Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

SUPPORTING INFORMATION

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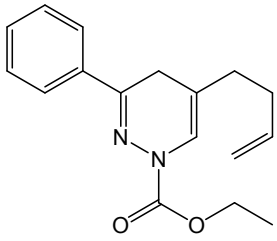
1. General Remarks.

All the commercially available reagents and solvents were used without further purification. 5-Methylene-6-methoxy-1,4,5,6-tetrahydropyridazines **1a–g** were prepared as described previously.[1] Chromatographic purification of compounds was carried out on silica gel (60–200 μm). TLC analysis was performed on pre-loaded (0.25 mm) glass supported silica gel plates (Kieselgel 60); compounds were visualized by exposure to UV light and by dipping the plates in 1% $Ce(SO_4)\cdot 4H_2O$, 2.5% $(NH_4)_6Mo_7O_{24}\cdot 4H_2O$ in 10% sulphuric acid followed by heating on a hot plate. All ^1H NMR and ^{13}C NMR spectra were recorded at 400 and 100 MHz, respectively, using $CDCl_3$ as solvent. Chemical shift (δ scale) are reported in parts per million (ppm) relative to the central peak of the solvent and are sorted in ascending order within each group. The following abbreviations are used to describe peak patterns where appropriate: s = singlet, d = doublet, t = triplet q = quartet and m = multiplet. All coupling constants (J value) are given in Hertz [Hz]. FT-IR spectra were obtained as Nujol mulls. Mass spectral data were obtained by electrospray ionization using a Q-TOF mass spectrometer in the positive ion mode (M+H or M+Na) as indicated. Elemental analyses were within ± 0.4 of the theoretical values (C, H, N).

2. Experimental procedures and spectral data.

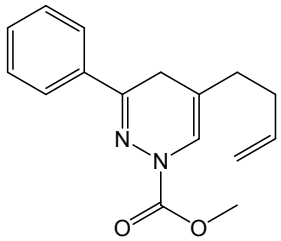
General Procedure for the Synthesis of 5-Methylenyl-1,4-dihydropyridazine Derivatives (3): To a solution of 5-methylene-6-methoxy-1,4,5,6-tetrahydropyridazine **1** (0.1 mmol) in CH_2Cl_2 (2 mL) at room temperature was added the appropriate nucleophile **2** (0.4 mmol) followed by the addition of $BF_3\cdot OEt_2$ (0.12 mmol). After completion (0.1–0.5 h, TLC monitoring), the reaction solvent was evaporated under reduced pressure and the crude mixture was purified by column chromatography on silica gel (ethyl acetate/cyclohexane) to afford the corresponding adduct **3**.

Note that the products **3a–r** were unstable, so they were immediately characterized after chromatographic purification.



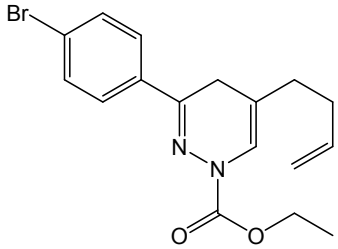
3a

Ethyl 5-(but-3-enyl)-3-phenylpyridazine-1(4*H*)-carboxylate (3a): Isolated by column chromatography on silica gel (ethyl acetate/cyclohexane, 1:9) in 73% yield. oil; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.40 (t, *J* = 7.2 Hz, 3H, OCH$_2$*CH$_3$*), 2.17–2.21 (m, 2H, *CH$_2$*CH$_2$CH=CH$_2$), 2.25–2.31 (m, 2H, CH$_2$*CH$_2$*CH=CH$_2$), 3.17 (s, 2H, C*CH$_2$*C), 4.37 (q, *J* = 7.2 Hz, 2H, O*CH$_2$*CH$_3$), 4.99–5.10 (m, 2H, CH$_2$CH$_2$CH=*CH$_2$*), 5.78–5.88 (m, 1H, CH$_2$CH$_2$*CH*=CH$_2$), 6.99 (s, 1H, N*CH*), 7.40–7.42 (m, 3H, Ph-H), 7.82–7.84 (m, 2H, Ph-H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.5 (q), 26.3 (t), 30.7 (t), 33.3 (t), 62.9 (t), 113.7 (s), 116.0 (t), 117.6 (d), 125.9 (d), 128.3 (d), 129.8 (d), 136.4 (s), 137.4 (d), 146.5 (s), 152.6 (s); IR (nujol): ν_{max} = 1726 cm^{-1}; MS *m/z* (ESI): 285 [M + H]$^+$; anal. calcd. for $C_{17}H_{20}N_2O_2$ (284,35): C 71.81, H 7.09, N 9.85; found: C 71.68, H 5.05, N 9.96.



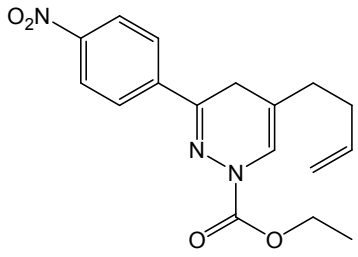
3b

Methyl 5-(but-3-en-1-yl)-3-phenylpyridazine-1(4*H*)-carboxylate (3b): Isolated by column chromatography on silica gel (ethyl acetate/cyclohexane, 1:9) in 69% yield. oil; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 2.17–2.21 (m, 2H, *CH$_2$*CH$_2$CH=CH$_2$), 2.25–2.31 (m, 2H, CH$_2$*CH$_2$*CH=CH$_2$), 3.17 (s, 2H, C*CH$_2$*C), 3.92 (s, 3H, O*CH$_3$*), 4.99–5.10 (m, 2H, CH$_2$CH$_2$CH=*CH$_2$*), 5.77–5.87 (m, 1H, CH$_2$CH$_2$*CH*=CH$_2$), 7.00 (s, 1H, N*CH*), 7.40–7.41 (m, 3H, Ph-H), 7.81–7.83 (m, 2H, Ph-H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 26.5 (t), 30.7 (t), 33.3 (t), 53.8 (q), 113.9 (s), 115.4 (t), 117.6 (d), 126.0 (d), 128.4 (d), 129.9 (d), 136.4 (s), 137.4 (d), 146.4 (s), 152.6 (s); IR (nujol): ν_{max} = 1721 cm^{-1}; MS *m/z* (ESI): 271 [M + H]$^+$; anal. calcd. for $C_{16}H_{18}N_2O_2$ (270,33): C, 71.09; H, 6.71; N, 10.36; found: C, 71.22; H, 6.64; N, 10.25.



3c

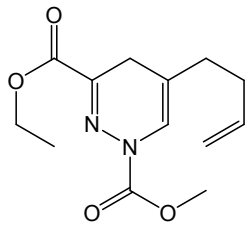
Ethyl 3-(4-bromophenyl)-5-(but-3-en-1-yl)pyridazine-1(4*H*)-carboxylate (3c): Isolated by column chromatography on silica gel (ethyl acetate/cyclohexane, 1:9) in 75% yield. oil; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.38 (t, *J* = 7.2 Hz, 3H, OCH$_2$*CH$_3$*), 2.16–2.20 (m, 2H, *CH$_2$*CH$_2$CH=CH$_2$), 2.24–2.28 (m, 2H, CH$_2$*CH$_2$*CH=CH$_2$), 3.13 (s, 2H, C*CH$_2$*C), 4.38 (q, *J* = 7.2 Hz, 2H, O*CH$_2$*CH$_3$), 5.00–5.09 (m, 2H, CH$_2$CH$_2$CH=*CH$_2$*), 5.78–5.84 (m, 1H, CH$_2$CH$_2$*CH*=CH$_2$), 6.98 (s, 1H, N*CH*), 7.54 (d, *J* = 8.8 Hz, 2H, Ph-H), 7.70 (d, *J* = 8.8 Hz, 2H, Ph-H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.5 (q), 26.2 (t), 30.6 (t), 33.3 (t), 63.0 (t), 113.6 (s), 115.4 (t), 117.6 (d), 124.1 (d), 127.5 (d), 131.5 (s), 135.3 (s), 137.4 (d), 144.8 (s), 152.6 (s); IR (nujol): ν_{max} = 1732 cm^{-1}; MS *m/z* (ESI): 365 (100), 363 (100) [M + H]$^+$; anal. calcd. for $C_{17}H_{19}BrN_2O_2$ (363,25): C, 56.21; H, 5.27; N, 7.71; found: C, 56.36; H, 5.19; N, 7.63.



3d

Ethyl 5-(but-3-enyl)-3-(4-nitrophenyl)pyridazine-1(4*H*)-carboxylate (3d):

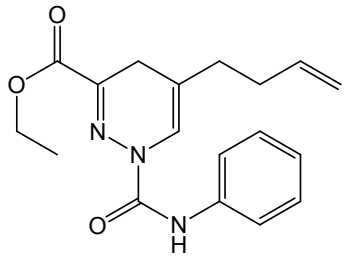
Isolated by column chromatography on silica gel (ethyl acetate/cyclohexane, 1:9) in 79% yield. oil; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.40 (t, *J* = 7.2 Hz, 3H, OCH_2CH_3), 2.18–2.22 (m, 2H, $CH_2CH_2CH{=}CH_2$), 2.26–2.35 (m, 2H, $CH_2CH_2CH{=}CH_2$), 3.19 (s, 2H, CCH_2C), 4.38 (q, *J* = 7.2 Hz, 2H, OCH_2CH_3), 5.01–5.10 (m, 2H, $CH_2CH_2CH{=}CH_2$), 5.81–5.83 (m, 1H, $CH_2CH_2CH{=}CH_2$), 6.99 (s, 1H, NCH), 7.98 (d, *J* = 8.8 Hz, 2H, Ph-H), 8.25 (d, *J* = 8.8 Hz, 2H, Ph-H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.5 (q), 26.2 (t), 30.5 (t), 33.2 (*t*), 63.3 (t), 114.0 (*s*), 115.6 (t), 117.5 (d), 123.6 (d), 126.7 (d), 136.4 (s), 137.2 (d), 142.3 (s), 148.3 (s), 152.0 (s); IR (nujol): ν_{max} = 1725 cm^{-1}; MS *m/z* (ESI): 330 [M + H$^+$]; anal. calcd. for $C_{17}H_{19}N_3O_4$ (329,35): C, 62.00; H, 5.81; N, 12.76; found: C, 62.14; H, 5.85; N, 12.66.



3e

3-Ethyl 1-methyl 5-(but-3-en-1-yl)pyridazine-1,3(4*H*)-dicarboxylate (3e):

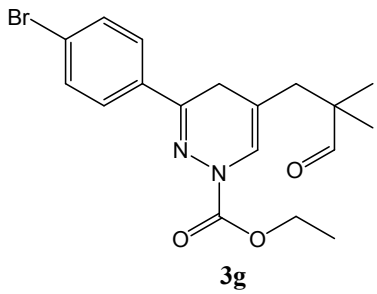
Isolated by column chromatography on silica gel (ethyl acetate/cyclohexane, 1:9) in 26% yield. oil; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C δ = 1.38 (t, *J* = 7.2 Hz, 3H, OCH_2CH_3), 2.10–2.14 (m, 2H, $CH_2CH_2CH{=}CH_2$), 2.20–2.23 (m, 2H, $CH_2CH_2CH{=}CH_2$), 3.04 (s, 2H, CCH_2C), 3.91 (s, 3H, OCH_3), 4.35 (q, *J* = 7.2 Hz, 2H OCH_2CH_3) 5.01–5.07 (m, 2H, $CH_2CH_2CH{=}CH_2$), 5.74–5.81 (m, 1H, $CH_2CH_2CH{=}CH_2$), 6.85 (s, 1H, NCH); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.1 (q), 25.3 (t), 30.3 (t), 33.0 (t), 54.4 (q), 62.2 (t), 115.6 (s), 116.1 (t), 117.0 (d), 137.4 (d), 139.8 (s), 152.4 (s) 164.0 (s); IR (nujol): ν_{max} = 1723, 1706 cm^{-1}; MS *m/z* (ESI): 267 [M + H$^+$]; anal. calcd. for $C_{13}H_{18}N_2O_4$ (266,29): C, 58.63; H, 6.81; N, 10.52; found: C, 58.74; H, 6.75; N, 10.59.



3f

Ethyl 5-(but-3-enyl)-1-(phenylcarbamoyl)-1,4-dihydropyridazine-3-carboxylate (3f):

Isolated by column chromatography on silica gel (ethyl acetate/cyclohexane, 1:9) in 31% yield. oil; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C δ = 1.39 (t, *J* = 7.2 Hz, 3H, OCH_2CH_3), 2.12–2.16 (m, 2H, $CH_2CH_2CH{=}CH_2$), 2.22–2.27 (m, 2H, $CH_2CH_2CH{=}CH_2$), 3.11 (s, 2H, CCH_2C), 4.35 (q, *J* = 7.2 Hz, 2H OCH_2CH_3) 4.99–5.09 (m, 2H, $CH_2CH_2CH{=}CH_2$), 5.79–5.80 (m, 1H, $CH_2CH_2CH{=}CH_2$), 7.08–7.12 (m, 2H, NCH and Ph-H), 7.31–7.35 (m, 2H, Ph-H), 7.51–7.53 (m, 2H, Ph-H), 8.62 (s, H, NH);^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.2 (q), 25.5 (t), 30.2 (t), 33.2 (t), 61.9 (t), 114.9 (s), 115.4 (t), 115.5 (d), 119.7 (d), 123.8 (d), 129.0 (d), 136.6 (s), 137.2 (d), 137.5 (s), 149.6 (s) 163.7 (s); IR (nujol): ν_{max} = 1718, 1702 cm^{-1}; MS *m/z* (ESI): 350 [M + Na]$^+$, 328 [M + H]$^+$; anal. calcd. for $C_{18}H_{21}N_3O_3$ (327,38): C, 66.04; H, 6.47; N, 12.84; found: C, 66.19; H, 6.41; N, 12.76.

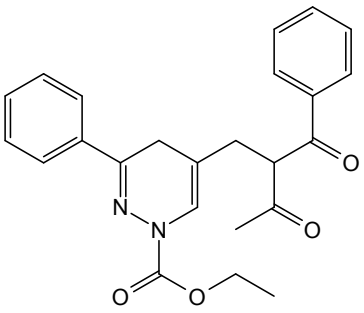


3g

Ethyl 3-(4-bromophenyl)-5-(2,2-dimethyl-3-oxopropyl)pyridazine-1(4*H*)-carboxylate (3g):

Isolated by column chromatography on silica gel (ethyl acetate/cyclohexane, 1:9) in 65% yield. oil; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.12 (s, 6H, $CH_2C(CH_3)_2CHO$) 1.39 (t, *J* = 7.2 Hz, 3H, OCH_2CH_3), 2.32 (s, 2H, $CH_2C(CH_3)_2CHO$), 3.01 (s, 2H, CCH_2C), 4.36 (q, *J* = 7.2 Hz, 2H, OCH_2CH_3), 6.98 (s, 1H, NCH), 7.52

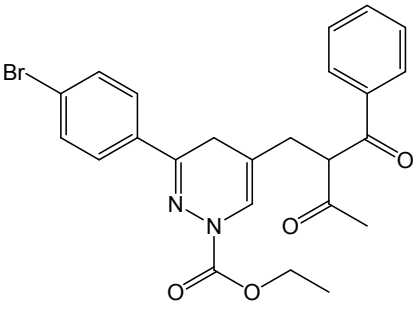
(d, *J* = 8.8 Hz, 2H, Ph-H), 7.64 (d, *J* = 8.8 Hz, 2H, Ph-H), 9.58 (s, 1H $CH_2C(CH_3)_2CHO$); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.5 (q), 22.1 (q), 27.6 (t), 41.6 (t), 46.2 (s), 63.2 (t), 110.2 (s), 120.7 (d), 124.4 (s), 127.6 (d), 131.6 (d), 135.0 (s), 139.4 (s), 144.9 (s), 205.6 (d); IR (nujol): ν_{max} = 1725, 1717 cm^{-1}; MS *m/z* (ESI): 395 (100), 393 (100) $[M + H]^+$; anal. calcd. for $C_{18}H_{21}BrN_2O_3$ (393,27): C, 54.97; H, 5.38; N, 7.12; found: C, 54.82; H, 5.31; N, 7.17.



3h

Ethyl 5-(2-benzoyl-3-oxobutyl)-3-phenylpyridazine-1(4*H*)-carboxylate (3h):

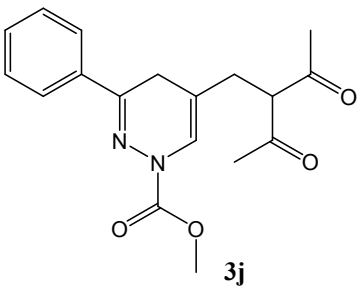
Isolated by column chromatography on silica gel (ethyl acetate/cyclohexane, 1:9) in 94% yield. oil; ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.37 (t, *J* = 7.2 Hz, 3H, OCH_2CH_3), 2.17 (s, 3H CH_3CO), 2.81 (d, *J* = 7.2 Hz, 2H, CCH_2CH), 3.15 (s, 2H, CCH_2C), 4.33 (q, *J* = 7.2 Hz, 2H, OCH_2CH_3), 4.70 (t, *J* = 7.2 Hz, 1H, CCH_2CH), 7.01 (s, 1H, NCH), 7.49–8.01 (m, 10H, Ph-H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.5 (q), 26.4 (q), 28.0 (t), 33.0 (t), 61.0 (d), 63.0 (t), 110.5 (s), 119.4 (d), 126.0 (d), 128.4 (d), 128.7 (d), 129.0 (d), 130.0 (d), 134.0 (d), 136.0 (s), 136.1 (s), 145.9 (s), 153.9 (s), 195.4 (s), 203.0 (s); IR (nujol): ν_{max} = 1725, 1714 cm^{-1}; MS *m/z* (ESI): 405 $[M + H^+]$; anal. calcd. for $C_{24}H_{24}N_2O_4$ (404,46): C, 71.23; H, 5.98; N, 6.93; found: C, 71.10; H, 5.89; N, 6.84.



3i

Ethyl 5-(2-benzoyl-3-oxobutyl)-3-(4-bromophenyl)pyridazine-1(4*H*)-carboxylate (3i):

Isolated by column chromatography on silica gel (ethyl acetate/cyclohexane, 1:9) in 83% yield. oil; ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.36 (t, *J* = 7.2 Hz, 3H, OCH_2CH_3), 2.17 (s, 3H CH_3CO), 2.80 (d, *J* = 7.2 Hz, 2H, CCH_2CH), 3.10 (s, 2H, CCH_2C), 4.33 (q, *J* = 7.2 Hz, 2H, OCH_2CH_3), 4.69 (t, *J* = 7.2 Hz, 1H, CCH_2CH), 6.99 (s, 1H, NCH), 7.49–8.00 (m, 9H, Ph-H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.5 (q), 26.2 (q), 28.0 (t), 32.9 (t), 61.0 (d), 63.1 (t), 110.5 (s), 119.4 (d), 124.3 (d), 127.5 (d), 128.7 (d), 129.0 (d), 131.5 (d), 134.0 (s), 134.9 (s), 136.1 (s), 144.7 (s), 152.2 (s), 195.3 (s), 202.9 (s); IR (nujol): ν_{max} = 1732, 1721 cm^{-1}; MS *m/z* (ESI): 485 (100), 483 (100) $[M + H]^+$; anal. calcd. for $C_{24}H_{23}BrN_2O_4$ (483,35): C, 59.64; H, 4.80; N, 5.80; found: C, 59.51; H, 4.75; N, 5.89.

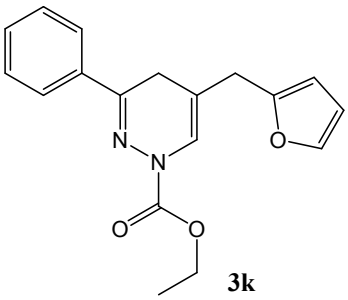


3j

Methyl 5-(2-acetyl-3-oxobutyl)-3-phenylpyridazine-1(4*H*)-carboxylate (3j):

Isolated by column chromatography on silica gel (ethyl acetate/cyclohexane, 1:9) in 42% yield. oil; ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 2.14 (s, 6H, $COCH_3$ enol form), and 2.22 (s, 6H, $COCH_3$), 2.64 (d, *J* = 7.2 Hz, 2H, CCH_2CH) and 2.99 (s, 2H, CCH_2C= enol form), 3.14 (s, 2H, CCH_2C) and 3.19 (s, 2H, CCH_2C enol form), 3.92 (s, 3H, OCH_3), 3.95–3.99 (m, 1H, CCH_2CH), 6.89 (s, 1H, NCH enol form) and 7.01 (s, 1H, NCH), 7.40–7.43 (m, 3H, Ph-H) and 7.80–7.82 (m, 2H, Ph-H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 23.1 (q, enol form), 26.4 (q) 26.8 (q, enol form), 29.1 (t, enol form) 29.7 (t), 32.0 (t, enol form), 32.1 (t), 54.0 (q), 66.1 (d), 104.9 (s, enol form), 110.5

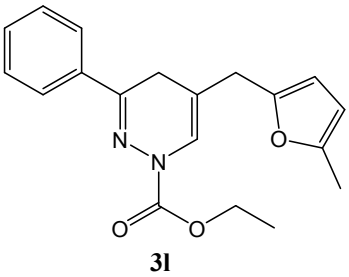
(s), 112.7 (s, enol form), 117.8 (d, enol form), 119.4 (d), 125.9 (d, enol form), 126.0 (d), 128.4 (d), 128.5 (d, enol form), 130.0 (d, enol form), 130.1 (d), 136.0 (s), 136.1 (s, enol form), 145.9 (s, enol form), 146.1 (s), 153.0 (s), 191.8 (s, enol form), 202.9 (s); IR (nujol): ν_{max} = 1730, 1708 cm^{-1}; MS *m/z* (ESI): 329 [M + H^+]; anal. calcd. for $C_{18}H_{20}N_2O_4$ (328,36): C, 65.84; H, 6.14; N, 8.53; found: C, 65.71; H, 6.19; N, 8.47.



3k

Ethyl 5-(furan-2-ylmethyl)-3-phenylpyridazine-1(4*H*)-carboxylate (3k):

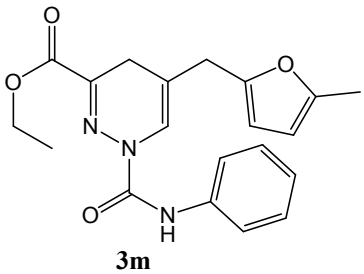
Isolated by column chromatography on silica gel (ethyl acetate/cyclohexane, 1:4) in 56% yield. oil; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.40 (t, *J* = 7.2 Hz, 3H, OCH_2CH_3), 3.15 (s, 2H, CCH_2C), 3.43 (s, 2H, $CCH_2C_4H_4O$), 4.37 (q, *J* = 7.2 Hz, 2H, OCH_2CH_3), 6.12 (dd, 1H, J_1 = 2.8 Hz, J_2 = 0.8 Hz, furan), 6.31 (dd, 1H, J_1 = 2.8 Hz, J_2 = 2.0 Hz, furan), 7.11 (s, 1H, N*CH*), 7.34 (dd, 1H, J_1 = 2.0 Hz, J_2 = 0.8 Hz, furan), 7.34–7.40 (m, 3H, Ph-H), 7.79–7.81 (m, 2H, Ph-H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.5 (q), 26.0 (t), 32.9 (t), 63.0 (t), 106.9 (d), 110.4(d), 110.8 (s), 118.9 (d), 126.0 (d), 128.3 (d), 129.8 (d), 136.4 (s), 141.8 (d), 146.5 (s), 151.6 (s), 152.6 (s); IR (nujol): ν_{max} = 1705 cm^{-1}; MS *m/z* (ESI): 333 [M + Na]$^+$, 311 [M + H]$^+$; anal. calcd. for $C_{18}H_{18}N_2O_3$ (310,35): C, 69.66; H, 5.85; N, 9.03; found: C, 69.73; H, 5.81; N, 9.09.



3l

Ethyl 5-((5-methylfuran-2-yl)methyl)-3-phenylpyridazine-1(4*H*)-carboxylate (3l):

Isolated by column chromatography on silica gel (ethyl acetate/cyclohexane, 1:4) in 94% yield. oil; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.40 (t, *J* = 7.2 Hz, 3H, OCH_2CH_3), 2.26 (d, *J* = 0.8 Hz, 3H, CCH_3), 3.15 (s, 2H, CCH_2C), 3.37 (s, 2H, $CCH_2C_4H_3O$), 4.37 (q, *J* = 7.2 Hz, 2H, OCH_2CH_3), 5.87 (d, J_1 = 2.8 Hz, J_2 = 0.8 Hz, 1H, furan), 5.98 (d, *J* = 2.8 Hz, 1H, furan), 7.10 (s, 1H, N*CH*), 7.39–7.40 (m, 3H, Ph-H), 7.79–7.82 (m, 2H, Ph-H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 13.5 (q) 14.5 (q), 25.9 (t), 33.0 (t), 63.0 (t), 106.1 (d), 107.6 (d), 111.1 (s), 118.8 (d), 126.0 (d), 128.3 (d), 129.8 (d), 136.3 (s), 146.2 (d), 149.5 (s), 151.3 (s), 152.4 (s); IR (nujol): ν_{max} = 1728 cm^{-1}; MS *m/z* (ESI): 325 [M + H^+]; anal. calcd. for $C_{19}H_{20}N_2O_3$ (324,37): C, 70.35; H, 6.21; N, 8.64; found: C, 70.20; H, 6.25; N, 8.58.

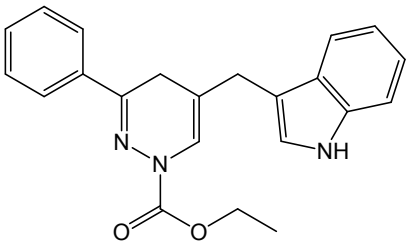


3m

Ethyl 5-((5-methylfuran-2-yl)methyl)-1-(phenylcarbamoyl)-1,4-dihydropyridazine-3-carboxylate (3m):

Isolated by column chromatography on silica gel (ethyl acetate/cyclohexane, 1:4) in 30% yield. oil; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.38 (t, *J* = 7.2 Hz, 3H, OCH_2CH_3), 2.25 (d, *J* = 0.8 Hz, 3H, CCH_3), 3.09 (s, 2H, CCH_2C), 3.31 (s, 2H, $CCH_2C_4H_3O$), 4.33 (q, *J* = 7.2 Hz, 2H, OCH_2CH_3), 5.87 (d, J_1 = 2.8 Hz, J_2 = 0.8 Hz, 1H, furan), 5.98 (d, *J* = 2.8 Hz, 1H, furan), 7.10 (t, *J* = 7.6 Hz, 1H, Ph-H),7.17 (s, 1H, N*CH*), 7.34 (t, *J* = 7.6 Hz, 2H, Ph-H), 7.52 (t, *J* = 7.6 Hz, 2H, Ph-H), 8.61 (s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 13.6 (q),14.5 (q), 25.3 (t), 32.9 (t), 61.9 (t), 106.2 (d), 107.9 (d), 112.6 (s), 116.5 (d), 119.7 (d), 123.9 (d), 129.0 (d), 137.0 (s), 137.4 (s), 148.7 (s), 149.6 (s), 151.5 (s), 163.6 (s); IR (nujol): ν_{max}

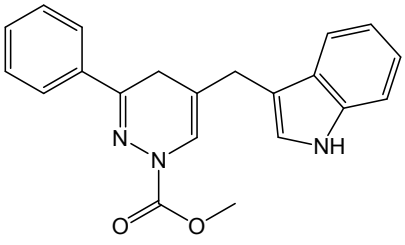
= 1726 cm^{-1}; MS *m/z* (ESI): 368 [M + H^+]; anal. calcd. for $C_{20}H_{21}N_3O_4$ (367,40): C, 65.38; H, 5.76; N, 11.44; found: C, 65.25; H, 5.74; N, 11.54.



3n

Ethyl 5-[(1*H*-indol-3-yl)methyl]-3-phenylpyridazine-1(4*H*)-carboxylate (3n):

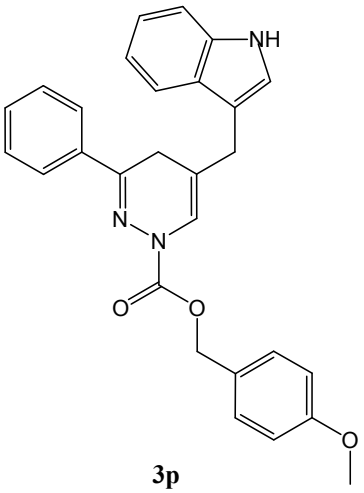
Isolated by column chromatography on silica gel (ethyl acetate/cyclohexane, 2:3) in 41% yield. oil; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.41 (t, *J* = 7.2 Hz, 3H, $OCH_2\mathit{CH_3}$) 3.15 (s, 2H, $C\mathit{CH_2}C$), 3.57 (s, 2H, $C\mathit{CH_2}C_8H_6N$), 4.38 (q, *J* = 7.2 Hz, 2H, $O\mathit{CH_2}CH_3$), 7.04 (d, *J* = 2.4 Hz, 1H, Indole-H), 7.13–7.26, (m, 3H, N*CH,* Indole-H) 7.32–7.38 (m, 4H, Ph-H, Indole-H) 7.64 (d, *J* = 7.6 Hz, 1H, Indole-H) 7.74–7.76 (m, 2H, Ph-H) 8.12 (s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 15.5 (q), 26.1 (t), 30.2 (t), 62.9 (t), 111.2 (d), 111.6 (s), 113.7(s), 117.9 (d), 118.9 (d), 119.5 (d*)*, 122.1 (d), 122.5 (d), 126.0 (d), 127.5 (s), 128.2 (d), 129.7 (d), 136.4 (s), 136.4 (s), 146.4 (s), 152.5 (s); IR (nujol): ν_{max} = 3285, 1713 cm^{-1}; MS *m/z* (ESI): 360 [M + H^+]; anal. calcd. for $C_{22}H_{21}N_3O_2$ (359,42): C, 73.52; H, 5.89; N, 11.69; found: C, 73.67; H, 5.96; N, 11.74.



3o

Methyl 5-[(1*H*-indol-3-yl)methyl]-3-phenylpyridazine-1(4*H*)-carboxylate (3o):

Isolated by column chromatography on silica gel (ethyl acetate/cyclohexane, 2:3) in 49% yield. oil; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 3.15 (s, 2H, $C\mathit{CH_2}C$), 3.57 (s, 2H, $C\mathit{CH_2}C_8H_6N$), 3.94 (s, 3H, $O\mathit{CH_3}$), 7.03 (d, *J* = 1.6 Hz, 1H, Indole-H), 7.13–7.21, (m, 3H, N*CH,* Indole-H) 7.35–7.37 (m, 4H, Ph-H, Indole-H) 7.64 (d, *J* = 7.6 Hz, 1H, Indole-H) 7.73–7.75 (m, 2H, Ph-H), 8.14 (s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 26.2 (t), 30.1 (t), 53.8 (q), 111.2 (d), 111.4 (s), 114.0 (s), 117.8 (d), 118.8 (d), 119.5 (d), 122.1 (d), 122.5 (d), 126.0 (d), 127.5 (s), 128.3 (d), 129.8 (d), 136.3 (s), 136.4 (s), 146.9 (s), 153.3 (s); IR (nujol): ν_{max} = 3285, 1732 cm^{-1}; MS *m/z* (ESI): 346 [M + H^+]; anal. calcd. for $C_{21}H_{19}N_3O_2$ (345,39): C, 73.03; H, 5.54; N, 12.17; found: C, 73.17; H, 5.58; N, 12.10.

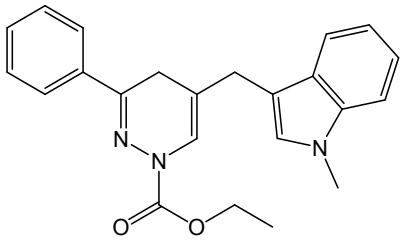


3p

4-Methoxybenyl 5-[(1*H*-indol-3-yl)methyl]-3-phenylpyridazine-1(4*H*)-carboxylate (3p):

Isolated by column chromatography on silica gel (ethyl acetate/cyclohexane, 2:3) in 47% yield. oil; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 3.14 (s, 2H, $C\mathit{CH_2}C$), 3.55 (s, 2H, $C\mathit{CH_2}C_8H_6N$), 3.81 (s, 3H, $O\mathit{CH_3}$), 5.39 (s, 2H, $O\mathit{CH_2}$Ph), 6.90 (d, *J* = 8.8 Hz, 2H, Ph-H), 7.04 (d, *J* = 2.4 Hz, 1H, Indole), 7.10–7.20, (m, 3H, N*CH,* Indole-H) 7.35–7.30 (m, 6H, Ph-H, Indole-H) 7.62 (d, *J* = 8.0 Hz, 1H, Indole-H), 7.73–7.75 (m, 2H, Ph-H) 8.07 (s, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 26.1 (t), 30.1 (t), 55.3 (q), 68.1 (t), 111.2 (d), 111.6 (s), 113.9 (s), 117.9 (d), 118.9 (d), 119.6 (d), 122.2 (d), 122.5 (d), 126.0 (d), 127.5 (s), 128.2 (d), 128.2 (d), 128.6 (s), 129.7 (d), 130.0 (d), 136.3 (s), 136.4 (s), 146.6 (s), 152.7 (s), 159.6 (s); IR (nujol): ν_{max} = 3295, 1724 cm^{-1}; MS *m/z*

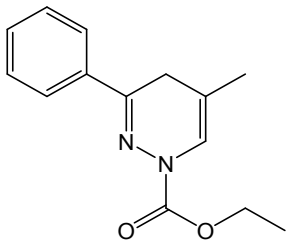
(ESI): 452 [M + H^+]; anal. calcd. for $C_{28}H_{25}N_3O_3$ (451,52): C, 74.48; H, 5.58; N, 9.31; found: C, 74.31; H, 5.52; N, 9.39.



3q

Ethyl 5-[(1-methyl-1*H*-indol-3-yl)methyl]-3-phenylpyridazine-1(4*H*)-carboxylate (3q):

Isolated by column chromatography on silica gel (ethyl acetate/cyclohexane, 2:3) in 58% yield. oil; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.40 (t, *J* = 7.2 Hz, 3H, OCH_2CH_3) 3.15 (s, 2H, CCH_2C), 3.56 (s, 2H, $CCH_2C_9H_8N$), 3.76 (s, 3H, NCH_3) 4.38 (q, *J* = 7.2 Hz, 2H, OCH_2CH_3), 6.91 (s, 1H, Indole-H), 7.09–7.31, (m, 4H, N*CH,* Indole-H) 7.35–7.37 (m, 3H, Ph-H) 7.62 (d, *J* = 8.0 Hz, 1H, Indole-H) 7.74–7.76 (m, 2H, Ph-H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.6 (q), 26.1 (t), 30.1 (t), 32.7 (q), 62.9 (t), 109.2 (d), 110.0 (s), 113.9 (s), 117.8 (d), 118.9 (d), 119.0 (d), 121.7 (d), 126.0 (d), 127.2 (d), 127.9 (s), 128.2 (d), 129.7 (d), 136.4 (s), 137.2 (s), 146.4 (s), 152.7 (s); IR (nujol): ν_{max} = 1718 cm^{-1}; MS *m/z* (ESI): 374 [M + H^+]; anal. calcd. for $C_{23}H_{23}N_3O_2$ (373,45): C, 73.97; H, 6.21; N, 11.25; found: C, 73.79; H, 6.25; N, 11.31.



3r

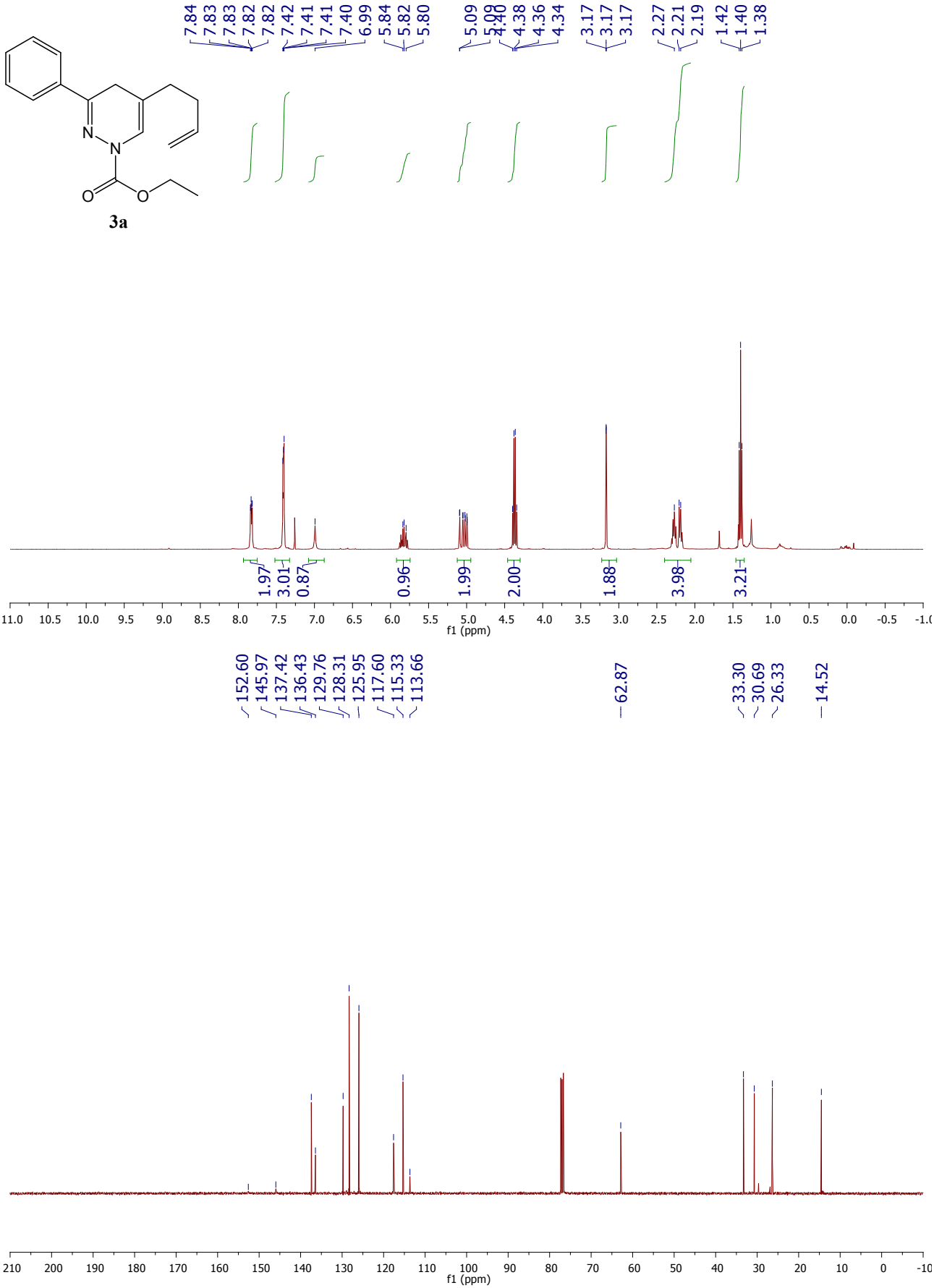
Ethyl 5-methyl-3-phenylpyridazine-1(4*H*)-carboxylate (3r):

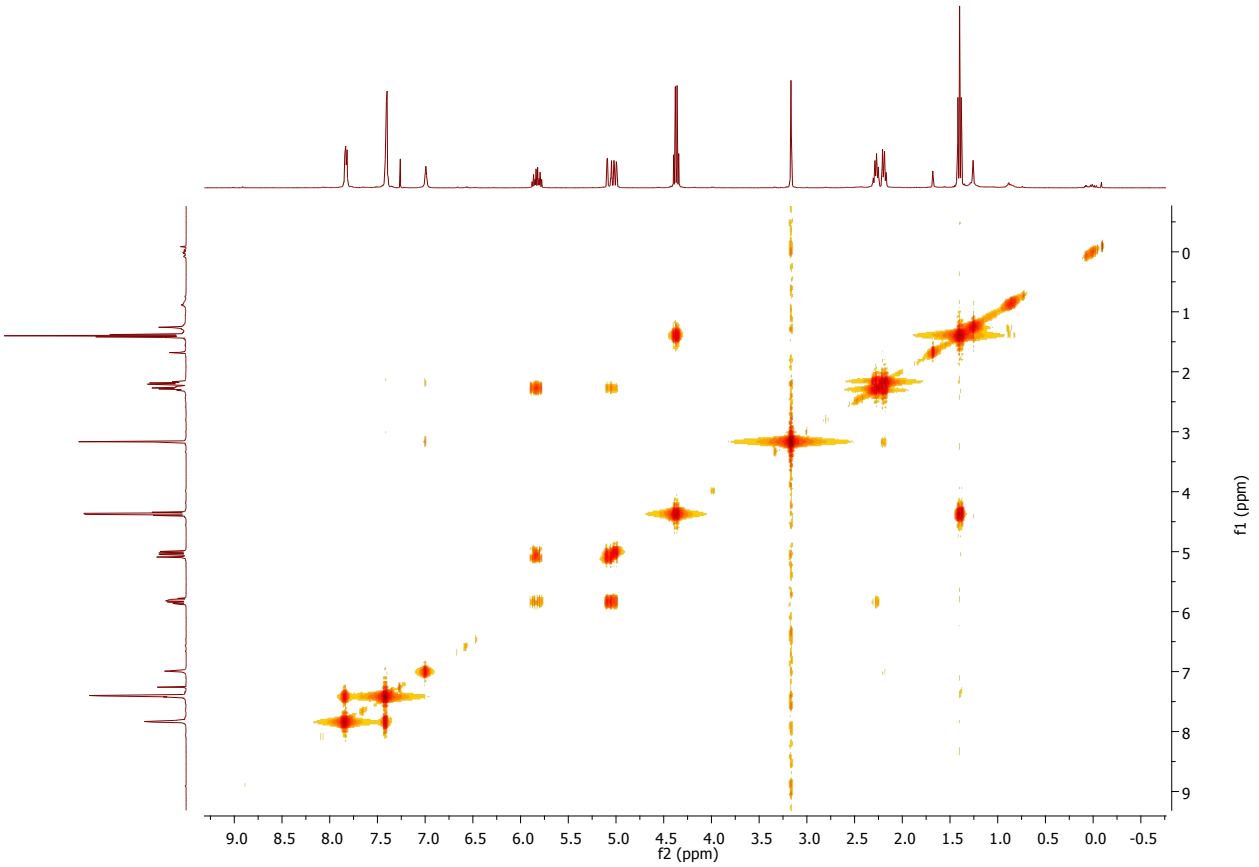
Isolated by column chromatography on silica gel (ethyl acetate/cyclohexane, 1:9) in 53% yield. oil; ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.40 (t, *J* = 7.2 Hz, 3H OCH_2CH_3) 1.78 (s, 3H, CCH_3), 3.15 (s, 2H, CCH_2C), 4.36 (q, *J* = 7.2 Hz, 2H, OCH_2CH_3), 6.97 (s, 1H, N*CH*), 7.40–7.42 (m, 3H, Ph-H), 7.83 (m, 2H, Ph-H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.6 (q), 19.8 (q), 27.9 (t), 62.9 (t), 110.7 (s), 117.2 (d), 125.9 (d), 128.3 (d), 129.8 (d), 136.4 (s), 145.9 (s), 152.6 (s); IR (nujol): ν_{max} =1725 cm^{-1}; MS *m/z* (ESI): 245 [M + H^+]; anal. calcd. for $C_{14}H_{16}N_2O_2$ (244,29): C, 68.83; H, 6.60; N, 11.47; found: C, 68.96; H, 6.65; N, 11.40.

3. References and notes

1 O. A. Attanasi, G. Favi, F. Mantellini, S. Mantenuto, G. Moscatelli and S. Nicolini, *Synlett* 2015, 193.

4. ^{1}H and ^{13}C NMR spectra of products.

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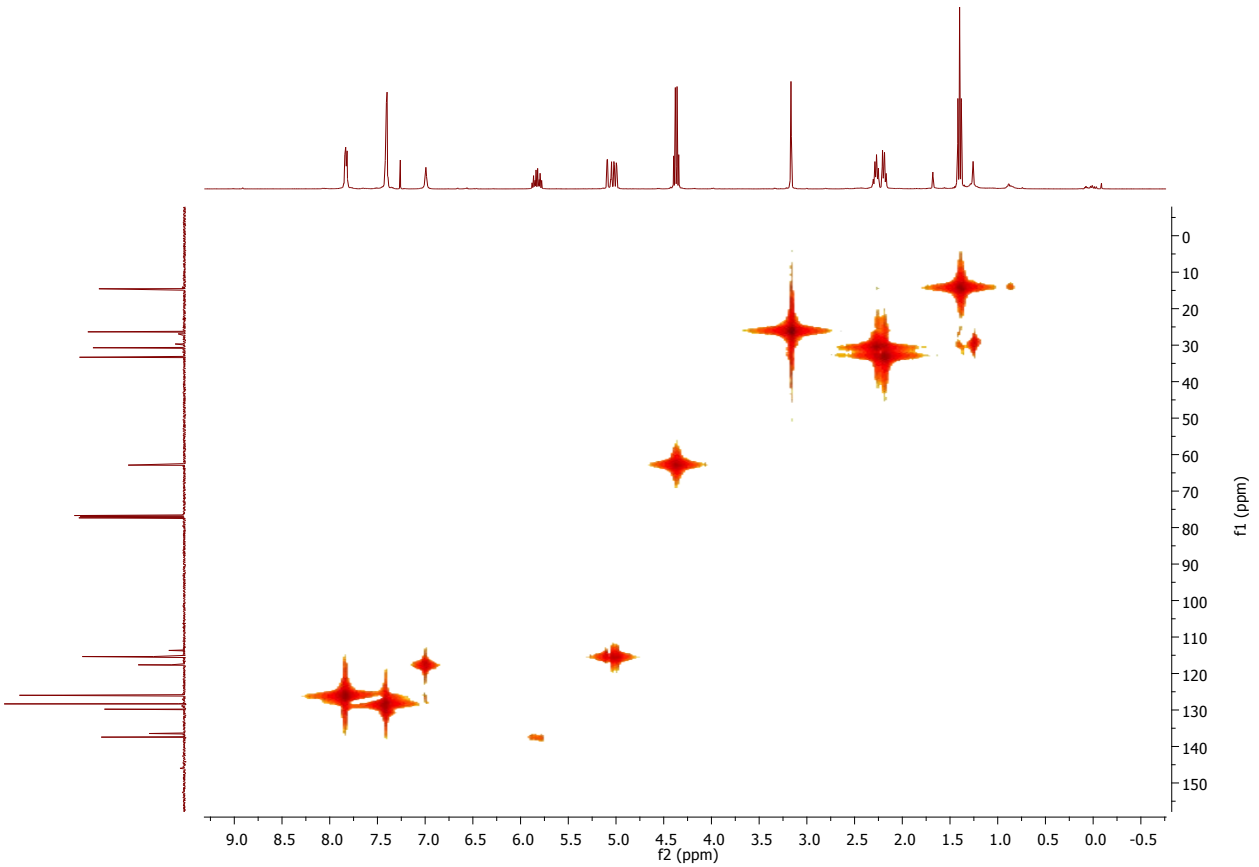
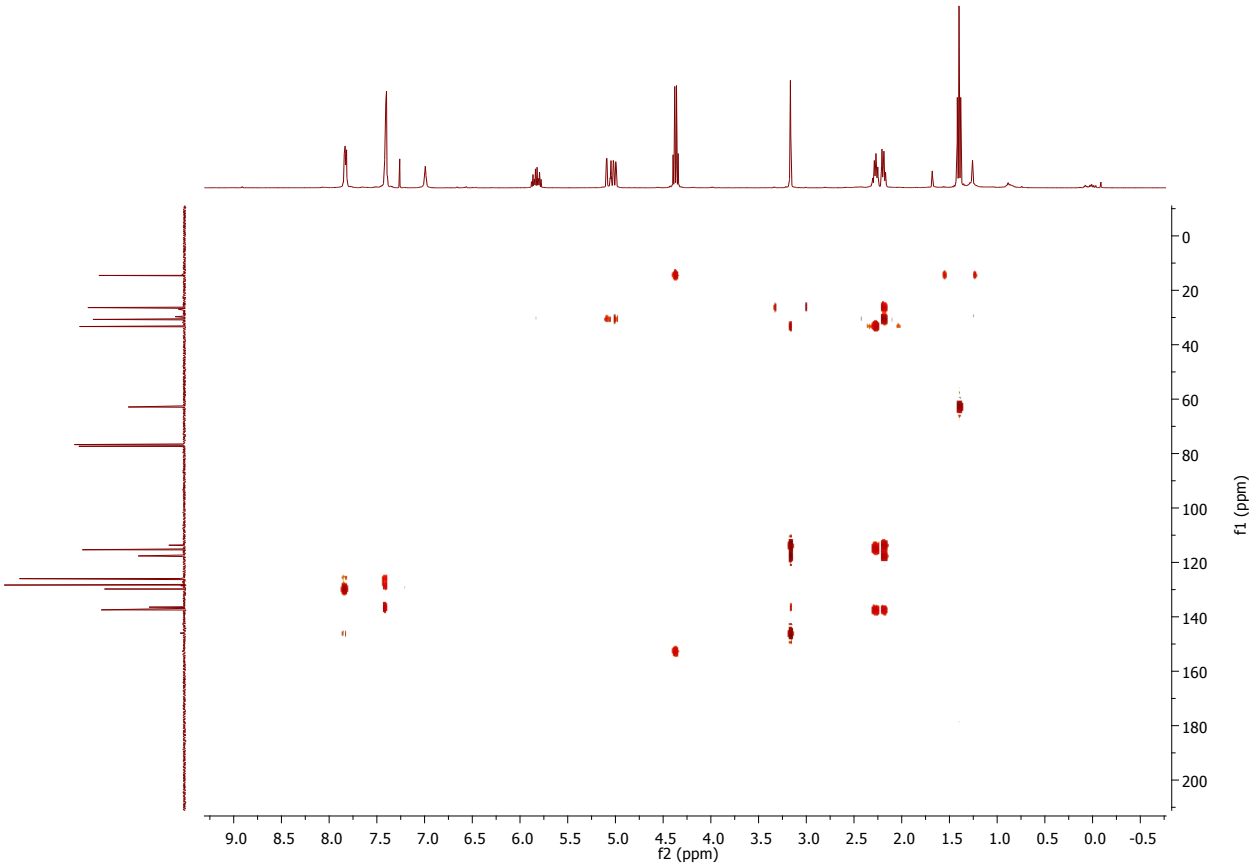
f2 (ppm)


f1 (ppm)
f2 (ppm)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80
100
120
140
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200
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6.5
6.0
5.5
5.0
4.5
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2.5
2.0
1.5
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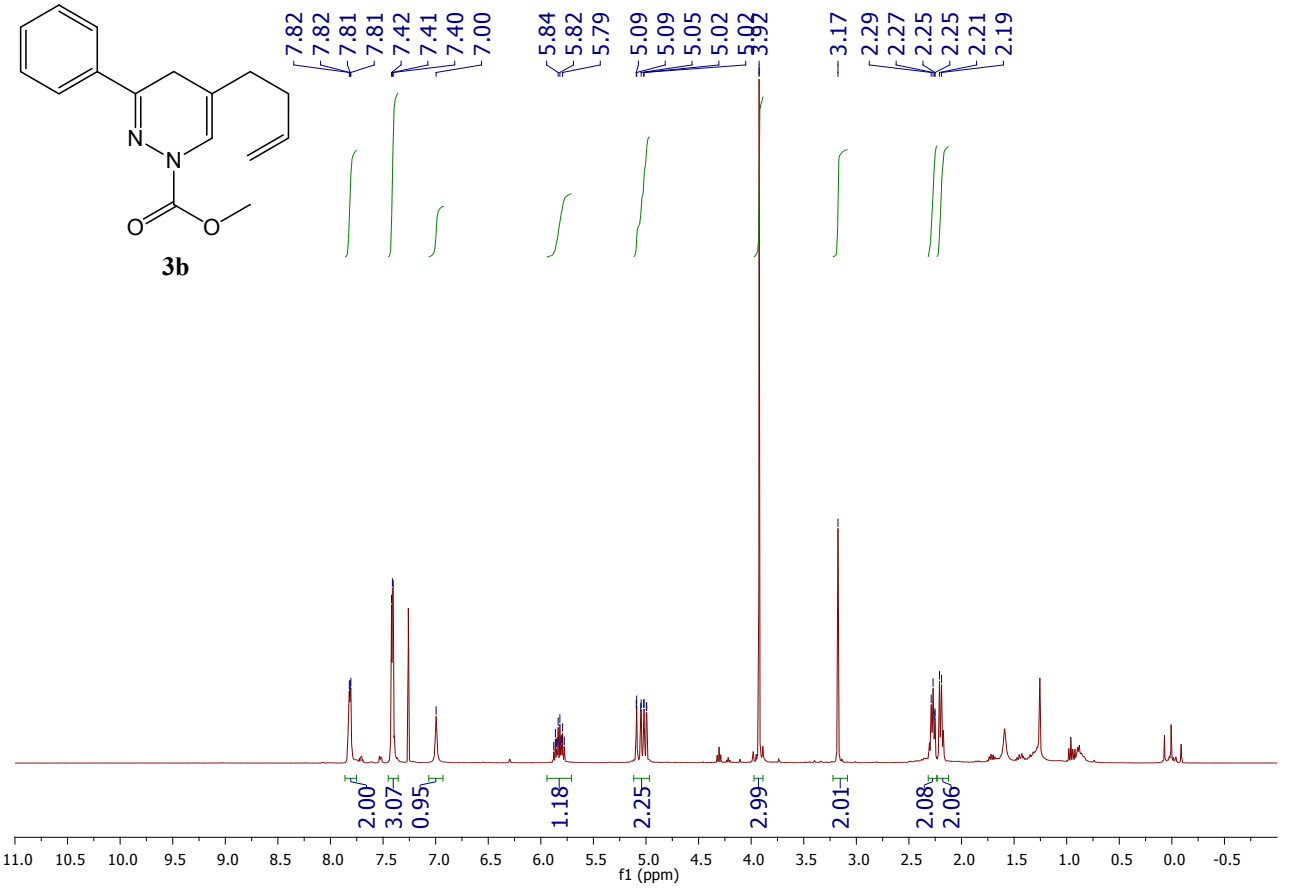
f2 (ppm)

3b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5.05
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3.17
2.29
2.27
2.25
2.25
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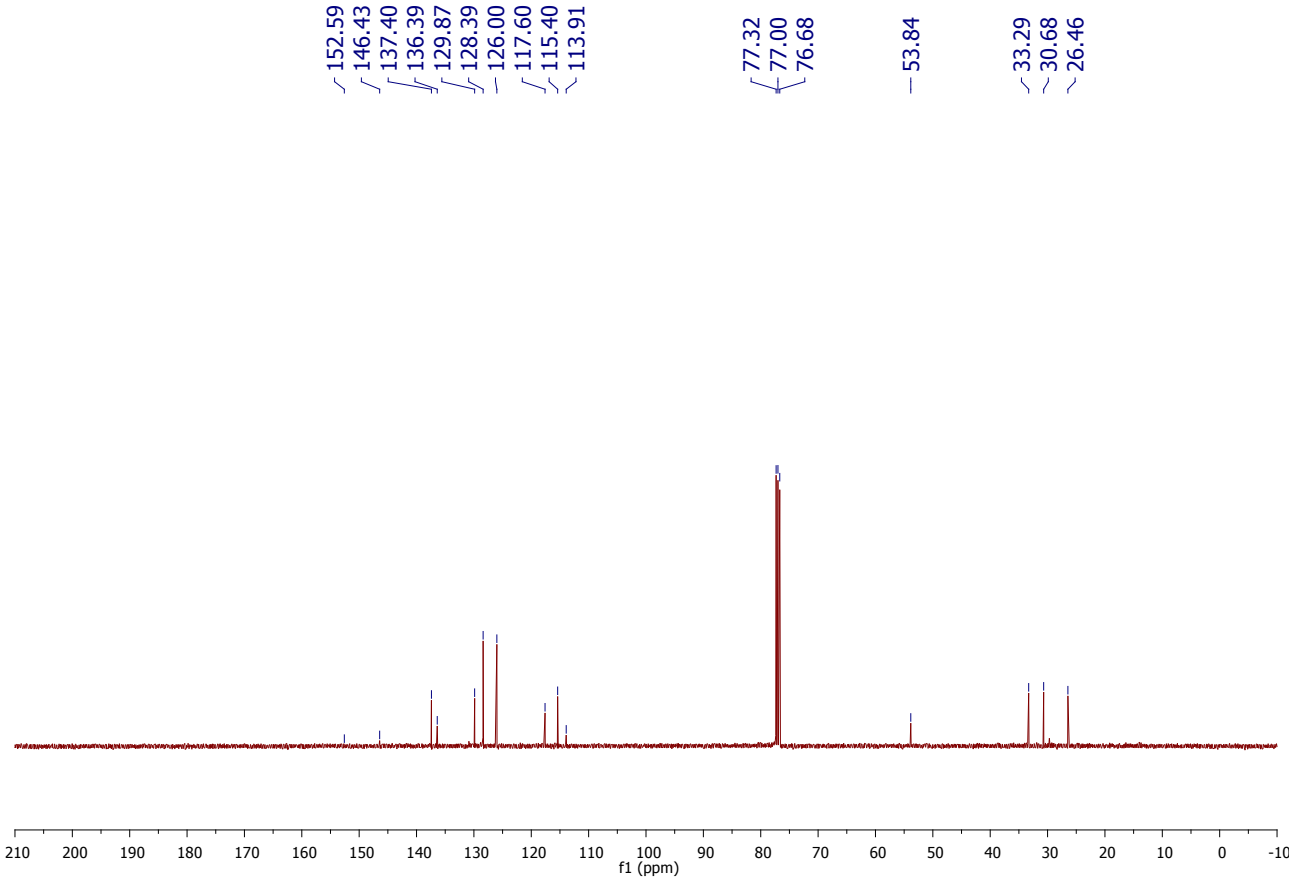
2.06
f1 (ppm)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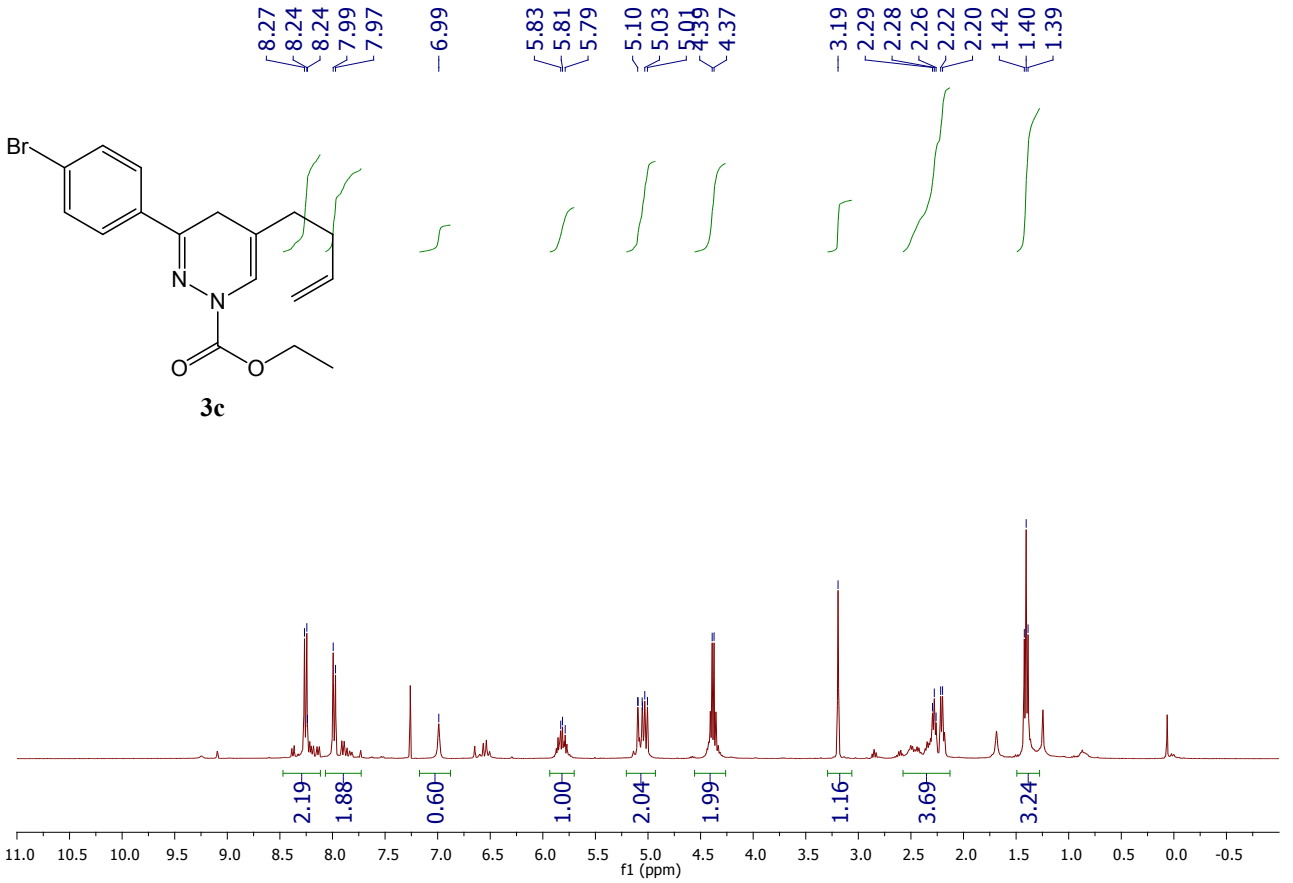
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2.28
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2.20
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1.40
1.39
Br
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3.24
f1 (ppm)
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142.31
137.17
136.41
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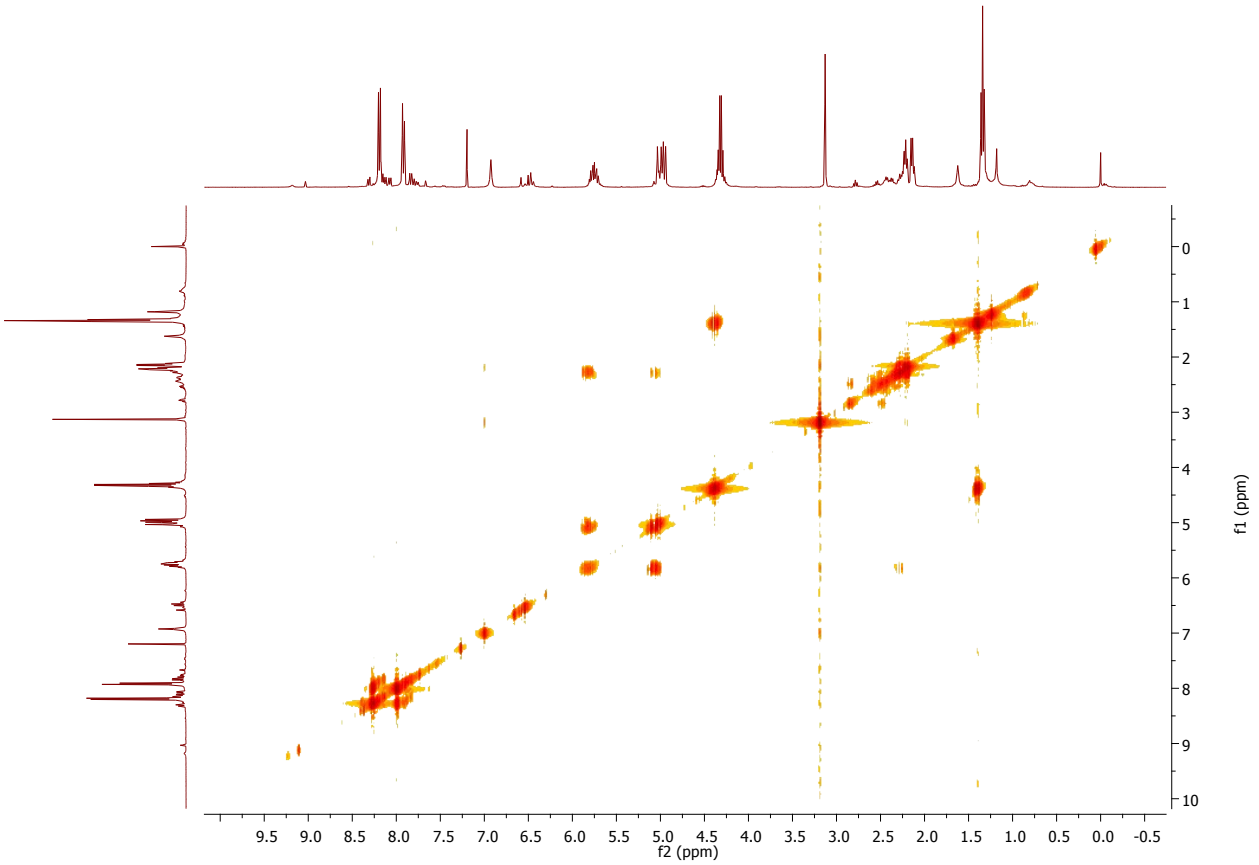
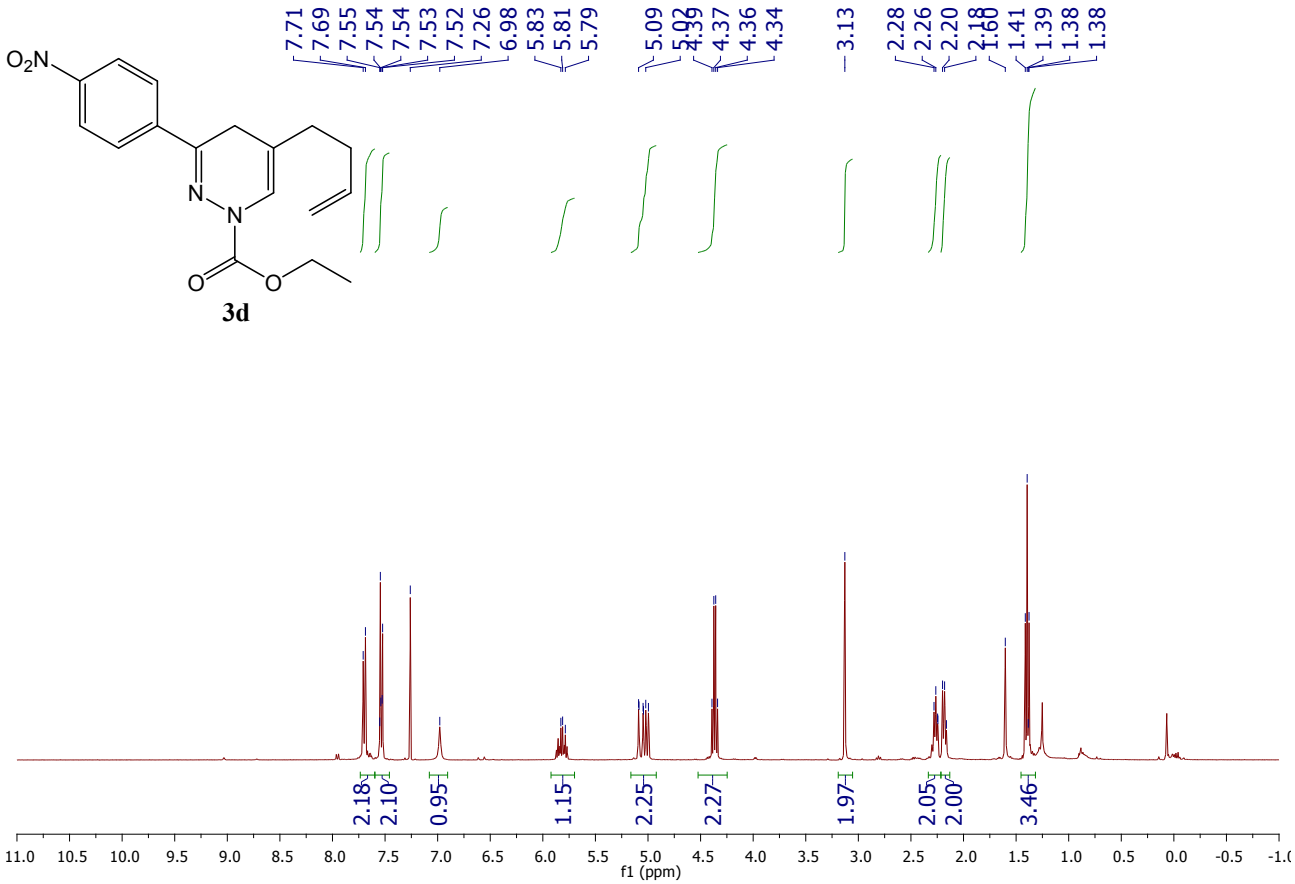
f1 (ppm)

3c


f1 (ppm)
f2 (ppm)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3.46
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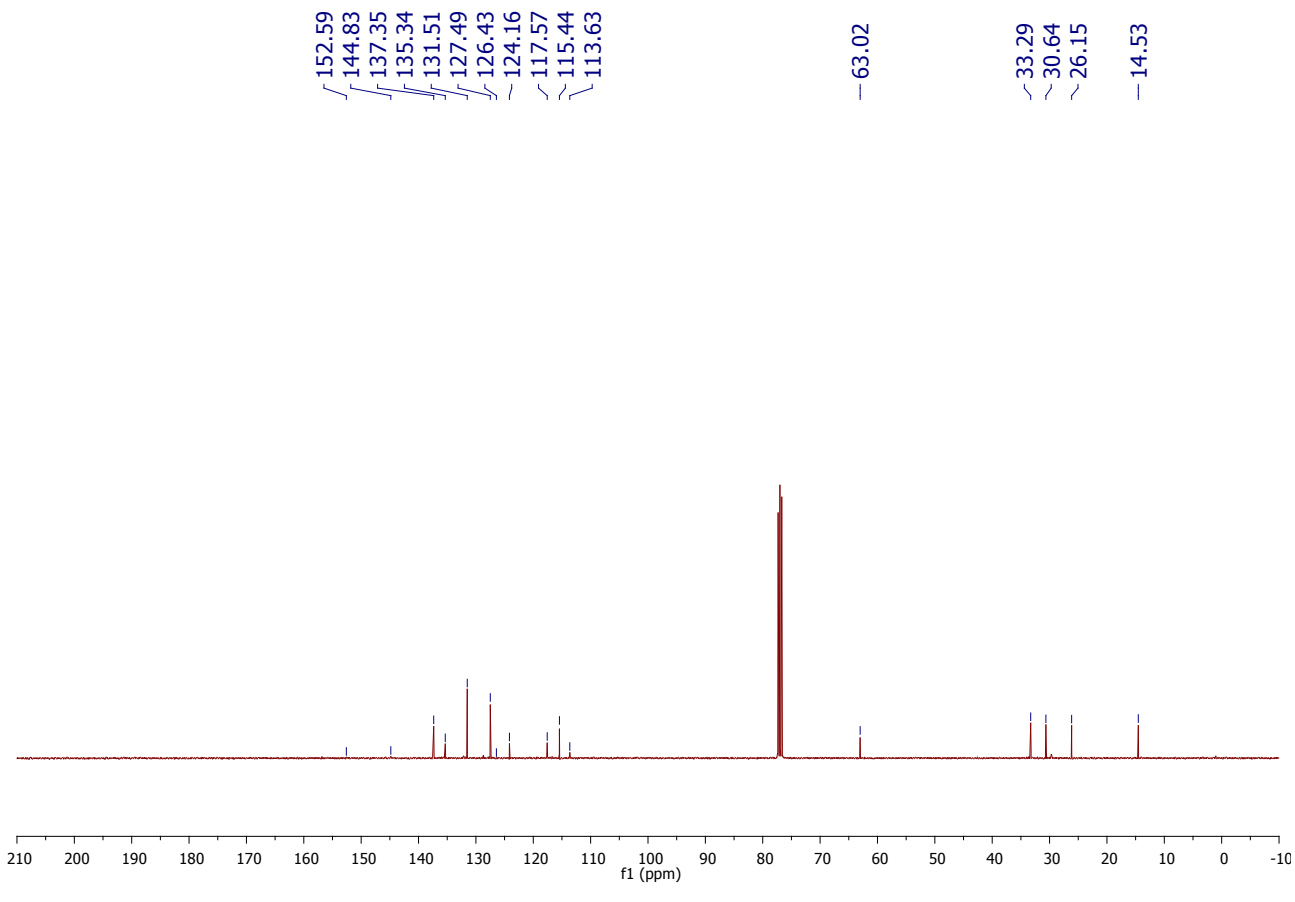
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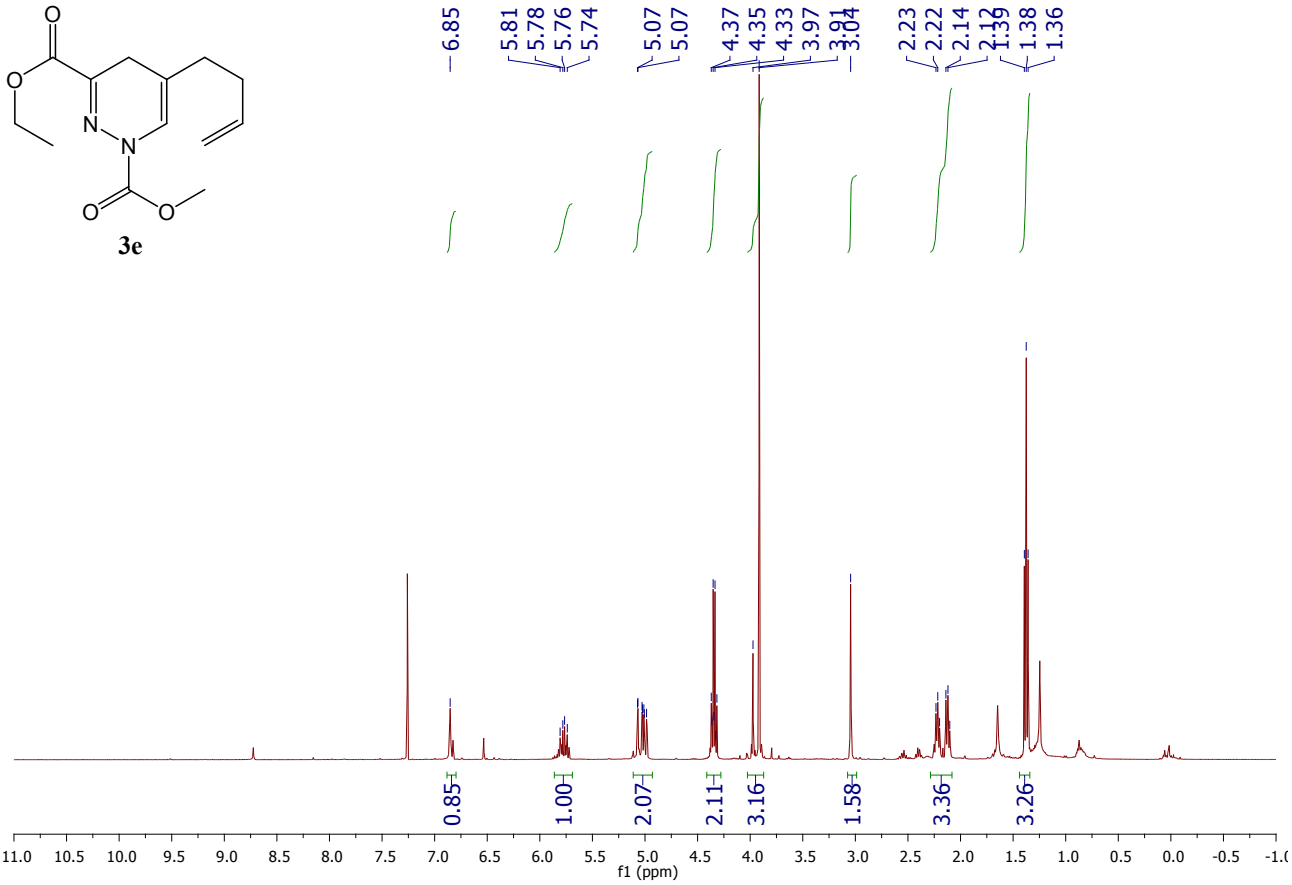
f1 (ppm)

3e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2.23
2.22
2.14
2.12
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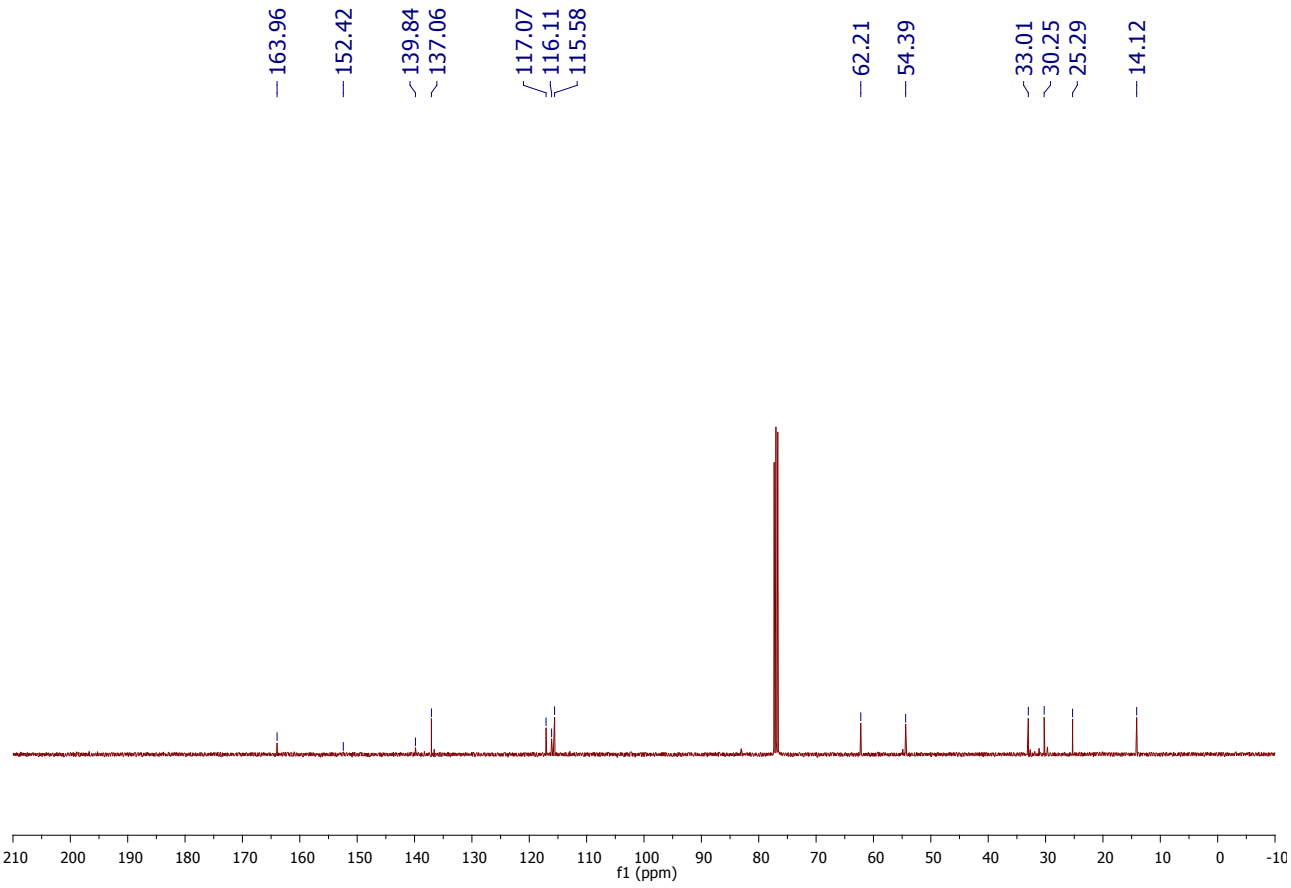
3.26
f1 (ppm)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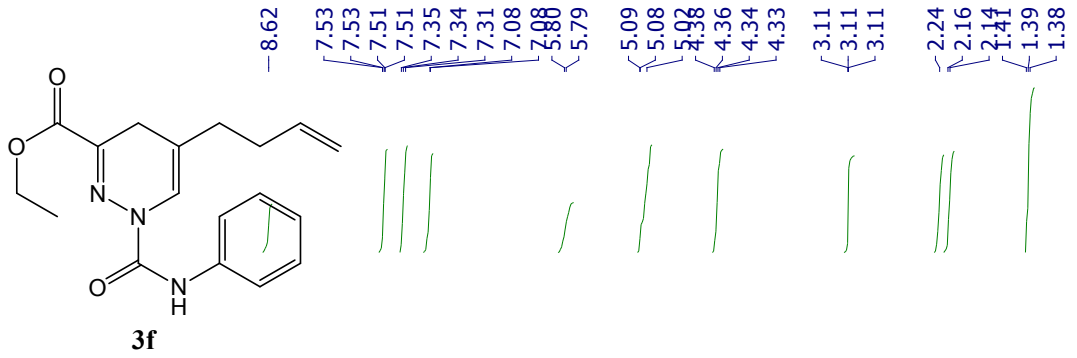
f1 (ppm)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O
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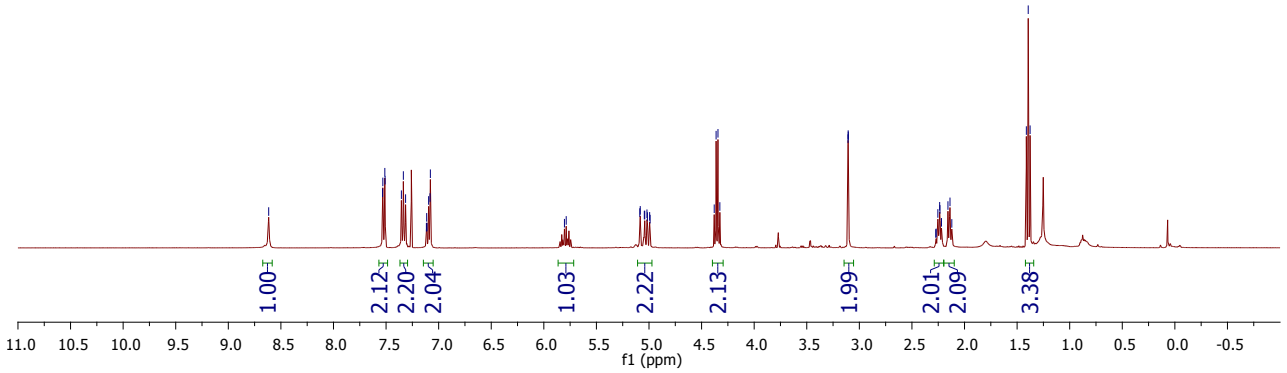
N
H

3f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3.38
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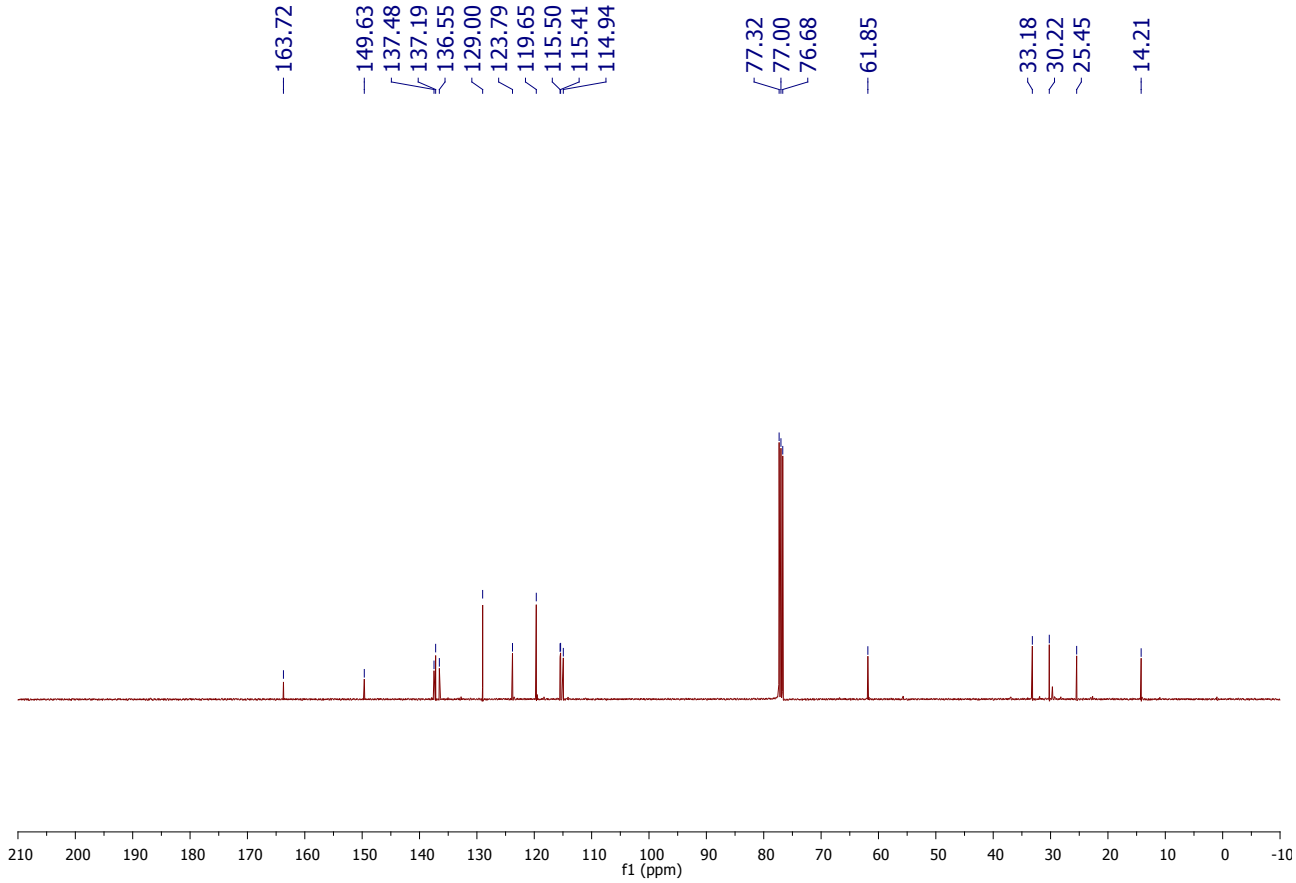
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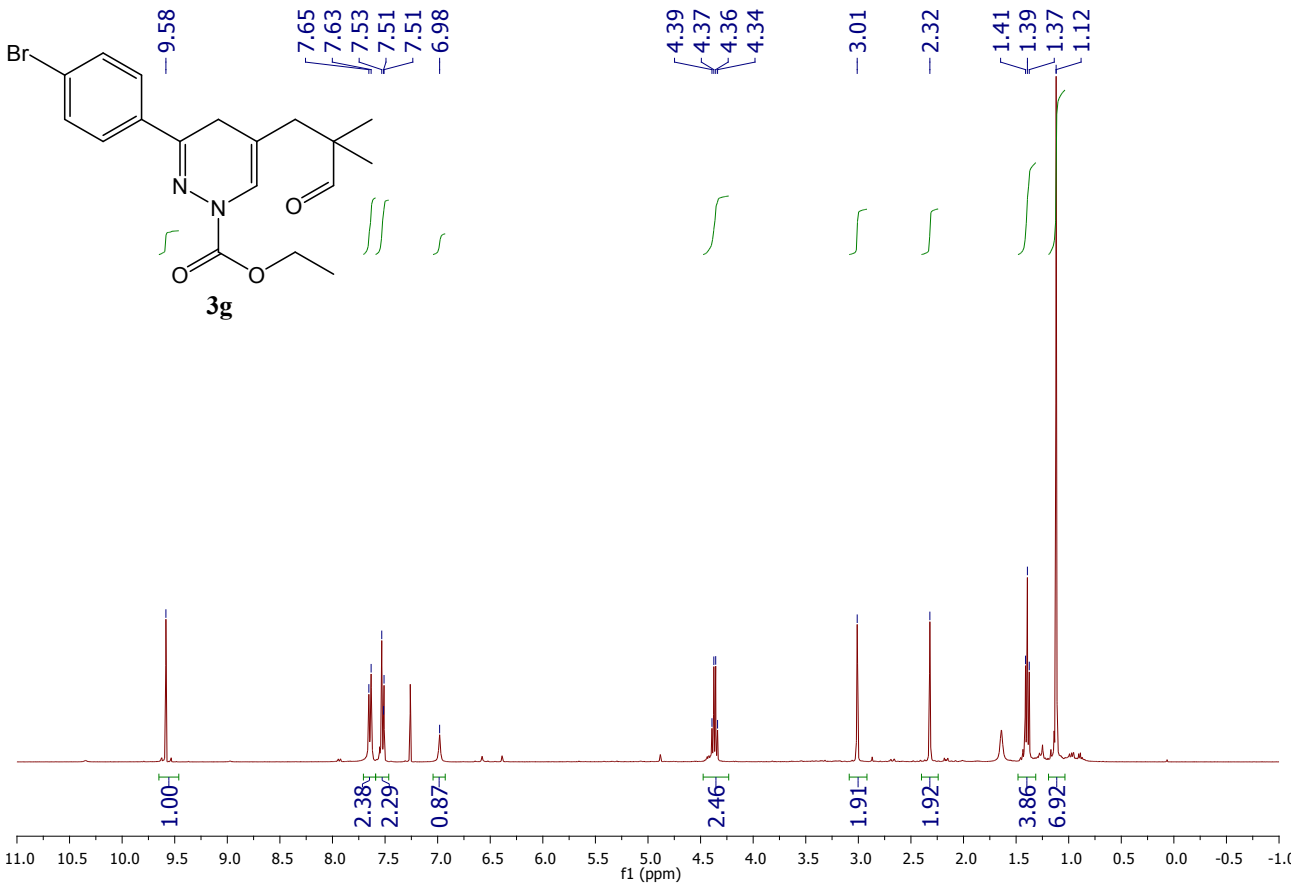
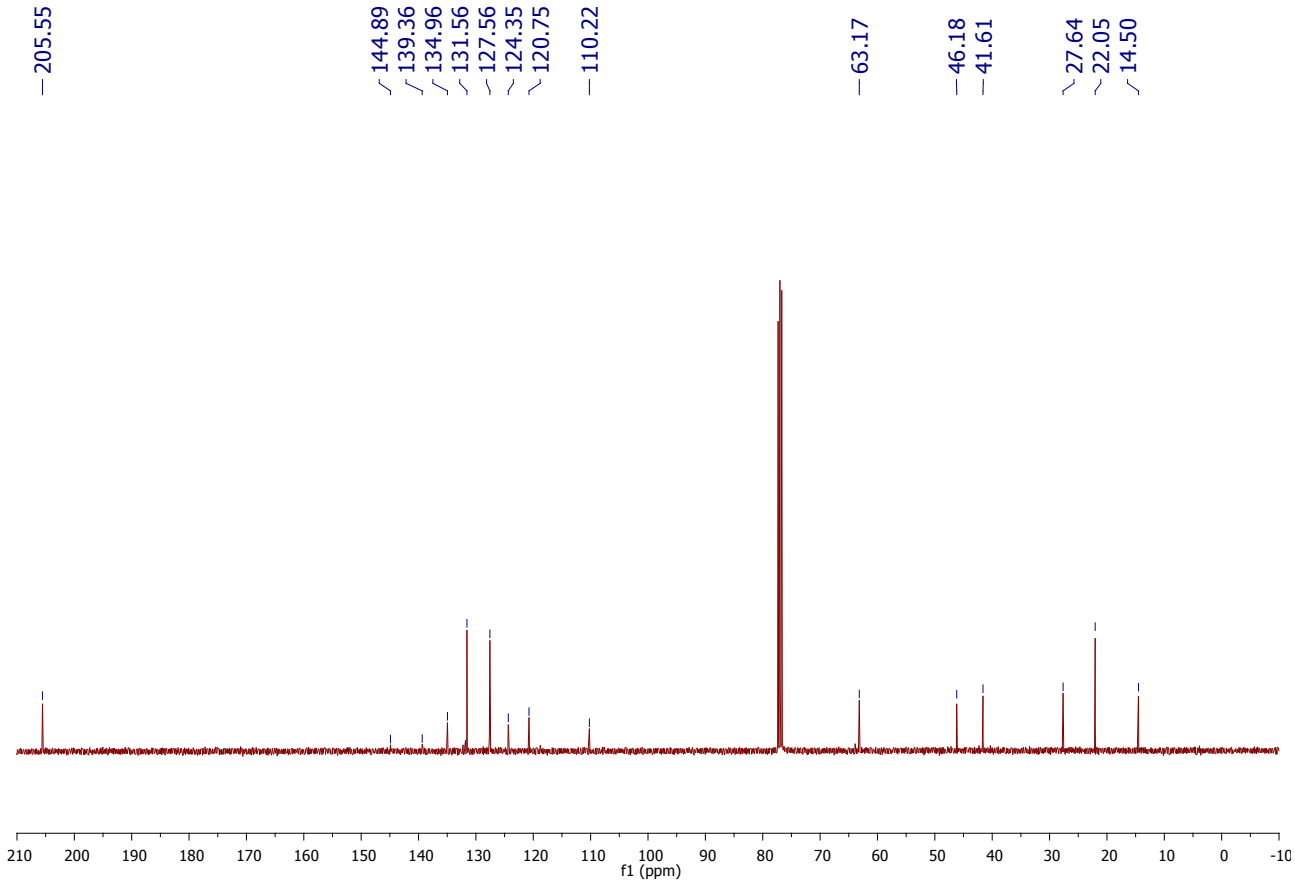
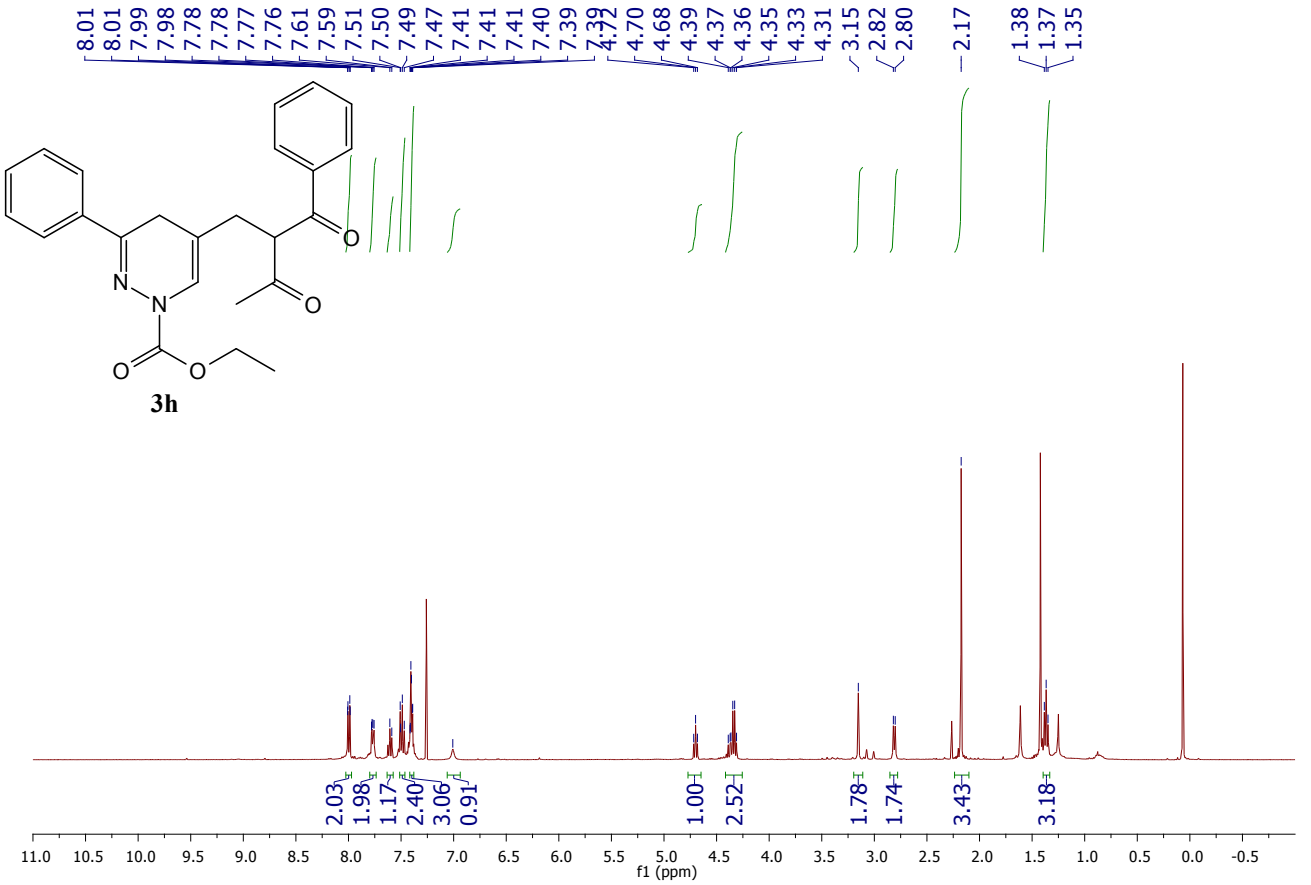
25.45
14.21
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

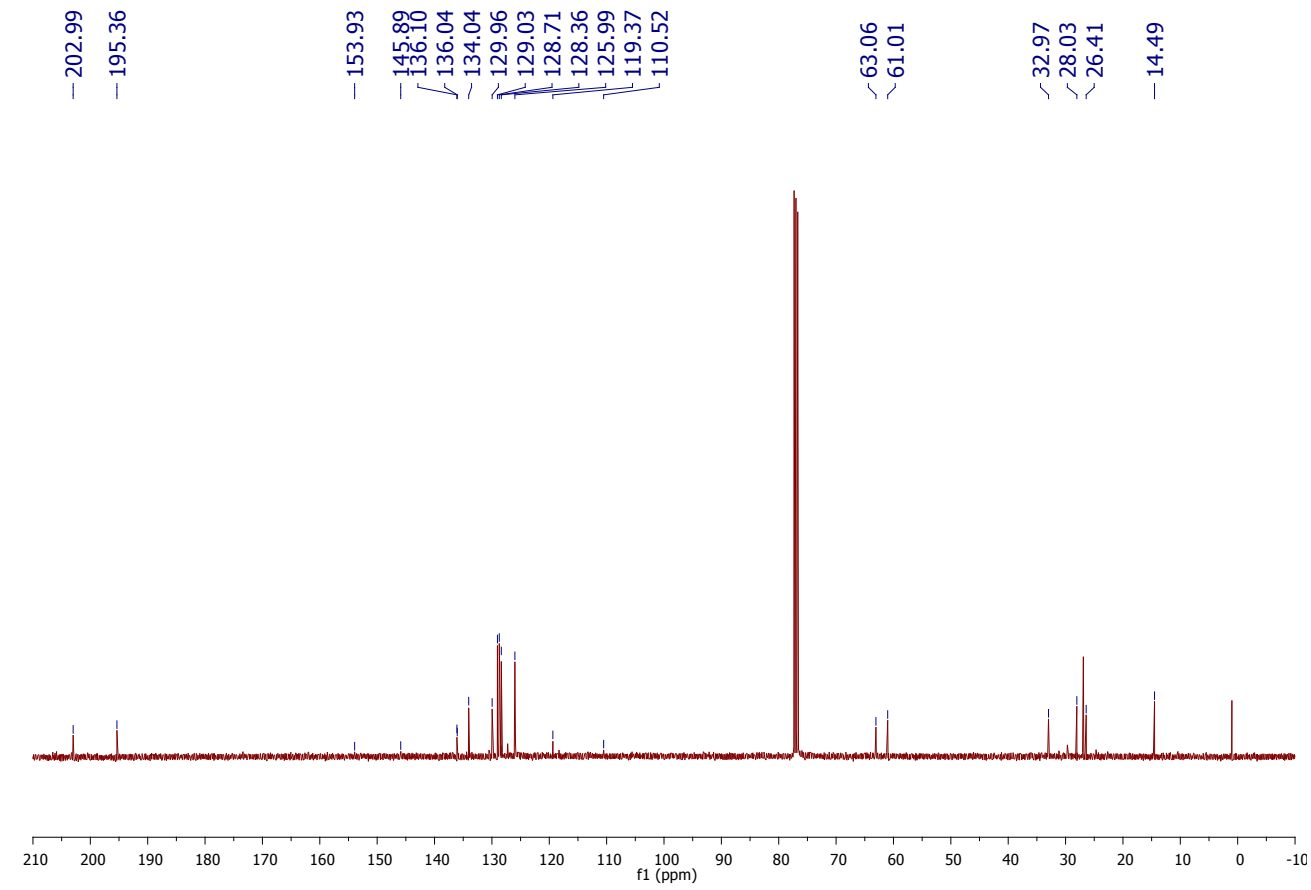

Br
N
N
O
O
O
9.58
7.65
7.63
7.53
7.51
7.51
6.98
4.39
4.37
4.36
4.34
3.01
2.32
1.41
1.39
1.37
1.12
1.00
2.38
2.29
0.87
2.46
1.91
1.92
3.86
6.92
f1 (ppm)

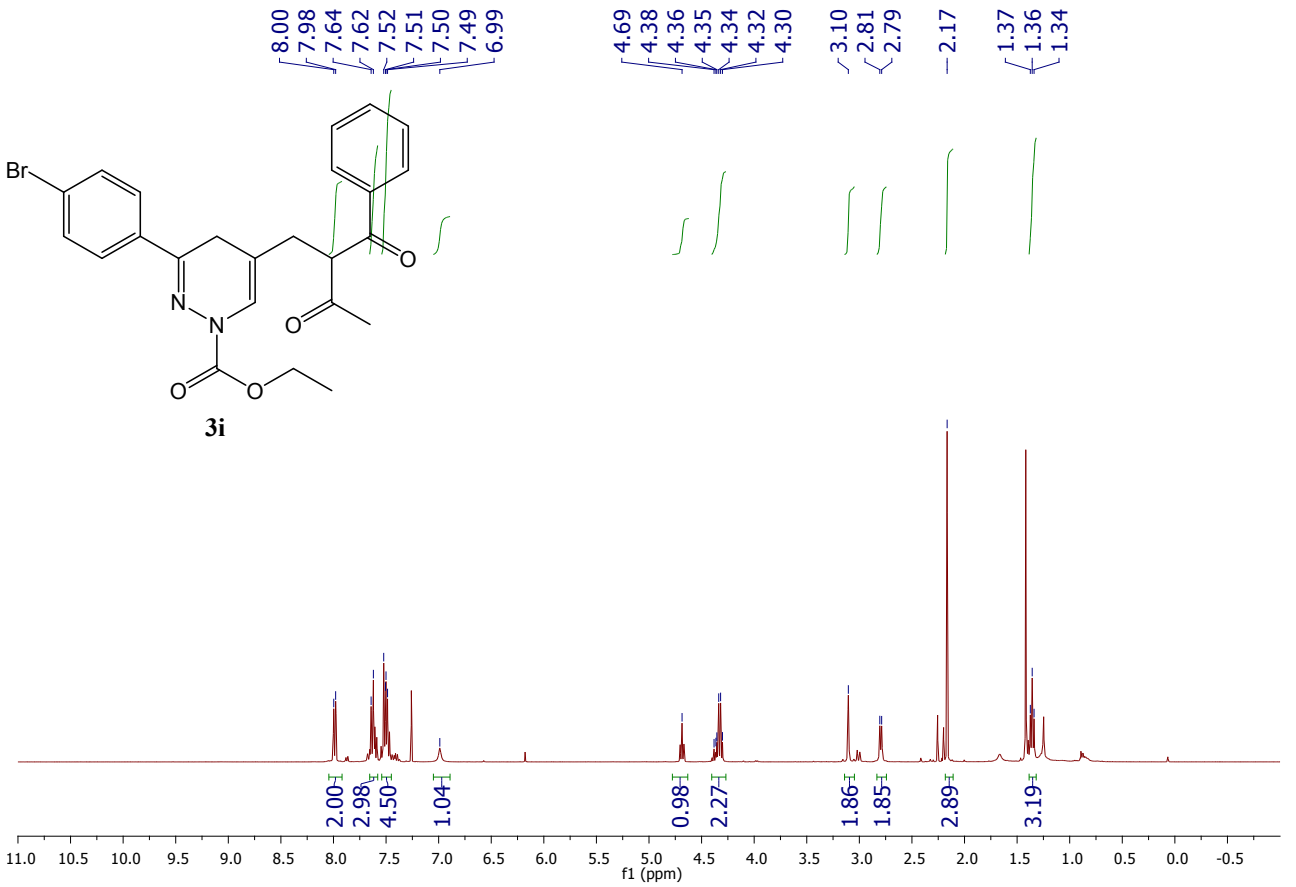
3g


205.55
144.89
139.36
134.96
131.56
127.56
124.35
120.75
110.22
63.17
46.18
41.61
27.64
22.05
14.50
f1 (ppm)

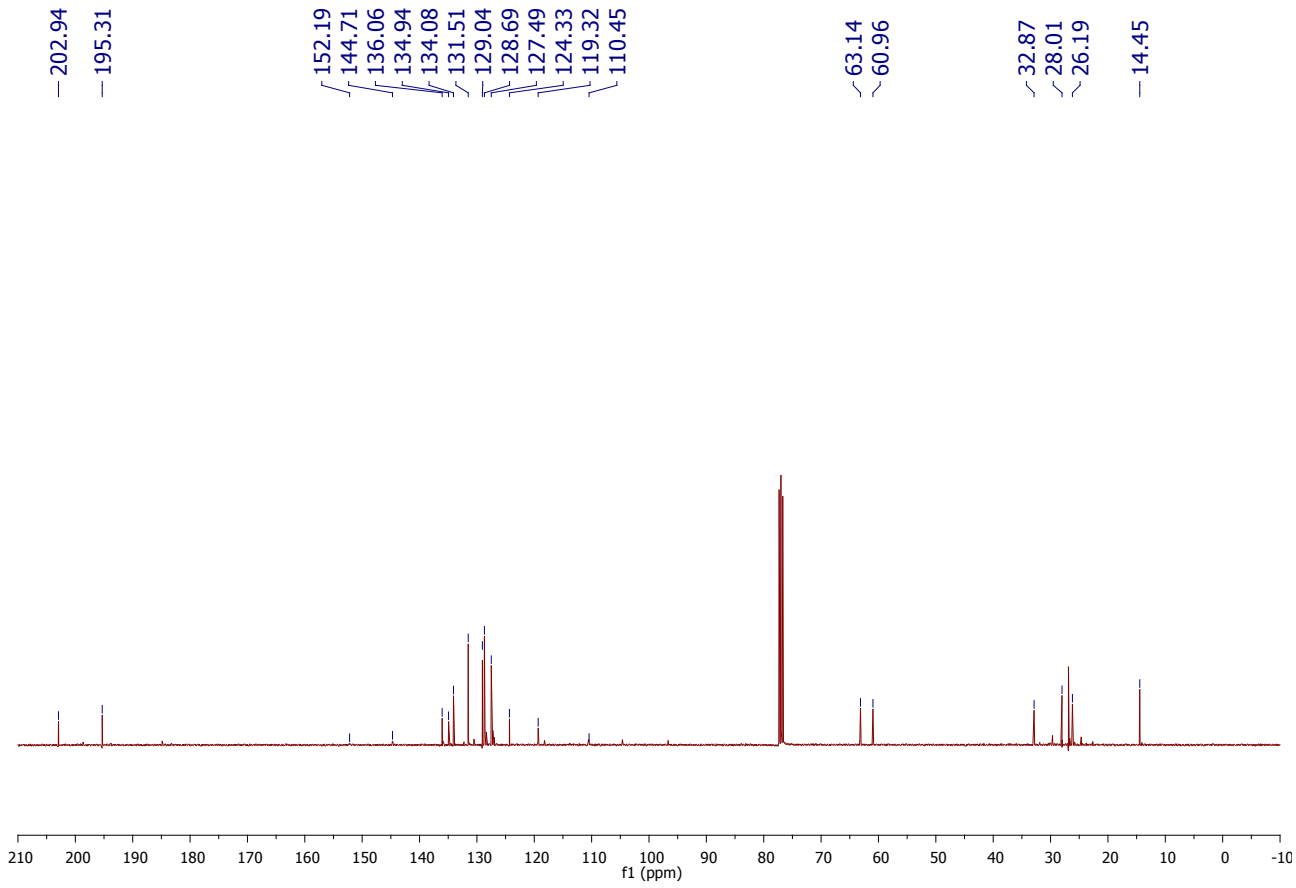

8.01
8.01
7.99
7.98
7.78
7.78
7.77
7.76
7.61
7.59
7.51
7.50
7.49
7.47
7.41
7.41
7.41
7.40
7.39
7.39
4.72
4.70
4.68
4.39
4.37
4.36
4.35
4.33
4.31
3.15
2.82
2.80
2.17
1.38
1.37
1.35
O
N
N
O
O
O
2.03
1.98
1.17
2.40
3.06
0.91
1.00
2.52
1.78
1.74
3.43
3.18
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

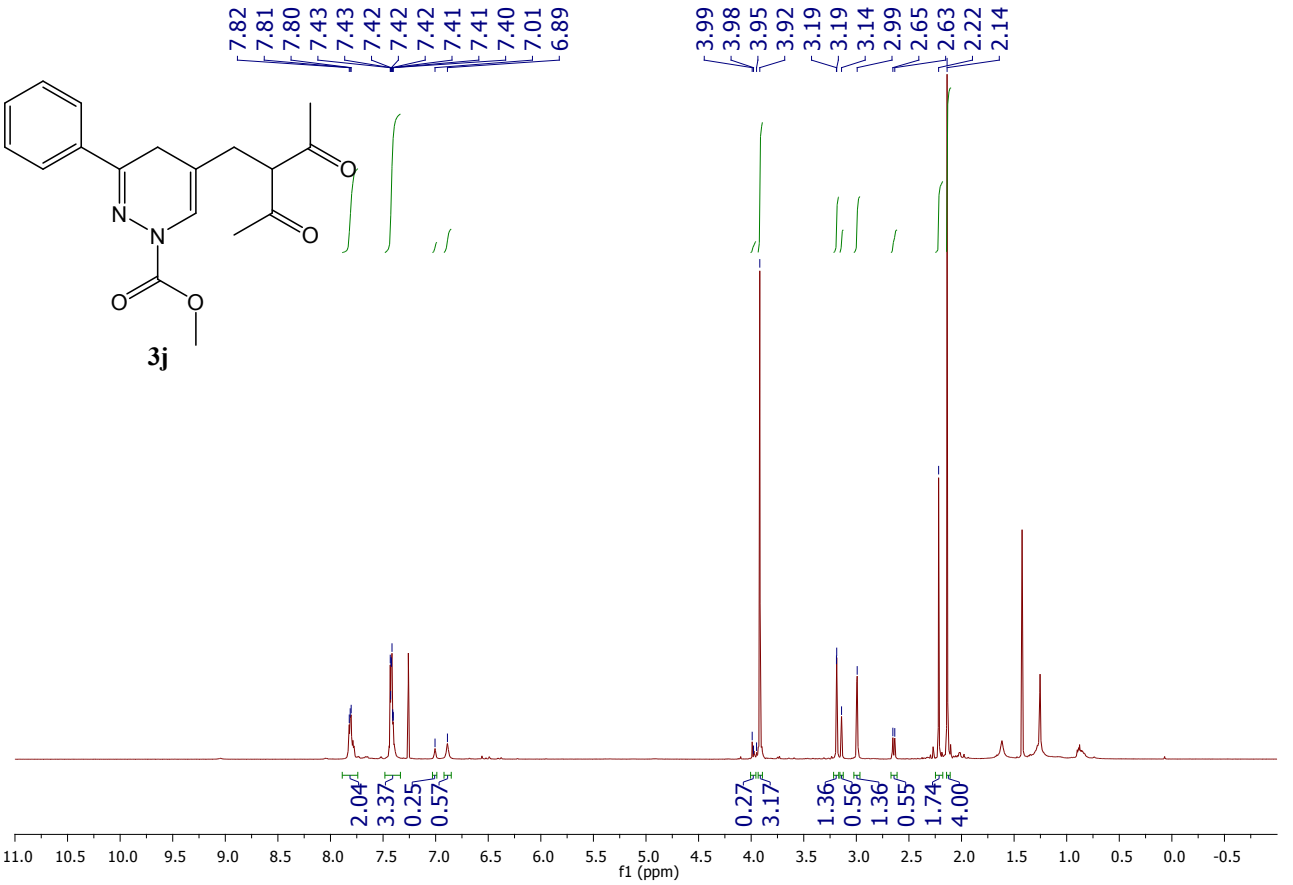
3h


202.99
195.36
153.93
145.89
136.10
136.04
134.04
129.96
129.03
128.71
128.36
125.99
119.37
110.52
63.06
61.01
32.97
28.03
26.41
14.49
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)

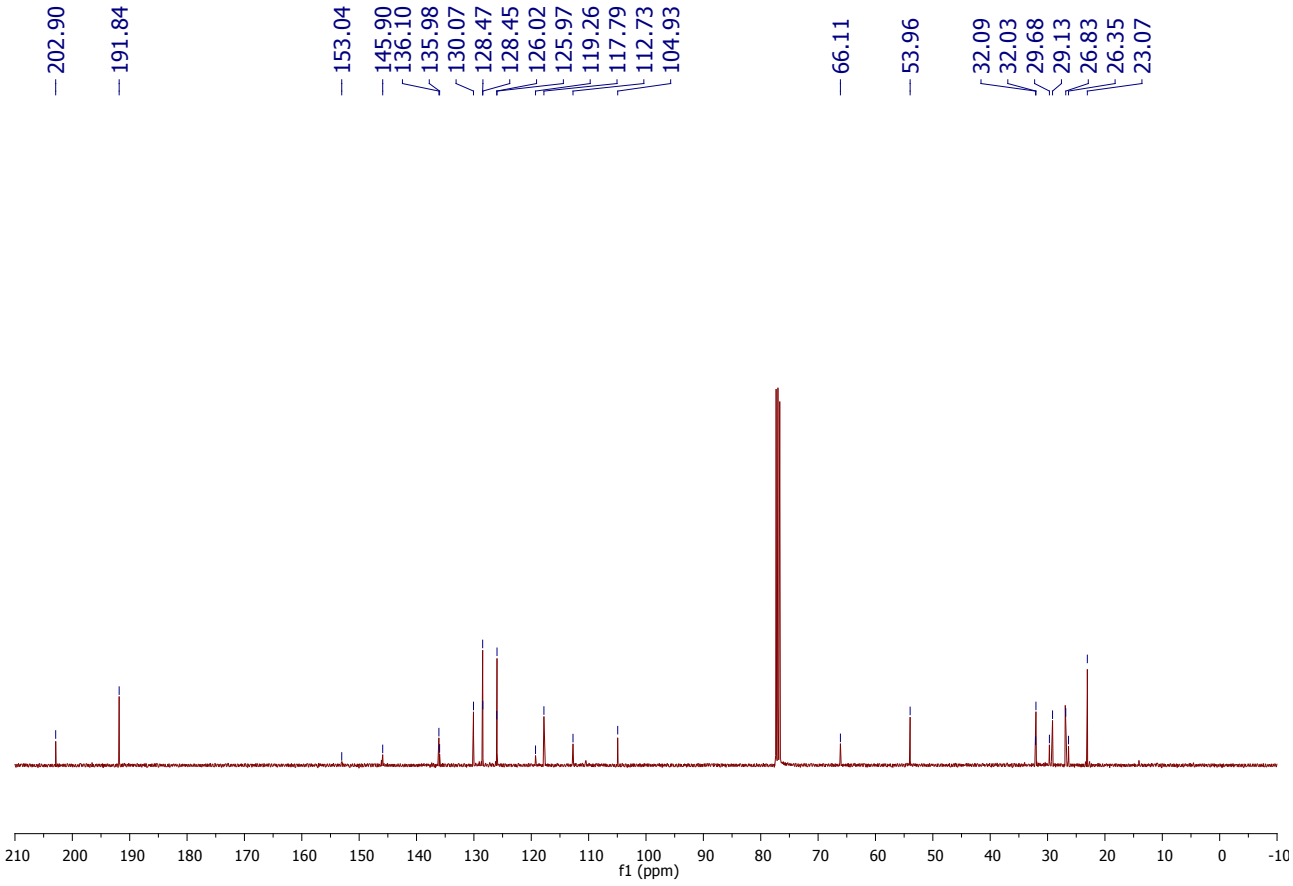

8.00
7.98
7.64
7.62
7.52
7.51
7.50
7.49
6.99
4.69
4.38
4.36
4.35
4.34
4.32
4.30
3.10
2.81
2.79
2.17
1.37
1.36
1.34
Br
O
N
N
O
O
O
2.00
2.98
4.50
1.04
0.98
2.27
1.86
1.85
2.89
3.19
f1 (ppm)

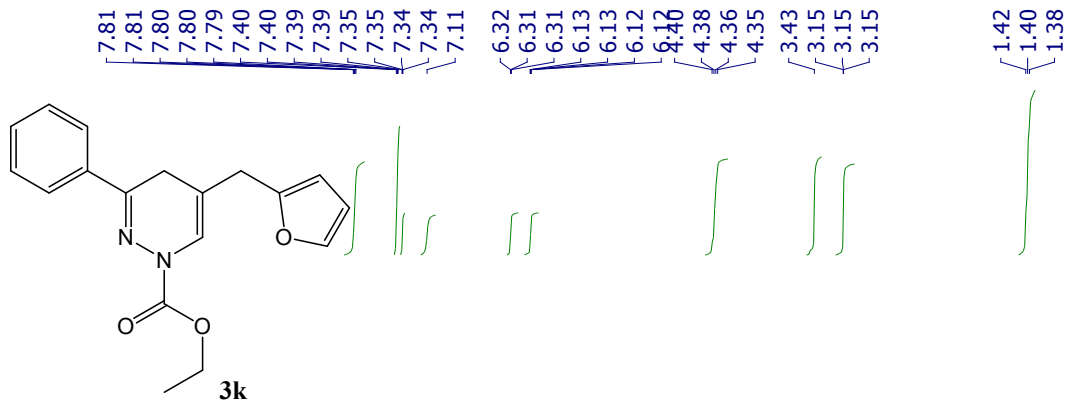
3i


202.94
195.31
152.19
144.71
136.06
134.94
134.08
131.51
129.04
128.69
127.49
124.33
119.32
110.45
63.14
60.96
32.87
28.01
26.19
14.45
f1 (ppm)

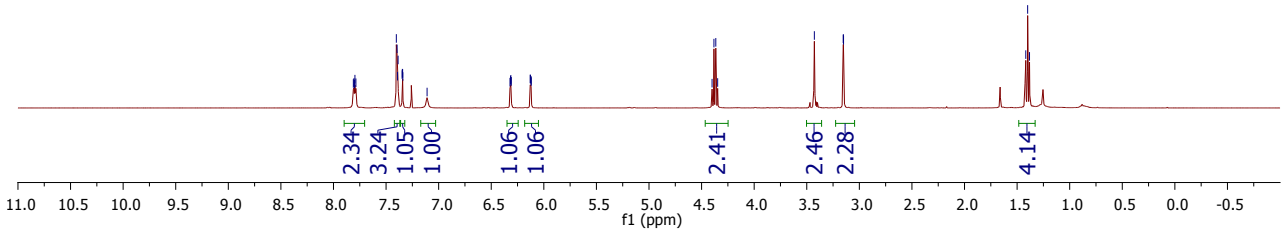

7.82
7.81
7.80
7.43
7.43
7.42
7.42
7.42
7.41
7.41
7.40
7.01
6.89
3.99
3.98
3.95
3.92
3.19
3.19
3.14
2.99
2.65
2.63
2.22
2.14
O
O
N
N
O
O
2.04
3.37
0.25
0.57
0.27
3.17
1.36
0.56
1.36
0.55
1.74
4.00
f1 (ppm)

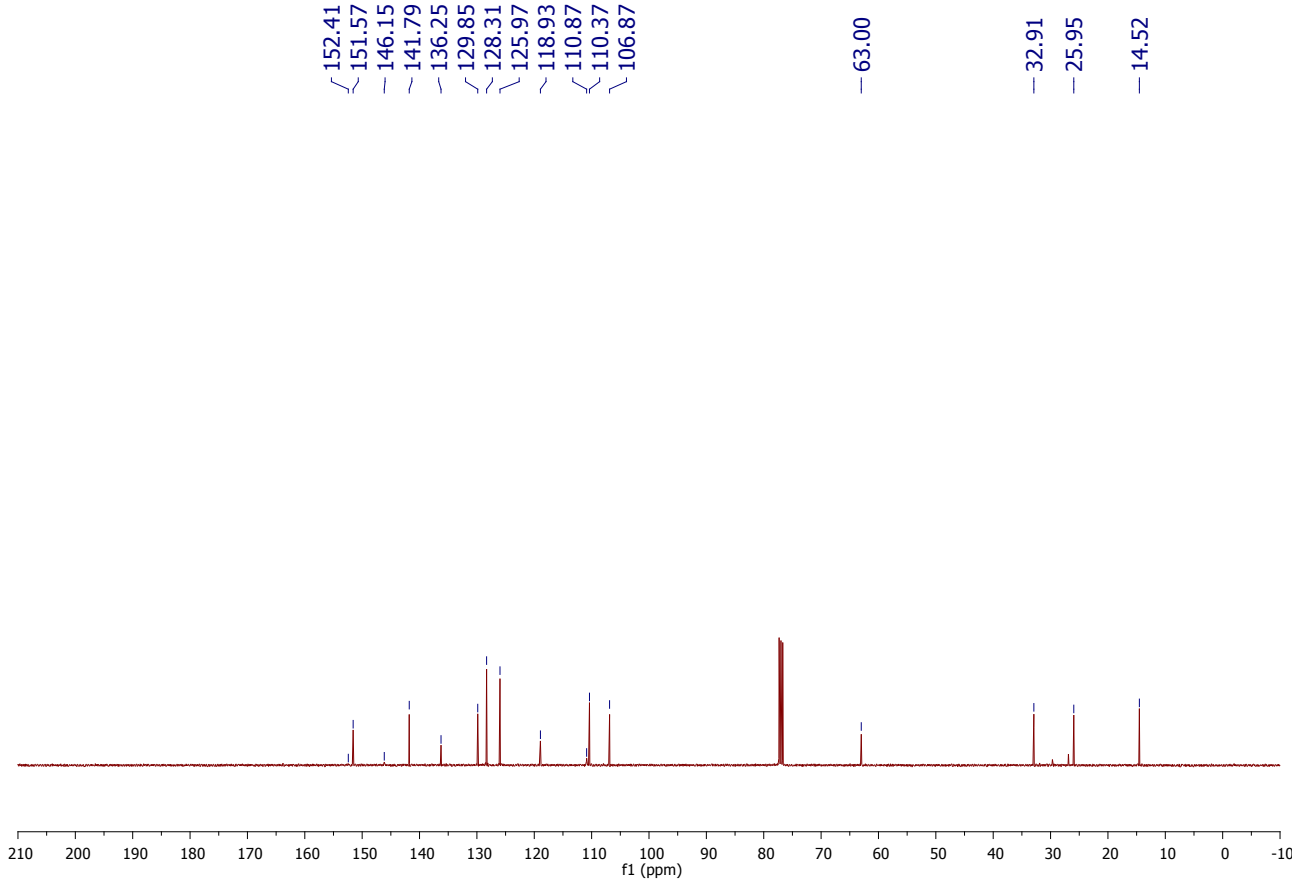
3j

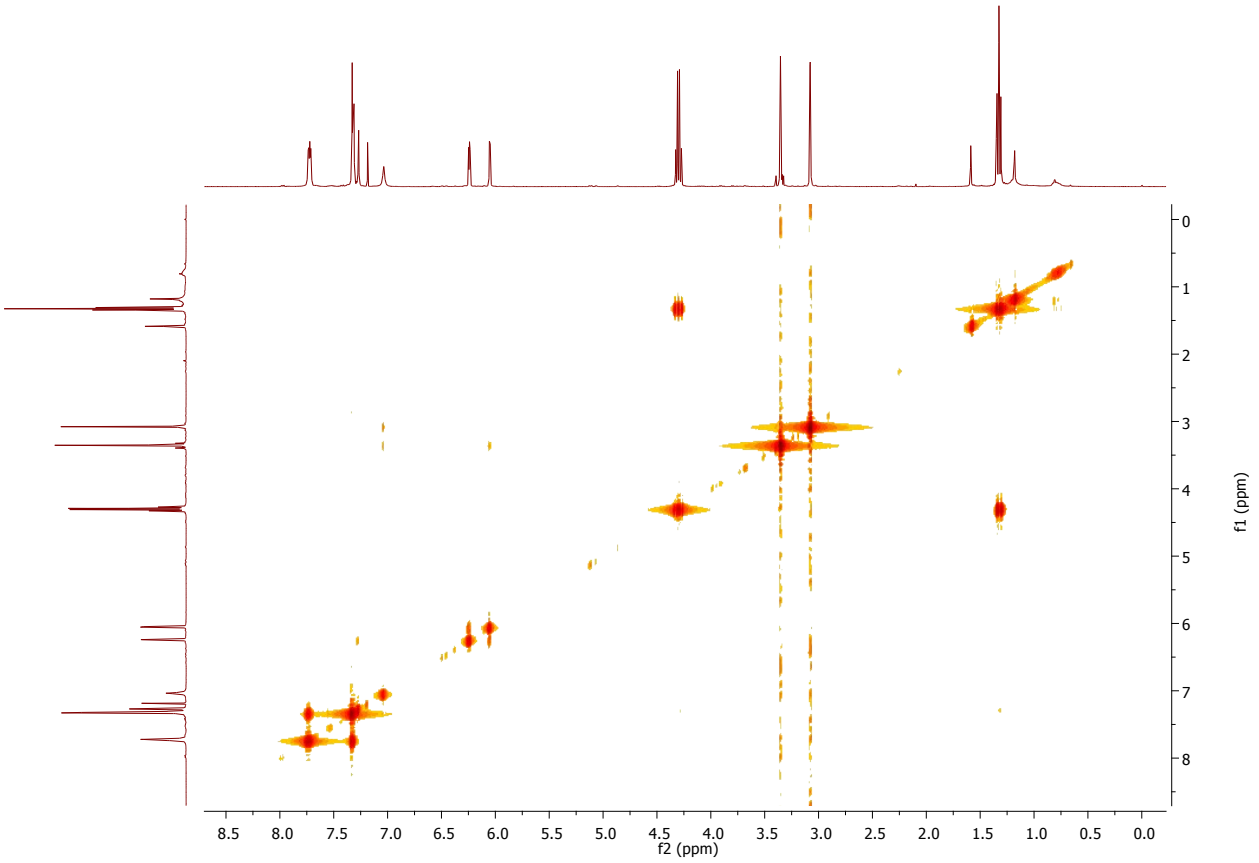

202.90
191.84
153.04
145.90
136.10
135.98
130.07
128.47
128.45
126.02
125.97
119.26
117.79
112.73
104.93
66.11
53.96
32.09
32.03
29.68
29.13
26.83
26.35
23.07
f1 (ppm)

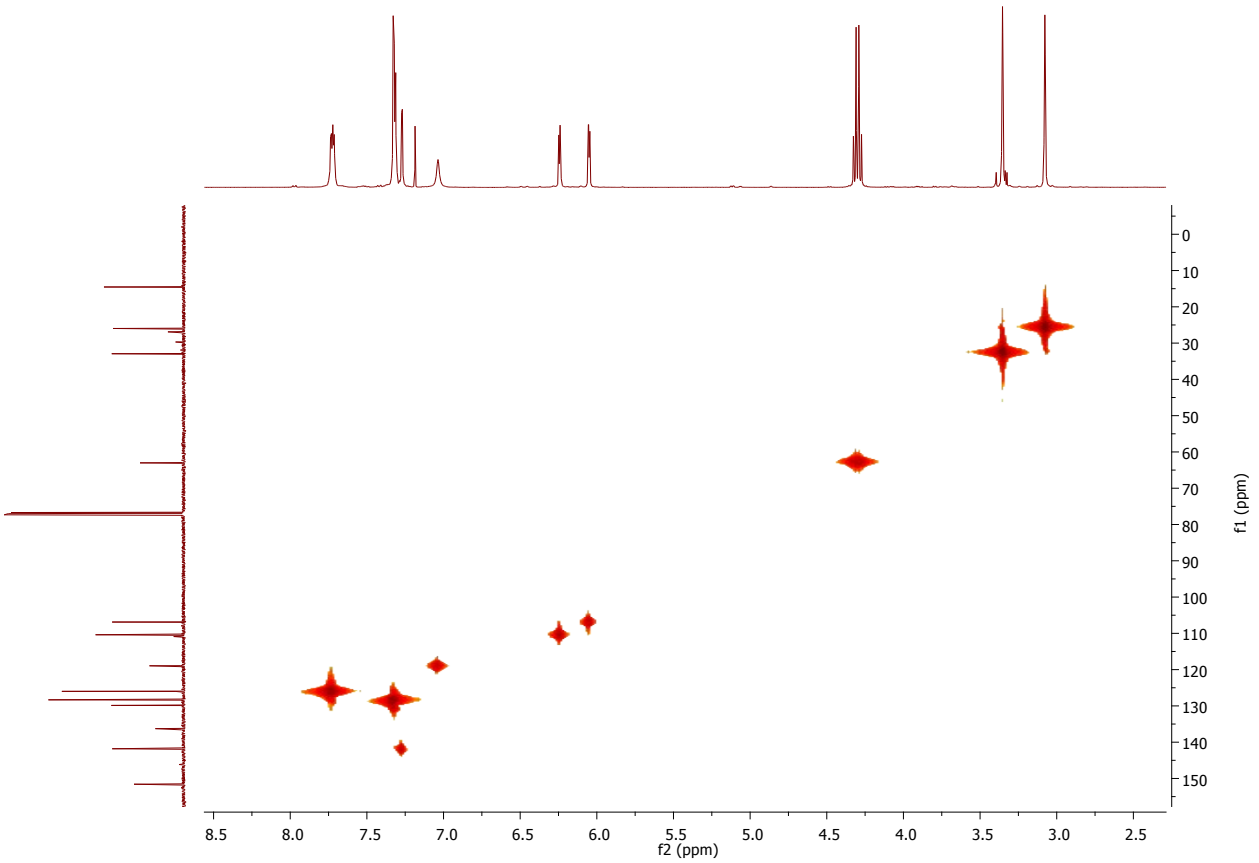

7.81
7.81
7.80
7.80
7.79
7.40
7.40
7.39
7.39
7.35
7.35
7.34
7.34
7.11
6.32
6.31
6.31
6.13
6.13
6.12
4.40
4.38
4.36
4.35
3.43
3.15
3.15
3.15
1.42
1.40
1.38
N
N
O
O
O

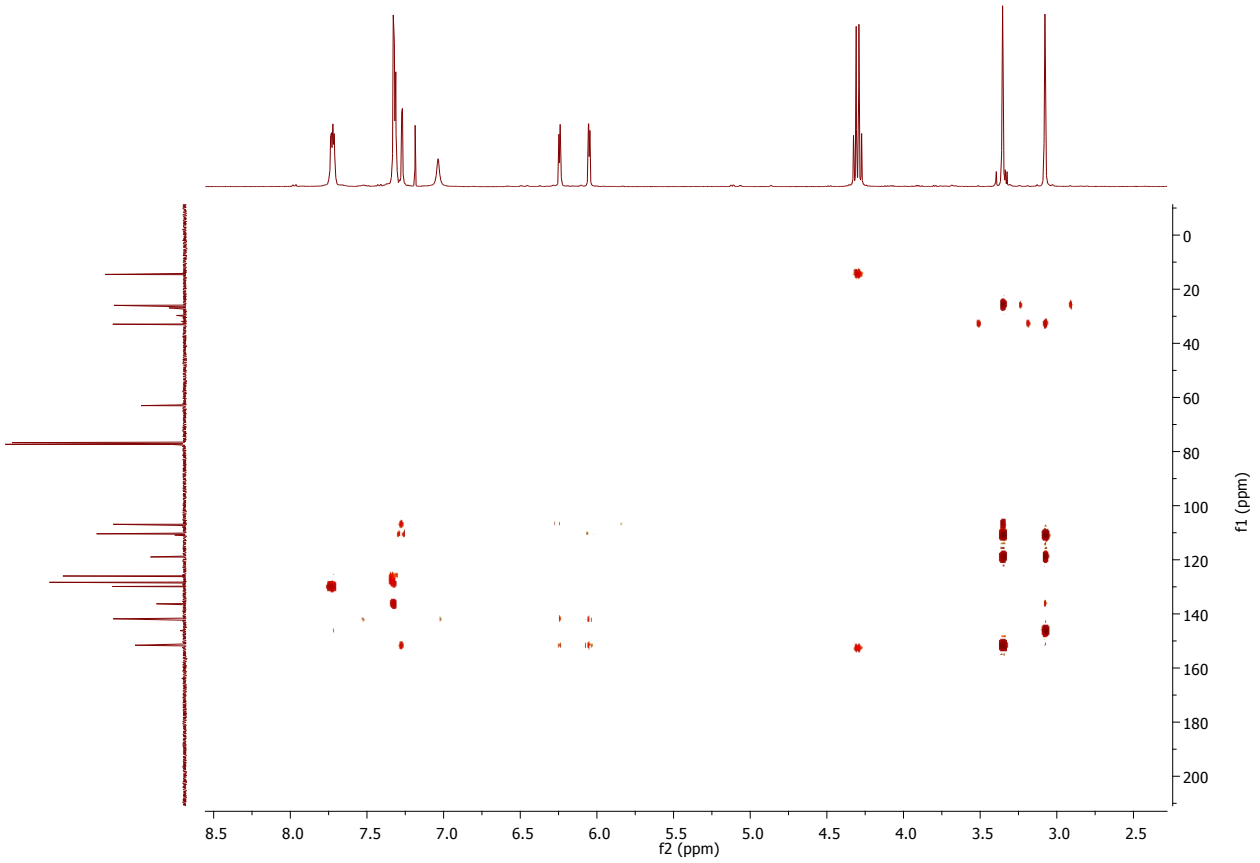
3k

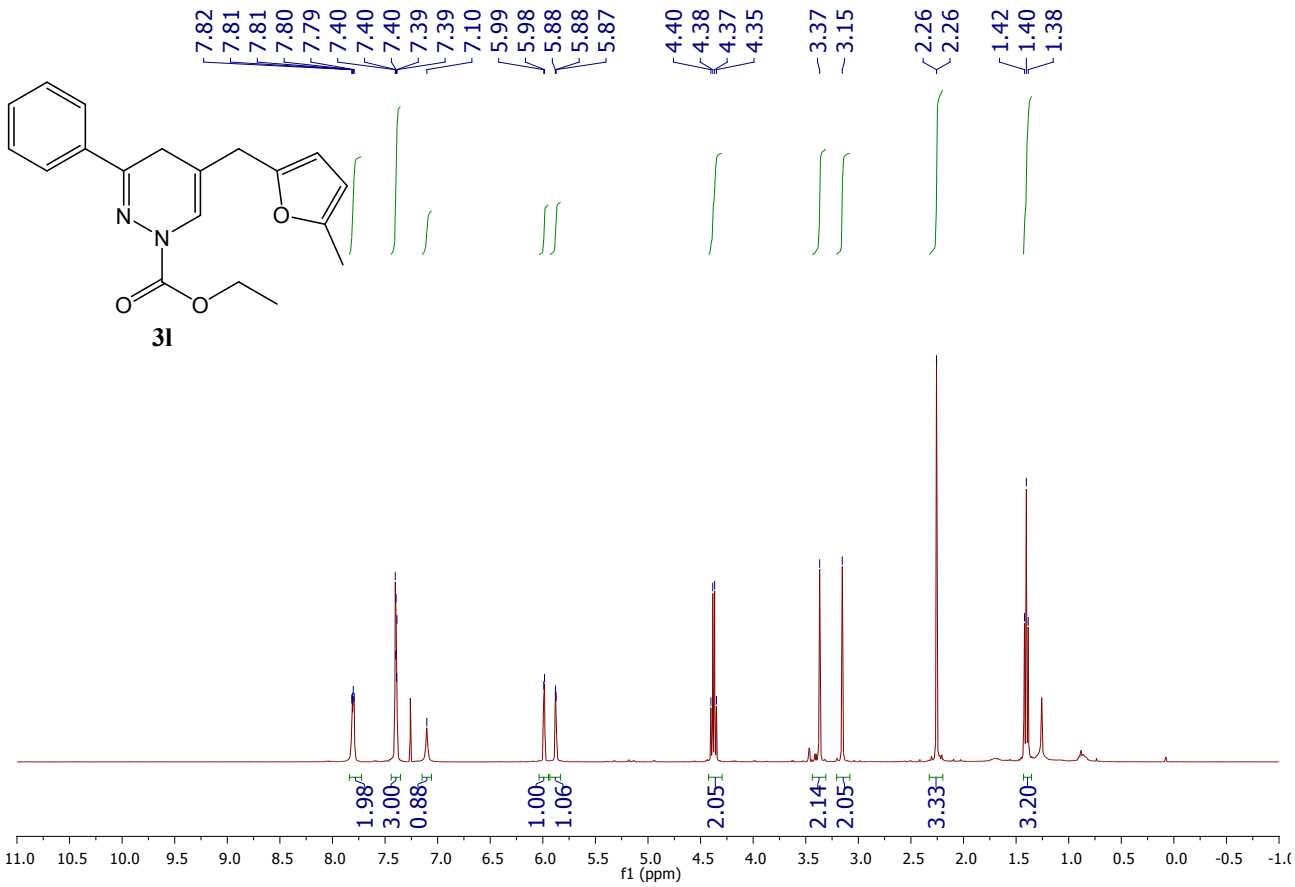

2.34
3.24
1.05
1.00
1.06
1.06
2.41
2.46
2.28
4.14
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


152.41
151.57
146.15
141.79
136.25
129.85
128.31
125.97
118.93
110.87
110.37
106.87
63.00
32.91
25.95
14.52
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)

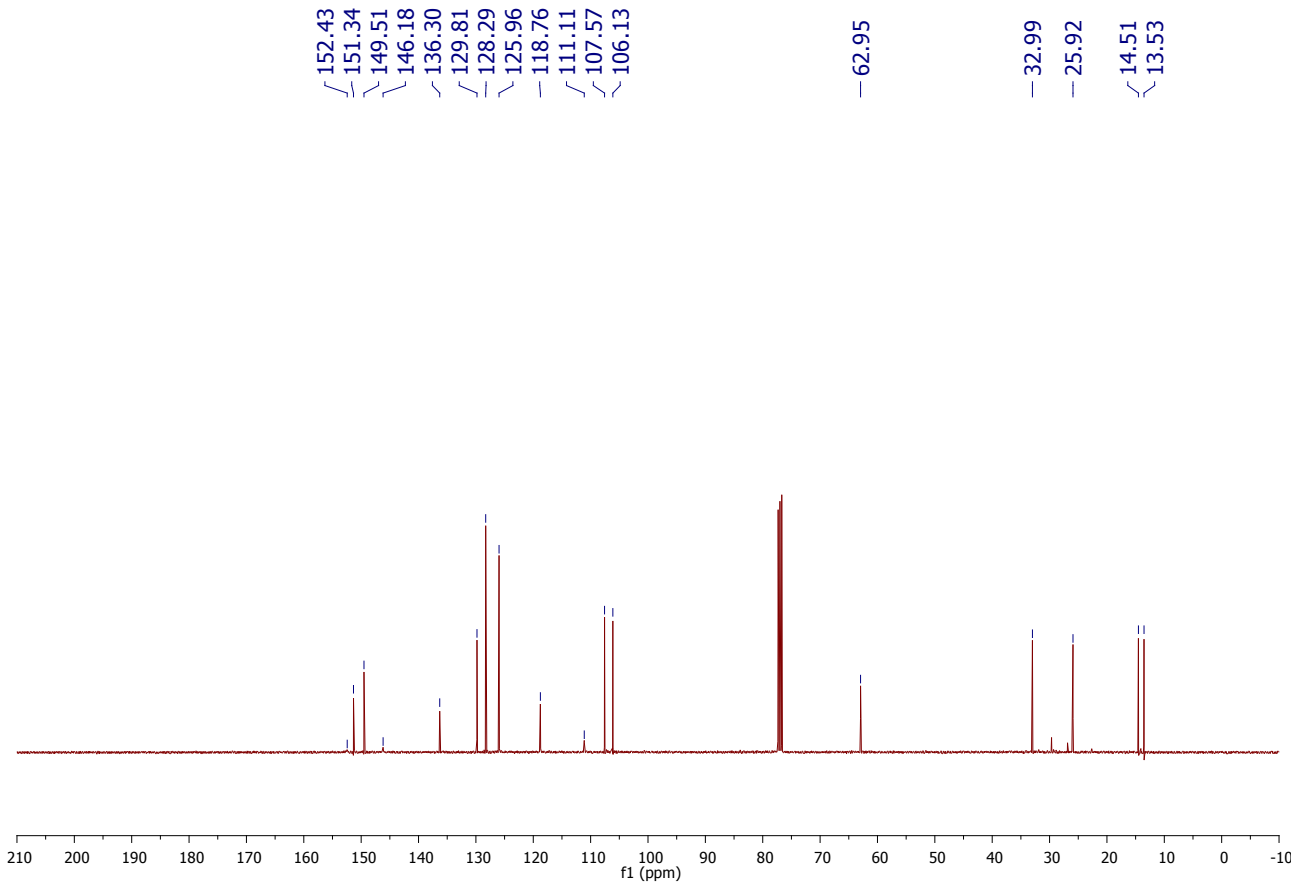

f1 (ppm)
f2 (ppm)

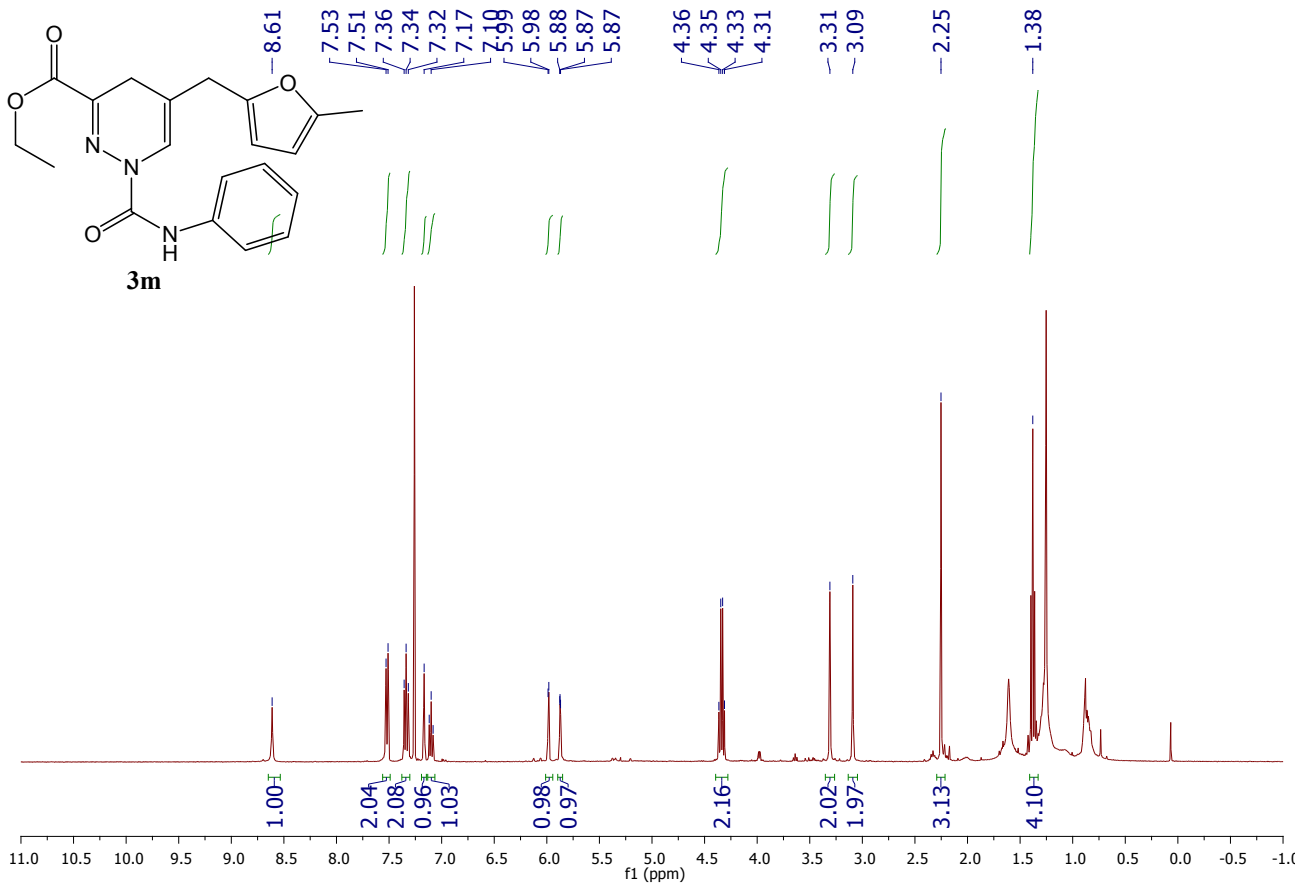

f1 (ppm)
f2 (ppm)


0
20
40
60
80
100
120
140
160
180
200
f1 (ppm)
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
f2 (ppm)

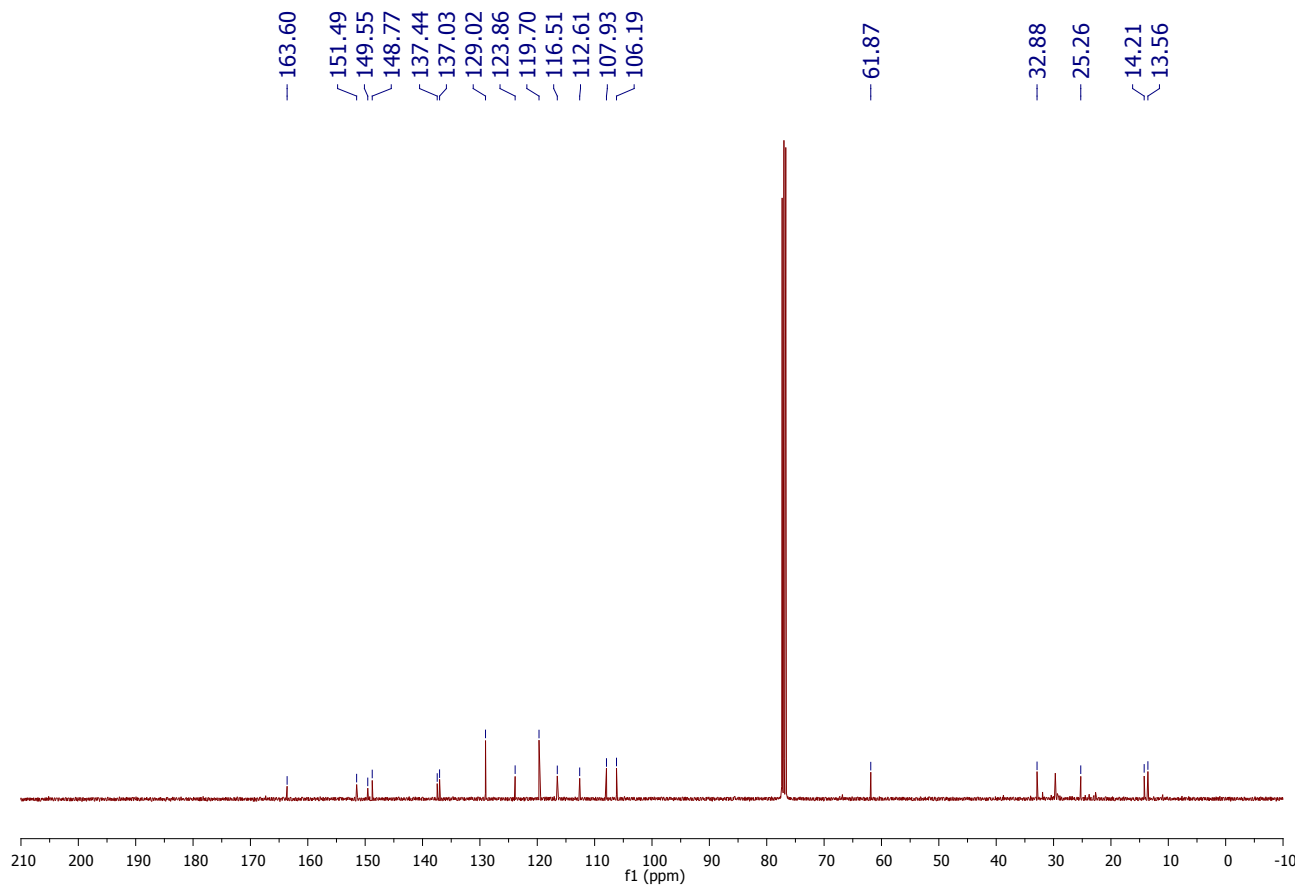

7.82
7.81
7.81
7.80
7.79
7.40
7.40
7.40
7.39
7.39
7.10
5.99
5.98
5.88
5.88
5.87
4.40
4.38
4.37
4.35
3.37
3.15
2.26
2.26
1.42
1.40
1.38
N
N
O
O
O
1.98
3.00
0.88
1.00
1.06
2.05
2.14
2.05
3.33
3.20
11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)

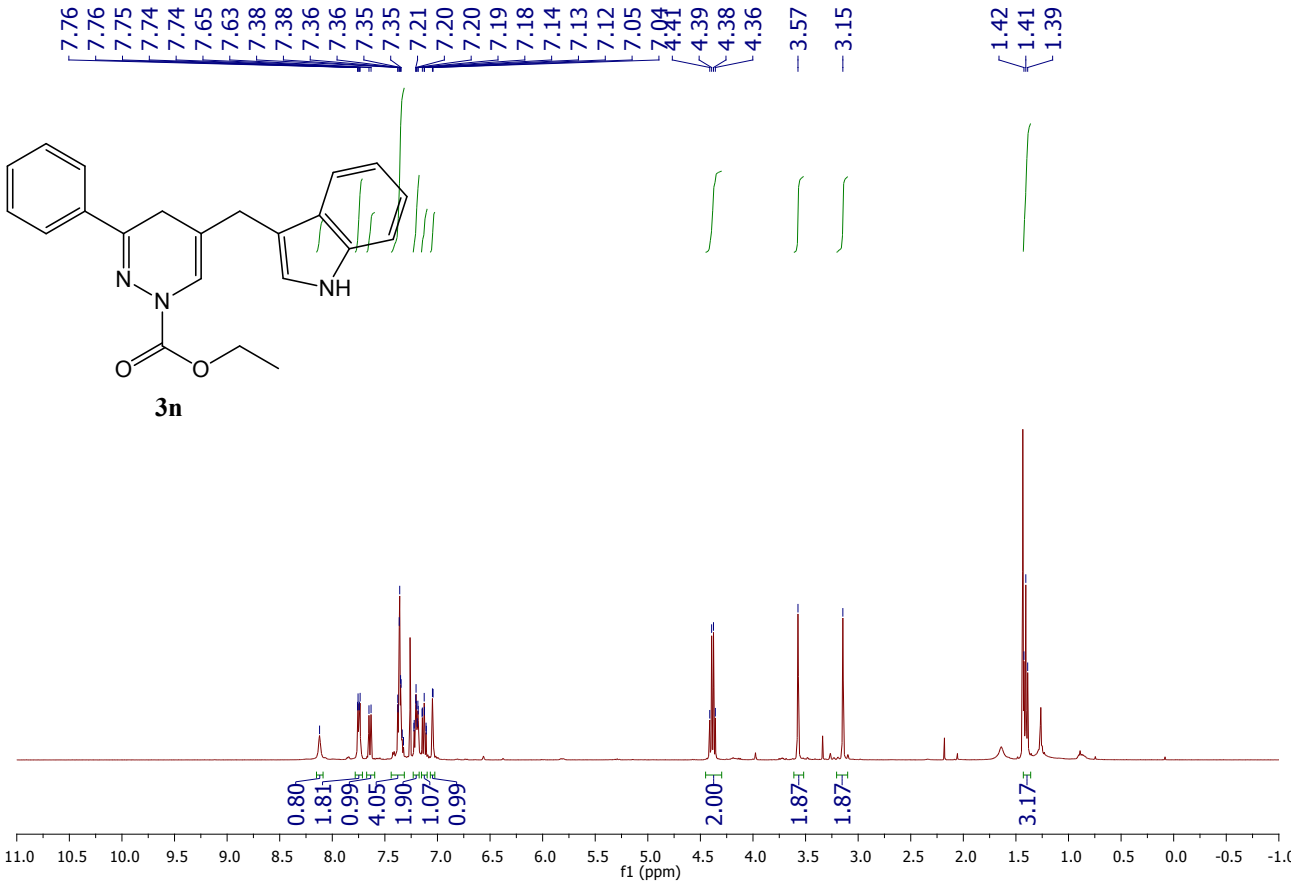
3l


152.43
151.34
149.51
146.18
136.30
129.81
128.29
125.96
118.76
111.11
107.57
106.13
62.95
32.99
25.92
14.51
13.53
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

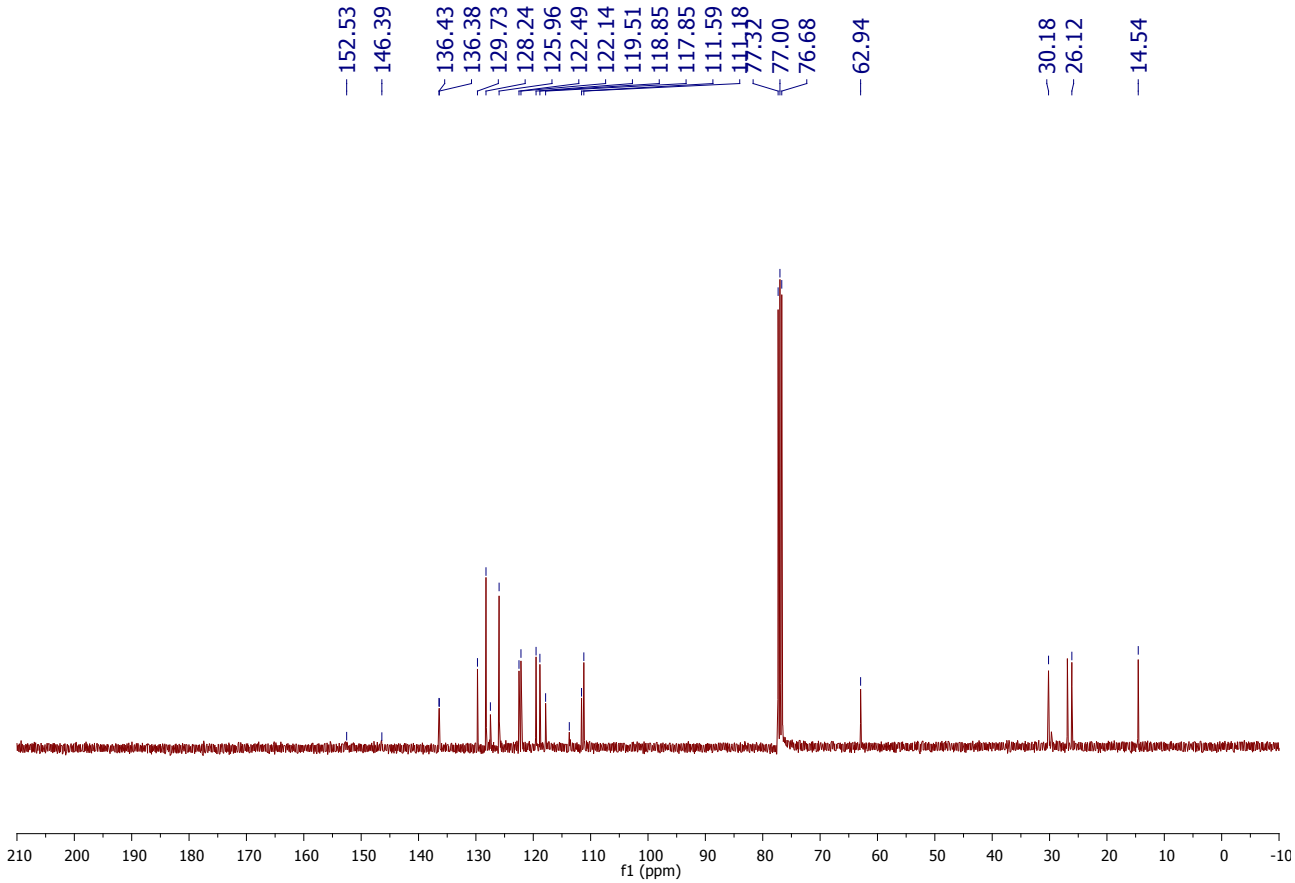

8.61
7.53
7.51
7.36
7.34
7.32
7.17
5.99
5.98
5.88
5.87
5.87
4.36
4.35
4.33
4.31
3.31
3.09
2.25
1.38
1.00
2.04
2.08
0.96
1.03
0.98
0.97
2.16
2.02
1.97
3.13
4.10
f1 (ppm)

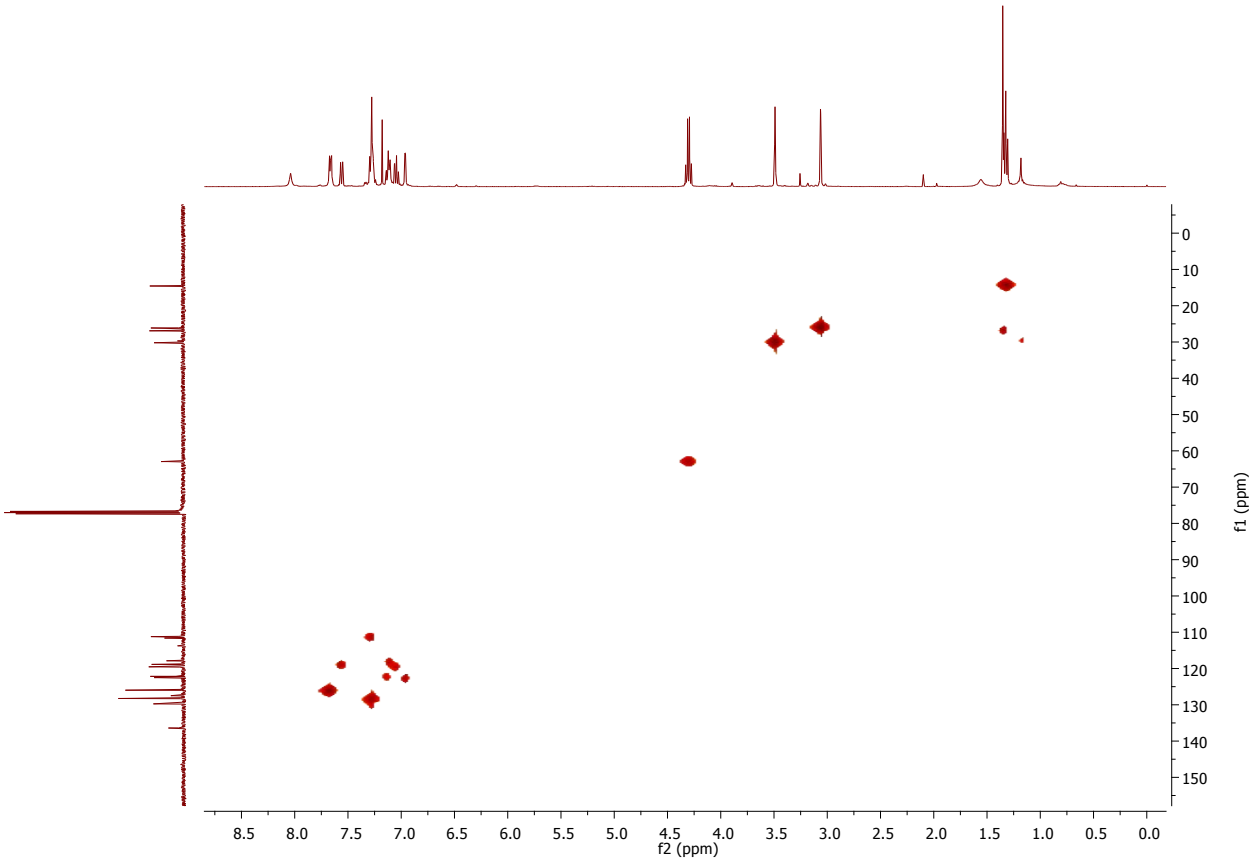
3m

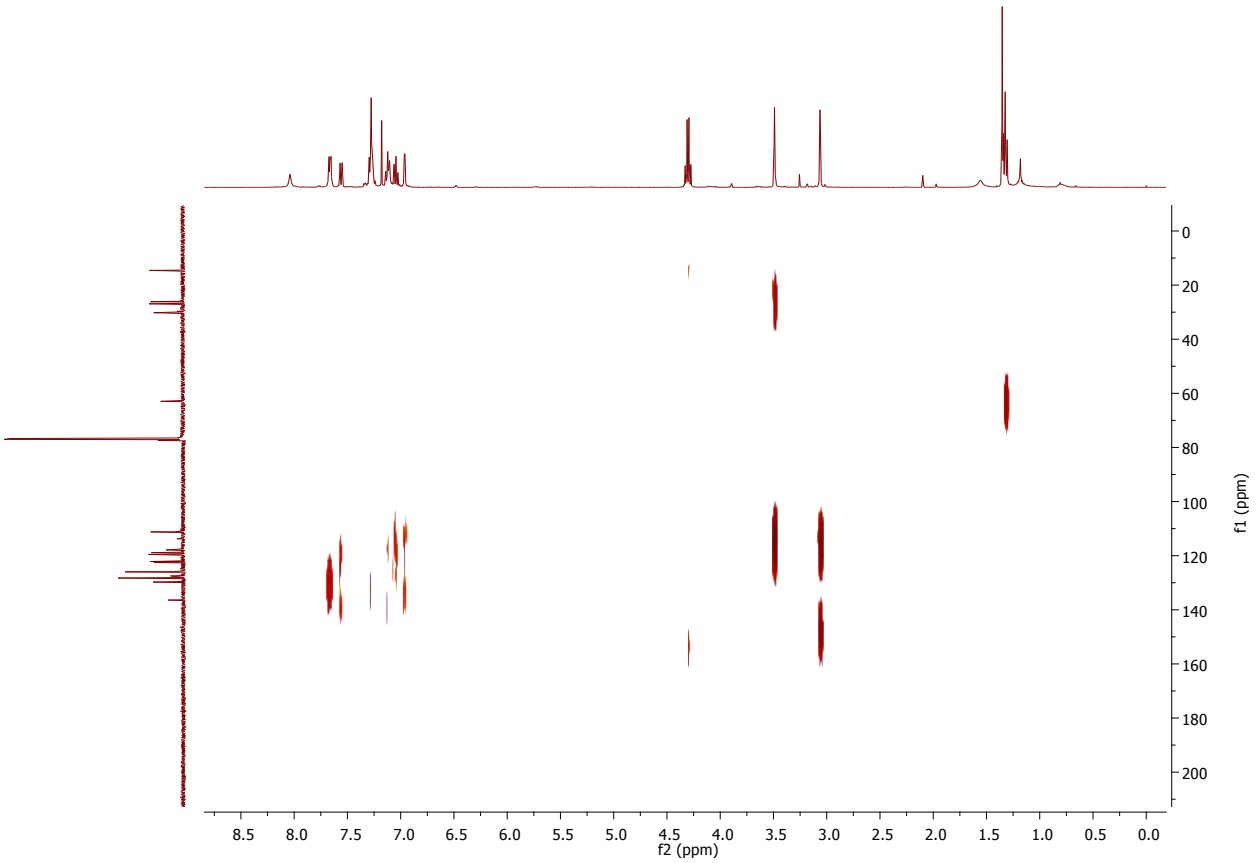

163.60
151.49
149.55
148.77
137.44
137.03
129.02
123.86
119.70
116.51
112.61
107.93
106.19
61.87
32.88
25.26
14.21
13.56
f1 (ppm)

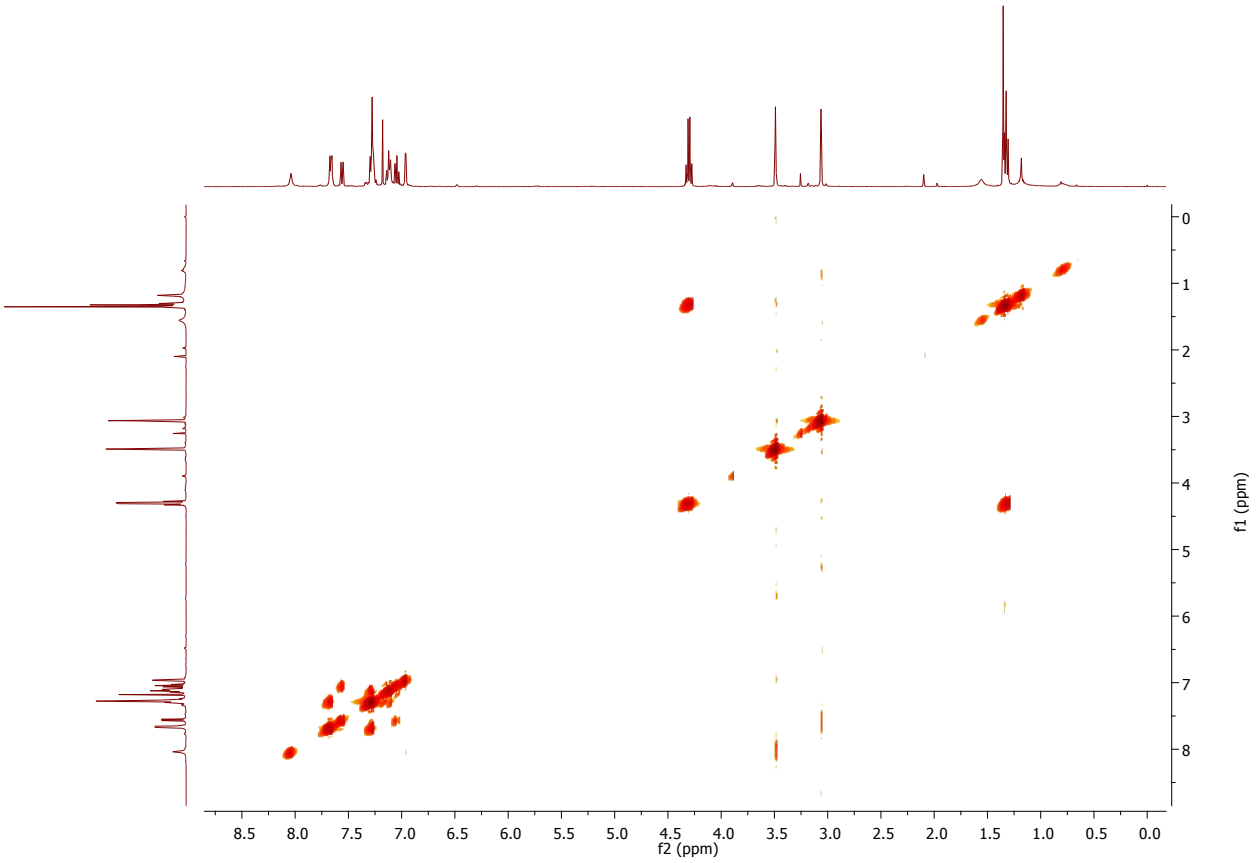

7.76
7.76
7.75
7.74
7.74
7.65
7.63
7.38
7.38
7.36
7.36
7.35
7.35
7.21
7.20
7.20
7.19
7.18
7.14
7.13
7.12
7.05
7.04
4.41
4.39
4.38
4.36
3.57
3.15
1.42
1.41
1.39
N
N
NH
O
O
0.80
1.81
0.99
4.05
1.90
1.07
0.99
2.00
1.87
1.87
3.17
f1 (ppm)

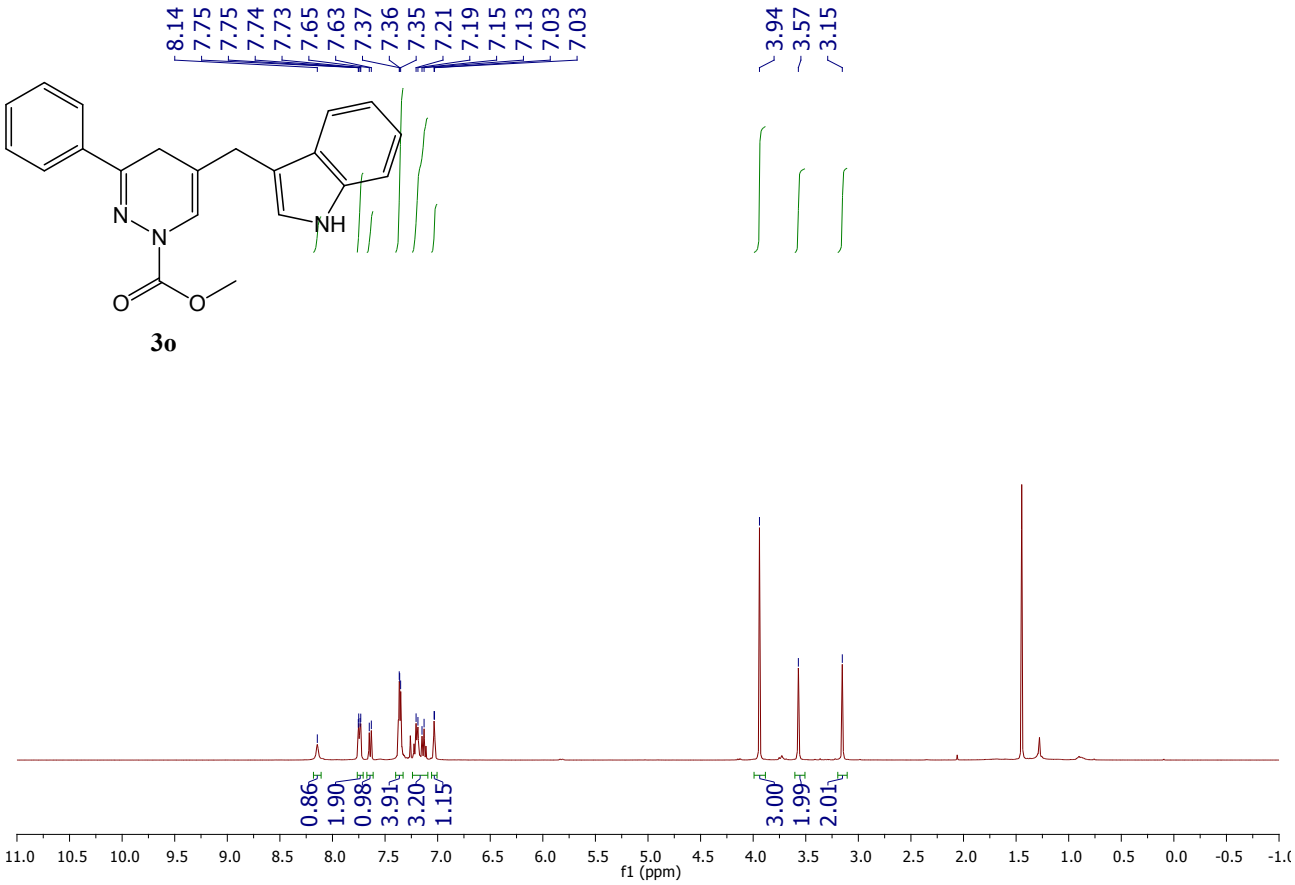
3n


152.53
146.39
136.43
136.38
129.73
128.24
125.96
122.49
122.14
119.51
118.85
117.85
111.59
111.18
77.32
77.00
76.68
62.94
30.18
26.12
14.54
f1 (ppm)

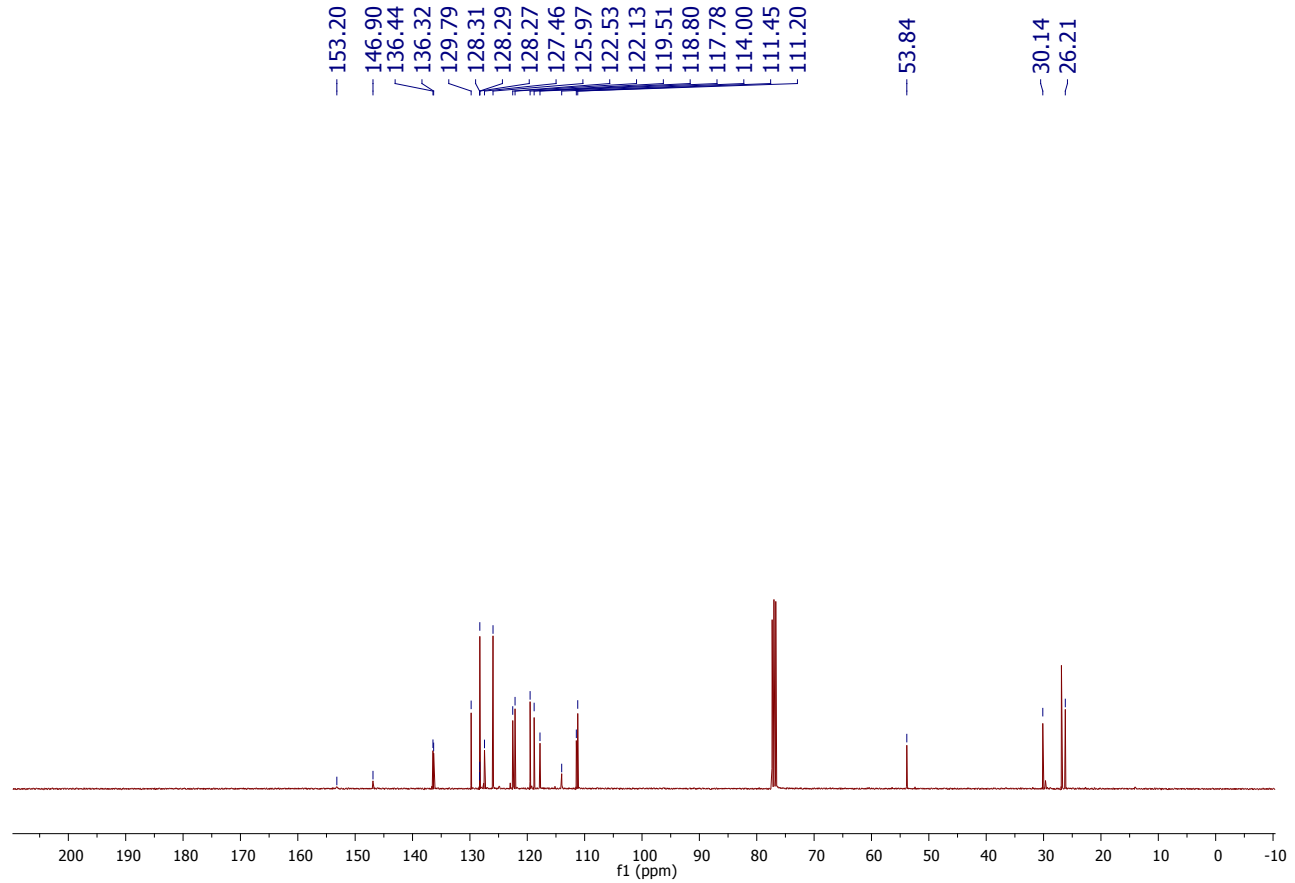

f2 (ppm)
f1 (ppm)

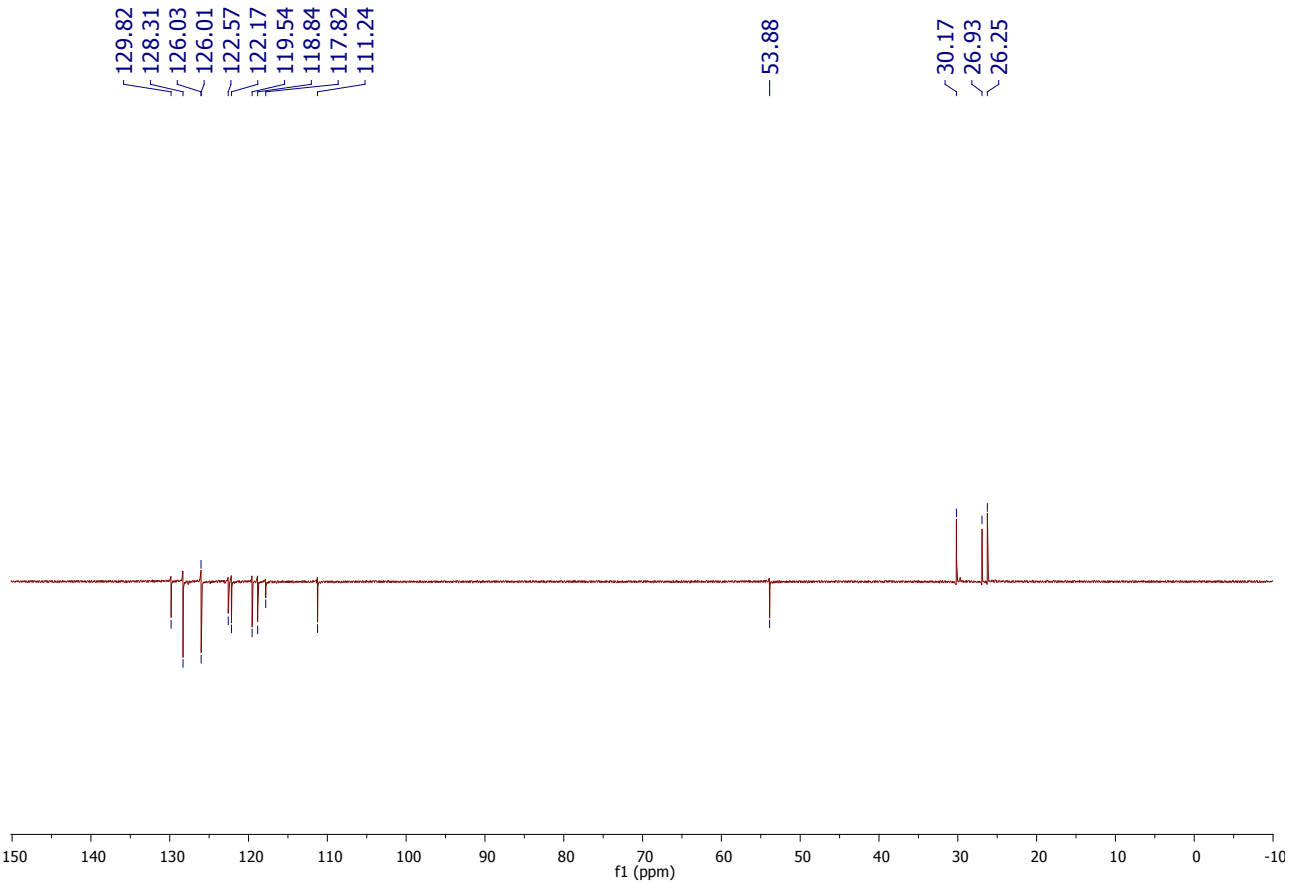

f2 (ppm)
f1 (ppm)

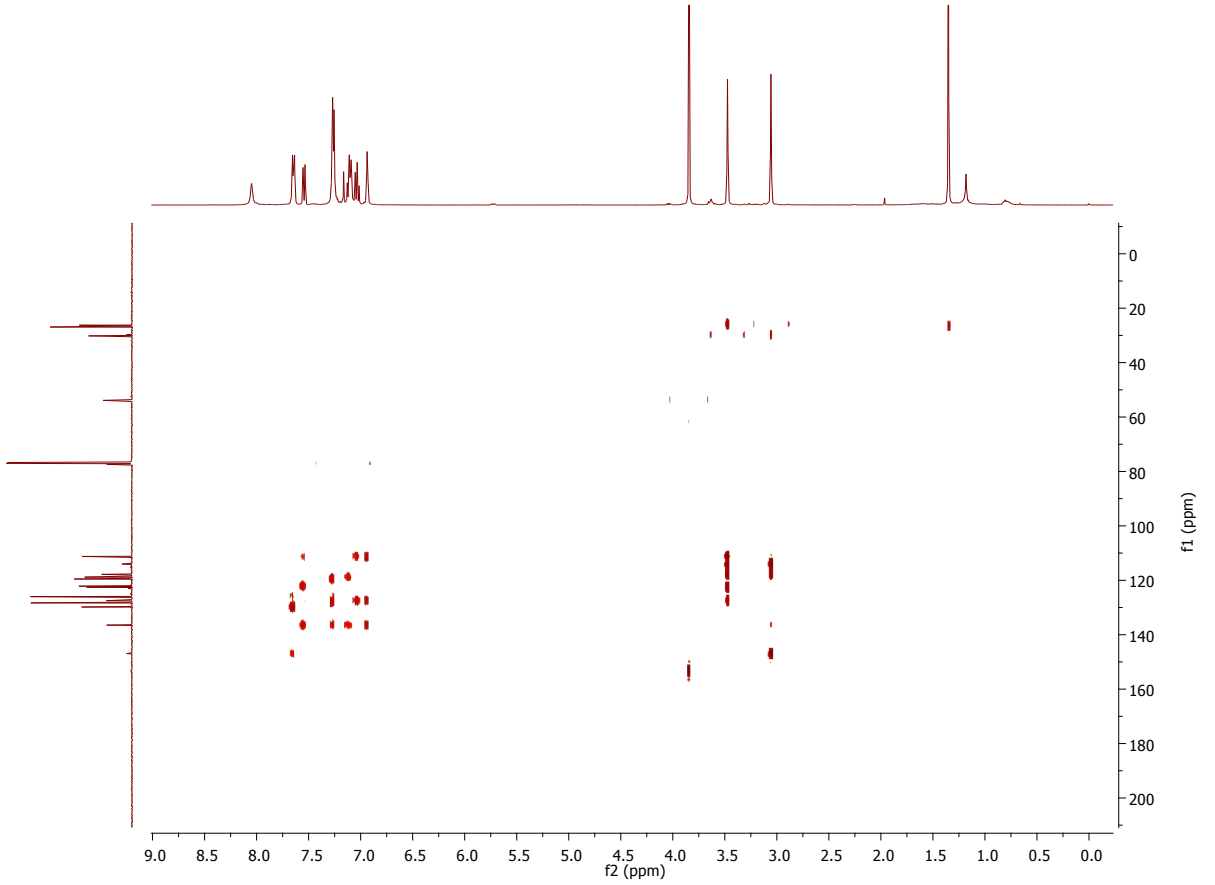

0
1
2
3
4
5
6
7
8
f1 (ppm)
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f2 (ppm)

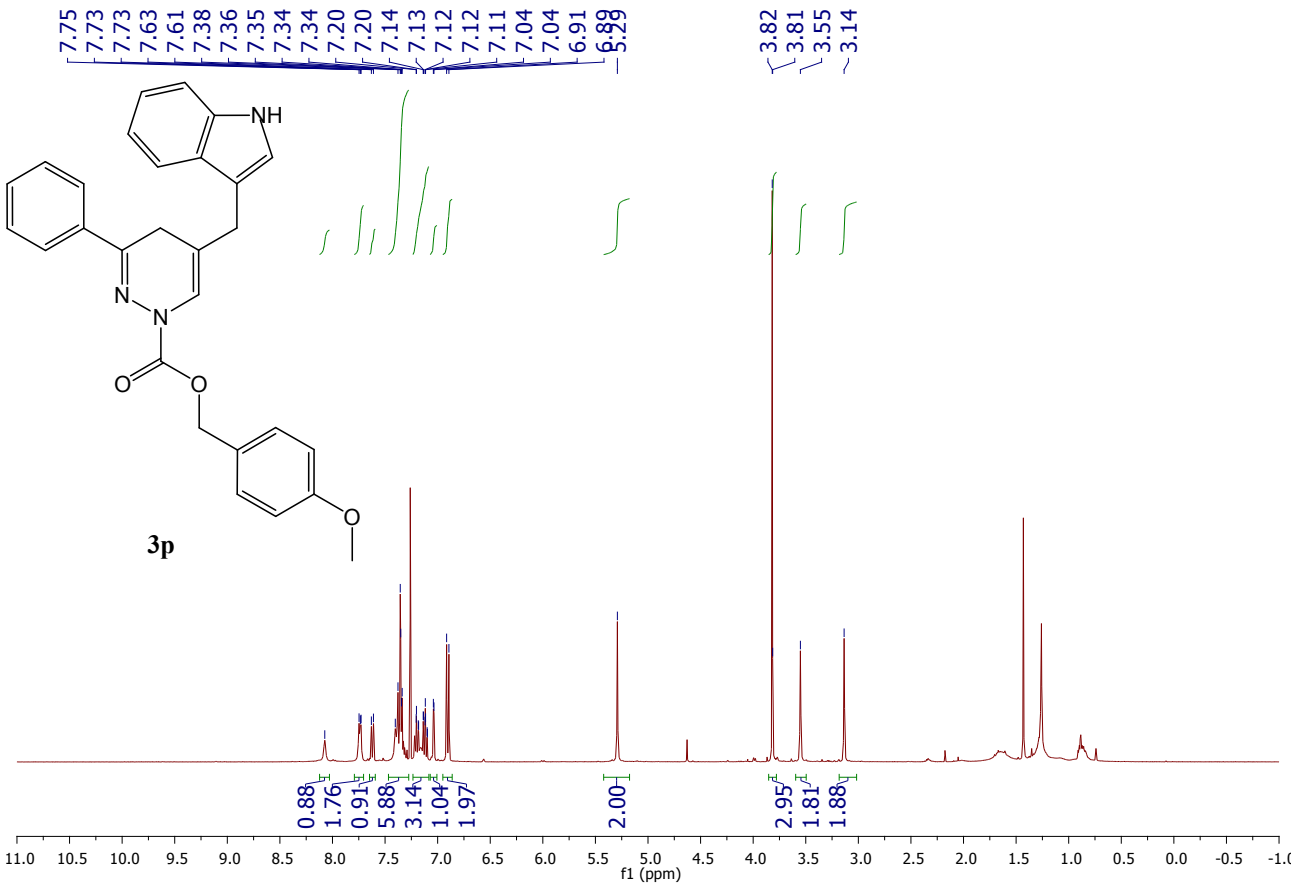

8.14
7.75
7.75
7.74
7.73
7.65
7.63
7.37
7.36
7.35
7.21
7.19
7.15
7.13
7.03
7.03
3.94
3.57
3.15
N
N
NH
O
O
0.86
1.90
0.98
3.91
3.20
1.15
3.00
1.99
2.01
f1 (ppm)

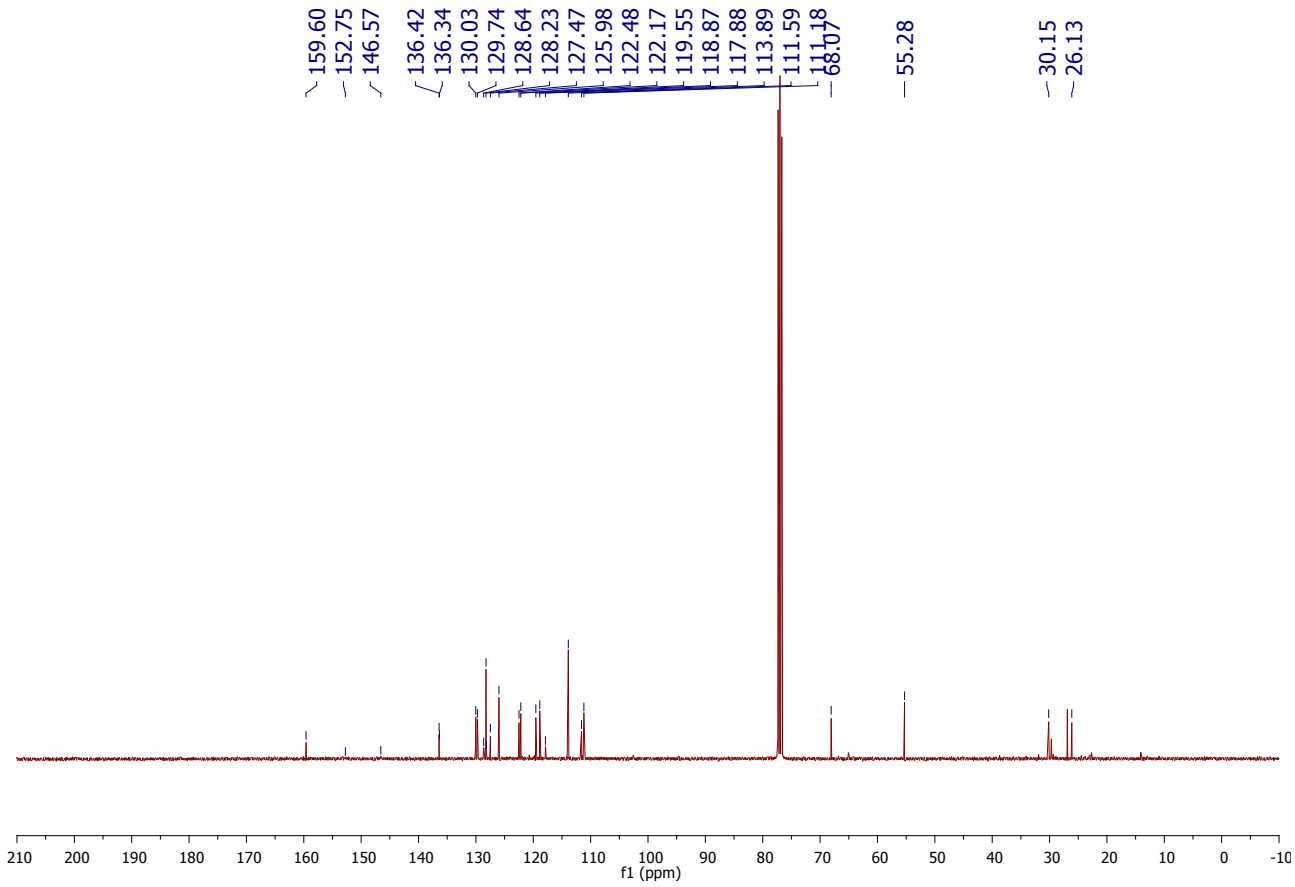
3o

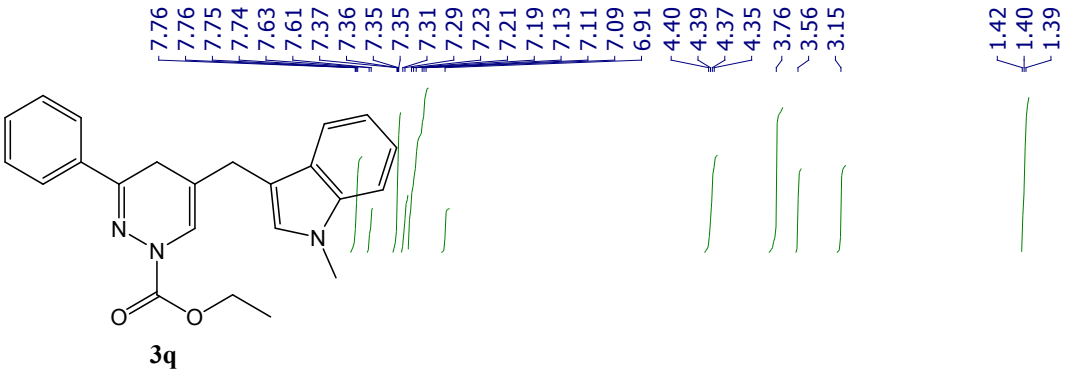

153.20
146.90
136.44
136.32
129.79
128.31
128.29
128.27
127.46
125.97
122.53
122.13
119.51
118.80
117.78
114.00
111.45
111.20
53.84
30.14
26.21
f1 (ppm)


129.82
128.31
126.03
126.01
122.57
122.17
119.54
118.84
117.82
111.24
53.88
30.17
26.93
26.25
150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

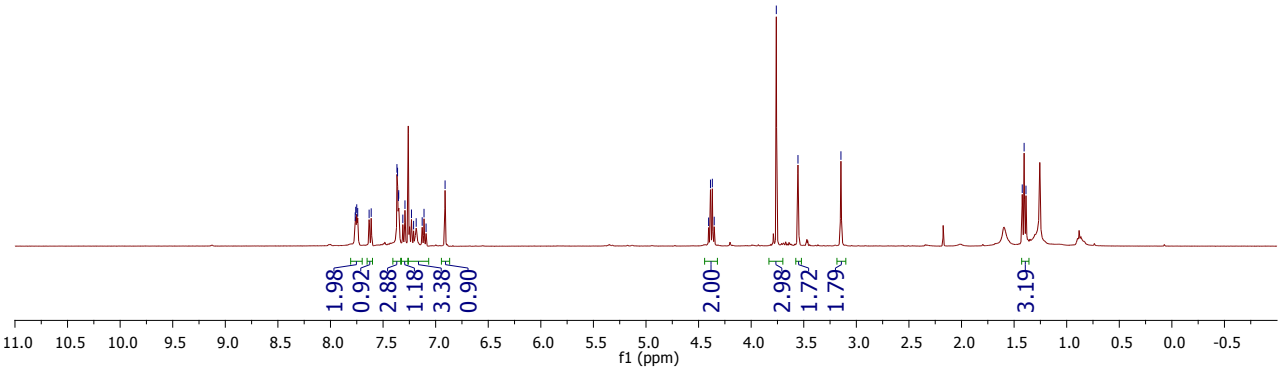

0 20 40 60 80 100 120 140 160 180 200
f1 (ppm)
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f2 (ppm)

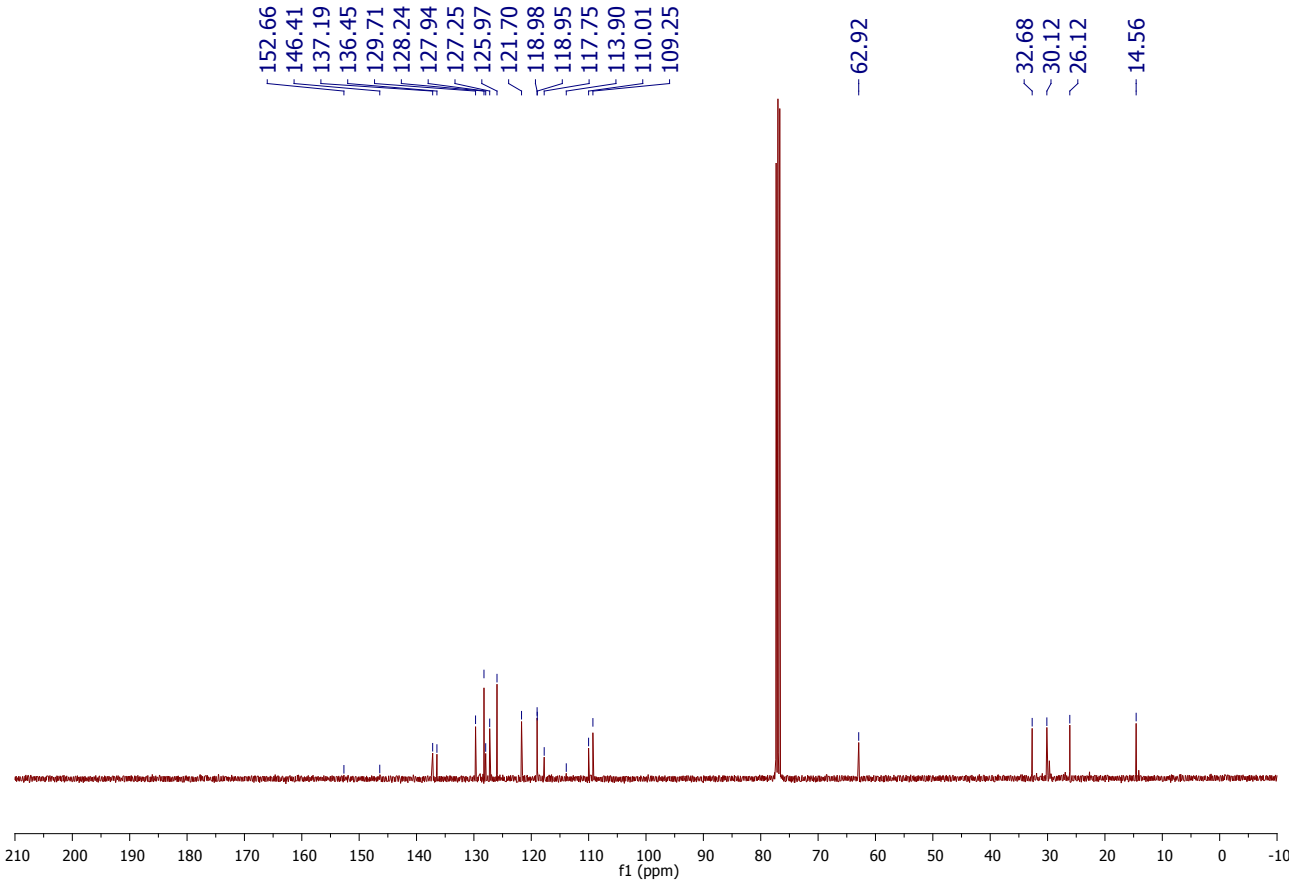

7.75
7.73
7.73
7.63
7.61
7.38
7.36
7.35
7.34
7.34
7.20
7.20
7.14
7.13
7.12
7.12
7.11
7.04
7.04
6.91
6.89
5.29
3.82
3.81
3.55
3.14
NH
N
N
O
O
O
3p
0.88
1.76
0.91
5.88
3.14
1.04
1.97
2.00
2.95
1.81
1.88
f1 (ppm)

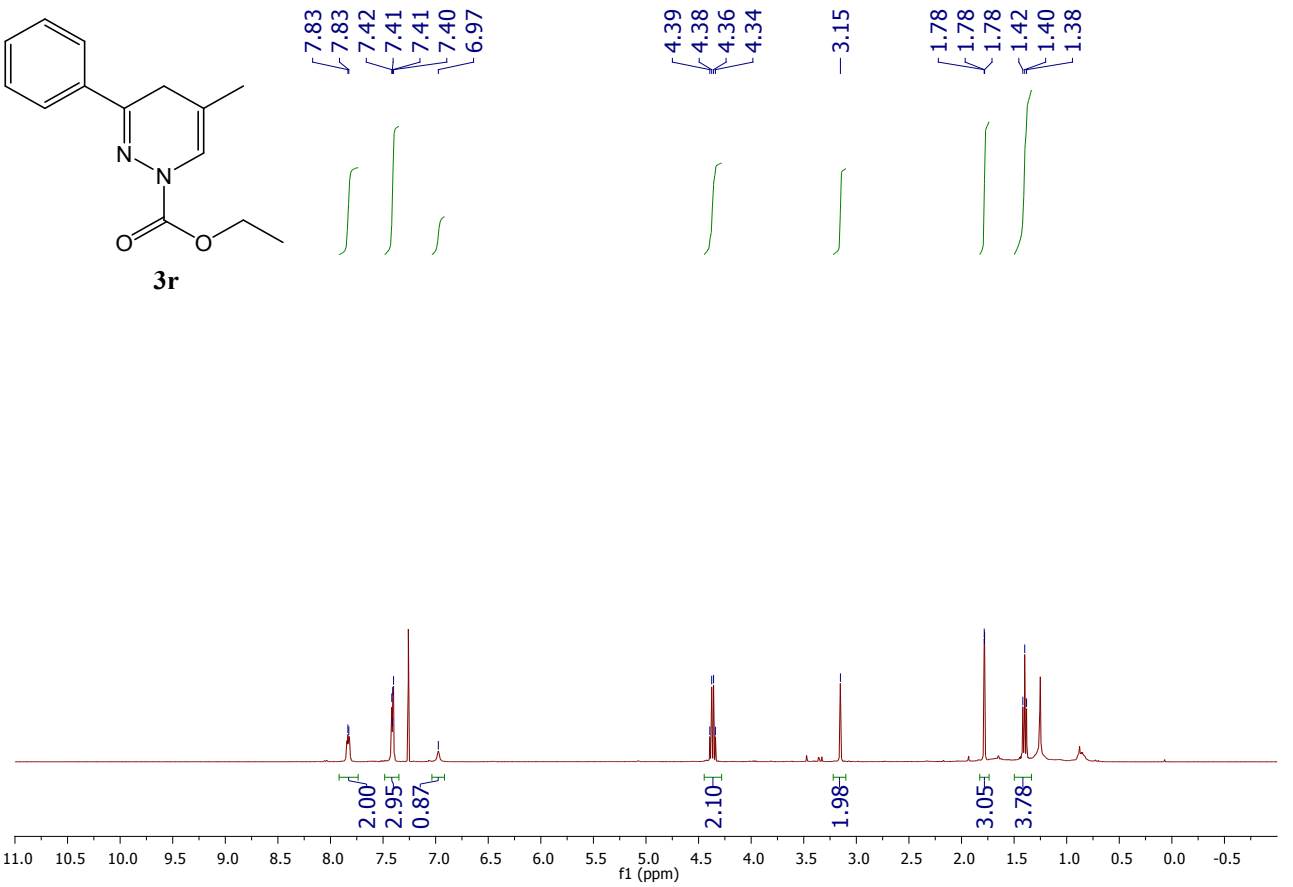

159.60
152.75
146.57
136.42
136.34
130.03
129.74
128.64
128.23
127.47
125.98
122.48
122.17
119.55
118.87
117.88
113.89
111.59
111.18
68.07
55.28
30.15
26.13
f1 (ppm)


7.76
7.76
7.75
7.74
7.63
7.61
7.37
7.36
7.35
7.35
7.31
7.29
7.23
7.21
7.19
7.13
7.11
7.09
6.91
4.40
4.39
4.37
4.35
3.76
3.56
3.15
1.42
1.40
1.39
N
N
N
O
O

3q


1.98
0.92
2.88
1.18
3.38
0.90
2.00
2.98
1.72
1.79
3.19
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
f1 (ppm)


152.66
146.41
137.19
136.45
129.71
128.24
127.94
127.25
125.97
121.70
118.98
118.95
117.75
113.90
110.01
109.25
62.92
32.68
30.12
26.12
14.56
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)


7.83
7.83
7.42
7.41
7.41
7.40
6.97
4.39
4.38
4.36
4.34
3.15
1.78
1.78
1.78
1.42
1.40
1.38
N
N
O
O
2.00
2.95
0.87
2.10
1.98
3.05
3.78
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
f1 (ppm)
152.58
145.87
136.43
129.77
128.33
125.92
117.24
110.69
62.87
27.88
19.83
14.55
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)

3r