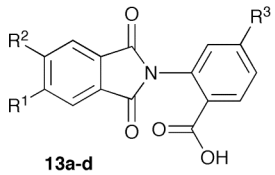
Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

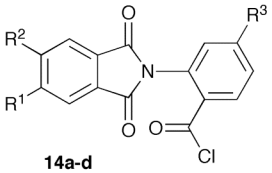
A novel approach to isoindolo[2,1-*a*]indol-6-ones

Philip Duncanson, Yuen-Ki Cheong, Majid Motevalli and D. Vaughan Griffiths*

Electronic Supplementary Information

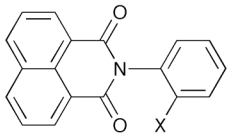


13a-d

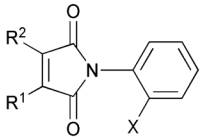


14a-d

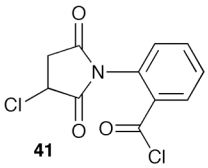
a $R^1 = R^2 = R^3 = H$,
b $R^1 = R^2 = H$, $R^3 = Cl$,
c $R^1 = R^2 = Cl$, $R^3 = H$,
d $R^1 = R^2 = R^3 = Cl$



24 X = CO_2H, **25** X = COCl



31a and **31c** X = CO_2H
32a and **32c** X = COCl



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Experimental

General details

Melting points were obtained on a Buchi SMP-20 capillary melting point apparatus and are uncorrected. IR spectra were recorded either a Shimadzu FTIR-8300 or a Perkin Elmer Spectrum 65 FT-IR spectrophotometer and selected bands are reported below. Low resolution mass spectra were obtained using a Bruker Esquire LC mass spectrometer equipped with an electrospray ionisation source or an Agilent GC mass spectrometer equipped with an electron ionisation detector. High resolution mass spectrometry was carried out by the EPSRC facility at Swansea. TLC was performed with alumina backed silica gel 60 F_{254} eluting with the solvent system used for the column chromatography unless otherwise stated and the plates were visualised under UV light or developed in an iodine tank. Column chromatography used silica gel with particle size 33–50 μm and was purchased from BDH. All other materials were purchased from Sigma-Aldrich Ltd. and used as received unless indicated otherwise.

General procedure to prepare the benzoic acid derivatives 13

A mixture of the appropriate anhydride **11** (20 mmol), 2-aminobenzoic acid **12** (20.5 mmol) and glacial acetic acid (25 cm^3) was heated at 110 °C for 16 h. The solution was then cooled and the solvent evaporated to leave a solid residue, which was purified as indicated below.

2-(1,3-Dioxoisoindolin-2-yl)benzoic acid **13a**[1] was prepared from phthalic anhydride and 2-aminobenzoic acid. A pure sample of the acid **13a** (2.51 g, 47%) was isolated as a cream coloured solid, mp 221-222 °C [lit.,[2] 217 °C (aq EtOH)] by the slow evaporation of an ethanolic solution of the crude product, δ_H(270 MHz, d_6-DMSO)[1] 7.57 (1 H, dd, *J* 8 and 1, 3-H), 7.65 (1 H, td, *J* 8 and 1, 5-H), 7.78 (1 H, td, *J* 8 and 2, 4-H), 7.89-7.95 (2 H, m, 5'/6'-H), 7.96-8.03 (2 H, m, 4'/7'-H), 8.07 (1 H, dd, *J* 8 and 2, 6-H), 13.13(1 H, br s, CO_2H); δ_C(67.9 MHz, d_6-DMSO)[1] 123.5 (x2)(C-4'/7'), 129.3 (C-1), 129.3 (C-5), 130.7 (C-3), 131.0 (C-6), 131.5 (C-2), 131.8 (x2)(C-3a'/7a'), 133.1 (C-4), 134.9 (x2)(C-5'/6'), 166.2 (CO_2H), 167.2 (x2)(C-1'/3'); ν_{max}/cm^{-1} (ATM) 3170 br, 3091, 1701, 1603, 1495, 1457, 1384, 1293, 1232, 1219, 1174, 1118, 1085, 1074, 896, 882, 833, 791, 774, 755, 718, 705.

4-Chloro-2-(1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)benzoic acid **13b** was prepared from phthalic anhydride and 2-amino-4-chlorobenzoic acid. The crude product was recrystallised from glacial acetic acid to give the pure acid **13b** (4.3 g, 71%) as a white powder, mp 280-281 °C (lit.,[3] 269-270 °C (AcOH)); δ_H(270 MHz, d_6-DMSO) 7.72 (1 H, dd, *J* 8.5 and 2, 5-H), 7.75 (1 H, d, *J* 2, 3-H), 7.91-7.96 (2 H, m, 5'/6'-H), 7.98-8.02 (2 H, m, 4'/7'-H), 8.07 (1 H, d, *J* 8, 6-H), 13.37 (1 H, br s, CO_2H); δ_C(67.9 MHz, d_6-DMSO) 123.7 (x2)(C-4'/7'), 128.3 (C-1), 129.5 (C-5), 130.6 (C-3), 131.8 (x2)(C-3a'/7a'), 132.8 (C-6), 133.0 (C-2), 135.0 (x2)(C-5'/6'), 137.2 (C-4), 165.5 (CO_2H), 166.9 (x2)(C-1'/3'); ν_{max}/cm^{-1} (ATM) 1707, 1681, 1594, 1492, 1419, 1317, 1276, 1220, 1105, 896, 867, 841, 779, 712, 693, 680; *m/z* (ESI)[4] 324 ($M+Na^+$. $C_{15}H_8ClNNaO_4$ requires 324).

2-(5,6-Dichloro-1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)benzoic acid **13c** was prepared from 4,5-dichlorophthalic anhydride and 2-aminobenzoic acid. The crude product was recrystallised from a chloroform/methanol (98:2) mixture to give the pure acid **13c** (4.2 g, 63 %) as a fawn coloured solid, mp 245-246 °C; δ_H(270 MHz, d_6-DMSO) 7.54 (1 H, d, *J* 7.5, 3-H), 7.63 (1 H, t, *J* 7.5, 5-H), 7.77 (1 H, t, *J*

7.5, 4-H), 8.10 (1 H, d, *J* 7.5, 6-H) 8.29 (2 H, s, 4'/7'-H), 13.22 (1 H, br s, CO_2H); δ_C(67.9 MHz, d_6-DMSO) 125.8 (x2)(C-4'/7'), 129.0 (C-1), 129.7 (C-5), 130.6 (C-3), 131.2 (C-2), 131.3 (C-6), 131.6 (x2)(C-3a'/7a'), 133.2 (C-4), 138.0 (x2)(C-5'/6'), 165.4 (x2)(C-1'/3'), 166.1 (CO_2H); ν_{max}/cm^{-1} (ATM) 3000-2600, 1718, 1687, 1601, 1491, 1452, 1371, 1310, 1280, 1263, 1223, 1140, 1109, 919, 871, 802, 693, 667; ; *m/z* (ESI)[4] 333.9671 ($M-H^-$. $C_{15}H_6Cl_2NO_4$ requires 333.9679).

4-Chloro-2-(5,6-dichloro-1,3-dioxo-1,3-dihydro-2H-isoindol-2-yl)benzoic acid **13d** was prepared from 4,5-dichlorophthalic anhydride and 2-amino-4-chlorobenzoic acid. The crude product was recrystallised by the slow evaporation of a solution in a chloroform/methanol (98:2) mixture. The pure acid **13d** (4.9 g, 66%) was isolated as a white powder, mp 254-255 °C; δ_H(270 MHz, d_6-DMSO) 7.71-7.76 (2 H, m, 3/5-H), 8.06-8.15 (1 H, m, 6-H), 8.34 (2 H, s, 4'/7'-H), 13.43 (1 H, br s, CO_2H); δ_C(67.9 MHz, d_6-DMSO) 125.9 (x2)(C-4'/7'), 128.0 (C-1), 129.7 (C-5), 130.3 (C-3), 131.4 (x2)(C-3a'/7a'), 132.4 (C-2), 132.8 (C-6), 137.2 (C-4), 138.1 (x2)(C-5'/6'), 164.9 (x2)(C-1'/3'), 165.2 (CO_2H); ν_{max}/cm^{-1} (ATM) 3050-2650, 1720, 1696, 1595, 1434, 1402, 1364, 1311, 1278, 1221, 1141, 1115, 1096, 890, 760, 736; *m/z* (ESI)[4] 369.9428 ($M+H^+$. $C_{15}H_7Cl_3NO_4$ requires 369.9435).

N,N-(1,8-Naphthaloyl)-2-aminobenzoic acid 24[5]

A mixture of 1,8-naphthalic anhydride (6.0 g, 30 mmol), 2-aminobenzoic acid (4.3, 30 mmol), triethylamine (4.5 g, 43.5 mmol) and DMF (50 cm^3) was heated and stirred at 140 °C for 16 h. Volatile components were then removed by heating under reduced pressure (75 °C at 15 mmHg) and the residue heated in boiling methanol (50 cm^3) for 30 min. The resulting solid was then filtered off and dried at 150 °C to give the pure acid **24** (6.5 g, 72 %) as a colourless powder, mp 294-295 °C (lit.,[5] 298-299 °C, lit.,[6] 292 °C), δ_H(270 MHz, d_6-DMSO) 7.56 (1 H, d, *J* 8, 3-H), 7.61 (1 H, t, *J* 8, 5-H), 7.79 (1 H, t, *J* 8, 4-H), 7.89 (2 H, t, *J* 8, 5'/8'-H), 8.16 (1 H, d, *J* 8, 6-H), 8.45-8.53 (4 H, m, 4'/6'/7'/9'-H); δ_C(67.9 MHz, d_6-DMSO) 122.4 (x2)(C-3a'/9a'), 127.3 (x2)(C-5'/8'), 127.9 (C-1), 128.0 (C-5), 129.0 (C-6a'), 130.8 (x2)(C-4'/9'), 131.1 (C-3), 131.3 (C-6), 131.5 (C-9b'), 133.2 (C-4), 134.6 (x2)(C-6'/7'), 136.4 (C-2), 163.8 (x2)(C-1'/3'), 166.0 (CO_2H).

2-(2,5-Dioxo-2,5-dihydro-1*H*-pyrrol-1-yl)benzoic acid 31a

A mixture of 2-aminobenzoic acid (4.2 g, 30 mmol), maleic anhydride (3.0 g, 30 mmol) and acetic acid was heated under reflux in an oil bath at 120-125 °C for 16 h. The reaction mixture was cooled and solvent evaporated under reduced pressure (75 °C at 15 mmHg) to leave a green slurry. DCM (50 cm^3) was added, the mixture stirred for 2 h and any solid filtered off, washed with DCM (50 cm^3) and air dried. This minor product (850 mg, 12 %) was shown to be 2-{[(2*Z*)-3-carboxyprop-2-enoyl]amino}benzoic acid; δ_H(400 MHz, d_6-DMSO) 6.68 (1 H, d, *J* 15.5, 2'-H), 7.00 (1 H, d, *J* 15.5, 3'-H), 7.21 (1 H, t, *J* 7.5, 5-H), 7.60 (1 H, td, *J* 7.5 and 1.3, 4-H), 7.98 (1 H, dd, *J* 7.5 and 1.3, 6-H), 8.41 (1 H, *J* 7.5, 3-H), 11.41 (1 H, s, NH), 13.3 (1 H, bs, CO_2H); δ_C(109.2 MHz, d_6-DMSO) 118.3 (C-1), 121.0 (C-3), 123.8 (C-5), 131.1 (C-6), 131.6 (C-2'), 133.9 (C-4), 137.3 (C-3'), 139.7 (C-2), 161.4 (C-4'), 166.2 (C-1'), 169.2 (CO_2H); ν_{max}/cm^{-1} (ATM) 3312, 3100-2500 br, 1688, 1668, 1632, 1605, 1582, 1531, 1411, 1311, 1266, 1170, 971, 883. The major product **31a** was isolated by removing the solvent from the filtrate under reduced pressure (35 °C at 15 mmHg) to give a viscous oil which was then purified by column chromatography on silica gel eluting with a DCM/MeOH 9:1 mixture. The resulting solid was crystallised by the slow evaporation of a DCM solution to give the pure 2-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)benzoic acid **31a** (2.8 g, 43%) as a fawn coloured solid (r_f = 0.15) mp 161-163 °C [lit.,[7] 160-162 °C (EtOH)]; δ_H(270 MHz, d_6-DMSO) 7.23 (2 H, s, 3'/4'-H), 7.41 (1 H, dd, *J* 8 and 2, 3-H), 7.59 (1 H, td, *J* 8 and 2, 5-H), 7.72 (1 H, td, *J* 8 and 2, 4-H), 8.01 (1 H, dd, *J* 8 and 2, 6-H), 13.12 (1 H, br s, CO_2H); δ_C(67.9 MHz, d_6-DMSO) 129.7 (x2)(C-1, C-5), 131.2 (C-3), 131.6 (C-6), 131.7 (C-2), 133.6 (C-4), 135.7 (x2)(C-3'/4'), 166.7 (CO_2H), 170.7 (x2)(C-2'/5'); ν_{max}/cm^{-1} (ATM) 2973, 2861, 2666, 1683, 1600, 1576, 1494, 1422, 1301, 1269, 1212, 1154, 1096, 1060, 1040, 1008, 955, 909, 831, 805, 772.

2-(3,4-Dichloro-2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)benzoic acid 31c

This compound was prepared from dichloromaleic anhydride and 2-aminobenzoic acid using the procedure previously described for the benzoic acids **13** and purified by recrystallisation from a chloroform/methanol 95:5 mixture. The pure product **31c** (3.9 g, 69 %) was isolated as a yellow powder, mp 241-242 °C (lit.,[8] 237-239 °C), δ_H(270 MHz, d_6-DMSO) 7.50 (1 H, d, *J* 8, 3-H), 7.65 (1 H, t, *J* 8, 5-H), 7.89 (1 H, t, *J* 8, 4-H), 8.08 (1 H, d, *J* 8, 6-H), 13.37 (1 H, br s, CO_2H); δ_C(67.9 MHz, d_6-DMSO) 128.7 (C-1), 130.1 (C-5), 130.3 (C-2), 130.7 (C-3), 131.5 (C-6), 133.2 (x2)(C-3'/4'), 133.6 (C-4), 162.3 (x2)(C-2'/5'), 165.9 (CO_2H); ν_{max}/cm^{-1} (ATM) 3222, 1718, 1603, 1491, 1453, 1372, 1226, 1122, 1081, 1018, 901, 883, 820, 758, 732, 648.

General procedure for the preparation of acid chlorides 14

DMF (1 drop) was added to a mixture of the benzoic acid derivative **13** (3.0 mmol) and thionyl chloride (10 cm^3) and the mixture stirred at room temperature for 16 h. If any solid remained the mixture was then heated under reflux for 5 min. Volatile components were removed under reduced pressure (40 °C at 15 mmHg). To ensure the removal of any residual thionyl chloride, the residue was redissolved in warm dry toluene (20 cm^3) and the toluene and other volatile compounds were then removed under reduced pressure (55 °C at 15 mmHg) taking care to rigorously exclude moisture from the product. The resulting acid chloride **14** was used without further purification.

2-(1,3-Dioxoisoindolin-2-yl)benzoyl chloride **14a** gave δ_H(270 MHz, $CDCl_3$) 7.42 (1 H, dd, *J* 8 and 1, 3-H), 7.58 (1 H, td, *J* 8 and 1, 5-H), 7.74 (1 H, td, *J* 8 and 1, 4-H), 7.74-7.78 (2 H, m, 5'/6'-H), 7.86-7.91 (1 H, m, 4'/7'-H), 8.27 (1 H, dd, *J* 8 and 1, 6-H); δ_C(67.9 MHz, $CDCl_3$) 124.1 (x2)(C-4'/7'), 129.5 (C-5), 130.4 (C-3), 131.1 (C-1), 131.4 (C-2), 131.8 (x2)(C-3a'/7a'), 133.8 (C-6), 134.7 (x2)(C-5'/6'), 135.3 (C-4), 166.3 (COCl), 166.9 (x2)(C-1'/3').

4-Chloro-2-(1,3-dioxoisoindolin-2-yl)benzoyl chloride **14b** gave δ_H(270 MHz, $CDCl_3$) 7.45 (1 H, d, *J* 2, 3-H), 7.57 (1 H, dd, *J* 8 and 2, 5-H), 7.77-7.82 (2 H, m, 5'/6'-H), 7.90-7.95 (2 H, m, 4'/7'-H), 8.24 (1 H, d, *J* 8, 6-H); δ_C(67.9 MHz, $CDCl_3$) 124.3 (x2)(C-4'/7'), 129.7 (C-5), 129.8 (C-1), 130.7 (C-3), 131.7 (x2)(C-3a'/7a'), 132.3 (C-2), 134.9 (C-6), 135.0 (x2)(C-5'/6'), 141.5 (C-4), 165.5 (COCl), 165.5 (x2)(C-1'/3').

2-(5,6-Dichloro-1,3-dioxoisoindolin-2-yl)benzoyl chloride **14c** gave δ_H(270 MHz, $CDCl_3$) 7.45 (1 H, dd, *J* 7.5 and 1, 3-H), 7.68 (1 H, td, *J* 7.5 and 1, 5-H), 7.82 (1 H, td, *J* 7.5 and 1, 4-H), 8.05 (2 H, s, 4'/7'-H), 8.37 (1 H, dd, *J* 7.5 and 1, 6-H); δ_C(67.9 MHz, $CDCl_3$) 126.3 (x2)(C-4'/7'), 130.0 (C-5), 130.6 (C-3), 130.8 (C-1), 131.1 (x2)(C-3a'/7a'), 131.3 (C-2), 134.4 (C-6), 135.5 (C-4), 139.9 (x2)(C-5'/6'), 165.1 (x2)(C-1'/3'), 166.4 (COCl).

4-Chloro-2-(5,6-dichloro-1,3-dioxoisoindolin-2-yl)benzoyl chloride **14d** gave δ_H(270 MHz, $CDCl_3$) 7.43 (1 H, d, *J* 2, 3-H), 7.58 (1 H, dd, *J* 8 and 2, 5-H), 7.98 (2 H, s, 4'/7'-H), 8.24 (1 H, d, *J* 8, 6-H); δ_C(67.9 MHz, $CDCl_3$) 126.1 (x2)(C-4'/7'), 128.3 (C-1), 129.9 (C-3), 130.6 (C-5), 130.7 (x2)(C-3a'/7a'), 131.7 (C-2), 135.0 (C-6), 139.8 (x2)(C-5'/6'), 141.6 (C-4), 164.5 (x2)(C-1'/3'), 165.4 (COCl).

N,N-(1,8-Naphthaloyl)-2-aminobenzoyl chloride **25** was prepared from the acid **24** using the same procedure as that used to prepare the acid chlorides **14** and gave δ_H(270 MHz,$CDCl_3$) 7.42(1 H, dd, *J* 8 and 1.5, 3-H), 7.67 (1 H , td, *J* 8 and 1.5, 5-H), 7.76 (2 H, t, *J* 7.5, 5'/8'-H), 7.82 (1 H, td, *J* 8 and 1.5, 4-H), 8.26 (2 H, d, *J* 7.5, 6'/7'-H), 8.40 (1 H, dd, *J* 8 and 1.5, 6-H), 8.60 (2 H, d, *J* 7.5, 4'/9'-H); δ_C(67.9 MHz, $CDCl_3$) 122.7 (x2)(C-3a'/9a'), 127.2 (x2)(C-5'/8'), 129.2 (C-9b'), 129.7 (C-3), 131.3 (C-5), 131.4 (C-6a'), 131.9 (x2)(C-4'/9'), 132.0 (C-1), 134.8 (x2)(C-6'/7'), 135.0 (C-6), 135.8 (C-4), 136.3 (C-2), 164.4 (x2)(C-1'/3'), 165.9 (COCl).

2-(3,4-Dichloro-2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)benzoyl chloride **32c** was prepared from the acid **31c** using the same procedure as that used to prepare the acid chlorides **14** and gave δ_H(270 MHz, $CDCl_3$) 7.32 (1 H, d, *J* 8, 3-H), 7.62 (1 H, t, *J* 8, 5-H), 7.74 (1 H, t, *J* 8, 4-H), 8.32 (1 H, d, *J* 8, 6-H); δ_C(67.9 MHz, $CDCl_3$) 130.0 (C-2), 130.5 (C-5), 130.9 (C-3), 131.0 (C-1), 134.3 (x2)(C-3'/4'), 134.9 (C-6), 135.8 (C-4), 161.8 (x2)(C-2'/5'), 166.5 (COCl).

The reaction of 2-(2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)benzoic acid 31a with oxalyl chloride and thionyl chloride

1. Limited reaction with oxalyl chloride

A mixture of the benzoic acid **31a** (540 mg, 2.5 mmol), oxalyl chloride (5 cm^3) and DMF (1 drop) was stirred for 1 h at room temperature and volatile components were then removed under reduced pressure (40 °C at 15 mmHg). Toluene (15 cm^3) was then added and removed under reduced pressure (40 °C at 15 mmHg) to give a brown viscous residue that contained the desired acid chloride **32a** [δ_H(270 MHz, $CDCl_3$) 6.85 (s, =CH)] as only the minor component (*ca.* 23%). The major component was the halogenated derivative **41** [δ_H(270 MHz, $CDCl_3$) 3.05 (1 H, dd, *J* 18.8 and 4), 3.48 (1 H, dd , *J* 18.8 and 8.5), 4.82 (1 H, dd, *J* 8.5 and 4)] (*ca.* 77%). Since these components could not be readily separated, the mixture was used to investigate their reactions with triethyl phosphite.

2. Reaction with thionyl chloride for a more extended period.

2-(2,5-Dioxo-2,5-dihydro-1*H*-pyrrol-1-yl)benzoic acid **31a** (1.5 g, 6.9 mmol), thionyl chloride (3 cm^3) and dry DCM (15 cm^3) were stirred at room temperature for 16 h by which time a dark brown/orange solution had been obtained. The solution was filtered and the filtrate evaporated under reduced pressure (50 °C at 15 mmHg) to leave a viscous residue. Final traces of thionyl chloride were removed by repeatedly adding DCM (20 cm^3) and then evaporating the solution under reduced pressure (50 °C, 15 mmHg). The resulting viscous residue was shown to be *2-(3-chloro-2,5-dioxopyrrolidin-1-yl)benzoyl chloride* **41** (1.72 g, 92 %) in a good state of purity and this was used without further purification; δ_H(270 MHz, $CDCl_3$) 3.05 (1 H, dd, *J* 18.5 and 4, 4'-H), 3.45 (1 H, dd, *J* 18.5 and 8.5, 4-H), 4.82(1 H, dd, *J* 8.5 and 4, 3-H), 7.18-7.32 (1 H, br m, 4-H), 7.58 (1 H, t, *J* 8, 5-H), 7.71 (1 H, br d, *J* 8, 6-H), 8.32 (1 H, d, *J* 8, 3-H); δ_C(67.9 MHz, $CDCl_3$) 39.6 (C-4'), 49.2 (C-3'), 129.9 (C-3), 130.3 (C-5), 130.9 (C-1), 134.5 (C-6), 134.9 (C-2), 135.8 (C-4), 166.3 (COCl), 171.8 (C-5'), 172.0 (C-2')

X-Ray crystallography

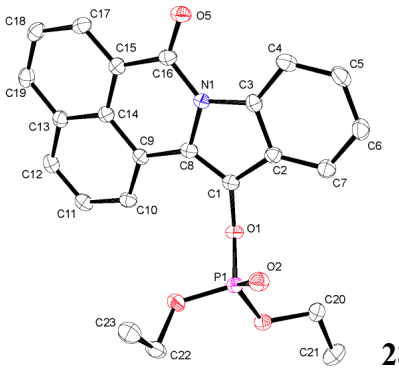
For all complexes, the crystals were glued to a glass fibre and mounted on the diffractometer head. Intensity data for all crystals were collected at 120 K, using a Bruker-Nonius FR591CCD deffractometer, equipped with a Mo-K_α rotating anode (λ = 0.71073 Å), monochromated by graphite (**15a**) or 10 cm confocal focusing mirrors (**28**, **35c** and **37c**). The crystals were positioned 30 mm from the CCD and all intensities were measured using a counting time of 20 seconds with 1.0° increments (ω and Ω) to fill the Ewald sphere. The unit cell parameters were determined by least-squares refinement of all data automatically centred reflections with setting angles of $2.91 \leq 2\theta \leq 27.48°$.

All intensities were collected using the programs COLLECT[9]. Data reductions and refinements were performed using both DENZO[10] and COLLECT according to Lorentz and polarisation effects. Absorption corrections were applied based on multi-scan method and were obtained using SADABS[11]. X-ray crystal structures were determined using the DirAx[12] program. The programs ORTEP-3[13] and PLATON[14] were used for drawing the molecules. WINGX[15] was used to prepare material for publication.

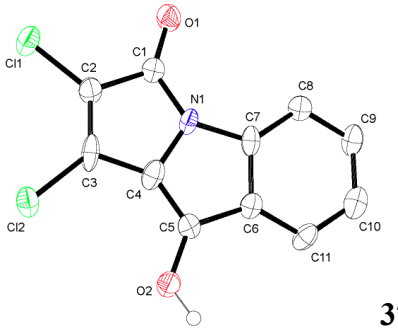
All structures were solved by the heavy-atom method using the DIRDIFF99[16] program and refined anisotropically (non-hydrogen atoms) by full-matrix least-squares technique against F^2 using the SHELXL-97[17] program. All H atoms were calculated geometrically and refined by a riding model.

Table 1: Crystallographic data for **15a**, **28**, **35c** and **37c**[18]

Compound	**15a**	**28**	**35c**	**37c**
Formula	$C_{19}H_{18}NO_5P$	$C_{23}H_{20}NO_5P$	$C_{15}H_{14}Cl_2NO_5P$	$C_{11}H_5Cl_2NO_2$
M_r (Da)	371.31	421.37	390.14	254.06
T (K)	120 (2)	120 (2)	120 (2)	120 (2)
Crystal system	Triclinic	Monoclinic	Monoclinic	Orthorhombic
Space group	P -1	I 2/a	$P2_1/n$	P 2_1 n b
a (Å)	8.5690 (2)	22.2526 (5)	12.4096 (3)	3.7524(7)
b (Å)	8.7336 (2)	7.0132 (2)	9.6934 (2)	12.666(3)
c (Å)	11.8798 (3)	25.1963 (6)	27.4755 (7)	21.009(4)
α (°)	81.6460 (10)	90	90	90
β (°)	85.9310 (10)	106.297 (2)	92.9430 (10)	90
γ (°)	88.264 (2)	90	90	90
V (Å^3)	877.23 (4)	3774.19 (16)	3300.70 (13)	998.5(4)
D_{Calc} (Mg/m^3) (*Z*)	1.406 (2)	1.483 (8)	1.570 (8)	1.690 (4)
μ_{ω}(mm^{-1})	0.187	0.184	0.516	0.629
Crystal size (mm^3)	0.32 x 0.27 x 0.17	0.30 x 0.17 x 0.04	0.20 x 0.12 x 0.06	0.30 x 0.06 x 0.03
Index ranges for *h*, *k*, *l*	-11/11,-11/11,-15/15	-28/28, -9/9, -27/32	-14/16,-12/12,-34/35	-4/4, -16/16, -26/27
No. of reflections collected	20152	19986	29073	5015
No.of reflections unique (R_{int})	4033 (0.0416)	4293 (0.0538)	7515 (0.0494)	1941 (0.0560)
No. of reflections observed	3408	3406	6115	1681
$T_{max/min}$	0.9688 and 0.9425	0.9927 and 0.9468	0.9697 and 0.9038	0.9814 and 0.8337
Data/restraints/parameters	4033 / 0 / 237	4293/0/273	7515/0/437	1941 / 1 / 149
Goodness-of-fit (GOF)	1.052	1.092	1.144	1.078
R1, wR_2 [$I > 2\sigma(I)$]	0.0408, 0.0982	0.0540, 0.1035	0.0648, 0.1204	0.0842, 0.2141
(all data)	0.0498, 0.1037	0.0747, 0.1142	0.0838, 0.1298	0.0983, 0.2260
Largest diff. peak and hole (e/Å^3)	0.452 and -0.410	0.325 and -0.396	0.407 and -0.435	0.587 and -0.653



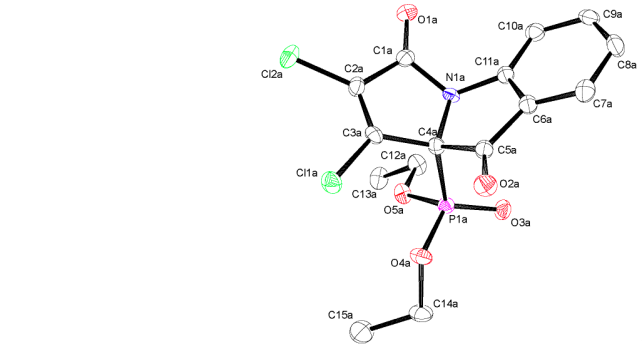
28



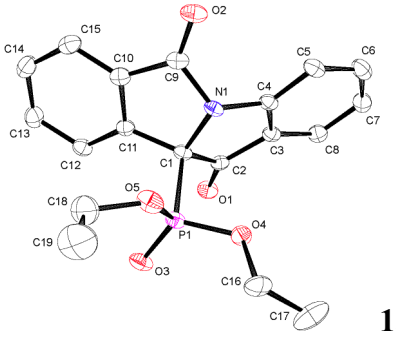
37c

Table 1 Selected bond lengths and angles for compounds **28** and **37c**

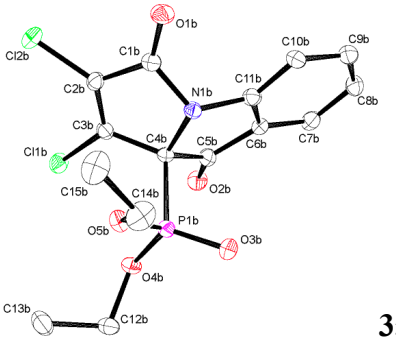
	28		**37c**
Bond lengths (Å)			
O(1)-C(1)	1.392 (3)	O(1)-C(1)	1.231 (9)
O(5)-C(16)	1.219 (3)	O(2)-C(5)	1.325 (9)
N(1)-C(3)	1.402 (3)	N(1)-C(1)	1.362 (9)
N(1)-C(8)	1.420 (3)	N(1)-C(4)	1.412 (10)
N(1)-C(16)	1.396 (3)	N(1)-C(7)	1.440 (8)
P(1)-O(1)	1.597 (2)	C(1)-C(2)	1.468 (10)
C(1)-C(2)	1.429 (3)	C(2)-C(3)	1.349 (12)
C(1)-C(8)	1.364 (3)	C(3)-C(4)	1.435 (10)
C(2)-C(3)	1.411 (3)	C(4)-C(5)	1.358 (10)
C(8)-C(9)	1.451 (3)	C(5)-C(6)	1.460 (10)
C(9)-C(14)	1.424 (3)	C(6)-C(7)	1.415 (11)
C(15)-C(16)	1.480 (3)		
Bond angles (°)			
C(2)-C(1)-C(8)	110.4 (2)	N(1)-C(1)-C(2)	104.9 (6)
O(1)-C(1)-C(8)	124.8 (2)	N(1)-C(4)-C(3)	105.6 (7)
O(1)-C(1)-C(2)	124.6 (2)	N(1)-C(4)-C(5)	110.2 (6)
P(1)-O(1)-C(1)	122.1 (2)	N(1)-C(7)-C(6)	106.2 (6)
C(1)-C(2)-C(3)	106.0 (2)	C(1)-N(1)-C(4)	111.4 (6)
C(2)-C(3)-N(1)	107.9 (2)	C(4)-N(1)-C(7)	108.0 (6)
C(3)-N(1)-C(8)	108.8 (2)	C(1)-C(2)-C(3)	109.4 (7)
C(8)-N(1)-C(16)	124.8 (2)	C(2)-C(3)-C(4)	108.5 (7)
C(1)-C(8)-N(1)	106.9 (2)	C(3)-C(4)-C(5)	144.2 (8)
N(1)-C(8)-C(9)	119.8 (2)	C(4)-C(5)-C(6)	107.4 (7)
C(8)-C(9)-C(14)	117.4 (2)	C(5)-C(6)-C(7)	108.1 (6)
C(9)-C(14)-C(15)	121.6 (2)		
C(14)-C(15)-C(16)	121.3 (2)		
C(15)-C(16)-N(1)	115.1 (2)		



35c (a)



15a



35c (b)

Table 2 Selected bond lengths and angles for β-ketophosphonates **15a** and **35c** (structures A and B)[§]

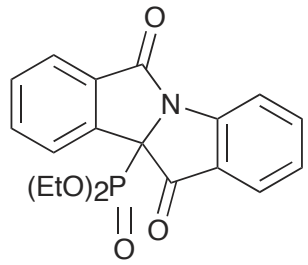
	15a		**35c**	
Bond lengths (Å)			**(a)**	**(b)**
C(9)-O(2)	1.215 (2)	C(1)-O(1)	1.209 (4)	1.207 (4)
C(2)-O(1)	1.214 (2)	C(5)-O(2)	1.206 (4)	1.206 (4)
C(1)-P(1)	1.842 (2)	C(4)-P(1)	1.858 (3)	1.855 (3)
C(10)-C(11)	1.393 (2)	C(2)-C(3)	1.335 (5)	1.330 (4)
C(11)-C(1)	1.504 (2)	C(3)-C(4)	1.498 (5)	1.498 (4)
C(1)-C(2)	1.549 (2)	C(4)-C(5)	1.555 (5)	1.552 (5)
C(9)-C(10)	1.479 (2)	C(1)-C(2)	1.476 (5)	1.477 (5)
C(2)-C(3)	1.468 (2)	C(5)-C(6)	1.478 (5)	1.473 (5)
C(3)-C(4)	1.395 (2)	C(6)-C(11)	1.390 (5)	1.394 (5)
N(1)-C(9)	1.409 (2)	N(1)-C(1)	1.404 (4)	1.409 (4)
N(1)-C(1)	1.474 (2)	N(1)-C(4)	1.474 (4)	1.474 (4)
N(1)-C(4)	1.417 (2)	N(1)-C(11)	1.421 (4)	1.434 (4)
Bond angles (°)				
C(2)-C(1)-C(11)	120.31 (12)	C(5)-C(4)-C(3)	119.0(3)	118.6 (3)
P(1)-C(1)-N(1)	109.91 (9)	P(1)-C(4)-N(1)	105.7 (2)	105.7 (2)
C(2)-C(1)-N(1)	104.40 (11)	C(5)-C(4)-N(1)	104.9 (3)	104.9 (3)
C(11)-C(1)-N(1)	103.48 (11)	C(3)-C(4)-N(1)	102.7 (3)	102.8 (2)
P(1)-C(1)-C(2)	108.24 (10)	P(1)-C(4)-C(5)	109.2 (2)	109.7 (2)
P(1)-C(1)-C(11)	108.24 (10)	P(1)-C(4)-C(3)	113.8 (2)	113.6 (2)
C(1)-(2)-C(3)	105.24 (12)	C(4)-C(5)-C(6)	104.6 (3)	104.7 (3)
C(2)-C(3)-C(4)	109.49 (13)	C(5)-C(6)-C(11)	109.7 (3)	109.9 (3)
C(3)-C(4)-N(1)	110.87 (13)	C(6)-C(11)-N(1)	111.2 (3)	110.6 (3)
C(4)-N(1)-C(1)	108.87 (11)	C(11)-N(1)-C(4)	108.5 (3)	108.5 (3)
C(1)-N(1)-C(9)	111.47 (12)	C(4)-N(1)-C(1)	110.8 (3)	110.7 (3)
N(1)-C(9)-C(10)	106.05 (13)	N(1)-C(1)-C(2)	105.5 (3)	105.3 (3)
C(9)-C(10)-C(11)	109.50 (14)	C(1)-C(2)-C(3)	110.1 (3)	110.6 (3)
C(10)-C(11)-C(1)	108.92 (13)	C(2)-C(3)-C(4)	110.3 (3)	110.2 (3)

[§] Values on the same row of the table show the corresponding bond lengths or bond angles in the two compounds

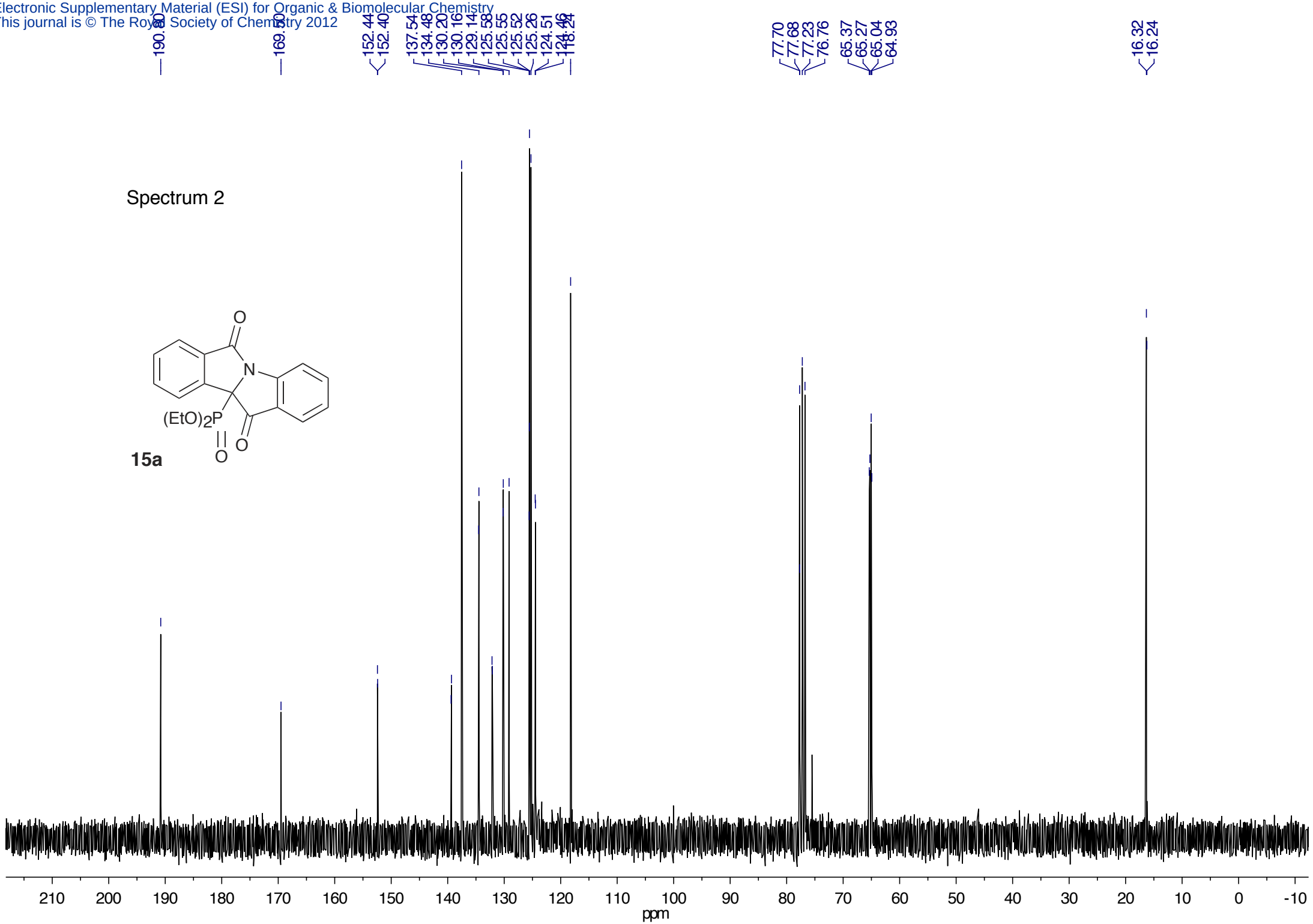
Further information on NMR spectra provided.

1. ^{31}P NMR spectrum of **15a** in $CDCl_3$ at 109.3 MHz
2. ^{13}C NMR spectrum of **15a** in $CDCl_3$ at 67.9 MHz
3. ^{31}P NMR spectrum of **16a** in $CDCl_3$ at 109.3 MHz
4. ^{13}C NMR spectrum of **16a** in $CDCl_3$ at 67.9 MHz
5. ^{31}P NMR spectrum of **20a** in $CDCl_3$ at 109.3 MHz
6. ^{13}C NMR spectrum of **20a** in $CDCl_3$ at 100.6 MHz
7. ^{13}C NMR spectrum of **23a** in $CDCl_3$ at 67.9 MHz
8. ^{31}P NMR spectrum of **15b** in $CDCl_3$ at 109.3 MHz
9. ^{13}C NMR spectrum of **15b** in $CDCl_3$ at 100.6 MHz
10. ^{31}P NMR spectrum of **20b** in $CDCl_3$ at 109.3 MHz
11. ^{13}C NMR spectrum of **20b** in $CDCl_3$ at 67.9 MHz
12. ^{13}C NMR spectrum of **23b** in $CDCl_3$ at 100.6 MHz
13. ^{13}C NMR spectrum of **13c** in d_6-DMSO at 67.9 MHz
14. ^{31}P NMR spectrum of **15c** in $CDCl_3$ at 109.3 MHz
15. ^{13}C NMR spectrum of **15c** in $CDCl_3$ at 100.6 MHz
16. ^{31}P NMR spectrum of **20c** in $CDCl_3$ at 109.3 MHz
17. ^{13}C NMR spectrum of **20c** in $CDCl_3$ at 100.6 MHz
18. ^{1}H NMR spectrum of **23c** in CCl_4 at 270 MHz
19. ^{13}C NMR spectrum of **13d** in d_6-DMSO at 67.9 MHz
20. ^{31}P NMR spectrum of **15d** in $CDCl_3$ at 109.3 MHz
21. ^{13}C NMR spectrum of **15d** in $CDCl_3$ at 100.6 MHz
22. ^{31}P NMR spectrum of **20d** in $CDCl_3$ at 109.3 MHz
23. ^{13}C NMR spectrum of **20d** in $CDCl_3$ at 100.6 MHz
24. ^{1}H NMR spectrum of **23d** in d_6-DMSO at 270 MHz
25. ^{31}P NMR spectrum of **26** in $CDCl_3$ at 109.3 MHz
26. ^{13}C NMR spectrum of **26** in $CDCl_3$ at 67.9 MHz
27. ^{31}P NMR spectrum of **27** in $CDCl_3$ at 109.3 MHz
28. ^{13}C NMR spectrum of **27** in $CDCl_3$ at 100.6 MHz
29. ^{31}P NMR spectrum of **28** in $CDCl_3$ at 109.3 MHz
30. ^{13}C NMR spectrum of **28** in $CDCl_3$ at 100.6 MHz
31. ^{13}C NMR spectrum of **29** in $CDCl_3$ at 100.6 MHz
32. ^{31}P NMR spectrum of **35a** in $CDCl_3$ at 109.3 MHz
33. ^{13}C NMR spectrum of **35a** in $CDCl_3$ at 67.9 MHz
34. ^{31}P NMR spectrum of **44** in $CDCl_3$ at 109.3 MHz
35. ^{13}C NMR spectrum of **44** in $CDCl_3$ at 100.6 MHz
36. ^{13}C NMR spectrum of **50** in $CDCl_3$ at 67.9 MHz
37. ^{31}P NMR spectrum of **52** in $CDCl_3$ at 109.3 MHz
38. ^{13}C NMR spectrum of **52** in $CDCl_3$ at 100.6 MHz
39. ^{31}P NMR spectrum of **35c** in $CDCl_3$ at 109.3 MHz
40. ^{13}C NMR spectrum of **35c** in $CDCl_3$ at 67.9 MHz
41. ^{13}C NMR spectrum of **38c** in $CDCl_3$ at 100.6 MHz
42. ^{13}C NMR spectrum of **40** in $CDCl_3$ at 100.6 MHz

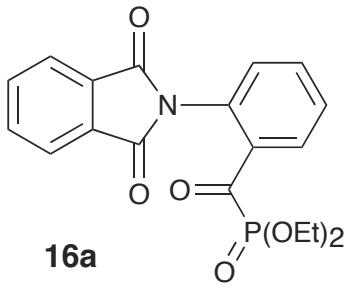
Spectrum 1



15a

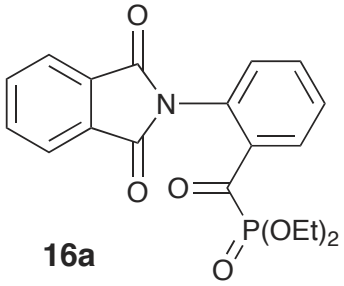


Spectrum 3



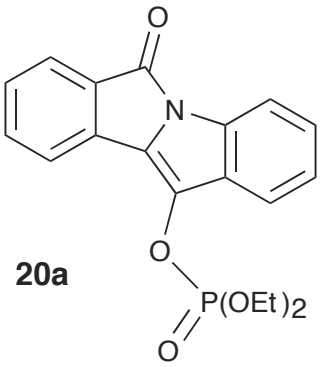
16a

Spectrum 4

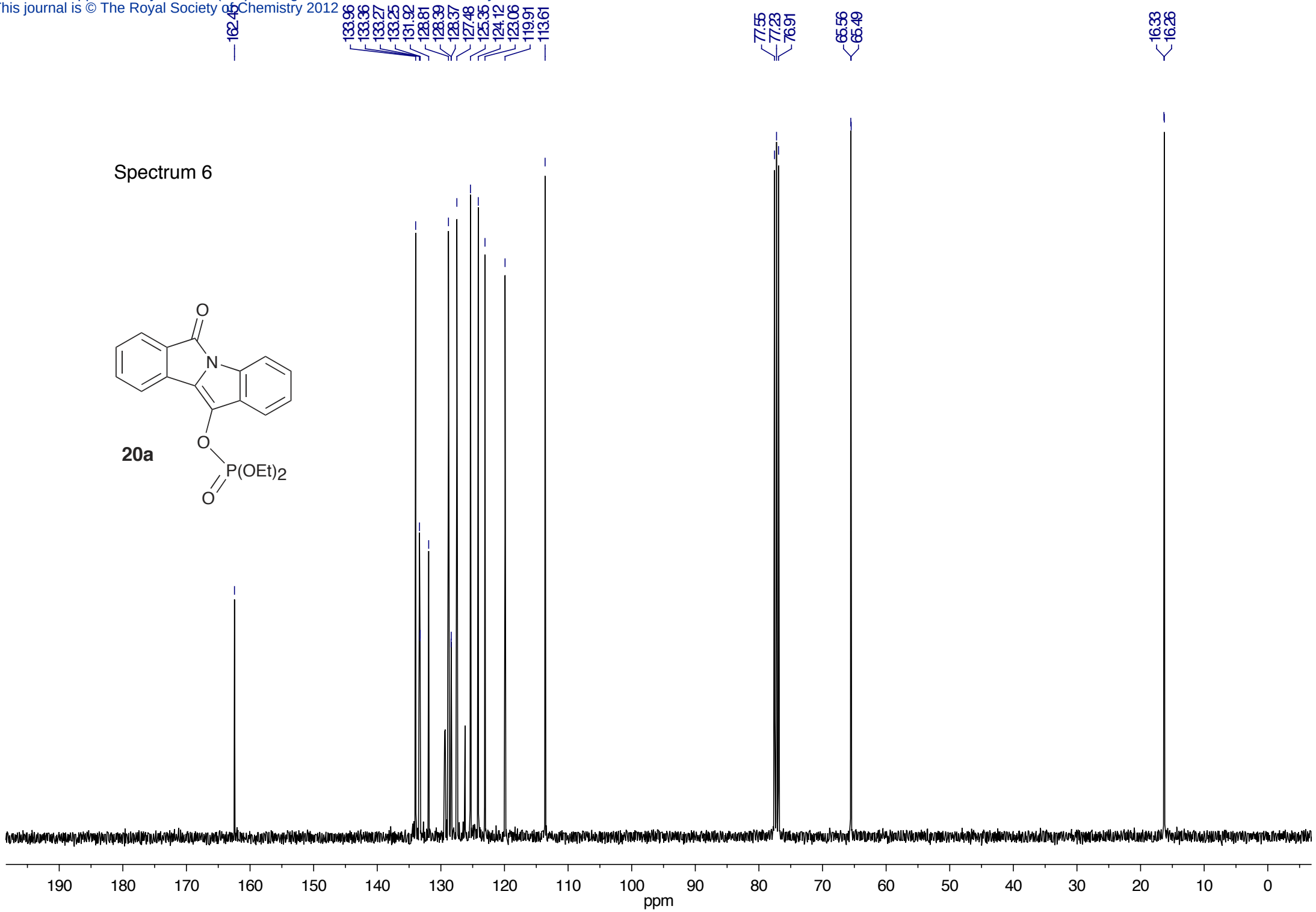


16a

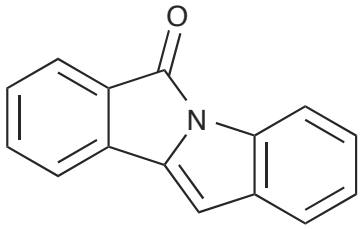
Spectrum 5



20a



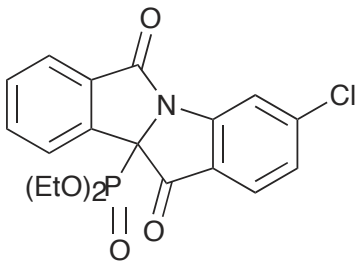
Spectrum 7



23a

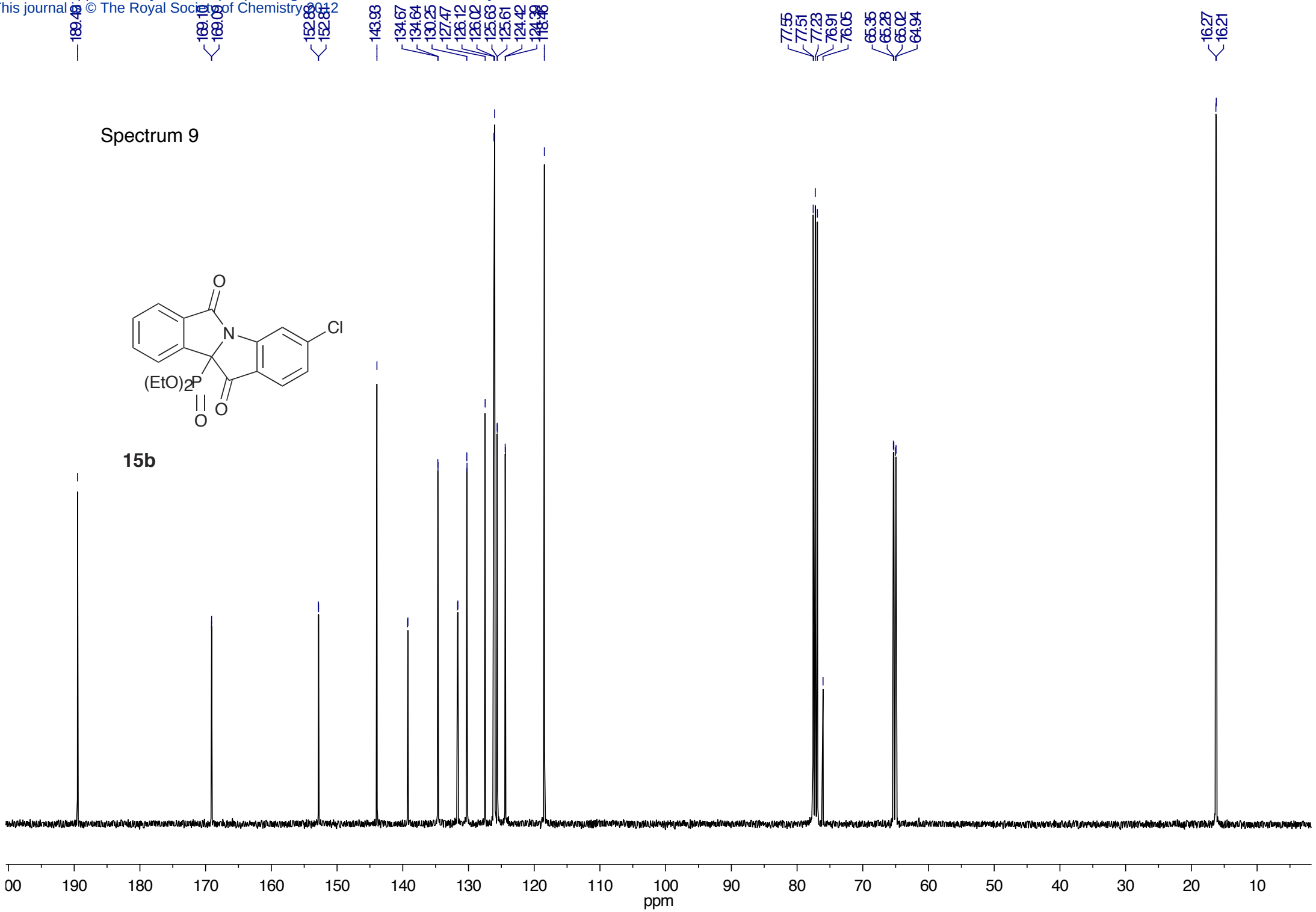
12.25

Spectrum 8

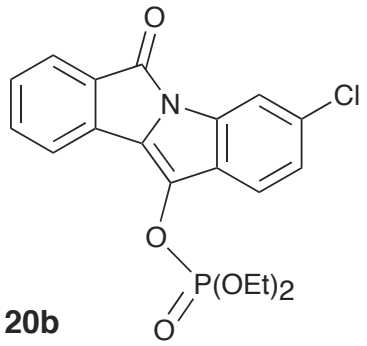


15b

150 130 110 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -110 -130 -150
ppm



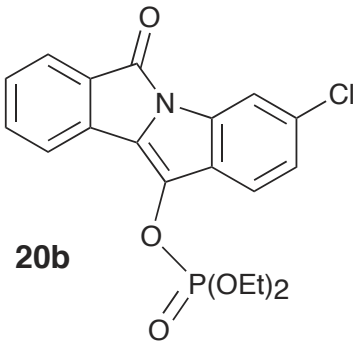
Spectrum 10



20b

162.12
134.15
133.48
133.04
133.01
132.84
131.94
129.01
128.85
128.72
126.81
126.77
126.60
125.51
124.57
123.10
120.71
113.81
77.70
77.23
76.76
65.61
65.52
65.50
16.34
16.24

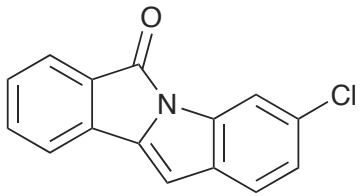
Spectrum 11



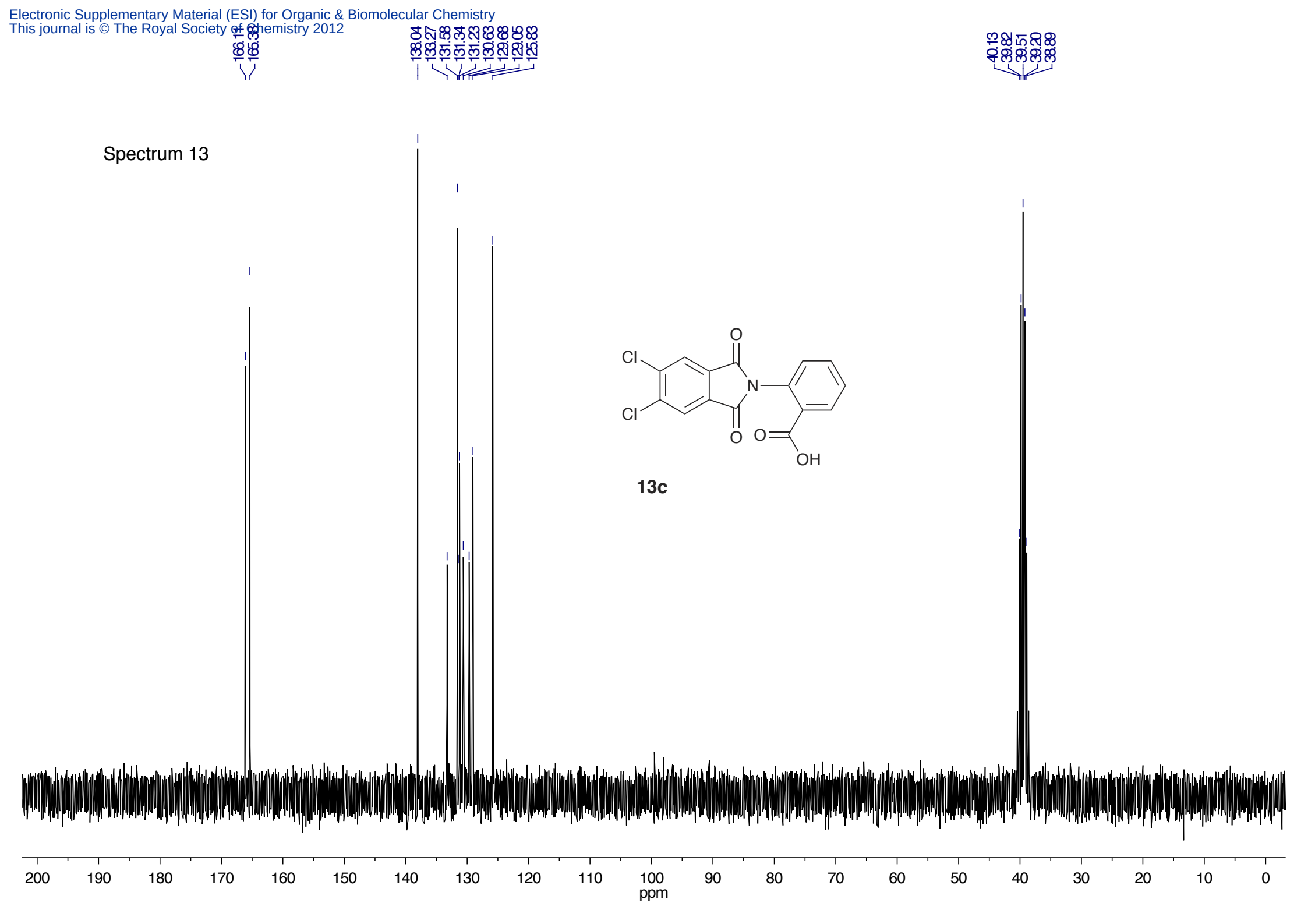
20b

200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
ppm

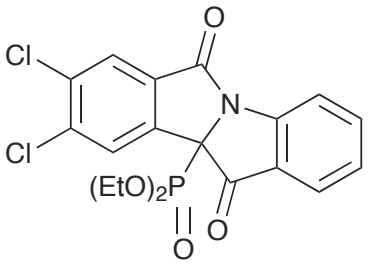
Spectrum 12



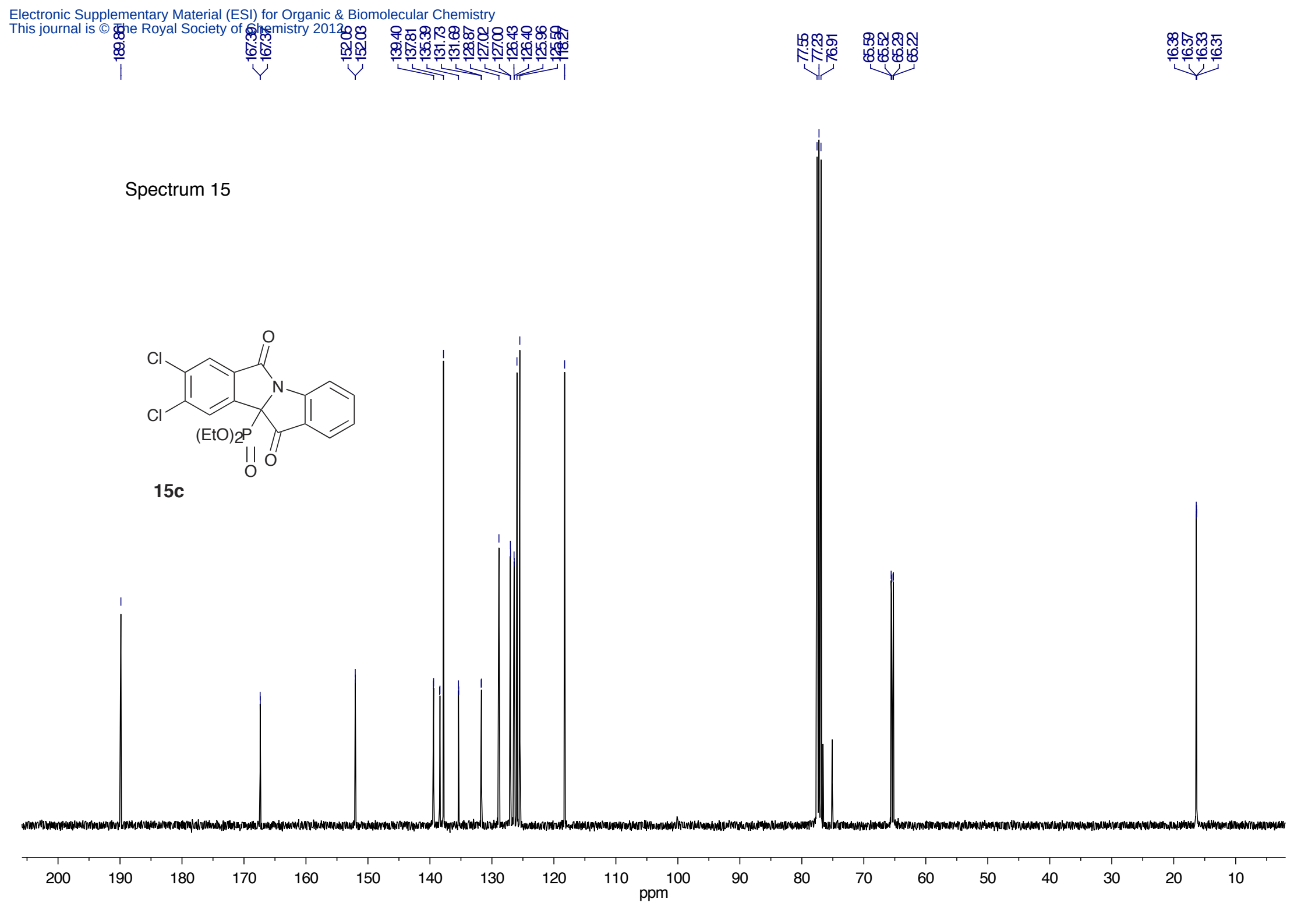
23b



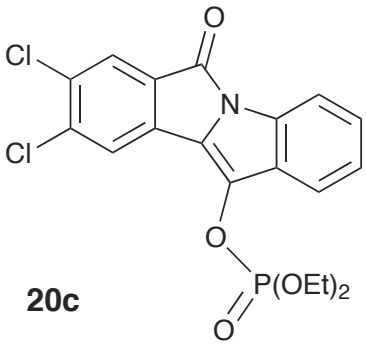
Spectrum 14



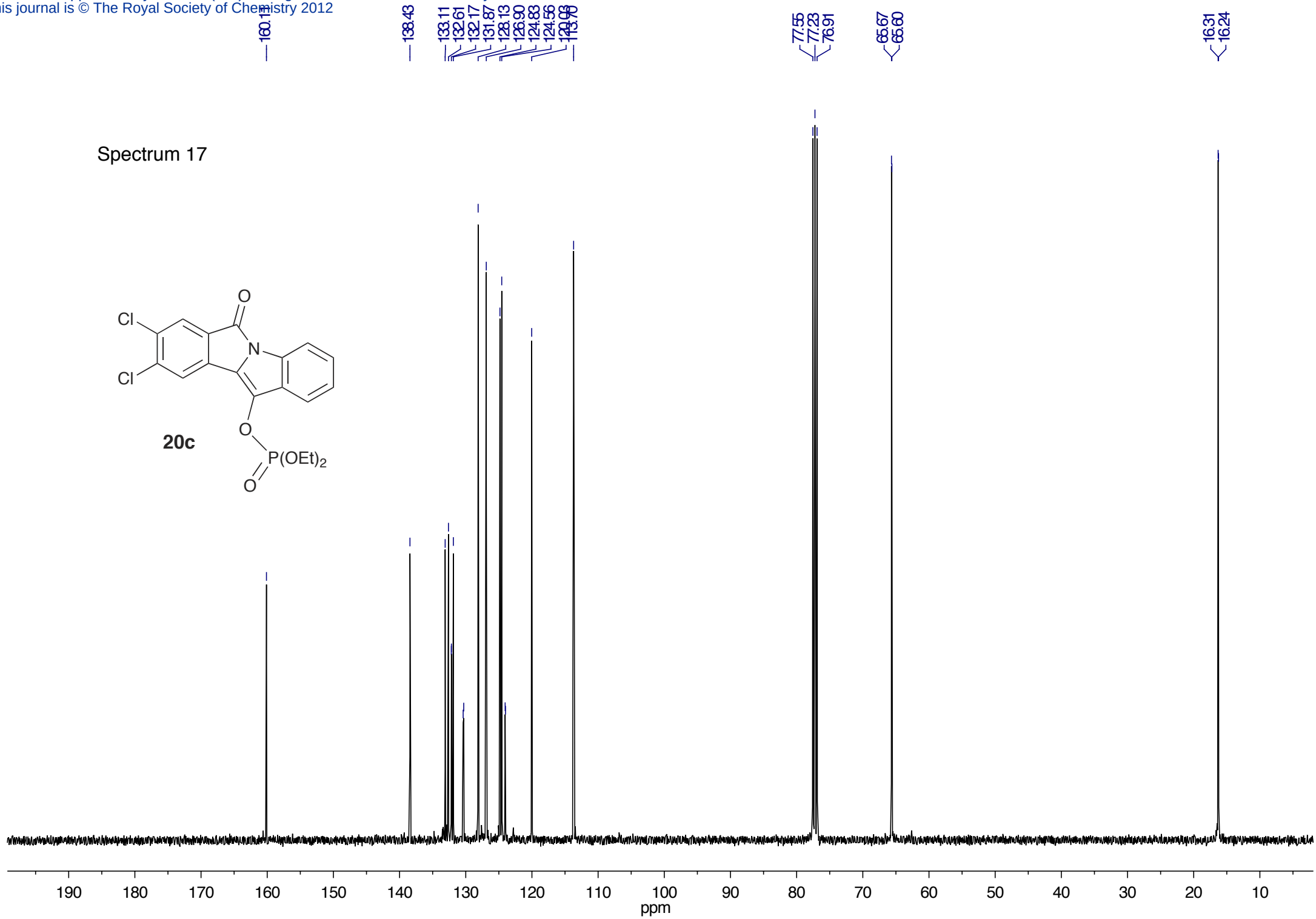
15c



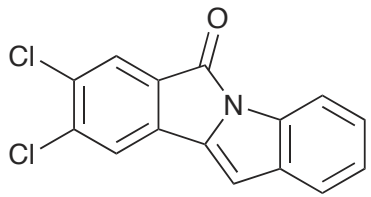
Spectrum 16



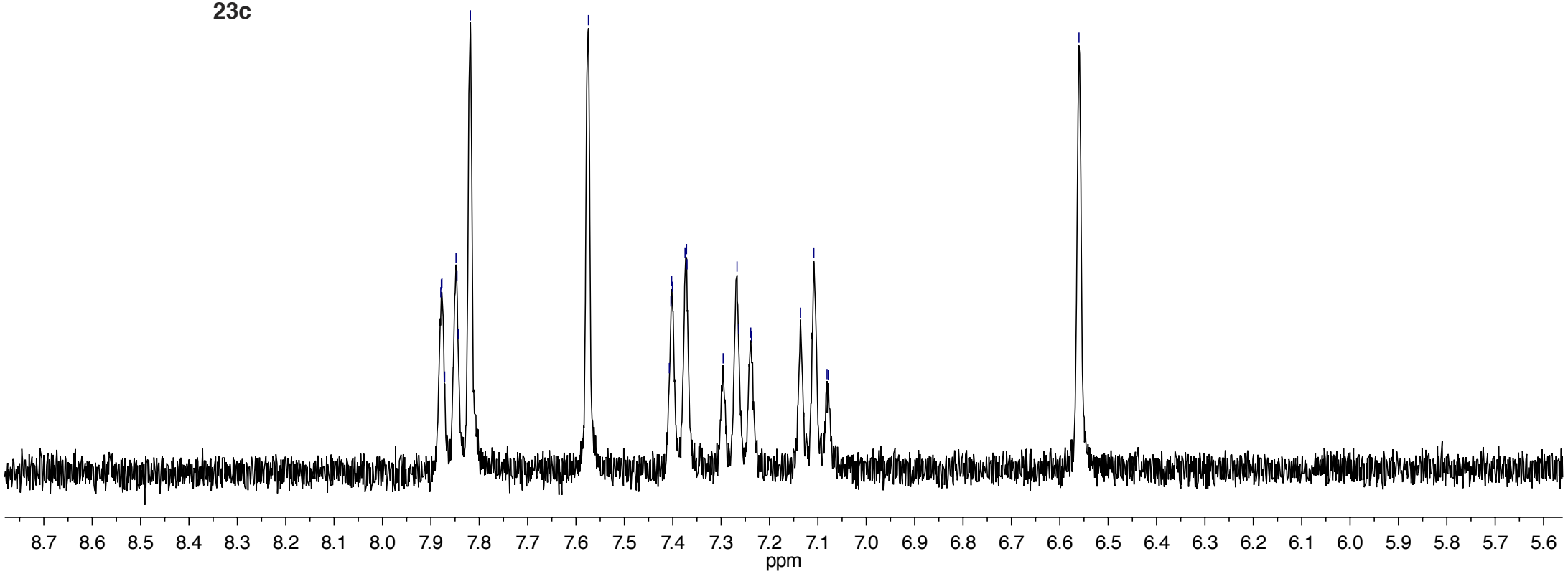
20c

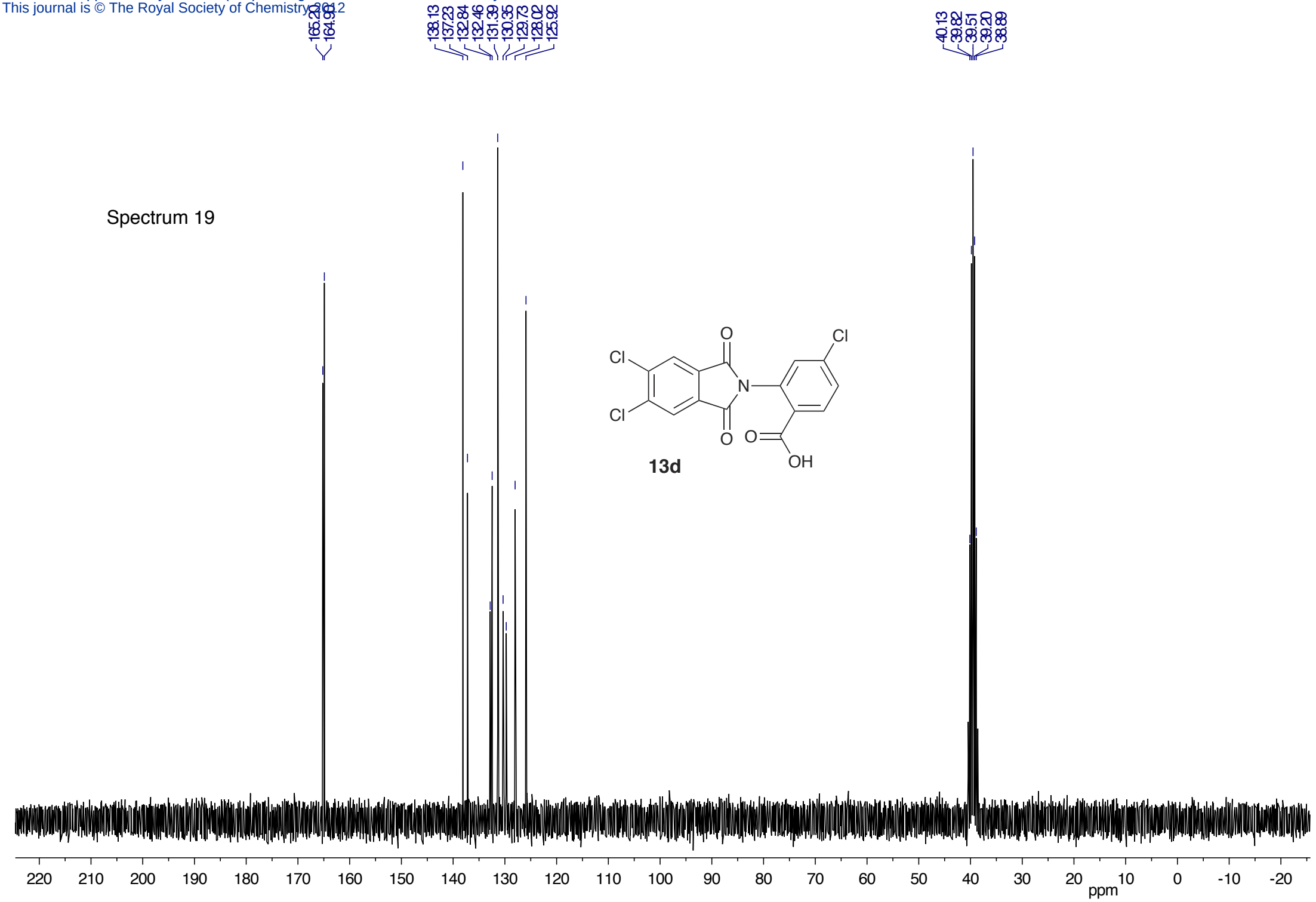


Spectrum 18

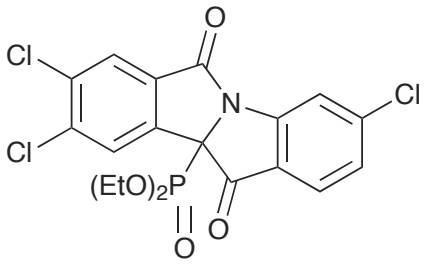


23c

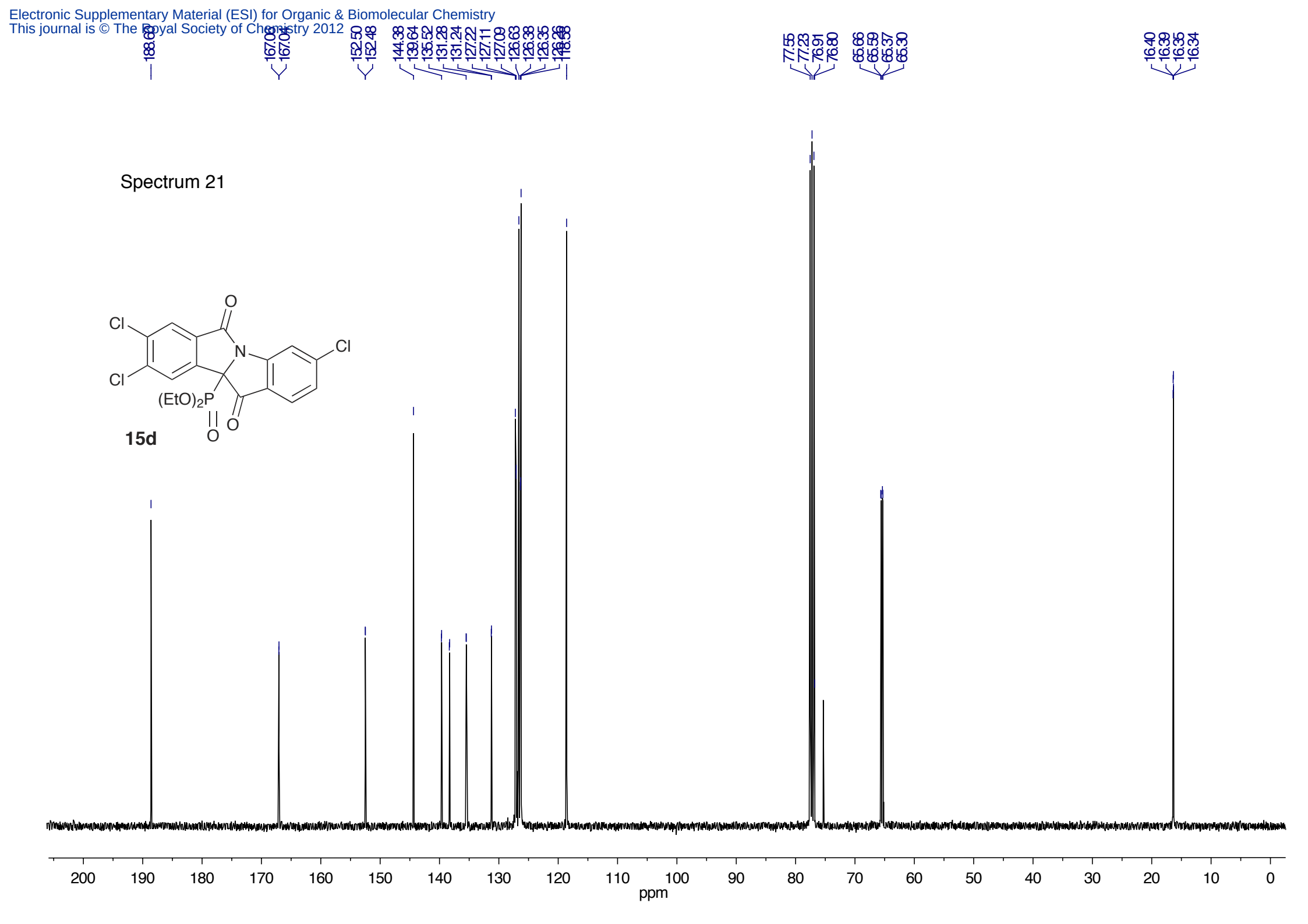




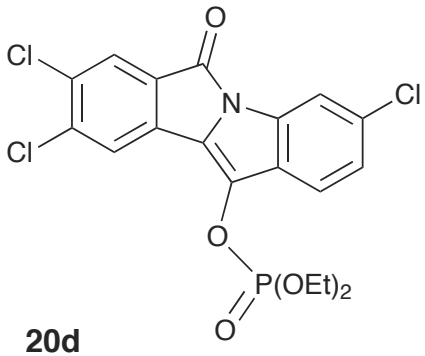
Spectrum 20



15d

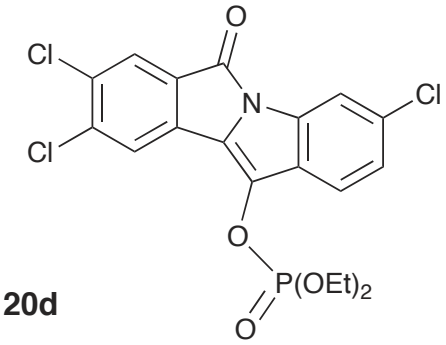


Spectrum 22



20d

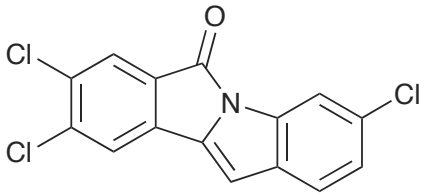
Spectrum 23



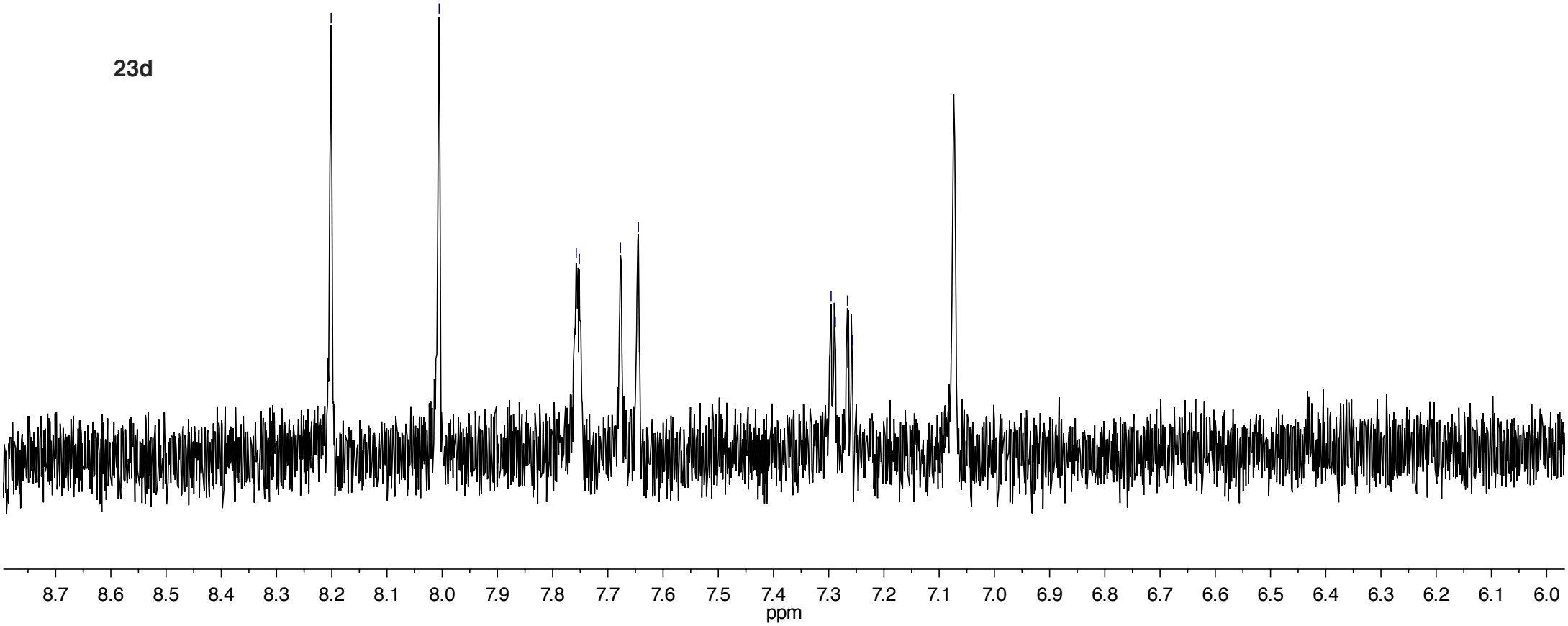
20d

8.2011
8.0054
7.7571
7.7516
7.6772
7.6447
7.2957
7.2881
7.2661
7.2570
7.0706

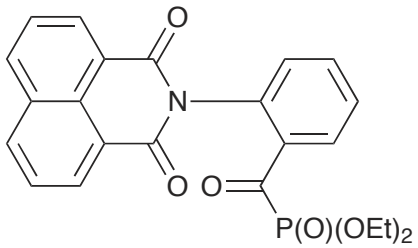
Spectrum 24



23d



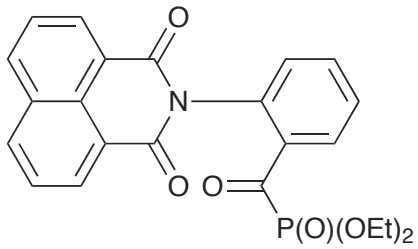
Spectrum 25



26

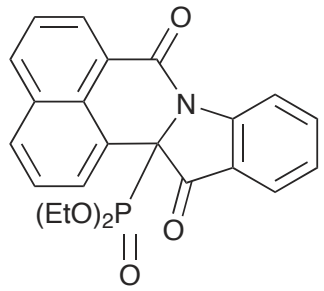
200.66
198.10
164.48
134.85
134.78
134.68
134.51
133.62
133.59
133.57
132.63
131.96
131.56
131.29
131.24
129.34
128.89
127.05
127.03
122.95
77.70
77.23
76.76
64.32
64.21
16.48
16.39

Spectrum 26

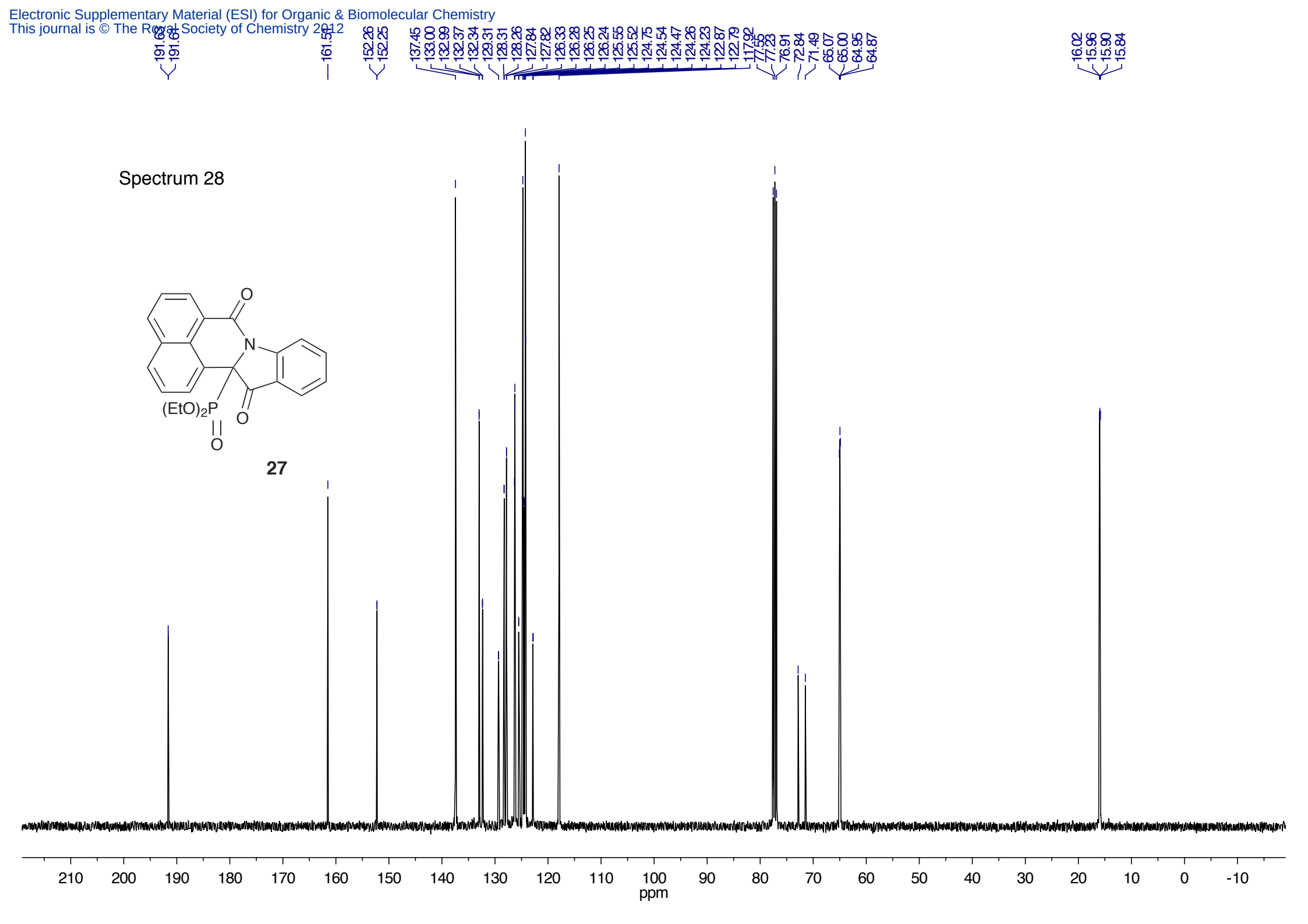


26

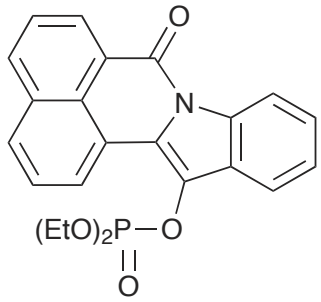
Spectrum 27



27

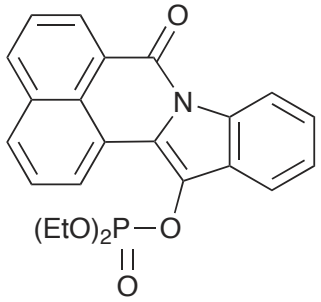


Spectrum 29



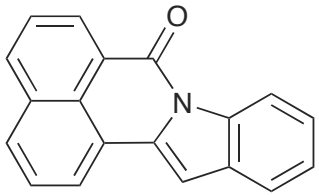
28

Spectrum 30



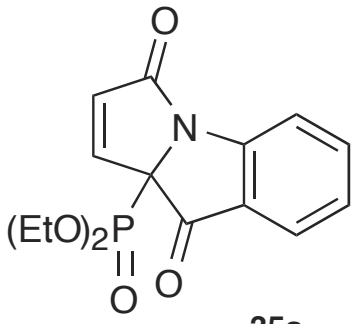
28

Spectrum 31



29

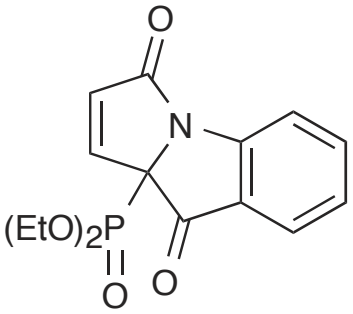
Spectrum 32



35a

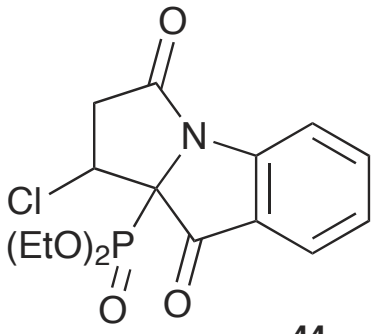
189.2533
172.1899
152.0130
151.9846
146.0967
145.9978
137.8000
129.9538
129.8427
129.4004
125.8492
125.5596
118.4990
82.3173
80.1691
77.7011
77.2298
76.7596
65.4085
65.3395
65.3034
65.2318
16.5188
16.5077
16.4352
16.4227

Spectrum 33



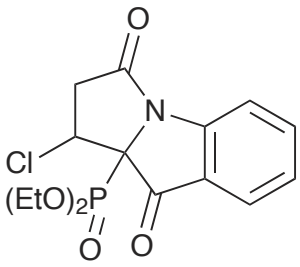
35a

Spectrum 34



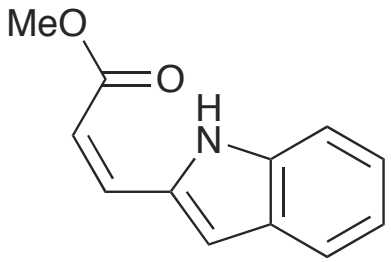
44

Spectrum 35



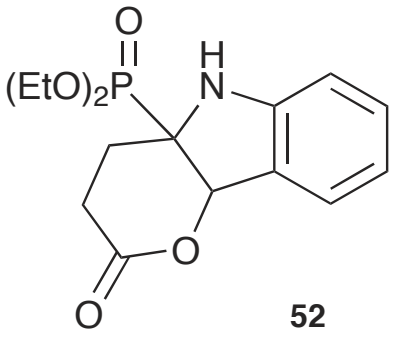
44

Spectrum 36



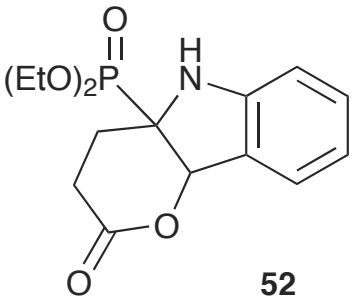
50

Spectrum 37



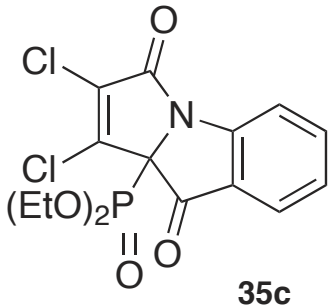
52

Spectrum 38

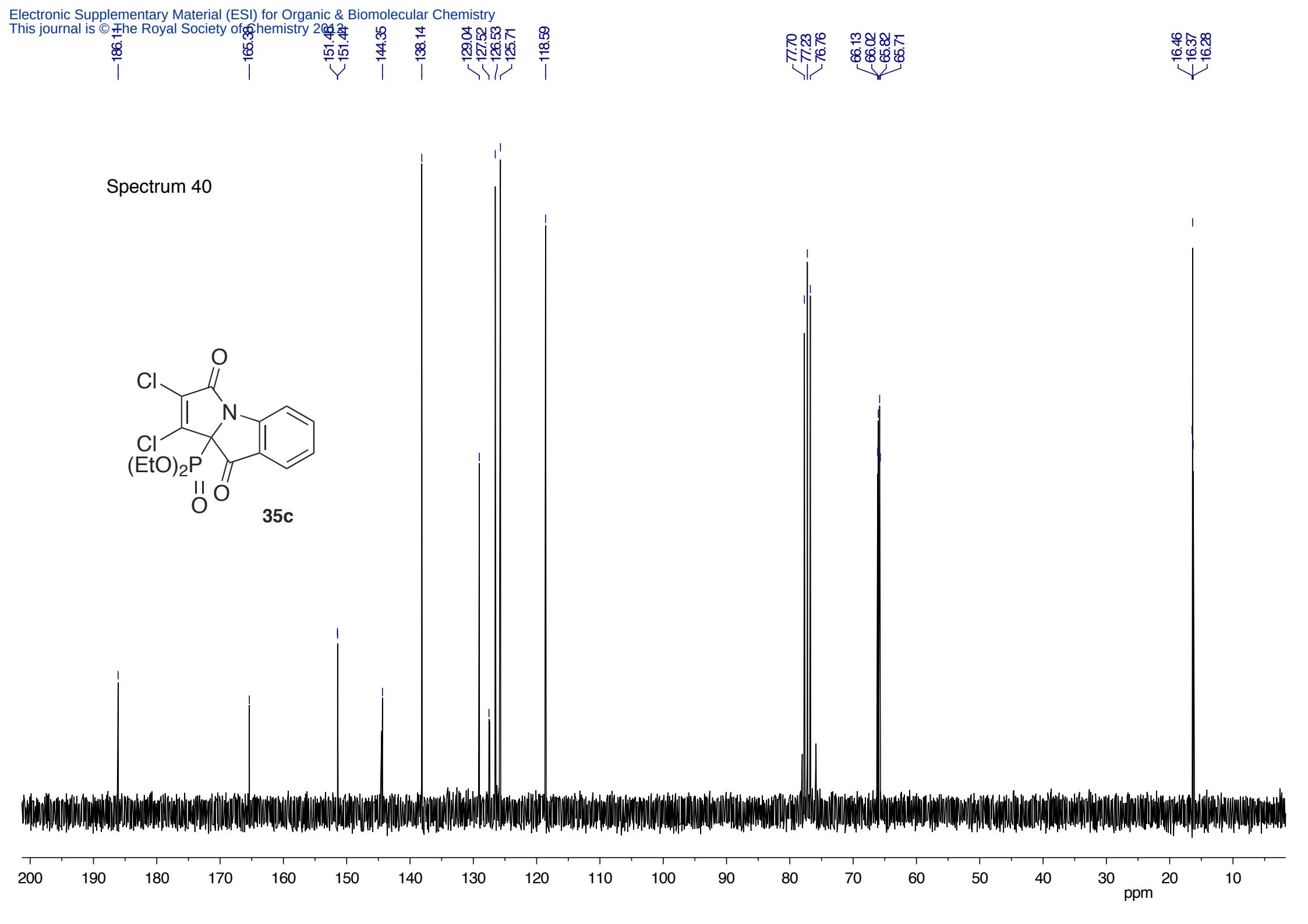


52

Spectrum 39

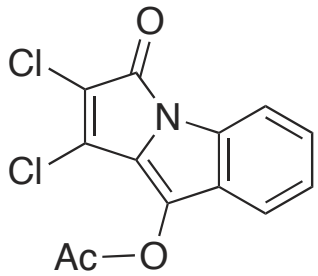


35c

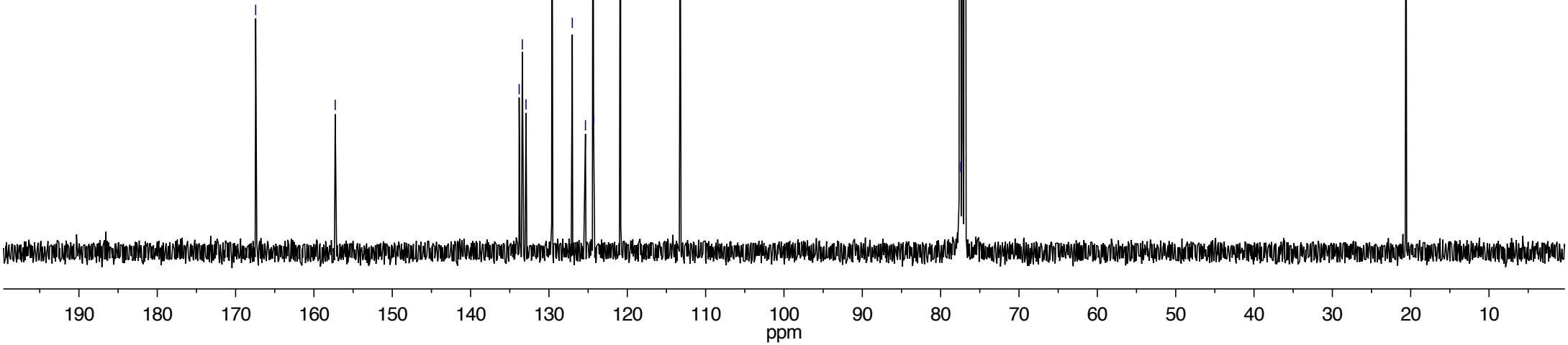


167.49
157.28
133.80
133.40
132.93
129.63
127.02
125.34
124.38
124.30
120.87
113.29
77.55
77.43
77.23
76.91
20.60

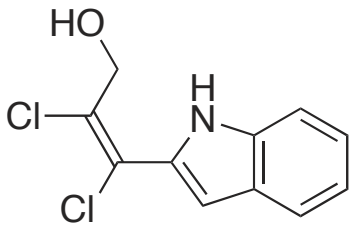
Spectrum 41



38c



Spectrum 42



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Notes and references

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