Supplementary information for:

Efficient and Mild Microwave Assisted Stepwise Functionalization of Naphthalenediimide with α-Amino Acids

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Contents:

SYNTHESIS

General: All solvents were of reagent grade quality and purchased commercially. All purchased starting materials were used without further purification. The determined melting points are uncorrected. NMR spectra were recorded on 400 MHz or 500 MHz instruments. The NMR spectra were referenced to solvent. All the spectra were recorded at 298K. ^{1}H NMR, data are reported as follows: chemical shift in ppm on the δ scale, integration, multiplicity (s: singlet, d: doublet, t: triplet, q: quartet, dd: doublet of doublets, bs: broad singlet, bt: broad triplet), coupling constants (Hz) and assignment. TLC analyses were carried out using silica gel 60 Å TLC plates. Column chromatography was performed on silica gel 60 Å (0.040-0.063mm) for column chromatography (230 – 400 mesh ASTM). The sonication was performed using a tabletop ultrasonic cleaner. The microwave experiments were conducted using a domestic microwave oven or a dedicated microwave synthesizer.

Work-up and Characterization Data:

(R)-2-[7-((R)-1-Carboxy-2-tritylsulfanyl-ethyl)-1,3,6,8-tetraoxo-3,6,7,8-tetrahydro-1*H*-benzo[*lmn*][3,8]phenanthrolin-2-yl]-3-tritylsulfanyl-propionic acid, (*R,R*)-2b

The reaction was performed on 0.746 mmol (200 mg) 1,4,5,8-naphthalenetetracarboxylic dianhydride and 1.491 mmol (542 mg) of H-(L)-Cys(Trt)-OH using both synthetic methods (A and B), as well as on 3.728 mmol (1g) 1,4,5,8-naphthalenetetracarboxylic dianhydride and 7.457 mmol (2.71g) H-(L)-Cys(Trt)-OH using synthetic method B.

Work up: the brown residue was taken-up with chloroform (150 ml). The organic phase was washed with 1.5 N HCl (2 x 50 ml), brine (1 x 50 ml), water (1 x 50 ml) and dried over Na_2SO_4, the solvent was removed and the product dried under vacuum. The product was obtained in 95% yield as a yellow-brown powder. m.p. 185-187 °C (dec); ^{1}H NMR (500 MHz, $CDCl_3$) δ(ppm): 8.63 (s, 4H), 7.32-7.28 (t, J = 7.5, 12H), 7.21-7.18 (t, J = 7.5, 12H), 7.18-7.12 (d, J = 7.5, 6H), 5.49 (dd, J_1 = 10.4, J_2 = 4.7, 2H), 3.25 (dd, J_1 = 14.2, J_2 = 10.4, 2H), 3.13 (dd, J_1 = 14.2, J_2 = 4.7, 2H); ^{13}C NMR {^{1}H} (100.62 MHz, $CDCl_3$) δ(ppm): 174.7, 161.9, 144.2, 131.4, 129.6, 127.9, 126.8, 126.1, 119.6, 67.6, 52.8; HRMS (ESI+) calcd. for: $C_{58}H_{42}N_2NaO_8S_2$ $[M+Na]^+$ (m/z): 981.2280, found: 981.2275.

(S)-2-[7-((S)-1-Carboxy-2-tritylsulfanyl-ethyl)-1,3,6,8-tetraoxo-3,6,7,8-tetrahydro-1*H*-benzo[*lmn*][3,8]phenanthrolin-2-yl]-3-tritylsulfanyl-propionic acid (*S,S*)-2b

Work up: the dark brown oil was taken up into $CHCl_3$ (100 ml). The organic phase was washed with 1N HCl (2 x 50 ml), brine (1 x 75 ml) and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure and dried under high-vacuum. The product was obtained in the form of a yellow solid in 86% yield. m.p. 182-184°C (dec); ^{1}H NMR (400 MHz, $CDCl_3$) δ(ppm): 11.47 (bs, 2H), 8.66 (s, 4H), 7.35-7.32 (d, J = 10.0, 12H), 7.23-7.14 (m, 18H), 5.55-5.51 (dd, J_1 = 15.0, J_2 = 4.5, 2H), 3.31-3.25 (dd, J_1 = 24.0, J_2 = 10.5, 2H), 3.19-3.14 (dd, J_1 = 18.0, J_2 = 4.5, 2H); ^{13}C NMR {^{1}H} (100.62 MHz, $CDCl_3$) δ(ppm): 174.1, 163.5, 144.2, 131.4, 129.5, 127.9, 127.8, 126.7, 126.2, 67.5, 52.8, 30.2; HRMS (ESI+) calcd. for: $C_{58}H_{42}N_2NaO_8S_2$ $[M+Na]^+$ (m/z): 981.2280, found: 981.2281.

2-Amino-3-tritylsulfanyl-propionic acid methyl ester trifluoro-acetic acid salt

0.5 g of H-(L)-Cys-OMe·HCl (2.912 mmol) and 0.812 g of trityl chloride (2.912 mmol) were co-dissolved in 6 ml of trifluoroacetic acid obtaining a deep brown solution. After stirring the reaction mixture under nitrogen for 10 minutes, the solvent was removed under reduced pressure and the thick oily residue was taken-up with dichloromethane (10 ml). The dichloromethane was removed under reduced pressure and the procedure was repeated four times until a foaming solid was obtained. The crude product was dissolved in dichloromethane (150 ml) and washed with water (2 x 100 ml), the organic layer was dried over Na_2SO_4 and the solvent removed. 1.245 g of product were obtained as a white powder, the title product was clean by NMR analysis and was used without any further purification. Yield 87%. m.p. 66-68°C; ^{1}H NMR (400 MHz, $CDCl_3$) δ(ppm): 7.42-7.20 (m, 15H), 3.63 (s, 3H), 3.06-2.90 (m, 2H), 2.84 (dd, J_1 = 14, J_2 = 4.5, 2H), 2.35 (t, 4H, J = 7), 2.27 (m, 2H), 1.27 (s, 18H, OtBu); ^{13}C NMR (100.62 MHz, $CDCl_3$) δ(ppm): 168.4, 162.0, 143.7, 129.3, 128.2, 127.1, 67.5, 53.2, 51.9, 32.1.

(R)-2-[7-((R)-1-Methoxycarbonyl-2-tritylsulfanyl-ethyl)-1,3,6,8-tetraoxo-3,6,7,8-tetrahydro-1*H*-benzo[*lmn*][3,8]phenanthrolin-2-yl]-3-tritylsulfanyl-propionic acid methyl ester, (*R*,*R*)-2c

Work up: the dark brown oil was taken up into $CHCl_3$ (100 ml). The organic phase was washed with 1N HCl (2 x 50 ml), brine (1 x 75 ml) and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure. The crude product was purified by colum chromatography (silica, CH_2Cl_2/MeOH 98/2 v/v). The product was obtained in the form of a yellow solid in 70% yield over two steps from H-(L)-Cys-OMe·HCl. m.p. 125-127 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ(ppm): 8.73 (s, 4H), 7.34-7.32 (d, J = 7.0, 12H), 7.22-7.15 (m, 18H), 5.57-5.53 (dd, J_1 = 15.0, J_2 = 6.0, 2H), 3.66-3.64 (m, 5H), 3.24-3.22 (dd, J_1 = 9.5, J_2 = 4.0, 2H); ^{13}C NMR {^{1}H} (100.62 MHz, $CDCl_3$) δ(ppm): 168.6, 162.1, 144.3, 131.4, 129.6, 127.9, 126.7, 126.4, 67.4, 53.0, 52.7, 30.5; HRMS (ESI+) calcd. for: $C_{60}H_{46}N_2NaO_8S_2$ $[M+Na]^+$ (m/z): 1009.2593, found: 1009.2588.

(S)-3-Benzyloxy-2-[7-((S)-2-benzyloxy-1-carboxy-ethyl)-1,3,6,8-tetraoxo-3,6,7,8-tetrahydro-1*H*-benzo[*lmn*][3,8]phenanthrolin-2-yl]-propionic acid, (*S*,*S*)-2d

Work-up: the residue was taken-up with 50 ml of chloroform; the organic solution was extracted with 1.5 N HCl (2 x 50 ml), brine (1 x 30 ml) and water (1 x 30 ml). The solution was dried over Na_2SO_4 and the solvent removed under reduced pressure. To remove the residual DMF, the crude product was dissolved in 5 ml of acetonitrile and added drop wise to a vigorously stirred 2.5% aqueous solution of $KHSO_4$. The product coagulates as brown-pink flakes, the precipitate was filtered using a Büchner funnel, washed with water and dried under vacuum. The product was obtained as a brown-red powder in 86% yield. m.p. 137-139 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ(ppm): 8.66 (s, 4H), 7.20-7.08 (m, 30H), 6.11 (dd, J_1 = 9.03, J_2 = 5.5, 2H), 4.2 (AB system, J_{AB}= 12, 4H), 4.34-4.18 (m, 4H); ^{13}C NMR {^{1}H} (100.62 MHz, DMSO-d_6) δ(ppm): 169.13, 162.3, 138.1, 131.4, 128.2, 127.5, 127.4, 126. 4, 125.9, 71.9, 66.7, 52.9; HRMS (ESI+) calcd. for: $C_{34}H_{26}N_2NaO_{10}$ $[M+Na]^+$ (m/z): 645.1485, found: 645.1480.

(S)-2-[7-((S)-1-Methoxycarbonyl-3-methyl-butyl)-1,3,6,8-tetraoxo-3,6,7,8-tetrahydro-1*H*-benzo[*lmn*][3,8]phenanthrolin-2-yl]-4-methyl-pentanoic acid methyl ester, (*S*,*S*)-2e

Work-up: the residue was taken-up with water, the suspension was filtered using a Büchner funnel, the precipitate was washed with water (200 ml) and dried under vacuum. The crude product was purified by filtration through a short plug of silica using ethylacetate as eluent. 370 mg of product were obtained as a pale orange-yellow powder. Yield 95%. TLC

(silica, $CHCl_3$/MeOH 50/1 v/v) Rf: 0.53; m.p. 117 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ(ppm): 8.78 (s, 4H), 5.78 (dd, J_1 = 9.5, J_2 = 5, 2H), 3.73 (s, 6H), 2.29-2.22 (m, 2H), 2.16-2.09 (m, 2H), 1.54 (m, 2H), 1.01 (d, J = 6.6, 6H), 0.923 (d, J = 6.6, 6H); ^{13}C NMR {^{1}H} (125.78 MHz, $CDCl_3$) δ(ppm): 170.3, 162.5, 131.4, 126.9, 126.5, 52.6, 52.5, 37.9, 25.4, 23.1, 22.0; HRMS (ESI+) calcd. for: $C_{28}H_{31}N_2O_8$ $[M+H]^+$ (m/z): 523.2080, found: 523.2090.

(S)-2-[7-((S)-1-Methoxycarbonyl-2-phenyl-ethyl)-1,3,6,8-tetraoxo-3,6,7,8-tetrahydro-1*H*-benzo[*lmn*][3,8]phenanthrolin-2-yl]-3-phenyl-propionic acid methyl ester, (*S*,*S*)-2f

Work-up: the residue was taken-up with 50 ml of acetonitrile and evaporated to dryness. The yellow residue was triturated with water (100 ml), the solution was discarded and the precipitate was washed with a further amount of water (200 ml) and dried under vacuum. The crude product was purified by filtration on a short silica plug, ethyl acetate was used as eluent. The product was obtained as a bright yellow powder in 74% yield. TLC (silica, AcOEt/EP 1/1 v/v) Rf: 0.75; m.p. 224-225 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ(ppm): 8.63 (s, 4H), 7.20-7.00 (m, 10H), 5.93 (dd, J_1 = 9.10, J_2 = 5.5, 2H), 3.65 (s, 6H), 3.60 (dd, J_1 = 14.0, J_2 = 5.5, 2H), 3.29 (dd, J_1 = 14, J_2 = 9.1, 2H); ^{13}C NMR {^{1}H} (100.61 MHz, DMSO-d_6) δ(ppm): 169.2, 161.8, 137.2, 131.3, 128.9, 128.1, 126.4, 125.9, 125.5, 54.2, 52.3, 34.0; HRMS (ESI+) calcd. for: $C_{34}H_{27}N_2O_8$ $[M+H]^+$ (m/z): 591.1767, found: 591.1762.

(S)-2-{7-[(S)-1-Carboxy-2-(4-hydroxy-phenyl)-ethyl]-1,3,6,8-tetraoxo-3,6,7,8-tetrahydro-1*H*-benzo[*lmn*][3,8]phenanthrolin-2-yl}-3-(4-hydroxy-phenyl)-propionic acid, (*S*,*S*)-2g

Work up: the dark brown oil was taken up into MeOH (100 ml). This solution was added under stirring to 200 ml of 1N HCl. The resulting suspension was allowed to coagulate overnight and then filtered through a P4 sintered glass funnel. The solid was then washed with 100 ml deionized water and dried *in vacuo*. The product was obtained in the form of a dark-orange solid in 91% yield. m.p. 269-272°C (dec); ^{1}H NMR (400 MHz, DMSO-d_6) δ(ppm): 12.91 (bs, 2H), 9.04 (s, 2H), 8.65 (s, 4H), 6.94-6.92 (d, J = 8.5, 2H), 6.49-6.47 (d, J = 8.5, 2H), 5.78-5.74 (dd, J_1 = 15.0, J_2 = 5.5, 2H), 3.48-3.43 (dd, J_1 = 19.5, J_2 = 5.5, 2H), 3.23-3.17 (dd, J_1 = 23.5, J_2 = 9.5, 2H); ^{13}C NMR {^{1}H} (100.62 MHz, DMSO-d_6) δ(ppm): 170.3, 161.9, 155.6, 136.5, 131.2, 129.8, 127.7, 126.0, 125.6, 114.9, 54.8, 33.3; HRMS (ESI+) calcd. for: $C_{32}H_{23}N_2O_{10}$ $[M+H]^+$ (m/z): 595.1353, found: 595.1351.

(S)-2-{7-[(S)-1-Methoxycarbonyl-2-(1-trityl-1*H*-imidazol-4-yl)-ethyl]-1,3,6,8-tetraoxo-3,6,7,8-tetrahydro-1*H*-benzo[*lmn*][3,8]phenanthrolin-2-yl}-3-(1-trityl-1*H*-imidazol-4-yl)-propionic acid methyl ester, (*S*,*S*)-2h

Work-up: the residue was taken-up with water. The suspension was filtered with a Büchner funnel, the precipitate was washed with water (200 ml) and dried under vacuum. The crude product was purified by column chromatography (silica, $CHCl_3$/methanol 200/10 v/v). 575 mg of product were obtained as a bright yellow powder, yield 73%. TLC (silica, $CHCl_3$/methanol 9/1 v/v) Rf: 0.84; m.p. 165-170 °C (dec); ^{1}H NMR (400 MHz, $CDCl_3$) δ(ppm): 8.65 (s, 4H), 7.40-7.10 (m, 20H), 6.96-6.88 (m, 12H), 6.58 (s, 2H), 5.99 (dd, J_1 = 9.5, J_2 = 6.0, 2H), 3.75 (s, 6H), 3.65-3.50 (m, 4H); ^{13}C NMR {^{1}H} (125.78 MHz, $CDCl_3$) δ(ppm): 169.7, 162.3, 142.2, 138.6, 136.7, 131.0, 129.6, 127.8, 127.8, 126.8, 126.4, 119.1, 74.9, 54.1, 52.6, 27.1; HRMS (ESI+) calcd. for: $C_{66}H_{51}N_6O_8$ $[M+H]^+$ (m/z): 1055.3768, found: 1055.3755.

(S)-2-{7-[(S)-1-Carboxy-2-(1-trityl-1*H*-imidazol-4-yl)-ethyl]-1,3,6,8-tetraoxo-3,6,7,8-tetrahydro-1*H*-benzo[*lmn*][3,8]phenanthrolin-2-yl}-3-(1-trityl-1*H*-imidazol-4-yl)-propionic acid, (S,S)-2i

Work up: the dark brown oil was taken up into $CHCl_3$ (100 ml). The organic phase was washed with 1N HCl (2 x 50 ml), brine (1 x 75 ml) and dried over anhydrous Na_2SO_4. The

solvent was removed under reduced pressure and dried under high-vacuum. The product was obtained in the form of a yellow solid in 75% yield. m.p. 251-254°C (dec); ^{1}H NMR (400 MHz, DMSO-d_6) δ(ppm): 8.72 (s, 4H), 7.91 (bs, 2H), 7.25-7.21 (m, 18H), 6.95 (bs, 2H), 6.88-6.86 (m, 12H), 5.84-5.80 (dd, J_1 = 14.5, J_2 = 4.0, 2H), 3.54-3.49 (dd, J_1 = 18.0, J_2 = 4.0, 2H), 3.42-3.35 (dd, J_1 = 25.5, J_2 = 11.0, 2H); ^{13}C NMR {^{1}H} (100.62 MHz, $CDCl_3$) δ(ppm): 169.6, 169.5, 162.1, 147.7, 141.0, 137.1, 131.3, 128.9, 128.2, 127.7, 127.5, 126.6, 127.1, 125.8, 53.3, 37.4, 34.4, 21.4; HRMS (ESI+) calcd. for: $C_{64}H_{47}N_6O_8$ $[M+H]^+$ (m/z): 1027.3455, found: 1027.3449.

(S)-2-{7-[(S)-1-Carboxy-2-(1*H*-indol-3-yl)-ethyl]-1,3,6,8-tetraoxo-3,6,7,8-tetrahydro-1*H*-benzo[*lmn*][3,8]phenanthrolin-2-yl}-3-(1*H*-indol-3-yl)-propionic acid, (*S*,*S*)-2j

Work-up: the dark brown oil was taken up into MeOH (400 ml). This solution was added under stirring to 600 ml of 1N HCl. The resulting suspension was allowed to coagulate overnight and then filtered through a P4 sintered glass funnel. The solid was then washed with 100 ml deionized water and dried *in vacuo*. The product was obtained in the form of a brown solid in 90% yield. m.p. 263-265 °C (dec) (Lit:[1] 286-288); ^{1}H NMR (400 MHz, DMSO-d_6) δ(ppm): 12.97 (bs, 2H), 10.63 (bs, 2H), 8.59 (s, 4H), 7.46-7.44 (d, J = 7.5, 2H), 7.19-7.17 (d, J = 8.0, 2H), 7.03 (s, 2H), 6.94-6.90 (dd, J_1 = 15.0, J_2 = 7.0, 2H), 6.80-6.77 (dd, J_1 = 15.0, J_2 = 7.5, 2H), 5.86-5.82 (dd, J_1 = 14.0, J_2 = 8.5, 2H), 3.69-3.65 (dd, J_1 = 19.5, J_2 = 5.0, 2H), 3.51-3.45 (dd, J_1 = 23.5, J_2 = 9.0, 2H); ^{13}C NMR {^{1}H} (100.62 MHz, DMSO-d_6) δ(ppm): 173.8, 170.4, 161.9, 135.8, 131.0, 126.9, 125.9, 125.6, 123.6, 120.7, 118.1, 117.8, 111.2, 110.0, 54.2, 24.0; HRMS (ESI+) calcd. for: $C_{36}H_{24}N_4NaO_8$ $[M+Na]^+$ (m/z): 663.1492, found: 663.1507.

(S)-3-(1*H*-Indol-3-yl)-2-{7-[(S)-2-(1*H*-indol-3-yl)-1-methoxycarbonyl-ethyl]-1,3,6,8-tetraoxo-3,6,7,8-tetrahydro-1*H*-benzo[*lmn*][3,8]phenanthrolin-2-yl}-propionic acid methyl ester, (*S*,*S*)-2k

Work up: the dark brown oil was taken up into $CHCl_3$ (200 ml). The organic phase was washed with 1N HCl (2 x 75 ml), brine (1 x 100 ml) and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure and the resulting solid dried under high-vacuum. The product was obtained in the form of a red-brown solid in 82% yield. m.p. 258-260 °C (dec); ^{1}H NMR (400 MHz, DMSO-d_6) δ(ppm): 10.67 (bs, 2H), 8.59 (s, 4H), 7.48-7.46 (d, J = 7.5, 2H), 7.20-7.18 (d, J = 8.0, 2H), 7.05 (s, 2H), 6.94-6.90 (dd, J_1 = 14.5, J_2 = 7.0, 2H), 6.81-6.77 (dd, J_1 = 15.0, J_2 = 7.5, 2H), 5.96-5.22 (dd, J_1 = 14.0, J_2 = 5.5, 2H), 3.72-3.66 (m, 5H), 3.49-3.43 (dd, J_1 = 23.5, J_2 = 9.0, 2H); ^{13}C NMR {^{1}H} (100.62 MHz, DMSO-d_6) δ(ppm): 169.4, 161.9, 135.8, 131.1, 126.9, 125.9, 125.5, 123.8, 120.7, 118.1, 117.8, 111.2, 109.5, 53.9, 52.2, 23.9; HRMS (ESI+) calcd. for: $C_{39}H_{29}N_4O_8$ $[M+H]^+$ (m/z): 669.1985, found: 669.1960.

(S)-2-[7-((S)-3-*tert*-Butoxycarbonyl-1-carboxy-propyl)-1,3,6,8-tetraoxo-3,6,7,8-tetrahydro-1*H*-benzo[*lmn*][3,8]phenanthrolin-2-yl]-pentanedioic acid 5-*tert*-butyl ester, (*S*,*S*)-2l

Work-up: the dark brown oil was taken-up with 3 ml of acetonitrile and added drop wise to a vigorously stirred 2.5% aqueous solution of $KHSO_4$. The product coagulates as a pink powder, the precipitate was filtered with a Büchner funnel, washed with water and dried under vacuum. 421 mg of product were obtained as a light pink powder, 88% yield. m.p. 145°C (dec); ^{1}H NMR (400 MHz, DMSO-d_6) δ(ppm): 12.90 (bs, 2H), 8.72 (s, 4H), 5.55 (dd, J_1 = 9.4, J_2 = 4.3, 2H), 2.45 (m, 4H), 2.35 (t, 4H, J = 7), 2.27 (m, 2H), 1.27 (s, 18H); ^{13}C NMR {^{1}H} (100.61 MHz, DMSO-d_6) δ(ppm): 171.6, 170.2, 162.4, 130.9, 126.3, 126.0, 79.5, 52.8, 31.5, 27.5, 23.4; HRMS (ESI+) calcd. for: $C_{32}H_{35}N_2O_{12}$ $[M+H]^+$ (m/z): 639.2190, found: 639.2194.

(S)-6-*tert*-Butoxycarbonylamino-2-[7-((S)-5-*tert*-butoxycarbonylamino-1-carboxy-pentyl)-1,3,6,8-tetraoxo-3,6,7,8-tetrahydro-1*H*-benzo[*lmn*][3,8]phenanthrolin-2-yl]-hexanoic acid, (*S*,*S*)-2m

Work-up: the dark brown oil was taken up with 3 ml of acetonitrile and added drop wise to a vigorously stirred 2.5% aqueous solution of $KHSO_4$. The product coagulates as a pink yellow powder, the precipitate was filtered with a Büchner funnel, washed with water and dried under vacuum. 498 mg of product were obtained as a light pink powder, 92% yield. m.p. 150 °C (dec) ^{1}H NMR (400 MHz, DMSO-d_6) δ(ppm): 12.83 (bs, 2H), 8.69 (s, 4H), 5.52 (dd, J_1 = 9.2, J_2 = 5.0, 2H), 2.81 (m, 4H), 2.21 (m, 2H), 2.05 (m, 2H) 1.44-1-1.12 (m, 26H); ^{13}C NMR {^{1}H} (100.61 MHz, DMSO-d_6) δ(ppm): 170.5, 162.2, 155.4, 131.1, 126.3, 125.9, 77.0, 53.3, 29.2, 28.0, 23.1; HRMS (ESI+) calcd. for: $C_{36}H_{45}N_4O_{12}$ $[M+H]^+$ (m/z): 725.3034, found: 725.3062.

2-[7-(1-Carboxy-ethyl)-1,3,6,8-tetraoxo-3,6,7,8-tetrahydro-1*H*-benzo[*lmn*][3,8]phenanthrolin-2-yl]-propionic acid, (*S*,*S*)-2n

The reaction was performed on 3.728 mmol (1g) 1,4,5,8-naphthalenetetracarboxylic dianhydride and 7.457 mmol (664 mg) H-(L)-Ala-OH using synthetic method B.

Work-up: the dark brown residue was taken up into CH_3CN/MeOH (10 ml 2:1 v/v). This solution was added under stirring to 200 ml of 1N HCl. The resulting suspension was allowed to coagulate for 1 hour and then filtered using a Büchner funnel. The solid was then washed with 50 ml deionized water and dried *in vacuo*. The product was obtained in the form of a brown solid in 84% yield. m.p. 324-326°C (dec); ^{1}H NMR (400 MHz, DMSO-d_6) δ(ppm): 12.84 (bs, 2H), 8.74 (s, 4H), 6.66 (bt, 2H), 5.62-5.56 (dd, J_1 = 21.0, J_2 = 7.0, 2H), 1.57-1.56 (d, J_1 = 7.0, 3H); ^{13}C NMR {^{1}H} (100.61 MHz, DMSO-d_6) δ(ppm): 171.0, 162.0, 130.9, 126.1, 49.0, 14.3; HRMS (ESI+) calcd. for: $C_{20}H_{15}N_2O_8$ $[M+H]^+$ (m/z): 411.0828, found: 411.0833.

2-{7-{1-Carboxy-4-[*N*'-(2,2,5,7,8-pentamethyl-1-benzopyran-6-sulfonyl)-guanidino]-butyl}-1,3,6,8-tetraoxo-3,6,7,8-tetrahydro-1*H*-benzo[*lmn*][3,8]phenanthrolin-2-yl}-5-[*N*'-(2,2,5,7,8-pentamethyl-1-benzopyran-6-sulfonyl)-guanidino]-pentanoic acid, (*S*,*S*)-2o

The reaction was performed on 0.373 mmol (100 mg) 1,4,5,8- naphthalenetetracarboxylic dianhydride and 0.746 mmol (329 mg) H-Arg(Pmc)-OH using synthetic method B.

Work-up: the dark brown residue was taken up into CH_3CN (4 ml). This solution was added under stirring to 80 ml of 1N HCl. The resulting suspension was allowed to coagulate for 1 hour and then filtered using a Büchner funnel. The solid was then washed with 50 ml deionized water and dried *in vacuo*. The product was obtained in the form of a pink-yellow solid in 98% yield. m.p. 280-284°C (dec); ^{1}H NMR (400 MHz, DMSO-d_6) δ(ppm): 8.73 (s, 4H), 6.72 (bs, 3H), 6.34 (bs, 3H), 5.53-5.49 (dd, J_1 = 14.0, J_2 = 4.5, 2H), 3.09-2.97 (m, 4H), 2.40 (s, 6H), 2.38 (s, 6H), 2.27-2.18 (m, 2H), 2.06-1.96 (m, 8H), 1.73-1.70 (t, 4H), 1.51-1.35 (t, 4H), 1.22 (s, 12H); ^{1}H NMR (400 MHz, CD_3OD) δ(ppm): 8.68 (s, 4H), 5.62-5.58 (dd, J_1 = 14.5, J_2 = 5.0, 2H), 3.19-3.15 (m, 4H), 2.58-2.55 (m, 4H), 2.44 (s, 6H), 2.42 (s, 6H), 2.35-2.28 (m, 2H), 2.18-2.09 (m, 2H), 2.02 (s, 6H), 1.77-1.74 (t, 4H), 1.61-1.45 (m, 4H), 1.25 (s, 12H); ^{13}C NMR {^{1}H} (100.61 MHz, DMSO-d_6) δ(ppm): 170.4, 162.3, 155.8, 152.3, 134.5, 134.3, 134.0, 131.2, 126.3, 125.9, 122.6, 117.7, 113.8, 73.4, 53.3, 35.7, 32.0, 26.4, 25.8, 20.6, 18.0, 16.9, 11.8.

1-[7-(1-Carboxy-cyclohexyl)-1,3,6,8-tetraoxo-3,6,7,8-tetrahydro-1*H*-benzo[*lmn*][3,8]phenanthrolin-2-yl]-cyclohexanecarboxylic acid, 2p

The reaction was performed on 0.373 mmol (100 mg) 1,4,5,8- naphthalenetetracarboxylic dianhydride and 0.746 mmol (107 mg) H-Ac6c-OH using synthetic method B.

Work-up: the dark brown residue was taken up into MeOH (10 ml). This suspension was added under stirring to 80 ml 0.1% $Mg(ClO_4)_2$ aqueous solution. The resulting suspension

was allowed to coagulate for 15 minutes and then filtered using a Büchner funnel. The solid was taken up into MeOH (10 ml) and added to 80 ml 1N HCl. The resulting suspension was allowed to coagulate for 1 hour and then filtered using a Büchner funnel. The solid was then washed with 50 ml deionized water and dried *in vacuo*. The product was obtained in the form of a pale-green solid in 40% yield. It is worth mentioning the poor solubility of the product as it precipitates upon standing from DMSO or DMF solutions. m.p. > 330 °C; ^{1}H NMR (400 MHz, DMF-d_7) δ(ppm): 8.66 (s, 4H), 2.95-2.94 (m, 2H), 2.71-2.67 (m, 2H), 2.21-2.18 (m, 4H), 1.84-1.77 (m, 4H), 1.63-1.61 (m, 6H), 1.44-1.41 (m, 2H); ^{1}H NMR (400 MHz, DMSO-d_6) δ(ppm): 12.45 (bs, 2H), 8.56 (s, 4H), 2.85-2.79 (m, 4H), 2.10-2.07 (m, 4H), 1.73-1.52 (m, 10H), 1.39-1.32 (m, 2H); ^{13}C NMR {^{1}H} (100.61 MHz, DMF-d_7) δ(ppm): 173.6, 165.0, 130.9, 128.5, 126.6, 67.8, 32.0, 25.8, 23.4; HRMS (ESI+) calcd. for: $C_{28}H_{27}N_2O_8$ $[M+H]^+$ (m/z): 519.1767, found: 519.1772.

1-(1,3,6,8-Tetraoxo-1,3,6,8-tetrahydro-2-oxa-7-aza-pyren-7-yl)-cyclohexane-carboxylic acid, 3p

The compound was isolated from the reaction between 1,4,5,8- naphthalene-tetracarboxylic dianhydride (1.865 mmol, 500 mg) and H-Ac6c-OH (3.73 mmol, 535 mg) using synthetic method B. The dark brown residue was taken up into MeOH (40 ml) and added to 150 ml 1N HCl. The resulting suspension was allowed to coagulate for 1 hour and then filtered using a Büchner funnel. The a third of the solid was then dissolved in sat. $NaHCO_3$ (200 ml). The pH of the solution was lowered to 8 and the precipitate formed was allowed to coagulate over night and filtered. The filtrate was washed with 1N HCl (50 ml), followed by deionized water (50 ml) and dried *in vacuo*. The product was obtained in the form of a brown-green solid in 2% yield, containing *ca.* 10% (by ^{1}H NMR) H-Ac6c-OH (starting material) impurity. It is worth mentioning the poor solubility of product as it precipitates upon standing from under-saturated solutions in DMSO. m.p. > 330 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ(ppm): 12.06 (bs, 1H), 8.55-8.51 (d, J = 14.0, 4H), 2.82-2.77 (m, 2H), 2.07-2.04 (m, 2H), 1.73-1.53 (m, 5H), 1.38-1.32 (m, 1H); ^{13}C NMR {^{1}H} (100.61 MHz, DMSO-d_6) δ(ppm): 172.9, 163.9, 163.2, 130.1, 129.7, 127.6, 127. 3, 126.8, 125.3, 67.9, 30.9, 24.8, 22.4.

(R)-2-{7-[(S)-1-Carboxy-2-(1-trityl-1*H*-imidazol-4-yl)-ethyl]-1,3,6,8-tetraoxo-3,6,7,8-tetrahydro-1*H*-benzo[*lmn*][3,8]phenanthrolin-2-yl}-3-tritylsulfanyl-propionic acid, (*R*,*S*)-4a

Work up: the dark brown oil was taken up into $CHCl_3$ (100 ml). The organic phase was washed with 1N HCl (2 x 50 ml), brine (1 x 75 ml) and dried over anhydrous Na_2SO_4. The solvent was removed under reduced pressure and dried under high-vacuum. The product was obtained in the form of a tan solid in 81% yield. m.p. 170-172°C (dec); ^{1}H NMR (400 MHz, DMSO-d_6) δ(ppm): 13.21 (bs, 2H), 8.75-8.68 (dd, J_1 = 26.5, J_2 = 7.5, 4H), 7.23-7.12 (m, 26H), 6.80-6.78 (d, J_1 = 7.5, 5H), 5.84-5.80 (dd, J_1 = 15.0, J_2 = 4.5, 1H), 5.61-5.57 (dd, J_1 = 15.0, J_2 = 4.5, 1H), 3.48-3.33 (m, 2H), 3.13-3.08 (dd, J_1 = 17.0, J_2 = 4.5, 1H), 3.00-2.94 (dd, J_1 = 23.5, J_2 = 10.5, 1H); ^{13}C NMR {^{1}H} (100.62 MHz, $CDCl_3$) δ(ppm): 169.7, 169.5, 169.1, 143.9, 141.1, 131.6, 131.3, 129.5, 128.9, 128.9, 128.5, 128.0, 127.9, 127.7, 127.5, 126.7, 126.6, 126.2, 126.1, 125.5, 66.5, 66.4; HRMS (ESI+) calcd. for: $C_{61}H_{45}N_4O_8S$ $[M+H]^+$ (m/z): 993.2958, found: 993.2909.

(S)-2-{7-[(S)-1-Carboxy-2-(4-hydroxy-phenyl)-ethyl]-1,3,6,8-tetraoxo-3,6,7,8-tetrahydro-1*H*-benzo[*lmn*][3,8]phenanthrolin-2-yl}-succinic acid 1-methyl ester, (*S*,*S*)-4c

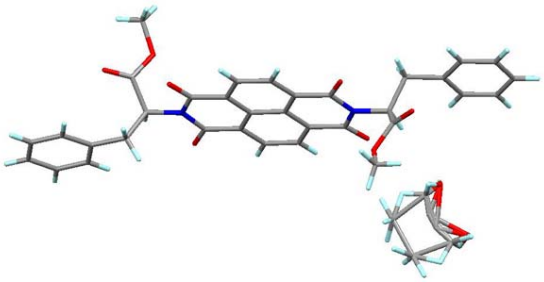
Work up: the dark brown oil was taken up into $CHCl_3$ (10 ml). This solution was added under stirring to 75 ml of 1N HCl. The resulting suspension was filtered using a Büchner funnel. The brown solid was then recrystallized from acetone/hexane and dried *in vacuo*. The product was obtained in the form of a orange solid in 90% yield. m.p. 160-162°C (dec); ^{1}H NMR (400 MHz, Acetone-d_6) δ(ppm): 10.81 (bs, 1H), 8.77-8.71 (dd, J_1 = 24.5, J_2 = 7.5, 4H), 7.02-6.99 (d, 2H, J = 8.5), 6.55-6.53 (d, J = 8.5, 2H), 6.27-6.24 (dd, J_1 = 13.5, J_2 = 5.0, 1H), 6.02-5.98 (dd, J_1 = 15.5, J_2 = 5.5, 1H), 3.68 (s, 3H), 3.61-3.38 (m, 3H), 2.97-2.91 (m, 1H); ^{13}C NMR {^{1}H} (100.62 MHz, Acetone-d_6) δ(ppm): 171.8, 170.5, 170.0, 163.2, 163.1, 156.7, 131.9, 131.0, 129.0, 127.8, 127.5, 127.5, 127.2, 115.8, 54.5, 52.9, 50.6, 34.4; HRMS (ESI+) calcd. for: $C_{22}H_{21}N_2O_{11}$ $[M+H]^+$ (m/z): 561.1145, found: 561.1169.

(S)-2-{7-[(S)-2-(1*H*-Indol-3-yl)-1-methoxycarbonyl-ethyl]-1,3,6,8-tetraoxo-3,6,7,8-tetrahydro-1*H*-benzo[*lmn*][3,8]phenanthrolin-2-yl}-3-methyl-pentanoic acid methyl ester, (S,S)-4d

Work up: the dark brown oil was taken up into CH_3CN (15 ml). This solution was added under stirring to 75 ml of 1N HCl. The resulting suspension was allowed to coagulate overnight and then filtered using a Büchner funnel. The solid was then washed with 100 ml deionized water and dried *in vacuo*. The product was obtained in the form of a red-brown solid in 65% yield. m.p. 122-124°C; ^{1}H NMR (400 MHz, DMSO-d_6) δ(ppm): 10.66 (bs, 1H), 8.71-8.64 (dd, J_1 = 26.5, J_2 = 7.5, 4H), 7.51-7.49 (d, J = 8.0, 1H), 7.20-7.18 (d, J = 8.0, 1H), 7.05-7.04 (d, J = 2.0, 1H), 6.95-6.91 (dd, J_1 = 16.0, J_2 = 8.0, 1H), 6.84-6.81 (dd, J_1 = 16.0, J_2 = 8.0, 1H), 6.00-5.90 (dd, J_1 = 15.0, J_2 = 5.5, 1H), 5.33-5.30 (d, J = 8.5, 1H), 3.73-3.67 (m, 4H), 3.57 (s, 3H), 3.52-3.46 (dd, J_1 = 23.5, J_2 = 9.0, 1H), 2.47-2.40 (m, 1H), 1.33-1.26 (m, 1H), 1.18-1.16 (d, J = 6.5, 3H), 0.95-0.86 (m, 1H), 0.76-0.72 (t, 3H); ^{13}C NMR {^{1}H} (100.62 MHz, DMSO-d_6) δ(ppm): 169.5, 169.1, 135.9, 131.5, 131.3, 127.0, 123.8, 120.8, 118.2, 117.9, 111.2, 109.5, 79.1, 57.6, 53.9, 52.3, 52.1, 33.3, 24.5, 24.0, 17.5, 10.9; HRMS (ESI+) calcd. for: $C_{33}H_{29}N_3NaO_8$ $[M+Na]^+$ (m/z): 618.1852, found: 618.1838.

X-ray Characterization Data:

Table S1. Crystal data and structure refinement for $C_{34}H_{26}N_2O_8 \cdot C_3H_6O$



Identification code	js0611	
Empirical formula	$C_{37}H_{32}N_2O_9$	
Formula weight	648.65	
Temperature	180(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	C222(l)	
Unit cell dimensions	a = 9.2755(2) Å	α = 90°
	b = 13.5333(3) Å	β = 90°
	c = 25.1099(7) Å	γ = 90°
Volume	3152.00(13) $Å^3$	
Z	4	
Density (calculated)	1.367 Mg/m^3	
Absorption coefficient	0.099 mm^{-1}	
F(000)	1360	
Crystal size	0.46 x 0.12 x 0.02 mm^3	
Theta range for data collection	2.66 to 27.47°	
Index ranges	-11 <= h <= 11, -16 <= k <= 17, -32 <= l <= 32	
Reflections collected	13658	
Independent reflections	2015 [R(int) = 0.0909]	
Completeness to theta = 30.04°	99.2 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	1.001 and 0.861	
Averaged Friedel pairs	1524	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2015 / 0 / 217	
Goodness-of-fit on F2	1.053	
Final R indices [I>2sigma(I)]	Rl = 0.0488, wR2 = 0.1199	
R indices (all data)	Rl= 0.0961, wR2 = 0.1423	
Absolute structure parameter	-3(2)	
Extinction coefficient	0.0057(11)	
Largest diff. peak and hole	0.317 and -0.394 e.$Å^{-3}$	

Diffractometer: *Nonius KappaCCD* area detector. **Data collection:** Collect (Collect: Data collection software, R. Hooft, Nonius B.V., 1998). **Data reduction**: *Denzo* (Z. Otwinowski & W. Minor, *Methods in Enzymology* (1997) Vol. **276**: *Macromolecular Crystallography*, part A, pp. 307–326; C. W. Carter, Jr. & R. M. Sweet, Eds., Academic Press). S**tructure refinement**: *SHELXL97* (G. M. Sheldrick (1997), University of Göttingen, Germany). **Graphics:** Mercury ver. 1.4.1 (CCDC) and Ortep-3 for Windows ver. 1.08 (L. J. Farrugia, *J. Appl. Cryst* (1997), **30**, 565).

Special details: All hydrogen atoms were placed in idealized positions and refined using a riding model. The solvent is disordered acetone.

Figure S1. Top view of the molecular structure of **2f** showing the atom labeling scheme Single crystals obtained from acetone solution. Displacement ellipsoids are scaled to the 50% probability level. A discordered acetone molecule has been removed for clarity.

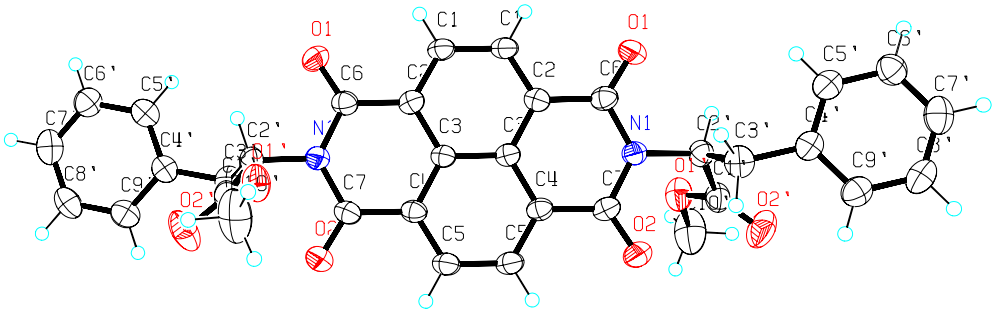


Figure S2. View of the molecular structure of **2f** normal to the (010) plane. Single crystals obtained from acetone solution. Displacement ellipsoids are scaled to the 50% probability level. A discordered acetone molecule has been removed for clarity.

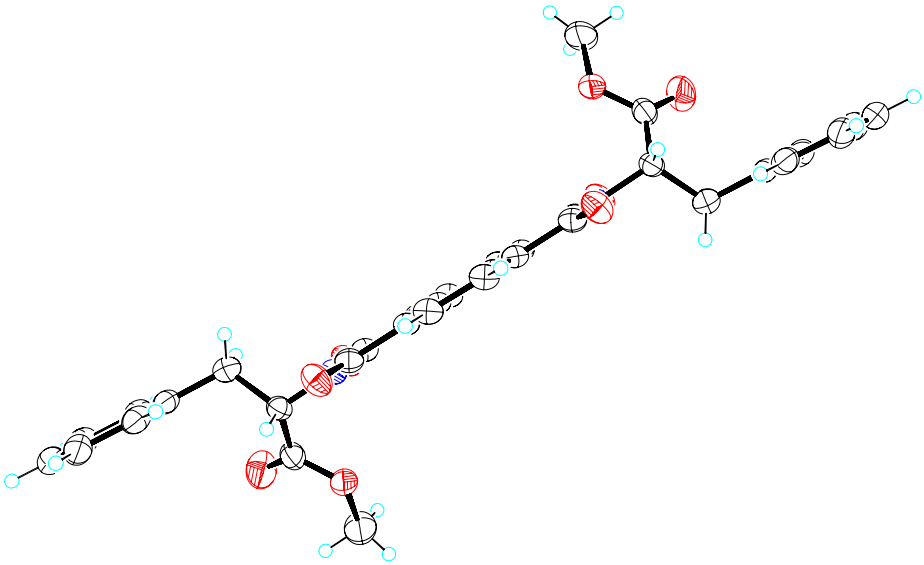


Figure S3. Unit cell packing diagram for single crystals of **2f** obtained from acetone. View normal to (010) plane.

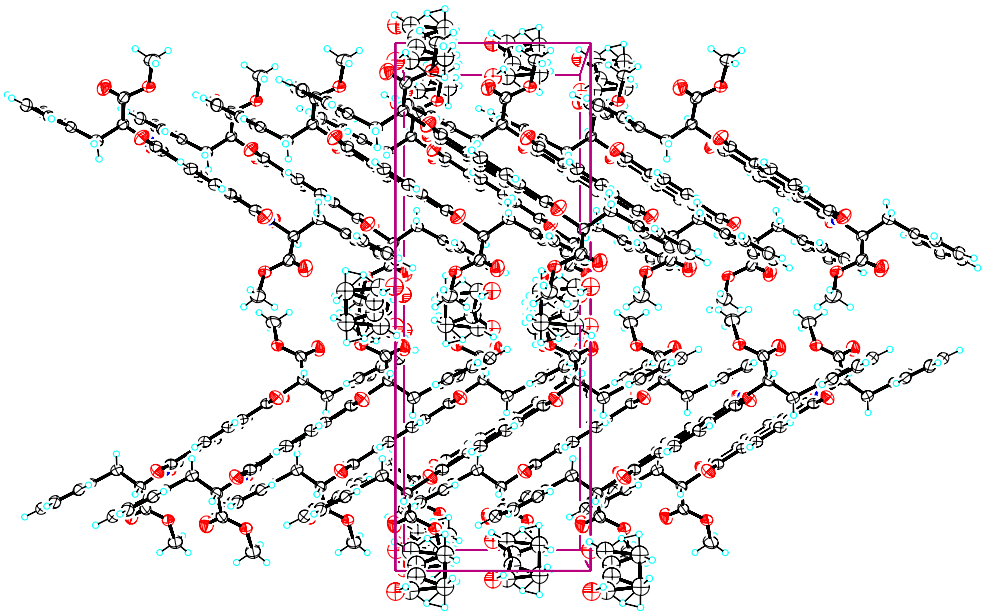


Table S2. Crystal data and structure refinement for $C_{34}H_{26}N_2O_8 \cdot C_2H_3N$

Identification code	js0614	
Empirical formula	$C_{36}H_{29}N_3O_8$	
Formula weight	631.62	
Temperature	120(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P1	
Unit cell dimensions	a = 8.0870(1) Å	α = 82.999(1)°
	b = 8.2484(1) Å	β = 81.897(1)°
	c = 12.1896(3) Å	γ = 68.672(1)°
Volume	747.65(2) $Å^3$	
Z	1	
Density (calculated)	1.403Mg/m^3	
Absorption coefficient	0.100 mm^{-1}	
F(000)	330	
Crystal size	0.46 x 0.46 x 0.14 mm^3	
Theta range for data collection	3.73 to 30.04°	
Index ranges	-11 <= h <= 11, -11 <= k <= 11, -17 <= l <= 17	
Reflections collected	11161	
Independent reflections	4330 [R(int) = 0.0209]	
Completeness to theta = 30.04°	98.9 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.990 and 0.945	
Averaged Friedel pairs	2465	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4330 / 3 / 426	
Goodness-of-fit on F2	1.095	
Final R indices [I>2sigma(I)]	Rl = 0.0339, wR2 = 0.0957	
R indices (all data)	Rl = 0.0347, wR2 = 0.0965	
Absolute structure parameter	0.6(6)	
Largest diff. peak and hole	0.408 and -0.434 e.$Å^{-3}$	

Diffractometer: *Nonius KappaCCD* area detector. **Data collection:** Collect (Collect: Data collection software, R. Hooft, Nonius B.V., 1998). **Data reduction**: *Denzo* (Z. Otwinowski & W. Minor, *Methods in Enzymology* (1997) Vol. **276**: *Macromolecular Crystallography*, part A, pp. 307–326; C. W. Carter, Jr. & R. M. Sweet, Eds., Academic Press). S**tructure refinement**: *SHELXL97* (G. M. Sheldrick (1997), University of Göttingen, Germany). **Graphics:** Mercury ver. 1.4.1 (CCDC) and Ortep-3 for Windows ver. 1.08 (L. J. Farrugia, *J. Appl. Cryst* (1997), **30**, 565).

Special details: All hydrogen atoms were placed in idealized positions and refined using a riding model.

Figure S4. Top view of of the molecular structure of **2f** showing the atom labeling scheme Single crystals obtained from CH_2Cl_2 / CH_3CN mixture. Displacement ellipsoids are scaled to the 50% probability level.

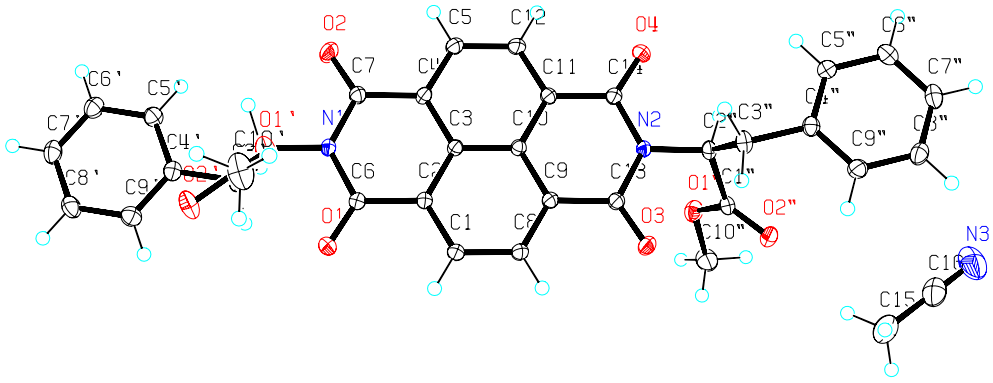
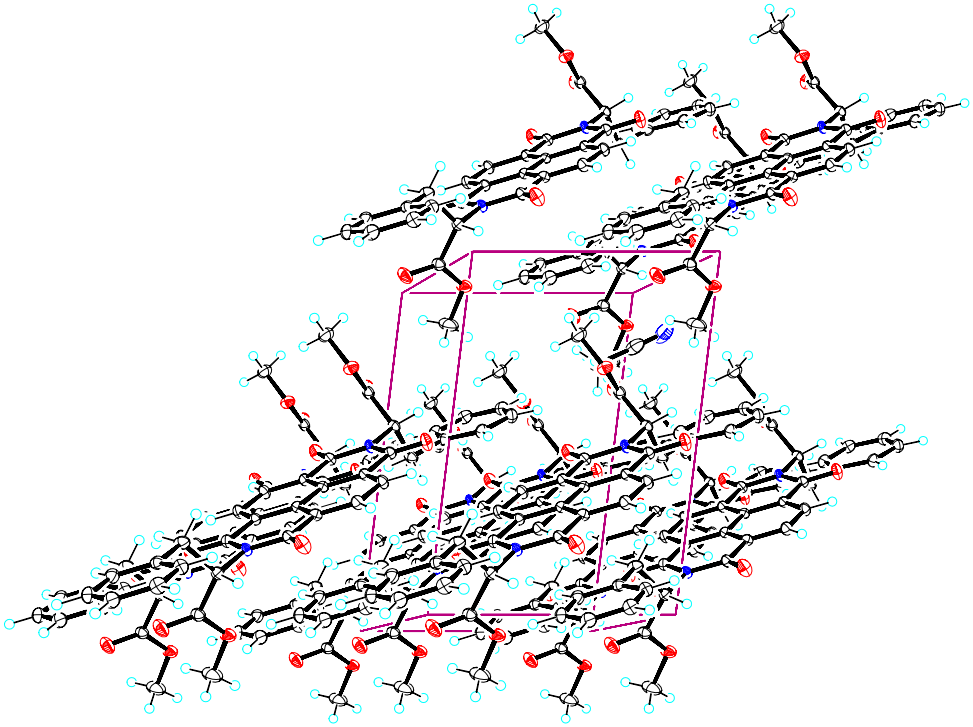
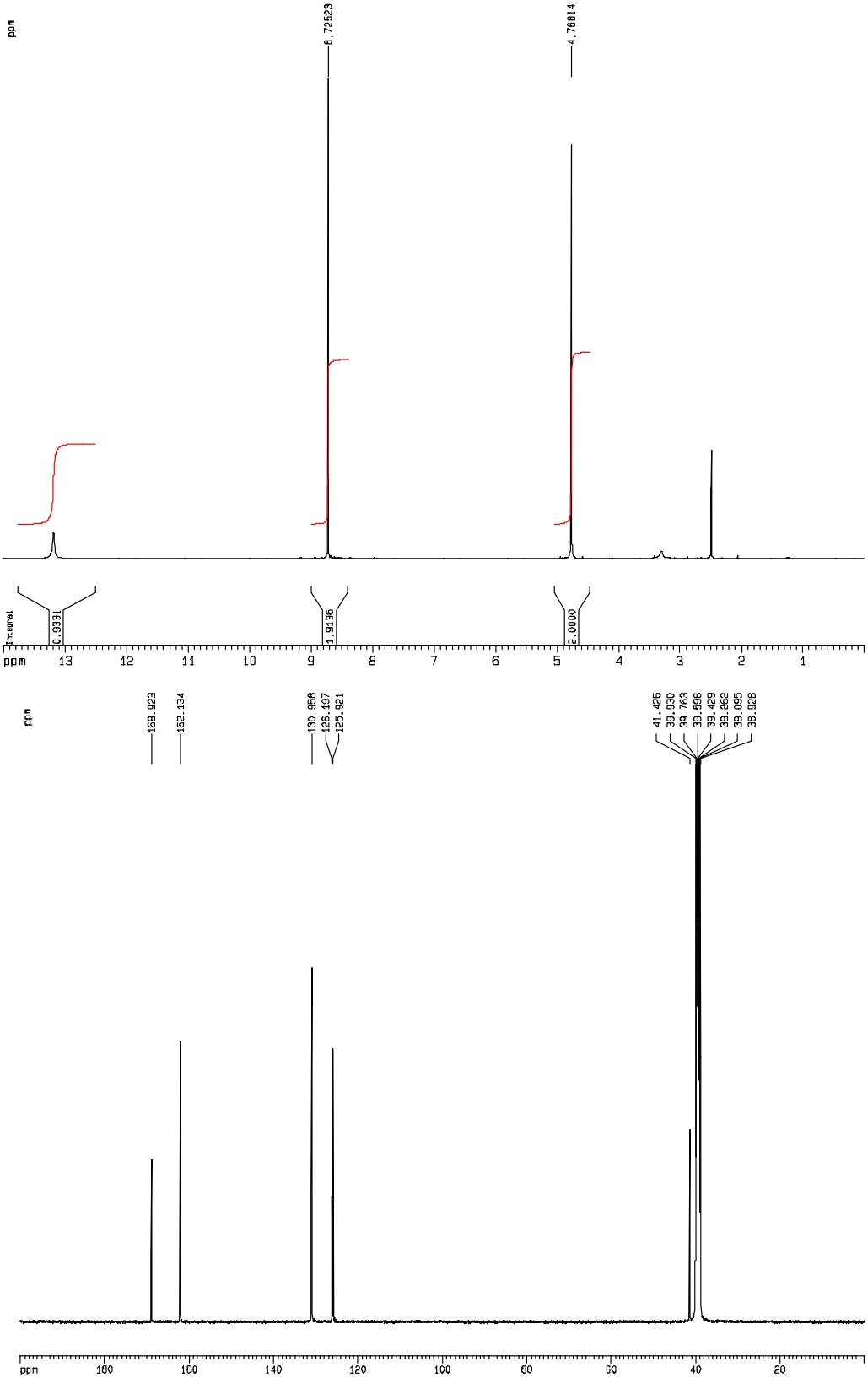


Figure S4. Unit cell packing diagram for single crystals of **2f** obtained from CH_2Cl_2 / CH_3CN mixture. View normal to (100) plane.



^{1}H NMR and ^{13}C NMR Spectra of Compounds 2a-2p and 4a-4d

2a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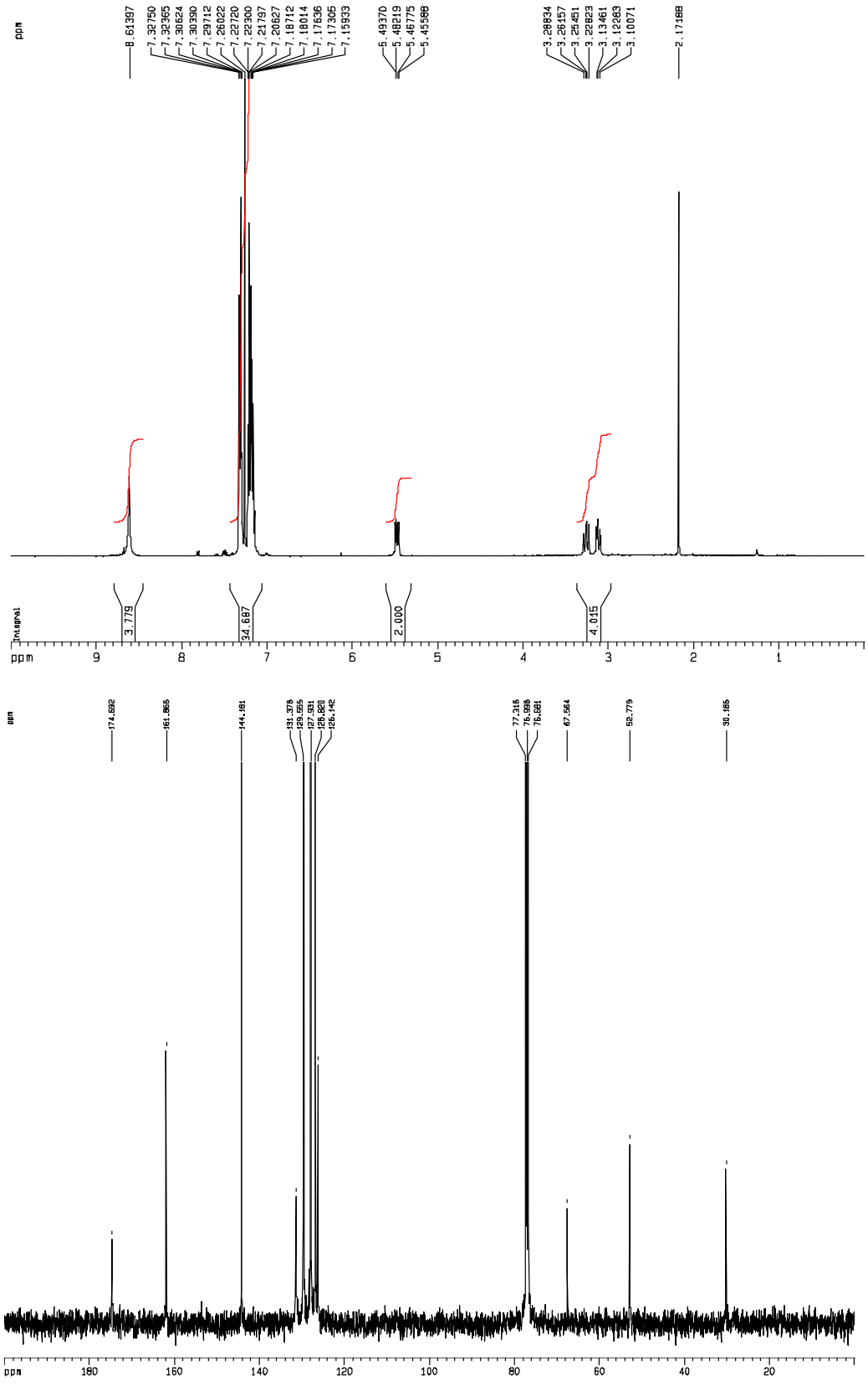
(*R*,*R*)-**2b**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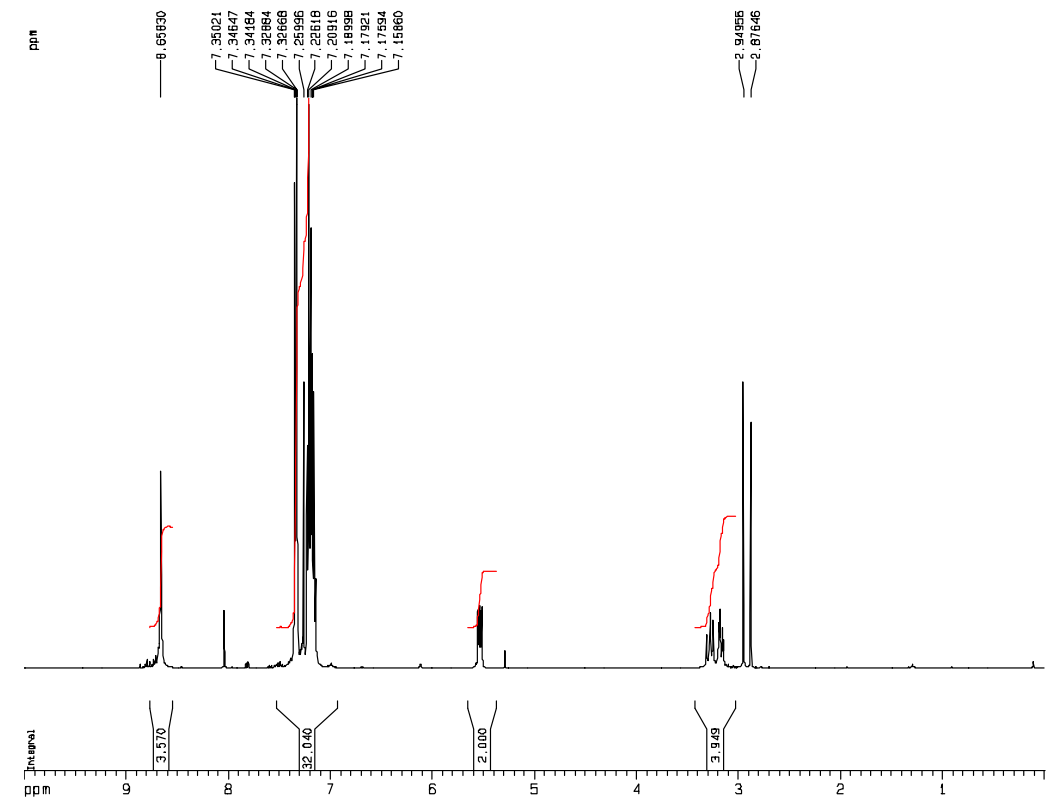
(*S*,*S*)-**2b**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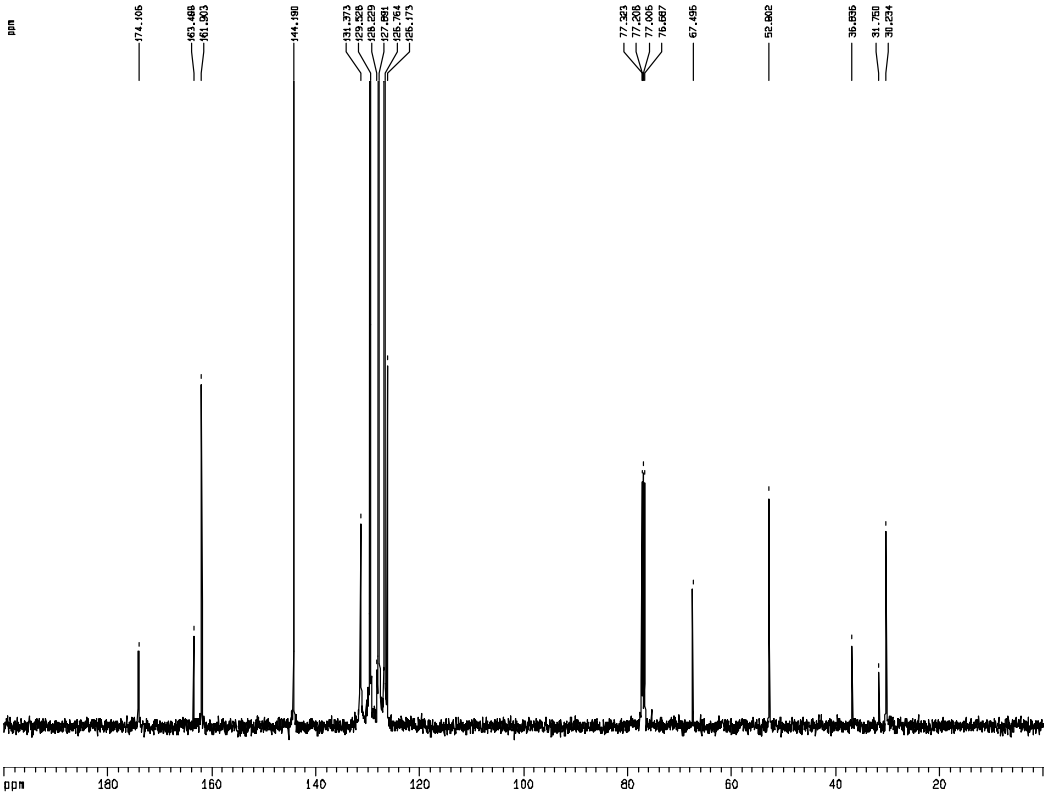
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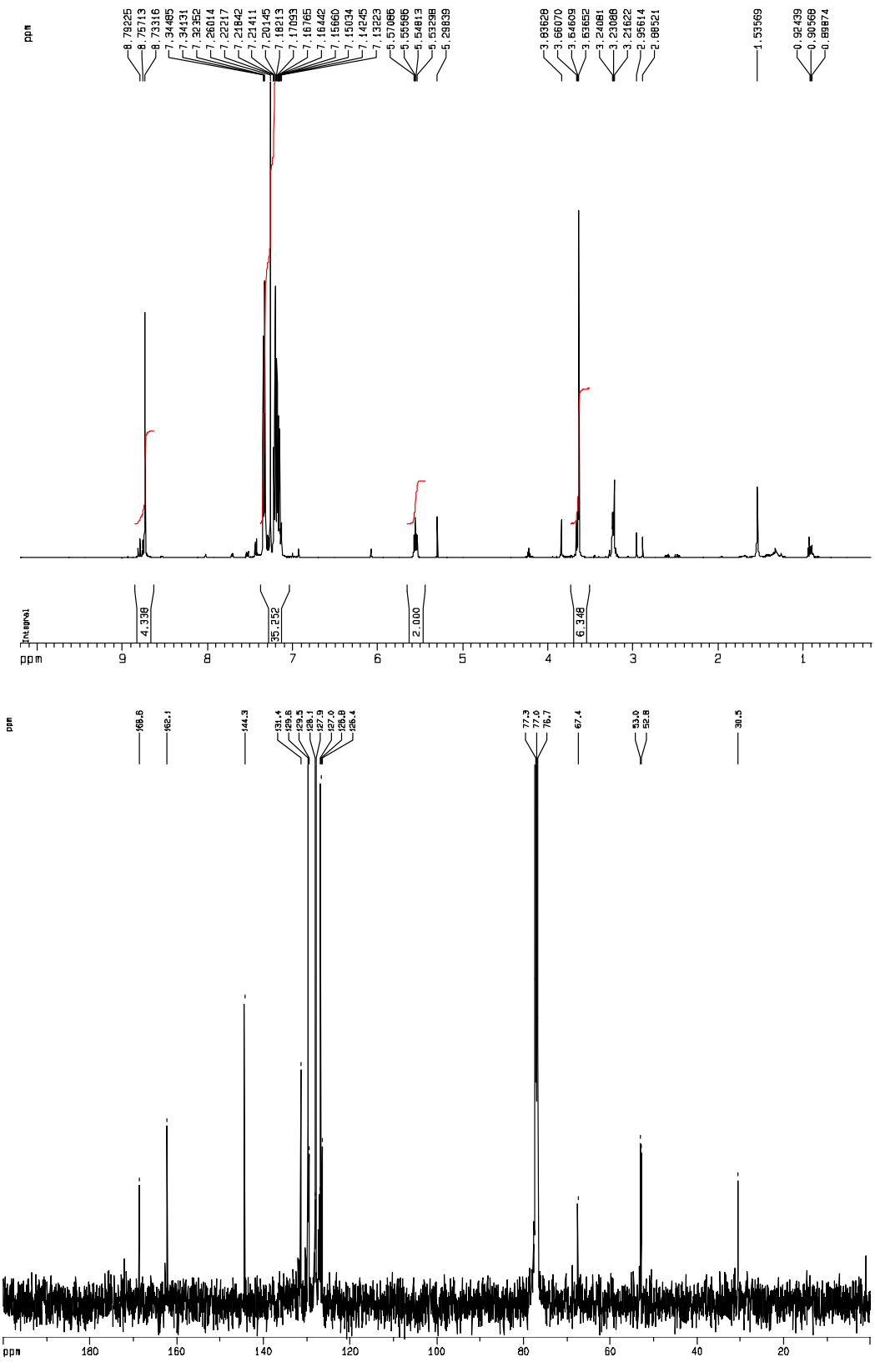
(*R*,*R*)-**2c**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ppm
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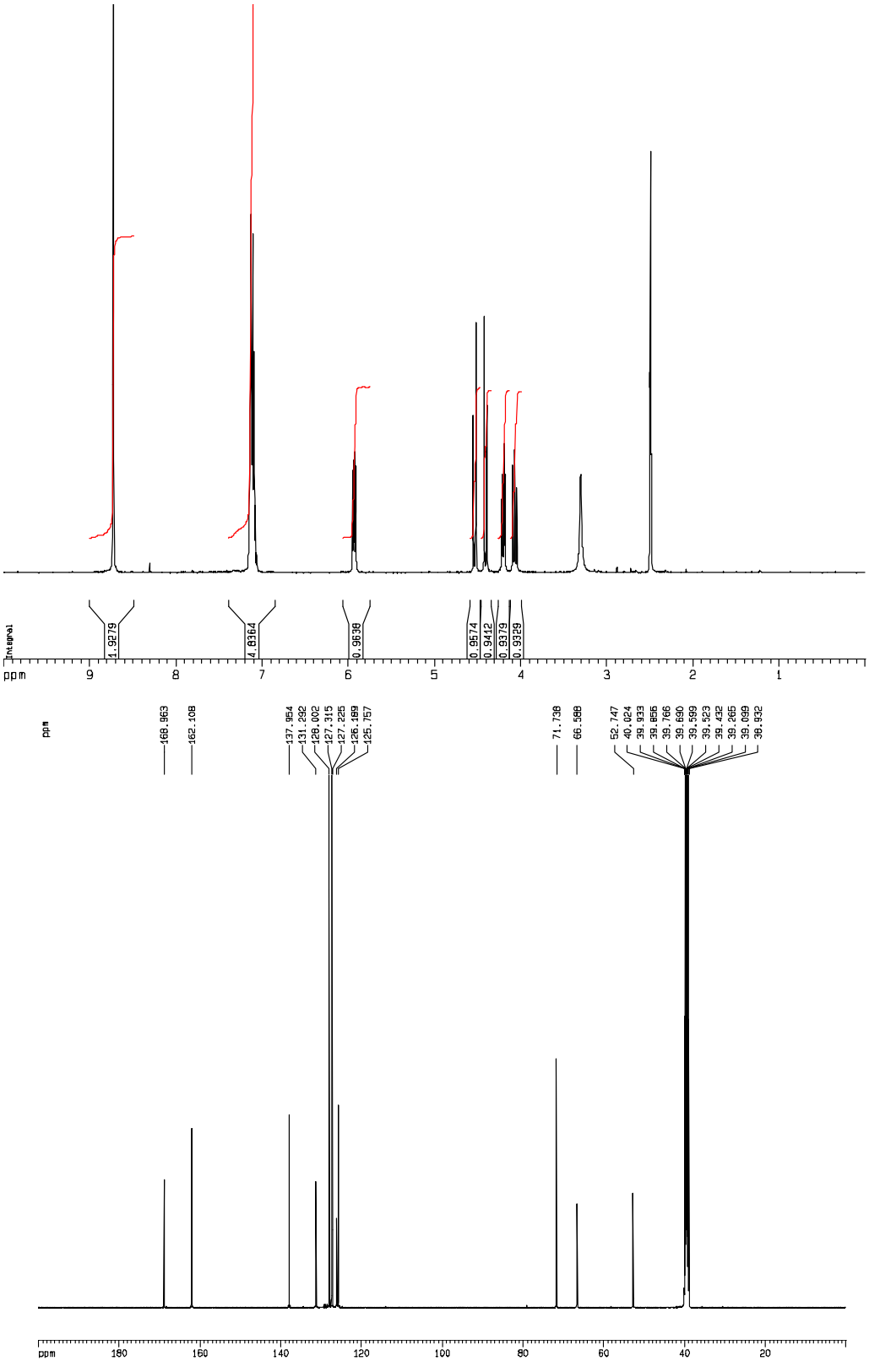
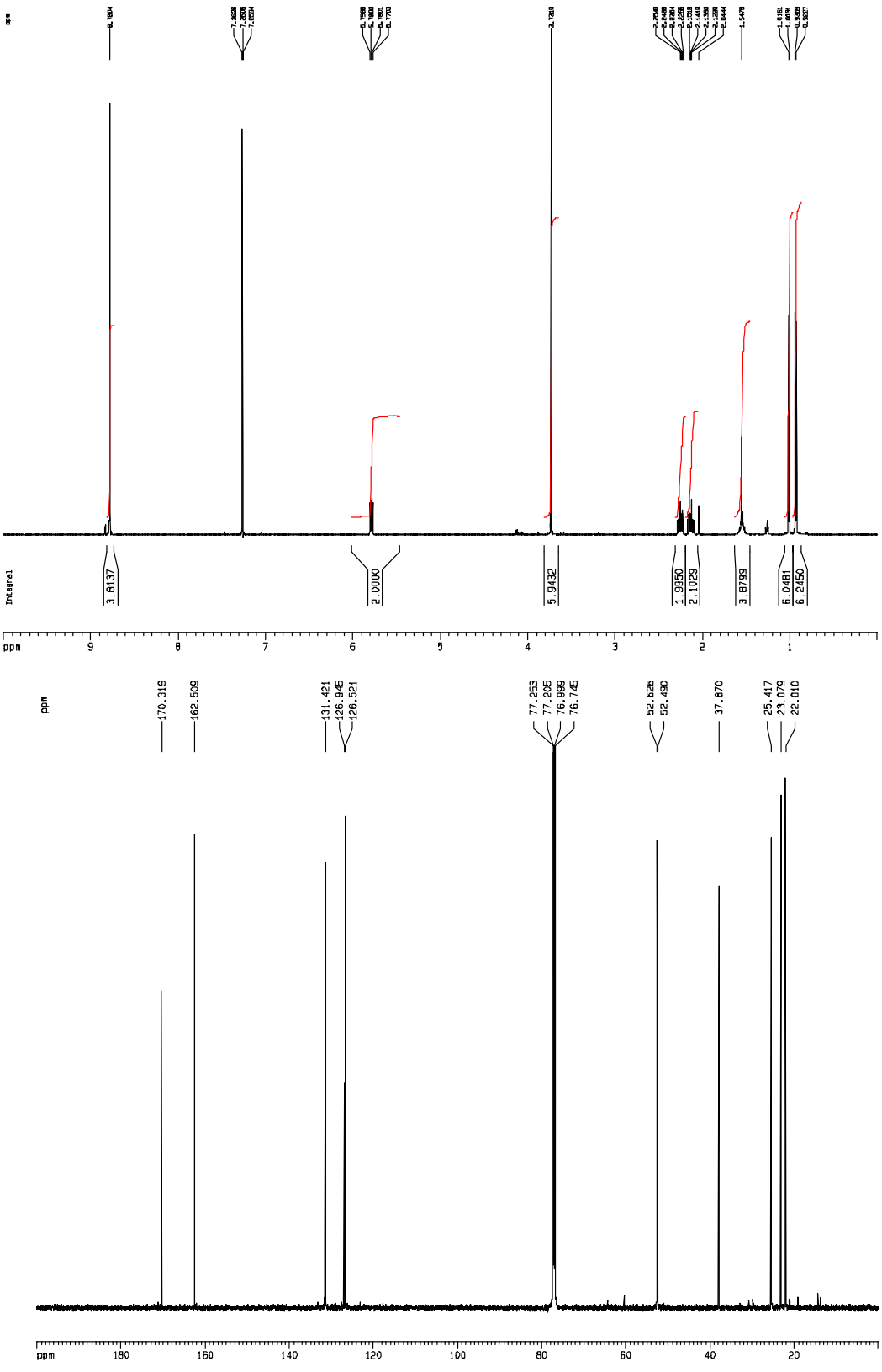
120
100
80
60
40
20

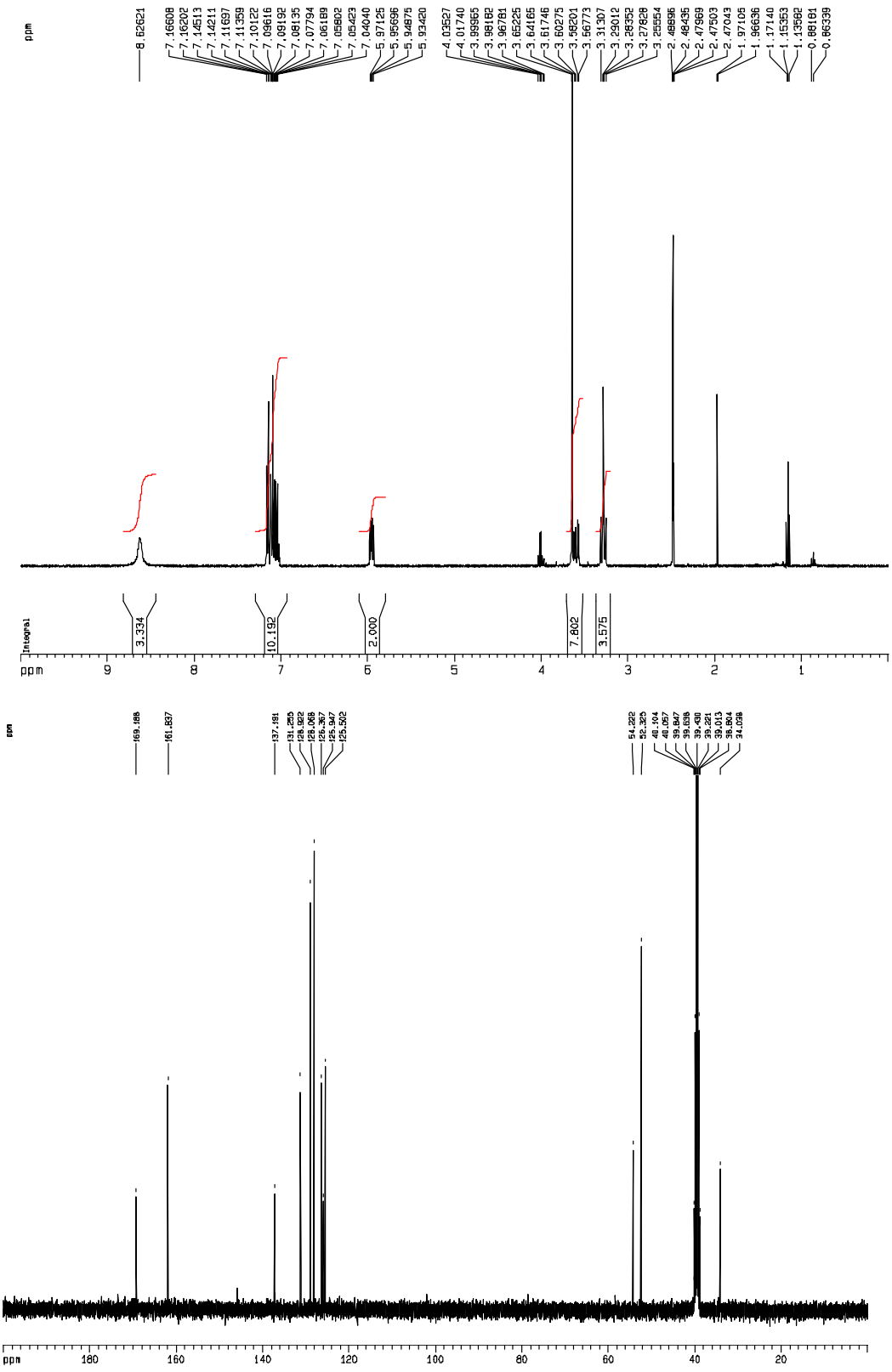
(*S*,*S*)-**2d**


Integral
1.9279
4.8364
0.9638
0.9574
0.9412
0.9379
0.9329
ppm
9
8
7
6
5
4
3
2
1
ppm
168.963
162.108
137.954
131.292
128.002
127.315
127.225
126.189
125.757
71.738
66.588
52.747
40.024
39.933
39.856
39.766
39.690
39.599
39.523
39.432
39.265
39.099
38.932
ppm
180
160
140
120
100
80
60
40
20

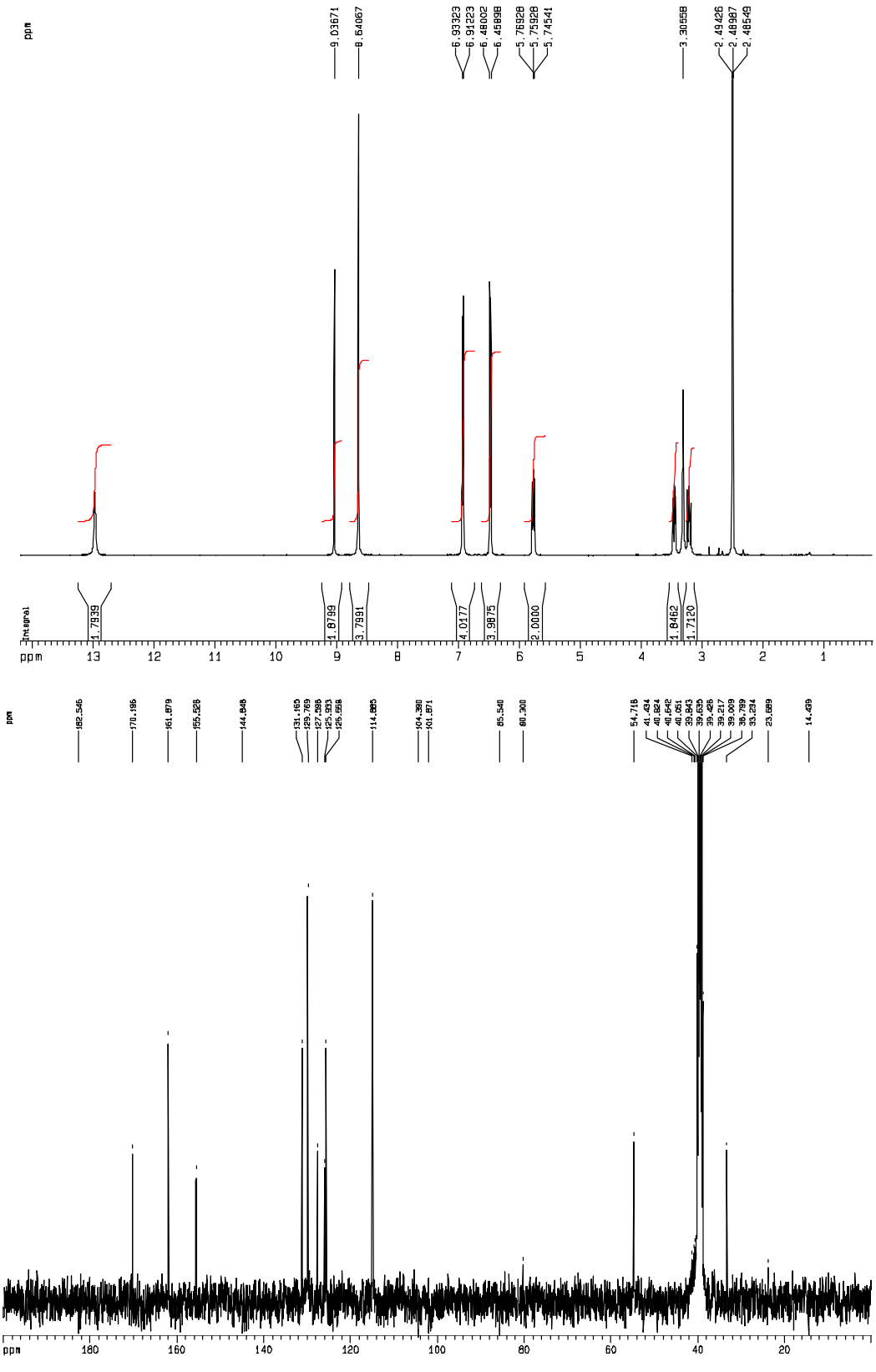
(*S*,*S*)-**2e**


ppm
Integral
3.8137
2.0000
5.9432
1.9950
2.1029
3.8799
6.0481
6.2450
ppm
170.319
162.509
131.421
126.945
126.521
77.253
77.205
76.999
76.745
52.625
52.490
37.870
25.417
23.079
22.010
ppm

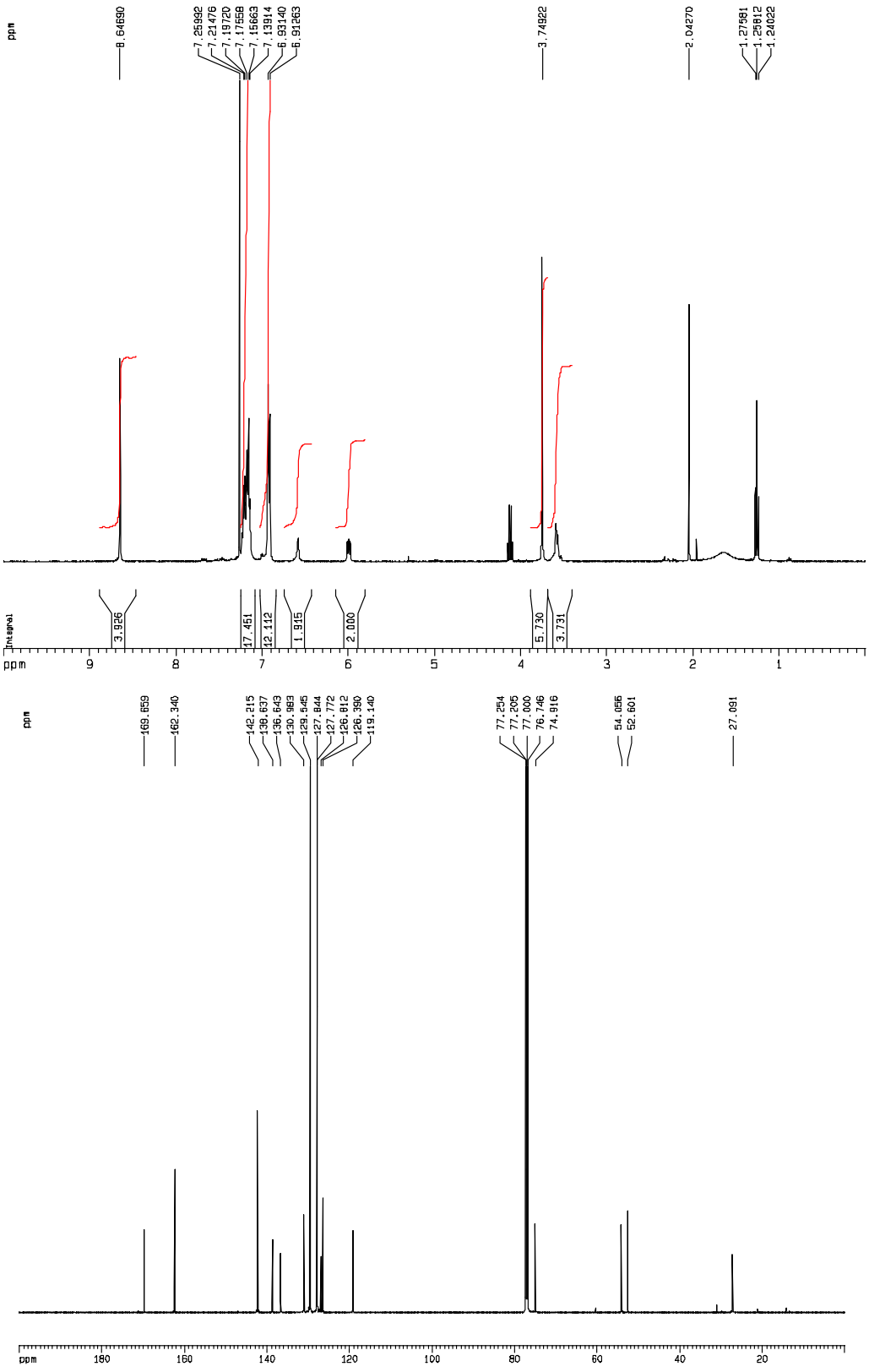
(*S*,*S*)-**2f**


ppm
8.82621
7.16608
7.16202
7.14513
7.14211
7.11697
7.11359
7.10122
7.09616
7.09192
7.08135
7.07794
7.06189
7.05802
7.05423
7.04040
5.97125
5.95696
5.94875
5.93420
4.03527
4.01740
3.99965
3.98182
3.96781
3.65225
3.64165
3.61746
3.60275
3.58201
3.56773
3.31307
3.29012
3.28352
3.27828
3.25554
2.48996
2.48435
2.47969
2.47503
2.47043
1.97105
1.96636
1.17140
1.15353
1.13582
0.88181
0.86339
Integral
3.334
10.192
2.000
7.802
3.575
ppm
9
8
7
6
5
4
3
2
1
ppm
169.168
161.837
137.191
131.255
128.922
128.068
125.367
125.947
125.502
54.222
52.325
40.104
40.057
39.847
39.638
39.430
39.221
39.013
35.804
34.036
ppm
180
160
140
120
100
80
60
40
20

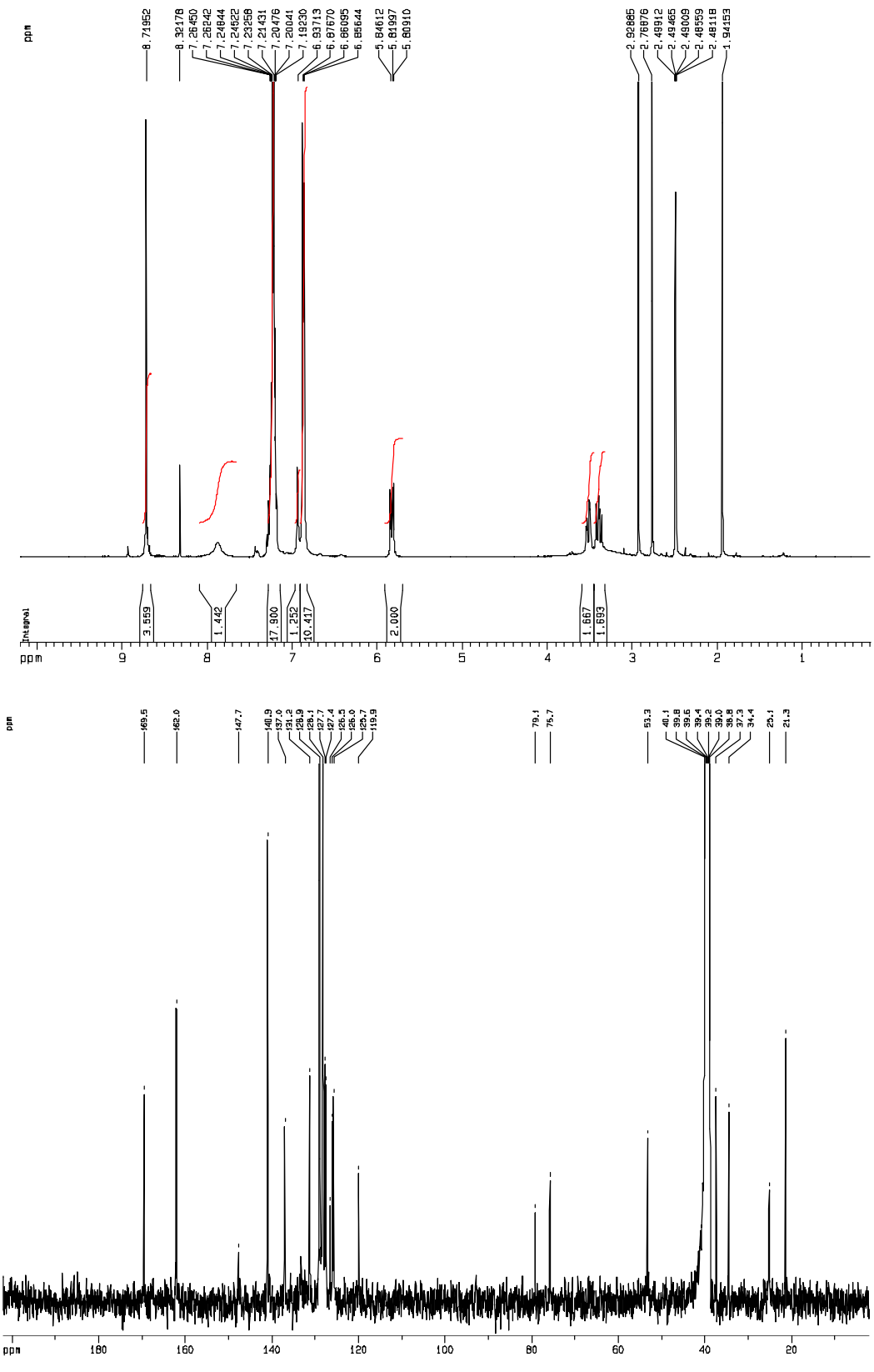
(*S*,*S*)-**2g**


ppm
9.03671
8.64067
6.93323
6.91223
6.48002
6.45898
5.76928
5.75928
5.74541
3.30558
2.49426
2.48987
2.48549
Integral
1.7939
4.8799
3.7991
4.0477
3.9875
2.0000
1.8462
1.7120
ppm
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm
182.546
170.196
161.879
155.528
144.846
131.165
129.769
127.298
125.933
125.556
114.885
104.380
101.871
85.540
80.300
54.718
41.434
40.824
40.642
40.051
39.843
39.635
39.426
39.217
39.009
38.799
33.234
23.689
14.439
ppm
180
160
140
120
100
80
60
40
20

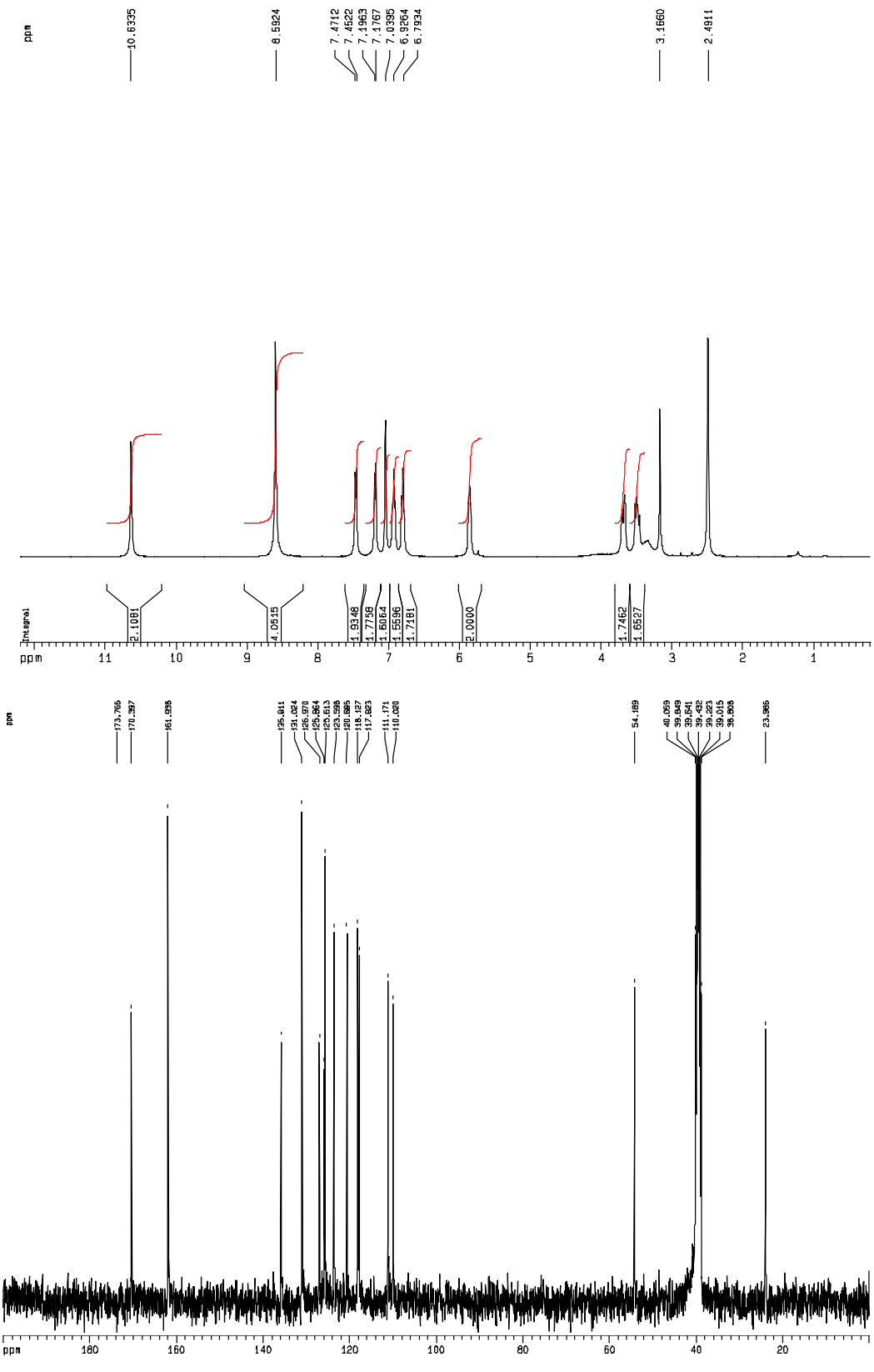
(*S*,*S*)-**2h**


ppm
8.64690
7.25992
7.21476
7.19720
7.17558
7.15663
7.13914
6.93140
6.91263
3.74922
2.04270
1.27581
1.25812
1.24022
Integral
3.926
17.451
12.112
1.915
2.000
5.730
3.731
ppm
9
8
7
6
5
4
3
2
1
ppm
169.659
162.340
142.215
138.637
136.643
130.983
129.645
127.844
127.772
126.812
126.390
119.140
77.254
77.205
77.000
76.746
74.916
54.056
52.601
27.091
ppm
180
160
140
120
100
80
60
40
20

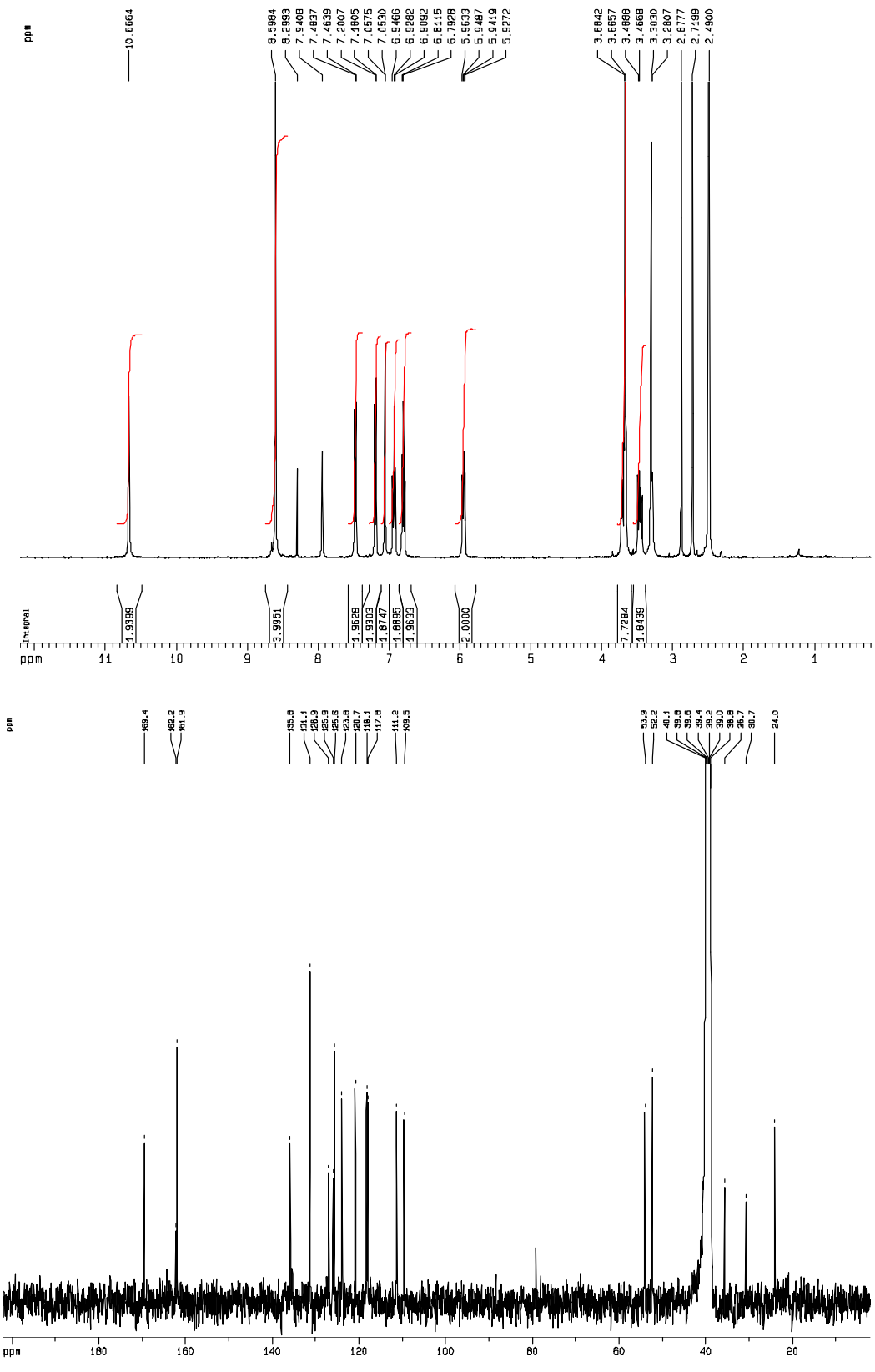
(*S*,*S*)-**2i**



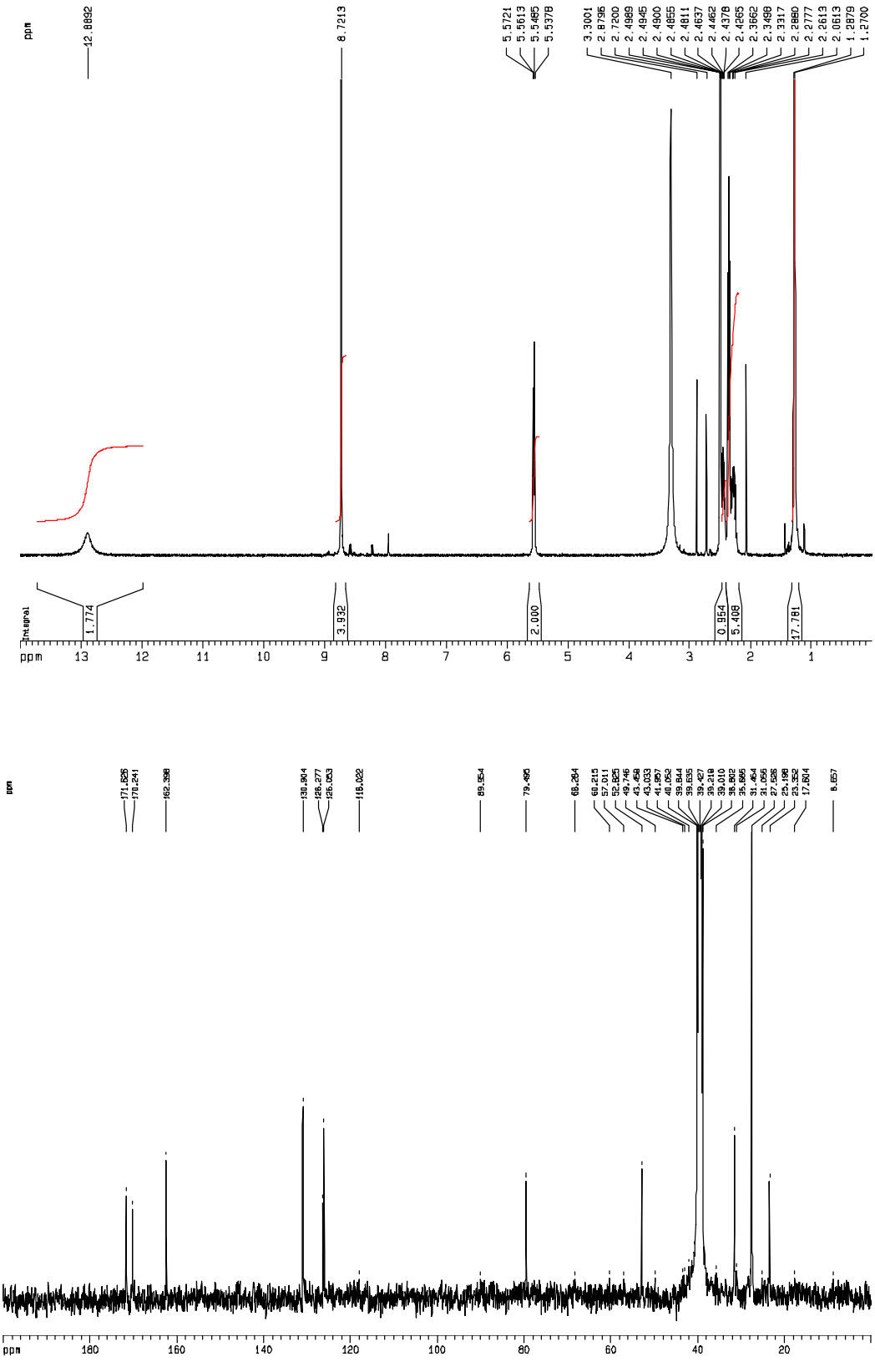
(*S*,*S*)-**2j**


ppm
10.6335
8.5924
7.4712
7.4522
7.1963
7.1767
7.0395
6.9264
6.7934
3.1660
2.4911
Integral
2.1081
4.0515
1.9348
1.7758
1.6064
1.5596
1.7181
2.0000
1.7462
1.6527
ppm
11
10
9
8
7
6
5
4
3
2
1
ppm
173.766
170.397
161.938
135.811
131.024
126.970
125.864
125.513
123.596
120.886
118.127
117.823
111.171
110.020
54.189
40.059
39.849
39.641
39.432
39.223
39.015
38.806
23.986
ppm
180
160
140
120
100
80
60
40
20

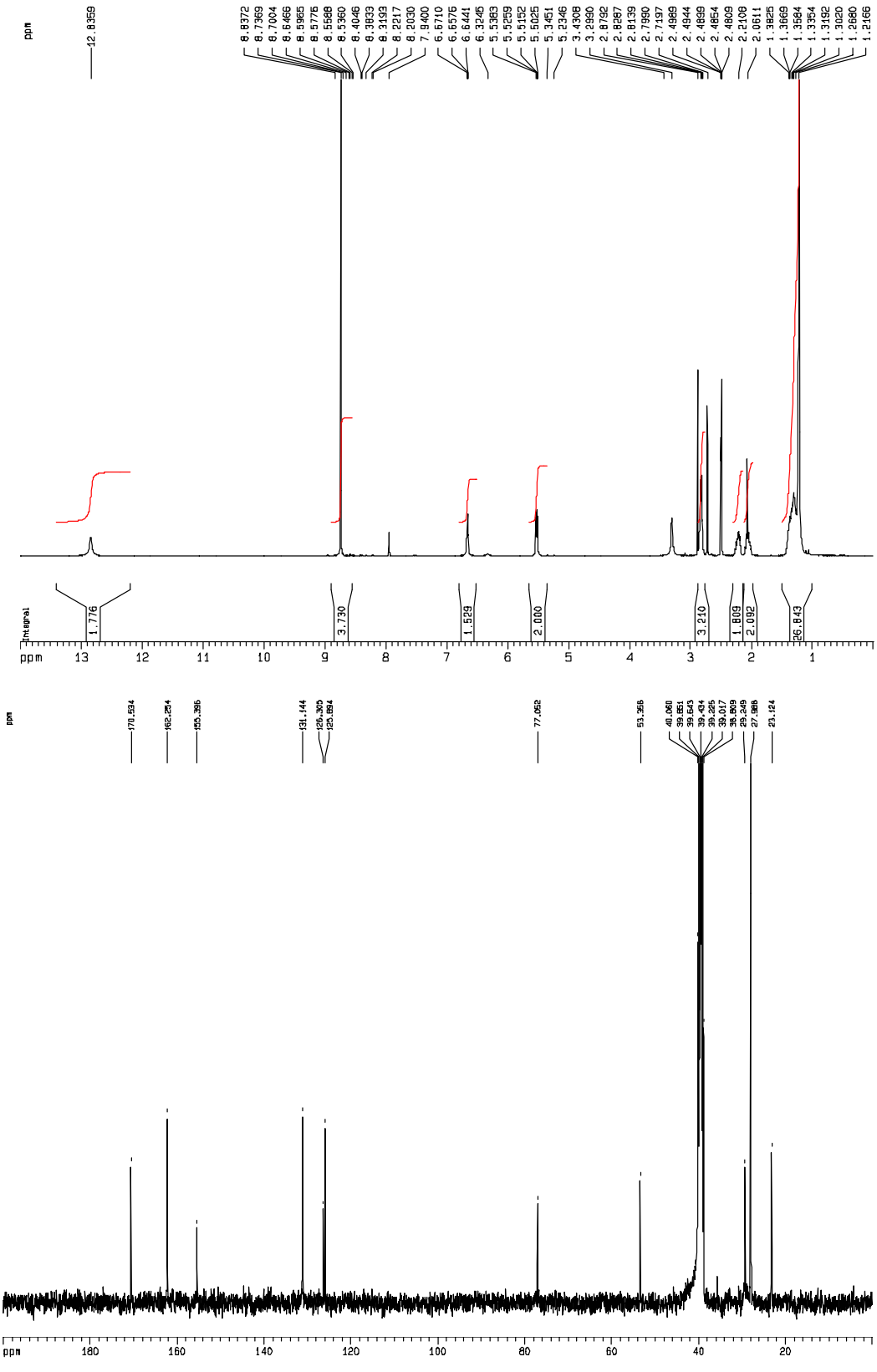
(*S*,*S*)-**2k**


ppm
10.6664
8.5984
8.2993
7.9408
7.4837
7.4639
7.2007
7.1805
7.0575
7.0530
6.9466
6.9282
6.9092
6.8115
6.7928
5.9633
5.9487
5.9419
5.9272
3.6842
3.6657
3.4888
3.4668
3.3030
3.2807
2.8777
2.7199
2.4900
Integral
1.9399
3.9961
1.9528
1.9303
1.8747
1.8895
1.9633
2.0000
7.7284
1.8439
ppm
11
10
9
8
7
6
5
4
3
2
1
ppm
169.4
162.2
161.9
135.8
131.1
128.9
125.9
125.6
123.8
120.7
118.1
117.8
111.2
109.5
53.9
52.2
40.1
39.8
39.6
39.4
39.2
39.0
38.8
38.7
38.7
24.0
ppm
180
160
140
120
100
80
60
40
20

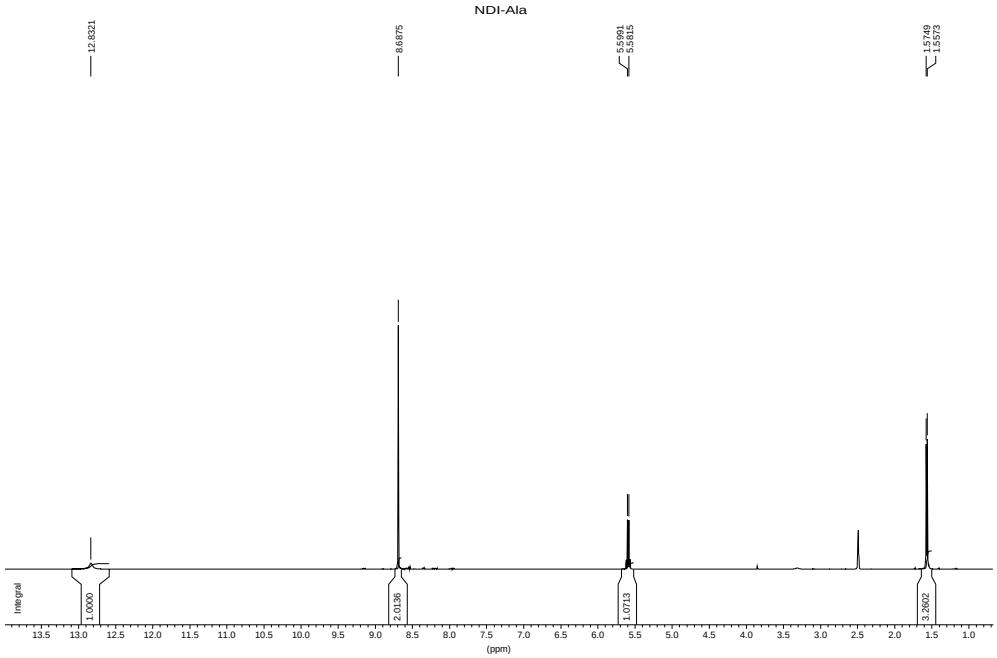
(*S*,*S*)-**21**

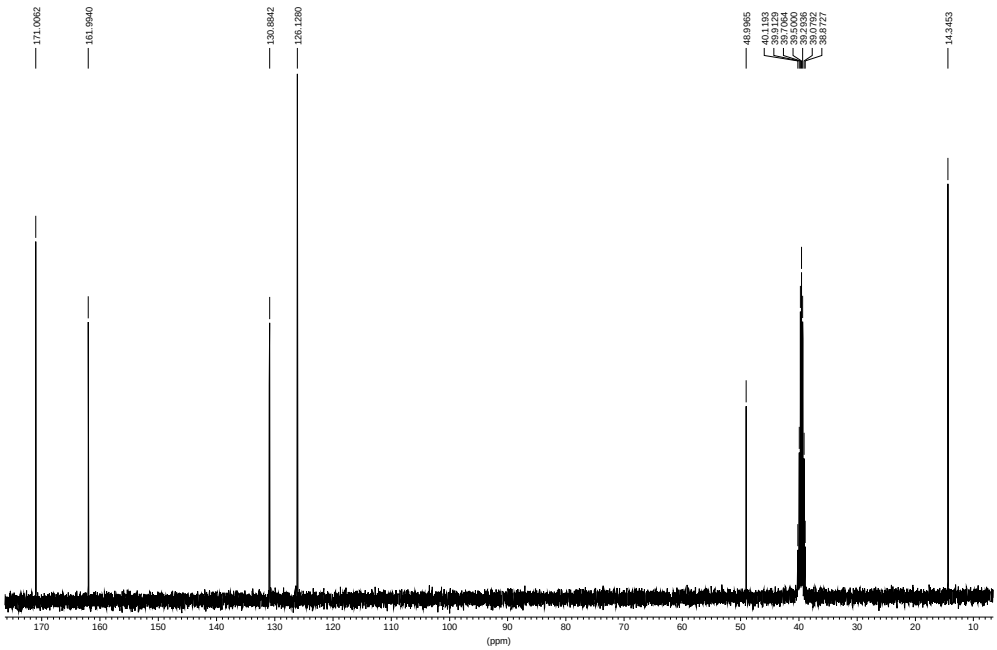

ppm
12.8932
8.7213
5.5721
5.5613
5.5485
5.5378
3.3001
2.8795
2.7200
2.4989
2.4945
2.4900
2.4855
2.4811
2.4637
2.4462
2.4378
2.4265
2.3662
2.3498
2.3317
2.2880
2.2777
2.2613
2.0613
1.2879
1.2700
Integral
1.774
3.932
2.000
0.954
5.408
17.781
ppm
13
12
11
10
9
8
7
6
5
4
3
2
1
ppm
171.825
170.241
162.398
130.904
128.277
126.053
118.022
89.954
79.495
68.264
60.215
57.011
52.825
49.746
43.033
41.857
41.052
39.844
39.635
39.427
39.218
39.010
36.802
35.865
31.454
31.055
27.526
25.198
23.352
17.804
8.857
ppm
180
160
140
120
100
80
60
40
20

(*S*,*S*)-**2m**

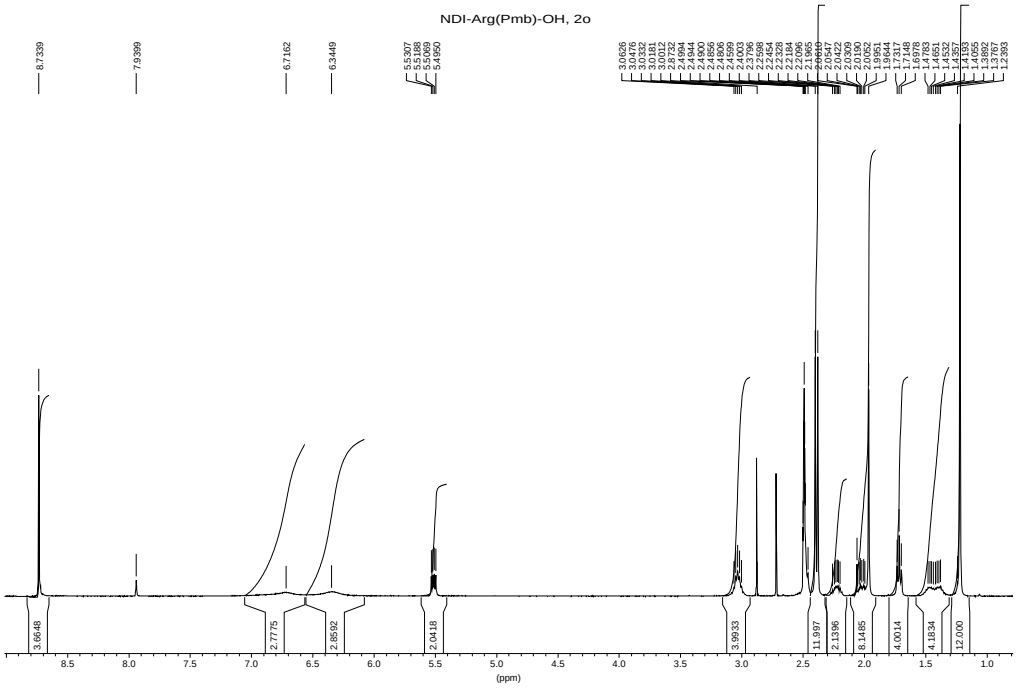


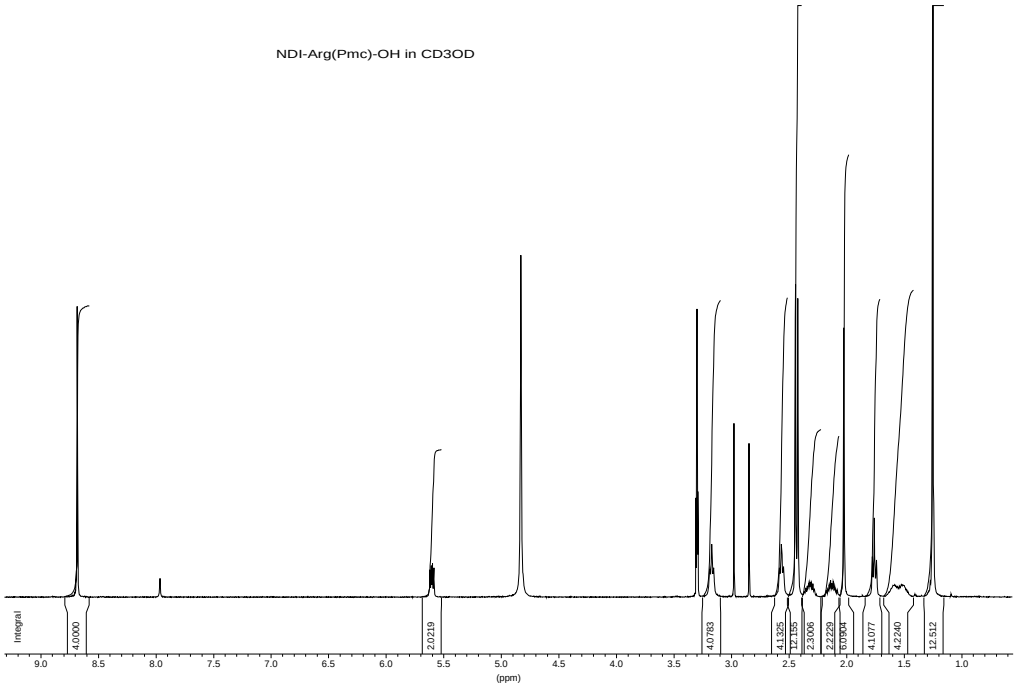
(*S*,*S*)-**2n**


NDI-Ala
12.8321
8.6875
5.5991
5.5815
1.5749
1.5573
Integral
1.0000
2.0136
1.0713
3.2602
(ppm)

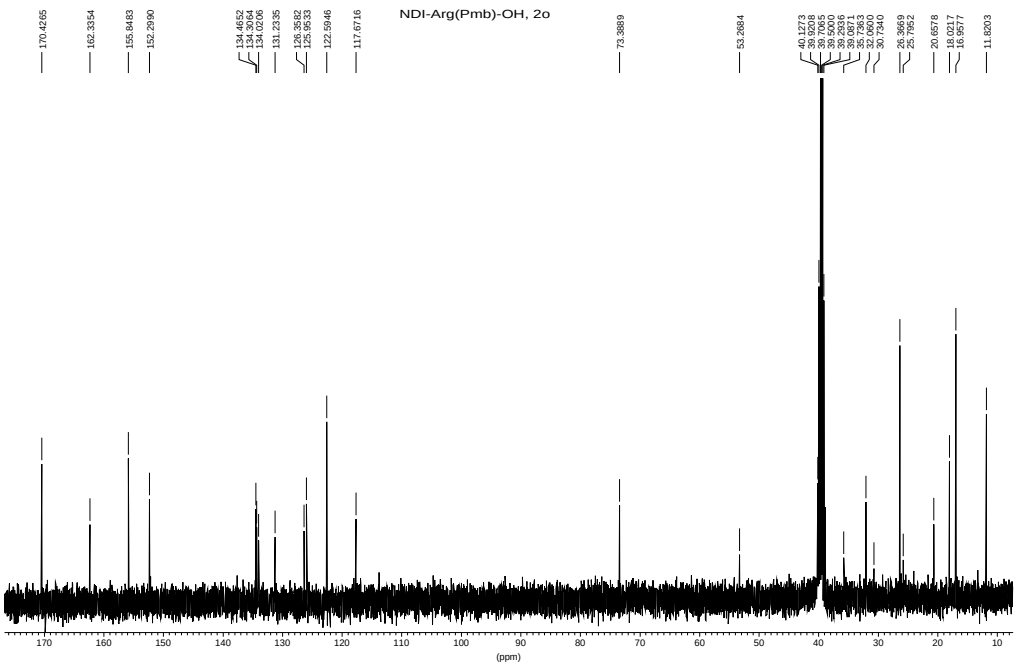

171.0062
161.9940
130.8842
126.1280
48.9965
40.1193
39.9129
39.7064
39.5000
39.2936
39.0792
38.8727
143.453
(ppm)

(*S*,*S*)-**2o**

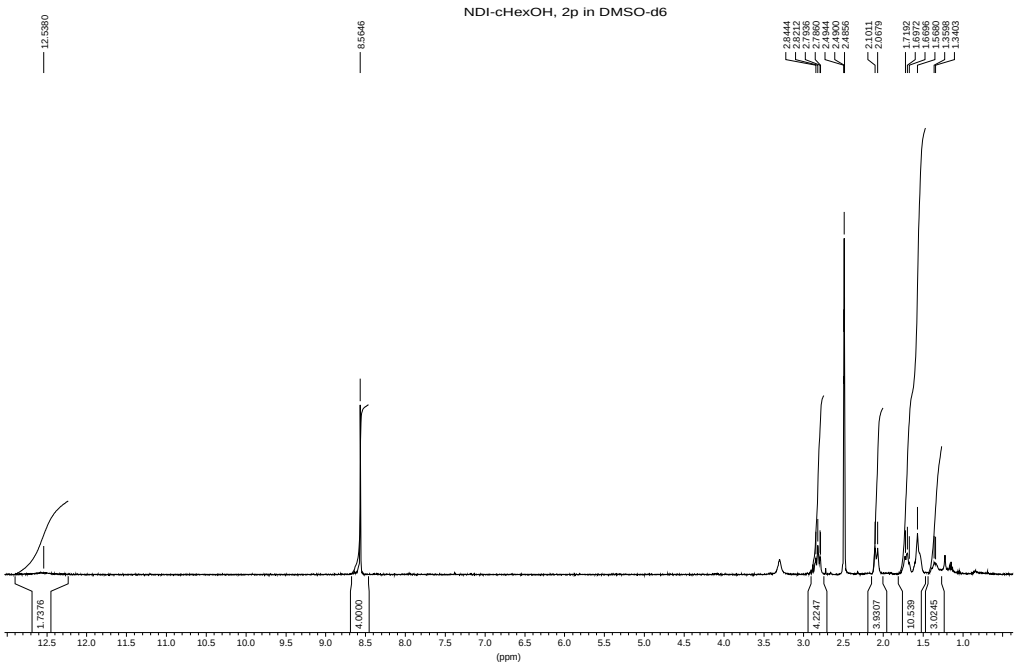

NDI-Arg(Pmb)-OH, 2o
8.7339
7.9399
6.7162
6.3449
5.5307
5.5198
5.5069
5.4950
3.66:48
2.7775
2.8592
2.0418
3.9933
11.997
2.1396
8.1485
4.0014
4.1834
12.000
(ppm)

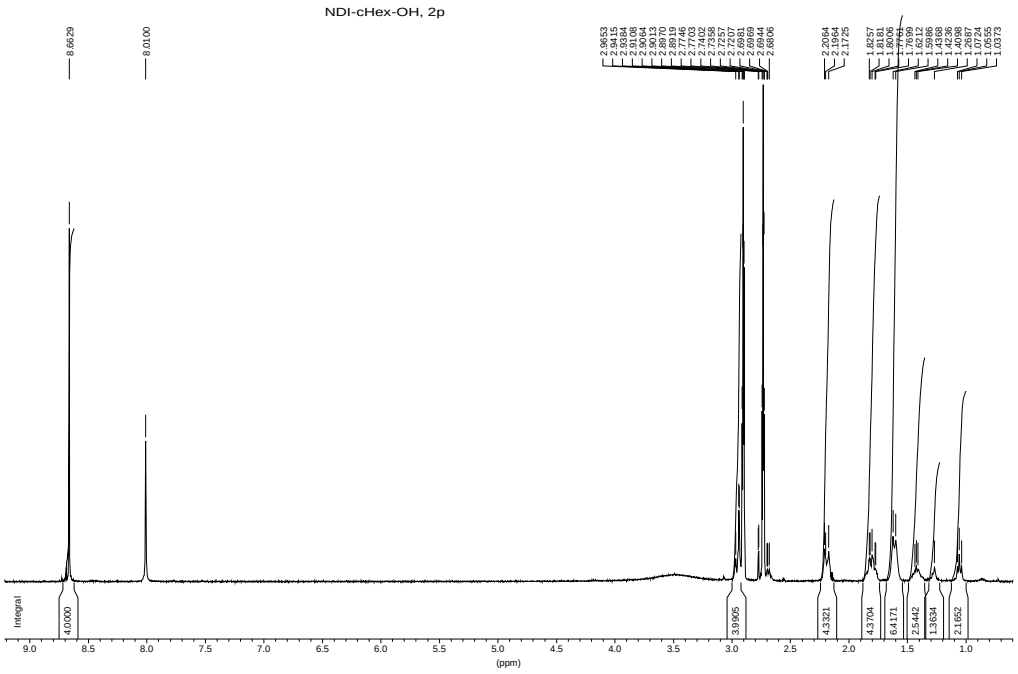

NDI-Arg(Pmc)-OH in CD3OD
Integral
4.0000
2.0219
4.0763
4.1325
12.2135
2.3006
2.2229
6.0304
4.1077
4.2240
12.512
(ppm)

(*S*,*S*)-**2o**

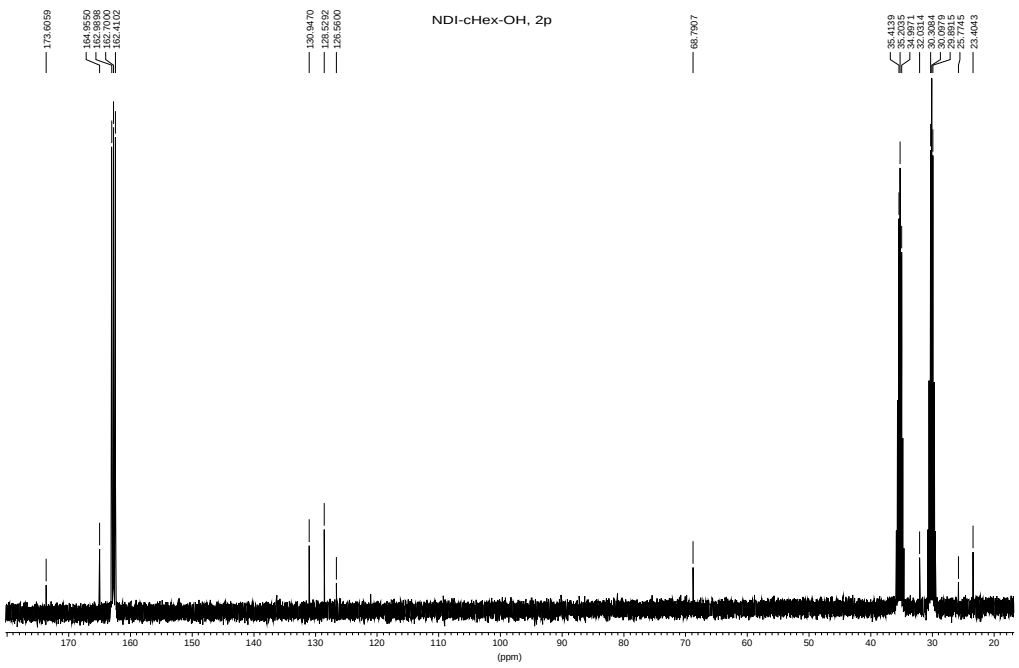

NDI-Arg(Pmb)-OH, 2o
170.4265
162.3354
155.8483
152.2990
134.4652
134.3644
134.0206
131.2335
126.3582
125.9533
122.5946
117.6716
73.3889
53.2684
40.1273
39.9208
39.7055
39.5000
39.2936
39.0871
35.7363
32.0600
30.7340
26.3669
25.7952
20.6578
18.0577
16.9577
11.8203
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
(ppm)

2p

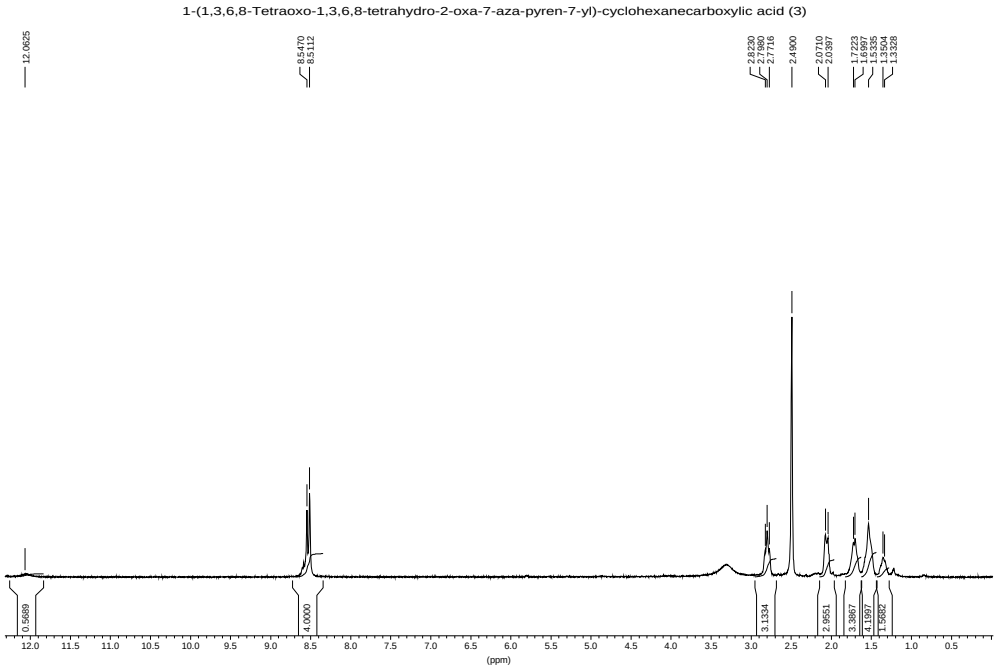

NDI-cHexOH, 2p in DMSO-d6
12.5380
8.5646
2.8444
2.8212
2.8096
2.7860
2.4944
2.4900
2.4856
2.1011
2.0879
1.7192
1.6972
1.6696
1.5990
1.3598
1.3403
1.7376
4.0000
4.2247
3.9307
10.539
3.0245
(ppm)

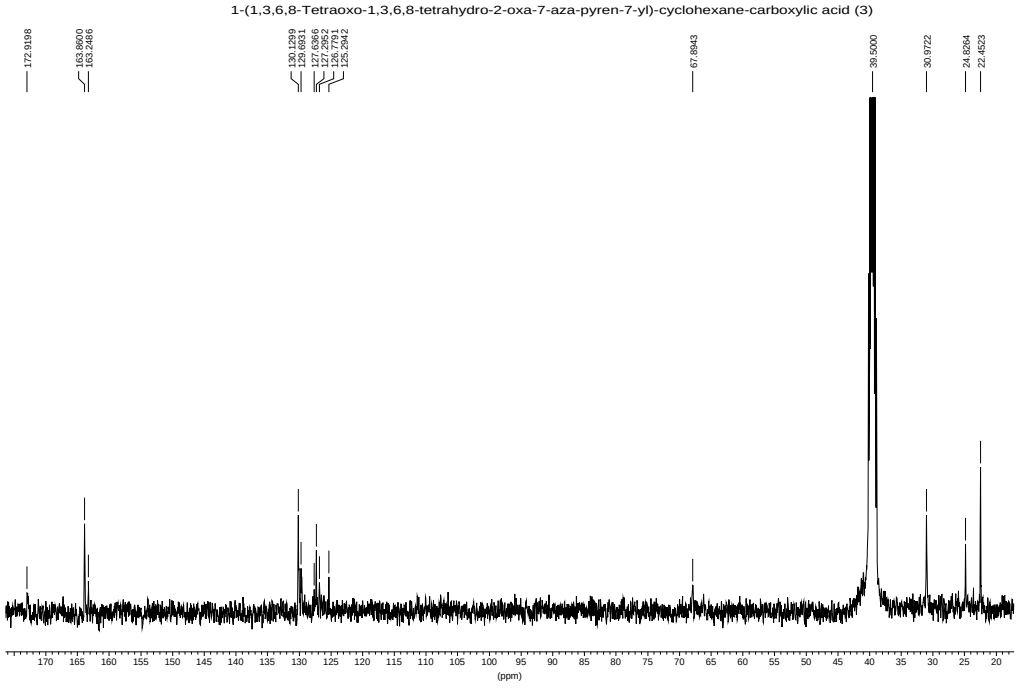

NDI-cHex-OH, 2p
8.6629
8.0100
2.9653
2.9415
2.9334
2.9108
2.9054
2.8915
2.8919
2.8746
2.7703
2.7402
2.7357
2.7257
2.7207
2.6981
2.6969
2.6944
2.6806
2.2064
2.1954
2.1725
1.8257
1.8061
1.8006
1.7761
1.7699
1.7527
1.5986
1.4368
1.4236
1.4098
1.2687
1.2574
1.0755
1.0373
Integral
4.0000
3.9905
4.3321
4.3704
6.4171
2.5442
1.3634
2.1652
(ppm)

2p

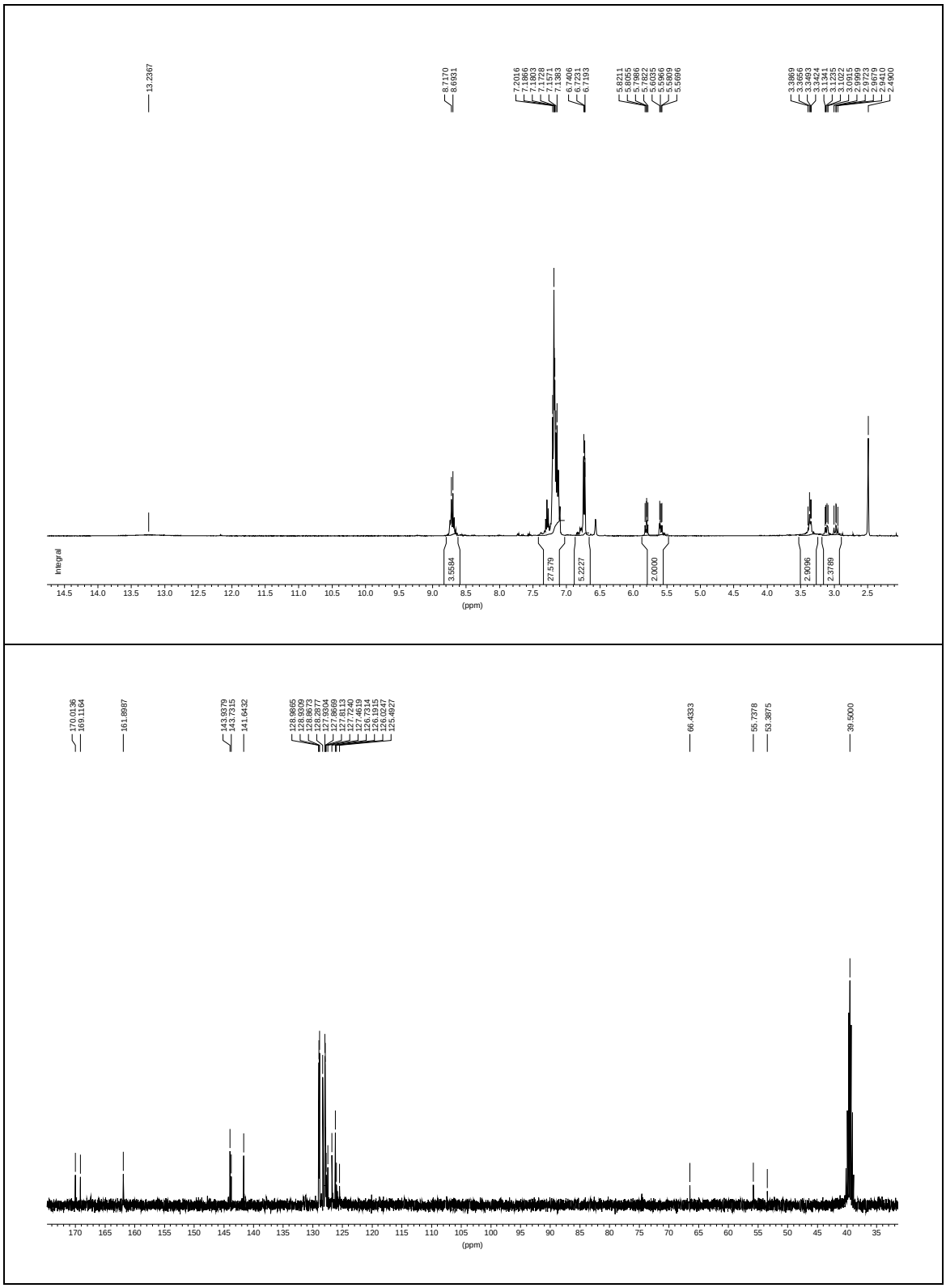

NDI-cHex-OH, 2p
173.6059
164.9550
164.6698
162.7000
162.4102
130.9470
128.5292
126.5600
68.7907
35.4139
35.2035
34.9971
32.1014
30.3084
30.0979
29.8845
25.7745
23.4043
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
(ppm)

3p

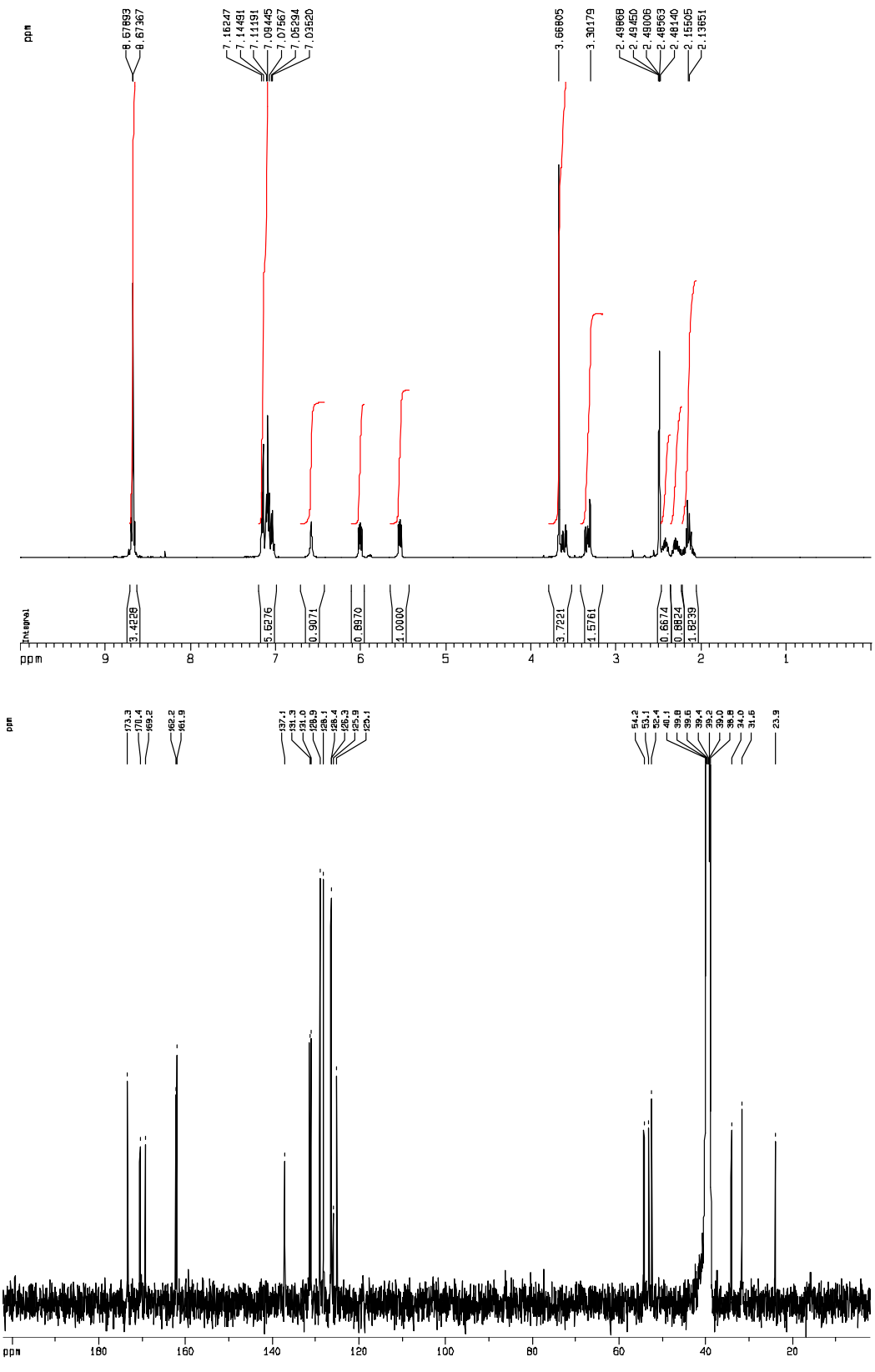

1-(1,3,6,8-Tetraoxo-1,3,6,8-tetrahydro-2-oxa-7-aza-pyren-7-yl)-cyclohexanecarboxylic acid (3)
12.0625
8.5470
8.5112
2.8220
2.7980
2.7716
2.4900
2.0710
2.0397
1.7223
1.6967
1.5335
1.3504
1.3328
0.5689
4.0000
3.1334
2.9551
3.3867
4.1997
1.5882
(ppm)


1-(1,3,6,8-Tetraoxo-1,3,6,8-tetrahydro-2-oxa-7-aza-pyren-7-yl)-cyclohexane-carboxylic acid (3)
172.9198
163.8600
163.2486
130.1299
129.6631
127.6366
127.2952
125.3701
125.2042
67.8943
39.5000
30.9722
24.8264
22.4523
(ppm)

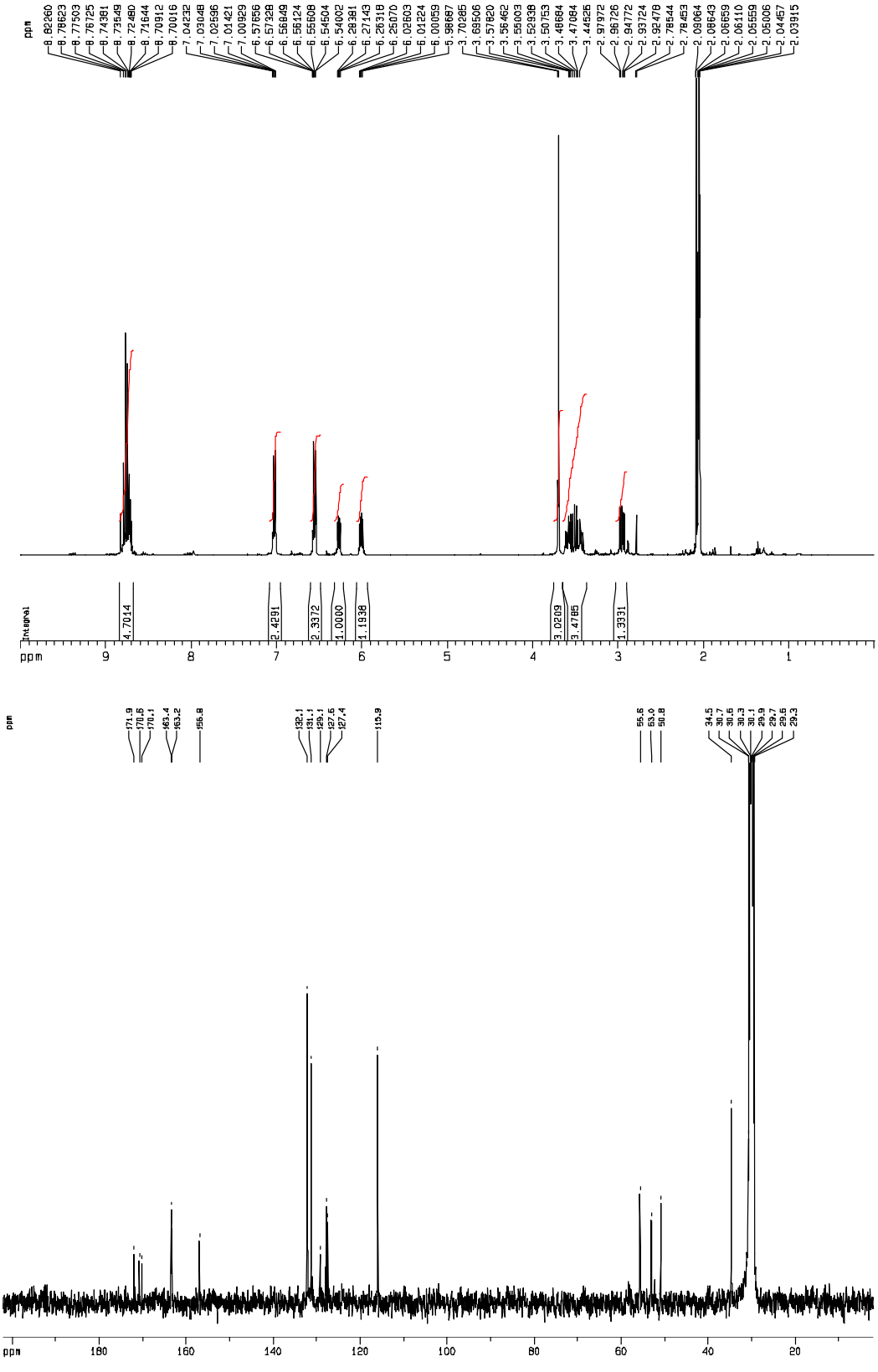
(*R*,*S*)-4a


13.2367
8.7170
8.6931
7.2016
7.1986
7.1803
7.1728
7.1572
7.1383
6.7406
6.7231
6.7193
5.8211
5.8055
5.7986
5.7822
5.6035
5.5866
5.5809
5.5696
3.3869
3.3656
3.3496
3.3424
3.1341
3.1225
3.1022
3.0915
2.9999
2.9723
2.9679
2.9410
2.4900
Integral
3.5584
27.579
5.2227
2.0000
2.9096
2.3789
(ppm)
170.0136
169.1164
161.8887
143.9379
143.7315
141.6432
128.9865
128.8709
128.8573
128.2877
127.9304
127.8969
127.8113
127.7240
127.4619
126.7214
126.1915
126.0247
125.4927
66.4333
55.7378
53.3875
39.5000
(ppm)

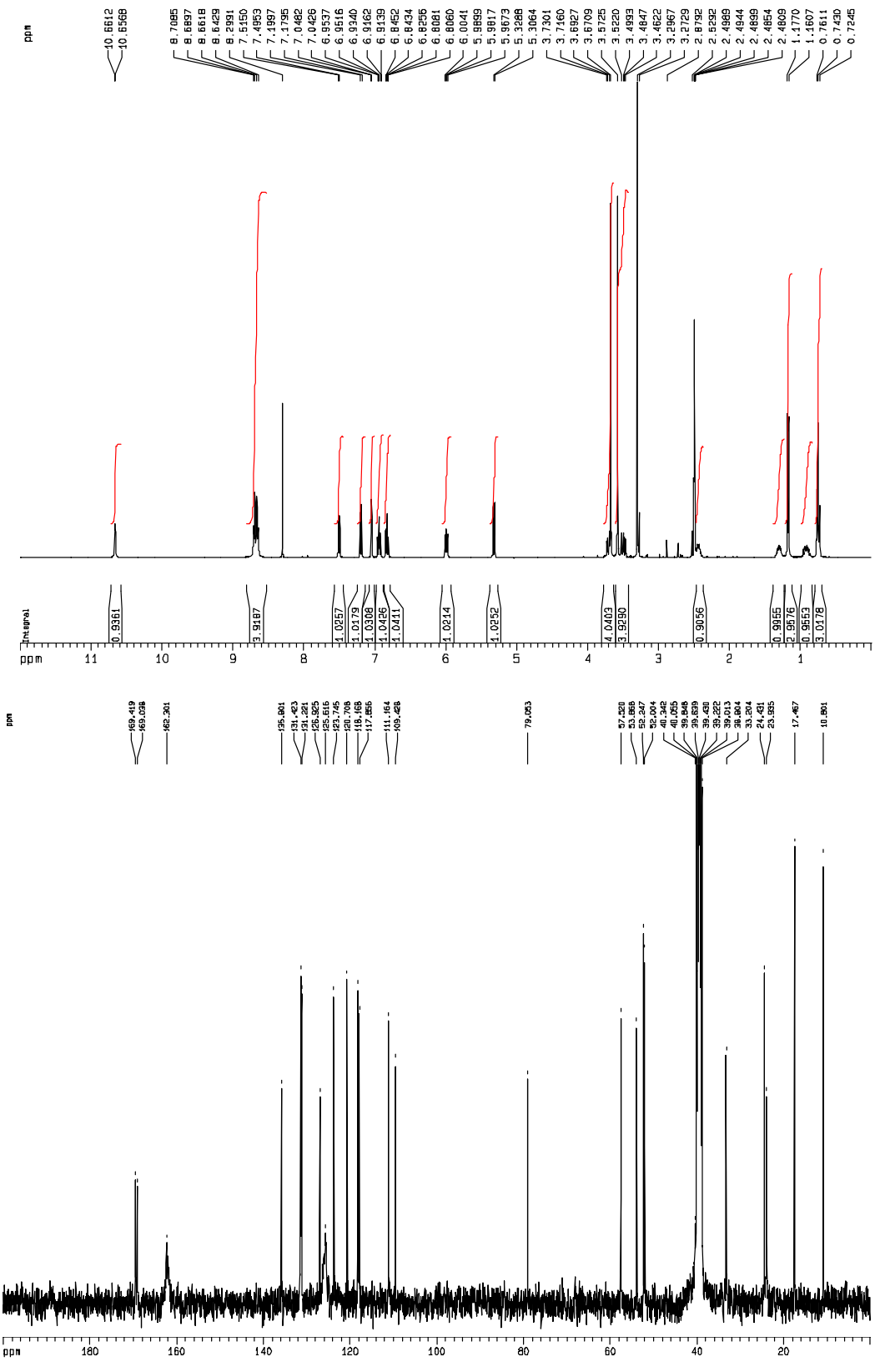
(*S*,*S*)-**4b**


ppm
8.67893
8.67367
7.16247
7.14491
7.11191
7.09445
7.07567
7.05294
7.03520
3.66805
3.30179
2.49868
2.49450
2.49006
2.48563
2.48140
2.15505
2.13651
Integral
3.4238
5.6276
0.9071
0.8870
1.0000
3.7221
1.5761
0.6674
0.8824
1.8239
ppm
9
8
7
6
5
4
3
2
1
ppm
173.3
170.4
169.2
162.2
161.9
137.1
131.3
131.0
129.9
128.1
128.4
125.3
125.0
120.1
64.2
53.1
52.4
40.1
39.8
39.6
39.4
39.2
39.0
38.8
34.0
31.6
23.9
ppm
180
160
140
120
100
80
60
40
20

(*S*,*S*)-**4c**



(*S*,*S*)-**4d**



[1] Jursic, B. S.; Patel, P. K. *Carbohydr. Res.* **2005**, *340*, 1413-1418