Electronic Supplementary Information

Transition Metal-Free One-Pot Synthesis of 2-Substituted 3-Carboxy-4-Quinolone and Chromone Derivatives

Jian-Ping Lin, Ya-Qiu Long*

CAS Key Laboratory of Receptor Research, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, 555 Zuchongzhi Road, Shanghai 201203, China

E-mail:yqlong@mail.shcnc.ac.cn

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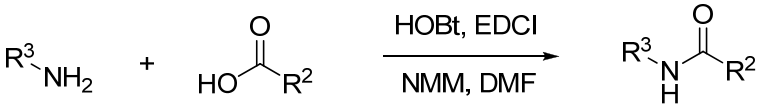
* To whom correspondence should be addressed. Tel: 86-21-50806876; Fax: 86-21-50807088.

General Methods, Materials, and Instrumentation

Unless otherwise specified, all reactions were carried out in flame-dried glassware with magnetic stirring. Commercial reagents were used as received with the following exceptions: K_2CO_3, Na_2CO_3, Cs_2CO_3 and DIPEA were purchased from Aldrich (>99%, reagent grade). Solvents were dried and distilled by standard procedures[1]. All reagents were weighed and handled in air at room temperature. Column chromatography was performed on silica gel (200 ~ 300 mesh). NMR spectra were recorded on Brucker AVANCE 300 NMR spectrometer or Brucker AVANCE III 400 NMR spectrometer or Brucker AVANCE III 500 NMR spectrometer. Chemical shifts for Proton magnetic resonance spectra (^{1}H NMR) were quoted in parts per million (ppm) referenced to the appropriate solvent peak or 0.0 ppm for tetramethylsilane (TMS). The following abbreviations were used to describe peak splitting patterns when appropriate: br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multriplet, dd = doublet of doublet. Coupling constants, *J*, were reported in hertz unit (Hz). Chemical shifts for ^{13}C NMR were reported in ppm referenced to the center line at 77.16 ppm of $CDCl_3$ or 39.52 of DMSO-*d*. Mass spectra were recorded using an ES ion source unless stated otherwise. All melting points were measured using a BÜCHI 510 melting point apparatus.

General Procedure for Synthesis of Amides[2]

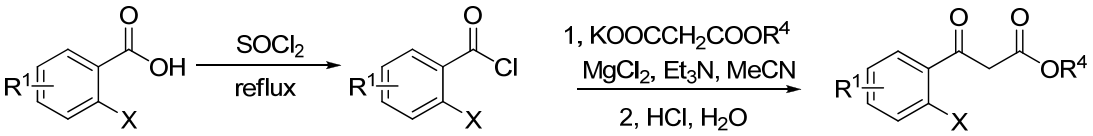


R_3= alkyl or aryl

A flame dried flask was charged with carboxylic acid (4.4 mmol, 1.1 equiv) in dry N,N-dimethylformamide (40 ml), and the solution was stirred at 0 ºC. To this solution was added 1-hydroxybenzotriazole (4.8 mmol, 1.2 equiv) and 1-[3-(dimethylamino)propyl]-3-ethylamine (4.8 mmol, 1.2 equiv). After 30 min, N-methylmorpholin (10.0 mmol, 2.5 equiv) and amine (4.0 mmol, 1 equiv) was added to the resulting mixture. The reaction was slowly warmed to room temperature and

keeped stirring for 6 h. Then solvent were removed in vacuo and the resulting residue was resuspended in EtOAc (150 mL) and washed with water (2 x 40 mL), 0.1 N HCl (2 x 40 mL), 0.1 N NaOH (2 x 40 mL), and brine (1 x 40 mL). The organic phase was dried over Na_2SO_4, concentrated in vacuo, and purified by silica gel chromatography.

General Procedure for Synthesis of 3-oxo-3-arylpropanoates[3]

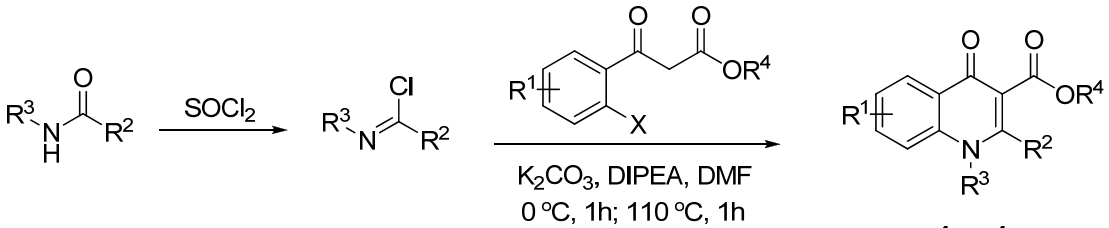


X= F, Cl, Br, I

A solution of carboxylic acid (4.0 mmol, 1.0 equiv) in thionyl chloride (2 ml) was refluxed for 2 h. After cooling to room temperature, the mixture was concentrated under reduced pressure. Toluene was added (2 x 2 ml) and the mixture concentrated again to yield the corresponding acyl chloride as a TLC pure residual oil.

Potassium malonate (5.2 mmol, 1.3 equiv)was placed in a flask under a nitrogen blanket. Acetonitrile (40 ml) was added and the mixture was allowed to stir at 10 °C. To this mixture was added triethylamine (16 mmol, 4 equiv) followed by magnesium chloride (8 mmol, 2 equiv) and stirring continued at 50 °C for 2 h. The resulting slurry was re-cooled to 0 ºC. and a solution of the acyl chloride in dry acetonitrile (10 ml) was added dropwise. The mixture allowed to stir continued at 70 °C for 3 h, next cooled to room temperature. The solvent was distilled off and poured into ice water and acidified to pH 5-6 with 1N HCl, then extracted with ethyl acetate (3 x 50 ml) and dried over Na_2SO_4, concentrated in vacuo, and purified by silica gel chromatography.

General Procedure for Synthesis of Quinolones 4a ~ 4y.

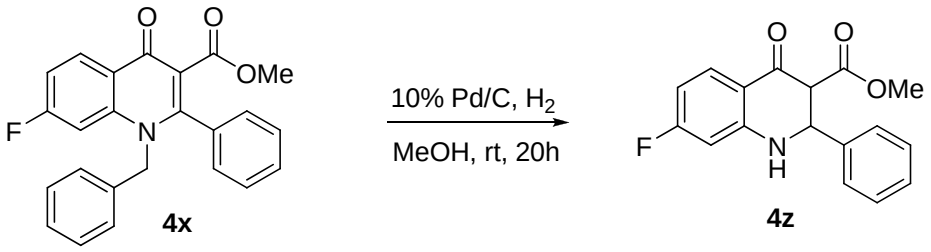


4a ~ 4y

A solution of amide (2.4 mmol, 1.2 equiv) in thionyl chloride (12 mmol, 6 equiv) was stirred at room temperature overnight or refluxed for 3 h. After cooling to room temperature, the mixture was concentrated under reduced pressure. The residue was dissolved in toluene (2 x 1 ml) and the mixture was evaporated again to generate the corresponding imidoyl chloride as a TLC pure residual oil.

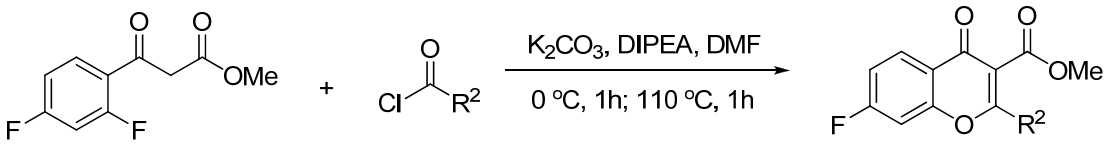
3-Oxopropanoate (2.0 mmol, 1 equiv), potassium carbonate (6.0 mmol, 3 equiv) and *N*,*N*-diisopropylethylamine (4.0 mmol, 2 equiv) were mixed in dry DMF (5 ml) and stirred at 0°C for 15 min. To this mixture, was added a solution of the imidoyl chloride in dry DMF (5 ml). The reaction mixture was stirred at 0 °C for 1 h and heated at 110°C for another 1h. The solvent was distilled off and the residue was poured into water, then extracted with CH_2Cl_2 (50 ml x 3) and dried over Na_2SO_4, concentrated in vacuo, and purified by silica gel chromatography. Recrystallization from ethanol and n-hexane gave further purified product.

Procedure for Synthesis of Quinolone 4z.



A solution of **4x** (194 mg, 0.50 mmol) in EtOH (5 ml) was hydrogenated over 10% Pd/C (60 mg 30% w/w) at room temperature for 20 h with stirring. The catalyst was filtered out, and the filtrate was concentrated in vacuo affording a crude product, which was purified by column chromatography on silica gel with petroleum ether-ethyl acetate (1:1, v/v) to yield **4z** (145mg, 97%) as a white powder.

General Procedure for Synthesis of Chromones 6a ~ 6i.



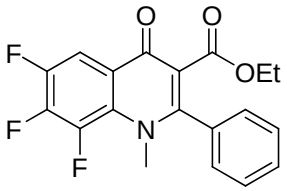
6a ~ 6i

3-Oxopropanoate (2.0 mmol, 1 equiv), potassium carbonate (6.0 mmol, 3 equiv) and *N*,*N*-diisopropylethylamine (4.0 mmol, 2 equiv) were mixed in dry DMF (5 ml) and stirred at 0°C for 15 min. To this mixture was added a solution of the acyl chloride in dry DMF (5 ml). The reaction solution was stirred at 0 °C for 1 h and heated at 110°C for another 1h. The solvent was distilled off and poured into water, then extracted with CH_2Cl_2 (3 x 50 ml) and dried over Na_2SO_4, concentrated in vacuo, and purified by silica gel chromatography. Recrystallization from ethanol and n-hexane gave further purified product.

Characterization data for the products 4a-4z and 6a-6i

Ethyl

6,7,8-trifluoro-1-methyl-4-oxo-2-phenyl-1,4-dihydroquinoline-3-carboxylate (4a).

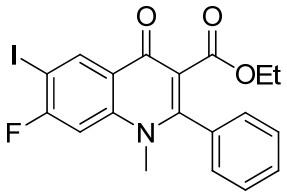


Eluent: petroleum ether/ ethyl acetate = 6:1. Yield 74% (532 mg). White solid, mp 126-128℃. ^{1}H NMR (300 MHz, CD_3OD) δ 8.02 (ddd, *J* = 10.3, 8.4, 2.3 Hz, 1H), 7.65 – 7.52 (m, 3H), 7.52 – 7.43 (m, 2H), 3.92 (q, *J* = 7.1 Hz, 2H), 3.71 (d, *J* = 8.7 Hz, 3H), 0.88 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.79, 165.46, 155.02, 148.28 (dd, *J* = 251.6, 12.2 Hz), 143.91 (dt, *J* = 32.8, 16.7 Hz), 142.38 (dd, *J* = 254.6, 15.9 Hz), 132.93, 130.71, 129.44, 129.22, 128.91, 123.58 (d, *J* = 5.5 Hz), 119.01, 108.77(dd, *J* = 18.3, 3.3 Hz), 61.38, 41.66 (d, *J* = 15.4 Hz), 13.86. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{19}H_{15}NO_3F_3$ 362.1004; found 362.1007.

Ethyl

7-fluoro-6-iodo-1-methyl-4-oxo-2-phenyl-1,4-dihydroquinoline-3-carboxylate

(4b).

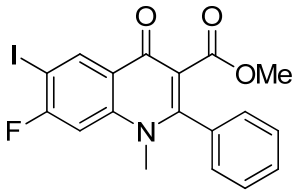


Eluent: petroleum ether/ ethyl acetate = 6:1. Yield 74% (668 mg). White solid, mp 235-236℃. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.86 (d, *J* = 7.2 Hz, 1H), 7.55 – 7.46 (m, 3H), 7.42 – 7.35 (m, 2H), 7.21 (d, *J* = 9.8 Hz, 1H), 3.95 (q, *J* = 7.1 Hz, 2H), 3.45 (s, 3H), 0.88 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.13 (s), 165.73 (s), 163.76 (d, *J* = 250.5 Hz), 152.98 (s), 142.60 (d, *J* = 10.4 Hz), 139.07 (s), 133.04 (s), 130.31 (s), 128.97 (s), 128.75 (s), 125.04 (s), 120.06 (s), 103.06 (d, *J* = 29.6 Hz), 61.19 (s), 37.42 (s), 13.78 (s). HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{19}H_{15}NO_3NaFI$ 473.9978; found 473.9968.

Methyl

7-fluoro-6-iodo-1-methyl-4-oxo-2-phenyl-1,4-dihydroquinoline-3-carboxylate

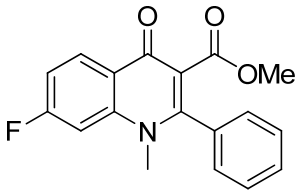
(4c).



Eluent: petroleum ether/ ethyl acetate = 3:1. Yield 64% (561 mg). White solid, mp 232-233℃. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.86 (d, *J* = 7.2 Hz, 1H), 7.56 – 7.42 (m, 3H), 7.42 – 7.31 (m, 2H), 7.21 (d, *J* = 9.7 Hz, 1H), 3.48 (s, 3H), 3.46 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.16, 166.41, 163.85 (d, *J* = 250.6 Hz), 153.23, 142.63 (d, *J* = 10.5 Hz), 139.16, 139.12, 133.02, 130.38, 129.04, 128.60, 125.08, 119.87, 103.07 (d, *J* = 29.8 Hz), 52.27, 37.48. HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{18}H_{14}NO_3FI$ 438.0002; found 438.0003.

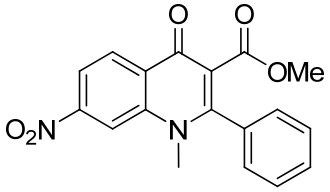
Methyl 7-fluoro-1-methyl-4-oxo-2-phenyl-1,4-dihydroquinoline-3-carboxylate

(4d).



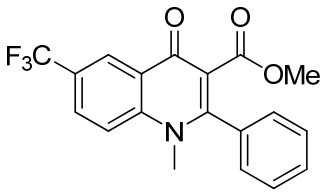
Eluent: petroleum ether/ ethyl acetate = 2:1. Yield 65% (403 mg). White solid, mp 212-213℃. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.58 – 8.48 (m, 1H), 7.57 – 7.38 (m, 5H), 7.24 – 7.11 (m, 2H), 3.51 (s, 3H), 3.48 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.54, 166.83, 165.66 (d, *J* = 252.2 Hz), 153.06, 142.82 (d, *J* = 11.3 Hz), 133.36, 130.42, 130.32, 129.07, 128.72, 123.68, 119.52, 113.19 (d, *J* = 22.8 Hz), 102.68 (d, *J* = 26.8 Hz), 52.32, 37.52. HRMS (ESI) m/z: $[M + Na]^+$ Calcd for $C_{18}H_{14}NO_3FNa$ 334.0855; found 334.0873.

Methyl 1-methyl-7-nitro-4-oxo-2-phenyl-1,4-dihydroquinoline-3-carboxylate (4e).



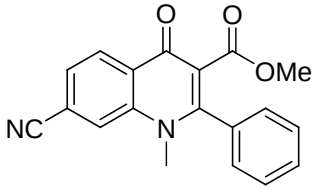
Eluent: petroleum ether/ ethyl acetate = 3:1. Yield 85% (574 mg). Light yellow solid, mp 261-263℃. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.68 (d, *J* = 8.8 Hz, 1H), 8.49 (d, *J* = 1.9 Hz, 1H), 8.22 (dd, *J* = 8.8, 2.0 Hz, 1H), 7.63 – 7.52 (m, 3H), 7.44 – 7.40 (m, 2H), 3.63 (s, 3H), 3.52 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.08, 166.24, 154.34, 150.40, 141.21, 132.83, 130.71, 130.31, 129.58, 129.26, 128.59, 120.66, 118.35, 112.71, 52.51, 37.83. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{15}N_2O_5$ 339.0981; found 339.0984.

Methyl 1-methyl-4-oxo-2-phenyl-6-(trifluoromethyl)-1,4-dihydroquinoline-3-carboxylate (4f).



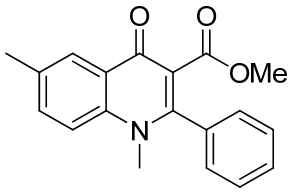
Eluent: petroleum ether/ ethyl acetate = 3:1. Yield 73% (524 mg). White solid, mp 194-196℃. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.81 (s, 1H), 7.92 (dd, *J* = 9.0, 2.2 Hz, 1H), 7.67 (d, *J* = 8.8 Hz, 1H), 7.60 – 7.46 (m, 3H), 7.45 – 7.32 (m, 2H), 3.57 (s, 3H), 3.51 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.59, 166.50, 153.46, 143.11, 133.10, 130.50, 129.28 (d, *J* = 3.2 Hz), 129.15, 128.66, 126.63, 126.59 (d, *J* = 33.7 Hz), 125.33, 125.28 (d, *J* = 4.0 Hz), 120.15, 117.33, 52.40, 37.67. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{19}H_{14}NO_3F_3$ Na 384.0823; found 384.0815.

Methyl 7-cyano-1-methyl-4-oxo-2-phenyl-1,4-dihydroquinoline-3-carboxylate (4g).



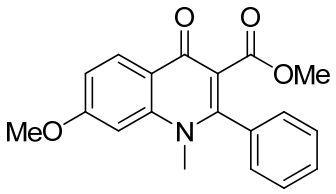
Eluent: petroleum ether/ ethyl acetate = 3:1. Yield 68% (430 mg). White solid, mp 265-267℃. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.61 (d, *J* = 8.2 Hz, 1H), 7.91 (s, 1H), 7.66 (d, *J* = 8.2 Hz, 1H), 7.57 – 7.50 (m, 3H), 7.44 – 7.37 (m, 2H), 3.57 (s, 3H), 3.51 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.16, 166.31, 153.82, 141.02, 132.87, 130.63, 129.28, 129.21, 128.77, 128.61, 126.49, 121.28, 120.45, 118.14, 116.41, 52.46, 37.60. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{19}H_{14}N_2O_3$ Na 341.0902; found 341.0897.

Methyl 1,6-dimethyl-4-oxo-2-phenyl-1,4-dihydroquinoline-3-carboxylate (4h).



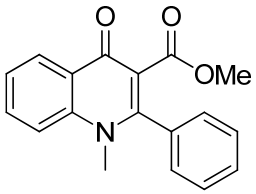
Eluent: petroleum ether/ ethyl acetate = 3:1. Yield 43% (264 mg). White solid, mp 167-168℃. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.30 (s, 1H), 7.54 – 7.37 (m, 7H), 3.51 (s, 3H), 3.49 (s, 3H), 2.49 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.14, 167.32, 152.30, 139.37, 134.58, 134.45, 133.79, 130.08, 128.93, 128.78, 126.90, 126.70, 118.78, 116.13, 52.21, 37.34, 21.10. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{19}H_{18}NO_3$ 308.1287; found 308.1259.

Methyl 7-methoxy-1-methyl-4-oxo-2-phenyl-1,4-dihydroquinoline-3-carboxylate (4i).



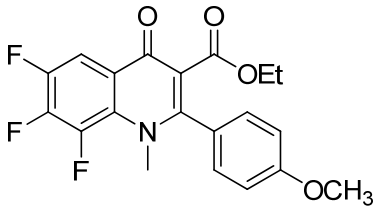
Eluent: petroleum ether/ ethyl acetate = 3:1. Yield 48% (309 mg). White solid, mp 213-214℃. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.44 (d, J = 8.9 Hz, 1H), 7.61 – 7.30 (m, 5H), 7.03 (dd, J = 8.7, 2.0 Hz, 1H), 6.86 (d, J = 1.9 Hz, 1H), 3.95 (s, 3H), 3.50 (s, 3H), 3.46 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.72, 167.23, 163.49, 152.44, 143.00, 133.77, 130.07, 129.21, 128.95, 128.77, 121.12, 118.93, 112.60, 99.47, 55.92, 52.19, 37.36. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{19}H_{18}NO_4$ 324.1236; found 324.1266.

Methyl 1-methyl-4-oxo-2-phenyl-1,4-dihydroquinoline-3-carboxylate (4j).



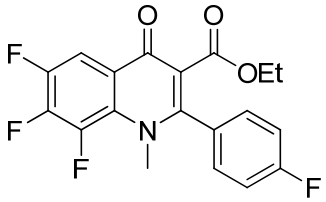
Eluent: petroleum ether/ ethyl acetate = 3:1. Yield 50% (293 mg). White solid, mp 197-199℃. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.51 (d, J = 8.0 Hz, 1H), 7.76 – 7.68 (m, 1H), 7.56 – 7.36 (m, 7H), 3.52 (s, 3H), 3.50 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.22, 167.14, 152.67, 141.26, 133.68, 133.08, 130.15, 128.98, 128.74, 127.30, 126.99, 124.53, 119.09, 116.22, 52.24, 37.39. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{18}H_{15}NO_3Na$ 316.0950; found 316.0924.

Ethyl 6,7,8-trifluoro-2-(4-methoxyphenyl)-1-methyl-4-oxo-1,4-dihydroquinoline-3-carboxylate (4k).



Eluent: petroleum ether/ ethyl acetate = 6:1. Yield 70% (542 mg). White solid, mp 132-133℃. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.15 – 8.04 (m, 1H), 7.36 (d, *J* = 8.6 Hz, 2H), 7.01 (d, *J* = 8.6 Hz, 2H), 4.03 (q, *J* = 7.1 Hz, 2H), 3.87 (s, 3H), 3.62 (d, *J* = 8.4 Hz, 3H), 0.99 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.93, 165.76, 161.43, 155.08, 148.27 (dd, *J* = 250.9, 11.3 Hz), 143.87 (d, *J* = 256.4 Hz), 142.39 (dd, *J* = 250.8, 9.0 Hz), 130.51, 129.63, 125.04, 123.63 (d, *J* = 4.4 Hz), 119.23, 114.63, 108.76 (dd, *J* = 18.2, 3.4 Hz), 61.43, 55.69, 41.75 (d, *J* = 15.0 Hz), 14.06. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{20}H_{17}NO_4F_3$ 392.1110; found 392.1121.

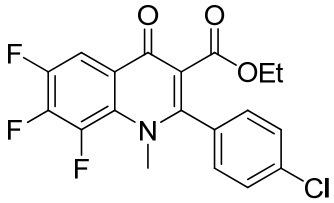
Ethyl 6,7,8-trifluoro-2-(4-fluorophenyl)-1-methyl-4-oxo-1,4-dihydroquinoline-3-carboxylate (4l).



Eluent: petroleum ether/ ethyl acetate = 6:1. Yield 66% (498 mg). White solid, mp 138-139℃. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.07 (ddd, *J* = 10.4, 8.3, 2.3 Hz, 1H), 7.44 (dd, *J* = 8.8, 5.2 Hz, 2H), 7.25 – 7.19 (m, 2H), 4.01 (q, *J* = 7.1 Hz, 2H), 3.62 (d, *J* = 8.3 Hz, 3H), 0.97 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.83, 165.45, 153.90, 148.38 (dd, *J* = 252.0, 11.2 Hz), 143.99 (dt, *J* = 33.0, 16.9 Hz), 142.37 (dd, *J* = 256.2, 14.7 Hz), 131.80 (d, *J* = 9.1 Hz), 131.15 (d, *J* = 8.6 Hz), 128.93 (d, *J* = 3.6

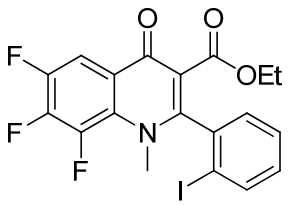
Hz), 123.59 (d, J = 4.3 Hz), 119.28, 116.60 (d, J = 22.0 Hz), 115.87 (d, J = 22.1 Hz), 108.82 (dd, J = 24.2, 9.4 Hz), 61.57, 41.70 (d, J = 15.4 Hz), 14.01. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{19}H_{13}NO_3F_4Na$ 402.0729; found 402.0720.

Ethyl 2-(4-chlorophenyl)-6,7,8-trifluoro-1-methyl-4-oxo-1,4-dihydroquinoline-3-carboxylate (4m).



Eluent: petroleum ether/ ethyl acetate = 6:1. Yield 71% (560 mg). White solid, mp 166-168℃. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.11 – 8.05 (m, 1H), 7.51 (d, J = 8.4 Hz, 2H), 7.39 (d, J = 8.4 Hz, 2H), 4.02 (q, J = 7.1 Hz, 2H), 3.62 (d, J = 8.2 Hz, 3H), 0.98 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.76, 165.32, 153.79, 148.38 (dd, J = 252.3, 11.7 Hz), 145.63 – 142.34 (m), 142.38 (dd, J = 253.1, 14.4 Hz), 137.16, 131.26, 130.37, 129.61, 129.49 (d, J = 3.1 Hz), 123.57 (d, J = 3.8 Hz), 119.10, 108.81 (dd, J = 18.1, 3.2 Hz), 61.59, 41.70 (d, J = 15.5 Hz), 13.95. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{19}H_{13}NO_3F_3NaCl$ 418.0434; found 418.0432.

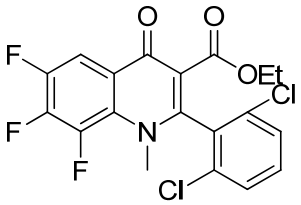
Ethyl 6,7,8-trifluoro-2-(2-iodophenyl)-1-methyl-4-oxo-1,4-dihydroquinoline-3-carboxylate (4n).



Eluent: petroleum ether/ ethyl acetate = 6:1. Yield 77% (750 mg). White solid, mp 114-115℃. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.19 – 8.13 (m, 1H), 7.98 (d, J = 7.7 Hz, 1H), 7.53 – 7.48 (m, 1H), 7.41 – 7.33 (m, 1H), 7.25 – 7.20 (m, 1H), 3.98 (q, J = 7.1 Hz, 2H), 3.66 (d, J = 8.3 Hz, 3H), 0.94 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz,

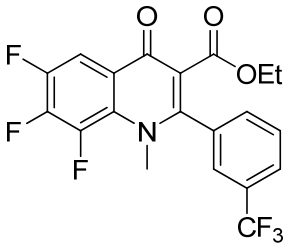
$CDCl_3$) δ 171.95, 164.90, 155.25, 148.38 (dd, *J* = 252.1, 11.3 Hz), 144.09 (d, *J* = 257.5 Hz), 142.45 (dd, *J* = 254.1, 13.1 Hz), 139.75, 138.14, 131.77, 130.16, 128.89, 128.70, 123.87 (d, *J* = 4.0 Hz), 118.23, 109.01 (d, *J* = 18.4 Hz), 98.51, 61.37, 39.85 (d, *J* = 16.5 Hz), 13.92. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{19}H_{14}NO_3F_3I$ 487.9971; found 487.9973.

Ethyl 2-(2,6-dichlorophenyl)-6,7,8-trifluoro-1-methyl-4-oxo-1,4-dihydroquinoline-3-carboxylate (4o).



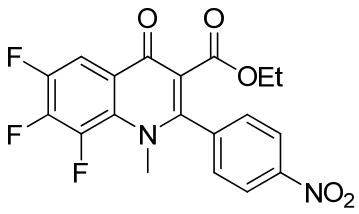
Eluent: petroleum ether/ ethyl acetate = 6:1. Yield 74% (633 mg). White solid, mp 135-137℃. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.22 – 8.08 (m, 1H), 7.53 – 7.36 (m, 3H), 4.06 (q, *J* = 7.1 Hz, 2H), 3.69 (d, *J* = 7.7 Hz, 3H), 1.02 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.93, 164.52, 150.05, 148.47 (dd, *J* = 252.8, 11.5 Hz), 144.13 (dt, *J* = 34.1, 16.8 Hz), 142.37 (dd, *J* = 255.8, 14.6 Hz), 135.20, 132.37, 131.42, 128.63, 128.52, 124.00 (d, *J* = 3.7 Hz), 117.71, 109.16 (dd, *J* = 18.1, 3.4 Hz), 61.42, 39.16 (d, *J* = 17.2 Hz), 13.99. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{19}H_{13}NO_3F_3Cl_2$ 430.0225; found 430.0232.

Ethyl 6,7,8-trifluoro-1-methyl-4-oxo-2-(3-(trifluoromethyl)phenyl)-1,4-dihydroquinoline-3-carboxylate (4p).



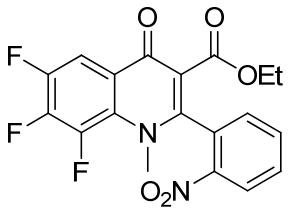
Eluent: petroleum ether/ ethyl acetate = 6:1. Yield 72% (620 mg). White solid, mp 111-112℃. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.17 – 8.06 (m, 1H), 7.83 (d, *J* = 7.1 Hz, 1H), 7.77 – 7.63 (m, 3H), 3.99 (q, *J* = 7.1 Hz, 2H), 3.63 (d, *J* = 8.2 Hz, 3H), 0.95 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.80, 165.16, 153.16, 148.55 (dd, *J* = 253.5, 11.3 Hz), 144.14 (dt, *J* = 258.1, 16.8 Hz), 142.43 (dd, *J* = 255.6, 13.4 Hz), 133.78, 132.41, 131.99 (d, *J* = 33.3 Hz), 130.08, 129.44, 127.57 (d, *J* = 3.6 Hz), 125.91 (d, *J* = 3.6 Hz), 123.77 (d, *J* = 24.7 Hz), 122.23, 119.37, 109.06 (dd, *J* = 18.8, 2.9 Hz), 61.73, 41.82 (d, *J* = 15.6 Hz), 13.86. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{20}H_{14}NO_3F_6$ 430.0878; found 430.0887.

Ethyl 6,7,8-trifluoro-1-methyl-2-(4-nitrophenyl)-4-oxo-1,4-dihydroquinoline-3-carboxylate (4q).



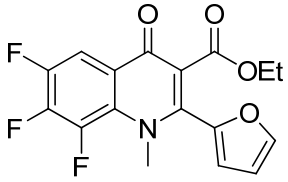
Eluent: petroleum ether/ ethyl acetate = 6:1. Yield 65% (528 mg). White solid, mp 210-211℃. ^{1}H NMR (300 MHz, CD_3OD) δ 8.44 (d, *J* = 8.9 Hz, 2H), 8.11 – 8.02 (m, 1H), 7.80 (d, *J* = 8.9 Hz, 2H), 3.96 (q, *J* = 7.1 Hz, 2H), 3.71 (d, *J* = 8.4 Hz, 3H), 0.94 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.54, 164.94, 152.62, 149.08, 148.51 (dd, *J* = 253.9, 11.5 Hz), 145.67 – 142.43 (m), 142.43 (dd, *J* = 255.3, 15.1 Hz), 138.96, 130.40, 129.40, 124.39, 123.52 (d, *J* = 4.3 Hz), 118.87, 108.78 (dd, *J* = 18.3, 2.6 Hz), 61.76, 41.83 (d, *J* = 15.8 Hz), 13.97. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{19}H_{13}N_2O_5F_3Na$ 429.0674; found 429.0678.

Ethyl 6,7,8-trifluoro-1-methyl-2-(2-nitrophenyl)-4-oxo-1,4-dihydroquinoline-3-carboxylate (4r).



Eluent: petroleum ether/ ethyl acetate = 3:1. Yield 81% (654 mg). Light yellow solid, mp 163-164℃. ^{1}H NMR (300 MHz, CD_3OD) δ 8.38 (d, *J* = 7.7 Hz, 1H), 8.12 – 8.02 (m, 1H), 7.96 – 7.85 (m, 2H), 7.63 (d, *J* = 6.8 Hz, 1H), 3.93 – 3.80 (m, 2H), 3.79 (d, *J* = 8.3 Hz, 3H), 0.91 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.44, 164.88, 152.21, 148.39 (dd, *J* = 253.1, 10.4 Hz), 147.92, 144.12 (dt, *J* = 258.9, 17.1 Hz), 142.32 (dd, *J* = 253.6, 16.2 Hz), 134.61, 131.93, 130.80, 128.77, 128.03, 125.12, 123.66 (d, *J* = 3.8 Hz), 116.62, 109.01 (dd, *J* = 18.3, 3.3 Hz), 61.59, 40.71 (d, *J* = 17.0 Hz), 13.89. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{19}H_{14}N_2O_5F_3$ 407.0855; found 407.0863.

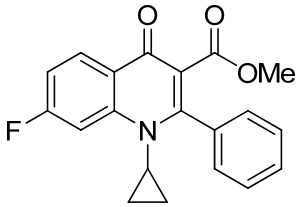
Ethyl 6,7,8-trifluoro-2-(furan-2-yl)-1-methyl-4-oxo-1,4-dihydroquinoline-3-carboxylate (4s).



Eluent: petroleum ether/ ethyl acetate = 6:1. Yield 41% (287 mg). White solid, mp 179-180℃. ^{1}H NMR (300 MHz, CD_3OD) δ 7.97 (ddd, *J* = 10.3, 8.3, 2.3 Hz, 1H), 7.91 – 7.86 (m, 1H), 6.95 (d, *J* = 3.5 Hz, 1H), 6.71 (dd, *J* = 3.5, 1.8 Hz, 1H), 4.13 (q, *J* = 7.1 Hz, 2H), 3.78 (d, *J* = 8.4 Hz, 3H), 1.14 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.20, 165.35, 148.43 (dd, *J* = 251.8, 10.4 Hz), 144.57, 144.51, 145.57 – 142.32 (m), 142.50 (dd, *J* = 255.5, 14.3 Hz), 129.90, 123.68 (d, *J* = 5.5 Hz), 119.01, 116.17, 112.10, 108.59 (dd, *J* = 18.3, 3.3 Hz), 61.85, 42.30 (d, *J* = 14.6 Hz), 14.22. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{17}H_{13}NO_4F_3$ 352.0797; found 352.0798.

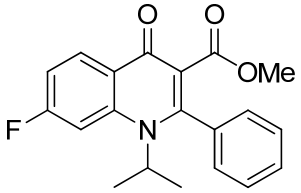
Methyl

1-cyclopropyl-7-fluoro-4-oxo-2-phenyl-1,4-dihydroquinoline-3-carboxylate (4t).



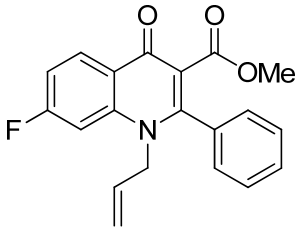
Eluent: petroleum ether/ ethyl acetate = 2:1. Yield 56% (378 mg). White solid, mp 210-212℃. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.45 (dd, *J* = 8.8, 6.7 Hz, 1H), 7.59 (dd, *J* = 11.1, 2.0 Hz, 1H), 7.48 (s, 5H), 7.14 (t, *J* = 8.4 Hz, 1H), 3.54 (s, 3H), 3.20 – 3.10 (m, 1H), 0.92 (d, *J* = 6.9 Hz, 2H), 0.64 (d, *J* = 3.7 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.04, 166.83, 165.12 (d, *J* = 251.6 Hz), 153.95, 144.15 (d, *J* = 11.7 Hz), 134.34, 130.05, 129.94, 128.78, 128.71, 123.43, 120.10, 113.09 (d, *J* = 23.0 Hz), 104.34 (d, *J* = 27.1 Hz), 52.45, 33.05, 13.11. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{20}H_{16}NO_3FNa$ 360.1012; found 360.1024.

Methyl 7-fluoro-1-isopropyl-4-oxo-2-phenyl-1,4-dihydroquinoline-3-carboxylate (4u).



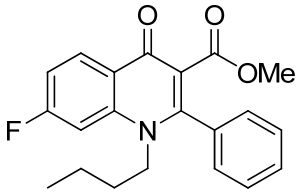
Eluent: petroleum ether/ ethyl acetate = 3:1. Yield 77% (521 mg). White solid, mp 196-198℃. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.54 (dd, *J* = 9.0, 7.0 Hz, 1H), 7.54 – 7.43 (m, 4H), 7.40 – 7.37 (m, 2H), 7.13 (ddd, *J* = 9.6, 7.7, 2.2 Hz, 1H), 4.63 (dt, *J* = 14.4, 7.2 Hz, 1H), 3.45 (s, 3H), 1.57 (d, *J* = 7.2 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.24, 166.95, 164.44 (d, *J* = 250.7 Hz), 153.25, 140.74 (d, *J* = 11.3 Hz), 133.96, 130.67 (d, *J* = 10.7 Hz), 130.16, 129.11, 128.14, 124.91, 119.89, 112.97 (d, *J* = 22.9 Hz), 105.13 (d, *J* = 27.3 Hz), 54.01, 52.31, 21.05. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{20}H_{19}NO_3F$ 340.1349; found 340.1339.

Methyl 1-allyl-7-fluoro-4-oxo-2-phenyl-1,4-dihydroquinoline-3-carboxylate (4v).



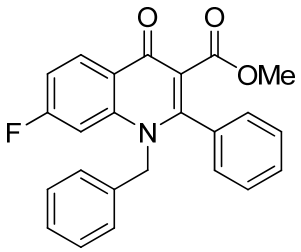
Eluent: petroleum ether/ ethyl acetate = 2:1. Yield 64% (430 mg). White solid, mp 139-140℃. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.53 (dd, *J* = 9.5, 6.7 Hz, 1H), 7.58 – 7.33 (m, 5H), 7.21 – 7.06 (m, 2H), 5.86 – 5.74 (m, 1H), 5.31 (d, *J* = 10.7 Hz, 1H), 5.01 (d, *J* = 17.2 Hz, 1H), 4.58 – 4.45 (m, 2H), 3.50 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.54, 166.77, 165.60 (d, *J* = 251.9 Hz), 153.06, 141.99 (d, *J* = 11.5 Hz), 132.86, 131.31, 130.41, 130.30 (d, *J* = 10.7 Hz), 128.78, 128.42, 123.77, 119.76, 118.62, 113.31 (d, *J* = 22.9 Hz), 103.67 (d, *J* = 27.2 Hz), 52.32, 51.30. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{20}H_{17}NO_3F$ 338.1192; found 338.1202.

Methyl 1-butyl-7-fluoro-4-oxo-2-phenyl-1,4-dihydroquinoline-3-carboxylate (4w).



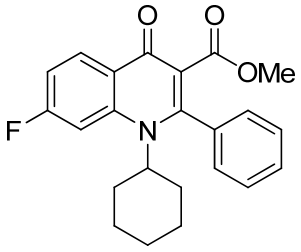
Eluent: petroleum ether/ ethyl acetate = 2:1. Yield 75% (529 mg). White solid, mp 110-111℃. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.57 – 8.50 (m, 1H), 7.53 – 7.45 (m, 3H), 7.43 – 7.35 (m, 2H), 7.19 – 7.10 (m, 2H), 3.90 – 3.79 (m, 2H), 3.48 (d, *J* = 1.2 Hz, 3H), 1.69 –1.59 (m, 2H), 1.23 – 1.09 (m, 2H), 0.76 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.39, 166.86, 165.67 (d, *J* = 251.6 Hz), 152.74, 141.63 (d, *J* = 11.2 Hz), 133.11, 130.60 (d, *J* = 10.7 Hz), 130.19, 128.88, 128.66, 124.10, 119.68, 113.15 (d, *J* = 22.8 Hz), 102.81 (d, *J* = 26.9 Hz), 52.30, 48.69, 30.63, 19.84, 13.53. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{21}H_{21}NO_3F$ 354.1505; found 354.1489.

Methyl 1-benzyl-7-fluoro-4-oxo-2-phenyl-1,4-dihydroquinoline-3-carboxylate (4x).



Eluent: petroleum ether/ ethyl acetate = 2:1. Yield 63% (487 mg). White solid, mp 185-186℃. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.54 (dd, *J* = 8.8, 6.7 Hz, 1H), 7.47 – 7.26 (m, 8H), 7.17 – 7.05 (m, 1H), 7.01 – 6.96 (m, 3H), 5.16 (s, 2H), 3.51 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.66, 166.79, 165.59 (d, *J* = 252.2 Hz), 153.37, 142.18 (d, *J* = 11.5 Hz), 135.25, 132.80, 130.41, 130.32, 129.41, 128.88, 128.41, 128.20, 125.54, 123.95, 119.92, 113.45 (d, *J* = 22.9 Hz), 103.97 (d, *J* = 27.1 Hz), 52.65, 52.40. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{24}H_{19}NO_3F$ 388.1349; found 388.1327.

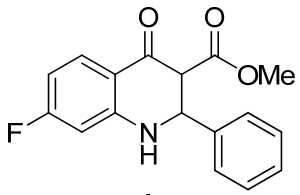
Methyl 1-cyclohexyl-7-fluoro-4-oxo-2-phenyl-1,4-dihydroquinoline-3-carboxylate (4y).



Eluent: petroleum ether/ ethyl acetate = 3:1. Yield 85% (645 mg). White solid, mp 221-223℃. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.58 – 8.48 (m, 1H), 7.59 (d, *J* = 11.8 Hz, 1H), 7.53 – 7.43 (m, 3H), 7.42 – 7.32 (m, 2H), 7.12 (t, *J* = 8.3 Hz, 1H), 4.10 (t, *J* = 12.7 Hz, 1H), 3.47 (s, 3H), 2.35 (dd, *J* = 24.0, 11.9 Hz, 2H), 1.81 (d, *J* = 11.5 Hz, 4H), 1.59 (d, *J* = 12.2 Hz, 1H), 1.17 (dd, *J* = 27.1, 13.2 Hz, 1H), 0.92 (dd, *J* = 25.7, 13.1 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.24, 166.69, 164.40 (d, *J* = 250.3 Hz), 153.57, 141.54 (d, *J* = 10.7 Hz), 134.12, 130.48 (d, *J* = 10.7 Hz), 130.14,129.01,

128.04, 124.84, 119.97, 112.91 (d, J = 22.9 Hz), 105.47 (d, J = 27.6 Hz), 63.67, 52.32, 30.62, 26.56, 25.10. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{23}H_{23}NO_3F$ 380.1662; found 380.1675.

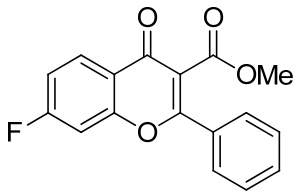
Methyl 7-fluoro-4-oxo-2-phenyl-1,2,3,4-tetrahydroquinoline-3-carboxylate (4z).



4z

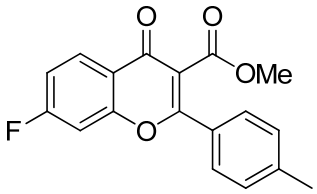
Eluent: petroleum ether/ ethyl acetate = 1:1. Yield 97% (145 mg). White solid, mp 253-255℃. ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.14 (s, 1H), 7.85 (dd, J = 9.0, 6.1 Hz, 1H), 7.46-7.50 (m, 3H), 7.34 – 7.26 (m, 3H), 6.91-6.96 (m, 1H), 3.50 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ 173.08, 166.72, 163.60 (d, J = 150.4 Hz), 149.83, 140.94 (d, J = 10.0 Hz), 133.42, 128.83, 128.32 (d, J = 15.2 Hz), 128.04, 121.55, 115.54, 112.83 (d, J = 28.1 Hz), 103.84 (d, J = 26.8 Hz), 51.74. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{17}H_{13}NO_3F$ 298.0879; found 298.0894.

Methyl 7-fluoro-4-oxo-2-phenyl-4H-chromene-3-carboxylate (6a).



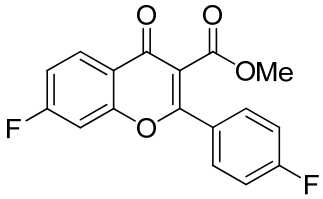
Eluent: petroleum ether/ ethyl acetate = 10:1. Yield 64% (380 mg). White solid, mp 101-102℃. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.29 (dd, J = 8.8, 6.2 Hz, 1H), 7.76 – 7.67 (m, 2H), 7.62 – 7.46 (m, 3H), 7.26 – 7.14 (m, 2H), 3.80 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.30, 166.20 (d, J = 256.2 Hz), 165.58, 163.59, 157.01 (d, J = 13.3 Hz), 132.11, 131.74, 129.14, 128.96 (d, J = 10.7 Hz), 128.17, 120.16, 118.33, 114.82 (d, J = 22.8 Hz), 105.11 (d, J = 25.3 Hz), 53.14. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{17}H_{11}O_4FNa$ 321.0539; found 321.0550.

Methyl 7-fluoro-4-oxo-2-p-tolyl-4H-chromene-3-carboxylate (6b).



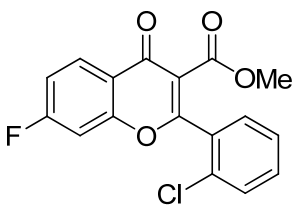
Eluent: petroleum ether/ ethyl acetate = 6:1. Yield 61% (380 mg). White solid, mp 122-123℃. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.27 (dd, *J* = 8.7, 6.3 Hz, 1H), 7.62 (d, *J* = 8.1 Hz, 2H), 7.31 (d, *J* = 8.1 Hz, 2H), 7.25 – 7.12 (m, 2H), 3.81 (s, 3H), 2.44 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.32, 166.17 (d, *J* = 256.1 Hz), 165.76, 163.67, 157.01 (d, *J* = 13.4 Hz), 142.82, 129.86, 128.97, 128.86, 128.11, 120.18, 117.92, 114.67 (d, *J* = 22.8 Hz), 105.05 (d, *J* = 25.5 Hz), 53.08, 21.82. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{18}H_{13}O_4FNa$ 335.0696; found 335.0672.

Methyl 7-fluoro-2-(4-fluorophenyl)-4-oxo-4H-chromene-3-carboxylate (6c).



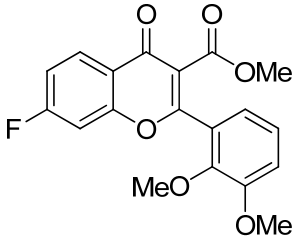
Eluent: petroleum ether/ ethyl acetate = 6:1. Yield 69% (432 mg). White solid, mp 129-131℃. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.33 – 8.21 (m, 1H), 7.79 – 7.68 (m, 2H), 7.25 – 7.10 (m, 4H), 3.81 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 174.16, 166.24 (d, *J* = 256.5 Hz), 165.48, 164.93 (d, *J* = 254.2 Hz), 162.44, 156.94 (d, *J* = 13.3 Hz), 130.57 (d, *J* = 9.0 Hz), 128.98 (d, *J* = 10.7 Hz), 127.88, 120.11, 118.31, 116.50 (d, *J* = 22.1 Hz), 114.90 (d, *J* = 22.8 Hz), 105.08 (d, *J* = 25.5 Hz), 53.19. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{17}H_{10}O_4F_2Na$ 339.0445; found 339.0441.

Methyl 2-(2-chlorophenyl)-7-fluoro-4-oxo-4H-chromene-3-carboxylate (6d).



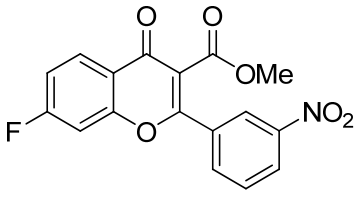
Eluent: petroleum ether/ ethyl acetate = 6:1. Yield 73% (485 mg). White solid, mp 111-112℃. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.31 (dd, *J* = 8.7, 6.2 Hz, 1H), 7.57 – 7.35 (m, 4H), 7.25 – 7.14 (m, 2H), 3.68 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.79, 166.24 (d, *J* = 256.6 Hz), 164.26, 163.63, 157.03 (d, *J* = 13.3 Hz), 133.36, 132.46, 131.22, 130.60, 130.38, 129.07 (d, *J* = 10.7 Hz), 127.06, 120.58, 120.02, 115.01 (d, *J* = 22.8 Hz), 105.22 (d, *J* = 25.5 Hz), 52.90. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{17}H_{10}O_4FClNa$ 355.0149; found 355.0157.

Methyl 2-(2,3-dimethoxyphenyl)-7-fluoro-4-oxo-4H-chromene-3-carboxylate (6e).



Eluent: petroleum ether/ ethyl acetate = 6:1. Yield 61% (435 mg). White solid, mp 119-120℃. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.34 – 8.27 (m, 1H), 7.22 – 7.07 (m, 4H), 7.04 (dd, *J* = 7.3, 2.0 Hz, 1H), 3.92 (s, 3H), 3.87 (s, 3H), 3.71 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.00, 166.10 (d, *J* = 256.1 Hz), 164.77, 163.79, 157.08 (d, *J* = 13.4 Hz), 153.04, 147.38, 129.01 (d, *J* = 10.6 Hz), 126.53, 124.41, 121.32, 120.49, 119.70, 115.60, 114.69 (d, *J* = 22.8 Hz), 105.07 (d, *J* = 25.4 Hz), 61.51, 56.16, 52.78. HRMS (ESI) m/z: $[M+H]^+$ Calcd for $C_{19}H_{16}O_6F$ 359.0931; found 359.0934.

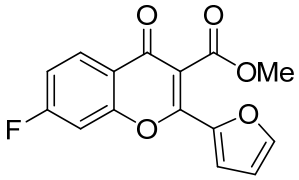
Methyl 7-fluoro-2-(3-nitrophenyl)-4-oxo-4H-chromene-3-carboxylate (6f).



Eluent: petroleum ether/ ethyl acetate = 6:1. Yield 50% (344 mg). White solid, mp 124-126℃. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.63 (s, 1H), 8.43 (d, *J* = 8.3 Hz, 1H), 8.30 (dd, *J* = 8.8, 6.2 Hz, 1H), 8.07 (d, *J* = 7.8 Hz, 1H), 7.75 (t, *J* = 8.0 Hz, 1H), 7.30

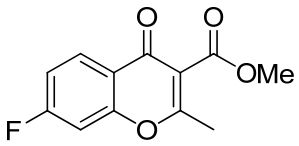
– 7.20 (m, 2H), 3.87 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.86, 166.38 (d, *J* = 257.4 Hz), 164.92, 160.55, 156.86 (d, *J* = 13.4 Hz), 148.57, 133.87, 133.20, 130.42, 129.07 (d, *J* = 10.7 Hz), 126.50, 123.37, 120.08, 119.30, 115.32 (d, *J* = 22.8 Hz), 105.24 (d, *J* = 25.7 Hz), 53.43. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{17}H_{10}NO_6FNa$ 366.0390; found 366.0390.

Methyl 7-fluoro-2-(furan-2-yl)-4-oxo-4H-chromene-3-carboxylate (6g).



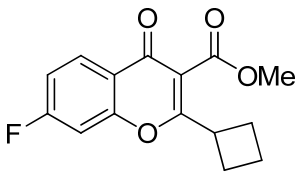
Eluent: petroleum ether/ ethyl acetate = 6:1. Yield 63% (362 mg). White solid, mp 129-130℃. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.24 (dd, *J* = 8.8, 6.3 Hz, 1H), 7.69 – 7.63 (m, 1H), 7.23 – 7.12 (m, 3H), 6.65 – 6.63 (m, 1H), 3.99 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.06, 169.77, 166.17 (d, *J* = 256.1 Hz), 164.94, 156.41 (d, *J* = 13.5 Hz), 152.14, 147.12, 129.84, 128.78 (d, *J* = 10.7 Hz), 120.20 (d, *J* = 2.0 Hz), 116.15, 114.61 (d, *J* = 22.7 Hz), 112.96, 104.96 (d, *J* = 25.7 Hz), 53.22. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{15}H_9O_5FNa$ 311.0332; found 311.0320.

Methyl 7-fluoro-2-methyl-4-oxo-4H-chromene-3-carboxylate (6h).



Eluent: petroleum ether/ ethyl acetate = 6:1. Yield 36% (171 mg). White solid, mp 124-125℃. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.22 (dd, *J* = 8.6, 6.2 Hz, 1H), 7.19 – 7.08 (m, 2H), 3.94 (s, 3H), 2.52 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.63, 167.74, 165.96 (d, *J* = 255.9 Hz), 165.54, 156.63 (d, *J* = 13.2 Hz), 128.93 (d, *J* = 10.6 Hz), 120.35, 118.05, 114.60 (d, *J* = 22.8 Hz), 104.78 (d, *J* = 25.4 Hz), 53.00, 19.80. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{12}H_9O_4FNa$ 259.0383; found 259.0406.

Methyl 2-cyclobutyl-7-fluoro-4-oxo-4H-chromene-3-carboxylate (6i).



Eluent: petroleum ether/ ethyl acetate = 10:1. Yield 43% (235 mg). Colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.21 (dd, *J* = 8.8, 6.3 Hz, 1H), 7.24 – 7.04 (m, 2H), 3.93 (s, 3H), 3.83 – 3.68 (m, 1H), 2.59 – 2.41 (m, 2H), 2.39 – 2.23 (m, 2H), 2.14 – 1.91 (m, 2H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 173.91, 170.14, 165.95 (d, *J* = 255.6 Hz), 165.43, 156.76 (d, *J* = 13.3 Hz), 128.81 (d, *J* = 10.7 Hz), 120.32, 116.72, 114.51 (d, *J* = 22.8 Hz), 104.96 (t, *J* = 26.2 Hz), 52.99, 37.36, 26.54, 18.38. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{15}H_{13}O_4FNa$ 299.0696; found 299.0712.

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1. W. L. F. Armarego and C. L. L. Chai, *Purification of Laboratory Chemicals*, Elsevier, 2003.
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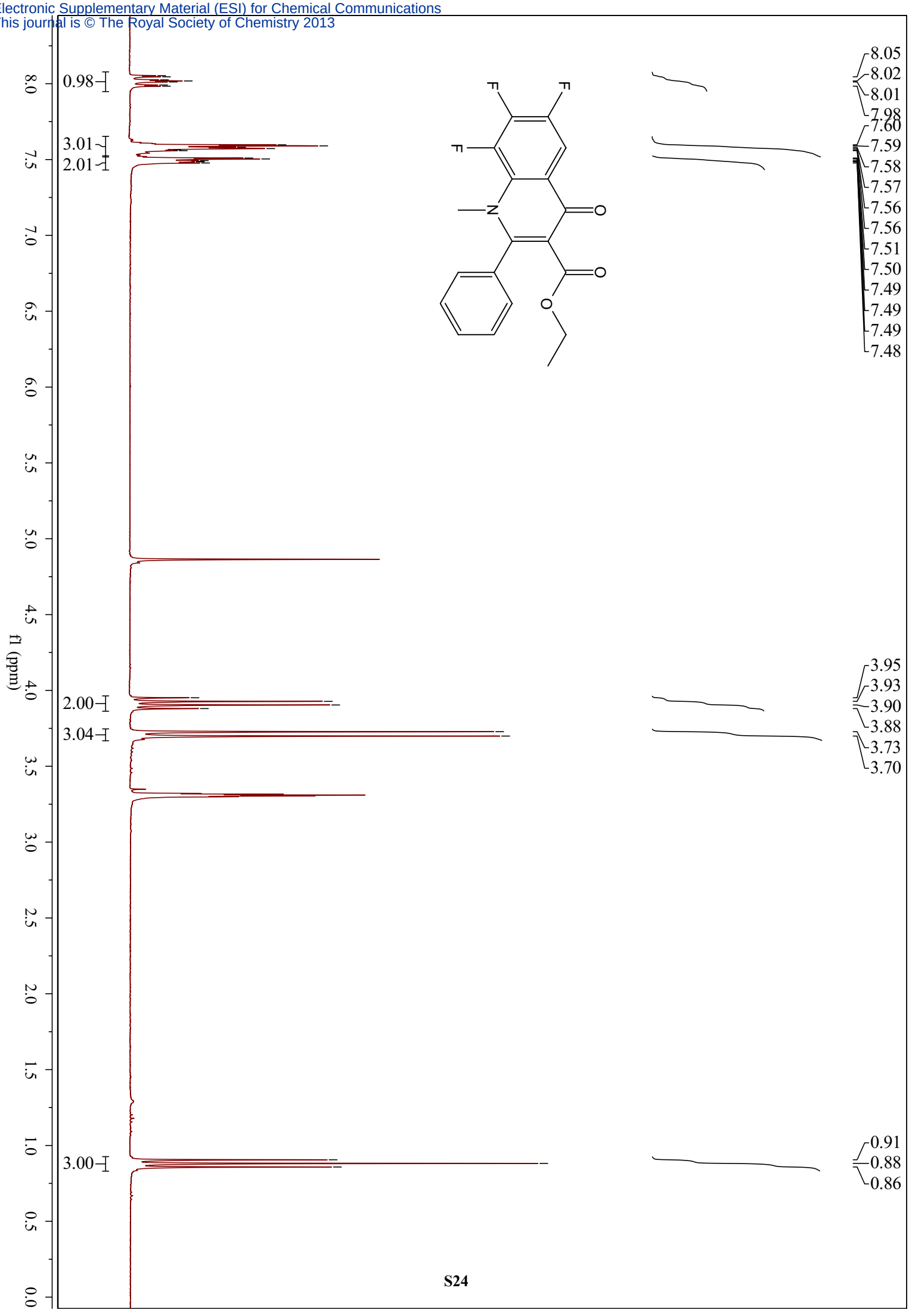
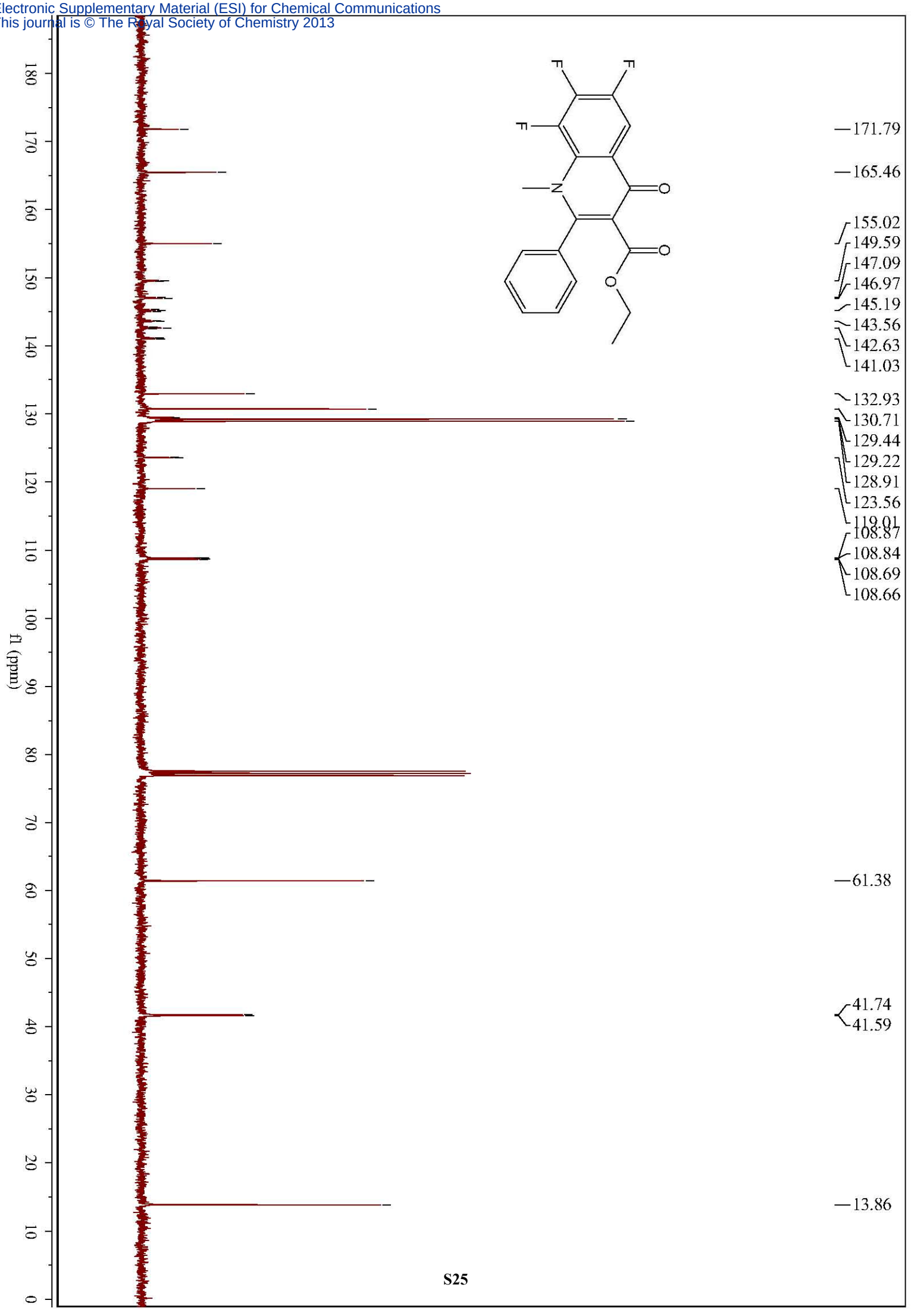
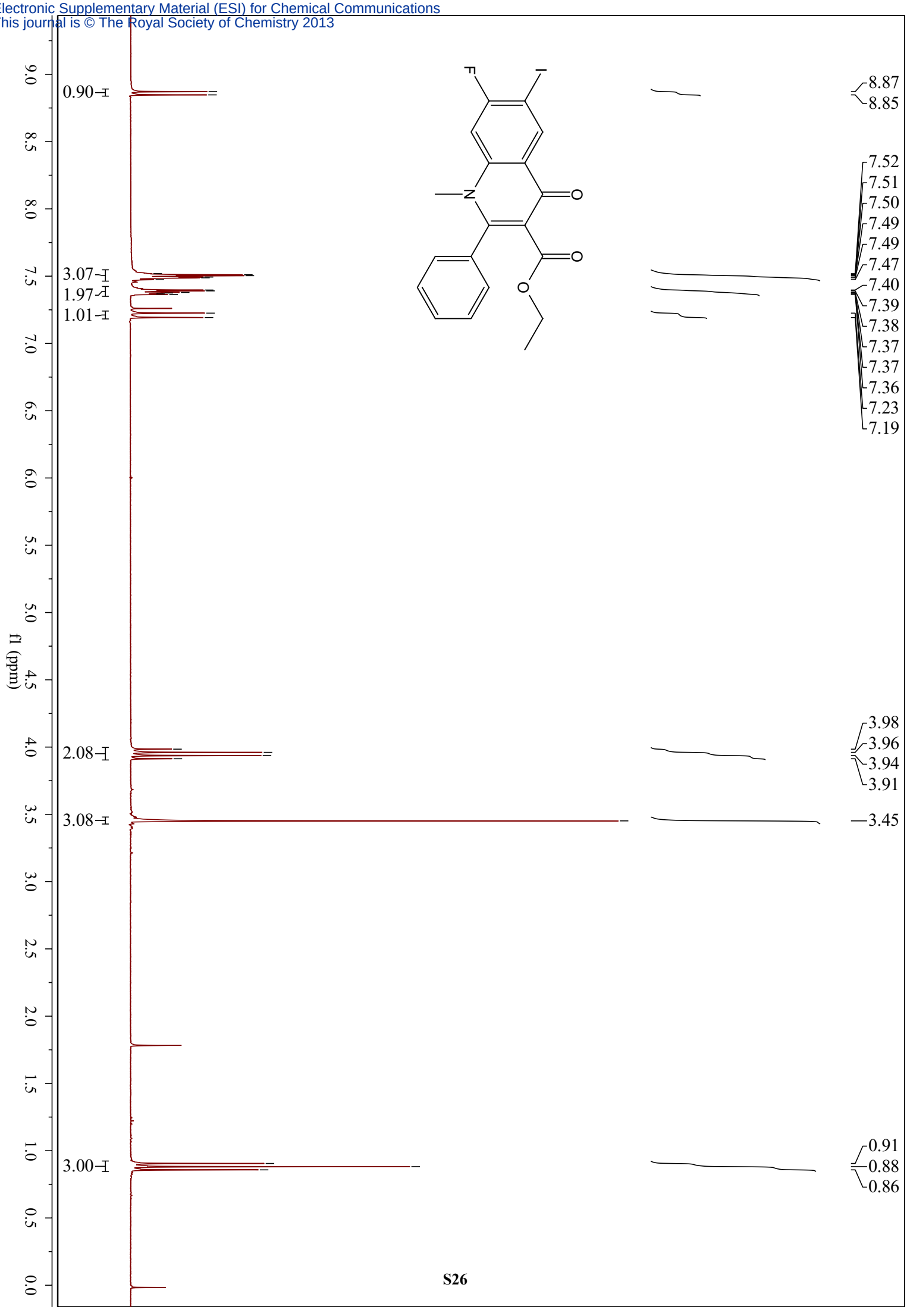
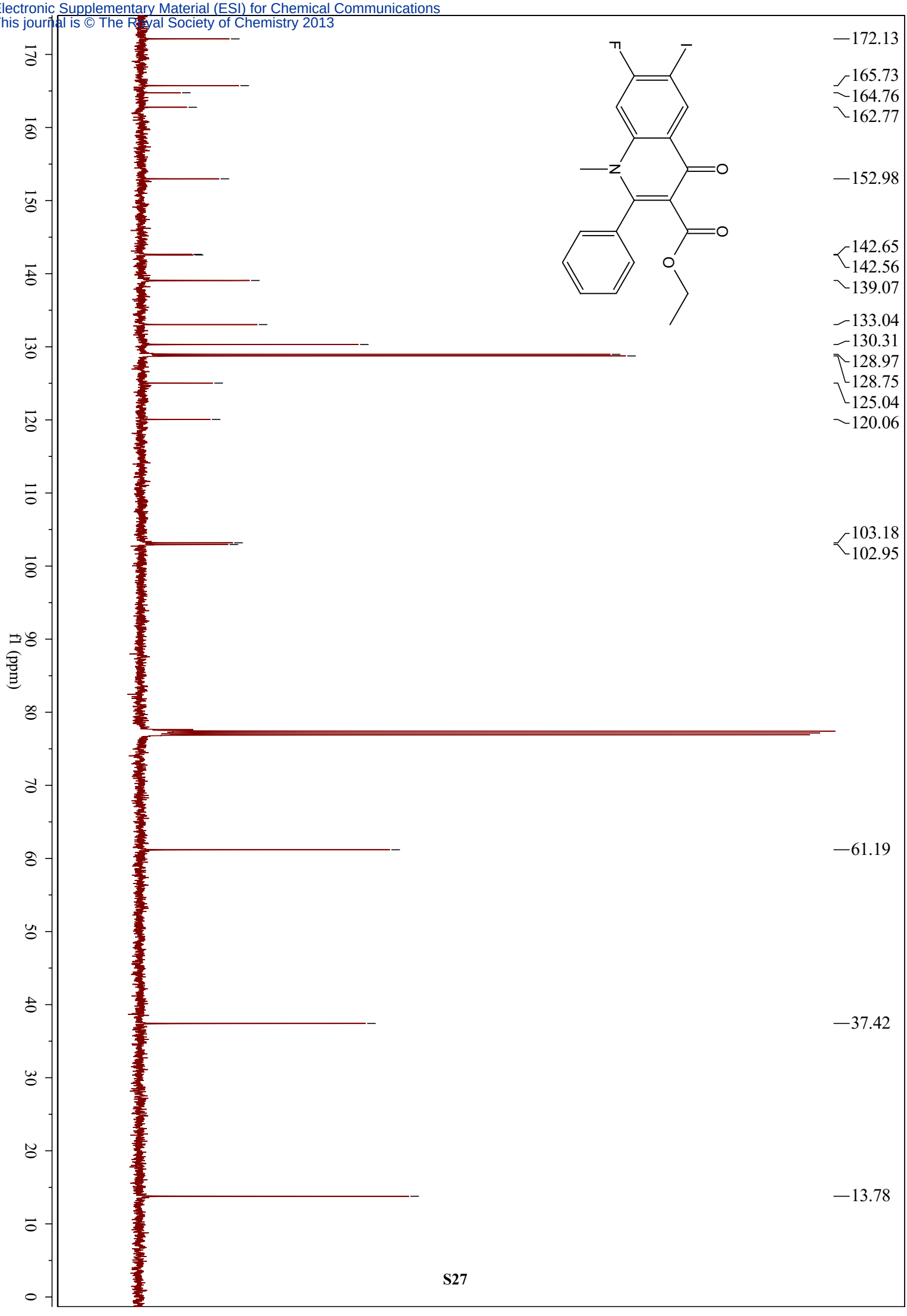
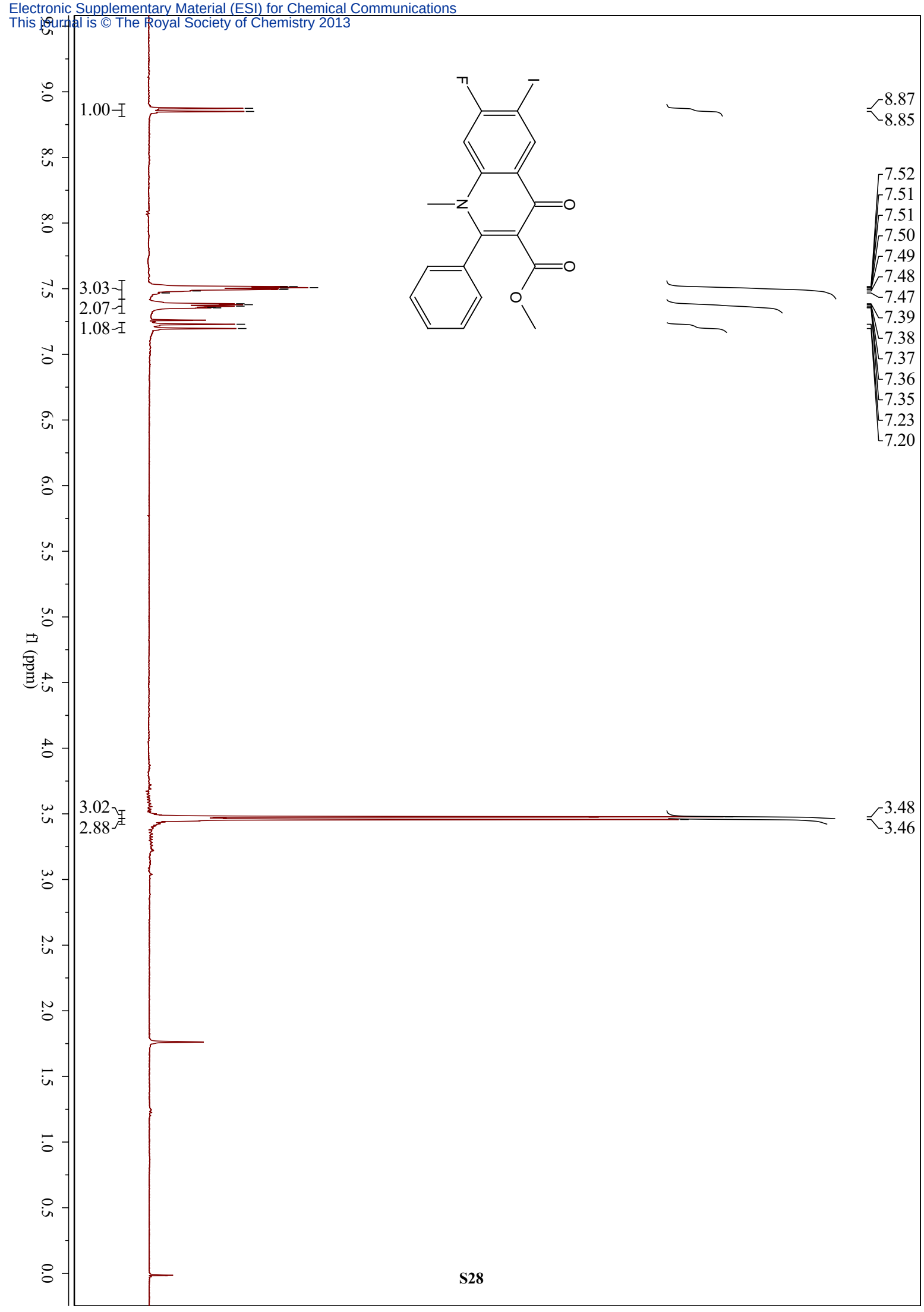
3. G. Sbardella, A. Mai, M. Artico, M. G. Setzu, G. Poni and P. La Colla, *Farmaco*, 2004, **59**, 463-471.

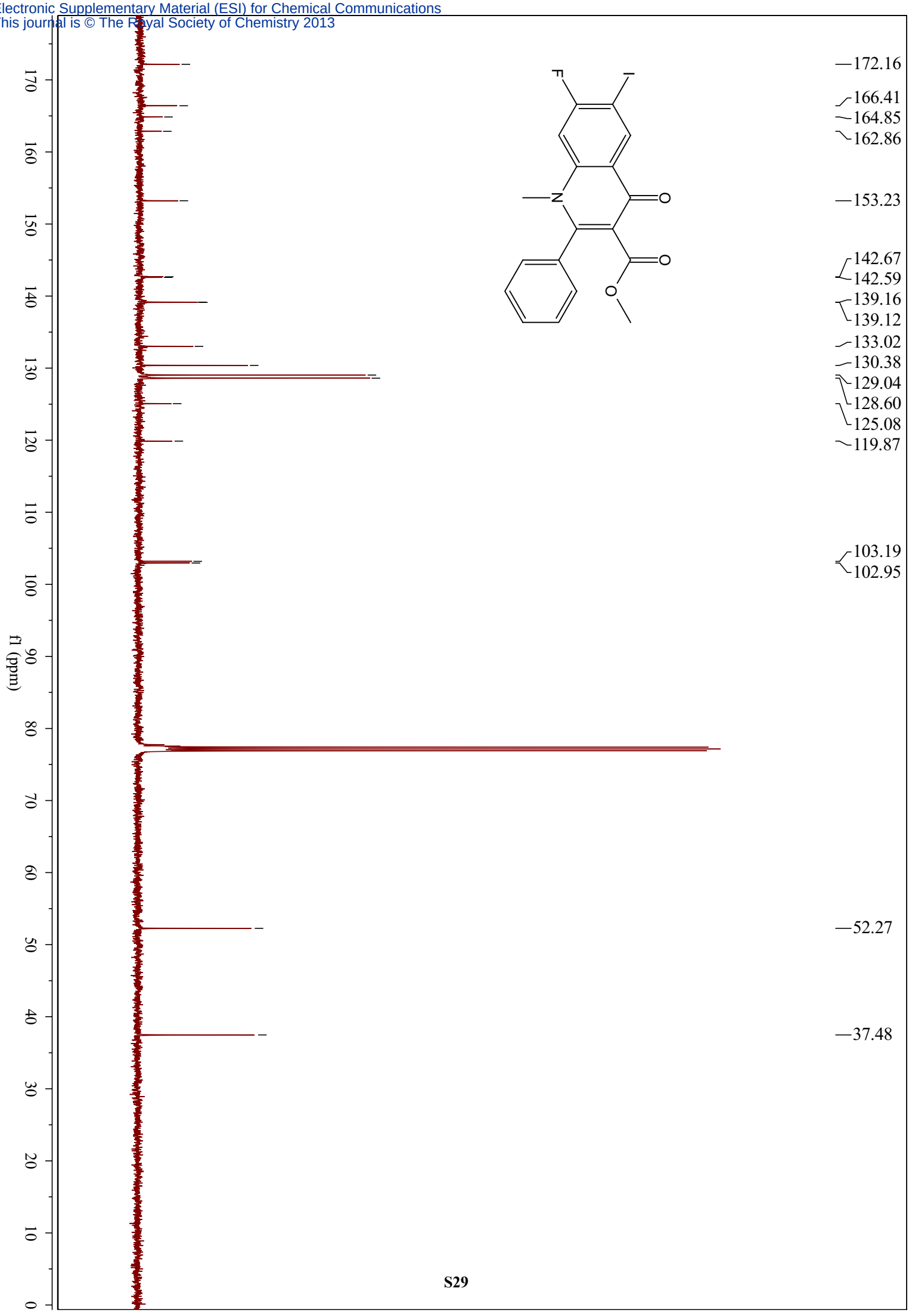


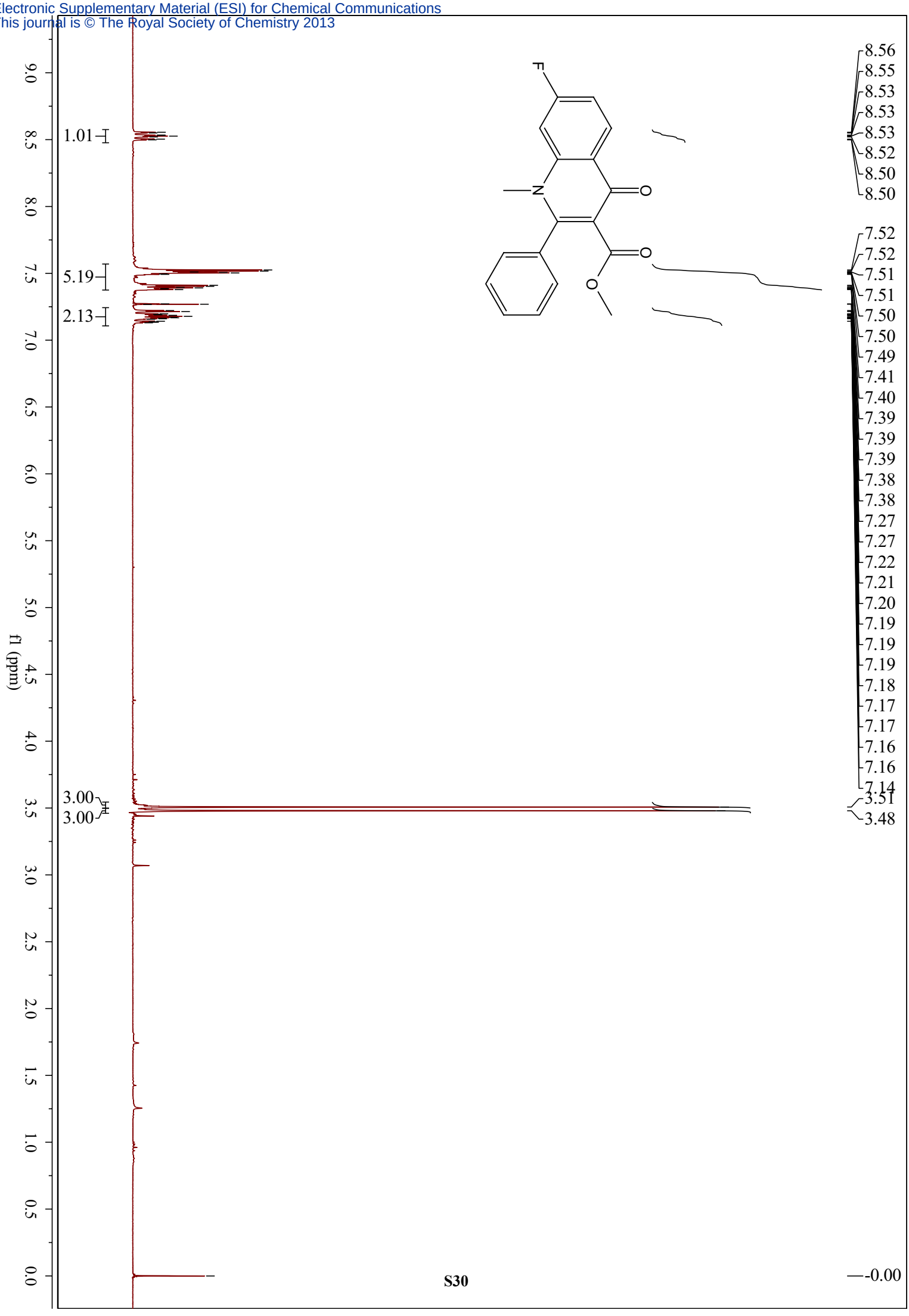


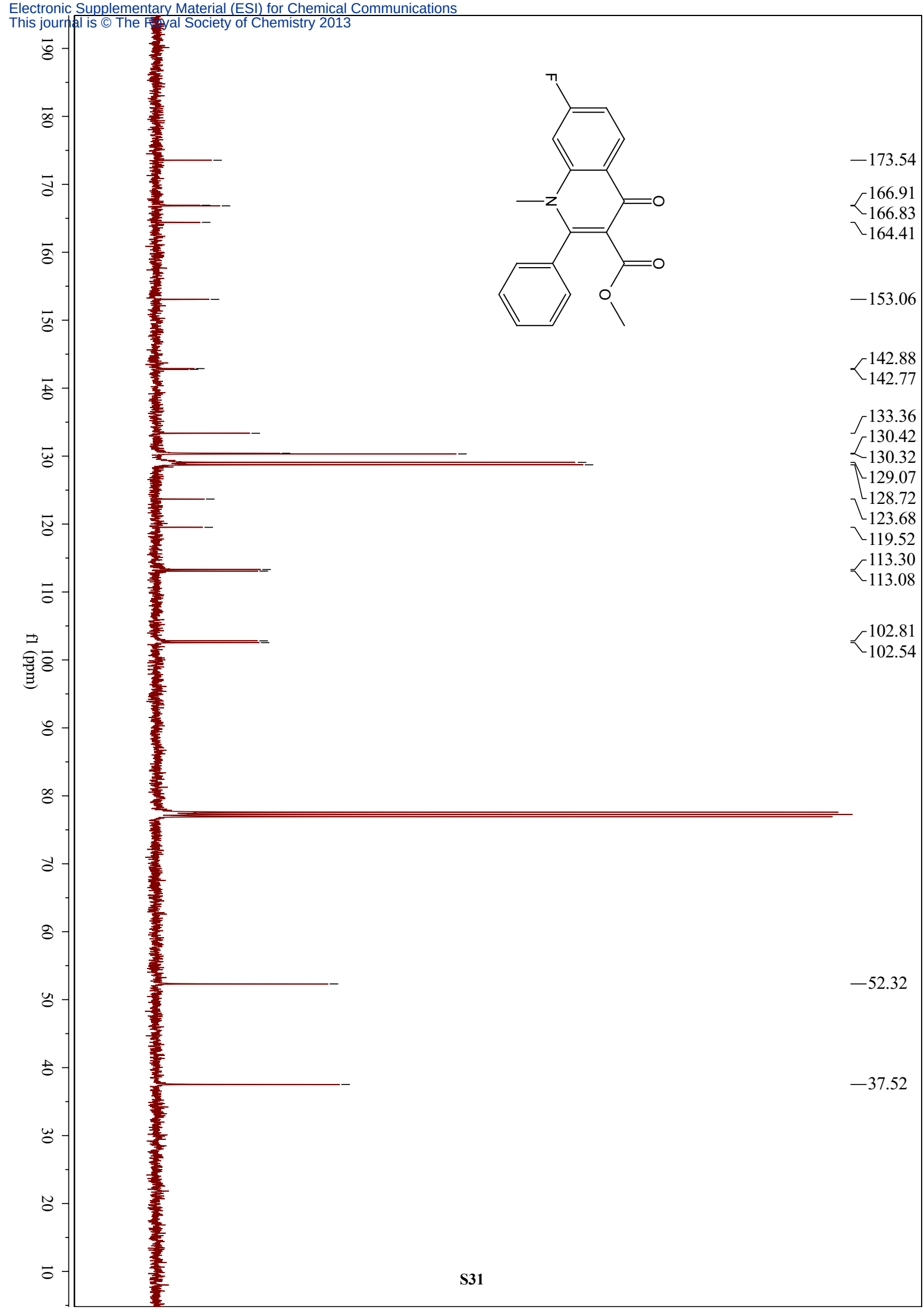


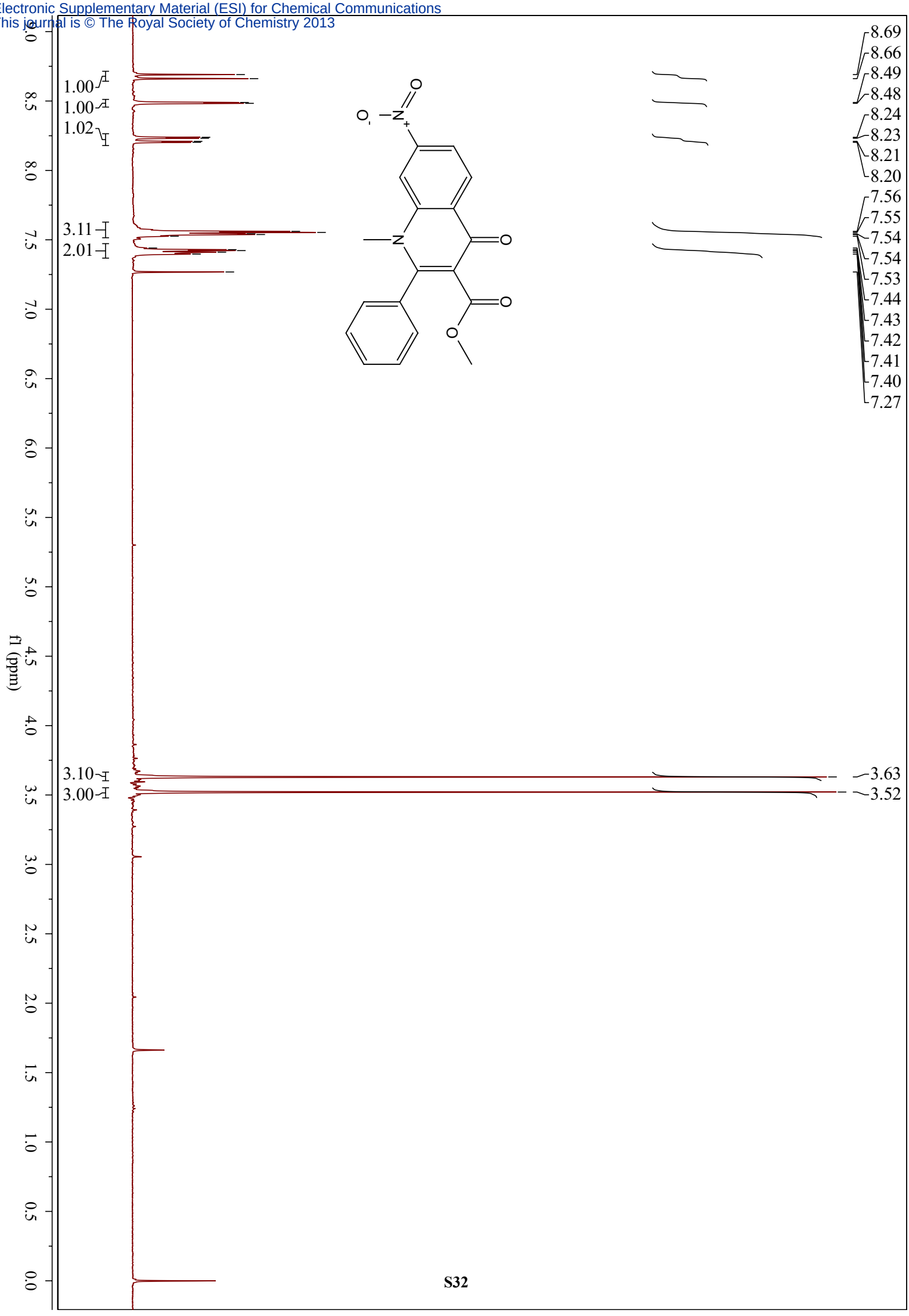


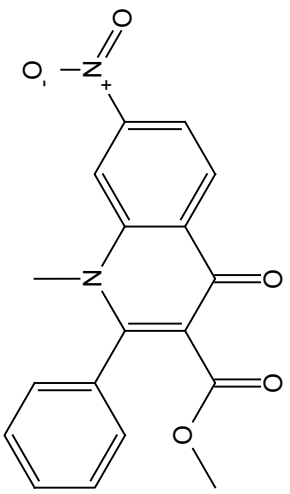












173.08
166.24
154.34
150.40
141.21
132.83
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129.58
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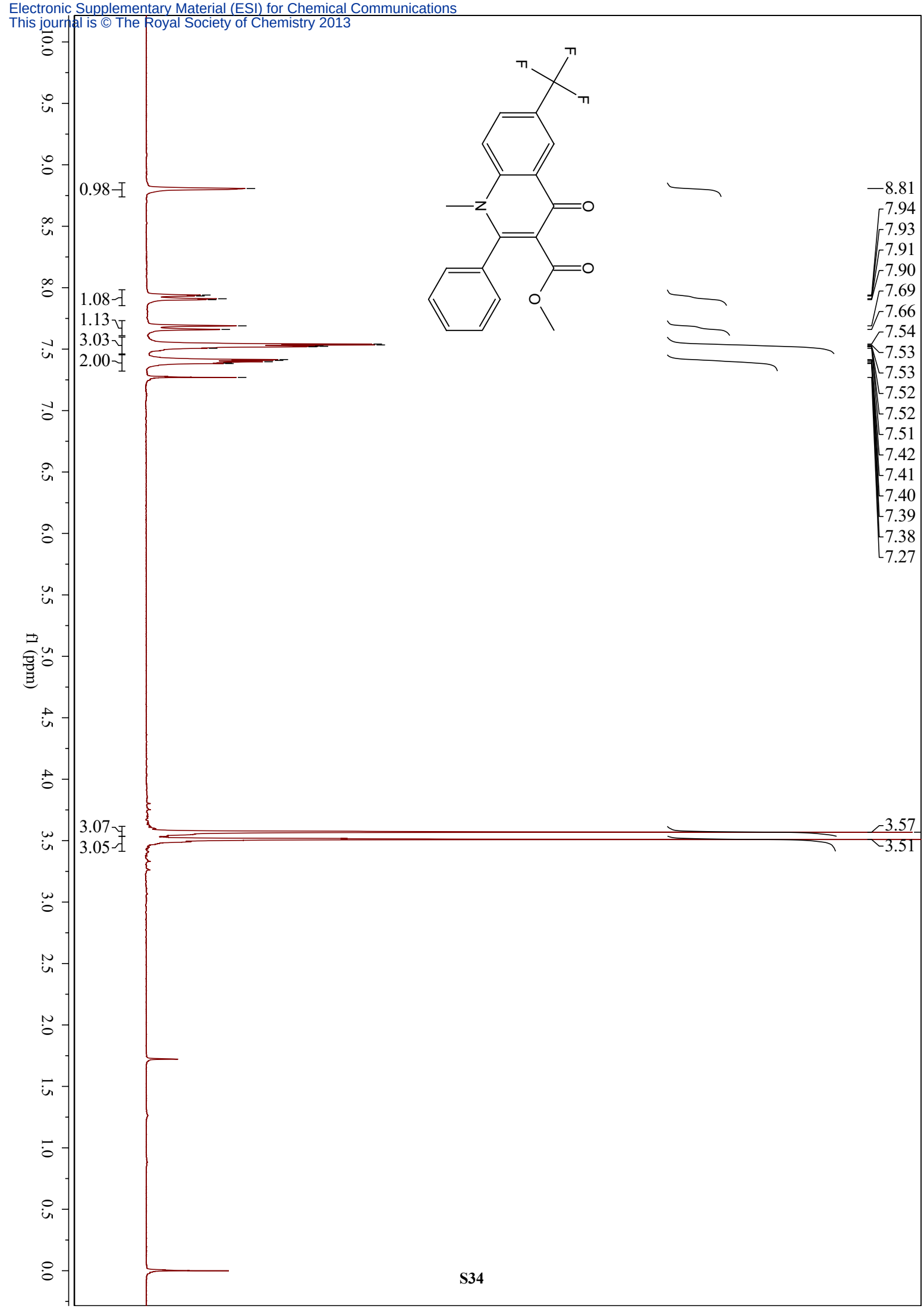
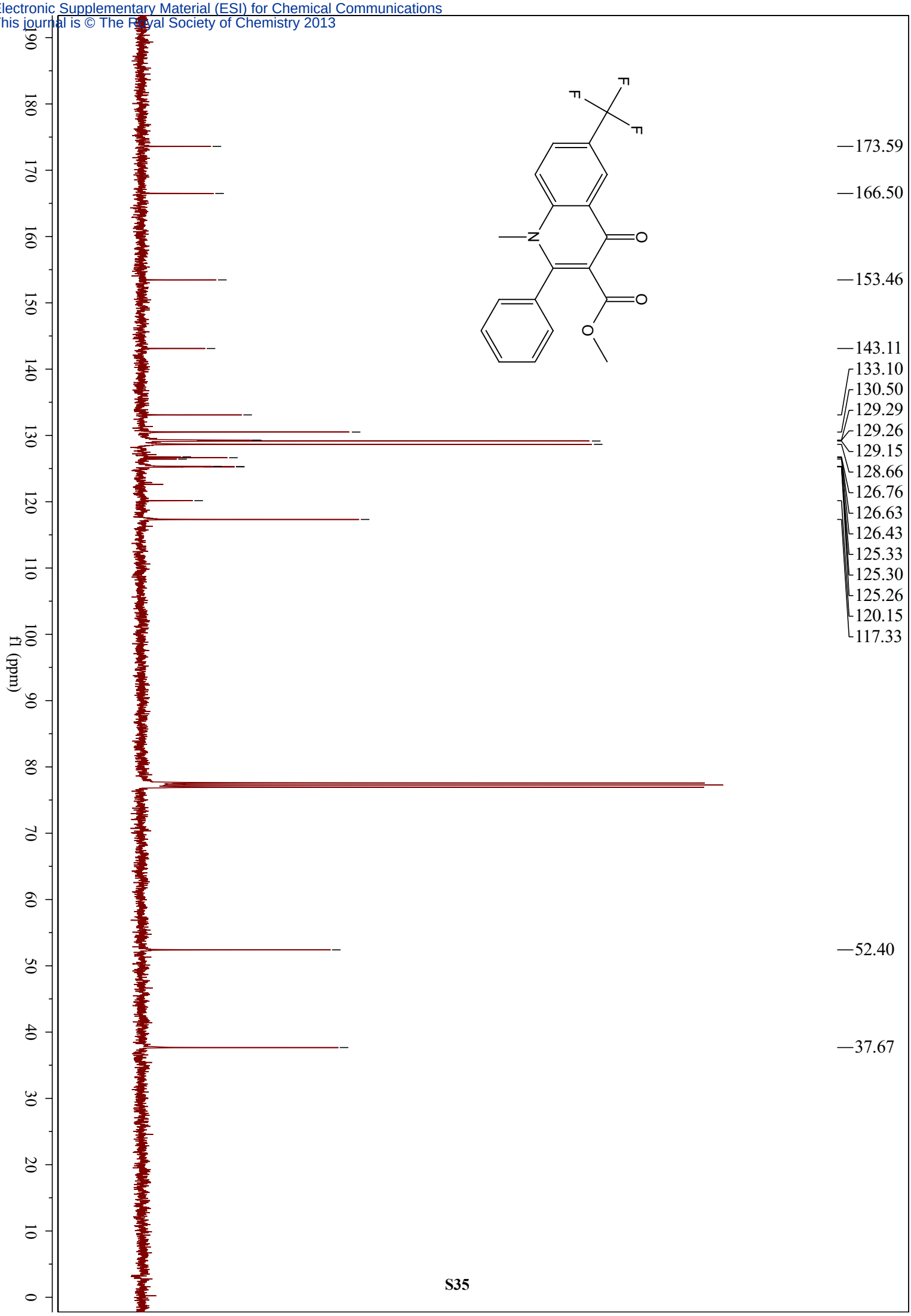
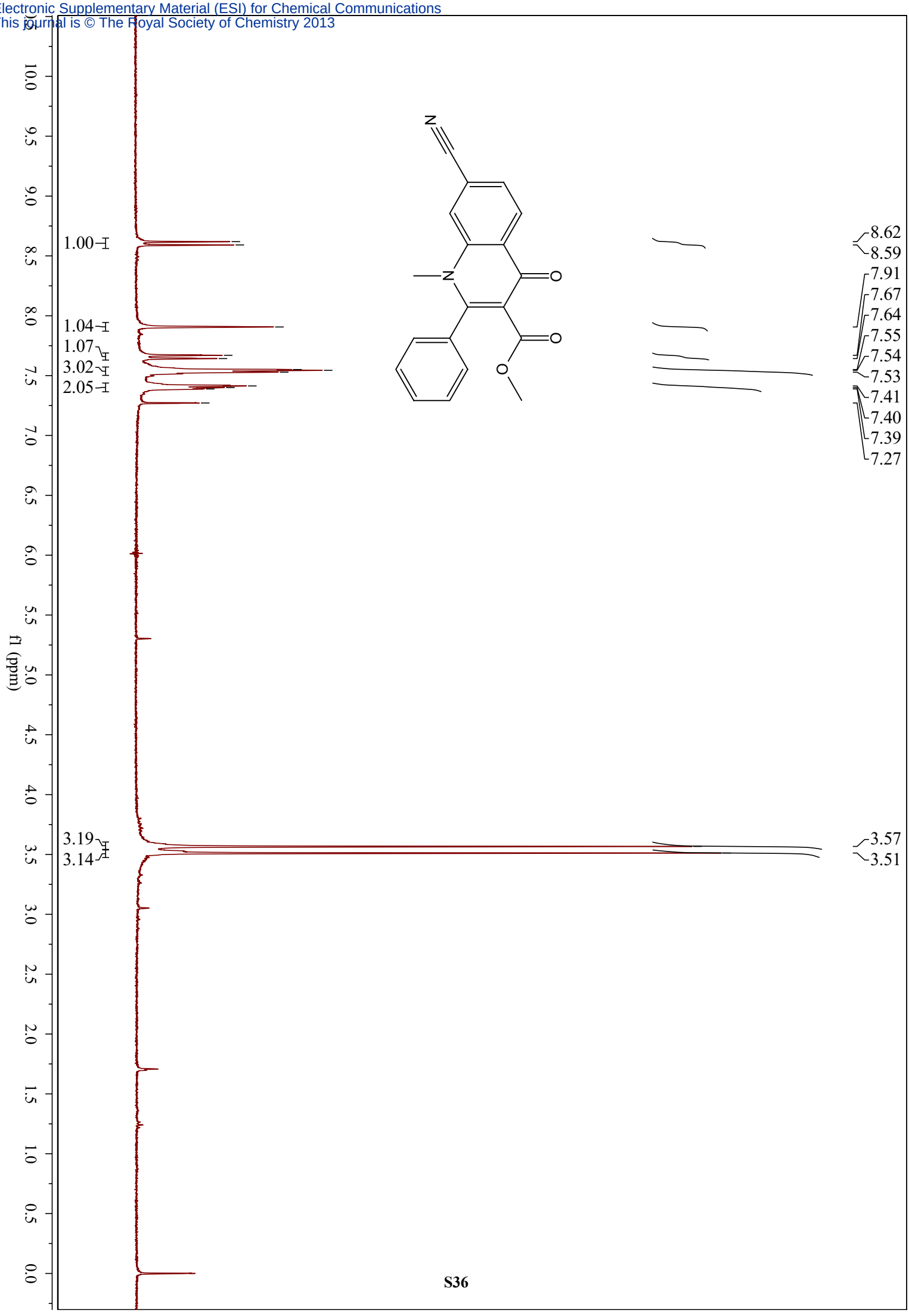
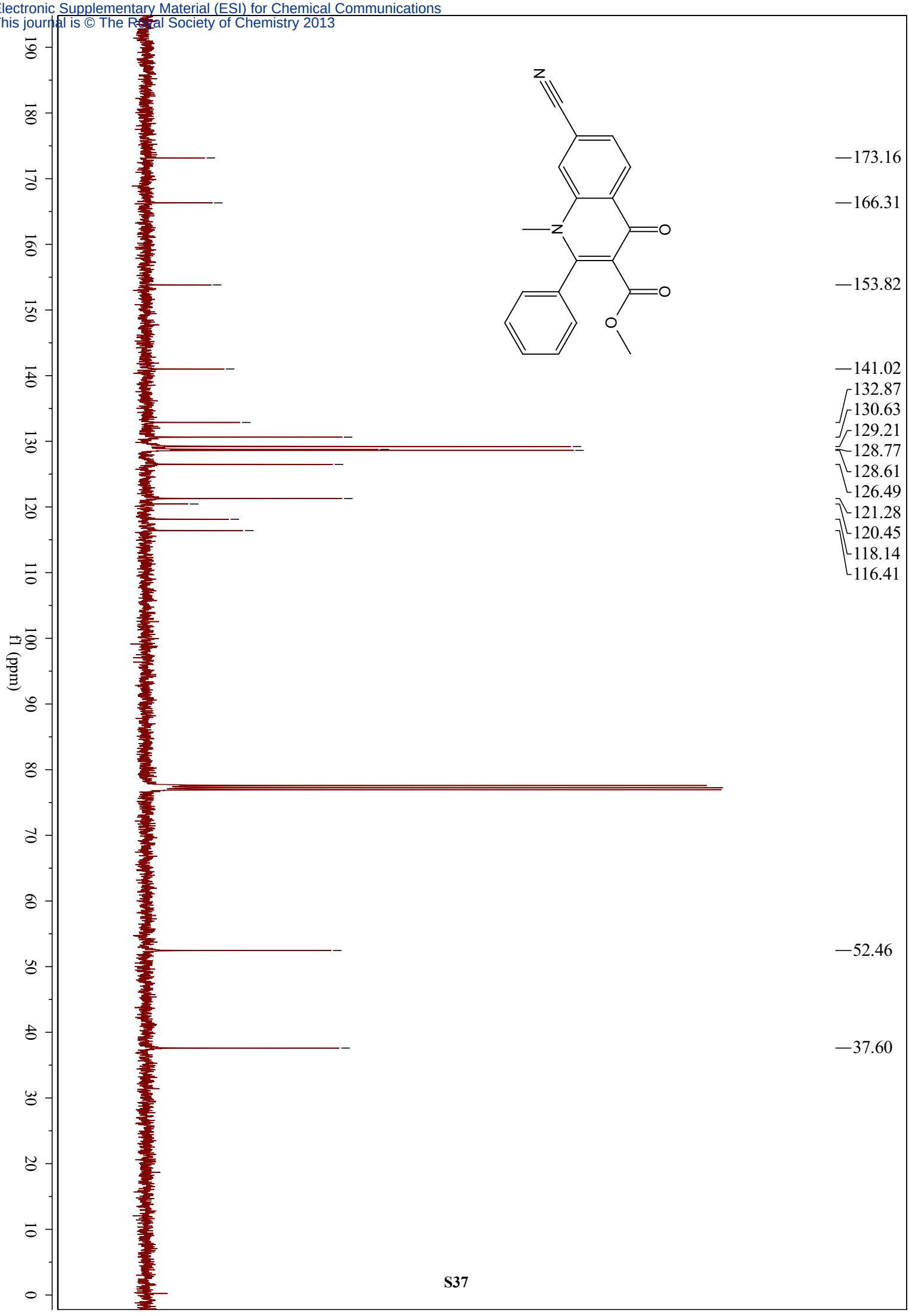
128.59
120.66
118.35
112.71
52.51
37.83

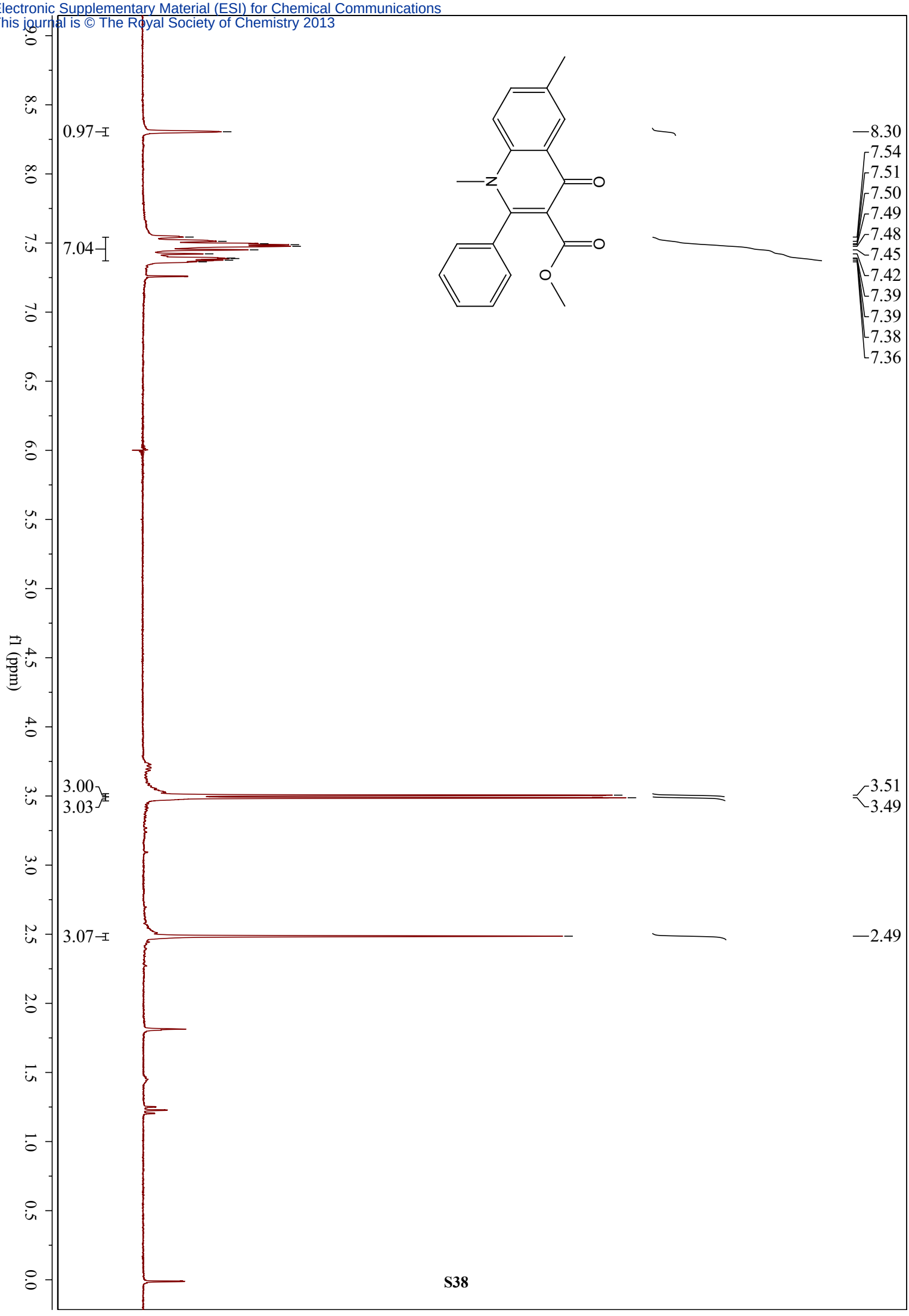
f1 (ppm)

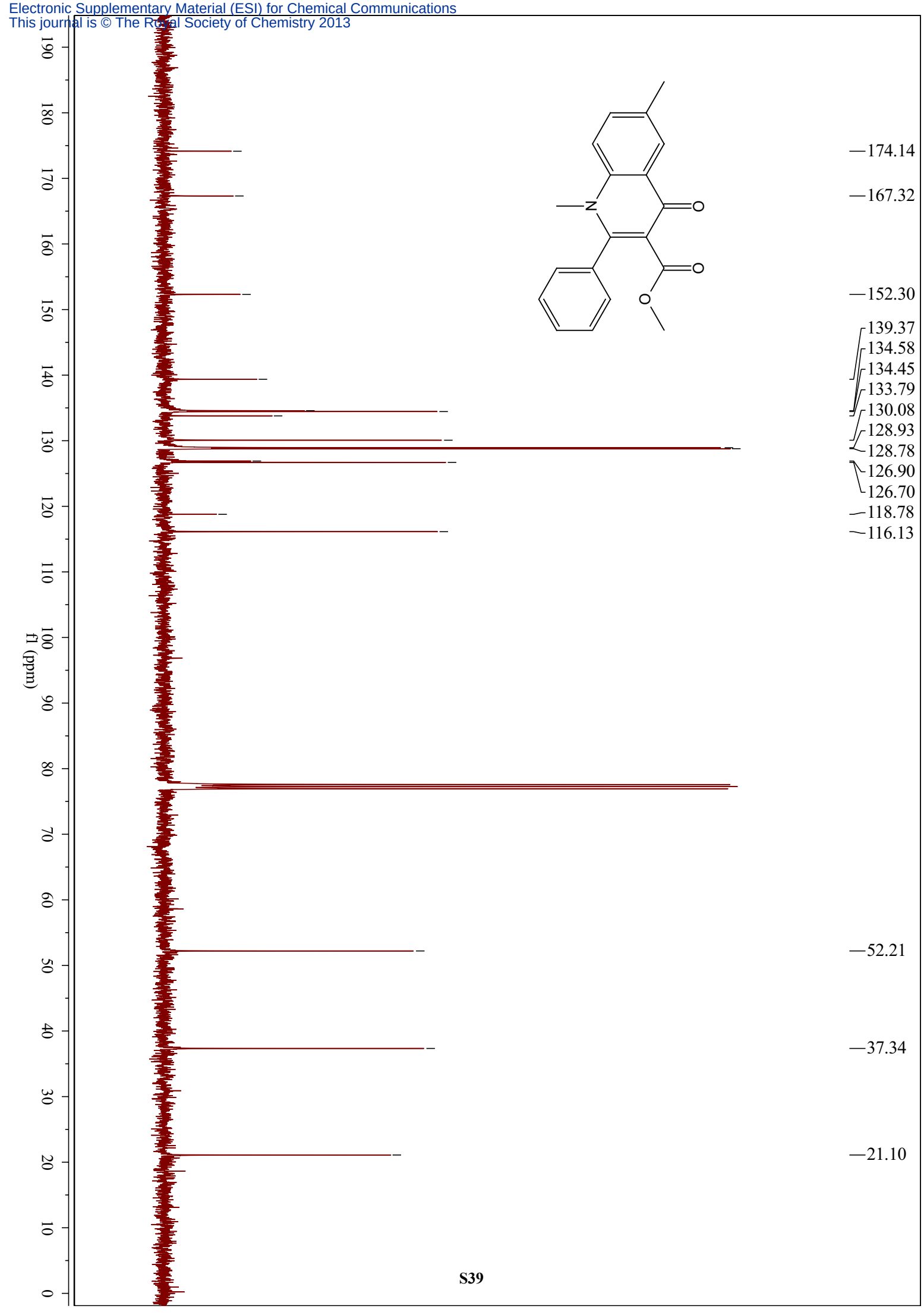


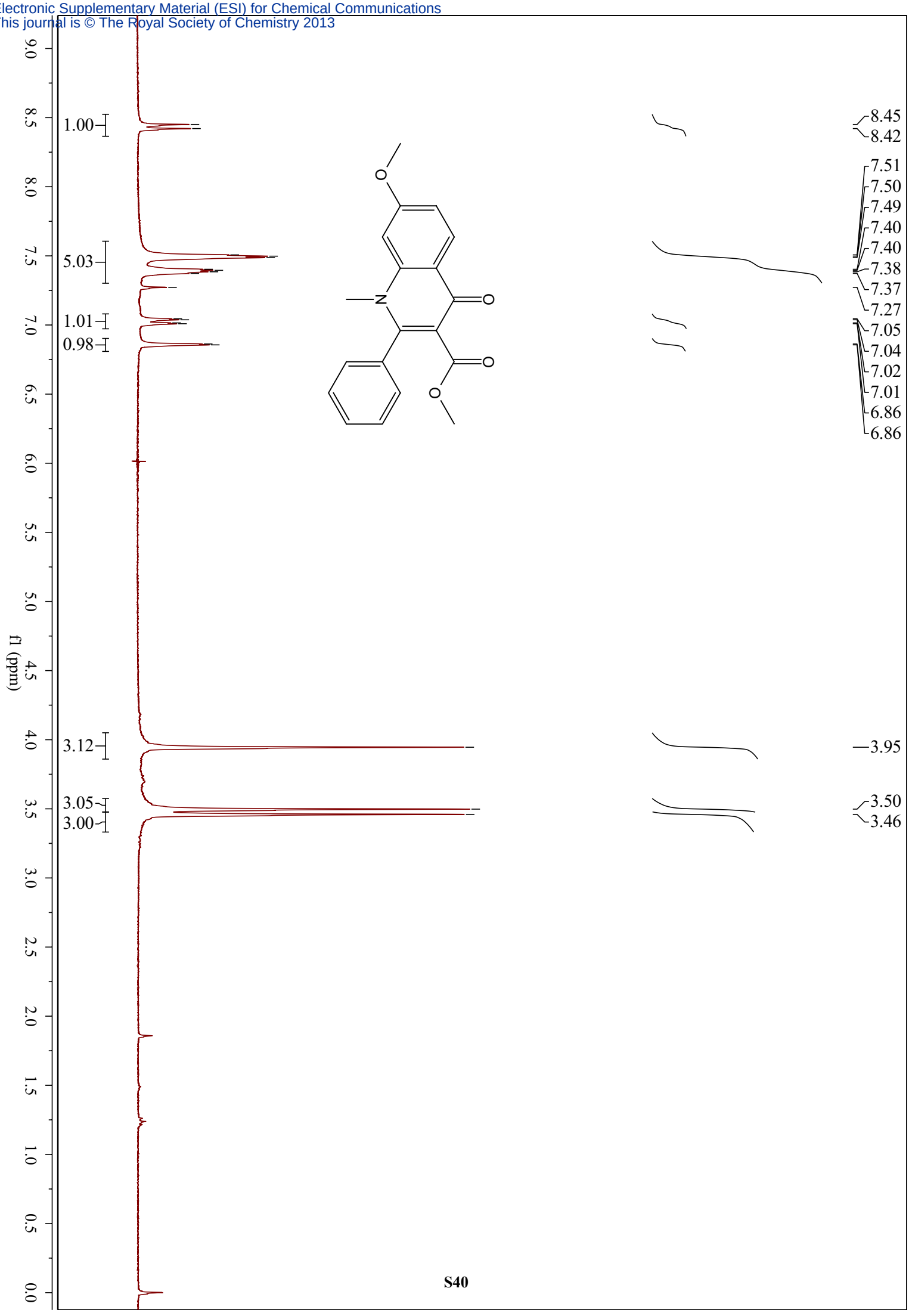


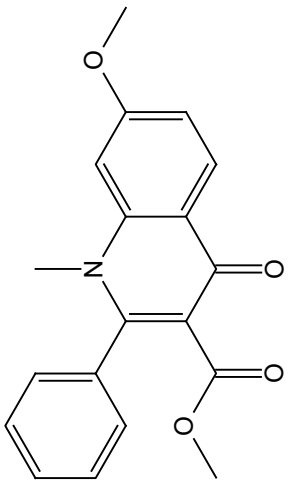


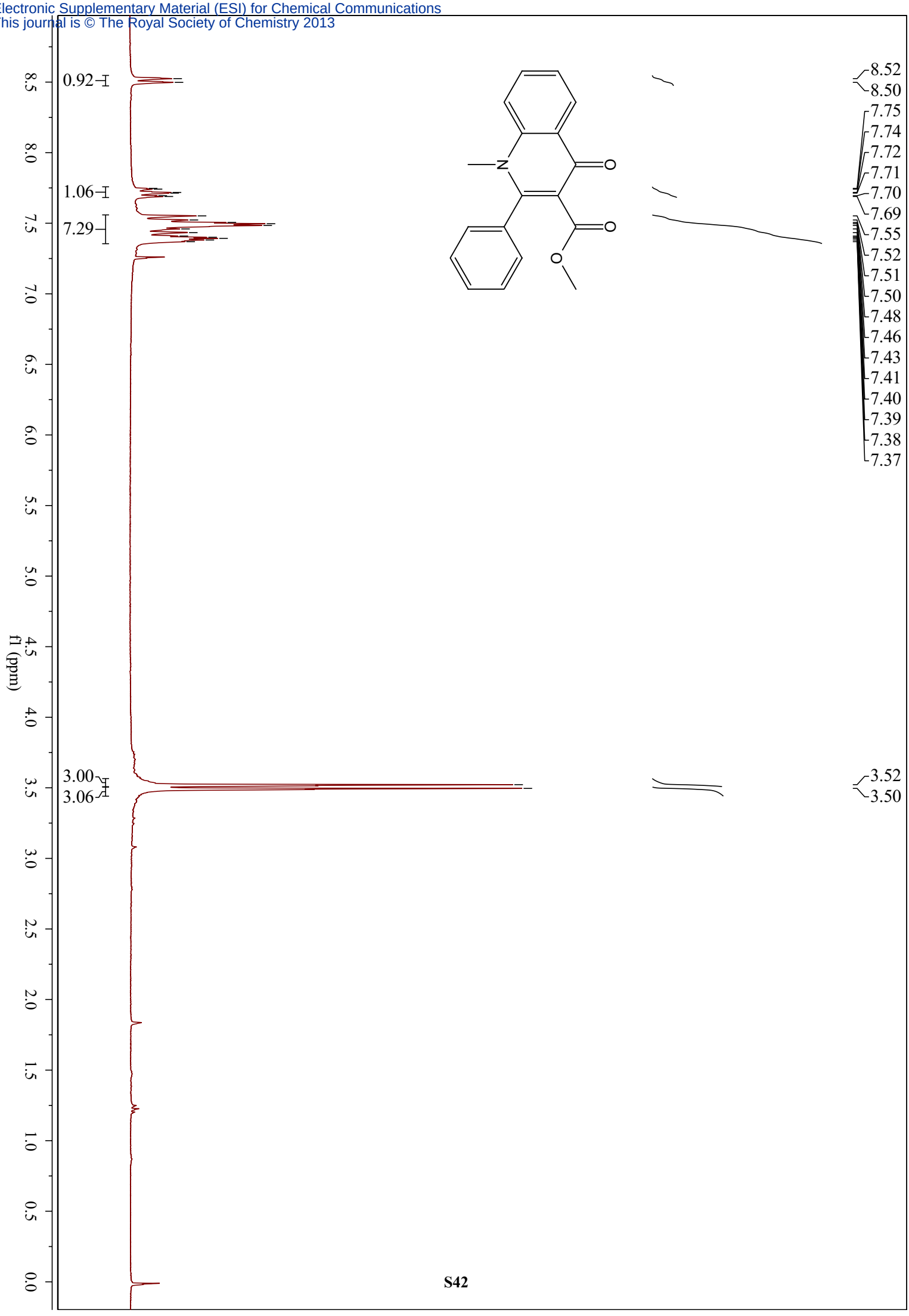


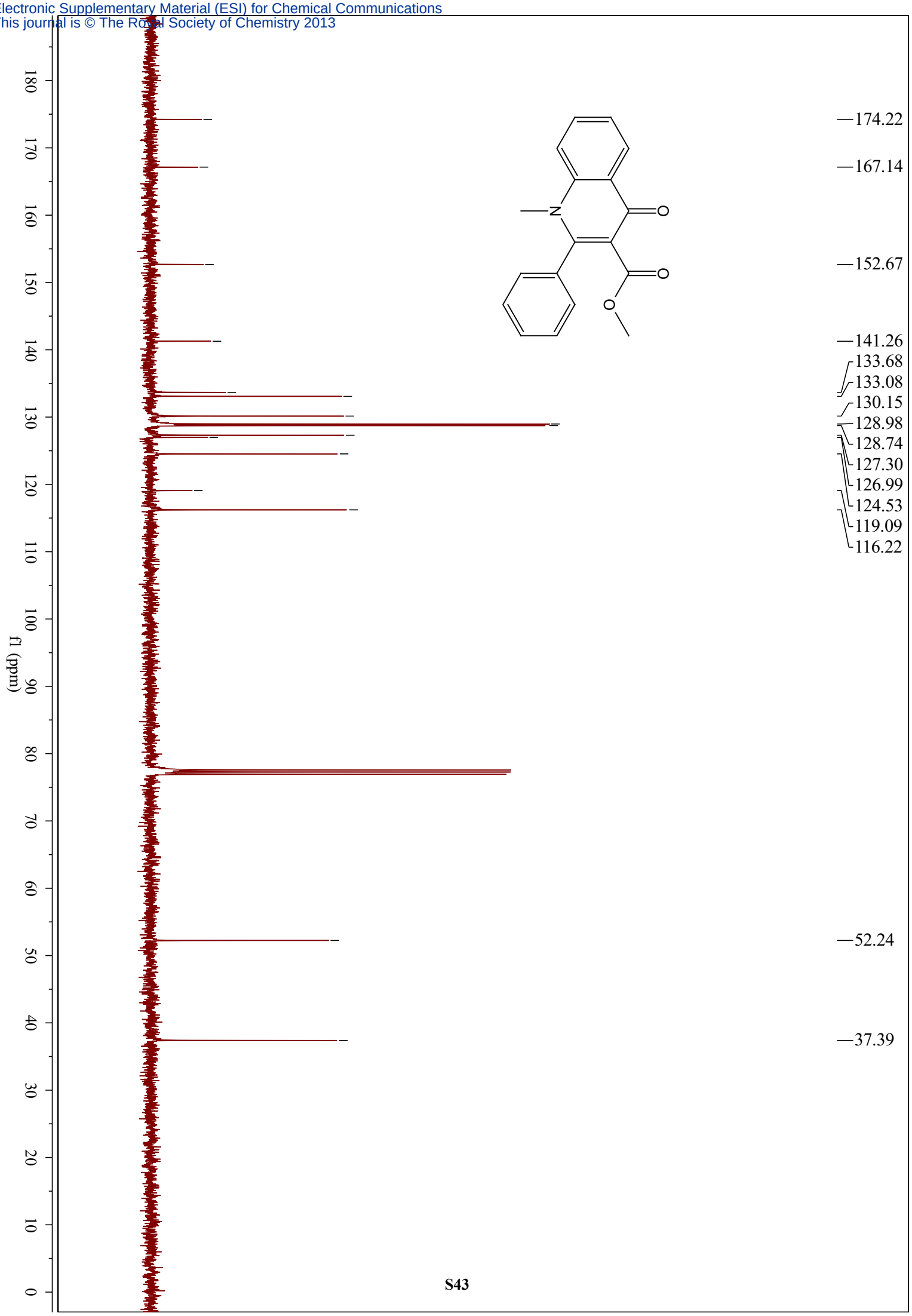


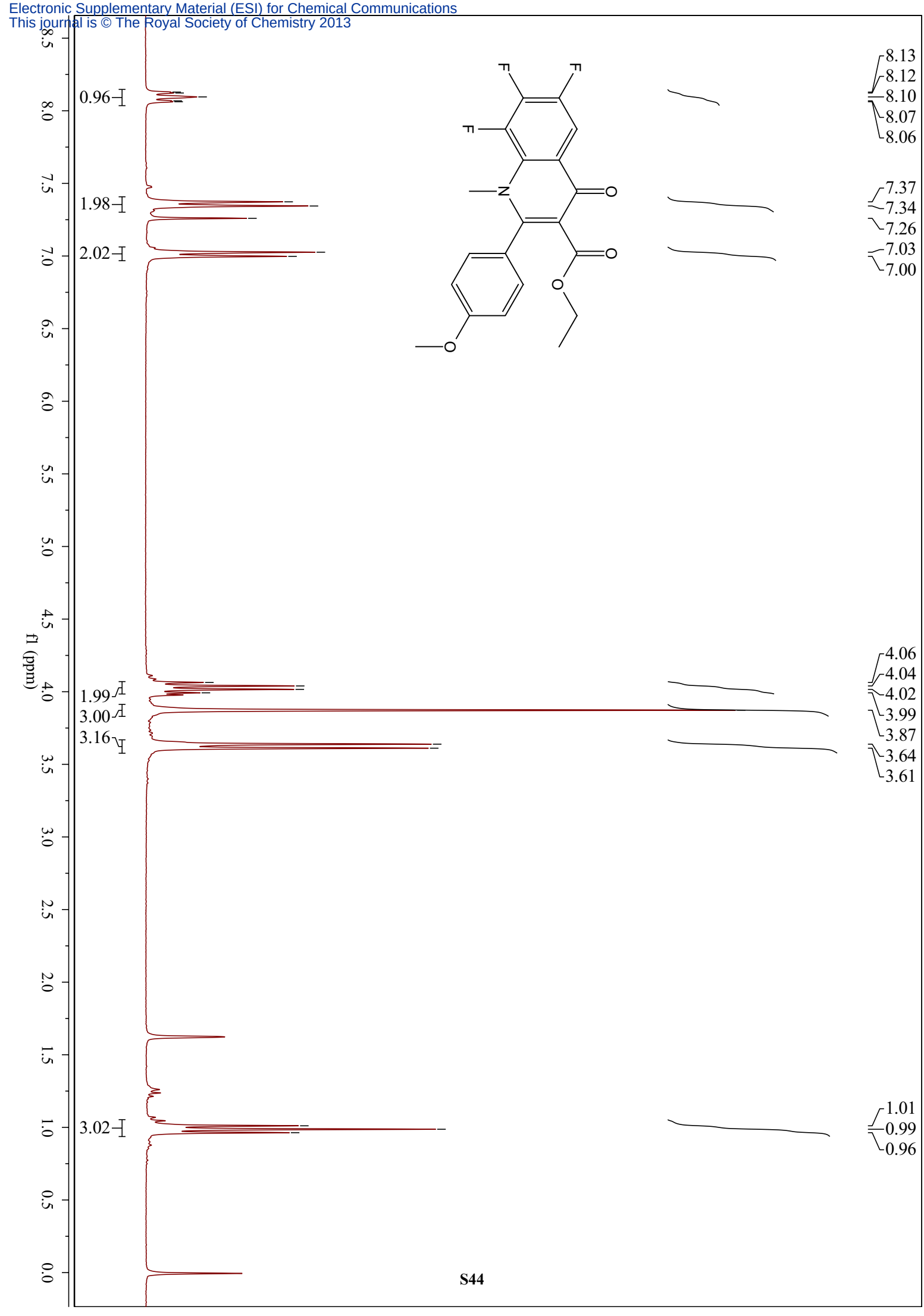


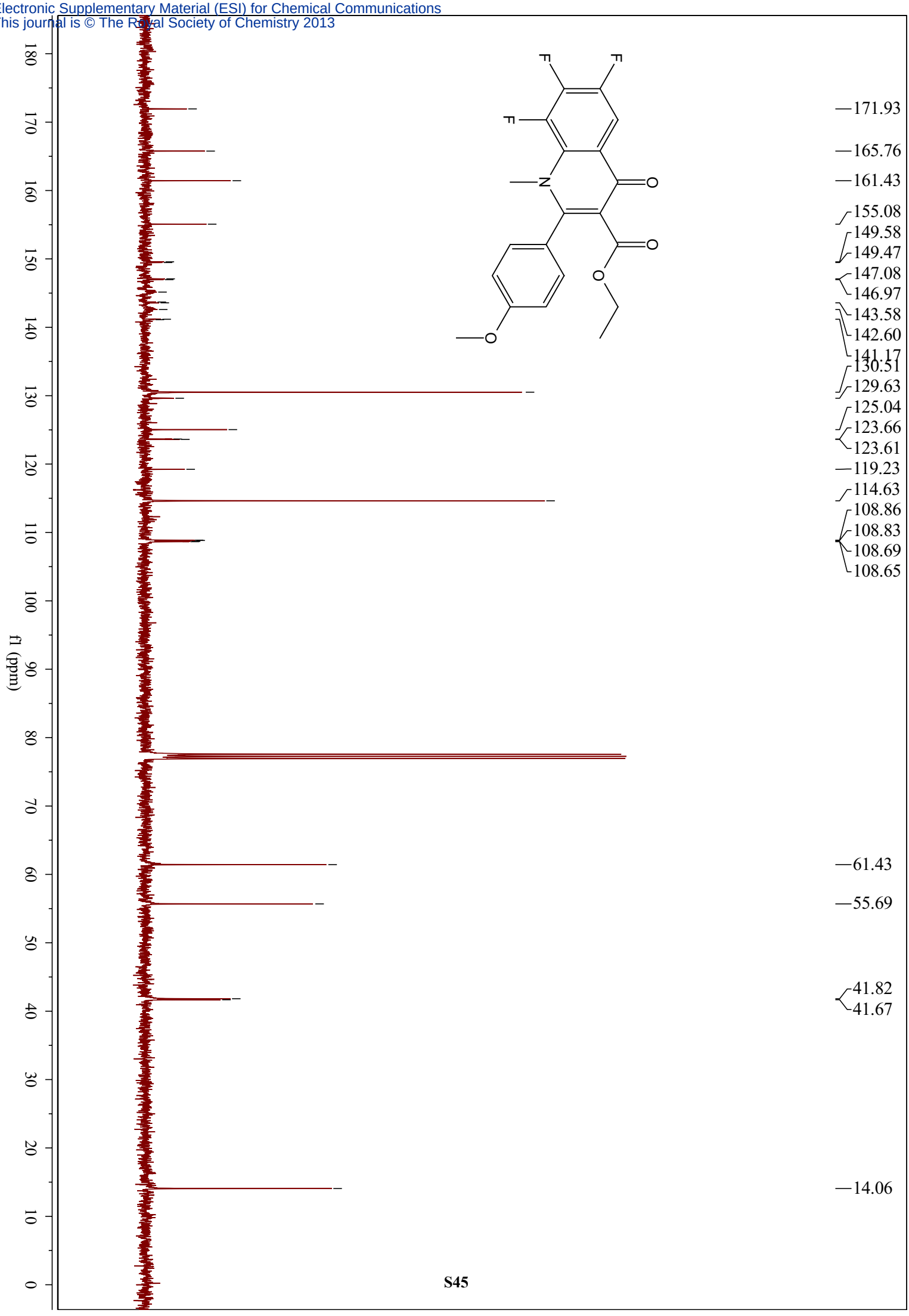


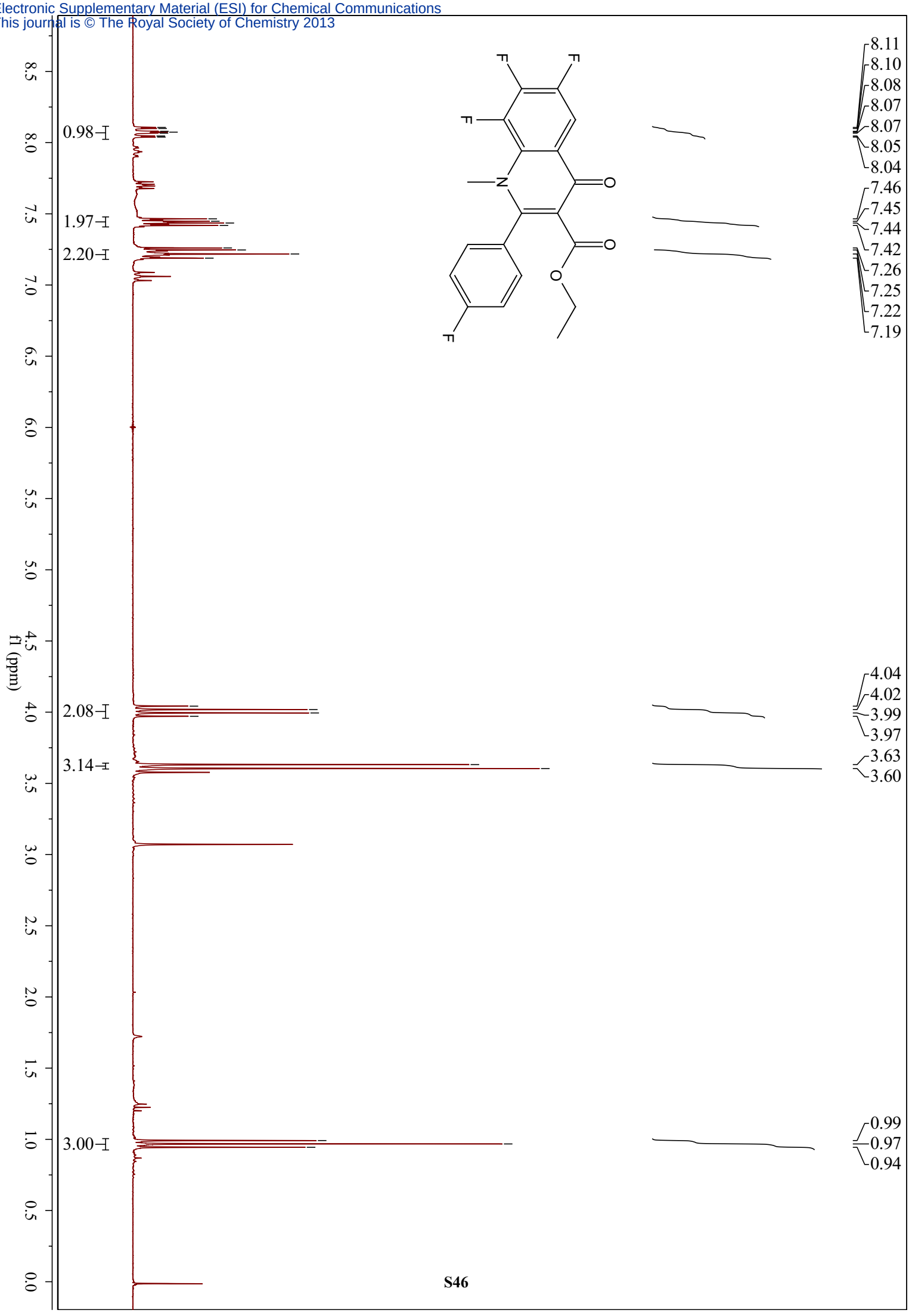


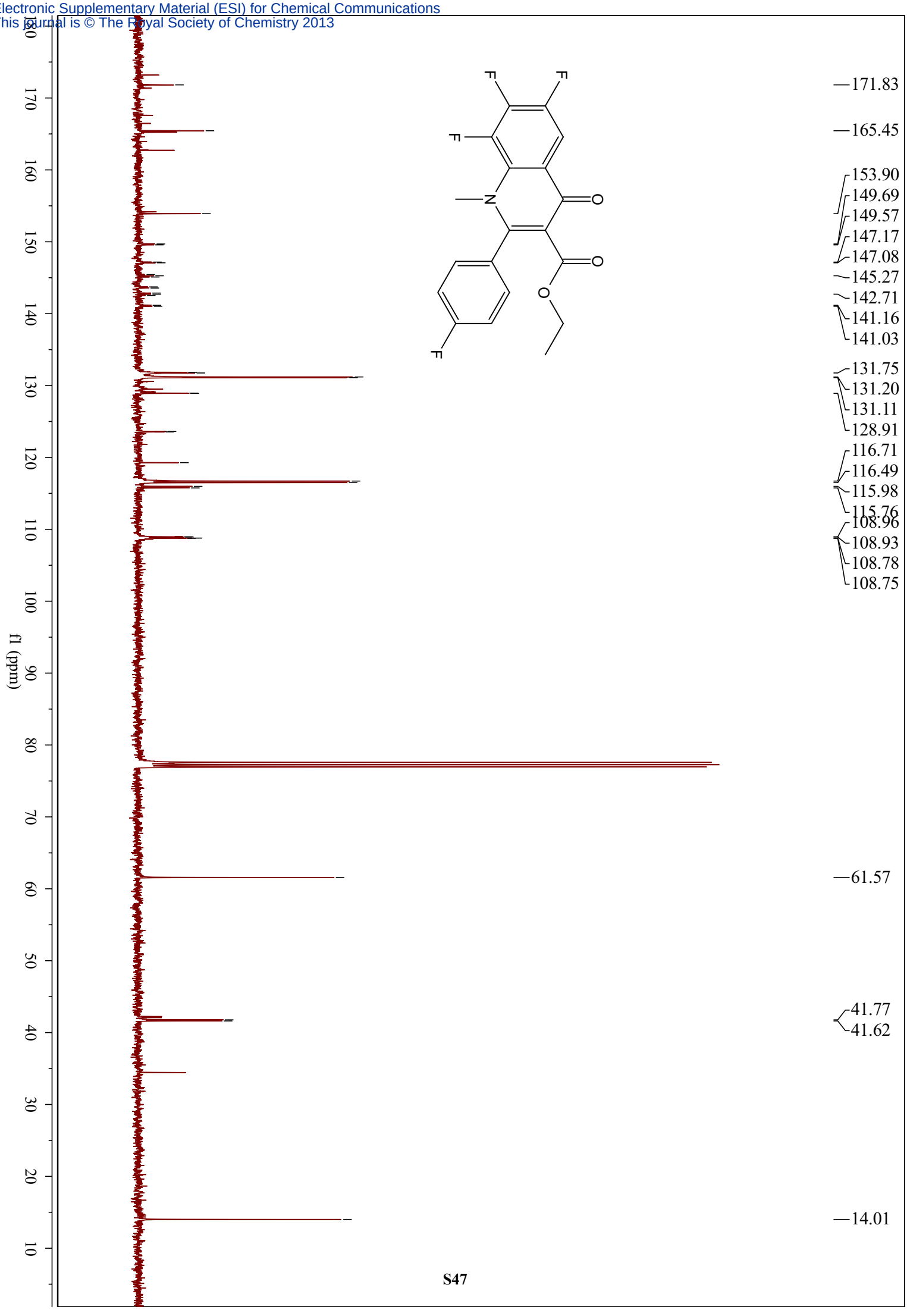


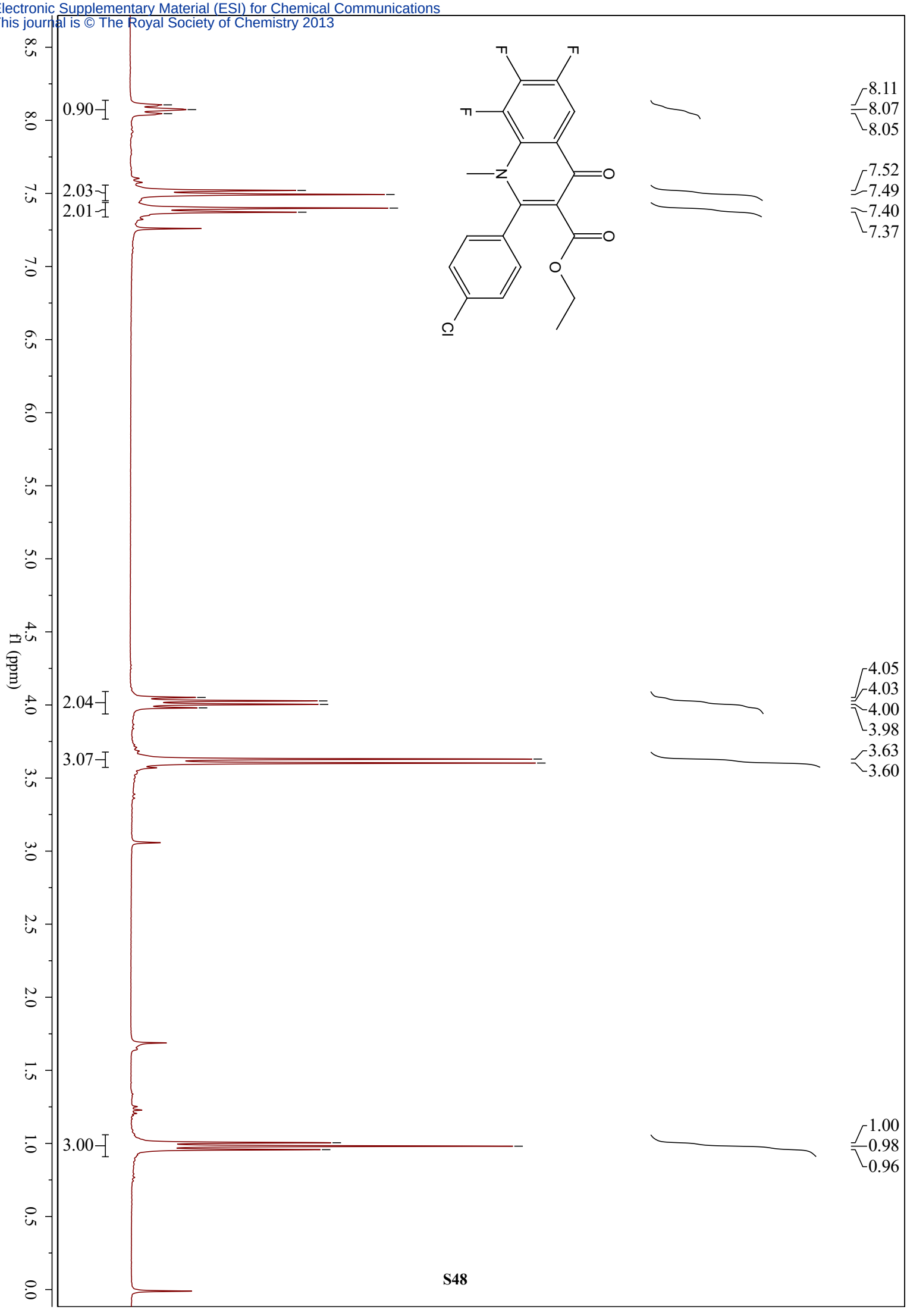


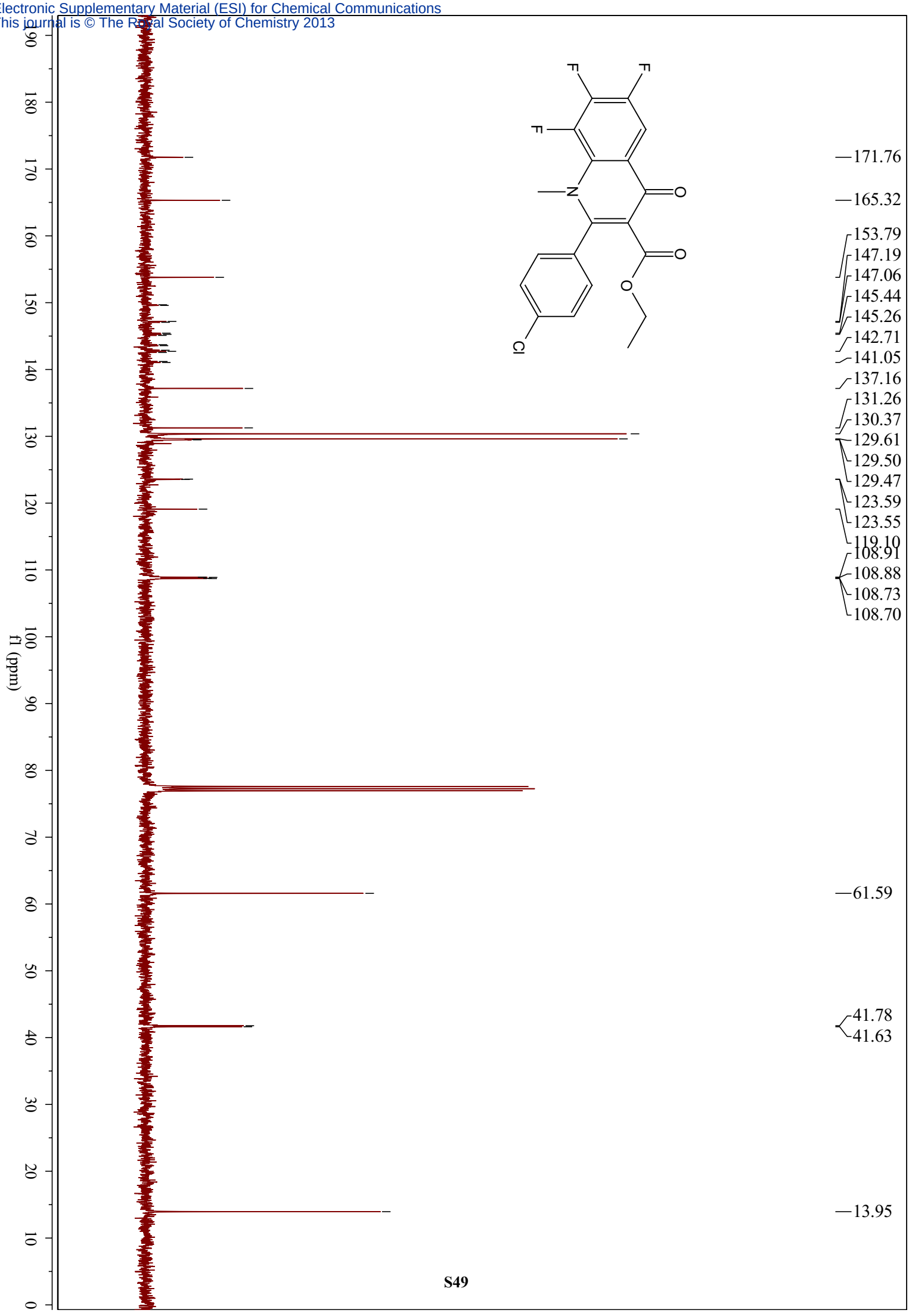


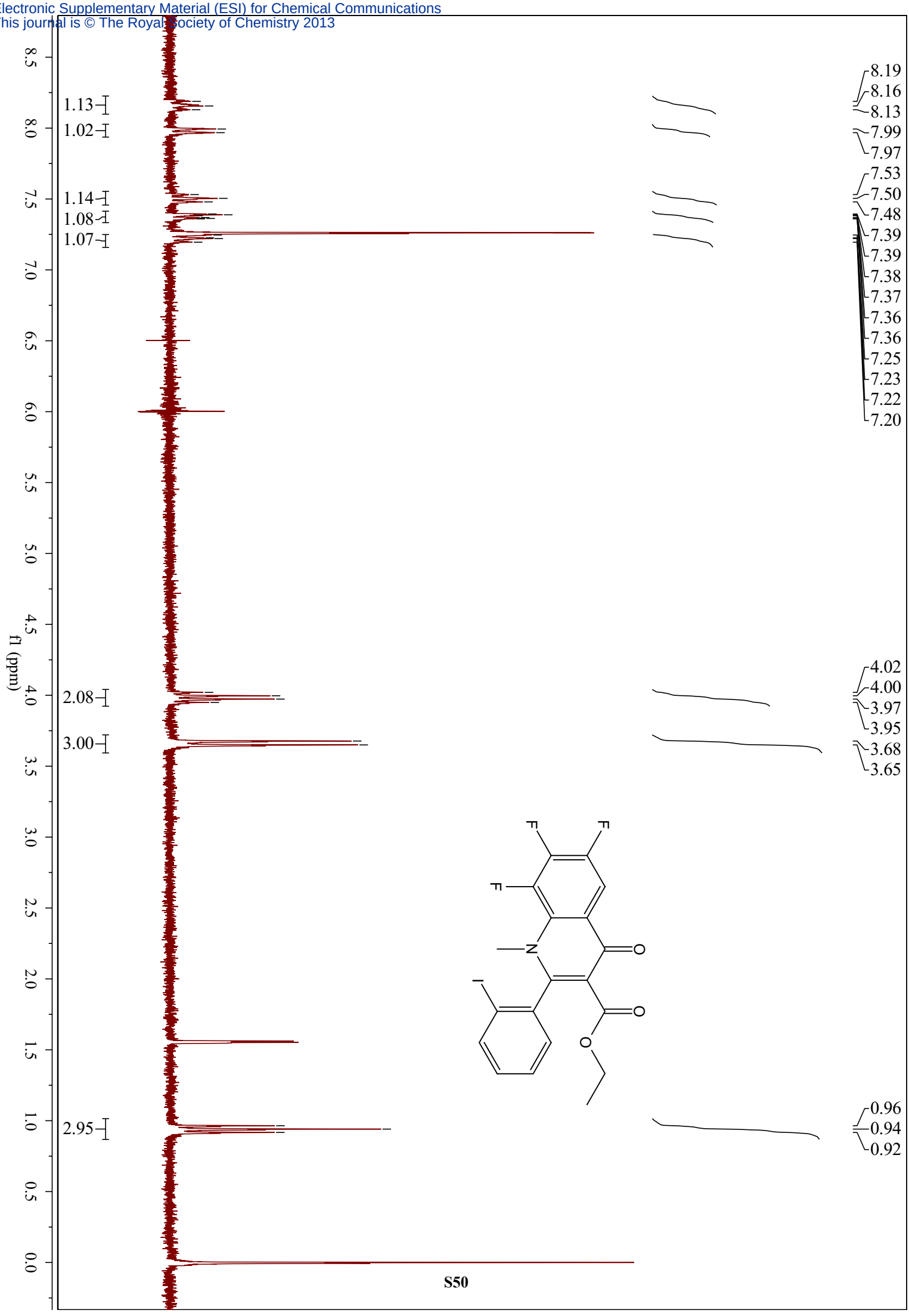


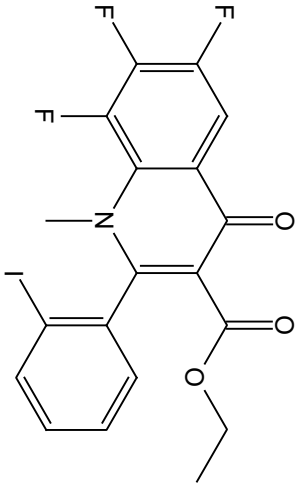


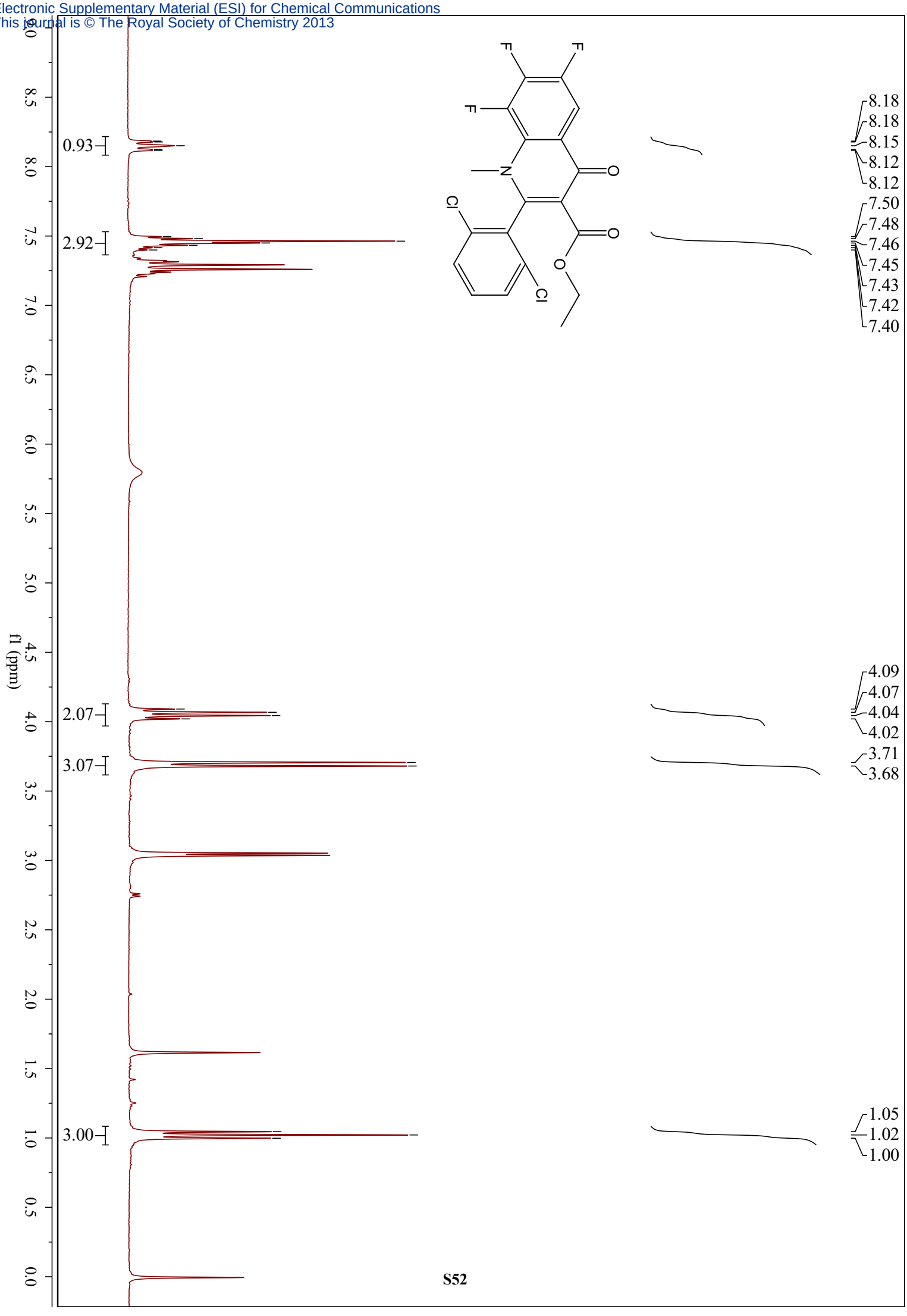


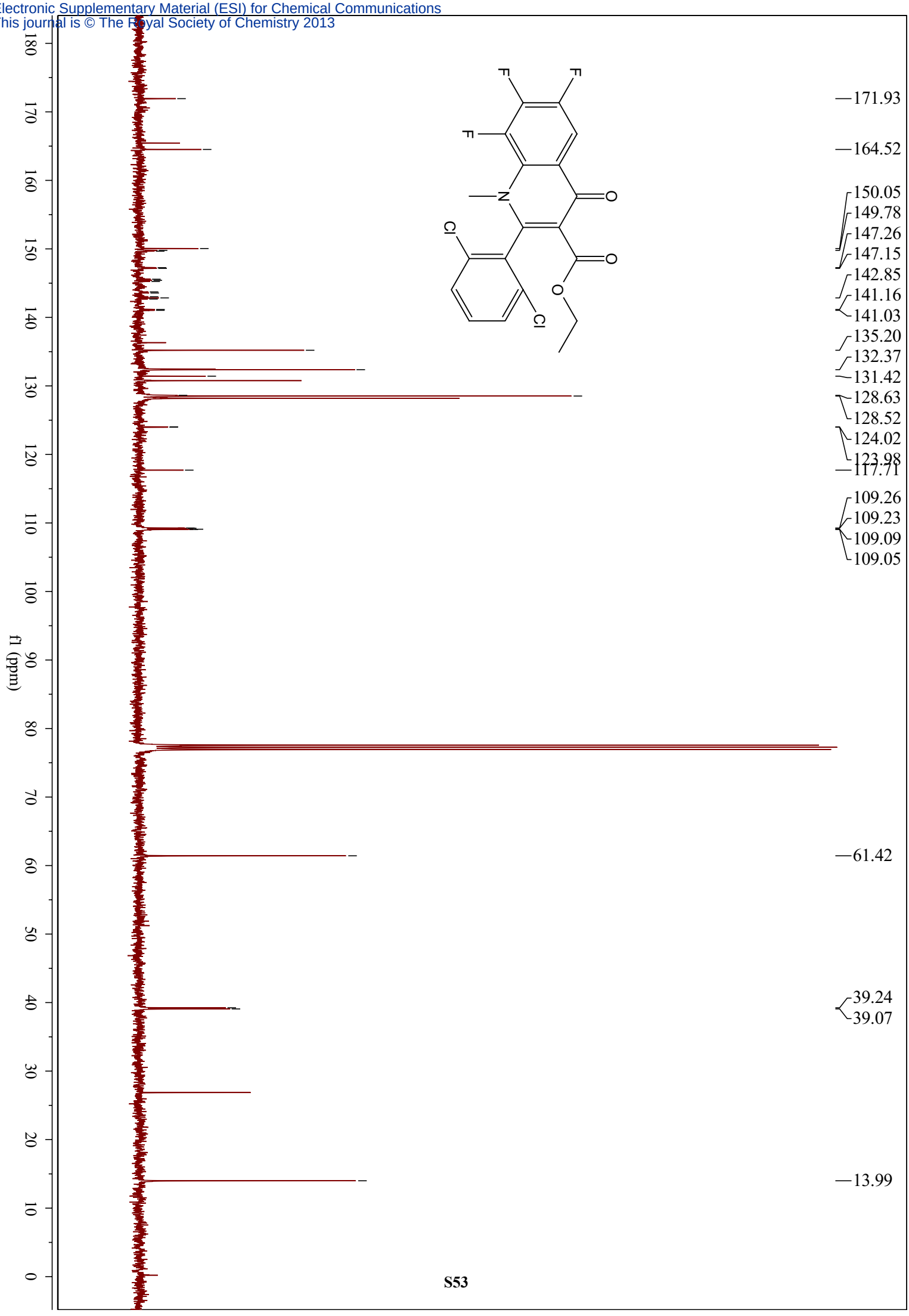


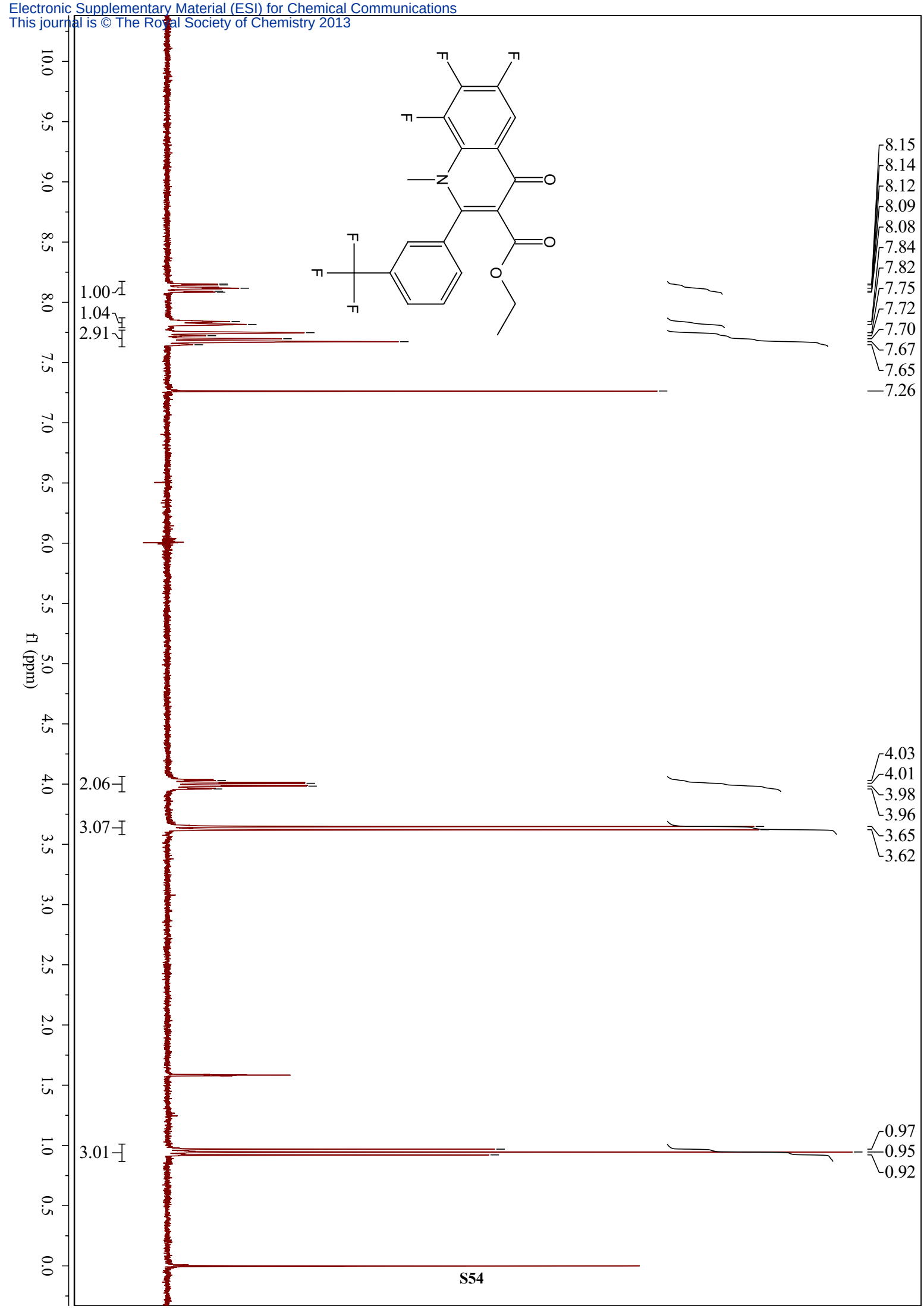


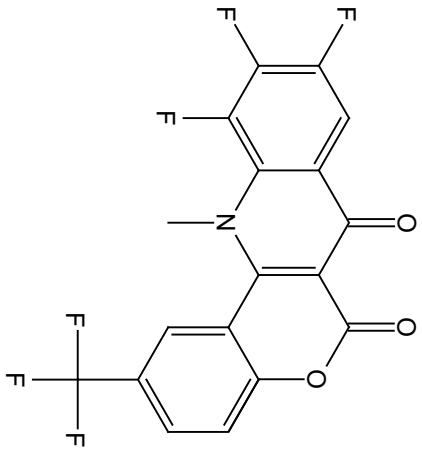


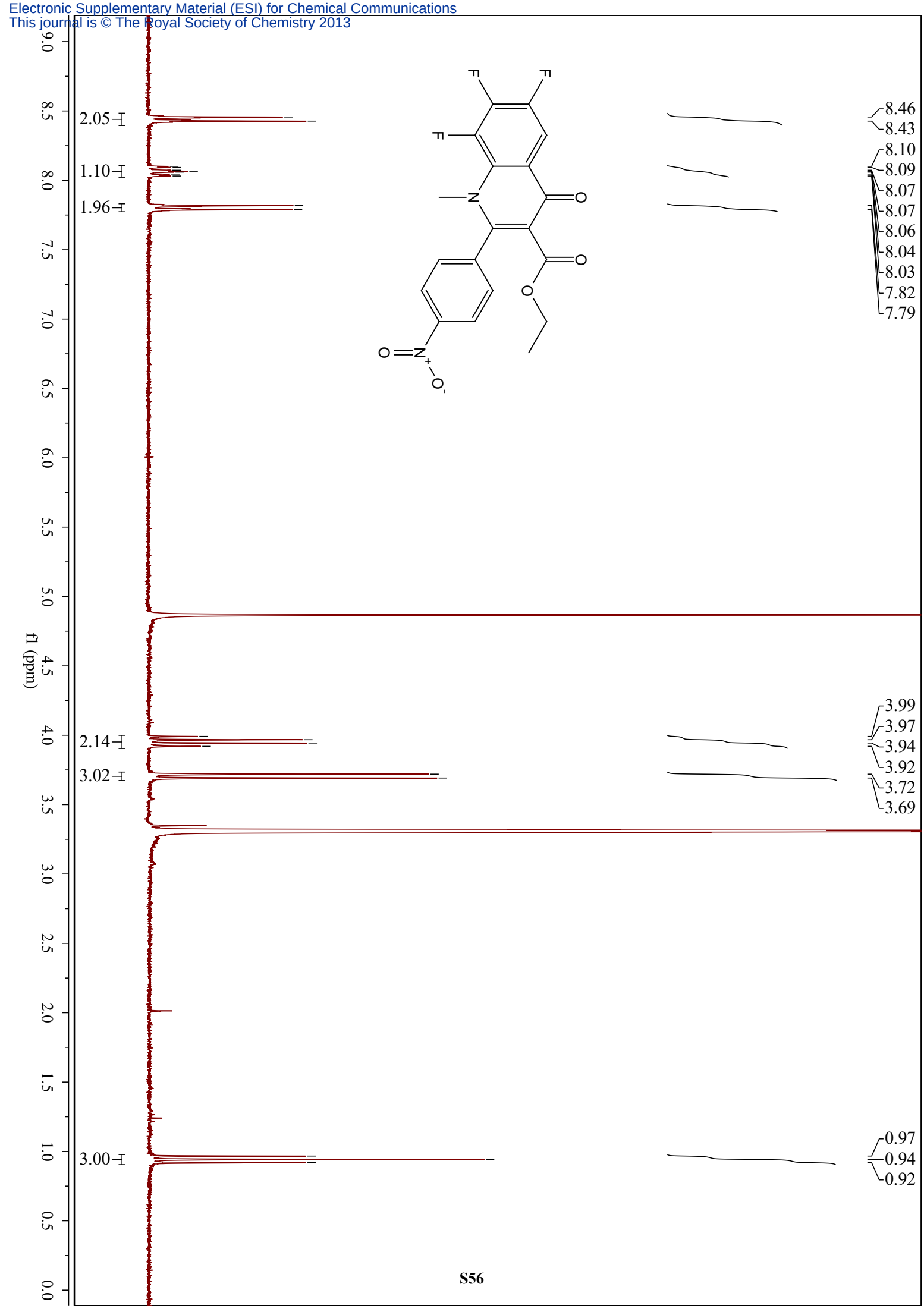


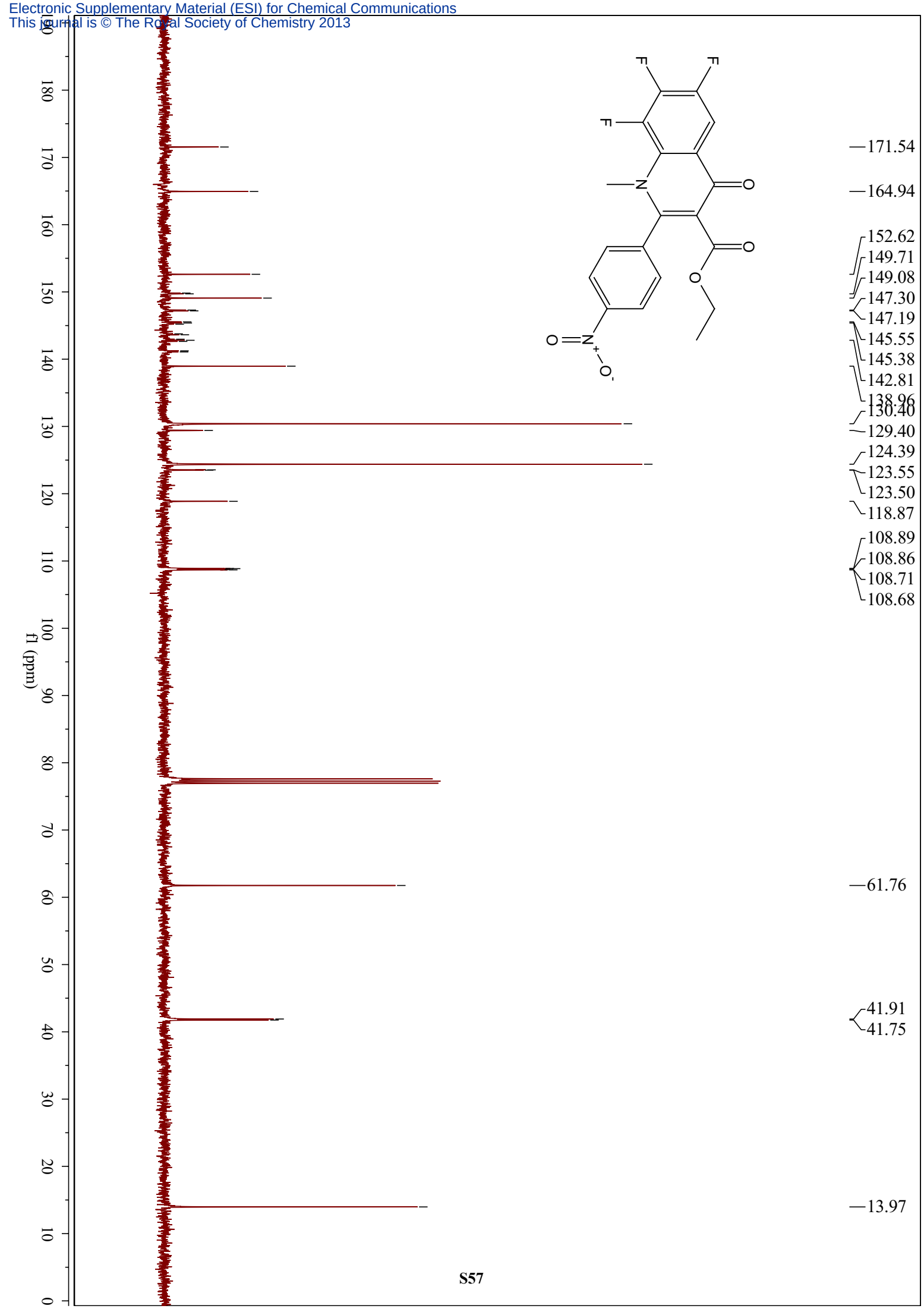


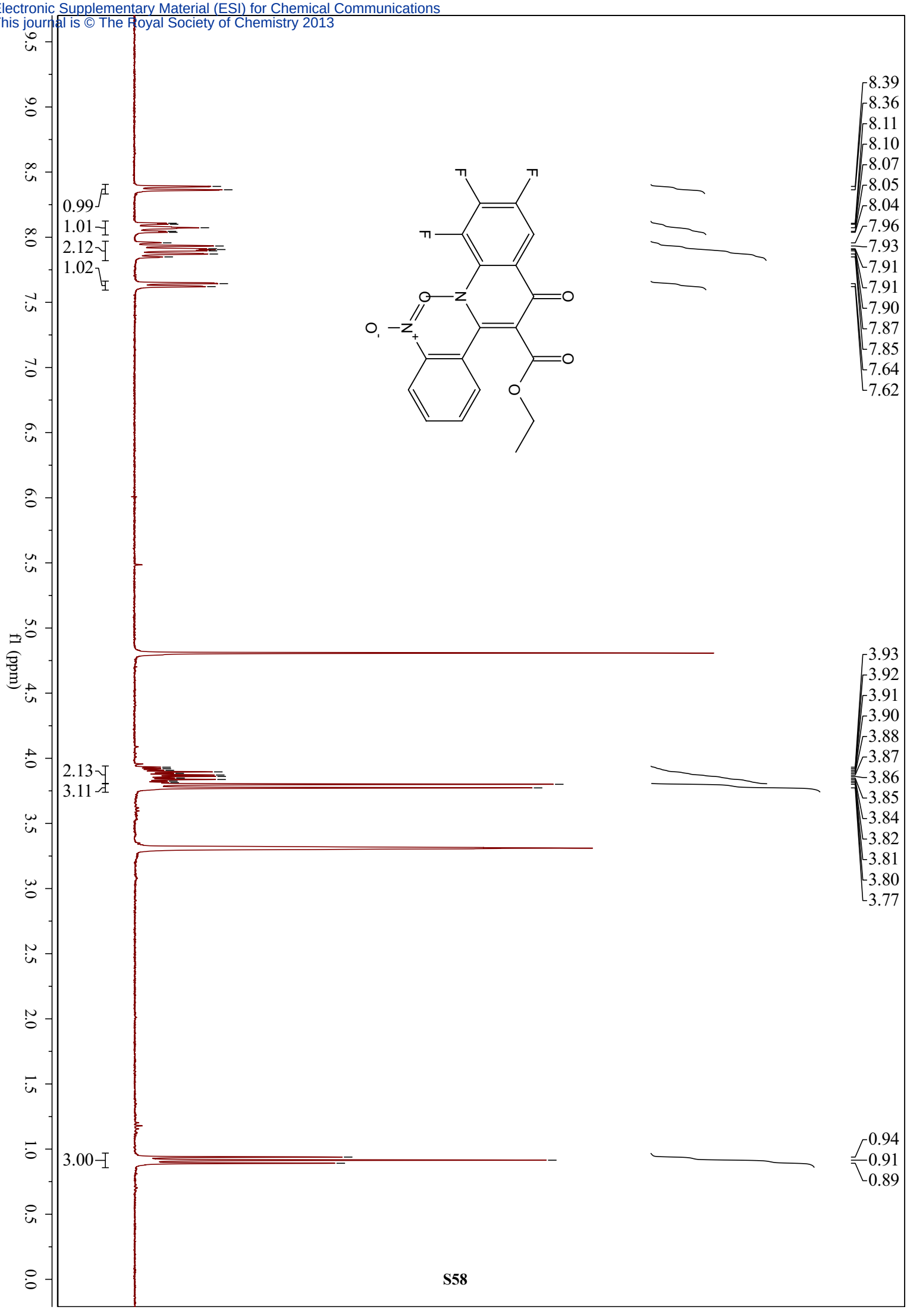


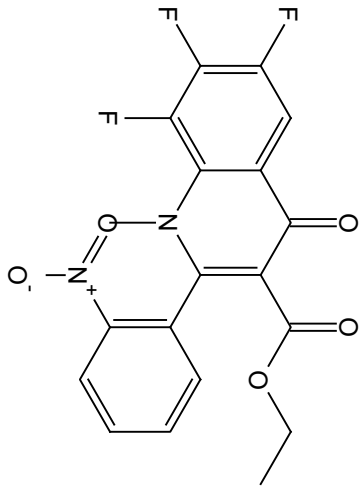


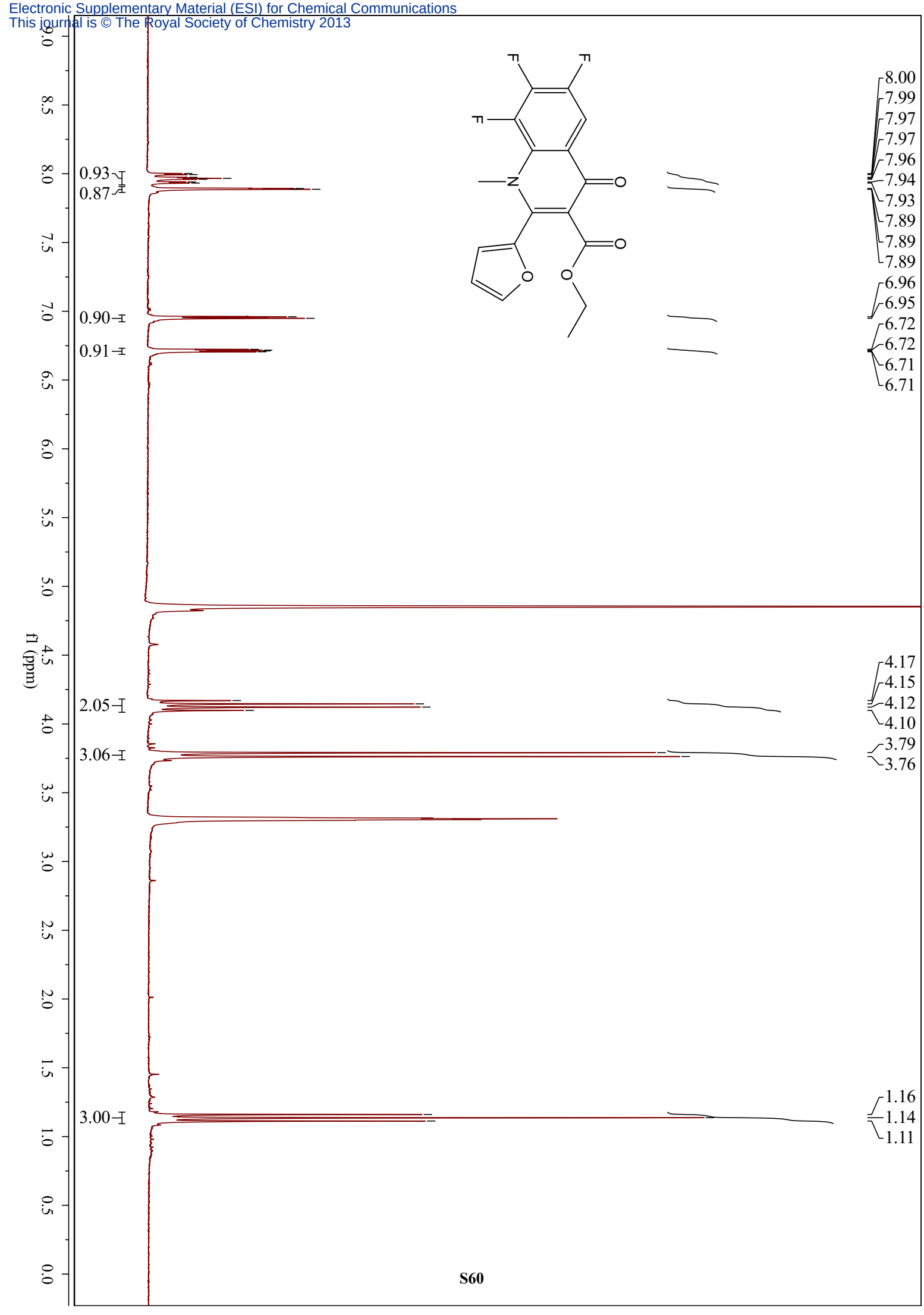


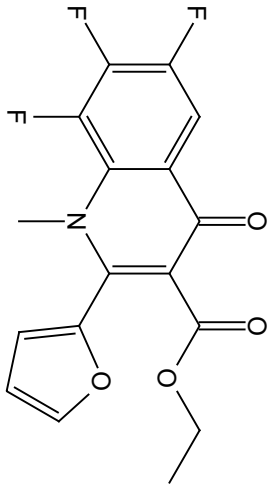






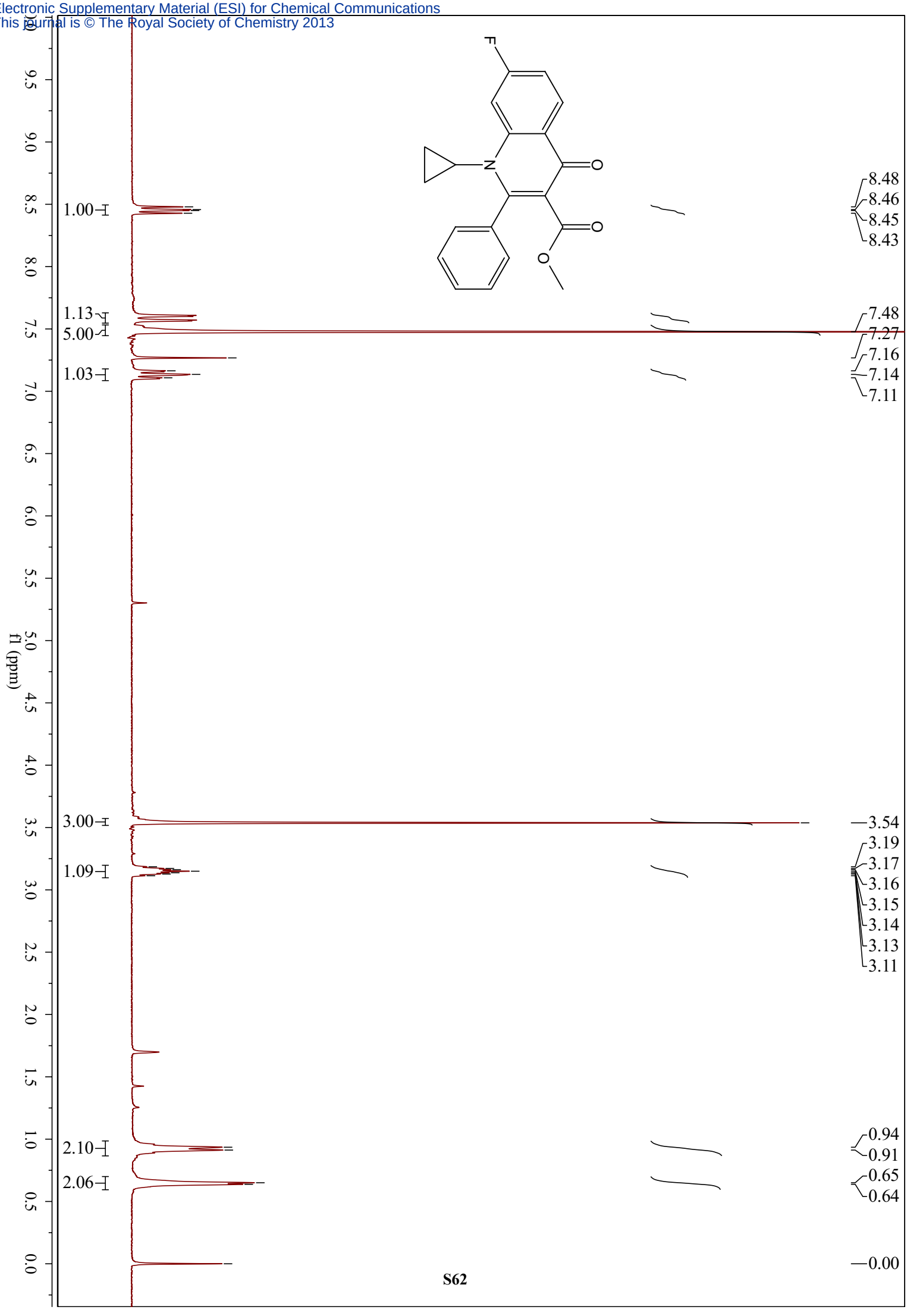


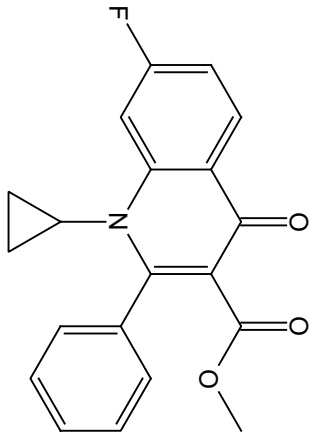




172.20
165.35
149.74
147.13
145.73
145.45
144.57
144.51
142.73
141.30
141.16
129.90
123.70
123.65
119.01
116.17
112.10
108.70
108.67
108.52
108.48
61.85
42.37
42.23
14.22

f1 (ppm)





174.04
166.83
166.37
163.87
153.95
144.21
144.09
134.34
130.05
129.94
128.78
128.71
123.43
120.10
113.21
112.98
104.47
104.20
52.45
33.05
13.11

f1 (ppm)