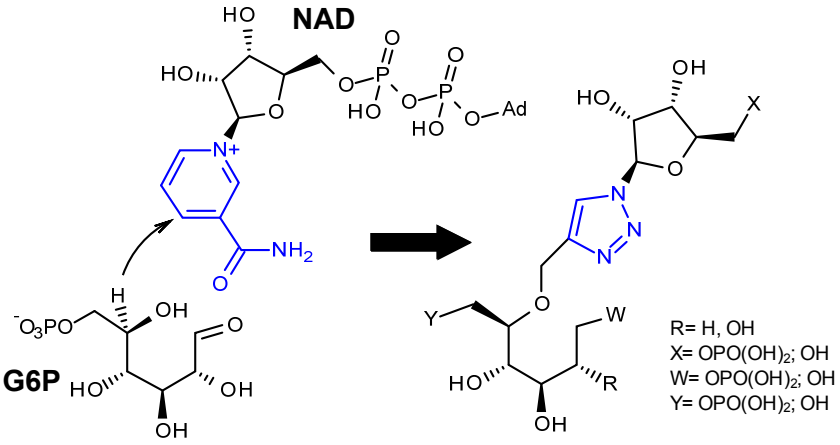
Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry


Probing *myo*-inositol 1-phosphate synthase with multisubstrate adducts

*Rania M. Deranieh,*[a] *Miriam L. Greenberg,*[a] *Pierre-B. Le Calvez,*[b] *Maura C. Mooney,*[c] *Marie E. Migaud*[b,d]

# Electronic Supplementary Information




The first carbohydrate-nucleotide hybrids, designed to be multisubstrate adducts mimicking *myo*-inositol 1-phosphate synthase first oxidative transition state, are reported.

**Allyl-2,3,4-tri-*O*-benzyl-6-*O*-trityl-D-glucopyranoside (3)**

To a suspension of D-glucose (30.0 g, 166.7 mmol) in allyl alcohol (100 mL) was added sulfuric acid (1.00 g, 10.2 mmol) drop-wise. The reaction mixture was stirred at 85 °C until the solid dissolved (4 hours), then cooled to rt. The allyl alcohol was removed *in vacuo* and the gummy residue was purified by silica column chromatography ($CHCl_3$/EtOH 1/0-7/3 v/v) to give the intermediate 1-*O*-allyl-D-glucopyranoside (21.7g) as a colourless oil.

To a solution of 1-*O*-allyl-D-glucopyranoside (21.6 g, 98.2 mmol) in dry pyridine (100 mL) was added trityl chloride (29.8 g, 107.0 mmol) portion-wise and the solution was heated at 50 °C for 24 hours. The pyridine was then removed *in vacuo* and the residue was solubilised with chloroform (200 mL), and washed with a saturated copper sulfate aqueous solution (3 × 50 mL), water (3 × 50 mL), brine (50 mL) and was then dried over $MgSO_4$. The dry extract was concentrated under reduced pressure and the residue was purified by silica column

chromatography ($CHCl_3$/EtOH/TEA: 9/0.9/0.1 v/v/v) to give 1-*O*-allyl-6-trityl-D-glucopyranoside (40.6 g, 52% overall) as a white wax. (mixture α/β 0.3/0.7).
$^1H$ (500 MHz, $CDCl_3$), δ 7.45-7.38 (6H, m, $H_{Ar}$), 7.21-7.05 (9H, m, $H_{Ar}$, Tr), 5.99-5.89 (1H, m, $CH=CH_2$), 5.31 (1H, dd, J = 1.6 Hz, 17.4 Hz, $CH_2=CH$), 5.22-5.19 (1H, dd, J = 1.6 Hz, 10.5 Hz, $CH_2=CH$), 4.91 (1H, d, J = 3.9 Hz, H1β), 4.39-4.34 (1H, ddt, J = 1.4 Hz, 5.4 Hz, 12.6 Hz, H5α), 4.26-4.22 (1H, ddt, J = 1.4 Hz, 5.4 Hz, 12.6 Hz, H5β), 4.32 (1H, d, J = 7.8Hz, H1α), 4.16-4.12 (1H, m, H4α), 4.06-4.02 (1H, m, H4β), 3.74-3.68 (1H, m, H2), 3.52-3.44 (3H, m, H6, H3), 3.41-3.36 (2H, m, $CH_2$-CH=CH2). $^{13}C$ (125 MHz, $CDCl_3$), δ 143.7, 143.6(2) ($C_{Ar}$ Tr), 133.7, 133.6 ($CH=CH_2$ α, β), 128.6, 127.9(2), 127.1(2) ($CH_{Ar}$), 118.1, 118.0 ($CH_2=CH$ α, β), 101.4, 97.1 (C1 α, β), 87.0, 86.9 ($C(Ph_3)$ α, β), 76.3, 74.7 (C2 α, β), 74.1, 73.5 (C5 α, β), 72,1 (C3), 71.8, 71.6 (C4 α, β), 70.1, 68,4 ($CH_2$-CH=$CH_2$ α, β), 64.2, 63.9 (C6 α, β). HRMS $ES^+$-TOF: Calculated for $C_{28}H_{31}O_6$ $[M+H]^+$ = 461.1964, found $[M+H]^+$= 461.1994.

To a solution of allyl 6-O-trityl-D-glucopyranoside (7.50 g, 16.2 mmol) in dry DMF (150 mL) was added sodium hydride (2.60 g, 64.9 mmol, 60% in oil) portion-wise at 0 °C. After 20 minutes, the reaction mixture was warmed up to rt and *tetra*butyl ammonium iodide (1.20 g, 3.2 mmol) was added followed by benzyl bromide (7.7 mL, 64.9 mmol). After 12 hours at rt, the reaction was carefully quenched with water (500 mL). The precipitate was then filtered under vacuum and then dissolved in EtOAc (200 mL). The organic solution was washed with water (3 × 50 mL), brine (50 mL) and dried over $MgSO_4$. The filtrate was then concentrated under reduced pressure to afford a gummy brown solid which was purified by column chromatography (Hex/EtOAc/TEA 1/0/0.1-75/24/1 v/v/v) to give (**3**) (11.1 g, 92%) as a white wax. (mixture α/β 0.3/0.7). $^1H$ (500 MHz, $CDCl_3$) δ 7.55-7.45 (6H, m, $H_{Ar}$), 7.41-7.14 (22H, m, $H_{Ar}$), 6.88-6.87 (2H, m, $H_{Ar}$), 6.10-5.95 (1H, m, $CH=CH_2$), 5.43-5.34 (1H, dd, J = 1.6 Hz, 17.2 Hz, $CH=CH_2$), 5.30-5.22 (1H, m, $CH=CH_2$), 5.04-4.68 (6H, m, $CH_2$-Ph), 4.52 (1H, d, J = 7.3Hz, H1α), 4.96 (1H, d, J = 3.9Hz, H1β), 4.37-4.32 (1H, ddt, J = 1.4 Hz, 5.4 Hz, 12.6 Hz, H5α), 4.24-4.20 (1H, ddt, J = 1.4 Hz, 5.4 Hz, 12.6 Hz, H5β), 4.14-4.09 (1H, m, H4α), 4.05-4.00 (1H, m, H4β), 3.73-3.69 (1H, m, H2), 3.53-3.47 (3H, m, H6, H3), 3.41-3.33 (2H, m, $CH_2$-CH=$CH_2$). $^{13}C$ (125 MHz, $CDCl_3$), δ 143.9, 143.7(2) ($C_{Ar}$ Tr), 138.8, 138.4, 137.9 ($C_{Ar}$ Bn), 134.2, 133.8 ($CH=CH_2$ α, β), 128.8, 128.4, 128.2, 128.1(2), 127.9, 127.7, 127.6, 127.5 ($CH_{Ar}$), 118.2, 117.4 ($CH_2=CH$ α, β), 102.7, 95.2 (C1 α, β), 86.3(2) ($C(Ph)_3$, α, β), 84.7 (C4α), 82.6 (C2β), 82.3 (C5α), 80.3 (C4β), 78.2 (C3), 77.8 (C2α), 75.9, 75.6, 74.6 ($CH_2$-Ph),

70.5 (C5β), 70.1, 68.0 ($CH_2$-CH=$CH_2$ α, β), 62.5, 62.4 (C6 α, β). HRMS $ES^+$-TOF: Calculated for $C_{49}H_{48}O_6Na$ $[M+Na]^+$ = 755.3349, found $[M+Na]^+$= 755.3324.

**2,3,4-Tri-*O*-benzyl-6-*O*-trityl-D-glucitol (4).**

To (**3**) (3.00 g, 4.0 mmol) was added potassium tert-butoxide (2.00 g, 16.1 mmol) neat. The solid suspension was stirred at 100 °C for 1 hour under strong stirring. DMSO (3 mL) was then added and the solution was stirred for a further 1 hour at the same temperature. Once cool, the reaction mixture was diluted with water (100 mL) and extracted with chloroform (3 × 20 mL). The organic extracts were concentrated under reduced pressure affording crude black oil. Without any further purification, the crude product was solubilised in wet acetone (20 mL). To this, mercury(II) oxide (1.30 g, 6.0 mmol) was added and after 5 minutes, a solution of mercury(II) chloride (1.60 g, 6.0 mmol) in acetone (5 mL) was added drop-wise over a 20 minutes period. After stirring for 4 hours at rt, the reaction mixture was filtered through a pad of celite. The filtrate was then concentrated under reduced pressure and the residue was dissolved with EtOAc (10 mL). This organic solution was washed with water (3 × 5 mL), brine (5 mL) and dried over $MgSO_4$. The dry extract was concentrated under reduced pressure and the crude product was purified by column chromatography (Hex/EtOAc/TEA: 75/24/1 v/v/v) to give 2,3,4-tri-*O*-benzyl-6-*O*-trityl-D-glucopyranose intermediate (2.70 g, 96%) as a colourless oil (mixture α/β 0.3/0.7). $^1H$ (500 MHz, $CDCl_3$) δ 7.52-7.50 (6H, m, $H_{Ar}$), 7.40-7.17 (22H, m, $H_{Ar}$), 6.90-6.89 (2H, m, $H_{Ar}$), 5.39 (1H, d, J = 2.5 Hz, H1β), 5.01-4.70 (6H, m, $CH_2$-Ph, H1α), 4.36 (1H, d, J = 11.0 Hz, $CH_2$-Ph), 4.07-4.05 (1H, m, H5β), 3.99 (1H, t, J = 9.5 Hz, H4β), 3.81 (1H, t, J = 9.5 Hz, H3β), 3.76 (1H, t, J = 9.5 Hz, H2α), 3.70 (1H, dd, J = 3.5 Hz, 9.5 Hz, H2β), 3.62 (1H, t, J = 9.5 Hz, H4α), 3.50-3.48 (1H, m, H5α), 3.52-3.44 (3H, m, H6, H3α). $^{13}C$ (125 MHz, $CDCl_3$) δ 143.8, 143.7(2) ($C_{Ar}$ Tr), 138.5, 138.4, 137.9, ($C_{Ar}$ Bn), 128.7, 128.5, 128.4, 128.3, 128.1(2), 128.0 (2), 127.8(3), 127.8, 127.7, 127.6, 127.5, 127.4, 126.9(2) ($CH_{Ar}$), 97.5 (C1α), 91.2 (C1β), 86.8 ($C(Ph)_3$), 84.6 (C4α), 83.3 (C2β), 81.7 (C5α), 80.4 (C4β), 77.8 (C3), 77.7 (C2α), 75.8, 74.8, 73.3 ($CH_2$-Ph), 70.5 (C5β), 62.6, 62.3 (C6). HRMS $ES^+$-TOF: Calculated for $C_{46}H_{44}O_6Na$ $[M+Na]^+$ =715.3036, found $[M+Na]^+$= 715.3032.

To a solution of 2,3,4-tri-*O*-benzyl-6-*O*-trityl-D-glucopyranose (2.00 g, 2.9 mmol) in dry $Et_2O$ (20 mL) was added lithium aluminium hydride (0.22 g, 5.8 mmol) portion-wise at 0 °C. The reaction was then warmed to rt and stirred for 2 hours. The reaction mixture was then diluted with $Et_2O$ (10 mL) and carefully quenched with water (50 mL). After being filtered

through a pad of celite, the organic layer was isolated and washed with water (3 × 10 mL), brine (10 mL) and dried with $MgSO_4$. $Et_2O$ was then removed under reduced pressure to give (**4**) (1.95 g, 98%) as a white foam. $^1H$ (500 MHz, $CDCl_3$) δ 7.45-7.43 (6H, m, $H_{Ar}$), 7.32-7.21 (22H, m, $H_{Ar}$), 7.10-7.08 (2H, m, $H_{Ar}$), 4.67-4.58 (3H, m, $CH_2$-Ph), 4.53-4.51 (1H, m, $CH_2$-Ph), 4.45-4.39 (2H, m, $CH_2$-Ph), 4.07-4.03 (1H, m, H5), 3.87-3.84 (1H, dd, J = 3.3 Hz, 6.8 Hz, H4), 3.82-3.76 (2H, m, H2,H3), 3.72-3.54 (1H, dd, J = 4.3 Hz, 11.8 Hz, H1), 3.57-3.54 (1H, dd, J = 4.3 Hz, 11.8 Hz, H1), 3.38-3.35 (1H, dd, J = 4.3 Hz, 9.6 Hz, H6), 3.32-3.29 (1H, dd, J = 4.3 Hz, 9.6 Hz, H6'), 3.08 (1H, s br, OH). 2.56 (1H, s br, OH). $^{13}C$ (125 MHz, $CDCl_3$) δ 143.8(3) ($C_{Ar}$ Tr), 138.1, 137.7, 137.6 ($C_{Ar}$ Bn), 128.7, 128.4(3), 128.3, 128.2, 127.9(2), 127.8(2), 127.7, 127.1 ($CH_{Ar}$), 79.4 (C2), 79.3 (C3), 76.9 (C4), 74.4, 73.0, 72.7 ($CH_2$-Ph), 70.7 (C5), 64.6 (C6), 61.9 (C1). HRMS ES+-TOF: Calculated for $C_{46}H_{46}O_6Na$ $[M+Na]^+$= 717.3190, $[M+Na]^+$= 717.3192.

**Azido-2,3,5-tri-*O*-benzoyl-β-D-ribofuranoside (11).**

To a suspension of commercially available 2,3,5-*O*-tribenzoyl-1-*O*-acetate riboside (**10**) (10.0 g, 19.8 mmol) in dry acetonitrile (150 mL) was added aluminium chloride (3.90 g, 29.7 mmol). After stirring for ten minutes, azidotrimethylsilane (3.1 mL, 23.8 mmol) was added drop-wise to the solution. The reaction mixture was stirred for three hours at rt. The acetonitrile was then removed under reduced pressure, and the residue was dissolved in DCM (100 mL). The organic solution was washed with water (3 × 50 mL), brine (50 mL) and dried over $MgSO_4$. The DCM was removed under reduced pressure to give (**11**) (9.20 g, 96%) as colourless oil which crystallised after one week.

$^1H$ (500 MHz, $CDCl_3$) δ 8.10 (2H, dd, J = 1.2 Hz, 8.3 Hz, $H_{Ar}$), 8.00 (2H, dd, J = 1.2 Hz, 8.3 Hz, $H_{Ar}$), 7.90 (2H, dd, J = 1.2 Hz, 8.3 Hz, $H_{Ar}$), 7.61-7.52 (3H, m, $H_{Ar}$), 7.49-7.33 (6H, m, $H_{Ar}$), 5.85 (1H, dd, J = 5.0 Hz, 5.8 Hz, H3), 5.69 (1H, d, J = 1.6 Hz, H1), 5.59 (1H, dd, J = 1.6 Hz, 5.8 Hz, H2), 4.80-4.76 (2H, m, H5, H4), 4.58-4.55 (1H, m, H5). $^{13}C$ (125 MHz, $CDCl_3$) δ 166.1, 165.2, 165.0 (C=O, Bz), 133.7, 133.6, 133.2, 129.8, 129.7(2) ($CH_{Ar}$), 129.4, 128.7, 128.6 ($C_{Ar}$ Bz), 128.5, 128.4(2) ($CH_{Ar}$), 93.3 (C1), 79.8 (C4), 75.2 (C2), 71.4 (C3), 63.7 (C5). HRMS ES $^+$-TOF: Calculated for $C_{26}H_{22}N_3O_7$ $[M+H]^+$ = 488.1458, found $[M+H]^+$= 488.1460.

**6-*O*-Trityl-D-glucal (26).**

To a suspension of tri-*O*-acetyl-D-glucal (**25**) (2.0g, 7.3 mmol) in methanol (30 mL) was added MeONa (1 mL, 25% wt. in MeOH) and the reaction was stirred for 30 minutes at rt. After repeated filtration through a pad of Dowex $H^+$ until pH 7, methanol was removed under reduced pressure. The residue was taken up in dry pyridine (50 mL) and TrCl (3.10 g, 11.0 mmol) was added portion-wise and the resulting mixture was stirred overnight at rt. Pyridine was removed *in vacuo* and the dry residue was dissolved in chloroform (50 mL). The organic solution was washed with a saturated copper sulfate solution (4 × 20 mL), water (3 × 20 mL), brine (20 mL) and dried over $MgSO_4$. The crude product was purified by silica column chromatography ($CHCl_3$/EtOH/TEA: 9/0.9/0.1 v/v/v) to yield **2** (1.95 g, 63%) as a white wax. $\delta_H$ (500 MHz; $CDCl_3$; $Me_4Si$) 7.46-7.42 (5H, m, Ph), 7.29-7.19 (10H, m, Ph), 6.34 (1H, dd, *J* = 1.1 Hz, 6.2 Hz, H-1), 4.70 (1H, dd, *J* = 2.6 Hz, 6.2 Hz, H-2), 4.19-4.17 (1H, m, H-5), 3.86-3.78 (2H, m, H3, H-4), 3.53 (1H, dd, *J* = 3.4 Hz, 9.8 Hz, H-6), 3.31 (1H, dd, *J* = 4.9 Hz, 9.8 Hz, H-6). $\delta_C$ (125 MHz; $CDCl_3$; $Me_4Si$) 144.5 (C-1), 143.5(3) 128.5, 128.0, 127.2, 102.5 (C-2), 87.0 (C-$(Ph)_3$), 76.6 (C-5), 71.6 (C-3), 69.5 (C-4), 62.9 (C-6). HRMS (ES) calculated $[M+Na]^+$= 411.1572; found $[M+Na]^+$= 411.1569. FTIR ($cm^{-1}$) 3392 (υO–H), 3058 ($\upsilon C_{sp2}$-H), 2924 (υC-H Alkyl), 1646 (υC=C), 1055 (υC-O). $[\alpha_D]_D^{22}$ +6.12 (*c* 0.94 in $CHCl_3$).

**3,4-Di-*O*-benzyl-6-*O*-trityl-D-glucal (27).**

To a solution of 6-*O*-trityl-D-glucal (**26**) (5.00 g, 12.9 mmol) in dry DMF (100 mL) was added sodium (0.77 g, 32.2 mmol, 60% wt. in oil) portionwise at rt. The reaction mixture was stirred for 30 minutes and benzyl bromide (3.8 mL, 32.2 mmol) was then added dropwise. After being stirred for 8 hours at rt, the reaction was carefully quenched with water (200 mL) and extracted with EtOAc (3 × 50 mL). The organic phase was isolated and was then washed with water (3 × 50 mL), brine (50 mL) and dry over $MgSO_4$. After removal of EtOAc under reduced pressure, the crude product was purified by silica column chromatography (Hex/EtOAc/TEA: 9/0.9/0.1 v/v/v) to yield (**27**) (3.9 g, 53%) as a colourless wax. $\delta_H$ (500 MHz; $CDCl_3$; $Me_4Si$) 7.52-7.51 (6H, m, Ph), 7.31-7.19 (17H, m, Ph), 7.06-7.03 (2H, m, Ph), 6.51 (1H, dd, *J* = 1.0 Hz, 6.1 Hz, H-1), 4.89 (1H, dd, *J* = 2.5 Hz, 6.1 Hz, H-2), 4.76 (1H, d, *J* = 11.0 Hz, $CH_2$-Ph), 4.62 (1H, d, *J* = 11.6 Hz, $CH_2$-Ph), 4.55 (1H, d, *J* = 11.6 Hz, $CH_2$-Ph), 4.53 (1H, d, *J* = 11.0 Hz, $CH_2$-Ph), 4.21-4.19 (1H, m, H-5), 4.04-4.03 (2H, m, H-3, H-4), 3.57

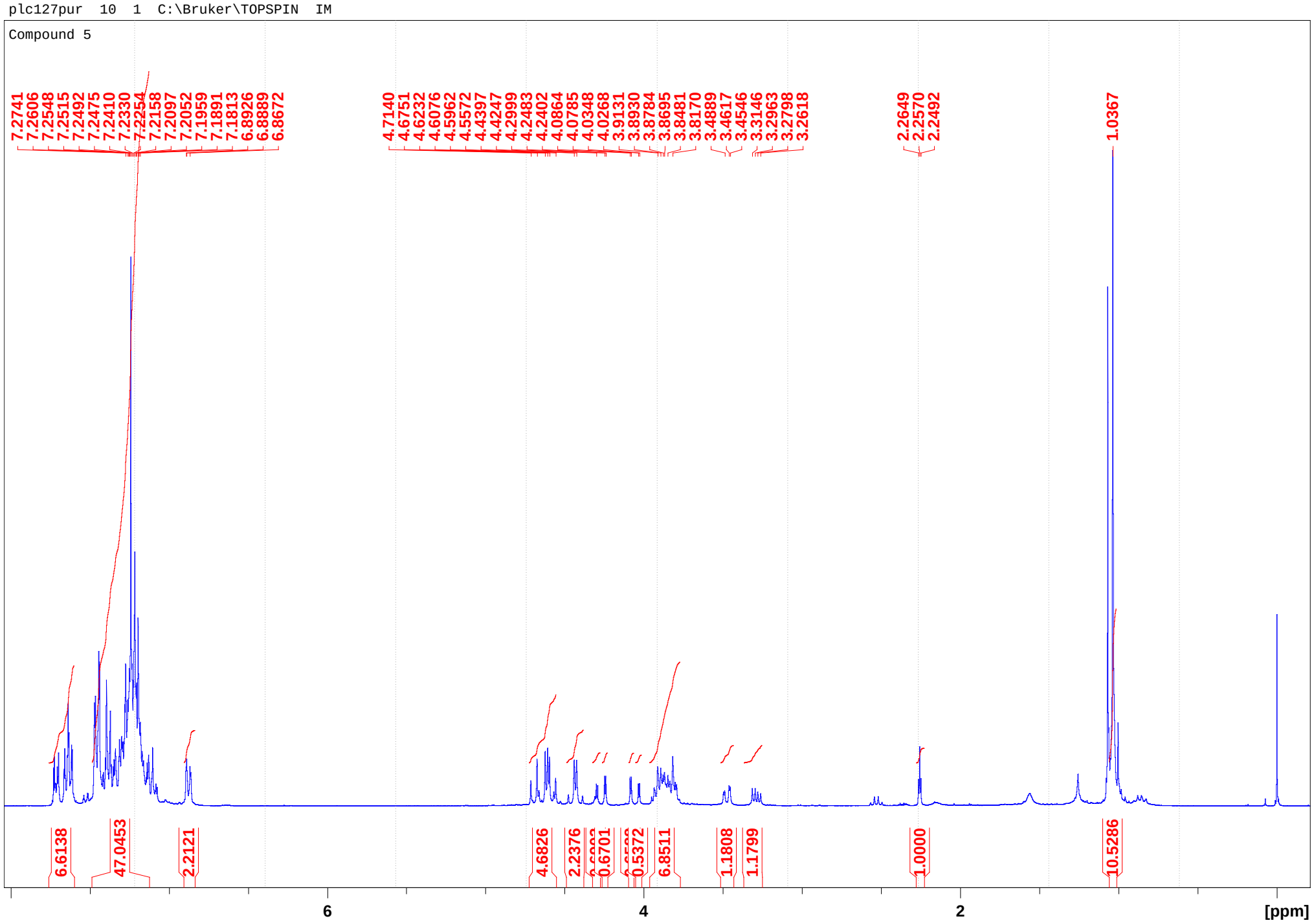
(1H, dd, *J* = 3.5 Hz, 9.8 Hz, H-6), 3.43 (1H, dd, *J* = 5.0 Hz, 9.8 Hz, H-6). $\delta_C$ (125 MHz; $CDCl_3$; $Me_4Si$) 144.7 (C-1), 143.8(3) 138.2, 138.0, 128.2, 128.3, 128.1, 127.7(2), 127.5, 127.4, 126.8, 99.7 (C-2), 86.3 (C-$(Ph)_3$), 76.8 (C-5), 76.0 (C-3), 74.5 (C-4), 73.7, 70.6 ($CH_2$-Ph), 62.0 (C-6). HRMS (ES) calculated $[M+Na]^+$= 591.2511; found $[M+Na]^+$= 591.2525. FTIR ($cm^{-1}$): 3434 (υO-H), 3060 ($\upsilon C_{sp2}$-H), 3029 ($\upsilon C$-$H_{Ar}$), 2876 (υC-H Alkyl), 1646 (υC=C), 1067 (υC-O), 745 ($\upsilon C_{sp3}$-H). $[\alpha_D]_D^{22}$ +5.26, (*c* 1.33 in $CHCl_3$).

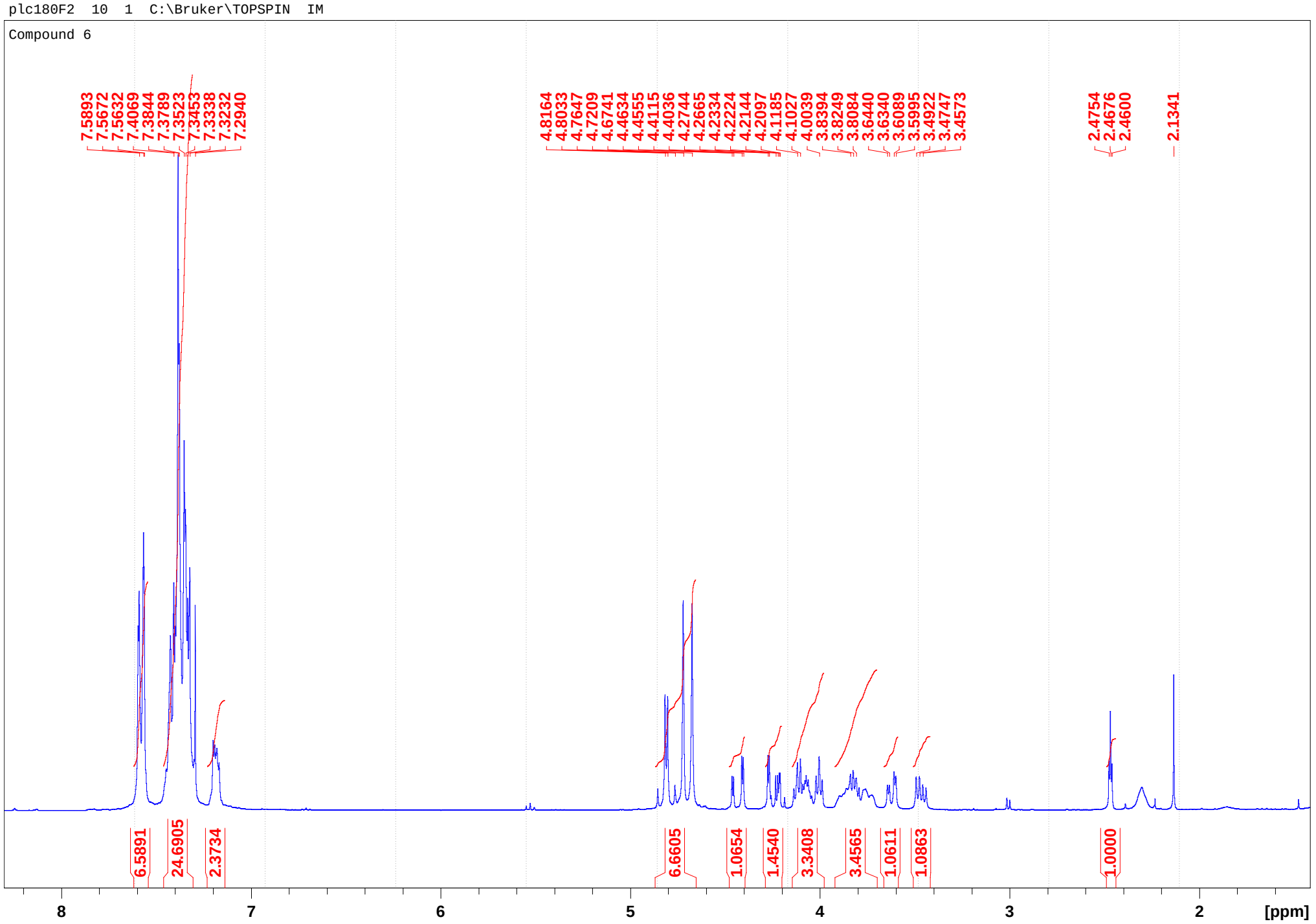
**3,4-Di-*O*-benzyl-6-*O*-trityl-2-deoxy-D-glucopyranose (28).**

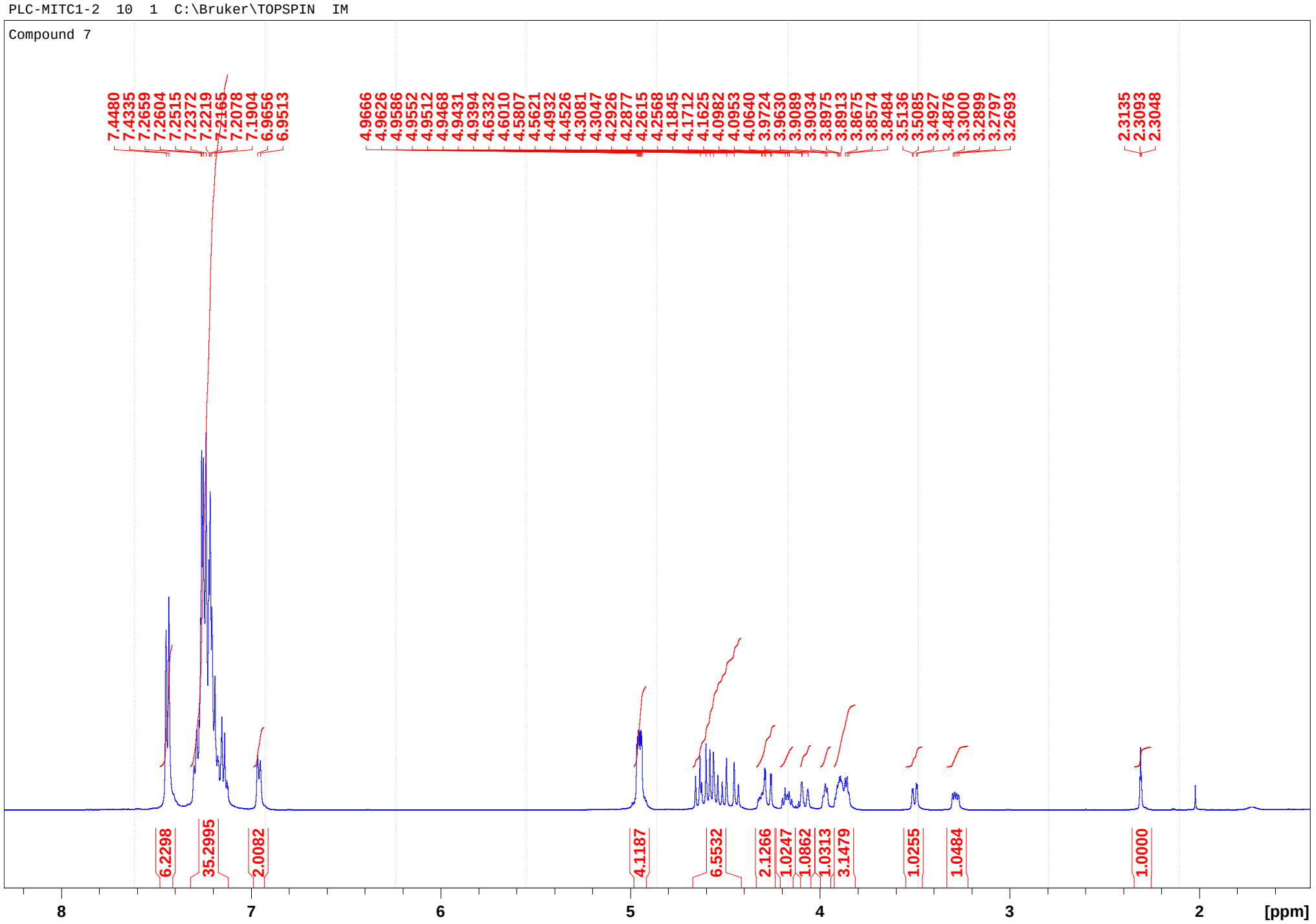
To a solution of 3,4-di-*O*-benzyl-6-*O*-trityl-D-glucal (**27**) (2.00 g, 3.5 mmol) in THF/water mixture (30 mL: 4/1, v/v) was added mercury acetate (2.20 g, 7.0 mmol) portion-wise at 0°C. The reaction mixture was stirred for 2 hours at 0°C, then diluted with a THF/water mixture (50 mL: 1/1, v/v) to which sodium borohydride was carefully added (0.66 g, 17.6 mmol). After 5 minutes at 0°C, the reaction mixture was then diluted with water (20 mL). The aqueous solution was extracted with EtOAc (3 × 20 mL) and the organic layer was then washed with water (3 × 20 mL), brine (20 mL) and dried over $MgSO_4$. After removal of EtOAc under reduced pressure, the crude product was purified by silica column chromatography (Hex/EtOAc/TEA: 9/0.9/0.1-75/24/1 v/v/v) to yield (**28**) (1.06 g, 51% overall) as a colourless wax (mixture α/β 0.4/0.6). $\delta_H$ (500 MHz; $CDCl_3$; $Me_4Si$) 7.53 (6H, d, *J* = 7.4 Hz, Ph), 7.40-7.21 (17H, m, Ph) 6.98-6.69 (2H, m, Ph), 5.50 (1H, d, *J* = 2.5 Hz, H-1β), 4.83-4.79 (2H, m, $CH_2$-Ph), 4.72-4.62 (2H, m, H-1α, $CH_2$-Ph), 4.42-4.38 (1H, m, $CH_2$-Ph), 4.09-4.04 (2H, m, H-5β, H-3β), 3.75 (1H, t, *J* = 9.5 Hz, H-4β), 3.66 (1H, q, *J* = 8.8 Hz, H-4α), 3.64-3.59 (2H, m, H-6α, H-3α), 3.55 (1H, dd, *J* = 1.8 Hz, 10.1 Hz, H-6β), 3.50-3.47 (1H, m, H-5α), 3.31-3.27 (1H, m, H-6α), 2.40 (1H, ddd, *J* = 1.9 Hz, 4.8 Hz, 12.8 Hz, H-2α), 2.36 (1H, ddd, *J* = 1.9 Hz, 4.8 Hz, 12.8 Hz, H-2β), 1.81 (1H, dt, *J* = 3.5 Hz, 12.8 Hz, H-2β), 1.67 (1H, dq, *J* = 1.6 Hz, 10.2 Hz, H-2α). $\delta_C$ (125 MHz; $CDCl_3$; $Me_4Si$) 144.0, 143.9(2) 138.6, 138.3, 138.2, 138.1 128.8, 128.4(α, β), 128.1(α, β), 128.0(α, β), 127.7, 127.5(α, β), 127.4, 126.9 94.1 (C-1α), 92.1 (C-1β), 86.3, 86.5 79.2 (C-4α), 78.7 (C-4β), 77.8 (C-3α), 77.1(C-3β), 75.2 (C-5α), 74.8, 72.1, 71.7 , 71.2 (C-5β), 63.0 (C-6α, β), 38.2 (C-2α), 35.7 (C-2β). HRMS (ES) calculated $[M+Na]^+$= 609.2617; found $[M+Na]^+$= 609.2642. FTIR ($cm^{-1}$): 3425 (υO-H), 3060, 3029 ($\upsilon C$-$H_{Ar}$), 2928 (υC-H Alkyl), 1090 (υC-O), 747 ($\upsilon C_{sp3}$-H). $[\alpha_D]_D^{22}$ +8.89 (*c* 0.90 in $CHCl_3$).

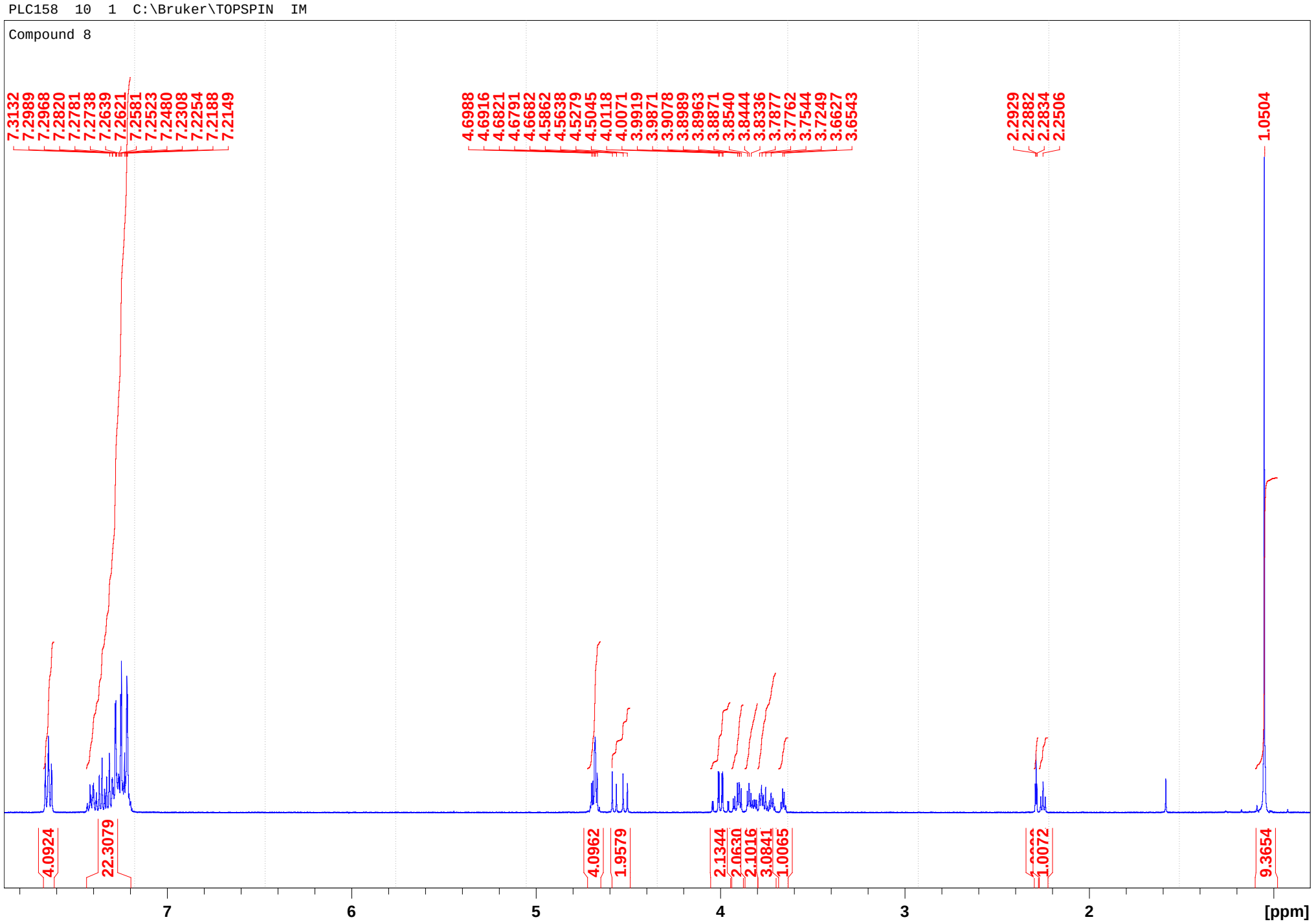
**3,4-Di-*O*-benzyl-1-*O*-*tert*-butyldiphenylsilyl-6-*O*-trityl-2-deoxy-D-glucitol (29).**

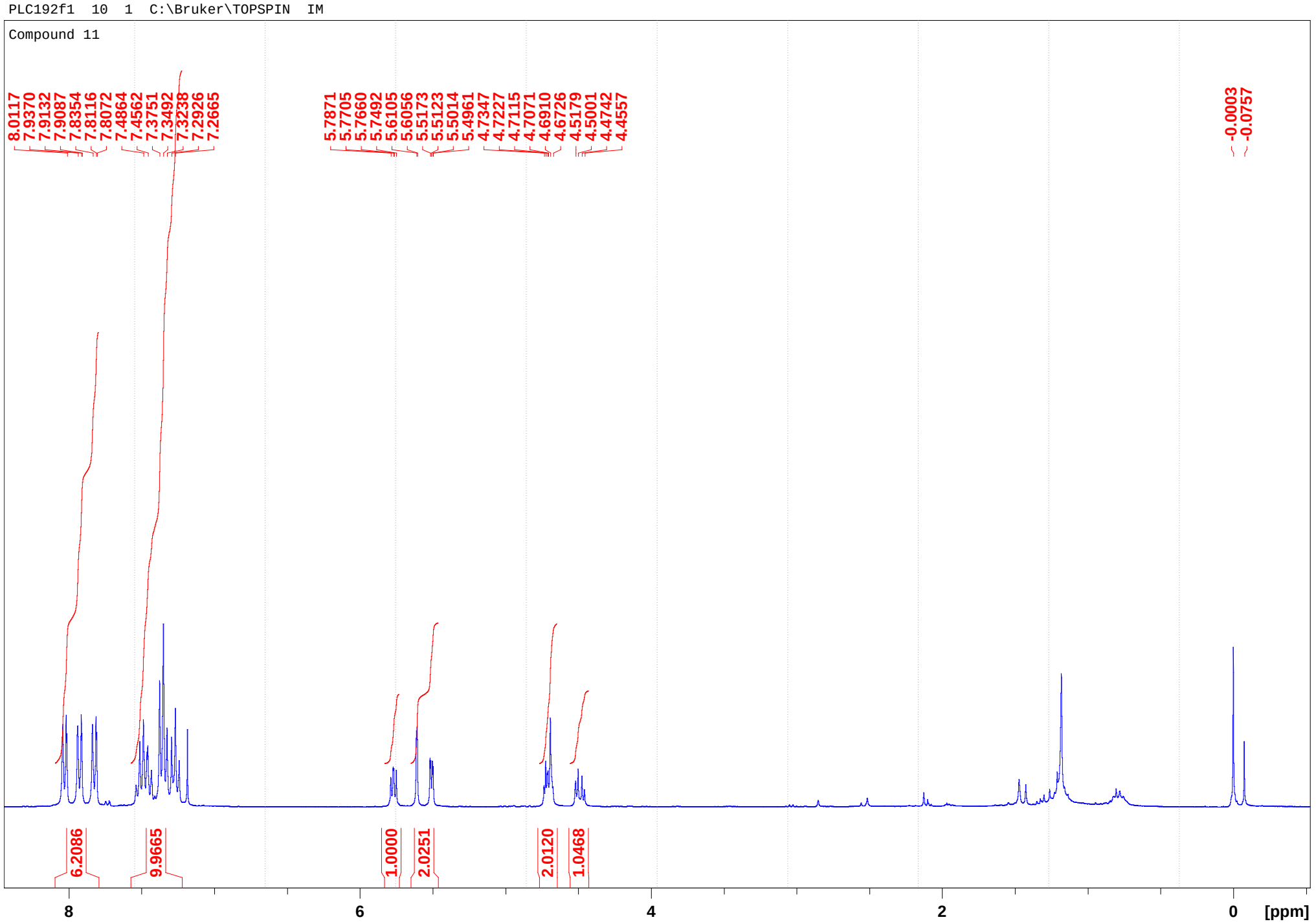
To a solution of 3,4-di-*O*-benzyl-6-*O*-trityl-2-deoxy-D-glucopyranose (**28**) (1.10 g, 1.9 mmol) in dry $Et_2O$ (30 mL) was carefully added lithium aluminium hydride (0.14 g, 3.7 mmol) portion-wise at 0°C. The reaction mixture was warmed to rt over a 30 minutes period and then stirred for a further 2 hours. The reaction mixture was diluted with $Et_2O$ (30 mL) and carefully quenched with water until total precipitation of lithium salts (about 20 mL). The reaction mixture was filtered off and the organic layer was washed with water (3 × 20 mL), brine (20 mL) and dried over $MgSO_4$. The dry organic solution was concentrated under reduced pressure to give 3,4-di-*O*-benzyl-6-*O*-trityl-2-deoxy-D-glucitol as a crude colourless oil. $\delta_H$ (500 MHz; $CDCl_3$; $Me_4Si$) 7.45-7.43 (6H, m, Ph), 7.32-7.19 (17H, m, Ph), 7.08-7.06 (2H, m, Ph), 4.54 (1H, d, $J$ = 11.4 Hz, $CH_2$-Ph), 4.47 (1H, d, $J$ = 11.4 Hz, $CH_2$-Ph), 4.39 (2H, s, $CH_2$-Ph), 4.02-3.95 (1H, m, H-5), 3.77-3.75 (2H, m, H-1), 3.58-3.55 (2H, m, H-3, H-4), 3.41 (1H, dd, $J$ = 3.6 Hz, 9.7 Hz, H-6), 3.27 (1H, br, OH), 3.22 (1H, dd, $J$ = 4.9 Hz, 9.7 Hz, H-6), 1.83-1.81 (2H, m, H-2). $\delta_C$ (125 MHz; $CDCl_3$; $Me_4Si$) 143.9(3), 137.8, 137.7, 128.7, 128.5, 128.3 128.2, 128.1, 127.9, 127.8, 127.7, 127.0, 86.61, 77.7 (C-5), 77.6 (C-4), 73.4, 72.7 ($CH_2$-Ph), 70.9 (C-3), 64.6 (C-1), 59.9 (C-6), 32.9 (C-2). The crude product was then dissolved in dry DCM (20 mL) and dry TEA (0.78 mL, 5.62 mmol) and 4-DMAP (0.063 g, 0.56 mmol) were added. The reaction mixture was stirred at rt for 30 minutes and TBDPSCl (0.54 mL, 2.1 mmol) was then added drop-wise and the resulting solution was stirred at rt overnight. The reaction mixture was concentrated to dryness and the crude product was purified by silica column chromatography (Hex/EtOAc/TEA: 9/0.9/0.1 v/v/v) to yield **(29)** (1.05 g, 96% overall) as a colourless wax. $\delta_H$ (500 MHz; $CDCl_3$; $Me_4Si$)7.65-7.62 (4H, m, Ph), 7.47-7.38 (5H, m, Ph), 7.41-7.37 (24H, m, Ph), 7.10-7.07 (2H, m, Ph), 4.61-4.47 (4H, m, $CH_2$-Ph), 4.00-3.89 (3H, m, H-5, H-1), 3.87-3.70 (2H, m, H-3, H-4), 3.50 (1H, dd, $J$ = 2.4 Hz, 10.5 Hz, H-6), 3.33 (1H, dd, $J$ = 5.6 Hz, 10.5 Hz, H-6), 1.87-1.81 (2H, m, H-2), 1.09 (9H, s, C-$(CH_3)_3$). $\delta_C$ (125 MHz; $CDCl_3$; $Me_4Si$)143.8(3), 138.4, 138.1, 133.5, 133.5, 129.6, 128.7, 128.3, 128.1(2), 128.0, 127.9, 127.8(2), 127.6, 127.4, 86.9, 80.7 (C-5), 79.4 (C-3), 76.7 (C-4), 74.5, 73.2 ($CH_2$-Ph), 63.1 (C-1), 60.4 (C-6), 33.2 (C-2), 26.8 ($CH_3$), 19.4 (C-$(CH_3)_3$). HRMS (ES) calculated $[M+Na]^+$= 849.3951; found $[M+Na]^+$= 849.3966. $[\alpha_D]_D^{22}$ +3.17 (*c* 0.63 in $CHCl_3$).

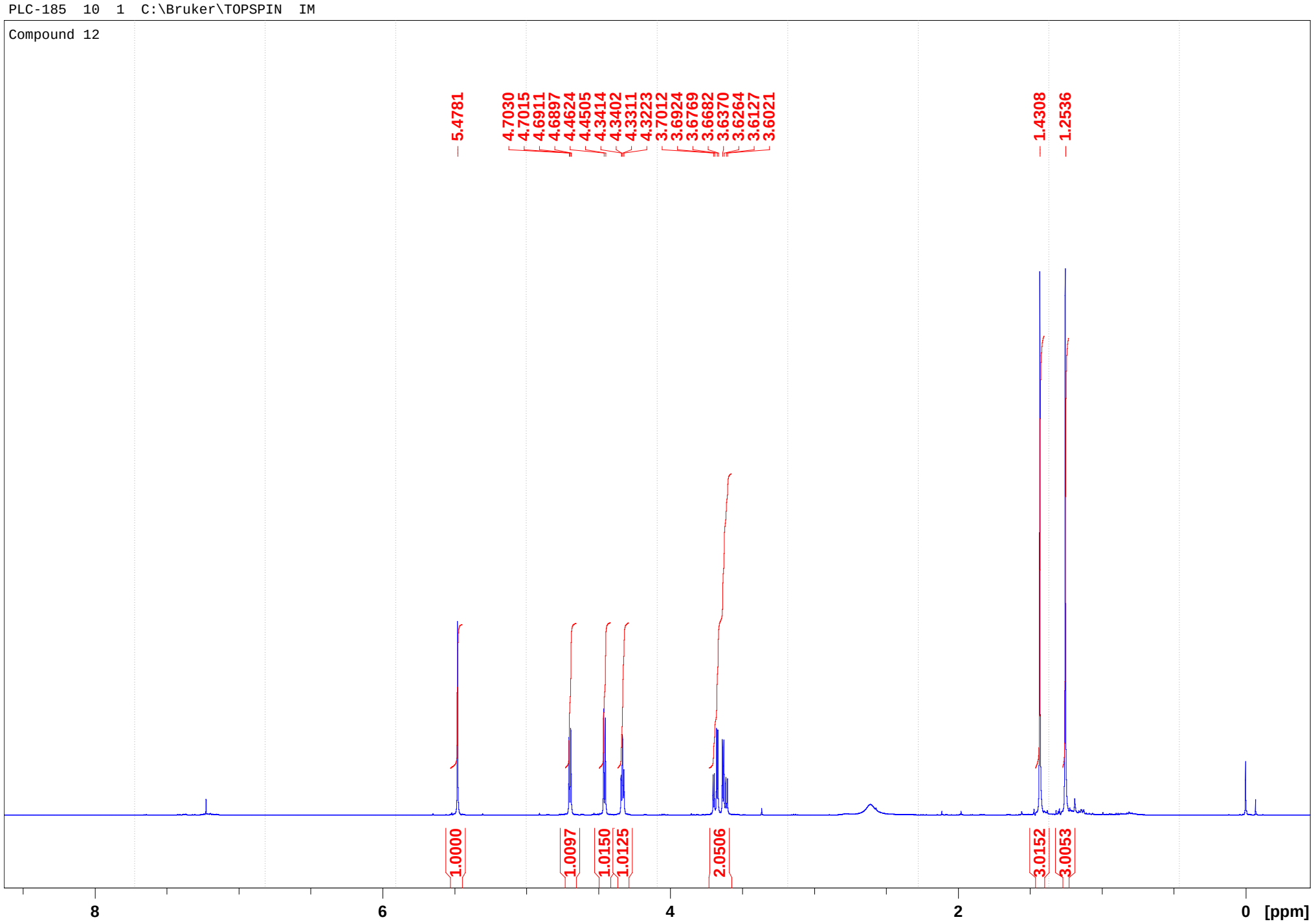


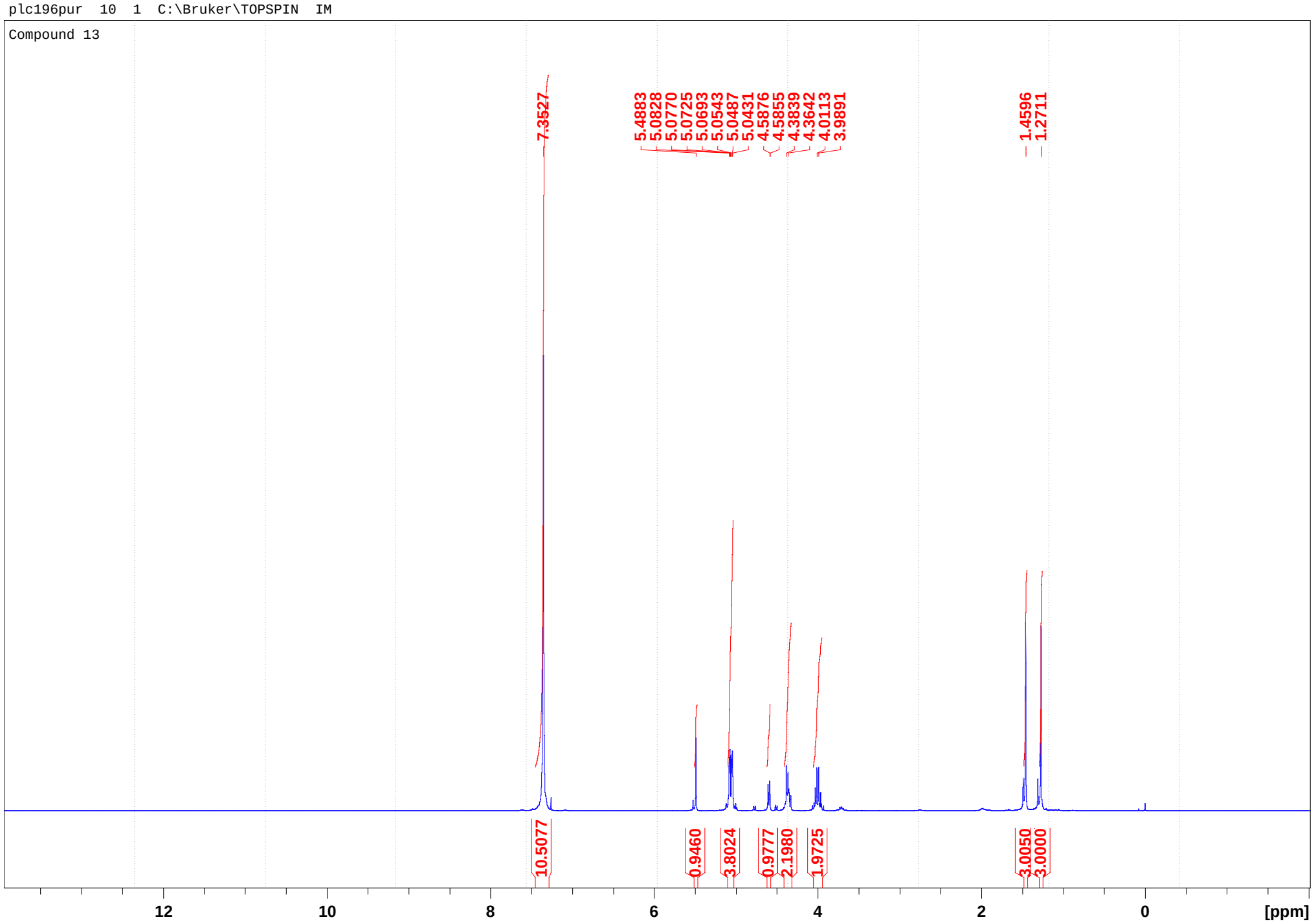


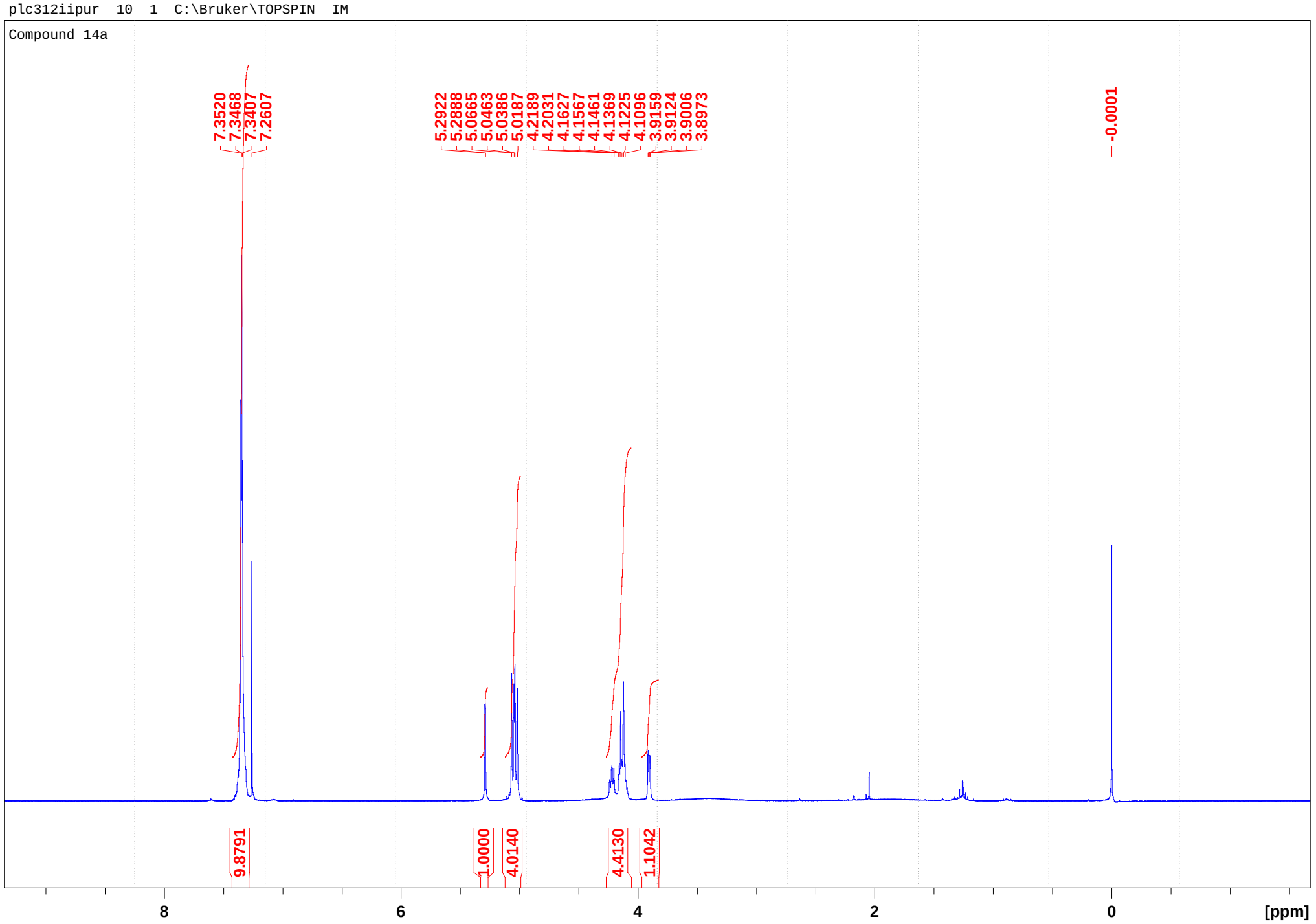


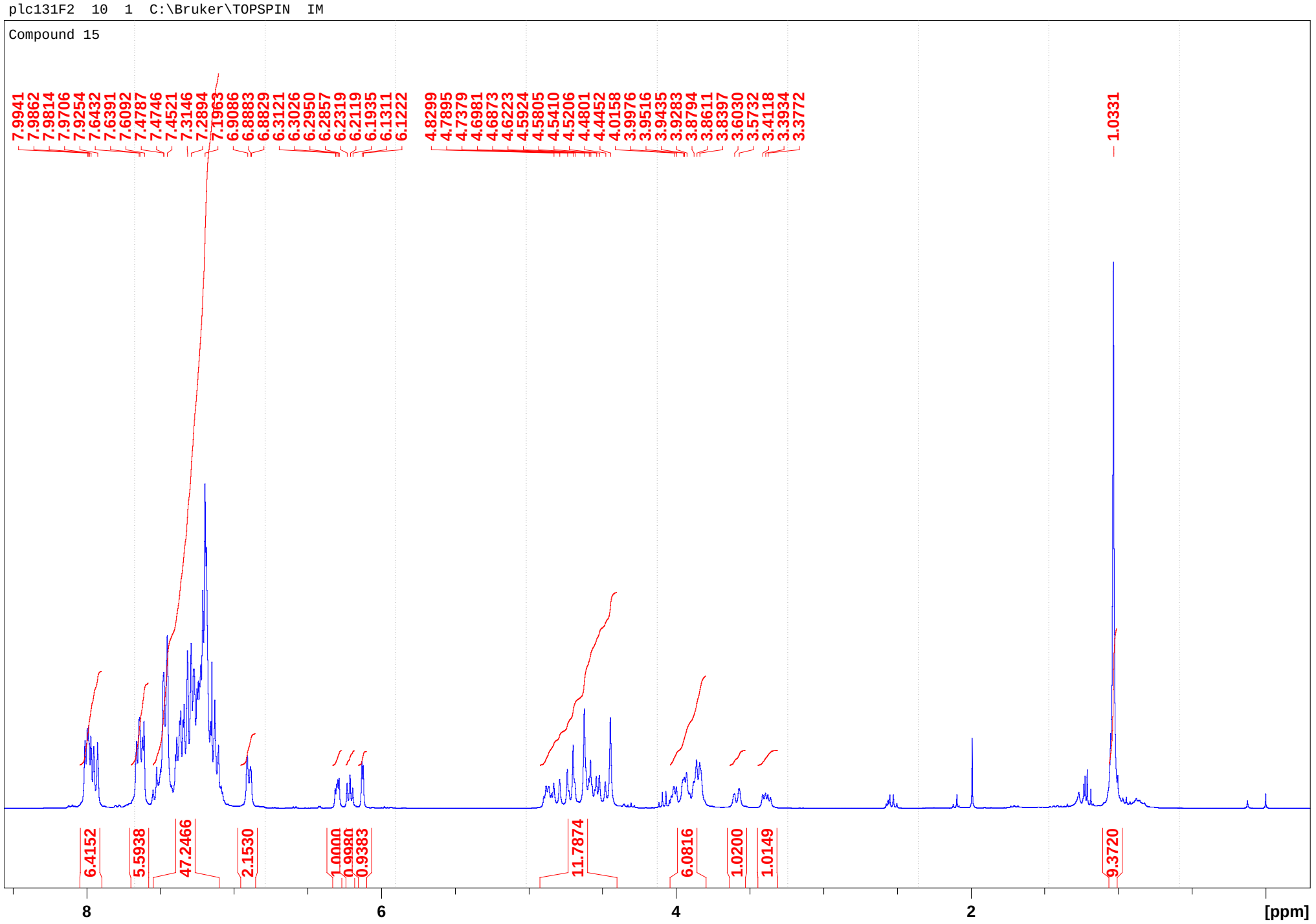




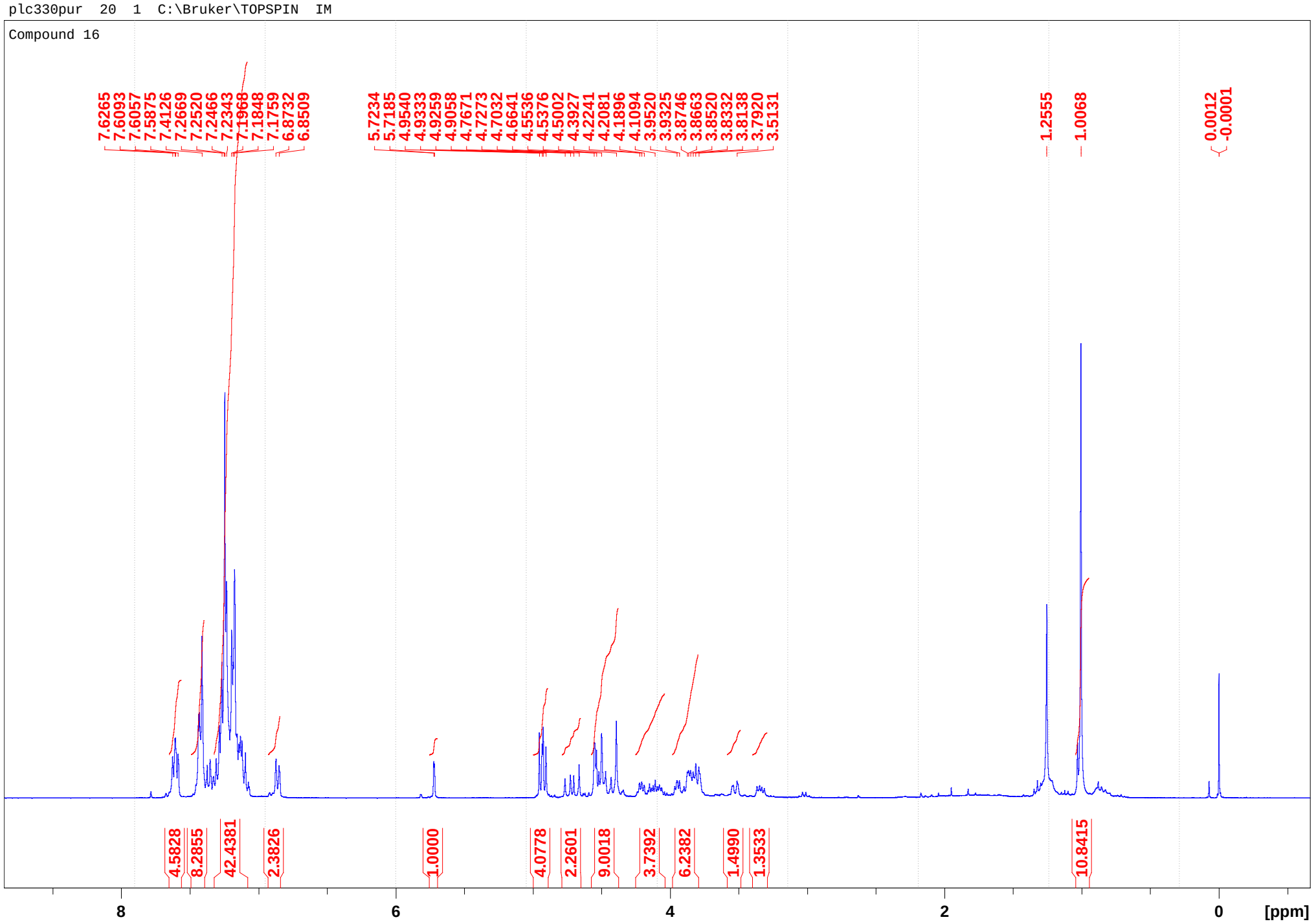


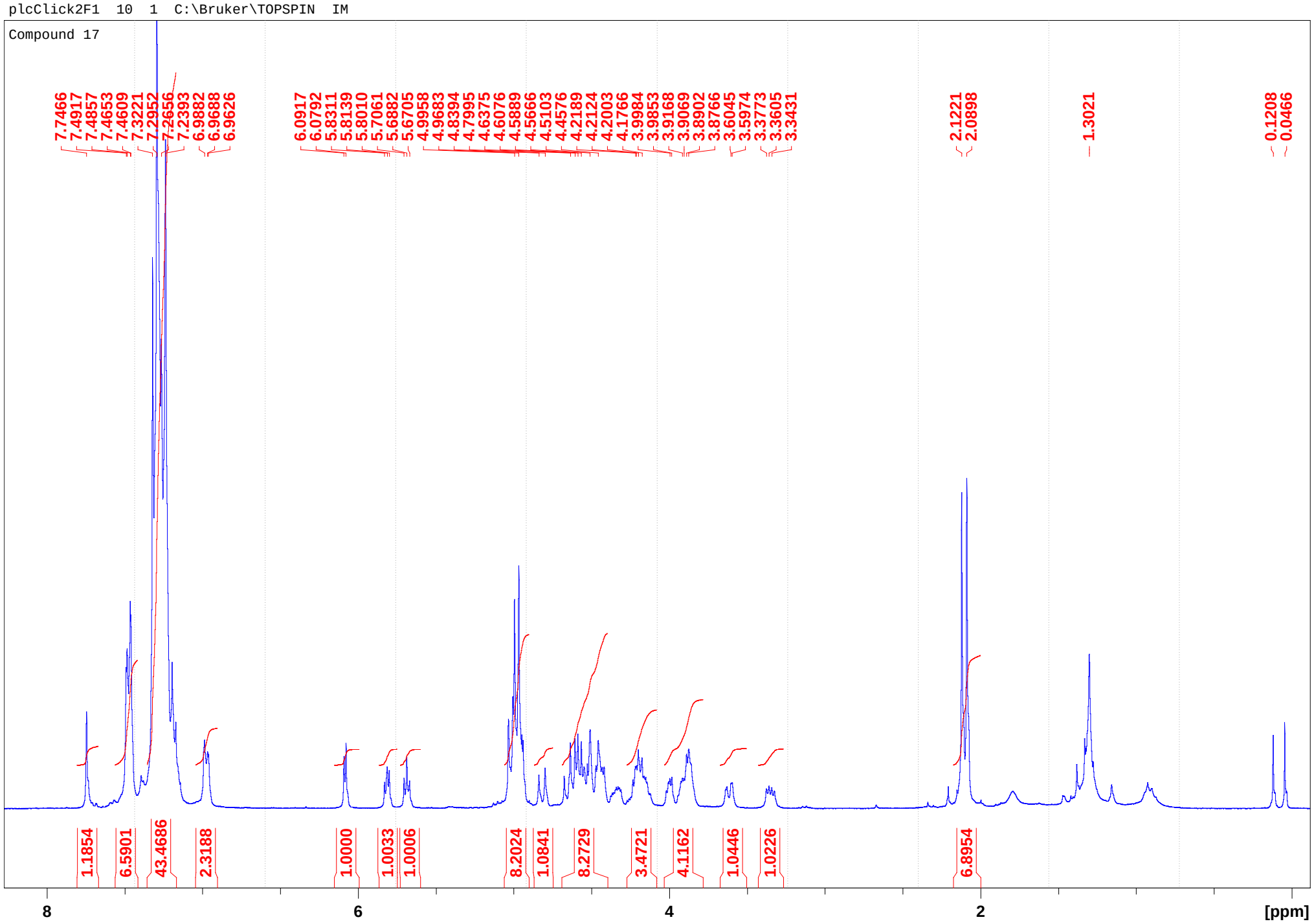


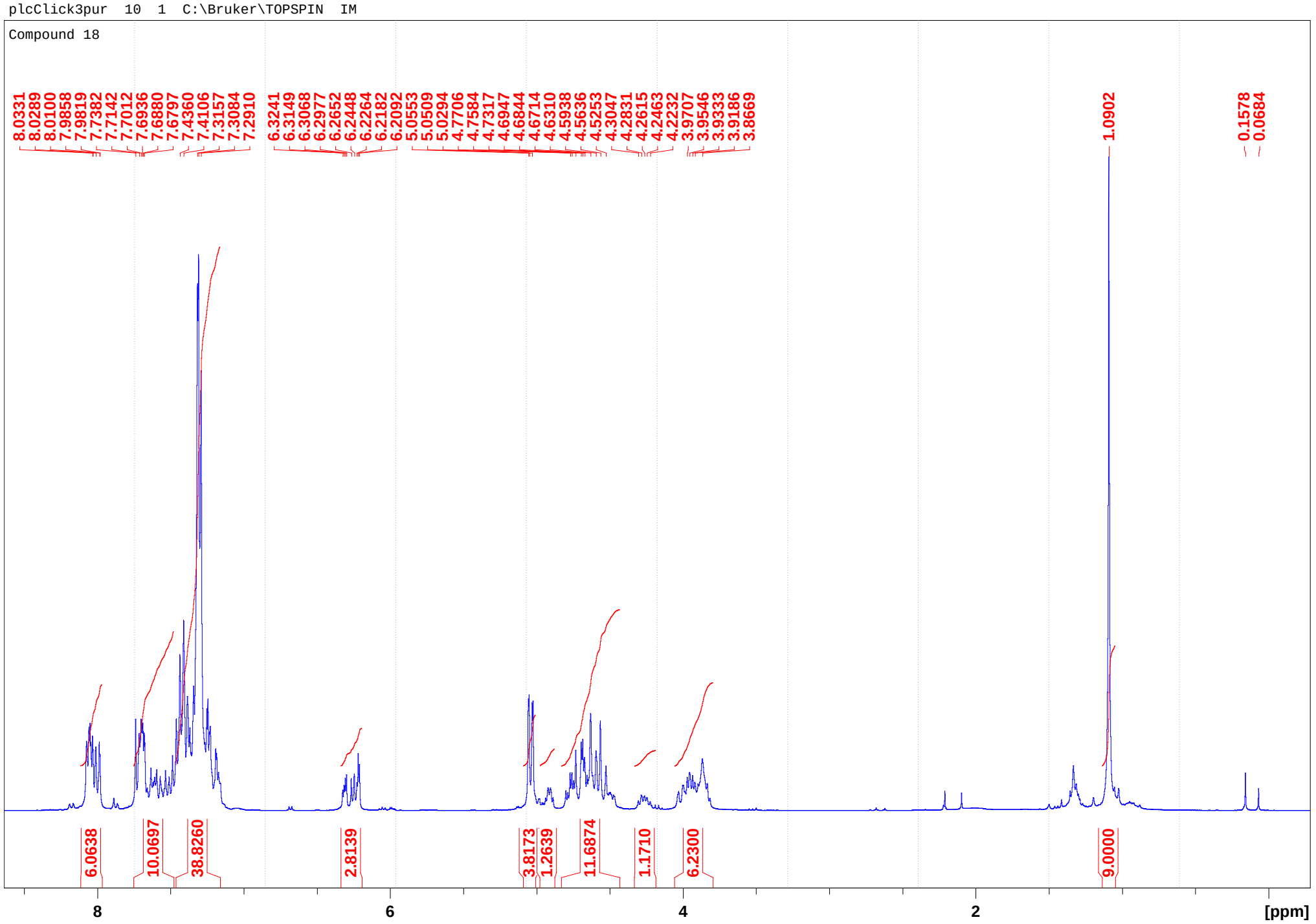


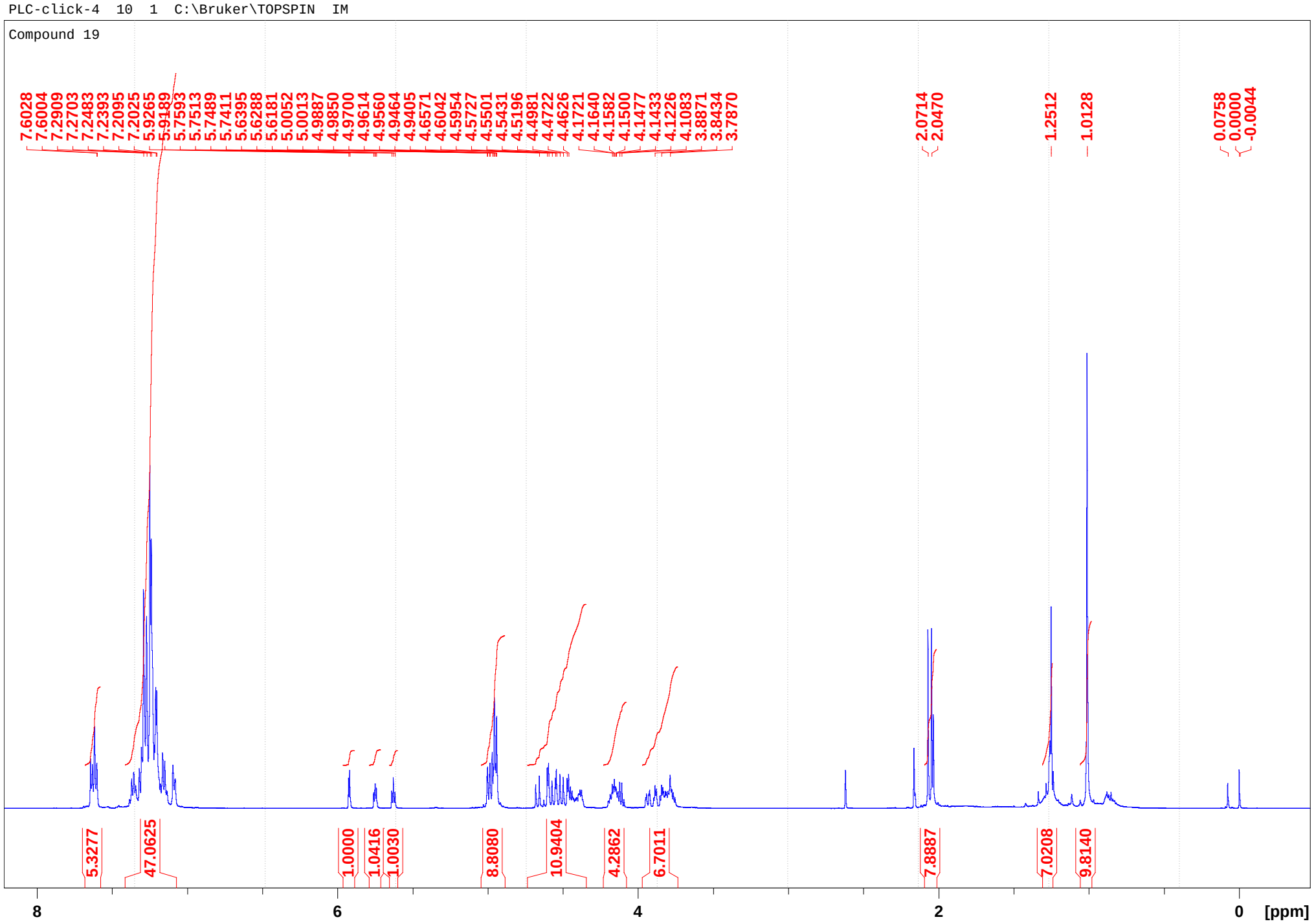


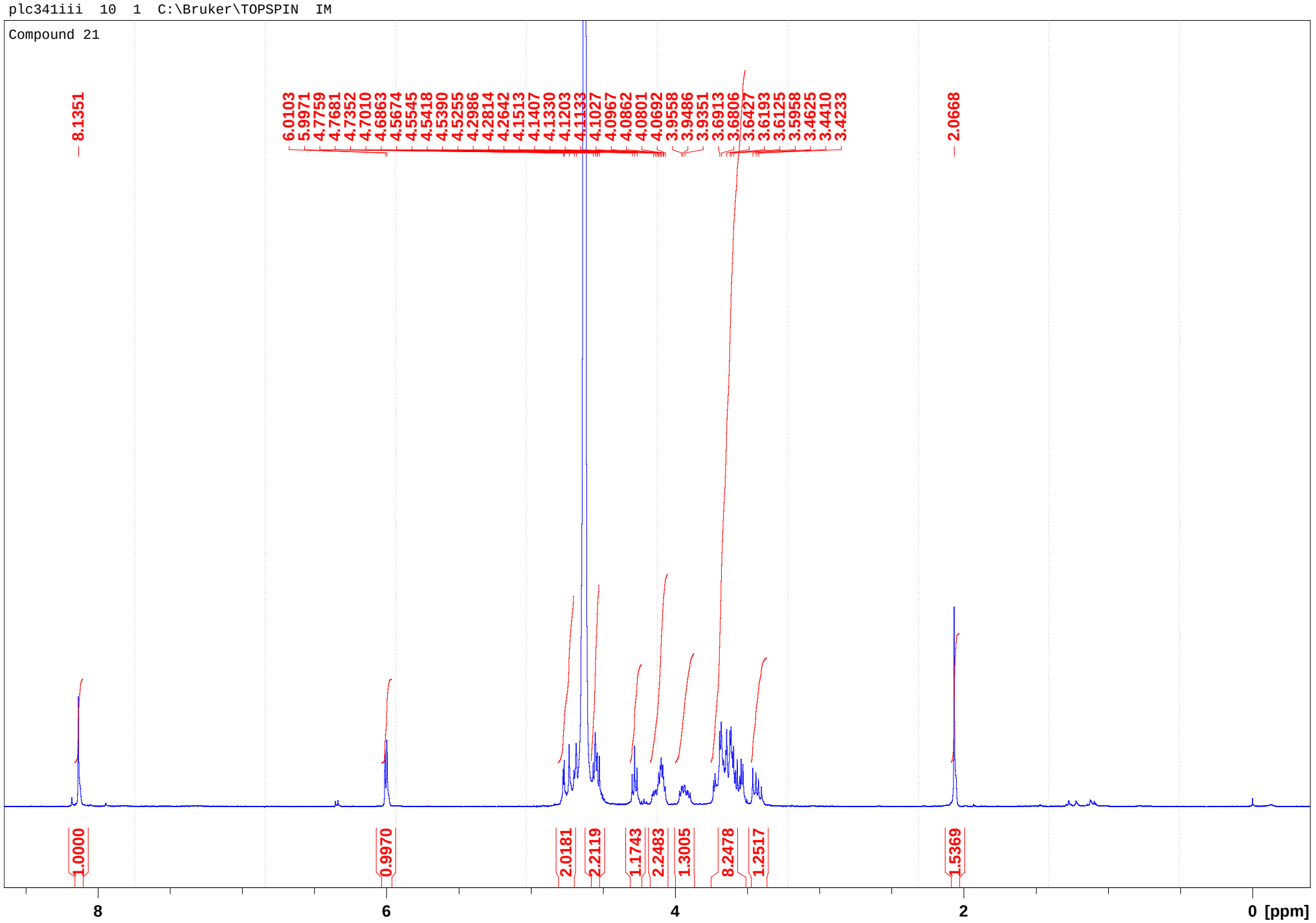
Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

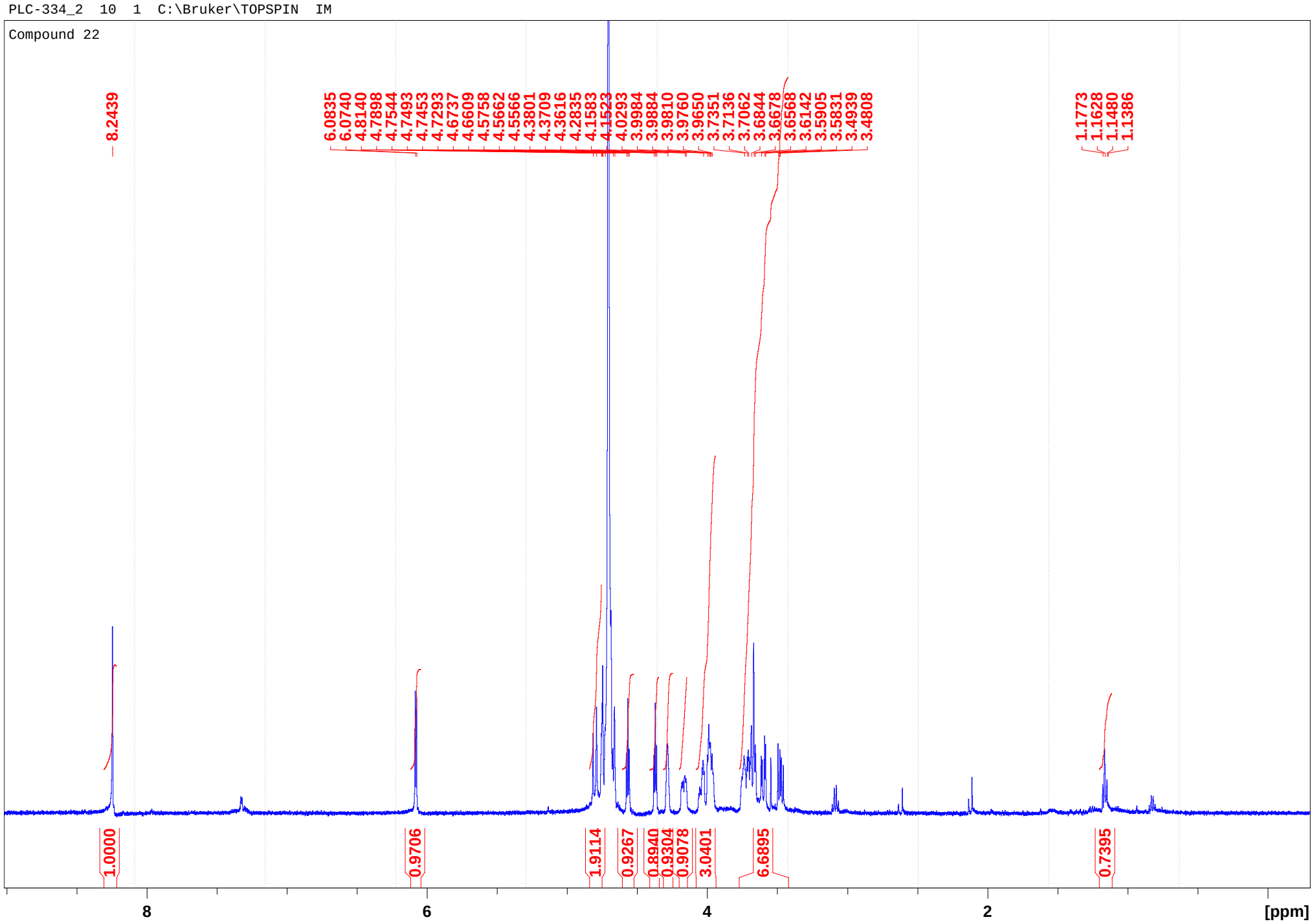



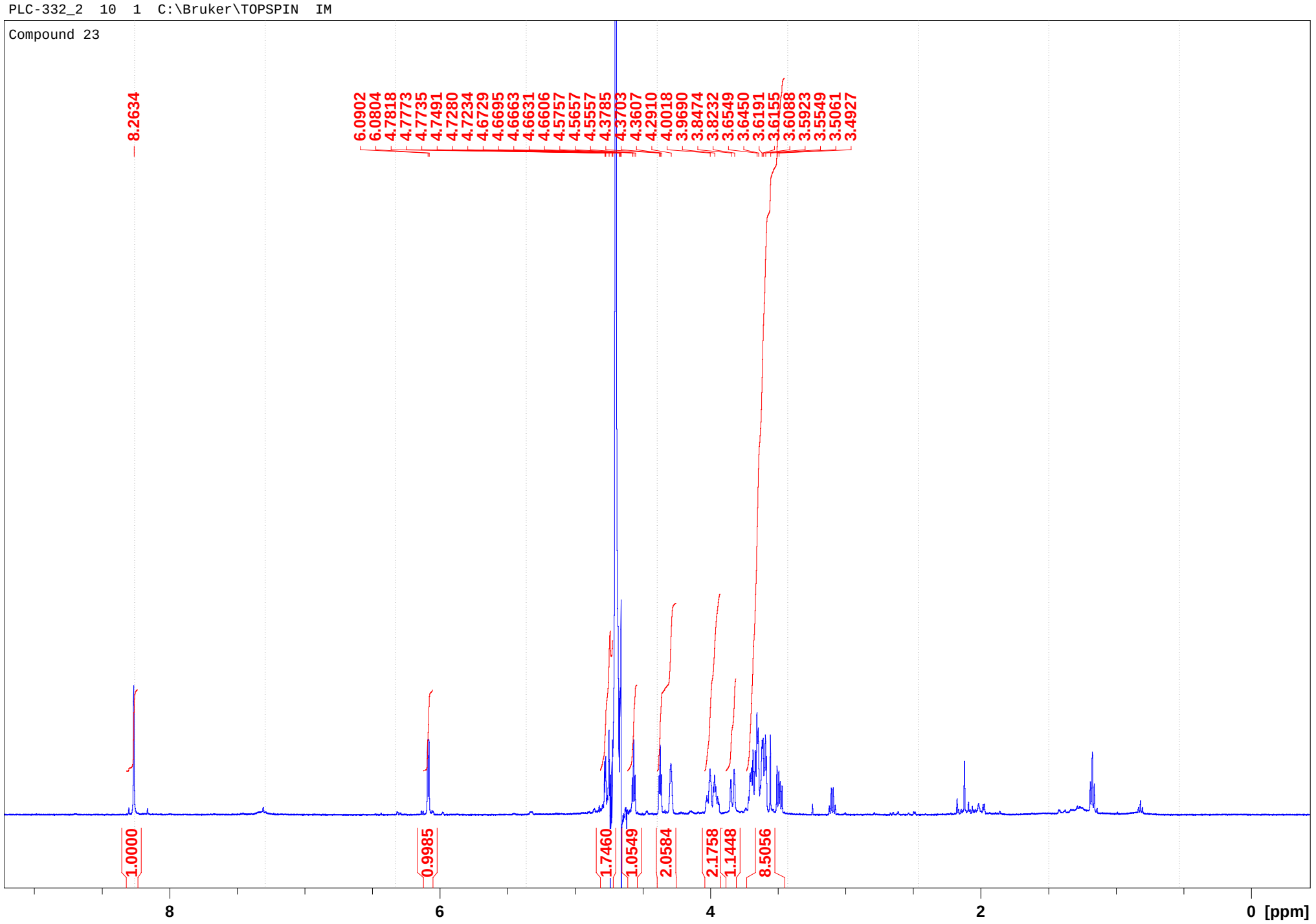


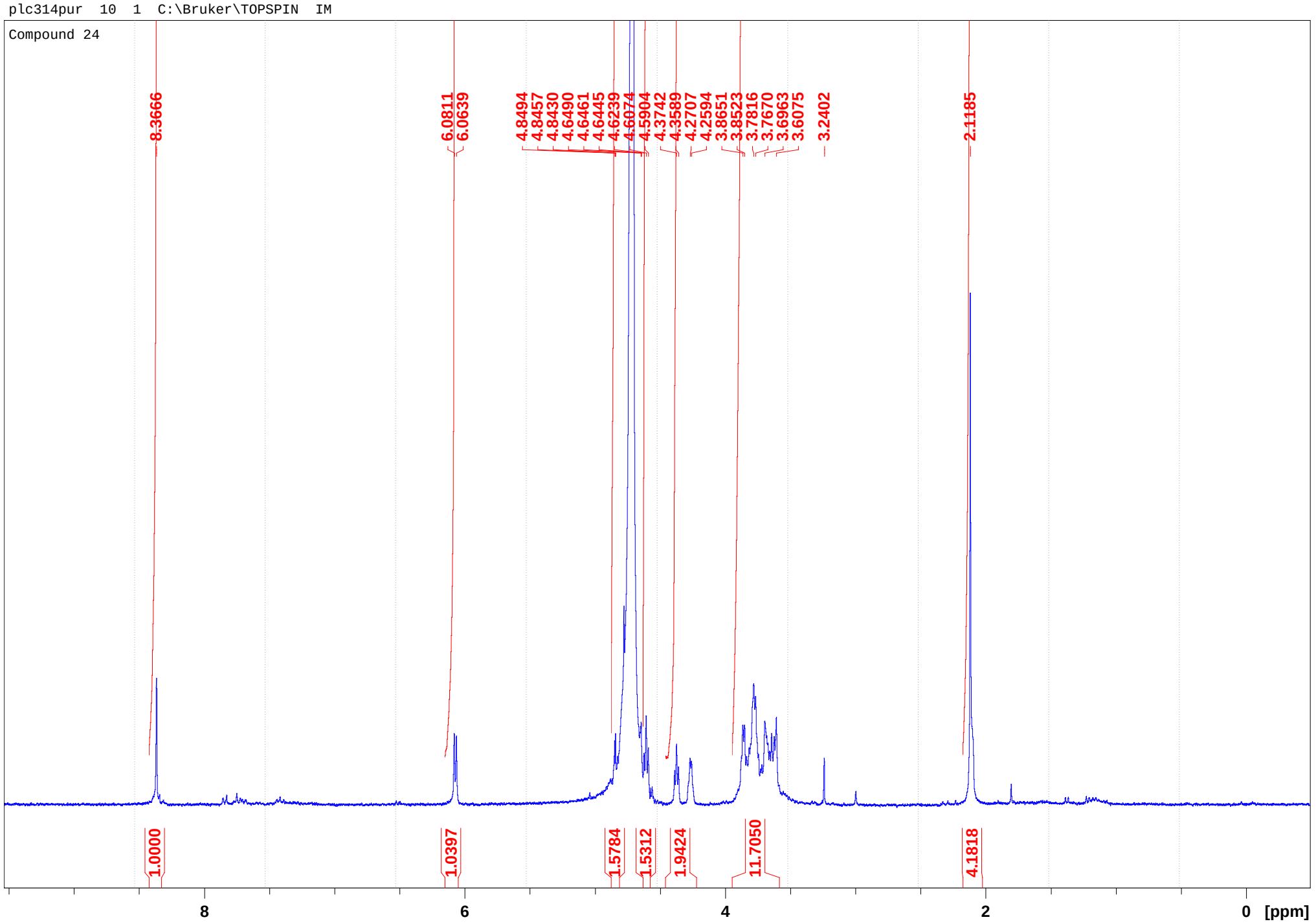


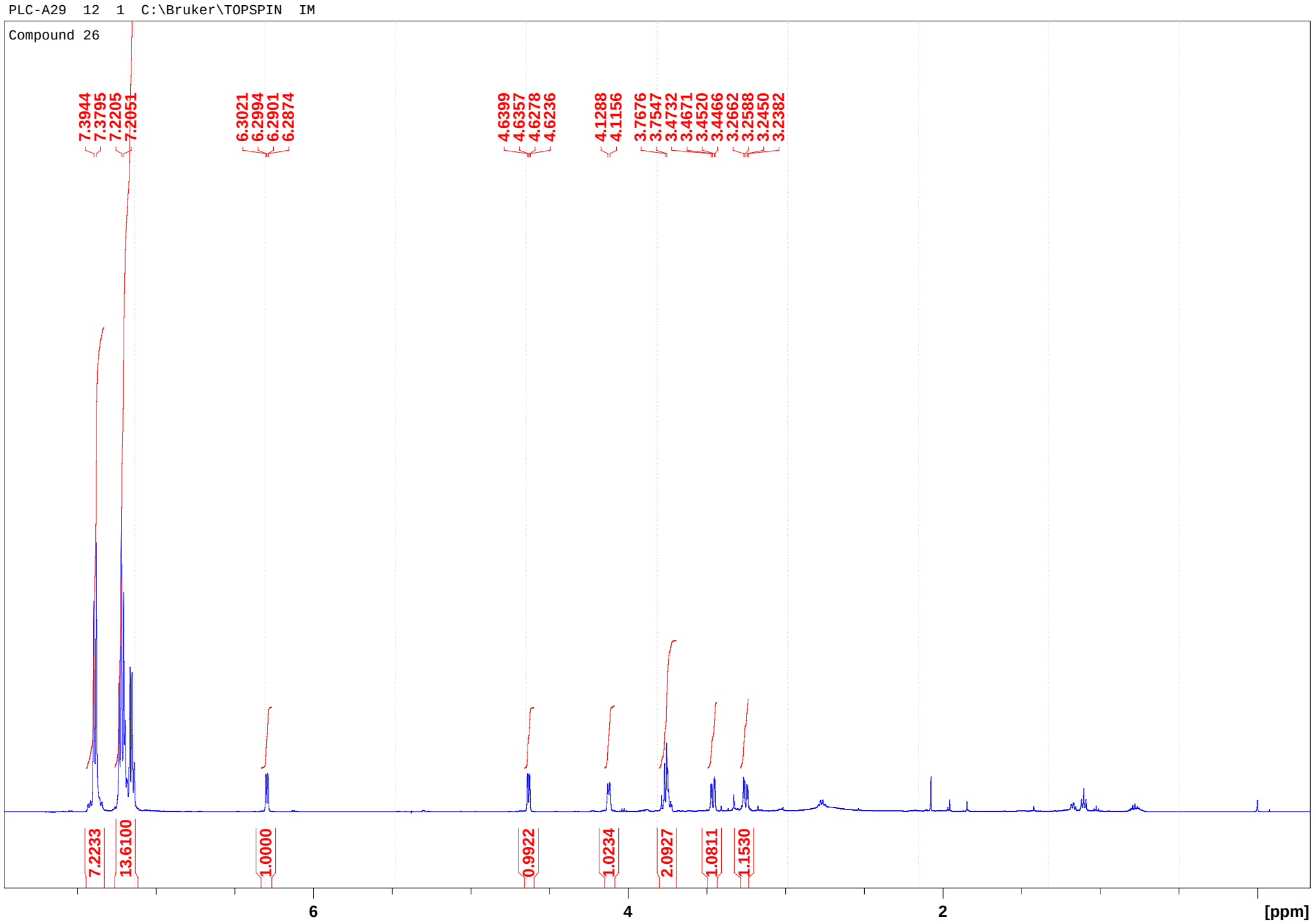


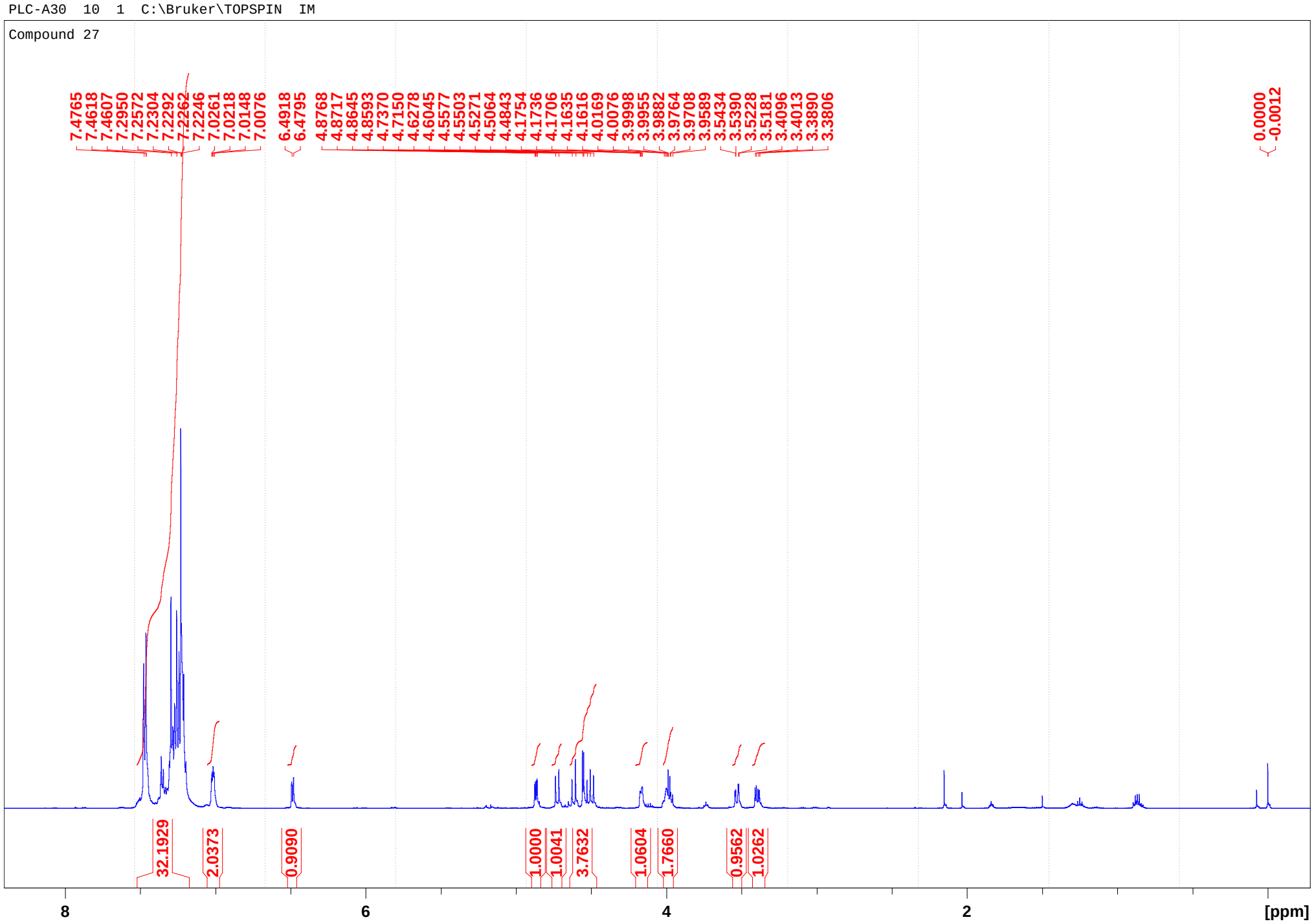


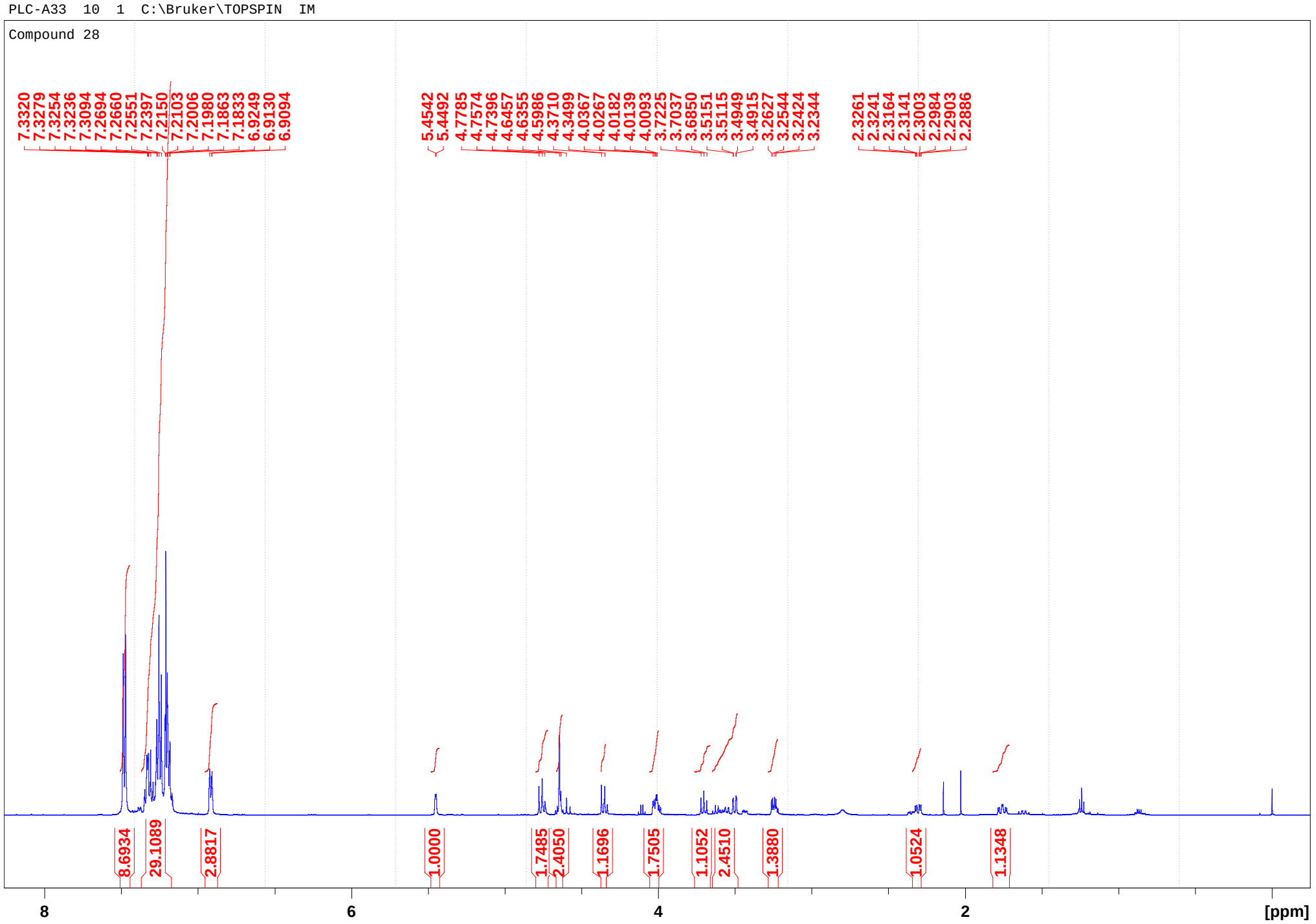


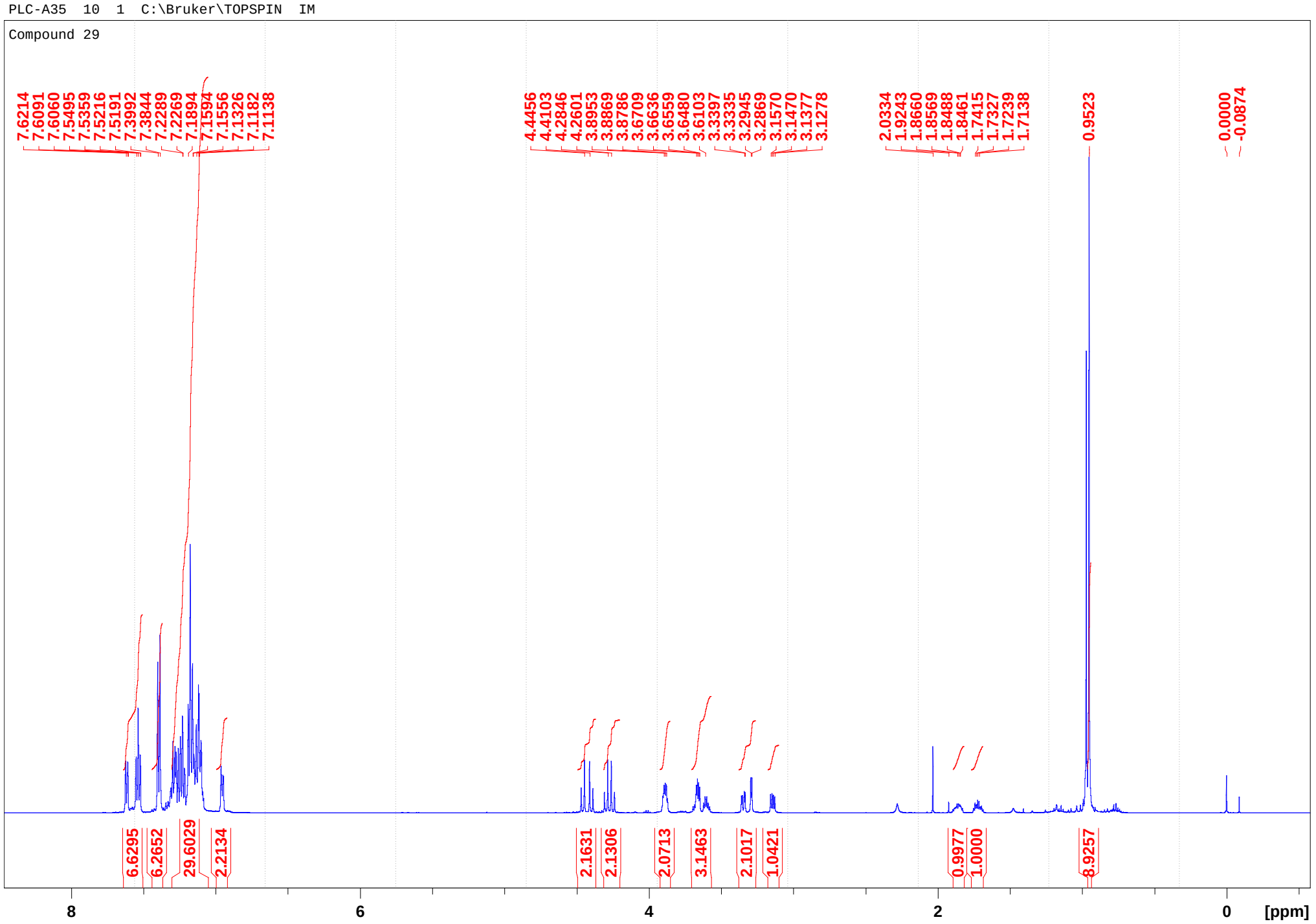


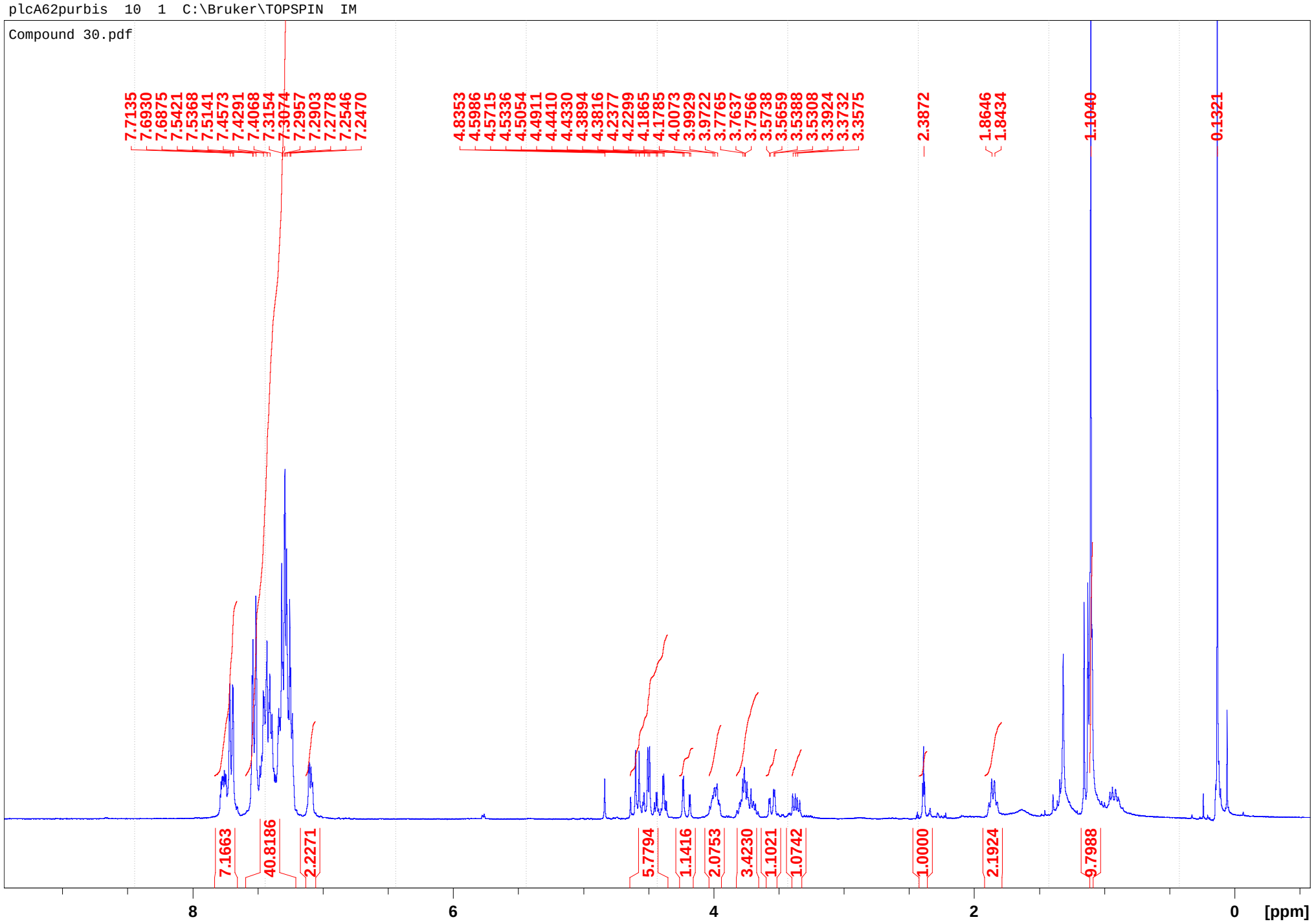


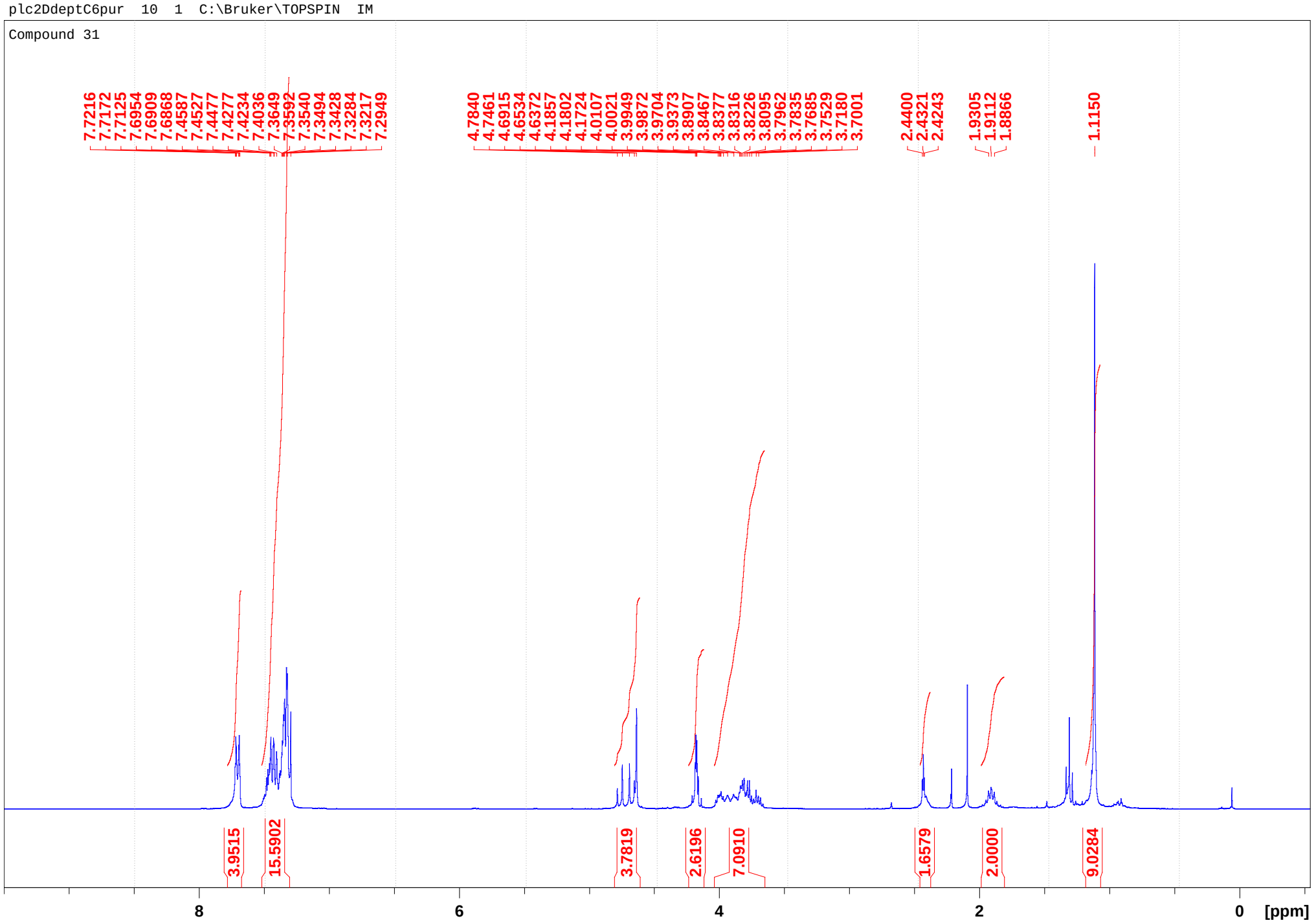


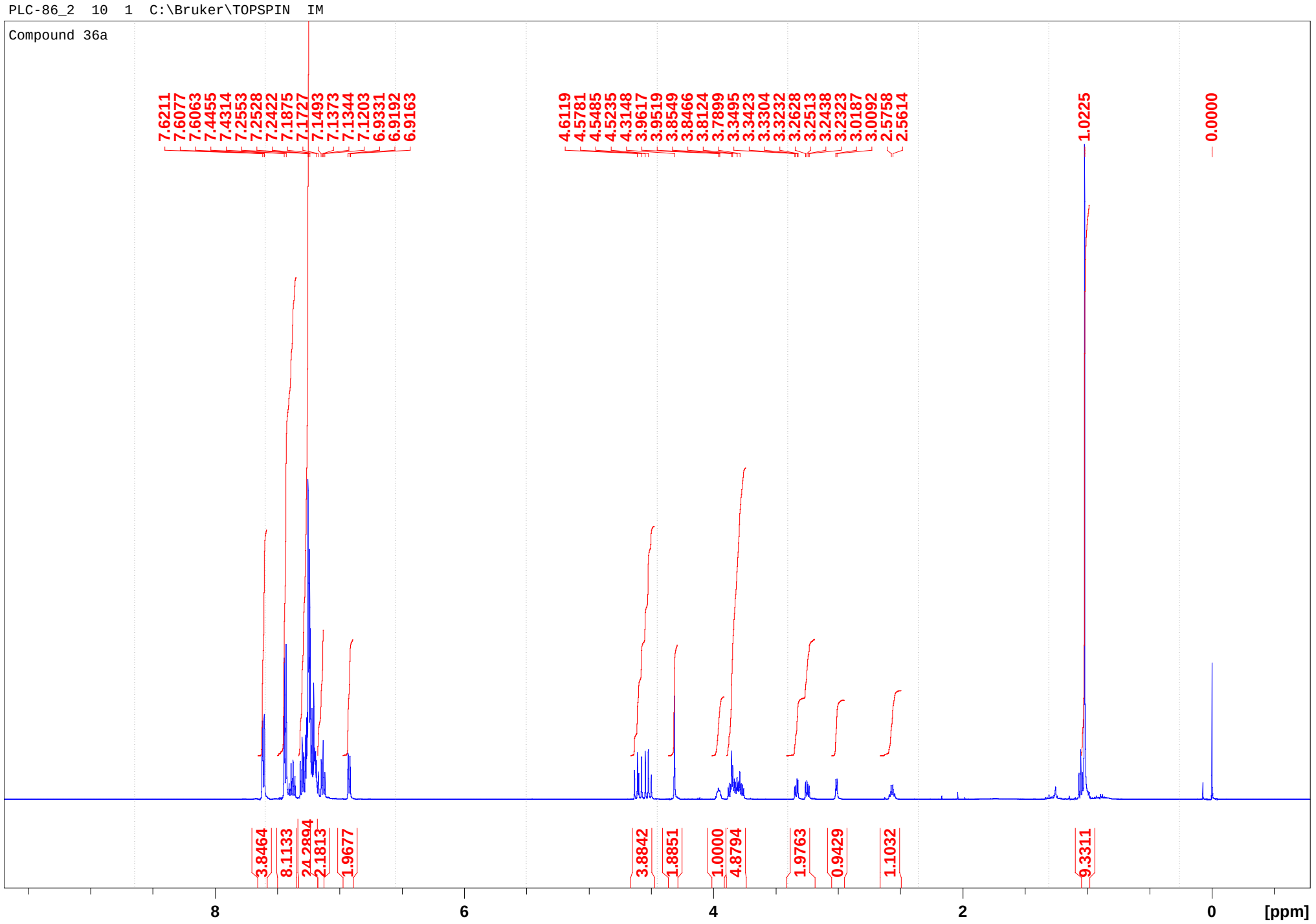


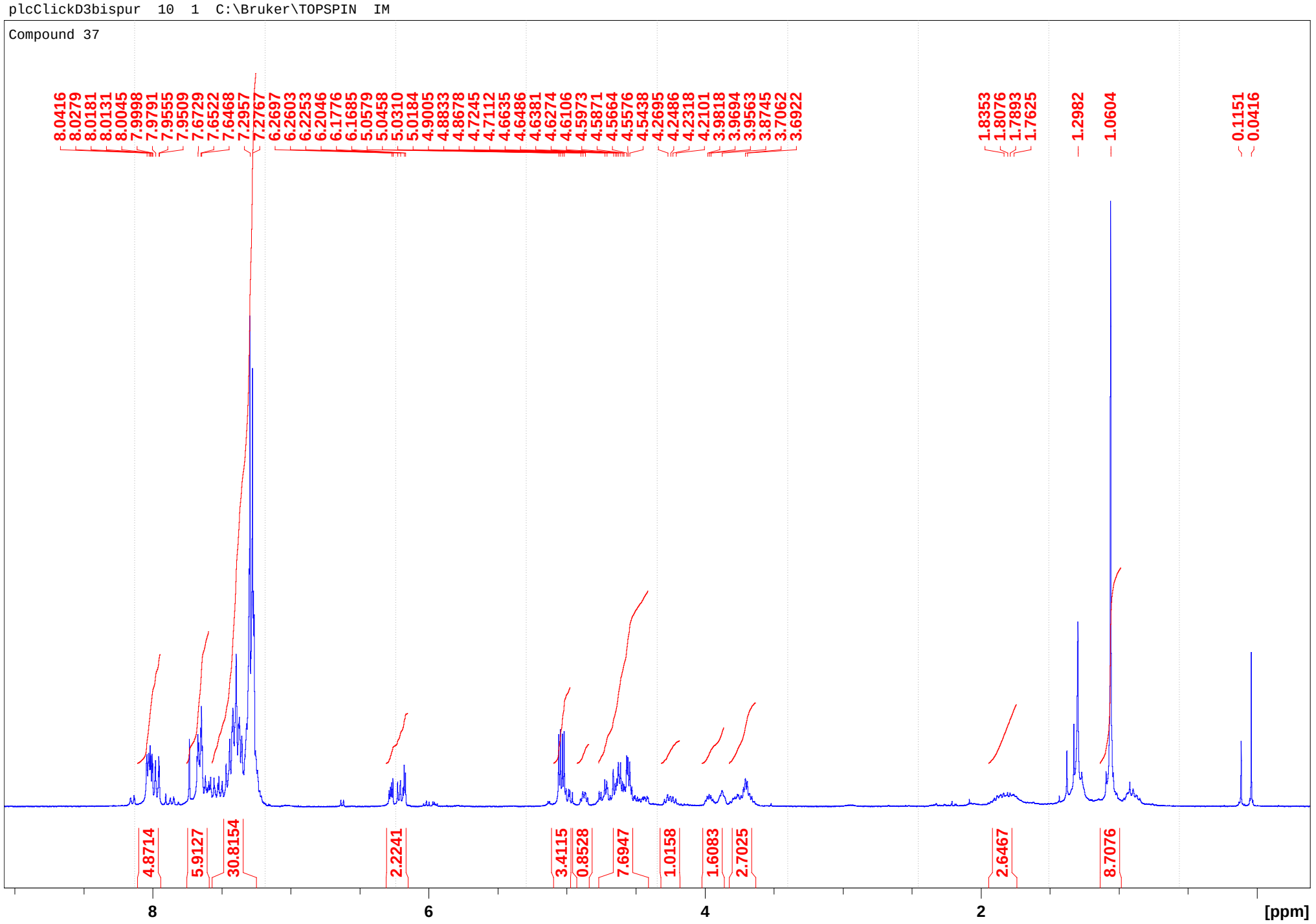


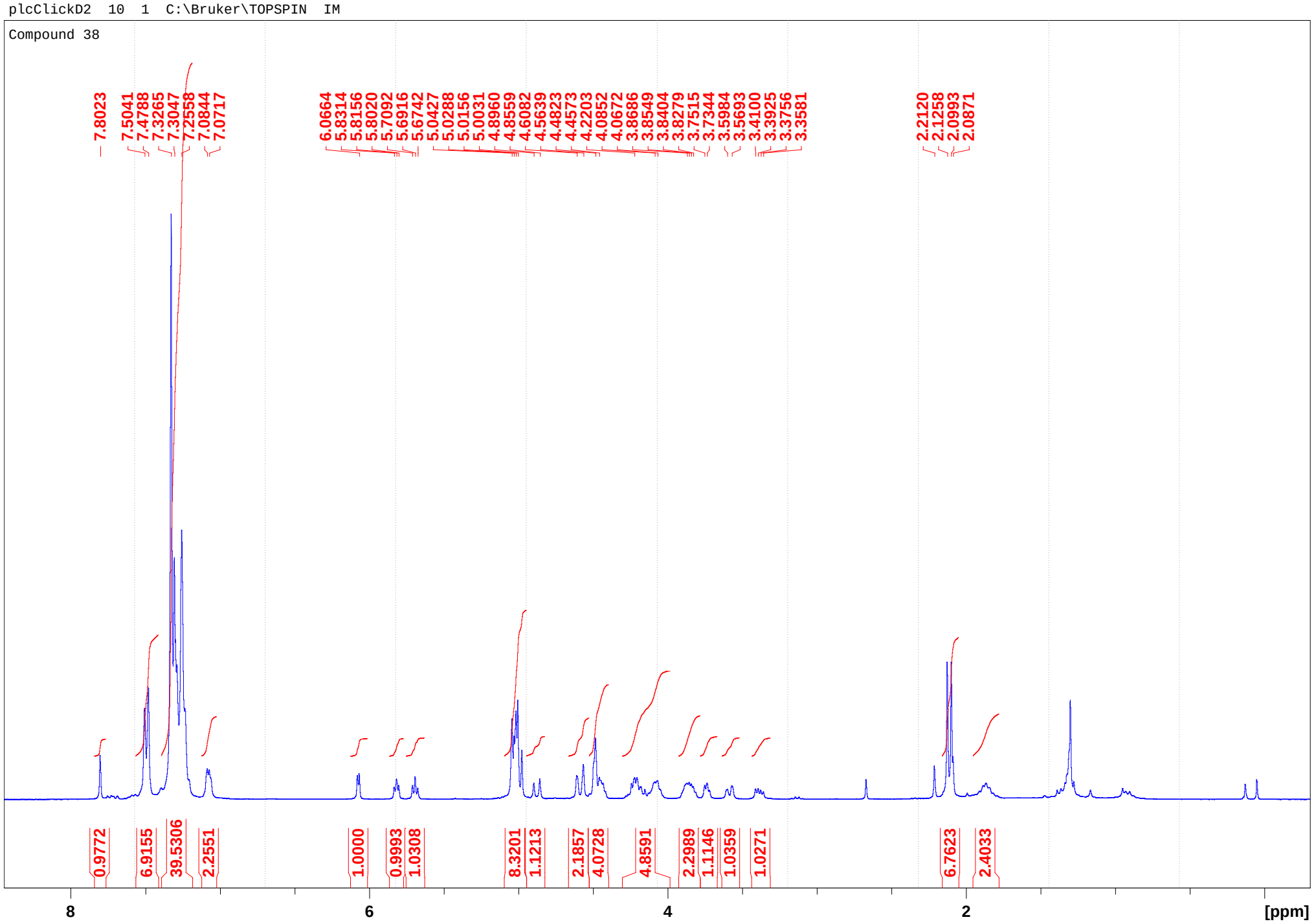


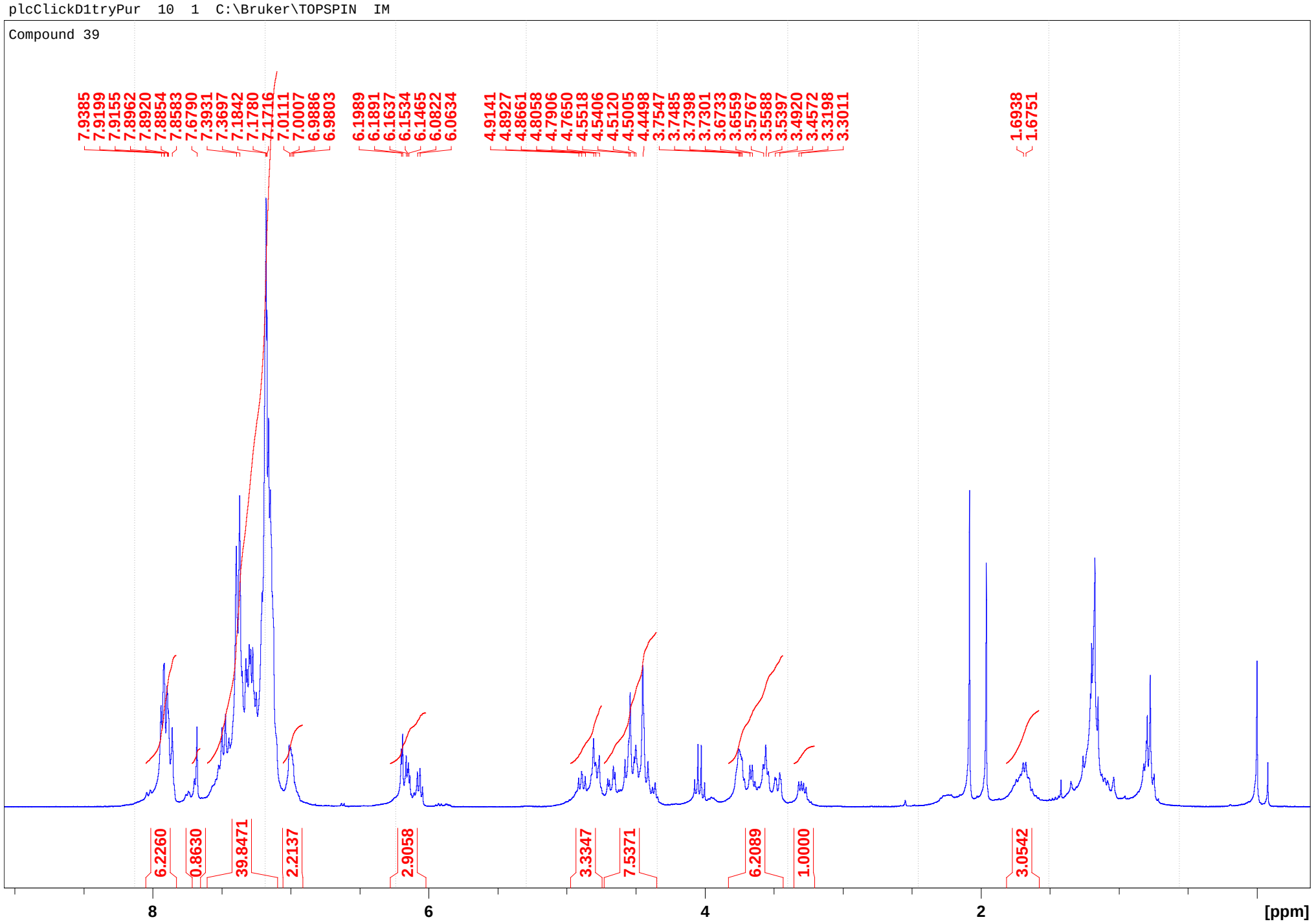


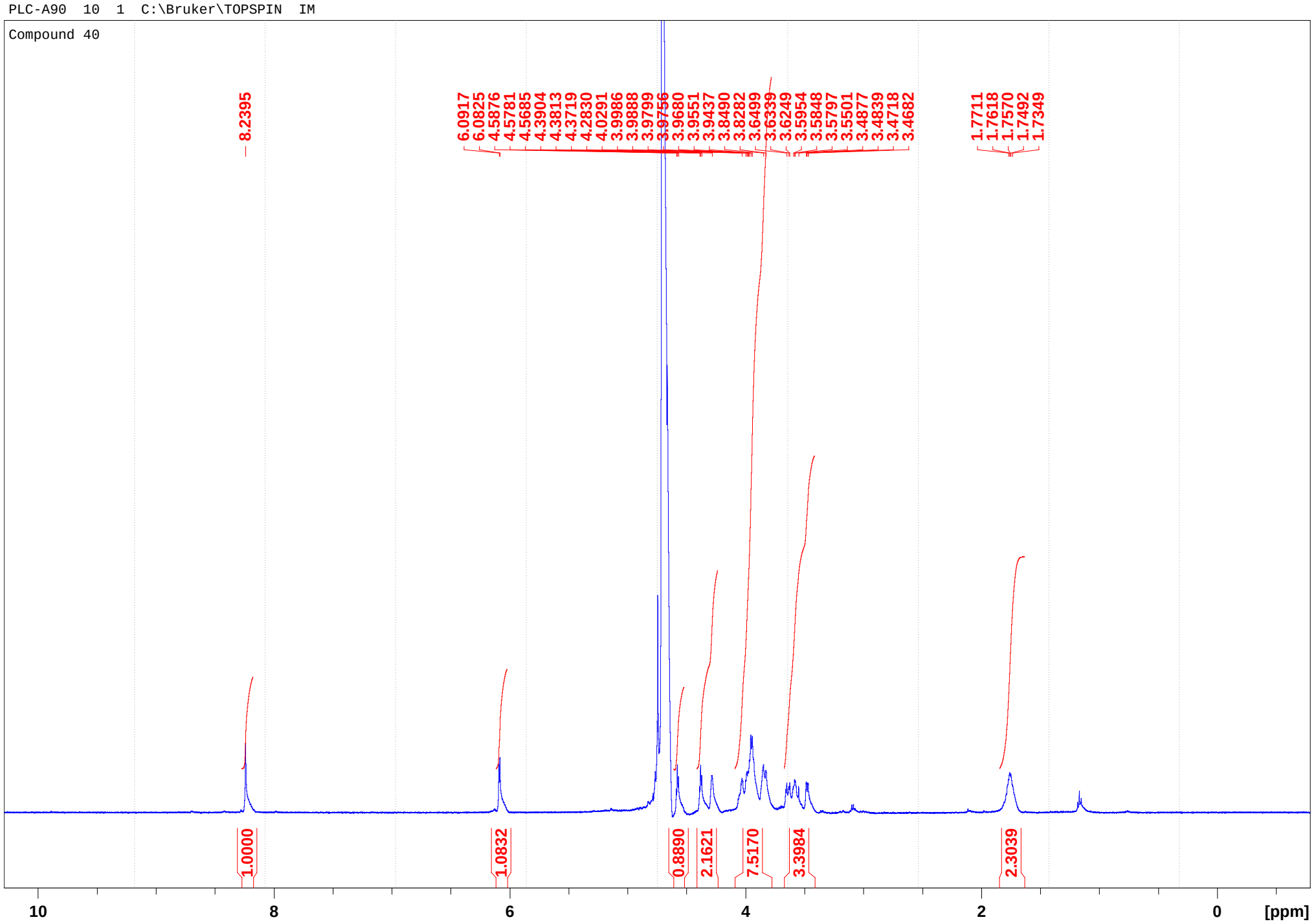


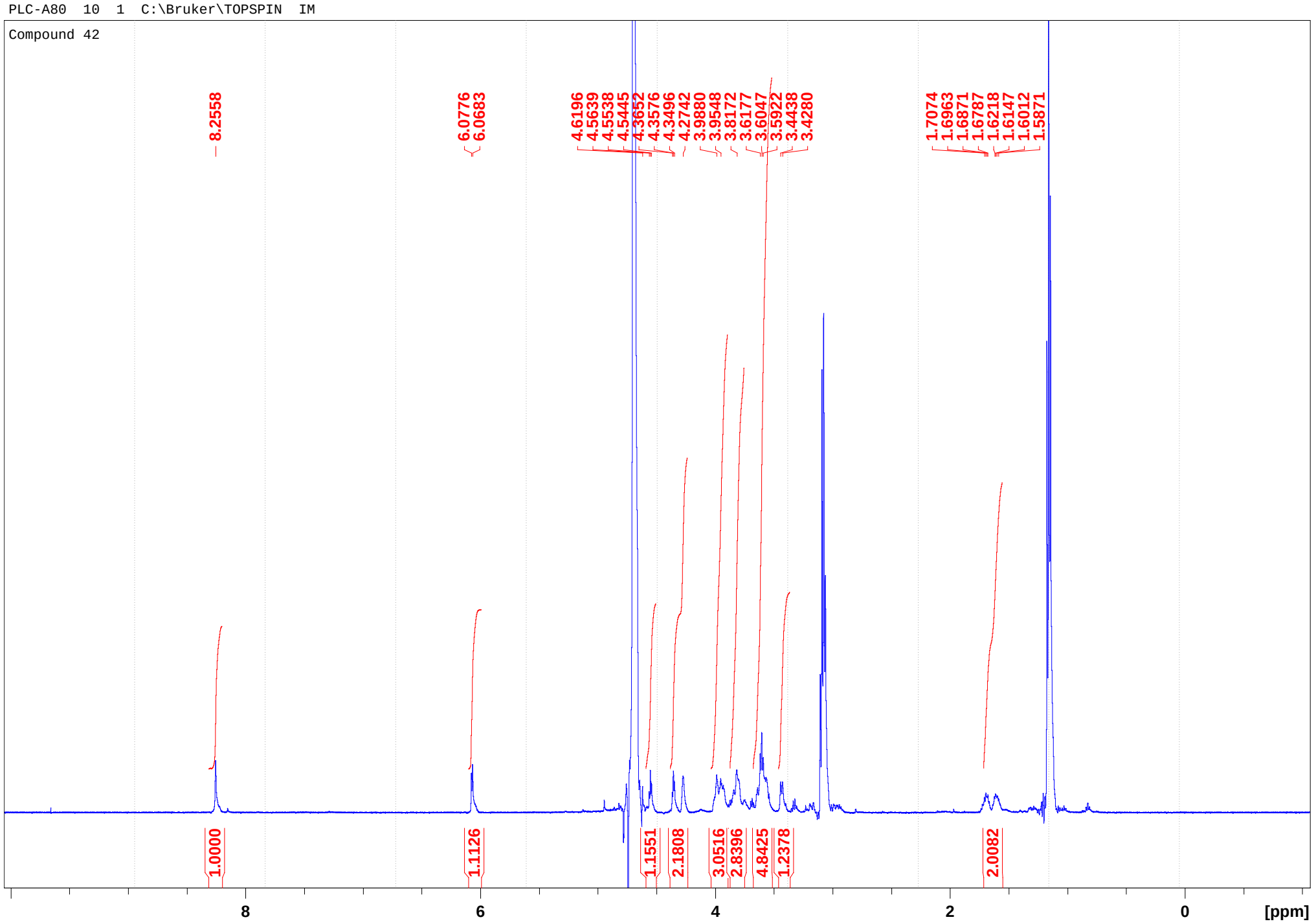


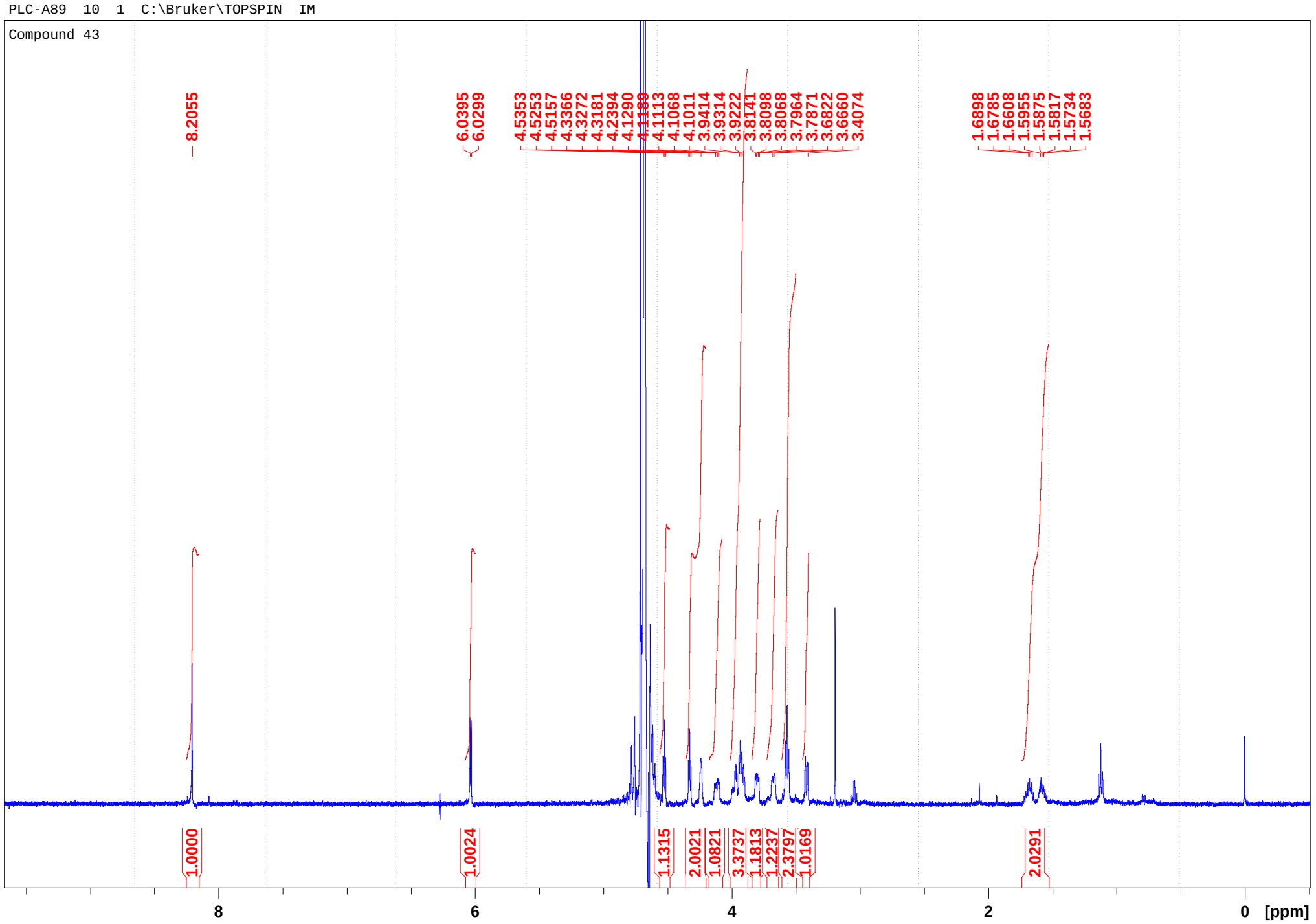


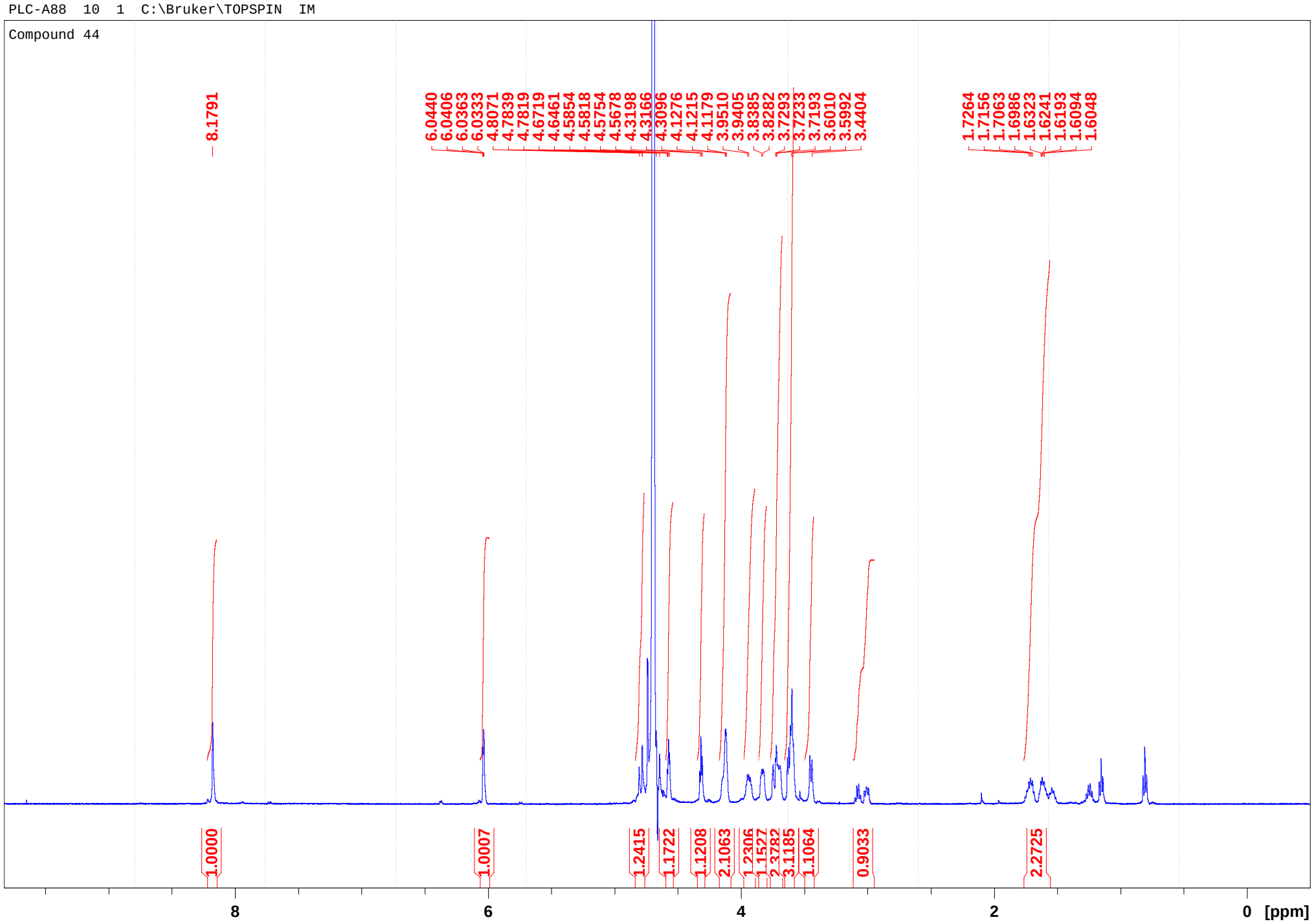






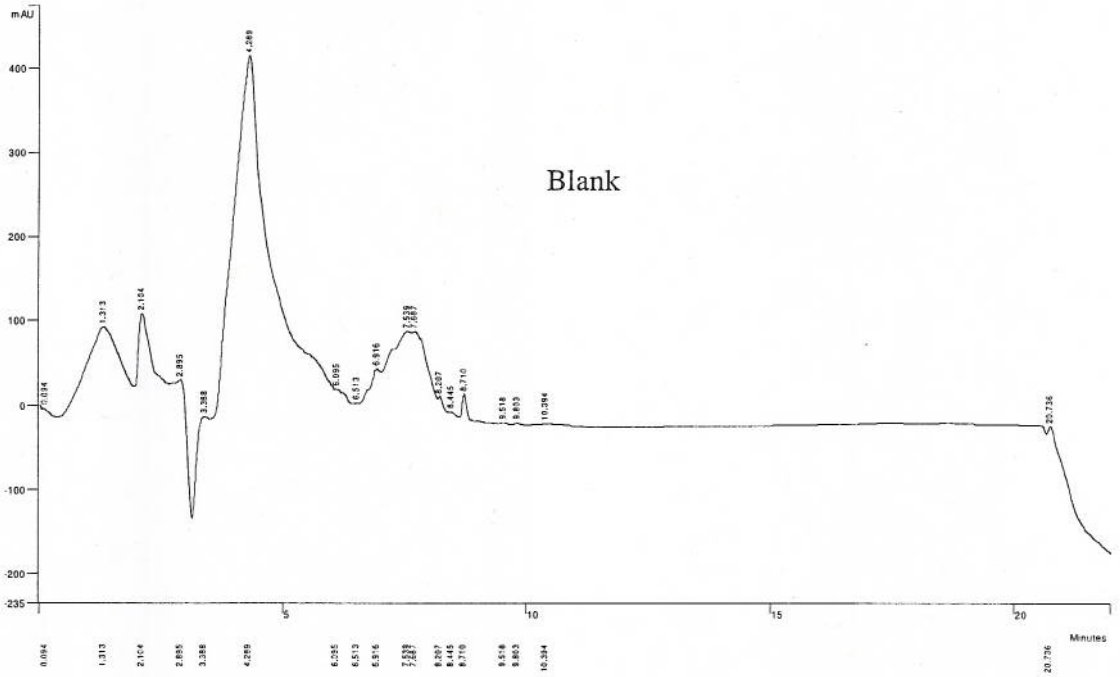


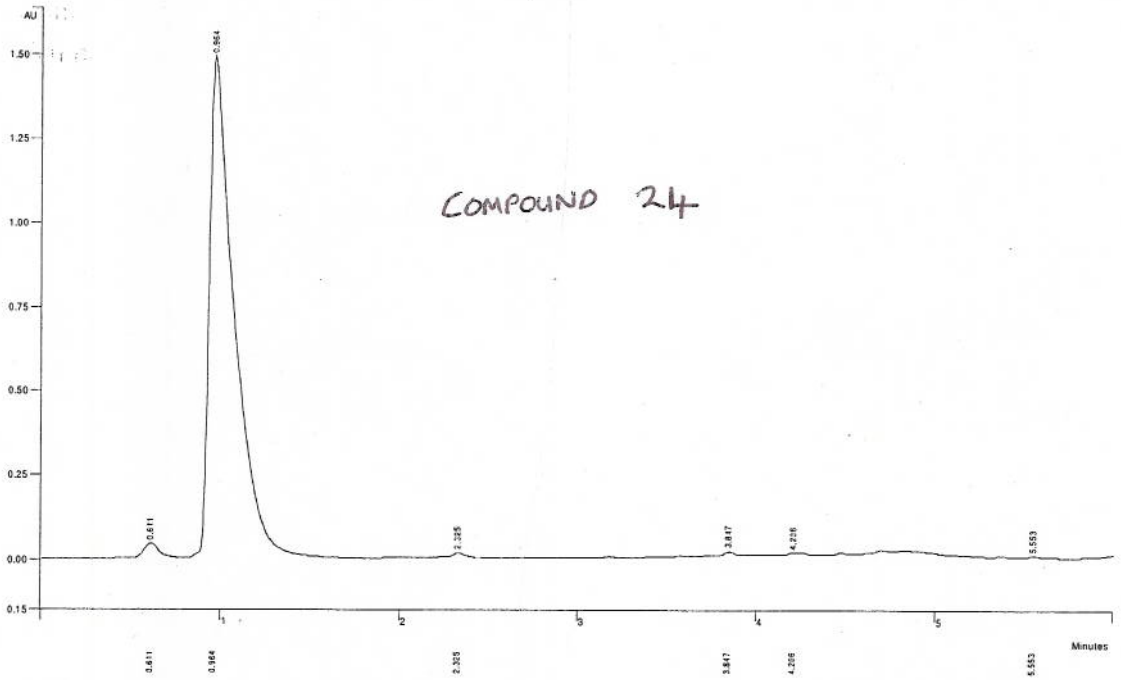




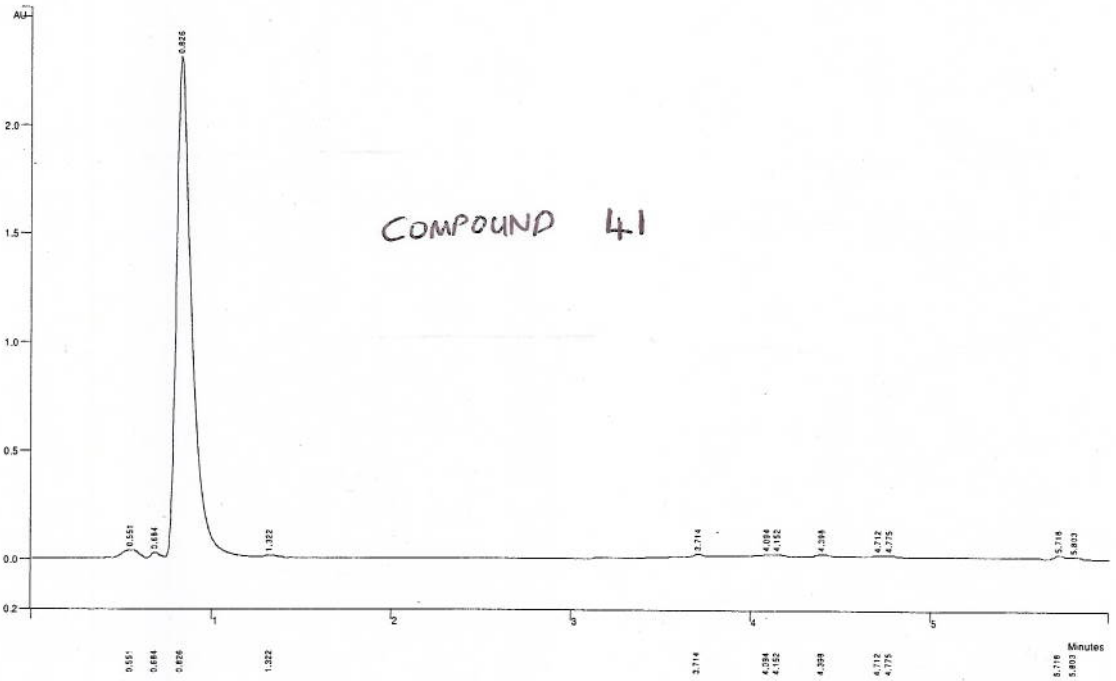
# HPLC TRACES OF COMPOUNDS 21-24 AND 40-44

Column: C18 Waters, 3.5 mm, 5 × 150 mm
Temperature: 25 °C
Detection wave: 280 nm
Flow rate: 0.5 mL.min$^{-1}$
Injection: 50µL
Mobile phase: $H_2O$/MeOH: 95/5

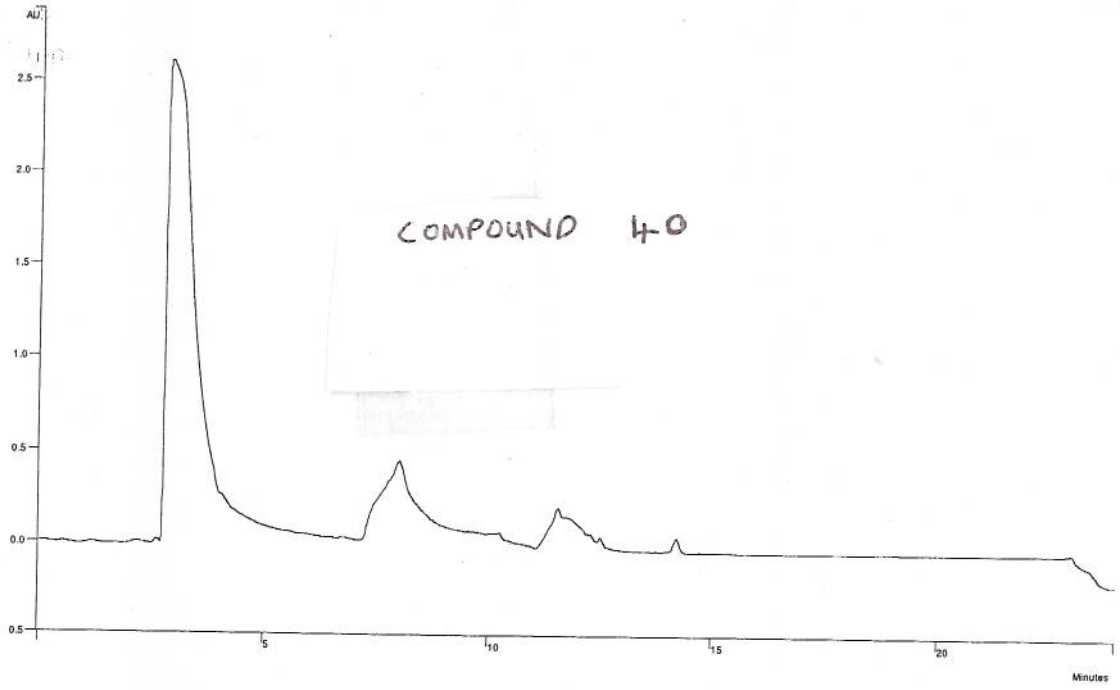




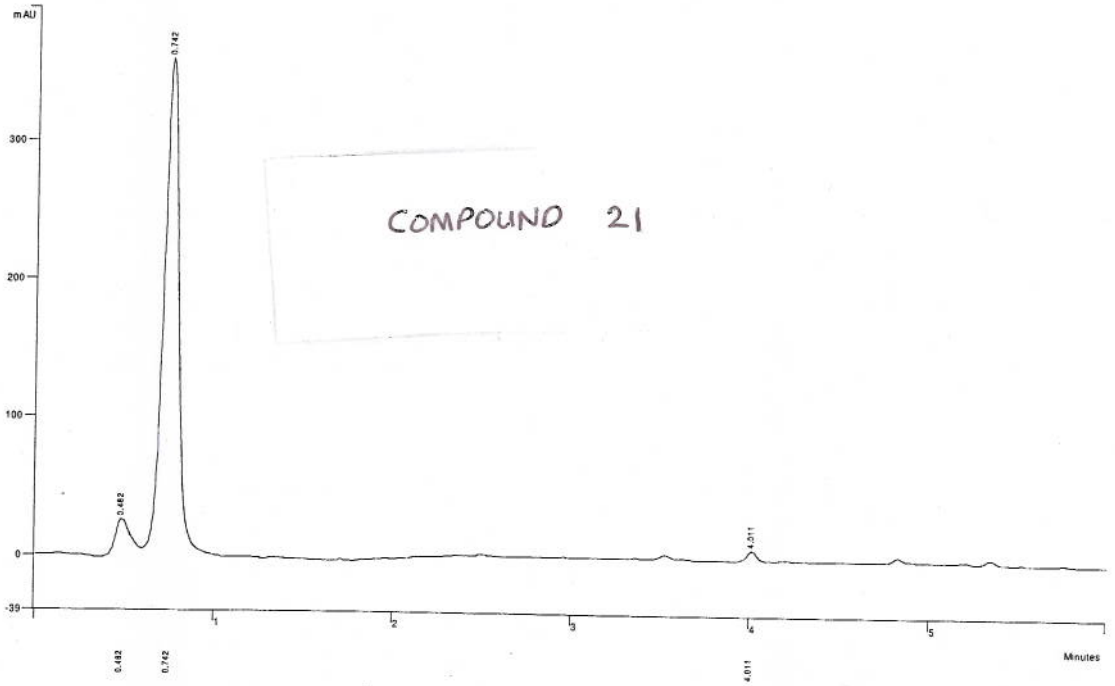

COMPOUND 24



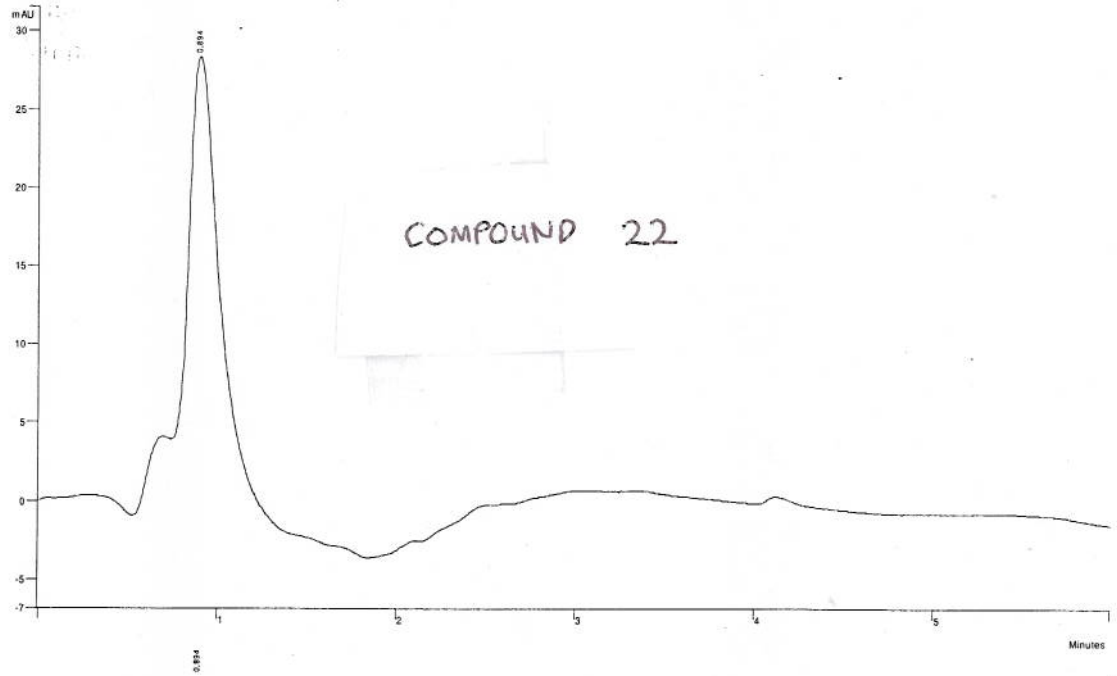

COMPOUND 41



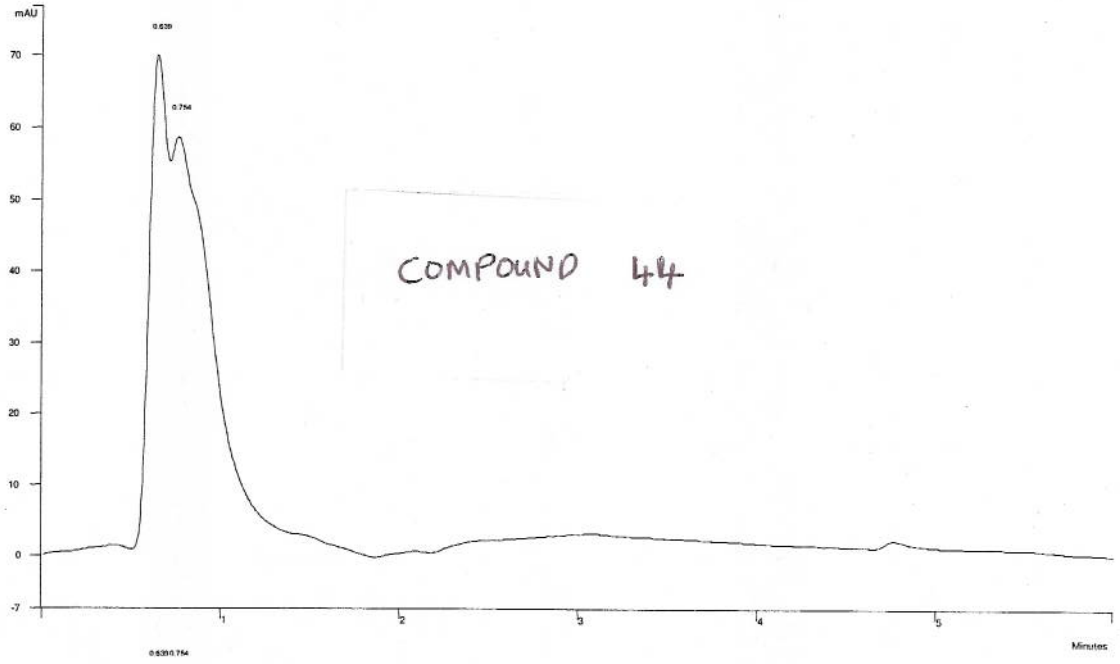

COMPOUND 40



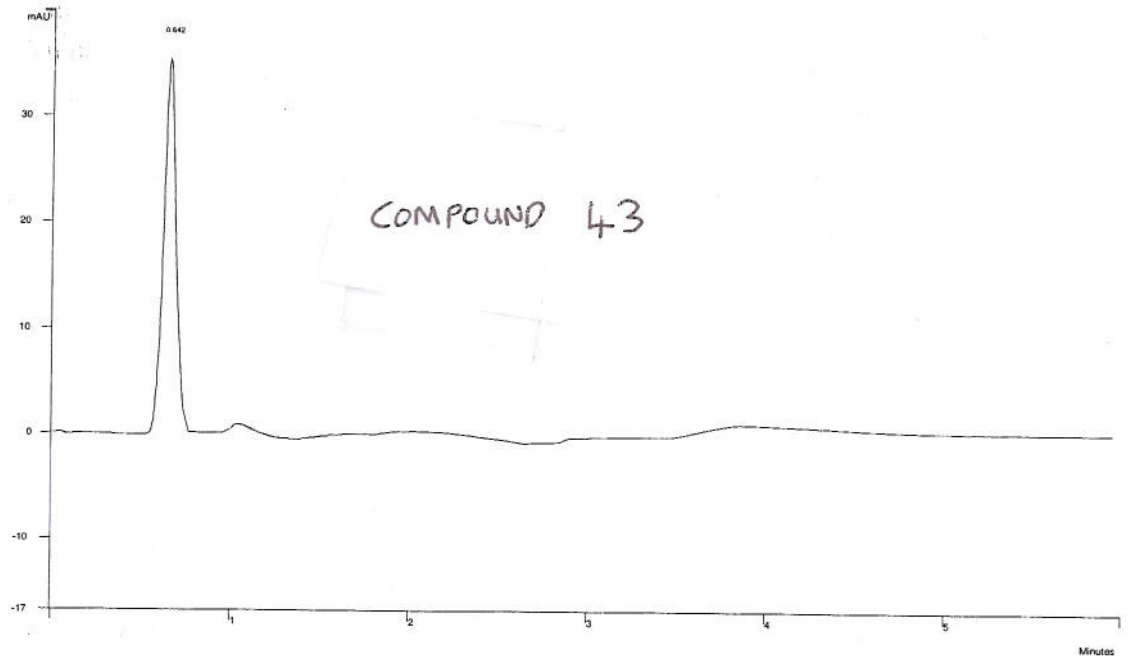

COMPOUND 21



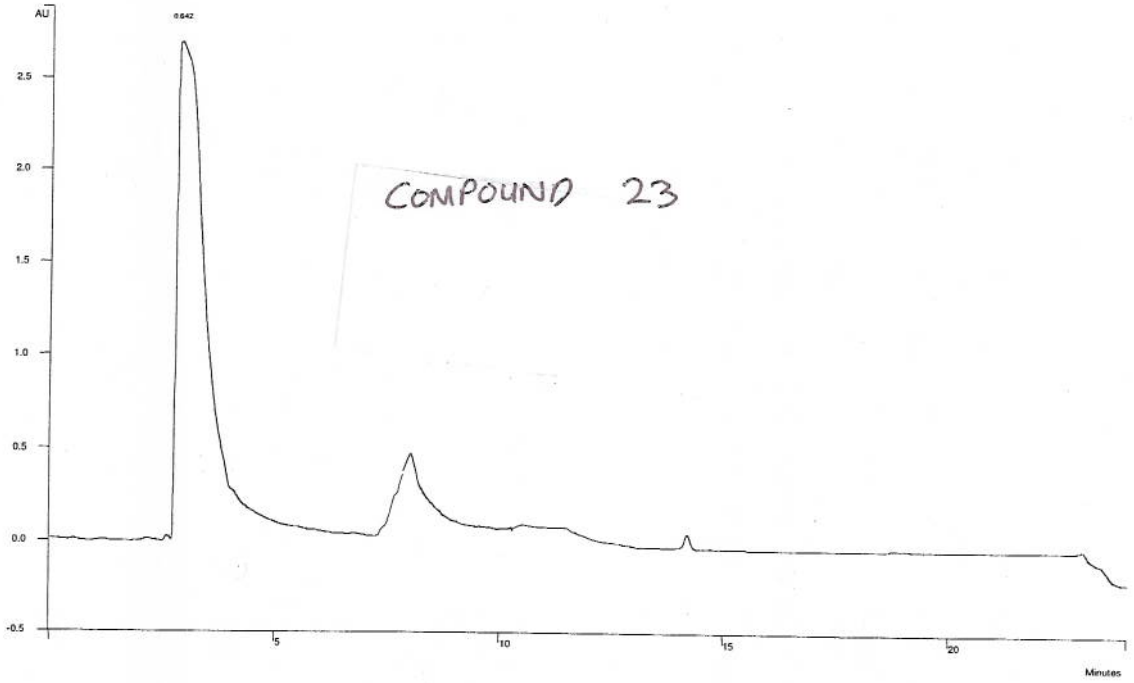

COMPOUND 22



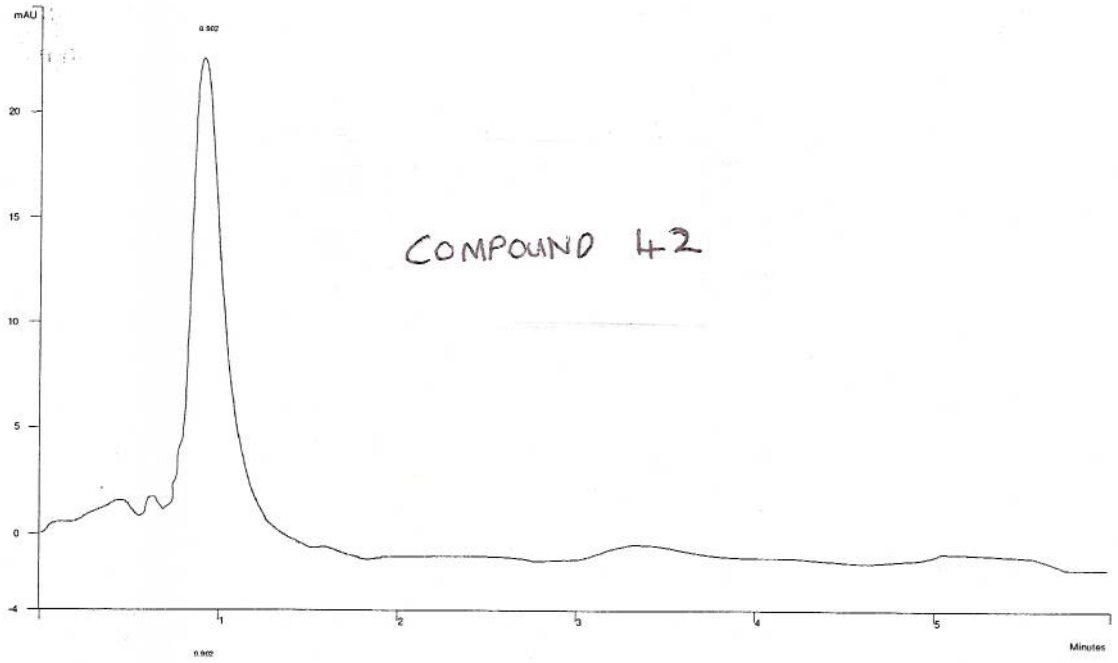

COMPOUND 44




COMPOUND 43




COMPOUND 23




COMPOUND 42