Acylboronates in Polarity-Reversed Generation of Acyl Palladium(II) Intermediates

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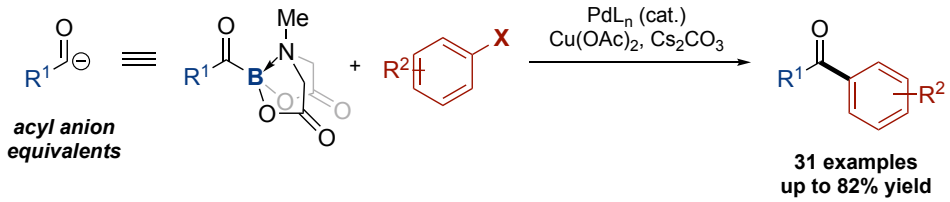
Abstract: We report a catalytic cross-coupling process between aryl (pseudo)halides and boron-based acyl anion equivalents. This mode of acylboronate reactivity represents polarity reversal, which is supported by the observation of tetracoordinated boronate and acyl palladium(II) species by ^{11}B, ^{31}P NMR, and mass spectrometry. A broad scope of aliphatic and aromatic acylboronates has been examined, as well as a variety of aryl (pseudo)halides.



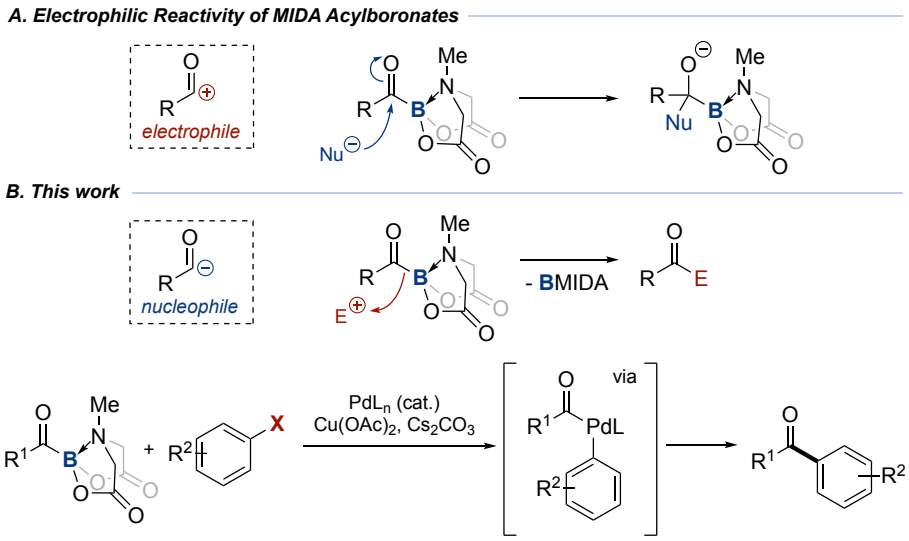
Introduction:

Polarity reversal (umpolung) allows one to switch the natural polarization of a functional group.[1] A number of established examples of this phenomenon demonstrate how electrophilic functional groups can be turned into nucleophiles and *vice versa*. Carbonyl compounds, which are electrophiles of prominence in organic synthesis, react with a broad range of nucleophilic species.[2] An umpolung transformation can reverse polarization such that the carbonyl functionality is made to react with electrophiles as an acyl or formyl anion.[2]

Acylboron compounds, which are a class of functionalized carbonyl group-containing molecules, have emerged as useful reagents in organic synthesis.[3,4] While effective as boron-containing building blocks, these molecules are not stable in their free boronic acid form.[5] Synthetic applications of acylboronates are enabled by the utilization of a MIDA (*N*-methyliminodiacetic acid) ligand[4c-g,7] or potassium organotrifluoroborates,[4a,b,g,h] which provide enhanced stability to borylated compounds. It is now well understood that acylboronates display reactivity that is similar to the ketone functionality.[8] The ability of acylboronates to undergo nucleophilic addition has found application in the synthesis of valuable boron-containing heterocycles, peptides, and proteins (Scheme 1a).[4,8] α-Functionalization of acylboronates reveals another mode of reactivity, further underscoring the relative stability of BMIDA under a range of reaction conditions.[4f,8c] Acylboronates have shown to participate in rearrangement reactions yielding *N*-, *O*-, and *C*-borylated species that are difficult to prepare by alternate routes as a result of boron atom migration.[8d] After derivatization, the MIDA ligand can be removed,[7] leading to the

isolation of stable molecules in free boronic acid form or non-borylated compounds afforded by rapid protodeboronation.[9]

While there are numerous reports on the electrophilic reactivity of acylboronates, a polarity-reversed application in catalyst has not been realized to date.[10] Herein, we report that readily available MIDA acylboronates[4g] give rise to boron analogs of α-keto acids. The boron-based acyl anion equivalents have been evaluated in the Pd-catalyzed Suzuki-Miyaura reaction of acylboronates and aryl (pseudo)halides in the construction of C(sp^2)-C(sp^2) bonds (Scheme 1b). The observation of tetracoordinated boronate and acyl palladium(II) intermediates provides additional insights into transmetalation in the Suzuki-Miyaura reaction and complements the previously published reports about this least understood step of the catalytic cycle.[11] A broad scope of aryl (pseudo)halides has been investigated, as well as a number of aryl and alkyl acylboronates.

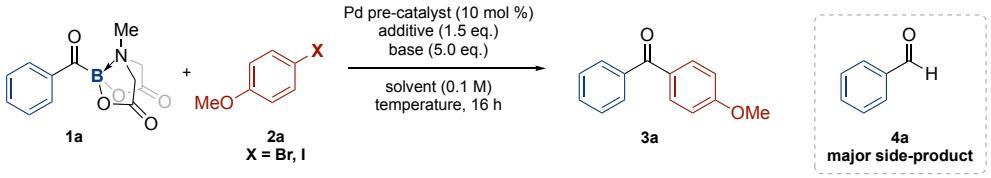


Scheme 1: a) Previous work on electrophilic reactivity of MIDA acylboronates; b) This work: Pd-catalyzed Suzuki-Miyaura cross-coupling reaction of acylboronates as acyl anion equivalents.

Results and Discussion:

We hypothesized that the polarity-reversed application of acylboronates could be examined in the Pd-catalyzed cross-coupling reaction of aryl halides. As a model reaction for our initial investigations, acylboronate **1a** and *p*-iodoanisole were combined with catalytic XPhos Pd G2, $Cu(OAc)_2$ as the stoichiometric additive, and K_2CO_3 as a base in 4:1 solvent mixture of DMF:*tert*-amyl alcohol (*t*-amylOH). The reaction afforded the desired ketone product **3a** in 44% yield (Table 1, entry 1). Analysis of the crude reaction mixture by ^{1}H NMR and GC-MS revealed the major side-product of the reaction to be benzaldehyde **4a**, owing to the protodeboronation of **1a**. Other side-products observed were products of aryl iodide homocoupling, deiodination, and decarbonylative cross-coupling. To optimize the reaction conditions, solvent, palladium species, base, additive, and temperature were screened. Switching *t*-amylOH to IPA led to lower yields of **3a** (Entry 2), but omitting alcoholic co-solvent resulted in a slight increase in yield (Entry 3). Changing *p*-iodoanisole to *p*-bromoanisole did not have a major impact on the yield but limited the formation of other side-products, such as biaryl derivatives to <10%, which aids purification

(Entry 4). Other solvents, such as MeCN, toluene, and dioxane were ineffective, likely due to the reduced solubility of **1a** (Entries 5 – 7). Switching the stoichiometric additive to CuCl and CuI, or decreasing the equivalents of $Cu(OAc)_2$ had a negative impact on the reaction (Entries 8 – 10). Other Pd species were inferior compared to XPhos Pd G2 (Entries 11 – 14). Increasing the temperature of the reaction to 100°C also decreased the yield of **3a** (Entry 15). While K_3PO_4 was found to be a less efficient base (Entry 16), Cs_2CO_3 was significantly more effective (Entry 17). Decreasing the reaction temperature to 60°C led to the formation of **3a** in 73% yield (Entry 18).



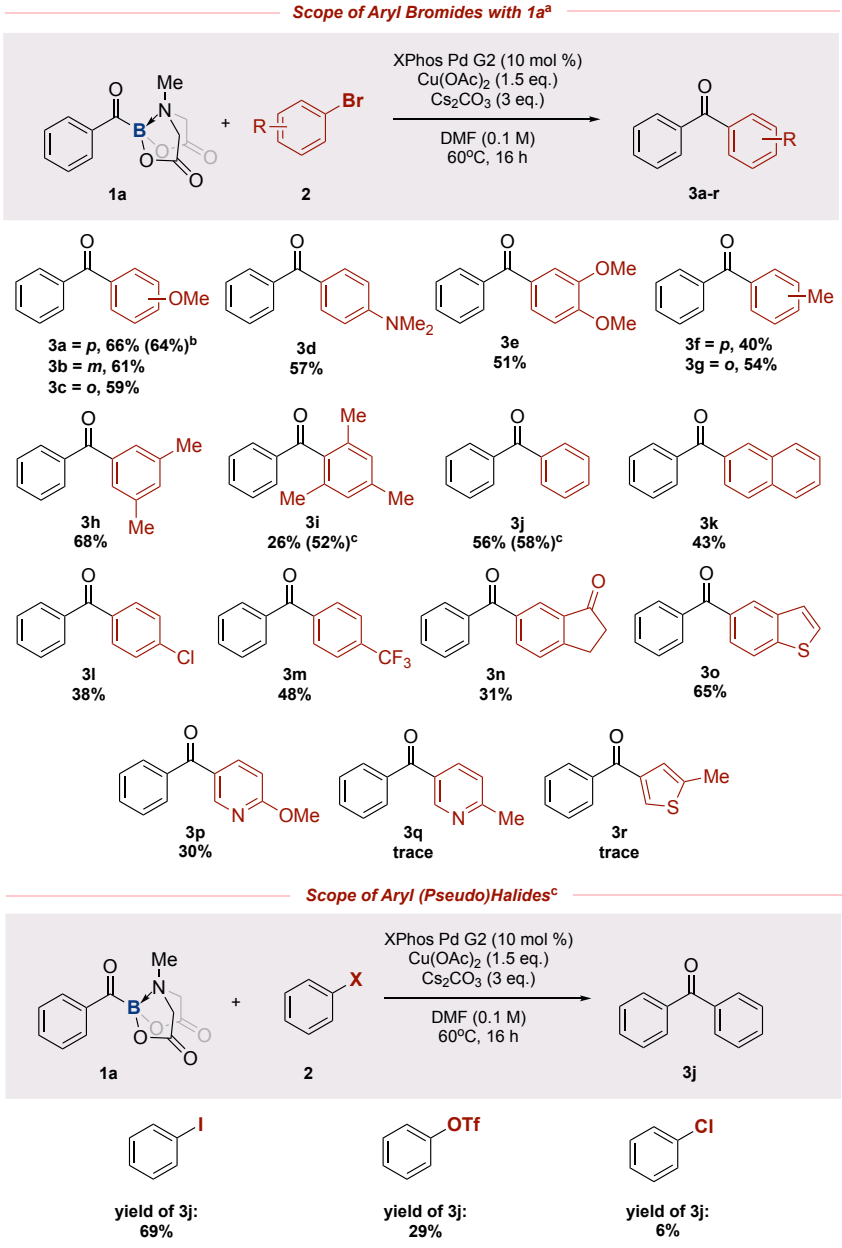
entry	Pd pre-catalyst	base	additive	solvent	temp	yield (%)
1[a]	XPhos Pd G2	K_2CO_3	$Cu(OAc)_2$	4:1 DMF:*t*-amylOH	80	44
2[a]	XPhos Pd G2	K_2CO_3	$Cu(OAc)_2$	4:1 DMF:IPA	80	33
3[a]	XPhos Pd G2	K_2CO_3	$Cu(OAc)_2$	DMF	80	49
4[b]	XPhos Pd G2	K_2CO_3	$Cu(OAc)_2$	DMF	80	47
5[b]	XPhos Pd G2	K_2CO_3	$Cu(OAc)_2$	MeCN	80	13
6[b]	XPhos Pd G2	K_2CO_3	$Cu(OAc)_2$	toluene	80	19
7[b]	XPhos Pd G2	K_2CO_3	$Cu(OAc)_2$	dioxane	80	12
8[b]	XPhos Pd G2	K_2CO_3	CuCl	DMF	80	10
9[b]	XPhos Pd G2	K_2CO_3	CuI	DMF	80	6
10[b]	XPhos Pd G2	K_2CO_3	$Cu(OAc)_2$[c]	DMF	80	17
11[b]	XPhos Pd G3	K_2CO_3	$Cu(OAc)_2$	DMF	80	37
12[b]	CPhos Pd G2	K_2CO_3	$Cu(OAc)_2$	DMF	80	36
13[b]	SPhos Pd G2	K_2CO_3	$Cu(OAc)_2$	DMF	80	30
14[b]	RuPhos Pd G2	K_2CO_3	$Cu(OAc)_2$	DMF	80	26
15[b]	XPhos Pd G2	K_2CO_3	$Cu(OAc)_2$	DMF	100	36
16[b]	XPhos Pd G2	K_3PO_4	$Cu(OAc)_2$	DMF	80	24
17[b]	XPhos Pd G2	Cs_2CO_3	$Cu(OAc)_2$	DMF	80	61
18[b]	**XPhos Pd G2**	**Cs_2CO_3**	**$Cu(OAc)_2$**	**DMF**	**60**	**73 (66%)**

Table 1. The Suzuki-Miyaura reaction optimization. Reaction conditions: **1a** (1.5 eq.), Pd pre-catalyst (10 mol %), additive (1.5 eq.) and base (5.0 eq.) were combined in a flame-dried 0.5-dram vial under nitrogen atmosphere. Solvent (0.1 M) was added followed by *p*-bromo- or iodoanisole (0.05 mmol, 1.0 eq.). The reaction was capped and stirred for 16 hours at the indicated temperature. Production of **3a** was referenced to 1,3,5-trimethoxybenzene and the NMR yield was calculated accordingly. [b] Reactions were carried out with *p*-iodoanisole. [c] Reactions were carried out with *p*-bromoanisole. [d] 0.75 eq. was used.

The scope of the reaction was explored with respect to aryl bromide utilizing the optimized reaction conditions (Scheme 2). *para-*, *meta-*, and *ortho*-Bromoanisole were employed in the transformation to afford the corresponding ketones **3a-3c** in good yield. The position of the substituent on the aromatic ring of aryl bromide did not have a significant influence on the reaction outcome. Notably, the reaction producing **3a** was successfully scaled up to 1 mmol under standard conditions. The amine functional group was tolerated in the reaction (**3d**). An arene with increased electron density was a suitable coupling partner and led to product formation in a good yield (**3e**). Reactions with mono-, di-, and tri-methylated aryl bromides provided ketones **3f-i** in moderate yields. Ketones **3j** and **3k** were synthesized in 56% and 43% yield, respectively. The use

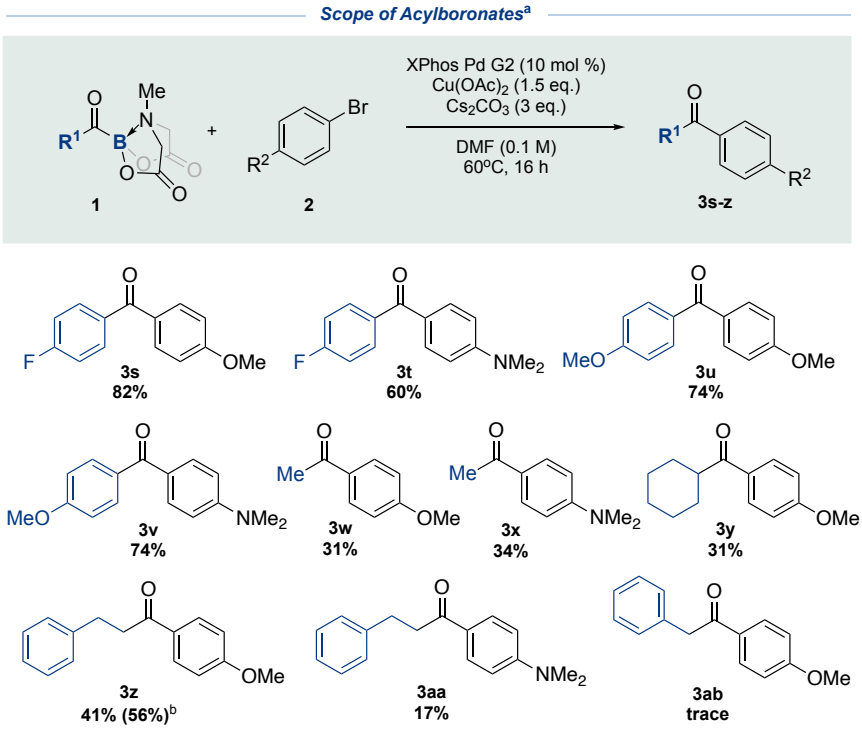
of *p*-bromochlorobenzene afforded the corresponding ketone **3l** in 38%, showing that aryl bromides were more reactive in the transformation than aryl chlorides. In general, substrates bearing electron-donating groups reacted more efficiently in the cross-coupling reaction, whereas the presence of electron-withdrawing groups, such as trifluoromethyl (**3m**), cyclic ketone (**3n**), benzothiophene (**3o**), and methoxypyridine (**3p**) on the arene resulted in lower yields of the corresponding ketone products. Pyridyl and methylthiophene were not compatible under the reaction conditions and provided only a trace amount of the corresponding ketones (**3q** and **3r**).

Next, we investigated the scope of electrophilic partners. The reaction of iodobenzene afforded the desired ketone **3j** in higher yield compared to the reaction of bromobenzene, albeit with more side-product formation. The same ketone was synthesized in 29% assay yield when phenyl trifluoromethanesulfonate was used. Only a trace amount of **3j** was observed when chlorobenzene was used due to the relative difficulty of oxidative addition into the C-Cl bond.



Scheme 2. Scope of the Pd-catalyzed Suzuki-Miyaura reaction of MIDA acylboronate **1a** with aryl bromides. Yields refer to the isolated product. [a] Reactions were performed on a 0.1 mmol scale using **1a** (1.5 eq.), aryl bromide (1.0 eq.), XPhos Pd G2 (10 mol %), $Cu(OAc)_2$ (1.5 eq.), Cs_2CO_3 (3.0 eq.) in DMF (0.1 M), 60°C, 16 h. [b] Performed on a 1 mmol scale under standard conditions. [c] NMR yield was determined by using 1,3,5-trimethoxybenzene as an internal standard.

The compatibility of other acylboronates to the cross-coupling conditions was also evaluated (Scheme 3). The introduction of an electron-withdrawing group, such as fluorine, to the aromatic ring of acylboronate resulted in successful reactions with *p*-bromoanisole and *p*-bromo-*N,N*-dimethylaniline (**3s** and **3t**). The reactions of *p*-methoxybenzoyl boronate with the same aryl halides afforded the corresponding ketones **3u** and **3v** in 74% and 60% yield, respectively. We next investigated the compatibility of aliphatic acylboronates in the cross-coupling reaction. Gratifyingly, when acetyl boronate was employed as the nucleophilic partner, the reactions were successful and provided the desired ketones **3w** and **3x**. The reaction of cyclohexanecarbonyl boronate gave the product (**3y**) in good yield. Ketones **3z** and **3aa** were synthesized in 41% and 17% yield, respectively, in the reaction with 3-phenylpropanoyl boronate. The reaction of phenylacetyl boronate provided only trace amount of the desired ketone **3ab**.



Scheme 3. Scope of the Pd-catalyzed Suzuki-Miyaura reaction of MIDA acylboronate **1** with aryl bromides. Yields refer to the isolated product. [a] Reactions were performed on a 0.1 mmol scale using **1** (1.5 eq.), aryl bromide (1.0 eq.), XPhos Pd G2 (10 mol %), $Cu(OAc)_2$ (1.5 eq.), Cs_2CO_3 (3.0 eq.) in DMF (0.1 M), 60°C, 16 h. [b] NMR yield was determined by using 1,3,5-trimethoxybenzene as an internal standard.

In order to gain insight into the mechanism of the reaction and identify possible intermediates, analysis by *in situ* NMR spectroscopy was employed. Due to the poor solubility of Cs_2CO_3 and the formation of insoluble by-products, the reaction of **1a** and **2a** in DMF-d_7 under standard conditions was not homogeneous and signals of the ^{1}H NMR spectrum were too broad to be

analyzed quantitatively and qualitatively. Instead, a series of control reactions was conducted and monitored by ^{11}B NMR spectroscopy. The reaction of **1a** and **2a** under standard conditions in DMF was monitored over 17 hours (Table 2, entry 1). After 1 hour, a ^{11}B NMR spectrum consisted of a signal at 5.5 ppm corresponding to **1a** and a new resonance at 0.47 ppm. The intensity of the latter continued to rise over the course of the reaction, accompanied by the disappearance of the resonance of **1a** within 11 hours. When **1a** was mixed with 1.5 equivalents of $Cu(OAc)_2$ and 3.0 equivalents of Cs_2CO_3 in DMF at 60°C in the absence of Pd catalyst, the same signal at 0.47 ppm in the ^{11}B NMR spectrum was observed (Entry 2). Further analysis was required to probe the intermediacy of the species with the distinct resonance at 0.47 ppm that appeared in the course of both control reactions.

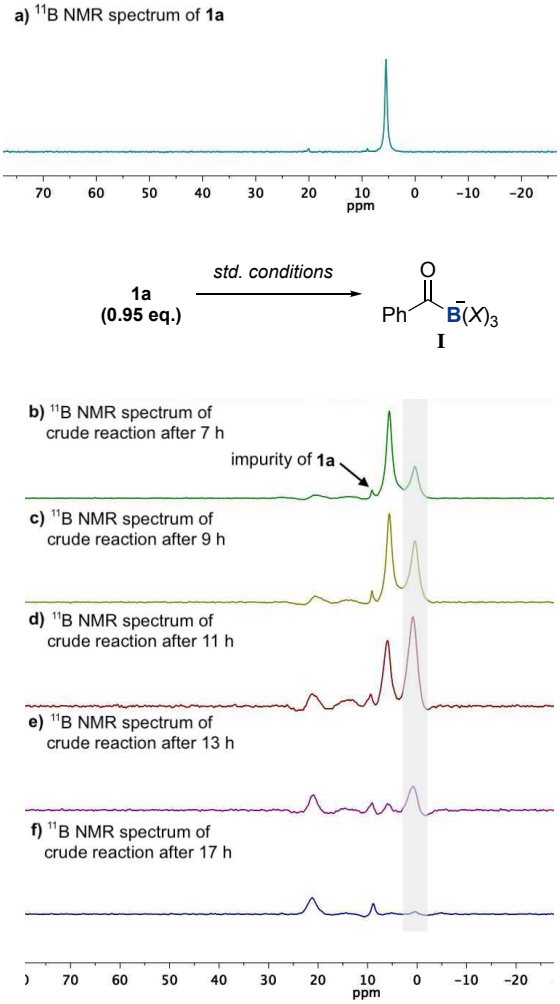
entry	deviation from standard conditions[a]	^{11}B NMR resonances
1	none	0.47 ppm
2	no XPhos Pd G2, no **2a**	0.47 ppm
3	no $Cu(OAc)_2$	no conversion
4	only **1a** and $Cu(OAc)_2$	no conversion
5	only **1a** and Cs_2CO_3	no conversion
6	only **1a** and CsOAc	no conversion
7	only **1a**, $Cu(OAc)_2$, and CsOAc	no conversion

Table 2. Control reactions monitored by ^{11}B NMR spectroscopy. [a]Standard conditions: **1a** (1.5 eq.), aryl bromide (1.0 eq.), XPhos Pd G2 (10 mol %), $Cu(OAc)_2$ (1.5 eq.), Cs_2CO_3 (3.0 eq.) in DMF (0.1 M), 60°C, 16 h.

Additional control reactions were performed to get a better understanding of the reaction mechanism. No conversion of **1a** was observed by ^{11}B NMR spectrometry when the reaction was conducted without $Cu(OAc)_2$ but otherwise standard conditions (Entry 3). No conversion (<5%) was detected when **1a** was mixed with only $Cu(OAc)_2$ at 60°C (Entry 4). No change in ^{11}B NMR spectrum was observed when **1a** was reacted with 3.0 equivalents of Cs_2CO_3 at 60°C (Entry 5). Since CsOAc is potentially generated *in situ* (from the metathesis reaction between $Cu(OAc)_2$ and Cs_2CO_3), we conducted two control reactions of **1a** with only CsOAc (Entry 6) and with CsOAc and $Cu(OAc)_2$ (Entry 7) as additives. No reaction was observed in either experiment. Based on these results, both $Cu(OAc)_2$ and Cs_2CO_3 are needed for the generation of the species with the ^{11}B NMR signal at 0.47 ppm. The ^{11}B NMR resonance in the area between 9 and -7 ppm is typical of tetracoordinated boron compounds bearing -OR groups.[12] A tetracoordinated acylboron intermediate with the ^{11}B NMR chemical shift of 2.32 ppm was recently observed by Mankad and co-workers in the copper-catalyzed carbonylative borylation of alkyl halides, as tricoordinated pinacol-acylboron coordinated with one equivalent of Li*O*t*Bu*.[4g] Bode and co-workers originally proposed that hydrolysis of MIDA acylboronate leads to the highly reactive boron-ligated intermediate,[8a] which either undergoes ligation with *O*-Me hydroxylamines or rapid protodeboronation in the presence of water.[9] In our study, the observed intermediate with the ^{11}B NMR signal of 0.47 ppm likely corresponds to the tetracoordinated boron species **I**, where X is either acetate or carbonate anions.

To assess whether or not **I** is the reactive intermediate in the reaction, a sub-stoichiometric amount of **1a** was subjected to the standard conditions (Scheme 4). The signal at 0.47 ppm appeared after 1 hour and its intensity continued to increase, while the peak corresponding to **1a**

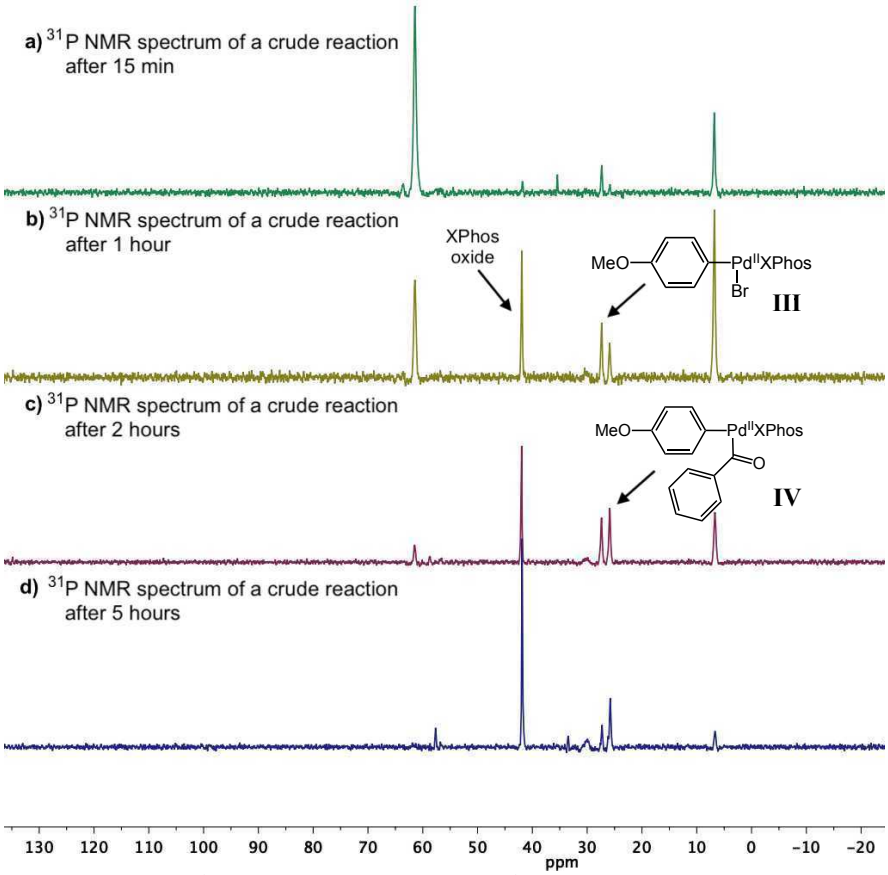
decreased. Gratifyingly, once **1a** was consumed (~11 hours), the resonance at 0.47 ppm began to disappear. After 16 hours, complete consumption of **I** was observed confirming the intermediacy of the species.



Scheme 4. Mechanistic analysis by ^{11}B NMR spectroscopy. a) ^{11}B NMR spectrum of **1a**; ^{11}B NMR spectra of the cross-coupling reaction of MIDA acylboronate **1a** (0.95 eq.), aryl bromide (1.0 eq.), XPhos Pd G2 (10 mol %), $Cu(OAc)_2$ (1.5 eq.), Cs_2CO_3 (3.0 eq.) in DMF (0.1 M), 60°C, monitored over b) 7 hours; c) 9 hours; d) 11 hours; e) 13 hours; f) 17 hours.

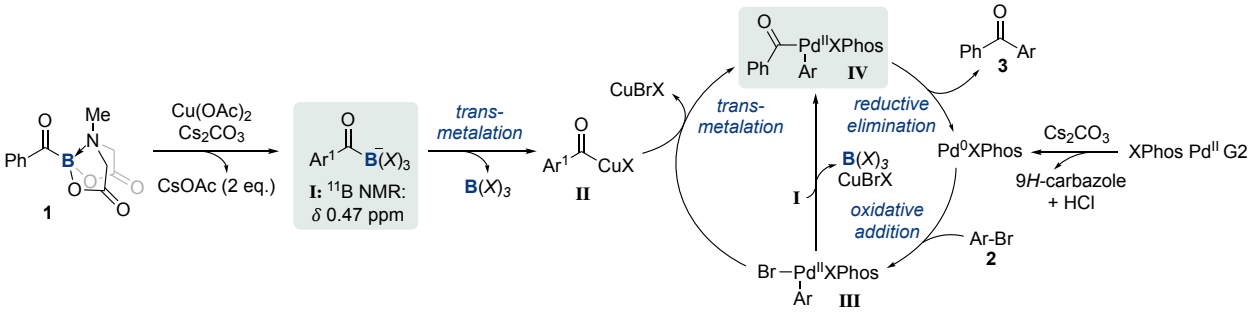
We then turned our attention to detecting the hypothesized intermediacy of an acyl palladium complex. The progress of a stoichiometric reaction of **1a**, **2a**, and Pd pre-catalyst was monitored by ^{31}P NMR spectrometry over 16 hours under standard conditions (Scheme 5). After 15 minutes, the signals at 41.9 ppm, which corresponded to XPhos oxide, and 27.4 ppm appeared. The latter was assigned to the oxidative addition palladium complex **III**, which chemical shift was consistent with previous literature reports.[13] After 1 hour, a new signal at 25.9 ppm appeared and its intensity continued to rise while the resonance of **III** slowly disappeared. This new signal, upfield of 1.5 ppm from that of complex **III**, was assigned to the acyl palladium species **IV**. A similar upfield shift for analogous carbonylated complexes was observed by the Moser[14] and Yamamoto[15]

groups in Pd-catalyzed carbonylation reactions with carbon monoxide. Moreover, **IV** was detected by HRMS (ESI+) under stoichiometric conditions with the expected isotopic distribution.



Scheme 5. Mechanistic analysis by ^{31}P NMR spectroscopy. a)-d) ^{31}P NMR spectrum of the stoichiometric reaction of MIDA acylboronate **1a** (1.5 eq.), 4-bromoanisole (1.0 eq.), XPhos Pd G2 (1.0 eq.), $Cu(OAc)_2$ (1.5 eq.), Cs_2CO_3 (3.0 eq.) in DMF (0.1 M), 60°C; a) 15 min; b) 1 hour; c) 2 hours; d) 5 hours.

Based on the experimental results and previously reported literature, a plausible reaction mechanism shown in Scheme 6 was proposed. According to this scheme, acylboronate **1** reacts with $Cu(OAc)_2$ and Cs_2CO_3 to generate intermediate **I**, which was observed by ^{11}B NMR spectrometry, and 2 equivalents of CsOAc. Further transmetalation affords acyl copper species **II**. The Pd(0) active catalyst is generated from the base-mediated reductive elimination of the Pd(II) pre-catalyst. Oxidative addition with aryl bromide affords intermediate **III**. Subsequent transmetalation with **II** or directly with **I** gives acyl palladium complex **IV**. Further reductive elimination provides the desired ketone **3** and regenerates the active catalyst.



Scheme 6. Proposed mechanism of the Suzuki-Miyaura reaction reaction of MIDA acylboronates.

In summary, we have developed a new Pd-catalyzed cross-coupling reaction between aryl (pseudo)halides and MIDA acylboronates that serve as acyl anion equivalents. The mild reaction conditions were found to be compatible with various aliphatic and aromatic acylboronates. ^{11}B and ^{31}P NMR mechanistic studies, as well as mass spectrometry, revealed that the tetracoordinated boron and acyl palladium(II) species are possible reaction intermediates. Further exploration of boron-based acyl anion equivalents in chemical synthesis as well as studies aimed at defining broader utility for the $ArC(O)B(OH)_2$ class of molecules are underway in our laboratory.

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Acylboronates in Polarity-Reversed Generation of Acyl Palladium(II) Intermediates

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Supplementary Information

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General Information

Solvents

All solvents and reagents were purchased from commercial sources and dried over 4Å MS prior to use unless otherwise stated. Dioxane and toluene were distilled from sodium benzophenone ketyl prior to use. Acetonitrile (MeCN) was distilled from calcium hydride prior to use. Dimethylformamide (DMF) was purchased from MilliporeSigma in a Sure/Seal^{TM} bottle and used as received. Acyl MIDA boronates (**1a-1g**) were synthesized according to literature procedures.[1, 2]

Chromatography

Flash column chromatography was carried out using Silicycle 230-400 mesh silica gel. Thin-layer chromatography was performed on Merck Aluminum-backed TLC Silica gel 60 F254 and visualized using a UV lamp (254 nm) and curcumin stain.

Nuclear Magnetic Resonance Spectroscopy

^{1}H, ^{11}B, ^{13}C, ^{31}P, and ^{19}F NMR and 2D NMR experiments were performed on Varian Mercury 300 MHz, 400 MHz, 500 MHz, 600 MHz or Bruker 400 MHz spectrometers. ^{11}B NMR chemical shifts(δ) are reported in parts per million (ppm) referenced to an external standard of $BF_3 \cdot Et_2O$ (δ = 0 ppm). ^{1}H NMR chemical shifts (δ) are reported in parts per million (ppm) referenced to residual protonated solvent peak (CD_3CN δ = 1.94 ppm, $CDCl_3$ δ = 7.26 ppm). Spectral data is reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, dt = doublet of triplets, ddt = doublet of doublet of triplets, dtd = doublet of triplet of doublets, m = multiplet, br = broad), coupling constant (J) in Hertz (Hz), and integration. ^{13}C NMR spectra chemical shifts (δ) are reported in parts per million (ppm) and were referenced to carbon resonances in the corresponding NMR solvent (CD_3CN δ = 118.2, 1.3 (center line), $CDCl_3$ δ = 77.1 (center line)). Carbon atoms exhibiting significant line broadening brought about by boron substituents were not reported due to quadrupolar relaxation. ^{19}F NMR chemical shifts (δ) are reported in parts per million (ppm) and referenced to an external standard of $CFCl_3$ (δ = 0.0).

Mass Spectroscopy

High resolution mass spectra were obtained on a VG 70-250S (double focusing) mass spectrometer at 70 eV or on an ABI/Sciex Qstar mass spectrometer with ESI or DART source, MS/MS and accurate mass capabilities.

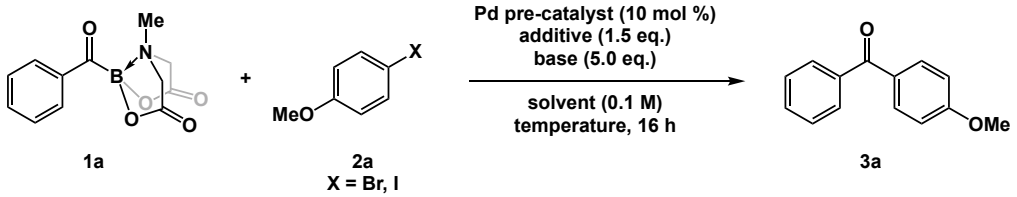
RP-HPLC/MS

Low-resolution mass spectra (ESI) were collected on an Agilent Technologies 1200 series HPLC paired to a 6130 Mass Spectrometer. Compounds were resolved on Phenomenex's Kinetex 2.6u C18 50x4.6mm column at room temperature with a flow of 1 mL/min. The gradient consisted of eluents A (0.1% formic acid in double distilled water) and B (0.1% formic acid in HPLC-grade acetonitrile).

Experimental procedure and characterization of compounds

Optimization of SMCC reaction conditions

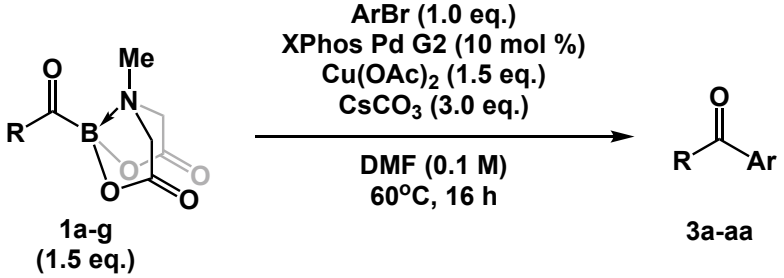
To a flame-dried vial equipped with a stir bar was added acyl MIDA boronate (**1a**) (0.075 mmol, 1.5 eq.), Pd pre-catalyst (0.005 mmol, 10 mol %), additive (0.075 mmol, 1.5 eq.), and a base (0.25 mmol, 5.0 eq.). The vial was evacuated and backfilled with nitrogen. This was repeated three times. Aryl halide (0.05 mmol, 1.0 eq.) and solvent (0.1 M) were subsequently added, and the reaction was stirred for 16 h in a heating block set to the indicated temperature. Upon completion, as indicated by TLC, the reaction was filtered. The assay yield of **3a** was determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as an internal standard.



entry	Pd pre-catalyst	base	additive	solvent	temp	yield (%)
1[a]	XPhos Pd G2	K_2CO_3	$Cu(OAc)_2$	4:1 DMF:*t*-amylOH	80	44
2[a]	XPhos Pd G2	K_2CO_3	$Cu(OAc)_2$	4:1 DMF:IPA	80	33
3[a]	XPhos Pd G2	K_2CO_3	$Cu(OAc)_2$	DMF	80	49
4[b]	XPhos Pd G2	K_2CO_3	$Cu(OAc)_2$	DMF	80	47
5[b]	XPhos Pd G2	K_2CO_3	$Cu(OAc)_2$	MeCN	80	13
6[b]	XPhos Pd G2	K_2CO_3	$Cu(OAc)_2$	toluene	80	19
7[b]	XPhos Pd G2	K_2CO_3	$Cu(OAc)_2$	dioxane	80	12
8[b]	XPhos Pd G2	K_2CO_3	CuCl	DMF	80	10
9[b]	XPhos Pd G2	K_2CO_3	CuI	DMF	80	6
10[b]	XPhos Pd G2	K_2CO_3	$Cu(OAc)_2$[c]	DMF	80	17
11[b]	XPhos Pd G3	K_2CO_3	$Cu(OAc)_2$	DMF	80	37
12[b]	CPhos Pd G2	K_2CO_3	$Cu(OAc)_2$	DMF	80	36
13[b]	SPhos Pd G2	K_2CO_3	$Cu(OAc)_2$	DMF	80	30
14[b]	RuPhos Pd G2	K_2CO_3	$Cu(OAc)_2$	DMF	80	26
15[b]	XPhos Pd G2	K_2CO_3	$Cu(OAc)_2$	DMF	100	36
16[b]	XPhos Pd G2	K_3PO_4	$Cu(OAc)_2$	DMF	80	24
17[b]	XPhos Pd G2	Cs_2CO_3	$Cu(OAc)_2$	DMF	80	61
18[b]	**XPhos Pd G2**	**Cs_2CO_3**	**$Cu(OAc)_2$**	**DMF**	**60**	**73 (66%)**

Table S1. The SMCC reaction optimization. **1a** (1.5 eq.), Pd pre-catalyst (10 mol %), additive (1.5 eq.) and base (5.0 eq.) were combined in a flame-dried 0.5-dram vial under nitrogen atmosphere. Solvent (0.1 M) was added followed by *p*-bromo- or iodoanisole (0.05 mmol, 1.0 eq.). The reaction was capped and stirred for 16 hours at the indicated temperature. Production of **3a** was referenced to 1,3,5-trimethoxybenzene and the NMR yield was calculated accordingly. [a] Reactions were carried out with *p*-iodoanisole. [b] Reactions were carried out with *p*-bromoanisole. [c] 0.75 eq. was used.

General procedure of the SMCC reaction with MIDA acylboronates

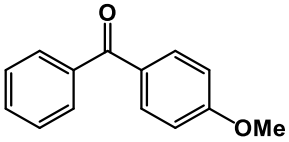


To a flame-dried vial equipped with a stir bar was added acyl MIDA boronate (**1a-g**) (0.15 mmol, 1.5 eq.), XPhos Pd G2 (0.01 mmol, 10 mol %), Cs_2CO_3 (0.3 mmol, 3.0 eq.) and $Cu(OAc)_2$ (0.15 mmol, 1.5 eq.). The vial was evacuated and backfilled with nitrogen. This was repeated three times. DMF (0.1 M) and aryl bromide (0.1 mmol, 1.0 eq.) were subsequently added, and the reaction was

stirred for 16 h in a heating block set to a temperature of 60 °C. Upon completion, as indicated by TLC, the reaction was filtered and loaded onto Celite. Purification via column chromatography provided the corresponding ketone products (**3a-3aa**).

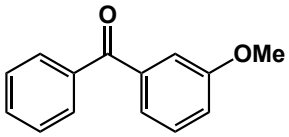
Characterization of ketones (3)

(4-Methoxyphenyl)(phenyl)methanone (3a)[3]



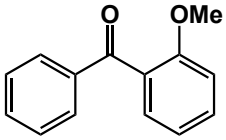
Yellow solid; 0.1 mmol scale: 66% yield, 0.066 mmol, 14.0 mg; 1 mmol scale: 64% yield, 0.643 mmol, 136.5 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.89 – 7.80 (m, 2H), 7.78 – 7.73 (m, 2H), 7.60 – 7.54 (m, 1H), 7.50 – 7.45 (m, 2H), 7.00 – 6.94 (m, 2H), 3.89 (s, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.7, 163.4, 138.4, 132.7, 132.0, 130.3, 129.9, 128.3, 113.7, 55.6 ppm.

(3-Methoxyphenyl)(phenyl)methanone (3b)[3]



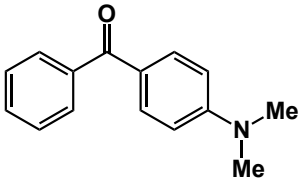
Yellow oil; 61% yield, 0.061 mmol, 12.9 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 – 7.78 (m, 2H), 7.62 – 7.52 (m, 1H), 7.52 – 7.42 (m, 2H), 7.40 – 7.31 (m, 3H), 7.12 (ddd, J = 8.0, 2.6, 1.4 Hz, 1H), 3.84 (s, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 196.5, 159.6, 138.9, 137.7, 132.5, 130.1, 129.3, 128.3, 122.9, 118.9, 114.4, 55.5 ppm.

(2-Methoxyphenyl)(phenyl)methanone (3c)[3]



Yellow oil; 59% yield, 0.059 mmol, 12.5 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 – 7.77 (m, 2H), 7.62 – 7.55 (m, 1H), 7.51 – 7.44 (m, 2H), 7.38 – 7.32 (m, 3H), 7.13 (ddd, J = 7.8, 2.8, 1.3 Hz, 1H), 3.85 (s, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 196.6, 159.7, 139.0, 137.7, 132.5, 130.1, 129.3, 128.3, 122.9, 118.9, 114.4, 55.5 ppm.

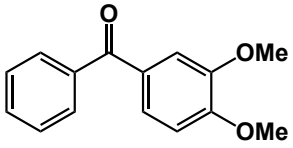
(4-(Dimethylamino)phenyl)(phenyl)methanone (3d)[4]



Green solid; 57% yield, 0.057 mmol, 12.8 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.83 – 7.79 (m, 2H), 7.76 – 7.69 (m, 2H), 7.56 – 7.48 (m, 1H), 7.48 – 7.42 (m, 2H), 6.72 – 6.63 (m, 2H), 3.06 (d, J = 0.9 Hz, 6H) ppm;

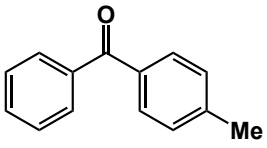
^{13}C NMR (126 MHz, $CDCl_3$) δ 195.2, 153.4, 139.4, 132.8, 131.2, 129.5, 128.1, 124.8, 110.6, 40.1 ppm.

(3,4-Dimethoxyphenyl)(phenyl)methanone (3e)[3]



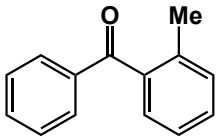
White solid; 51% yield, 0.051 mmol, 12.3 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 – 7.71 (m, 2H), 7.56 (d, *J* = 7.5 Hz, 1H), 7.52 – 7.43 (m, 3H), 7.38 (dd, *J* = 8.3, 2.0 Hz, 1H), 6.89 (d, *J* = 8.3 Hz, 1H), 3.96 (s, 3H), 3.94 (s, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.7, 153.1, 149.1, 138.4, 132.0, 130.4, 129.8, 128.3, 125.6, 112.2, 109.9, 56.2, 56.2 ppm.

Phenyl(*p*-tolyl)methanone (3f)[3]



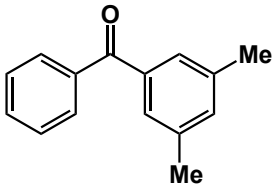
Yellow oil; 41% yield, 0.041 mmol, 8 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.81 – 7.76 (m, 2H), 7.75 – 7.71 (m, 2H), 7.60 – 7.55 (m, 1H), 7.50 – 7.45 (m, 2H), 7.32 – 7.27 (m, 2H), 2.50 – 2.34 (m, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 196.6, 143.4, 138.1, 135.0, 132.3, 130.4, 130.1, 129.1, 128.3, 21.8, 21.8 ppm.

Phenyl(*o*-tolyl)methanone (3g)[3]



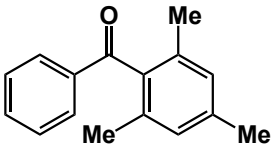
Colorless oil; 54% yield, 0.054 mmol, 10.6 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.85 – 7.78 (m, 2H), 7.63 – 7.55 (m, 1H), 7.52 – 7.43 (m, 2H), 7.39 (dd, *J* = 7.4, 1.5 Hz, 1H), 7.35 – 7.28 (m, 2H), 7.28 – 7.21 (m, 1H), 2.34 (s, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 198.8, 138.7, 137.9, 136.9, 133.3, 131.1, 130.4, 130.3, 128.6, 128.6, 125.3, 20.1 ppm.

(2,6-Dimethylphenyl)(phenyl)methanone (3h)[5]



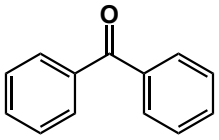
Yellow solid; 68% yield, 0.068 mmol, 14.2 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 – 7.76 (m, 2H), 7.61 – 7.55 (m, 1H), 7.50 – 7.45 (m, 2H), 7.41 (dt, *J* = 1.6, 0.8 Hz, 2H), 7.22 (tt, *J* = 1.7, 0.8 Hz, 1H), 2.38 (s, 6H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.3, 138.0, 138.0, 137.8, 134.2, 132.4, 130.2, 130.1, 128.4, 128.3, 127.9, 21.3 ppm.

Mesityl(phenyl)methanone (3i)[6]



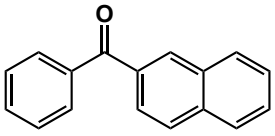
Yellow oil; 26 % yield, 0.026 mmol, 5.9 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.88 – 7.73 (m, 2H), 7.64 – 7.51 (m, 1H), 7.51 – 7.38 (m, 2H), 6.90 (t, *J* = 1.1 Hz, 2H), 2.33 (s, 3H), 2.08 (s, 6H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 200.9, 138.6, 137.4, 137.0, 134.3, 133.7, 129.5, 128.9, 128.5, 21.2, 19.5 ppm.

Benzophenone (3j)[3]



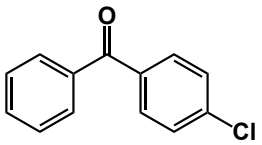
Off-white solid; 56% yield, 0.056 mmol, 10.1 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 – 7.78 (m, 4H), 7.63 – 7.54 (m, 2H), 7.52 – 7.45 (m, 4H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 196.9, 137.7, 132.5, 130.2, 128.4 ppm.

Naphthalen-2-yl(phenyl)methanone (3k)[3]



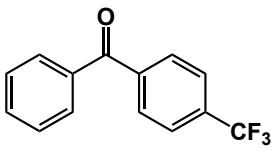
Yellow oil; 43% yield, 0.043 mmol, 10.0 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28 – 8.26 (m, 1H), 7.97 – 7.85 (m, 6H), 7.67 – 7.49 (m, 5H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 196.9, 138.0, 135.4, 134.9, 132.5, 132.4, 132.0, 130.2, 129.5, 128.5, 128.4, 128.4, 127.9, 126.9, 125.9 ppm.

(4-Chlorophenyl)(phenyl)methanone (3l)[3]



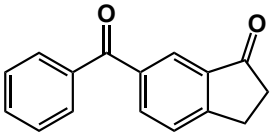
White solid; 38% yield, 0.038 mmol, 8.2 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.79 – 7.71 (m, 4H), 7.62 – 7.57 (m, 1H), 7.52 – 7.42 (m, 4H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.6, 139.0, 137.3, 136.0, 132.7, 131.6, 130.0, 128.7, 128.5 ppm.

Phenyl(4-(trifluoromethyl)phenyl)methanone (3m)[3]



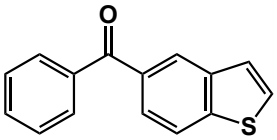
White solid; 48% yield, 0.048 mmol, 12 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.90 (dq, *J* = 7.6, 0.8 Hz, 2H), 7.82 – 7.79 (m, 2H), 7.78 – 7.74 (m, 2H), 7.66 – 7.61 (m, 1H), 7.51 (ddt, *J* = 8.5, 6.6, 1.1 Hz, 2H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 195.7, 140.9, 136.9, 133.9 (q, *J* = 32.7 Hz), 133.2, 130.3, 130.2, 128.7, 125.5 (q, *J* = 3.8 Hz), 123.8 (d, *J* = 272.6 Hz) ppm; ^{19}F NMR (377 MHz, $CDCl_3$) δ -63.01 (s, 3F) ppm.

6-Benzoyl-2,3-dihydro-1H-inden-1-one (3n)



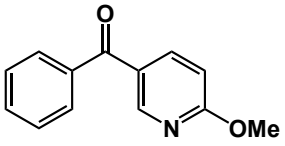
Yellow oil; 31% yield, 0.31 mmol, 7.4 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15 – 8.02 (m, 2H), 7.87 – 7.66 (m, 2H), 7.68 – 7.55 (m, 2H), 7.55 – 7.36 (m, 2H), 3.33 – 3.16 (m, 2H), 2.84 – 2.69 (m, 2H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 206.2, 195.8, 159.2, 137.2, 137.17, 137.0, 135.8, 132.9, 130.0, 128.6, 127.2, 125.8, 36.6, 26.2 ppm. HRMS (DART): m/z calcd. for $C_{16}H_{13}O_2$ ($[M+H]^+$), 237.09101; found, 237.09149.

Benzo[*b*]thiophen-5-yl(phenyl)methanone (3o)



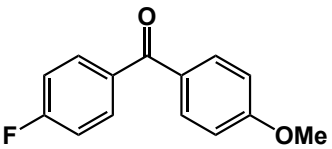
Off-white solid; 65% yield, 0.065 mmol, 15.4 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.25 (dd, J = 1.7, 0.7 Hz, 1H), 7.97 (dt, J = 8.3, 0.8 Hz, 1H), 7.84 (dt, J = 8.3, 1.8 Hz, 3H), 7.66 – 7.57 (m, 1H), 7.57 – 7.47 (m, 3H), 7.41 (dd, J = 5.5, 0.8 Hz, 1H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 196.8, 143.9, 139.2, 138.1, 134.0, 132.4, 130.1, 130.1, 128.4, 128.0, 126.4, 125.4, 124.6, 122.5 ppm. HRMS (DART): m/z calcd. for $C_{15}H_{11}OS$ ($[M+H]^+$), 239.05251; found, 239.05307.

(6-Methoxypyridin-3-yl)(phenyl)methanone (3p)[7]



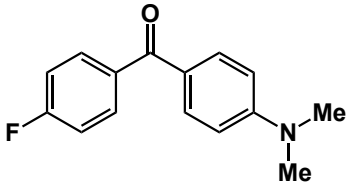
Colorless oil; 30% yield, 0.030 mmol, 6.5 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.62 (dd, J = 2.5, 0.7 Hz, 1H), 8.11 (dd, J = 8.7, 2.4 Hz, 1H), 7.82 – 7.75 (m, 2H), 7.60 (ddt, J = 8.0, 6.9, 1.3 Hz, 1H), 7.53 – 7.47 (m, 2H), 6.85 (dd, J = 8.7, 0.7 Hz, 1H), 4.03 (s, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.3, 166.6, 150.9, 140.2, 137.7, 132.6, 129.9, 128.6, 127.1, 111.2, 54.2 ppm.

(4-Fluorophenyl)(4-methoxyphenyl)methanone (3s)[5]



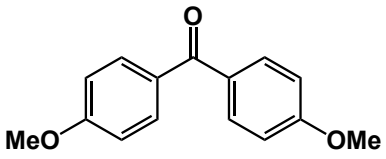
White solid; 82% yield, 0.82 mmol, 18.9 mg; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (dt, J = 8.7, 2.6 Hz, 4H), 7.15 (t, J = 8.6 Hz, 2H), 6.97 (d, J = 8.9 Hz, 2H), 3.88 (s, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.2, 166.2, 164.2, 163.4, 134.6 (d, J = 3.2 Hz), 132.5, 132.4 (d, J = 9.0 Hz), 130.1, 115.4 (d, J = 21.8 Hz), 113.8, 55.6 ppm; ^{19}F NMR (377 MHz, $CDCl_3$) δ -106.91 (s, 1F) ppm.

(4-(Dimethylamino)phenyl)(4-fluorophenyl)methanone (3t)[8]



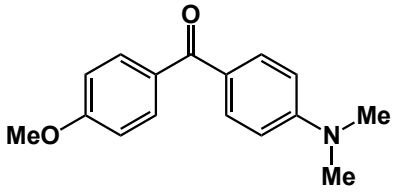
Yellow solid; 60% yield, 0.060 mmol, 14.7 mg; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 – 7.68 (m, 4H), 7.13 (t, *J* = 8.7 Hz, 2H), 6.69 (d, *J* = 9.0 Hz, 2H), 3.07 (s, 6H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 193.8, 165.7, 163.7, 153.3, 135.5 (d, *J* = 3.1 Hz), 132.7, 132.0 (d, *J* = 8.7 Hz), 115.2 (d, *J* = 21.8 Hz), 110.8, 40.2 ppm; ^{19}F NMR (377 MHz, $CDCl_3$) δ -108.32 (s, 1F) ppm.

Bis(4-methoxyphenyl)methanone (3u)[9]



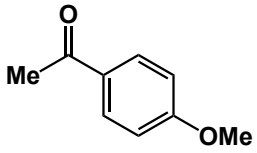
White solid; 74% yield, 0.074 mmol, 17.8 mg; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.9 Hz, 4H), 6.95 (d, *J* = 8.8 Hz, 4H), 3.87 (s, 6H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.5, 162.9, 132.3, 130.8, 113.6, 55.6 ppm.

(4-(Dimethylamino)phenyl)(4-methoxyphenyl)methanone (3v)[9]



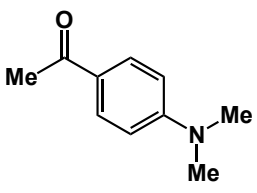
Yellow solid; 60% yield, 0.060 mmol, 15.6 mg; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7. 76 (dd, *J* = 9.0, 7.1 Hz, 4H), 6.94 (d, *J* = 8.8 Hz, 2H), 6.70 (d, *J* = 9.0 Hz, 2H), 3.87 (s, 3H), 3.06 (s, 6H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 194.1, 162.3, 152.9, 132.4, 131.9, 131.7, 125.5, 113.3, 110.7, 55.4, 40.1 ppm.

4-Methoxyacetophenone (3w)[10]



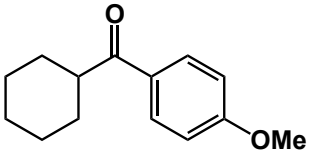
White solid; 31% yield, 0.031 mmol, 4.7 mg; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.9 Hz, 2H), 6.92 (d, *J* = 8.9 Hz, 2H), 3.86 (s, 3H), 2.55 (s, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 196.9, 163.6, 130.7, 130.5, 113.8, 55.6, 26.5 ppm.

4-Dimethylaminoacetophenone (3x)[11]



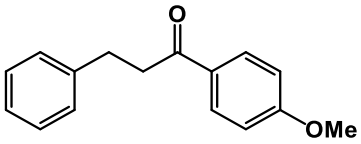
White solid; 34% yield, 0.034 mmol, 5.6 mg; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 – 7.81 (m, 2H), 6.64 (dt, *J* = 9.2, 1.8 Hz, 2H), 3.04 (d, *J* = 1.2 Hz, 6H), 2.50 (d, *J* = 1.2 Hz, 3H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 196.4, 153.4, 130.5, 125.3, 110.5, 40.0, 26.0 ppm.

Cyclohexyl(4-methoxyphenyl)methanone (3y)[12]



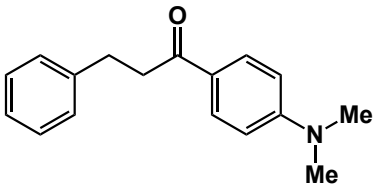
White solid; 31% yield, 0.031 mmol, 6.8 mg; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03 – 7.87 (m, 2H), 7.01 – 6.88 (m, 2H), 3.85 (s, 3H), 3.21 (tt, *J* = 11.6, 3.2 Hz, 1H), 1.85 (dddd, *J* = 17.6, 10.4, 4.4, 2.4 Hz, 4H), 1.72 (dtt, *J* = 13.0, 3.4, 1.5 Hz, 1H), 1.54 – 1.44 (m, 2H), 1.43 – 1.32 (m, 2H), 1.27 (tt, *J* = 12.2, 3.3 Hz, 1H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 202.4, 163.2, 130.5, 129.2, 113.7, 55.4, 45.3, 29.5, 26.0, 25.9 ppm.

1-(4-Methoxyphenyl)-3-phenylpropan-1-one (3z)[12]



White solid; 41% yield, 0.041 mmol, 9.9 mg; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, *J* = 8.9 Hz, 2H), 7.34 – 7.15 (m, 5H), 6.92 (d, *J* = 8.9 Hz, 2H), 3.87 (s, 3H), 3.25 (dd, *J* = 8.7, 6.8 Hz, 2H), 3.11 – 3.00 (m, 2H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 198.0, 163.6, 141.6, 130.4, 130.1, 128.6, 128.6, 126.2, 113.9, 55.6, 40.2, 30.5 ppm.

1-(4-(Dimethylamino)phenyl)-3-phenylpropan-1-one (3aa)[12]



Colorless oil; 17% yield, 0.017 mmol, 4.4 mg; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 – 7.80 (m, 2H), 7.34 – 7.23 (m, 4H), 7.23 – 7.16 (m, 1H), 6.68 – 6.60 (m, 2H), 3.25 – 3.16 (m, 2H), 3.05 (m, 8H) ppm; ^{13}C NMR (126 MHz, $CDCl_3$) δ 197.6, 153.5 142.0, 130.4, 128.6, 128.6, 126.1, 125.0, 110.8, 40.2, 39.9, 30.9 ppm.

General procedure for control reactions monitored by ^{11}B NMR of the SMCC reaction

To an oven-dried 5-mm NMR tube was added acyl MIDA boronate (**1a**) (0.075 mmol, 1.5 eq.), XPhos Pd G2 (0.005 mmol, 10 mol %), and $Cu(OAc)_2$ (0.075 mmol, 1.5 eq.). The tube was transferred to a nitrogen-filled glovebox. Cs_2CO_3 (0.15 mmol, 3.0 eq.) and aryl bromide (0.05 mmol, 1.0 eq.) were subsequently added in a glove box. DMF (0.1 M) was added. The NMR tube was taken out of the glovebox and was heated to a temperature of 60 °C for 17 h. ^{11}B NMR spectra were obtained in the time intervals indicated.

entry	deviation from standard conditions[a]	^{11}B NMR resonances appeared in the course of the reaction
1	none	0.47 ppm
2	no XPhos Pd G2, no **2a**	0.47 ppm
3	no $Cu(OAc)_2$	no conversion
4	only **1a** and $Cu(OAc)_2$	no conversion
5	only **1a** and Cs_2CO_3	no conversion
6	only **1a** and CsOAc	no conversion
7	only **1a**, $Cu(OAc)_2$, and CsOAc	no conversion

Table S2. Control reactions monitored by ^{11}B NMR spectroscopy. [a] Standard conditions: **1a** (1.5 eq.), aryl bromide (1.0 eq.), XPhos Pd G2 (10 mol %), $Cu(OAc)_2$ (1.5 eq.), Cs_2CO_3 (3.0 eq.) in DMF (0.1 M), 60°C, 16 h.

^{11}B NMR spectra of the control reactions of the SMCC reaction

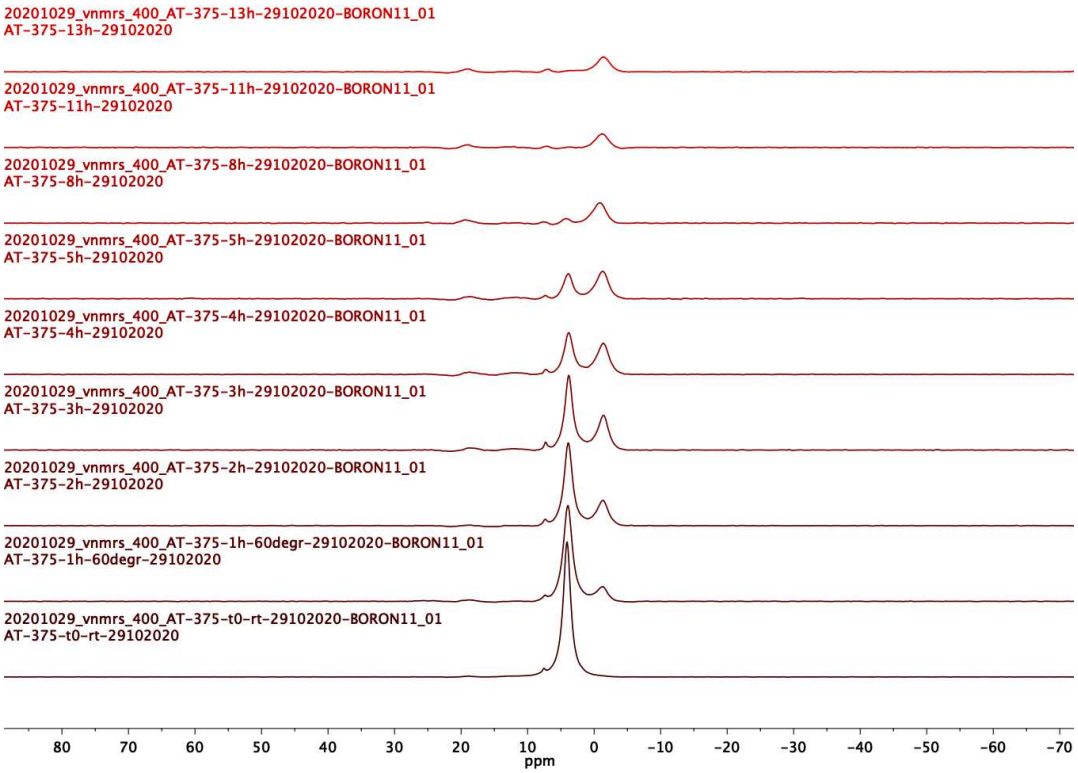


Figure S1. ^{11}B NMR spectra of the reaction of MIDA acylboronate **1a** under standard conditions. Standard conditions: **1a** (1.5 eq.), 4-bromoanisole (1.0 eq.), XPhos Pd G2 (10 mol %), $Cu(OAc)_2$ (1.5 eq.), Cs_2CO_3 (3.0 eq.) in DMF (0.1 M), 60°C.

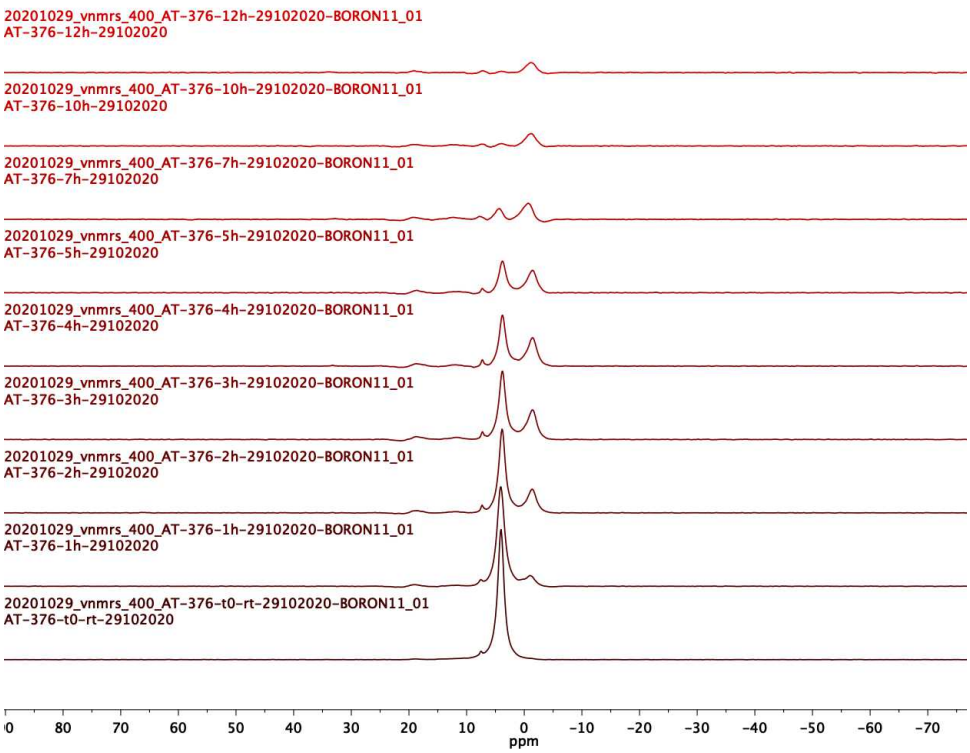


Figure S2. ^{11}B NMR spectra of the reaction of MIDA acylboronate **1a** without Pd catalyst. Reaction conditions: **1a** (1.5 eq.), $Cu(OAc)_2$ (1.5 eq.), Cs_2CO_3 (3.0 eq.) in DMF (0.1 M), 60ºC.

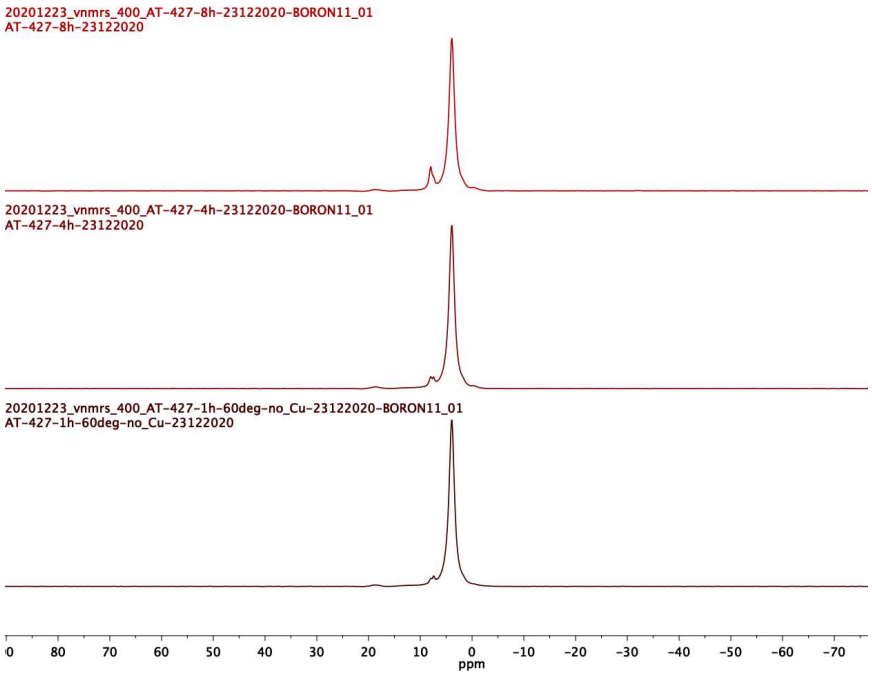


Figure S3. ^{11}B NMR spectra of the reaction of MIDA acylboronate **1a** with no copper additive. Reaction conditions: **1a** (1.5 eq.), 4-bromoanisole (1.0 eq.), XPhos Pd G2 (10 mol %), Cs_2CO_3 (3.0 eq.) in DMF (0.1 M), 60ºC.

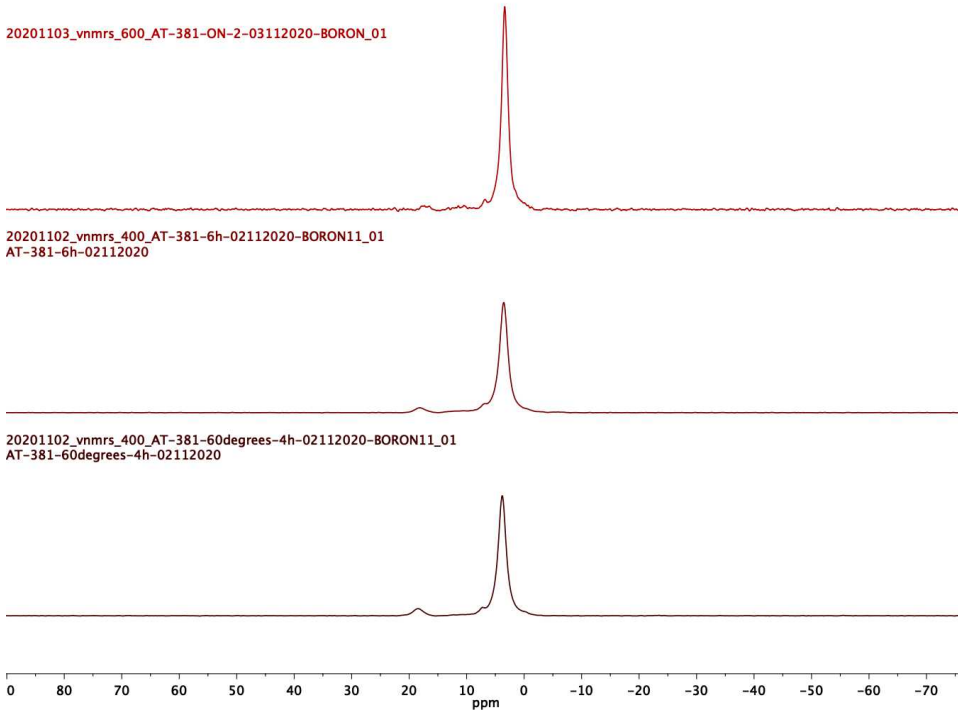


Figure S4. ^{11}B NMR spectra of the reaction of MIDA acylboronate **1a** with $Cu(OAc)_2$ only. Reaction conditions: **1a** (1.5 eq.), $Cu(OAc)_2$ (1.5 eq.) in DMF (0.1 M), 60ºC.

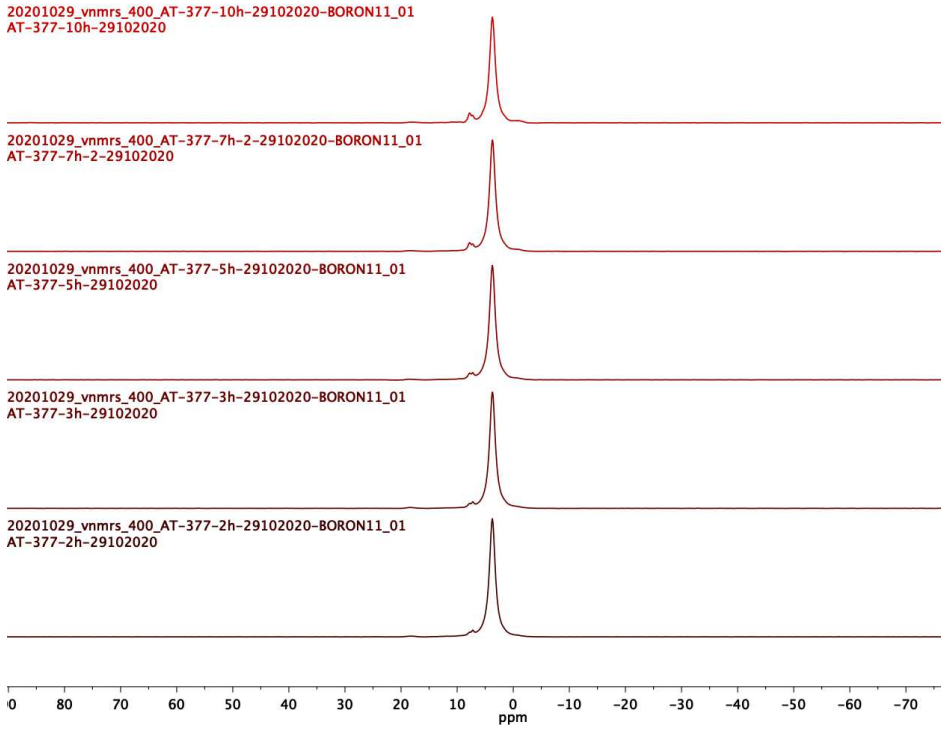


Figure S5. ^{11}B NMR spectra of the reaction of MIDA acylboronate **1a** with base only. Reaction conditions: **1a** (1.5 eq.), Cs_2CO_3 (3.0 eq.) in DMF (0.1 M), 60ºC.

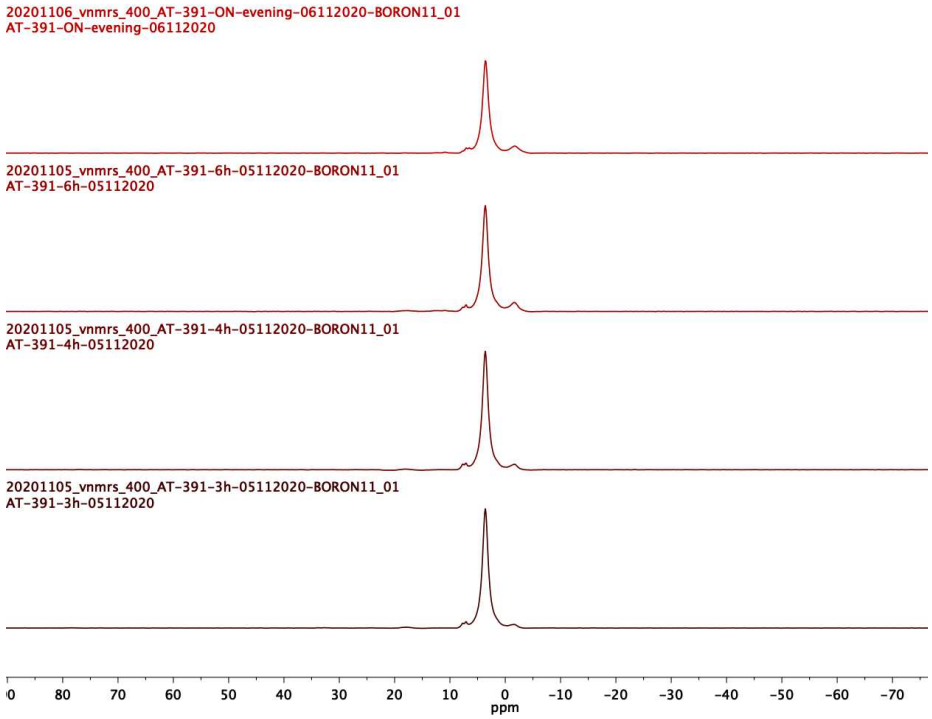


Figure S6. ^{11}B NMR spectra of the reaction of MIDA acylboronate **1a** with only CsOAc. Reaction conditions: **1a** (1.5 eq.), CsOAc (3.0 eq.) in DMF (0.1 M), 60ºC.

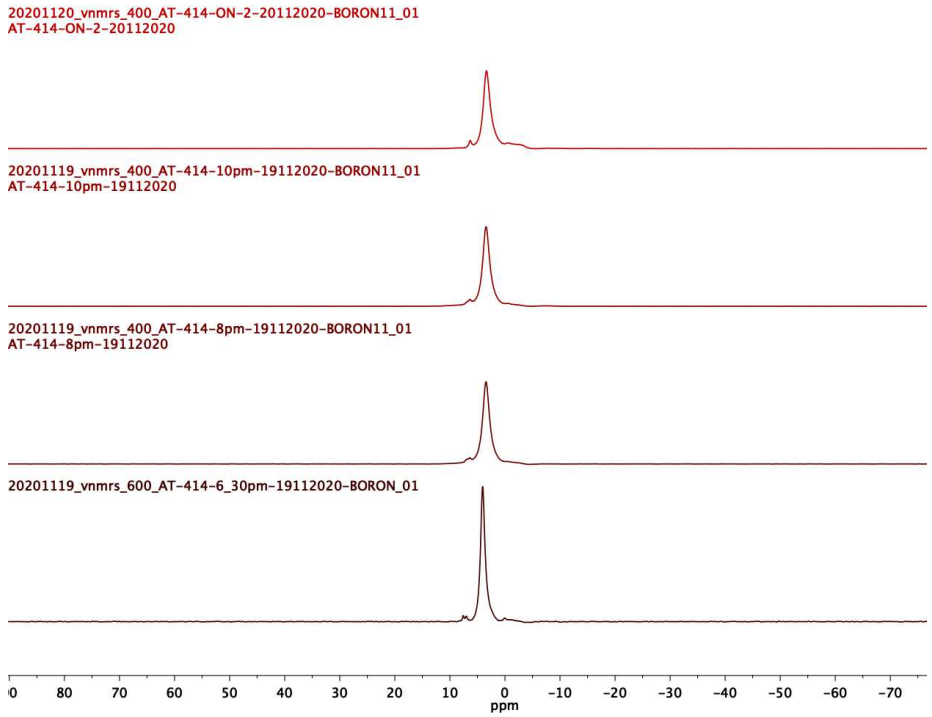


Figure S7. ^{11}B NMR spectra of the reaction of MIDA acylboronate **1a** with CsOAc as a base. Reaction conditions: **1a** (1.5 eq.), $Cu(OAc)_2$ (1.5 eq.), CsOAc (3.0 eq.) in DMF (0.1 M), 60ºC.

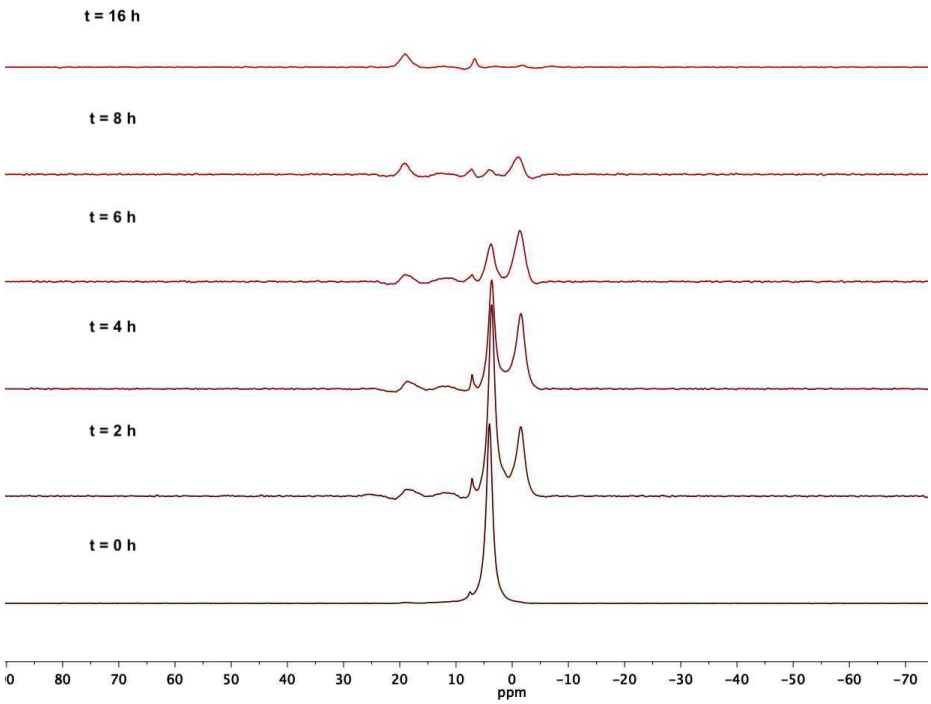


Figure S8. ^{11}B NMR spectra of the reaction of MIDA acylboronate **1a** (0.95 eq.) under standard conditions. Reaction conditions: **1a** (0.95 eq.), 4-bromoanisole (1.0 eq.), XPhos Pd G2 (10 mol %), $Cu(OAc)_2$ (1.5 eq.), Cs_2CO_3 (3.0 eq.) in DMF (0.1 M), 60°C.

General procedure for the stoichiometric reaction monitored by ^{31}P NMR of the SMCC reaction

To an oven-dried 5-mm NMR tube was added acyl MIDA boronate (**1a**) (0.075 mmol, 1.5 eq.), XPhos Pd G2 (0.05 mmol, 1 eq.), and $Cu(OAc)_2$ (0.075 mmol, 1.5 eq.). The tube was transferred to a nitrogen-filled glovebox. Cs_2CO_3 (0.15 mmol, 3.0 eq.) and aryl bromide (0.05 mmol, 1.0 eq.) were subsequently added in a glovebox. DMF (0.1 M) was added. The NMR tube was taken out of the glovebox and was heated to a temperature of 60 °C for 17 h. ^{31}P NMR spectra were obtained in the time intervals indicated.

^{31}P NMR and mass spectrometry spectra of the stoichiometric reactions of the SMCC reaction

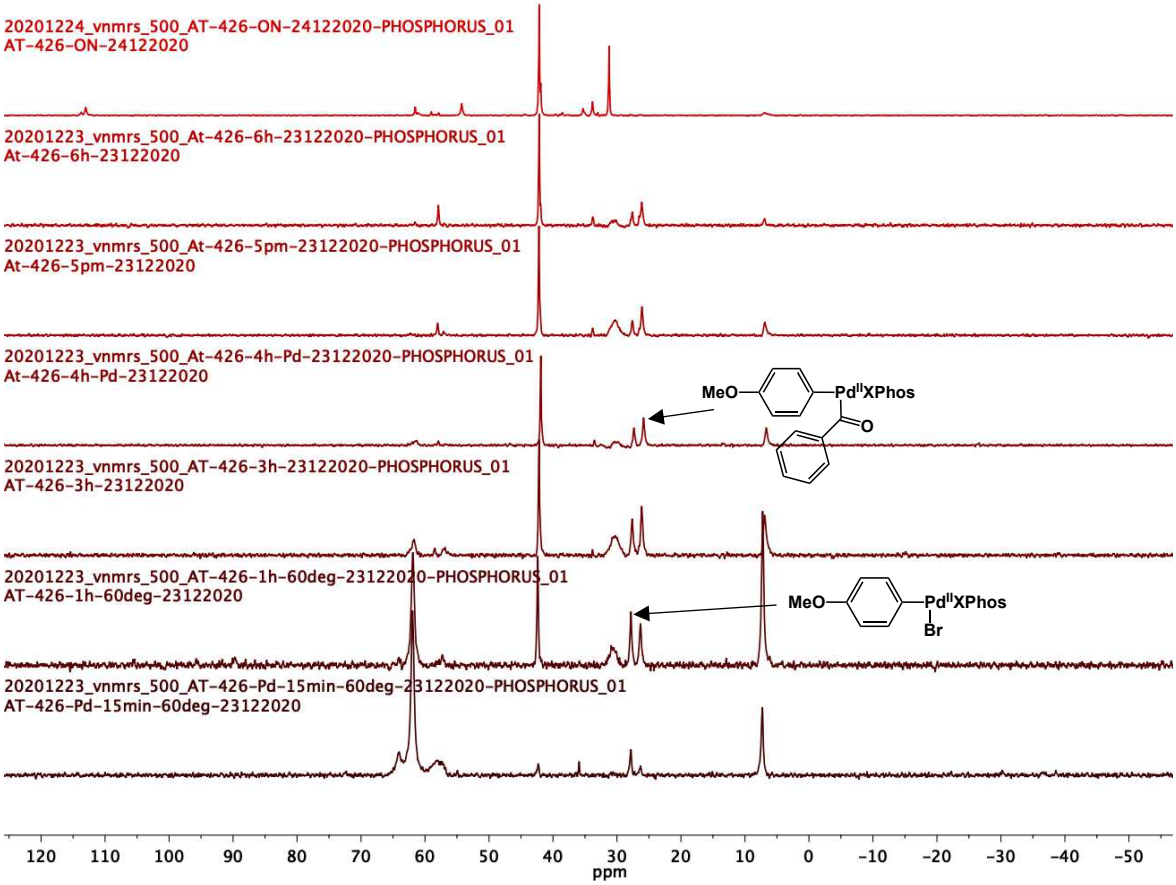


Figure S9. ^{31}P NMR spectra of the stoichiometric reaction of MIDA acylboronate **1a** (1.5 eq.), 4-bromoanisole (1.0 eq.), XPhos Pd G2 (1.0 eq.), $Cu(OAc)_2$ (1.5 eq.), Cs_2CO_3 (3.0 eq.) in DMF (0.1 M), 60ºC.

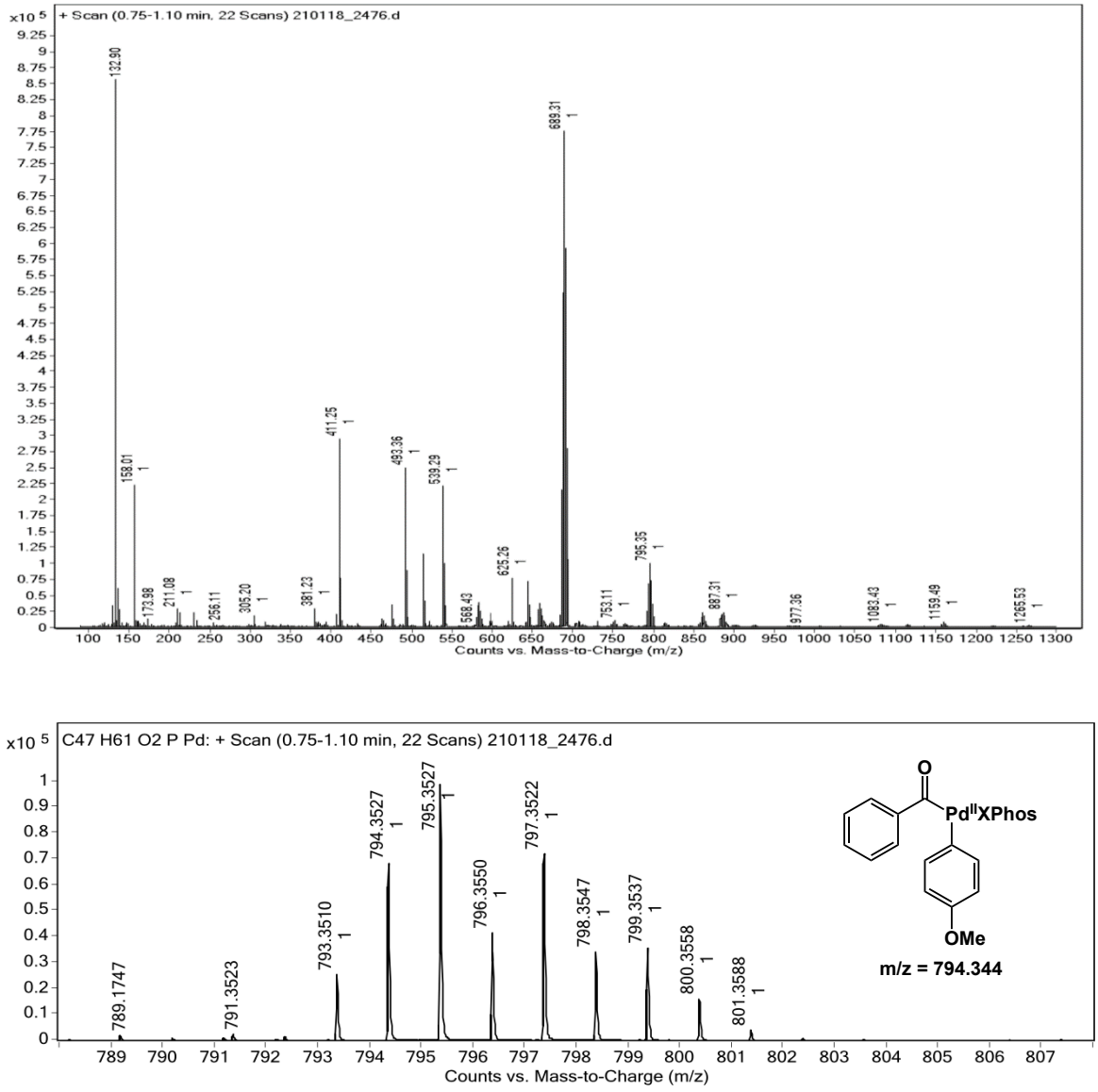


Figure S10. Mass spectrum of the crude reaction of MIDA acylboronate **1a** and 4-bromoanisole showing the peak attributable to a transmetalation complex (m/z = 794.344).

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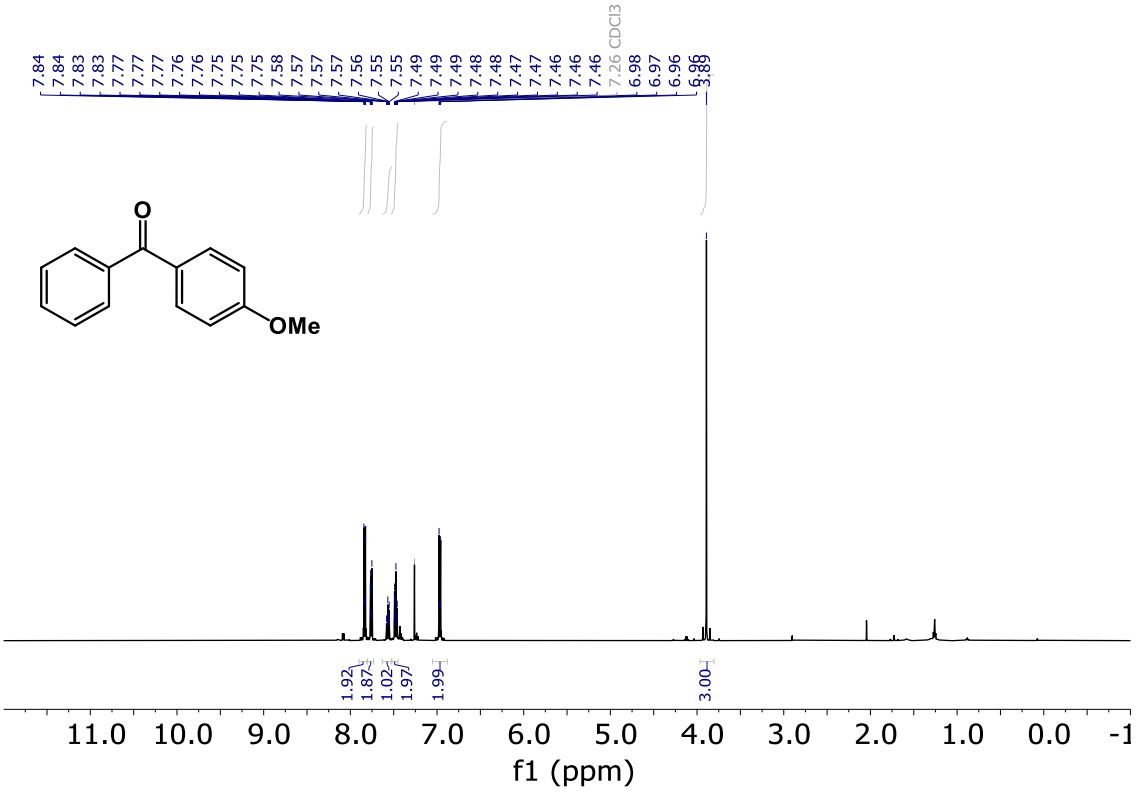
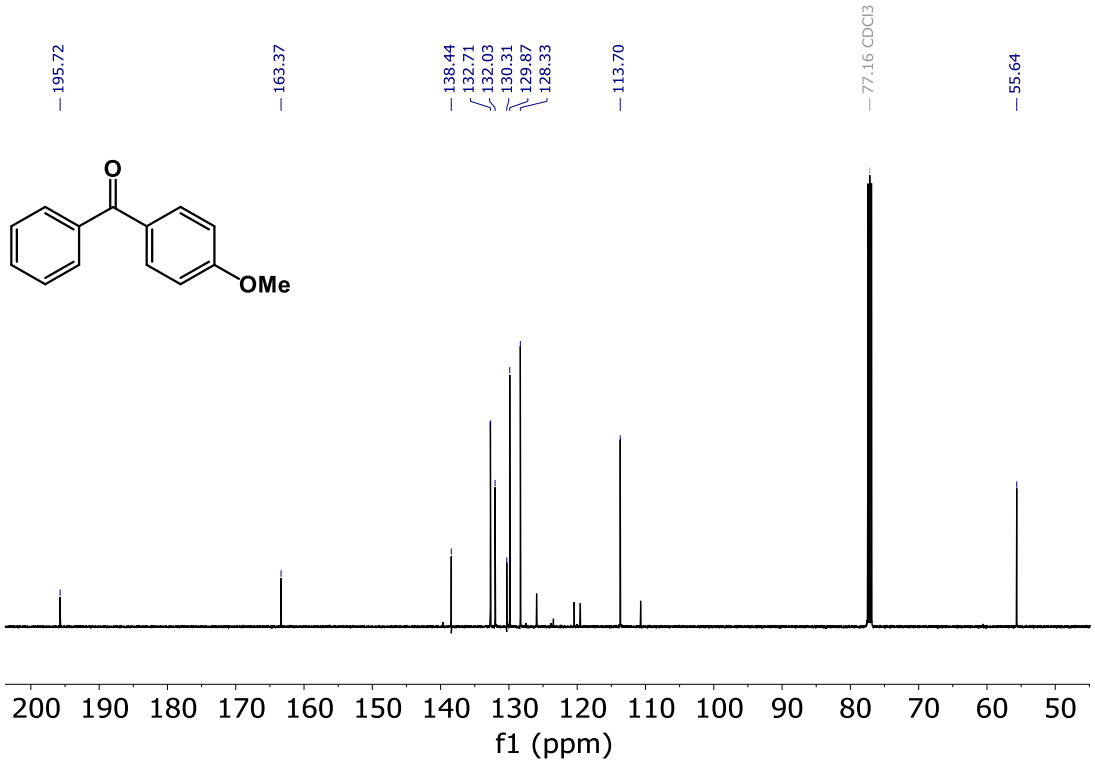
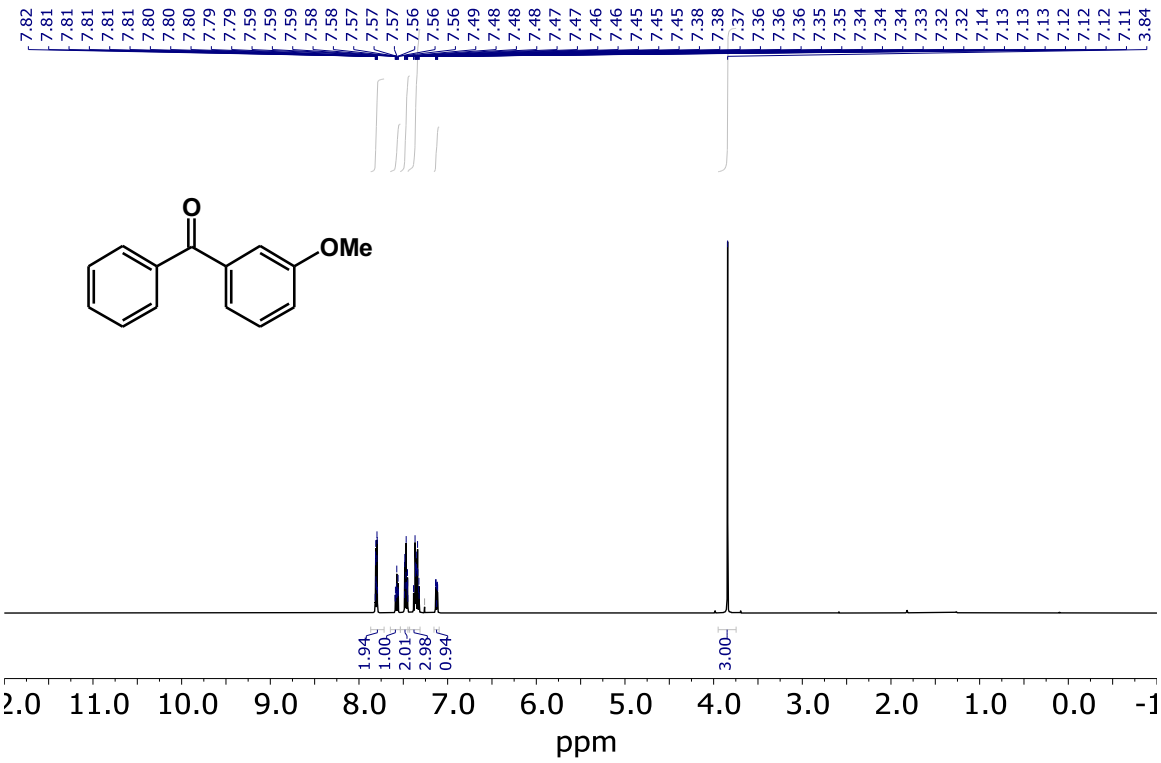
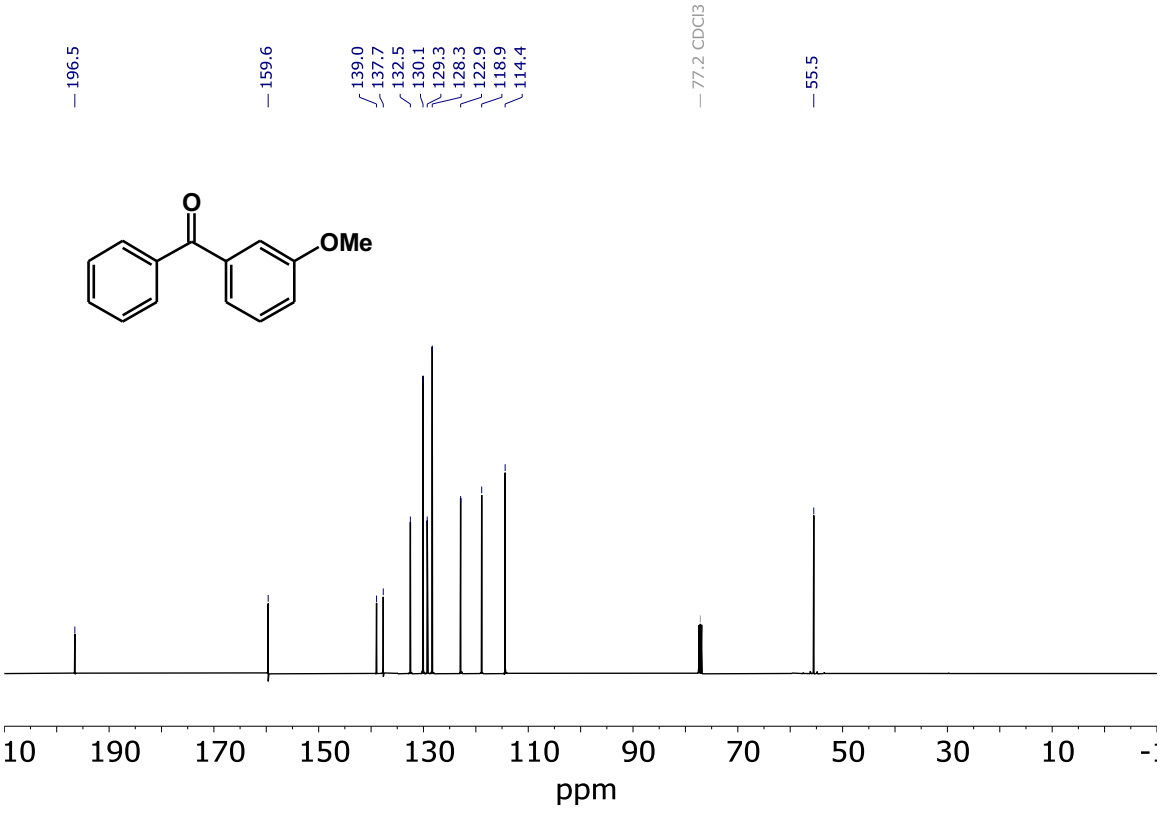
(4-methoxyphenyl)(phenyl)methanone (3a)



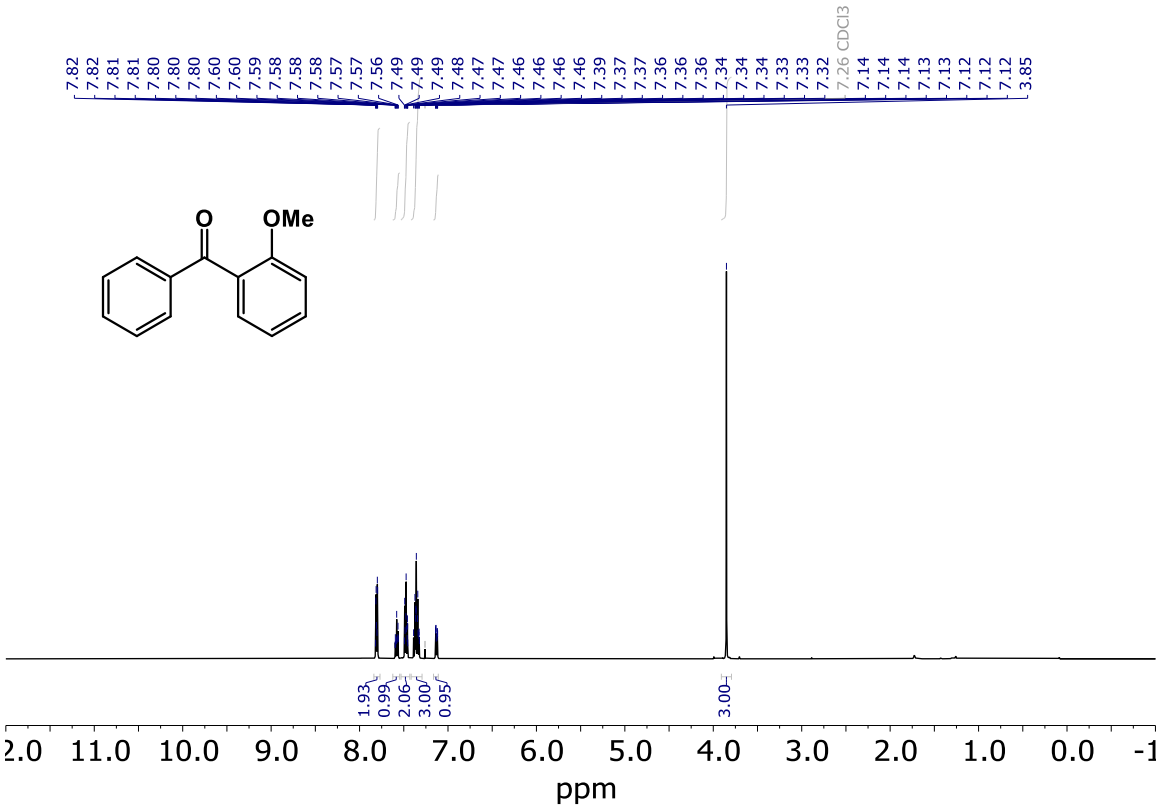


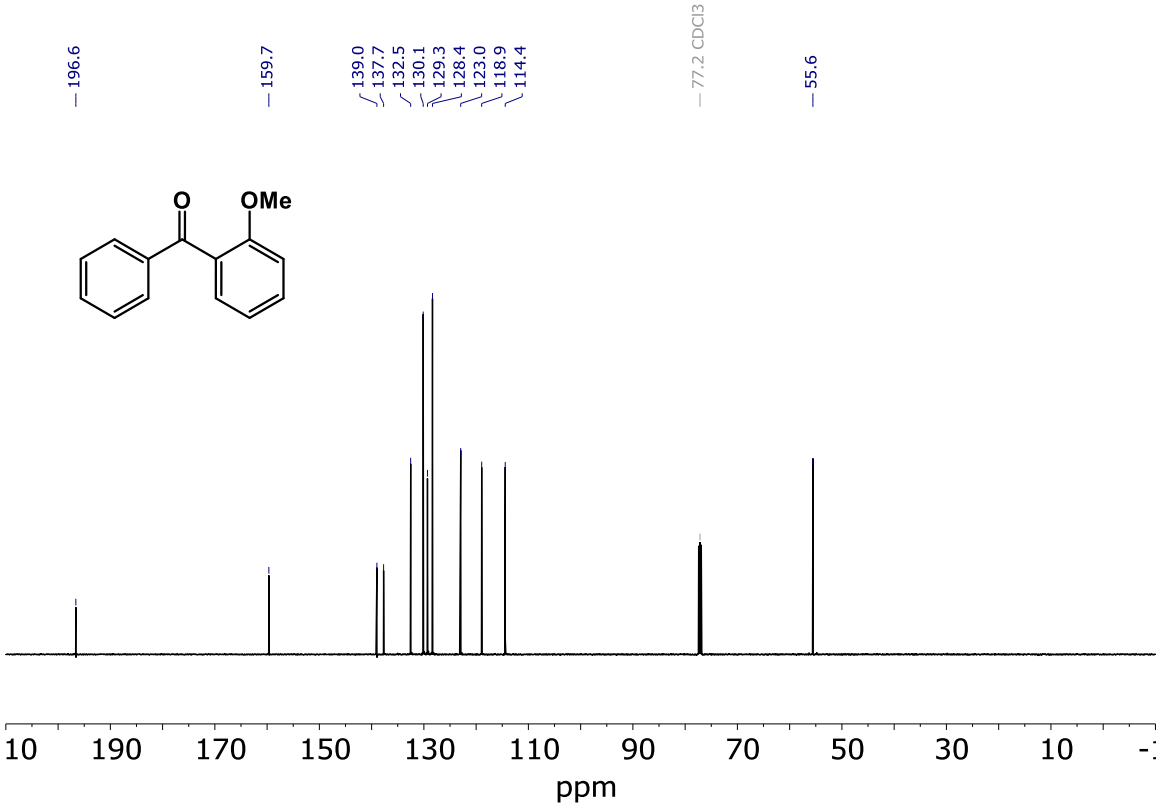
(3-methoxyphenyl)(phenyl)methanone (3b)



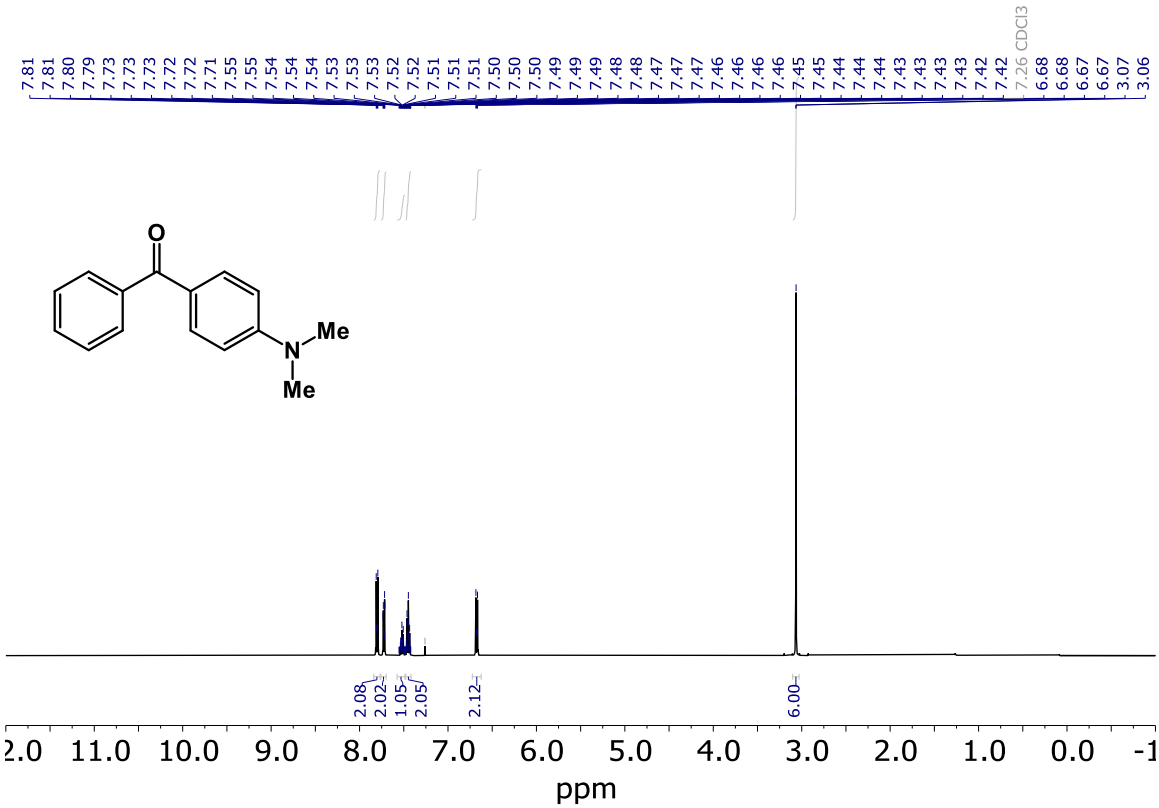


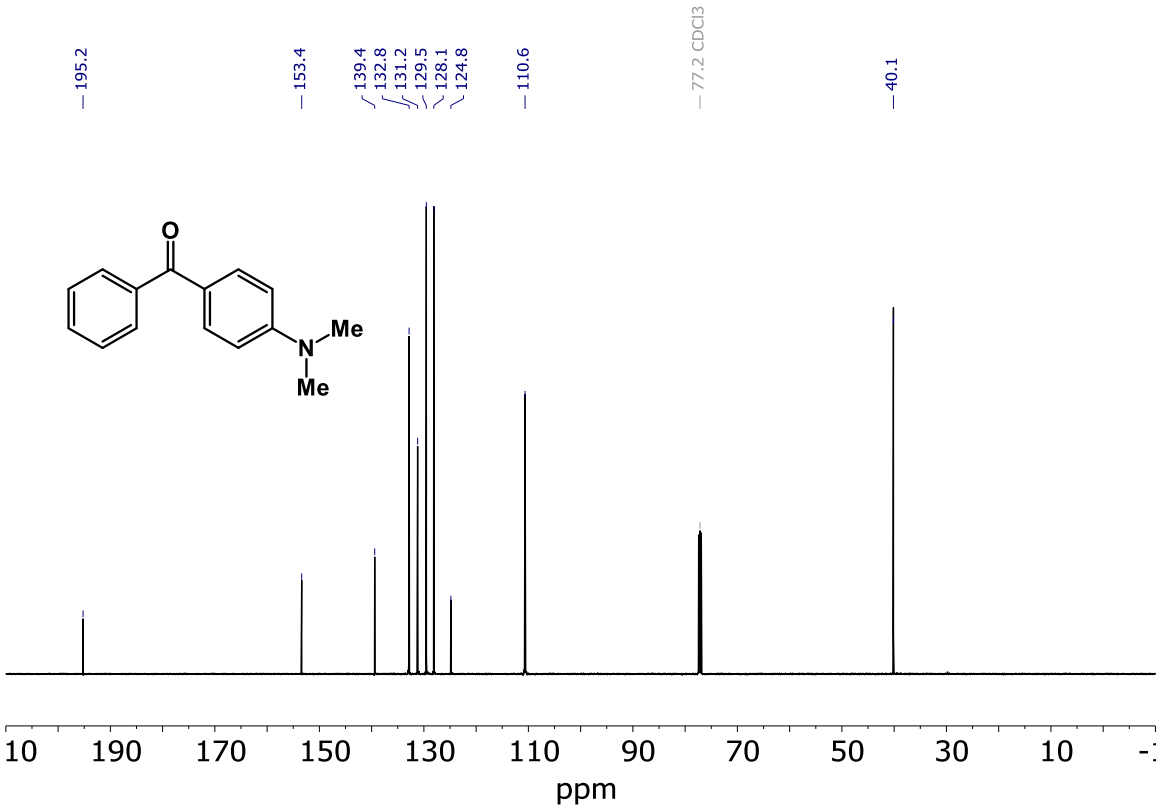
(2-methoxyphenyl)(phenyl)methanone (3c)



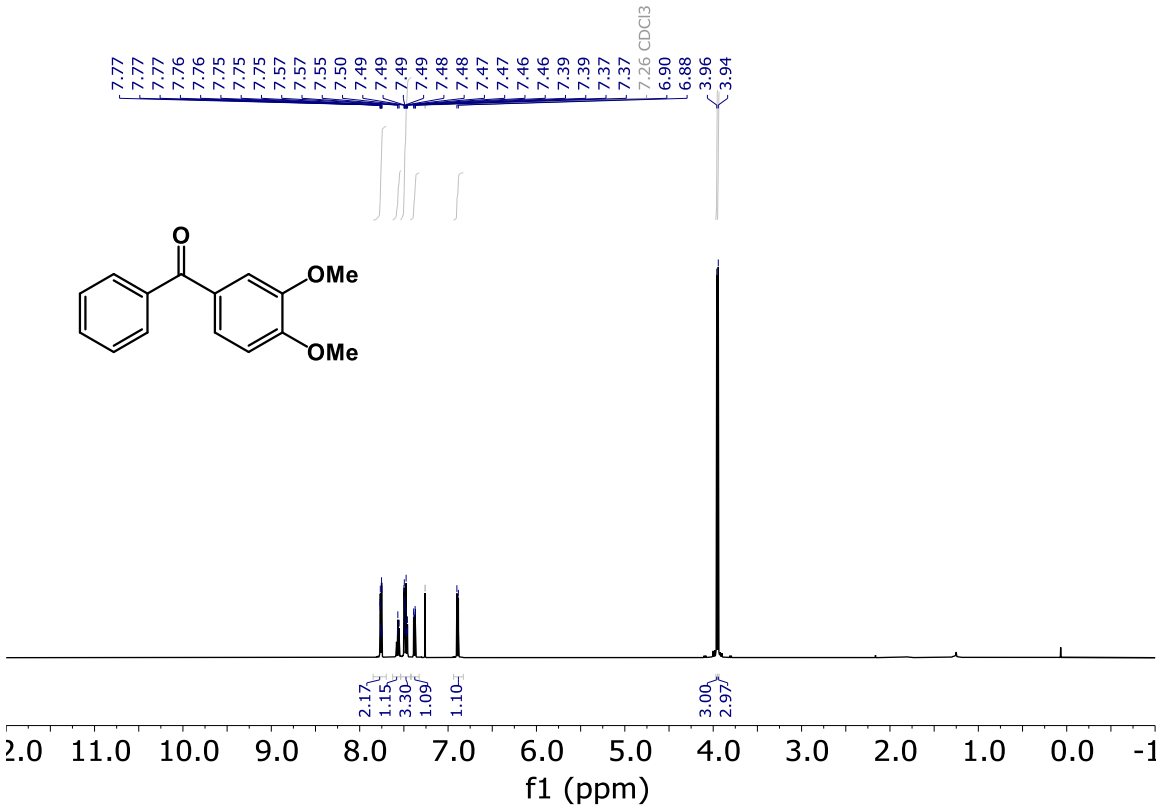


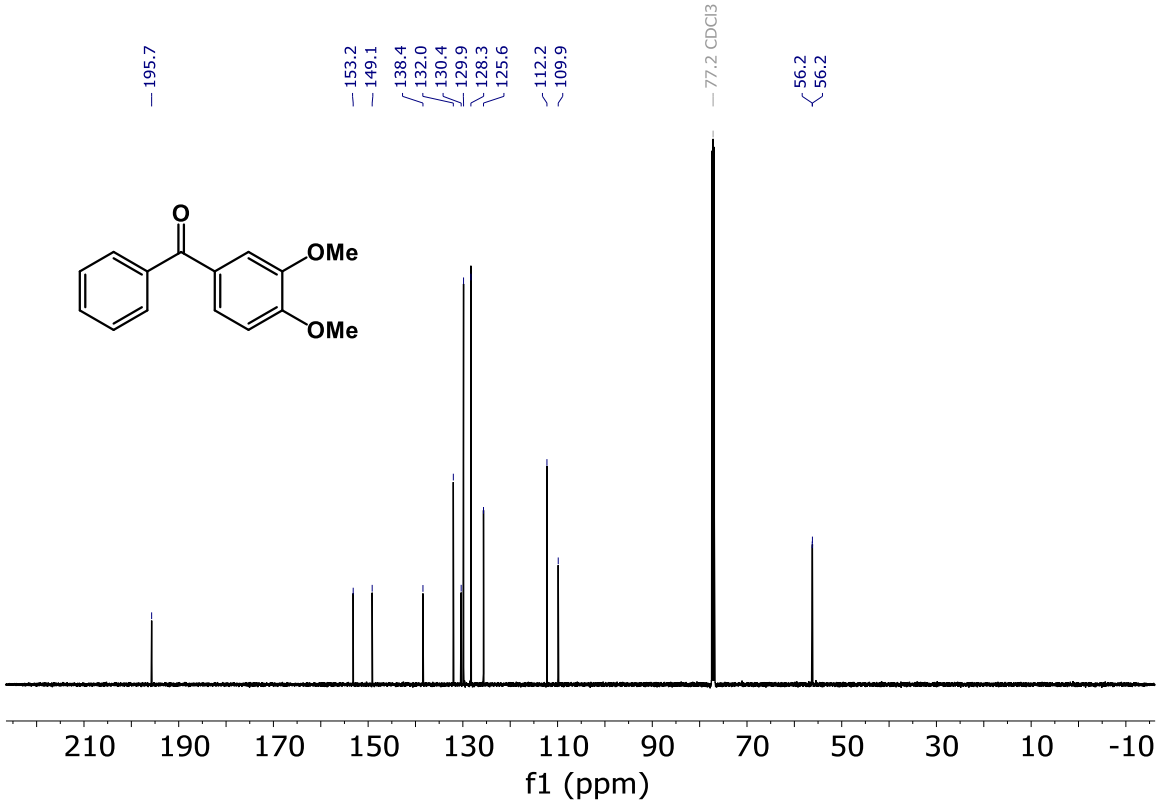
(4-(dimethylamino)phenyl)(phenyl)methanone (3d)



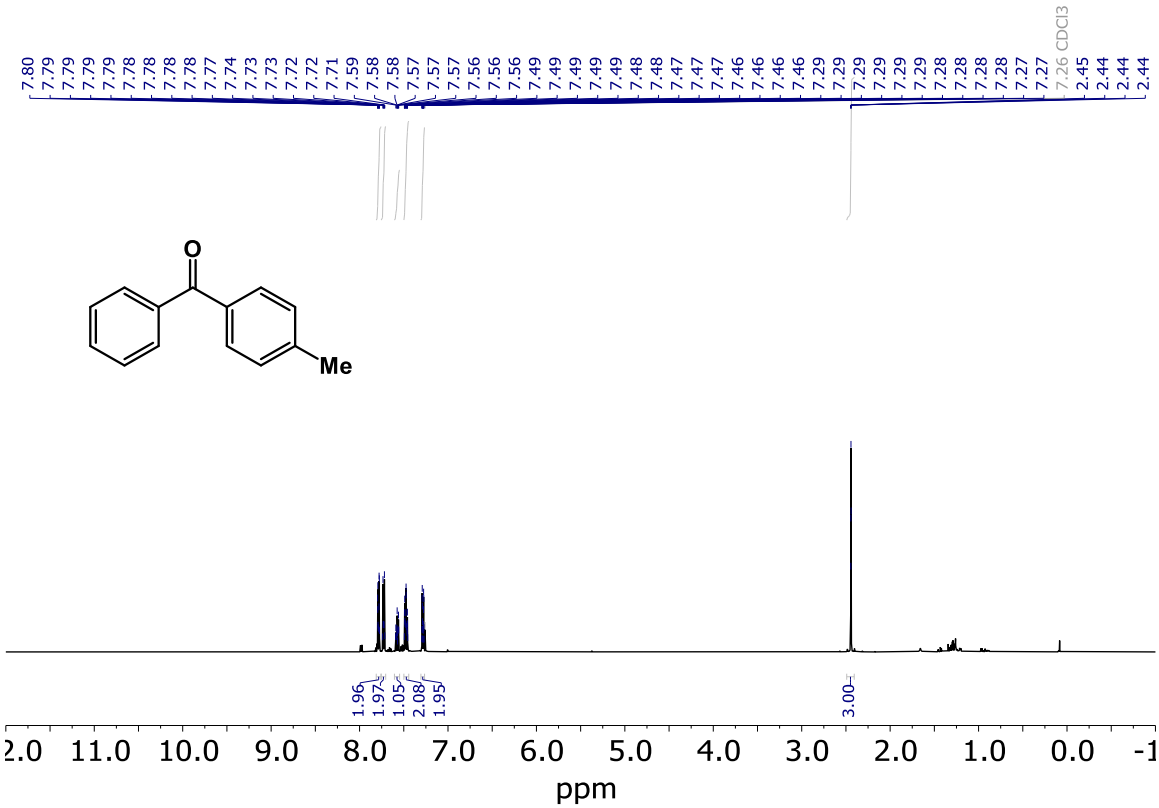


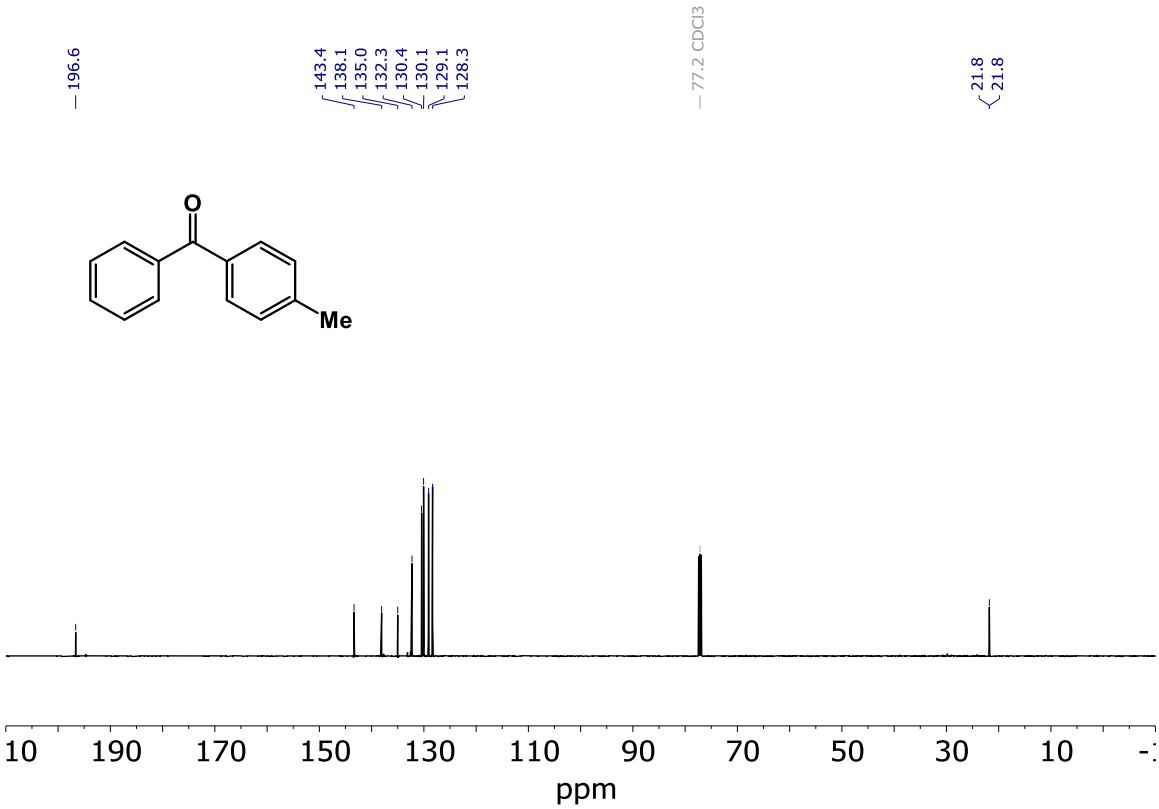
(3,4-dimethoxyphenyl)(phenyl)methanone (3e)



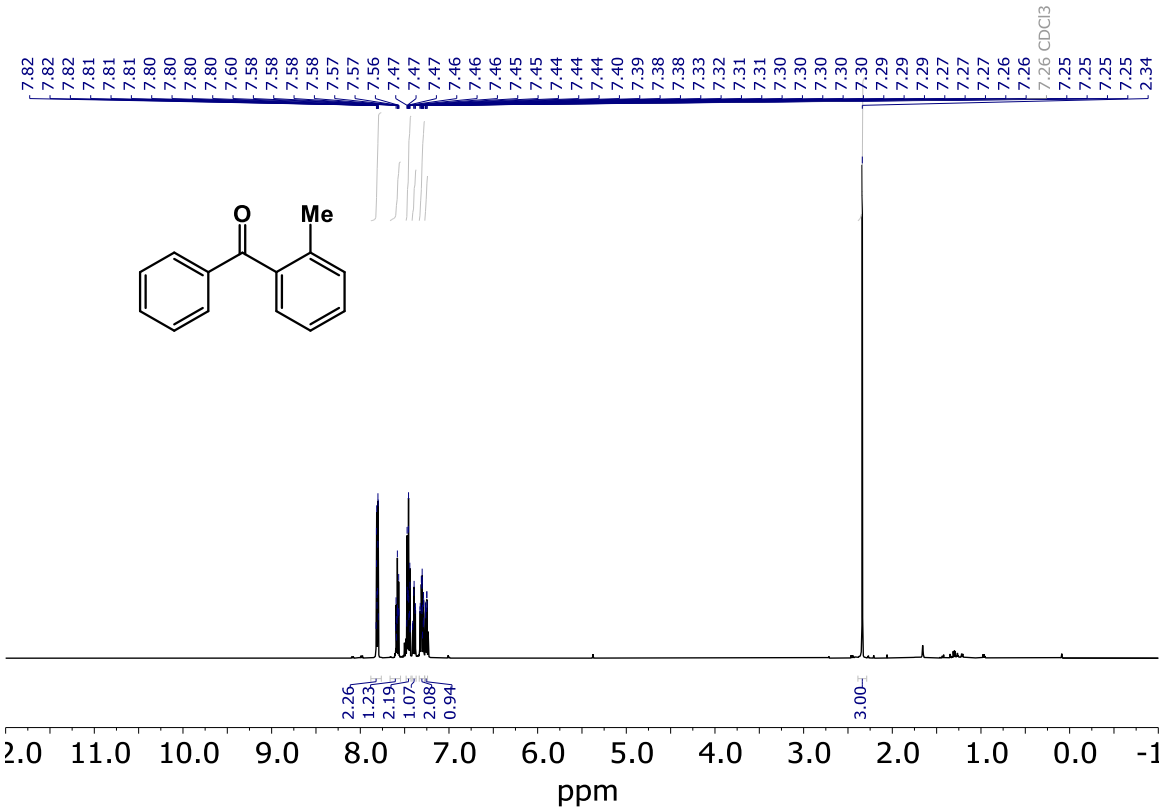


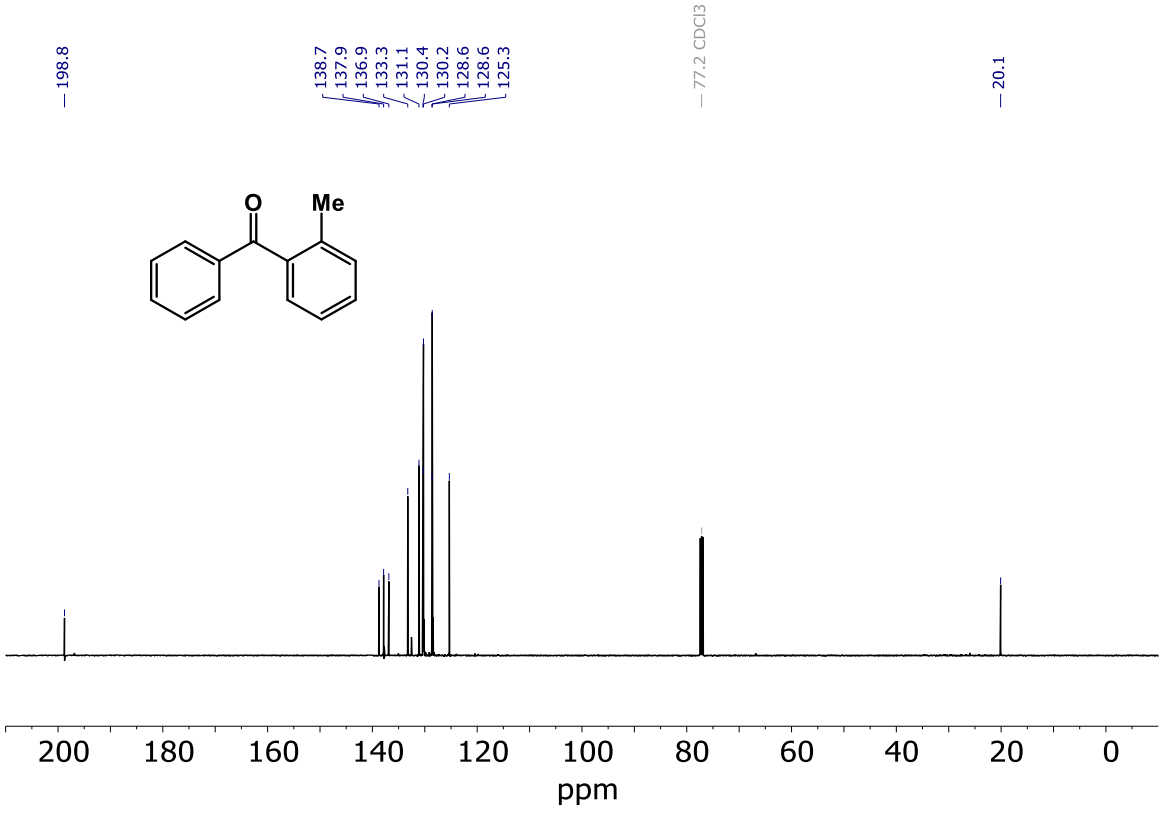
phenyl(*p*-tolyl)methanone (3f)



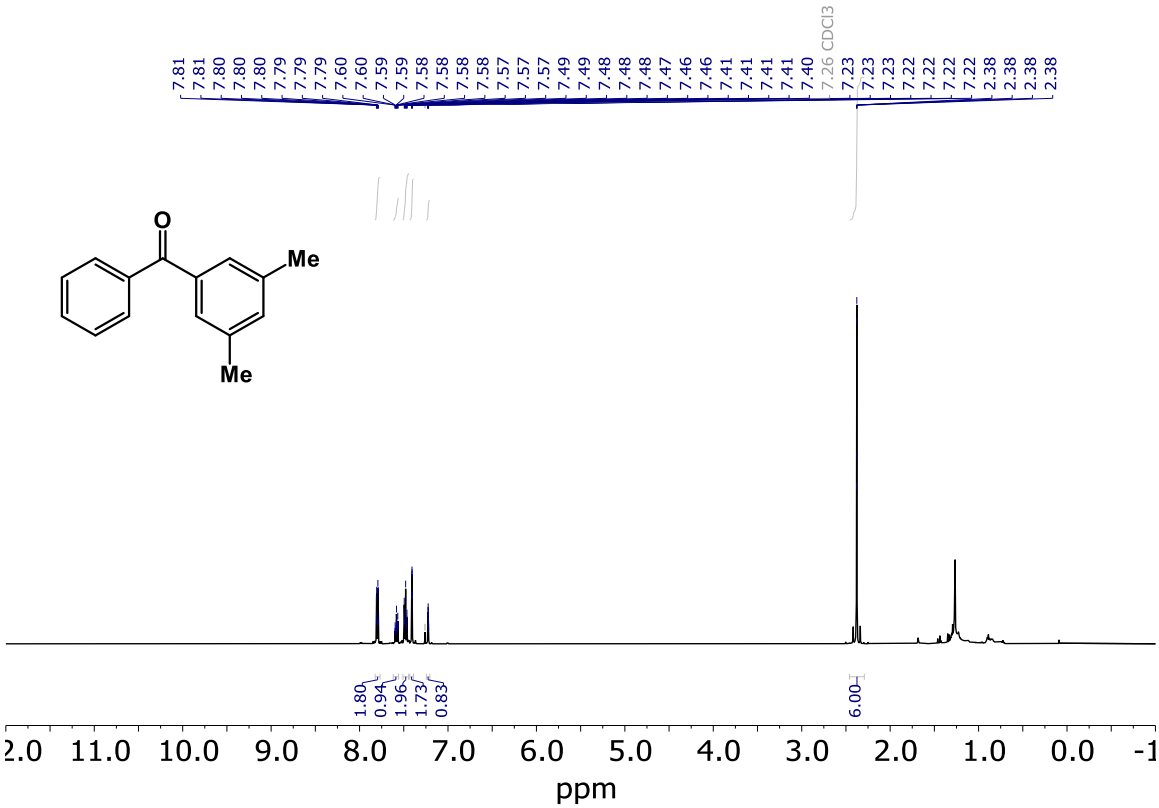


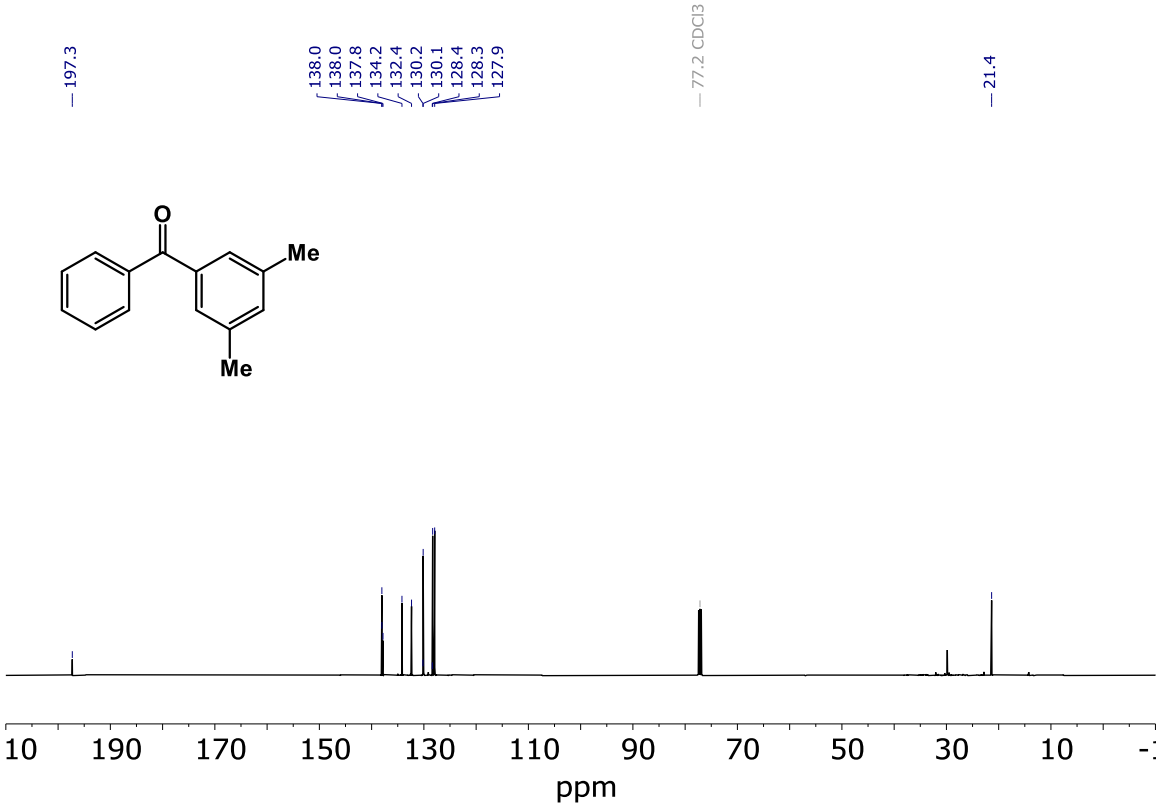
phenyl(o-tolyl)methanone (3g)



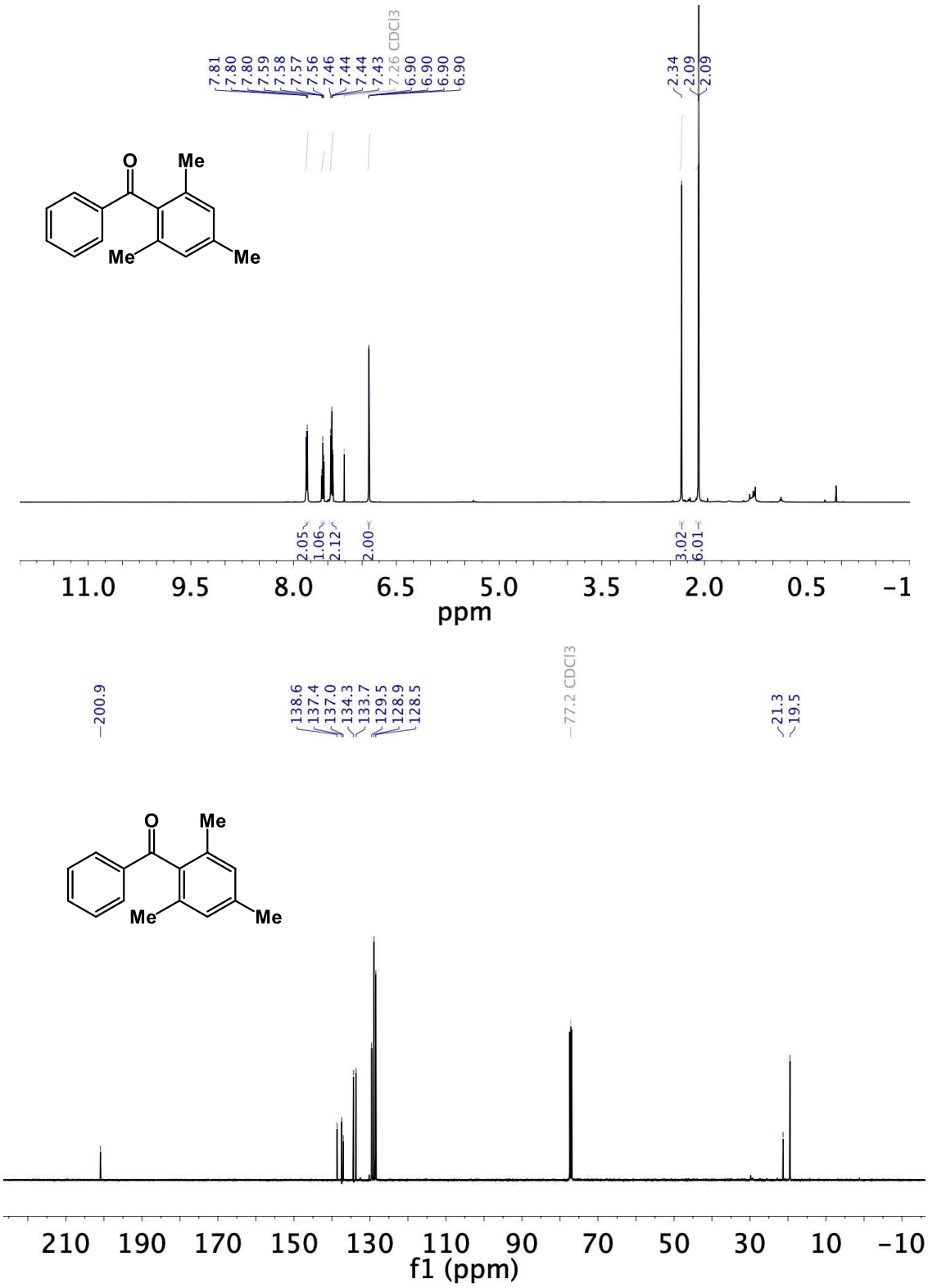


(2,6-dimethylphenyl)(phenyl)methanone (3h)

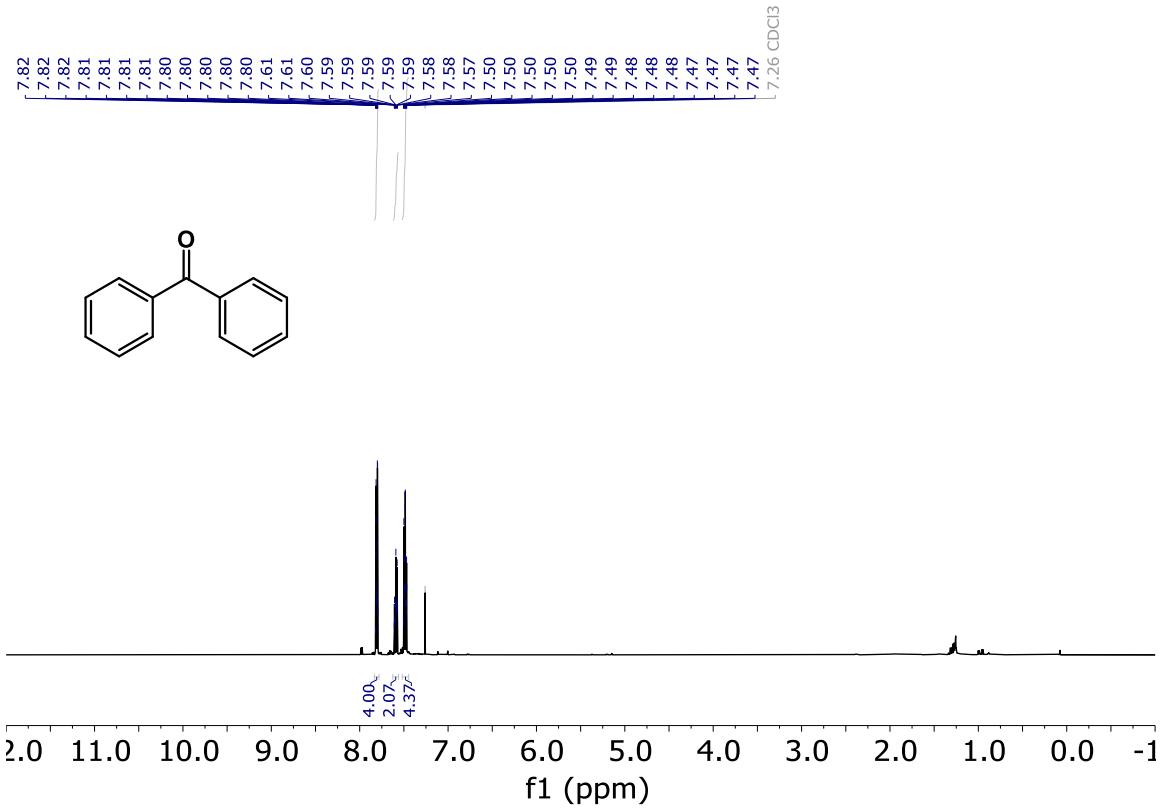


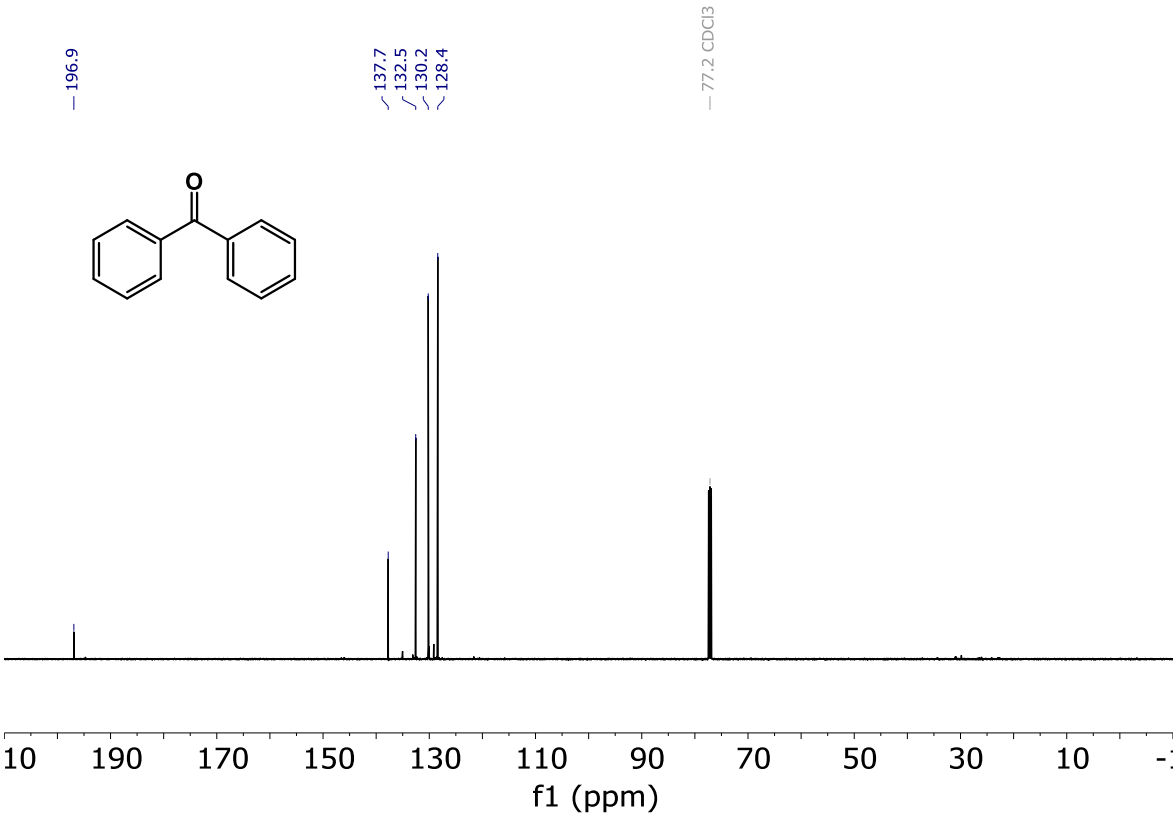


mesityl(phenyl)methanone (3i)

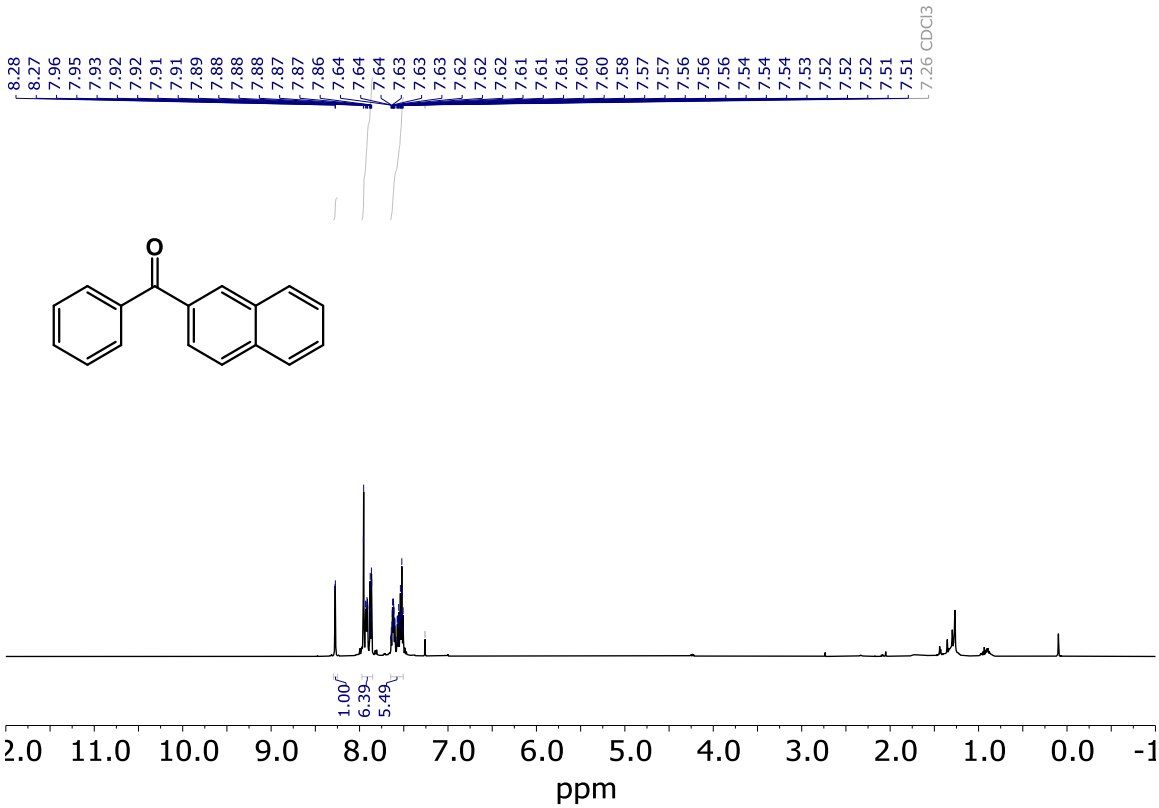


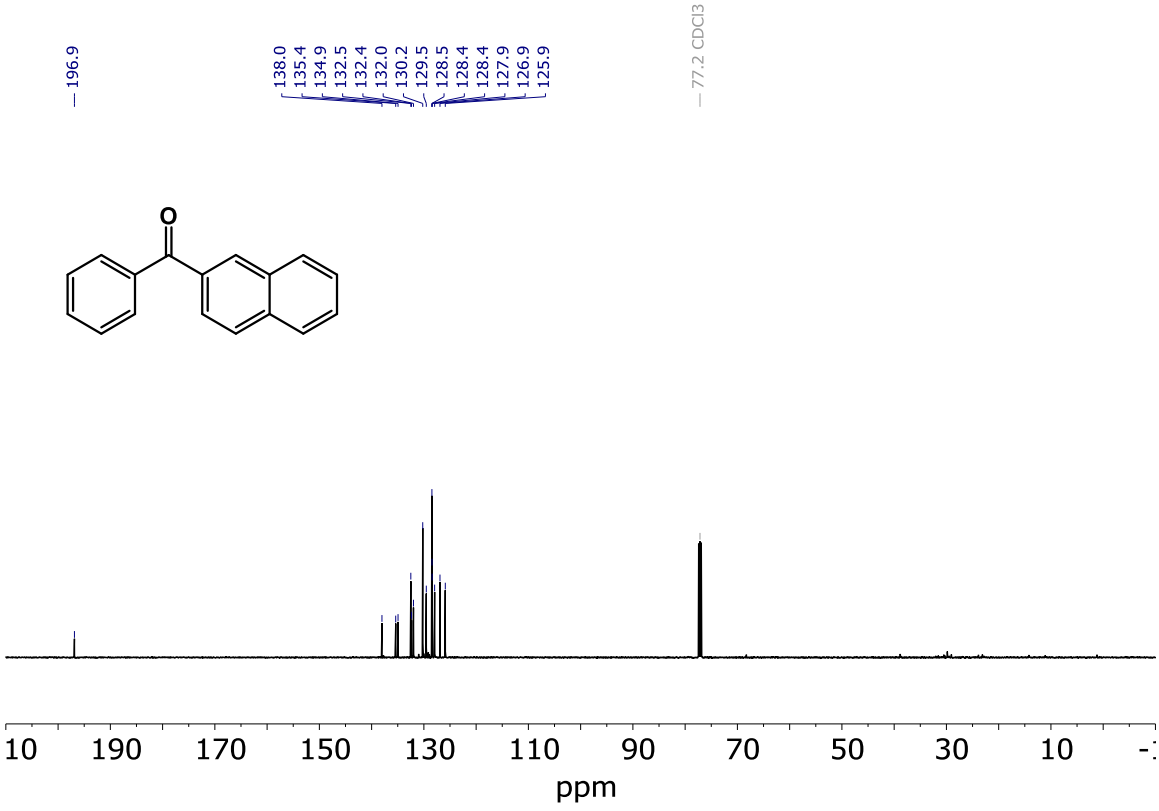
benzophenone (3j)



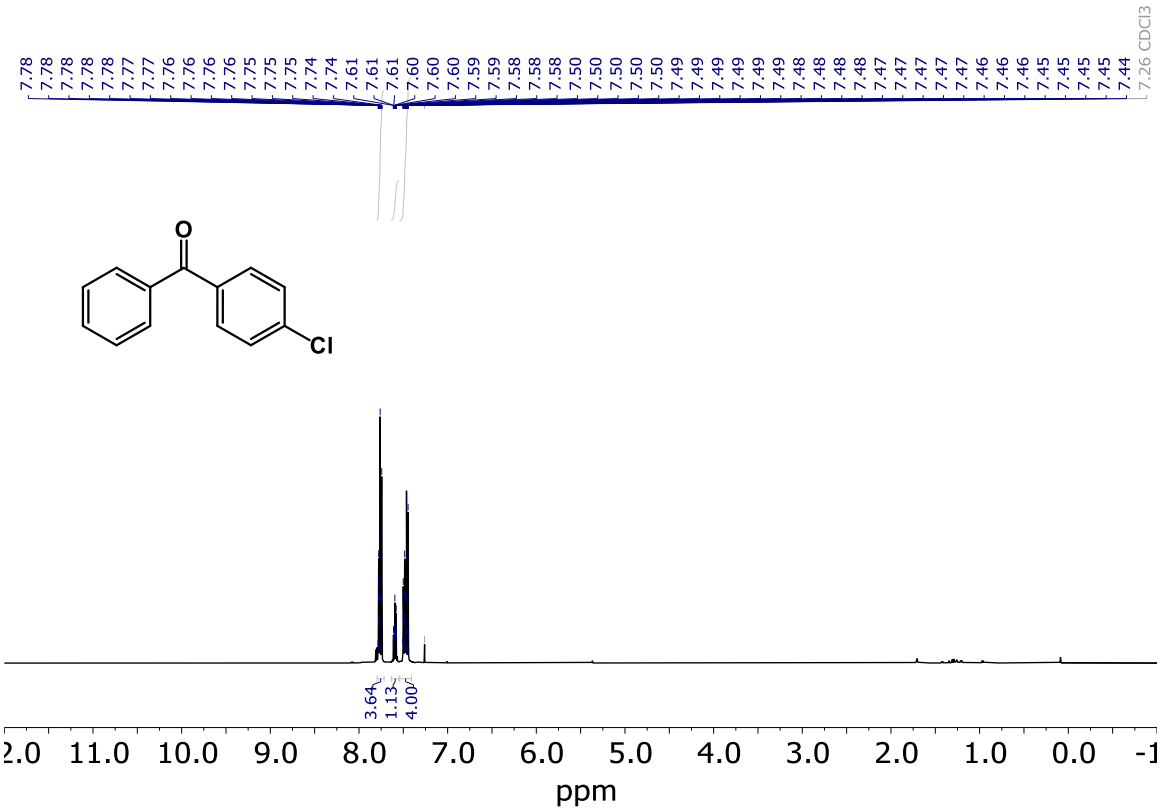


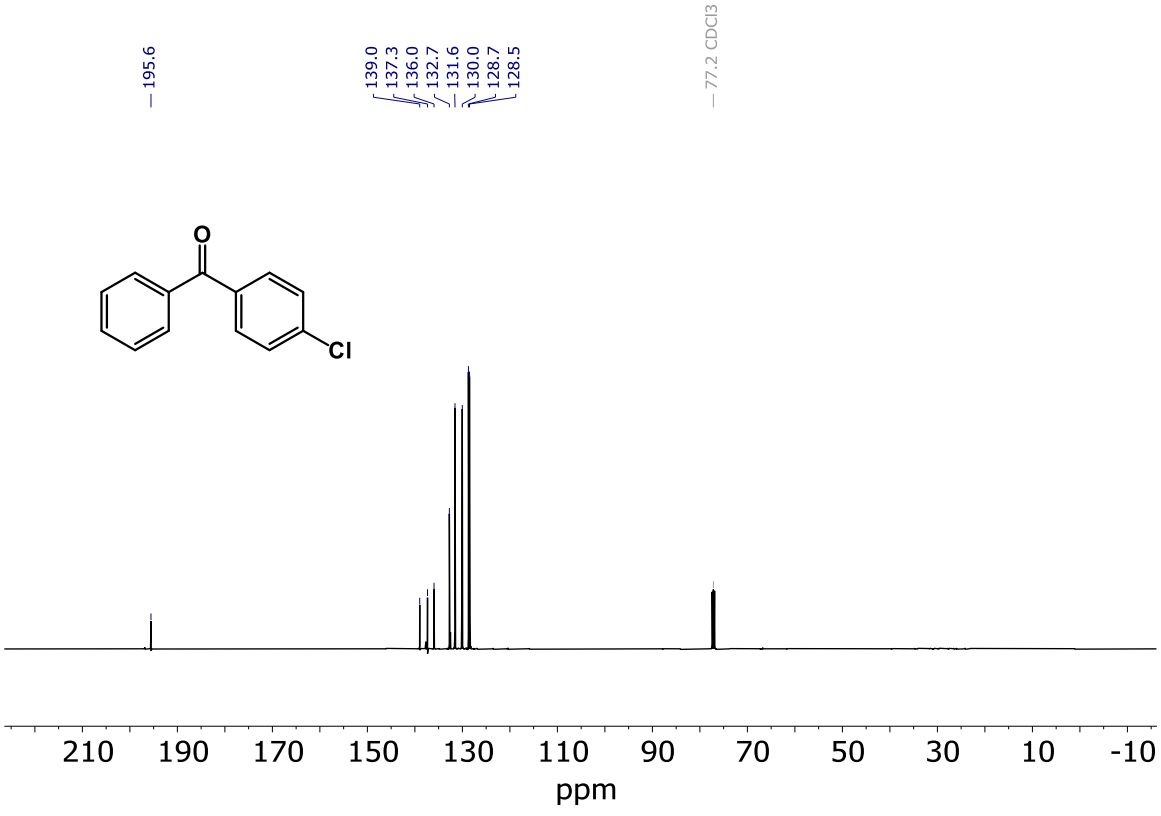
naphthalen-2-yl(phenyl)methanone (3k)



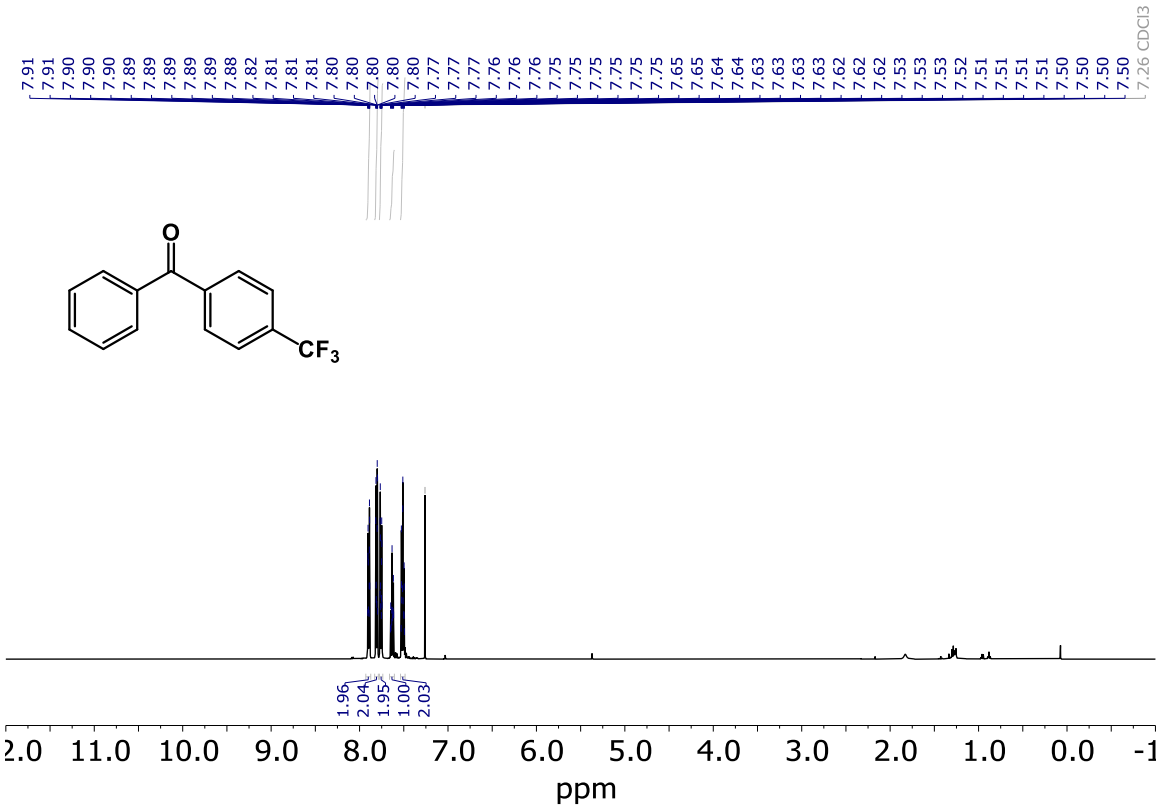


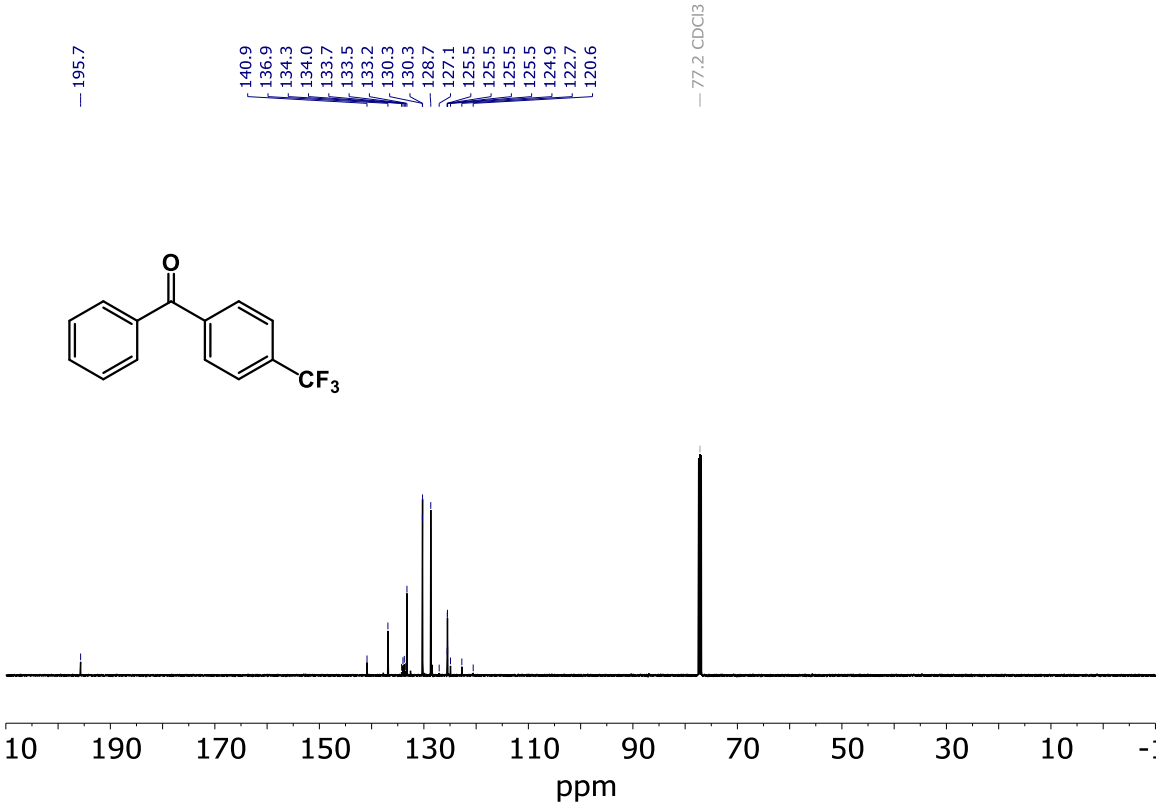
(4-chlorophenyl)(phenyl)methanone (3l)



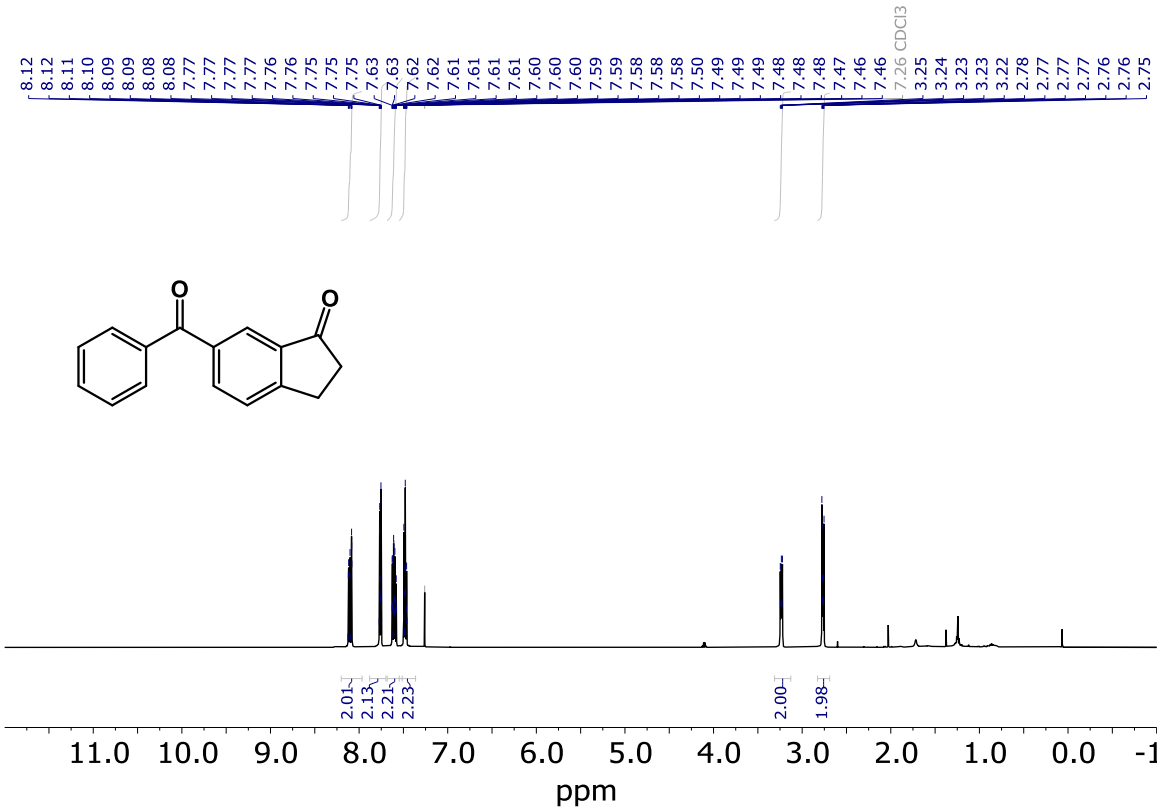


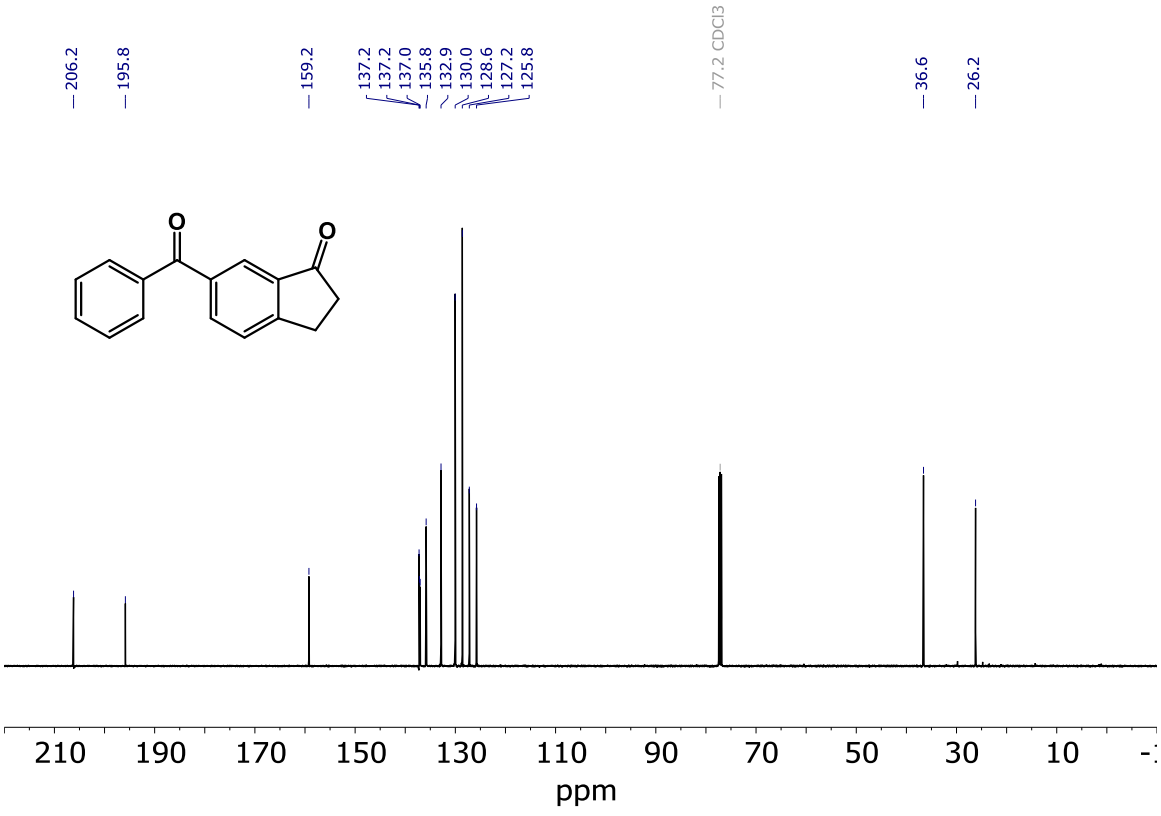
phenyl(4-(trifluoromethyl)phenyl)methanone (3m)



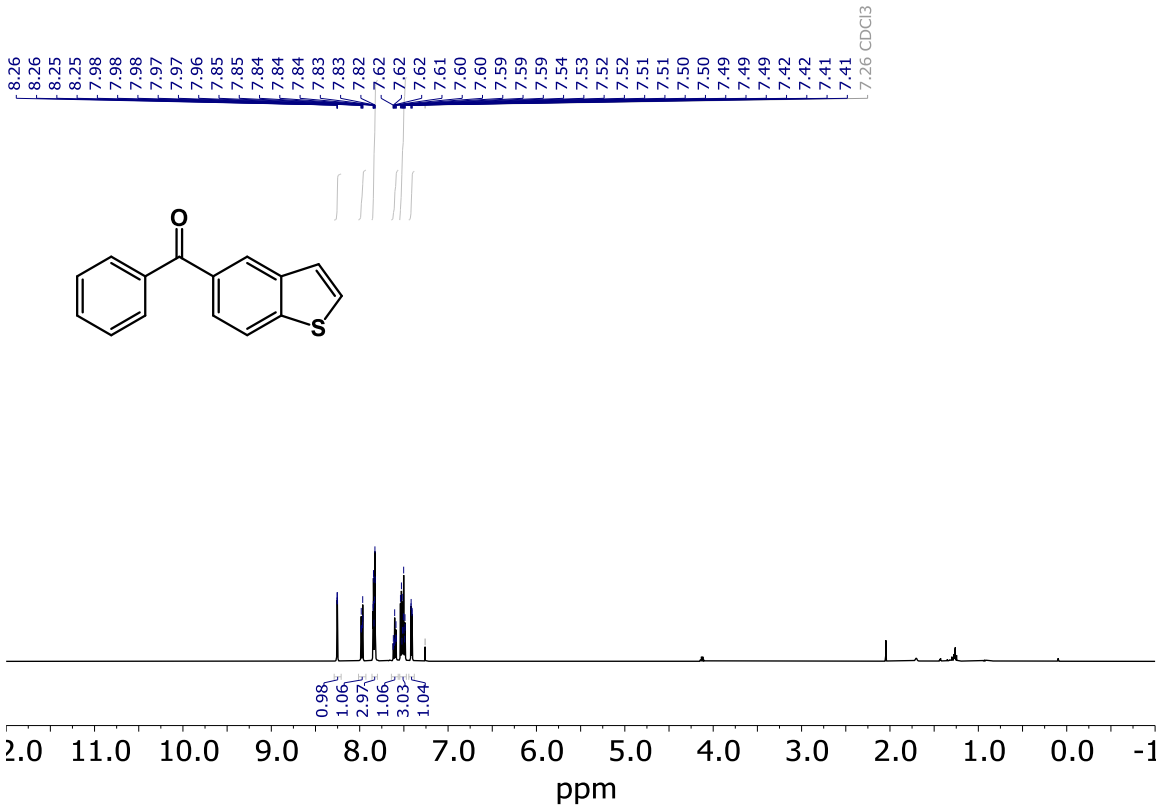


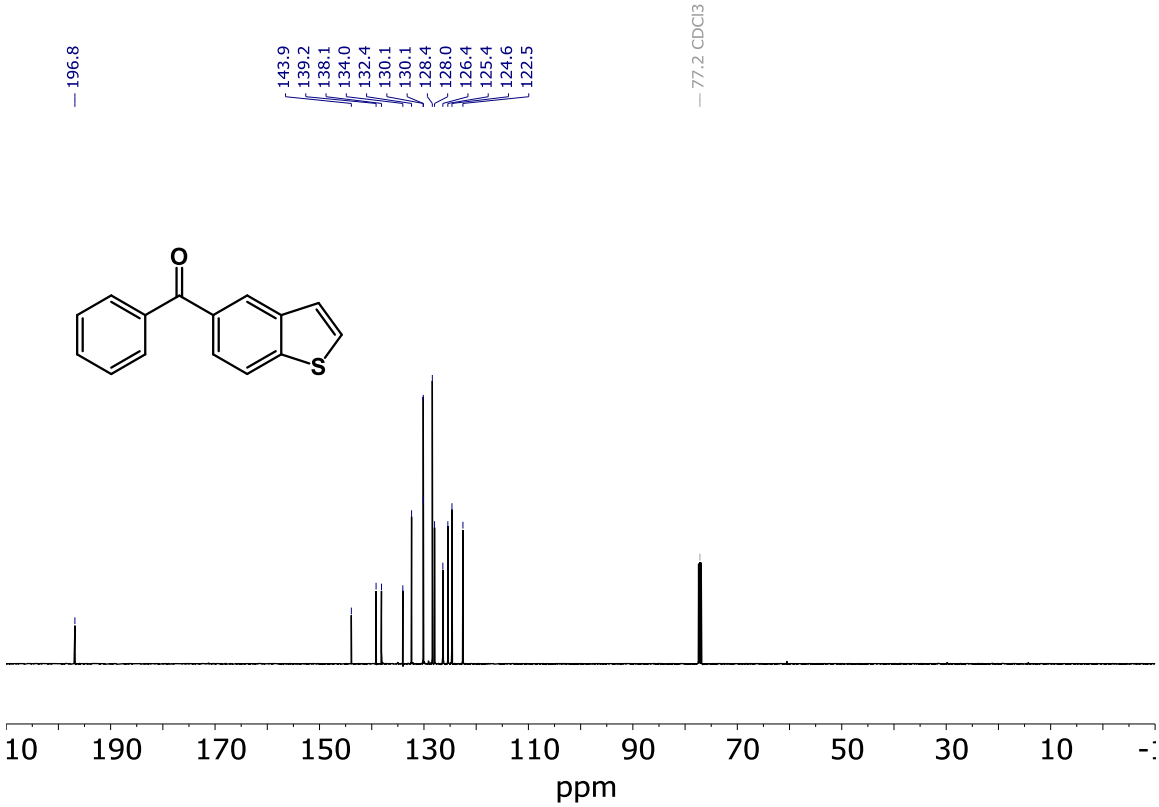
6-benzoyl-2,3-dihydro-1H-inden-1-one (3n)



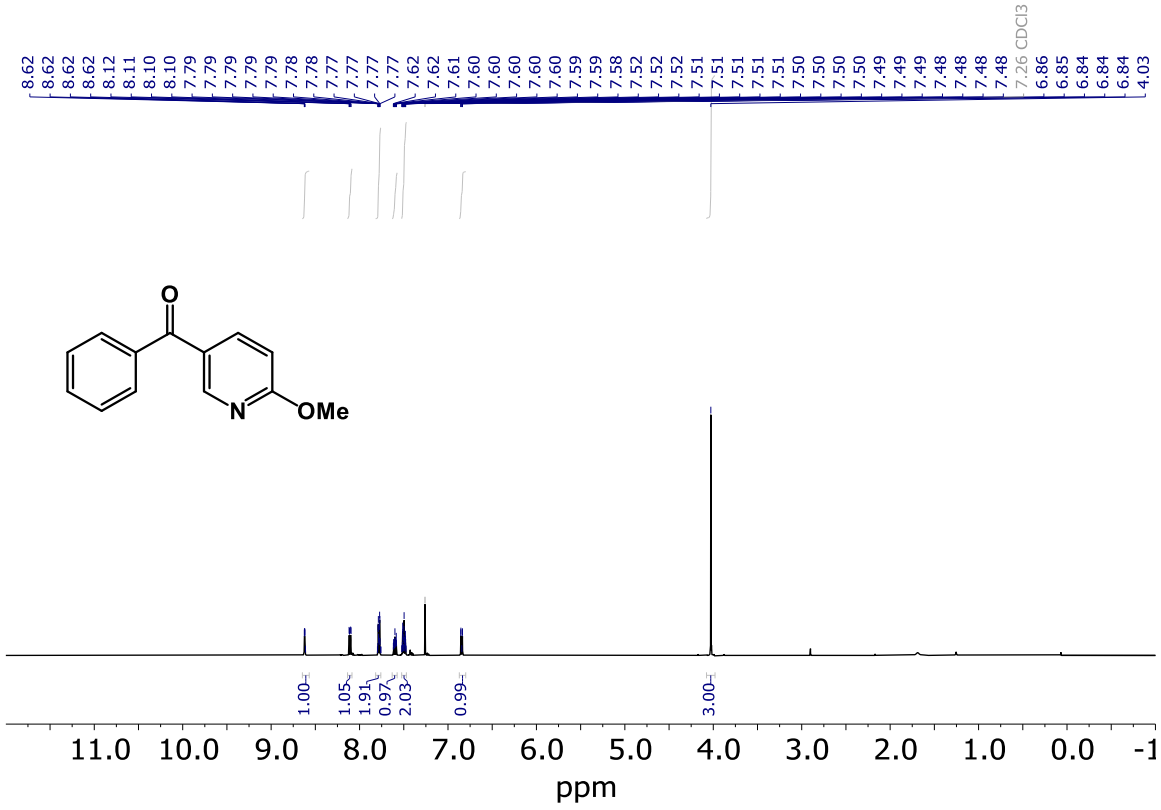


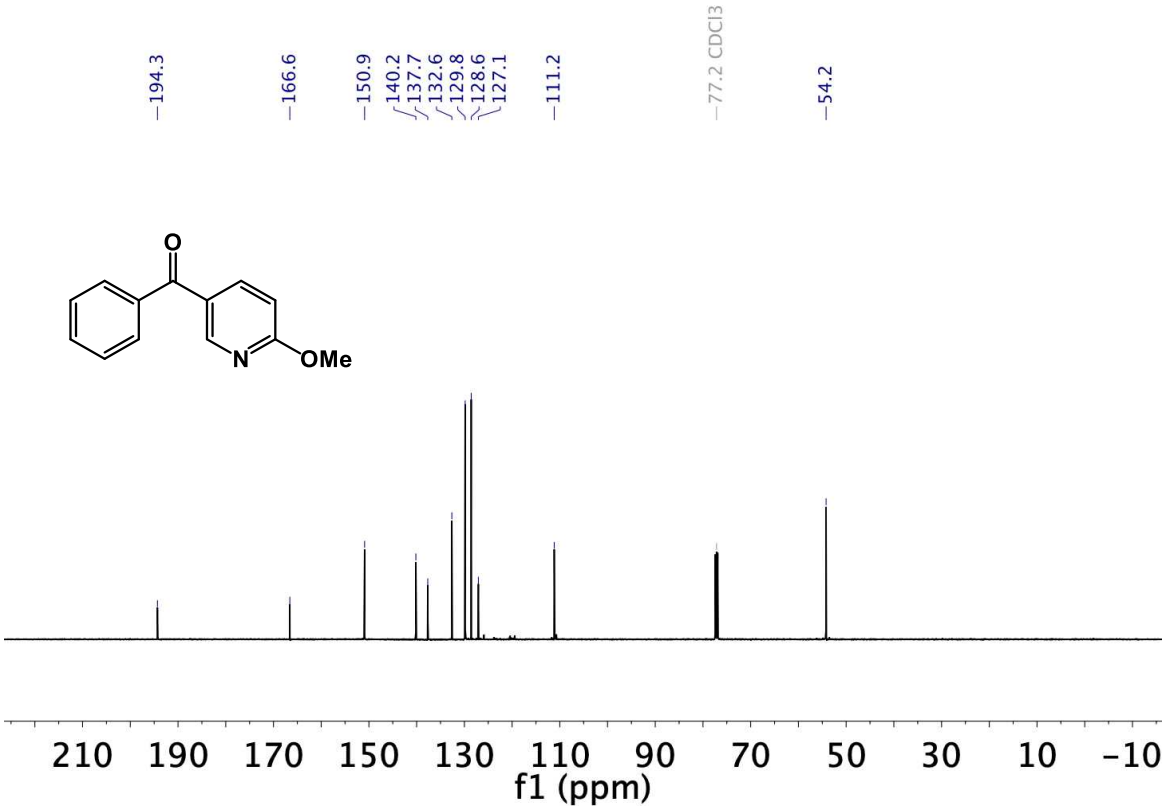
benzo[b]thiophen-5-yl(phenyl)methanone (3o)



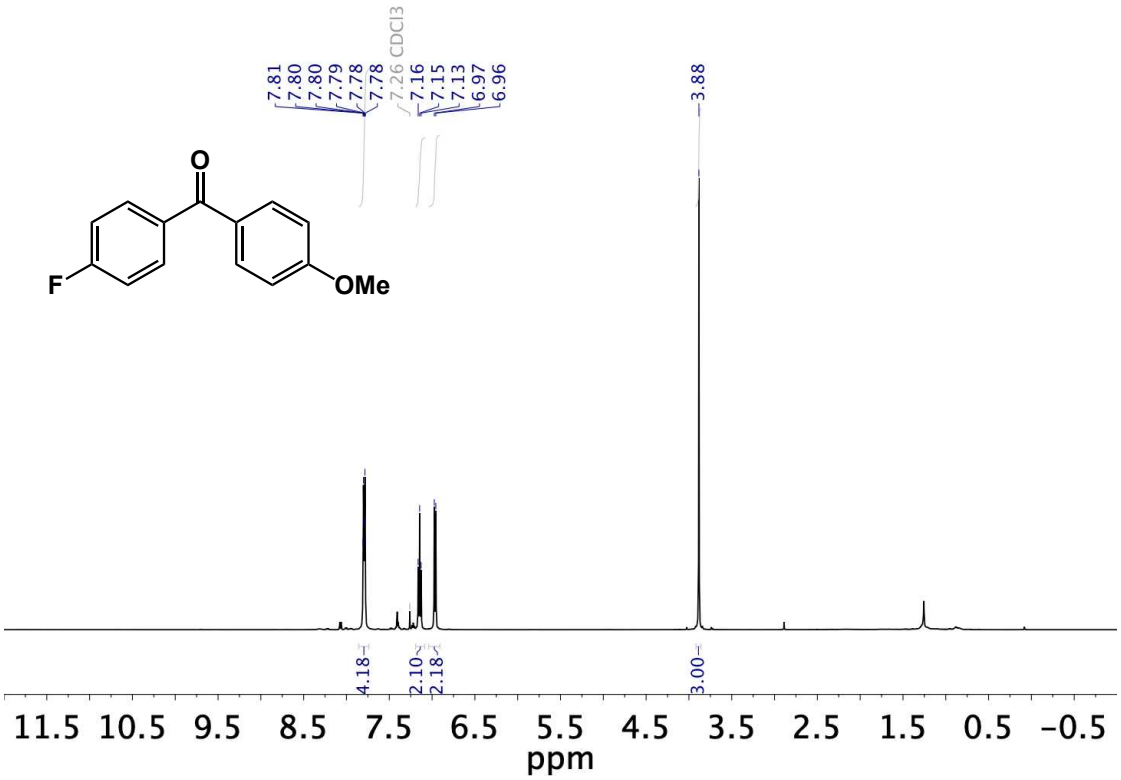


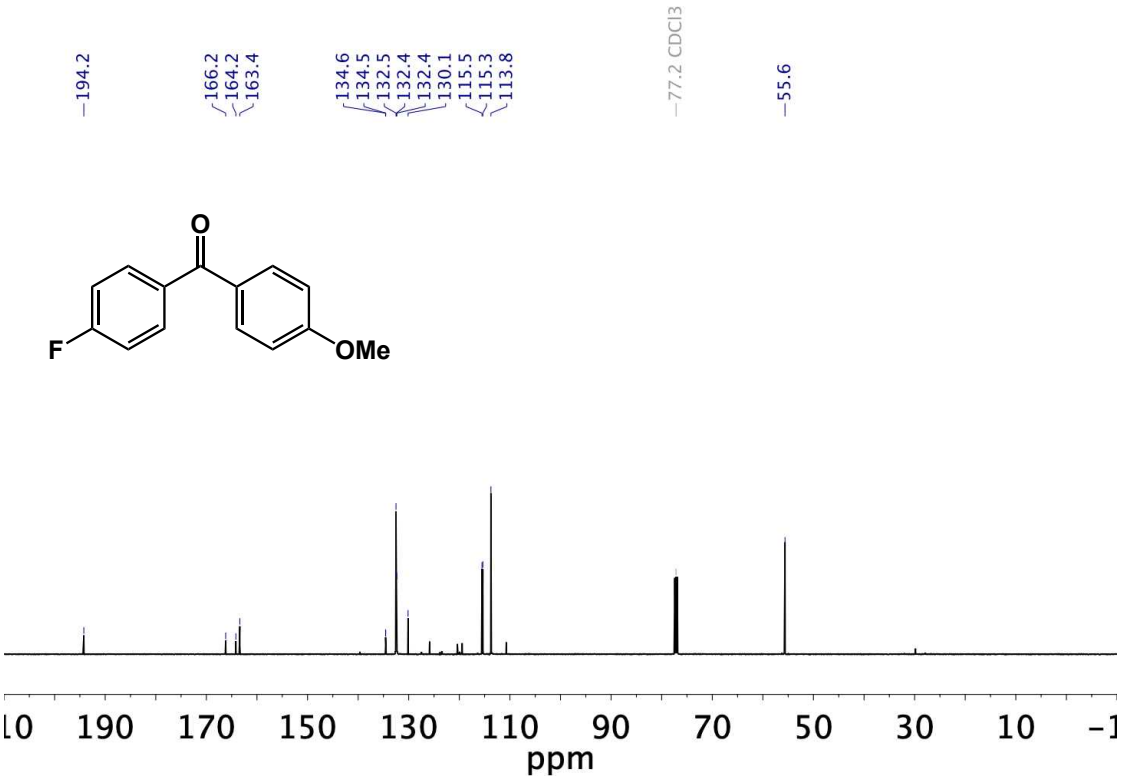
(6-methoxypyridin-3-yl)(phenyl)methanone (3p)

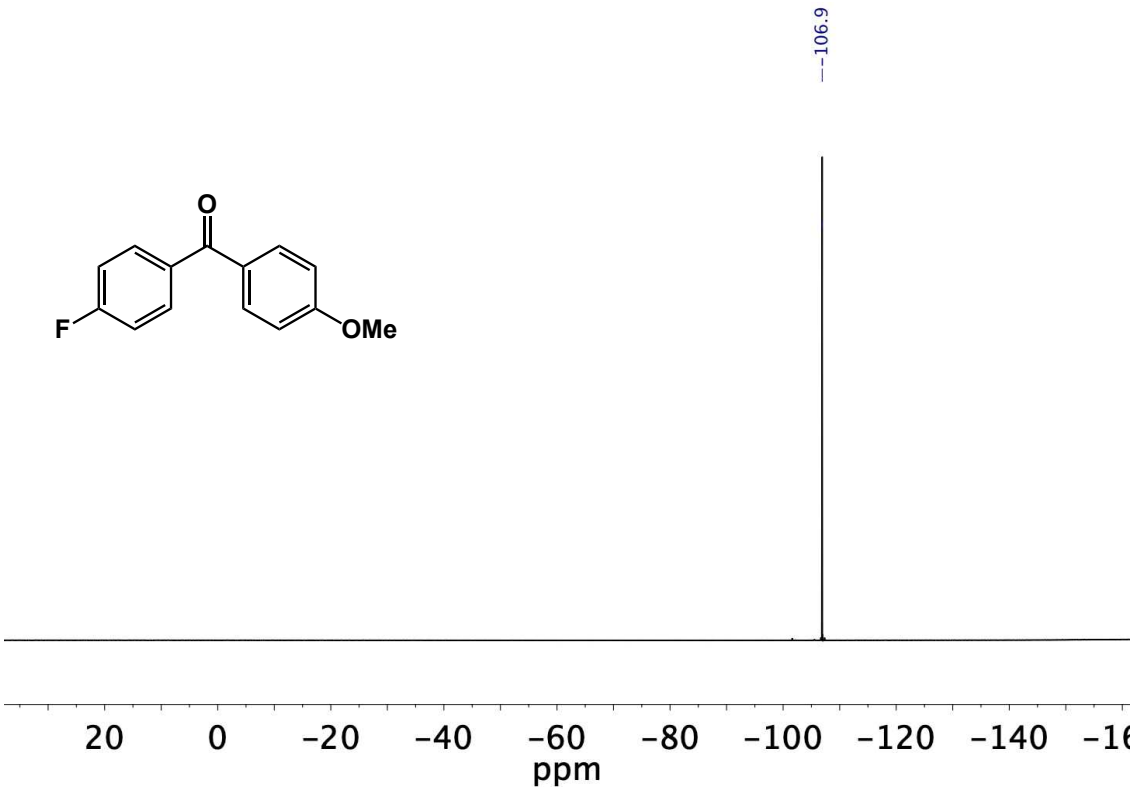




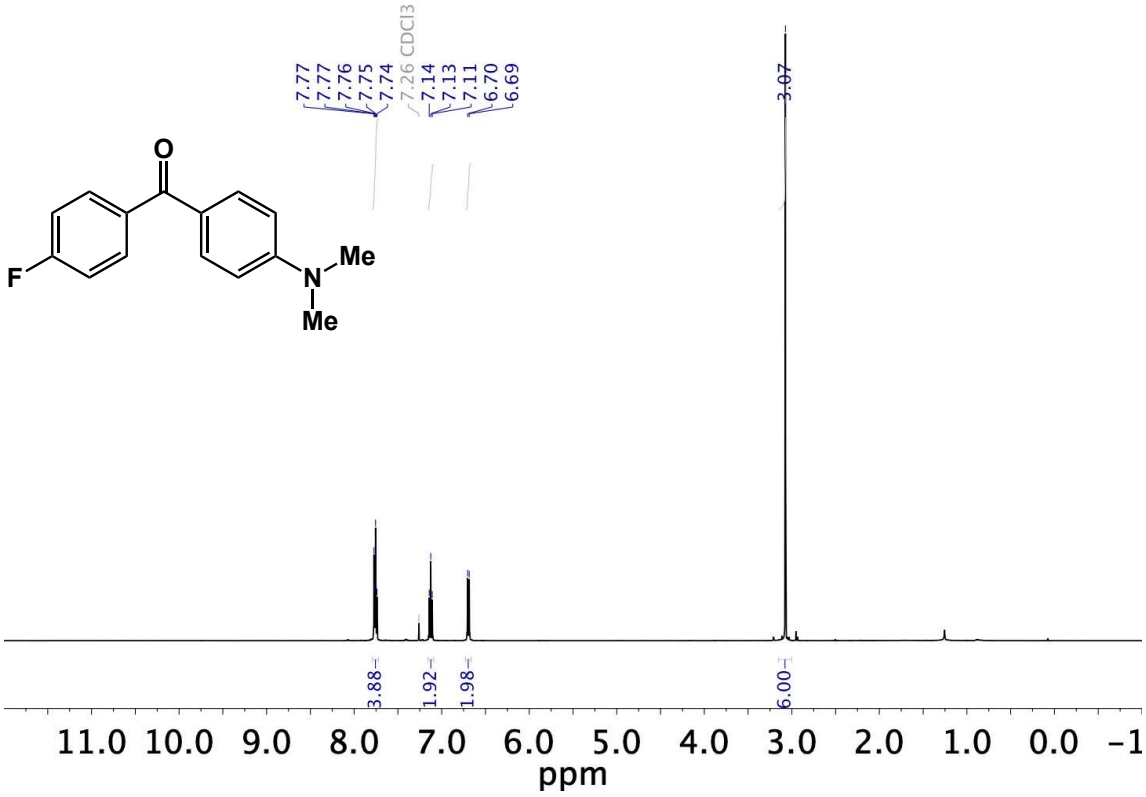
(4-fluorophenyl)(4-methoxyphenyl)methanone (3s)

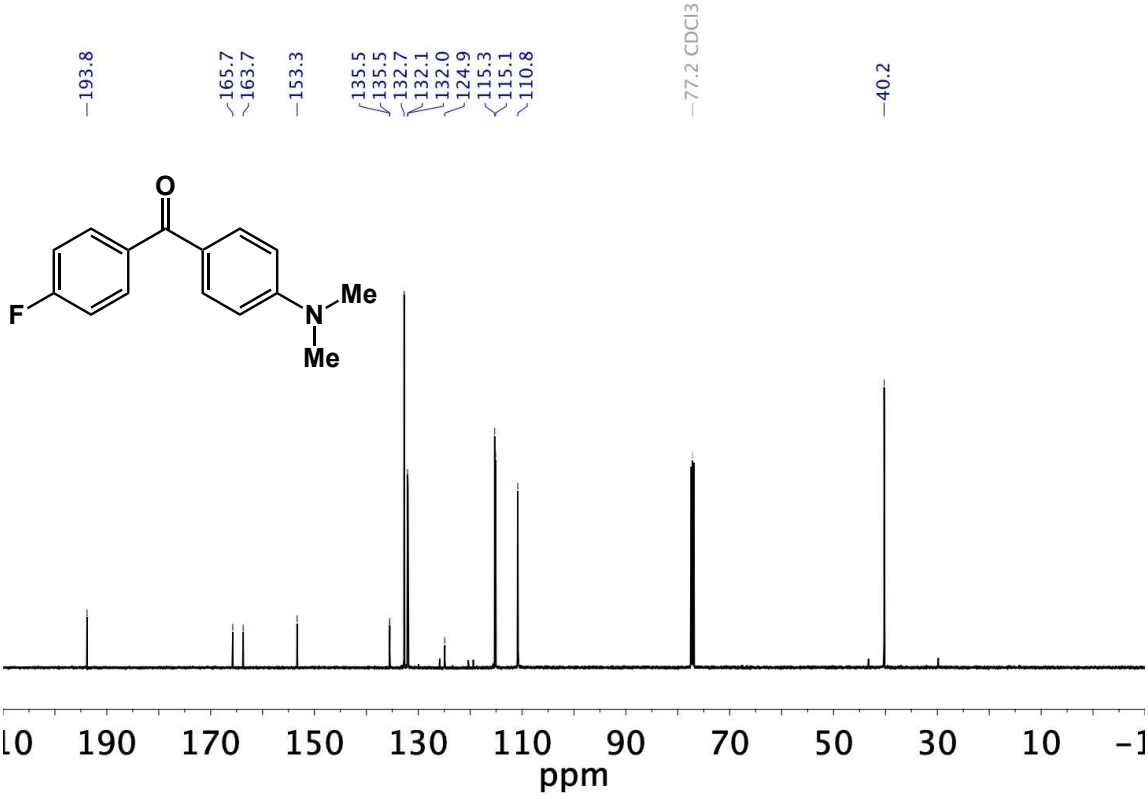


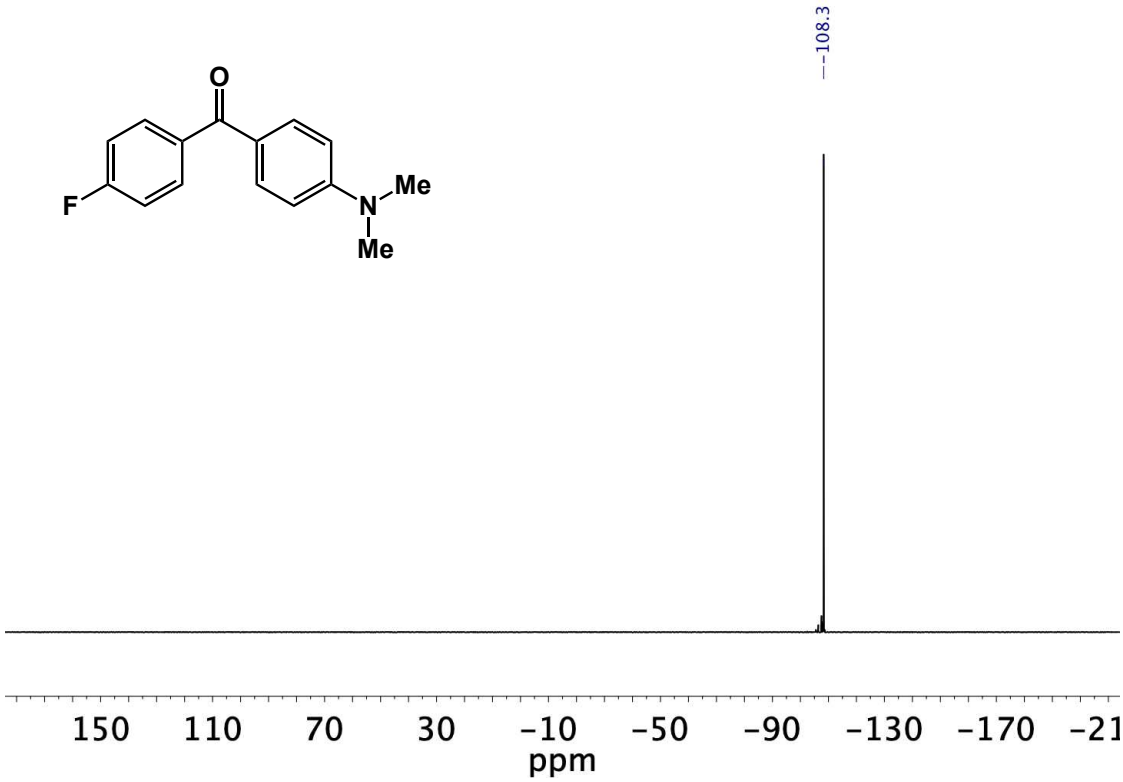



-106.9
O
F
OMe
20
0
-20
-40
-60
-80
-100
-120
-140
-16
ppm

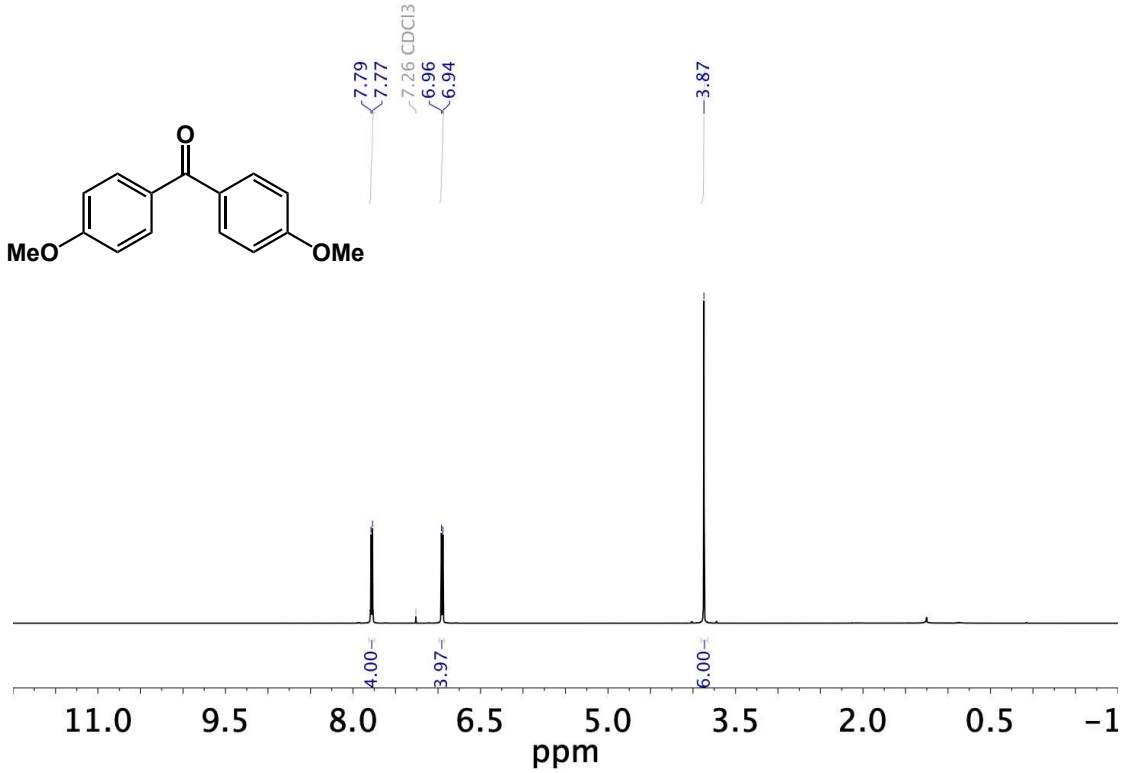
(4-(dimethylamino)phenyl)(4-fluorophenyl)methanone (3t)

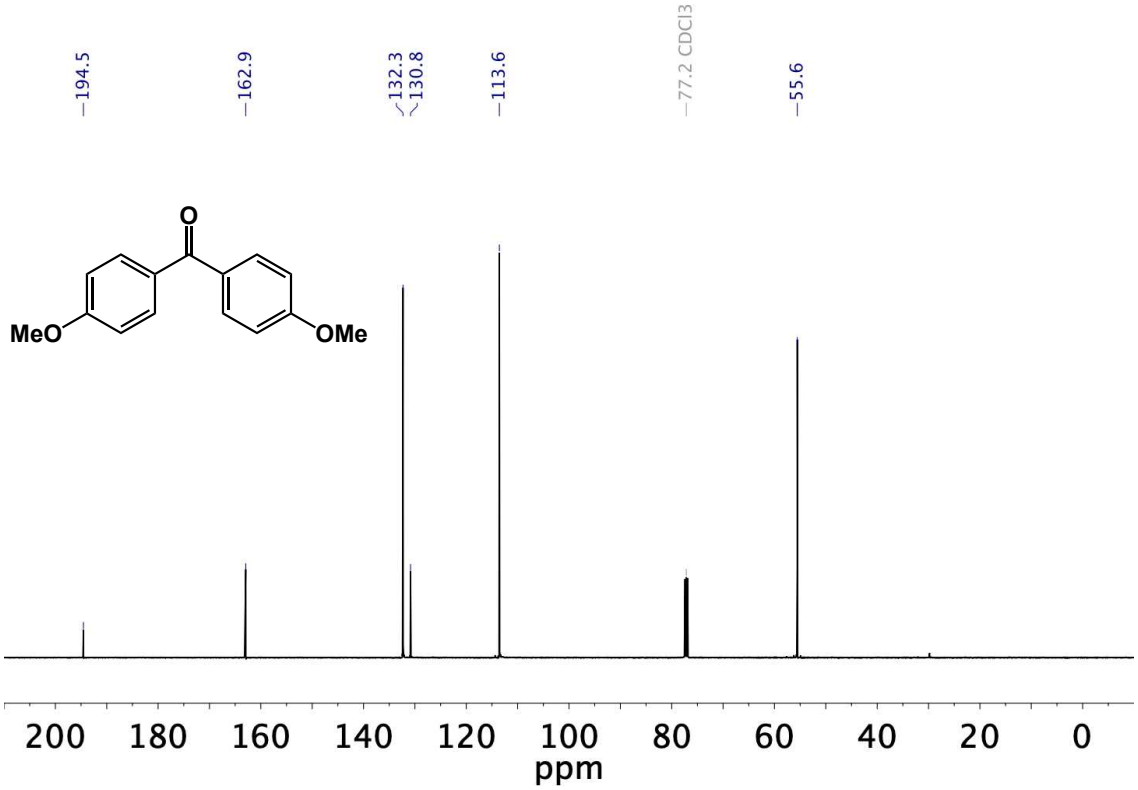




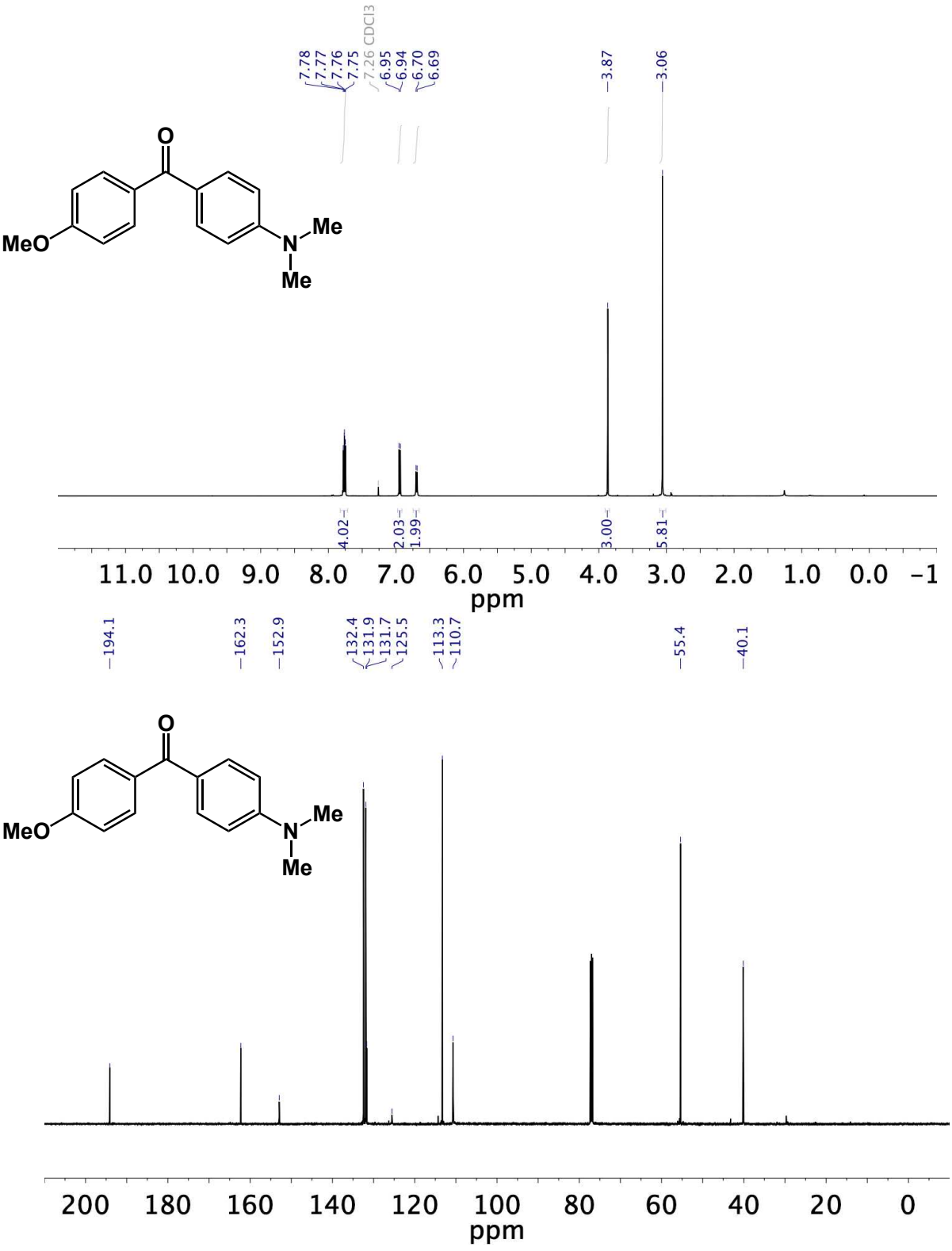

O
F
N
Me
Me
-108.3
150
110
70
30
-10
-50
-90
-130
-170
-21
ppm

bis(4-methoxyphenyl)methanone (3u)

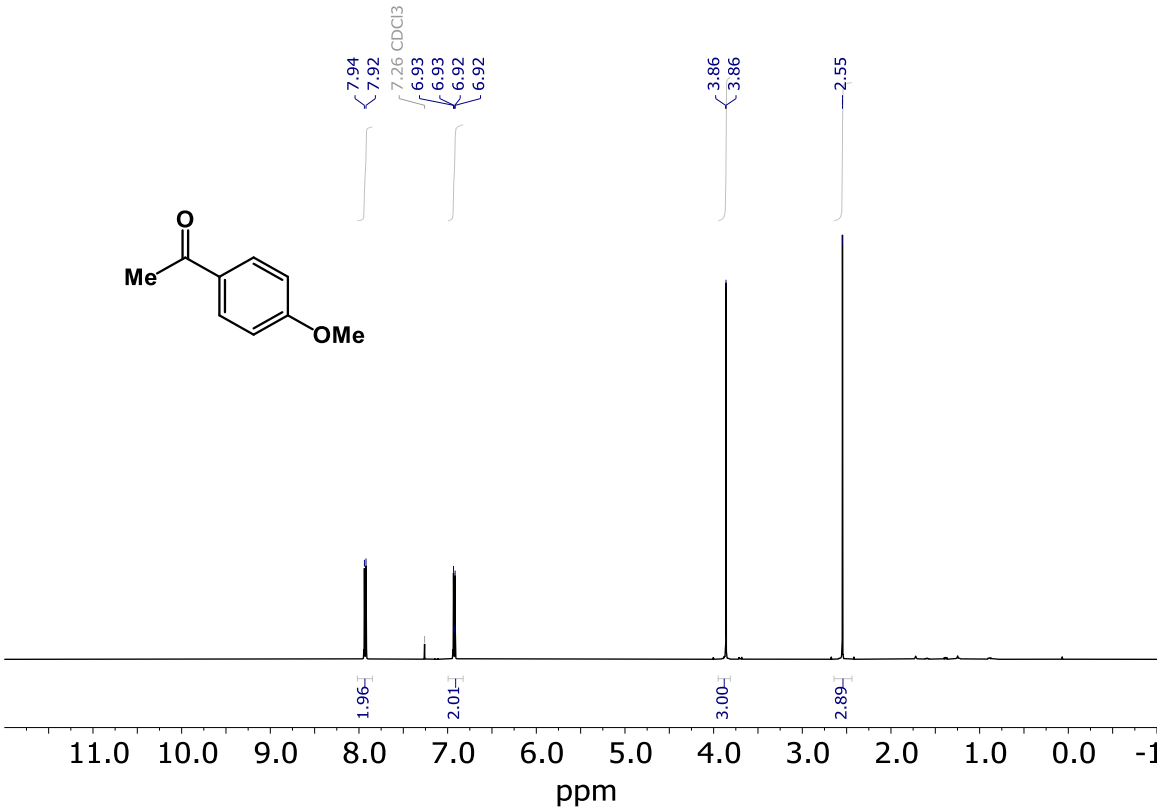


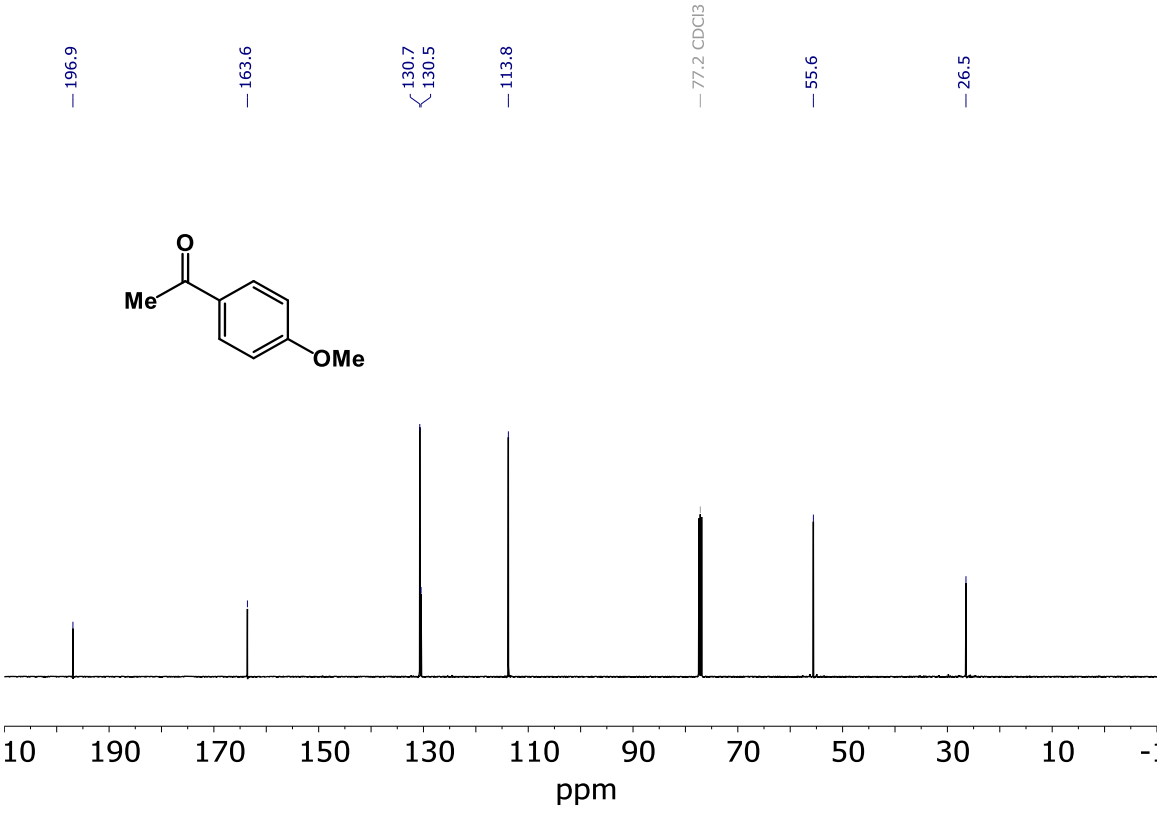


(4-(dimethylamino)phenyl)(4-methoxyphenyl)methanone (3v)

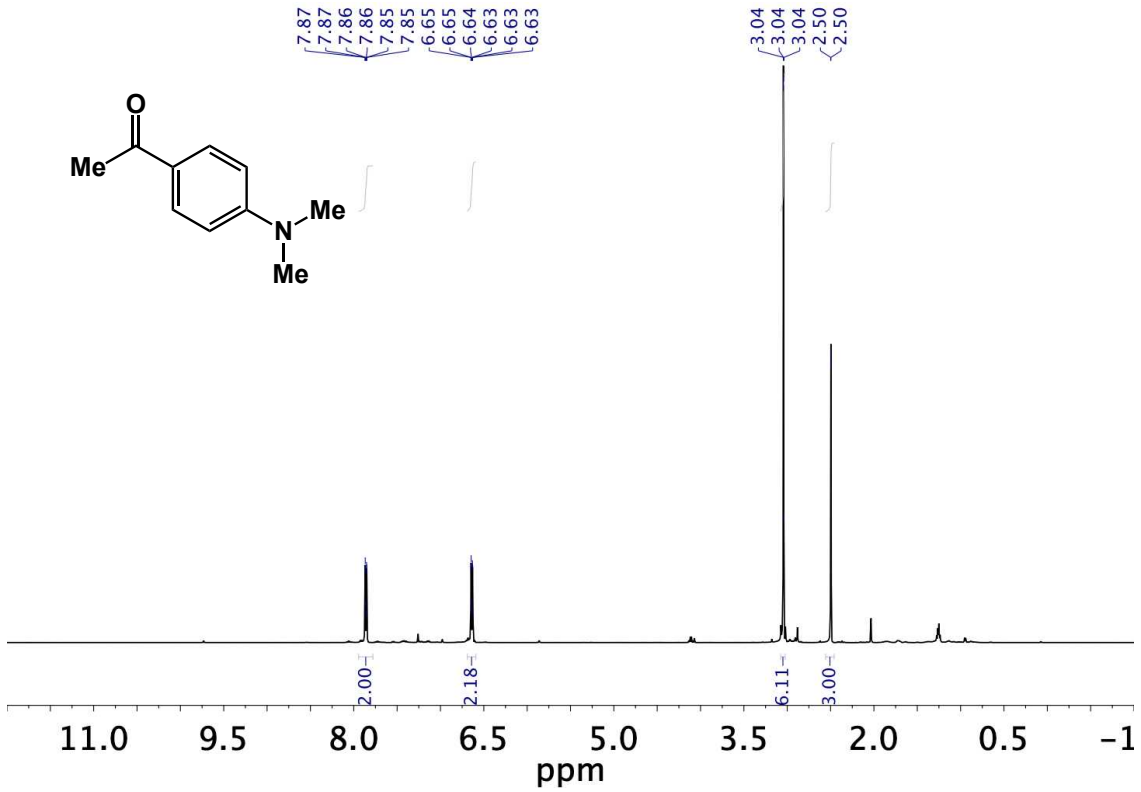


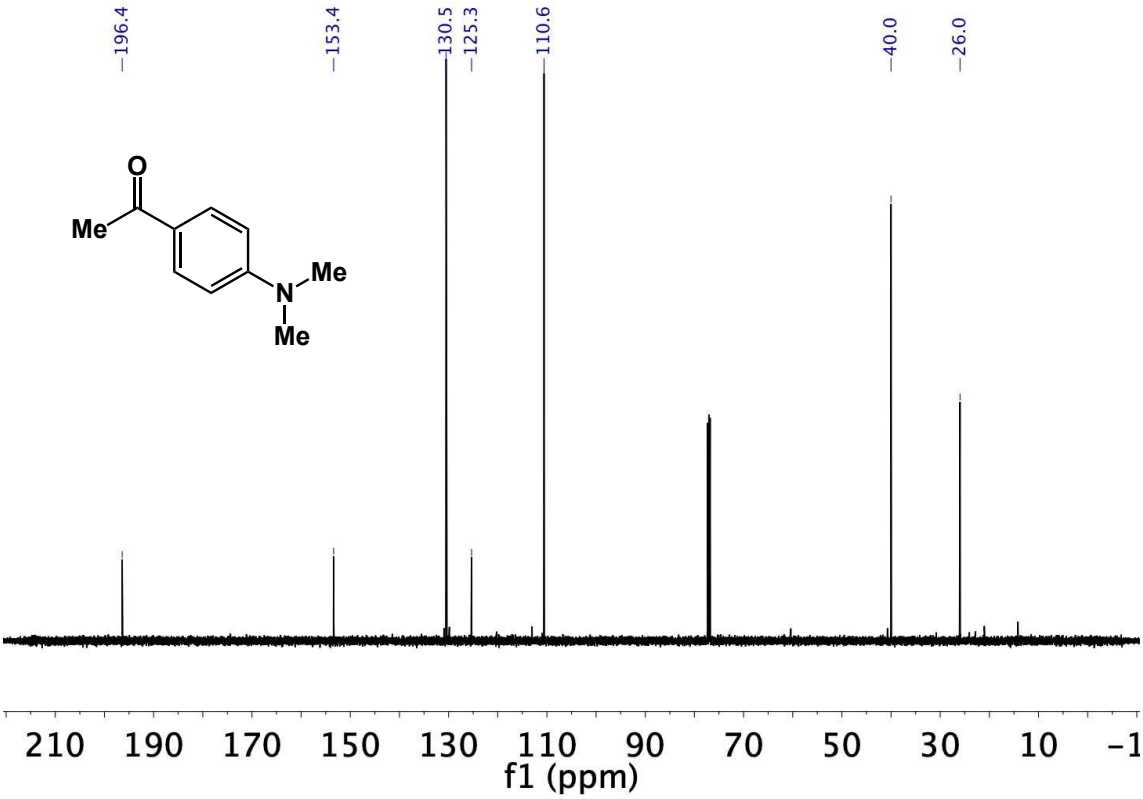
4-methoxyacetophenone (3w)



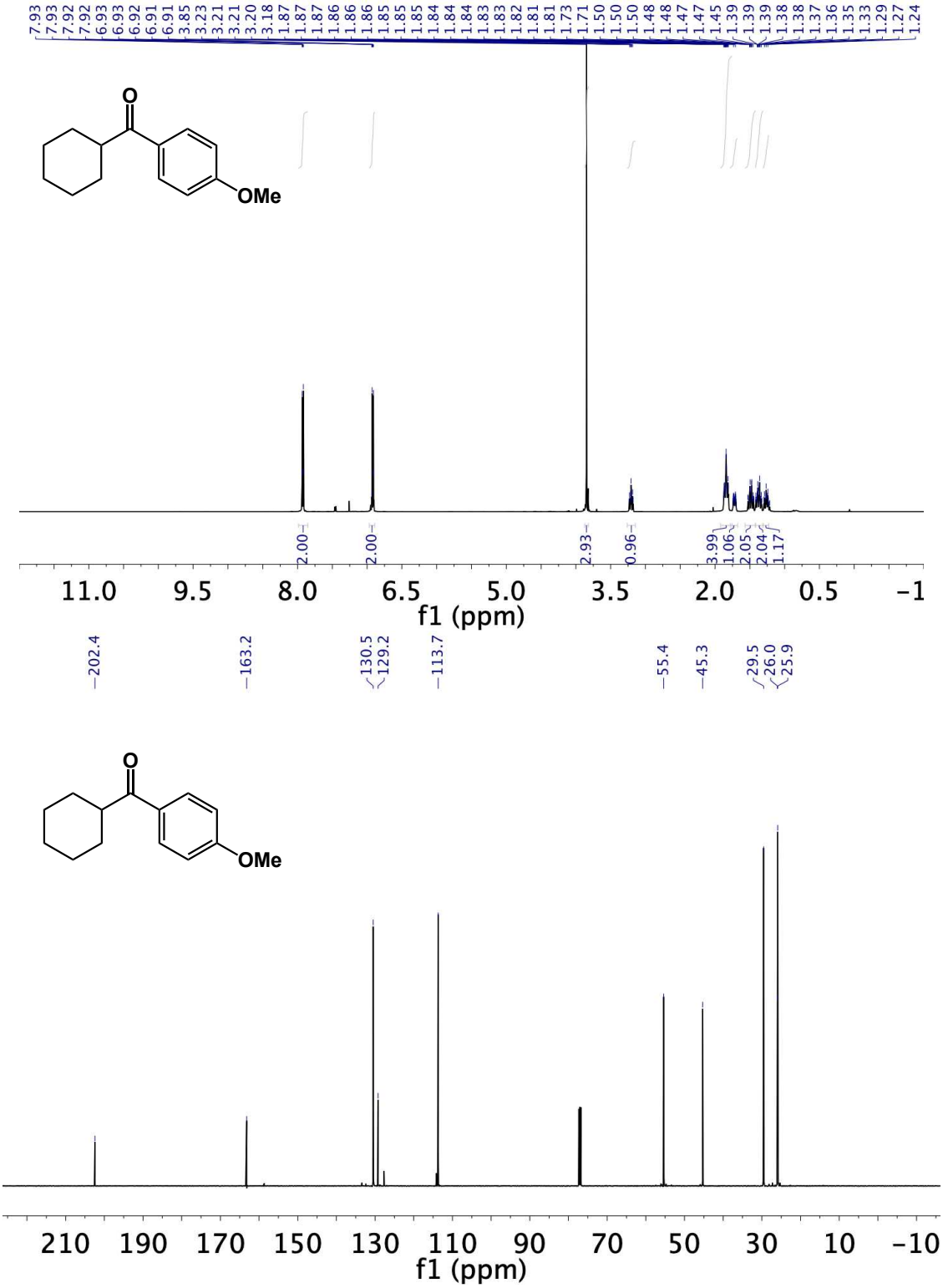


4-dimethylaminoacetophenone (3x)

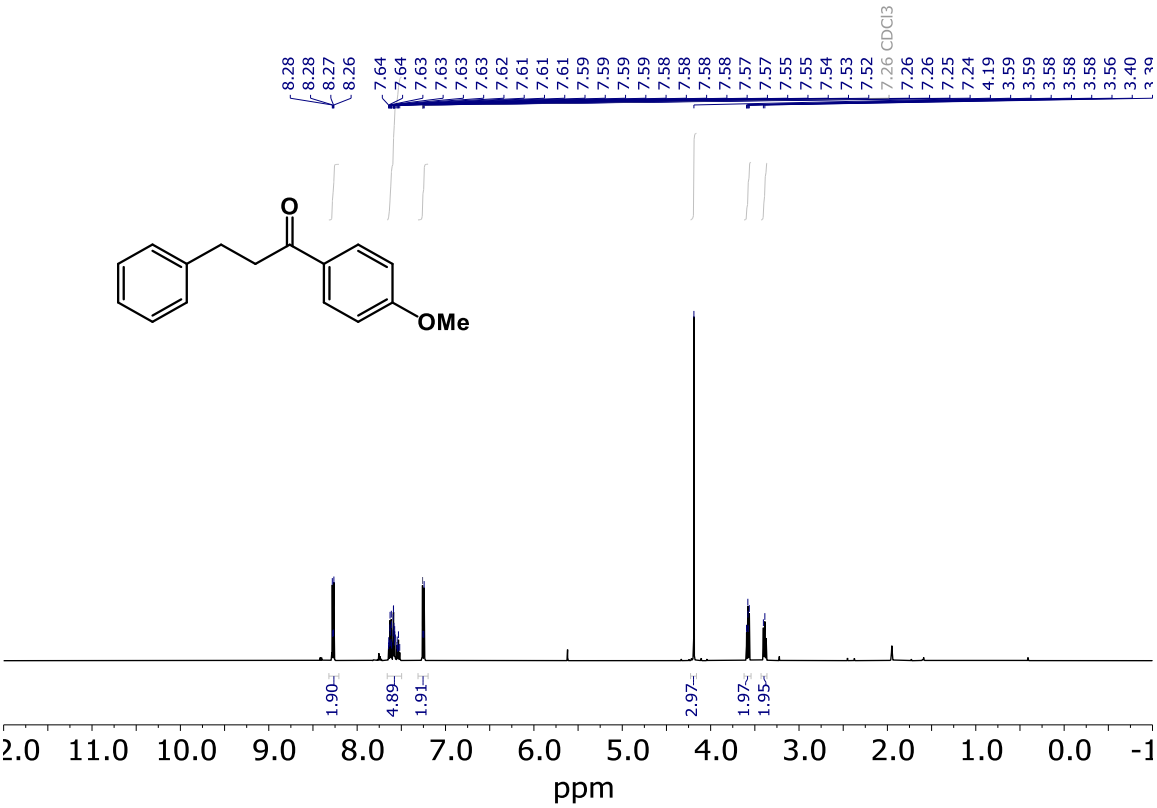


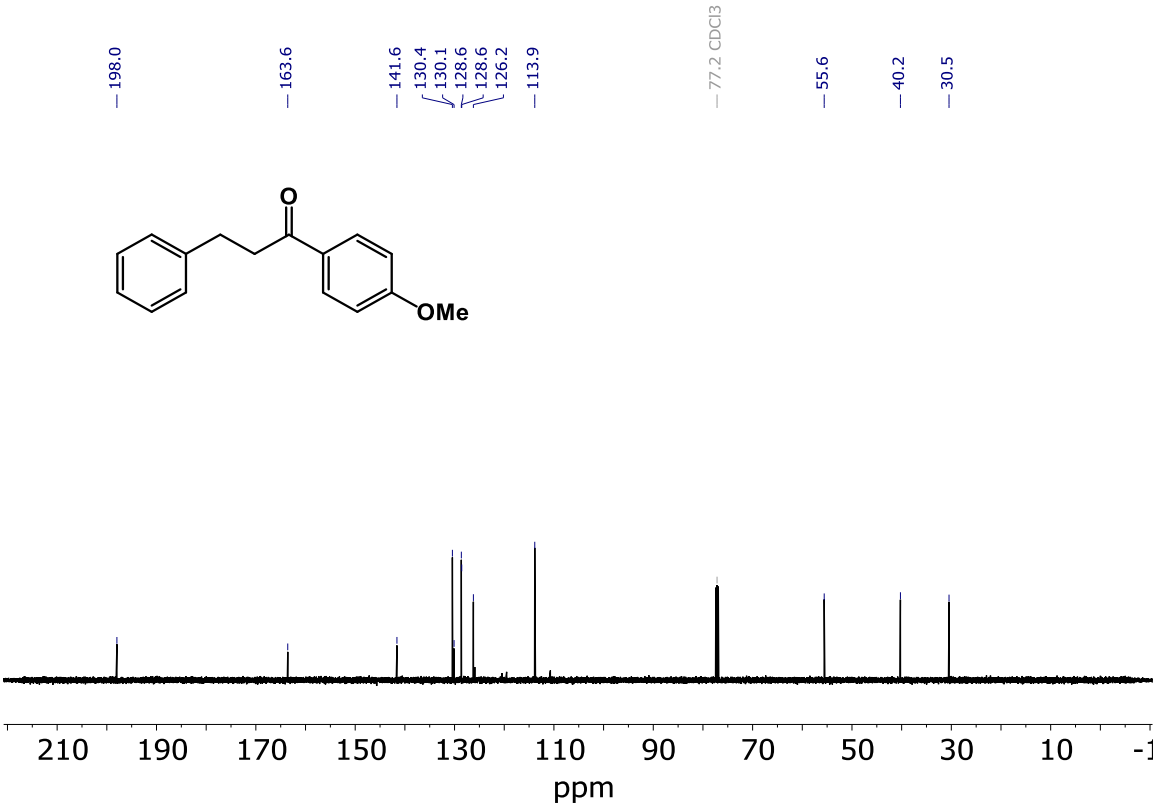


cyclohexyl(4-methoxyphenyl)methanone (3y)



1-(4-methoxyphenyl)-3-phenylpropan-1-one (3z)





1-(4-(dimethylamino)phenyl)-3-phenylpropan-1-one (3aa)