Electronic Supplementary Material (ESI) for Green Chemistry.

SUPPORTING INFORMATION

Highly Stereoselective and Catalyst-Free Synthesis of Annulated Tetrahydropyridines by Intramolecular Imino-Diels-Alder Reaction under Microwave Irradiation in Water

N. Lezana,[a] M. Matus-Pérez,[a] A. Galdámez,[a] S. Lühr [b] and M. Vilches-Herrera.[a]*

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General Experiment

All microwave reactions were performed in a Monowave 300, in sealed reaction vessels. The temperature was controlled using an IR sensor. TLC were performed on silica gel 60 F254 plates. GC-MS spectra were recorded on a Varian 450 GC triple quadrupole coupled to a Varian 320 MS mass spectrometer equipped with an electronic impact source (EI). HPLC-ESI-MS experiments were performed on an Exactive Plus Orbitrap MS Thermo Scientific. The accurate mass measurements were performed at a resolution of 140.000 in positive mode. 1H NMR (200 and 400 MHz) and 13C NMR (50 and 100 MHz) spectra were recorded on a Bruker Biospin GmbH NMR.

General procedure for the preparations of imines (3a-c and 4a,b)

5-Amino-1-(*tert*-butyl)-1H-pyrrole-3-carbonitrile (1 mmol, 1 eq.) or 5-amino-1-(phenyl)-pyrazole-3-methyl, were dissolved in methanol (60 mL) and the corresponding salicylaldehyde (1 mmol, 1 eq.) was added. The mixture was stirred at reflux for 6-8 hours and left overnight at room temperature. The crystals were filtered and washed with cold methanol and used without further purification.

General procedure for the preparation of 5a-g and 6a-d

The corresponding imine derivative (1 mmol, 1eq.) was dissolved in acetonitrile (20 mL) and K_2CO_3 (3 mmol, 3eq.) and the corresponding allyl bromide (1 mmol, 1eq.) was added. The mixture was refluxed for 8 hours. After cooling, the solvent was evaporated and the residue was dissolved in AcOEt (8mL), avoiding the undesirable dichloromethane for extractions.[1] Water (12mL) was added and the mixture stirred for 15 min at room temperature. The organic phase was separated and the aqueous layer was extracted with AcOEt (2x12mL). The combined organic phases were dried over Na_2SO_4 anhydrous, filtered and concentrated under reduce pressure, dissolved in 5mL of methanol or in a mixture of hexane/AcOet (4:1, 5mL) for crystallization and left overnight. The formed crystals were filtered to give the corresponding products. No other purification method was used (e.g column chromatography).

[1] Alternative Solvents for Green Chemistry, Francesca M. Kerton, The Royal Society of Chemistry, 2009, ch. 1.

General procedure for the preparation of 7a-k and 8a-d.

5a-g, **6a-d** or **9** (0.5 mmol) and water (2-4 mL) were introduced in a microwave reaction vial which was sealed with a PTFE-coated silicone septum and closed with a PEEK cap. The solution was heated for 5 minutes at 200°C. After cooling the aqueous solution was sonicated to break the compact precipitated formed and left overnight. Method A: for compounds 7a-f and 8a-d (Figure 1) the formed precipitate was filtered and washed with water. Method B: for compounds 7h-k, the aqueous solution was extracted with 1 mL (x2) of ethyl acetate,[1] dried over sodium sulfate concentrated and crystallized from methanol. No column chromatography was necessary for purification, except for compounds 7a´ and 7b´ for *cis* isomer isolation.

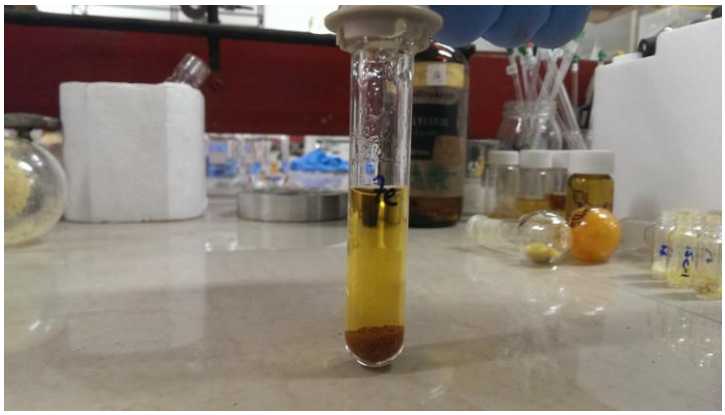
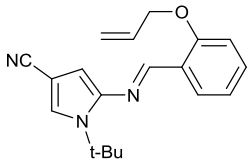
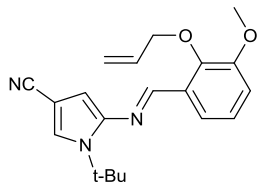


Figure 1

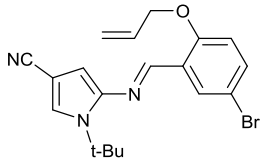
Compound Characterisation



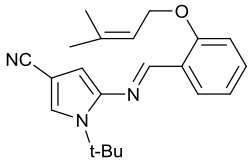
(E)-5-(2-(Allyloxy)benzylideneamino)-1-*tert*-butyl-1H-pyrrole-3-carbonitrile (5a), (380 mg, 52%). mp 82.7-83.7°C (from MeOH). ^{1}H (200 MHz, $CDCl_3$) δ 8.95 (1H, s, N=CH), 8.07 (1H, dd, J_1 = 1.1 Hz, J_2 = 7.7 Hz), 7.41 (1H, t, *J* = 11.3, 4.3 Hz), 7.25 (1H, d, *J* = 1.9 Hz,), 7.03 (1H , t), 6.94 (1H, d, *J* = 8.5 Hz), 6.39 (1H, d, *J* = 1.6 Hz), 6.19 – 6.00 (1H, m), 5.45 (1H, d, *J* = 17.3 Hz), 5.34 (1H, d, *J* = 10.5 Hz), 4.64 (2H, d, *J* = 5.1 Hz), 1.71 (9H, s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.53, 151.32, 132.78, 132.52, 128.88, 128.51, 127.10, 125.07, 124.68, 121.08, 117.95, 112.59, 98.22, 90.07, 69.24, 58.32, 30.14. MS(GC, 70eV): m/z(%) = 307.1 (M^+,100%), 250.2(75). HRMS (ESI): Mass calculated for $C_{19}H_{21}N_3O$ $[M-H]^+$ 307.1685. Found: 308.1757.



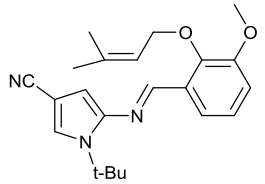
(E)-5-(2-(allyloxy)-3-methoxybenzylideneamino)-1-tert-butyl-1H-pyrrole-3-carbonitrile (5b), (487 mg, 60%). mp 139.7-141.5°C. ^{1}H NMR (200 MHz, $CDCl_3$) δ 8.82 (1H ,s), 7.62 (1H, d, *J* = 7.82 Hz), 7.23 (1H, s), 7.10 (1H, t, J_1 = 8.80; J_2 = 7.82 Hz), 6.99 (1H, d, *J* = 3.91,7.82Hz), 6.36 (1H , d, *J* = 1.22 Hz), 6.05 (1H, m, *J*=5.38, 6.11Hz), 5.36 (1H, d), 5.26 (1H, d, *J* = 10.27 Hz), 4.58 (2H, d, *J* = 5.87 Hz), 3.87(3H, s) 1.68 (9H, s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.04, 151.61, 148.78, 143.67, 133.51, 130.34, 124.86, 124.24, 118.50, 118.37, 117.22, 114.78, 98.41, 90.20, 74.98, 58.38, 55.94, 30.16. MS(GC, 70eV) m/z 337.1(M^+, 62%), 280.3 (33), 162(100). HRMS (ESI): Mass calculated for $C_{19}H_{21}N_3O$ $[M-H]^+$ 337.1790. Found: 338.1864.



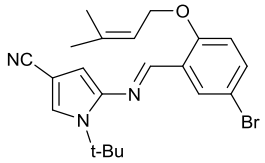
(E)-5-(2-(allyloxy)-5-bromobenzylideneamino)-1-tert-butyl-1H-pyrrole-3-carbonitrile (5c), (554 mg, 56%). mp 121.5-122.0°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.89 (1H , s), 8.11 (1H, d, *J* = 2.2 Hz), 7.47 (1H, dd, *J* = 8.8, 2.4 Hz), 7.26 (1H, s), 6.83 (1H, d, *J* = 8.8 Hz), 6.41 (1H, s), 6.13 – 5.98 (1H, m), 5.43 (1H, d, *J* = 17.3 Hz), 5.36 (1H, d, *J* = 10.5 Hz), 4.62 (2H, d, *J* = 5.1 Hz), 1.71 (9H, s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.41, 149.68, 143.45, 134.81, 132.31, 129.59, 126.85, 125.07, 118.36, 117.10, 114.48, 113.78, 98.76, 90.29, 69.55, 58.44, 30.21. MS(GC, 70eV): m/z 385.1(M^+,65%), 329.1(63), 222.1(100). HRMS (ESI): Mass calculated for $C_{19}H_{20}BrN_3O$ $[M-H]^+$ 385.0790. Found: 386.08863.



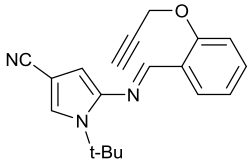
(E)-1-tert-butyl-5-(2-(3-methylbut-2-enyloxy)benzylideneamino)-1H-pyrrole-3-carbonitrile (5d), (480 mg, 48%). mp 115.2-116.3°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.91 (1H ,s), 8.06 (1H, dd, *J* = 7.6, 1.5 Hz), 7.40 (1H, t), 7.24 (1H, d, *J* = 1, 7 Hz), 7.01 (1H, t), 6.95(1H, d, *J* = 8.3 Hz), 6.39 (1H, d, 1.9 Hz), 5.51(1H, m) 4.61 (1H, d, *J* = 6.6 Hz), 1.82 (3H, s), 1.76 (3H, s), 1.70 (9H s).^{13}C NMR (101 MHz, $CDCl_3$). δ 159.00, 151.76, 144.19, 138.40, 132.62, 127.15, 125.15, 124.69, 120.89, 119.46, 117.44, 112.73, 98.31, 90.09, 65,57, 58.38, 30.23, 25.92, 18.41. MS (GC, 70eV): m/z 335.2(M^+, 55%), 264.0(100), 172.1(60).



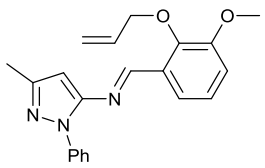
(E)-1-tert-butyl-5-(3-methoxy-2-(3-methylbut-2-enyloxy)benzylideneamino)-1H-pyrrole-3-carbonitrile (5e), (492 mg, 60%). mp 92.1-93.5°C ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.84(1H, s) 7.65 (1H, d, *J* = 7.8 Hz), 7.25 (1H, d, *J* = 1.9 Hz), 7.12 (1H, t), 7.01 (1H, d, *J* = 9.0 Hz), 6.38 (1H, d, 1.9 Hz), 5.54 (1H, m), 4.59 (2H, d, *J* = 7.6 Hz), 3.91 (3H, s), 1.76 (3H, s), 1.71 (9H, s), 1.65 (3H, s). ^{13}C NMR (101 MHz, DMSO) δ 153.35, 152.18, 149.07, 143.90, 139.84, 130.79, 124.91, 124.23, 119.82, 118.41, 117.38, 114.79, 98.33, 90.26, 70.46, 58.48, 56.07, 30.26, 25.96, 18.09. MS (GC, 70eV): m/z 365.1(M^+, 66%), 294(1200), 1662.1(68).



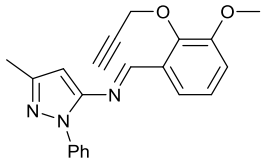
(E)-5-(5-bromo-2-(3-methylbut-2-enyloxy)benzylideneamino)-1-tert-butyl-1H-pyrrole-3-carbonitrile (5f), (376 mg, 55 %). mp 122.3-123.5°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80 (1H, s) 8.10 (1H, d, *J* = 2.7 Hz), 7.45 (1H, dd, *J* = 8.8, 2.4 Hz), 7.26 (1H ,s), 6.84 (1H, d, *J* = 8.8 Hz), 6.41 (1H, d, J = 1.7 Hz), 5.48 (1H,m), 4.60 (2H, d, *J* = 6.6 Hz), 1.82 (3H, s), 1.76 (3H, s), 1.71 (9H ,s).^{13}C NMR (101 MHz, $CDCl_3$) δ 157.90, 150.15, 143.66, 138.95, 134.91, 129.64, 126.98, 125.11, 119.01, 117.27, 114.64, 113.57, 98.87, 90.33, 65.91, 58.53, 30.31, 25.93, 18.45. MS(GC, 70eV): m/z 413.1(M^+, 52%), 342.1(100), 250.1(50).



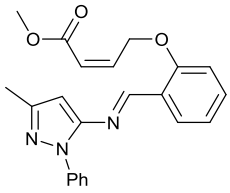
(E)-1-tert-butyl-5-(2-(prop-2-ynyloxy)benzylideneamino)-1H-pyrrole-3-carbonitrile (5g), (378 mg, 51%). mp 101.3-102.8°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.82 (1H, s), 8.01 (1H, dd, *J* = 8.07, 1.7 Hz), 7.39 – 7.33 (1H, m, *J* =1.71, 8.3Hz), 7.17 (1H, d, *J* = 1.9 Hz), 7.02 (1H, d, *J* = 6.6 Hz), 6.99 (1H, d, *J* = 8.07Hz), 6.34(1H, dd, *J* =1.9 Hz), 4.74 (2H, dd, *J* = 9.7, 2.4 Hz), 2.48 (1H, t, *J* = 2.4 Hz), 1.63 (1H, s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.52 (s), 151.11 (s), 143.93 (s), 132.51 (s), 127.31 (s), 125.63 (s), 124.87 (s), 122.00 (s), 117.36 (s), 113.07 (s), 98.52 (s), 90.22 (s), 78.15 (s), 76.30 (s), 58.44 (s), 56.53 (s), 30.25 (s).



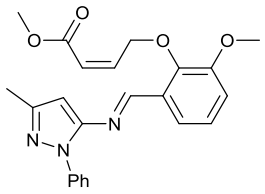
(E)-N-(2-(allyloxy)-3-methoxybenzylidene)-3-methyl-1-phenyl-1H-pyrazol-5-amine (6a), (64%, 498 mg). mp 96-97°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.03 (1H, s), 7.65 (1H, d, *J* = 8.07 Hz), 7.65 (1H, d, *J* = 7.8Hz), 7.43 (1H, t), 7.29 (1H, t), 7.09 (1H, t), 7.03 (1H, d, J = 7.8 Hz), 6.17 (1H, s), 6.08 (1H, m), 5.40 (1H, d), 5.29 (1H, d), 4.62 (1H, 5.9 Hz), 3.89 (3H, s), 2.37 (3H, s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.60, 152.88, 150.96, 149.19, 149.13, 139.53, 133.53, 129.96, 128.51, 126.35, 124.29, 124.12, 118.99, 118.53, 115.41, 93.38, 75.02, 55.94, 14.21.



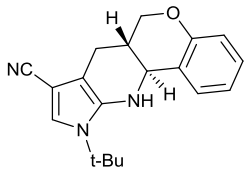
(E)-N-(3-methoxy-2-(prop-2-ynyloxy)benzylidene)-3-methyl-1-phenyl-1H-pyrazol-5-amine (6b), (356 mg, 59%). mp 111-112°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.12 (1H, s), 7 .76 (1H, d, *J* = 7.9 Hz), 7.69 (1H, d, 7.8 Hz), 7.44 (1H, t), 7.30 (1H, t), 7.14 (1H, t), 7.03 (1H, 8.1 Hz), 6.23 (1H, s), 4.84 (2H, d), 3.89 (3H, s), 2.48 (1H, m), 2.37 (3H, s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 157.02, 152.67, 150.95, 149.20, 147.56, 139.54, 130.96, 128.50, 126.34, 124.99, 124.12, 118.91, 115.17, 93.60, 78.74, 78.41, 60.79, 55.92, 14.22.



(Z)-methyl 4-(2-((E)-(3-methyl-1-phenyl-1H-pyrazol-5-ylimino)methyl)phenoxy)but-2-enoate (6c), (364 mg, 58%). mp 115-116°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.12 (1H, s), 8.09 (1H, dd, J =1.7, J = 7.7 Hz), 7 .75 (1H, d, *J* = 7.9 Hz), 7.44 (3H, m), 7.30 (1H, t), 7.13 (1H, dt), 7.03 (1H, t), 6.86 (1H, d, *J* = 8.4 Hz), 6.21 (2H, m), 4.81 (2H, dd, *J* = 1.7, 3.8 Hz), 3.87 (3H, s), 3.78 (3H, s), 2.38 (3H, s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.25, 158.15, 155.59, 151.07, 149.19, 142.02, 139.57, 133.24, 128.52, 128.00, 126.33, 124.73, 124.08, 122.14, 121.71, 112.23, 93.46, 66.99, 51.83, 14.21.

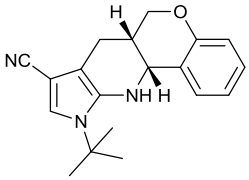


(E)-N-(2-(allyloxy)-3-methoxybenzylidene)-3-methyl-1-phenyl-1H-pyrazol-5-amine (6d), (280 mg, 62%). mp 110-111°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.99 (1H, s), 7.73 (1H, d, *J* = 7.7 Hz), 7.63 (1H, d, *J* =7.9Hz), 7.43 (2H, t), 7.29 (1H, t), 7.11 (1H, m), 7.03(1H, d, *J* = 7.9 Hz), 6.28 (1H, td), 6.18 (1H, s), 4.74 (2H, dd, *J* = 1.7, 6.2 Hz), 3.87 (3H, s), 3.78 (3H, s), 2.36 (3H, s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.55, 155.86, 152.63, 150.77, 149.24, 148.65, 143.01, 139.46, 129.66, 128.52, 126.42, 124.70, 124.15, 121.65, 119.15, 115.50, 93.50, 72.28, 55.97, 14.16.



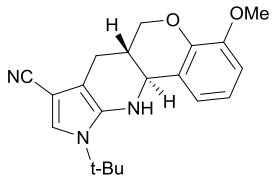
10-(tert-butyl)-6,6a,7,10,11,11a-hexahydrochromeno[4,3-b]pyrrolo[3,2-e]pyridine-8-carbonitrile (7a), (106 mg, 87%), mp 202.5-203.5°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (1H, d, *J* = 7.6 Hz), 7.22 (1H, t), 7.02 (1H, s), 6.96 (1H, t, *J* = 7.5 Hz), 6.87 (1H, d, *J* = 8.1 Hz), 4.42 (1H, dd, *J* = 11.1, 3.0 Hz), 4.00 (1H, t, *J* = 10.5 Hz), 3.90 (1H , t, *J* = 9.2 Hz), 2.81 (1H, dd, *J* = 15.2, 5.1 Hz), 2.58 (1H, d, *J* = 10.5 Hz), 2.29 (1H, t), 2.18 – 1.92 (1H ,m), 1.65 (9H, s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.88, 156.89, 153.82, 144.65, 128.83, 126.99, 123.45, 120.88, 116.52, 110.52, 109.75, 68.71, 59.46, 59.30, 34.76, 29.19, 25.88. MS(GC, 70eV) m/z 307.4(M^+, 100%), 251.3 (63.3), 157.1(28.7). HRMS (ESI): Mass calculated for $C_{19}H_{21}N_3O$ $[M-H]^+$ 307.1685. Found: 308.1755.

A coupling constant of $J_{6a,11a}$ = 10.5 Hz for the signal at δ = 3.96 – 4.01 ppm can be measured. Interestingly a coupling constant of *J* = 10.3 Hz between the proton at C-11a and the nitrogen is observed.

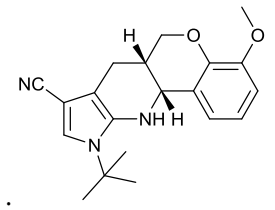


10-(tert-butyl)-6,6a,7,10,11,11a-hexahydrochromeno[4,3-b]pyrrolo[3,2-e]pyridine-8-carbonitrile (7a´).(55mg, 30%). mp 186.2-188.3°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.78 (d, *J* = 7.6 Hz, 1H), 7.26 (s, 1H), 7.21 (t, 1H), 7.01 (t, *J* = 7.5 Hz, 1H), 6.85 (d, *J* = 8.3 Hz, 1H),4.59(d, *J* = 10.5 Hz, 1H), 4.36 (dd, *J* = 11.1, 3.4 Hz, 1H), 4.11 (t, *J* = 11.0 Hz, 1H), 3.15 (dd, *J* = 17.6, 3.9 Hz, 1H), 2.46 (dd, *J* = 17.2, 14.2 Hz, 1H), 2.33-2.27 (m, 1H), 1.71 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.87, 156.87, 153.81, 144.64, 128.81, 126.97, 123.43, 120.87, 116.51, 110.61, 109.73, 68.69, 59.44, 59.28, 34.75, 29.17,

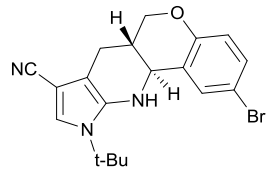
25.87. MS(GC, 70eV): m/z (%) = 307.4(M^+,100), 251.3 (63.3), 157.1(28.7). HRMS (ESI): Mass calculated for $C_{19}H_{21}N_3O$ $[M-H]^+$ 307.1685. Found: 308.1755.
The isolated *cis* isomer showed a signal at 4.38- 4.34 ppm with a coupling constant $J_{6a,11a}$ = 3.4 Hz.



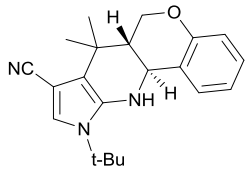
10-(tert-butyl)-4methoxy-6,6a,7,10,11,11a-hexahydrochromeno[4,3-b]pyrrolo[3,2-e]pyridine-8-carbonitrile (7b), (138 mg, 82%) mp 235-237.7°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (1H, d, *J* = 7.8 Hz), 7.01(1H, s), 6.95 (1H, t, *J* = 7.8 Hz), 6.85 (1H, d, *J* = 7.82 Hz), 4.57 (1H, dd, *J* = 11.2, 3.6 Hz), 4.00 (1H, t, *J* = 10.5 Hz), 3.94 (1H, t, *J* = 11.25 Hz), 3.89 (3H, s), 2.83(1H, dd, *J* =10.27, 5.2 Hz), 2.57 (1H, d, *J* = 10.5 Hz), 2.30 (1H, t, *J* = 11.98 Hz), 2.12 (1H, m, 4.9 Hz), 1.64 (9H, s).^{13}C NMR (101 MHz, $CDCl_3$) δ 148.49, 144.39, 135.15, 123.88, 120.97, 120.67, 118.03, 116.97, 110.83, 108.29, 88.81, 69.64, 68.60, 57.19, 56.11, 55.15, 34.50, 29.75, 22.76. MS(GC, 70eV): m/z 337.3 (M^+, 89.5 %), 280.3(28.6), 162.2(100). HRMS (ESI): Mass calculated for $C_{20}H_{23}N_3O_2$ $[M-H]^+$ 337.1790. Found: 338.1860.
For the reaction carried out in water under microwave irradiation, the isolated *trans* isomer showed a signal at 4.03- 3.98 ppm with a coupling constant $J_{6a,11a}$ = 10.5 Hz.



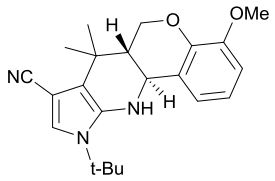
10-(tert-butyl)-4methoxy-6,6a,7,10,11,11a-hexahydrochromeno[4,3-b]pyrrolo[3,2-e]pyridine-8-carbonitrile (7b´), (30mg, 25%). mp ND. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 7.6 Hz, 1H), 7.08 (s, 1H), 6.96-6.90 (m, *2*H), 4.63 (dd, *J* = 11.1, 5.6 Hz, 1H), 4.23 (t, *J* = 12.2 Hz, 1H), 3.93 (t, *J* = 5.8Hz, 1H) 3.90 (s, 3H), 3.44-3.35 (m, *J* = 15.8, 4.9 Hz, 1H) 2.9 (dd, *J* = 16.1, 9.5 Hz, 1H), 2.47 (t, *J* = 16.4 Hz, 1H), 1.71 (s, 9H).^{13}C NMR (101 MHz, $CDCl_3$) δ 154.59, 148.87, 138.64, 129.25, 123.07, 122.24, 121.19, 117.00, 116.30, 113.44, 108.79, 88.63,70.69, 58.00, 56.13, 35.62, 30.05, 19.99. MS(GC, 70eV): m/z(%) = 337.3 (M^+,89.5), 280.3(28.6), 162.2(100). HRMS (ESI): Mass calculated for $C_{20}H_{23}N_3O_2$ $[M-H]^+$ 337.1790. Found: 338.1860.
For the reaction carried out in *p*-xylene, the isolated *cis* isomer showed a signal at 3.95- 3.88 ppm with a coupling constant $J_{6a,11a}$ = 5.8 Hz.



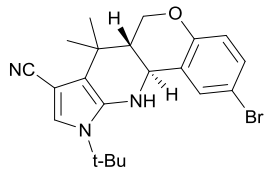
2-bromo-10-(tert-butyl)-6,6a,7,10,11,11a-hexahydrochromeno[4,3-b]pyrrolo[3,2-e]pyridine-8-carbonitrile (7c). (144 mg, 75%) mp 236.2-238.5°C. ^{1}H NMR (400 MHz, DMSO) δ 7.62 (1H, s), 7.36 (1H, d, *J* = 2.0, 8.80 Hz), 7.33 (1H, s), 6.82 (1H, d, *J* = 8.8 Hz), 4.44 (1H, d, *J* = 4.1, 10.52 Hz), 4.41 (1H, d, *J* = 10.76 Hz), 3.92 (1H, d, *J*=11.15 Hz), 3.87 (1H, t, *J*=3.32, 6.60 Hz), 2.66 (1H, dd, *J* = 9.78, 5.4 Hz), 2.23 – 2.14 (1H, m), 2.02 (1H, dd, *J* = 10.8, 5.5 Hz), 1.60 (9H, s). ^{13}C NMR (101 MHz, DMSO) δ 140.02, 136.54, 131.41, 129.77, 127.00, 126.96, 123.80, 122.05, 119.02, 112.18, 107.77, 87.63, 57.51, 54.50, 32.85, 29.89, 22.34. HRMS (ESI): Mass calculated for $C_{19}H_{20}BrN_3O$ $[M-H]^+$ 385.0790. Found: 386.0862.



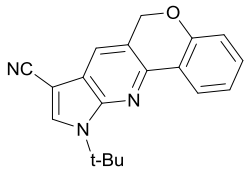
10-(tert-butyl)-7.7-dimethyl-6,6a,7,10,11,11a-hexahydrochromenol[4,3-b]pyrrolo[3,2-e]pyridine-8-carbonitrile (7d) (139 mg, 83%). mp 212.5-213.4°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (1H, d, *J* = 7.6 Hz), 7.21 (1H, t, *J* = 7.6 Hz), 7.03 (1H, s), 6.98 (1H, t), 6.86 (1H, d, *J* = 11.6 Hz), 4.47 (1H, dd, *J* = 11.0, 3.2 Hz), 4.15 (1H, t), 3.92 (1H, t), 2.52 (1H, d, *J* = 10.5 Hz), 1.88 – 1.78 (1H, m), 1.64 (9H, s), 1.56 (3H s), 1.21 (3H, s). ^{13}C NMR (101 MHz, DMSO) δ 150.20, 128.61, 124.17, 122.50, 118.89, 117.48, 116.25, 114.01, 113.11, 112.13, 81.61, 60.85, 52.30, 46.65, 41.13, 28.01, 24.80, 22.43, 19.66. MS(GC, 70eV): m/z 335.3 (M^+, 83%), 264.2(100), 172(41). HRMS (ESI): Mass calculated for $C_{21}H_{23}N_3O_3$ $[M-H]^+$ 335.1998. Found: 336.2070.



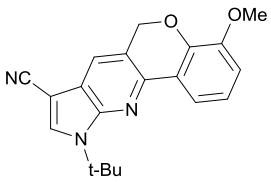
10-(tert-butyl)-4.methoxy-7,7-dimethyl-6,6a,7,10,11,11a-hexahydrochromeno[4,3-b]pyrrolo[3,2-e]pyridine-8-carbonitrile (7e), (153 mg, 84%). mp 214.8-216.6°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (1H, d, *J* = 9.4 Hz), 7.23 (1H, s), 7.15 (1H, dd, *J* = 10.0, 5.8 Hz), 7.04 (1H, d, *J* = 8.0 Hz), 4.81 (1H, dd, *J* = 10.9, 2.7 Hz), 4.37 (1H, t, *J* = 10.7 Hz), 4.15 (1H, t, *J* = 11.3 Hz), 4.09 (2H, s), 3.92 (1H, q, *J* = 7.0 Hz), 2.71 (1H, d, *J* = 10.4 Hz), 1.83 (6H, s), 1.75 (2H, s, *J* = 5.9 Hz), 1.41 (1H, s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.41 , 144.48 , 133.33 , 124.37 , 122.17 , 120.66 , 118.80 , 117.84 , 110.53 , 110.50 , 86.34 , 66.01 , 57.04 , 55.99 , 51.33 ,8 45.72 , 32.70 , 29.61 , 27.09 , 24.50 , 18.44. MS(GC, 70eV) m/z 365.4(M^+, 83.5%), 294.3(99.7), 202.3(68.1), 162.2(100). HRMS (ESI): Mass calculated for $C_{22}H_{27}N_3O_2$ $[M-H]^+$ 365.2103. Found: 366.2176.



2-bromo-10-(tert-butyl)-7,7-dimethyl-6,6a,7,10,11,11a-hexahydrochromeno[4,3-b]pyrrolo[3,2-e]pyridine-8-carbonitrile (7f), (173 mg, 84%). mp 266.4-267.1°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (1H,, s), 7.48 (1H, d, *J* = 8.7 Hz), 7.23 (1H, s), 6.94 (1H, t, *J* = 8.4 Hz), 4.66 (1H, dd, *J* = 11.1, 2.8 Hz), 4.30 (1H, t, *J* = 10.5 Hz), 4.08 (1H, t, *J* = 11.3 Hz), 3.90 (1H, q, *J* = 7.0 Hz), 2.67 (1H, d, *J* = 10.7 Hz), 1.83 (9H, s), 1.74 (3H, s), 1.38 (3H, s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.16, 132.95, 131.88, 129.99, 125.68, 122.44, 118.88, 117.71, 113.13, 86.37, 65.76, 57.16, 51.31, 45.54, 32.75, 29.90, 27.18, 24.37, 18.44. MS(GC, 70eV) m/z 414(M+, 24.2%), 357.2(´46.5), 342.2(100). HRMS (ESI): Mass calculated for $C_{21}H_{24}BrN_3O$ $[M-H]^+$ 413.1103. Found: 414.1176.



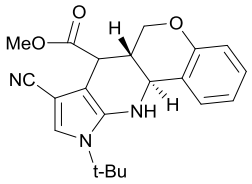
10-(tert-butyl)6,10,dihydrochromenol[4,3-b]pyrrolo[3,2-e]pyridine-8-carbonitrile (7g), (91 mg, 60%). mp 178.3-179.1°C. ^{1}H NMR (400 MHz, DMSO) δ 8.47 (1H, s), 8.15 (1H, dd, *J* = 7.6, 1.2 Hz), 7.98 (1H, s), 7.38 – 7.30 (1H, m), 7.14 (1H, dd, *J* = 9.5, 5.3 Hz), 7.00 (1H, dd, *J* = 6.4 Hz), 5.34 (2H, s), 3.18 (1H, s, *J* = 17.2 Hz), 1.81 (9H, s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.62, 147.16, 144.02, 133.23, 131.08, 124.72, 123.71, 123.68, 122.30, 121.19, 120.48, 117.18, 115.48, 83.41, 77.33, 77.01, 76.70, 68.56, 58.68, 29.23. MS(GC, 70eV) m/z 303.3 (M^+, 58%), 246.2 (58). HRMS (ESI): Mass calculated for $C_{19}H_{17}N_3O$ $[M-H]^+$ 303.1372. Found: 304.1454.



10-(tert-butyl)-4.methoxy-6,10,dihydrochromeno[4,3-b]pyrrolo[3,2-e]pyridine-8-carbonitrile (7h), (116 mg, 70%). mp 237.7-239.3°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (1H, dd, *J* = 7.9, 1.4 Hz), 7.80 (1H, s), 7.77 (1H, s), 7.04 (1H, dd, *J* = 10.1, 5.8 Hz), 6.92 (1H, dd, *J* = 8.0, 1.3 Hz), 5.37 (2H, s), 3.90 (3H, s), 1.85 (9H, s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.79 , 147.11 , 145.98 , 143.90 , 133.31 , 124.47 , 123.72 , 121.83 , 121.06 , 120.54 , 116.64 , 115.44 , 113.07 , 83.42 , 68.94 , 58.69 , 56.19 ,

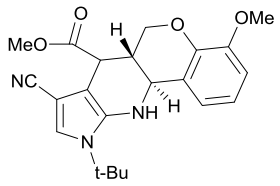
29.22. MS(GC, 70eV): m/z 333.1(M^+, 51.3%), 277.2(100). HRMS (ESI): Mass calculated for $C_{20}H_{19}N_3O_2$ $[M-H]^+$ 333.1477. Found: 334.1562.

7i

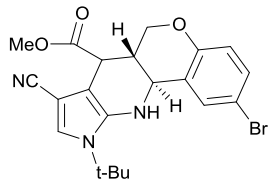


methyl-10-(tert-butyl)-8-cyano-6,6a,7,10,11,11a-hexahydrochromenol[4,3-b]pyrrolo[3,2-e]pyridine-7-carboxylate (7i), (88 mg, 48%). mp 162.5-164.3°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 14.36 – 14.30 (1H, m), 7.58 (1H, d, *J* = 7.7 Hz), 7.23 (1H, t), 7.06 (1H, s), 7.00 (1H, t, *J* = 8.2, 6.1, 2.4 Hz), 6.88 (1H, dd, *J* = 8.2, 0.9 Hz), 4.48 (1H, dd), 4.12 – 4.06 (1H, m), 3.94 (1H, dd, *J* = 14.9, 7.7 Hz), 3.85 (3H, s), 3.51 (1H, dd, *J* = 10.9, 2.1 Hz), 2.67 (1H, dd, *J* = 10.6, 1.6 Hz), 2.41 – 2.33 (1H, m, *J* = 10.9, 7.2 Hz), 1.65 (9H, s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 172.97 , 154.54 , 135.65 , 129.32 , 126.27 , 122.31 , 121.09 , 116.95 , 106.25 , 88.49 , 67.63 , 57.45 , 54.36 , 52.33 , 41.53 , 38.16 , 29.64. MS(GC, 70eV) m/z 365.3 (M^+, 100%), 294.3(76) 202.3(39). HRMS (ESI): Mass calculated for $C_{21}H_{23}N_3O_3$ $[M-H]^+$ 365.1739. Found: 366.1822.

7j



methyl-10-(tert-butyl)-8-cyano-4-methoxy-6,6a,7,10,11,11a-hexahydrochromeno[4,3-b]pyrrolo[3,2-e]pyridine-7-carboxylate (7j),(87 mg, 44%). mp 237.7-238.3°C. ^{1}H NMR (400 MHz, CDCl3) δ 7.20 (1H, d, J = 7.8 Hz), 7.06 (1H, s), 6.96 (1H, t, J = 7.9 Hz), 6.86 (1H, d, J = 8.0 Hz), 4.62 (1H, dd, *J* = 11.1, 2.9 Hz), 4.09 (1H, t, *J* = 10.5 Hz), 3.98 (1H, t, J = 11.3 Hz), 3.89 (3H, s), 3.84 (3H, s), 3.76 – 3.66 (1H, m), 3.51 (1H, d, J = 10.8 Hz), 2.67 (1H, d, J = 10.5 Hz), 2.39 (1H, tt, J = 10.9, 5.5 Hz), 1.65 (9H s). 13C NMR (101 MHz, CDCl3) δ 172.80 , 148.39 , 144.04 , 135.63 , 123.03 , 122.30 , 120.82 , 117.84 ,116.10, 111.02 , 106.15 , 88.53 , 67.99 , 57.43 , 56.03 , 54.28 , 52.31 , 41.43 , 38.04 , 29.62. MS(GC, 70eV): m/z 395.3(M+, 100%), 280.3(50), 232.3(32). HRMS (ESI): Mass calculated for C22H25N3O4 [M-H]+ 395.1845. Found: 396.1931.



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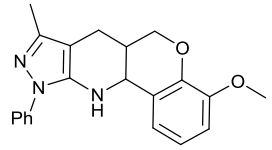
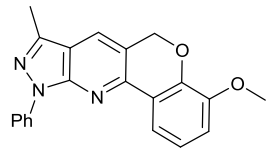
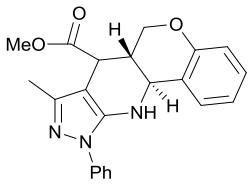
methyl-2-bromo-10-(tert-butyl)-8-cyano-6,6a,7,10,11,11a-hexahydrochromeno[4,3-b]pyrrolo[3,2-e]pyridine-7-carboxylate (7k), (89 mg, 40%). mp 235.5-237.5°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (1H, s), 7.30 (1H, d, *J* = 88 Hz), 7.06 (1H, s), 6.75 (1H, d, *J* = 8.5 Hz), 4.46 (1H, dd, *J* = 11.3, 2.2 Hz), 4.02 (1H, t, *J* = 10.5 Hz), 3.90 (1H, t, *J* = 10.8 Hz), 3.84 (3H, s), 3.48 (1H, d, *J* = 10.8, 2.1 Hz), 2.67 (1H, d, *J* = 10.8), 2.37 – 2.29 (1H ,m), 1.65 (9H, s). ^{13}C NMR (101 MHz, $CDCl_3$) δ .172.77, 153.71, 135.29, 132.24, 129.05, 124.32, 122.52, 118.88, 1nnnn16.00, 113.23, 106.44, 88.50, 67.74, 57.56, 54.15, 52.37, 41.38, 37.78, 29.71. MS(GC, 70eV): m/z 445.2(M^+, 100%), 444.3(42), 280.1(32.9). HRMS (ESI): Mass calculated for $C_{21}H_{22}BrN_3O_3$ $[M-H]^+$ 443.0845. Found: 444.0905.



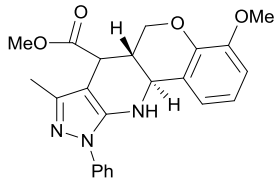
4-methoxy-8-methyl-10-phenyl-6,6a,7,10,11,11a-hexahydrochromeno[3,4-e]pyrazolo[3,4-b]pyridine (8a), (142 m**g,** 82%). mp 231-233 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (1H, d, J = 7.8 Hz), 7.23 (1H, t), 7.06 (1H, t), 6.78 (1H, d, *J* = 7.8 Hz), 6.72 (1H, t), 6.70 (1H, t), 6.91 (1H, d, J = 7.8 Hz), 4.36 (1H, dd, *J* = 2.7, J = 11 Hz), 3.99 (1H, t, *J* = 8.8 Hz), 3.76 (1H, t, J = 10.7 Hz), 3.66 (3H,s), 3.42 (1H, 6d, J = 6.1 Hz), 2.46 (1H, m), 2.02 (3H ,s), 1.97 (2H, m). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.42, ,146.95, 143.82, 143.65, 139.2, 129.39, 129.35, 126.03, 123.16, 121.69, 120.62, 117.21, 110.64, 100.49, 69.48, 55.97, 54.23, 34.24, 21.50, 12.23. HRMS (ESI): Mass calculated for $C_{21}H_{21}N_3O_2$ $[M-H]^+$ 347.1634. Found: 347.1925.



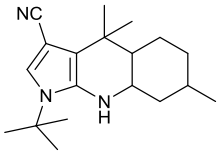
4-methoxy-8-methyl-10-phenyl-6,10-dihydrochromeno[3,4-e]pyrazolo[3,4-b]pyridine (8b), (128 mg**,** 75%). mp 232-233°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.38 (1H, d, J = 7.8 Hz), 8.23 (1H, s), 7.87 (1H, m), 7.59 (2H, t), 7.32 (1H, t), 7.14 (2H, m), 5.358 (2H, s), 3.84 (3H, s), 2.60 (3H, s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.72, 149.14, 148.54, 147.03, 143.51, 139.79, 129.70, 127.20, 125.73, 123.93, 122.44, 121.27, 120.18, 117.02, 116.35, 115.11, 68.35, 56.29, 12.67. HRMS (ESI): Mass calculated for $C_{21}H_{17}N_3O_2$ $[M-H]^+$ 343.1321. Found: 344.1215.



Methyl 8-methyl-10-phenyl-6,6a,7,10,11,11a-hexahydrochromeno[3,4-e]pyrazolo[3,4-b]pyridine-7-carboxylate (8c), (166 mg, 89%). mp 185-187 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (1H, d, J = 8.1 Hz), 7.56 (1H, d, J = 7.6 Hz), 7.48 (2H, t), 7.25 (1H, dt), 6.98 (1H, t), 6.84 (1H, d, J = 8.1 Hz), 5.78 (1H, d), 4.34 (1H, dd, J = 3.7, 11.3 Hz), 4.23 (1H, dd, J = 7.6, 10.6 Hz), 4.06 (1H, t), 3.77 (3H, s), 3.53 (1H, d), 2.26 (1H, m), 2.02 (3H, s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.70, 154.22, 145.85, 145.45, 139.74, 129.41, 128.99, 127.44, 125.87, 121.51, 121.09, 116.57, 100.42, 99.99, 67.17, 53.12, 52.58, 37.87, 12.89. HRMS (ESI): Mass calculated for $C_{22}H_{21}N_3O_3$ $[M-H]^+$ 375.1583.

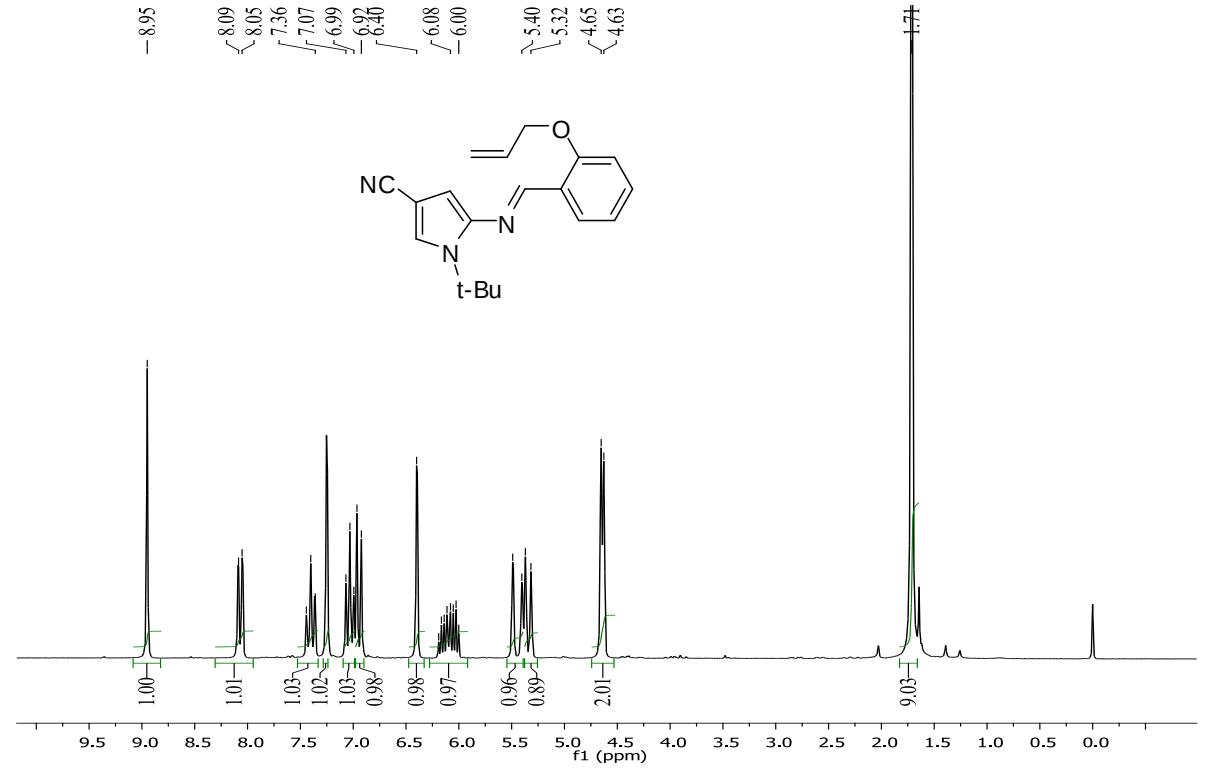


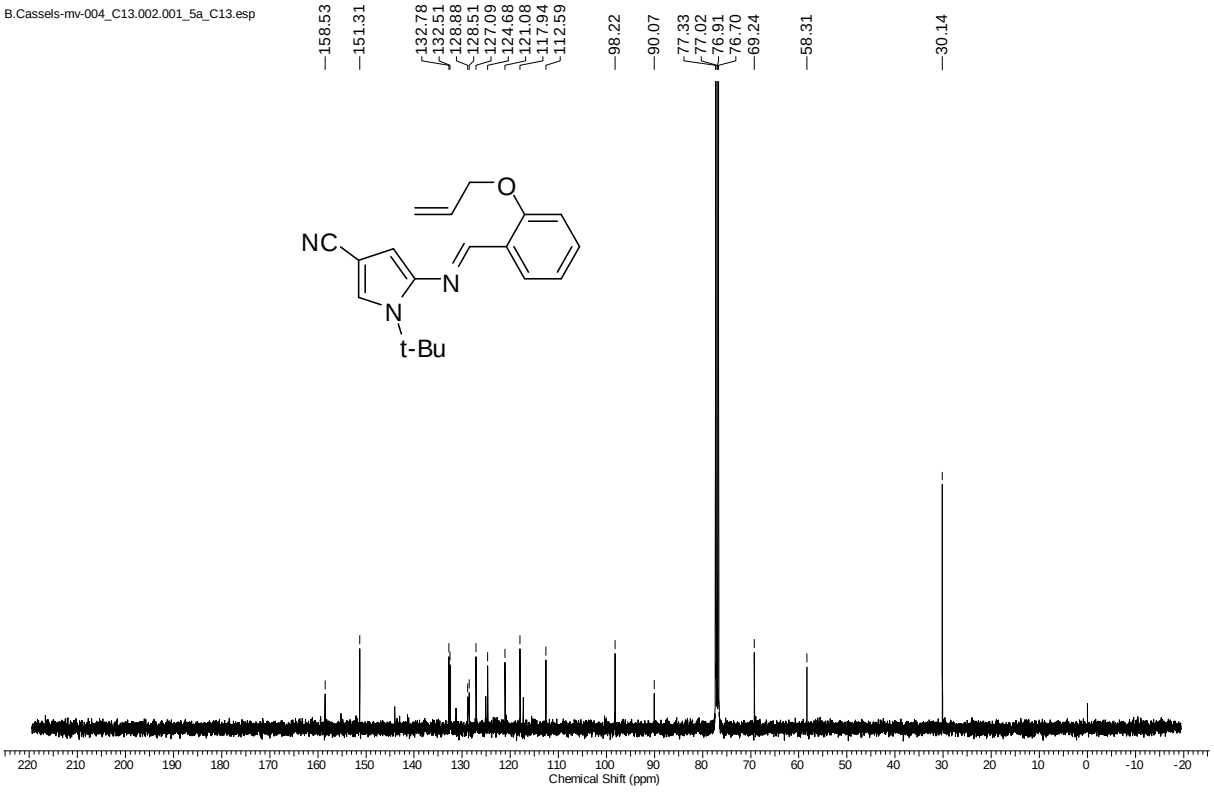
Methyl- 4-methoxy-8-methyl-10-phenyl-6,6a,7,10,11,11a-hexahydrochromeno[3,4-e]pyrazolo[3,4-b]pyridine-7-carboxylate (8d), (170 mg, 84%). mp 238-239°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (2H, d, J = 8.3 Hz), 7.49 (2H, t), 7.28 (1H, t), 7.14 (1H, t), 6.92 (2H, 4.7 Hz), 5.7 (1H, d, J = 7.3 Hz), 4.36 (1H, dd, J = 3.4, 11.0 Hz), 4.22 (1H, dd, J = 7.2, 10.3 Hz) 4.02 (1H, t), 3.07 (3H, s), 2.95 (3H, s), 3.54 (1H, d), 2.23 (1H, m), 2.02 (3H, s). ^{13}C NMR (101 MHz, $CDCl_3$) δ 173.73, 148.37, 145.85, 145.52, 143.94, 139.75, 129.46, 125.90, 123.71, 121.49, 120.68, 118.85, 111.58, 100.44, 67.04, 56.10, 56.10, 53.16, 52.61, 37.80, 12.90. HRMS (ESI): Mass calculated for $C_{23}H_{23}N_3O_4$ $[M-H]^+$ 405.1689. Found: 406.2223.



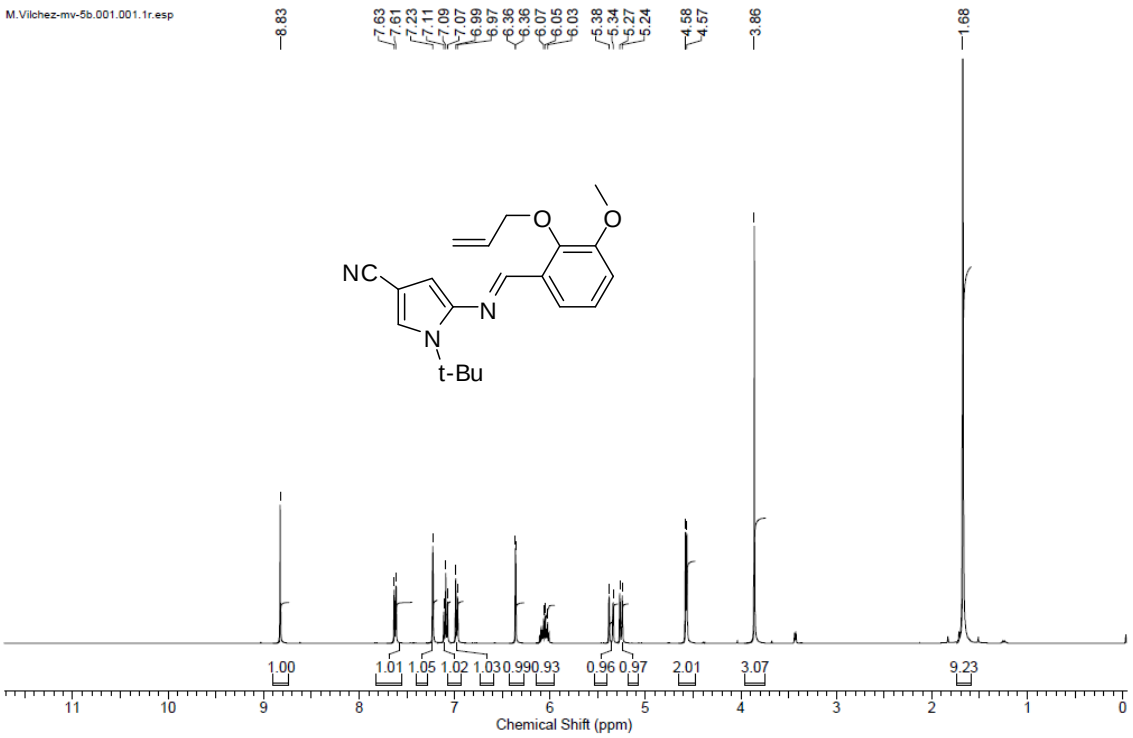
1-tert-butyl-4,4,7-trimethyl-4,4a,5,6,7,8,8a,9-octahydro-1H-pyrrolo[2,3-b]quinoline-3-carbonitrile (10), (97 mg, 65%). m.p 164.6-165.5°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (1H, s), 4.02 (1H, m), 2.25 (1H, d), 1.61 (9H, s), 1.61(2H, m), 1.48 (1H, m), 1.44 (3H, s), 1.35 (3H, m), 1.27 (3H, s), 0.89 (3H, d). ^{13}C NMR (101 MHz, $CDCl_3$) δ 165.45, 156.02, 152.86, 111.85, 107.72, 58.85, 55.30, 45.34, 42.34, 36.77, 34.20, 29.18, 27.22, 26.53, 23.91, 22.65, 22.27. MS(GC, 70eV): m/z 298.2(M^+, 100%), 258(41). HRMS (ESI): Mass calculated for $C_{19}H_{29}N_3$ [M-H]+ 299.2361.

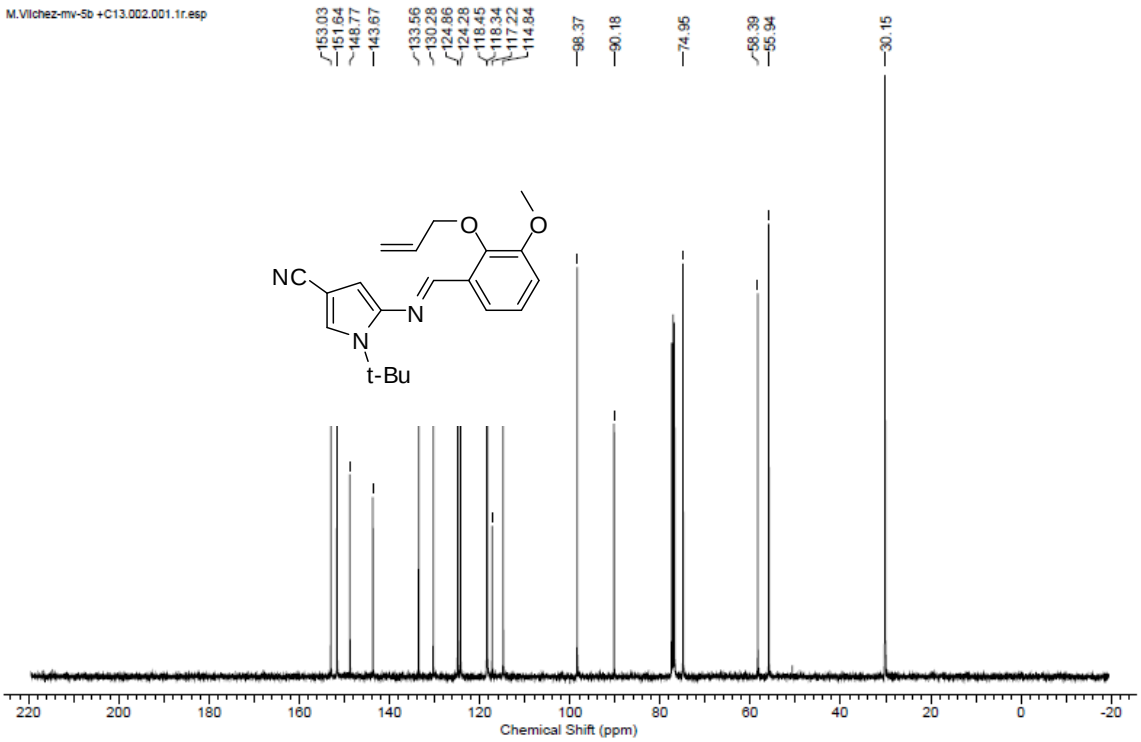
5a


8.95
8.09
8.05
7.36
7.07
6.99
6.92
6.40
6.08
6.00
5.40
5.32
4.65
4.63
1.71
O
NC
N
N
t-Bu
1.00
1.01
1.03
1.02
1.03
0.98
0.98
0.97
0.96
0.89
2.01
9.03
f1 (ppm)

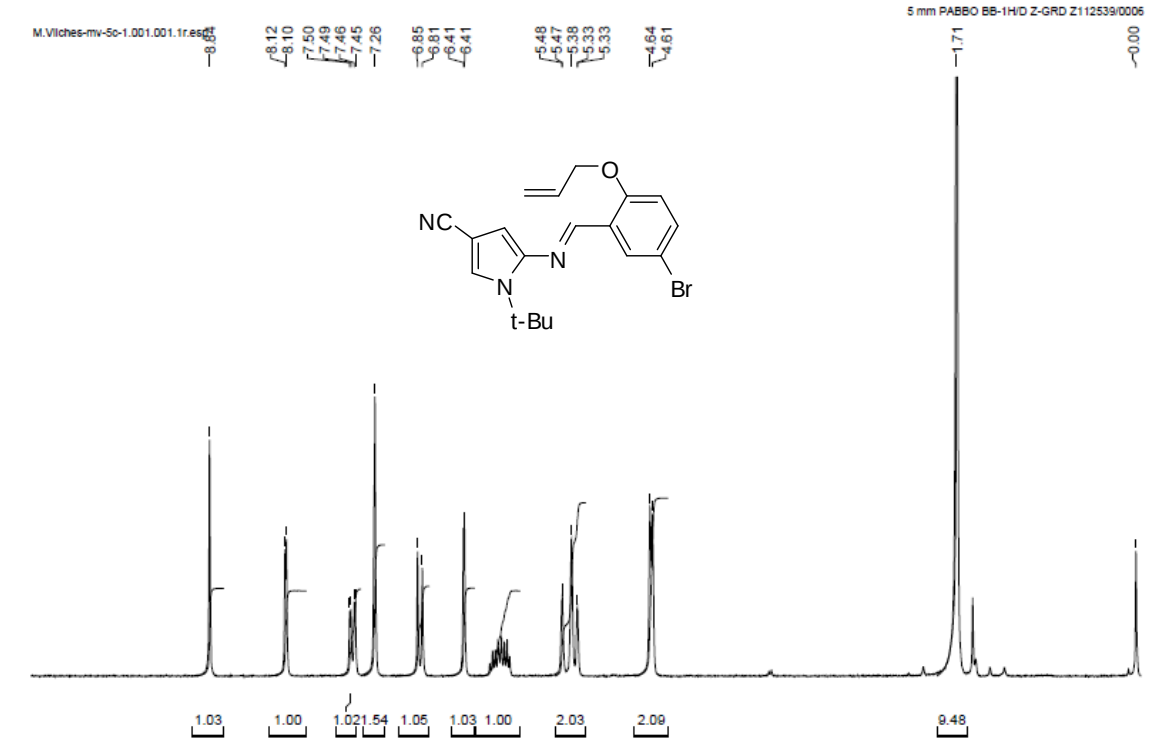

B.Cassels-mv-004_C13.002.001_5a_C13.esp
158.53
151.31
132.78
132.51
128.88
128.51
127.09
124.68
121.08
117.94
112.59
98.22
90.07
77.33
77.02
76.91
76.70
69.24
58.31
30.14
O
NC
N
N
t-Bu
Chemical Shift (ppm)

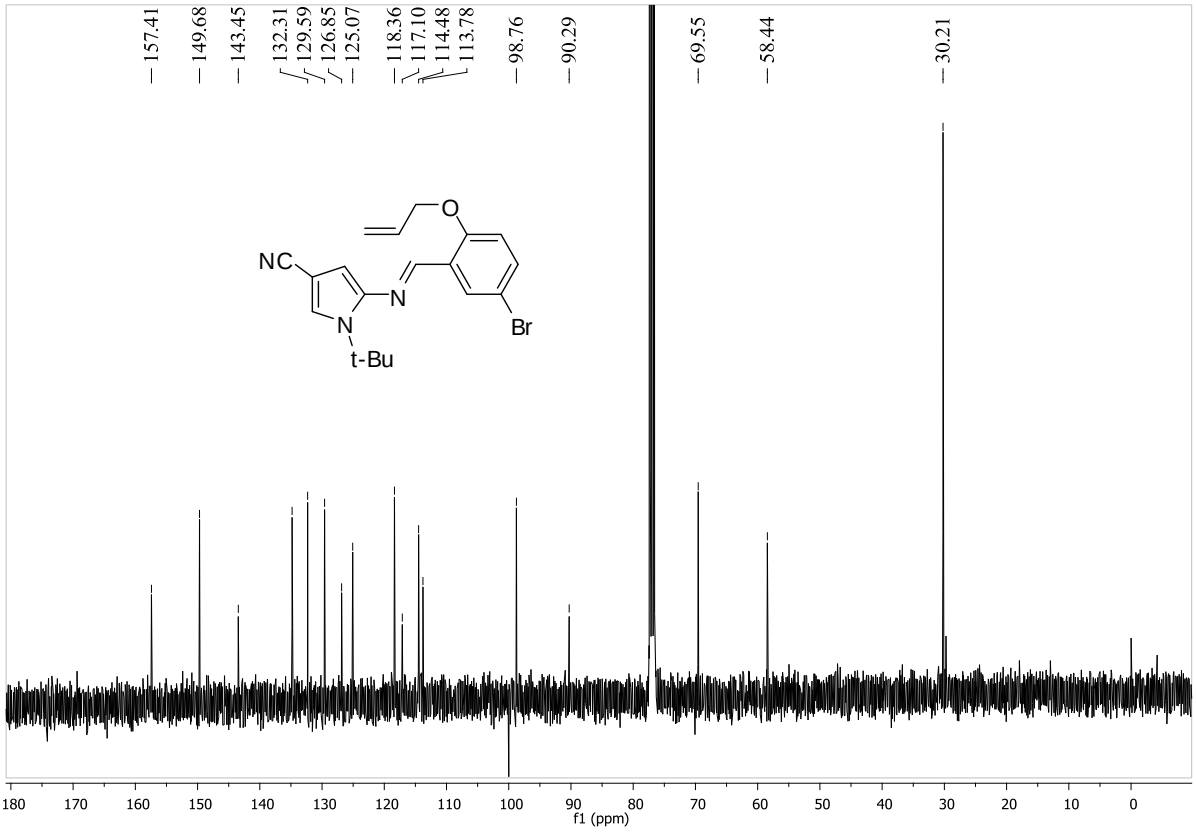
5b


M.Vilchez-mv-5b.001.001.1r.esp
8.83
7.63
7.61
7.23
7.11
7.09
7.07
6.99
6.97
6.36
6.36
6.07
6.05
6.03
5.38
5.34
5.27
5.24
4.58
4.57
3.86
1.68
NC
N
N
t-Bu
O
O
1.00
1.01
1.05
1.02
1.03
0.99
0.93
0.96
0.97
2.01
3.07
9.23
Chemical Shift (ppm)

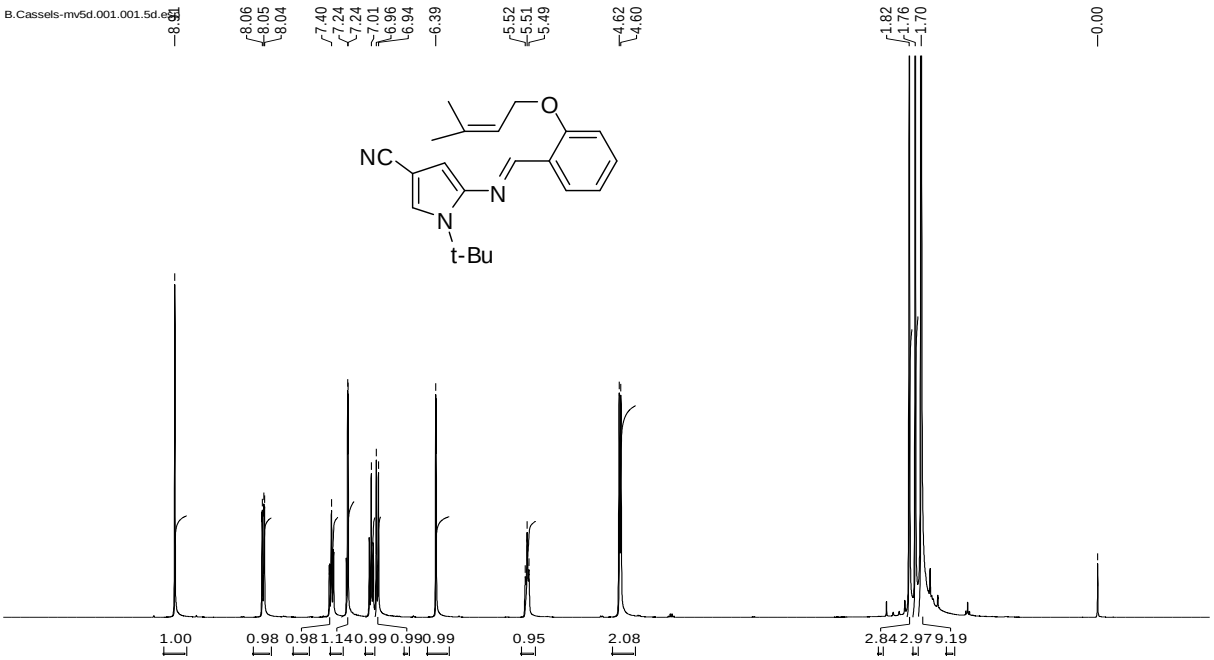

M.Vilchez-mv-5b +C13.002.001.1r.esp
153.03
151.64
148.77
143.67
133.56
130.28
124.86
124.28
118.45
118.34
117.22
114.84
98.37
90.18
74.95
58.39
55.94
30.15
NC
N
N
t-Bu
O
O
Chemical Shift (ppm)

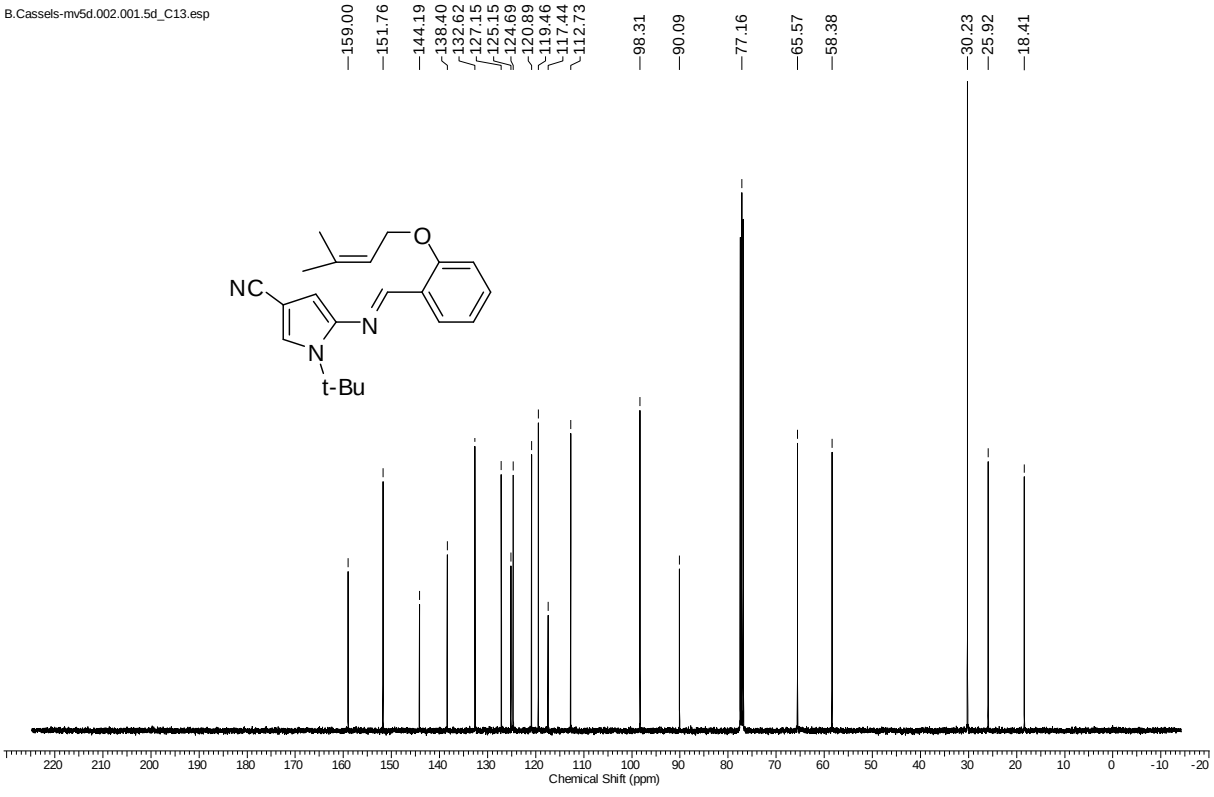
5c


5 mm PABBO BB-1H/D Z-GRD Z112539/0006
M.Vilches-mv-5c-1.001.001.1r.esp
8.84
8.12
8.10
7.50
7.49
7.46
7.45
7.26
6.85
6.81
6.41
6.41
5.48
5.47
5.38
5.33
5.33
4.64
4.61
1.71
0.00
NC
N
N
t-Bu
O
Br
1.03
1.00
1.02
1.54
1.05
1.03
1.00
2.03
2.09
9.48

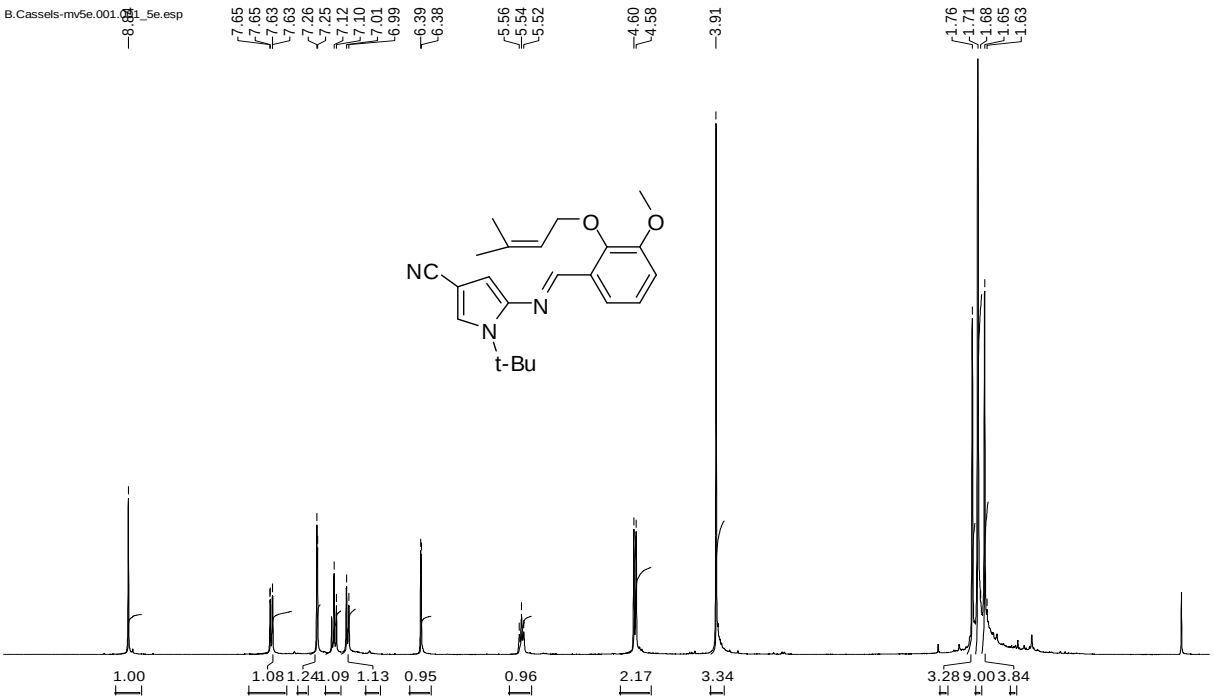

157.41
149.68
143.45
132.31
129.59
126.85
125.07
118.36
117.10
114.48
113.78
98.76
90.29
69.55
58.44
30.21
NC
N
N
t-Bu
O
Br
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

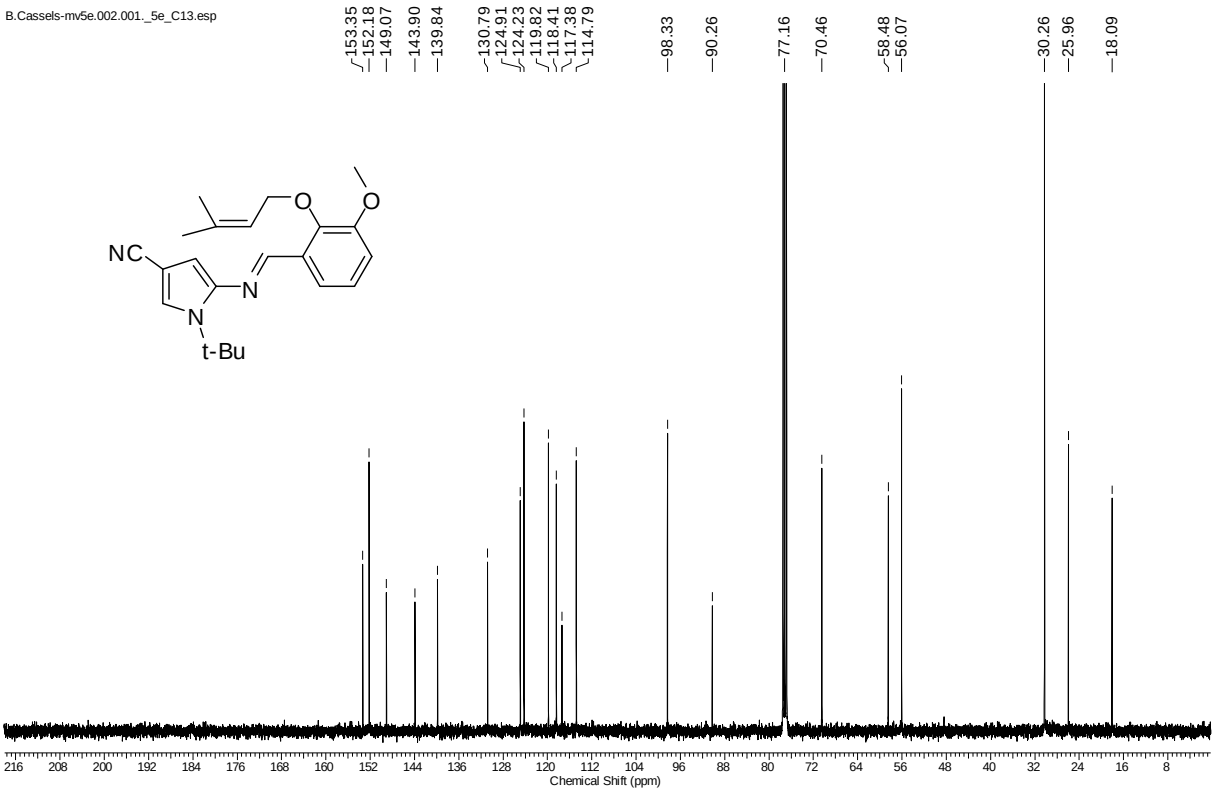
5d


B.Cassels-mv5d.001.001.5d.esp
8.06
8.05
8.04
7.40
7.24
7.24
7.01
6.96
6.94
6.39
5.52
5.51
5.49
4.62
4.60
1.82
1.76
1.70
0.00
NC
O
N
N
t-Bu
1.00
0.98
0.98
1.14
0.99
0.99
0.99
0.95
2.08
2.84
2.97
9.19

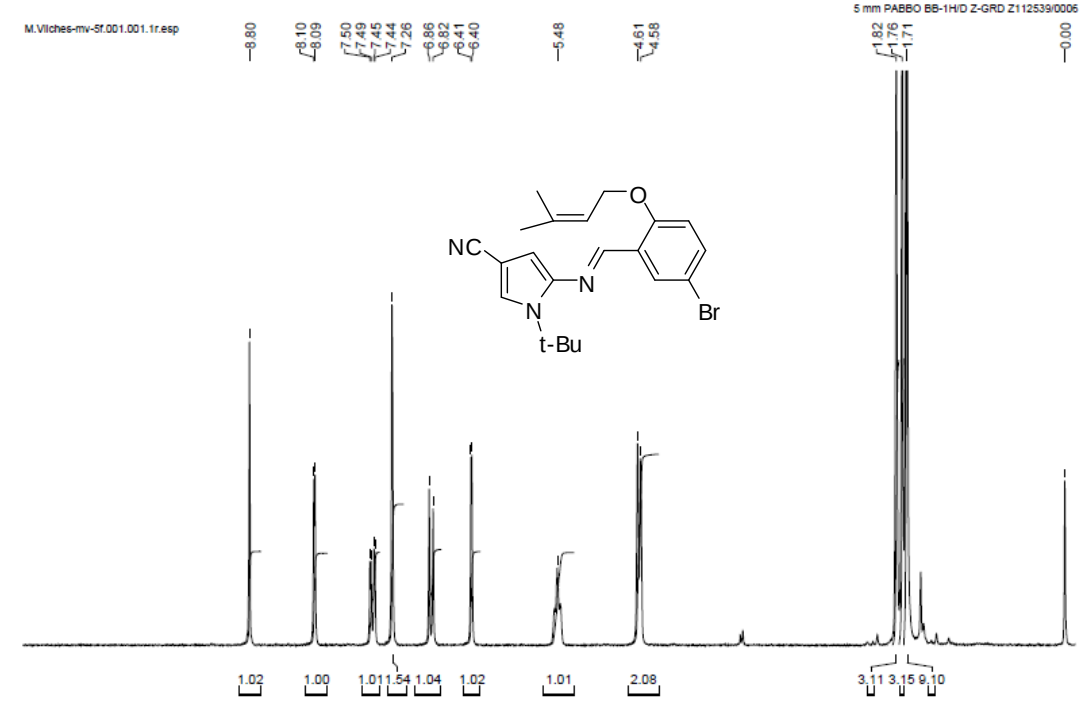

B.Cassels-mv5d.002.001.5d_C13.esp
159.00
151.76
144.19
138.40
132.62
127.15
125.15
124.69
120.89
119.46
117.44
112.73
98.31
90.09
77.16
65.57
58.38
30.23
25.92
18.41
NC
O
N
N
t-Bu
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
-20
Chemical Shift (ppm)

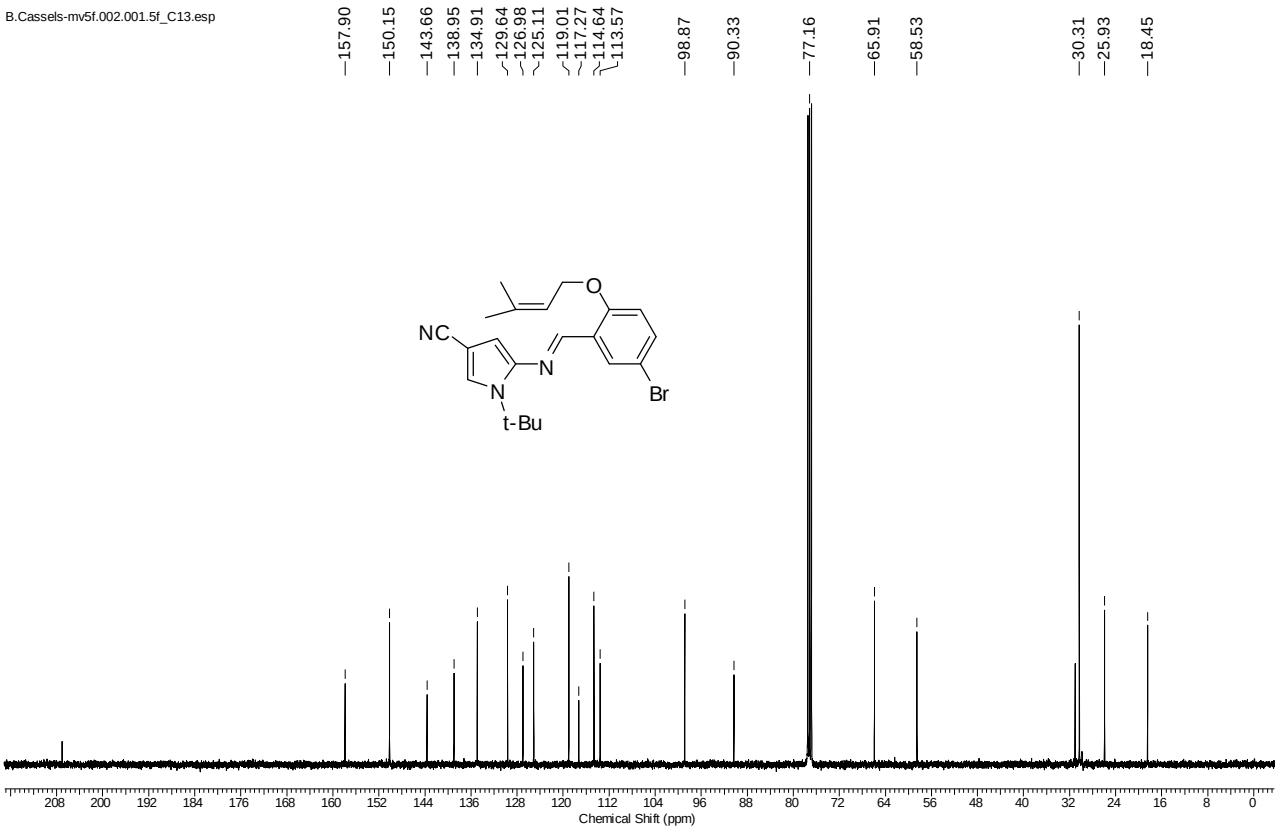
5e


B.Cassels-mv5e.001.001._5e.esp
8.64
7.65
7.65
7.63
7.63
7.26
7.25
7.12
7.10
7.01
6.99
6.39
6.38
5.56
5.54
5.52
4.60
4.58
3.91
1.76
1.71
1.68
1.65
1.63
NC
N
N
t-Bu
O
O
1.00
1.08
1.24
1.09
1.13
0.95
0.96
2.17
3.34
3.28
9.00
3.84

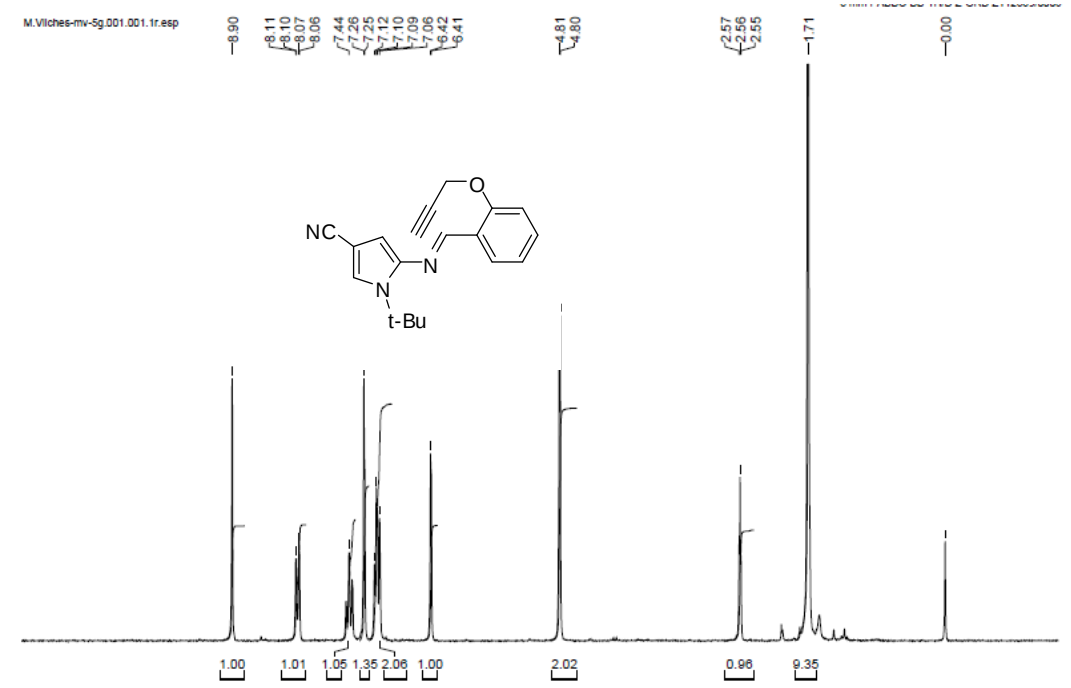

B.Cassels-mv5e.002.001._5e_C13.esp
153.35
152.18
149.07
143.90
139.84
130.79
124.91
124.23
119.82
118.41
117.38
114.79
98.33
90.26
77.16
70.46
58.48
56.07
30.26
25.96
18.09
NC
N
N
t-Bu
O
O
216
208
200
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
Chemical Shift (ppm)

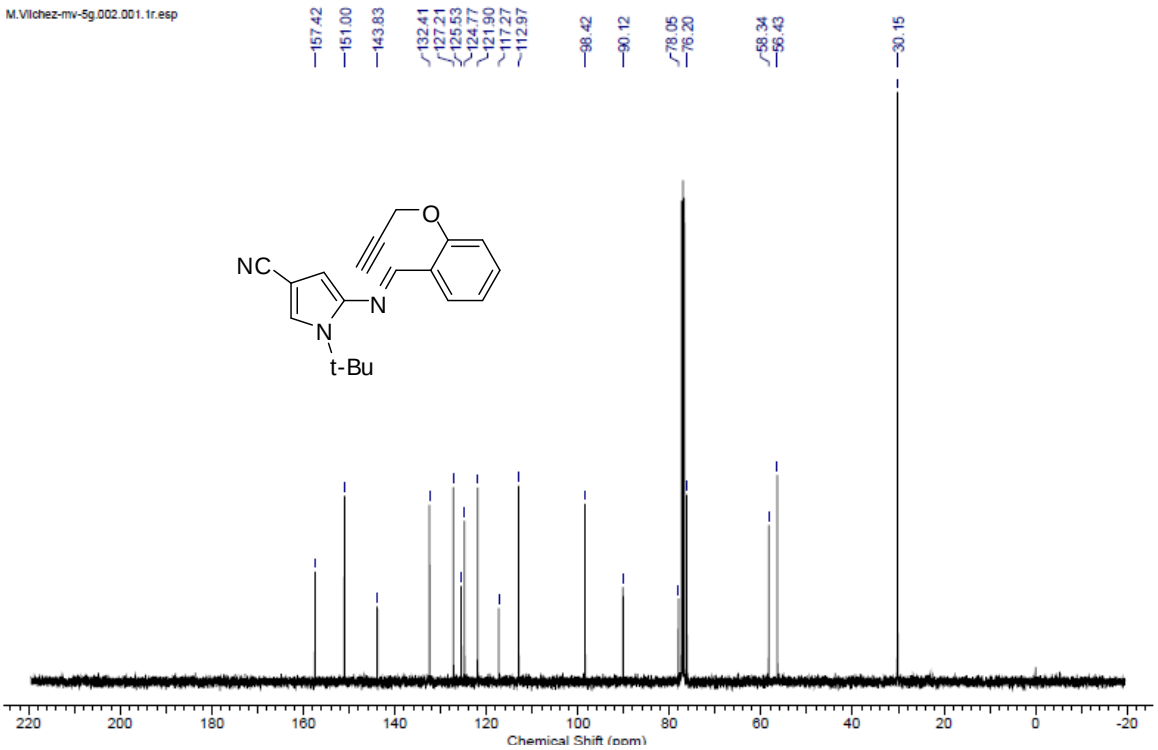
5f


M.Vilches-mv-5f.001.001.1r.esp
5 mm PABBO BB-1H/D Z-GRD Z112539/0006
8.80
8.10
8.09
7.50
7.49
7.45
7.44
7.26
6.86
6.82
6.41
6.40
5.48
4.61
4.58
1.82
1.76
1.71
0.00
NC
N
N
t-Bu
O
Br
1.02
1.00
1.01
1.54
1.04
1.02
1.01
2.08
3.11
3.15
9.10

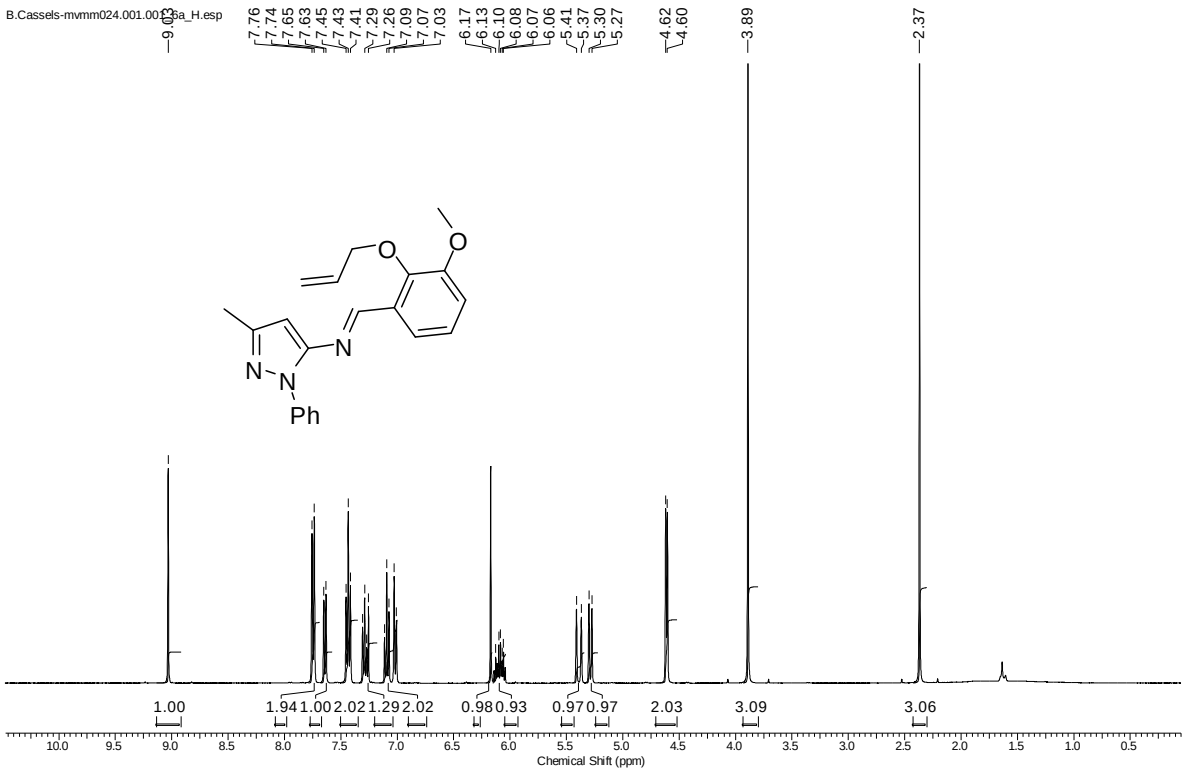

B.Cassels-mv5f.002.001.5f_C13.esp
157.90
150.15
143.66
138.95
134.91
129.64
126.98
125.11
119.01
117.27
114.64
113.57
98.87
90.33
77.16
65.91
58.53
30.31
25.93
18.45
NC
N
N
t-Bu
O
Br
208
200
192
184
176
168
160
152
144
136
128
120
112
104
96
88
80
72
64
56
48
40
32
24
16
8
0
Chemical Shift (ppm)

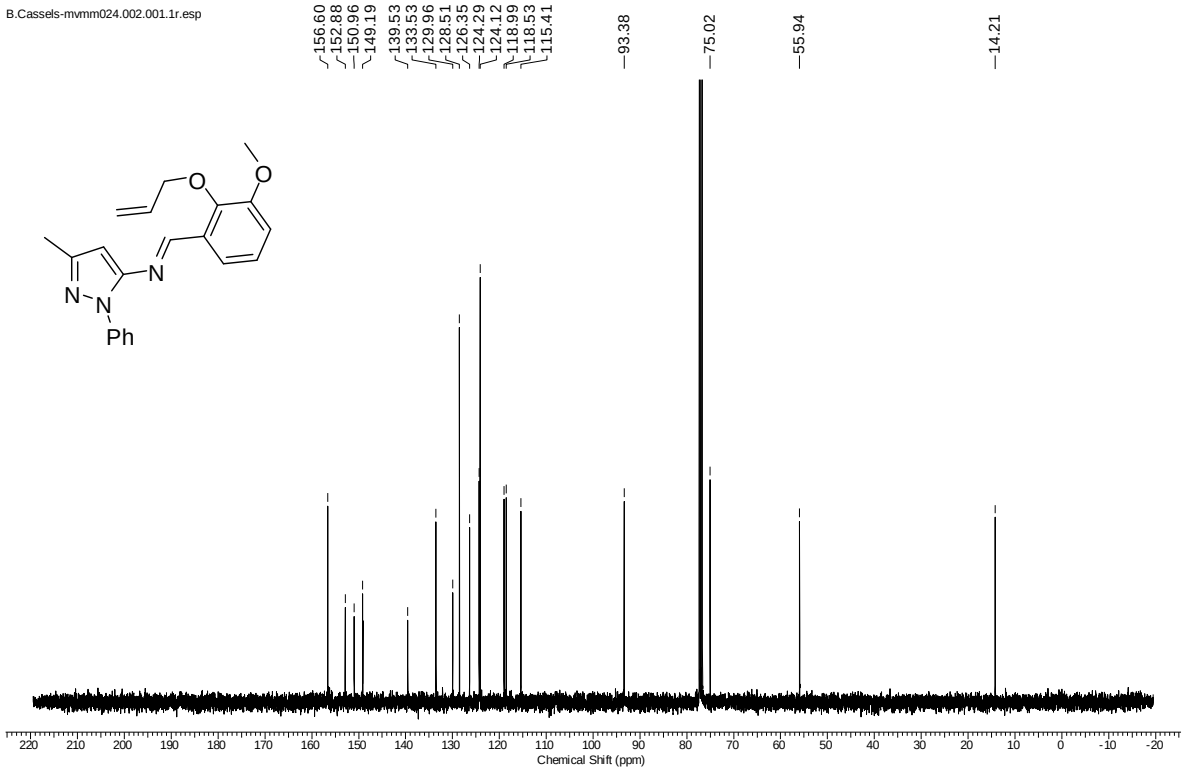
5g


M.Vilches-mv-5g.001.001.1r.esp
8.90
8.11
8.10
8.07
8.06
7.44
7.26
7.25
7.12
7.10
7.09
7.06
6.42
6.41
4.81
4.80
2.57
2.56
2.55
1.71
0.00
NC
N
N
t-Bu
O
1.00
1.01
1.05
1.35
2.06
1.00
2.02
0.96
9.35

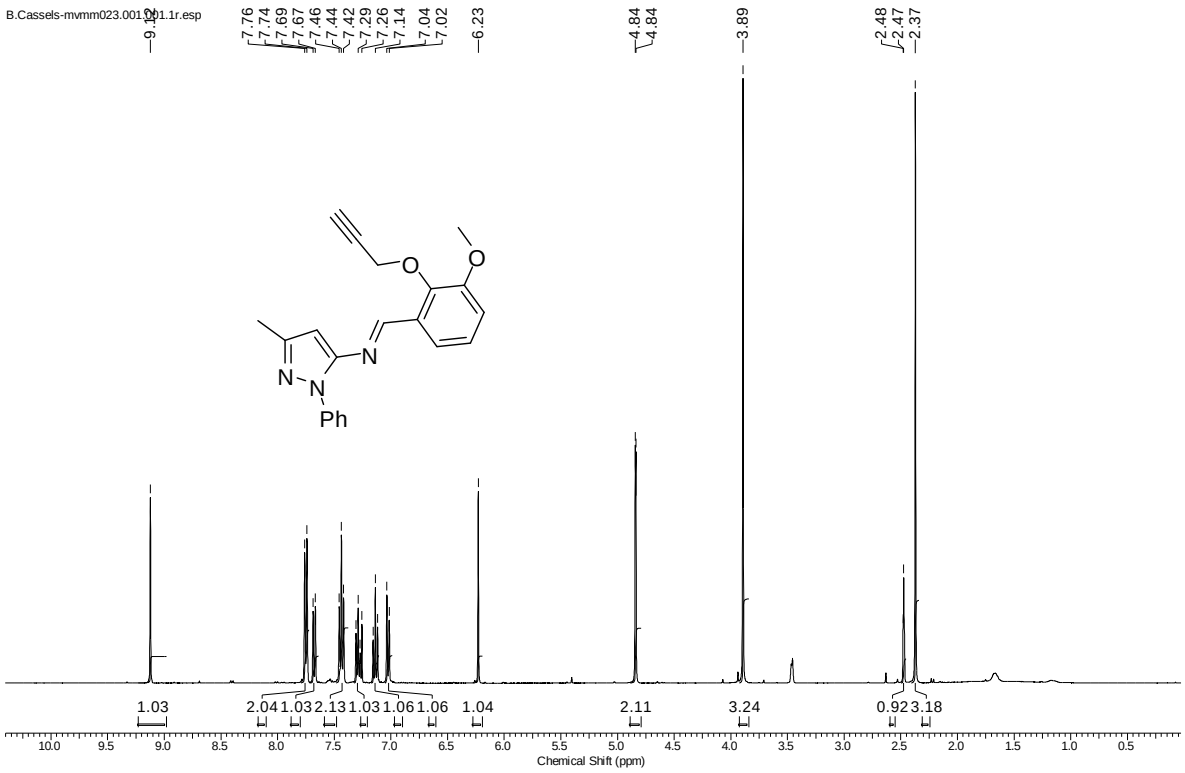

M.Vilchez-mv-5g.002.001.1r.esp
157.42
151.00
143.83
132.41
127.21
125.53
124.77
121.90
117.27
112.97
98.42
90.12
78.05
76.20
58.34
56.43
30.15
NC
N
N
t-Bu
O
220
200
180
160
140
120
100
80
60
40
20
0
-20
Chemical Shift (ppm)

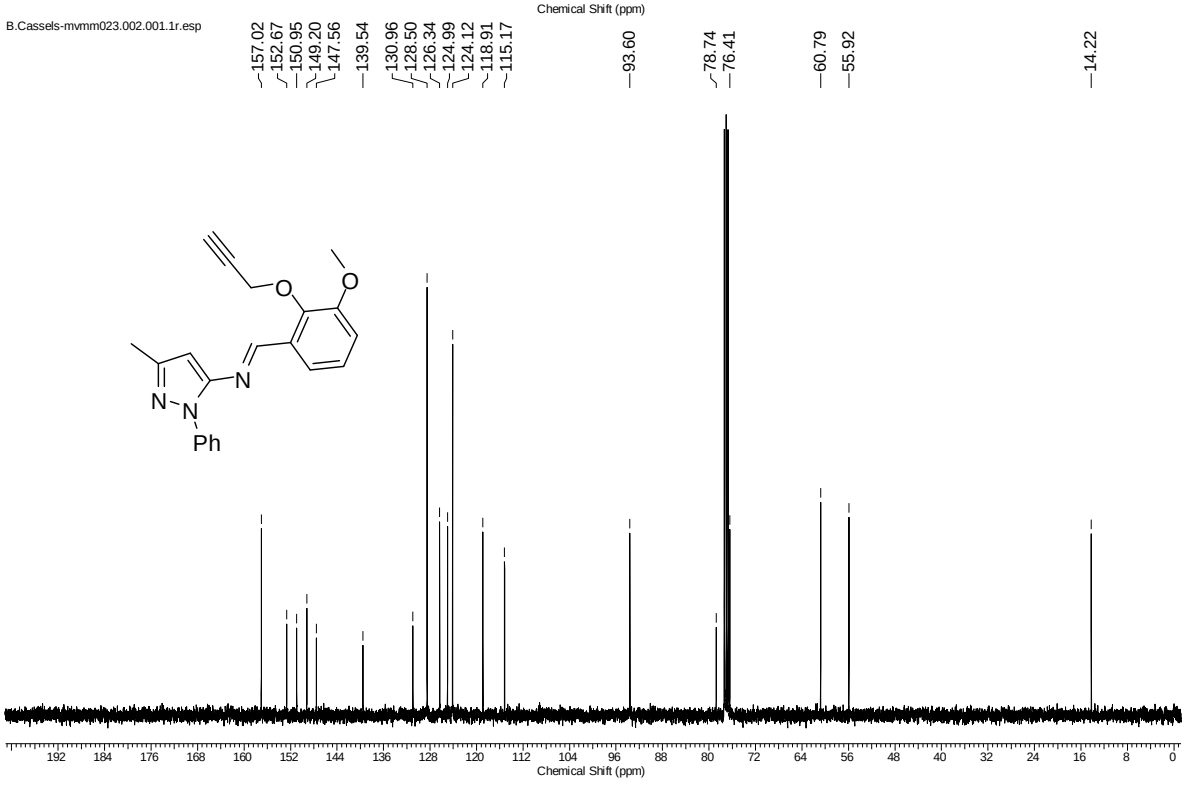
6a


B.Cassels-mvmm024.001.001.6a_H.esp
9.03
7.76
7.74
7.65
7.63
7.45
7.43
7.41
7.29
7.26
7.09
7.07
7.03
6.17
6.13
6.10
6.08
6.07
6.06
5.41
5.37
5.30
5.27
4.62
4.60
3.89
2.37
O
O
N
N
N
Ph
1.00
1.94
1.00
2.02
1.29
2.02
0.98
0.93
0.97
0.97
2.03
3.09
3.06
Chemical Shift (ppm)

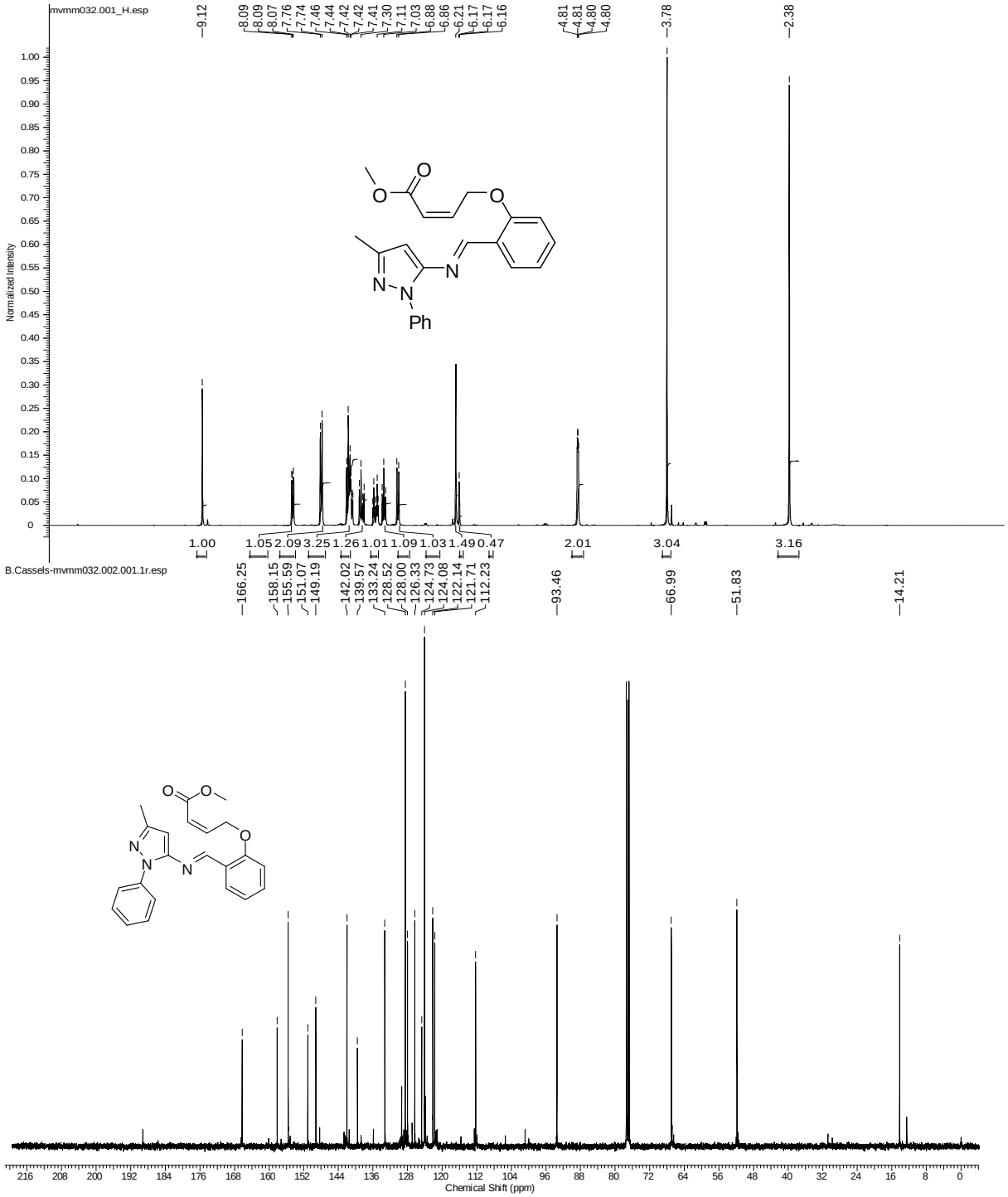

B.Cassels-mvmm024.002.001.1r.esp
156.60
152.88
150.96
149.19
139.53
133.53
129.96
128.51
126.35
124.29
124.12
118.99
118.53
115.41
93.38
75.02
55.94
14.21
O
O
N
N
N
Ph
Chemical Shift (ppm)

6b

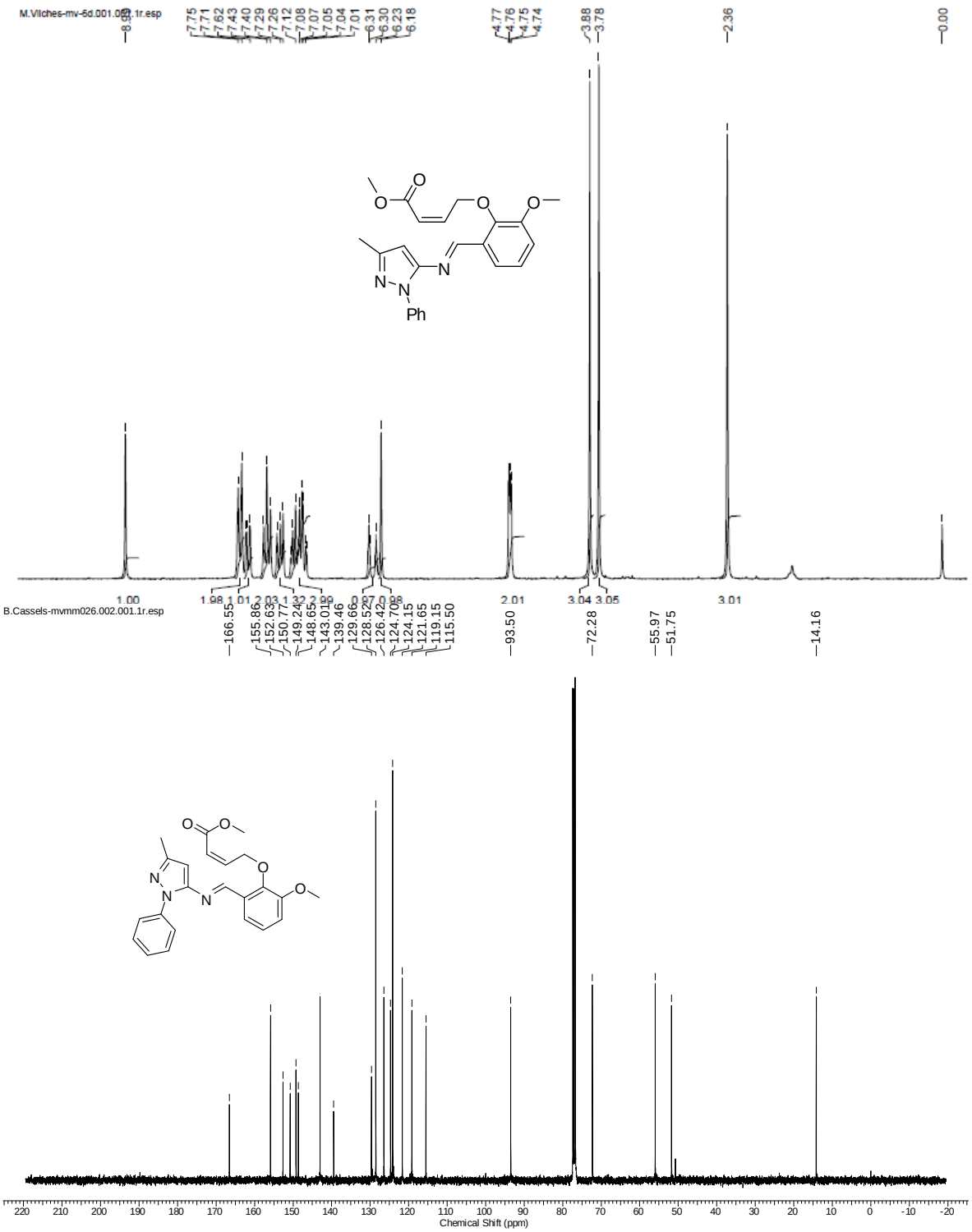

B.Cassels-mvmm023.001.001.1r.esp
9.12
7.76
7.74
7.69
7.67
7.46
7.44
7.42
7.29
7.26
7.14
7.04
7.02
6.23
4.84
4.84
3.89
2.48
2.47
2.37
O
O
N
N
N
Ph
1.03
2.04
1.03
2.13
1.03
1.06
1.06
1.04
2.11
3.24
0.92
3.18
Chemical Shift (ppm)


B.Cassels-mvmm023.002.001.1r.esp
157.02
152.67
150.95
149.20
147.56
139.54
130.96
128.50
126.34
124.99
124.12
118.91
115.17
93.60
78.74
76.41
60.79
55.92
14.22
O
O
N
N
N
Ph
Chemical Shift (ppm)

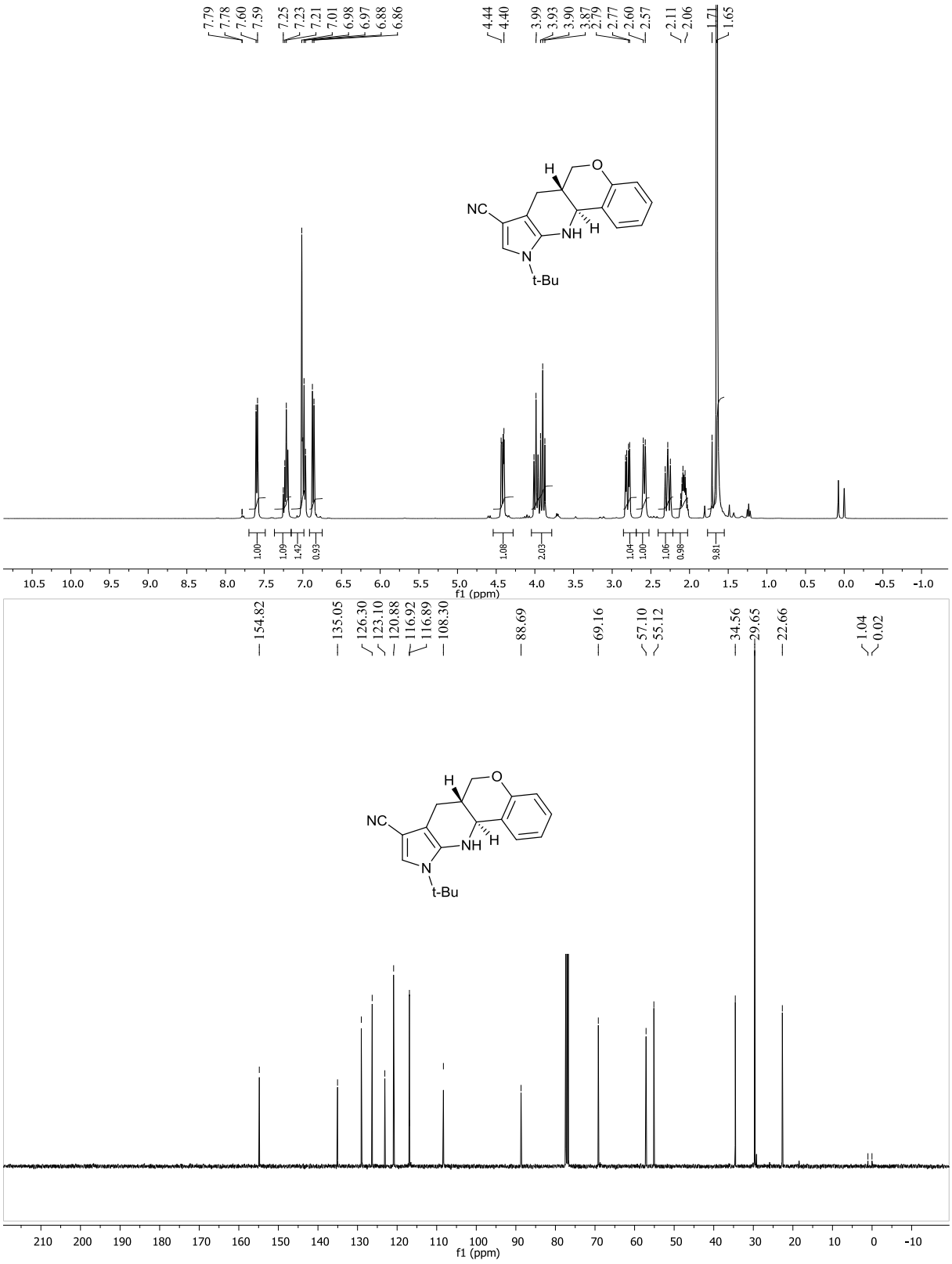
6c

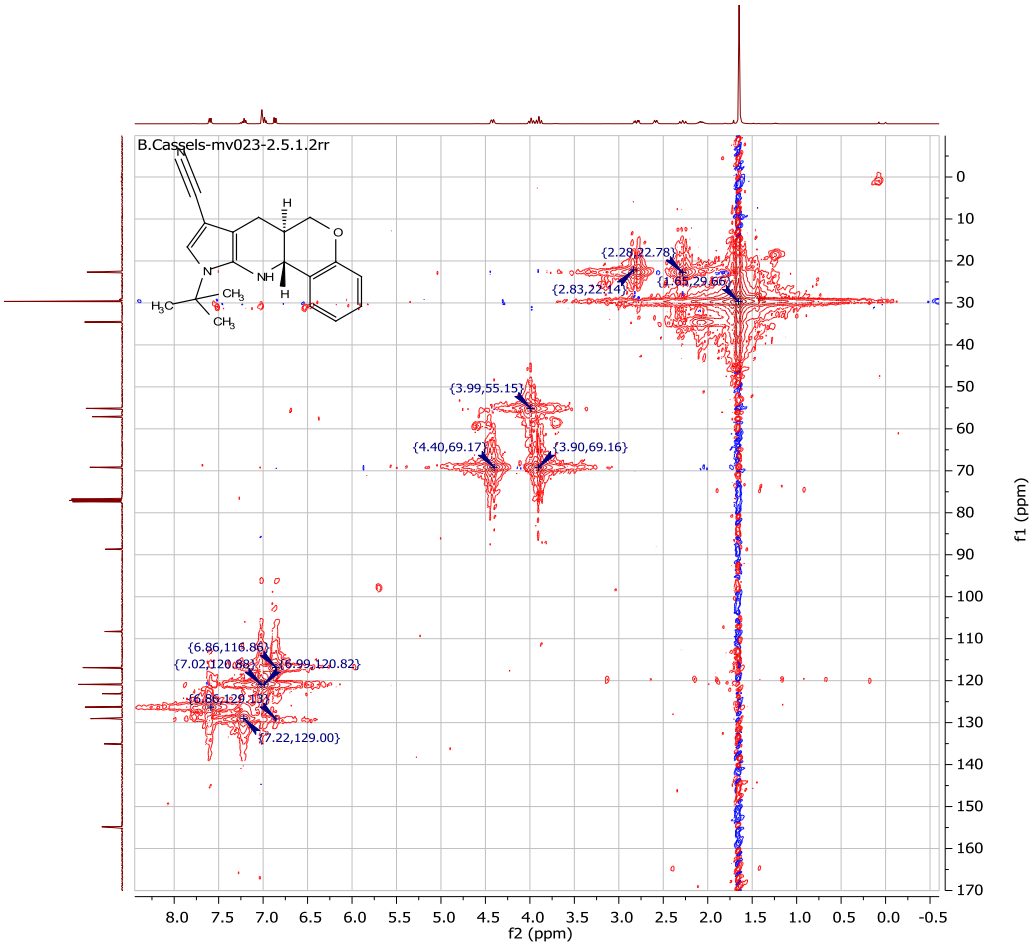

mvmm032.001_H.esp
9.12
8.09
8.09
8.07
7.76
7.74
7.46
7.44
7.42
7.42
7.41
7.30
7.11
7.03
6.88
6.86
6.21
6.17
6.17
6.16
4.81
4.81
4.80
4.80
3.78
2.38
Normalized Intensity
1.00
1.05
2.09
3.25
1.26
1.01
1.09
1.03
1.49
0.47
2.01
3.04
3.16
B.Cassels-mvmm032.002.001.1r.esp
166.25
158.15
155.59
151.07
149.19
142.02
139.57
133.24
128.52
128.00
126.33
124.73
124.08
122.14
121.71
112.23
93.46
66.99
51.83
14.21
Chemical Shift (ppm)

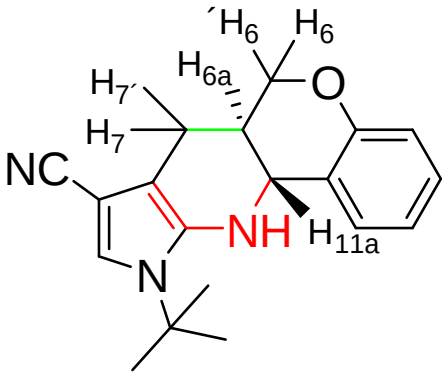
6d


M.Vilches-mv-6d.001.001.1r.esp
8.59
7.75
7.71
7.62
7.43
7.40
7.29
7.26
7.12
7.08
7.07
7.05
7.04
7.01
6.31
6.30
6.23
6.18
4.77
4.76
4.75
4.74
3.88
3.78
2.36
0.00
1.00
1.98
1.01
2.03
1.41
2.09
2.07
2.08
2.01
3.04
3.05
3.01
B.Cassels-mvmm026.002.001.1r.esp
166.55
155.86
152.63
150.77
149.24
148.65
143.01
139.46
129.66
128.52
126.42
124.70
124.15
121.65
119.15
115.50
93.50
72.28
55.97
51.75
14.16
Chemical Shift (ppm)

7a

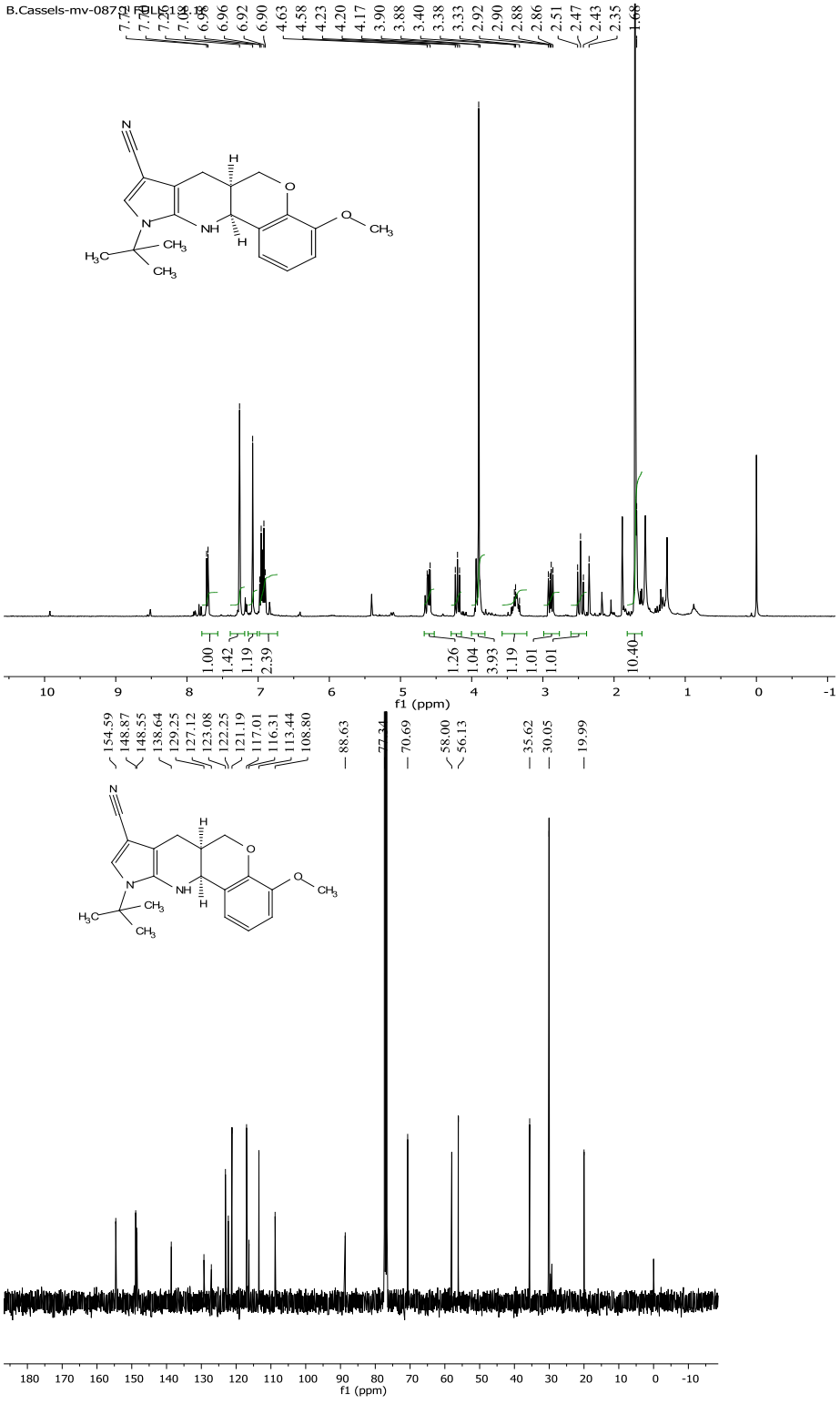

7.79
7.78
7.60
7.59
7.25
7.23
7.21
7.01
6.98
6.97
6.88
6.86
4.44
4.40
3.99
3.93
3.90
3.87
2.79
2.77
2.60
2.57
2.11
2.06
1.71
1.65
NC
H
O
NH
H
N
t-Bu
1.00
1.09
1.42
0.93
1.08
2.03
1.04
1.00
1.06
0.98
9.81
f1 (ppm)
154.82
135.05
126.30
123.10
120.88
116.92
116.89
108.30
88.69
69.16
57.10
55.12
34.56
29.65
22.66
1.04
0.02
f1 (ppm)

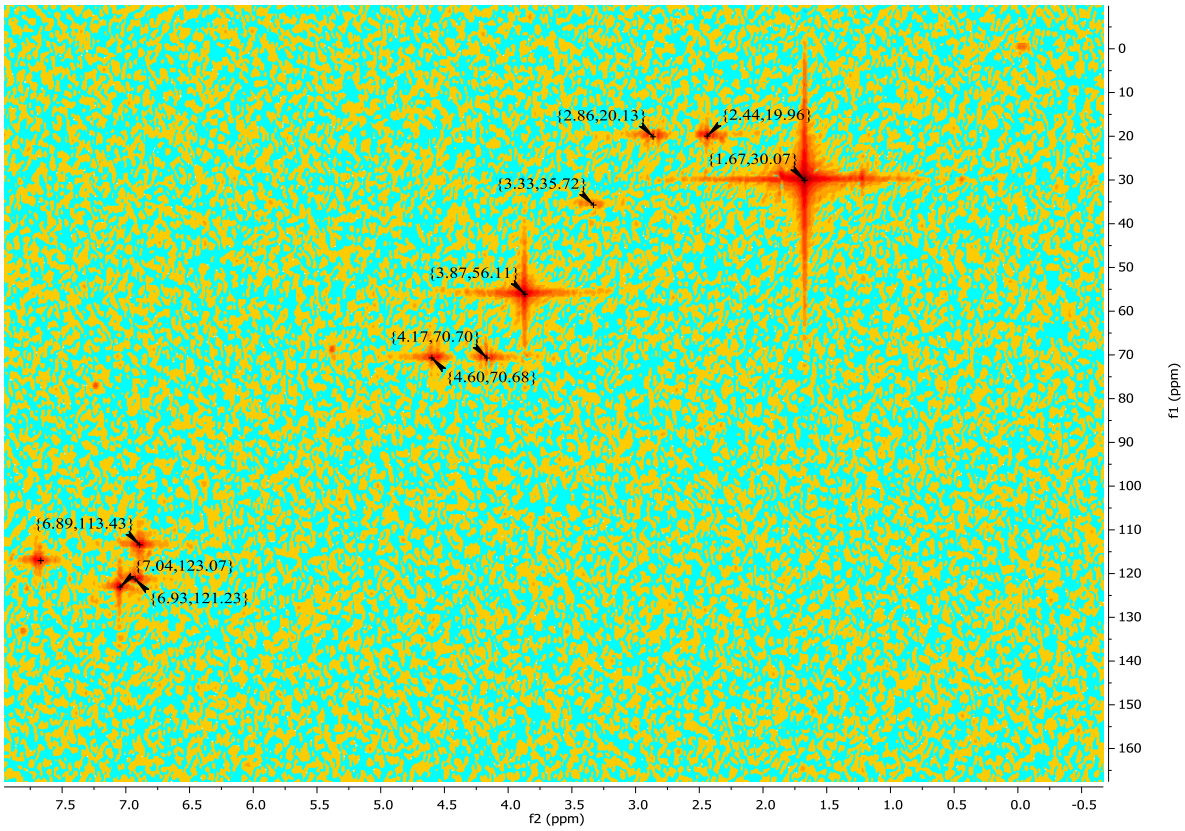


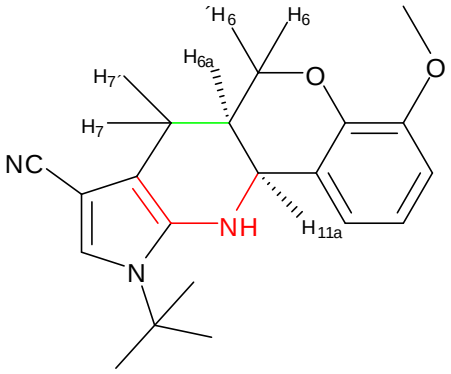


	H δ ppm	C δ ppm
H-6	4.42	69.49
H11a	3.99	54.89
H6´	3.90	69.49
H7	2.82	22.66
H7´	2.29	22.66
H6a	2.08	34.55

cis 7a

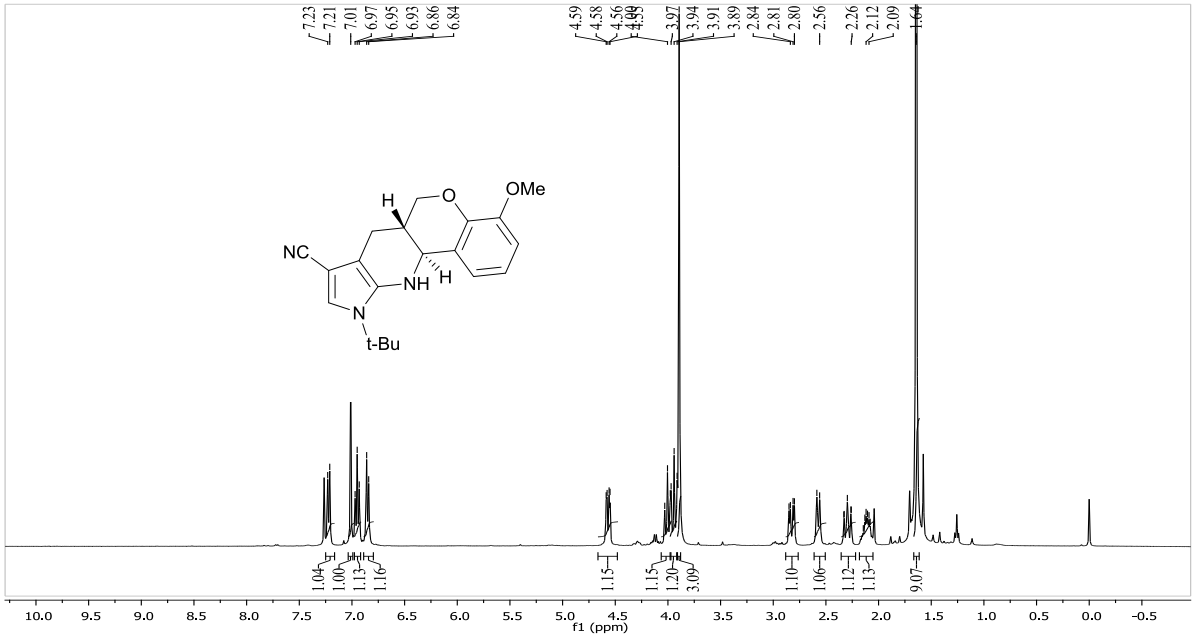

B.Cassels-mv-0872 FDLC13.11
7.72
7.71
7.26
7.08
6.98
6.96
6.92
6.90
4.63
4.58
4.23
4.20
4.17
3.90
3.88
3.40
3.38
3.33
2.92
2.90
2.88
2.86
2.51
2.47
2.43
2.35
1.68
N
H
O
N
NH
H
O
CH3
H3C
CH3
CH3
1.00
1.42
1.19
2.39
1.26
1.04
3.93
1.19
1.01
1.01
10.40
10 9 8 7 6 5 4 3 2 1 0 -1
f1 (ppm)
154.59
148.87
148.55
138.64
129.25
127.12
123.08
122.25
121.19
117.01
116.31
113.44
108.80
88.63
77.34
70.69
58.00
56.13
35.62
30.05
19.99
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

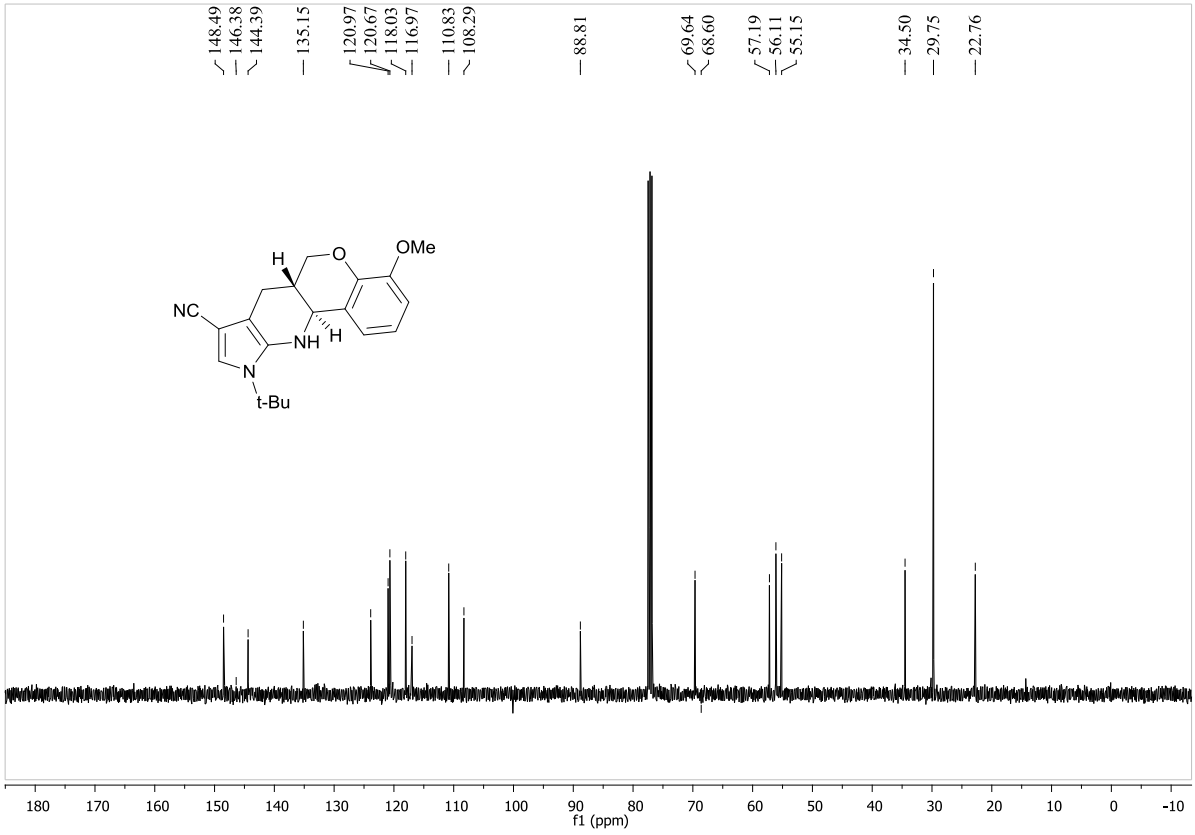




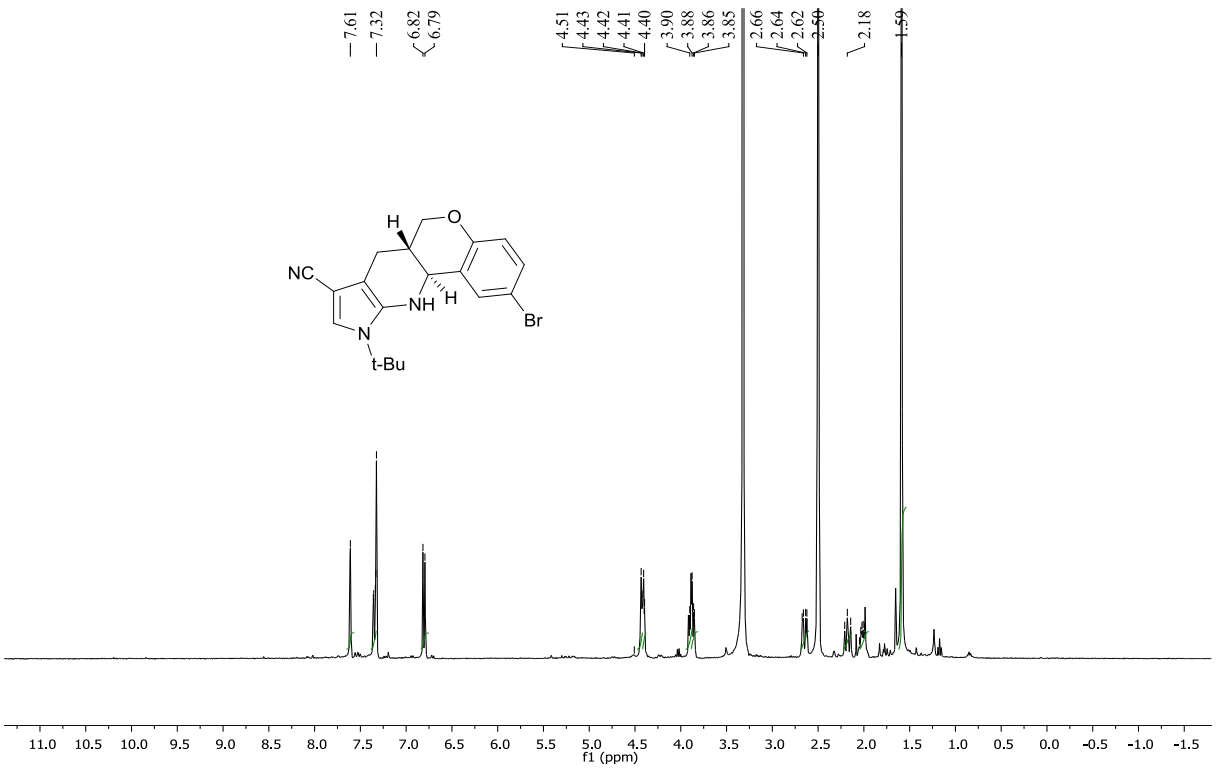
	H δ ppm	C δ ppm
H-6	4.60	70.68
H6´	4.17	70.68
H11a	Not observed	Not observed
H6a	3.33	35.72
H7	2.86	20.13
H7´	2.44	20.13

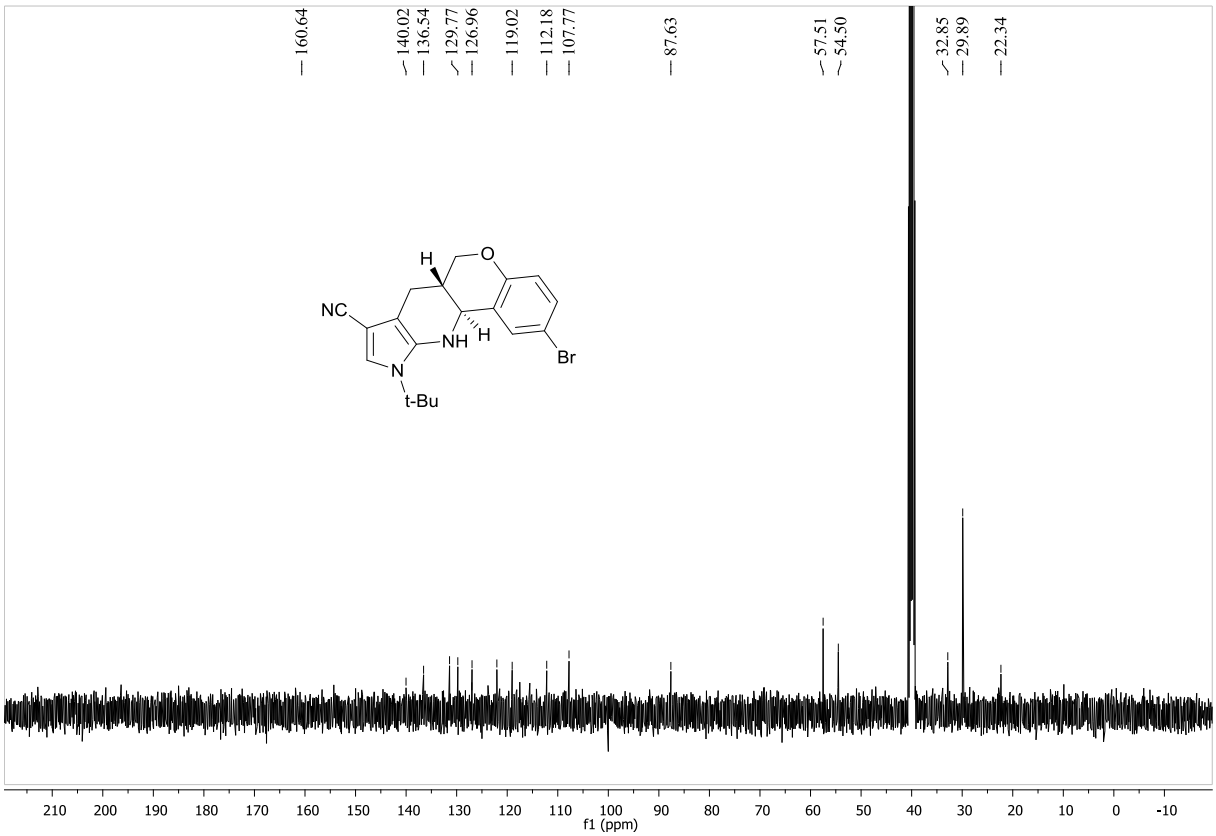
7b


7.23
7.21
7.01
6.97
6.95
6.93
6.86
6.84
4.59
4.58
4.56
3.97
3.94
3.91
3.89
2.84
2.81
2.80
2.56
2.26
2.12
2.09
1.64
H
O
OMe
NC
NH
H
N
t-Bu
1.04
1.00
1.13
1.16
1.15
1.15
1.20
3.09
1.10
1.06
1.12
1.13
9.07
f1 (ppm)

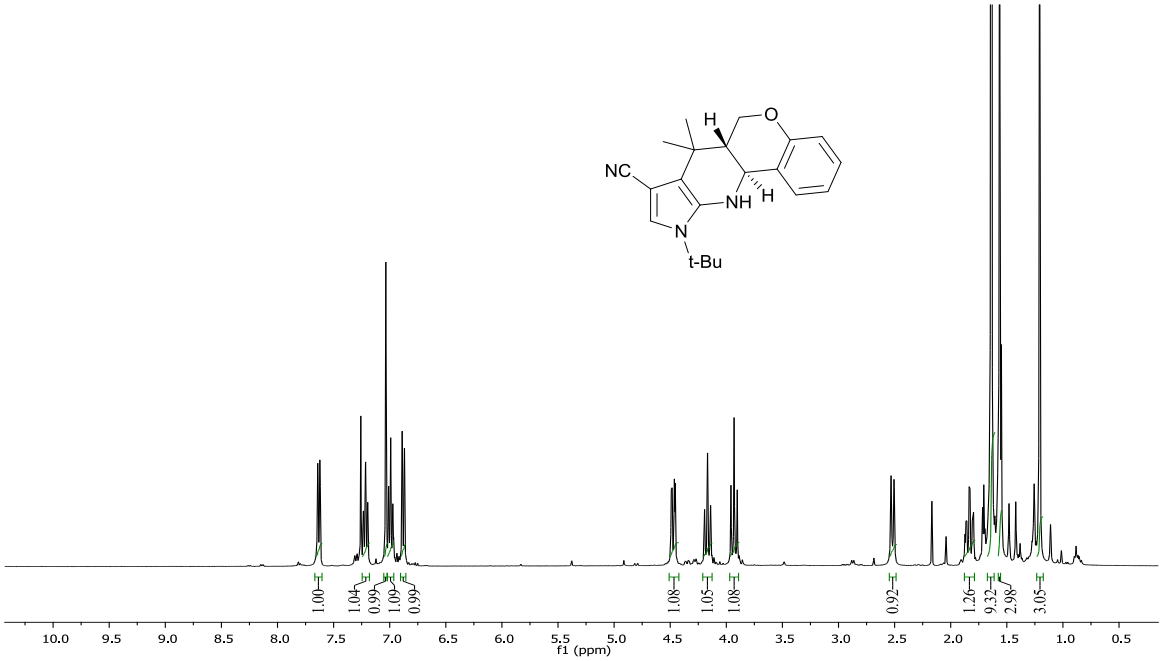

148.49
146.38
144.39
135.15
120.97
120.67
118.03
116.97
110.83
108.29
88.81
69.64
68.60
57.19
56.11
55.15
34.50
29.75
22.76
H
O
OMe
NC
NH
H
N
t-Bu
f1 (ppm)

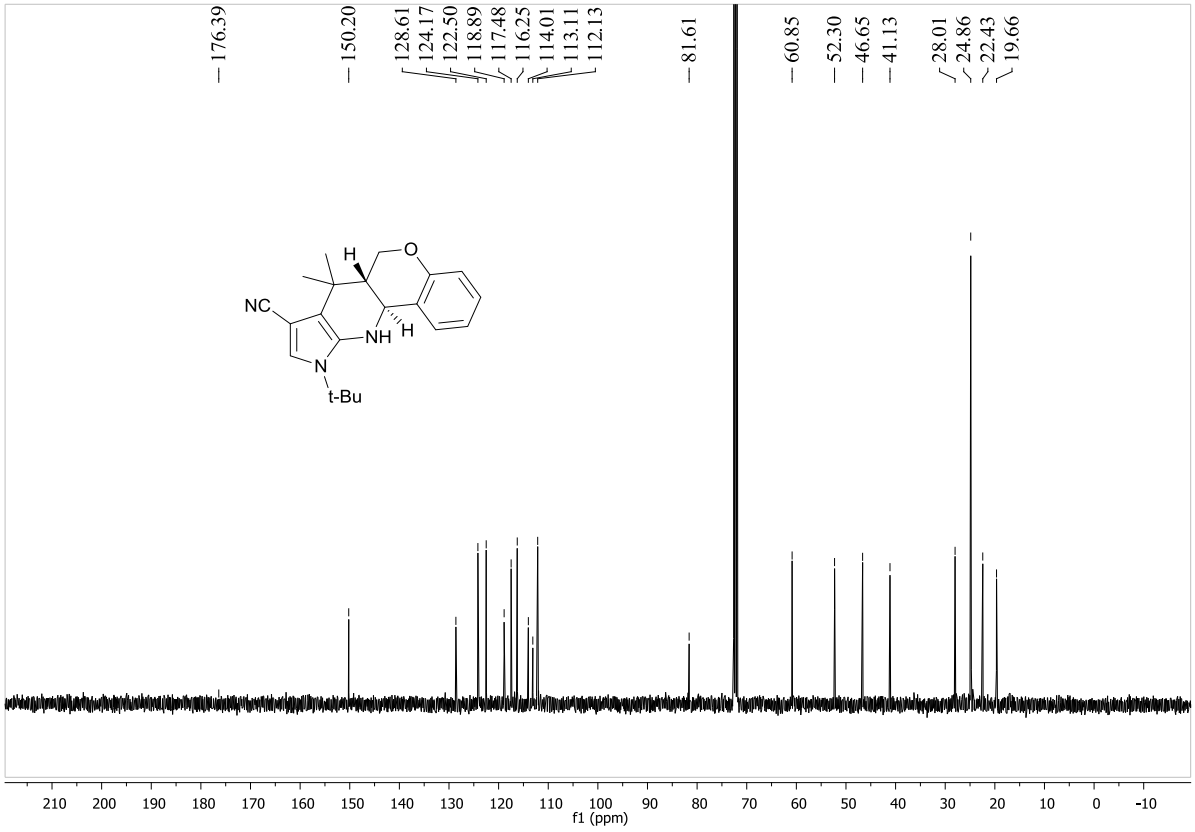
7c


7.61
7.32
6.82
6.79
4.51
4.43
4.42
4.41
4.40
3.90
3.88
3.86
3.85
2.66
2.64
2.62
2.50
2.18
1.59
H
O
NC
NH
H
Br
N
t-Bu
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5 -1.0 -1.5
f1 (ppm)

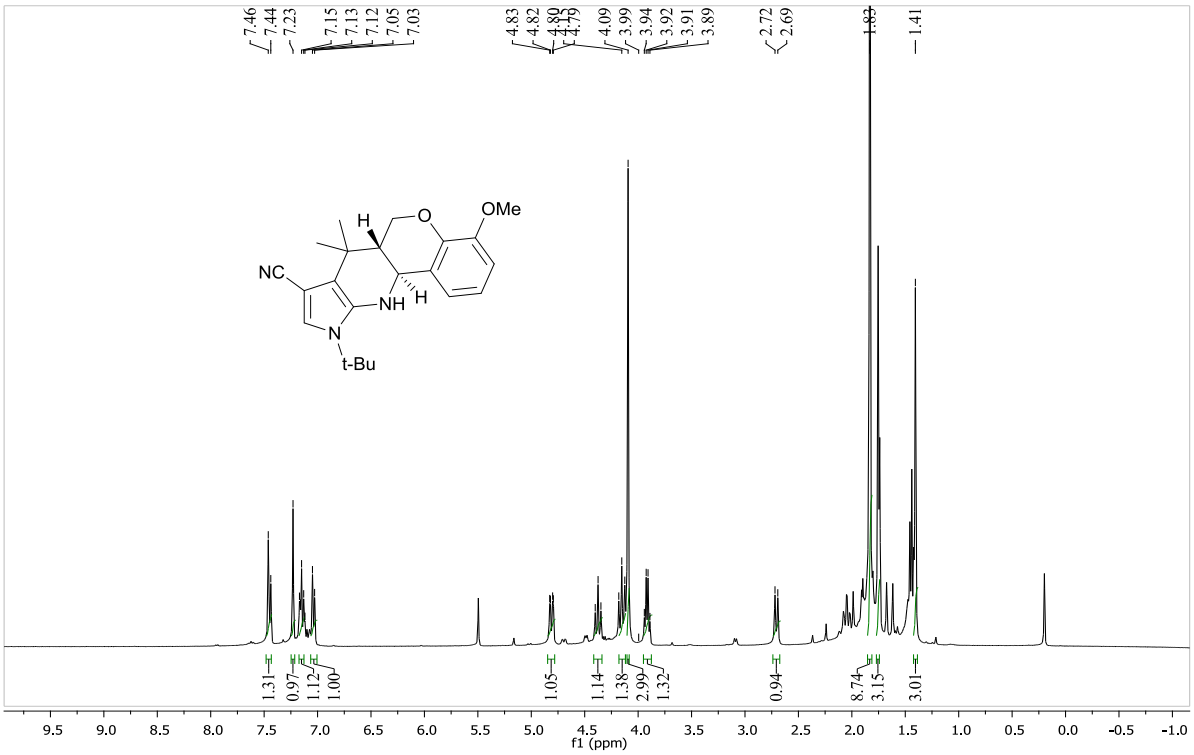

160.64
140.02
136.54
129.77
126.96
119.02
112.18
107.77
87.63
57.51
54.50
32.85
29.89
22.34
H
O
NC
NH
H
Br
N
t-Bu
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

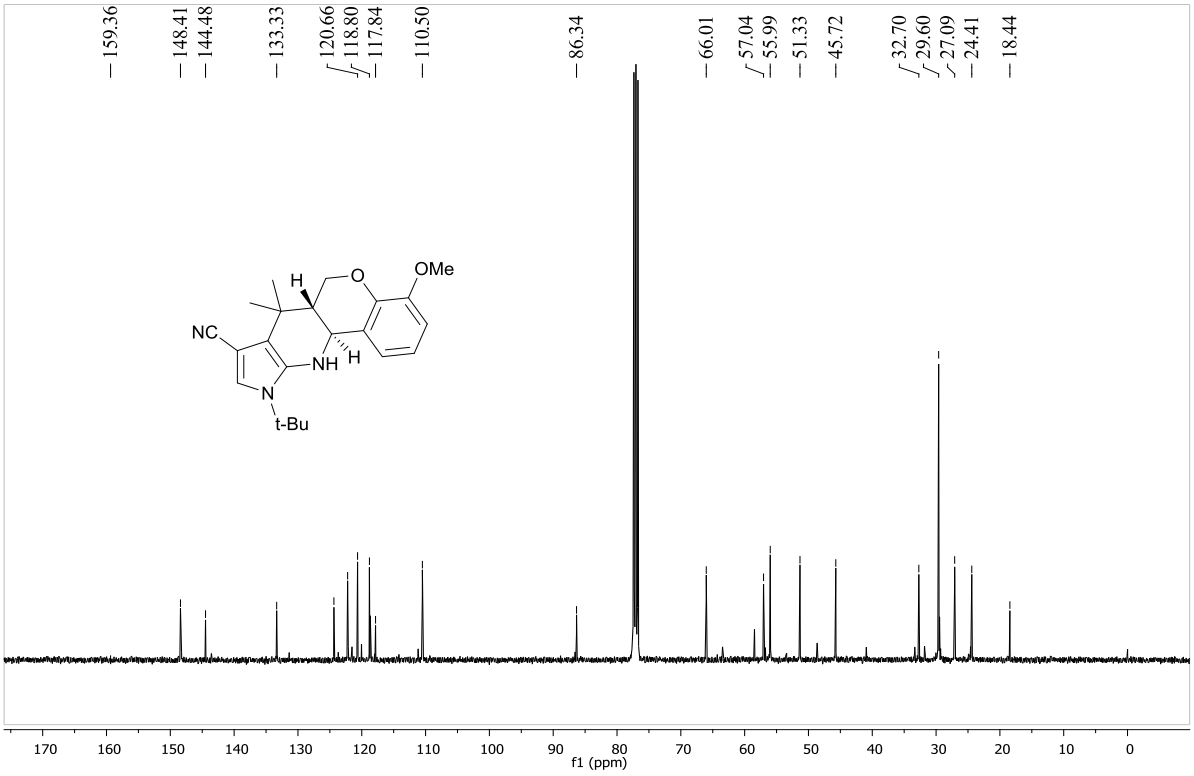
7d


NC
H
O
NH
H
N
t-Bu
1.00
1.04
0.99
1.09
0.99
1.08
1.05
1.08
0.92
1.26
9.32
2.98
3.05
f1 (ppm)

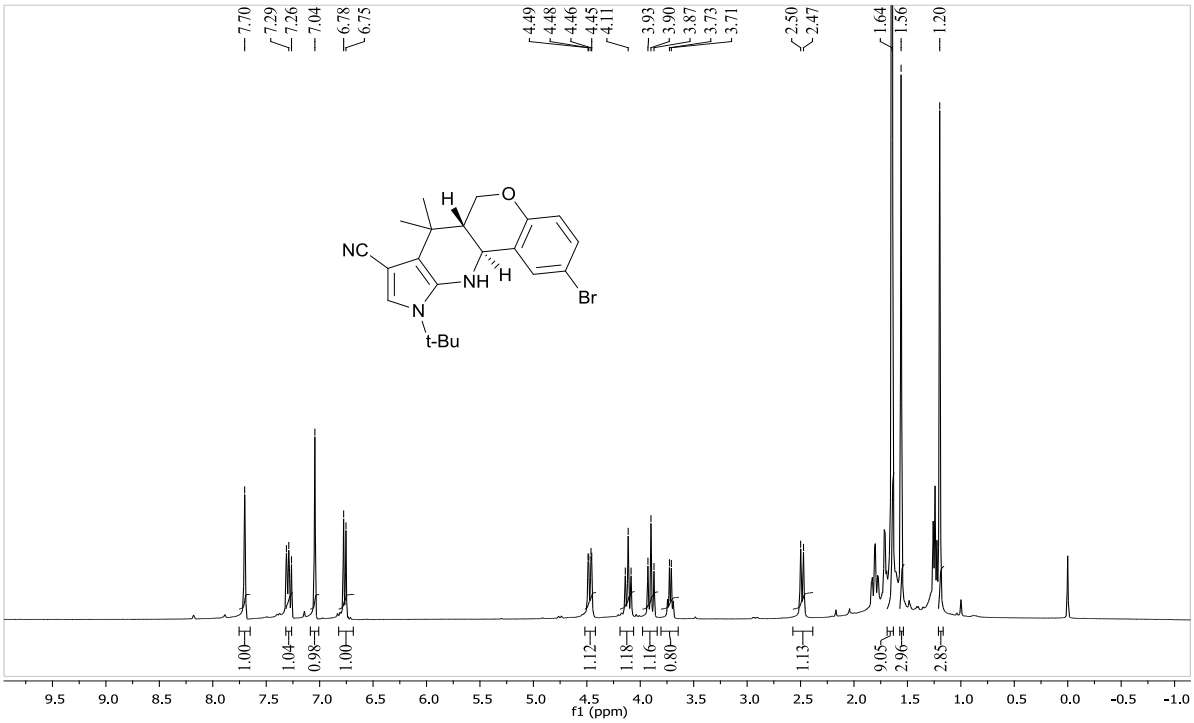

176.39
150.20
128.61
124.17
122.50
118.89
117.48
116.25
114.01
113.11
112.13
81.61
60.85
52.30
46.65
41.13
28.01
24.86
22.43
19.66
NC
H
O
NH
H
N
t-Bu
f1 (ppm)

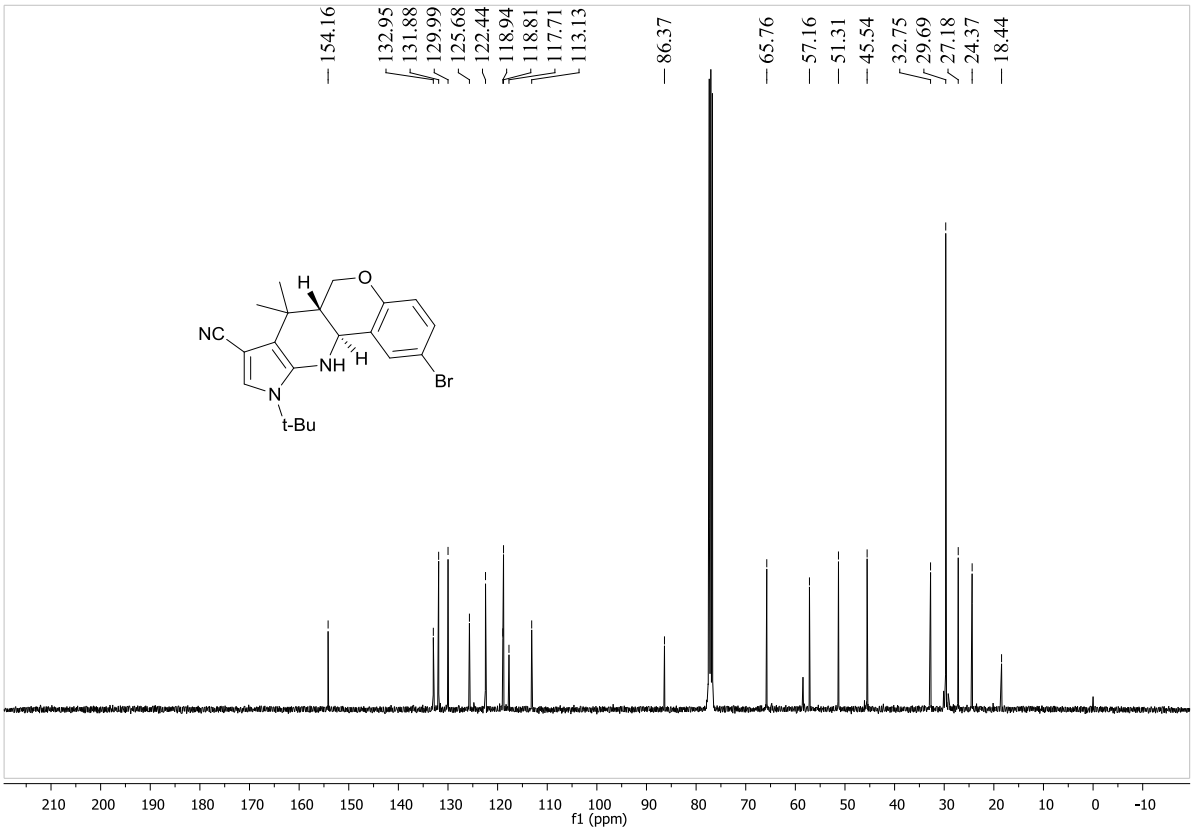
7e


7.46
7.44
7.23
7.15
7.13
7.12
7.05
7.03
4.83
4.82
4.80
4.79
4.09
3.99
3.94
3.92
3.91
3.89
2.72
2.69
1.83
1.41
OMe
H
O
NC
NH
H
N
t-Bu
1.31
0.97
1.12
1.00
1.05
1.14
1.38
2.99
1.32
0.94
8.74
3.15
3.01
f1 (ppm)

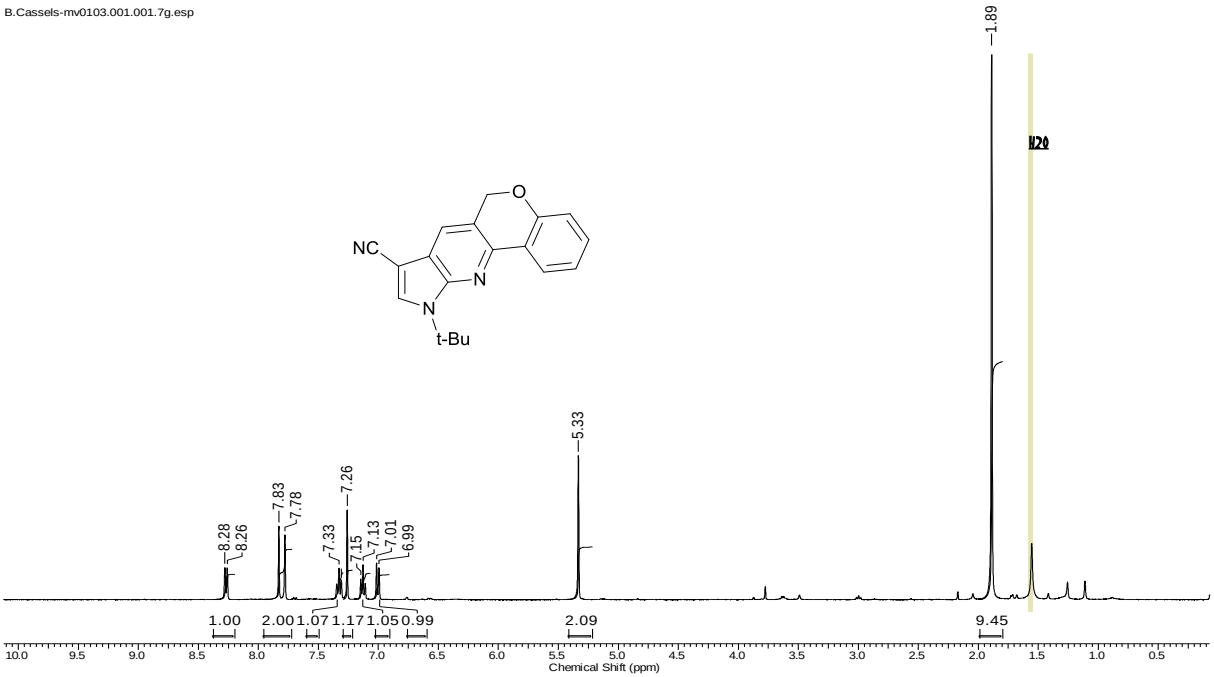

159.36
148.41
144.48
133.33
120.66
118.80
117.84
110.50
86.34
66.01
57.04
55.99
51.33
45.72
32.70
29.60
27.09
24.41
18.44
OMe
H
O
NC
NH
H
N
t-Bu
f1 (ppm)

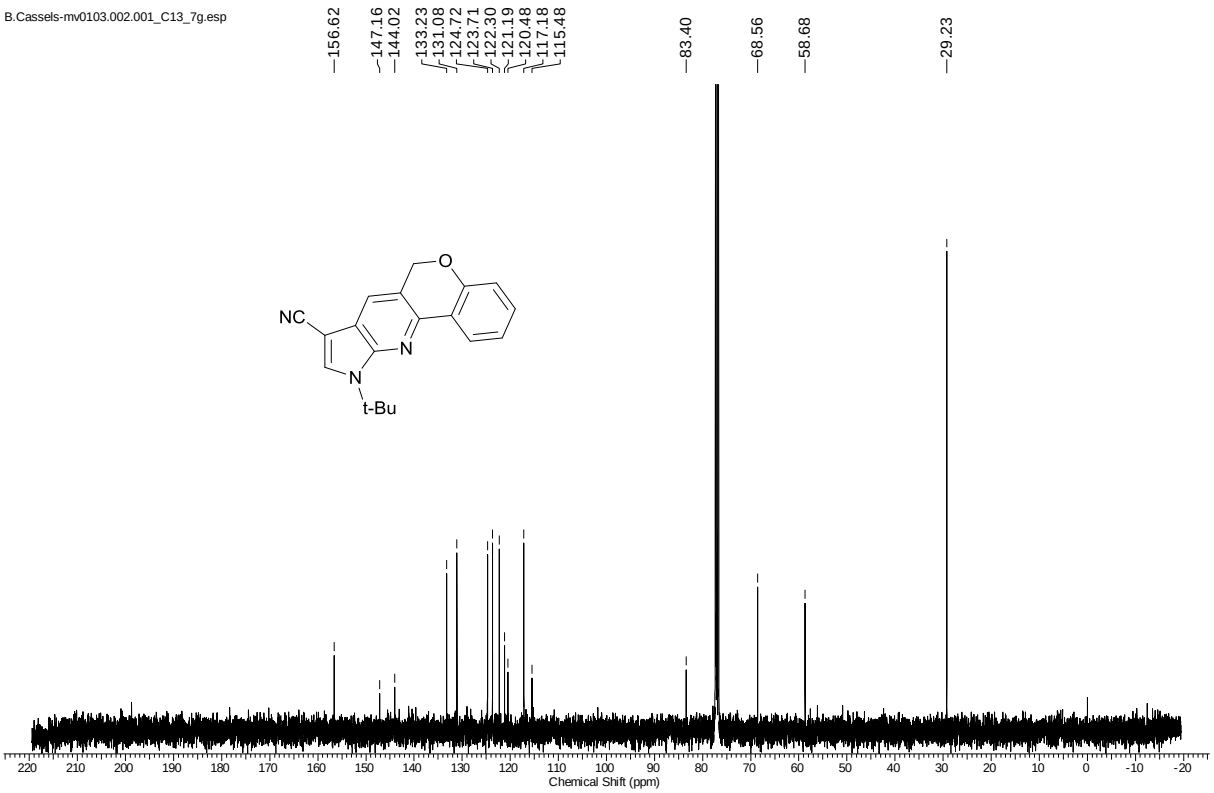
7f


7.70
7.29
7.26
7.04
6.78
6.75
4.49
4.48
4.46
4.45
4.11
3.93
3.90
3.87
3.73
3.71
2.50
2.47
1.64
1.56
1.20
NC
H
O
NH
H
Br
N
t-Bu
1.00
1.04
0.98
1.00
1.12
1.18
1.16
0.80
1.13
9.05
2.96
2.85
f1 (ppm)

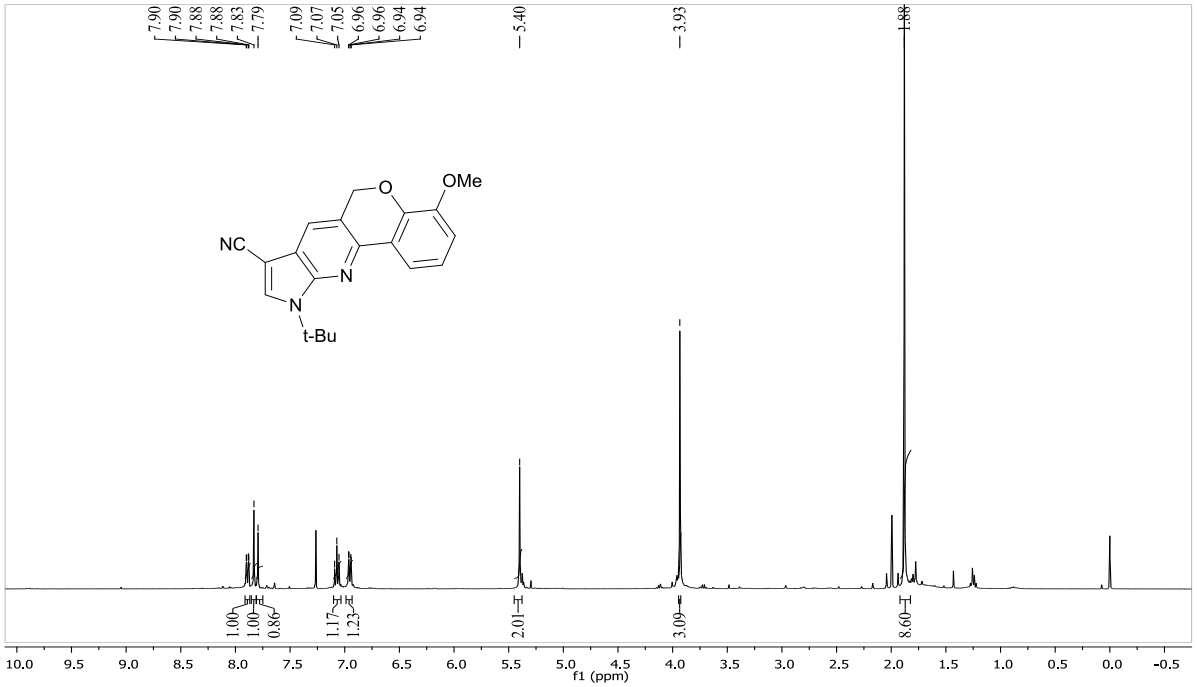

154.16
132.95
131.88
129.99
125.68
122.44
118.94
118.81
117.71
113.13
86.37
65.76
57.16
51.31
45.54
32.75
29.69
27.18
24.37
18.44
NC
H
O
NH
H
Br
N
t-Bu
f1 (ppm)

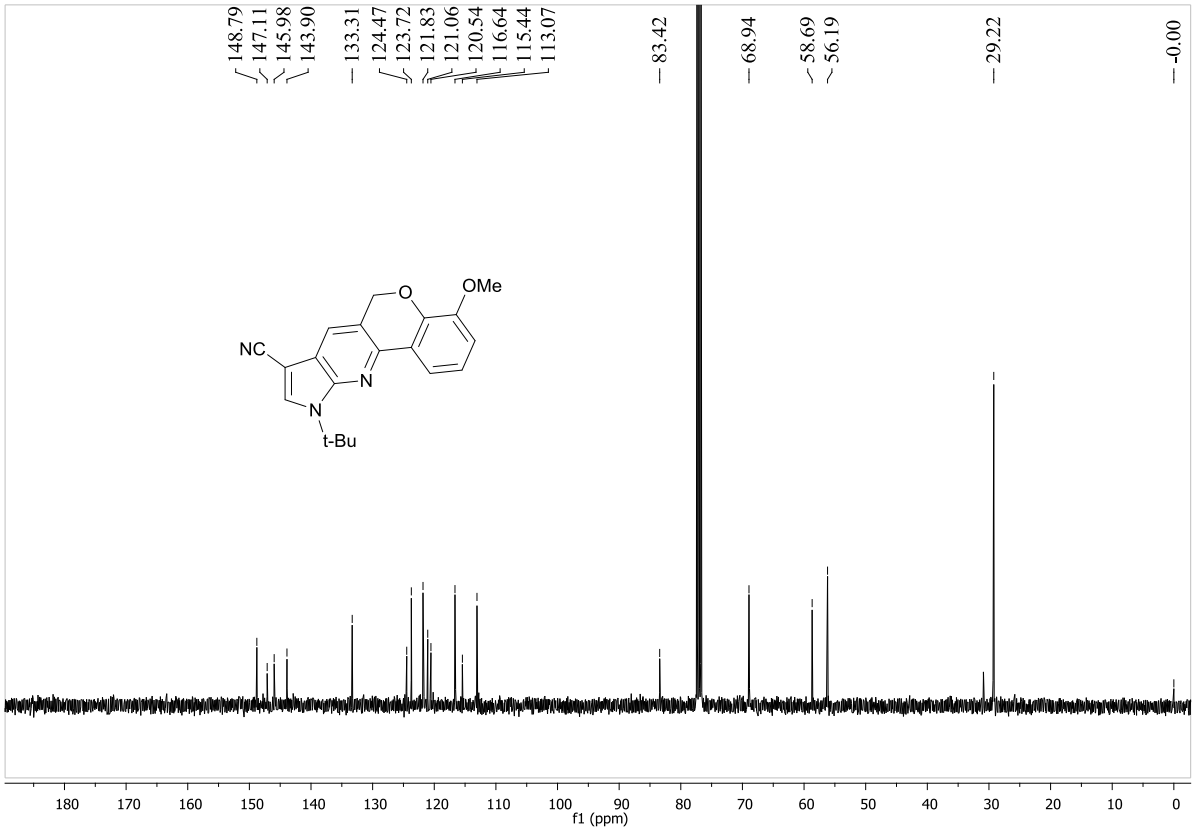
7g


B.Cassels-mv0103.001.001.7g.esp
1.89
H20
NC
O
N
N
t-Bu
5.33
8.28
8.26
7.83
7.78
7.33
7.26
7.15
7.13
7.01
6.99
1.00
2.00
1.07
1.17
1.05
0.99
2.09
9.45
Chemical Shift (ppm)

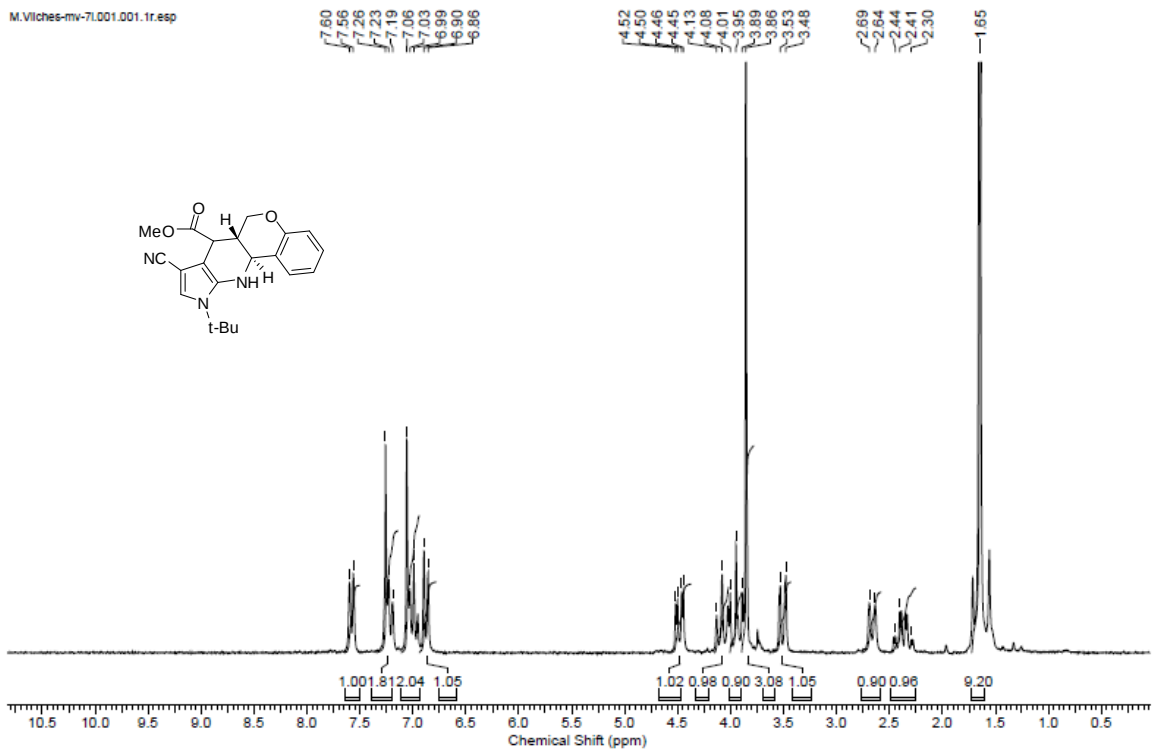

B.Cassels-mv0103.002.001_C13_7g.esp
156.62
147.16
144.02
133.23
131.08
124.72
123.71
122.30
121.19
120.48
117.18
115.48
83.40
68.56
58.68
29.23
NC
O
N
N
t-Bu
Chemical Shift (ppm)

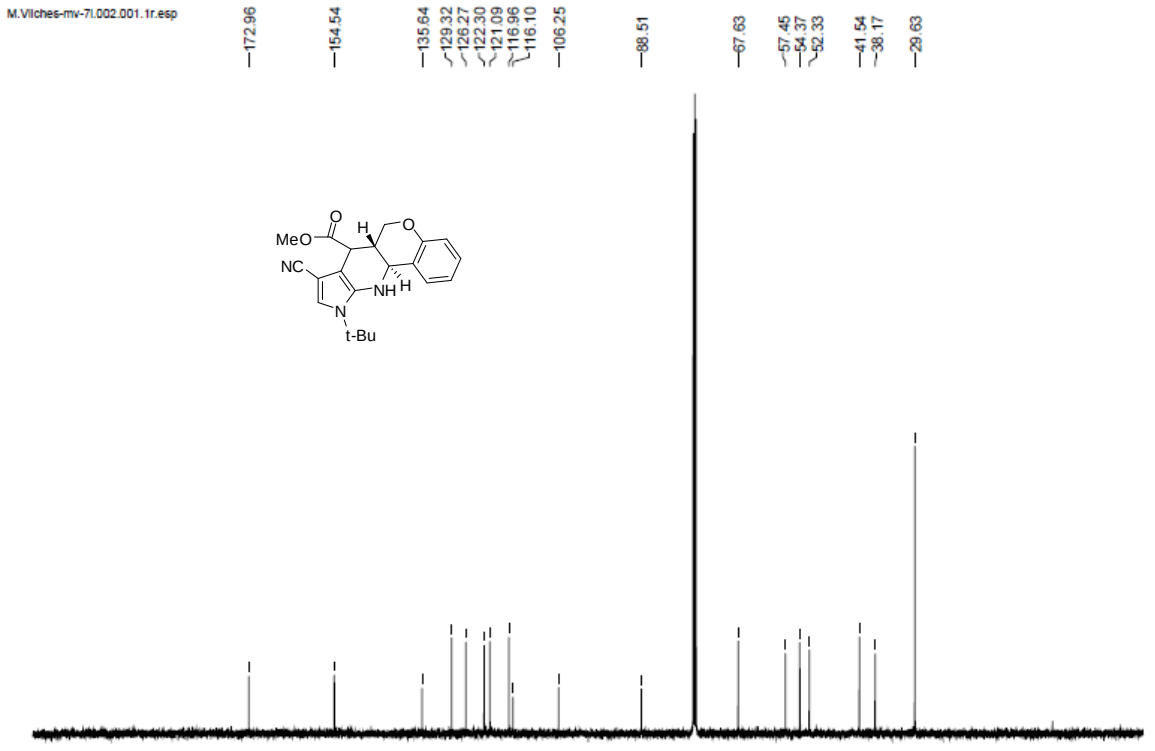
7h


7.90
7.90
7.88
7.88
7.83
7.79
7.09
7.07
7.05
6.96
6.96
6.94
6.94
5.40
3.93
1.88
OMe
O
NC
N
N
t-Bu
1.00
1.00
0.86
1.17
1.23
2.01
3.09
8.60
f1 (ppm)

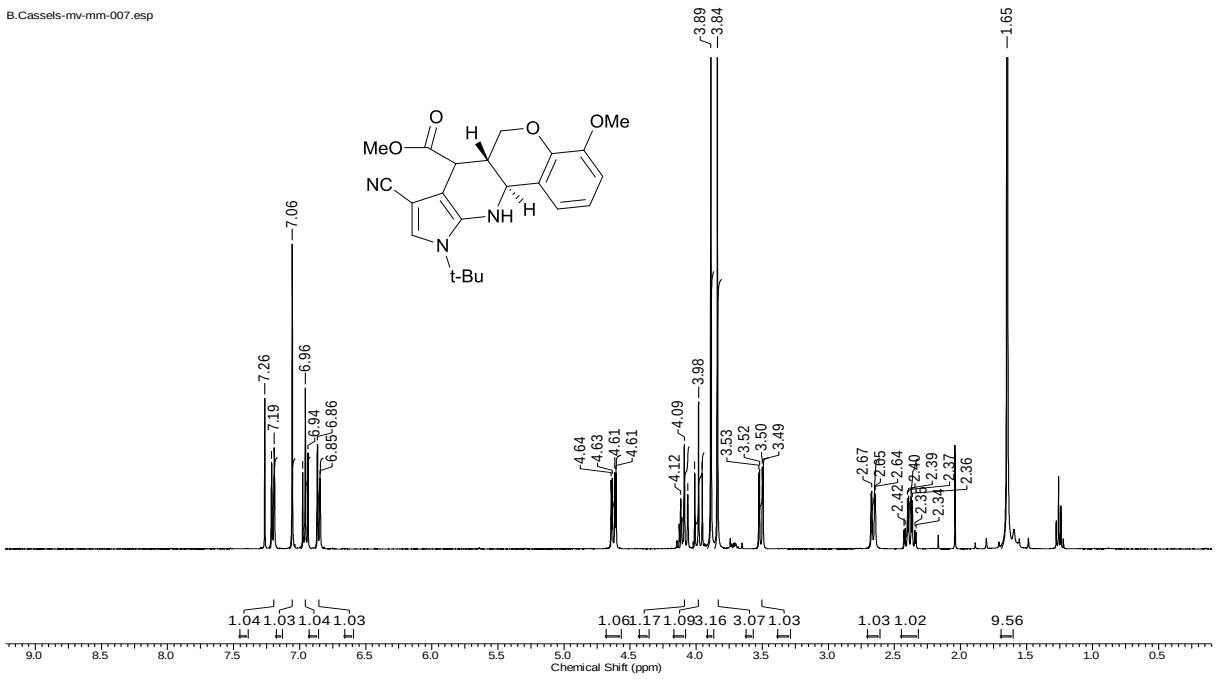

148.79
147.11
145.98
143.90
133.31
124.47
123.72
121.83
121.06
120.54
116.64
115.44
113.07
83.42
68.94
58.69
56.19
29.22
-0.00
OMe
O
NC
N
N
t-Bu
f1 (ppm)

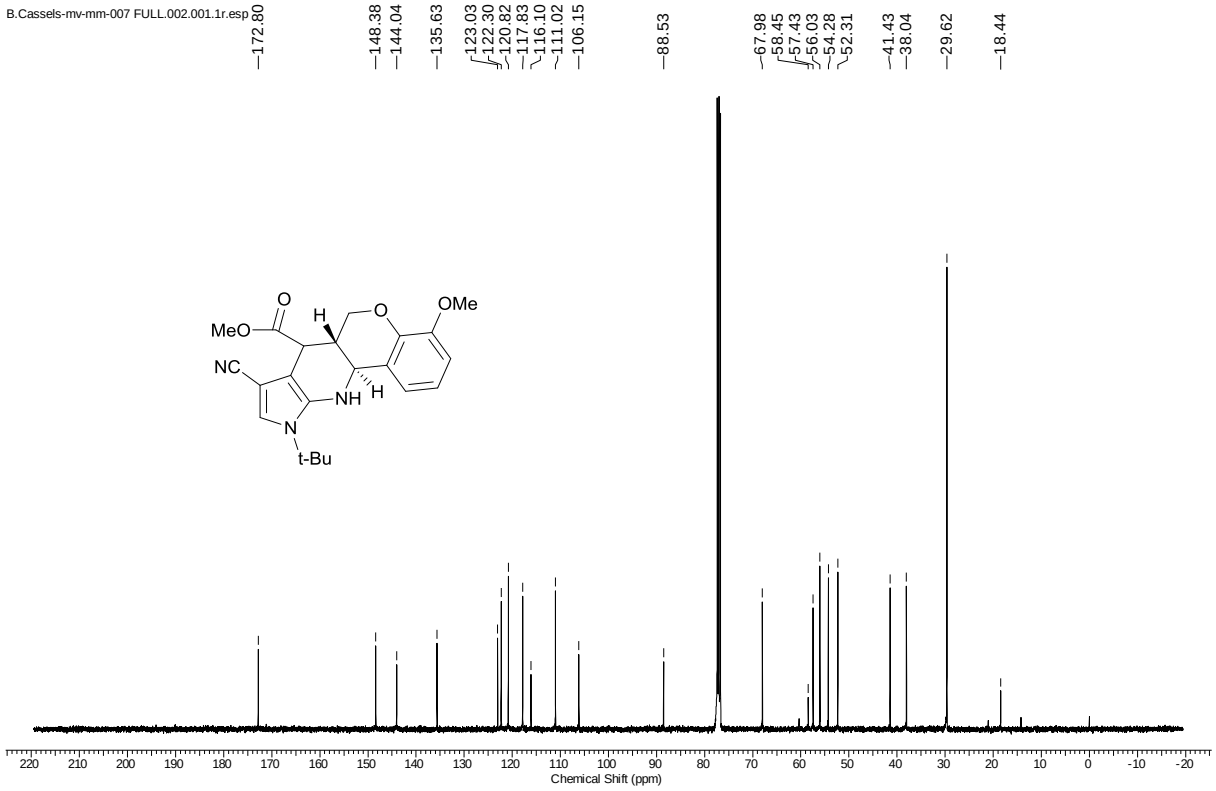
7i


M.Vilches-mv-7l.001.001.1r.esp
7.60
7.56
7.26
7.23
7.19
7.06
7.03
6.99
6.90
6.86
4.52
4.50
4.46
4.45
4.13
4.08
4.01
3.95
3.89
3.86
3.53
3.48
2.69
2.64
2.44
2.41
2.30
1.65
MeO
NC
NH
H
O
H
N
t-Bu
1.00 1.81 2.04 1.05
1.02 0.98 0.90 3.08 1.05
0.90 0.96
9.20
Chemical Shift (ppm)

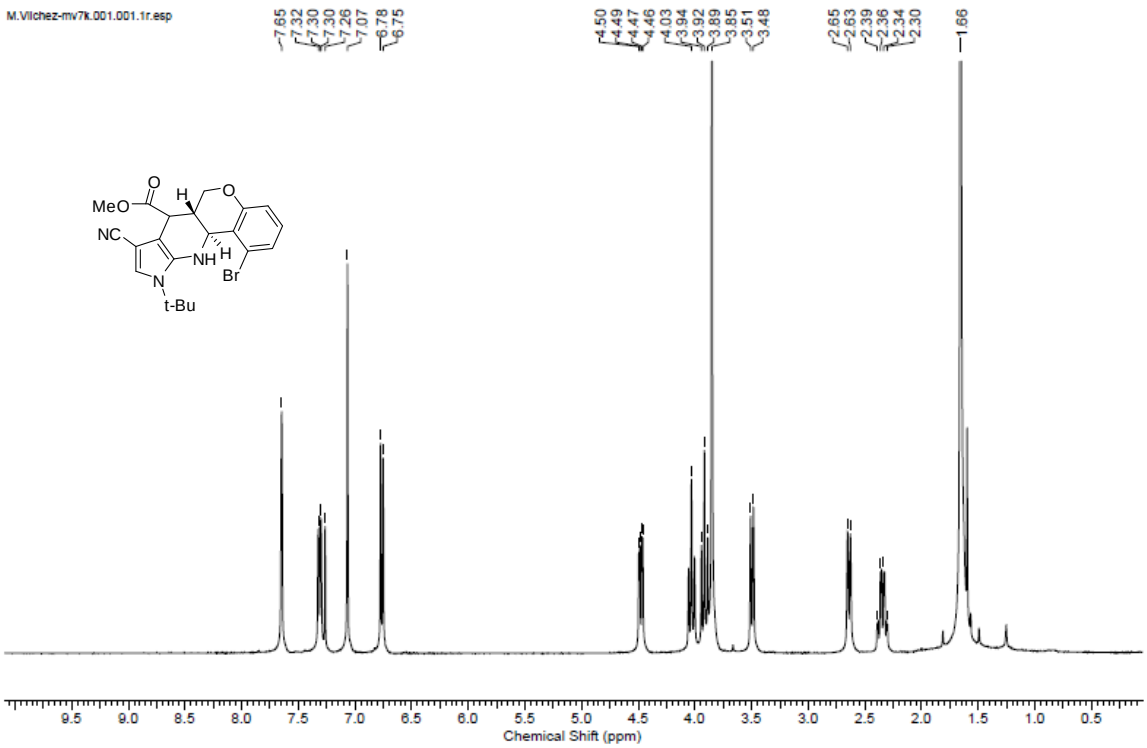

M.Vilches-mv-7l.002.001.1r.esp
172.96
154.54
135.64
129.32
126.27
122.30
121.09
116.96
116.10
106.25
88.51
67.63
57.45
54.37
52.33
41.54
38.17
29.63
MeO
NC
NH
H
O
H
N
t-Bu

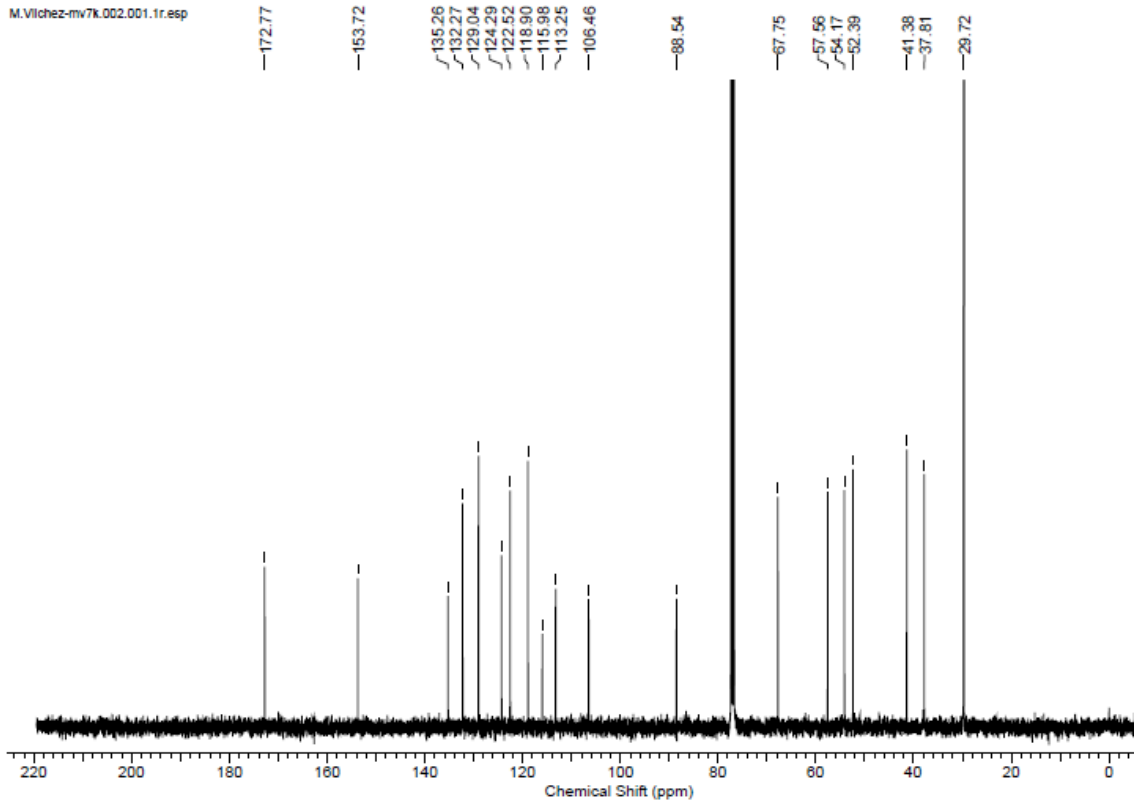
7j


B.Cassels-mv-mm-007.esp
3.89
3.84
1.65
7.06
7.26
7.19
6.96
6.94
6.86
6.85
4.64
4.63
4.61
4.61
4.12
4.09
3.98
3.53
3.52
3.50
3.49
2.67
2.65
2.64
2.42
2.40
2.39
2.34
2.37
2.36
MeO
NC
NH
N
t-Bu
OMe
1.04 1.03 1.04 1.03
1.06 1.17 1.09 3.16 3.07 1.03
1.03 1.02
9.56
Chemical Shift (ppm)

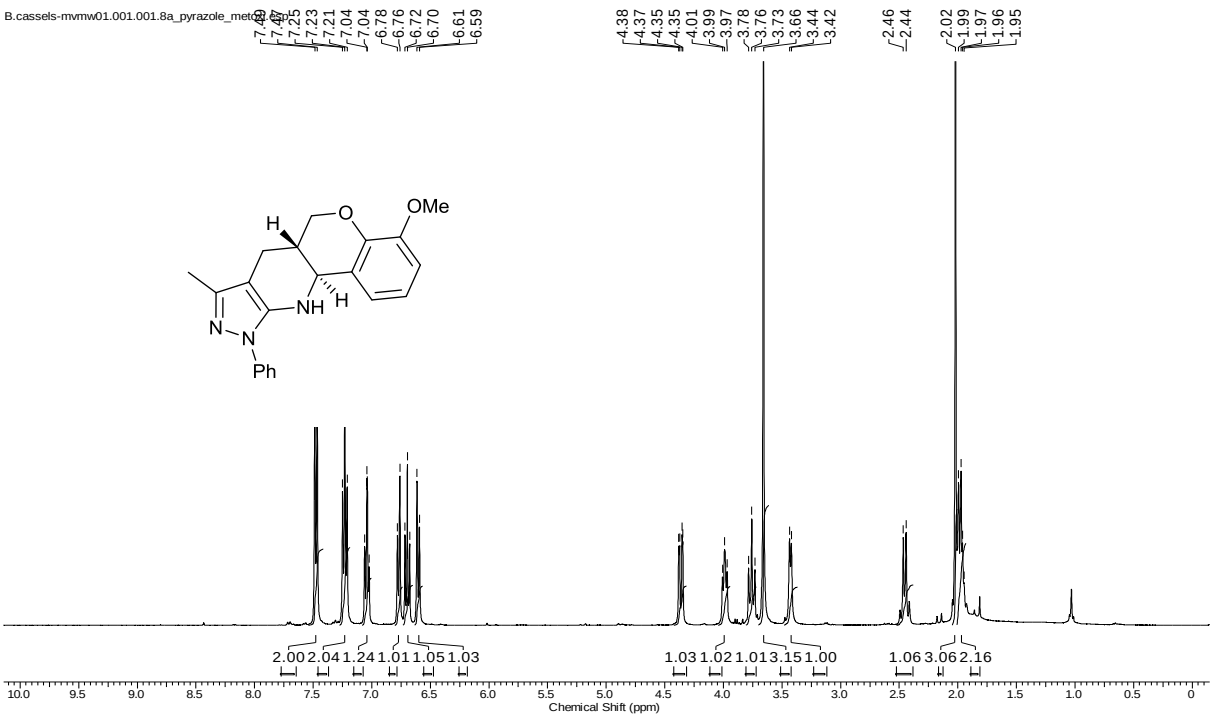

B.Cassels-mv-mm-007 FULL.002.001.1r.esp
172.80
148.38
144.04
135.63
123.03
122.30
120.82
117.83
116.10
111.02
106.15
88.53
67.98
58.45
57.43
56.03
54.28
52.31
41.43
38.04
29.62
18.44
MeO
NC
NH
N
t-Bu
OMe
Chemical Shift (ppm)

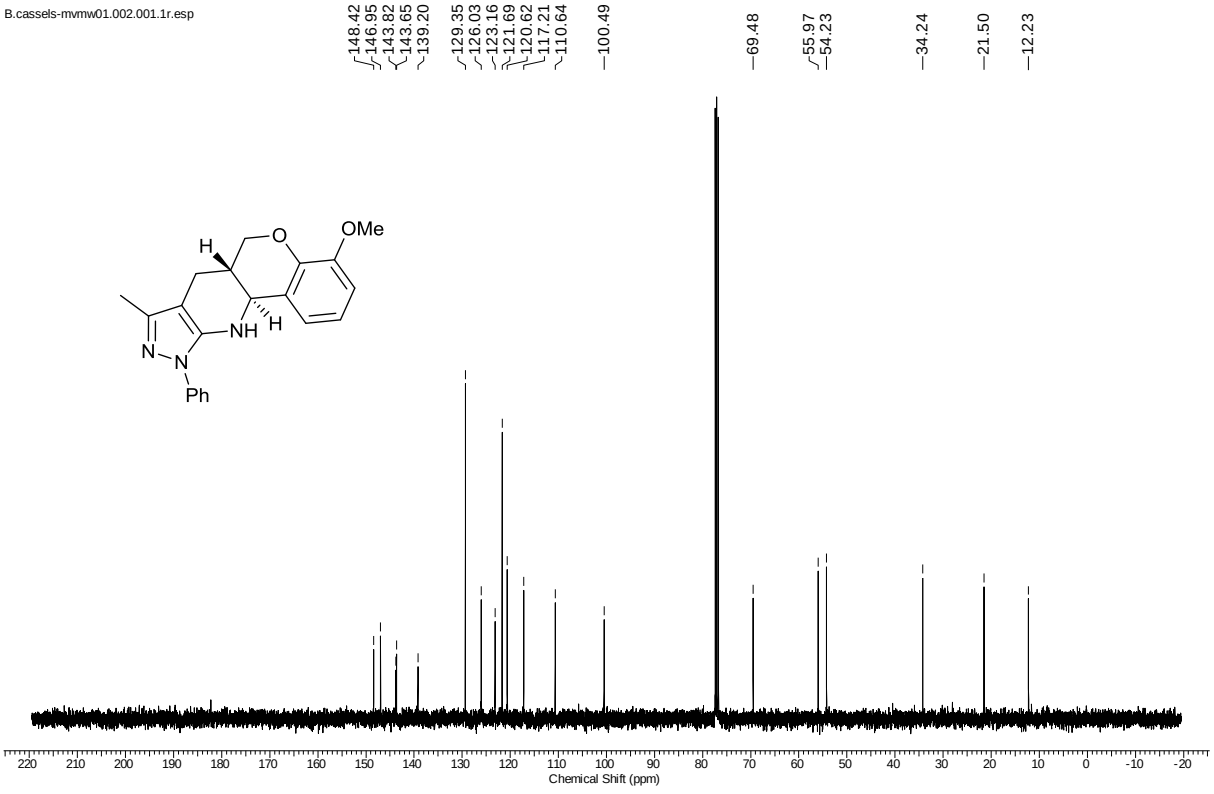
7k


M.Vilchez-mv7k.001.001.1r.esp
7.65
7.32
7.30
7.30
7.26
7.07
6.78
6.75
4.50
4.49
4.47
4.46
4.03
3.94
3.92
3.89
3.85
3.51
3.48
2.65
2.63
2.39
2.36
2.34
2.30
1.66
MeO
O
H
O
NC
NH
H
Br
N
t-Bu
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
Chemical Shift (ppm)

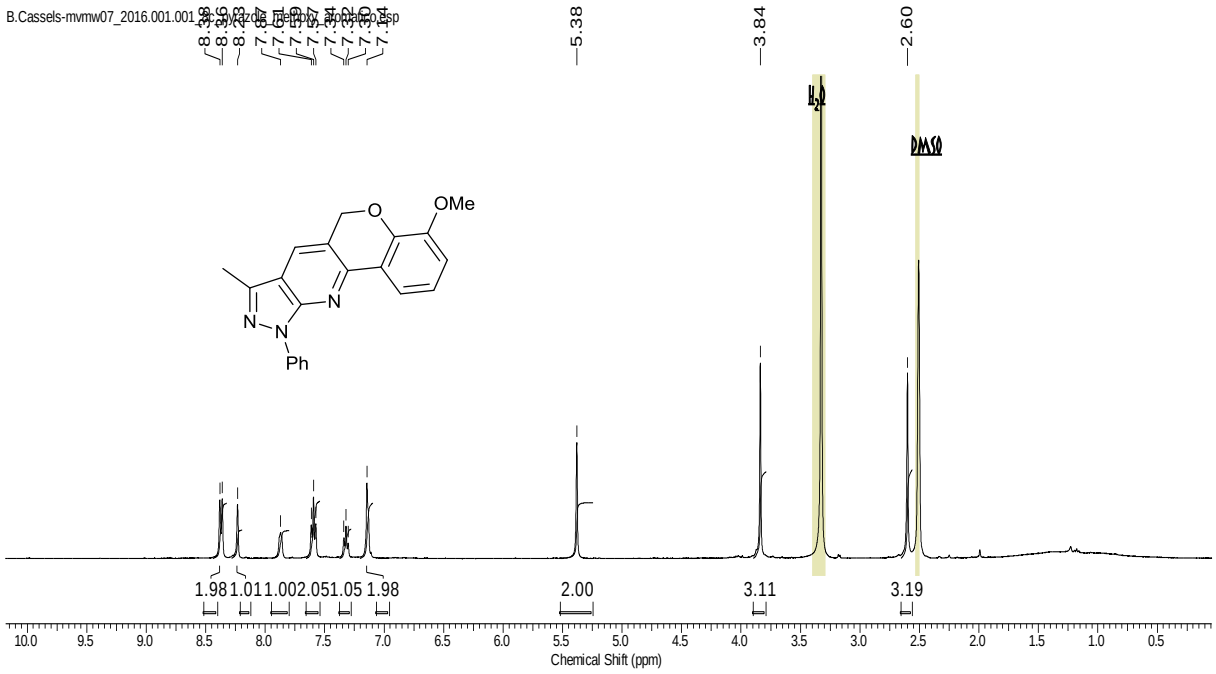

M.Vilchez-mv7k.002.001.1r.esp
172.77
153.72
135.26
132.27
129.04
124.29
122.52
118.90
115.98
113.25
106.46
88.54
67.75
57.56
54.17
52.39
41.38
37.81
29.72
220
200
180
160
140
120
100
80
60
40
20
0
Chemical Shift (ppm)

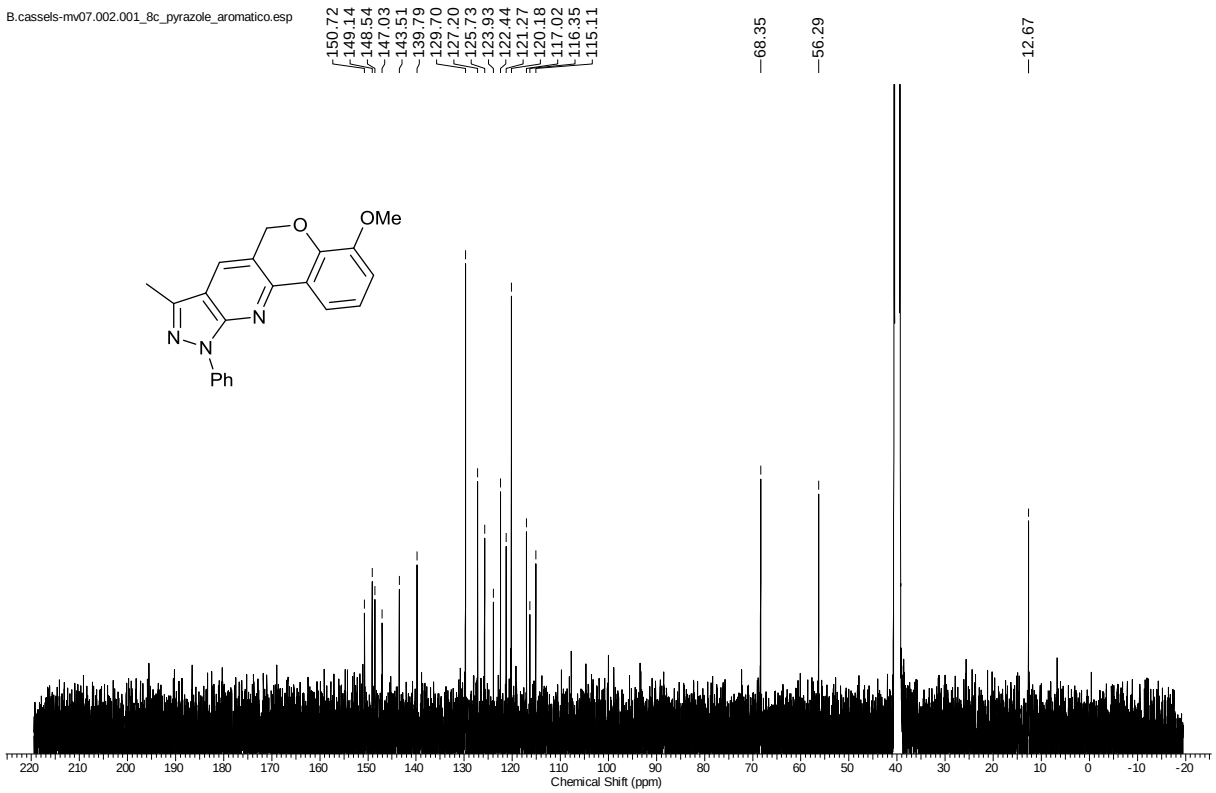
8a


B.cassels-mvmw01.001.001.8a_pyrazole_metoxy.esp
7.48
7.47
7.25
7.23
7.21
7.04
7.04
6.78
6.76
6.72
6.70
6.61
6.59
4.38
4.37
4.35
4.35
4.01
3.99
3.97
3.78
3.76
3.73
3.66
3.44
3.42
2.46
2.44
2.02
1.99
1.97
1.96
1.95
OMe
H
O
NH
H
N
N
Ph
2.00 2.04 1.24 1.01 1.05 1.03
1.03 1.02 1.01 3.15 1.00
1.06 3.06 2.16
Chemical Shift (ppm)

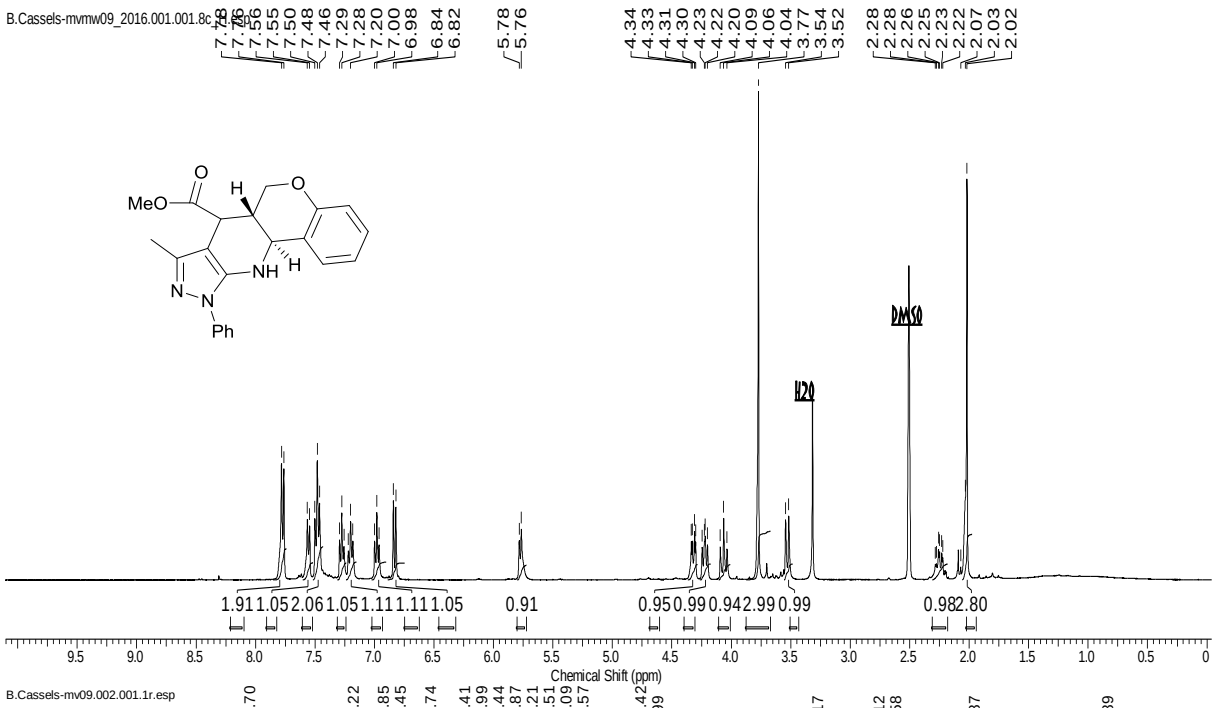

B.cassels-mvmw01.002.001.1r.esp
148.42
146.95
143.82
143.65
139.20
129.35
126.03
123.16
121.69
120.62
117.21
110.64
100.49
69.48
55.97
54.23
34.24
21.50
12.23
OMe
H
O
NH
H
N
N
Ph
Chemical Shift (ppm)

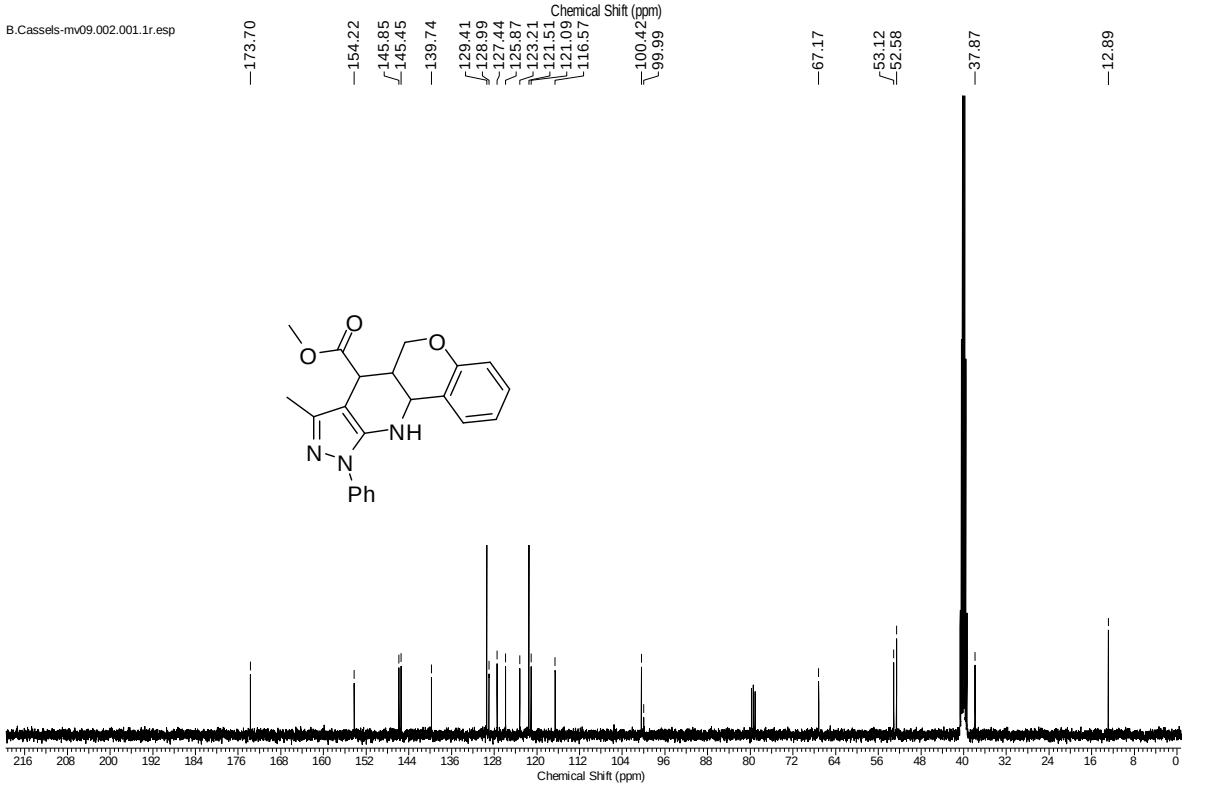
8b

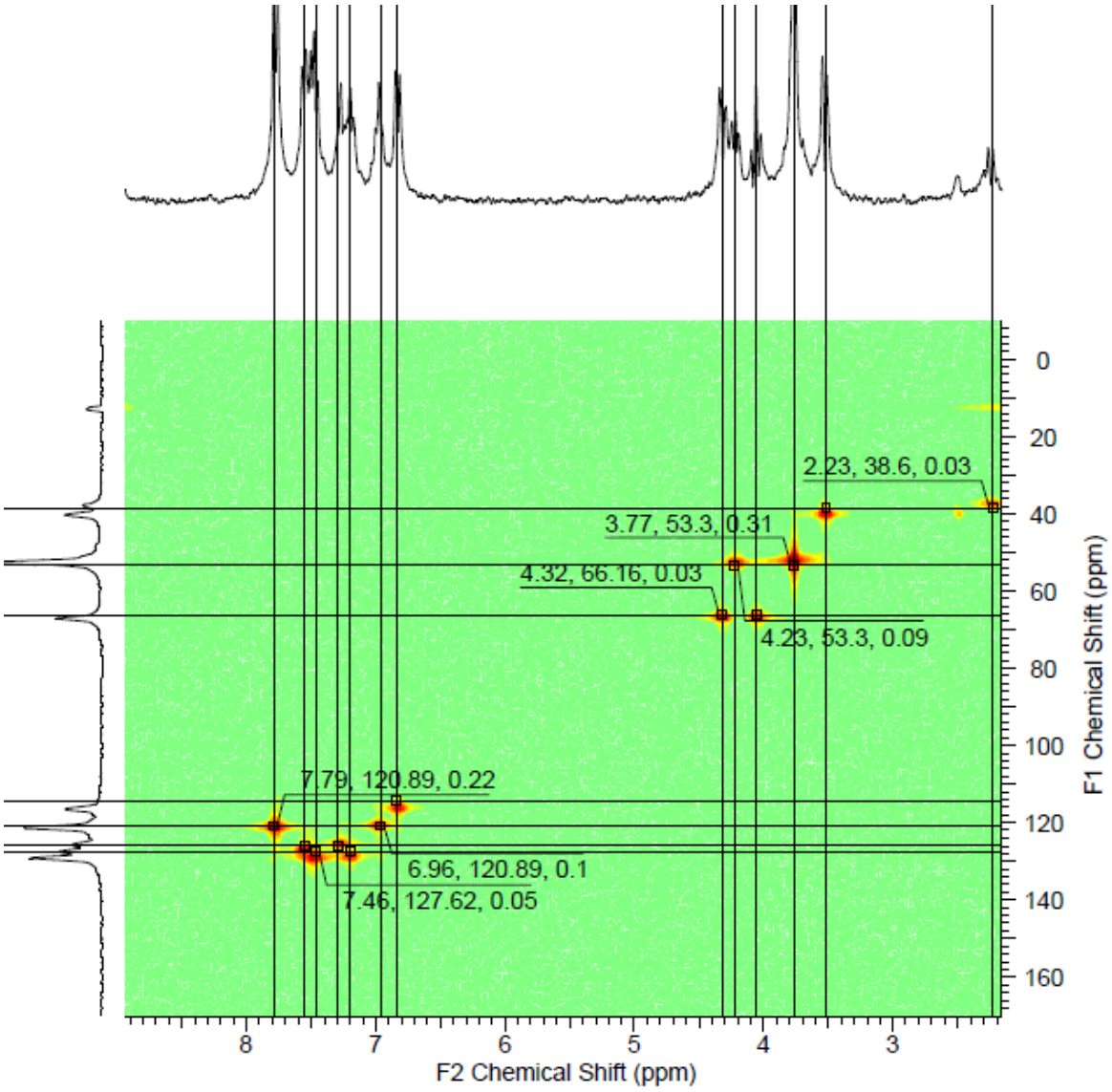

B.Cassels-mvmw07_2016.001.001_8b_pyrazole_heteroxy_aromatico.esp
5.38
3.84
2.60
H2O
DMSO
OMe
O
N
N
N
Ph
1.98
1.01
1.00
2.05
1.05
1.98
2.00
3.11
3.19
Chemical Shift (ppm)

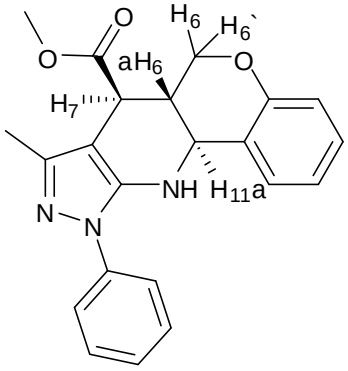

B.cassels-mv07.002.001_8c_pyrazole_aromatico.esp
150.72
149.14
148.54
147.03
143.51
139.79
129.70
127.20
125.73
123.93
122.44
121.27
120.18
117.02
116.35
115.11
68.35
56.29
12.67
OMe
O
N
N
N
Ph
Chemical Shift (ppm)

8c


B.Cassels-mvmw09_2016.001.001.8c.esp
7.78
7.56
7.55
7.50
7.48
7.46
7.29
7.28
7.20
7.00
6.98
6.84
6.82
5.78
5.76
4.34
4.33
4.31
4.30
4.23
4.22
4.20
4.09
4.06
4.04
3.77
3.54
3.52
2.28
2.28
2.26
2.25
2.23
2.22
2.07
2.03
2.02
MeO
O
H
O
NH
H
N
N
Ph
DMSO
H2O
1.91 1.05 2.06 1.05 1.11 1.11 1.05 0.91 0.95 0.99 0.94 2.99 0.99 0.98 2.80
Chemical Shift (ppm)

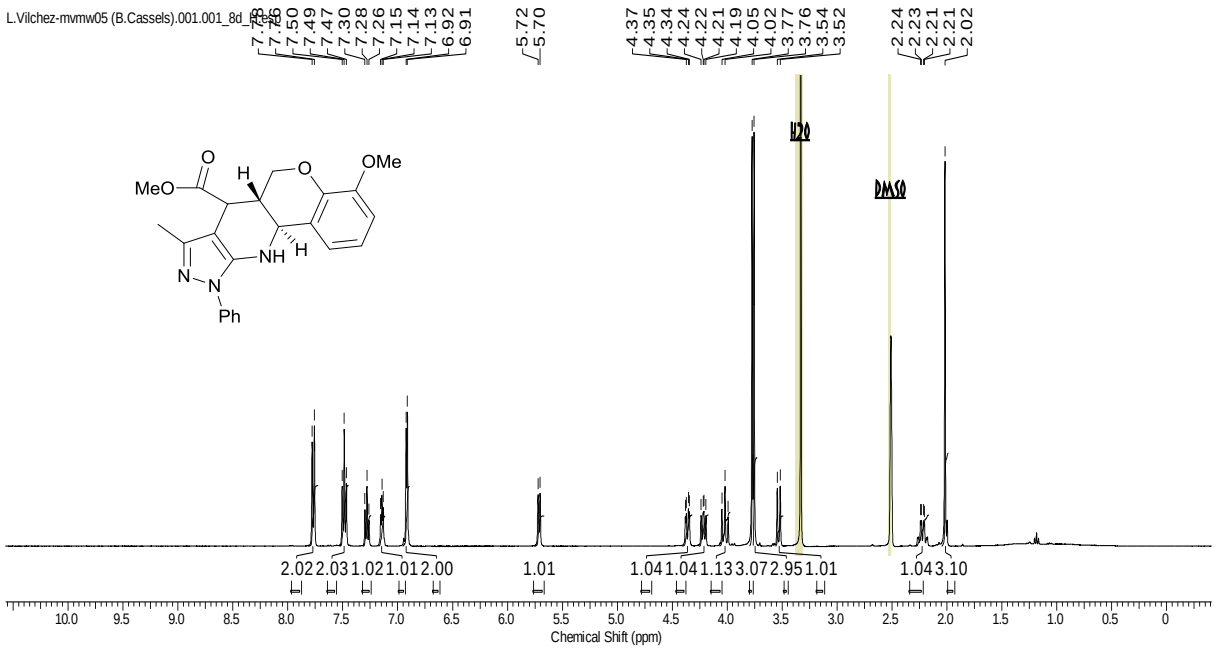

B.Cassels-mv09.002.001.1r.esp
173.70
154.22
145.85
145.45
139.74
129.41
128.99
127.44
125.87
123.21
121.51
121.09
116.57
100.42
99.99
67.17
53.12
52.58
37.87
12.89
O
O
O
NH
N
N
Ph
Chemical Shift (ppm)

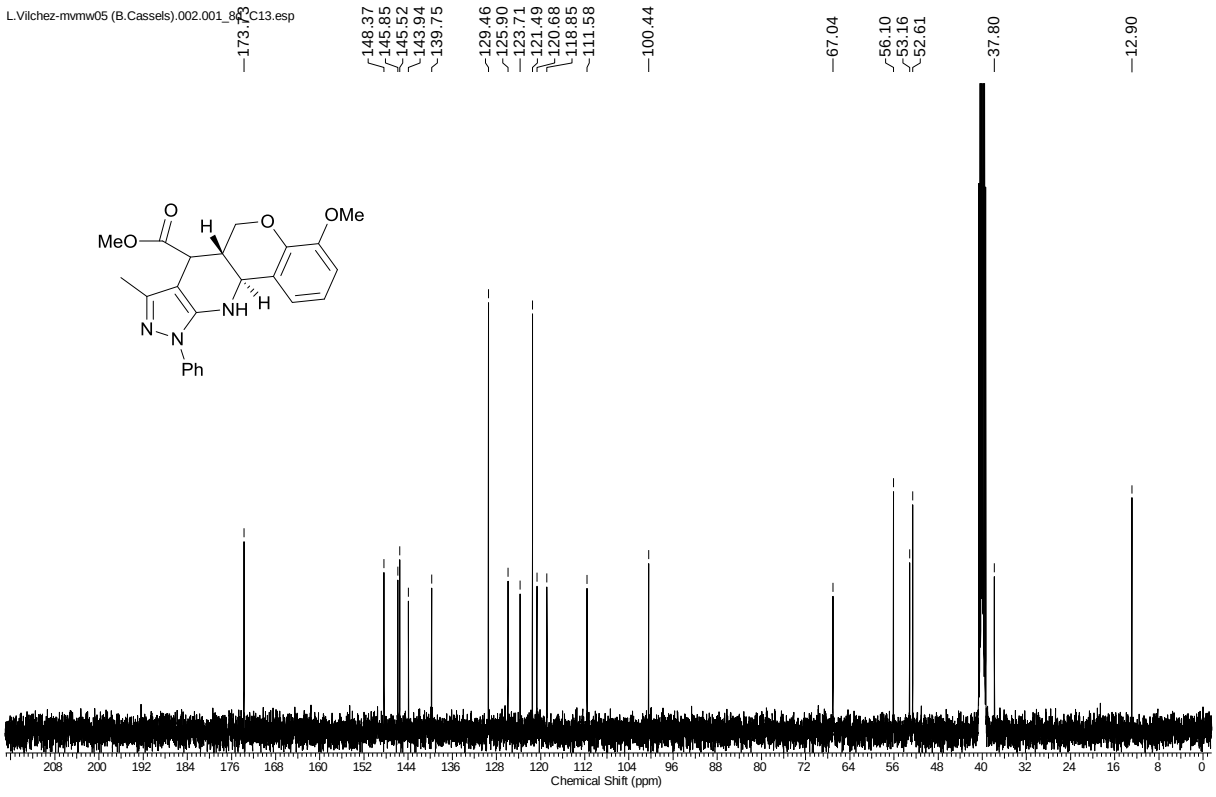




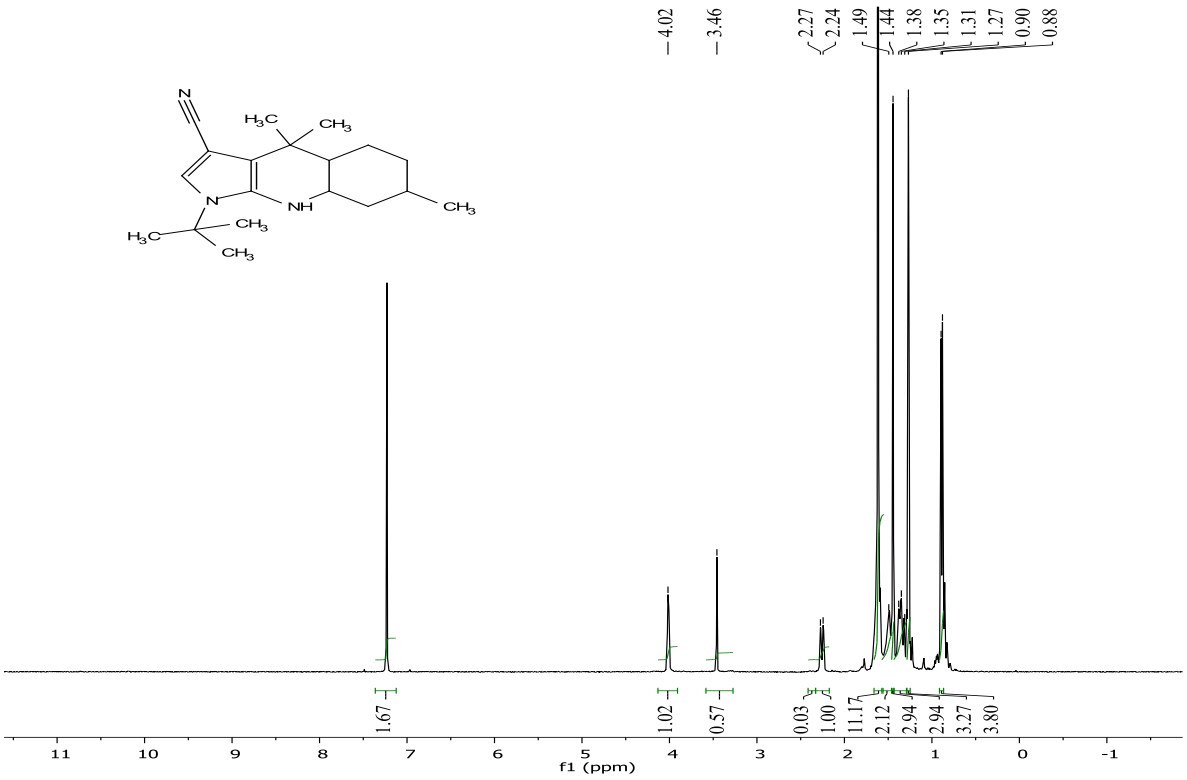
	H δ ppm	C δ ppm
H-6	4.34	67.17
H6´	4.06	67.17.
H11a	4.21	53.12
H6a	2.25	37.87
H7	3.51	40.41

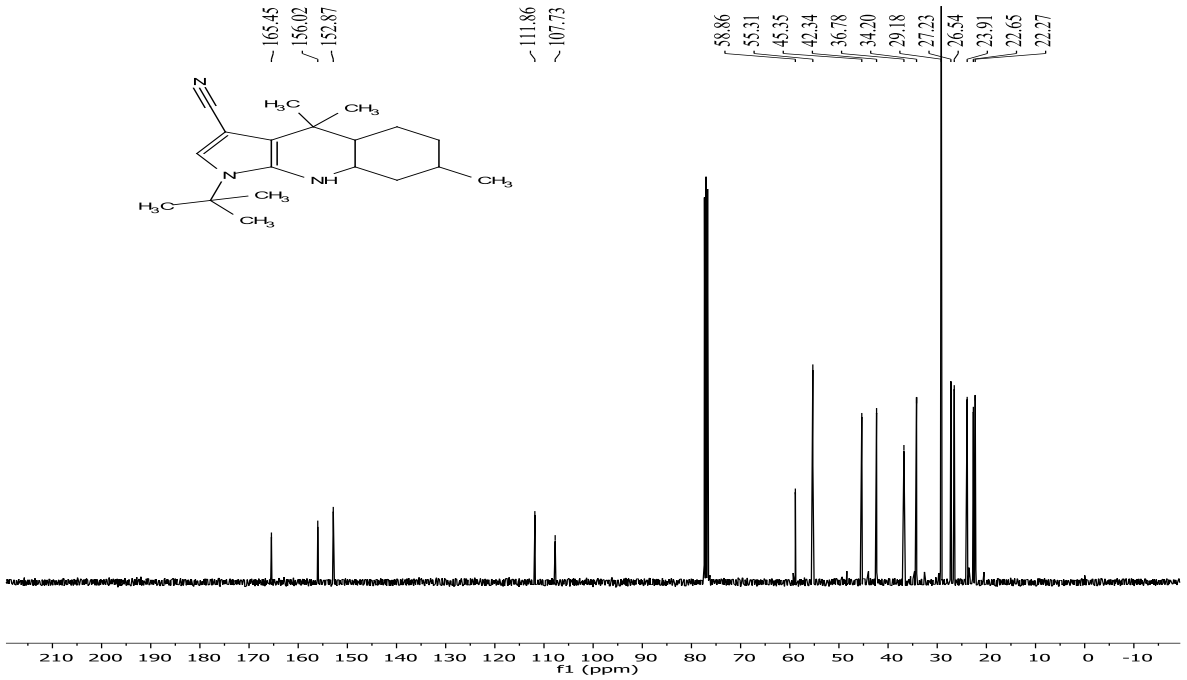
8d


L.Vilchez-mvmw05 (B.Cassels).001.001_8d_1H.esp
7.76
7.50
7.49
7.47
7.30
7.28
7.26
7.15
7.14
7.13
6.92
6.91
5.72
5.70
4.37
4.35
4.34
4.24
4.22
4.21
4.19
4.05
4.02
3.77
3.76
3.54
3.52
2.24
2.23
2.21
2.21
2.02
H2O
DMSO
MeO
O
H
O
OMe
NH
H
N
N
Ph
2.02 2.03 1.02 1.01 2.00
1.01
1.04 1.04 1.13 3.07 2.95 1.01
1.04 3.10
Chemical Shift (ppm)


L.Vilchez-mvmw05 (B.Cassels).002.001_8d_C13.esp
173.
148.37
145.85
145.52
143.94
139.75
129.46
125.90
123.71
121.49
120.68
118.85
111.58
100.44
67.04
56.10
53.16
52.61
37.80
12.90
MeO
O
H
O
OMe
NH
H
N
N
Ph
Chemical Shift (ppm)

10


4.02
3.46
2.27
2.24
1.49
1.44
1.38
1.35
1.31
1.27
0.90
0.88
1.67
1.02
0.57
0.03
1.00
11.17
2.12
2.94
2.94
3.27
3.80
f1 (ppm)


165.45
156.02
152.87
111.86
107.73
58.86
55.31
45.35
42.34
36.78
34.20
29.18
27.23
26.54
23.91
22.65
22.27
f1 (ppm)