Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Supporting Information

Phosphine Catalyzed δ-Carbon Addition and Isomerization of Alkynones to Ketimines: Preparation of 1,3-Dienes Substituted Dihydroquinazolinones and 3-aminooxindoles

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CONTENTS

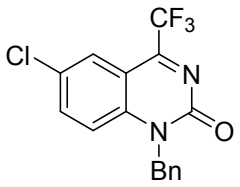
General Remarks. ^{1}H NMR spectra were recorded on a Varian Mercury-300 and 400 spectrometer for solution in $CDCl_3$ with tetramethylsilane (TMS) as an internal standard; coupling constants J are given in Hz. ^{13}C NMR spectra were recorded on a Varian Mercury-300 and 400 spectrophotometers (75 or 100 MHz) with complete proton decoupling spectrophotometers ($CDCl_3$: 77.0 ppm). Mass and HRMS spectra were recorded by EI or ESI method. Organic solvents used were dried by standard methods when necessary. Infrared spectra were recorded on a Perkin-Elmer PE-983 spectrometer with absorption in cm^{-1}. Melting points were determined on a digital melting point apparatus and temperatures were uncorrected. Commercially obtained reagents were used without further purification. All these reactions were monitored by TLC with silica gel coated plates. Flash column chromatography was carried out using silica gel at increased pressure.

Compound **1a** was commercially available compound. Compounds **1b-1d** are known compounds and prepared according to the previous literature.[1]

Compounds **4a-4g**, **6a**, and **8a** are known compounds and prepared according to the previous literature.[2]

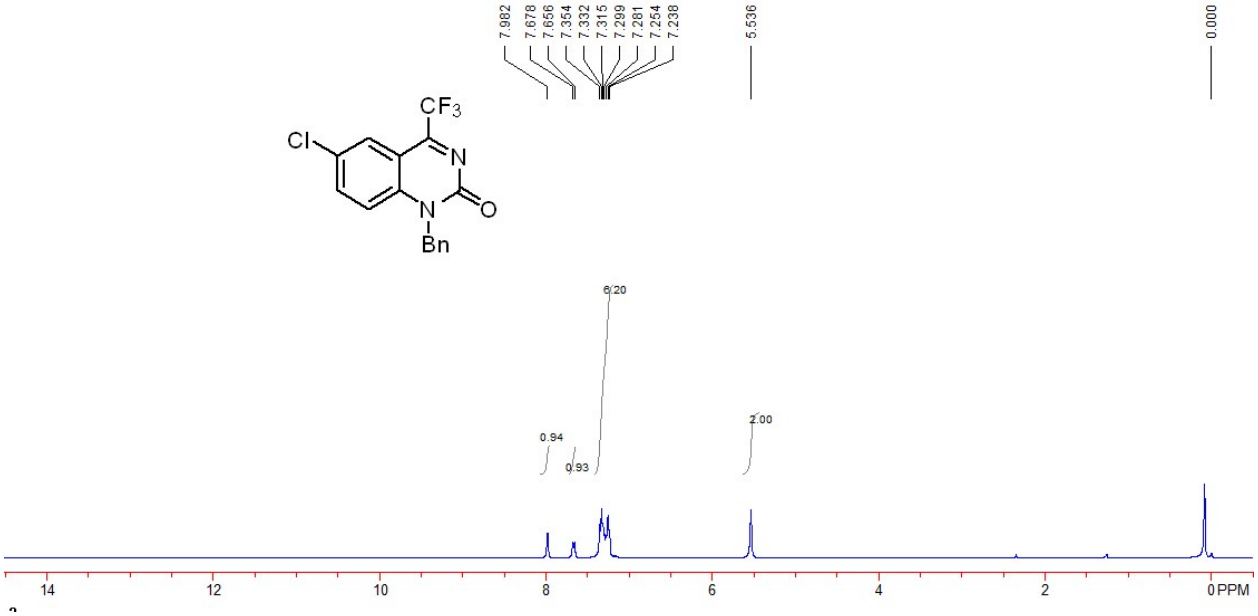
General Procedure for Synthesis of Cyclic Ketimines 2 and Spectroscopic Data of the Products

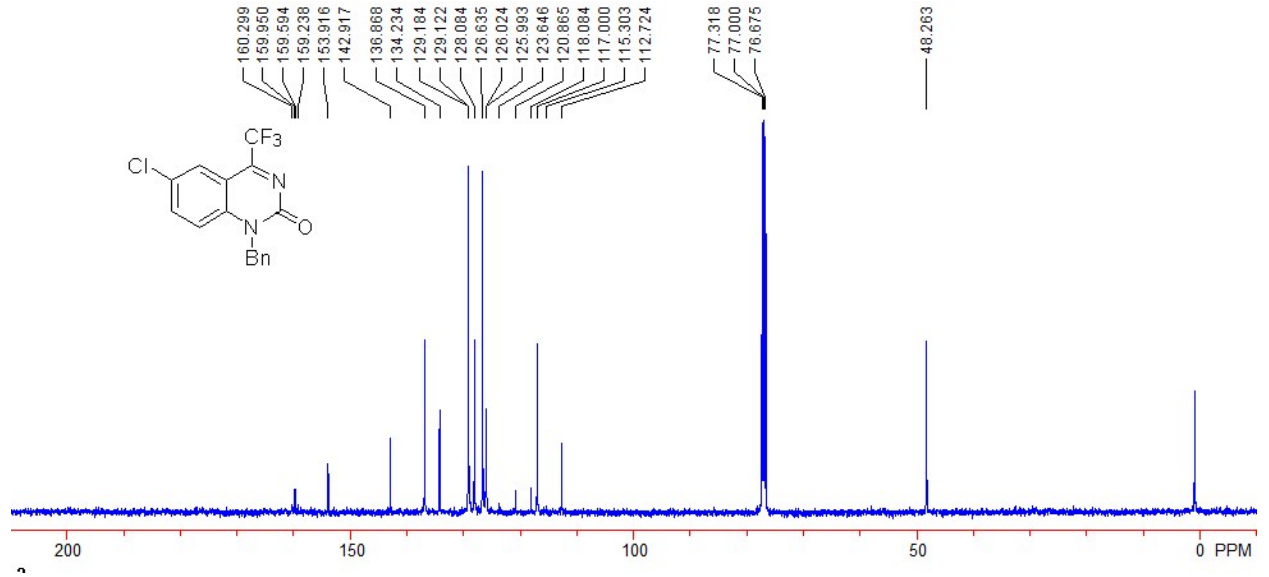
Cyclic ketimines **2** were prepared according to a reported procedure in the previous literature.[3] Among them, **2a-2d** are known compounds.

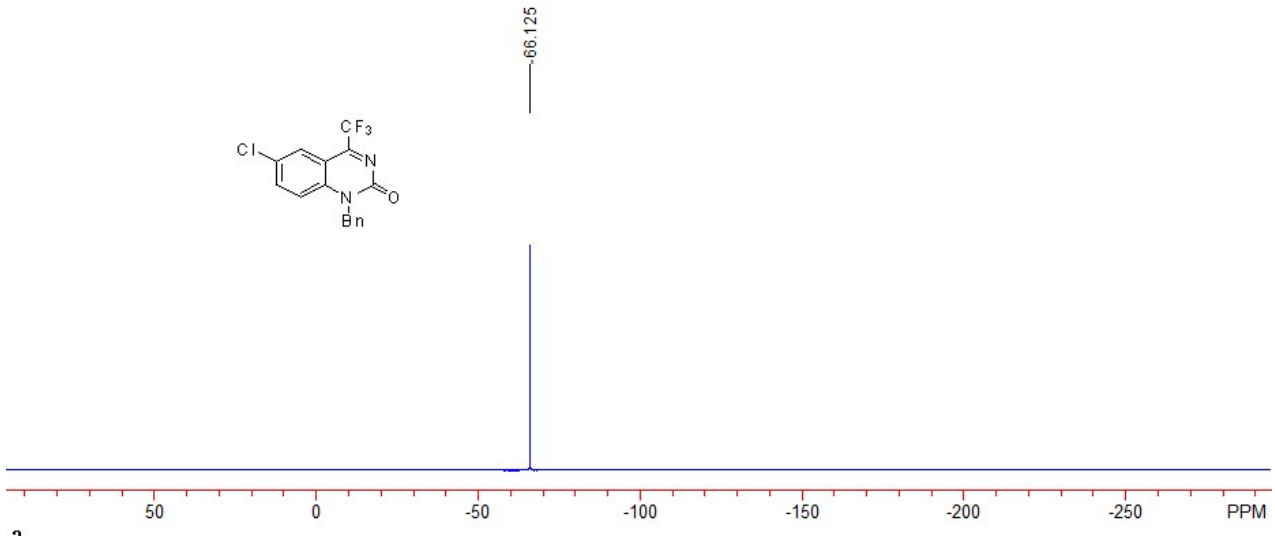


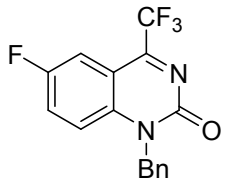
1-benzyl-6-chloro-4-(trifluoromethyl)quinazolin-2(1H)-one (2e).

A yellow solid, 54% yield. M.p.: 154-156 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ, 5.54 (s, 2H, CH_2), 7.23-7.36 (m, 6H, ArH), 7.67 (d, J = 8.8 Hz, 1H, ArH), 7.98 (s, 1H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 48.26, 112.7, 115.3, 119.5 (q, J = 278.1 Hz), 126.0 (d, J = 3.1 Hz), 126.6, 128.1, 129.1, 129.2, 134.2, 136.9, 142.9, 153.9, 159.8 (q, J = 35.6 Hz). ^{19}F NMR (376 MHz, $CDCl_3$, $CFCl_3$) δ -66.13. IR (CH_2Cl_2) ν 2955, 2923, 2851, 1681, 1622, 1555, 1221, 1200, 1142, 974, 734 cm^{-1}. MS (ESI) *m/z* (%): 339.1 (100) $[M+H]^+$; HRMS (ESI) Calcd. For $C_{16}H_{11}ClF_3N_2O^{+1}(M+H)^+$ requires 339.0507, Found: 339.0505.





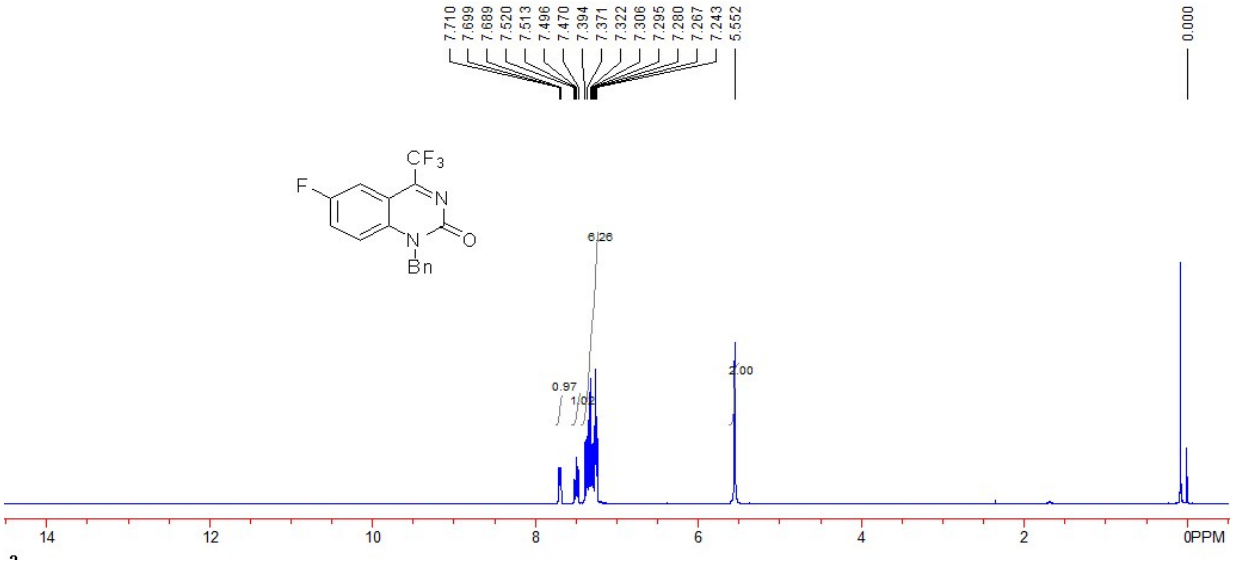


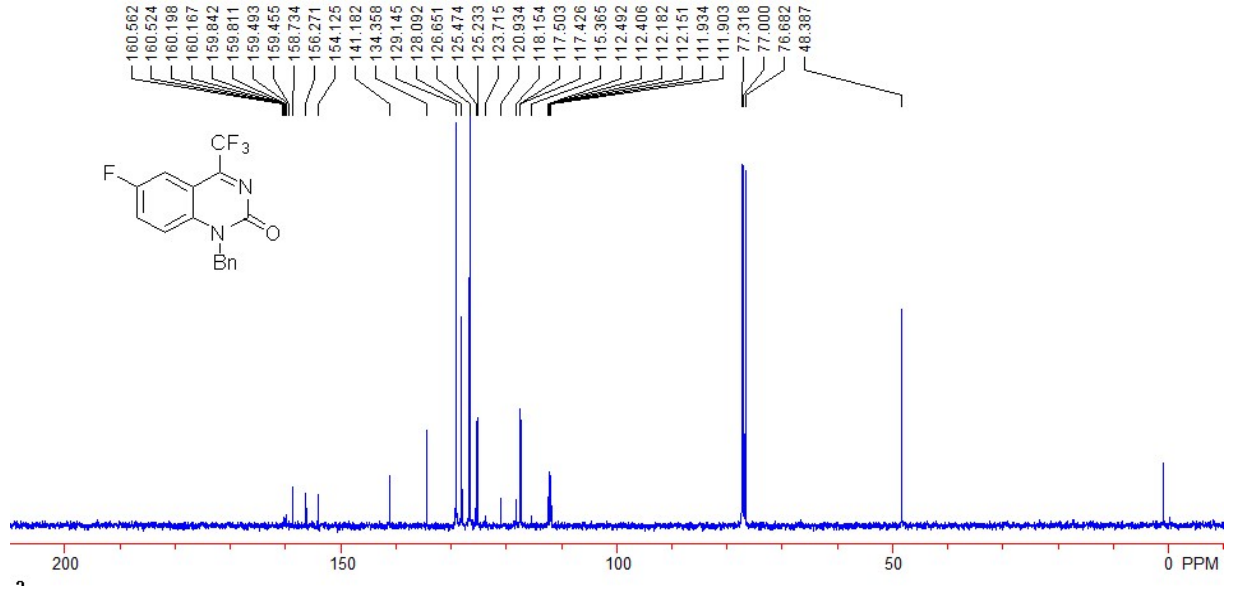


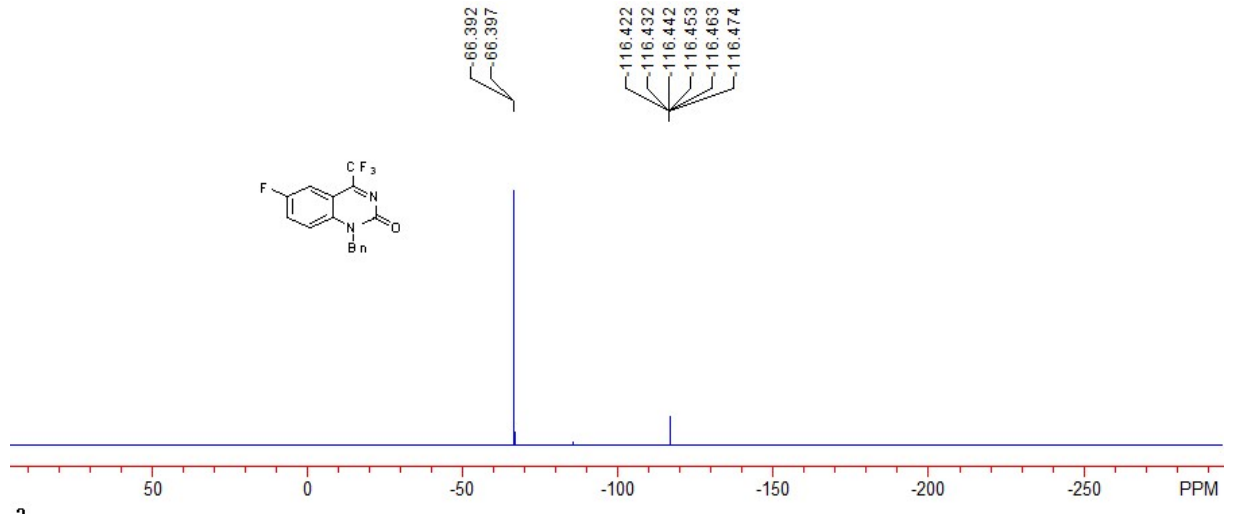
1-benzyl-6-fluoro-4-(trifluoromethyl)quinazolin-2(1H)-one (2f).

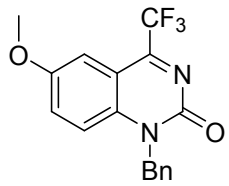
A yellow solid, 59% yield. M.p.: 142-144 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 5.55 (s, 2H, CH_2), 7.24-7.40 (m, 6H, ArH), 7.47-7.52 (m, 1H, ArH), 7.68-7.71 (m, 1H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 48.39, 112.0 (dd, J = 3.1, 24.8 Hz), 112.4 (d, J = 8.6 Hz), 117.5 (d, J = 7.7 Hz), 119.5 (q, J = 278.0 Hz), 125.4 (d, J = 24.1 Hz), 126.7, 128.1, 129.1, 134.5, 141.2, 154.1, 157.5 (d, J = 246.3 Hz), 160.0 (dd, J = 3.1, 35.6 Hz). ^{19}F NMR (376 MHz, $CDCl_3$, $CFCl_3$) δ -66.39-(-66.40), -116.42-(-116.47). IR (CH_2Cl_2) ν 2954, 2923, 2853, 1682, 1566, 1445, 1238, 1203, 799, 728 cm^{-1}.

MS (ESI) *m/z* (%): 323.1 (100) $[M+H]^+$; HRMS (ESI) Calcd. For $C_{16}H_{11}F_4N_2O^{+1}(M+H)^+$ requires 323.0802, Found: 323.0805.



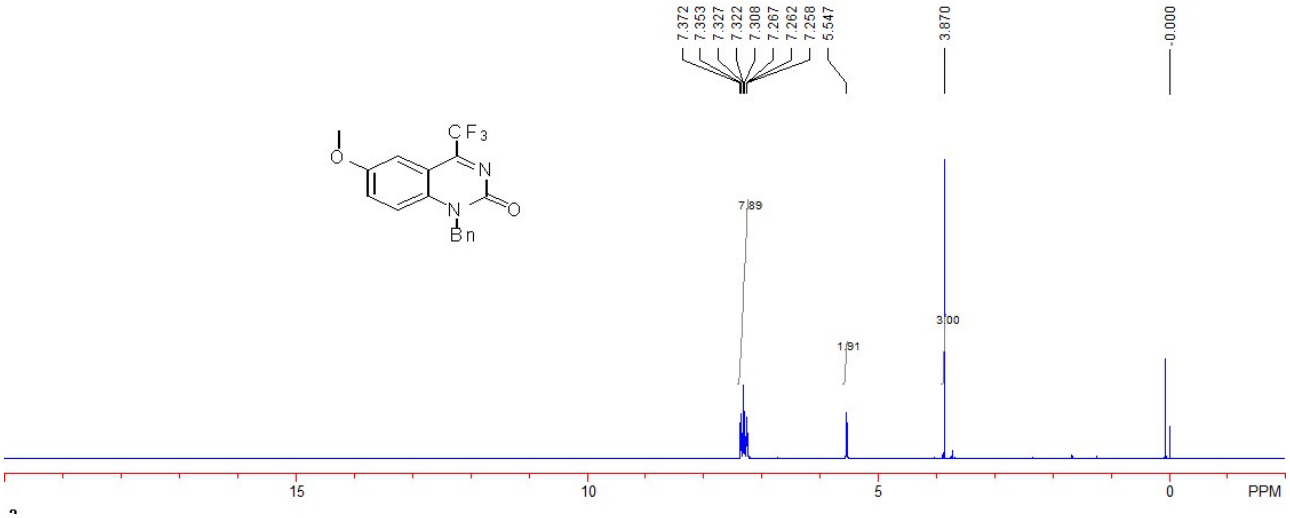


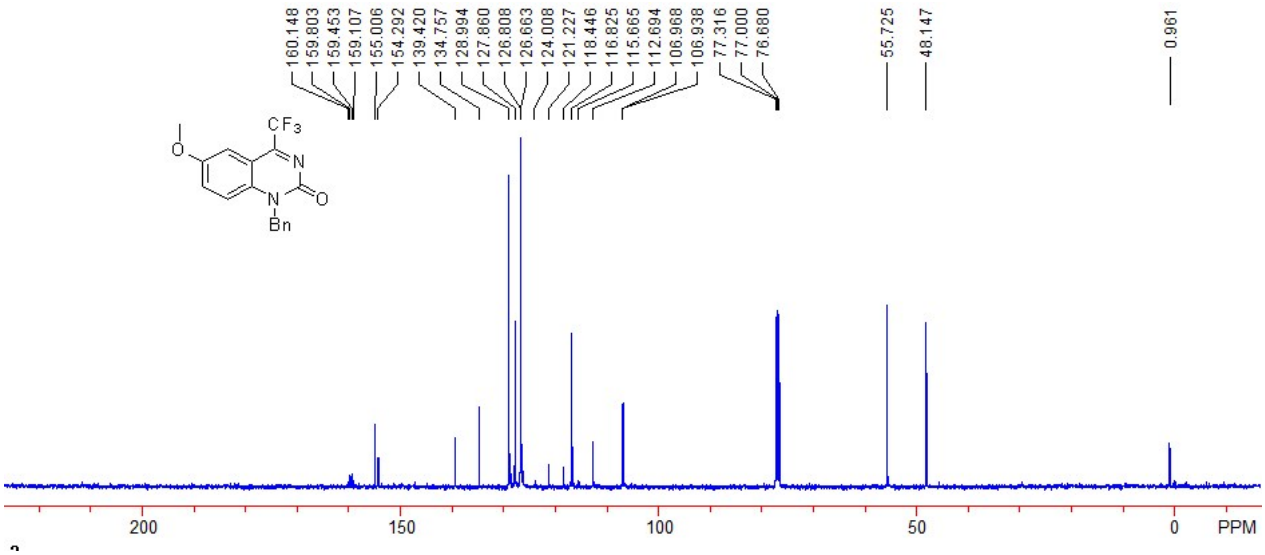


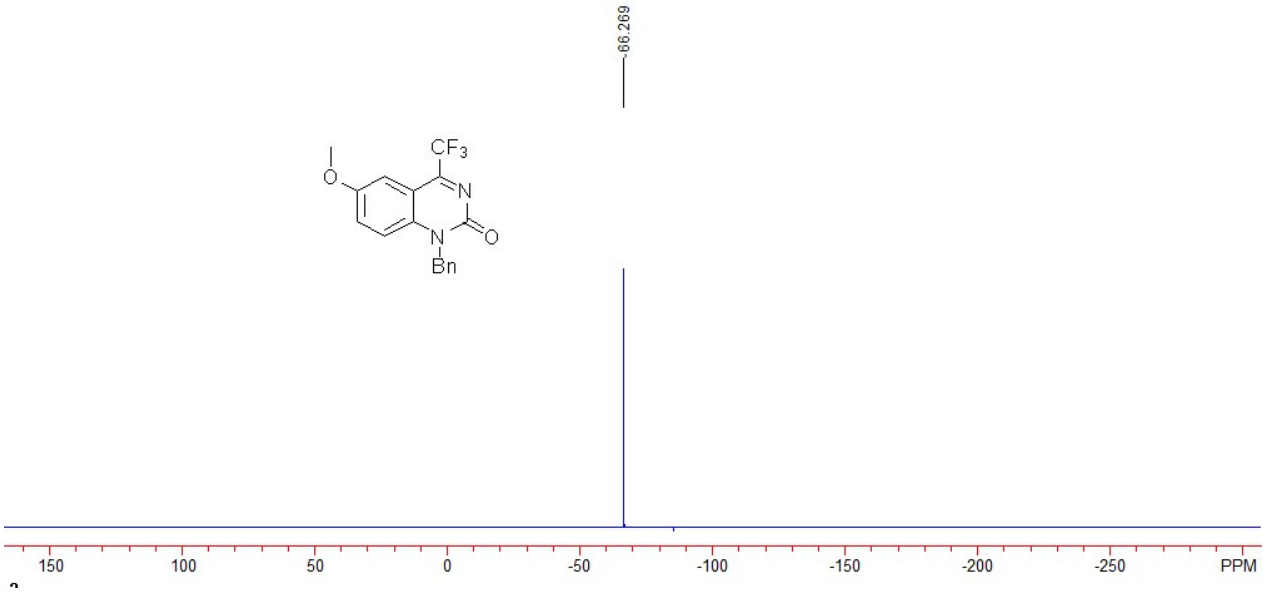


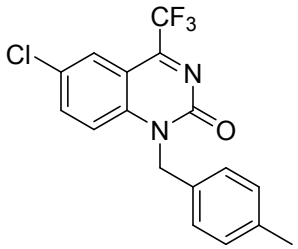
1-benzyl-6-methoxy-4-(trifluoromethyl)quinazolin-2(1H)-one (2g).

A green solid, 73% yield. M.p.: 161-163 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 3.87 (s, 3H, CH_3), 5.55 (s, 2H, CH_2), 7.25-7.38 (m, 8H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 48.15, 55.73, 107.0 (d, J = 3.0 Hz), 112.7, 116.8, 119.8 (q, J = 278.1 Hz), 126.7, 126.8, 127.9, 129.0, 134.8, 139.4, 154.3, 155.0, 159.6 (q, J = 35.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$, $CFCl_3$) δ -66.27. IR (CH_2Cl_2) ν 2956, 2923, 2852, 1456, 1400, 1259, 1088, 1017, 850, 798, 729 cm^{-1}. MS (ESI) *m/z* (%): 335.1 (100) $[M+H]^+$; HRMS (ESI) Calcd. For $C_{17}H_{14}F_3N_2O_2^{+1}(M+H)^+$ requires 335.1002, Found: 335.1008.





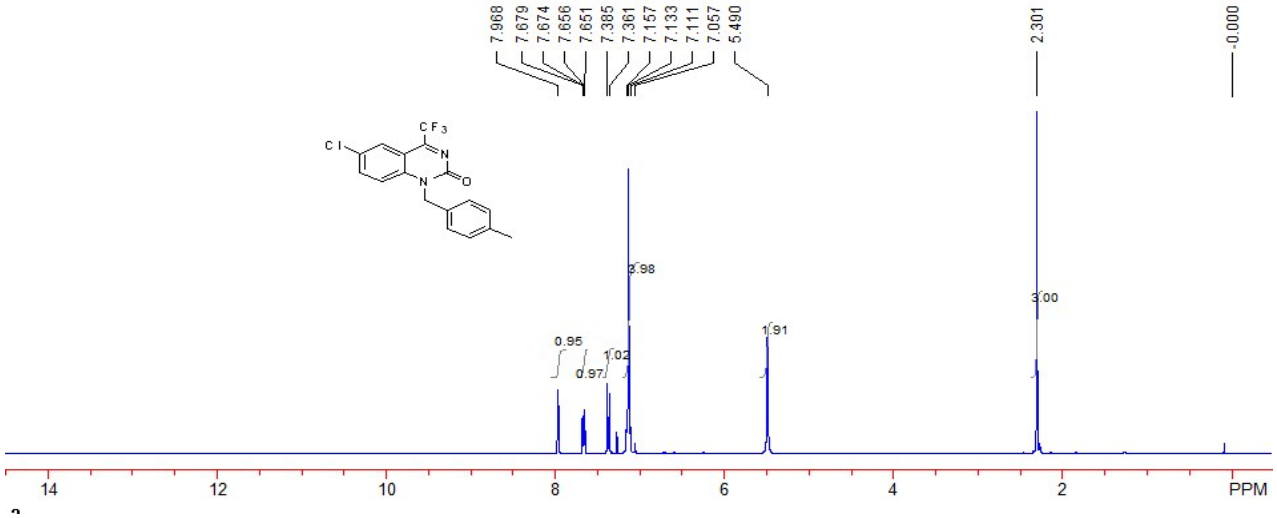


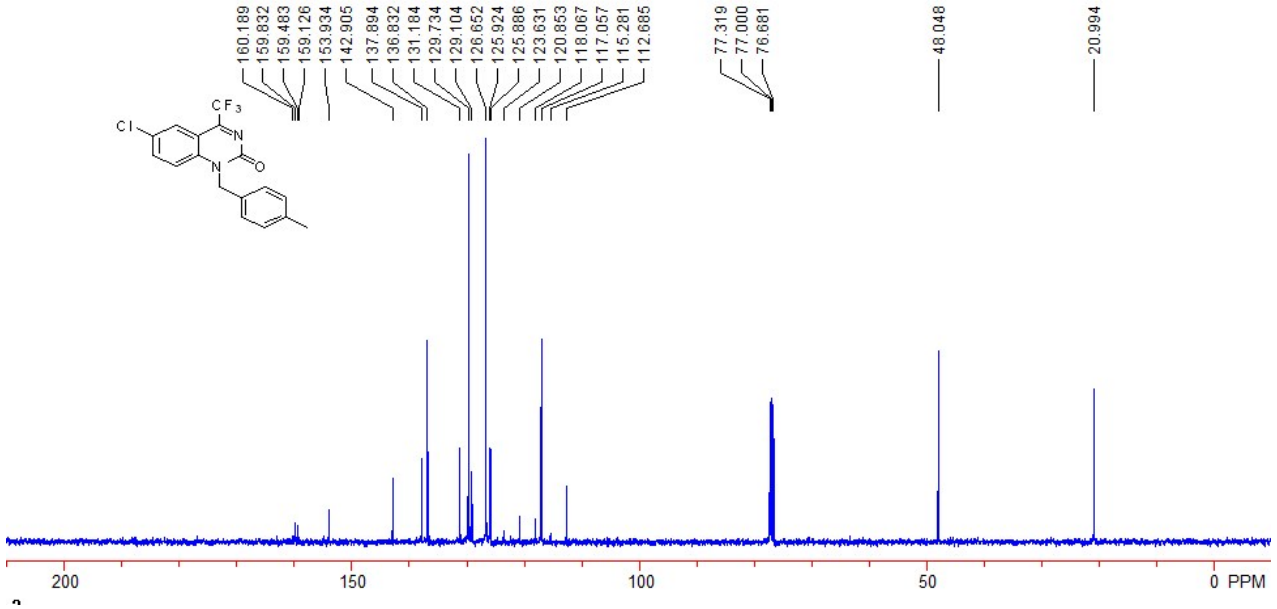


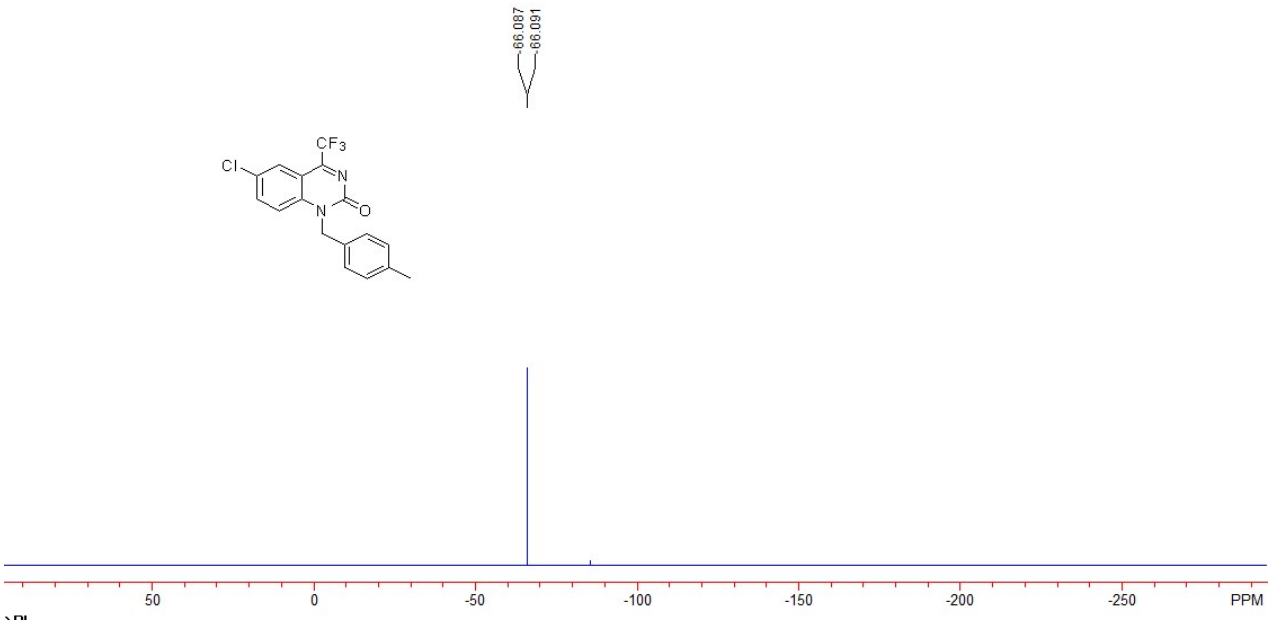
6-chloro-1-(4-methylbenzyl)-4-(trifluoromethyl)quinazolin-2(1H)-one (2h).

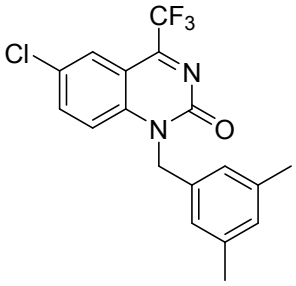
A yellow solid, 72% yield. M.p.: 158-160 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 2.30 (s, 3H, CH_3), 5.49 (s, 2H, CH_2), 7.05-7.16 (m, 4H, ArH), 7.37(d, J = 9.6 Hz, ArH), 7.67(dd, J = 2.0, 9.2 Hz, ArH), 7.97 (s, 1H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 21.0, 48.05, 112.7, 117.1, 119.5 (q, J = 278.6 Hz), 125.9 (d, J =3.8 Hz), 126.7, 129.1, 129.7, 131.2, 136.8, 137.7, 153.9, 159.7 (q, J =

34.9 Hz). ^{19}F NMR (376 MHz, $CDCl_3$, $CFCl_3$) δ -66.09 (d, *J* =1.5 Hz). IR (CH_2Cl_2) ν 3214, 3078, 2921, 1697, 1668, 1622, 1556, 1223, 1200, 973, 822 cm^{-1}. MS (ESI) *m/z* (%): 353.1 (100) $[M+H]^+$; HRMS (ESI) Calcd. For $C_{17}H_{13}ClF_3N_2O^{+1}(M+H)^+$ requires 353.0663, Found: 353.0662.



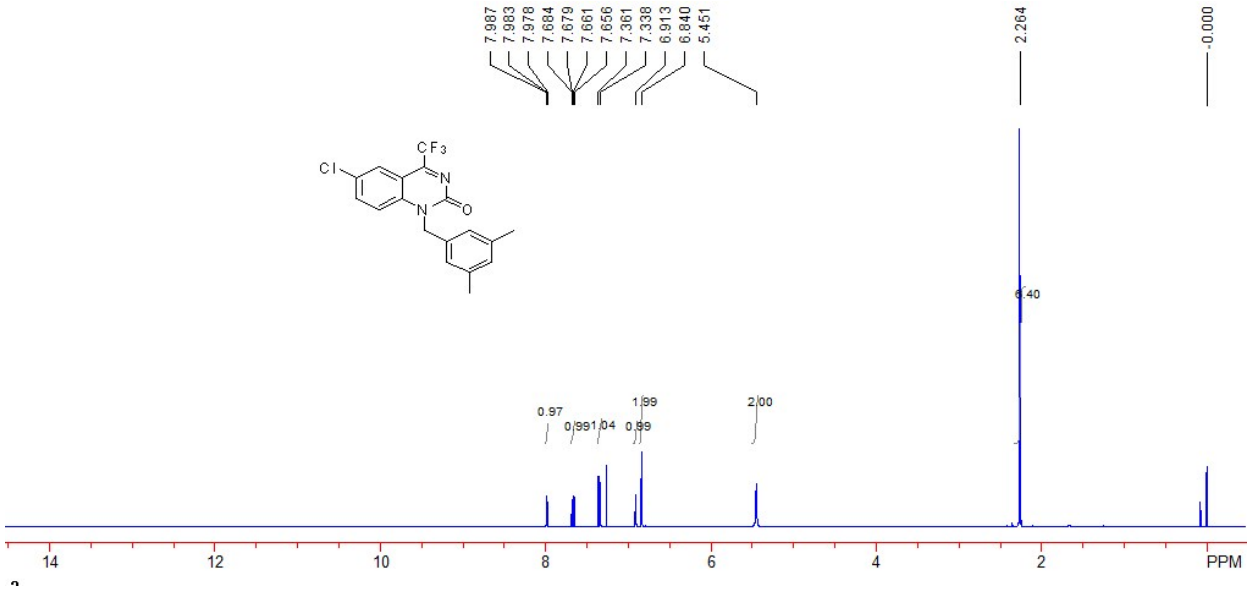






6-chloro-1-(3,5-dimethylbenzyl)-4-(trifluoromethyl)quinazolin-2(1H)-one (2i).

A yellow solid, 76% yield. M.p.: 153-155 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 2.26 (s, 6H, CH_3), 5.45 (s, 2H, CH_2), 6.84 (s, 1H, ArH), 6.91 (s, 1H, ArH), 7.35(d, *J* = 9.2 Hz, ArH), 7.67(dd, *J* = 2.0, 9.2 Hz, ArH), 7.97-7.99 (m, 1H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 21.2, 48.34, 112.7, 117.1, 119.5 (q, *J* = 277.8 Hz), 124.3, 125.9 (d, *J* =3.0 Hz), 129.1, 129.8, 134.2, 136.9, 138.8, 143.0, 154.0, 159.7 (q, *J* = 35.0 Hz). ^{19}F NMR (376 MHz, $CDCl_3$, $CFCl_3$) δ -66.08 (d, *J* =1.9 Hz). IR (CH_2Cl_2) ν 2970, 1680, 1622, 1556, 1449, 1222, 1200, 1142, 976, 816 cm^{-1}. MS (ESI) *m/z* (%): 367.1 (100) $[M+H]^+$; HRMS (ESI) Calcd. For $C_{18}H_{15}F_3N_2O^{+1}(M+H)^+$ requires 367.0820, Found: 367.0822.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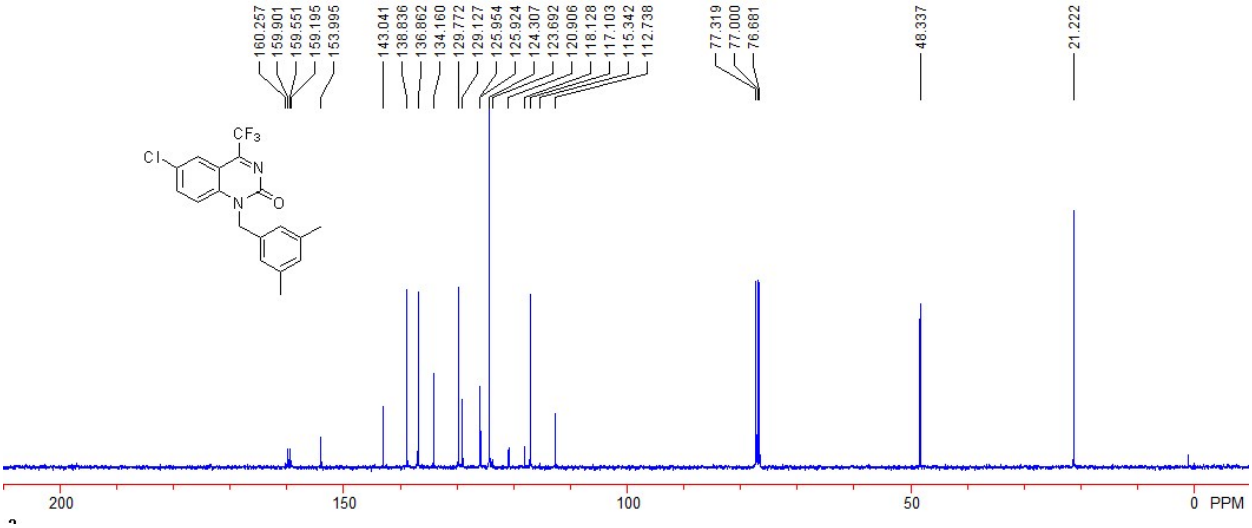
2
PPM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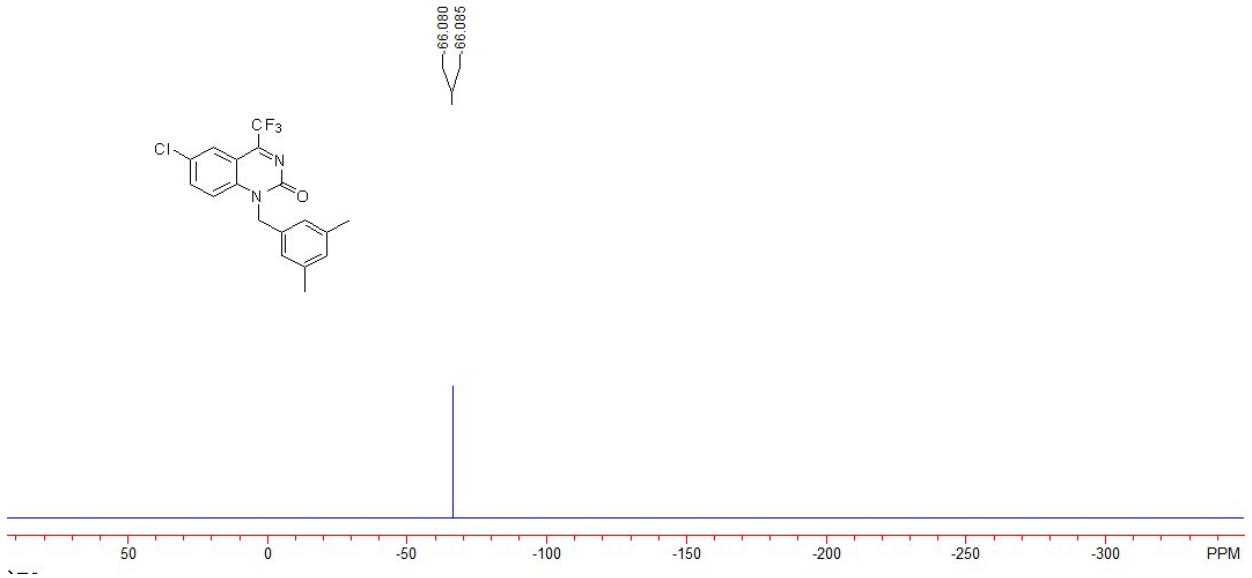
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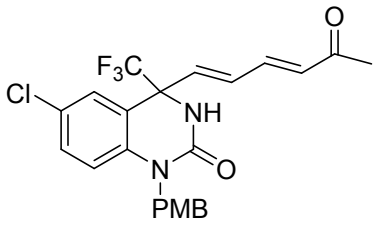
PPM

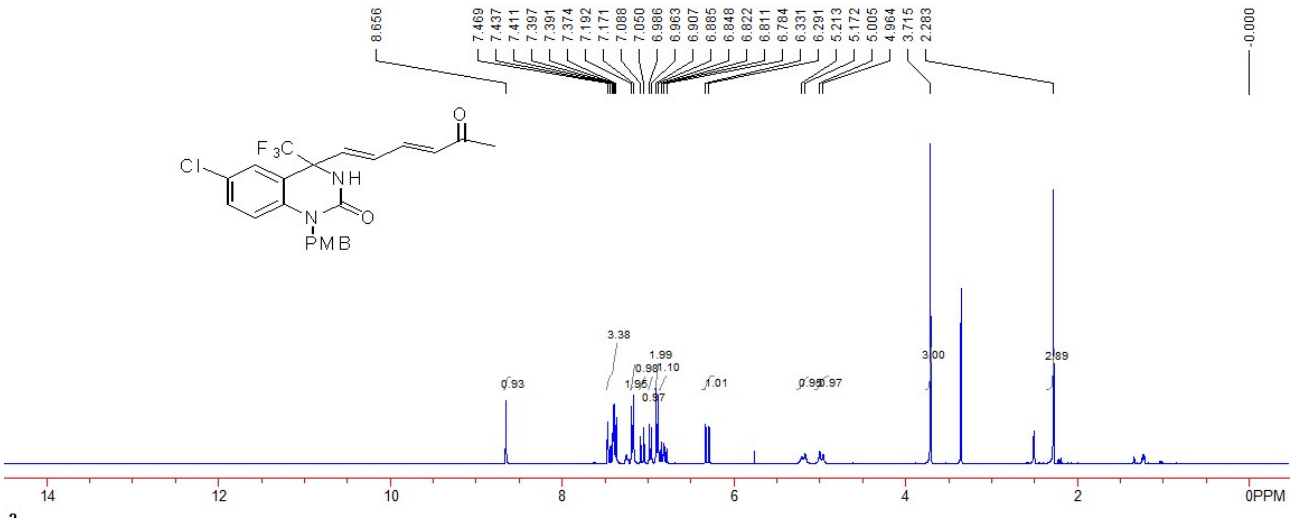
General Procedure for Hex-3-yn-2-one 1a to Cyclic Trifluoromethyl Ketimines 2 and Spectroscopic Data of the Products

General procedure: The 4Å MS was added to a Schlenk tube and heated under vacuum to remove ambient moisture and water, then filled with argon. After the Schlenk tube was returned to room temperature, cyclic trifluoromethyl ketimines **2** (0.2 mmol) and $P(4\text{-}FC_6H_4)_3$ (13 mg, 0.04 mmol) was added. Under argon atmosphere, to a solution of cyclic trifluoromethyl ketimines **2** (0.2 mmol) and $P(4\text{-}FC_6H_4)_3$ (13 mg, 0.04 mmol) in toluene (1.0 mL) was added the hex-3-yn-2-one **1a** (0.8 mmol) at room temperature. Then the resulting mixture was heated to 65 ^oC and continued stirring at 65 ^oC until the reaction completed (monitoring by TLC). Then the solvent was removed under reduced pressure and the residue was directly subjected to a flash column chromatography on silica gel to afford the desired products **3a-3i**. Trace impurity was contained, which has been described in detail in Page S47.



6-chloro-1-(4-methoxybenzyl)-4-((1E,3E)-5-oxohexa-1,3-dien-1-yl)-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1H)-one (3a).

A white solid, 92% yield (85 mg). M.p.: 243-245 ^oC. ^1H NMR (d_6-DMSO, TMS, 400 MHz) δ 2.28 (s, 3H, CH_3), 3.72 (s, 3H, CH_3), 4.98 (d, *J* = 16.4 Hz, 1H, CH_2), 5.19 (d, *J* = 16.4 Hz, 1H, CH_2), 6.31 (d, *J* = 16.0 Hz, 1H, =CH), 6.82 (dd, *J* = 10.4, 15.2 Hz, 1H, =CH), 6.90 (d, *J* = 8.8 Hz, 2H, ArH), 6.97 (d, *J* = 9.2 Hz, 1H, ArH), 7.07 (d, *J* = 15.2 Hz, 1H, =CH), 7.18 (d, *J* = 8.8 Hz, 2H, ArH), 7.37-7.47 (m, 3H, =CH, ArH), 7.45 (s, 1H, NH). ^{13}C NMR ($CDCl_3$, TMS, 75 MHz) δ 27.6, 45.5, 55.2, 62.5 (q, *J* = 28.9 Hz), 114.3, 116.3, 118.9, 124.6 (q, *J* = 286.2 Hz), 127.6, 127.7, 127.8, 127.9, 128.4, 128.5, 128.7, 130.4, 133.3, 133.8, 135.1, 136.2, 140.1, 158.9, 198.0. ^{19}F NMR (376 MHz, $CDCl_3$, $CFCl_3$) δ -80.10. IR (CH_2Cl_2) ν 3214, 2960, 2925, 1682, 1601, 1513, 1502, 1428, 1393, 1250, 1175, 1066, 1045, 808 cm^{-1}. MS (ESI) *m/z* (%): 487.0 (100) $[M+Na]^+$; HRMS (ESI) Calcd. For $C_{23}H_{21}F_3N_2ClO_3{}^{+1}(M+H)^+$ requires 465.1187, Found: 465.1180.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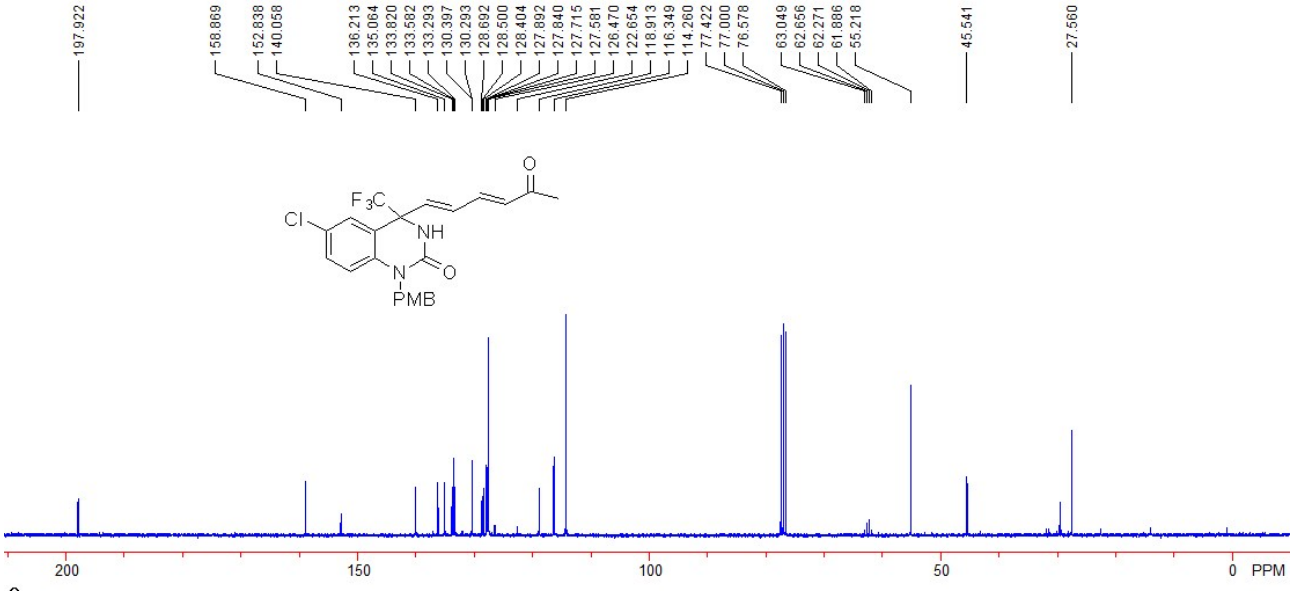
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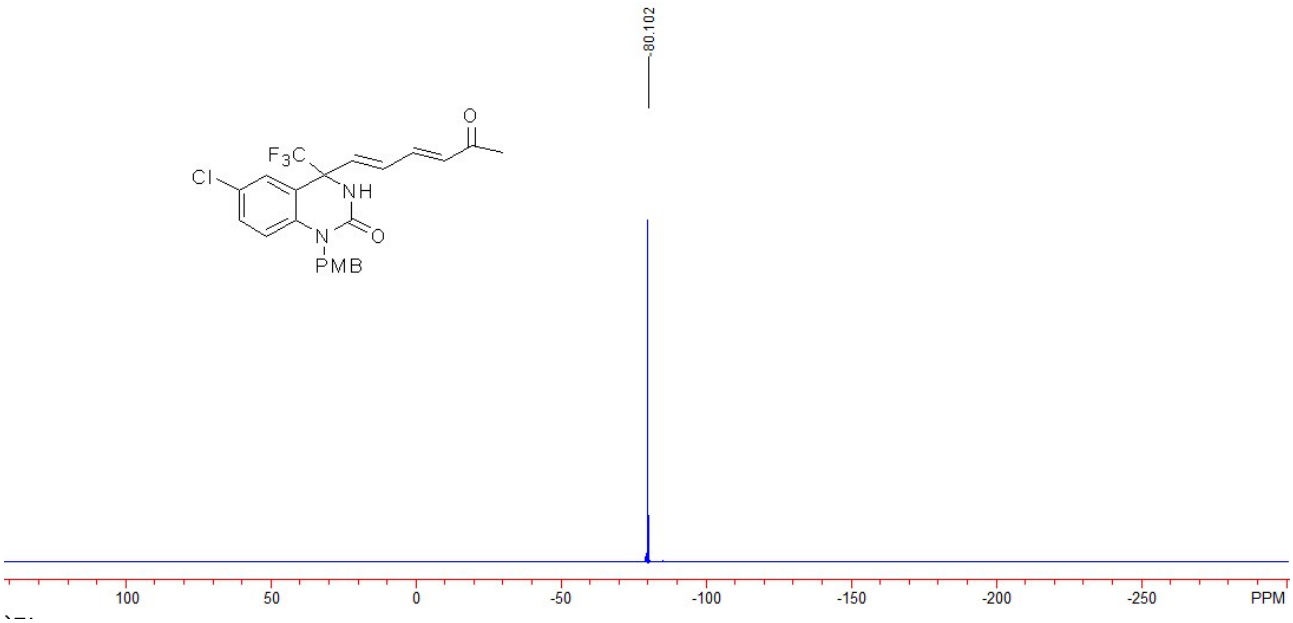
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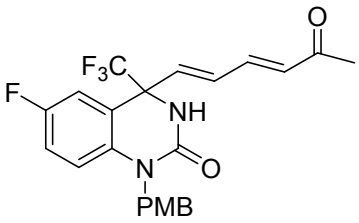
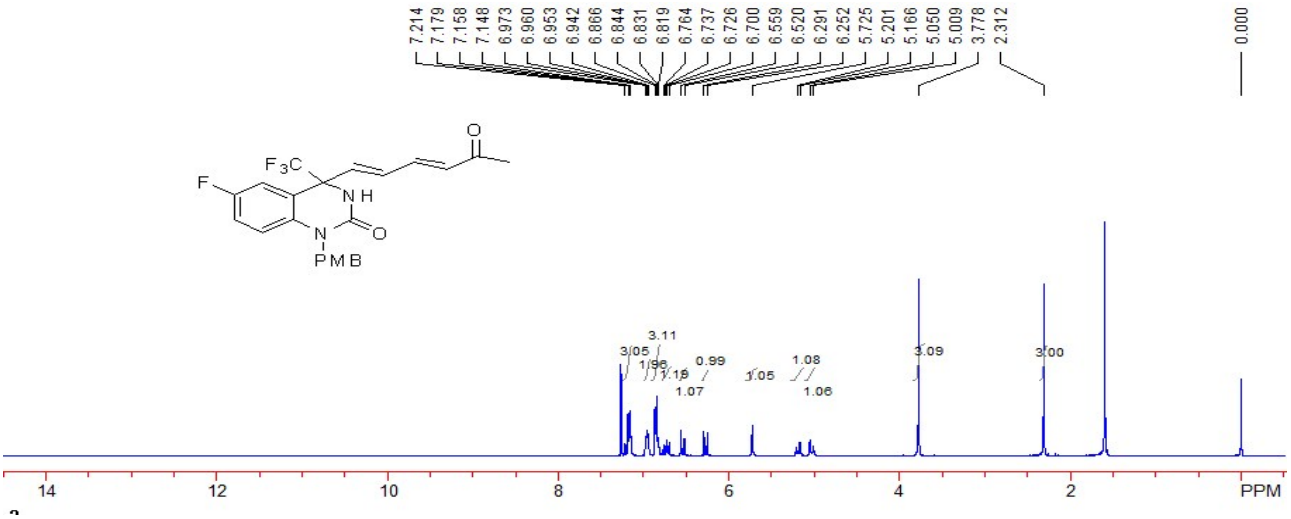
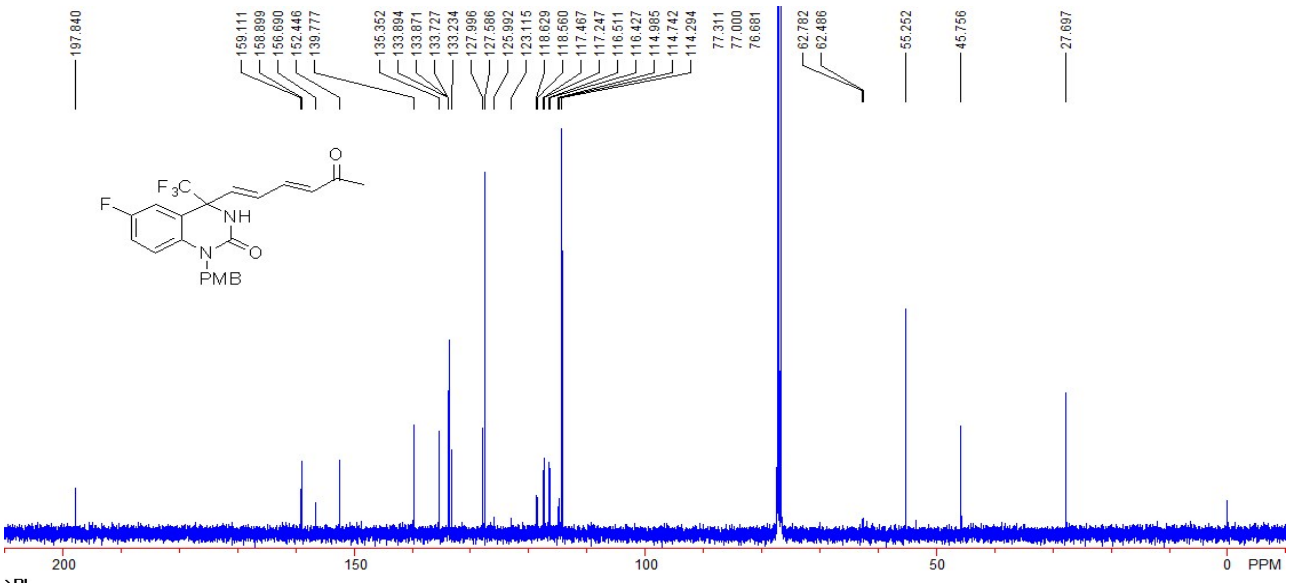
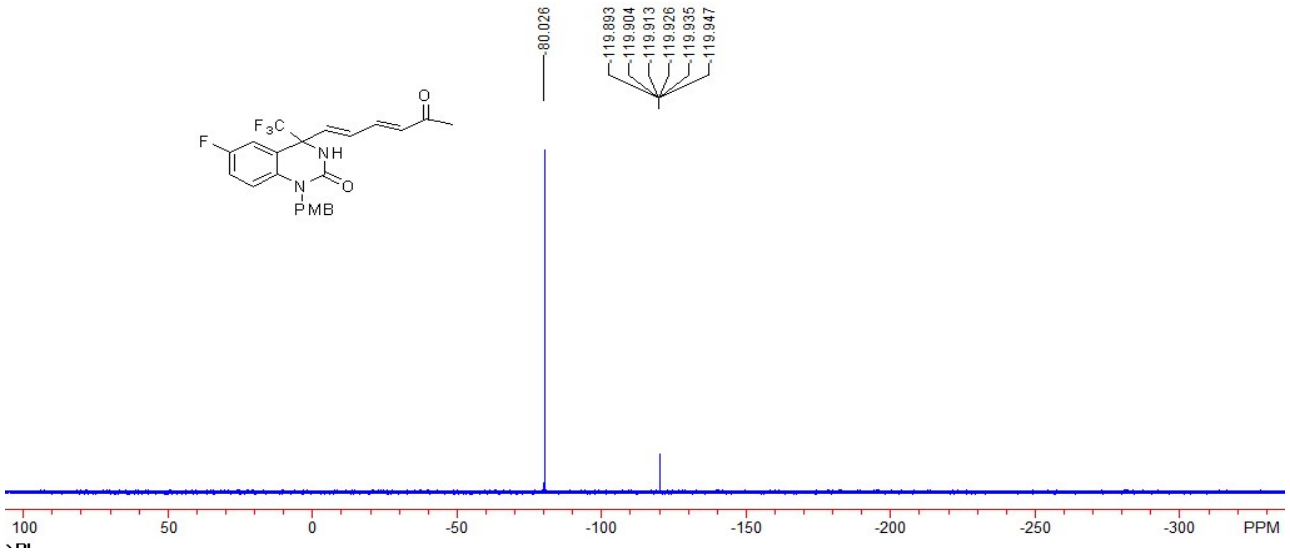


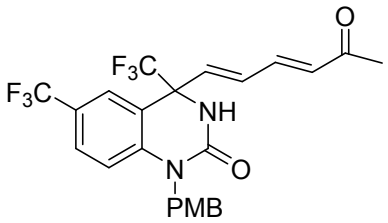
6-fluoro-1-(4-methoxybenzyl)-4-((1E,3E)-5-oxohexa-1,3-dien-1-yl)-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1H)-one (3b).

A white solid, 83% yield (74 mg). M.p.: 231-233 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 2.31 (s, 3H, CH_3), 3.78 (s, 3H, CH_3), 5.03 (d, *J* = 16.4 Hz, 1H, CH_2), 5.18 (d, *J* = 16.4 Hz, 1H, CH_2), 5.73 (s, 1H, NH), 6.27 (d, *J* = 15.6 Hz, 1H, =CH), 6.54 (d, *J* = 15.6 Hz, 1H, =CH), 6.73 (dd, *J* = 10.8, 15.6 Hz, 1H, =CH), 6.81-6.87 (m, 3H, ArH, =CH), 6.94-6.97 (m, 2H, ArH), 7.14-7.22 (m, 3H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 27.7, 45.8, 55.3, 62.6 (q, *J* = 29.6 Hz), 114.3, 114.9 (d, *J* = 24.3 Hz), 116.5 (d, *J* = 8.4 Hz), 117.4 (d, *J* = 22.0 Hz), 118.6 (d, *J* = 6.9 Hz), 124.6 (q, *J* = 287.7 Hz), 127.6, 128.0, 133.2, 133.7, 133.9 (d, *J* = 2.3 Hz), 135.4, 139.8, 152.4, 157.9 (d, *J* = 242.1 Hz), 158.9, 197.8. ^{19}F NMR (376 MHz, $CDCl_3$, $CFCl_3$) δ -80.03, -119.89-(-119.95) (m). IR (CH_2Cl_2) ν 3366, 2955, 2923, 2853, 1678, 1513, 1457, 1377, 1259, 1089, 1017, 800 cm^{-1}. MS (ESI) *m/z* (%): 449.1 (100) $[M+H]^+$; HRMS (ESI) Calcd. For $C_{23}H_{21}F_4N_2O_3^{+1}(M+H)^+$ requires 449.1483, Found: 449.1487.





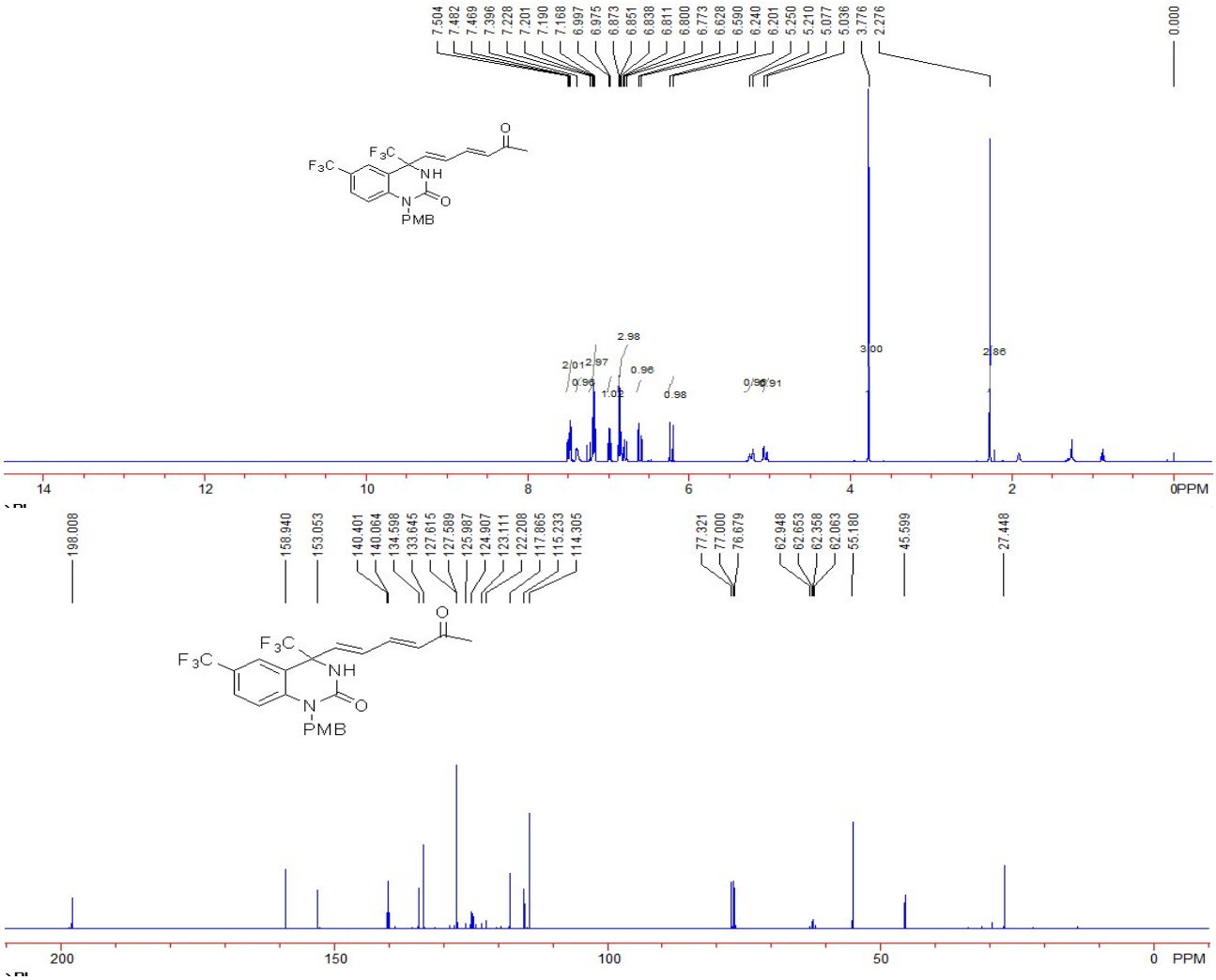


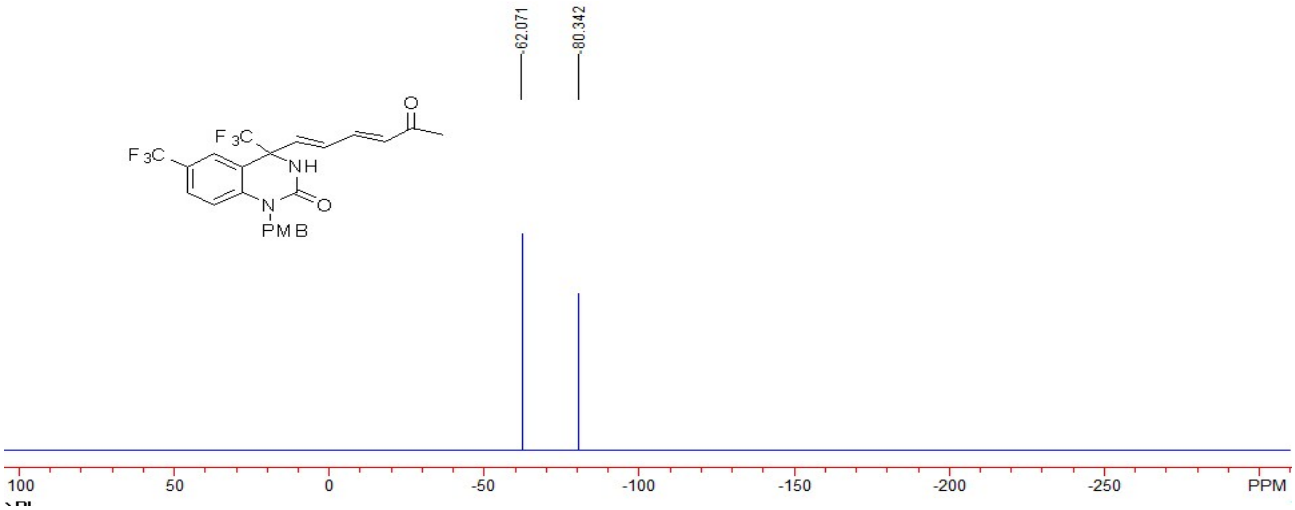


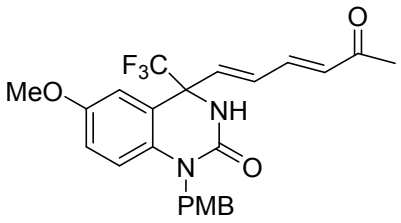
1-(4-methoxybenzyl)-4-((1E,3E)-5-oxohexa-1,3-dien-1-yl)-4,6-bis(trifluoromethyl)-3,4-dihydroquinazolin-2(1H)-one (3c).

A white solid, 73% yield (72 mg). M.p.: 165-167 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 2.28 (s, 3H, CH_3), 3.78 (s, 3H, CH_3), 5.07 (d, J = 16.4 Hz, 1H, CH_2), 5.23 (d, J = 16.4 Hz, 1H, CH_2), 6.22 (d, J = 15.6 Hz, 1H, =CH), 6.61 (d, J = 15.2 Hz, 1H, =CH), 6.77-6.88 (m, 3H, ArH, =CH), 6.99 (d, J = 8.8 Hz, 1H, ArH), 7.16-7.23 (m, 3H, ArH, =CH), 7.40 (br, 1H, NH) 7.46-7.51 (m, 2H, ArH).

^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 27.4, 45.6, 55.2, 62.5 (q, J = 29.5 Hz), 114.3, 115.2, 117.9, 123.5 (q, J = 269.9 Hz), 124.5 (q, J = 287.7 Hz), 127.59, 127.62, 133.6, 134.6, 140.1, 140.4, 153.1, 158.9, 198.0. ^{19}F NMR (376 MHz, $CDCl_3$, $CFCl_3$) δ -62.07, -80.34. IR (CH_2Cl_2) ν 3219, 3091, 2955, 2915, 2853, 1685, 1624, 1598, 1513, 1394, 1370, 1329, 1290, 1249, 1171, 1121, 1090, 998, 821, 738 cm^{-1}. MS (ESI) *m/z* (%): 516.2 (100) $[M+NH_4]^+$; HRMS (ESI) Calcd. For $C_{24}H_{24}F_6N_3O_3^{+1}(M+NH_4)^+$ requires 516.1716, Found: 516.1713.

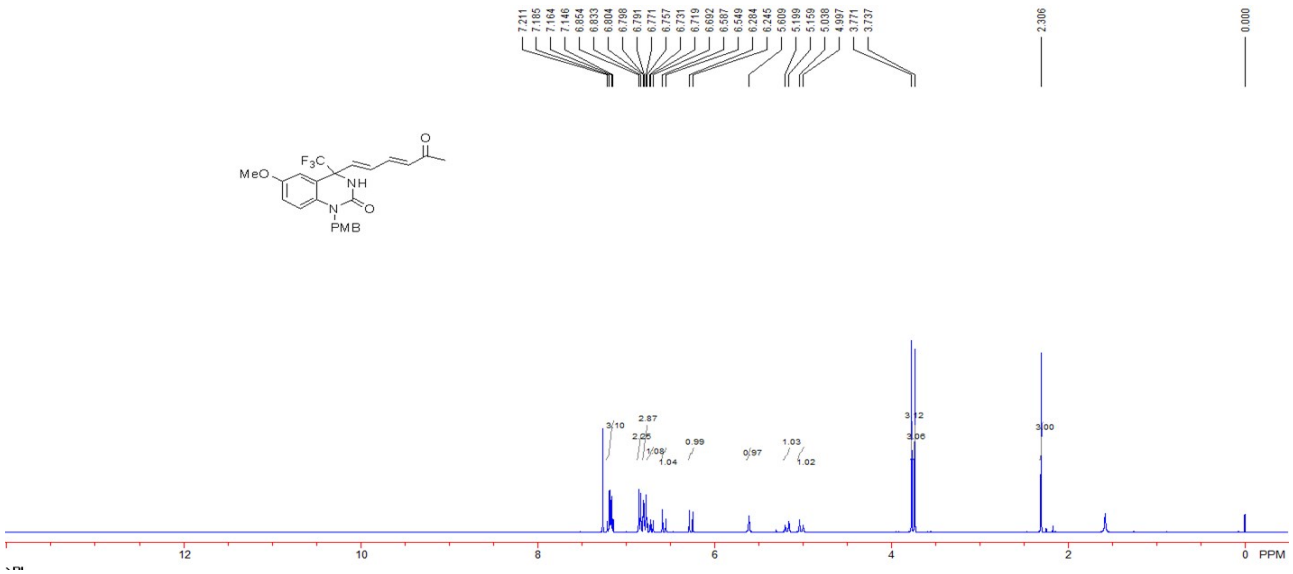






6-methoxy-1-(4-methoxybenzyl)-4-((1E,3E)-5-oxohexa-1,3-dien-1-yl)-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1H)-one (3d).

A white solid, 76% yield (70 mg). M.p.: 215-217 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 2.31 (s, 3H, CH_3), 3.74 (s, 3H, CH_3), 3.77 (s, 3H, CH_3), 5.02 (d, J = 16.0 Hz, 1H, CH_2), 5.18 (d, J = 16.0 Hz, 1H, CH_2), 5.61 (s, 1H, NH), 6.27 (d, J = 15.6 Hz, 1H, =CH), 6.57 (d, J = 15.2 Hz, 1H, =CH), 6.73 (dd, J = 10.4, 15.2 Hz, 1H, =CH), 6.77-6.81 (m, 3H, ArH, =CH), 6.84 (d, J = 8.4 Hz, 2H, ArH), 7.14-7.22 (m, 3H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 27.7, 45.6, 55.2, 55.6, 62.8 (q, J = 28.9 Hz), 114.1, 114.2, 115.0, 116.1, 118.4, 124.7 (q, J = 287.7 Hz), 127.6, 128.5, 131.0, 132.7, 133.4, 136.1, 140.0, 152.7, 154.9, 158.8, 197.9. ^{19}F NMR (376 MHz, $CDCl_3$, $CFCl_3$) δ -79.79. IR (CH_2Cl_2) ν 3344, 2954, 2922, 2852, 1673, 1596, 1513, 1455, 1401, 1377, 1259, 1175, 1089, 1018, 800, 762 cm^{-1}. MS (ESI) *m/z* (%): 461.2 (100) $[M+H]^+$; HRMS (ESI) Calcd. For $C_{24}H_{24}F_3N_2O_4^{+1}(M+H)^+$ requires 461.1683, Found: 461.1689.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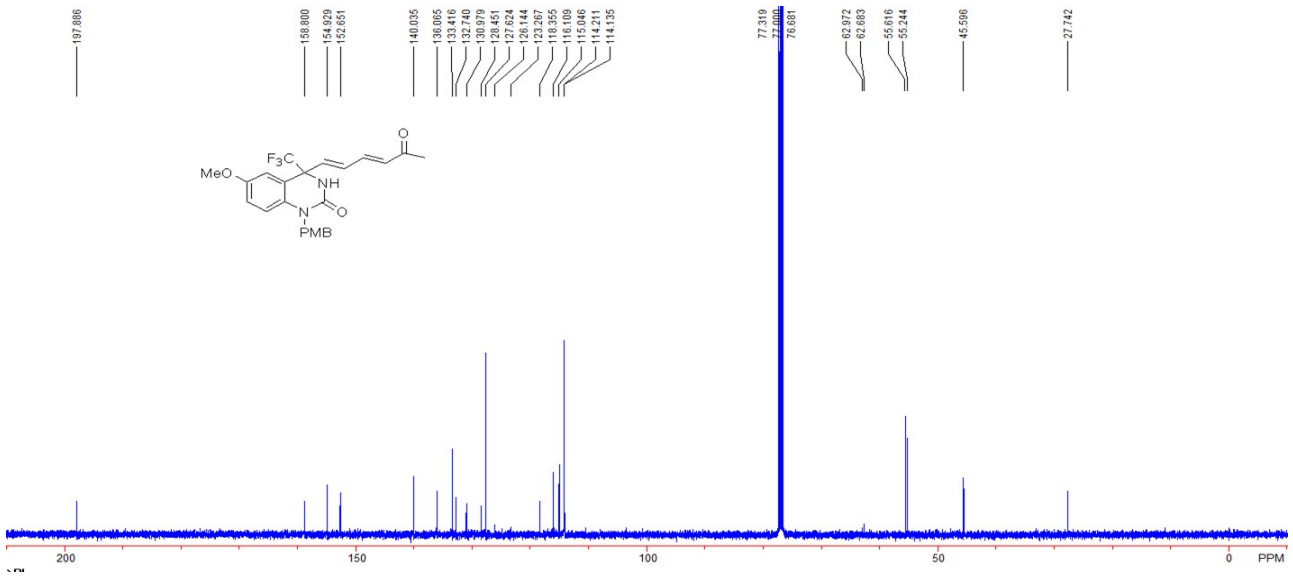
6.692
6.587
6.549
6.284
6.245
5.609
5.199
5.159
5.038
4.997
3.771
3.737
2.306
0.000
MeO
F3C
NH
N
O
PMB
3.10
2.87
2.06
3.08
1.04
0.99
0.97
1.03
1.02
3.12
3.06
3.00
12
10
8
6
4
2
0
PPM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136.085
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123.267
118.365
116.109
115.046
114.211
114.135
77.319
77.000
76.681
62.972
62.663
55.616
55.244
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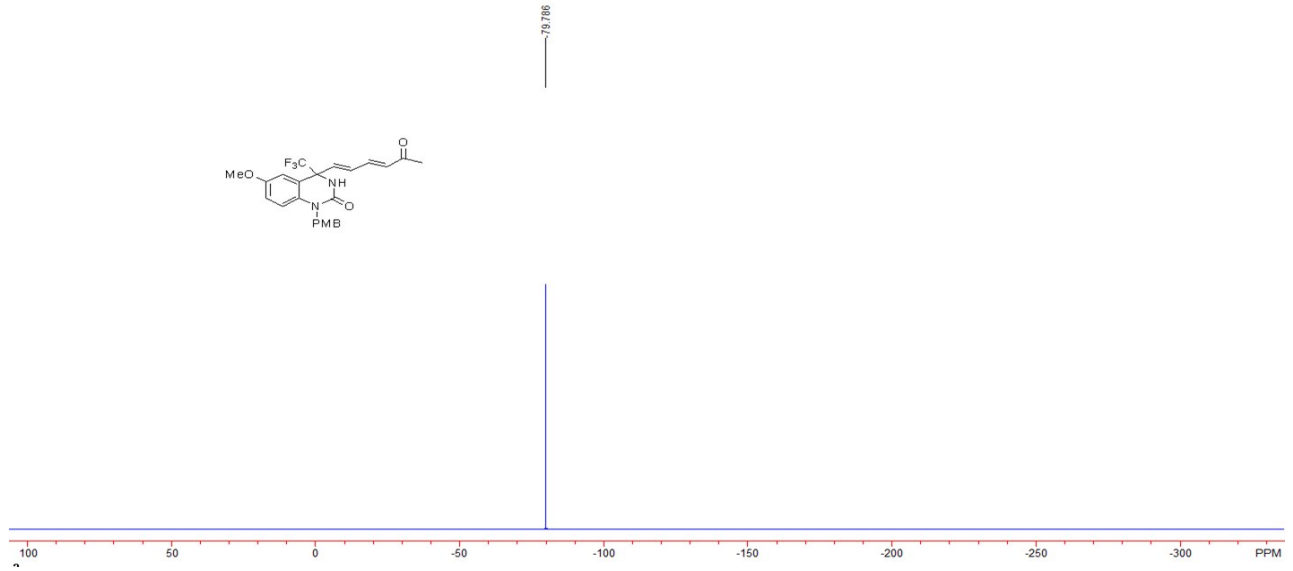
27.742
MeO
F3C
NH
N
O
PMB
200
150
100
50
0
PPM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PMB
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50
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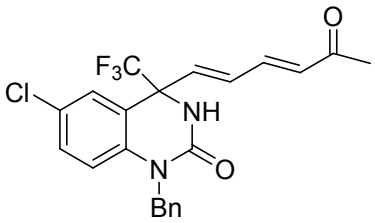
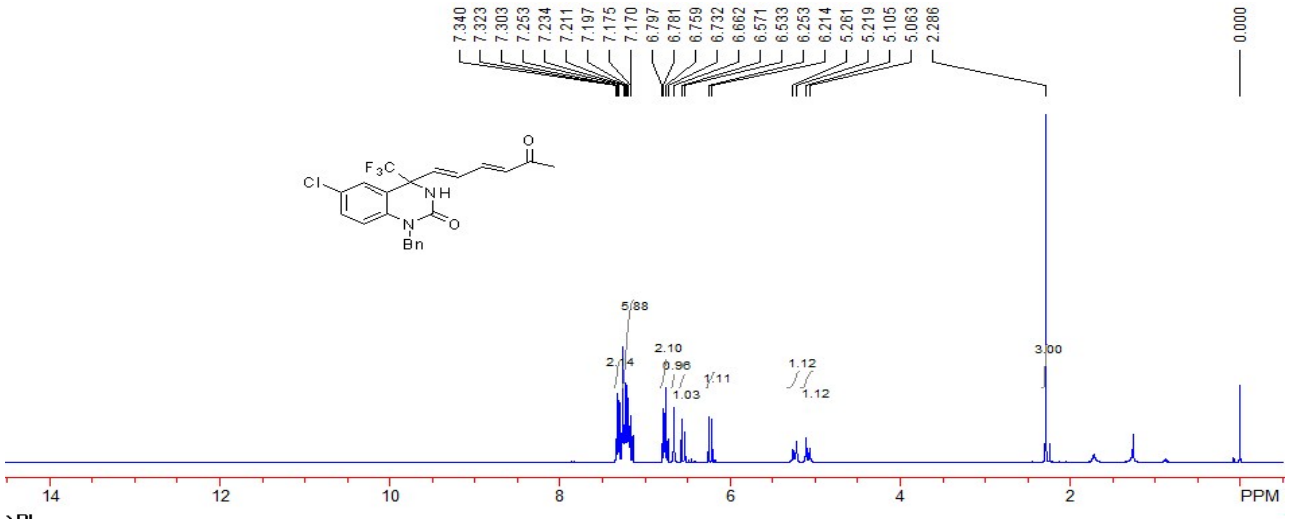
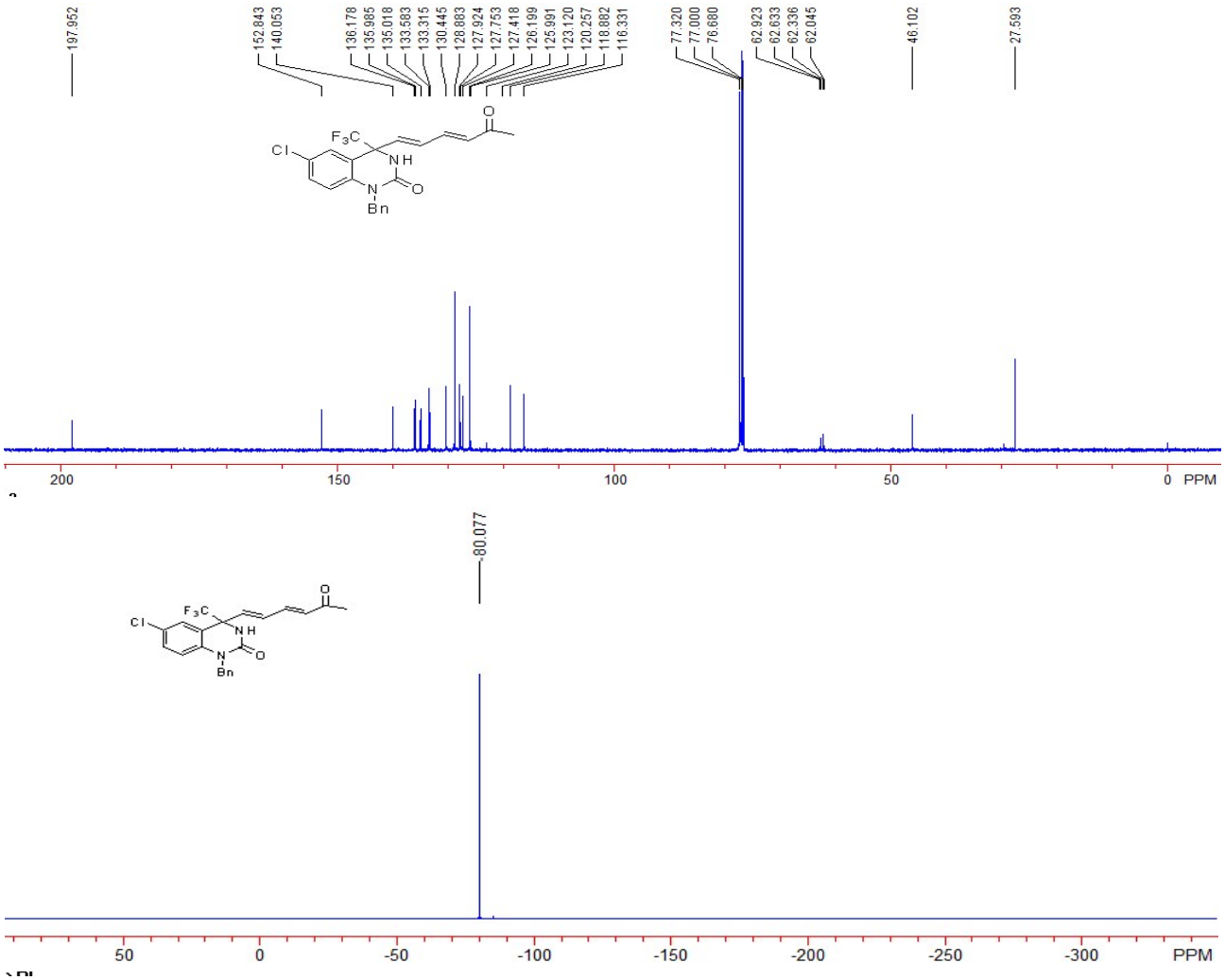
-100
-150
-200
-250
-300
PPM

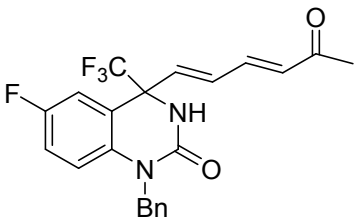


1-benzyl-6-chloro-4-((1E,3E)-5-oxohexa-1,3-dien-1-yl)-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1H)-one (3e).

A white solid, 82% yield (71 mg). M.p.: 213-215 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 2.29 (s, 3H, CH_3), 5.08 (d, *J* = 16.8 Hz, 1H, CH_2), 5.24 (d, *J* = 16.8 Hz, 1H, CH_2), 6.23 (d, *J* = 15.6 Hz, 1H, =CH), 6.55 (d, *J* = 15.2 Hz, 1H, =CH), 6.66 (s, 1H, NH), 6.73-6.80 (m, 2H, =CH), 7.17-7.26 (m, 6H, ArH), 7.30-7.34 (m, 2H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 27.6, 46.1, 62.5 (d, *J* = 29.7 Hz), 116.3, 118.9, 124.6 (q, *J* = 287.1 Hz), 126.2, 127.4, 127.8, 127.9, 128.9, 130.4, 133.3, 133.6, 135.0, 136.0, 136.2, 140.1, 152.8, 198.0. ^{19}F NMR (376 MHz, $CDCl_3$, $CFCl_3$) δ -80.08. IR (CH_2Cl_2) ν 3216, 3084, 2954, 2923, 2851, 1682, 1599, 1501, 1425, 1175 cm^{-1}. MS (ESI) *m/z* (%): 435.1 (100) $[M+H]^+$; HRMS (ESI) Calcd. For $C_{22}H_{19}F_3N_2O_3$ $^{+1}(M+H)^+$ requires 435.1082, Found: 435.1080.



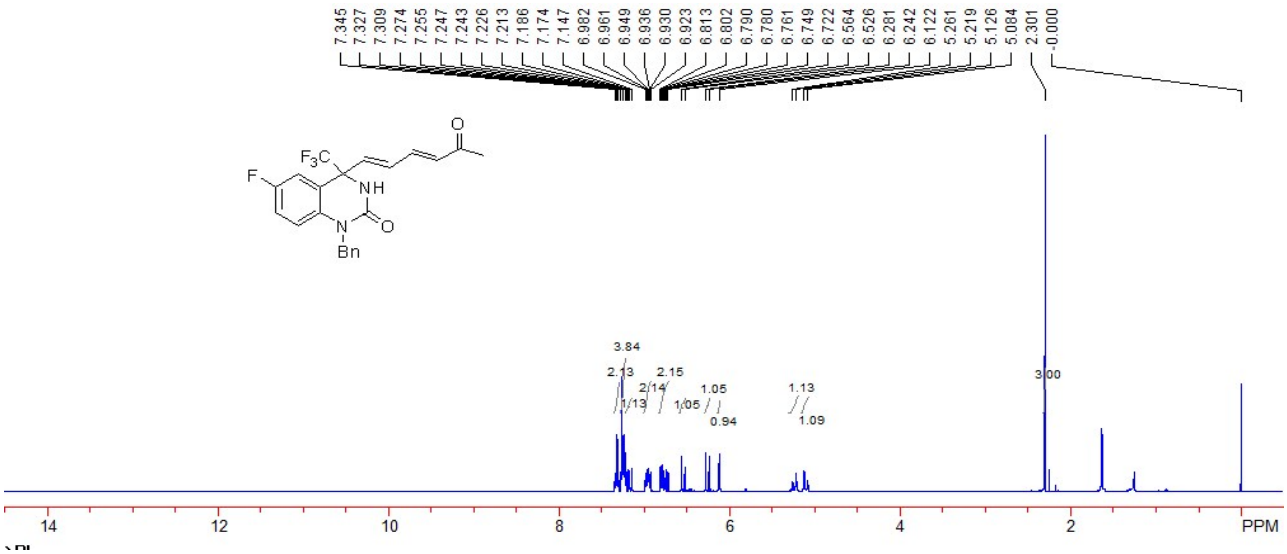


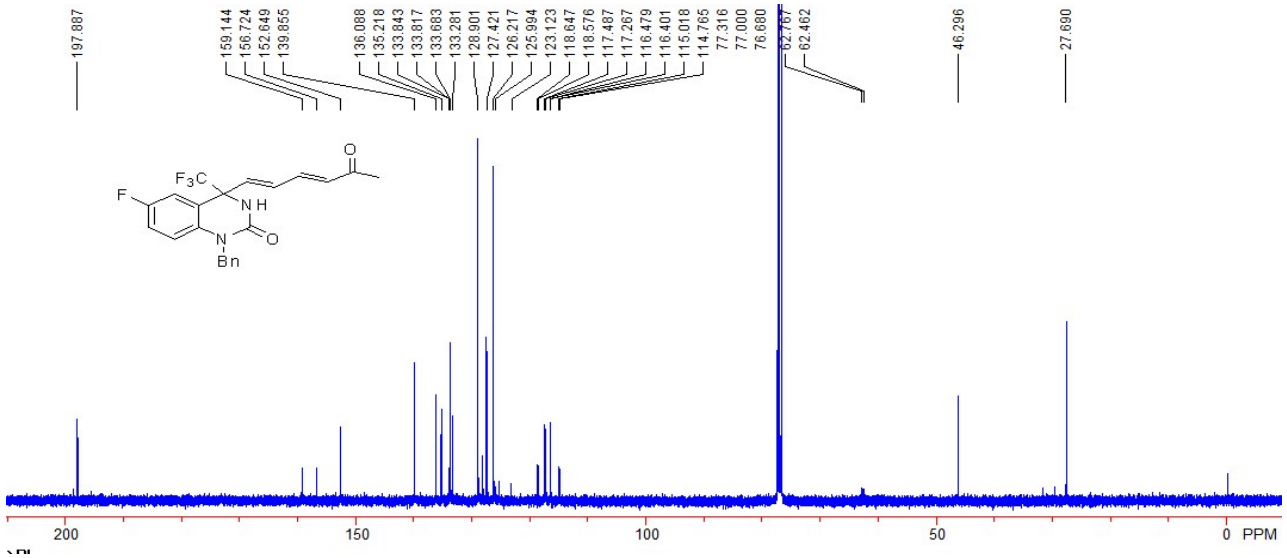


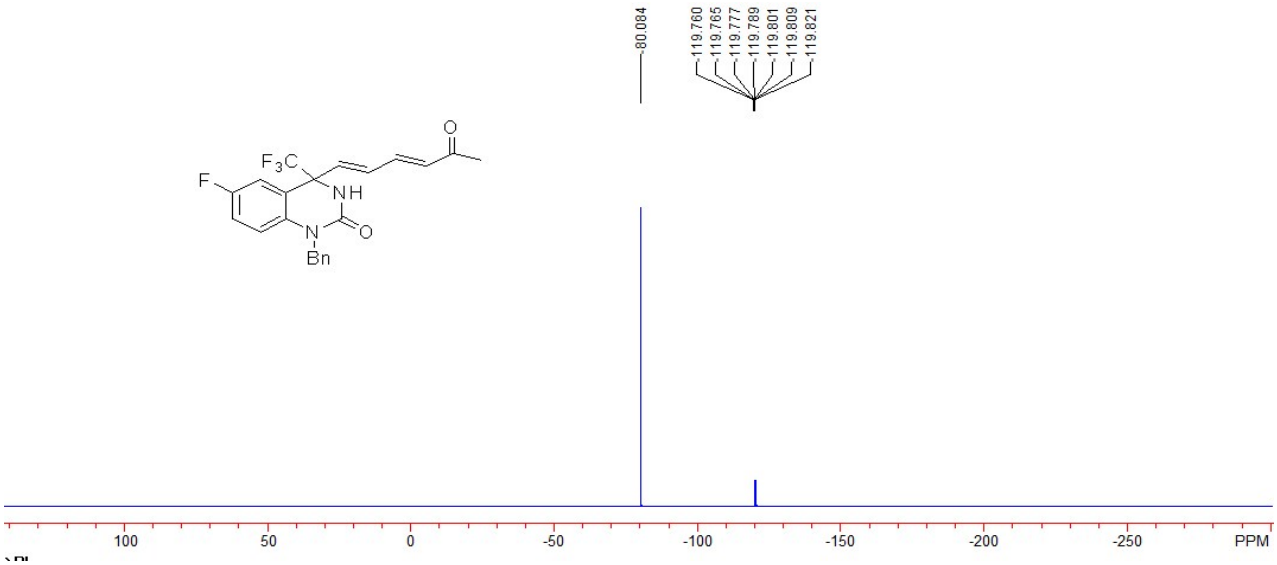
1-benzyl-6-fluoro-4-((1E,3E)-5-oxohexa-1,3-dien-1-yl)-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1H)-one (3f).

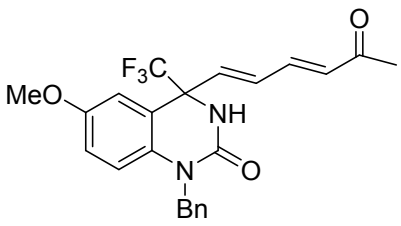
A white solid, 90% yield (75 mg). M.p.: 226-228 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 2.30 (s, 3H, CH_3), 5.11 (d, J = 16.8 Hz, 1H, CH_2), 5.24 (d, J = 16.8 Hz, 1H, CH_2), 6.12 (s, 1H, NH), 6.26 (d, J = 15.6 Hz, 1H, =CH), 6.55 (d, J = 15.2 Hz, 1H, =CH), 6.72-6.82 (m, 2H, ArH, =CH), 6.92-6.99 (m, 2H, ArH), 7.18 (dd, J = 10.8, 15.6 Hz, 1H, =CH), 7.22-7.27 (m, 3H, ArH), 7.30-7.35 (m, 2H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 27.7, 46.3, 62.6 (q, J = 30.5 Hz), 114.9 (d, J = 25.3 Hz), 116.4 (d, J = 3.9 Hz), 117.4 (d, J = 22.0 Hz), 118.6 (d, J = 7.1 Hz), 124.6 (q, J = 287.1 Hz), 126.2,

127.4, 128.9, 133.3, 133.7, 133.8 (d, J = 2.6 Hz), 135.2, 136.1, 139.9, 152.6, 157.9 (d, J = 242.0 Hz), 197.9. ^{19}F NMR (376 MHz, $CDCl_3$, $CFCl_3$) δ -80.08, -119.76-(-119.83) (m). IR (CH_2Cl_2) ν 3210, 3080, 2955, 2919, 2850, 1678, 1599, 1515, 1439, 1397, 1255, 1175, 999, 724 cm^{-1}. MS (ESI) *m/z* (%): 441.1 (100) $[M+Na]^+$; HRMS (ESI) Calcd. For $C_{22}H_{18}F_4N_2NaO_2^{+1}(M+Na)^+$ requires 441.1197, Found: 441.1200.



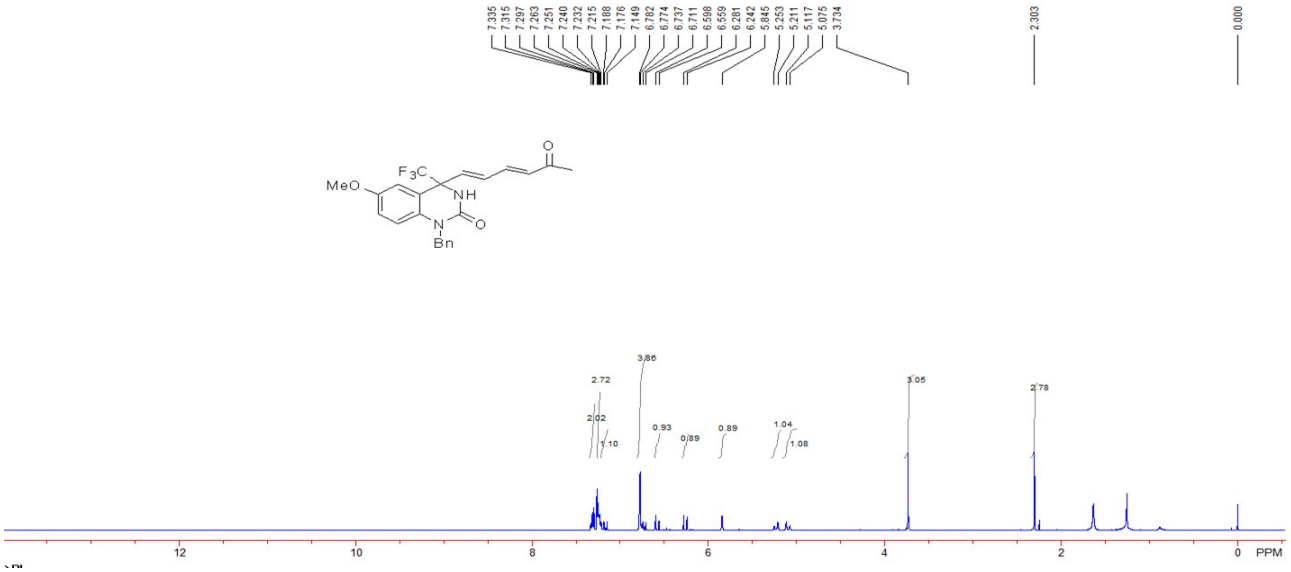






1-benzyl-6-methoxy-4-((1E,3E)-5-oxohexa-1,3-dien-1-yl)-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1H)-one (3g).

A white solid, 60% yield (51 mg). M.p.: 201-203 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 2.30 (s, 3H, CH_3), 3.73 (s, 3H, CH_3), 5.10 (d, *J* = 16.8 Hz, 1H, CH_2), 5.23 (d, *J* = 16.8 Hz, 1H, CH_2), 5.85 (s, 1H, NH), 6.26 (d, *J* = 15.6 Hz, 1H, =CH), 6.58 (d, *J* = 15.6 Hz, 1H, =CH), 6.71-6.79 (m, 4H, ArH, =CH), 7.18 (dd, *J* = 10.8, 15.6 Hz, 1H, =CH), 7.23-7.27 (m, 2H, ArH), 7.29-7.34 (m, 2H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 27.7, 46.1, 55.6, 62.8 (q, *J* = 28.9 Hz), 114.2, 115.0, 116.1, 118.3, 124.7 (q, *J* = 287.7 Hz), 126.3, 127.2, 128.8, 131.0, 132.7, 133.4, 136.0, 136.5, 140.1, 152.7, 154.9, 158.8, 198.0. ^{19}F NMR (376 MHz, $CDCl_3$, $CFCl_3$) δ -79.78. IR (CH_2Cl_2) ν 3216, 3073, 2954, 2923, 2852, 1675, 1596, 1516, 1454, 1434, 1403, 1255, 1231, 1180, 725 cm^{-1}. MS (ESI) *m/z* (%): 431.2 (100) $[M+H]^+$; HRMS (ESI) Calcd. For $C_{23}H_{23}F_3N_2O_3^{+1}(M+H)^+$ requires 431.1577, Found: 431.1573.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6.711
6.598
6.559
6.261
6.242
5.845
5.253
5.211
5.117
5.075
3.734
2.303
0.000
MeO
F3C
NH
N
O
Bn
3.86
2.72
3.05
2.78
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12
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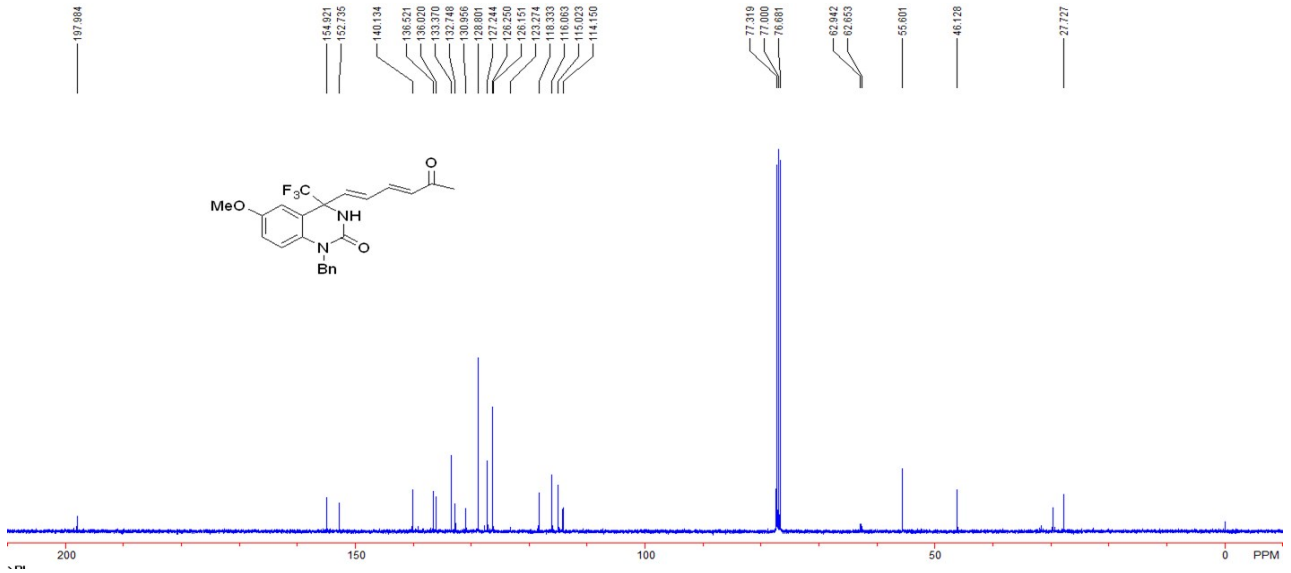
PPM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115.023
114.150
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77.000
76.681
62.942
62.653
55.601
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27.727
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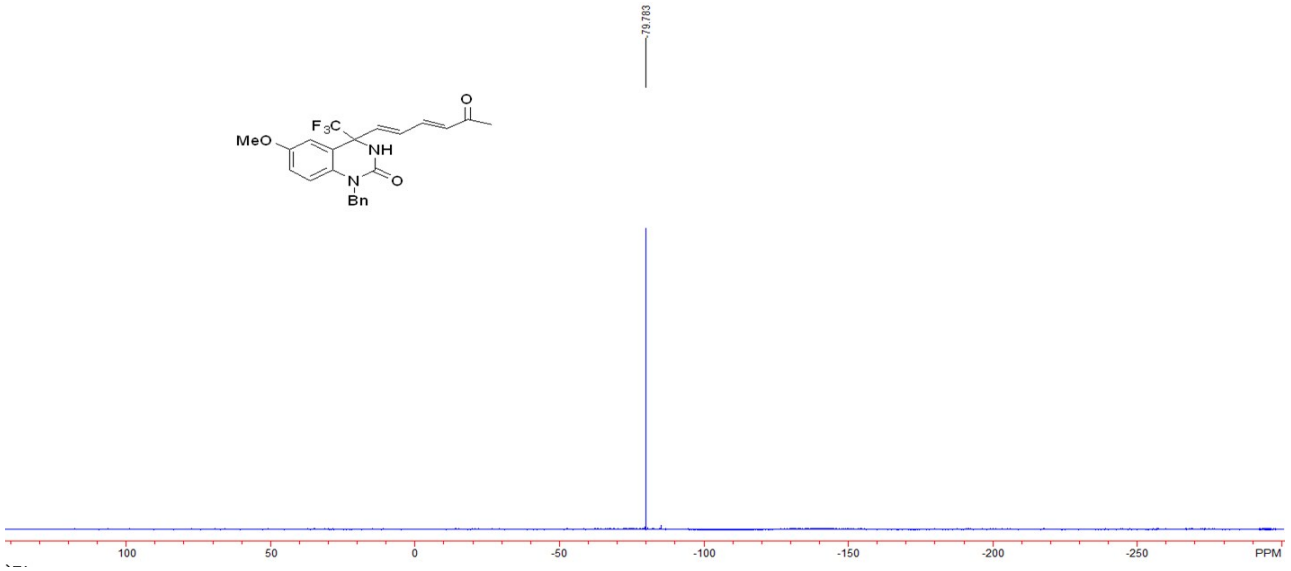
F3C
NH
N
O
Bn
200
150
100
50
0
PPM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O
Bn
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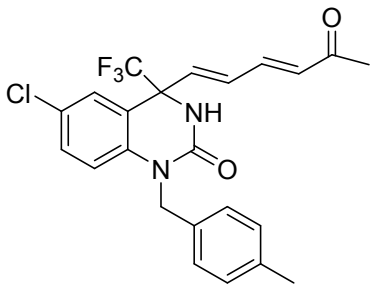
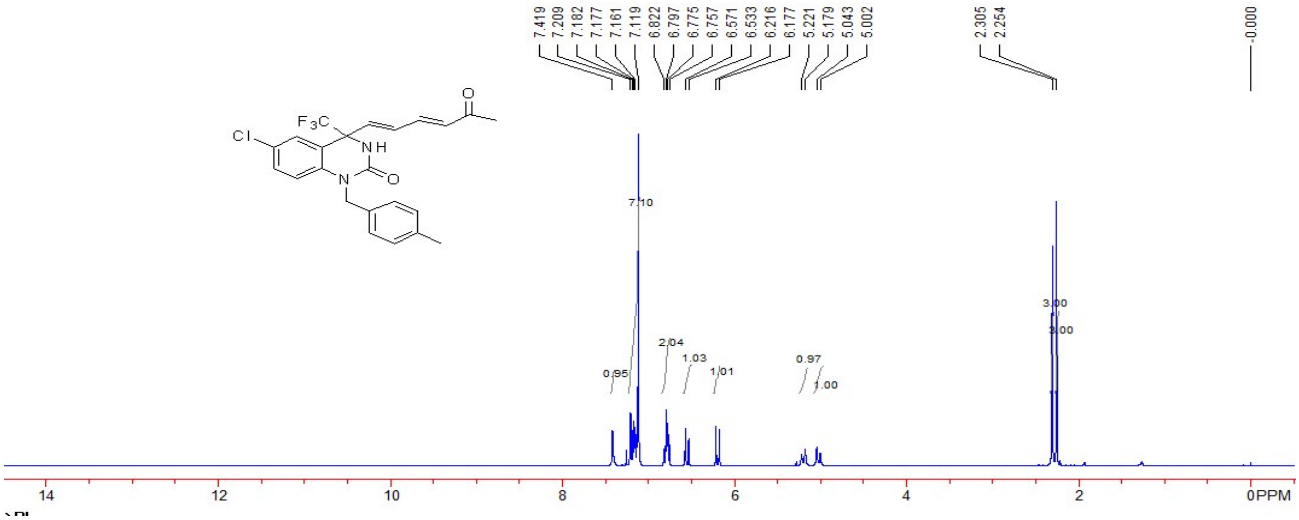
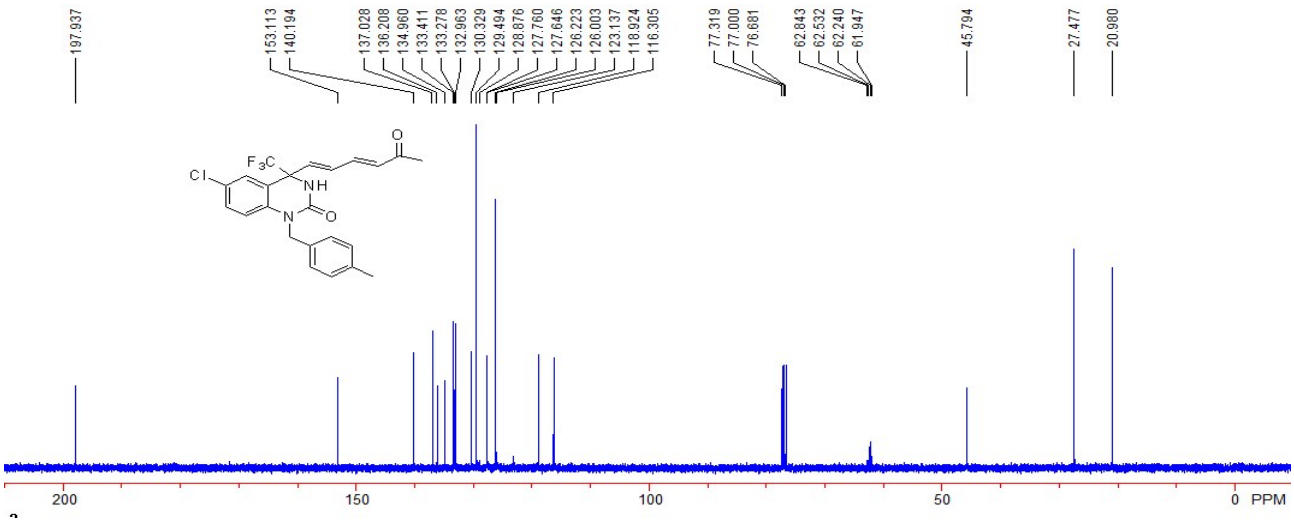
-50
-100
-150
-200
-250
PPM

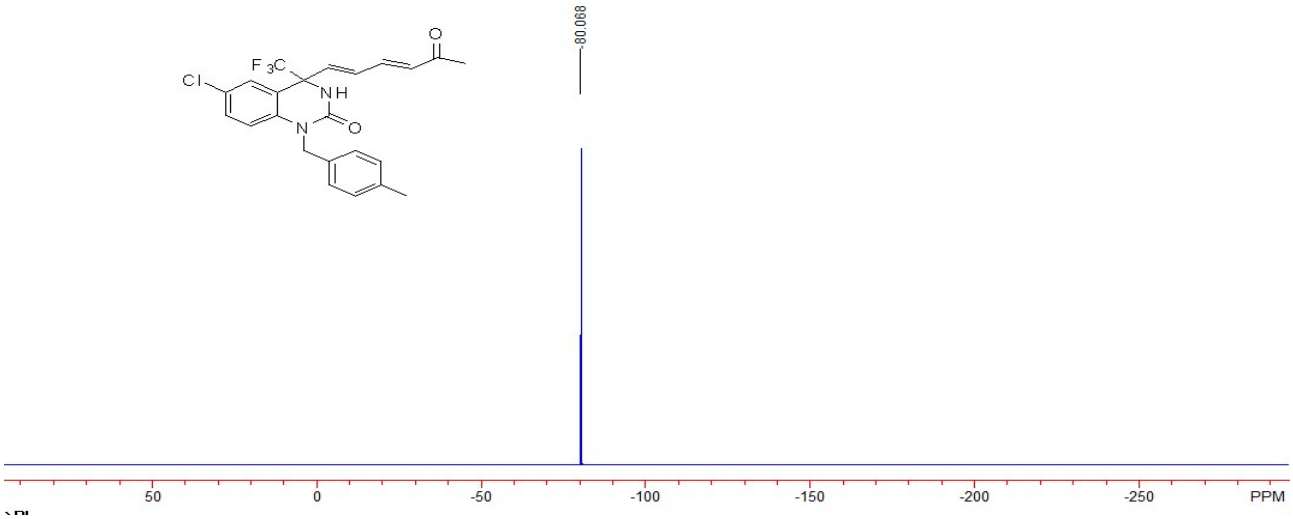


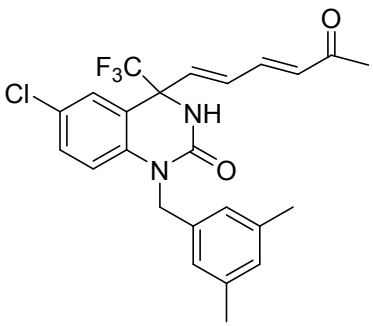
6-chloro-1-(4-methylbenzyl)-4-((1E,3E)-5-oxohexa-1,3-dien-1-yl)-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1H)-one (3h).

A white solid, 87% yield (78 mg). M.p.: 242-244 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 2.25 (s, 3H, CH_3), 2.31 (s, 3H, CH_3), 5.02 (d, J = 16.4 Hz, 1H, CH_2), 5.20 (d, J = 16.0 Hz, 1H, CH_2), 6.20 (d, J = 15.6 Hz, 1H, =CH), 6.55 (d, J = 15.2 Hz, 1H, =CH), 6.75-6.83 (m, 2H, =CH), 7.11-7.21 (m, 7H, ArH), 7.42 (s, 1H, NH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 21.0, 27.5, 45.8, 62.4 (q, J = 29.2 Hz), 116.3, 118.9, 124.6 (q, J = 286.6 Hz), 126.2, 127.6, 127.8, 129.5, 130.3, 133.0, 133.3, 133.4, 135.0, 136.2, 137.0, 140.2, 153.1, 197.9. ^{19}F NMR (376 MHz, $CDCl_3$, $CFCl_3$) δ -80.07. IR (CH_2Cl_2) ν 3394, 2922, 1681, 1592, 1451, 1337, 1123, 1020, 955, 912, 847, 818, 668, 626 cm^{-1}. MS (ESI) *m/z* (%): 449.1 (100) $[M+H]^+$; HRMS (ESI) Calcd. For $C_{23}H_{21}ClF_3N_2O_2^{+1}(M+H)^+$ requires 449.1238, Found: 449.1238.





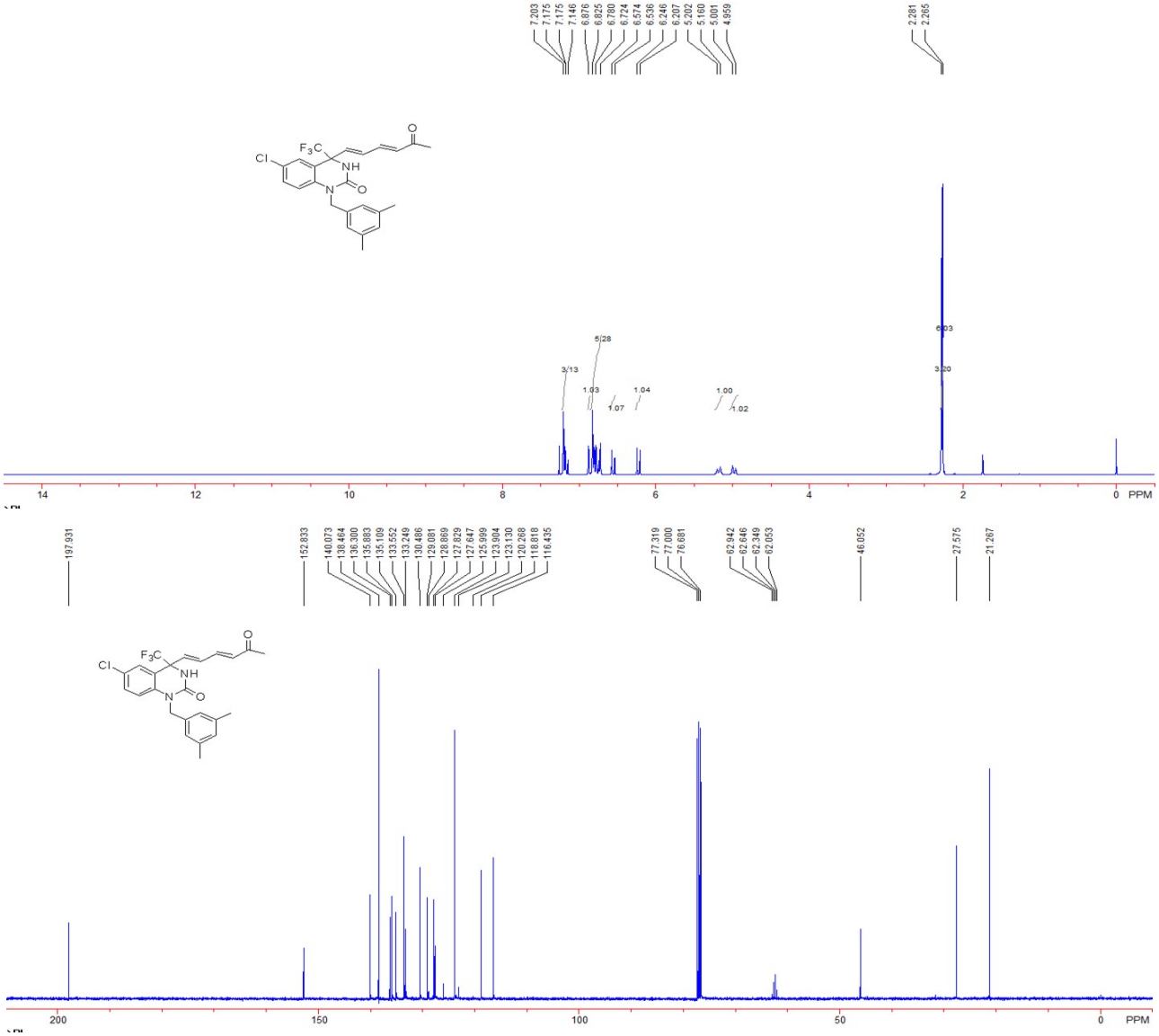


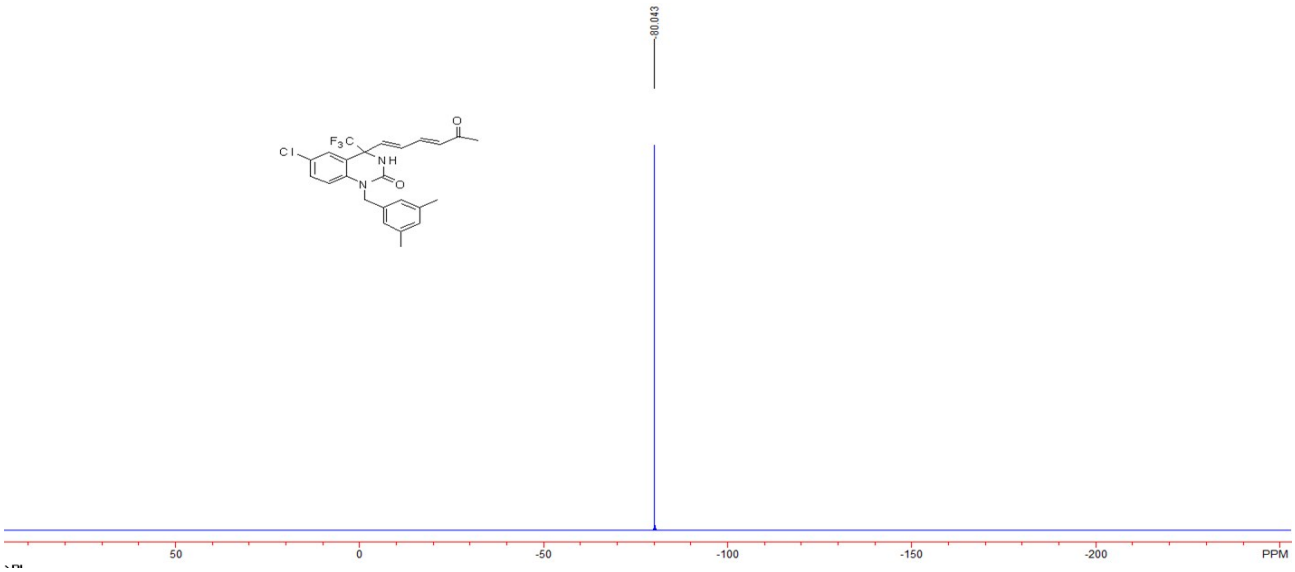


6-chloro-1-(3,5-dimethylbenzyl)-4-((1E,3E)-5-oxohexa-1,3-dien-1-yl)-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1H)-one (3i).

A white solid, 96% yield (87 mg). M.p.: 251-253 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 2.27 (s, 6H, CH_3), 2.28 (s, 3H, CH_3), 4.98 (d, J = 16.8 Hz, 1H, CH_2), 5.28 (d, J = 16.0 Hz, 1H, CH_2), 6.23 (d, J = 15.6 Hz, 1H, =CH), 6.56 (d, J = 15.2 Hz, 1H, =CH), 6.72-6.83 (m, 5H, ArH, =CH), 6.88 (s, 1H, NH), 7.14-7.21 (m, 3H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 21.3, 27.6, 46.1, 62.5 (q, J

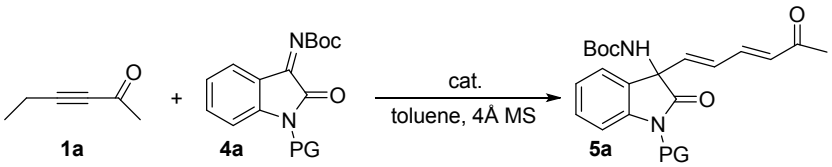
= 29.7 Hz), 116.4, 118.8, 123.9, 124.6 (q, J = 286.9 Hz), 127.6, 127.8, 129.1, 130.5, 133.2, 133.6, 135.1, 135.9, 136.3, 138.5, 140.1, 152.8, 197.9. ^{19}F NMR (376 MHz, $CDCl_3$, $CFCl_3$) δ -80.04. IR (CH_2Cl_2) ν 3206, 3085, 2922, 2851, 1681, 1600, 1503, 1425, 1392, 1259, 1175, 1118, 1000, 810 cm^{-1}. MS (ESI) *m/z* (%): 463.1 (100) $[M+H]^+$; HRMS (ESI) Calcd. For $C_{24}H_{23}ClF_3N_2O_2^{+1}(M+H)^+$ requires 463.1395, Found: 463.1392.




-80.043
Cl
F3C
NH
N
O
O
50
0
-50
-100
-150
-200
PPM

Optimal Conditions for the Synthesis of 5a

Table S1. Optimization of the reaction conditions.



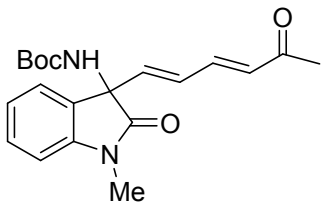
1a **4a** **5a**

entry[a]	PG	**1a** (equiv)	Cat.	4Å MS	temp (°C)	time (h)	yield%
1	Bn	3	PPh_3	0	rt	72	53[b]
2	allyl	3	PPh_3	0	rt	72	34[b]
3	allyl	3	$MePPh_2$	0	rt	72	complex
4	Me	2	PPh_3	0	rt	42	35[b]
5	allyl	2	$P(4\text{-}FC_6H_4)_3$	0	rt	24	trace
6[d]	Me	2	PPh_3	200 mg	60	42	56[c]
7	Me	4	$P(4\text{-}FC_6H_4)_3$	100 mg	65	96	86[b]

[*a*] The reaction was carried out using **1a** (0.2~0.8 mmol), **4a** (0.2 mmol), cat. (0.02 mmol), in the indicated solvent (1.0 mL) in a Schlenk tube at the indicated temperature. [*b*] Isolated yield. [*c*] The reaction was carried out using **1a** (2.0 mmol), **4a** (1.0 mmol), cat. (0.25 mmol), in the indicated solvent (3 mL) in a Schlenk tube at the indicated temperature.

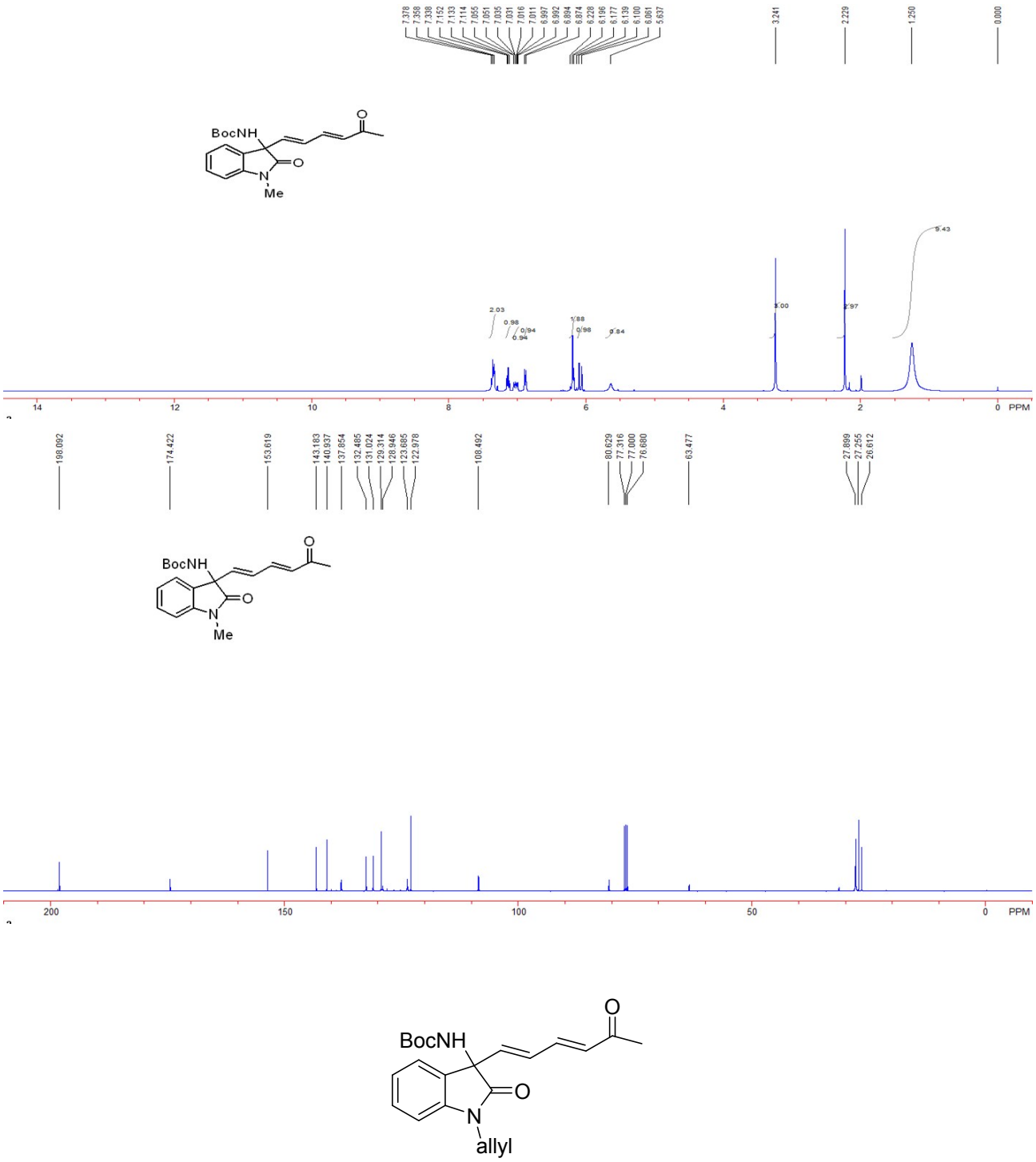
General Procedure for Hex-3-yn-2-one 1a to Isatin-derived N-Boc Ketimines 4 and Spectroscopic Data of the Products

General procedure: The 4Å MS was added to a Schlenk tube and heated under vacuum to remove ambient moisture and water, then filled with argon. After the Schlenk tube was returned to room temperature, isatin-derived *N*-Boc ketimines **4** (0.2 mmol) and $P(4\text{-}FC_6H_4)_3$ (13 mg, 0.04 mmol) was added. Under argon atmosphere, to a solution of isatin-derived *N*-Boc ketimines **4** (0.2 mmol) and $P(4\text{-}FC_6H_4)_3$ (13 mg, 0.04 mmol) in toluene (1.0 mL) was added the hex-3-yn-2-one **1a** (0.8 mmol) at room temperature. Then the resulting mixture was heated to 65 ^oC and continued stirring at 65 ^oC until the reaction completed (monitoring by TLC). Then the solvent was removed under reduced pressure and the residue was directly subjected to a flash column chromatography on silica gel to afford the desired products **5a**-**5g**.



tert-butyl (1-methyl-2-oxo-3-((1E,3E)-5-oxohexa-1,3-dien-1-yl)indolin-3-yl)carbamate (5a).

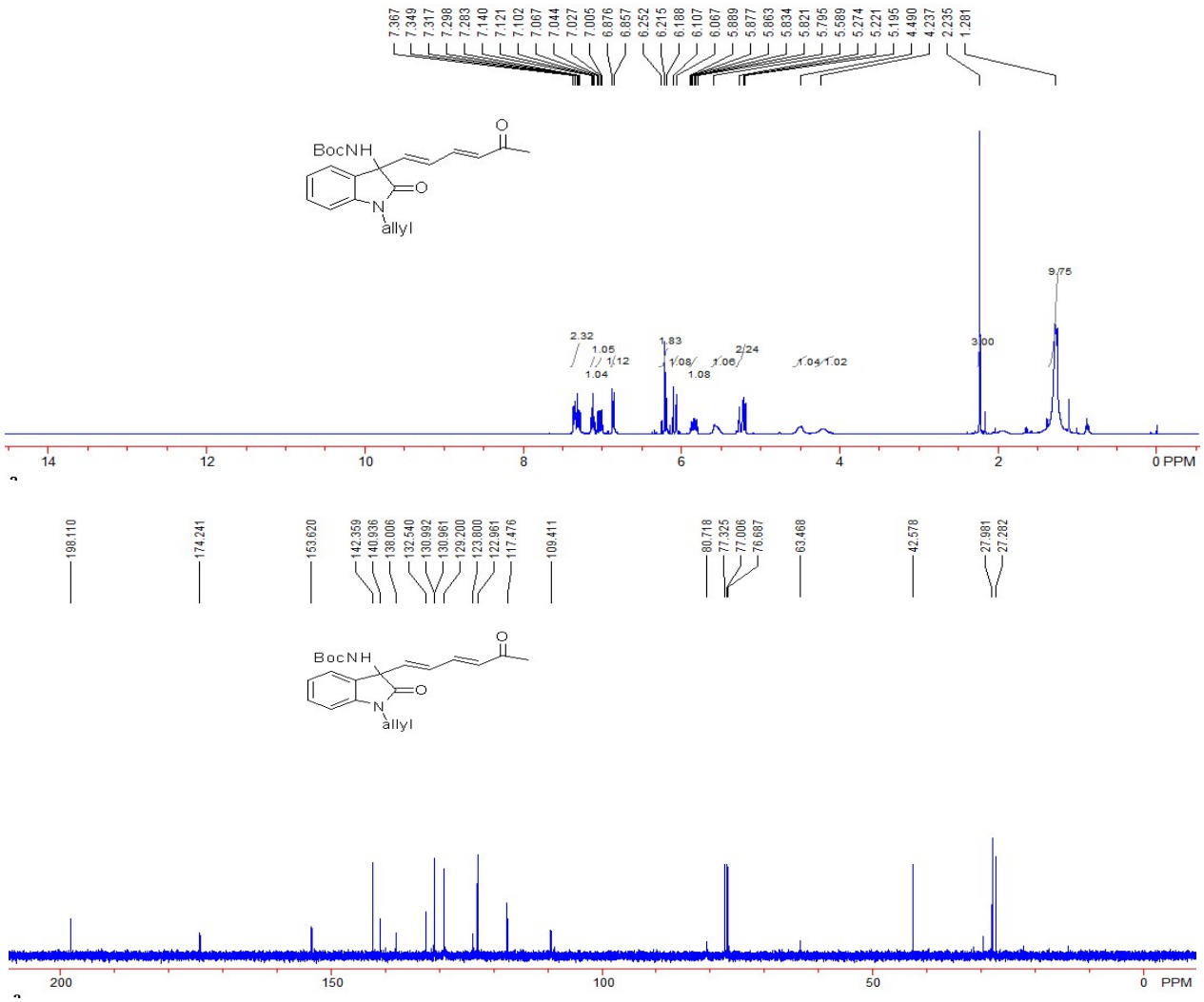
A white solid, 86% yield (61 mg). M.p.: 180-182 ^oC. ^1H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.25 (s, 9H, $C(CH_3)_3$), 2.23 (s, 3H, CH_3), 3.24 (s, 3H, CH_3), 5.64 (s, 1H, NH), 6.08 (d, *J* = 15.6 Hz, 1H, =CH), 6.13-6.23 (m, 2H, =CH), 6.89 (d, *J* = 8.0 Hz, 1H, ArH), 7.02 (ddd, *J* = 1.6, 8.0, 15.6 Hz, 1H, =CH), 7.11-7.16 (m, 1H, ArH), 7.33-7.38 (m, 2H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 26.6, 27.3, 27.9, 63.5, 80.6, 108.5, 123.0, 123.7, 128.9, 129.3, 131.0, 132.5, 137.9, 140.9, 143.2, 153.6, 174.4, 198.1. IR (CH_2Cl_2) ν 3323, 2956, 2922, 2851, 1722, 1494, 1464, 1376, 1259, 1161, 1088, 852, 761, 692 cm^{-1}. MS (ESI) *m/z* (%): 357.2 (100) $[M+H]^+$; HRMS (ESI) Calcd. For $C_{20}H_{25}N_2O_4^{+1}(M+H)^+$ requires 357.1809, Found: 357.1813.

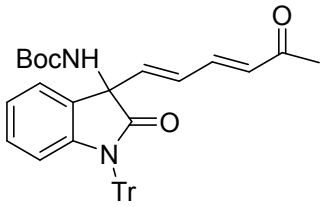


tert-butyl (1-methyl-2-oxo-3-((1E,3E)-5-oxohexa-1,3-dien-1-yl)indolin-3-yl)carbamate (5b).

A white solid, 90% yield (64 mg). M.p.: 119-121 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.28 (s, 9H, $C(CH_3)_3$), 2.24 (s, 3H, CH_3), 4.23 (br, 1H, CH_2), 4.49 (br, 1H, CH_2), 5.19-5.28 (m, 2H, =CH), 5.59 (br, 1H, NH), 5.79-5.89 (m, 1H, =CH), 6.08 (d, J = 16.0 Hz, 1H, =CH), 6.18-6.25 (m, 2H, =CH), 6.87 (d, J = 7.6 Hz, 1H, ArH), 7.04 (dd, J = 9.2, 16.0 Hz, 1H, =CH), 7.12 (dd, J = 7.6, 7.6 Hz, 1H, ArH), 7.28-7.37 (m, 2H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 27.3, 28.0, 42.6, 63.5,

80.7, 109.4, 117.5, 123.0, 123.8, 129.2, 131.0, 132.5, 138.0, 140.9, 142.4, 153.6, 174.2, 198.1. IR (CH_2Cl_2) ν 3322, 2970, 2922, 1708, 1670, 1611, 1487, 1466, 1363, 1250, 1159, 995, 753, 734 cm^{-1}. MS (ESI) *m/z* (%): 383.2 (100) $[M+H]^+$; HRMS (ESI) Calcd. For $C_{22}H_{27}N_2O_4^{+1}(M+H)^+$ requires 383.1965, Found: 383.1965.

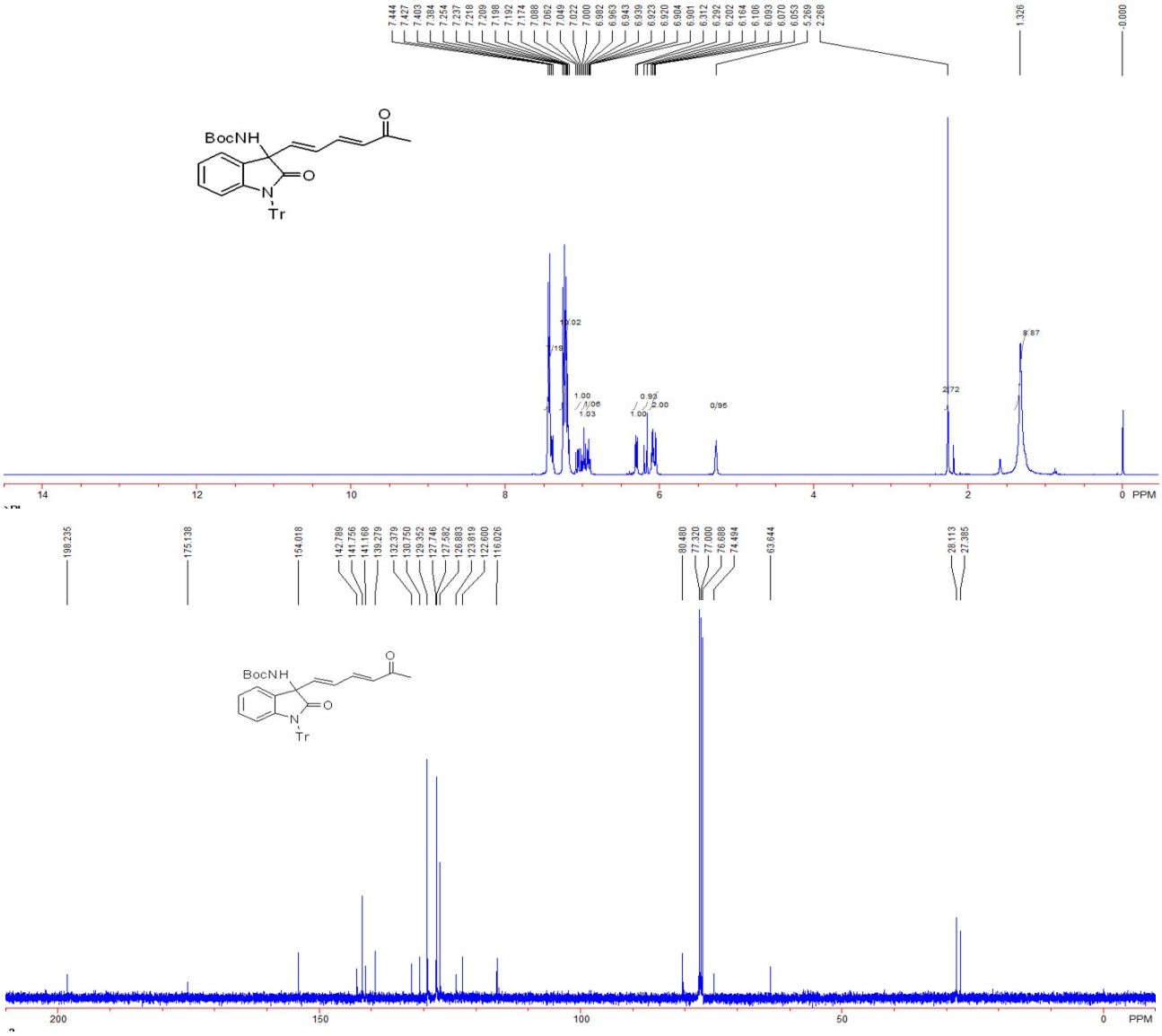


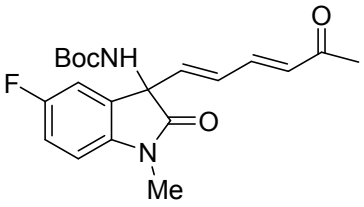


tert-butyl (1-methyl-2-oxo-3-((1E,3E)-5-oxohexa-1,3-dien-1-yl)indolin-3-yl)carbamate (5c).

A white solid, 84% yield (92 mg). M.p.: 235-237 ^oC. ^1H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.33 (s, 9H, $C(CH_3)_3$), 2.27 (s, 3H, CH_3), 5.27 (s, 1H, NH), 6.05-6.11 (m, 2H, =CH), 6.18 (d, *J* = 15.2 Hz,

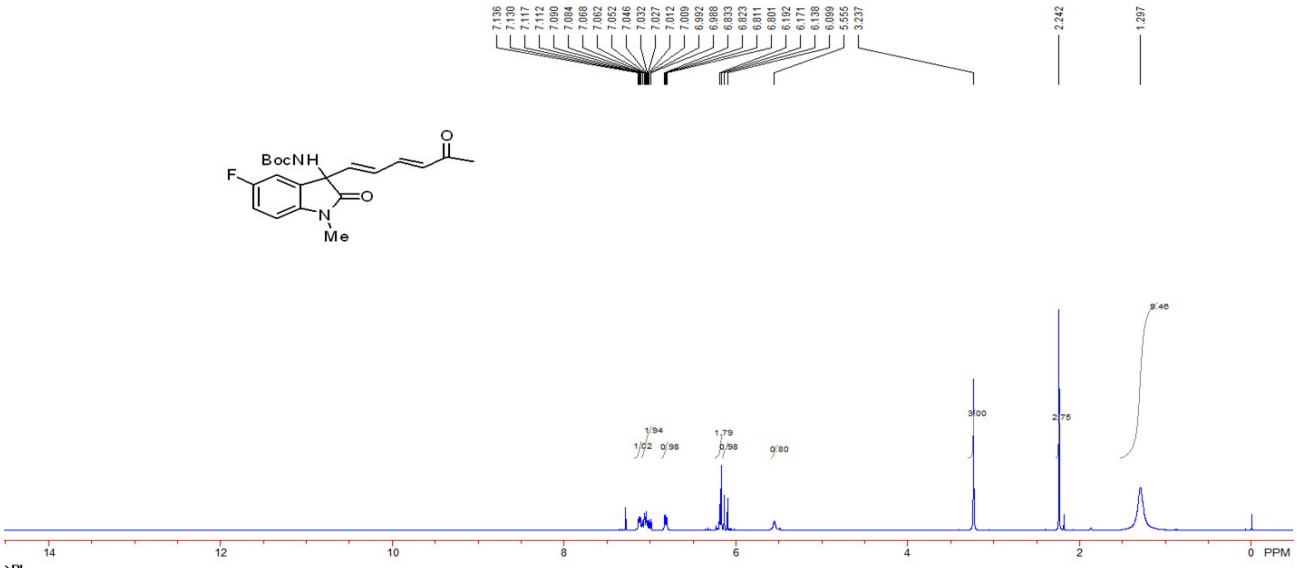
1H, =CH), 6.30 (d, *J* = 8.0 Hz, 1H, ArH), 6.92 (ddd, *J* = 1.2, 8.0, 8.0 Hz, 1H, ArH), 6.98 (dd, *J* = 7.6, 7.6 Hz, 1H, ArH), 7.06 (dd, *J* = 10.4, 15.6 Hz, 1H, ArH), 7.17-7.26 (m, 10H, ArH), 7.38-7.45 (m, 7H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 27.4, 28.1, 63.6, 74.5, 80.5, 116.0, 122.6, 123.8, 126.9, 127.6, 127.7, 129.4, 130.8, 132.4, 139.3, 141.2, 141.8, 142.8, 154.0, 175.1, 198.2. IR (CH_2Cl_2) ν 3303, 2971, 2927, 2850, 1715, 1670, 1596, 1490, 1462, 1449, 1365, 1256, 1156, 1021, 998, 908, 730, 703 cm^{-1}. MS (ESI) *m/z* (%): 602.3 (100) $[M+NH_4]^+$; HRMS (ESI) Calcd. For $C_{38}H_{40}N_3O_4^{+1}(M+NH_4)^+$ requires 602.3013, Found: 602.3015.

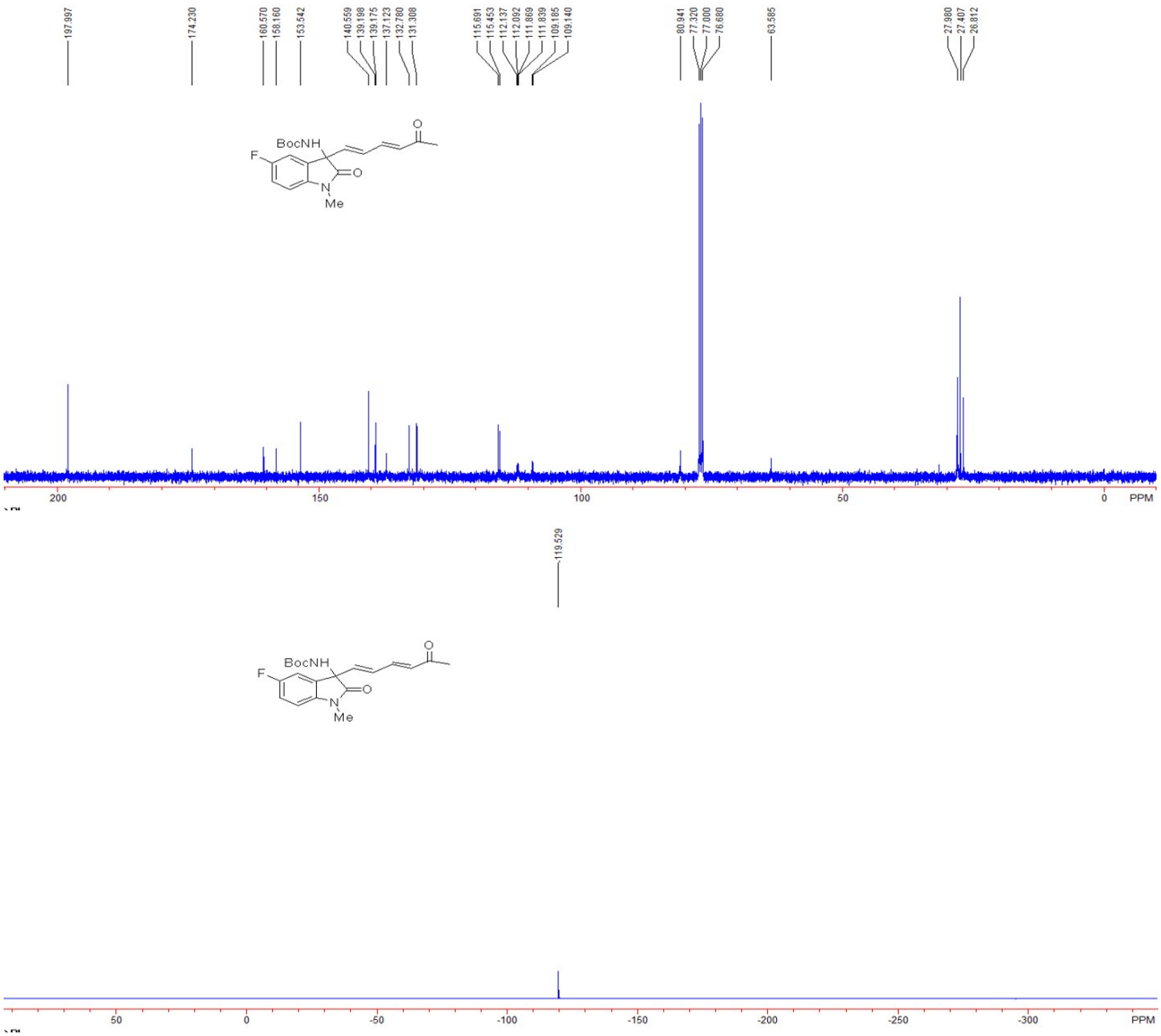


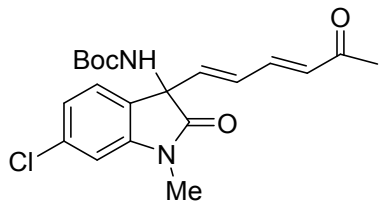


tert-butyl (5-fluoro-1-methyl-2-oxo-3-((1E,3E)-5-oxohexa-1,3-dien-1-yl)indolin-3-yl)carbamate (5d).

A white solid, 82% yield (61 mg). M.p.: 188-190 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.30 (s, 9H, $C(CH_3)_3$), 2.24 (s, 3H, CH_3), 3.24 (s, 3H, CH_3), 5.56 (s, 1H, NH), 6.12 (d, *J* = 15.6, 1H, =CH), 6.17-6.23 (m, 2H, =CH), 6.82 (dd, *J* = 4.0, 8.8 Hz, 1H, ArH), 6.98-7.09 (m, 2H, =CH, ArH), 7.12 (dd, *J* = 2.4, 8.8 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 26.8, 27.4, 28.0, 63.6, 80.9, 109.2 (d, *J* = 4.5 Hz), 111.9 (d, *J* = 3.0 Hz), 112.1 (d, *J* = 4.5 Hz), 115.6 (d, *J* = 23.8 Hz), 131.3, 132.8, 137.1, 139.2 (d, *J* = 2.3 Hz), 140.6, 153.5, 159.4 (d, *J* = 241.0 Hz), 174.2, 198.0. ^{19}F NMR (376 MHz, $CDCl_3$, $CFCl_3$) δ -119.53. IR (CH_2Cl_2) ν 3289, 2925, 2849, 1723, 1593, 1497, 1469, 1366, 1266, 1235, 1159, 1116, 830, 813, 733, 702, 661 cm^{-1}. MS (ESI) *m/z* (%): 293.1 (100) $[M+NH_4]^+$; HRMS (ESI) Calcd. For $C_{20}H_{27}FN_3O_4^{+1}(M+NH_4)^+$ requires 392.1980, Found: 392.1980.



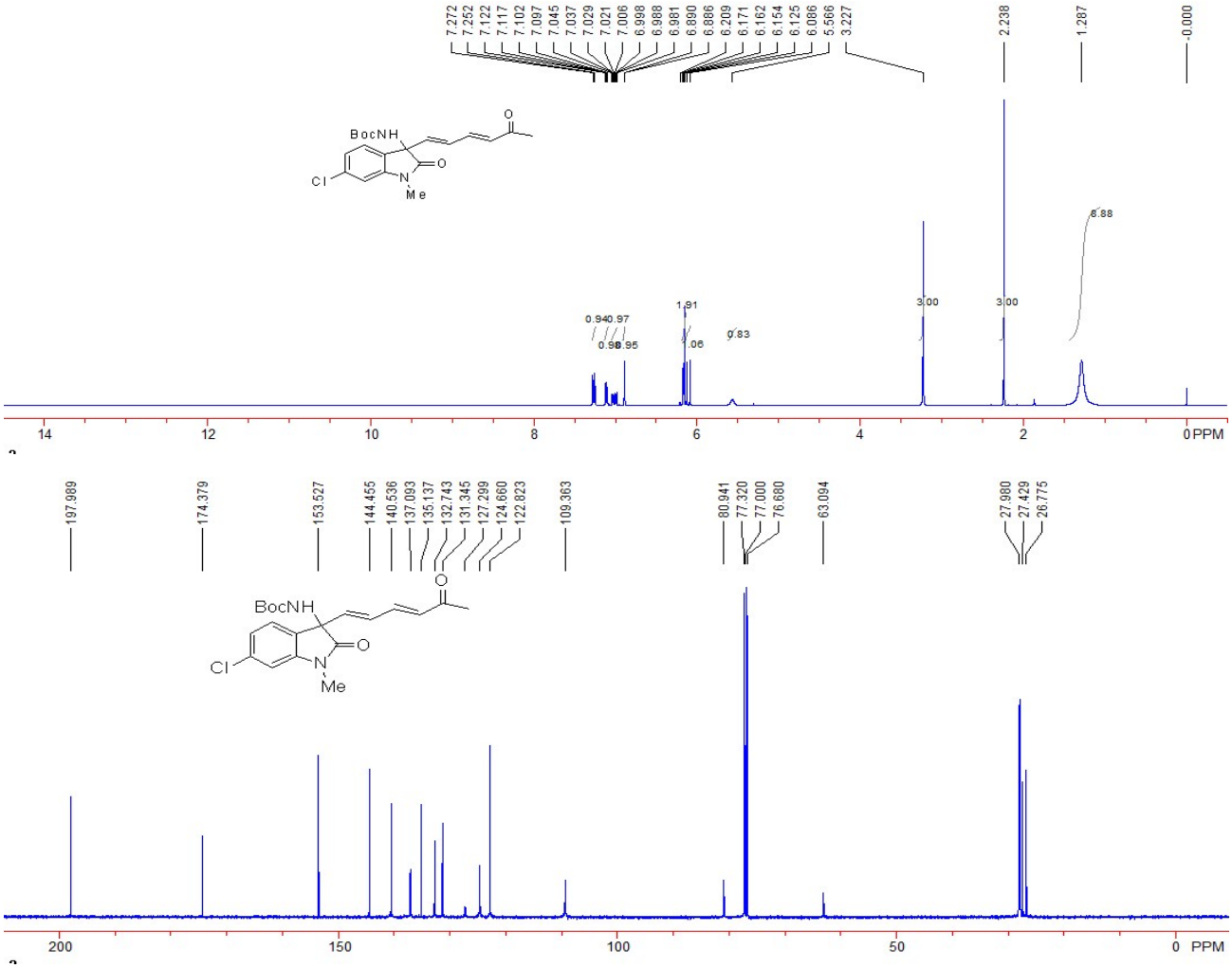


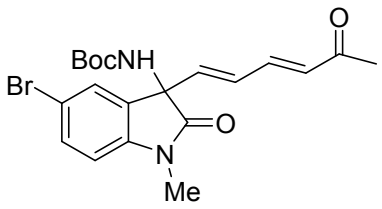


tert-butyl (6-chloro-1-methyl-2-oxo-3-((1E,3E)-5-oxohexa-1,3-dien-1-yl)indolin-3-yl)carbamate (5e).

A white solid, 92% yield (72 mg). M.p.: 236-238 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.29 (s, 9H, $C(CH_3)_3$), 2.24 (s, 3H, CH_3), 3.23 (s, 3H, CH_3), 5.57 (s, 1H, NH), 6.11 (d, J = 15.6 Hz, 1H, =CH), 6.15-6.21 (m, 2H, =CH), 6.89 (d, J = 1.6 Hz, 1H, ArH), 7.01 (ddd, J = 3.2, 6.4, 15.6 Hz, 1H, =CH), 7.11 (dd, J = 2.0, 8.0 Hz, 1H, ArH), 7.26 (d, J = 8.0 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 26.8, 27.4, 28.0, 63.1, 80.9, 109.4, 122.8, 124.7, 127.3, 131.3, 132.7, 135.1, 137.1,

140.5, 144.5, 153.5, 174.4, 198.0. IR (CH_2Cl_2) ν 3316, 2980, 2917, 2848, 1724, 1671, 1610, 1595, 1489, 1364, 1263, 1160, 1116, 997, 812, 701 cm^{-1}. MS (ESI) *m/z* (%): 391.1 (100) $[M+H]^+$; HRMS (ESI) Calcd. For $C_{20}H_{24}ClN_2O_4^{+1}(M+NH_4)^+$ requires 391.1419, Found: 391.1417.

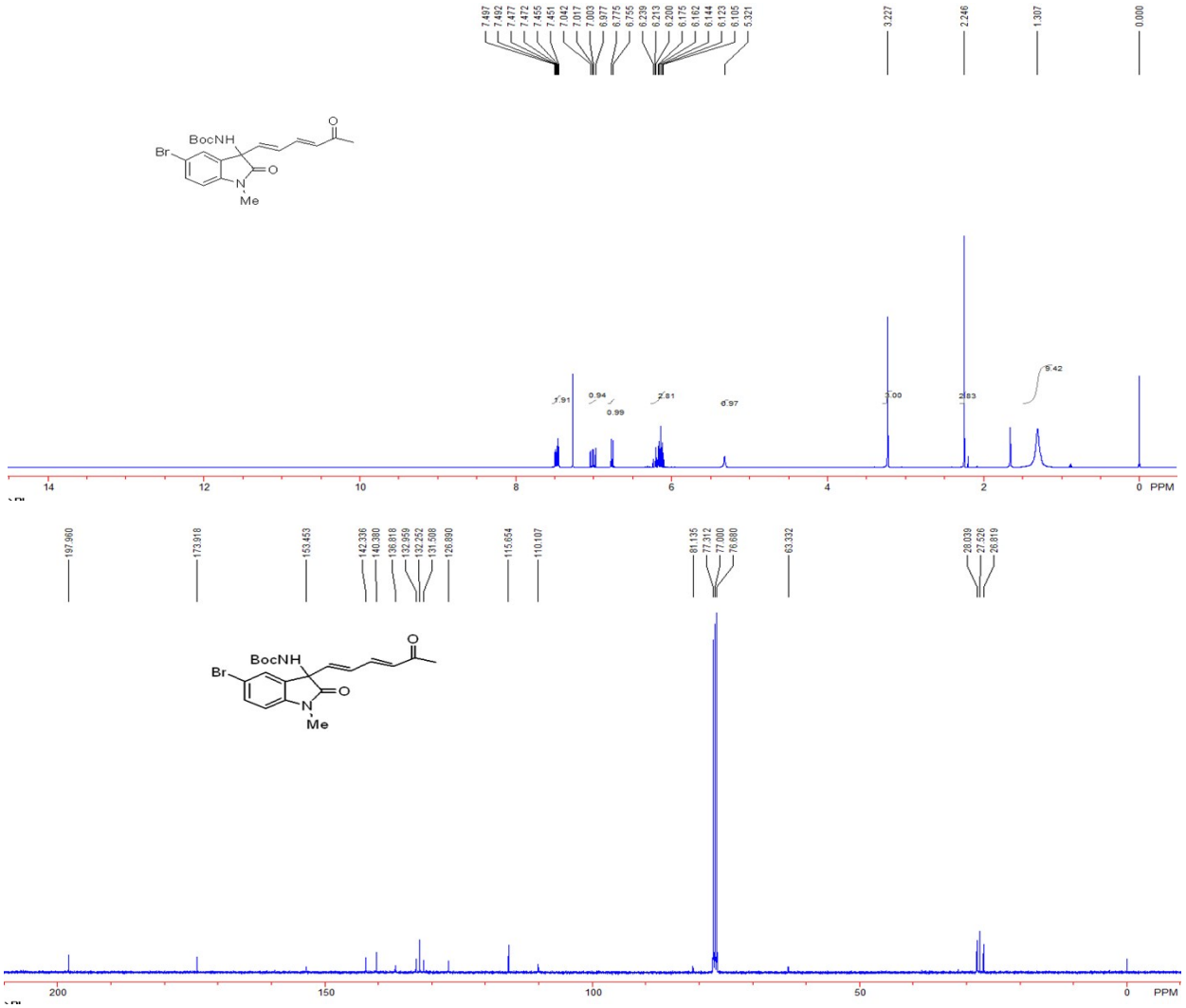


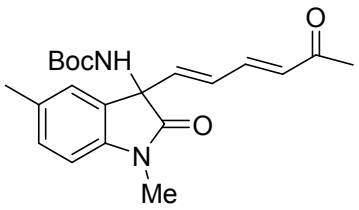


tert-butyl (5-bromo-1-methyl-2-oxo-3-((1E,3E)-5-oxohexa-1,3-dien-1-yl)indolin-3-yl)carbamate (5f).

A white solid, 88% yield (77 mg). M.p.: 289-290 ^oC. ^1H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.31 (s, 9H, $C(CH_3)_3$), 2.25 (s, 3H, CH_3), 3.23 (s, 3H, CH_3), 5.32 (s, 1H, NH), 6.10-6.24 (m, 3H, =CH), 6.77 (d, *J* = 8.0 Hz, 1H, ArH), 7.01 (dd, *J* = 10.0, 15.6 Hz, 1H, =CH), 7.45-7.50 (m, 2H, ArH). ^{13}C NMR

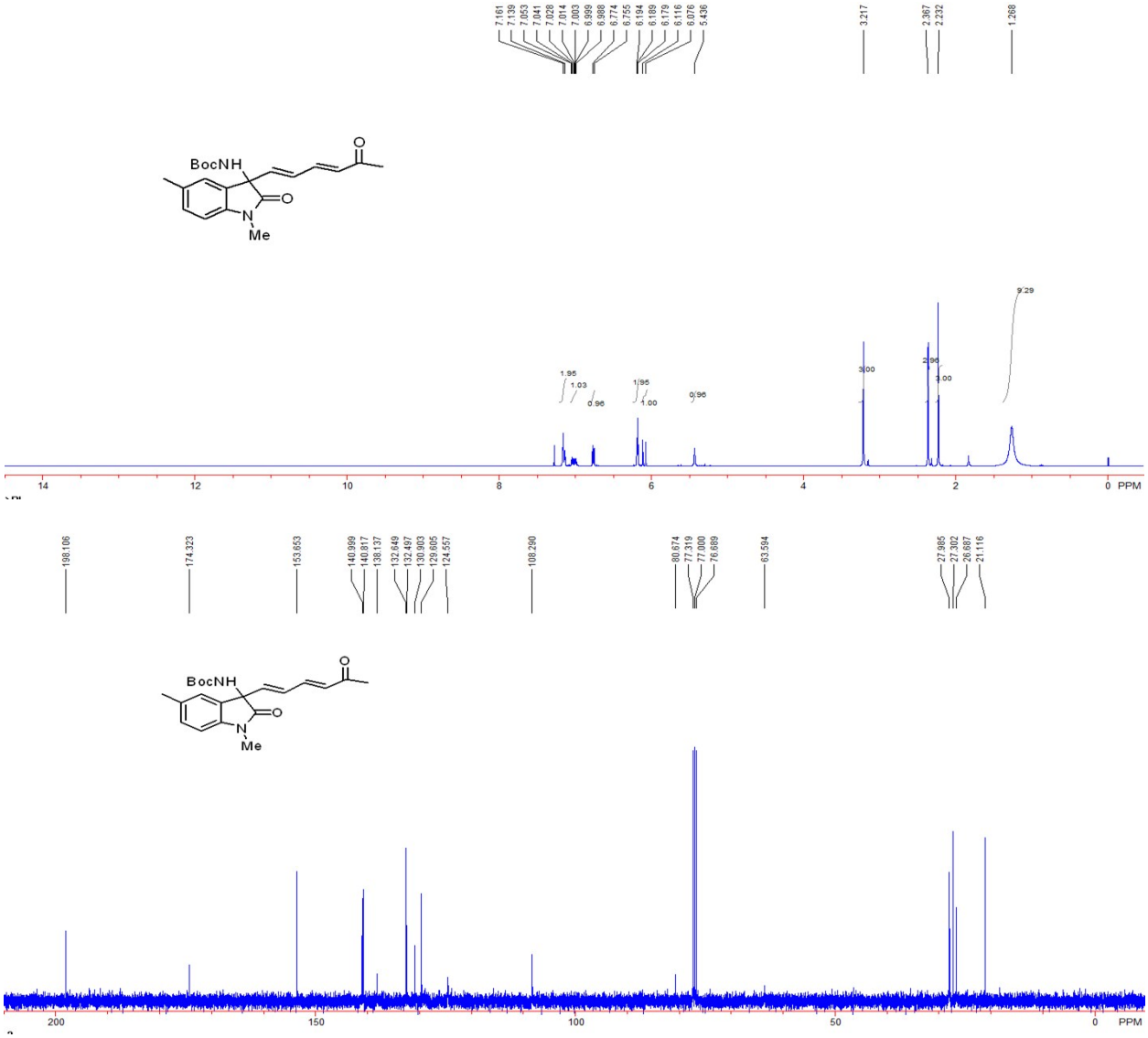
($CDCl_3$, TMS, 100 MHz) δ 26.8, 27.5, 28.0, 63.3, 81.1, 110.1, 115.7, 126.9, 131.5, 132.3, 133.0, 136.8, 140.4, 142.3, 153.5, 173.9, 198.0. IR (CH_2Cl_2) ν 3315, 2959, 2925, 2846, 1727, 1671, 1607, 1488, 1364, 1254, 1162, 1116, 999, 810 cm^{-1}. MS (ESI) *m/z* (%): 452.1 (100) $[M+NH_4]^+$; HRMS (ESI) Calcd. For $C_{20}H_{27}BrN_3O_4^{+1}(M+NH_4)^+$ requires 452.1179, Found: 452.1178.





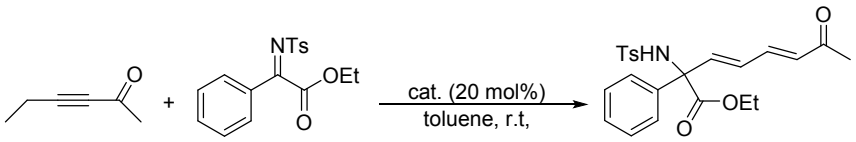
tert-butyl (1,5-dimethyl-2-oxo-3-((1E,3E)-5-oxohexa-1,3-dien-1-yl)indolin-3-yl)carbamate (5g). A white solid, 64% yield (47 mg). M.p.: 142-144 °C. ^1H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.27 (s, 9H, $C(CH_3)_3$), 2.23 (s, 3H, CH_3), 2.37 (s, 3H, CH_3), 3.22 (s, 3H, CH_3), 5.44 (s, 1H, NH), 6.10 (d, *J*

= 16.0 Hz, 1H, =CH), 6.17-6.20 (m, 2H, =CH), 6.76 (d, *J* = 7.6 Hz, 1H, ArH), 6.98-7.06 (m, 1H, =CH), 7.13-7.17 (m, 2H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 21.1, 26.7, 27.3, 28.0, 63.6, 80.7, 108.3, 124.6, 129.6, 130.9, 132.5, 132.6, 138.1, 140.8, 141.0, 153.7, 174.3, 198.1. IR (CH_2Cl_2) ν 3318, 2974, 2926, 1708, 1670, 1602, 1499, 1363, 1281, 1251, 1165, 997, 810, 732 cm^{-1}. MS (ESI) *m/z* (%): 371.2 (100) $[M+H]^+$; HRMS (ESI) Calcd. For $C_{21}H_{27}N_2O_4^{+1}(M+NH_4)^+$ requires 371.1965, Found: 371.1964.



Optimal Conditions for the Synthesis of 7a

Table S2. Optimization of the reaction conditions.



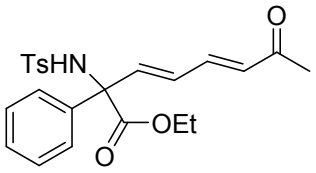
1a **6a** **7a**

entry[a]	Cat.	4ÅMS	temp (°C)	time (h)	yield%
1	PPh_3	0	rt	144	30[b]
2	PPh_3	100	65	72	24[b]
3	$MePPh_2$	100	rt	144	complex
4	PPh_3	100	rt	144	14[b]
5	$P(4\text{-}FC_6H_4)_3$	100	rt	144	24[b]

[*a*] The reaction was carried out using **1a** (0.3 mmol), **6a** (0.2 mmol), cat. (0.02 mmol), in the indicated solvent (1.0 mL) in a Schlenk tube at the indicated temperature. [*b*] Isolated yield.

General Procedure for Hex-3-yn-2-one 1a to N-tosyl α-Ketimine Esters 6a and Spectroscopic Data of the Products

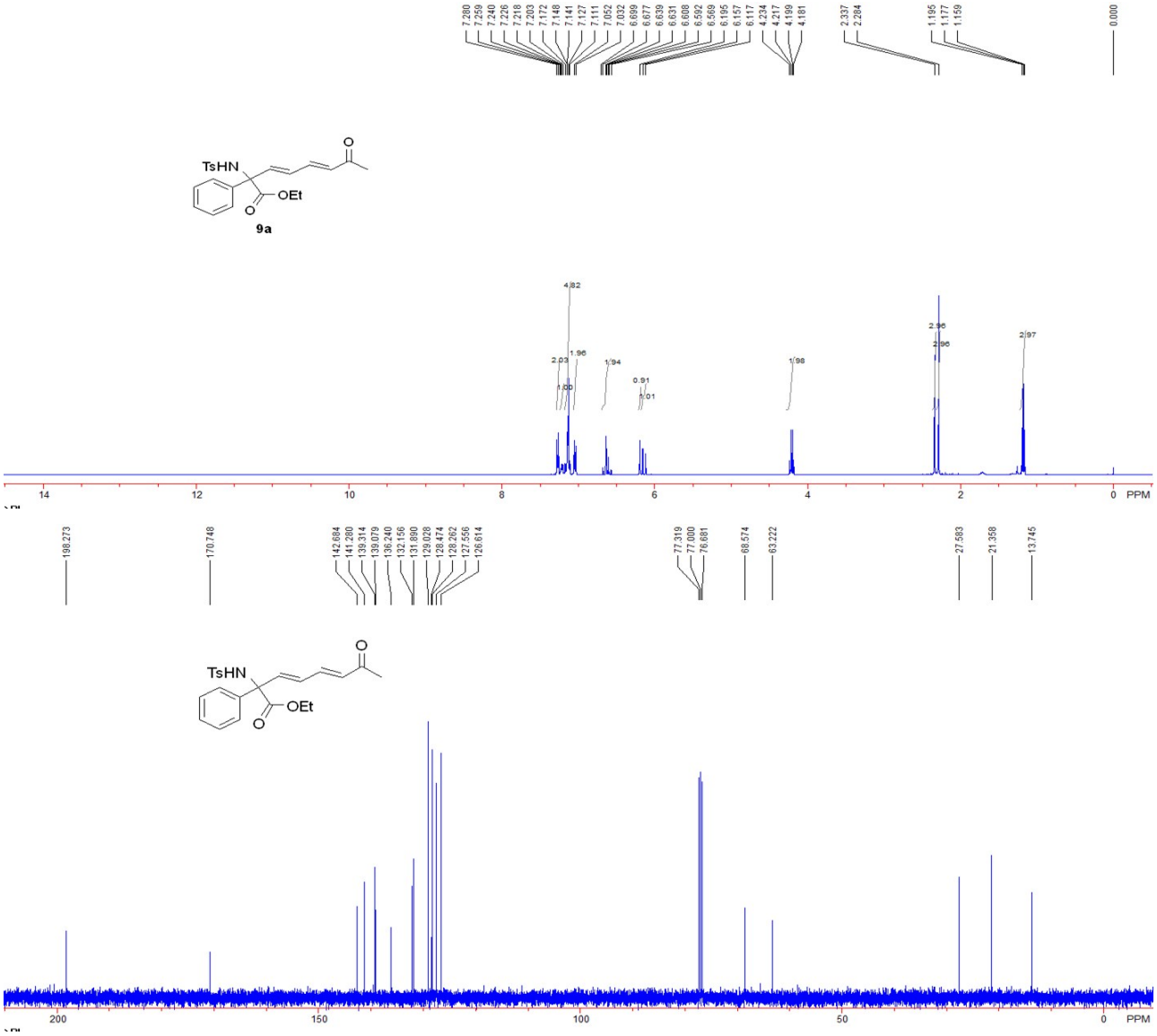
General procedure: Under argon atmosphere, to a solution of N-tosyl α-ketimine esters **6a** (0.2 mmol) and PPh_3 (11 mg, 0.04 mmol) in toluene (1.0 mL) was added the hex-3-yn-2-one **1a** (0.3 mmol) at room temperature. Then the resulting mixture was stirred at 65 °C until the reaction completed (monitoring by TLC). Then the solvent was removed under reduced pressure and the residue was directly subjected to a flash column chromatography on silica gel to afford the desired product **7a**.



Ethyl (3E,5E)-2-((4-methylphenyl)sulfonamido)-7-oxo-2-phenylocta-3,5-dienoate (7a).

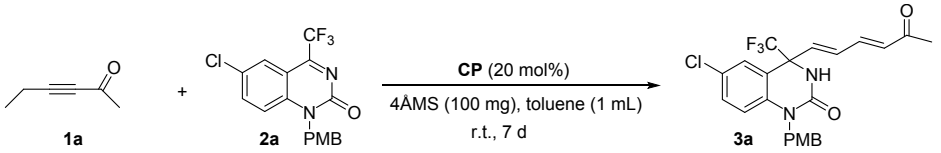
A white solid, 30% yield (62 mg). M.p.: 156-158 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.18 (t, *J* = 7.2 Hz, 3H, CH_3), 2.28 (s, 3H, CH_3), 2.34 (s, 3H, CH_3), 4.21 (q, *J* = 7.2 Hz, 2H, CH_2), 6.14 (d, *J* = 16.0 Hz, 1H, =CH), 6.20 (s, 1H, NH), 6.56-6.68 (m, 2H, =CH), 7.04 (d, *J* = 8.0 Hz, 2H, ArH), 7.11-7.18 (m, 5H, =CH), 7.19-7.24 (m, 1H, ArH), 7.27 (d, *J* = 8.0 Hz, 2H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 13.7, 21.4, 27.6, 63.2, 68.6, 126.6, 127.6, 128.3, 128.5, 129.0, 131.9, 132.2, 136.2, 139.1, 139.3, 141.3, 142.7, 170.7, 198.3. IR (CH_2Cl_2) ν 3255, 2923, 1733, 1663, 1590, 1329, 1246,

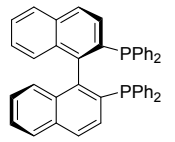
1155, 1092, 999, 813, 698, 662 cm^{-1}. MS (ESI) *m/z* (%): 445.2 (100) $[M+NH_4]^+$; HRMS (ESI) Calcd. For $C_{23}H_{29}N_2O_5S^{+1}(M+NH_4)^+$ requires 445.1792, Found: 445.1792.



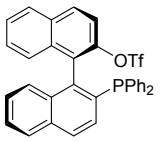
Screening of Chiral Phosphine Catalysts of δ-Carbon Activation of Hex-3-yn-2-one 1a and Addition to Cyclic Trifluoromethyl Ketimine 2a.

Table S3. Screening of chiral phosphine catalysts in the enantioselective addition of **1a** and **2a**.[a]

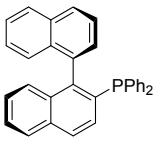




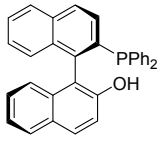
CP-12
no reaction



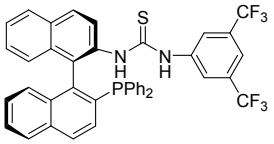
CP-2
no product



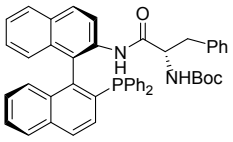
CP-3
trace



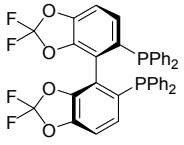
CP-4
complex



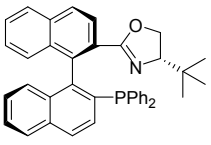
CP-5
r.t, n.r.
70 °C, complex



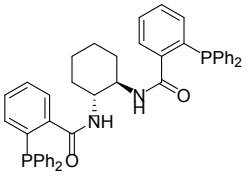
CP-6
trace



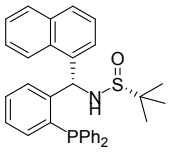
CP-7
trace



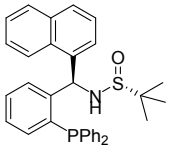
CP-8
no product



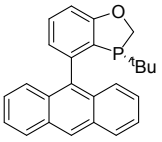
CP-9
trace



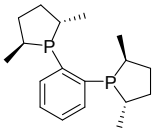
CP-10
complex



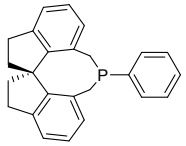
CP-11
complex



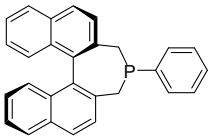
antPhos
no product



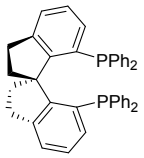
DuPhos
no product



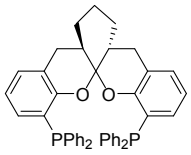
R-SITCP
71% yield, 0% ee[c]



CP-14
r.t, 62% yield[b], 6% ee[c]



(*R*)-SDP
r.t, 56% yield[b], 6% ee[c]

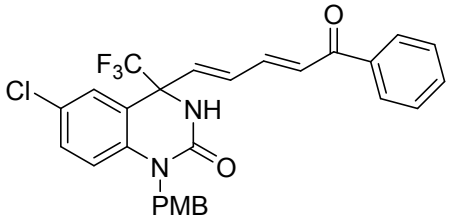


(*S,S,S*)-SKP
r.t, 63% yield[b], 7% ee[c]

[a] Reactions were performed with **1a** (0.40 mmol) and **2a** (0.20 mmol) in the presence of 20 mol% of **CP** in toluene (1 mL) for 7 days. [b] Isolated yields.
[c] Determined by chiral HPLC analysis.

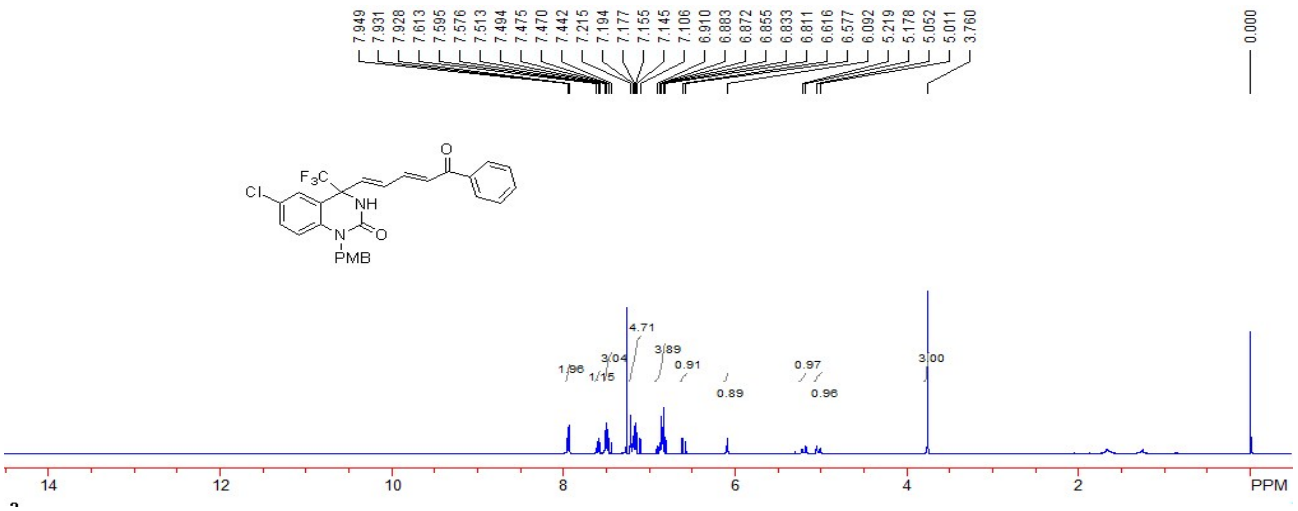
General Procedure for Alkynones 1 to Cyclic Trifluoromethyl Ketimines 2a and Spectroscopic Data of the Products

General procedure: The 4Å MS was added to a Schlenk tube and heated under vacuum to remove ambient moisture and water, then filled with argon. After the Schlenk tube was returned to room temperature, cyclic trifluoromethyl ketimines **2a** (0.2 mmol) and $P(4\text{-}FC_6H_4)_3$ (13 mg, 0.04 mmol) was added. Under argon atmosphere, to a solution of cyclic trifluoromethyl ketimines **2** (0.2 mmol) and $P(4\text{-}FC_6H_4)_3$ (13 mg, 0.04 mmol) in toluene (1.0 mL) was added the alkynones **1** (0.8 mmol) at room temperature. Then the resulting mixture was heated to 65 ^oC and continued stirring at 65 ^oC until the reaction completed (monitoring by TLC). Then the solvent was removed under reduced pressure and the residue was directly subjected to a flash column chromatography on silica gel to afford the desired products **3j** and **3k**.



6-chloro-1-(4-methoxybenzyl)-4-((1E,3E)-5-oxo-5-phenylpenta-1,3-dien-1-yl)-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1H)-one (3j).

A white solid, 88% yield (93 mg). M.p.: 221-223 ^oC. ^1H NMR ($CDCl_3$, TMS, 400 MHz) δ 3.76 (s, 3H, CH_3), 5.03 (d, J = 16.4 Hz, 1H, CH_2), 5.20 (d, J = 16.0 Hz, 1H, CH_2), 6.09 (s, 1H, NH), 6.60 (d, J = 15.6 Hz, 1H, =CH), 6.81-6.91 (m, 4H, ArH, =CH), 7.11-7.12 (m, 5H, ArH, =CH), 7.44-7.52 (m, 3H, ArH, =CH), 7.58-7.61 (m, 1H, ArH), 7.92-7.95 (m, 1H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 45.6, 62.6 (q, J = 29.6 Hz), 114.3, 116.4, 118.9, 124.5 (q, J = 286.9 Hz), 127.6, 127.78, 127.82, 128.1, 128.5, 128.7, 129.1, 130.5, 133.2, 133.5, 135.5, 136.1, 137.4, 141.2, 152.8, 158.9, 189.9. ^{19}F NMR (376 MHz, $CDCl_3$, $CFCl_3$) δ -79.95. IR (CH_2Cl_2) ν 3205, 3065, 2952, 2924, 2853, 1678, 1599, 1513, 1503, 1428, 1247, 1173, 1013, 734, 695 cm^{-1}. MS (ESI) *m/z* (%): 527.1 (100) $[M+H]^+$; HRMS (ESI) Calcd. For $C_{28}H_{23}ClF_3N_2O_3^{+1}(M+H)^+$ requires 527.1344, Found: 527.1343.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7.931
7.928
7.613
7.595
7.576
7.513
7.494
7.475
7.470
7.442
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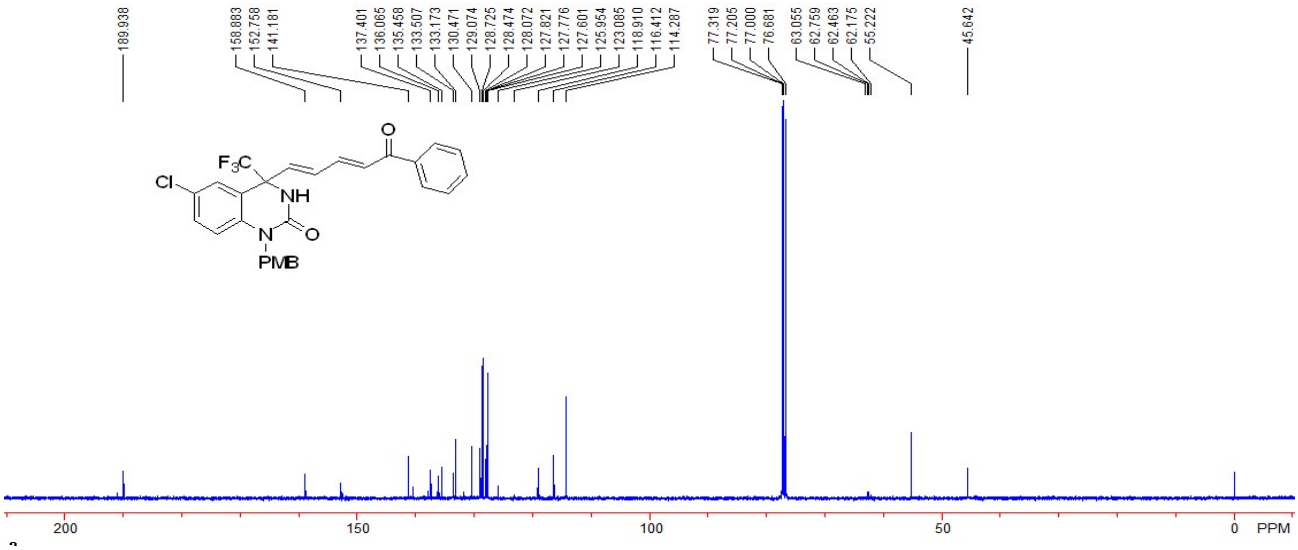
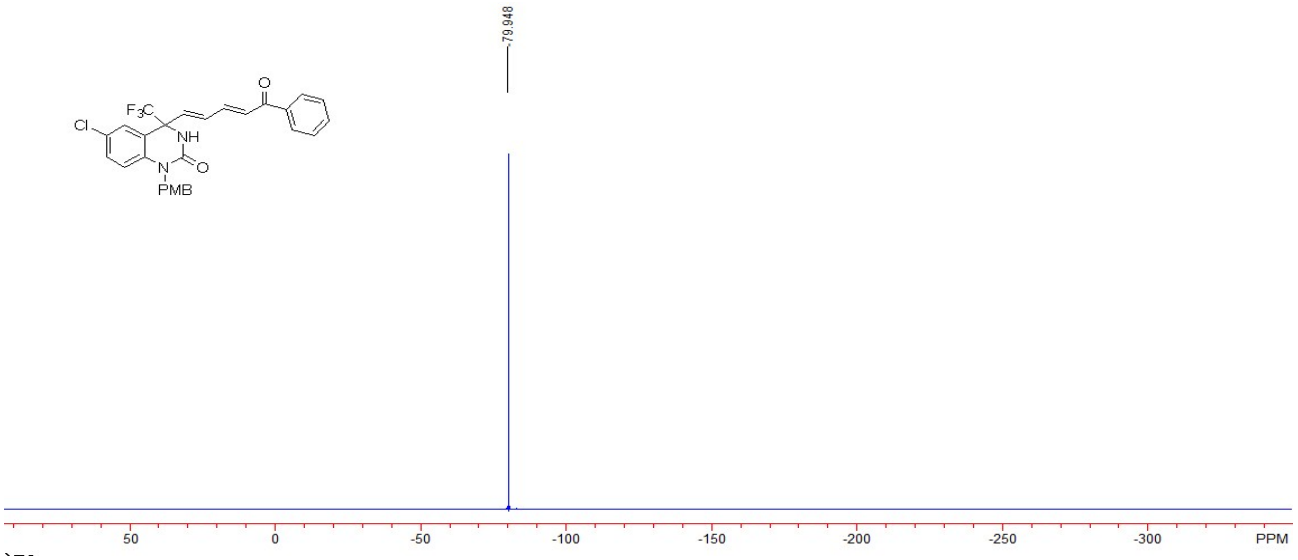
7.194
7.177
7.155
7.145
7.106
6.910
6.883
6.872
6.855
6.833
6.811
6.616
6.577
6.092
5.219
5.178
5.052
5.011
3.760
0.000
F3C
Cl
NH
N
O
PMB
4.71
3.89
3.04
1.96
1.15
0.91
0.89
0.97
0.96
3.00
14
12
10
8
6
4
2
PPM


189.938
158.883
152.758
141.181
137.401
136.065
135.458
133.507
133.173
130.471
129.074
128.725
128.474
128.072
127.821
127.776
127.601
125.954
123.085
118.910
116.412
114.287
77.319
77.205
77.000
76.681
63.055
62.759
62.463
62.175
55.222
45.642
F3C
Cl
NH
N
O
PMB
200
150
100
50
0
PPM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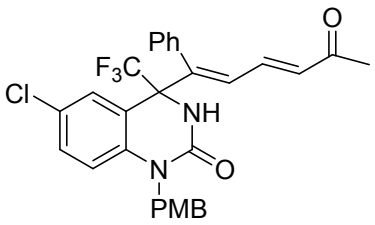
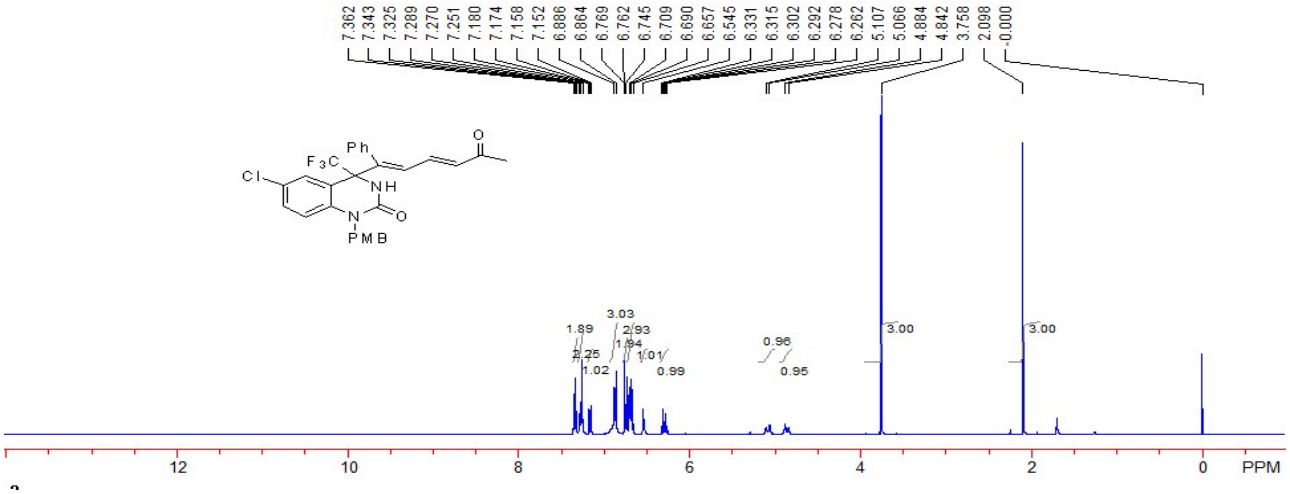
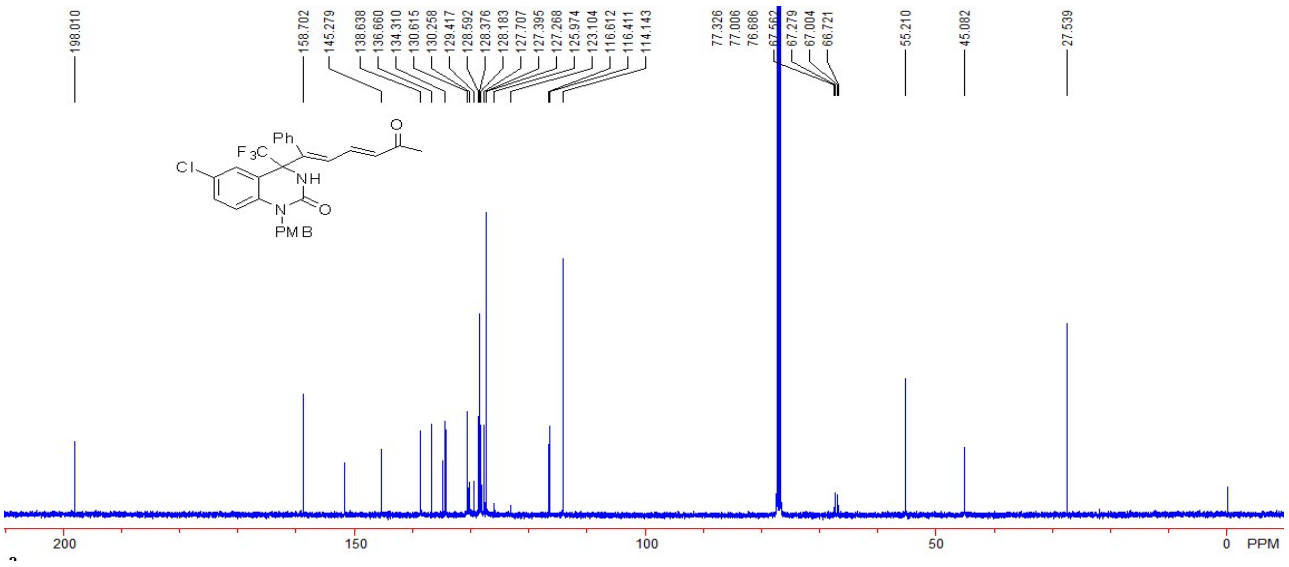
F3C
Cl
NH
N
O
PMB
50
0
-50
-100
-150
-200
-250
-300
PPM



6-chloro-1-(4-methoxybenzyl)-4-((1E,3E)-5-oxo-1-phenylhexa-1,3-dien-1-yl)-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1H)-one (3k).

A white solid, 65% yield (70 mg). M.p.: 172-174 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 2.10 (s, 3H, CH_3), 3.76 (s, 3H, CH_3), 4.86 (d, *J* = 16.8 Hz, 1H, CH_2), 5.09 (d, *J* = 16.8 Hz, 1H, CH_2), 6.30 (td, *J* = 6.4, 14.8 Hz, 1H, =CH), 6.55 (br, 1H, NH), 6.65-6.71 (m, 3H, ArH, =CH), 6.74-6.77 (m, 2H, ArH), 6.88 (d, *J* = 8.8 Hz, 3H, ArH, =CH), 7.17 (dd, *J* = 2.4, 8.8 Hz, 1H, ArH), 7.25-7.29 (m, 2H, ArH), 7.32-7.37 (m, 2H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 27.5, 45.1, 55.2, 67.1 (q, *J* = 31.3 Hz), 114.1, 116.4, 116.6, 124.5 (q, *J* = 287.0 Hz), 127.3, 127.4, 128.2, 128.4, 129.4, 130.3, 130.6, 134.3, 136.7, 138.6, 145.3, 158.7, 198.0. ^{19}F NMR (376 MHz, $CDCl_3$, $CFCl_3$) δ -73.31. IR (CH_2Cl_2) ν 3205, 3080, 2959, 2922, 2849, 1675, 1601, 1512, 1425, 1392, 1248, 1174, 1091, 1066, 1028, 805, 737, 705 cm^{-1}. MS (ESI) *m/z* (%): 541.2 (100) $[M+H]^+$; HRMS (ESI) Calcd. For $C_{29}H_{25}ClF_3N_2O_3^{+1}(M+H)^+$ requires 541.1500, Found: 541.1500.




198.010
158.702
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136.660
134.310
130.615
130.258
129.417
128.592
128.376
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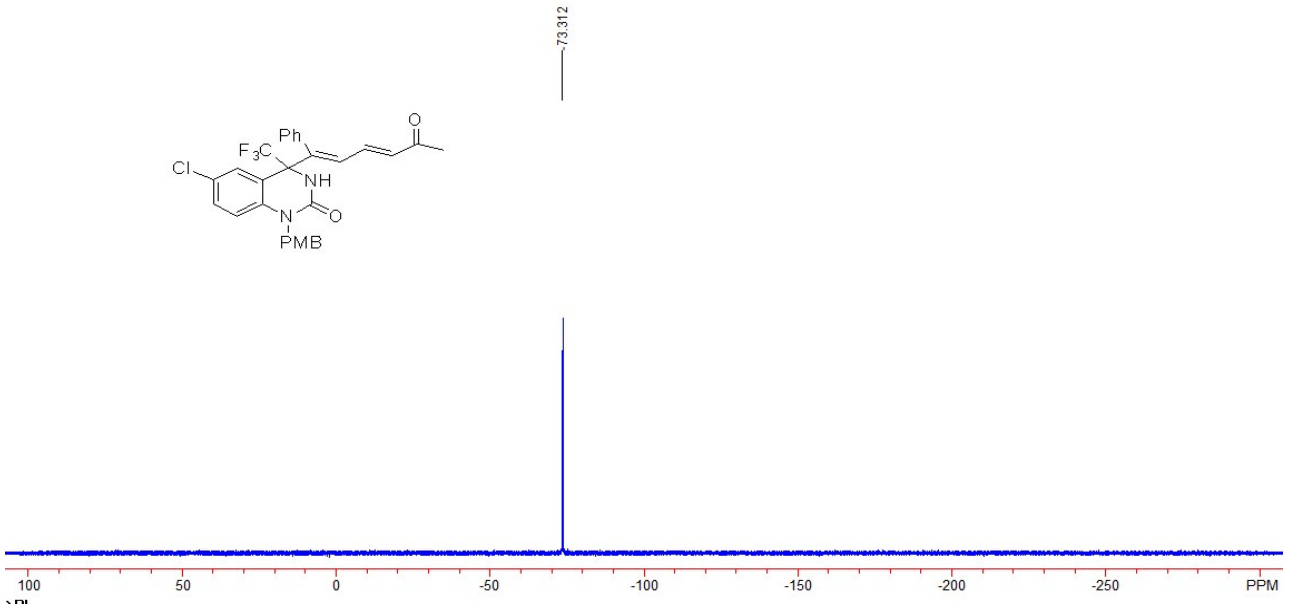
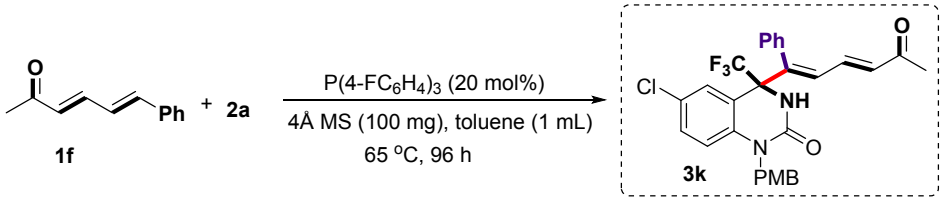
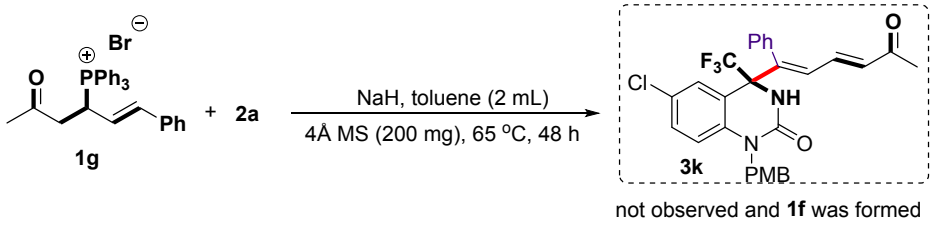
127.707
127.395
127.268
125.974
123.104
116.612
116.411
114.143
77.326
77.006
76.686
67.562
67.279
67.004
66.721
55.210
45.082
27.539
Ph
F3C
Cl
NH
O
N
PMB
200
150
100
50
0
PPM


73.312
Ph
F3C
Cl
NH
O
N
PMB
100
50
0
-50
-100
-150
-200
-250
PPM

Control Experiments and Spectroscopic Data of the Products.

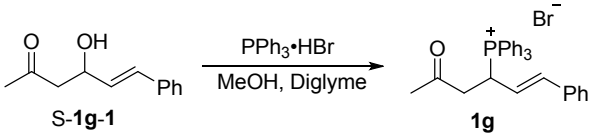


The 4Å MS was added to a Schlenk tube and heated under vacuum to remove ambient moisture and water, then filled with argon. After the Schlenk tube was returned to room temperature, cyclic trifluoromethyl ketimine **2a** (0.2 mmol) and $P(4\text{-}FC_6H_4)_3$ (13 mg, 0.04 mmol) were added. Under argon atmosphere, to a solution of cyclic trifluoromethyl ketimines **2a** (0.2 mmol) and $P(4\text{-}FC_6H_4)_3$ (13 mg, 0.04 mmol) in toluene (1.0 mL) was added the (3E,5E)-6-phenylhexa-3,5-dien-2-one **1f** (0.8 mmol) at room temperature. Then the resulting mixture was heated to 65 °C and continued stirring at 65 °C for 96 hours. Product **3k** was not obtained and **1f** was recovered.



NaH (2.0 equiv) was added slowly into a solution of the phosphonium salt **1g** (2.0 equiv) and cyclic trifluoromethyl ketimine **2a** (0.20 mmol) in toluene (2 mL) at room temperature. After stirring the mixture at 65 °C for 48 h, the solvent was evaporated under reduced pressure. Product **3k** was not obtained and **1f** was formed.

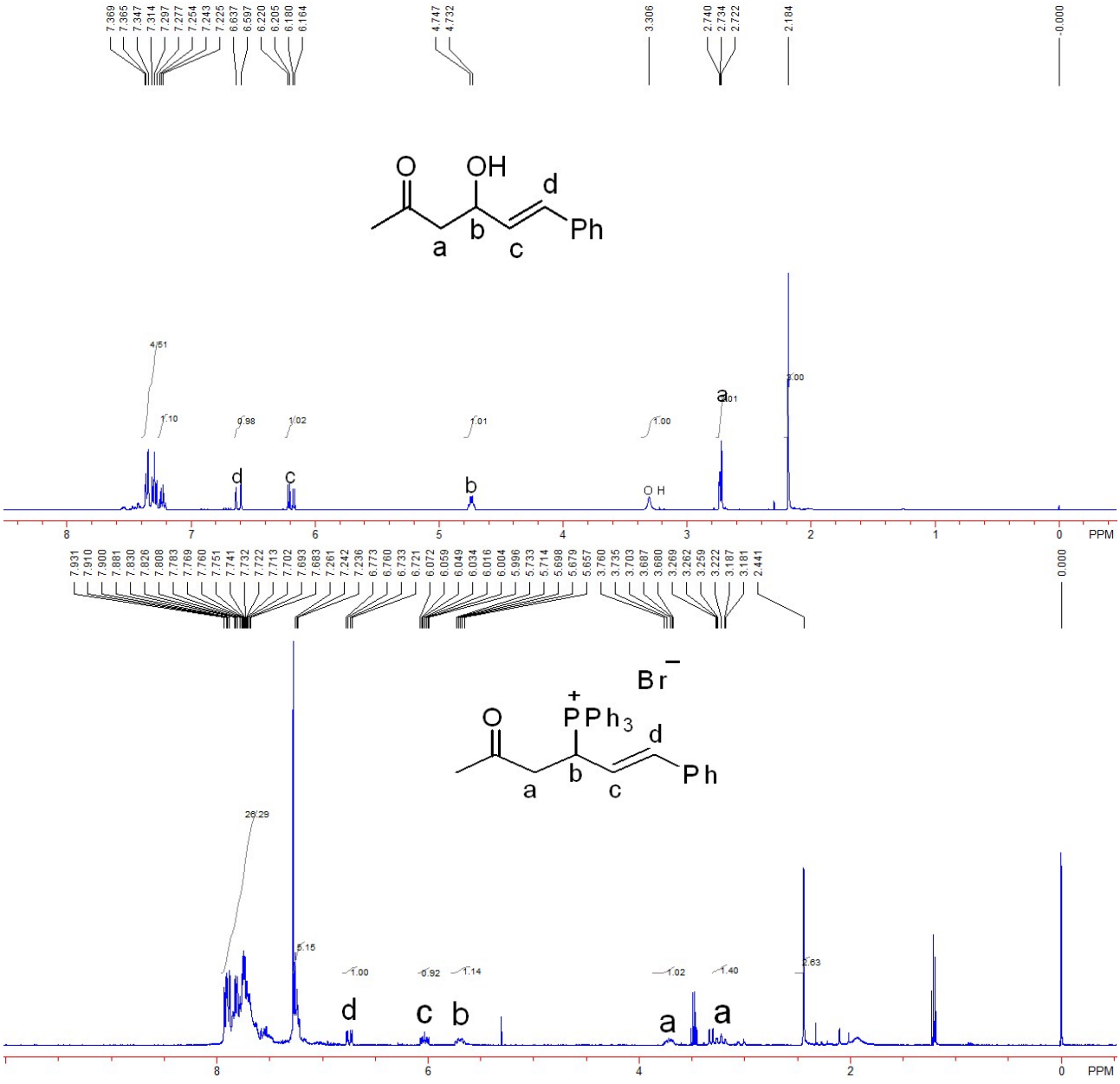
Compound **1g** was prepared following a slightly modified literature procedure.[4]

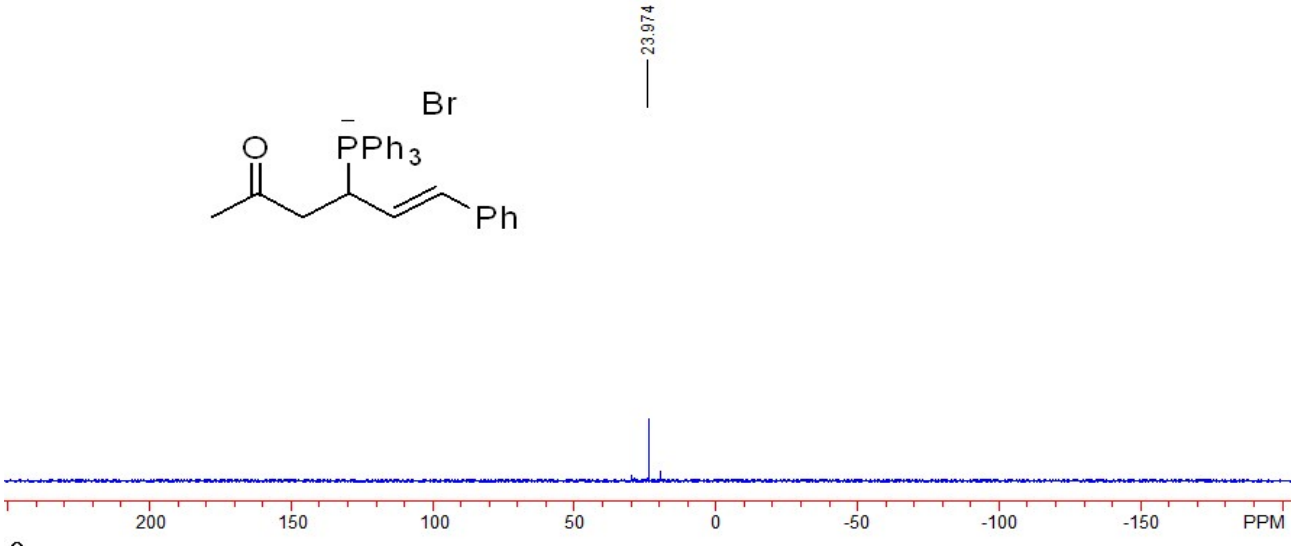


S-**1g-1** (4 mmol) was dissolved in a mixture of MeOH (5 mL) and Diglyme (5 mL) followed by addition of triphenylphosphine hydrobromide, and the resulting mixture was stirred overnight. After the reaction completed, most of the solvent was removed by vacuum evaporation, then Et_2O (20 mL)

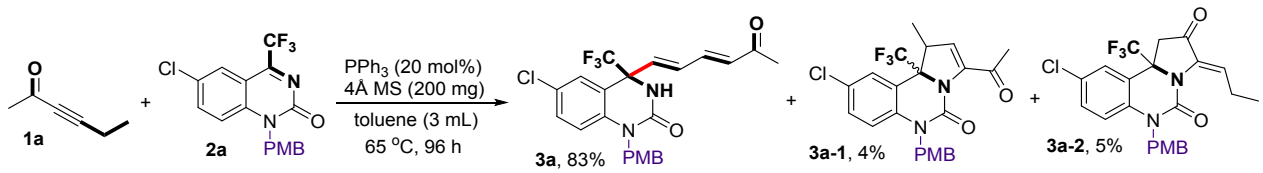
was added. The crude solid product containing small amount of triphenylphosphine hydrobromide was obtained by filtration.

^{31}P NMR (121 MHz, $CDCl_3$) δ 24.0; HRMS (ESI) Calcd. For $C_{30}H_{28}OP^{+1}[M\text{-}Br]^+$ requires 435.1872, Found: 435.1874.

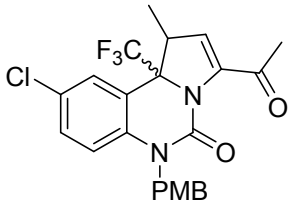



23.974
Br
PPh3
O
Ph
200
150
100
50
0
-50
-100
-150
PPM

Large-scale Testing and Transformations of Product 3a and Spectroscopic Data of the Products.



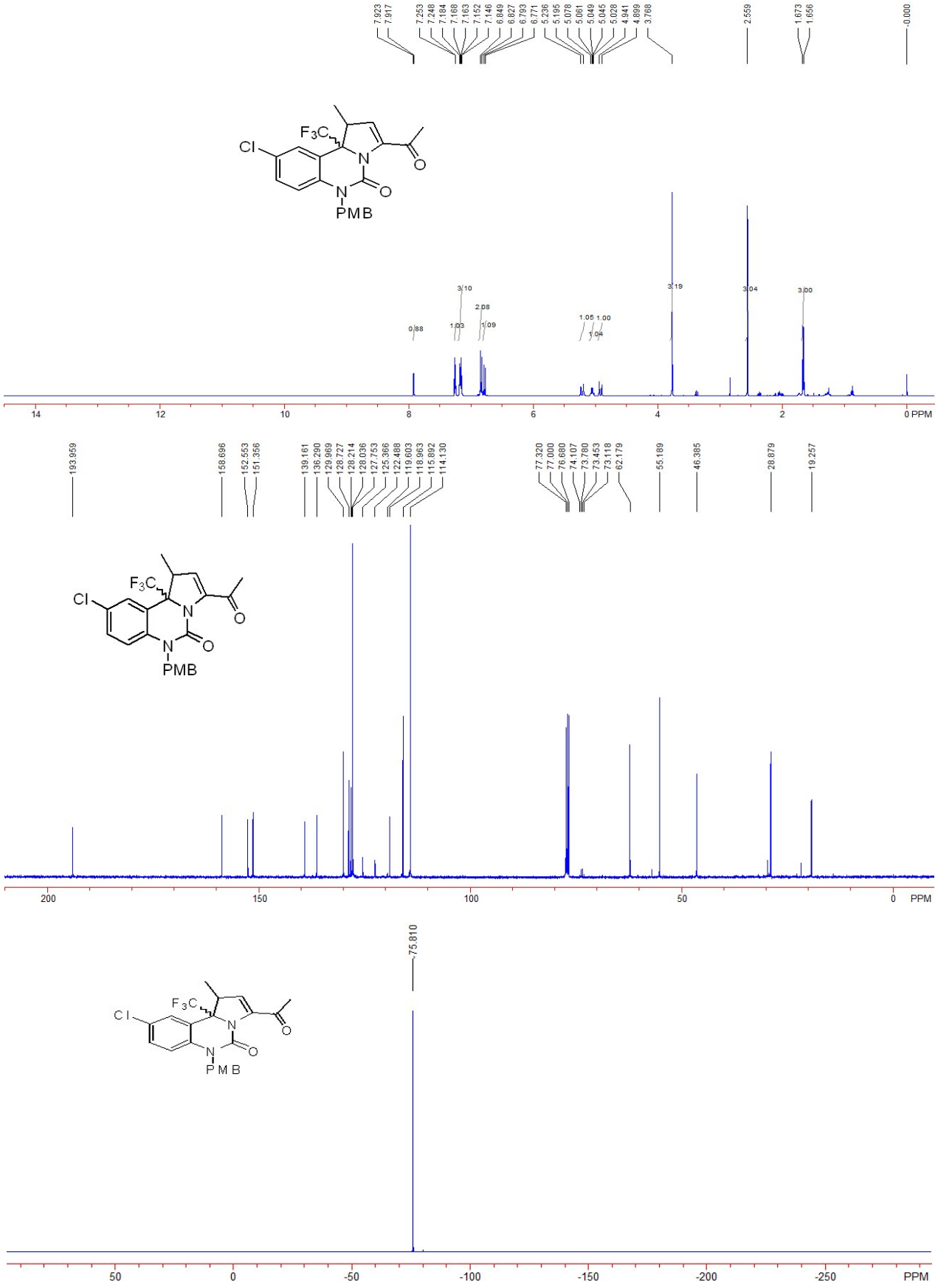
The used 4Å MS (200 mg) was added to a Schlenk tube and was heated under vacuum to remove ambient moisture and water, then filled with argon. After the Schlenk tube was returned to room temperature, cyclic trifluoromethyl ketimine **2a** (1.0 mmol) and PPh_3 (53 mg, 0.2 mmol) was added, followed by addition of toluene (3.0 mL) and then hex-3-yn-2-one **1a** (4.0 mmol) was added at room temperature. Then the resulting mixture was heated to 65 °C and continued stirring at 65 °C until the reaction complete (monitoring by TLC). Then the solvent was removed under reduced pressure and the residue was directly subjected to a flash column chromatography on silica gel to afford the desired product **3a**. Products **3a-1** and **3a-2** were separated as byproducts in a very small amount. The polarity of **3a** and **3a-1** is very similar, which led to the isolation of these two compounds become very difficult.

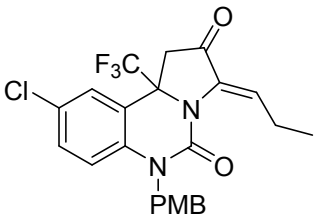


3-acetyl-9-chloro-6-(4-methoxybenzyl)-1-methyl-10b-(trifluoromethyl)-6,10b-dihydropyrrolo[1,2-c]quinazolin-5(1H)-one (3a-1).

A viscous liquid, 4% yield (19 mg). ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.66 (d, J = 6.8 Hz, 3H, CH_3), 2.56 (s, 3H, CH_3), 3.77 (s, 3H, CH_3), 4.92 (d, J = 16.8 Hz, 1H, CH_2), 5.02-5.08 (m, 1H, CH), 5.22 (d, J = 16.8 Hz, 1H, CH_2), 6.78 (d, J = 8.8 Hz, 1H, ArH), 6.84 (d, J = 8.8 Hz, 1H, ArH), 7.14-7.19 (m, 3H, ArH, =CH), 7.25 (d, J = 2.0 Hz, 1H, ArH), 7.92 (d, J = 2.0 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 19.3, 28.9, 46.4, 55.2, 62.2, 73.6 (d, J = 32.7 Hz), 114.1, 115.9, 119.0, 119.6, 123.9 (q, J = 287.8 Hz), 127.8, 128.2, 128.7, 130.0, 136.3, 139.2, 151.4, 152.6, 158.7, 194.0. ^{19}F NMR (376 MHz, $CDCl_3$, $CFCl_3$) δ -75.81. IR (CH_2Cl_2) ν 2984, 2363, 1673, 1615, 1514, 1390, 1246, 1189, 1174, 1033, 808, 718 cm^{-1}. MS (ESI) *m/z* (%): 487.0 (100) $[M+Na]^+$; HRMS (ESI)

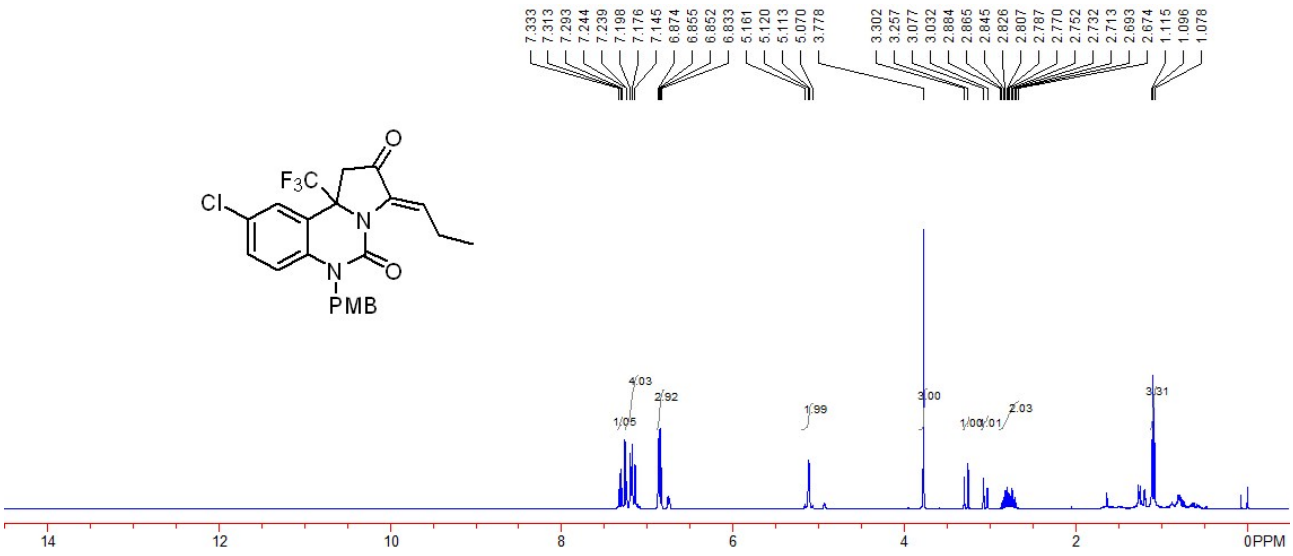
Calcd. For $C_{23}H_{21}F_3N_2ClO_3^{+1}(M+H)^+$ requires 465.1187, Found: 465.1186.

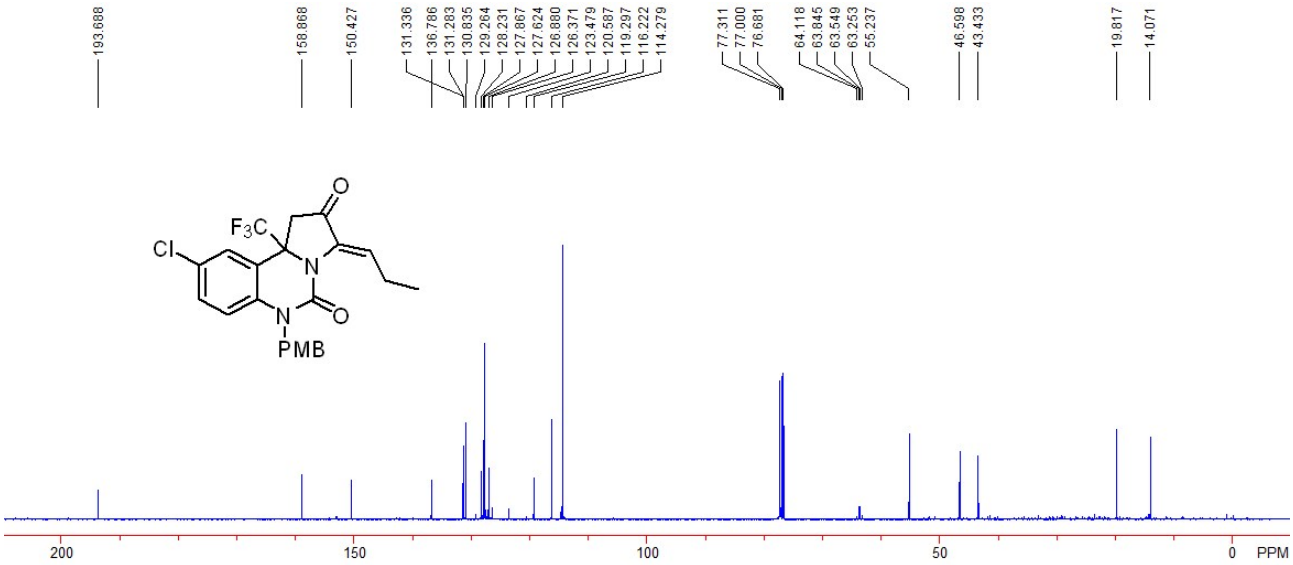


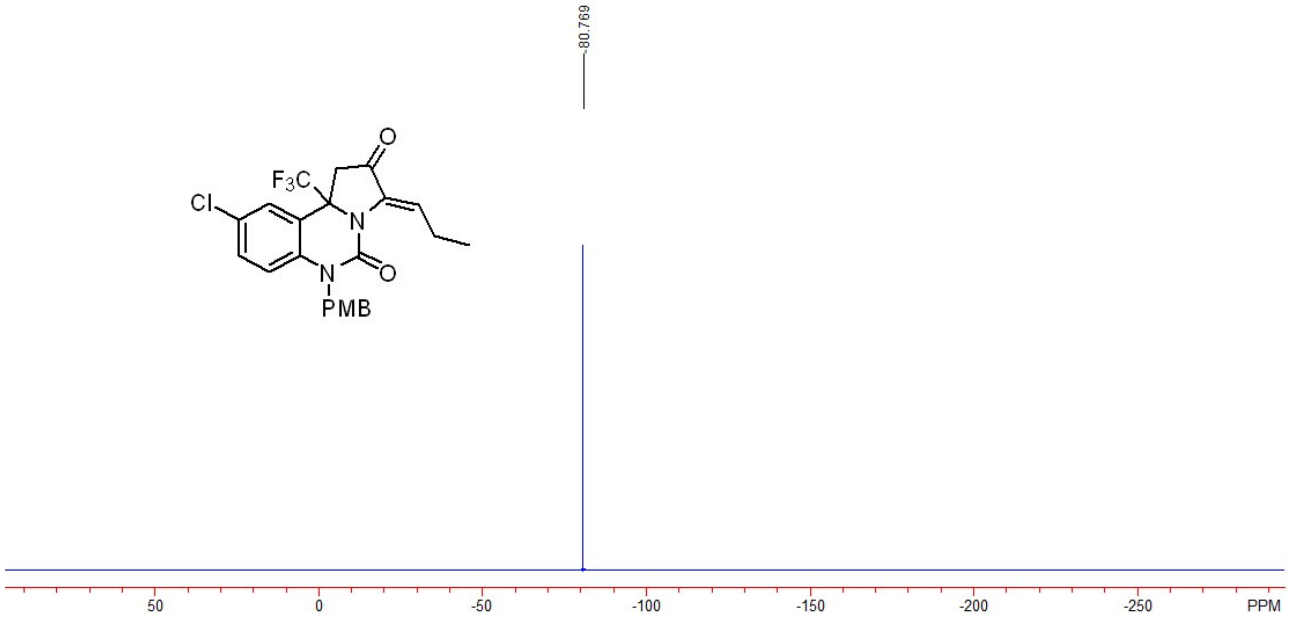


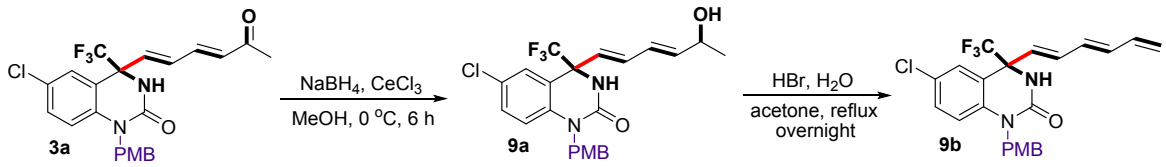
2-chloro-8-ethyl-5-(4-methoxybenzyl)-11a-(trifluoromethyl)-11,11a-dihydro-6H-pyrido[1,2-c]quinazoline-6,10(5H)-dione (3a-2).

A viscous liquid, 5% yield (23 mg). ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.10 (t, *J* = 8.0 Hz, 3H, CH_3), 2.67-2.89 (m, 2H, CH_2), 3.05 (d, *J* = 18.0 Hz, 1H, CH_2), 3.28 (d, *J* = 18.0 Hz, 1H, CH_2), 3.78 (s, 3H, CH_3), 5.07-5.17 (m, 2H, CH_2), 6.83-6.87 (m, 3H, ArH), 7.14-7.24 (m, 4H, ArH), 7.92 (dd, *J* = 8.0, 8.0 Hz, 1H, ArH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 14.1, 19.8, 43.4, 46.6, 55.2, 63.7 (d, *J* = 29.6 Hz), 114.3, 116.2, 119.3, 120.6, 124.9 (q, *J* = 289.2 Hz), 126.9, 127.6, 127.9, 128.2, 129.3, 130.8, 131.28, 131.34, 136.8, 150.4, 158.9, 193.7. ^{19}F NMR (376 MHz, $CDCl_3$, $CFCl_3$) δ -80.77. IR (CH_2Cl_2) ν 2970, 2933, 2357, 2336, 1677, 1514, 1500, 1384, 1177, 1065, 998 cm^{-1}. MS (ESI) *m/z* (%): 486.9 (100) $[M+Na]^+$; HRMS (ESI) Calcd. For $C_{23}H_{21}F_3N_2ClO_3^{+1}(M+H)^+$ requires 465.1187, Found: 465.1182.



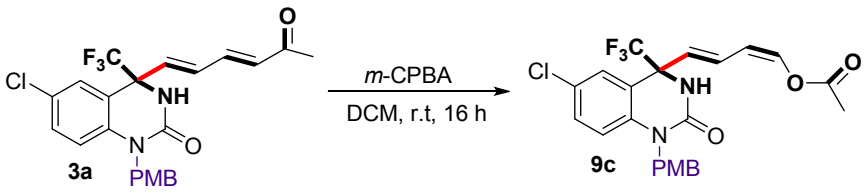




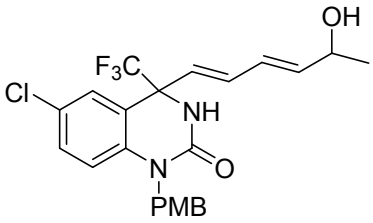


Under argon atmosphere, to a solution of **3a** (0.2 mmol) in methanol (2.0 mL) was added $CeCl_3$ (0.2 mmol) at 0 °C. After 10 minutes, $NaBH_4$ (0.3 mmol) was added to the resulting mixture and continued to stir for another 15 minutes at 0 °C. Then the reaction mixture was allowed to rise to room temperature. After 4 hours, the solvent was removed under reduced pressure and the residue was directly subjected to a flash column chromatography on silica gel to afford the desired product **9a**.

9a (0.178 mmol) was dissolved in acetone/H_2O (4.32 mL/25 μL) and was heated to reflux, followed by addition of HBr (10 μL). The reaction mixture was under reflux overnight. After return to room temperature, trace amount of saturated sodium carbonate solution was added into the reaction mixture to quench the reaction. The solvent was removed under reduced pressure and the residue was directly subjected to a flash column chromatography on silica gel to afford the desired product **9b**.



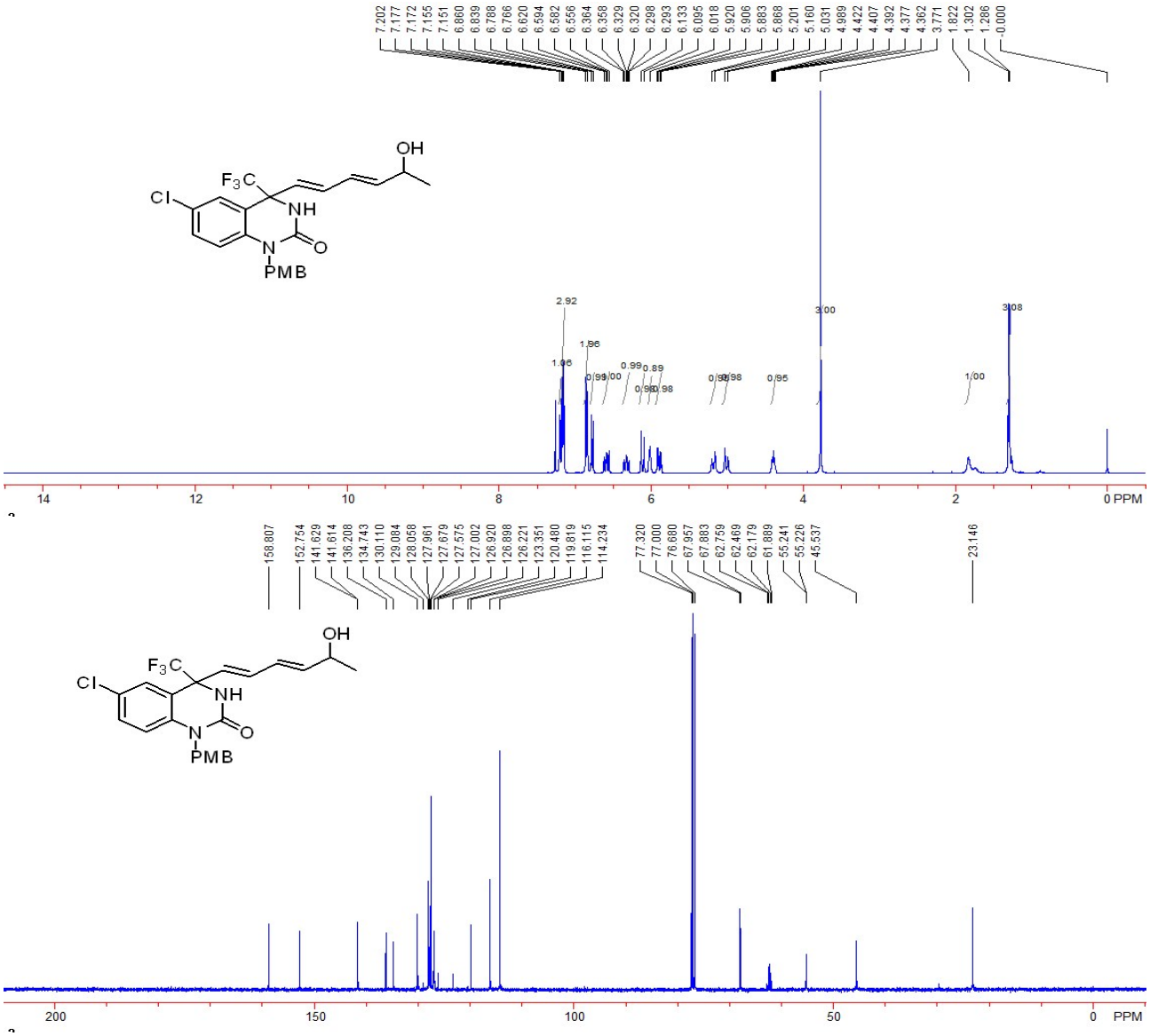
Under argon atmosphere, to a solution of **3a** (0.2 mmol) in dichloromethane (1.0 mL) was added $CeCl_3$ (0.2 mmol) at 0 °C. After 10 minutes, *m*-CPBA (0.26 mmol) was added to the resulting mixture and continued to stir for another 15 minutes at the 0 °C. Then the reaction mixture was allowed to rise to room temperature. After 4 hours, Me_2S was added to quench the reaction. The solvent was removed under reduced pressure and the residue was directly subjected to a flash column chromatography on silica gel to afford the desired product **9c**.

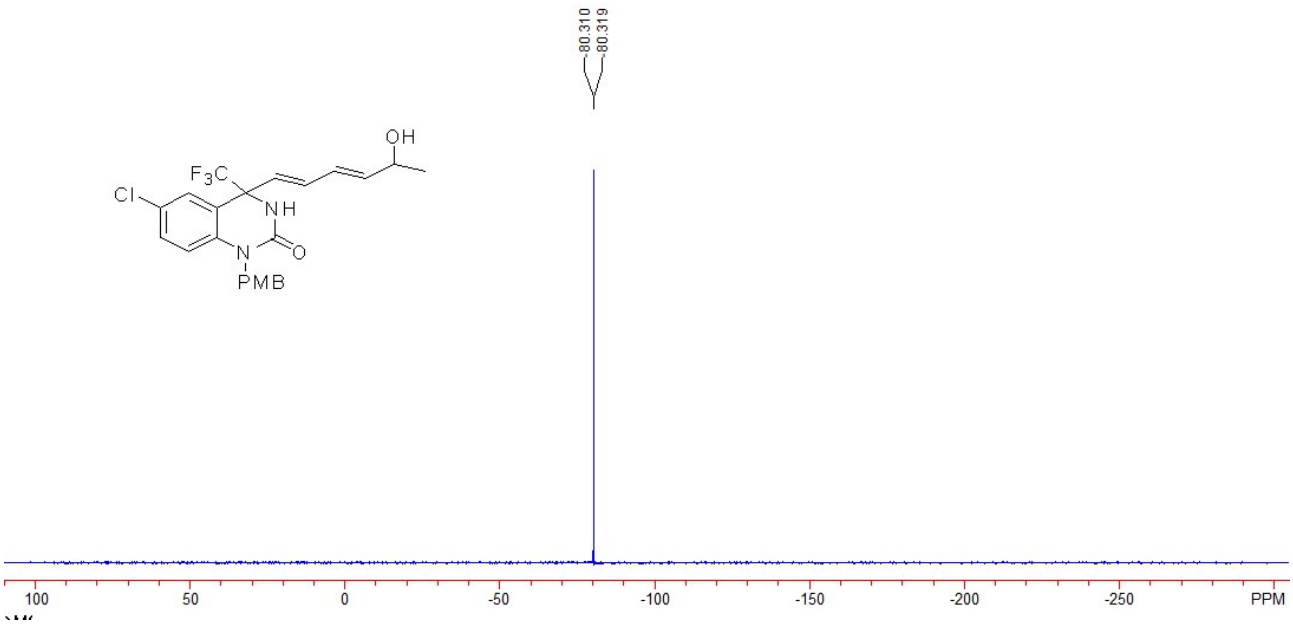


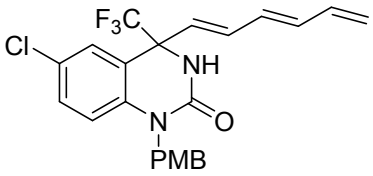
6-chloro-4-((1E,3E)-5-hydroxyhexa-1,3-dien-1-yl)-1-(4-methoxybenzyl)-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1H)-one (9a).

A white solid, 89% yield (83 mg). M.p.: 256-258 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.29 (d, *J* = 6.4 Hz, 3H, CH_3), 1.82 (br, 1H, OH), 3.77 (s, 3H, CH_3), 4.36-4.43 (m, 1H, CH), 5.01 (d, *J* = 16.8 Hz, 1H, CH_2), 5.18 (d, *J* = 16.8 Hz, 1H, CH_2), 5.89 (dd, *J* = 5.6, 14.8 Hz, 1H, =CH), 6.02 (s, 1H, NH), 6.11 (d, *J* = 15.2 Hz, 1H, =CH), 6.29-6.37 (m, 1H, =CH), 6.59 (dd, *J* = 10.4, 15.2 Hz, 1H, =CH), 6.78 (d, *J* = 8.8 Hz, 1H, ArH), 6.85 (d, *J* = 8.4 Hz, 2H, ArH), 7.15-7.18 (m, 3H, ArH), 7.20

(s, 1H, Ar). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 23.1, 45.5, 55.2 (d, J = 1.4 Hz), 62.3 (q, J = 29.0 Hz), 114.2, 116.1, 119.8, 124.8 (q, J = 287.0 Hz), 126.90, 126.92, 127.0, 127.6, 127.8, 128.0, 128.1, 130.1, 134.7, 136.2, 141.6 (d, J = 1.5 Hz), 152.8, 158.8, 158.8. ^{19}F NMR (376 MHz, $CDCl_3$, $CFCl_3$) δ -80.31 (d, J =3.4 Hz). IR (CH_2Cl_2) ν 3380, 3090, 2971, 2929, 1678, 1603, 1513, 1427, 1392, 1249, 1174, 1032, 993, 809, 742 cm^{-1}. MS (ESI) *m/z* (%): 467.1 (100) $[M+H]^+$; HRMS (ESI) Calcd. For $C_{23}H_{23}ClF_3N_2O_3^{+1}(M+H)^+$ requires 467.1344, Found: 467.1340.

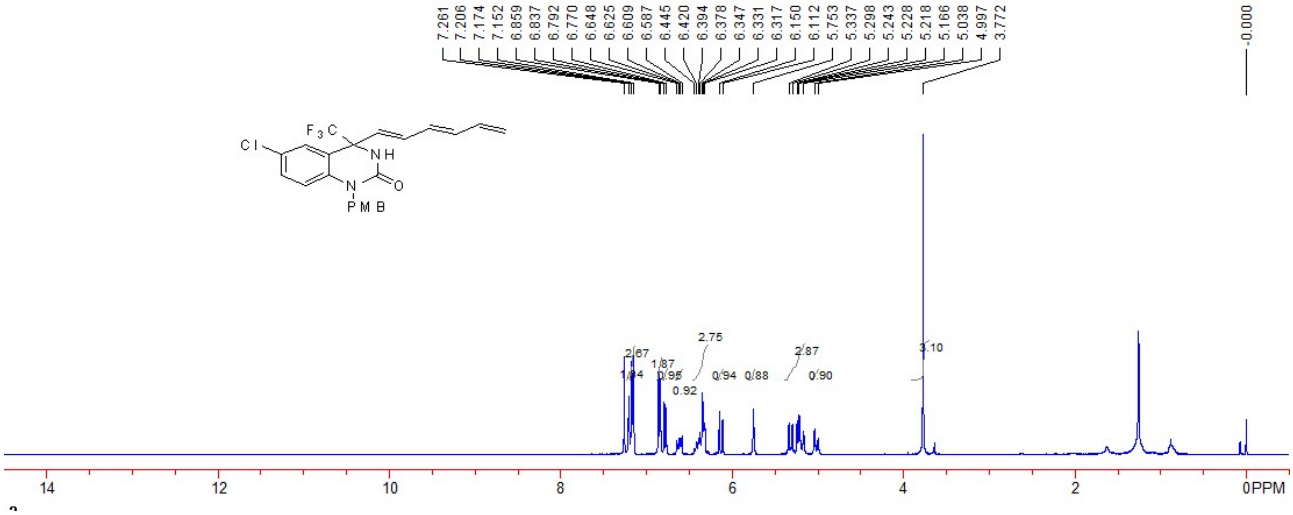






6-chloro-4-((1E,3E)-5-hydroxyhexa-1,3-dien-1-yl)-1-(4-methoxybenzyl)-4-(trifluoromethyl)-3,4-dihydroquinazolin-2(1H)-one (9b).

A white solid, 43% yield (34 mg). M.p.: 201-203 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 3.77 (s, 3H, CH_3), 5.02 (d, *J* = 16.4 Hz, 1H, CH_2), 5.16-5.34 (m, 3H, CH_2, =CH), 5.75 (s, 1H, NH), 6.13 (d, *J* = 15.2 Hz, 1H, =CH), 6.32-6.45 (m, 3H, =CH), 6.62 (dd, *J* = 8.8, 15.6 Hz, 1H, =CH), 6.78 (d, *J* = 8.8 Hz, 1H, ArH), 6.85 (d, *J* = 8.8 Hz, 2H, ArH), 7.16 (d, *J* = 8.8 Hz, 3H, ArH), 7.21 (s, 1H, Ar). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 45.6, 55.2, 62.5 (d, *J* = 1.4 Hz), 62.3 (q, *J* = 29.2 Hz), 114.3, 116.2, 119.8, 120.1, 124.8 (q, *J* = 286.9 Hz), 127.0, 127.6, 127.7, 128.0, 130.2, 130.4, 135.2, 136.1, 137.3, 152.5, 158.8. ^{19}F NMR (376 MHz, $CDCl_3$, $CFCl_3$) δ -80.28. IR (CH_2Cl_2) ν 3032, 2925, 2863, 1681, 1513, 1502, 1427, 1390, 1174, 1007, 809 cm^{-1}. MS (ESI) *m/z* (%): 471.1 (100) $[M+Na]^+$; HRMS (ESI) Calcd. For $C_{23}H_{21}ClF_3N_2O_3^{+1}(M+H)^+$ requires 449.1238, Found: 449.1235.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6.770
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6.625
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6.420
6.394
6.378
6.347
6.331
6.317
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5.218
5.166
5.038
4.997
3.772
0.000
Cl
F3C
NH
O
N
PMB
2.67
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0.95
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14
12
10
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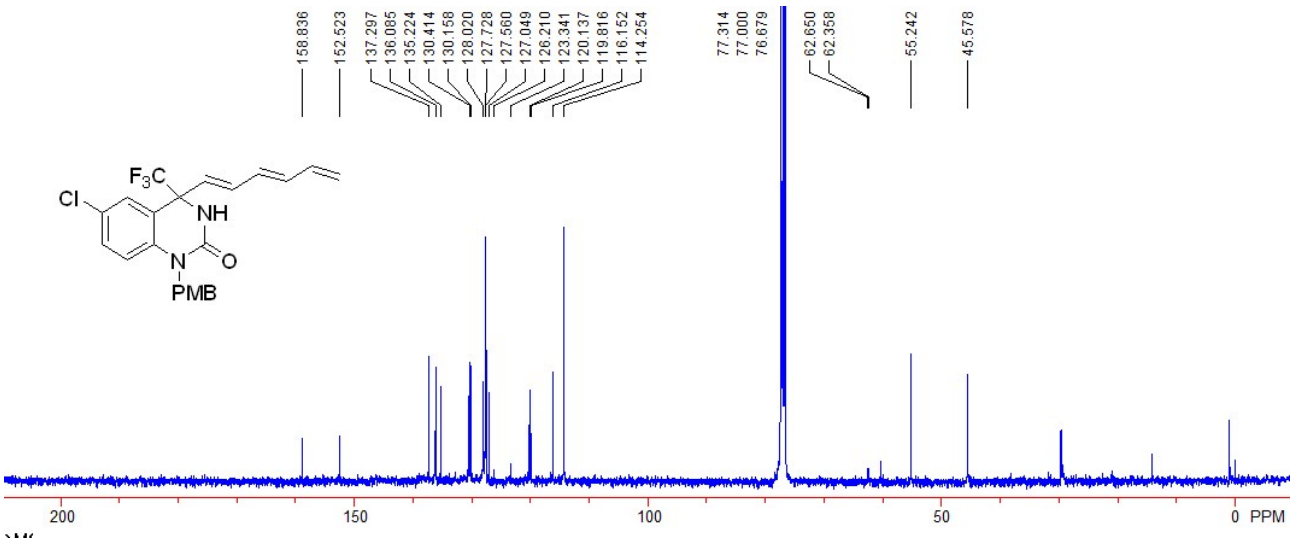
4
2
0PPM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120.137
119.816
116.152
114.254
77.314
77.000
76.679
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Cl
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O
N
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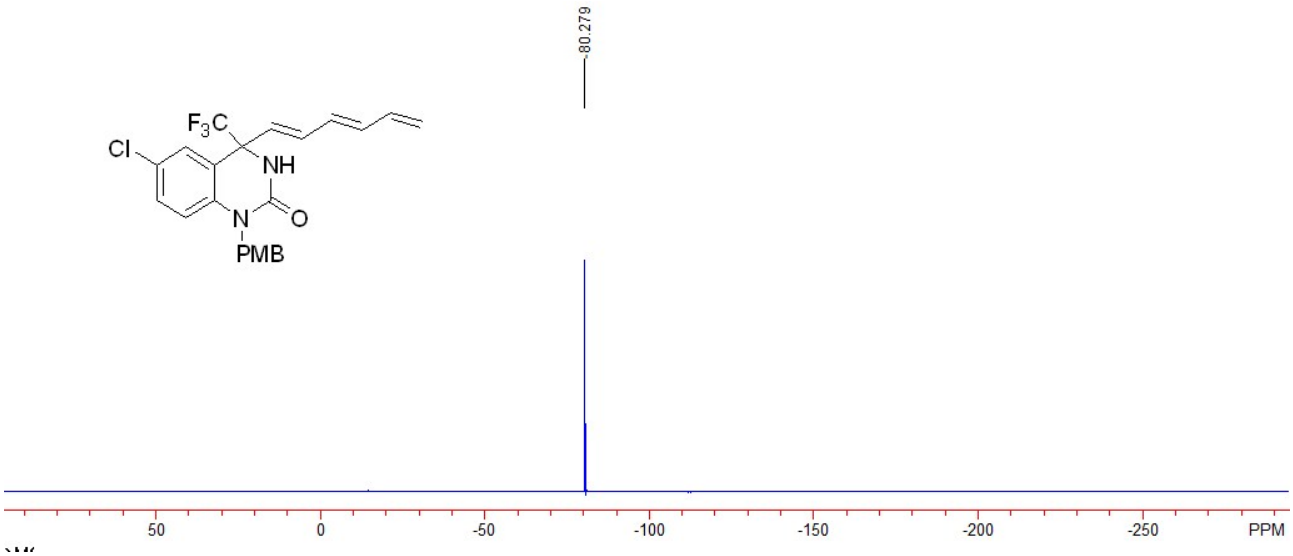
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-200
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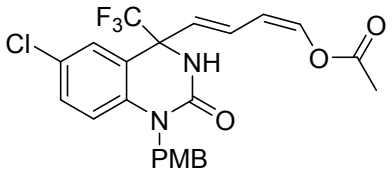
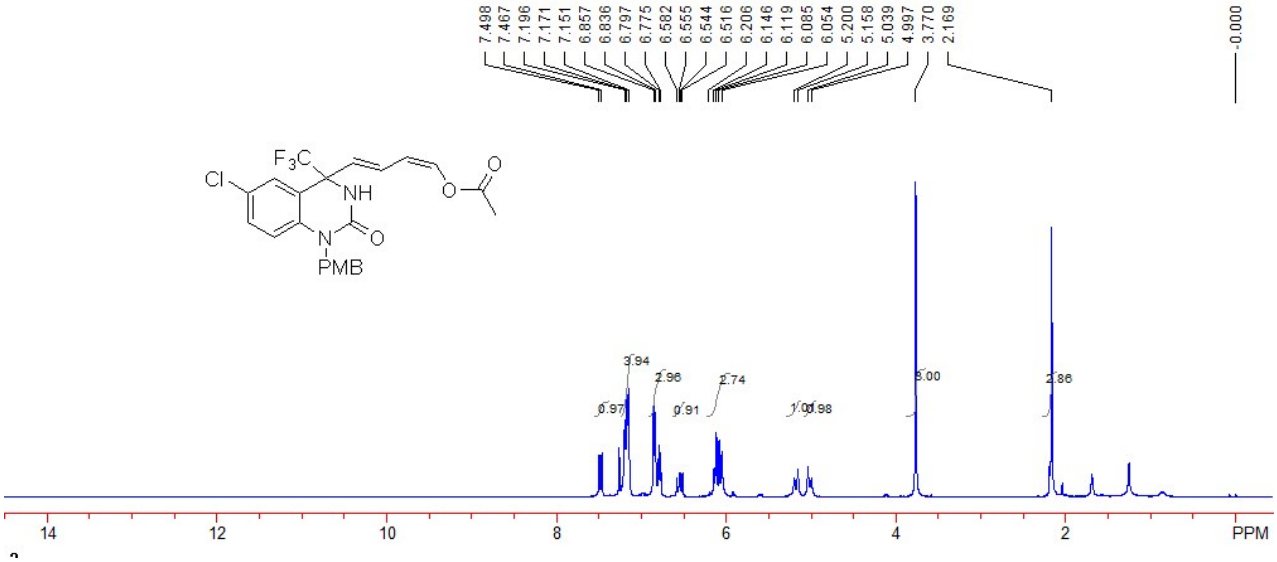
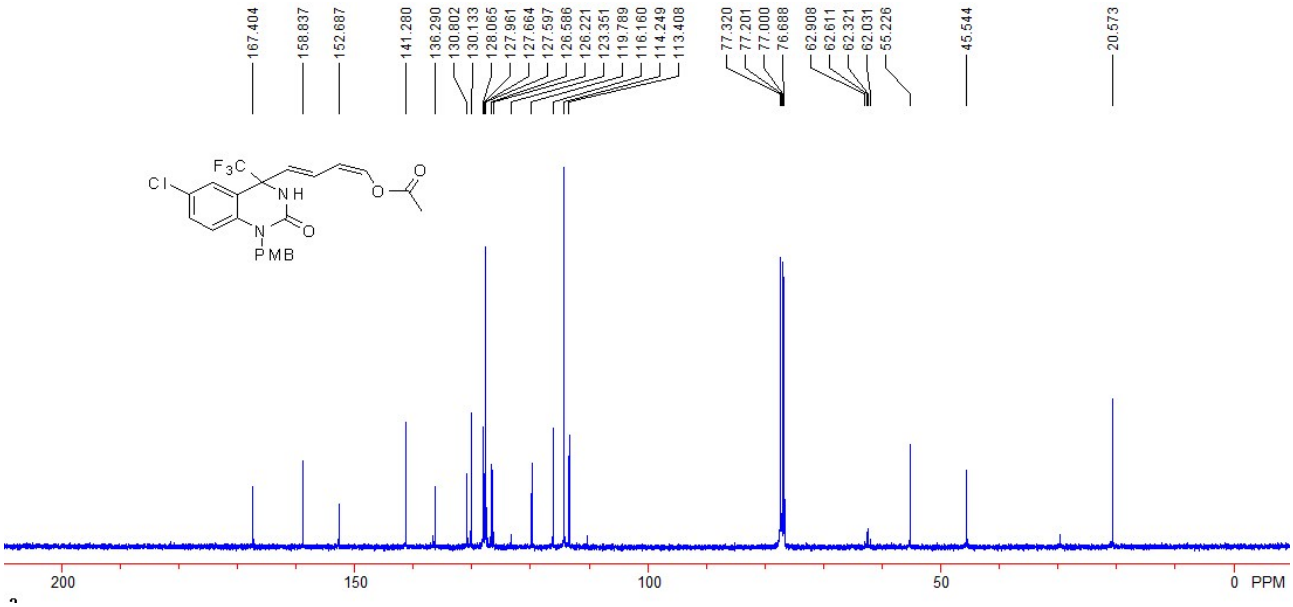


(1Z,3E)-4-(6-chloro-1-(4-methoxybenzyl)-2-oxo-4-(trifluoromethyl)-1,2,3,4-tetrahydroquinazolin-4-yl)buta-1,3-dien-1-yl acetate (9c).

A white solid, 53% yield (47 mg). M.p.: 157-159 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 2.17 (s, 3H, CH_3), 3.77 (s, 3H, CH_3), 5.02 (d, *J* = 16.8 Hz, 1H, CH_2), 5.18 (d, *J* = 16.8 Hz, 1H, CH_2), 6.05-6.14 (m, 3H, =CH, ArH), 6.81 (dd, *J* = 11.2, 15.2 Hz, 1H, =CH), 6.77-6.86 (m, 3H, =CH, ArH), 7.15-7.20 (m, 4H, =CH, NH, ArH), 7.48 (d, *J* = 12.4 Hz, 1H, =CH). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 20.6, 45.5, 55.2, 62.5 (d, *J* = 29.0 Hz), 114.2, 116.2, 119.8, 124.8 (q, *J* = 287.0 Hz), 126.6, 127.6, 127.7, 128.0, 128.1, 130.1, 130.8, 136.3, 141.3, 152.7, 152.8, 167.4. ^{19}F NMR (376 MHz, $CDCl_3$, $CFCl_3$) δ -80.27. IR (CH_2Cl_2) ν 2958, 2923, 2358, 2332, 1763, 1681, 1427, 1210, 1109, 1038, 895, 741 cm^{-1}. MS (ESI) *m/z* (%): 481.1 (100) $[M+H]^+$; HRMS (ESI) Calcd. For $C_{23}H_{21}F_3N_2ClO_4^{+1}(M+H)^+$ requires 481.1142, Found: 481.1097.

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127.961
127.664
127.597
126.586
126.221
123.351
119.789
116.160
114.249
113.408
77.320
77.201
77.000
76.688
62.908
62.611
62.321
62.031
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45.544
20.573
F3C
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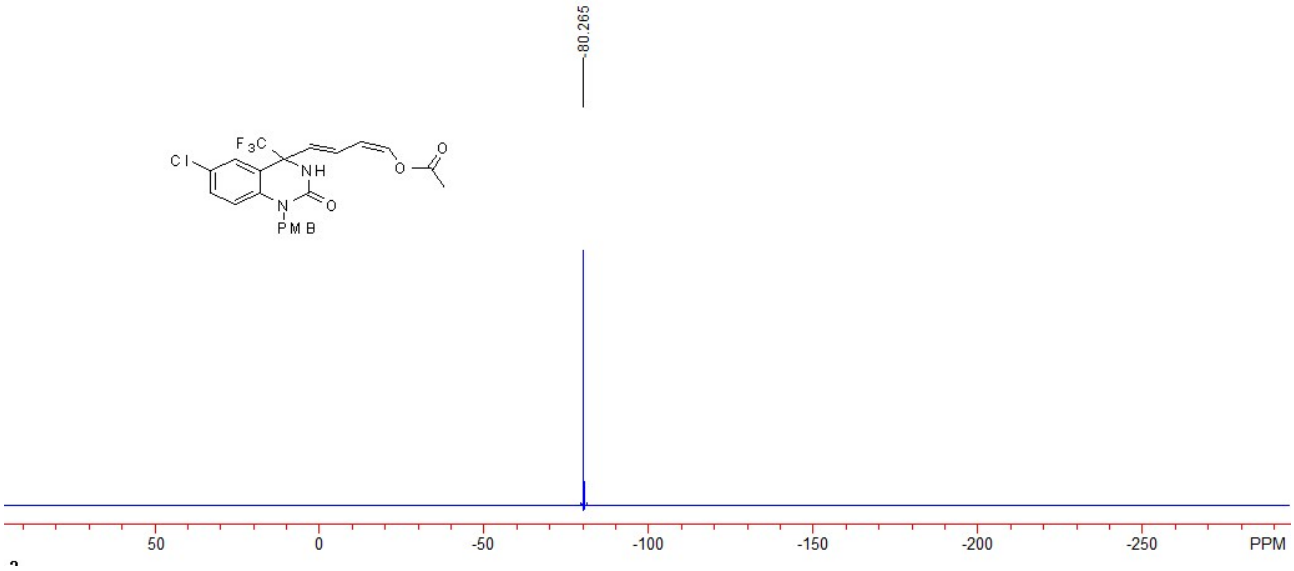
NH
O
N
PMB
200
150
100
50
0 PPM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N
PMB
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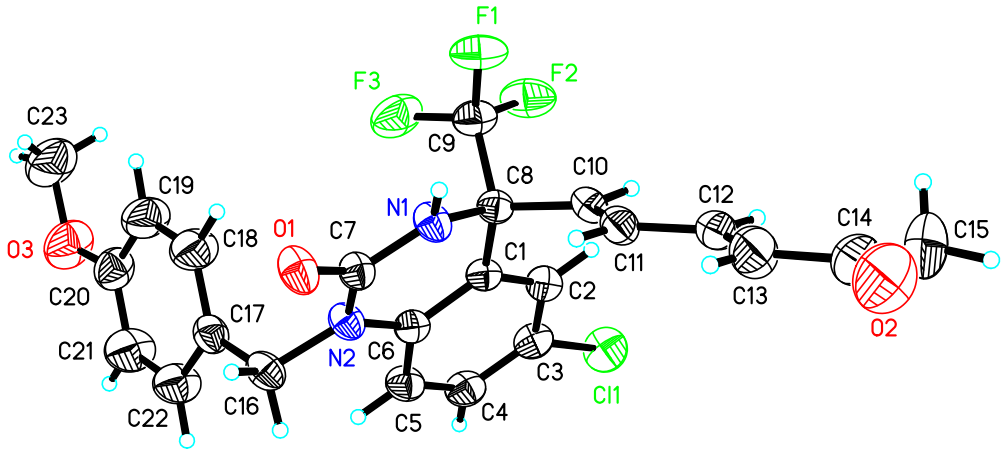
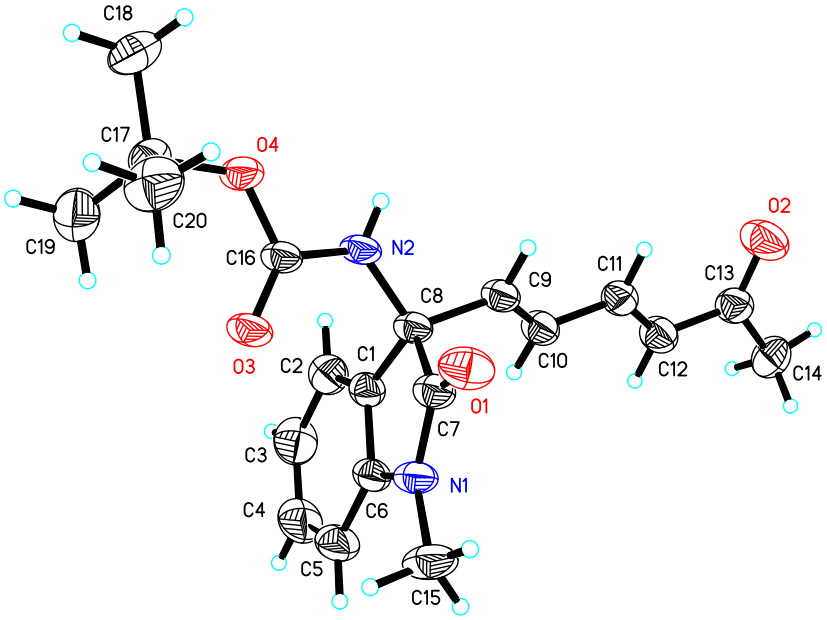
-50
-100
-150
-200
-250
PPM

X-ray Crystal Data of 3a and 5a.



The crystal data of **3a** have been deposited in CCDC with number 1005236. Empirical Formula: $C_{23}H_{20}ClF_3N_2O_3$; Formula Weight: 464.86; Crystal Color, Habit: colorless; Crystal Dimensions: 0.211 x 0.175 x 0.112 mm^3; Crystal System: Orthorhombic; Lattice Parameters: a = 18.1727(15) Å, alpha = 90 deg. b = 10.5743(9) Å, beta = 90 deg. c = 23.8130(19) Å, gamma = 90 deg.; V = 4576.0(7) $Å^3$; Space group: Pbca; Z = 8; D_{calc} = 1.350 g/cm^3; F_{000} = 1920; Diffractometer: Rigaku AFC7R; Residuals: R; R_w: 0.0596, 0.1255.



The crystal data of **5a** have been deposited in CCDC with number 1011176. Empirical Formula: $C_{20}H_{24}N_2O_4$; Formula Weight: 356.41; Crystal Color, Habit: colorless; Crystal Dimensions: 0.211 x 0.156 x 0.123 mm^3; Crystal System: Monoclinic; Lattice Parameters: a = 18.416(5) Å, alpha = 90 deg. b = 11.310(3) Å, beta = 93.907(7) deg. c = 9.759(3) Å, gamma = 90 deg.; V = 2027.9(10) $Å^3$; Space group: P 21/c; Z = 4; D_{calc} = 1.167 g/cm^3; F_{000} = 760; Diffractometer: Rigaku AFC7R; Residuals: R; R_w: 0.0457, 0.1271.

References:

1. (a) O. Lifchits, M. Mahlau, C. M. Reisinger, A. Lee, C. Farès, I. Polyak, G. Gopakumar, W. Thiel and B. List, *J. Am. Chem. Soc.*, 2013, **135**, 6677; (b) D.-Y. Li, Y. Wei and M. Shi, *Eur. J. Org. Chem.*, 2015, **2015**, 4108.
2. (a) S. Takizawa, F. A. Arteaga, Y. Yoshida, M. Suzuki and H. Sasai, *Org. Lett.*, 2013, **15**, 4142; (b) K. Kato, H. Nakamura and K. Nakanishi, *Appl. Surf. Sci.*, 2014, **293**, 312; (c) S. Nakamura, S. Takahashi, D. Nakane and H. Masuda, *Org. Lett.*, 2015, **17**, 106; (d) X. Ren and H. Du, *J. Am. Chem. Soc.*, 2016, **138**, 810.
3. N. A. Magnus, P. N. Confalone, L. Storace, M. Patel, C. C. Wood, W. P. Davis and R. L. Parsons, *J. Org. Chem.*, 2003, **68**, 754.
4. G. E. Magoulas, S. E. Bariamis, C. M. Athanassopoulos, A. Haskopoulos, P. G. Dedes, M. G. Krokidis, N. K. Karamanos, D. Kletsas, D. Papaioannou and G. Maroulis, *Eur. J. Med. Chem.*, 2011, **46**, 721.