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# Efficient One-Pot Synthesis of Dihydroquinolinones in Water at Room Temperature

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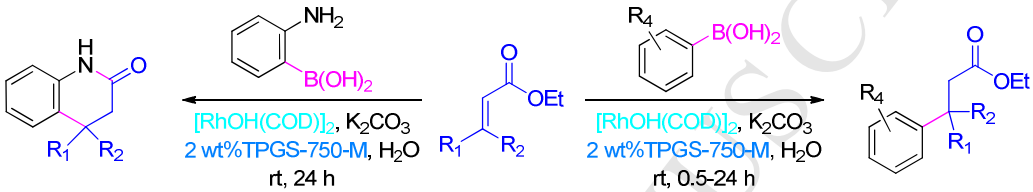
**Abstract:**




A mild and robust one-pot protocol for the Rh-catalyzed 1,4-addition of 2-aminoboronic acid to α,β-unsaturated esters for the efficient synthesis of dihydroquinolinones has been developed. Furthermore the addition of a variety of substituted boronic acids to diverse α,β-unsaturated esters has been investigated. The reactions proceed in water containing catalytic amounts of the commercially available designer surfactant TPGS-750-M (via the formation of nanomicelles). This mild and easy to perform process proceeds at room temperature and tolerates a wide range of functionalities.

Keywords: Rh-catalyzed 1,4-addition; Dihyroquinolinone; Micelles; Green Chemistry

## 1. Introduction

The dihydroquinolinone (dihydroquinolin-2-one) core structure can not only be found in a large number of natural products but also in important drug candidates. Examples shown in Figure 1 include drugs like cilostazol (**1**) (a PDE3 phosphodiesterase inhibitor for the treatment of peripheral vascular disease) and aripiprazole (**2**) (an anti-psychotic used for the treatment of schizophrenia). Natural products like the insecticidal antibiotic Yaequinolone A1 (**3**), isolated from the fungal strain *Penicillium sp.* FKI-2140,[1] and the alkaloid Trigolutesin A (**4**), isolated from *Trigonostemon lutescens*,[2] also contain the dihydroquinolinone core.

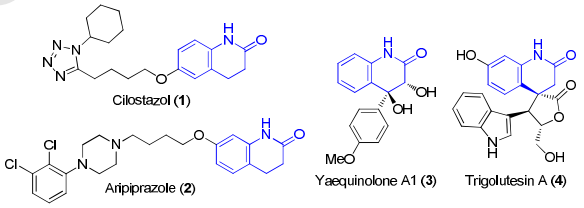



**Figure 1.** Drugs and natural products containing the dihydroquinolinone core.

Methods which allow efficient access to substituted dihydroquinolinones are therefore of significant interest, in particular if such a process allows high functional group tolerance. In addition to the classical Friedel-Crafts cyclization approaches,[3] several other methods for the synthesis of dihydroquinolinones have been published over the last few years, e.g. triflic acid-mediated cyclization of N-benzylcinnamanilides[4] or hypervalent iodine oxidative cyclization of aryl-methoxyamides[5] and various metal catalyzed reactions.[6-8]Alternatively, free radical cyclization of allylsulfonyl substituted N-aryl amide derivatives[9] and radical cyclization of butenyl arylhydroxamate[10] were recently disclosed. However, most of the reported reactions are either multi-step or require reaction conditions which are not suited for the synthesis of dihydroquinolinones containing sensitive functional groups. Similar limitations are described for a one-pot rhodium catalyzed 1,4-addition of

2-aminoarylboronates to α,β-unsaturated esters. The reactions were carried out at reflux in aqueous dioxane using KOH as base to give the corresponding dihydroquinolinones, albeit in moderate yields.[11] Since sensitive substrates may not be stable under such harsh reaction conditions the goal of the present study was to explore a methodology which proceeds under milder reaction conditions. In 2012 Lipshutz et al. reported an asymmetric rhodium catalyzed 1,4-addition of aryl boronic acids to acyclic and cyclic enones in water at room temperature using the nanomicellar system PQS.[12] In this particular publication chiral BINAP was covalently attached to the PQS surfactant and the rhodium catalyst was subsequently inserted to form the first described chiral transition metal catalyst-tethered surfactant. This alternative to classical organic chemistry is called micellar catalysis: Instead of using organic solvents the reaction is conducted in water containing nanomicelles derived from adding catalytic amounts of commercially available and environmentally benign designer surfactants to the water (e.g. PTS or TPGS-750-M).[13] In this case water serves as the macroscopic medium that drives nanoparticle organization due to entropic factors. Depending on size, shape, concentration and nature of the surfactant two plausible reaction mechanisms have been proposed: a.) reactions take place in the inner core of a micelle, b.) a phase-transfer-like mechanism where reactions take place at the interface between nanoparticle and water. With limited levels of surfactant, usually 2 to 5 weight percent, concentrations of reactants are typically high in the inner core or at the interface of the micelle. As a consequence reaction rates at room temperature are comparable to those commonly seen at elevated temperatures in organic solvents.

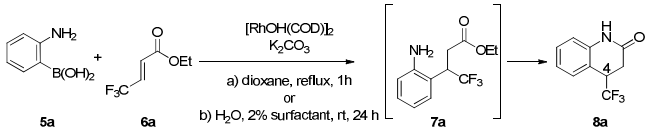
Herein, we applied this methodology of micellar catalysis to the Rh-catalyzed 1,4-addition of 2-aminoboronic acid (**5a**) to different α,β-unsaturated esters. Compared to conventional reaction conditions in organic solvents we noted several additional benefits: The risk of protodeboronation was minimized due to the absence of heating leading to higher yields; the impurity profile improved significantly which in turn simplified purification; and finally cost savings due to easier product isolation and the reduced use of organic solvents.

## 2. Results and discussion

The goal of the present study was to identify a flexible, efficient and green one-pot synthesis of dihydroquinolones (**8**). We were particularly interested in fluorinated substituents or sensitive functional groups because a fundamental strategy for medicinal chemistry is the fluorination of new drug molecules in order to alter activity, selectivity or metabolic stability. Therefore the synthesis of fluorinated dihydroquinolinones is of significant interest to the pharmaceutical industry. To date, only a single publication has disclosed the synthesis of 4-perfluoroalkylquinolinones by reacting 2-alkylperfluororinated anilines with the lithium enolate of acetaldehyde. Unfortunately, the reported yields were poor (less than 15%).[14]

Our initial work focused on the synthesis of fluorinated alkyl substituents at the 4-position of dihydroquinolinones using commercially available 2-aminophenylboronic acid (**5a**) and the trifluoromethyl crotonester **6a** (see Table 1). At first, the 1,4-addition was carried out under conventional reaction conditions using 5 mol% $[RhOH(COD)]_2$ and 2 equivalents of $K_2CO_3$ in dioxane at reflux for 1 hour (Table 1, entry 1). The moderate yield can be rationalized by the competing protodeboronation which occurs at elevated temperatures. Using more than the typically used 2 equivalents of the 2-aminophenylboronic acid (**5a**) did not further improve the yield. In order to minimize the risk of protodeboronation the reaction was carried out at room temperature. Unfortunately, when using the standard reaction conditions at room temperature the desired product could only be isolated in 20% yield. Performing the reaction in water without any surfactant at room temperature (Table 1, entry 2) also afforded the desired product, albeit in poor yields. The same reaction was then investigated under micellar catalysis conditions using 2 mol% of different surfactants in water (Table 1, entries 2-7). The best results were obtained using the commercially available designer surfactant TPGS-750-M (Table 1, entry 7) yielding the desired 4-trifluoromethyl-dihydroquinolinone **8a** in 78% yield. Other non-ionic surfactants (Table 1, entries 3,4,6,7) and the anionic surfactant SDS (Table 1, entry 5) gave inferior results. Interestingly, the intermediate **7a** could be detected in LC-MS during the course of the reaction. However upon completion after 24 hours, **8a** was the only observed and isolated product.

**Table 1.** Impact of different solvents.



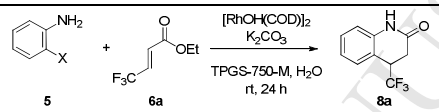

| Entry | Method | Surfactant | Yield [%] |
|---|---|---|---|
| 1 | A | - | 33 (20)* |
| 2 | B | - | 15 |

| | | | |
|---|---|---|---|
| 3 | B | Triton-X-100 | 20 |
| 4 | B | PTS | 23 |
| 5 | B | SDS | 39 |
| 6 | B | TPGS-1000-M | 40 |
| 7 | B | Solutol/Kolliphor | 46 |
| 8 | B | TPGS-750-M | 78 |

Method A: 1 eq **6a**, 2 eq **5a**, 5 mol% $[RhOH(COD)]_2$, 2 eq $K_2CO_3$, dioxane, reflux, 1h; Method B: 1 eq **6a**, 2.00 eq **5a**, 5 mol% $[RhOH(COD)]_2$, 2 eq $K_2CO_3$, 2 wt% surfactant, $H_2O$, rt, 24 h; * reaction at room temperature.

Since some degree of protodeboronation of the 2-aminophenylboronic acid (**5a**) was always observed via LC-MS, the use of the more stable pinacol ester **5b** and the potassium trifluoroborate salt **5c** (see Table 2) were investigated. While the related pinacol ester **5b** gave the desired product in good yield (but still lower compared to the boronic acid **5a**; Table 2, entry 2), the potassium trifluoroborate salt **5c** gave no conversion of starting materials (Table 2, entry 3).

**Table 2.** Impact of the boron species.

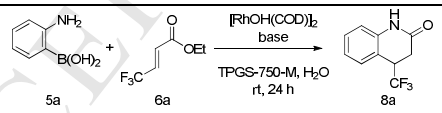



5 6a 8a

| Entry | X | Boron derivative 5 | Yield [%] |
|---|---|---|---|
| 1 | $-B(OH)_2$ | **5a** | 78 |
| 2 | pinacol ester | **5b** | 61 |
| 3 | $-BF_3K$ | **5c** | 0 |

Subsequently the role of the base was investigated. As described in previous publications, the use of more lipophilic bases like TIPSOH/KOH and TMSOK may be beneficial for micellar catalysis due to better penetration of such based into the inner core of a micelle.[15] However for this particular reaction, the influence of the base was minimal and comparable yields using four different bases were observed (Table 3), which would be in agreement with an (at least partly) interfacial mechanism.

**Table 3.** Impact of different bases.

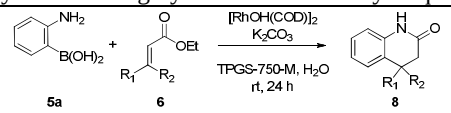



5a 6a 8a

| Entry | Base | Yield [%] |
|---|---|---|
| 1 | $K_2CO_3$ | 78 |
| 2 | TMSOK | 73 |
| 3 | TIPSOH/KOH | 73 |
| 4 | $Et_3N$ | 70 |

Using the now optimized conditions, a series of functionalized 4-dihydroquinolinones were isolated in good to excellent yields using differently substituted α,β-unsaturated esters (see Table 4). Fluorinated compounds such as **8a-c** (Table 4, entries 1-3) were isolated in good yields. The methyl-derivative **8d** and the phenyl-derivative **8e** (Table 4, entries 4 and 5) were obtained with improved yields of 78% and 95% yield compared to the previously published yields of 47% and 58% respectively.[11] Furthermore, products containing quaternary centers could also be formed and the two tricyclic compounds spiro-cyclobutane **8h** and oxetane **8i** were isolated in 29% and 30% yield.

**Table 4.** Synthesis of highly functionalized dihydroquinolinones 8a-e.



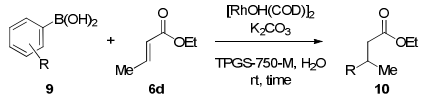

| Entry | $R_1$ | $R_2$ | Product 8 | Yield [%] |
|---|---|---|---|---|
| 1 | $CF_3$ | H | **a** | 78 |
| 2 | $CH_2CF_3$ | H | **b** | 75 |
| 3 | $CHF_2$ | H | **c** | 61 |
| 4 | Me | H | **d** | 95 |
| 5 | Ph | H | **e** | 78 % |
| 6 |  | H | **f** | 83 |
| 7 |  | H | **g** | 44 |
| 8 |  | | **h** | 29 |
| 9 |  | | **i** | 30 |

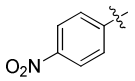
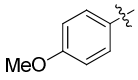
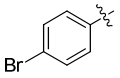
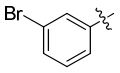
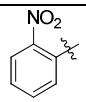
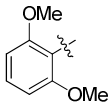
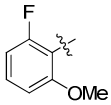
Method: 1 eq **6**, 2 eq **5a**, 5 mol% $[RhOH(COD)]_2$, 2 eq $K_2CO_3$, 2 wt% TPGS-750-M, $H_2O$, rt, 24 h.

After investigating the reaction of 2-aminophenylboronic acid (**5a**) with different Michael acceptors **6** we turned our attention to the synthesis of "open chain" analogues in order to explore the influence of different substituents on the boronic acid. The rhodium catalyzed 1,4-addition of bronic acids to α,β-unsaturated esters is generally a powerful methodology in organic chemistry, documented by the large number of publications since the first disclosure by Hayashi and Miyaura in 1997.[16] However, most described reactions require high temperatures and organic solvents. Interestingly literature examples are usually restricted to para- and meta-substituted aryl boronic acids.[17] In the case of sterically more hindered ortho substituted boronic acids, the corresponding products were only isolated in poor to moderate yields.[18] One reason for the lower yields might be the aforementioned protodeboronation of the boronic acid which occurs faster at elevated temperatures. Again, performing chemistry in micelles would be an attractive alternative since reactions can be performed at room temperature.

Para- and meta-substituted phenylboronic acids **9** added very smoothly and in high yields to crotonester **6d** using our standard reaction conditions. For example ethyl 3-(4-nitrophenyl)butanoate (**10a**) (Table 5, entry 1) could be isolated after 60 min reaction time in 83% yield and ethyl 3-(4-methoxyphenyl)butanoate (**10b**) (Table 5, entry 2) after an even shorter time period of 30 min in 95% yield. The para- and meta- substituted bromo phenylboronic acids **10c** and **10d** were also isolated in high yields (Table 5, entries 3 and 4). We then investigated the more challenging reaction of ortho substituted phenylboronic acids **9f-k** (Table 5, entries 5-10). Boronic acids with functionalities such as ortho-methoxy and ortho-methyl reacted smoothly with crotonester **6d** and the desired products **10f** and **10g** could be isolated in very high yields. However ortho-nitro- and ortho-hydroxyl-groups slowed down the reaction and corresponding products **10h** and **10i** were only detected only in traces (Table 5, entries 7 and 8). The sterically even more hindered ortho-bismethoxy boronic acid **9j** gave the desired product **10j** in 80% yield, whereas the ortho-methoxy fluoride substituted compound **10k** was isolated only in 34% yield (Table 5, entries 9 and 10).

**Table 5.** Impact of substitution on arylboronic acids 9.

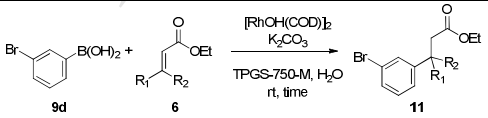


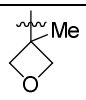

| Entry | R = | 10 | Time [h] | Yield [%] |
|---|---|---|---|---|
| 1 |  | **a** | 1 | 83 |
| 2 |  | **b** | 0.5 | 95 |
| 3 |  | **c** | 0.5 | 80 |
| 4 |  | **d** | 1 | 95 |
| 5 |  | **e** | 1 | 87 |
| 6 |  | **f** | 1 | 95 |
| 7 |  | **g** | 24 | traces |
| 8 |  | **h** | 24 | traces |
| 9 |  | **i** | 1 | 80 |
| 10 |  | **j** | 24 | 34 |

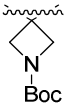
Method: 1 eq **6d**, 2 eq **9**, 5 mol% $[RhOH(COD)]_2$, 2 eq $K_2CO_3$, 2 wt% TPGS-750-M, $H_2O$, rt, time.

Finally we investigated the influence of substitution on the α,β-unsaturated ester moiety **6**. Even sensitive functionalities on the α,β-unsaturated esters such as oxetanes were well tolerated and compounds **11a** and **11b**[19] (Table 6, entries 1, 2) were isolated in 70% and 47% yield respectively. The lower yield of 47% of oxetane **11b** might be rationalized by the more difficult formation of a quaternary center. Similarly the spiro-cyclobutyl compound **11c** was isolated in 43% yield (Table 6, entry 3). A longer reaction time did not improve the yield further. Surprisingly spiro-azetidine compound[20] **11d** was obtained in an excellent 88% yield (Table 6, entry 4).

**Table 6.** Impact of substitution on α,β-unsaturated esters 6.




| Entry | $R_1$ = | $R_2$ = | 11 | Time [h] | Yield [%] |
|---|---|---|---|---|---|
| 1 |  | H | **a** | 1 | 70 |

| | | | | |
|---|---|---|---|---|
| 2 |  | **b** | 2 | 47 |
| 3 |  | **c** | 2 | 43 |
| 4 |  | **d** | 2 | 88 |

Method: 1 eq **6**, 2 eq **9d**, 5 mol% $[RhOH(COD)]_2$, 2 eq $K_2CO_3$, 2 wt% TPGS-750-M, $H_2O$, rt, time.

## 3. Conclusion

In conclusion we were able to develop an efficient and mild green chemistry procedure for the rhodium catalyzed 1,4-addition of 2-aminophenylboronic acid (**5a**) to a series of different α,β-unsaturated esters to yield highly functionalized dihydroquinolinones. The use of catalytic amounts of the surfactant TPGS-750-M allows the use of water as solvent and the performance of the reactions at ambient temperature. In addition, the described method herein was successfully applied to the rhodium catalyzed 1,4-addition of substituted phenylboronic acids to various α,β-unsaturated esters to give products in good to excellent yields. These highly functionalized intermediates are of interest to the medicinal chemist.

## 4. Experimental section

### 4.1 General information

Reactions were performed in a 5 mL vial containing a Teflon coated stirring bar. All commercially available reagents were used without further purification. TPGS (2 wt. %) solution in water was purchased from Aldrich. Column chromatography was performed with an Isco CombiFlash® Companion™ using Grace Reveleris® cartridge (Silica 40 µm). 1H and 13C NMR spectra were measured on a Bruker DRX 500 spectrometer (500 and 125, 470 MHz, respectively) or on a Bruker Avance 600 spectrometer (600 and 151 MHz, respectively). Proton NMR data were recorded as follows: chemical shift in ppm referenced from residual solvent peak (CDCl3, 7.26 ppm), multiplicity (s = singlet; d = doublet; t = triplet; q = quartet; p = pentet; sx = sextet; m = multiplet), coupling constant (Hz), and integration. 13C Chemical shifts were recorded in ppm from the solvent resonance employed as the internal standard (CDCl3, 77.00 ppm). Mass spectral data were acquired on a QExactive (Thermo Scientific).

### 4.2 General procedure

In a 5 mL microwave vial containing α,β-unsaturated ethyl ester (100 mg, 1.00 eq), boronic ester (2.00 eq), potassium carbonate (2.00 eq) and $[RhOH(COD)]_2$ (0.05 eq) was added 2% wt. TPGS-750-M solution in water (3 mL). The mixture was stirred vigorously at ambient temperature for the indicated time. The reaction mixture was then extracted with ethyl acetate. The organic phase was subsequently dried over $MgSO_4$, filtrated and reduced under vacuum. The crude product was purified by column chromatography on silica (eluent: 0-10% methanol in dichloromethane) to yield the desired product.

### 4.3 4-(trifluoromethyl)-3,4-dihydroquinolin-2(1H)-one (8a)

Prepared from ethyl 4,4,4-trifluorobut-2-enoate (100 mg, 0.595 mmol, 1.00 eq) and 2-aminoboronic acid (163 mg, 1.19 mmol, 2.00 eq) according to the general procedure. The reaction mixture was stirred for 24 h. Purification by column chromatography on silica gel (MeOH in $CH_2Cl_2$; 0-10%) afforded the pure product (100 mg, 78%) as white solid. $^1$H NMR (500 MHz, $CDCl_3$): δ 9.05 (s, 1H), 7.32 (td, *J* = 7.7, 1.5 Hz, 1H), 7.29 (d, *J* = 7.5 Hz, 1H), 7.08 (td, *J* = 7.6, 1.2 Hz, 1H), 6.90 (dd, *J* = 8.0, 1.2 Hz, 1H), 3.64 (qdd, *J* = 9.6, 7.1, 2.9 Hz, 1H), 3.00 – 2.89 (m, 2H) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$): δ 168.39, 137.83, 130.38, 130.08, 126.12, 123.43, 116.30, 115.57, 41.15, 30.07 ppm. $^{19}$F NMR (470 MHz, $CDCl_3$): δ -72.51 ppm. HRMS (ESI) m/z $[M + H]^+$ calcd for $[C_{10}H_9F_3NO]^+$ 216.0631, found 216.0630.

### 4.4 4-(2,2,2-trifluoroethyl)-3,4-dihydroquinolin-2(1H)-one (8b)

Prepared from ethyl 5,5,5-trifluoropent-2-enoate (100 mg, 0.549 mmol, 1.00 eq) and 2-aminoboronic acid (150 mg, 1.10 mmol, 2.00 eq) according to the general procedure. The reaction mixture was stirred for 24 h. Purification by column chromatography on silica gel (MeOH in $CH_2Cl_2$; 0-10%) afforded the pure product (95 mg, 75%) as white solid. $^1$H NMR (500 MHz, $CDCl_3$): δ 9.28 (s, 1H), 7.28 – 7.17 (m, 2H), 7.05 (td, *J* = 7.5, 1.2 Hz, 1H), 6.92 – 6.86 (m, 1H), 3.40 (dq, *J* = 9.1, 5.0 Hz, 1H), 2.84 (dd, *J* = 16.4, 5.9 Hz, 1H), 2.71 (dd, *J* = 16.4, 3.6 Hz, 1H), 2.47 – 2.32 (m, 2H) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$): δ 170.43, 136.39, 128.62, 127.67, 126.20, 124.94, 123.67, 116.23, 37.82, 35.80, 30.96 ppm. $^{19}$F NMR (470 MHz, $CDCl_3$): δ -63.33 ppm. HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{11}H_{11}F_3NO$ 230.0787, found 230.0783.

**4.5 4-(Difluoromethyl)-3,4-dihydroquinolin-2(1H)-one (8c)**

Prepared from ethyl 4,4-difluorobut-2-enoate (100 mg, 0.666 mmol, 1.00 eq) and 2-aminoboronic acid (182 mg, 1.33 mmol, 2.00 eq) according to the general procedure. The reaction mixture was stirred for 24 h. Purification by column chromatography on silica gel (MeOH in $CH_2Cl_2$; 0-10%) afforded the pure product (80 mg, 61%) as white solid. $^1$H NMR (500 MHz, $CDCl_3$): δ 9.05 (s, 1H), 7.29 (dt, *J* = 7.5, 1.4 Hz, 1H), 7.27 – 7.22 (m, 1H), 7.06 (td, *J* = 7.5, 1.1 Hz, 1H), 6.88 (dd, *J* = 7.9, 1.2 Hz, 1H), 5.85 (td, *J* = 56.0, 4.3 Hz, 1H), 3.44 – 3.33 (m, 1H), 2.94 – 2.82 (m, 2H) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$): δ 169.41, 137.65, 129.55, 129.46, 123.48, 117.92, 116.26, 116.12, 40.95, 29.64 ppm. $^{19}$F NMR (470 MHz, $CDCl_3$): δ -120.87, -123.60 ppm. HRMS (ESI) m/z $[M + H]^+$ calcd for $[C_{10}H_{10}F_2NO]^+$ 198.0725, found 198.0730.

**4.6 4-Methyl-3,4-dihydroquinolin-2(1H)-one (8d)**

Prepared from ethyl but-2-enoate (100 mg, 0.876 mmol, 1.00 eq) and 2-aminoboronic acid (240 mg, 1.75 mmol, 2.00 eq) according to the general procedure. The reaction mixture was stirred for 24 h. Purification by column chromatography on silica gel (MeOH in $CH_2Cl_2$; 0-10%) afforded the pure product (134 mg, 95%) as white solid. $^1$H NMR (500 MHz, $CDCl_3$): δ 9.10 (s, 1H), 7.22 – 7.14 (m, 2H), 7.02 (td, *J* = 7.5, 1.1 Hz, 1H), 6.88 – 6.81 (m, 1H), 3.14 (h, *J* = 6.7 Hz, 1H), 2.74 (dd, *J* = 16.1, 5.8 Hz, 1H), 2.43 (dd, *J* = 16.1, 7.2 Hz, 1H), 1.32 (d, *J* = 7.0 Hz, 3H) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$): δ 136.44, 128.72, 127.53, 126.52, 123.35, 115.72, 115.69, 38.38, 30.76, 19.80 ppm. HRMS (ESI) m/z $[M + H]^+$ calcd for $[C_{10}H_{12}NO]^+$ 162.0913, found 162.0908.

**4.7 4-Phenyl-3,4-dihydroquinolin-2(1H)-one (8e)**

Prepared from ethyl cinnamate (100 mg, 0.568 mmol, 1.00 eq) and 2-aminoboronic acid (156 mg, 1.14 mmol, 2.00 eq) according to the general procedure. The reaction mixture was stirred for 24 h. Purification by column chromatography on silica gel (MeOH in $CH_2Cl_2$; 0-10%) afforded the pure product (99 mg, 78%) as white solid. $^1$H NMR (500 MHz, $CDCl_3$): δ 8.92 (s, 1H), 7.33 (dd, *J* = 8.2, 6.7 Hz, 2H), 7.32 – 7.23 (m, 1H), 7.24 – 7.15 (m, 3H), 6.96 (td, *J* = 7.5, 1.1 Hz, 1H), 6.94 – 6.85 (m, 2H), 4.30 (t, *J* = 7.5 Hz, 1H), 3.00 – 2.87 (m, 2H) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$): δ 170.87, 141.43, 136.99, 128.89 (2), 128.35, 127.99, 127.79 (2), 127.21, 126.64, 123.35, 115.68, 41.99, 38.40 ppm. HRMS (ESI) m/z $[M + H]^+$ calcd for $[C_{15}H_{14}NO]^+$ 224.1070, found 224.1063.

**4.8 4-(3-Methyloxetan-3-yl)-3,4-dihydroquinolin-2(1H)-one (8f)**

Prepared from ethyl 3-(3-methyloxetan-3-yl)acrylate (100 mg, 0.588 mmol, 1.00 eq) and 2-aminoboronic acid (161 mg, 1.18 mmol, 2.00 eq) according to the general procedure. The reaction mixture was stirred for 24 h. Purification by column chromatography on silica gel (MeOH in $CH_2Cl_2$; 0-10%) afforded the pure product (106 mg, 83%) as white solid. $^1$H NMR (500 MHz, $CDCl_3$): δ 9.15 (s, 1H), 7.22 (ddd, *J* = 8.0, 6.5, 2.3 Hz, 1H), 7.06 – 6.97 (m, 2H), 6.89 – 6.83 (m, 1H), 4.83 (d, *J* = 5.9 Hz, 1H), 4.63 (d, *J* = 5.8 Hz, 1H), 4.41 (d, *J* = 5.7 Hz, 1H), 4.29 (d, *J* = 6.0 Hz, 1H), 3.57 (dd, *J* = 7.3, 4.7 Hz, 1H), 2.70 (dd, *J* = 16.6, 7.3 Hz, 1H), 2.40 (dd, *J* = 16.7, 4.7 Hz, 1H), 1.32 (s, 3H) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$): δ 171.45, 137.42, 128.34, 128.06, 123.40, 122.79, 116.16, 82.07, 81.95, 43.56, 42.78, 31.98, 19.10 ppm. HRMS (ESI) m/z $[M + H]^+$ calcd for $[C_{13}H_{16}NO_2]^+$ 218.1176, found 218.1173.

**4.9 4-Cyclobutyl-3,4-dihydroquinolin-2(1H)-one (8g)**

Prepared from ethyl 3-cyclobutylacrylate (100 mg, 0.648 mmol, 1.00 eq) and 2-aminoboronic acid (178 mg, 1.30 mmol, 2.00 eq) according to the general procedure. The reaction mixture was stirred for 24 h. Purification by column chromatography on silica gel (MeOH in $CH_2Cl_2$; 0-10%) afforded the pure product (58 mg, 44%) as white solid. $^1$H NMR (500 MHz, $CDCl_3$): δ 8.97 (s, 1H), 7.21 – 7.10 (m, 2H), 6.98 (td, *J* = 7.5, 1.1 Hz, 1H), 6.83 (d, *J* = 7.8 Hz, 1H), 2.84 – 2.80 (m, 1H), 2.68 (dd, *J* = 16.2, 6.2 Hz, 1H), 2.53 – 2.40 (m, 2H), 2.18 – 2.07 (m, 1H), 1.92 – 1.68 (m, 5H) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$): δ 171.56, 136.37, 127.98, 127.54, 125.99, 122.86, 115.74, 42.71, 38.76, 33.68, 27.24, 26.70, 17.56 ppm. HRMS (ESI) m/z $[M + H]^+$ calcd for $[C_{13}H_{16}NO]^+$ 202.1226, found 202.1224.

**4.10 1'H-Spiro[cyclobutane-1,4'-quinolin]-2'(3'H)-one (8h)**

Prepared from ethyl 2-cyclobutylideneacetate (100 mg, 0.713 mmol, 1.00 eq) and 2-aminoboronic acid (196 mg, 1.43 mmol, 2.00 eq) according to the general procedure. The reaction mixture was stirred for 24 h. Purification by column chromatography on silica gel (MeOH in $CH_2Cl_2$; 0-10%) afforded the pure product (39 mg, 29%) as white solid. $^1$H NMR (500 MHz, $CDCl_3$): δ 8.66 (d, *J* = 68.4 Hz, 1H), 7.47 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.19 (td, *J* = 7.6, 1.5 Hz, 1H), 7.14 – 7.07 (m, 1H), 6.82 (dd, *J* = 8.1, 3.7 Hz, 1H), 2.77 (s, 2H), 2.40 – 2.28 (m, 2H), 2.16 – 2.06 (m, 3H), 2.09 – 1.94 (m, 1H) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$): δ 170.36, 135.68, 131.03, 127.48, 124.21, 123.55, 115.75, 31.82, 27.39 (2), 14.91 (2) ppm. HRMS (ESI) m/z $[M + H]^+$ calcd for $[C_{12}H_{14}NO]^+$ 188.1070, found 188.1065.

**4.11 1'H-Spiro[oxetane-3,4'-quinolin]-2'(3'H)-one (8i)**

Prepared from ethyl 2-(oxetan-3-ylidene)acetate (100 mg, 0.703 mmol, 1.00 eq) and 2-aminoboronic acid (193 mg, 1.40 mmol, 2.00 eq) according to the general procedure. The reaction mixture was stirred for 24 h. Purification by column chromatography on silica gel (MeOH in $CH_2Cl_2$; 0-10%) afforded the pure product (40 mg, 30%) as white solid. $^1$H NMR (500 MHz, $CDCl_3$): δ 8.93 (s, 1H), 7.70 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.31 – 7.24 (m, 1H), 7.18 (dd, *J* = 7.9, 6.8 Hz, 1H), 6.87 (dd, *J* = 7.7, 1.2 Hz, 1H), 4.88 (d, *J* = 6.3 Hz, 2H), 4.70 (d, *J* = 6.2 Hz, 2H), 3.06 (s, 2H) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$): δ 169.61, 135.98, 128.74 (2), 125.66, 124.95, 124.08, 116.10, 81.17, 41.24, 40.93 ppm. HRMS (ESI) m/z $[M + H]^+$ calcd for $[C_{11}H_{12}NO]^+$ 190.0863, found 190.0862

**4.12 Ethyl 3-(4-nitrophenyl)butanoate (10a)**

Prepared from ethyl but-2-enoate (100 mg, 0.876 mmol, 1.00 eq) and (4-nitrophenyl)boronic acid (292 mg, 1.75 mmol, 2.00 eq) according to the general procedure. The reaction mixture was stirred for 1 h. Purification by column chromatography on silica gel (MeOH in $CH_2Cl_2$; 0-10%) afforded the pure product (173 mg, 83%) as yellow oil. $^1$H NMR (500 MHz, $CDCl_3$): δ 8.19 – 8.11 (m, 2H), 7.41 – 7.36 (m, 2H), 4.06 (qd, *J* = 7.1, 2.8 Hz, 2H), 3.40 (h, *J* = 7.2 Hz, 1H), 2.61 (dd, *J* = 7.6, 1.9 Hz, 2H), 1.33 (d, *J* = 7.0 Hz, 3H), 1.17 (t, *J* = 7.1 Hz, 3H) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$): δ 171.53, 153.32, 146.62, 127.71 (2), 123.78 (2), 60.52, 42.25, 36.39, 21.64, 14.12 ppm. HRMS (ESI) m/z $[M + H]^+$ calcd for $[C_{12}H_{16}NO_4]^+$ 238.1074, found 238.1072.

**4.13 Ethyl 3-(4-methoxyphenyl)butanoate (10b)**

Prepared from ethyl but-2-enoate (100 mg, 0.876 mmol, 1.00 eq) and (4-methoxyphenyl)boronic acid (266 mg, 1.75 mmol, 2.00 eq) according to the general procedure. The reaction mixture was stirred for 30 min. Purification by column chromatography on silica gel (MeOH in $CH_2Cl_2$; 0-10%) afforded the pure product (178 mg, 91%) as yellow oil. $^1$H NMR (500 MHz, $CDCl_3$): δ 7.17 – 7.10 (m, 2H), 6.87 – 6.80 (m, 2H), 4.07 (qd, *J* = 7.2, 1.1 Hz, 2H), 3.78 (s, 3H), 3.23 (h, *J* = 7.2 Hz, 1H), 2.53 (qd, *J* = 14.9, 7.6 Hz, 2H), 1.27 (d, *J* = 7.0 Hz, 3H), 1.18 (t, *J* = 7.1 Hz, 3H) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$): δ 172.45, 158.06, 137.87, 127.66 (2), 113.81 (2), 60.22, 55.24, 43.27, 35.74, 21.98, 14.20. HRMS (ESI) m/z $[M + H]^+$ calcd for $[C_{13}H_{19}O_3]^+$ 223.1329, found 223.1326.

**4.14 Ethyl 3-(4-bromophenyl)butanoate (10c)**

Prepared from ethyl but-2-enoate (100 mg, 0.876 mmol, 1.00 eq) and (4-bromophenyl)boronic acid (352 mg, 1.75 mmol, 2.00 eq) according to the general procedure. The reaction mixture was stirred for 2 h. Purification by column chromatography

on silica gel (MeOH in $CH_2Cl_2$; 0-10%) afforded the pure product (189 mg, 80%) as yellow oil. $^1$H NMR (500 MHz, $CDCl_3$): δ 7.43 – 7.38 (m, 2H), 7.11 – 7.08 (m, 2H), 4.07 (qd, *J* = 7.1, 1.3 Hz, 2H), 3.24 (h, *J* = 7.2 Hz, 1H), 2.59 – 2.49 (m, 2H), 1.27 (d, *J* = 7.0 Hz, 3H), 1.18 (t, *J* = 7.1 Hz, 3H) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$): δ 172.01, 144.66, 131.49 (2), 128.54 (2), 120.01, 60.33, 42.72, 35.98, 21.75, 14.14 ppm. HRMS (ESI) m/z $[M + H]^+$ calcd for $[C_{12}H_{16}BrO_2]^+$ 271.0328, found 271.0092.

**4.15 Ethyl 3-(3-bromophenyl)butanoate (10d)**

Prepared from ethyl but-2-enoate (100 mg, 0.876 mmol, 1.00 eq) and (3-bromophenyl)boronic acid (352 mg, 1.75 mmol, 2.00 eq) according to the general procedure. The reaction mixture was stirred for 1 h. Purification by column chromatography on silica gel (MeOH in $CH_2Cl_2$; 0-10%) afforded the pure product (228 mg, 96%) as yellow oil. $^1$H NMR (500 MHz, $CDCl_3$): δ 7.36 (q, *J* = 1.3 Hz, 1H), 7.35 – 7.30 (m, 1H), 7.19 – 7.13 (m, 2H), 4.08 (q, *J* = 7.1 Hz, 2H), 3.25 (sx, *J* = 7.2 Hz, 1H), 2.61 – 2.49 (m, 2H), 1.29 (d, *J* = 7.0 Hz, 3H), 1.19 (t, *J* = 7.1 Hz, 3H) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$): δ 171.98, 148.08, 130.07, 129.97, 129.52, 125.54, 122.52, 60.40, 42.72, 36.28, 21.71, 14.18 ppm. HRMS (ESI) m/z $[M + H]^+$ calcd for $[C_{12}H_{16}BrO_2]^+$ 273.0328, found 273.0324.

**4.16 Ethyl 3-(2-methoxyphenyl)butanoate (10e)**

Prepared from ethyl but-2-enoate (100 mg, 0.876 mmol, 1.00 eq) and (2-methoxyphenyl)boronic acid (266 mg, 1.75 mmol, 2.00 eq) according to the general procedure. The reaction mixture was stirred for 1 h. Purification by column chromatography on silica gel (MeOH in $CH_2Cl_2$; 0-10%) afforded the pure product (169 mg, 87%) as yellow oil. $^1$H NMR (500 MHz, $CDCl_3$): δ 7.21 – 7.15 (m, 2H), 6.91 (dt, *J* = 7.5, 1.1 Hz, 1H), 6.85 (dd, *J* = 8.1, 1.1 Hz, 1H), 4.09 (q, *J* = 7.1 Hz, 2H), 3.83 (s, 3H), 3.69 – 3.60 (m, 1H), 2.68 (dd, *J* = 15.0, 6.0 Hz, 1H), 2.50 (dd, *J* = 15.0, 8.9 Hz, 1H), 1.27 (d, *J* = 7.0 Hz, 3H), 1.20 (t, *J* = 7.1 Hz, 3H) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$): δ 172.85, 156.91, 133.81, 127.21, 126.95, 120.51, 110.53, 60.12, 55.30, 41.28, 30.20, 20.07, 14.22 ppm. HRMS (ESI) m/z $[M + H]^+$ calcd for $[C_{13}H_{19}O_3]^+$ 223.1329, found 223.1324.

**4.17 Ethyl 3-(o-tolyl)butanoate (10f)**

Prepared from ethyl but-2-enoate (100 mg, 0.876 mmol, 1.00 eq) and o-tolylboronic acid (238 mg, 1.75 mmol, 2.00 eq) according to the general procedure. The reaction mixture was stirred for 1 h. Purification by column chromatography on silica gel (MeOH in $CH_2Cl_2$; 0-10%) afforded the pure product (175 mg, 97%) as yellow oil. $^1$H NMR (500 MHz, $CDCl_3$): δ 7.22 – 7.06 (m, 4H), 4.09 (q, *J* = 7.2 Hz, 2H), 3.58 – 3.51 (m, 1H), 2.63 (dd, *J* = 15.2, 6.6 Hz, 1H), 2.53 (dd, *J* = 15.2, 8.5 Hz, 1H), 2.38 (s, 3H), 1.26 (d, *J* = 6.9 Hz, 3H), 1.19 (t, *J* = 7.1 Hz, 3H) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$): δ 172.52, 143.92, 135.27, 130.40, 126.25, 126.03, 125.05, 60.26, 42.19, 31.49, 21.28, 19.43, 14.17 ppm. HRMS (ESI) m/z $[M + H]^+$ calcd for $[C_{13}H_{19}O_2]^+$ 207.1380, found 207.1377.

**4.18 Ethyl 3-(2,6-dimethoxyphenyl)butanoate (10i)**

Prepared from ethyl but-2-enoate (100 mg, 0.876 mmol, 1.00 eq) and (2,6-dimethoxyphenyl)boronic acid (319 mg, 1.75 mmol, 2.00 eq) according to the general procedure. The reaction mixture was stirred for 1 h. Purification by column chromatography on silica gel (MeOH in $CH_2Cl_2$; 0-10%) afforded the pure product (176 mg, 80%) as yellow oil. $^1$H NMR (500 MHz, $CDCl_3$): δ 7.11 (t, *J* = 8.3 Hz, 1H), 6.52 (d, *J* = 8.3 Hz, 2H), 4.06 (q, *J* = 7.1 Hz, 2H), 4.02 – 3.93 (m, 1H), 3.80 (s, 6H), 2.82 (dd, *J* = 15.1, 8.6 Hz, 1H), 2.72 (dd, *J* = 15.1, 6.6 Hz, 1H), 1.29 (d, *J* = 7.1 Hz, 3H), 1.17 (t, *J* = 7.1 Hz, 3H) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$): δ 173.60, 158.56 (2), 127.16, 121.51, 104.29 (2), 59.87, 55.69 (2), 39.59, 26.30, 18.66, 14.20 ppm. HRMS (ESI) m/z $[M + H]^+$ calcd for $[C_{14}H_{21}O_4]^+$ 253.1434, found 253.1428.

**4.19 Ethyl 3-(2-fluoro-6-methoxyphenyl)butanoate (10j)**

Prepared from ethyl but-2-enoate (100 mg, 0.876 mmol, 1.00 eq) and (2-fluoro-6-methoxyphenyl)boronic acid (298 mg, 1.75 mmol, 2.00 eq) according to the general procedure. The reaction mixture was stirred for 24 h. Purification by column chromatography on silica gel (MeOH in $CH_2Cl_2$; 0-10%) afforded the pure product (71 mg, 37%) as yellow oil. $^1$H NMR (500 MHz, $CDCl_3$): δ 7.10 (td, *J* = 8.3, 6.4 Hz, 1H), 6.64 (td, *J* = 8.7, 8.2, 1.2 Hz, 2H), 4.06 (q, *J* = 7.1 Hz, 2H), 3.87 – 3.81

(m, 1H), 3.82 (s, 3H), 2.76 – 2.72 (m, 2H), 1.32 (d, *J* = 6.9 Hz, 3H), 1.16 (t, *J* = 7.1 Hz, 3H) ppm. $^{19}$F NMR (470 MHz, $CDCl_3$): δ -115.04 ppm. $^{13}$C NMR (125 MHz, $CDCl_3$): δ 172.86, 161.85, 158.67, 127.47, 120.73, 108.36, 106.54, 60.08, 55.85, 39.75, 26.34, 19.09, 14.13 ppm. HRMS (ESI) m/z $[M + H]^+$ calcd for $[C_{13}H_{18}FO_3]^+$ 241.1234, found 241.1233.

#### 4.20 Ethyl 3-(3-bromophenyl)-3-(3-methyloxetan-3-yl)propanoate (11a)

Prepared from ethyl 3-(3-methyloxetan-3-yl)acrylate (100 mg, 0.588 mmol, 1.00 eq) and (3-bromophenyl)boronic acid (236 mg, 1.18 mmol, 2.00 eq) according to the general procedure. The reaction mixture was stirred for 2 h. Purification by column chromatography on silica gel (MeOH in $CH_2Cl_2$; 0-10%) afforded the pure product (135 mg, 70%) as yellow oil. $^1$H NMR (600 MHz, $CDCl_3$): δ 7.36 (ddd, *J* = 7.9, 2.0, 1.1 Hz, 1H), 7.32 (t, *J* = 1.9 Hz, 1H), 7.16 (t, *J* = 7.8 Hz, 1H), 7.11 (dt, *J* = 7.7, 1.4 Hz, 1H), 4.62 (dd, *J* = 10.2, 5.9 Hz, 2H), 4.32 (d, *J* = 5.8 Hz, 1H), 4.08 (d, *J* = 6.1 Hz, 1H), 4.00 (qq, *J* = 7.3, 3.7 Hz, 2H), 3.58 (dd, *J* = 10.9, 4.5 Hz, 1H), 2.73 (dd, *J* = 15.6, 10.9 Hz, 1H), 2.58 (dd, *J* = 15.6, 4.5 Hz, 1H), 1.29 (s, 3H), 1.10 (t, *J* = 7.1 Hz, 3H) ppm. $^{13}$C NMR (151 MHz, $CDCl_3$): δ 171.62, 141.96, 131.26, 130.18, 129.89, 127.03, 122.44, 81.56, 81.15, 60.63, 47.97, 42.50, 35.01, 20.64, 14.00 ppm. HRMS (ESI) m/z $[M + H]^+$ calcd for $[C_{15}H_{20}BrO_3]^+$ 327.0590, found 327.0583.

#### 4.21 Ethyl 2-(3-(3-bromophenyl)oxetan-3-yl)acetate (11b)

Prepared from ethyl 2-(oxetan-3-ylidene)acetate (100 mg, 0.703 mmol, 1.00 eq) and (3-bromophenyl)boronic acid (283 mg, 1.41 mmol, 2.00 eq) according to the general procedure. The reaction mixture was stirred for 2 h. Purification by column chromatography on silica gel (MeOH in $CH_2Cl_2$; 0-10%) afforded the pure product (99 mg, 47%) as yellow oil. $^1$H NMR (500 MHz, $CDCl_3$): δ 7.38 (dt, *J* = 8.0, 1.5 Hz, 1H), 7.31 (t, *J* = 1.9 Hz, 1H), 7.21 (t, *J* = 7.7 Hz, 1H), 7.13 – 7.08 (m, 1H), 4.97 (d, *J* = 6.1 Hz, 2H), 4.84 (d, *J* = 6.5 Hz, 2H), 4.07 – 3.98 (m, 2H), 3.10 (s, 2H), 1.13 (t, *J* = 7.1 Hz, 3H) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$): δ 170.32, 145.94, 130.05, 129.94, 129.12, 124.54, 122.61, 81.51 (2), 60.57, 45.23, 44.61, 14.05 ppm. HRMS (ESI) m/z $[M + H]^+$ calcd for $[C_{13}H_{16}BrO_3]^+$ 299.0277, found 299.0272.

#### 4.22 Ethyl 2-(1-(3-bromophenyl)cyclobutyl)acetate (11c)

Prepared from ethyl 2-cyclobutylideneacetate (100 mg, 0.713 mmol, 1.00 eq) and (3-bromophenyl)boronic acid (287 mg, 1.43 mmol, 2.00 eq) according to the general procedure. The reaction mixture was stirred for 2 h. Purification by column chromatography on silica gel (MeOH in $CH_2Cl_2$; 0-10%) afforded the pure product (90 mg, 43%) as yellow oil. $^1$H NMR (500 MHz, $CDCl_3$): δ 7.31 – 7.29 (m, 2H), 7.18 – 7.13 (m, 1H), 7.10 (dt, *J* = 7.7, 1.5 Hz, 1H), 3.95 (q, *J* = 7.1 Hz, 2H), 2.76 (s, 2H), 2.46 – 2.34 (m, 4H), 2.09 (dp, *J* = 11.5, 8.7 Hz, 1H), 1.91 – 1.82 (m, 1H), 1.08 (t, *J* = 7.2 Hz, 3H) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$): δ 171.20, 151.12, 129.57, 129.05, 128.82, 124.45, 122.15, 60.04, 46.50, 44.81, 32.91 (2), 15.81, 14.06 ppm. HRMS (ESI) m/z $[M + H]^+$ calcd for $[C_{14}H_{18}BrO_2]^+$ 297.0485, found 297.1539.

#### 4.23 tert-Butyl 3-(3-bromophenyl)-3-(2-ethoxy-2-oxoethyl)azetidine-1-carboxylate (11d)

Prepared from tert-butyl 3-(2-ethoxy-2-oxoethylidene)azetidine-1-carboxylate (100 mg, 0.414 mmol, 1.00 eq) and (3-bromophenyl)boronic acid (166 mg, 0.829 mmol, 2.00 eq) according to the general procedure. The reaction mixture was stirred for 2 h. Purification by column chromatography on silica gel (MeOH in $CH_2Cl_2$; 0-10%) afforded the pure product (146 mg, 88%) as yellow oil. $^1$H NMR (500 MHz, $CDCl_3$): δ 7.40 – 7.36 (m, 1H), 7.34 (t, *J* = 1.9 Hz, 1H), 7.21 (t, *J* = 7.8 Hz, 1H), 7.14 (dt, *J* = 7.8, 1.4 Hz, 1H), 4.23 (d, *J* = 8.6 Hz, 2H), 4.18 (d, *J* = 8.8 Hz, 2H), 4.02 (q, *J* = 7.1 Hz, 2H), 2.95 (s, 2H), 1.44 (s, 9H), 1.14 (t, *J* = 7.2 Hz, 3H) ppm. $^{13}$C NMR (125 MHz, $CDCl_3$): δ 170.09, 156.28, 146.21, 130.03, 129.97, 129.38, 124.79, 122.56, 79.83, 60.59 (2), 45.51 (2), 39.46, 28.33 (3), 14.04 ppm. HRMS (ESI) m/z $[M + H]^+$ calcd for $[C_{18}H_{25}BrNO_4]^+$ 398.0961, found 398.0951.

## Acknowledgements

We thank Monika Franck, Johanna Klee and Tanja Lindner for supporting chemical synthesis, Gisela Backfisch for support in measuring HRMS, Claudia Krack, Sarah Zauchner, Manuela Diehl, Renate Kostiza and Christian Müller for analytical support.

## Supplementary data

Copies of $^{1}H$ $^{19}F$ and $^{13}C$ NMR spectra for compound **8a-i**, **10a-f**, **10i**, **10j** and **11a-d**. Supplementary data related to this article can be found at (insert link).

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# Efficient One-Pot Synthesis of Dihydroquinolinones in Water at Room Temperature

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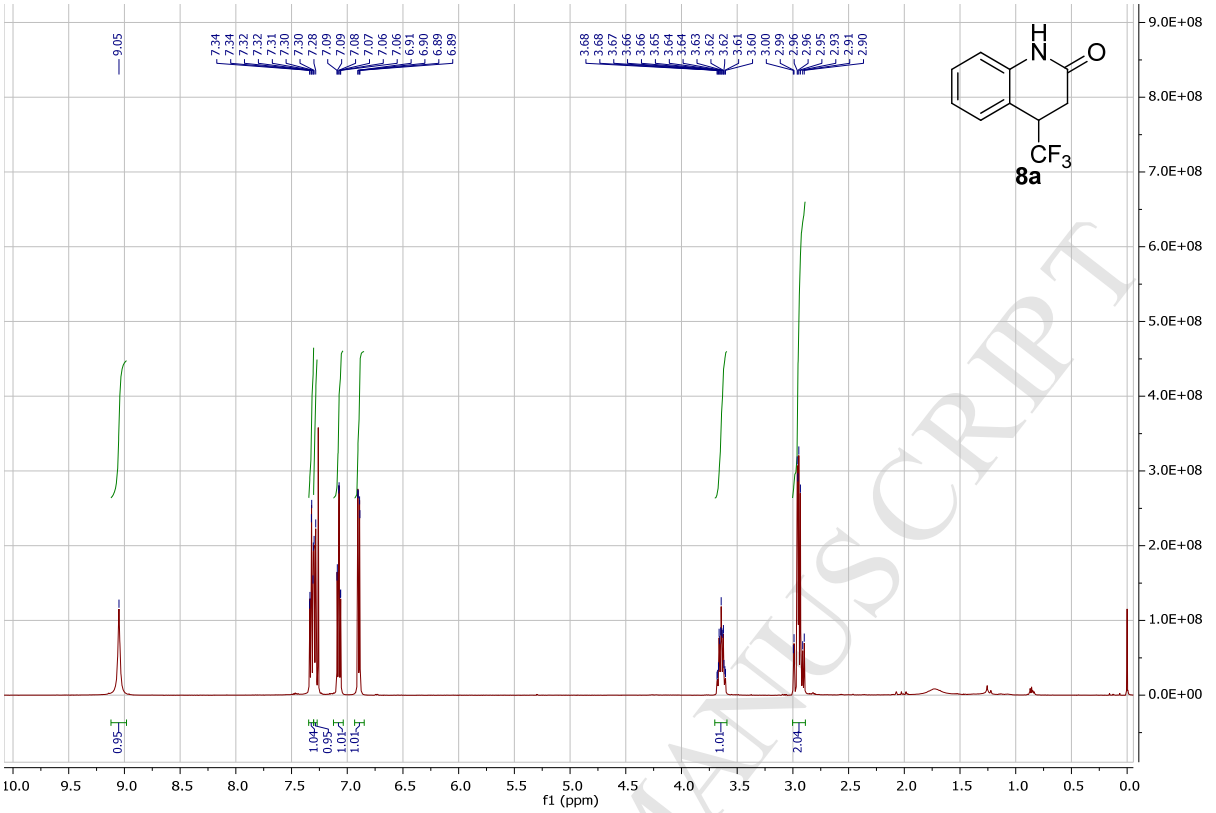
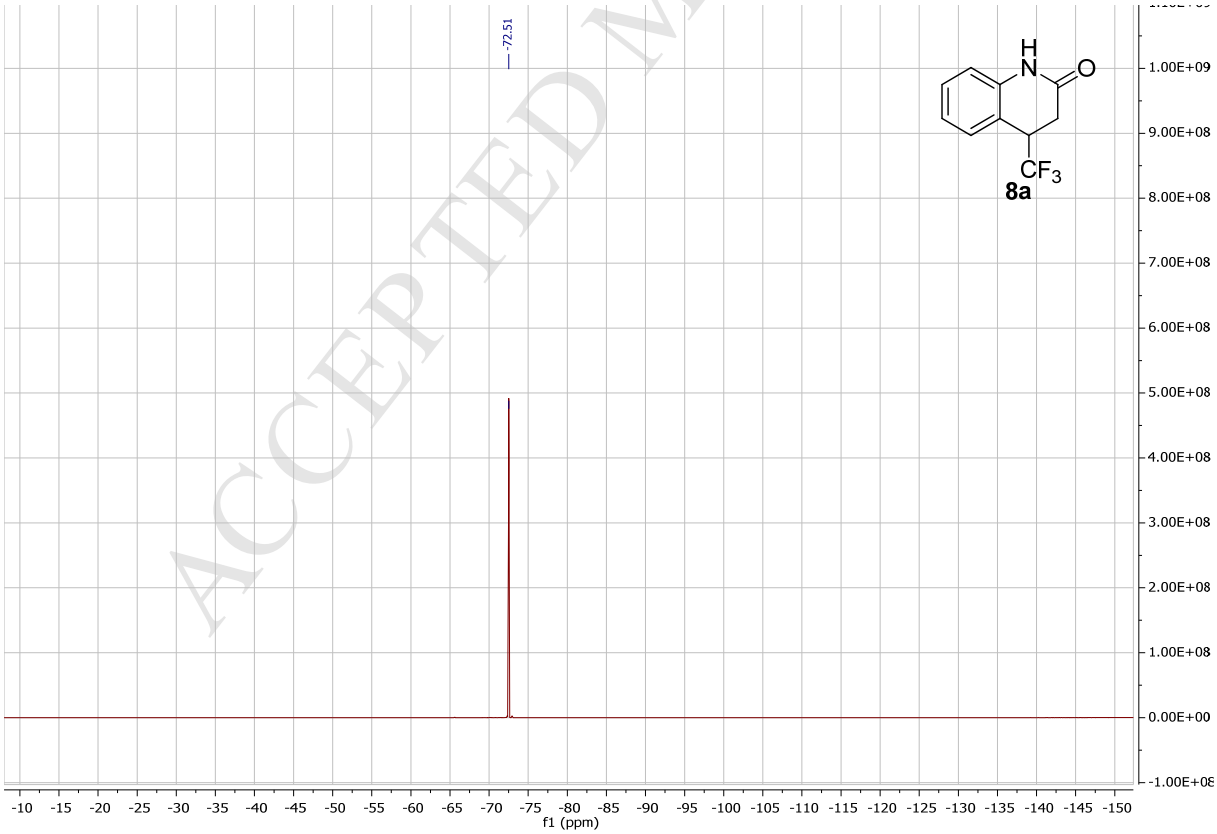
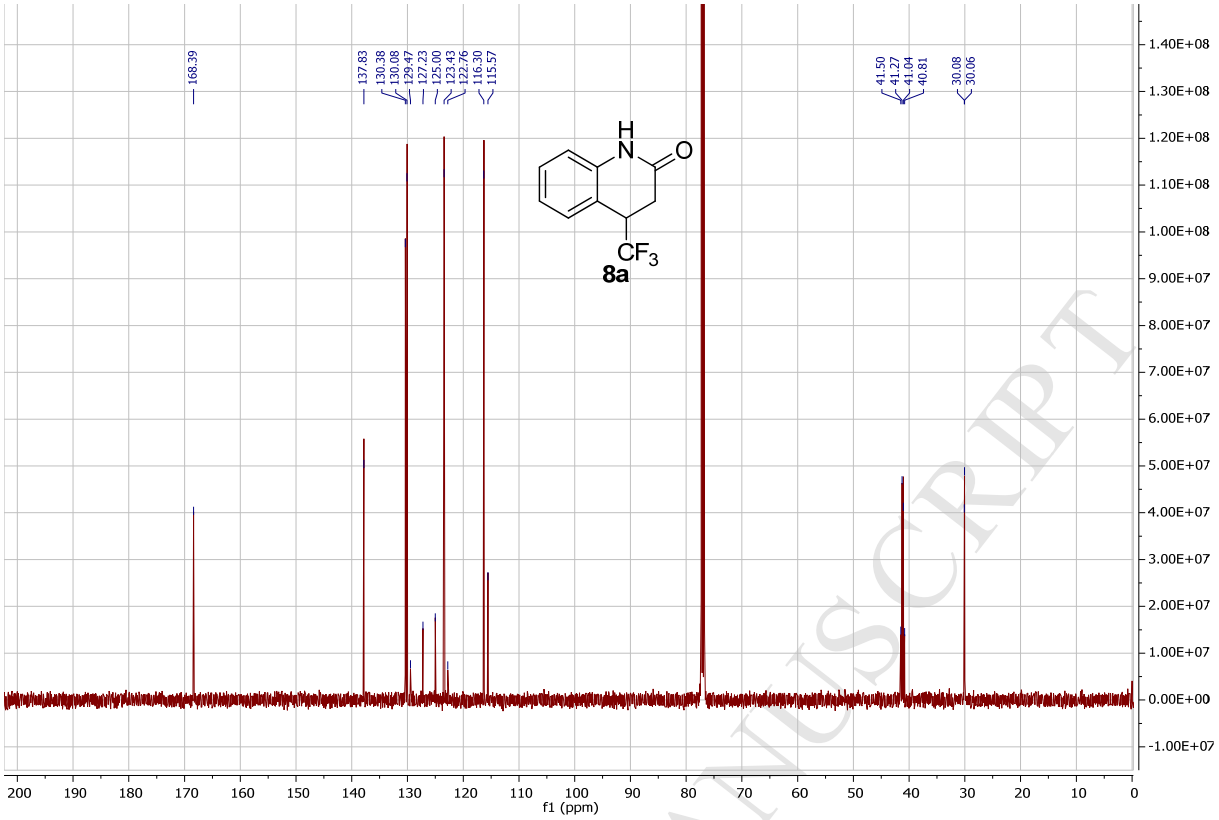
## Supplementary Data

**4-(trifluoromethyl)-3,4-dihydroquinolin-2(1H)-one (8a)**



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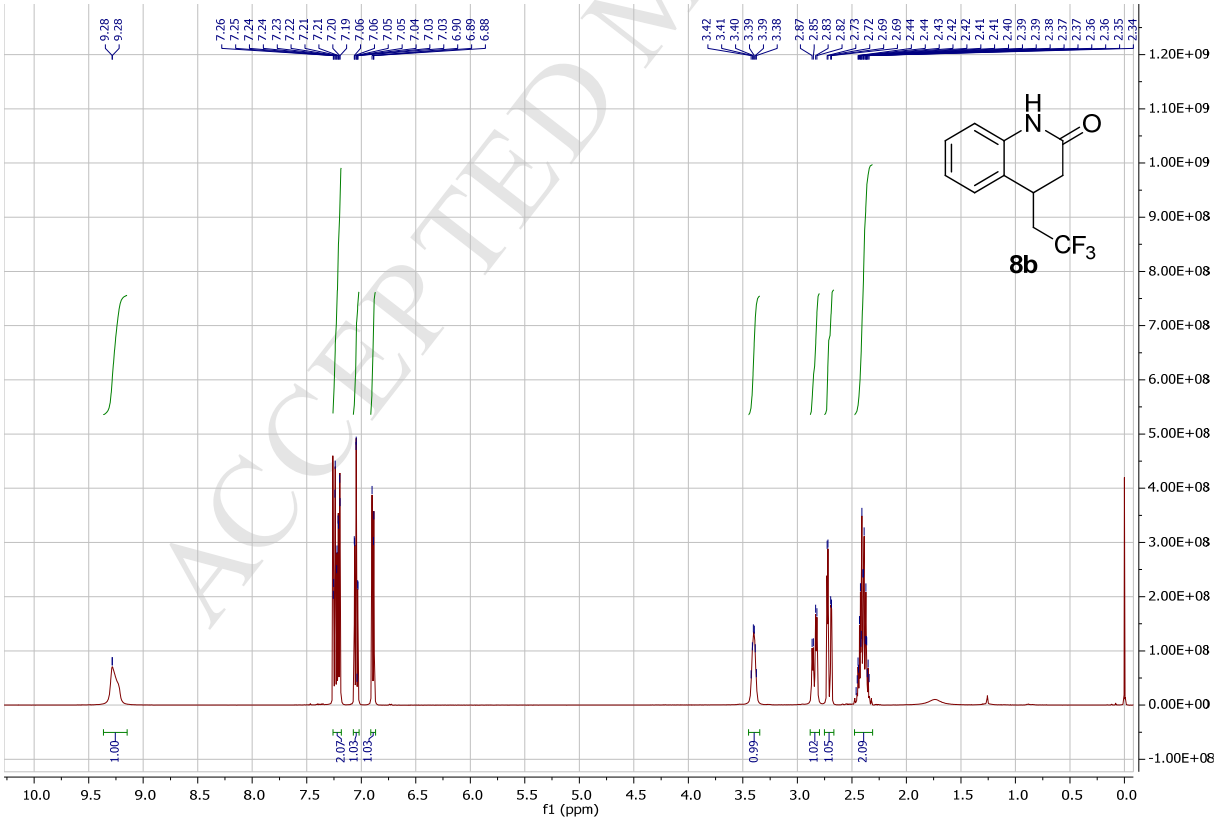
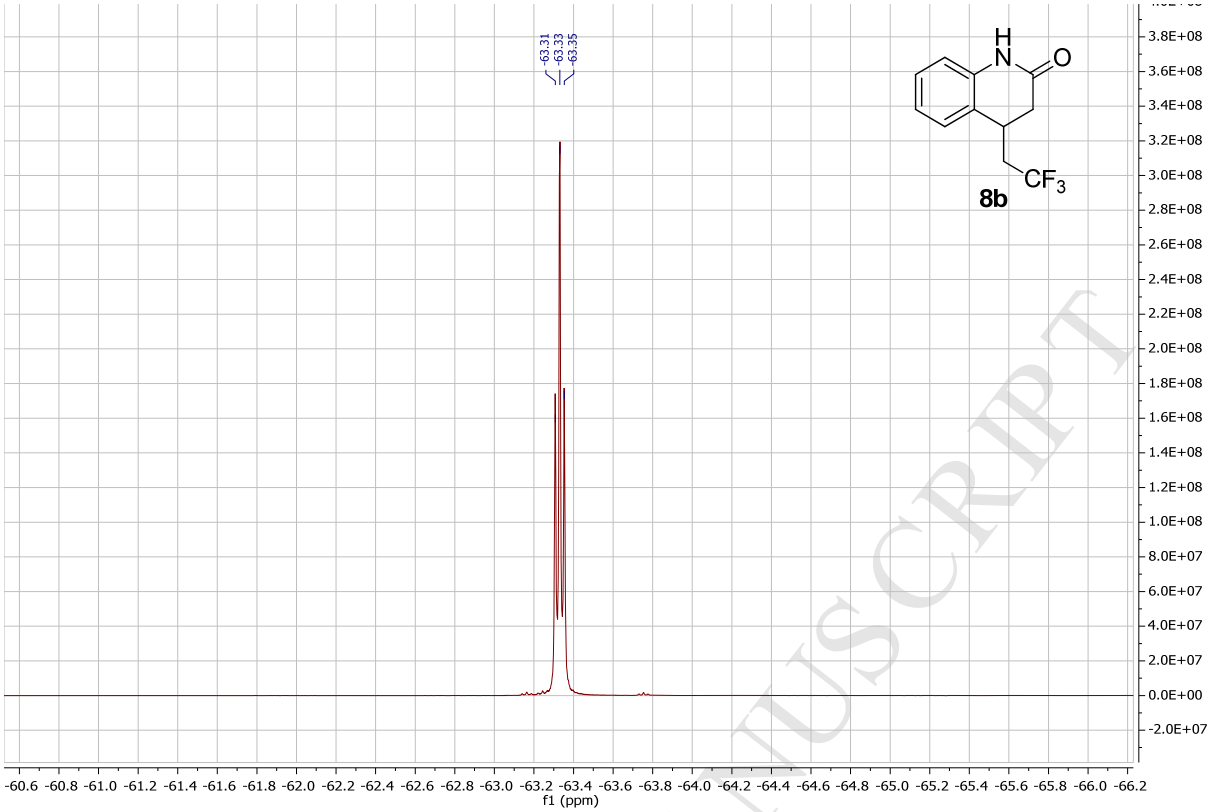
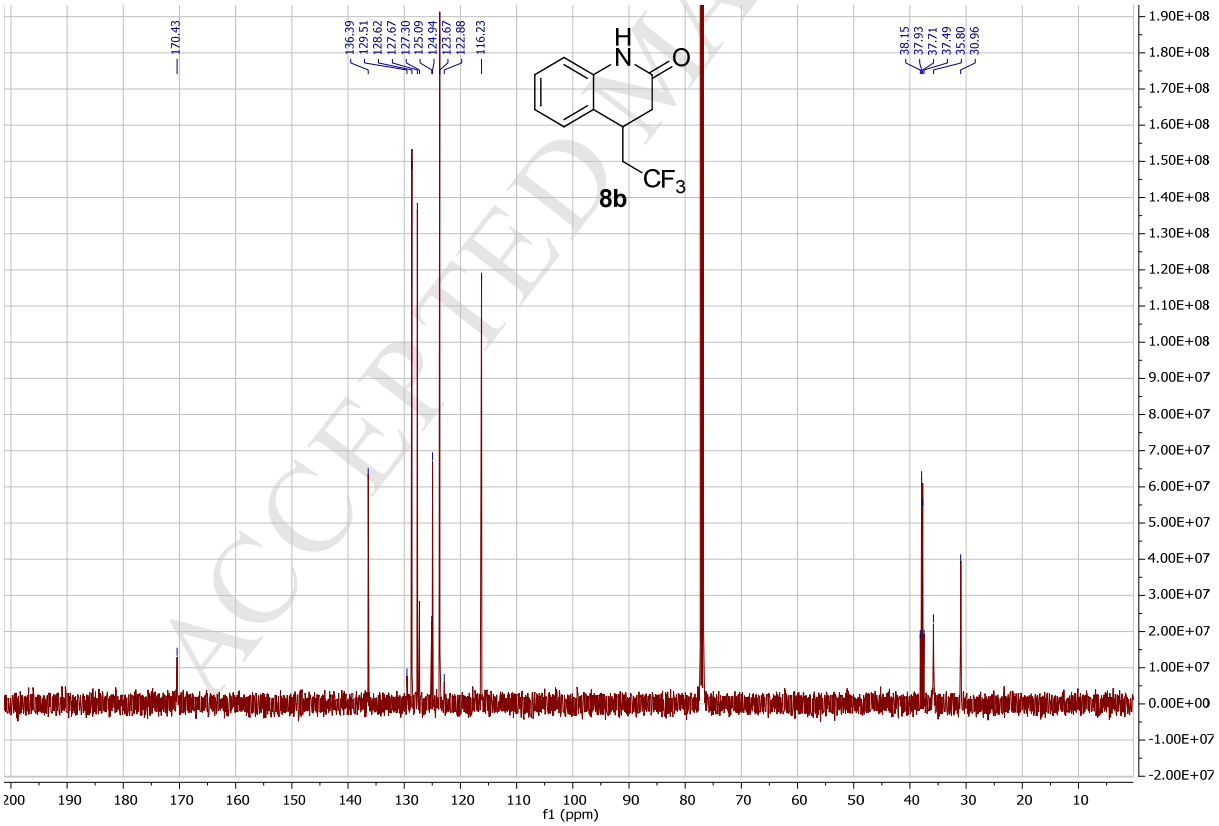
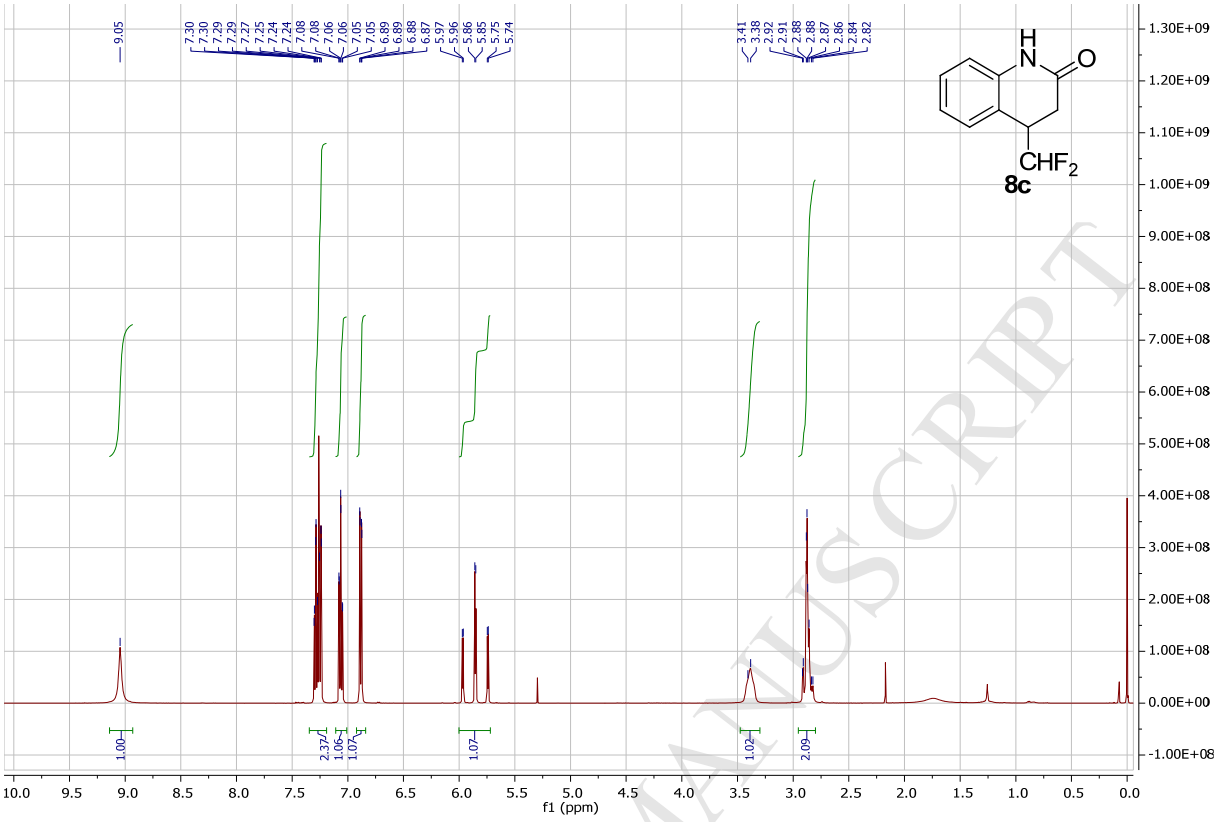
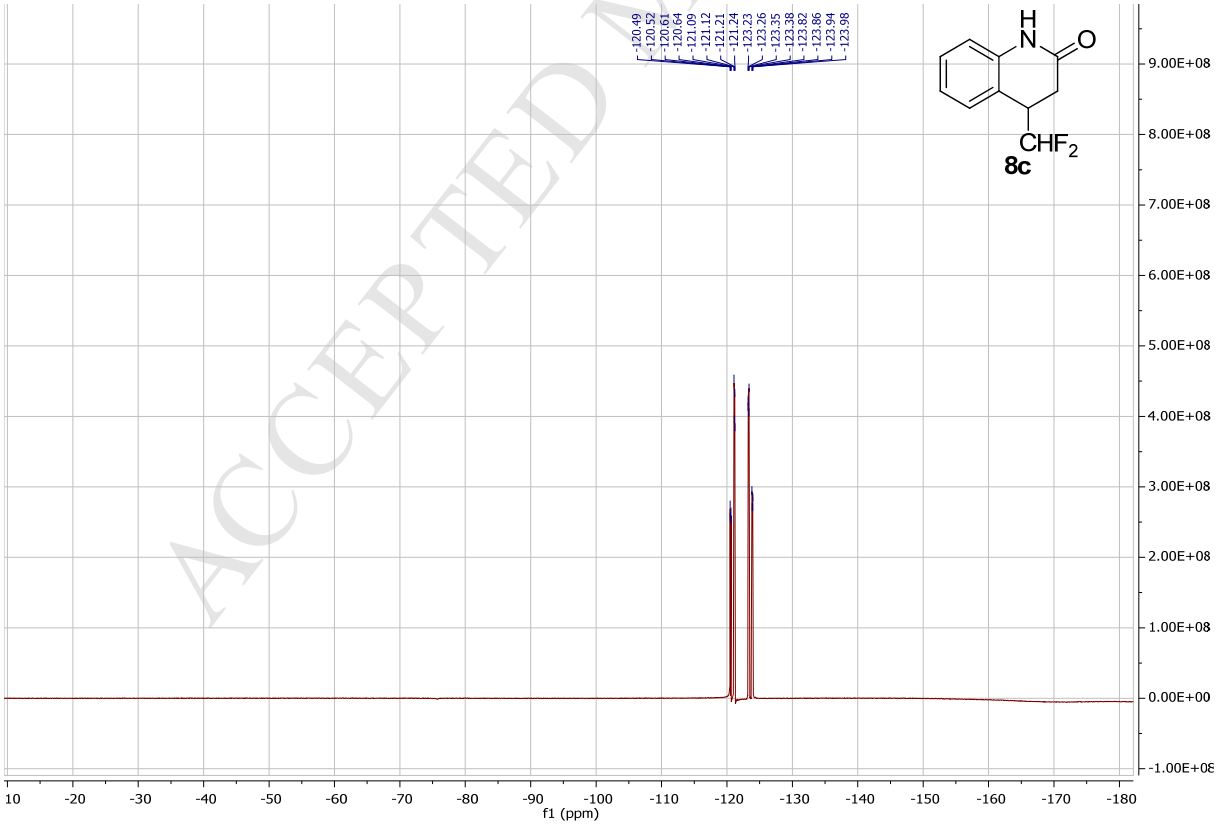


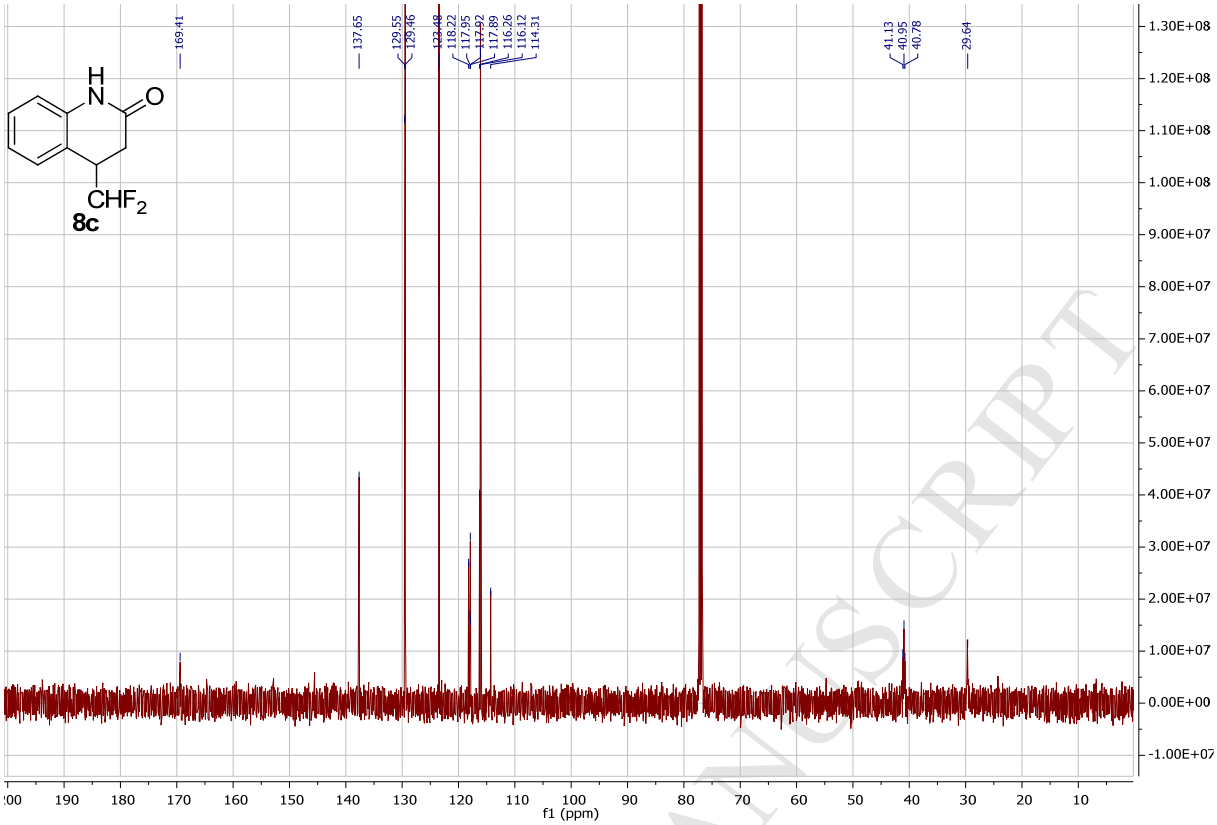


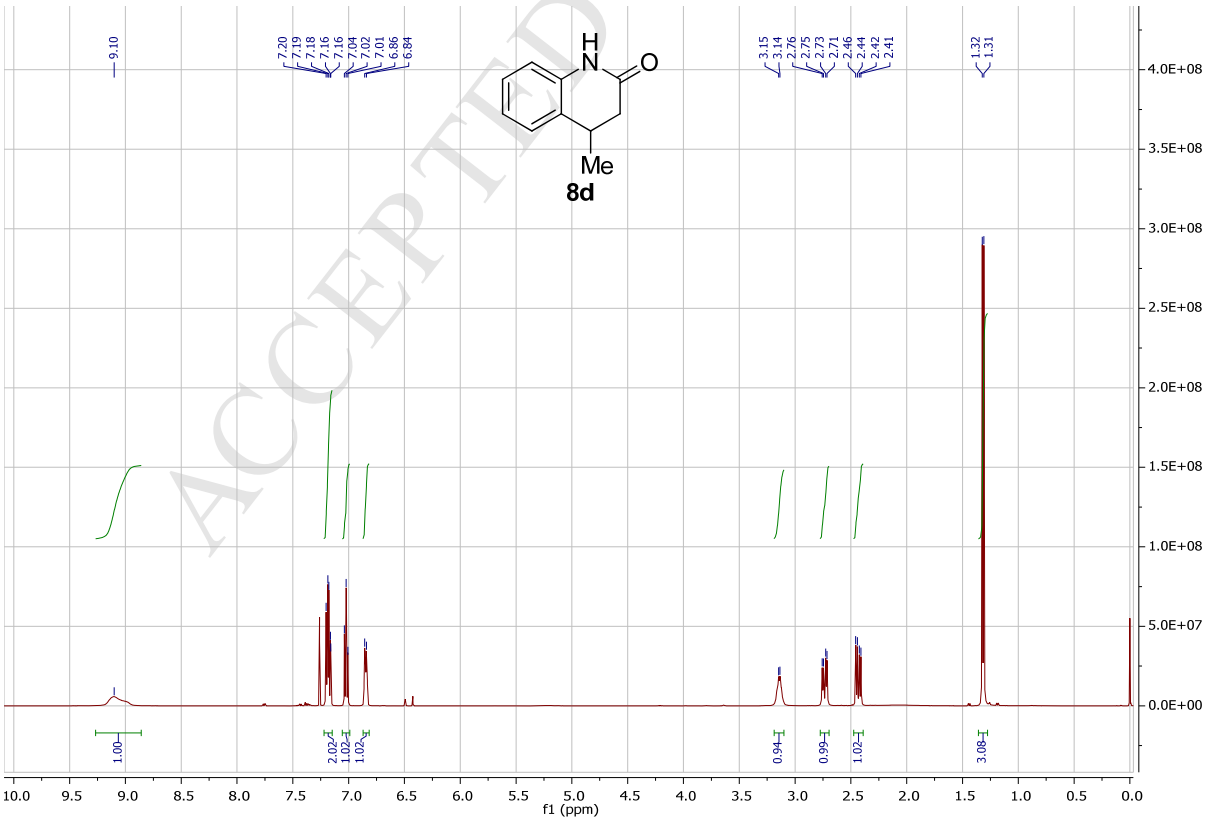
**4-(difluoromethyl)-3,4-dihydroquinolin-2(1H)-one (8c)**

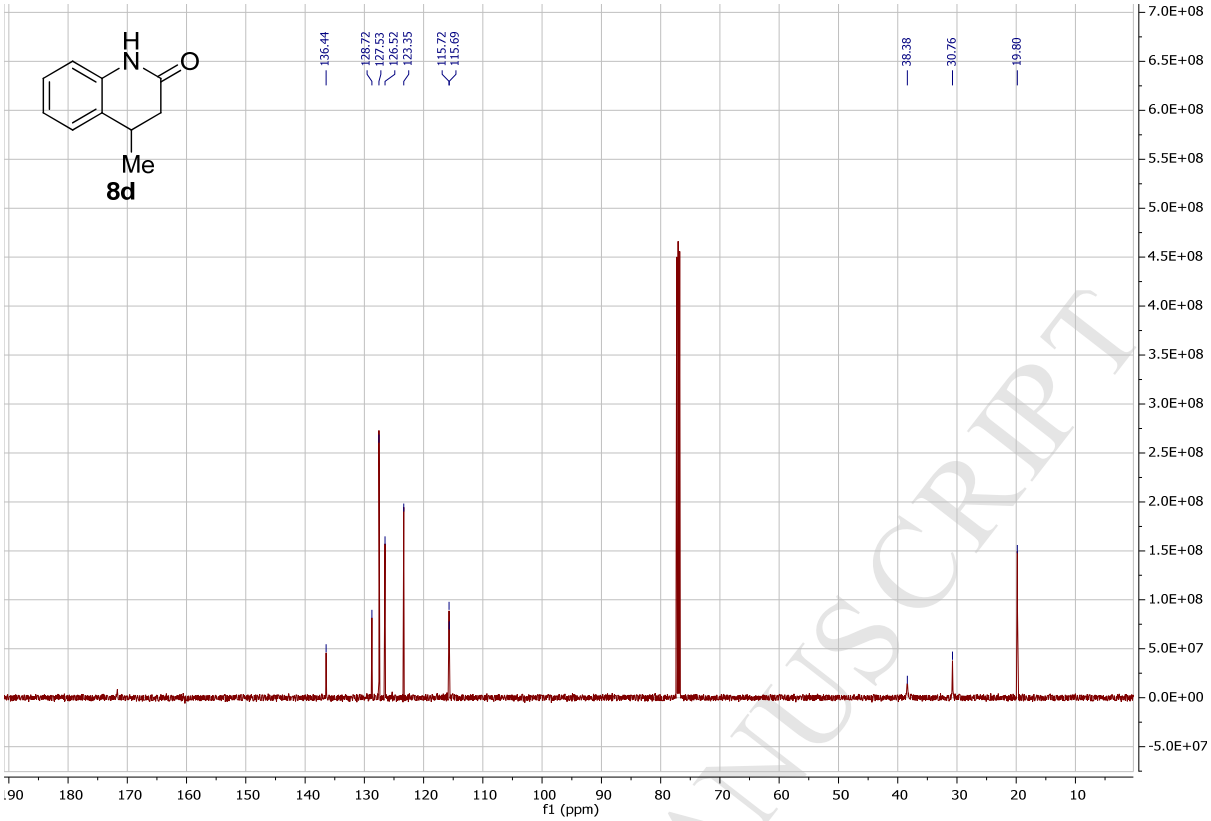


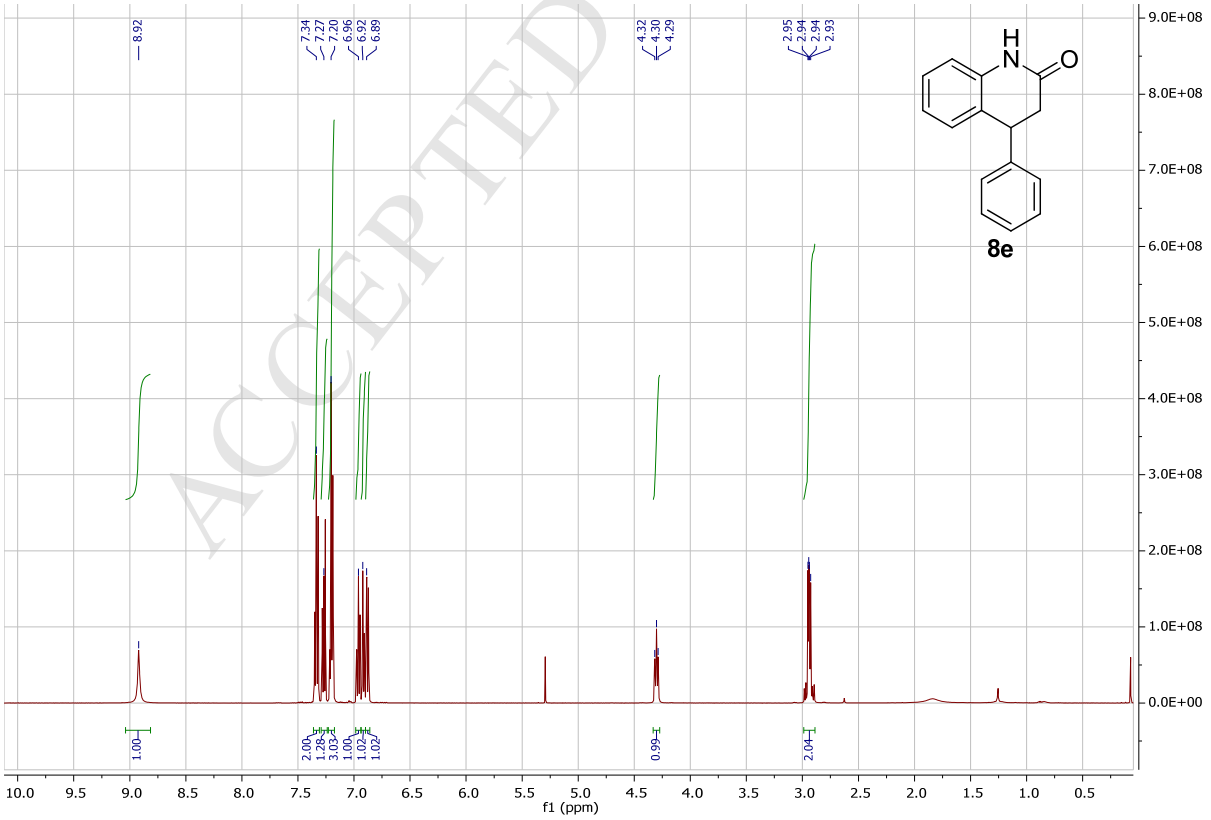


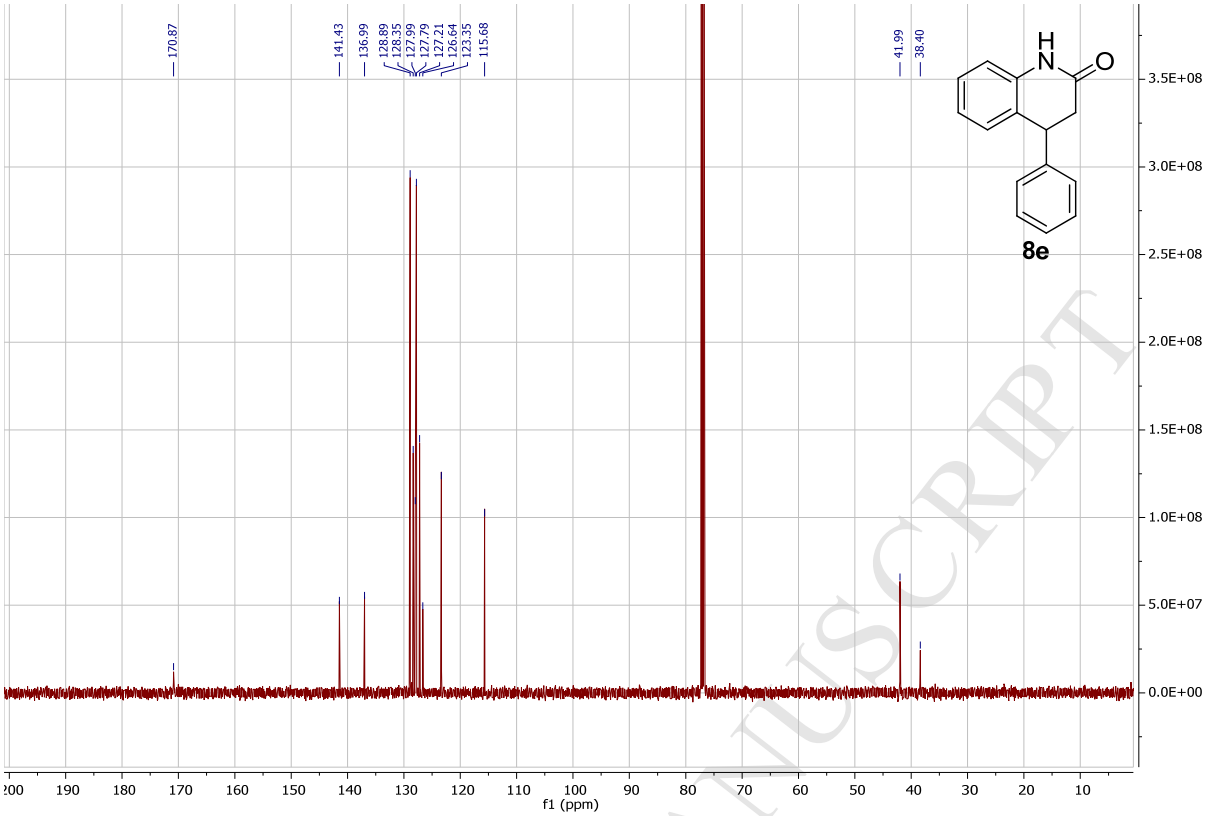

**4-methyl-3,4-dihydroquinolin-2(1H)-one (8d)**



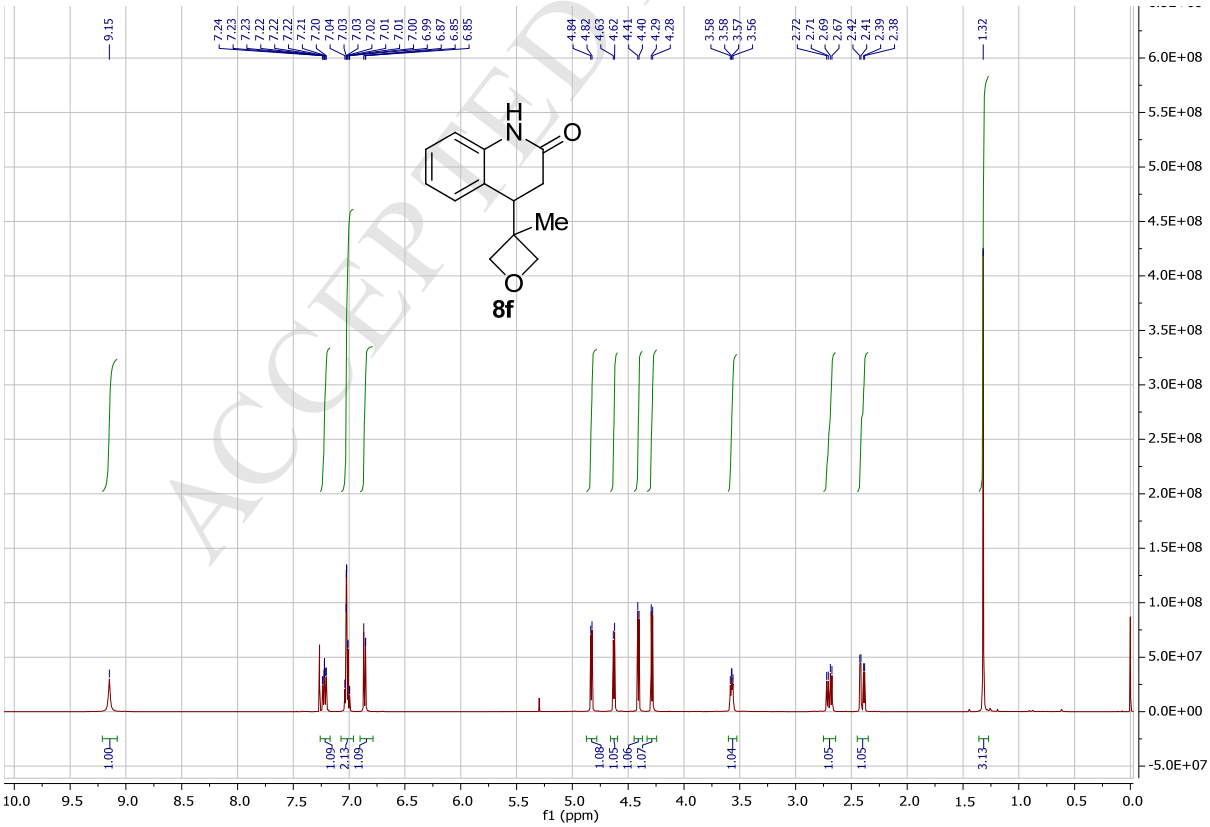


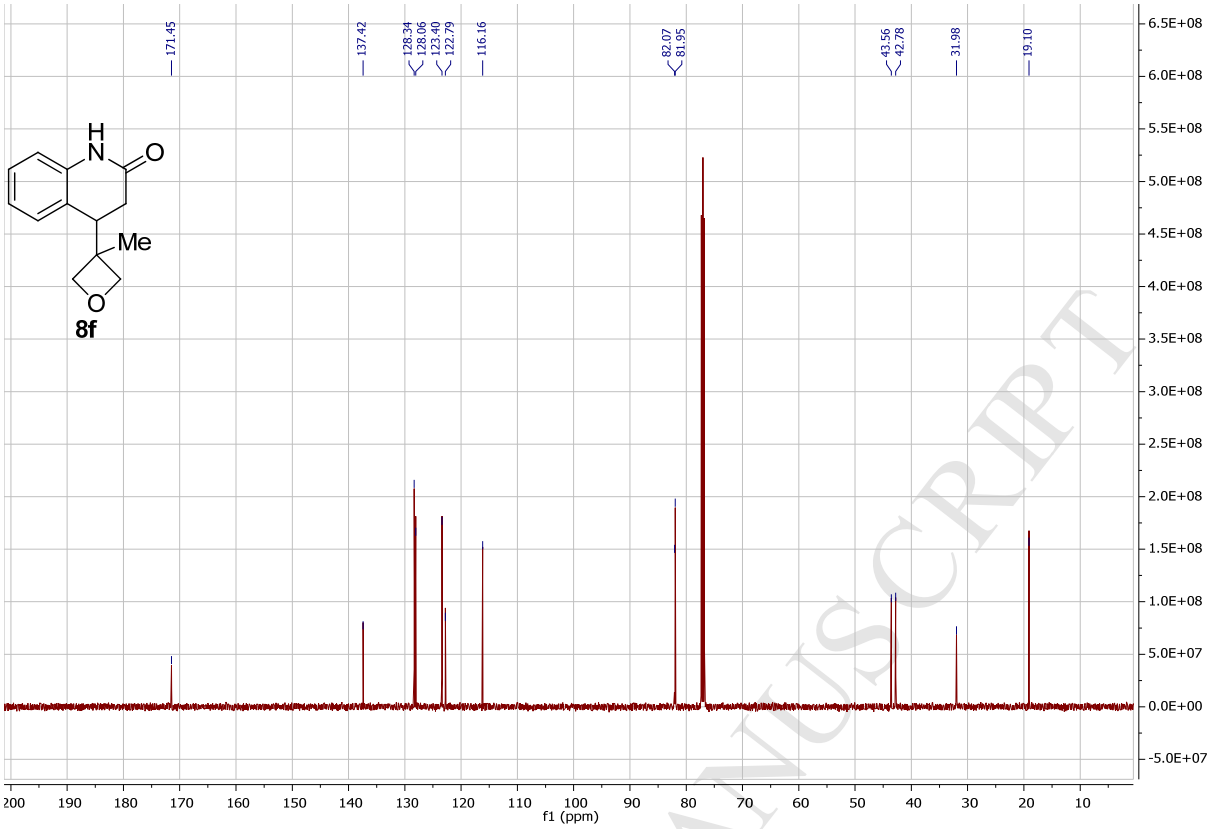

**4-phenyl-3,4-dihydroquinolin-2(1H)-one (8e)**



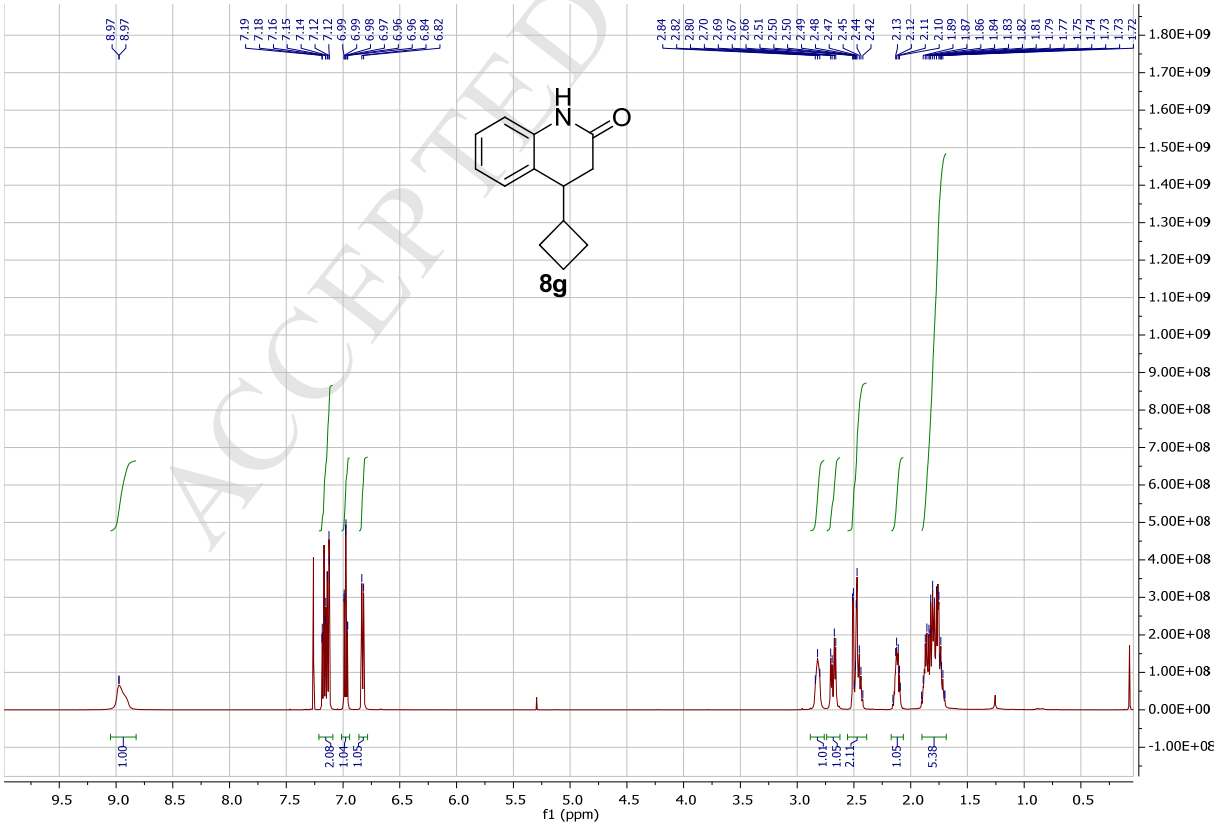


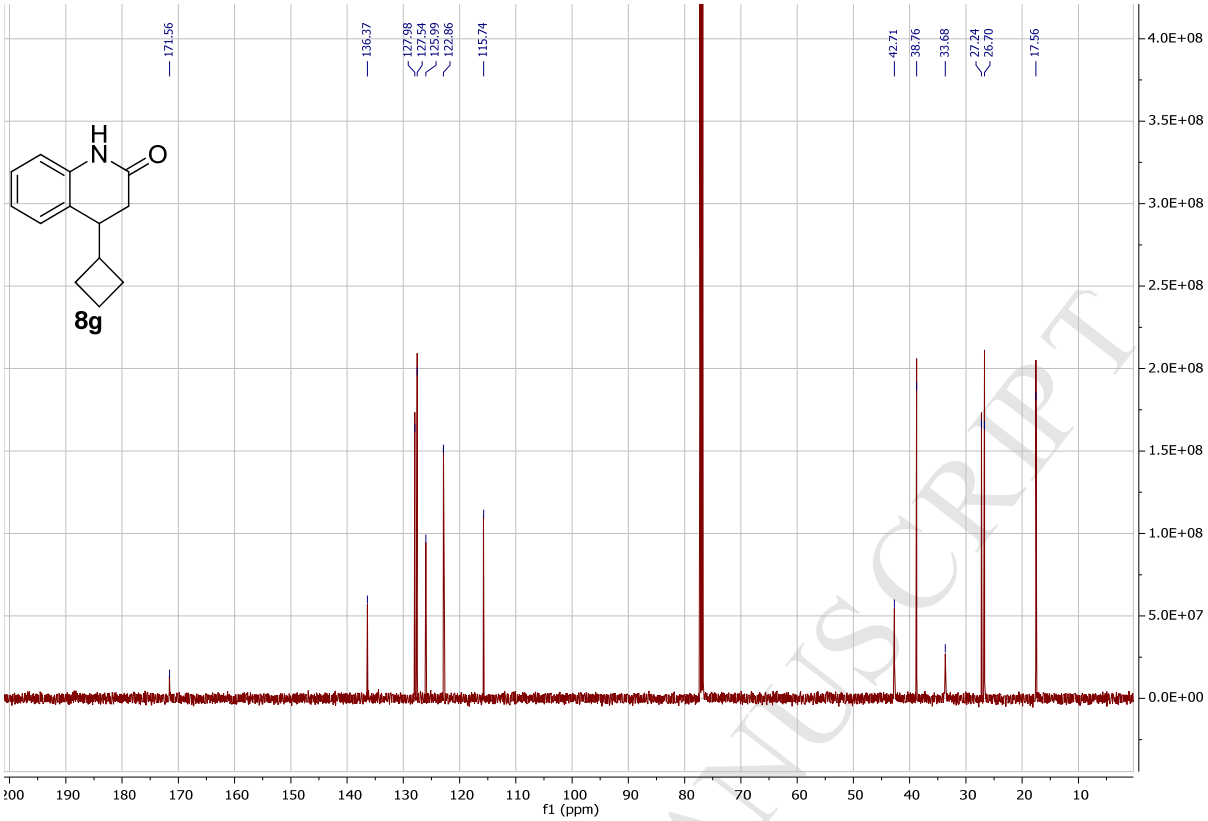

**4-(3-methyloxetan-3-yl)-3,4-dihydroquinolin-2(1H)-one (8f)**



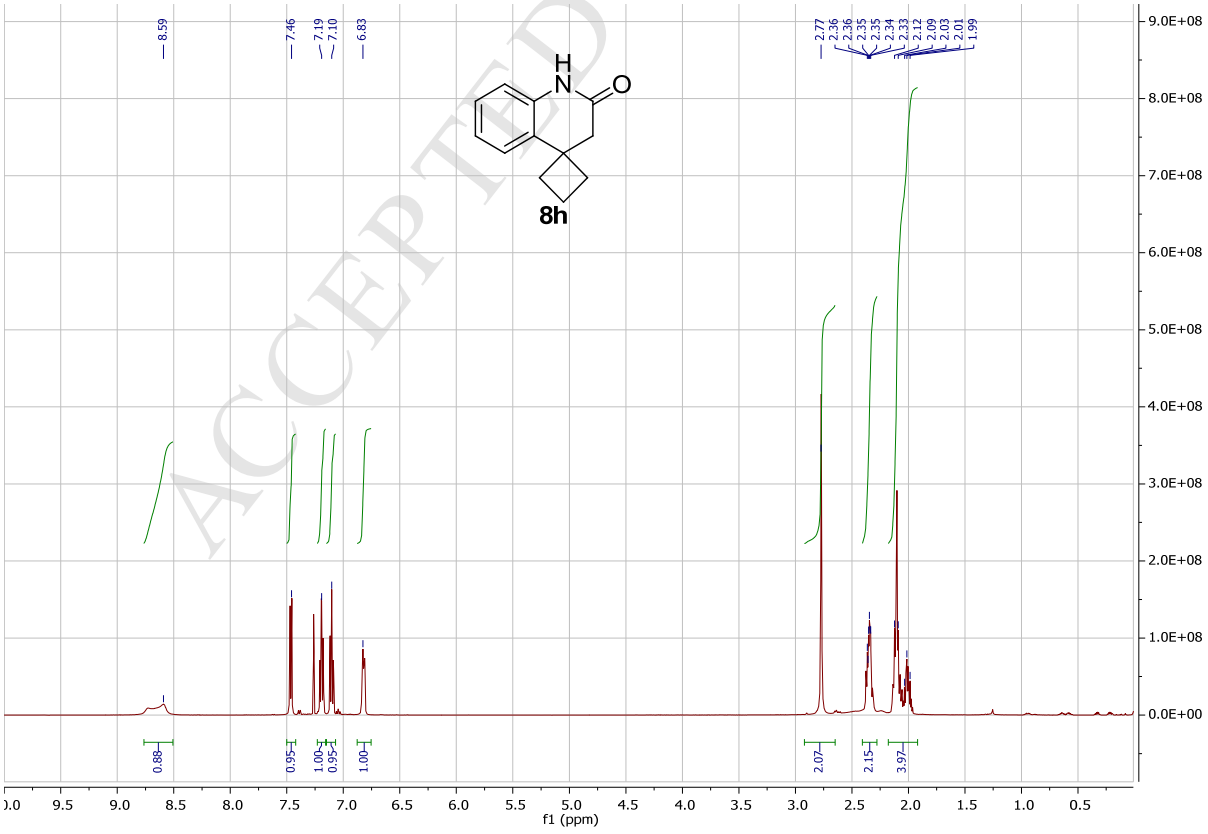


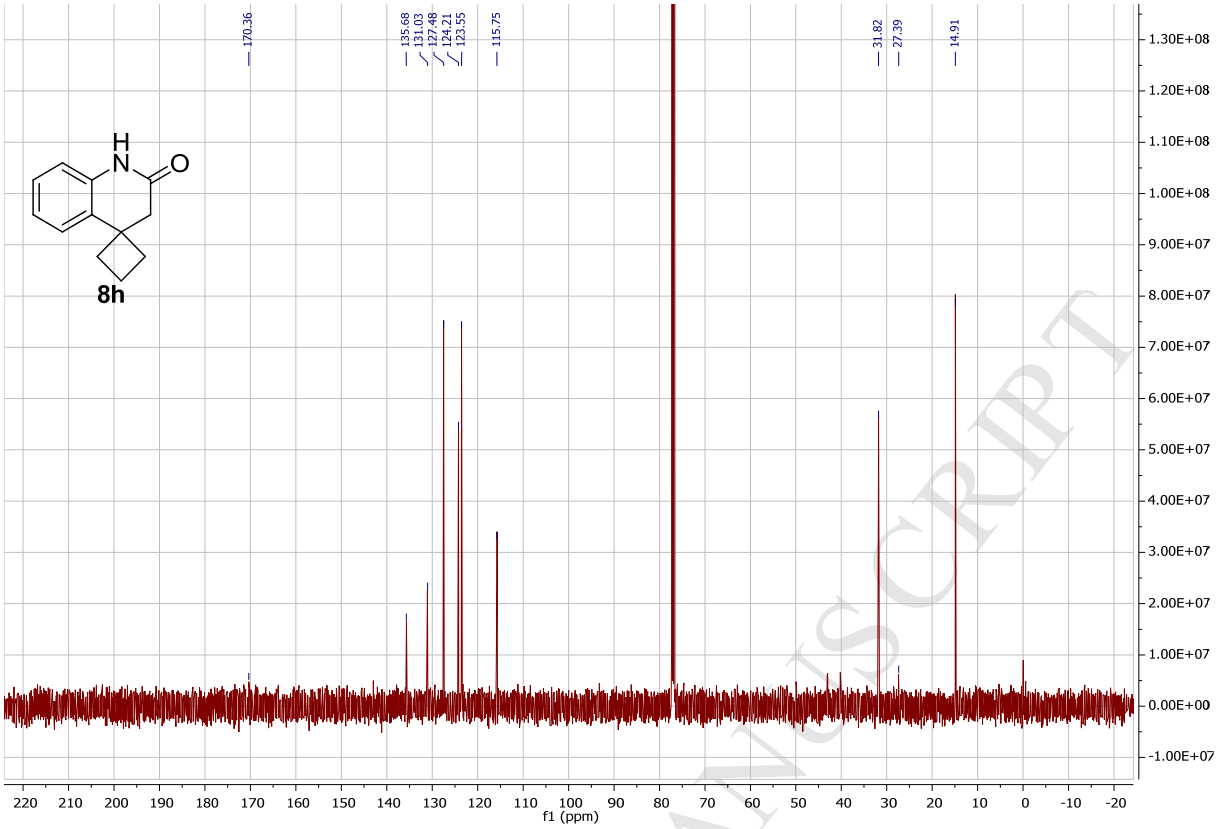

**4-cyclobutyl-3,4-dihydroquinolin-2(1H)-one (8g)**



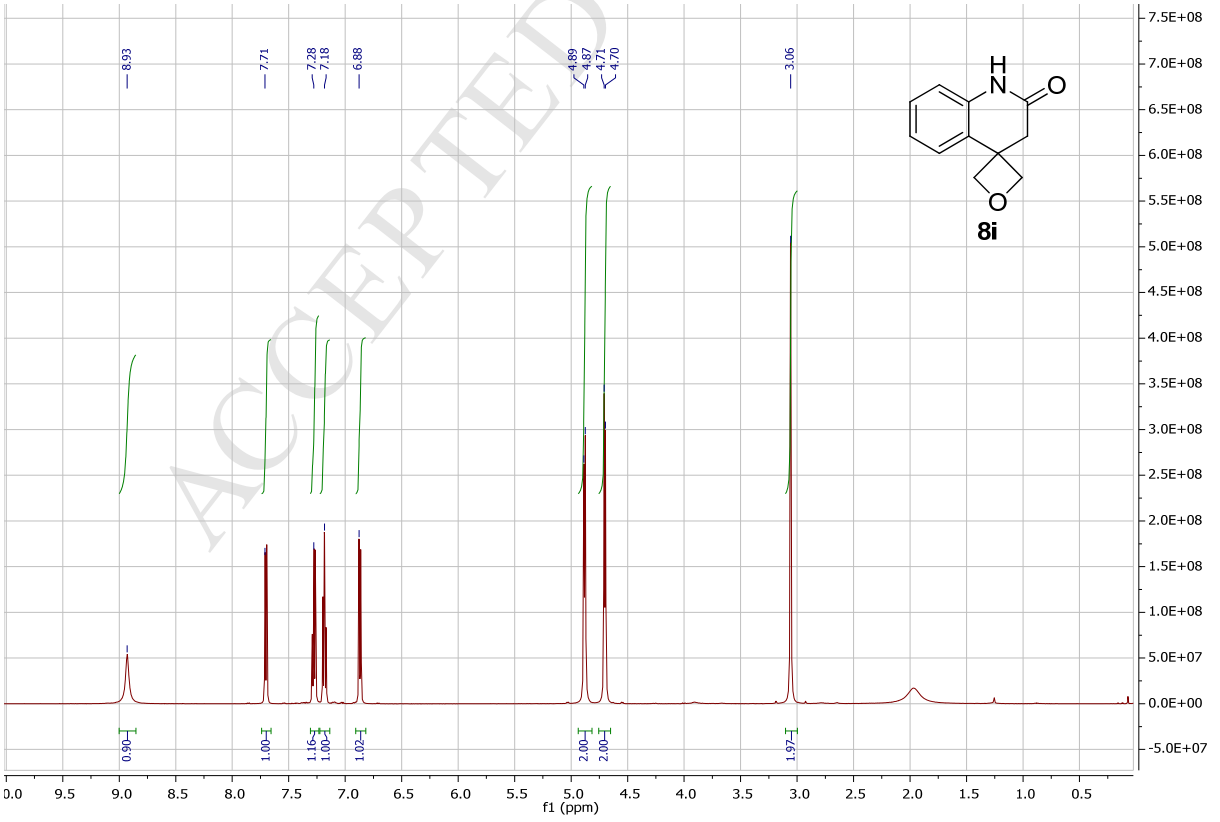


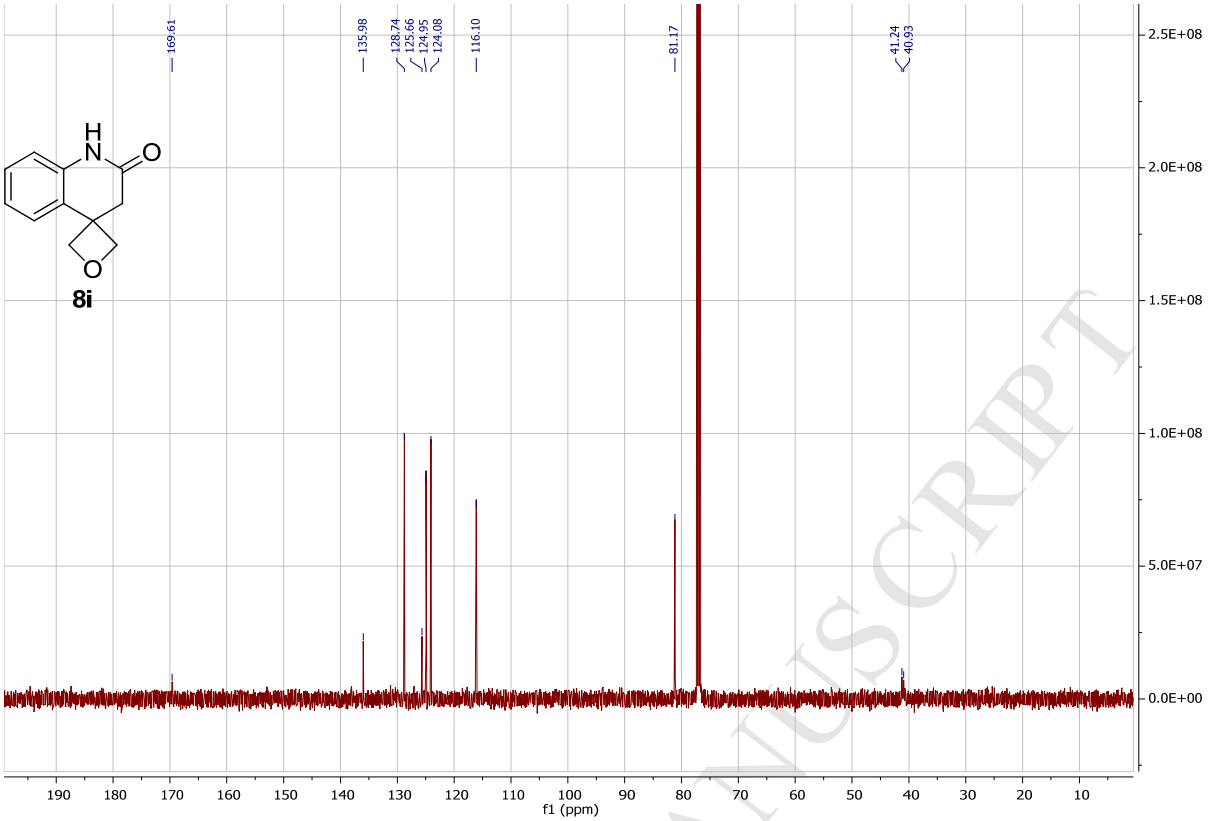

**1'H-spiro[cyclobutane-1,4'-quinolin]-2'(3'H)-one (8h)**



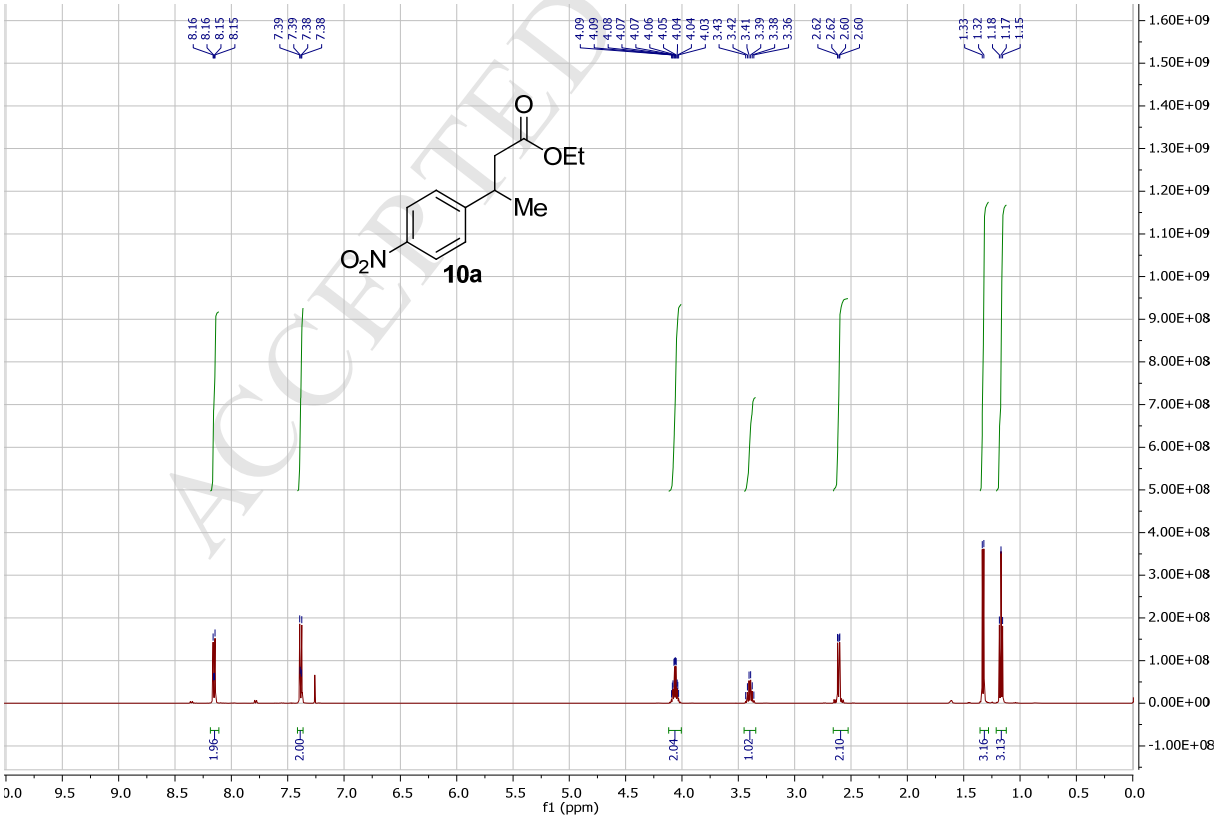


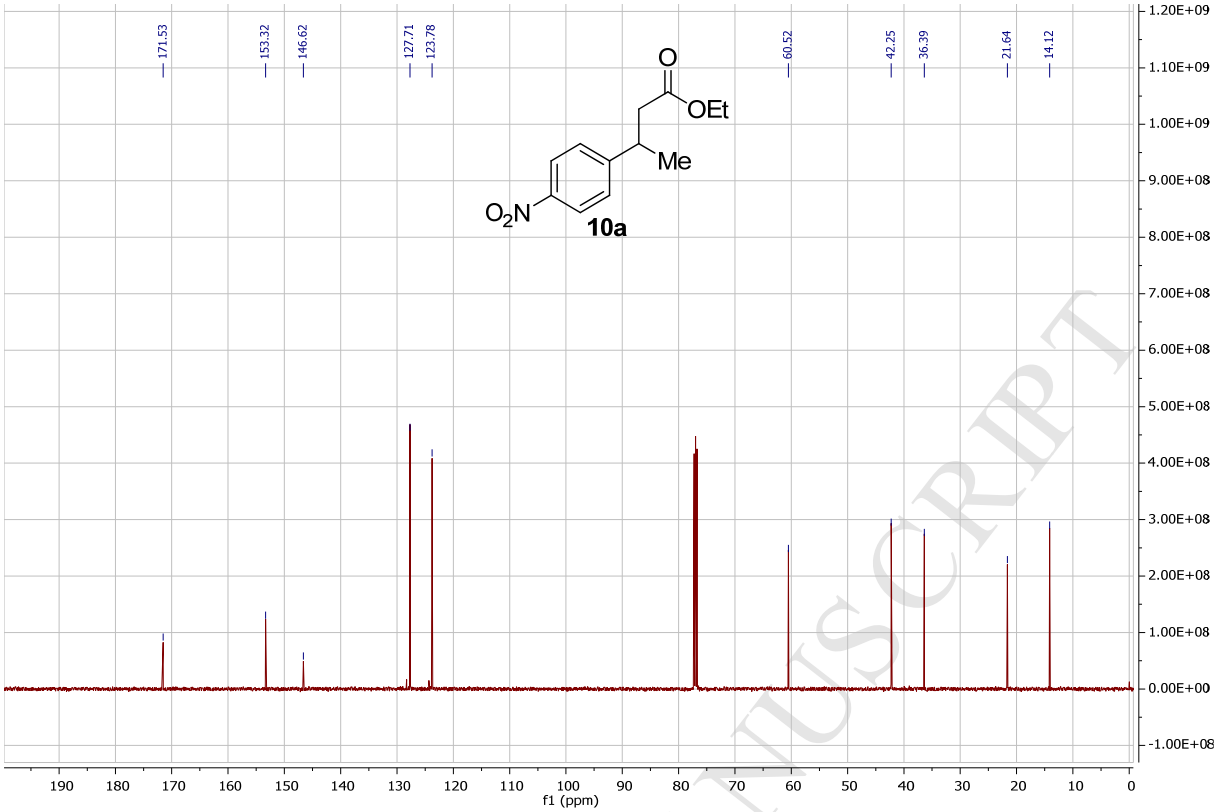

**1'H-spiro[oxetane-3,4'-quinolin]-2'(3'H)-one (8i)**



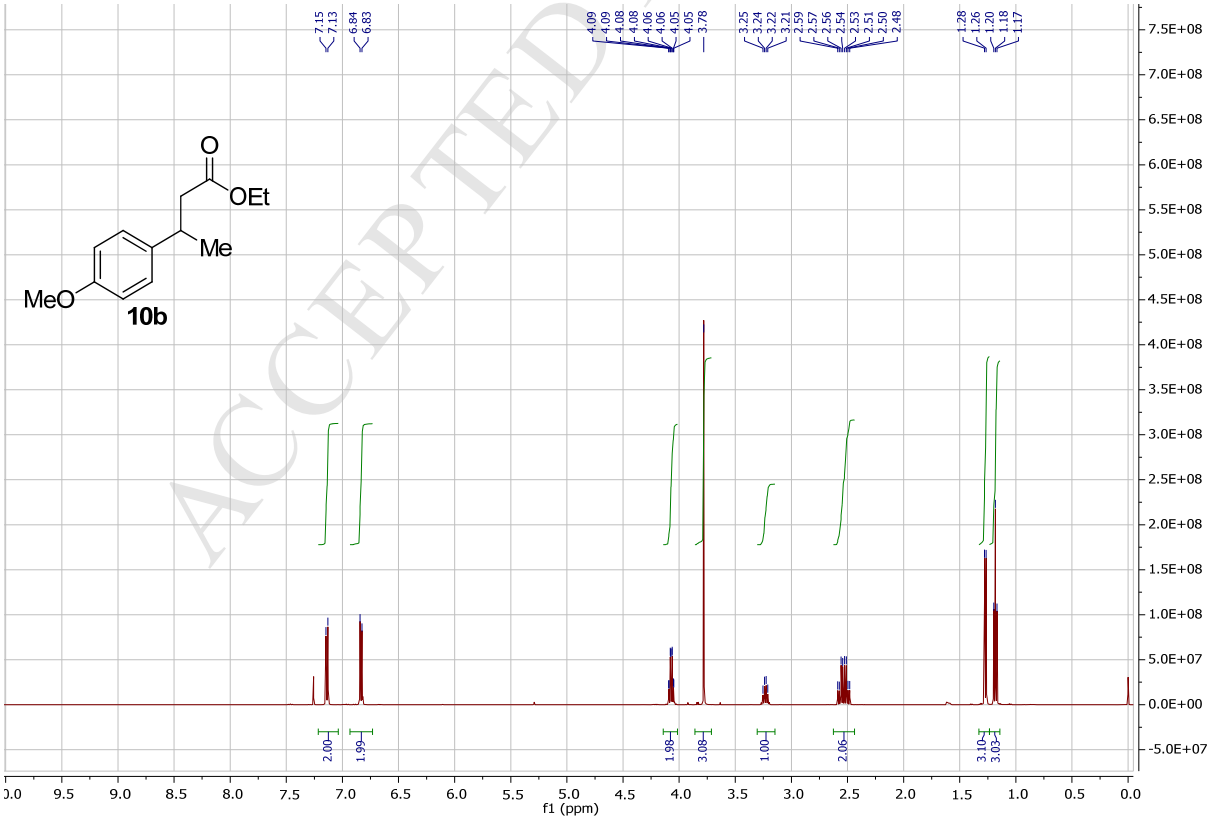


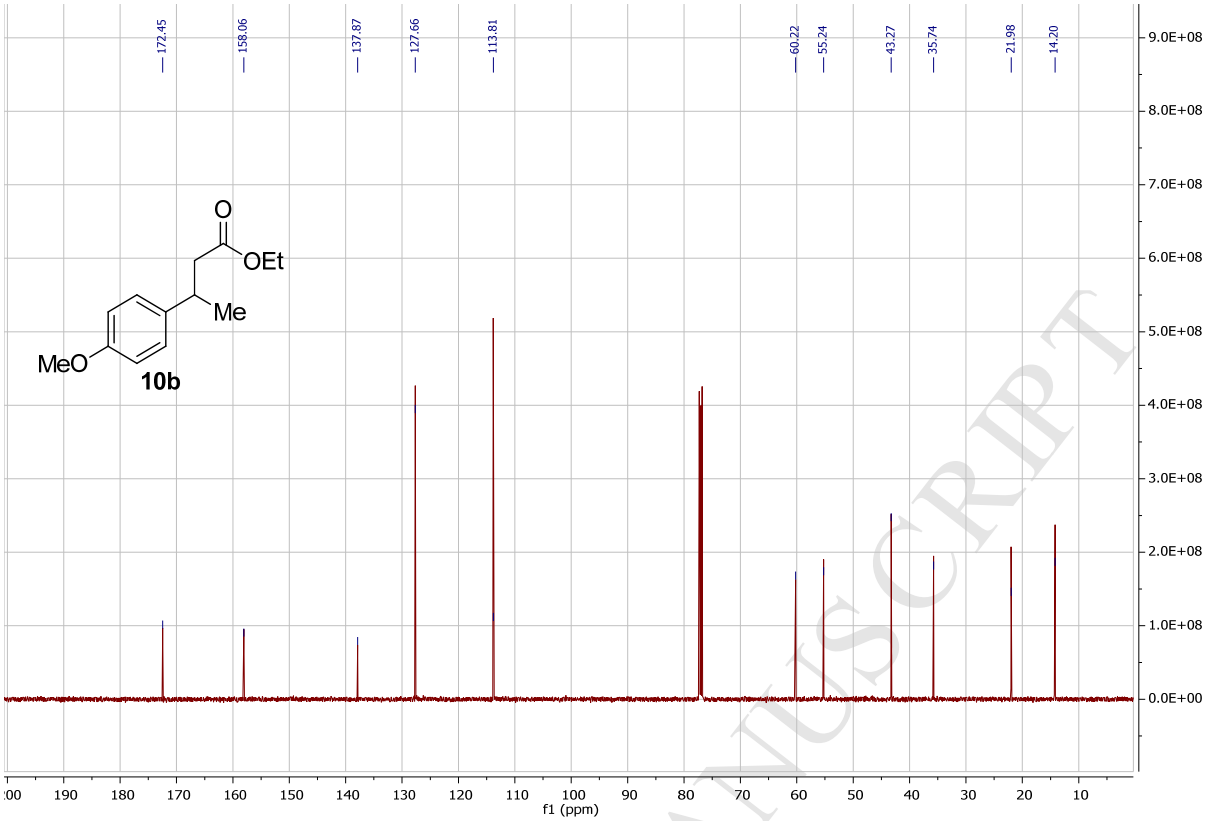

**ethyl 3-(4-nitrophenyl)butanoate (10a)**



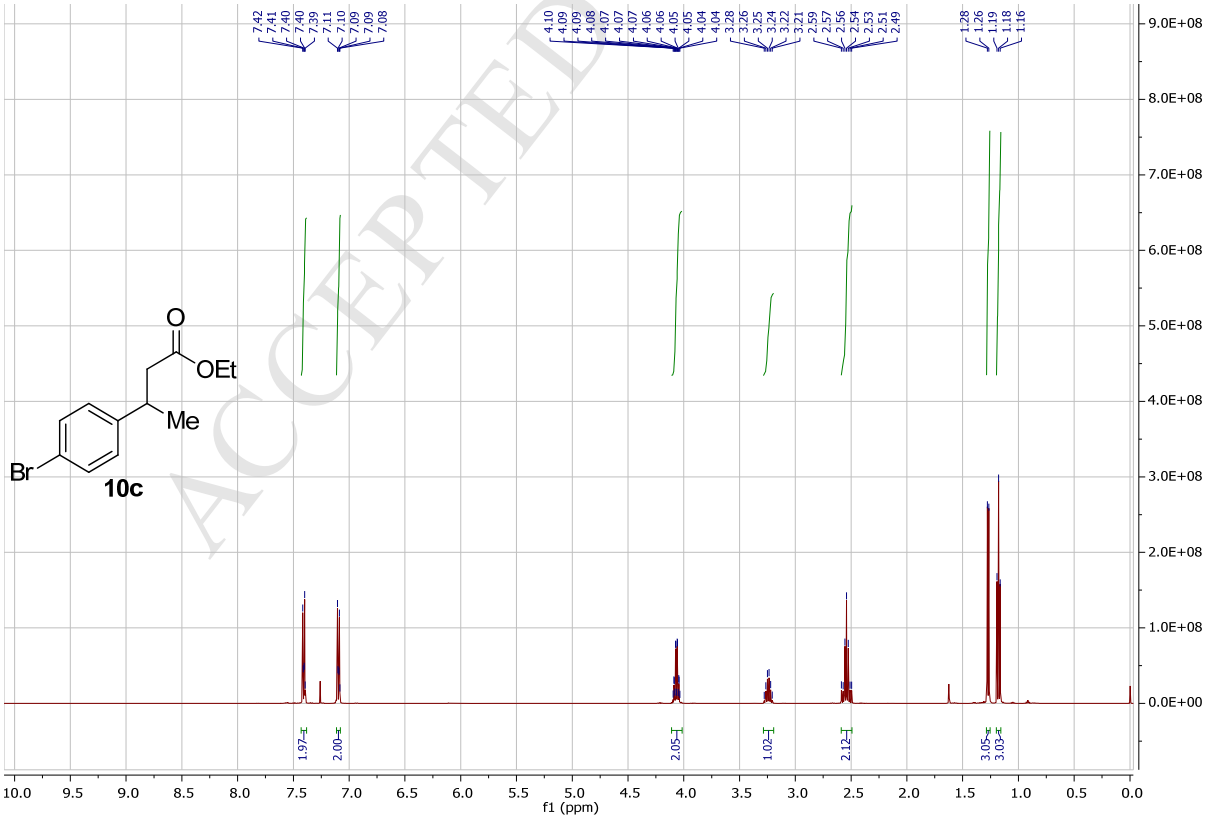


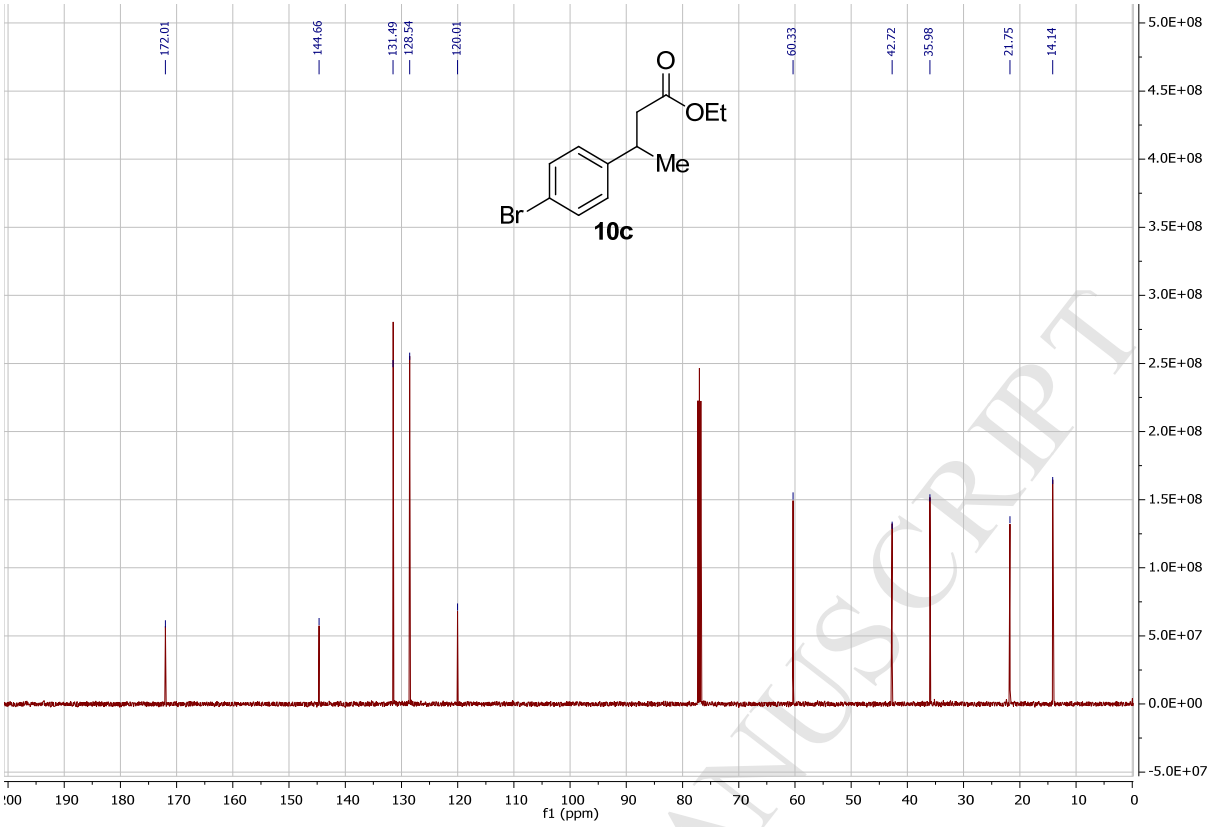

**ethyl 3-(4-methoxyphenyl)butanoate (10b)**






**ethyl 3-(4-bromophenyl)butanoate (10c)**



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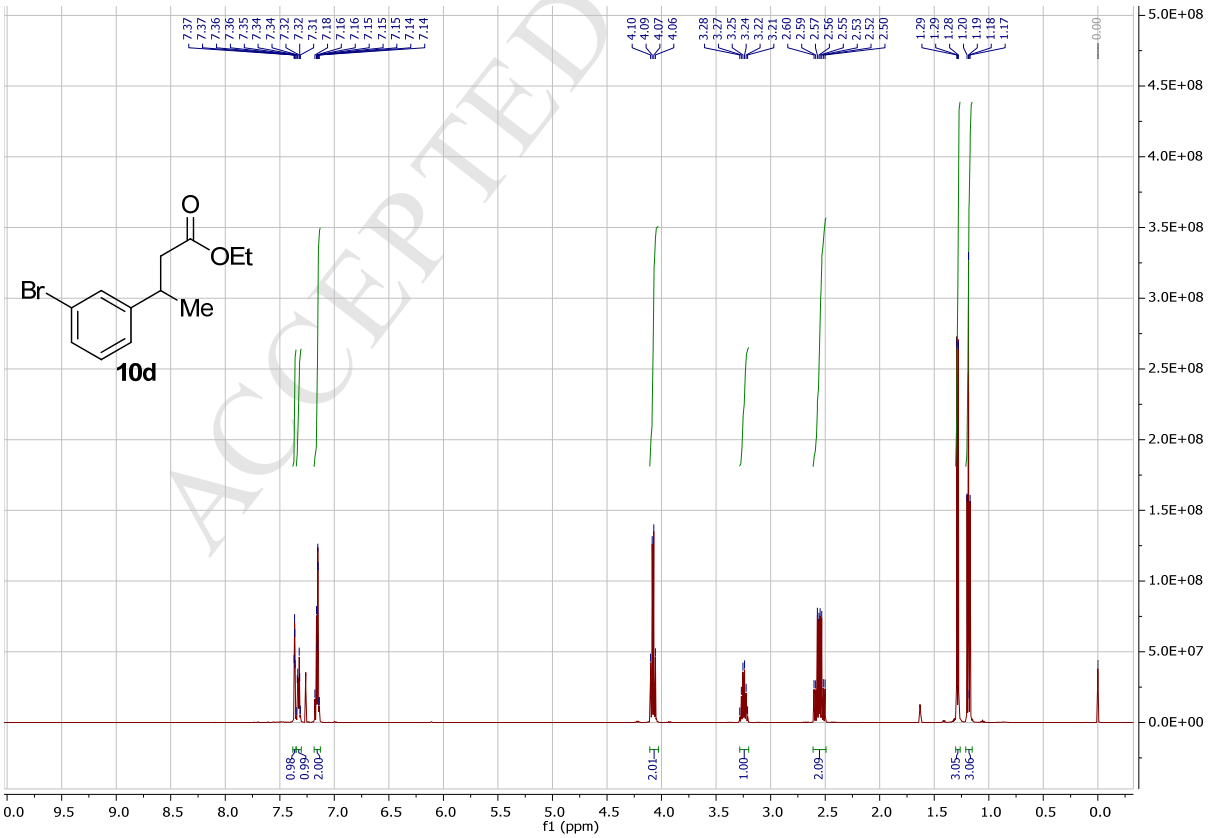

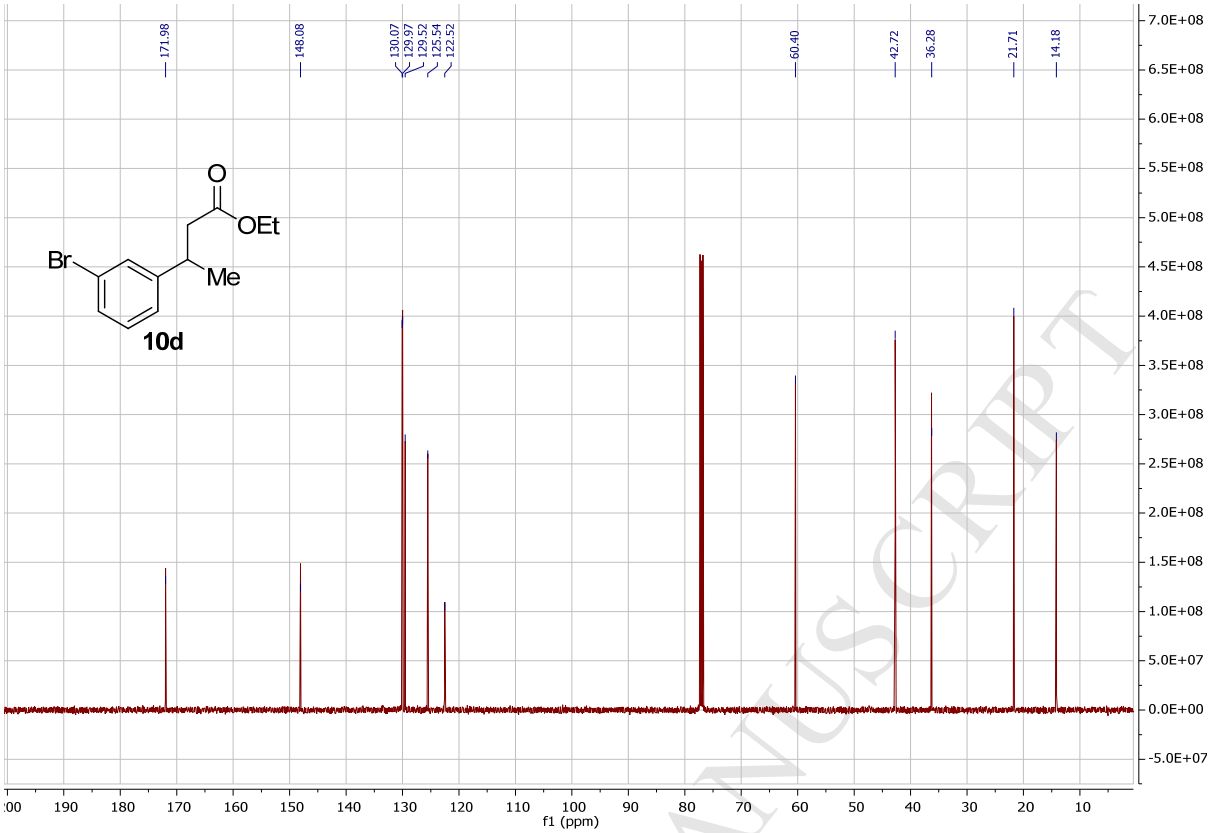


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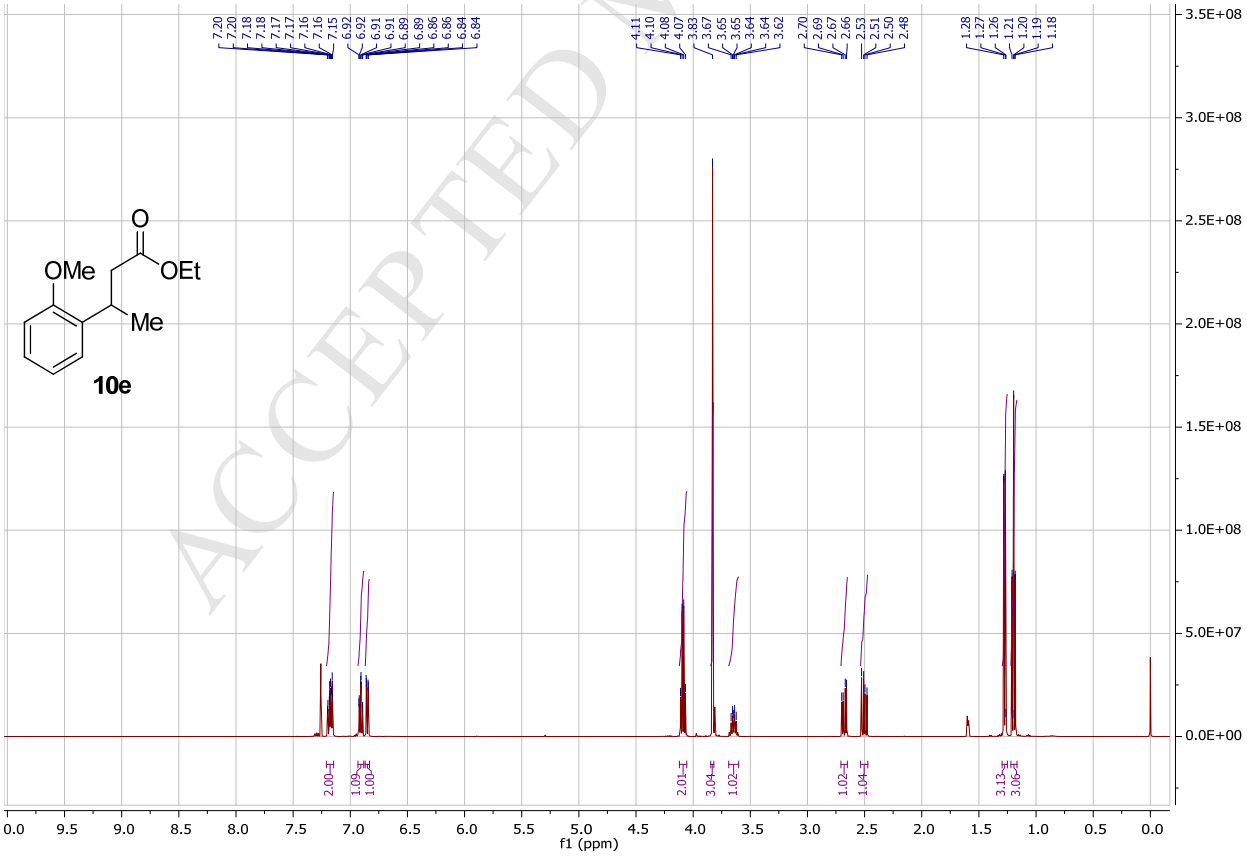
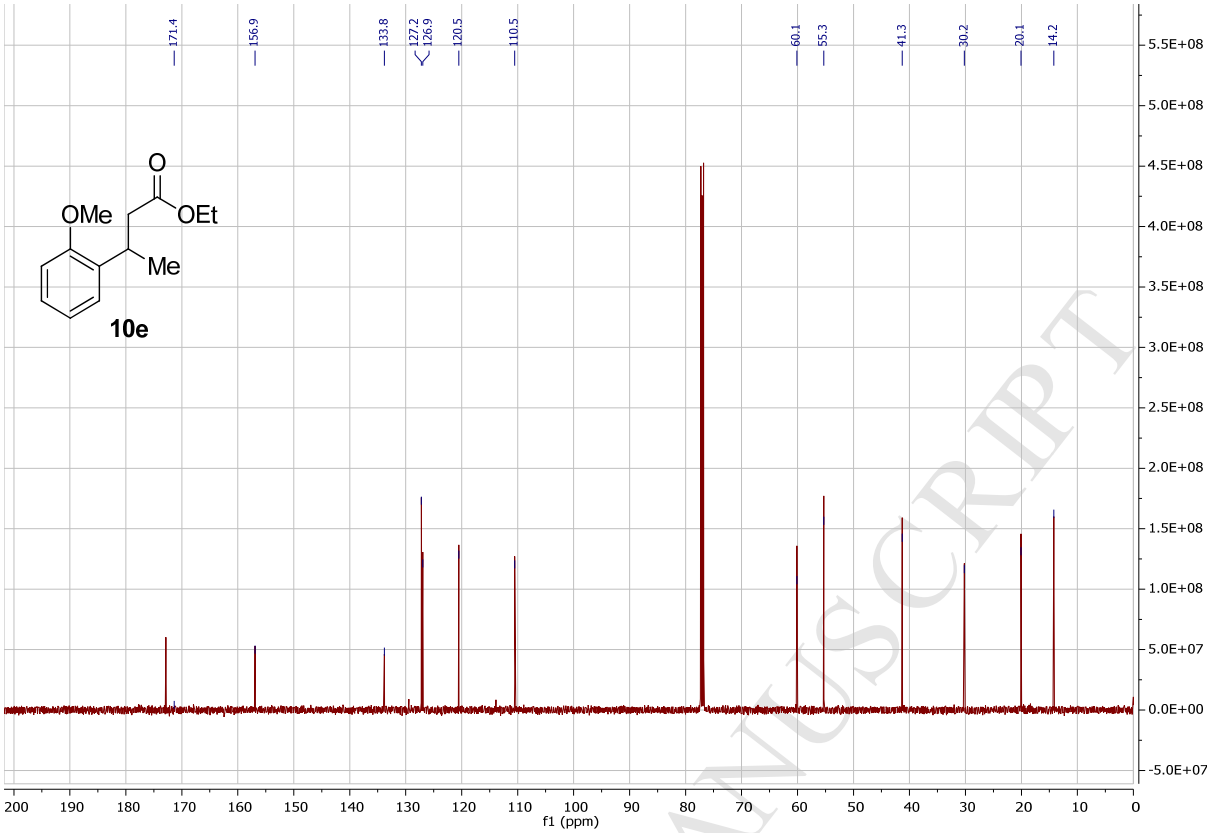
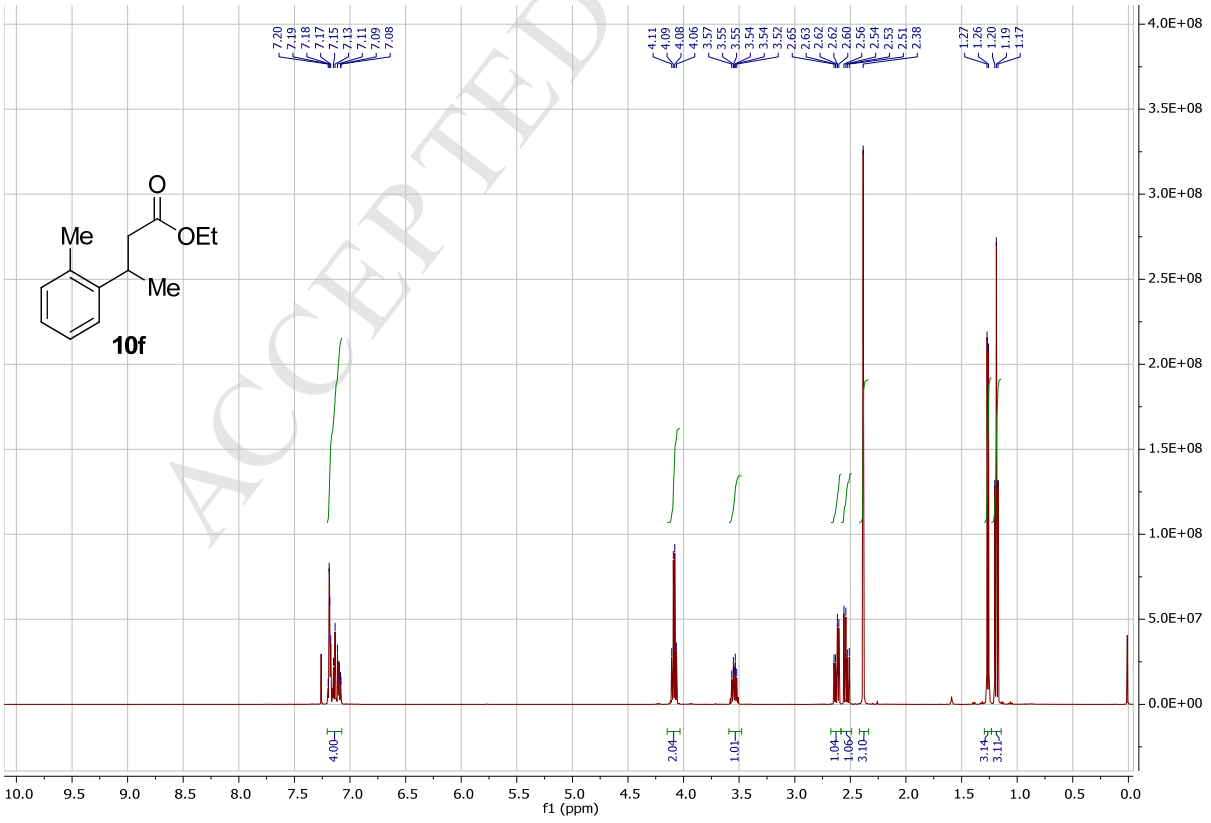
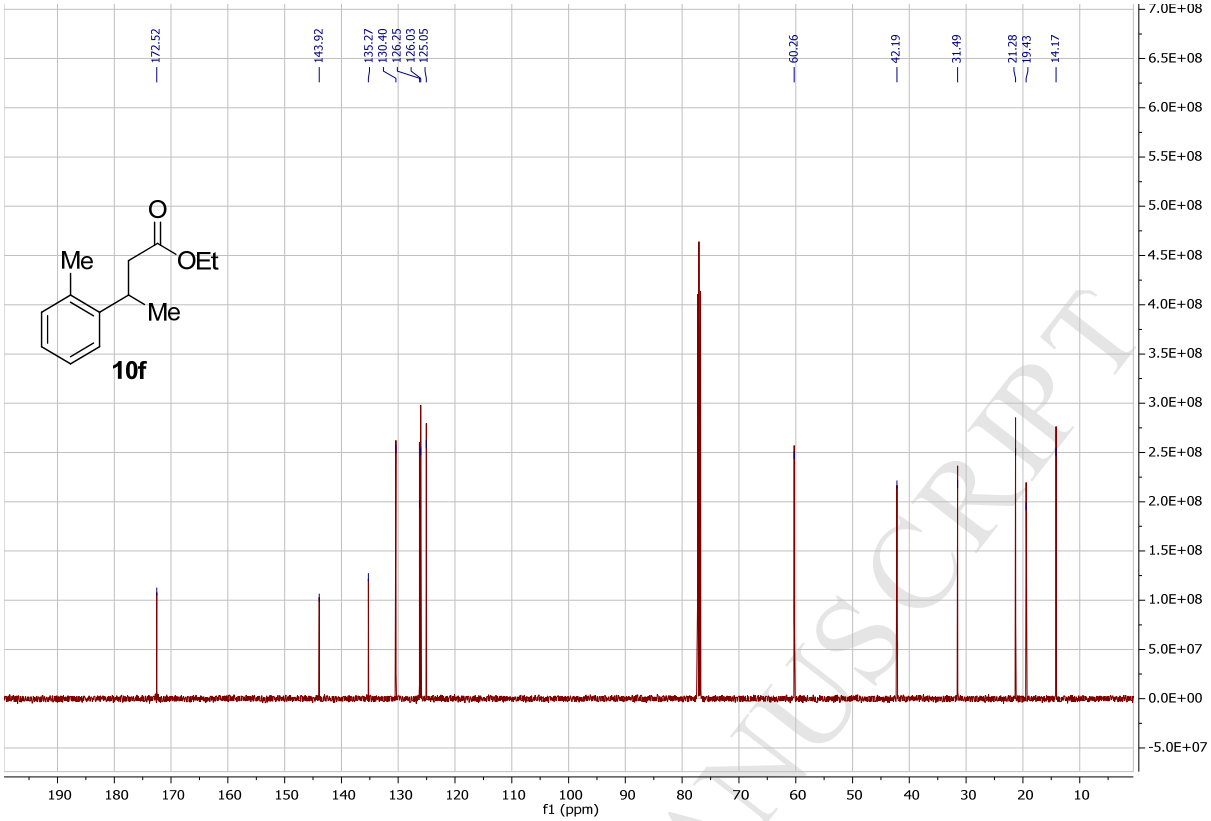





**ethyl 3-(o-tolyl)butanoate (10f)**



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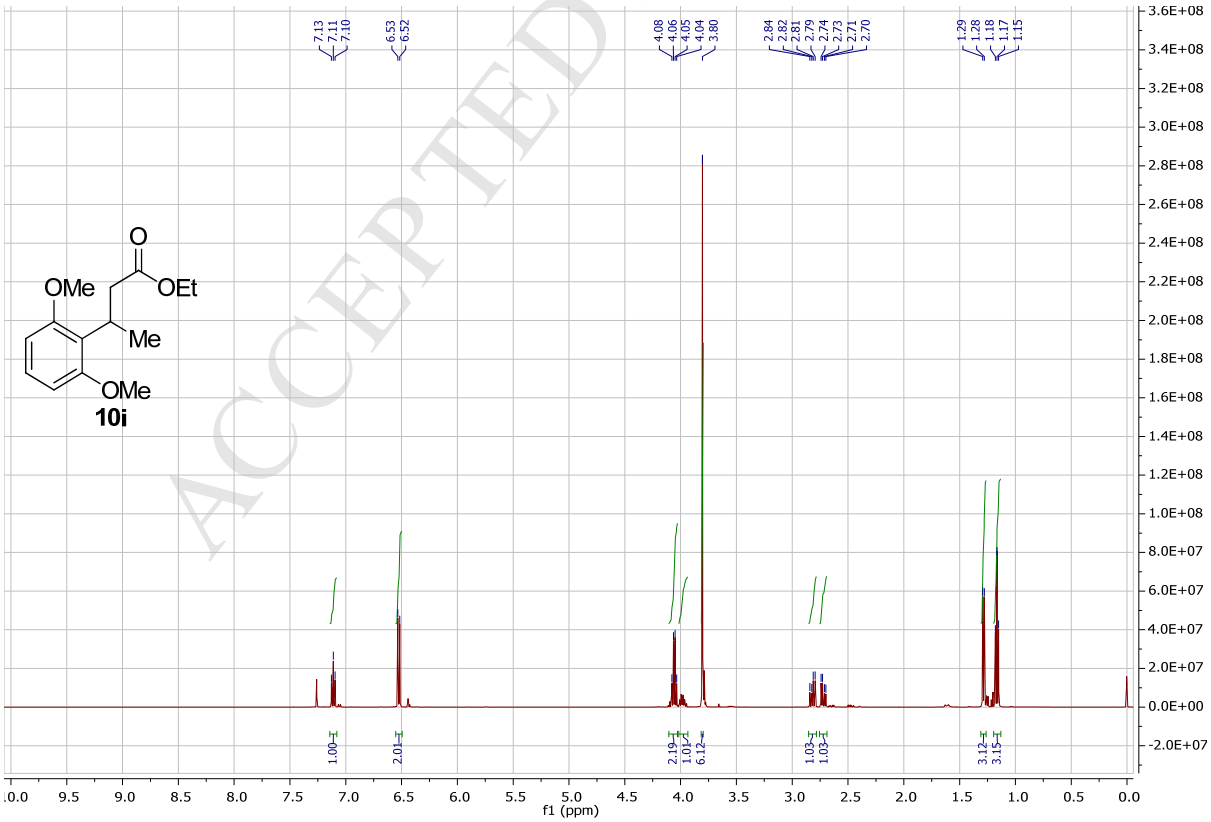
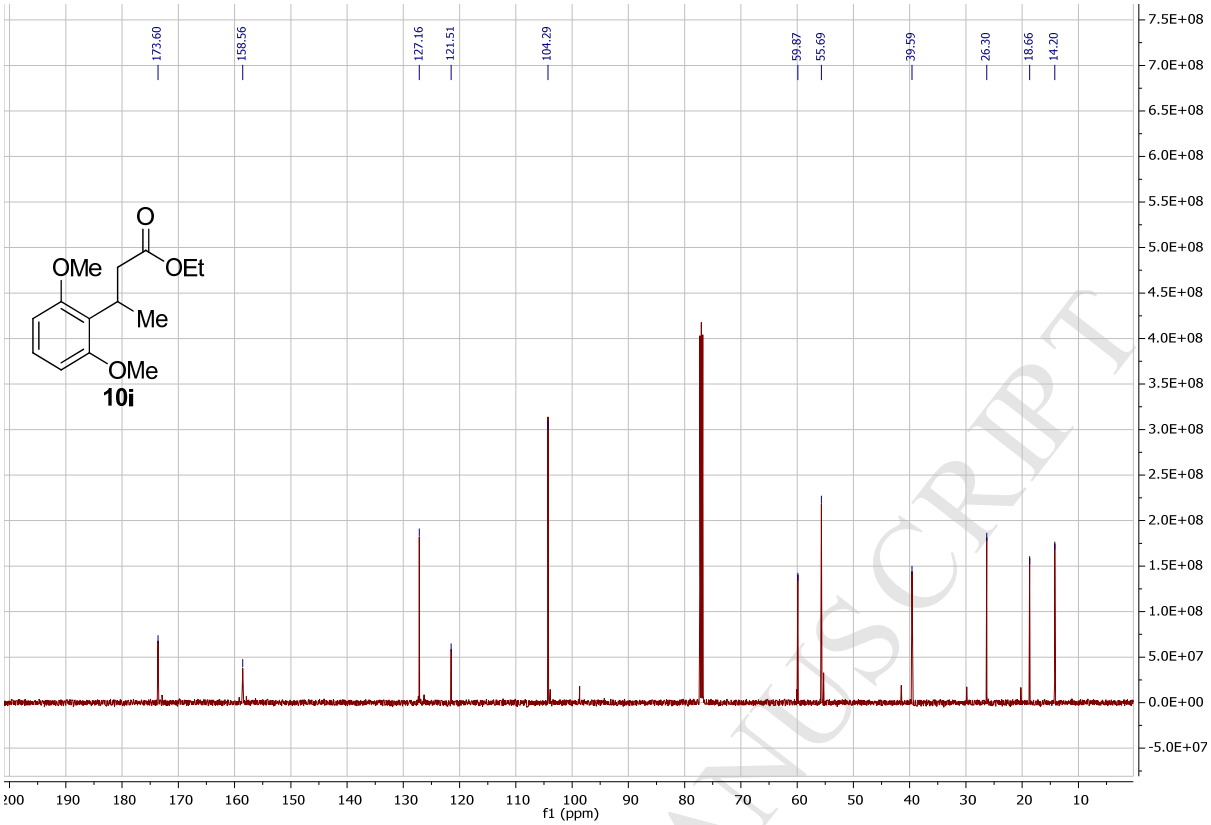
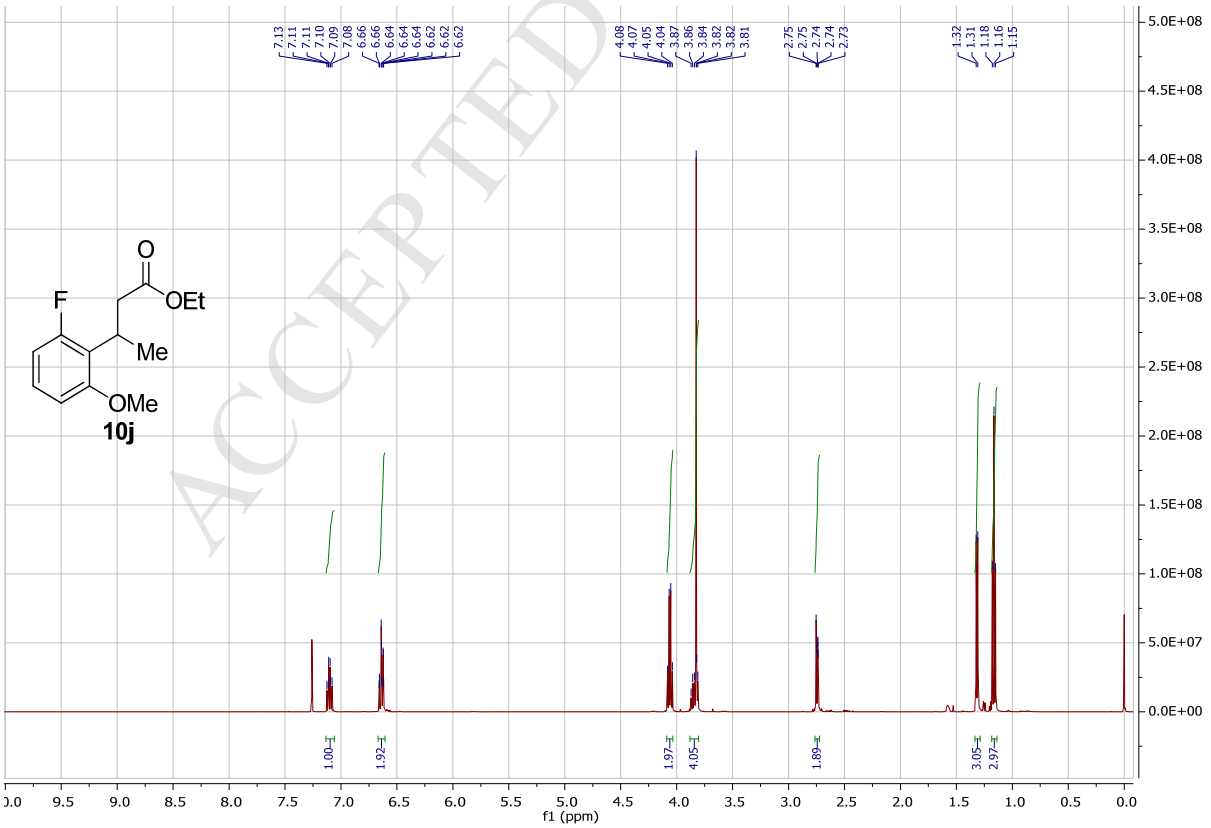
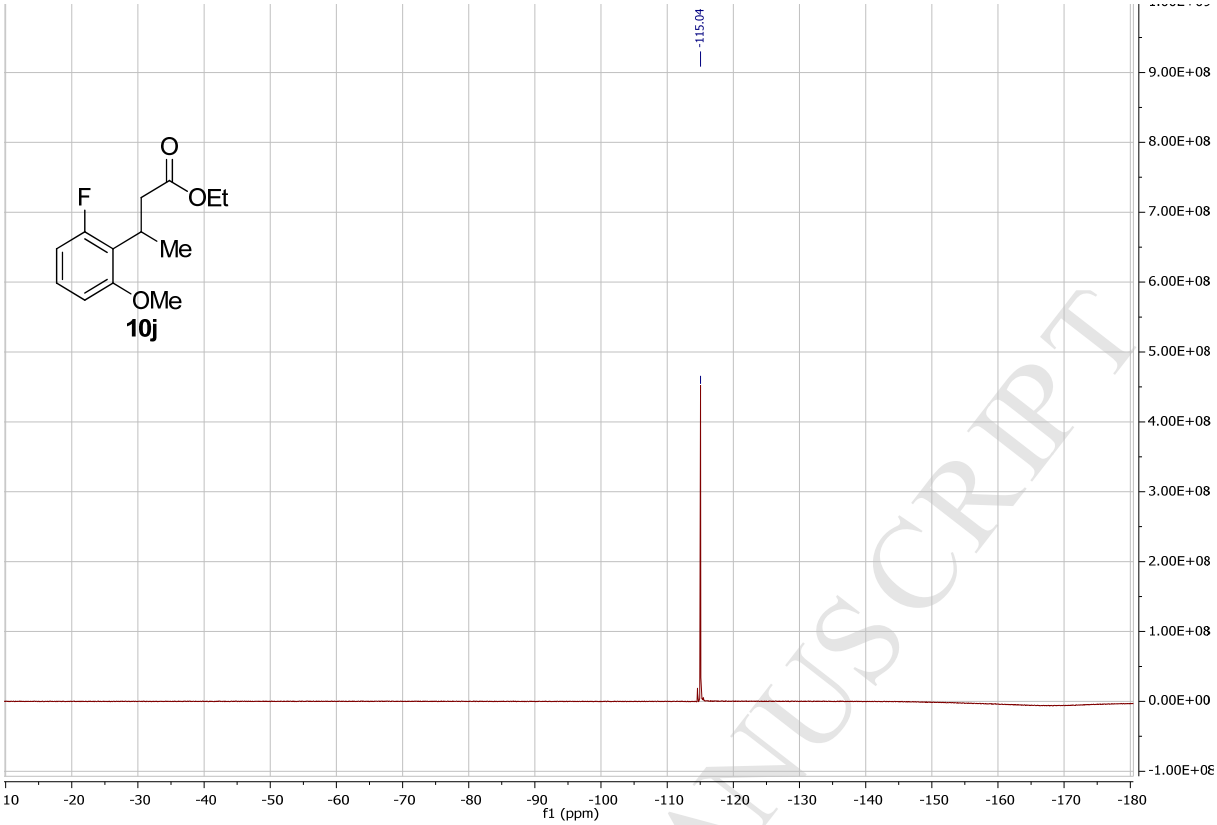
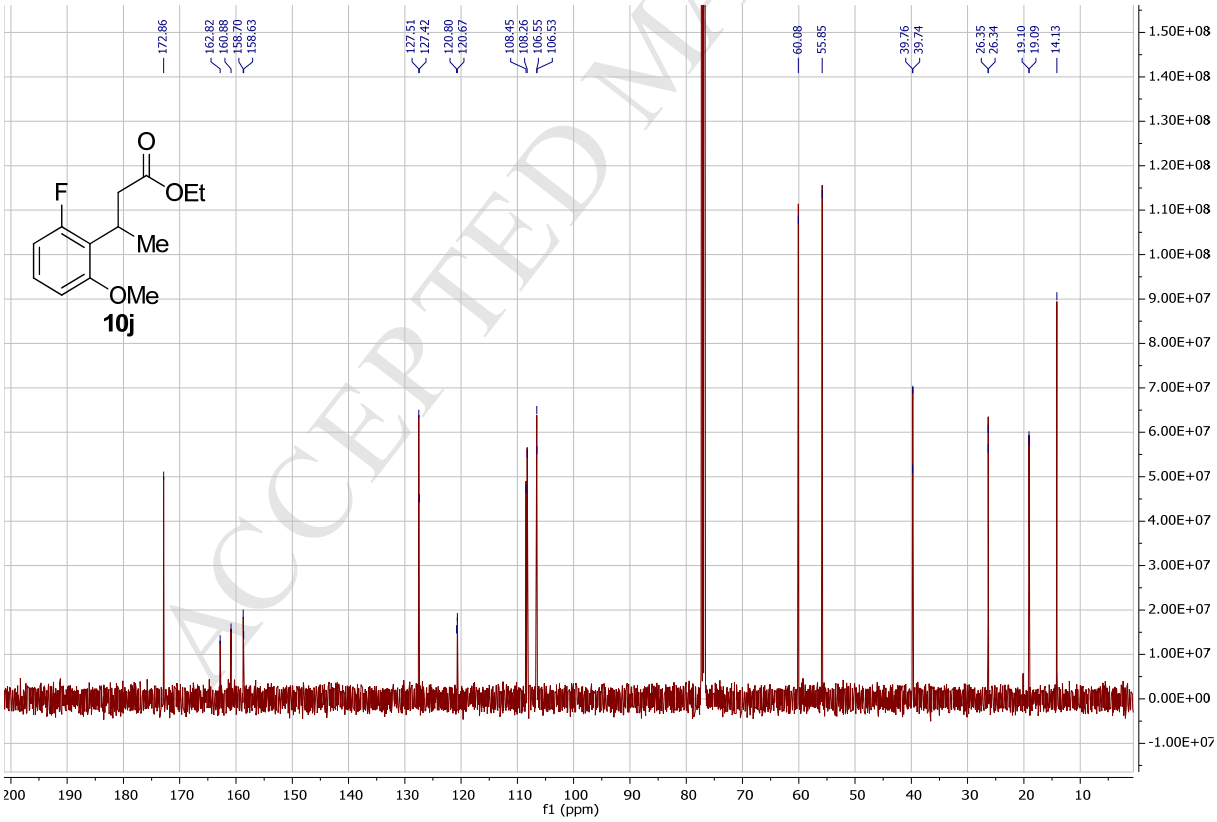




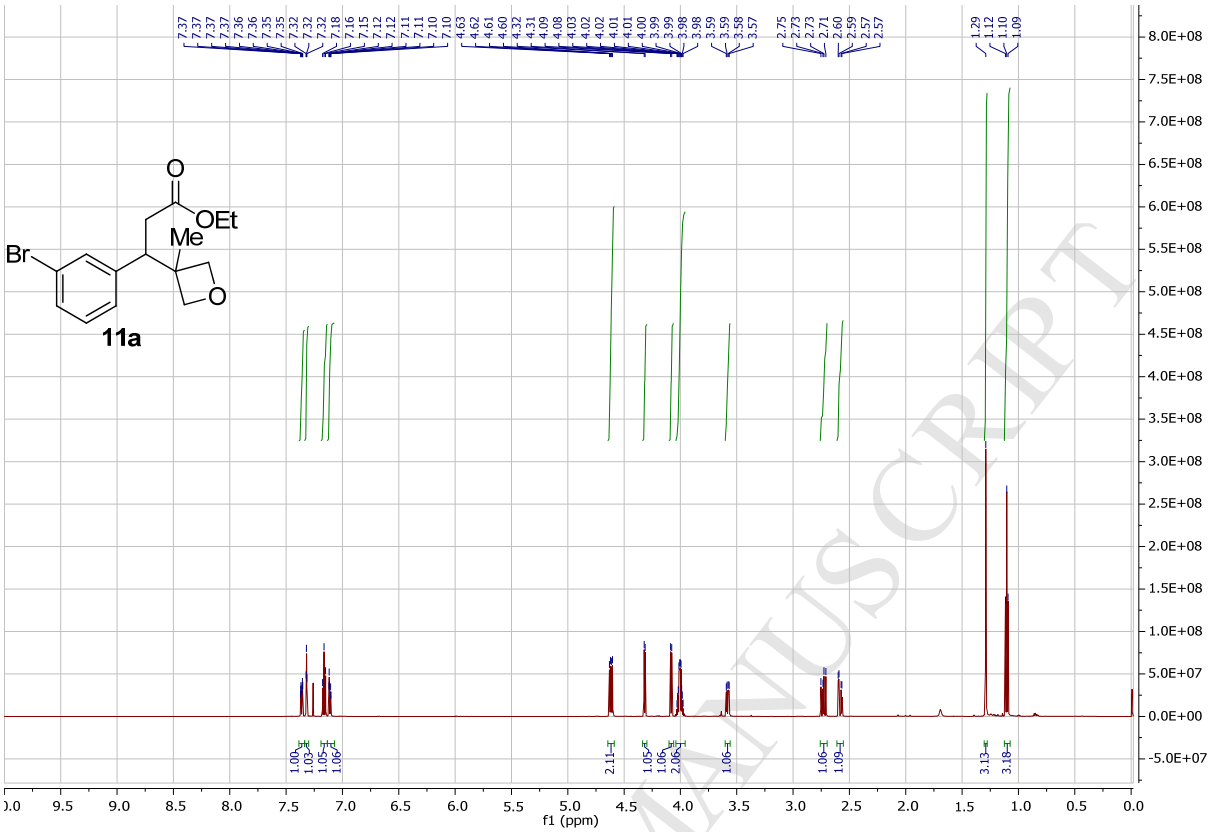

**ethyl 3-(2-fluoro-6-methoxyphenyl)butanoate (10j)**

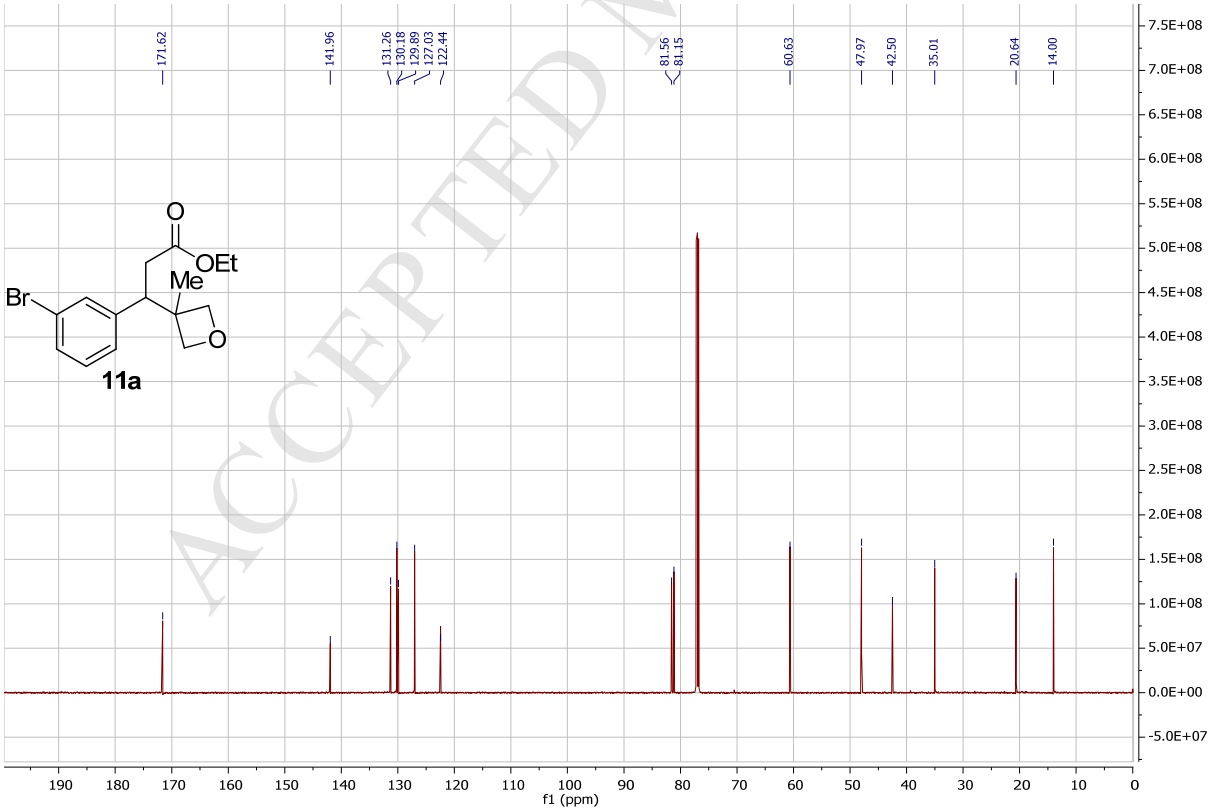




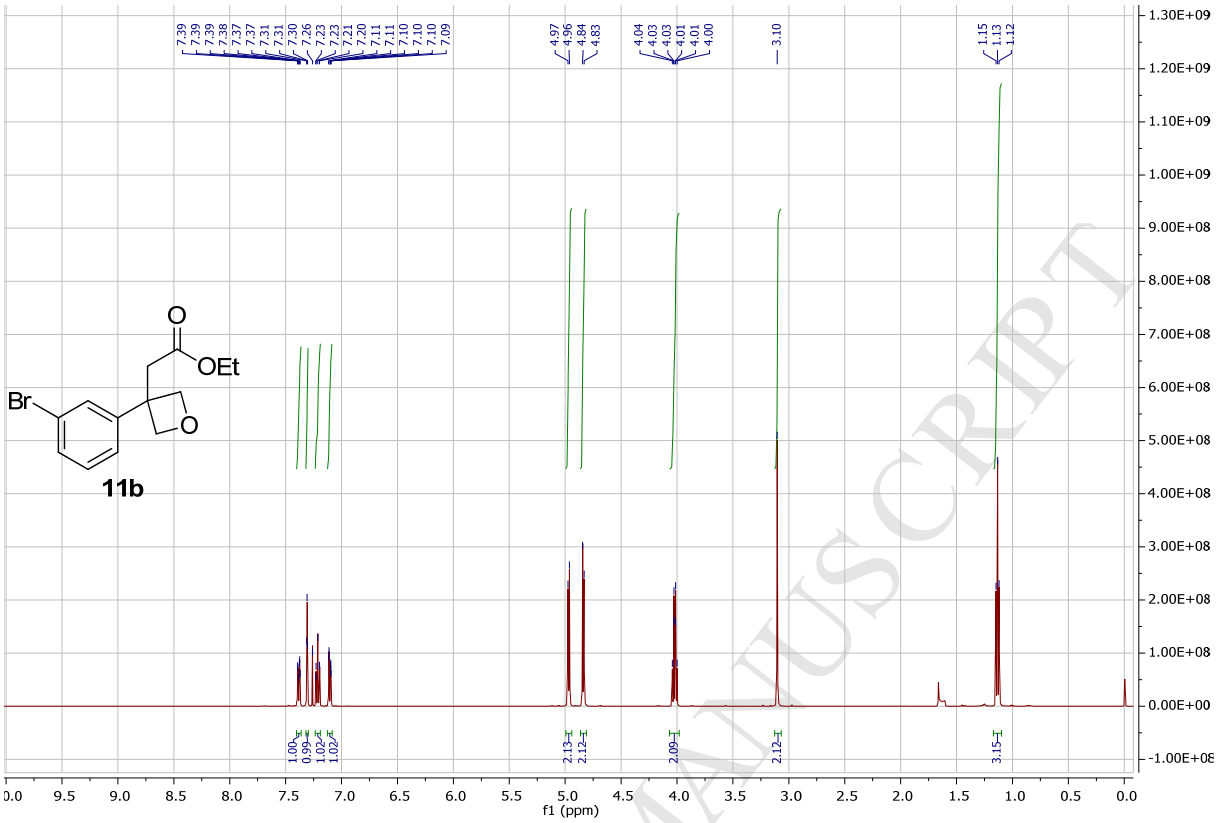



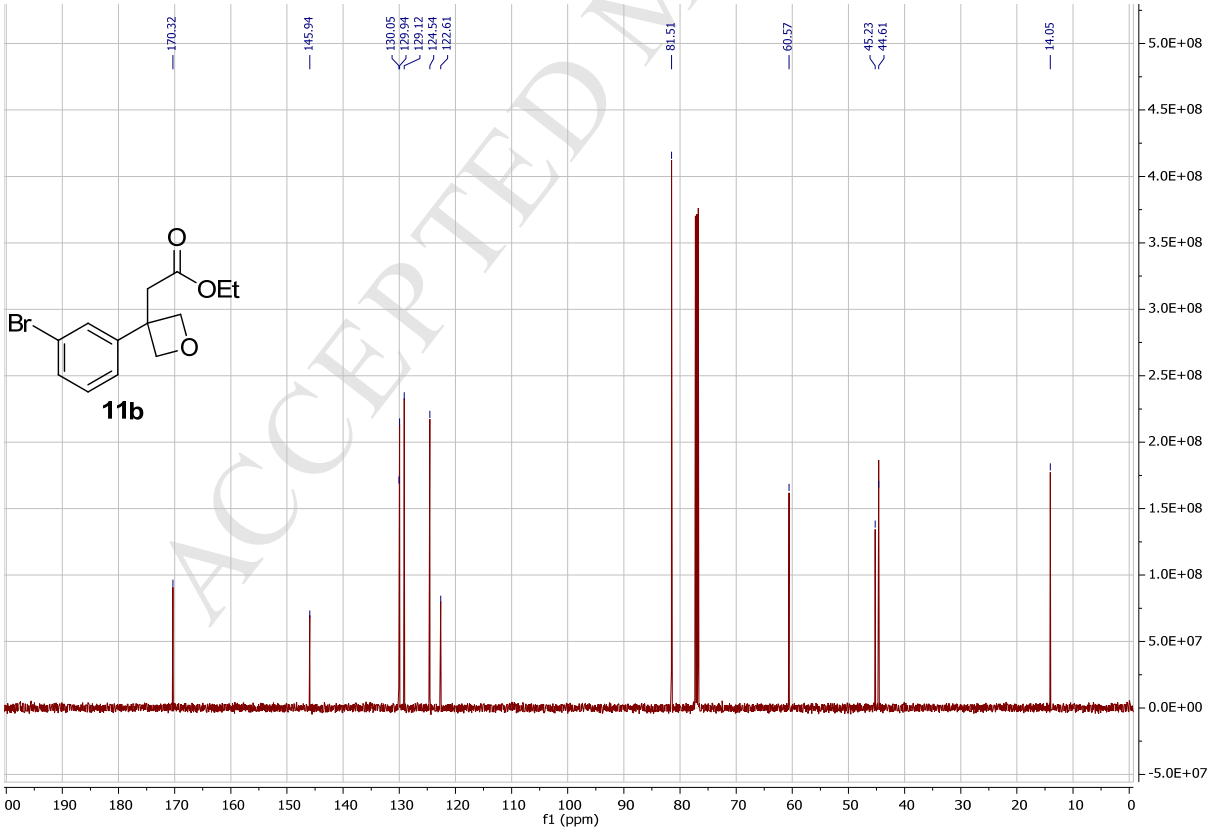
**ethyl 3-(3-bromophenyl)-3-(3-methyloxetan-3-yl)propanoate (11a)**



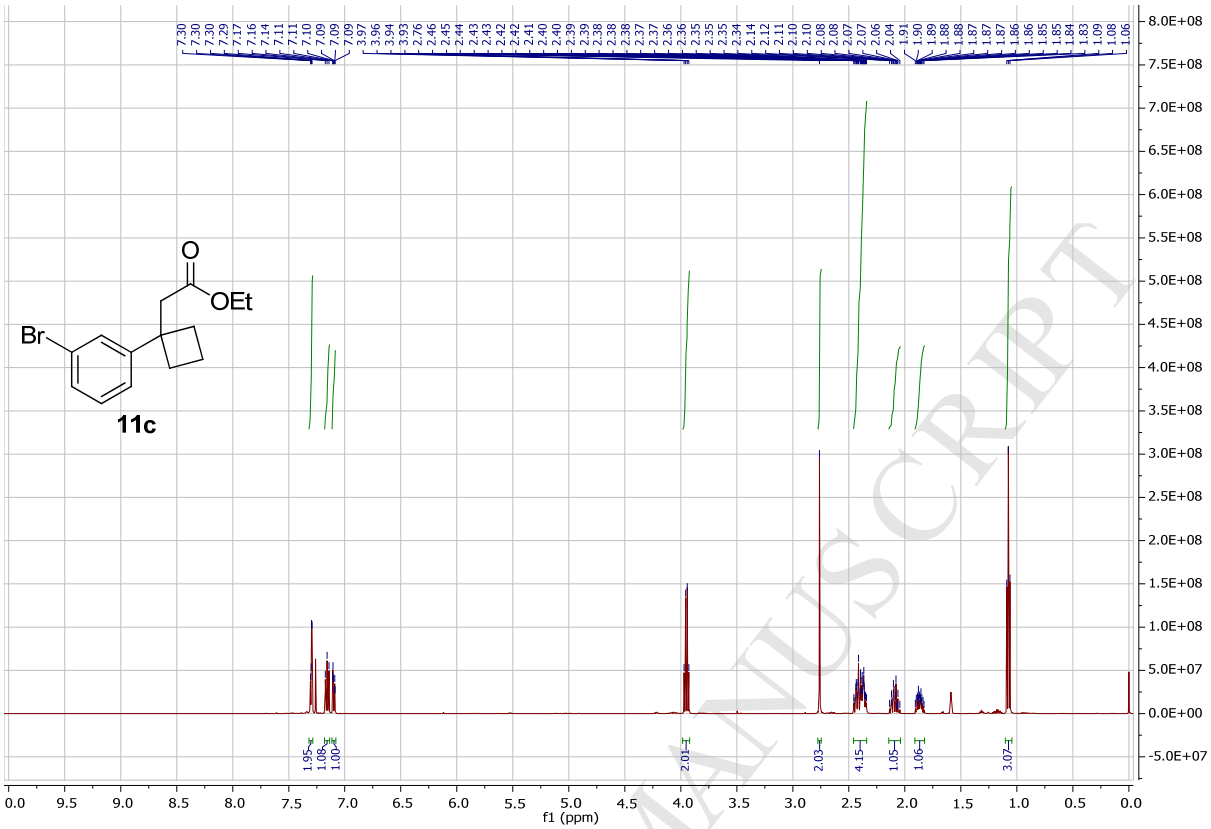



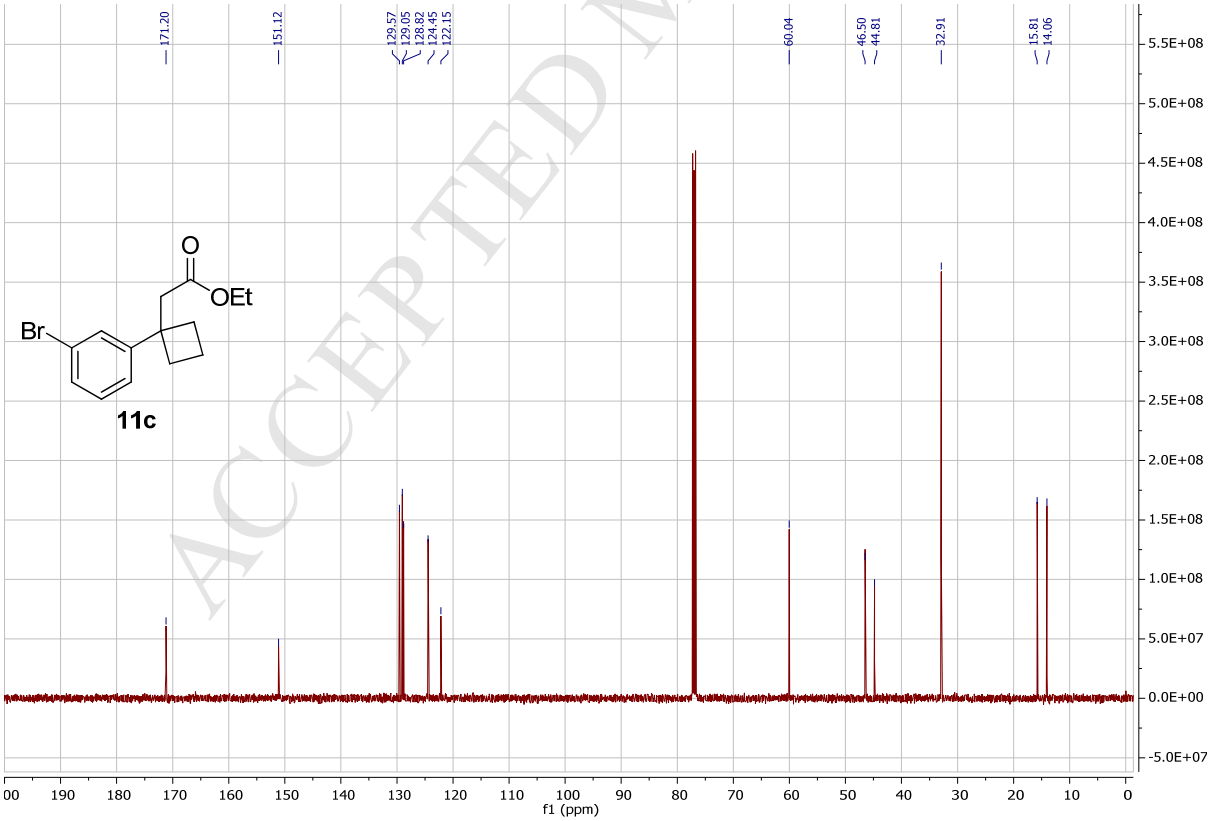
**ethyl 2-(3-(3-bromophenyl)oxetan-3-yl)acetate (11b)**



**ethyl 2-(1-(3-bromophenyl)cyclobutyl)acetate (11c)**



**tert-butyl 3-(3-bromophenyl)-3-(2-ethoxy-2-oxoethyl)azetidine-1-carboxylate (11d)**