Supporting Information

for

PMDTA-Catalyzed multicomponent synthesis and biological activity of 2-amino-4*H*-chromenes containing phosphonate or phosphine oxide moiety

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General information

The reactions under conventional heating were carried out in an oil bath.

High-performance liquid chromatography-mass spectrometry (HPLC-MS) measurements were performed with an Agilent 1200 liquid chromatography system coupled with a 6130 quadrupole mass spectrometer equipped with an ESI ion source (Agilent Technologies, Palo Alto, CA, USA). Analysis was performed at 40 ºC on a Gemini C18 column (150 mm × 4.6 mm, 3 μm; Phenomenex, Torrance, CA, USA) with a mobile phase flow rate of 0.6 mL/min. Composition of eluent A was 0.1% (NH_4)(HCOO) in water; eluent B was 0.1% (NH_4)(HCOO) and 8% water in acetonitrile, 0–3 min 5% B, 3–13 min gradient, 13–20 min 100% B. The injection volume was 2 μL. The chromatographic profile was registered at 254 nm. The MSD operating parameters were as follows: positive ionization mode, scan spectra from m/z 120 to 1000, drying gas temperature 300 ºC, nitrogen flow rate 12 L/min, nebulizer pressure 60 psi, capillary voltage 4000 V.

High resolution mass spectrometric measurements were performed using a Sciex 5600+ Q-TOF mass spectrometer in positive electrospray mode.

The ^{31}P, ^{1}H, ^{13}C, NMR spectra were taken in $CDCl_3$ solution on a Bruker AV-300 spectrometer operating at 121.5, 75.5 and 300 MHz, respectively. Chemical shifts are downfield relative to 85% H_3PO_4 and TMS. Non-equivalence effect was observed in ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra. Corresponding pairs of resonances were marked with (I) and (II).

General procedure for the synthesis of (2-amino-3-cyano-4H-chromen-4-yl) phosphonate derivatives

The mixture of 1.0 mmol salicylaldehyde derivative (0.11 ml of salicylaldehyde, 0.14 g of 5-fluoro-2-hydroxybenzaldehyde, 0.16 g of 2-chloro-5-hydroxybenzaldehyde, 0.20 g of 3-bromo-2-hydroxybenzaldehyde, 0.17 g of 3-ethoxy-5-hydroxybenzaldehyde, 0.14 g of 2,3-dihydroxybenzaldehyde), 1.0 mmol malononitrile (0.066 g) and 1.0 mmol dialkyl phosphite (0.10 ml of dimethyl phosphite, 0.13 ml of diethyl phosphite, 0.17 ml of di(*i*-propyl) phosphite, 0.20 ml of dibutyl phosphite, 0.22 ml of dibenzyl phosphite, 0.19 ml of diphenyl phosphite, 0.15 ml of ethyl phenyl-*H*-phosphinate), and basic catalysts (0.05 mmol [0.007 ml of DPA, 0.007 ml of TEA, 0.009 ml of DIPEA, 0.008 ml of DBU, 0.008 ml of DMAP, 0.005 ml of DABCO, 0.007 ml of TMEDA or 0.010 ml of PMDTA] or 0.10 mmol [0.021 ml] of PMDTA) was stirred at 60-80 °C for 15-45 min in an oil bath. In the experiments marked by *Table 1, entries 9 and 10* 1 ml of ethanol or acetonitrile was used as the solvent. The composition of the

reaction mixtures was analysed by high pressure liquid chromatography (HPLC). The mixtures were dissolved in ethyl acetate and were cooled down to 5 °C. After 3-4 h, precipitated product was filtered out. The following products were thus prepared:

*Diethyl (2-amino-3-cyano-4H-chromen-4-yl)phosphonate (**2a**)*

Yield: 92% (0.28 g), pale yellow crystal; Mp: 138-140 °C; Mp[S1]: 138-140 °C; ^{1}H NMR ($CDCl_3$) δ: 1.17 (t, J_{HH} = 7.1, 3H, CH_3^{I}), 1.34 (t, J_{HH} = 7.0, 3H, CH_3^{II}), 3.88 (d, $^{2}J_{HP}$ = 17.9, 1H, CHP), 3.90-4.04 (m, 2H, CH_2^{I}), 4.08-4.15 (m, 2H, CH_2^{II}), 4.91 (brs, 2H, NH_2), 6.97 (d, J_{HH} = 8.2, 1H, ArH), 7.11-7.16 (m, 1H, ArH), 7.22-7.28 (m, 1H, ArH), 7.32-7.36 (m, 1H, ArH); ^{1}H NMR ($CDCl_3$) δ [S1]: 1.22 (t, J_{HH} = 6.93, 3H, CH_3^{I}), 1.34 (t, J_{HH} = 6.97, 3H, CH_3^{II}), 3.89 (d, $^{2}J_{HP}$ = 17.95, 1H, CHP), 3.15-4.15 (m, 4H, CH_2), 5.09 (brs, 2H, NH_2), 6.94 (d, J_{HH} = 8.12, 1H, ArH), 7.11 (d, J_{HH} = 7.64, 1H, ArH), 7.21-7.32 (m, 2H, ArH), 7.32-7.36 (m, 1H, ArH); ^{31}P NMR ($CDCl_3$) δ: 21.8; δ[S2] ($CDCl_3$) 21.2; $[M+H]^{+}_{found}$ = 309.1005, $C_{14}H_{18}N_2O_4P$ requires 309.1004.

*Dimethyl (2-amino-3-cyano-4H-chromen-4-yl)phosphonate (**2b**)*

Yield: 90% (0.25 g), pale yellow crystal; Mp: 146-148 °C; Mp[S1]: 148-152 °C; ^{1}H NMR ($CDCl_3$) δ: 3.65 (d, J_{HP} = 10.4, 3H, CH_3^{I}), 3.76 (d, J_{HP} = 10.7, 3H, CH_3^{II}), 3.92 (d, $^{2}J_{HP}$ = 17.9, 1H, CHP), 4.95 (brs, 2H, NH_2), 6.99 (d, J_{HH} = 8.2, 1H, ArH), 7.12-7.17 (m, 1H, ArH), 7.24-7.29 (m, 1H, ArH), 7.31-7.35 (m, 1H, ArH); ^{1}H NMR ($CDCl_3$) δ [S1]: 3.67 (d, J_{HP} = 10.47, 3H, CH_3^{I}), 3.76 (d, J_{HP} = 9.15, 3H, CH_3^{II}), 3.96 (d, $^{2}J_{HP}$ = 17.68, 1H, CHP), 5.11 (brs, 2H, NH_2), 6.97 (d, J_{HH} = 8.06, 1H, ArH), 7.15 (d, J_{HH} = 7.42, 1H, ArH), 7.23-7.33 (m, 2H, ArH); ^{31}P NMR ($CDCl_3$+DMSO-d6) δ: 29.4; δ[S2] ($CDCl_3$) 24.2; $[M+H]^{+}_{found}$ = 281.0699, $C_{12}H_{15}N_2O_4P$ requires 281.0691.

*Dibutyl (2-amino-3-cyano-4H-chromen-4-yl)phosphonate (**2c**)*

Yield: 92% (0.33 g), pale yellow crystal; Mp: 145-147 °C; Mp[S2]:149-152 °C; ^{1}H NMR ($CDCl_3$) δ: 0.85 (t, J_{HH} = 7.4, 3H, $CH_3^{I}CH_2$), 0.92 (t, J_{HH} = 7.4, 3H, $CH_3^{II}CH_2$), 1.23-1.31 (m, 2H, $CH_3CH_2^{I}CH_2$), 1.35-1.43 (m, 2H, $CH_3CH_2^{II}CH_2$), 1.46-1.52 (m, 2H, $CH_2^{I}CH_2O$), 1.63-1.70 (m, 2H, $CH_2^{II}CH_2O$), 3.80-3.96 [3.89 (d, $^{2}J_{HP}$ = 18.1, CHP) overlapped by the multiplet of OCH_2^{I} total int. 3H], 3.80-3.96 (m, 2H, OCH_2^{II}), 4.86 (brs, 2H, NH_2), 6.97 (d, J_{HH} = 8.3, 1H, ArH), 7.11-7.15 (m, 1H, ArH), 7.23-7.27 (m, 1H, ArH), 7.32-7.36 (m, 1H, ArH); ^{1}H NMR ($CDCl_3$) δ [S2]: 0.83 (t, J_{HH} = 7.4, 3H, $CH_3^{I}CH_2$), 0.89 (t, J_{HH} = 7.4, 3H, $CH_3^{II}CH_2$), 1.17-1.65 (m, 8H, $CH_3CH_2CH_2$, CH_2CH_2O), 4.07-3.96 (m, 5H, OCH_2, CHP), 5.15 (brs, 2H, NH_2), 6.94 (d, J_{HH} = 8.2, 1H, ArH), 7.10 (t, J_{HH} = 7.5, 1H, ArH), 7.21-7.24 (m, 1H, ArH), 7.30 (dt, J_{HH} =

7.6, 1H, ArH); ^{31}P NMR ($CDCl_3$) δ: 21.9; δ[S2] ($CDCl_3$) 21.8; $[M+H]^+_{found}$ = 365.1639, $C_{18}H_{28}N_2O_4P$ requires 365.1630.

*Di(i-propyl) (2-amino-3-cyano-4H-chromen-4-yl)phosphonate (**2d**)*

Yield: 84% (0.28 g); Mp: 125-130 °C; Mp[S3]: 115-117 °C; ^{1}H NMR ($CDCl_3$) δ: 1.05(d, J_{HH} = 6.1, 3H, CH_3^I), 1.25 (d, J_{HH} = 6.3, 3H, CH_3^{II}), 1.34 (d, J_{HH} = 6.3, 3H, CH_3^{III}), 1.35 (d, J_{HH} = 6.3, 3H, CH_3^{IV}), 3.80 (d, $^2J_{HP}$ = 18.0, 1H, CHP), 4.36-4.50 (m, 1H, OCH^I), 4.61-4.75 (m, 1H, OCH^{II}), 5.75 (brs, 2H, NH_2), 6.97 (d, J_{HH} = 8.1, 1H, ArH), 7.08-7.18 (m, 1H, ArH), 7.20-7.30 (m, 1H, ArH), 7.36 (d, J_{HH} = 7.7, 1H, ArH); ^{1}H NMR ($CDCl_3$) δ [S4]: 1.02(d, J_{HH} = 6.4, 3H, CH_3^I), 1.22 (d, J_{HH} = 4.0, 3H, CH_3^{II}), 1.33 (t, J_{HH} = 6.4, 6H, CH_3^{III}, CH_3^{IV}), 3.77 (d, $^2J_{HP}$ = 18.4, 1H, CHP), 4.39-4.69 (m, 2H, OCH), 4.94 (brs, 2H, NH_2), 6.93 (d, J_{HH} = 8.4, 1H, ArH), 7.12 (t, J_{HH} = 7.6, 1H, ArH), 7.20 (d, J_{HH} = 6.0, 1H, ArH), 7.34 (d, J_{HH} = 7.6, 1H, ArH); ^{31}P NMR ($CDCl_3$+DMSO-d6) δ: 21.2; δ[S4] ($CDCl_3$) 19.4; $[M+H]^+_{found}$ = 337.1318, $C_{16}H_{22}N_2O_4P$ requires 337.1317.

*Dibenzyl (2-amino-3-cyano-4H-chromen-4-yl)phosphonate (**2e**)*

Yield: 85% (0.37 g), pale yellow crystal; Mp: 139-140 °C; ^{1}H NMR ($CDCl_3$+DMSO-d6) δ: 3.97 (d, $^2J_{HP}$ = 17.4, 1H, CHP), 4.80-4.93 (m, 2H, PhCH_2^I), 4.96 (d, J_{HH} = 8.3, 2H, PhCH_2^{II}), 6.04 (brs, 2H, NH_2), 6.90-7.00 (m, 1H, ArH), 7.04-7.13 (m, 1H, ArH), 7.16-7.38 (m, 12H, ArH); ^{13}C NMR ($CDCl_3$+DMSO-d6) δ: 35.8 (d, $^1J_{CP}$ = 147.4, C_4), 49.2 (d, $^2J_{CP}$ = 7.9, C_3), 68.0 (d, $^2J_{CP}$ = 10.2, PhCH$_2^I$), 68.1 (d, $^2J_{CP}$ = 10.3, PhCH$_2^{II}$), 116.4 (d, J_{CP} = 3.3), 116.5 (d, J_{CP} = 5.6), 120.0, 124.6 (d, J_{CP} = 2.9), 127.7 ($C_3'^I$), 127.9 ($C_3'^{II}$), 128.1 ($C_4'^I$), 128.2 ($C_4'^{II}$), 128.3 ($C_2'^I$), 128.4 ($C_2'^{II}$), 128.9 (d, J_{CP} = 3.4), 129.4 (d, $^3J_{CP}$= 4.2), 136.0 (d, $^3J_{CP}$ = 5.8, $C_1'^I$), 136.1 (d, $^3J_{CP}$ = 5.5, $C_1'^{II}$), 149.9 (d, $^3J_{CP}$ = 5.3, C_{8a}), 162.6 (d, $^3J_{CP}$ = 3.2, C_2); ^{31}P NMR ($CDCl_3$+DMSO-d6) δ: 28.0; $[M+H]^+_{found}$ = 433.1317, $C_{24}H_{22}N_2O_4P$ requires 433.1317.

*Diphenyl (2-amino-3-cyano-4H-chromen-4-yl)phosphonate (**2f**)*

Yield: 90% (0.36 g), pale yellow crystal; Mp: 139-140 °C; ^{1}H NMR (DMSO-d6) δ: 4.77 (d, $^2J_{HP}$ = 17.0, 1H, CHP), 6.80-6.95 (m, 2H, ArH), 6.96-7.60 [7.42 (brs, NH_2) overlapped by the multiplet of ArH total int. 14H]; ^{13}C NMR (DMSO-d6) δ: 36.1 (d, $^1J_{CP}$ = 147.0, C_4), 47.0 (d, $^2J_{CP}$ = 7.9, C_3), 116.7 (d, J_{CP} = 3.4), 117.0 (d, J_{CP} = 5.1), 120.5, 120.7 (d, J_{CP} = 10.1, $C_3'^I$), 120.8 (d, J_{CP} = 10.1, $C_3'^{II}$), 125.1 (d, J_{CP} = 3.4), 125.6 ($C_4'^I$), 125.7 ($C_4'^{II}$), 129.9 (d, J_{CP} = 3.8), 130.29 (d, $^3J_{CP}$ = 4.0, $C_2'^I$), 130.31 (d, $^3J_{CP}$ = 3.9, $C_2'^{II}$), 130.4 (d, $^3J_{CP}$= 4.7, C_5), 150.56 (d, $^2J_{CP}$ = 10.3, $C_1'^I$), 150.59 (d, $^3J_{CP}$ = 5.9, C8A), 150.64 (d, $^2J_{CP}$ = 10.5, $C_1'^{II}$), 163.6 (d, $^3J_{CP}$ = 2.7, C_2); ^{31}P NMR (DMSO-d6) δ: 16.2; $[M+H]^+_{found}$ = 404.1006, $C_{22}H_{18}N_2O_4P$ requires 404.1004.

*Ethyl (2-amino-3-cyano-4H-chromen-4-yl)(phenyl)phosphinate (**2g**)*

Yield: 86% (0.29 g), pale yellow crystal; Mp: 173-180 °C; **Isomer A**: ^{1}H NMR ($CDCl_3$+DMSO-d6) δ: 1.40 (t, J_{HH} = 7.0, 3H, CH_3), 3.84-4.25 [4.03 (d, $^{2}J_{HP}$ = 14.6, CHP) overlapped by the multiplet of CH_2 total int. 3H], 6.43 (brs, 2H, NH_2), 6.66-6.75 (m, 1H, ArH), 6.95-7.04 (m, 1H, ArH), 7.05-7.25 (m, 2H, ArH), 7.28-7.59 (m, 5H, ArH); ^{13}C NMR ($CDCl_3$+DMSO-d6) δ: 16.5 (d, $^{3}J_{CP}$ = 6.0, CH_3), 38.6 (d, $^{1}J_{CP}$ = 98.6, C_4), 48.5 (d, $^{2}J_{CP}$ = 4.4, C_3), 61.3 (d, $^{2}J_{CP}$ = 7.6, CH_2O), 115.7 (d, J_{CP} = 3.0), 116.7 (d, J_{CP} = 2.7), 120.1, 124.3 (d, J_{CP} = 2.4), 127.95 (d, $^{1}J_{CP}$ = 124.3, C_1'), 128.00 (d, $^{3}J_{CP}$ = 11.9, C_3'), 128.6 (d, J_{CP} = 3.4, C_4'), 129.8 (d, J_{CP} = 3.9), 132.3 (d, $^{2}J_{CP}$ = 7.5, C_2'), 132.4 (d, $^{3}J_{CP}$ = 2.6), 149.9 (d, $^{3}J_{CP}$ = 4.9, C_{8a}), 162.5 (d, $^{3}J_{CP}$ = 2.7, C_2); ^{31}P NMR ($CDCl_3$+DMSO-d6) δ: 42.8; **Isomer B**: ^{1}H NMR ($CDCl_3$+DMSO-d6) δ: 1.30 (t, J_{HH} = 7.0, 3H, CH_3), 3.84-4.25 [3.98 (d, $^{2}J_{HP}$ = 14.9, CHP) overlapped by the multiplet of CH_2 total int. 3H], 6.50 (brs, 2H, NH_2), 6.77-6.85 (m, 1H, ArH), 6.87-6.94 (m, 1H, ArH), 7.05-7.25 (m, 2H, ArH), 7.28-7.59 (m, 5H, ArH); ^{13}C NMR ($CDCl_3$+DMSO-d6) δ: 16.5 (d, $^{3}J_{CP}$ = 5.7, CH_3), 39.0 (d, $^{1}J_{CP}$ = 100.6, C_4), 47.8 (d, $^{2}J_{CP}$ = 5.4, C_3), 61.3 (d, $^{2}J_{CP}$ = 6.9, CH_2O), 116.1 (d, J_{CP} = 2.7), 117.4 (d, J_{CP} = 3.1), 120.1, 124.1 (d, J_{CP} = 2.7), 128.2 (d, $^{3}J_{CP}$ = 11.9, C_3'), 128.4 (d, $^{1}J_{CP}$ = 120.8, C_1'), 128.7 (d, J_{CP} = 3.5, C_4'), 129.2 (d, J_{CP} = 4.0), 132.4 (d, $^{2}J_{CP}$ = 7.9, C_2'), 132.5 (d, $^{3}J_{CP}$ = 3.2), 150.2 (d, $^{3}J_{CP}$ = 4.7, C_{8a}), 162.8 (d, $^{3}J_{CP}$ = 2.5, C_2); ^{31}P NMR ($CDCl_3$+DMSO-d6) δ: 41.8; $[M+H]^{+}_{found}$ = 341.1057, $C_{18}H_{18}N_2O_3P$ requires 341.1055.

*Diethyl (2-amino-3-cyano-6-fluoro-4H-chromen-4-yl)phosphonate (**3a**)*

Yield: 91% (0.30 g), pale orange crystal; Mp: 159-161 °C; ^{1}H NMR ($CDCl_3$) δ: 1.25 (t, J_{HH} = 7.0, 3H, CH_3^{I}), 1.35 (t, J_{HH} = 7.1, 3H, CH_3^{II}), 3.86 (d, $^{2}J_{HP}$ = 18.4, 1H, CHP), 3.98-4.21 (m, 4H, CH_2), 5.17 (brs, 2H, NH_2), 6.89-7.01 (m, 2H, ArH), 7.02-7.13 (m, 1H, ArH); ^{13}C NMR ($CDCl_3$) δ: 16.34 (d, $^{3}J_{CP}$ = 6.0, CH_3^{I}), 16.35 (d, $^{3}J_{CP}$ = 5.6, CH_3^{II}), 35.7 (dd, $^{1}J_{CP}$ = 148.9, J_{CF} = 1.4, C_4), 50.6 (d, $^{2}J_{CP}$ = 8.1, C_3), 63.1 (d, $^{2}J_{CP}$ = 7.4, CH_2O^{I}), 63.4 (d, $^{2}J_{CP}$ = 7.5, CH_2O^{II}), 115.8 (t, J_{CP} = 3.9), 116.1 (dd, J_{CP} = 3.7, J_{CF} = 5.0), 117.8 (dd, J_{CP} = 3.3, J_{CF} = 8.6), 118.4 (dd, J_{CP} = 5.9, J_{CF} = 8.4), 119.3, 146.0 (dd, $^{3}J_{CP}$ = 5.1, J_{CF} = 2.6, C_{8a}), 159.1 (dd, J_{CP} = 3.5, $^{1}J_{CF}$ = 244.4, C_6), 162.1 (d, $^{3}J_{CP}$ = 3.5, C_2); ^{31}P NMR ($CDCl_3$) δ: 21.1; $[M+H]^{+}_{found}$ = 327.0913, $C_{14}H_{17}FN_2O_4P$ requires 327.0910.

*Dibutyl (2-amino-3-cyano-6-fluoro-4H-chromen-4-yl)phosphonate (**3c**)*

Yield: 88% (0.34 g), pale yellow crystal; Mp: 115-117 °C; ^{1}H NMR ($CDCl_3$) δ: 0.88 (t, J_{HH} = 7.3, 3H, $CH_3CH_2^{I}$), 0.93 (t, J_{HH} = 7.4, 3H, $CH_3CH_2^{II}$), 1.17-1.48 (m, 4H, CH_3CH_2), 1.48-1.78 (m, 4H, CH_2CH_2O), 3.76-4.16 [3.87 (d, $^{2}J_{HP}$ = 18.5, CHP) overlapped by the multiplet of CH_2O

total int. 5H], 5.01 (brs, 2H, NH_2), 6.81-7.01 (m, 2H, ArH), 7.01-7.16 (m, 1H, ArH); ^{13}C NMR ($CDCl_3$) δ: 13.51 ($CH_3CH_2^{I}$), 13.54 ($CH_3CH_2^{II}$), 18.5 ($CH_3CH_2^{I}$), 18.6 ($CH_3CH_2^{II}$), 32.49 (d, $^3J_{CP}$ = 6.2, $CH_2CH_2O^{I}$), 32.50 (d, $^3J_{CP}$ = 6.1, $CH_2CH_2O^{II}$), 35.6 (dd, $^1J_{CP}$ = 149.4, J_{CF} = 1.1, C_4), 51.2 (d, $^2J_{CP}$ = 8.1, C_3), 66.7 (d, $^2J_{CP}$ = 7.6, CH_2O^{I}), 67.0 (d, $^2J_{CP}$ = 7.7, CH_2O^{II}), 115.7 (dd, J_{CP} = 3.6, J_{CF} = 11.6), 116.1 (dd, J_{CP} = 3.2, J_{CF} = 13.1), 117.7 (dd, J_{CP} = 3.2, J_{CF} = 8.6), 118.4 (dd, J_{CP} = 2.5, J_{CF} = 5.9), 119.1, 145.9 (dd, $^3J_{CP}$ = 5.2, J_{CF} = 2.1, C_{8a}), 159.1 (dd, J_{CP} = 3.8, $^1J_{CF}$ = 240.7, C_6), 161.8 (d, $^3J_{CP}$ = 3.4, C_2); ^{31}P NMR ($CDCl_3$) δ: 21.2; $[M+H]^+_{found}$ = 383.1539, $C_{18}H_{25}FN_2O_4P$ requires 383.1536.

*Dibenzyl (2-amino-3-cyano-6-fluoro-4H-chromen-4-yl)phosphonate (**3e**)*

Yield: 83% (0.37 g), pale yellow crystal; Mp: 177-179 °C; ^{1}H NMR (DMSO-d6) δ: 4.35 (d, $^2J_{HP}$ = 18.3, 1H, CHP), 4.89-4.98 (m, 4H, PhCH_2), 7.00-7.05 (m, 2H, ArH), 7.10-7.16 (m, 1H, ArH), 7.22-7.35 [7.25 (brs, NH_2) overlapped by the multiplet of ArH, total int. 12H]; ^{13}C NMR (DMSO-d6) δ: 35.4 (dd, $^1J_{CP}$ = 144.8, J_{CF} = 1.3, C_4), 47.1 (d, $^2J_{CP}$ = 7.5, C_3), 67.8 (d, $^2J_{CP}$ = 7.1, PhCH_2^{I}), 68.0 (d, $^2J_{CP}$ = 7.1, PhCH_2^{II}), 116.0 (t, J_{CP} = 4.1), 116.3 (t, J_{CP} = 4.8), 118.1 (dd, J_{CP} = 2.7, J_{CF} = 5.7), 120.1 (dd, J_{CP} = 5.3, J_{CF} = 8.6), 120.5, 128.0 ($C_2'^{I}$), 128.1 ($C_2'^{II}$), 128.64 ($C_4'^{I}$), 128.65 ($C_4'^{II}$), 128.86 ($C_3'^{I}$), 128.87 ($C_3'^{II}$), 136.78 (d, $^3J_{CP}$ = 6.2, $C_1'^{I}$), 136.84 (d, $^3J_{CP}$ = 6.0, $C_1'^{II}$), 146.8 (dd, $^3J_{CP}$ = 5.2, J_{CF} = 2.3, C_{8a}), 158.5 (dd, J_{CP} = 3.5, $^1J_{CF}$ = 240.6, C_6), 163.3 (d, $^3J_{CP}$ = 2.7, C_2); ^{31}P NMR (DMSO-d6) δ: 23.1; $[M+H]^+_{found}$ = 451,1225, $C_{24}H_{21}FN_2O_4P$ requires: 451,1223.

*Diethyl (2-amino-3-cyano-5-chloro-4H-chromen-4-yl)phosphonate (**4a**)*

Yield: 90% (0.31 g), pale yellow crystal; Mp: 178-180 °C; ^{1}H NMR ($CDCl_3$) δ: 1.28 (t, J_{HH} = 7.1, 3H, CH_3^{I}), 1.32 (t, J_{HH} = 7.0, 3H, CH_3^{II}), 3.94-4.19 (m, 4H, CH_2), 4.24 (d, $^2J_{HP}$ = 17.5, 1H, CHP), 5.03 (brs, 2H, NH_2), 6.87-7.02 (m, 1H, ArH), 7.12-7.32 (m, 2H, ArH); ^{13}C NMR ($CDCl_3$) δ: 16.4 (d, $^3J_{CP}$ = 5.7, CH_3^{I}), 16.5 (d, $^3J_{CP}$ = 5.7, CH_3^{II}), 34.1 (d, $^1J_{CP}$ = 149.4, C_4), 51.9 (d, $^2J_{CP}$ = 8.2, C_3), 63.2 (d, $^2J_{CP}$ = 7.6, CH_2O^{I}), 63.3 (d, $^2J_{CP}$ = 7.5, CH_2O^{II}), 115.4 (d, J_{CP} = 3.2), 117.4 (d, J_{CP} = 4.6), 119.1, 126.2 (d, J_{CP} = 2.8), 129.2 (d, J_{CP} = 3.4), 133.4 (d, J_{CP} = 5.3, C_5), 151.7 (d, $^3J_{CP}$ = 5.0, C_{8a}), 162.8 (d, $^3J_{CP}$ = 3.5, C_2); ^{31}P NMR ($CDCl_3$) δ: 21.4; $[M+H]^+_{found}$ = 343.0618, $C_{14}H_{17}ClN_2O_4P$ requires 343.0615.

*Dibutyl (2-amino-3-cyano-5-chloro-4H-chromen-4-yl)phosphonate (**4c**)*

Yield: 90% (0.36 g), pale yellow crystal; Mp: 129-130 °C; ^{1}H NMR ($CDCl_3$) δ: 0.89 (t, J_{HH} = 7.1, 3H, C$H_3CH_2^{I}$), 0.91 (t, J_{HH} = 7.1, 3H, C$H_3CH_2^{II}$), 1.23-1.47 (m, 4H, $CH_3CH_2CH_2$), 1.50-

1.73 (m, 4H, C*H*$_2$CH$_2$O), 3.82-4.15 (m, 4H, CH$_2$), 4.23 (d, $^2J_{HP}$ = 17.5, 1H, CHP), 5.28 (brs, 2H, NH$_2$), 6.84-7.06 (m, 1H, ArH), 7.08-7.36 (m, 2H, ArH); ^{13}C NMR (CDCl$_3$) δ: 13.60 (*C*H$_3$CH$_2^{I}$), 13.62 (*C*H$_3$CH$_2^{II}$), 18.6 (CH$_3$*C*H$_2$CH$_2$), 32.55 (d, $^3J_{CP}$ = 4.1, *C*H$_2$CH$_2$O^{I}), 32.63 (d, $^3J_{CP}$ = 4.6, *C*H$_2$CH$_2$O^{II}), 34.0 (d, $^1J_{CP}$ = 149.5, C$_4$), 52.0 (d, $^2J_{CP}$ = 8.1, C$_3$), 66.7 (d, $^2J_{CP}$ = 7.8, CH$_2$O^{I}), 66.9 (d, $^2J_{CP}$ = 7.9, CH$_2$O^{II}), 115.3 (d, J_{CP} = 3.3), 117.5 (d, J_{CP} = 4.7), 119.0, 126.1 (d, J_{CP} = 2.8), 129.1 (d, J_{CP} = 3.3), 133.3 (d, J_{CP} = 5.2, C$_5$), 151.6 (d, $^3J_{CP}$ = 5.2, C$_{8a}$), 162.7 (d, $^3J_{CP}$ = 3.5, C$_2$); ^{31}P NMR (CDCl$_3$) δ: 21.5; $[M+H]^+_{found}$ = 399.1245, $C_{18}H_{25}ClN_2O_4P$ requires 399.1241.

*Dibenzyl (2-amino-3-cyano-5-chloro-4H-chromen-4-yl)phosphonate (**4e**)*

Yield: 82% (0.38 g), pale yellow crystal; Mp: 182-184 °C; ^{1}H NMR (DMSO-d6) δ: 4.25 (d, $^2J_{HP}$ = 17.1, 1H, CHP), 4.83-5.08 (m, 4H, PhC*H*$_2$), 7.05 (d, J_{HH} = 7.6, 1H, ArH), 7.18-7.41 (m, 12H, ArH), 7.46 (brs, 2H, NH$_2$); ^{13}C NMR (DMSO-d6) δ: 35.6 (d, $^1J_{CP}$ = 146.6, C$_4$), 47.9 (d, $^2J_{CP}$ = 7.6, C$_3$), 67.95 (d, $^2J_{CP}$ = 13.4, Ph*C*H$_2^{I}$), 68.04 (d, $^2J_{CP}$ = 13.3, Ph*C*H$_2^{II}$), 115.9 (d, J_{CP} = 2.8), 117.9 (d, J_{CP} = 4.3), 120.1, 126.1 (d, J_{CP} = 2.4), 128.0 (C$_2$'^{I}), 128.1 (C$_2$'^{II}), 128.59 (C$_4$'^{I}), 128.60 (C$_4$'^{II}), 128.81 (C$_3$'^{I}), 128.83 (C$_3$'^{II}), 130.3 (d, J_{CP} = 3.5), 132.7 (d, $^3J_{CP}$= 5.3, C$_5$), 136.7 (d, $^3J_{CP}$ = 5.9, C$_1$'^{I}), 136.8 (d, $^3J_{CP}$ = 6.0, C$_1$'^{II}), 151.9 (d, $^3J_{CP}$ = 4.9, C$_{8a}$), 163.7 (d, $^3J_{CP}$ = 2.8, C$_2$); ^{31}P NMR (DMSO-d6) δ: 22.7; $[M+H]^+_{found}$ = 467.0930, $C_{24}H_{21}ClN_2O_4P$ requires 467.0927.

*Diethyl (2-amino-3-cyano-8-bromo-4H-chromen-4-yl)phosphonate (**5a**)*

Yield: 87% (0.34 g), pale yellow crystal; Mp: 183-185 °C; ^{1}H NMR (CDCl$_3$+DMSO-d6) δ: 1.21 (t, J_{HH} = 7.0, 3H, CH$_3^{I}$), 1.33 (t, J_{HH} = 7.0, 3H, CH$_3^{II}$), 3.91 (d, $^2J_{HP}$ = 18.0, 1H, CHP), 3.95-4.16 (m, 4H, CH$_2$), 6.44 (brs, 2H, NH$_2$), 6.96-7.08 (m, 1H, ArH), 7.21-7.32 (m, 1H, ArH), 7.43-7.54 (m, 1H, ArH); ^{13}C NMR (CDCl$_3$+DMSO-d6) δ: 16.3 (d, $^3J_{CP}$ = 5.3, CH$_3^{I}$), 16.4 (d, $^3J_{CP}$ = 5.5, CH$_3^{II}$), 36.0 (d, $^1J_{CP}$ = 147.9, C$_4$), 49.4 (d, $^2J_{CP}$ = 8.0, C$_3$), 62.8 (d, $^2J_{CP}$ = 7.3, CH$_2$O^{I}), 63.1 (d, $^2J_{CP}$ = 7.5, CH$_2$O^{II}), 110.1 (d, J_{CP} = 3.9), 119.2 (d, J_{CP} = 5.4), 119.6, 125.3 (d, J_{CP} = 3.1), 128.6 (d, J_{CP} = 4.3), 132.5 (d, J_{CP} = 3.7, C$_8$), 146.9 (d, $^3J_{CP}$ = 5.1, C$_{8a}$), 162.2 (d, $^3J_{CP}$ = 3.4, C$_2$); ^{31}P NMR (CDCl$_3$+DMSO-d6) δ: 26.4; $[M+H]^+_{found}$ = 387.0109, $C_{14}H_{17}BrN_2O_4P$ requires 387.0109.

*Dibenzyl (2-amino-3-cyano-8-bromo-4H-chromen-4-yl)phosphonate (**5e**)*

Yield: 70% (0.36 g), pale yellow crystal; Mp: 163-165 °C; ^{1}H NMR (DMSO-d6) δ: 4.43 (d, $^2J_{HP}$ = 18.0, 1H, CHP), 4.83-5.04 (m, 4H, PhCH$_2$), 7.00-7.12 (m, 1H, ArH), 7.16-7.44 [7.38 (brs, NH$_2$) overlapped by the multiplet of ArH total int. 13H], 7.53-7.64 (m, 1H, ArH); ^{13}C

NMR (DMSO-d6) δ: 35.6 (d, $^{1}J_{CP}$ = 144.4, C_4), 48.0 (d, $^{2}J_{CP}$ = 7.6, C_3), 67.8 (d, $^{2}J_{CP}$ = 7.0, Ph*C*H_2^{I}), 67.9 (d, $^{2}J_{CP}$ = 7.0, Ph*C*H_2^{II}), 109.9 (d, J_{CP} = 4.0), 120.1, 120.4 (d, J_{CP} = 5.2), 126.0 (d, J_{CP} = 3.1), 127.95 ($C_2'^{I}$), 128.01 ($C_2'^{II}$), 128.59 ($C_4'^{I}$), 128.60 ($C_4'^{II}$), 128.8 (C_3'), 129.4 (d, J_{CP} = 5.0), 132.9 (d, $^{3}J_{CP}$= 2.9, C_8), 136.8 (d, $^{3}J_{CP}$ = 6.2, C_1'), 147.3 (d, $^{3}J_{CP}$ = 4.9, C_{8a}), 162.8 (d, $^{3}J_{CP}$ = 2.7, C_2); ^{31}P NMR (DMSO-d6) δ: 23.4; $[M+H]^{+}_{found}$ = 511.0425, $C_{24}H_{21}N_2O_4P$ requires 511.0422.

*Diethyl (2-amino-3-cyano-8-ethoxy-4H-chromen-4-yl)phosphonate (**6a**)*

Yield: 96% (0.34 g), white crystal; Mp: 181-183 °C; Mp[S2]: 181-183 °C; ^{1}H NMR ($CDCl_3$) δ: 1.17 (t, J_{HH} = 7.0, 3H, CH_3^{I}), 1.34 (t, J_{HH} = 7.0, 3H, CH_3^{II}), 1.42 (t, J_{HH} = 7.0, 3H, $C_8OCH_2CH_3$), 3.87 (d, $^{2}J_{HP}$ = 17.8, 1H, CHP), 3.90-4.02 (m, 2H, CH_2^{I}), 4.04-4.16 (m, 4H, CH_2^{II}, OCH_2CH_3), 4.94 (brs, 2H, NH_2), 6.82-6.85 (m, 1H, ArH), 6.89-6.92 (m, 1H, ArH), 7.02-7.06 (m, 1H, ArH); ^{1}H NMR ($CDCl_3$) δ [S2]: 1.17 (t, J_{HH} = 7.1, 3H, CH_3^{I}), 1.34 (t, J_{HH} = 7.1, 3H, CH_3^{II}), 1.41 (t, J_{HH} = 7.0, 3H, $C_8OCH_2CH_3$), 3.87 (d, $^{2}J_{HP}$ = 17.8, 1H, CHP), 3.91-4.14 (m, 6H, CH_2, OCH_2CH_3), 5.06 (brs, 2H, NH_2), 6.83 (dt, J_{HH} = 8.2, J_{HH} = 1.6, 1H, ArH), 6.90 (dd, J_{HH} = 6.4, J_{HH} = 1.4, 1H, ArH), 7.04 (t, J_{HH} = 8.0, 1H, ArH); ^{31}P NMR ($CDCl_3$+DMSO-d6) δ: 26.1; δ[S2] ($CDCl_3$) 22.3; $[M+H]^{+}_{found}$ = 353.1267, $C_{16}H_{22}N_2O_5P$ requires 353.1266.

*Dibenzyl (2-amino-3-cyano-8-ethoxy-4H-chromen-4-yl)phosphonate (**6e**)*

Yield: 85% (0.40 g), white crystal; Mp: 160-162 °C; ^{1}H NMR (DMSO-d6) δ: 1.33 (t, J_{HH} = 6.9, 3H, OCH_2CH_3), 3.98-4.16 (m, 2H, OCH_2CH_3), 4.29 (d, $^{2}J_{HP}$ = 17.5, 1H, CHP), 4.84-5.02 (m, 4H, PhCH_2), 6.75-6.89 (m, 1H, ArH), 6.94-7.10 (m, 2H, ArH), 7.14-7.43 [7.22 (brs, NH_2) overlapped by the multiplet of ArH total int. 12H]; ^{13}C NMR (DMSO-d6) δ: 15.1 (OCH_2CH_3), 35.5 (d, $^{1}J_{CP}$ = 144.8, C_4), 47.6 (d, $^{2}J_{CP}$ = 7.5, C_3), 64.7 (OCH_2CH_3), 67.7 (d, $^{2}J_{CP}$ = 7.0, Ph*C*H_2^{I}), 67.8 (d, $^{2}J_{CP}$ = 7.1, Ph*C*H_2^{II}), 113.6 (d, J_{CP} = 2.6), 119.0 (d, J_{CP} = 4.9), 120.6, 121.2 (d, J_{CP} = 4.2), 124.6 (d, J_{CP} = 2.4), 127.9 ($C_2'^{I}$), 128.0 ($C_2'^{II}$), 128.52 ($C_4'^{I}$), 128.54 ($C_4'^{II}$), 128.81 ($C_3'^{I}$), 128.82 ($C_3'^{II}$), 136.9 (d, $^{3}J_{CP}$ = 6.2, C_1'), 140.1 (d, $^{3}J_{CP}$= 5.5, C_8), 146.9 (d, $^{3}J_{CP}$ = 3.4, C_{8a}), 163.2 (d, $^{3}J_{CP}$ = 2.7, C_2); ^{31}P NMR (DMSO-d6) δ: 23.9; $[M+H]^{+}_{found}$ = 477.1579, $C_{26}H_{26}N_2O_5P$ requires 477.1579.

*Diethyl (2-amino-3-cyano-8-hydroxy-4H-chromen-4-yl)phosphonate (**7a**)*

Yield: 82% (0.27 g), pale yellow crystal; Mp: 217-218 °C; ^{1}H NMR ($CDCl_3$+DMSO-d6) δ: 1.22 (t, J_{HH} = 7.0, 3H, CH_3^{I}), 1.31 (t, J_{HH} = 7.1, 3H, CH_3^{II}), 3.84 (d, J_{HP} = 17.8, 1H, CHP), 3.91-

4.14 (m, 4H, CH_2), 6.34 (brs, 2H, NH_2), 6.68-6.78 (m, 1H, ArH), 6.78-6.87 (m, 1H, ArH), 6.87-6.97 (m, 1H, ArH), 9.04 (brs, 1H, OH); ^{13}C NMR ($CDCl_3$+DMSO-d6) δ: 16.37 (d, $^3J_{CP}$ = 5.3, CH_3^I), 16.41 (d, $^3J_{CP}$ = 5.4, CH_3^{II}), 35.8 (d, $^1J_{CP}$ = 147.8, C_4), 49.2 (d, $^2J_{CP}$ = 7.7, C_3), 62.6 (d, $^2J_{CP}$ = 7.3, CH_2O^I), 62.9 (d, $^2J_{CP}$ = 7.5, CH_2O^{II}), 115.8 (d, J_{CP} = 3.3), 118.2 (d, J_{CP} = 5.0), 119.2 (d, J_{CP} = 4.3), 120.2, 124.4 (d, J_{CP} = 3.0), 138.7 (d, $^3J_{CP}$ = 5.3, C_{8a}), 145.3 (d, J_{CP} = 3.3, C_8), 162.8 (d, $^3J_{CP}$ = 3.0, C_2); ^{31}P NMR ($CDCl_3$+DMSO-d6) δ: 27.1; $[M+H]^+_{found}$ = 325.0954, $C_{14}H_{18}N_2O_5P$ requires 325.0953.

General procedure for the synthesis of (2-amino-3-cyano-4*H*-chromen-4-yl) phosphine oxide derivatives

A mixture of 1.0 mmol salicylaldehyde derivative (0.11 ml of salicylaldehyde, 0.14 g of 5-fluoro-2-hydroxybenzaldehyde, 0.16 g of 2-chloro-5-hydroxybenzaldehyde, 0.20 g of 3-bromo-2-hydroxybenzaldehyde, 0.17 g of 3-ethoxy-5-hydroxybenzaldehyde), 1.0 mmol malononitrile (0.066 g), 1.0 mmol secunder phophine oxide (0.20 g of diphenylphosphine oxide, 0.23 g of bis(*para*-tolyl)phosphine oxide, 0.26 g bis(3,5-dimethylphenyl)phosphine oxide, or 0.30 g of di(naphtalene-2-yl)phosphine oxide), 0.05 mmol (0.010 ml) of PMDTA was stirred in 2 ml of acetonitrile at 60 °C for 15 min in an oil bath. The reaction mixtures were cooled down to 5 °C. After 3-4 h, precipitated product was filtered out and washed with acetonitrile. The following products were thus prepared:

*(Diphenyl)(2-amino-3-cyano-4H-chromen-4-yl)phosphine oxide (**8a**)*

Yield: 92% (0.34 g), white crystal; Mp: 213-214 °C; ^{1}H NMR ($CDCl_3$+DMSO-d6) δ: 4.70 (d, $^2J_{HP}$ = 5.9, 1H, CHP), 6.70 (brs, 2H, NH_2), 6.71-6.75 (m, 1H, ArH), 6.82-6.88 (m, 2H, ArH), 7.15 (t, J_{HH} = 7.7, 1H, ArH), 7.41-7.51 (m, 4H, ArH), 7.51-7.59 (m, 2H, ArH), 7.70-7.76 (m, 2H, ArH), 7.84-7.91 (m, 2H, ArH); ^{13}C NMR ($CDCl_3$+DMSO-d6) δ: 38.8 (d, $^1J_{CP}$ = 68.5, C_4), 47,3 (d, $^2J_{CP}$ = 4.0, C_3), 116.0 (d, J_{CP} = 1.0), 117.6 (d, J_{CP} = 3.5), 120.1, 123.9 (d, J_{CP} = 1.3), 128.29 (d, $^3J_{CP}$ = 11.0, $C_3'^I$), 128.32 (d, $^3J_{CP}$ = 11.1, $C_3'^{II}$), 128.4 (d, J_{CP} = 2.9), 129.16 (d, J_{CP} = 1.8, $C_4'^I$), 129.17 (d, J_{CP} = 1.9, $C_4'^{II}$), 130.4 (d, $^1J_{CP}$ = 93.8, $C_1'^I$), 131.0 (d, $^1J_{CP}$ = 91.7, $C_1'^{II}$), 131.8 (d, $^2J_{CP}$ = 9.0, $C_2'^I$), 131.9 (d, $^2J_{CP}$ = 9.4, $C_2'^{II}$), 132.1 (d, $^3J_{CP}$ = 8.2), 150.9 (d, $^3J_{CP}$ = 4.0, C_{8a}), 163.9 (d, $^3J_{CP}$ = 2.2, C_2); ^{31}P NMR ($CDCl_3$+DMSO-d6) δ: 34.3; $[M+H]^+_{found}$ = 373.1110, $C_{22}H_{18}N_2O_2P$ requires: 373.1106.

*[Bis(p-tolyl)](2-amino-3-cyano-4H-chromen-4-yl)phosphine oxide (**8b**)*

Yield: 95% (0.38 g), white crystal; Mp: 218-220 °C; ^{1}H NMR (DMSO-d6) δ: 2.33 (s, 3H, CH_3^{I}), 2.35 (s, 3H, CH_3^{II}), 4.94 (d, $^{2}J_{HP}$ = 4.1, 1H, CHP), 6.68 (d, J_{HH} = 7.5, 1H, ArH), 6.85 (t, J_{HH} = 7.5, 2H, ArH), 6.92 (d, J_{HH} = 8.1, 2H, ArH), 7.08 (brs, 2H, NH_2), 7.17 (t, J_{HH} = 7.8, 1H, ArH), 7.26 (d, J_{HH} = 5.8, 2H, ArH), 7.31 (d, J_{HH} = 5.1, 2H, ArH), 7.62 (dd, J_{HH} = 10.5, J_{HH} = 7.8, 2H, ArH), 7.77 (dd, J_{HH} = 10.5, J_{HH} = 7.8, 2H, ArH); ^{13}C NMR (DMSO-d6) δ: 21.57 (CH_3^{I}), 21.61 (CH_3^{II}), 38.0 (d, $^{1}J_{CP}$ = 67.9, C_4), 47.1 (d, $^{2}J_{CP}$ = 4.4, C_3), 116.3 (d, J_{CP} = 2.2), 118.9 (d, J_{CP} = 3.5), 120.5, 124.2 (d, J_{CP} = 1.4), 128.7 (d, $^{1}J_{CP}$ = 95.5, $C_1'^{I}$), 128.8 (d, J_{CP} = 2.6), 129.1 (d, $^{1}J_{CP}$ = 9.9, $C_1'^{II}$), 129.3 (d, $^{3}J_{CP}$ = 11.4, $C_3'^{I}$), 129.4 (d, $^{3}J_{CP}$ = 11.8, $C_3'^{II}$), 131.88 (d, J_{CP} = 6.5), 131.94 (d, $^{2}J_{CP}$ = 8.1, $C_2'^{I}$), 132.2 (d, $^{2}J_{CP}$ = 8.5, $C_2'^{II}$), 142.1 (d, J_{CP} = 2.7, $C_4'^{I}$), 142.2 (d, J_{CP} = 2.7, $C_4'^{II}$), 151.4 (d, $^{3}J_{CP}$ = 4.0, C_{8a}), 164.4 (d, $^{3}J_{CP}$ = 2.0, C_2); ^{31}P NMR (DMSO-d6) δ: 29.3; $[M+H]^{+}_{found}$ = 401.1421, $C_{24}H_{22}N_2O_2P$ requires: 401.1419.

*[Bis(3,5-dimethylphenyl)](2-amino-3-cyano-4H-chromen-4-yl)phosphine oxide (**8c**)*

Yield: 89% (0.38 g), white crystal; Mp: 250-252 °C; ^{1}H NMR ($CDCl_3$+DMSO-d6) δ: 2.28 (s, 6H, CH_3^{I}), 2.33 (s, 6H, CH_3^{II}), 4.75 (d, $^{2}J_{HP}$ = 6.9, 1H, CHP), 6.69 (d, J_{HH} = 7.8, 1H, ArH), 6.81-6.94 [6.89 (brs, NH_2) overlapped by the multiplet of ArH total int. 4H], 7.10-7.20 (m, 3H, ArH), 7.27 (d, J_{HH} = 11.0, 2H, ArH), 7.44 (d, J_{HH} = 10.8, 2H, ArH); ^{13}C NMR ($CDCl_3$+DMSO-d6) δ: 21.2 (CH_3^{I}), 21.3 (CH_3^{II}), 38.2 (d, $^{1}J_{CP}$ = 74.2, C_4), 47.3 (d, $^{2}J_{CP}$ = 3.3, C_3), 115.9 (d, J_{CP} = 2.5), 118.3 (d, J_{CP} = 3.5), 120.5, 123.8 (d, J_{CP} = 1.5), 128.4 (d, J_{CP} = 2.9), 129.3 (d, J_{CP} = 2.5), 129.4 (d, $^{2}J_{CP}$ = 9.1, $C_2'^{I}$), 129.8 (d, $^{2}J_{CP}$ = 8.6, $C_2'^{II}$), 130.6 (d, $^{1}J_{CP}$ = 92.6, $C_1'^{I}$), 131.2 (d, $^{1}J_{CP}$ = 90.5, $C_1'^{II}$), 133.3 (d, J_{CP} = 2.7, $C_4'^{I}$), 133.4 (d, J_{CP} = 2.1, $C_4'^{II}$), 137.59 (d, $^{3}J_{CP}$ = 11.7, $C_3'^{I}$), 137.60 (d, $^{3}J_{CP}$ = 11.9, $C_3'^{II}$), 151.2 (d, $^{3}J_{CP}$ = 3.5, C_{8a}), 164.0 (d, $^{3}J_{CP}$ = 2.8, C_2); ^{31}P NMR ($CDCl_3$+DMSO-d6) δ: 30.2; $[M+H]^{+}_{found}$ = 429.1736, $C_{26}H_{26}N_2O_2P$ requires: 429.1732.

*[Di(naphthalene-2-yl)](2-amino-3-cyano-4H-chromen-4-yl)phosphine oxide (**8d**)*

Yield: 85% (0.40 g), white crystal; Mp: 147-148 °C; ^{1}H NMR (DMSO-d6) δ: 5.35 (d, $^{2}J_{HP}$ = 3.3, 1H, CHP), 6.69-6.83 (m, 2H, ArH), 6.95 (d, J_{HH} = 8.1, 1H, ArH), 7.09-7.26 [7.18 (brs, NH_2) overlapped by the multiplet of ArH total int. 3H], 7.52-7.71 (m, 4H, ArH), 7.91-8.20 (m, 8H, ArH), 8.45 (d, J_{HH} = 12.5, 1H, ArH), 8.62 (d, J_{HH} = 12.6, 1H, ArH); ^{13}C NMR (DMSO-d6) δ: 37.9 (d, $^{1}J_{CP}$ = 67.7, C_4), 46.7 (d, $^{2}J_{CP}$ = 4.6, C_3), 116.5 (d, J_{CP} = 2.6), 118.7 (d, J_{CP} = 3.7), 120.5, 124.3 (d, J_{CP} = 2.6), 126.9 (d, J_{CP} = 10.4, $C_{(naphtyl)}$), 127.2 (d, J_{CP} = 10.3, $C_{(naphtyl)}$), 127.4 (d, J_{CP} = 9.9, $C_{(naphtyl)}$), 128.2 ($C_{(naphtyl)}$), 128.4 (d, J_{CP} = 11.0, $C_{(naphtyl)}$), 128.7 (d, J_{CP} = 4.7, $C_{(naphtyl)}$), 128.9 (d, J_{CP} = 2.9), 129.27 (d, J_{CP} = 3.2), 129.30 (d, J_{CP} = 8.5, $C_{(naphtyl)}$), 129.4 (d,

$^{1}J_{CP}$ = 92.7, $C_{1(naphtyl)^{I}}$), 129.7 (d, $^{1}J_{CP}$ = 89.9, $C_{1(naphtyl)^{II}}$), 132.4 (d, J_{CP} = 10.3, $C_{(naphtyl)}$), 132.6 (d, J_{CP} = 10.1, $C_{(naphtyl)}$), 133.7 (d, J_{CP} = 8.0, $C_{(naphtyl)}$), 134.2 (d, J_{CP} = 7.8 $C_{(naphtyl)}$), 134.6 (d, J_{CP} = 2.3, $C_{(naphtyl)}$), 134.8 (d, J_{CP} = 2.4, $C_{(naphtyl)}$), 151.5 (d, $^{3}J_{CP}$ = 4.0, C_{8a}), 164.6 (d, $^{3}J_{CP}$ = 2.1, C_2); ^{31}P NMR (DMSO-d6) δ: 29.1; $[M+H]^{+}_{found}$ = 473.1422, $C_{30}H_{22}N_2O_2P$ requires: 473.1419.

*(Diphenyl)(2-amino-3-cyano-6-fluoro-4H-chromen-4-yl)phosphine oxide (**9a**)*

Yield: 88% (0.34 g), white crystal; Mp: 230-232 °C; ^{1}H NMR (DMSO-d6) δ: 5.05 (d, $^{2}J_{HP}$ = 4.3, 1H, CHP), 6.38 (d, J_{HH} = 9.0, 1H, ArH), 6.91-7.08 (m, 2H, ArH), 7.17 (brs, 2H, NH_2), 7.41-7.66 (m, 6H, ArH), 7.78 (dd, J_{HH} = 10.9, J_{HH} = 6.7, 2H, ArH), 7.94 (dd, J_{HH} = 10.8, J_{HH} = 6.7, 2H, ArH); ^{13}C NMR (DMSO-d6) δ: 38.3 (dd, $^{1}J_{CP}$ = 67.0, J_{CF} = 1.0, C_4), 46.1 (d, $^{2}J_{CP}$ = 4.5, C_3), 115.4 (t, J_{CP} = 2,9), 115.7 (t, J_{CP} = 3.9), 117.8 (dd, J_{CP} = 2.1, J_{CF} = 8.3), 120.1, 120.6 (dd, J_{CP} = 3.6, J_{CF} = 8.6), 128.88 (d, $^{3}J_{CP}$ = 10.9, $C_3{}'^{I}$), 128.89 (d, $^{3}J_{CP}$ = 10.8, $C_3{}'^{II}$), 131.2 (d, $^{1}J_{CP}$ = 93.4, $C_1{}'^{I}$), 131.8 (d, $^{3}J_{CP}$ = 8.9, $C_2{}'^{I}$), 131.9 (d, $^{1}J_{CP}$ = 90.5, $C_1{}'^{II}$), 132.2 (d, $^{2}J_{CP}$ = 8.9, $C_2{}'^{II}$), 132.4 (d, J_{CP} = 2.6, $C_4{}'^{I}$), 132.5 (d, J_{CP} = 2.2, $C_4{}'^{II}$), 147.7 (dd, $^{3}J_{CP}$ = 4.2, J_{CF} = 2.2, C_{8a}), 158.0 (dd, J_{CP} = 3.0, $^{1}J_{CF}$ = 240.7, C_6), 164.4 (d, $^{3}J_{CP}$ = 2.1, C_2); ^{31}P NMR (DMSO-d6) δ: 28.8; $[M+H]^{+}_{found}$ = 391.1014, $C_{22}H_{17}FN_2O_2P$ requires: 391.1012.

*[Bis(p-tolyl)](2-amino-3-cyano-6-fluoro-4H-chromen-4-yl)phosphine oxide (**9b**)*

Yield: 92% (0.39 g), white crystal; Mp: 258-260 °C; ^{1}H NMR (DMSO-d6) δ: 2.30 (s, 3H, $CH_3{}^{I}$), 2.36 (s, 3H, $CH_3{}^{II}$), 4.96 (d, $^{2}J_{HP}$ = 4.9, 1H, CHP), 6.42 (d, J_{HH} = 7.4, 1H, ArH), 6.92-6.98 (m, 1H, ArH), 6.99-7.06 (m, 1H, ArH), 7.13 (brs, 2H, NH_2), 7.29 (d, J_{HH} = 5.7, 2H, ArH), 7.33 (d, J_{HH} = 5.6, 2H, ArH), 7.62 (t, J_{HH} = 9.1, 2H, ArH), 7.76 (t, J_{HH} = 9.2, 2H, ArH);^{13}C NMR (DMSO-d6) δ: 21.56 ($CH_3{}^{I}$), 21.62 ($CH_3{}^{II}$), 38.3 (d, $^{1}J_{CP}$ = 67.3, C_4), 46.5 (d, $^{2}J_{CP}$ = 4.2, C_3), 115.5 (dd, J_{CP} = 2.2, J_{CF} = 23.4), 115.7 (dd, J_{CP} = 2.9, J_{CF} = 24.7), 117.7 (dd, J_{CP} = 1.9, J_{CF} = 8.3), 120.3, 120.9 (dd, J_{CP} = 3.3, J_{CF} = 8.3), 128.1 (d, $^{1}J_{CP}$ = 95.3, $C_1{}'^{I}$), 128.8 (d, $^{1}J_{CP}$ = 92.8, $C_1{}'^{II}$), 129.45 (d, $^{3}J_{CP}$ = 11.4, $C_3{}'^{I}$), 129.48 (d, $^{3}J_{CP}$ = 11.4, $C_3{}'^{II}$), 131.9 (d, $^{2}J_{CP}$ = 9.3, $C_2{}'^{I}$), 132.2 (d, $^{2}J_{CP}$ = 9.2, $C_2{}'^{II}$), 142.3 (d, J_{CP} = 2.6, $C_4{}'^{I}$), 142.3 (d, J_{CP} = 2.8, $C_4{}'^{II}$), 147.6 (dd, $^{3}J_{CP}$ = 3.4, J_{CF} = 2.2, C_{8a}), 158.0 (dd, $^{3}J_{CP}$ = 2.8, $^{1}J_{CF}$ = 240.1, C_6), 164.3 (d, $^{3}J_{CP}$ = 2.0, C_2); ^{31}P NMR (DMSO-d6) δ: 29.2; $[M+H]^{+}_{found}$ = 419.1327, $C_{24}H_{21}FN_2O_2P$ requires: 419.1325.

*[Bis(3,5-dimethylphenil)](2-amino-3-cyano-6-fluoro-4H-chromen-4-yl)phosphine oxide (**9c**)*

Yield: 97% (0.43 g), white crystal; Mp: 268-270 °C; ^{1}H NMR (DMSO-d6) δ: 2.27 (s, 6H, $CH_3{}^{I}$), 2.32 (s, 6H, $CH_3{}^{II}$), 4.97 (d, $^{2}J_{HP}$ = 5.0, 1H, CHP), 6.43 (d, J_{HH} = , 19.2, 1H, ArH), 6.91-6.97

(m, 1H, ArH), 7.00-7.07 (m, 1H, ArH), 7.13 (brs, 2H, NH_2), 7.17 (d, J_{HH} = 10.9, 2H, ArH), 7.33 (d, J_{HH} = 11.1, 2H, ArH), 7.47 (d, J_{HH} = 10.9, 2H, ArH); ^{13}C NMR (DMSO-d6) δ: 21.3 (CH_3^{I}), 21.4 (CH_3^{II}), 38.2 (d, $^1J_{CP}$ = 66.7, C_4), 46.6 (d, $^2J_{CP}$ = 4.0, C_3), 115.4 (dd, J_{CP} = 2.7, J_{CF} = 23.7), 115.8 (dd, J_{CP} = 3.3, J_{CF} = 24.9), 117.6 (dd, J_{CP} = 2.0, J_{CF} = 8.8), 120.5, 120.9 (dd, J_{CP} = 3.3, J_{CF} = 8.5), 129.5 (d, $^2J_{CP}$ = 9.0, $C_2'^{I}$), 129.9 (d, $^2J_{CP}$ = 8.6, $C_2'^{II}$), 130.8 (d, $^1J_{CP}$ = 93.0, $C_1'^{I}$), 131.7 (d, $^1J_{CP}$ = 90.3, $C_1'^{II}$), 133.6 (d, J_{CP} = 2.6, $C_4'^{I}$), 133.8 (d, J_{CP} = 2.7, $C_4'^{II}$), 137.96 (d, $^3J_{CP}$ = 11.8, $C_3'^{I}$), 138.02 (d, $^3J_{CP}$ = 11.8, $C_3'^{II}$), 147.7 (dd, $^3J_{CP}$ = 3.8, J_{CF} = 2,1, C_{8a}), 158.0 (dd, $^3J_{CP}$ = 2.5, $^1J_{CF}$ = 239.6, C_6), 164.4 (d, $^3J_{CP}$ = 1.7, C_2); ^{31}P NMR (DMSO-d6) δ: 26.3; $[M+H]^+_{found}$ = 447.1640, $C_{26}H_{25}FN_2O_2P$ requires: 447.1638.

*[Bis(naphthalene-2-yl)](2-amino-3-cyano-6-fluoro-4H-chromen-4-yl)phosphine oxide (**9d**)*

Yield: 90% (0.44 g), white crystal; Mp: 215-216 °C; ^{1}H NMR (DMSO-d6) δ: 5.34 (d, $^2J_{HP}$ = 3.9, 1H, CHP), 6.51 (d, J_{HH} = 5.3, 1H, ArH), 6.94-7.06 (m, 2H, ArH), 7.20 (brs, 2H, NH_2), 7.56-7.71 (m, 4H, ArH),), 8.01 (t, J_{HH} = 8.5, 3H, ArH), 8.04-8.13 (m, 4H, ArH), 8.45 (d, J_{HH} = 12.5, 1H, ArH), 8.59 (d, J_{HH} = 12.6, 1H, ArH);^{13}C NMR (DMSO-d6) δ: 38.2 (d, $^1J_{CP}$ = 66.8, C_4), 46.2 (d, $^2J_{CP}$ = 4.4, C_3), 115.5 (dd, J_{CP} = 2.6, J_{CF} = 12.8), 115.7 (dd, J_{CP} = 2.5, J_{CF} = 12.3), 117.9 (dd, J_{CP} = 1.8, J_{CF} = 8.6), 120.2, 120.7 (dd, J_{CP} = 3.6, J_{CF} = 8.6), 126.8 (d, J_{CP} = 10.3, $C_{(naphtyl)}$), 127.1 (d, J_{CP} = 10.2, $C_{(naphtyl)}$), 127.1 (d, J_{CP} = 18.1, $C_{(naphtyl)}$), 128.2 ($C_{(naphtyl)}$), 128.4 (d, J_{CP} = 8.3, $C_{(naphtyl)}$), 128.5 (d, J_{CP} = 10.8, $C_{(naphtyl)}$), 128.77 (d, J_{CP} = 9.4, $C_{(naphtyl)}$), 128.78 (d, $^1J_{CP}$ = 74.7, $C_{1(naphtyl)}^{I}$), 129.30 (d, J_{CP} = 13.6, $C_{(naphtyl)}$), 129.34 (d, $^1J_{CP}$ = 90.5, $C_{1(naphtyl)}^{II}$), 132.3 (d, J_{CP} = 12.2, $C_{(naphtyl)}$), 132.5 (d, J_{CP} = 12.3, $C_{(naphtyl)}$), 133.7 (d, J_{CP} = 7.8, $C_{(naphtyl)}$), 134.3 (d, J_{CP} = 7.8, $C_{(naphtyl)}$), 134.6 (d, J_{CP} = 2.1, $C_{(naphtyl)}$), 134.8 (d, J_{CP} = 2.2, $C_{(naphtyl)}$), 147.7 (dd, $^3J_{CP}$ = 3.8, J_{CF} = 2,3, C_{8a}), 158.0 (dd, $^3J_{CP}$ = 2.7, $^1J_{CF}$ = 236.8, C_6), 164.5 (d, $^3J_{CP}$ = 1.9, C_2); ^{31}P NMR (DMSO-d6) δ: 27.4; $[M+H]^+_{found}$ = 491.1329, $C_{30}H_{21}FN_2O_2P$ requires: 491.1325.

*(Diphenyl)(2-amino-3-cyano-5-chloro-4H-chromen-4-yl)phosphine oxide (**10a**)*

Yield: 92% (0.37 g), white crystal; Mp: 241-243 °C; ^{1}H NMR (DMSO-d6) δ: 4.82 (d, $^2J_{HP}$ = 4.0, 1H, CHP), 7.03 (d, J_{HH} = 8.1, 1H, ArH), 7.10 (d, J_{HH} = 7.9, 1H, ArH), 7.18-7.72 [7.28 (brs, NH_2) overlapped by the multiplet of ArH total int. 11H], 7.92 (dd, J_{HH} = 10.8, J_{HH} = 6.8, 2H, ArH); ^{13}C NMR (DMSO-d6) δ: 38.0 (d, $^1J_{CP}$ = 66.6, C_4), 47.3 (d, $^2J_{CP}$ = 4.1, C_3), 115.6 (d, J_{CP} = 1.7), 118.0 (d, J_{CP} = 2.8), 120.0, 125.6 (d, J_{CP} = 1.9), 128.6 (d, $^3J_{CP}$ = 11.2, $C_3'^{I}$), 129.0 (d, $^3J_{CP}$ = 11.0, $C_3'^{II}$), 129.98 (d, J_{CP} = 2.6, $C_4'^{I}$), 129.99 (d, J_{CP} = 2.7, $C_4'^{II}$), 130.2 (d, $^1J_{CP}$ = 93.9, $C_1'^{I}$), 131.9 (d, $^2J_{CP}$ = 9.3, $C_2'^{I}$), 132.1 (d, $^1J_{CP}$ = 85.1, $C_1'^{II}$), 132.4 (d, J_{CP} = 2.7), 132.6 (d, $^2J_{CP}$

= 8.7, C_2'^{II}), 132.7 (d, J_{CP} = 3.7, C_5), 152.6 (d, $^3J_{CP}$ = 4.0, C_{8a}), 164.6 (d, $^3J_{CP}$ = 2.1, C_2); ^{31}P NMR (DMSO-d6) δ: 29.3; $[M+H]^+_{found}$ = 407.0719, $C_{22}H_{17}ClN_2O_2P$ requires: 407.0716.

*[Bis(p-tolyl)](2-amino-3-cyano-5-chloro-4H-chromen-4-yl)phosphine oxide (**10b**)*

Yield: 90% (0.39 g), white crystal; Mp: 188-190 °C; ^{1}H NMR (DMSO-d6) δ: 2.31 (s, 3H, CH_3^I), 2.40 (s, 3H, CH_3^{II}), 4.74 (d, $^2J_{HP}$ = 4.3, 1H, CHP), 7.01 (d, J_{HH} = 8.2, 1H, ArH), 7.12 (d, J_{HH} = 8.0, 1H, ArH), 7.19 (d, J_{HH} = 8.2, 2H, ArH), 7.25 (brs, 2H, NH_2), 7.27-7.41 (m, 5H, ArH), 7.75 (dd, J_{HH} = 10.4, J_{HH} = 7.7, 2H, ArH); ^{13}C NMR (DMSO-d6) δ: 21.6 (CH_3^I), 21.7 (CH_3^{II}), 38.0 (d, $^1J_{CP}$ = 66.8, C_4), 47.6 (d, $^2J_{CP}$ = 4.0, C_3), 115.6 (d, J_{CP} = 2.2), 118.3 (d, J_{CP} = 2.8), 120.1, 125.6 (d, J_{CP} = 1.2), 127.2 (d, $^1J_{CP}$ = 96.4, C_1'^{I}), 129.20 (d, $^1J_{CP}$ = 93.0, C_1'^{II}), 129.21 (d, $^3J_{CP}$ = 11.5, C_3'^{I}), 129.6 (d, $^3J_{CP}$ = 11.5, C_3'^{II}), 129.9 (d, J_{CP} = 2.1), 131.9 (d, $^2J_{CP}$ = 9.6, C_2'^{I}), 132.6 (d, $^2J_{CP}$ = 8.9, C_2'^{II}), 132.8 (d, J_{CP} = 4.1, C_5), 142.3 (d, J_{CP} = 2.7, C_4'^{I}), 142.6 (d, J_{CP} = 2.5, C_4'^{II}), 152.5 (d, $^3J_{CP}$ = 3.9, C_{8a}), 164.5 (d, $^3J_{CP}$ = 2.0, C_2); ^{31}P NMR (DMSO-d6) δ: 29.5; $[M+H]^+_{found}$ = 435.1031, $C_{24}H_{21}ClN_2O_2P$ requires: 435.1029.

*[Bis(3,5-dimethylphenyl)](2-amino-3-cyano5-chloro-4H-chromen-4-yl)phosphine oxide (**10c**)*

Yield: 94% (0.43 g), white crystal; Mp: 258-260 °C; ^{1}H NMR (DMSO-d6) δ: 2.20 (s, 6H, CH_3^I), 2.35 (s, 6H, CH_3^{II}), 4.74 (d, $^2J_{HP}$ = 4.8, 1H, CHP), 6.95-7.02 (m, 3H, ArH), 7.09-7.18 (m, 2H, ArH), 7.21-7.35 [7.24 (brs, NH_2) overlapped by the multiplet of ArH total int. 5H], 7.33 (d, J_{HH} = 11.0, 2H, ArH);^{13}C NMR (DMSO-d6) δ: 21.3 (CH_3^I), 21.4 (CH_3^{II}), 37.9 (d, $^1J_{CP}$ = 66.6, C_4), 47.6 (d, $^2J_{CP}$ = 3.9, C_3), 115.5 (d, J_{CP} = 2.3), 118.3 (d, J_{CP} = 2.8), 120.3, 125.5 (d, J_{CP} = 1.6), 129.5 (d, $^2J_{CP}$ = 9.3, C_2'^{I}), 129.8 (d, J_{CP} = 3.0), 129.9 (d, $^1J_{CP}$ = 93.3, C_1'^{I}), 130.2 (d, $^2J_{CP}$ = 8.5, C_2'^{II}), 132.0 (d, $^1J_{CP}$ = 90.5, C_1'^{II}), 132.9 (d, J_{CP} = 4.1, C_5), 133.6 (d, J_{CP} = 2.2, C_4'^{I}), 134.1 (d, J_{CP} = 2.3, C_4'^{II}), 137.7 (d, $^3J_{CP}$ = 11.9, C_3'^{I}), 138.0 (d, $^3J_{CP}$ = 11.7, C_3'^{II}), 152.7 (d, $^3J_{CP}$ = 3.9, C_{8a}), 164.6 (d, $^3J_{CP}$ = 2.1, C_2); ^{31}P NMR (DMSO-d6) δ: 29.9; $[M+H]^+_{found}$ = 463.1345, $C_{26}H_{25}ClN_2O_2P$ requires: 463.1342.

*[Bis(naphthalene-2-yl)](2-amino-3-cyano5-chloro-4H-chromen-4-yl)phosphine oxide (**10d**)*

Yield: 89% (0.45 g), white crystal; Mp: 232-233 °C; ^{1}H NMR (DMSO-d6) δ: 5.11 (d, $^2J_{HP}$ = 3.9, 1H, CHP), 7.04 (d, J_{HH} = 5.3, 1H, ArH), 7.06 (d, J_{HH} = 5.1, 1H, ArH), 7.24-7.37 [7.30 (brs, NH_2) overlapped by the multiplet of ArH total int. 3H], 7.51-7.74 (m, 5H, ArH), 7.87-7.99 (m, 3H, ArH), 8.01-8.24 (m, 5H, ArH), 8.64 (d, J_{HH} = 12.6, 1H, ArH); ^{13}C NMR (DMSO-d6) δ: 38.0 (d, $^1J_{CP}$ = 66.9, C_4), 47.5 (d, $^2J_{CP}$ = 4.0, C_3), 115.8 (d, J_{CP} = 2.4), 118.1 (d, J_{CP} = 2.9), 120.1, 125.7 (d, J_{CP} = 1.3), 127.1 (d, J_{CP} = 10.2, $C_{(naphtyl)}$), 127.4 ($C_{(naphtyl)}$), 127.5 (d, J_{CP} = 9.7, $C_{(naphtyl)}$), 127.9 (d, $^1J_{CP}$ = 94.5, $C_{1(naphtyl)}^I$), 128.15 (d, J_{CP} = 11.0, $C_{(naphtyl)}$), 128.22 (d, J_{CP} = 8.4,

$C_{(naphtyl)}$), 128.5 (d, J_{CP} = 11.0, $C_{(naphtyl)}$), 128.5 (d, J_{CP} = 6.5, $C_{(naphtyl)}$), 129.4 (d, J_{CP} = 19.7, $C_{(naphtyl)}$), 130.4 (d, J_{CP} = 2.3), 129.7 (d, $^{1}J_{CP}$ = 90.3, $C_{1(naphtyl)}{}^{II}$), 132.3 (d, J_{CP} = 12.4, $C_{(naphtyl)}$), 132.61 (d, J_{CP} = 4.2, C_5), 132.66 (d, J_{CP} = 12.3, $C_{(naphtyl)}$), 133.7 (d, J_{CP} = 8.8, $C_{(naphtyl)}$), 134.7 (d, J_{CP} = 2.2, $C_{(naphtyl)}$), 134.8 (d, J_{CP} = 8.0, $C_{(naphtyl)}$), 135.0 (d, J_{CP} = 2.2, $C_{(naphtyl)}$), 152.7 (d, $^{3}J_{CP}$ = 4.0, C_{8a}), 164.7 (d, $^{3}J_{CP}$ = 2.1, C_2); ^{31}P NMR (DMSO-d6) δ: 29.8; $[M+H]^{+}_{found}$ = 507.1032, $C_{30}H_{21}ClN_2O_2P$ requires: 507.1029.

*(Diphenyl)(2-amino-3-cyano-8-bromo-4H-chromen-4-yl)phosphine oxide (**11a**)*

Yield: 86% (0.39 g), pale yellow crystal; Mp: 261-263 °C; ^{1}H NMR (DMSO-d6) δ: 5.15 (d, $^{2}J_{HP}$ = 3.7, 1H, CHP), 6.62 (d, J_{HH} = 7.7, 1H, ArH), 6.79 (t, J_{HH} = 7.9, 1H, ArH), 7.30 (brs, 2H, NH_2), 7.41-7.50 (m, 3H, ArH), 7.50-7.67 (m, 4H, ArH), 7.80 (t, J_{HH} = 9.0, 2H, ArH), 7.97 (t, J_{HH} = 9.0, 2H, ArH); ^{13}C NMR (DMSO-d6) δ: 42.4 (d, $^{1}J_{CP}$ = 66.8, C_4), 51.0 (d, $^{2}J_{CP}$ = 4.5, C_3), 113.8 (d, J_{CP} = 3.0), 123.9, 124.9 (d, J_{CP} = 3.4), 129.3 (d, J_{CP} = 1.9), 132.7 (d, J_{CP} = 3.5), 132.85 (d, $^{3}J_{CP}$ = 11.0, $C_3{}'^{I}$), 132.91 (d, $^{3}J_{CP}$ = 11.0, $C_3{}'^{II}$), 135.5 (d, $^{1}J_{CP}$ = 93.3, $C_1{}'^{I}$), 135.77 (d, $^{1}J_{CP}$ = 90.3, $C_1{}'^{II}$), 135.82 (d, $^{2}J_{CP}$ = 9.2, $C_2{}'^{I}$), 136.2 (d, $^{2}J_{CP}$ = 8.3, $C_2{}'^{II}$), 136.36 (d, J_{CP} = 3.0, $C_4{}'^{I}$), 136.38 (d, J_{CP} = 3.5, $C_4{}'^{II}$), 136.5 (d, J_{CP} = 1.9, C_8), 152.2 (d, $^{3}J_{CP}$ = 3.9, C_{8a}), 168.1 (d, $^{3}J_{CP}$ = 2.1, C_2);^{31}P NMR (DMSO-d6) δ:33.8; $[M+H]^{+}_{found}$ = 451.0212, $C_{22}H_{17}BrN_2O_2P$ requires: 451.0211.

*[Bis(p-tolyl)](2-amino-3-cyano-8-bromo-4H-chromen-4-yl)phosphine oxide (**11b**)*

Yield: 87% (0.42 g), pale yellow crystal; Mp: 232-234 °C; ^{1}H NMR (DMSO-d6) δ: 2.30 (s, 3H, $CH_3{}^{I}$), 2.33 (s, 3H, $CH_3{}^{II}$), 5.00 (d, $^{2}J_{HP}$ = 3.8, 1H, CHP), 6.60 (d, J_{HH} = 7.6, 1H, ArH), 6.76 (t, J_{HH} = 7.9, 1H, ArH), 7.14-7.27 [7.20 (brs, NH_2) overlapped by the multiplet of ArH total int. 4H], 7.30 (d, J_{HH} = 5.6, 2H, ArH), 7.42 (d, J_{HH} = 7.9, 1H, ArH), 7.59 (t, J_{HH} = 9.1, 2H, ArH), 7.75 (t, J_{HH} = 9.2, 2H, ArH); ^{13}C NMR (DMSO-d6) δ: 21.58 ($CH_3{}^{I}$), 21.62 ($CH_3{}^{II}$), 38.5 (d, $^{1}J_{CP}$ = 67.0, C_4), 47.3 (d, $^{2}J_{CP}$ = 4.5, C_3), 109.8 (d, J_{CP} = 3.0), 120.0, 121.2 (d, J_{CP} = 3.4), 125.3 (d, J_{CP} = 2.1), 128.4 (d, $^{1}J_{CP}$ = 95.7, $C_1{}'^{I}$), 128.7 (d, $^{1}J_{CP}$ = 93.3, $C_1{}'^{II}$), 128.8 (d, J_{CP} = 2.7), 129.4 (d, $^{3}J_{CP}$ = 11.3, $C_3{}'^{I}$), 129.5 (d, $^{3}J_{CP}$ = 11.5, $C_3{}'^{II}$), 131.8 (d, $^{2}J_{CP}$ = 9.2, $C_2{}'^{I}$), 132.1 (d, $^{2}J_{CP}$ = 9.1, $C_2{}'^{II}$), 132.3 (d, J_{CP} = 2.5, C_8), 142.24 (d, J_{CP} = 2.6, $C_4{}'^{I}$), 142.30 (d, J_{CP} = 2.7, $C_4{}'^{II}$), 148.1 (d, $^{3}J_{CP}$ = 3.9, C_{8a}), 164.0 (d, $^{3}J_{CP}$ = 2.2, C_2); ^{31}P NMR (DMSO-d6) δ: 29.6; $[M+H]^{+}_{found}$ = 479.0524, $C_{24}H_{21}BrN_2O_2P$ requies: 479.0524.

*[Bis(3,5-dimethylphenyl)](2-amino-3-cyano-8-bromo-4H-chromen-4-yl)phosphine oxide (**11c**)*

Yield: 82% (0.41 g), pale yellow crystal; Mp: 265-267°C; ^{1}H NMR (DMSO-d6) δ: 2.26 (s, 6H, CH_3^{I}), 2.32 (s, 6H, CH_3^{II}), 5.04 (d, $^{2}J_{HP}$ = 4.4, 1H, CHP), 6.65 (d, J_{HH} = 7.6, 1H, ArH), 6.83 (t, J_{HH} = 7.9, 1H, ArH), 7.14-7.23 [7.20 (brs, NH_2) overlapped by the multiplet of ArH total int. 4H], 7.32 (d, J_{HH} = 11.0, 2H, ArH), 7.47 (d, J_{HH} = 11.4, 3H, ArH); ^{13}C NMR (DMSO-d6) δ: 21.3 (CH_3^{I}), 21.4 (CH_3^{II}), 38.3 (d, $^{1}J_{CP}$ = 66.8, C_4), 47.6 (d, $^{2}J_{CP}$ = 4.3, C_3), 109.8 (d, J_{CP} = 3.1), 120.2, 121.2 (d, J_{CP} = 3.2), 125.3 (d, J_{CP} = 2.7), 128.8 (d, J_{CP} = 3.5), 129.5 (d, $^{2}J_{CP}$ = 8.9, $C_2'^{I}$), 129.8 (d, $^{2}J_{CP}$ = 8.8, $C_2'^{II}$), 131.2 (d, $^{1}J_{CP}$ = 93.1, $C_1'^{I}$), 131.5 (d, $^{1}J_{CP}$ = 90.3, $C_1'^{II}$), 132.3 (d, J_{CP} = 2.9, C_8), 133.67 (d, J_{CP} = 2.8, $C_4'^{I}$), 133.70 (d, J_{CP} = 2.7, $C_4'^{II}$), 137.93 (d, $^{3}J_{CP}$ = 11.8, $C_3'^{I}$), 137.97 (d, $^{3}J_{CP}$ = 11.8, $C_3'^{II}$), 148.2 (d, $^{3}J_{CP}$ = 3.9, C_{8a}), 163.9 (d, $^{3}J_{CP}$ = 2.2, C_2); ^{31}P NMR (DMSO-d6) δ: 25.0; $[M+H]^{+}_{found}$ = 507.0837, $C_{26}H_{25}BrN_2O_2P$ requies: 507.0837.

*[Bis(naphthalene-2-yl)](2-amino-3-cyano-8-bromo-4H-chromen-4-yl)phosphine oxide (**11d**)*

Yield: 73% (0.40 g), white crystal; Mp: 245-246°C; ^{1}H NMR (DMSO-d6) δ: 5.42 (d, $^{2}J_{HP}$ = 2.9, 1H, CHP), 6.61-6.77 (m, 2H, ArH), 7.31 (brs, 2H, NH_2), 7.44 (d, J_{HH} = 6.4, 1H, ArH), 7.52-7.72 (m, 4H, ArH), 7.89-8.19 (m, 8H, ArH), 8.43 (d, J_{HH} = 12.6, 1H, ArH), 8.61 (d, J_{HH} = 12.7, 1H, ArH); ^{13}C NMR (DMSO-d6) δ: 38.3 (d, $^{1}J_{CP}$ = 66.7, C_4), 47.1 (d, $^{2}J_{CP}$ = 4.7, C_3), 110.0 (d, J_{CP} = 3.2), 120.0, 121.1 (d, J_{CP} = 3.6), 125.4 (d, J_{CP} = 1.6), 126.8 (d, J_{CP} = 10.3, $C_{(naphtyl)}$), 127.1 (d, J_{CP} = 10.3, $C_{(naphtyl)}$), 127.5 (d, J_{CP} = 9.1, $C_{(naphtyl)}$), 128.2 ($C_{(naphtyl)}$), 128.7 (d, J_{CP} = 8.8, $C_{(naphtyl)}$), 129.1 (d, $^{1}J_{CP}$ = 100.5, $C_{1(naphtyl)}^{I}$), 129.2 (d, $^{1}J_{CP}$ = 103.1, $C_{1(naphtyl)}^{II}$), 129.3 (d, J_{CP} = 8.0, $C_{(naphtyl)}$), 132.4 (d, J_{CP} = 7.5, $C_{(naphtyl)}$), 130.5 (d, J_{CP} = 1.5, C_8), 132.6 (d, J_{CP} = 10.8, $C_{(naphtyl)}$), 133.7 (d, J_{CP} = 8.1, $C_{(naphtyl)}$), 134.2 (d, J_{CP} = 8.1, $C_{(naphtyl)}$), 134.6 (d, J_{CP} = 2.3, $C_{(naphtyl)}$), 134.8 (d, J_{CP} = 2.2, $C_{(naphtyl)}$), 148.3 (d, $^{3}J_{CP}$ = 3.8, C_{8a}), 164.2 (d, $^{3}J_{CP}$ = 2.3, C_2); ^{31}P NMR (DMSO-d6) δ: 29.6; $[M+H]^{+}_{found}$ = 551.0525, $C_{30}H_{21}BrN_2O_2P$ requies: 551.0524.

*(Diphenyl)(2-amino-3-cyano-8-ethoxy-4H-chromen-4-yl)phosphine oxide (**12a**)*

Yield: 92% (0.38 g), white crystal; Mp: 178-180 °C; ^{1}H NMR (DMSO-d6) δ: 1.29 (t, J_{HH} = 6.9, 3H, $OCH_2C\mathit{H}_3$), 3.97-4.05 (tq, J_{HH} = 7.2, J_{HH} = 3.7, 2H, $OC\mathit{H}_2CH_3$), 4.97 (d, $^{2}J_{HP}$ = 3.0, 1H, CHP), 6.15 (d, J_{HH} = 7.7, 1H, ArH), 6.70 (t, J_{HH} = 8.0, 1H, ArH), 6.84 (d, J_{HH} = 7.6, 1H, ArH), 7.06 (brs, 2H, NH_2), 7.38-7.44 (m, 2H, ArH), 7.45-7.58 (m, 4H, ArH), 7.74 (t, J_{HH} = 8.7, 2H, ArH), 7.92 (t, J_{HH} = 8.9, 2H, ArH); ^{13}C NMR (DMSO-d6) δ: 15.1 ($OCH_2\mathit{C}H_3$), 38.2 (d, $^{1}J_{CP}$ = 67.7, C_4), 46.7 (d, $^{2}J_{CP}$ = 4.5, C_3), 64.7 ($O\mathit{C}H_2CH_3$), 113.2 (d, J_{CP} = 2.7), 119.6 (d, J_{CP} =

3.3), 120.4, 120.8 (d, J_{CP} = 3.3), 124.0 (d, J_{CP} = 2.2), 128.8 (d, $^{3}J_{CP}$ = 11.0, $C_3{}^{'I}$), 128.9 (d, $^{3}J_{CP}$ = 11.0, $C_3{}^{'II}$), 131.8 (d, $^{2}J_{CP}$ = 8.7, $C_2{}^{'I}$), 132.0 (d, $^{1}J_{CP}$ = 92.4, $C_1{}^{'I}$), 132.18 (d, J_{CP} = 2.7, $C_4{}^{'I}$), 132.20 (d, $^{2}J_{CP}$ = 8.5, $C_2{}^{'II}$), 132.31 (d, J_{CP} = 2.3, $C_4{}^{'II}$), 132.33 (d, $^{1}J_{CP}$ = 89.9, $C_1{}^{'II}$), 141.0 (d, J_{CP} = 4.1, C_8), 146.8 (d, $^{3}J_{CP}$ = 2.6, C_{8a}), 164.5 (d, $^{3}J_{CP}$ = 2.1, C_2); ^{31}P NMR (DMSO-d6) δ: 28.7; $[M+H]^{+}_{found}$ = 417.1369, $C_{24}H_{22}N_2O_3P$ requires: 417.1368.

*[Bis(p-tolyl)](2-amino-3-cyano-8-ethoxy-4H-chromen-4-yl)phosphine oxide (**12b**)*

Yield: 90% (0.40 g), white crystal; Mp: 228-230 °C; ^{1}H NMR (DMSO-d6) δ: 1.31 (t, J_{HH} = 7.0, 3H, $OCH_2C\mathit{H}_3$), 2.32 (s, 3H, $CH_3{}^{I}$), 2.35 (s, 3H, $CH_3{}^{II}$), 4.03 (qt, J_{HH} = 6.9, J_{HH} = 3.3, 2H, $OC\mathit{H}_2CH_3$), 4.90 (d, $^{2}J_{HP}$ = 3.9, 1H, CHP), 6.21 (d, J_{HH} = 7.6, 1H, ArH), 6.75 (t, J_{HH} = 8.0, 1H, ArH), 6.86 (d, J_{HH} = 8.2, 1H, ArH), 7.04 (brs, 2H, NH_2), 7.24 (d, J_{HH} = 5.5, 2H, ArH), 7.31 (d, J_{HH} = 5.4, 2H, ArH), 7.60 (t, J_{HH} = 10.5, 2H, ArH), 7.77 (t, J_{HH} = 10.4, 2H, ArH); ^{13}C NMR (DMSO-d6) δ: 15.1 ($OCH_2\mathit{C}H_3$), 21.56 ($CH_3{}^{I}$), 21.60 ($CH_3{}^{II}$), 38.2 (d, $^{1}J_{CP}$ = 68.2, C_4), 47.0 (d, $^{2}J_{CP}$ = 4.4, C_3), 64.7 ($O\mathit{C}H_2CH_3$), 113.2 (d, J_{CP} = 2.1), 119.9 (d, J_{CP} = 3.4), 120.5, 120.9 (d, J_{CP} = 3.1), 123.9 (d, J_{CP} = 2.0), 128.9 (d, $^{1}J_{CP}$ = 95.1, $C_1{}^{'I}$), 129.2 (d, $^{1}J_{CP}$ = 92.6, $C_1{}^{'II}$), 129.3 (d, $^{3}J_{CP}$ = 12.2, $C_3{}^{'I}$), 129.4 (d, $^{3}J_{CP}$ = 12.3, $C_3{}^{'II}$), 131.9 (d, $^{2}J_{CP}$ = 9.1, $C_2{}^{'I}$), 132.2 (d, $^{2}J_{CP}$ = 9.0, $C_2{}^{'II}$), 141.0 (d, J_{CP} = 4.0, C_8), 141.95 (d, J_{CP} = 2.6, $C_4{}^{'I}$), 142.03 (d, J_{CP} = 2.5, $C_4{}^{'II}$), 146.7 (d, $^{3}J_{CP}$ = 2.8, C_{8a}), 164.3 (d, $^{3}J_{CP}$ = 1.7, C_2); ^{31}P NMR (DMSO-d6) δ: 29.1; $[M+H]^{+}_{found}$ = 445.1682, $C_{26}H_{26}N_2O_3P$ requires: 445.1681.

*[Bis(3,5-dimethylphenyl)](2-amino-3-cyano-8-ethoxy-4H-chromen-4-yl)phosphine oxide (**12c**)*

Yield: 88% (0.42 g), white crystal; Mp: 272-274 °C; ^{1}H NMR (DMSO-d6) δ: 1.31 (t, J_{HH} = 7.0, 3H, $OCH_2C\mathit{H}_3$), 2.25 (s, 6H, $CH_3{}^{I}$), 2.31 (s, 6H, $CH_3{}^{II}$), 4.00-4.07 (m, 2H, $OC\mathit{H}_2CH_3$), 4.91 (d, $^{2}J_{HP}$ = 4.1, 1H, CHP), 6.22 (d, J_{HH} = 7.7, 1H, ArH), 6.77 (t, J_{HH} = 8.0, 1H, ArH), 6.87 (d, J_{HH} = 8.2, 1H, ArH), 7.02 (brs, 2H, NH_2), 7.15 (d, J_{HH} = 21.0, 2H, ArH), 7.30 (d, J_{HH} = 10.8, 2H, ArH), 7.47 (d, J_{HH} = 10.9, 2H, ArH); ^{13}C NMR (DMSO-d6) δ: 15.1 ($OCH_2\mathit{C}H_3$), 21.3 ($CH_3{}^{I}$), 21.4 ($CH_3{}^{II}$), 38.1 (d, $^{1}J_{CP}$ = 67.7, C_4), 47.2 (d, $^{2}J_{CP}$ = 4.1, C_3), 64.7 ($O\mathit{C}H_2CH_3$), 113.1 (d, J_{CP} = 2.7), 120.0 (d, J_{CP} = 3.0), 120.7, 120.9 (d, J_{CP} = 1.9), 123.9 (d, J_{CP} = 1.4), 129.5 (d, $^{2}J_{CP}$ = 8.0, $C_2{}^{'I}$), 129.8 (d, $^{2}J_{CP}$ = 8.0, $C_2{}^{'II}$), 131.8 (d, $^{1}J_{CP}$ = 92.1, $C_1{}^{'I}$), 132.0 (d, $^{1}J_{CP}$ = 89.6, $C_1{}^{'II}$), 133.4 (d, J_{CP} = 5.5, $C_4{}^{'I}$), 133.6 (d, J_{CP} = 5.2, $C_4{}^{'II}$), 137.8 (d, $^{3}J_{CP}$ = 11.7, $C_3{}^{'I}$), 137.9 (d, $^{3}J_{CP}$ = 11.5, $C_3{}^{'II}$), 141.1 (d, J_{CP} = 4.0, C_8), 146.7 (d, $^{3}J_{CP}$ = 2.6, C_{8a}), 164.3 (d, $^{3}J_{CP}$ = 1.8, C_2); ^{31}P NMR (DMSO-d6) δ: 25.2; $[M+H]^{+}_{found}$ = 473.1997, $C_{28}H_{30}N_2O_3P$ requires: 473.1994.

*[Bis(3,5-dimethylphenyl)](2-amino-3-cyano-8-ethoxy-4H-chromen-4-yl)phosphine oxide (**12d**)*

Yield: 82% (0.42 g), white crystal; Mp: 237-238 °C; ^{1}H NMR (DMSO-d6) δ: 1.28 (t, J_{HH} = 6.9, 3H, OCH_2CH_3), 4.01 (qd, J_{HH} = 7.0, 2.6, 2H, OCH_2CH_3), 5.29 (d, $^{2}J_{HP}$ = 3.1, 1H, CHP), 6.29 (d, J_{HH} = 7.6, 1H, ArH), 6.68 (t, J_{HH} = 8.0, 1H, ArH), 6.84 (d, J_{HH} = 8.1, 1H, ArH), 7.12 (brs, 2H, NH_2), 7.54-7.67 (m, 4H, ArH), 7.94-8.16 (m, 8H, ArH), 8.42 (d, J_{HH} = 12.5, 1H, ArH), 8.60 (d, J_{HH} = 12.5, 1H, ArH); ^{13}C NMR (DMSO-d6) δ: 15.1 (OCH_2CH_3), 38.0 (d, $^{1}J_{CP}$ = 67.8, C_4), 46.7 (d, $^{2}J_{CP}$ = 4.4, C_3), 64.6 (OCH_2CH_3), 113.2 (d, J_{CP} = 2.1), 119.7 (d, J_{CP} = 3.1), 120.5, 120.6 (d, J_{CP} = 3.1), 124.1 (d, J_{CP} = 1.3), 126.9 (d, J_{CP} = 10.0, $C_{(naphtyl)}$), 127.2 (d, J_{CP} = 10.1, $C_{(naphtyl)}$), 127.3 (d, J_{CP} = 14.1, $C_{(naphtyl)}$), 128.2 ($C_{(naphtyl)}$), 128.3 (d, J_{CP} = 8.0, $C_{(naphtyl)}$), 128.4 (d, J_{CP} = 7.9, $C_{(naphtyl)}$), 128.6 (d, J_{CP} = 6.3, $C_{(naphtyl)}$), 129.3 (d, J_{CP} = 16.2, $C_{(naphtyl)}$), 129.6 (d, $^{1}J_{CP}$ = 93.1, $C_{1(naphtyl)^{I}}$), 129.8 (d, $^{1}J_{CP}$ = 89.9, $C_{1(naphtyl)^{II}}$), 132.4 (d, J_{CP} = 12.1, $C_{(naphtyl)}$), 132.6 (d, J_{CP} = 12.3, $C_{(naphtyl)}$), 133.6 (d, J_{CP} = 7.8, $C_{(naphtyl)}$), 133.1 (d, J_{CP} = 7.9, $C_{(naphtyl)}$), 134.5 (d, J_{CP} = 2.2, $C_{(naphtyl)}$), 134.7 (d, J_{CP} = 2.2, $C_{(naphtyl)}$), 141.1 (d, $^{3}J_{CP}$ = 4.1, C_8), 146.8 (d, $^{3}J_{CP}$ = 2.7, C_{8a}), 164.5 (d, $^{3}J_{CP}$ = 1.9, C_2); ^{31}P NMR (DMSO-d6) δ: 27.8; $[M+H]^{+}_{found}$ = 517.1683, $C_{32}H_{26}N_2O_3P$ requires: 517.1681.

Single crystal X-ray diffraction measurements

Single-crystal X-ray diffraction data of **2c**, **6e** and **8a-c** were collected on an Agilent Technologies SuperNova Dual diffractometer using Mo-Kα radiation (λ = 0.71073 Å) or or Cu-Kα radiation (λ = 1.54184 Å) at 150 K. The data were processed using CrysAlis Pro [S5]. Structure was solved by ShelXT [S6] using intrinsic phasing and refined by a full-matrix least-squares procedure based on F^2 with ShelXL [S7] using Olex2 program suite [S8]. All the non-hydrogen atoms were refined anisotropically. Hydrogen atoms were readily located in difference Fourier maps, and were subsequently treated as riding atoms in geometrically idealized positions with C–H = 0.95 Å (aromatic), 1.00 Å (methine), 0.99 Å (methylene) or 0.98 Å (methyl), and with U_{iso}(H) = kU_{eq}(C), where k = 1.5 for methyl group and 1.2 for all H atoms. The amino H atoms were refined fixing the bond lengths in **2c**, **6e** while in **8a-c** they were refined freely and were treated with U_{iso}(H) = 1.2 U_{eq}(N). The crystallographic data are listed in Table S1. Deposition Numbers 2083632–2083636 (for **2c**, **6e** and **8a-c**) contain the supplementary crystallographic data for this paper. These data are provided free of charge by the joint Cambridge Crystallographic Data Centre and Fachinformationszentrum Karlsruhe Access Structures service www.ccdc.cam.ac.uk/structures.

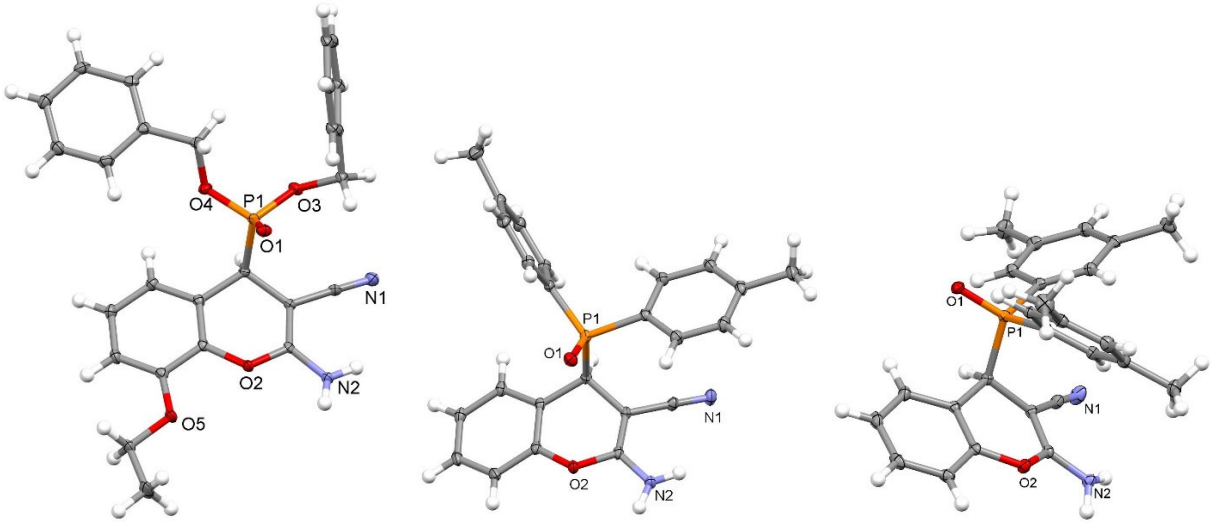


Figure S1. Molecular structures of **6e** (left), **8b** (middle) and **8c** (right).

Table **S1**: Crystal data and structure refinement for **2c**, **6e**, **8a**·CH_3CN, **8b** and **8c**.

	2c	**6e**	**8a**·CH_3CN	**8b**	**8c**
CCDC number	2083632	2083633	2083634	2083635	2083636
Empirical formula	$C_{18}H_{25}N_2O_4P$	$C_{26}H_{25}N_2O_5P$	$C_{24}H_{20}N_3O_2P$	$C_{24}H_{21}N_2O_2P$	$C_{26}H_{25}N_2O_2P$
Formula weight	364.37	476.45	413.40	400.40	428.45
***T*/K**	150.00(10)	150.00(10)	150.00(10)	150.00(10)	150.00(10)
Crystal system	monoclinic	triclinic	monoclinic	triclinic	monoclinic
Space group	$P2_1/n$	$P\bar{1}$	$P2_1/c$	$P\bar{1}$	$P2_1/c$
***a*/Å**	14.4732(3)	9.9066(4)	12.3634(7)	9.0000(5)	12.9952(5)
***b*/Å**	8.9061(2)	9.9454(4)	10.7573(6)	11.1653(8)	11.0767(5)
***c*/Å**	15.9214(4)	12.3415(6)	15.9936(8)	12.3858(7)	15.1578(6)
***α*/°**	90	102.791(4)	90	115.027(7)	90
***β*/°**	109.314(2)	101.823(4)	101.939(5)	91.058(5)	93.224(4)
***γ*/°**	90	90.163(3)	90	113.010(6)	90
***V*/Å^3**	1936.76(8)	1159.14(9)	2081.1(2)	1012.50(13)	2178.42(16)
Z	4	2	4	2	4
D_{calc}**/g cm^{-3}**	1.250	1.365	1.319	1.313	1.306
***μ*/mm^{-1}**	1.462	1.398	0.158	0.159	0.152
***F*(000)**	776.0	500.0	864.0	420.0	904.0
Reflections collected	7323	7877	10972	8457	11113
Data/restraints/parameters	3670/2/234	4385/2/314	4755/0/278	4649/0/270	4993/0/290
R_{int}	0.0338	0.0300	0.0243	0.0229	0.0272
GOF, *S*	1.075	1.043	1.040	1.030	1.019
R_1, wR_2 [$I \geq 2\sigma(I)$]	0.0534, 0.1380	0.0417, 0.1130	0.0426, 0.1064	0.0433, 0.0999	0.0416, 0.1038
R_1, wR_2 **[all data]**	0.0575, 0.1431	0.0442, 0.1163	0.0552, 0.1167	0.0593, 0.1114	0.0553, 0.1128
$\Delta\rho_{min}$, $\Delta\rho_{max}$ **[e Å^{-3}]**	0.53, –0.72	0.32, –0.54	0.55, –0.46	0.38, –0.36	0.36, –0.40

Table S2. Hydrogen bond geometry for **2c**, **6e**, **8a**·CH_3CN, **8b** and **8c**.

D–H···A	D–H (Å)	H···A (Å)	D···A (Å)	D–H···A (°)	Symmetry code
2c					
N2–H2A···O1	0.908(16)	1.887(16)	2.793(2)	175(2)	1½ – *x*, ½ + *y*, ½ – *z*
N2–H2B···N1	0.875(16)	2.157(17)	3.015(2)	167(2)	2 – *x*, 1 – *y*, 1 – *z*
6e					
N2–H2A···O1	0.866(15)	1.989(16)	2.8102(17)	157.7(18)	1 – *x*, 2 – *y*, 1 – *z*
C1–H1···N1	1.00	2.59	3.391(2)	136.7	2 – *x*, 2 – *y*, 1 – *z*
8a·CH_3CN					
N2–H2A···O1	0.90(2	1.92(2)	2.823(2)	174.0(19)	–*x*, ½ + *y*, 1½ – *z*
N2–H2B···N1	0.87(2)	2.39(2)	3.186(2)	151.6(18)	–*x*, 1 – *y*, 1 – *z*
8b					
N2–H2A···O1	0.92(2)	1.89(2)	2.811(2)	177.2(19)	2 – *x*, 1 – *y*, 1 – *z*
N2–H2B···N1	0.85(2)	2.23(2)	3.065(2)	167.6(19)	1 – *x*, 1 – *y*, 1 – *z*
8c					
N2–H2A···O1	0.88(2)	2.03(2)	2.9060(19)	171.4(18)	*x*, 1½ – *y*, ½ + *z*
N2–H2B···N1	0.88(2)	2.24(2)	3.073(2)	159.5(18)	–*x*, 1 – *y*, 1 – *z*

Biological Evaluation

Cell culture

Cells were purchased from the American Type Culture Collection (ATCC, Manassas, Virginia, USA). Human lung adenocarcinoma A549 cells were maintained in Dulbecco's Modified Eagle Medium (DMEM), while mouse fibroblast NIH/3T3 and human promyelocytic leukemia HL-60 cells were maintained in Roswell Park Memorial Institute 1640 medium (RPMI-1640) containing 10% FCS. Media were supplemented with 2 mM GlutaMAX, 100 U/mL penicillin, and 100 µg/mL streptomycin (Life Technologies, Carlsbad, California, USA). Cell cultures were maintained at 37 °C in a humidified incubator in an atmosphere of 5% CO_2 (Sanyo, Japan).

Antibacterial activity

All reagents were purchased from Sigma-Aldrich (Hungary, Budapest). *E. coli-GFP* and *B. subtilis-GFP* bacteria were grown in Lysogeny Broth (Luria-Bertani broth, LB, 10 g tryptone, 5 g yeast extract, 10 g/L NaCl, pH 7.0) medium overnight (ON) at 37 °C in an incubator with continuous shaking [S9,S10]. The ON bacterial culture was diluted (*E. coli-GFP:* 1:10000, *B. subtilis-GFP*: 1:1000) in LB medium containing 10 µg/ml ampicillin. 200 µl of diluted *E. coli* suspension per well were transferred to 96-well plates and different agents were added in the appropriate concentration, then incubated in a shaker (600 rpm) for 3 h at 37 °C. Test compounds were dissolved in 3-fold amounts of dimethyl sulfoxide (DMSO). Cells were treated with an increasing concentration of test compounds (1 µM – 30 µM). Doxycyclin (IC_{50}= 0.10±0.02 and 0.04±0.01 µM for *E. coli* and *B. subtilis*) and gentamicine (IC_{50}= 4.23±0.99 and 0.49±0.14 µM for *E. coli* and *B. subtilis*) were used as positive controls. For induction of the GFP expression IPTG (0.1 mM final concentration) was added to each well and incubated for 3 h at 37 °C.

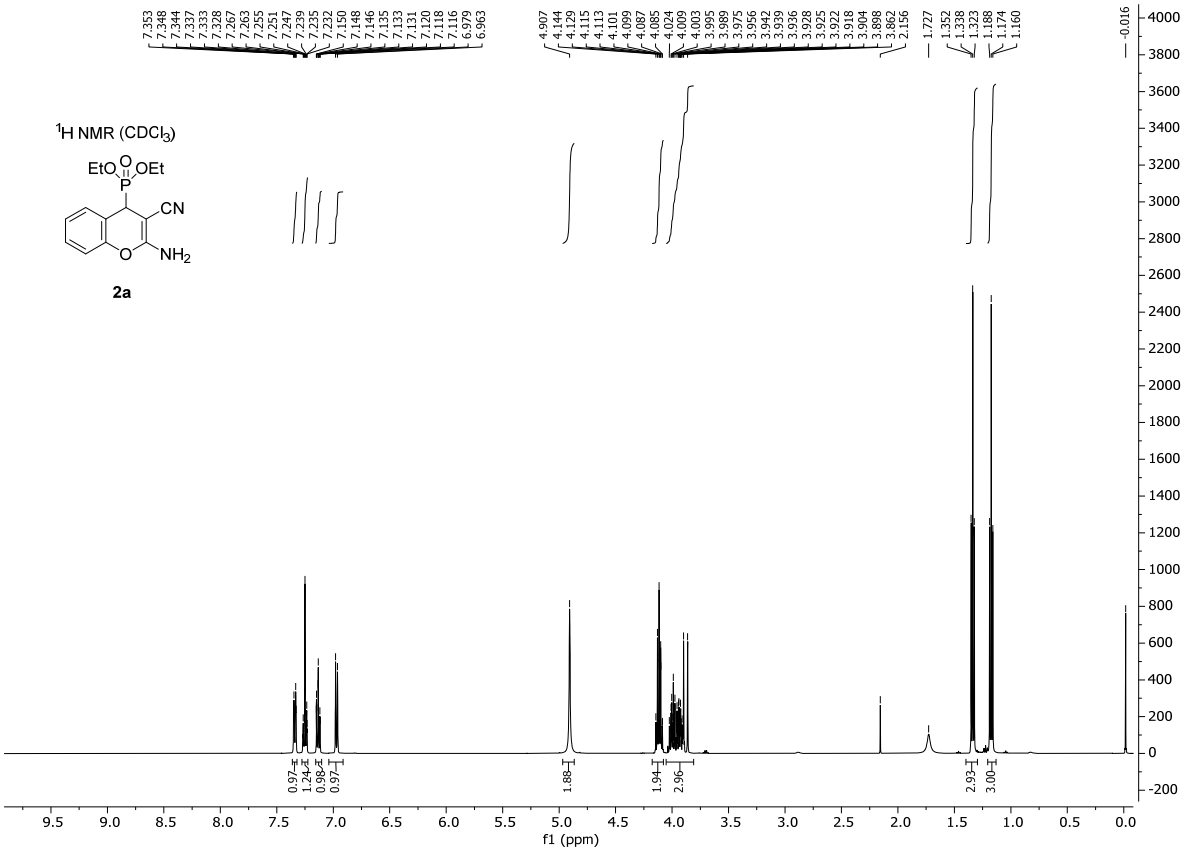
Following incubation samples were centrifuged at 2750 rpm, room temperature (RT) for 5 min and washed twice with 200 µl PBS, intermitted with a centrifugation step between the two washes. After a third centrifugation step the bacterial cells were suspended in 100 µl PBS. The quantity of bacteria was estimated according to the fluorimetric measurements. The fluorescence of the bacterial cells was measured by Victor™ 1420 Multilabel Counter (Perkin Elmer, Waltham, MA, U.S.) at 485/535 nm for 1 sec per well controlled by Wallac 1420 Manager software. Each treatment was repeated in at least 2 wells per plate during the experiments. % fluorescence intensity based on the quantity of *E. coli-GFP* cells was calculated using untreated control values as 100%. Error was represented by standard deviation (SD). IC_{50} values (50% inhibiting concentration) were calculated by GraphPad Prism® 5.

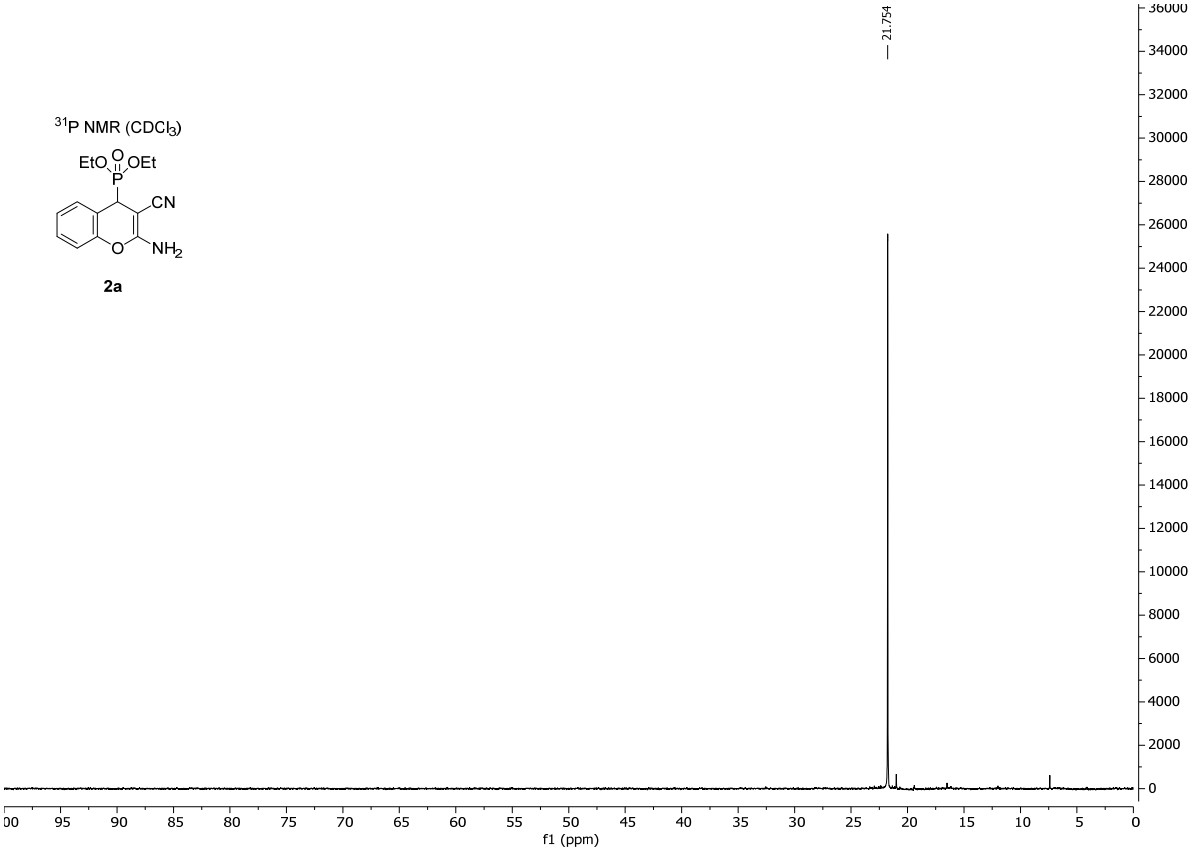
Cytotoxicity assay

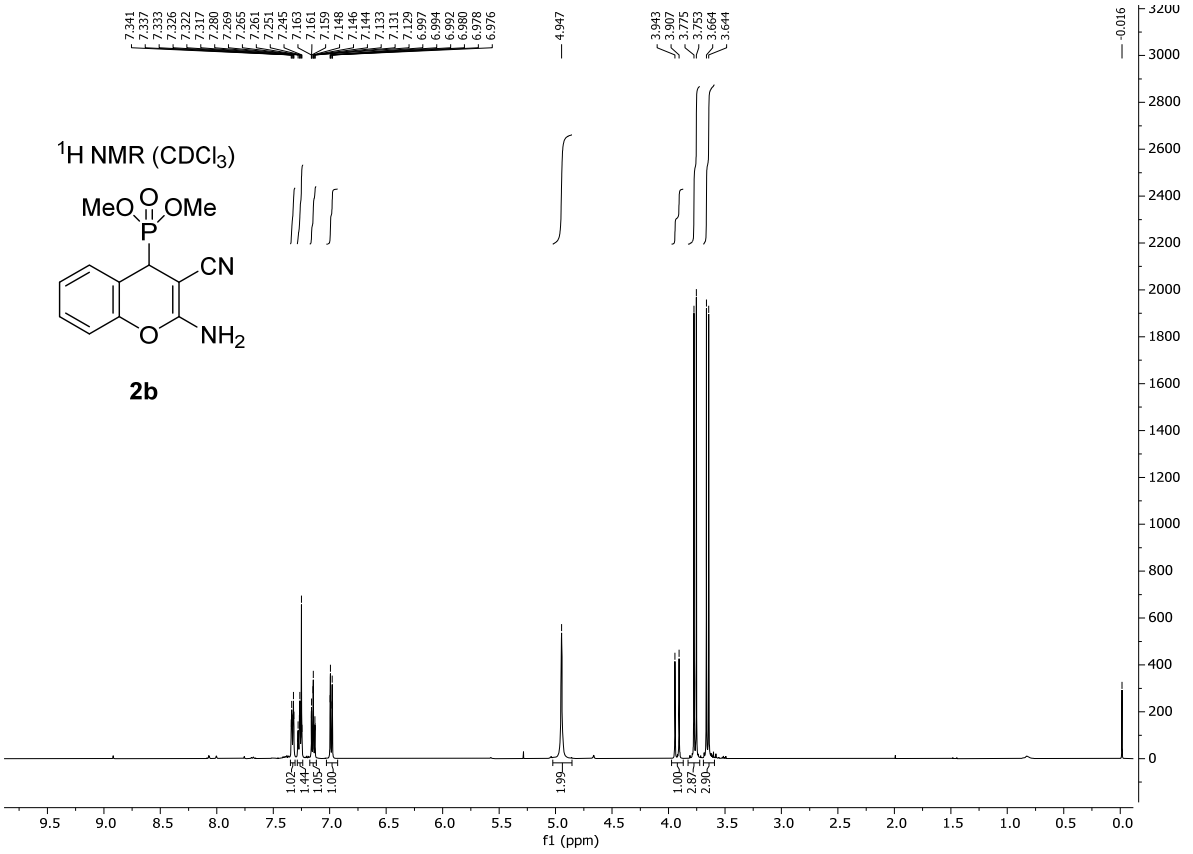
Cytotoxicity of the synthesized molecules was determined on A549, NIH/3T3 and HL-60 cells using the fluorescent Resazurin assay as described previously [S11].

Briefly, cells (A549 and NIH/3T3: 6000, HL-60: 120.000 cells/well) were seeded into 96-well plates (Corning Life Sciences) in media and incubated overnight. Test compounds were dissolved in 3-fold amounts of dimethyl sulfoxide (DMSO). Cells were treated with an increasing concentration of test compounds (1 μM – 30 μM). Positive controls were doxorubicin for A549 and NIH/3T3 (IC_{50}= 0.31±0.24 μM and 5.65±0.81 μM, respectively), and bortezomib for HL60 (IC_{50}= 7.42±2.60 nM). Cell viability was determined after 72 h incubation. Resazurin reagent (Sigma-Aldrich) was added at a final concentration of 25 μg/mL. After a 2 h incubation for at 37 °C, 5% CO_2, fluorescence (530 nm excitation /580 nm emission) was recorded on a multimode microplate reader (Cytofluor4000, PerSeptive Biosytems). Viability was calculated with relation to untreated control cells and blank wells containing media without cells. IC_{50} values (50% inhibiting concentration) were calculated by GraphPad Prism® 5 (La Jolla, CA, USA). Student's t test was performed for individual test compound concentrations with relation to untreated control cell viability values.

^{1}H NMR, ^{13}C NMR and ^{31}P NMR spectra



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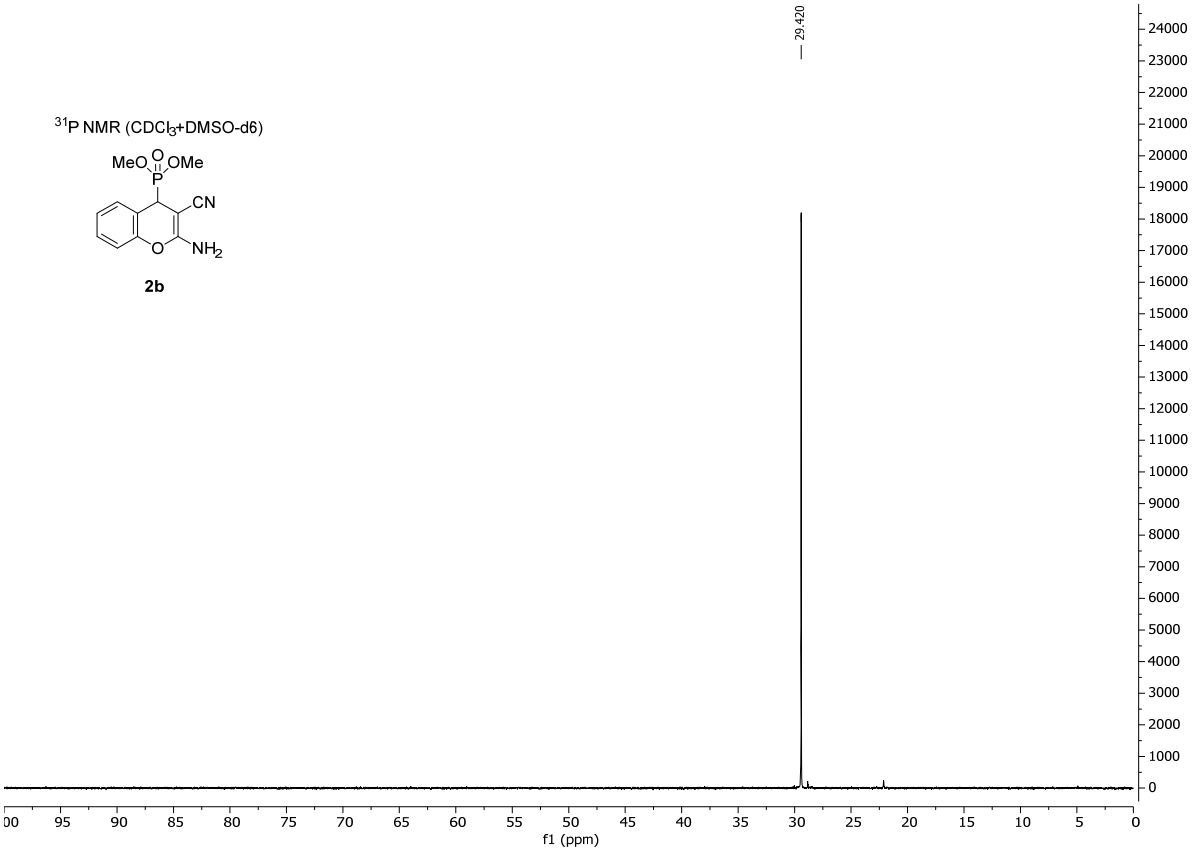
7.163
7.161
7.159
7.148
7.146
7.144
7.133
7.131
7.129
6.997
6.994
6.992
6.980
6.978
6.976
4.947
3.943
3.907
3.775
3.753
3.664
3.644
-0.016
1H NMR (CDCl3)
MeO
O
OMe
P
CN
O
NH2
2b
1.02
1.44
1.05
1.00
1.99
1.00
2.87
2.90
f1 (ppm)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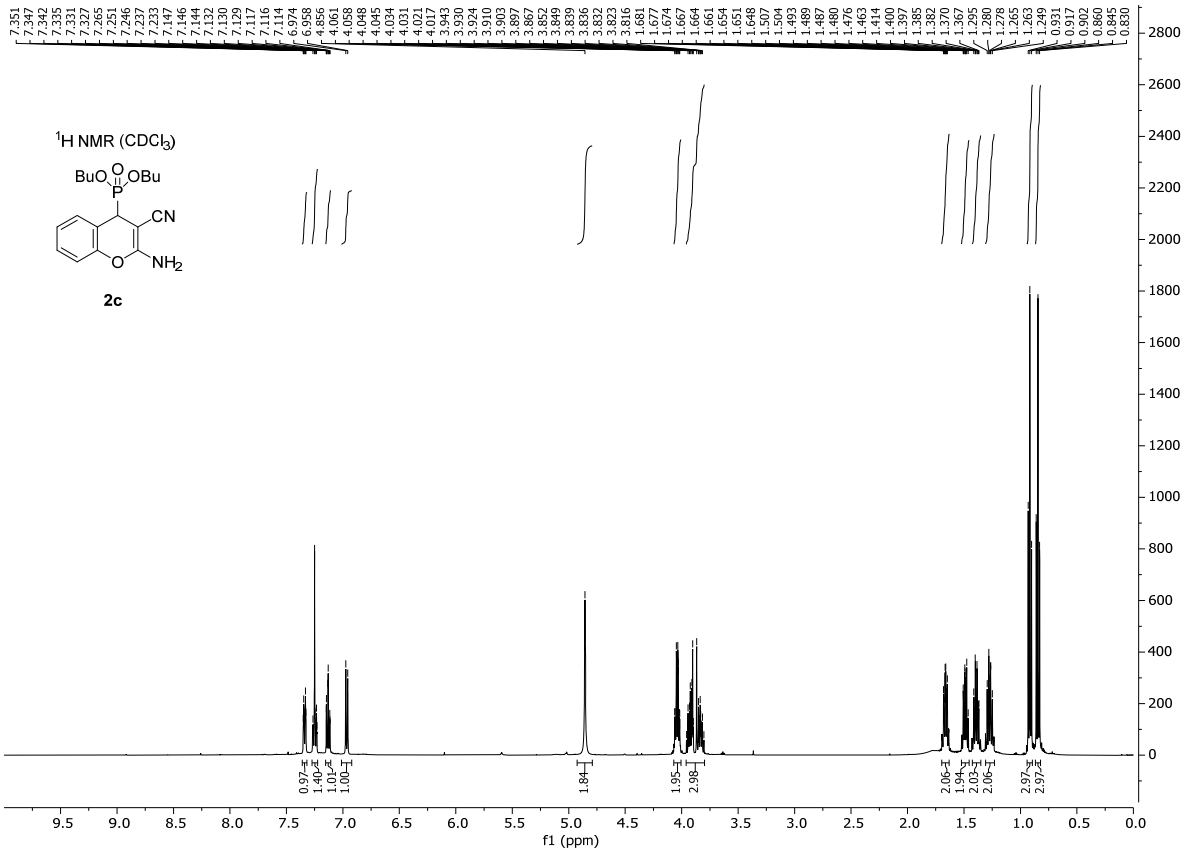
O
OMe
P
CN
O
NH2
2b
f1 (ppm)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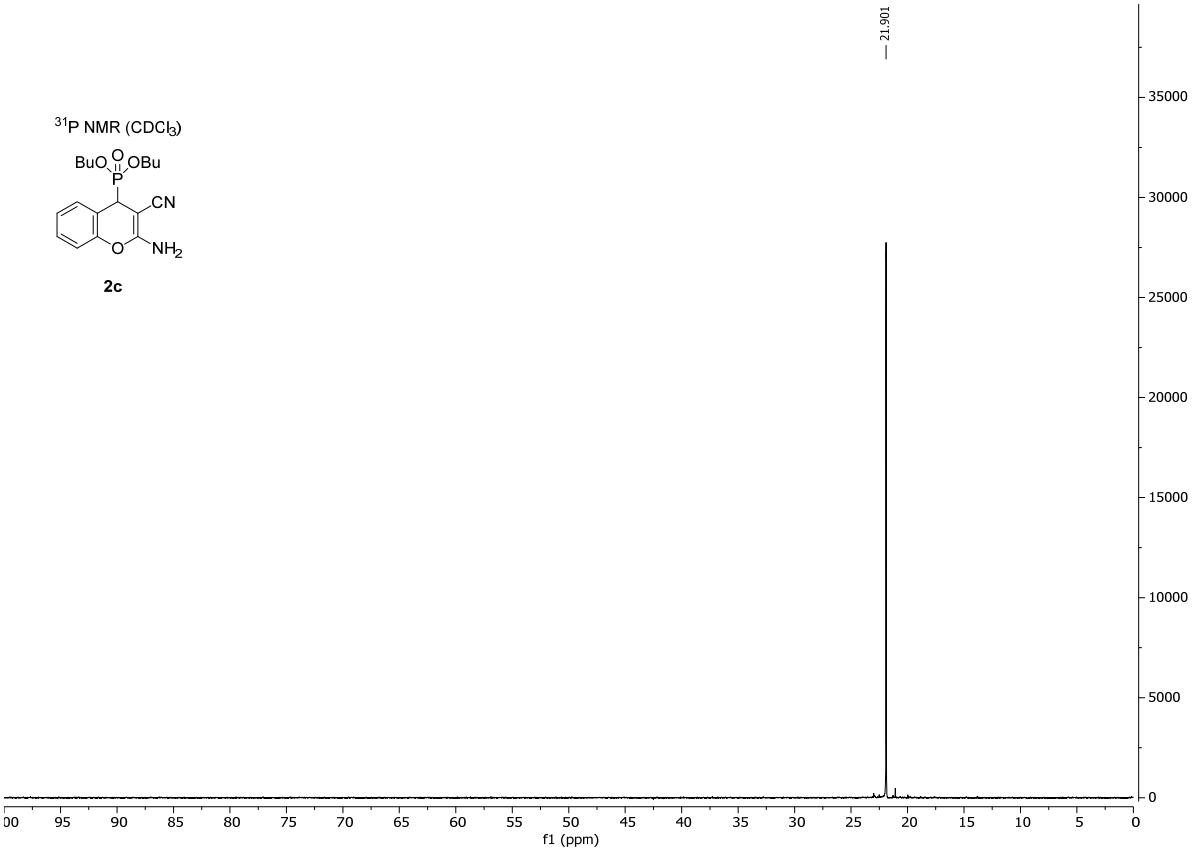
BuO
OBu
P
O
CN
NH$_2$
O
2c
f1 (ppm)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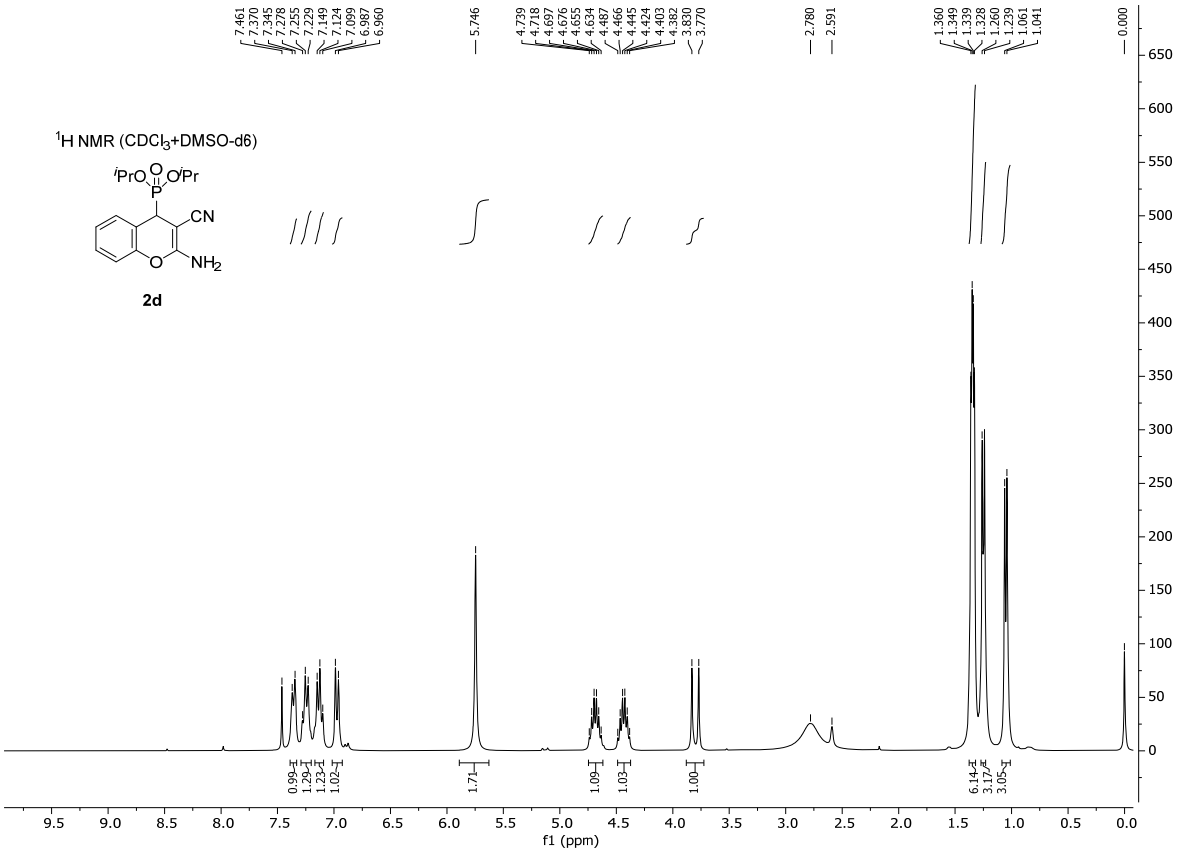
OBu
P
O
CN
NH$_2$
O
2c
f1 (ppm)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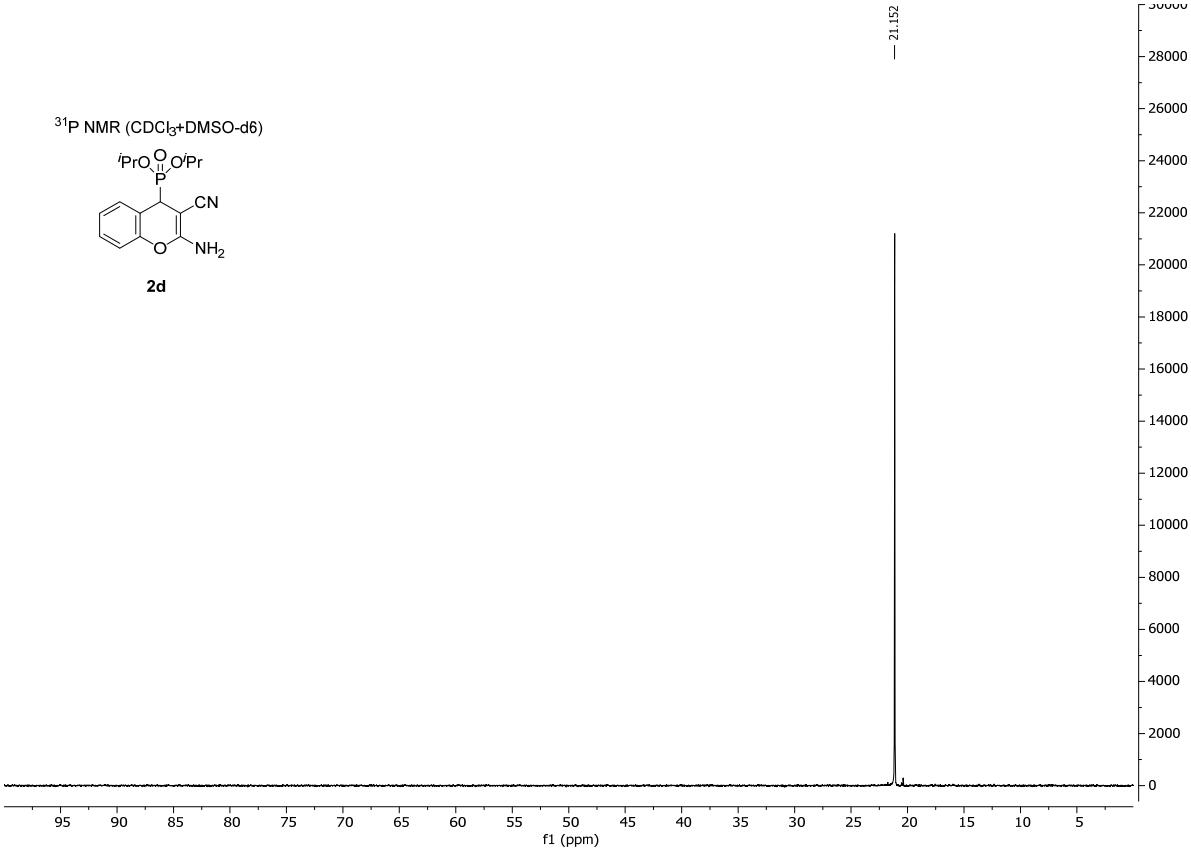
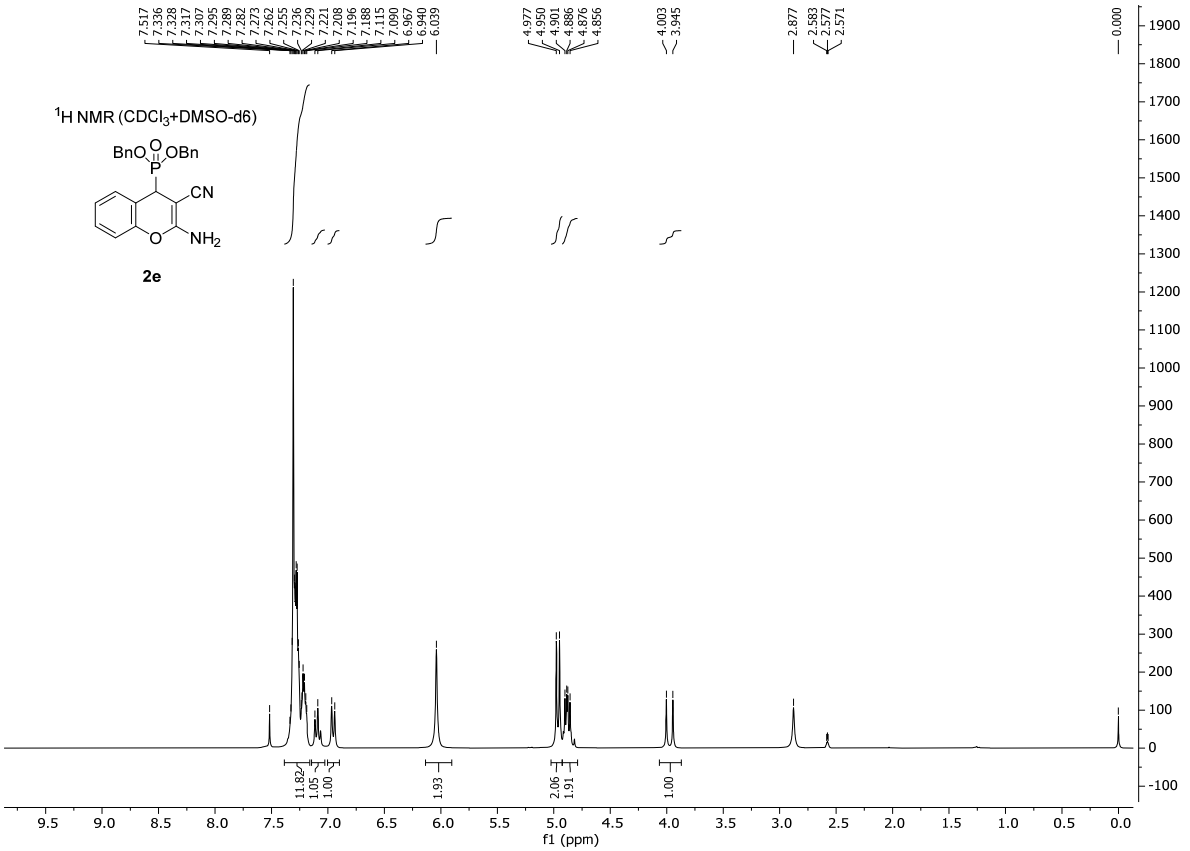
7.229
7.149
7.124
7.099
6.987
6.960
5.746
4.739
4.718
4.697
4.676
4.655
4.634
4.487
4.466
4.445
4.424
4.403
4.382
3.830
3.770
2.780
2.591
1.360
1.349
1.339
1.328
1.260
1.239
1.061
1.041
0.000
^{1}H NMR (CDCl$_3$+DMSO-d6)
^{i}PrO
O
O^{i}Pr
P
CN
O
NH$_2$
2d
0.99
1.29
1.23
1.02
1.71
1.09
1.03
1.00
6.14
3.17
3.05
f1 (ppm)


21.152
^{31}P NMR (CDCl$_3$+DMSO-d6)
^{i}PrO
O
O^{i}Pr
P
CN
O
NH$_2$
2d
f1 (ppm)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7.336
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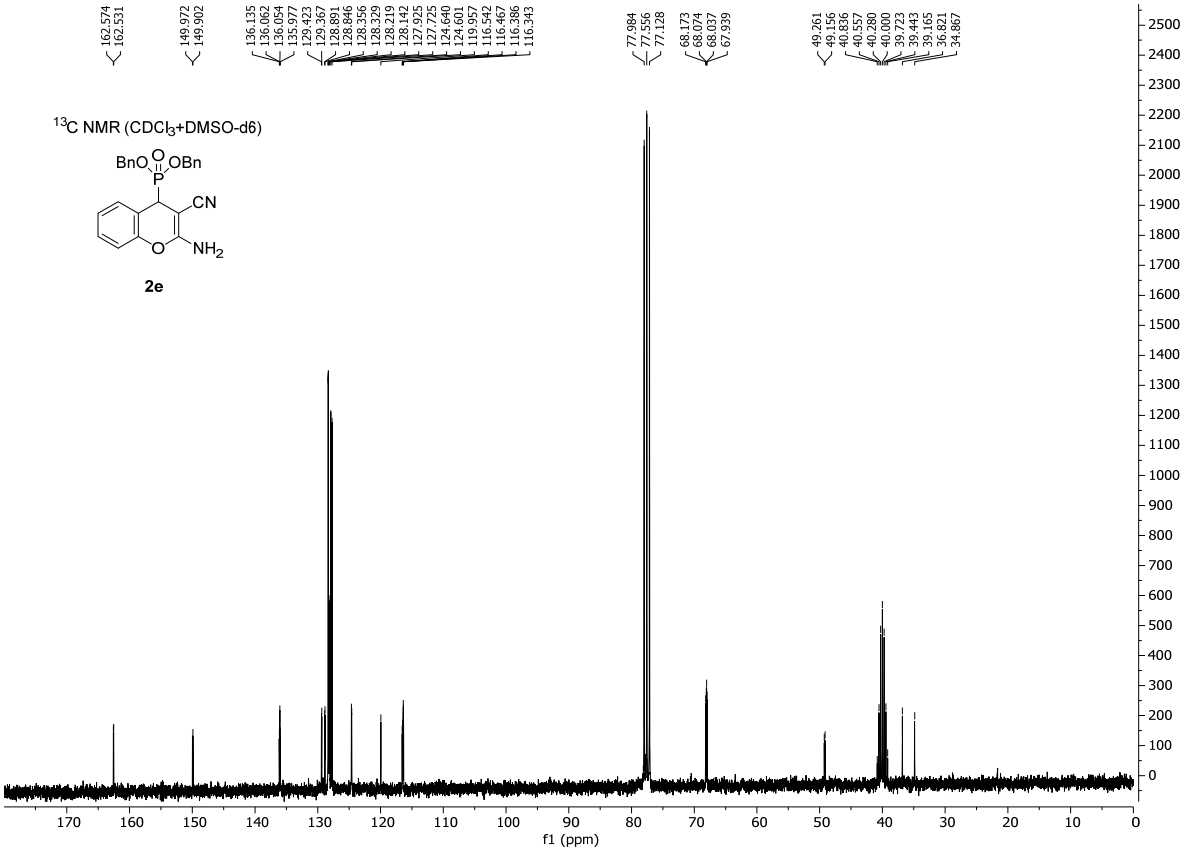
7.317
7.307
7.295
7.289
7.282
7.273
7.262
7.255
7.236
7.229
7.221
7.208
7.196
7.188
7.115
7.090
6.967
6.940
6.039
4.977
4.950
4.901
4.886
4.876
4.856
4.003
3.945
2.877
2.583
2.577
2.571
0.000
^{1}H NMR (CDCl$_3$+DMSO-d6)
BnO
OBn
P
O
CN
NH$_2$
2e
11.82
1.05
1.00
1.93
2.06
1.91
1.00
f1 (ppm)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149.902
136.135
136.062
136.054
135.977
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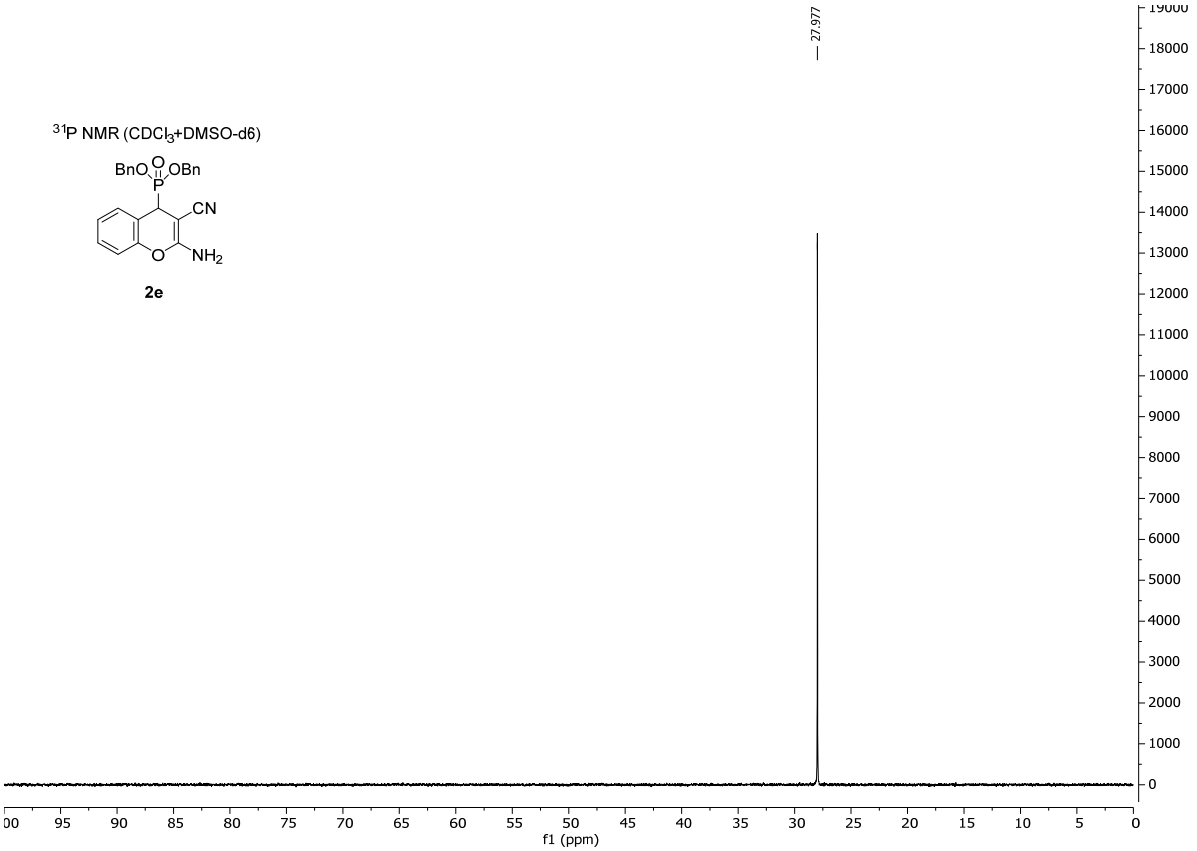
128.891
128.846
128.356
128.329
128.219
128.142
127.925
127.725
124.640
124.601
119.937
116.542
116.467
116.386
116.343
77.984
77.556
77.128
68.173
68.074
68.037
67.939
49.261
49.156
40.836
40.557
40.280
40.000
39.723
39.443
39.165
36.821
34.867
^{13}C NMR (CDCl$_3$+DMSO-d6)
BnO
OBn
P
O
CN
NH$_2$
2e
f1 (ppm)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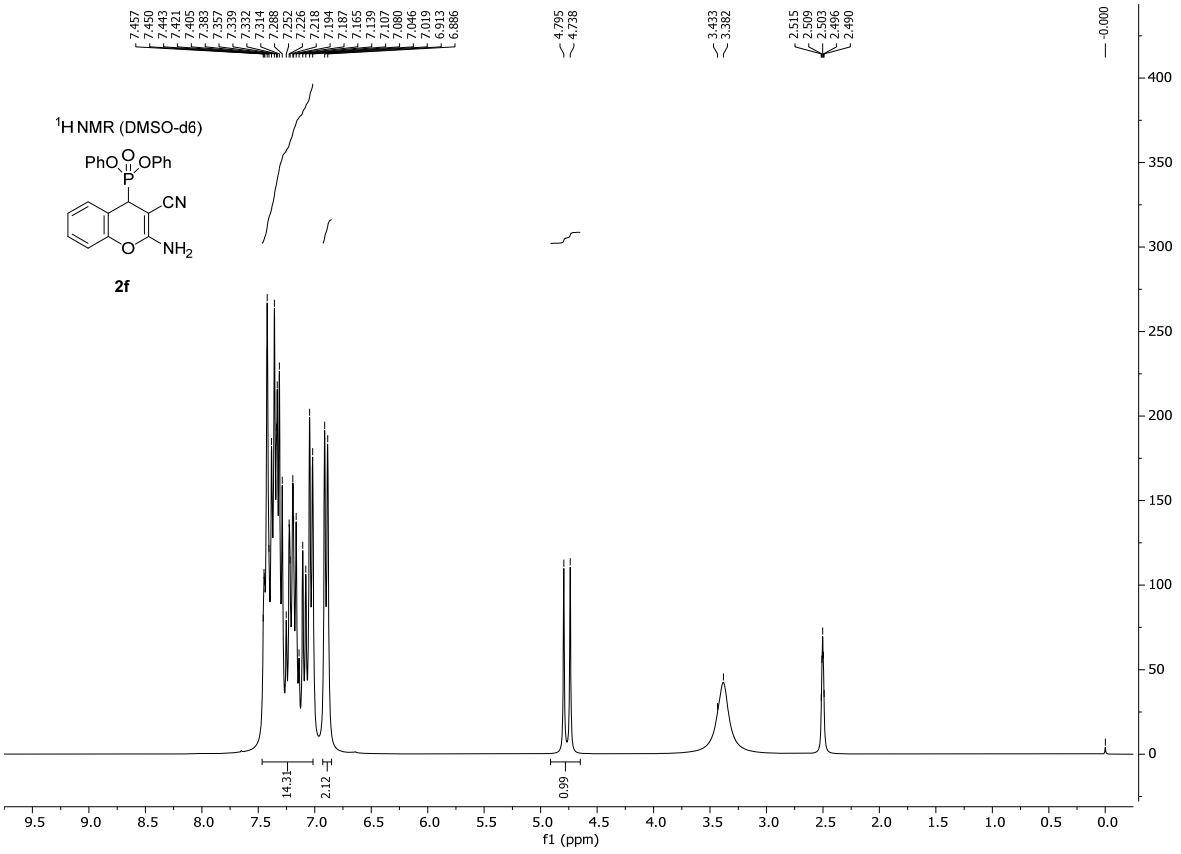
BnO
OBn
P
CN
NH2
O
2e
27.977
f1 (ppm)


1H NMR (DMSO-d6)
PhO
OPh
P
CN
NH2
O
2f
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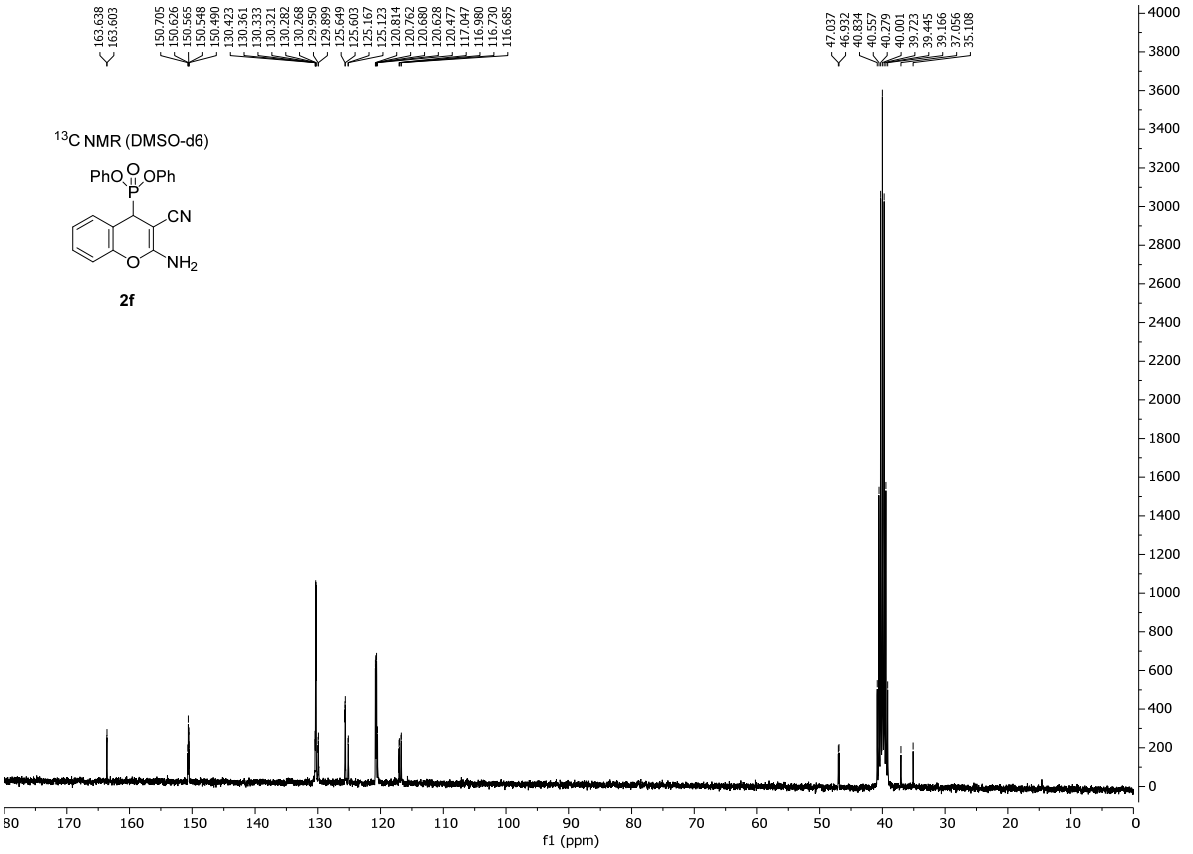
7.450
7.443
7.421
7.405
7.383
7.357
7.339
7.332
7.314
7.288
7.252
7.226
7.218
7.194
7.187
7.165
7.139
7.107
7.080
7.046
7.019
6.913
6.886
4.795
4.738
3.433
3.382
2.515
2.509
2.503
2.496
2.490
-0.000
14.31
2.12
0.99
f1 (ppm)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130.333
130.321
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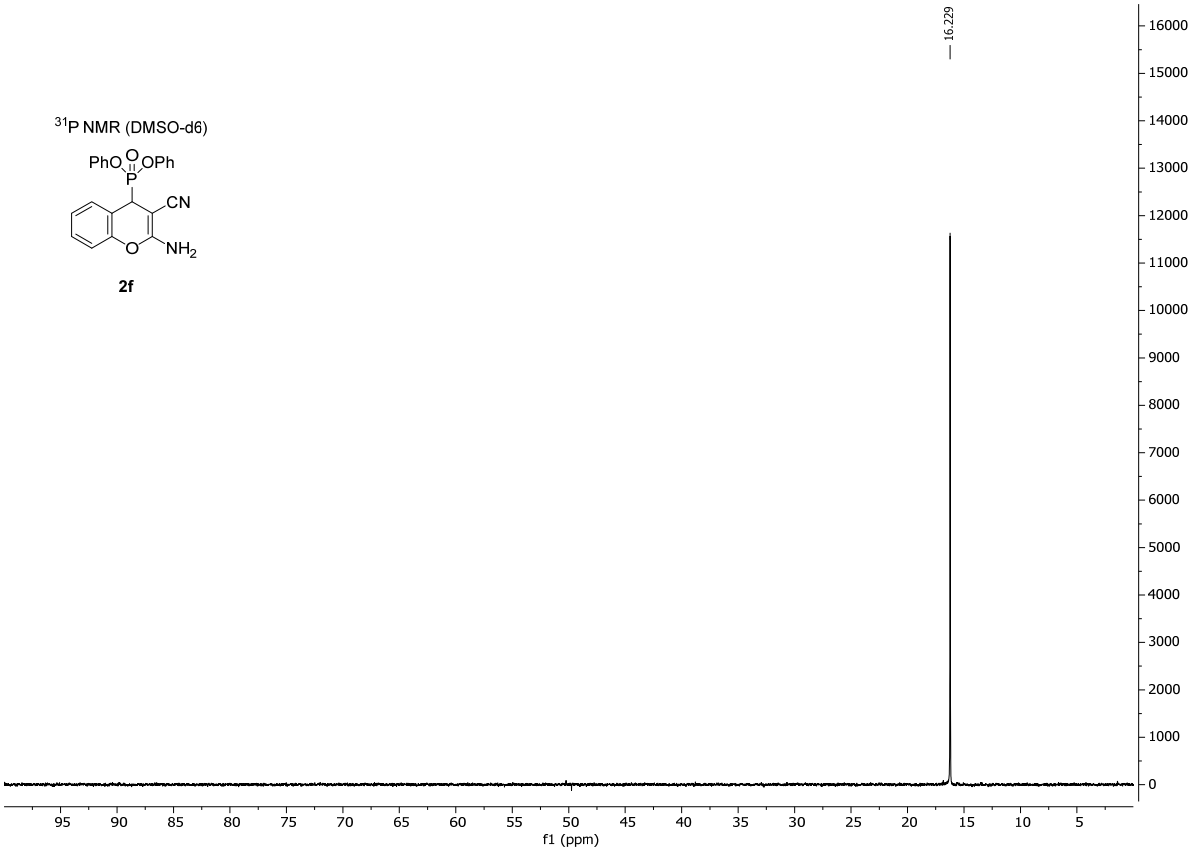
130.268
129.950
129.899
125.649
125.603
125.167
125.123
120.814
120.762
120.680
120.628
120.477
117.047
116.980
116.730
116.685
47.037
46.932
40.834
40.557
40.279
40.001
39.723
39.445
39.166
37.056
35.108
13C NMR (DMSO-d6)
PhO
OPh
P
CN
O
NH2
2f
f1 (ppm)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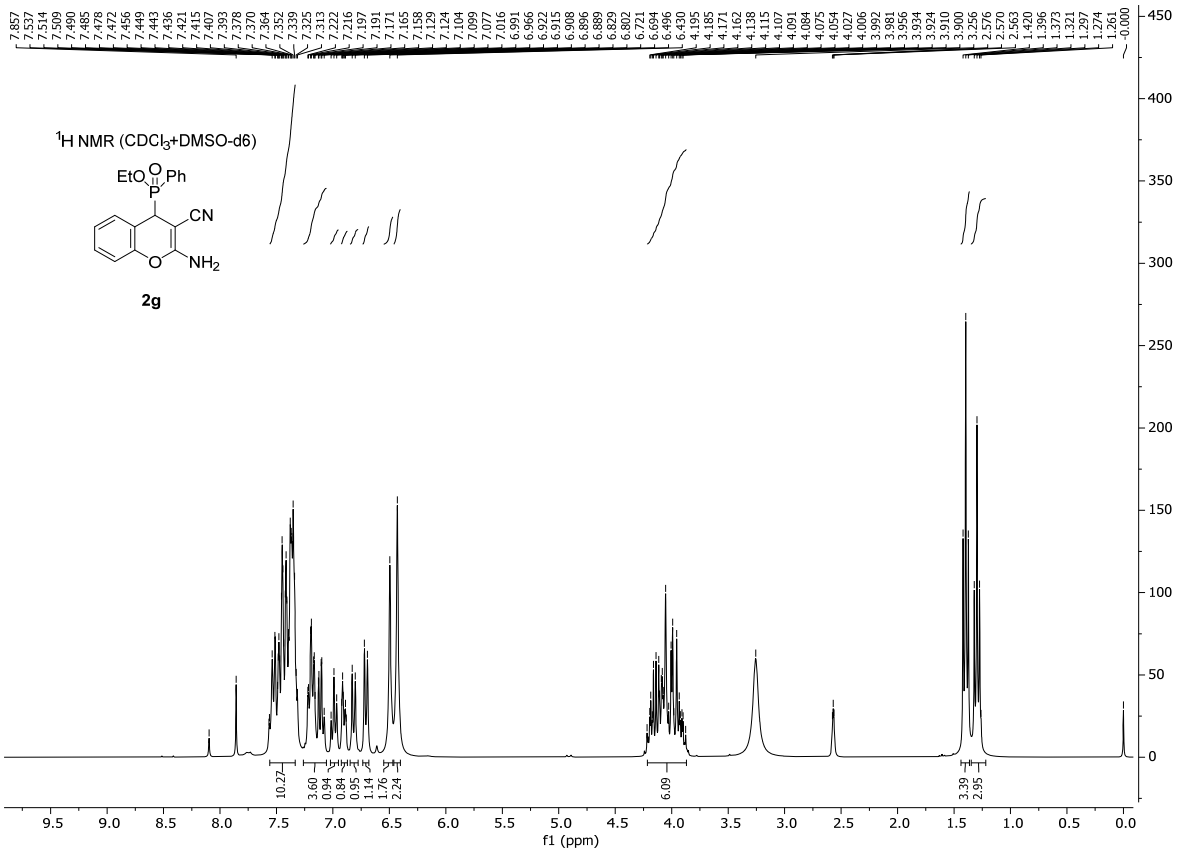
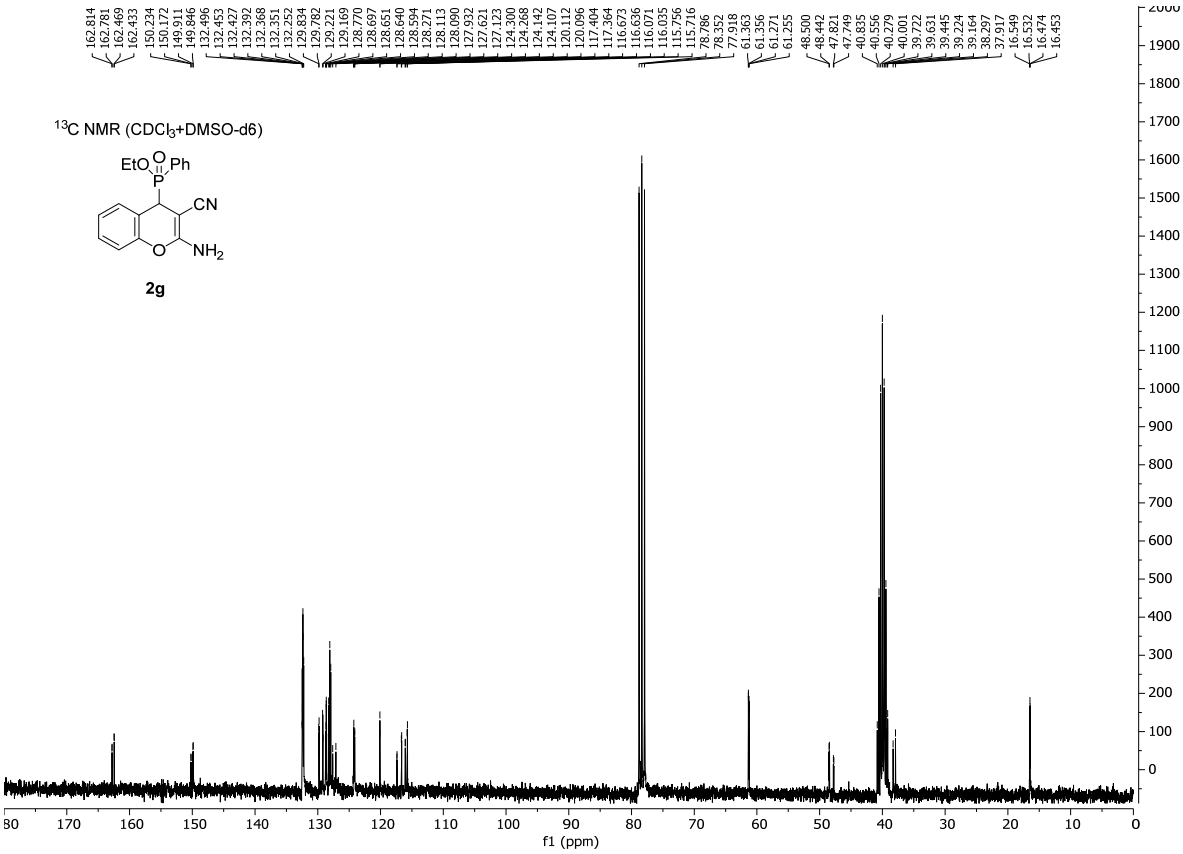
PhO
OPh
P
CN
O
NH2
2f
f1 (ppm)


^{1}H NMR (CDCl$_3$+DMSO-d6)
EtO
O
Ph
P
CN
O
NH$_2$
2g
f1 (ppm)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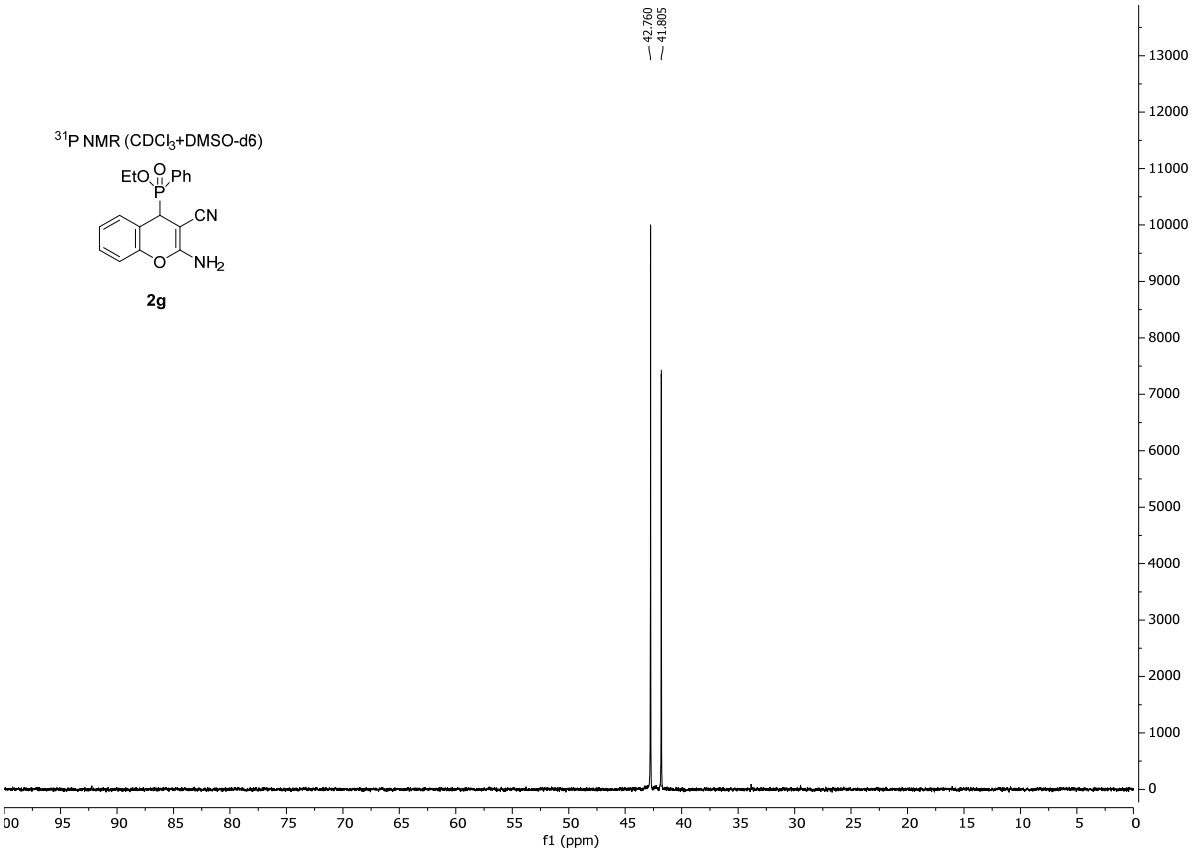
EtO
O
Ph
P
CN
O
NH$_2$
2g
f1 (ppm)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Ph
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O
NH2
2g
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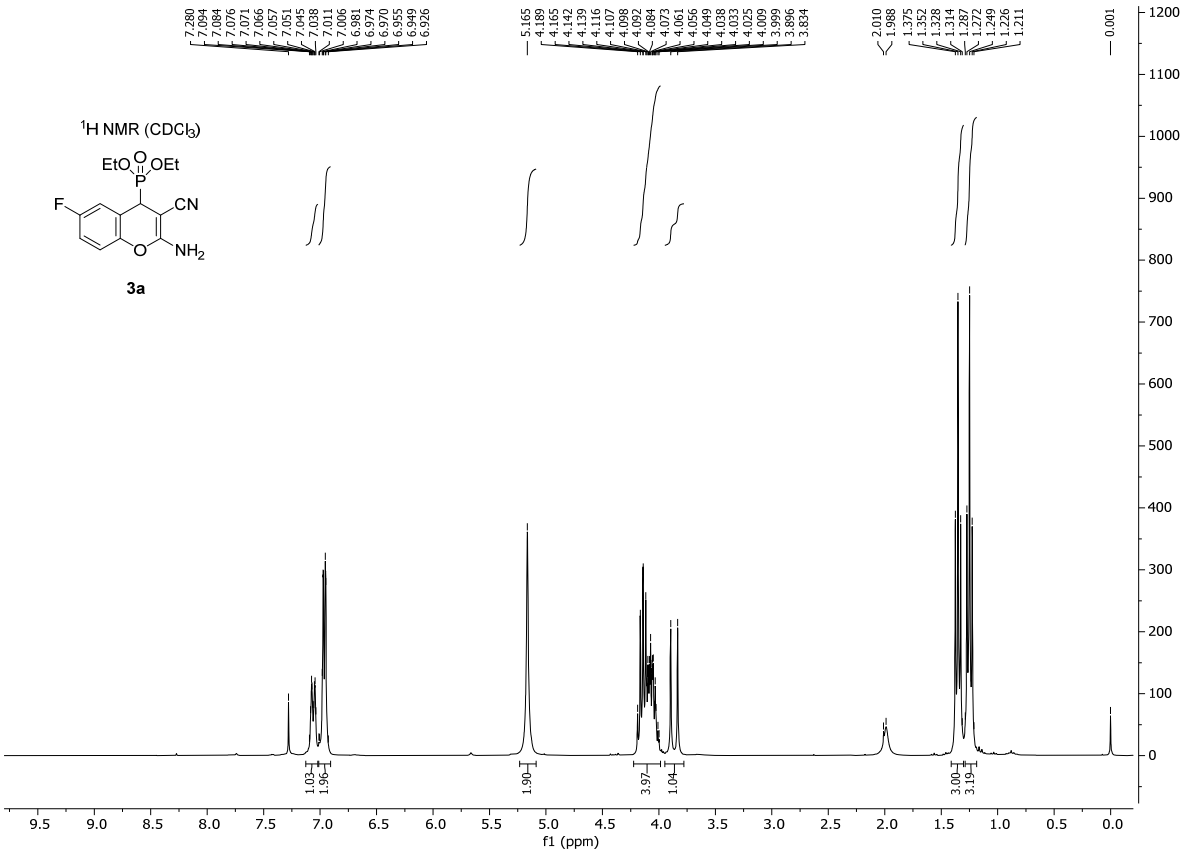
f1 (ppm)


1H NMR (CDCl3)
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O
P
OEt
F
CN
O
NH2
3a
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7.094
7.084
7.076
7.071
7.066
7.057
7.051
7.045
7.038
7.011
7.006
6.981
6.974
6.970
6.955
6.949
6.926
5.165
4.189
4.165
4.142
4.139
4.116
4.107
4.098
4.092
4.084
4.073
4.061
4.056
4.049
4.038
4.033
4.025
4.009
3.999
3.896
3.834
2.010
1.988
1.375
1.352
1.328
1.314
1.287
1.272
1.249
1.226
1.211
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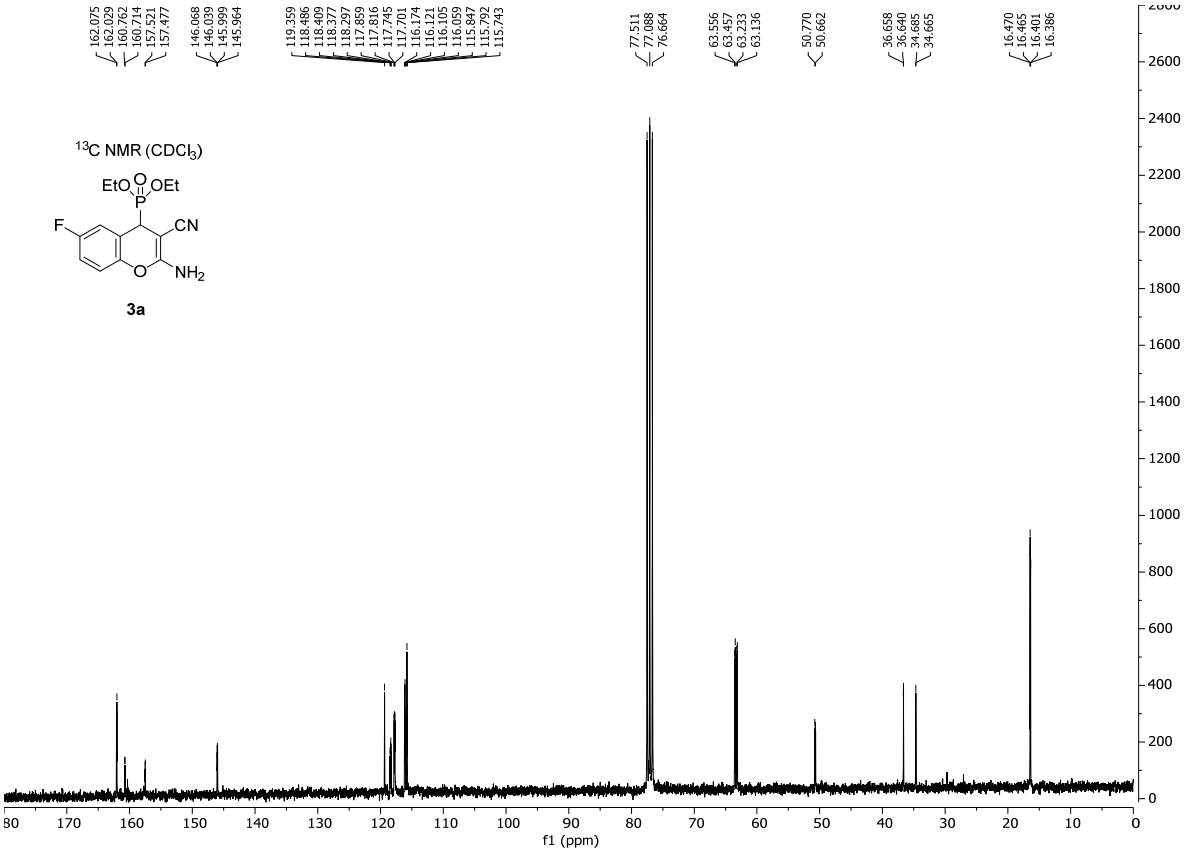
1.96
1.90
3.97
1.04
3.00
3.19
f1 (ppm)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118.409
118.377
118.297
117.859
117.816
117.745
117.701
116.174
116.121
116.105
116.059
115.847
115.792
115.743
77.511
77.088
76.664
63.556
63.457
63.233
63.136
50.770
50.662
36.658
36.640
34.685
34.665
16.470
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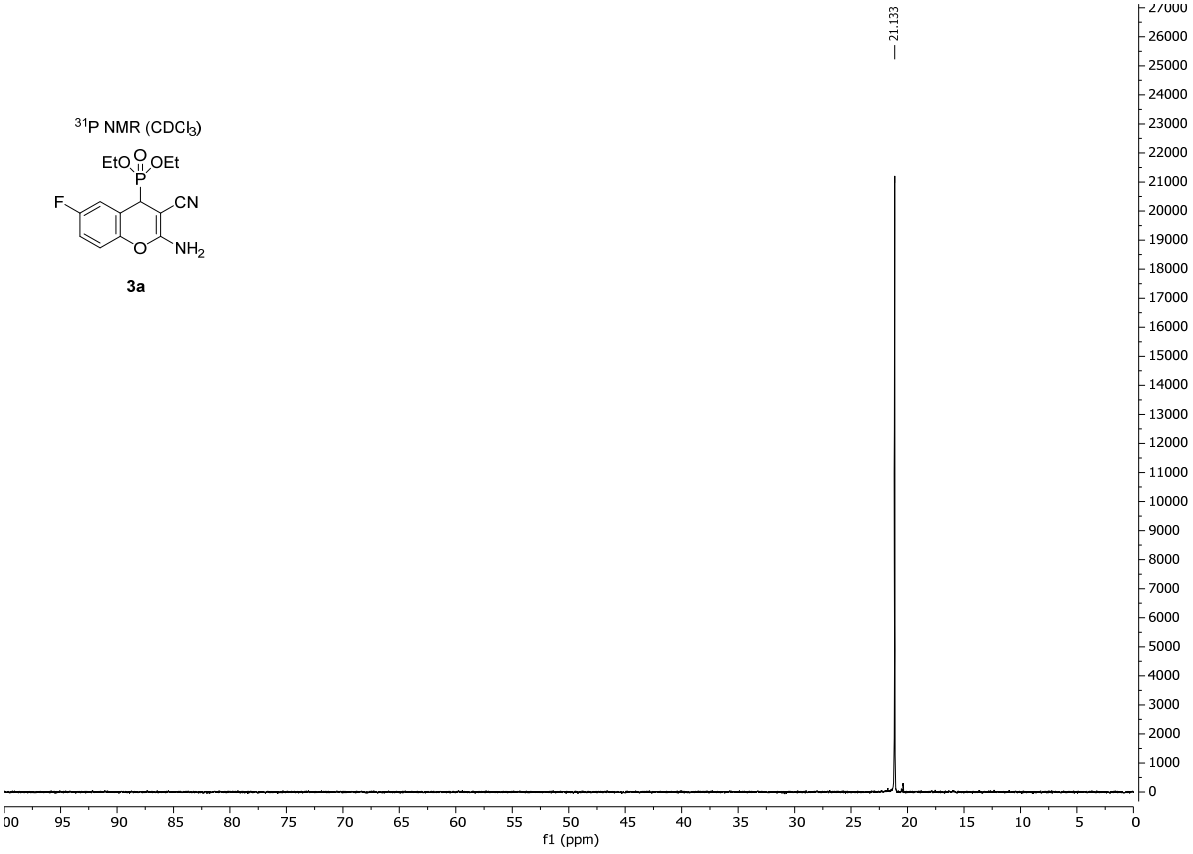
13C NMR (CDCl3)
EtO
O
OEt
P
F
CN
O
NH2
3a
f1 (ppm)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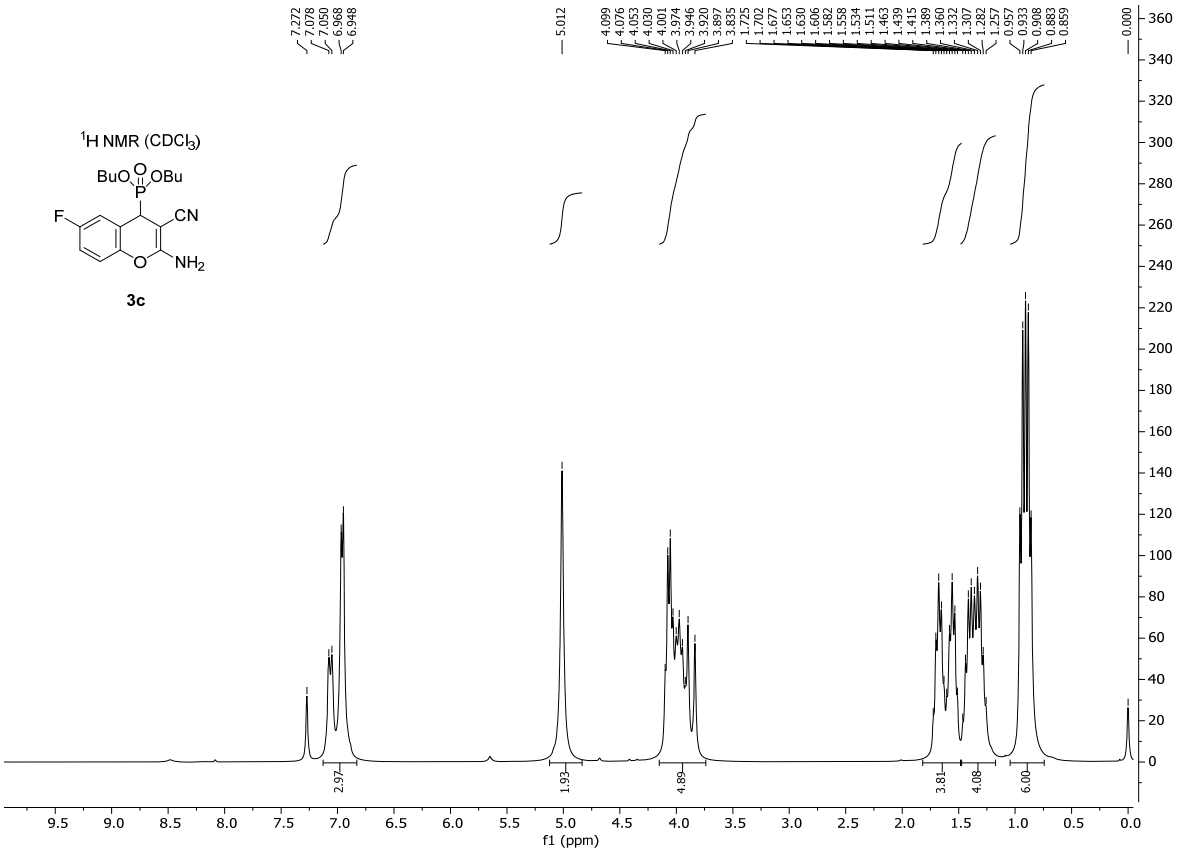
O
OEt
P
F
CN
O
NH2
3a
f1 (ppm)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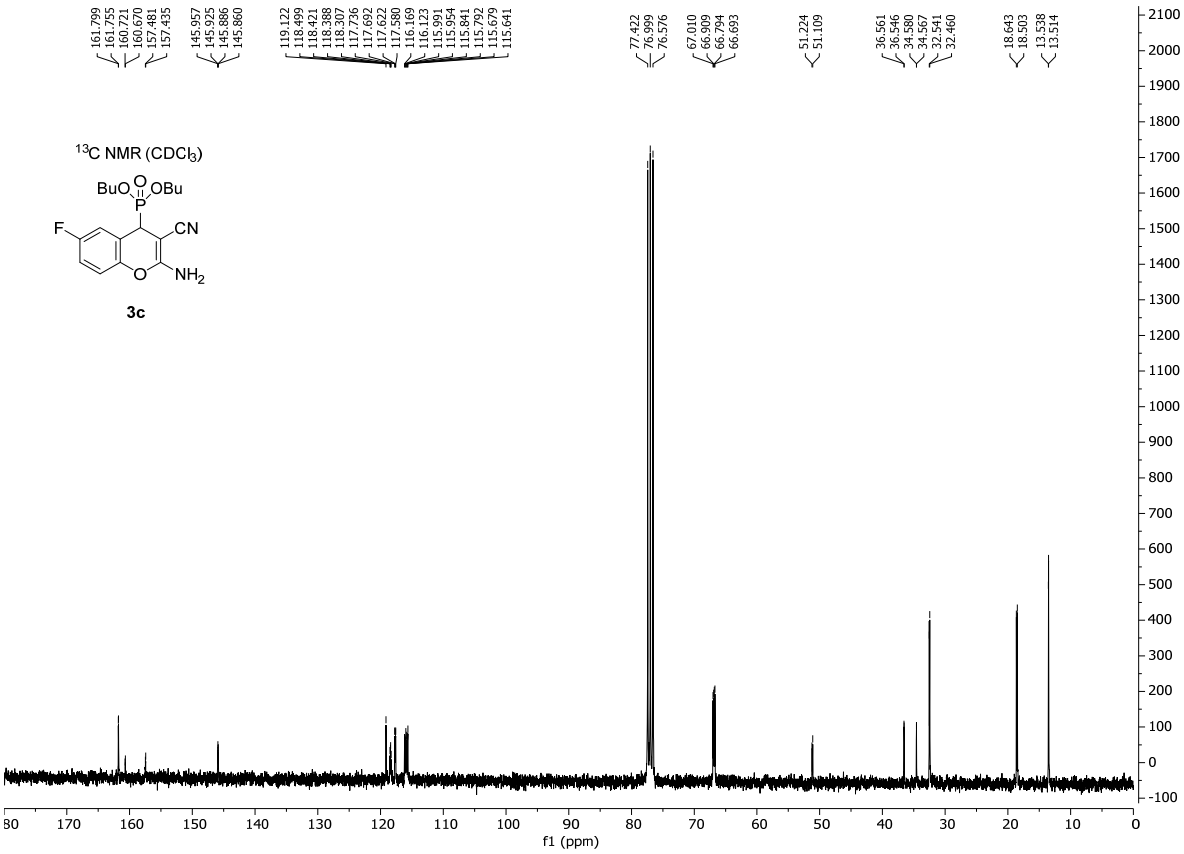
1.558
1.534
1.511
1.463
1.439
1.415
1.389
1.360
1.332
1.307
1.282
1.257
0.957
0.933
0.908
0.883
0.859
0.000
^{1}H NMR ($CDCl_3$)
BuO
OBu
P
O
F
CN
NH$_2$
3c
2.97
1.93
4.89
3.81
4.08
6.00
f1 (ppm)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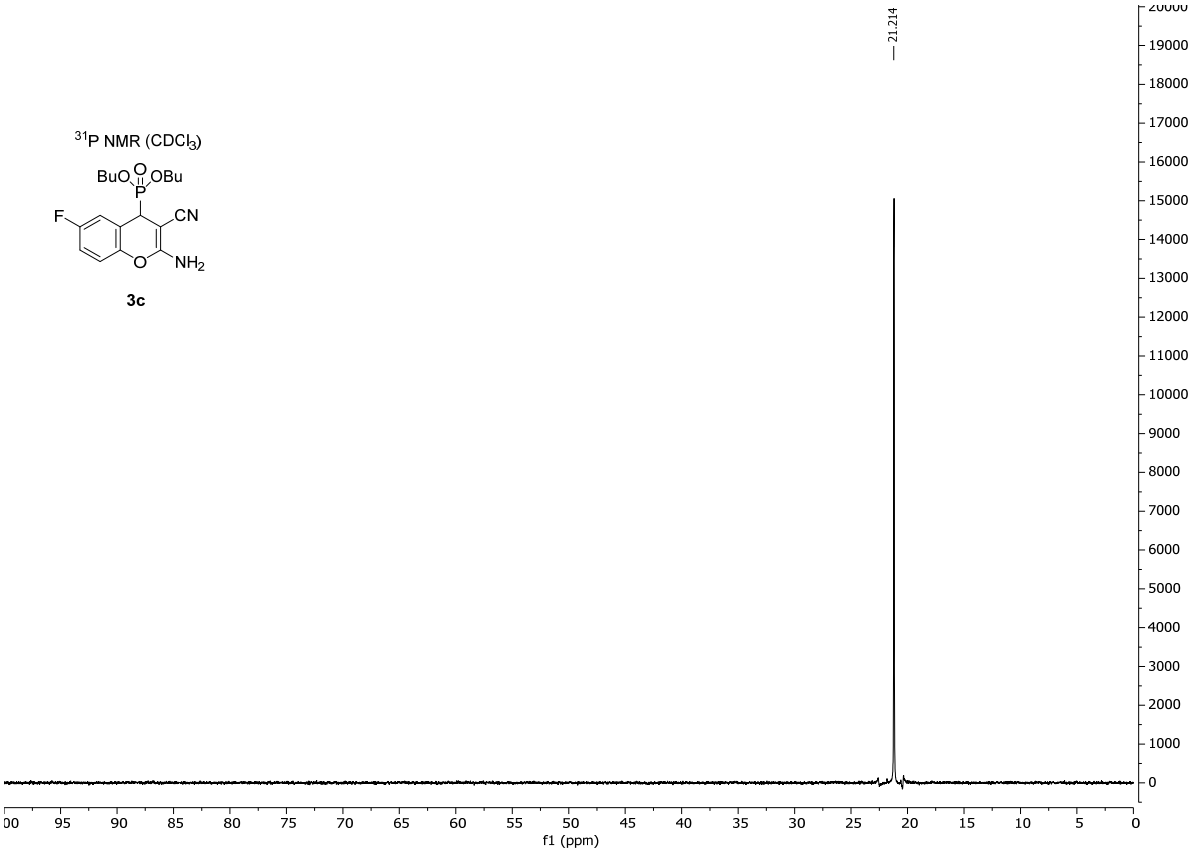
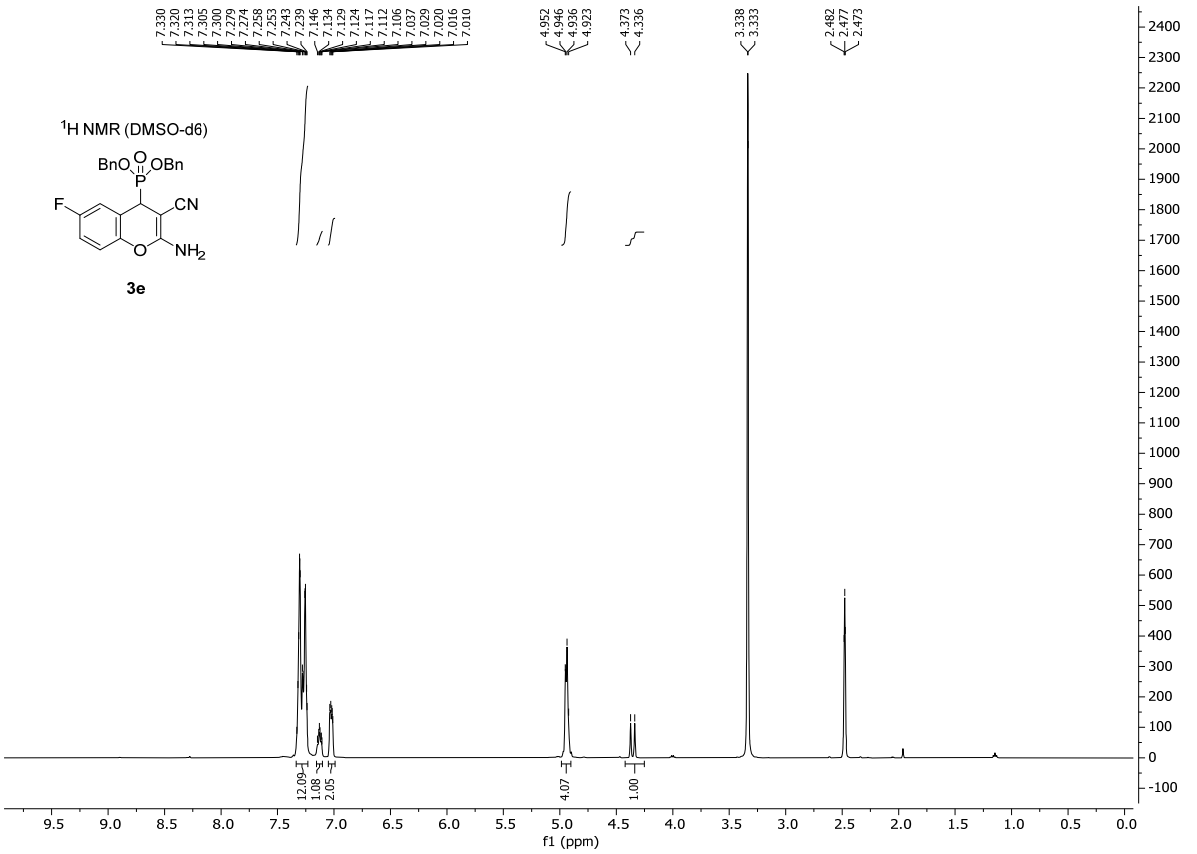
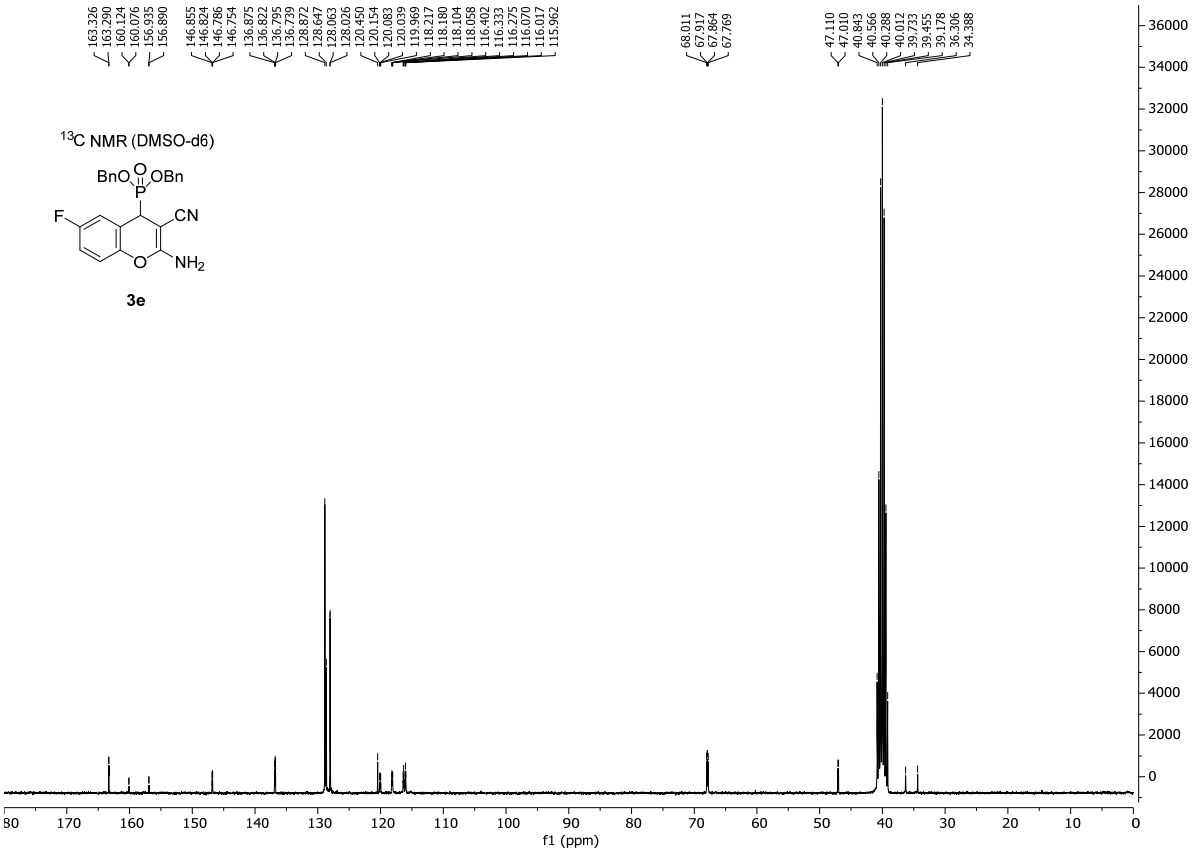
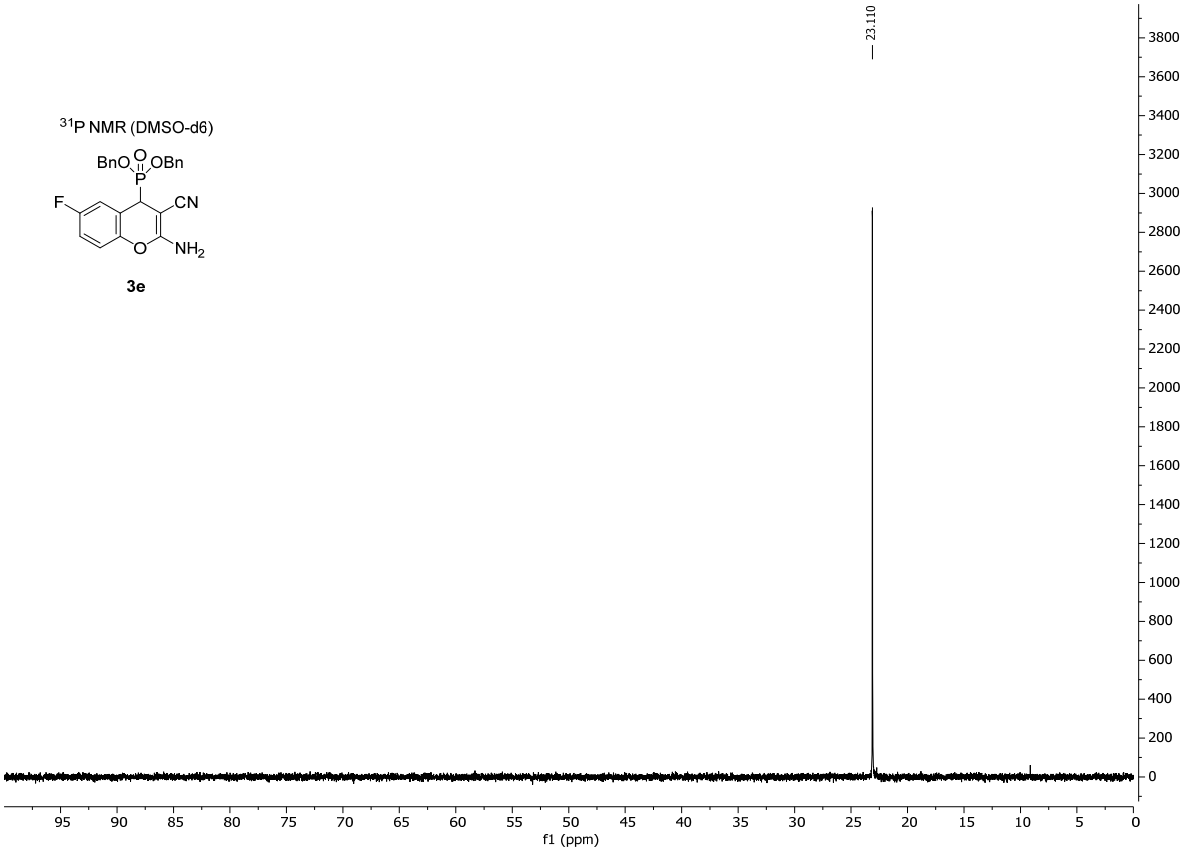
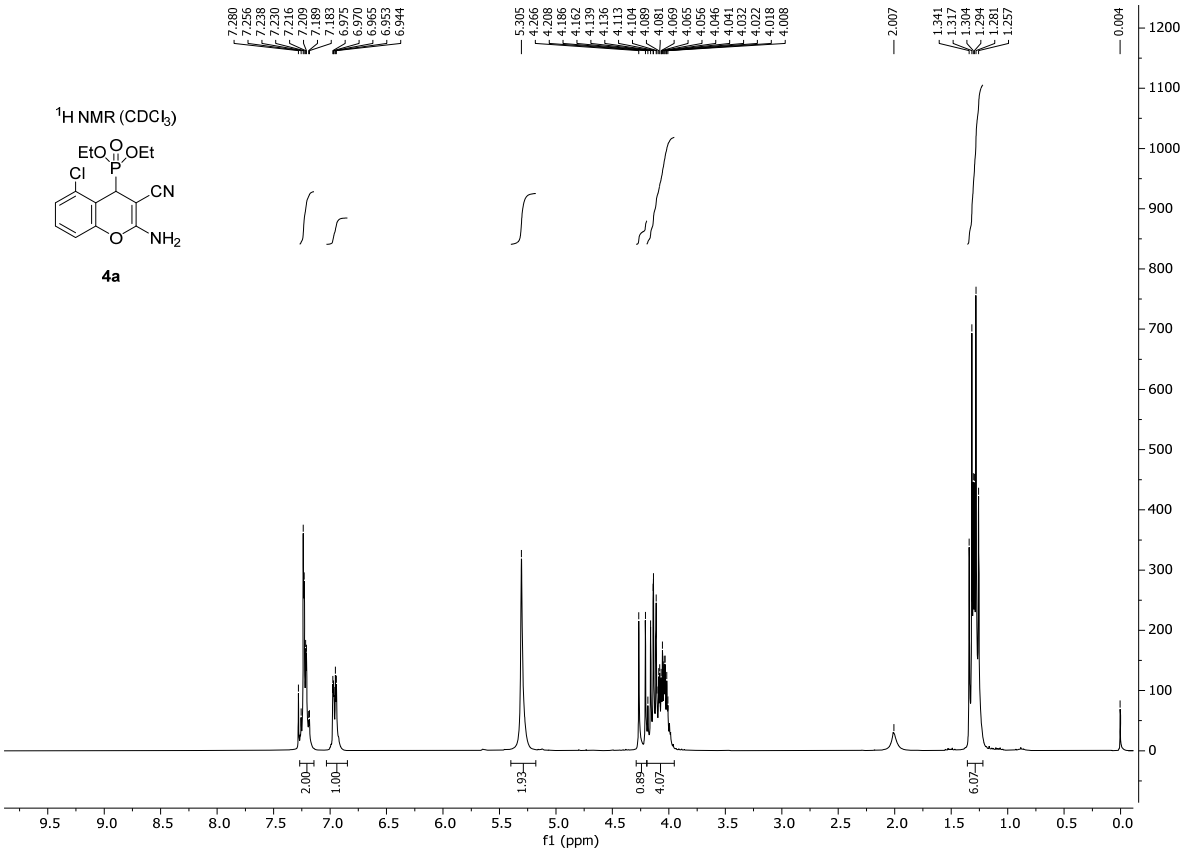
118.388
118.307
117.736
117.692
117.622
117.580
116.169
116.123
115.991
115.954
115.841
115.792
115.679
115.641
77.422
76.999
76.576
67.010
66.909
66.794
66.693
51.224
51.109
36.561
36.546
34.580
34.567
32.541
32.460
18.643
18.503
13.538
13.514
^{13}C NMR ($CDCl_3$)
BuO
OBu
P
O
F
CN
NH$_2$
3c
f1 (ppm)

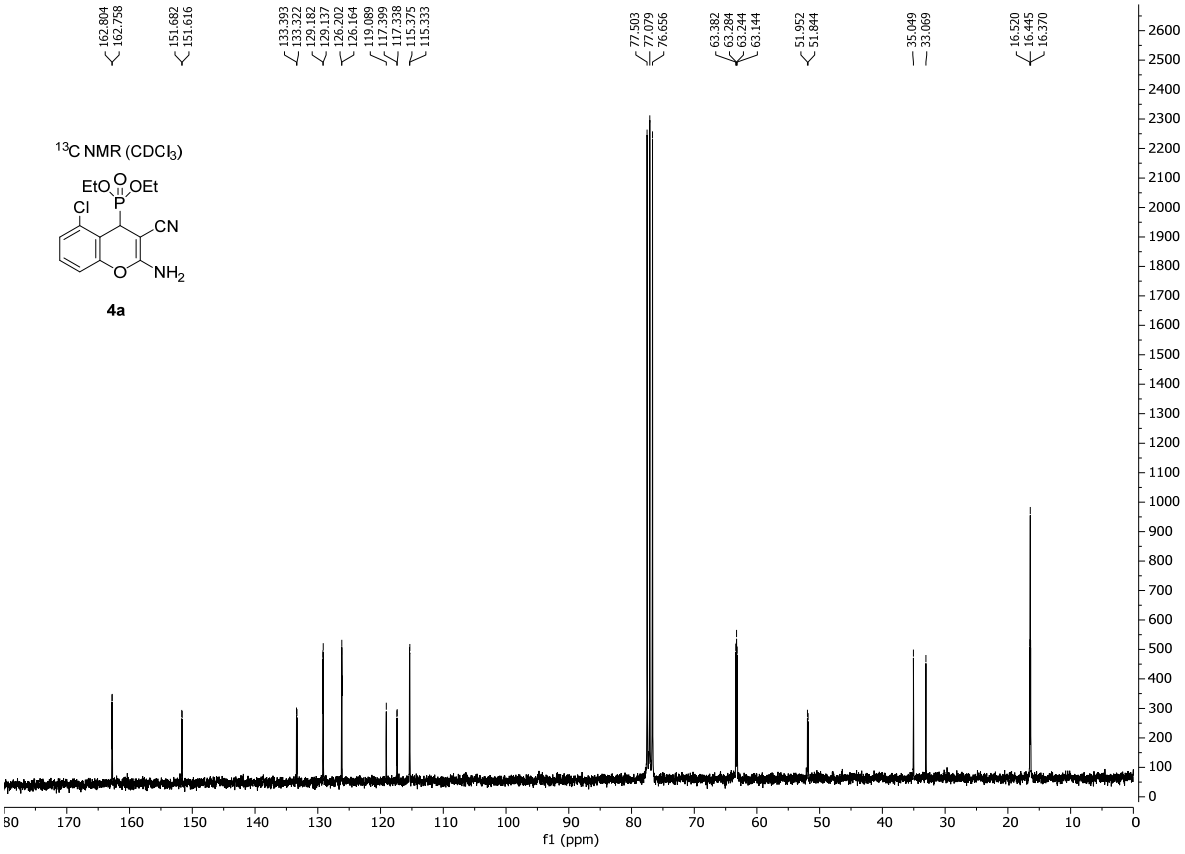

^{31}P NMR ($CDCl_3$)
BuO
OBu
P
O
F
CN
O
NH_2
3c
21.214
f1 (ppm)

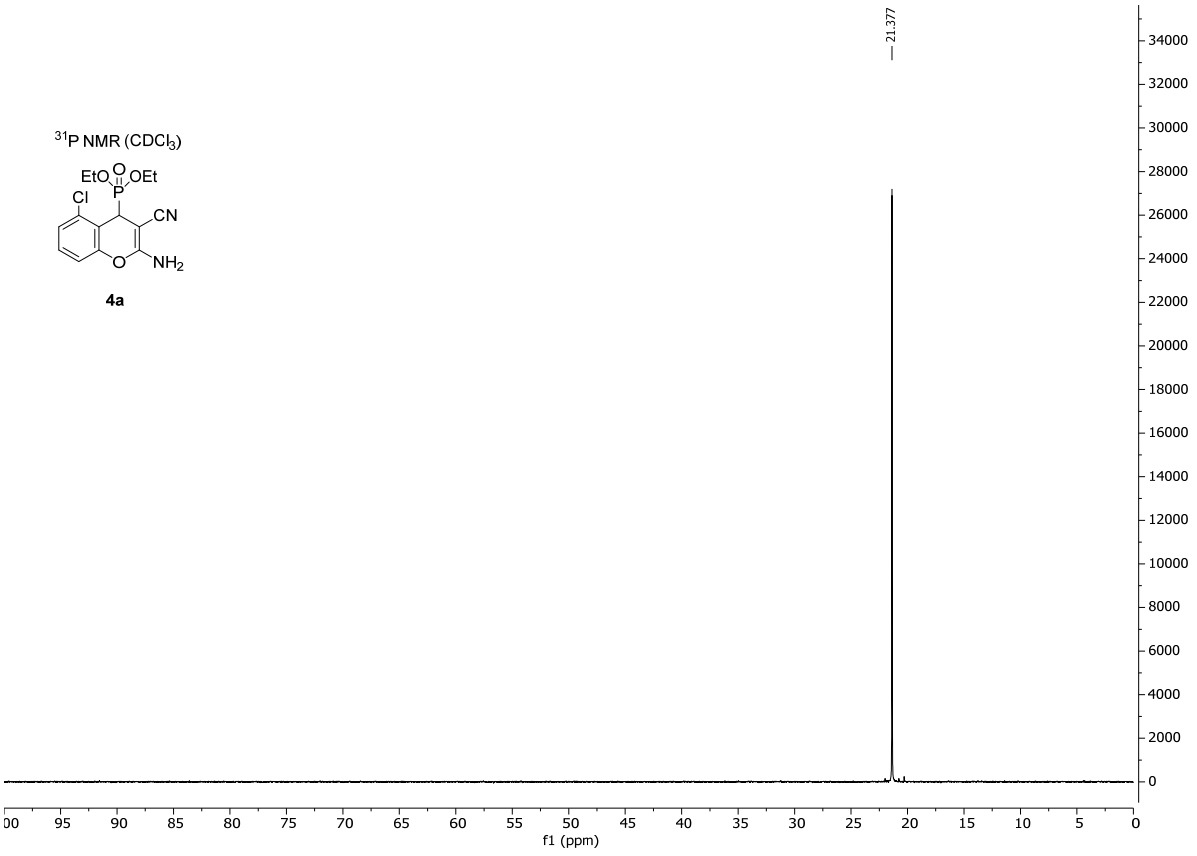

^{1}H NMR (DMSO-d6)
BnO
OBn
P
O
F
CN
O
NH_2
3e
7.330
7.320
7.313
7.305
7.300
7.279
7.274
7.258
7.253
7.243
7.239
7.146
7.134
7.129
7.124
7.117
7.112
7.106
7.037
7.029
7.020
7.016
7.010
4.952
4.946
4.936
4.923
4.373
4.336
3.338
3.333
2.482
2.477
2.473
12.09
1.08
2.05
4.07
1.00
f1 (ppm)

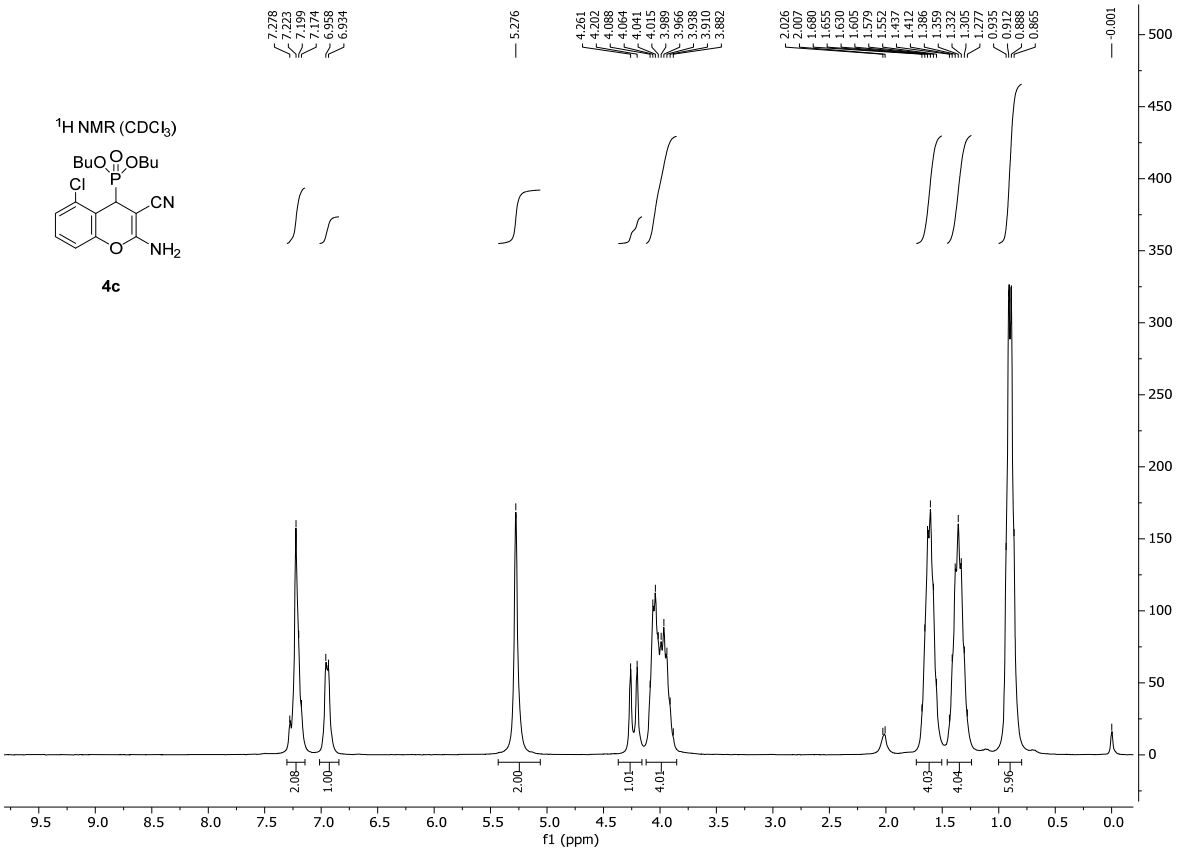

163.326
163.290
160.124
160.076
156.935
156.890
146.855
146.824
146.786
146.754
136.875
136.822
136.795
136.739
128.872
128.647
128.063
128.026
120.450
120.154
120.083
120.039
119.969
118.217
118.180
118.104
118.058
116.402
116.333
116.275
116.070
116.017
115.962
68.011
67.917
67.864
67.769
47.110
47.010
40.843
40.566
40.288
40.012
39.733
39.455
39.178
36.306
34.388
^{13}C NMR (DMSO-d6)
BnO
OBn
P
O
F
CN
O
NH$_2$
3e
f1 (ppm)

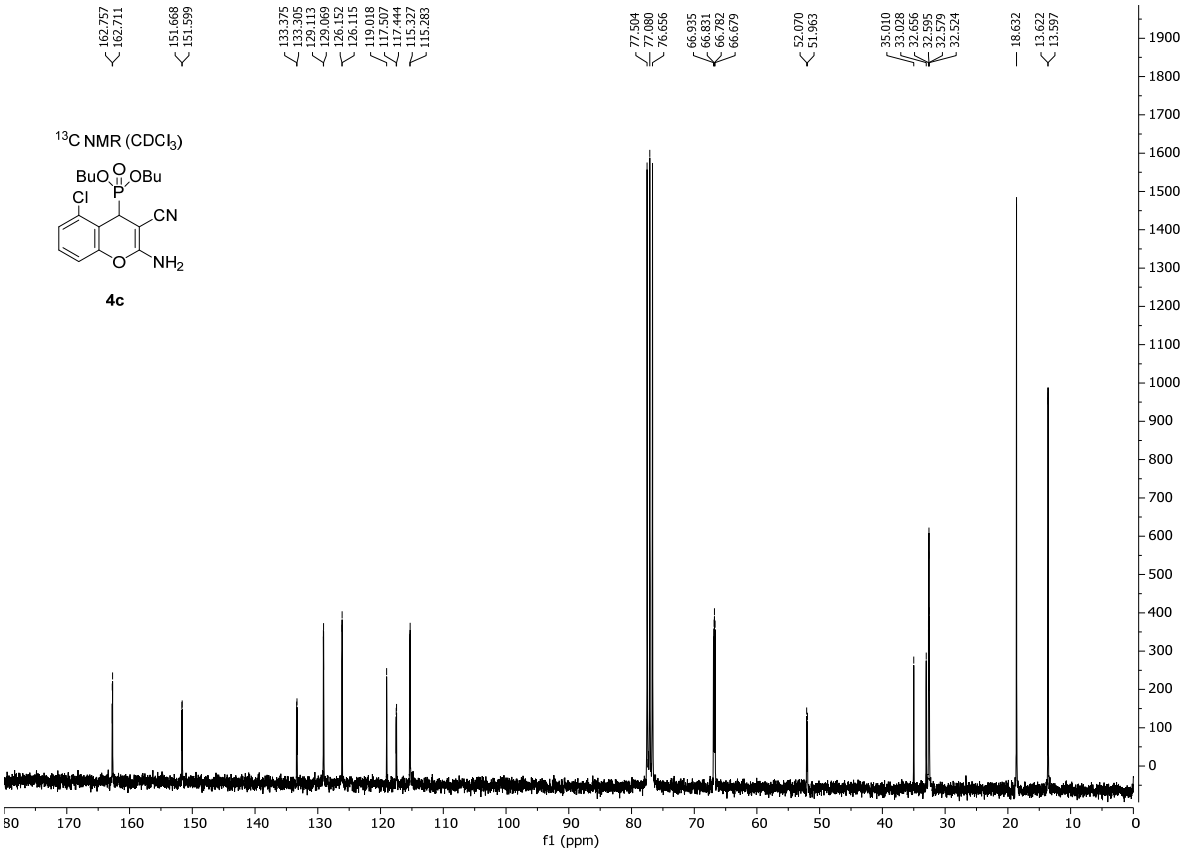

23.110
^{31}P NMR (DMSO-d6)
BnO
OBn
P
O
F
CN
O
NH$_2$
3e
f1 (ppm)

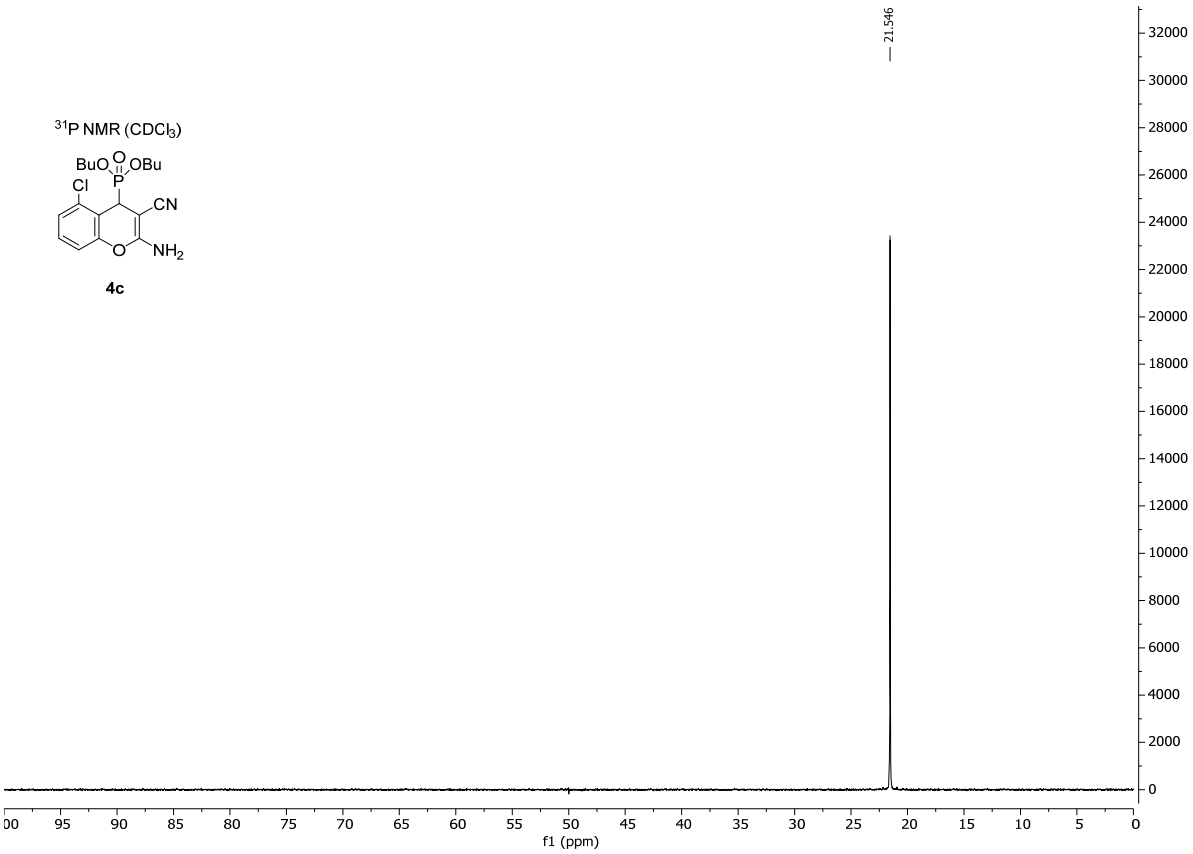

7.280
7.256
7.238
7.230
7.216
7.209
7.189
7.183
6.975
6.970
6.965
6.953
6.944
5.305
4.266
4.208
4.186
4.162
4.139
4.136
4.113
4.104
4.089
4.081
4.069
4.065
4.056
4.046
4.041
4.032
4.022
4.018
4.008
2.007
1.341
1.317
1.304
1.294
1.281
1.257
0.004
^{1}H NMR ($CDCl_3$)
EtO
OEt
Cl
CN
NH$_2$
4a
2.00
1.00
1.93
0.89
4.07
6.07
f1 (ppm)

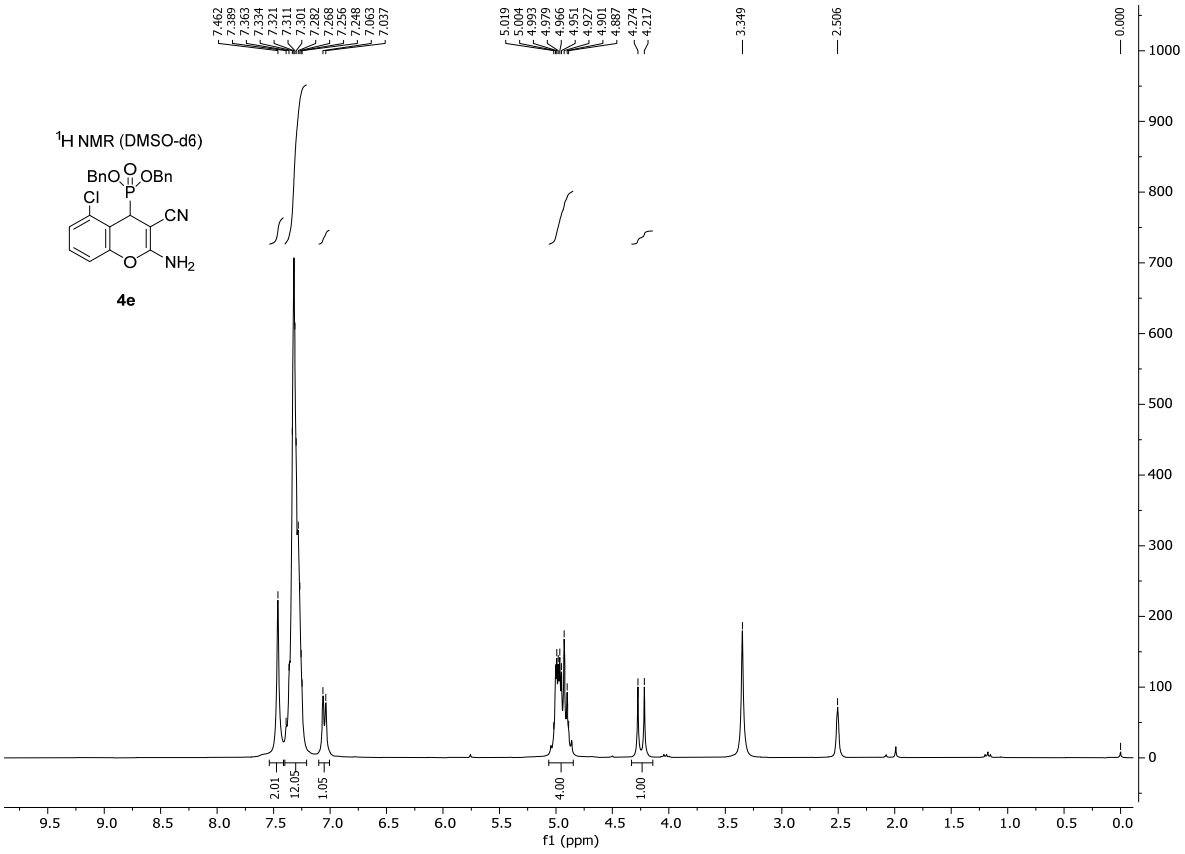

162.804
162.758
151.682
151.616
133.393
133.322
129.182
129.137
126.202
126.164
119.089
117.399
117.338
115.375
115.333
77.503
77.079
76.656
63.382
63.284
63.244
63.144
51.952
51.844
35.049
33.069
16.520
16.445
16.370
^{13}C NMR ($CDCl_3$)
EtO
OEt
Cl
CN
NH$_2$
4a
f1 (ppm)

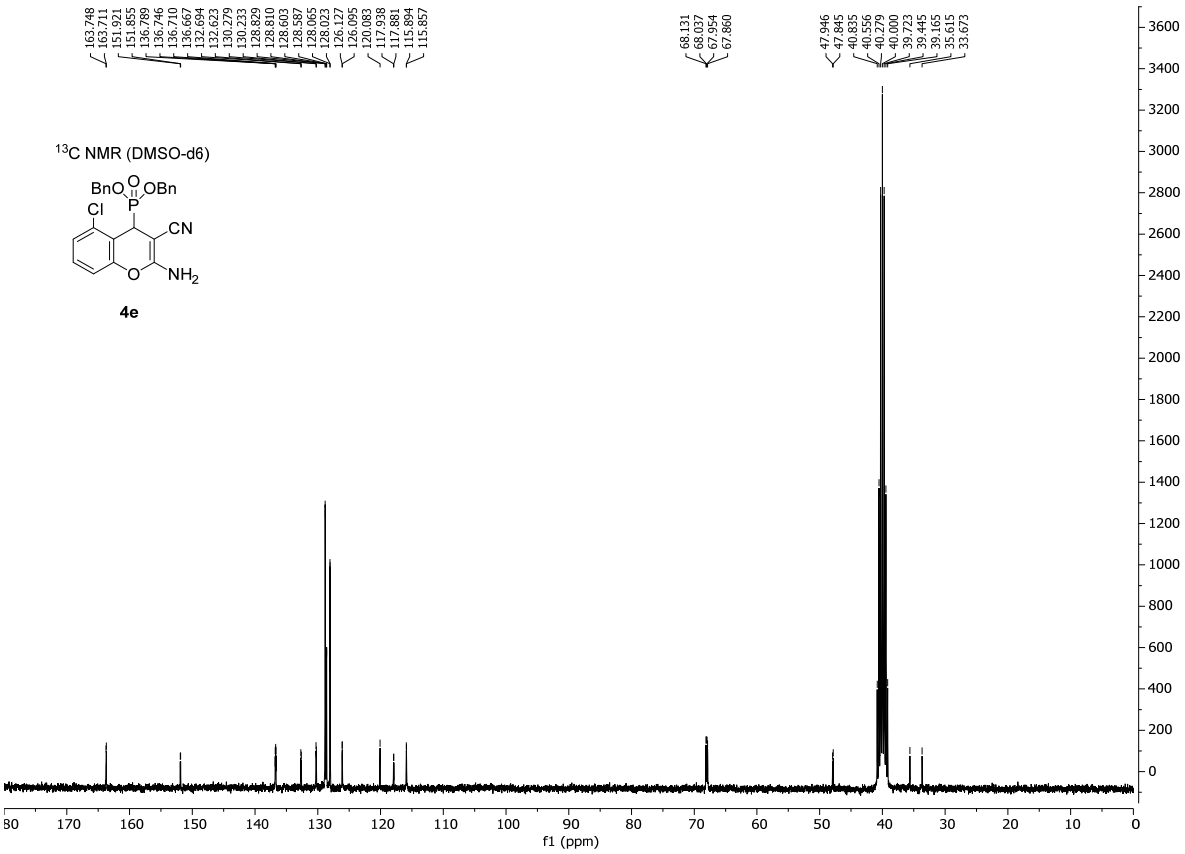

^{31}P NMR ($CDCl_3$)
EtO
OEt
Cl
CN
NH_2
4a
21.377
f1 (ppm)

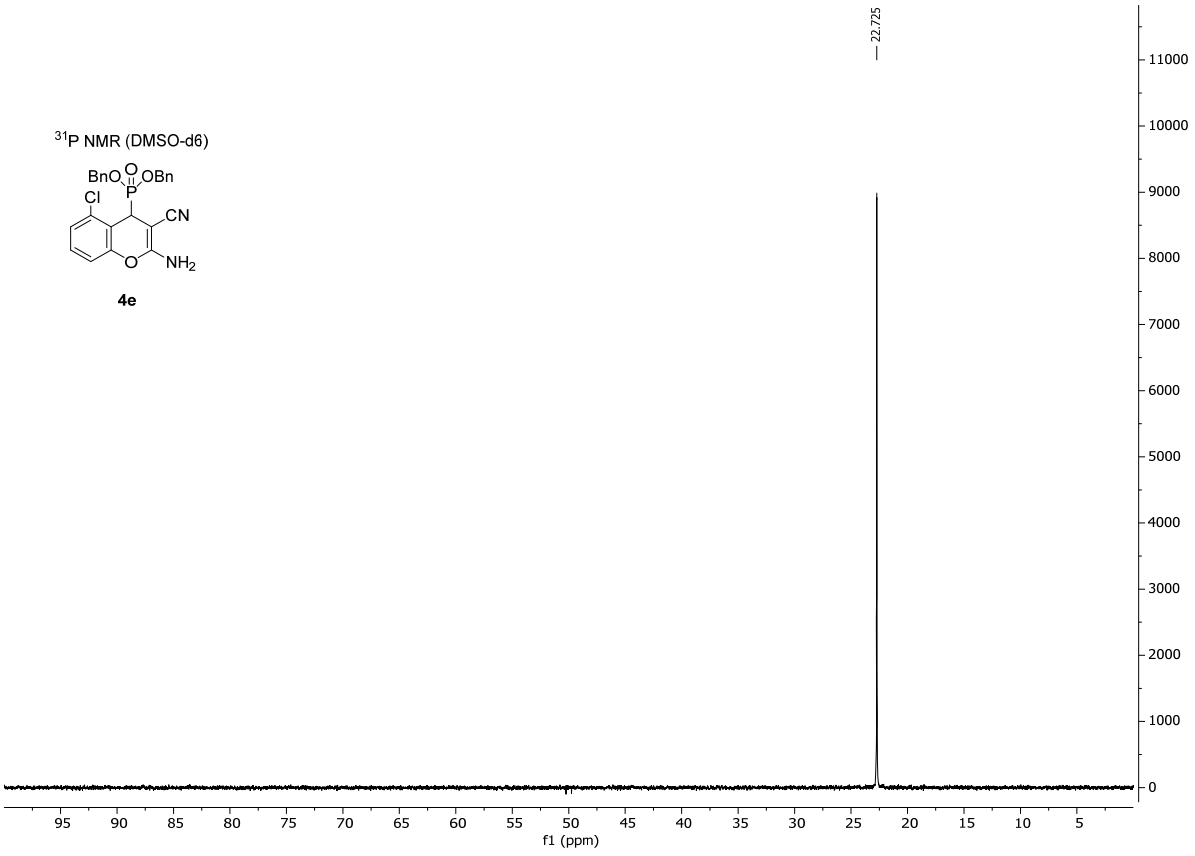

^{1}H NMR ($CDCl_3$)
BuO
OBu
Cl
CN
NH_2
4c
7.278
7.223
7.199
7.174
6.958
6.934
5.276
4.261
4.202
4.088
4.064
4.041
4.015
3.989
3.966
3.938
3.910
3.882
2.026
2.007
1.680
1.655
1.630
1.605
1.579
1.552
1.437
1.412
1.386
1.359
1.332
1.305
1.277
0.935
0.912
0.888
0.865
-0.001
2.08
1.00
2.00
1.01
4.01
4.03
4.04
5.96
f1 (ppm)

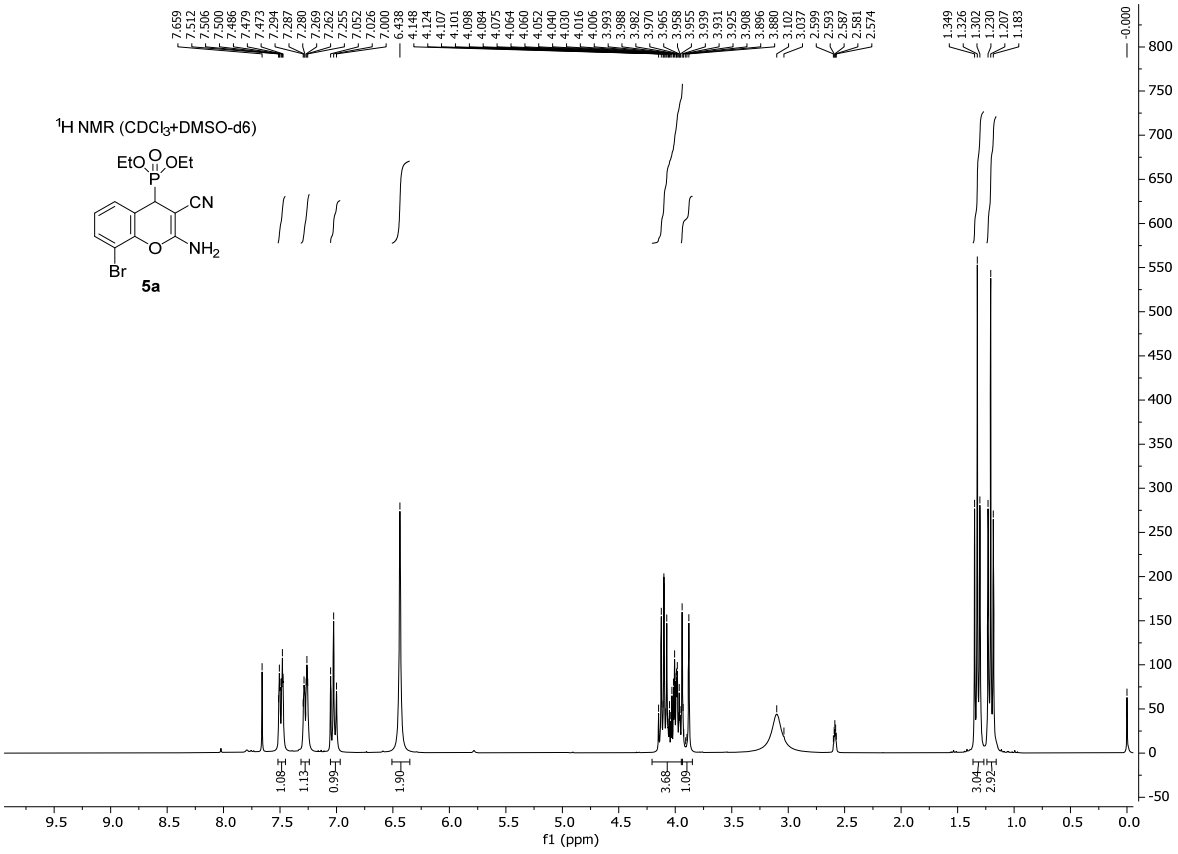

162.757
162.711
151.668
151.599
133.375
133.305
129.113
129.069
126.152
126.115
119.018
117.507
117.444
115.327
115.283
77.504
77.080
76.656
66.935
66.831
66.782
66.679
52.070
51.963
35.010
33.028
32.656
32.595
32.579
32.524
18.632
13.622
13.597
13C NMR (CDCl3)
BuO
OBu
Cl
CN
NH2
4c
f1 (ppm)

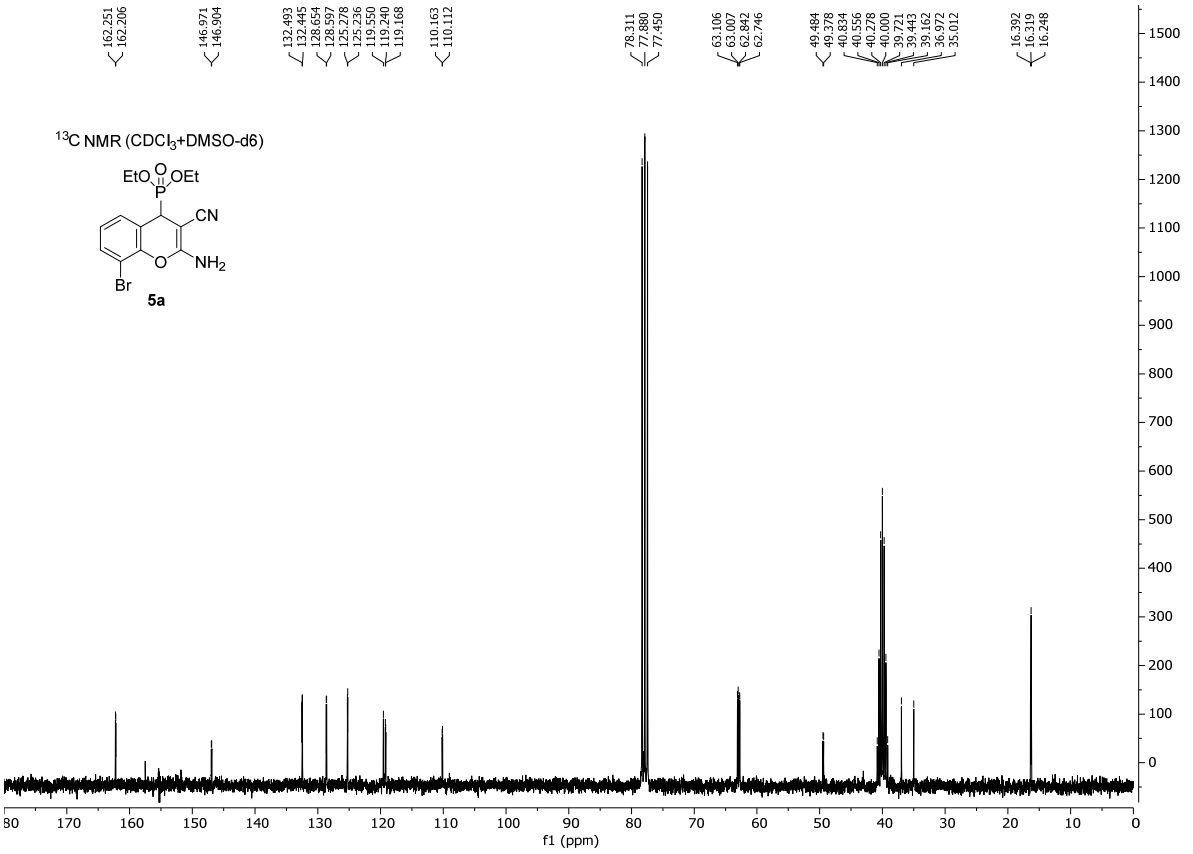

21.546
31P NMR (CDCl3)
BuO
OBu
Cl
CN
NH2
4c
f1 (ppm)

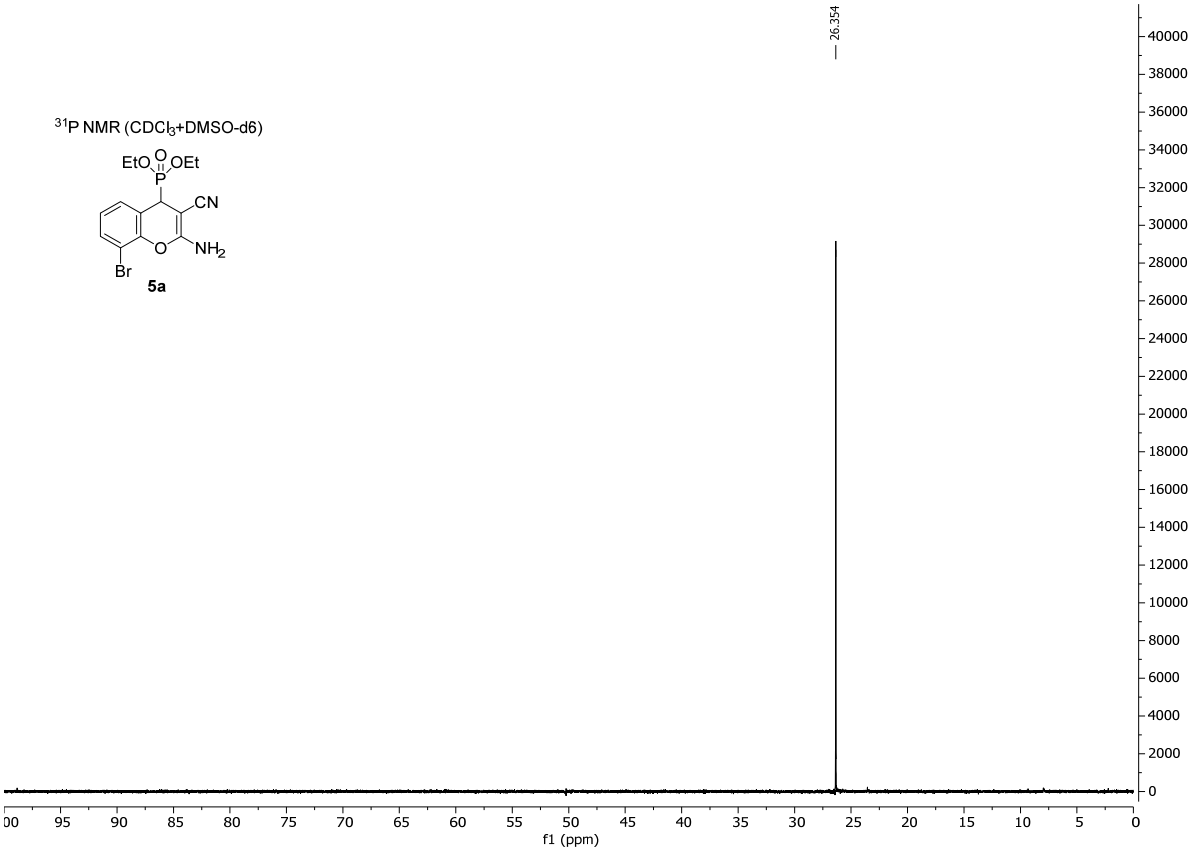

7.462
7.389
7.363
7.334
7.321
7.311
7.301
7.282
7.268
7.256
7.248
7.063
7.037
5.019
5.004
4.993
4.979
4.966
4.951
4.927
4.901
4.887
4.274
4.217
3.349
2.506
0.000
1H NMR (DMSO-d6)
BnO
OBn
Cl
CN
NH2
4e
2.01
12.05
1.05
4.00
1.00
f1 (ppm)

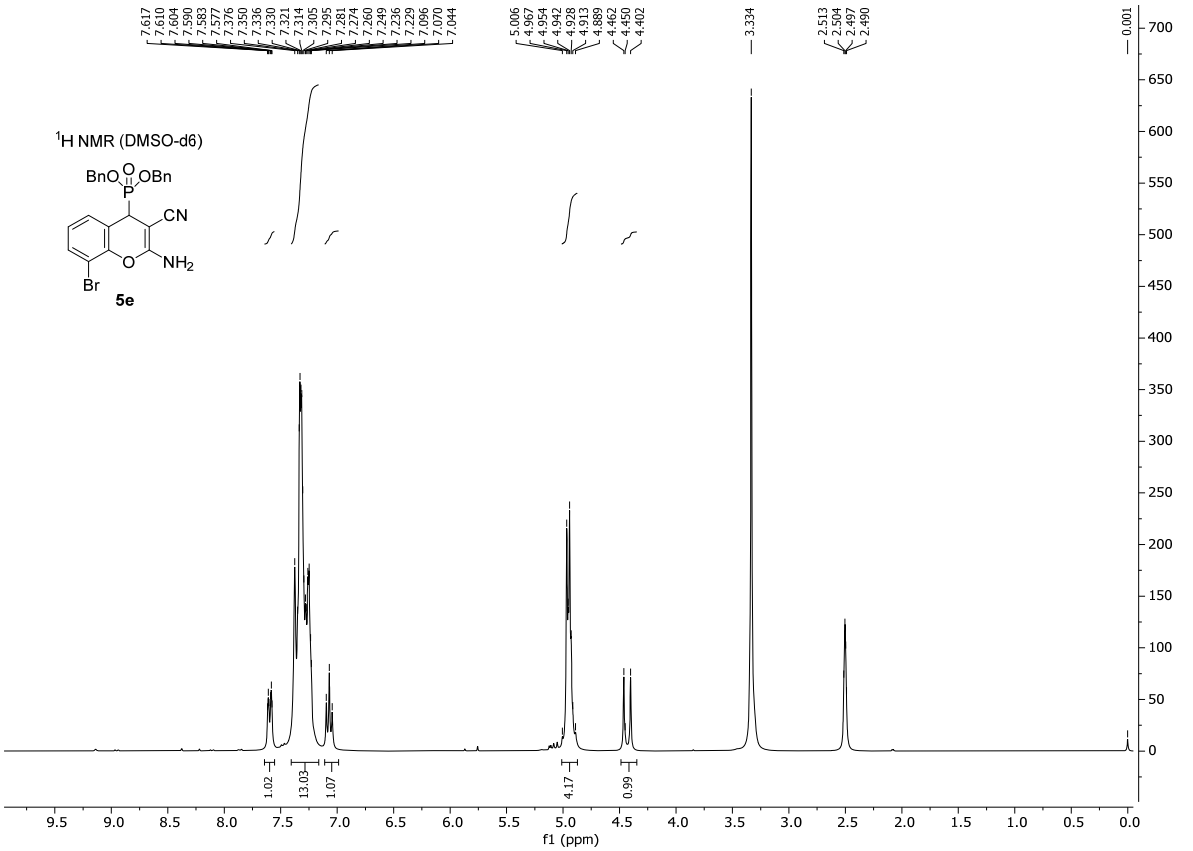

163.748
163.711
151.921
151.855
136.789
136.746
136.710
136.667
132.694
132.623
130.279
130.233
128.829
128.810
128.603
128.587
128.065
128.023
126.127
126.095
120.083
117.938
117.881
115.894
115.857
68.131
68.037
67.954
67.860
47.946
47.845
40.835
40.556
40.279
40.000
39.723
39.445
39.165
35.615
33.673
13C NMR (DMSO-d6)
BnO
OBn
Cl
CN
NH2
4e
f1 (ppm)

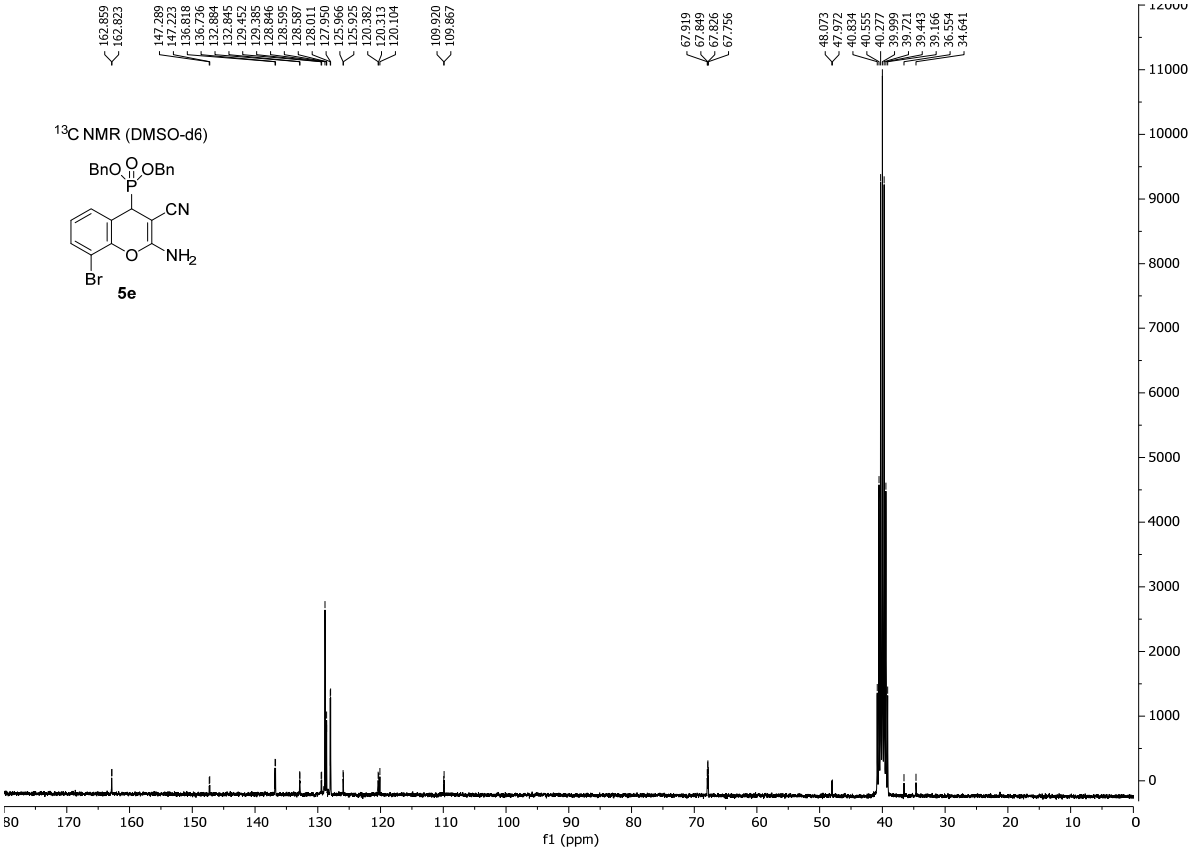

31P NMR (DMSO-d6)
BnO
OBn
Cl
CN
NH2
4e
22.725
f1 (ppm)

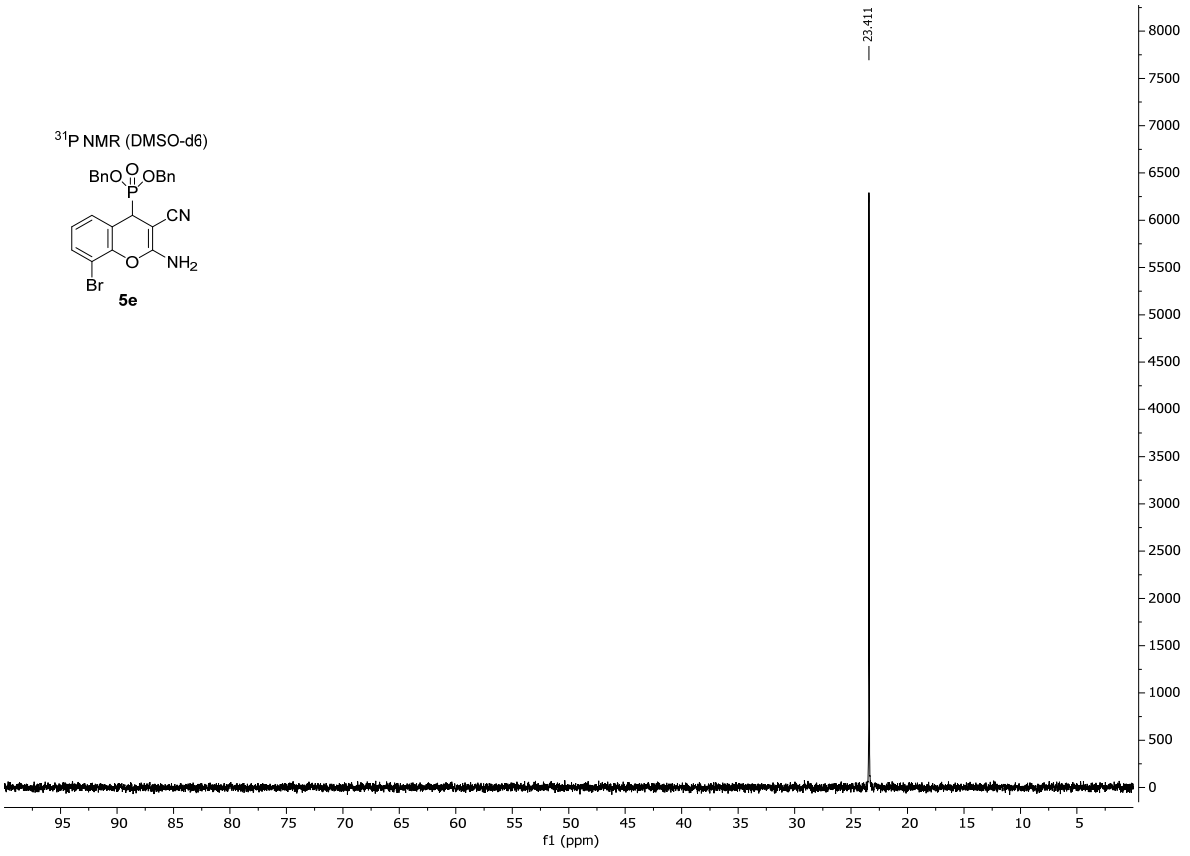

1H NMR (CDCl3+DMSO-d6)
EtO
OEt
CN
NH2
Br
5a
f1 (ppm)

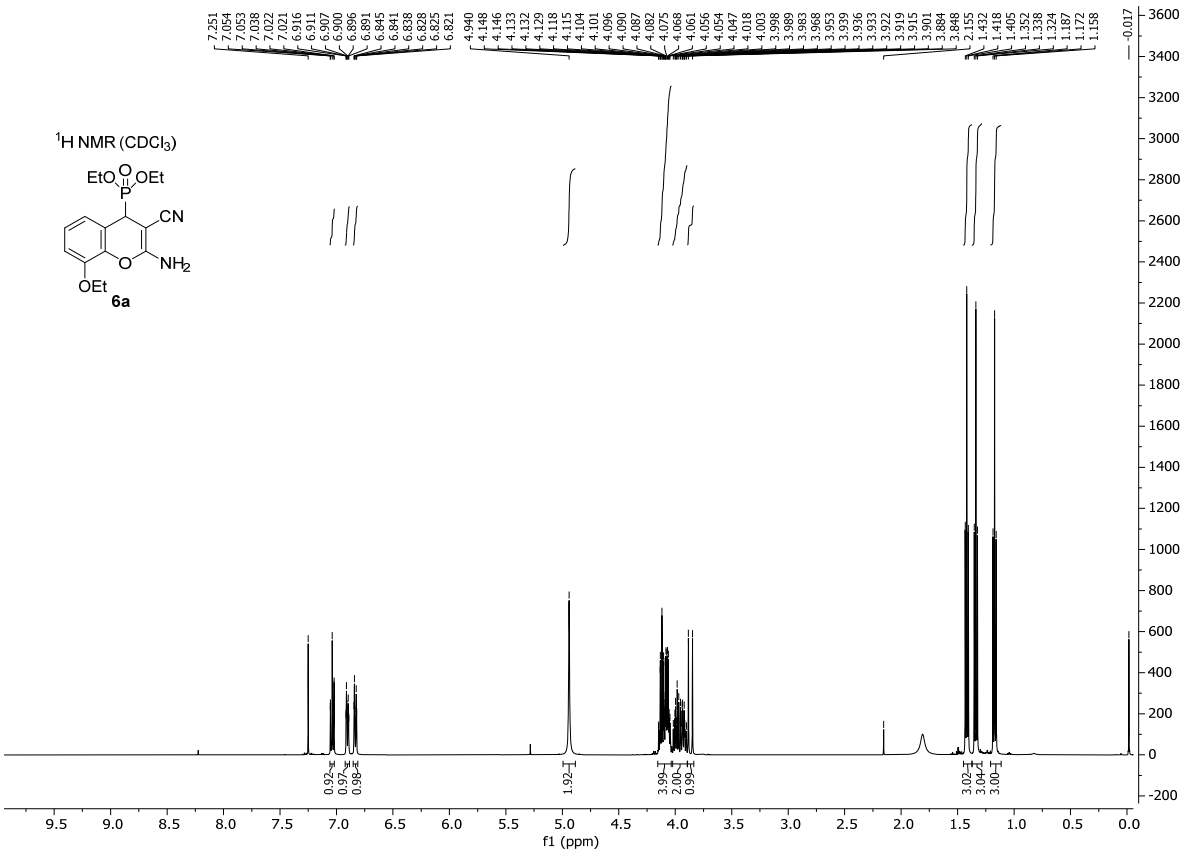

162.251
162.206
146.971
146.904
132.493
132.445
128.654
128.597
125.278
125.236
119.550
119.240
119.168
110.163
110.112
78.311
77.880
77.450
63.106
63.007
62.842
62.746
49.484
49.378
40.834
40.556
40.278
40.000
39.721
39.443
39.162
36.972
35.012
16.392
16.319
16.248
13C NMR (CDCl3+DMSO-d6)
EtO
OEt
P
O
CN
NH2
Br
5a
f1 (ppm)

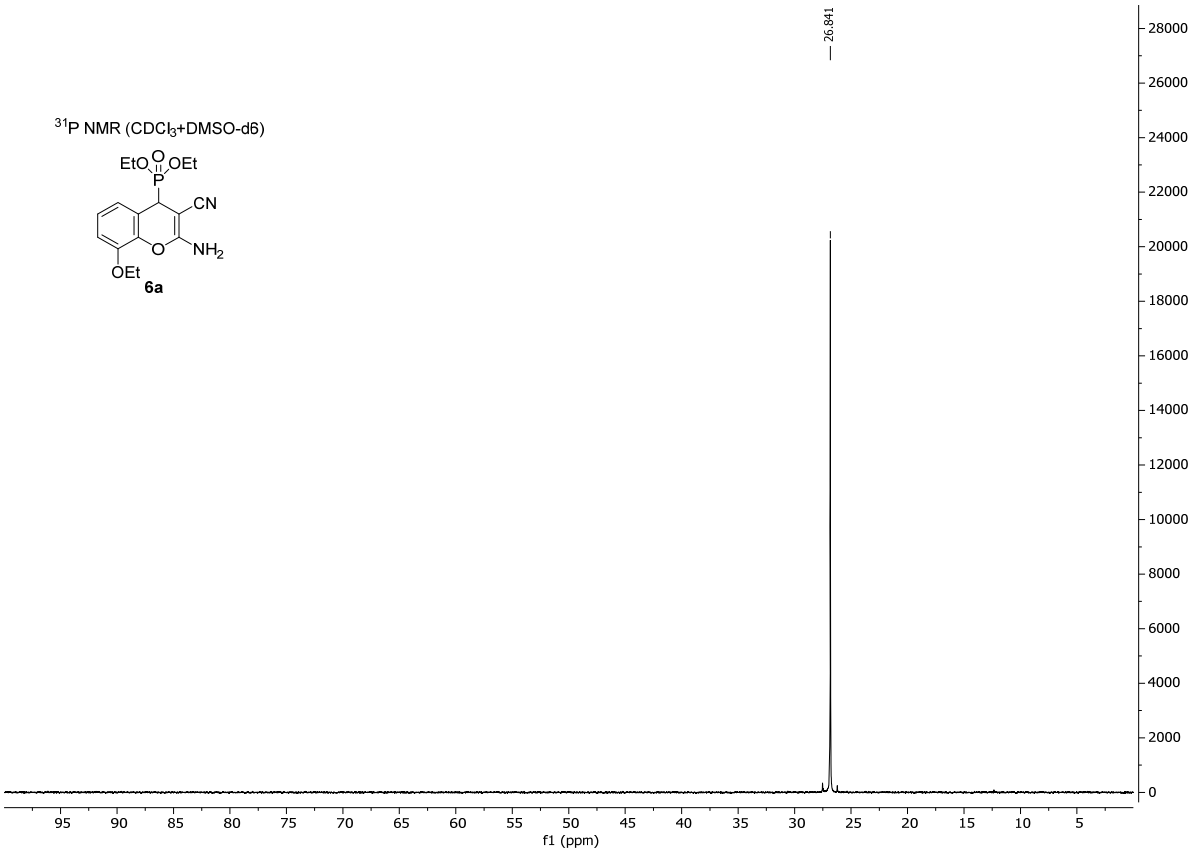

26.354
31P NMR (CDCl3+DMSO-d6)
EtO
OEt
P
O
CN
NH2
Br
5a
f1 (ppm)

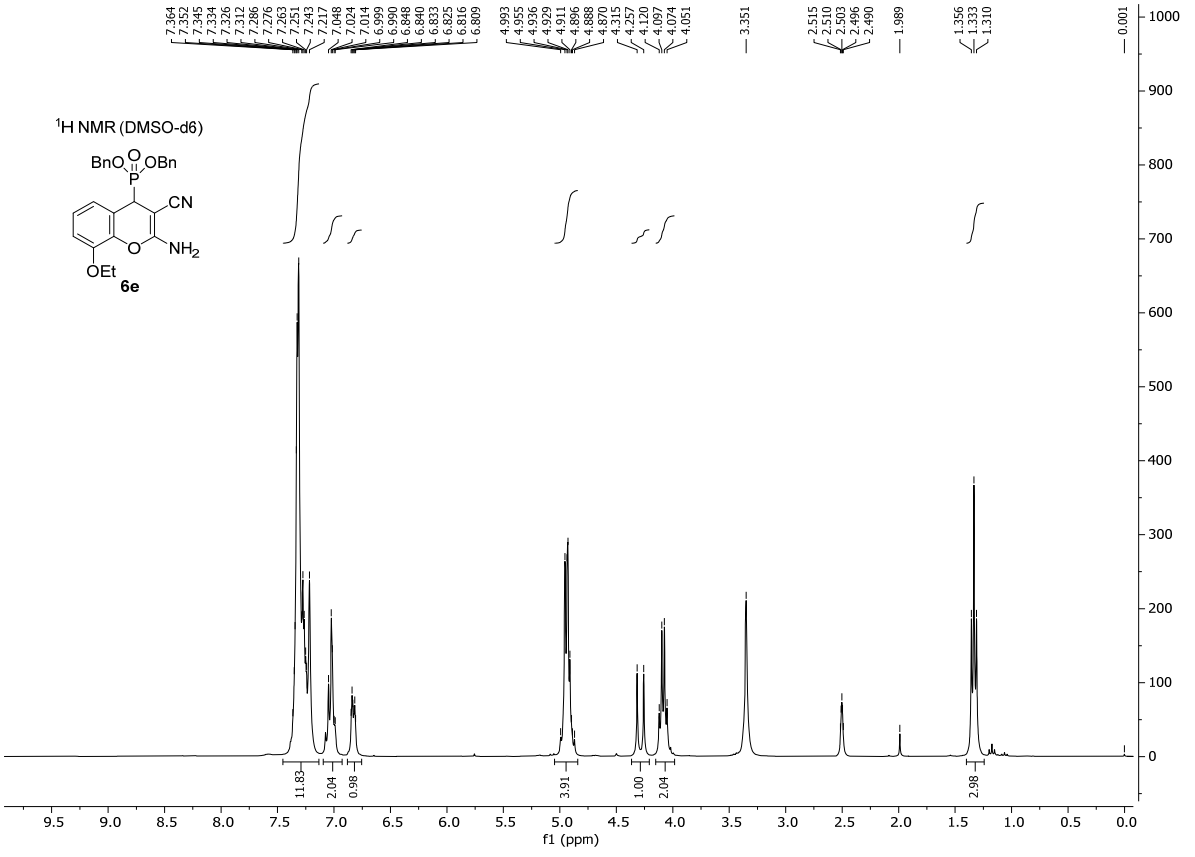

7.617
7.610
7.604
7.590
7.583
7.577
7.376
7.350
7.336
7.330
7.321
7.314
7.305
7.295
7.281
7.274
7.260
7.249
7.236
7.229
7.096
7.070
7.044
5.006
4.967
4.954
4.942
4.928
4.913
4.889
4.462
4.450
4.402
3.334
2.513
2.504
2.497
2.490
0.001
1H NMR (DMSO-d6)
BnO
OBn
P
O
CN
NH2
Br
5e
1.02
13.03
1.07
4.17
0.99
f1 (ppm)

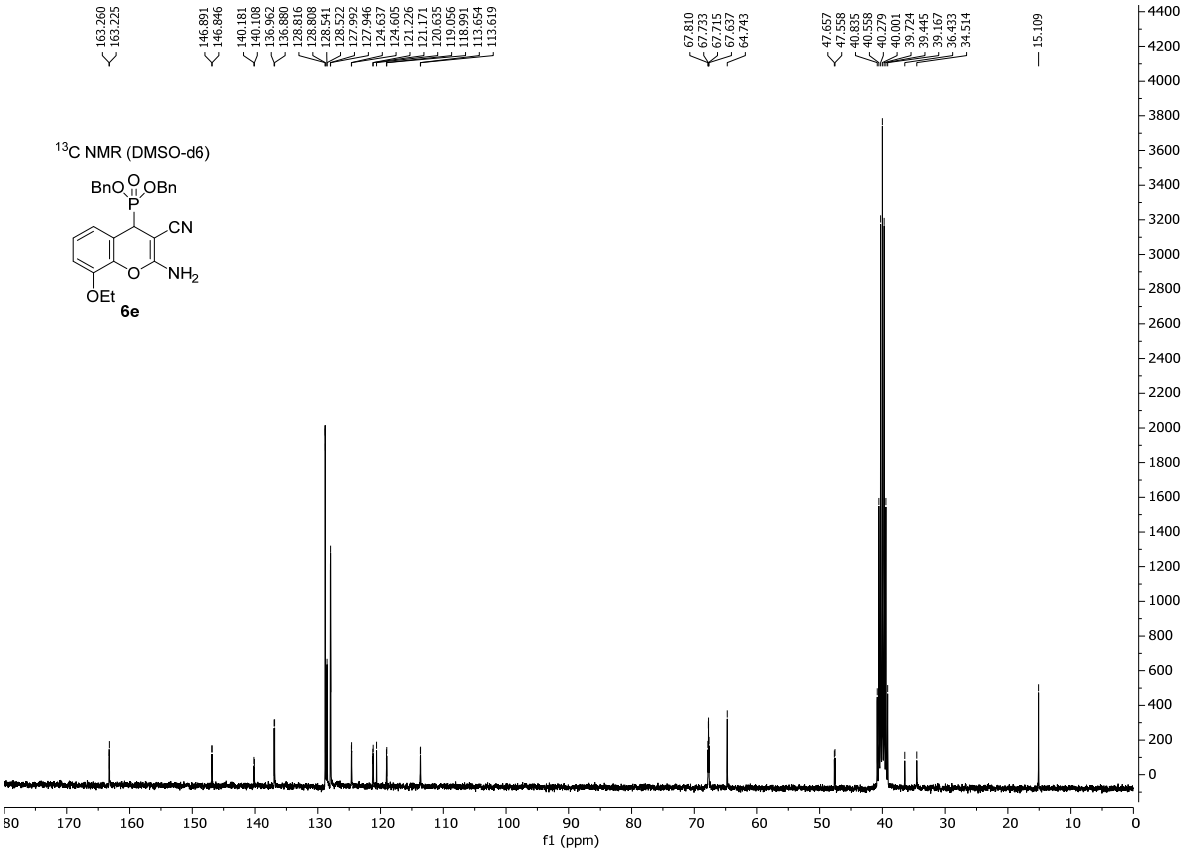

162.859
162.823
147.289
147.223
136.818
136.736
132.884
132.845
129.452
129.385
128.846
128.595
128.587
128.011
127.950
125.966
125.925
120.382
120.313
120.104
109.920
109.867
67.919
67.849
67.826
67.756
48.073
47.972
40.834
40.555
40.277
39.999
39.721
39.443
39.166
38.554
34.641
13C NMR (DMSO-d6)
BnO
OBn
P
O
CN
NH2
Br
5e
f1 (ppm)

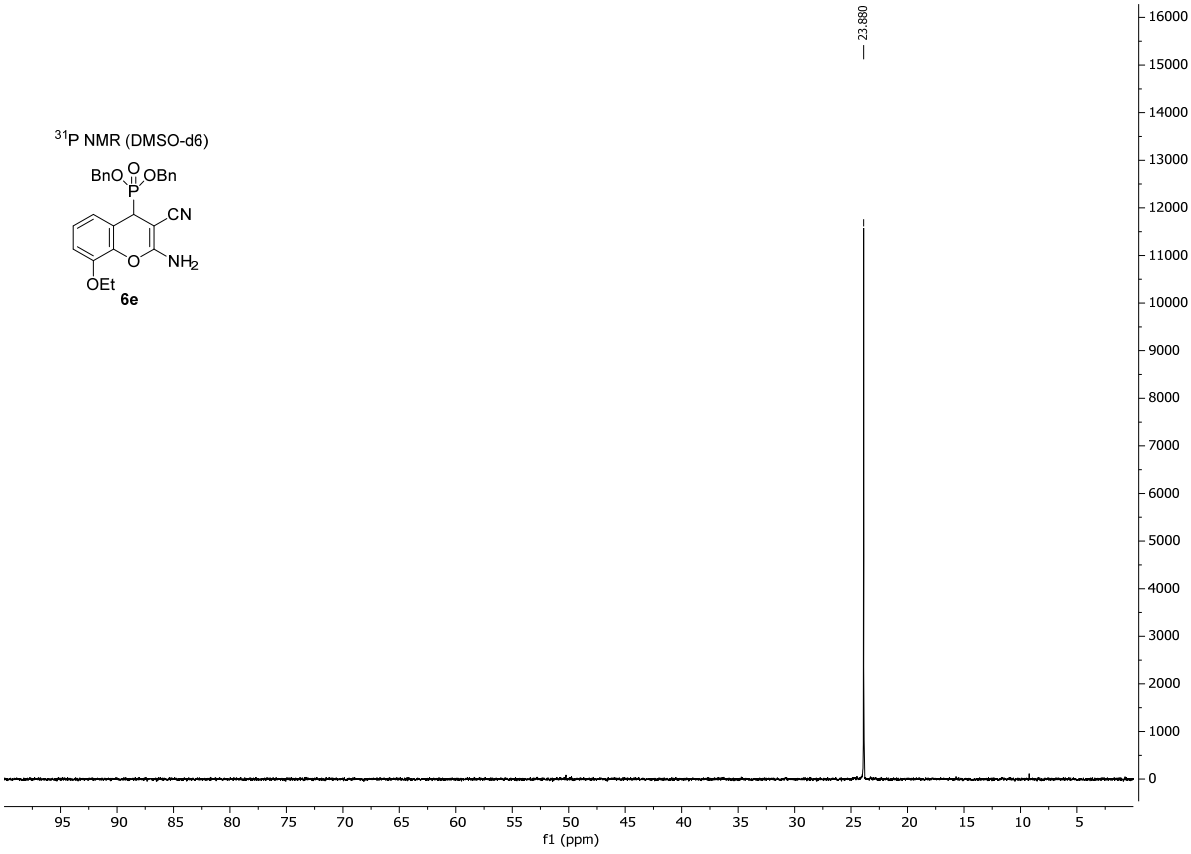

31P NMR (DMSO-d6)
BnO
OBn
P
O
CN
NH2
O
Br
5e
23.411
f1 (ppm)

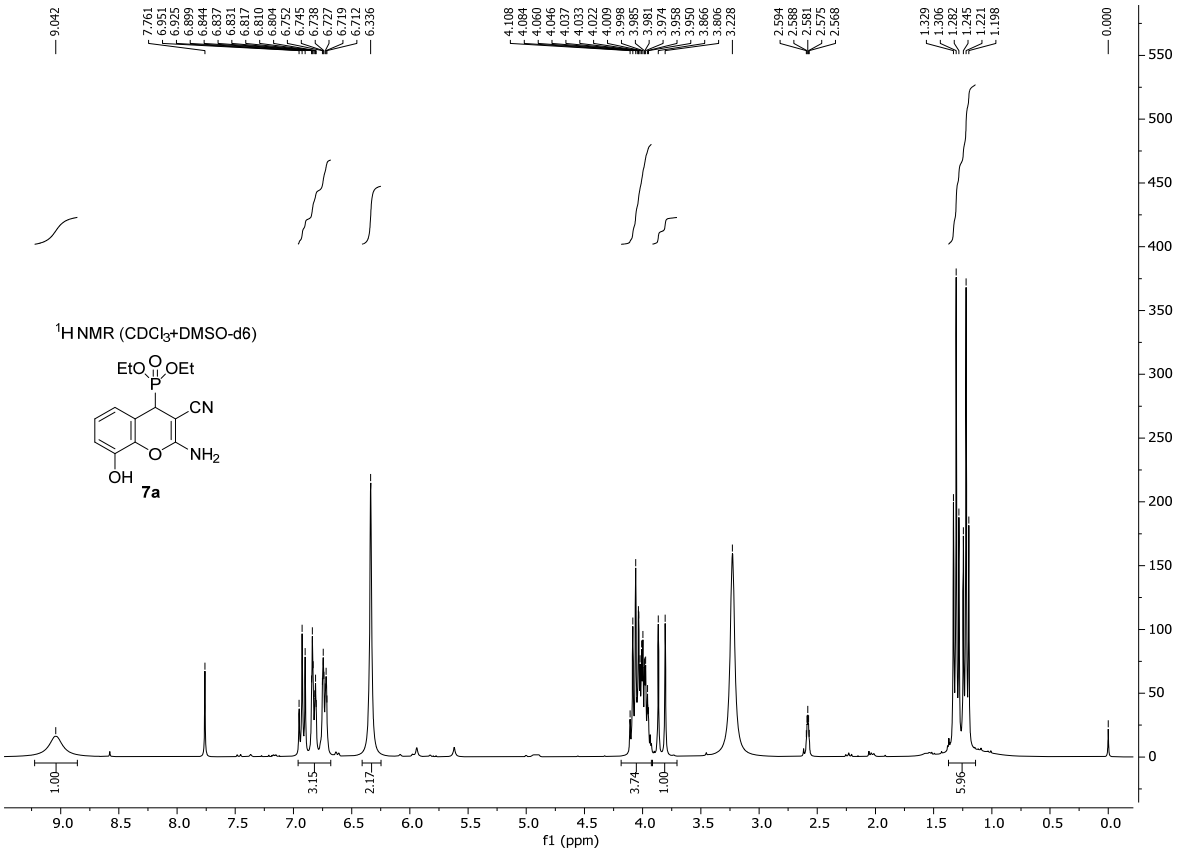

1H NMR (CDCl3)
EtO
OEt
P
O
CN
NH2
O
OEt
6a
f1 (ppm)

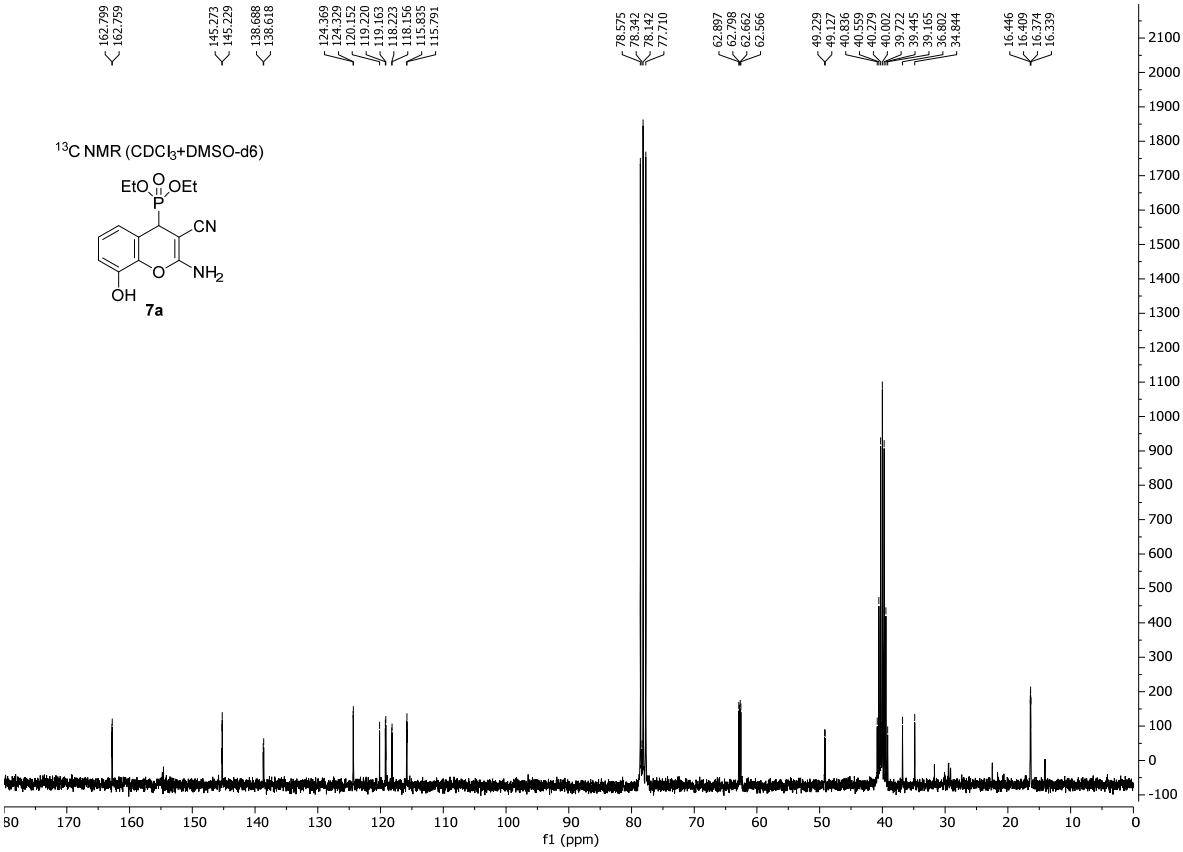

31P NMR (CDCl3+DMSO-d6)
EtO
OEt
P
O
CN
NH2
O
OEt
6a
26.841
f1 (ppm)

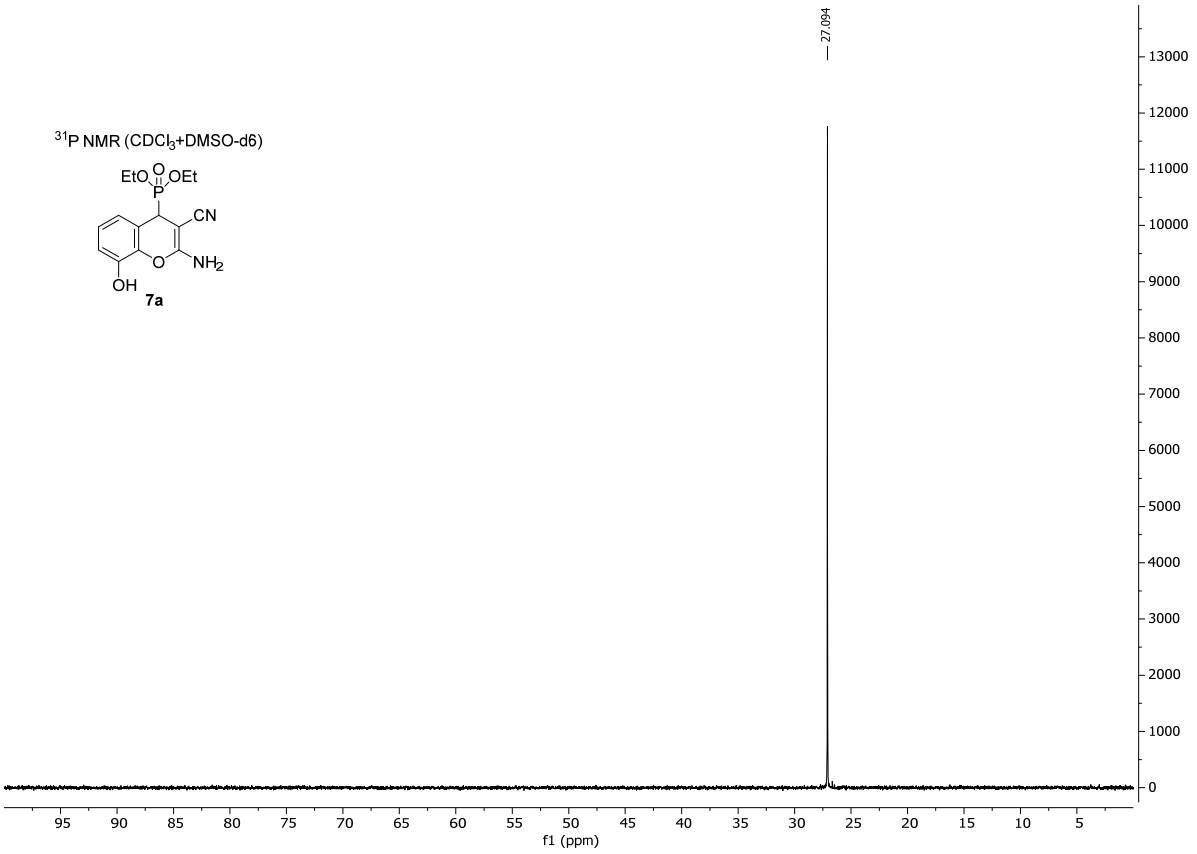

1H NMR (DMSO-d6)
BnO
OBn
P
O
CN
NH2
O
OEt
6e
7.364
7.352
7.345
7.334
7.326
7.312
7.286
7.276
7.263
7.251
7.243
7.217
7.048
7.024
7.014
6.999
6.990
6.848
6.840
6.833
6.825
6.816
6.809
4.993
4.955
4.936
4.929
4.911
4.896
4.888
4.870
4.315
4.257
4.120
4.097
4.074
4.051
3.351
2.515
2.510
2.503
2.496
2.490
1.989
1.356
1.333
1.310
0.001
11.83
2.04
0.98
3.91
1.00
2.04
2.98
f1 (ppm)

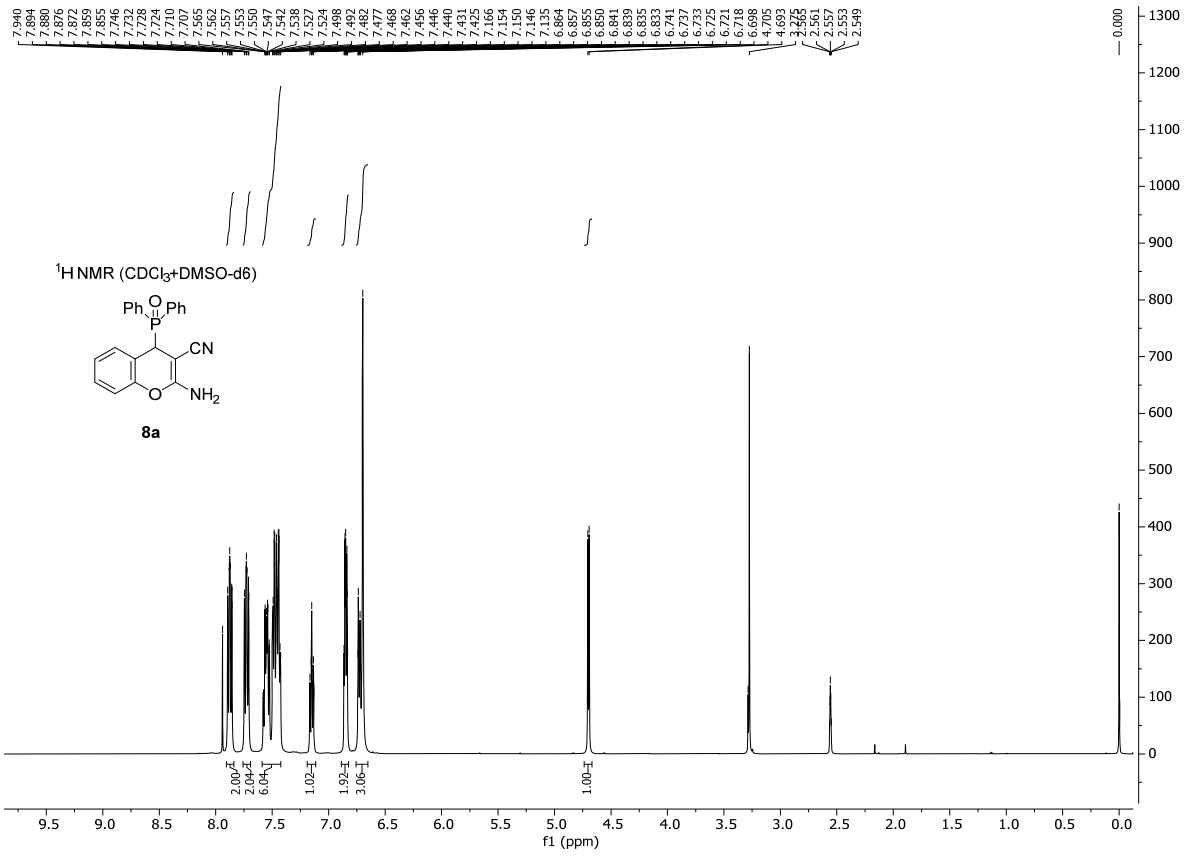

163.260
163.225
146.891
146.846
140.181
140.108
136.962
136.880
128.816
128.808
128.541
128.522
127.992
127.946
124.637
124.605
121.226
121.171
120.635
119.056
118.991
113.654
113.619
67.810
67.733
67.715
67.637
64.743
47.657
47.558
40.835
40.558
40.279
40.001
39.724
39.445
39.167
36.433
34.514
15.109
13C NMR (DMSO-d6)
BnO
OBn
CN
NH2
OEt
6e
f1 (ppm)

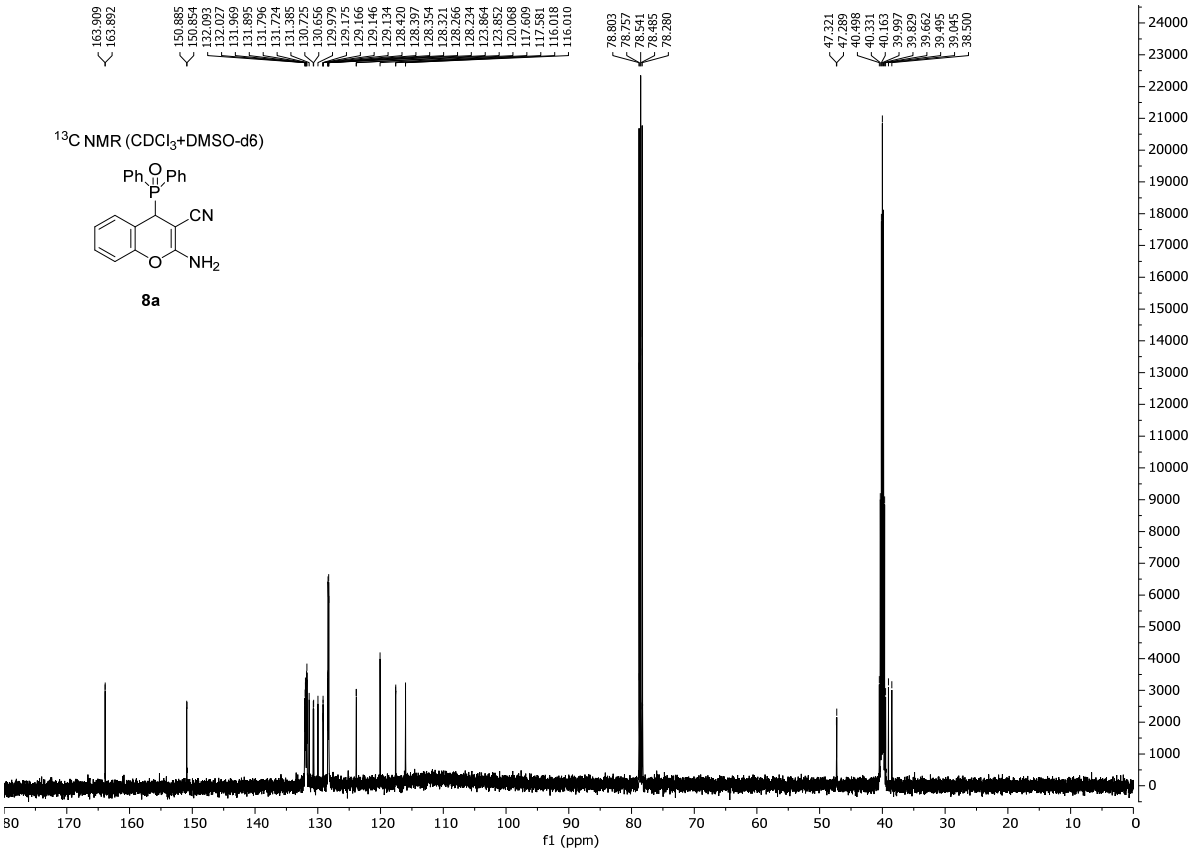

23.880
31P NMR (DMSO-d6)
BnO
OBn
CN
NH2
OEt
6e
f1 (ppm)


9.042
7.761
6.951
6.925
6.899
6.844
6.837
6.831
6.817
6.810
6.804
6.752
6.745
6.738
6.727
6.719
6.712
6.336
4.108
4.084
4.060
4.046
4.037
4.033
4.022
4.009
3.998
3.985
3.981
3.974
3.958
3.950
3.866
3.806
3.228
2.594
2.588
2.581
2.575
2.568
1.329
1.306
1.282
1.245
1.221
1.198
0.000
1H NMR (CDCl3+DMSO-d6)
EtO
OEt
P
O
CN
NH2
OH
7a
1.00
3.15
2.17
3.74
1.00
5.96
f1 (ppm)


162.799
162.759
145.273
145.229
138.688
138.618
124.369
124.329
120.152
119.220
119.163
118.223
118.156
115.835
115.791
78.575
78.342
78.142
77.710
62.897
62.798
62.662
62.566
49.229
49.127
40.836
40.559
40.279
40.002
39.722
39.445
39.165
36.802
34.844
16.446
16.409
16.374
16.339
13C NMR (CDCl3+DMSO-d6)
EtO
OEt
P
O
CN
NH2
OH
7a
f1 (ppm)


31P NMR (CDCl3+DMSO-d6)
EtO
OEt
P
O
CN
NH2
OH
O
7a
27.094
f1 (ppm)


1H NMR (CDCl3+DMSO-d6)
Ph
Ph
P
O
CN
NH2
O
8a
0.000
2.00
2.04
6.04
1.02
1.92
3.06
1.00
f1 (ppm)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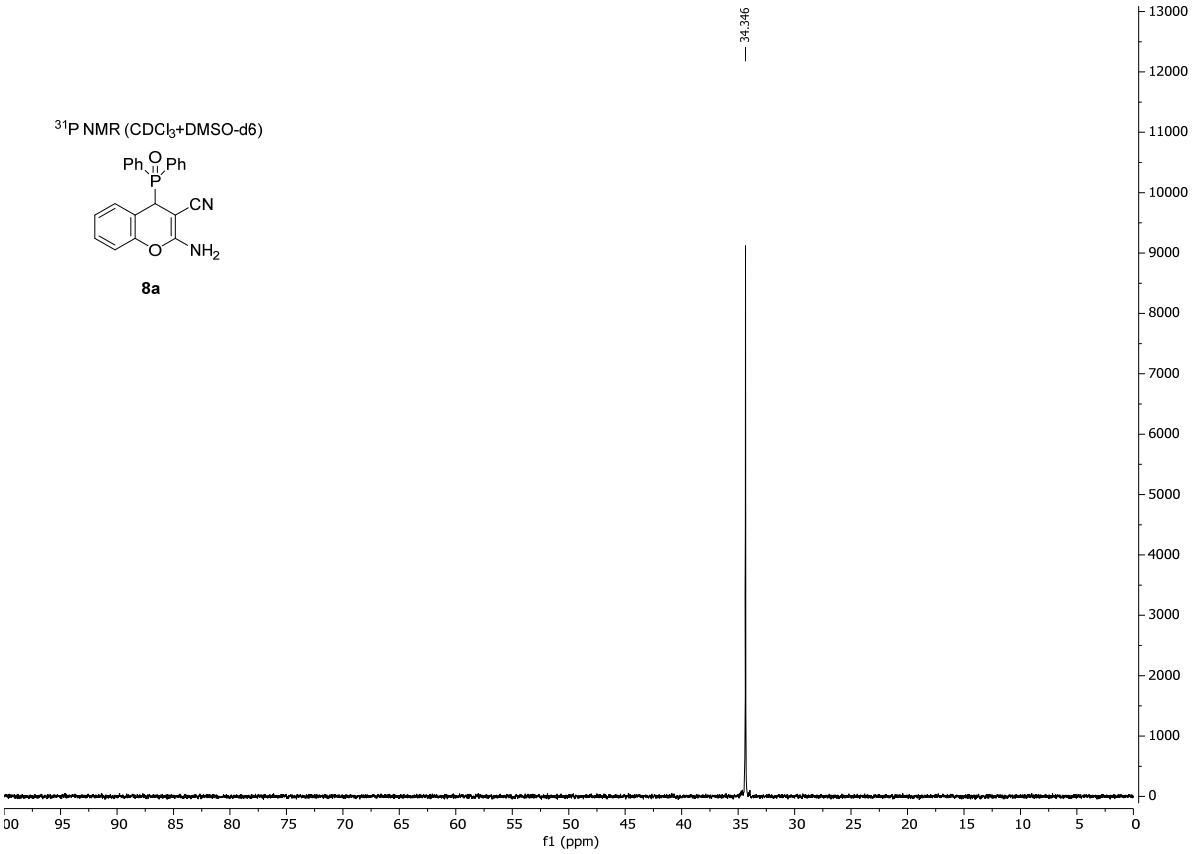
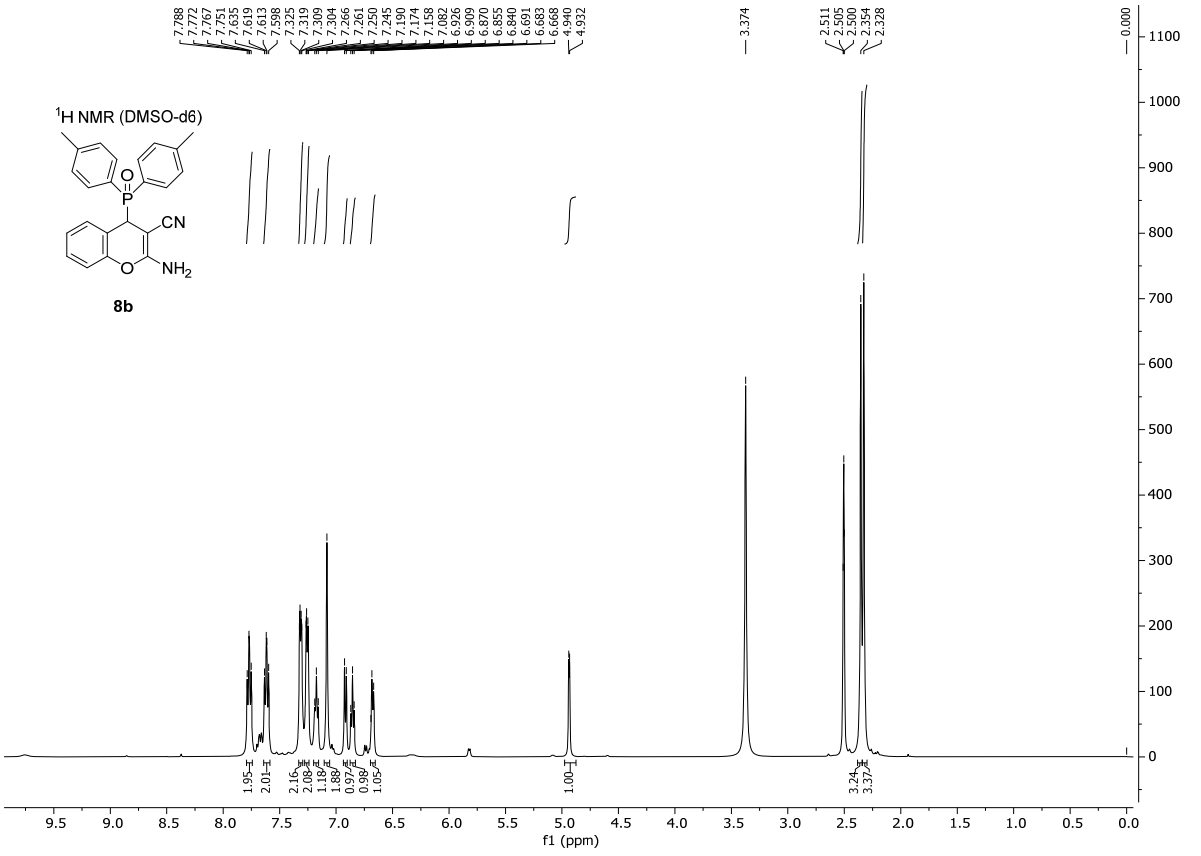
163.892
150.885
150.854
132.093
132.027
131.969
131.895
131.796
131.724
131.385
130.725
130.656
129.979
129.175
129.166
129.146
129.134
128.420
128.397
128.354
128.321
128.266
128.234
123.864
123.852
120.068
117.609
117.581
116.018
116.010
78.803
78.757
78.541
78.485
78.280
47.321
47.289
40.498
40.331
40.163
39.997
39.829
39.662
39.495
39.045
38.500
13C NMR (CDCl3+DMSO-d6)
Ph
O
Ph
P
CN
O
NH2
8a
f1 (ppm)


34.346
31P NMR (CDCl3+DMSO-d6)
Ph
O
Ph
P
CN
O
NH2
8a
f1 (ppm)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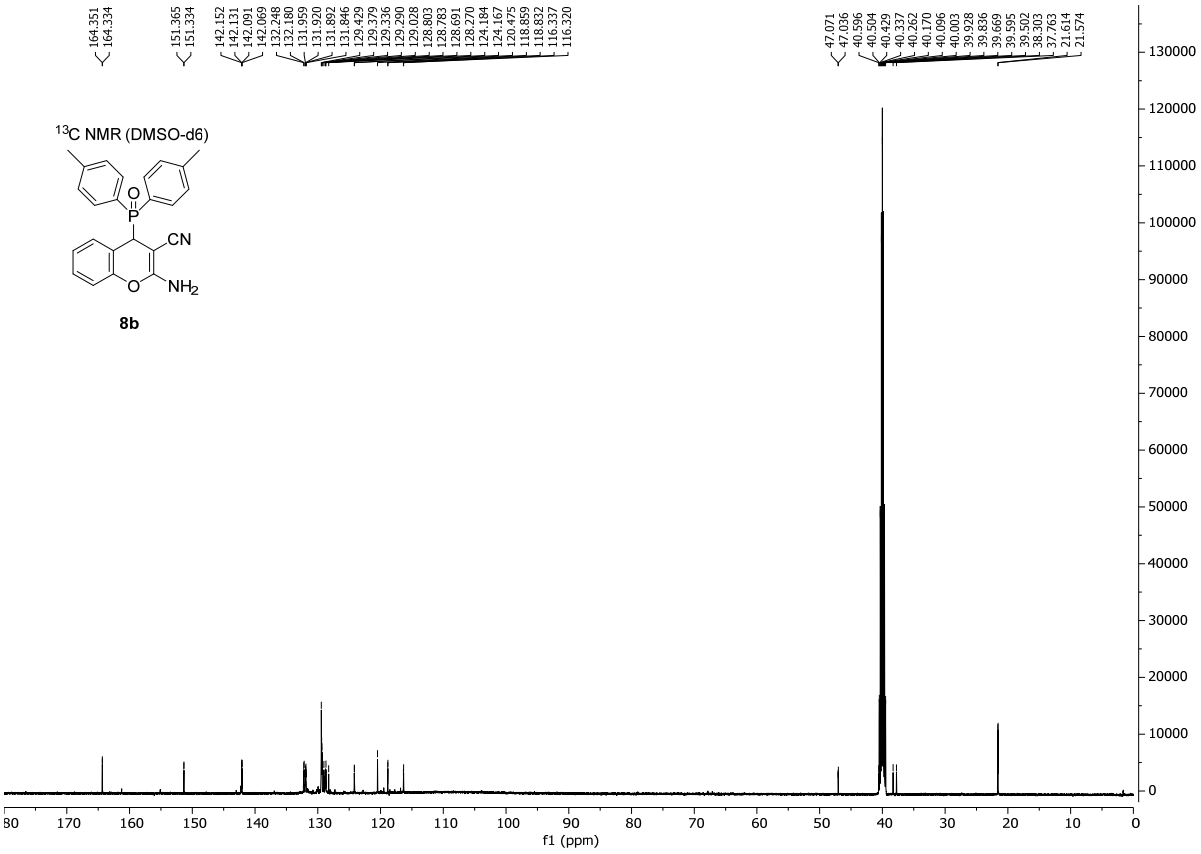
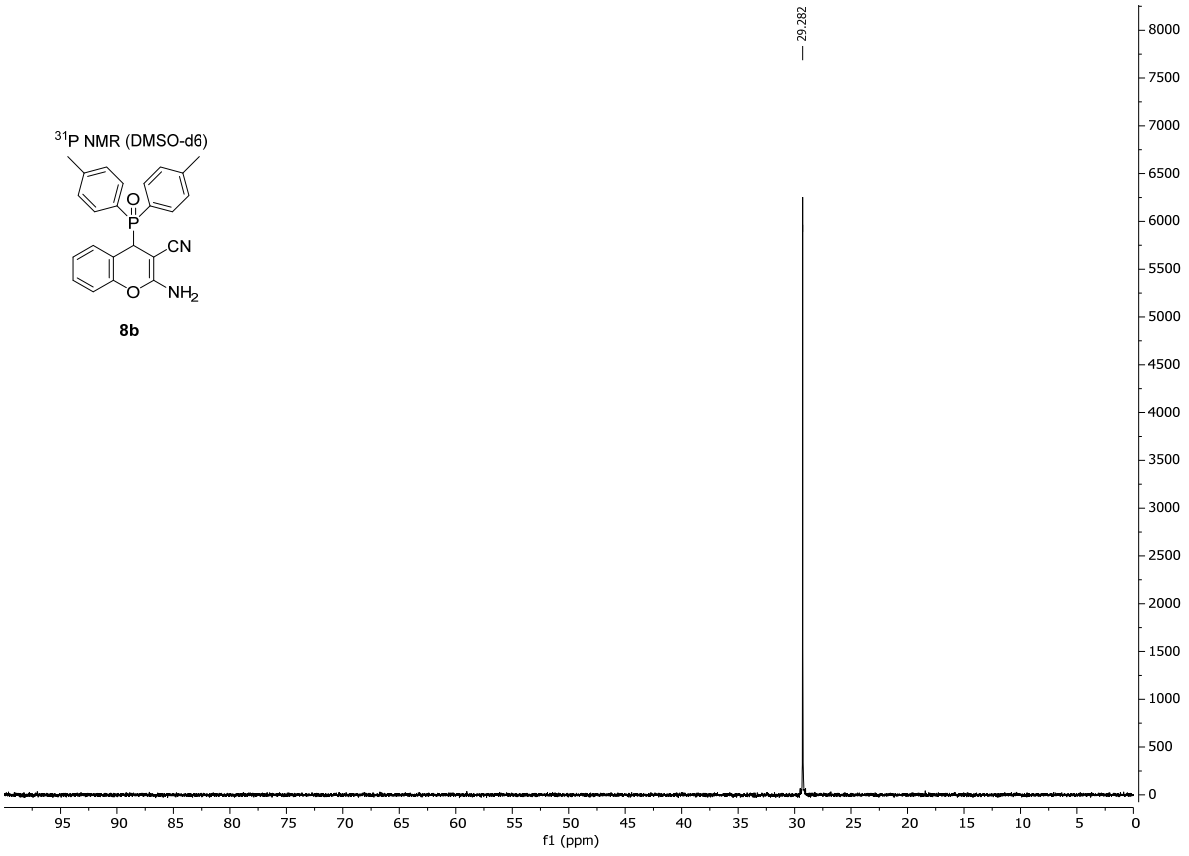
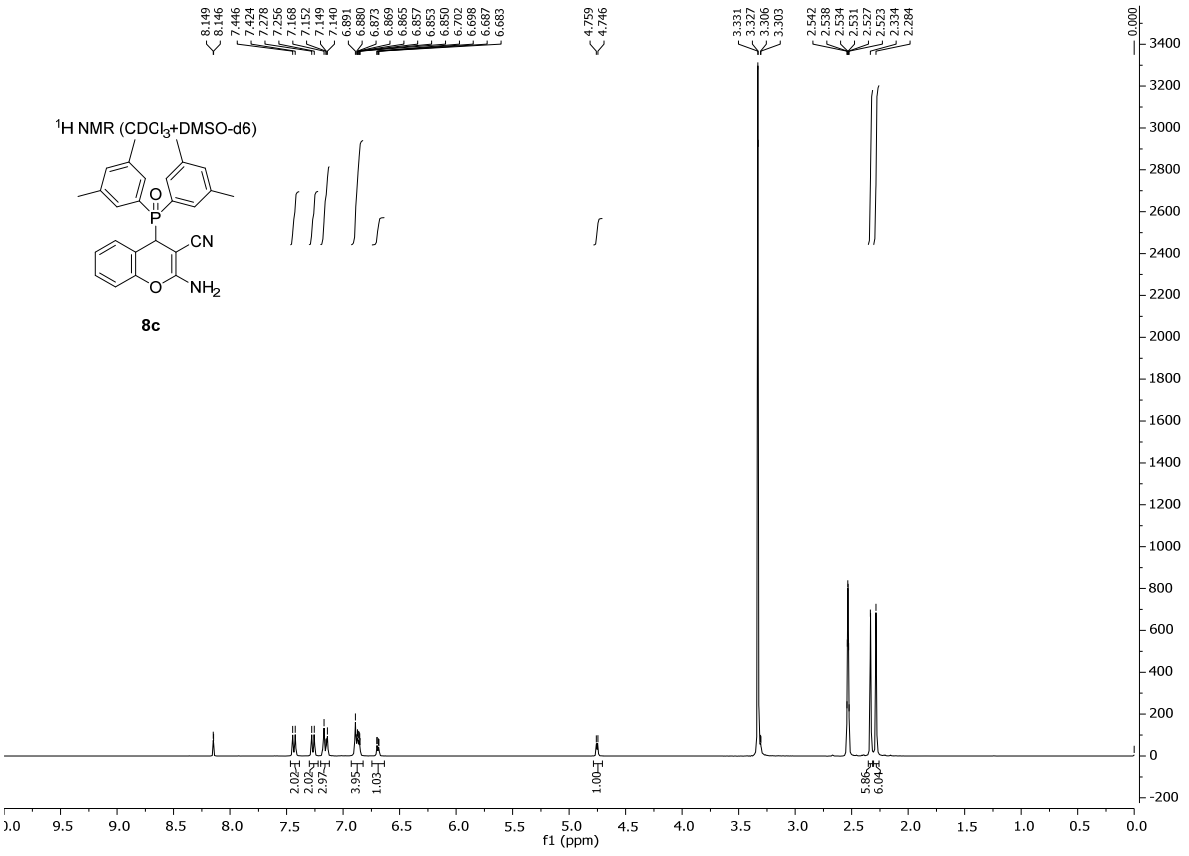
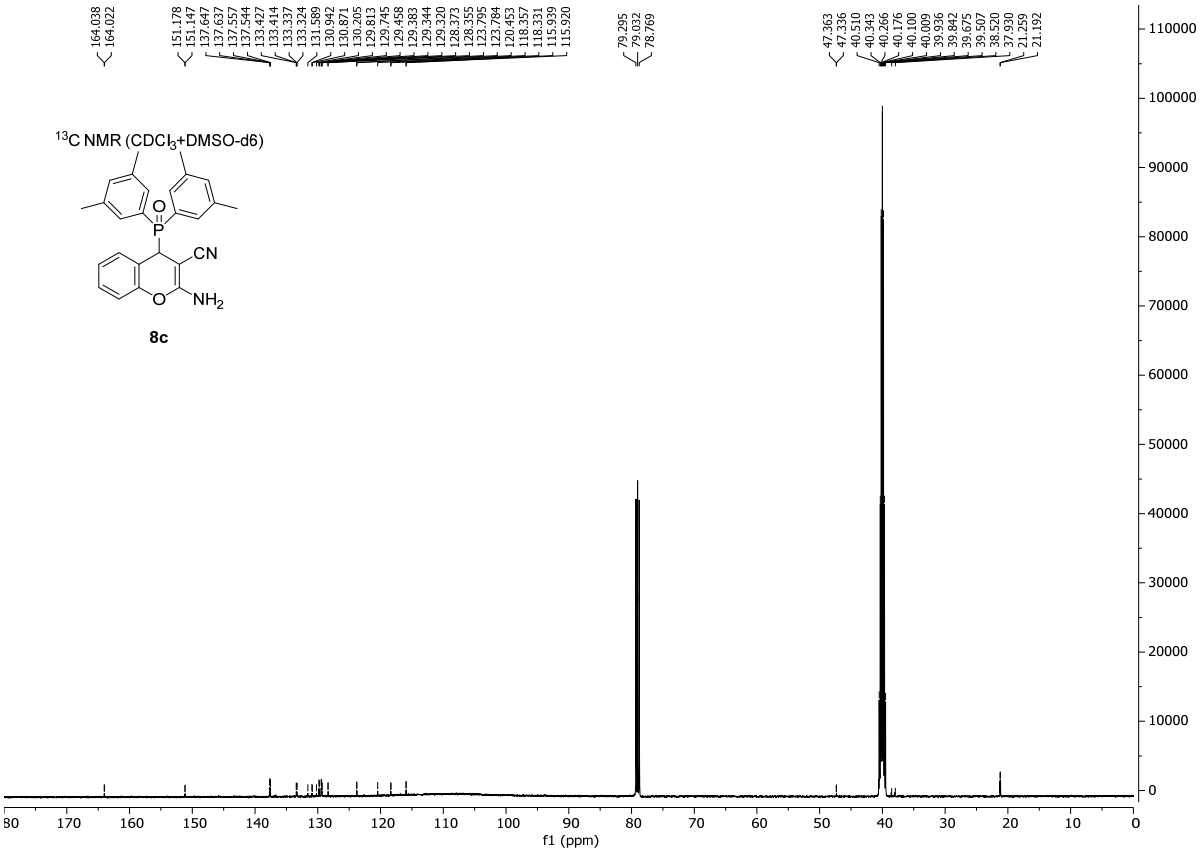
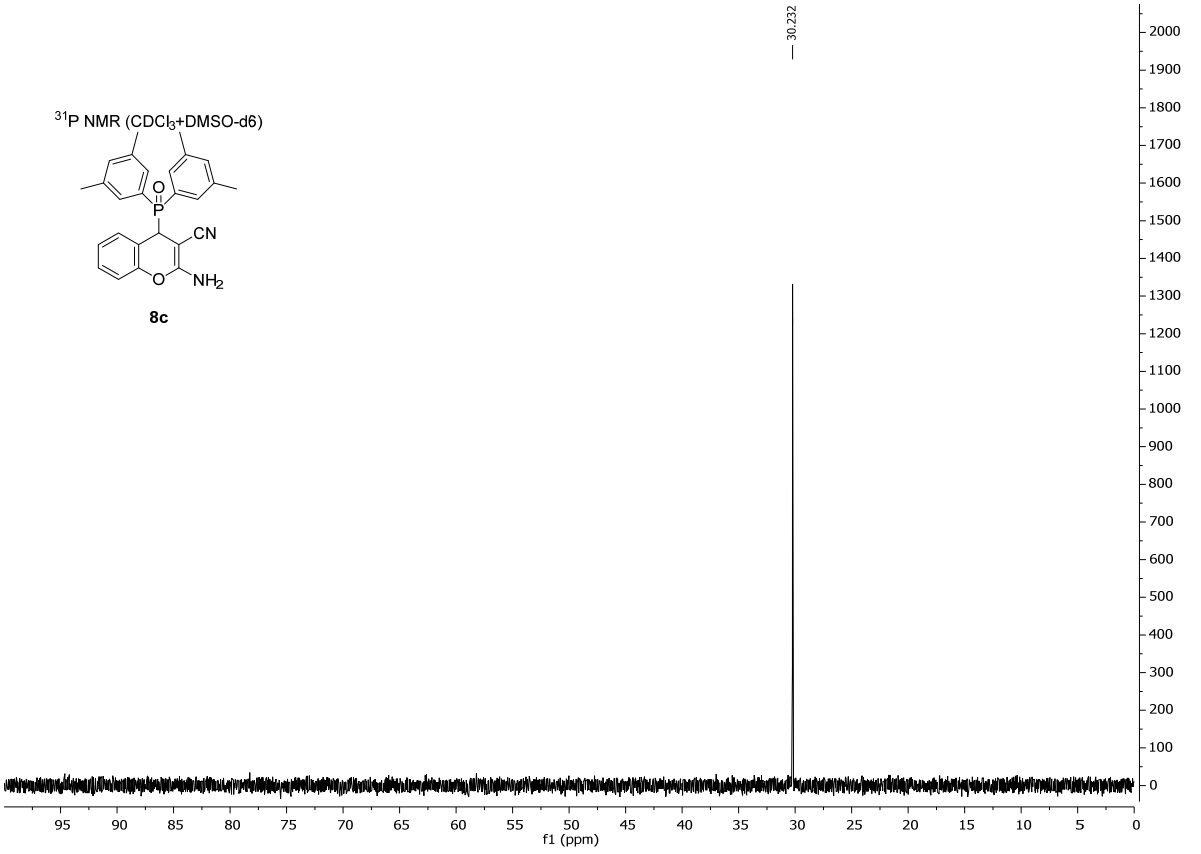
7.772
7.767
7.751
7.635
7.619
7.613
7.598
7.325
7.319
7.309
7.304
7.266
7.261
7.250
7.245
7.190
7.174
7.158
7.082
6.926
6.909
6.870
6.855
6.840
6.691
6.683
6.668
4.940
4.932
3.374
2.511
2.505
2.500
2.354
2.328
0.000
1H NMR (DMSO-d6)
O
P
CN
O
NH2
8b
1.95
2.01
2.16
2.08
1.18
1.89
0.97
0.98
1.05
1.00
3.24
3.37
f1 (ppm)

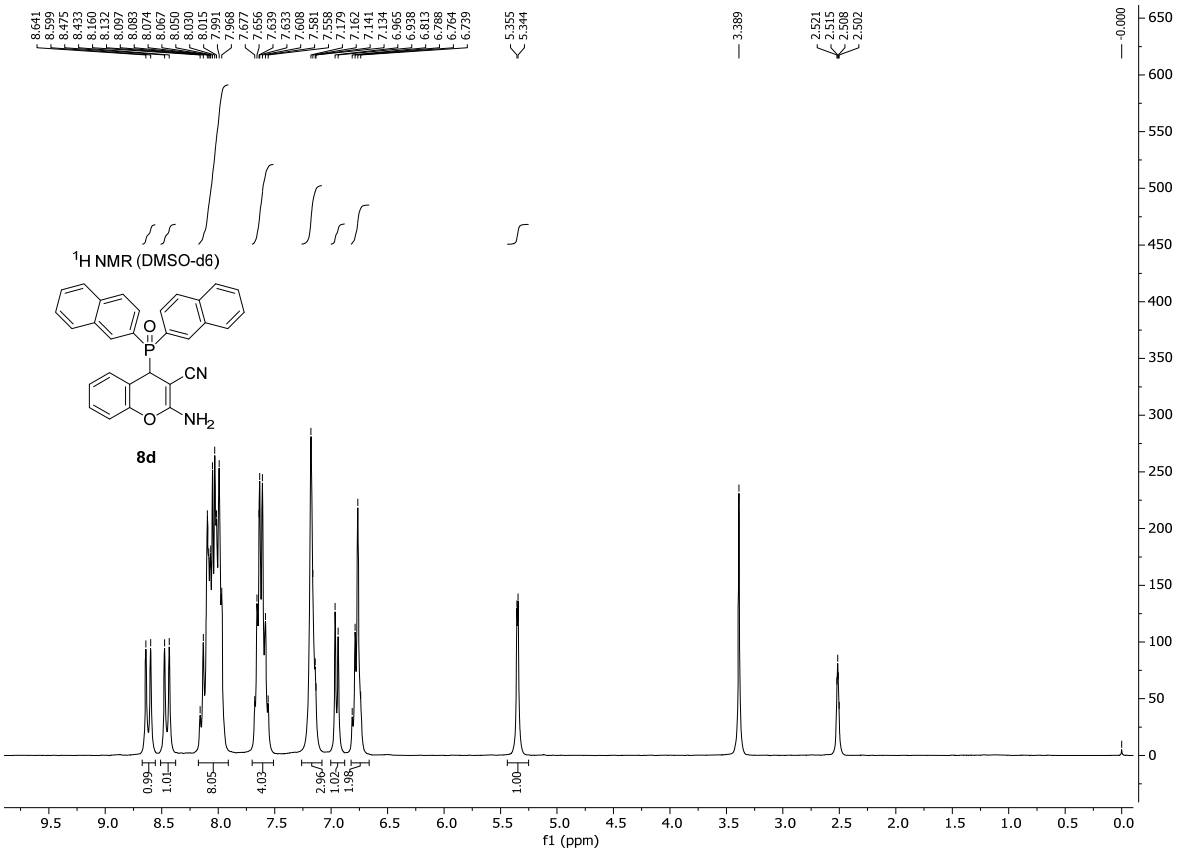

164.351
164.334
151.365
151.334
142.152
142.131
142.091
142.069
132.248
132.180
131.959
131.920
131.892
131.846
129.429
129.379
129.336
129.290
129.028
128.803
128.783
128.691
128.270
124.184
124.167
120.475
118.859
118.832
116.337
116.320
47.071
47.036
40.596
40.504
40.429
40.337
40.262
40.170
40.096
40.003
39.928
39.836
39.669
39.595
39.502
38.303
37.763
21.614
21.574
13C NMR (DMSO-d6)
O
P
CN
O
NH2
8b
f1 (ppm)

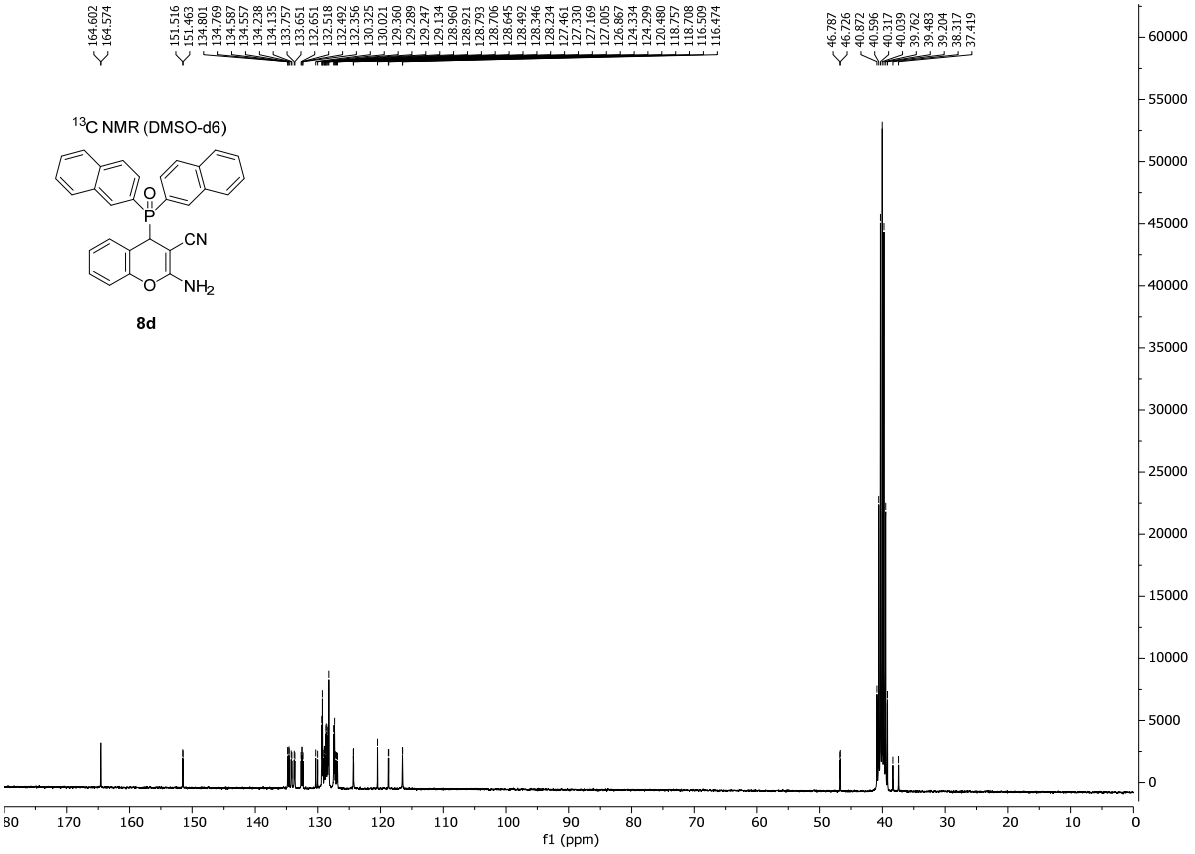

31P NMR (DMSO-d6)
8b
29.282
f1 (ppm)

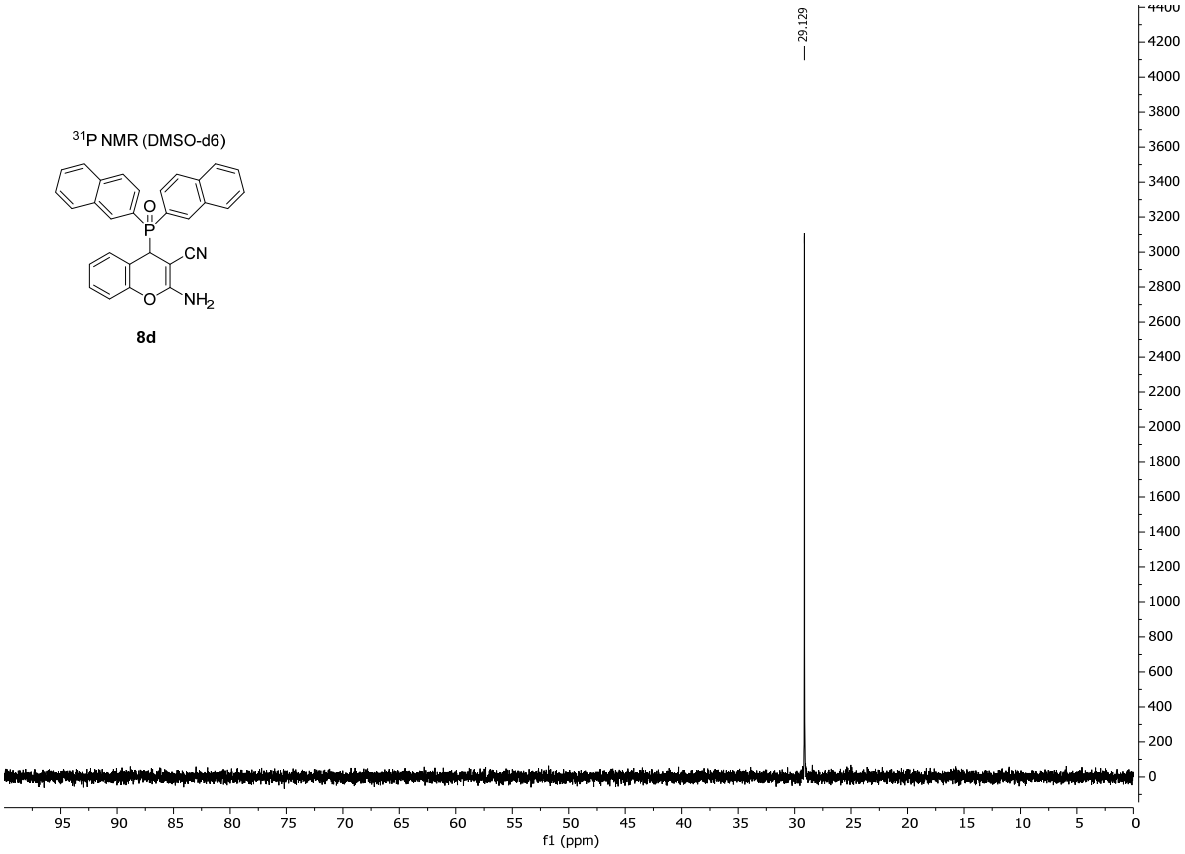

1H NMR (CDCl3+DMSO-d6)
8c
f1 (ppm)

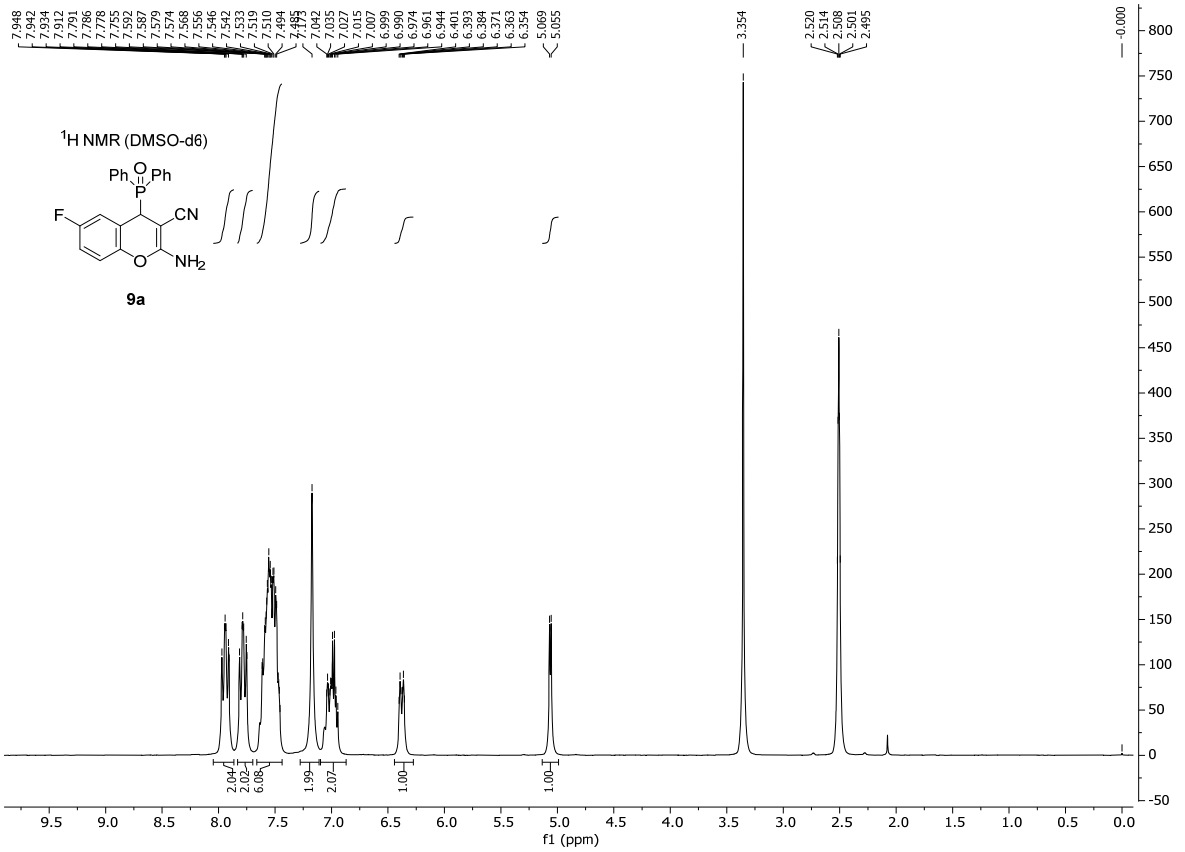

164.038
164.022
151.178
151.147
137.647
137.637
137.557
137.544
133.427
133.414
133.337
133.324
131.589
130.942
130.871
130.205
129.813
129.745
129.458
129.383
129.344
129.320
128.373
128.355
123.795
123.784
120.453
118.357
118.331
115.939
115.920
79.295
79.032
78.769
47.363
47.336
40.510
40.343
40.266
40.176
40.100
40.009
39.936
39.842
39.675
39.507
38.520
37.930
21.259
21.192
13C NMR (CDCl3+DMSO-d6)
O
P
CN
O
NH2
8c
f1 (ppm)

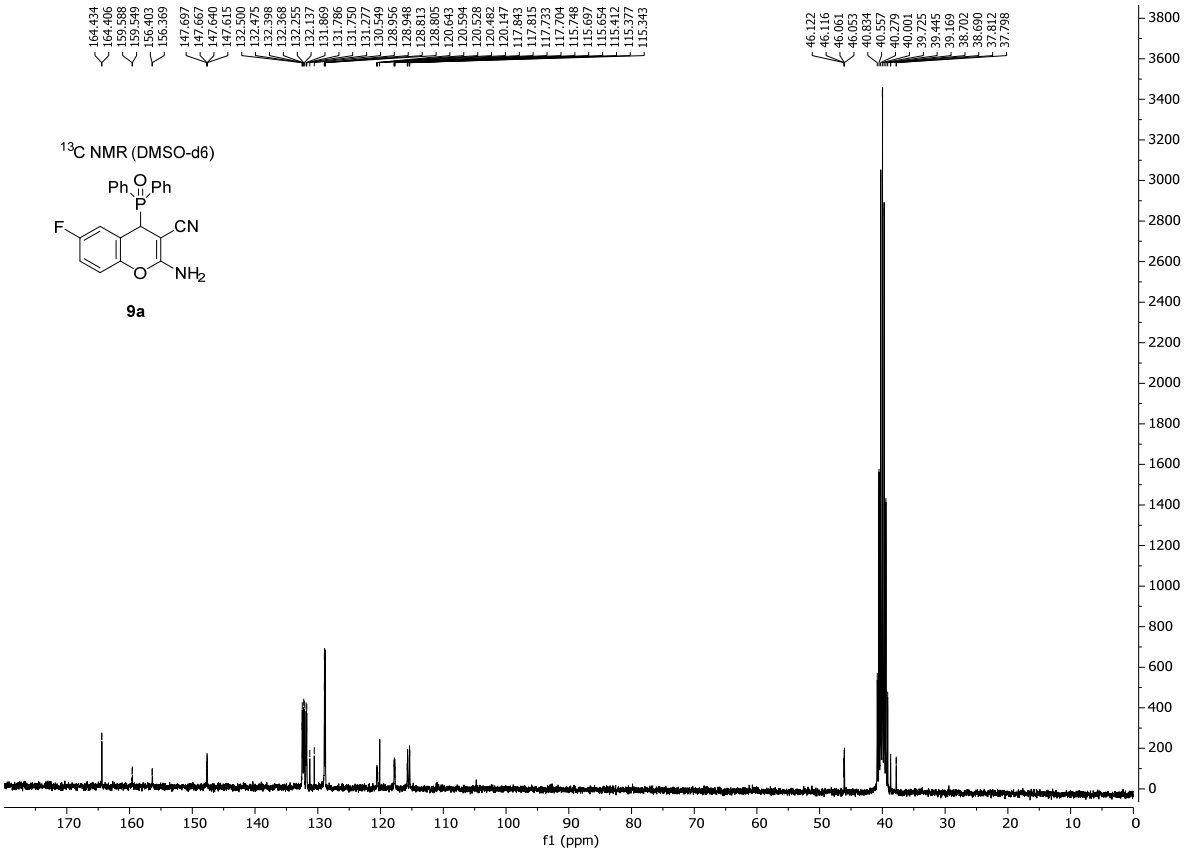

30.232
31P NMR (CDCl3+DMSO-d6)
O
P
CN
O
NH2
8c
f1 (ppm)

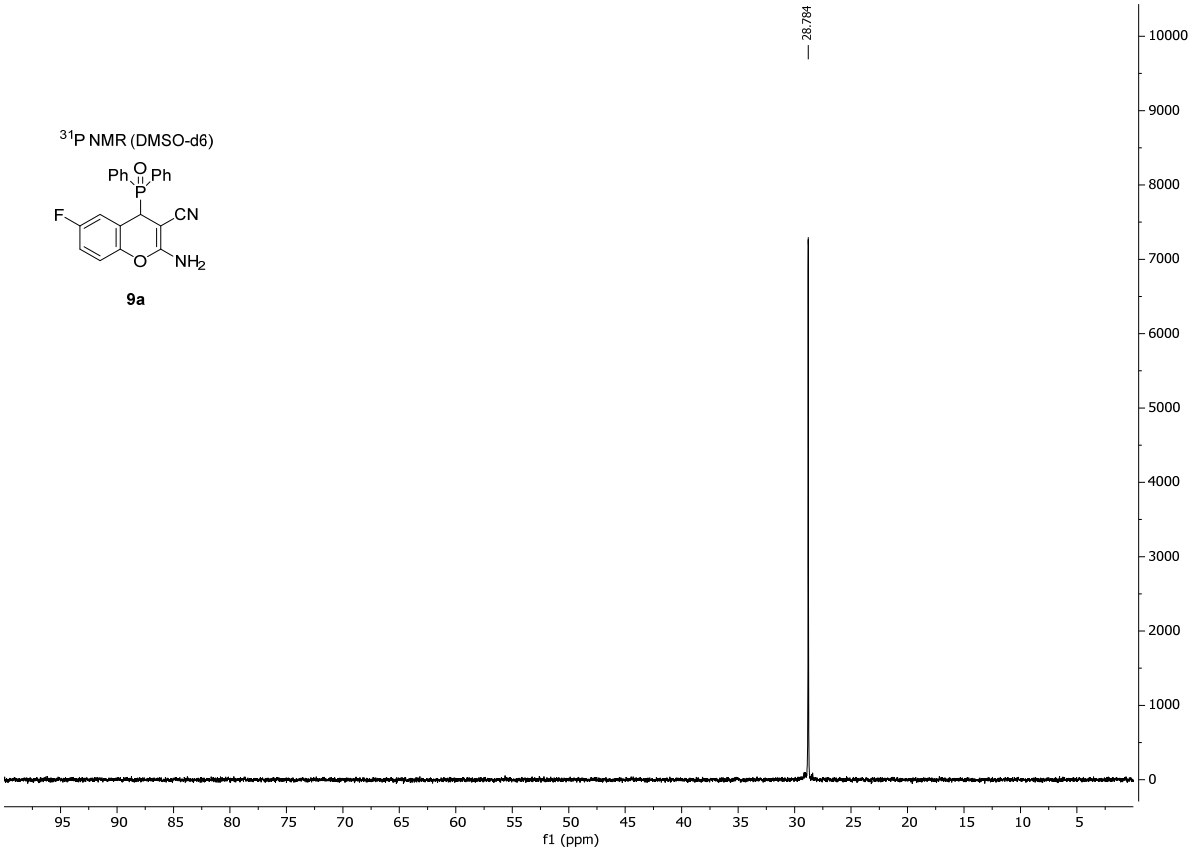

^{1}H NMR (DMSO-d6)
8d
f1 (ppm)

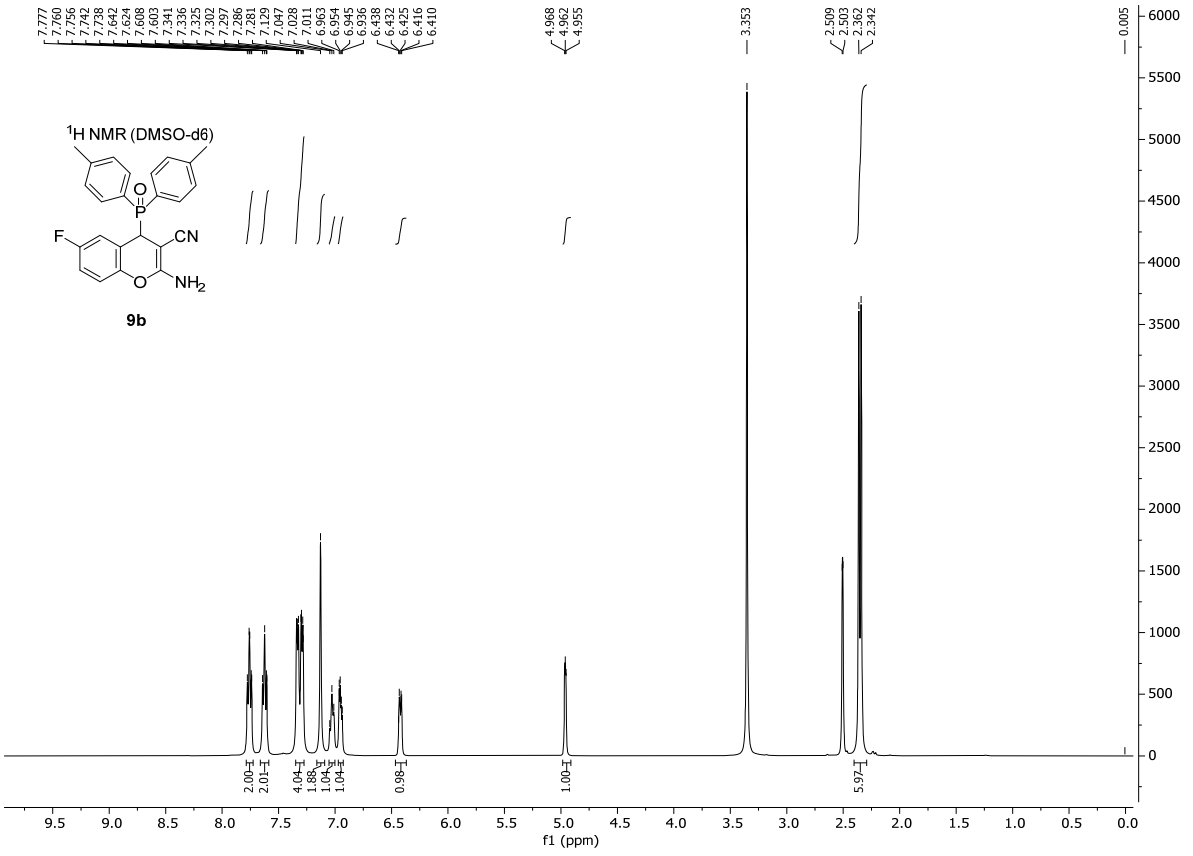

^{13}C NMR (DMSO-d6)
8d
f1 (ppm)

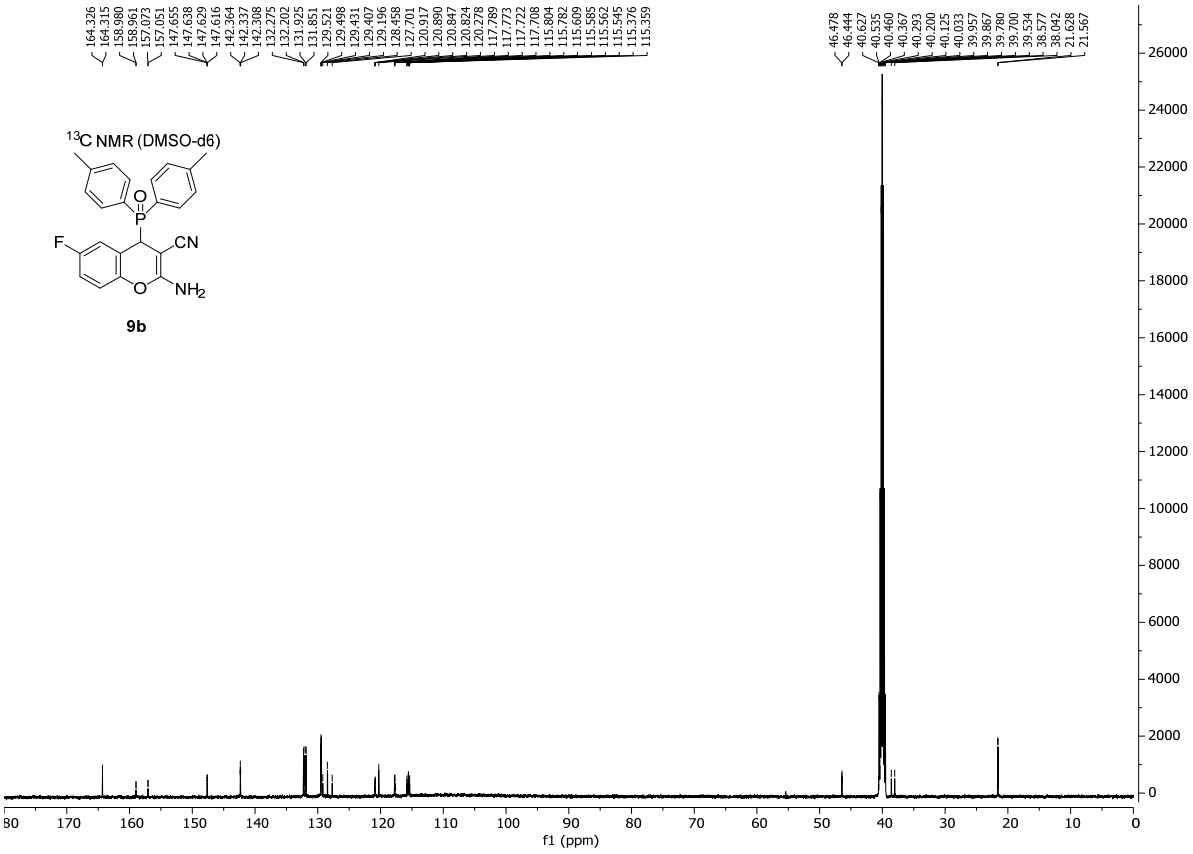

31P NMR (DMSO-d6)
8d
29.129
f1 (ppm)


1H NMR (DMSO-d6)
9a
7.948
7.942
7.934
7.912
7.791
7.786
7.778
7.755
7.592
7.587
7.579
7.574
7.568
7.556
7.546
7.542
7.533
7.519
7.510
7.494
7.042
7.035
7.027
7.015
7.007
6.999
6.990
6.974
6.961
6.944
6.401
6.393
6.384
6.371
6.363
6.354
5.069
5.055
3.354
2.520
2.514
2.508
2.501
2.495
-0.000
2.04
2.02
6.08
1.99
2.07
1.00
1.00
f1 (ppm)


164.434
164.406
159.588
159.549
156.403
156.369
147.697
147.667
147.640
147.615
132.500
132.475
132.398
132.368
132.255
132.137
131.869
131.786
131.750
131.277
130.549
128.956
128.948
128.813
128.805
120.643
120.594
120.528
120.482
120.147
117.843
117.815
117.733
117.704
115.748
115.697
115.654
115.412
115.377
115.343
46.122
46.116
46.061
46.053
40.834
40.557
40.279
40.001
39.725
39.445
39.169
38.702
38.690
37.812
37.798
^{13}C NMR (DMSO-d6)
Ph
O
Ph
P
F
CN
O
NH$_2$
9a
f1 (ppm)


28.784
^{31}P NMR (DMSO-d6)
Ph
O
Ph
P
F
CN
O
NH$_2$
9a
f1 (ppm)


7.777
7.760
7.756
7.742
7.738
7.642
7.624
7.608
7.603
7.341
7.336
7.325
7.302
7.297
7.286
7.281
7.129
7.047
7.028
7.011
6.963
6.954
6.945
6.936
6.438
6.432
6.425
6.416
6.410
4.968
4.962
4.955
3.353
2.509
2.503
2.362
2.342
0.005
^{1}H NMR (DMSO-d6)
O
P
F
CN
O
NH$_2$
9b
2.00
2.01
4.04
1.88
1.04
1.04
0.98
1.00
5.97
f1 (ppm)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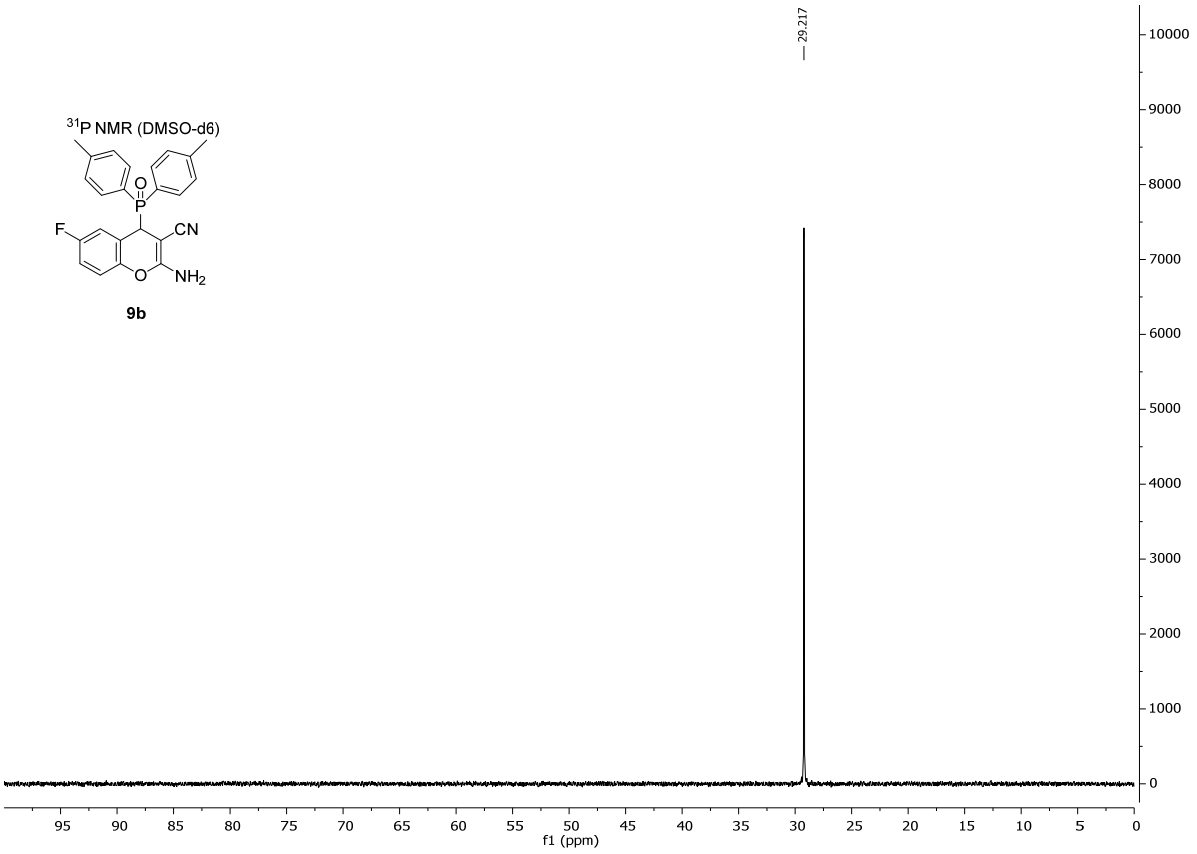
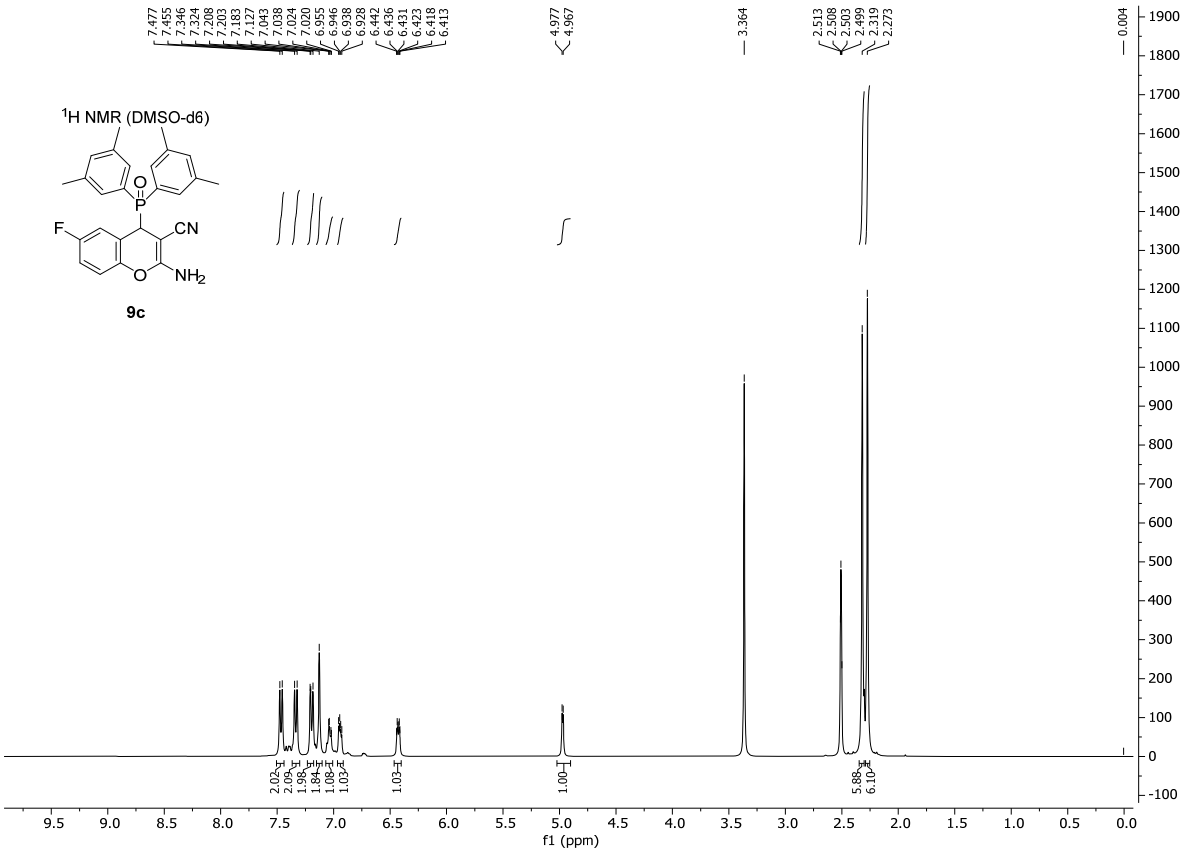
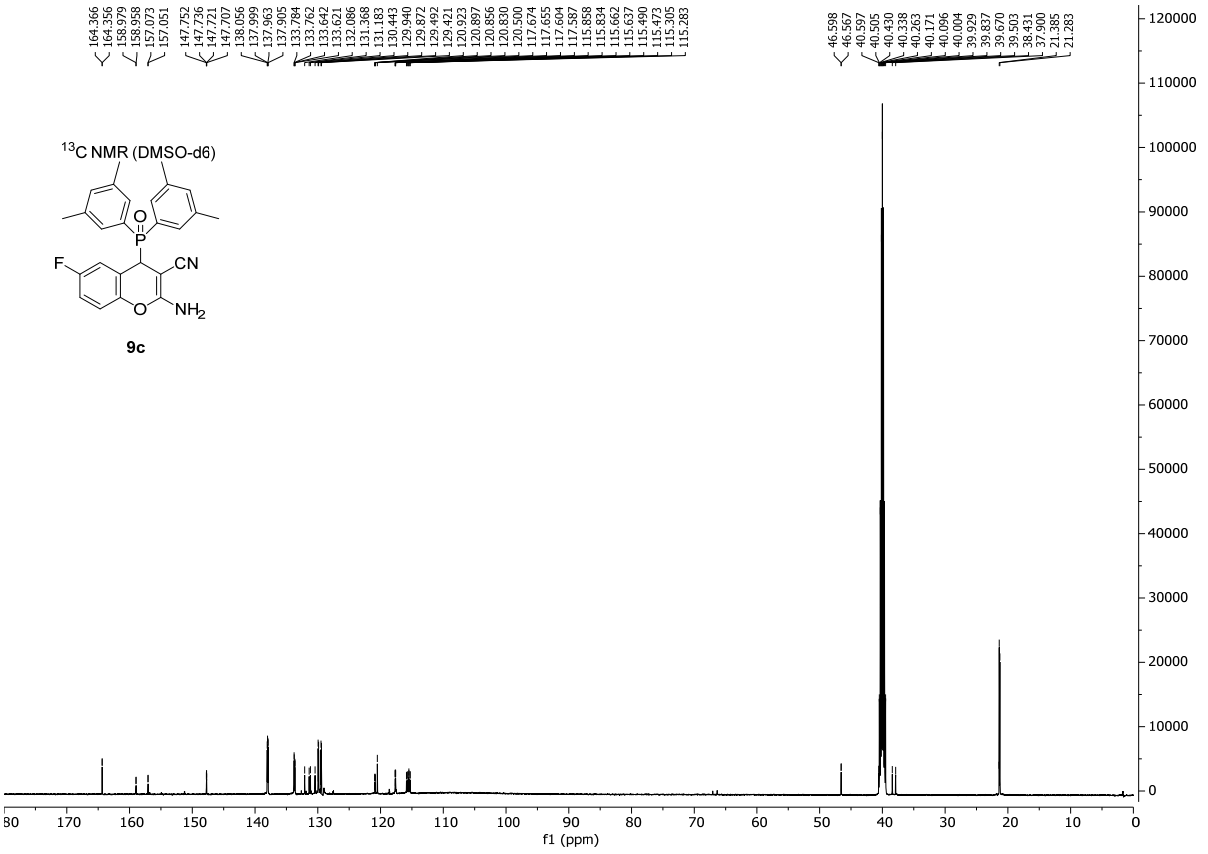
164.315
158.980
158.961
157.073
157.051
147.655
147.638
147.629
147.616
142.364
142.337
142.308
132.275
132.202
131.925
131.851
129.521
129.498
129.431
129.407
129.196
128.458
127.701
120.917
120.890
120.847
120.824
120.278
117.789
117.773
117.722
117.708
115.804
115.782
115.609
115.585
115.562
115.545
115.376
115.359
46.478
46.444
40.627
40.535
40.460
40.367
40.293
40.200
40.125
40.033
39.957
39.867
39.780
39.700
39.534
38.577
38.042
21.628
21.567
^{13}C NMR (DMSO-d6)
O
P
F
CN
O
NH$_2$
9b
f1 (ppm)


31P NMR (DMSO-d6)
9b
29.217
f1 (ppm)


1H NMR (DMSO-d6)
9c
7.477
7.455
7.346
7.324
7.208
7.203
7.183
7.127
7.043
7.038
7.024
7.020
6.955
6.946
6.938
6.928
6.442
6.436
6.431
6.423
6.418
6.413
4.977
4.967
3.364
2.513
2.508
2.503
2.499
2.319
2.273
0.004
2.02
2.09
1.98
1.84
1.08
1.03
1.03
1.00
5.88
6.10
f1 (ppm)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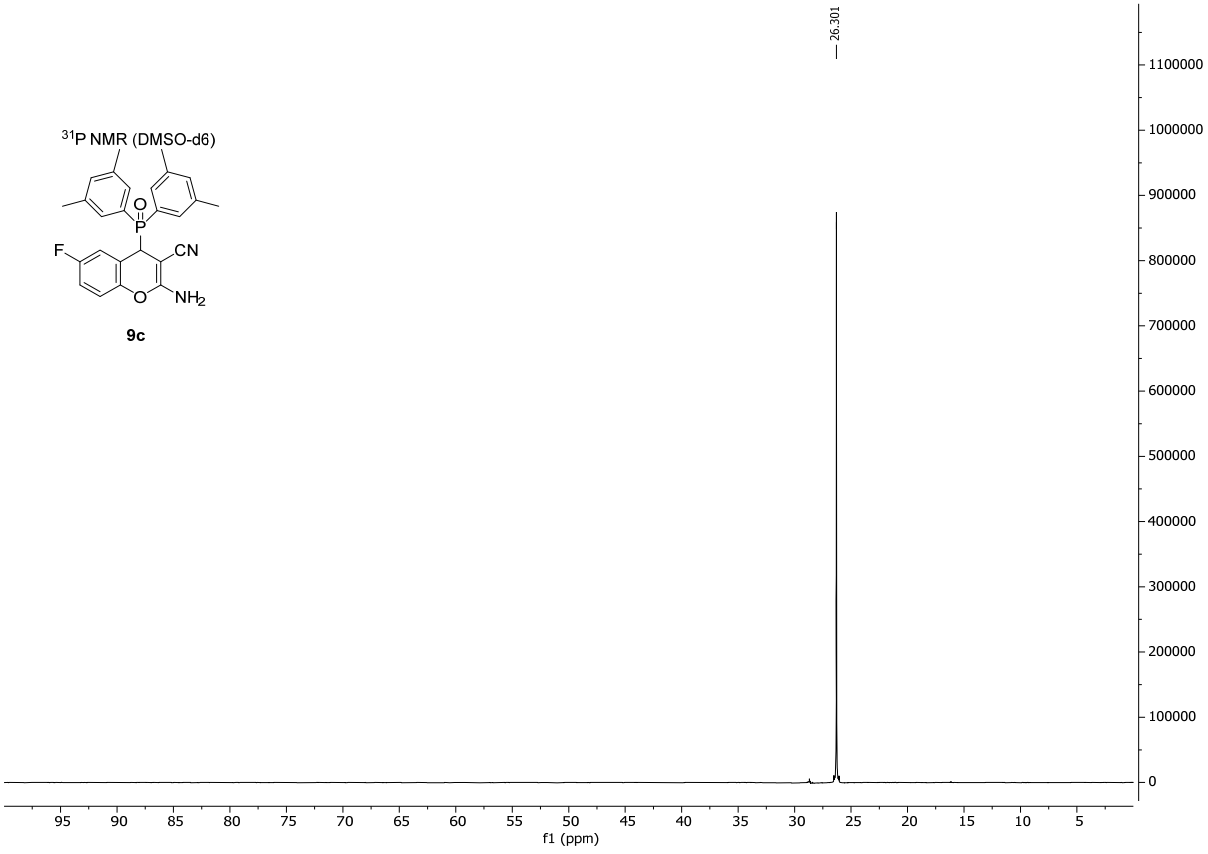
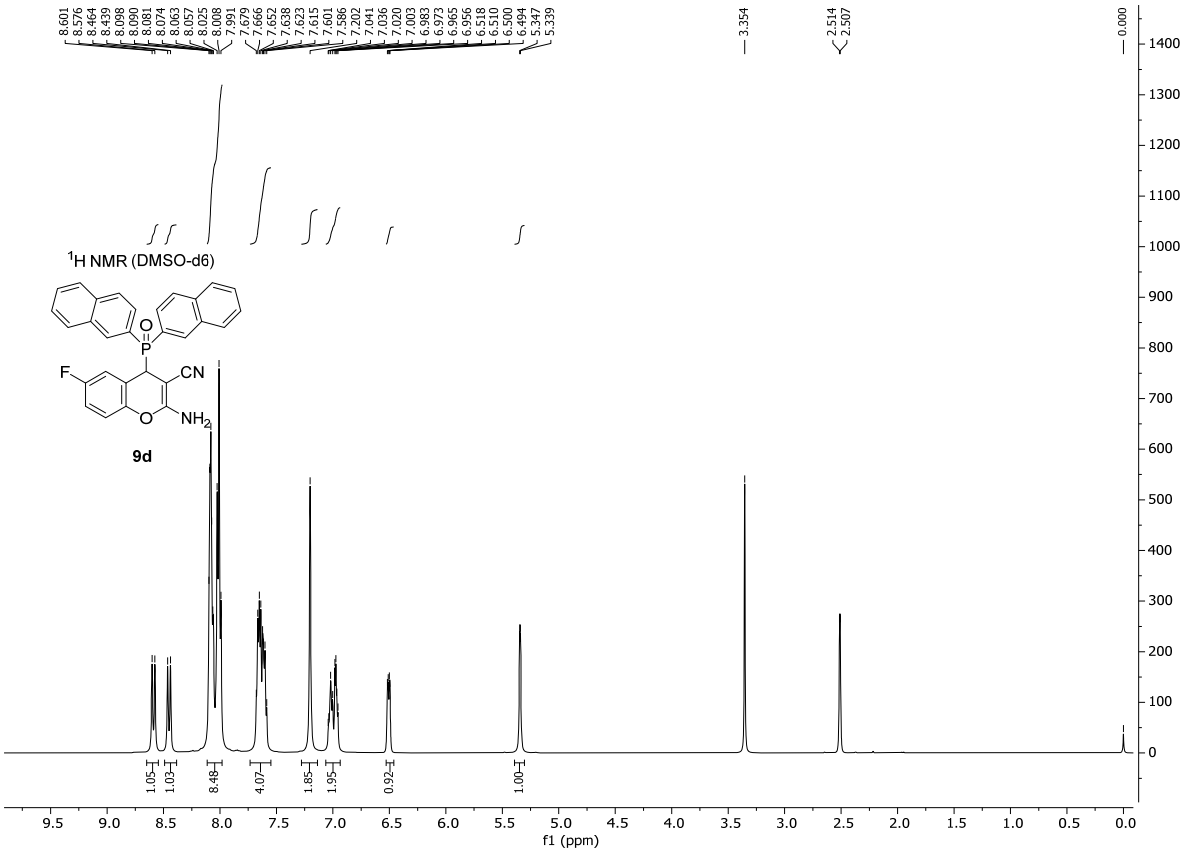
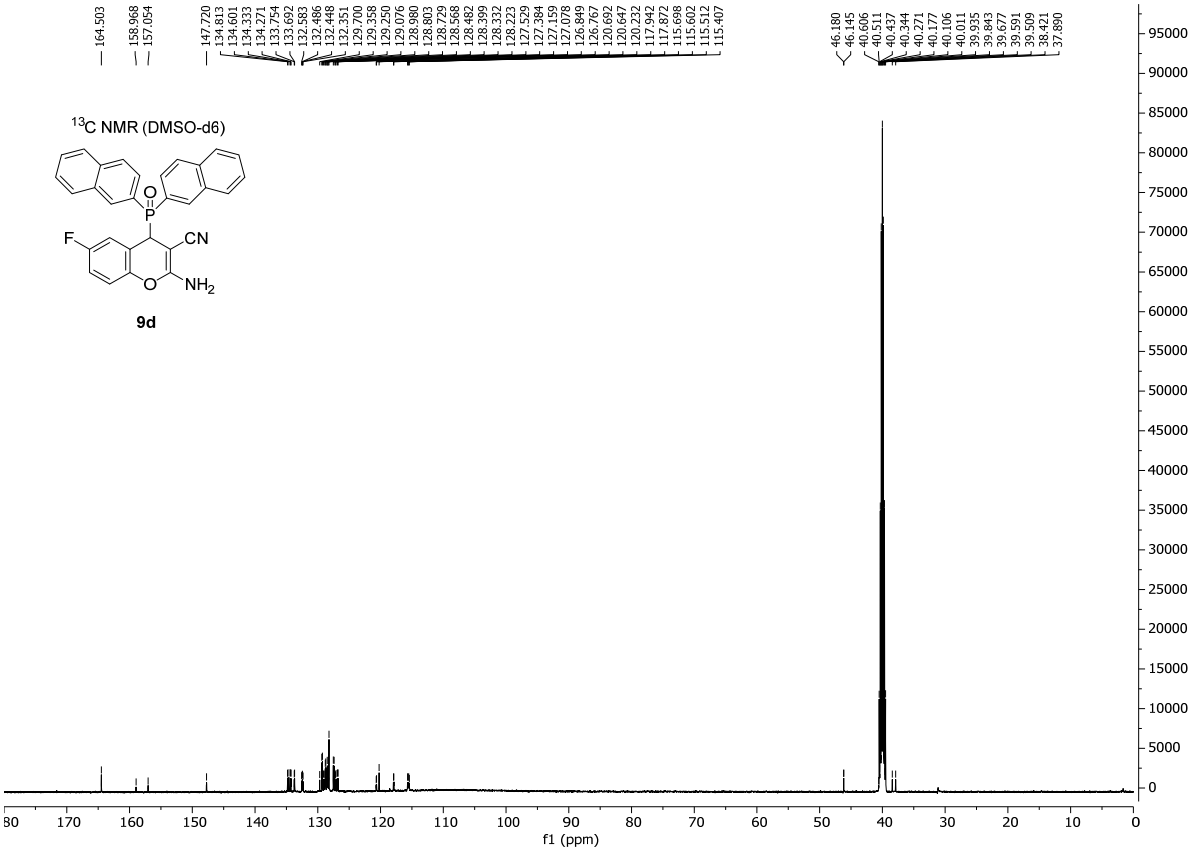
164.356
158.979
158.958
157.073
157.051
147.752
147.736
147.721
147.707
138.056
137.999
137.963
137.905
133.784
133.762
133.642
133.621
132.086
131.368
131.183
130.443
129.940
129.872
129.492
129.421
120.923
120.897
120.856
120.830
120.500
117.674
117.655
117.604
117.387
115.858
115.834
115.662
115.637
115.490
115.473
115.305
115.283
46.598
46.567
40.597
40.505
40.430
40.338
40.263
40.171
40.096
40.004
39.929
39.837
39.670
39.503
38.431
37.900
21.385
21.283
13C NMR (DMSO-d6)
O
P
F
CN
O
NH2
9c
f1 (ppm)


26.301
31P NMR (DMSO-d6)
O
P
F
CN
O
NH2
9c
f1 (ppm)


8.601
8.576
8.464
8.439
8.098
8.090
8.081
8.074
8.063
8.057
8.025
8.008
7.991
7.679
7.666
7.652
7.638
7.623
7.615
7.601
7.586
7.202
7.041
7.036
7.020
7.003
6.983
6.973
6.965
6.956
6.518
6.510
6.500
6.494
5.347
5.339
3.354
2.514
2.507
0.000
1H NMR (DMSO-d6)
O
P
F
CN
O
NH2
9d
1.05
1.03
8.48
4.07
1.85
1.95
0.92
1.00
f1 (ppm)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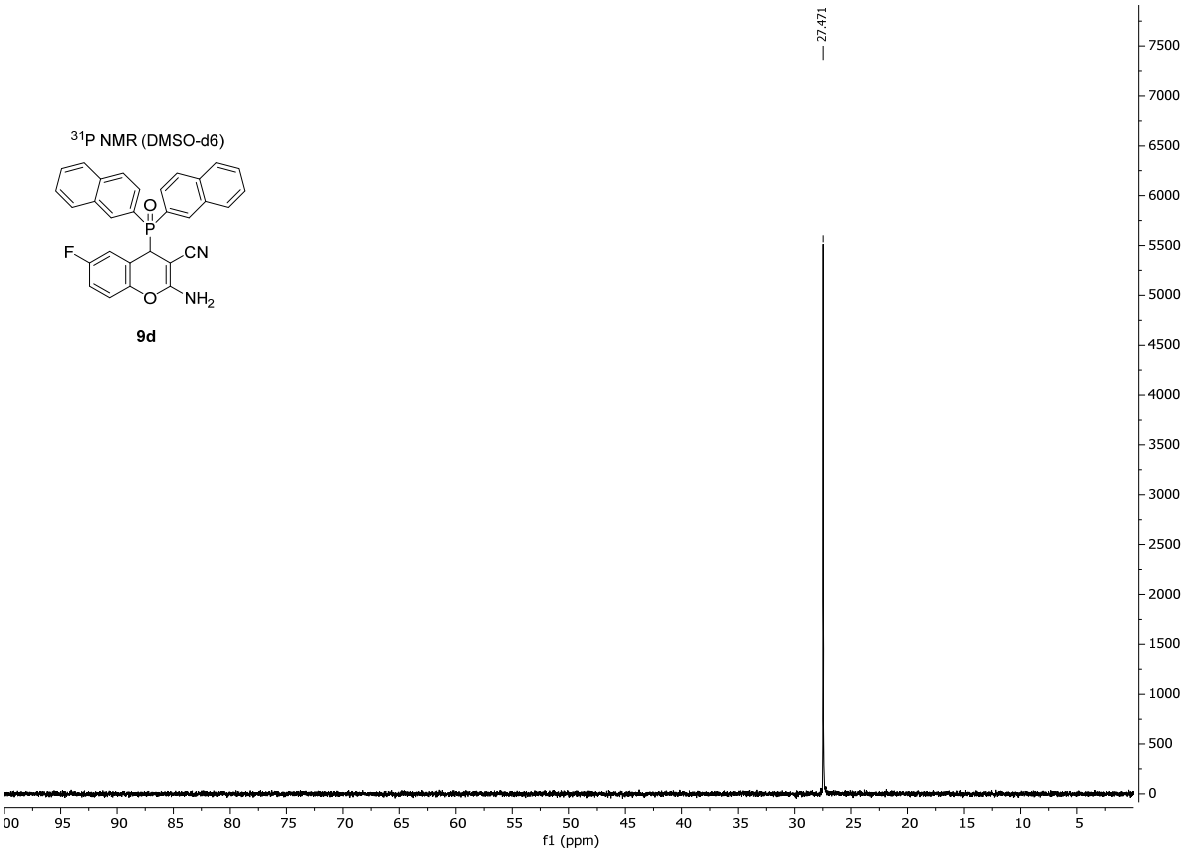
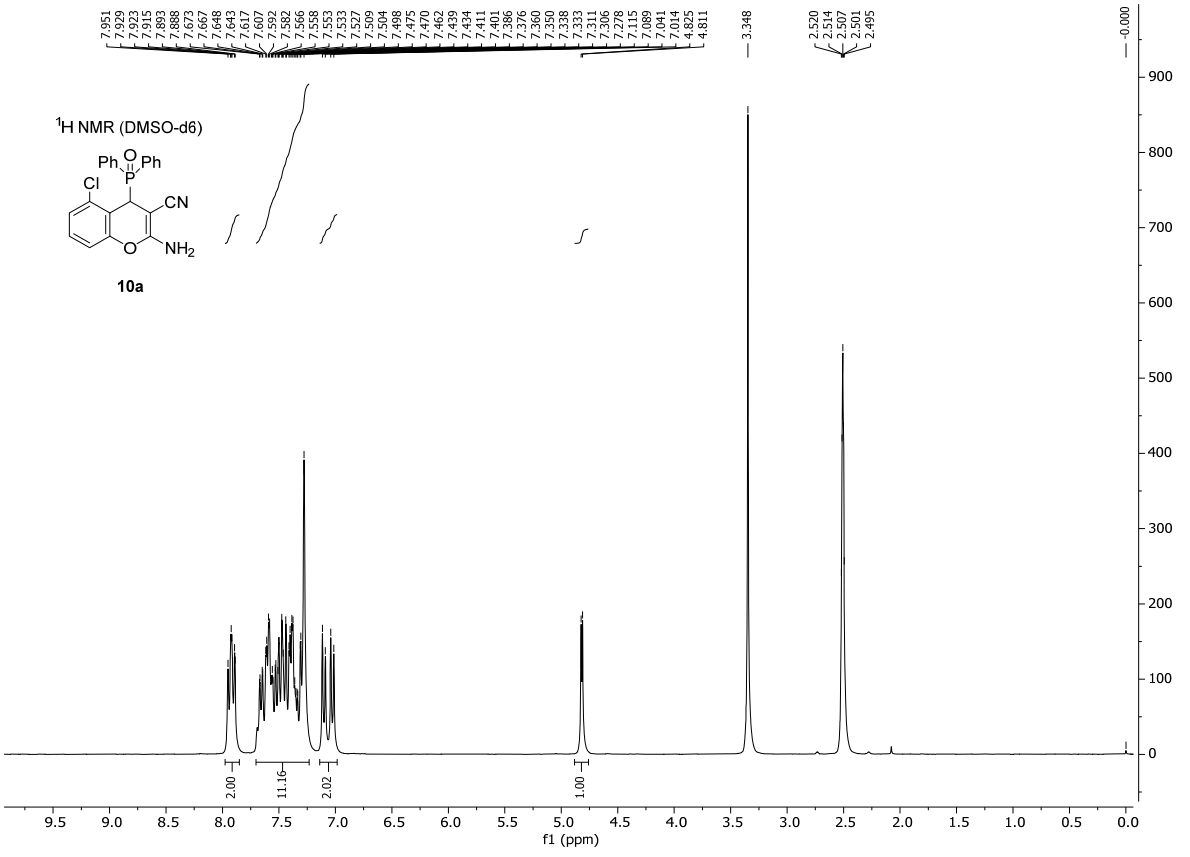
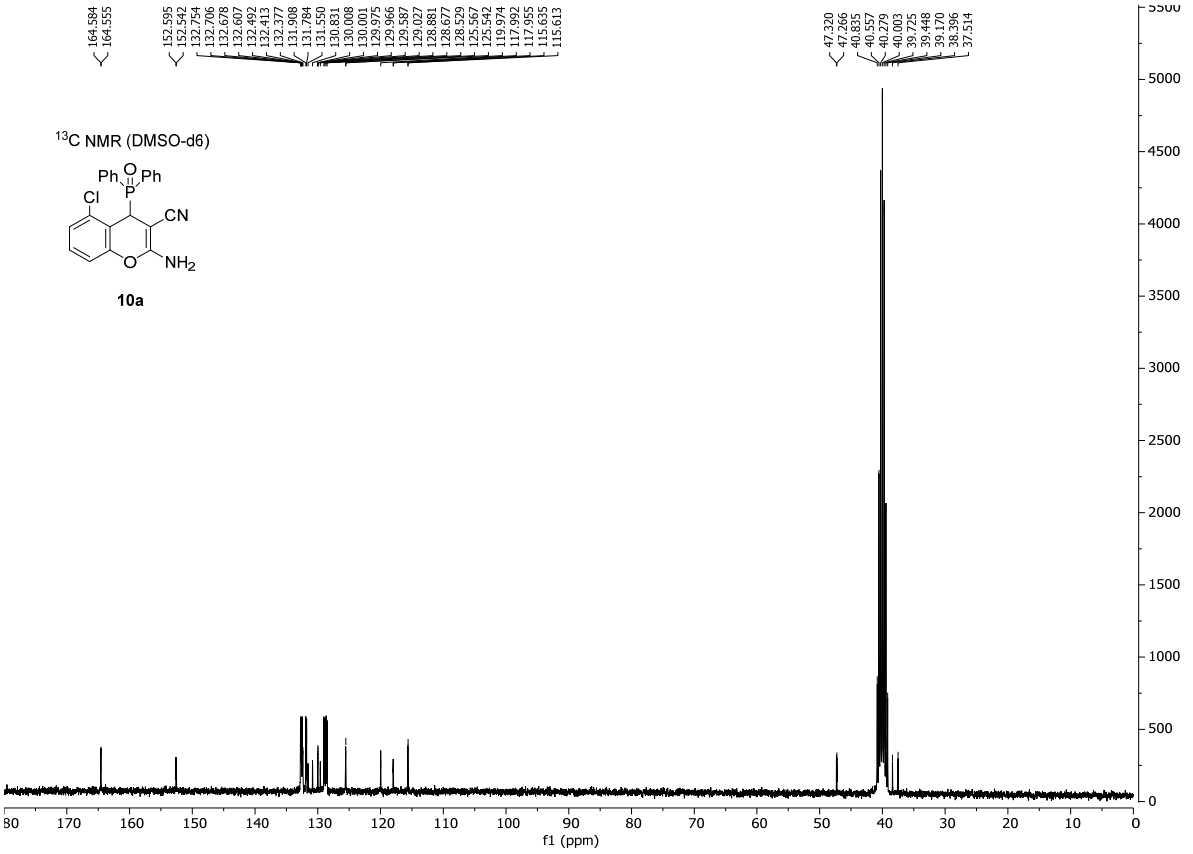
158.968
157.054
147.720
134.813
134.601
134.333
134.271
133.754
133.692
132.583
132.486
132.448
132.351
129.700
129.358
129.250
129.076
128.980
128.803
128.729
128.568
128.482
128.399
128.332
128.223
127.529
127.384
127.159
127.078
126.849
126.767
120.692
120.647
120.232
117.942
117.872
115.698
115.602
115.512
115.407
46.180
46.145
40.606
40.511
40.437
40.344
40.271
40.177
40.106
40.011
39.935
39.843
39.677
39.591
39.509
38.421
37.890
13C NMR (DMSO-d6)
O
P
F
CN
O
NH2
9d
f1 (ppm)


31P NMR (DMSO-d6)
9d
27.471
f1 (ppm)


1H NMR (DMSO-d6)
10a
3.348
2.520
2.514
2.507
2.501
2.495
-0.000
2.00
11.16
2.02
1.00
f1 (ppm)


164.584
164.555
152.595
152.542
132.754
132.706
132.678
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132.377
131.908
131.784
131.550
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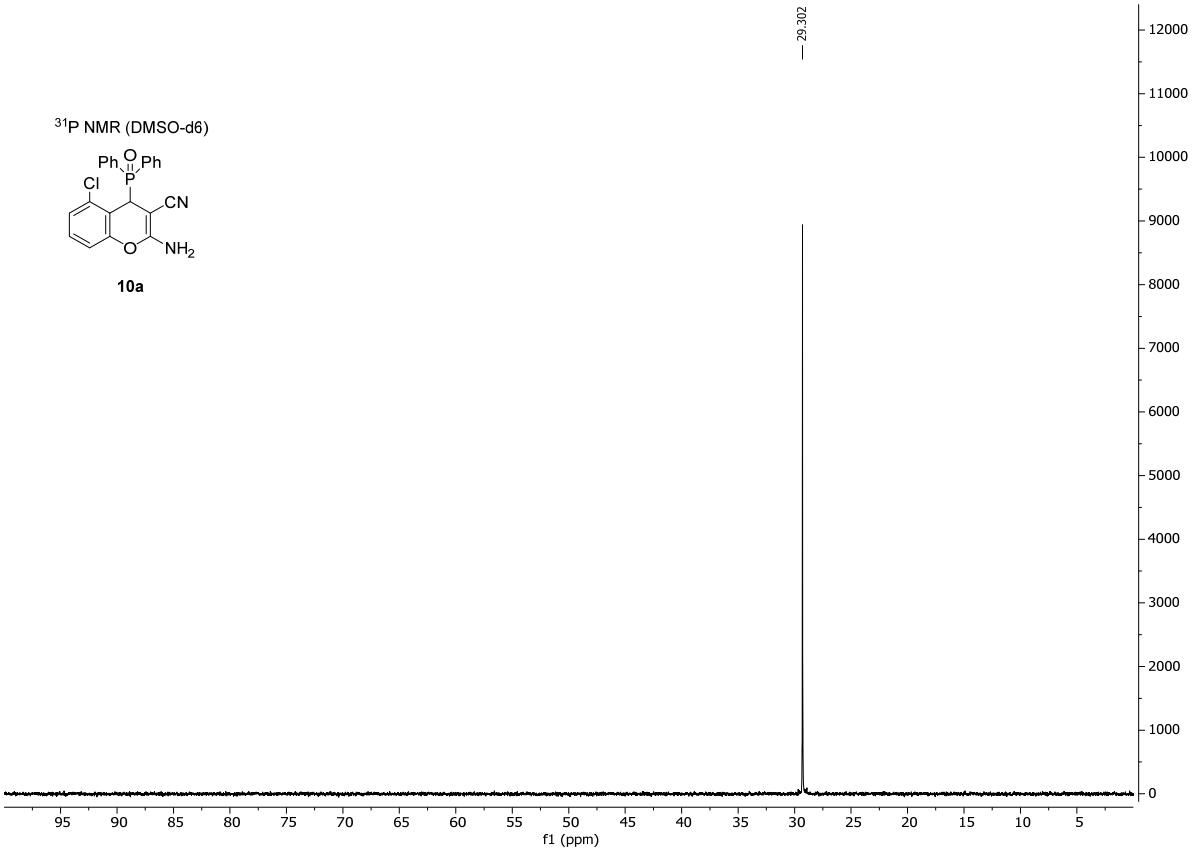
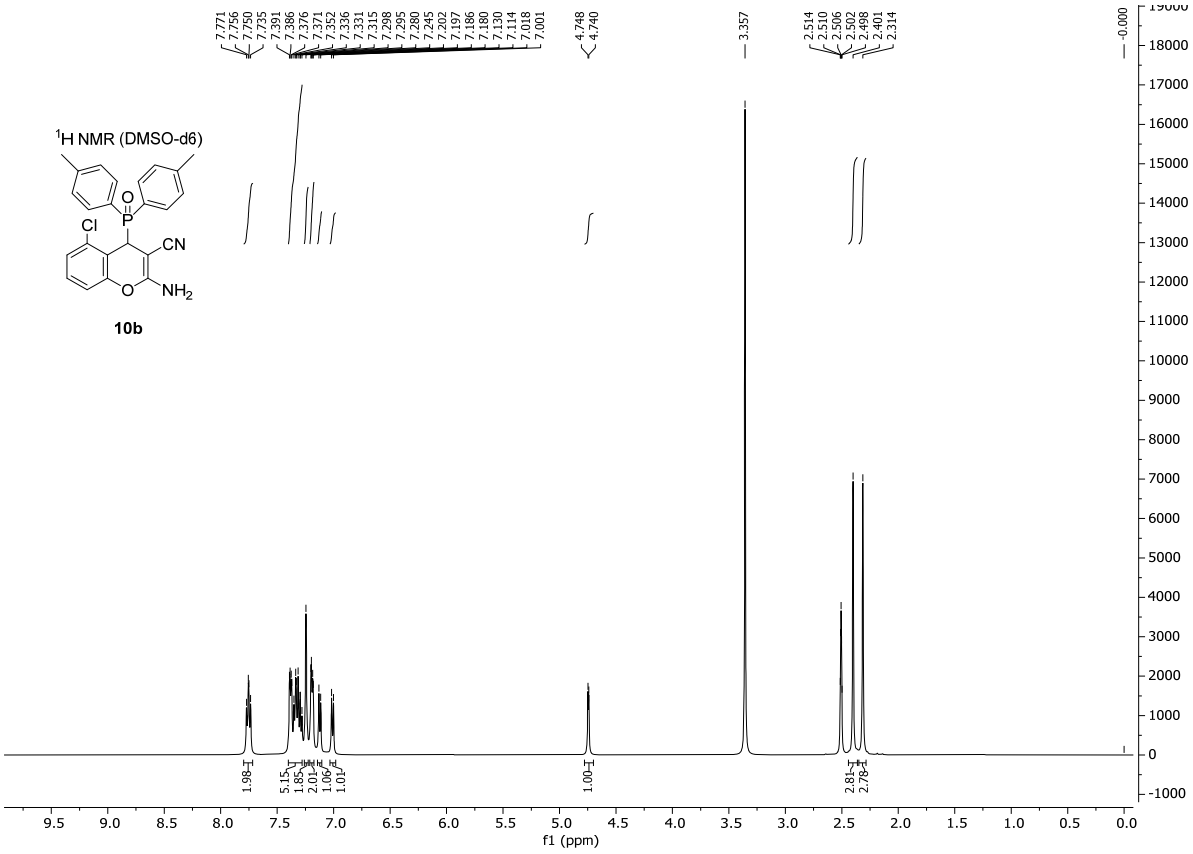
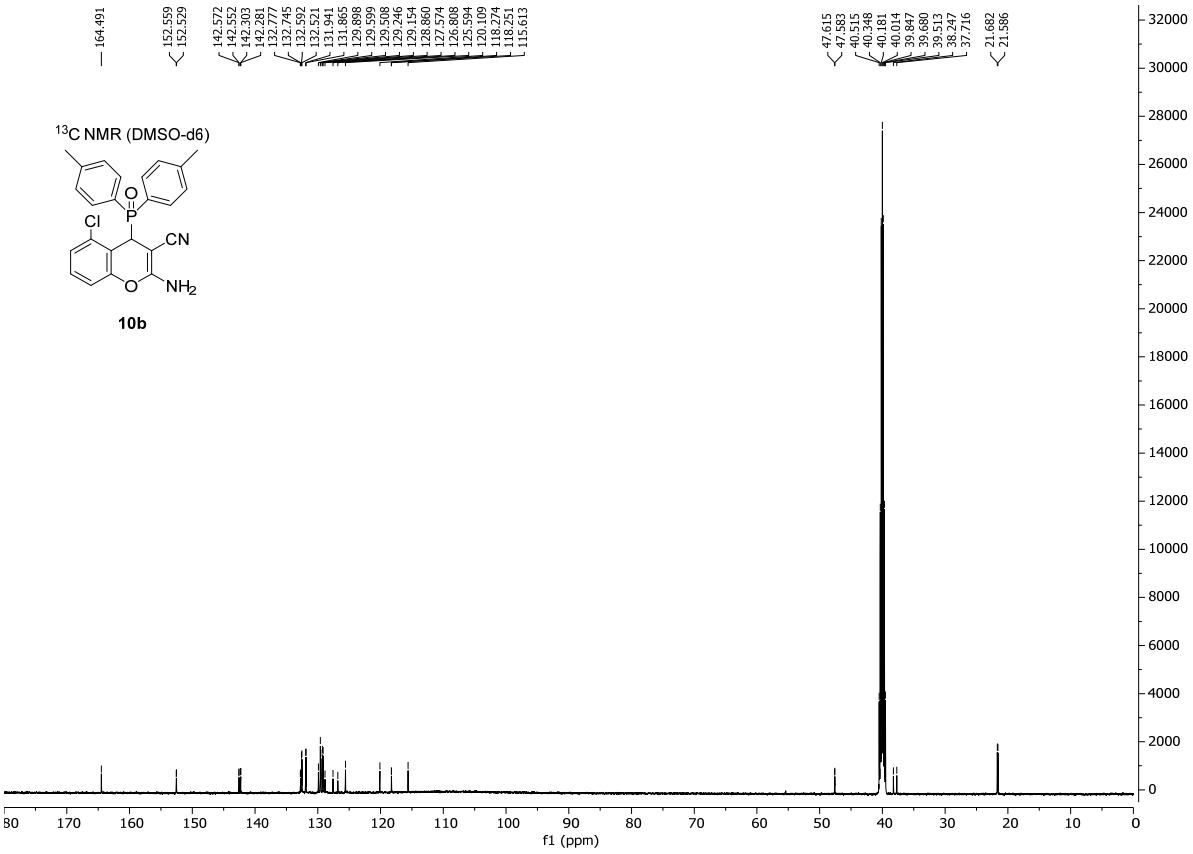
130.001
129.975
129.966
129.587
129.027
128.881
128.677
128.529
125.567
125.542
119.974
117.992
117.955
115.635
115.613
47.320
47.266
40.835
40.557
40.279
40.003
39.725
39.448
39.170
38.396
37.514
13C NMR (DMSO-d6)
Ph
O
Ph
P
Cl
CN
O
NH2
10a
f1 (ppm)


29.302
31P NMR (DMSO-d6)
Ph
O
Ph
P
Cl
CN
O
NH2
10a
f1 (ppm)


7.771
7.756
7.750
7.735
7.391
7.386
7.376
7.371
7.352
7.336
7.331
7.315
7.298
7.295
7.280
7.245
7.202
7.197
7.186
7.180
7.130
7.114
7.018
7.001
4.748
4.740
3.357
2.514
2.510
2.506
2.502
2.498
2.401
2.314
-0.000
1.98
5.15
1.85
2.01
1.06
1.01
1.00
2.81
2.78
f1 (ppm)

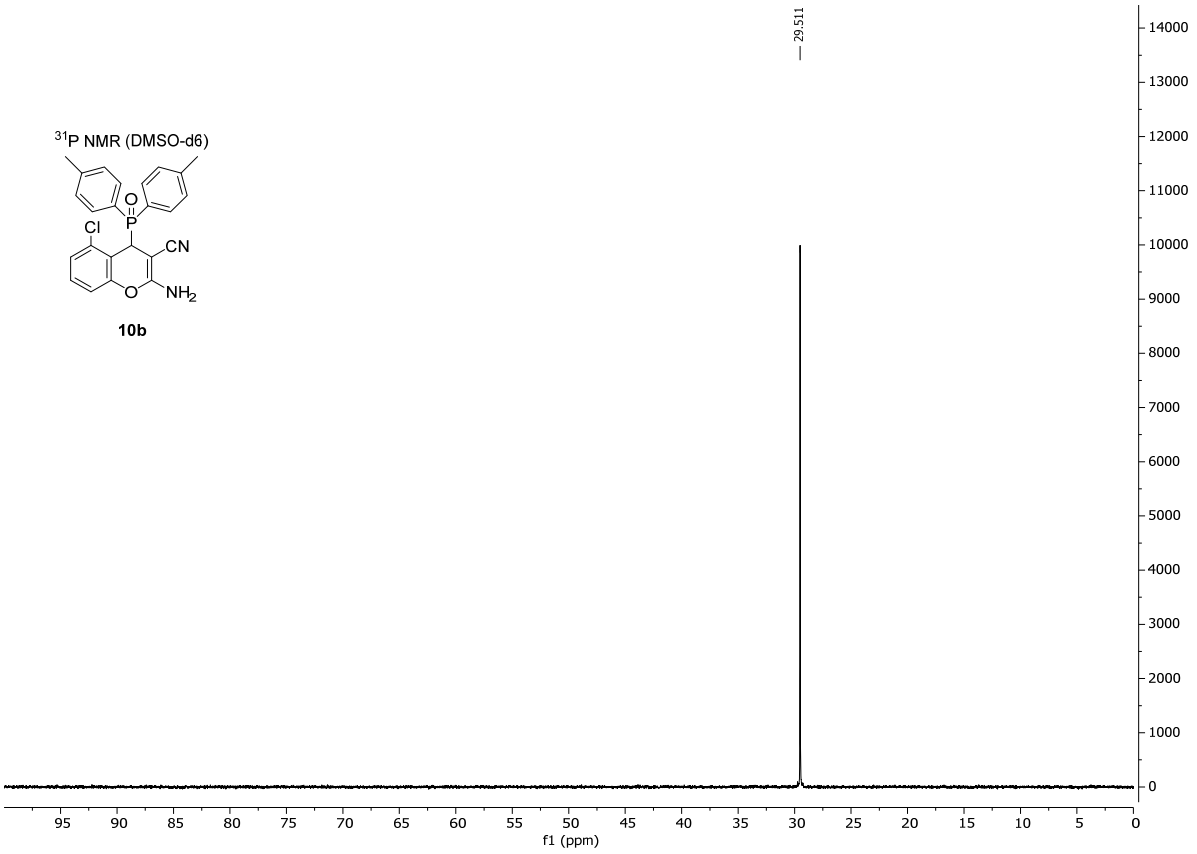
1H NMR (DMSO-d6)
O
P
Cl
CN
O
NH2

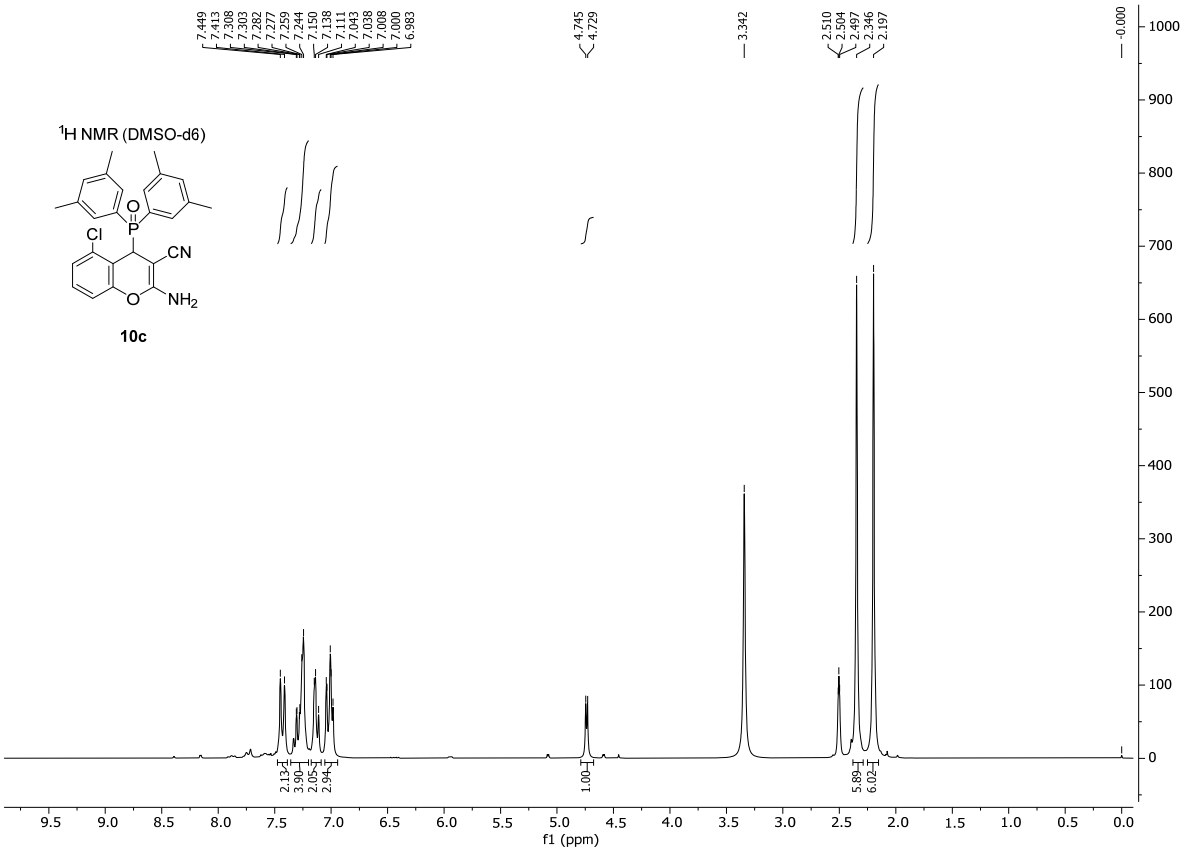
10b

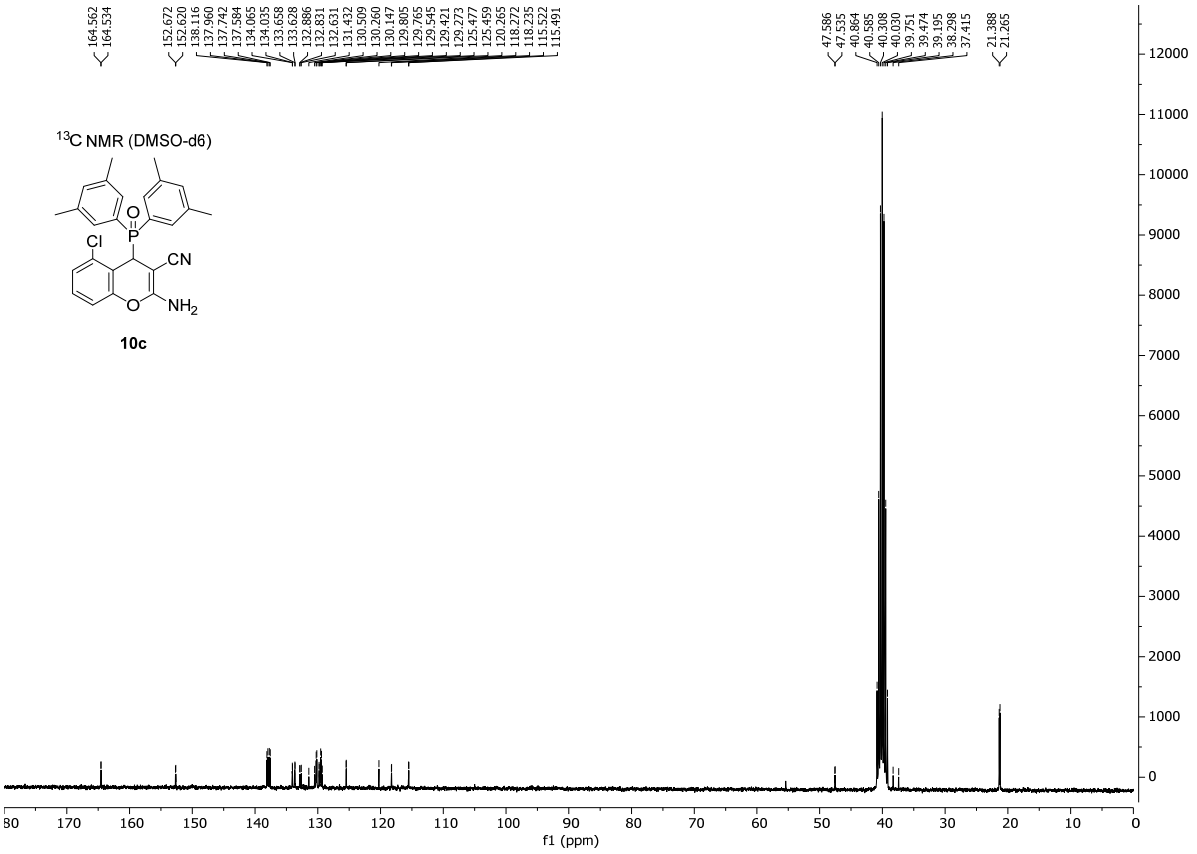

164.491
152.559
152.529
142.572
142.552
142.303
142.281
132.777
132.745
132.592
132.521
131.941
131.865
129.898
129.599
129.508
129.246
129.154
128.860
127.574
126.808
125.594
120.109
118.274
118.251
115.613
47.615
47.583
40.515
40.348
40.181
40.014
39.847
39.680
39.513
38.247
37.716
21.682
21.586
f1 (ppm)

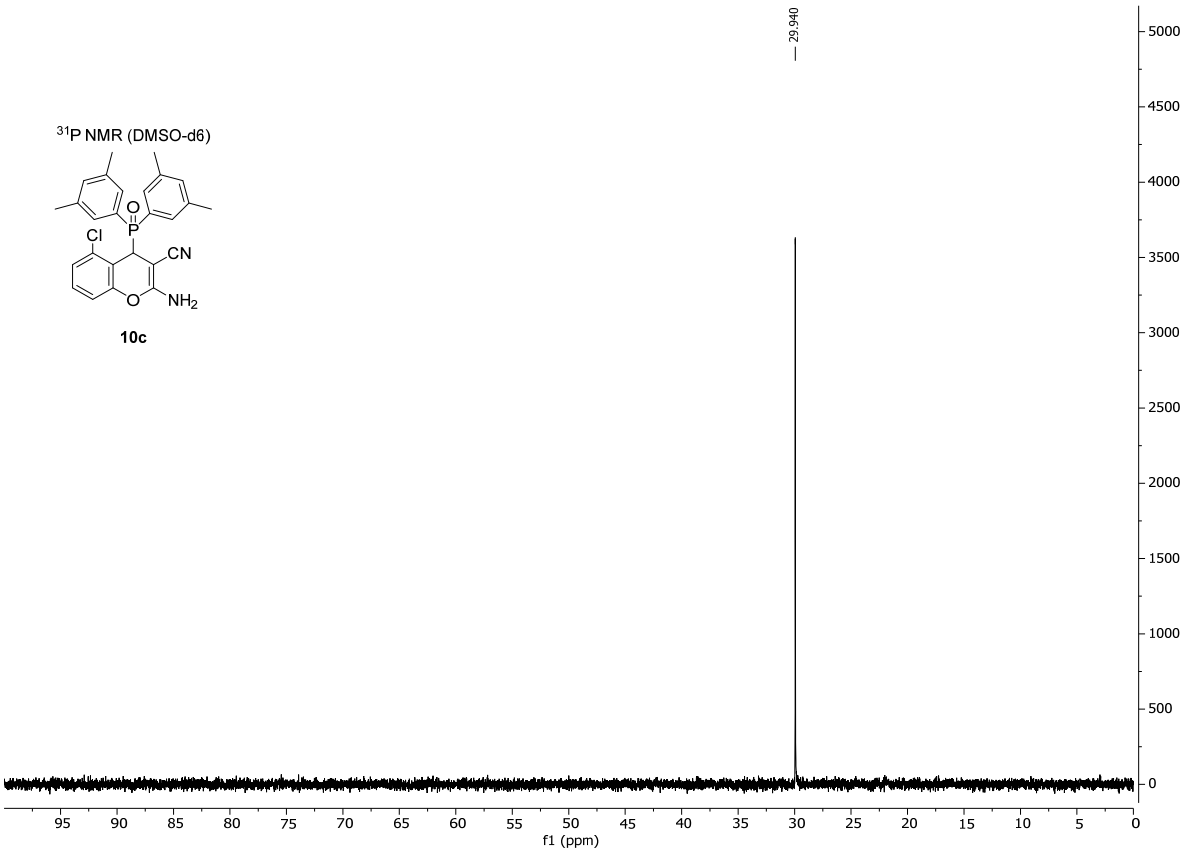
13C NMR (DMSO-d6)
O
P
Cl
CN
O
NH2

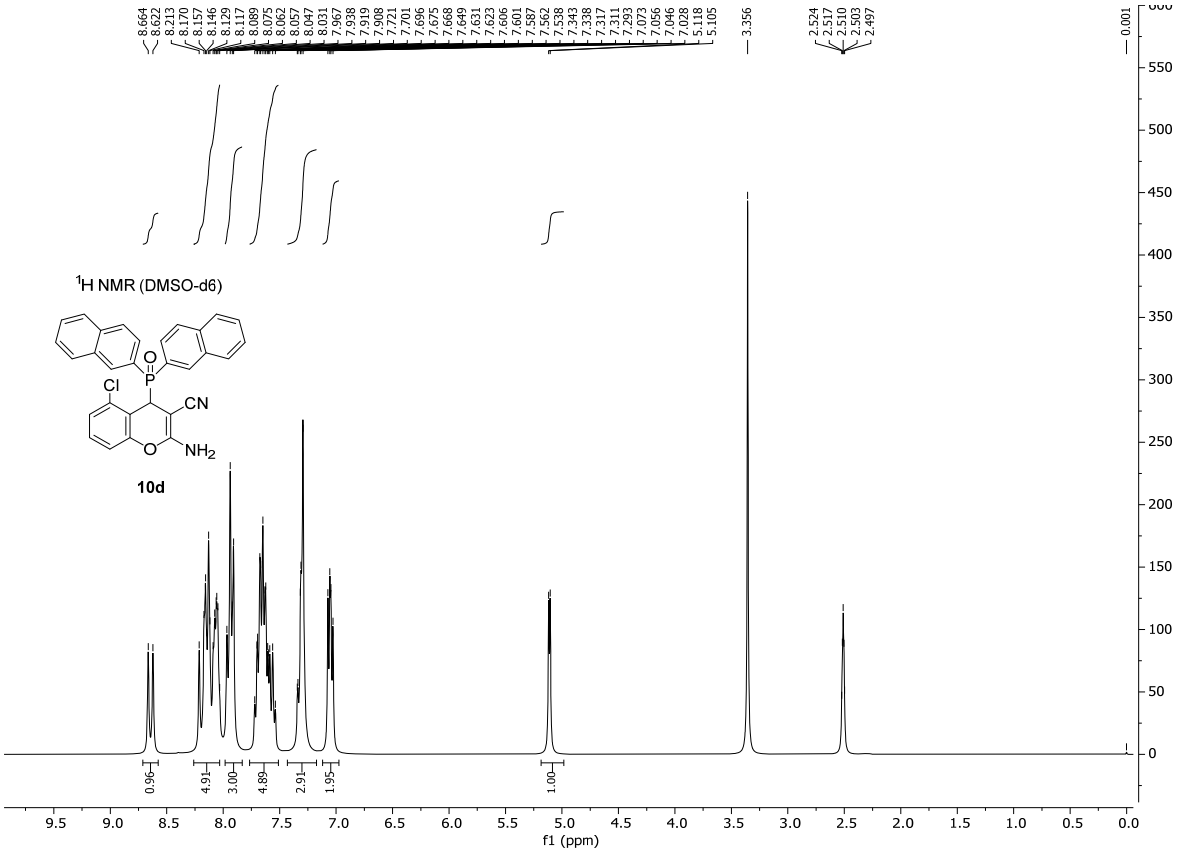
10b

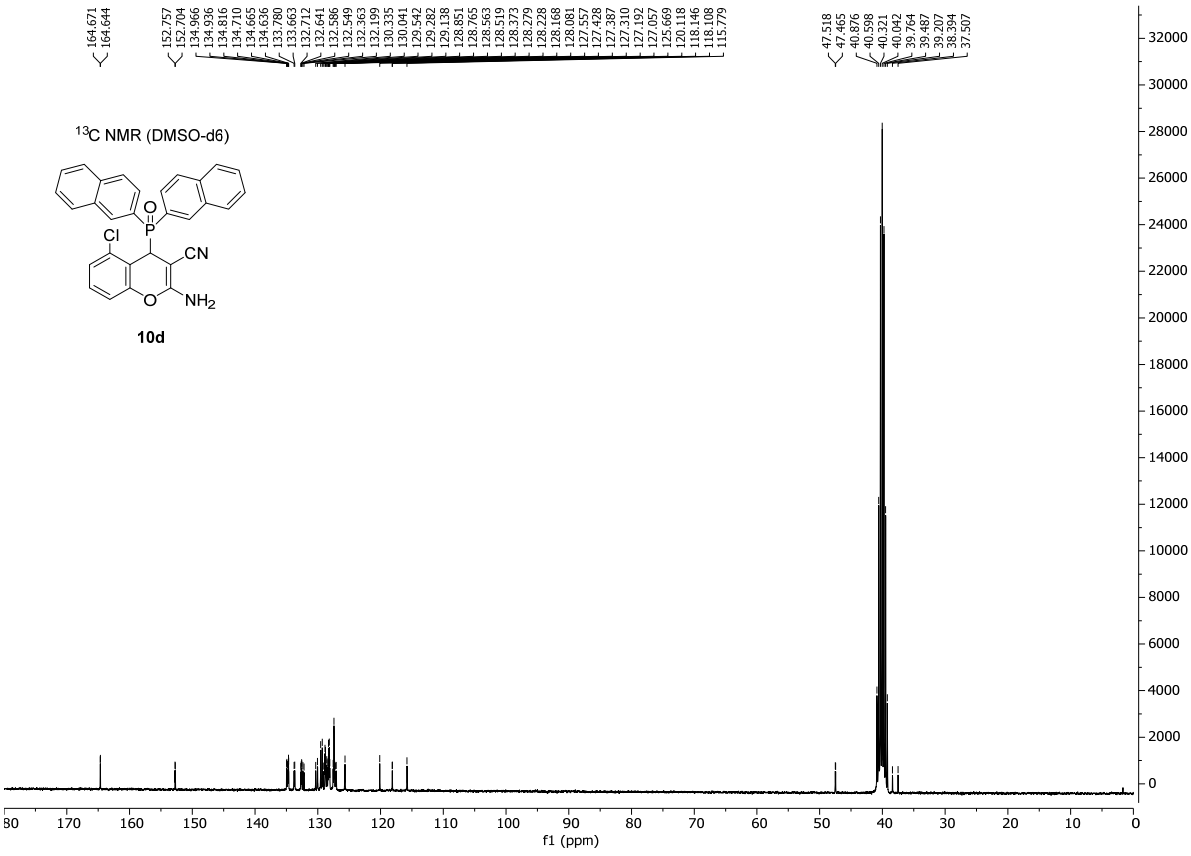

31P NMR (DMSO-d6)
10b
29.511
f1 (ppm)

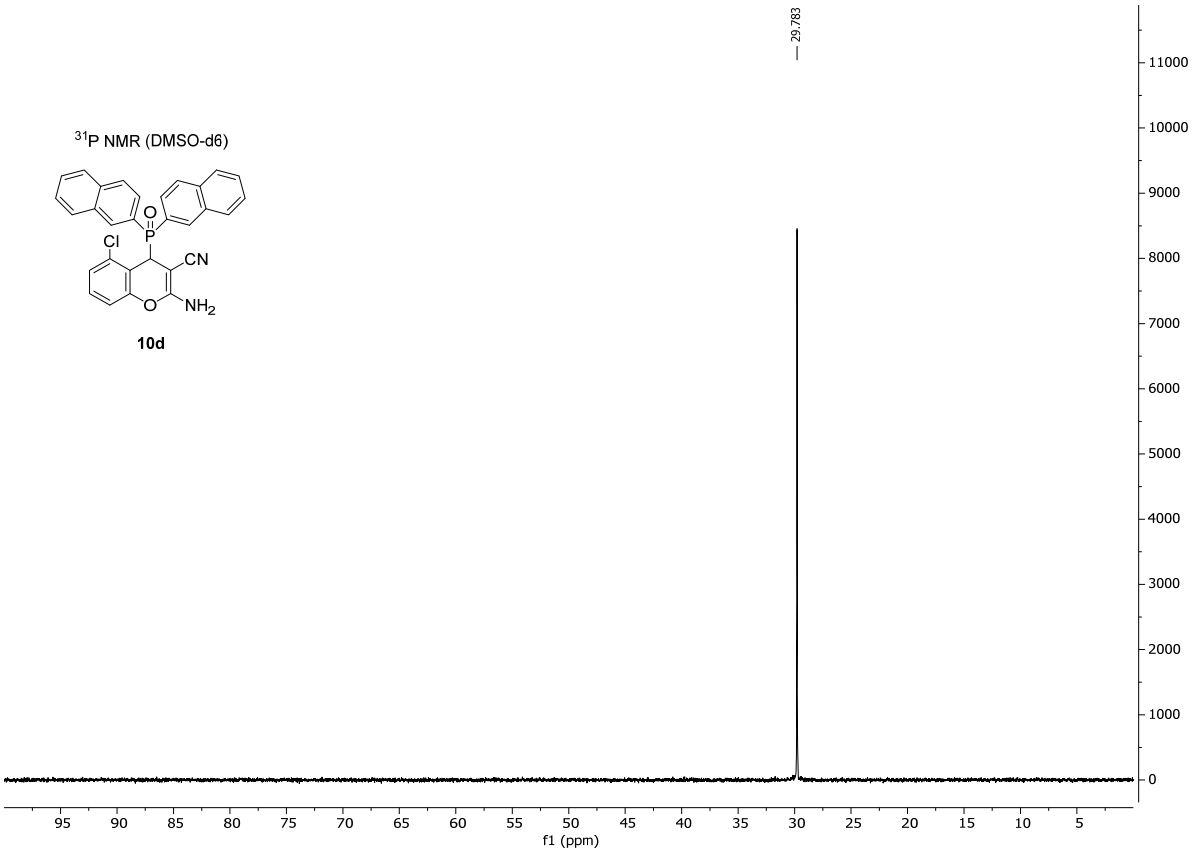

1H NMR (DMSO-d6)
10c
7.449
7.413
7.308
7.303
7.282
7.277
7.259
7.244
7.150
7.138
7.111
7.043
7.038
7.008
7.000
6.983
4.745
4.729
3.342
2.510
2.504
2.497
2.346
2.197
-0.000
2.13
3.90
2.05
2.94
1.00
5.89
6.02
f1 (ppm)

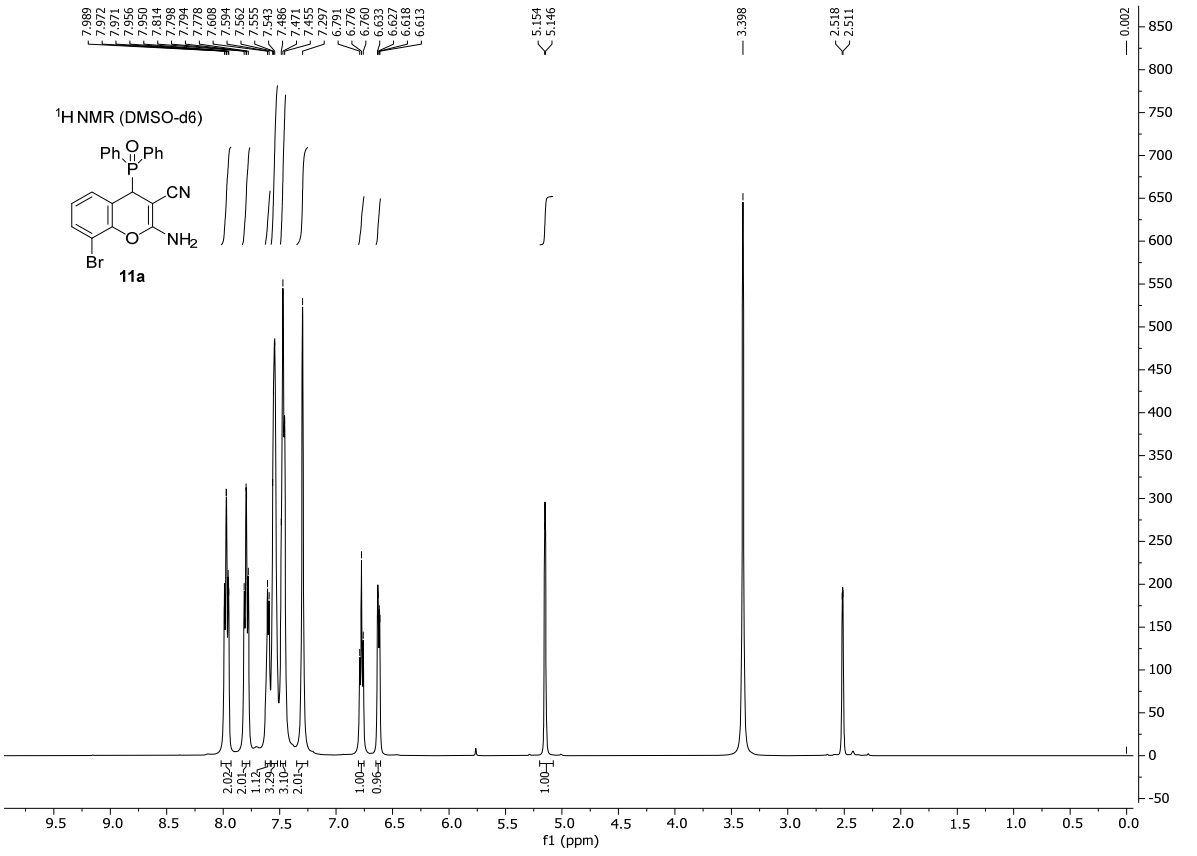

164.562
164.534
152.672
152.620
138.116
137.960
137.742
137.384
134.065
134.035
133.658
133.628
132.886
132.831
132.631
131.432
130.509
130.260
130.147
129.805
129.765
129.545
129.471
129.273
125.459
120.265
118.272
118.255
116.522
115.491
47.586
47.535
40.864
40.585
40.308
40.030
39.751
39.474
39.195
38.298
37.415
21.388
21.265
^{13}C NMR (DMSO-d6)
O
P
Cl
CN
O
NH$_2$
10c
f1 (ppm)

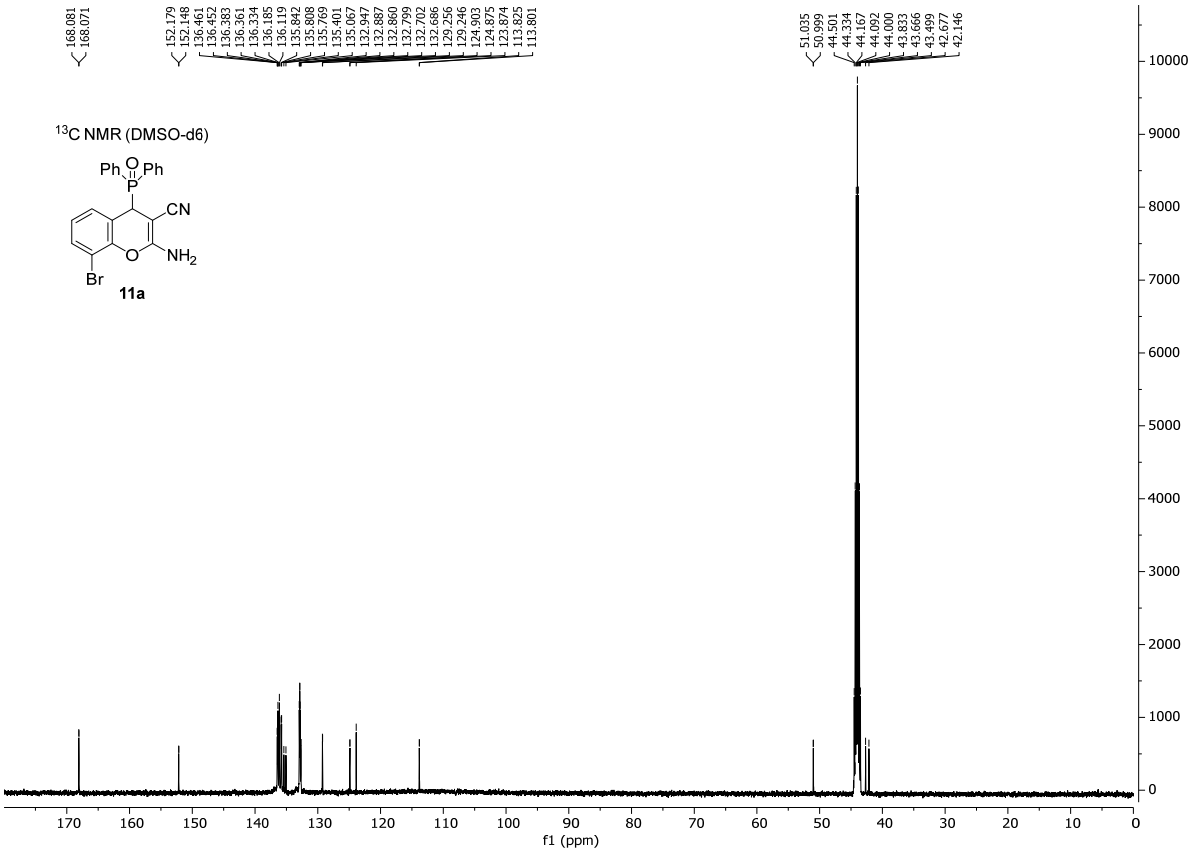

29.940
^{31}P NMR (DMSO-d6)
O
P
Cl
CN
O
NH$_2$
10c
f1 (ppm)

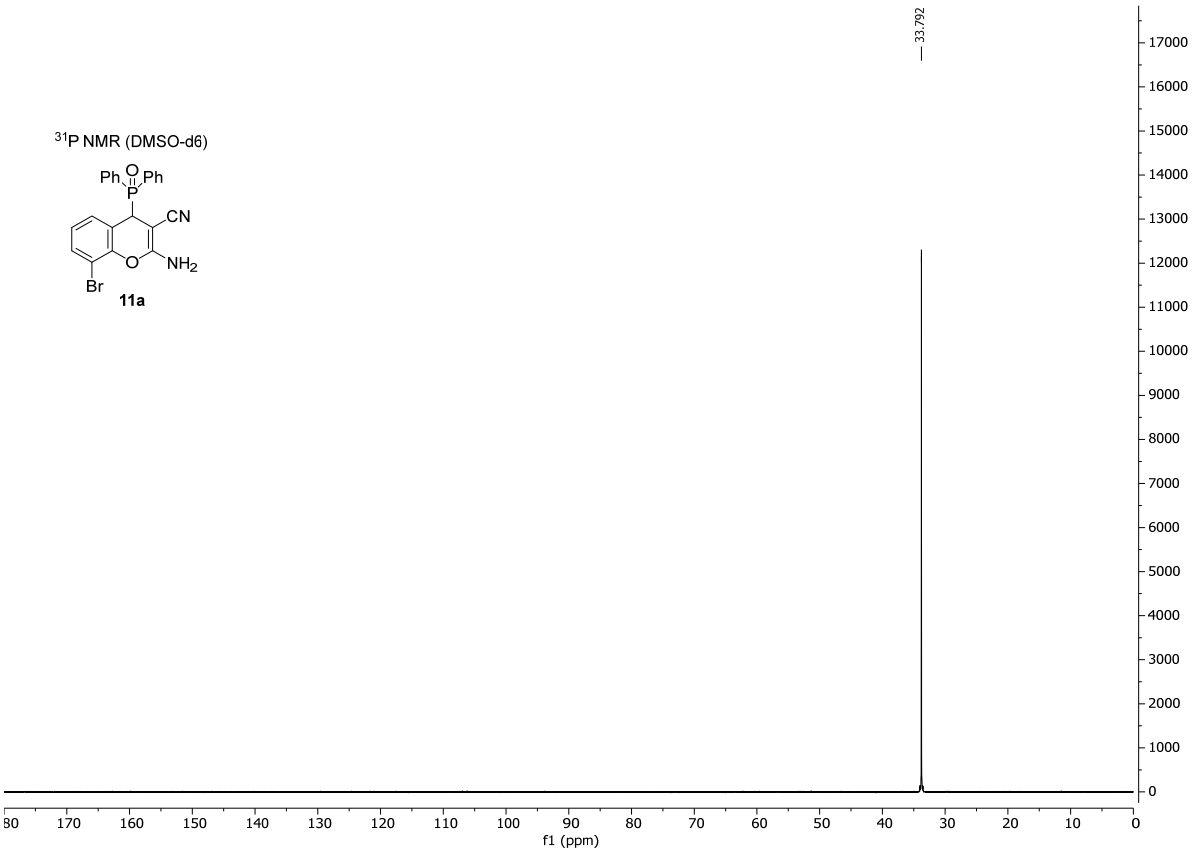

1H NMR (DMSO-d6)
10d
f1 (ppm)

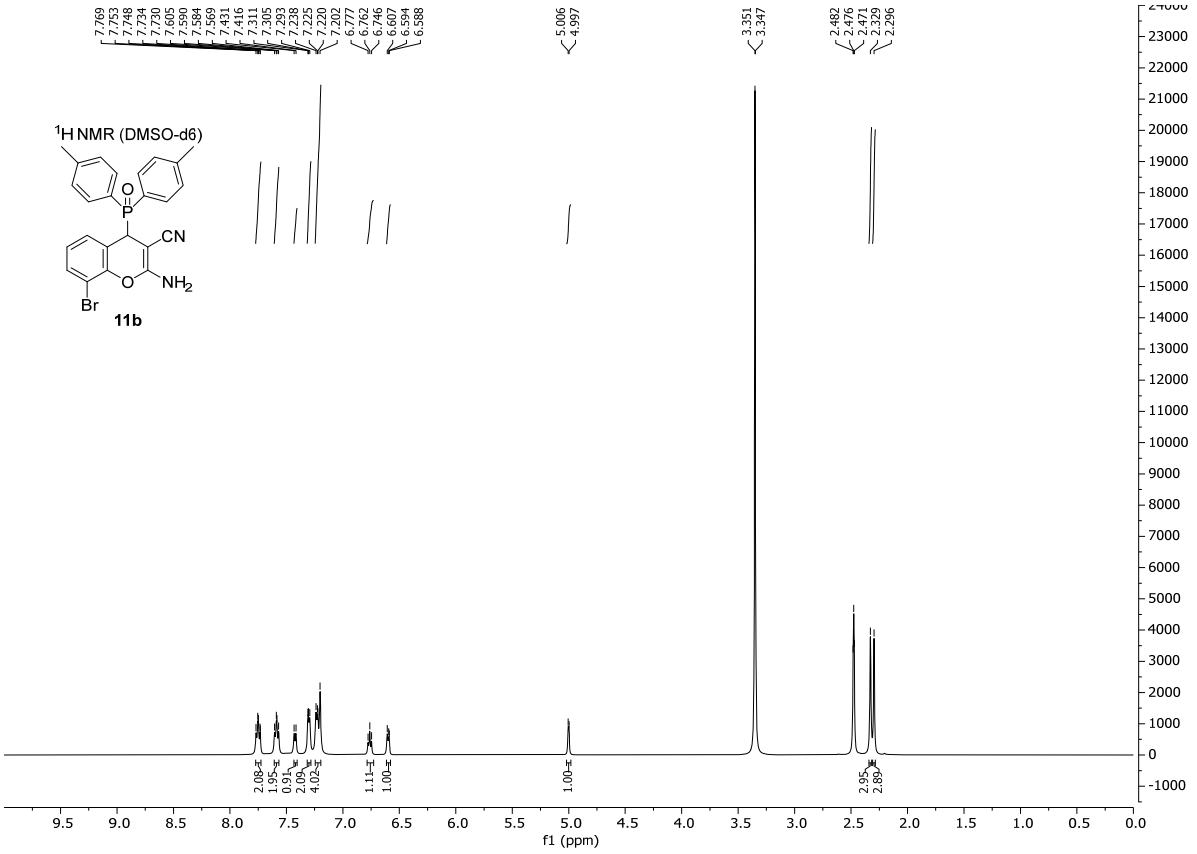

13C NMR (DMSO-d6)
10d
f1 (ppm)

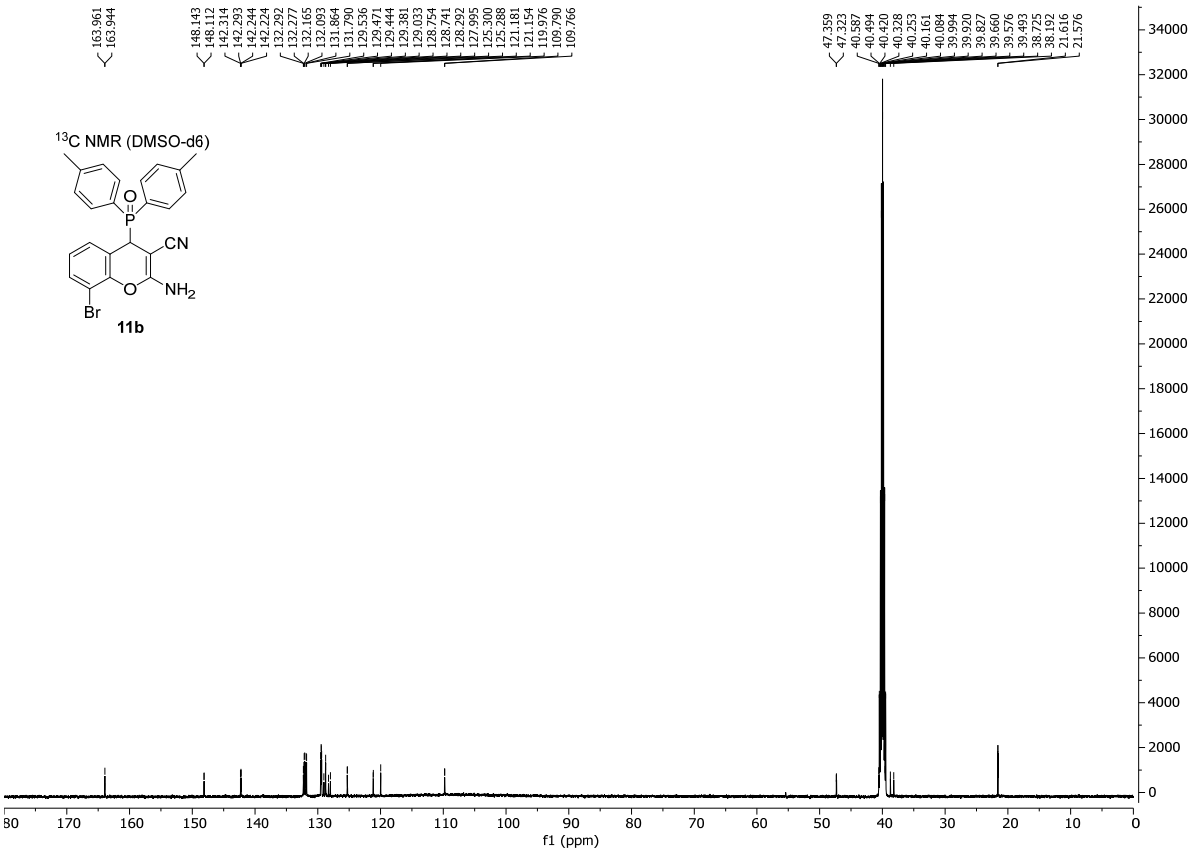

31P NMR (DMSO-d6)
10d
29.783
f1 (ppm)

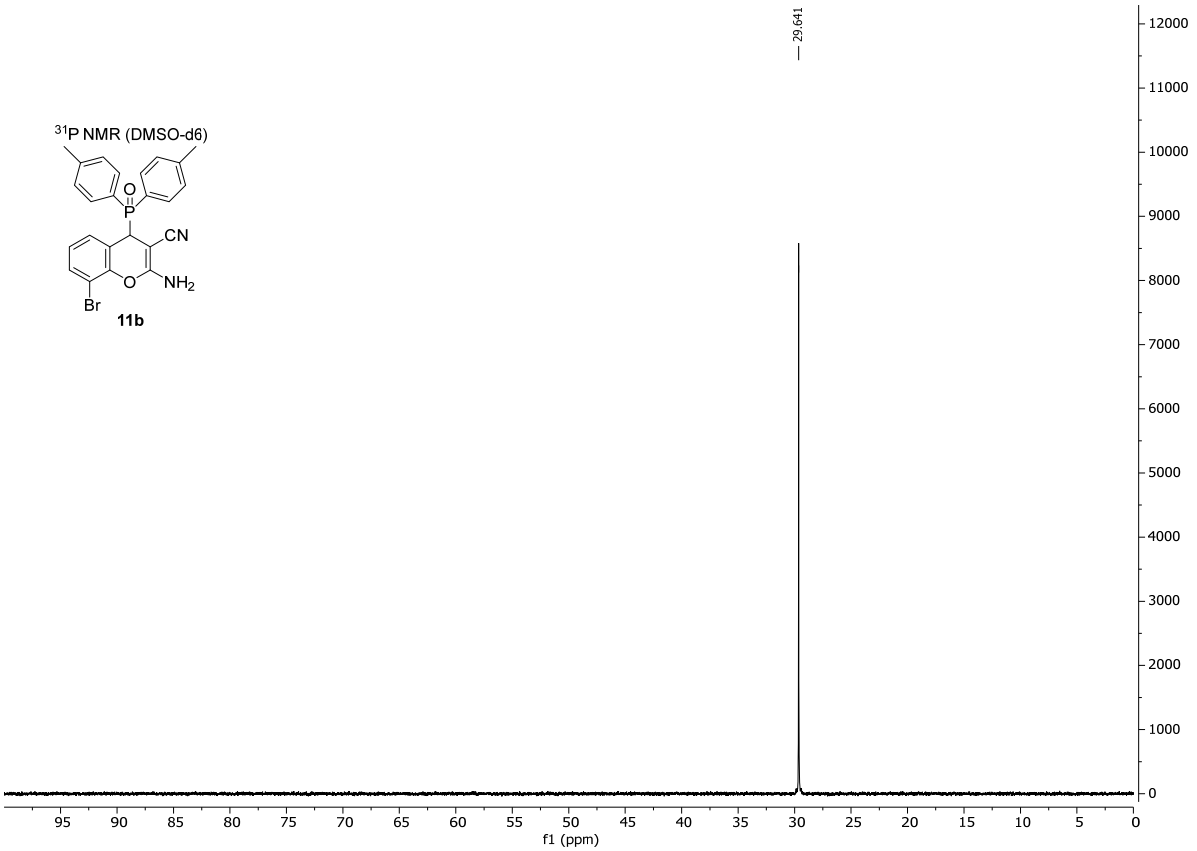

1H NMR (DMSO-d6)
11a
7.989
7.972
7.971
7.956
7.950
7.814
7.798
7.794
7.778
7.608
7.594
7.562
7.555
7.543
7.486
7.471
7.455
7.297
6.791
6.776
6.760
6.633
6.627
6.618
6.613
5.154
5.146
3.398
2.518
2.511
0.002
2.02
2.01
1.12
3.29
3.10
2.01
1.00
0.96
1.00
f1 (ppm)

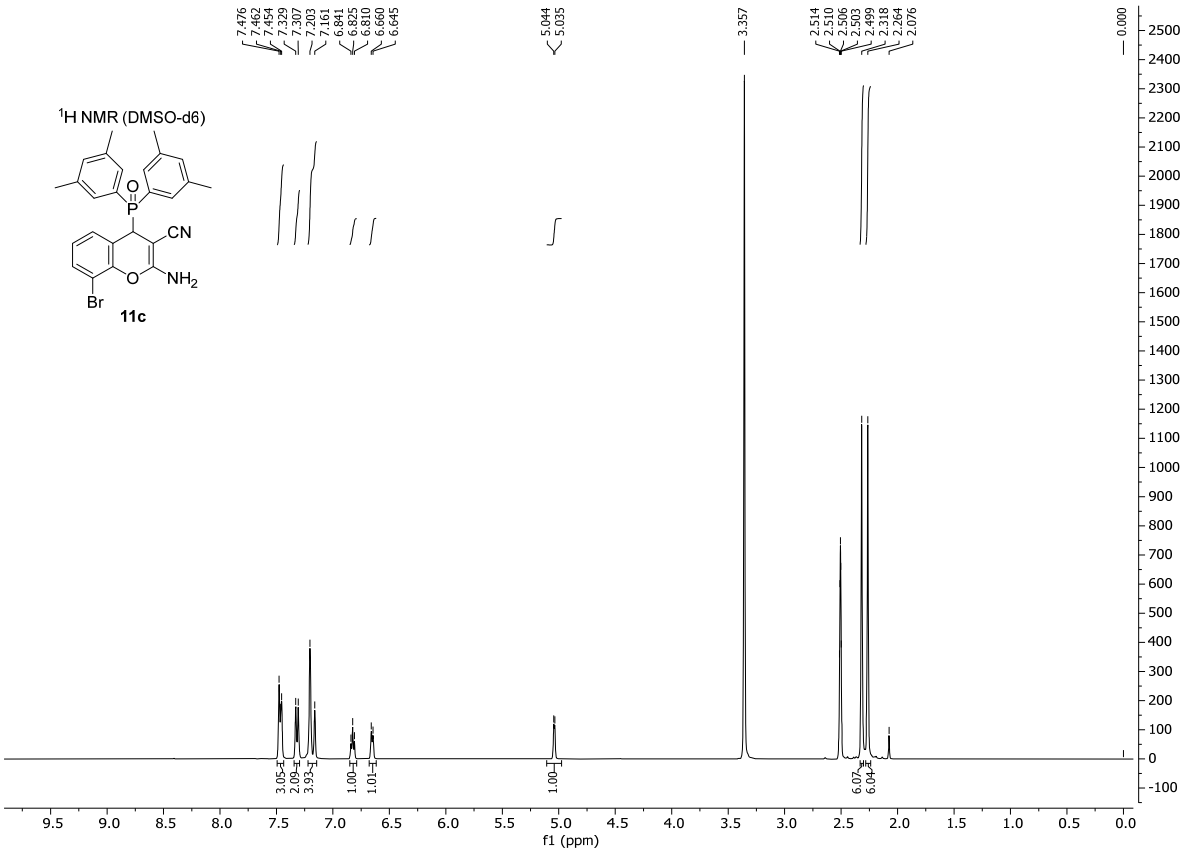

168.081
168.071
152.179
152.148
136.461
136.452
136.383
136.361
136.334
136.185
136.119
135.842
135.808
135.769
135.401
135.067
132.947
132.887
132.860
132.799
132.702
132.686
129.256
129.246
124.903
124.875
123.874
113.825
113.801
51.035
50.999
44.501
44.334
44.167
44.092
44.000
43.833
43.666
43.499
42.677
42.146
13C NMR (DMSO-d6)
Ph
O
Ph
P
CN
O
NH2
Br
11a
f1 (ppm)

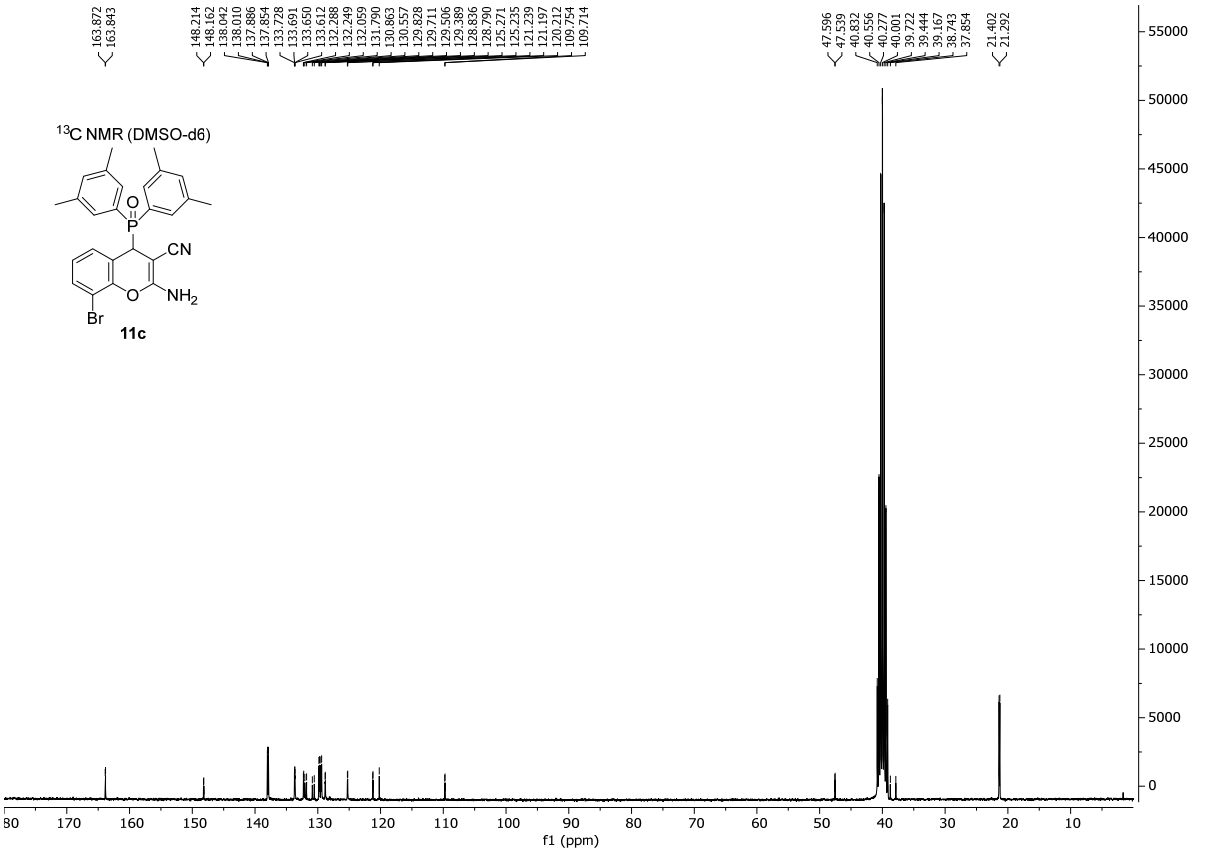

33.792
31P NMR (DMSO-d6)
Ph
O
Ph
P
CN
O
NH2
Br
11a
f1 (ppm)

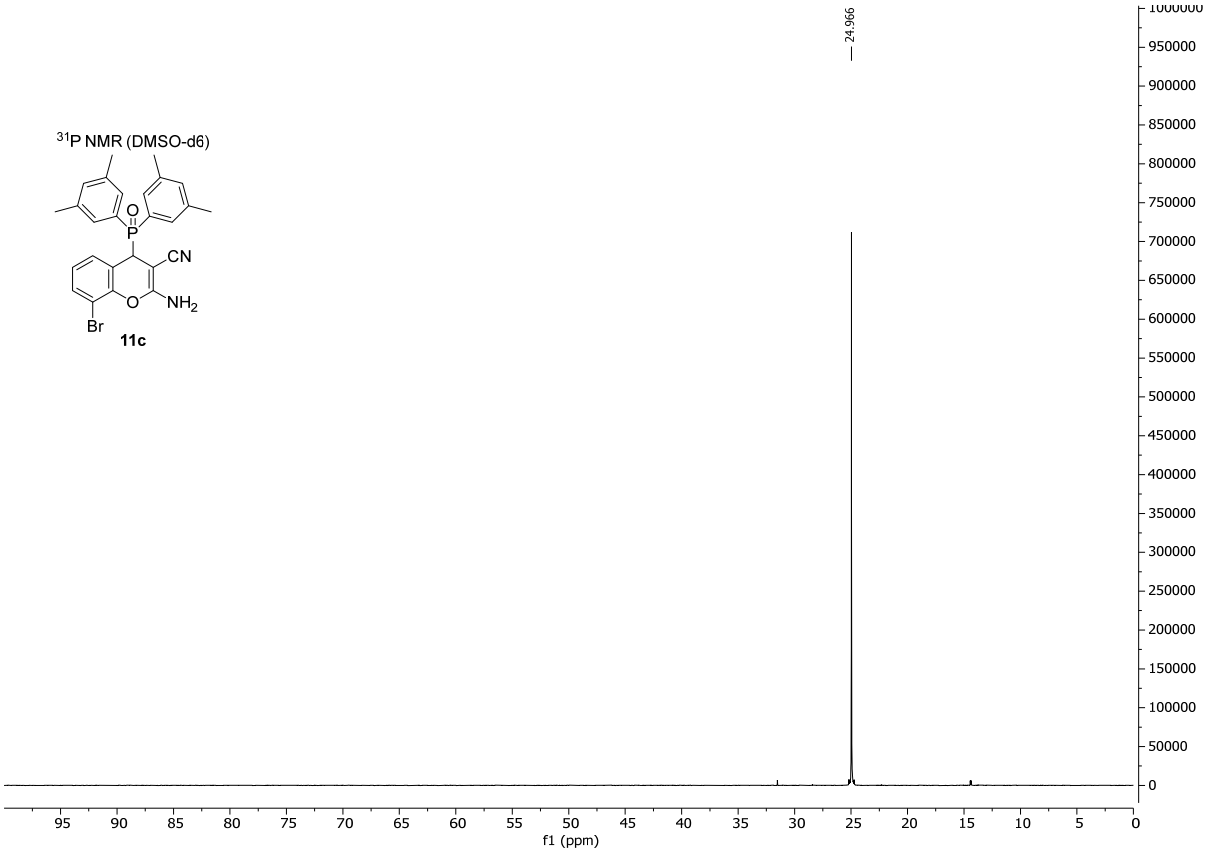

7.769
7.753
7.748
7.734
7.730
7.605
7.590
7.584
7.569
7.431
7.416
7.311
7.305
7.293
7.238
7.225
7.220
7.202
6.777
6.762
6.746
6.607
6.594
6.588
5.006
4.997
3.351
3.347
2.482
2.476
2.471
2.329
2.296
^{1}H NMR (DMSO-d6)
O
P
CN
O
NH$_2$
Br
11b
2.08
1.95
0.91
2.09
4.02
1.11
1.00
1.00
2.95
2.89
f1 (ppm)

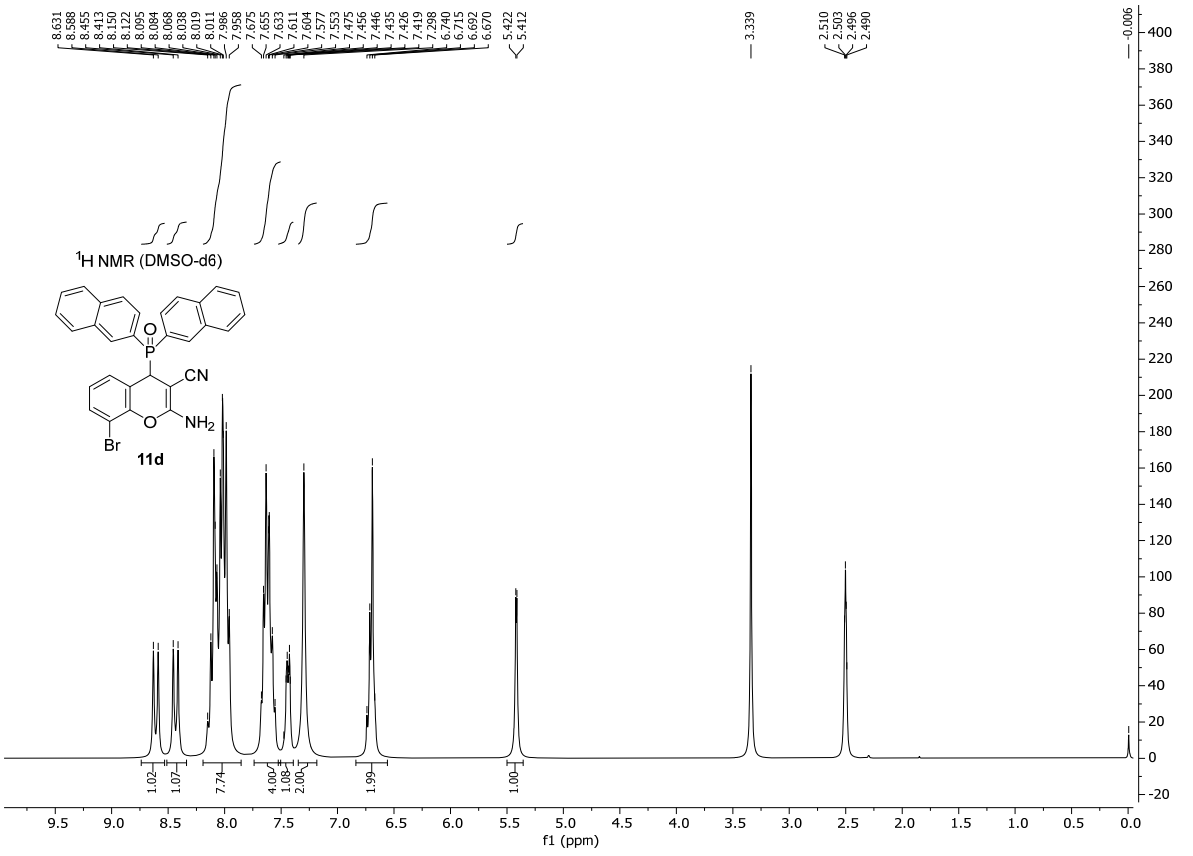

163.961
163.944
148.143
148.112
142.314
142.293
142.244
142.224
132.292
132.277
132.165
132.093
131.864
131.790
129.536
129.471
129.444
129.381
129.033
128.754
128.741
128.292
127.995
125.300
125.288
121.181
121.154
119.976
109.790
109.766
47.359
47.323
40.587
40.494
40.420
40.328
40.253
40.161
40.084
39.994
39.920
39.827
39.660
39.576
39.493
38.725
38.192
21.616
21.576
^{13}C NMR (DMSO-d6)
O
P
CN
O
NH$_2$
Br
11b
f1 (ppm)

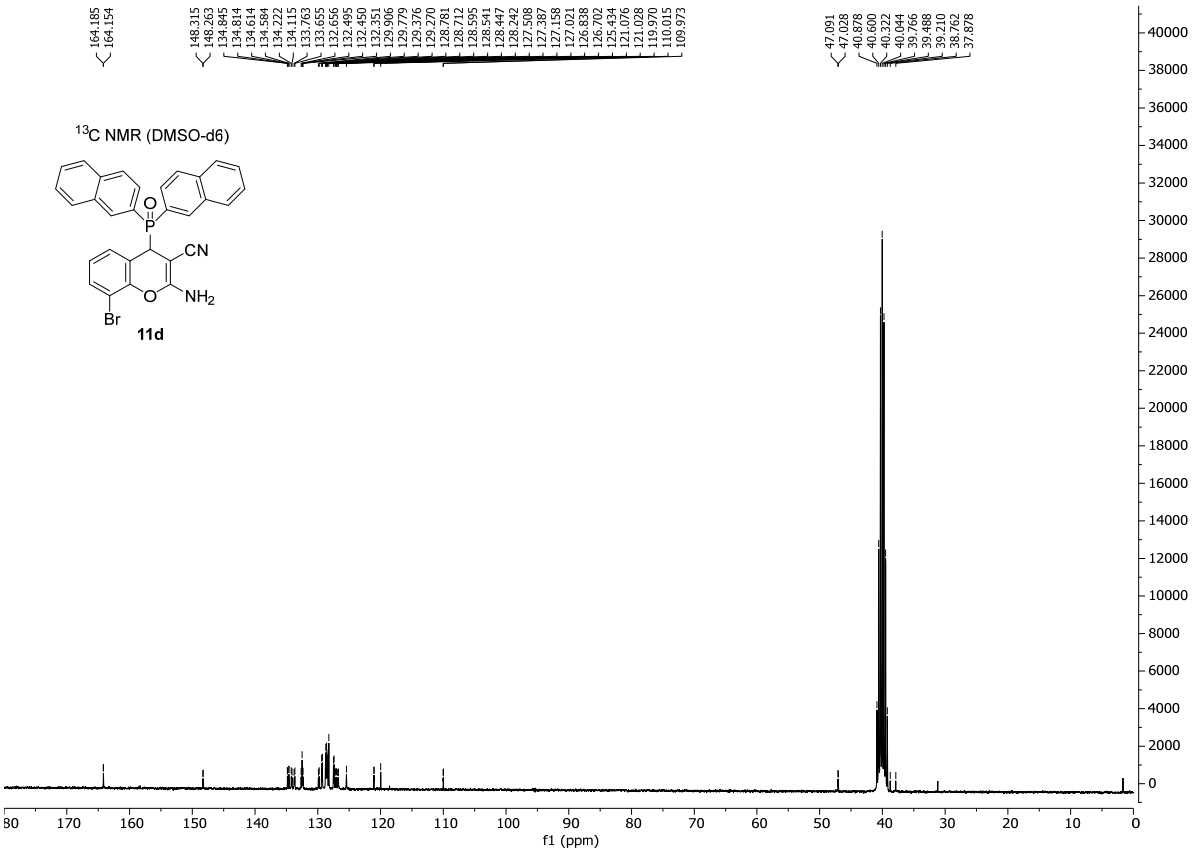

31P NMR (DMSO-d6)
11b
29.641
f1 (ppm)

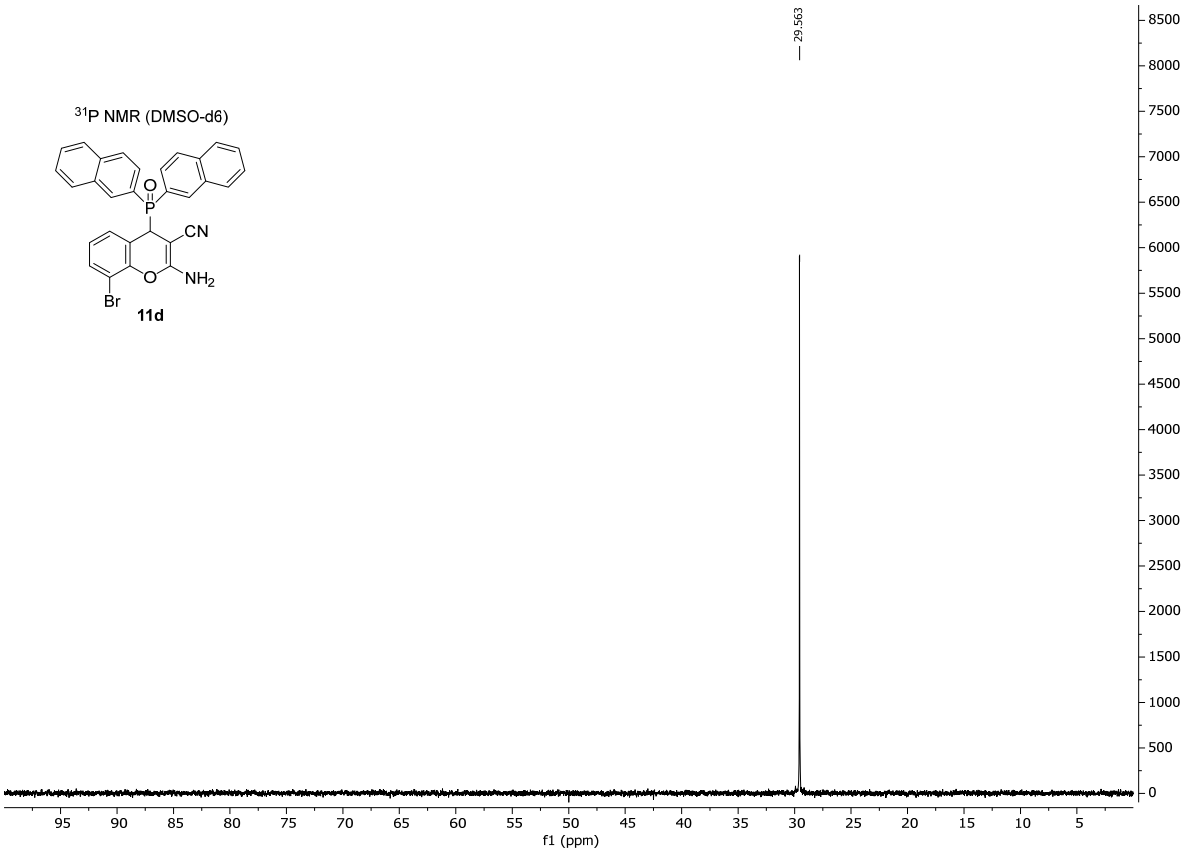

1H NMR (DMSO-d6)
11c
7.476
7.462
7.454
7.329
7.307
7.203
7.161
6.841
6.825
6.810
6.660
6.645
5.044
5.035
3.357
2.514
2.510
2.506
2.503
2.499
2.318
2.264
2.076
0.000
3.05
2.09
3.93
1.00
1.01
1.00
6.07
6.04
f1 (ppm)

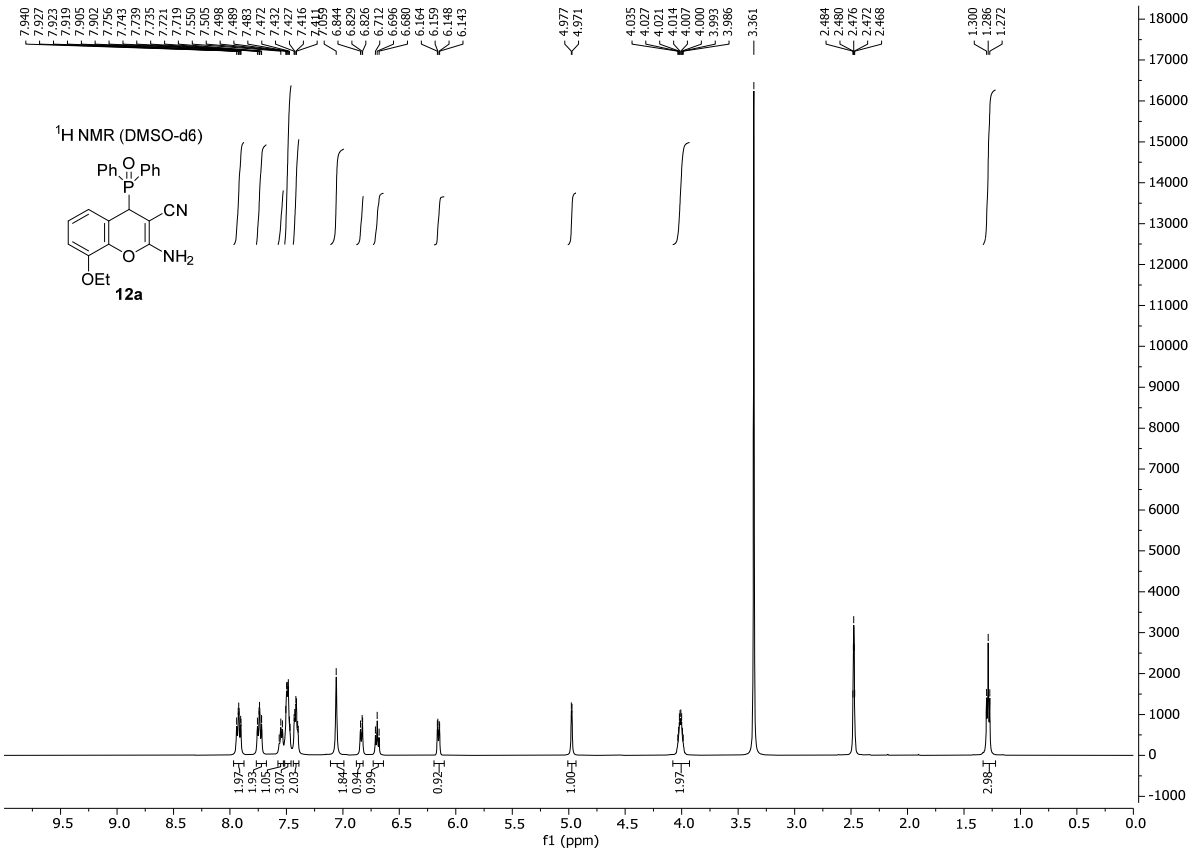

163.872
163.843
148.214
148.162
138.042
138.010
137.886
137.854
133.728
133.691
133.650
133.612
132.288
132.249
132.059
131.790
130.863
130.557
129.828
129.711
129.566
129.389
128.896
128.790
125.271
125.235
121.239
121.197
120.212
109.754
109.714
47.596
47.539
40.832
40.556
40.277
40.001
39.722
39.444
39.167
38.743
37.854
21.402
21.292
55000
50000
45000
40000
35000
30000
25000
20000
15000
10000
5000
0
80
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
f1 (ppm)
13C NMR (DMSO-d6)
O
P
CN
O
NH2
Br
11c

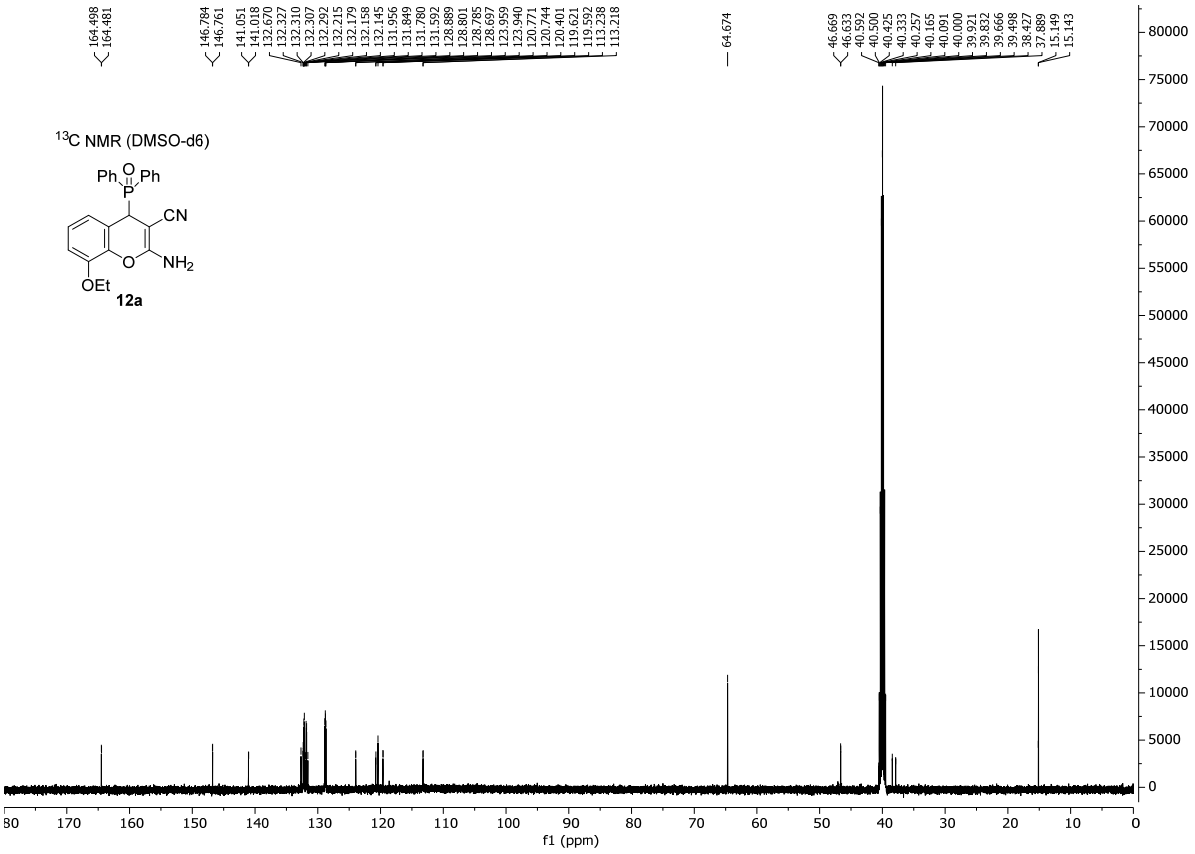

24.966
950000
900000
850000
800000
750000
700000
650000
600000
550000
500000
450000
400000
350000
300000
250000
200000
150000
100000
50000
0
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
f1 (ppm)
31P NMR (DMSO-d6)
O
P
CN
O
NH2
Br
11c


8.631
8.588
8.455
8.413
8.150
8.122
8.095
8.084
8.068
8.038
8.019
8.011
7.986
7.958
7.675
7.655
7.633
7.611
7.604
7.577
7.553
7.475
7.456
7.446
7.435
7.426
7.419
7.298
6.740
6.715
6.692
6.670
5.422
5.412
3.339
2.510
2.503
2.496
2.490
-0.006
1H NMR (DMSO-d6)
O
P
CN
O
NH2
Br
11d
1.02
1.07
7.74
4.00
1.08
2.00
1.99
1.00
f1 (ppm)


164.185
164.154
148.315
148.263
134.845
134.814
134.614
134.584
134.222
134.115
133.763
133.655
132.656
132.495
132.450
132.351
129.906
129.779
129.376
128.781
128.712
128.595
128.541
128.447
128.242
127.508
127.387
127.158
127.021
126.838
126.702
125.434
121.076
121.028
119.970
110.015
109.973
47.091
47.028
40.878
40.600
40.322
40.044
39.766
39.488
39.210
38.762
37.878
13C NMR (DMSO-d6)
O
P
CN
O
NH2
Br
11d
f1 (ppm)


31P NMR (DMSO-d6)
11d
29.563
f1 (ppm)


1H NMR (DMSO-d6)
12a
f1 (ppm)


164.498
164.481
146.784
146.761
141.051
141.018
132.670
132.327
132.310
132.307
132.292
132.215
132.179
132.158
132.145
131.956
131.849
131.780
131.592
128.889
128.801
128.785
128.697
123.959
123.940
120.771
120.744
120.401
119.621
119.592
113.238
113.218
64.674
46.669
46.633
40.592
40.500
40.425
40.333
40.257
40.165
40.091
40.000
39.921
39.832
39.666
39.498
38.427
37.889
15.149
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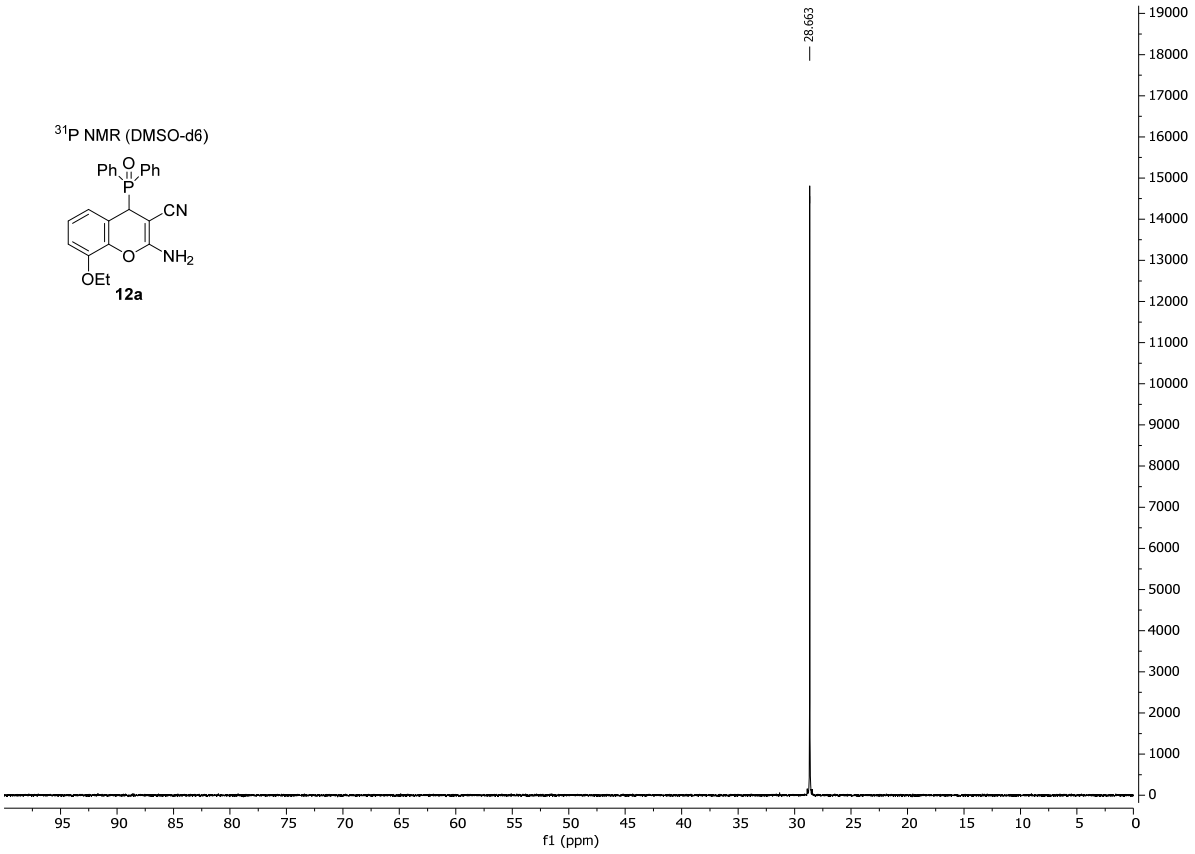
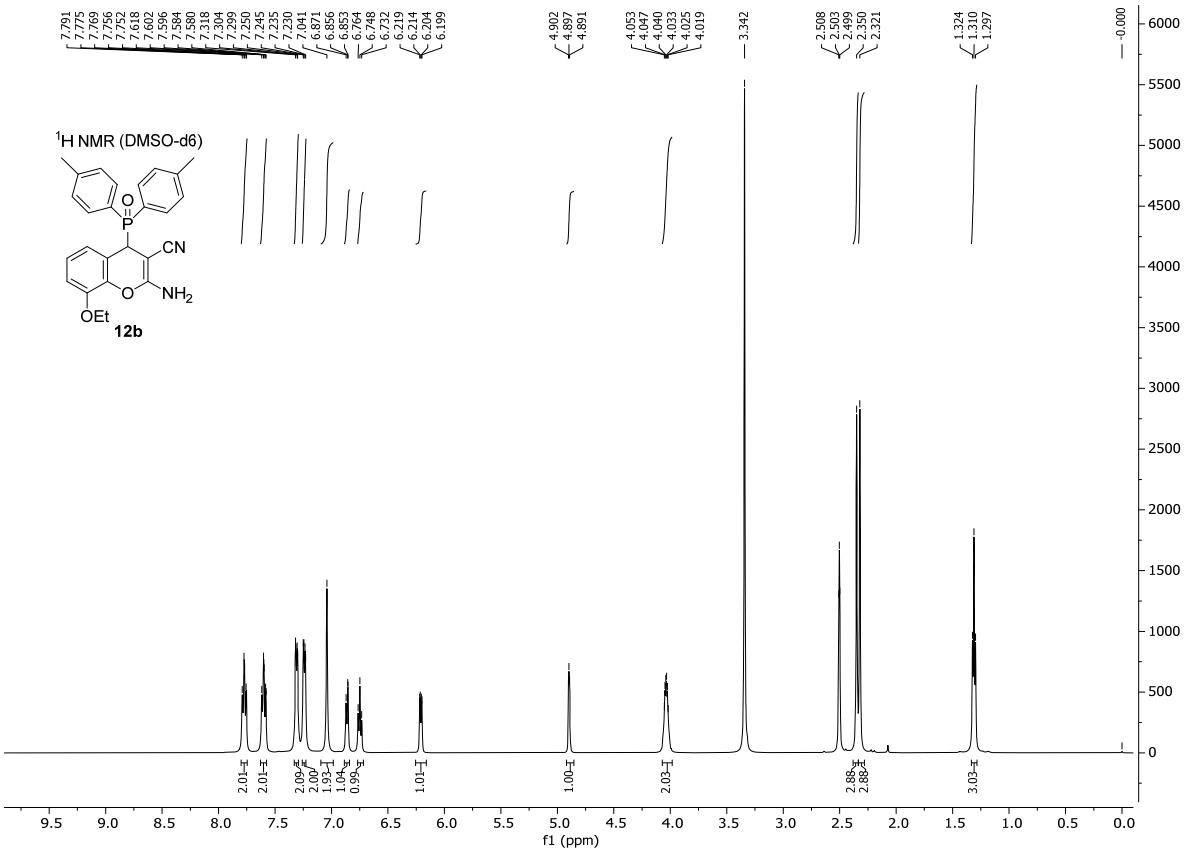
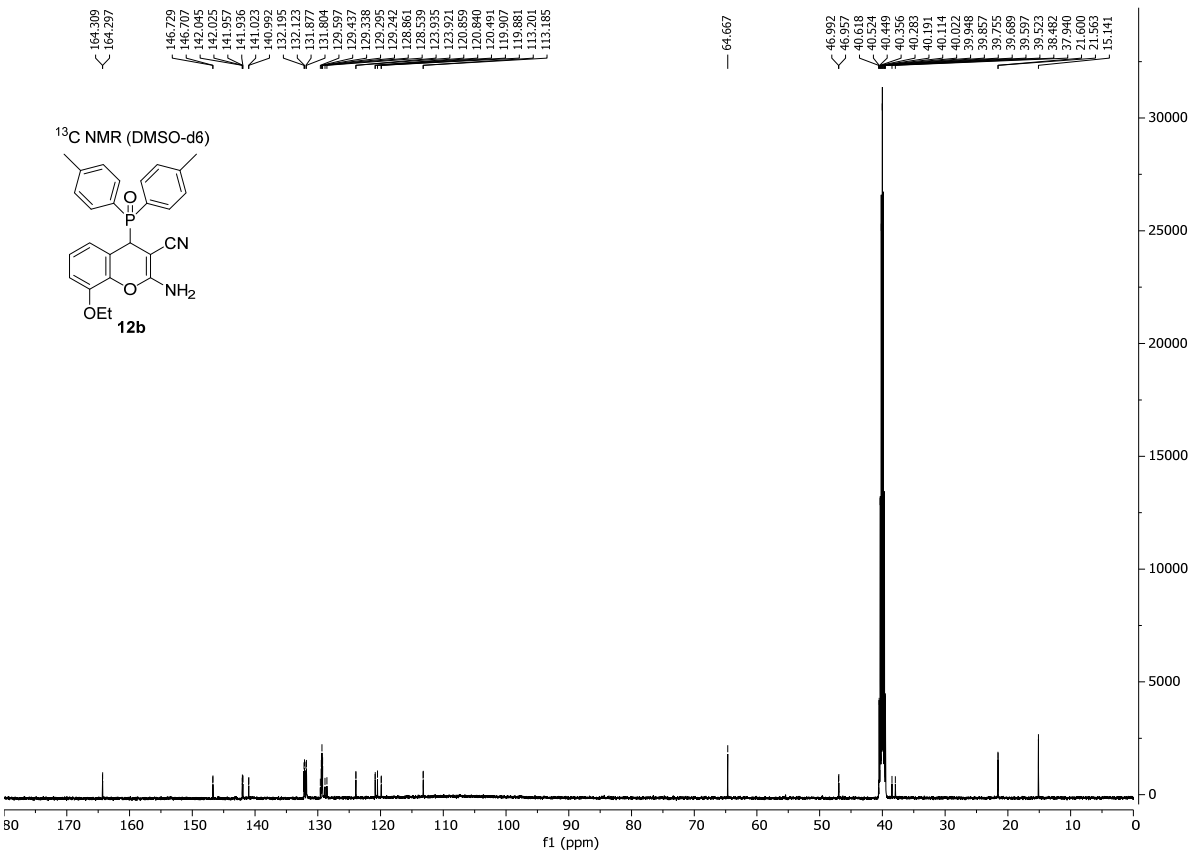
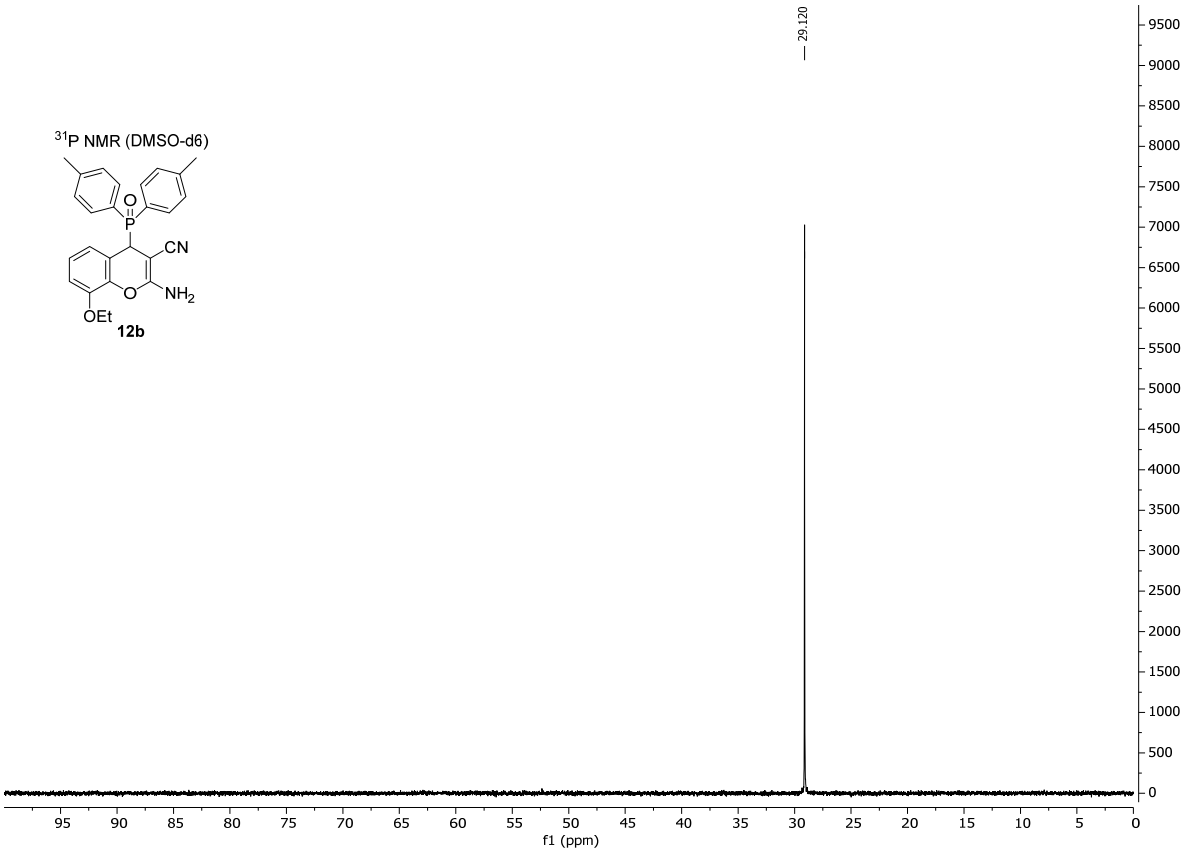
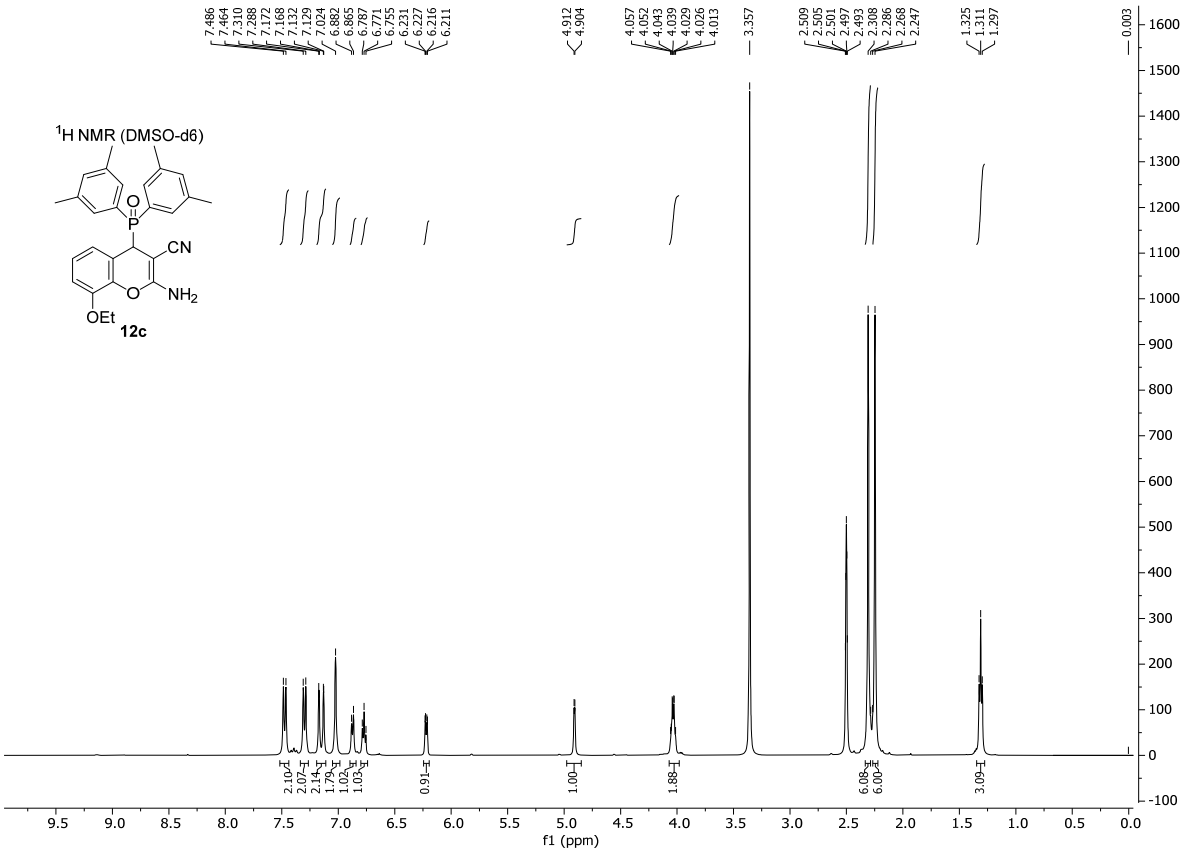
13C NMR (DMSO-d6)
Ph
O
Ph
P
CN
NH2
O
OEt
12a
f1 (ppm)

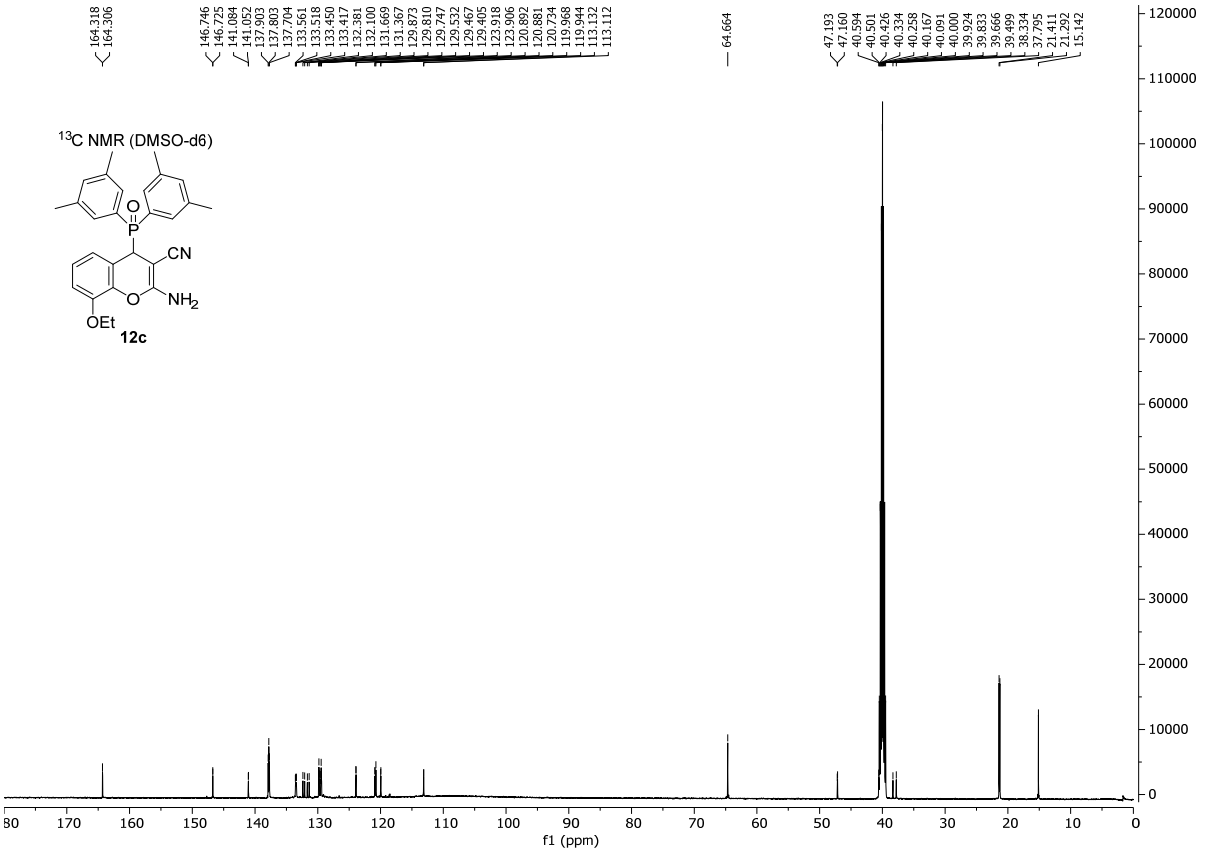

28.663
31P NMR (DMSO-d6)
Ph
O
Ph
P
CN
NH2
O
OEt
12a
f1 (ppm)

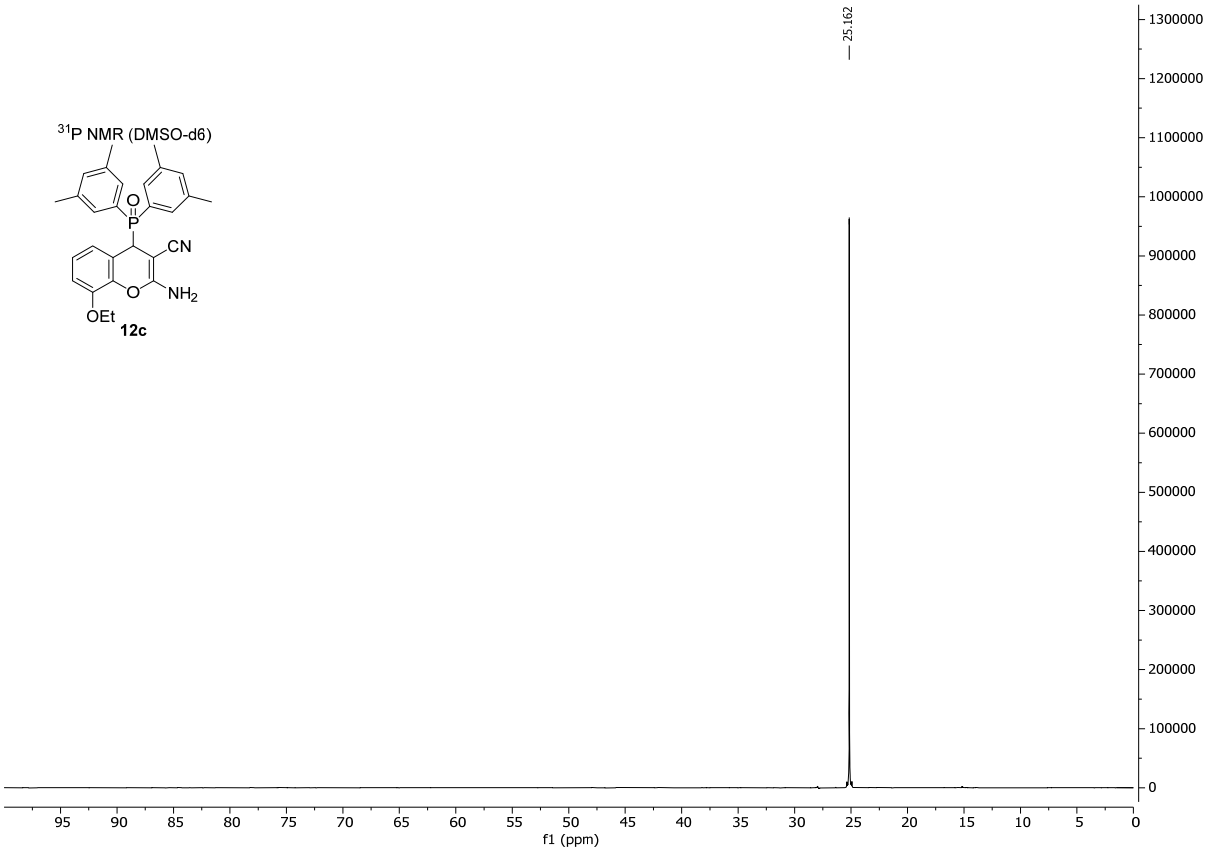

^{1}H NMR (DMSO-d6)
12b

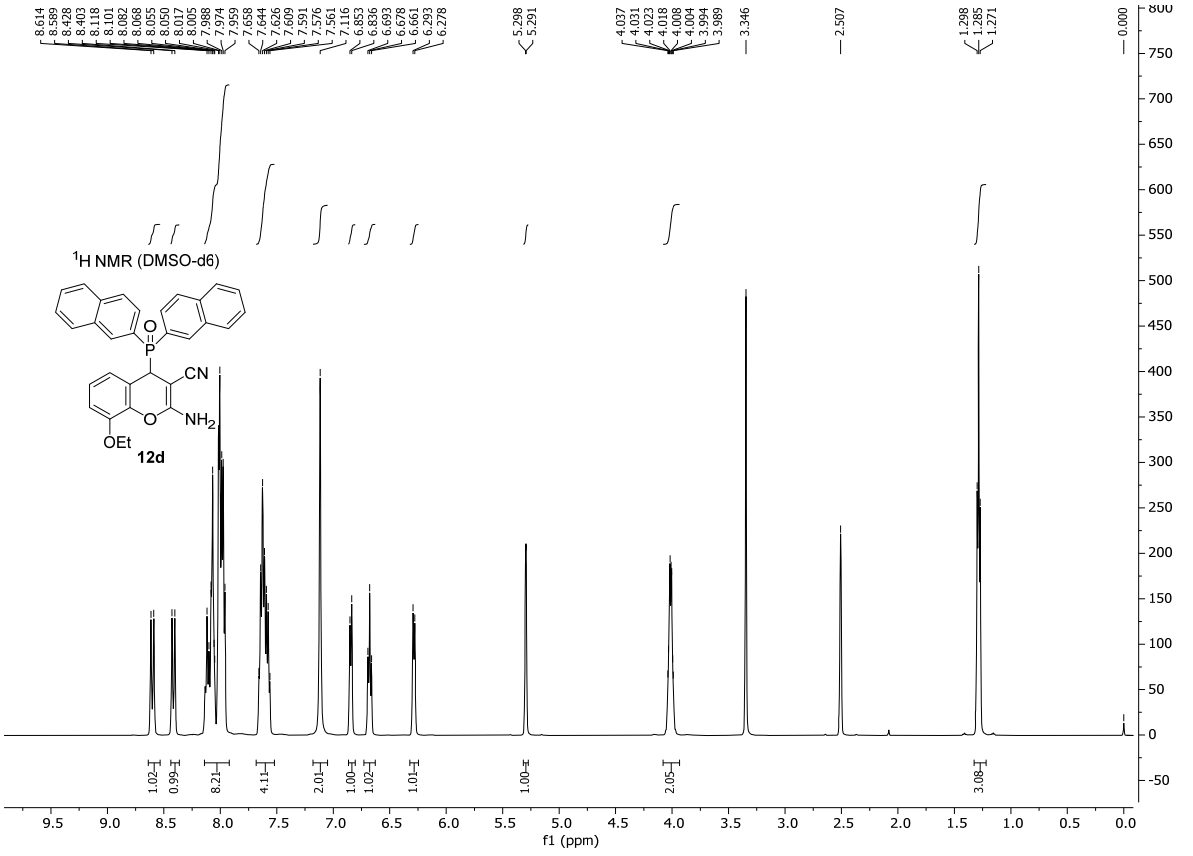

^{13}C NMR (DMSO-d6)
12b

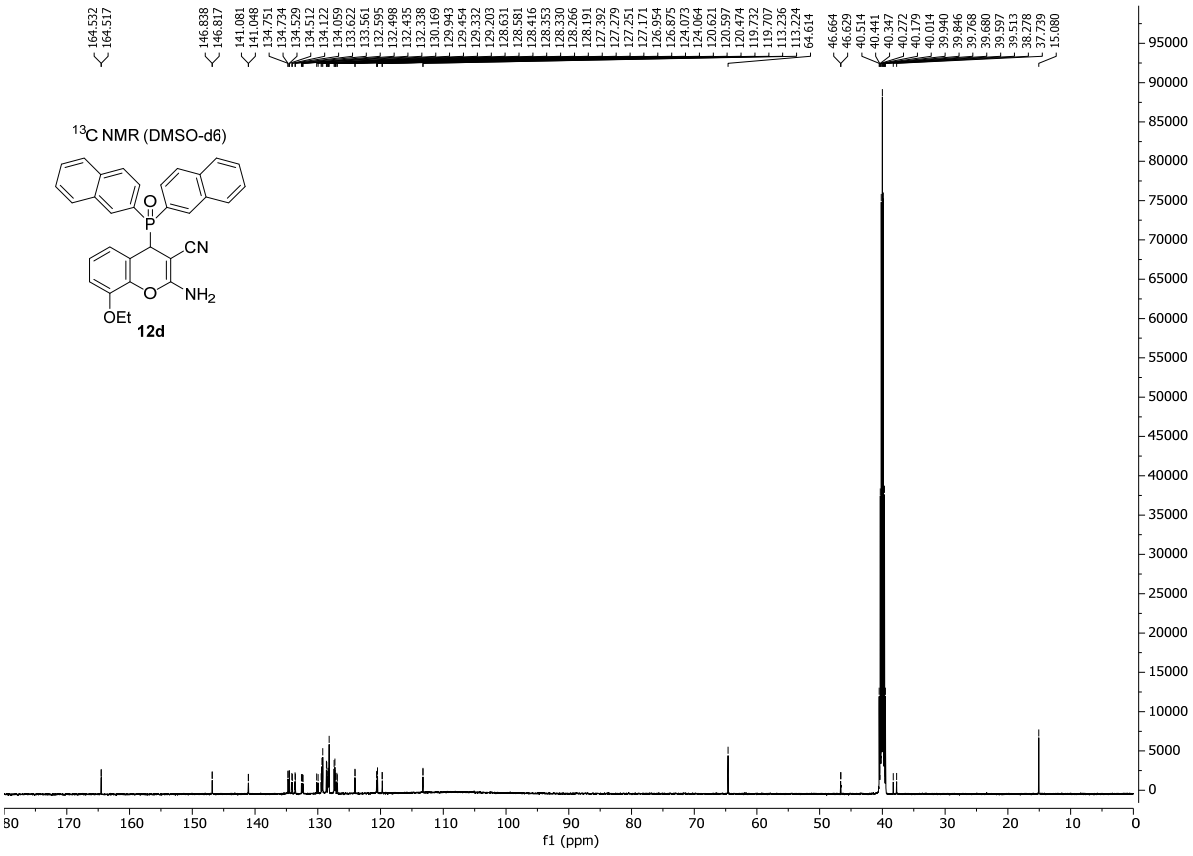

31P NMR (DMSO-d6)
12b
29.120
f1 (ppm)


1H NMR (DMSO-d6)
12c
7.486
7.464
7.310
7.288
7.172
7.168
7.132
7.129
7.024
6.882
6.865
6.787
6.771
6.755
6.231
6.227
6.216
6.211
4.912
4.904
4.057
4.052
4.043
4.039
4.029
4.026
4.013
3.357
2.509
2.505
2.501
2.497
2.493
2.308
2.286
2.268
2.247
1.325
1.311
1.297
0.003
2.10
2.07
2.14
1.79
1.02
1.03
0.91
1.00
1.88
6.08
6.00
3.09
f1 (ppm)


164.318
164.306
146.746
146.725
141.084
141.052
137.903
137.803
137.704
133.561
133.518
133.450
133.417
132.381
132.100
131.669
131.367
129.873
129.810
129.747
129.532
129.467
129.405
123.918
123.906
120.892
120.881
120.734
119.968
119.944
113.132
113.112
64.664
47.193
47.160
40.594
40.501
40.426
40.334
40.258
40.167
40.091
40.000
39.924
39.833
39.666
39.499
38.334
37.795
21.411
21.292
15.142
13C NMR (DMSO-dδ)
O
P
CN
O
NH2
OEt
12c
f1 (ppm)


25.162
31P NMR (DMSO-dδ)
O
P
CN
O
NH2
OEt
12c
f1 (ppm)


8.614
8.599
8.498
8.403
8.118
8.101
8.082
8.068
8.055
8.050
8.017
8.005
7.988
7.974
7.959
7.658
7.644
7.626
7.609
7.591
7.576
7.561
7.116
6.853
6.836
6.693
6.678
6.661
6.293
6.278
5.298
5.291
4.037
4.031
4.023
4.018
4.008
4.004
3.994
3.989
3.346
2.507
1.298
1.285
1.271
0.000
1H NMR (DMSO-d6)
O
P
CN
O
NH2
OEt
12d
1.02
0.99
8.21
4.11
2.01
1.00
1.02
1.01
1.00
2.05
3.08
f1 (ppm)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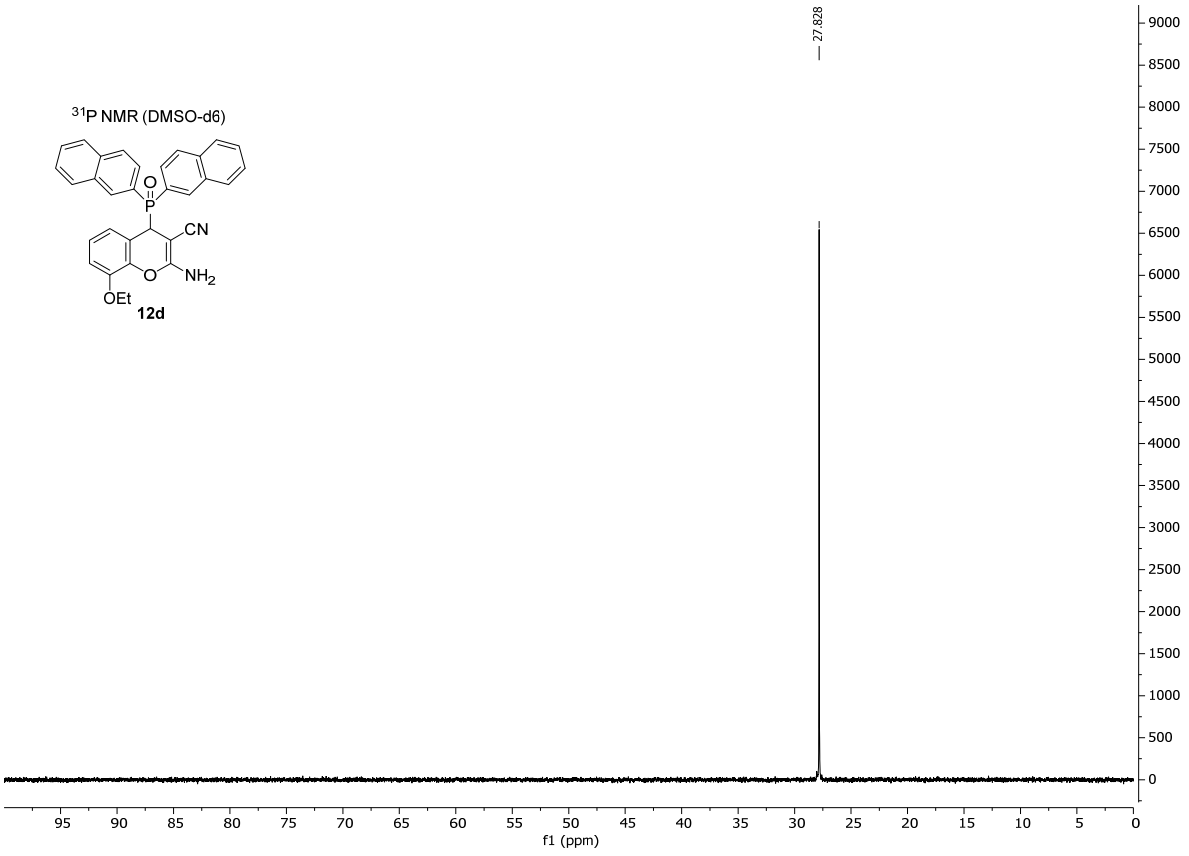
164.517
146.838
146.817
141.081
141.048
134.751
134.734
134.529
134.512
134.122
134.059
133.622
133.561
132.595
132.498
132.435
132.338
130.169
129.943
129.454
129.332
129.203
128.631
128.581
128.416
128.353
128.330
128.266
128.191
127.392
127.279
127.251
127.171
126.954
126.875
124.073
124.064
120.621
120.597
120.474
119.732
119.707
113.236
113.224
64.614
46.664
46.629
40.514
40.441
40.347
40.272
40.179
40.014
39.940
39.846
39.768
39.680
39.597
39.513
38.278
37.739
15.080
13C NMR (DMSO-d6)
O
P
CN
O
NH2
OEt
12d
f1 (ppm)


31P NMR (DMSO-d6)
O
P
CN
O
NH2
OEt
12d
27.828
9000
8500
8000
7500
7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
95
90
85
80
75
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
f1 (ppm)

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