Supporting Information

Asymmetric cyclopropanation of olefins catalysed by Cu(I) complexes of chiral pyridine-containing macrocyclic ligands (Pc-L*)

Brunilde Castano[a], Stefano Guidone,[a,e] Emma Gallo,[a] Fabio Ragaini,[a] Nicola Casati,[b] Piero Macchi,[c] Massimo Sisti[d] and Alessandro Caselli*[a]

[a] *Dipartimento di Chimica, Università di Milano, and ISTM-CNR; Via Golgi 21, 20133 Milano, Italy. Fax: (+39)02 5031 4405; Tel: (+39)02 5031 4372; E-mail: alessandro.caselli@unimi.it*

[b] *Laboratory for Synchrotron Radiation - Condensed Matter, Swiss Light Source, Paul Scherrer Institut,Villigen PSI CH-5232 Villigen Switzerland.*

[c] *Department of Chemistry and Biochemistry, University of Bern, Freiestrasse 3, CH3012, Bern, Switzerland.*

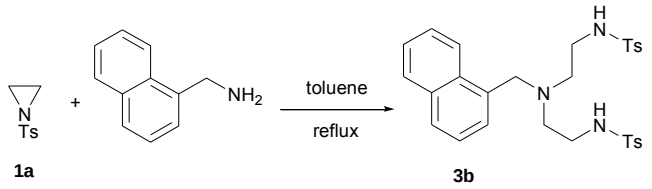
[d] *Dip. Scienza e Alta Tecnologia, Università degli Studi dell'Insubria, Via Valleggio 11, 22100 Como, Italy.*

[e] *Present address: EaStCHEM School of Chemistry, University of St Andrews, St Andrews, UK, KY16 9ST*

General. NMR spectra were recorded on Bruker Avance 300-DRX or Avance 400-DRX spectrometers. Chemical shifts (ppm) are reported relative to TMS. The ^{1}H NMR signals of the compounds described in the following have been attributed by COSY and NOESY techniques. Assignments of the resonance in ^{13}C NMR were made using the APT pulse sequence and HSQC and HMBC techniques. The ^{15}N NMR signals of the compound described have been attributed by HMBC technique. Infrared spectra were recorded on a BIO-RAD FTS-7 spectrophotometer. Elemental analyses and mass spectra were recorded in the analytical laboratories of Milan University. GC-MS analysis were performed on a Shimadzu GCMS-QP5050A instrument. Optical rotation were measured on a Perkin Elmer instruments model 343 plus; $[\alpha]_D$ values are given in 10^{-1} deg cm^2 g^{-1}. Microwave assisted reactions were performed with a MILESTONE® microSYNT multimode labstation, using 12 mL sealed glass vessels. The internal temperature was detected with a fiber optic sensor. Unless otherwise specified, all the reactions were carried out in a dinitrogen atmosphere employing standard Schlenk techniques and magnetic stirring. Solvents were dried prior use by standard procedures and stored under dinitrogen. α -Methylstyrene was distilled over CaH_2 and stored under dinitrogen. Copper(I) triflate benzene complex, copper(I) tetrakis-acetonitrile esafluorophosphate complex and copper(I) tetrakis-acetonitrile tetrafluoro borate

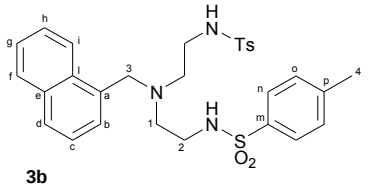
complex were synthesized following literature methods.[1] All other starting materials were commercial products and were used as received. The synthesis and characterization of bis(sulfonamides) **3a**, the macrocycles **4a** and the copper(I) complexes **6a** were already reported.[2] The synthesis and characterization of bis(sulfonamides) **3c-d**, the macrocycles **4c-d** and the copper(I) complexes **6c-d, 8d-10d** were reported in a previous communication.[3] The collected analytical data for *cis* and *trans* ethyl-2-methyl-2-phenylcyclopropanecarboxylate,[4], *cis* and *trans* *tert*-butyl 2-methyl-2-phenylcyclopropanecarboxylate,[5] *cis* and *trans* ethyl-2-phenylcyclopropanecarboxylate,[6] *cis* and *trans* ethyl-2-*p*-tolyl-cyclopropanecarboxylate,[7] *cis* and *trans* ethyl 2-(4-chlorophenyl)cyclopropanecarboxylate,[7] ethyl-2,2-diphenylcyclopropanecarboxylate,[6] *cis* and *trans* ethyl 2,2-dimethyl-3-(2-methylpropenyl)cyclopropanecarboxylate (ethyl chrysanthemate),[5] dimethyl-2-oxabicyclo[3.1.0]hex-3-ene-3,6-dicarboxylate[8] and *cis* and *trans* ethyl-2-hexylcyclopropanecarboxylate[9] are in agreement with those reported in the literature.

Synthesis of 3b



1a **3b**

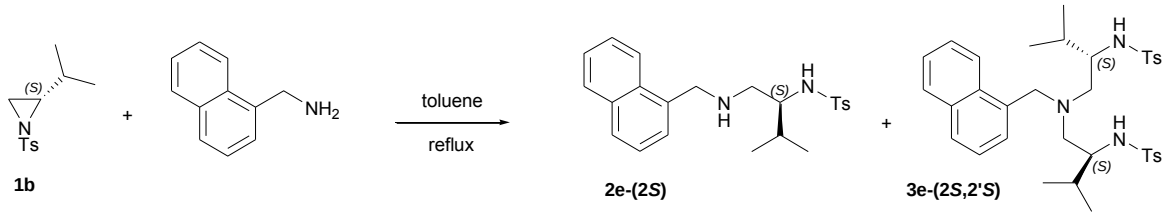
This synthesis can be performed in the air. A solution of 1-tosylaziridine **1a** (2.24 g, 11.5 mmol) and 1-naphthylmethylamine (0.811 g, 5.16 mmol) in distilled toluene (11 mL) was stirred and heated under reflux for 5 h. The mixture was dried and purified by silica gel chromatography using *n*-hexane:ethyl acetate = 6:4 as eluant, obtaining pure amine **3b** (2.14 g, 5.04 mmol, yield: 75%).



3b

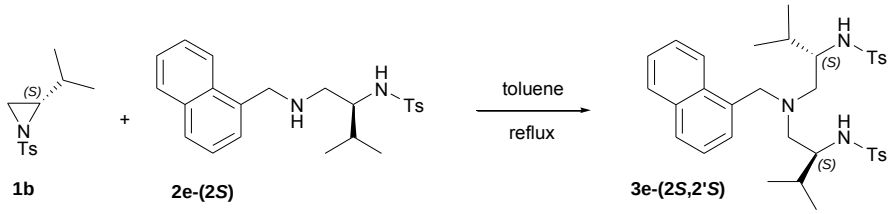
^{1}H NMR (300 MHz; $CDCl_3$; T = 300 k) δ 8.14 (1H, d, *J* = 8.3 Hz, H^i), 7.86 (1H, d, *J* = 8.3 Hz, Ar*H*), 7.78 (1H, m, Ar*H*), 7.54 (4H, d, *J* = 8.0 Hz, H^n) overlapping with 7.61-7.49 (2H, m, Ar*H*), 7.42-7.32 (2H, m, Ar*H*), 7.19 (4H, d, *J* = 8.0 Hz, H^o), 4.83 (2H, bs, N*H*), 4.00 (2H, br, CH_2^3), 2.90 (4H, m, CH_2), 2.66 (4H, m, CH_2), 2.38 (6H, s, CH_3^4). ^{13}C NMR (75 MHz; $CDCl_3$; T = 300 k) δ 143.5 (*C*), 136.7 (*C*), 134.0 (*C*), 132.0 (*C*), 129.8 (*C*H), 129.0 (C^0H), 127.1 (C^nH), 126.3 (*C*H), 125.4 (*C*H), 123.7 (C^iH), 54.2(CH_2), 40.8 (C^3H_2), 21.6 (C^4H_3). Signals relative to quaternary carbons, aromatic *C*H and CH_2 were not detected. Elemental Analysis: Found: C, 63.1; H, 6.2; N, 7.5% Calc. for $C_{29}H_{33}N_3O_4S_2$: C, 63.1; H, 6.0; N, 7.6%.

Synthesis of 2e-(2*S*) and 3e-(2*S*,2'*S*)



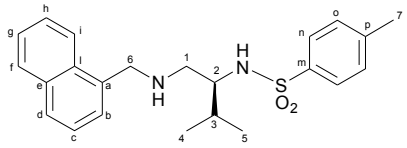
This synthesis can be performed in the air. A solution of (*S*)-2-isopropyl-1-tosylaziridine **1b** (1.732 g, 7.23 mmol) and 1-naphthylmethylamine (0.494 g, 3.14 mmol) in distilled toluene (15 mL) was stirred and heated under reflux for 5 h. The mixture was dried and purified by silica gel chromatography using *n*-hexane:ethyl acetate = 7:3 as eluant, obtaining monoamine **2e-(2*S*)** (0.875 g, 2.21 mmol, yield: 70%) and pure amine **3e-(2*S*,2'*S*)** (0.600 g, 0.944 mmol, yield: 30%).

Synthesis of 3e-(2*S*,2'*S*) from 2e-(2*S*) under conventional heating



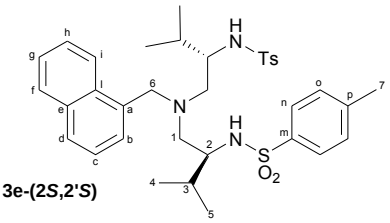
A solution of (*S*)-2-isopropyl-1-tosylaziridine **1b** (0.258 g, 1.08 mmol) and monoamine **2e-(2*S*)** (0.349 g, 0.88 mmol) in toluene (10 mL) was stirred and heated under reflux for 33 h. The mixture

was dried and purified by silica gel chromatography using *n*-hexane:ethyl acetate = 7:3 as eluant, obtaining the amine **3e-(2*S*,2'*S*)** (0.330 g, 0.519 mmol, yield: 74%).



2e-(2S)

^{1}H NMR (300 MHz; $CDCl_3$; T = 300 k) δ 8.02 (1H, dd, *J* = 7.7 Hz, *J* = 1.3 Hz, H^{i}), 7.89 (1H, dd, *J* = 7.7 Hz, *J* = 1.3 Hz, H^{f}), 7.81 (1H, dd, *J* = 7.7 Hz, *J* = 1.3 Hz, H^{d}), 7.62 (2H, d, *J* = 7.9 Hz, H^{n}), 7.55 (1H, t, *J* = 7.7 Hz, H^{g}), 7.54 (1H, t, *J* = 7.7 Hz, H^{h}), 7.42 (1H, t, *J* = 7.7 Hz, H^{c}), 7.38 (1H, d, *J* = 7.7 Hz, H^{b}), 7.08 (2H, d, *J* = 7.9 Hz, H^{o}), 4.14 (1H, d, *J* = 13.4 Hz, H^{6}), 4.08 (1H, d, *J* = 13.4 Hz, $H^{6'}$), 3.09 (1H, ddd, *J* = 6.8 Hz, *J* = 6.8 Hz, *J* = 4.4 Hz, H^{2}), 2.73 (1H, dd, *J* = 12.4 Hz, *J* = 6.8 Hz, $H^{1'}$), 2.60 (1H, dd, *J* = 12.4 Hz, *J* = 4.4 Hz, H^{1}), 2.29 (3H, s, CH_3^{7}), 1.85 (1H, m, H^{3}), 0.81 (3H, d, *J* = 6.81 Hz, CH_3^{4}), 0.79 (3H, d, *J* = 6.81 Hz, CH_3^{5}). The signals relative to NH were not detected. ^{13}C NMR (75 MHz; $CDCl_3$; T = 300 k) δ 129.6 (C^{n}H), 129.0 (C^{f}H), 128.5 (C^{d}H), 127.2 (C^{o}H), 126.7 (*C*H), 126.6 (*C*H), 126.1 (*C*H), 125.5 (*C*H), 123.6 (C^{i}H), 58.2 (C^{2}H), 50.9 ($C^{6}H_2$), 49.0 ($C^{1}H_2$), 30.5 (C^{3}H), 21.5 ($C^{7}H_3$), 18.9 ($C^{4}H_3$), 18.4 ($C^{5}H_3$). The signals relative to quaternary carbons were not detected. Elemental Analysis: Found: C, 69.8; H, 7.0; N, 6.9% Calc. for $C_{23}H_{28}N_2O_2S$: C, 69.7; H, 7.1; N, 7.1%. MS (EI): m/z 397 (M^{+}+1). $[\alpha]_D^{20}$ = - 3.611° (c 1.082 in $CHCl_3$).

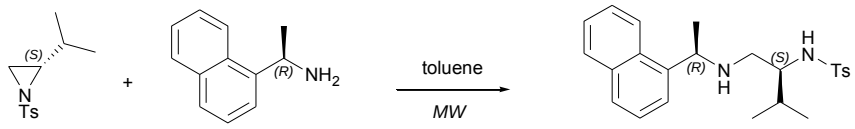


3e-(2S,2'S)

^{1}H NMR (300 MHz; $CDCl_3$; T = 300 k) δ 8.18 (1H, d, *J* = 8.0 Hz, H^{i}), 7.85-7.76 (2H, m, H^{d} and H^{f}), 7.75 (4H, d, *J* = 8.2 Hz, H^{n}), 7.51-7.38 (3H, m, H^{c}, H^{h} and H^{g}), 7.34 (1H, d, *J* = 8.0 Hz, H^{b}), 7.23 (4H, d, *J* = 8.2 Hz, H^{o}), 4.99 (2H, d, *J* = 6.0 Hz, N*H*), 4.04 (1H, d, *J* = 13.1, H^{6}), 3.80 (1H, d, *J* = 13.1 Hz, $H^{6'}$), 3.45 (2H, m, H^{2}), 2.55-2.35 (4H, m, H^{1}), overlapping with 2.38 (6H, s, CH_3^{7}), 1.79

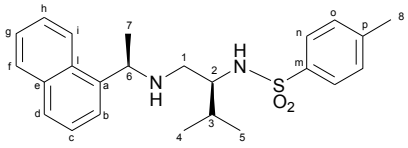
(2H, m, H^3), 0.53 (6H, d, J = 6.9 Hz, CH_3^4), 0.52 (6H, J = 6.9 Hz, CH_3^5). ^{13}C NMR (75 MHz; $CDCl_3$; T = 300 k) δ 143.2 (*C*), 138.6 (*C*), 133.9 (*C*), 132.2 (*C*), 129.6 (C^nH), 128.6 (*C*H), 128.2 (*C*H), 127.1 (C^oH), 126.3 (*C*H), 125.8 (*C*H), 125.3 (*C*H), 124.3 (C^iH), 56.9 (C^6H_2), 55.9 (C^2H), 54.9 (C^1H_2), 29.3 (C^3H), 21.6 (C^7H_3), 17.9 (C^4H_3), 16.9 (C^5H_3). A signal relative to a quaternary carbon was not detected. Elemental Analysis: Found: C, 66.3; H, 7.2; N, 6.3% Calc. for $C_{35}H_{45}N_3O_4S_2$: C, 66.1; H, 7.1; N, 6.6%. MS (EI): m/z 636 (M^++1). $[\alpha]_D^{20}$ = + 9.92 (*c* 1.31 in $CHCl_3$).

Synthesis of 2f-(1*R*,2*S*) under microwave heating



1b **2f-(1*R*,2*S*)**

This synthesis can be performed in the air. A solution of (*S*)-2-isopropyl-1-tosylaziridine **1b** (0.811 g, 3.39 mmol) and (*R*)-1-(1-naphthyl)ethyl amine (0.529 g, 3.09 mmol) in toluene (21 mL) was added in a microwave tube. The solution was stirred and heated by microwave irradiation for 3 h at 150 °C. The resulting mixture was dried and purified by silica gel chromatography using *n*-hexane:ethyl acetate = 7:3 as eluant, obtaining a yellow solid **2f-(1*R*,2*S*)** (0.904 g, 2.20 mmol, yield: 71%).

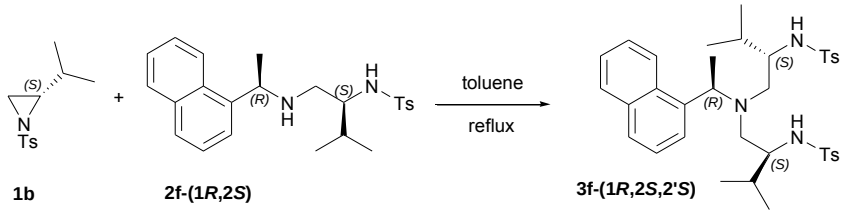


2f-(1*R*,2*S*)

^{1}H NMR (300 MHz; $CDCl_3$; T = 300 k) δ 8.03 (1H, m, H^i), 7.89 (1H, m, Ar*H*), 7.78 (2H, d, J = 8.4 Hz, H^n) overlapping with 7.79-7.75 (1H, m, Ar*H*) 7.52-7.45 (4H, m, Ar*H*), 7.25 (2H, d, J = 8.4 Hz, H^o), 5.22 (1H, br, N*H*), 4.35 (1H, q, J = 6.6 Hz, H^6), 3.08 (1H, m, H^2), 2.46-2.42 (2H, m, H^1), 2.40 (3H, s, CH_3^8), 1.85 (1H, dh, J = 13.4 Hz, J = 6.8 Hz, H^3), 1.36 (3H, d, J = 6.6 Hz, CH_3^7), 0.81 (3H, d, J = 6.8 Hz, CH_3^4), 0.78 (3H, d, J = 6.8 Hz, CH_3^5) One NH signal is too broad to be detected.

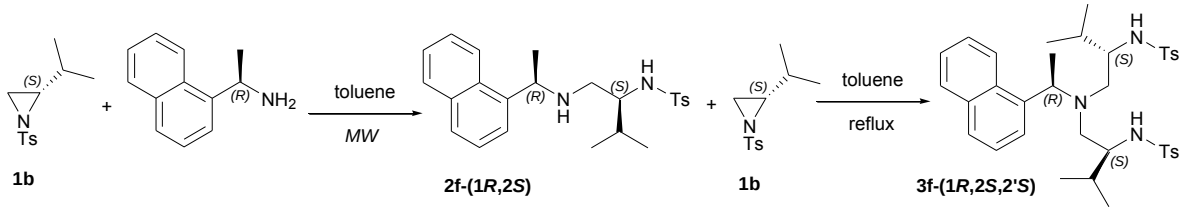
^{13}C NMR (75 MHz; $CDCl_3$; T = 300 k) δ 143.2 (*C*), 140.8 (*C*), 138.2 (*C*), 134.1 (*C*),131.3 (*C*),129.6 (*C*^{o}H), 129.1 (*C*H),127.4 (*C*H), 127.2 (*C*H), 125.9 (*C*H), 125.7 (*C*H), 125.5 (*C*H), 122.8 (*C*^{i}H),122.6 (*C*H), 59.0 (*C*^{2}H), 53.3 (*C*^{6}H), 47.4 (*C*^{1}H$_2$), 30.4 (*C*^{3}H), 23.5 (*C*^{7}H$_3$), 21.5 (*C*^{8}H$_3$), 18.8 (*C*^{4}H$_3$), 18.4 (*C*^{5}H$_3$). ^{15}N NMR (40 MHz; $CDCl_3$; T = 300 k) δ 98.0 (*N*HTs), 40.1 (*N*HC^{6}). Elemental Analysis: Found: C, 70.4; H, 7.4; N, 6.6% Calc. for $C_{24}H_{30}N_2O_2S$: C, 70.2; H, 7.4; N, 6.8%. $[\alpha]_D^{20}$ = + 9.92 (*c* 1.31 in $CHCl_3$).

Synthesis of 3f-(1*R*,2*S*,2'*S*) from 2f-(1*R*,2*S*) under conventional heating



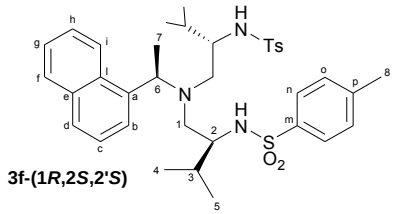
A solution of (*S*)-2-isopropyl-1-tosylaziridine **1b** (0.307 g, 1.28 mmol) and monoamine **2f-(1*R*,2*S*)** (0.478 g, 1.16 mmol) in toluene (10 mL) was stirred and heated under reflux for 90 h. The mixture was dried and purified by silica gel chromatography using *n*-hexane:ethyl acetate = 7:3 as eluant, obtaining a yellow solid **3f-(1*R*,2*S*,2'*S*)** (0.302 g, 0.464 mmol, yield: 40%).

Direct synthesis of 3f-(1*R*,2*S*,2'*S*)



A solution of (*S*)-2-isopropyl-1-tosylaziridine **1b** (0.781 g, 3.21 mmol) and (*R*)-1-(1-naphthyl)ethyl amine (0.514 g, 3.0 mmol) in toluene (21 mL) was added in a microwave tube. The solution was stirred and heated by microwave irradiation for 3h at 150°C. The resulting mixture, without any purification, was added to a solution of (*S*)-2-isopropyl-1-tosylaziridine **1b** (0.785 g, 3.28 mmol) in distilled toluene (4 mL) and was stirred and heated under reflux for 45 h. The

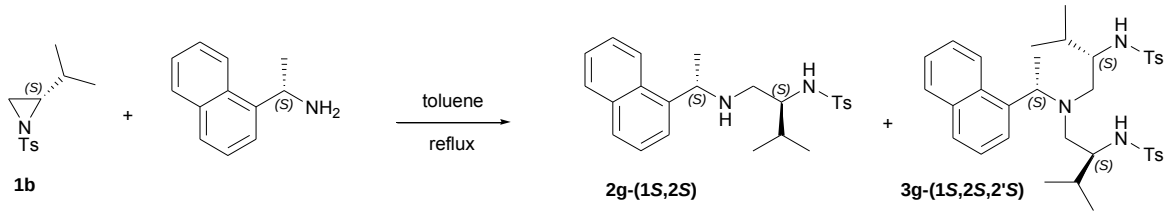
mixture was dried and purified by silica gel chromatography using *n*-hexane:ethyl acetate = 7:3 as eluant, obtaining a yellow solid **3f-(1*R*,2*S*,2'*S*)** (0.785 g, 1.21 mmol, yield: 40%).



3f-(1*R*,2*S*,2'*S*)

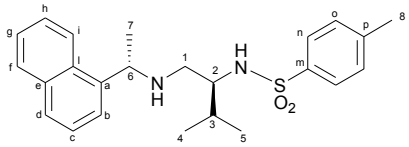
^{1}H NMR (400 MHz; $CDCl_3$; T = 300 k) δ 7.94 (1H, m, H^{i}) 7.79(4H, d, J = 8.0 Hz, H^{n}) overlapping with 7.79 (1H, m, Ar*H*), 7.73 (1H, dd, J = 5.8 Hz, J = 3.4 Hz, Ar*H*), 7.45-7.42 (2H, m, Ar*H*), 7.40-7.39 (2H, m, Ar*H*), 7.29 (4H, d, J = 8.0 Hz, H^{o}), 4.66 (2H, d, J = 7.9 Hz, N*H*), 4.59 (1H, q, J = 6.6 Hz, H^{6}), 3.26 (1H, m, H^{2}), 2.46 (2H, dd, J = 13.4 Hz, J = 5.1 Hz, H^{1}), 2.41 (6H, s, CH_3^{8}), 1.55 (2H, m, H^{3}), 1.20 (3H, d, J = 6.6 Hz, CH_3^{7}) 0.56 (6H, d, J = 6.9 Hz, CH_3^{4}), 0.19 (6H, d, J = 6.8 Hz, CH_3^{5}). ^{13}C NMR (75 MHz; $CDCl_3$; T = 300 k) δ 143.4 (*C*), 138.2 (*C*), 138.0 (*C*), 134.1 (*C*), 132.1 (*C*), 129.7 (C^{n}H), 128.8 (*C*H), 128.2 (*C*H), 127.3 (C^{o}H), 125.6 (*C*H), 125.5 (*C*H), 125.1 (*C*H), 125.0 (*C*H), 123.9 (*C*H), 56.6 (C^{2}H), 53.6 (C^{6}H), 52.3 ($C^{1}H_2$), 27.6 (C^{3}H), 21.6 ($C^{8}H_3$), 19.3 ($C^{4}H_3$), 14.8 ($C^{5}H_3$), 12.4 ($C^{7}H_3$). ^{15}N NMR (40 MHz; $CDCl_3$; T = 300 k) δ 94.0 (*N*HTs), 38.3 (*N*HC^{6}). Elemental Analysis: Found: C, 66.6; H, 7.6; N, 6.5% Calc. for $C_{36}H_{47}N_3O_4S_2$: C, 66.5; H, 7.3; N, 6.5%. $[\alpha]_D^{20}$ = - 47.22 (*c* 1.37 in $CHCl_3$).

Synthesis of 2g-(1*S*,2*S*) and 3g-(1*S*,2*S*, 2'*S*)



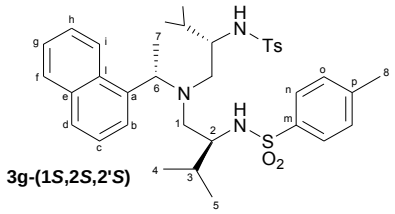
1b **2g-(1*S*,2*S*)** **3g-(1*S*,2*S*,2'*S*)**

This synthesis can be performed in the air. A solution of (*S*)-2-isopropyl-1-tosylaziridine **1b** (2.080 g, 8.7 mmol) and (*S*)-1-(1-naphthyl)ethyl amine (0.498 g, 2.90 mmol) in distilled toluene (38 mL) was stirred and heated under reflux for 220 h. The mixture was dried and purified by silica gel chromatography using *n*-hexane:ethyl acetate = 7:3 as eluant, obtaining monoamine **2g-(1*S*,2*S*)** (0.686 g, 1.67 mmol, yield: 58%) and pure amine **3g-(1*S*,2*S*, 2'*S*)** (0.754 g, 1.16 mmol, yield: 40%).



2g-(1*S*,2*S*)

^{1}H NMR (300 MHz; $CDCl_3$; T = 300 k) δ 8.15 (1 H, m, Ar*H*), 7.90 (1H, m, Ar*H*), 7.78 (1H, dd, *J* = 7.9 Hz, *J* = 1.8 Hz, Ar*H*), 7.55-7.43 (6H, m, Ar*H*), 6.96 (2H, d, *J* = 7.9 Hz, Ar*H*), 5.09 (1H, bs, N*H*), 4.38 (1H, q, *J* = 6.5 Hz, H^6), 2.92 (1H, m, H^2), 2.59 (1H, dd, , *J* = 12.3 Hz, *J* = 5.5 Hz, H^1), 2.26 (3H, s, CH_3^8), 2.19 (1H, dd, *J* = 12.3 Hz, *J* = 4.5 Hz, $H^{1'}$), 1.84 (1H, m, H^3), 1.40 (3H, d, *J* = 6.5 Hz, CH_3^7), 0.88 (3H, d, *J* = 6.8 Hz, CH_3^4), 0.83 (3H, d, *J* = 6.8 Hz, CH_3^5). ^{13}C NMR (75 MHz; $CDCl_3$; T = 300 k) δ 142.9 (*C*), 140.9 (*C*), 137.7 (*C*), 134.2 (*C*), 131.4 (*C*), 129.4 (*C*H), 129.1 (*C*H), 127.5 (*C*H), 127.0 (*C*H), 125.9 (*C*H), 125.8 (*C*H), 125.6 (*C*H), 123.3 (*C*H), 123.1 (*C*H), 59.3 (C^2H), 54.5 (C^6H), 48.0 (C^1H_2), 30.3 (C^3H), 23.7 (C^7H_3), 21.4 (C^8H_3), 19.0 (C^4H_3), 18.8 (C^5H_3). Elemental Analysis: Found: C, 70.3; H, 7.5; N, 6.7% Calc. for $C_{24}H_{30}N_2O_2S$: C, 70.2; H, 7.4; N, 6.8%. $[\alpha]_D^{20}$ = - 45.09 (c 1.02 in $CHCl_3$).

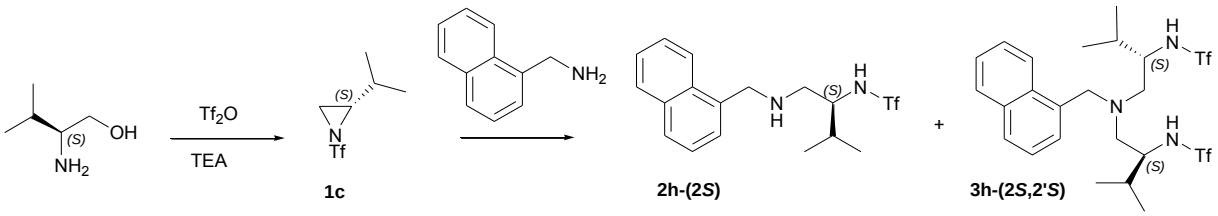


3g-(1*S*,2*S*,2'*S*)

^{1}H NMR (300 MHz; $CDCl_3$; T = 300 k) δ 8.73 (1H, d, *J* = 8.2 Hz, H^i), 7.73 (2H, d, *J* = 7.8 Hz, Ar*H*), 7.70 (4H, d, *J* = 8.3 Hz, H^n), 7.56 (1H, pt, *J* = 8.2 Hz, Ar*H*), 7.43-7.37 (2H, m, Ar*H*), 7.29 (1H, m, Ar*H*), 7.24 (4H, d, *J* = 8.3 Hz, H^o), 5.36 (2H, d, *J* = 5.4 Hz, N*H*), 5.13 (1H, q, *J* = 6.5 Hz, H^6), 3.68 (2H, m, H^2), 2.48-2.42 (4H, m, H^1), overlapping with 2.42 (6H, s, CH_3^8), 1.76 (2H, m, H^3), 1.48 (3H, d, *J* = 6.5 Hz, CH_3^7), 0.68 (6H, d, *J* = 7.0 Hz, CH_3^4), 0.35 (6H, d, *J* = 7.0 Hz, CH_3^5) ^{13}C NMR (75 MHz; $CDCl_3$; T = 300 k) δ 143.0 (C^p), 139.3 (*C*), 137.9 (*C*), 134.1 (*C*), 131.7 (*C*), 129.5 (C^nH), 128.4 (*C*H), 127.4 (*C*H), 127.1 (C^oH), 125.9 (*C*H), 125.2 (*C*H), 124.9 (*C*H), 124.6 (*C*H), 54.7 (C^2H), 53.3 (C^6H), 48.1 (C^1H_2), 29.6 (C^3H), 21.7 (C^8H_3), 18.0 (C^4H_3), 15.9 (C^5H_3), 11.1 (C^7H_3). A signal relative to an aromatic carbon was not detected. Elemental Analysis: Found: C,

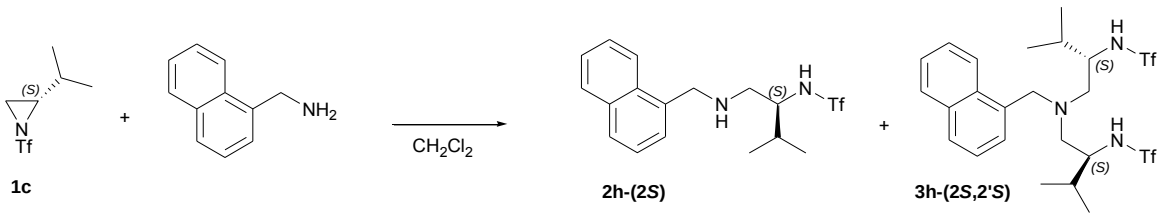
66.4; H, 7.3; N, 6.7% Calc. for $C_{36}H_{47}N_3O_4S_2$: C, 66.5; H, 7.3; N, 6.5%. MS (EI): m/z 650 (M^++1). $[\alpha]_D^{20}$ = - 33.65 (c 0.28 in $CHCl_3$).

Direct synthesis of 2h-(2*S*) and 3h-(2*S*,2'*S*)

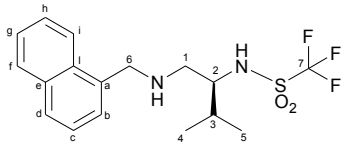


Triethylamine (2.4 mL) was added to a solution of L-valinole (0.837 g, 8.12 mmol) in CH_2Cl_2 (30 mL). Then trifluoromethanesulfonic anhydride (5.031 g, 17.8 mmol) was added dropwise to the solution cooled to -78°C. The resulting yellow solution was heated to -30 °C and stirred overnight. The solution was washed with HCl 0.1 M (120 mL) and brine (120 mL); organic phase was anhydrified with Na_2SO_4, filtered and diluted with CH_2Cl_2 (30 mL). The solution was cooled to -40 °C and a solution of 1-naphthylmethylamine (0.441 g, 2.80 mmol) in CH_2Cl_2 (10 mL) was added dropwise. After 30', the solution was carried to room temperature. A white suspension immediately formed. After 48 h, reaction was dried and purified by silica gel chromatography using *n*-hexane:ethyl acetate = 7:3 as eluant. Main product was monoamine **2h-(2*S*)** (560 mg, 1.50 mmol, yield: 53%), while amine **3h-(2*S*,2'*S*)** was obtained mixed with unreacted aziridine **1c** and was recrystallized from n-hexane in CH_2Cl_2 (182 mg, 0.310 mmol, yield: 11%). Crystals suitable for X-Ray analysis of monoamine **2h-(2*S*)** were obtained from CH_2Cl_2. Crystals suitable for X-Ray analysis of amine **3h-(2*S*,2'*S*)** were obtained by layering n-hexane (4 mL) to a CH_2Cl_2 solution (5 mL).

Synthesis of 2h-(2*S*) and 3h-(2*S*,2'*S*)

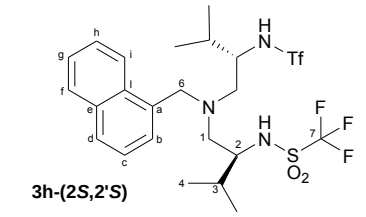


A solution of 1-naphthylmethylamine (0.306 g, 1.94 mmol) in distilled CH_2Cl_2 (10 mL) was added dropwise to a solution of (*S*)-2-isopropyl-1-triflylaziridine **1c** (0.879 g, 4.01 mmol) in distilled CH_2Cl_2 (20 mL) cooled to.-40°C. After 30 minutes the solution was carried to room temperature. A white suspension immediately formed. The reaction was followed by TLC. After 48 h the white suspension was filtered giving pure monoamine **2h-(2*S*)** (0.226 g, 0.604 mmol, yield: 31%); pure amine **3h-(2*S*,2'*S*)** (0.600 g, 1.01 mmol, yield: 52%) were obtained by layering *n*-hexane (5 mL) to a CH_2Cl_2 solution (5 mL).



2h-(2*S*)

^{1}H NMR (400 MHz; $CDCl_3$; T = 300 k) δ 8.09 (1H, d, *J* = 8.0 Hz, H^i), 7.88 (1H, d, *J* = 8.0 Hz, H^f), 7.80 (1H, pst, *J* = 8.0 Hz, Ar*H*), 7.61-7.48 (2H, m, $H^{h\text{-}g}$), 7.43-7.42 (2H, m, Ar*H*), 4.28 (1H, d, *J* = 13.2 Hz, $H^{6'}$), 4.25 (1H, d, *J* = 13.2 Hz, H^6), 3.35 (1H, ddd, *J* = 8.0 Hz, *J* = 4.2 Hz, *J* = 4.8 Hz, H^2), 3.02 (1H, dd, *J* = 12.9 Hz, *J* = 4.2 Hz, $H^{1'}$), 2.80 (1H, dd, *J* = 12.9 Hz, *J* = 4.8 Hz, H^1), 1.86 (1H, dq, *J* = 8.0 Hz, *J* = 6.8 Hz, H^3), 0.97 (3H, d, *J* = 6,8 Hz, CH_3^4), 0.92 (3H, d, *J* = 6,8 Hz, CH_3^5), 0.51 (1H, bs, N*H*). ^{13}C NMR (75 MHz; $CDCl_3$; T = 300 k) δ 129.0 (*C*H), 128.5 (C^4H), 126.5 (*C*H), 126.0 (*C*H), 125.4 (C^iH), 123.6 (C^gH), 61.0 (C^2H), 52.1 (C^6H_2), 49.5 (C^1H_2), 30.4 (C^3H), 19.2 (C^4H_3), 18.8 (C^5H_3). Signals relative to quaternary carbons were not detected. ^{19}F NMR (282 MHz; $CDCl_3$; T = 300 k) δ -77.7 (m). Elemental Analysis: Found: C, 54.7; H, 5.8; N, 7.3% Calc. for $C_{17}H_{21}F_3N_2O_2S$: C, 54.5; H, 5.6; N, 7.5%.

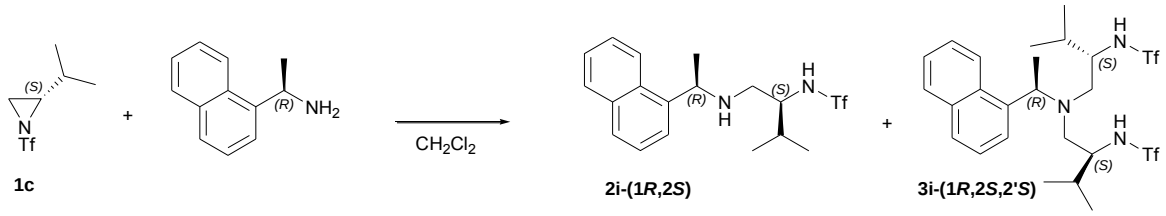


3h-(2*S*,2'*S*)

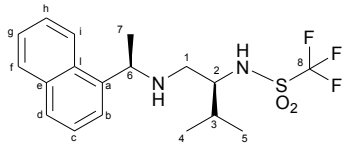
^{1}H NMR (300 MHz; $CDCl_3$; T = 300 k) δ 8.14 (1H, d, *J* = 8.1 Hz, H^i), 7.86 (1H, d, *J* = 8.1 Hz, Ar*H*), 7.81 (1H, d, *J* = 8.1 Hz, Ar*H*), 7.58-7.42 (4H, m, Ar*H*), 5.04 (2H, br, N*H*), 4.21 (1H, d, *J* =

13.2 Hz, H^6), 4.05 (1H, d, J = 13.2 Hz, $H^{6'}$), 3.61 (2H, m, H^2), 2.72-2.58 (4H, m, H^1), 1.92 (2H, m, H^3), 0.81 (6H, d, J = 6.9 Hz, CH_3^4), 0.65 (6H, d, J = 6.9 Hz, CH_3^5). ^{13}C NMR (75 MHz; $CDCl_3$; T = 300 k) δ 134.1 (*C*), 133.1 (*C*), 132.2 (*C*), 128.9 (*C*H), 128.8 (*C*H), 128.6 (*C*H), 126.5 (*C*H), 126.1 (*C*H), 125.4 (*C*H), 123.9 (C^iH), 119.5 (C_7, q, J = 321 Hz), 58.7 (C^2H), 57.0 (C^6H_2), 56.2 (C^1H_2), 29.4 (C^3H), 18.4 (C^4H_3), 16.6 (C^5H_3). ^{19}F NMR (282 MHz; $CDCl_3$; T = 300 k) δ -77.6 (bs). Elemental Analysis: Found: C, 46.6; H, 5.4; N, 7.1% Calc. for $C_{23}H_{31}F_6N_3O_4S_2$: C, 46.7; H, 5.3; N, 7.1%.

Synthesis of 2i-(1*R*,2*S*) and 3i-(1*R*,2*S*,2'*S*)



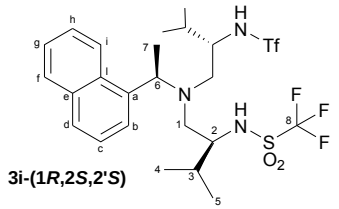
A solution of (*R*)-1-(1-naphthyl)ethyl amine (0.374 g, 2.18 mmol) in distilled CH_2Cl_2 (10 mL) was added dropwise to a solution of (*S*)-2-isopropyl-1-triflylaziridine **1c** (0.968 g, 4.46 mmol) in distilled CH_2Cl_2 (30 mL) cooled to.- 40 °C. After 30 minutes the solution was carried to room temperature. A white suspension immediately formed. The reaction was followed by TLC. After 90 h, the mixture was dried and purified by silica gel chromatography using *n*-hexane:ethyl acetate = 7:3 as eluant, obtaining a monoamine **2i-(1*R*,2*S*)** (0.0932 g, 0.240 mmol, yield: 11%) and pure amine **3i-(1*R*,2*S*,2'*S*)** (1.180 g, 1.95 mmol, yield: 89%).



2i-(1*R*,2*S*)

^{1}H NMR (300 MHz; $CDCl_3$; T = 300 k) δ 8.15 (1H, d, J = 8.2 Hz, H^i), 7.90 (1H, d, J = 7.7 Hz, Ar*H*), 7.79 (1H, d, J = 8.0 Hz, Ar*H*), 7.59-7.47 (4H, m, Ar*H*), 4.67 (1H, q, J = 6.5 Hz, H^6), 3.33 (1H, m, H^2), 3.20 (2H, br, N*H*), 2.84 (1H, dd, J = 13.0 Hz, J = 5.0 Hz, H^1), 2.70 (1H, dd, J = 13.0 Hz, J = 4.3 Hz, $H^{1'}$), 1.87 (1H, m, H^3), 1.57 (3H, d, J = 6.6 Hz, CH_3^7), 0.93 (3H, d, J = 6.8 Hz,

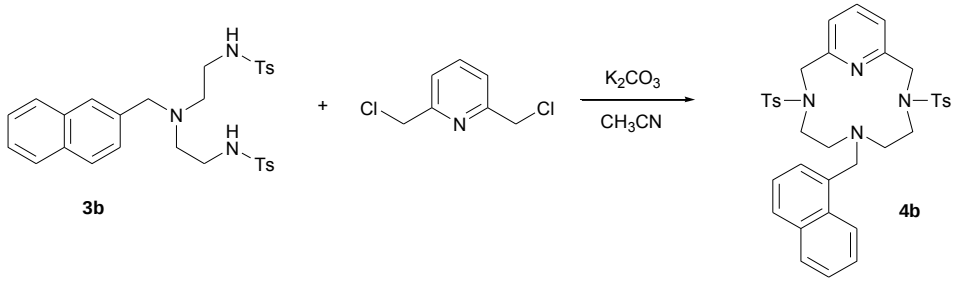
CH_3^4), 0.84 (3H, d, *J* = 6.8 Hz, CH_3^5). ^{13}C NMR (75 MHz; $CDCl_3$; T = 300 k) δ 139.7 (*C*), 134.2 (*C)*, 131.2 (*C*), 129.3 (*C*H), 128.1(*C*H), 126.4 (*C*H), 125.9 (*C*H), 125.8 (*C*H), 122.9 (*C*H), 122.6 (*C*^{i}H), 119.9 (*C*^{8}, q, *J* = 321 Hz*),* 60.9 (*C*^{2}H), 53.8 (*C*^{6}H), 47.8 (*C*^{3}H_2), 30.5 (*C*^{3}H), 23.1 (*C*^{7}H_3), 19.2 (*C*^{4}H_3), 18.8 (*C*^{5}H_3). ^{19}F NMR (282 MHz; $CDCl_3$; T = 300 k) δ -77.4 (s). Elemental Analysis: Found: C, 55.7; H, 6.2; N, 7.0% Calc. for $C_{18}H_{23}F_3N_2O_2S$: C, 55.7; H, 6.0; N, 7.2%. MS (EI): m/z 388 (M^+), 373 (M^+-CH_3), 255 (M^+-Tf), 184 (M^+-204).



3i-(1*R*,2*S*,2'*S*)

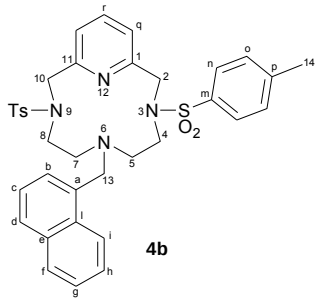
^{1}H NMR (300 MHz; $CDCl_3$; T = 300 k) δ 8.01 (1H, d, *J* = 9.4 Hz, *H*^{i}), 7.85 (1H, d, *J* = 9.4 Hz, Ar*H*), 7.80 (1H, d, *J* = 7.8 Hz, Ar*H*), 7.54-7.48 (3H, m, Ar*H*), 7.46 (1H, pst, *J* = 7.4 Hz, Ar*H*), 4.88 (1H, q, *J* = 6.5 Hz, *H*^{6}), 4.68 (2H, br, N*H*), 3.56 (2H, m, *H*^{2}), 2.75 (2H, dd, *J* = 13.5 Hz, *J* = 4.9 Hz, *H*^{1}), 2.63 (2H, dd, *J* = 13.5 Hz, *J* = 9.7 Hz, *H*$^{1'}$), 1.70 (2H, m, *H*^{3}), 1.57 (3H, d, *J* = 6.7 Hz, CH_3^7) 0.88 (6H, d, *J* = 6.9 Hz, CH_3^4), 0.31 (6H, d, *J* = 6.8 Hz, CH_3^5). ^{13}C NMR (75 MHz; $CDCl_3$; T = 300 k) δ 137.4 (*C*), 134.3 (*C)*, 132.1 (*C*), 129.1 (*C*H), 128.7(*C*H), 125.9 (*C*H), 125.8 (*C*H), 125.3 (*C*H), 125.1 (*C*H), 123.5 (*C*^{i}H), 119.6 (*C*^{8}, q, *J* = 321 Hz*),* 59.2 (*C*^{2}H), 53.9 (*C*^{6}H), 53.2(*C*^{1}H_2), 27.7 (*C*^{3}H), 19.5 (*C*^{4}H_3), 14.6 (*C*^{5}H_3), 12.4 (*C*^{7}H_3). ^{19}F NMR (282 MHz; $CDCl_3$; T = 300 k) δ - 77.56 (s). Elemental Analysis: Found: C, 47.4; H, 5.8; N, 6.6% Calc. for $C_{24}H_{33}F_6N_3O_4S_2$: C, 47.6; H, 5.5; N, 6.9%. MS (EI): m/z 590 (M^+-CH_3), 401 (M^+-Tf).

Synthesis of 4b



3b **4b**

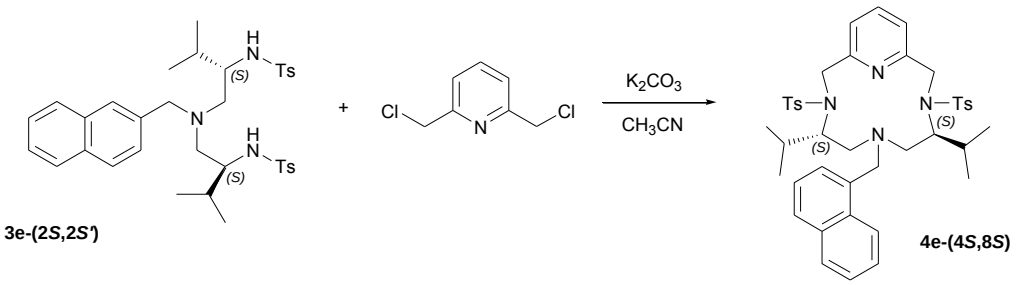
A solution of amine **3b** (0.842 g, 1.53 mmol), 2,6-bis(chloromethyl) pyridine (0.269 g, 1.53 mmol) and micronized anhydrous potassium carbonate (0.633 g, 4.58 mmol) in distilled acetonitrile (35 mL) was stirred and heated under reflux for 45 hours. The resulting mixture was washed with water end extracted with ethyl acetate, dried and purified by silica gel chromatography using toluene:dichloromethane:isopropanol = 90:10:5 as eluant, obtaining a white solid **4b** (0.508 g, 0.776 mmol, yield: 51%).



4b

^{1}H NMR (300 MHz; $CDCl_3$; T = 300 k) δ 8.11 (1H, d, J = 8.1 Hz, H^i), 7.90-7.83 (2H, m, ArH), 7.76 (1H, pst, J = 7.8 Hz, H^r), 7.50 (4H, d, J = 8.2 Hz, H^n), overlapping with 7.52-7.23 (6H, m, ArH), 7.19 (4 H, d, J = 8.2 Hz, H^o), 4.31 (4H, br, CH_2^2), 3.93 (2H, br, CH_2^{13}), 3.07 (4H, m, CH_2^4), 2.39 (6H, s, CH_3^{14}) overlapping with 2.36 (4H, m, CH_2^5). Elemental Analysis: Found: C, 66.2; H, 5.8; N, 8.4% Calc. for $C_{36}H_{38}N_4O_4S_2$: C, 66.0; H, 5.8; N, 8.6%.

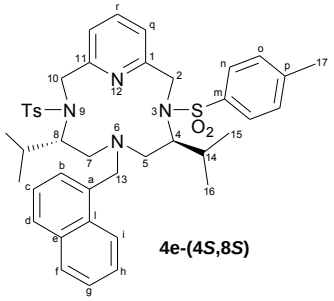
Synthesis of 4e-(4S,8S)



3e-(2*S*,2*S'*) **4e-(4S,8S)**

A solution of amine **3e-(2*S*,2*S'*)** (0.330 g, 0.520 mmol), 2,6-bis(chloromethyl) pyridine (0.0914 g, 0.520 mmol) and micronized anhydrous potassium carbonate (0.228 g, 1.65 mmol) in distilled acetonitrile (12 mL) was stirred and heated under reflux for 45 hours. The resulting mixture was washed with water end extracted with ethyl acetate, dried and purified by silica gel chromatography

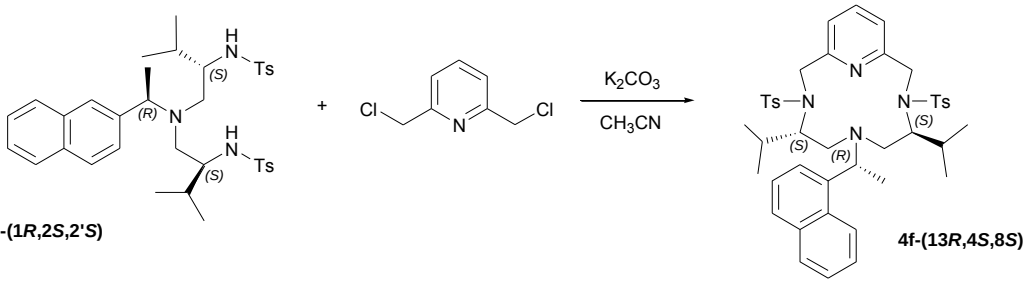
using toluene:dichloromethane:isopropanol = 90:10:5 as eluant, obtaining a white solid **4e-(4*S*,8*S*)** (0.215 g, 0.291 mmol, yield: 56%).



4e-(4*S*,8*S*)

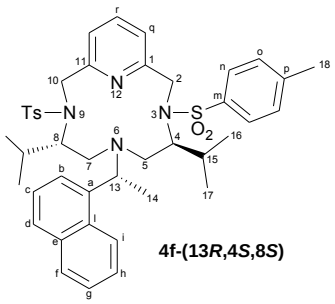
^{1}H NMR (300 MHz; $CDCl_3$; T = 300 k) δ 8.35 (1H, d, *J* = 8.0 Hz, H^{i}), 7.86 (1H, d, *J* = 8.0 Hz, Ar*H*), 7.76 (1H, d, *J* = 8.0 Hz, Ar*H*) 7.66-7.58 (3H, m, Ar*H*), 7.53 (1H, pt, *J* = 7.6 Hz, Ar*H*), 7.43 (1H, pt, *J* = 7.6 Hz, Ar*H*), 7.29-7.11 (6H, m, Ar*H*), 7.02 (4H, d, *J* = 7.8 Hz, H^{o}), 4.72 (2H, d, *J* = 15.6 Hz, H^{2}), 4.30 (1H, d, *J* = 13.5 Hz, H^{13}), 4.18 (1H, d, *J* = 13.5 Hz, $H^{13'}$), 3.78 (2H, d, *J* = 15.6 Hz, $H^{2'}$), 3.68 (2H, dd, *J* = 15.6 Hz *J* = 6.9 Hz, H^{5}), 3.51 (2H, m, H^{4}), 2.29 (6H, s, CH_3^{17}), 2.19 (2H, m, $H^{5'}$), 1.19 (2H, m, *H*), 0.58 (6H, d, *J* = 6.9 Hz, CH_3^{15}), 0.48 (6H, br, CH_3^{16}). ^{13}C NMR (75 MHz; $CDCl_3$; T = 300 k) δ 156.5 (*C*), 142.3 (*C*), 139.3 (*C*), 137.2 (*C*H), 135.7 (*C*), 134.0 (*C*), 132.7 (*C*), 128.9 (*C*H), 128.5 (*C*H), 128.0 (*C*H), 127.8 (*C*H), 127.7 (*C*H), 125.9 (*C*H), 125.7 (*C*H), 125.4 (*C*H), 125.0 (*C*H), 120.2 (*C*H), 65.6 (C^{4}H), 57.2 ($C^{13}H_2$), 53.1 ($C^{5}H_2$), 48.9 ($C^{2}H_2$), 30.5 (C^{14}H), 21.4 ($C^{17}H_3$), 20.4 ($C^{15}H_3$), 20.2 ($C^{16}H_3$). Elemental Analysis: Found: C, 68.4; H, 6.8; N, 7.4% Calc. for $C_{42}H_{50}N_4O_4S_2$: C, 68.3; H, 6.8; N, 7.6%. MS (FAB): m/z 739 (M^{+}+1). $[\alpha]_D^{20}$ = + 1.04 (*c* 1.01 in $CHCl_3$).

Synthesis of 4f-(13*R*,4*S*,8*S*)



3f-(1*R*,2*S*,2'*S*) **4f-(13*R*,4*S*,8*S*)**

A solution of amine **3f-(1*R*,2*S*,2'*S*)** (0.715 g, 1.10 mmol), 2,6-bis(chloromethyl) pyridine (0.194 g, 1.10 mmol) and micronized anhydrous potassium carbonate (0.608 g, 4.40 mmol) in distilled acetonitrile (37 mL) was stirred and heated under reflux for 116 h. The resulting mixture was washed with water end extracted with ethyl acetate, dried and purified by silica gel chromatography using *n*-hexane:ethyl acetate = 6:4 as eluant, obtaining a white solid **4f-(13*R*,4*S*,8*S*)** (0.471 g, 0.626 mmol, yield: 57%).

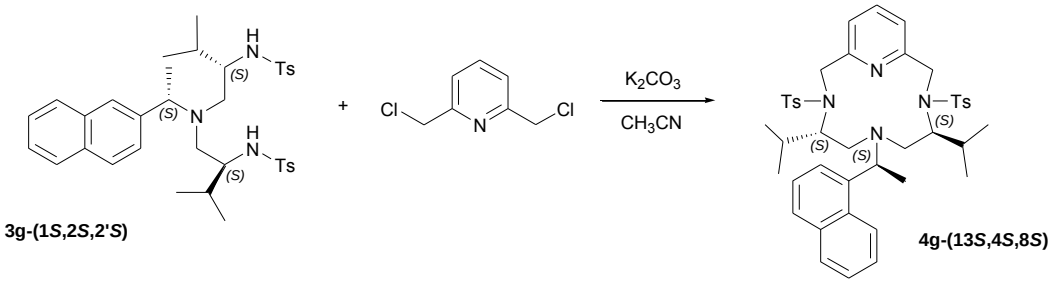


4f-(13*R*,4*S*,8*S*)

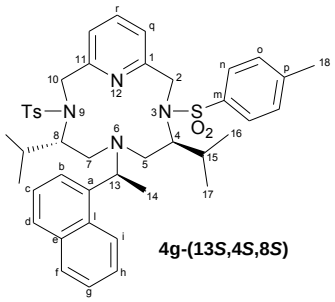
^{1}H NMR (300 MHz; $CDCl_3$; T = 300 k) δ 8.58 (1H, d, *J* = 8.1 Hz, H^{i}), 7.89 (1H, m, Ar*H*), 7.83 (1H, d, *J* = 8.1 Hz, Ar*H*), 7.69 (1H, d, *J* = 8.1 Hz, Ar*H*), 7.64-7.42 (8H, m, Ar*H*), 7.12 (4H, d, *J* = 7.8 Hz, H^{o}), 7.05 (2H, m, Ar*H*), 5.18 (1H, m, H^{13}), 4.72 (2H, m, H^{2}), 3.94-3.82 (6H, m, *H*), 2.63-2.60 (2H, m, *H*), 2.40 (2H, m, *H*) overlapping with 2.33 (6H, s, CH_3^{18}), 1.57 (3H, d, *J* = 6.5 Hz, CH_3^{14}), 0.44 (12H, m, $CH_3^{16\text{-}17}$). ^{13}C NMR (75 MHz; $CDCl_3$; T = 300 k) δ 156.5 (*C*), 142.5 (*C*), 142.2 (*C*), 138.9 (*C*), 137.0 (*C*H), 134.2 (*C*), 131.7 (*C*), 129.2 (C^{o}H), 128.9 (*C*H), 127.8 (C^{n}H), 127.0 (*C*H), 126.0 (*C*H), 125.9 (*C*H), 125.8 (*C*H), 125.2 (*C*H), 124.0 (C^{i}H), 120.7 (*C*H), 66.5 (*C*H), 50.8 (CH_2), 49.5 (CH_2), 30.0 (*C*H), 23.8 ($C^{14}H_3$), 21.5 ($C^{18}H_3$), 21.1 ($C^{16}H_3$). A signal relative to a CH was not detected. ^{15}N NMR (40 MHz; $CDCl_3$; T = 300 k) δ 33.2 (N^{6}). The signals relative to *N*-Ts and N^{12} were not detected. ^{1}H NMR (300 MHz; $C_6D_5CD_3$; T = 300 k) δ 8.74 (1H, d, *J* = 8.8 Hz, H^{i}), 7.99 (1H, d, *J* = 7.2 Hz, H^{b}), 7.68 (4H, pst, *J* = 8.0 Hz, H^{n}) overlapping with 7.69-7.66 (1H, m, H^{g}), 7.57-7.47 (2H, m, H^{d} and H^{h}), 7.38 (1H, pst, *J* = 7.5 Hz, H^{c}), 7.29 (1H, pst, *J* = 7.5 Hz, H^{f}), 7.05-7.03 (1H, m, H^{r}), 6.86 (4H, d, *J* = 8.0 Hz, H^{o}), 6.68 (2H, d, *J* = 7.8 Hz, H^{q}), 5.39 (1H, q, *J* = 6.6 Hz, H^{13}), 4.62 (2H, d, *J* = 15.9 Hz, H^{2}), 4.14-4.06 (4H, m, H^{4} and H^{5}), 4.02-3.93 (2H, m, $H^{2'}$),

2.96 (2H, d, J = 15.0 Hz, $H^{5'}$), 2.02 (6H, s, CH_3^{18}), 1.68 (3H, d, J = 6.6 Hz, CH_3^{14}), 1.39 (2H, m, H^{15}), 0.58 (12H, m, $CH_3^{16\text{-}17}$). ^{13}C NMR (75 MHz; $C_6D_5CD_3$; T = 300 k) δ 157.4 (*C*), 142.7 (*C*), 141.9 *(C)*, 140.4 (*C*), 136.3 (C^{r}H), 134.9 (C), 132.5 (C), 129.0 (C^{o}H), 128.2 (C^{n}H), 127.2 (C^{d}H), 126.3 (C^{b}H), 125.9 (C^{d}H) overlapping with 125.9 (C^{h}H), 125.2 (C^{f}H), 124.5 (C^{i}H), 120.5 (C^{q}H), 66.4 (C^{4}H), 57.2 (C^{13}H), 51.4 ($C^{2\text{-}5}H_2$), 30.9 (C^{15}H), 23.5 ($C^{14}H_3$), 21.0 ($C^{16}H_3$), 20.8 ($C^{18}H_3$). A signal relative to an aromatic carbon was not detected. Elemental Analysis: Found: C, 68.4; H, 7.4; N, 7.1% Calc. for $C_{43}H_{52}N_4O_4S_2$: C, 68.6; H, 7.0; N, 7.4%. MS (FAB): m/z 753 (M^++1).

Synthesis of 4g-(13*S*,4*S*,8*S*)



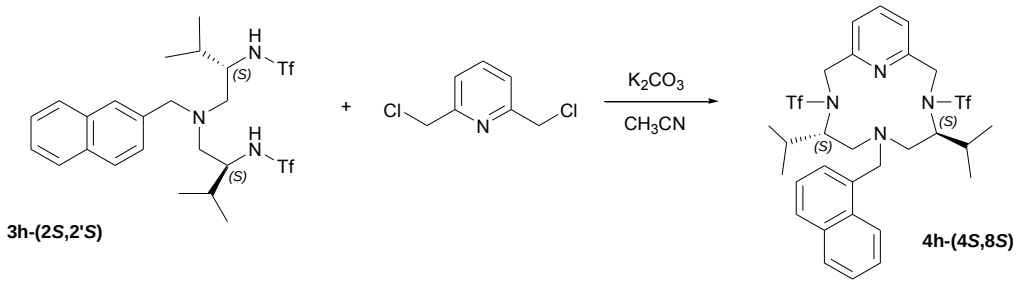
A solution of amine **3g-(1*S*,2*S*,2'*S*)** (0.0888 g, 0.137 mmol), 2,6-bis(chloromethyl) pyridine (0.0240 g, 0.136 mmol) and micronized anhydrous potassium carbonate (0.0700 g, 3.70 mmol) in distilled acetonitrile (6 mL) was stirred and heated under reflux for 53 h. The resulting mixture was washed with water end extracted with ethyl acetate, dried and purified by silica gel chromatography using n-hexane:dichloromethane:isopropanol = 80:17.5:2.5 as eluant, obtaining a white solid **4g-(13*S*,4*S*,8*S*)** (0.0512 g, 0.0679 mmol, yield: 50%).



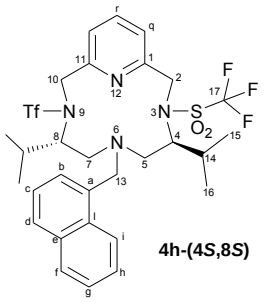
^{1}H NMR (300 MHz; $CDCl_3$;T = 300 k) δ 8.54 (1H, m, H^{i}), 7.89 (1H, m, Ar*H*), 7.85 (1H, d, J = 8.1 Hz, Ar*H*), 7.77 (1H, d, J = 8.1 Hz, Ar*H*), 7.64-7.41 (8H, m, Ar*H*), 7.09-6.99 (6H, m, Ar*H*), 5.01

(1H, m, H^{13}), 4.76 (2H, m, H^{2}), 3.86 (2H, m, $H^{2'}$), 3.77 (2H, m, H^{4}), 3.55 (2H, m, H^{5}), 2.36 (2H, m, $H^{5'}$), 2.29 (6H, s, CH_3^{18}), 1.48 (3H, d, J = 6.6 Hz, CH_3^{14}), 1.34-1.23 (2H, m, H^{15}), 0.60 (6H, m, CH_3^{16}), 0.38 (6H, m, CH_3^{17}). ^{13}C NMR (75 MHz; $CDCl_3$; T = 300 k) δ 156.3 (*C*), 142.3 (*C*), 141.4 (*C*), 139.2 (*C*), 137.3 (*C*H), 134.1 (*C*), 132.5 (*C*), 128.9 (C^{n}H), 128.8 (*C*H), 127.7 (C^{o}H), 127.6 (*C*H), 126.7 (*C*H), 126.2 (*C*H), 125.4 (*C*H), 124.1 (*C*H), 120.7 (*C*H), 66.0 (C^{4}H), 56.0 (C^{13}H), 51.0 ($C^{5}H_2$), 49.3 ($C^{2}H_2$), 30.2 (C^{15}H), 21.4 ($C^{18}H_3$), 20.8 ($C^{14}H_3$), 20.1 ($C^{16}H_3$) overlapping with 20.1 ($C^{17}H_3$). Elemental Analysis: Found: C, 68.6; H, 7.2; N, 7.4% Calc. for $C_{43}H_{52}N_4O_4S_2$: C, 68.6; H, 7.0; N, 7.4%. MS (FAB): m/z 753 (M^{+}+1).

Synthesis of 4h-(4*S*,8*S*)



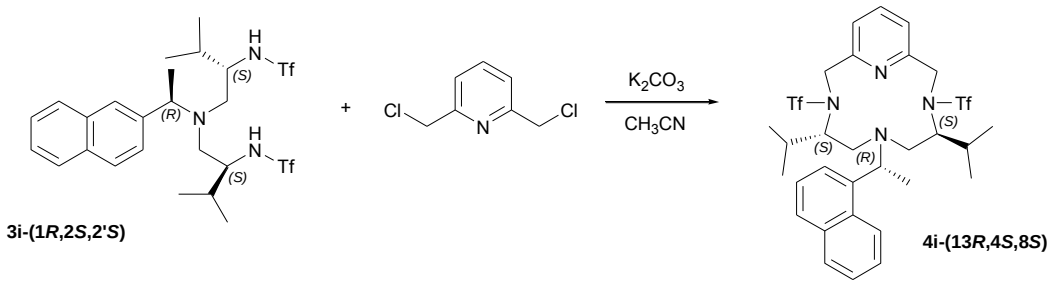
A solution of amine **3h-(2*S*,2*'S*)** (0.350 g, 0.592 mmol), 2,6-bis(chloromethyl) pyridine (0.108 g, 0.612 mmol) and micronized anhydrous potassium carbonate (0.245 g, 1.75 mmol) in distilled acetonitrile (15 mL) was stirred and heated under reflux for 28 h. The mixture was dried and purified by silica gel chromatography using toluene:dichloromethane:isopropanol = 85:10:5 as eluant, obtaining a yellow oil **4h-(4*S*,8*S*)** (0.218 g, 0.314 mmol, yield: 53%).



^{1}H NMR (400 MHz; C_6D_6; T = 300 k) δ 7.78-7.76 (2H, m, Ar*H*), 7.72-7.66 (2H, m, Ar*H*), 7.45-7.37 (2H, m, Ar*H*), 7.27-7.22 (1H, m, Ar*H*),7.17-7.07 (3H, m, Ar*H*), 4.77-4.47 (4H, m, C*H*), 3.89-

3.85 (4H, m, *H*), 3.10-3.05 (2H, m, *H*), 1.09 (2H, m, H^{14}), 0.69 (6H, bs, CH_3^{15}), 0.40 (6H, bs, CH_3^{16}). Two C*H* signals were not detected. At room temperature, this compound gives very broad signals in $CDCl_3$. ^{13}C NMR (100 MHz; C_6D_6; T = 300 k) δ 136.9 (*C*H), 129.1 (*C*H), 128.4 (*C*H), 128.3 (*C*H), 126.2 (*C*H), 126.0 (*C*H), 125.4 (*C*H), 56.9 (C^2H), 53.2 ($C^{13}H_2$), 49.9 (CH_2), 29.4 ($C^{14}H$), 19.9 ($C^{15}H_3$), 19.6 ($C^{16}H_3$). Signals relative to quaternary carbons and aromatic *C*H were not detected. ^{19}F NMR (376 MHz; C_6D_6; T = 300 k) δ - 74.5 (bs). Elemental Analysis: Found: C, 51.8; H, 5.4; N, 8.0% Calc. for $C_{30}H_{36}F_6N_4O_4S_2$: C, 51.9; H, 5.2; N, 8.1%. MS (FAB): m/z 695 (M^++1), 561 (M^+-Tf). $[\alpha]_D^{20}$ = - 0.85 (*c* 0.860 in $CHCl_3$).

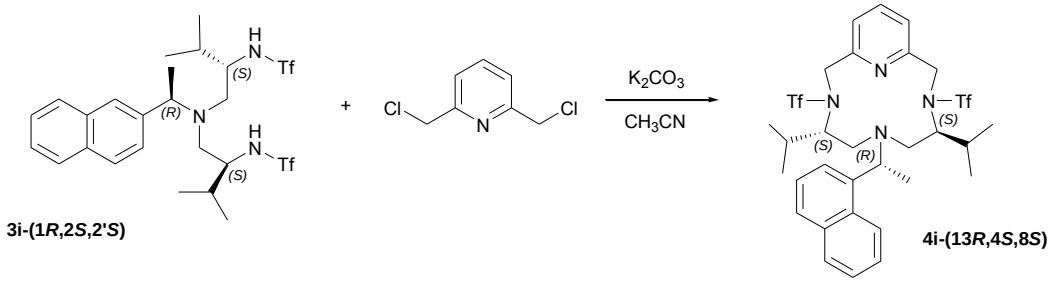
Synthesis of 4i-(13*R*,4*S*,8*S*) under conventional heating



3i-(1*R*,2*S*,2'*S*) **4i-(13*R*,4*S*,8*S*)**

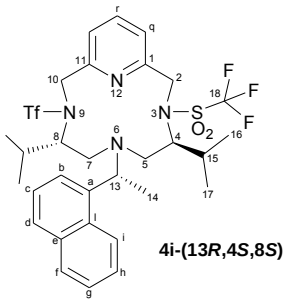
A solution of amine **3i-(1*R*,2*S*,2'*S*)** (0.402 g, 0.665 mmol), 2,6-bis(chloromethyl) pyridine (0.118 g, 0.671 mmol) and micronized anhydrous potassium carbonate (0.290 g, 2.10 mmol) in distilled acetonitrile (20 mL) was stirred and heated under reflux for 110 hours. The resulting mixture was washed with water end extracted with ethyl acetate, dried and purified by silica gel chromatography using toluene:dichloromethane:isopropanol = 85:10:5 as eluant, obtaining a white solid **4i-(13*R*,4*S*,8*S*)** (0.192 g, 0.271 mmol, yield: 39%).

Synthesis of 4i-(13*R*,4*S*,8*S*) under microwave heating



3i-(1*R*,2*S*,2'*S*) **4i-(13*R*,4*S*,8*S*)**

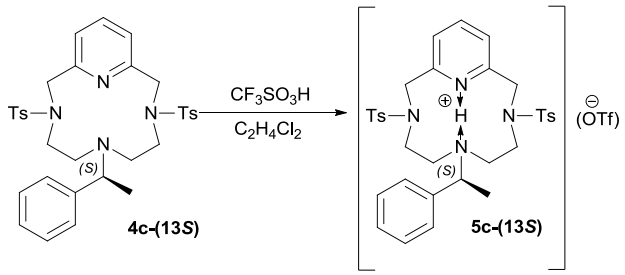
This synthesis can be performed in the air. A solution of amine **3i-(13*R*,4*S*,8*S*)** (0.387 g, 0.639 mmol), 2,6-bis(chloromethyl) pyridine (0.116 g, 0.658 mmol) and micronized potassium carbonate (0.265 g, 1.92 mmol) in distilled acetonitrile (13 mL) was added in a microwave tube. The mixture was stirred and heated by microwave irradiation for 4 hours and 30 minutes at 150°C. The resulting mixture was washed with water end extracted with ethyl acetate, dried and purified by silica gel chromatography using toluene:dichloromethane:isopropanol = 85:10:5 as eluant, obtaining a white solid **4i-(13*R*,4*S*,8*S*)** (0.250 g, 37.8 mmol, yield: 59%).



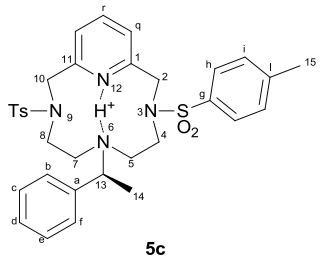
4i-(13*R*,4*S*,8*S*)

^{1}H NMR (300 MHz; $CDCl_3$; T = 300 k) δ 8.42 (1H, m, H^{i}), 7.81-7.78 (2H, m, Ar*H*), 7.68-7.62 (2H, m, Ar*H*), 7.52-7.40 (3H, m, Ar*H*), 7.20-7.17 (2H, m, Ar*H*), 5.16 (1H, q, *J* = 6.3 Hz, H^{13}), 4.91 (2H, d, *J* = 16.0 Hz, H^{2}), 4.40 (2H, d, *J* = 16.0 Hz, $H^{2'}$), 3.82 (2H, m, H^{5}), 2.98 (2H, m, $H^{5'}$), 1.65 (2H, m, H^{4}), 1.51 (3H, d, *J* = 6.3 Hz, CH_3^{14}), 0.73 (6H, bs, CH_3^{16}), 0.44 (6H, bs, CH_3^{17}). Two CH signals were not detected. ^{13}C NMR (75 MHz; $CDCl_3$; T = 300 k) δ 155.1 (*C*), 141.2 (*C*), 137.9 (*CH*), 134.2 (*C*), 131.6 (*C*), 128.9 (*C*H), 127.2 (*C*H), 126.4 (*C*H), 126.0 (*C*H), 125.3 (*C*H), 123.6 (*C*H), 122.1 (*C*H), 69.1 (C^{4}H), 57.4 (C^{13}H), 50.9 ($C^{2}H_2$), 50.4 ($C^{5}H_2$),29.9 (C^{15}H), 24.0 ($C^{14}H_3$), 21.0 ($C^{16}H_3$), 19.3 ($C^{17}H_3$). ^{15}N NMR (40 MHz; $CDCl_3$; T = 300 k) δ 31.35 (N^{6}), The signal relative to *N*-Tf and N^{12} were not detected. ^{19}F NMR (282 MHz; $CDCl_3$; T = 300 k) δ - 74.15 (s). Elemental Analysis: Found: C, 52.4; H, 5.3; N, 8.0% Calc. for $C_{31}H_{38}F_6N_4O_4S_2$: C, 52.5; H, 5.4; N, 7.9%. MS (FAB): m/z 709 (M^{+}+1), 575 (M^{+}-133). $[\alpha]_D^{20}$ = + 117 (*c* 0.005 in CH_2Cl_2).

Synthesis of 5c-(13*S*)



Ligand **4c-(13*S*)** (0.200 g, 0.323 mmol) was dissolved in distilled dichloroethane (5 mL). Triflic acid (0.0530 g, 0.355 mmol) was added and the solution stirred for 2 hours. The solution was dried, then *n*-hexane (10 mL) was added and the solid filtered in air (0.055 g, 0.0710 mmol, yield: 22%).

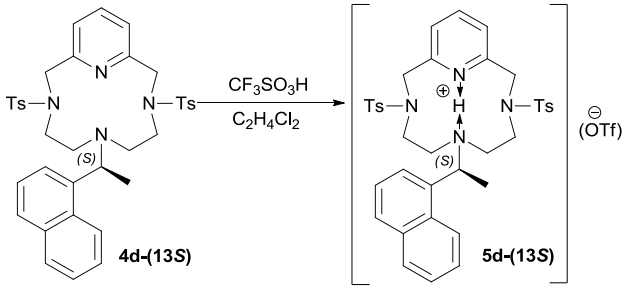


^{1}H NMR (300 MHz; $CDCl_3$; T = 300 k) δ 11.38 (1H, s, N*H*), 7.80 (2H, d, *J* = 8.2 Hz, Ar*H*), 7.71 (1H, pt, *J* = 7.7 Hz, Ar*H*), 7.61 (2H, d, *J* = 8.2 Hz, Ar*H*), 7.52 (2H, m, Ar*H*), 7.45-7.39 (5H, m, Ar*H*), 7.34 (2H, d, *J* = 8.1 Hz, Ar*H*), 7.22 (1H, d, *J* = 7.7 Hz, Ar*H*), 7.04 (1H, d *J* = 7.7 Hz, Ar*H*), 5.60 (1H, q, *J* = 7.0 Hz, *H*^{13}), 4.65 (1H, d, *J* = 17.1 Hz, C*H*$_2$), 4.17 (1H, d, *J* = 17.1 Hz, C*H*$_2$), 4.16-4.09 (2H, m, C*H*$_2$), 3.88 (1H, m, C*H*$_2$), 3.74-3.64 (3H, m, C*H*$_2$), 3.50-3.39 (3H, m, C*H*$_2$), 2.50 (3H, s, C*H*$_3$), 2.45 (3H, s, C*H*$_3$) overlapping with 2.45-2.40 (1H, m, C*H*$_2$), 1.85 (3H, d, *J* = 7.0 Hz, C*H*$_3$^{14}) overlapping with 1.85-1.80 (1H, m, C*H*$_2$). ^{13}C NMR (75 MHz; $CDCl_3$; T = 300 k) δ 156.8 (*C*), 155.5 (*C*), 145.4 (*C*), 144.8 (*C*), 139.6 (*C*H), 134.4 (*C*), 133.4 (*C*), 132.7 (*C*), 130.7 (*C*H), 130.6 (*C*H), 130.4 (*C*H), 129.9 (*C*H), 129.5 (*C*H), 127.9 (*C*H), 127.6 (*C*H), 122.8 (*C*H), 122.2 (*C*H), 58.3 (*C*^{13}H), 52.8 (*C*H$_2$), 51.7 (*C*H$_2$), 51.5 (*C*H$_2$), 46.2 (*C*H$_2$), 44.4 (*C*H$_2$), 21.8 (*C*H$_3$Ts), 21.7 (*C*H$_3$Ts). One *C*H$_2$ and *C*^{14}H$_3$ signals were not detected. ^{15}N NMR (40 MHz; $CDCl_3$; T = 300 k) δ 282,0 (*N*^{12}), 52.2 (*N*^{6}). The signals relative to *N*-Ts were not detected. Elemental Analysis: Found:

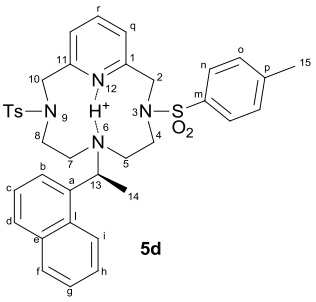
C, 52.9; H, 5.1; N, 7.6% Calc. for $C_{34}H_{39}F_3N_4O_7S_3$: C, 53.1; H, 5.1; N, 7.3%. m/z 619.2 (M^+ - $CF_3SO_3^-$).

5c-(13*R*) was synthesized in the same way starting from **4c-(13*R*)**.

Synthesis of 5d-(13*S*)



Ligand **4d-(13*S*)** (0.200 g, 0.299 mmol) was dissolved in distilled dichloroethane (5 mL). Triflic acid (0.046 g, 0.329 mmol) was added and the solution stirred for 2 hours. The solution was dried, then *n*-hexane (10 mL) was added and the solid filtered in air (0.118 g, 0.144 mmol, yield: 48%).

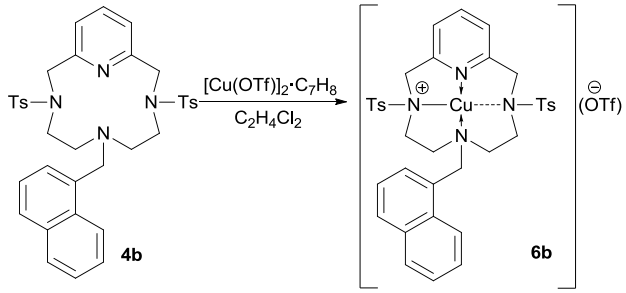


^{1}H NMR (400 MHz; $CDCl_3$; T = 300 k) δ 10.68 (1H, s, NH), 8.20 (1H, d, *J* = 8.6 Hz, Ar*H*), 7.94 (1H, d, *J* = 8.2 Hz, Ar*H*), 7.87-7.81 (4H, m, Ar*H*), 7.72 (1H, pt, *J* = 7.7 Hz, Ar*H*), 7.58 (1H, pt, *J* = 7.7 Hz, Ar*H*), 7.45 (2H, d, *J* = 8.1 Hz, Ar*H*), 7.41 (2H, d, *J* = 8.1 Hz, Ar*H*), 7.36-7.30 (2H, m, Ar*H*), 7.21 (2H, d, *J* = 8.1 Hz, Ar*H*), 6.81-6.77 (2H, m, Ar*H*), 6.22 (1H, q, *J* = 6.6 Hz, H^{13}), 4.53 (1H, m, CH_2) overlapping with 4.48 (1H, d, *J* = 16.6 Hz, CH_2), 4.07 (1H, d, *J* = 16.6 Hz, CH_2), 4.00-3.86 (3H, m, CH_2), 3.70 (1H, d, *J* = 16.3 Hz, CH_2), 3.52-3.30 (3H, m, CH_2), 2.49 (3H, s, CH_3), 2.35 (3H, s, CH_3), 2.20 (1H, m, CH_2), 2.06 (3H, d, *J* = 6.6 Hz, CH_3^{14}), 1.73 (1H, m, CH_2). ^{13}C NMR

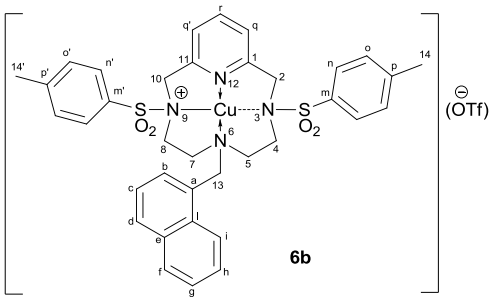
(100 MHz; $CDCl_3$; T = 300 k) δ 157.4 (*C*), 156.9 (*C*), 145.5 (*C*), 144.7 (*C*), 140.0 (*C*H), 133.9 (*C*), 133.8 (*C*), 132.5 (*C*), 131.5 (*C*H), 130.7 (*C*H), 130.7 (*C*), 130.1 (*C*H), 129.4 (*C*H), 129.3 (*C*), 128.0 (*C*H), 127.9 (*C*H), 127.5 (*C*H), 126.9 (*C*H), 126.8 (*C*H), 126.1 (*C*H), 122.8 (*C*H), 122.7 (*C*H), 121.9 (*C*H), 55.2 ($C^{13}H$), 54.3 (CH_2), 53.8 (CH_2), 53.5 (CH_2), 52.9 (CH_2), 47.8 (CH_2), 47.2 (CH_2), 21.8 (CH_3Ts), 21.6 (CH_3Ts), 11.3 ($C^{14}H_3$). ^{15}N NMR (40 MHz; $CDCl_3$; T = 300 k) δ 282,1 (N^{12}), 52.0 (N^6). The signals relative to *N*-Ts were not detected. Elemental Analysis: Found: C, 55.4; H, 5.2; N, 6.4% Calc. for $C_{38}H_{41}F_3N_4O_7S_3$: C, 55.7; H, 5.0; N, 6.8%. MS (FAB): m/z 669.2 (M^+-$CF_3SO_3^-$). $[\alpha]_D^{20}$ = - 168 (*c* 0.5 in CH_2Cl_2).

5d-(13*R*) was synthesized in the same way starting from **4d-(13*R*)**. $[\alpha]_D^{20}$ = + 168 (*c* 0.5 in CH_2Cl_2)

Synthesis of 6b

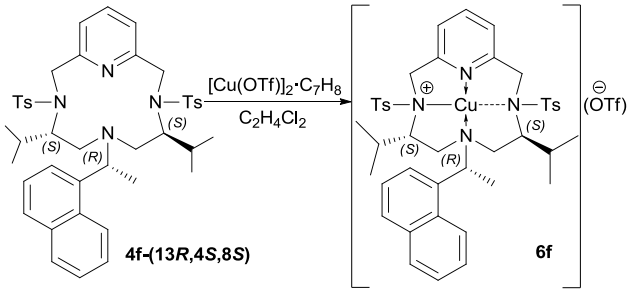


Copper (I) triflate benzene complex (0.0298 g, 0.0591 mmol) was added to a solution of macrocycle **4b** (0.0891 g, 0.118 mmol) in dichloroethane (10 mL). The solution was stirred at room temperature for one hour, concentrated to 5 mL and then 10 mL of *n*-hexane were layered. Then the solid was filtered and dried *in vacuo* under nitrogen, obtaining complex **6b** as a solid (0.111 g, 0.115 mmol, yield: 97%).

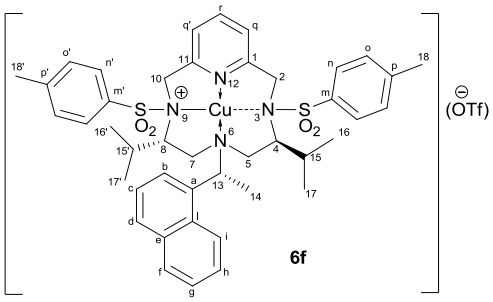


^{1}H NMR (300 MHz; $CDCl_3$; T = 300 k) δ 8.97 (1H, d, *J* = 7.8 Hz, H^i), 8.08-8.05 (2H, m, Ar*H*), 7.92 (1H, m, Ar*H*), 7.85-7.75 (2H, m, H^r) 7.65-7.52 (7H, m, Ar*H*), 7.42-7.37 (4H, m, Ar*H*), 7.27-7.17 (2H, m, Ar*H*), 4.89 (2H, d, *J* = 14.7 Hz, H^2 and H^{10}), 4.46 (2H, m, CH_2^{13}), 3.68 (2H, d, *J* = 14.7 Hz, H^2 and H^{10}), 3.53 (2H, m, H^4 and H^8), 2.93 (2H, m, H^4 and H^8), 2.82 (2H, m, H^5 and H^7), 2.50 (6H, s, CH_3^{14}), overlapping with 2.58-2.50 (2H, m, H^5 and H^7). Elemental Analysis: Found: C, 51.4; H, 4.3; N, 6.1% Calc. for $C_{37}H_{38}CuF_3N_4O_7S_3$: C, 51.2; H, 4.4; N, 6.6%.

Synthesis of 6f



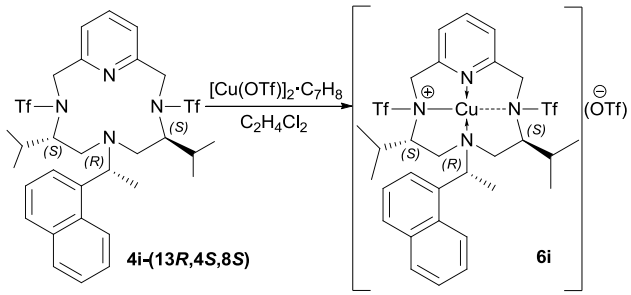
Copper (I) triflate benzene complex (0.0298 g, 0.0591 mmol) was added to a solution of macrocycle **4f-(13*R*,4*S*,8*S*)** (0.0891 g, 0.118 mmol) in dichloroethane (10 mL). The solution was stirred at room temperature for one hour, concentrated to 5 mL and then 10 mL of *n*-hexane were layered. Then the solid was filtered and dried *in vacuo* under nitrogen, obtaining complex **6f** as a solid (0.111 g, 0.115 mmol, yield: 97%).



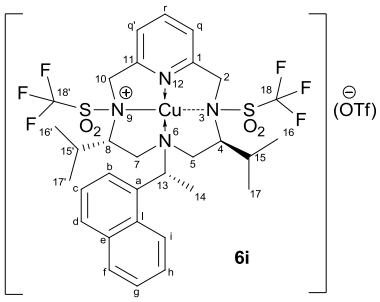
6f

^{1}H NMR (300 MHz; $CDCl_3$; T = 300 k) δ 8.68 (1H, d, *J* = 8.7 Hz, H^{i}), 7.93 (1H, d, *J* = 8.0 Hz, Ar*H*), 7.87 (4H, d, *J* = 8.1 Hz, H^{n} and $H^{n'}$), 7.80-7.69 (3H, m, Ar*H*), 7.62-7.40 (7H, m, Ar*H*), 7.23-7.16 (2H, m, Ar*H*), 5.95 (1H, q, *J* = 6.6 Hz, H^{14}), 5.25 (1H, d, *J* = 20 Hz, H^{2}), 4.79 (1H, d, *J* = 12.7 Hz, H^{7}), 4.71 (1H, d, *J* = 14.6 Hz, H^{10}), 4.62 (1H, d, *J* = 20 Hz, $H^{2'}$), overlapping with 4.61 (1H, m, H^{8}), 4.01 (1H, d, *J* = 14.6 Hz, $H^{10'}$), 2.78 (1H, d, *J* = 12.7 Hz, $H^{7'}$), 2.57 (3H, s, $CH_3^{18 \text{ or } 18'}$), overlapping with 2.57 (1H, m, H^{4}), 2.52 (3H, s, $CH_3^{18' \text{ or } 18}$), 2.42-2.37 (1H, m, H^{5}), 2.30-2.15 (2H, m, $H^{5'}$ and $H^{15'}$), 2.10 (3H, d, *J* = 6.8 Hz, CH_3^{14}), 1.59 (1H, m, H^{15}), 0.90 (3H, d, *J* = 6.7 Hz, $CH_3^{16'}$), 0.68 (3H, d, *J* = 6.2 Hz, CH_3^{17}), 0.29 (3H, d, *J* = 6.5 Hz, $CH_3^{17'}$), -0.49 (3H, d, *J* = 6.2 Hz, CH_3^{16}). ^{13}C NMR (75 MHz; $CDCl_3$; T = 300 k) δ 155.7 ($C^{1 \text{ or } 11}$), 151.2 ($C^{11 \text{ or } 1}$), 145.6 ($C^{p'}$), 145.3 (C^{p}), 140.4 (*C*H), 134.8 (C^{a}), 134.5 (C^{l}), 133.9 (*C*), 132.1 (*C*), 131.5 (*C*H), 130.4 (C^{o}), 129.8 (*C*H), 129.3 (*C*H), 128.9 (*C*H), 127.7 (CH^{h}), 127.3 (*C*H), 126.4 (*C*H), 125.2 (*C*H), 124.8 (*C*H), 124.5 (*C*H), 123.9 (*C*H), 122.8 (C^{i}), 64.7 (C^{4}H), 62.0 (C^{8}H), 57.4 ($C^{5}H_2$), 57.1 ($C^{10}H_2$), 56.4 (C^{13}H), 55.5 ($C^{7}H_2$), 46.8 ($C^{2}H_2$), 29.9 ($C^{15'}$H), 27.1 (C^{15}H), 24.5 ($C^{14}H_3$), 22.4 ($C^{16'}H_3$), 21.9 ($C^{18 \text{ and } 18'}H_3$), 21.3 ($C^{17'}H_3$), 20.3 ($C^{17}H_3$), 18.5 ($C^{16}H_3$), ^{19}F NMR (282 MHz; $CDCl_3$; T = 300 k) δ - 78.58 (s). Elemental Analysis: Found: C, 54.7; H, 5.2; N, 5.7% Calc. for $C_{44}H_{52}CuF_3N_4O_7S_3$: C, 54.7; H, 5.4; N, 5.8%.

Synthesis of 6i

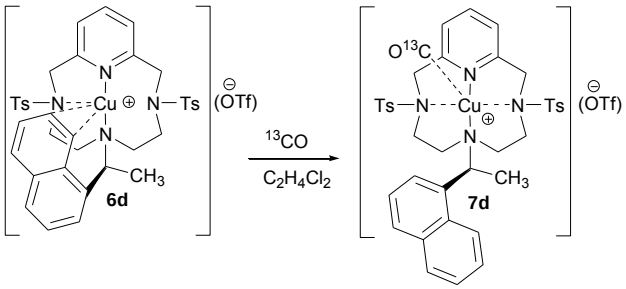


Copper (I) triflate benzene complex (0.231 g, 0.171 mmol) was added to a solution of macrocycle **4f-(13*R*,4*S*,8*S*)** (0.0860 g, 0.325 mmol) in dichloroethane (7 mL). The solution was stirred at room temperature for one hour and then 50 mL of *n*-hexane were layered. Then the solid was filtered and dried *in vacuo* under nitrogen, obtaining complex **6i** as a solid (0.140 g, 0.152 mmol, yield: 45%).

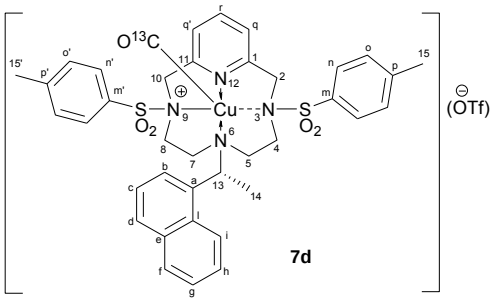


^{1}H NMR (300 MHz; $CDCl_3$; Me_4Si; T = 300 k) δ 8.16 (1H, d, *J* = 8.9 Hz, H^{i}), 8.01 (2H, pst, *J* = 7.5 Hz, Ar*H*), 7.80 (1H, pst, *J* = 7.7 Hz, Ar*H*), 7.73 (1H, m, Ar*H*), 7.68-7.63 (3H, m, Ar*H*), 7.31 (1H, m, Ar*H*), 7.20 (1H, m, Ar*H*), 6.46 (1H, m, H^{13}), 5.10-4.70 (5H, m, *H*), 4.40-4.01 (3H, m, *H*), 3.50 (1H, m, *H*), 2.95 (1H, m, *H*), 2.50-2.36 (1H, m, *H*), 2.06 (3H, d, *J* = 6.8 Hz, CH_3^{14}), 1.52 (1H, m, *H*), 1.27 (3H, bs, $CH_{3i\text{-}prop}$), 1.10 (3H, bs, $CH_{3i\text{-}prop}$), 0.80 (3H, bs, $CH_{3i\text{-}prop}$), 0.47 (3H, bs, $CH_{3i\text{-}prop}$). ^{13}C NMR (75 MHz; $CDCl_3$; T = 300 k) δ 139.3 (*C*H), 131.7 (*C*H), 130.4 (*C*H), 128.5 (*C*H), 127.4 (*C*H), 125.7 (*C*H), 122.6 (*C*H), 121.3 (C^{i}H), 57.1 (CH_2), 43.6 (CH_2), 31.7 (CH_2), 28.8 (*C*H), 22.8 (CH_2), 21.3 ($C^{14}H_3$), 20.8 ($CH_{3\ i\text{-}prop}$), 14.3 ($CH_{3\ i\text{-}prop}$). Signals relative to quaternary carbons, aromatic *C*H, aliphatic *C*H and CH_3 were not detected. Elemental Analysis: Found: C, 41.8; H, 3.7; N, 5.8% Calc. for $C_{32}H_{38}CuF_9N_4O_7S_3$: C, 41.7; H, 4.2; N, 6.1%.

Synthesis of 7d



20 mg of copper(I) complex **6d** were added to anhydrous and degassed $CDCl_3$ in a NMR tube and the solution was saturated with ^{13}CO, obtaining **7d**.

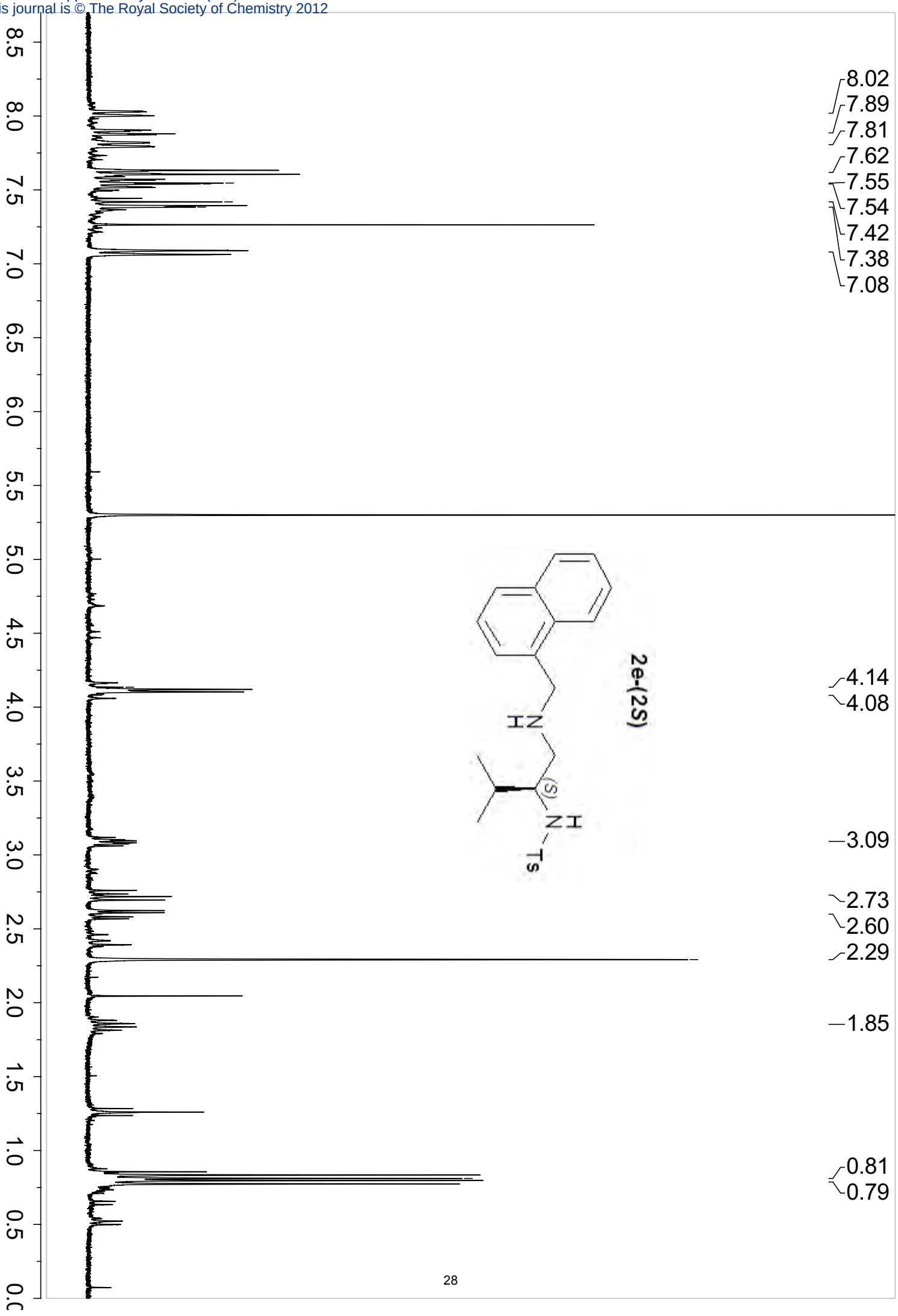


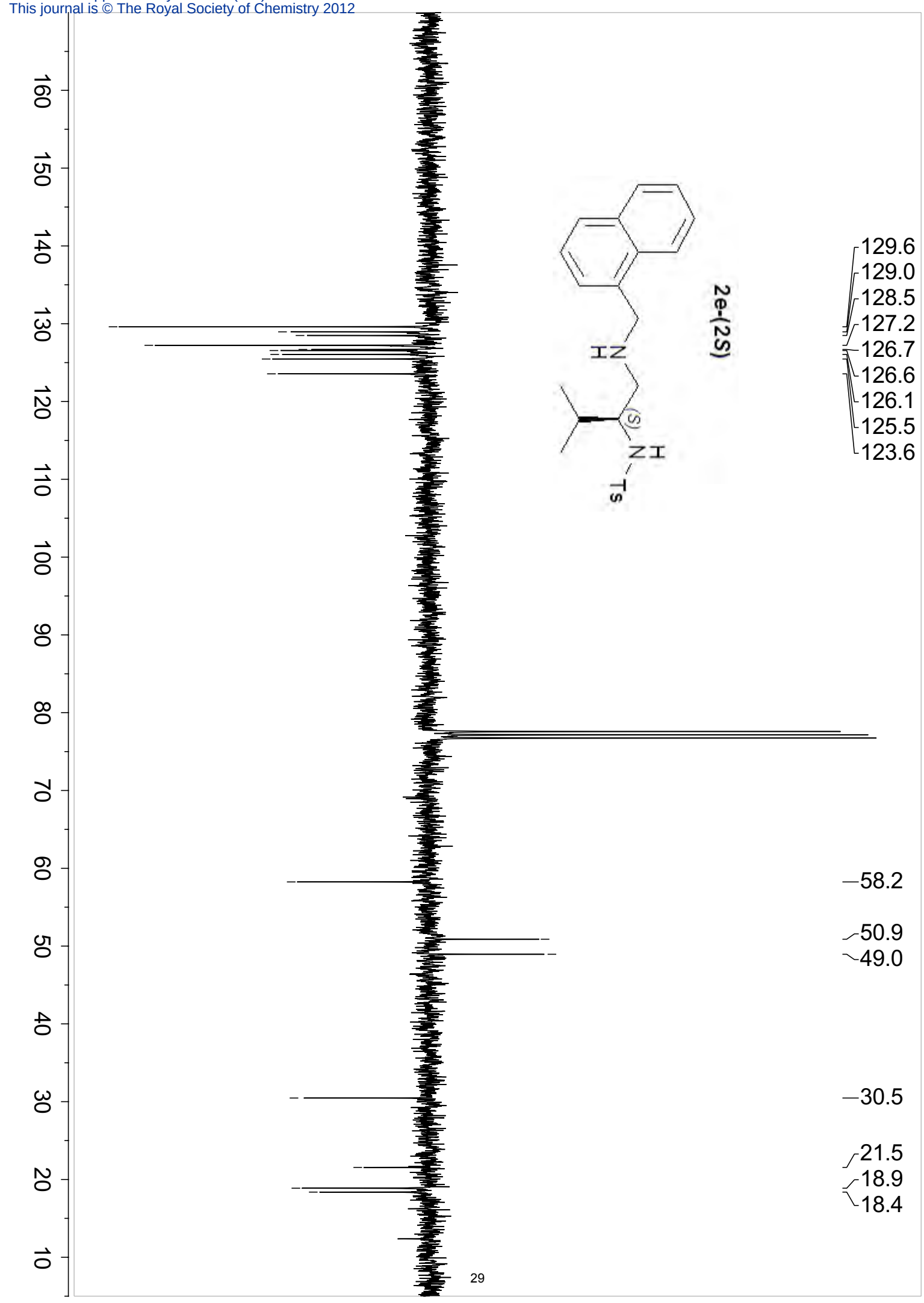
^{1}H NMR (300 MHz; $CDCl_3$; T = 300 k) δ 8.77 (1H, d, *J* = *8.7* Hz, H^{i}), 7.96 (1H, d, *J* = *8.3* Hz, Ar*H*), 7.88 (2H, d, *J* = 8.5 Hz, $H^{n \text{ or } n'}$), 7.84-7.82 (1H, m, Ar*H*) overlapping with 7.81 (2H, d, *J* = 8.2 Hz, $H^{n' \text{ or } n}$), 7.73 (1H, m, H^{h}), 7.68-7.59 (2H, m, Ar*H*), 7.53 (2H, d, *J* = 8.5 Hz, $H^{o \text{ or } o'}$), 7.49 (1H, m, Ar*H*), 7.40 (2H, d, *J* = *8.2* Hz, $H^{o' \text{ or } o}$), 7.31 (1H, m, Ar*H*), 7.23-7.16 (2H, m, Ar*H*), 6.19 (1H, q, *J* = 6.8 Hz, H^{13}), 5.24 (1H, d, *J* = 17.7 Hz, $H^{10 \text{ or } 2}$), overlapping with 5.19 (1H, d, *J* = 15.0 Hz, $H^{2 \text{ or } 10}$), 4.80 (1H, m, H^{7}), 4.30 (1H, m, H^{7}), 3.98 (1H, d, *J* = 17.7 Hz, $H^{10 \text{ or } 2}$), 3.64 (1H, d, *J* = 15.0 Hz, $H^{2 \text{ or } 10}$), 3.09-2.64 (4H, m, CH), 2.56 (3H, s, $CH_3^{15 \text{ or } 15'}$), 2.47 (3H, s, $CH_3^{15' \text{ or } 15}$), 2.36-2.28 (1H, m, $H^{7 \text{ or } 5}$), 2.16 (3H, *J* = *6.8* Hz, CH_3^{14}) overlapping with 2.15-2.07 (1H, m, $H^{8 \text{ or } 4}$). Highlighted signals are relative to compound **5d**. ^{13}C NMR (75 MHz; $CDCl_3$; T = 300 k) δ 184.4 (free ^{13}CO), 171.1 (^{13}CO), 156.1 (*C*), 152.2 (*C*), 145.9 (*C*), 140.4 (*CH*), 135.2 (*C*), 134.6 (*C*), 132.2 (*C*), 130.7 (2 CH_{Ts}), 130.0 (*C*H), 129.2 (CH_{Ts}), 129.2 (*C*H), 128.0 (CH_{Ts}), 126.8 ($C^{h}H$), 126.1 (*C*H), 125.5 (2 *C*H), 124.2 (*C*H), 123.6 (*C*H), 122.7 ($C^{i}H$), 56.8 ($C^{2}H_2$), 56.4 ($C^{2'}H_2$), 55.3 ($C^{13}H$), 52.7 ($C^{8}H_2$), 51.9 ($C^{5}H_2$), 50.7 ($C^{7}H_2$), 47.5 ($C^{4}H_2$), 23.4 ($C^{14}H_3$), 21.9 ($C^{15}H_3$), 21.7 ($C^{15'}H_3$). ^{15}N NMR

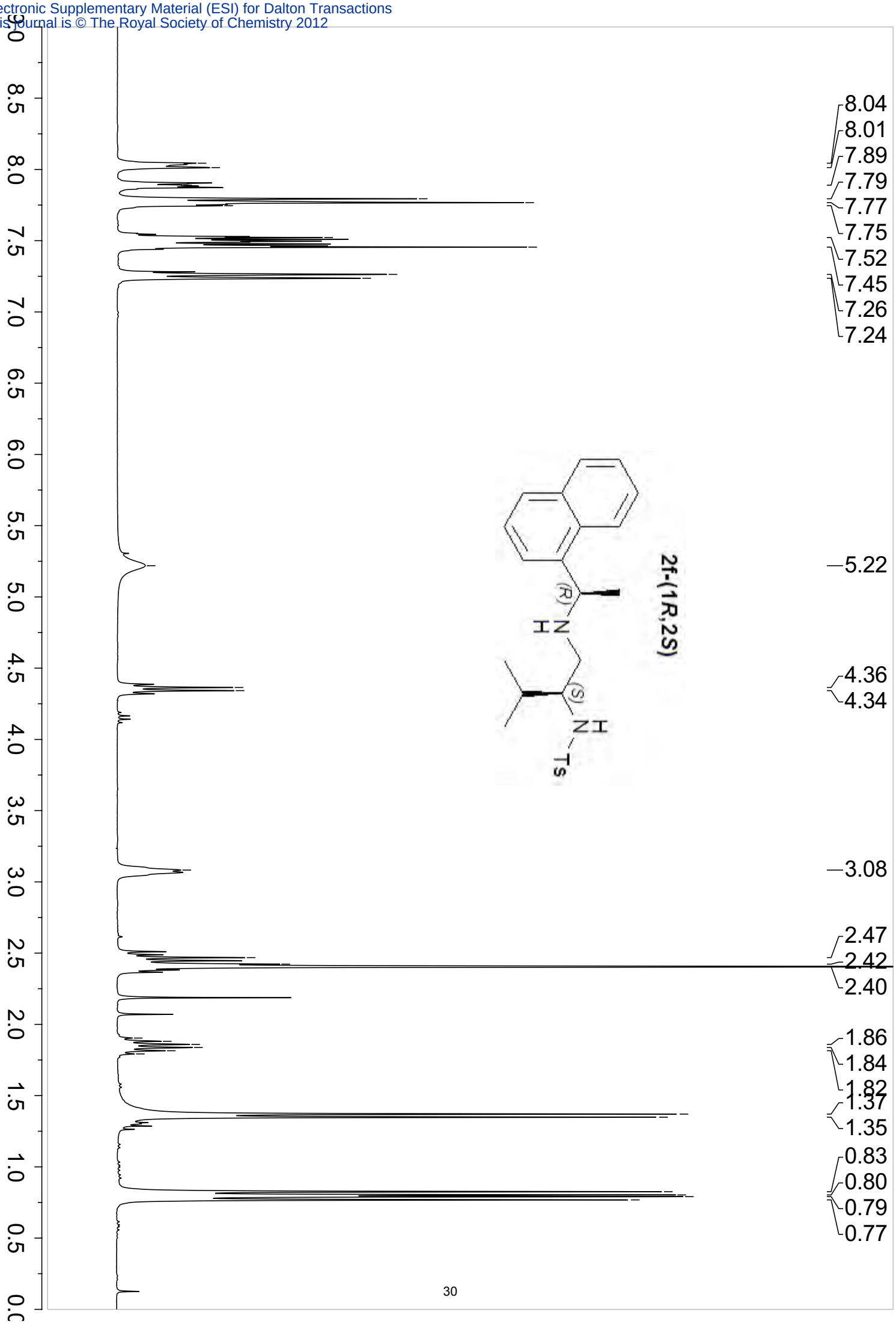
(40 MHz; $CDCl_3$; T = 300 k) δ 243.5 (N^{12}), 39.8 (N^6). The signals relative to *N*-Ts were not detected. IR (CH_2Cl_2 solution) $\nu_{CO} = 2111\ cm^{-1}$.

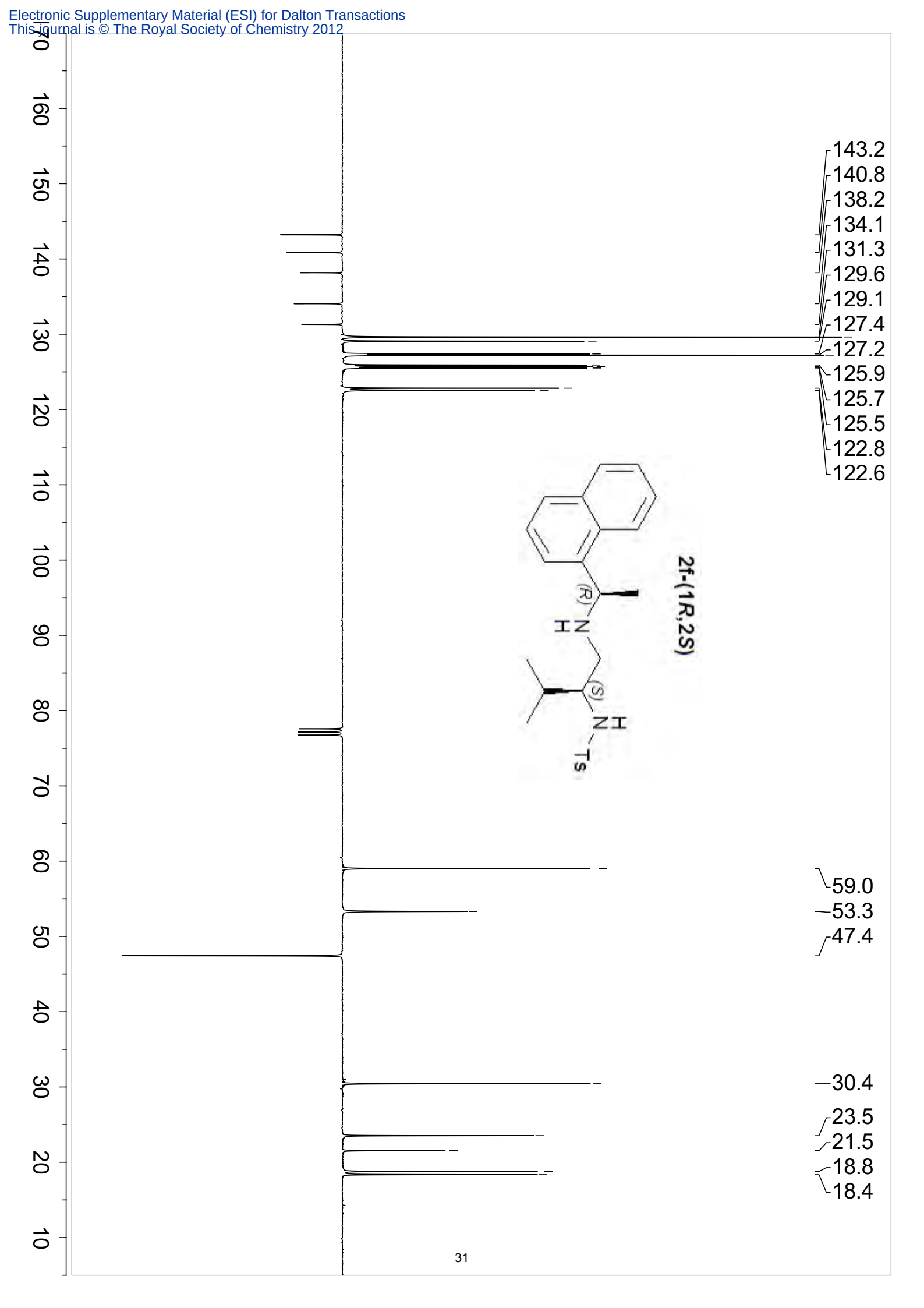
References

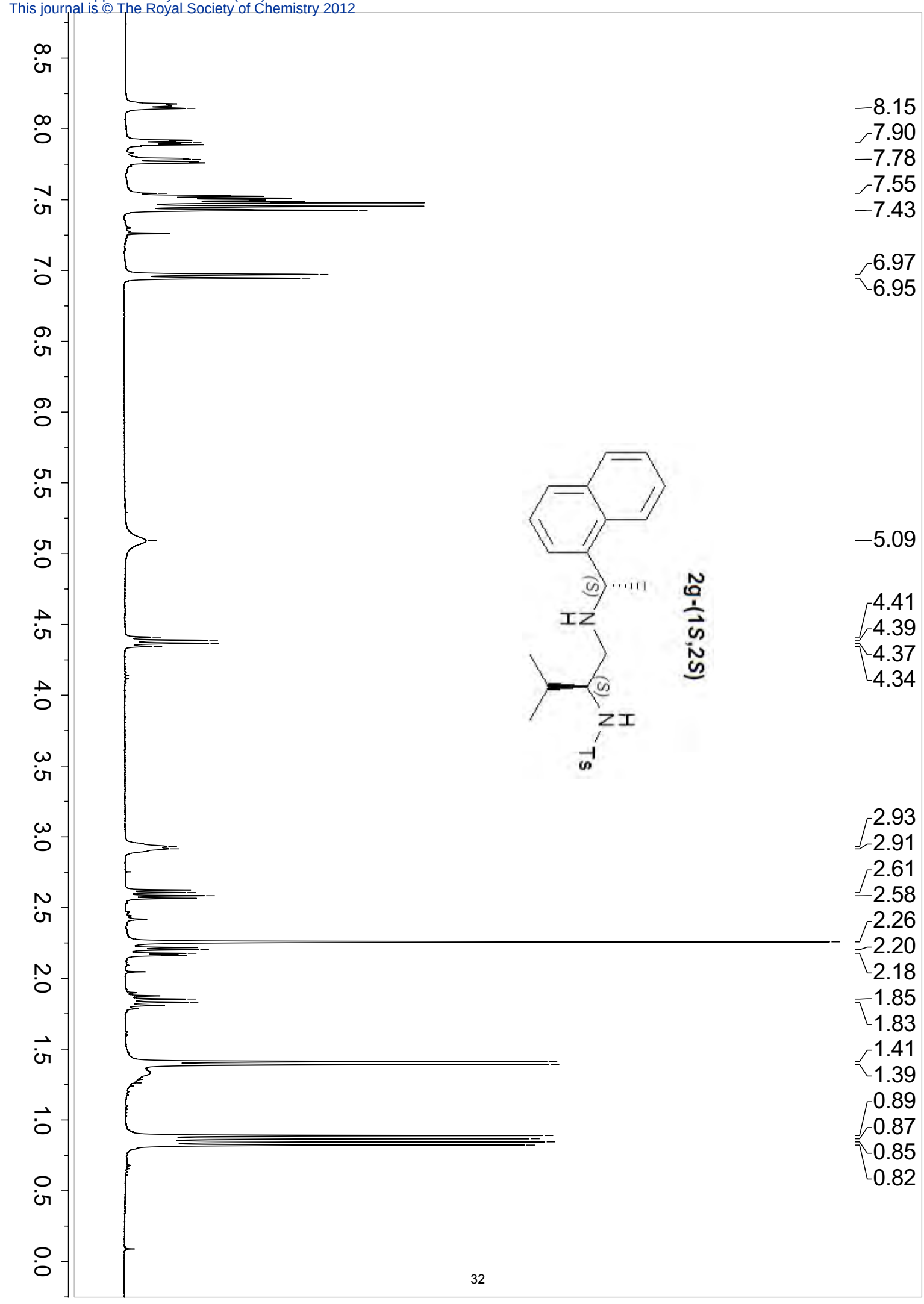
1. K. M. Gillespie, C. J. Sanders, P. O'Shaughnessy, I. Westmoreland, C. P. Thickitt and P. Scott, *J. Org. Chem.* , 2002, **67**, 3450-3458.
2. B. Castano, T. Pedrazzini, M. Sisti, E. Gallo, F. Ragaini, N. Casati and A. Caselli, *App. Organomet. Chem.*, 2011, **25**, 824-829.
3. A. Caselli, F. Cesana, E. Gallo, N. Casati, P. Macchi, M. Sisti, G. Celentano and S. Cenini, *Dalton Trans.*, 2008, 4202-4205.
4. A. Berkessel, P. Kaiser and J. Lex, *Chem. Eur. J.* , 2003, **9**, 4746-4756.
5. C. J. Sanders, K. M. Gillespie and P. Scott, *Tetrahedron: Asymmetry* 2001, **12**, 1055-1061.
6. L. Huang, Y. Chen, G.-Y. Gao and X. P. Zhang, *J. Org. Chem.* , 2003, **68**, 8179-8184.
7. Y. Chen, G.-Y. Gao and X. P. Zhang, *Tetrahedron Lett.*, 2005, **46**, 4965-4969.
8. C. Böhm, M. Schinnerl, C. Bubert, M. Zabel, T. Labahn, E. Parisini and O. Reiser, *Eur. J. Org. Chem.*, 2000, **2000**, 2955-2965.
9. A. G. M. Barrett, D. C. Braddock, I. Lenoir and H. Tone, *J. Org. Chem.*, 2001, **66**, 8260-8263.

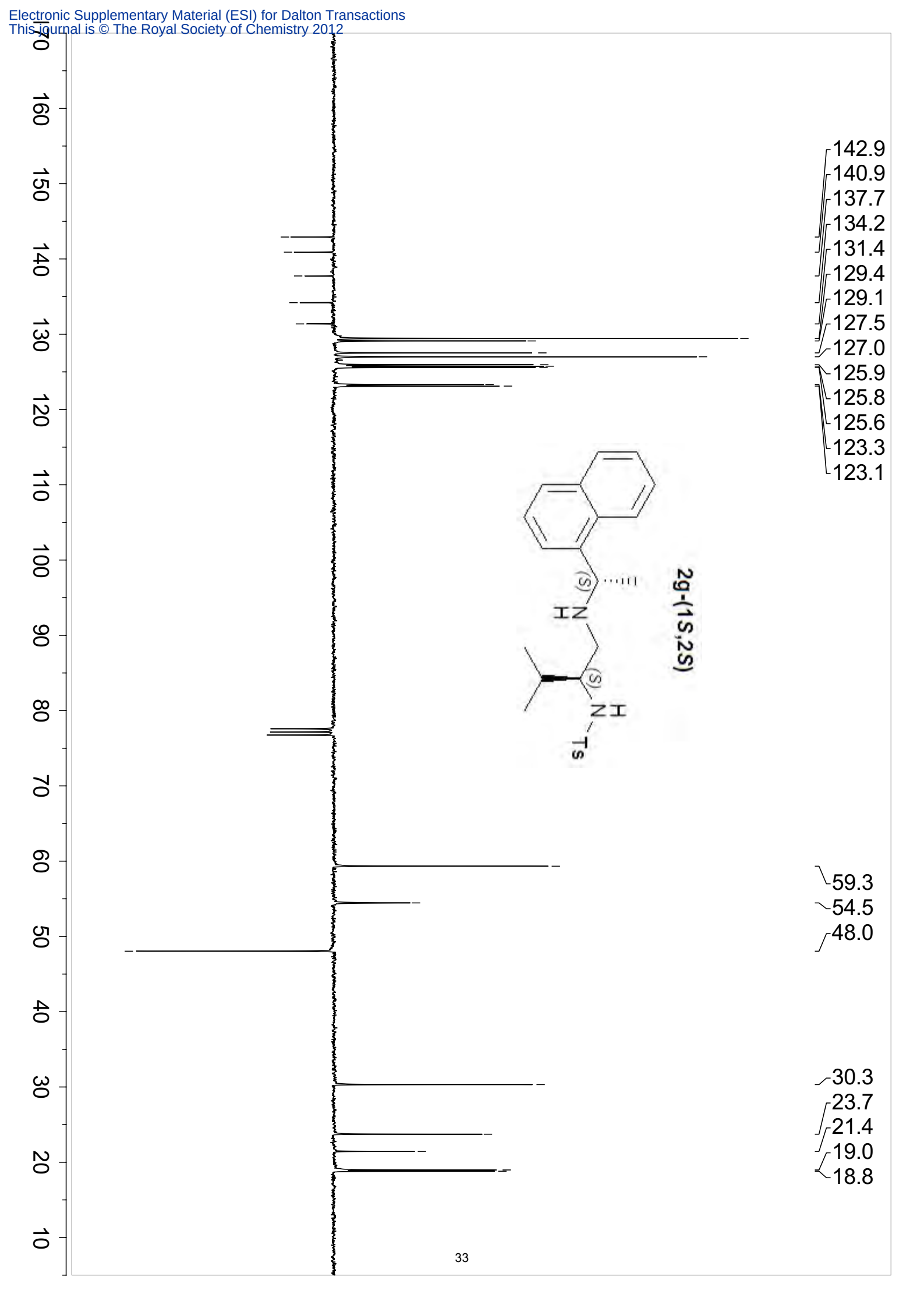


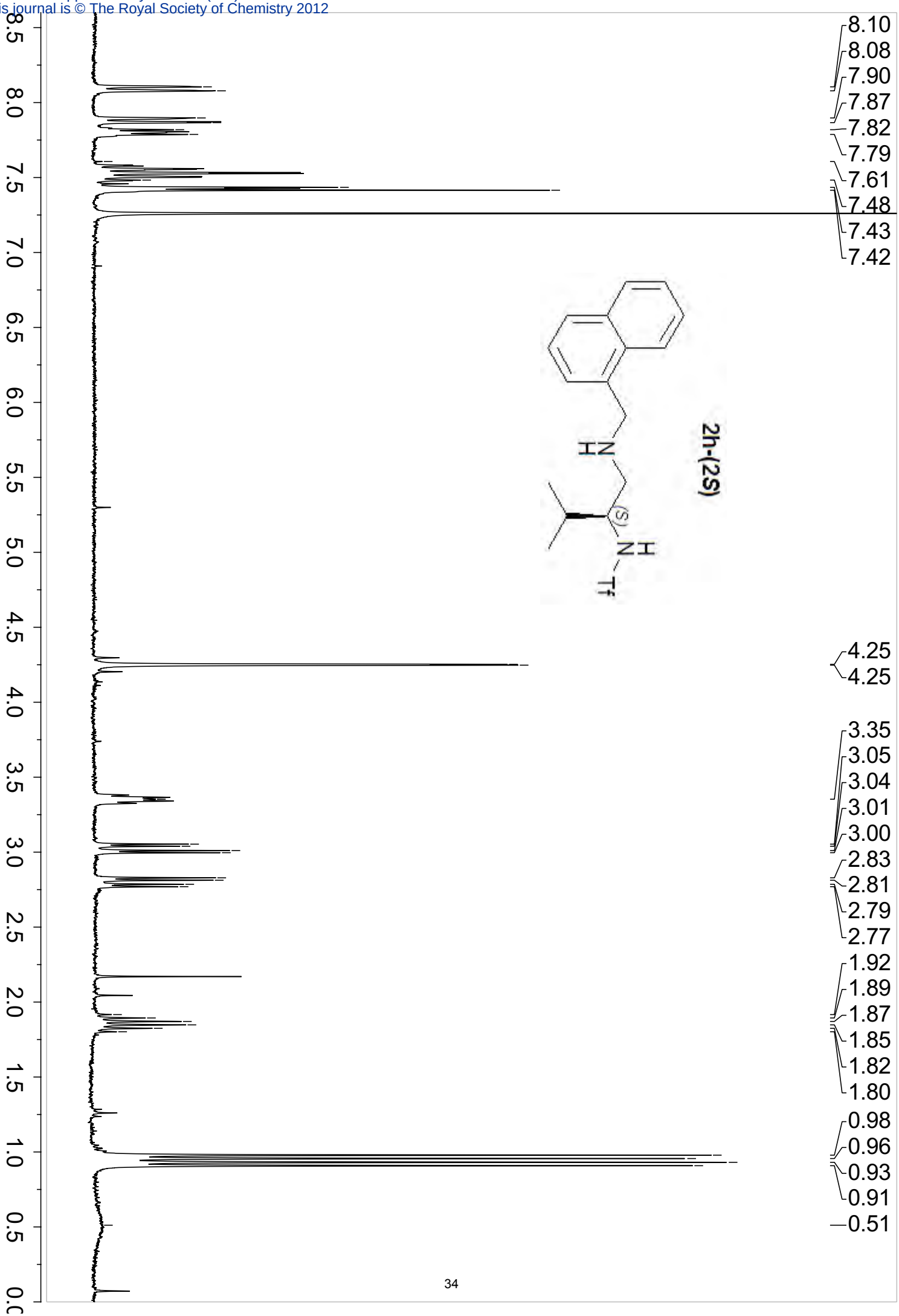


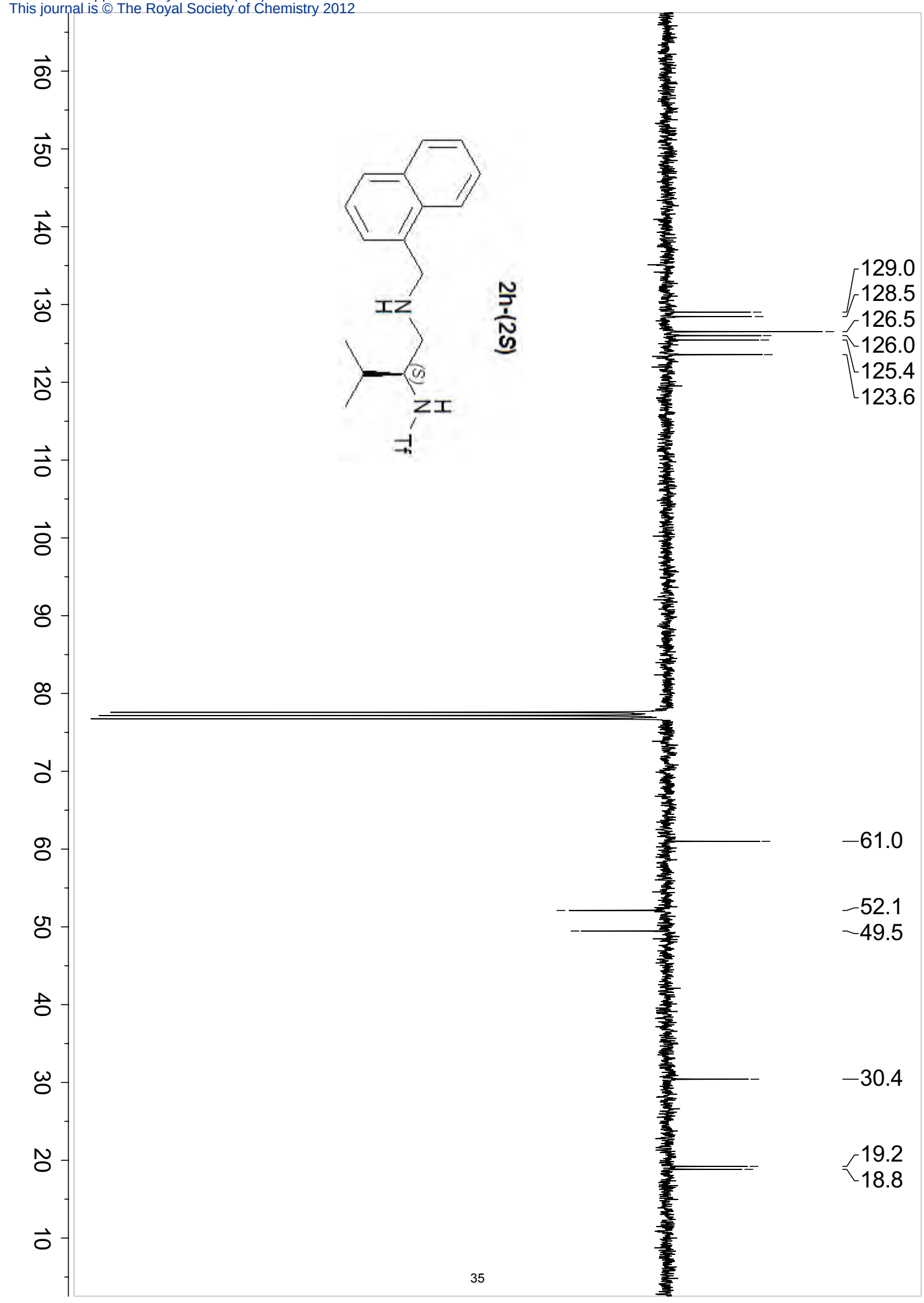


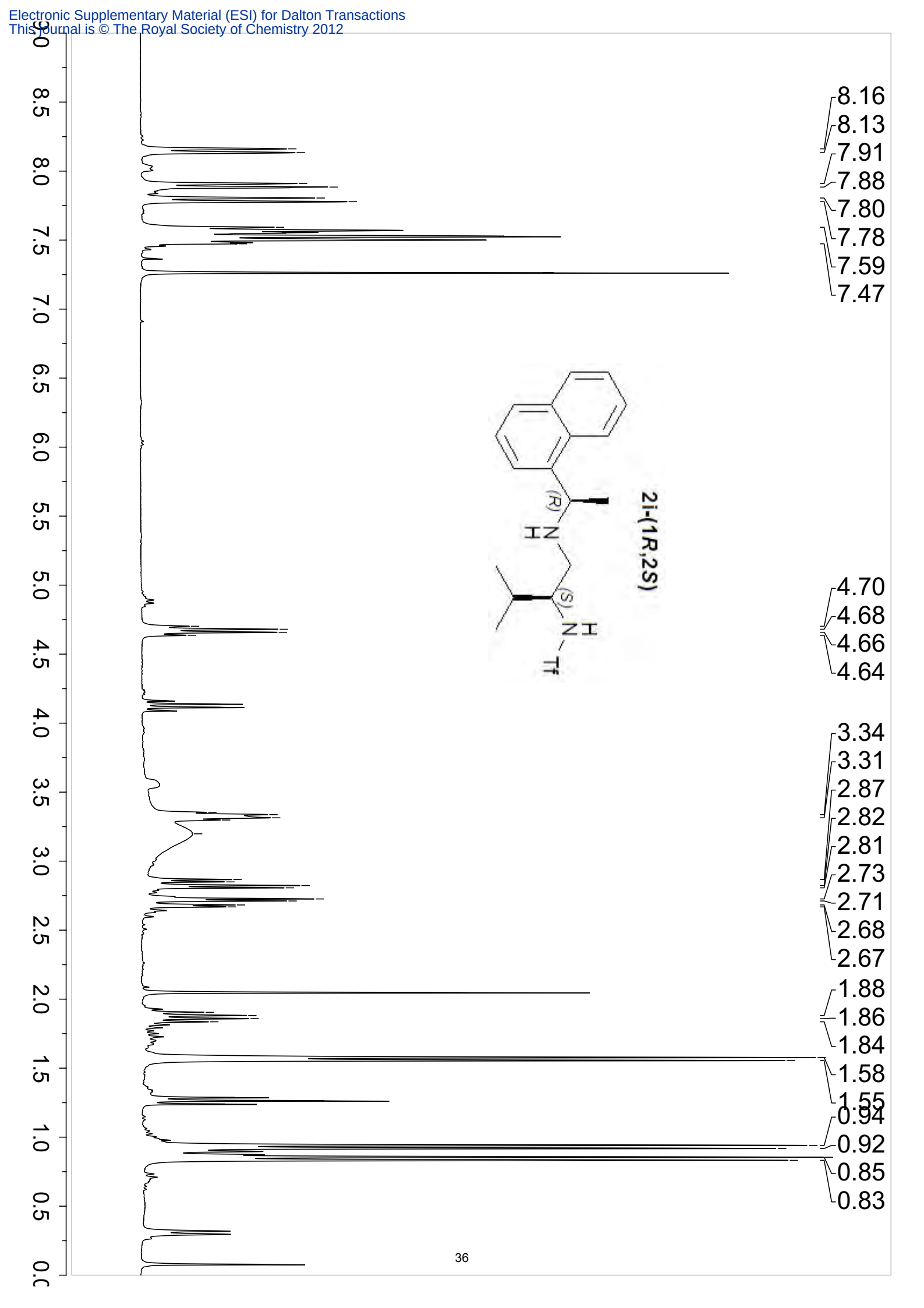

143.2
140.8
138.2
134.1
131.3
129.6
129.1
127.4
127.2
125.9
125.7
125.5
122.8
122.6
59.0
53.3
47.4
30.4
23.5
21.5
18.8
18.4
(R)
(S)
H
N
H
N
Ts
2f-(1R,2S)

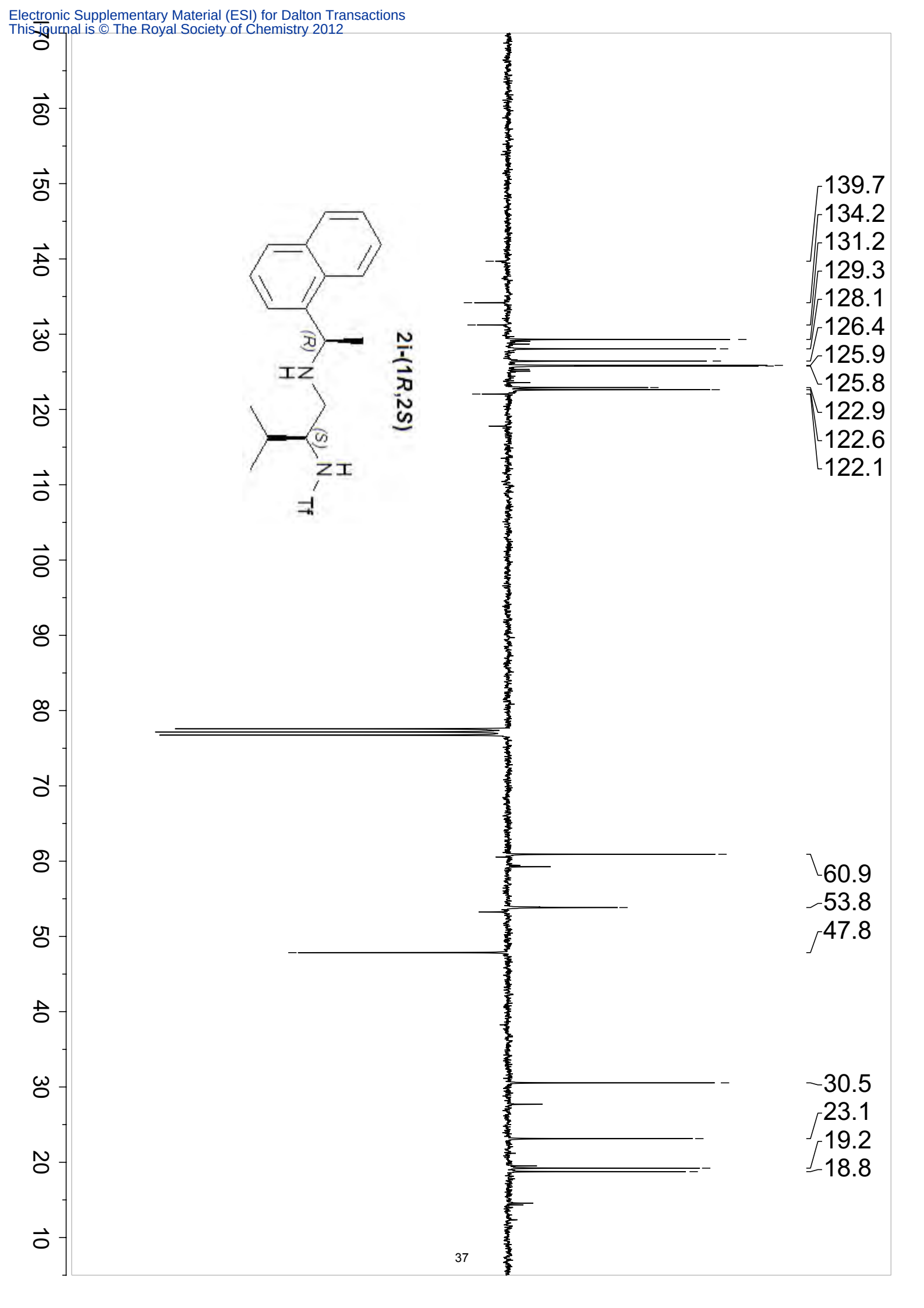


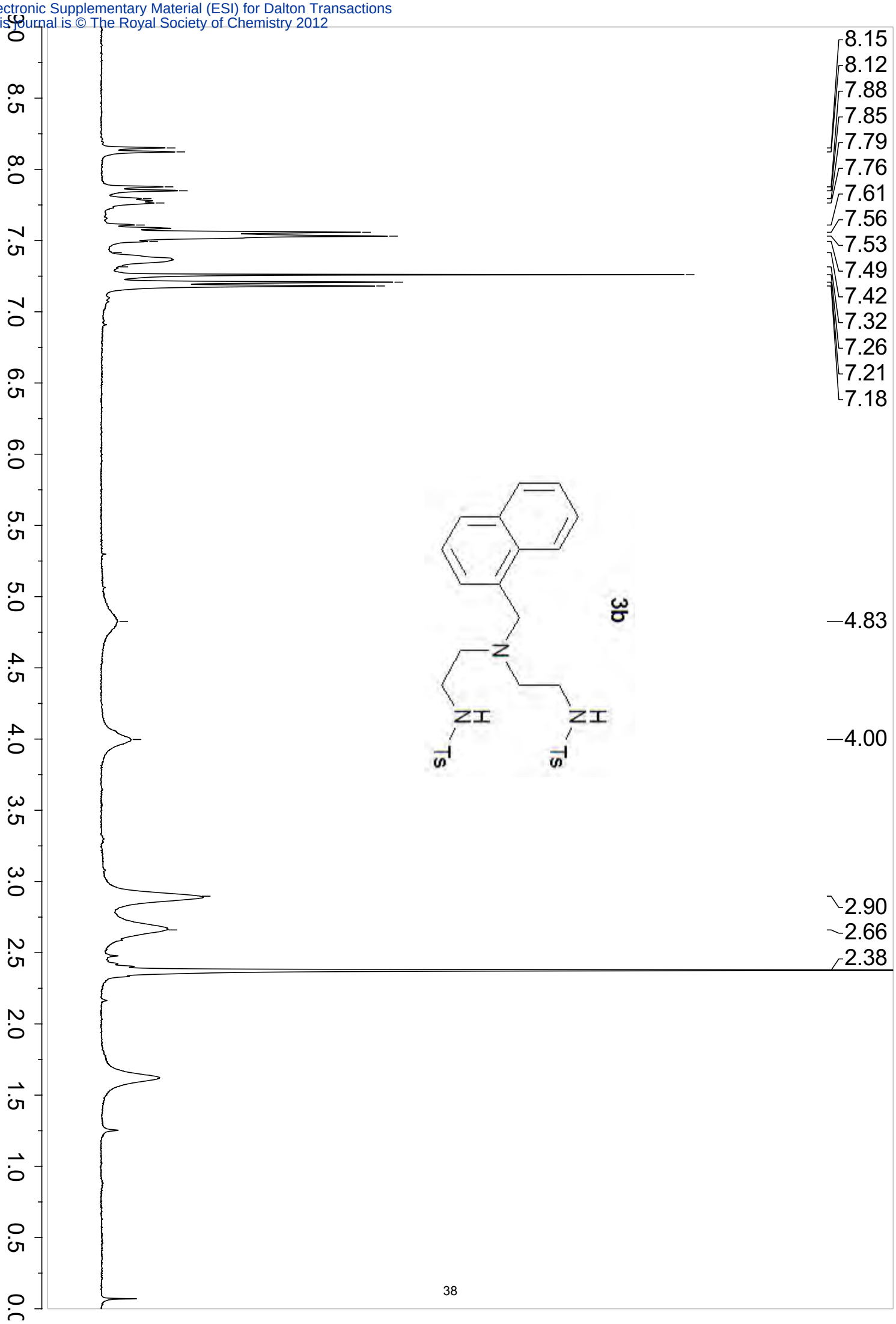


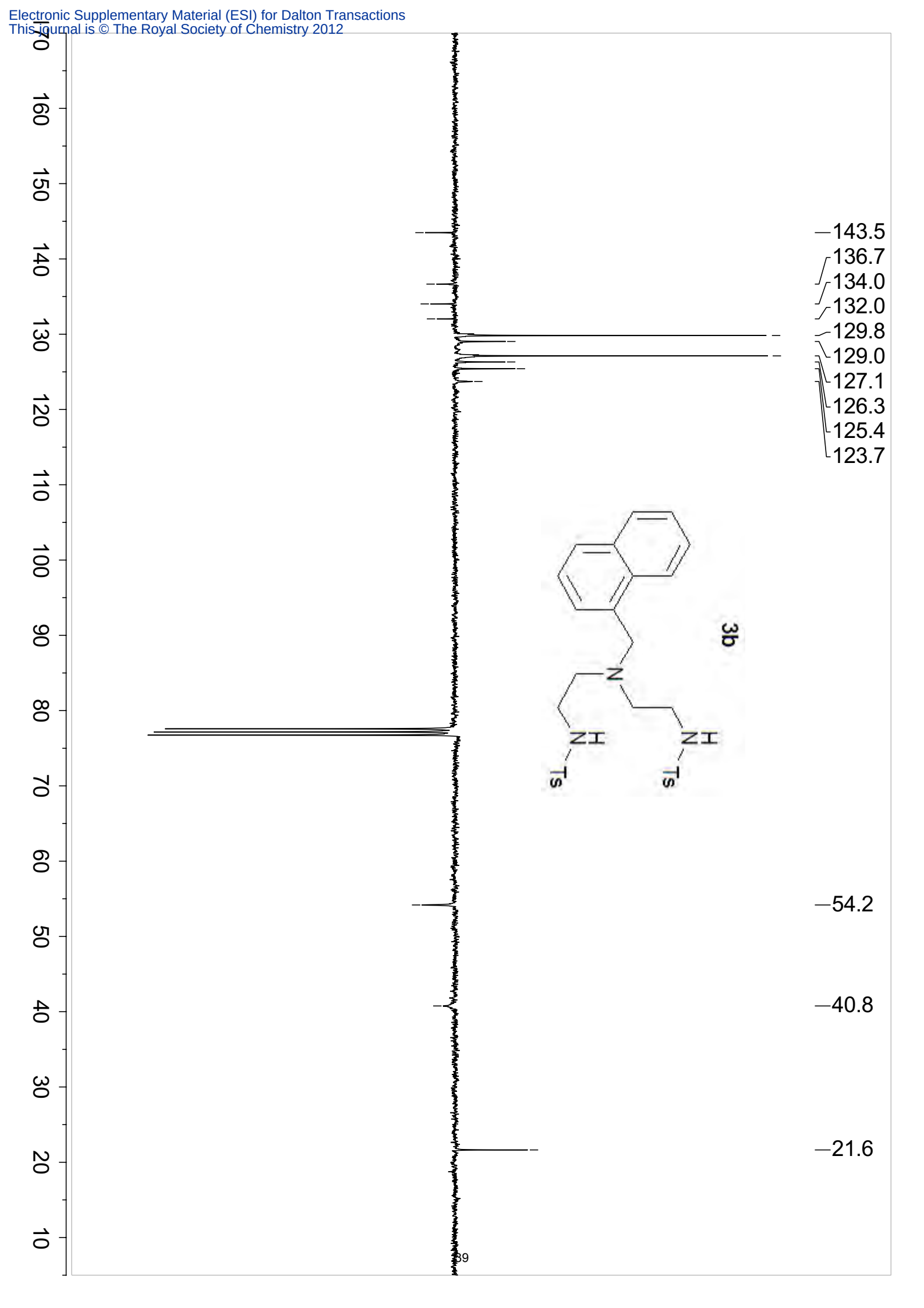


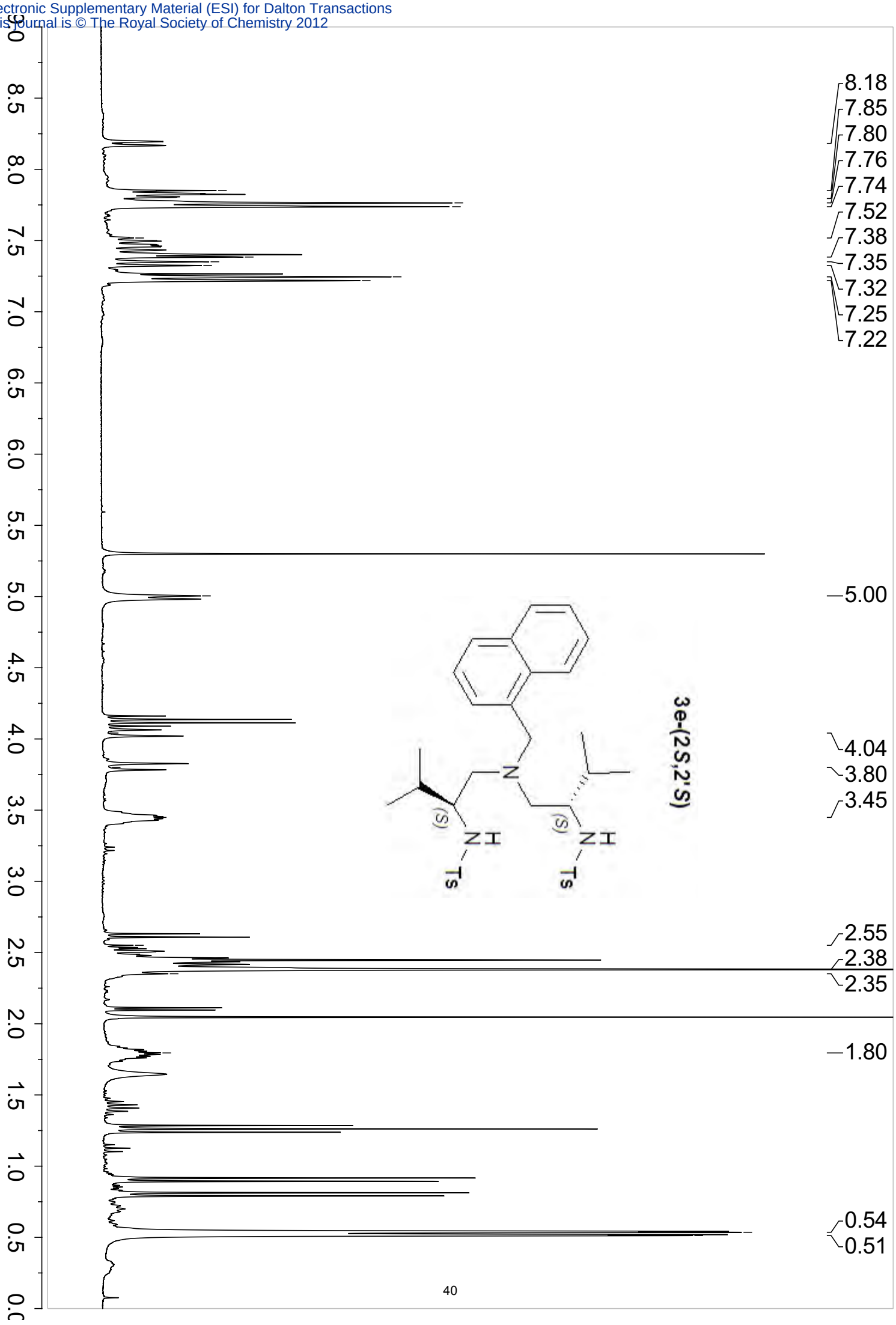


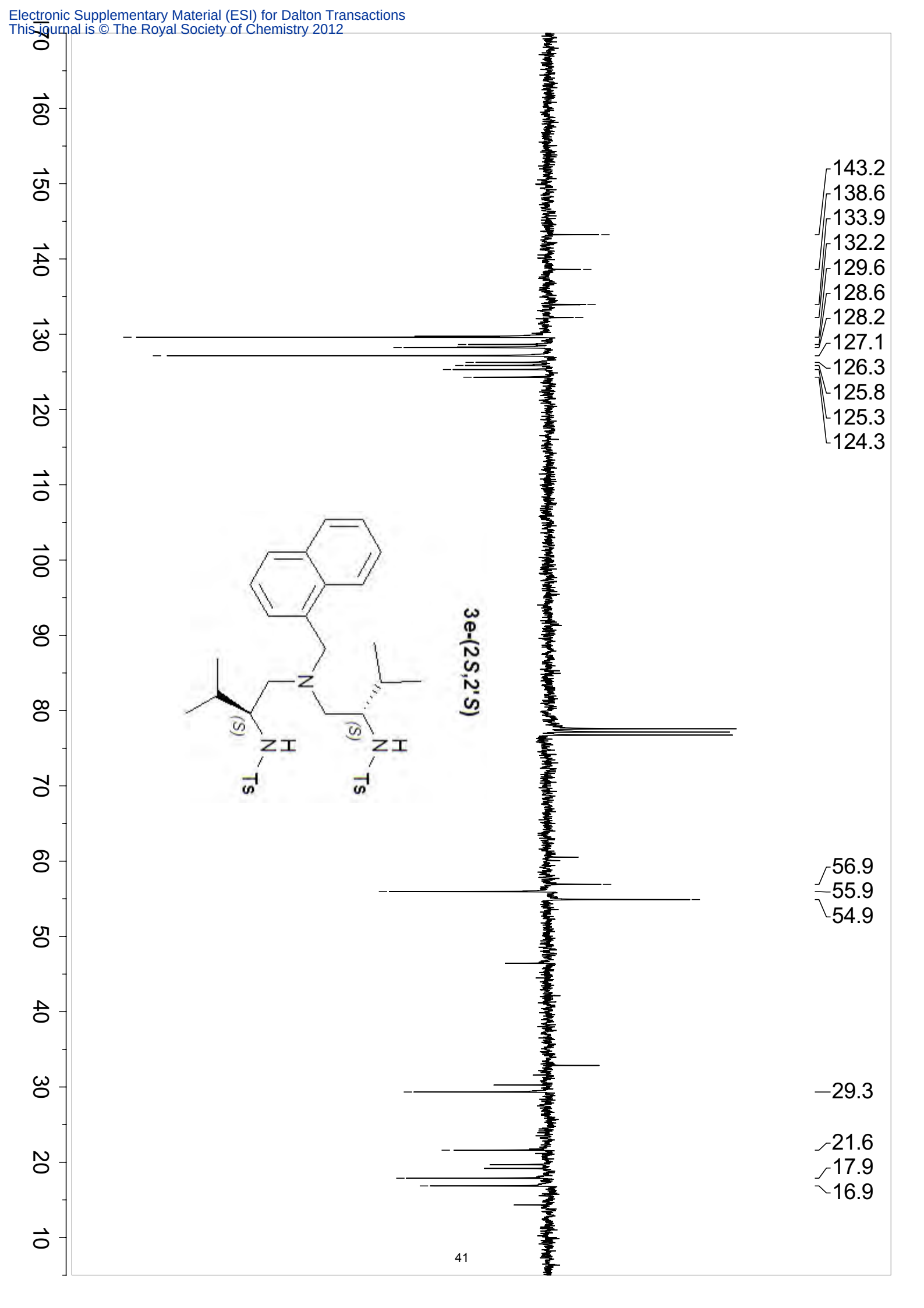


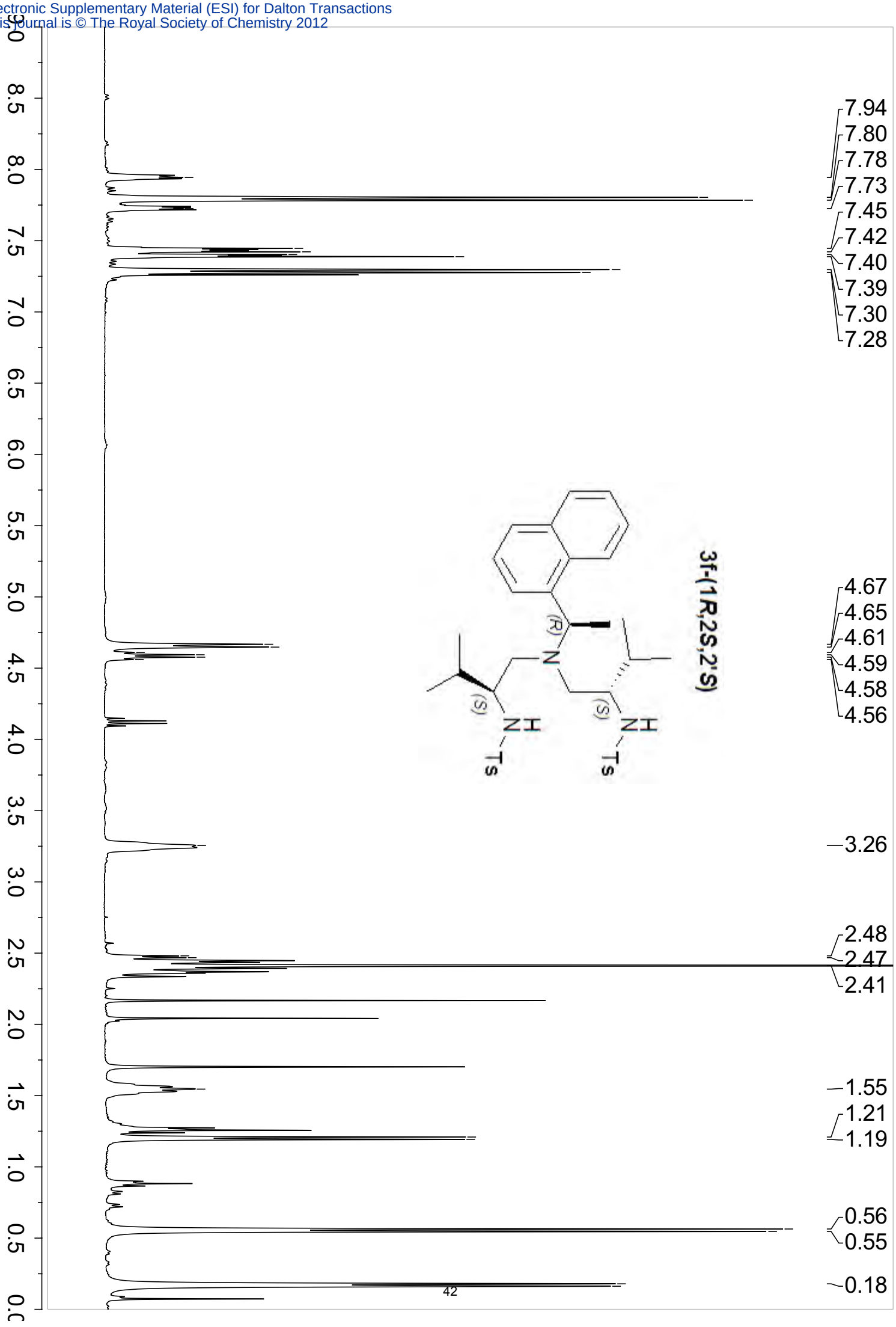


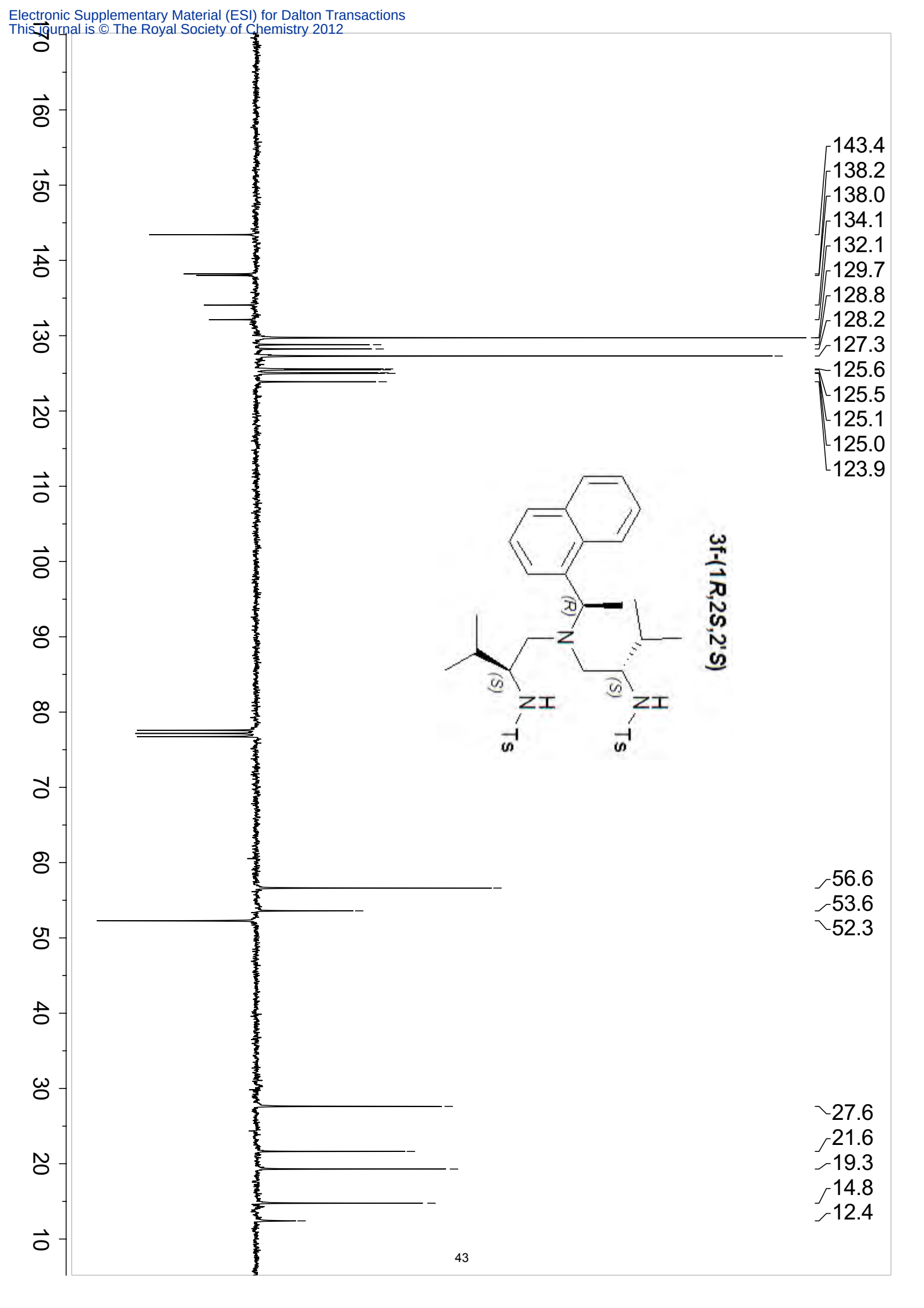


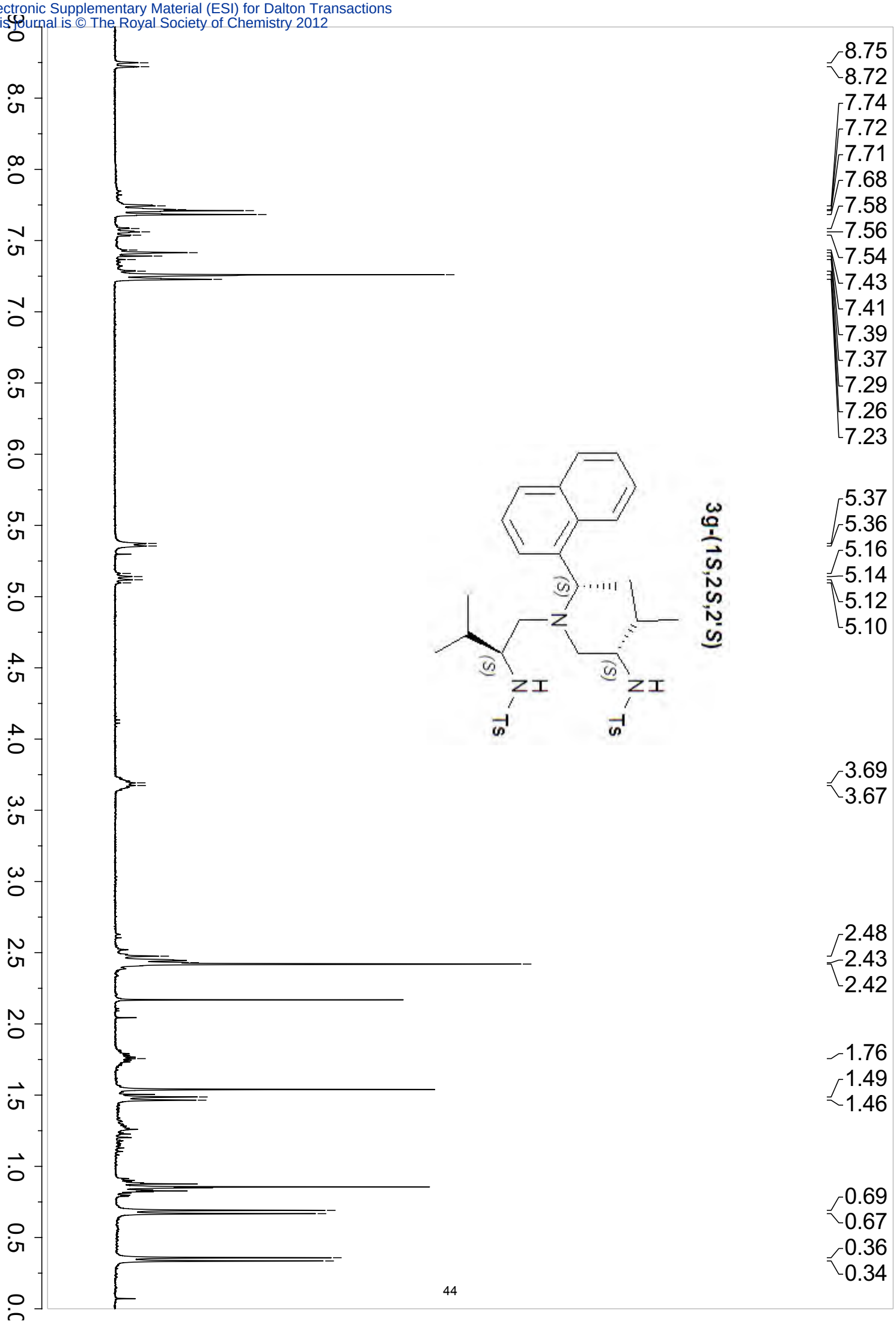


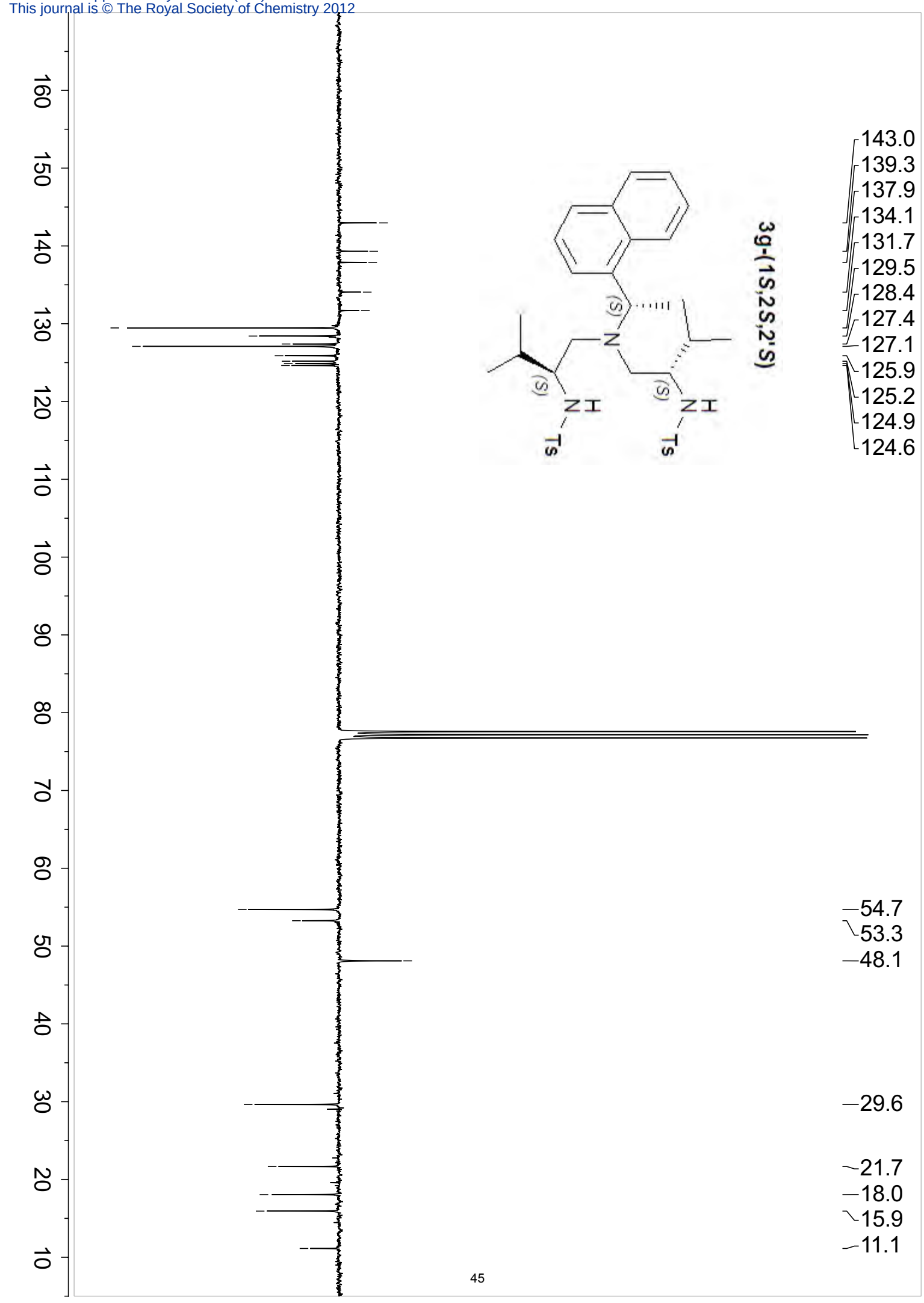


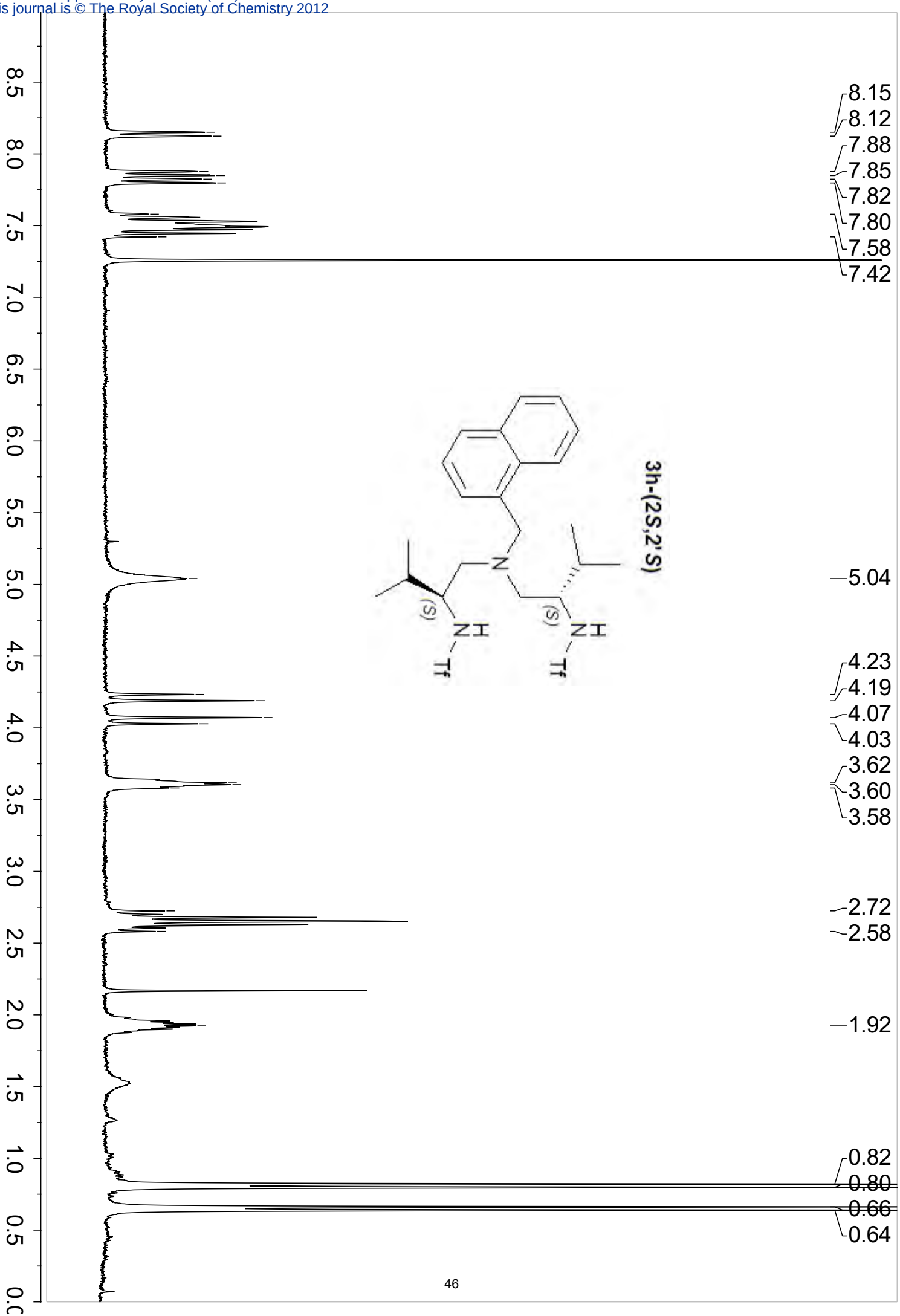


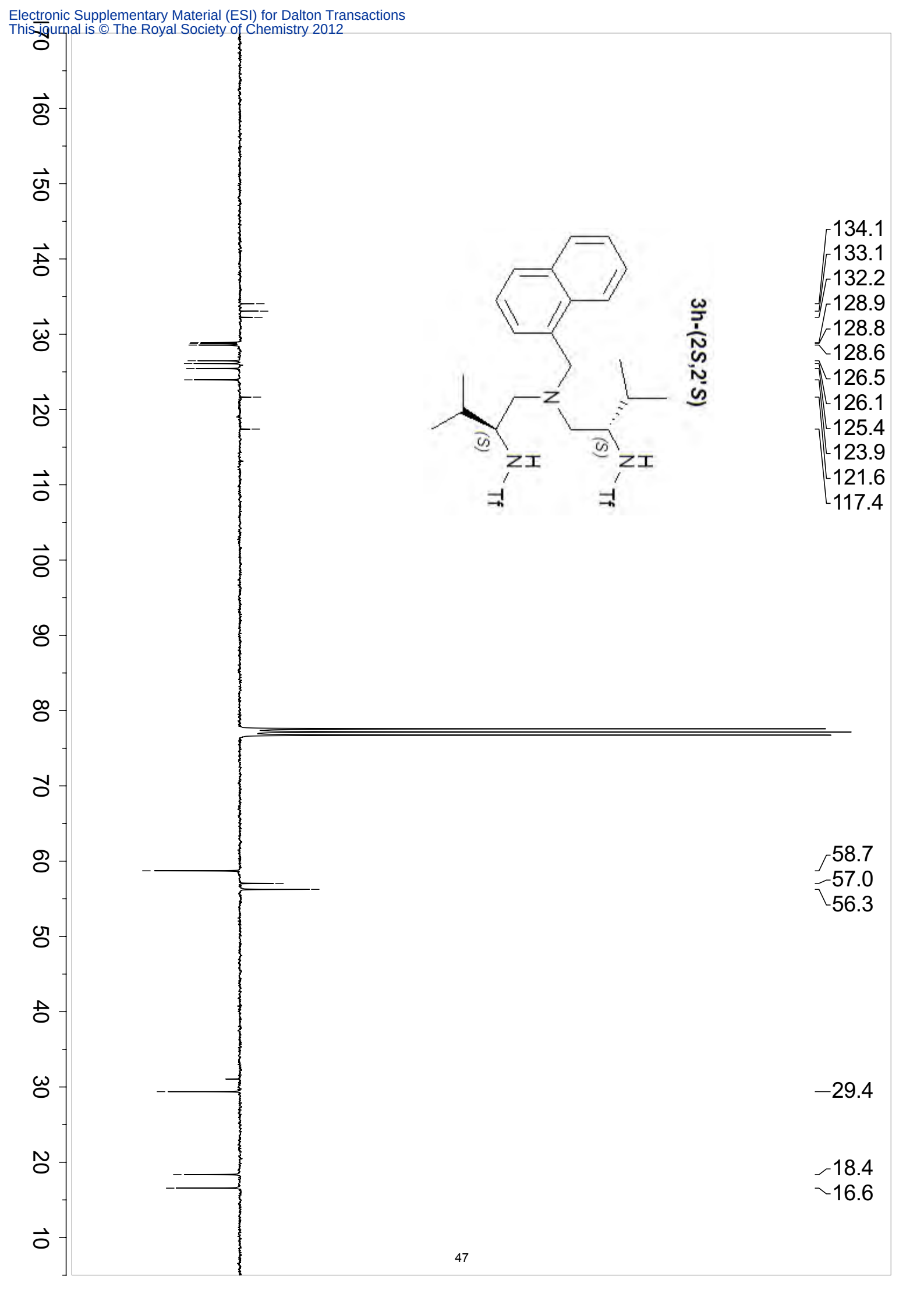


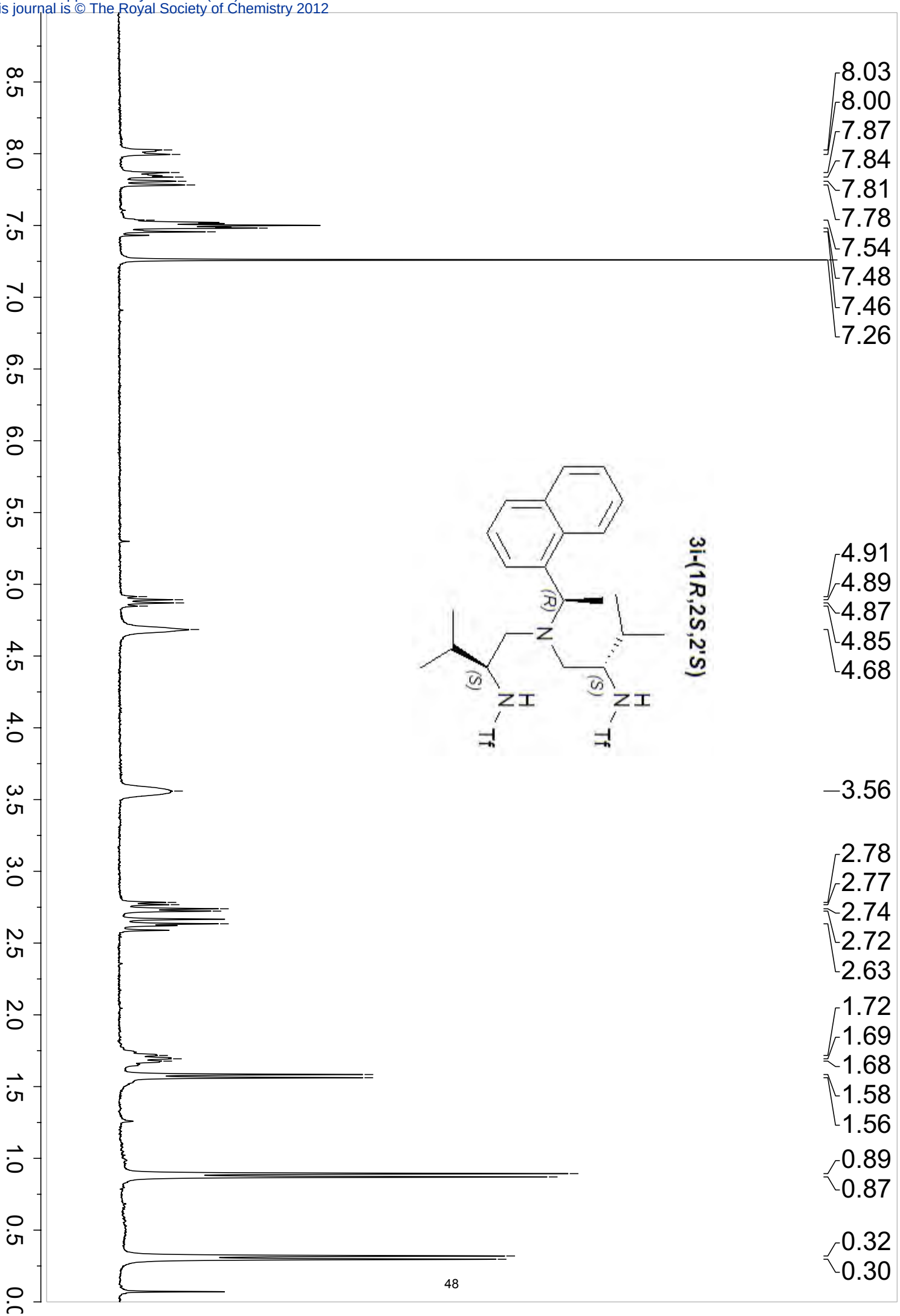


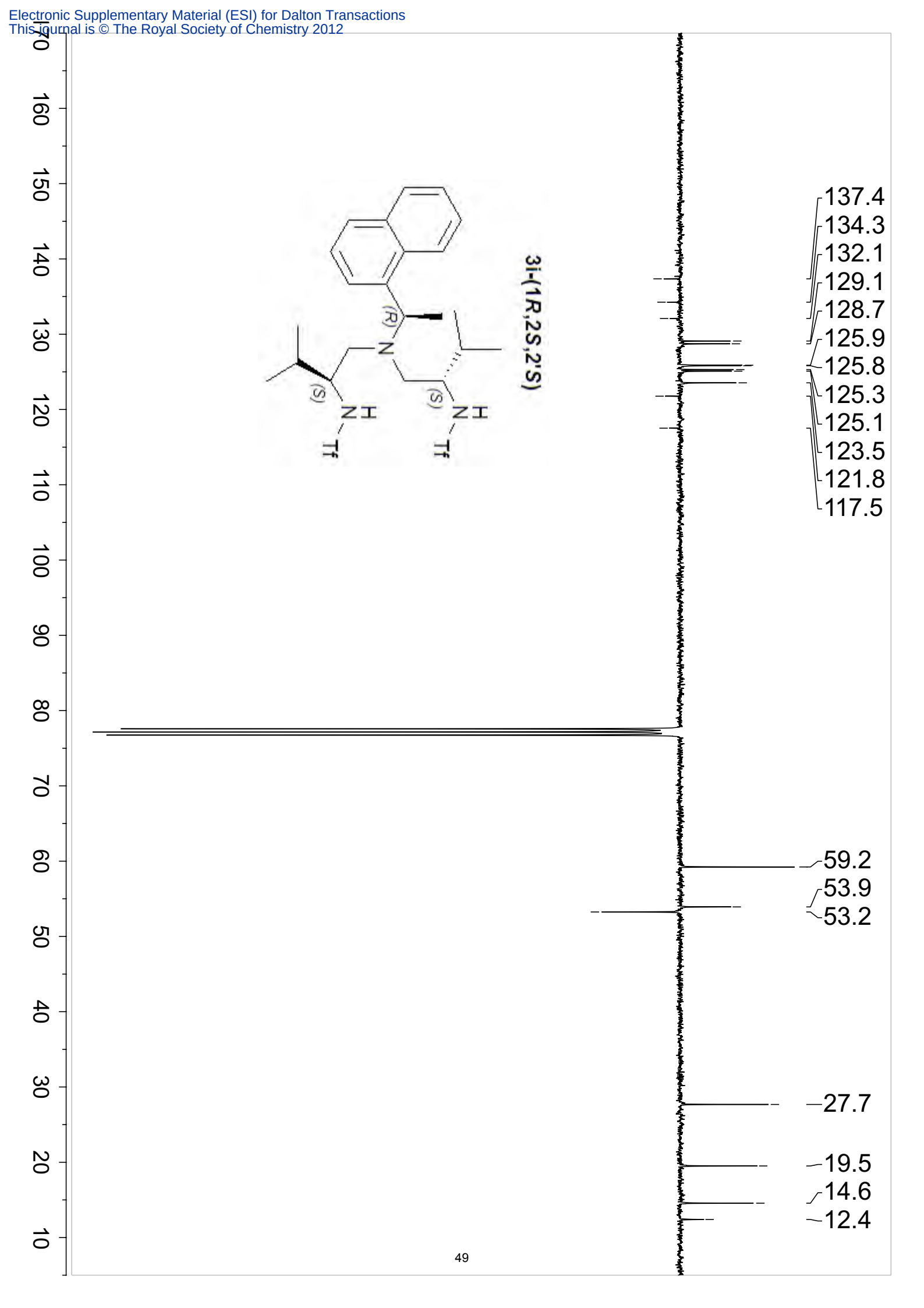


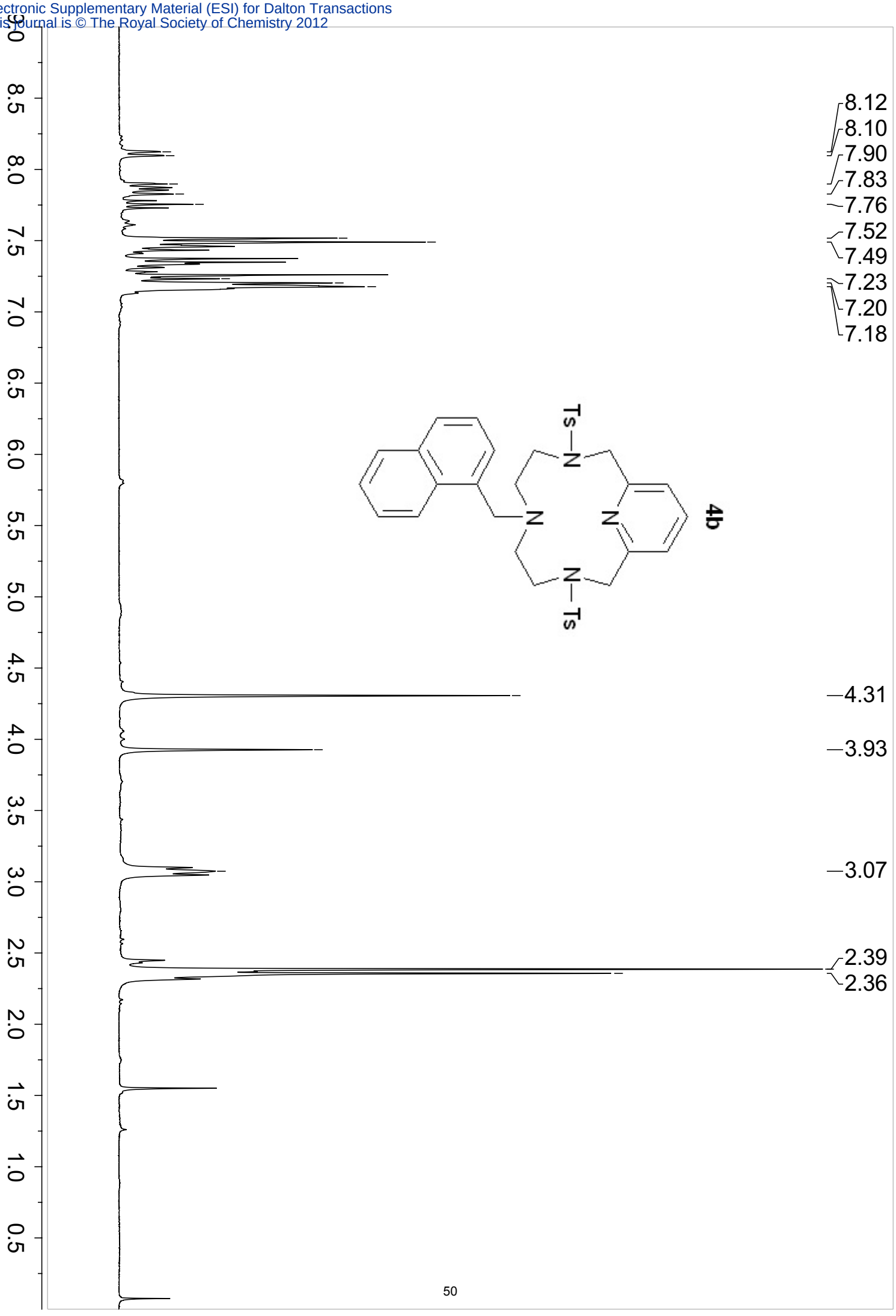


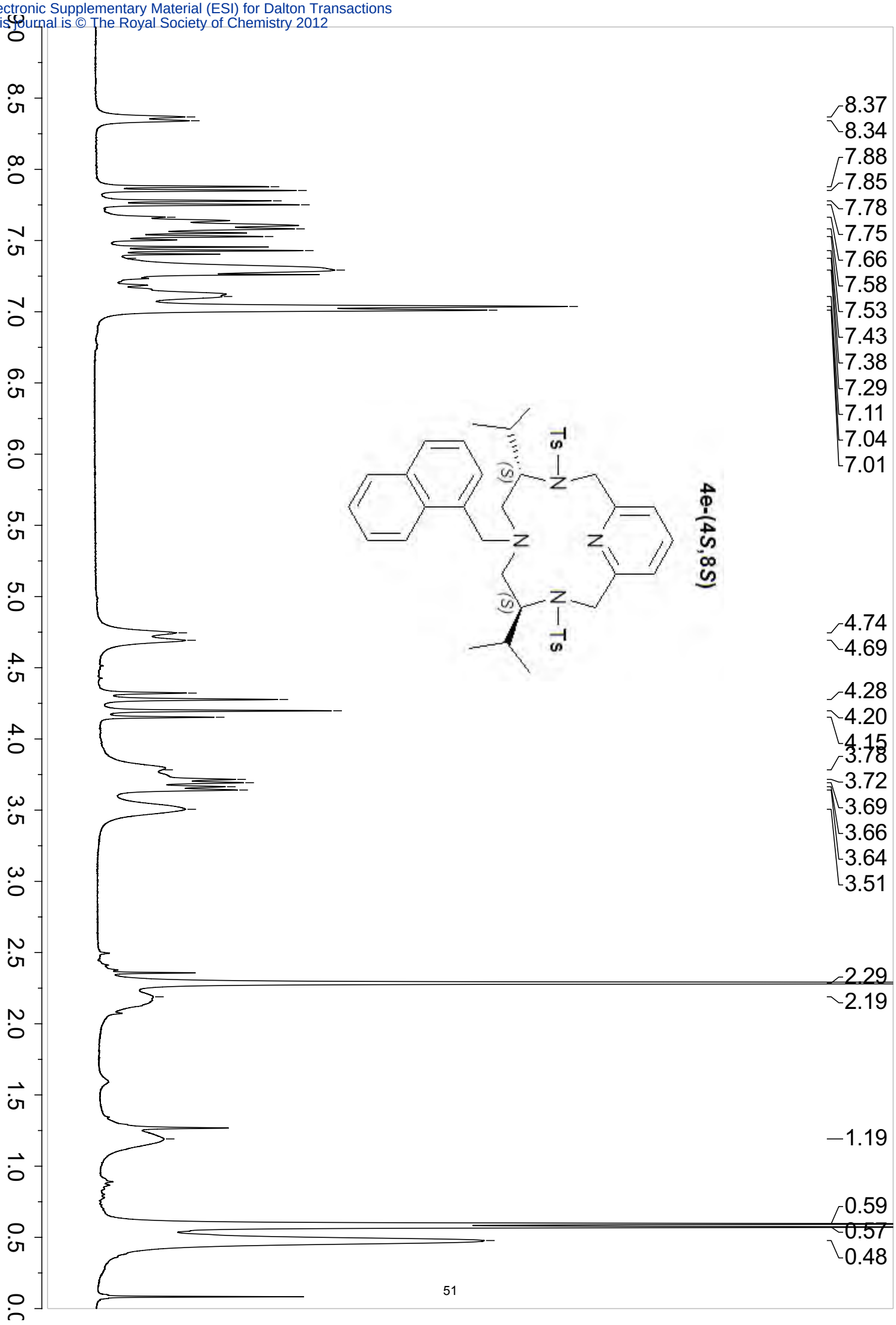


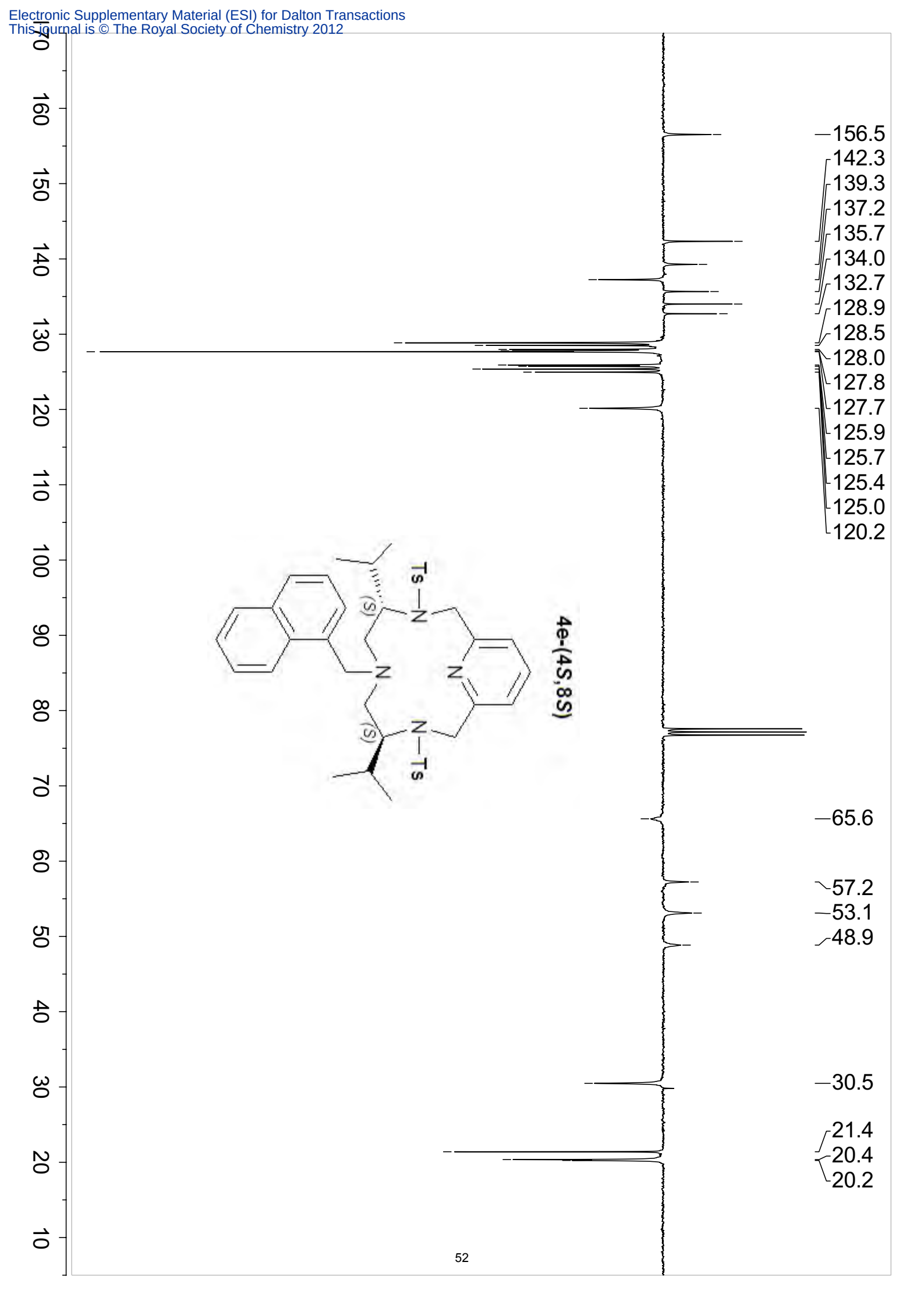


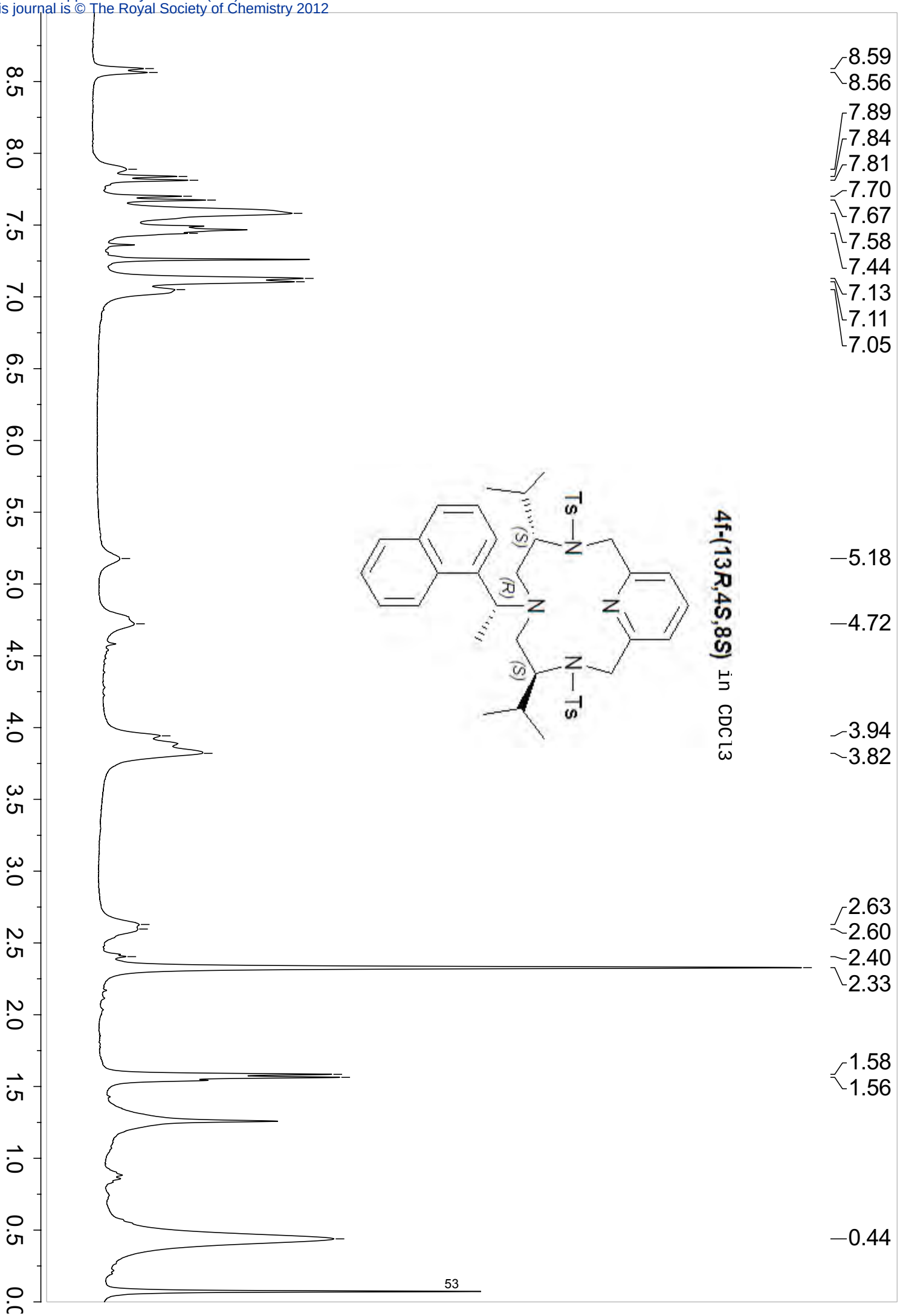

8.03
8.00
7.87
7.84
7.81
7.78
7.54
7.48
7.46
7.26
4.91
4.89
4.87
4.85
4.68
3.56
2.78
2.77
2.74
2.72
2.63
1.72
1.69
1.68
1.58
1.56
0.89
0.87
0.32
0.30
3i-(1R,2S,2'S)
(R)
(S)
(S)
N
H
N
Tf
H
N
Tf
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

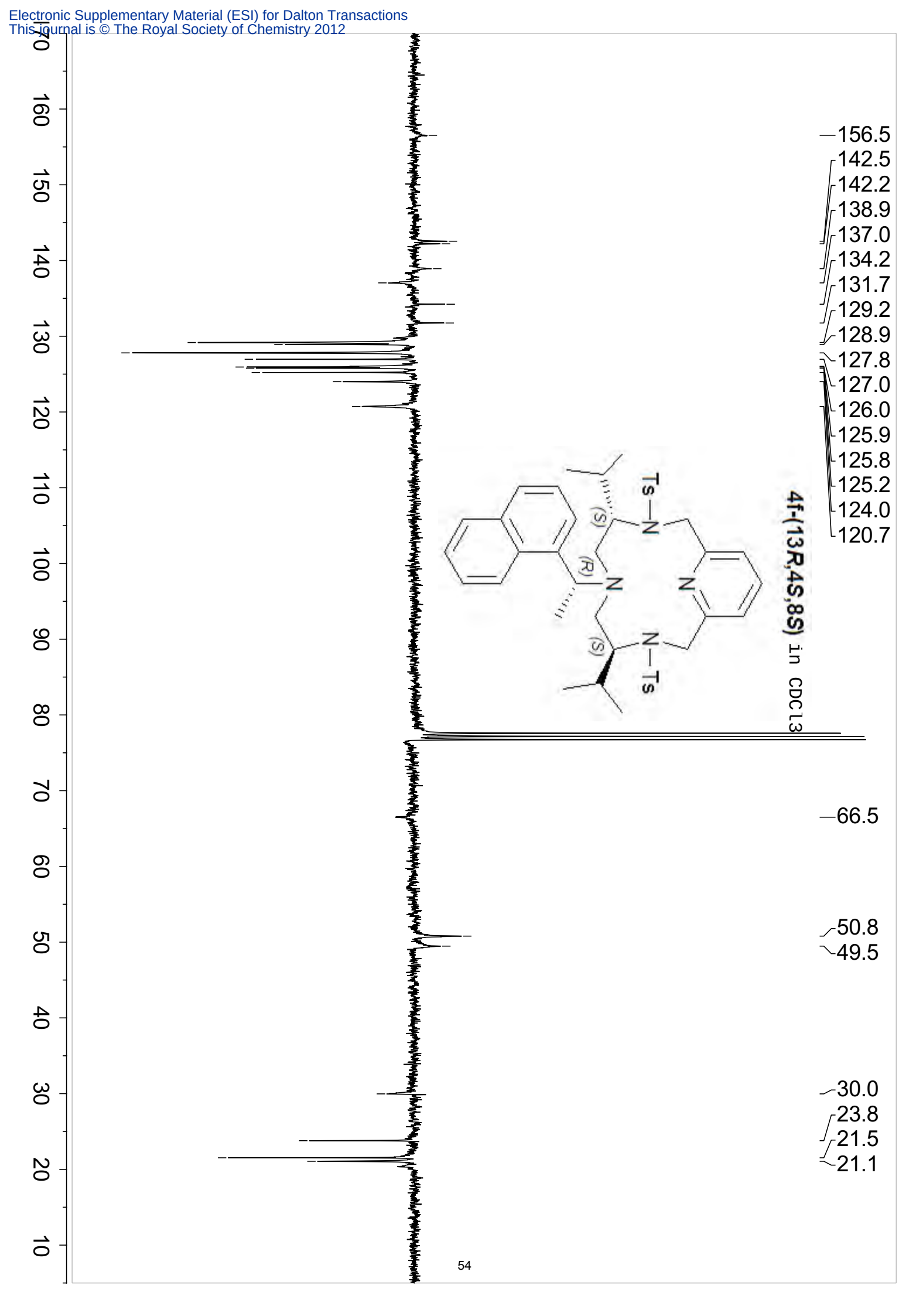


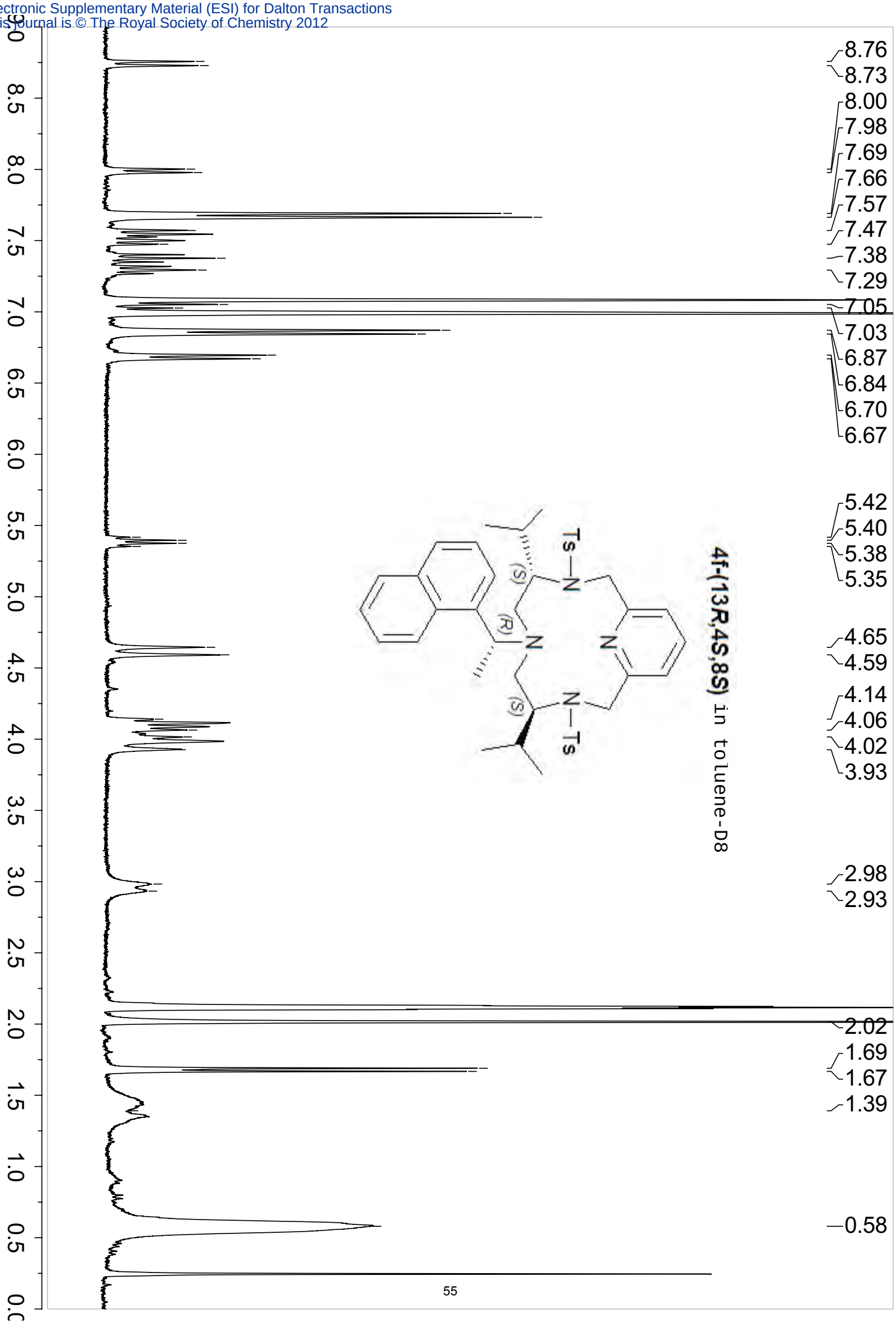


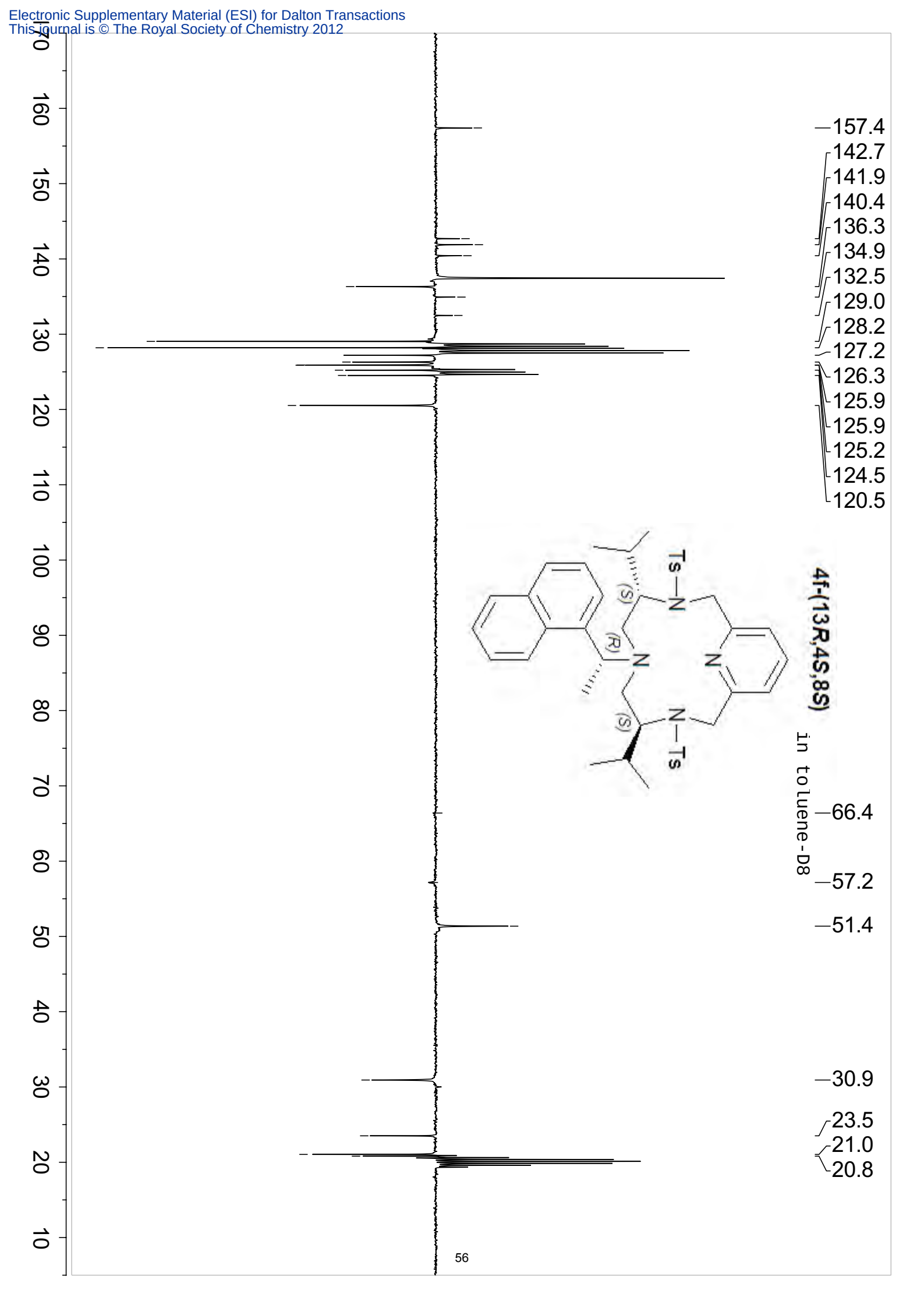


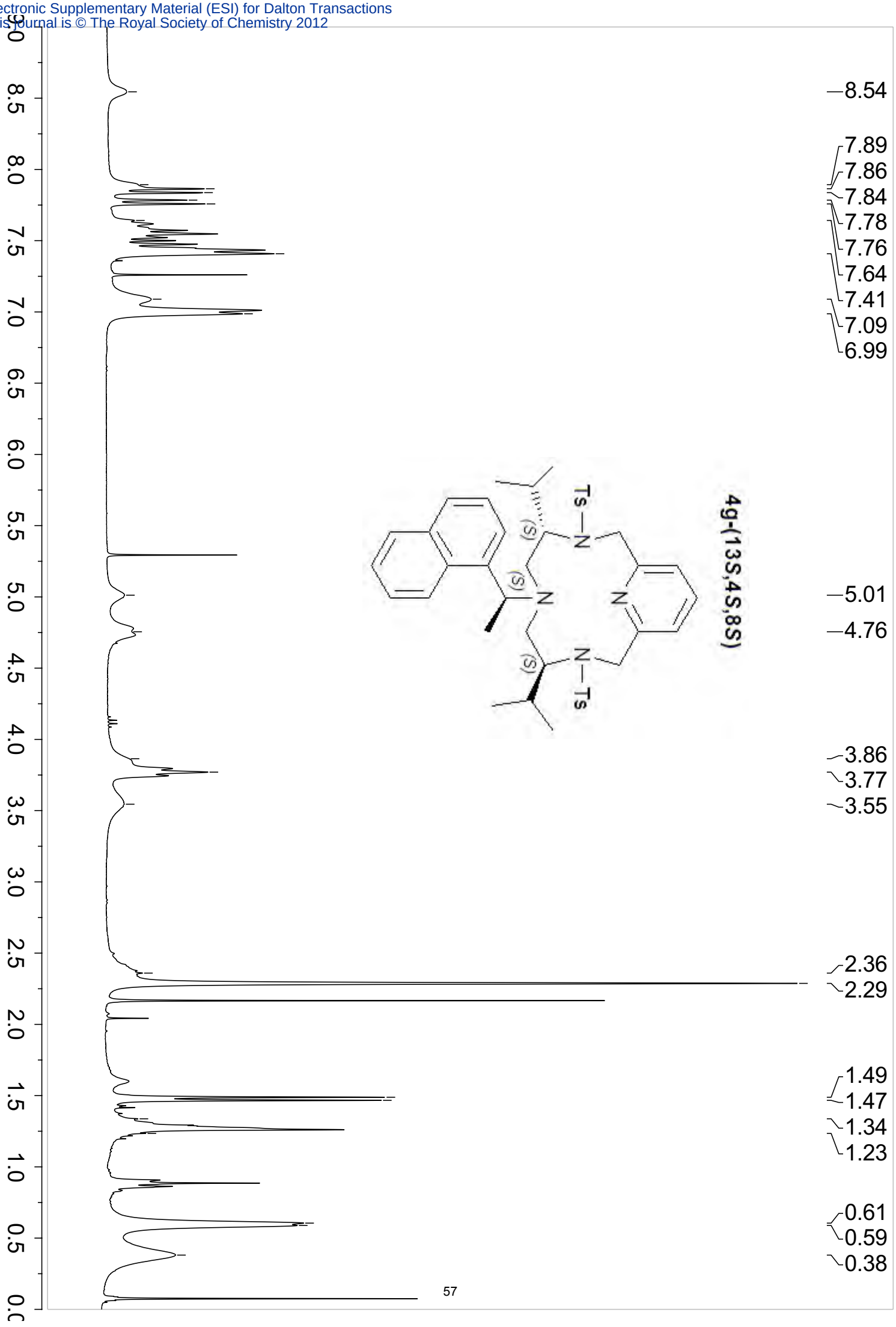


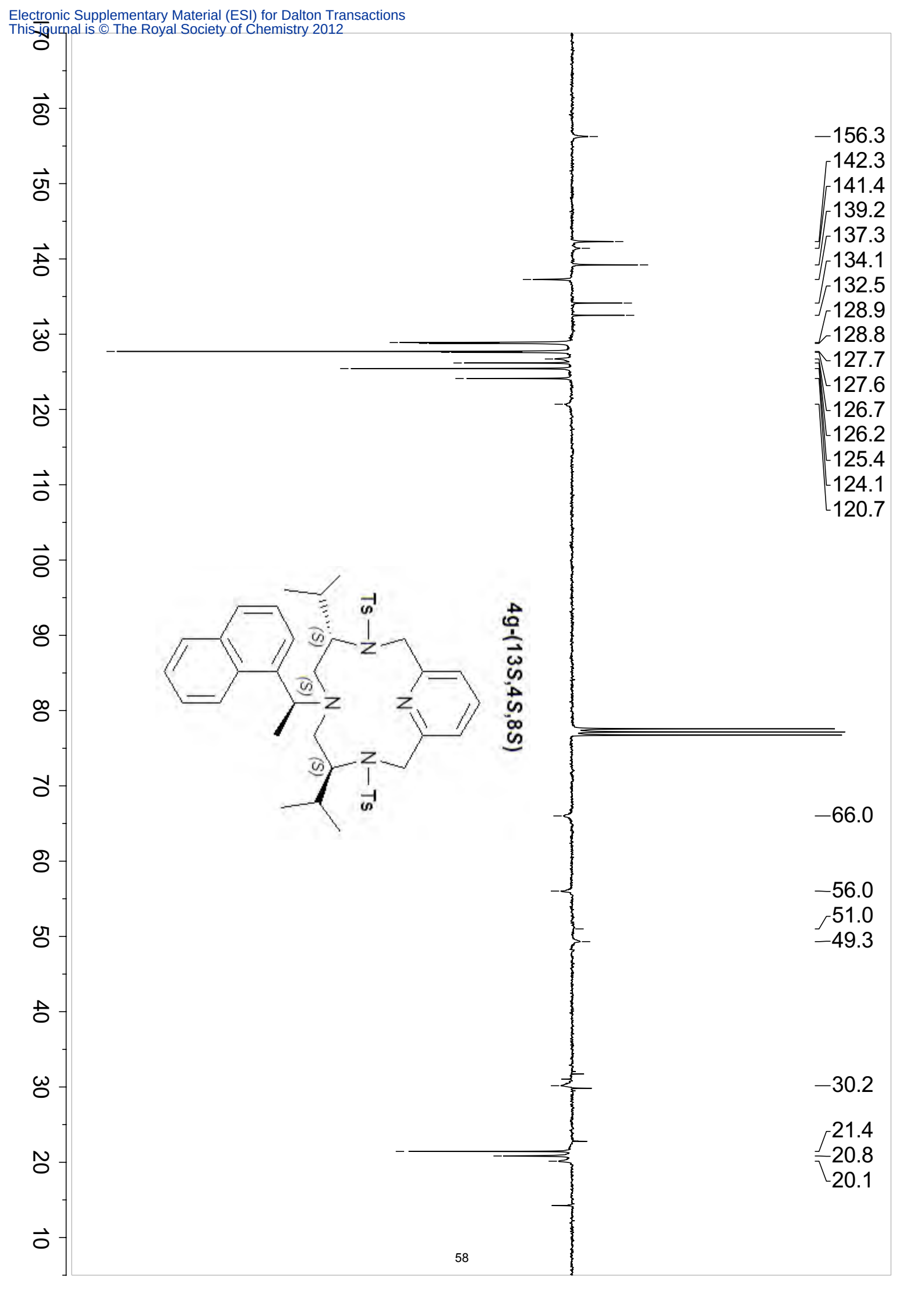


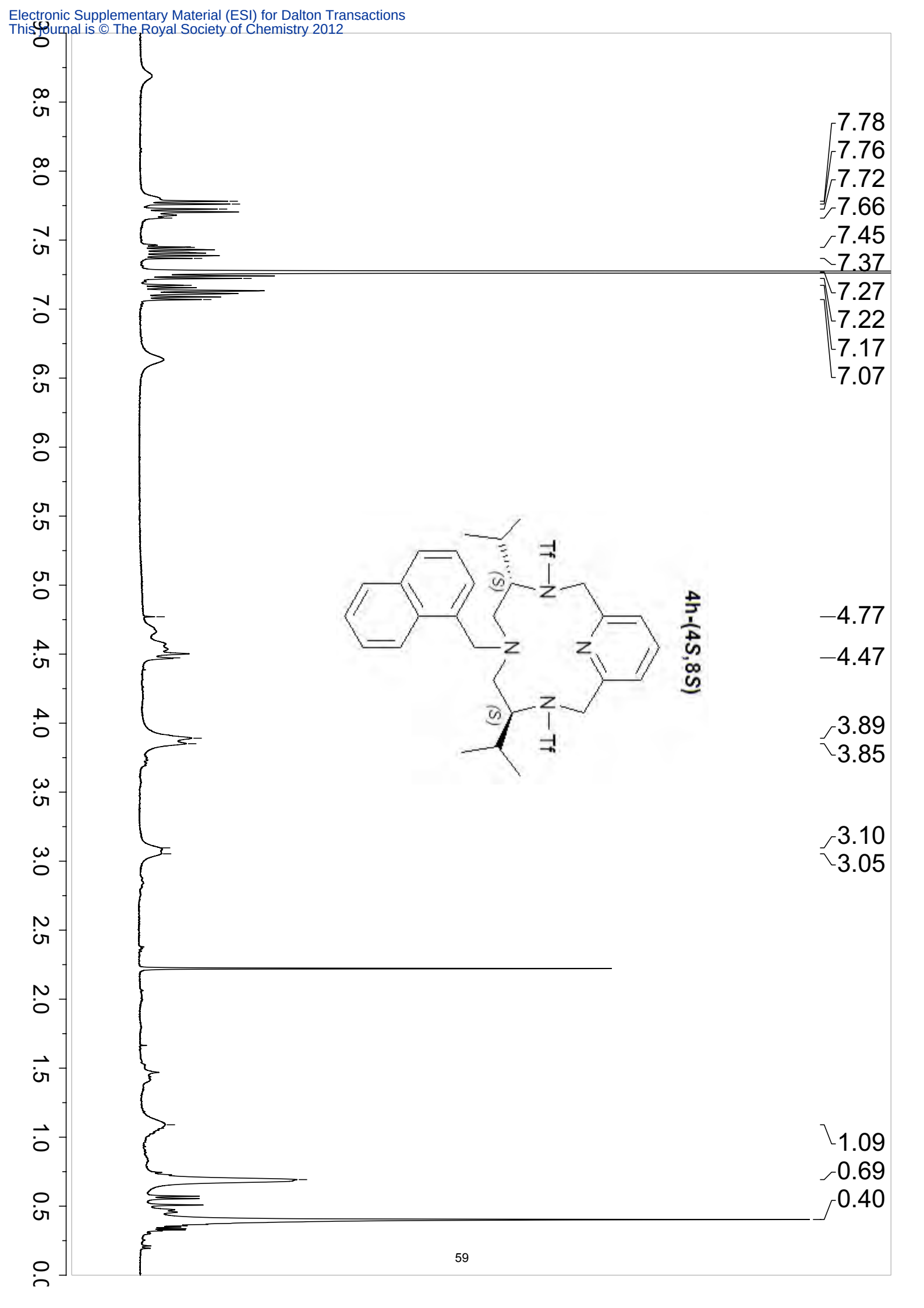


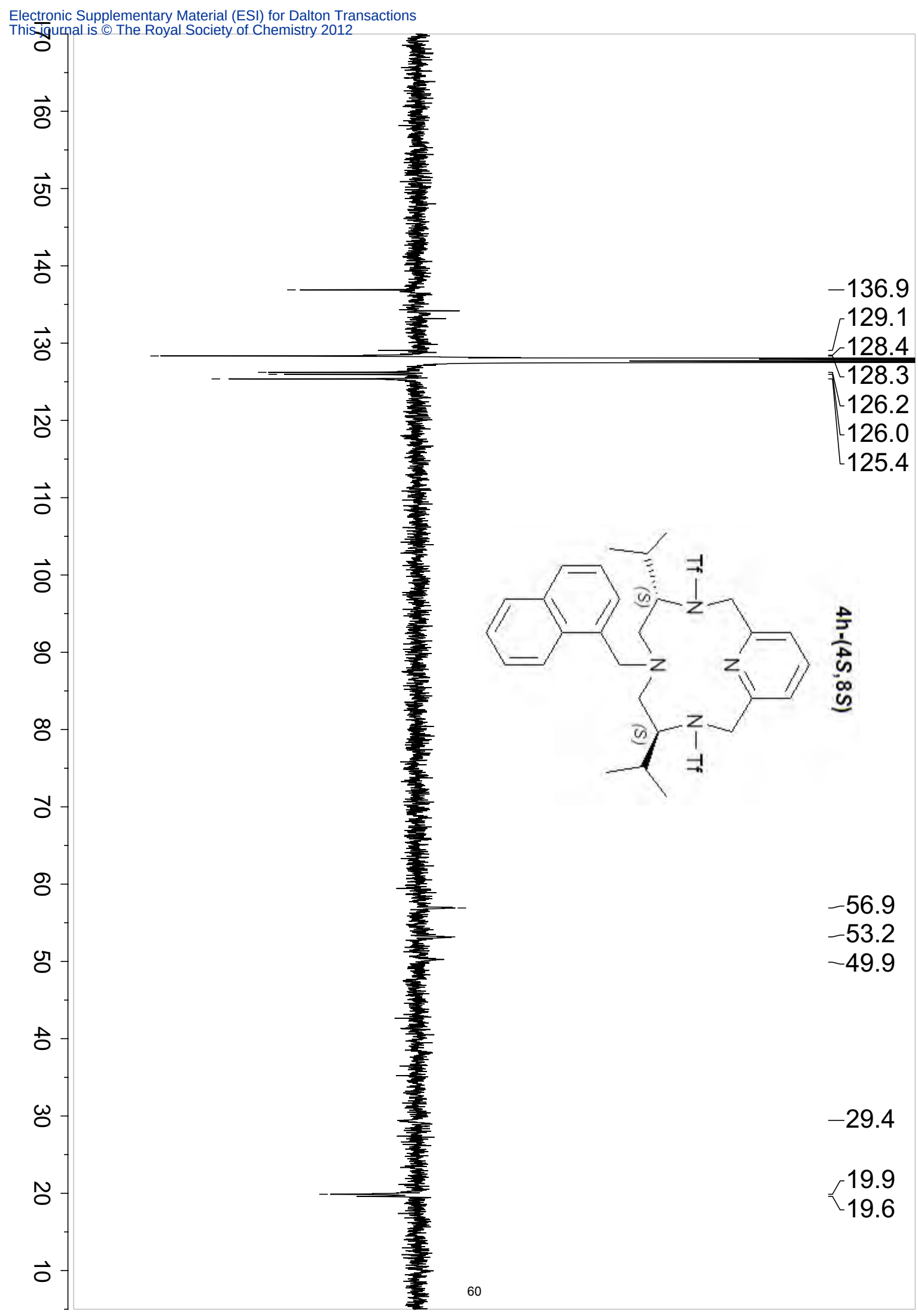


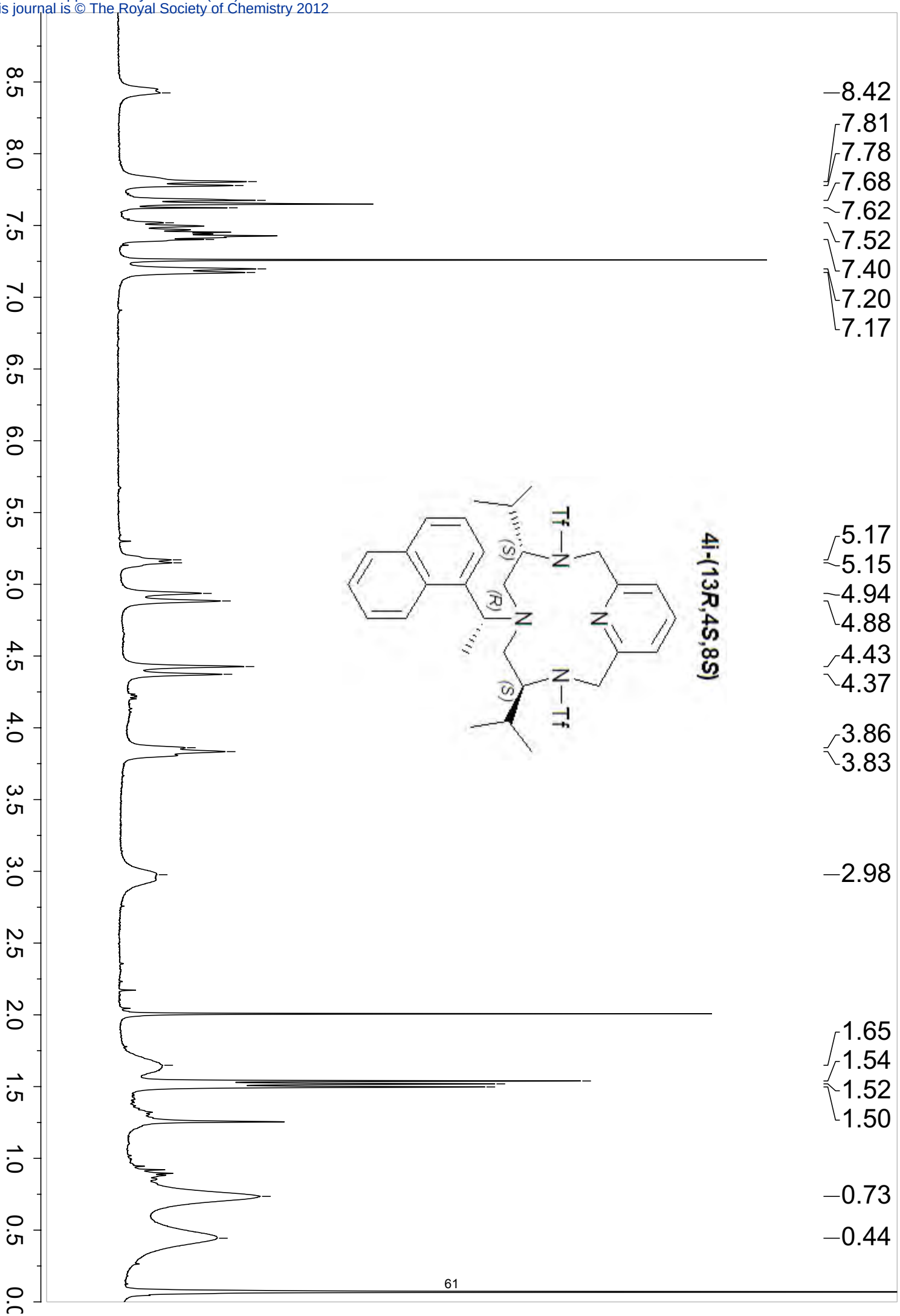


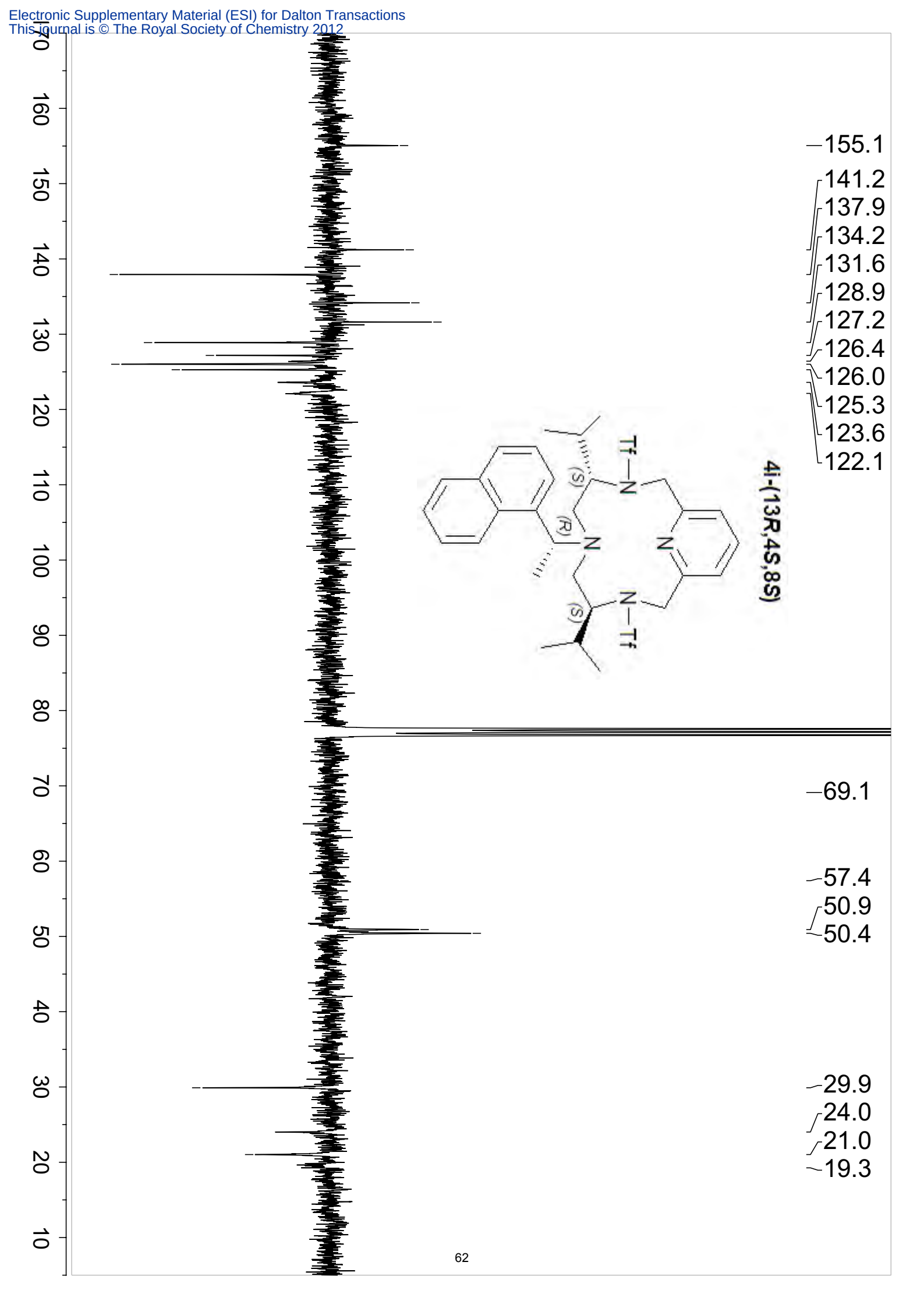


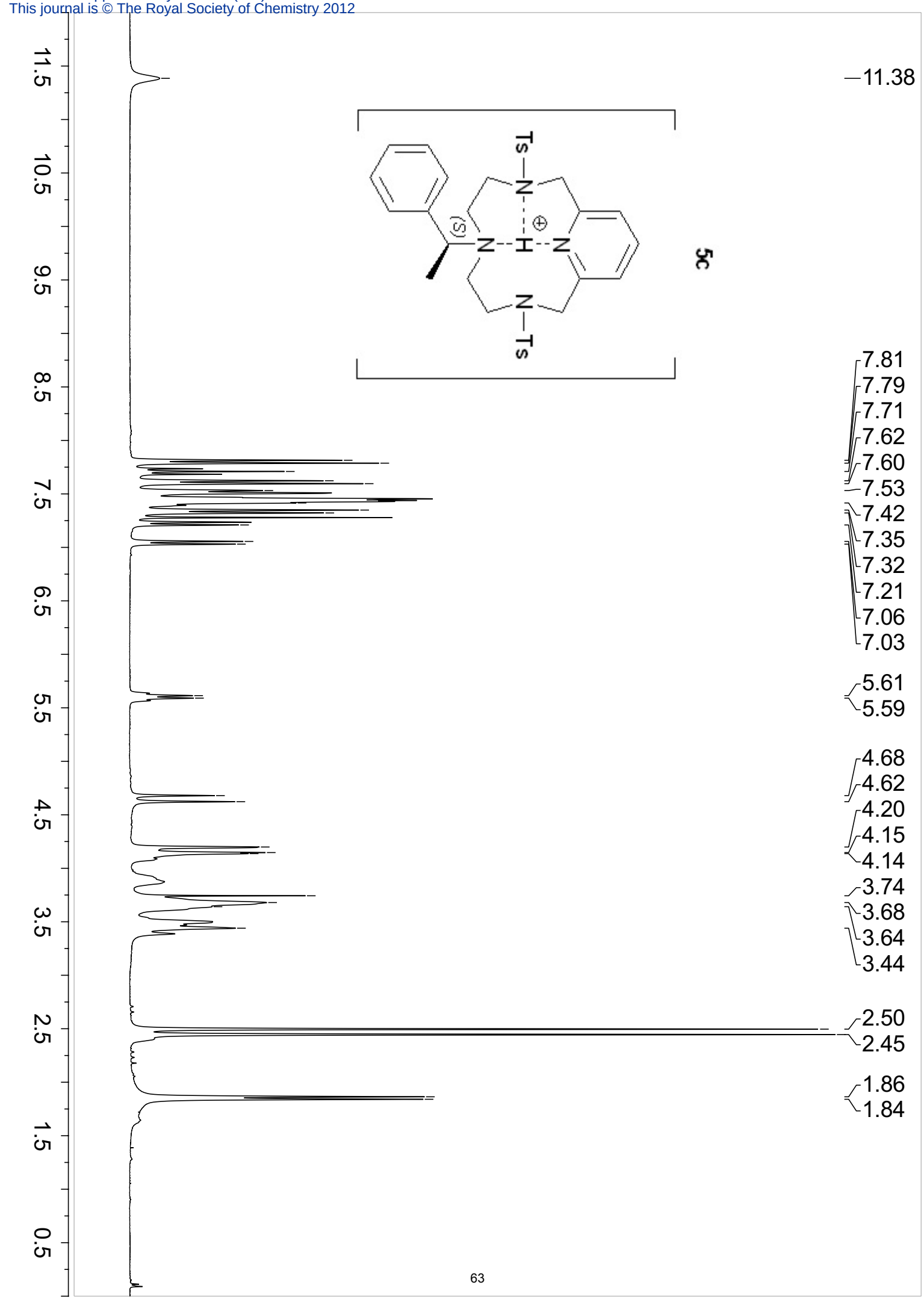


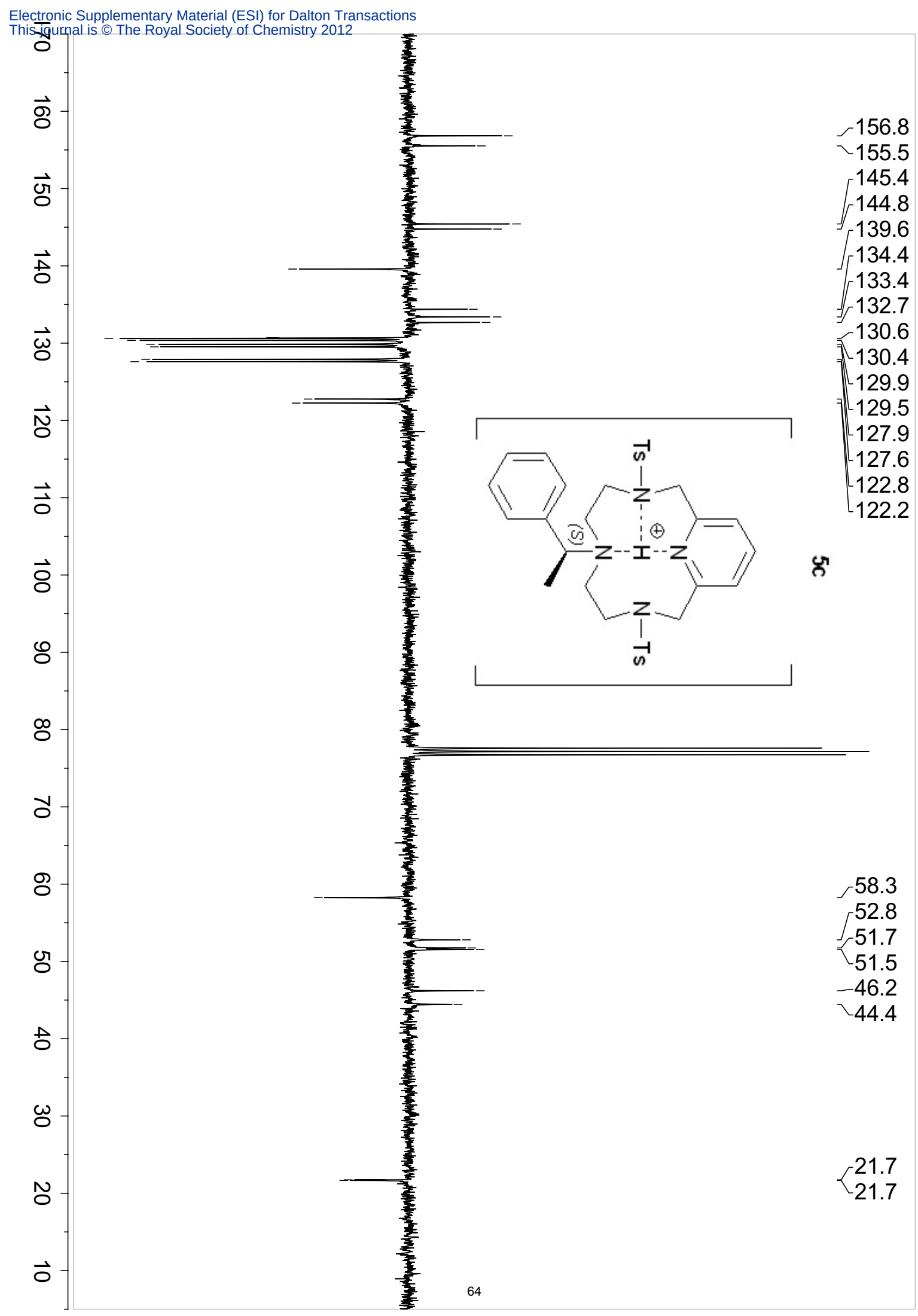


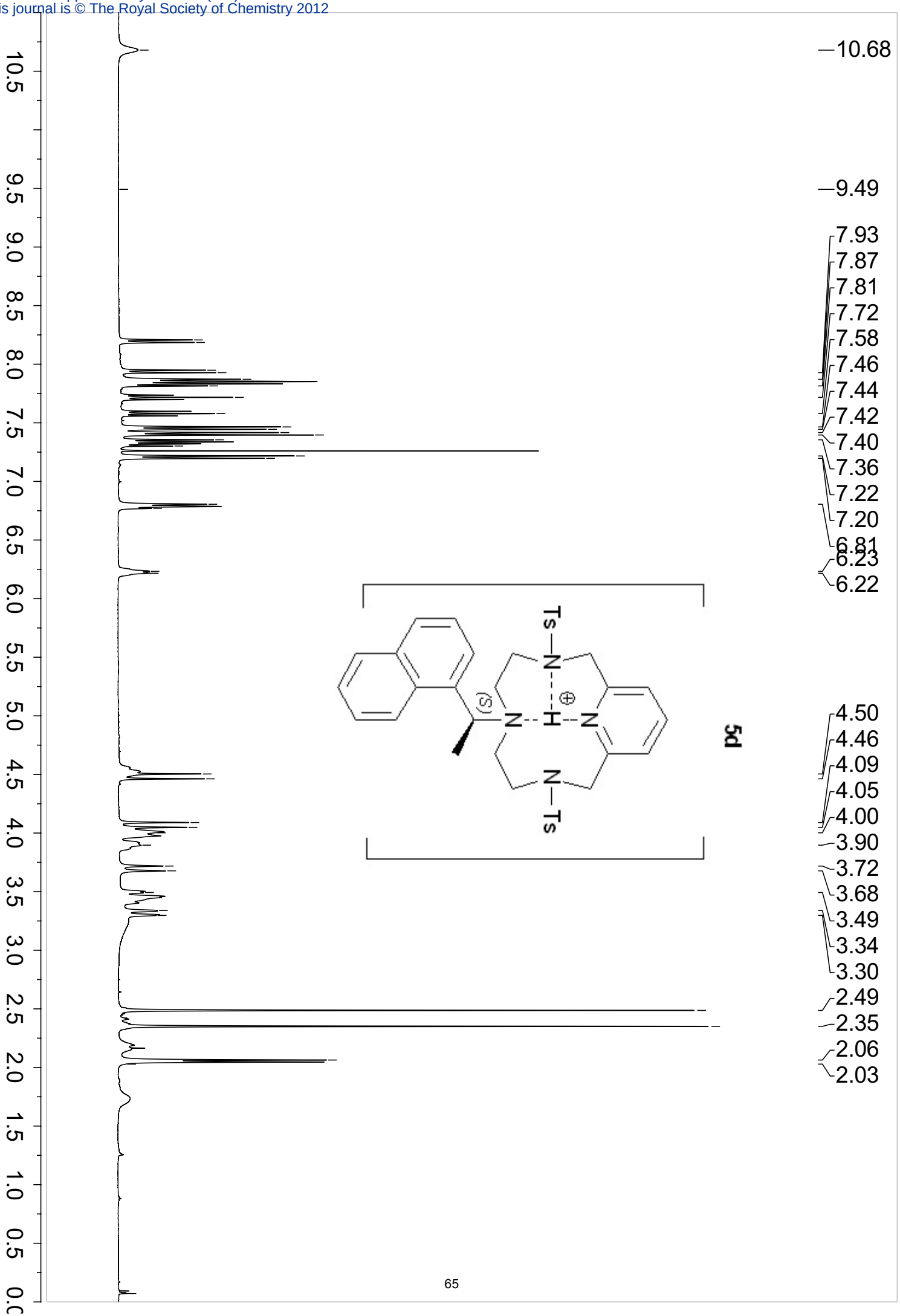


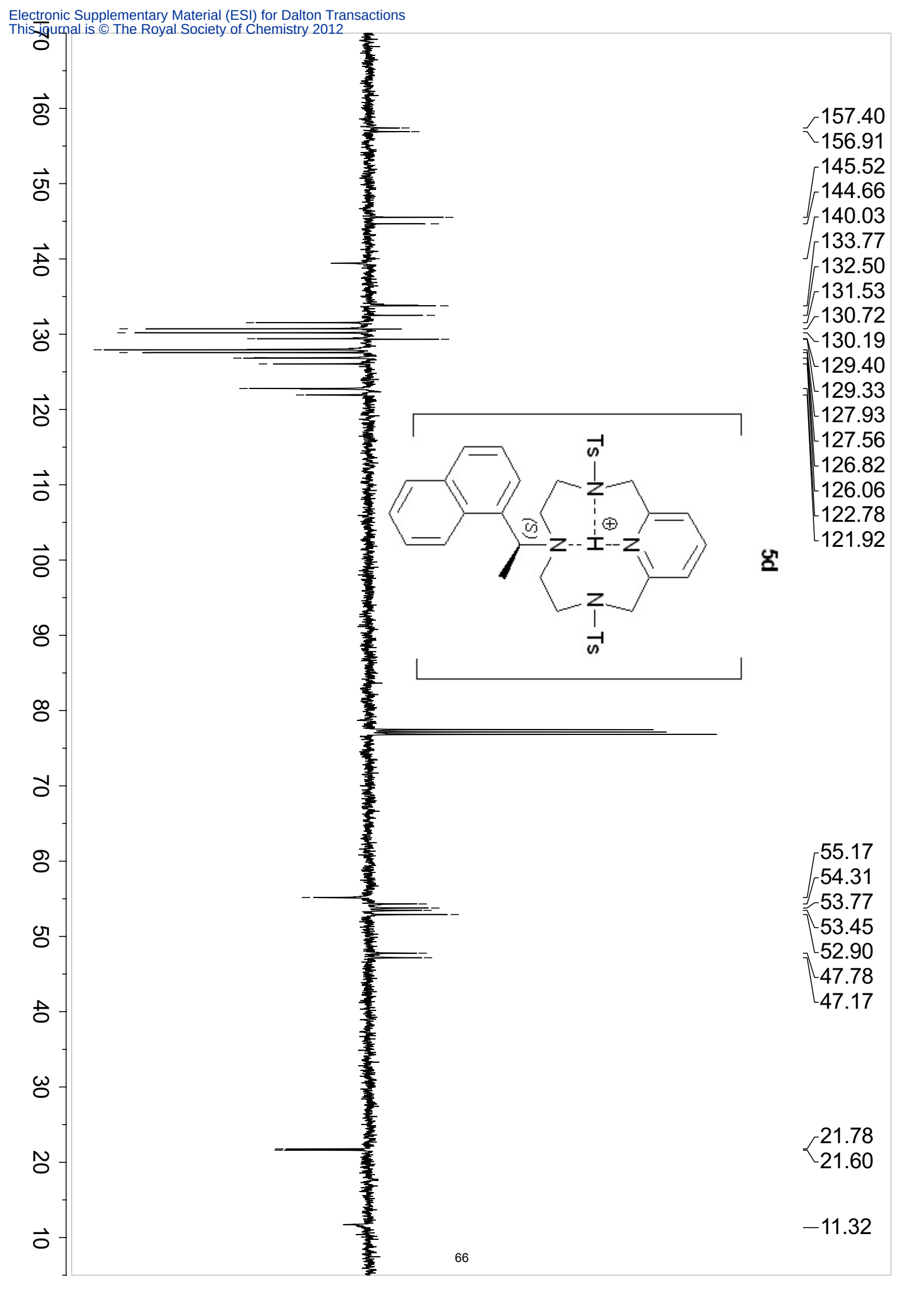


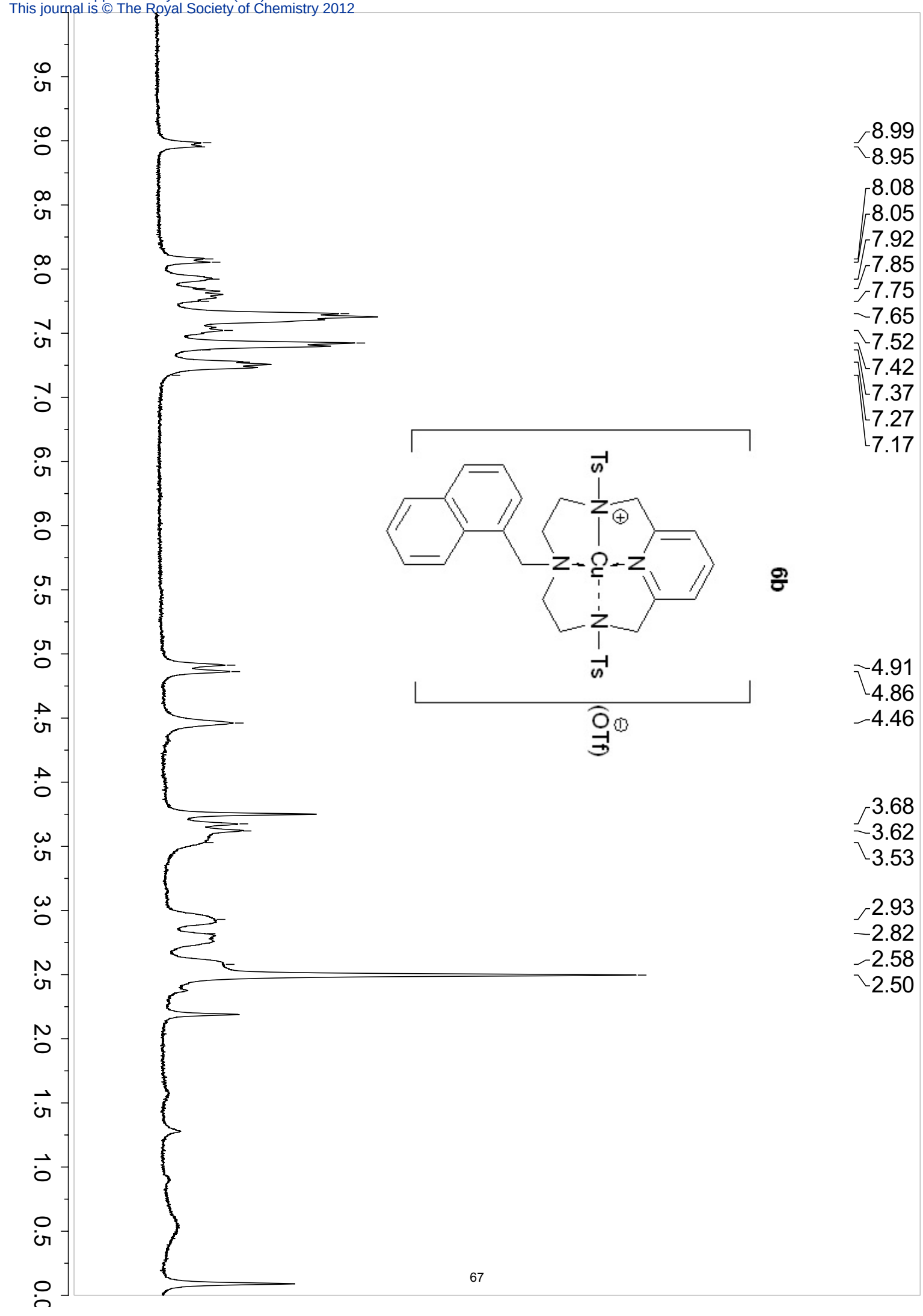


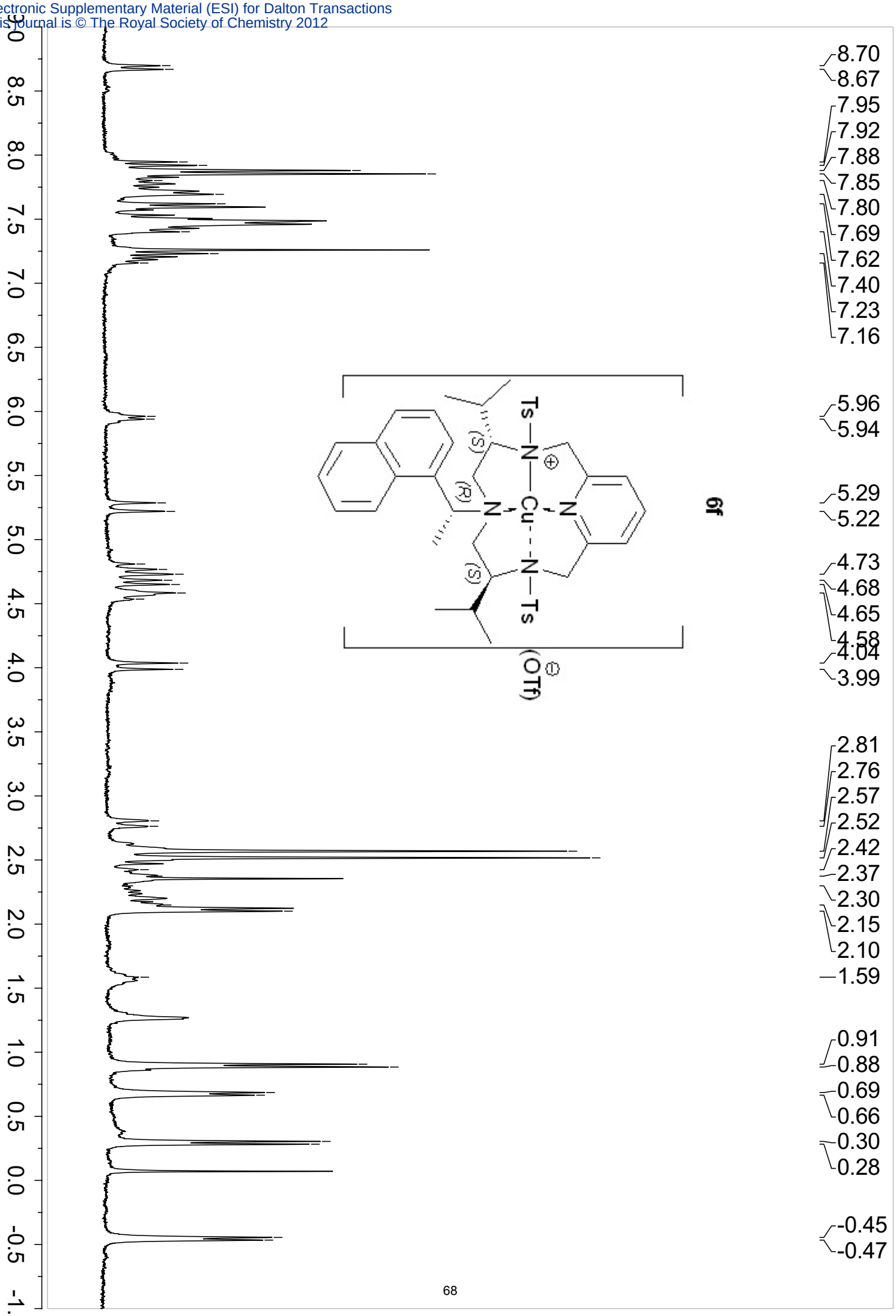


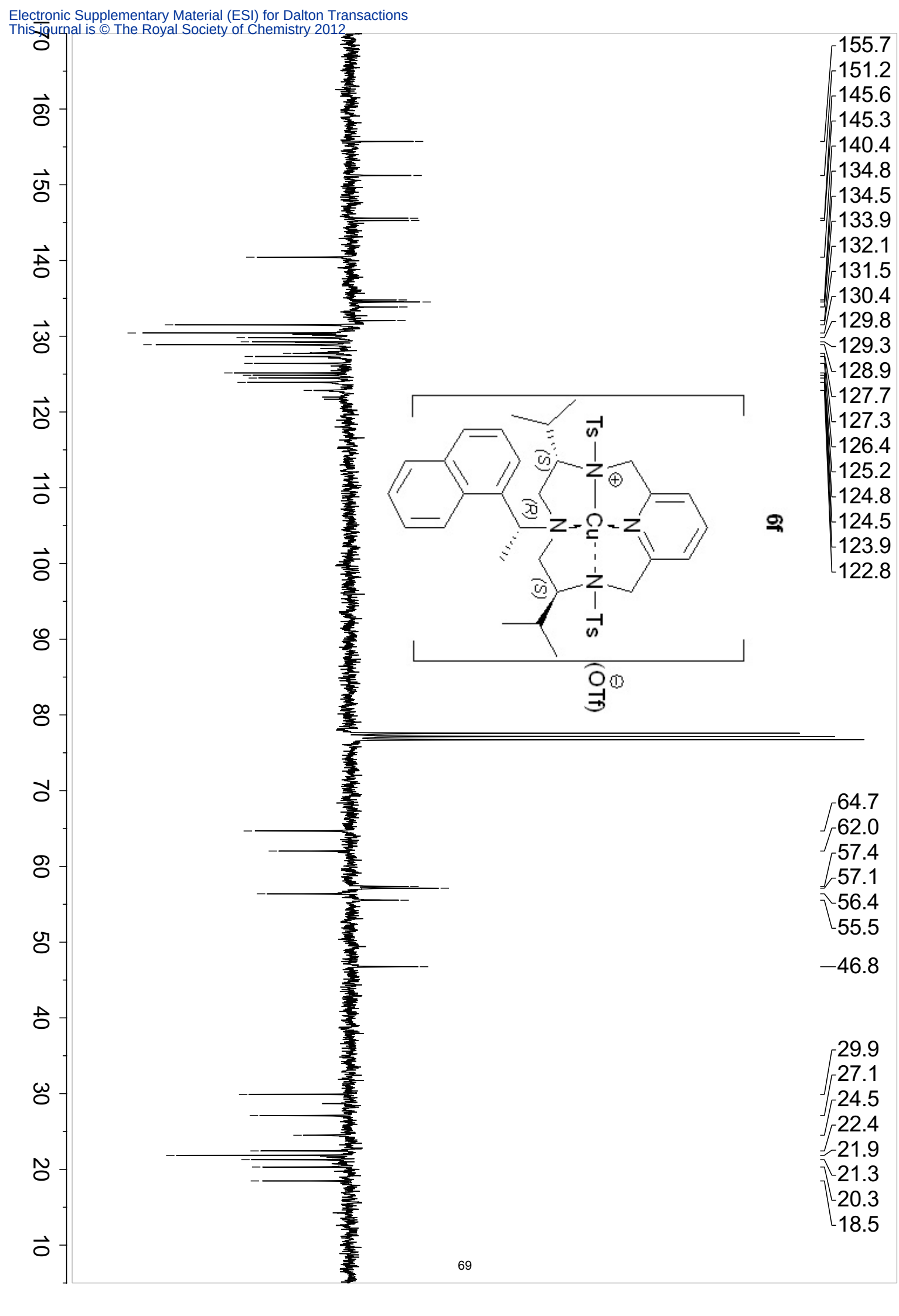


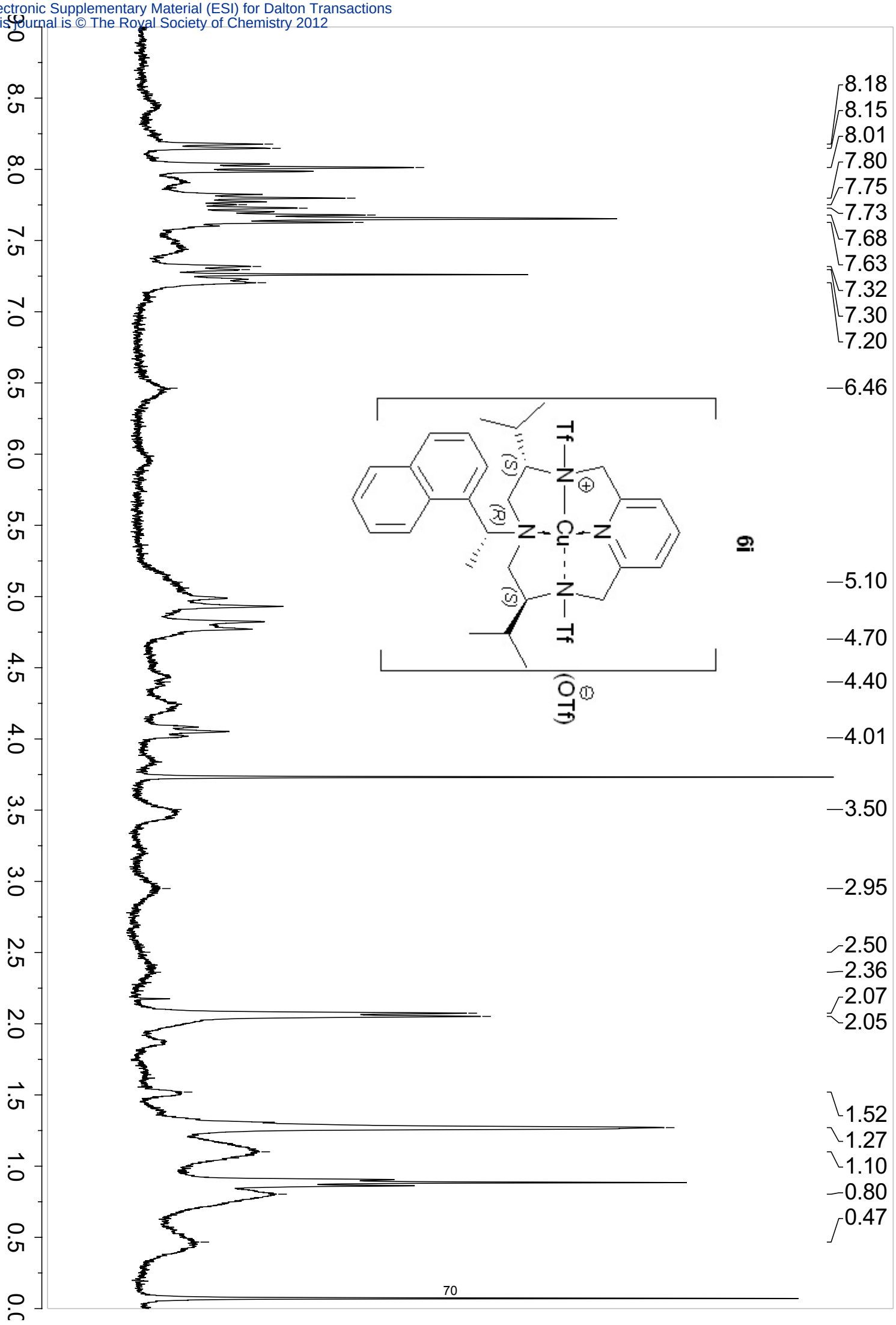


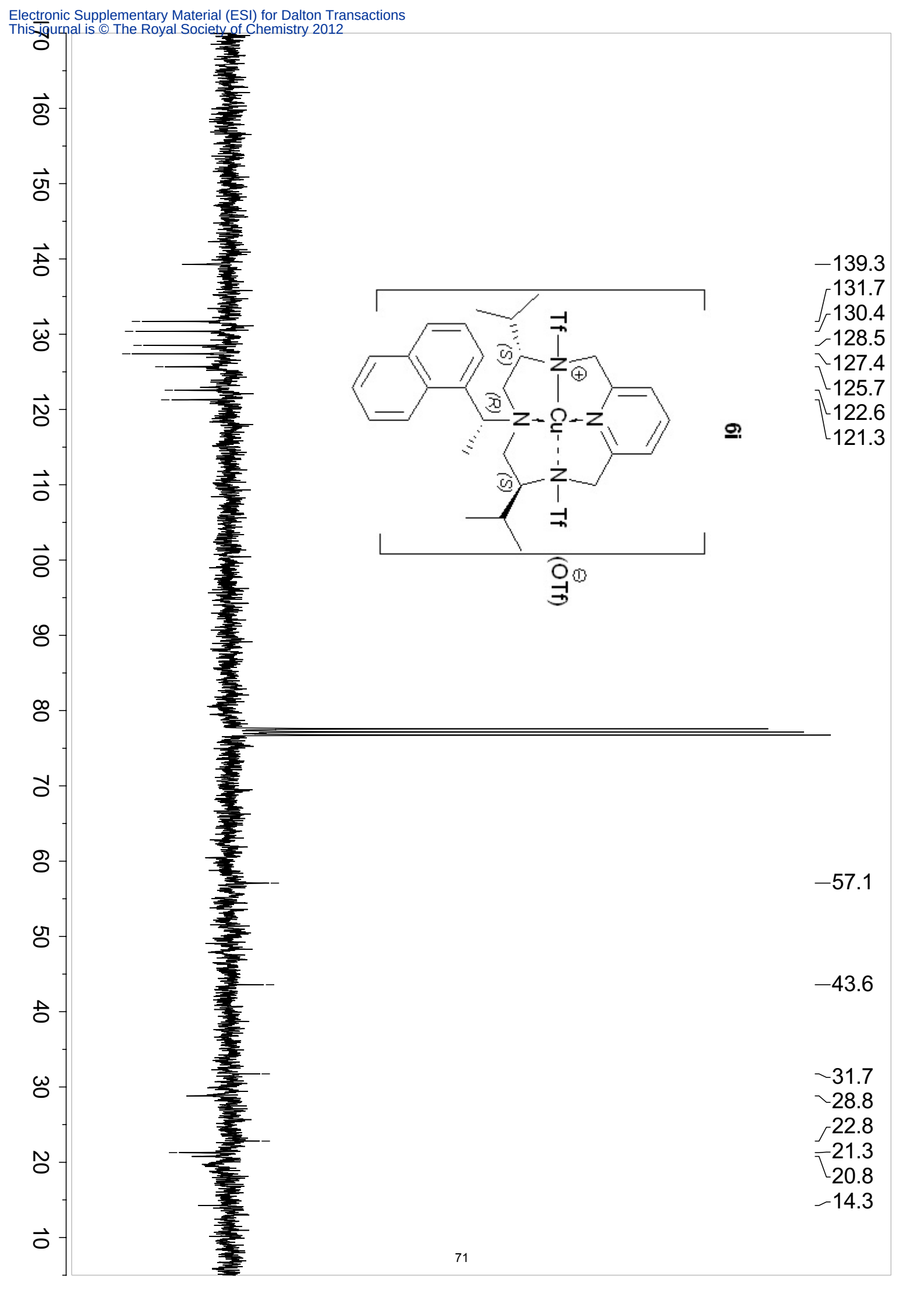


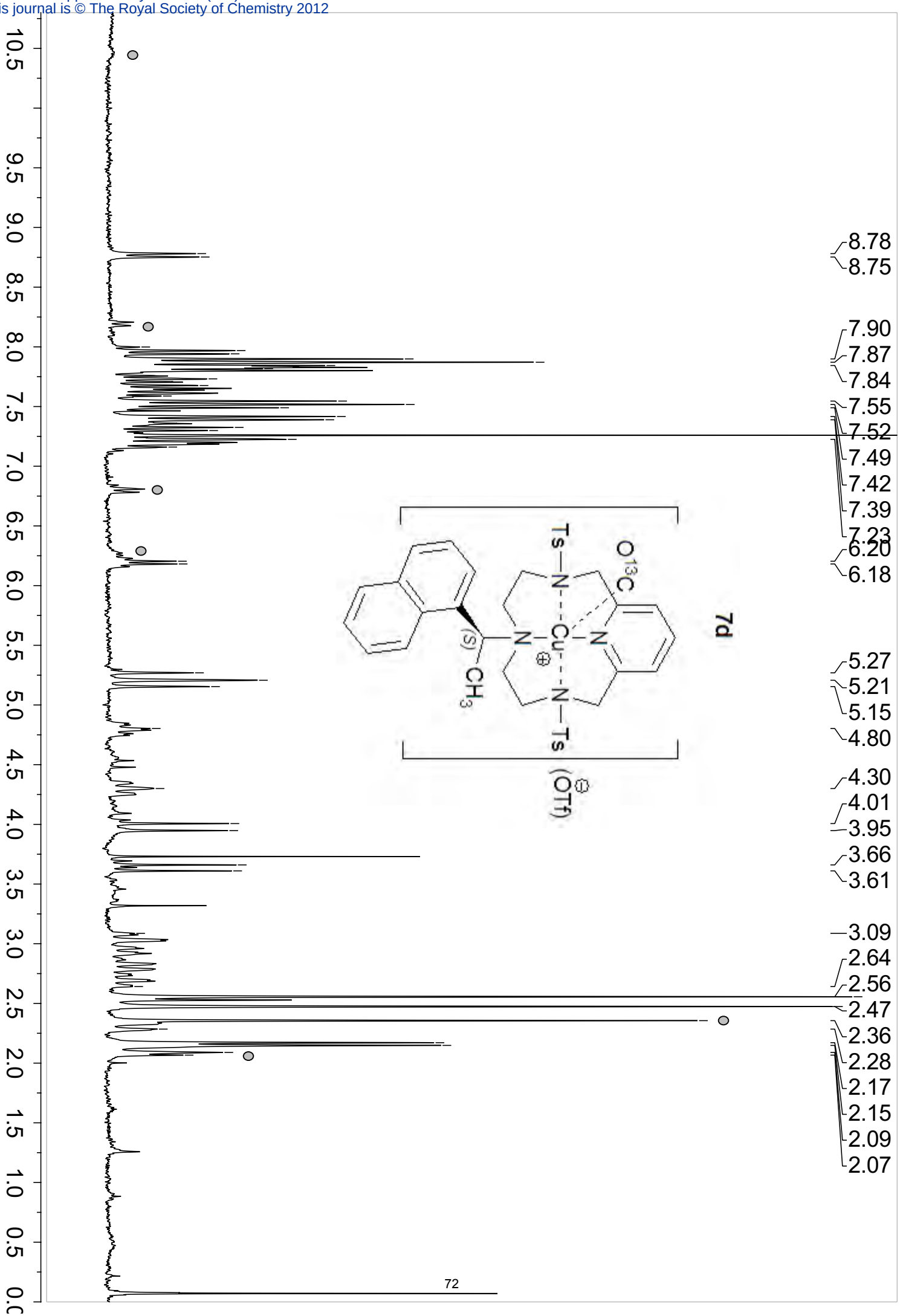












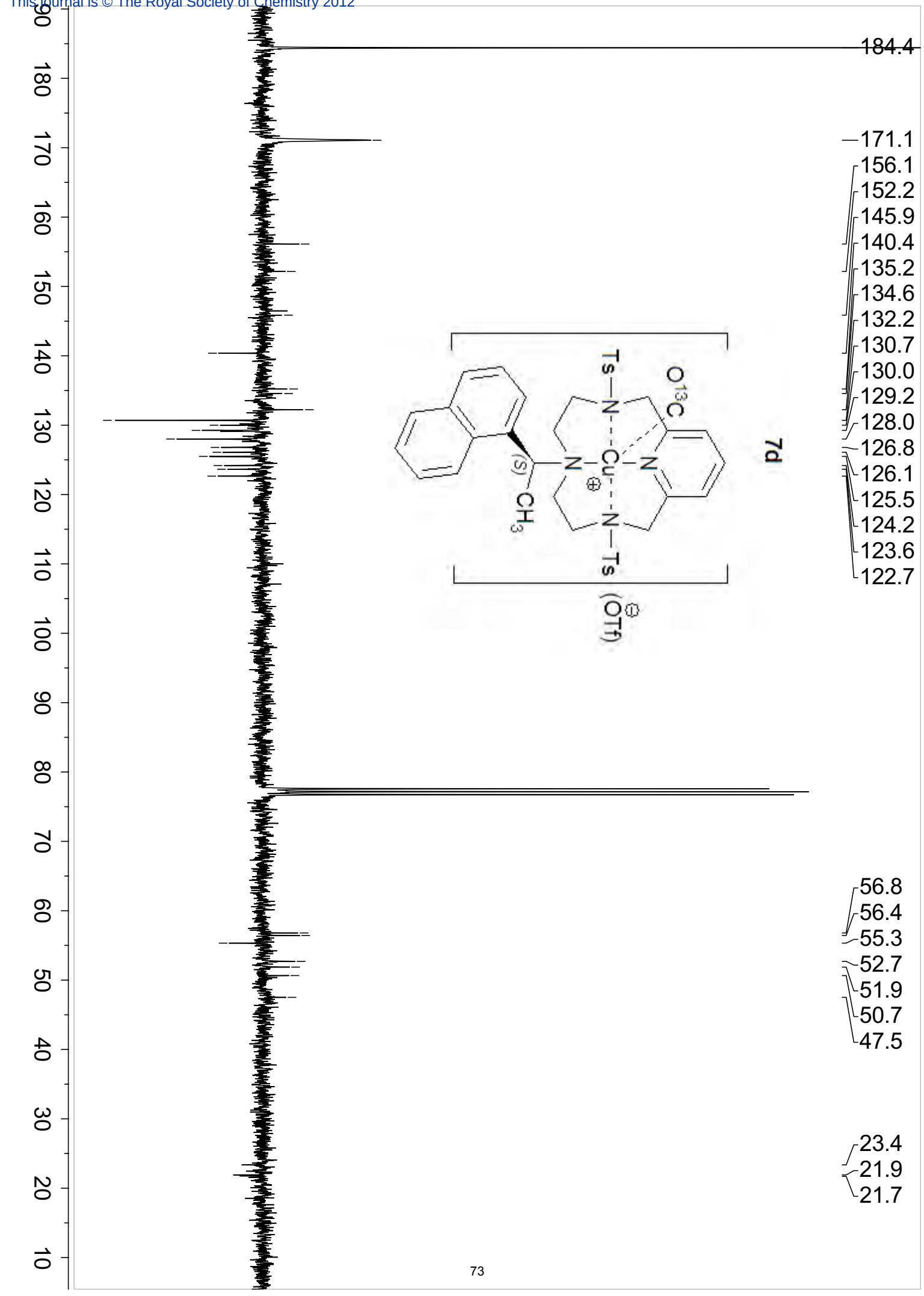


Table S1 - Crystal Data and Details of the Structure Determination of 4f

Crystal Data			
Formula			C43 H52 N4 O4 S2
Formula Weight			753.03
Crystal System			Orthorhombic
Space group		P212121	(No. 19)
a, b, c [Angstrom]	11.7359(2)	14.7577(2)	23.1185(3)
V [Ang**3]			4004.01(10)
Z			4
D(calc) [g/cm**3]			1.249
Mu(MoKa) [/mm]			0.180
F(000)			1608
Crystal Size [mm]		0.05 x	0.08 x 0.15
Data Collection			
Temperature (K)			293
Radiation [Angstrom]		MoKa	0.71073
Theta Min-Max [Deg]			1.6, 26.7
Dataset		-14: 14 ; -18: 18 ; -27: 28	
Tot., Uniq. Data, R(int)		29479,	7762, 0.051
Observed data [I > 0.0 sigma(I)]			5536
Refinement			
Nref, Npar			7762, 478
R, wR2, S		0.0498,	0.1010, 1.04
w = 1/[\s^2^(Fo^2^)+(0.0395P)^2^+0.1421P] where P=(Fo^2^+2Fc^2^)/3			
Max. and Av. Shift/Error			0.00, 0.00
Flack x			0.01(6)
Min. and Max. Resd. Dens. [e/Ang^3]			-0.25, 0.14

Table S2 - Bond Distances (Angstrom) for 4f

S1	-O11	1.432(2)	C16	-C33	1.517(5)
S1	-O12	1.438(2)	C29	-C30	1.523(3)
S1	-N3	1.632(2)	C29	-C31	1.526(4)
S1	-C101	1.760(3)	C101	-C102	1.391(4)
S2	-O21	1.436(2)	C101	-C106	1.375(4)
S2	-O22	1.434(2)	C102	-C103	1.360(5)
S2	-N9	1.624(2)	C2	-H2B	0.9700
S2	-C201	1.771(3)	C2	-H2A	0.9700
N3	-C2	1.469(3)	C103	-C104	1.391(5)
N3	-C4	1.494(3)	C104	-C105	1.382(5)
N6	-C5	1.464(3)	C4	-H4	0.9800
N6	-C7	1.474(3)	C104	-C107	1.506(5)
N6	-C12	1.470(3)	C5	-H5A	0.9700
N9	-C8	1.500(3)	C105	-C106	1.379(4)
N9	-C10	1.474(3)	C5	-H5B	0.9700
N12	-C1	1.324(4)	C7	-H7B	0.9700
N12	-C11	1.337(4)	C7	-H7A	0.9700
C1	-C2	1.518(5)	C8	-H8	0.9800
C1	-C403	1.389(5)	C10	-H10B	0.9700
C4	-C5	1.553(4)	C10	-H10A	0.9700
C4	-C16	1.556(4)	C12	-H12	0.9800
C7	-C8	1.537(4)	C13	-H13B	0.9600
C8	-C29	1.545(4)	C13	-H13C	0.9600
C10	-C11	1.501(4)	C13	-H13A	0.9600
C11	-C401	1.379(4)	C16	-H16	0.9800
C12	-C13	1.537(3)	C17	-H17A	0.9600
C12	-C301	1.527(4)	C17	-H17B	0.9600
C16	-C17	1.521(5)	C17	-H17C	0.9600
C29	-H29	0.9800	C301	-C310	1.434(4)
C30	-H30A	0.9600	C202	-H202	0.9300
C30	-H30B	0.9600	C302	-C303	1.408(4)
C30	-H30C	0.9600	C303	-C304	1.348(5)
C31	-H31A	0.9600	C203	-H203	0.9300
C31	-H31B	0.9600	C304	-C305	1.403(4)
C31	-H31C	0.9600	C205	-H205	0.9300

C33	-H33C	0.9600	C305	-C310	1.423(4)
C33	-H33A	0.9600	C305	-C306	1.425(5)
C33	-H33B	0.9600	C306	-C307	1.351(6)
C201	-C202	1.384(5)	C206	-H206	0.9300
C201	-C206	1.372(5)	C207	-H20A	0.9600
C102	-H102	0.9300	C207	-H20B	0.9600
C202	-C203	1.373(5)	C207	-H20C	0.9600
C203	-C204	1.375(5)	C307	-C308	1.391(6)
C103	-H103	0.9300	C308	-C309	1.370(5)
C204	-C205	1.384(6)	C309	-C310	1.418(4)
C204	-C207	1.526(5)	C401	-C402	1.368(5)
C105	-H105	0.9300	C402	-C403	1.367(6)
C205	-C206	1.383(4)	C302	-H302	0.9300
C106	-H106	0.9300	C303	-H303	0.9300
C107	-H10C	0.9600	C304	-H304	0.9300
C107	-H10D	0.9600	C306	-H306	0.9300
C107	-H10B	0.9600	C307	-H307	0.9300
C107	-H10F	0.9600	C308	-H308	0.9300
C107	-H10E	0.9600	C309	-H309	0.9300
C107	-H10A	0.9600	C401	-H401	0.9300
C301	-C302	1.368(4)	C402	-H402	0.9300

Table S3 - Crystal Data and Details of the Structure Determination for: 4d

Crystal Data			
Formula			C39 H44 N4 O4 S2
Formula Weight			696.92
Crystal System			Orthorhombic
Space group		P212121	(No. 19)
a, b, c [Angstrom]	9.7670(4)	14.2550(5)	25.9891(15)
V [Ang**3]			3618.4(3)
Z			4
D(calc) [g/cm**3]			1.279
Mu(MoKa) [/mm]			0.193
F(000)			1480
Crystal Size [mm]		0.08 x	0.08 x 0.17
Data Collection			
Temperature (K)			293
Radiation [Angstrom]		MoKa	0.71073
Theta Min-Max [Deg]			2.9, 28.9
Dataset		-11: 13 ; -19: 10 ; -34: 12	
Tot., Uniq. Data, R(int)		12636,	8019, 0.057
Observed data [I > 0.0 sigma(I)]			3437
Refinement			
Nref, Npar			8019, 442
R, wR2, S		0.0727,	0.1075, 0.97
w = 1/[\s^2^(Fo^2^)+(0.0089P)^2^]		where P=(Fo^2^+2Fc^2^)/3	
Max. and Av. Shift/Error			0.00, 0.00
Flack x			-0.09(10)
Min. and Max. Resd. Dens. [e/Ang^3]			-0.20, 0.19

Table S4 - Bond Distances (Angstrom) for 4d

S1	-O1	1.435(3)	C2	-H2	0.9800
S1	-O2	1.436(3)	C103	-C104	1.377(8)
S1	-N3	1.623(3)	C104	-C107	1.501(7)
S1	-C101	1.771(5)	C4	-H4B	0.9700
S2	-O3	1.444(3)	C104	-C105	1.390(8)
S2	-O4	1.455(4)	C4	-H4A	0.9700
S2	-N9	1.637(4)	C105	-C106	1.376(7)
S2	-C201	1.771(5)	C5	-H5A	0.9700
N3	-C2	1.485(6)	C5	-H5B	0.9700
N3	-C4	1.480(6)	C7	-H7A	0.9700
N6	-C5	1.471(6)	C7	-H7B	0.9700
N6	-C7	1.474(5)	C8	-H8B	0.9700
N6	-C311	1.492(6)	C8	-H8A	0.9700
N9	-C8	1.481(5)	C10	-H10	0.9800
N9	-C10	1.489(7)	C21	-H21B	0.9600
N12	-C1	1.335(6)	C21	-H21C	0.9600
N12	-C11	1.346(6)	C21	-H21A	0.9600
C1	-C2	1.532(6)	C22	-H22C	0.9600
C1	-C403	1.370(7)	C22	-H22A	0.9600
C2	-C21	1.516(7)	C22	-H22B	0.9600
C4	-C5	1.523(6)	C201	-C202	1.347(7)
C7	-C8	1.515(7)	C201	-C206	1.350(9)
C10	-C11	1.518(7)	C202	-C203	1.379(11)
C10	-C22	1.533(7)	C102	-H102	0.9300
C11	-C401	1.373(7)	C103	-H103	0.9300
C101	-C102	1.377(7)	C203	-C204	1.344(10)
C101	-C106	1.380(7)	C204	-C207	1.500(11)
C102	-C103	1.386(7)	C204	-C205	1.375(9)
C105	-H105	0.9300	C207	-H20C	0.9600
C205	-C206	1.378(11)	C307	-C308	1.399(11)
C106	-H106	0.9300	C308	-C309	1.376(11)
C107	-H10A	0.9600	C309	-C310	1.404(9)
C107	-H10C	0.9600	C311	-C312	1.530(7)
C107	-H10B	0.9600	C401	-C402	1.383(9)
C301	-C310	1.426(7)	C402	-C403	1.380(8)

C301	-C302	1.375(7)	C302	-H302	0.9300
C301	-C311	1.533(6)	C303	-H303	0.9300
C202	-H202	0.9300	C304	-H304	0.9300
C302	-C303	1.401(8)	C306	-H306	0.9300
C303	-C304	1.354(11)	C307	-H307	0.9300
C203	-H203	0.9300	C308	-H308	0.9300
C304	-C305	1.384(10)	C309	-H309	0.9300
C205	-H205	0.9300	C311	-H311	0.9800
C305	-C310	1.436(8)	C312	-H31A	0.9600
C305	-C306	1.426(11)	C312	-H31B	0.9600
C306	-C307	1.349(11)	C312	-H31C	0.9600
C206	-H206	0.9300	C401	-H401	0.9300
C207	-H20A	0.9600	C402	-H402	0.9300
C207	-H20B	0.9600	C403	-H403	0.9300

Table S5 - Crystal Data and Details of the Structure Determination for 5d

Crystal Data	
Formula	C37 H41 N4 O4 S2, C F3 O3 S
Formula Weight	818.96
Crystal System	Orthorhombic
Space group	P212121 (No. 19)
a, b, c [Angstrom]	11.1014(6) 12.1313(7) 29.7535(17)
V [Ang**3]	4007.0(4)
Z	4
D(calc) [g/cm**3]	1.358
Mu(MoKa) [/mm]	0.251
F(000)	1712
Crystal Size [mm]	0.08 x 0.10 x 0.15
Data Collection	
Temperature (K)	293
Radiation [Angstrom]	MoKa 0.71069
Theta Min-Max [Deg]	1.4, 27.0
Dataset	-14: 14 ; -15: 15 ; -38: 38
Tot., Uniq. Data, R(int)	33721, 8742, 0.033
Observed data [I > 0.0 sigma(I)]	6124
Refinement	
Nref, Npar	8742, 473
R, wR2, S	0.0728, 0.2337, 1.00
w = 1/[\s^2^(Fo^2^)+(0.1470P)^2^+1.6658P] where P=(Fo^2^+2Fc^2^)/3	
Max. and Av. Shift/Error	0.02, 0.00
Flack x	-0.03(11)
Min. and Max. Resd. Dens. [e/Ang^3]	-0.57, 0.64

Table S6 - Bond Distances (Angstrom) for 5d

S1	-O10	1.419(4)	F92	-C91	1.31(2)
S1	-O11	1.426(4)	F92	-C92	1.35(2)
S1	-N9	1.637(4)	F92	-F923	1.64(2)
S1	-C111	1.755(4)	F93	-C91	1.31(2)
S2	-O20	1.415(5)	F93	-F923	1.25(2)
S2	-O21	1.425(5)	F921	-C92	1.32(2)
S2	-N3	1.654(4)	F922	-C92	1.32(2)
S2	-C211	1.745(5)	F922	-C91	1.72(2)
S9	-S92	0.517(5)	F923	-C91	1.32(2)
S9	-O91	1.425(9)	F923	-C92	1.32(2)
S9	-O92	1.424(5)	O91	-O921	0.865(16)
S9	-O93	1.424(7)	O93	-O923	0.773(14)
S9	-O921	1.624(11)	N3	-C4	1.459(6)
S9	-O923	1.161(10)	N3	-C2	1.478(6)
S9	-C91	1.785(13)	N6	-C5	1.514(5)
S92	-O93	1.861(7)	N6	-C7	1.501(5)
S92	-O921	1.424(11)	N6	-C311	1.565(6)
S92	-O923	1.425(8)	N9	-C8	1.466(6)
S92	-C91	1.341(13)	N9	-C10	1.465(6)
S92	-C92	1.784(15)	N12	-C11	1.339(6)
S92	-O92	1.425(5)	N12	-C1	1.342(6)
S92	-O91	1.519(8)	N6	-H6	0.9100
F91	-F923	1.40(2)	C1	-C403	1.371(7)
F91	-F921	1.17(2)	C1	-C2	1.500(7)
F91	-C92	1.10(2)	C4	-C5	1.512(6)
F91	-C91	1.316(18)	C7	-C8	1.520(6)
F92	-F93	1.63(2)	C10	-C11	1.509(7)
F92	-F922	1.10(2)	C11	-C401	1.376(7)
C31	-C311	1.523(6)	C114	-C117	1.543(8)
C31	-C310	1.437(7)	C114	-C115	1.408(9)
C31	-C32	1.365(7)	C115	-C116	1.343(8)
C32	-C33	1.409(8)	C32	-H32	0.9300
C33	-C34	1.348(10)	C33	-H33	0.9300
C34	-C35	1.384(9)	C34	-H34	0.9300
C35	-C36	1.414(12)	C36	-H36	0.9300
C35	-C310	1.431(7)	C37	-H37	0.9300

C36	-C37	1.341(15)	C38	-H38	0.9300
C37	-C38	1.443(15)	C39	-H39	0.9300
C38	-C39	1.370(10)	C211	-C216	1.370(9)
C39	-C310	1.395(8)	C211	-C212	1.394(9)
C2	-H2A	0.9700	C112	-H112	0.9300
C2	-H2B	0.9700	C212	-C213	1.400(8)
C4	-H4A	0.9700	C113	-H113	0.9300
C4	-H4B	0.9700	C213	-C214	1.371(11)
C5	-H5B	0.9700	C214	-C215	1.352(11)
C5	-H5A	0.9700	C214	-C217	1.523(8)
C7	-H7B	0.9700	C115	-H115	0.9300
C7	-H7A	0.9700	C215	-C216	1.369(8)
C8	-H8B	0.9700	C116	-H116	0.9300
C8	-H8A	0.9700	C117	-H11A	0.9600
C10	-H10A	0.9700	C117	-H11B	0.9600
C10	-H10B	0.9700	C117	-H11C	0.9600
C111	-C112	1.394(7)	C91	-C92	0.71(2)
C111	-C116	1.395(7)	C311	-C312	1.519(7)
C112	-C113	1.368(8)	C212	-H212	0.9300
C113	-C114	1.339(9)	C213	-H213	0.9300
C215	-H215	0.9300	C311	-H311	0.9800
C216	-H216	0.9300	C312	-H31B	0.9600
C217	-H21C	0.9600	C312	-H31C	0.9600
C217	-H21A	0.9600	C312	-H31A	0.9600
C217	-H21B	0.9600	C401	-H401	0.9300
C401	-C402	1.346(8)	C402	-H402	0.9300
C402	-C403	1.381(8)	C403	-H403	0.9300