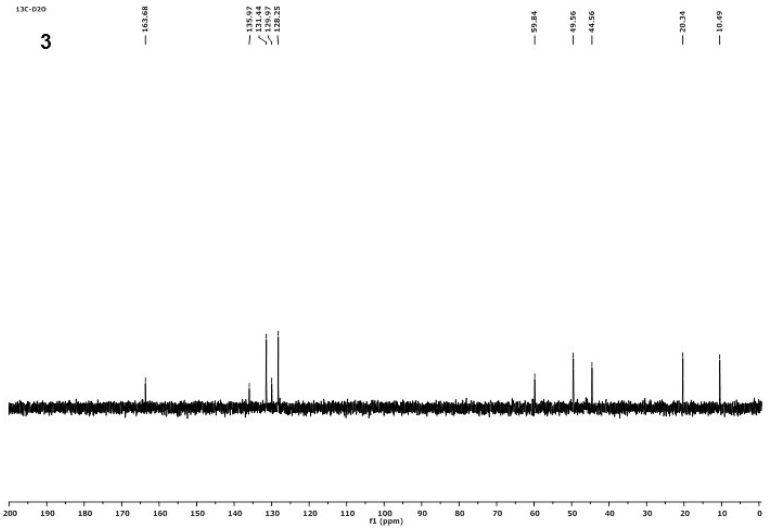
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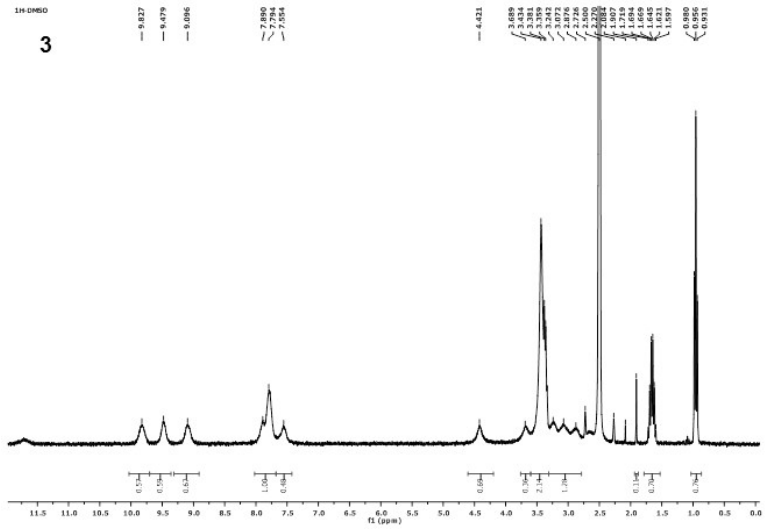
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2.220
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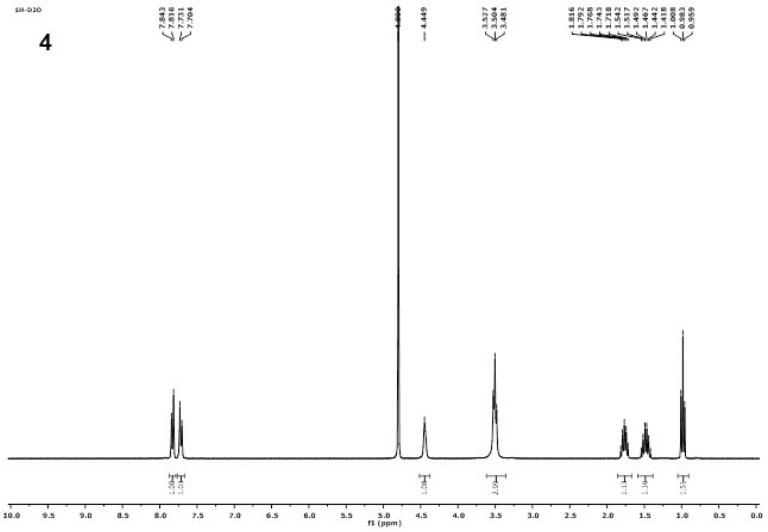
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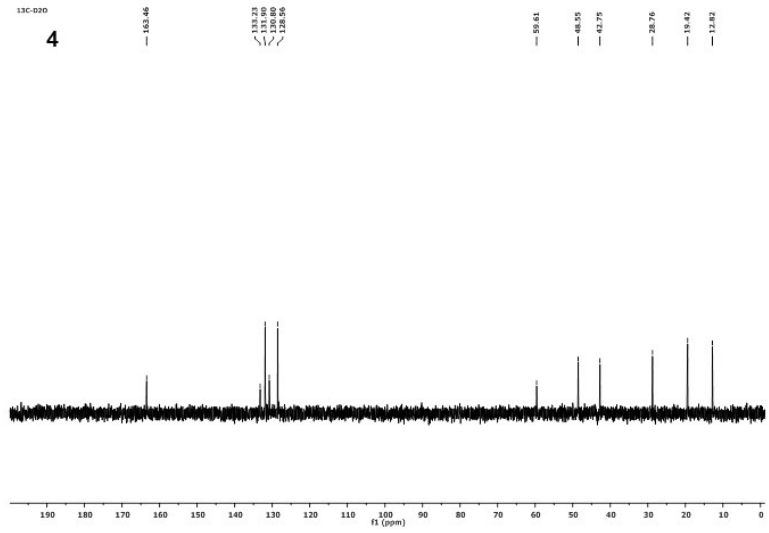
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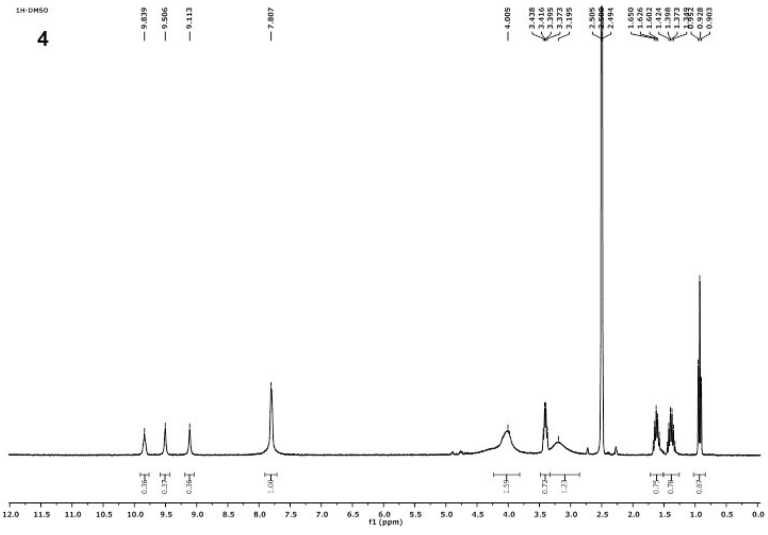
f1 (ppm)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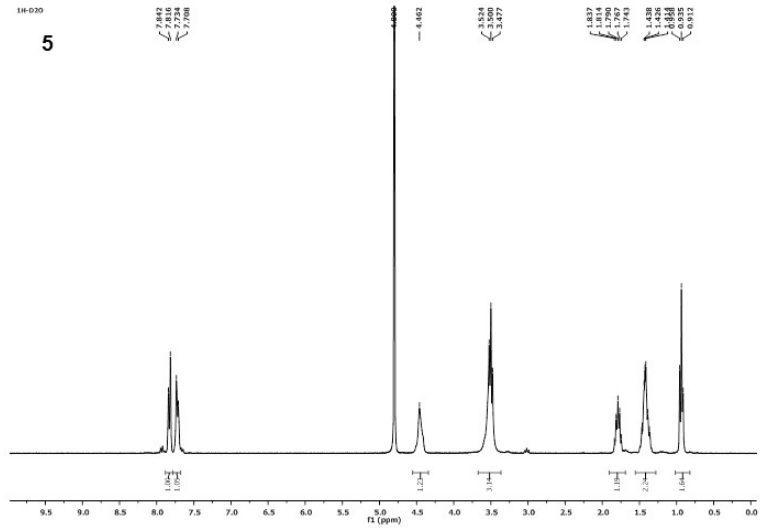
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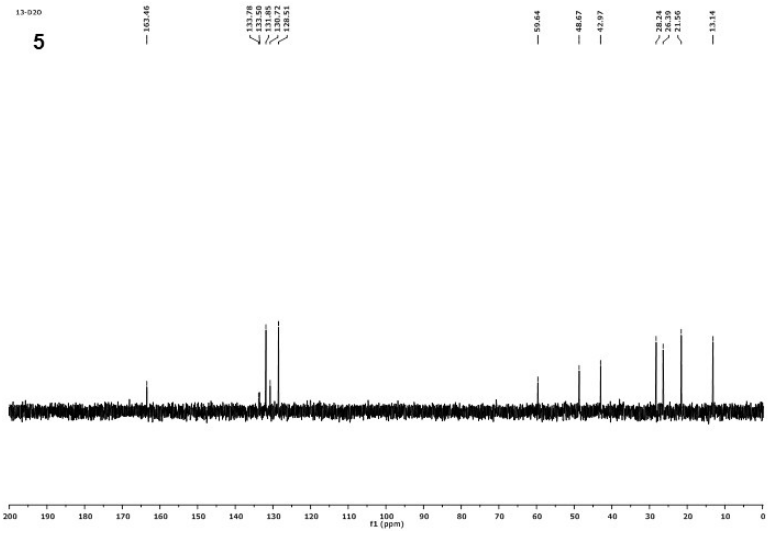
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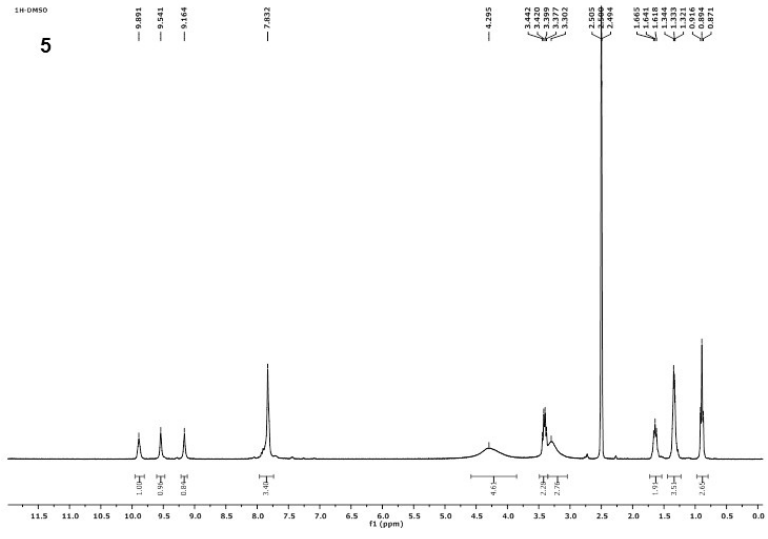
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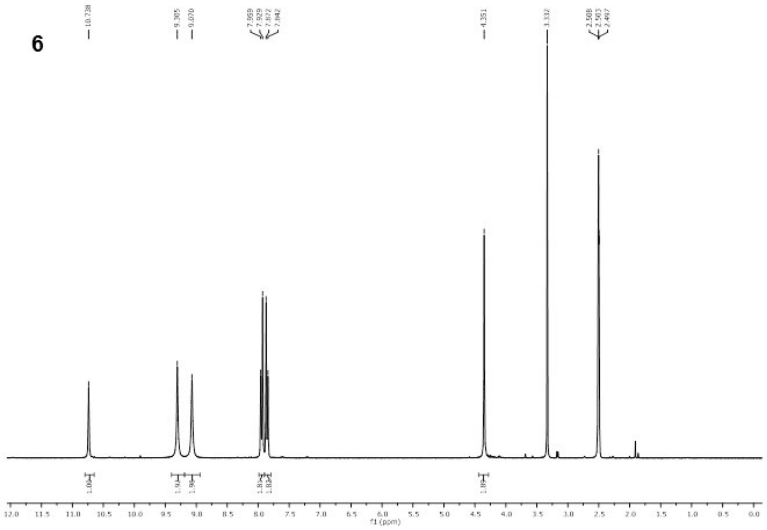
6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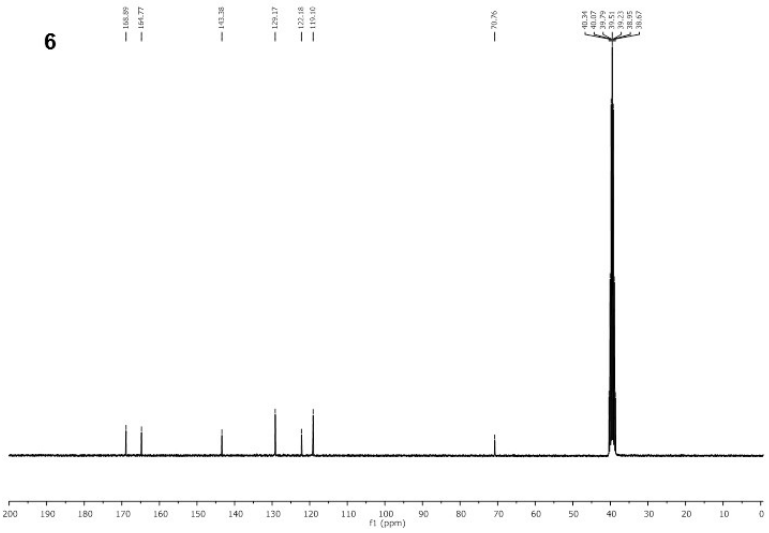
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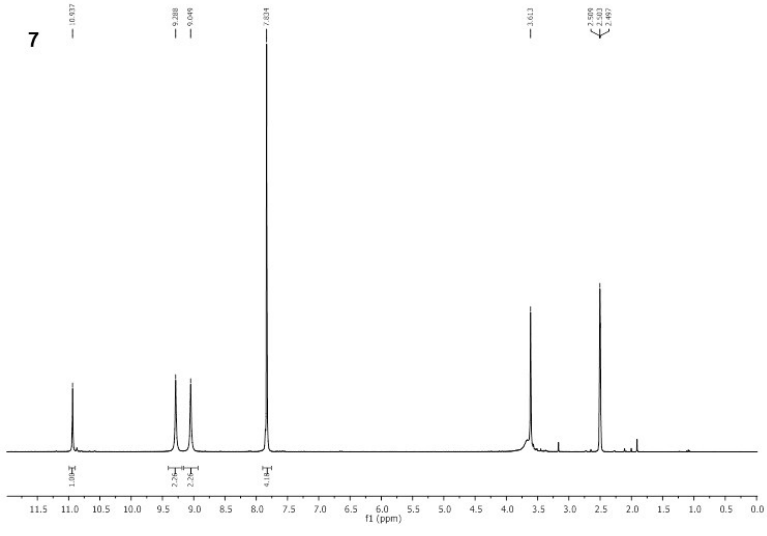
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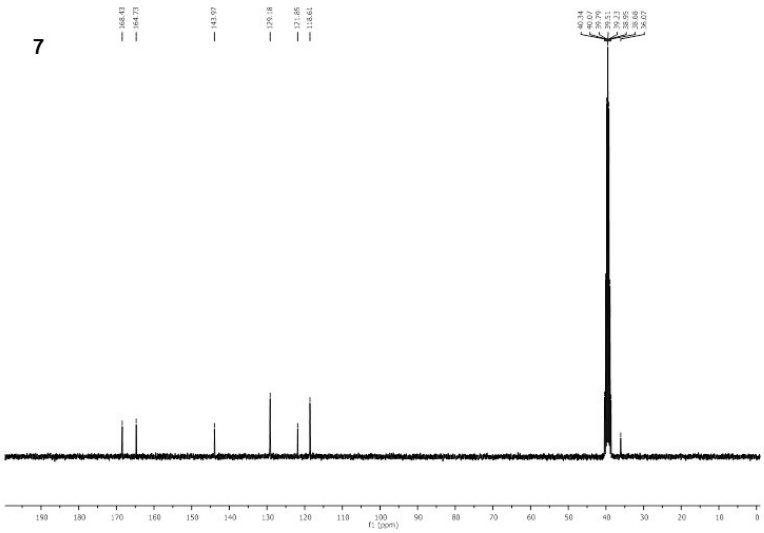

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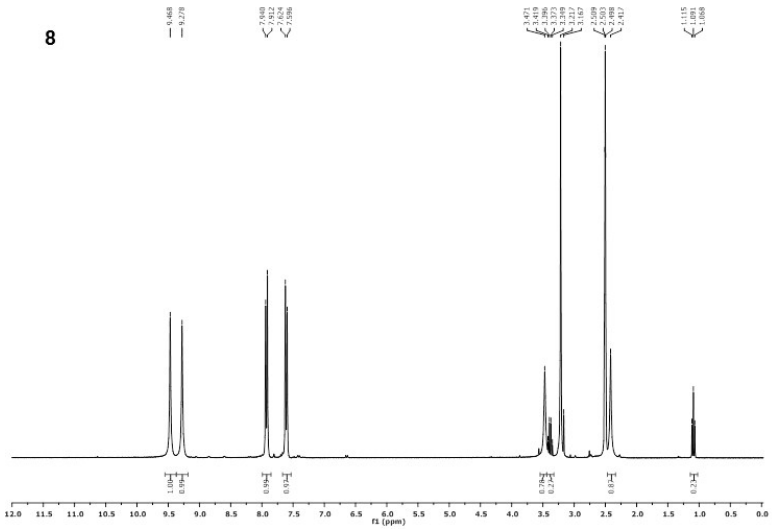

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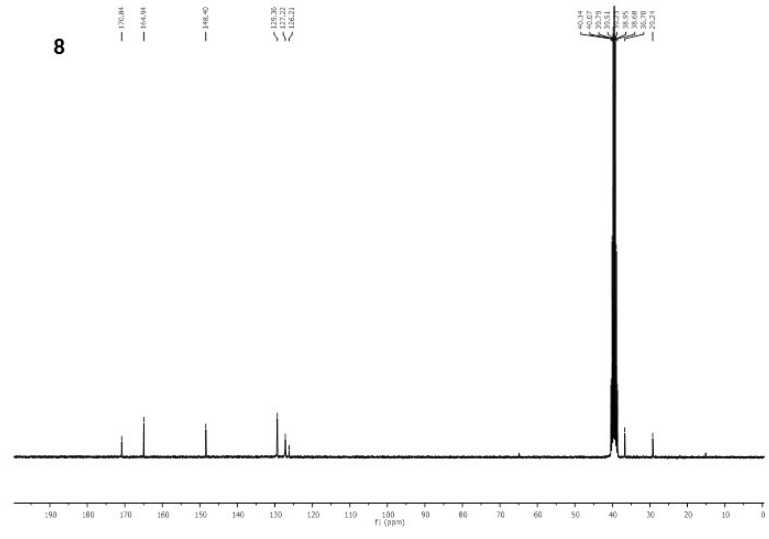

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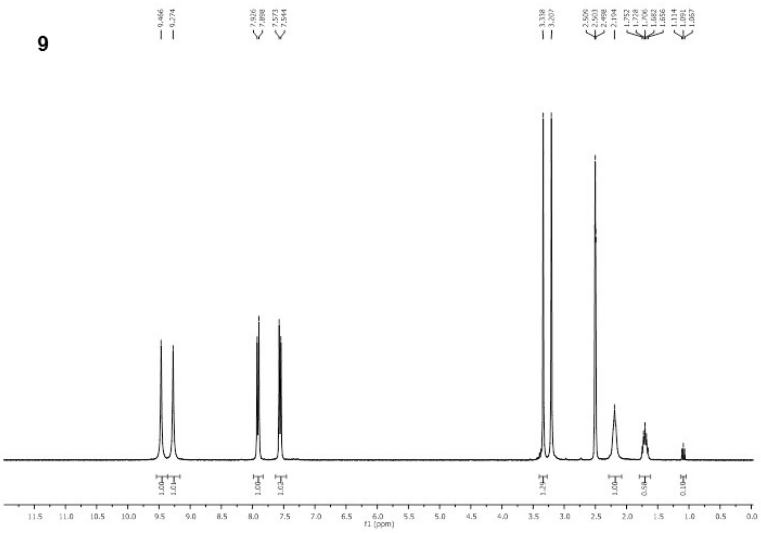

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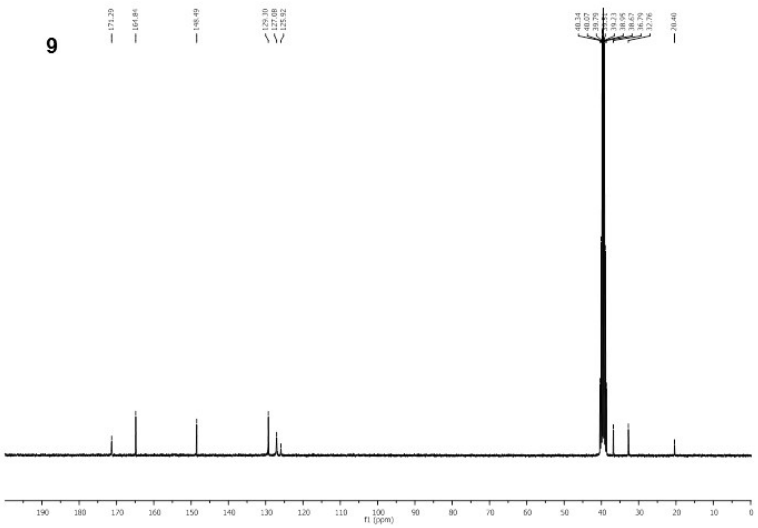

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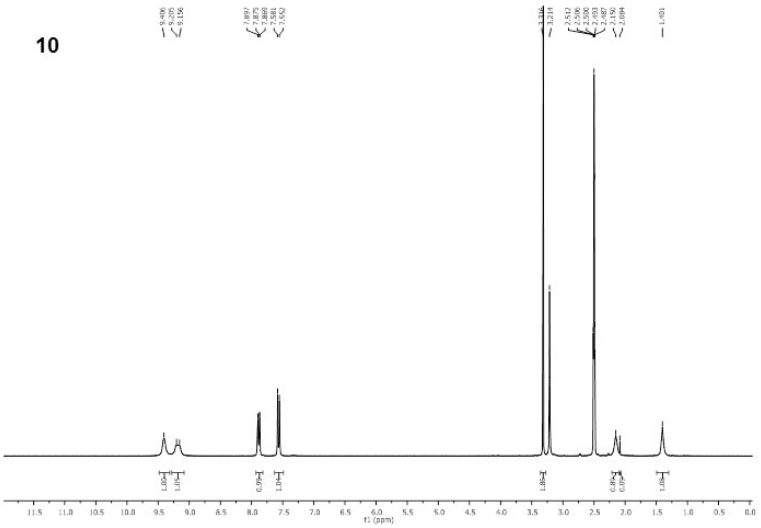

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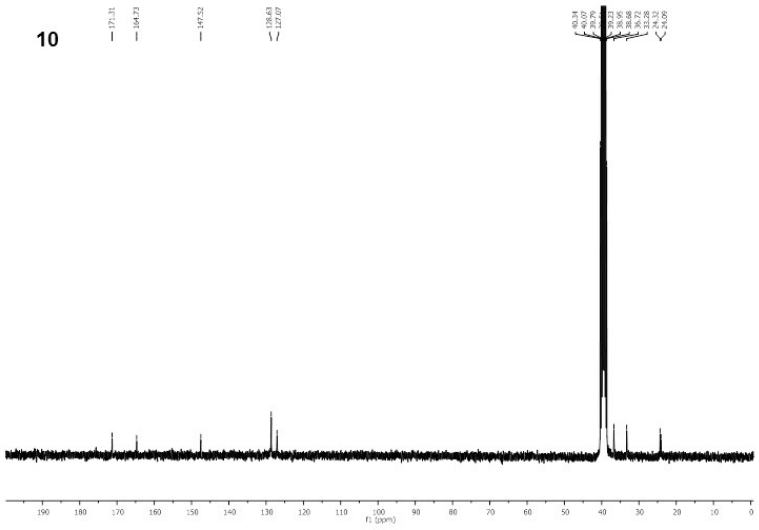

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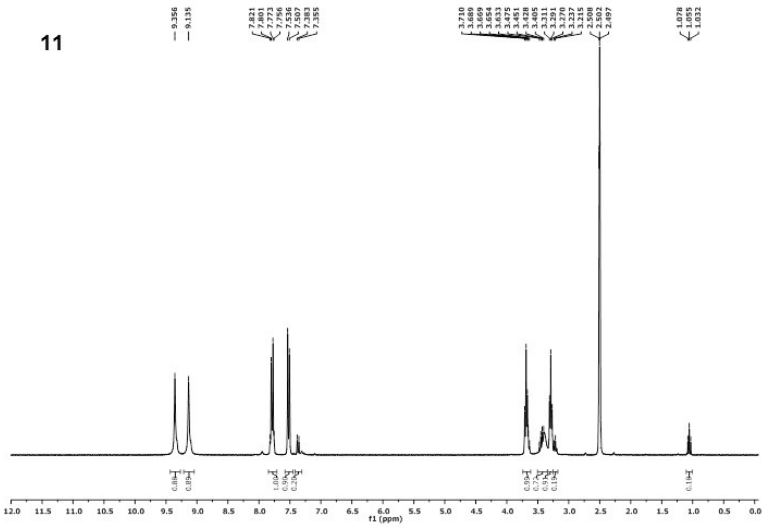

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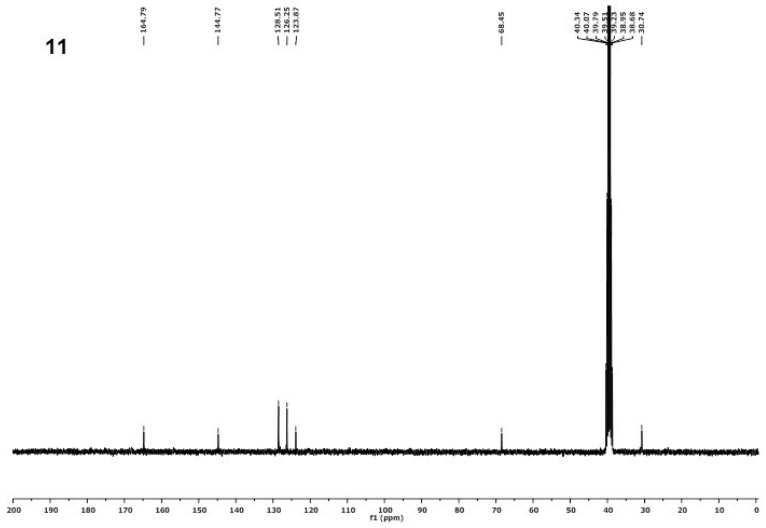

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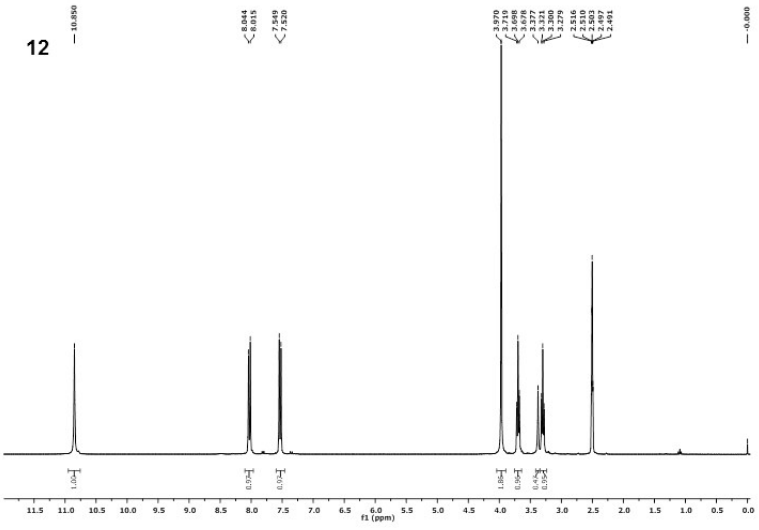

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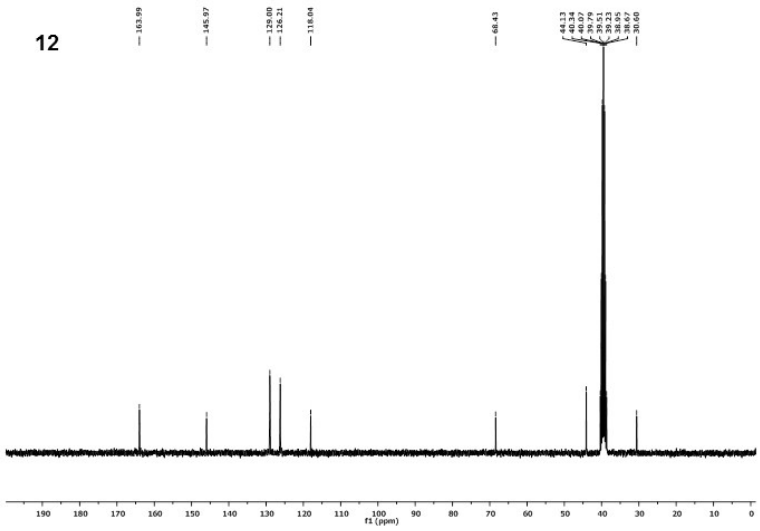

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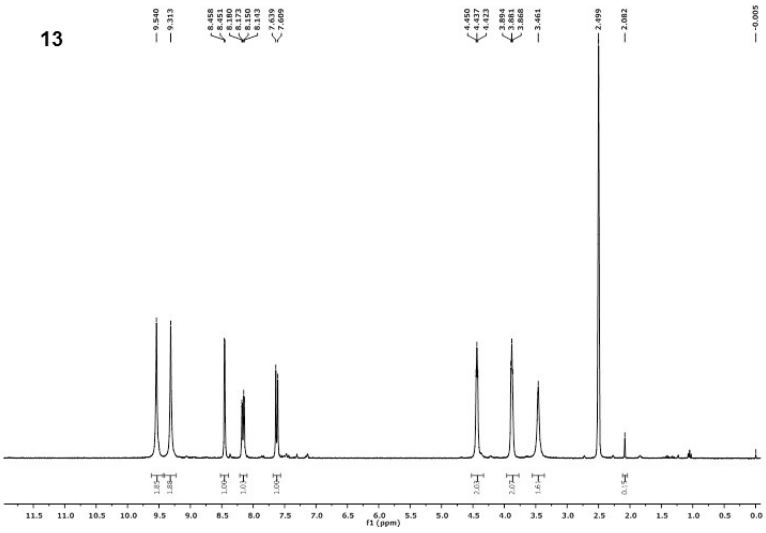

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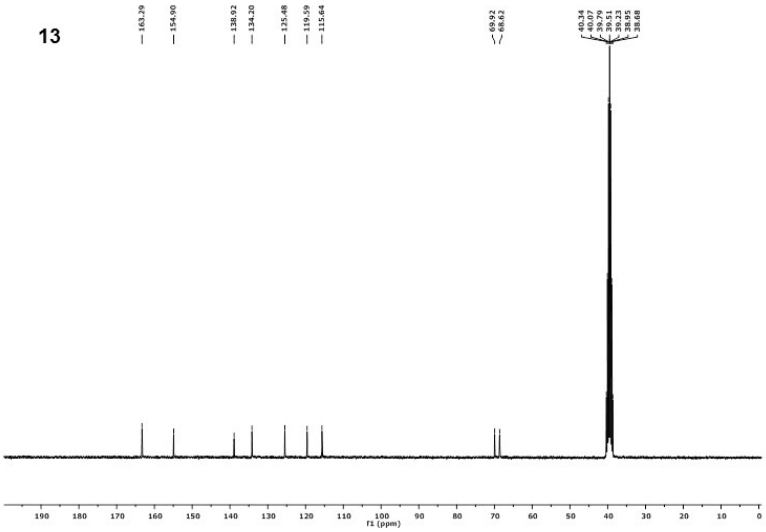
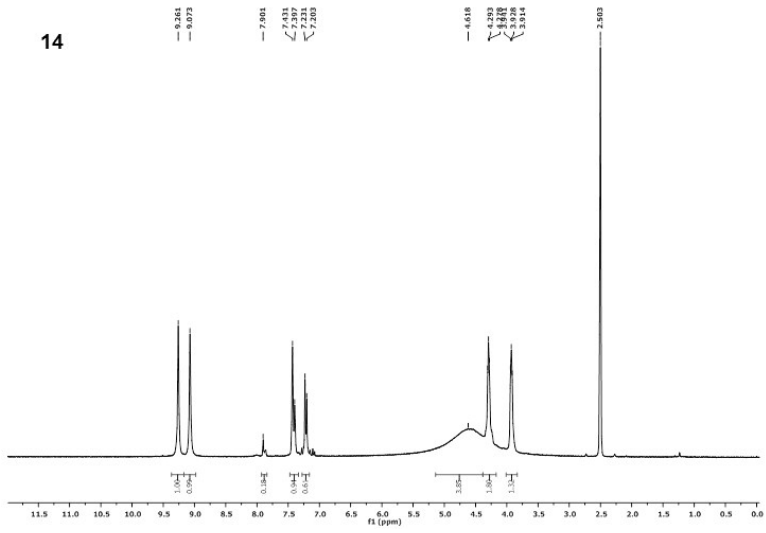
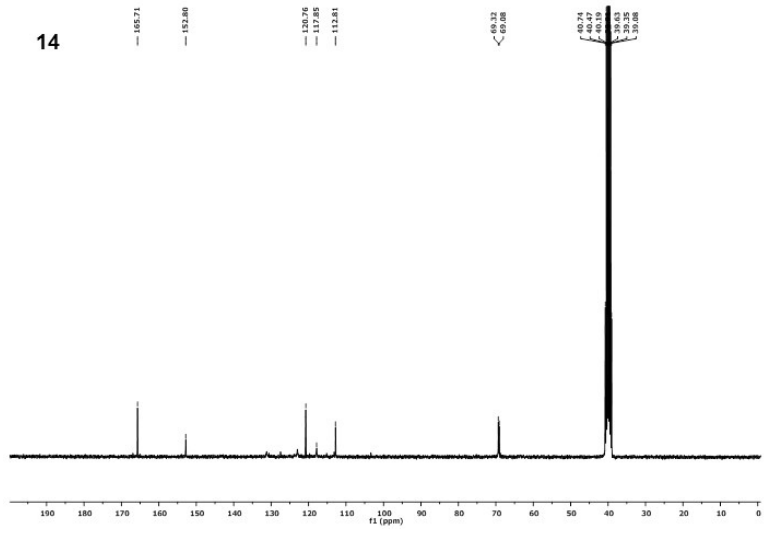

163.29
154.90
138.92
134.20
135.48
119.59
115.64
69.92
68.62
40.34
40.07
39.79
39.51
39.23
38.95
38.68
f1 (ppm)

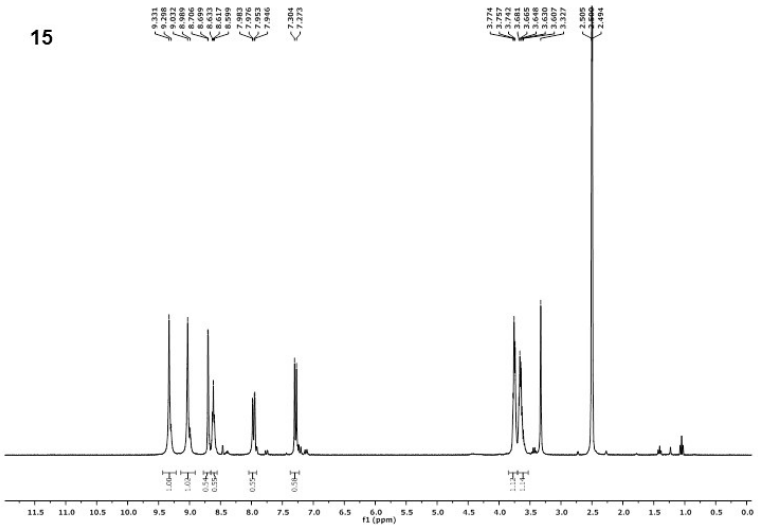
14


9.261
9.073
7.901
7.431
7.397
7.231
7.203
4.618
4.293
3.928
3.914
2.503
f1 (ppm)

14


165.71
153.80
120.76
117.85
112.81
69.32
69.08
40.74
40.47
40.19
39.63
39.35
39.08
f1 (ppm)

15



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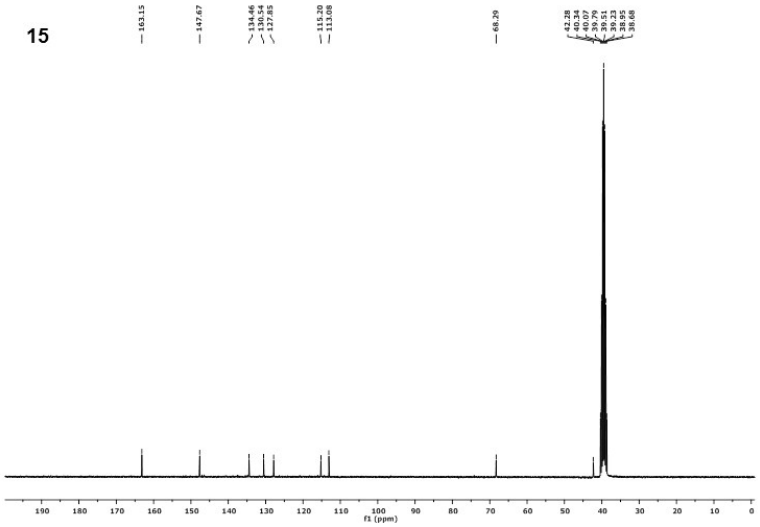
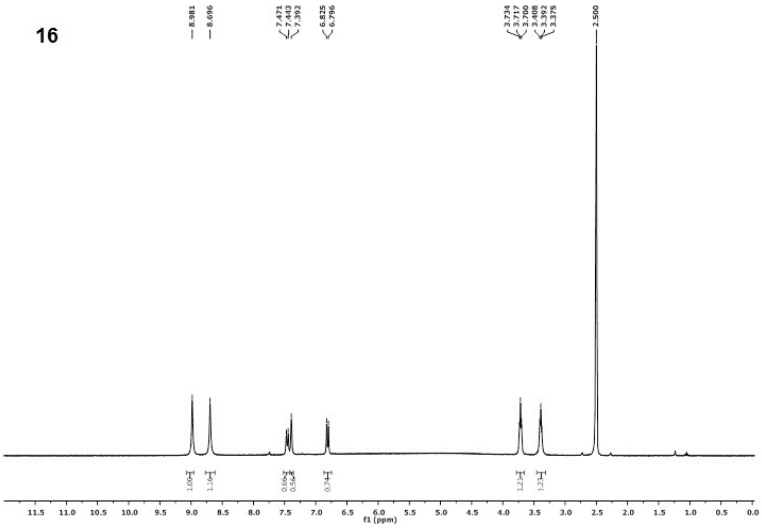
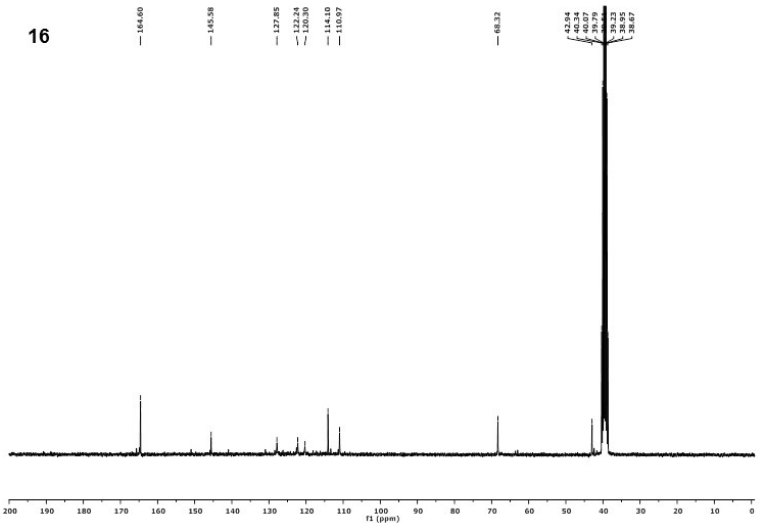


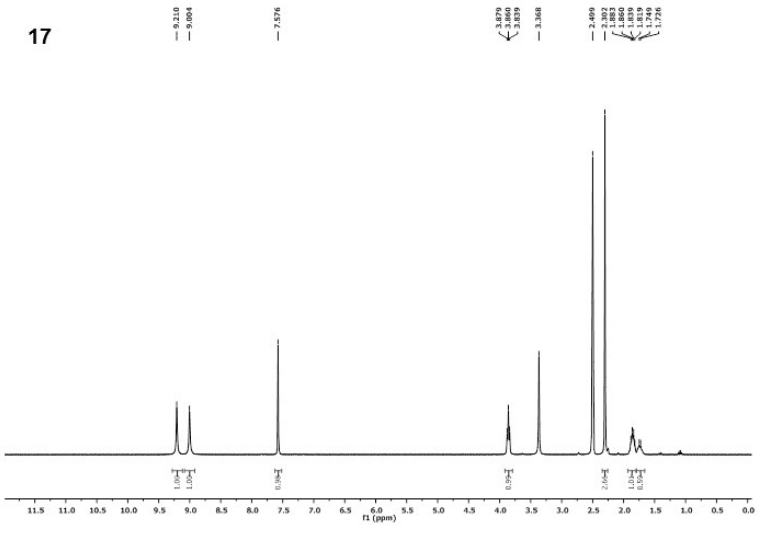
16



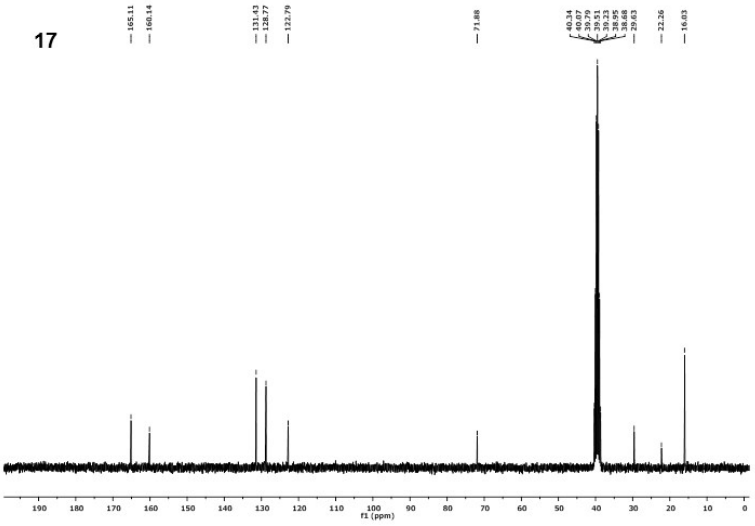
16


164.60
145.58
127.85
122.24
120.30
114.10
110.97
68.32
42.64
40.34
40.07
39.79
39.51
39.23
38.95
38.67
f1 (ppm)

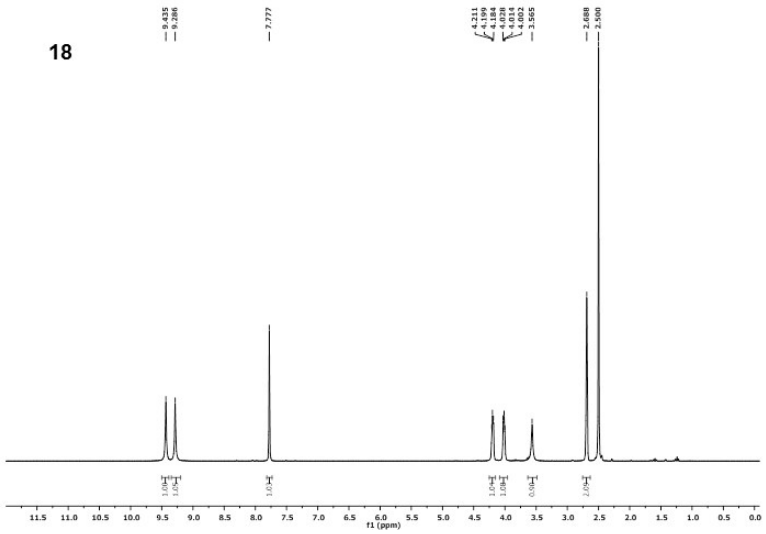
17


9.210
9.004
7.576
3.879
3.860
3.839
3.368
2.499
2.302
2.282
1.860
1.839
1.819
1.749
1.726
f1 (ppm)

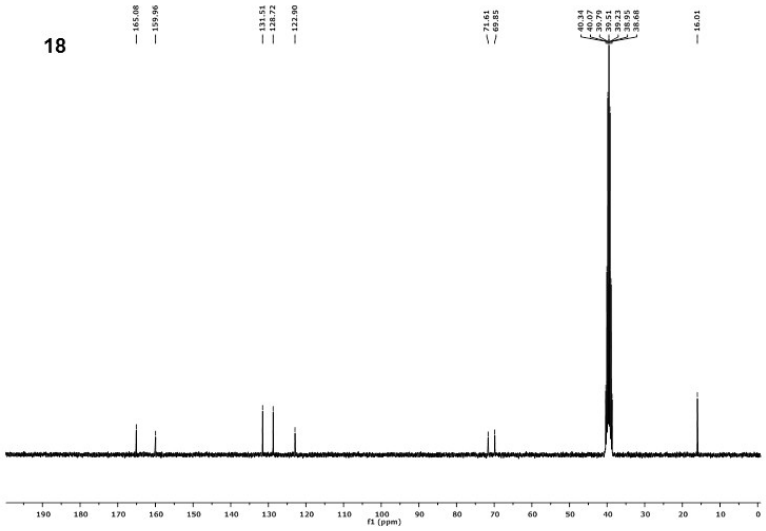
17


165.11
160.14
131.43
128.77
122.79
71.88
40.34
40.07
39.79
39.51
39.23
38.95
38.68
29.63
22.26
16.83
f1 (ppm)

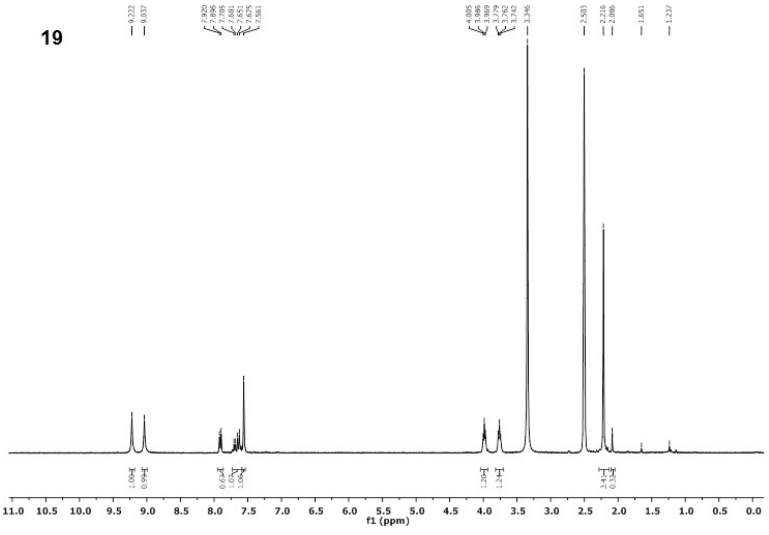
18


9.435
9.286
7.777
4.211
4.199
4.184
4.038
4.014
3.652
3.565
2.688
2.500
f1 (ppm)

18


165.08
159.96
131.51
128.72
122.90
71.61
69.85
40.34
40.07
39.79
39.51
39.23
38.95
38.68
16.01
f1 (ppm)

19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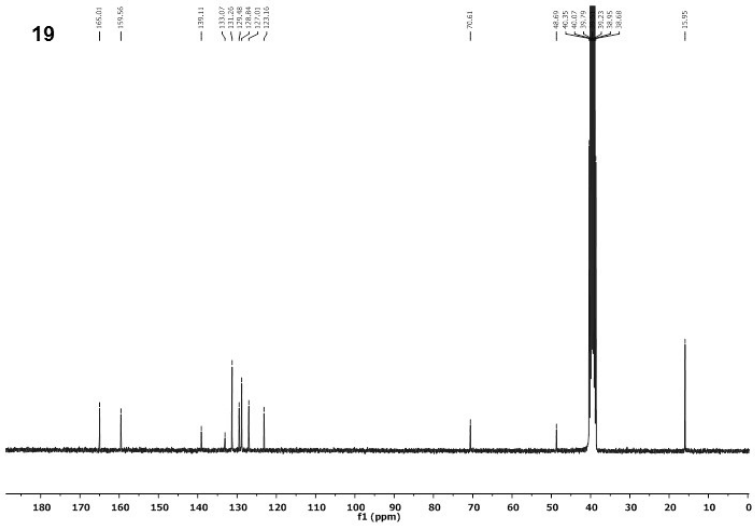
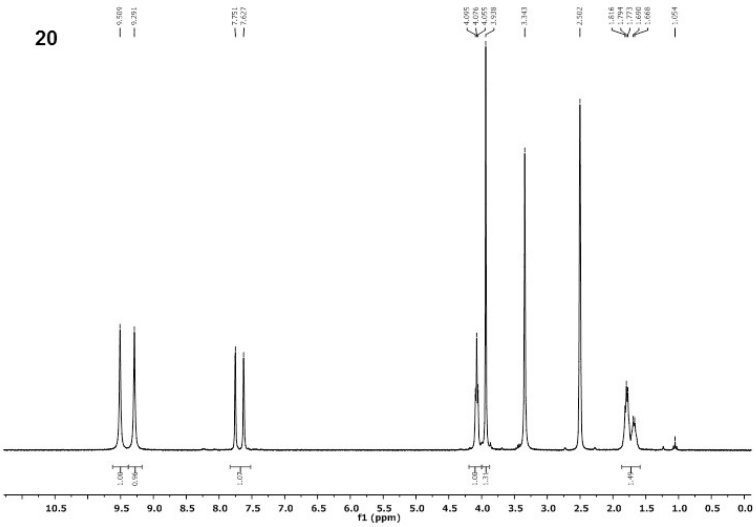
9.037
7.830
7.796
7.681
7.653
7.626
7.581
4.005
3.986
3.969
3.754
3.742
3.346
2.583
2.216
2.086
1.651
1.237
f1 (ppm)

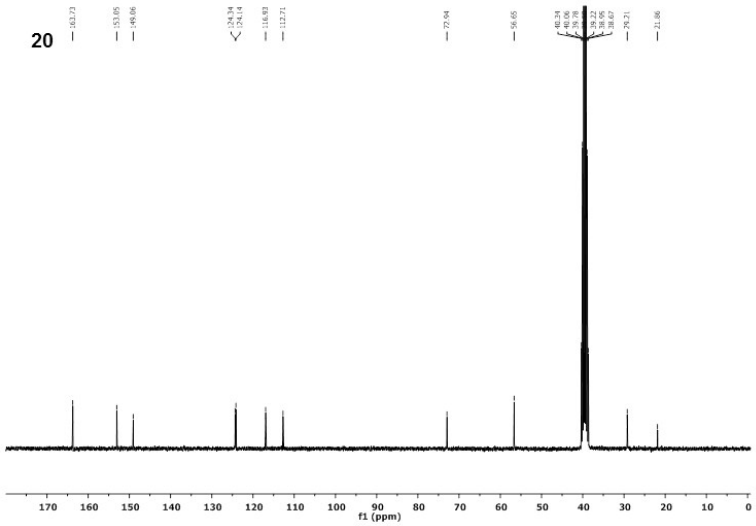
19


165.01
159.56
139.11
133.07
131.26
129.48
126.84
127.01
122.16
70.61
48.69
46.35
44.03
39.79
38.95
38.68
15.95
f1 (ppm)

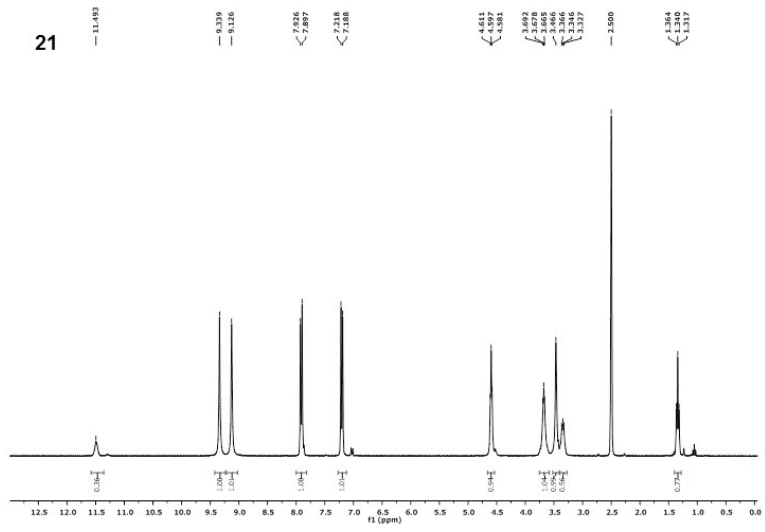
20


9.309
9.291
7.751
7.627
4.095
4.078
4.061
3.938
3.343
2.502
1.814
1.794
1.773
1.753
1.668
1.654
f1 (ppm)

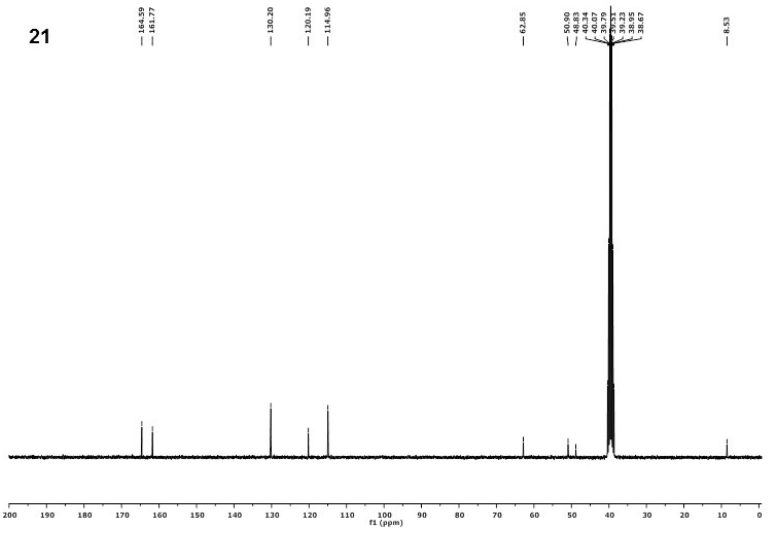
20


163.23
153.85
148.66
124.34
124.14
116.83
112.71
72.94
56.65
48.34
48.06
47.78
39.22
38.95
38.67
29.21
21.86
f1 (ppm)

21


11.493
9.339
9.126
7.926
7.897
7.218
7.188
4.611
4.597
4.581
3.692
3.678
3.665
3.466
3.346
3.327
2.500
1.364
1.350
1.337
f1 (ppm)

21


164.59
161.77
130.20
120.19
114.06
62.85
50.90
48.83
40.34
40.07
39.79
39.51
39.23
38.95
38.67
8.53
f1 (ppm)