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Supplementary Information

Carbonylative synthesis of 2-(trifluoromethyl)quinazolin-4(3*H*)-ones from trifluoroacetimidoyl chlorides and amines based on an activated carbon fibers supported palladium catalyst

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General Information

Unless otherwise noted, all reactions were carried out under air atmosphere. All reagents were from commercial sources and used as received without further purification. All solvents were dried by standard techniques and distilled prior to use. Column chromatography was performed on silica gel (200-300 meshes) using petroleum ether (bp. 60~90 °C) and ethyl acetate as eluent. ^{1}NMR spectra were recorded on a Bruker Avance operating at for ^{1}H NMR at 400 MHz, ^{13}C NMR at 100 MHz and spectral data were reported in ppm relative to tetramethylsilane (TMS) as internal standard and $CDCl_3$ (^{1}H NMR δ 7.26, ^{13}C NMR δ 77.16) as solvent. All coupling constants (*J*) are reported in Hz. The following abbreviations were used to describe peak splitting patterns when appropriate: s = singlet, d = doublet, dd = double doublet, ddd = double doublet of doublets, t = triplet, dt = double triplet, q = quatriplet, m = multiplet, br = broad.

1 General Procedures for the Preparation of Starting Materials

1.1 Preparation of Pd/ACFs[1]

1.1.1 Materials

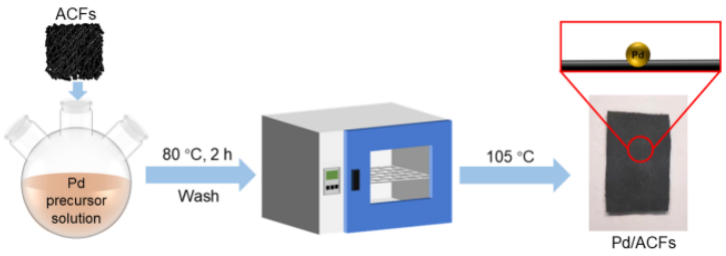
Palladium chloride ($PdCl_2$) was obtained from J&K Chemical Ltd (China). Sodium chloride (NaCl) was obtained from Wuxi Zhanwang Chemical Reagent Co., Ltd (China). ACFs was ordered from Ningbo Institute of Material Technology and Engineering,Chinese Academy of Sciences. All of the chemical reagents were of analytical grade and used without further purification.

1.1.2 Characterizations

The Pd content in the Pd/ACFs was measured through an inductively coupled plasma optical emission spectrometer (ICP-OES, Agilent 5100). The crystal structures of Pd/ACFs were revealed via a Bruker D8 Discover X-ray diffractometer (XRD) using Cu Kα radiation at 40 kV and 40 mA. The surface chemical composition of Pd

in ACFs was investigated by an X-ray photoelectron spectrometer (XPS, Thermo Scientific Escalab 250Xi). The morphology and microstructure of the samples was observed by scanning electron microscopy (SEM, Gemini500).

1.1.3 Synthesis of Pd/ACFs



The activated carbon fibers (ACFs) were employed as a carrier and palladium was used as the catalyst for the reaction.The ACFs were washed with deionized water and dried in an oven before the synthesis of the catalysts. $PdCl_2$ which was used as the metal precursor and NaCl ($PdCl_2$/NaCl=1/5, w/w) were dissolved in deionized water. Afterwards, the ACFs were added into the palladium solution and stirred in a water bath at 80 °C for 2 h. Eventually, the catalysts were washed with deionized water and dried in an oven at 105 °C.

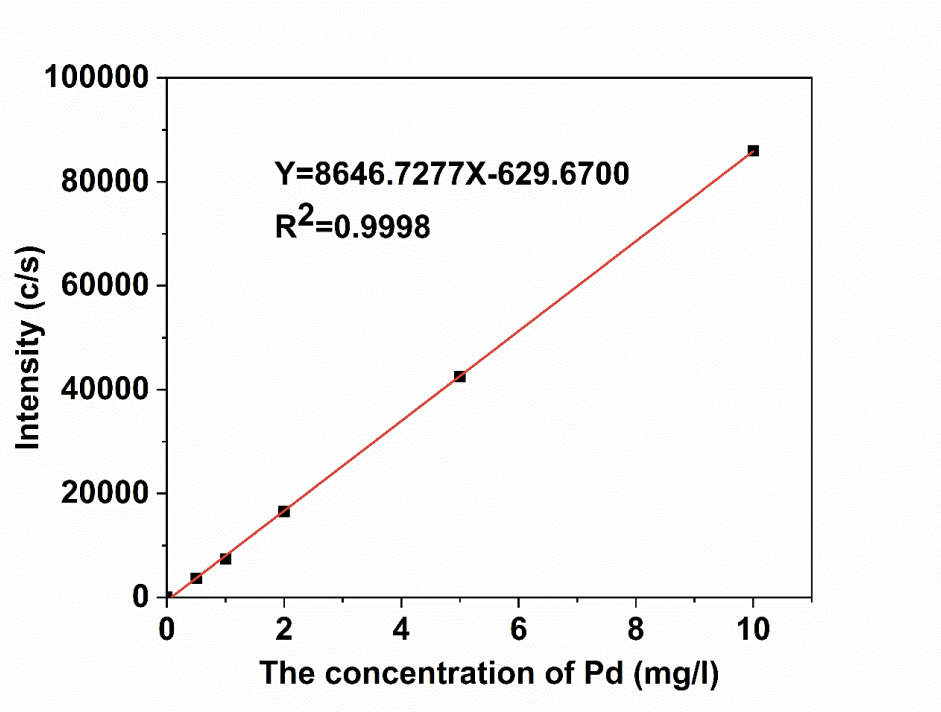
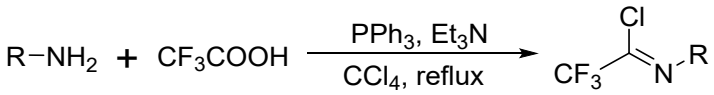


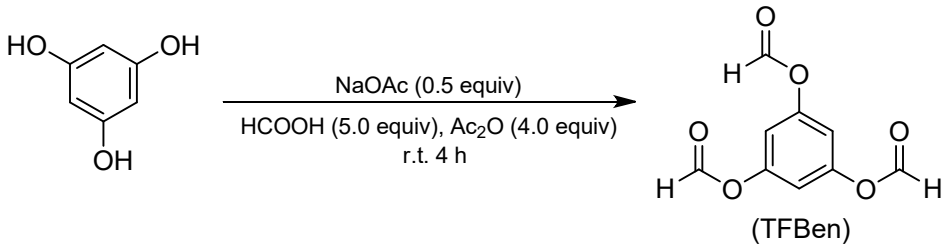
Fig.S1. The standard curve of Pd in inductively coupled plasma atomic emission spectra.

1.2 Preparation of trifluoroacetimidoyl chlorides[2]



A 100 mL two-necked flask equipped with a septum cap, a condenser, and a Teflon-coated magnetic stir bar was charged with PPh_3 (9.84 g, 37.5 mmol), Et_3N (2.1 mL, 15 mmol), CCl_4 (20.0 mL), and TFA (1.2 mL, 15 mmol). After the solution was stirred for about 10 min (ice bath), 2-iodoaniline (15 mmol) dissolved in CCl_4 (20.0 mL) was added. The mixture was then refluxed under stirring (3 h). After the reaction was completed, residual solid Ph_3PO, PPh_3 and Et_3N-HCl were washed with petroleum ether several times. Then the petroleum ether was filtered and concentrated under vacuum. The crude product was purified by column chromatography on silica gel or neutral alumina to afford the corresponding trifluoroacetimidoyl chloride product. All the trifluoroacetimidoyl chlorides are known compounds and have been reported previously by our group.[3]

1.3 Preparation of TFBen[4]

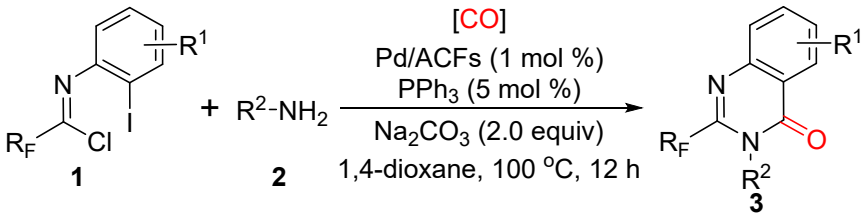


(TFBen)

Formic acid (8.4 mL, 222.8 mmol, 5.0 equiv.) was added to acetic anhydride (16.8 mL, 178.2 mmol, 4.0 equiv.) at room temperature. The mixture was stirred at 60 ^oC for 1 h and cooled to room temperature. The resulting solution was poured into a flask containing 1,3,5-trihydroxybenzene (5.62 g, 44.6 mmol, 1.0 equiv.) and NaOAc (1.83 g, 22.3 mmol, 0.5 equiv.). The mixture was stirred for 4 h in a water bath and then diluted with toluene (100 mL), washed with H_2O (50 mL) twice. The organic phase was kept in fridge (2-8 ^oC) overnight, then filtered and dried in vacuo to afford the desired product benzene-1,3,5-triyl triformate (TFBen) (5.1 g, 55%) as a white solid.

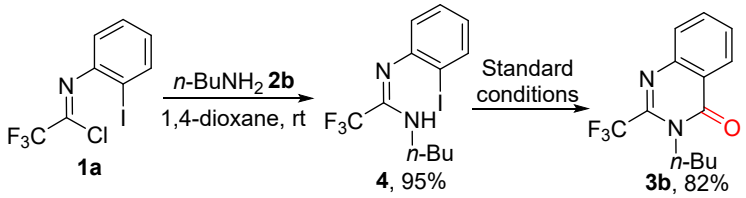
2. Experimental procedures

2.1 General procedure for the synthesis of products 3



Under N_2 atmosphere, Pd/ACFs (25 mg, 1 mol %), PPh_3 (2.6 mg, 0.01 mmol, 5 mol%), Na_2CO_3 (42.2 mg, 0.4 mmol, 2.0 equiv), and a 2.5 mL vial containing TFBen (210.0 mg, 1.0 mmol, 5.0 equiv), trifluoroacetimidoyl chloride **1** (0.2 mmol, 1.0 equiv), amine **2** (0.4 mmol, 2.0 equiv), 1,4-dioxane (2.0 mL) (extra dry) were added to an oven-dried 15 mL *In-Ex* tube. Then the tube was sealed and the mixture was stirred at 100 °C (oil bath) for 12 h. After the reaction was completed, the mixture was slowly cooled to room temperature, the reaction mixture was filtered and concentrated under vacuum. The residue was purified by column chromatography on silica gel (Petroleum Ether/EtOAc) to yield the 2-trifluoromethyl-quinazolin-4(3*H*)-one products **3**.

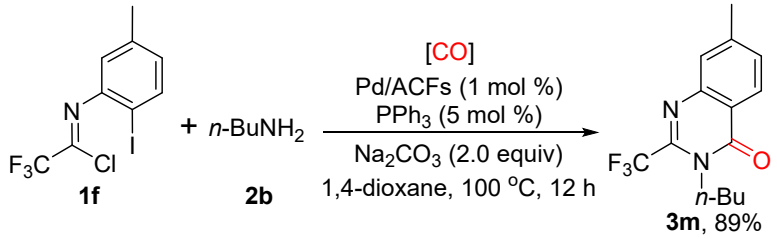
2.2 Control experiment



Under air atmosphere, trifluoroacetimidoyl chloride **1a** (0.2 mmol, 1.0 equiv), *n*-butylamine **2b** (0.4 mmol, 2.0 equiv) and 1,4-dioxane (2.0 mL) (extra dry) were added to an oven-dried 15 mL *In-Ex* tube. Then the tube was sealed and the mixture was stirred at room temperature for 2 h. After the reaction was completed, the reaction mixture was filtered and concentrated under vacuum. The residue was purified by column chromatography on silica gel (Petroleum Ether/EtOAc) to yield the amidine **4** in 95% yield.

Under N_2 atmosphere, Pd/ACFs (25 mg, 1 mol %), PPh_3 (2.6 mg, 0.01 mmol, 5 mol%), Na_2CO_3 (42.2 mg, 0.4 mmol, 2.0 equiv), amidine **4** (0.4 mmol, 2.0 equiv) and a 2.5 mL vial containing TFBen (210.0 mg, 1.0 mmol, 5.0 equiv), Then the tube was sealed and the mixture was stirred at 100 °C (oil bath) for 12 h. After the reaction was completed, the mixture was slowly cooled to room temperature, the reaction mixture was filtered and concentrated under vacuum. The residue was purified by column chromatography on silica gel (Petroleum Ether/EtOAc) to yield the 2-trifluoromethyl-quinazolin-4(3*H*)-one product **3b** in 82% yield.

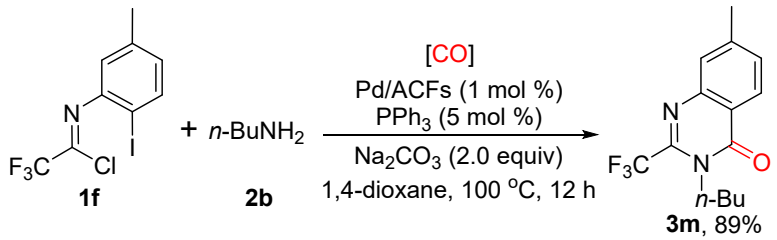
2.3 Scale-up reaction



1f **2b** **3m**, 89%

Under N_2 atmosphere, Pd/ACFs (125 mg, 0.5 mol %), PPh_3 (26 mg, 0.1 mmol, 5 mol%), Na_2CO_3 (422 mg, 4 mmol, 2.0 equiv), and a 25 mL vial containing TFBen (2.1 g, 10.0 mmol, 5.0 equiv), trifluoroacetimidoyl chloride **1f** (2 mmol, 1.0 equiv), *n*-butylamine **2b** (4 mmol, 2.0 equiv), 1,4-dioxane (20 mL) (extra dry) were added to an oven-dried 100 mL *In-Ex* tube. Then the tube was sealed and the mixture was stirred at 100 °C (oil bath) for 12 h. After the reaction was completed, the mixture was slowly cooled to room temperature, the reaction mixture was filtered and concentrated under vacuum. The residue was purified by column chromatography on silica gel (Petroleum Ether/EtOAc) to yield the product **3m** as a yellow oil in 89% yield (0.506 g).

2.4 Recycling experiment



1f **2b** **3m**, 89%

Under N_2 atmosphere, Pd/ACFs (25 mg, 1 mol %), PPh_3 (2.6 mg, 0.01 mmol, 5 mol%), Na_2CO_3 (42.2 mg, 0.4 mmol, 2.0 equiv), and a 2.5 mL vial containing TFBen (210.0 mg, 1.0 mmol, 5.0 equiv), trifluoroacetimidoyl chloride **1f** (0.2 mmol, 1.0 equiv), *n*-butylamine **2a** (0.4 mmol, 2.0 equiv), 1,4-dioxane (2.0 mL) (extra dry) were added to an oven-dried 15 mL *In-Ex* tube. Then the tube was sealed and the mixture was stirred at 100 °C (oil bath) for 12 h. After the reaction was completed, the mixture was slowly cooled to room temperature, the reaction mixture was filtered and concentrated under vacuum. The residue was purified by column chromatography on silica gel (Petroleum Ether/EtOAc) to yield the 2-trifluoromethyl-quinazolin-4(3*H*)-one product **3m** in 95% yield. The Pd/ACFs was reused in the next reaction for four times, and the yield of product **3m** was 93%, 87%, 82% and 75%, respectively.

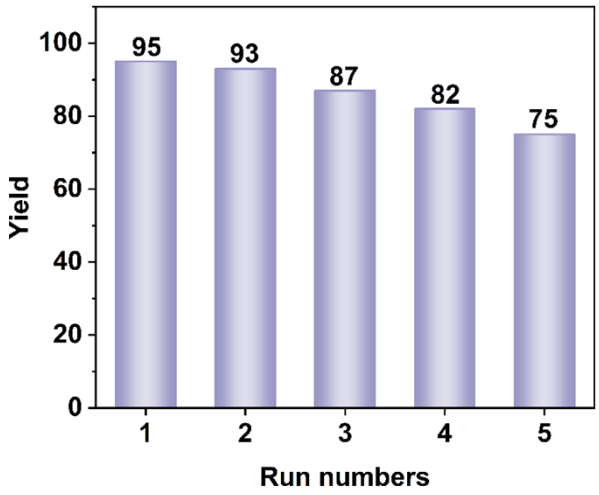
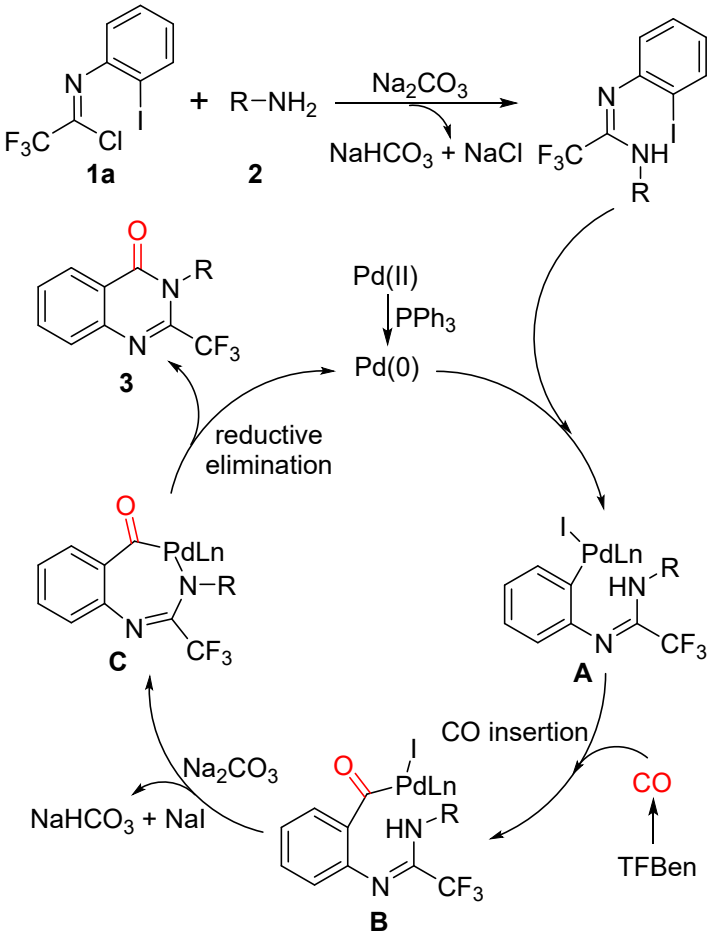
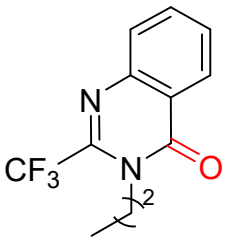


Fig. S2. Recycling of the Pd/ACFs catalyst for the carbonylative cyclization reaction.



Scheme S1. Plausible reaction mechanism.

3. Characterization data of the corresponding products

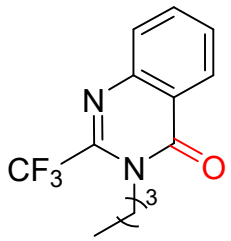


3-propyl-2-(trifluoromethyl)quinazolin-4(3*H*)-one (**3a**)[3]

General Procedure was followed with (2-iodophenyl)trifluoroacetimidoyl chloride **1a** (0.2 mmol, 1.0 equiv), amine **2a** (0.4 mmol, 2.0 equiv), Pd/ACFs (25 mg, 1.0 mol %), PPh_3 (2.6 mg, 0.01 mmol, 5 mol %), Na_2CO_3 (42.4 mg, 0.4 mmol, 2 equiv), TFBen (210 mg, 1 mmol, 5.0 equiv) and 1,4-dioxane (2.0 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.3) to give the titled product **3a** as a yellow oil (42.3 mg,

83%). ^{1}H NMR, ^{13}C NMR, ^{19}F NMR and HRMS data are consistent with the data we previously reported.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (d, J = 7.9 Hz, 1H), 7.83 – 7.77 (m, 2H), 7.62 – 7.56 (m, 1H), 4.13 – 4.02 (m, 2H), 1.79 (q, J = 7.6 Hz, 2H), 1.02 (t, J = 7.5 Hz, 3H).



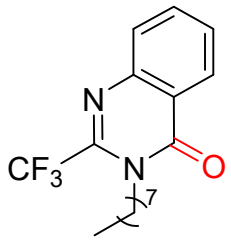
3-butyl-2-(trifluoromethyl)quinazolin-4(3*H*)-one (**3b**) [3]

General Procedure was followed with (2-iodophenyl)trifluoroacetimidoyl chloride **1a** (0.2 mmol, 1.0 equiv), amine **2b** (0.4 mmol, 2.0 equiv), Pd/ACFs (25 mg, 1.0 mol %), PPh_3 (2.6 mg, 0.01 mmol, 5 mol %), Na_2CO_3 (42.4 mg, 0.4 mmol, 2 equiv), TFBen (210 mg, 1 mmol, 5.0 equiv) and 1,4-dioxane (2.0 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.3) to give the titled product **3b** as a yellow oil (45.6 mg, 84%). ^{1}H NMR, ^{13}C NMR, ^{19}F NMR and HRMS data are consistent with the data we previously reported.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, J = 7.9 Hz, 1H), 7.88 – 7.75 (m, 2H), 7.64 – 7.54 (m, 1H), 4.16 – 4.08 (m, 2H), 1.75 (dd, J = 14.3, 5.9 Hz, 2H), 1.50 – 1.38 (m, 2H), 0.98 (t, J = 7.4 Hz, 3H).

^{13}C NMR (101 MHz, $CDCl_3$) δ 161.5, 145.2, 142.4 (C-F, q, $^{2}J_{(C-F)}$ = 35.5 Hz), 134.9, 129.3, 128.6, 127.1, 118.4 (C-F, q, $^{1}J_{(C-F)}$ = 277.0 Hz), 122.0, 45.4, 30.8, 20.3, 13.7.

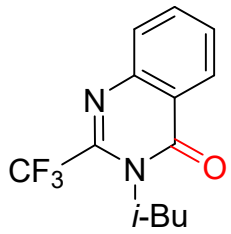
^{19}F NMR (376 MHz, $CDCl_3$) δ - 65.8.



3-octyl-2-(trifluoromethyl)quinazolin-4(3*H*)-one (**3c**) [3]

General Procedure was followed with (2-iodophenyl)trifluoroacetimidoyl chloride **1a** (0.2 mmol, 1.0 equiv), amine **2c** (0.4 mmol, 2.0 equiv), Pd/ACFs (25 mg, 1.0 mol %), PPh_3 (2.6 mg, 0.01 mmol, 5 mol %), Na_2CO_3 (42.4 mg, 0.4 mmol, 2 equiv), TFBen (210 mg, 1 mmol, 5.0 equiv) and 1,4-dioxane (2.0 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.3) to give the titled product **3c** as a yellow oil (48.4 mg, 74%). ^{1}H NMR, ^{13}C NMR, ^{19}F NMR and HRMS data are consistent with the data we previously reported.

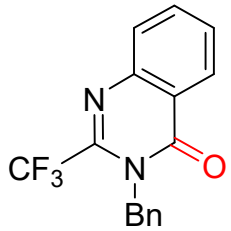
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, J = 7.3 Hz, 1H), 7.81 (dd, J = 3.8, 1.5 Hz, 2H), 7.59 (ddd, J = 8.3, 5.4, 3.0 Hz, 1H), 4.31 – 4.12 (m, 2H), 1.76 (p, J = 8.0, 7.5 Hz, 2H), 1.43 (dt, J = 13.9, 6.8 Hz, 2H), 1.36 – 1.21 (m, 8H), 0.96 – 0.76 (m, 3H).



3-isobutyl-2-(trifluoromethyl)quinazolin-4(3*H*)-one (**3d**) [3]

General Procedure was followed with (2-iodophenyl)trifluoroacetimidoyl chloride **1a** (0.2 mmol, 1.0 equiv), amine **2d** (0.4 mmol, 2.0 equiv), Pd/ACFs (25 mg, 1.0 mol %), PPh_3 (2.6 mg, 0.01 mmol, 5 mol %), Na_2CO_3 (42.4 mg, 0.4 mmol, 2 equiv), TFBen (210 mg, 1 mmol, 5.0 equiv) and 1,4-dioxane (2.0 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.3) to give the titled product **3d** as a yellow oil (50.1 mg, 93%). ^{1}H NMR, ^{13}C NMR, ^{19}F NMR and HRMS data are consistent with the data we previously reported.

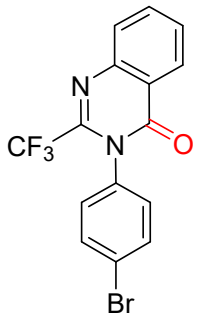
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, *J* = 7.6 Hz, 1H), 7.81 (d, *J* = 4.6 Hz, 2H), 7.61 (ddd, *J* = 8.2, 4.9, 3.5 Hz, 1H), 4.05 (d, *J* = 7.5 Hz, 2H), 2.32 (dt, *J* = 13.4, 6.6 Hz, 1H), 0.94 (d, *J* = 6.7 Hz, 6H).



4-benzyl-2-(trifluoromethyl)quinazolin-4(3*H*)-one (**3e**) [3]

General Procedure was followed with (2-iodophenyl)trifluoroacetimidoyl chloride **1a** (0.2 mmol, 1.0 equiv), amine **2e** (0.4 mmol, 2.0 equiv), Pd/ACFs (25 mg, 1.0 mol %), PPh_3 (2.6 mg, 0.01 mmol, 5 mol %), Na_2CO_3 (42.4 mg, 0.4 mmol, 2 equiv), TFBen (210 mg, 1 mmol, 5.0 equiv) and 1,4-dioxane (2.0 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.3) to give the titled product **3e** as a yellow oil (54.8 mg, 90%). ^{1}H NMR, ^{13}C NMR, ^{19}F NMR and HRMS data are consistent with the data we previously reported.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (d, *J* = 8.2 Hz, 1H), 7.86 (dd, *J* = 4.0, 1.7 Hz, 2H), 7.68 – 7.60 (m, 1H), 7.30 (q, *J* = 7.6 Hz, 3H), 7.18 (d, *J* = 7.5 Hz, 2H), 5.45 (s, 2H).

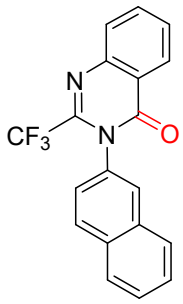


3-(4-bromophenyl)-2-(trifluoromethyl)quinazolin-4(3*H*)-one (**3f**) [3]

General Procedure was followed with (2-iodophenyl)trifluoroacetimidoyl chloride **1a** (0.2 mmol, 1.0 equiv), amine **2f** (0.4 mmol, 2.0 equiv), Pd/ACFs (25 mg, 1.0 mol %), PPh_3 (2.6 mg, 0.01 mmol, 5 mol %), Na_2CO_3 (42.4 mg, 0.4 mmol, 2.0 equiv), TFBen (210 mg, 1 mmol, 5.0 equiv) and 1,4-dioxane (2.0 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.3) to give the titled product **3f** as a yellow oil (59.2 mg,

80%). ^{1}H NMR, ^{13}C NMR, ^{19}F NMR and HRMS data are consistent with the data we previously reported.

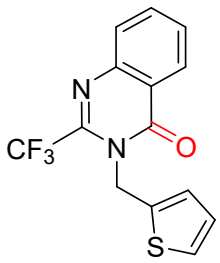
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, J = 7.8 Hz, 1H), 7.96 – 7.83 (m, 2H), 7.75 – 7.58 (m, 3H), 7.18 (d, J = 8.2 Hz, 2H).



3-(naphthalen-2-yl)-2-(trifluoromethyl)quinazolin-4(3*H*)-one (**3g**) [3]

General Procedure was followed with (2-iodophenyl)trifluoroacetimidoyl chloride **1a** (0.2 mmol, 1.0 equiv), amine **2g** (0.4 mmol, 2.0 equiv), Pd/ACFs (25 mg, 1.0 mol %), PPh_3 (2.6 mg, 0.01 mmol, 5 mol %), Na_2CO_3 (42.4 mg, 0.4 mmol, 2.0 equiv), TFBen (210 mg, 1 mmol, 5.0 equiv) and 1,4-dioxane (2.0 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.3) to give the titled product **3g** as a white solid (54.6 mg, 80%). ^{1}H NMR, ^{13}C NMR, ^{19}F NMR and HRMS data are consistent with the data we previously reported.

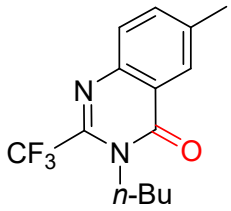
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, *J* = 7.7 Hz, 1H), 8.00 (d, *J* = 8.8 Hz, 1H), 7.97 – 7.92 (m, 2H), 7.91 – 7.86 (m, 2H), 7.84 (s, 1H), 7.70 – 7.63 (m, 1H), 7.62 – 7.53 (m, 2H), 7.39 (d, *J* = 8.6 Hz, 1H).



3-(thiophen-2-ylmethyl)-2-(trifluoromethyl)quinazolin-4(3*H*)-one (**3h**) [3]

General Procedure was followed with (2-iodophenyl)trifluoroacetimidoyl chloride **1a** (0.2 mmol, 1.0 equiv), amine **2g** (0.4 mmol, 2.0 equiv), Pd/ACFs (25 mg, 1.0 mol %), PPh_3 (2.6 mg, 0.01 mmol, 5 mol %), Na_2CO_3 (42.4 mg, 0.4 mmol, 2.0 equiv), TFBen (210 mg, 1 mmol, 5.0 equiv) and 1,4-dioxane (2.0 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.3) to give the titled product **3h** as a white solid (58 mg, 93%). ^{1}H NMR, ^{13}C NMR, ^{19}F NMR and HRMS data are consistent with the data we previously reported.

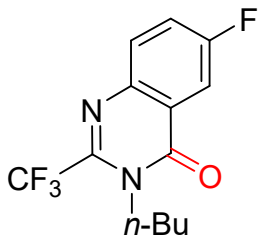
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, *J* = 8.1 Hz, 1H), 7.92 – 7.75 (m, 2H), 7.62 (ddd, *J* = 8.3, 5.3, 3.2 Hz, 1H), 7.24 (d, *J* = 5.2 Hz, 1H), 7.15 (d, *J* = 4.0 Hz, 1H), 6.94 (dd, *J* = 5.2, 3.5 Hz, 1H), 5.53 (s, 2H).



3-butyl-6-methyl-2-(trifluoromethyl)quinazolin-4(3*H*)-one (**3i**) [3]

General Procedure was followed with (2-iodophenyl)trifluoroacetimidoyl chloride **1b** (0.2 mmol, 1.0 equiv), amine **2a** (0.4 mmol, 2.0 equiv), Pd/ACFs (25 mg, 1.0 mol %), PPh_3 (2.6 mg, 0.01 mmol, 5 mol %), Na_2CO_3 (42.4 mg, 0.4 mmol, 2.0 equiv), TFBen (210 mg, 1 mmol, 5.0 equiv) and 1,4-dioxane (2.0 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.3) to give the titled product **3i** as a yellow oil (54.5 mg, 96%). ^{1}H NMR, ^{13}C NMR, ^{19}F NMR and HRMS data are consistent with the data we previously reported.

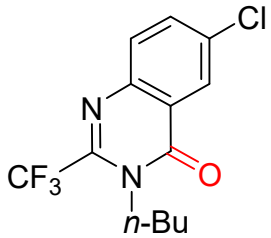
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 (s, 1H), 7.61 (d, *J* = 8.2 Hz, 1H), 7.54 (d, *J* = 8.4 Hz, 1H), 4.07 – 4.01 (m, 2H), 2.43 (s, 3H), 1.66 (p, *J* = 8.0, 7.6 Hz, 2H), 1.37 (dt, *J* = 14.8, 7.0 Hz, 2H), 0.90 (t, *J* = 7.4 Hz, 3H).



3-butyl-6-fluoro-2-(trifluoromethyl)quinazolin-4(3*H*)-one (**3j**) [3]

General Procedure was followed with (2-iodophenyl)trifluoroacetimidoyl chloride **1c** (0.2 mmol, 1.0 equiv), amine **2a** (0.4 mmol, 2.0 equiv), Pd/ACFs (25 mg, 1.0 mol %), PPh_3 (2.6 mg, 0.01 mmol, 5 mol %), Na_2CO_3 (42.4 mg, 0.4 mmol, 2.0 equiv), TFBen (210 mg, 1 mmol, 5.0 equiv) and 1,4-dioxane (2.0 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.3) to give the titled product **3j** as a yellow oil (54.1 mg, 94%). ^{1}H NMR, ^{13}C NMR, ^{19}F NMR and HRMS data are consistent with the data we previously reported.

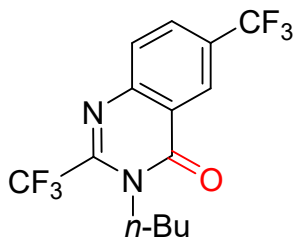
^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 8.2 Hz, 1H), 7.74 (dd, *J* = 8.9, 5.0 Hz, 1H), 7.44 (t, *J* = 8.5 Hz, 1H), 4.08 – 4.01 (m, 2H), 1.66 (p, *J* = 7.3 Hz, 2H), 1.39 (dt, *J* = 14.8, 7.4 Hz, 2H), 0.91 (t, *J* = 7.3 Hz, 3H).



3-butyl-6-chloro-2-(trifluoromethyl)quinazolin-4(3*H*)-one (**3k**) [3]

General Procedure was followed with (2-iodophenyl)trifluoroacetimidoyl chloride **1d** (0.2 mmol, 1.0 equiv), amine **2a** (0.4 mmol, 2.0 equiv), Pd/ACFs (25 mg, 1.0 mol %), PPh_3 (2.6 mg, 0.01 mmol, 5 mol %), Na_2CO_3 (42.4 mg, 0.4 mmol, 2.0 equiv), TFBen (210 mg, 1 mmol, 5.0 equiv) and 1,4-dioxane (2.0 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.3) to give the titled product **3k** as a yellow oil (46.6 mg, 76%). ^{1}H NMR, ^{13}C NMR, ^{19}F NMR and HRMS data are consistent with the data we previously reported.

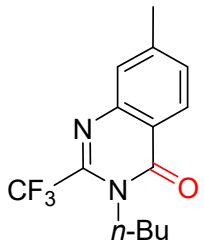
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (s, 1H), 7.74 (d, *J* = 1.6 Hz, 2H), 4.16 – 4.07 (m, 2H), 1.73 (p, *J* = 8.0, 7.6 Hz, 2H), 1.46 (dt, *J* = 14.8, 7.4 Hz, 2H), 0.98 (t, *J* = 7.4 Hz, 3H).



3-butyl-2,6-bis(trifluoromethyl)quinazolin-4(3*H*)-one (**3l**) [3]

General Procedure was followed with (2-iodophenyl)trifluoroacetimidoyl chloride **1e** (0.2 mmol, 1.0 equiv), amine **2a** (0.4 mmol, 2.0 equiv), Pd/ACFs (25 mg, 1.0 mol %), PPh_3 (2.6 mg, 0.01 mmol, 5 mol %), Na_2CO_3 (42.4 mg, 0.4 mmol, 2.0 equiv), TFBen (210 mg, 1 mmol, 5.0 equiv) and 1,4-dioxane (2.0 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.3) to give the titled product **3l** as a yellow oil (58.5 mg, 87%). ^{1}H NMR, ^{13}C NMR, ^{19}F NMR and HRMS data are consistent with the data we previously reported.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.59 (s, 1H), 8.01 (d, *J* = 8.5 Hz, 1H), 7.92 (d, *J* = 8.8 Hz, 1H), 4.26 – 4.02 (m, 2H), 1.82 – 1.64 (m, 2H), 1.48 (dt, *J* = 15.0, 7.4 Hz, 2H), 0.99 (t, *J* = 7.4 Hz, 3H).

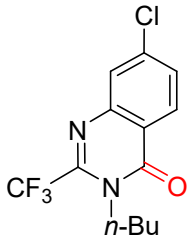


3-butyl-7-methyl-2-(trifluoromethyl)quinazolin-4(3*H*)-one (**3m**) [3]

General Procedure was followed with (2-iodophenyl)trifluoroacetimidoyl chloride **1f** (0.2 mmol, 1.0 equiv), amine **2a** (0.4 mmol, 2.0 equiv), Pd/ACFs (25 mg, 1.0 mol %), PPh_3 (2.6 mg, 0.01 mmol, 5 mol %), Na_2CO_3 (42.4 mg, 0.4 mmol, 2.0 equiv), TFBen (210 mg, 1 mmol, 5.0 equiv) and 1,4-dioxane (2.0 mL). Upon completion the mixture

was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.3) to give the titled product **3m** as a yellow oil (54 mg, 95%). ^{1}H NMR, ^{13}C NMR, ^{19}F NMR and HRMS data are consistent with the data we previously reported.

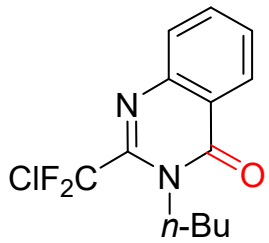
^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, *J* = 8.2 Hz, 1H), 7.59 (s, 1H), 7.40 (d, *J* = 8.2 Hz, 1H), 4.35 – 3.82 (m, 2H), 2.51 (s, 3H), 1.73 (p, *J* = 7.7 Hz, 2H), 1.46 (dt, *J* = 15.8, 7.9 Hz, 2H), 0.98 (t, *J* = 7.4 Hz, 3H).



3-butyl-7-chloro-2-(trifluoromethyl)quinazolin-4(3*H*)-one (**3n**) [3]

General Procedure was followed with (2-iodophenyl)trifluoroacetimidoyl chloride **1g** (0.2 mmol, 1.0 equiv), amine **2a** (0.4 mmol, 2.0 equiv), Pd/ACFs (25 mg, 1.0 mol %), PPh_3 (2.6 mg, 0.01 mmol, 5 mol %), Na_2CO_3 (42.4 mg, 0.4 mmol, 2.0 equiv), TFBen (210 mg, 1 mmol, 5.0 equiv) and 1,4-dioxane (2.0 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.3) to give the titled product **3n** as a yellow oil (40.6 mg, 66%). ^{1}H NMR, ^{13}C NMR, ^{19}F NMR and HRMS data are consistent with the data we previously reported.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, *J* = 8.6 Hz, 1H), 7.79 (s, 1H), 7.54 (d, *J* = 8.5 Hz, 1H), 4.14 – 4.07 (m, 2H), 1.73 (p, *J* = 7.5 Hz, 2H), 1.44 (dt, *J* = 14.5, 6.5 Hz, 2H), 0.98 (t, *J* = 7.2 Hz, 3H).



3-butyl-2-(chlorodifluoromethyl)quinazolin-4(3*H*)-one (**3o**) [3]

General Procedure was followed with (2-iodophenyl)trifluoroacetimidoyl chloride **1h** (0.2 mmol, 1.0 equiv), amine **2a** (0.4 mmol, 2.0 equiv), Pd/ACFs (25 mg, 1.0 mol %), PPh_3 (2.6 mg, 0.01 mmol, 5 mol %), Na_2CO_3 (42.4 mg, 0.4 mmol, 2.0 equiv), TFBen (210 mg, 1 mmol, 5.0 equiv) and 1,4-dioxane (2.0 mL). Upon completion the mixture was concentrated and purified via flash column chromatography (petroleum ether / ethyl acetate = 20:1, Rf = 0.3) to give the titled product **3o** as a yellow oil (27.5 mg, 48%). ^{1}H NMR, ^{13}C NMR, ^{19}F NMR and HRMS data are consistent with the data we previously reported.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (d, *J* = 7.7 Hz, 1H), 7.84 – 7.78 (m, 2H), 7.64 – 7.57 (m, 1H), 4.29 – 4.10 (m, 2H), 1.75 (p, *J* = 7.7 Hz, 2H), 1.46 (dt, *J* = 14.0, 7.0 Hz, 2H), 0.99 (t, *J* = 7.4 Hz, 3H).

4 References

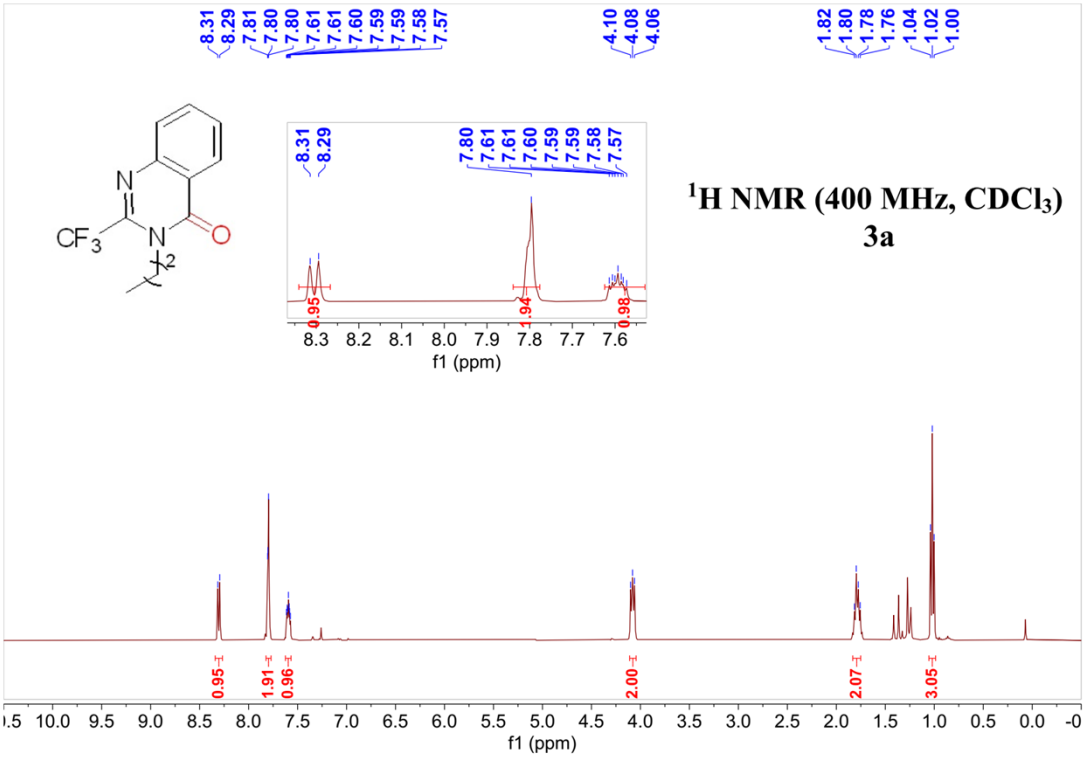
1. Wang, J.-S.; Li, C.; Ying, J.; Xu, T.; Lu, W.; Li, C.-Y.; Wu, X.-F., Activated carbon fibers supported palladium as efficient and easy-separable catalyst for carbonylative cyclization of o-alkynylphenols with nitroarenes: Facile construction of benzofuran-3-carboxamides. *J. Catal.* **2022,** *413*, 713-719.

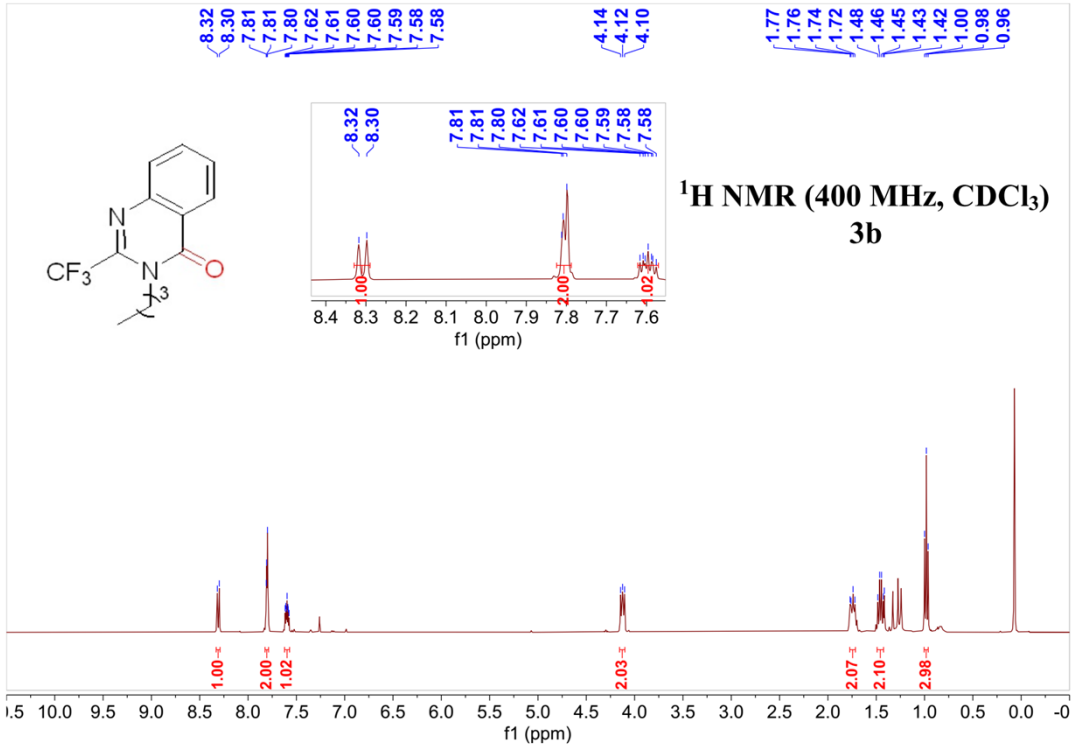
2. Chen, Z.; Hu, S.; Wu, X.-F., Trifluoroacetimidoyl halides: a potent synthetic origin. *Org. Chem. Front.* **2020,** *7*, 223-254.

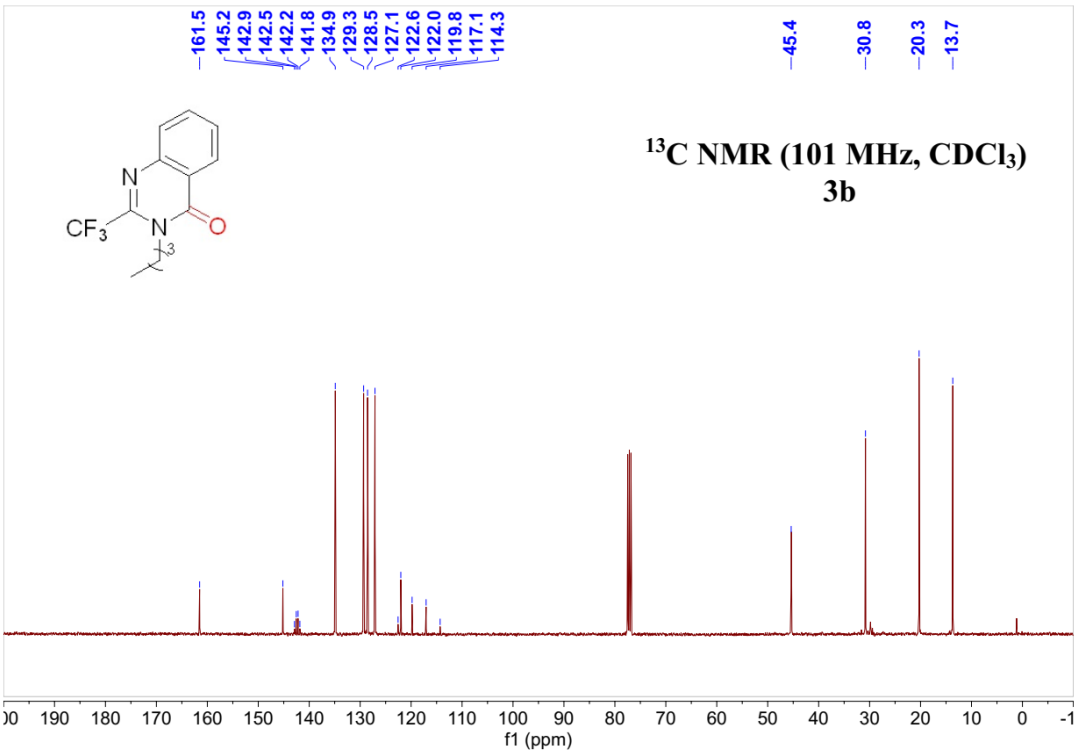
3. Chen, Z.; Wang, L.-C.; Zhang, J.; Wu, X.-F., Palladium-catalyzed three-component carbonylative synthesis of 2-(trifluoromethyl)quinazolin-4(3H)-ones from trifluoroacetimidoyl chlorides and amines. *Org. Chem. Front.* **2020,** *7*, 2499-2504.

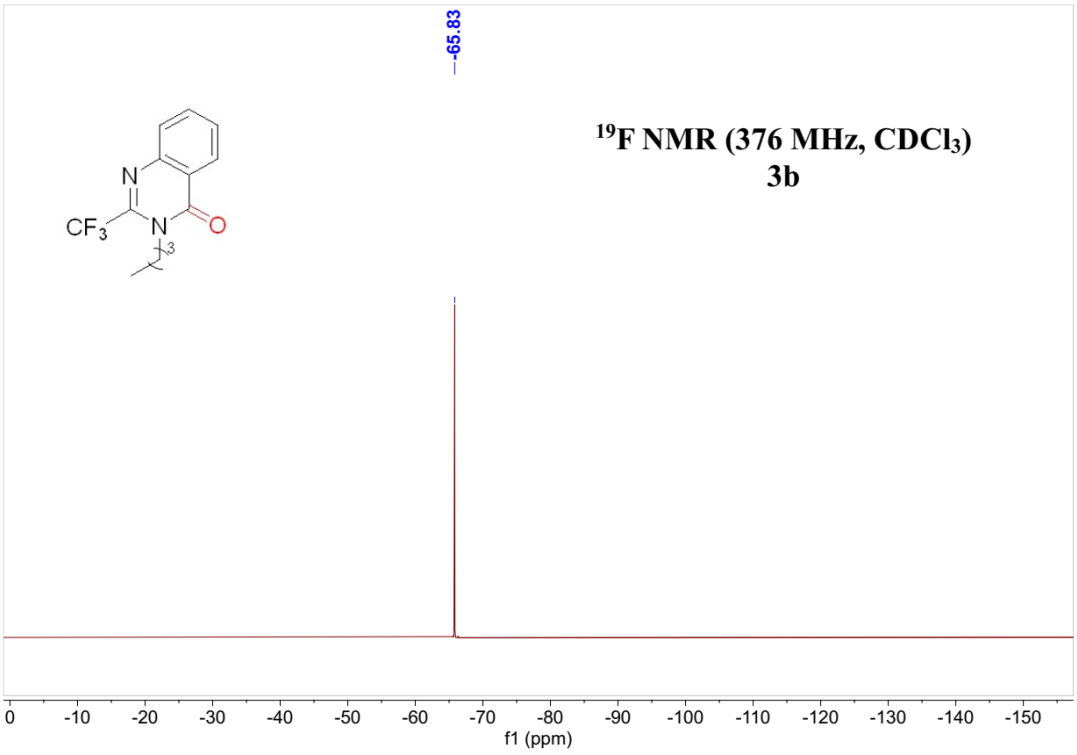
4. Yang, H.; Zhang, J.; Chen, Z.; Wu, X. F., TFBen (Benzene-1,3,5-triyl triformate): A Powerful and Versatile CO Surrogate. *Chem Rec* **2022,** *22*, e202100220.

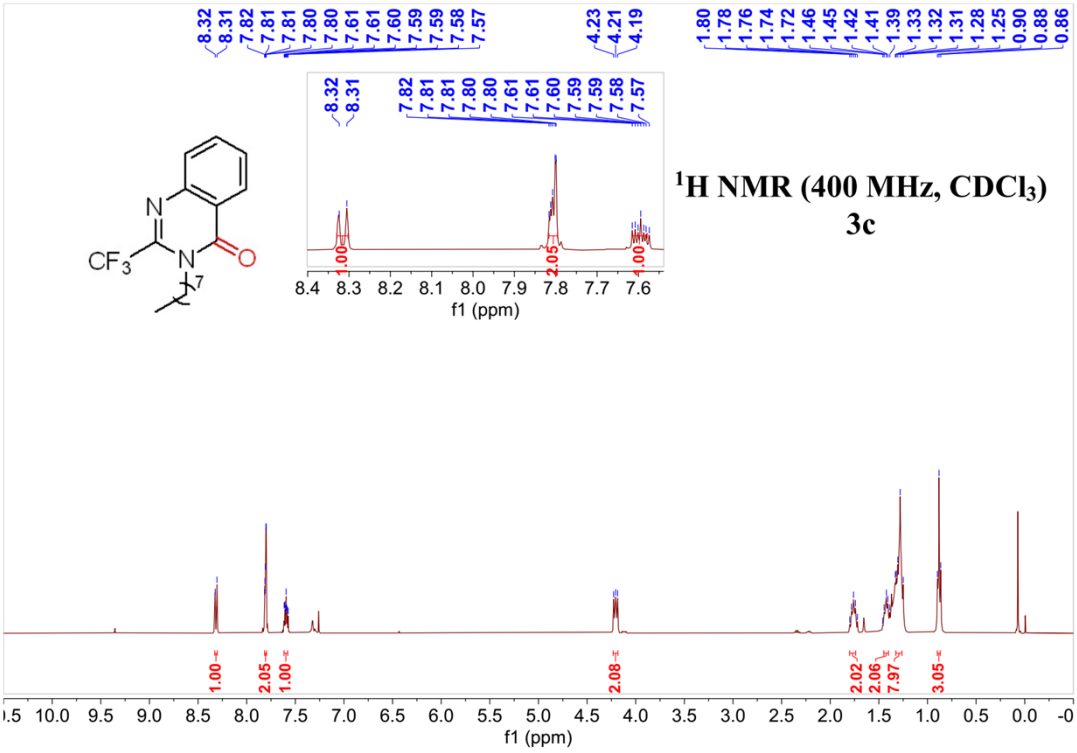
5 Copy of ^{1}H-NMR Spectra of Products



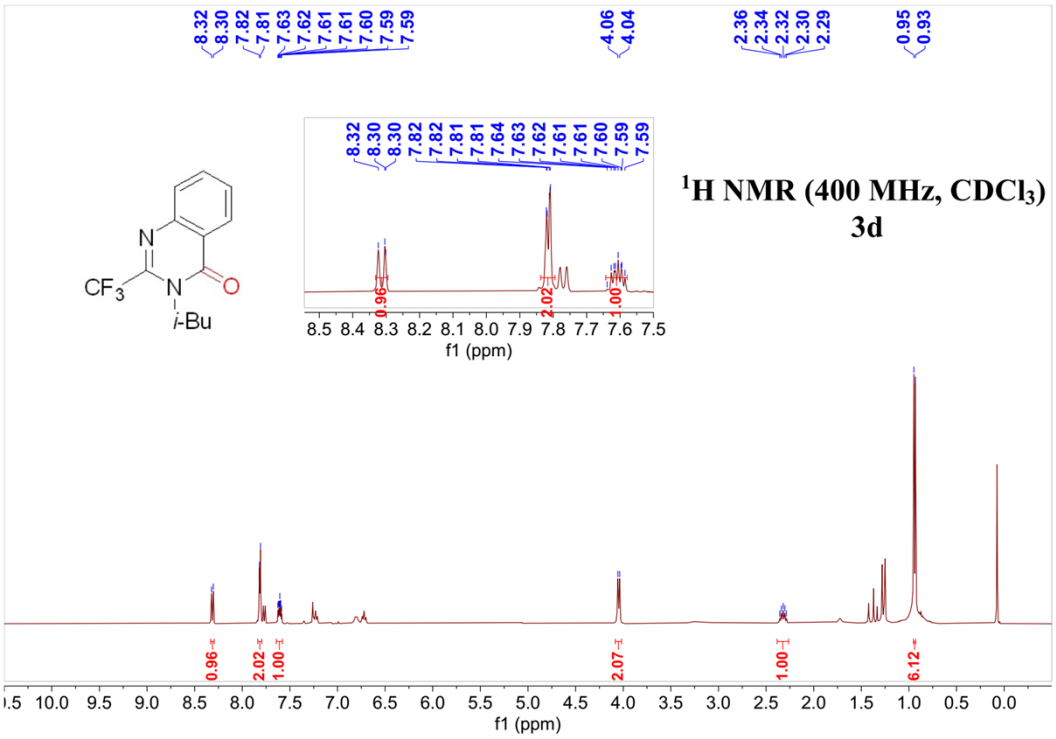



161.5
145.2
142.9
142.5
142.2
141.8
134.9
129.3
128.5
127.1
122.6
122.0
119.8
117.1
114.3
45.4
30.8
20.3
13.7
13C NMR (101 MHz, CDCl3)
3b
f1 (ppm)

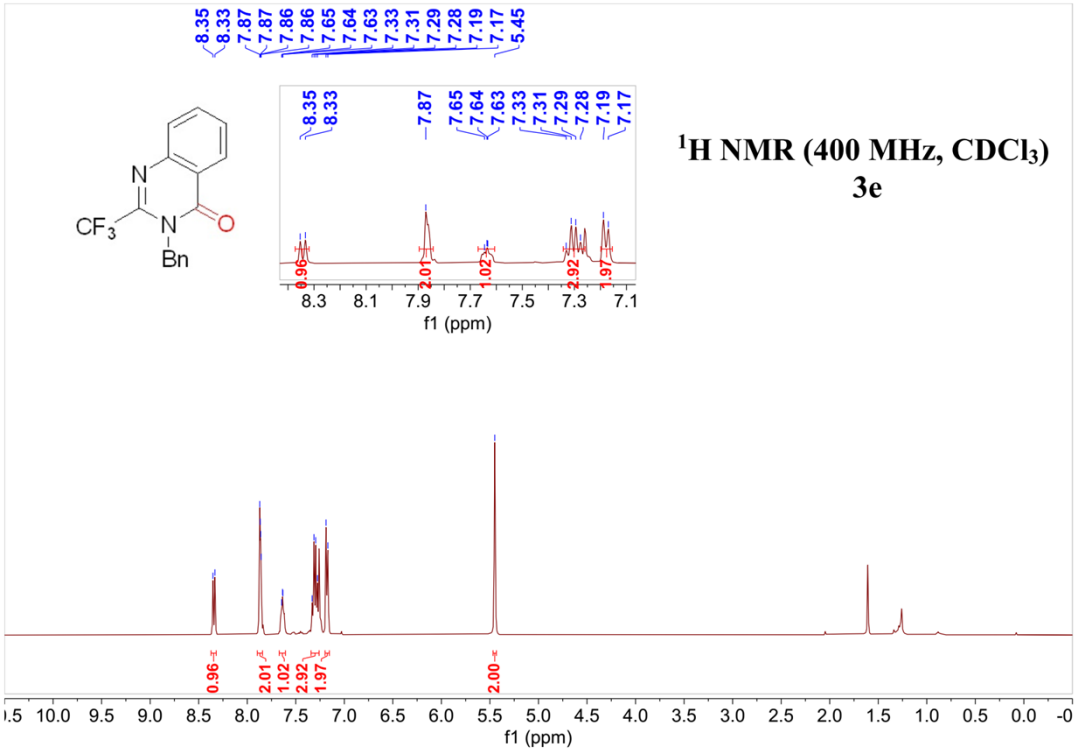

65.83
19F NMR (376 MHz, CDCl3)
3b
f1 (ppm)



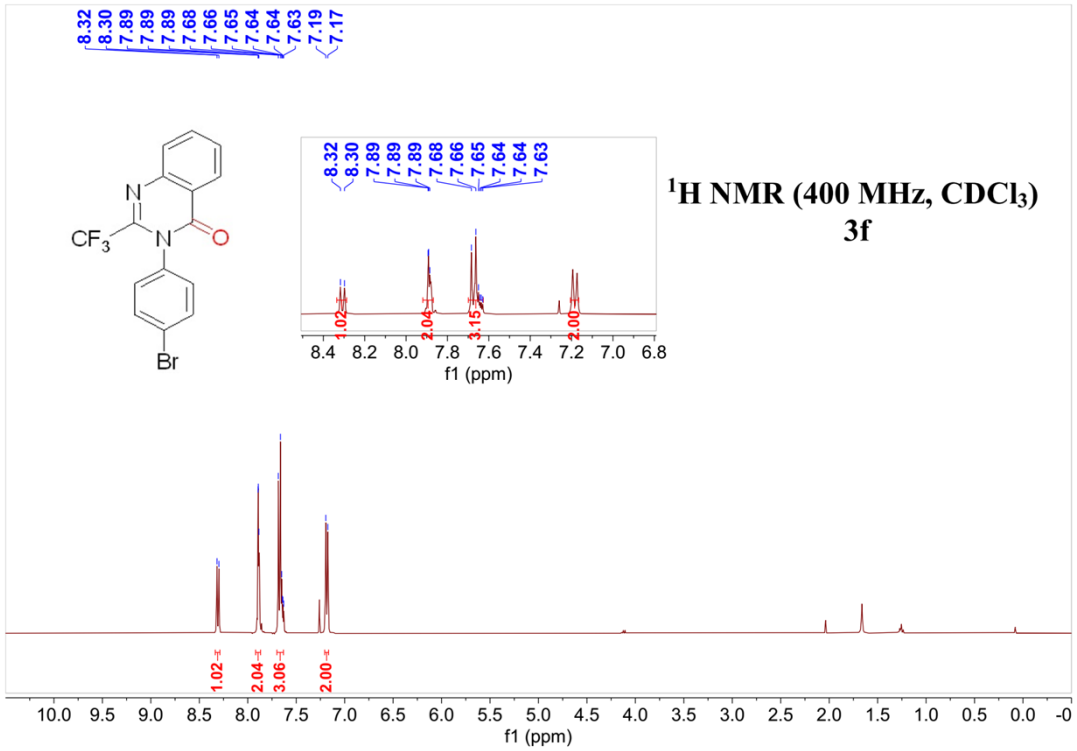
^{1}H NMR (400 MHz, $CDCl_3$)
3c



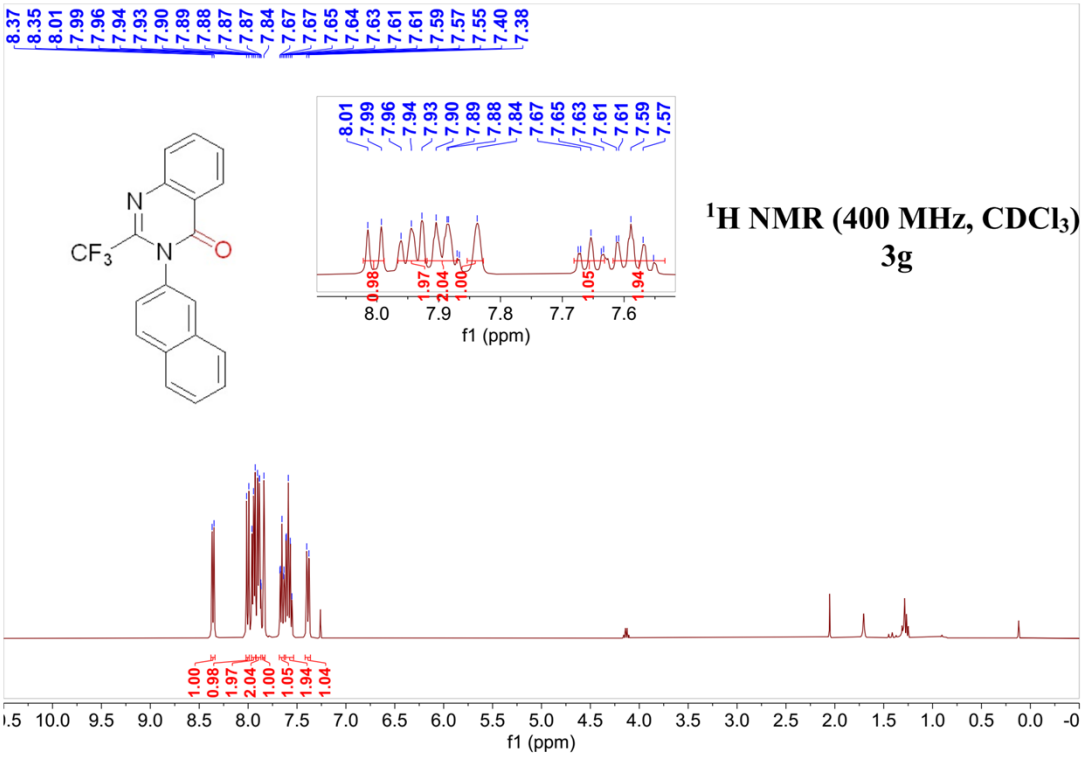
^{1}H NMR (400 MHz, $CDCl_3$)
3d



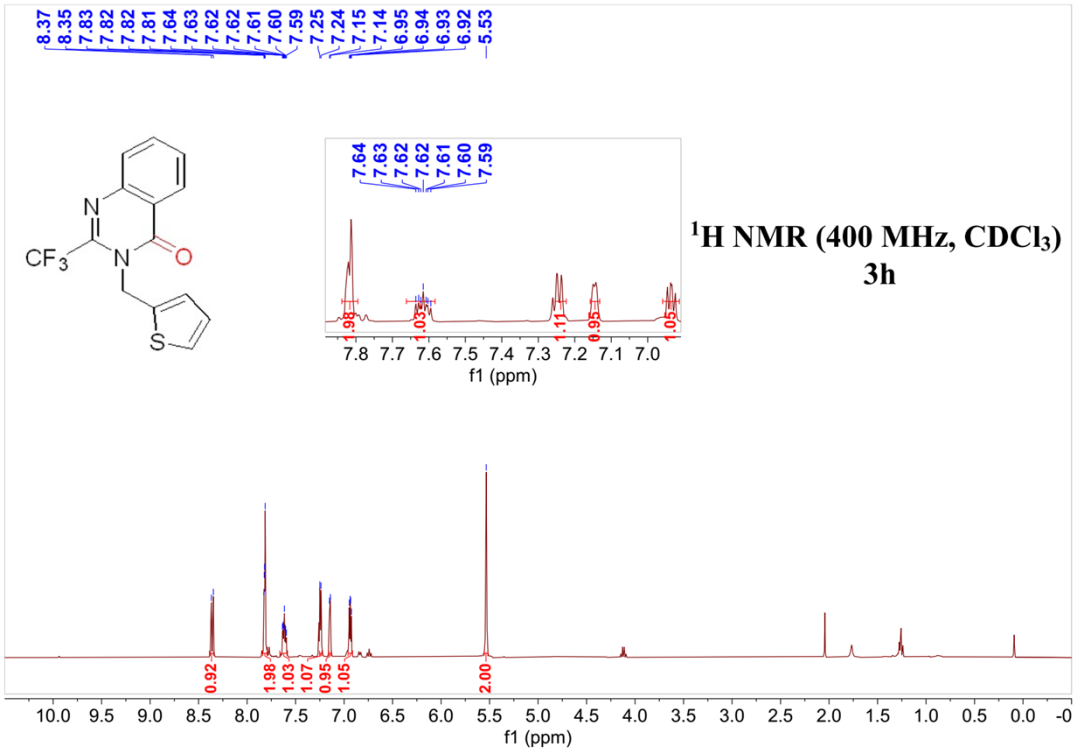
^{1}H NMR (400 MHz, $CDCl_3$)
3e



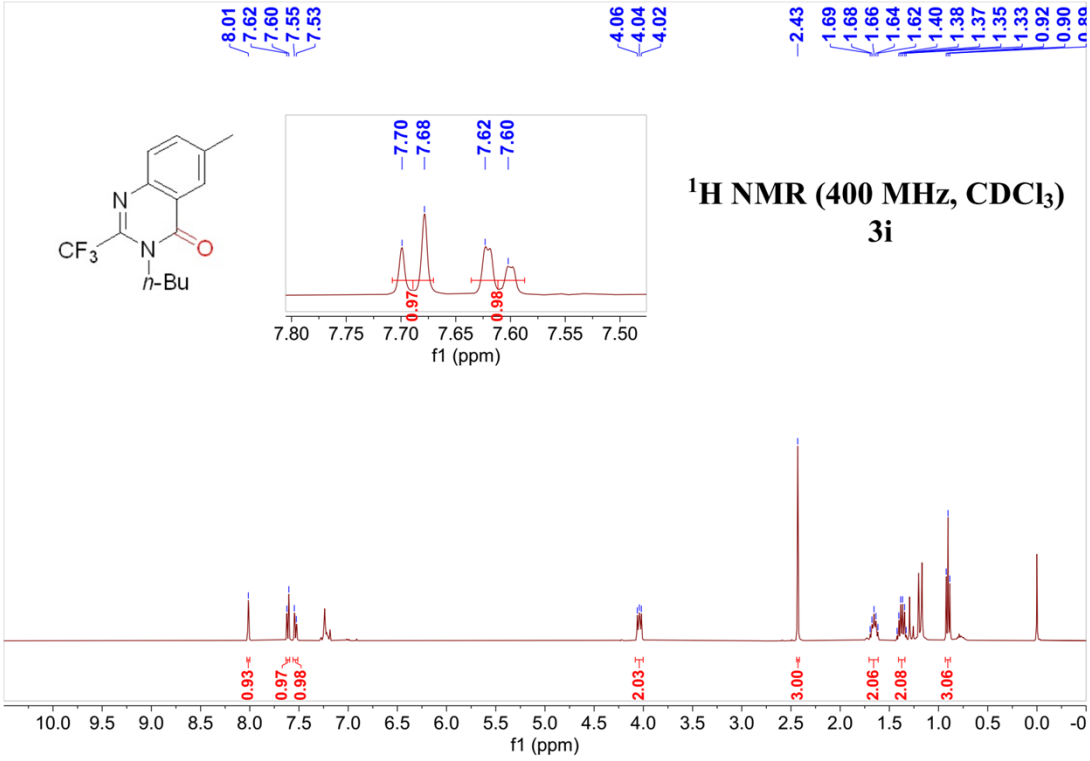
^{1}H NMR (400 MHz, $CDCl_3$)
3f



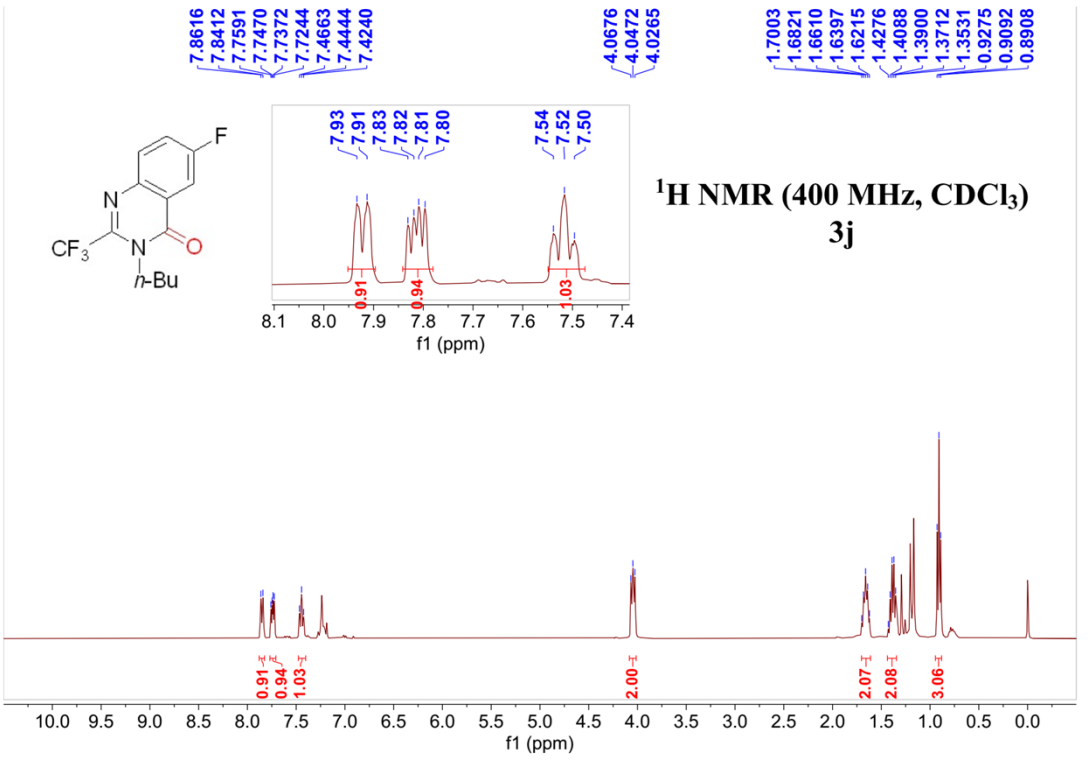
^{1}H NMR (400 MHz, $CDCl_3$)
3g



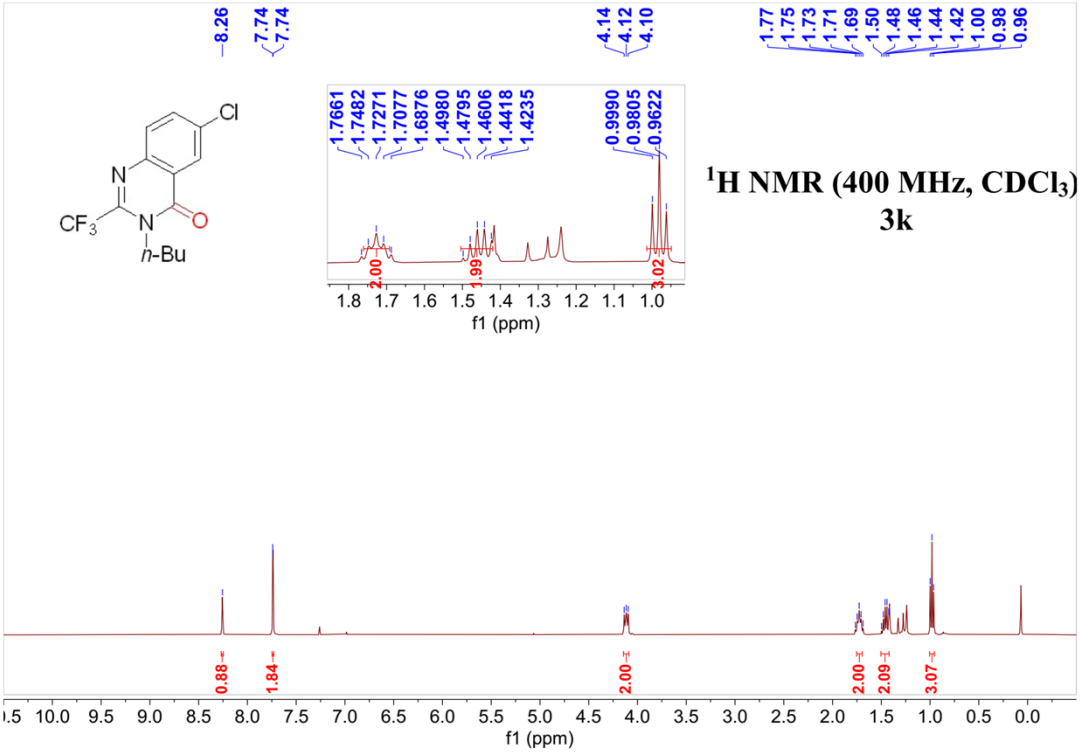
^{1}H NMR (400 MHz, $CDCl_3$)
3h

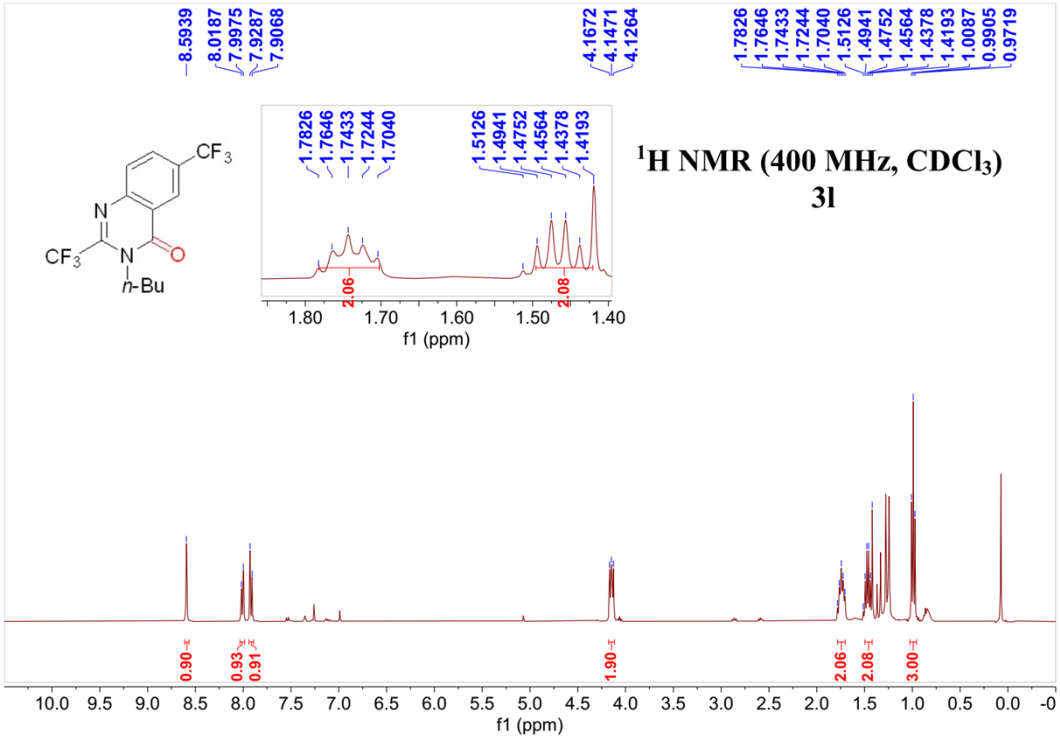


^{1}H NMR (400 MHz, $CDCl_3$)
3i



^{1}H NMR (400 MHz, $CDCl_3$)
3j


8.26
7.74
7.74
4.14
4.12
4.10
1.77
1.75
1.73
1.71
1.69
1.50
1.48
1.46
1.44
1.42
1.00
0.98
0.96
Cl
N
CF3
N
O
n-Bu
1.7661
1.7482
1.7271
1.7077
1.6876
1.4980
1.4795
1.4606
1.4418
1.4235
0.9990
0.9805
0.9622
2.00
1.99
3.02
1.8 1.7 1.6 1.5 1.4 1.3 1.2 1.1 1.0
f1 (ppm)
1H NMR (400 MHz, CDCl3)
3k
0.88
1.84
2.00
2.00
2.09
3.07
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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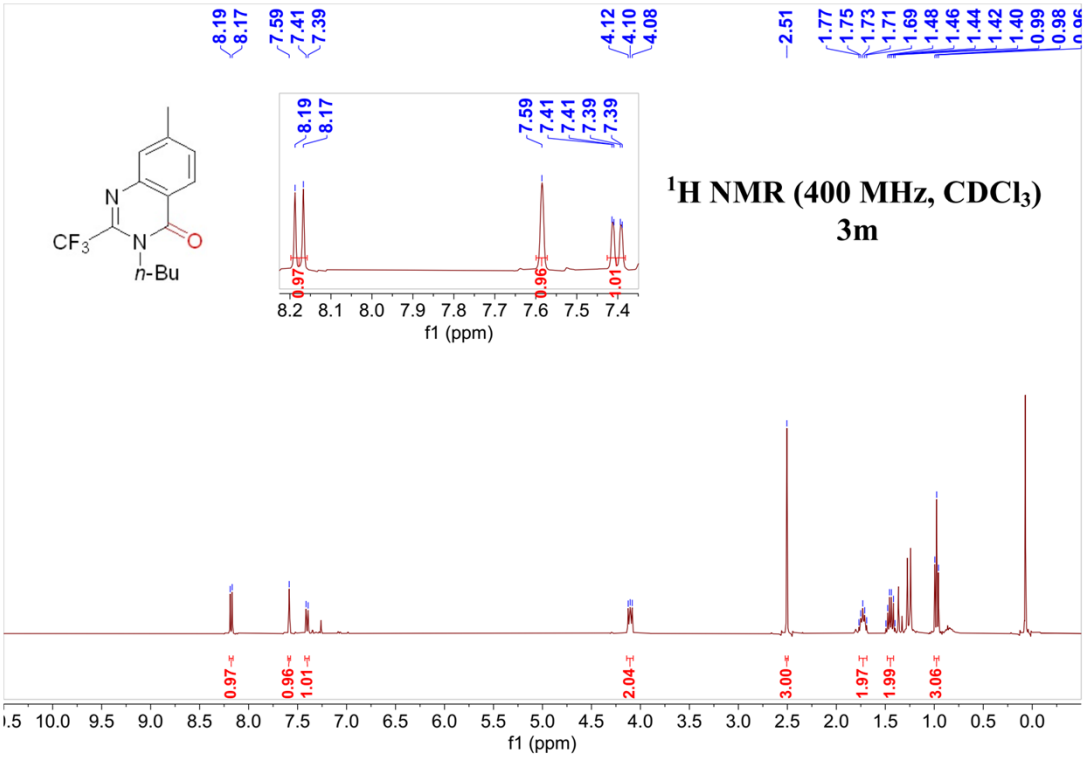
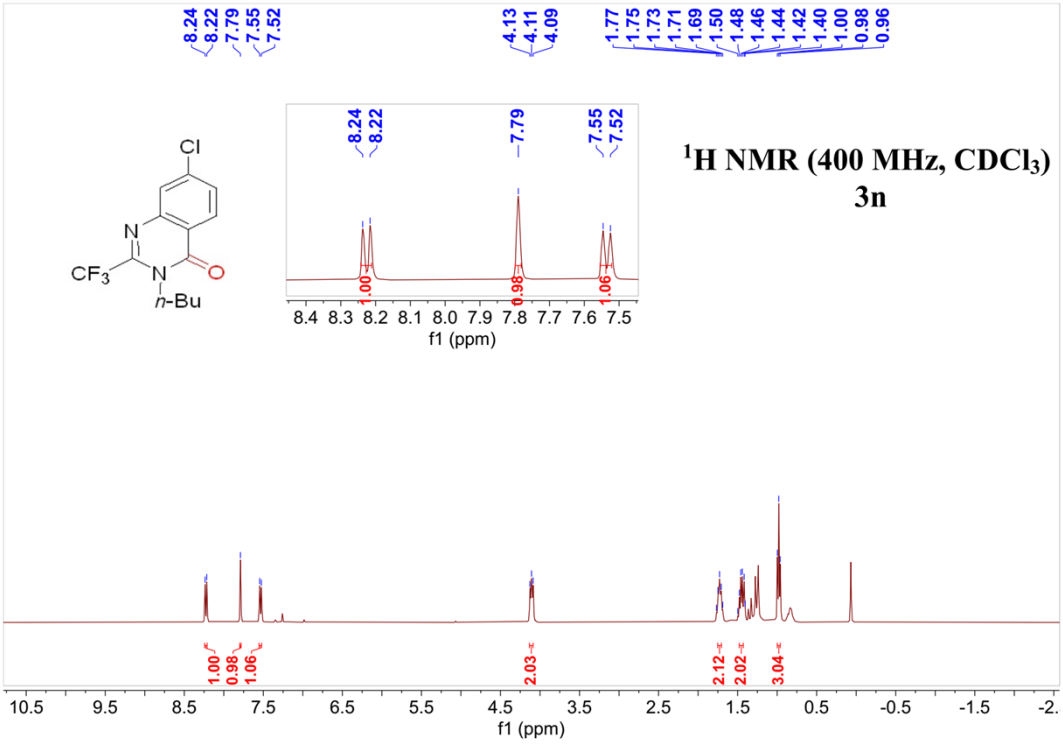
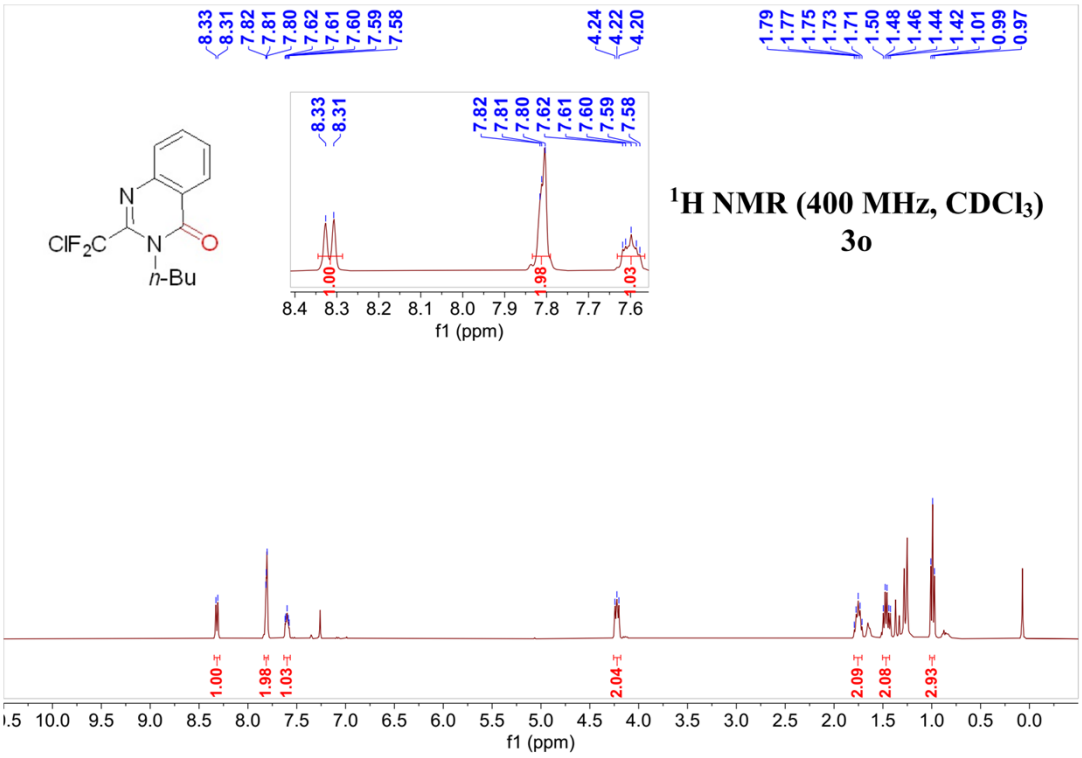
8.0187
7.9975
7.9287
7.9068
4.1672
4.1471
4.1264
1.7826
1.7646
1.7433
1.7244
1.7040
1.5126
1.4941
1.4752
1.4564
1.4378
1.4193
1.0087
0.9905
0.9719
CF3
N
CF3
N
O
n-Bu
1.7826
1.7646
1.7433
1.7244
1.7040
1.5126
1.4941
1.4752
1.4564
1.4378
1.4193
2.06
2.08
1.80 1.70 1.60 1.50 1.40
f1 (ppm)
1H NMR (400 MHz, CDCl3)
3l
0.90
0.93
0.91
1.90
2.06
2.08
3.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0
f1 (ppm)



^{1}H NMR (400 MHz, $CDCl_3$)
3m



^{1}H NMR (400 MHz, $CDCl_3$)
3n


8.33
8.31
7.82
7.81
7.80
7.62
7.61
7.60
7.59
7.58
4.24
4.22
4.20
1.79
1.77
1.75
1.73
1.71
1.50
1.48
1.46
1.44
1.42
1.01
0.99
0.97
N
ClF2C
N
O
n-Bu
1.00
1.98
1.03
8.4 8.3 8.2 8.1 8.0 7.9 7.8 7.7 7.6
f1 (ppm)
1H NMR (400 MHz, CDCl3)
3o
1.00
1.98
1.03
2.04
2.09
2.08
2.93
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)