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Supporting Information

Palladium-Catalyzed Cross-Coupling of Unreactive C(sp^3)−H Bonds with Azole C(sp^2)−H Bonds by Using Bromide as a Traceless Directing Group

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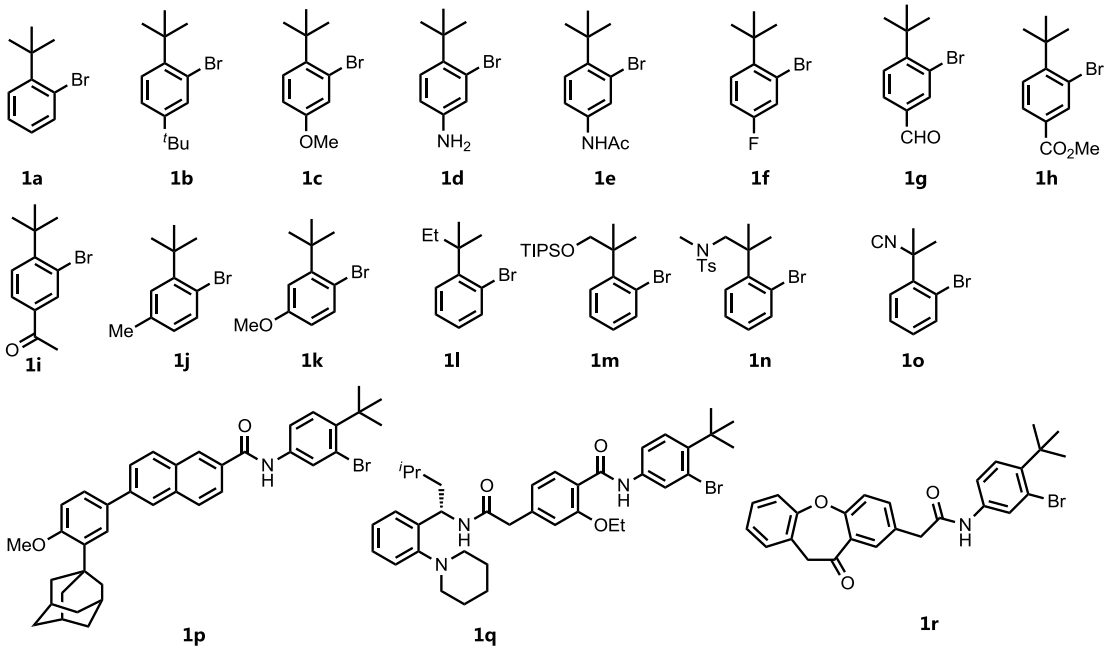
1. General Information

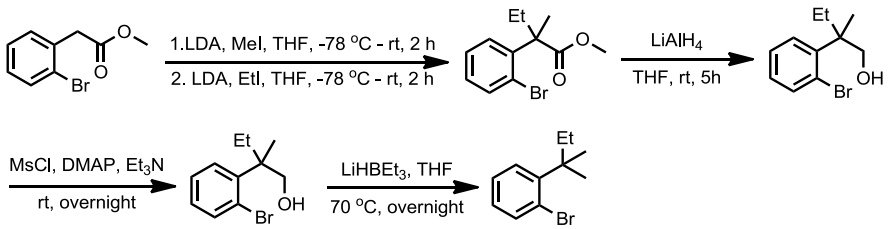
$Pd(OAc)_2$ was purchased from Strem Chemicals. All solvents were dried by JC Meyer Solvent Drying System. Unless otherwise noted, the other commercial chemicals were used without further purification. ^1H NMR and ^{13}C NMR spectra were recorded on Bruker DRX-600 instrument (600 MHz). High resolution mass spectra were measured on Bruker MicroTOF II ESI-TOF mass spectrometer. NMR spectra were recorded in $CDCl_3$. ^1H NMR spectra were referenced to residual $CHCl_3$ at 7.26 ppm, and ^{13}C NMR spectra were referenced to the central peak of $CDCl_3$ at 77.0 ppm. Chemical shifts (δ) are reported in ppm, and coupling constants (*J*) are in Hertz (Hz). Multiplicities are reported using the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet.

2. General Procedures for the Synthesis of Substrates



The known compounds (**1a-1k** and **1m-1r**) were prepared by following the reported procedures.[1-3] The known 1,3,4-oxadiazoles were prepared by following the reported procedures.[4]

Procedures for the Synthesis of the Compound 1l



1-Bromo-2-(*tert*-pentyl)benzene (**1l**) was made according to the modified procedures.[5,6] Methyl 2-(2-bromophenyl)acetate (4.58 g, 20 mmol) was dissolved in dry THF (1 M) under

nitrogen and LDA (11 mL, 22 mmol, 2 M in THF) was added at –78 °C *via* syringe. After stirring for 10 min at this temperature, MeI (3.12 g, 22 mmol) was added and the mixture was stirred for 2 h at room temperature. The reaction mixture was quenched with water and extracted with EtOAc (3 times). The combined organic layers were dried over sodium sulfate, filtered and evaporated under reduced pressure without further purification to provide desired product methyl 2-(2-bromophenyl)propanoate.

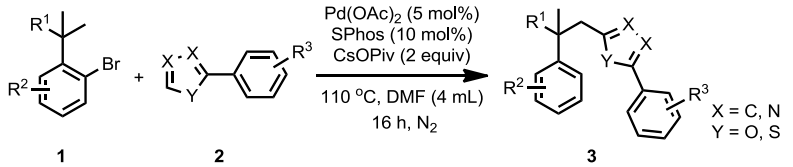
Dry THF (1 M) was added to dissolve the crude product under nitrogen and LDA (11 mL, 22 mmol, 2 M in THF) was added at –78 °C *via* syringe. After stirring for 10 min at this temperature, EtI (3.43 g, 22 mmol) was added and the mixture was stirred for 2 h at room temperature. The reaction mixture was quenched with water and extracted with EtOAc (3 times). The combined organic layers were dried over sodium sulfate, filtered and evaporated under vacuum. The residue was purified on silica gel to give 2-(2-bromophenyl)-2-methylbutanoate as a yellow oil (5.0 g, 92%).

Over a 0 ℃ solution of methyl 2-(2-bromophenyl)-2-methylbutanoate (2.51 g, 9 mmol) in anhydrous THF (45 mL) was added $LiAlH_4$ (345 mg, 9 mmol) portionwise. The reaction was stirred for 5 h at room temperature. The reaction mixture was quenched with water and extracted with EtOAc (3 times), washed with brine, dried over $MgSO_4$ and concentrated. The residue was purified on silica gel to give the corresponding alcohol product as a colorless oil (1.35 g, 62%).

Over a solution of the alcohol (1.51 g, 6 mmol) and DMAP (146 mg, 1.2 mmol) in dry DCM (30 mL) was added dry Et_3N (304 mg, 18 mmol). After stirring for 30 min at 0 ℃, MsCl (1.37 g, 12 mmol) was added. The reaction was stirred overnight while warming up to room temperature. When completed, Et_2O was added followed by NH_4Cl (aq.). The reaction was extracted with Et_2O (3 times), washed with brine, dried over $MgSO_4$ and concentrated. The crude was used in the next step without further purification.

Over a solution of the mesylate (321 mg, 1 mmol) in anhydrous THF (1mL) under nitrogen was added Super-Hydride (2.1 mL, 1M in THF). The reaction was heated at 70 ℃ overnight. When completed, the reaction was quenched by addition of NH_4Cl (aq.). The reaction was extracted with Et_2O (3 times), dried over $MgSO_4$, concentrated and purified on silica gel column to give 1-bromo-2-(*tert*-pentyl)benzene (**1l**) as a colorless oil (1.09 g, 80%).

3. General Procedures for the Cross-Coupling of C(sp^3)-H/C(sp^2)-H Bonds

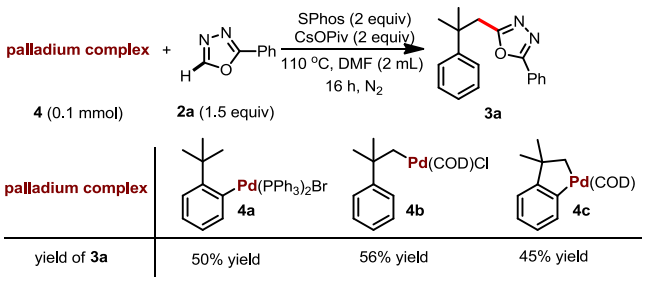


A 25 mL Schlenk-type tube (with a Teflon screw cap and a side arm) equipped with a magnetic stir bar was charged with $Pd(OAc)_2$ (2.2 mg, 0.01 mmol), SPhos (8.2 mg, 0.02 mmol), CsOPiv (93.6 mg, 0.4 mmol), the corresponding aryl bromide **1** (0.2 mmol), oxadiazole **2** (0.3 mmol, 1.5 equiv) and DMF (4 mL). The reaction was frozen with liquid nitrogen and then the tube was evacuated and backfilled with nitrogen (5 times). The mixture was stirred at 110 ℃ (preheated oil bath) for 16 hours. After cooling to room temperature, the reaction mixture was diluted with EtOAc (15 mL), washed with water (3 times), dried over Na_2SO_4 and concentrated

under reduced pressure. The residue was purified by preparative silica gel TLC with petroleum ether/ethyl acetate to give the corresponding products.

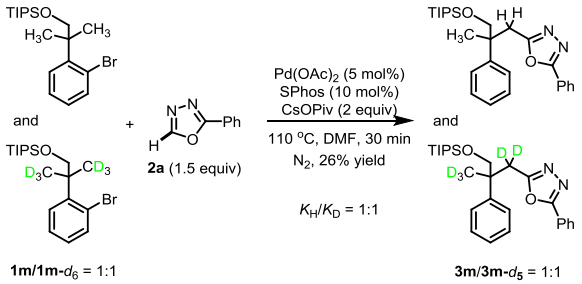
4. Preliminary Mechanistic Studies

4.1 Mechanistic Studies



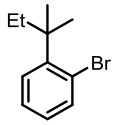
A 25 mL Schlenk-type tube (with a Teflon screw cap and a side arm) equipped with a magnetic stir bar was charged with the corresponding Pd complex **4** (0.1 mmol, 1 equiv),[2] SPhos (82.1 mg, 0.2 mmol), 2-phenyl-1,3,4-oxadiazole **2a** (21.9 mg, 0.15 mmol), CsOPiv (46.8 mg, 0.2 mmol), and DMF (2 mL). The reaction was frozen with liquid nitrogen and then the tube was evacuated and backfilled with nitrogen (5 times). The mixture was stirred at 110 °C (preheated oil bath) for 16 hours. After cooling to room temperature, the reaction mixture was diluted with EtOAc (15 mL), washed with water (3 times), dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by preparative thin layer chromatography (PTLC) affording cross-coupling product **3a** as a white solid.

4.2 Kinetic Isotope Effect Studies



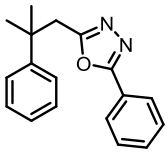
A 25 mL Schlenk-type tube (with a Teflon screw cap and a side arm) equipped with a magnetic stir bar was charged with $Pd(OAc)_2$ (2.2 mg, 0.01 mmol), SPhos (8.21 mg, 0.02 mmol), CsOPiv (93.6 mg, 0.4 mmol), 2-phenyl-1,3,4-oxadiazole **2a** (0.3 mmol, 1.5 equiv), aryl bromide **1m** (0.1 mmol), **1m-*d*^{6}** (0.1 mmol) and DMF (4 mL). The reaction was frozen with liquid nitrogen and then the tube was evacuated and backfilled with nitrogen (5 times). The mixture was stirred at 110 °C (preheated oil bath) for30 mins. After cooling to room temperature, the reaction mixture was diluted with EtOAc (15 mL), washed with water (3 times), dried over Na_2SO_4 and concentrated under reduced pressure. The product was analyzed by ^{1}H NMR after purification by preparative silica gel TLC with petroleum ether/ethyl acetate.

5. Characterization of the Substrates

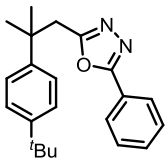


1-Bromo-2-(*tert*-pentyl)benzene (1l): colorless oil. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.57 (d, *J* = 7.8 Hz, 1H), 7.37 (d, *J* = 8.0 Hz, 1H), 7.24 (t, *J* = 7.6 Hz, 1H), 7.03 (t, *J* = 7.5 Hz, 1H), 2.04 (q, *J* = 7.5 Hz, 2H), 1.45 (s, 6H), 0.64 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 146.07, 135.63, 129.40, 127.34, 127.01, 122.54, 40.20, 32.30, 28.16, 9.35. MS (EI): (M^+): 225.9.

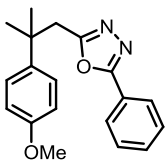
6. Characterization of the Products



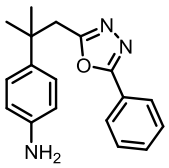
2-(2-Methyl-2-phenylpropyl)-5-phenyl-1,3,4-oxadiazole (3a): white solid (49.0 mg, 88%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.84 – 7.79 (m, 2H), 7.50 – 7.46 (m, 1H), 7.46 – 7.42 (m, 2H), 7.40 (dd, *J* = 8.4, 1.1 Hz, 2H), 7.36 – 7.31 (m, 2H), 7.25 – 7.21 (m, 1H), 3.24 (s, 2H), 1.51 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.93, 164.63, 147.23, 131.41, 128.90, 128.34, 126.65, 126.32, 125.56, 123.93, 40.01, 38.13, 28.50. HRMS (ESI-TOF) *m/z*: calcd for $C_{18}H_{18}N_2ONa^+$: 301.1311 $(M + Na)^+$, found: 301.1327.



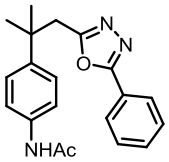
2-(2-(4-(*Tert*-butyl)phenyl)-2-methylpropyl)-5-phenyl-1,3,4-oxadiazole (3b)： white solid (57.0 mg, 85%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.79 – 7.75 (m, 2H), 7.47 (t, *J* = 7.4 Hz, 1H), 7.41 (t, *J* = 7.6 Hz, 2H), 7.35 (d, *J* = 8.5 Hz, 2H), 7.31 (d, *J* = 8.5 Hz, 2H), 3.22 (s, 2H), 1.50 (s, 6H), 1.32 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.98, 164.56, 148.98, 144.07, 131.35, 128.81, 126.59, 125.28, 125.11, 123.90, 40.15, 37.74, 34.27, 31.30, 28.41. HRMS (ESI-TOF) *m/z*: calcd for $C_{22}H_{26}N_2ONa^+$:357.1937 $(M + Na)^+$, found: 357.1941.



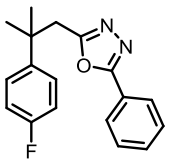
2-(2-(4-Methoxyphenyl)-2-methylpropyl)-5-phenyl-1,3,4-oxadiazole (3c): white solid (57.2 mg, 93%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.86 – 7.83 (m, 2H), 7.51 – 7.47 (m, 1H), 7.47 – 7.43 (m, 2H), 7.32 – 7.28 (m, 2H), 6.88 – 6.84 (m, 2H), 3.78 (s, 3H), 3.20 (s, 2H), 1.49 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.02, 164.62, 157.94, 139.36, 131.42, 128.91, 126.66, 126.65, 124.00, 113.63, 55.24, 40.19, 37.60, 28.68. HRMS (ESI-TOF) *m/z*: calcd for $C_{19}H_{21}N_2O_2^+$: 309.1598 $(M + H)^+$, found: 309.1606.



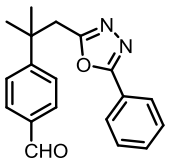
4-(2-Methyl-1-(5-phenyl-1,3,4-oxadiazol-2-yl)propan-2-yl)aniline (3d): brown oil (29.4 mg, 50%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.91 – 7.85 (m, 2H), 7.52 – 7.42 (m, 3H), 7.19 – 7.14 (m, 2H), 6.68 – 6.61 (m, 2H), 3.63 (brs, 2H), 3.17 (s, 2H), 1.46 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) 165.16, 164.56, 144.57, 137.23, 131.34, 128.88, 126.64, 126.37, 123.97, 114.93, 40.12, 37.41, 28.59. HRMS (ESI-TOF) *m/z*: calcd for $C_{18}H_{20}N_3O^+$: 294.1601 $(M + H)^+$, found: 294.1604.



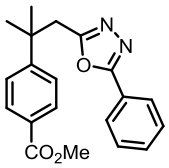
***N*-(4-(2-methyl-1-(5-phenyl-1,3,4-oxadiazol-2-yl)propan-2-yl)phenyl)acetamide (3e):** yellow solid (54.8 mg, 82%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.87 –7.83 (m, 2H), 7.65 (s, 1H), 7.50 – 7.41 (m, 5H), 7.34 – 7.29 (m, 2H), 3.20 (s, 2H), 2.14 (s, 3H), 1.48 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 168.41, 164.90, 164.66, 142.99, 136.25, 131.47, 128.94, 126.66, 126.09, 123.81, 119.85, 39.93, 37.82, 28.57, 24.44. HRMS (ESI-TOF) *m/z*: calcd for $C_{20}H_{21}N_3O_2Na^+$:358.1526 $(M + Na)^+$, found 358.1537.



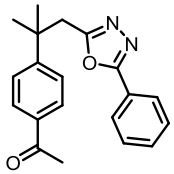
2-(2-(4-Fluorophenyl)-2-methylpropyl)-5-phenyl-1,3,4-oxadiazole (3f): white solid (42.6 mg, 72%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.85 – 7.82 (m, 2H), 7.52 – 7.43 (m, 3H), 7.37 – 7.32 (m, 2H), 7.01 (t, *J* = 8.7 Hz, 2H), 3.21 (s, 2H), 1.50 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) 164.71, 164.67, 161.33 (d, *J* = 245.2 Hz), 142.89 (d, *J* = 3.2 Hz), 131.51, 128.97, 127.24 (d, *J* = 7.7 Hz), 126.62, 123.87, 115.01 (d, *J* = 21.0 Hz), 40.11, 37.83, 28.75. ^{19}F NMR (565 MHz, $CDCl_3$) δ -117.07. HRMS (ESI-TOF) *m/z*: calcd for $C_{18}H_{17}FN_2ONa^+$: 319.1217 $(M + Na)^+$, found 319.1227.



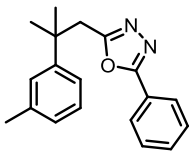
4-(2-Methyl-1-(5-phenyl-1,3,4-oxadiazol-2-yl)propan-2-yl)benzaldehyde (3g): yellow solid (27.6 mg, 45%). ^{1}H NMR (600 MHz, $CDCl_3$) 9.99 (s, 1H), 7.88 – 7.83 (m, 2H), 7.82 – 7.77 (m, 2H), 7.60 – 7.55 (m, 2H), 7.52 – 7.45 (m, 1H), 7.45 – 7.41 (m, 2H), 3.28 (s, 2H), 1.56 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 191.78, 164.70, 164.31, 154.24, 134.72, 131.59, 129.82, 128.98, 126.58, 126.42, 123.72, 39.64, 38.74, 28.49. HRMS (ESI-TOF) *m/z*: calcd for $C_{19}H_{18}N_2O_2Na^+$: 329.1260 $(M + Na)^+$, found 329.1264.



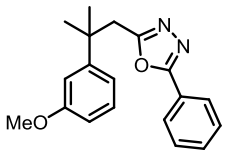
Methyl-4-(2-methyl-1-(5-phenyl-1,3,4-oxadiazol-2-yl)propan-2-yl)benzoate (3h): yellow solid (46.5mg, 69%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.01 – 7.98 (m, 2H), 7.82 – 7.79 (m, 2H), 7.50 – 7.45 (m, 3H), 7.43 (t, *J* =7.5 Hz, 2H), 3.90 (s, 3H), 3.26 (s, 2H), 1.53 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 166.82, 164.66, 164.46, 152.48, 131.49, 129.66, 128.93, 128.28, 126.61, 125.71, 123.77, 52.01, 39.67, 38.46, 28.44. HRMS (ESI-TOF) *m/z*: calcd for $C_{20}H_{20}N_2O_3Na^+$: 359.1366 $(M + Na)^+$, found 359.1379.



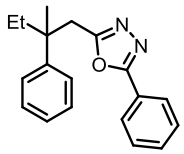
1-(4-(2-Methyl-1-(5-phenyl-1,3,4-oxadiazol-2-yl)propan-2-yl)phenyl)ethan-1-one (3i): white soild (38.6 mg, 60%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.94 – 7.89 (m, 2H), 7.82 – 7.78 (m, 2H), 7.51 – 7.45 (m, 3H), 7.43 (t, *J* =7.5 Hz, 2H), 3.26 (s, 2H), 2.57 (s, 3H), 1.54 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 197.61, 164.66, 164.41, 152.65, 135.32, 131.53, 128.93, 128.44, 126.58, 125.91, 123.75, 39.64, 38.50, 28.44, 26.54. HRMS (ESI-TOF) *m/z*: calcd for $C_{20}H_{20}N_2O_2Na^+$: 343.1417 $(M + Na)^+$, found 343.1428.



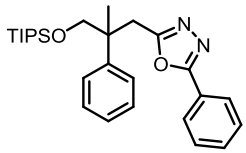
2-(2-Methyl-2-(*m*-tolyl)propyl)-5-phenyl-1,3,4-oxadiazole (3j): yellow solid (53.8 mg, 92%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.86 – 7.82 (m, 2H), 7.51 – 7.47 (m, 1H), 7.47 – 7.43 (m, 2H), 7.25 – 7.18 (m, 3H), 7.05 (dd, *J* = 7.1, 1.9 Hz, 1H), 3.22 (s, 2H), 2.34 (s, 3H), 1.50 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$)δ 165.02, 164.63, 147.31, 137.78, 131.41, 128.91, 128.24, 127.05, 126.66, 126.36, 124.00, 122.61, 40.01, 38.03, 28.50, 21.65. HRMS (ESI-TOF) *m/z*: calcd for $C_{19}H_{20}N_2ONa^+$: 315.1468 $(M + Na)^+$, found 315.1475.



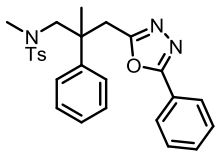
2-(2-(3-Methoxyphenyl)-2-methylpropyl)-5-phenyl-1,3,4-oxadiazole (3k): yellow oil (53.6 mg, 87%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.88 – 7.83 (m, 2H), 7.52 – 7.46 (m, 1H), 7.47 – 7.43 (m, 2H), 7.26 (t, *J* = 8.0 Hz, 1H), 6.99 (dd, *J* =7.8, 1.0Hz, 1H), 6.94 (t, *J* = 2.2 Hz, 1H), 6.78 (dd, *J* = 8.2, 2.3 Hz, 1H), 3.79 (s, 3H), 3.22 (s, 2H), 1.50 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.89, 164.65, 159.58, 149.11, 131.41, 129.29, 128.90, 126.66, 123.96, 118.07, 112.32, 110.93, 55.18, 39.92, 38.17, 28.46. HRMS (ESI-TOF) *m/z*: calcd for $C_{19}H_{20}N_2O_2Na^+$: 331.1417 $(M + Na)^+$, found 331.1423.



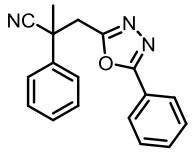
2-(2-Methyl-2-phenylbutyl)-5-phenyl-1,3,4-oxadiazole (3l): white solid (48.4 mg, 83%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.83 – 7.77 (m, 2H), 7.51 – 7.45 (m, 1H), 7.46-7.40 (m, 2H), 7.39 – 7.28 (m, 4H), 7.25 – 7.19 (m, 1H), 3.26 (d, *J* = 14.4 Hz, 1H), 3.22 (d, *J* = 14.4 Hz, 1H), 2.03 – 1.97 (m, 1H), 1.80 – 1.71 (m, 1H), 1.46 (s, 3H), 0.77 (t, *J* = 7.5 Hz, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.93, 164.59, 145.24, 131.36, 128.87, 128.27, 126.62, 126.24, 126.17, 123.94, 41.58, 38.90, 34.75, 23.56, 8.63. HRMS (ESI-TOF) *m/z*: calcd for $C_{19}H_{20}N_2ONa^+$: 315.1468 $(M + Na)^+$, found 315.1477.



2-(2-Methyl-2-phenyl-3-((triisopropylsilyl)oxy)propyl)-5-phenyl-1,3,4-oxadiazole (3m): yellow oil (65.2 mg, 72%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.81 – 7.75 (m, 2H), 7.48 – 7.45 (m, 1H), 7.43 – 7.40 (m, 4H), 7.33 (t, *J*=7.7Hz, 2H), 7.23 (t, *J* =7.3Hz, 1H), 3.95 (d, *J* = 9.6 Hz, 1H), 3.79 (d, *J* = 9.6 Hz, 1H), 3.47 (d, *J* = 15 Hz, 1H), 3.44 (d, *J* = 15 Hz, 1H), 1.54 (s, 3H), 1.15 – 1.06 (m, 3H), 1.06 - 1.02 (m, 18H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.20, 164.50, 143.68, 131.29, 128.82, 128.14, 126.59, 126.56, 126.48, 123.96, 72.00, 43.81, 34.05, 21.99, 17.96, 11.93. HRMS (ESI-TOF) *m/z*: calcd for $C_{27}H_{38}N_2O_2SiNa^+$: 473.2595 $(M + Na)^+$, found 473.2610.

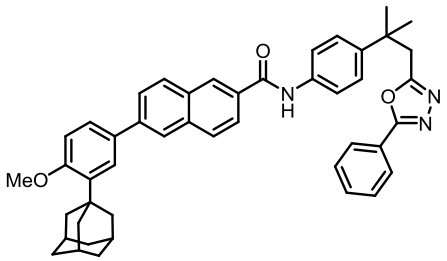


***N*-4-dimethyl-*N*-(2-methyl-2-phenyl-3-(5-phenyl-1,3,4-oxadiazol-2-yl)propyl)benzenesulfonamide (3n):** colorless oil (89.6 mg, 97%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.81 (d, *J* =7.0 Hz, 1H), 7.64 (d, *J* = 8.2 Hz, 2H), 7.48-7.46 (m, 1H), 7.45 – 7.39 (m, 4H), 7.33 – 7.30 (m, 4H), 7.23 (t, *J* =7.4Hz, 1H), 3.65 (d, *J* = 15.2 Hz, 1H), 3.49 (d, *J* = 14.0 Hz, 1H), 3.38 (d, *J* = 15.2 Hz, 1H), 3.18 (d, *J* = 14.0 Hz, 1H), 2.41 (s, 3H), 2.27 (s, 3H), 1.66 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.56, 164.45, 143.51, 143.12, 134.17, 131.40, 129.70, 128.86, 128.50, 127.48, 126.99, 126.61, 126.51, 123.81, 62.13, 42.50, 38.09, 35.66, 22.83, 21.44. HRMS (ESI-TOF) *m/z*: calcd for $C_{26}H_{27}N_3O_3SNa^+$: 484.1664 $(M + Na)^+$, found 484.1682.

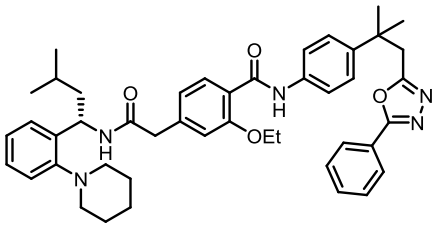


2-Methyl-2-phenyl-3-(5-phenyl-1,3,4-oxadiazol-2-yl)propanenitrile (3o): white solid (46.4 mg, 80%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.98 – 7.94 (m, 2H), 7.55 – 7.47 (m, 5H), 7.41(t, *J* =7.7 Hz, 2H), 7.35 (t, *J* =7.3Hz, 1H), 3.58 (dd, *J* =15, 3.6 Hz, 2H), 1.92 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.47, 161.71, 138.09, 131.87, 129.26, 129.06, 128.65, 126.92, 125.37, 123.46, 121.86, 40.82, 38.00,

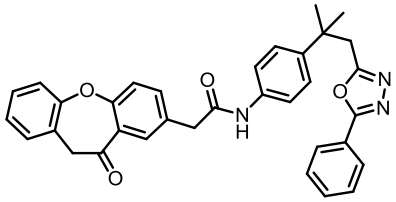
26.50. HRMS (ESI-TOF) *m/z*: calcd for $C_{18}H_{15}N_3ONa^+$: 312.1107 $(M + Na)^+$, found 312.1117.



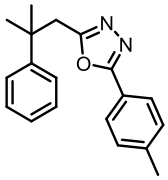
6-(3-((3*r*,5*r*,7*r*)-Adamantan-1-yl)-4-methoxyphenyl)-*N*-(4-(2-methyl-1-(5-phenyl-1,3,4-oxadiazol-2-yl)propan-2-yl)phenyl)-2-naphthamide (3p): white solid (96.6 mg, 70%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.37 (s, 1H), 8.11 (s, 1H), 8.02 (s, 1H), 7.98 – 7.90 (m, 3H), 7.90 – 7.85 (m, 2H), 7.81 (dd, *J* = 8.5, 1.8 Hz, 1H), 7.66 (d, *J* = 8.3 Hz, 2H), 7.61 (d, *J* = 2.4 Hz, 1H), 7.54 (dd, *J* = 8.3, 2.3 Hz, 1H), 7.49-7.43 (m, 3H), 7.40 (d, *J* = 8.4 Hz, 2H), 7.00 (d, *J* = 8.3 Hz, 1H), 3.91 (s, 3H), 3.23 (s, 2H),2.19 (s, 6H), 2.11 (s, 3H), 1.81 (s, 6H), 1.69 (s, 2H), 1.52 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.76, 164.90, 164.69, 158.90, 143.43, 141.04, 139.00, 136.33, 135.27, 132.46, 131.58, 131.46, 131.32, 129.29, 128.96, 128.76, 127.33, 126.73, 126.71, 126.30, 125.91, 125.68, 124.71, 123.88, 123.86, 120.21, 112.10, 55.15, 40.59, 39.98, 37.92, 37.19, 37.10, 29.08, 28.57. HRMS (ESI-TOF) *m/z*: calcd for $C_{46}H_{46}N_3O_3^+$: 688.3534 $(M + H)^+$, found 688.3551.



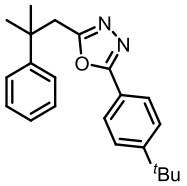
(*S*)-2-ethoxy-4-(2-((3-methyl-1-(2-(piperidin-1-yl)phenyl)butyl)amino)-2-oxoethyl)-*N*-(4-(2-methyl-1-(5-phenyl-1,3,4-oxadiazol-2-yl)propan-2-yl)phenyl)benzamide (3q): yellow solid (90.0 mg, 62%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 10.05 (s, 1H), 8.22 (d, *J* = 7.9 Hz, 1H), 7.88 – 7.82 (m, 2H), 7.64 – 7.59 (m, 2H), 7.47 – 7.41 (m, 3H), 7.40 – 7.35 (m, 2H), 7.24 – 7.16 (m, 2H), 7.11 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.05 (td, *J* = 7.2, 1.8 Hz, 1H), 6.96 (dd, *J* = 8.0, 1.5 Hz, 2H), 6.92 (d, *J* = 1.5 Hz, 1H), 5.42-5.35 (m, 1H), 4.20 – 4.04 (m, 2H), 3.56 (s, 2H), 3.22 (s, 2H), 2.94 (s, 2H), 2.61 (s, 2H), 1.94 (s, 1H), 1.77 – 1.68 (m, 2H), 1.67 – 1.55 (m, 4H), 1.56 – 1.48 (m, 10H), 1.43 (m, 1H), 0.91 (dd, *J* = 6.6, 1.6 Hz, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 168.73, 164.89, 164.63, 162.86, 156.77, 152.46, 142.86, 141.10, 138.64, 136.77, 132.70, 131.38, 128.89, 127.86, 127.71, 126.64, 126.20, 125.00, 123.83, 122.78, 122.17, 120.24, 119.85, 113.01, 65.00, 49.84, 46.61, 43.95, 39.96, 37.83, 28.52, 26.71, 25.28, 24.07, 22.72, 22.47, 14.77. HRMS (ESI-TOF) *m/z*: calcd for $C_{45}H_{54}N_5O_4^+$: 728.4170 $(M + H)^+$ found 728.4190.



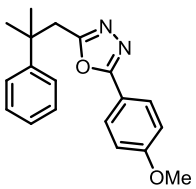
***N*-(4-(2-methyl-1-(5-phenyl-1,3,4-oxadiazol-2-yl)propan-2-yl)phenyl)-2-(11-oxo-10,11-dihydr odibenzo[*b,f*]oxepin-2-yl)acetamide (3r):** yellow oil (71.5 mg, 66%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.17 (d, *J* = 2.4 Hz, 1H), 7.89 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.84 – 7.81 (m, 2H), 7.58 (td, *J* = 7.5, 1.4 Hz, 1H), 7.52 – 7.44 (m, 3H), 7.43 – 7.37 (m, 5H), 7.32 – 7.29 (m, 2H), 7.24 (s, 1H), 7.08 (d, *J* = 8.4 Hz, 1H), 5.21 (s, 2H), 3.73 (s, 2H), 3.18 (s, 2H), 1.47 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 190.82, 168.80, 164.85, 164.65, 160.69, 143.35, 140.30, 136.35, 135.91, 135.46, 132.90, 132.45, 131.46, 129.47, 129.31, 128.93, 128.34, 127.87, 126.66, 126.11, 125.30, 123.80, 121.65, 119.91, 73.63, 43.57, 39.92, 37.84, 28.53. HRMS (ESI-TOF) *m/z*: calcd for $C_{34}H_{29}N_3O_4Na^+$: 566.2050 $(M + Na)^+$, found 566.2063.



2-(2-Methyl-2-phenylpropyl)-5-(*p*-tolyl)-1,3,4-oxadiazole (3u) : yellow oil (53.0 mg, 91%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.73 – 7.69 (m, 2H), 7.41 – 7.38 (m, 2H), 7.35 – 7.31 (m, 2H), 7.25 – 7.21 (m, 3H), 3.22 (s, 2H), 2.40 (s, 3H), 1.51 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.77, 164.64, 147.30, 141.89, 129.59, 128.33, 126.60, 126.29, 125.57, 121.19, 40.01, 38.11, 28.49, 21.56. HRMS (ESI-TOF) *m/z*: calcd for $C_{19}H_{20}N_2ONa^+$: 315.1468 $(M + Na)^+$, found 315.1478.

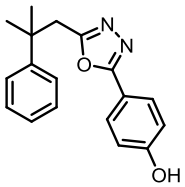


2-(4-(*Tert*-butyl)phenyl)-5-(2-methyl-2-phenylpropyl)-1,3,4-oxadiazole (3v): yellow solid (57.6 mg, 86%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.2 Hz, 2H), 7.46 (d, *J* = 8.2 Hz, 2H), 7.40 (d, *J* = 7.7 Hz, 2H), 7.34 (t, *J* = 7.6 Hz, 2H), 7.24 (t, *J* = 7.4 Hz, 1H), 3.23 (s, 2H), 1.51 (s, 6H), 1.34 (s, 9H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.67, 164.65, 154.95, 147.27, 128.31, 126.46, 126.28, 125.85, 125.54, 121.11, 39.96, 38.08, 34.97, 31.06, 28.48. HRMS (ESI-TOF) *m/z*: calcd for $C_{22}H_{26}N_2ONa^+$: 357.1937 $(M + Na)^+$, found 357.1952.

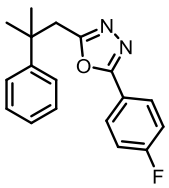


2-(4-Methoxyphenyl)-5-(2-methyl-2-phenylpropyl)-1,3,4-oxadiazole (3w): yellow oil (49.2 mg,

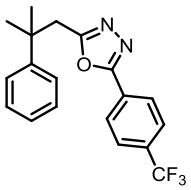
80%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.78 – 7.72 (m, 2H), 7.42 – 7.36 (m, 2H), 7.33 (t, *J* = 7.7 Hz, 2H), 7.23 (t, *J* = 7.3 Hz, 1H), 6.96 – 6.91 (m, 2H), 3.85 (s, 3H), 3.21 (s, 2H), 1.50 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.52, 164.36, 162.04, 147.30, 128.34, 128.28, 126.24, 125.55, 116.47, 114.29, 55.36, 39.95, 38.06, 28.46. HRMS (ESI-TOF) *m/z*: calcd for $C_{19}H_{20}N_2O_2Na^+$: 331.1417 $(M + Na)^+$, found 331.1430.



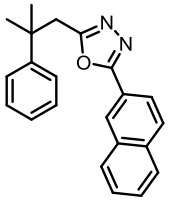
4-(5-(2-Methyl-2-phenylpropyl)-1,3,4-oxadiazol-2-yl)phenol (3x): yellow solid (32.5 mg, 55%). ^{1}H NMR (600 MHz, $(CD_3)_2SO$) δ 10.25 (s, 1H), 7.60 – 7.54 (m, 2H), 7.44 – 7.37 (m, 2H), 7.30 (t, *J* = 7.6 Hz, 2H), 7.19 (t, *J* = 7.3 Hz, 1H), 6.91 – 6.85 (m, 2H), 3.23 (s, 2H), 1.42 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.04, 163.81, 160.53, 147.27, 128.09, 128.06, 125.98, 125.64, 116.06, 114.20, 38.80, 37.78, 28.44. HRMS (ESI-TOF) *m/z*: calcd for $C_{18}H_{18}N_2O_2Na^+$: 317.1260 $(M + Na)^+$, found 317.1266.



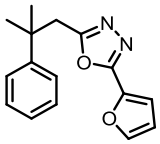
2-(4-Fluorophenyl)-5-(2-methyl-2-phenylpropyl)-1,3,4-oxadiazole (3y): white solid (47.0 mg, 79%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.82 – 7.78 (m, 2H), 7.40 – 7.38(m, 2H), 7.35 – 7.32 (m, 2H), 7.26 – 7.20 (m, 1H), 7.15 – 7.10 (m, 2H), 3.23 (s, 2H), 1.51 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.92, 164.56 (d, *J* =252.9 Hz), 163.81, 147.15, 128.87 (d, *J* = 8.8 Hz), 128.33, 126.33, 125.57, 120.25 (d, *J* = 3.4 Hz), 116.21 (d, *J* = 22.1 Hz), 40.01, 38.13, 28.50. ^{19}F NMR (565 MHz, $CDCl_3$) δ -107.30. HRMS (ESI-TOF) *m/z*: calcd for $C_{18}H_{17}FN_2ONa^+$: 319.1217 $(M + Na)^+$, found 319.1226.



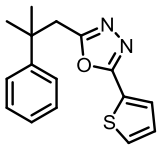
2-(2-Methyl-2-phenylpropyl)-5-(4-(trifluoromethyl)phenyl)-1,3,4-oxadiazole (3z): white solid (50.4 mg, 73%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.0 Hz, 2H), 7.70 (d, *J* = 8.2 Hz, 2H), 7.41 – 7.38 (m, 2H), 7.37 – 7.31 (m, 2H), 7.27 – 7.21 (m, 1H), 3.26 (s, 2H), 1.52 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.55, 163.46, 146.97, 133.04 (q, *J* = 32.9 Hz), 128.36, 127.11, 126.93, 126.39, 125.95 (q, *J* = 3.8 Hz), 125.57, 123.54 (q, *J* = 272.7 Hz), 40.08, 38.20, 28.52. ^{19}F NMR (565 MHz, $CDCl_3$) δ -63.08. HRMS (ESI-TOF) *m/z*: calcd for $C_{19}H_{17}F_3N_2ONa^+$: 369.1185 $(M + Na)^+$, found 369.1199.



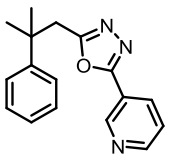
2-(2-Methyl-2-phenylpropyl)-5-(naphthalen-2-yl)-1,3,4-oxadiazole (3aa): yellow solid (50.7 mg, 77%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.20 (s, 1H), 7.93 (dd, *J* = 8.6, 1.7 Hz, 1H), 7.89 – 7.86 (m, 2H), 7.86 – 7.82 (m, 1H), 7.58 – 7.50 (m, 2H), 7.44 – 7.40 (m, 2H), 7.35 (t, *J* = 7.8 Hz, 2H), 7.29 – 7.23 (m, 1H), 3.26 (s, 2H), 1.53 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.95, 164.75, 147.23, 134.47, 132.71, 128.80, 128.67, 128.33, 127.84, 127.75, 126.97, 126.92, 126.27, 125.60, 122.96, 121.11, 40.05, 38.14, 28.49. HRMS (ESI-TOF) *m/z*: calcd for $C_{22}H_{20}N_2ONa^+$: 351.1468 $(M + Na)^+$, found 351.1475.



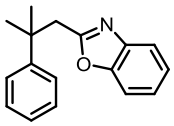
2-(Furan-2-yl)-5-(2-methyl-2-phenylpropyl)-1,3,4-oxadiazole (3ab): yellow oil (41.3 mg,77%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.58 (dd, *J* = 1.8, 0.8 Hz, 1H), 7.39 – 7.37 (m, 2H), 7.34 – 7.31 (m, 2H), 7.25 – 7.19 (m, 1H), 6.93 (dd, *J* = 3.5, 0.8 Hz, 1H), 6.54 (dd, *J* = 3.5, 1.8 Hz, 1H), 3.21 (s, 2H), 1.50 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.26, 157.54, 147.13, 145.41, 139.48, 128.33, 126.34, 125.46, 113.51, 111.93, 39.72, 38.11, 28.41. HRMS (ESI-TOF) *m/z*: calcd for $C_{16}H_{16}N_2O_2Na^+$: 291.1104 $(M + Na)^+$, found 291.1114.



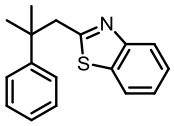
2-(2-Methyl-2-phenylpropyl)-5-(thiophen-2-yl)-1,3,4-oxadiazole (3ac): white solid (43.7 mg, 77%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.50 – 7.47 (m , 2H), 7.41 – 7.36 (m, 2H), 7.35 – 7.31 (m, 2H), 7.26 – 7.19 (m, 1H), 7.10 (dd, *J* = 5.0, 3.7 Hz, 1H), 3.21 (s, 2H), 1.51 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 164.33, 160.87, 147.13, 129.74, 129.31, 128.33, 127.96, 126.35, 125.53, 125.27, 39.87, 38.09, 28.45. HRMS (ESI-TOF) *m/z*: calcd for $C_{16}H_{16}N_2OSNa^+$: 307.0876 $(M + Na)^+$, found 307.0883.



2-(2-Methyl-2-phenylpropyl)-5-(pyridin-3-yl)-1,3,4-oxadiazole (3ad): yellow solid (39.2 mg, 70%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.96 (d, *J* = 2.5 Hz, 1H), 8.71 (dd, *J* = 4.9, 1.7 Hz, 1H), 8.11 (dt, *J* = 8.0, 1.9 Hz, 1H), 7.41 – 7.35 (m, 3H), 7.34 – 7.31 (m, 2H), 7.26 – 7.20 (m, 1H), 3.25 (s, 2H), 1.52 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.44, 162.51, 152.13, 147.61, 146.88, 133.82, 128.35, 126.42, 125.53, 123.63, 120.36, 40.02, 38.17, 28.51. HRMS (ESI-TOF) *m/z*: calcd for $C_{17}H_{17}N_3ONa^+$: 302.1264 $(M + Na)^+$, found 302.1269.



2-(2-Methyl-2-phenylpropyl)benzo[*d*]oxazole (3ae): yellow oil (49.3 mg, 77%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.71 – 7.63 (m, 1H), 7.45 – 7.39 (m, 3H), 7.36 – 7.30 (m, 2H), 7.32 – 7.26 (m, 2H), 7.25 – 7.19 (m, 1H), 3.23 (s, 2H), 1.52 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 165.01, 150.69, 148.07, 141.26, 128.27, 126.14, 125.46, 124.43, 123.99, 119.64, 110.28, 43.08, 38.49, 28.50. HRMS (ESI-TOF) *m/z*: calcd for $C_{17}H_{18}NO^+$: 252.1383$(M + H)^+$, found 252.1389.



2-(2-Methyl-2-phenylpropyl)benzo[*d*]thiazole (3af): yellow oil (33.7mg, 50%). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.97 (d, *J* = 8.1 Hz, 1H), 7.70 (d, *J* = 8.0 Hz, 1H), 7.44 – 7.39 (m, 3H), 7.38 –7.34 (m, 2H), 7.32 – 7.25 (m, 2H), 3.47 (s, 2H), 1.48 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 168.76, 152.46, 147.47, 135.57, 128.38, 126.33, 126.21, 125.62, 124.59, 122.51, 121.26, 48.98, 38.81, 28.79. HRMS (ESI-TOF) *m/z*: calcd for $C_{17}H_{18}NS^+$: 268.1154 $(M + H)^+$, found 268.1162.

7. References

(1) Z. Wu, D. Ma, B. Zhou, X. Ji, X. Ma, X. Wang, Y. Zhang, *Angew. Chem, Int. Ed.* 2017, **56**, 12288.

(2) T. Čarný, R. Rocaboy, A. Clemenceau, O. Baudoin, *Angew. Chem., Int. Ed*., 2020, **59**, 18980.

(3) X. Guo, S. He, Z. Xu, L. Chen, Z. Li, B. Song, J. Zuo, Z. Lin, W. Yang, *Nat. Commun.*, 2021, **12**, 1304.

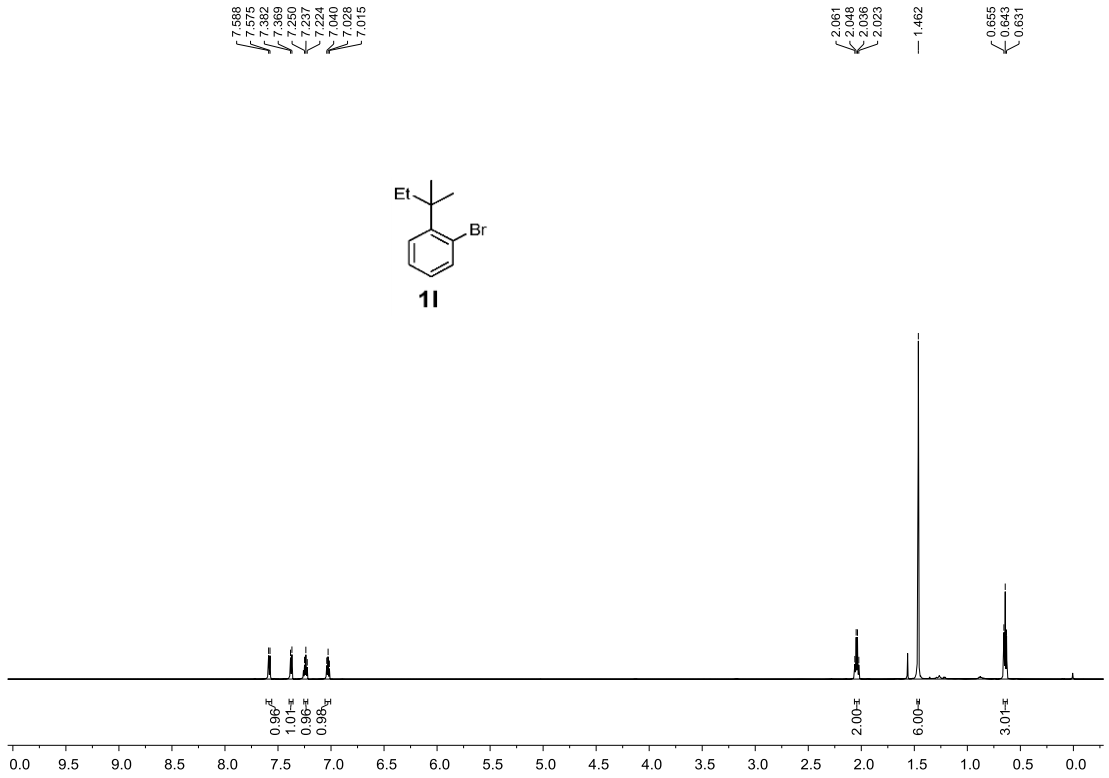
(4) J. Hédouin, C. Schneider, I. Gillaizeau, C. Hoarau. *Org. Lett.* 2018, **20**, 6027.

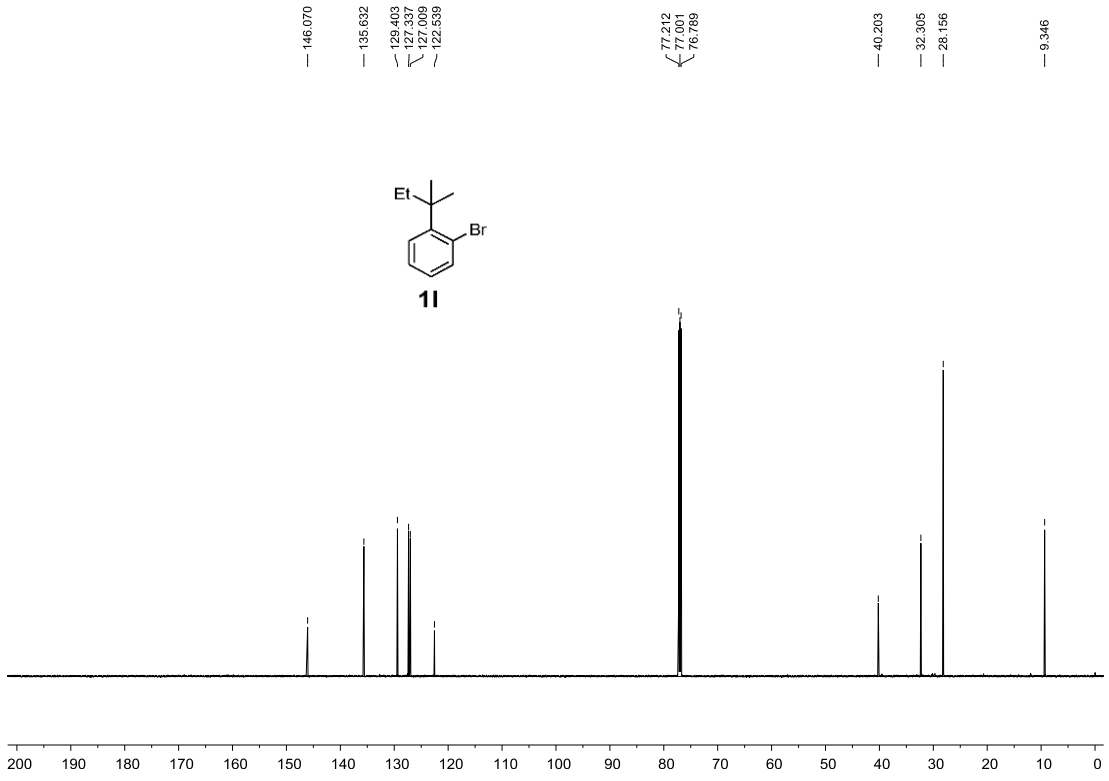
(5) P. Alvarez-Bercedo, A. Flores-Gaspar, A. Correa, R. Martin. *J. Am. Chem. Soc*.2010, **132**, 466.

(6) Á. Gutiérrez-Bonet, F. Juliá-Hernández, B. Luis, R. Martin. *J. Am. Chem. Soc.* 2016, **138**, 384.

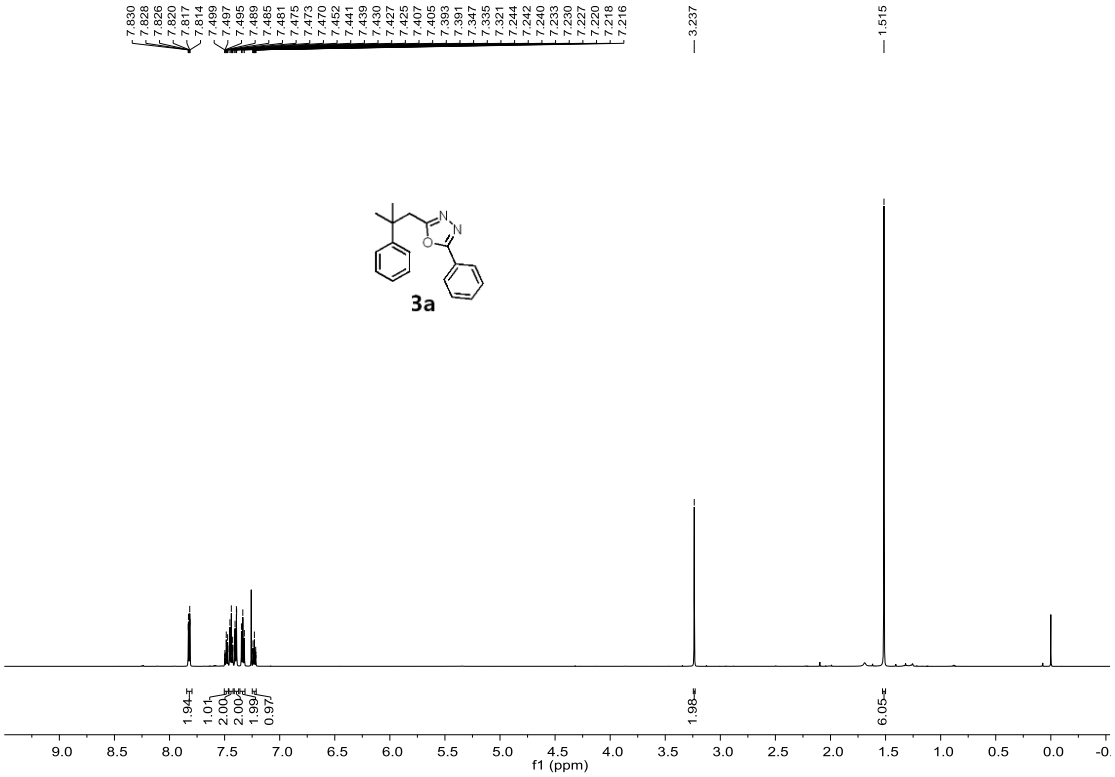
8. NMR Spectra

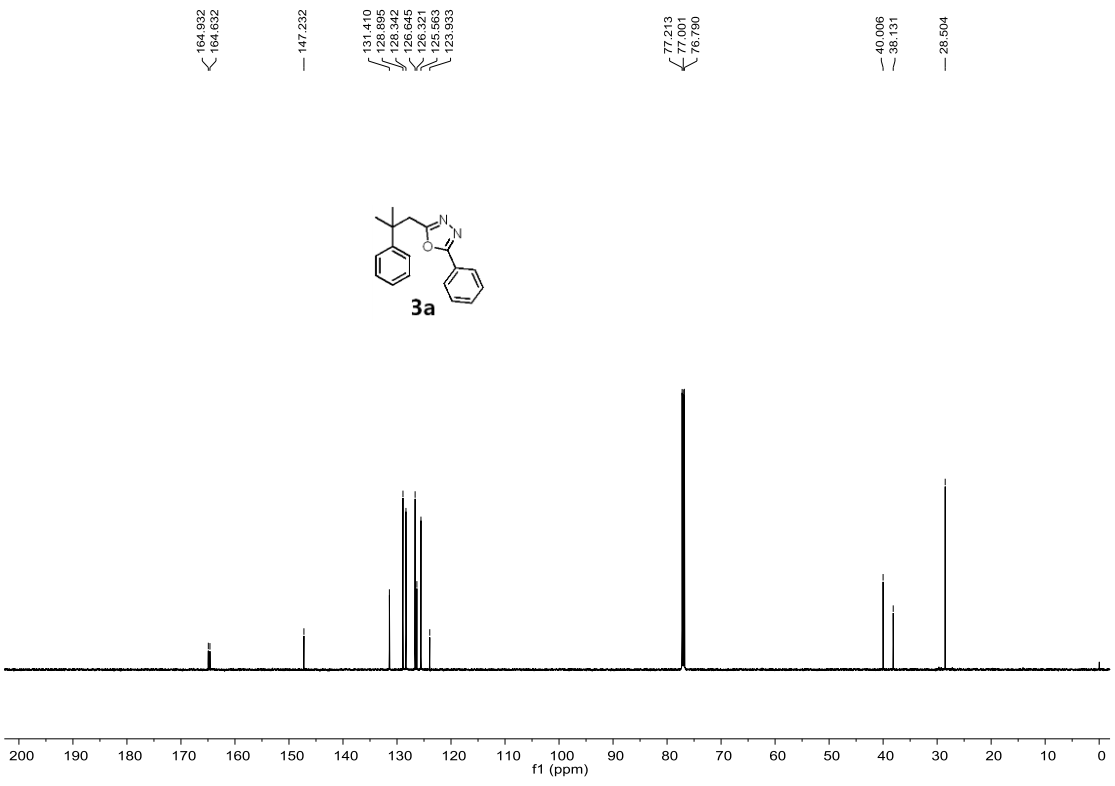
8.1 NMR Spectra of the Substrates

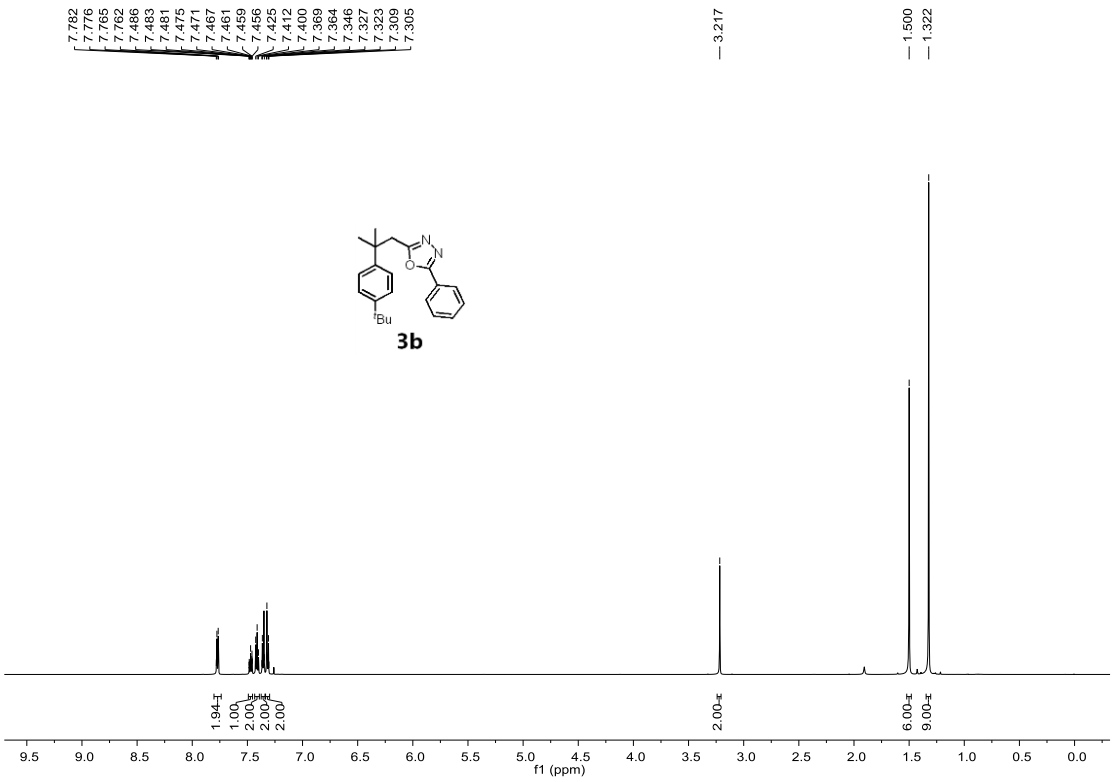




8.2 NMR Spectra of the Products



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7.483
7.481
7.475
7.471
7.467
7.461
7.459
7.456
7.425
7.412
7.400
7.369
7.364
7.346
7.327
7.323
7.309
7.305
3.217
1.500
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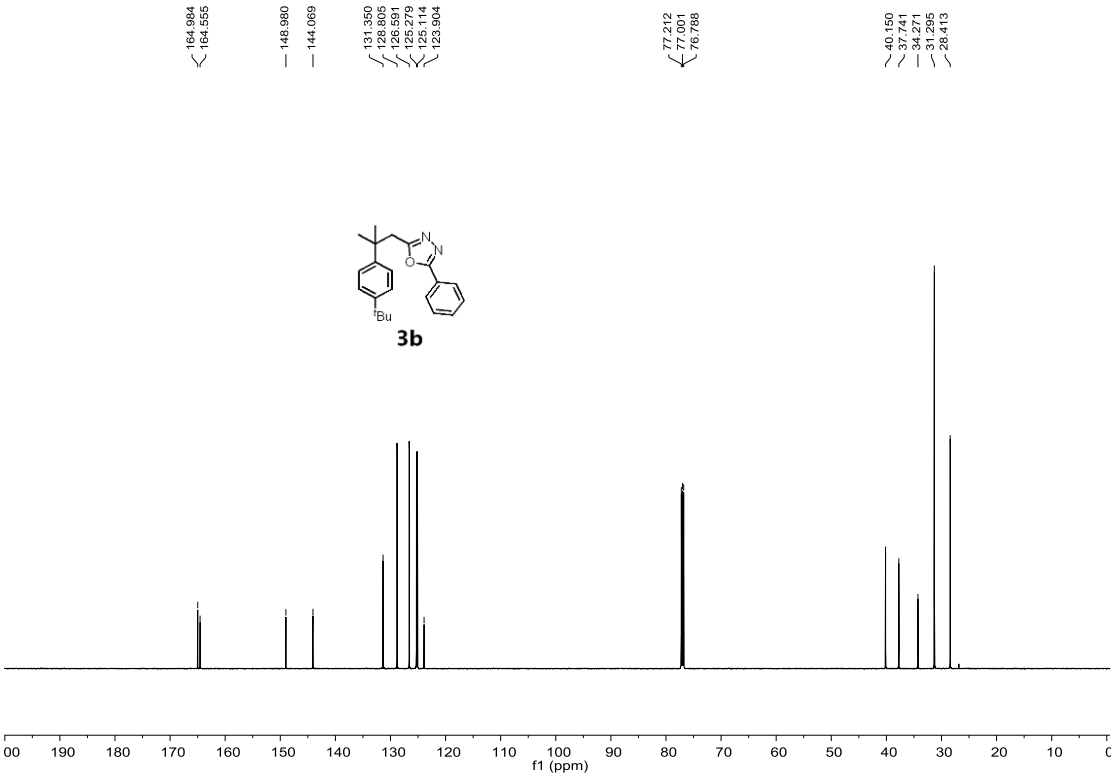
2.00
2.00
6.00
9.00
f1 (ppm)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148.980
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128.805
126.591
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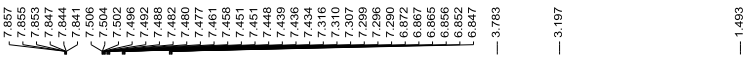
34.271
31.295
28.413
tBu
3b
f1 (ppm)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7.853
7.847
7.844
7.841
7.506
7.504
7.502
7.496
7.492
7.488
7.482
7.480
7.477
7.461
7.458
7.451
7.451
7.448
7.439
7.436
7.434
7.316
7.310
7.307
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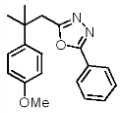
1.493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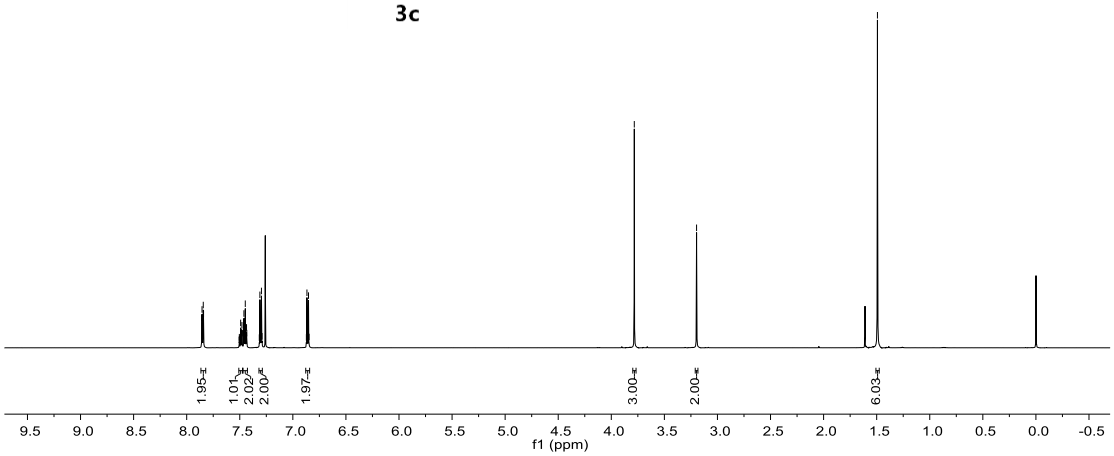
N
O
OMe

3c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1.97
3.00
2.00
6.03
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f1 (ppm)


165.016
164.618
157.937
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131.416
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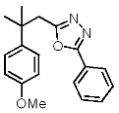
28.683


N
N
O
OMe

3c

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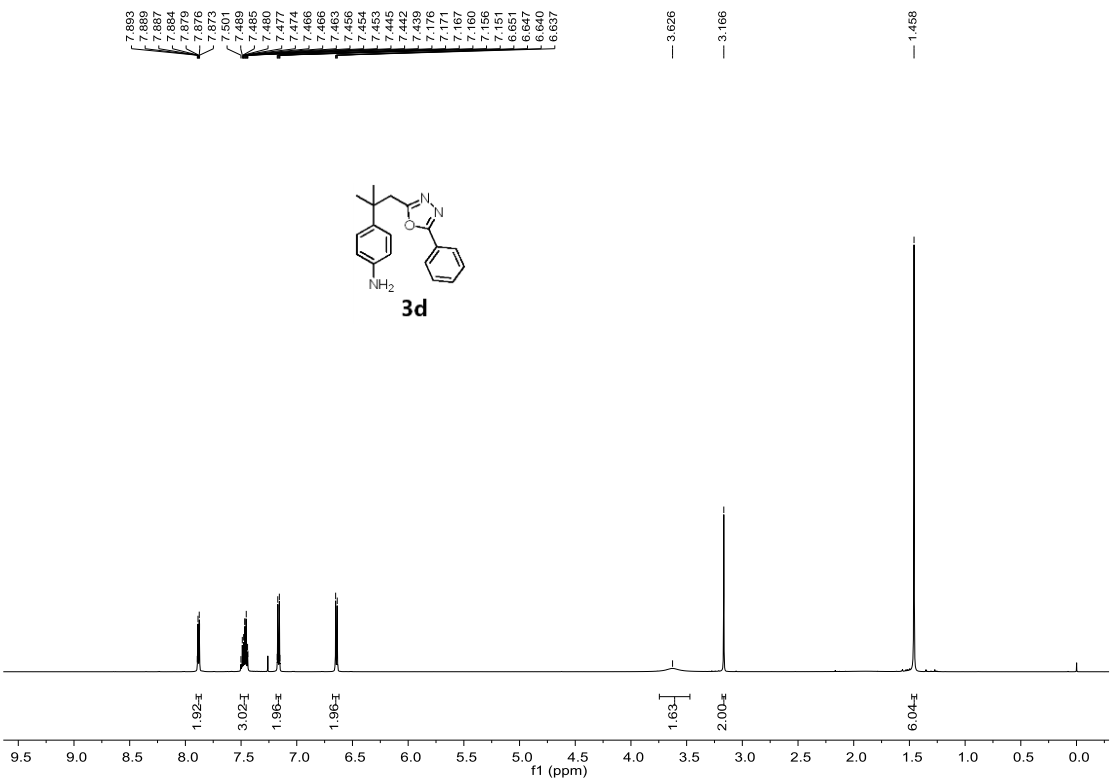
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7.463
7.456
7.454
7.453
7.445
7.442
7.439
7.176
7.171
7.167
7.160
7.156
7.151
6.651
6.647
6.640
6.637
3.626
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3.02
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1.63
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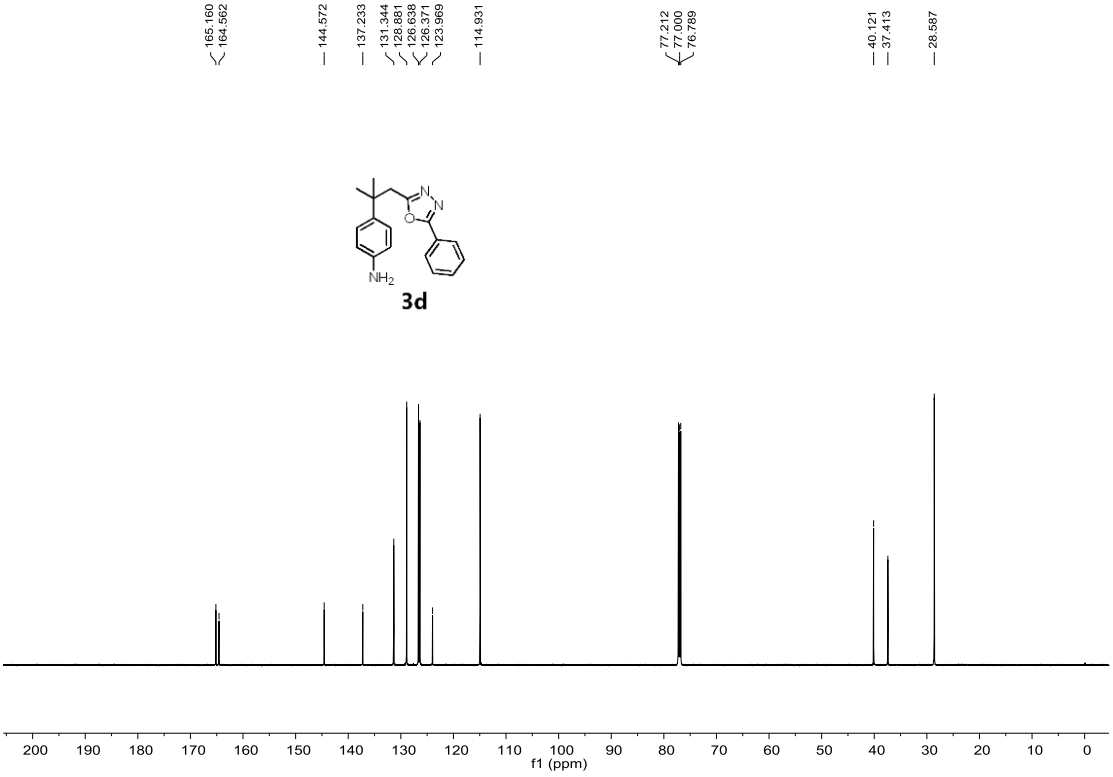
6.04
f1 (ppm)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37.413
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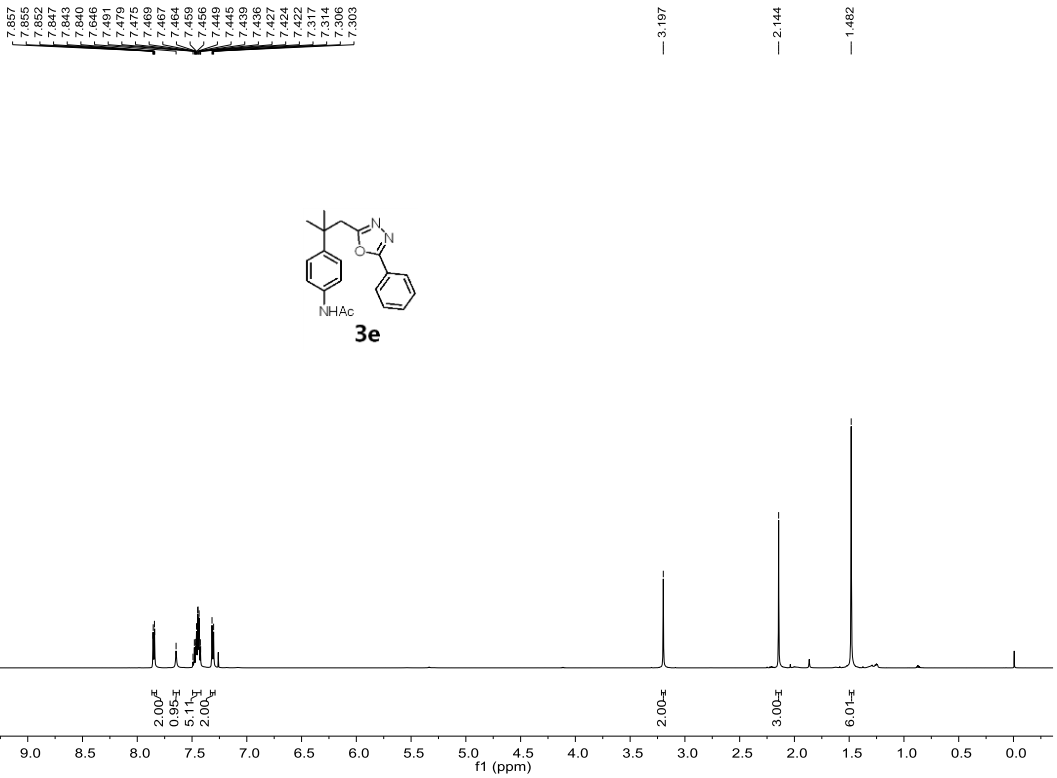
NH2
3d
f1 (ppm)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7.491
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7.469
7.467
7.464
7.459
7.456
7.449
7.445
7.439
7.436
7.427
7.424
7.422
7.317
7.314
7.306
7.303
3.197
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3e
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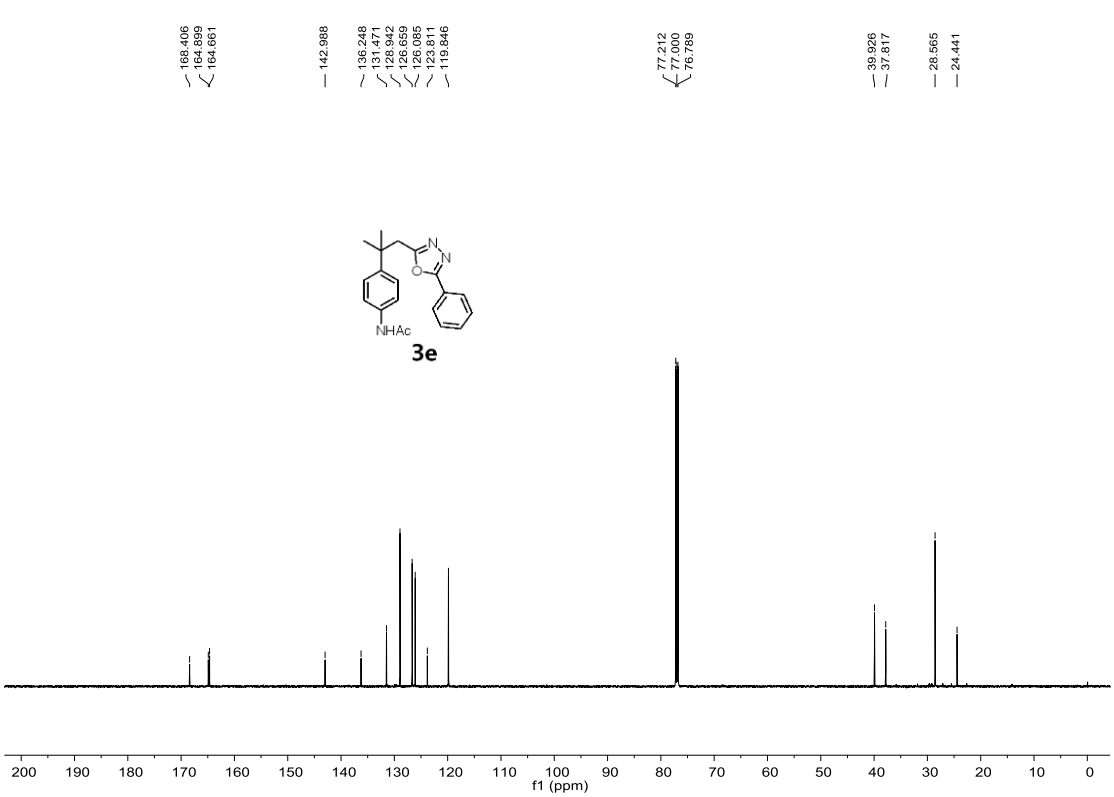
6.01
f1 (ppm)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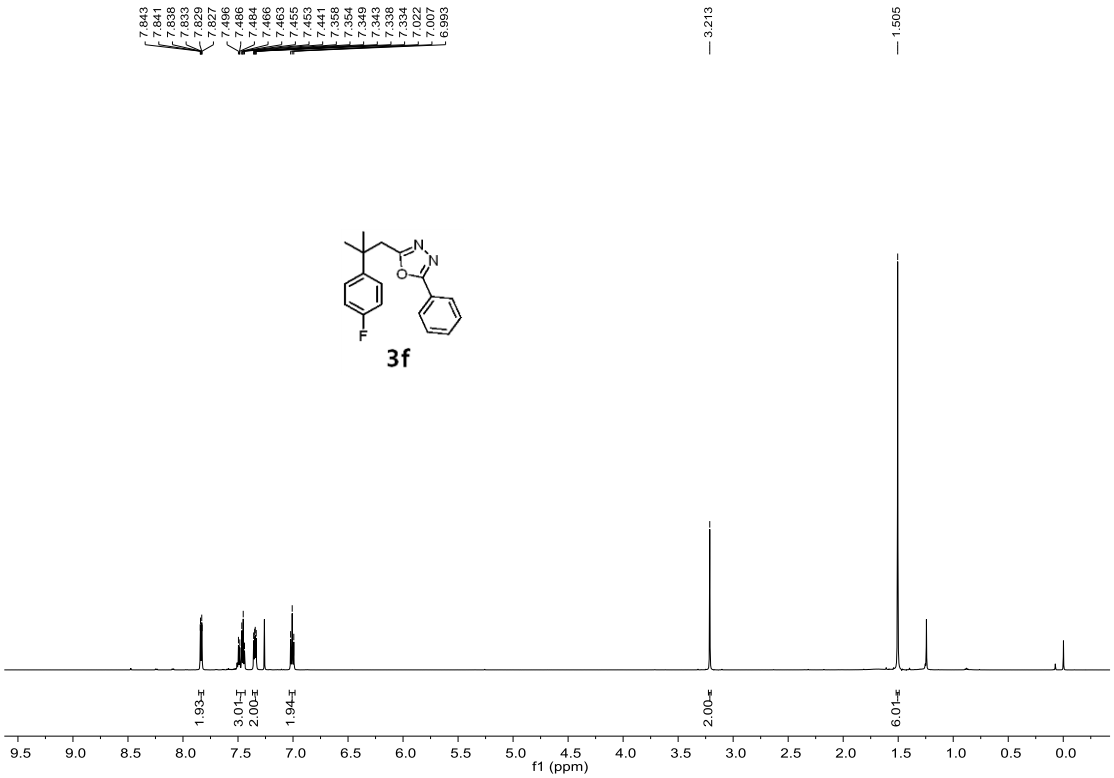
f1 (ppm)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7.453
7.441
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7.354
7.349
7.343
7.338
7.334
7.022
7.007
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1.505
F
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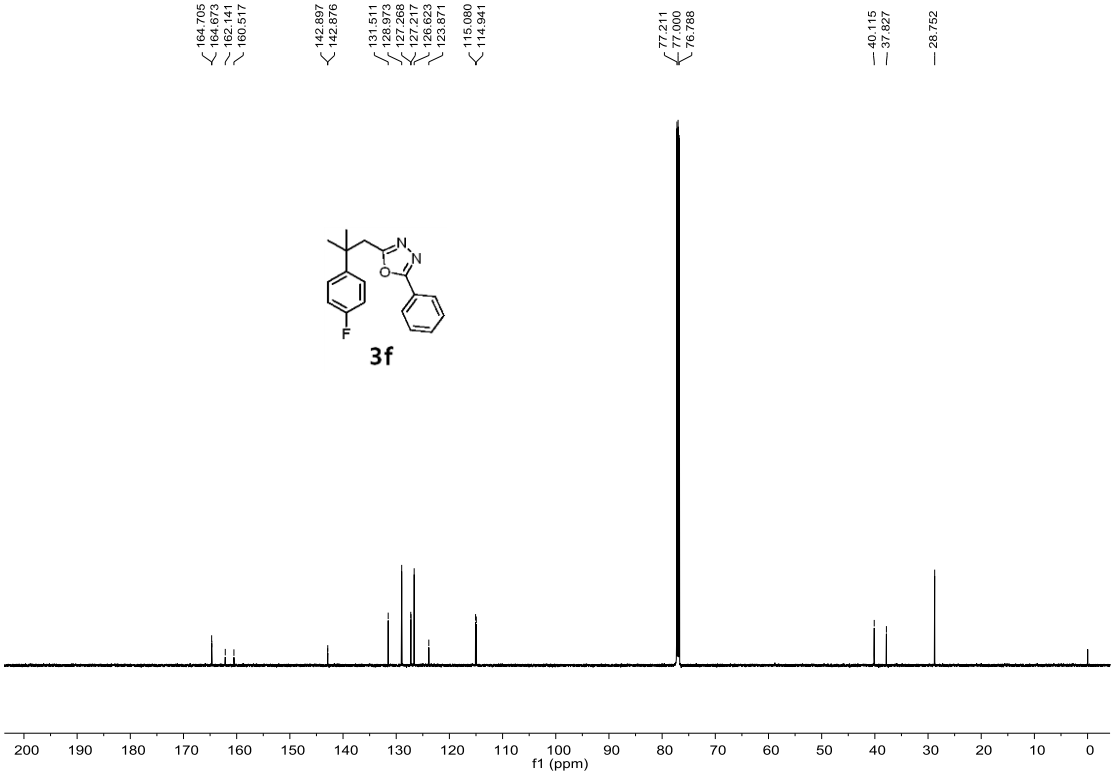
1.94
2.00
6.01
f1 (ppm)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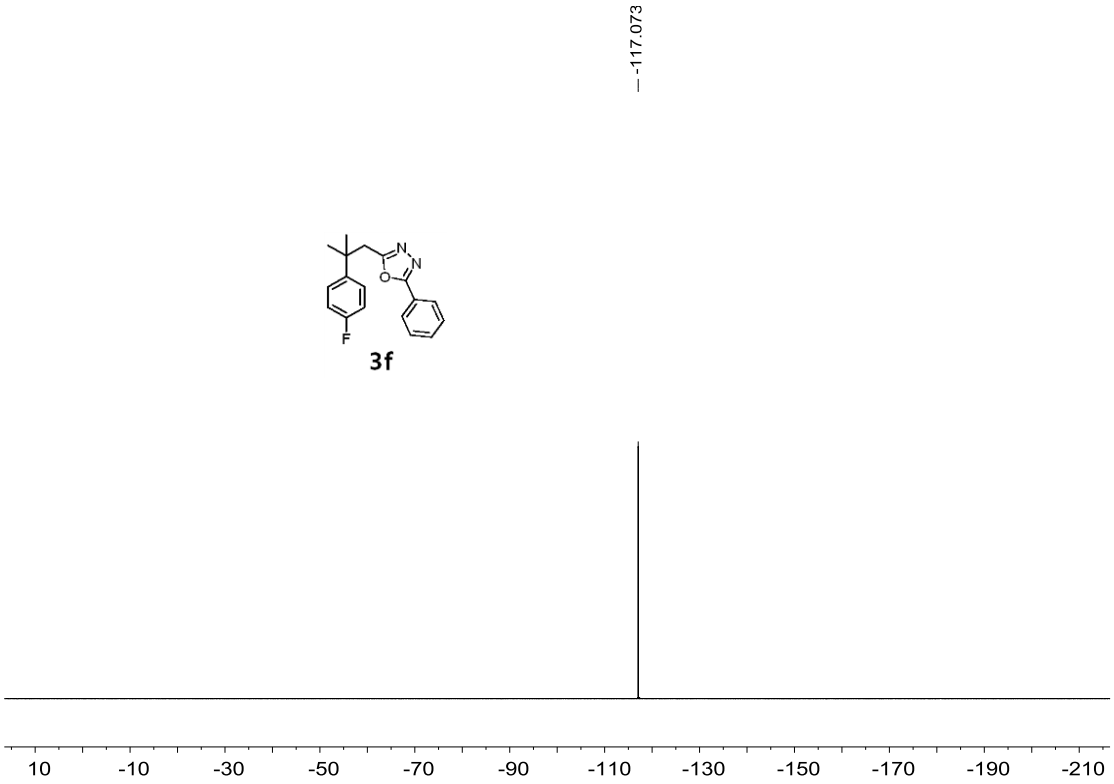
f1 (ppm)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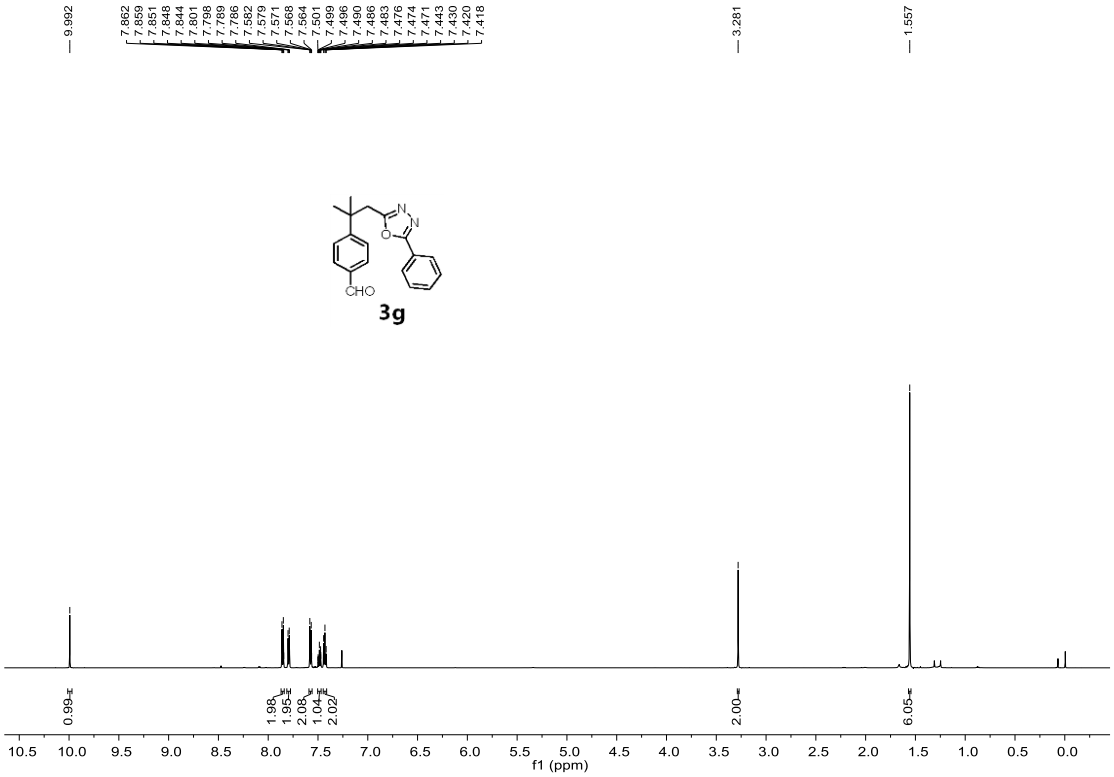
-210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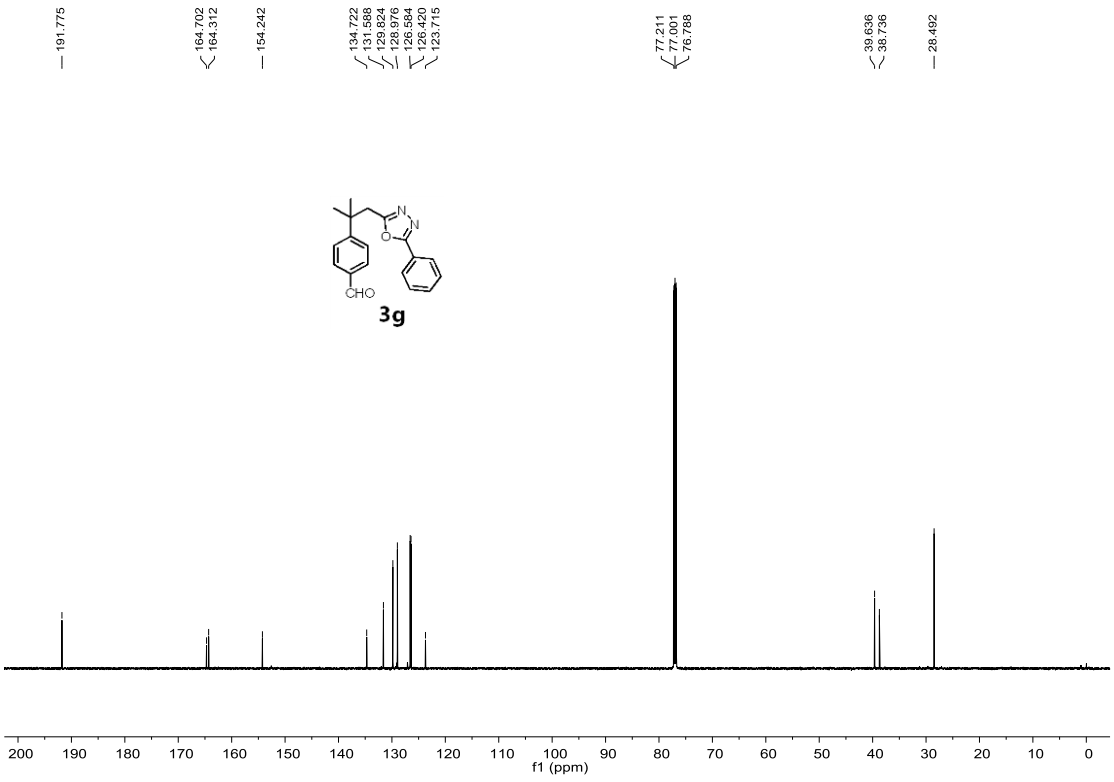
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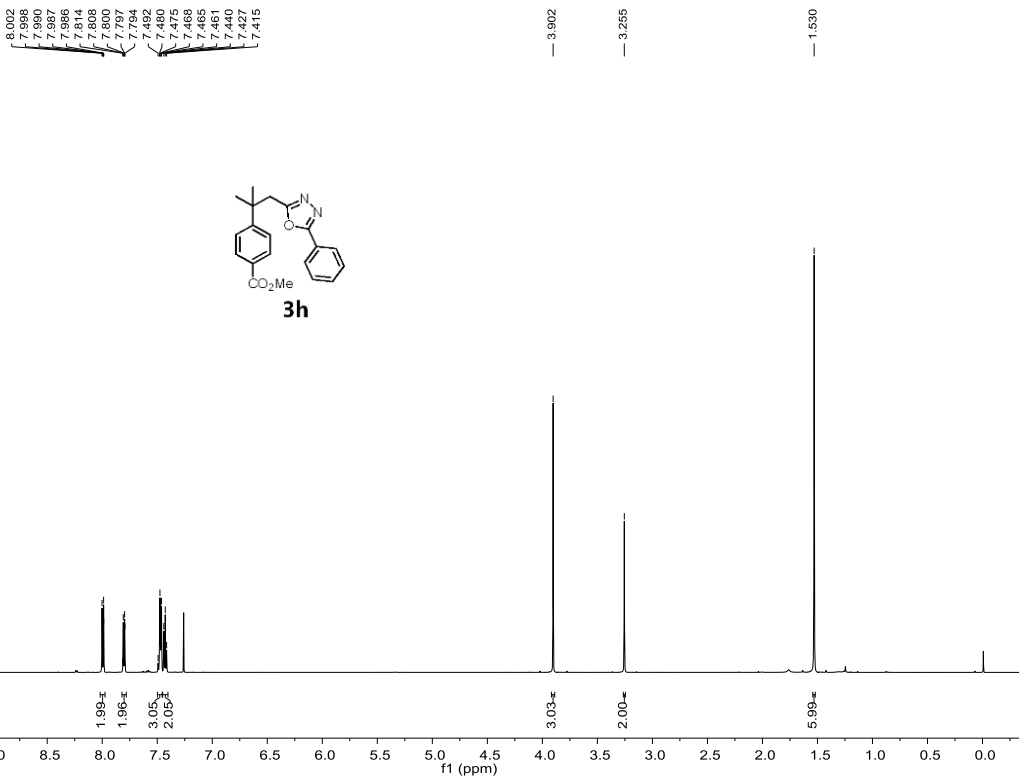
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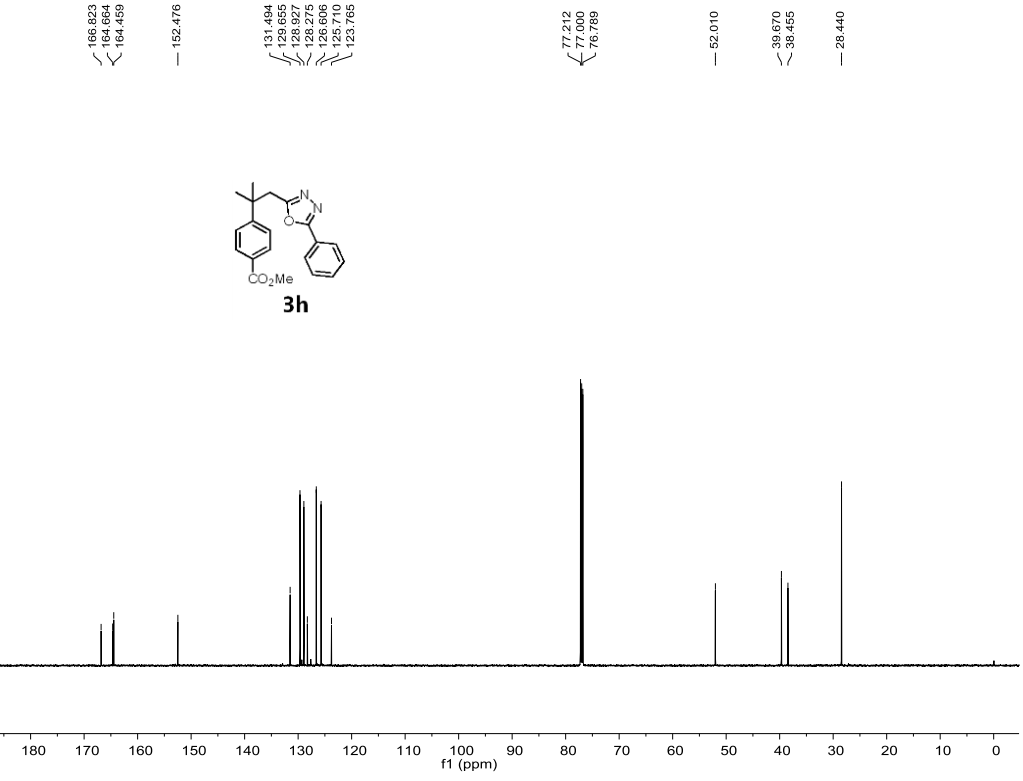
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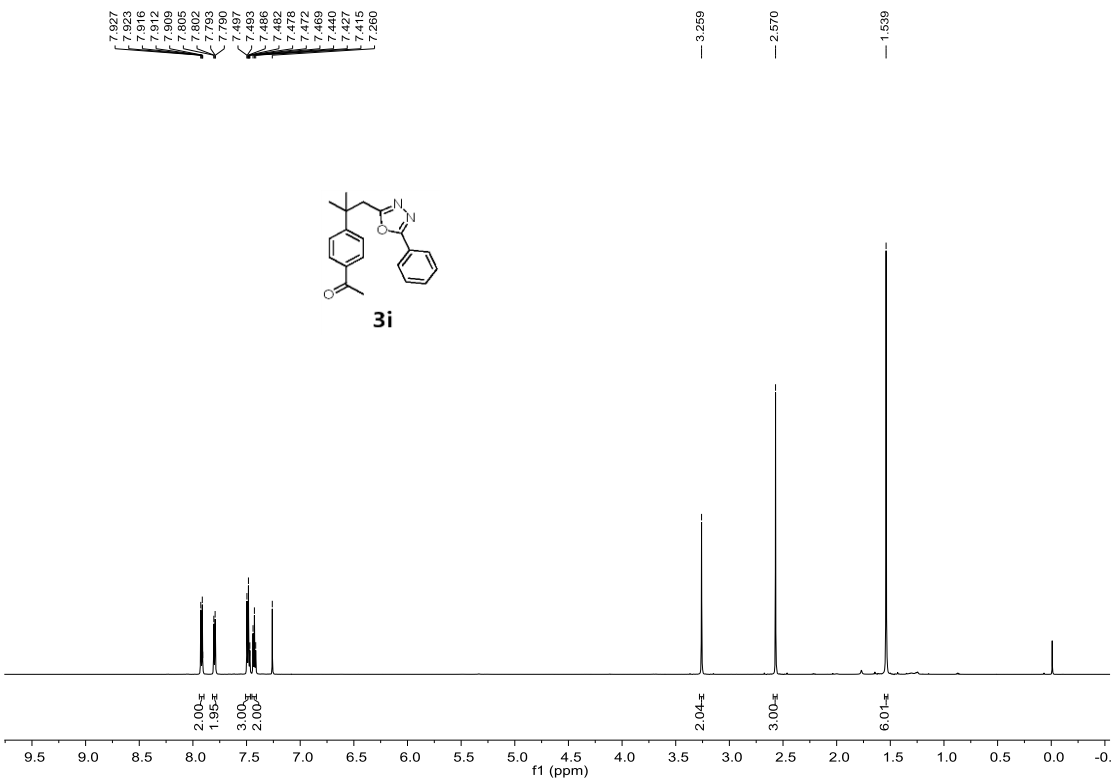
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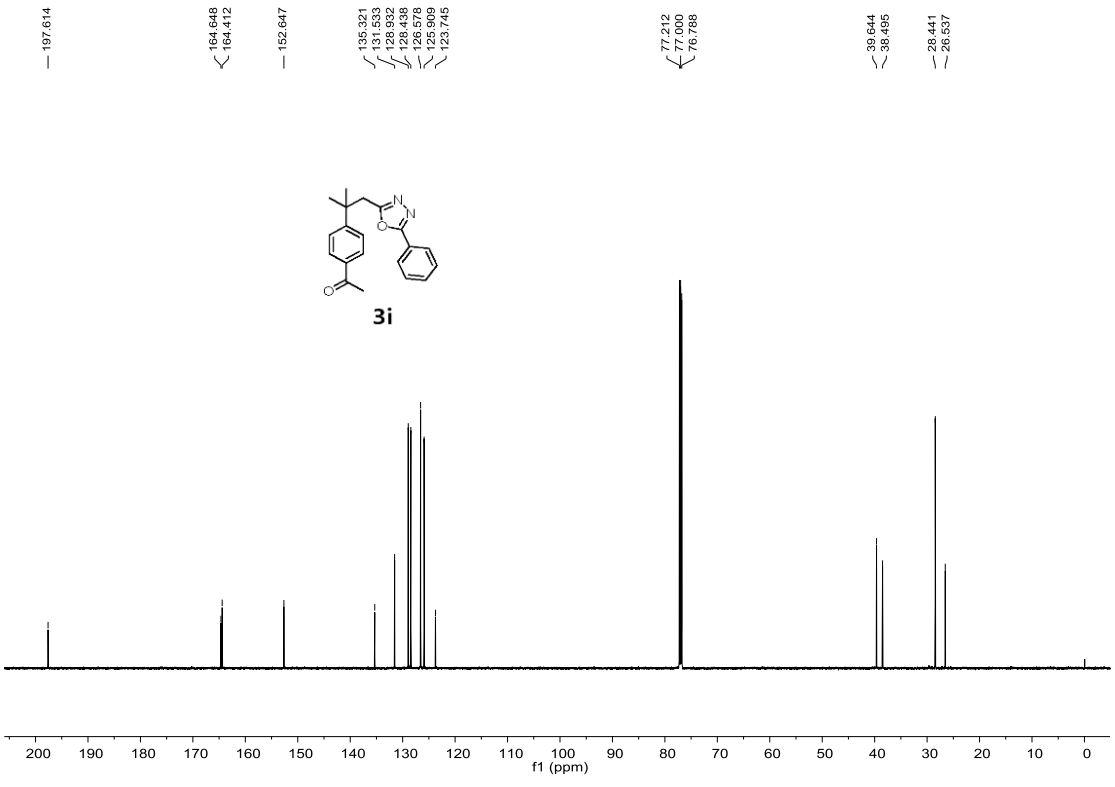
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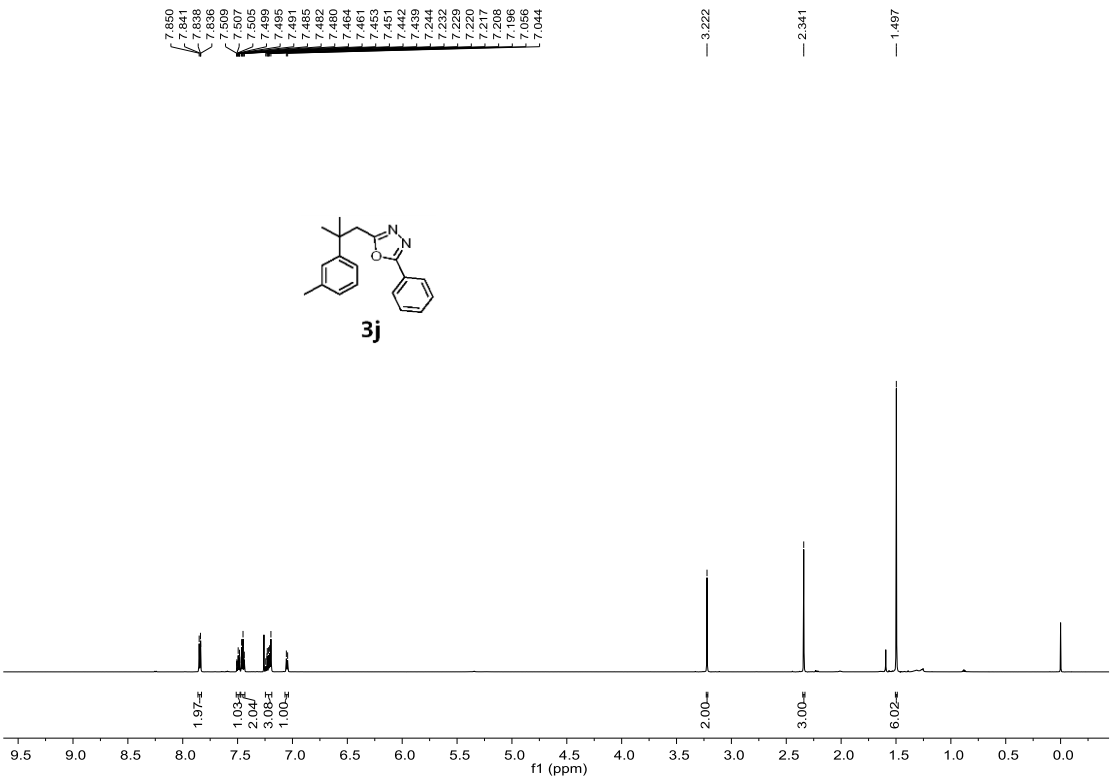
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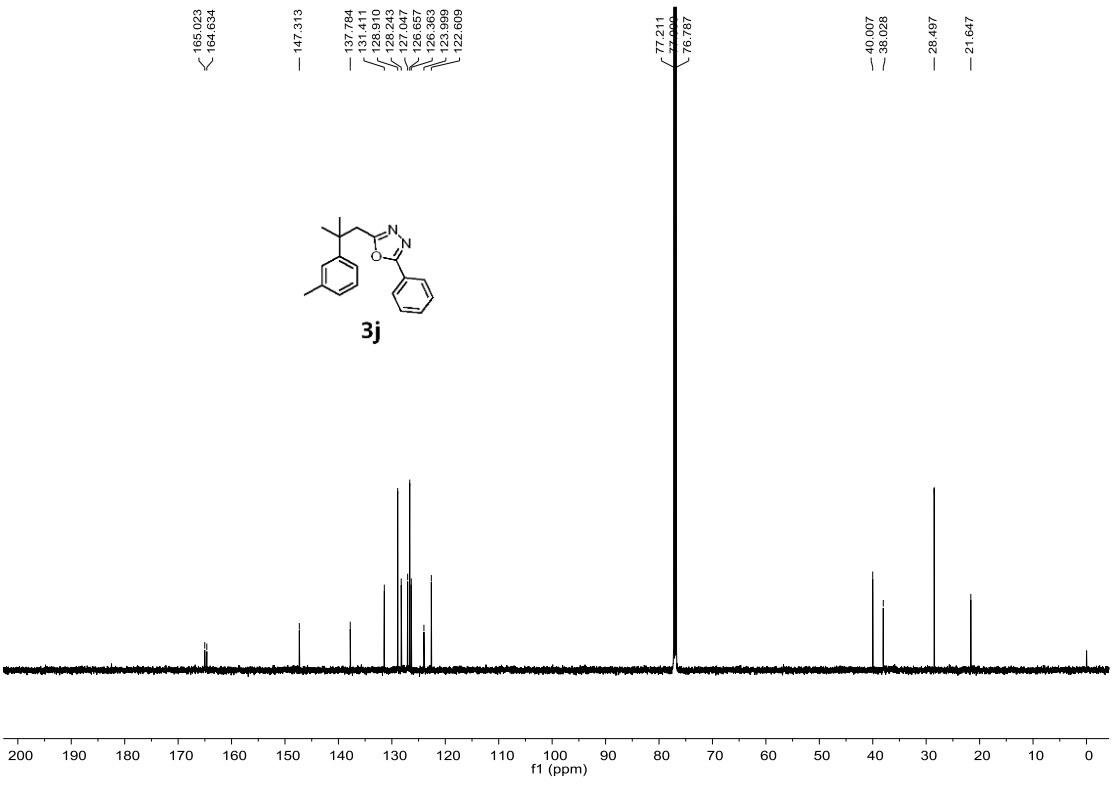
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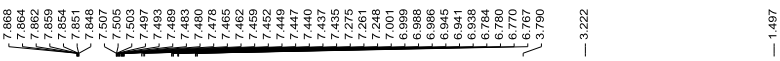
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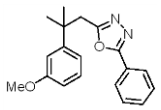
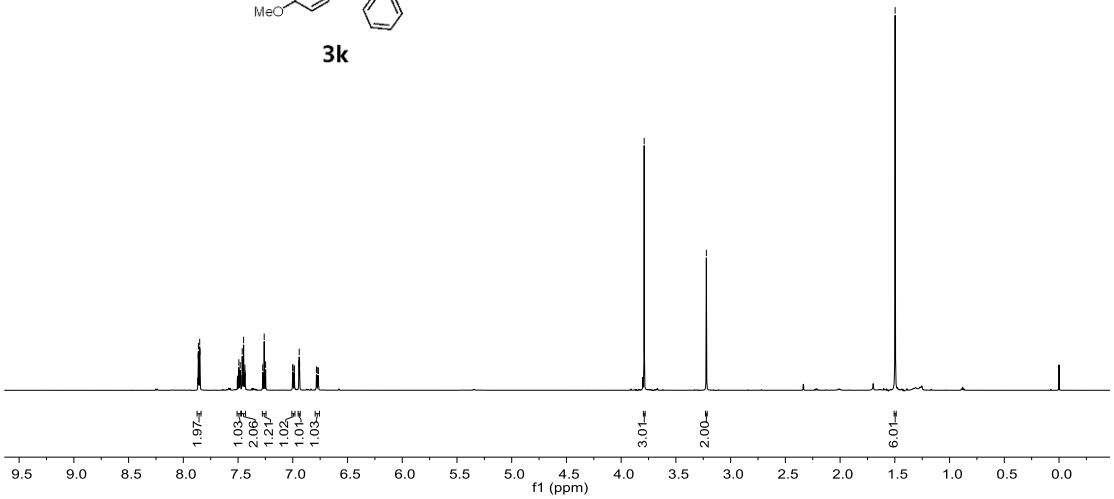
7.437
7.435
7.275
7.261
7.248
7.001
6.999
6.988
6.986
6.945
6.941
6.938
6.784
6.780
6.770
6.767
3.790
3.222
1.497


MeO
N
N
O

3k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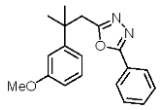
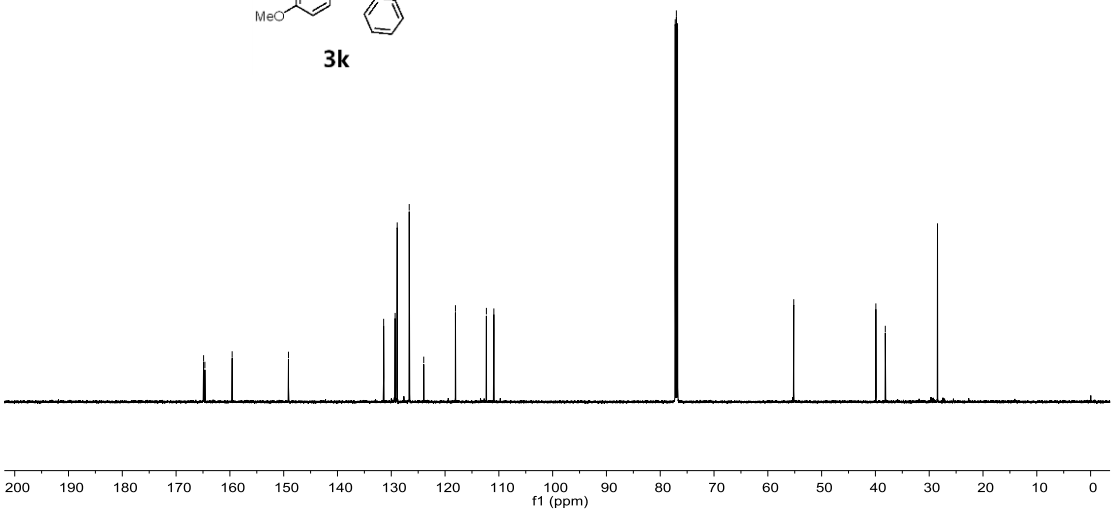
1.03
2.06
1.21
1.02
1.01
1.03
3.01
2.00
6.01
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


164.889
164.647
159.577
149.107
131.414
129.287
128.896
126.661
123.963
118.070
112.316
110.931
77.212
77.000
76.788
55.180
39.917
38.166
28.459


MeO
N
N
O

3k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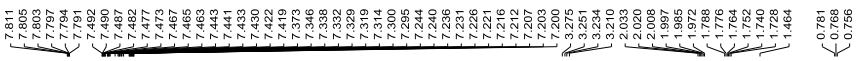
f1 (ppm)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7.490
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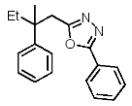
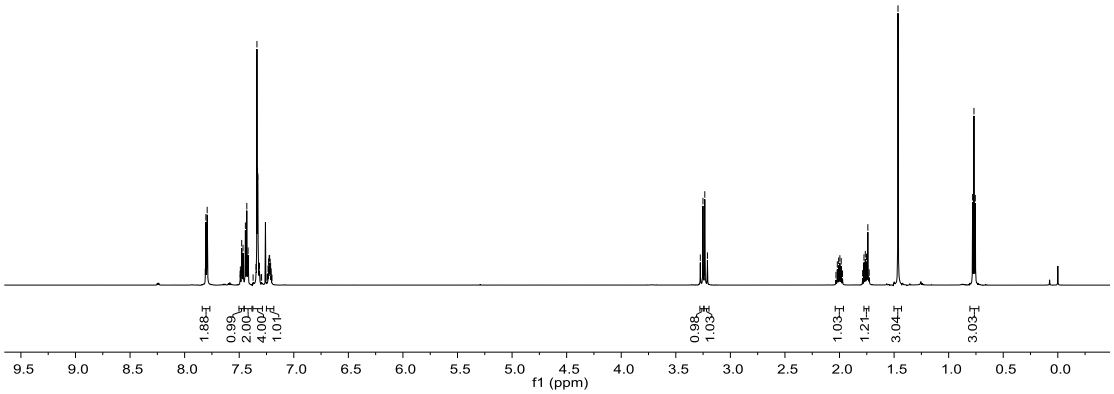
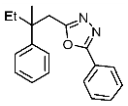
7.482
7.477
7.473
7.467
7.465
7.463
7.443
7.441
7.433
7.430
7.422
7.419
7.373
7.346
7.338
7.332
7.329
7.319
7.314
7.300
7.295
7.244
7.240
7.236
7.231
7.226
7.221
7.216
7.212
7.207
7.203
7.200
3.275
3.251
3.234
3.210
2.033
2.020
2.008
1.997
1.985
1.972
1.788
1.776
1.764
1.752
1.740
1.728
1.464
0.781
0.768
0.756


Et
N
N
O

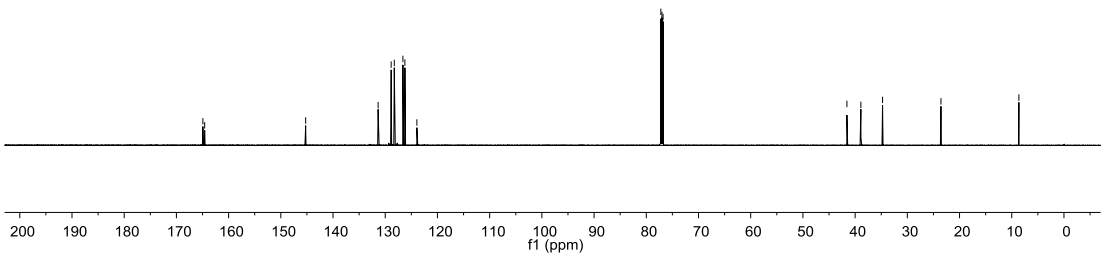
3l

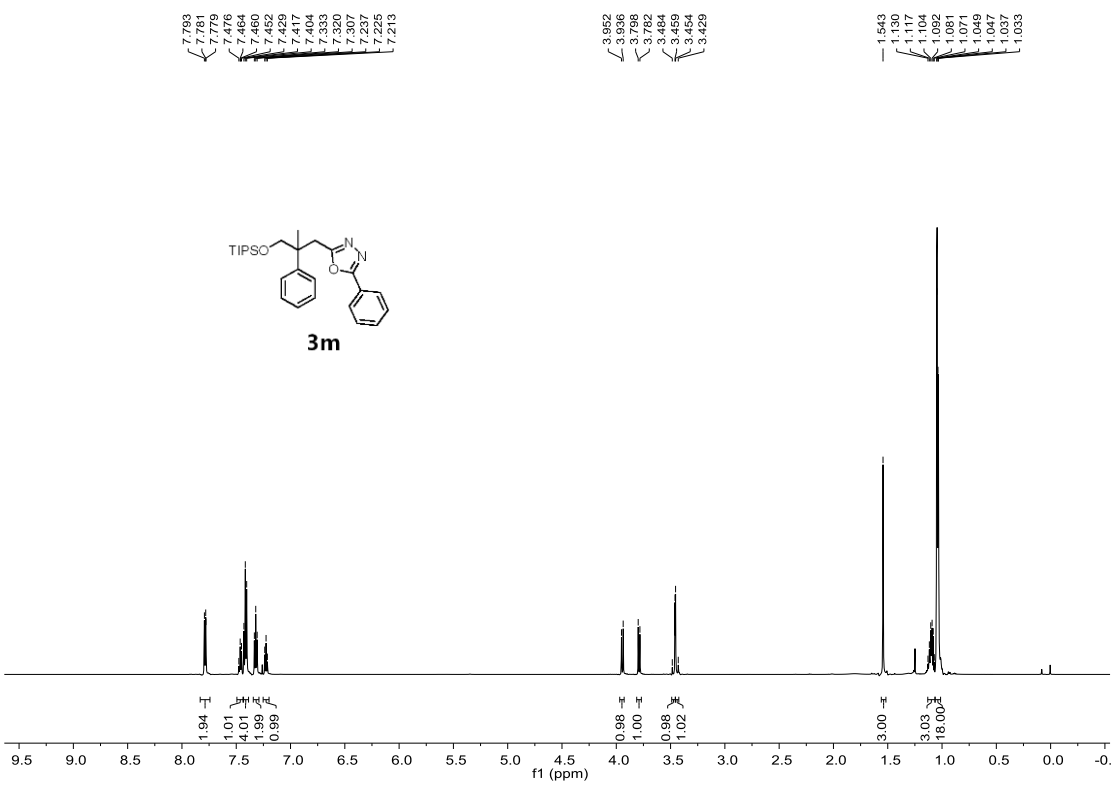

1.88
0.99
2.00
4.00
1.01
0.98
1.03
1.03
1.21
3.04
3.03
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

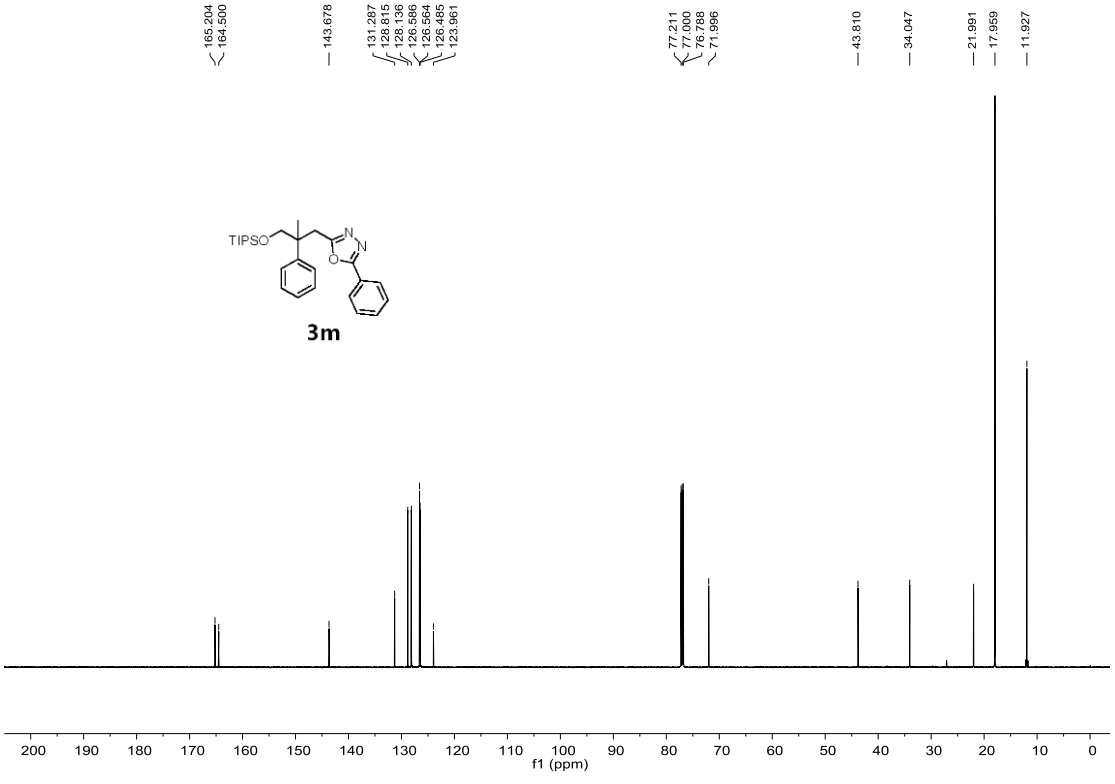

164.929
164.586
145.244
131.363
128.865
128.268
126.617
126.235
126.171
123.939
77.212
77.000
76.788
41.575
38.899
34.745
23.561
8.633


Et
N
N
O

3l


200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.793
7.781
7.779
7.476
7.464
7.460
7.452
7.429
7.417
7.404
7.333
7.320
7.307
7.237
7.225
7.213
3.952
3.936
3.798
3.782
3.484
3.459
3.454
3.429
1.543
1.130
1.117
1.104
1.092
1.081
1.071
1.049
1.047
1.037
1.033
TIPSO
3m
1.94
1.01
4.01
1.99
0.99
0.98
1.00
0.98
1.02
3.00
3.03
18.00
f1 (ppm)


165.204
164.500
143.678
131.287
128.815
128.136
126.586
126.564
126.485
123.961
77.211
77.000
76.788
71.996
43.810
34.047
21.991
17.959
11.927
TIPSO
3m
f1 (ppm)


7.820
7.808
7.649
7.635
7.483
7.471
7.459
7.439
7.425
7.409
7.334
7.322
7.309
7.297
7.240
7.228
7.216
3.664
3.638
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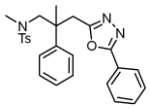
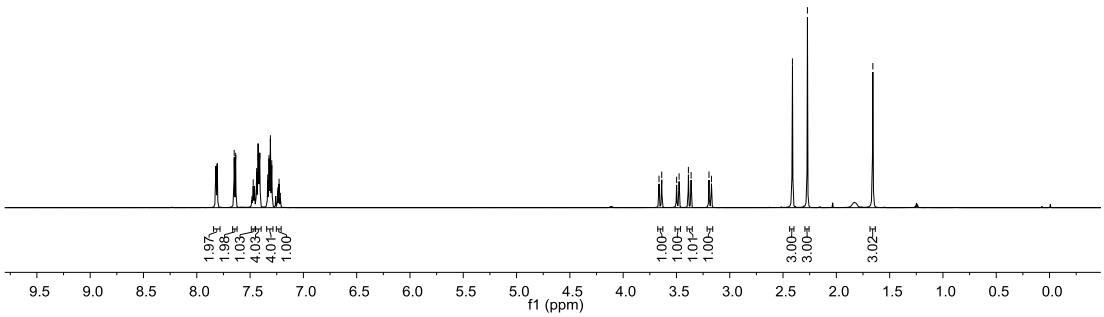
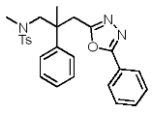
3.363
3.195
3.172
2.412
2.271
1.658



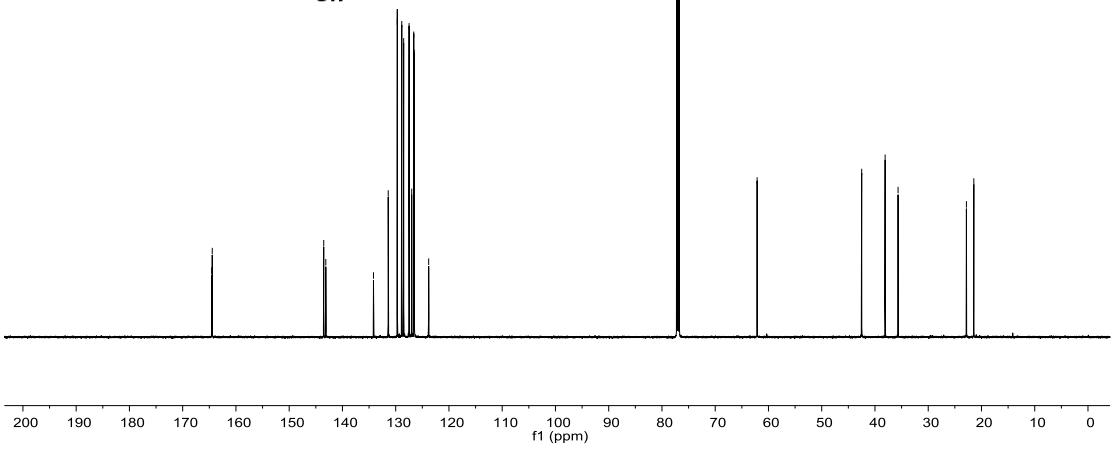
3n

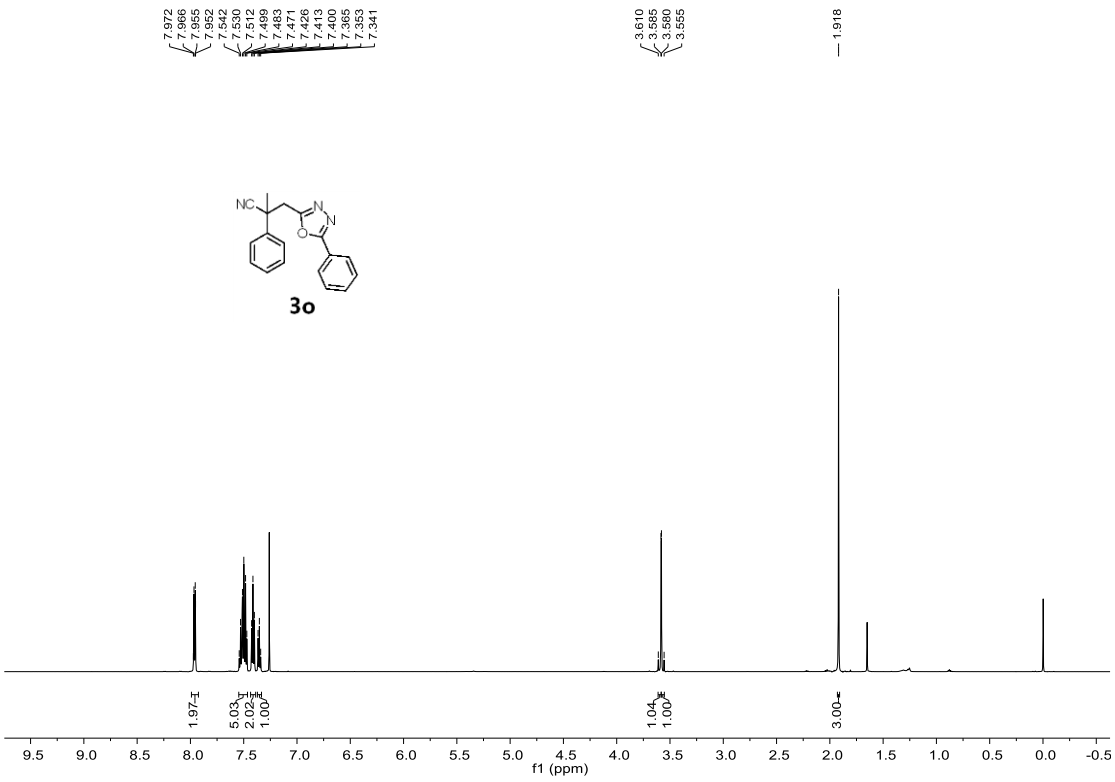

1.97
1.98
1.03
4.03
4.01
1.00
1.00
1.00
1.01
1.00
3.00
3.00
3.02
9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

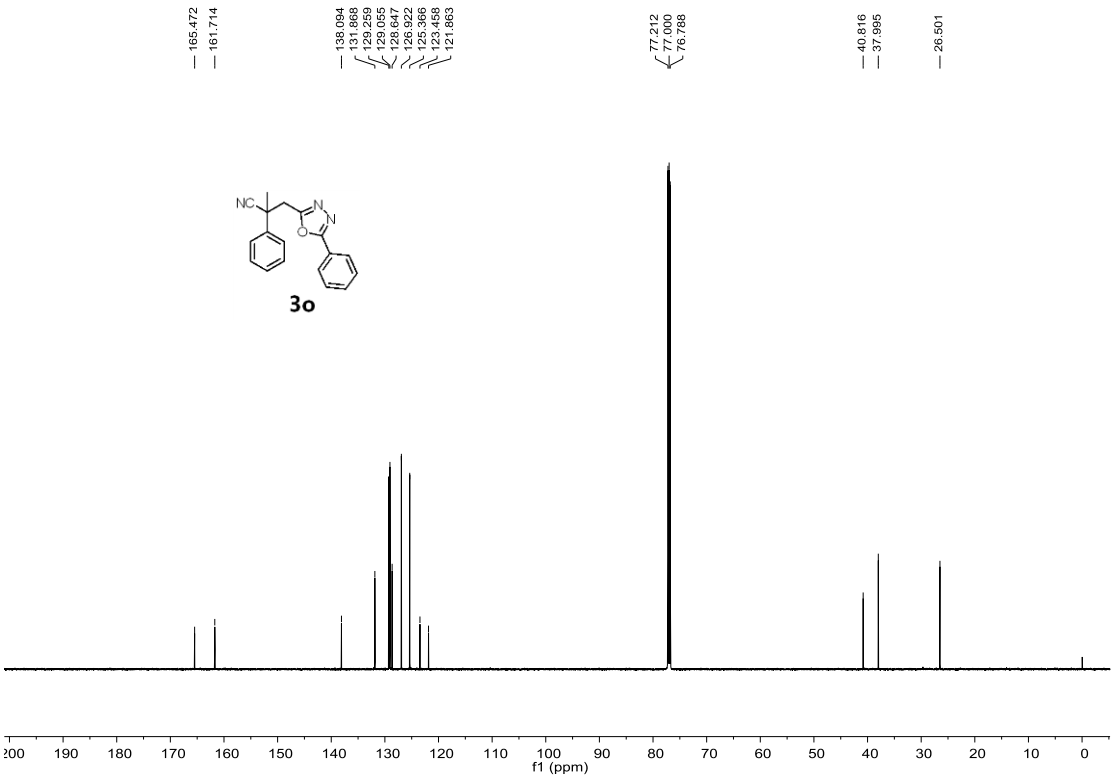

164.555
164.448
143.514
143.124
134.168
131.401
129.699
128.860
128.502
127.483
126.992
126.609
126.508
123.805
77.212
77.001
76.789
62.129
42.495
38.092
35.662
22.826
21.438



3n


200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.972
7.966
7.955
7.952
7.542
7.530
7.512
7.499
7.483
7.471
7.426
7.413
7.400
7.365
7.353
7.341
3.610
3.585
3.580
3.555
1.918
NC
N
N
O
3o
1.97
5.03
2.02
1.00
1.04
1.00
3.00
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)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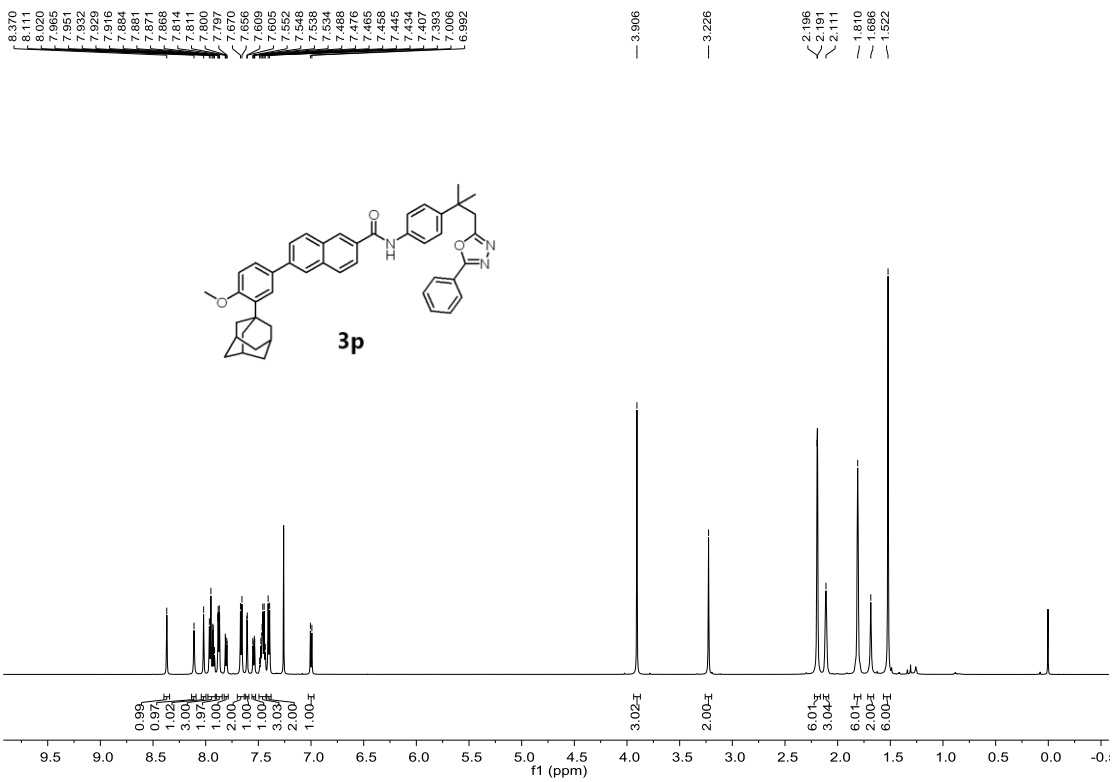
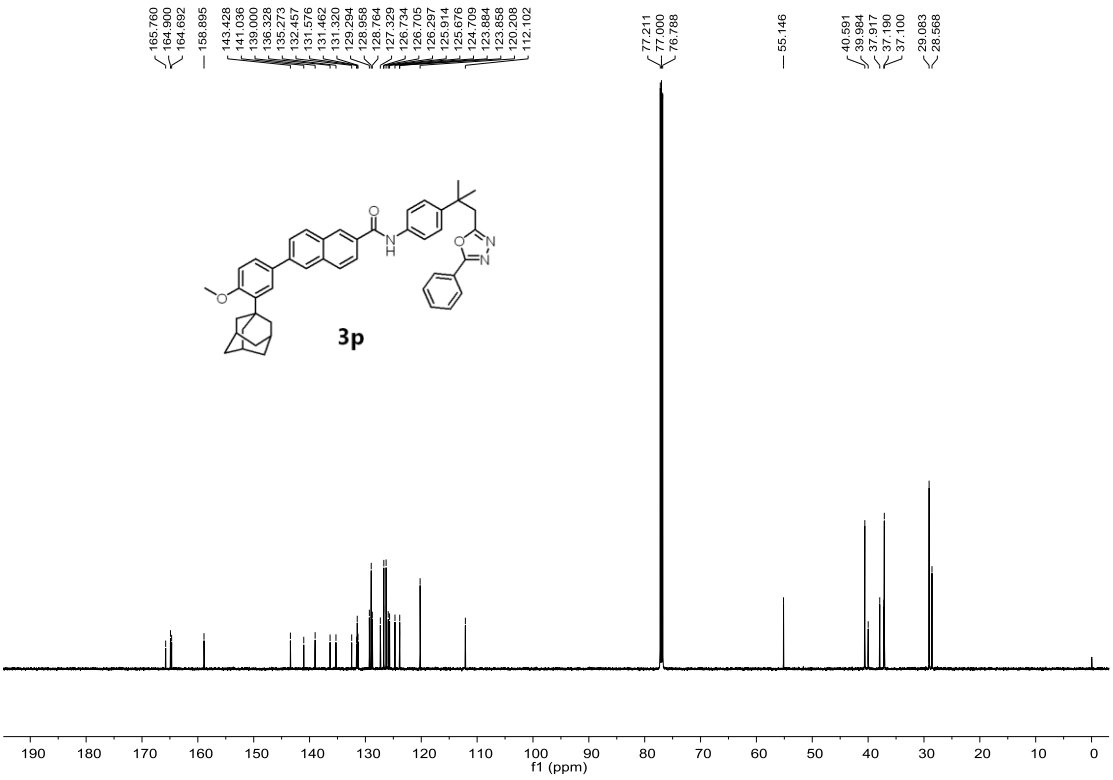
161.714
138.094
131.868
129.259
129.055
128.647
126.922
123.366
123.458
121.863
77.212
77.000
76.788
40.816
37.995
26.501
NC
N
N
O
3o
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


8.370
8.111
8.020
7.965
7.951
7.932
7.929
7.916
7.884
7.881
7.871
7.868
7.814
7.811
7.800
7.797
7.670
7.656
7.609
7.605
7.552
7.548
7.538
7.534
7.488
7.476
7.465
7.458
7.445
7.434
7.407
7.393
7.006
6.992
3.906
3.226
2.196
2.191
2.111
1.810
1.686
1.522
3p
0.99
0.97
1.02
3.00
1.97
2.00
1.00
1.00
3.03
2.00
1.00
3.02
2.00
6.01
3.04
6.01
2.00
6.00
f1 (ppm)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164.692
158.895
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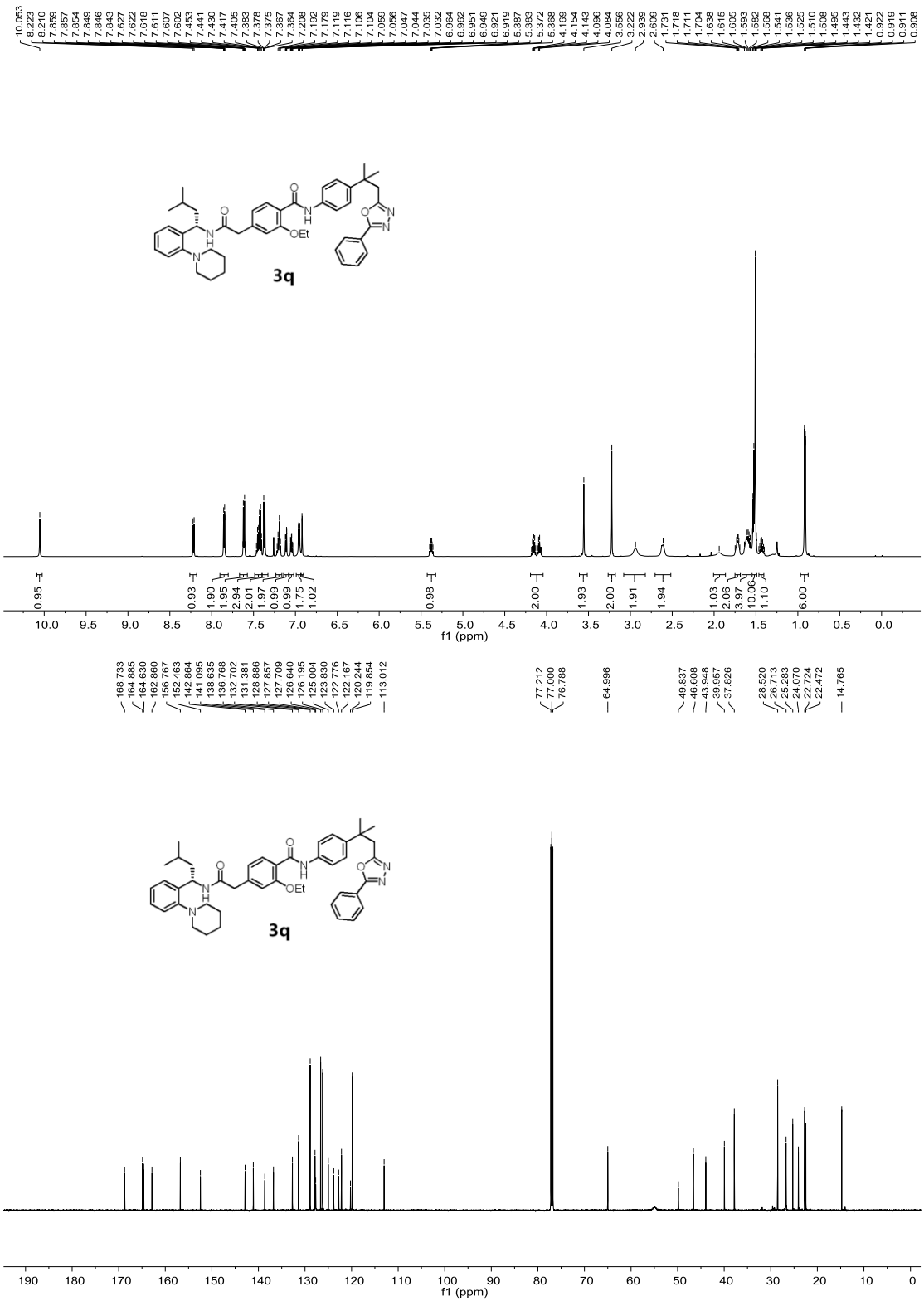
141.036
139.000
136.228
133.473
132.467
131.576
131.462
131.320
129.294
128.958
128.764
127.329
126.734
126.705
126.297
125.914
125.676
124.709
123.884
123.858
120.208
112.102
77.211
77.000
76.788
55.146
40.591
39.984
37.917
37.190
37.100
29.083
28.568
3p
f1 (ppm)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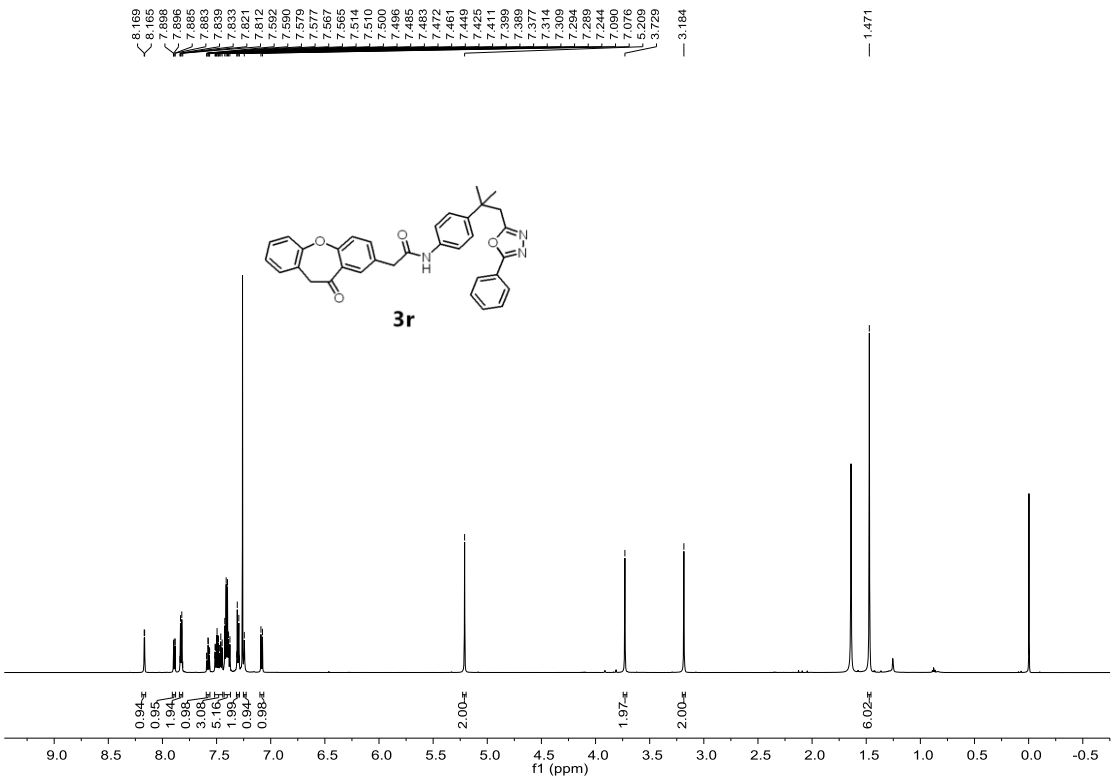
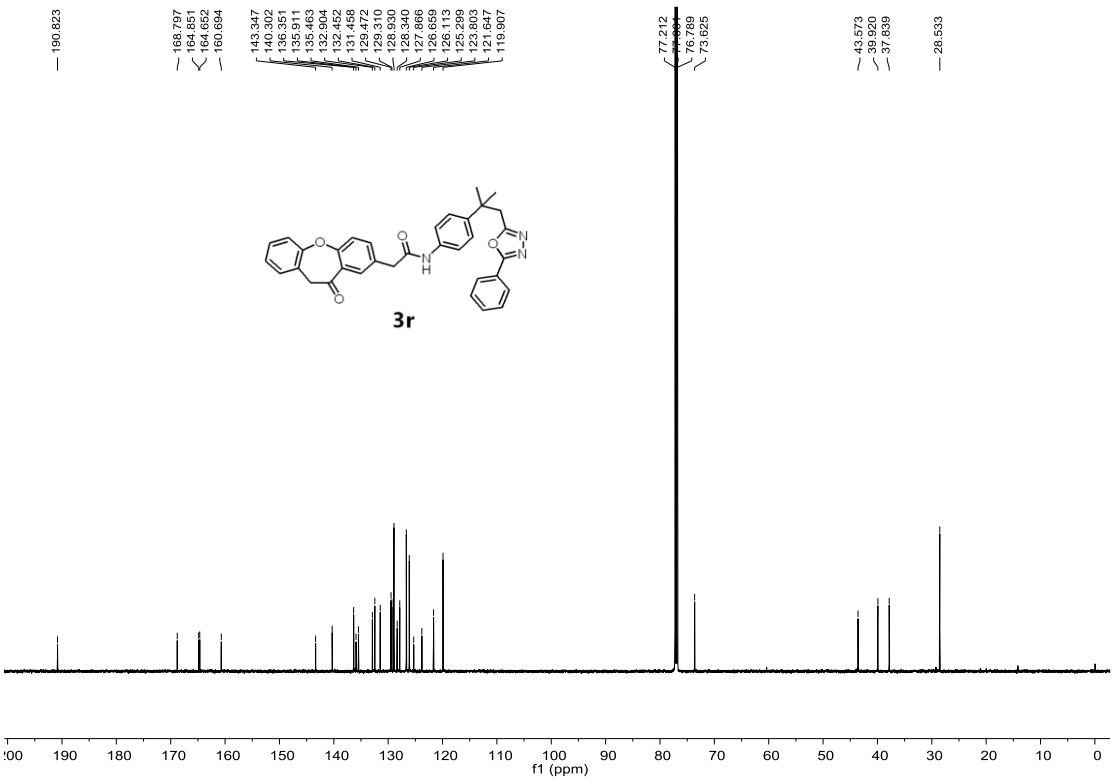
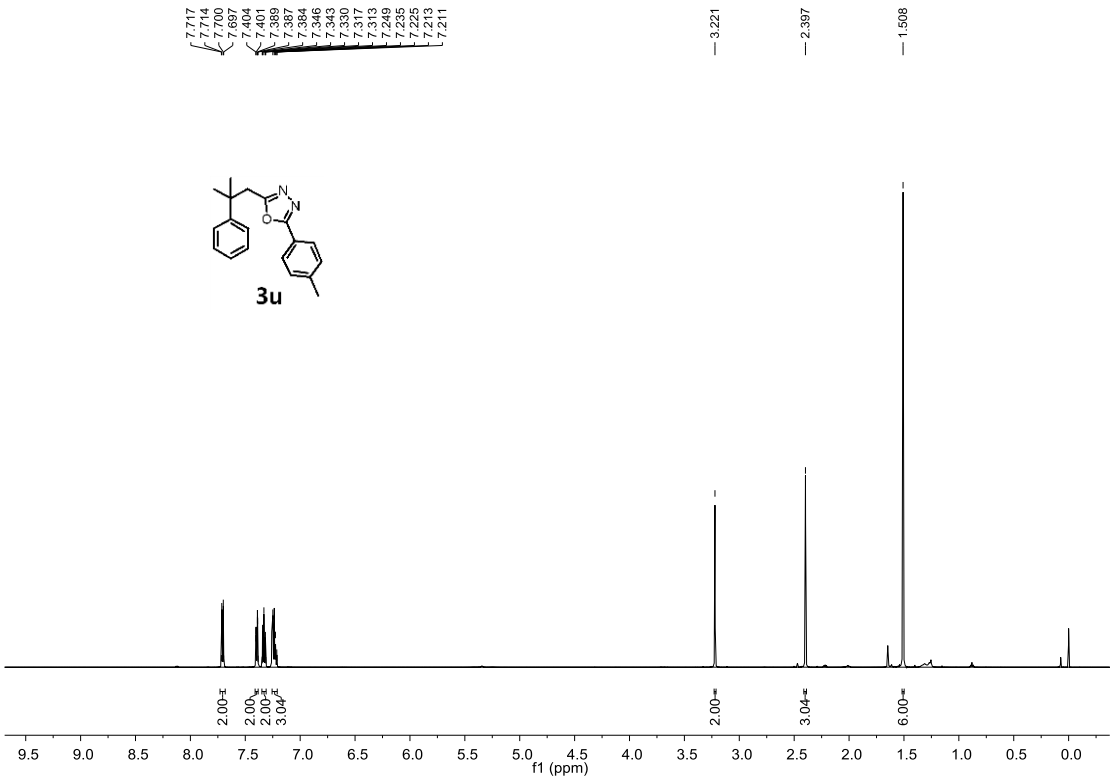
7.857
7.854
7.849
7.846
7.843
7.627
7.622
7.618
7.611
7.607
7.602
7.453
7.441
7.430
7.417
7.405
7.393
7.378
7.375
7.367
7.364
7.208
7.192
7.179
7.119
7.116
7.106
7.104
7.059
7.056
7.047
7.044
7.035
7.032
6.964
6.962
6.951
6.949
6.921
6.919
5.387
5.383
5.372
5.368
4.169
4.154
4.143
4.096
4.084
3.556
3.222
2.939
2.609
1.731
1.718
1.711
1.704
1.638
1.615
1.605
1.593
1.582
1.568
1.541
1.536
1.525
1.510
1.508
1.495
1.443
1.432
1.421
0.922
0.919
0.911
0.908
OEt
3q
0.95
0.93
1.90
1.95
2.94
2.01
1.97
0.99
0.99
1.75
1.02
0.98
2.00
1.93
2.00
1.91
1.94
1.03
2.06
3.97
10.06
1.10
6.00
f1 (ppm)
168.733
164.885
164.630
162.860
156.767
152.463
142.864
141.095
138.755
138.768
132.702
131.381
128.886
127.857
127.709
126.640
126.195
125.004
123.830
122.776
122.167
120.244
119.854
113.012
77.212
77.000
76.788
64.996
49.837
46.608
43.948
39.957
37.826
28.520
26.713
25.283
24.070
22.724
22.472
14.765
OEt
3q
f1 (ppm)


8.169
8.165
7.898
7.896
7.885
7.883
7.839
7.833
7.821
7.812
7.592
7.590
7.579
7.577
7.567
7.565
7.514
7.510
7.500
7.496
7.485
7.483
7.472
7.461
7.449
7.425
7.411
7.399
7.389
7.377
7.314
7.309
7.294
7.289
7.244
7.090
7.076
5.209
3.729
3.184
1.471
3r
0.94
0.95
1.94
0.98
3.08
5.16
1.99
0.94
0.98
2.00
1.97
2.00
6.02
f1 (ppm)


190.823
168.797
164.851
164.652
160.694
143.347
140.302
136.351
135.511
135.463
132.904
132.452
131.458
129.472
129.310
128.930
128.340
127.866
126.659
126.113
125.299
123.803
121.647
119.907
77.212
76.789
73.625
43.573
39.920
37.839
28.533
3r
f1 (ppm)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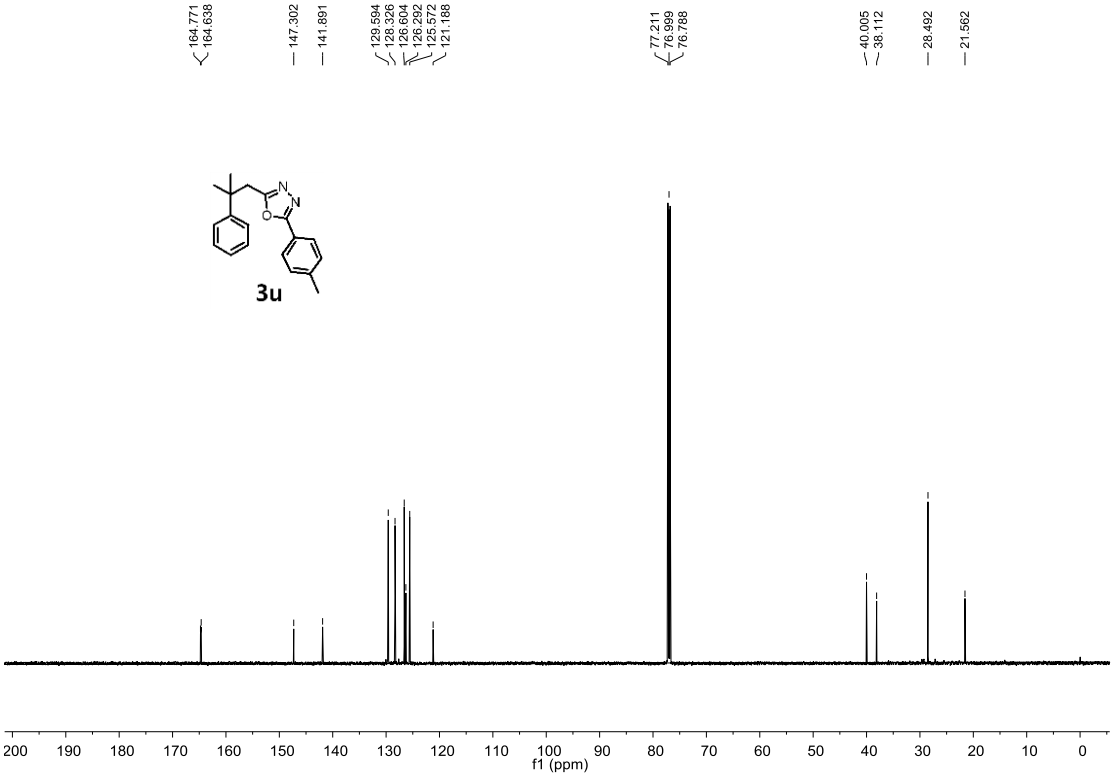
7.401
7.389
7.387
7.384
7.346
7.343
7.330
7.317
7.313
7.249
7.235
7.225
7.213
7.211
3.221
2.397
1.508
3u
2.00
2.00
2.00
3.04
2.00
3.04
6.00
f1 (ppm)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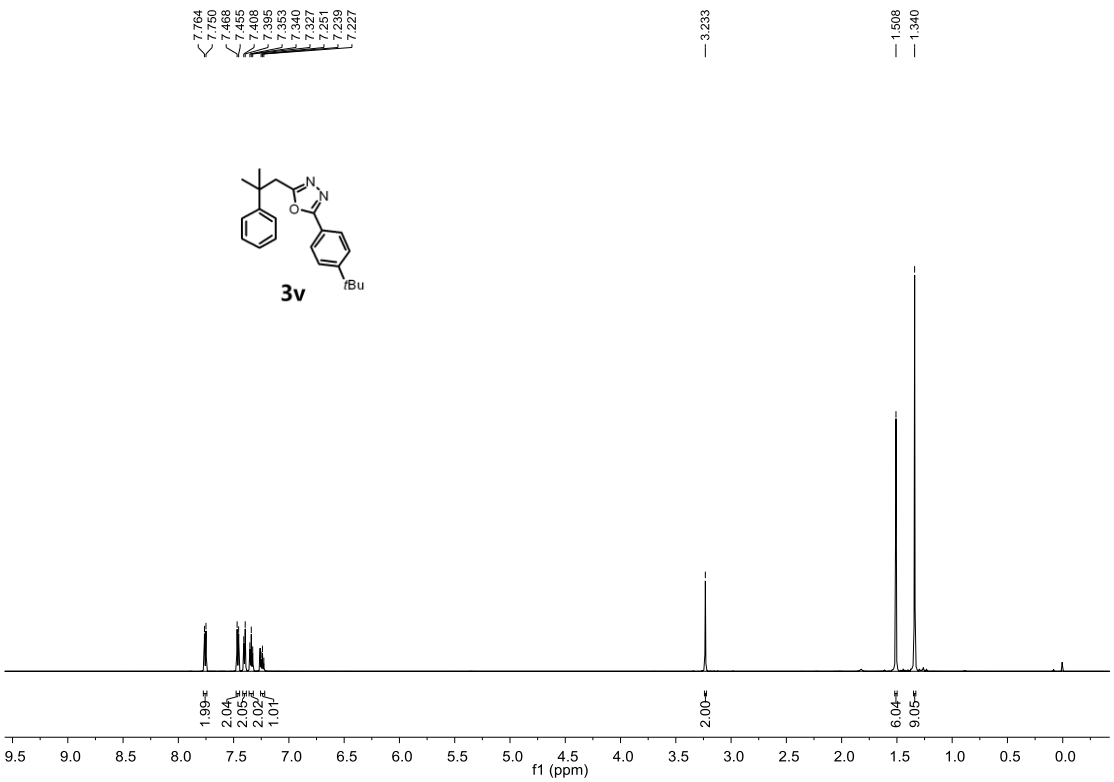
147.302
141.891
129.594
128.326
126.604
126.292
125.572
121.188
77.211
76.999
76.788
40.005
38.112
28.492
21.562
3u
f1 (ppm)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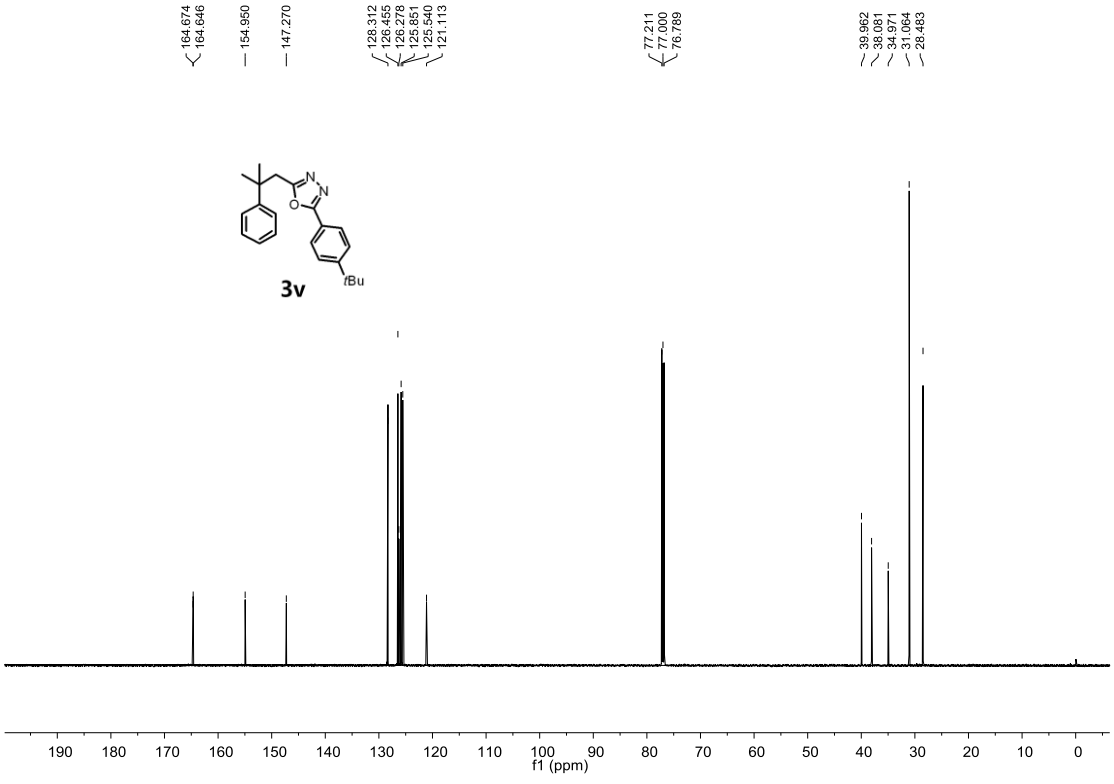
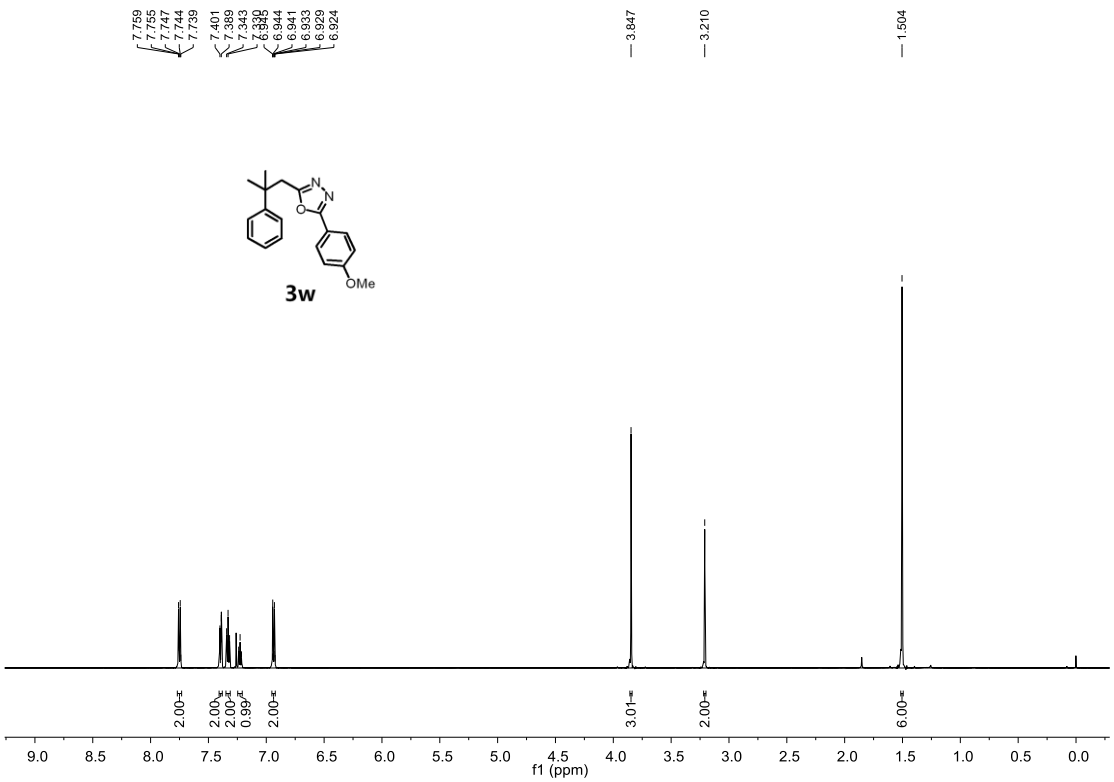
7.760
7.468
7.465
7.455
7.408
7.395
7.393
7.340
7.327
7.251
7.239
7.227
3.233
1.508
1.340
3v
tBu
1.99
2.04
2.05
2.02
1.01
2.00
6.04
9.05
f1 (ppm)


164.674
164.646
154.950
147.270
128.312
126.455
126.278
125.851
125.540
121.113
77.211
77.000
76.789
39.962
38.081
34.971
31.064
28.483
3v
tBu
f1 (ppm)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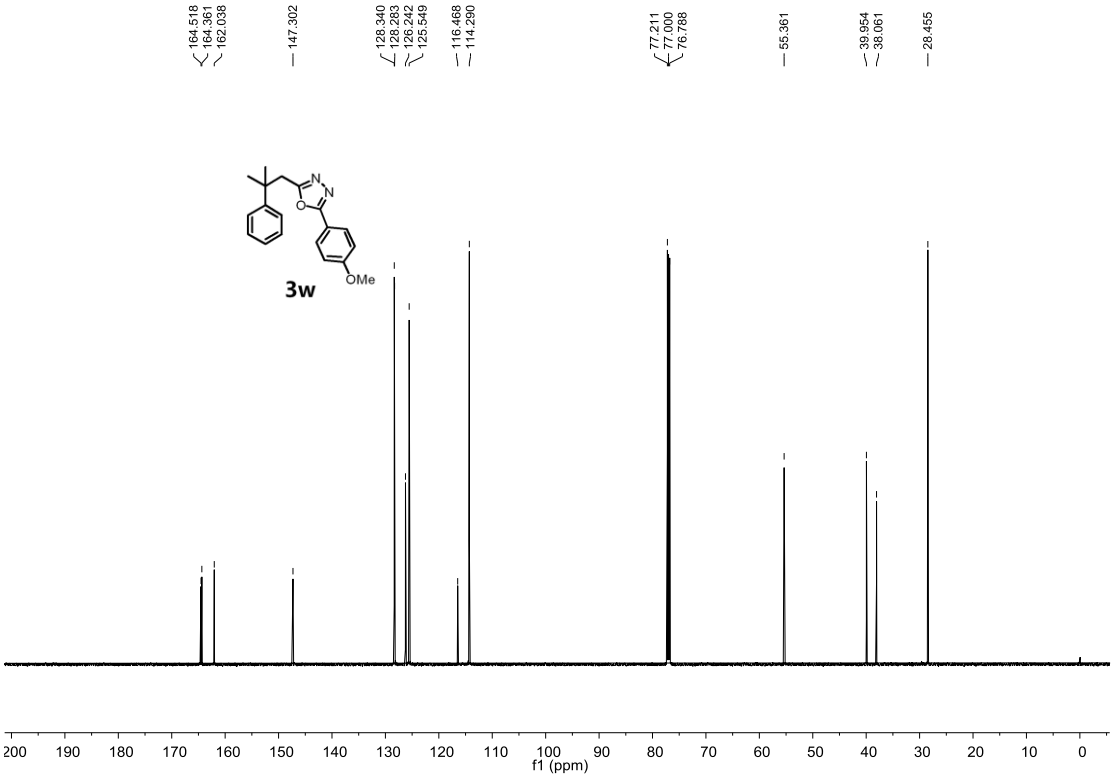
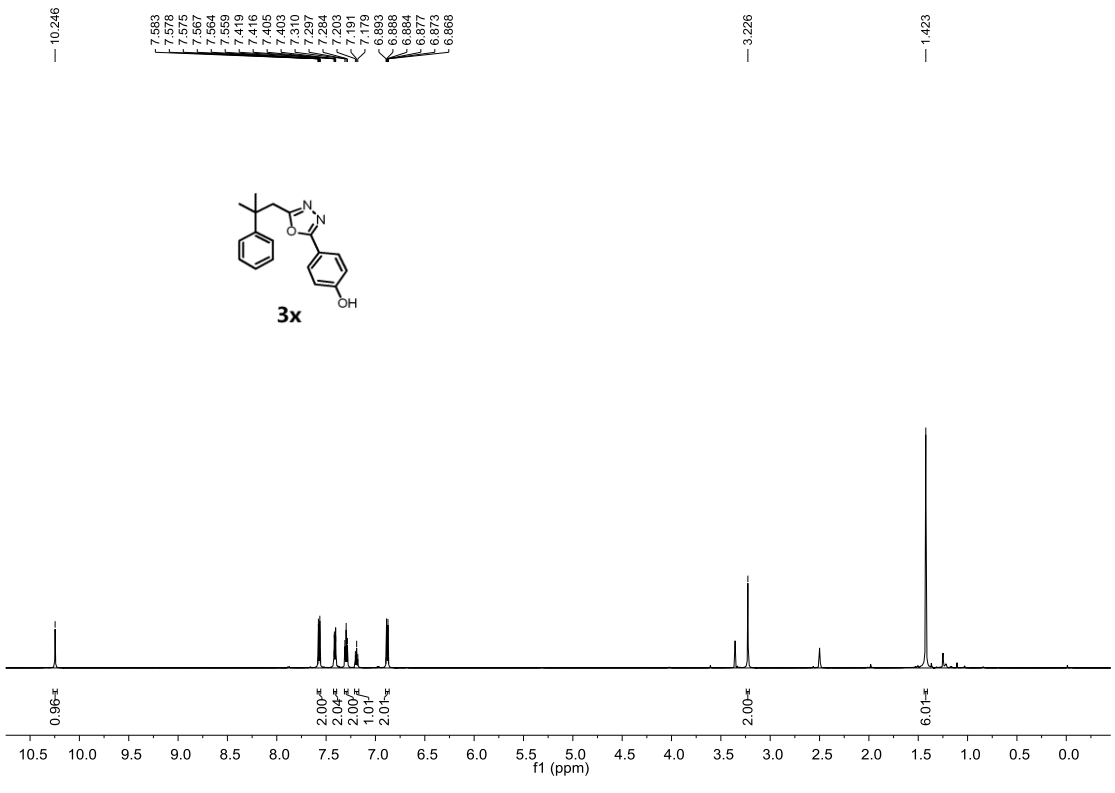
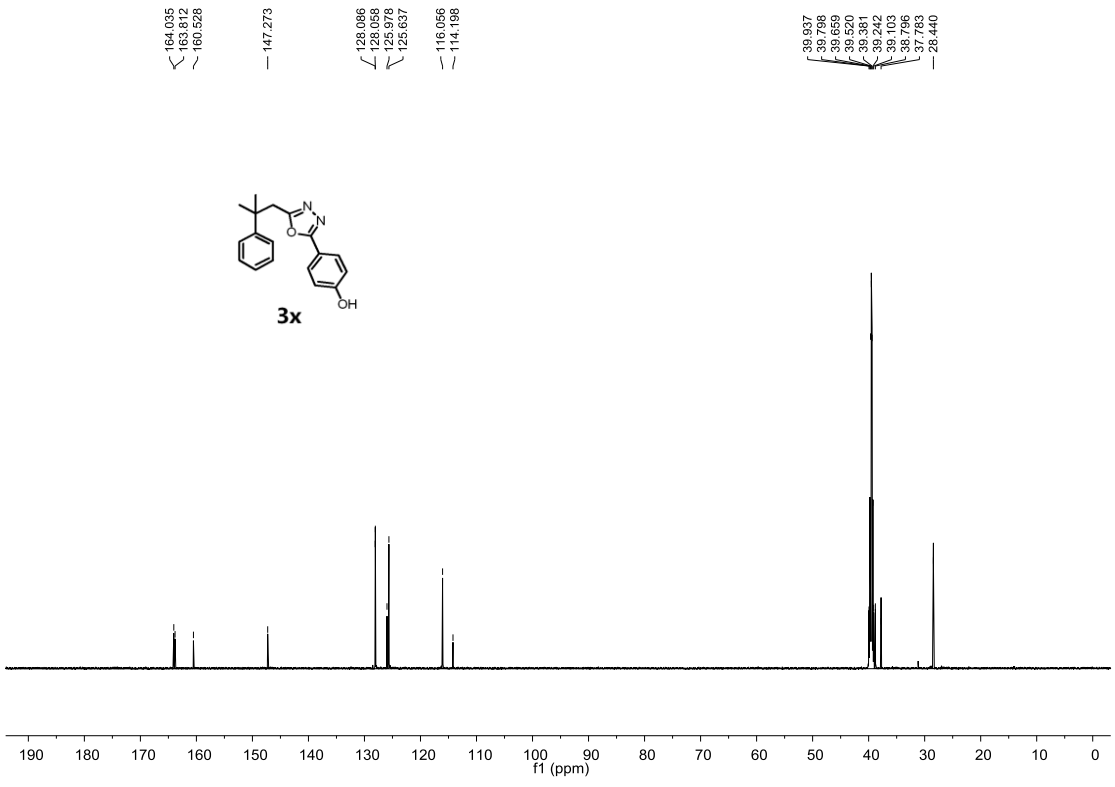
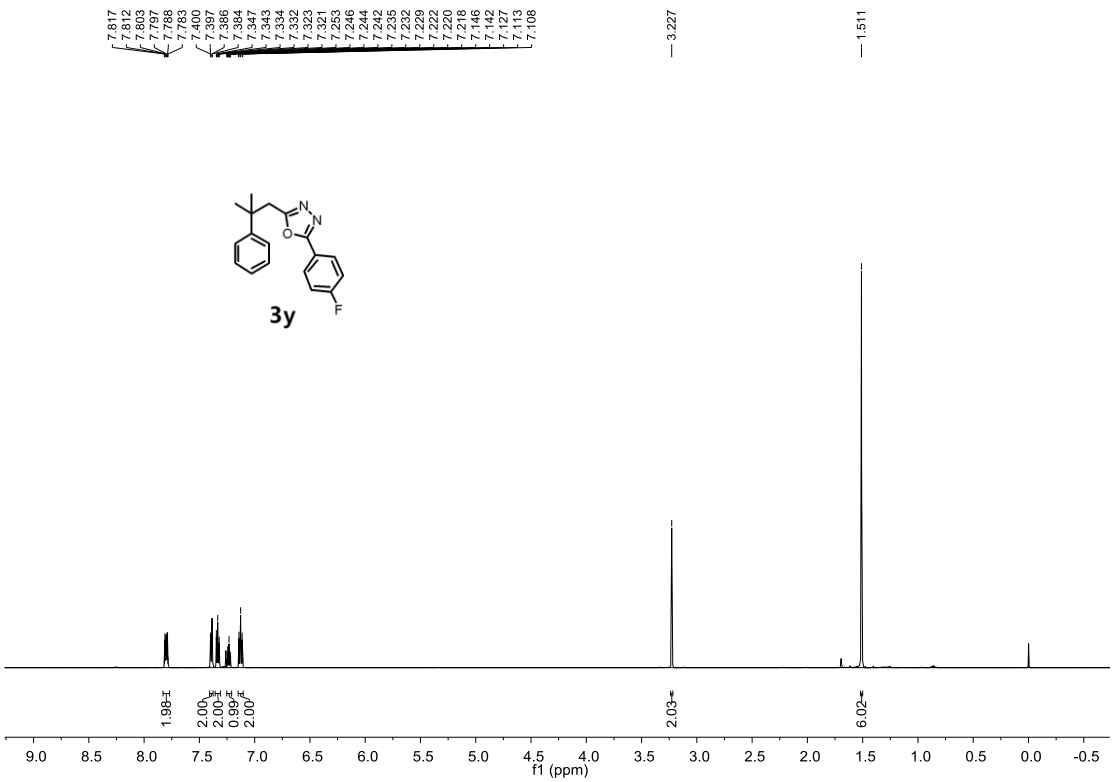
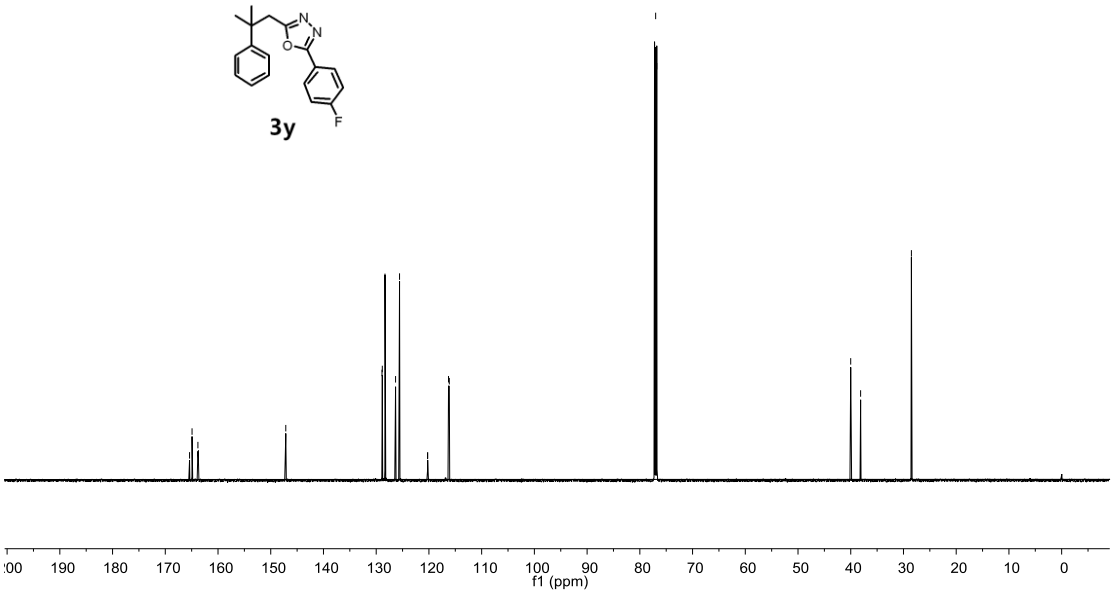
7.747
7.744
7.739
7.401
7.389
7.343
6.944
6.941
6.933
6.929
6.924
3.847
3.210
1.504
OMe
3w
2.00
2.00
2.00
0.99
2.00
3.01
2.00
6.00
f1 (ppm)

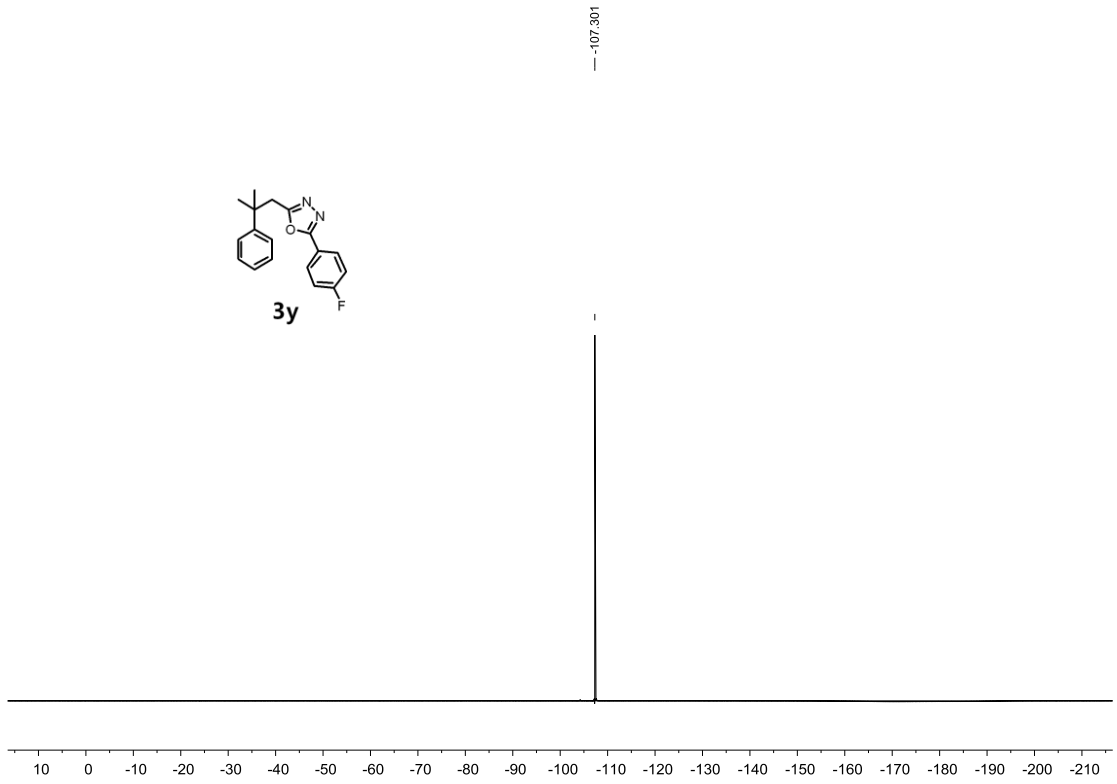

164.518
164.361
162.038
147.302
128.340
128.283
126.242
125.549
116.468
114.290
77.211
77.000
76.788
55.361
39.954
38.061
28.455
OMe
3w
f1 (ppm)

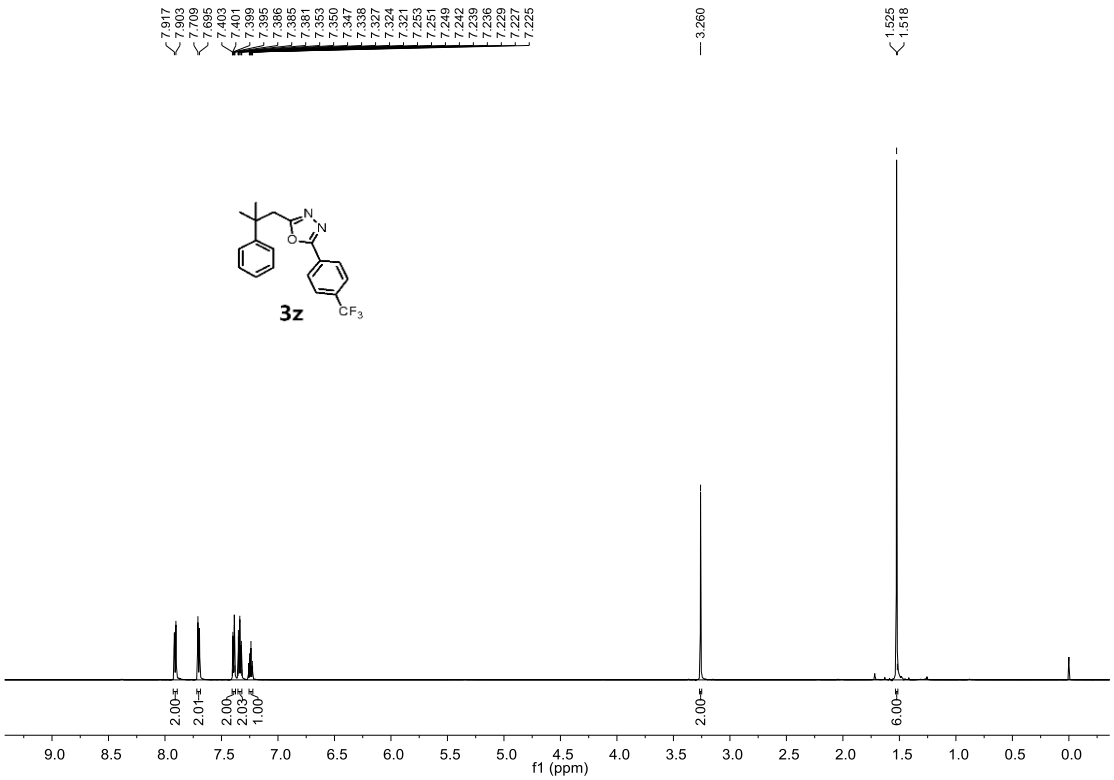

10.246
7.583
7.578
7.575
7.567
7.564
7.559
7.419
7.416
7.405
7.403
7.310
7.297
7.284
7.203
7.191
7.179
6.893
6.888
6.884
6.877
6.873
6.868
3.226
1.423
3x
0.96
2.00
2.04
2.00
1.01
2.01
2.00
6.01
f1 (ppm)

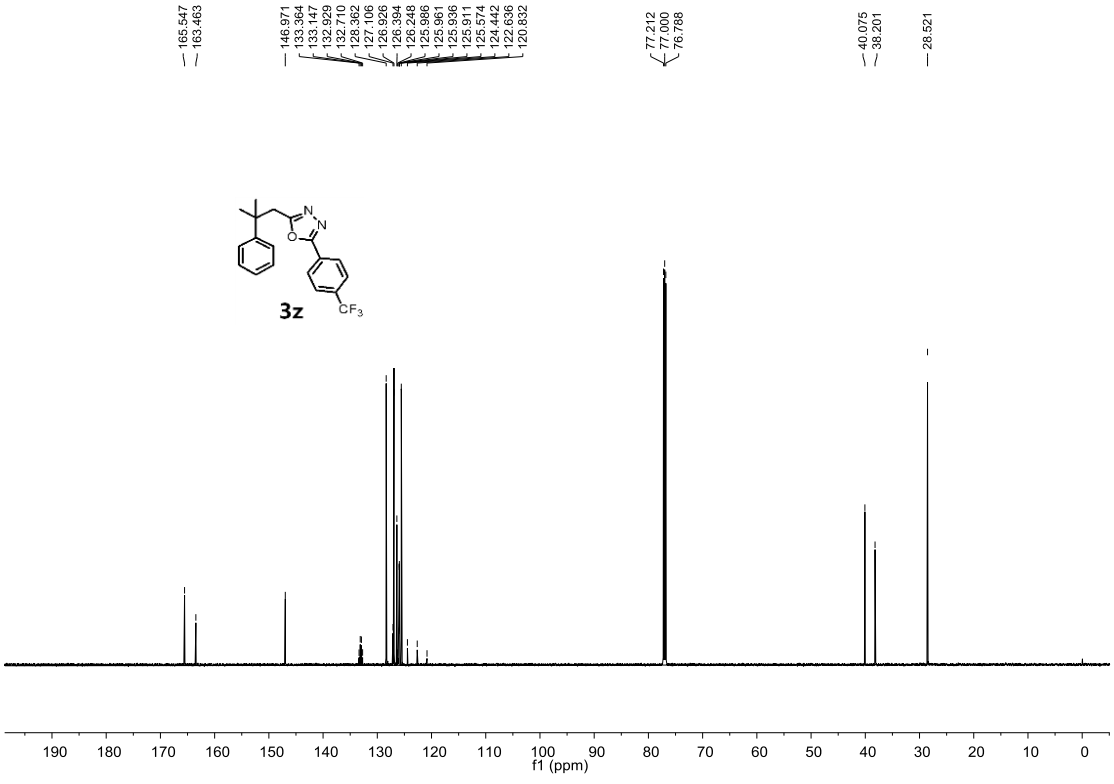

164.035
163.812
160.528
147.273
128.086
128.058
125.978
125.637
116.056
114.198
39.937
39.798
39.659
39.520
39.381
39.242
39.103
38.796
37.783
28.440
3x
f1 (ppm)


7.817
7.812
7.803
7.797
7.788
7.783
7.400
7.397
7.386
7.384
7.347
7.343
7.334
7.332
7.323
7.321
7.253
7.246
7.244
7.242
7.235
7.232
7.229
7.222
7.220
7.218
7.146
7.142
7.127
7.113
7.108
3.227
1.511
3y
1.98
2.00
2.00
0.99
2.00
2.03
6.02
f1 (ppm)


165.396
164.923
163.813
163.721
147.145
128.899
128.841
128.332
126.326
125.572
120.259
120.237
116.282
116.136
77.212
76.999
76.789
40.009
38.128
28.496
3y
f1 (ppm)


-107.301
3y
F
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210


7.917
7.903
7.709
7.695
7.403
7.401
7.399
7.395
7.386
7.385
7.381
7.353
7.350
7.347
7.338
7.327
7.324
7.321
7.253
7.251
7.249
7.242
7.239
7.236
7.229
7.227
7.225
3.260
1.525
1.518
3z
CF3
2.00
2.01
2.00
2.03
1.00
2.00
6.00
f1 (ppm)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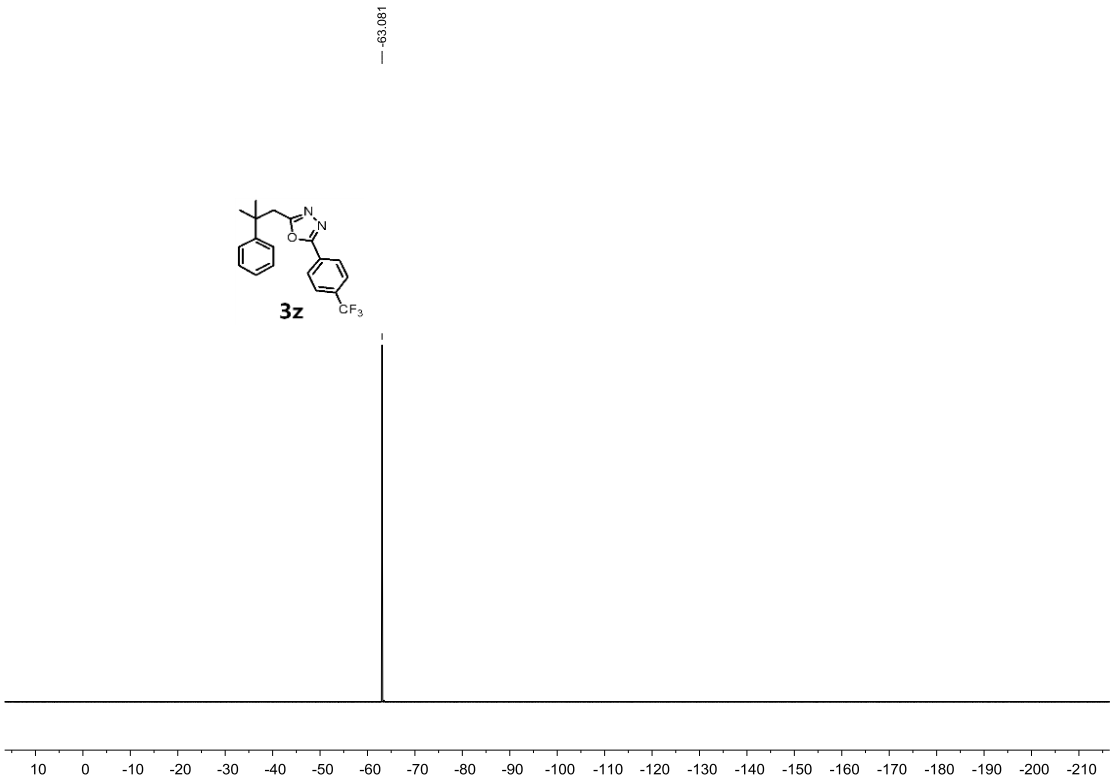
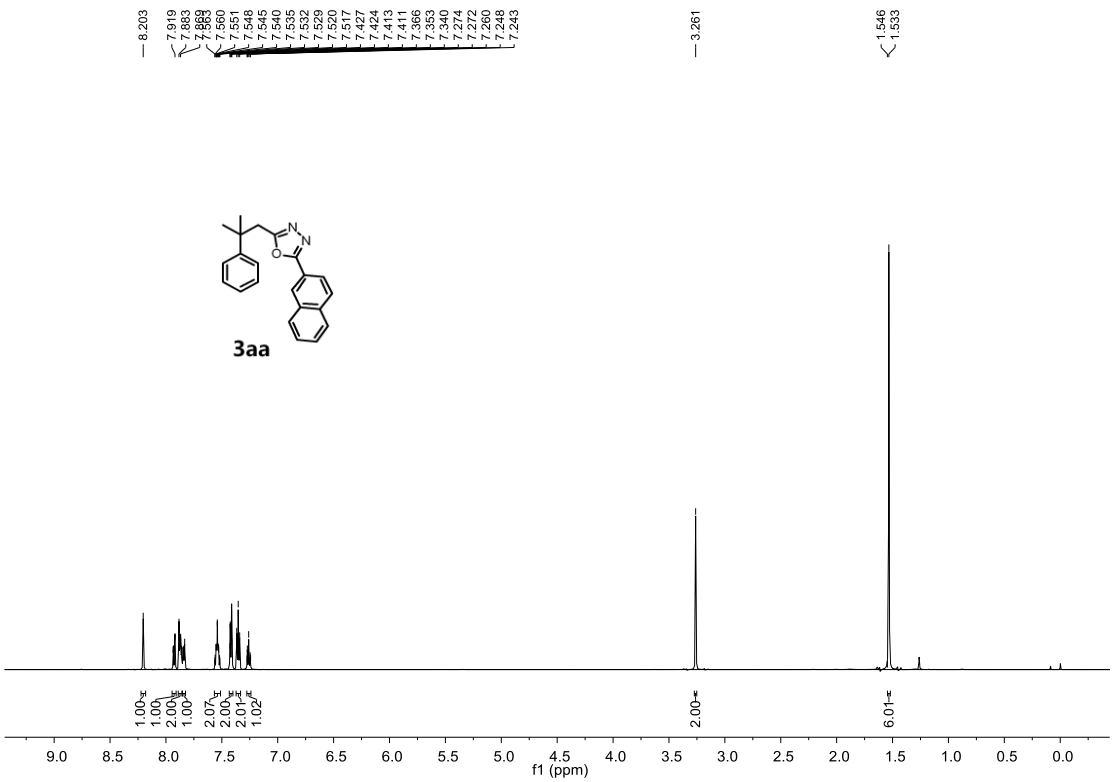
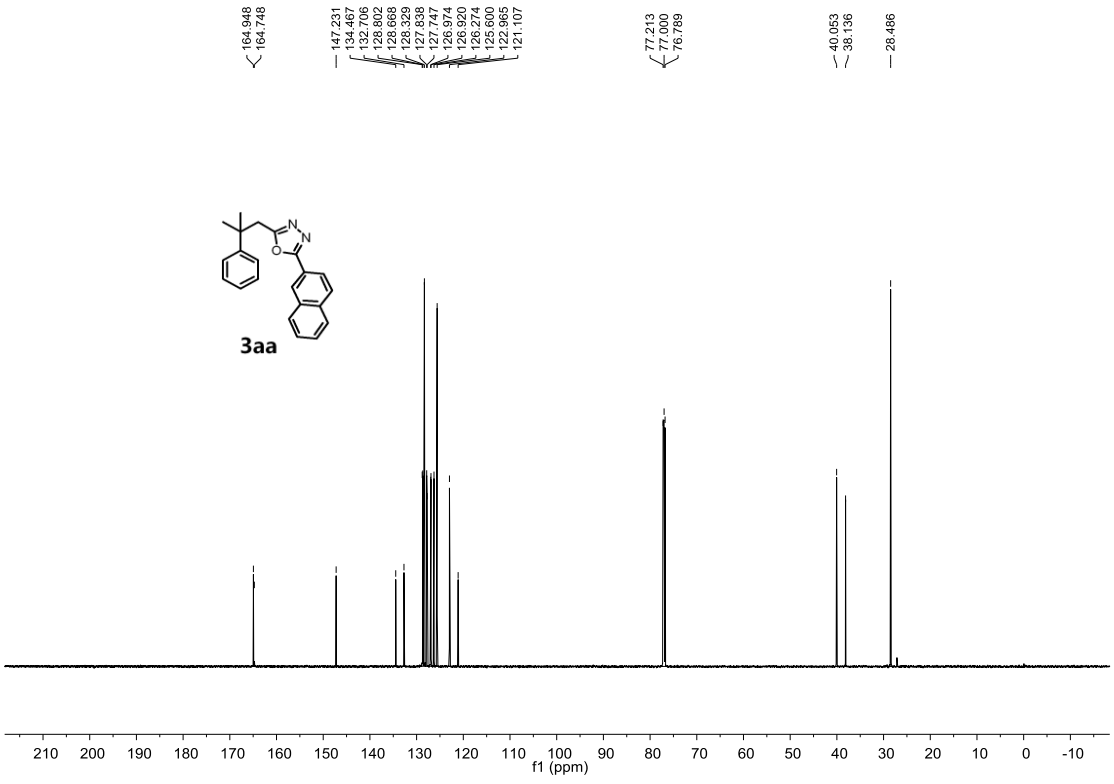
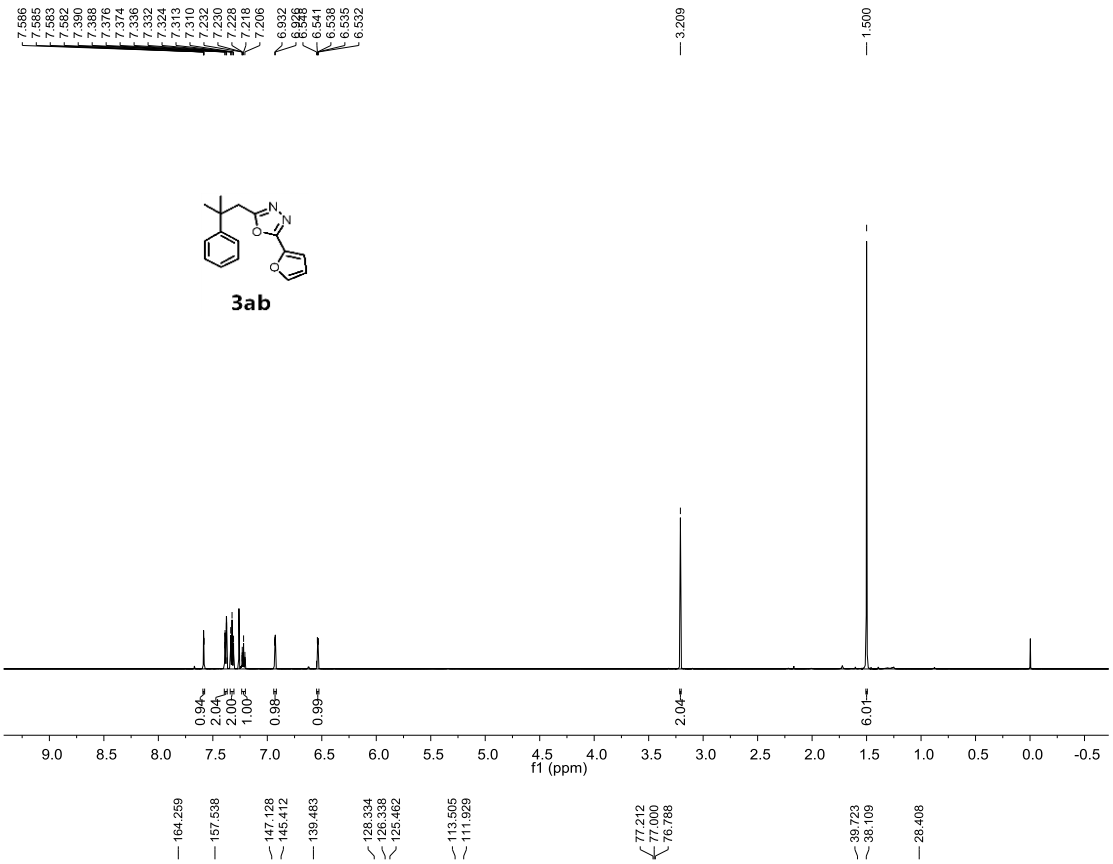
163.463
146.971
133.364
133.147
132.929
132.710
128.362
127.106
126.926
126.394
126.248
125.986
125.936
125.911
125.574
124.442
122.636
120.832
77.212
77.000
76.788
40.075
38.201
28.521
3z
CF3
f1 (ppm)

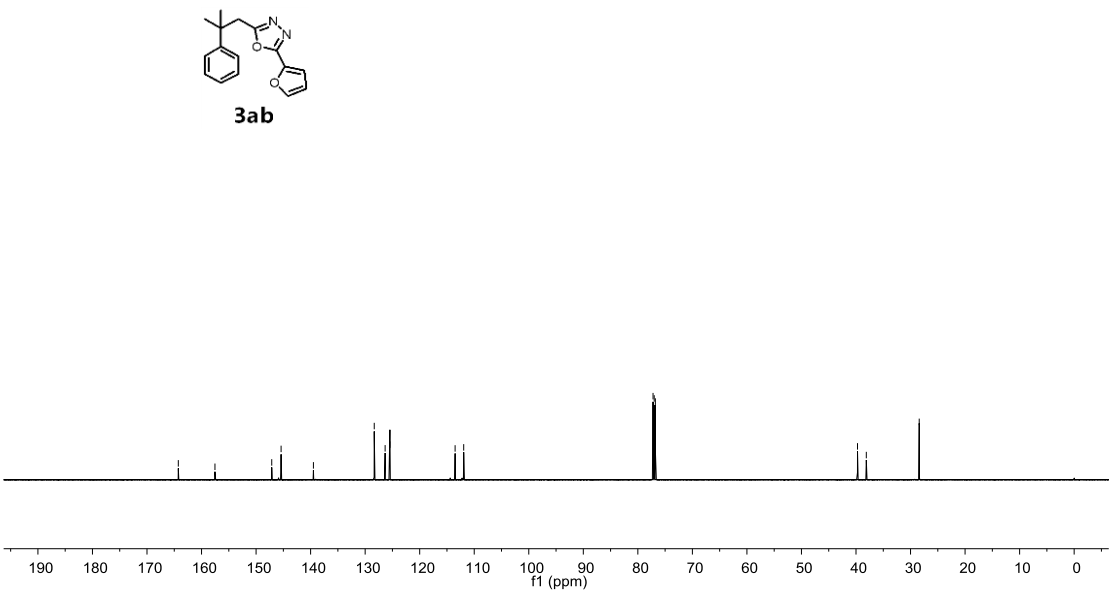

-63.081
3z
CF3
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210


8.203
7.919
7.883
7.560
7.551
7.548
7.545
7.540
7.535
7.532
7.529
7.520
7.517
7.427
7.424
7.413
7.411
7.366
7.353
7.340
7.274
7.272
7.260
7.248
7.243
3.261
1.546
1.533
3aa
1.00
1.00
2.00
1.00
2.07
2.00
2.01
1.02
2.00
6.01
f1 (ppm)

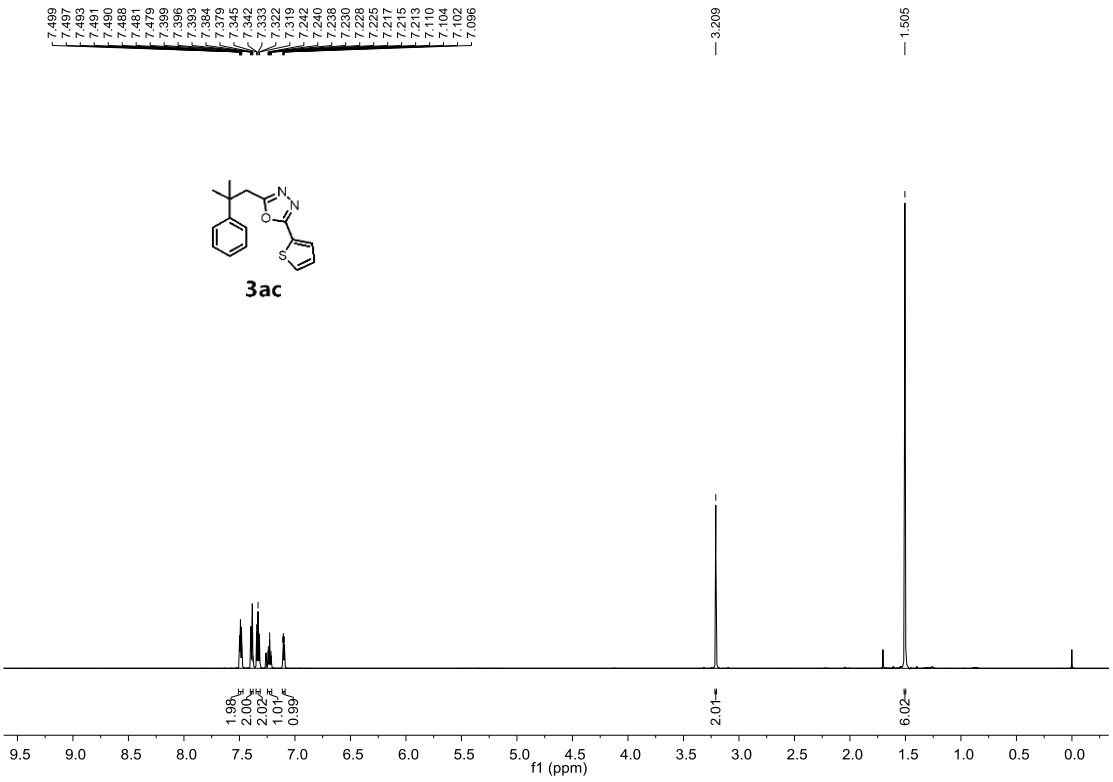

164.948
164.748
147.231
134.467
132.706
128.802
128.668
128.329
127.838
127.747
126.974
126.920
126.274
125.600
122.965
121.107
77.213
77.000
76.789
40.053
38.136
28.486
3aa
f1 (ppm)

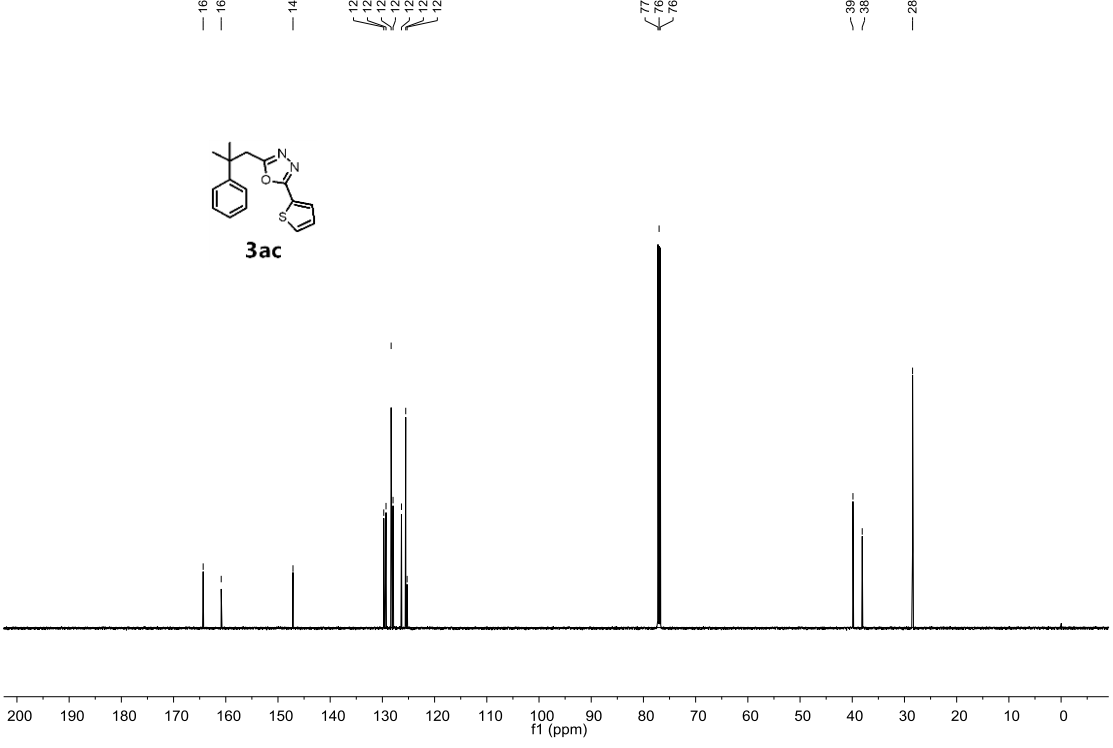

7.586
7.585
7.583
7.582
7.390
7.388
7.376
7.374
7.336
7.332
7.324
7.313
7.310
7.232
7.230
7.228
7.218
7.206
6.932
6.541
6.538
6.535
6.532
3.209
1.500
0.94
2.04
2.00
1.00
0.98
0.99
2.04
6.01
f1 (ppm)

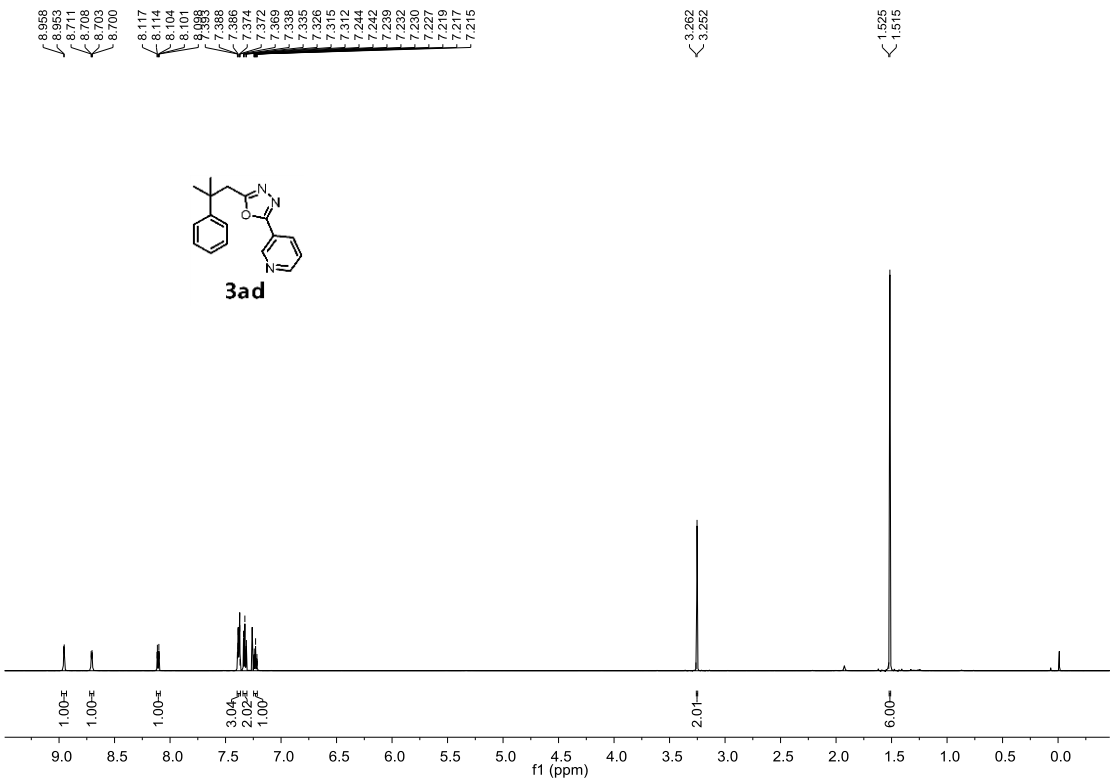
3ab

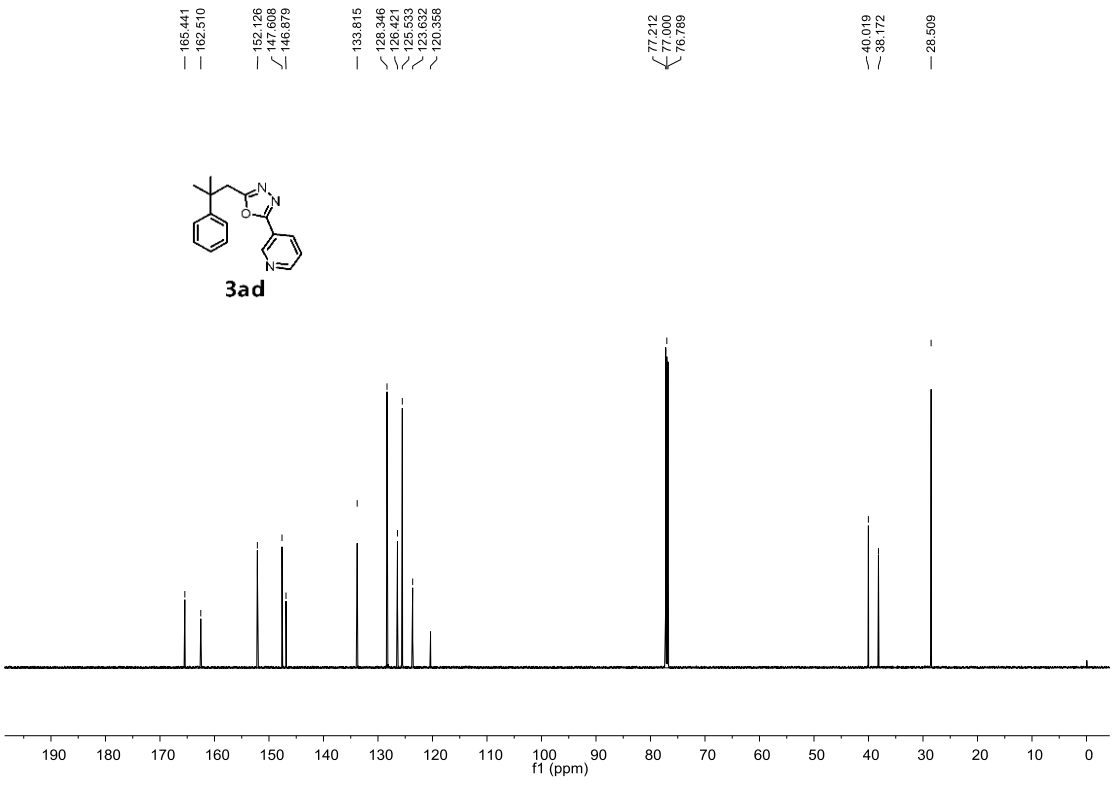

164.259
157.538
147.128
145.412
139.483
128.334
126.338
125.462
113.505
111.929
77.212
77.000
76.788
39.723
38.109
28.408
f1 (ppm)

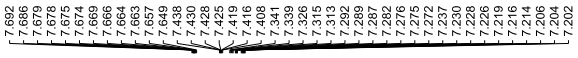
3ab

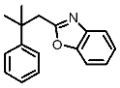

7.499
7.497
7.493
7.491
7.490
7.488
7.481
7.479
7.399
7.396
7.393
7.384
7.379
7.345
7.342
7.333
7.322
7.319
7.242
7.240
7.238
7.230
7.228
7.225
7.217
7.215
7.213
7.110
7.104
7.102
7.096
3.209
1.505
3ac
1.98
2.00
2.02
1.01
0.99
2.01
6.02
f1 (ppm)


164.331
160.873
147.125
129.740
129.306
128.325
127.956
126.345
125.528
125.265
77.212
76.999
76.788
39.868
38.092
28.446
3ac
f1 (ppm)

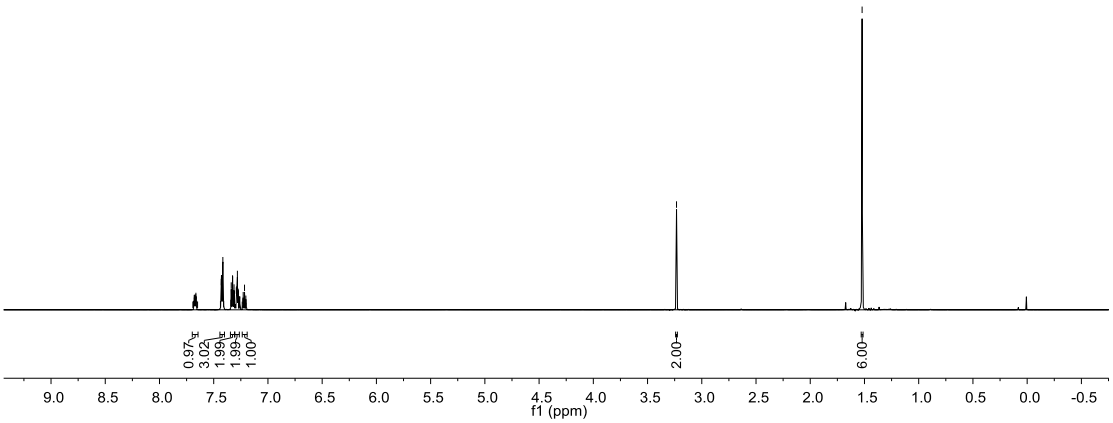

8.958
8.953
8.711
8.708
8.703
8.700
8.117
8.114
8.104
8.101
7.388
7.386
7.374
7.372
7.369
7.338
7.335
7.326
7.315
7.312
7.244
7.242
7.239
7.232
7.230
7.227
7.219
7.217
7.215
3.262
3.252
1.525
1.515
3ad
1.00
1.00
1.00
3.04
2.02
1.00
2.01
6.00
f1 (ppm)


165.441
162.510
152.126
147.608
146.879
133.815
128.346
128.421
125.533
123.632
120.358
77.212
77.000
76.789
40.019
38.172
28.509
3ad
f1 (ppm)

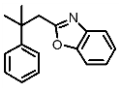

7.692
7.686
7.679
7.678
7.675
7.674
7.669
7.666
7.664
7.663
7.657
7.649
7.438
7.430
7.428
7.425
7.419
7.416
7.408
7.341
7.339
7.326
7.315
7.313
7.292
7.289
7.287
7.282
7.276
7.275
7.272
7.237
7.230
7.228
7.226
7.219
7.216
7.214
7.206
7.204
7.202
3.233
1.522



3ae

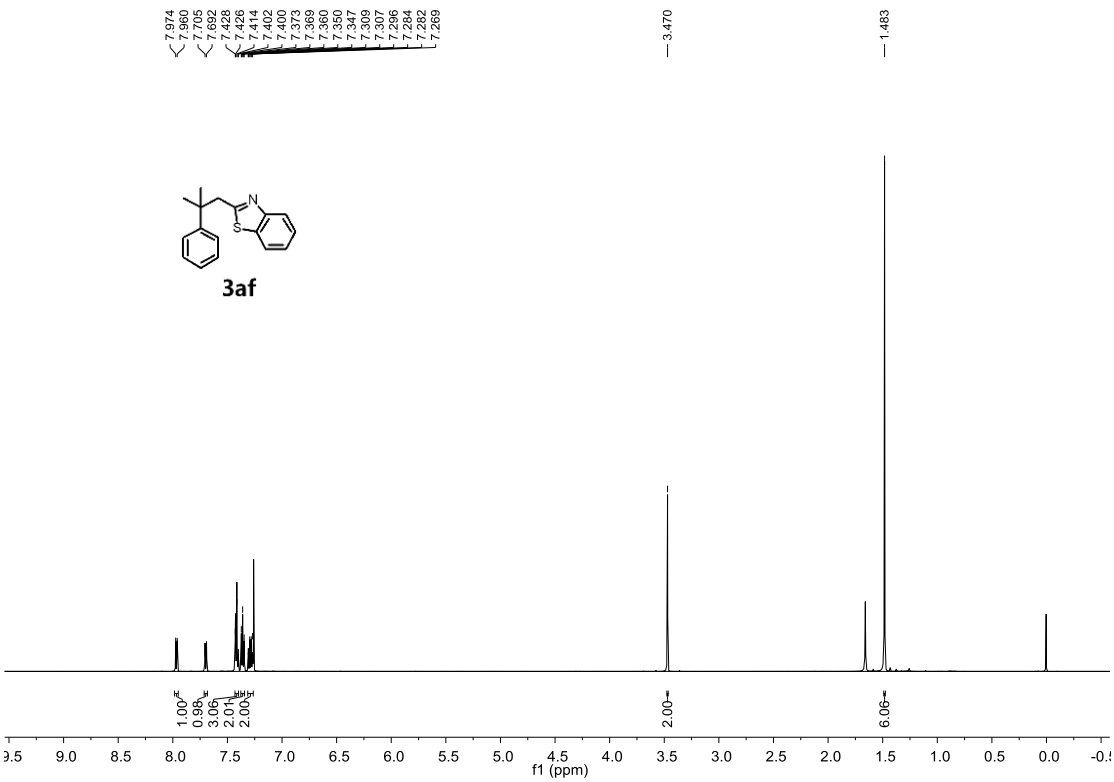

0.97
3.02
1.99
1.99
1.00
2.00
6.00
9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


165.012
150.694
148.069
141.258
128.272
126.141
125.464
124.426
123.986
119.638
110.277
77.211
76.999
76.788
43.084
38.485
28.498

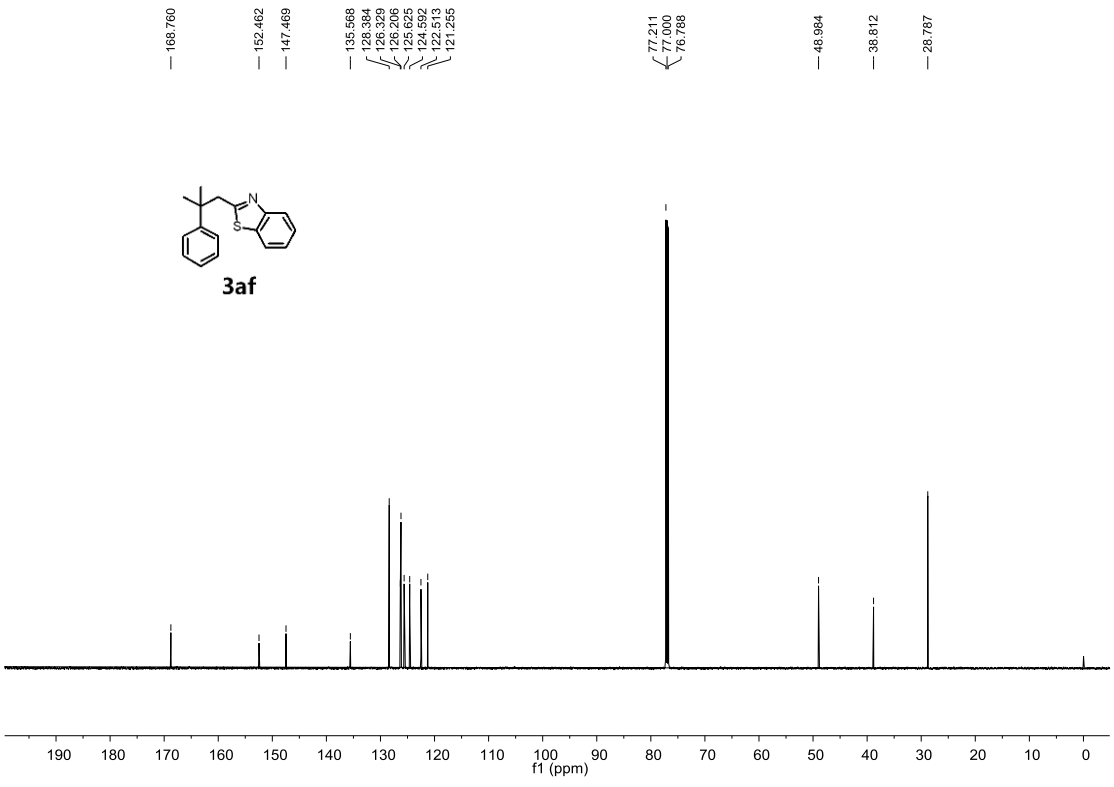


3ae

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


7.974
7.960
7.705
7.692
7.428
7.426
7.414
7.402
7.400
7.373
7.369
7.360
7.350
7.347
7.309
7.307
7.296
7.284
7.282
7.269
3.470
1.483
1.00
0.98
3.06
2.01
2.00
2.00
6.06
f1 (ppm)

3af


168.760
152.462
147.469
135.568
128.384
126.329
126.206
125.625
124.592
122.513
121.255
77.211
77.000
76.788
48.984
38.812
28.787
f1 (ppm)

3af

8.3 NMR Spectra for Kinetic Isotope Effect Studies