Alkynyliodonium Salt Mediated Alkynylation of Azlactones – Fast Access to C^{α}-Tetrasubstituted α-Amino Acid Derivatives

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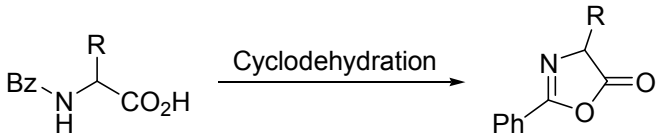
General Information

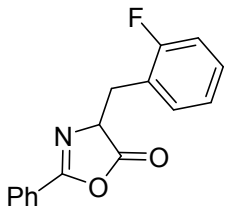
Unless otherwise stated, all reactions were performed using standard Schlenk techniques under a nitrogen atmosphere. Reagents were either used as received from their commercial supplier or purified according to *Purification of Common Laboratory Chemicals*.[1] Dry solvents were obtained from an MBraun SPS-800 solvent purification system and ethyldiisopropylamine was distilled from calcium hydride prior to use. Thin layer chromatography was performed on fluorescence indicator marked precoated silica gel 60 plates (Macherey-Nagel, ALUGRAM Xtra SIL G/UV_{254}) and visualized by UV light (254 nm/366 nm). Flash column chromatography was performed on silica gel (0.040 – 0.063 mm).

NMR spectra were recorded on an *Avance* 400 MHz instrument. Chemical shifts for ^{1}H NMR were reported as δ (parts per million) relative to the residual signals of $CHCl_3$ at 7.26 ppm (s) or DMSO at 2.50 ppm (qui). Chemical shifts for ^{13}C NMR were reported as δ (parts per million) relative to the $CDCl_3$ triplet at 77.0 ppm or the DMSO-D_6 septet at 39.5 ppm. The following abbreviations were used to describe splitting patterns: br = broad, s = singlet, d = doublet, t = triplet, q = quartet, qui = quintet, sept = septet, m = multiplet. Coupling constants *J* are given in Hertz. Mass spectra were recorded on a Finnigan MAT95 using EI or FAB method. High resolution mass spectra were recorded on an APEX II Bruker Daltonics using ESI method.

Alkynyl iodanes **1a-c** and **2a-c** were prepared according to a literature procedure.[2] All azlactones were prepared following literature procedures. Cyclodehydration of the corresponding *N*-benzoylated amino acids was performed using either EDCI (**3c**,[3] **3g**,[4] **3i**,[5] **3p**[3] and **3q**[3]),[3,6] or acetic anhydride (**3a**,[4] **3b**,[7] **3d**,[4] **3e**,[8] **3f**,[5] **3h**,[4] **3j**,[4] **3k**, **3l**, **3m**,[9] **3n,** and **3o**[9]). The spectroscopic data of the obtained compounds were in agreement with the given literature data.

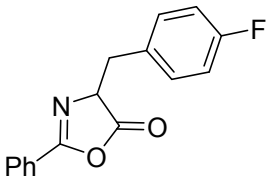


3



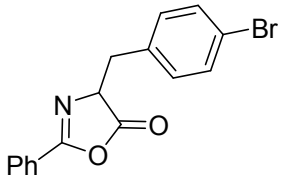
3k

4-(2-Fluorobenzyl)-2-phenyloxazol-5(4*H*)-one (**3k)**, yield: quantitative, colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 7.7 Hz, 2H), 7.61 – 7.53 (m, 1H), 7.52 – 7.43 (m, 2H), 7.36 – 7.28 (m, 1H), 7.26 – 7.20 (m, 1H), 7.13 – 7.00 (m, 2H), 4.77 – 4.66 (m, 1H), 3.41 (dd, *J* = 14.0, 5.6 Hz, 1H), 3.17 (dd, *J* = 14.0, 7.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.3 , 161.9 , 161.2 (d, *J* = 247 Hz), 132.8, 131.6 (d, *J* = 4 Hz), 129.1 (d, *J* = 8 Hz), 128.7 , 127.9 , 125.7 , 124.1 (d, *J* = 4 Hz), 122.7 (d, *J* = 15 Hz), 115.4 (d, *J* = 22 Hz), 65.5 (d, *J* = 1 Hz), 30.8 (d, *J* = 2 Hz). HRMS (ESI) calculated for $C_{16}H_{13}FNO_2$ $[M+H]^+$: m/z 270.092483, found: 270.092464.



3l

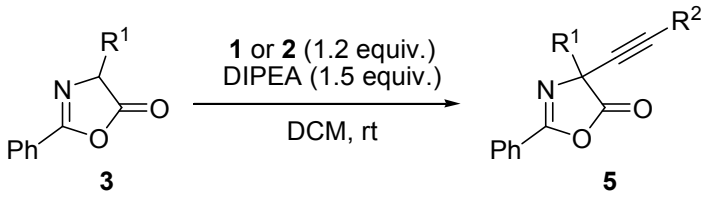
4-(4-Fluorobenzyl)-2-phenyloxazol-5(4*H*)-one (**3l)**, yield: quantitative, colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 – 7.86 (m, 2H), 7.62 – 7.52 (m, 1H), 7.52 – 7.43 (m, 2H), 7.26 – 7.18 (m, 2H), 7.01 – 6.90 (m, 2H), 4.74 – 4.63 (m, 1H), 3.35 (dd, *J* = 14.0, 4.8 Hz, 1H), 3.18 (dd, *J* = 14.0, 6.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.4, 162.0 (d, *J* = 246 Hz), 161.8, 132.8, 131.1 (d, *J* = 8.0 Hz), 130.8 (d, *J* = 3 Hz), 128.7, 127.8, 125.6, 115.2 (d, *J* = 21 Hz), 66.4, 36.4. HRMS (ESI) calculated for $C_{16}H_{13}FNO_2$ $[M+H]^+$: m/z 270.092483, found: 270.092575.



3n

4-(4-Bromobenzyl)-2-phenyloxazol-5(4*H*)-one (**3n**), yield: quantitative, colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 – 7.89 (m, 2H), 7.60 – 7.54 (m, 1H), 7.50 – 7.43 (m, 2H), 7.42 – 7.35 (m, 2H), 7.18 – 7.11 (m, 2H), 4.67 (dd, *J* = 6.6, 4.9 Hz, 1H), 3.34 (dd, *J* = 14.0, 4.9 Hz, 1H), 3.14 (dd, *J* = 14.0, 6.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.2, 161.8, 134.2, 132.8, 131.5, 131.3, 128.7, 127.8, 125.5, 121.3, 66.2, 36.5. HRMS (ESI) calculated for $C_{16}H_{13}BrNO_2$ $[M+H]^+$: m/z 330.012418, found: 330.012309.

General procedure for the electrophilic alkynylation of azlactones

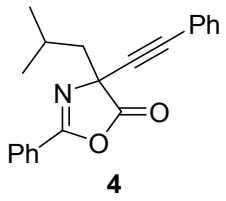


To a solution of azlactone **3a-q** (0.20 mmol, 1.0 equiv.) and ethyldiisopropylamine (0.30 mmol, 51.0 µL, 1.5 equiv.) in 4 mL DCM was added the appropriate alkynyl iodane (0.24 mmol, 1.2 equiv.) at room temperature. After complete conversion of the starting material (typically 30 minutes), the reaction was quenched by the addition of acetic acid. The resulting reaction mixture was directly loaded on silica gel and purified by flash-column chromatography.

Reactivity of azlactone 3a towards different alkynyl iodanes (Table 1)

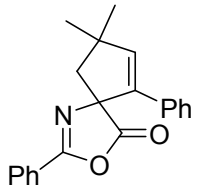
Reaction of **3a** with **1a** following the general procedure afforded 53.6 mg (84%) of **4** after column chromatography (cyclohexane/ethyl acetate 50:1 + 0.05% AcOH).

Reaction of **3a** with **2a** following the general procedure afforded 50.4 mg (79%) of **4** and 5.3 mg (8%) of **8a** after gradient column chromatography (cyclohexane/ethyl acetate 50:1→30:1 + 0.05% AcOH).



4

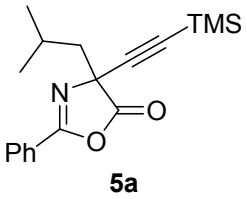
4-Isobutyl-2-phenyl-4-(2-phenylethynyl)oxazol-5(4*H*)-one (**4**), colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 – 8.05 (m, 2H), 7.63 – 7.58 (m, 1H), 7.54 – 7.48 (m, 2H), 7.48 – 7.44 (m, 2H), 7.36 – 7.27 (m, 3H), 2.27 (dd, *J* = 13.7, 5.2 Hz, 1H), 2.13 – 2.02 (m, 1H), 1.95 (dd, *J* = 13.7, 7.2 Hz, 1H), 1.06 (d, *J* = 6.6, 3H), 1.05 (d, *J* = 6.6, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.9, 161.3, 133.1, 131.9, 128.9, 128.8, 128.2, 128.2, 125.5, 121.7, 85.9, 83.3, 66.8, 47.4, 25.2, 23.9, 23.3. HRMS (ESI) calculated for $C_{21}H_{20}NO_2$ $[M+H]^+$: m/z 318.148855, found: 318.149138.



8a

8,8-Dimethyl-2,6-diphenyl-3-oxa-1-azaspiro[4.4]nona-1,6-dien-4-one (**8a**), colorless solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 – 8.01 (m, 2H), 7.61 – 7.55 (m, 1H), 7.52 – 7.45 (m, 2H), 7.24 – 7.15 (m, 5H), 6.26 (s, 1H), 2.43 (d, *J* = 13.4 Hz, 1H), 2.29 (d, *J* = 13.4 Hz, 1H), 1.55 (s, 2H), 1.38 (d, *J* = 2.9 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.0, 160.5, 145.7, 137.7, 134.1, 132.7, 128.8, 128.5, 128.1, 127.9, 126.3, 125.9, 81.5, 51.6, 45.0, 29.1, 29.0. HRMS (ESI) calculated for $C_{21}H_{20}NO_2$ $[M+H]^+$: m/z 318.148855, found: 318.149091.

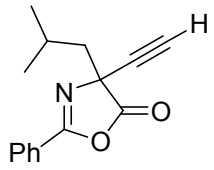
Reaction of **3a** with **1b** following the general procedure afforded 60.0 mg (96%) of **5a** after column chromatography (cyclohexane/ethyl acetate 50:1 + 0.05% AcOH).



5a

4-Isobutyl-4-(2-(trimethylsilyl)ethynyl)-2-phenyloxazol-5(4*H*)-one (**5a**), colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 – 8.00 (m, 2H), 7.62 – 7.55 (m, 1H), 7.53 – 7.46 (m, 2H), 2.15 (dd, *J* = 13.6, 5.1 Hz, 1H), 2.01 – 1.90 (m, 1H), 1.86 (dd, *J* = 13.6, 7.0 Hz, 1H), 1.00 (d, *J* = 6.6 Hz, 3H), 0.98 (d, *J* = 6.6 Hz, 3H), 0.17 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.7, 161.2, 133.0, 128.8, 128.2, 125.6, 98.6, 91.4, 66.9, 47.4, 25.1, 23.9, 23.3, -0.4. HRMS (ESI) calculated for $C_{19}H_{28}NO_3Si$ $[M+MeOH+H]^+$: m/z 346.183297, found: 346.183178.

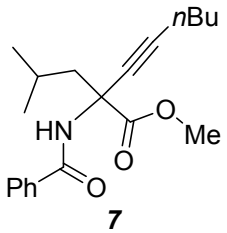
Reaction of **3a** with **2b** following the general procedure afforded 41.0 mg (85%) of **6** after column chromatography (cyclohexane/ethyl acetate 30:1 + 0.05% AcOH).



6

4-Ethynyl-4-isobutyl-2-phenyloxazol-5(4*H*)-one (**6**), colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 – 8.00 (m, 2H), 7.63 – 7.57 (m, 1H), 7.53 – 7.47 (m, 2H), 2.58 (s, 1H), 2.18 (dd, *J* = 13.8, 5.1 Hz, 1H), 2.05 – 1.93 (m, 1H), 1.85 (dd, *J* = 13.8, 7.4 Hz, 1H), 1.01 (d, *J* = 6.6, 3H), 1.00 (d, *J* = 6.6, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.5, 161.5, 133.2, 128.8, 128.2, 125.3, 78.2, 74.4, 66.2, 47.2, 25.1, 23.9, 23.2. HRMS (ESI) calculated for $C_{16}H_{20}NO_3$ $[M+MeOH+H]^+$: m/z 274.143770, found: 274.143722.

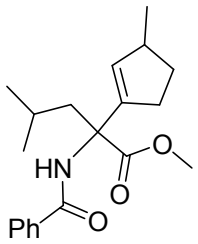
To a solution of **3a** (43.5 mg, 0.20 mmol, 1.0 equiv.) and ethyldiisopropylamine (0.30 mmol, 51.0 µL, 1.5 equiv.) in 4 mL DCM was added alkynyl iodane **1c** (109.5 mg, 0.24 mmol, 1.2 equiv.) at room temperature. After complete conversion of the starting material, a 0.5 M sodium methoxide solution (0.6 mL) was added to the reaction mixture and stirring was continued for further ten minutes. The reaction was quenched by the addition of acetic acid and the crude reaction mixture was loaded on silica gel. Purification by gradient flash-column chromatography (cyclohexane/ethyl acetate 30:1 → 7:1 + 0.05% AcOH) afforded 36.1 mg (55%) of **7** and 13.2 mg of **9a** (20%).



7

Methyl 2-(benzamido)-2-isobutyloct-3-ynoate (**7**), colorless solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 – 7.77 (m, 2H), 7.53 – 7.47 (m, 1H), 7.46 – 7.40 (m, 2H), 6.88 (br s, 1H), 3.82 (s, 3H), 2.37 (dd, *J* = 14.1, 5.8 Hz, 1H), 2.22 (t, *J* = 7.0 Hz, 2H), 2.16 (dd, *J* = 14.1, 6.8 Hz, 1H), 1.88 – 1.77 (m, 1H), 1.53 – 1.44 (m, 2H), 1.43 – 1.33 (m, 2H), 0.97 (d, *J* = 6.7 Hz, 3H), 0.92 (d, *J* = 6.7 Hz, 3H), 0.89 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 165.9, 134.0, 131.7, 128.5, 127.0, 85.3, 77.4, 57.3, 53.3, 44.7, 30.4, 24.9, 23.7, 23.3, 21.9, 18.4, 13.5. HRMS (ESI) calculated for $C_{20}H_{28}NO_3$ $[M+H]^+$: m/z 330.206370, found: 330.206325.

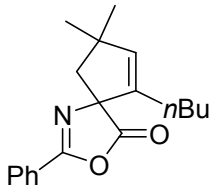
Methyl 2-(benzamido)-4-methyl-2-(3-methylcyclopent-1-enyl)pentanoate (**9a**, diastereomeric mixture), colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.84 – 7.78 (m, 2H), 7.53 – 7.41 (m, 4H), 5.74 – 5.67 (m, 1H), 3.78 (s, 3H), 2.86 – 2.74 (m, 2H), 2.43 – 2.18 (m, 2H), 2.18 – 2.03 (m, 2H), 1.65 – 1.53 (m, 1H), 1.43 – 1.30 (m, 1H), 1.03 – 0.99 (m, 3H), 0.94 – 0.89 (m, 3H), 0.83 – 0.78 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.2, 165.5, 165.5, 141.8, 141.4, 135.0, 135.0, 133.8, 133.6, 131.4, 128.6 (2×), 126.9, 63.9, 63.8, 53.0, 53.0, 40.8, 40.6, 40.0, 40.0, 32.0, 32.0, 31.7, 31.6, 24.7, 24.1, 24.1, 22.5, 22.4, 20.7, 20.6. HRMS (ESI) calculated for $C_{20}H_{27}NO_3Na$ $[M+Na]^+$: m/z 352.188315, found: 352.188143.



9a

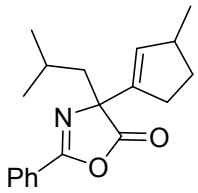
Reaction of **3a** with **2c** following the general procedure afforded 9.9 mg (17%) of **8b** and 41.3 mg (69%) of **9b** after gradient column chromatography (cyclohexane/ethyl acetate 100:1→50:1 + 0.05% AcOH).

6-Butyl-8,8-dimethyl-2-phenyl-3-oxa-1-azaspiro[4.4]nona-1,6-dien-4-one (**8b**), colorless solid: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 – 8.01 (m, 2H), 7.60 – 7.55 (m, 1H), 7.52 – 7.46 (m, 2H), 5.67 (t, *J* = 1.7 Hz, 1H), 2.26 (d, *J* = 13.5 Hz, 1H), 2.14 (d, *J* = 13.5 Hz, 1H), 1.87 – 1.70 (m, 2H), 1.48 – 1.38 (m, 2H), 1.33 – 1.22 (m, 8H), 0.85 (t, *J* = 7.3 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.4, 160.2, 141.7, 138.6, 132.6, 128.7, 128.0, 126.0, 82.4, 49.8, 45.0, 29.4, 29.4, 29.3, 26.5, 22.4, 13.9. HRMS (ESI) calculated for $C_{19}H_{24}NO_2$ $[M+H]^+$: m/z 298.180155, found: 298.180435.



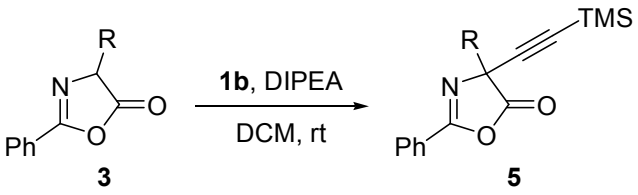
8b

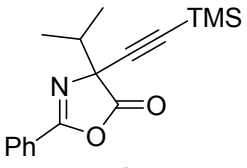
4-Isobutyl-4-(3-methylcyclopent-1-enyl)-2-phenyloxazol-5(4*H*)-one (**9b**, diastereomeric mixture), colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 – 8.01 (m, 2H), 7.61 – 7.54 (m, 1H), 7.53 – 7.46 (m, 2H), 5.70 – 5.66 (m, 1H), 2.81 – 2.68 (m, 1H), 2.64 – 2.29 (m, 2H), 2.18 – 2.04 (m, 2H), 1.93 – 1.85 (m, 1H), 1.75 – 1.65 (m, 1H), 1.47 – 1.33 (m, 1H), 1.03 – 0.97 (m, 3H), 0.95 – 0.91 (m, 3H), 0.90 (d, *J* = 6.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.6, 178.5, 159.7, 139.9, 139.7, 134.0, 133.9, 132.6, 128.8, 127.9, 127.9, 126.1, 73.3, 44.6, 44.6, 39.7, 39.7, 32.1, 32.0, 30.8, 30.7, 24.9, 24.1, 23.1, 23.1, 20.6, 20.6. HRMS (ESI) calculated for $C_{19}H_{24}NO_2$ $[M+H]^+$: m/z 298.180155, found: 298.180189.



9b

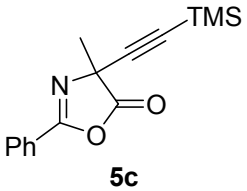
Substrate scope (Scheme 2)





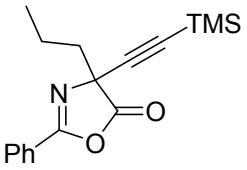
5b

4-Isopropyl-4-(2-(trimethylsilyl)ethynyl)-2-phenyloxazol-5(4*H*)-one (**5b**), yield (cyclohexane/ethylacetate 50:1 + 0.05% AcOH): 53.7 mg (90%), colorless oil**.** ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 – 8.02 (m, 2H), 7.61 – 7.56 (m, 1H), 7.52 – 7.46 (m, 2H), 2.33 (sept, *J* = 6.8 Hz, 1H), 1.20 (d, *J* = 6.8 Hz, 3H), 1.03 (d, *J* = 6.8 Hz, 3H), 0.18 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.9, 161.6, 133.0, 128.8, 128.2, 125.4, 98.1, 91.8, 71.2, 37.3, 17.0, 16.6, -0.3. HRMS (ESI) calculated for $C_{17}H_{21}NO_2SiNa$ $[M+Na]^+$: m/z 322.123377, found: 322.123401.



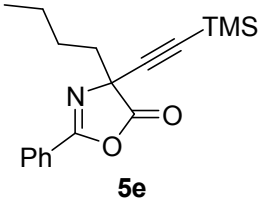
5c

4-Methyl-4-(2-(trimethylsilyl)ethynyl)-2-phenyloxazol-5(4*H*)-one (**5c**), yield (cyclohexane/ethyl acetate 30:1 + 0.05% AcOH): 49.7 mg (92%), colorless solid**.** ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 – 8.00 (m, 2H), 7.62 – 7.56 (m, 1H), 7.52 – 7.46 (m, 2H), 1.79 (s, 3H), 0.18 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.5, 161.5, 133.1, 128.8, 128.2, 125.4, 98.7, 90.9, 63.3, 26.0, -0.4. HRMS (ESI) calculated for $C_{15}H_{18}NO_2Si$ $[M+H]^+$: m/z 272.110132, found: 272.110276.



5d

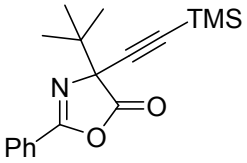
4-(2-(trimethylsilyl)ethynyl)-2-phenyl-4-propyloxazol-5(4*H*)-one (**5d**), yield (cyclohexane/ethyl acetate 50:1 + 0.05% AcOH)**:** 55.4 mg (93%), colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 – 8.01 (m, 2H), 7.62 – 7.56 (m, 1H), 7.52 – 7.46 (m, 2H), 2.16 – 2.06 (m, 1H), 2.04 – 1.95 (m, 1H), 1.62 – 1.48 (m, 1H), 1.48 – 1.35 (m, 1H), 0.95 (t, *J* = 7.4 Hz, 3H), 0.18 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.2, 161.5, 133.1, 128.8, 128.2, 125.4, 98.3, 91.3, 67.2, 41.2, 17.2, 13.7, -0.3. HRMS (ESI) calculated for $C_{17}H_{22}NO_2Si$ $[M+H]^+$: m/z 300.141432, found: 300.141493.



5e

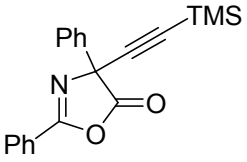
4-Butyl-4-(2-(trimethylsilyl)ethynyl)-2-phenyloxazol-5(4*H*)-one (**5e**), yield (cyclohexane/ethyl acetate 50:1 + 0.05% AcOH)**:** 60.8 mg (97%), colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 – 8.01 (m, 2H), 7.62 – 7.56 (m, 1H), 7.52 – 7.46 (m, 2H), 2.19 – 2.08 (m, 1H), 2.07 – 1.96 (m, 1H), 1.55 – 1.43 (m, 1H), 1.43 – 1.30 (m, 3H), 0.90 (t, *J* = 7.1 Hz, 3H), 0.18 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.2, 161.5, 133.1, 128.8, 128.2, 125.4, 98.4, 91.3, 67.2, 38.9, 25.8, 22.3, 13.7, -0.3. HRMS (ESI) calculated for $C_{18}H_{24}NO_2Si$ $[M+H]^+$: m/z 314.157082, found: 314.156910.

4-*tert*-Butyl-4-(2-(trimethylsilyl)ethynyl)-2-phenyloxazol-5(4*H*)-one (**5f**), yield (cyclohexane/DCM 5:1 + 0.05% AcOH): 37.8 mg (60%), colorless solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 – 8.02 (m, 2H), 7.61 – 7.56 (m, 1H), 7.52 – 7.46 (m, 2H), 1.17 (s, 9H), 0.19 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.4, 161.4, 133.0, 128.7, 128.2, 125.5, 98.0, 91.9, 74.1, 40.0, 24.5, -0.3. HRMS (ESI) calculated for $C_{18}H_{24}NO_2Si$ $[M+H]^+$: m/z 314.157082, found: 314.156844.



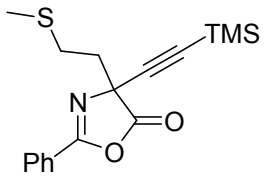
5f

4-(2-(Trimethylsilyl)ethynyl)-2,4-diphenyloxazol-5(4*H*)-one (**5g**), yield (cyclohexane/DCM 5:2 + 0.05% AcOH): 49.8 mg (75%), colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 – 8.12 (m, 2H), 7.67 – 7.60 (m, 3H), 7.57 – 7.51 (m, 2H), 7.44 – 7.36 (m, 3H), 0.23 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.7, 162.6, 135.5, 133.4, 129.2, 128.9, 128.9, 128.5, 126.0, 125.3, 98.1, 92.9, 69.2, -0.4. HRMS (ESI) calculated for $C_{20}H_{20}NO_2Si$ $[M+H]^+$: m/z 334.125782, found: 334.125703.



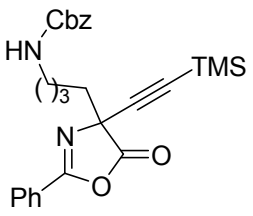
5g

4-(2-(Trimethylsilyl)ethynyl)-4-(2-(methylthio)ethyl)-2-phenyloxazol-5(4*H*)-one (**5h**), yield (cyclohexane/ethyl acetate 50:1 + 0.05% AcOH): 45.9 mg (69%), colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.05 – 8.01 (m, 2H), 7.62 – 7.57 (m, 1H), 7.52 – 7.47 (m, 2H), 2.78 – 2.69 (m, 1H), 2.68 – 2.59 (m, 1H), 2.46 – 2.37 (m, 1H), 2.34 – 2.25 (m, 1H), 2.09 (s, 3H), 0.18 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.7, 162.1, 133.3, 128.8, 128.3, 125.3, 97.5, 92.2, 66.3, 38.3, 28.4, 15.2, -0.4. HRMS (ESI) calculated for $C_{17}H_{21}NO_2SSiNa$ $[M+Na]^+$: m/z 354.095447, found: 354.095288.



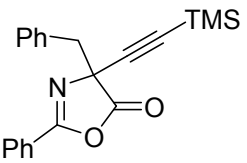
5h

Benzyl 4-(5-oxo-2-phenyl-4-((trimethylsilyl)ethynyl)-4,5-dihydrooxazol-4-yl)butylcarbamate (**5i**), yield (toluene/ethyl acetate 15:1 + 0.05% AcOH): 81.4 mg (88%), colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 – 7.99 (m, 2H), 7.63 – 7.57 (m, 1H), 7.52 – 7.46 (m, 2H), 7.39 – 7.27 (m, 5H), 5.07 (s, 2H), 4.78 (s, 1H), 3.24 – 3.11 (m, 2H), 2.19 – 1.94 (m, 2H), 1.62 – 1.42 (m, 4H), 0.18 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.0, 161.7, 156.3, 136.5, 133.2, 128.8, 128.5, 128.2, 128.1 (2×, shoulder peak), 125.3, 97.9, 91.7, 67.0, 66.6, 40.6, 38.6, 29.4, 21.1, -0.4. HRMS (ESI) calculated for $C_{26}H_{31}N_2O_4Si$ $[M+H]^+$: m/z 463.204760, found: 463.204699.



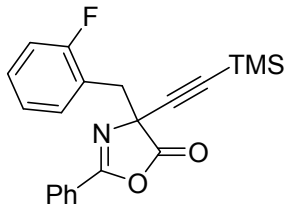
5i

4-Benzyl-4-(2-(trimethylsilyl)ethynyl)-2-phenyloxazol-5(4*H*)-one (**5j**), yield (cyclohexane/ethyl acetate 50:1 + 0.05% AcOH): 65.4 mg (94%), light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 – 7.87 (m, 2H), 7.57 – 7.52 (m, 1H), 7.46 – 7.40 (m, 2H), 7.25 – 7.17 (m, 5H), 3.49 (d, *J* = 13.4 Hz, 1H), 3.40 (d, *J* = 13.4 Hz, 1H), 0.20 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.4, 161.5, 133.0, 132.9, 130.5, 128.7, 128.1, 128.1, 127.6, 125.2, 98.0, 92.2, 68.1, 45.1, -0.4. HRMS (ESI) calculated for $C_{21}H_{21}NO_2SiNa$ $[M+Na]^+$: m/z 370.123377, found: 370.123295.



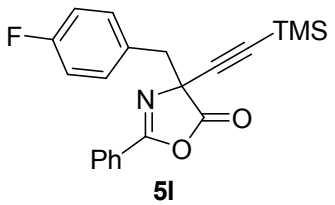
5j

4-(2-Fluorobenzyl)-4-(2-(trimethylsilyl)ethynyl)-2-phenyloxazol-5(4*H*)-one (**5k**), yield (cyclohexane/ethyl acetate 50:1 + 0.05% AcOH): 63.1 mg (86%), light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96 – 7.91 (m, 2H), 7.59 – 7.53 (m, 1H), 7.48 – 7.42 (m, 2H), 7.35 – 7.29 (m, 1H), 7.23 – 7.16 (m, 1H), 7.05 – 6.95 (m, 2H), 3.55 (d, *J* = 13.7 Hz, 1H), 3.39 (d, *J* = 13.7 Hz, 1H), 0.18 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.4 , 161.7 , 161.4 (d, *J* = 248 Hz), 133.1 , 132.5 (d, *J* = 4 Hz), 129.6 (d, *J* = 8 Hz), 128.7 , 128.2 , 125.2 , 123.7 (d, *J* = 4 Hz), 120.4 (d, *J* = 15 Hz), 115.4 (d, *J* = 22 Hz), 97.5 , 92.6 , 67.6 , 37.7 (d, *J* = 2 Hz), -0.4. HRMS (ESI) calculated for $C_{21}H_{21}FNO_2Si$ $[M+H]^+$: m/z 366.132010, found: 366.132114.



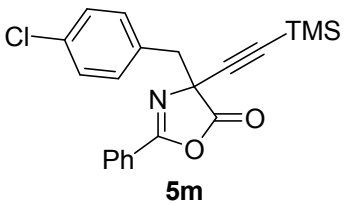
5k

4-(4-Fluorobenzyl)-4-(2-(trimethylsilyl)ethynyl)-2-phenyloxazol-5(4*H*)-one (**5l**), yield (cyclohexane/ethyl acetate 50:1 + 0.05% AcOH): 68.7 mg (94%), light yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 – 7.88 (m, 2H), 7.60 – 7.53 (m, 1H), 7.49 – 7.41 (m, 2H), 7.23 – 7.16 (m, 2H), 6.93 – 6.86 (m, 2H), 3.45 (d, *J* = 13.6 Hz, 1H), 3.36 (d, *J* = 13.6 Hz, 1H), 0.19 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.3, 162.3 (d, *J* = 246 Hz), 161.6, 133.2, 132.2 (d, *J* = 8 Hz), 128.7 (d, *J* = 2 Hz), 128.1, 125.1, 115.1 (d, *J* = 21 Hz), 97.7, 92.5, 68.0 (d, *J* = 2 Hz), 44.2, -0.4. HRMS (ESI) calculated for $C_{21}H_{21}FNO_2Si$ $[M+H]^+$: m/z 366.132010, found: 366.131931.



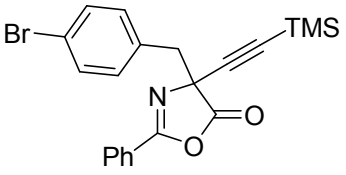
5l

4-(4-Chlorobenzyl)-4-(2-(trimethylsilyl)ethynyl)-2-phenyloxazol-5(4*H*)-one (**5m**), yield (cyclohexane/ethyl acetate 50:1 + 0.05% AcOH): 69.0 mg (90%), light yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 – 7.89 (m, 2H), 7.60 – 7.54 (m, 1H), 7.48 – 7.42 (m, 2H), 7.21 – 7.13 (m, 4H), 3.44 (d, *J* = 13.5 Hz, 1H), 3.34 (d, *J* = 13.5 Hz, 1H), 0.19 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.2, 161.7, 133.7, 133.2, 131.9, 131.5, 128.8, 128.3, 128.1, 125.0, 97.6, 92.6, 67.9, 44.2, -0.4. HRMS (ESI) calculated for $C_{21}H_{21}ClNO_2Si$ $[M+H]^+$: m/z 382.102460, found: 382.102460.



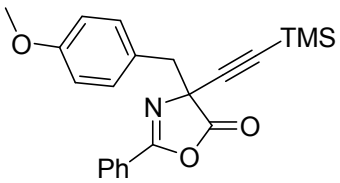
5m

4-(4-Bromobenzyl)-4-(2-(trimethylsilyl)ethynyl)-2-phenyloxazol-5(4*H*)-one (**5n**, yield (cyclohexane/ethyl acetate 50:1 + 0.05% AcOH): 71.1 mg (83%), light yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 – 7.89 (m, 2H), 7.60 – 7.54 (m, 1H), 7.48 – 7.43 (m, 2H), 7.36 – 7.31 (m, 2H), 7.13 – 7.08 (m, 2H), 3.42 (d, *J* = 13.5 Hz, 1H), 3.32 (d, *J* = 13.5 Hz, 1H), 0.19 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.2, 161.7, 133.2, 132.2, 132.0, 131.3, 128.8, 128.1, 125.0, 121.9, 97.6, 92.6, 67.8, 44.3, -0.4. HRMS (ESI) calculated for $C_{21}H_{21}BrNO_2Si$ $[M+H]^+$: m/z 427.051945, found: 427.051662.



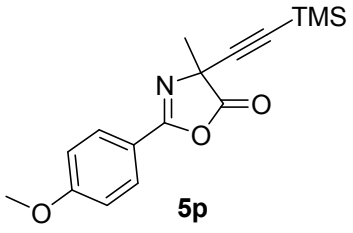
5n

4-(4-Methoxybenzyl)-4-(2-(trimethylsilyl)ethynyl)-2-phenyloxazol-5(4*H*)-one (**5o**), yield (cyclohexane/ethyl acetate 30:1 + 0.05% AcOH): 68.9 mg (91%), yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 – 7.87 (m, 2H), 7.57 – 7.52 (m, 1H), 7.46 – 7.40 (m, 2H), 7.15 – 7.10 (m, 2H), 6.75 – 6.70 (m, 2H), 3.70 (s, 3H), 3.44 (d, *J* = 13.6 Hz, 1H), 3.35 (d, *J* = 13.6 Hz, 1H), 0.20 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.5, 161.5, 159.0, 133.0, 131.6, 128.7, 128.1, 125.2, 124.9, 113.5, 98.1, 92.1, 68.3, 55.1, 44.4, -0.4. HRMS (ESI) calculated for $C_{22}H_{24}NO_3Si$ $[M+H]^+$: m/z 378.151997, found: 378.151934.



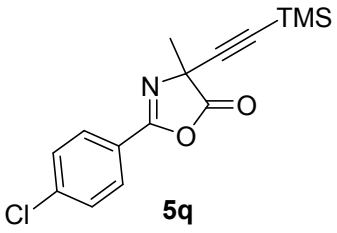
5o

2-(4-Methoxyphenyl)-4-methyl-4-(2-(trimethylsilyl)ethynyl)oxazol-5(4*H*)-one (**5p**), yield (cyclohexane/ethyl acetate 15:1 + 0.05% AcOH): 49.0 mg (81%), white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.99 – 7.93 (m, 2H), 7.01 – 6.95 (m, 2H), 3.87 (s, 3H), 1.77 (s, 3H), 0.17 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.7, 163.5, 161.2, 130.1, 117.6, 114.2, 99.1, 90.6, 63.2, 55.5, 26.1, -0.4. HRMS (ESI) calculated for $C_{16}H_{20}NO_3Si$ $[M+H]^+$: m/z 302.120696, found: 302.120504.



5p

2-(4-Chlorophenyl)-4-methyl-4-(2-(trimethylsilyl)ethynyl)oxazol-5(4*H*)-one (**5q**), yield (cyclohexane/ethyl acetate 30:1 + 0.05% AcOH): 47.7 mg (78%), white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 – 7.94 (m, 2H), 7.49 – 7.45 (m, 2H), 1.78 (s, 3H), 0.18 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.2, 160.7, 139.6, 129.5, 129.2, 123.9, 98.5, 91.1, 63.3, 26.0, -0.4. HRMS (ESI) calculated for $C_{15}H_{17}ClNO_2Si$ $[M+H]^+$: m/z 306.071159, found: 306.071099.



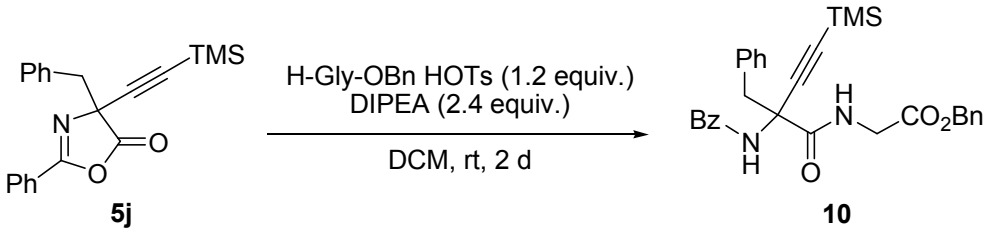
5q

Functionalizations (Scheme 3 and Scheme 4)

Large scale reaction

The reaction of **3j** (653.3 mg, 2.60 mmol, 1.0 equiv.), **1b** (3.12 mmol, 1.473 g, 1.2 equiv.) and ethyldiisopropylamine (3.9 mmol, 0.64 mL, 1.5 equiv.) in 52 mL of DCM was performed following the general procedure. Column chromatography on silica gel (cyclohexane/ethyl acetate 50:1 + 0.05% AcOH) afforded 860.4 mg (95%) of the corresponding product **5j**.

Peptide formation

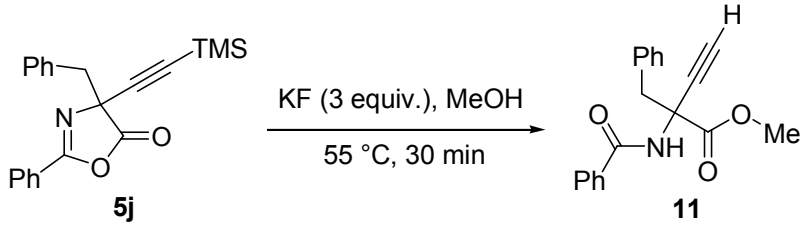


5j **10**

5j (69.5 mg, 0.20 mmol, 1.0 equiv.), H-Gly-OBn *p*-tosylate (81.0 mg, 0.24 mmol, 1.2 equiv.) and ethyldiisopropylamine (79.1 µL, 0.48 mmol, 2.4 equiv.) were dissolved in DMF (2 mL) and stirred at room temperature for two days. The solution was treated with a diluted solution of $NaHCO_3$ and extracted with EtOAc (3×). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and concentrated. The residue was purified by column chromatography (cyclohexane/ethyl acetate 4:1 + 0.5% AcOH) affording 92.0 mg (90%) of **10** as a colorless solid.

Benzyl *N*-benzoyl-α-(2-trimethylsilylethynyl)-phenylalanyl-glycinate (**10**): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93 – 7.85 (m, 2H), 7.67 – 7.61 (m, 1H), 7.58 – 7.39 (m, 13H), 7.05 (br s, 1H), 5.41 – 5.29 (m, 2H), 4.33 – 4.16 (m, 2H), 3.68 (d, *J* = 13.0 Hz, 1H), 3.54 (d, *J* = 13.0 Hz, 1H), 0.38 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.8, 168.6, 165.8, 135.0, 134.3, 133.8, 131.7, 130.4, 128.6, 128.5, 128.4, 128.3, 128.1, 127.6, 127.1, 101.8, 93.9, 67.1, 58.9, 44.1, 42.0, -0.4. HRMS (ESI) calculated for $C_{30}H_{32}N_2O_4SiNa$ $[M+Na]^+$: m/z 535.202355, found: 535.201862.

Methanolysis and removal of the TMS-group

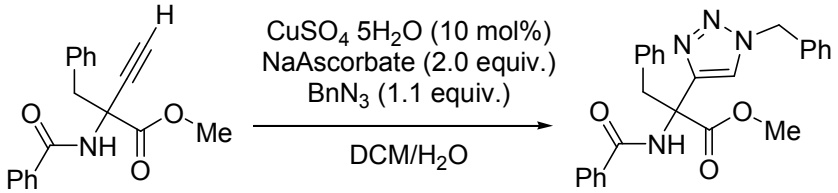


5j **11**

A solution of **5j** (694.3 mg, 2.00 mmol, 1.0 equiv.) and potassium fluoride (348.6 mg, 6.00 mmol, 3.0 equiv.) in 20 mL MeOH was heated to reflux for 30 minutes. The solvent was evaporated and the crude was loaded on silica gel. Flash-column chromatography (cyclohexane/ethyl acetate 3:1) afforded 603.2 mg (98%) of **11** as a colorless solid.

Methyl 2-(benzamido)-2-benzylbut-3-ynoate (**11**): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 – 7.69 (m, 2H), 7.54 – 7.49 (m, 1H), 7.45 – 7.40 (m, 2H), 7.29 – 7.26 (m, 3H), 7.21 – 7.17 (m, 2H), 6.78 (br s, 1H), 3.89 (s, 3H), 3.81 (d, *J* = 13.5 Hz, 1H), 3.57 (d, *J* = 13.5 Hz, 1H), 2.60 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.4, 166.3, 134.4, 133.7, 132.0, 130.3, 128.6, 128.4, 127.6, 127.1, 80.2, 73.7, 57.9, 53.7, 41.9. HRMS (ESI) calculated for $C_{19}H_{18}NO_3$ $[M+H]^+$: m/z 308.128120, found: 308.128139.

Click reaction

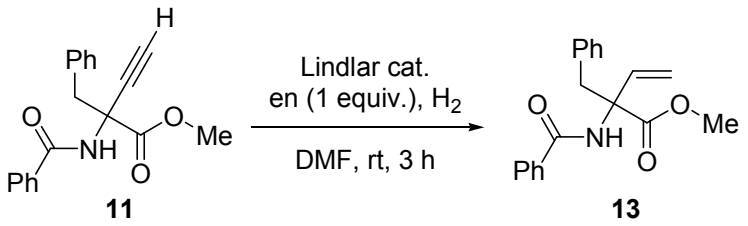


11 **12**

The reaction was performed following an adopted literature procedure using compound **11** (61.5 mg, 0.20 mmol) in 0.7 mL of DCM and 0.5 mL of H_2O.[10] Flash-column chromatography (cyclohexane/ethyl acetate 2:1) of the crude product afforded 83.5 mg (95%) of **12** as a colorless solid.

Methyl 2-(benzamido)-2-(1-benzyl-1*H*-1,2,3-triazol-4-yl)-3-phenylpropano-ate (**12**): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 – 7.73 (m, 3H), 7.67 (s, 1H), 7.53 – 7.47 (m, 1H), 7.45 – 7.36 (m, 5H), 7.27 – 7.24 (m, 2H), 7.19 – 7.07 (m, 3H), 6.90 – 6.84 (m, 2H), 5.58 (d, *J* = 14.9 Hz, 1H), 5.48 (d, *J* = 14.9 Hz, 1H), 3.89 (s, 2H), 3.77 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 166.5, 146.4, 134.9, 134.4, 134.1, 131.7, 130.1, 129.1, 128.7, 128.5, 128.0, 127.9, 127.0 (2×, shoulder peak), 122.2, 62.0, 54.3, 53.1, 40.5. HRMS (ESI) calculated for $C_{26}H_{25}N_4O_3$ $[M+H]^+$: m/z 441.192117, found: 441.192223.

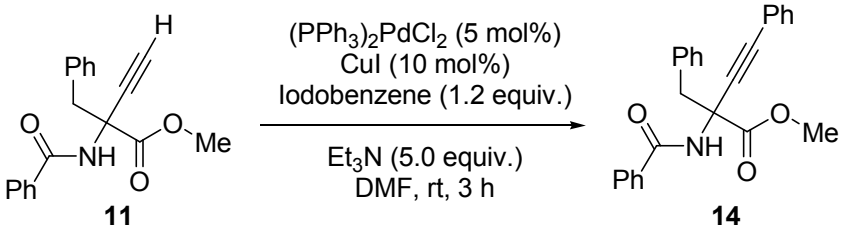
Reduction



The reaction was performed with compound **11** (61.5 mg, 0.20 mmol) in 2 mL of DMF following an adopted literature procedure.[11] Flash-column chromatography (cyclohexane/ethyl acetate 5:1) of the crude product afforded 52.7 mg (85%) of **13** as a colorless solid.

Methyl 2-(benzamido)-2-benzylbut-3-enoate (**13**): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 – 7.69 (m, 2H), 7.53 – 7.48 (m, 1H), 7.45 – 7.39 (m, 2H), 7.25 – 7.19 (m, 3H), 7.12 – 7.06 (m, 2H), 7.02 (s, 1H), 6.20 (dd, *J* = 17.3, 10.6 Hz, 1H), 5.35 (d, *J* = 10.6 Hz, 1H), 5.32 (d, *J* = 17.3 Hz, 1H), 3.92 (d, *J* = 13.5 Hz, 1H), 3.83 (s, 3H), 3.44 (d, *J* = 13.5 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.2, 166.3, 136.2, 135.7, 134.7, 131.6, 129.9, 128.6, 128.3, 127.1, 126.9, 116.3, 65.8, 53.0, 40.0. HRMS (ESI) calculated for $C_{19}H_{19}NO_3Na$ $[M+Na]^+$: m/z 332.125715, found: 332.125522.

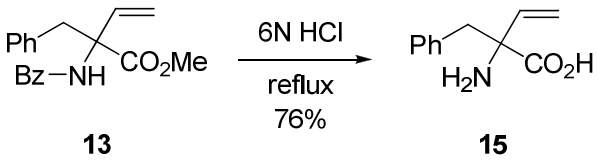
Sonogashira Coupling



The reaction was performed with compound **11** (61.5 mg, 0.20 mmol) in 3 mL of DMF following an adopted literature procedure.[12] Flash-column chromatography (toluene/ethyl acetate 40:1 + 0.05% AcOH) of the crude product afforded 63.2 mg (82%) of **14** as a colorless solid.

Methyl 2-(benzamido)-2-benzyl-4-phenylbut-3-ynoate (**14**): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 – 7.68 (m, 2H), 7.51 – 7.36 (m, 5H), 7.33 – 7.21 (m, 8H), 6.75 (br s, 1H), 3.87 (s, 3H), 3.79 – 3.69 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.5, 166.3, 135.1, 133.7, 131.9, 131.8, 130.5, 128.8, 128.5, 128.2, 128.1, 127.3, 127.0, 121.8, 85.8, 85.5, 58.7, 53.5, 41.6. HRMS (ESI) calculated for $C_{25}H_{21}NO_3Na$ $[M+Na]^+$: m/z 406.141365, found: 406.141037.

Deprotection of 13



13 **15**

Compound **13** (30 mg, 0.097 mmol) was dissolved in 6 N HCl (1 mL) and refluxed for 4 h until the TLC showed full conversion of the starting material. After extraction with $CHCl_3$ (5 mL) the aqueous layer was lyophilized. The residue was applied to an Amberlyst 15(H) cation exchange column. The column was consecutively washed with pure water, water-THF (1:1) and pure water again. Final elution with pyridine-water (1:9) afforded α-vinyl phenylalanine **15** as a white solid (14.2 mg, 76%).

2-Amino-2-benzylbut-3-enoic acid (**15**): ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.57 (br s, 2H), 7.30 – 7.17 (m, 5H), 6.09 (dd, *J* = 17.8, 11.2 Hz, 1H), 5.08 (d, *J* = 17.8 Hz, 1H), 5.06 (d, *J* = 11.2 Hz, 1H), 3.12 (d, *J* = 13.7 Hz, 1H), 2.95 (d, *J* = 13.7 Hz, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) δ 168.5, 138.8, 135.7, 130.7, 127.9, 126.5, 112.9, 65.5, 42.2. HRMS (ESI) calculated for $C_{11}H_{14}NO_2$ $[M+H]^+$: m/z 192.101905, found: 192.101828. The spectroscopic data was in accordance with the literature.[13]

Literature

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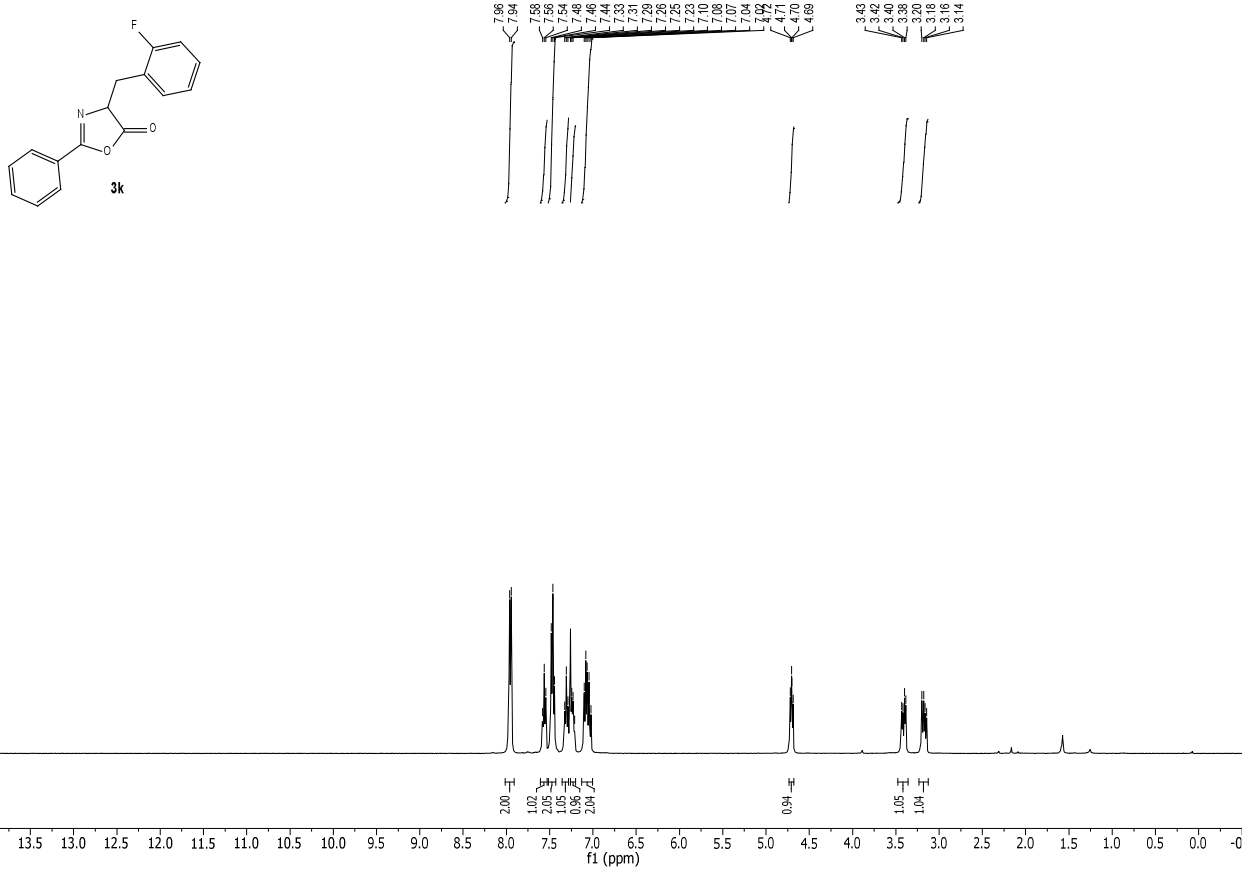
^{1}H and ^{13}C Spectra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O
O
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7.94
7.58
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7.48
7.46
7.44
7.33
7.31
7.29
7.26
7.25
7.23
7.10
7.08
7.07
7.04
7.02
4.72
4.71
4.70
4.69
3.43
3.42
3.40
3.38
3.20
3.18
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1.05
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2.04
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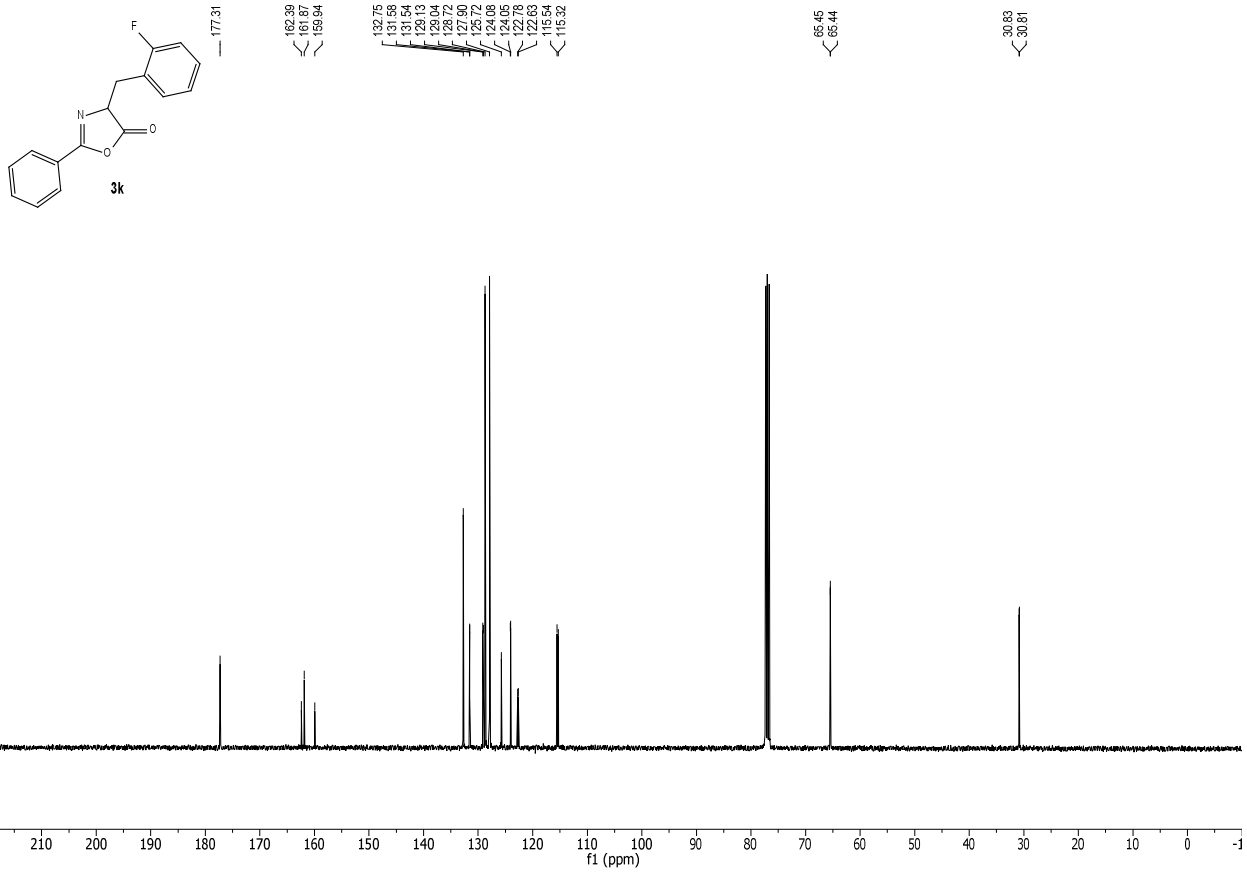
1.05
1.04
f1 (ppm)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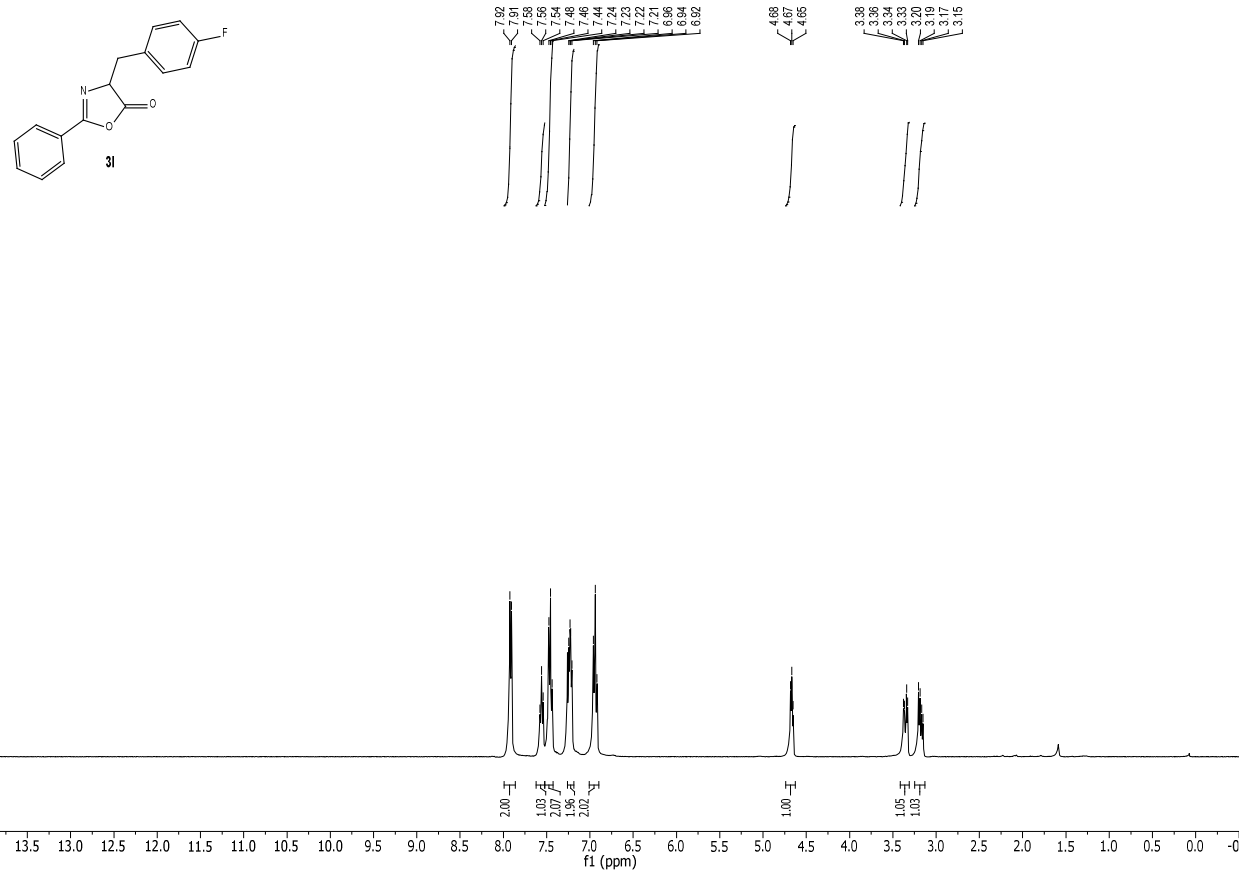
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7.23
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7.21
6.96
6.94
6.92
4.68
4.67
4.65
3.38
3.36
3.34
3.33
3.20
3.19
3.17
3.15
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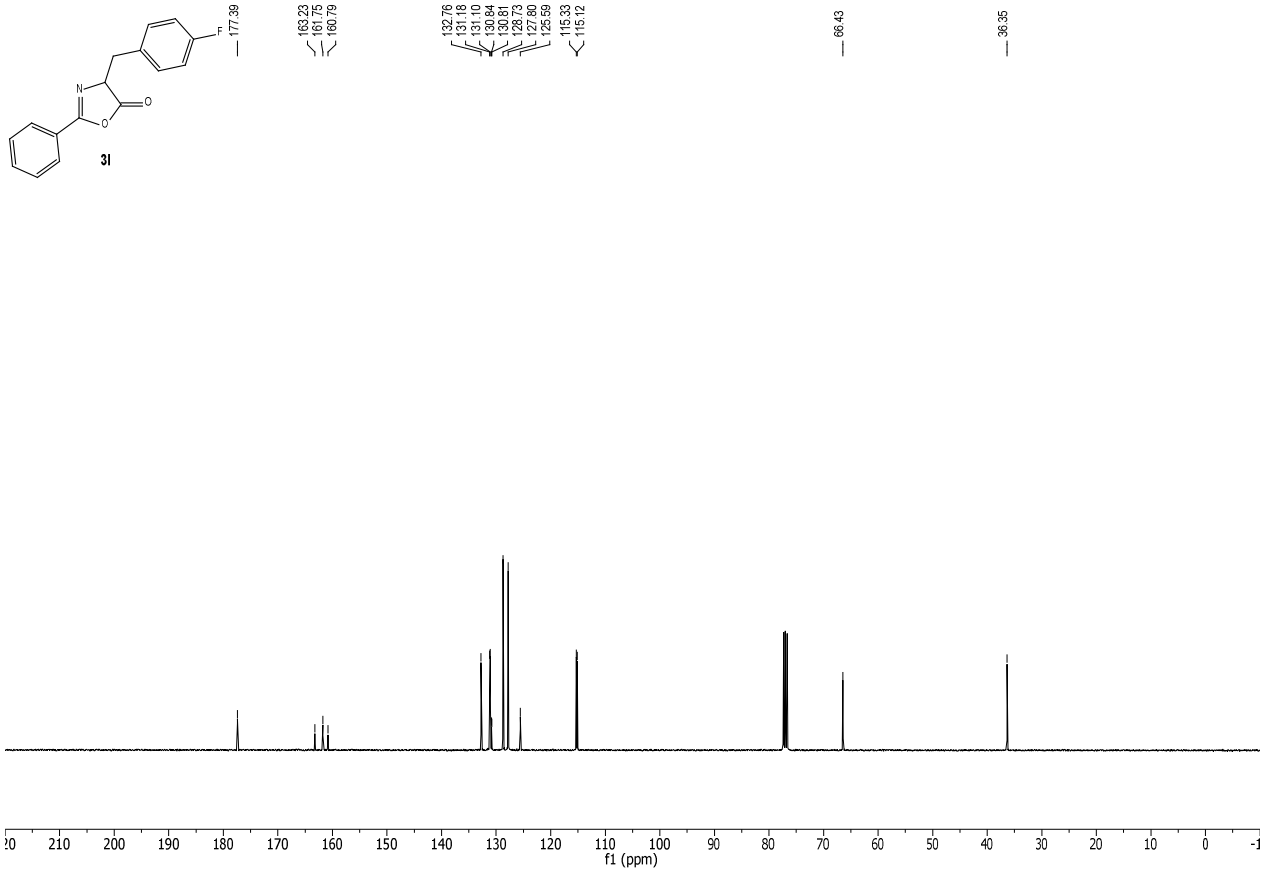
2.07
1.96
2.02
1.00
1.05
1.03
f1 (ppm)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115.12
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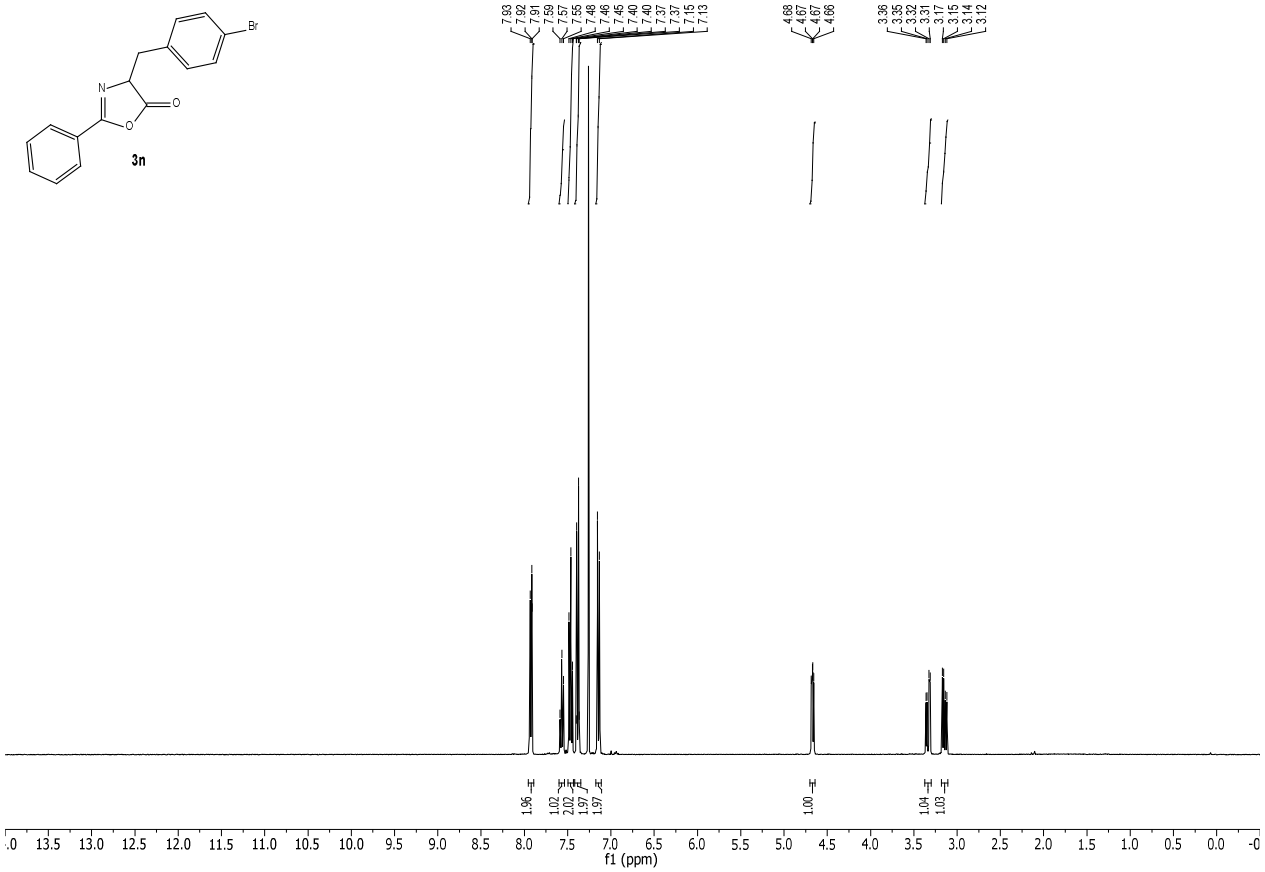
36.35
f1 (ppm)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7.37
7.15
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4.67
4.66
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3.32
3.31
3.17
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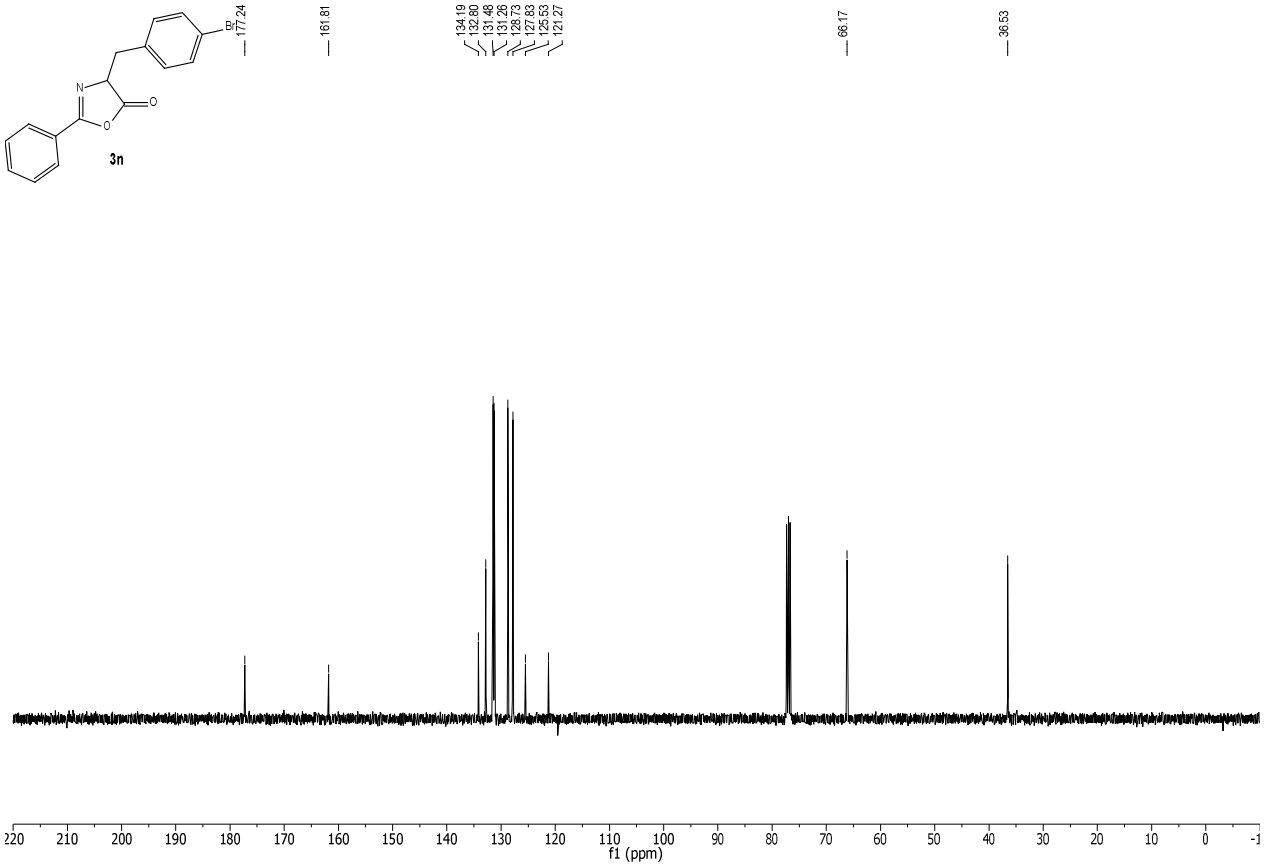
1.03
f1 (ppm)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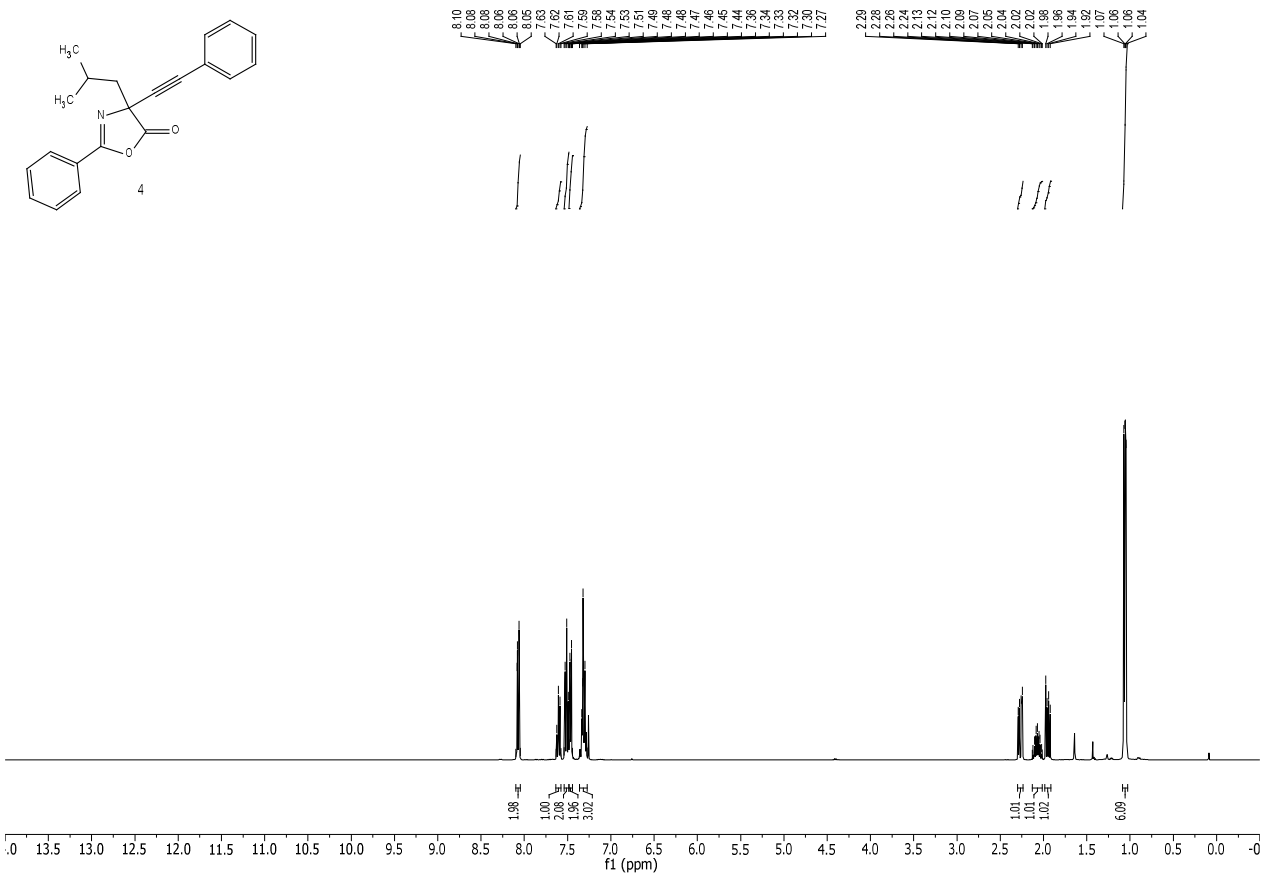
f1 (ppm)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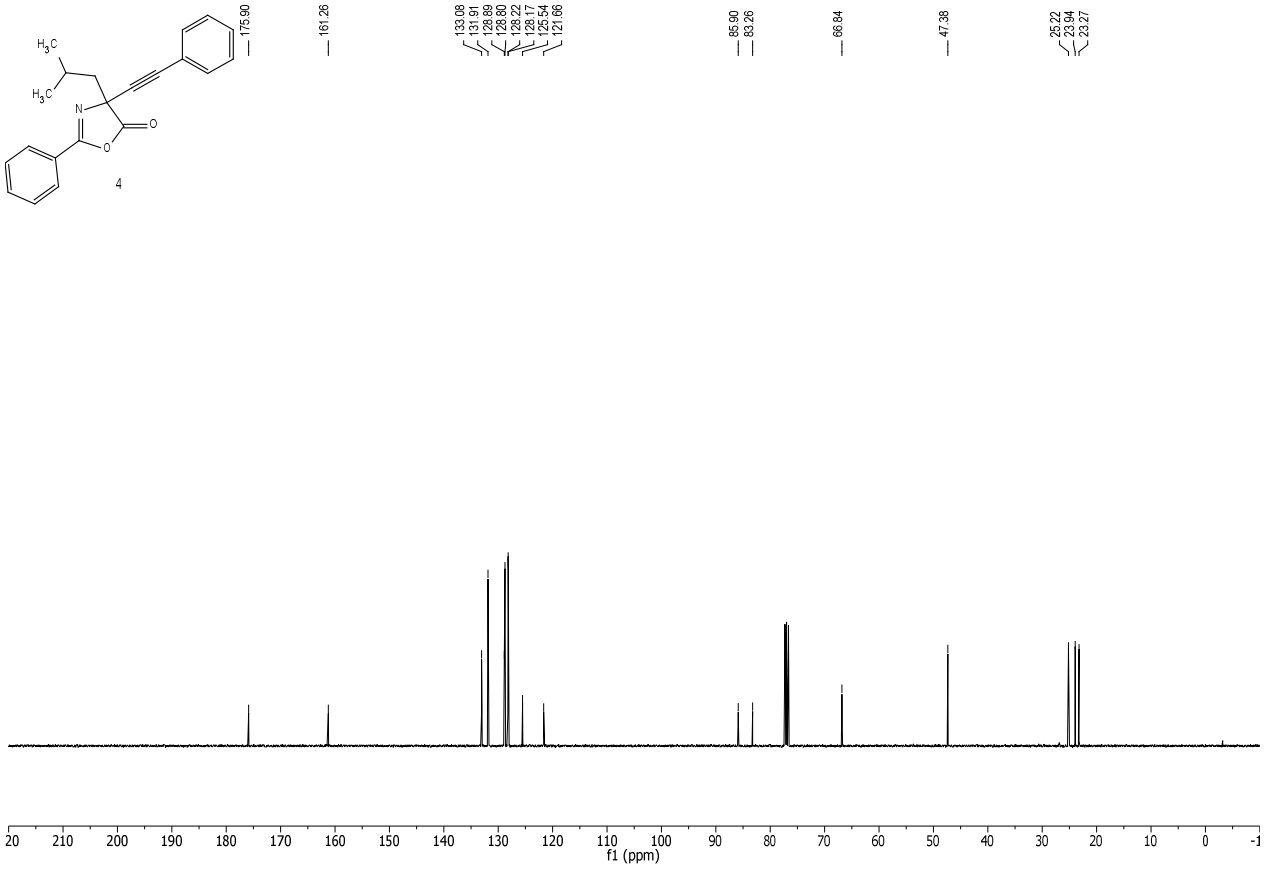
2.29 2.28 2.26 2.24 2.13 2.12 2.10 2.09 2.07 2.05 2.04 2.02 2.02 1.98 1.96 1.94 1.92 1.07 1.06 1.06 1.04
1.98 1.00 2.08 1.96 3.02 1.01 1.01 1.02 6.09
f1 (ppm)


4
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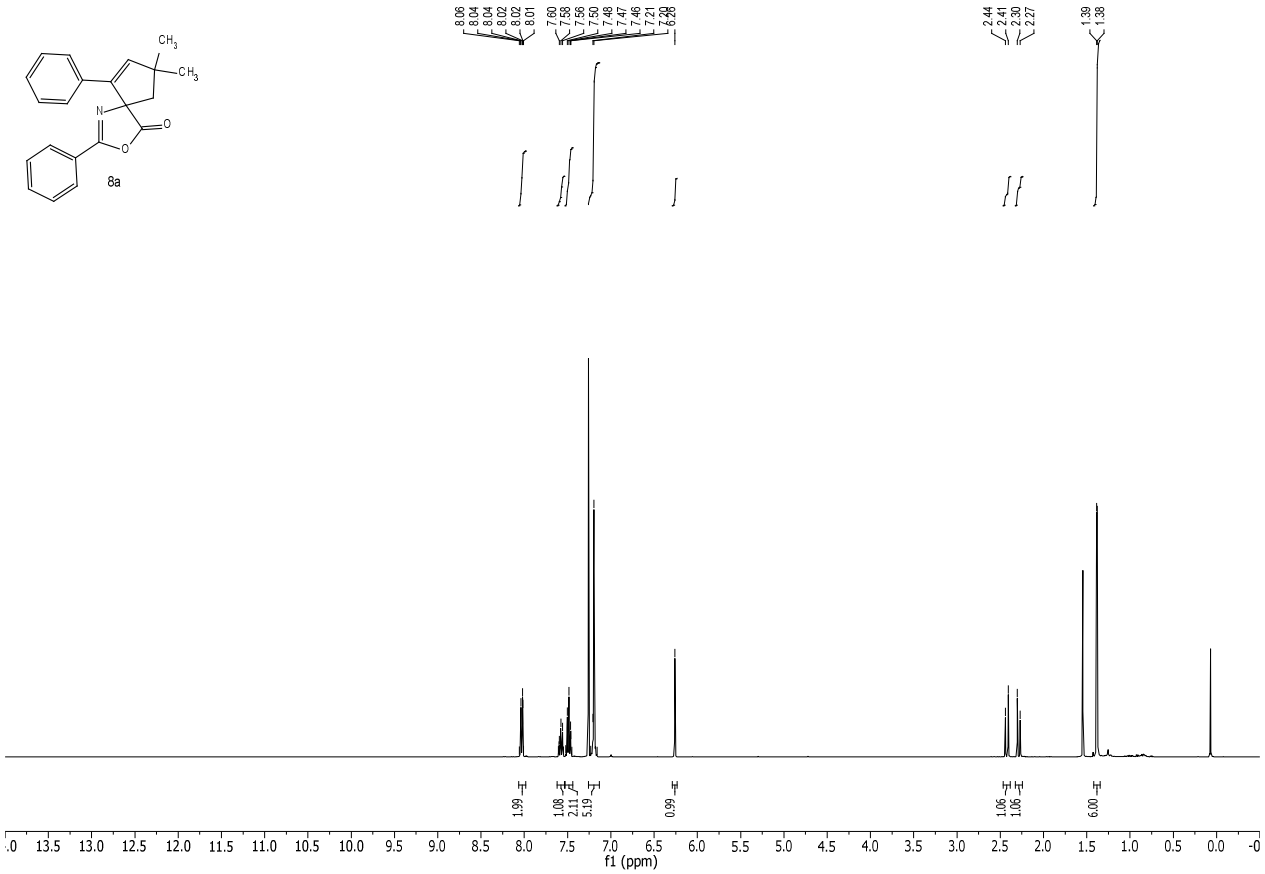
f1 (ppm)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8.02
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7.56
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7.47
7.46
7.21
7.20
6.26
2.44
2.41
2.30
2.27
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1.08
2.11
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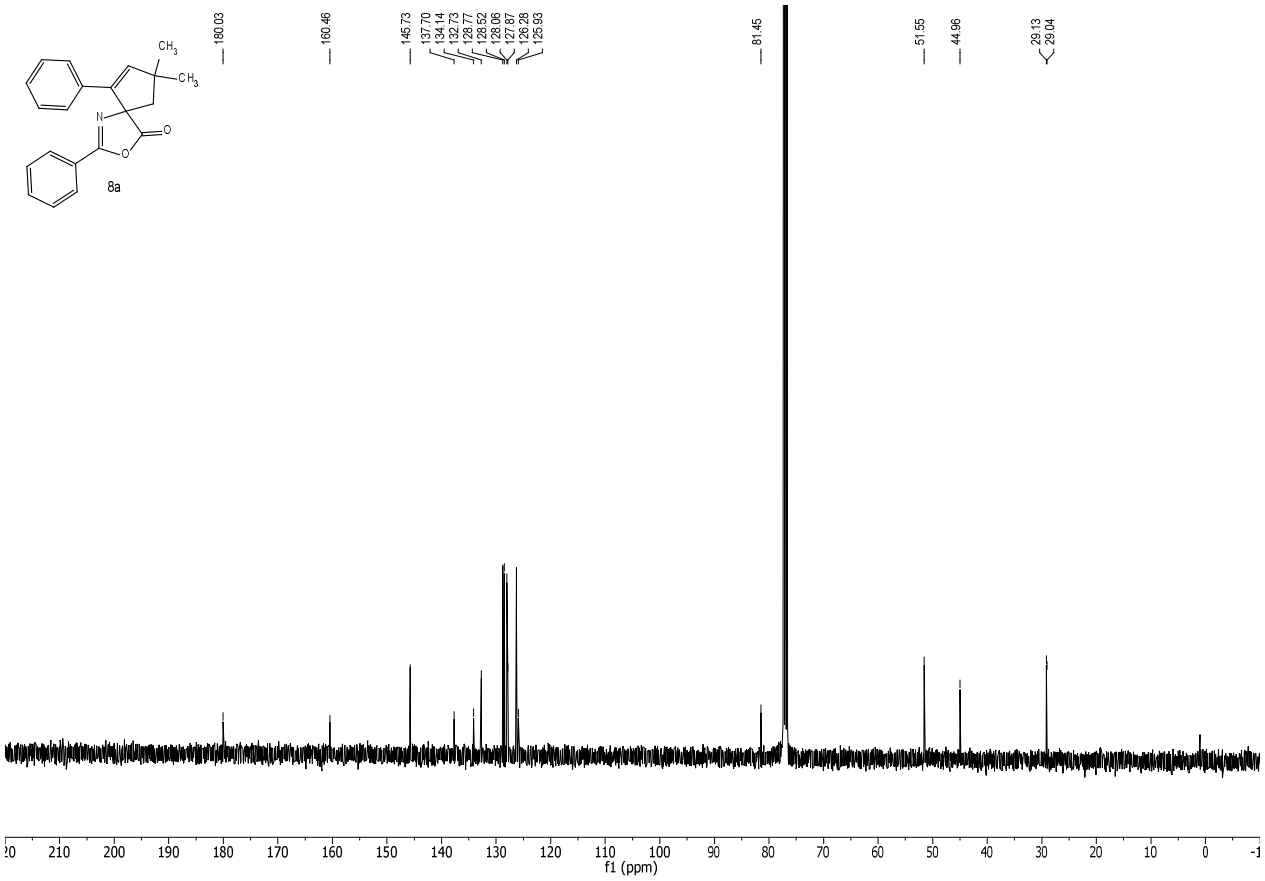
1.06
6.00
f1 (ppm)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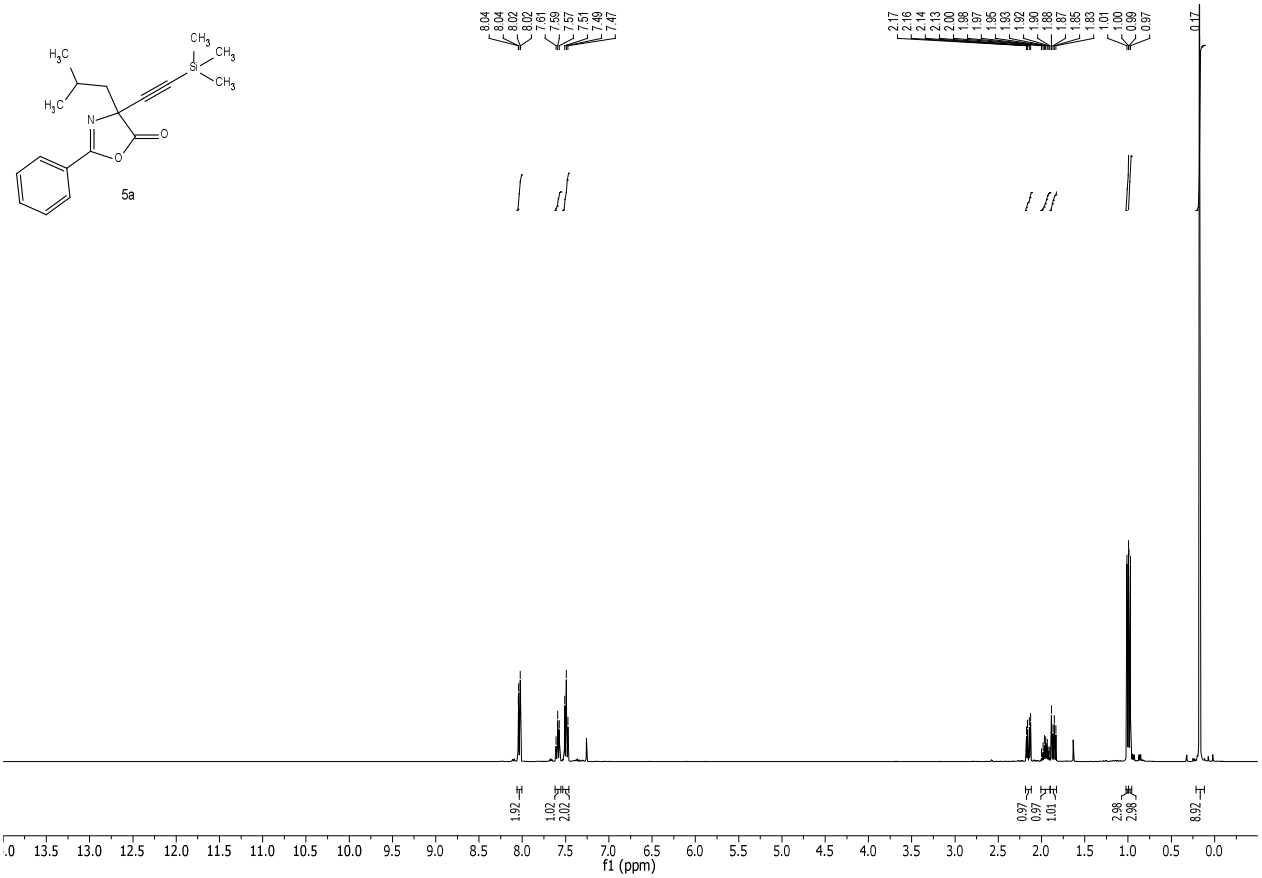
29.13
29.04
f1 (ppm)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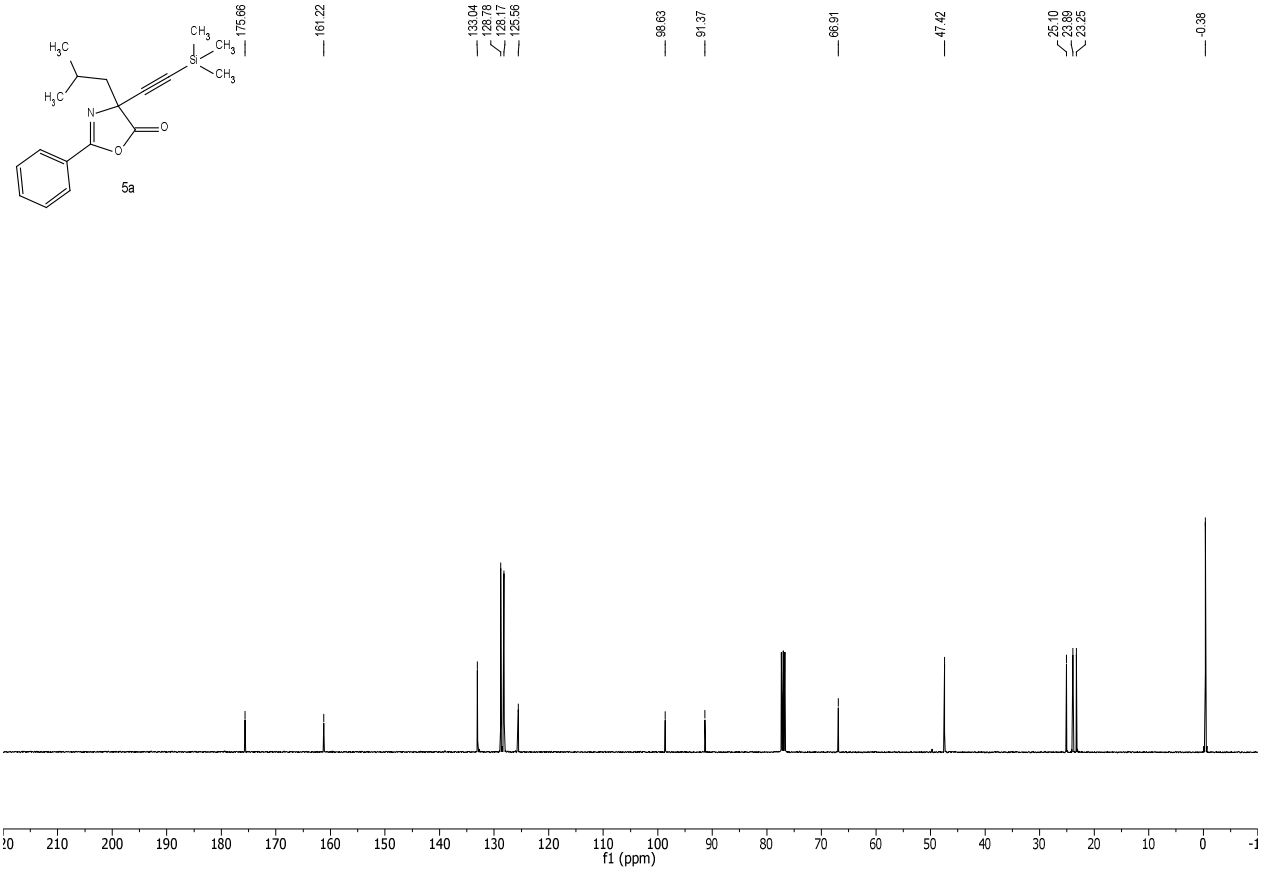
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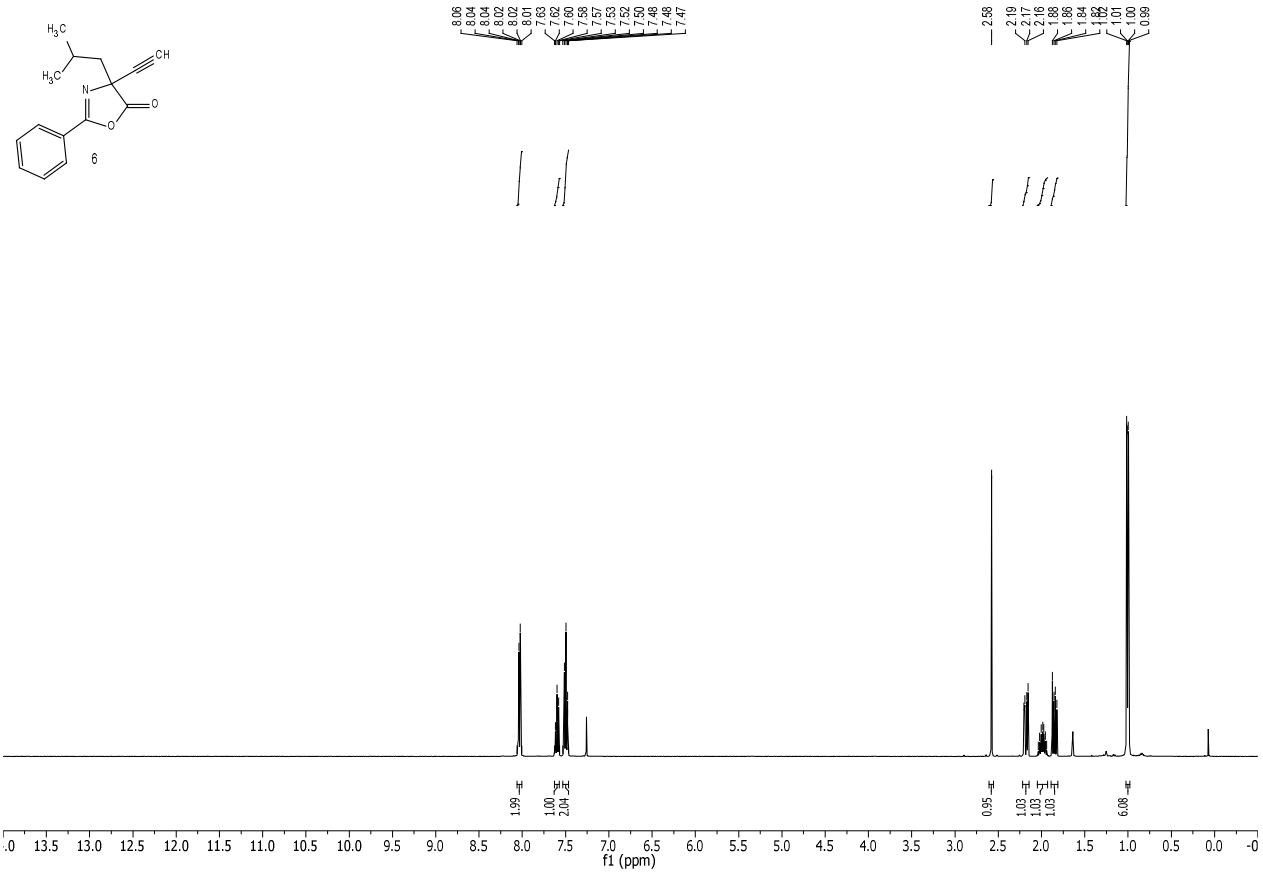
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7.53
7.52
7.50
7.48
7.48
7.47
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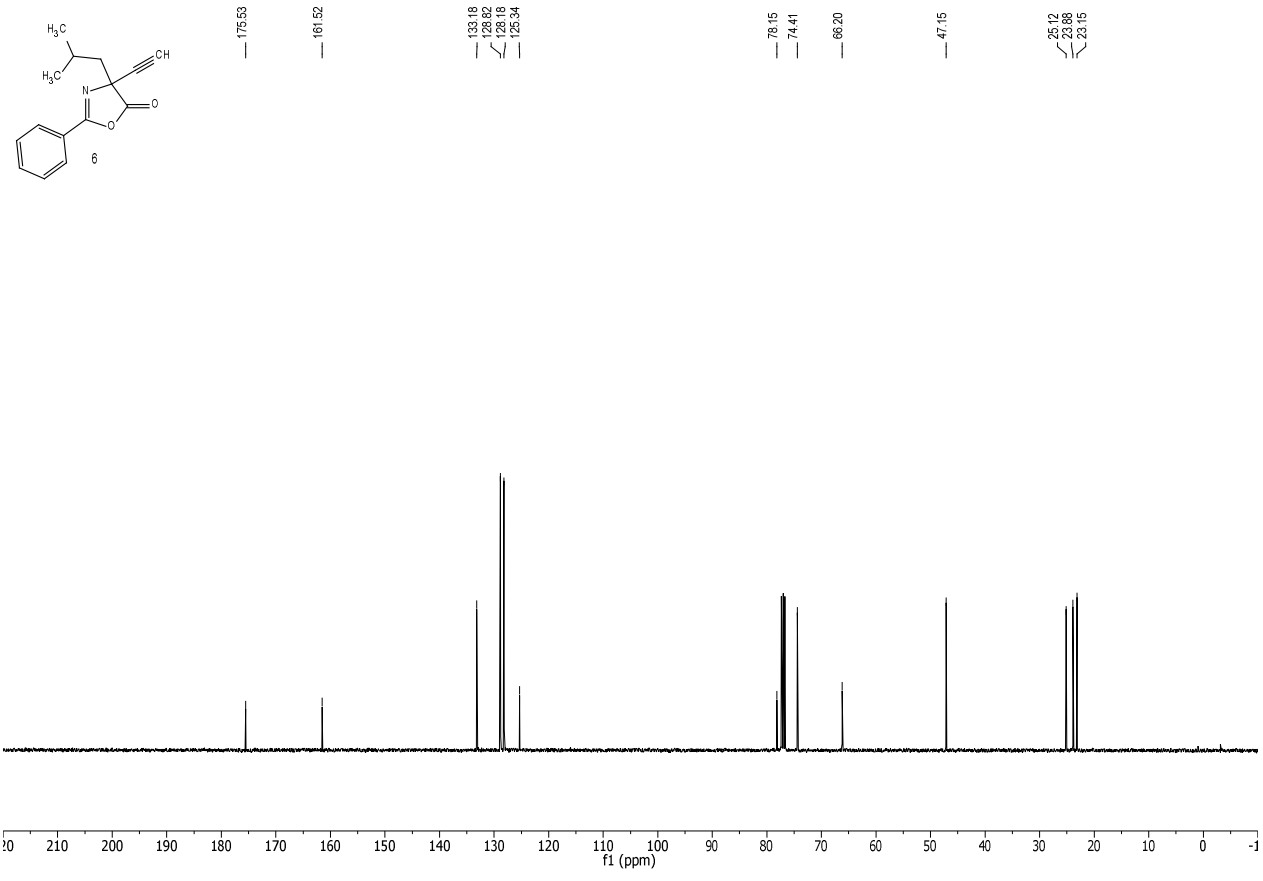
f1 (ppm)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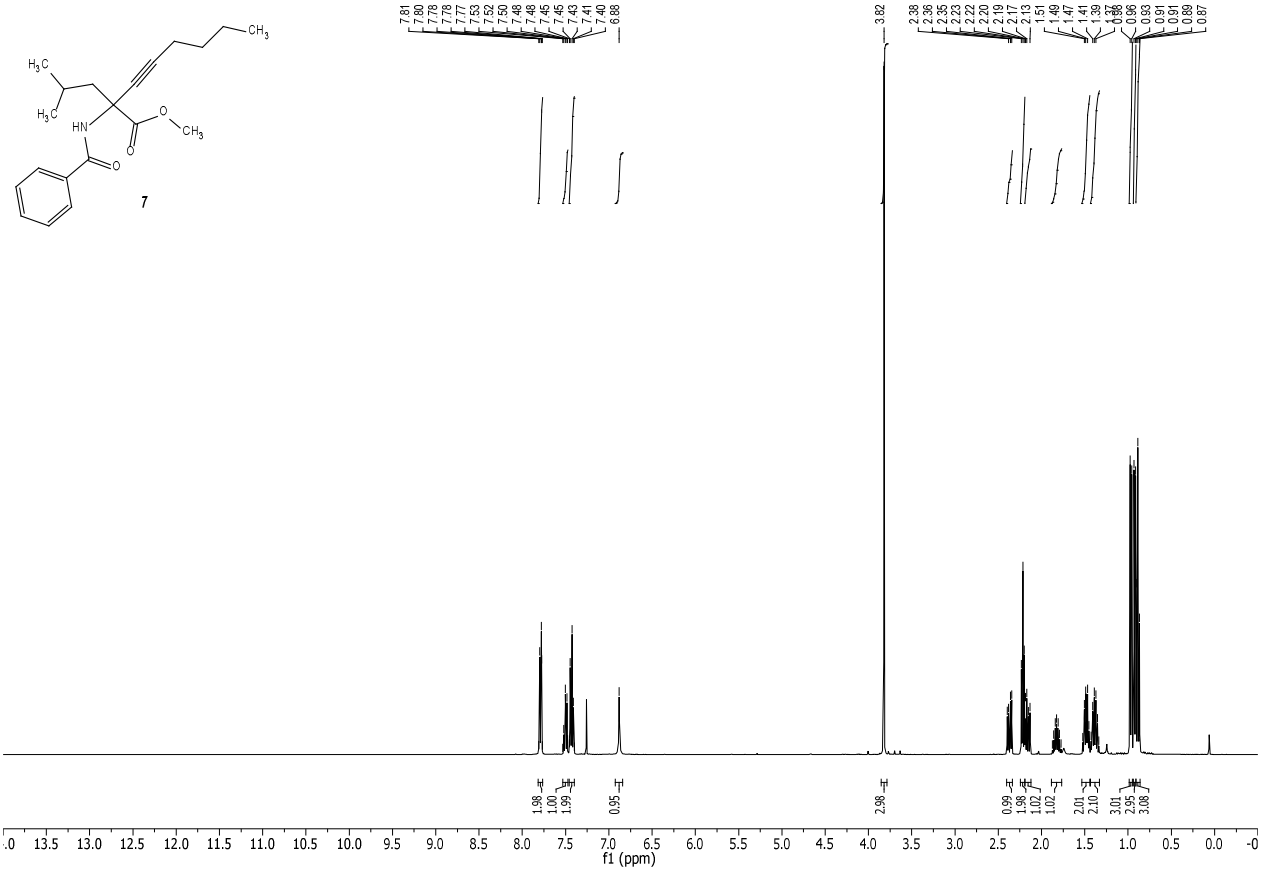
f1 (ppm)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7.41
7.40
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3.82
2.38
2.36
2.35
2.23
2.22
2.20
2.19
2.17
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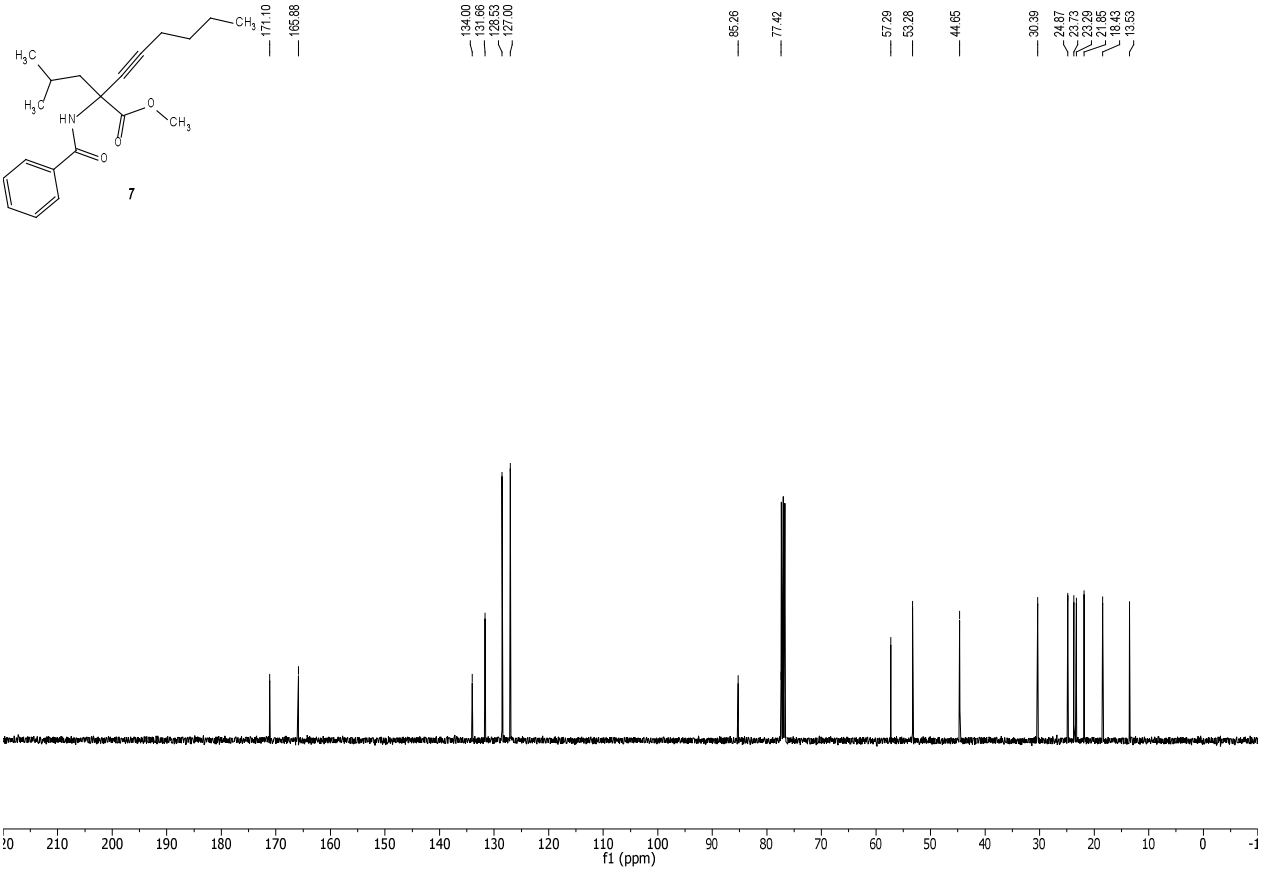
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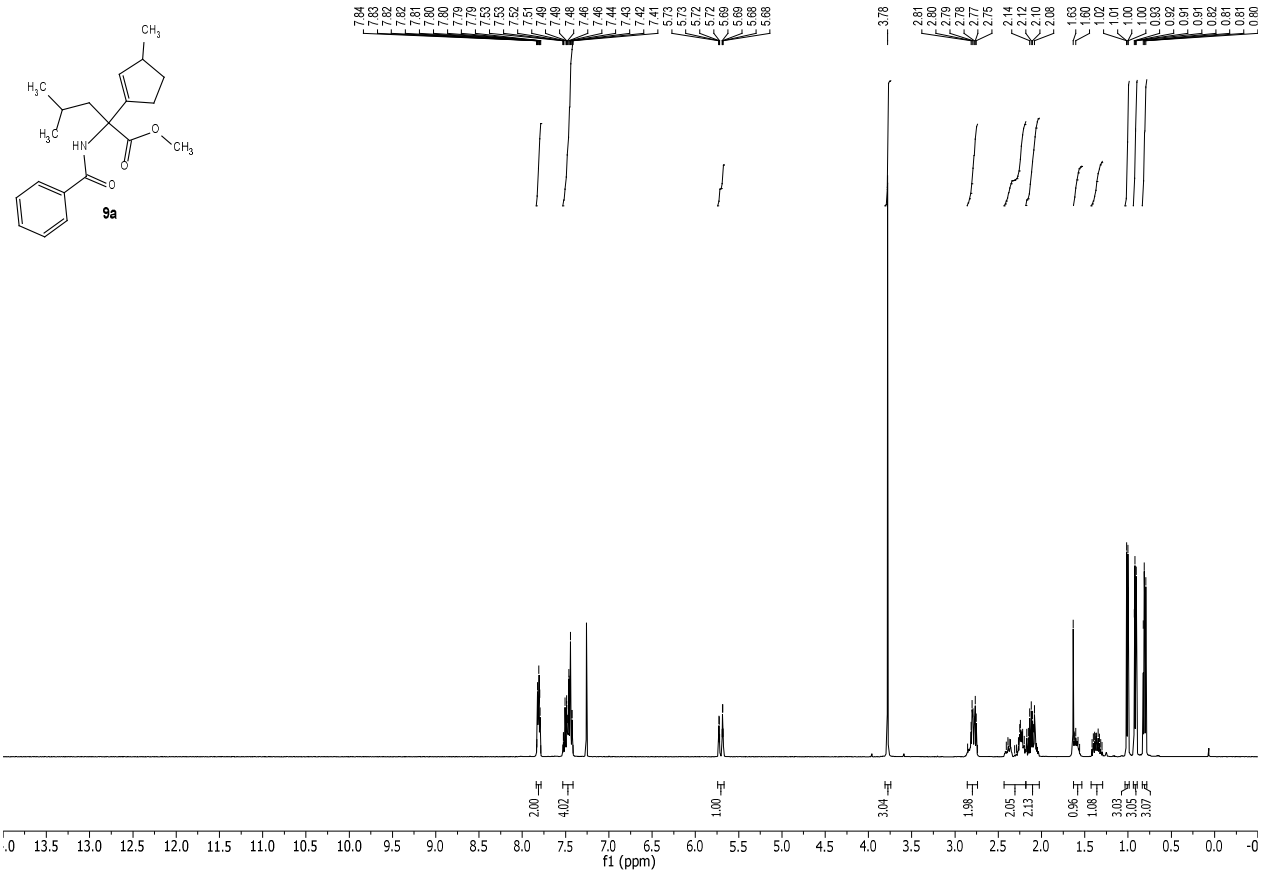
7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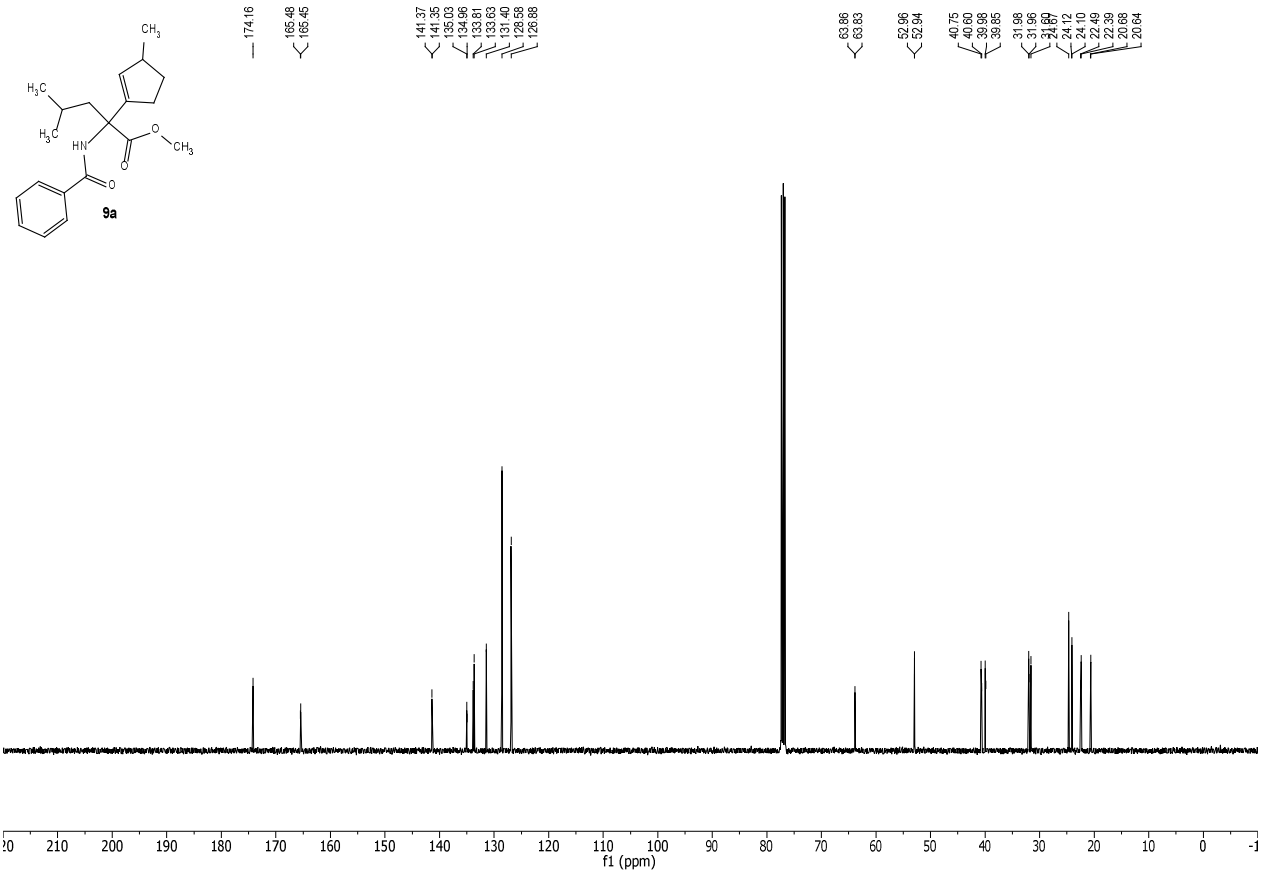
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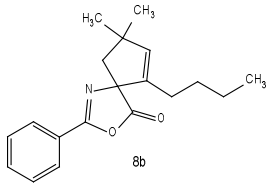
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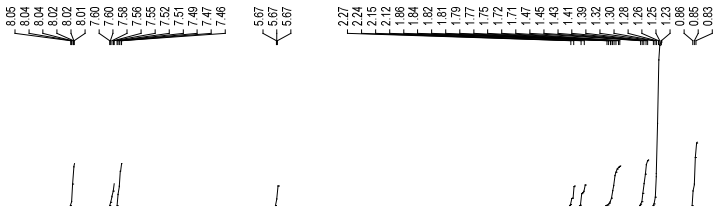
O
O
CH3

8b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7.60
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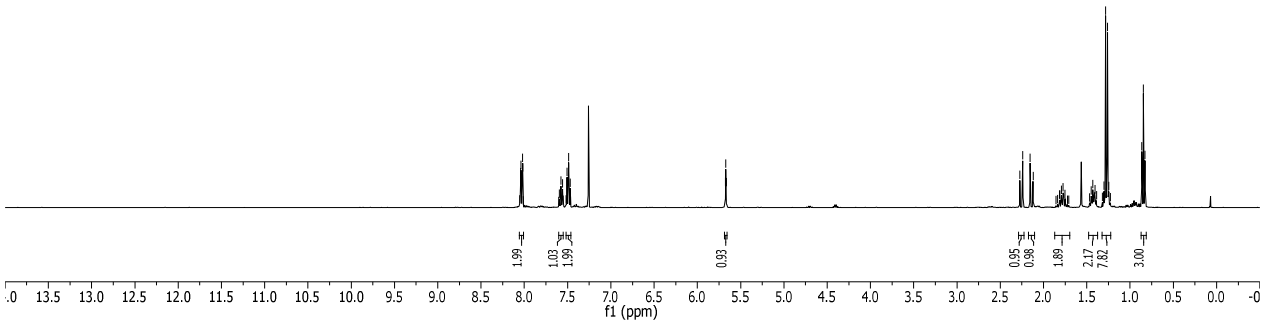
0.85
0.83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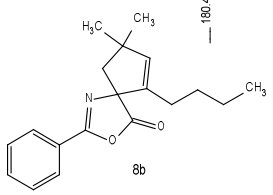
f1 (ppm)


H3C
CH3
N
O
O
CH3

8b

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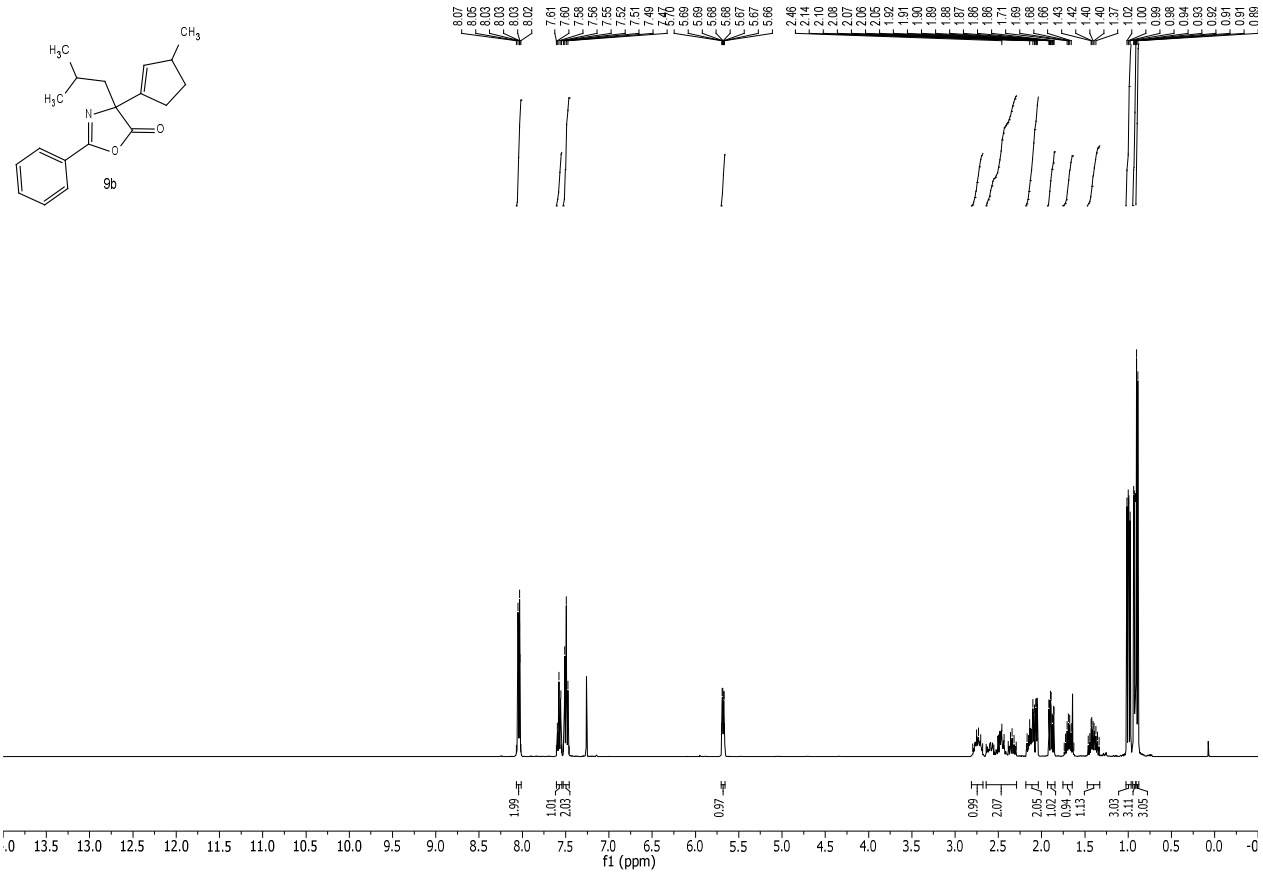
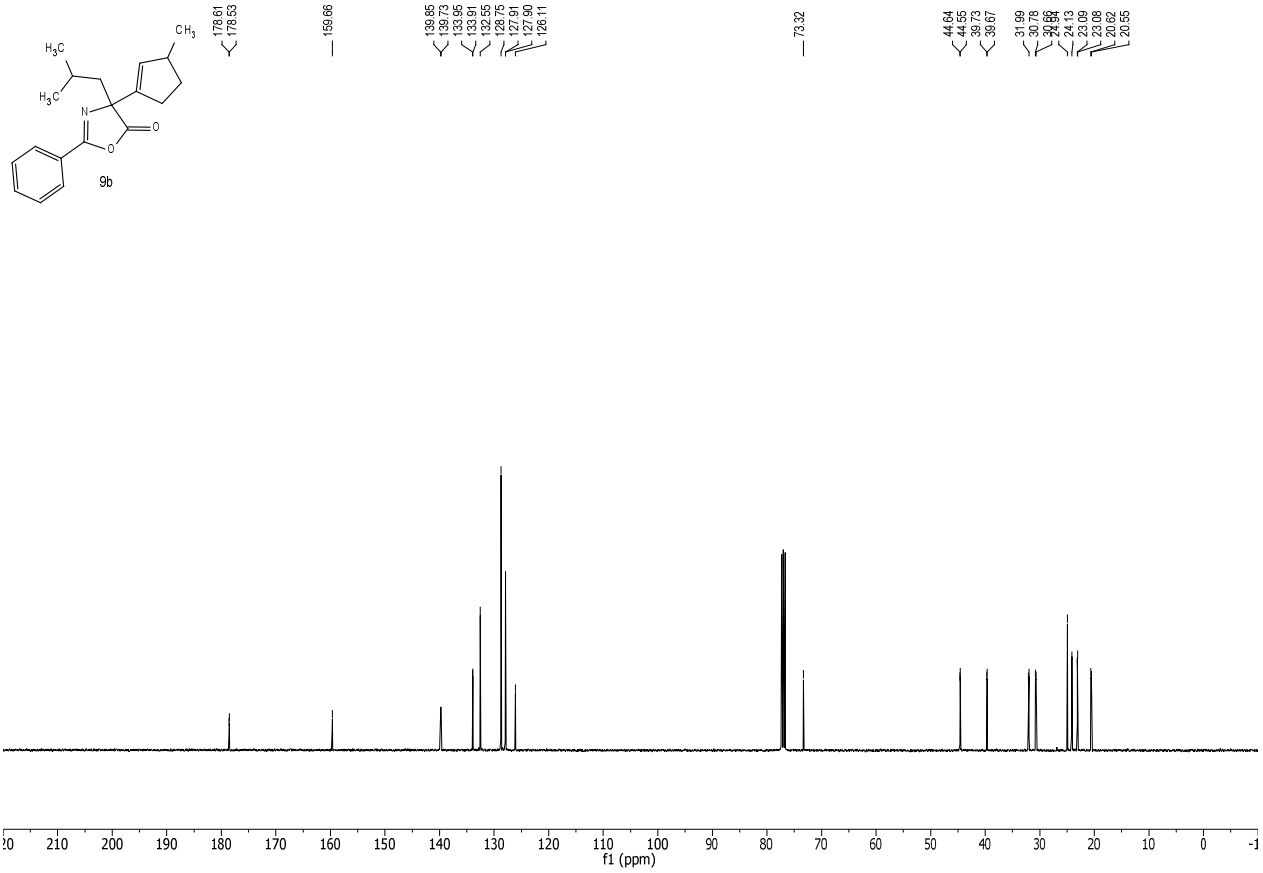
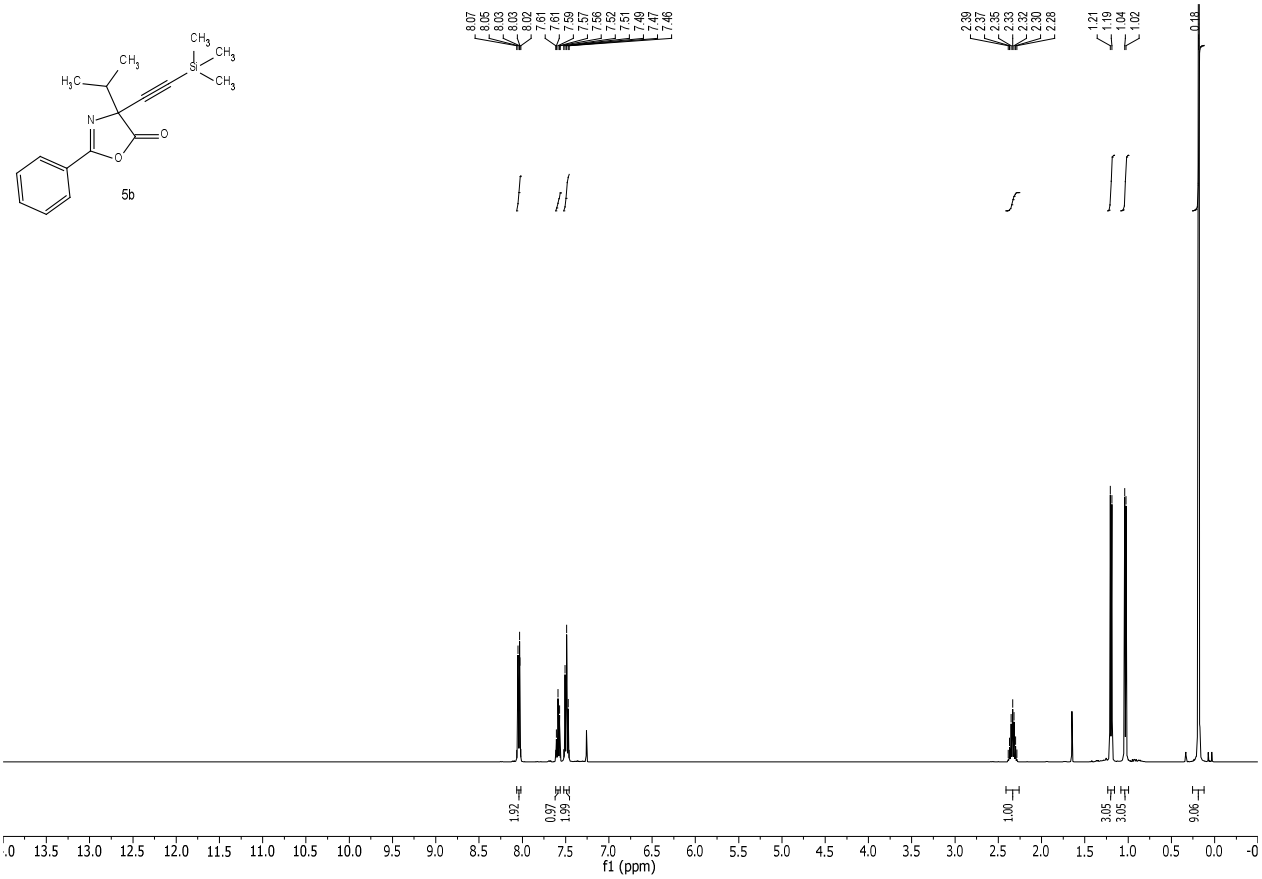
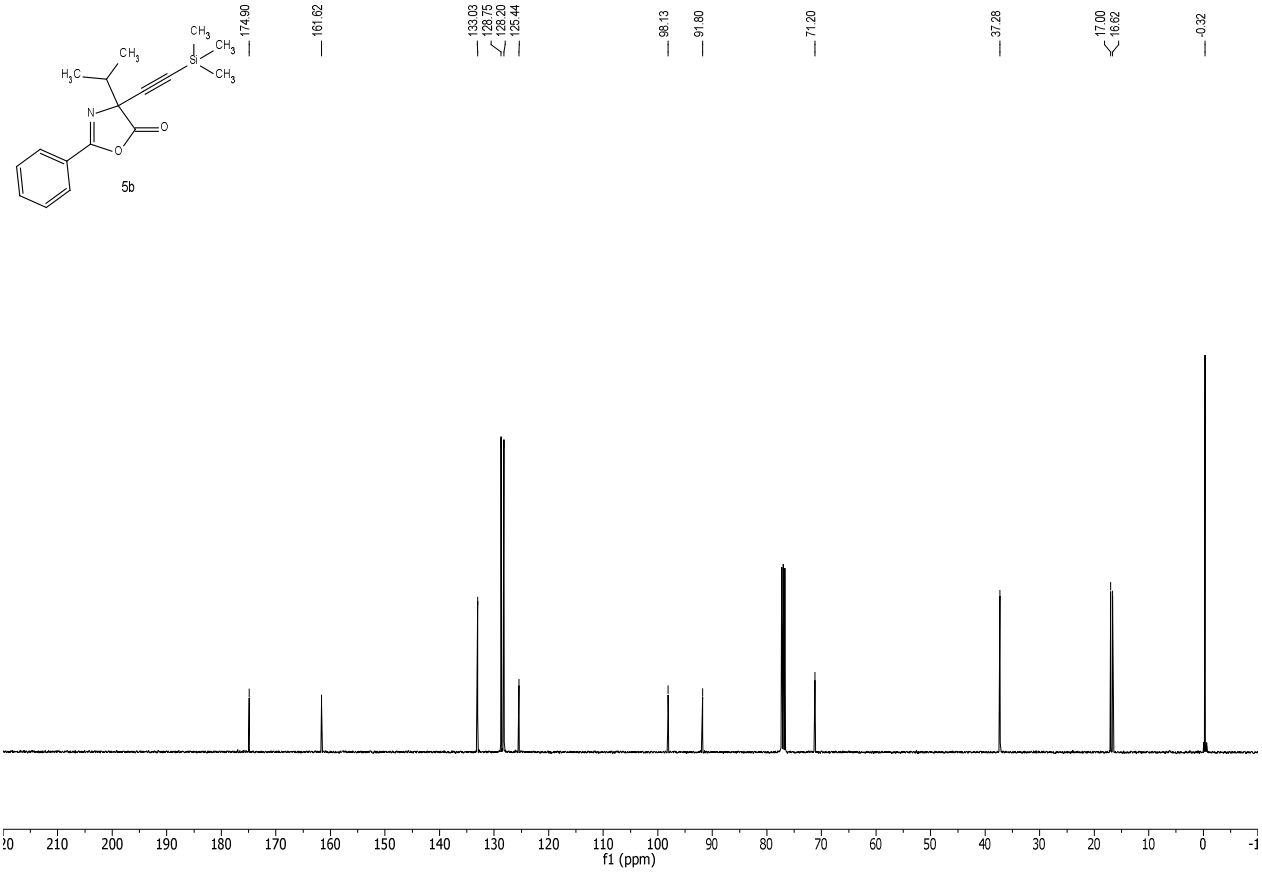
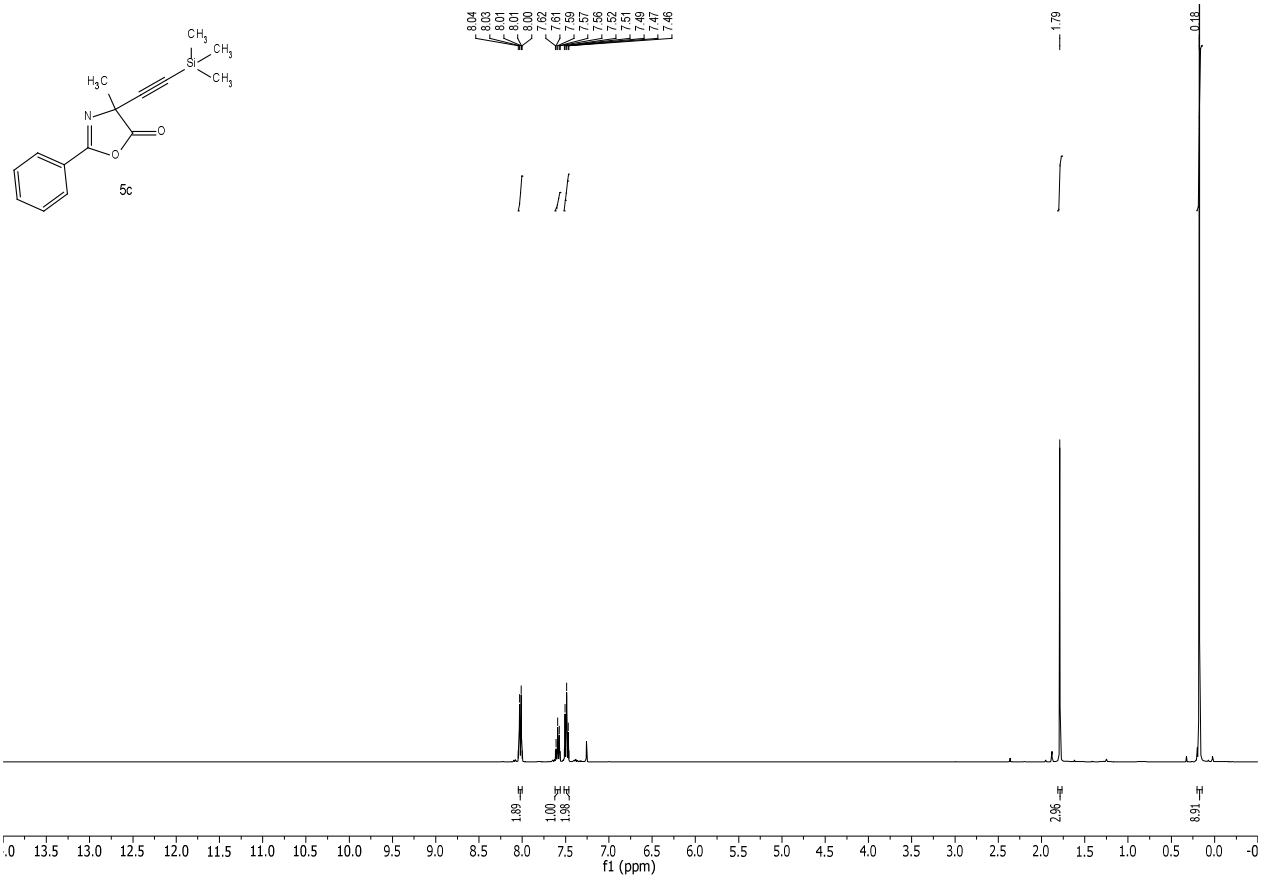
82.38
49.83
45.04
29.44
29.43
29.34
26.51
22.41
13.88
f1 (ppm)

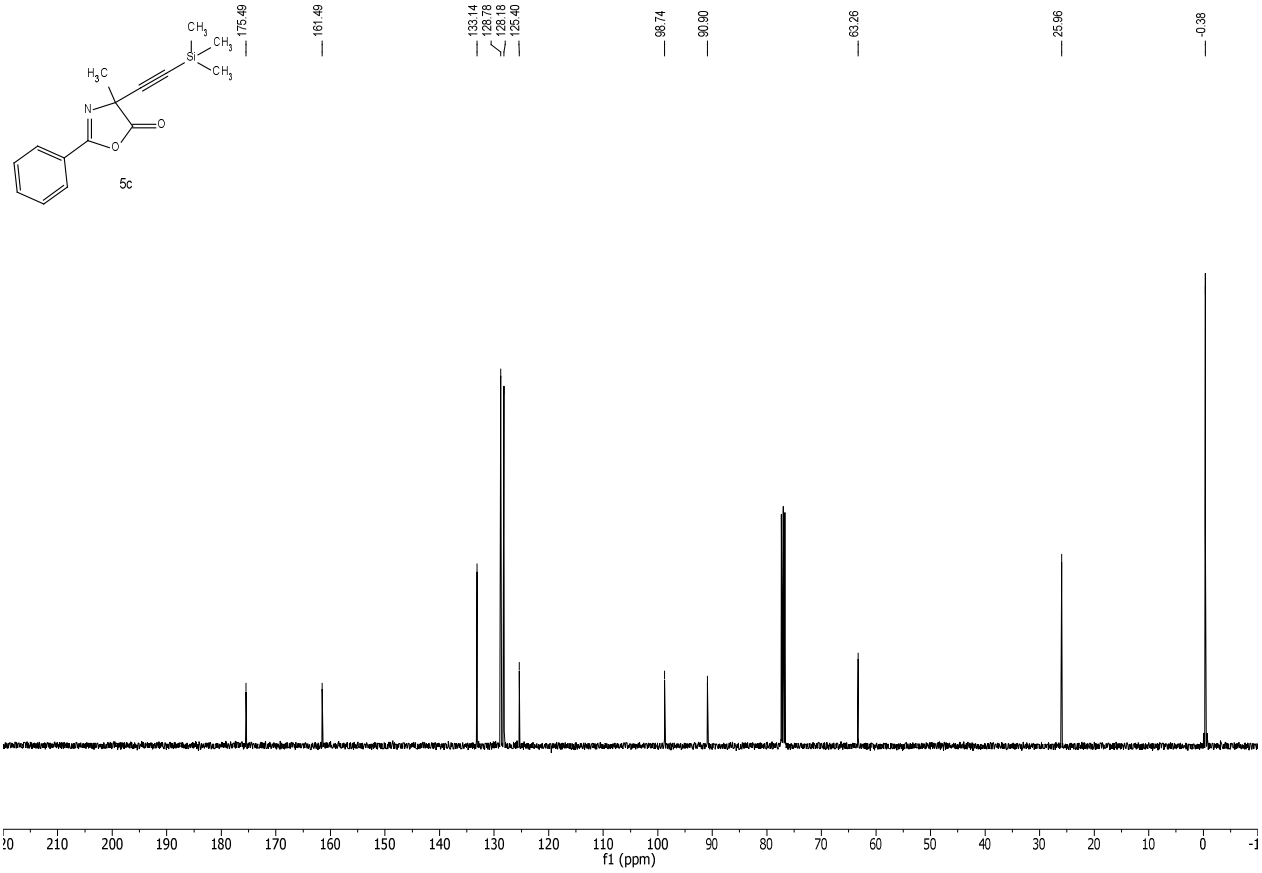

9b
f1 (ppm)

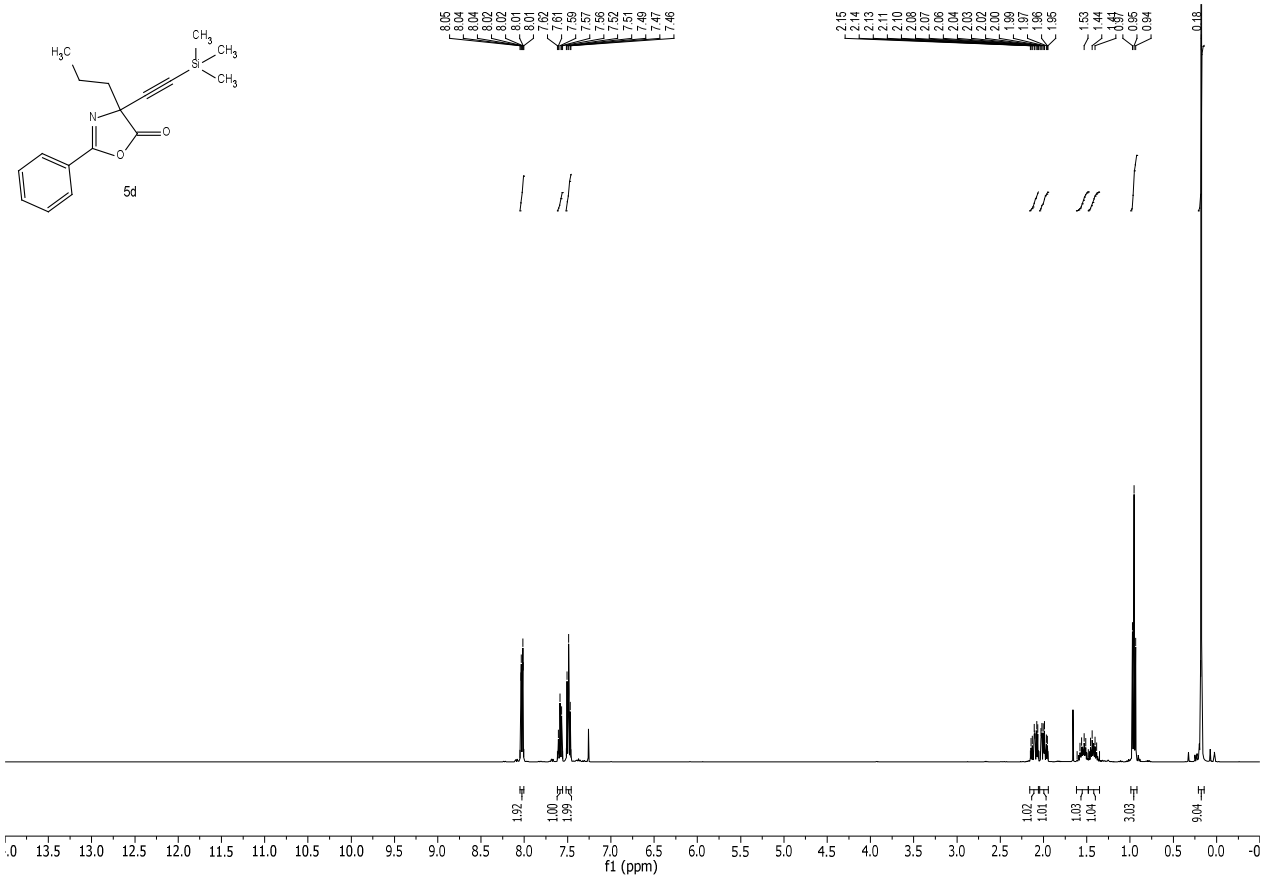

9b
f1 (ppm)

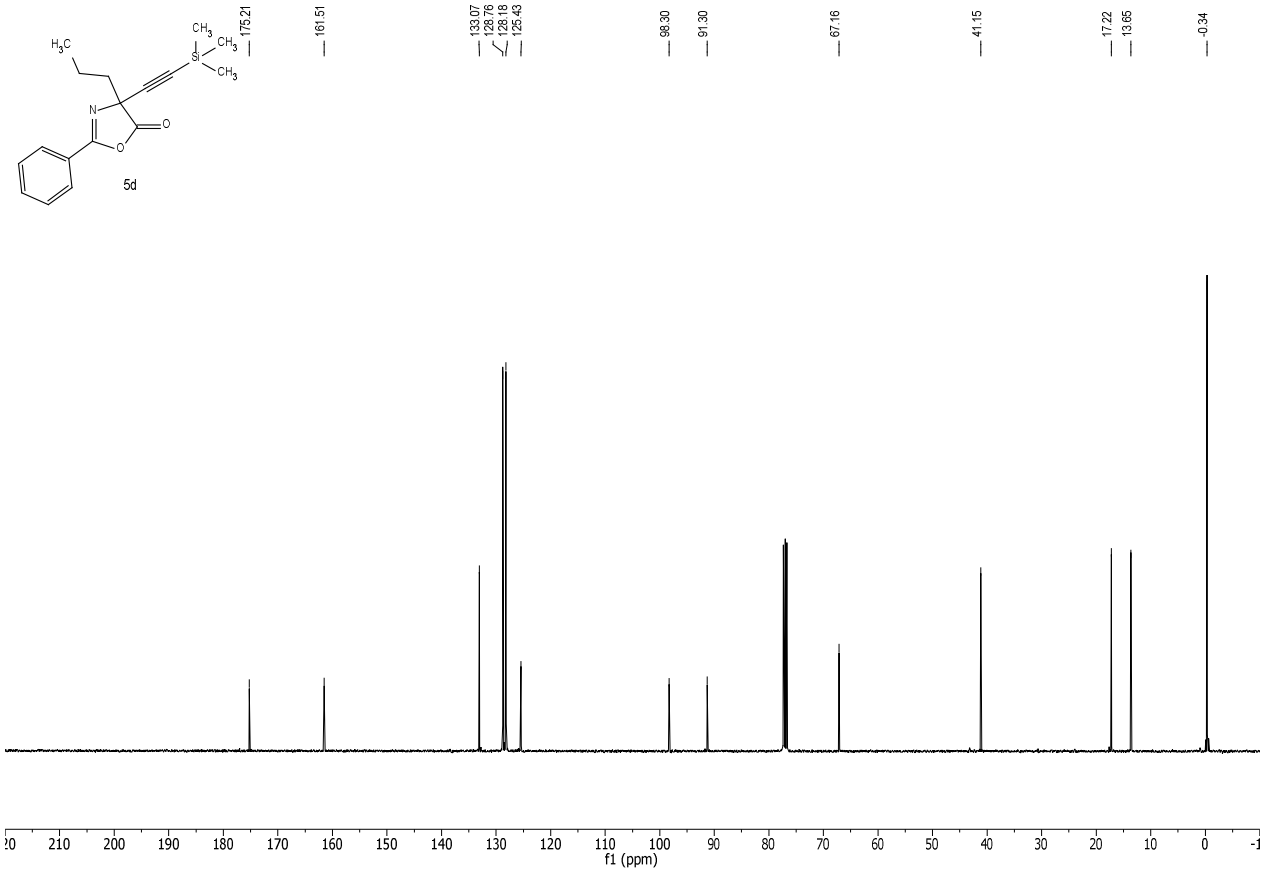

5b
8.07
8.05
8.03
8.03
8.02
7.61
7.59
7.57
7.56
7.52
7.51
7.49
7.47
7.46
2.39
2.37
2.35
2.33
2.32
2.30
2.28
1.21
1.19
1.04
1.02
0.18
1.92
0.97
1.99
1.00
3.05
3.05
9.06
f1 (ppm)

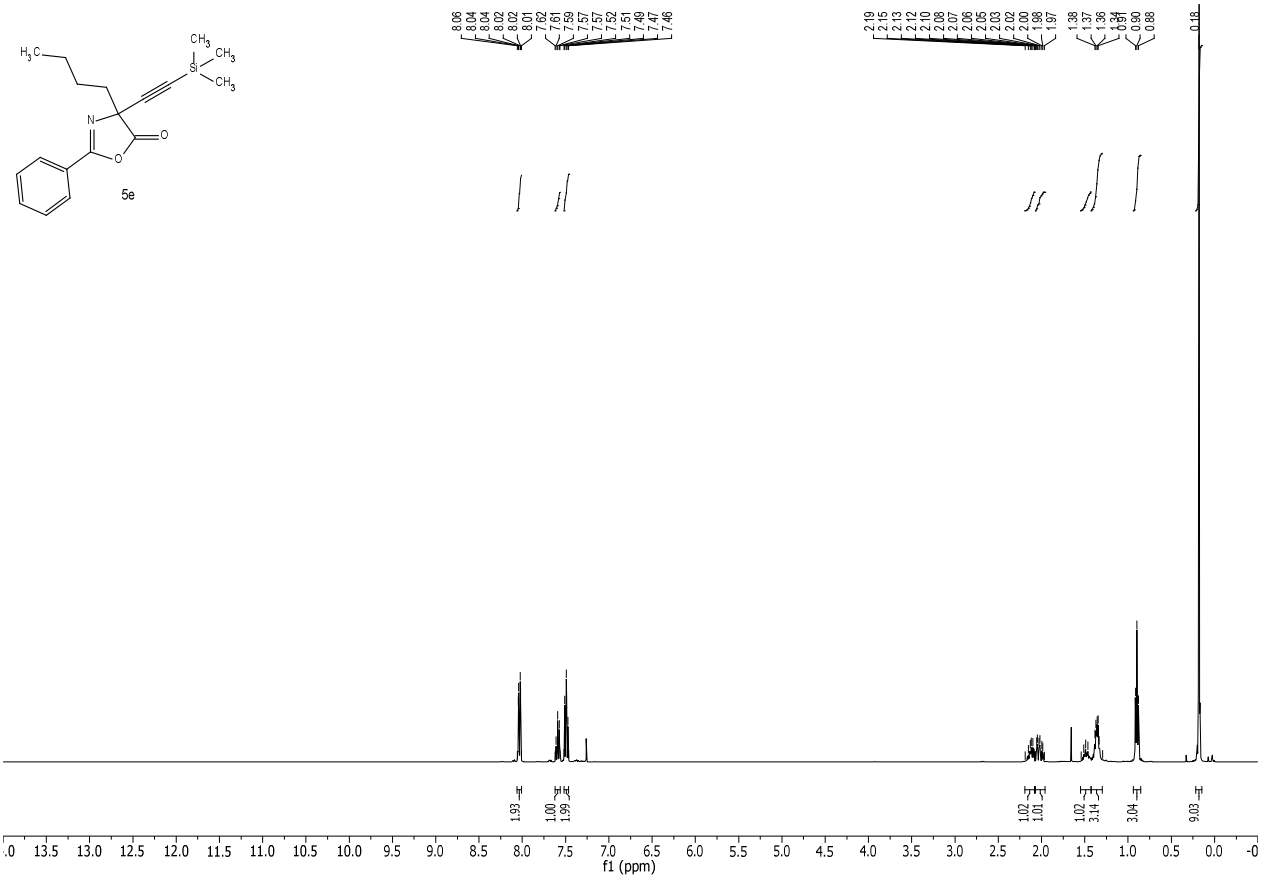

5b
174.90
161.62
133.03
128.75
128.20
125.44
98.13
91.80
71.20
37.28
17.00
16.62
-0.32
f1 (ppm)

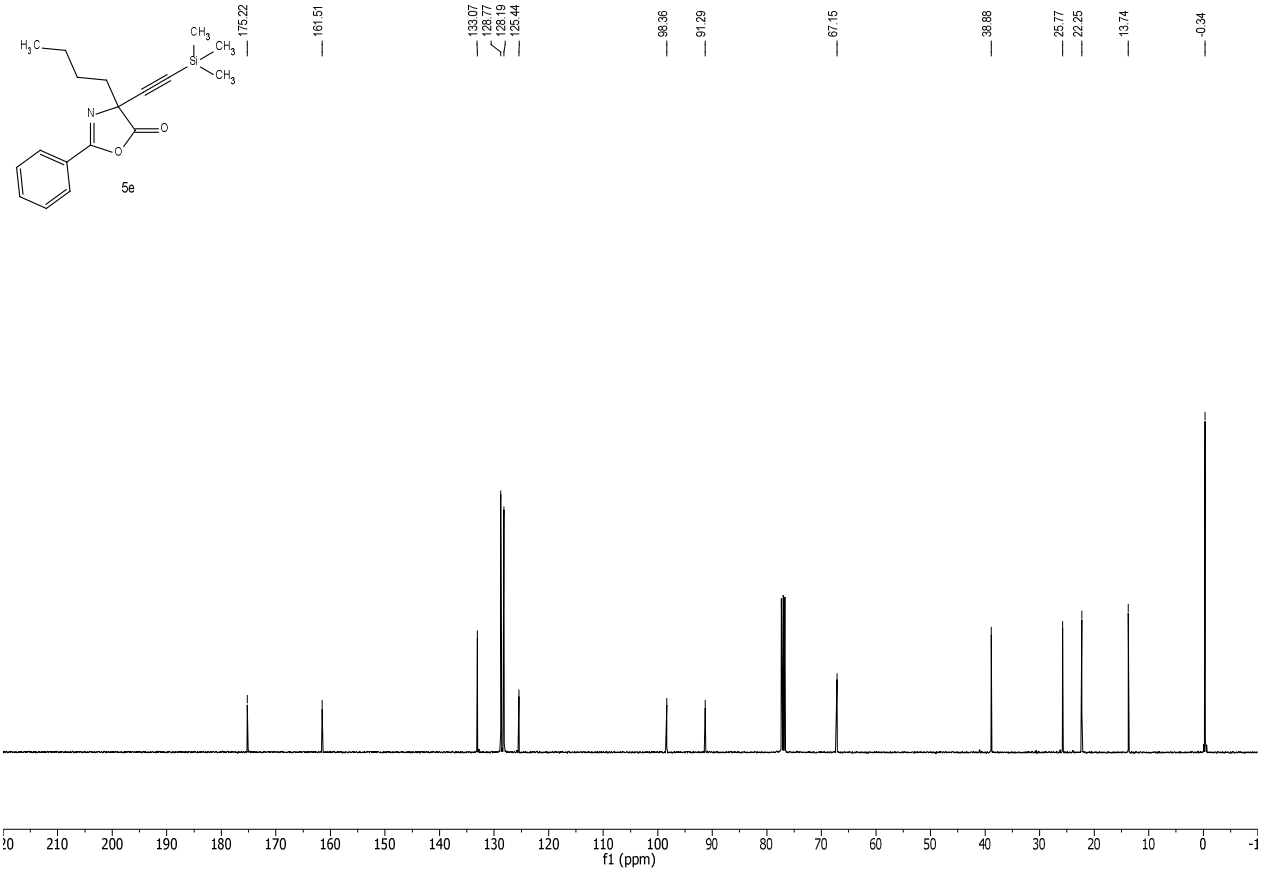

8.04
8.03
8.01
8.01
8.00
7.62
7.61
7.59
7.57
7.56
7.52
7.51
7.49
7.47
7.46
1.79
0.18
1.89
1.00
1.98
2.96
8.91
f1 (ppm)

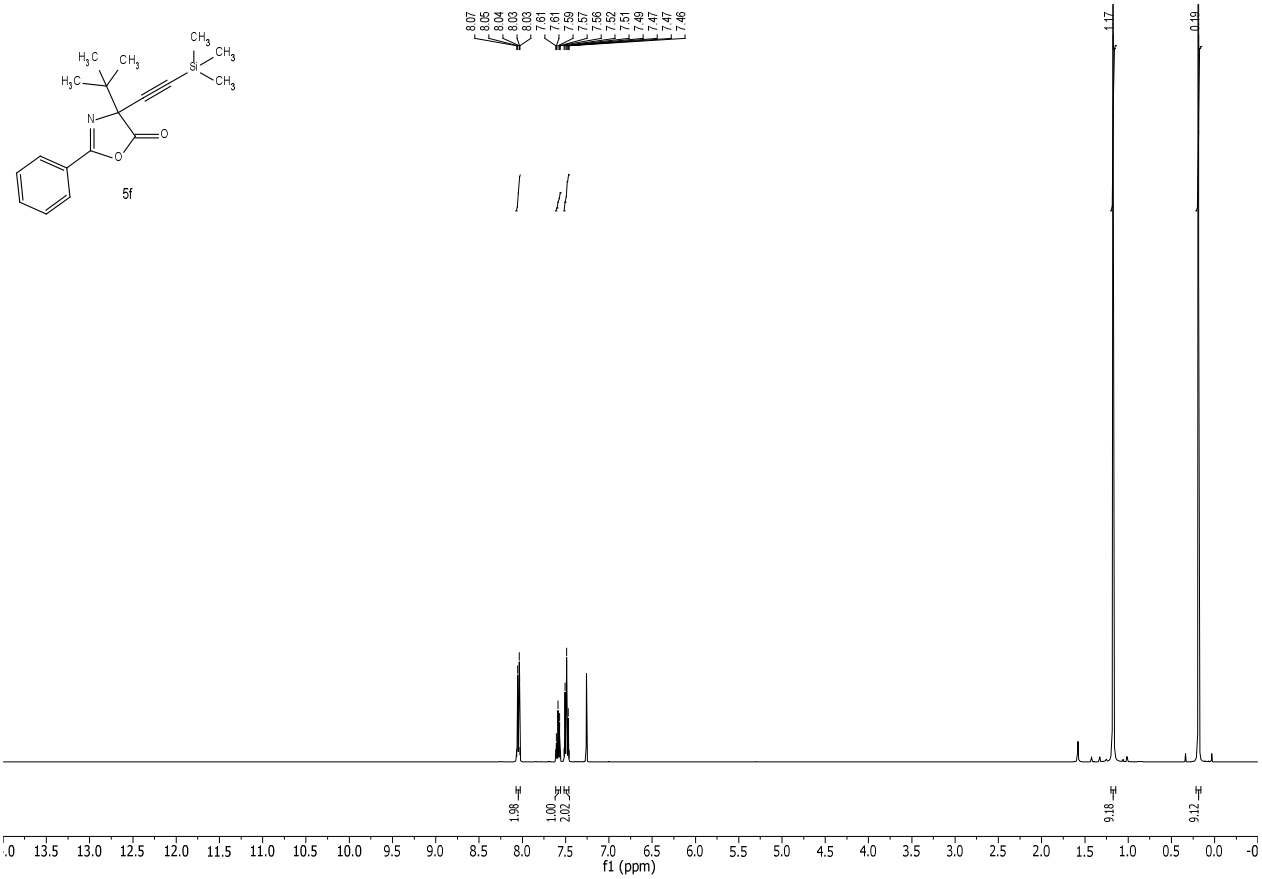

175.49
161.49
133.14
128.78
128.18
125.40
98.74
90.90
63.26
25.96
-0.38
f1 (ppm)

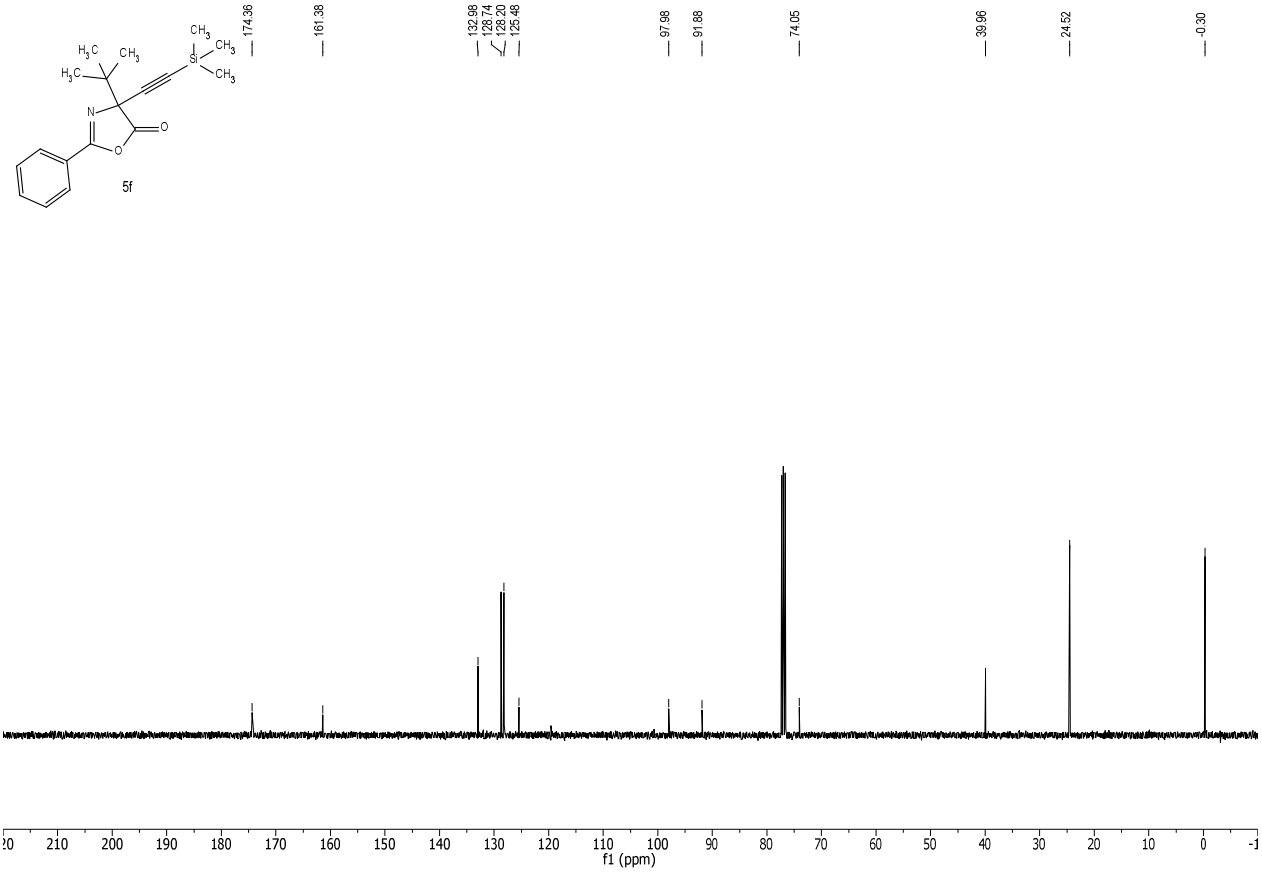

5d
f1 (ppm)

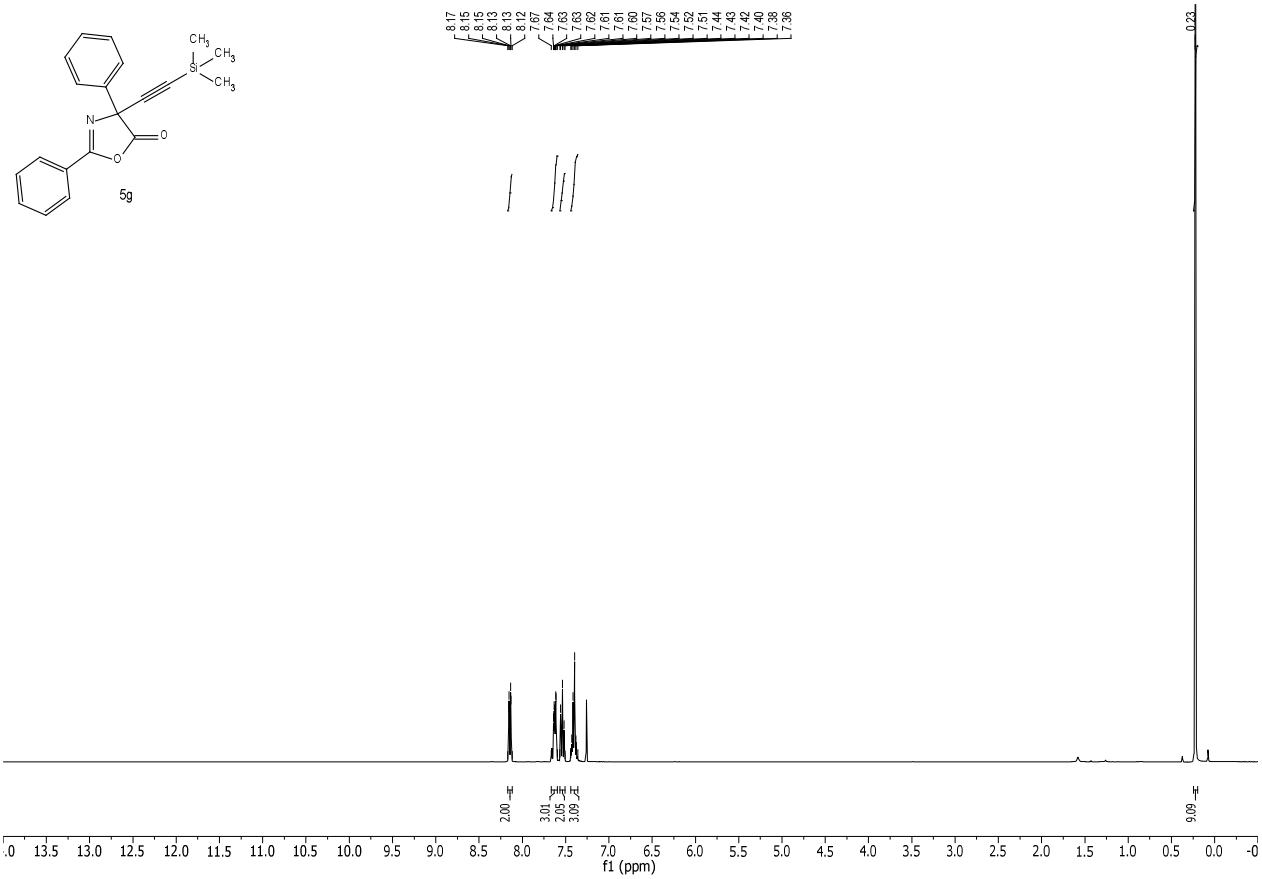

5d
f1 (ppm)

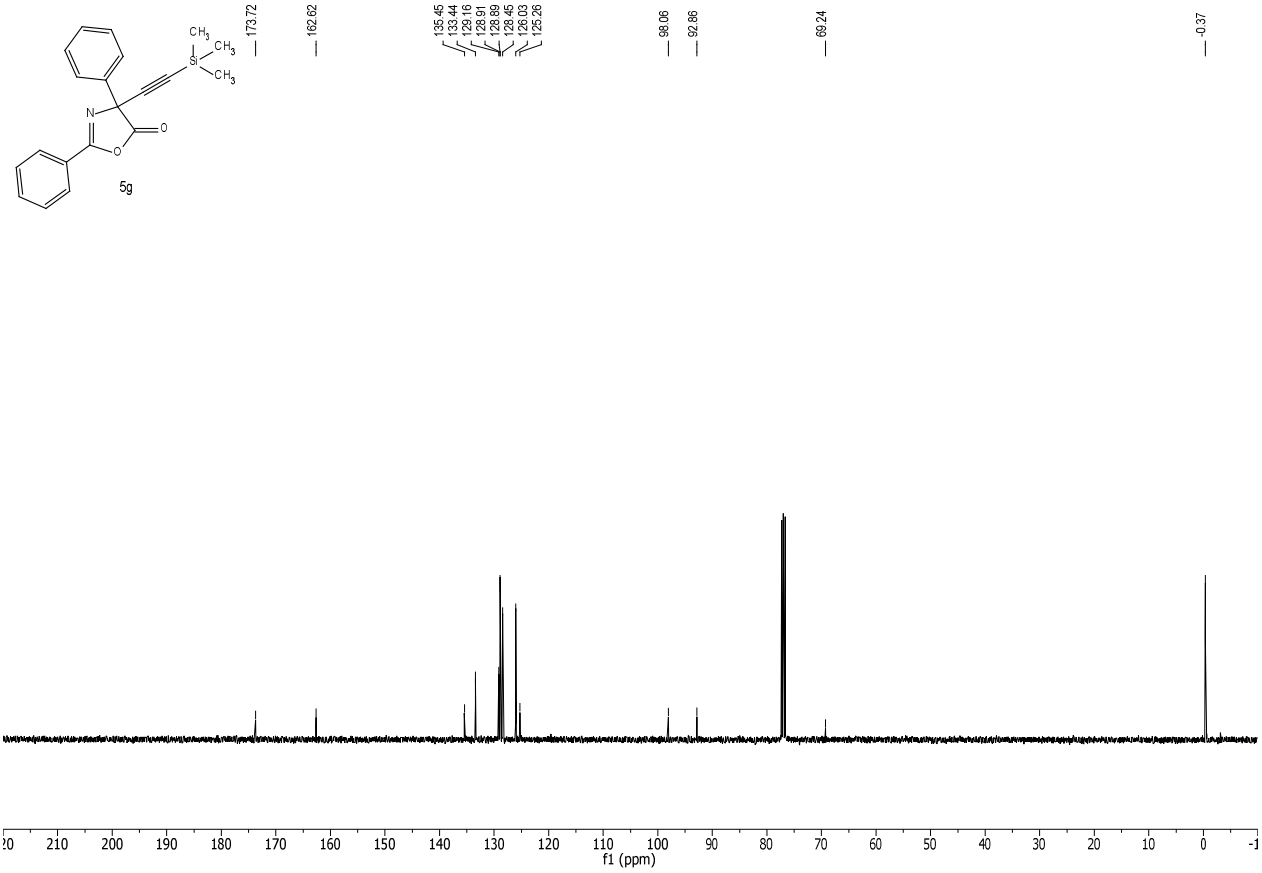

5e
f1 (ppm)

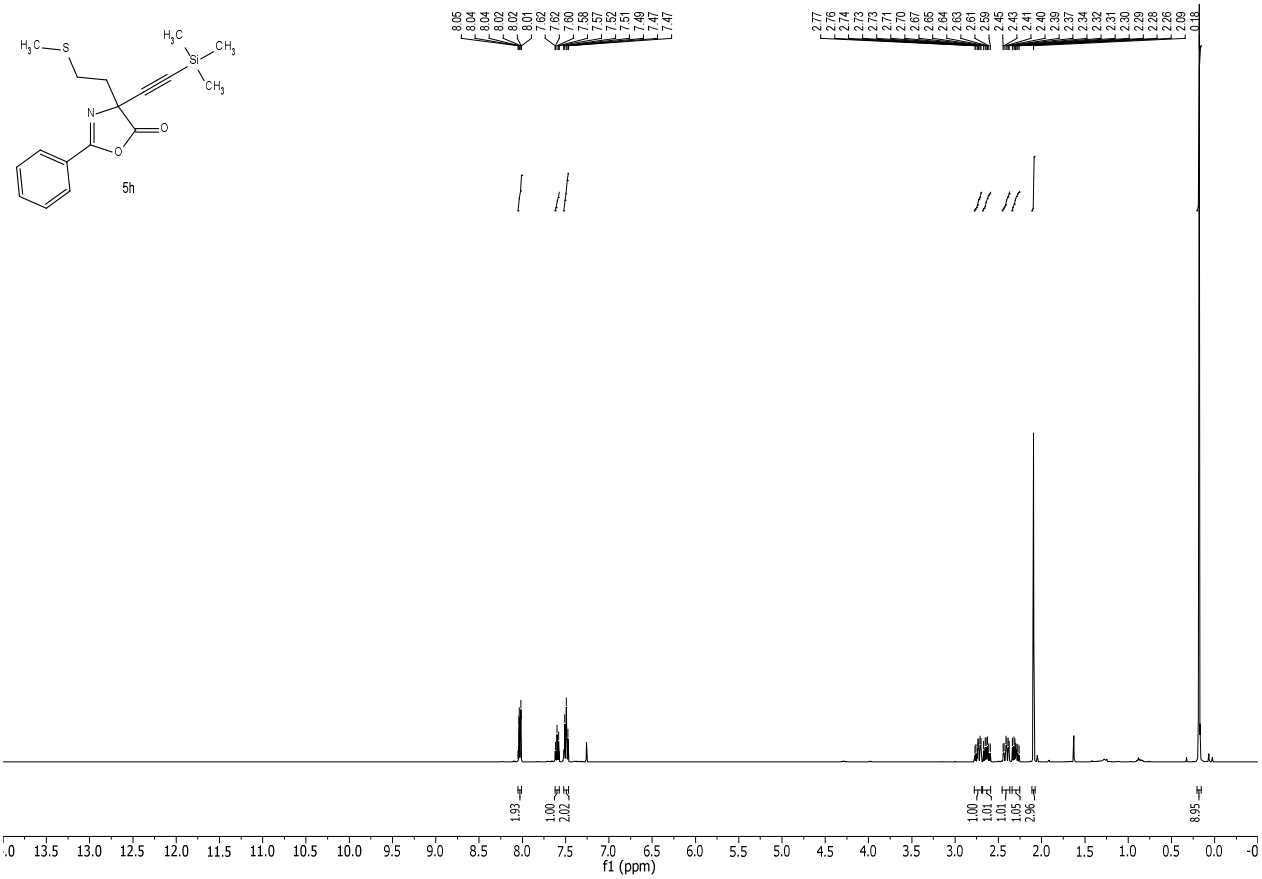

5e
f1 (ppm)

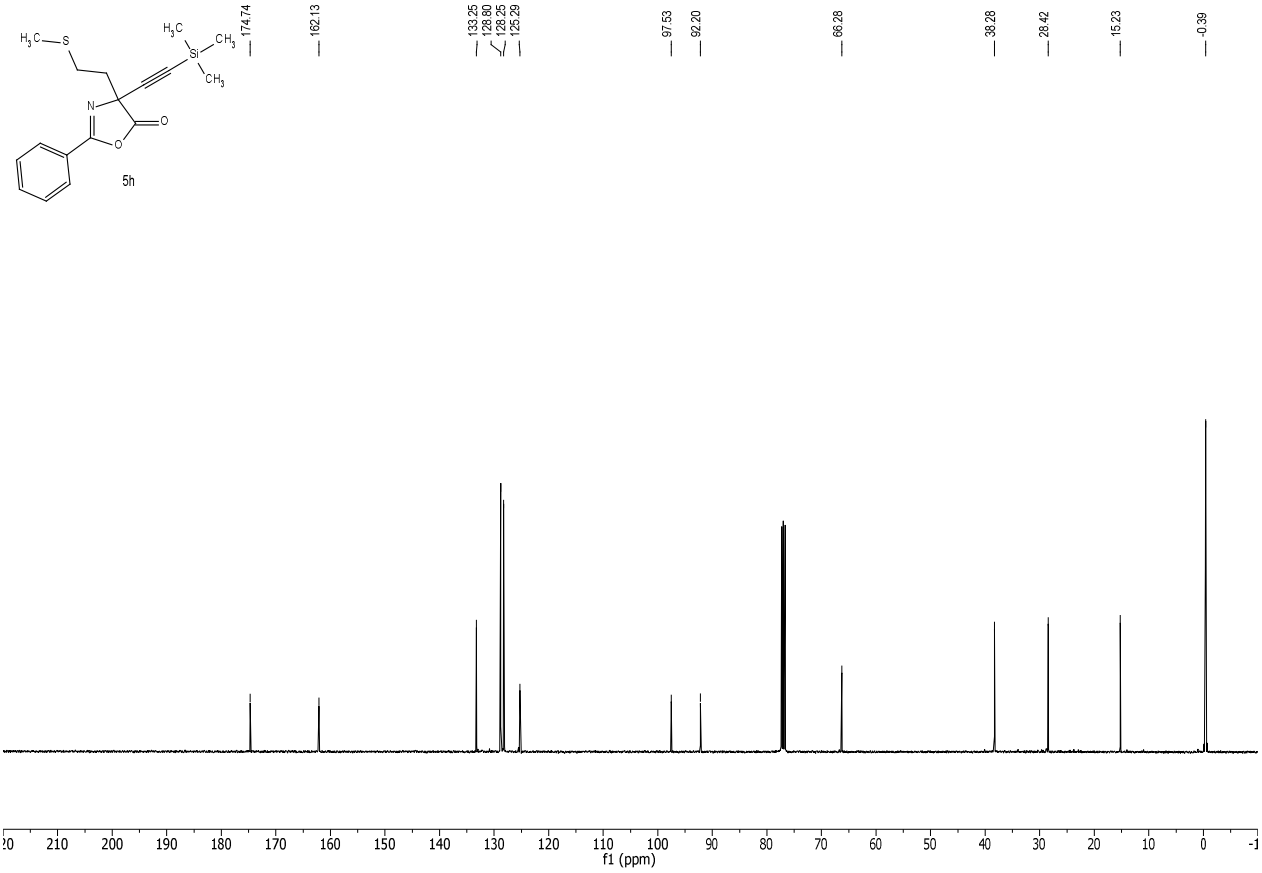

5f
8.07
8.05
8.04
8.03
7.61
7.59
7.57
7.56
7.52
7.51
7.49
7.47
7.47
7.46
1.17
0.19
1.98
1.00
2.02
9.18
9.12
f1 (ppm)

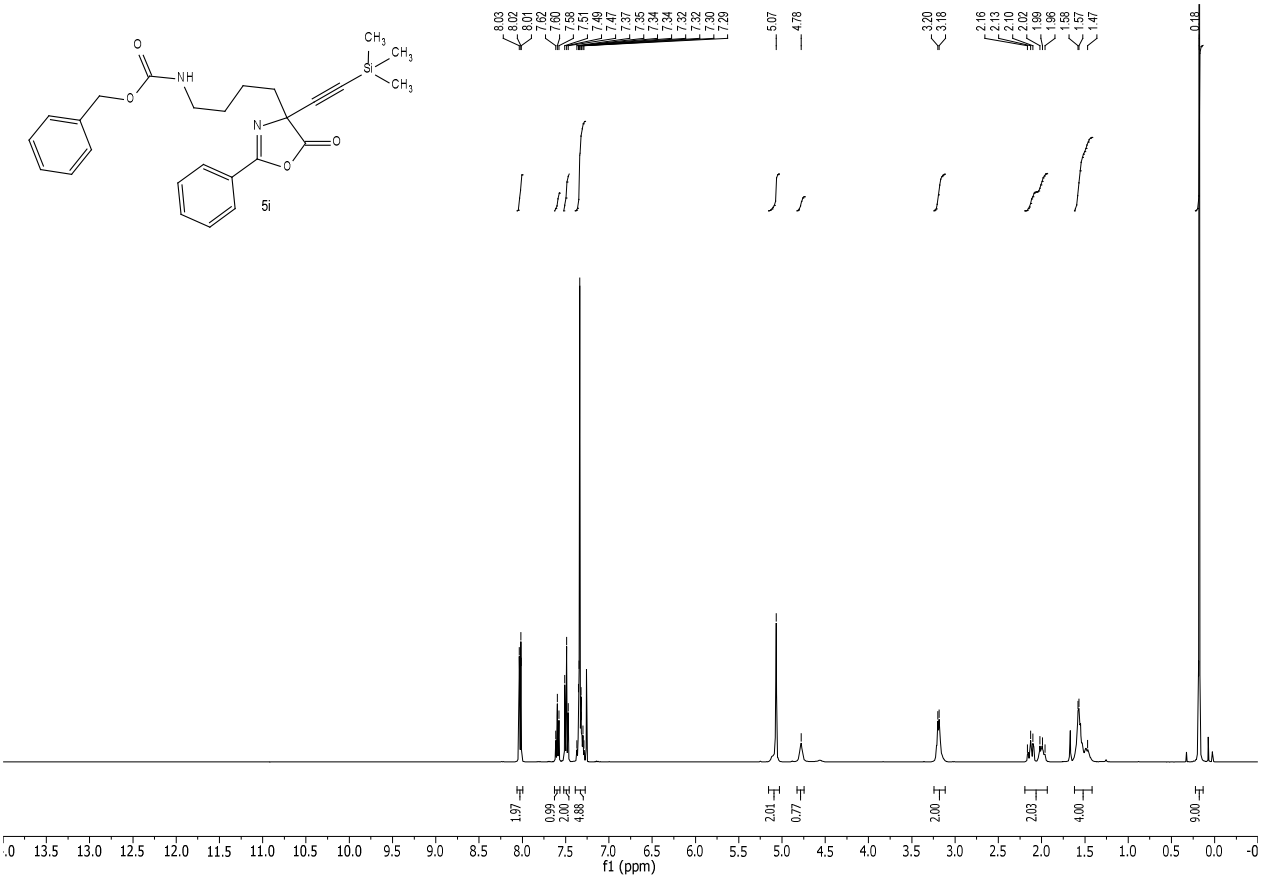

5f
174.36
161.38
132.98
128.74
128.20
125.48
97.98
91.88
74.05
39.96
24.52
-0.30
f1 (ppm)

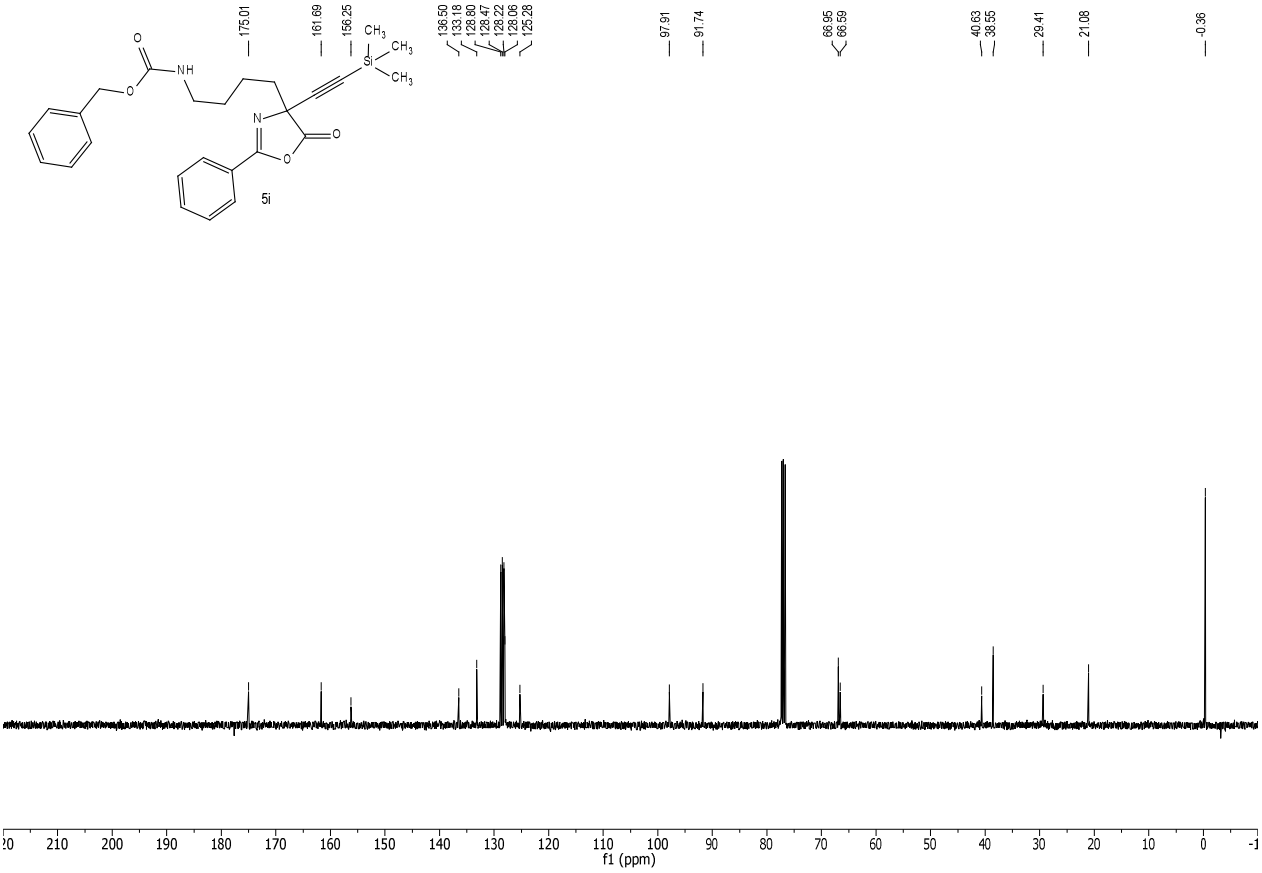

5g
8.17
8.15
8.15
8.13
8.13
8.12
7.67
7.64
7.63
7.63
7.62
7.61
7.61
7.60
7.57
7.56
7.54
7.52
7.51
7.44
7.43
7.42
7.40
7.38
7.36
0.23
2.00
3.01
2.05
3.09
9.09
f1 (ppm)

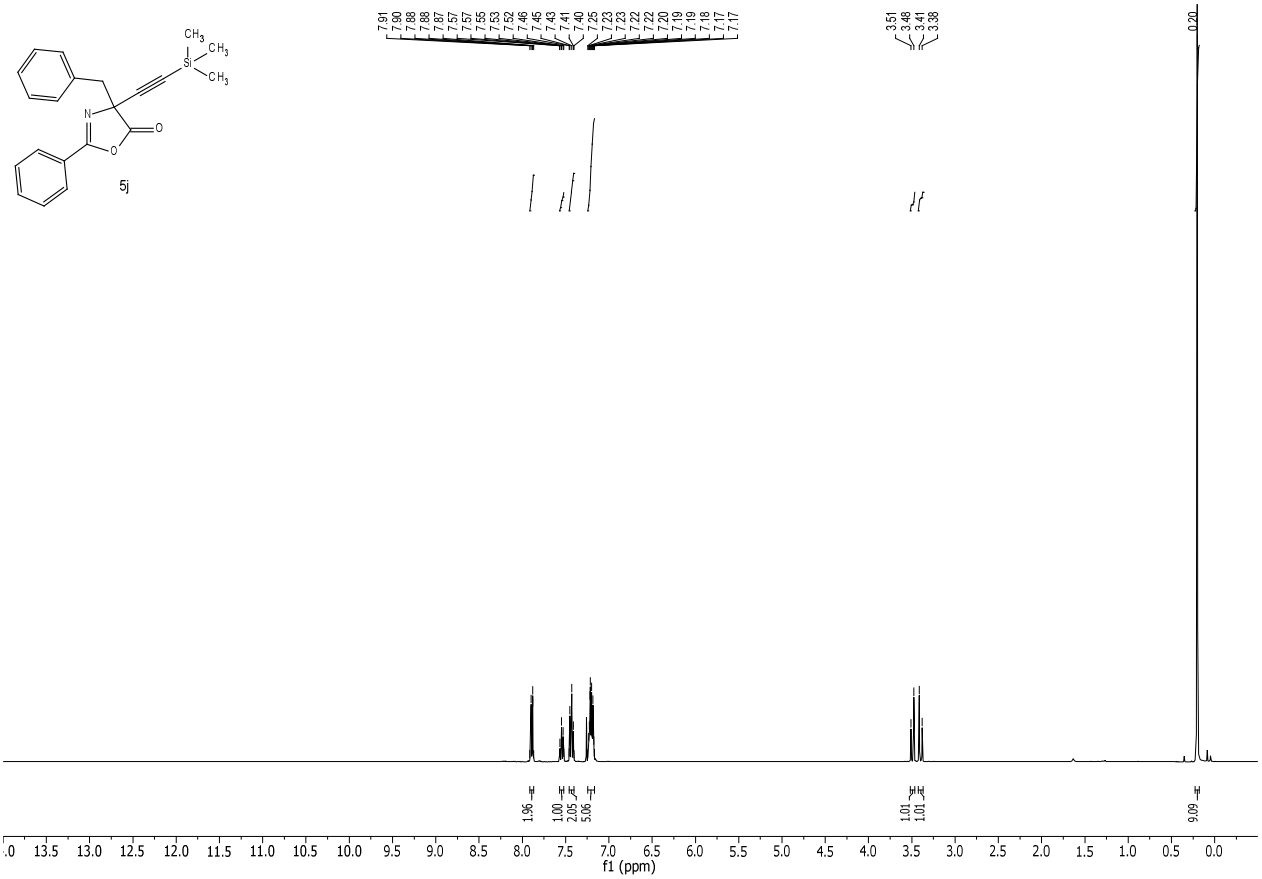

5g
173.72
162.62
135.45
133.44
129.16
128.91
128.89
128.45
126.03
125.26
98.06
92.86
69.24
-0.37
f1 (ppm)

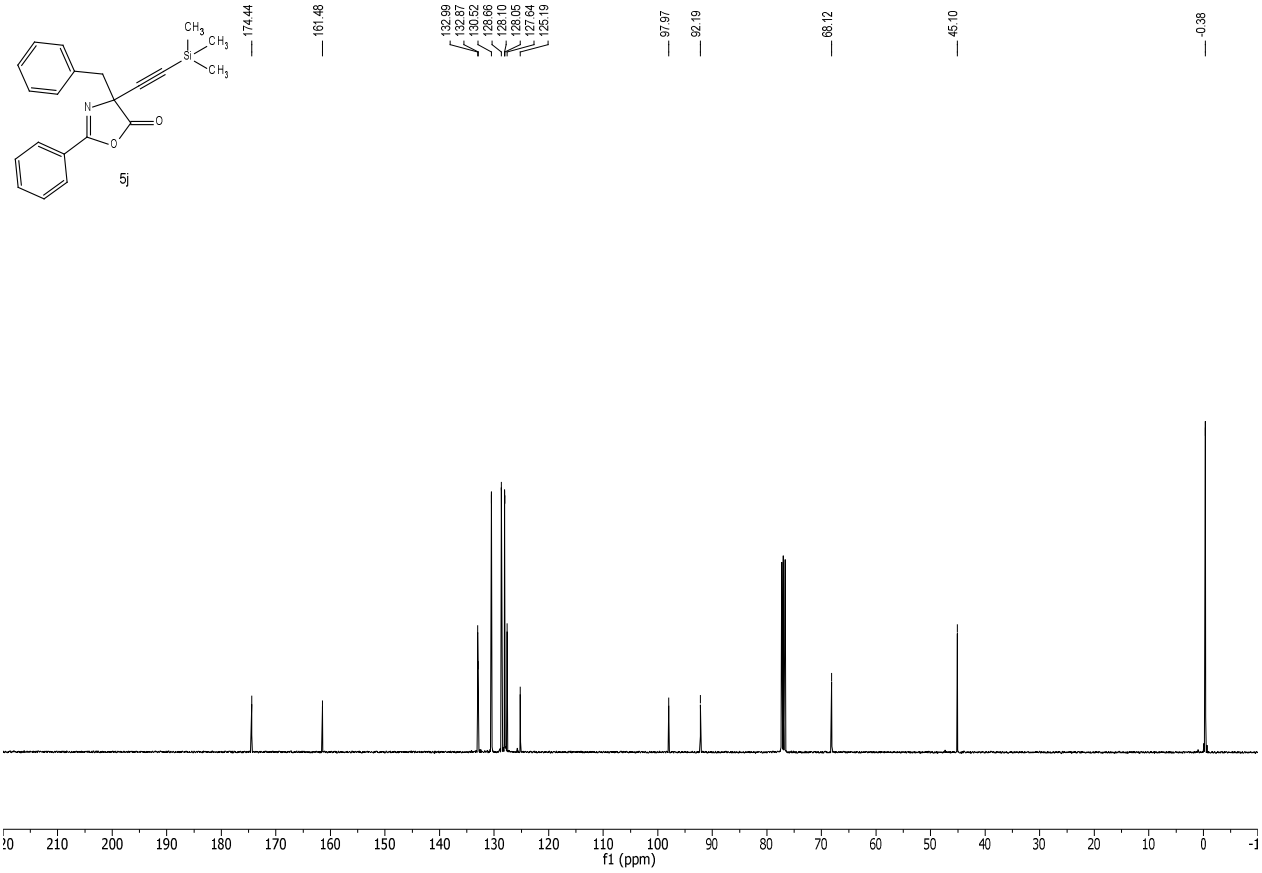

5h
f1 (ppm)

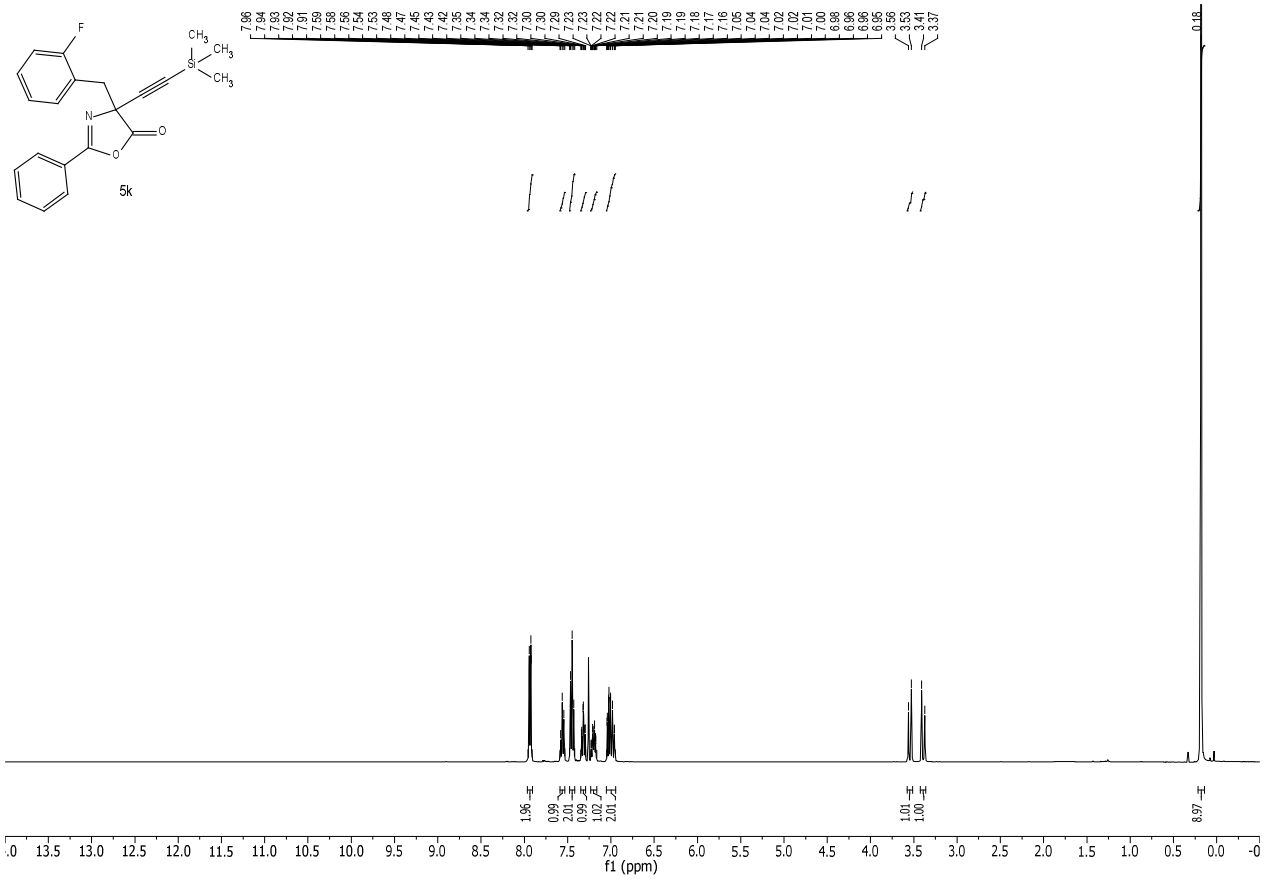

5h
f1 (ppm)

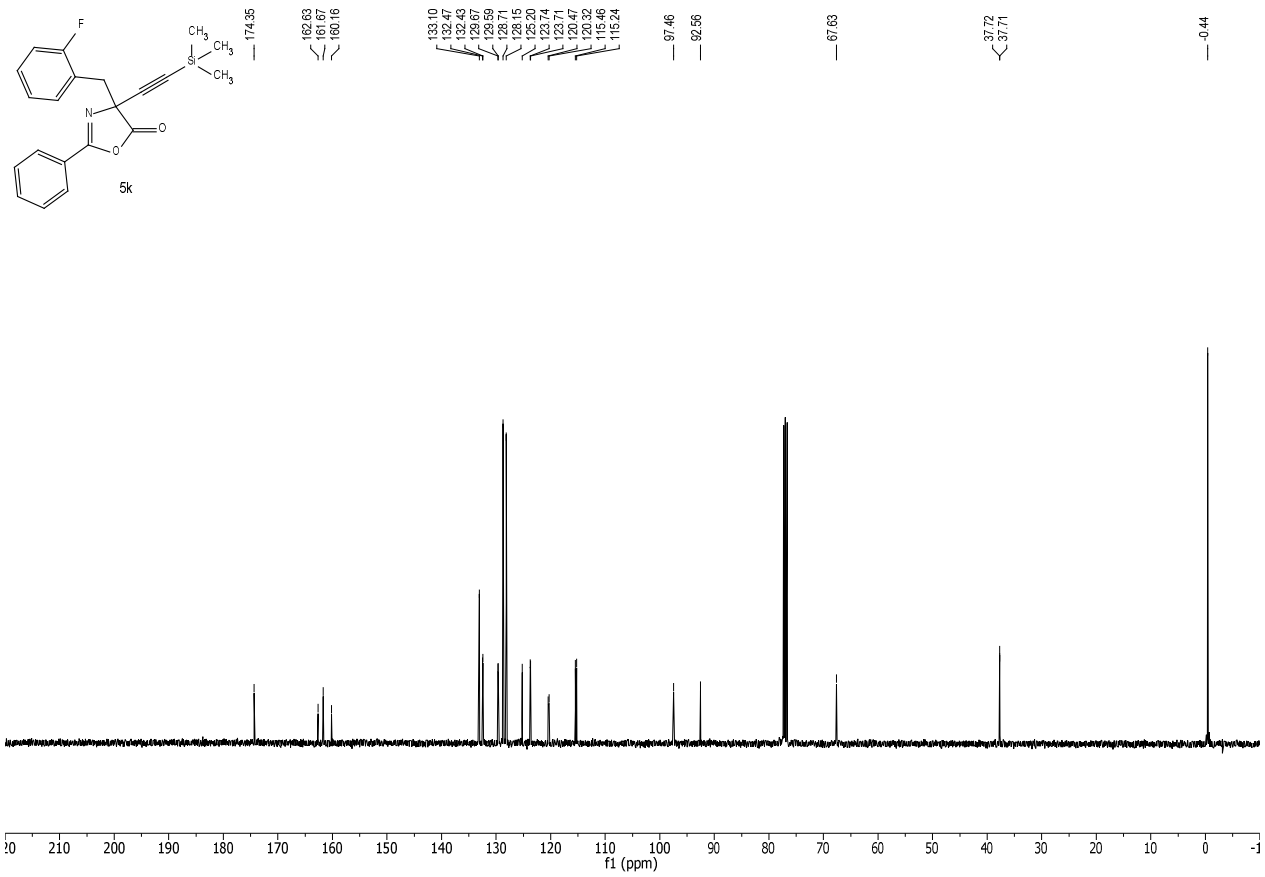

5i
8.03
8.02
8.01
7.62
7.60
7.58
7.51
7.49
7.47
7.37
7.35
7.34
7.32
7.30
7.29
5.07
4.78
3.20
3.18
2.16
2.13
2.10
2.02
1.99
1.96
1.58
1.57
1.47
0.18
1.97
0.99
2.00
4.88
2.01
0.77
2.00
2.03
4.00
9.00
f1 (ppm)

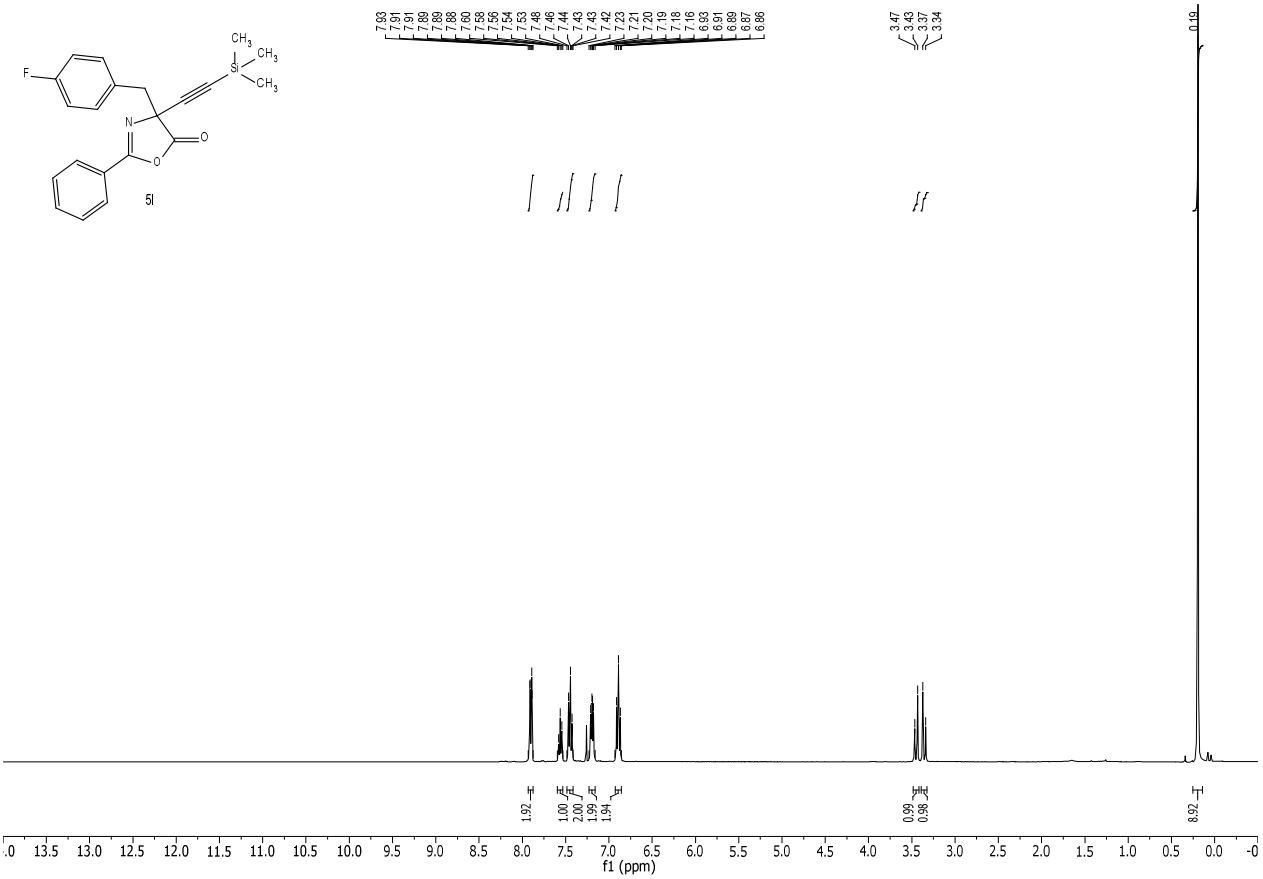

5i
175.01
161.69
156.25
136.50
133.18
128.80
128.47
128.22
126.06
125.28
97.91
91.74
66.95
66.59
40.63
38.55
29.41
21.08
-0.36
f1 (ppm)

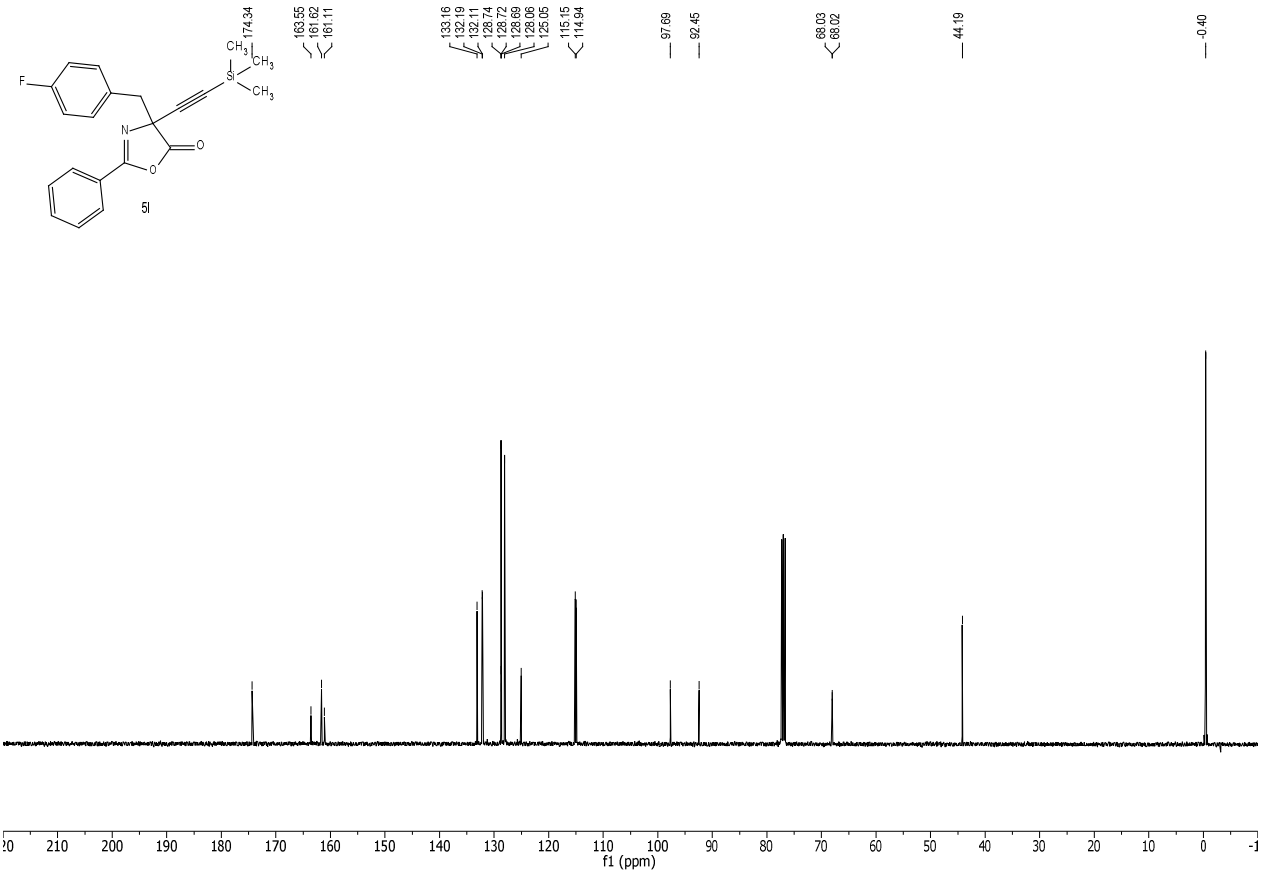

5j
7.91
7.90
7.88
7.88
7.87
7.57
7.57
7.55
7.53
7.52
7.46
7.45
7.43
7.41
7.40
7.25
7.23
7.23
7.22
7.22
7.20
7.19
7.19
7.18
7.17
7.17
3.51
3.48
3.41
3.38
0.20
1.96
1.00
2.05
5.06
1.01
1.01
9.09
f1 (ppm)

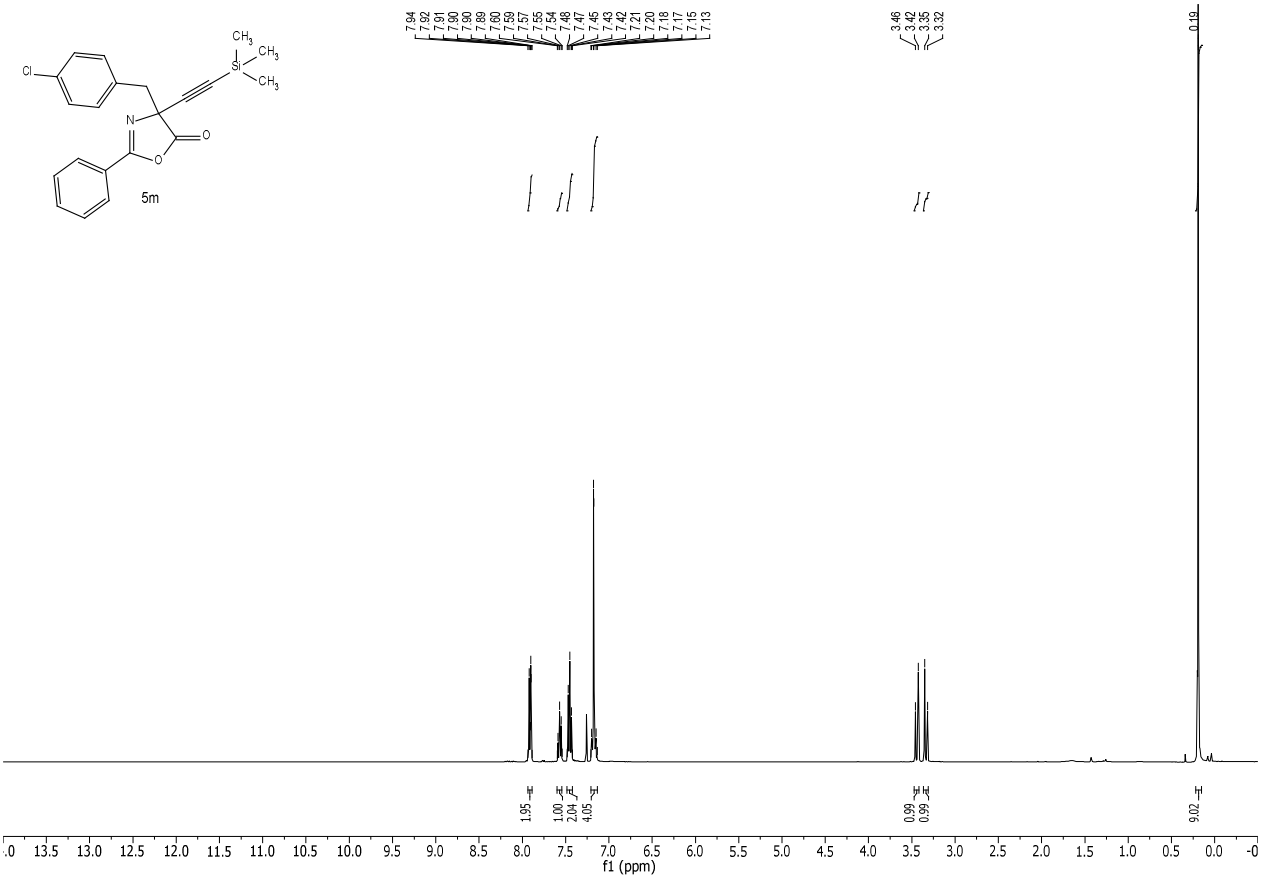

5j
174.44
161.48
132.99
132.87
130.52
128.66
128.10
128.05
127.64
125.19
97.97
92.19
68.12
45.10
-0.38
f1 (ppm)

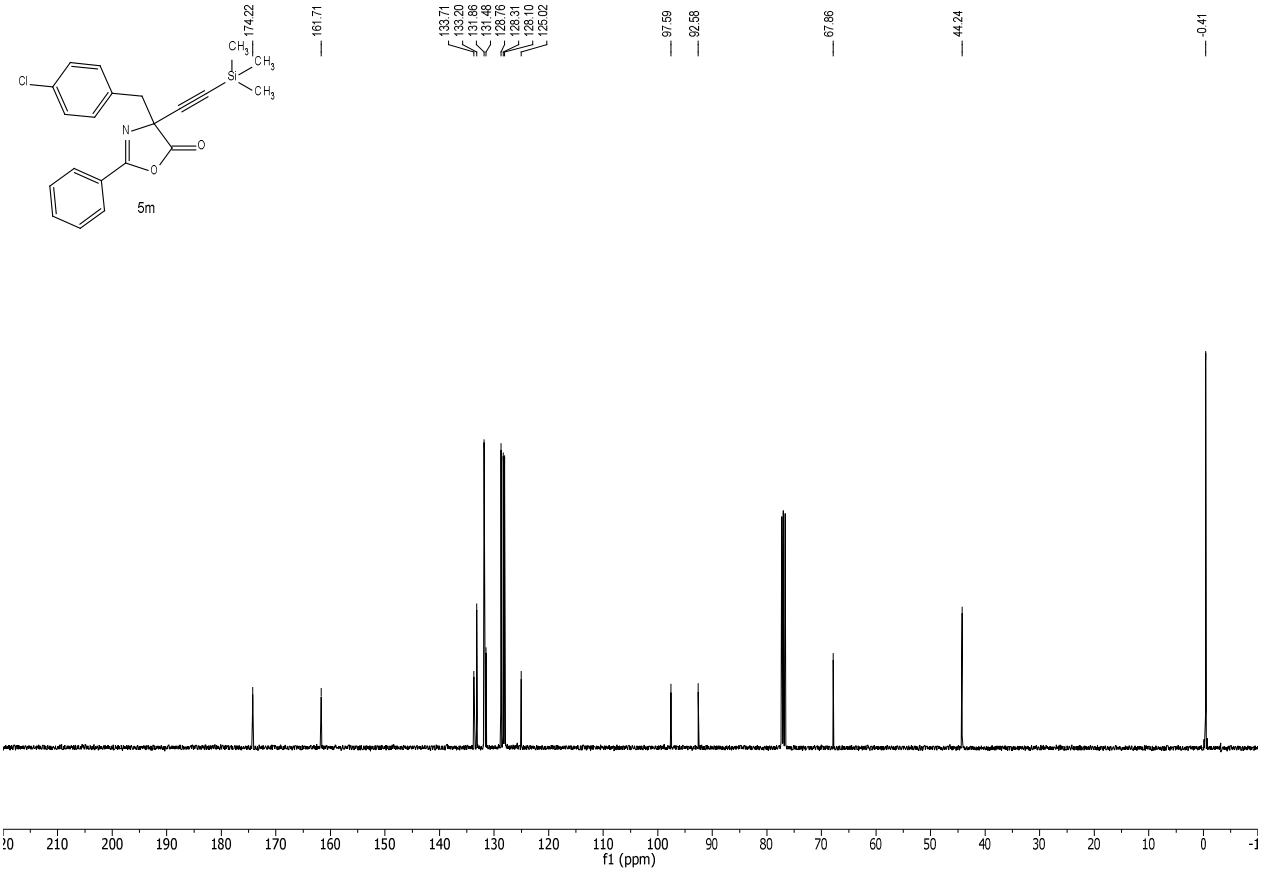

F
CH3
CH3
Si
CH3
N
O
O
5k
7.96
7.94
7.93
7.92
7.91
7.59
7.58
7.56
7.54
7.53
7.48
7.47
7.45
7.43
7.42
7.35
7.34
7.34
7.32
7.32
7.30
7.30
7.29
7.23
7.23
7.22
7.22
7.21
7.21
7.20
7.19
7.19
7.18
7.17
7.16
7.05
7.04
7.04
7.02
7.02
7.01
7.00
6.98
6.96
6.96
6.95
3.56
3.53
3.41
3.37
0.18
1.96
0.99
2.01
0.99
1.02
2.01
1.01
1.00
8.97
f1 (ppm)

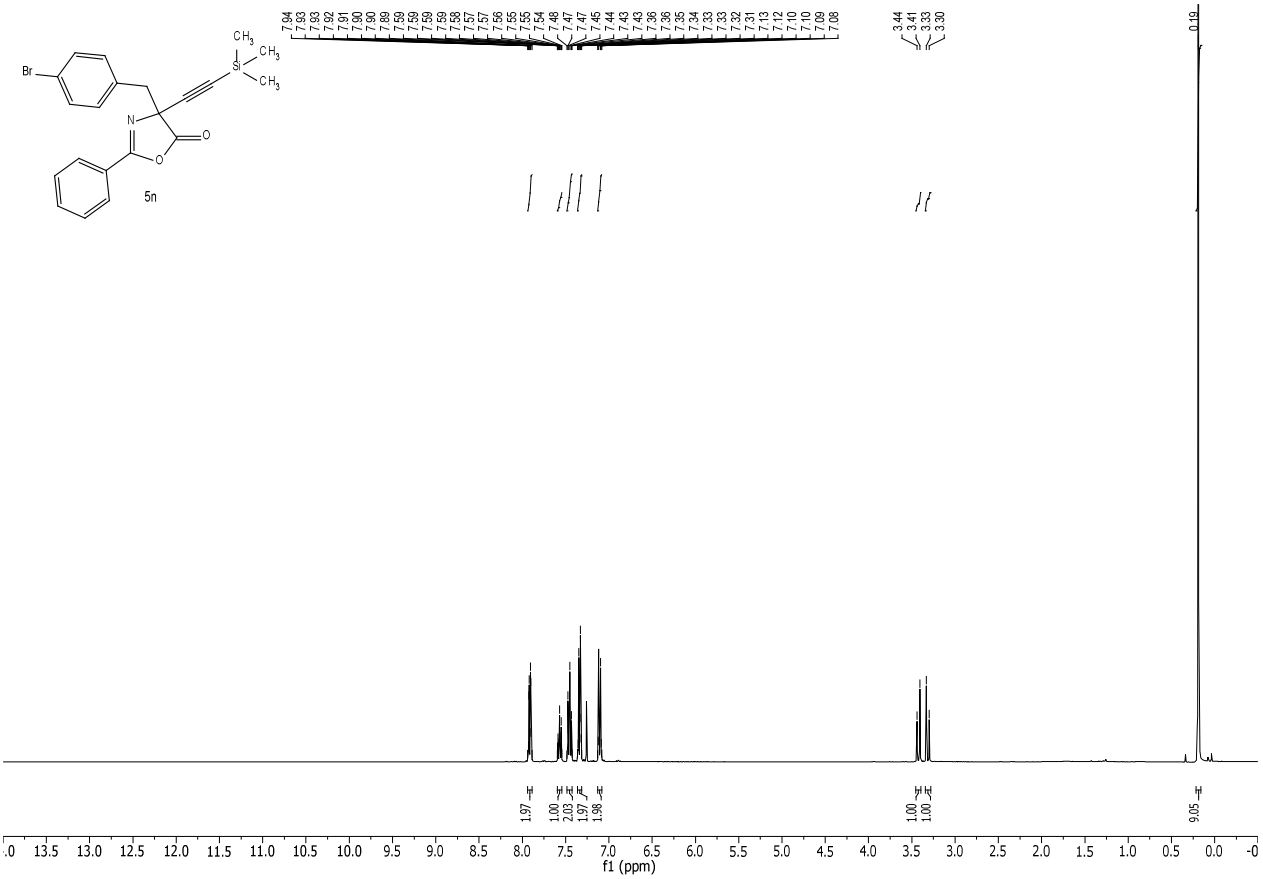

F
CH3
CH3
Si
CH3
N
O
O
5k
174.35
162.63
161.67
160.16
133.10
132.47
132.43
129.67
129.59
128.71
128.15
125.20
123.74
123.71
120.47
120.32
115.46
115.24
97.46
92.56
67.63
37.72
37.71
-0.44
f1 (ppm)

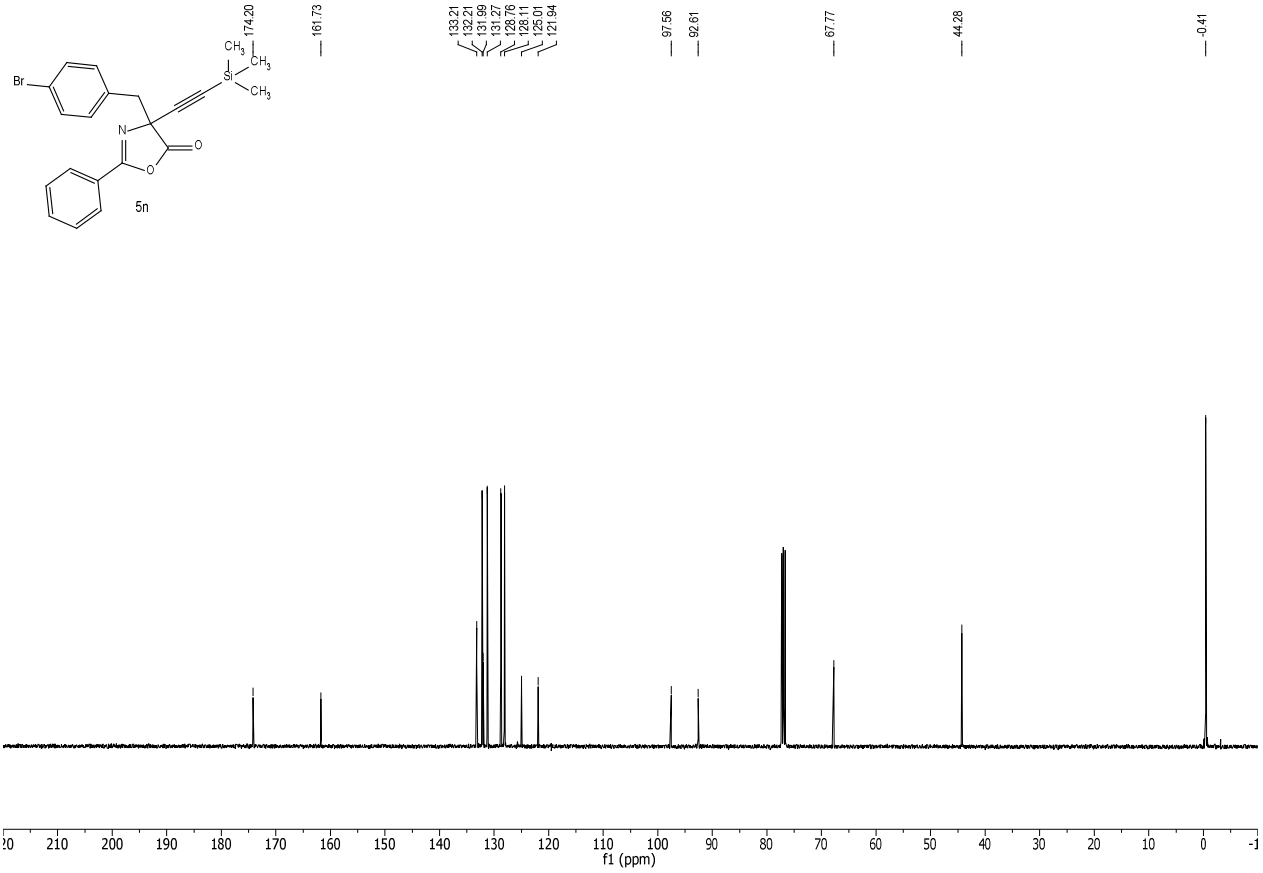

5l
7.93
7.91
7.91
7.89
7.89
7.88
7.60
7.58
7.56
7.54
7.53
7.48
7.46
7.44
7.43
7.43
7.42
7.23
7.21
7.20
7.19
7.18
7.16
6.93
6.91
6.89
6.87
6.86
3.47
3.43
3.37
3.34
0.19
1.92
1.00
2.00
1.99
1.94
0.99
0.98
8.92
f1 (ppm)

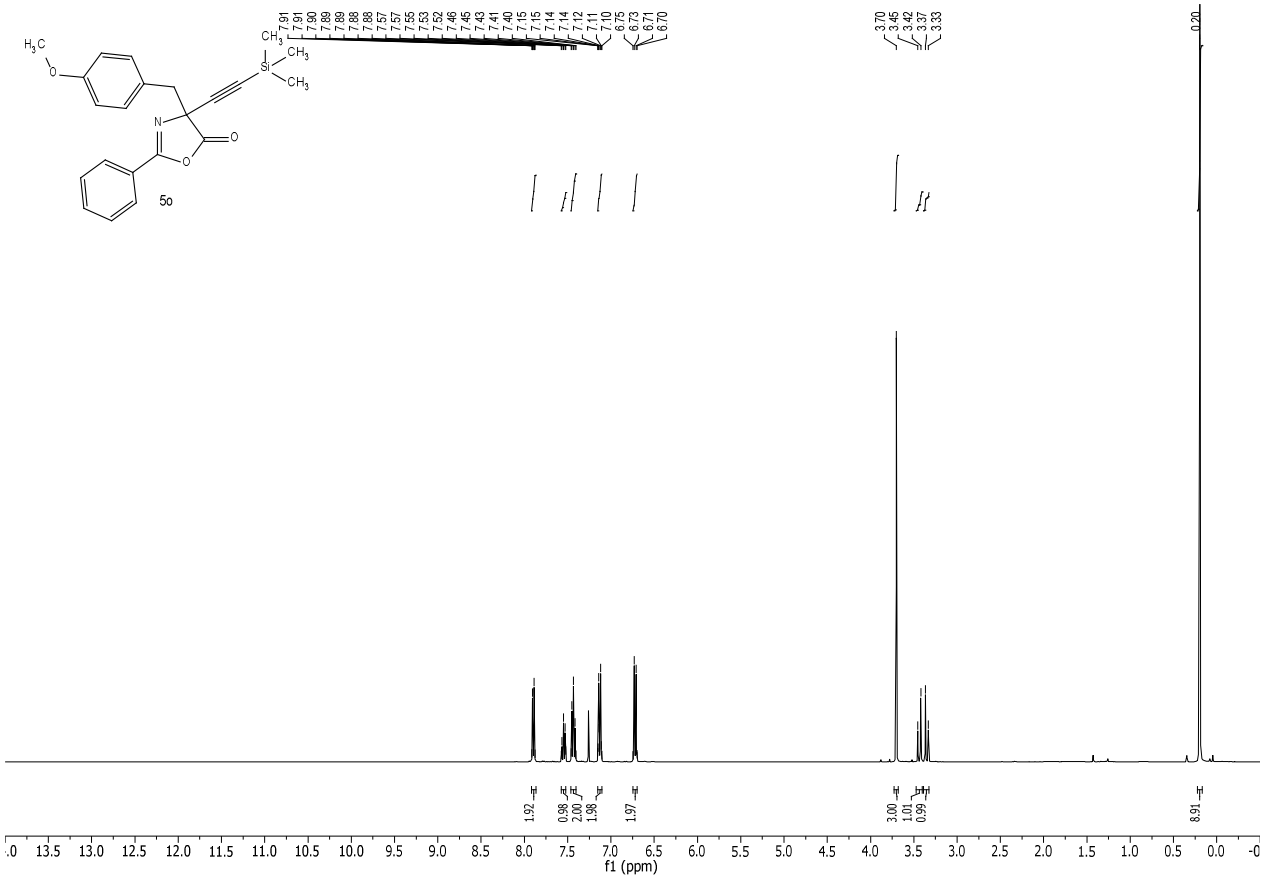

5l
174.34
163.55
161.62
161.11
133.16
132.19
132.11
128.74
128.72
128.69
128.06
125.05
115.15
114.94
97.69
92.45
68.03
68.02
44.19
-0.40
f1 (ppm)

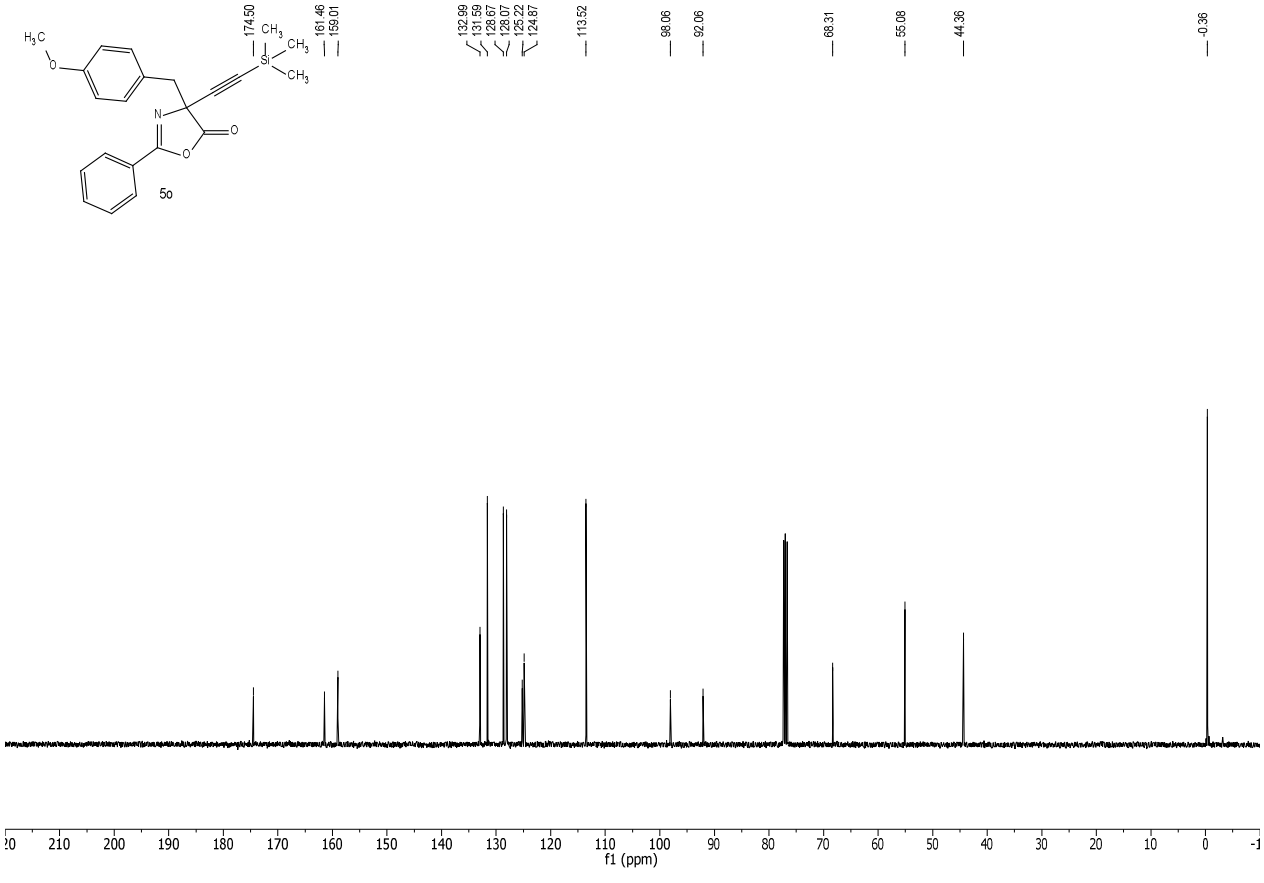

Cl
CH3
CH3
Si
CH3
N
O
O
5m
7.94
7.92
7.91
7.90
7.90
7.89
7.60
7.59
7.57
7.55
7.54
7.48
7.47
7.45
7.43
7.42
7.21
7.20
7.18
7.17
7.15
7.13
3.46
3.42
3.35
3.32
0.19
1.95
1.00
2.04
4.05
0.99
0.99
9.02
f1 (ppm)

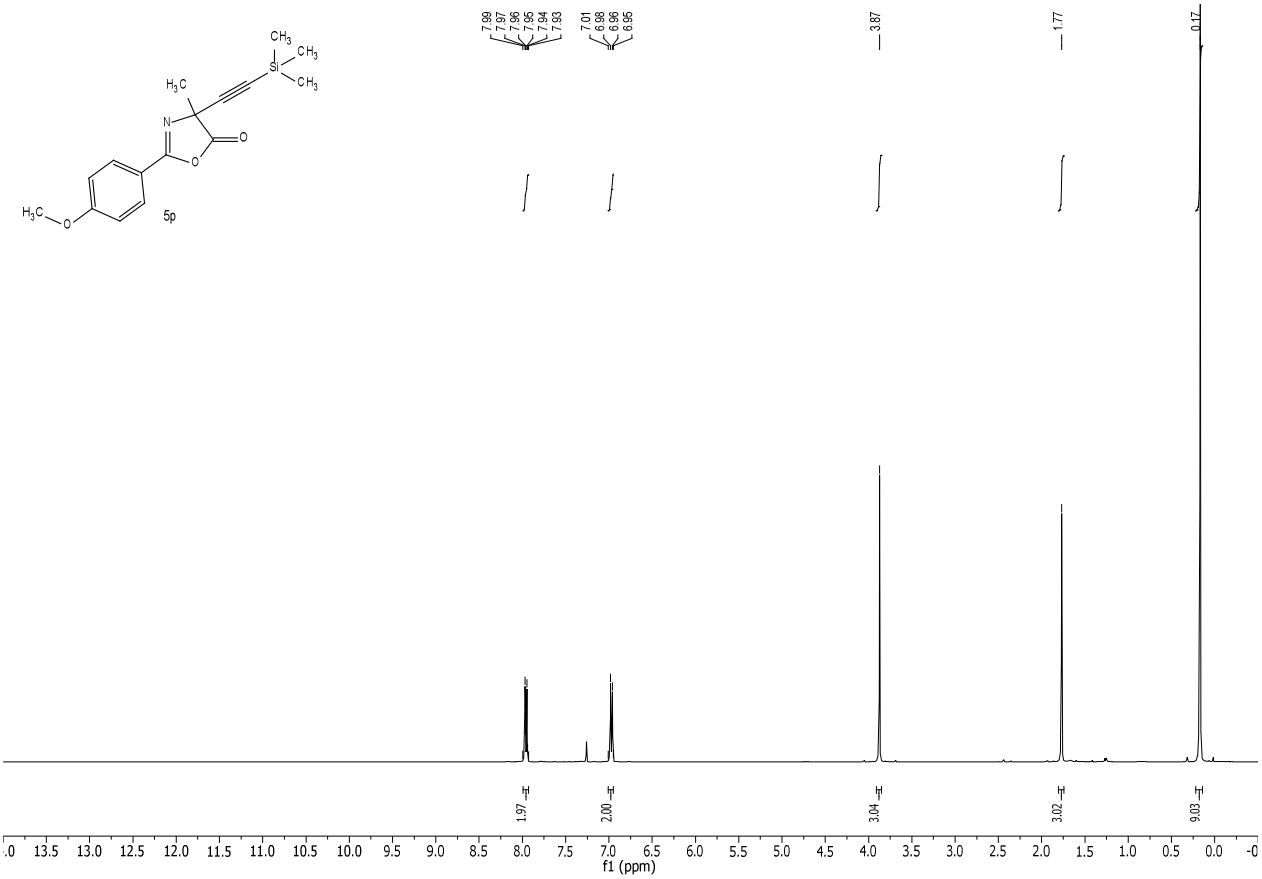

Cl
CH3
CH3
Si
CH3
N
O
O
5m
174.22
161.71
133.71
133.20
131.86
131.48
128.76
128.31
128.10
125.02
97.59
92.58
67.86
44.24
-0.41
f1 (ppm)

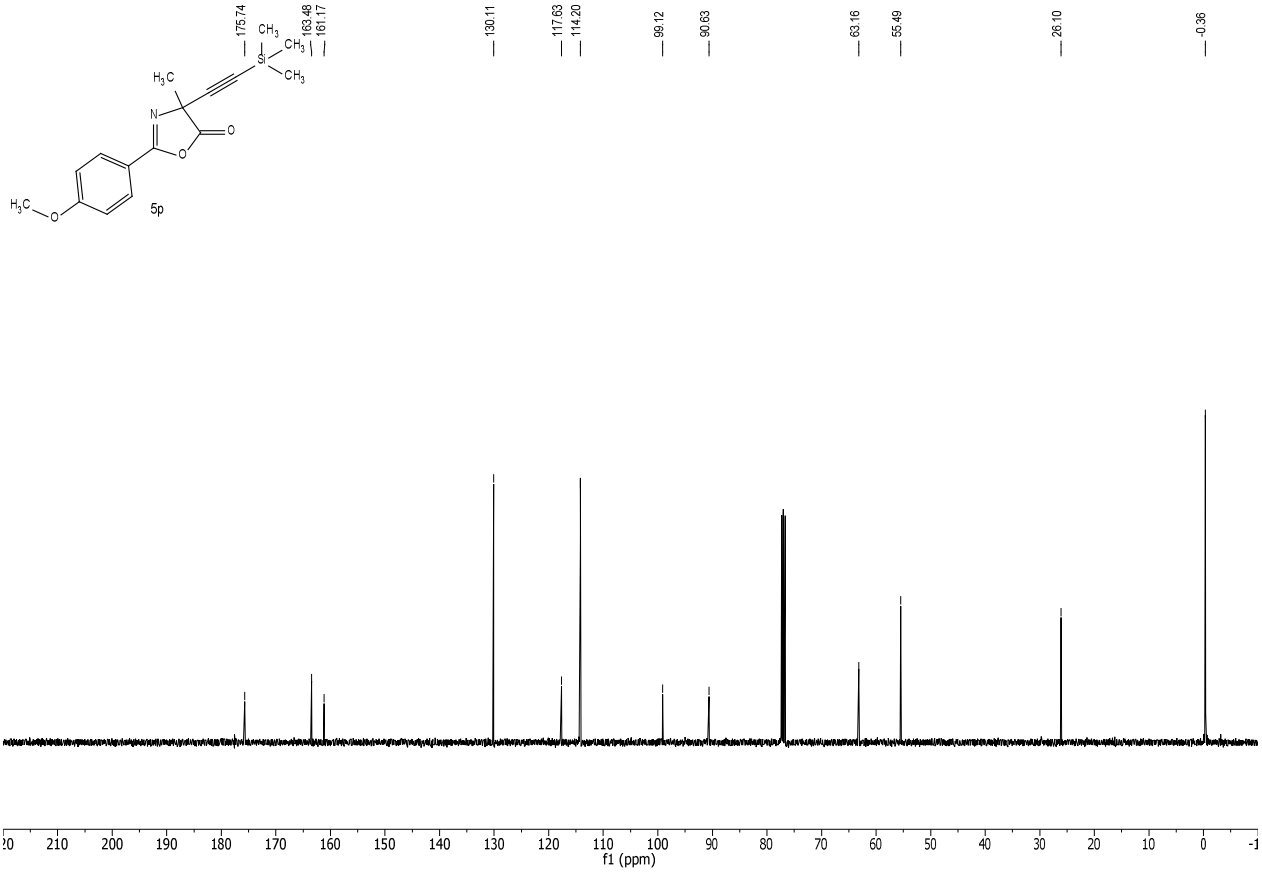

5n
f1 (ppm)

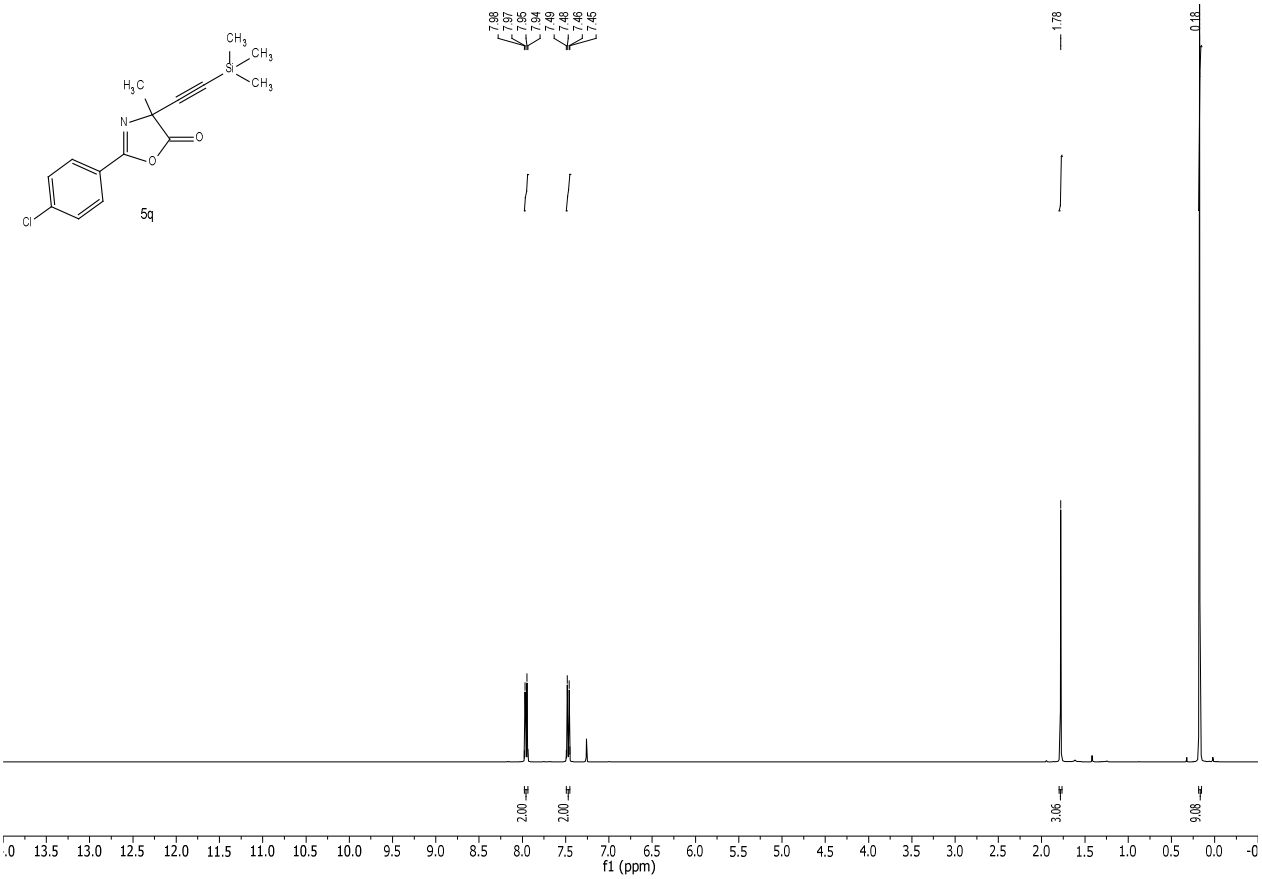

5n
f1 (ppm)

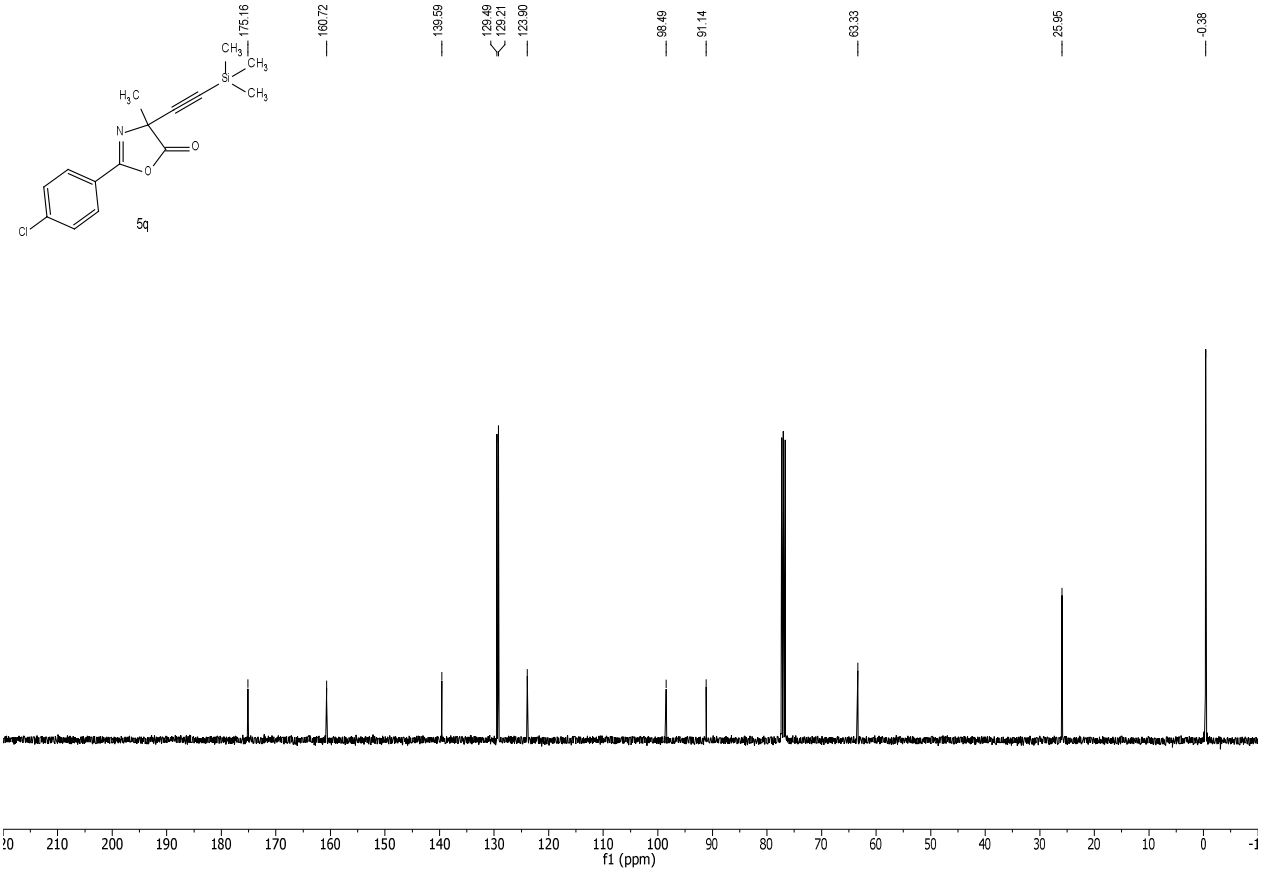

5o
7.91 7.91 7.90 7.89 7.89 7.88 7.88 7.57 7.57 7.55 7.53 7.52 7.46 7.45 7.43 7.41 7.40 7.15 7.15 7.14 7.14 7.12 7.11 7.10 6.75 6.73 6.71 6.70
3.70 3.45 3.42 3.37 3.33
0.20
1.92 0.98 2.00 1.98 1.97 3.00 1.01 0.99 8.91
f1 (ppm)

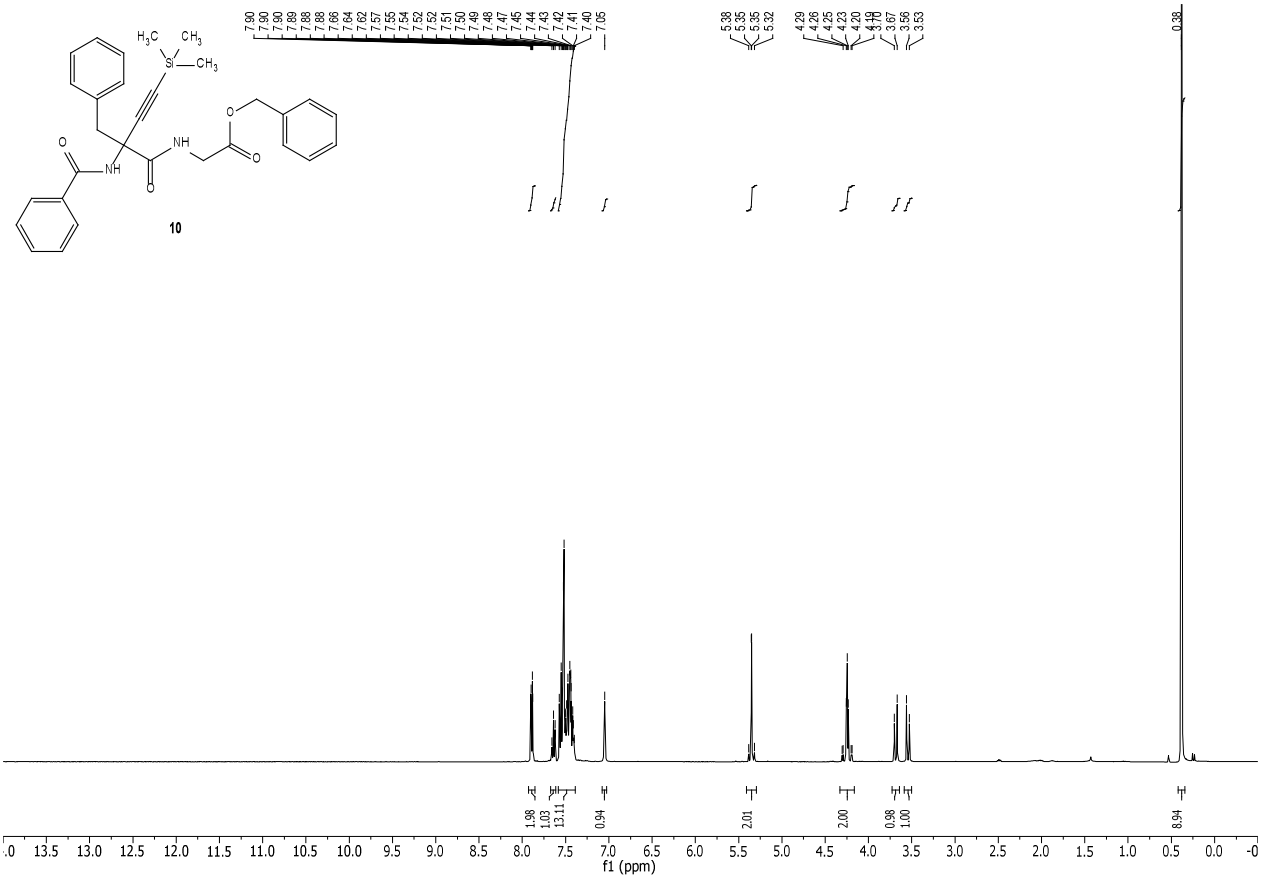

5o
174.50 161.46 159.01 132.99 131.59 128.67 128.07 125.22 124.87 113.52 98.06 92.06 68.31 55.08 44.36 -0.36
f1 (ppm)

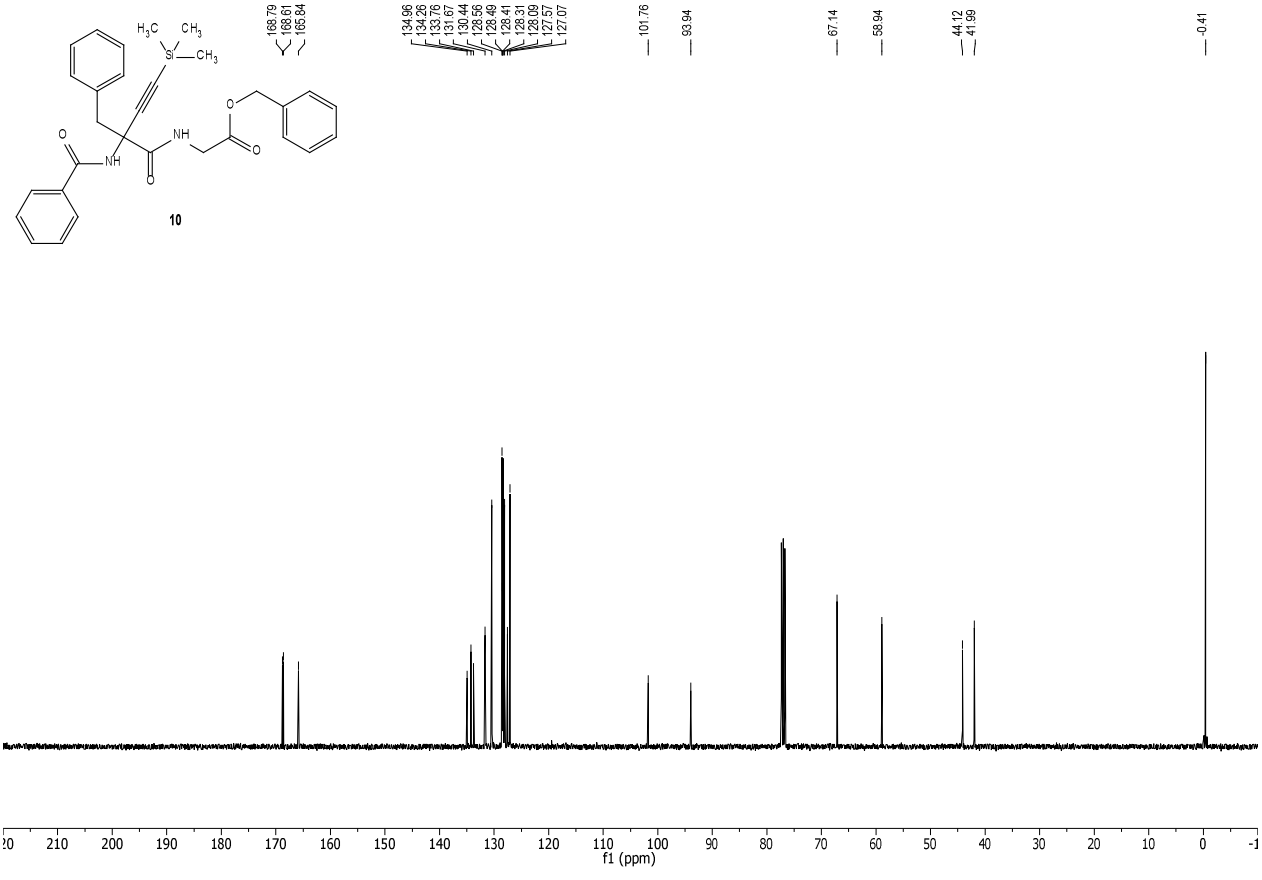

7.99
7.97
7.96
7.95
7.94
7.93
7.01
6.98
6.96
6.95
3.87
1.77
0.17
1.97
2.00
3.04
3.02
9.03
f1 (ppm)
5p

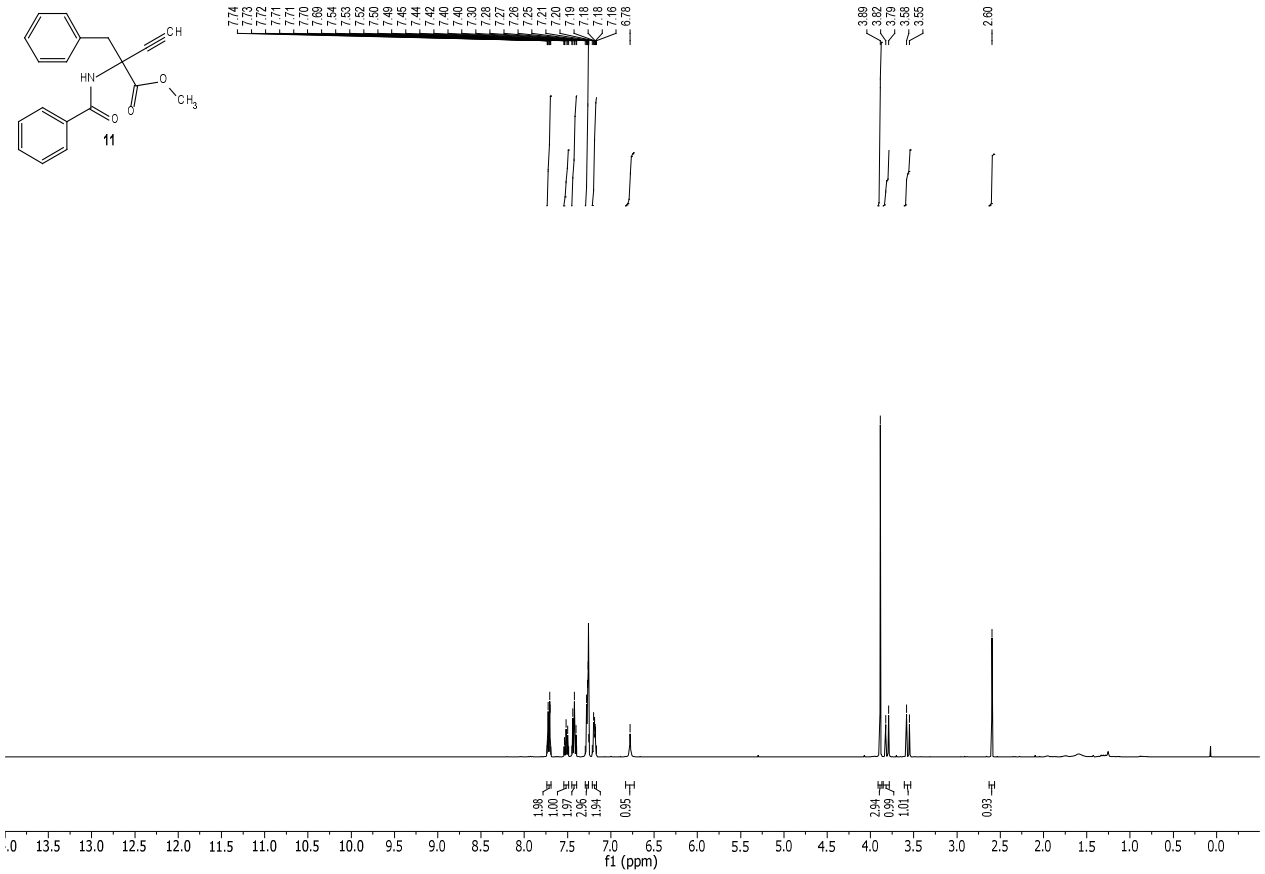

175.74
163.48
161.17
130.11
117.63
114.20
99.12
90.63
63.16
55.49
26.10
-0.36
f1 (ppm)
5p

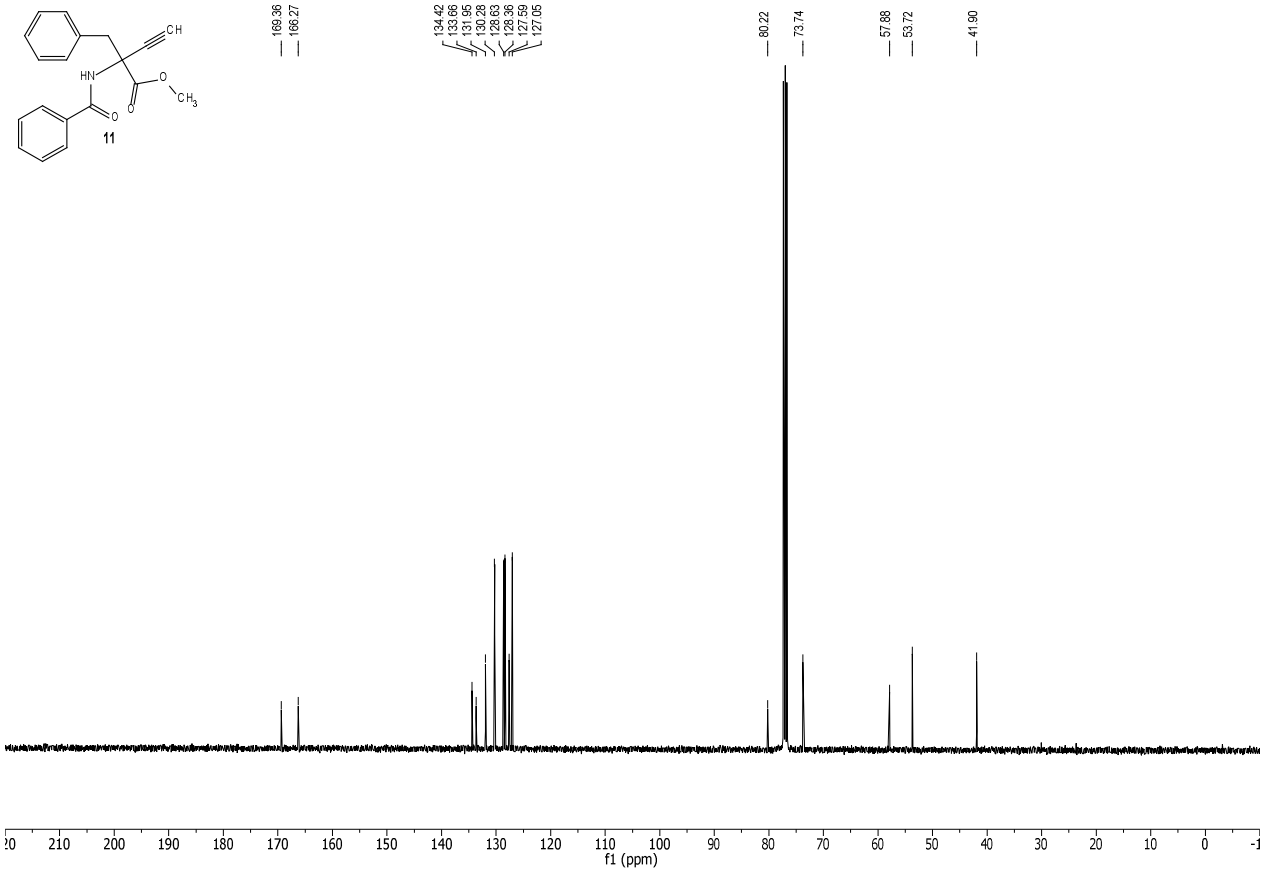

7.98
7.97
7.95
7.94
7.49
7.48
7.46
7.45
1.78
0.18
2.00
2.00
3.06
9.08
f1 (ppm)
5q

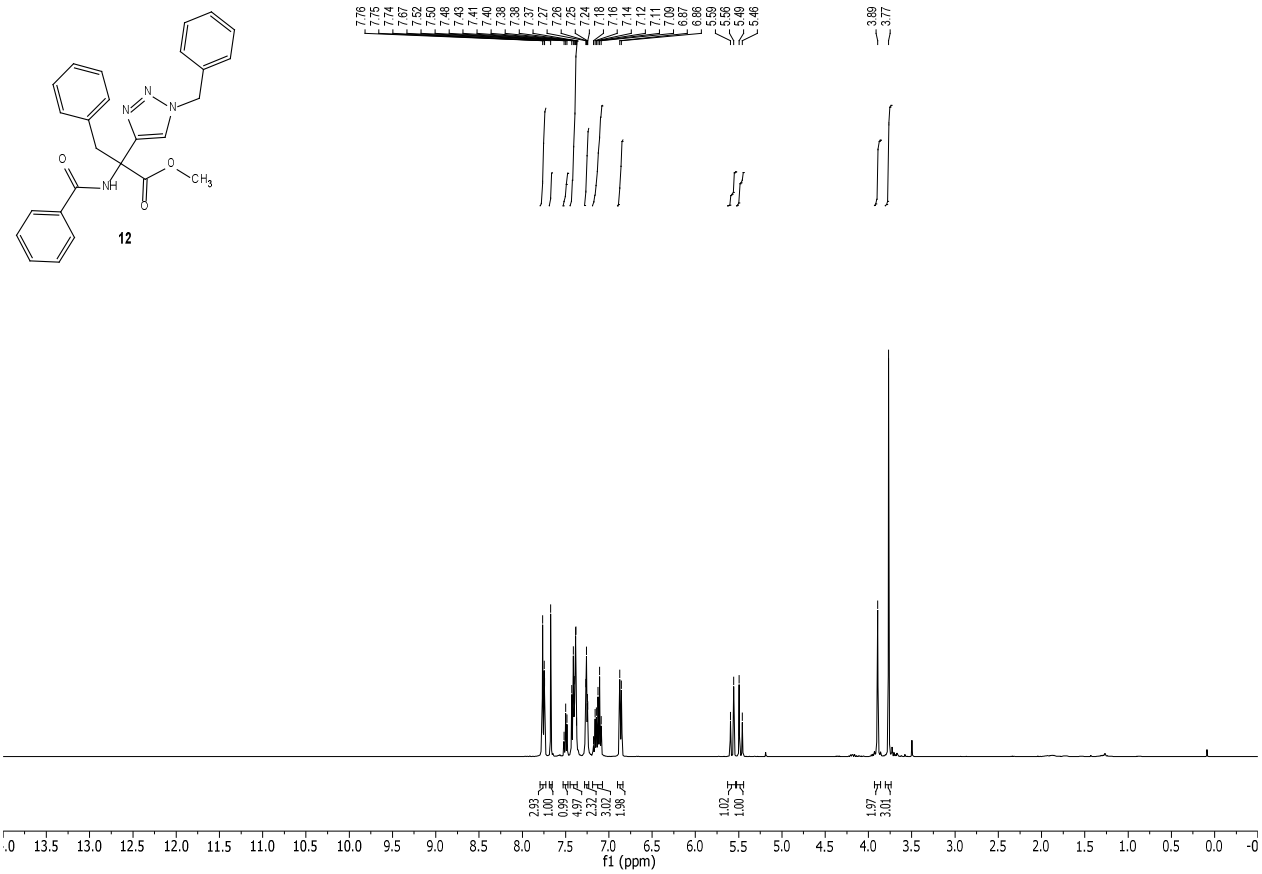

175.16
160.72
139.59
129.49
129.21
123.90
98.49
91.14
83.33
25.95
-0.38
f1 (ppm)
5q

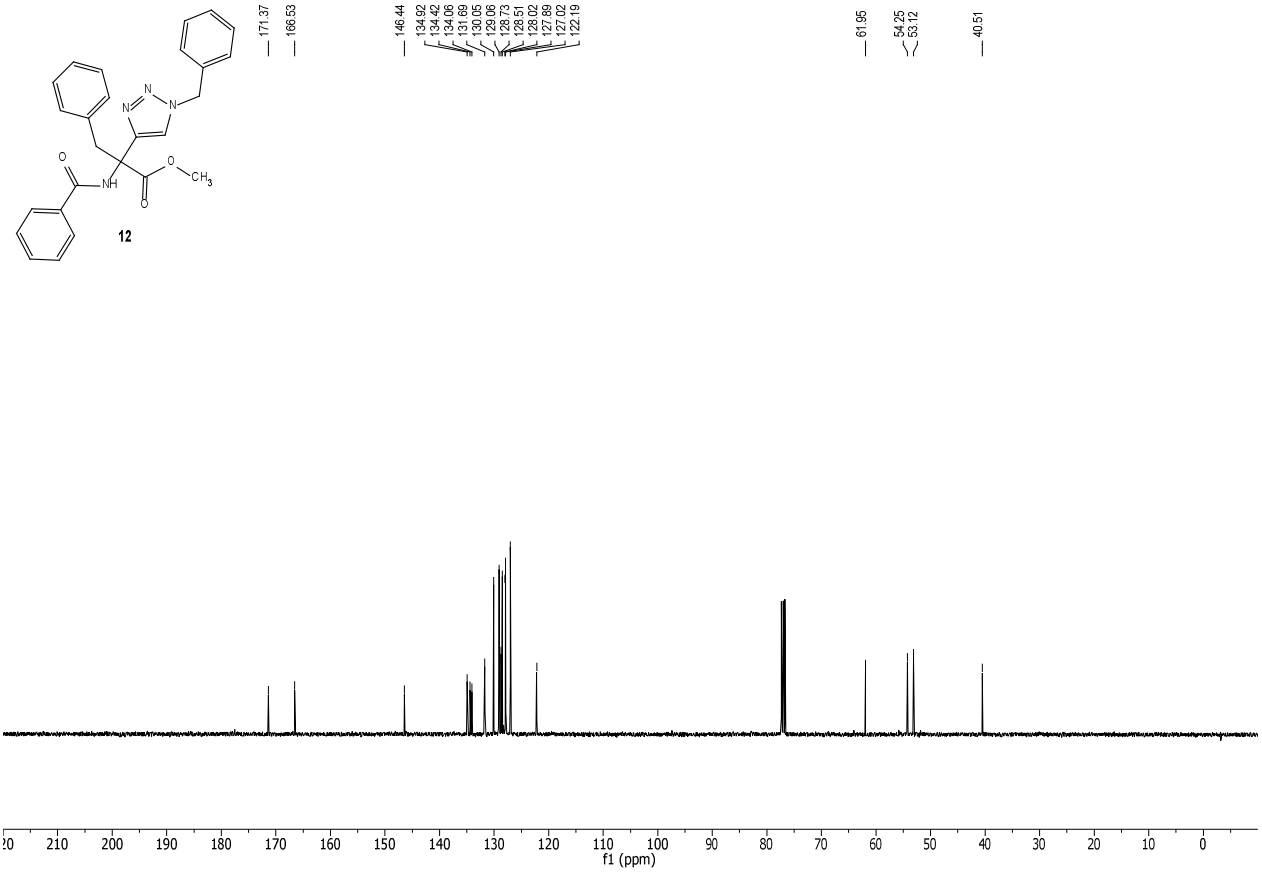

10
f1 (ppm)

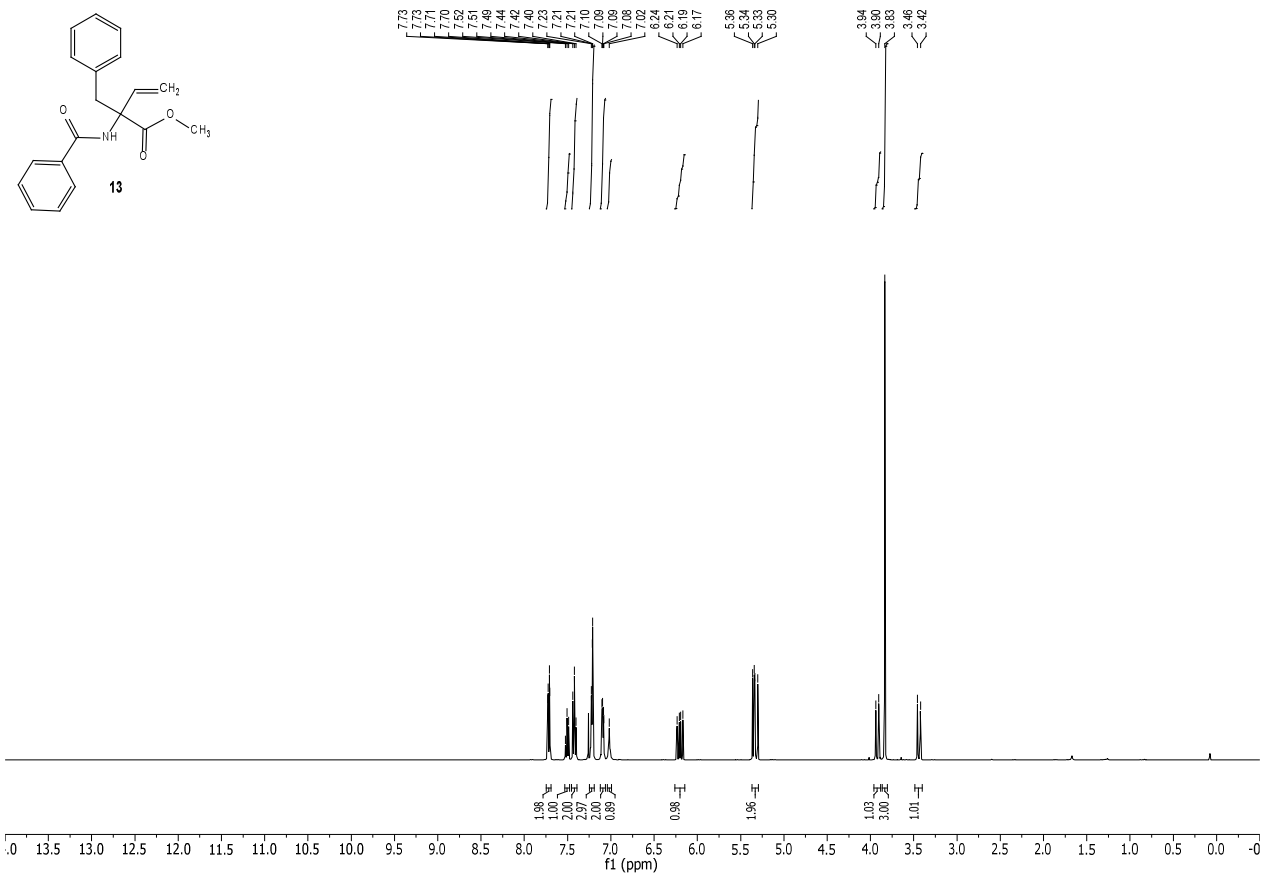

10
f1 (ppm)

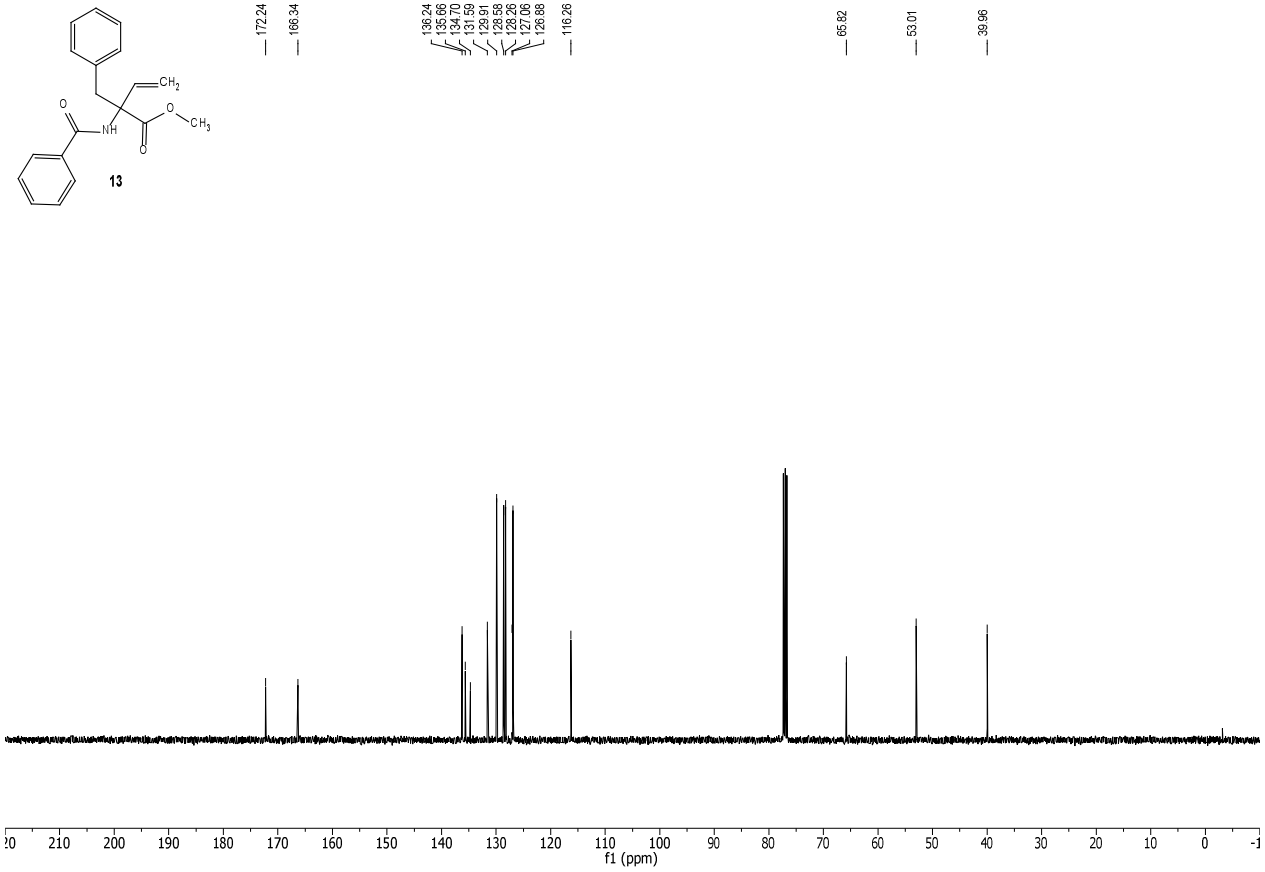

11
7.74
7.73
7.72
7.71
7.71
7.70
7.69
7.54
7.53
7.52
7.50
7.49
7.45
7.44
7.42
7.40
7.40
7.30
7.28
7.27
7.26
7.25
7.21
7.20
7.19
7.18
7.18
7.16
6.78
3.89
3.82
3.79
3.58
3.55
2.60
1.98
1.00
1.97
2.96
1.94
0.95
2.94
0.99
1.01
0.93
f1 (ppm)


11
169.36
168.27
134.42
133.66
131.95
130.28
128.63
128.36
127.59
127.05
80.22
73.74
57.88
53.72
41.90
f1 (ppm)


12
7.76
7.75
7.74
7.67
7.52
7.50
7.48
7.43
7.41
7.40
7.38
7.38
7.37
7.27
7.26
7.25
7.24
7.18
7.16
7.14
7.12
7.11
7.09
6.87
6.86
5.59
5.56
5.49
5.46
3.89
3.77
2.93
1.00
0.99
4.97
2.32
3.02
1.98
1.02
1.00
1.97
3.01
f1 (ppm)


12
171.37
166.53
146.44
134.92
134.42
134.06
131.69
130.05
129.06
128.73
128.51
128.02
127.89
127.02
122.19
61.95
54.25
53.12
40.51
f1 (ppm)


13
7.73
7.73
7.71
7.70
7.52
7.51
7.49
7.44
7.42
7.40
7.23
7.21
7.21
7.10
7.09
7.09
7.08
7.02
6.24
6.21
6.19
6.17
5.36
5.34
5.33
5.30
3.94
3.90
3.83
3.46
3.42
1.98
1.00
2.00
2.97
2.00
0.89
0.98
1.96
1.03
3.00
1.01
f1 (ppm)


13
172.24
166.34
136.24
135.66
134.70
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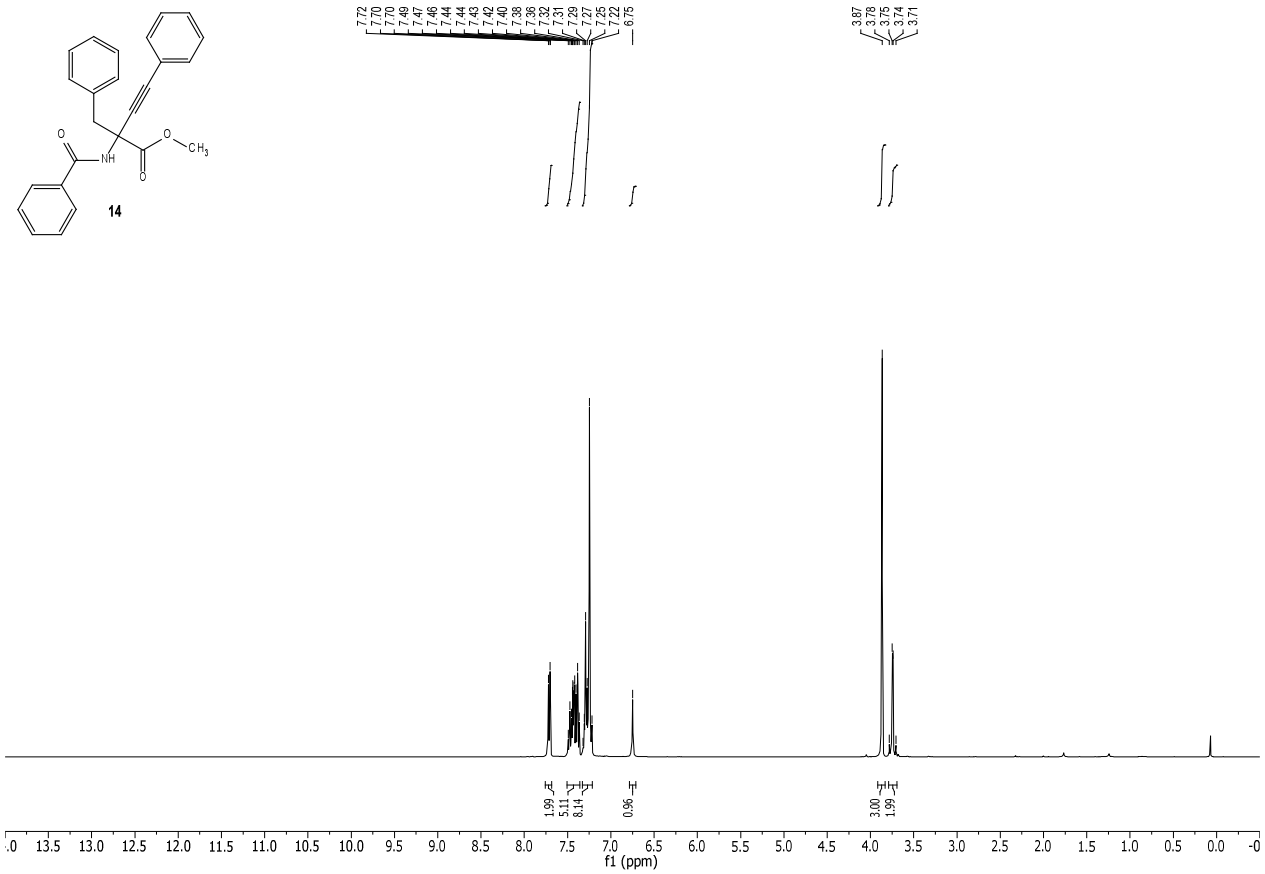
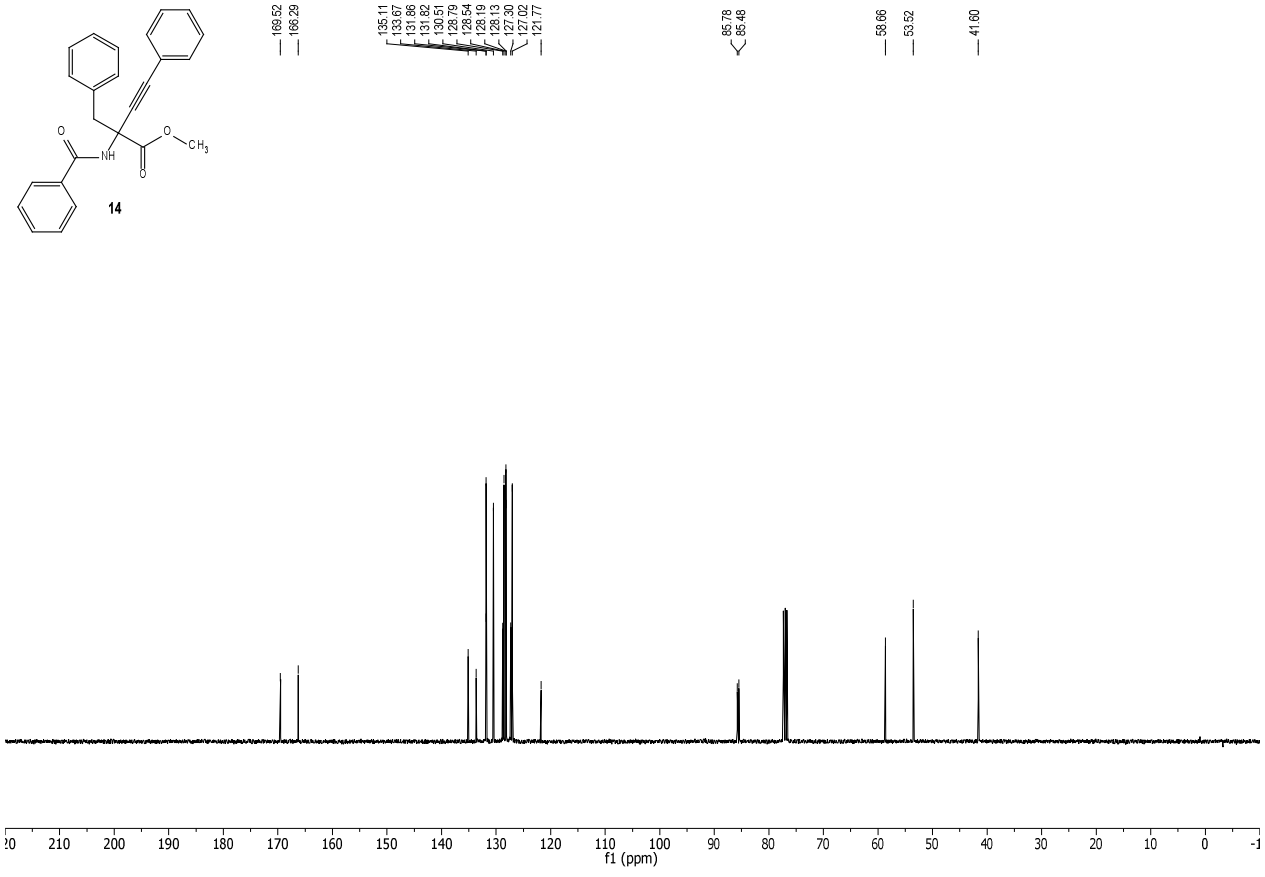
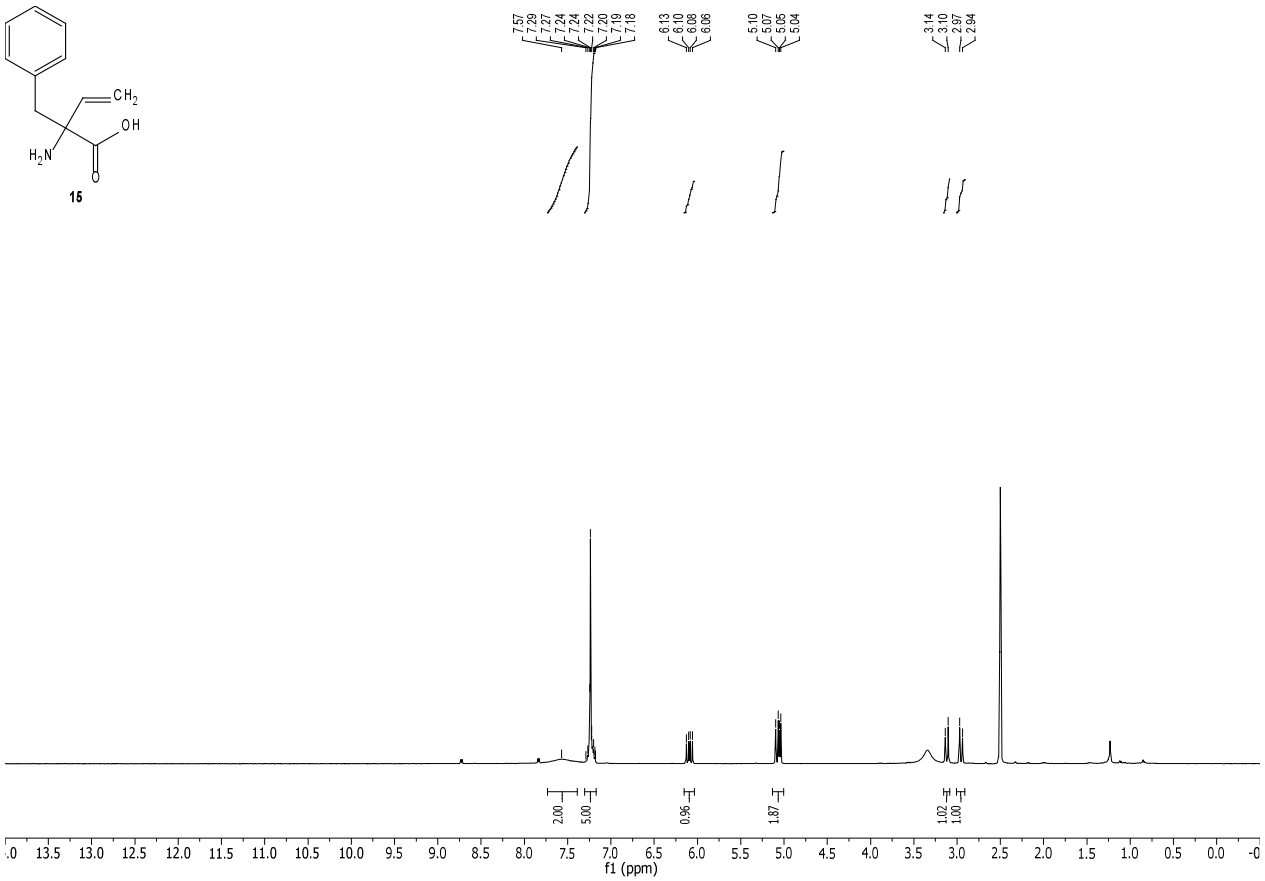
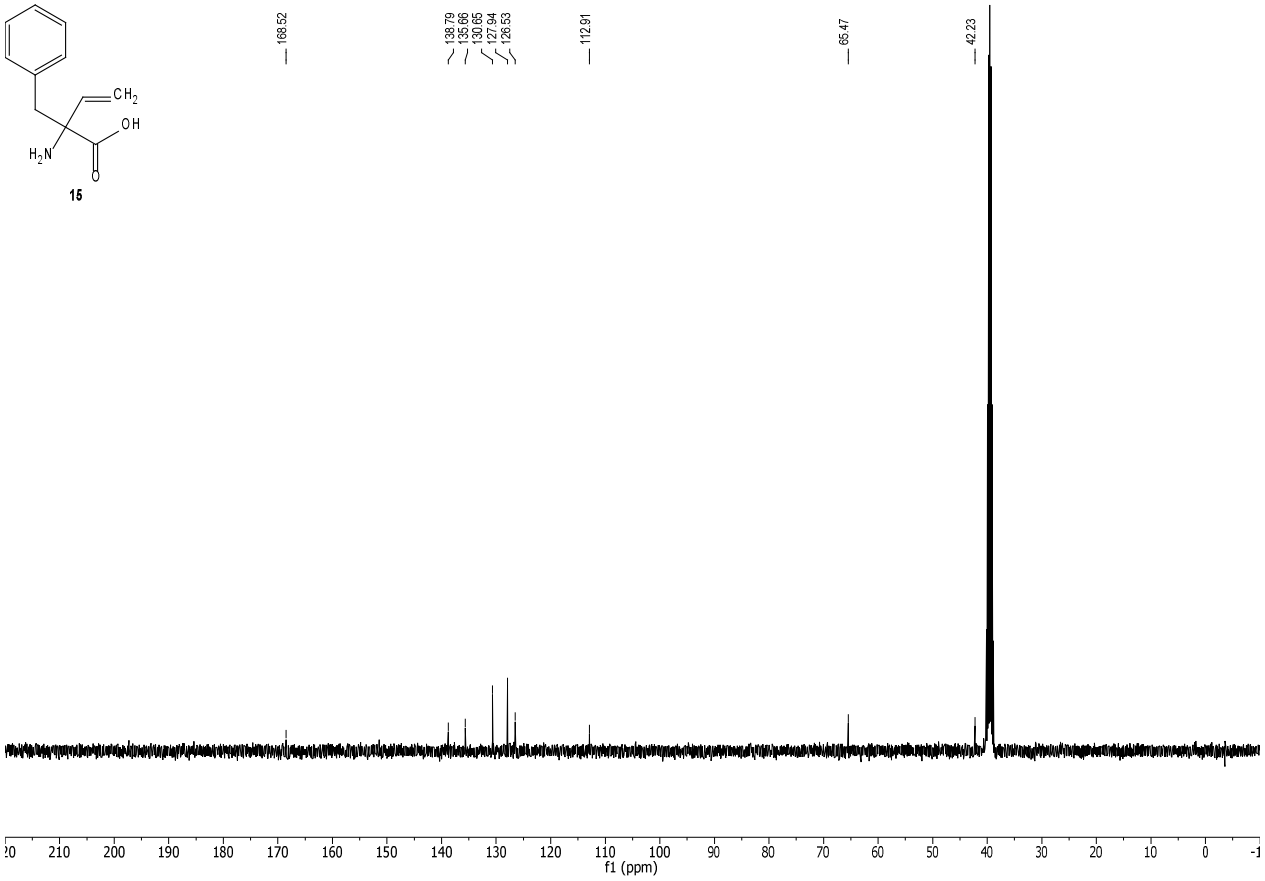
129.91
128.58
128.26
127.06
126.88
116.26
65.82
53.01
39.96
f1 (ppm)


14
7.72
7.70
7.70
7.49
7.47
7.46
7.44
7.43
7.42
7.40
7.38
7.36
7.32
7.31
7.29
7.27
7.25
7.22
6.75
3.87
3.78
3.75
3.74
3.71
1.99
5.11
8.14
0.96
3.00
1.99
f1 (ppm)


14
169.52
166.29
135.11
133.67
131.86
131.82
130.51
128.79
128.54
128.19
128.13
127.30
127.02
121.77
85.78
85.48
58.86
53.52
41.60
f1 (ppm)


7.57
7.29
7.27
7.24
7.24
7.22
7.20
7.19
7.18
6.13
6.10
6.08
6.06
5.10
5.07
5.05
5.04
3.14
3.10
2.97
2.94
CH2
OH
H2N
O
15
2.00
5.00
0.96
1.87
1.02
1.00
f1 (ppm)


168.52
138.79
135.66
130.65
127.94
126.53
112.91
65.47
42.23
CH2
OH
H2N
O
15
f1 (ppm)