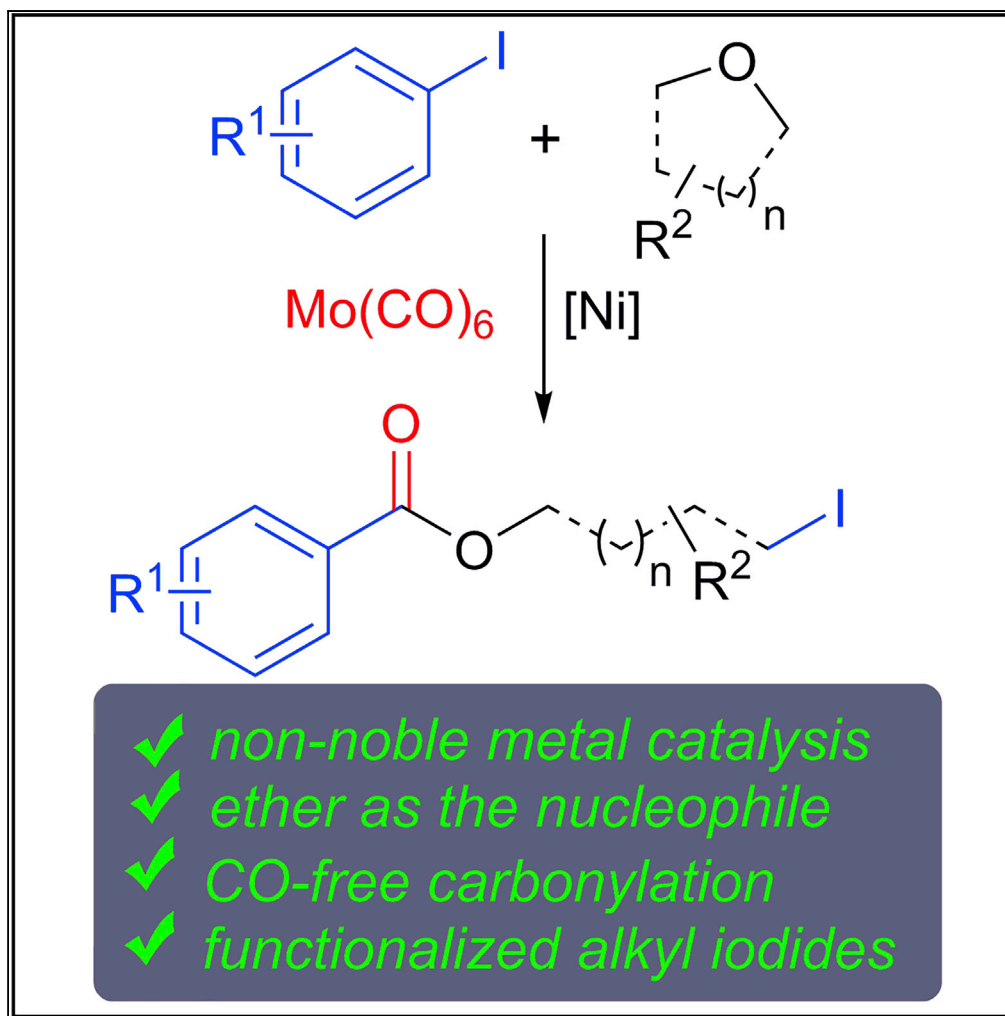


Article

Nickel-Catalyzed Carbonylative Synthesis of Functionalized Alkyl Iodides



Jin-Bao Peng, Fu-Peng Wu, Cong Xu, Xinxin Qi, Jun Ying, Xiao-Feng Wu

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HIGHLIGHTS

Nickel-catalyzed carbonylative synthesis of functionalized alkyl iodides

With Mo(CO)₆ as the solid CO source, carbonylative ether activation

Good yields of functionalized alkyl iodides

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Article

Nickel-Catalyzed Carbonylative Synthesis of Functionalized Alkyl Iodides

Jin-Bao Peng,^{1,3} Fu-Peng Wu,^{1,3} Cong Xu,¹ Xinxin Qi,¹ Jun Ying,¹ and Xiao-Feng Wu^{1,2,4,*}

SUMMARY

Functionalized alkyl iodides are important compounds in organic chemistry and biology. In this communication, we developed an interesting nickel-catalyzed carbonylative synthesis of functionalized alkyl iodides from aryl iodides and ethers. With Mo(CO)₆ as the solid CO source, both cyclic and acyclic ethers were activated, which is also a challenging topic in organic synthesis. Functionalized alkyl iodides were prepared in moderate to excellent yields with outstanding functional group tolerance. Besides the high value of the obtained products, all the atoms from the starting materials were incorporated in the final products and the reaction had high atom efficiency as well.

INTRODUCTION

Functionalized alkyl iodides are potent chemicals in organic chemistry and biology, and many drugs were effectively prepared from alkyl iodides (Trewick et al., 2002; DeGraw et al., 1997; Liu et al., 2014). Furthermore, ethers are widely used as solvents in organic transformations owing to their high chemical stability and relatively low boiling points. Besides, ethers are also used as strategic protecting groups for hydroxyl functions in organic synthesis (Wuts and Greene, 2014). The cleavage and functionalization of ethers is a versatile reaction in organic synthesis; several methods have been developed for the cleavage of ethers. In addition, many cyclic ethers are derived from biomass, and their ring-opening functionalization is synthetically useful for the synthesis of value-added chemicals (Christensen et al., 2014; Kumbhalkar et al., 2017; Mukherjee et al., 2017; Didiuk et al., 1995; Ohshita et al., 2006; Frei et al., 2018; Jones et al., 2017; Lübcke et al., 2017). However, owing to the high bond energy of C-O bond, relatively harsh conditions are usually needed for these transformations.

On the other hand, transition metal-catalyzed carbonylation reactions, using easily available starting materials to generate synthetically useful carbonyl-containing compounds by incorporating one or more CO into the substrate, have now emerged as one of the most powerful platform in synthetic chemistry (Gabriele et al., 2012; Wu, 2016; Peng and Wu, 2018). Typically, nucleophiles such as alcohols, amines, alkynes, and organic metallic compounds were usually used as the reactants for the carbonylative coupling reactions. Studies on carbonylative coupling reactions with weak nucleophiles (i.e., arenes and ethers) have been rarely reported. Recently, Arndtsen and co-workers developed an elegant procedure on carbonylation of arenes for the synthesis of ketones via the *in situ* formation of aroyl triflate as a highly reactive electrophile (Kinney et al., 2018; Tjutrins and Arndtsen, 2016; Torres et al., 2016; Quesnel and Arndtsen, 2013). However, to the best of our knowledge, the use of ether as the nucleophile in the carbonylation has not been reported because of its low reactivity (Seki et al., 1977; Tsuji et al., 1989; Watanabe et al., 1994; Getzler et al., 2004). Among the catalysts studied, palladium catalysts are more frequently applied. Although nickel catalysts have shown exceptional activities in certain bond activations, their related studies in carbonylation are still rare, which is mainly due to the fear of toxic and volatile Ni(CO)₄ formation, and the situation gets even worse with the usage of CO gas. To circumvent the discussed problems, the use of CO surrogates could provide high potential (Morimoto and Kakiuchi, 2004; Wu et al., 2017; Peng et al., 2017). Herein we wish to report our new results on nickel-catalyzed carbonylative cleavage of ethers with Mo(CO)₆ as the solid CO source. A broad range of functionalized alkyl iodides can be synthesized from aryl iodides and both cyclic and acyclic ethers. The control experiments showed that the carbonylative cleavage of ether was not proceeding via the intermediate acyl iodide. The ester formation step and the iodine attachment step took place simultaneously and synergistically.

RESULTS AND DISCUSSION

Optimization Study

Initially, iodobenzene **1a** and tetrahydrofuran **2b** were selected as the model substrates for this carbonylative ring opening of cyclic ethers. To our delight, upon stirring a solution of iodobenzene **1a**, tetrahydrofuran

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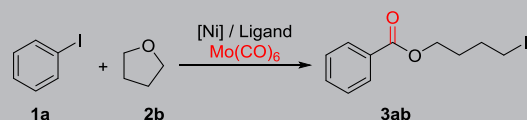
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Entry	[Ni]	Ligand	Solvent	Temperature °C	Yield (%) ^{a,b}
1	NiCl ₂	dtbbpy	Toluene	120	52
2	NiCl ₂	dtbbpy	Toluene	130	45
3	NiCl ₂	dtbbpy	Toluene	140	29
4	NiBr ₂	dtbbpy	Toluene	120	57
5	Ni(acac) ₂	dtbbpy	Toluene	120	30
6	Ni(OTf) ₂	dtbbpy	Toluene	120	58
7	Ni(OTf) ₂	bpy	Toluene	120	24
8	Ni(OTf) ₂	PCy ₃	Toluene	120	48
9	Ni(OTf) ₂	PPh ₃	Toluene	120	30
10 ^c	Ni(OTf) ₂	dtbbpy	Toluene	120	64
11 ^c	Ni(OTf) ₂	dtbbpy	Xylene	120	57
12 ^c	Ni(OTf) ₂	dtbbpy	Chlorobenzene	120	89
13 ^c	Ni(OTf) ₂	dtbbpy	Cyclohexane	120	42
14 ^{c,d}	Ni(OTf) ₂	dtbbpy	Chlorobenzene	120	95 (93)
15 ^{c,d,e}	Ni(OTf) ₂	dtbbpy	Chlorobenzene	120	32
16 ^{c,d,f}	Ni(OTf) ₂	dtbbpy	Chlorobenzene	120	41

Table 1. Optimization of the Reaction Conditions

See also Tables S1–S8.

^aReaction conditions: iodobenzene (0.5 mmol), THF (2.0 equiv), Ni(OTf)₂ (5 mol %), dtbbpy (5 mol %), Mo(CO)₆ (1.0 equiv), chlorobenzene (2 mL), 120°C.

^bYields were determined by gas chromatography using dodecane as an internal standard.

^cMo(CO)₆ (0.5 equiv).

^dTHF (3.0 equiv).

^eFe₃(CO)₁₂ (0.25 equiv).

^fCr(CO)₆ (0.5 equiv).

2b, and Mo(CO)₆ in the presence of NiCl₂ and dtbbpy (4,4'-di-tert-butyl-2,2'-bipyridine) in toluene at 120°C, the carbonylative ring-opening reaction proceeded successfully and the desired product δ -iodobutyl benzoate **3ab** was obtained in 52% yield (Table 1, entry 1). The reaction temperature played an important role in this reaction; increasing the reaction temperatures resulted in decreased yields (Table 1, entries 2 and 3). However, the yields decreased dramatically when the reaction was performed below 120°C (see details in Table S1). This is explainable since a high reaction temperature would facilitate the oxidative addition of transition metal into the C-I bond and the release of CO from Mo(CO)₆, whereas very high reaction temperature would result in the decarbonylation of acyl nickel complex. Subsequently, different nickel catalysts such as NiBr₂, Ni(acac)₂, and Ni(OTf)₂ were investigated (Table 1, entries 4–6, see details in Table S2). All the tested nickel catalysts showed comparable catalytic activity, with Ni(OTf)₂ giving the best result and a slightly higher yield of 58% (Table 1, entry 6). No carbonylation product was obtained in the absence of nickel catalyst (see in Table S2). Then, we investigated the effect of different ligands. A decreased yield of 24% was obtained when bpy (2,2'-bipyridine) was used as the ligand (Table 1, entry 7). Other bpy-based *N*-ligands including phenanthroline and terpyridine failed to catalyze this transformation (see details in Table S3). In addition to *N*-ligands, monodentate phosphine ligands and *N*-heterocyclic carbene also showed catalytic activity for this reaction, albeit leading to decreased yields (Table 1, entries 8 and 9, see details in Table S3).

The screening of the amount of $\text{Mo}(\text{CO})_6$ revealed that 0.5 equivalent of $\text{Mo}(\text{CO})_6$ is optimal and the product **3ab** was produced in 64% yield (Table 1, entry 10). Increasing the amount of $\text{Mo}(\text{CO})_6$ leads to lower yields, which might be caused by the formation of catalytically nonactive $\text{Ni}(\text{CO})_4$ in the presence of excess CO (see details in Table S4). Screening of the additives such as NaI and TBAI did not improve the yields (see details in Table S5). Notably, the selection of solvent also played an important role in the carbonylation reactions. The yields were decreased to 57% and 42% when the reaction was performed in xylene and cyclohexane, respectively (Table 1, entries 11 and 13). However, a high yield of 89% was obtained when chlorobenzene was used as the solvent (Table 1, entry 12; see details in Table S6). This may be due to the high polarity of PhCl and also the better solubility of substrates. Furthermore, increasing the amount of tetrahydrofuran improved the yield, and the desired product **3ab** was isolated in 93% yield (Table 1, entry 14; see details in Table S7). In addition to $\text{Mo}(\text{CO})_6$, other transition metal carbonyl complexes such as $\text{Fe}_3(\text{CO})_{12}$ and $\text{Cr}(\text{CO})_6$ were also capable of promoting this reaction, albeit giving lower yields (Table 1, entries 15 and 16). However, no desired product was obtained when gaseous CO (1 atm) was used instead of $\text{Mo}(\text{CO})_6$ (see Table S8). Notably, NaBr and NaCl were added into our optimized model system to attempt to produce the corresponding alkyl bromide and alkyl chloride, but no desired product could be detected.

Scope of the Investigation

With the optimized conditions in hand (Table 1, entry 14), we investigated the substrate scope of this transformation. First, as summarized in Figure 1, this reaction showed good generality to aryl iodides. A series of different aryl iodides were successfully applied to the optimized reaction conditions, and the corresponding iodoester products were obtained in moderate to excellent yields. Both electron-donating group- (Figure 1, **3ab–3ib**) and electron-withdrawing group- (Figure 1, **3jb–3qb**) substituted iodobenzenes were well tolerated and produced the corresponding iodoester products in 42%–93% yields. The steric properties of the iodobenzene affected the yields of the reaction significantly. For example, *meta*- and *para*-substituted iodobenzenes delivered the corresponding products in moderate to good yields under the standard conditions (Figure 1, **3cb** and **3db**, **3nb** and **3mb**). On the contrary, *ortho*-methyl iodobenzene gave a low yield of 51% (which could be improved to 70% by increasing the reaction temperature to 130°C, Figure 1, **3bb**). However, when *ortho*-chloro-iodobenzene was subjected to this reaction, only trace amount of the desired product was detected (Figure 1, **3ob**). Notably, a range of functional groups including ketone and ester were well tolerated in this reaction (**3jb** and **3kb**). Besides, fluoro and chloro substituents were compatible in this reaction and produced the corresponding products without breaking the C-X bonds (Figure 1, **3lb–3nb**). Interestingly, when 4-bromo-iodobenzene was used as the substrate, an inseparable mixture of **3pb** and **3pb'** (3.5:1) was obtained in 45% yield. However, no desired product could be detected when bromobenzene or 4-bromobenzotrifluoride was applied as the substrate, even though 1 equivalent of NaI additive was added. In addition to substituted iodobenzenes, other types of aromatic iodides were also tolerated in this transformation. For example, 1-iodonaphthalene, 2-iodonaphthalene, and 3-iodothiophene delivered the corresponding products in 77%, 72%, and 62% yields, respectively (Figure 1, **3rb**, **3sb**, and **3tb**). In addition, bromobenzene and 1-bromo-4-(trifluoromethyl)benzene were tested under our standard conditions as well, and no conversion of the substrates could be detected.

Subsequently, we turned our attention to test the generality of the ethers for this carbonylative ether cleavage reaction. As illustrated in Figure 2, a series of cyclic and acyclic ethers were tolerated in this reaction system. Symmetrical cyclic ethers such as tetrahydropyran **2c** and 7-oxabicyclo[2.2.1]heptane **2d** were well tolerated in this reaction, and the corresponding products were produced in moderate yields (Figure 2, **3ac** and **3hd**). It should be mentioned that when oxetane **2a** was applied to the standard reaction conditions, only trace amount of **3ha** was detected. However, **3ha** could be obtained in 41% yield when the reaction temperature was increased to 140°C. The low yield of **3ha** might be result from the polymerization of oxetane **2a**. In the case of unsymmetrical cyclic ethers, the cleavage of ether might take place via two different ways of C-O bond breaking. Generally, the C-O bond breaking prefers to take place at the sterically bulkier carbon of the ethers. For example, when 2-methyltetrahydrofuran **2f** was used as the starting material, carbonylative ring-opening product **3af** was obtained as the major products (Figure 2, **3af**: **3af'** = 9:1). However, when 3-methyltetrahydrofuran **2g** was used in this reaction, an inseparable mixture of **3ag** and **3ag'** was obtained in 68% yield with low selectivity (2:1). When 2,3-dihydrobenzofuran **2e** was applied to the optimized reaction condition, the carbonylative ring-opening product **3ae** was obtained in 37% yields. The C-O bond cleavage occurred selectively at the $\text{C}(\text{sp}^3)\text{-O}$ bond. In addition, acyclic ethers were also explored as substrates. The carbonylative cleavage of ethyl ether **2h**, butyl ether **2i**, and isopropyl ether **2j** took place smoothly and produced the corresponding esters in 65%, 48%, and 62% yields, respectively

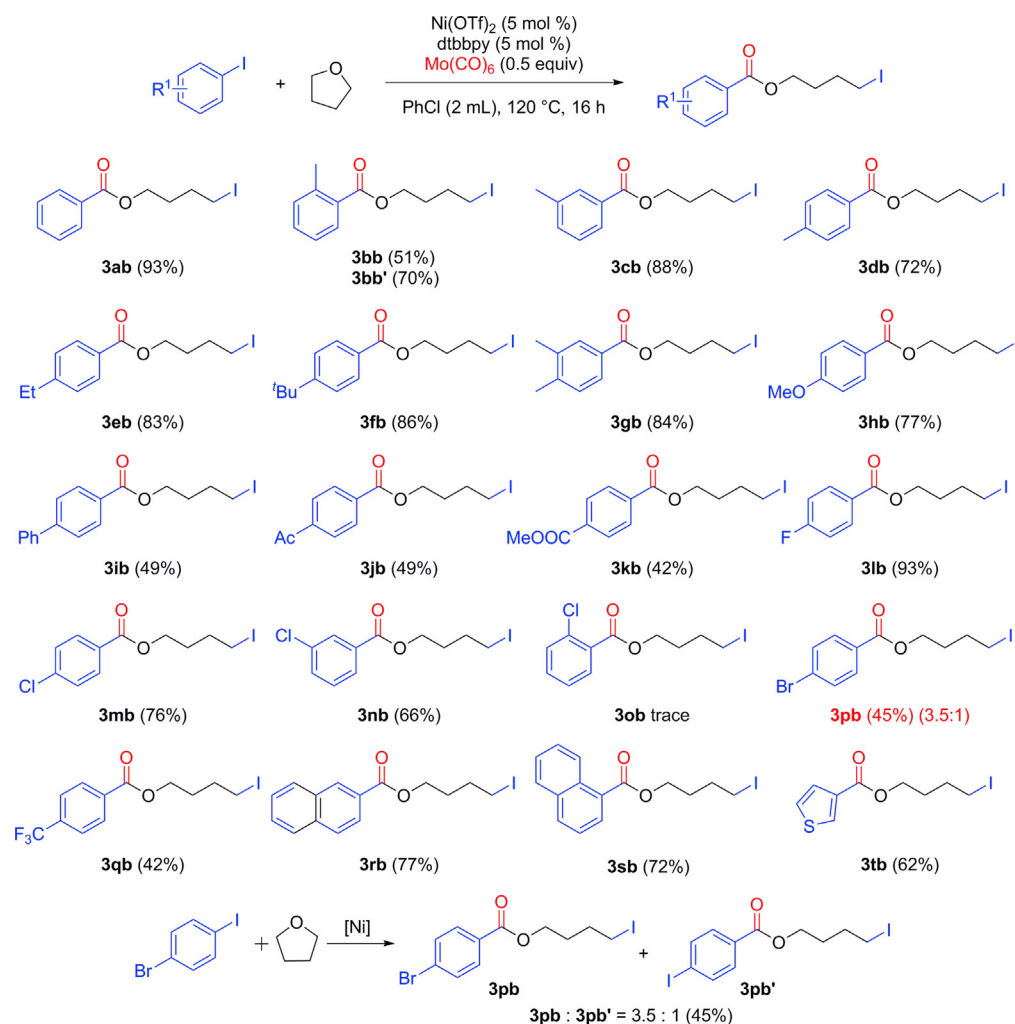


Figure 1. Substrate Scope of Aryl Iodides

Top: reaction conditions: aryl iodide (0.5 mmol), THF (3.0 equiv), Ni(OTf)₂ (5 mol %), dtbbpy (5 mol %), Mo(CO)₆ (0.5 equiv), chlorobenzene (2 mL), 120°C, isolated yields.

Bottom: aryl iodide (0.5 mmol), THF (3.0 equiv), Ni(OTf)₂ (5 mol %), dtbbpy (5 mol %), Mo(CO)₆ (0.5 equiv), chlorobenzene (2 mL), 130°C for **3bb'** and **3sb**.

See also Figures S1–S36.

(Figure 2, **3ah**, **3ai**, and **3aj**). When unsymmetrical ether **2k** was subjected to this reaction, a mixture of esters were obtained with a total yield of 70% (Figure 2, **3ak**: **3ak'** = 5:3). Moreover, when (methoxymethyl)benzene **2l** was reacted with iodobenzene under the optimized reaction condition, only 24% yield of methyl benzoate **3al** was obtained, whereas no benzyl benzoate was detected.

Mechanistic Study

To gain a better understanding of the reaction pathway of this carbonylative ether cleavage reaction, a series of supporting experiments were conducted (Scheme 1). First, when iodobenzene **1a** and THF (tetrahydrofuran) **2b** were subjected to the standard conditions in the presence of excess halide additives such as LiCl and LiBr, the iodoester **3ab** was obtained in good yields. No chloro- or bromoesters were observed (Scheme 1, A). Besides, 1,4-dioxane was reported to give the chloroester in acylative cleavage reactions. However, when 1,4-dioxane **2m** was used in this reaction, instead of iodoester **3am**, ethylene glycol dibenzoate **3am'** (Figures S59 and S60) was obtained in 40% yield (Scheme 1, B). This might result from the coordination of **3am** to the nickel catalyst, thus facilitating a second carbonylative cleavage. Furthermore,

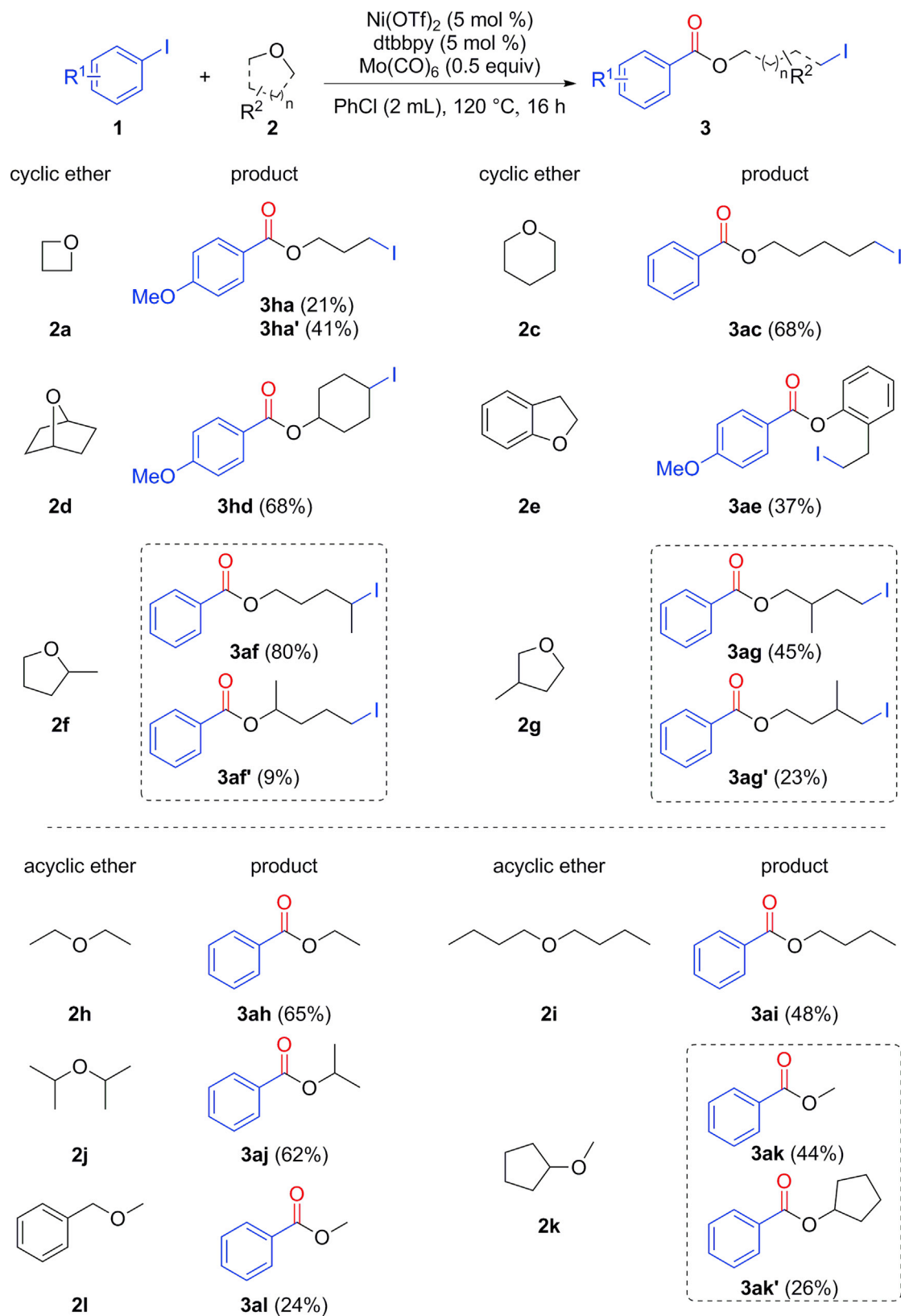


Figure 2. Substrate Scope of Ethers

Top: reaction conditions: aryl iodide (0.5 mmol), ether (3.0 equiv), Ni(OTf)₂ (5 mol %), dtbbpy (5 mol %), Mo(CO)₆ (0.5 equiv), chlorobenzene (2 mL), 120°C, isolated yields.

Middle: aryl iodide (0.5 mmol), ether (3.0 equiv), Ni(OTf)₂ (5 mol %), dtbbpy (5 mol %), Mo(CO)₆ (0.5 equiv), chlorobenzene (2 mL) at 130°C for **3ha**.

Bottom: aryl iodide (0.5 mmol), ether (3.0 equiv), Ni(OTf)₂ (5 mol %), dtbbpy (5 mol %), Mo(CO)₆ (0.5 equiv), chlorobenzene (2 mL) at 140°C for **3ha'**.

See also Figures S37–S58.

when unsymmetrical cyclic ether **2f** was reacted with iodobenzene, **3af** and **3af'** were obtained in a ratio of 9:1. However, the reaction of *in situ* prepared benzoyl iodide with 2-methyltetrahydrofuran **2f** produced **3af** and **3af'** with an opposite ratio of 1:2 (Scheme 1, C). These phenomena revealed that the carbonylative cleavage of ether did not proceed via the intermediate acyl iodide. The ester formation step and the iodine attachment step should take place simultaneously and synergistically.

Plausible Reaction Mechanism

Based on these results and previous literature, a plausible mechanism was proposed in Scheme 2. Initially, the oxidative addition of aryl iodide to the *in situ*-generated Ni(0) formed the aryl nickel complex **4**. Then, coordination and insertion of CO, which was released from Mo(CO)₆, generated the acyl nickel complex **5**. Then, the coordination of the oxygen of THF to nickel activated the oxygen and the adjacent carbon. Subsequently, the iodide attacked the carbon and the C–O bond broke to generate intermediate **7**. Finally, reductive elimination of **7** delivered the desired product **3** and regenerated Ni(0) for the next catalytic cycle.

Conclusion

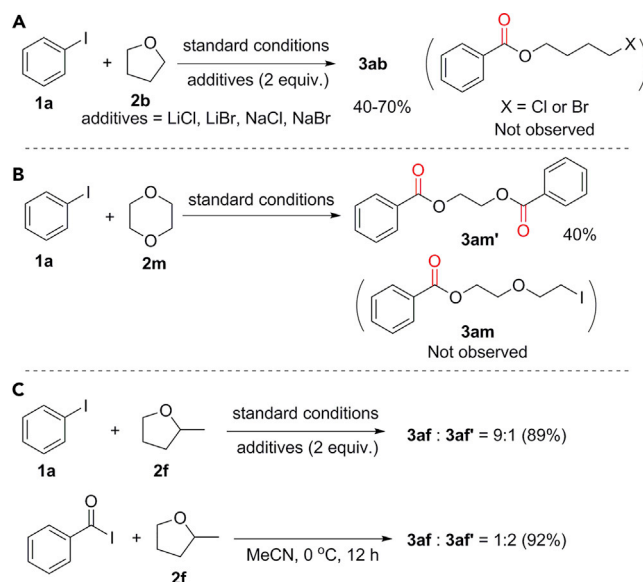
In summary, we have developed an interesting nickel-catalyzed carbonylative cleavage of ethers with Mo(CO)₆ as the solid CO source. Functionalized alkyl iodides were produced in moderate to good yields from aryl iodides and both cyclic and acyclic ethers. Beside the high value of the obtained products, all atoms from the starting materials were incorporated in the final products.

Limitations of Study

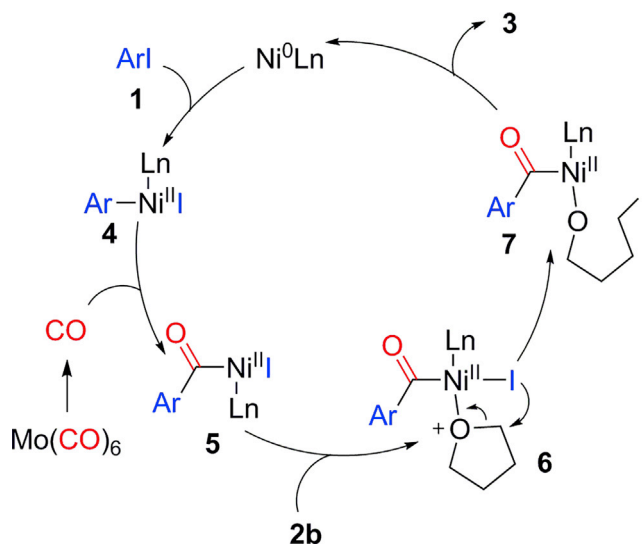
Substrates such as aryl bromides and aryl chlorides failed in this system. Alkyl bromides and alkyl chlorides cannot be prepared. More detailed mechanistic studies still need to be done.

METHODS

All methods can be found in the accompanying Transparent Methods supplemental file.



Scheme 1. Mechanistic Studies with Fuans and 1,4-Dioxane



Scheme 2. A Plausible Mechanism

SUPPLEMENTAL INFORMATION

Supplemental Information includes Transparent Methods, 60 figures, and 9 tables and can be found with this article online at <https://doi.org/10.1016/j.isci.2018.09.024>.

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AUTHOR CONTRIBUTIONS

X.-F.W. and J.-B.P. conceived and supervised the project. F.-P.W. and C.X. performed the experiments. F.-P.W. and C.X. analyzed and prepared the Supplemental Information. X.Q. and J.Y. participated in the discussions. X.-F.W. and J.-B.P. wrote and revised the manuscript.

DECLARATION OF INTERESTS

The authors declare no competing interests.

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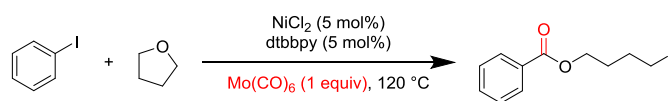
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Supplemental Information

Nickel-Catalyzed Carbonylative Synthesis of Functionalized Alkyl Iodides

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Table S1. Screening of the temperature, related to Table 1.

Entry	Temp.	Yield (%)
1	140	29
2	130	45
3	120	52
4	110	9
5	100	0
6	90	0

[a] Reaction conditions: Iodobenzene (0.5 mmol), THF (2 equiv.), NiCl_2 (5 mol%), dtbbpy (5 mol%), Mo(CO)_6 (1 equiv.), toluene (2 mL), x $^\circ\text{C}$, 16 h.

Table S2. Screening of the catalysts, related to Table 1.

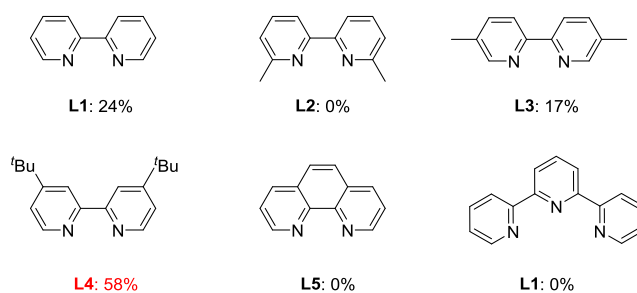
Entry	Catal.	Yield (%)
1	NiCl_2	52
2	NiBr_2	57
3	NiI_2	33
4	$\text{NiCl}_2 \cdot \text{glyme}$	57
5	Ni(acac)_2	30
6	Ni(OTf)_2	58
7	without Ni	0

[a] Reaction conditions: Iodobenzene (0.5 mmol), THF (2 equiv.), [Ni] (5 mol%), dtbbpy (5 mol%), Mo(CO)_6 (1 equiv.), toluene (2 mL), $120\text{ }^\circ\text{C}$, 16 h.

Table S3. Screening of the ligands, related to Table 1.

Entry	Ligand	Yield (%)
1	PCy ₃	48
2	dppp	0
3	BuPAd ₂	14
4	IPr•HCl	29
5	PPh ₃	30
6	(4-Tolyl) ₃ P	47
7	^t Bu ₃ P•HCl	21
8	Nitrogen ligands	see below

[a] Reaction conditions: Iodobenzene (0.5 mmol), THF (2 equiv.), Ni(OTf)₂ (5 mol%), Ligand (5 mol%), Mo(CO)₆ (1 equiv.), toluene (2 mL), 120 °C, 16 h.

**Table S4.** Screening of the amount of Mo(CO)₆, related to Table 1.

Entry	Mo(CO) ₆	Yield (%)
1	0.2 equiv.	34
2	0.3 equiv.	19
3	0.4 equiv.	44
4	0.5 equiv.	64
5	0.6 equiv.	58
6	1.0 equiv.	58
7	1.5 equiv.	51
8	2.0 equiv.	42

[a] Reaction conditions: Iodobenzene (0.5 mmol), THF (2 equiv.), Ni(OTf)₂ (5 mol%), dtbbpy (5 mol%), Mo(CO)₆ (X equiv.), toluene (2 mL), 120 °C, 16 h.

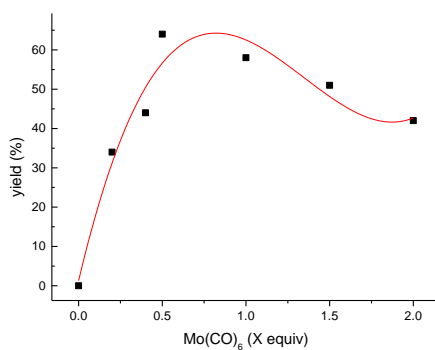


Table S5. Screening of the additives, related to Table 1.

Entry		Yield (%)
1	none	64
2	4 Å MS (80 mg)	60
3	NaI (20 mol%)	62
4	TBAI (20 mol%)	34
5	TBAB (20 mol%)	27
6	HCOOH (100 mol%)	10

[a] Reaction conditions: Iodobenzene (0.5 mmol), THF (2 equiv.), Ni(OTf)₂ (5 mol%), dtbbpy (5 mol%), Mo(CO)₆ (0.5 equiv.), toluene (2 mL), 120 °C, 16 h.

Table S6. Screening of the solvents, related to Table 1.

Entry	Solvent	Yield (%)
1	THF	48
2	Toluene	64
3 ^[b]	Toluene	60
4 ^[c]	Toluene	70
5	DMF	0
6	Acetonitrile	8
7	Cyclohexane	42
8	Chlorobenzene	89
9	Xylene	57

[a] Reaction conditions: Iodobenzene (0.5 mmol), THF (2 equiv.), Ni(OTf)₂ (5 mol%), dtbbpy (5 mol%), Mo(CO)₆ (0.5 equiv.), toluene (2 mL), 120 °C, 16 h. [b] THF (1.5 equiv.). [c] THF (3 equiv.).

Table S7. Screening of the amount of Ni(OTf)₂ and dtbbpy, related to Table 1.

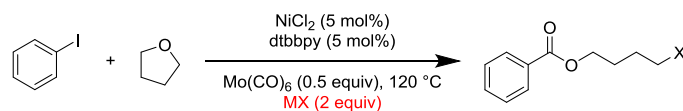
Entry	Ni(OTf) ₂ (X mol%), dtbbpy (X mol%)	Yield (%) ^[a]
1	X = 1	0
2	X = 2	46
3	X = 3	52
4	X = 4	82
5	X = 5	89
6 ^[b]	X = 3	74
7 ^[b]	X = 5	95(93) ^[c]

[a] Reaction conditions: Iodobenzene (0.5 mmol), THF (2 equiv.), Ni(OTf)₂ (X mol%), dtbbpy (X mol%), Mo(CO)₆ (0.5 equiv.), chlorobenzene (2 mL), 120 °C, 16 h. [b] THF (3 equiv.). [c] isolated yield.

Table S8. Screening of the CO sources, related to Table 1.

Entry	CO source	Yield (%) ^[a]
1	Mo(CO) ₆	95
2	Fe ₃ (CO) ₁₂	32
3	Co ₂ (CO) ₈	0
4	Cr(CO) ₆	41
5	W(CO) ₆	0
6	TFBen	0
7	HCOOH/DCC	0
8	CO (1 atm)	0

[a] Reaction conditions: Iodobenzene (0.5 mmol), THF (3 equiv.), Ni(OTf)₂ (5 mol%), dtbbpy (5 mol%), [CO] (1.5 mmol), chlorobenzene (2 mL), 120 °C, 16 h.

Table S9. Control experiments, related to Table 1.

Entry	MX	Yield (%) (X = Cl or Br)	Yield (%) (X = I)
1	none	0	95
2	NaCl	0	69
3	NaBr	0	66
4	LiCl	0	46
5	LiBr	0	41

[a] Reaction conditions: Iodobenzene (0.5 mmol), THF (3 equiv.), MX (2 equiv.), Ni(OTf)₂ (5 mol%), dtbbpy (5 mol%), Mo(CO)₆ (0.5 equiv.), chlorobenzene (2 mL), 120 °C, 16 h.

Copy of ^1H and ^{13}C NMR Spectra of Products

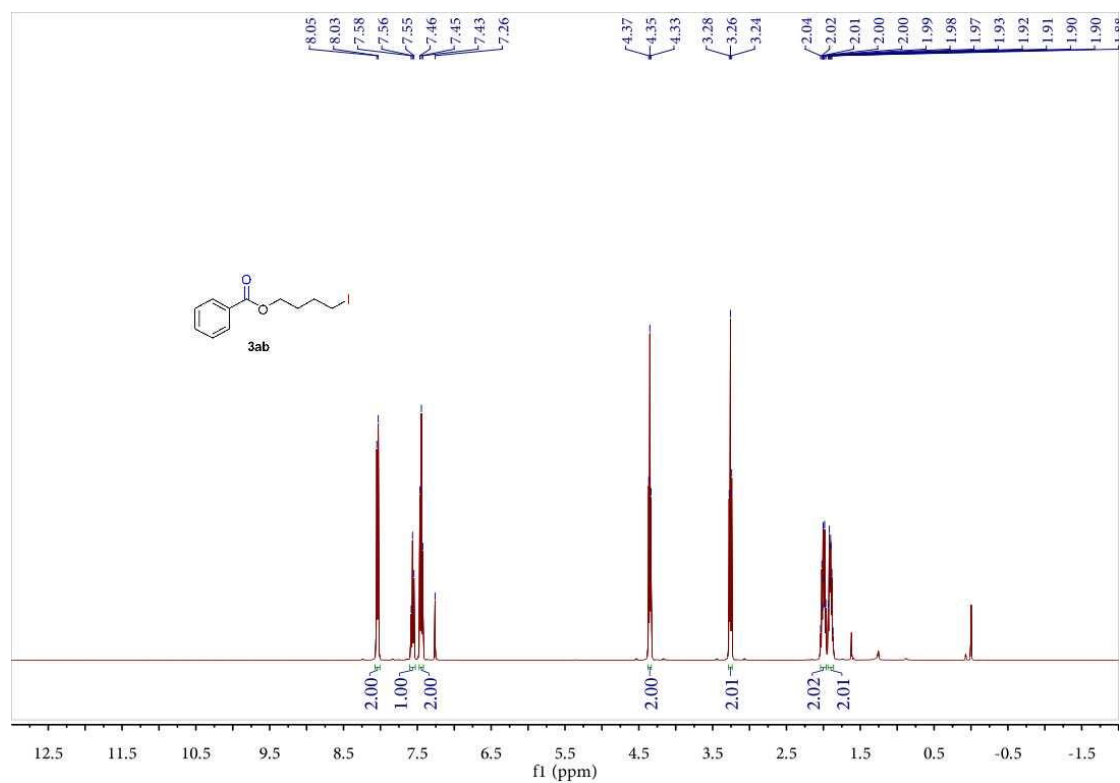


Figure S1. ^1H NMR spectrum of 3ab, related to Figure 1.

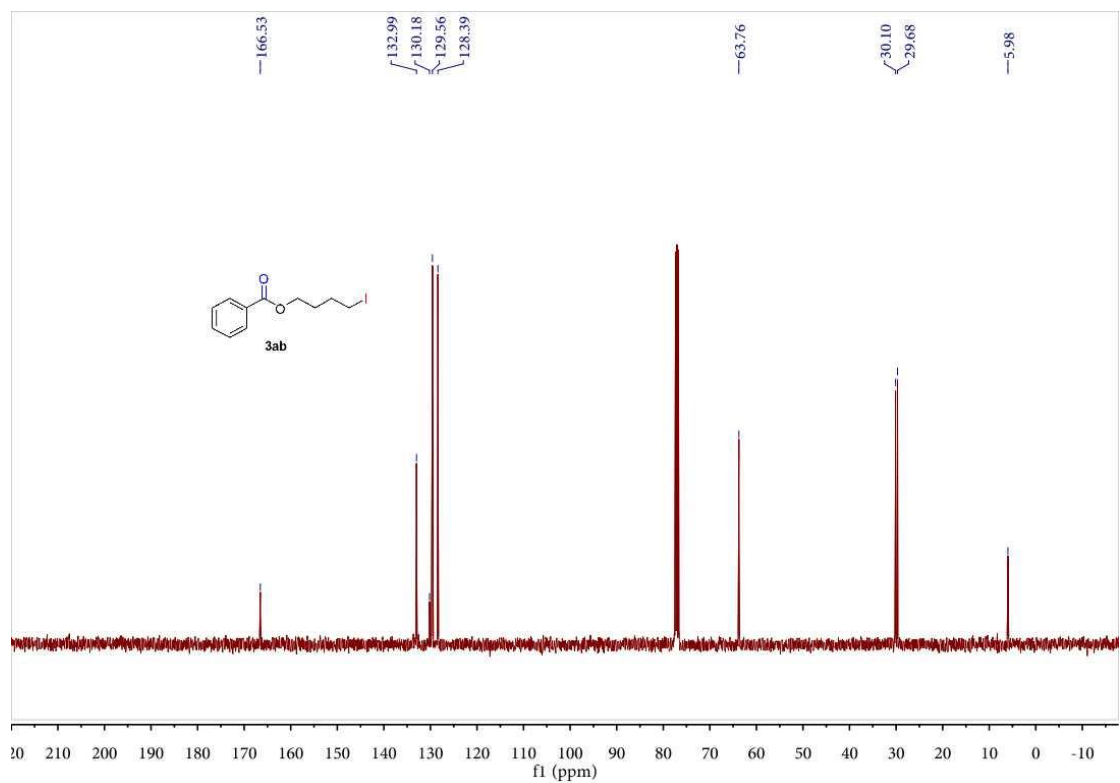


Figure S2. ^{13}C NMR spectrum of 3ab, related to Figure 1.

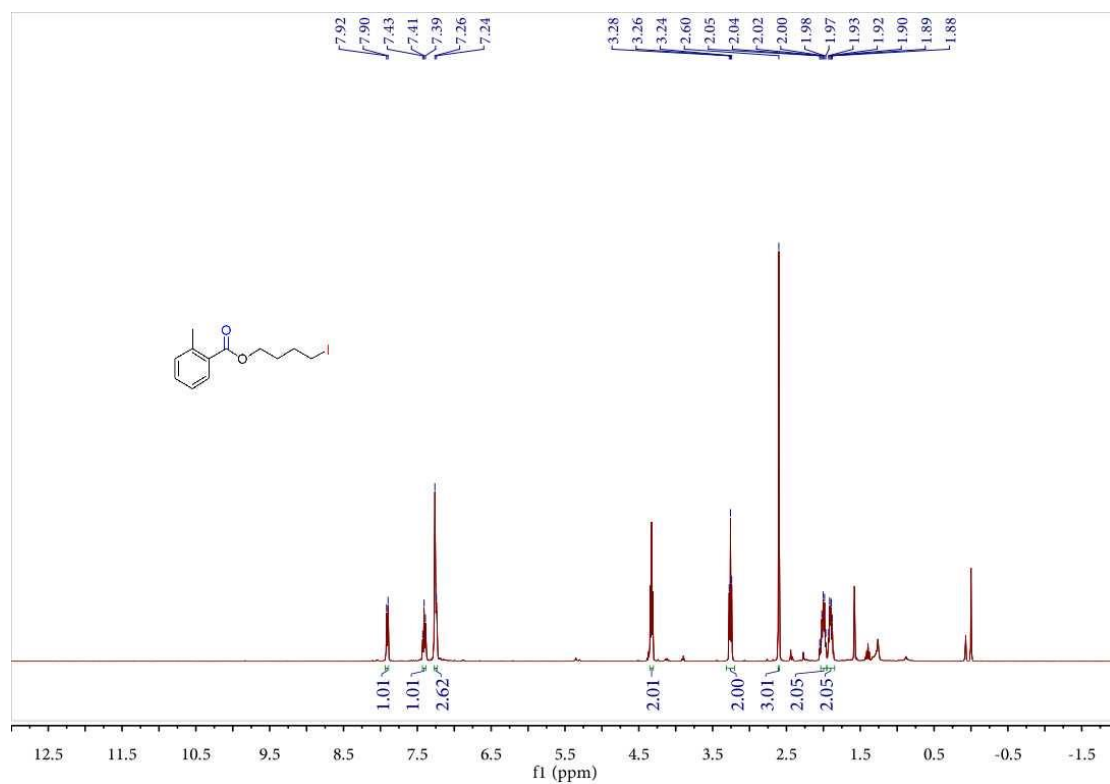


Figure S3. ^1H NMR spectrum of 3bb, related to Figure 1.

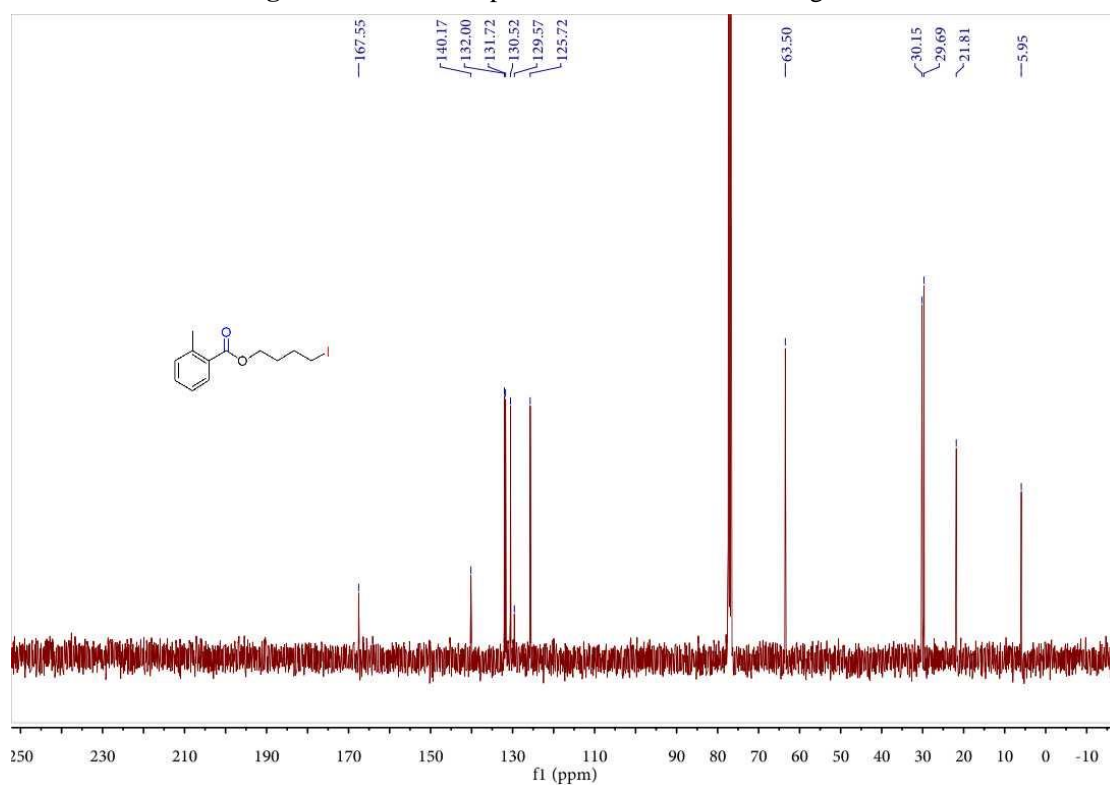


Figure S4. ^{13}C NMR spectrum of 3bb, related to Figure 1.

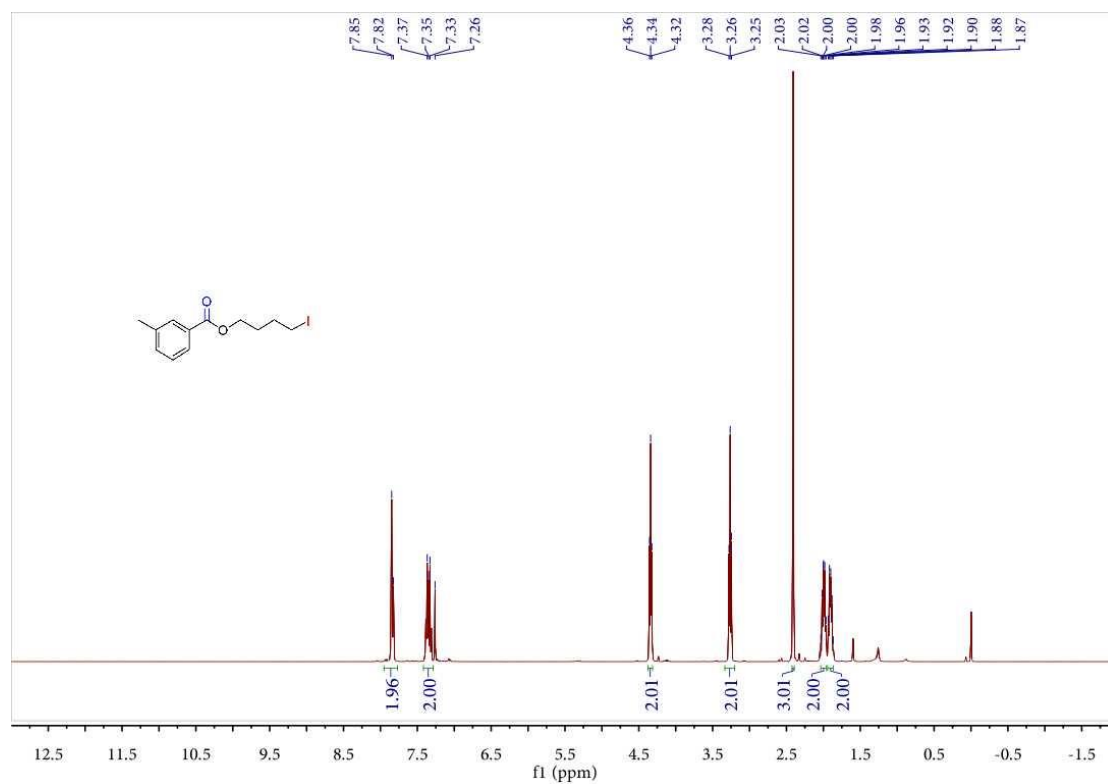


Figure S5. ^1H NMR spectrum of 3cb, related to Figure 1.

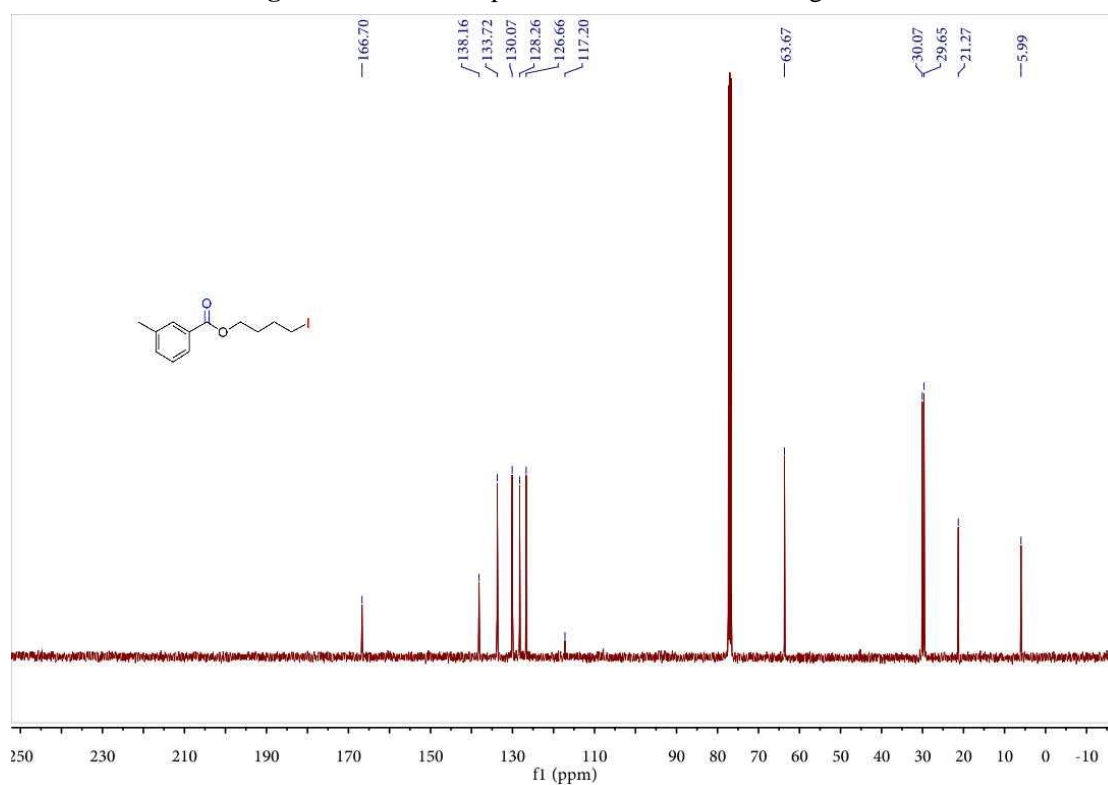


Figure S6. ^{13}C NMR spectrum of 3cb, related to Figure 1.

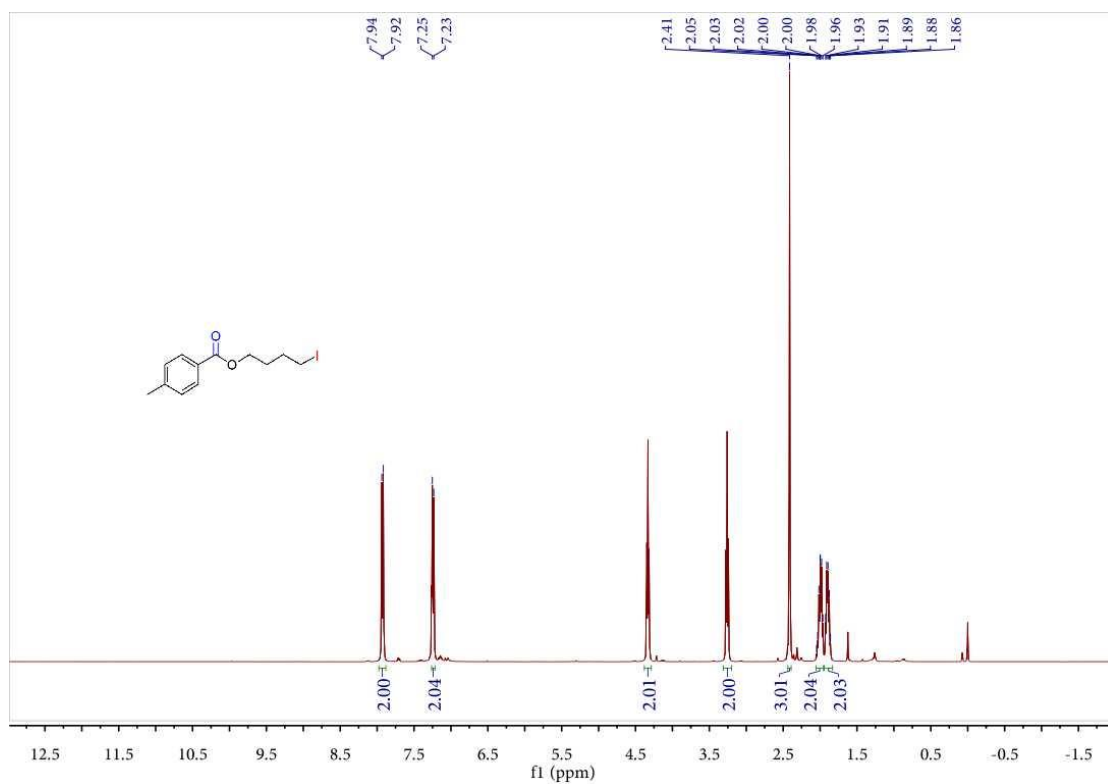


Figure S7. ^1H NMR spectrum of 3db, related to Figure 1.

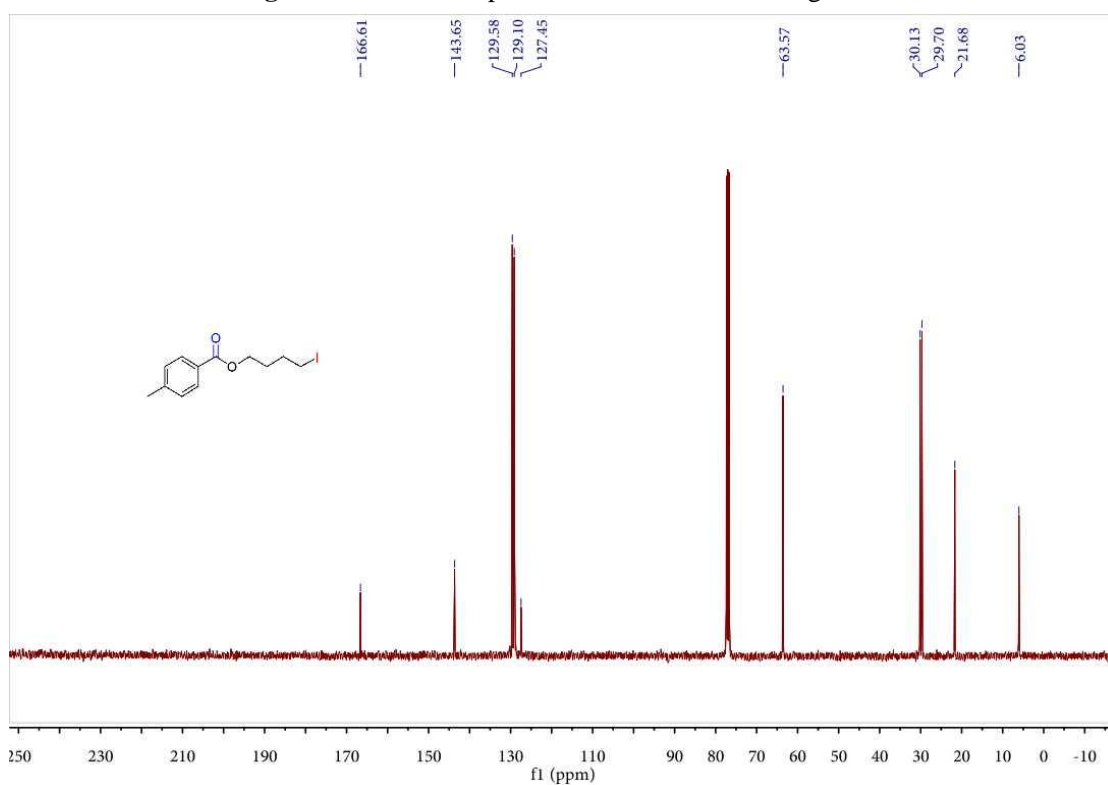


Figure S8. ^{13}C NMR spectrum of 3db, related to Figure 1.

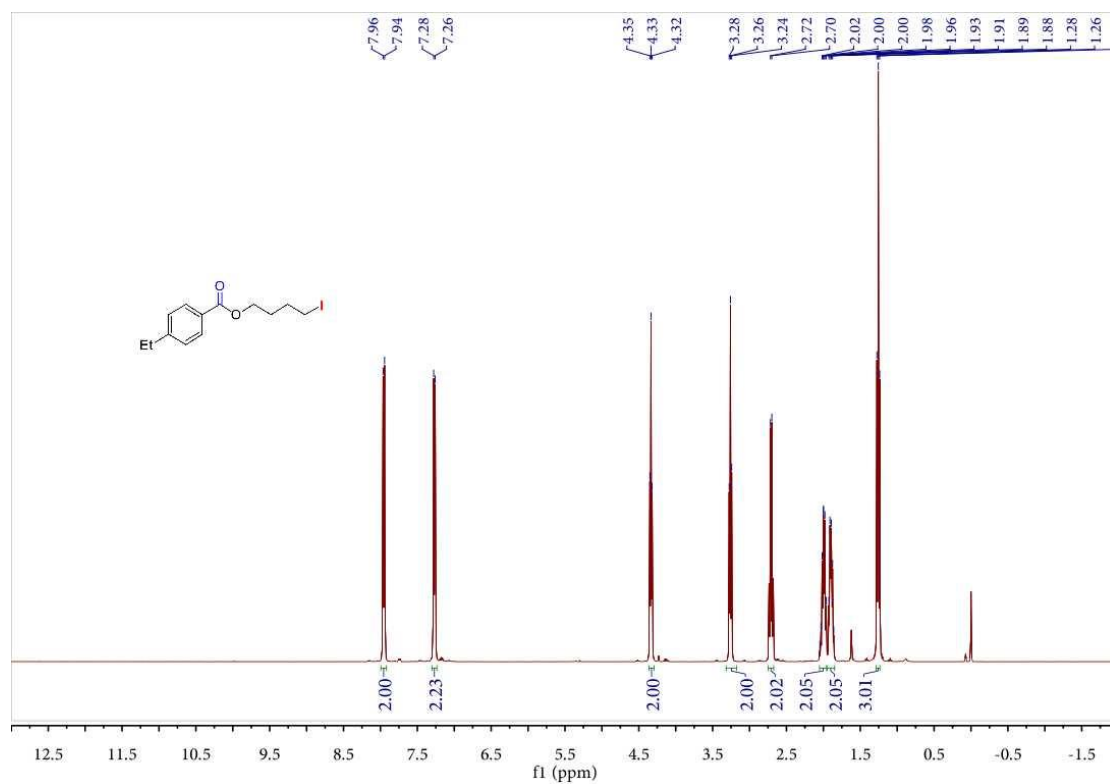


Figure S9. ¹H NMR spectrum of 3eb, related to Figure 1.

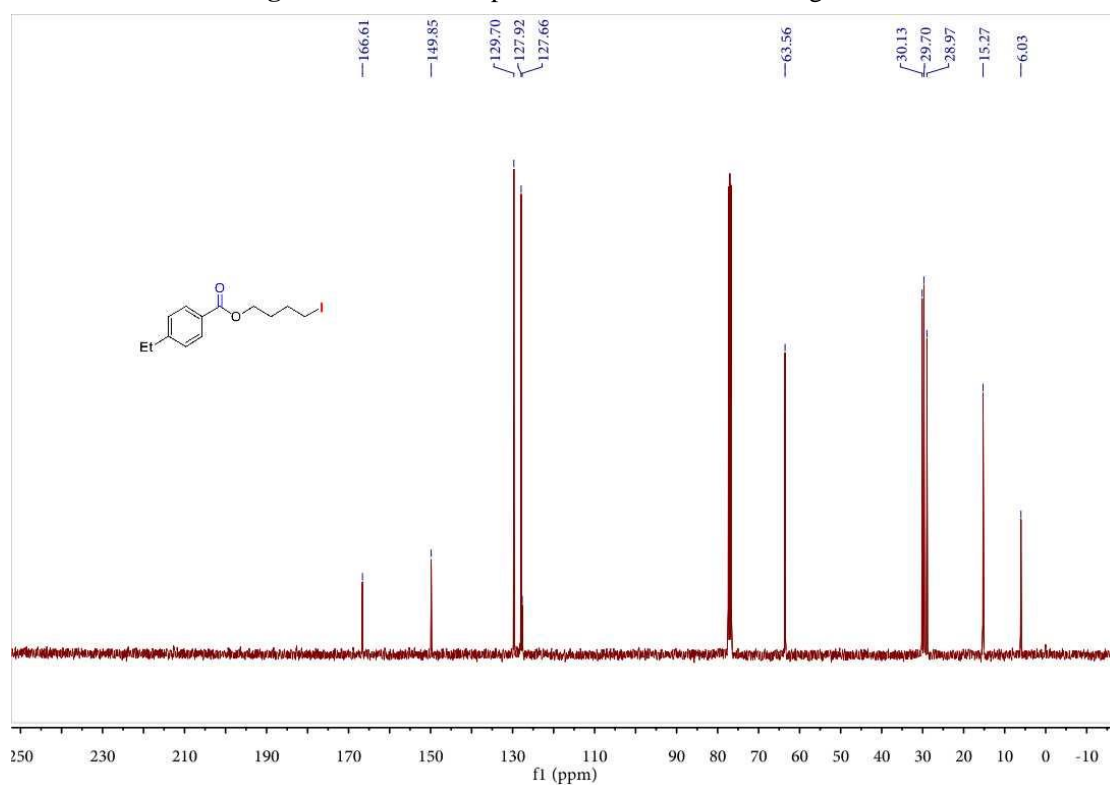


Figure S10. ¹³C NMR spectrum of 3eb, related to Figure 1.

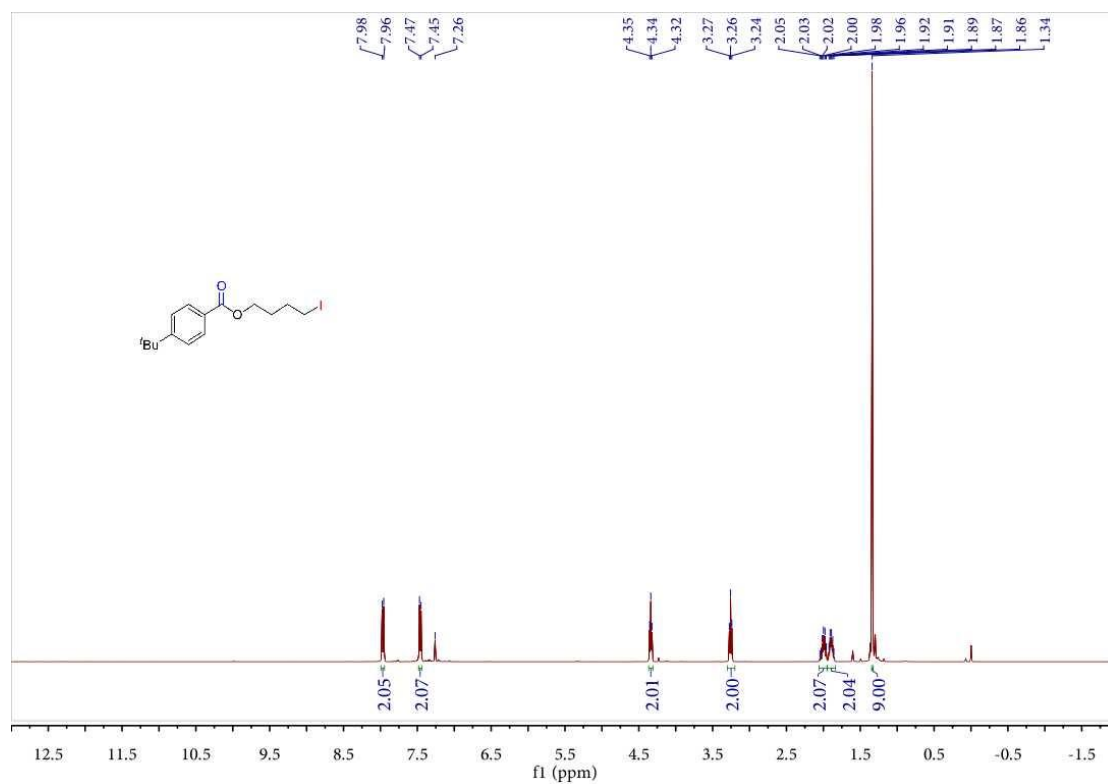


Figure S11. ^1H NMR spectrum of 3fb, related to Figure 1.

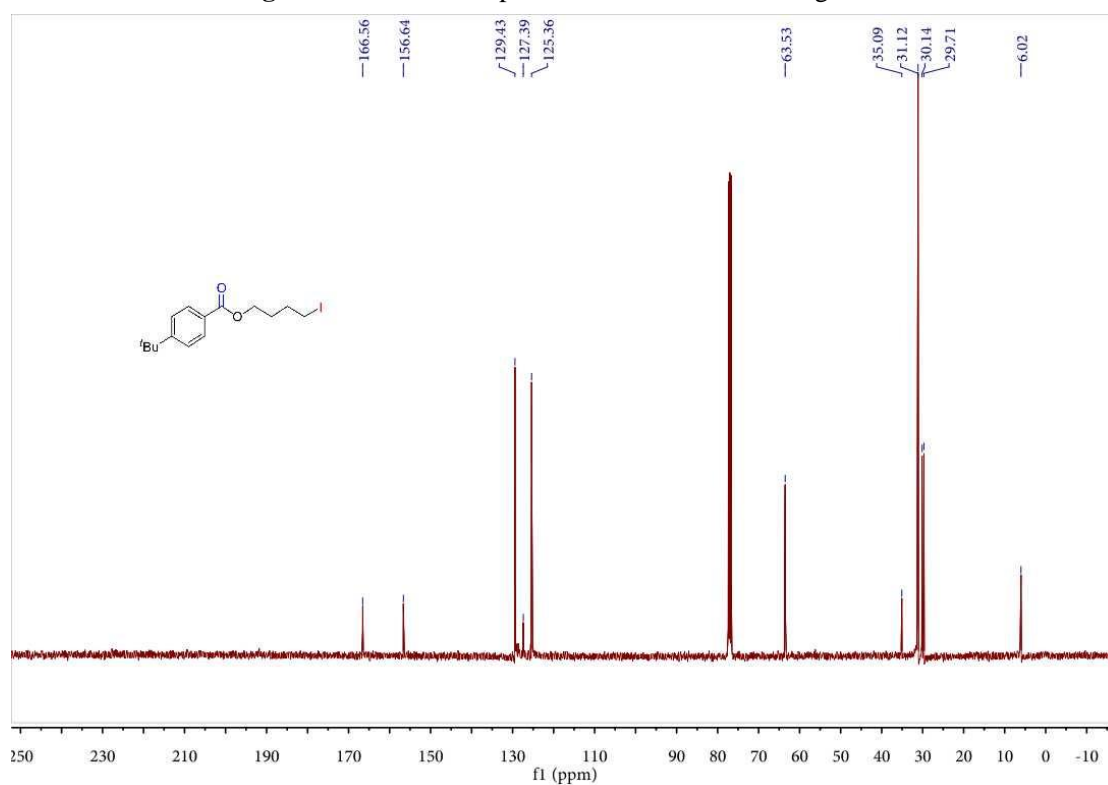


Figure S12. ^{13}C NMR spectrum of 3fb, related to Figure 1.

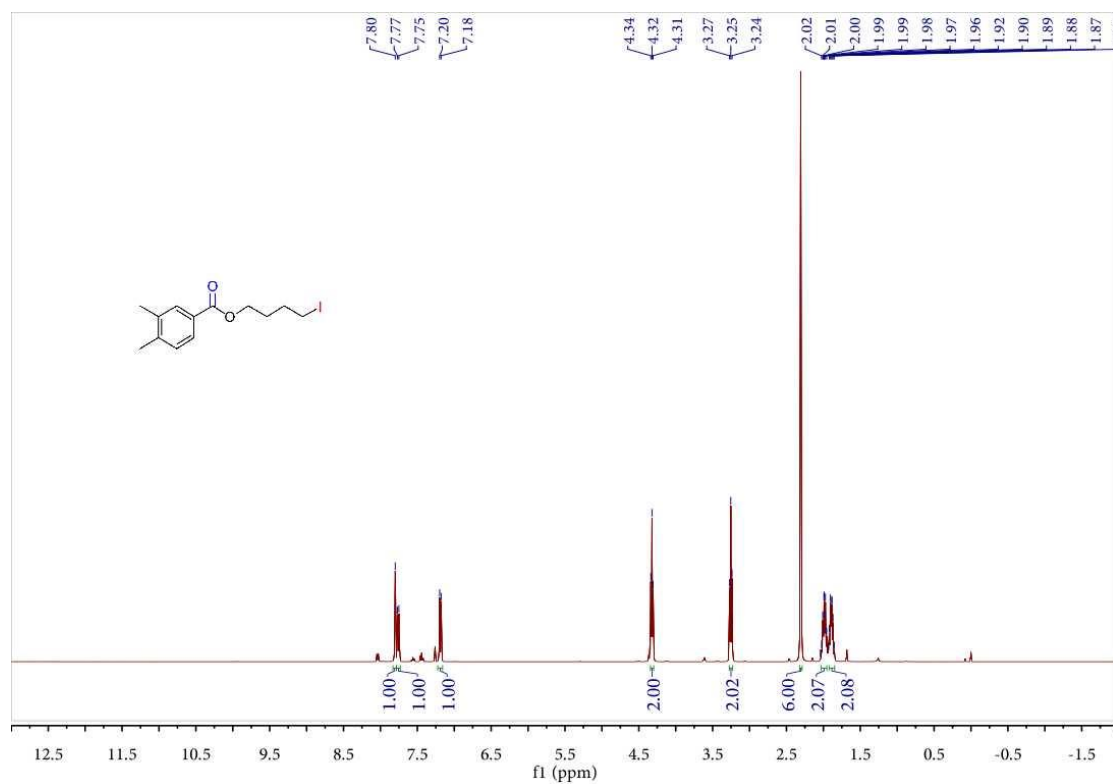


Figure S13. ^1H NMR spectrum of 3gb, related to Figure 1.

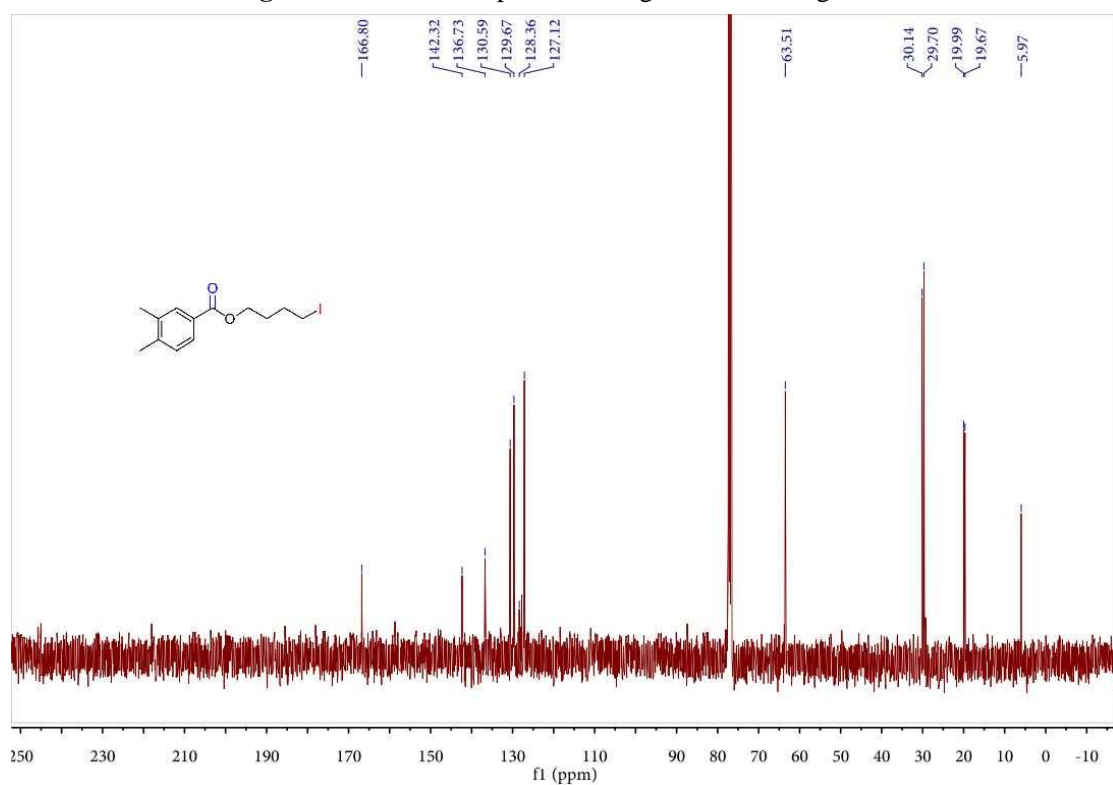


Figure S14. ^{13}C NMR spectrum of 3gb, related to Figure 1.

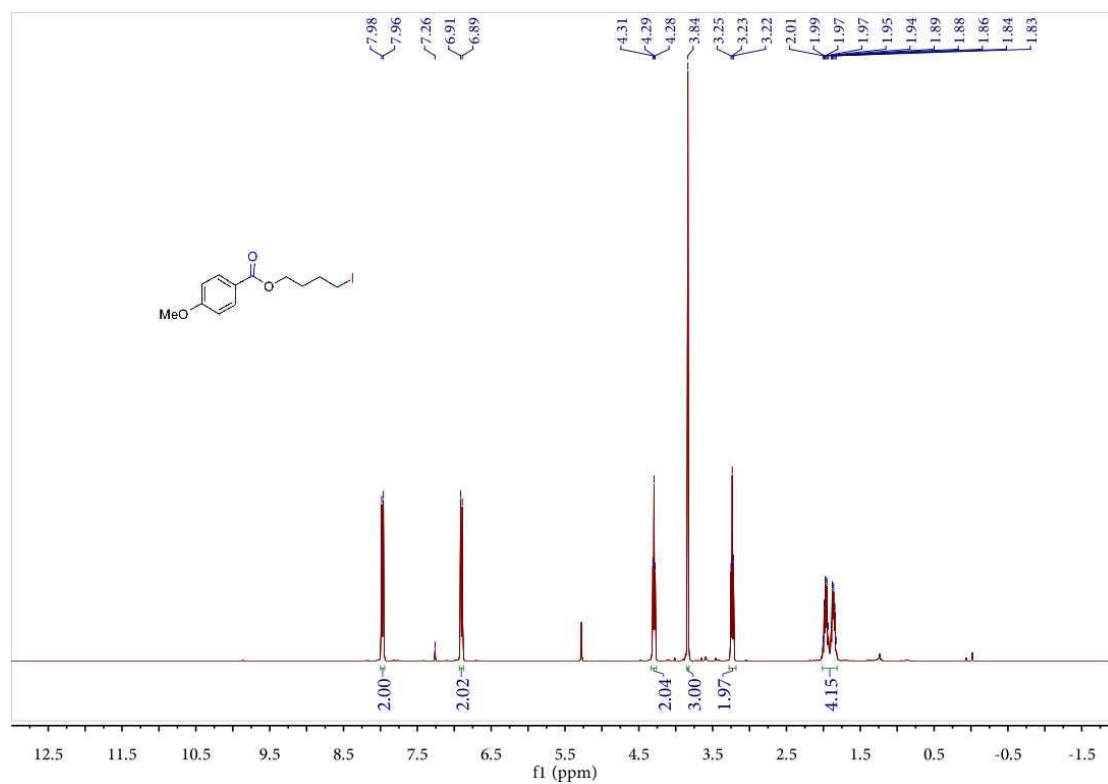


Figure S15. ^1H NMR spectrum of 3hb, related to Figure 1.

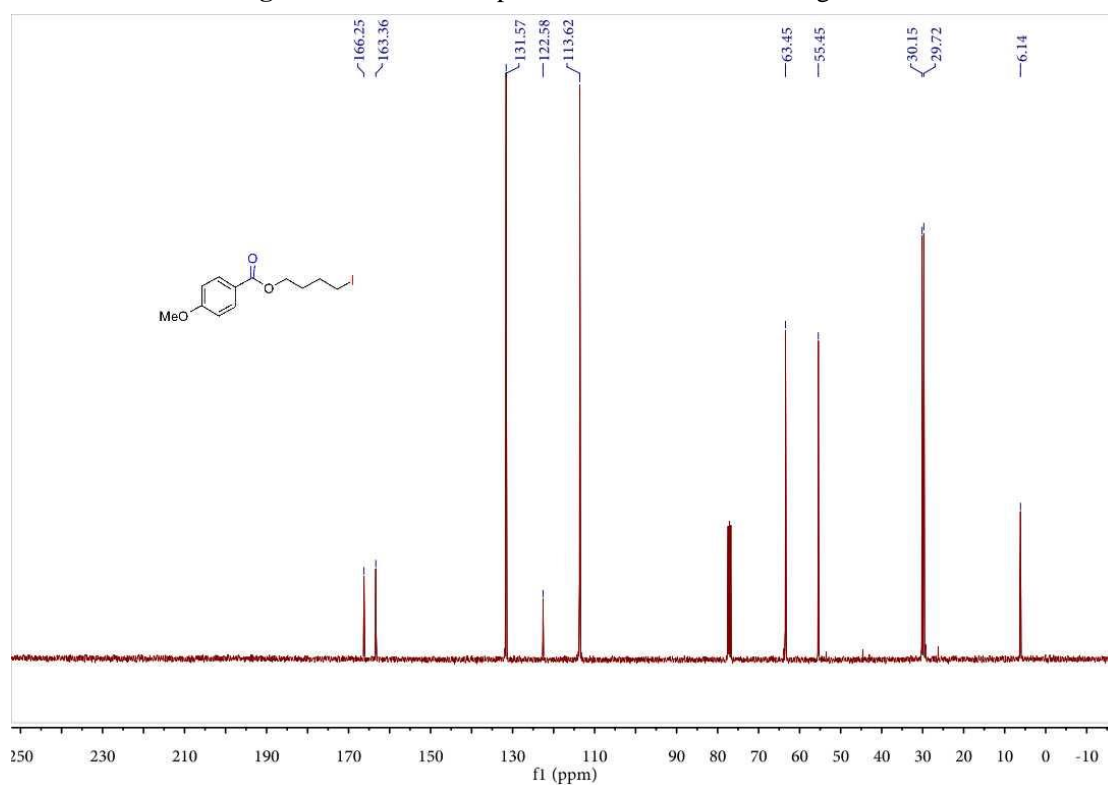


Figure S16. ^{13}C NMR spectrum of 3hb, related to Figure 1.

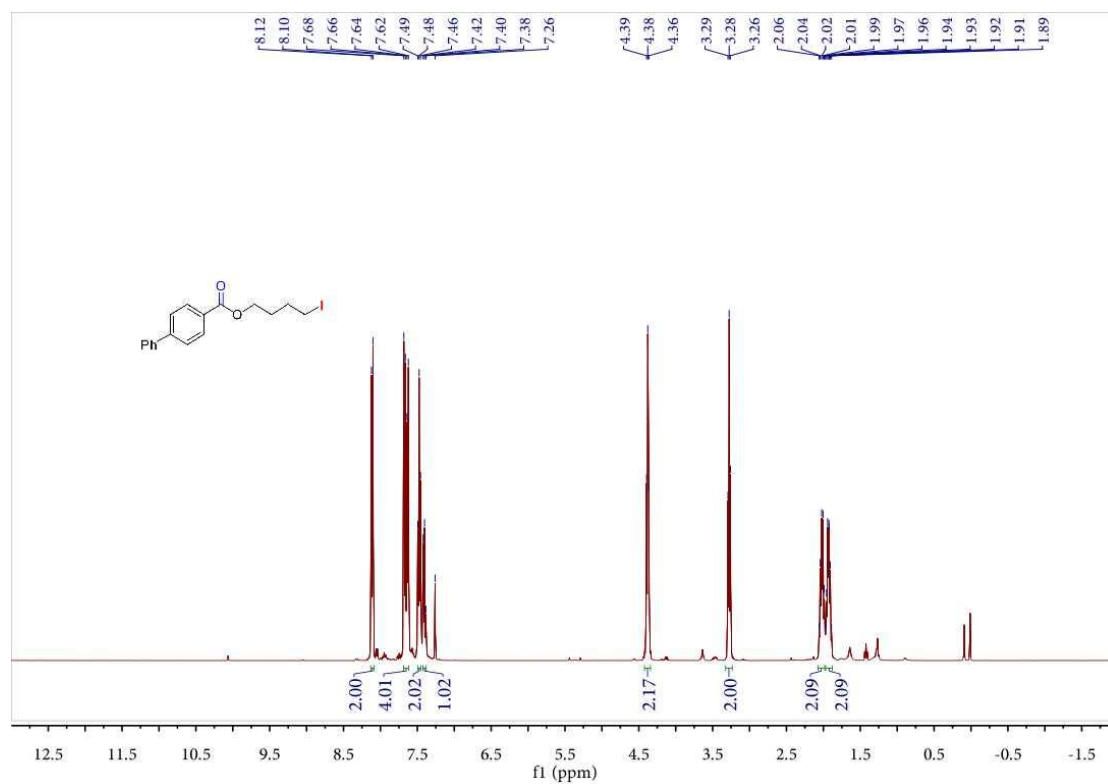


Figure S17. ^1H NMR spectrum of 3ib, related to Figure 1.

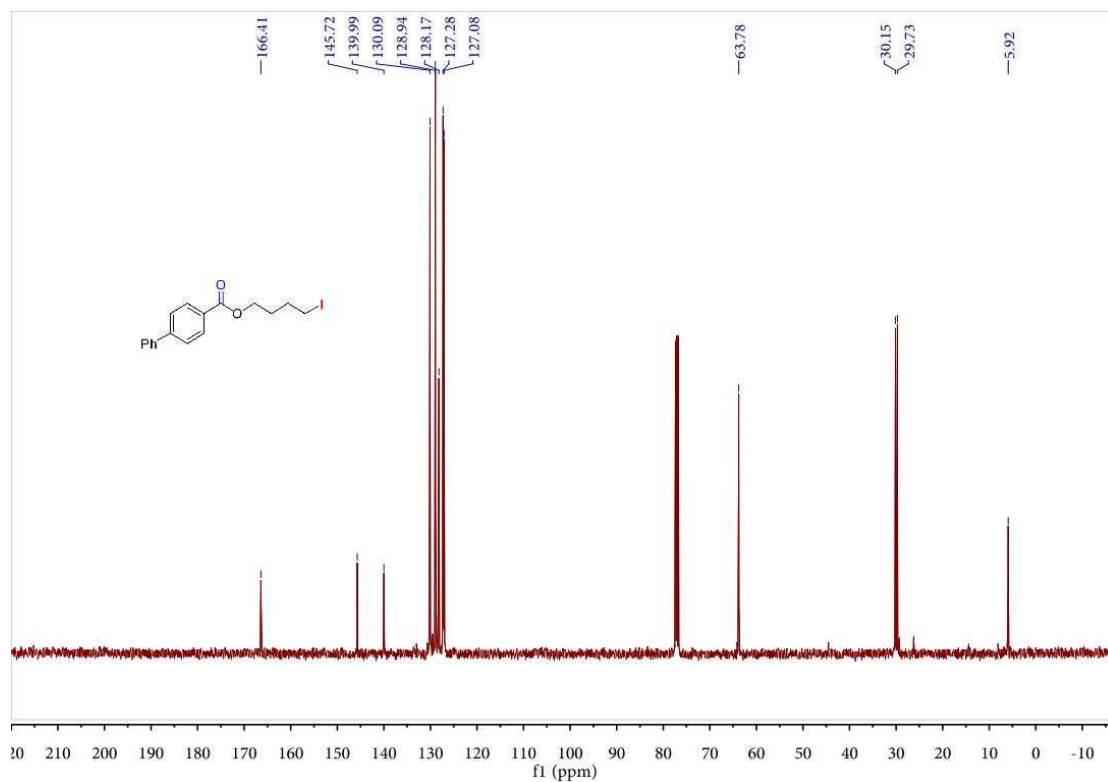


Figure S18. ^{13}C NMR spectrum of 3ib, related to Figure 1.

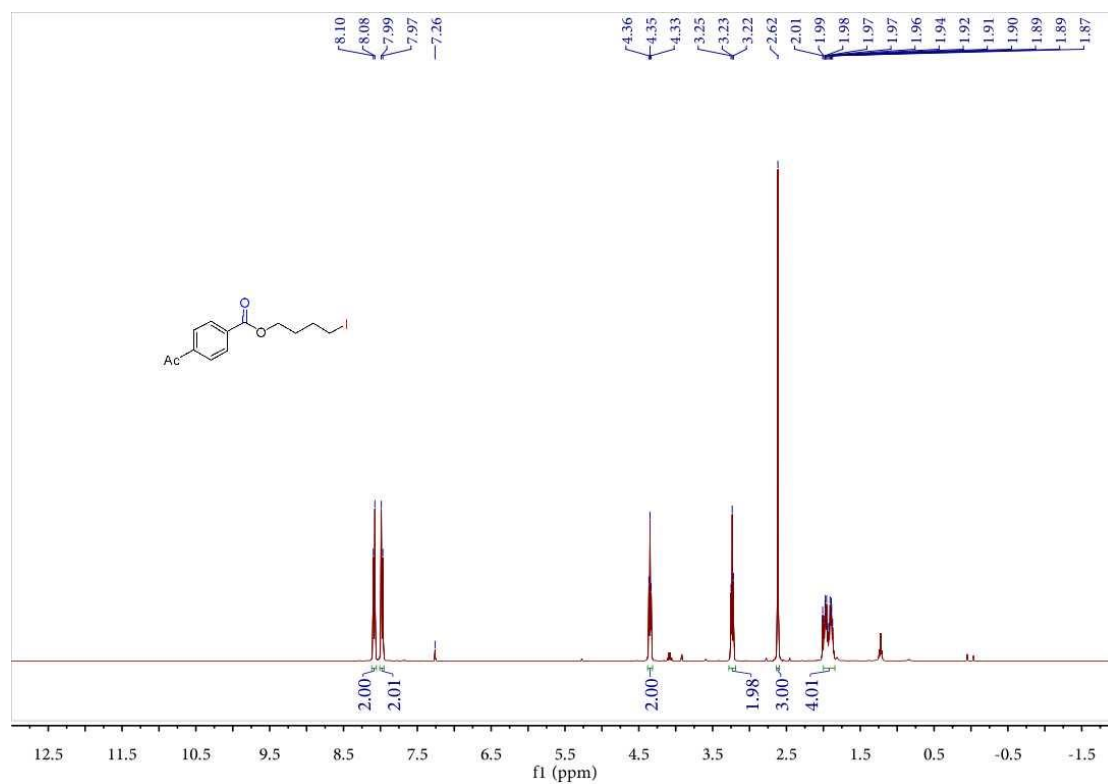


Figure S19. ¹H NMR spectrum of 3jb, related to Figure 1.

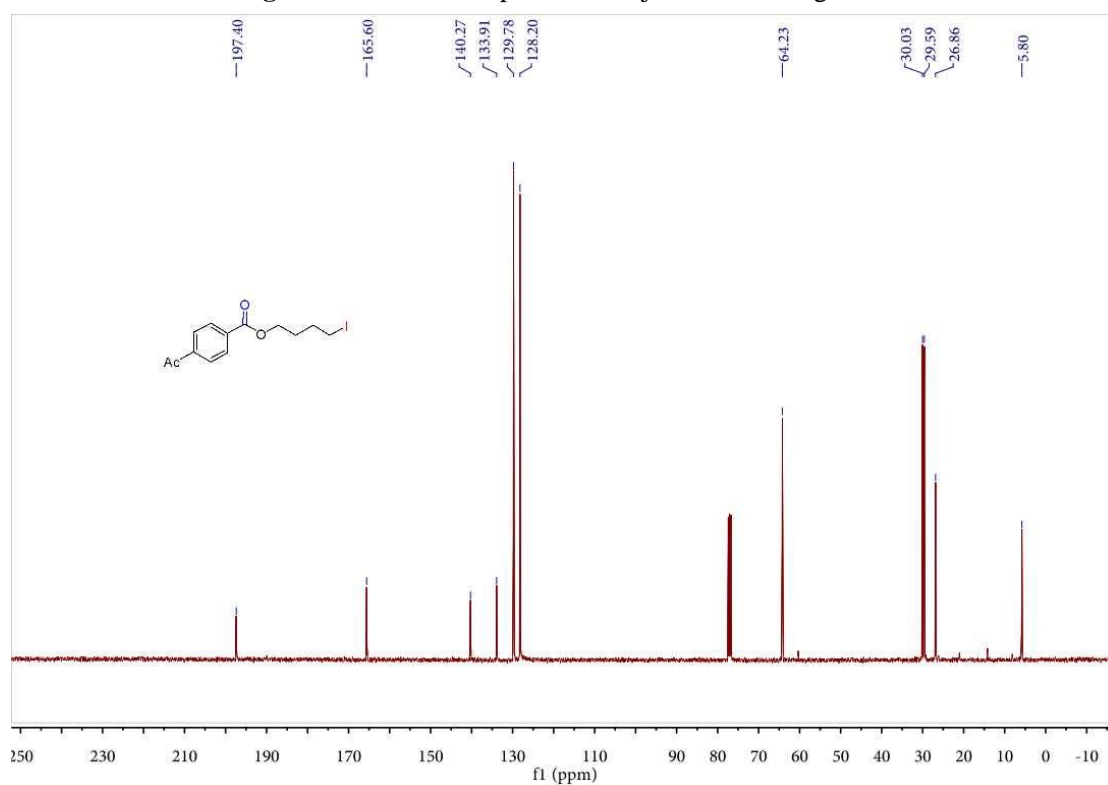


Figure S20. ¹³C NMR spectrum of 3jb, related to Figure 1.

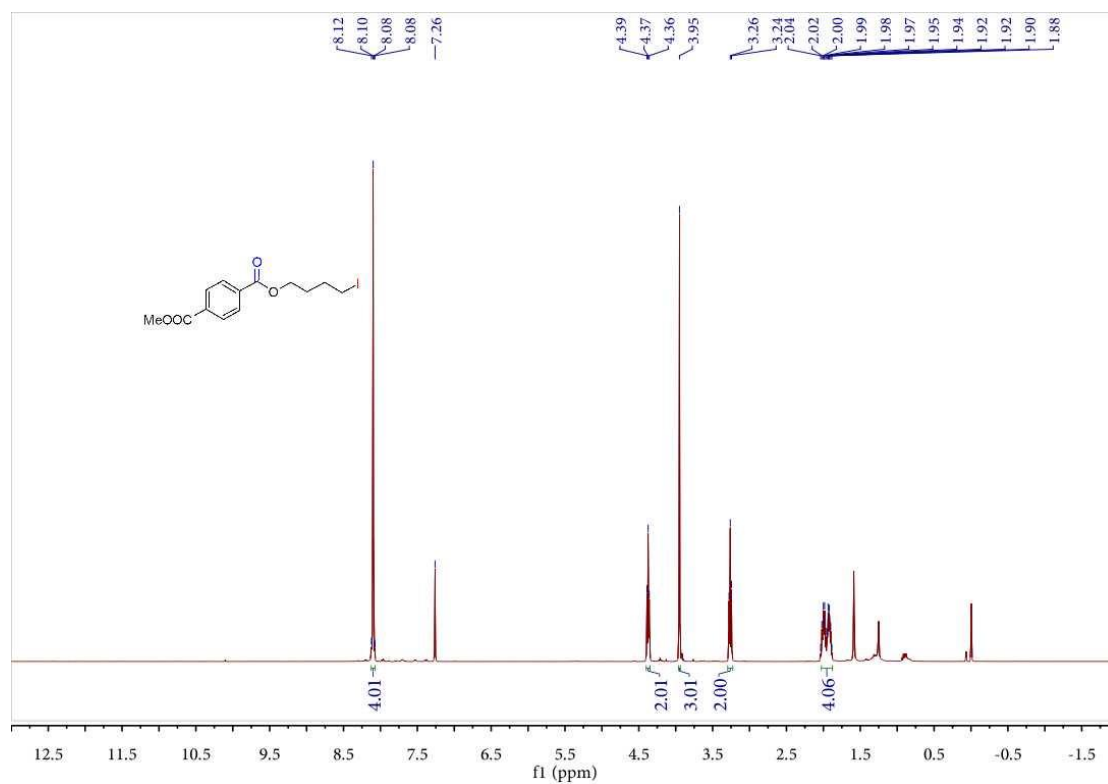


Figure S21. ¹H NMR spectrum of 3kb, related to Figure 1.

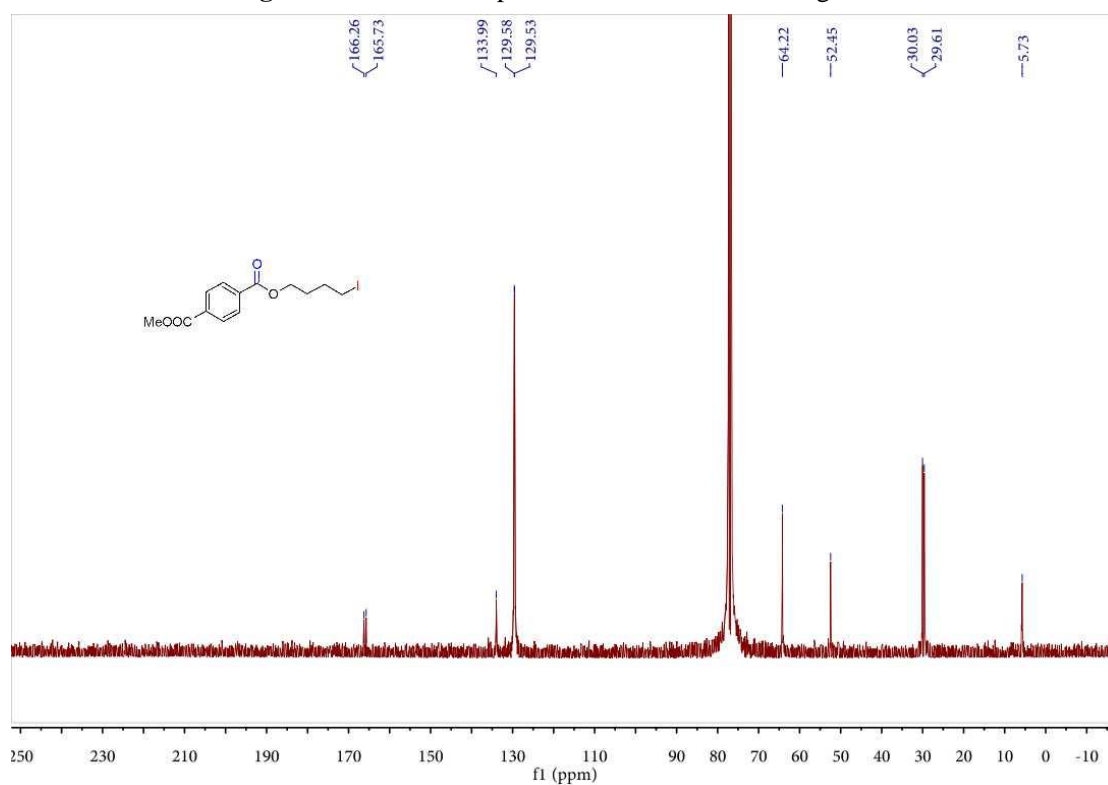


Figure S22. ¹³C NMR spectrum of 3kb, related to Figure 1.

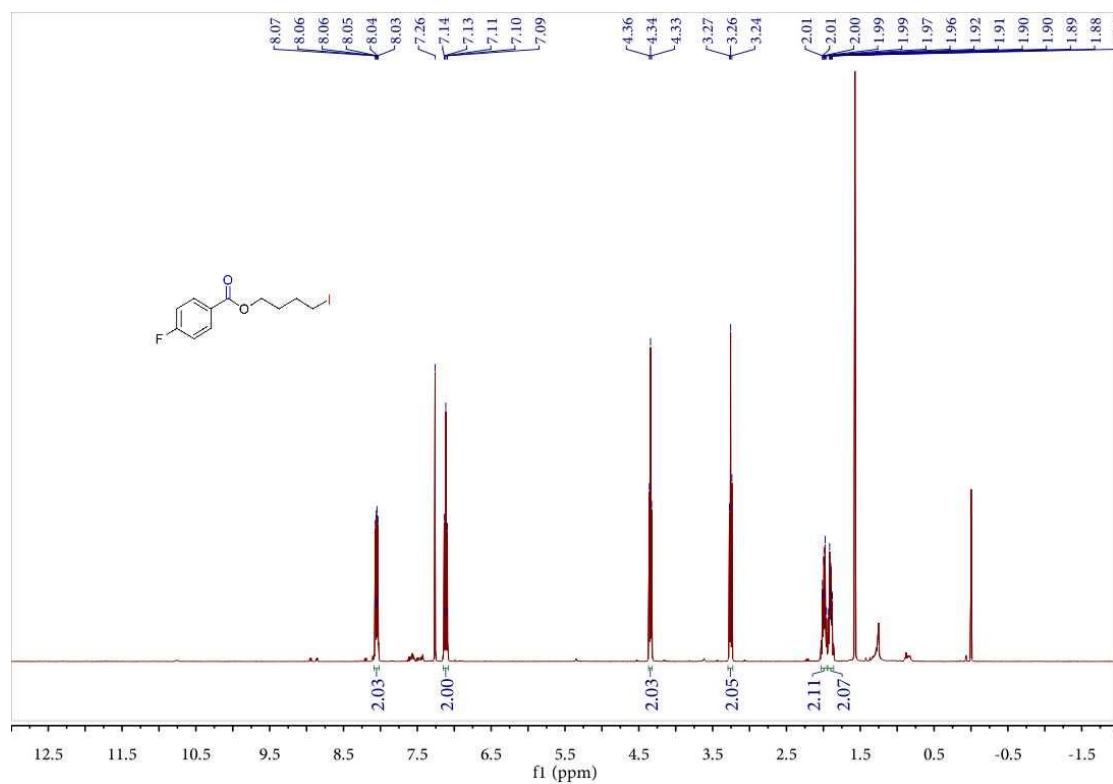


Figure S23. ^1H NMR spectrum of 3lb, related to Figure 1.

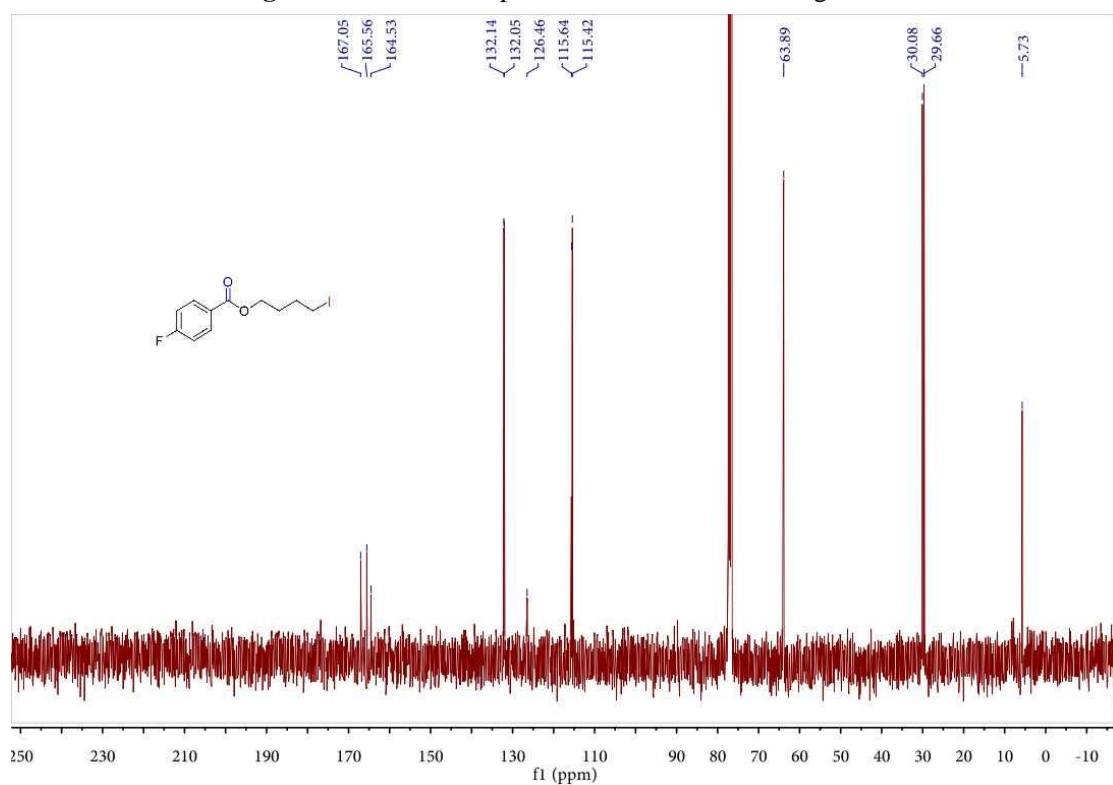


Figure S24. ^{13}C NMR spectrum of 3lb, related to Figure 1.

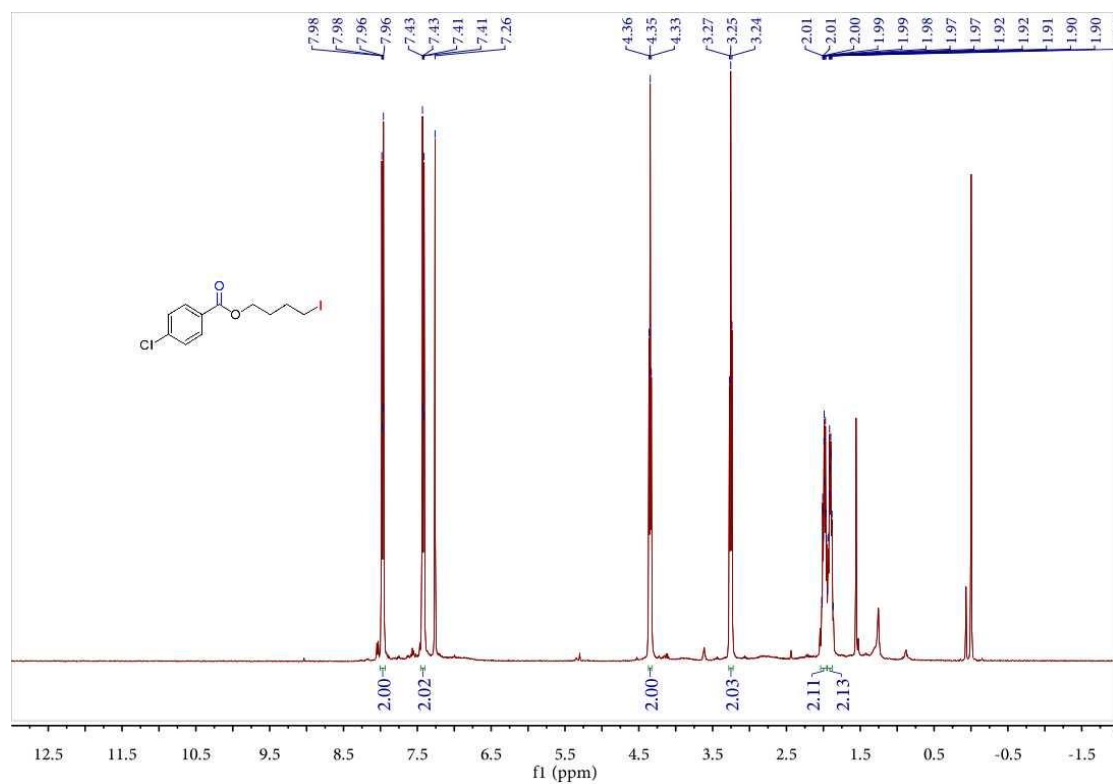


Figure S25. ¹H NMR spectrum of 3mb, related to Figure 1.

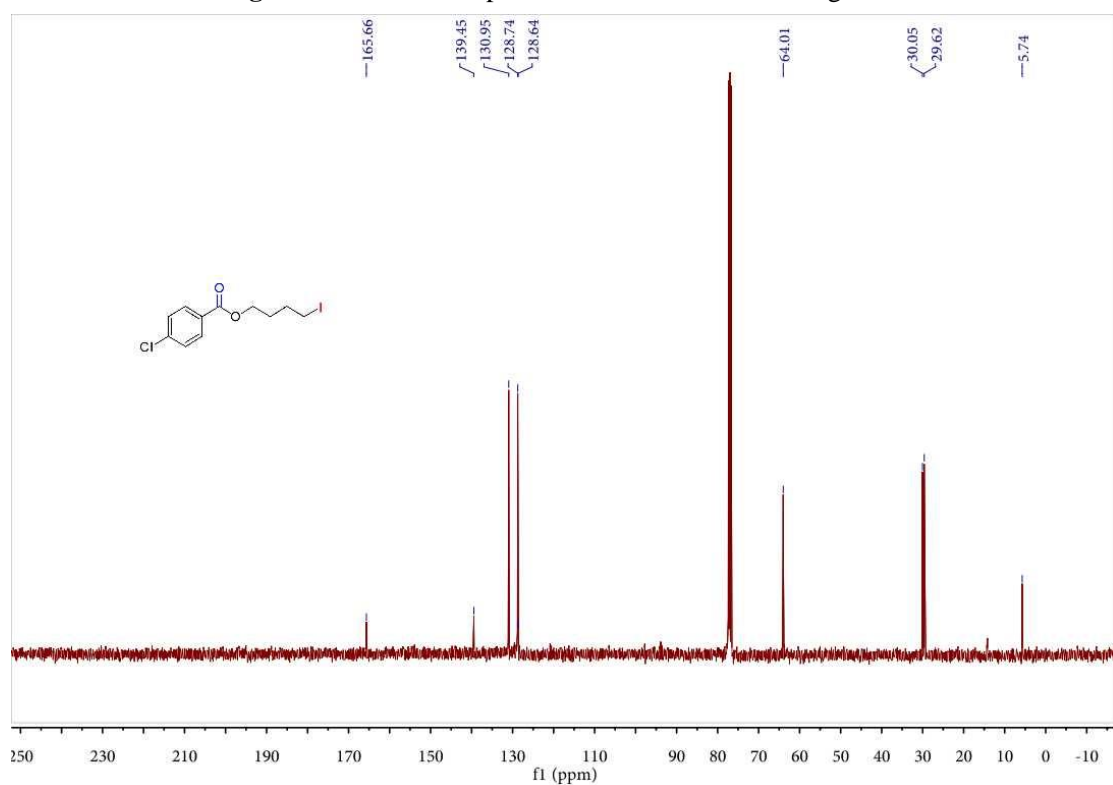
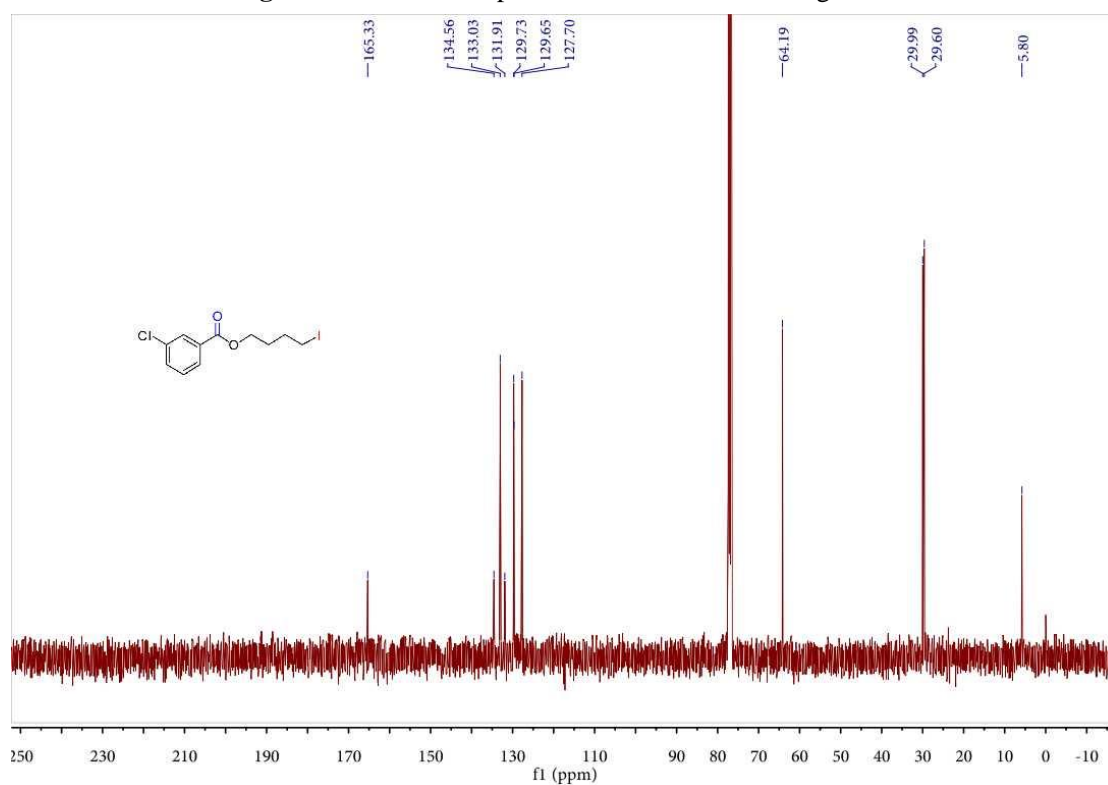
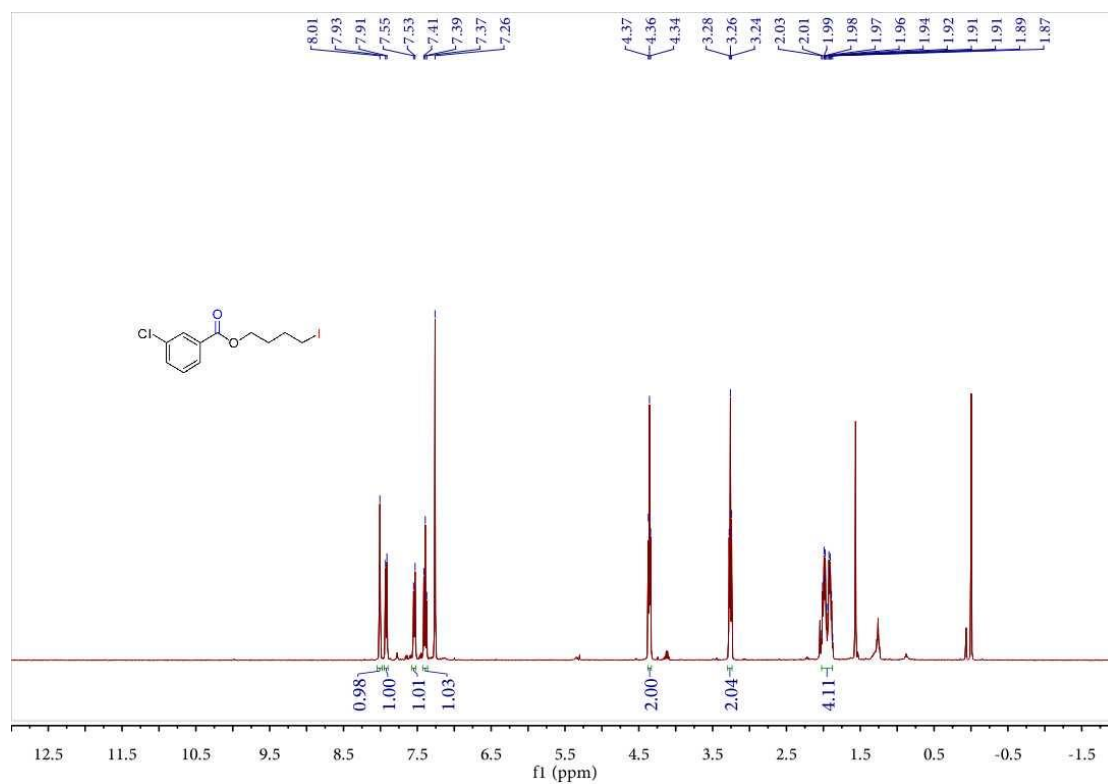


Figure S26. ¹³C NMR spectrum of 3mb, related to Figure 1.



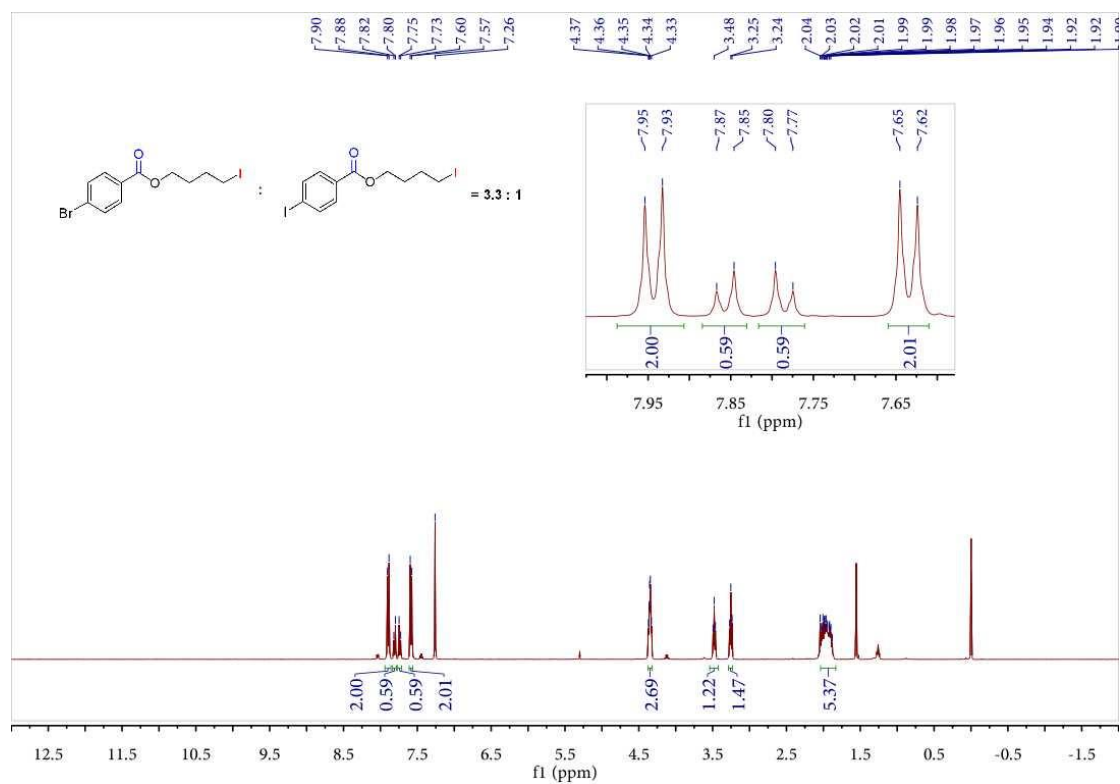


Figure S29. ¹H NMR spectrum of 3pb, related to Figure 1.

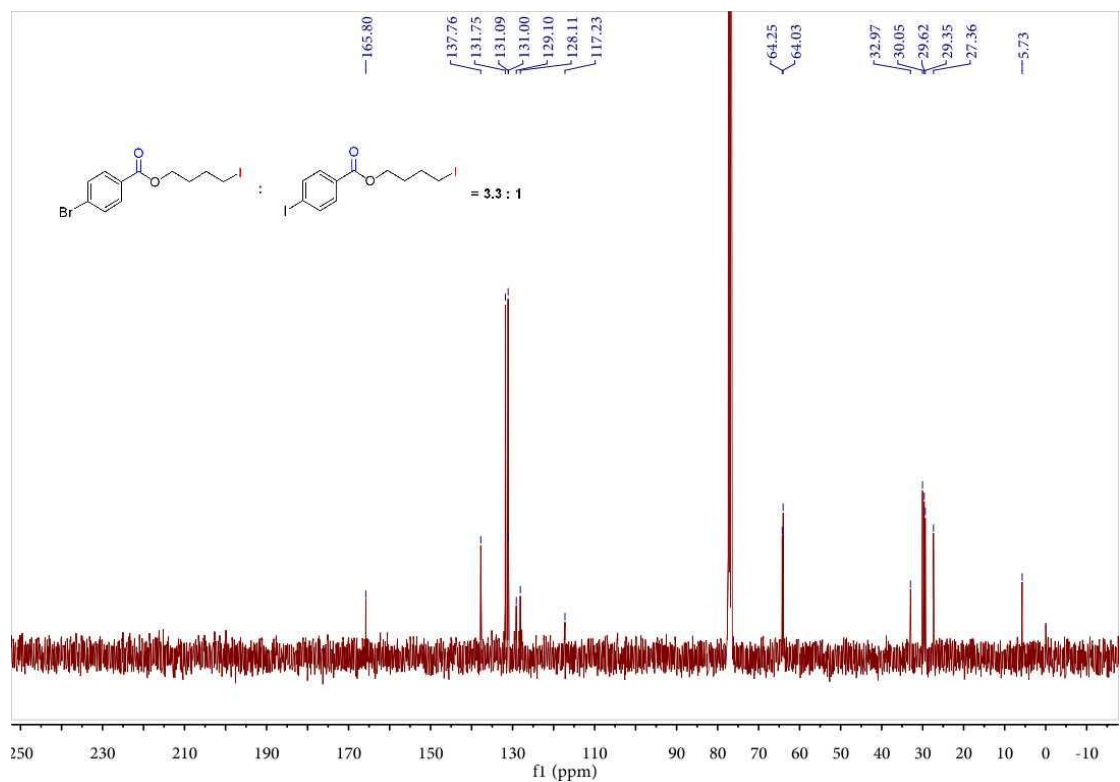


Figure S30. ¹³C NMR spectrum of 3pb, related to Figure 1.

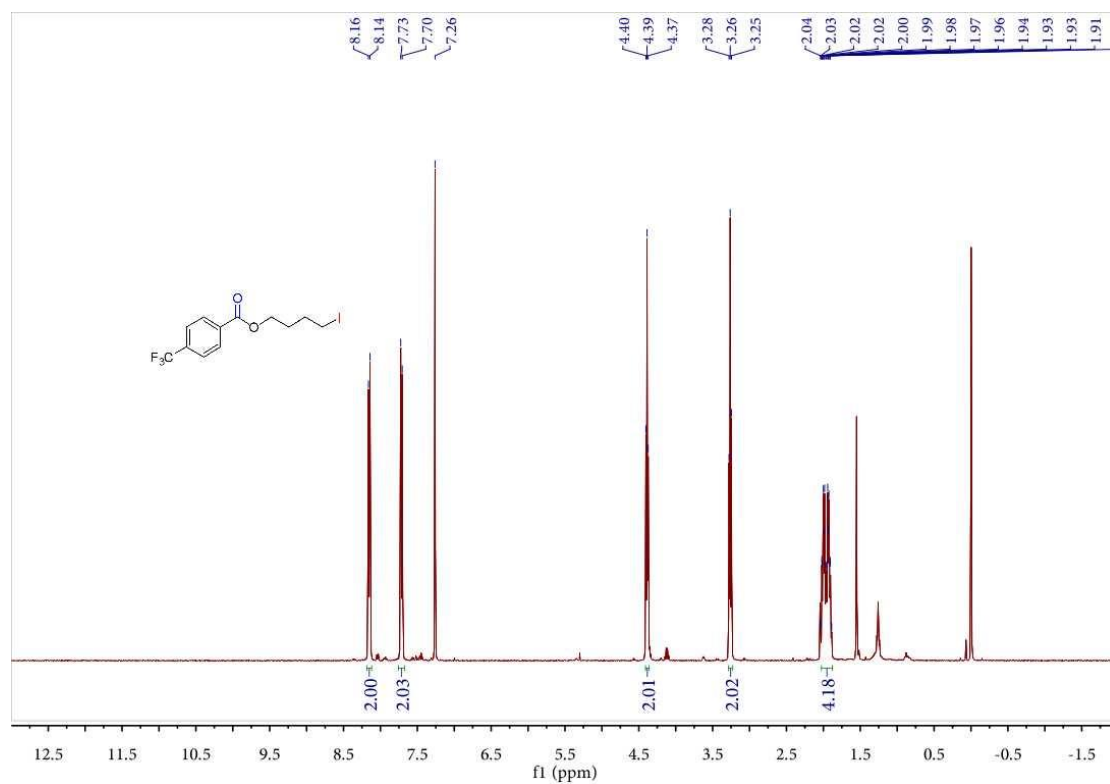


Figure S31. ^1H NMR spectrum of 3qb, related to Figure 1.

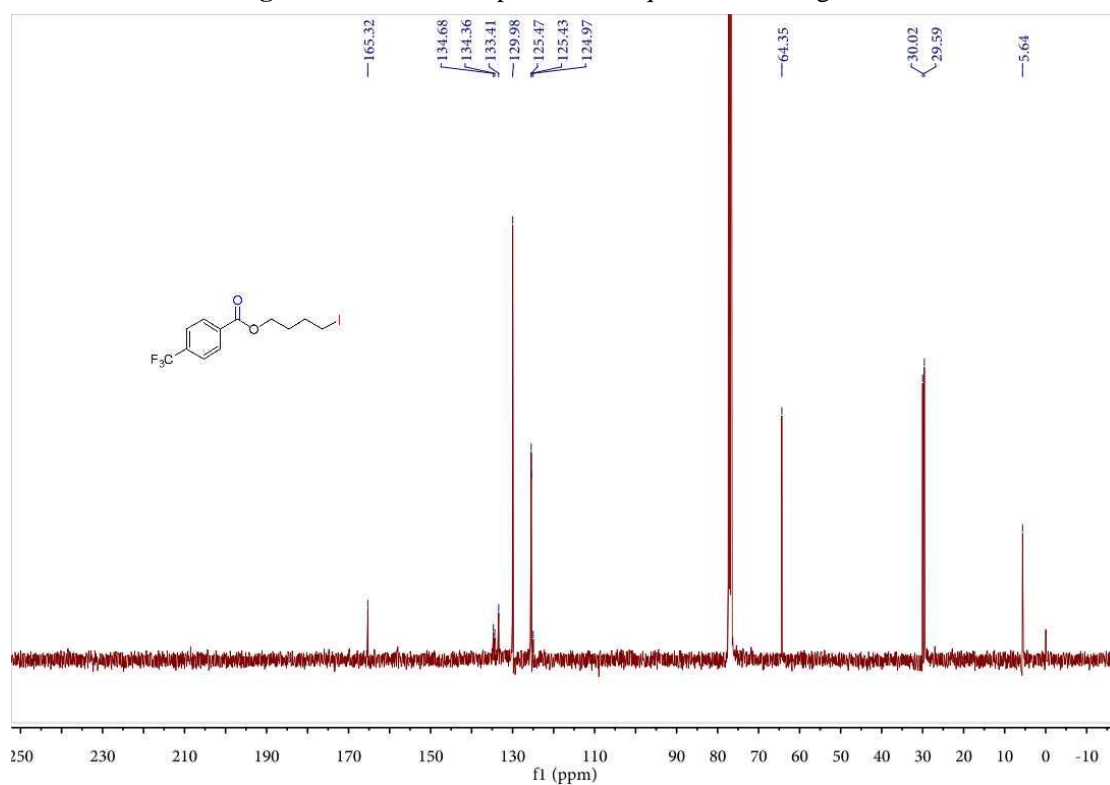


Figure S32. ^{13}C NMR spectrum of 3qb, related to Figure 1.

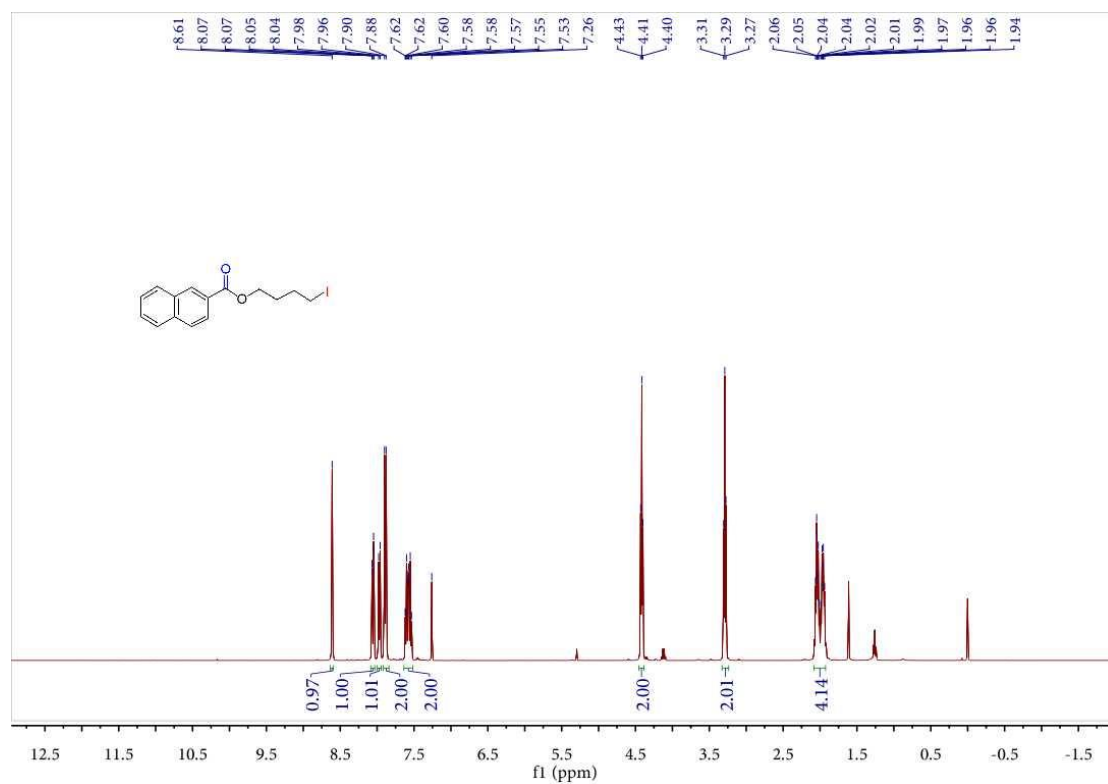


Figure S33. ^1H NMR spectrum of 3rb, related to Figure 1.

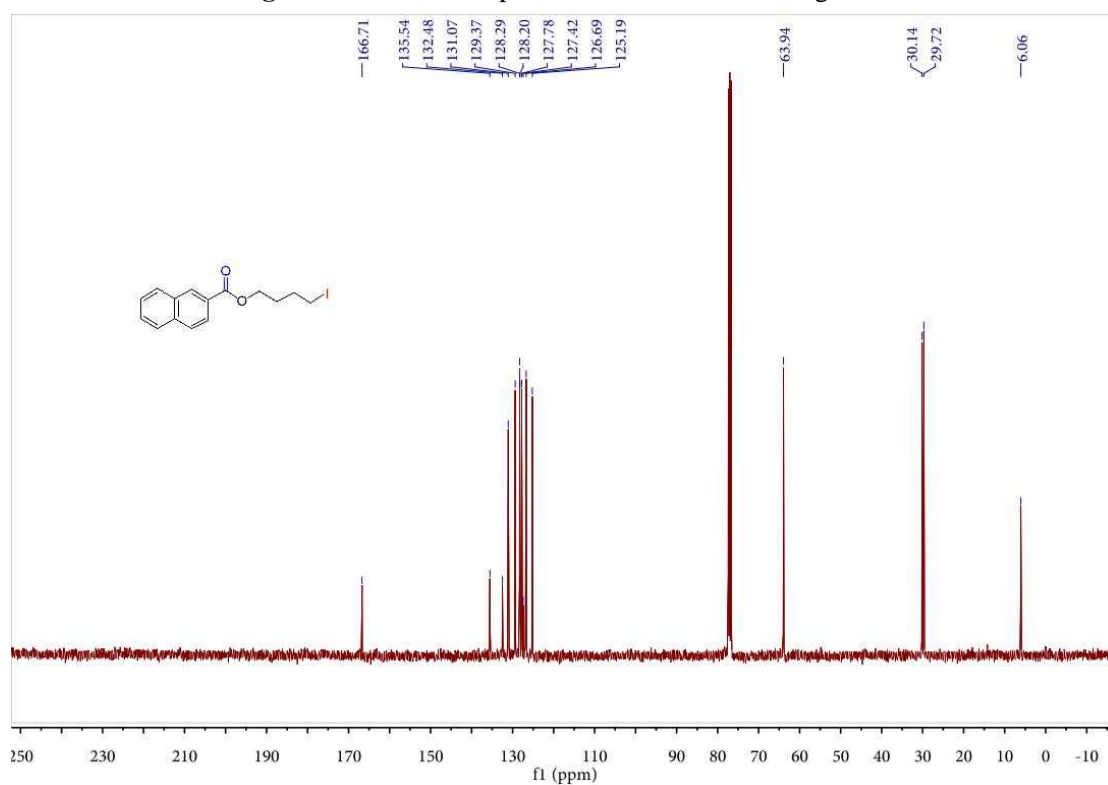


Figure S34. ^{13}C NMR spectrum of 3rb, related to Figure 1.

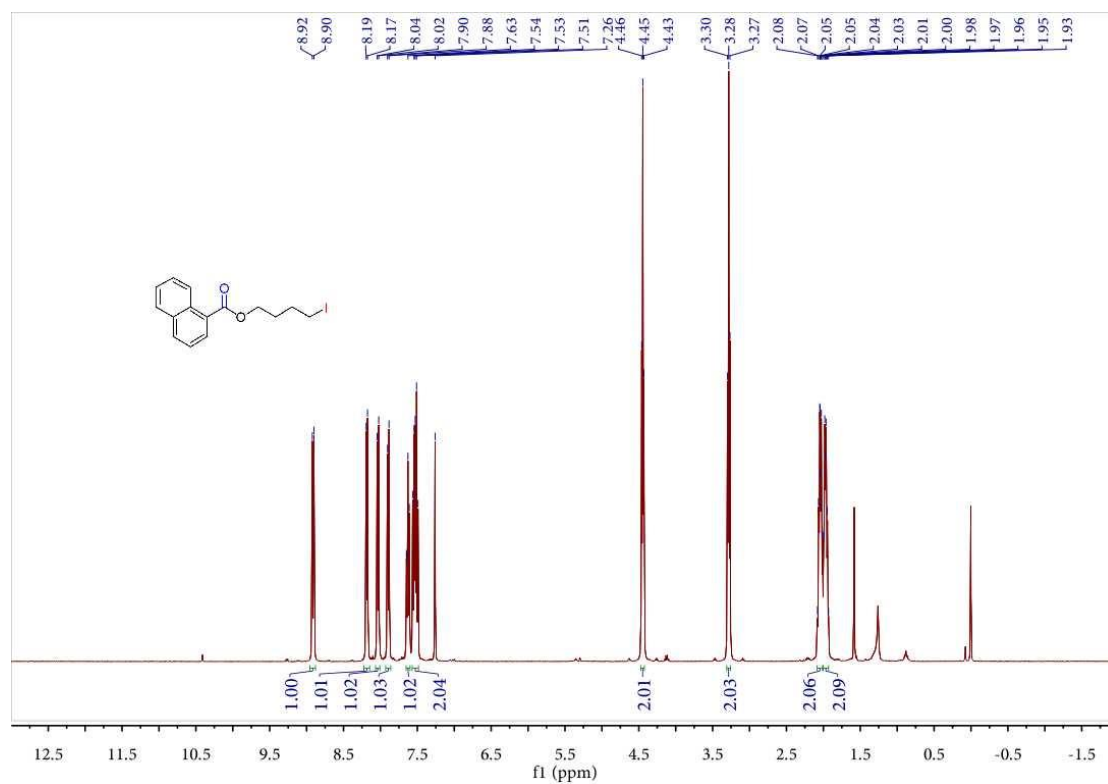


Figure S35. ^1H NMR spectrum of 3sb, related to Figure 1.

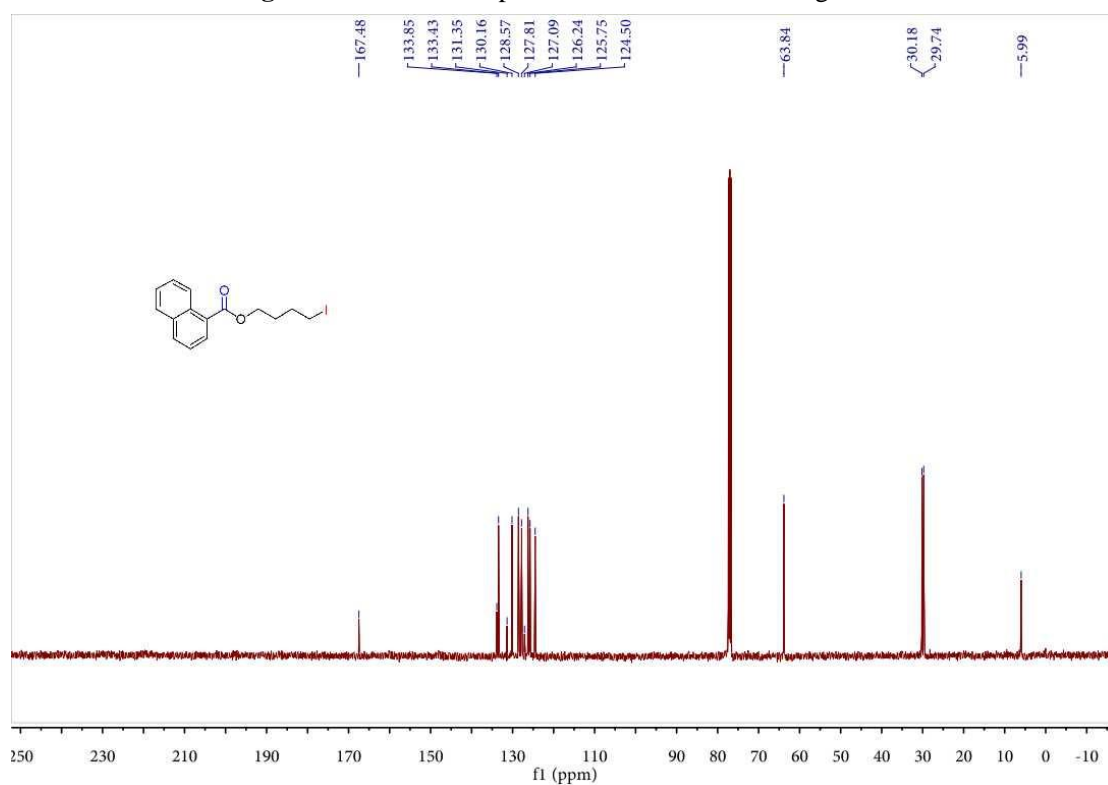


Figure S36. ^{13}C NMR spectrum of 3sb, related to Figure 1.

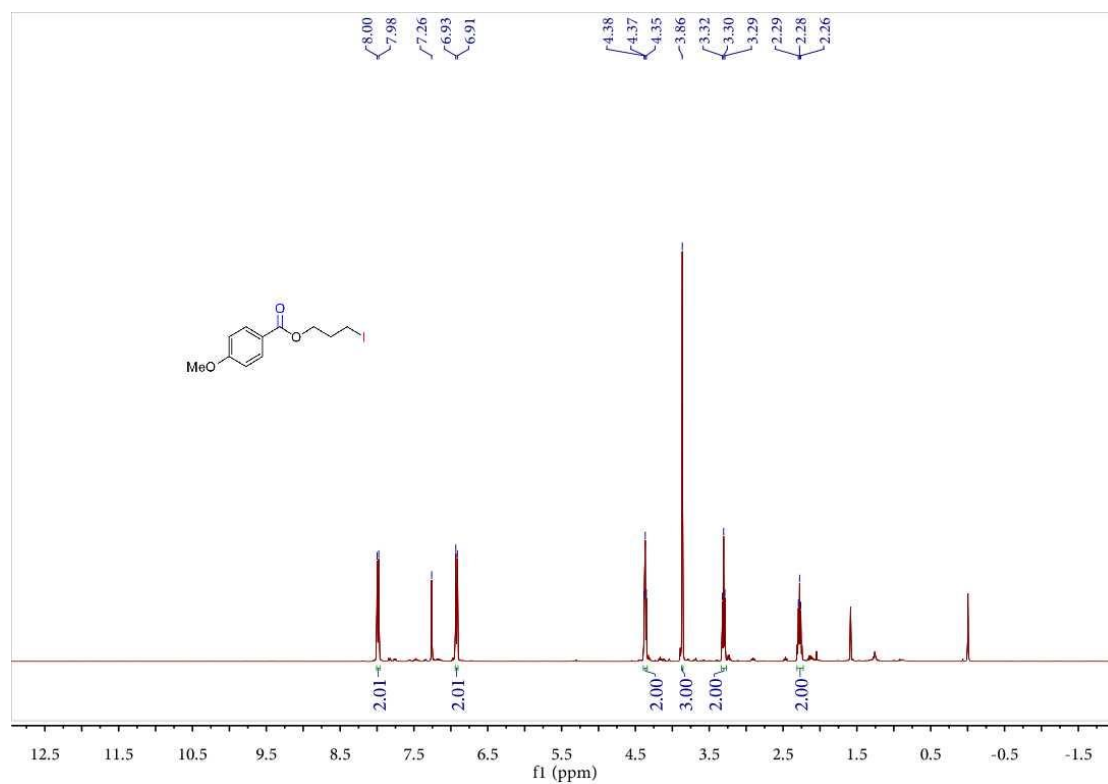


Figure S37. ^1H NMR spectrum of 3ha, related to Figure 2.

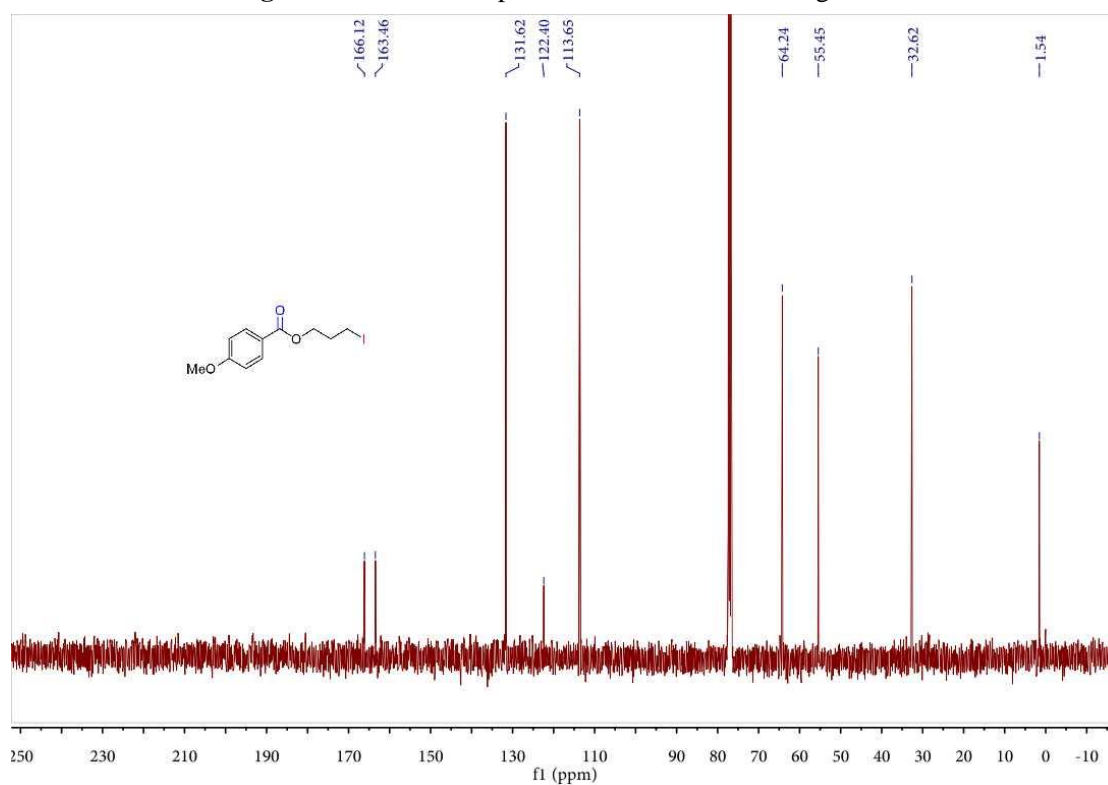


Figure S38. ^{13}C NMR spectrum of 3ha, related to Figure 2.

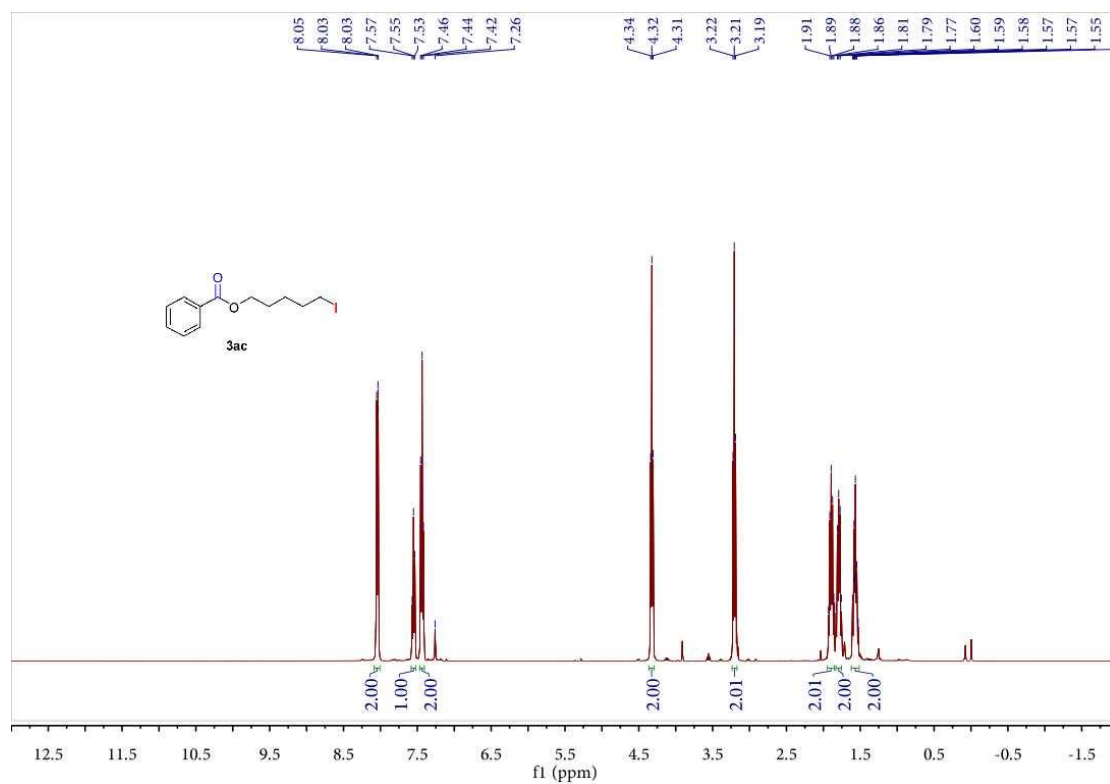


Figure S39. ¹H NMR spectrum of 3ac, related to Figure 2.

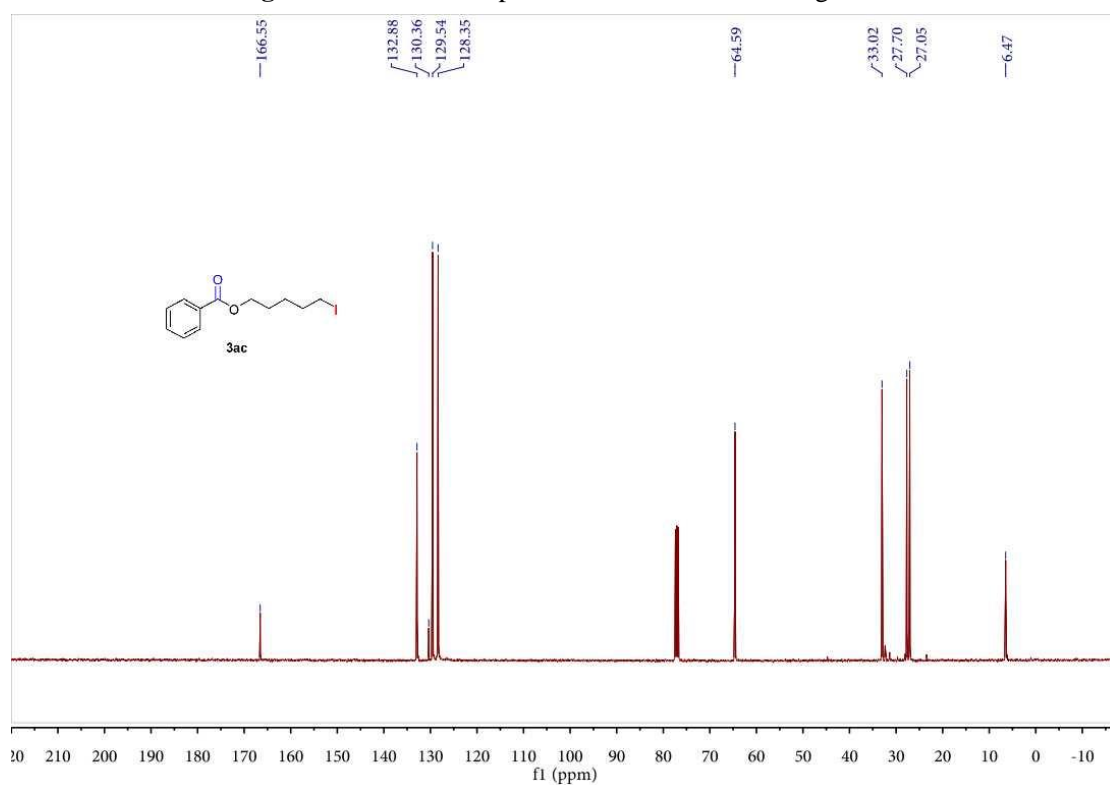


Figure S40. ¹³C NMR spectrum of 3ac, related to Figure 2.

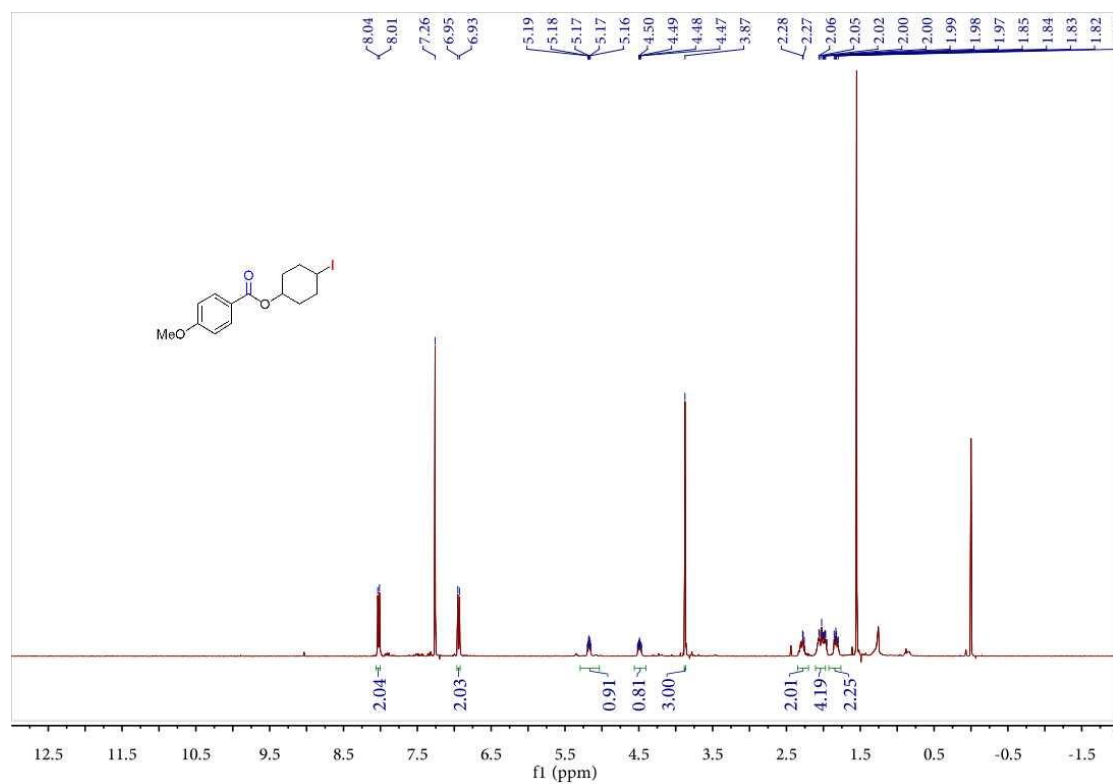


Figure S41. ¹H NMR spectrum of 3hd, related to Figure 2.

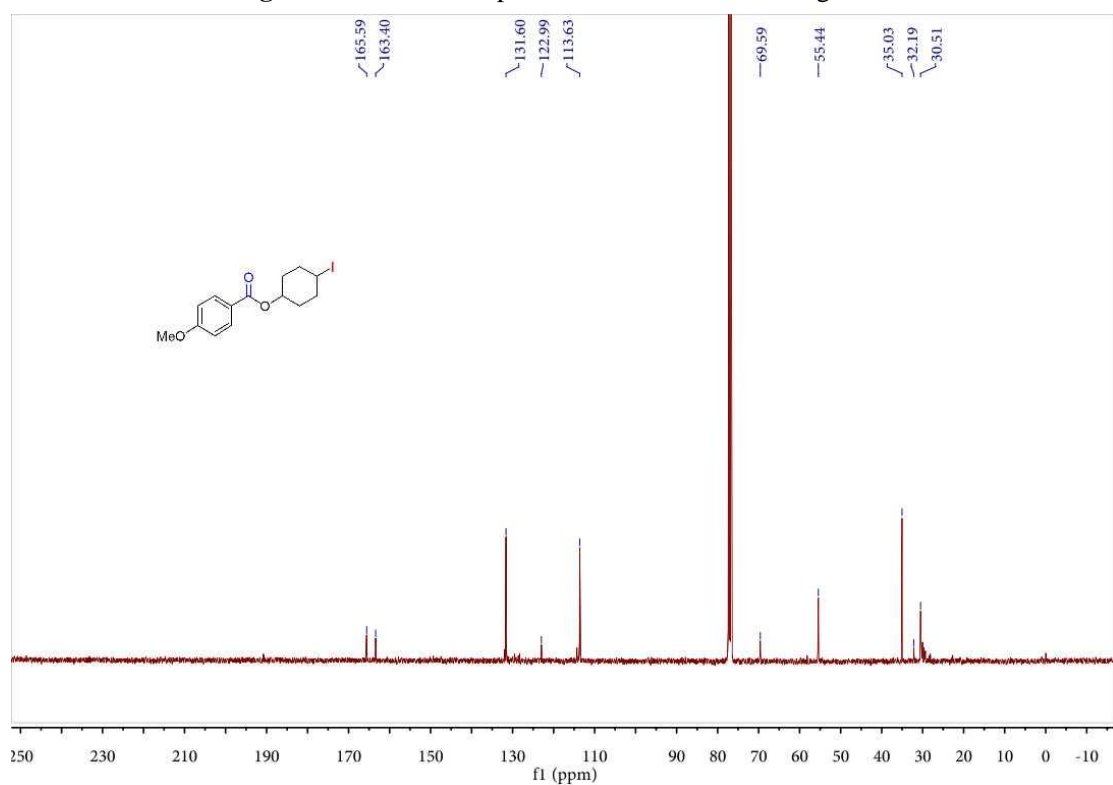


Figure S42. ¹³C NMR spectrum of 3hd, related to Figure 2.

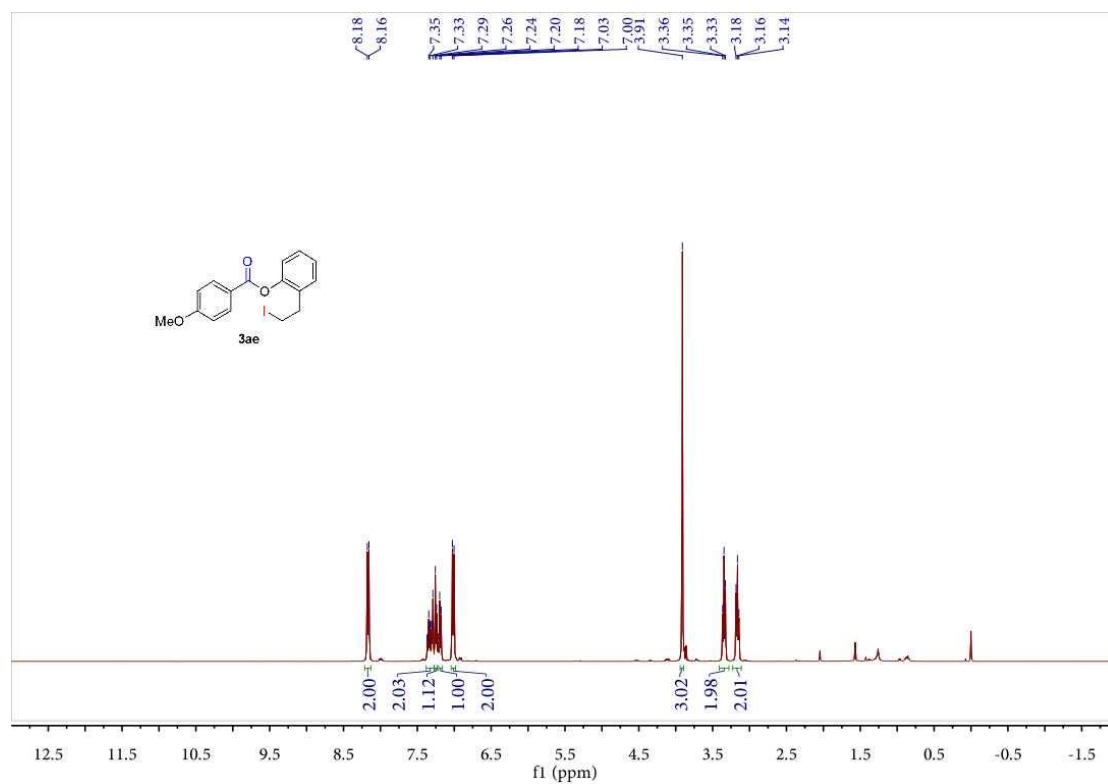


Figure S43. ¹H NMR spectrum of 3ae, related to Figure 2.

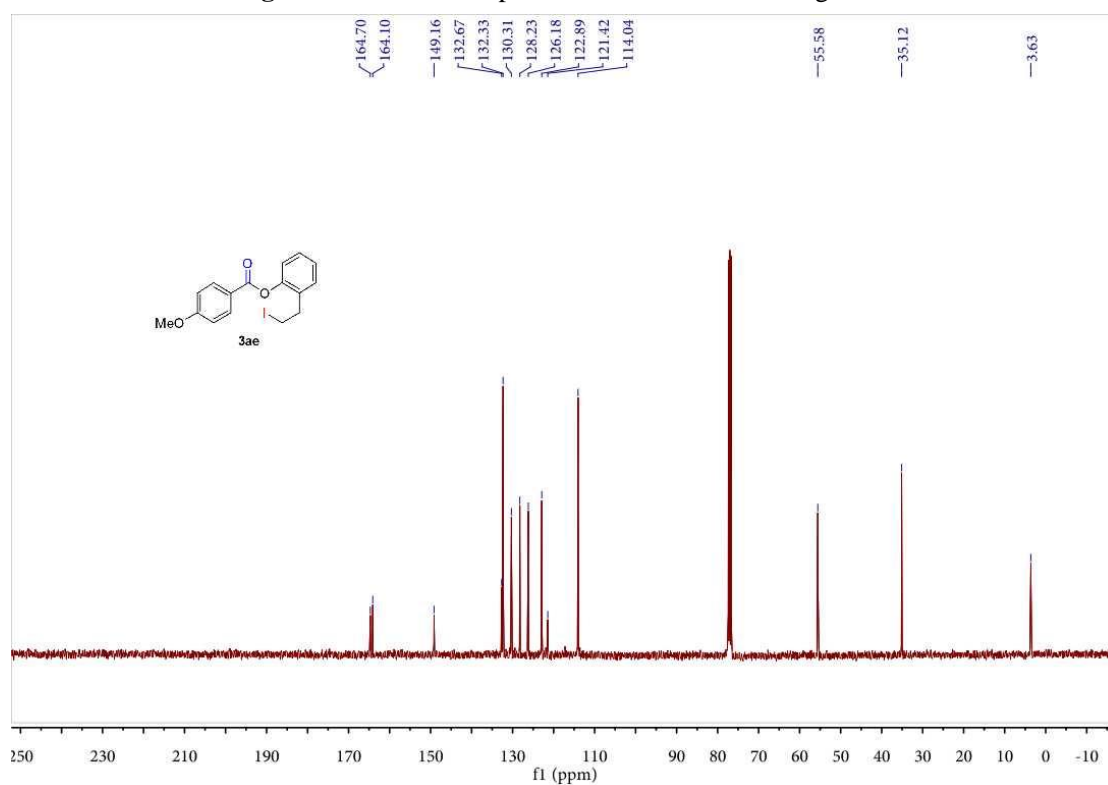


Figure S44. ¹³C NMR spectrum of 3ae, related to Figure 2.

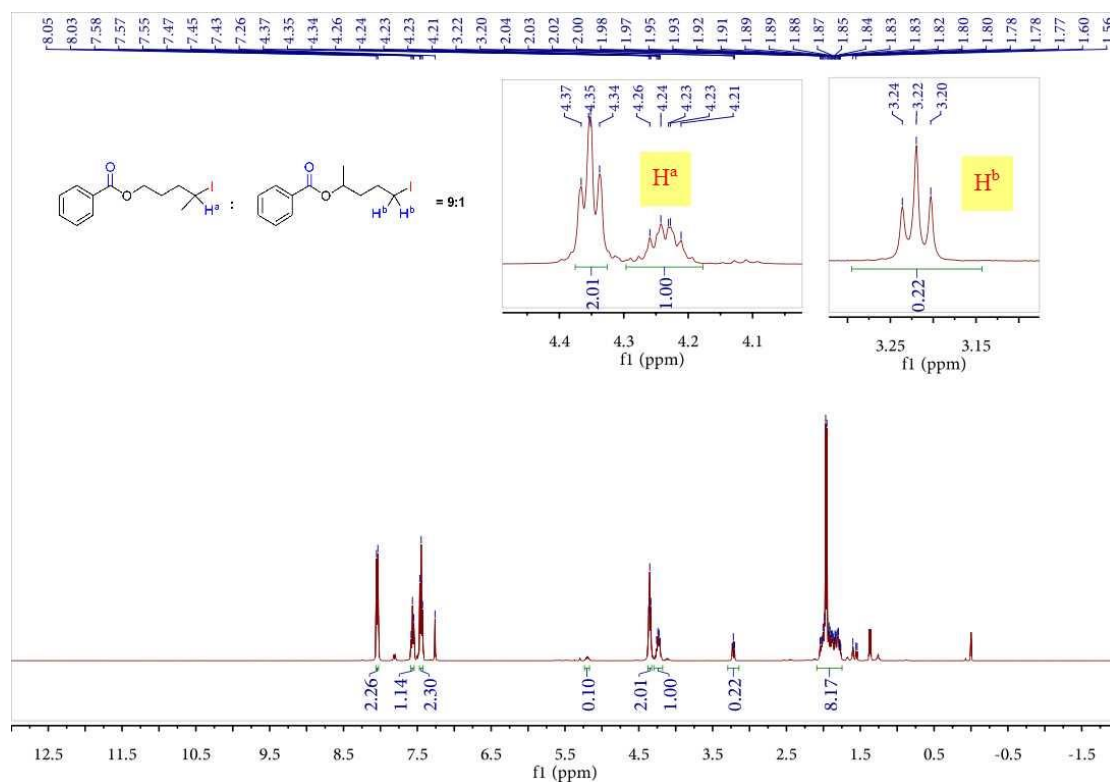


Figure S45. ^1H NMR spectrum of 3af + 3af', related to Figure 2.

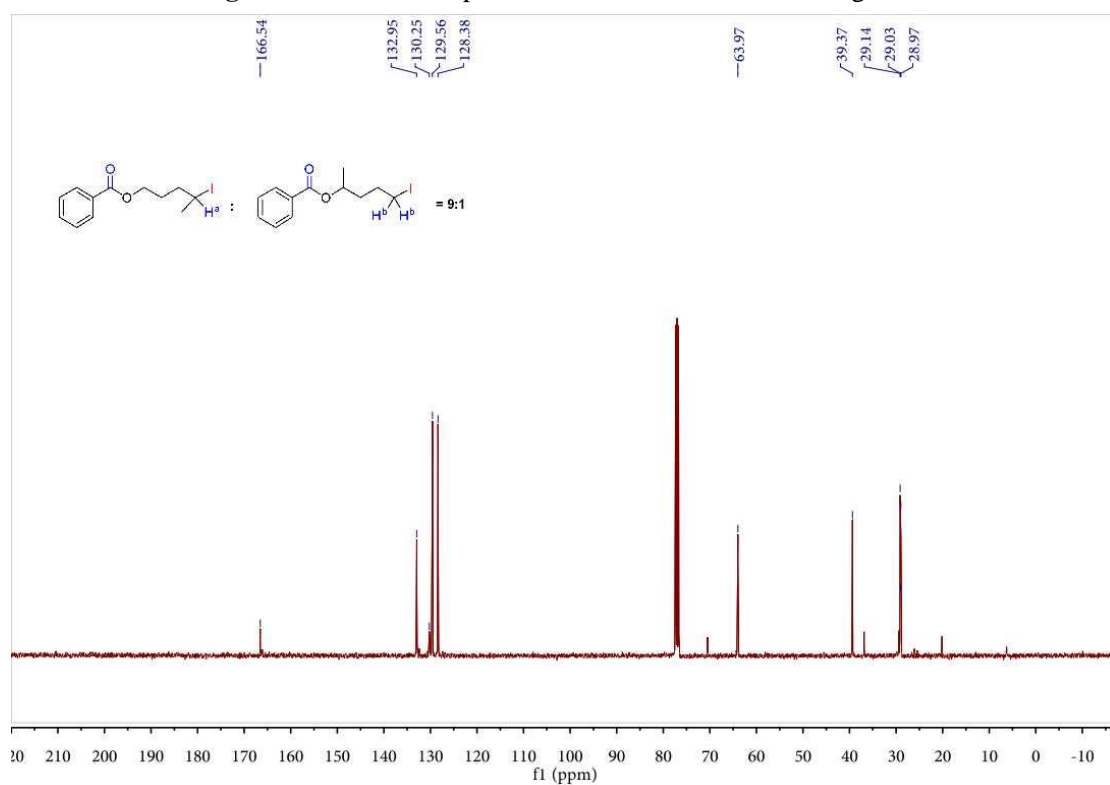


Figure S46. ^{13}C NMR spectrum of 3af + 3af', related to Figure 2.

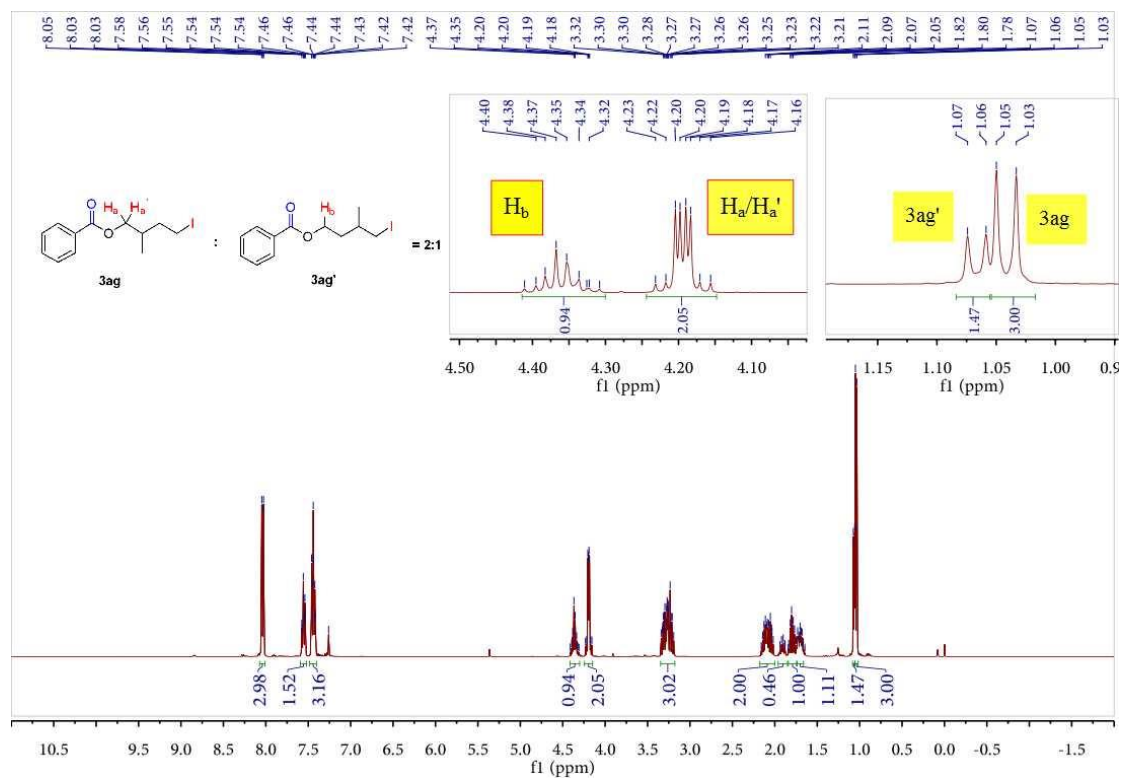


Figure S47. ^1H NMR spectrum of 3ag + 3ag', related to Figure 2.

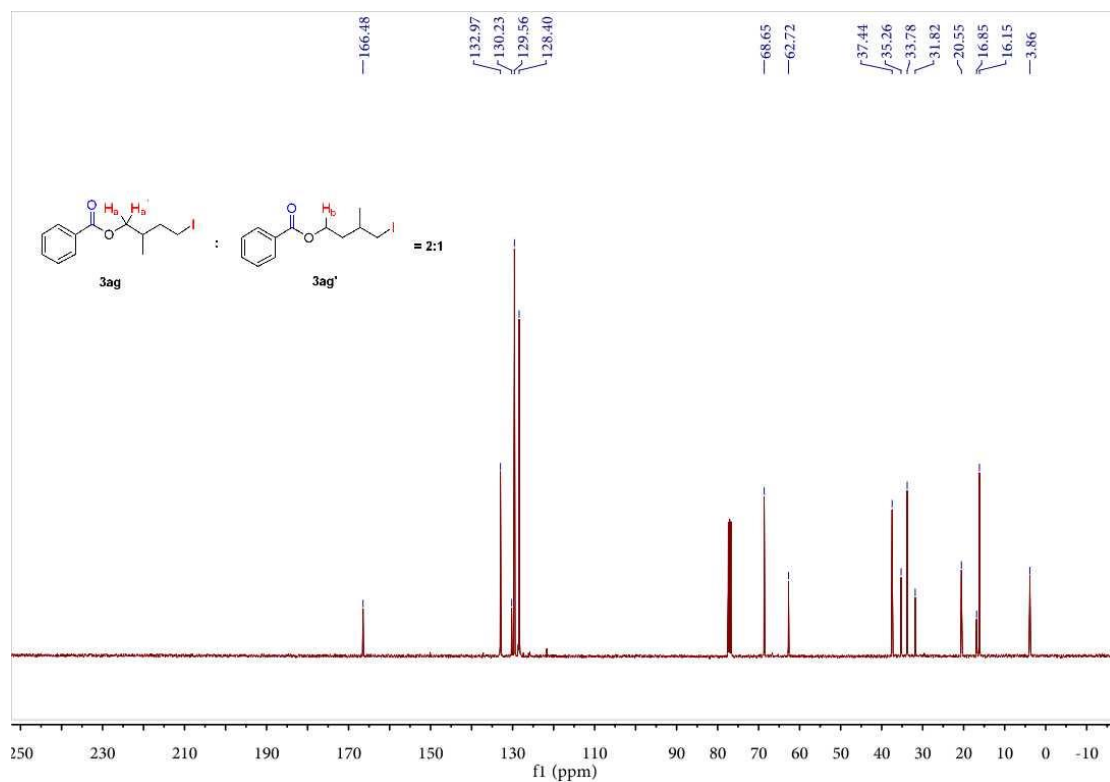


Figure S48. ^{13}C NMR spectrum of 3ag + 3ag', related to Figure 2.

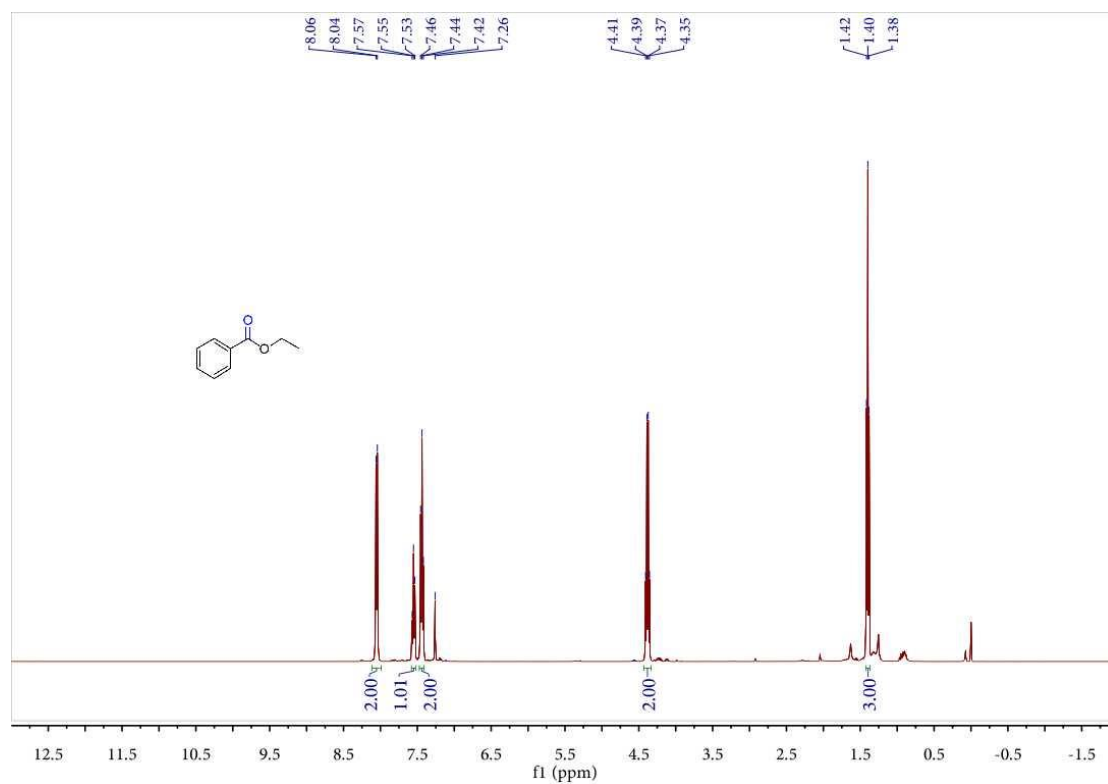


Figure S49. ¹H NMR spectrum of 3ah, related to Figure 2.

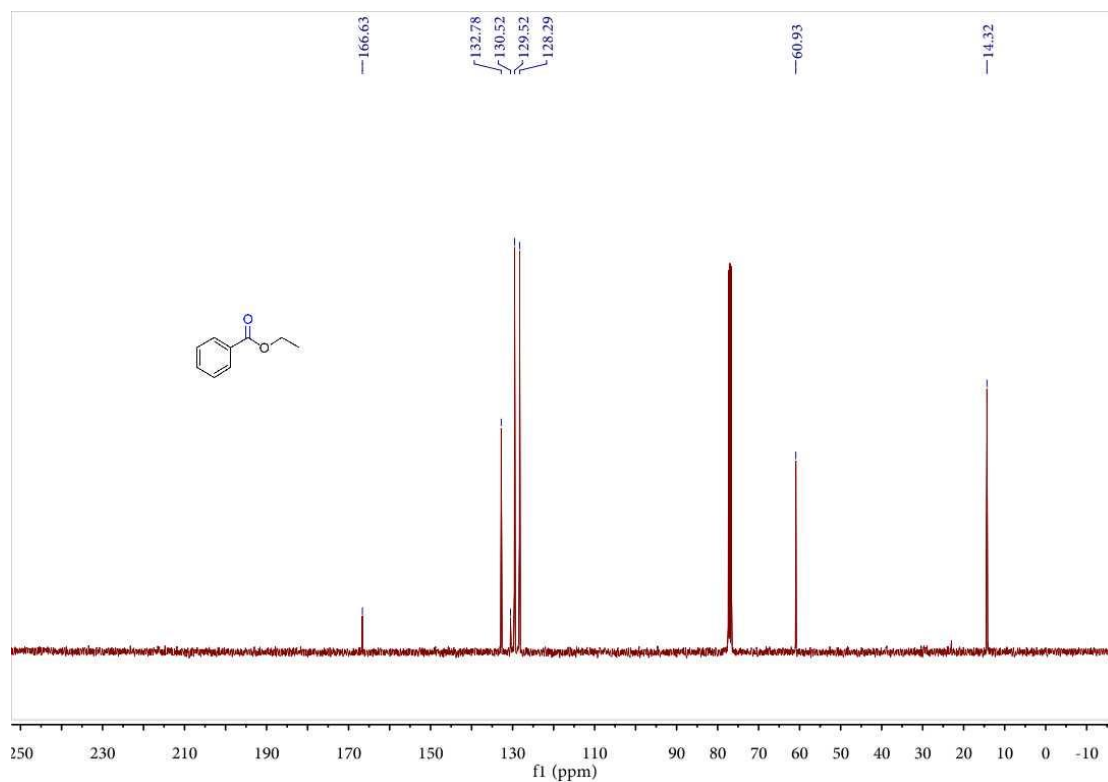


Figure S50. ¹³C NMR spectrum of 3ah, related to Figure 2.

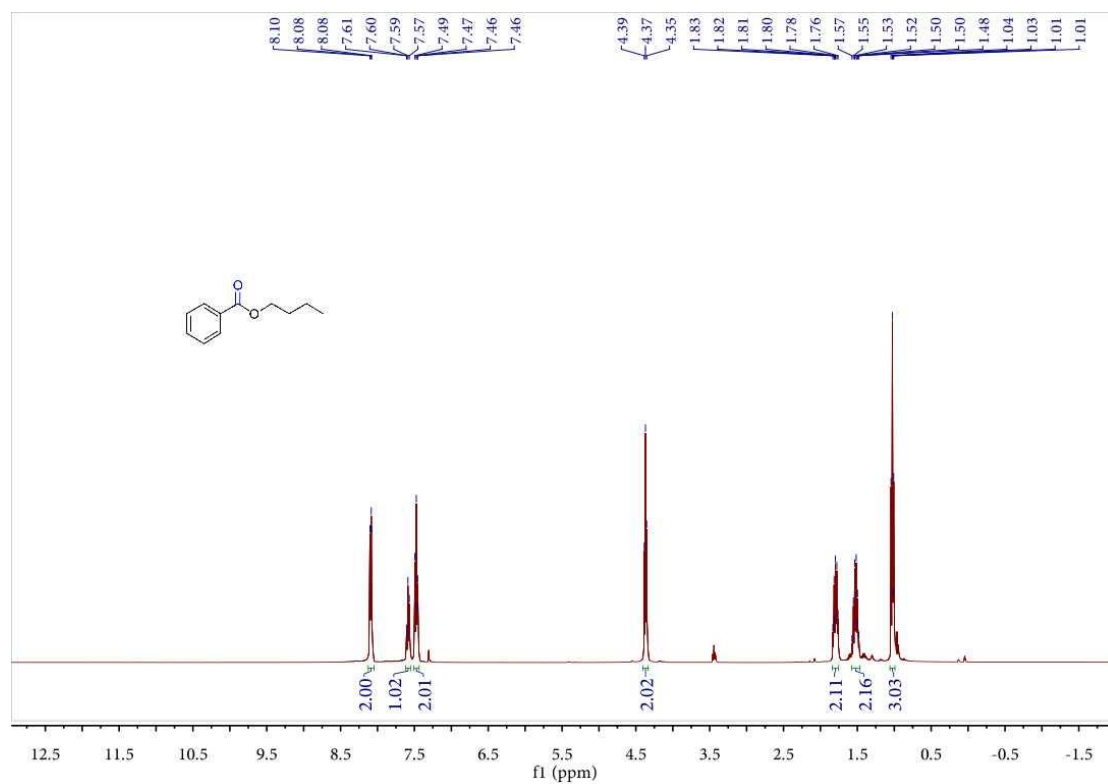


Figure S51. ^1H NMR spectrum of 3ai, related to Figure 2.

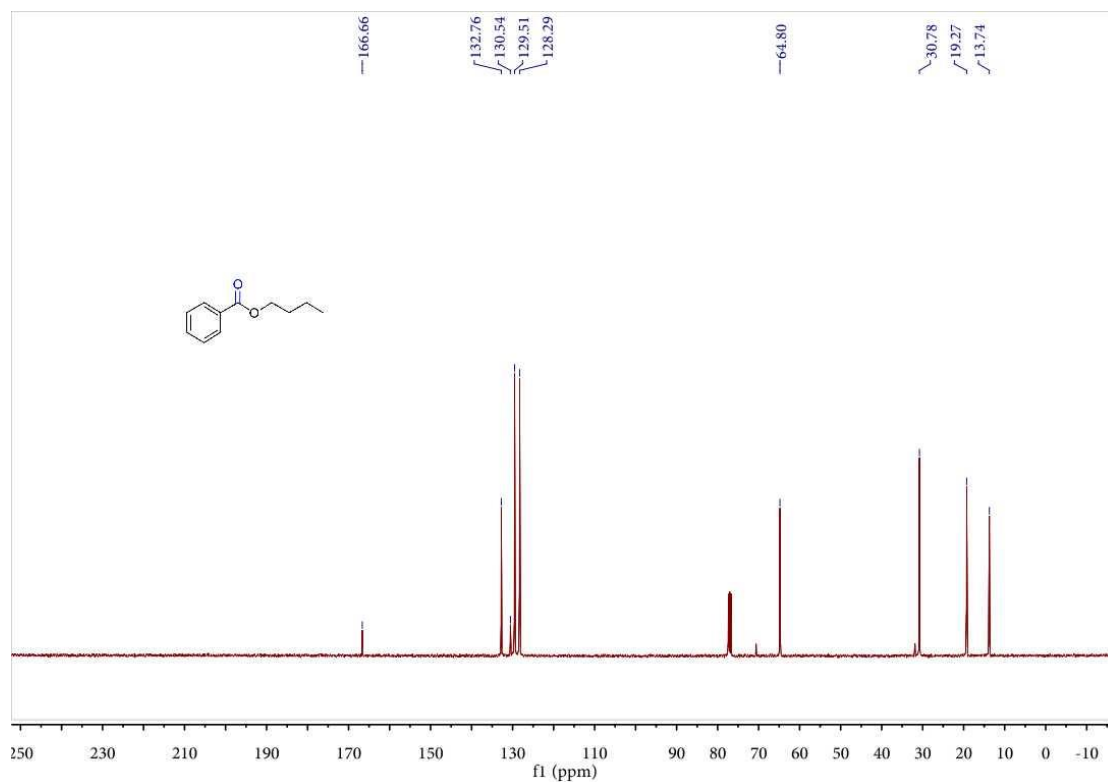


Figure S52. ^{13}C NMR spectrum of 3ai, related to Figure 2.

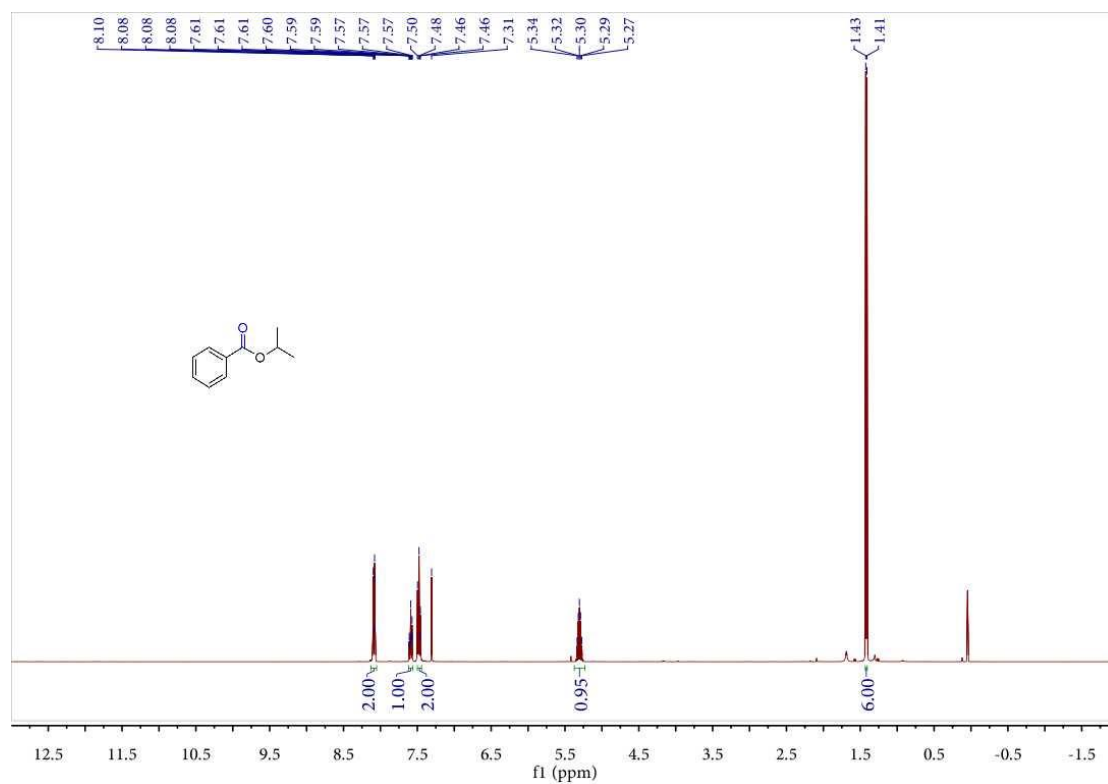


Figure S53. ^1H NMR spectrum of 3aj, related to Figure 2.

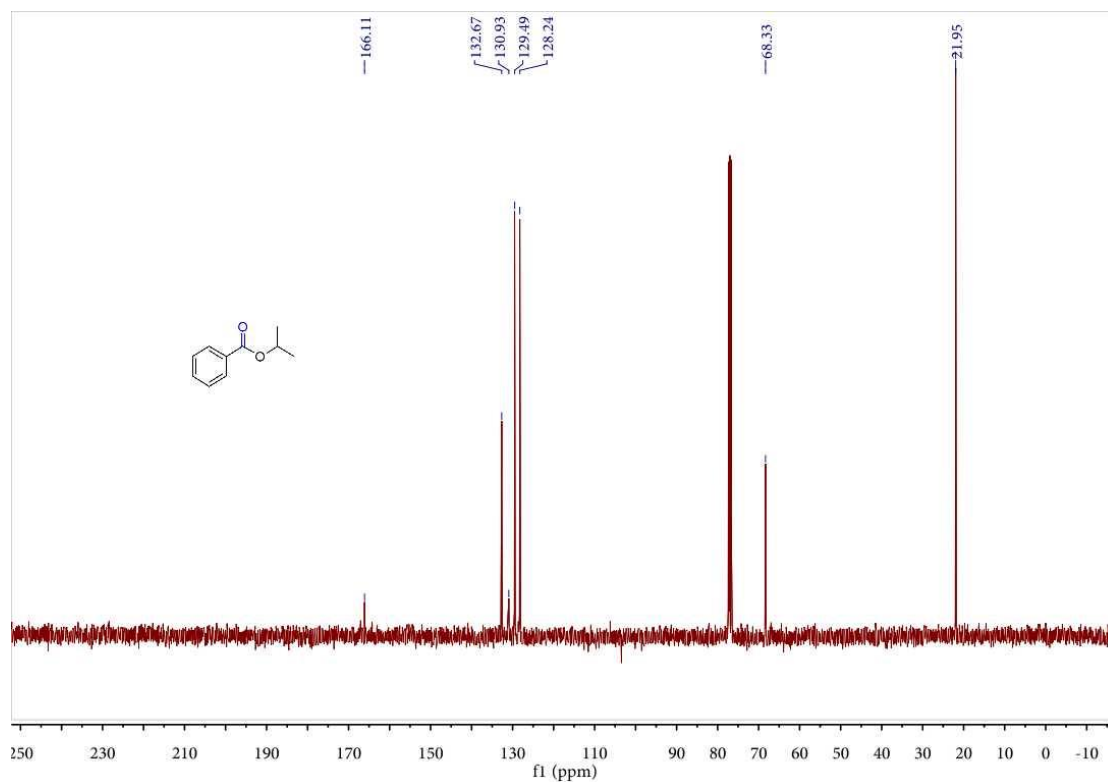


Figure S54. ^{13}C NMR spectrum of 3aj, related to Figure 2.

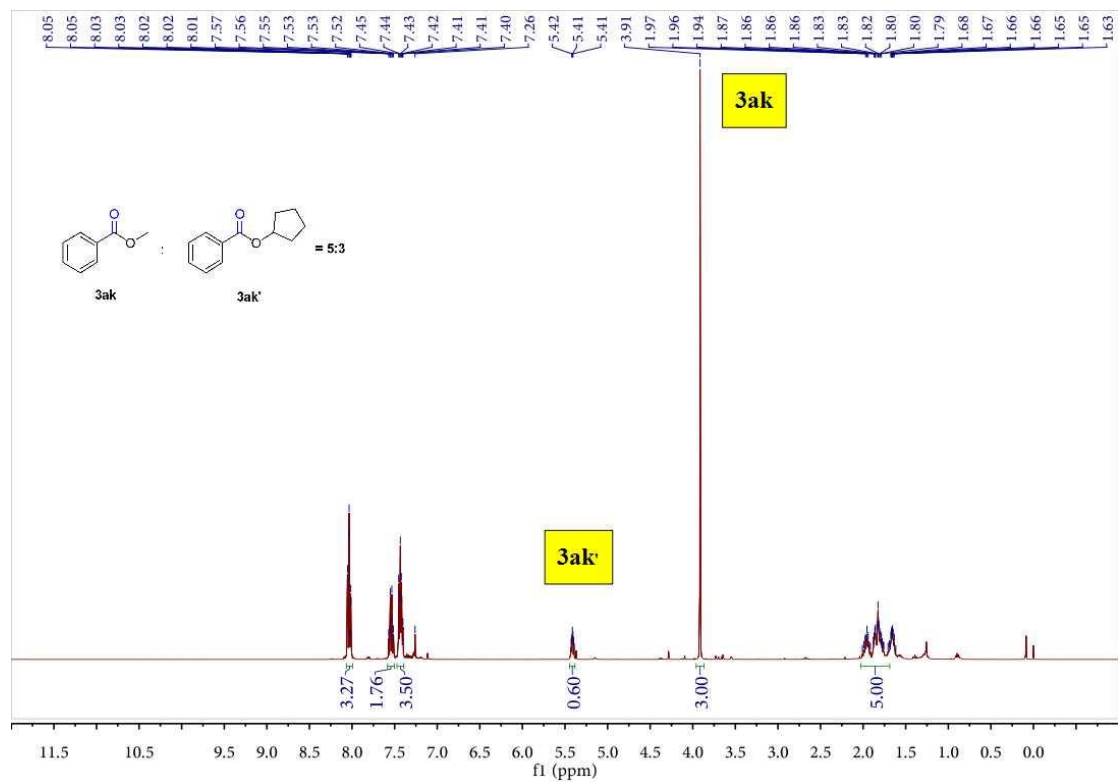


Figure S55. ¹H NMR spectrum of 3ak + 3ak', related to Figure 2.

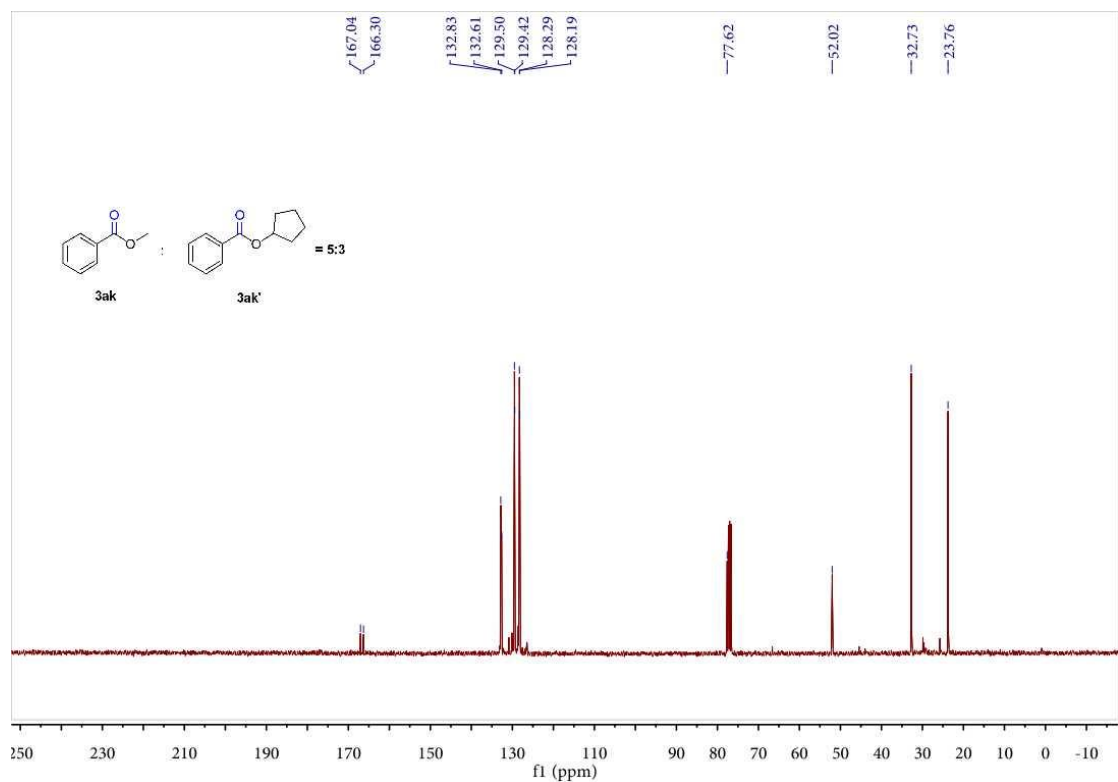


Figure S56. ¹³C NMR spectrum of 3ak + 3ak', related to Figure 2.

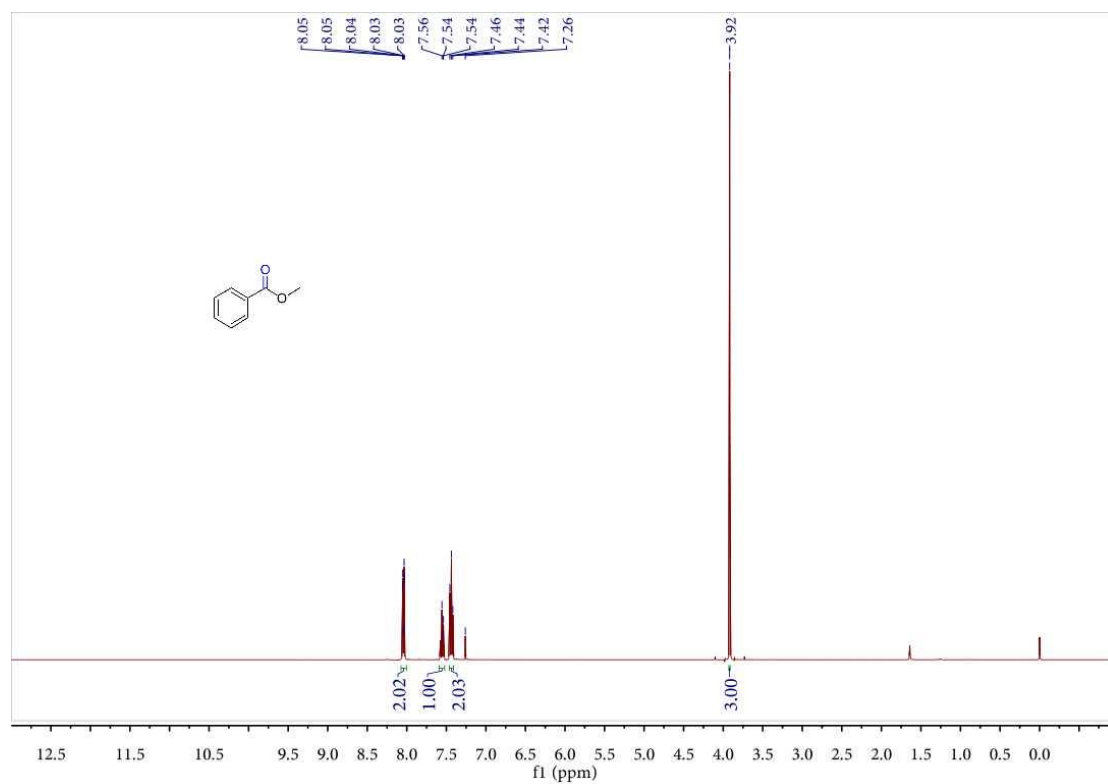


Figure S57. ¹H NMR spectrum of 3al, related to Figure 2.

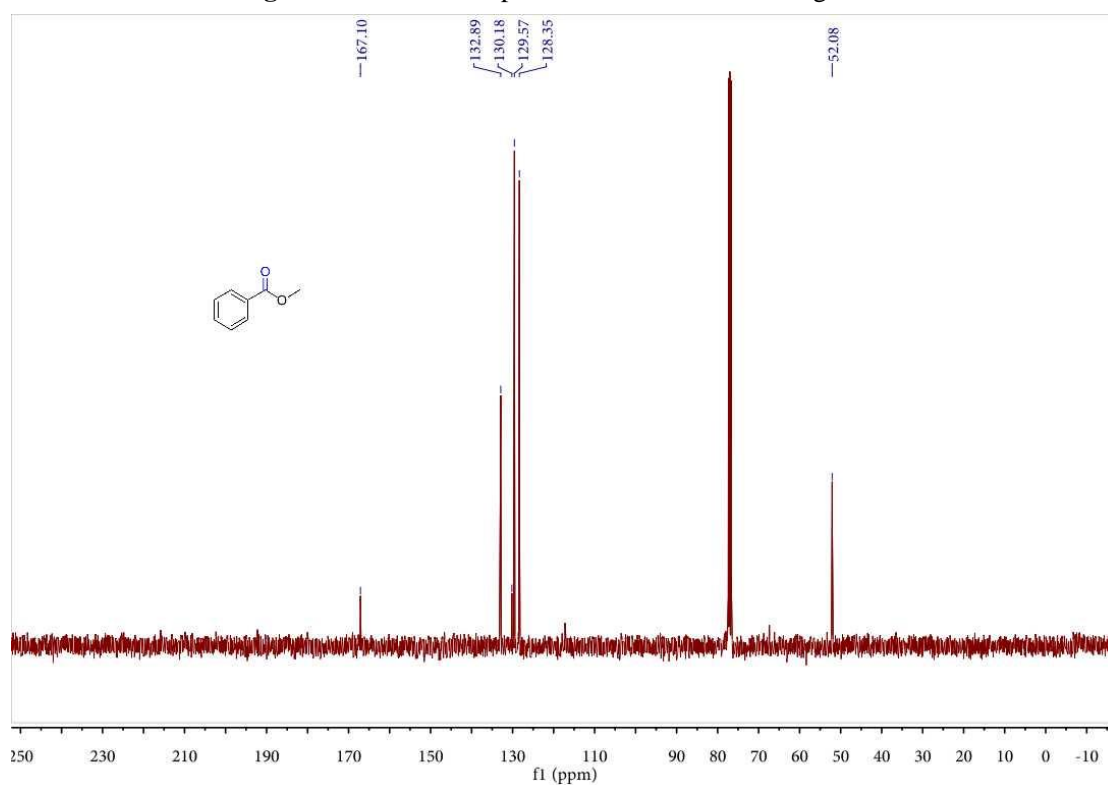


Figure S58. ¹³C NMR spectrum of 3al, related to Figure 2.

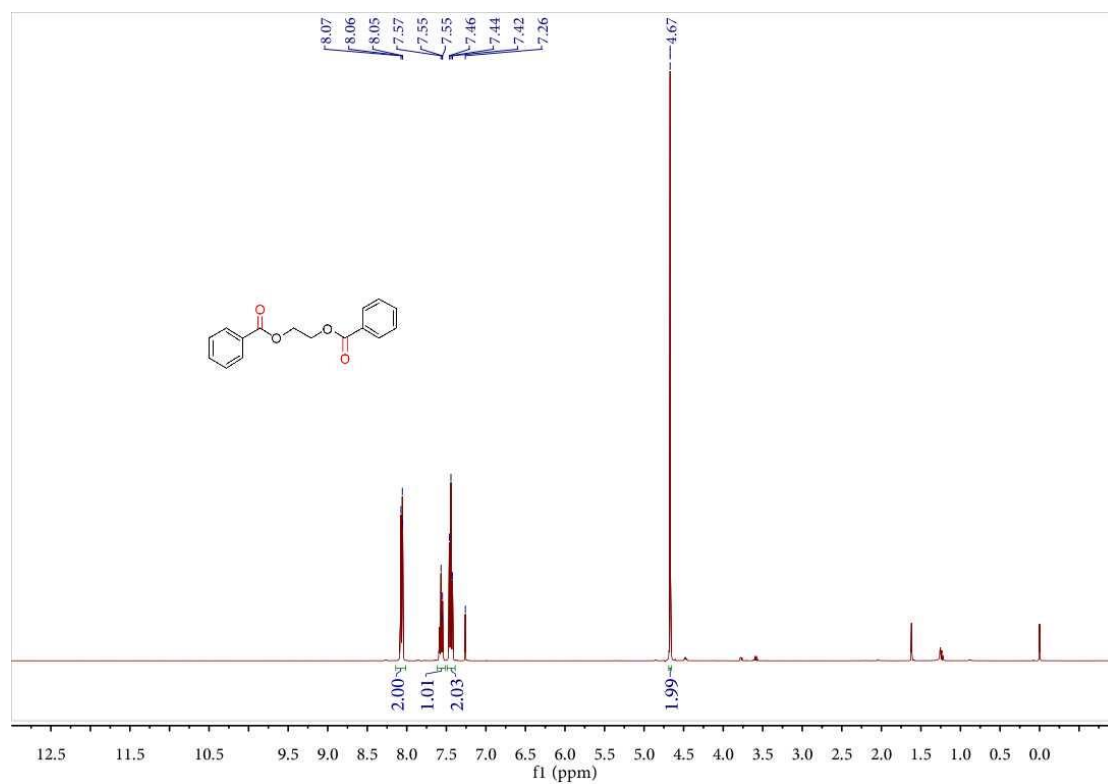


Figure S59. ^1H NMR spectrum of 3am', related to Scheme 1.

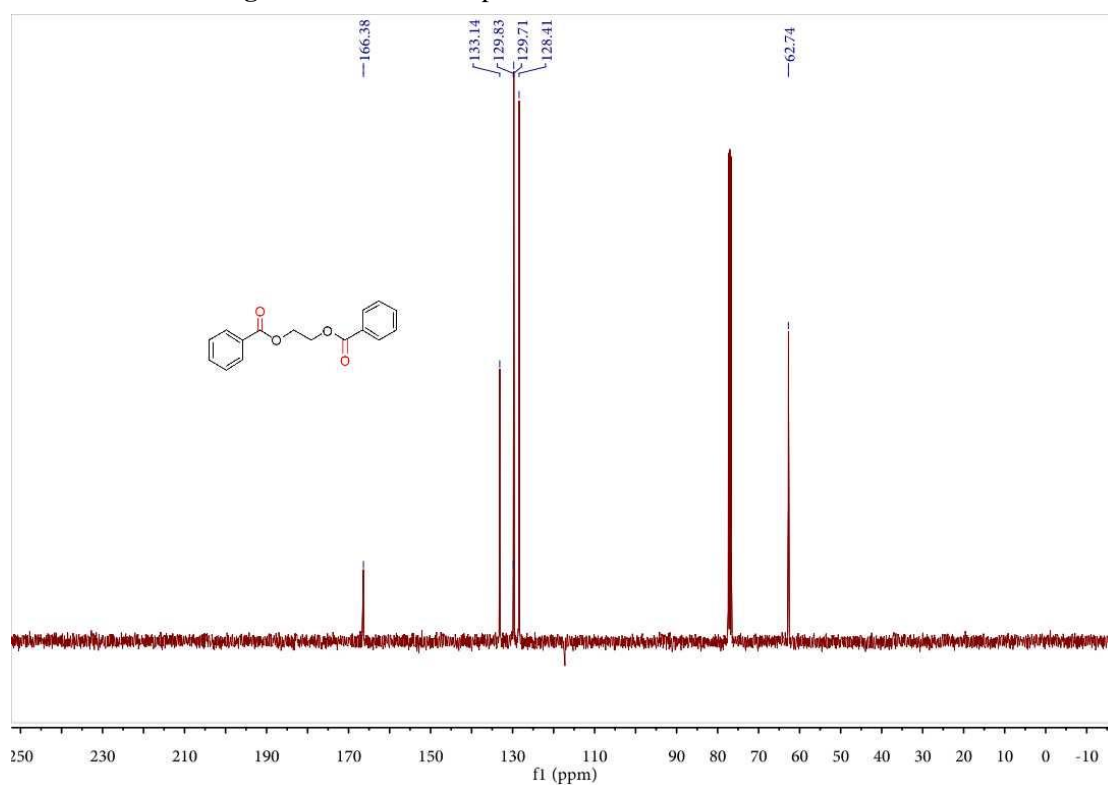
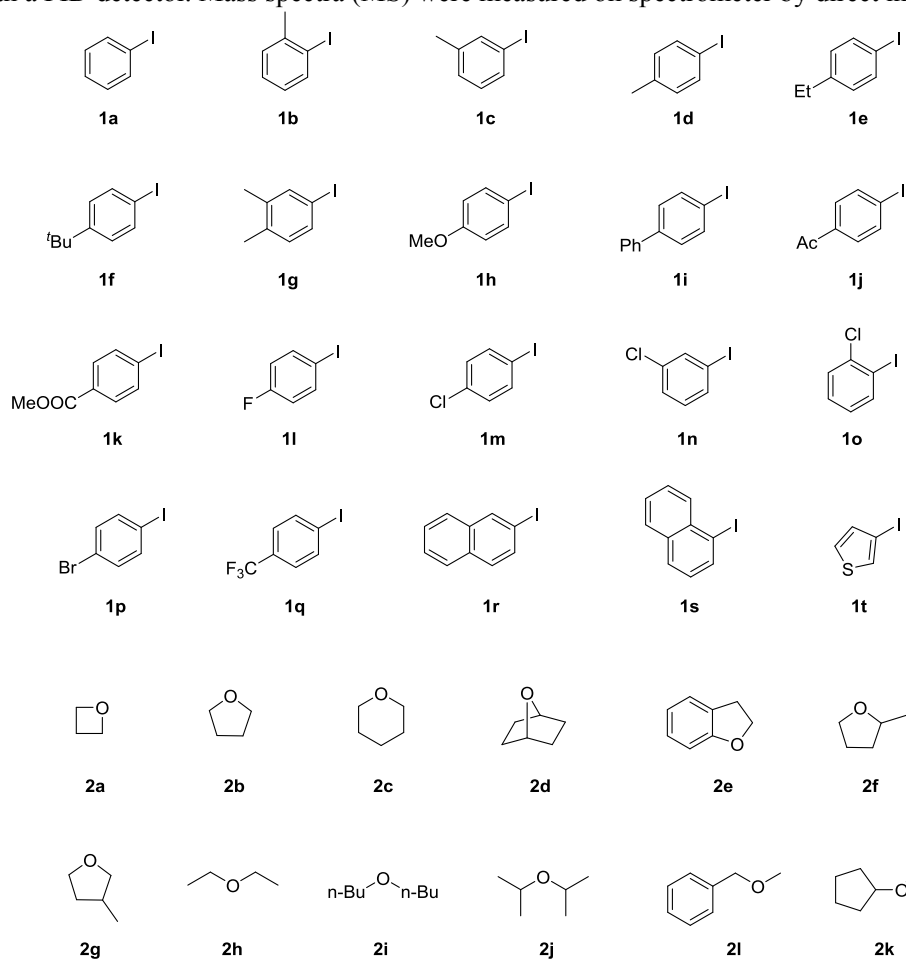


Figure S60. ^{13}C NMR spectrum of 3am', related to Scheme 1

Transparent Methods

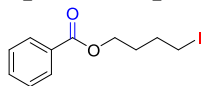
Unless otherwise noted, all reactions were carried out under a nitrogen atmosphere. All reagents were from commercial sources and used as received without further purification. All solvents were dried by standard techniques, and distilled prior to use. Column chromatography was performed on silica gel (200-300 meshes) using petroleum ether (bp. 60~90 °C) and ethyl acetate as eluent. ^1H and ^{13}C NMR spectra were taken on 400 MHz instruments and spectral data were reported in ppm relative to tetramethylsilane (TMS) as internal standard and CDCl_3 (^1H NMR δ 7.26, ^{13}C NMR δ 77.0) as solvent. All coupling constants (J) are reported in Hz with the following abbreviations: s = singlet, d = doublet, dd = double doublet, ddd = double doublet of doublets, t = triplet, dt = double triplet, q = quatriplet, m = multiplet, br = broad. Gas chromatography (GC) analyses were performed on a Shimadzu GC-2014C chromatograph equipped with a FID detector. Mass spectra (MS) were measured on spectrometer by direct inlet at 70 eV.



General Procedure

$\text{Ni}(\text{OTf})_2$ (8.9 mg, 5 mol%), dtbbpy (6.7 mg, 5 mol%) and $\text{Mo}(\text{CO})_6$ (66.0 mg, 0.25 mmol) were transferred into a 15 mL tube which was filled with nitrogen. Chlorobenzene (2.0 mL), THF (122 μL , 1.5 mol) and iodobenzene (0.5 mmol) were added to the reaction tube. The tube was sealed and the mixture was stirred at 120 °C for 16 h. After the reaction was completed, the reaction mixture was filtered and concentrated under vacuum. The crude product was purified by column chromatography on silica gel to afford the corresponding product.

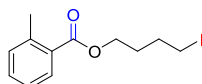
Spectroscopic Data of Products



4-Iodobutyl benzoate (3ab)

Prepared from iodobenzene (57 μL , 0.5 mmol) and tetrahydrofuran (122 μL , 1.5 mmol). After purification by column chromatography (petroleum ether/EtOAc = 50:1, R_f = 0.25) the desired compound was isolated as a colorless oil (142.8 mg, 93%).

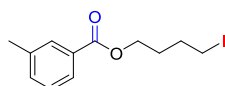
$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.04 (d, J = 7.8 Hz, 2H), 7.56 (t, J = 7.4 Hz, 1H), 7.45 (t, J = 7.7 Hz, 2H), 4.35 (t, J = 6.2 Hz, 2H), 3.26 (t, J = 6.7 Hz, 2H), 2.00 (dq, J = 11.1, 6.6 Hz, 2H), 1.90 (tt, J = 12.0, 6.2 Hz, 2H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 166.53, 132.99, 130.18, 129.56, 128.39, 63.76, 30.10, 29.68, 5.98.



4-Iodobutyl 2-methylbenzoate (3bb)

Prepared from 1-iodo-2-methylbenzene (65 μL , 0.5 mmol) and tetrahydrofuran (122 μL , 1.5 mmol). After purification by column chromatography (petroleum ether/EtOAc = 50:1, R_f = 0.25) the desired compound was isolated as a colorless oil (111.9 mg, 70%).

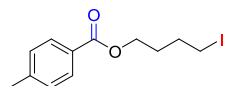
$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.91 (d, J = 8.3 Hz, 1H), 7.41 (t, J = 7.4 Hz, 1H), 7.25 (d, J = 8.2 Hz, 2H), 4.33 (t, J = 6.2 Hz, 2H), 3.26 (t, J = 6.7 Hz, 2H), 2.60 (s, 3H), 1.99 (dd, J = 14.3, 7.3 Hz, 2H), 1.95 – 1.85 (m, 2H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 167.55, 140.17, 132.00, 131.72, 130.52, 129.57, 125.72, 63.50, 30.15, 29.69, 21.81, 5.95. HRMS (ESI+): $\text{C}_{12}\text{H}_{15}\text{IO}_2$ $[\text{M}+\text{H}]^+$ found 319.0177, requires 319.0189 (3.7 ppm).



4-Iodobutyl 3-methylbenzoate (3cb)

Prepared from 1-iodo-3-methylbenzene (66 μL , 0.5 mmol) and tetrahydrofuran (122 μL , 1.5 mmol). After purification by column chromatography (petroleum ether/EtOAc = 50:1, R_f = 0.25) the desired compound was isolated as a colorless oil (139.0 mg, 88%).

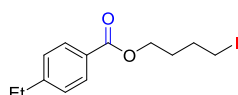
$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.84 (d, J = 9.3 Hz, 2H), 7.42 – 7.29 (m, 2H), 4.34 (t, J = 6.2 Hz, 2H), 3.26 (t, J = 6.7 Hz, 2H), 2.41 (s, 3H), 2.04 – 1.96 (m, 2H), 1.94 – 1.86 (m, 2H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 166.70, 138.16, 133.72, 130.07, 128.26, 126.66, 117.20, 63.67, 30.07, 29.65, 21.27, 5.99. HRMS (ESI+): $\text{C}_{12}\text{H}_{15}\text{IO}_2$ $[\text{M}+\text{H}]^+$ found 319.0194, requires 319.0189 (1.5 ppm).



4-Iodobutyl 4-methylbenzoate (3db)

Prepared from 1-iodo-4-methylbenzene (64 μL , 0.5 mmol) and tetrahydrofuran (122 μL , 1.5 mmol). After purification by column chromatography (petroleum ether/EtOAc = 50:1, R_f = 0.25) the desired compound was isolated as a colorless oil (113.9 mg, 72%).

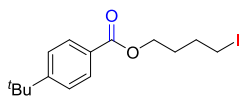
$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.93 (d, J = 8.1 Hz, 2H), 7.24 (d, J = 8.0 Hz, 2H), 4.33 (t, J = 6.2 Hz, 2H), 3.26 (t, J = 6.7 Hz, 2H), 2.41 (s, 3H), 2.05 – 1.95 (m, 2H), 1.94 – 1.83 (m, 2H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 166.61, 143.65, 129.58, 129.10, 127.45, 63.57, 30.13, 29.70, 21.68, 6.03.



4-Iodobutyl 4-ethylbenzoate (3eb)

Prepared from 1-ethyl-4-iodobenzene (74 μL , 0.5 mmol) and tetrahydrofuran (122 μL , 1.5 mmol). After purification by column chromatography (petroleum ether/EtOAc = 50:1, R_f = 0.25) the desired compound was isolated as a colorless oil (136.9 mg, 83%).

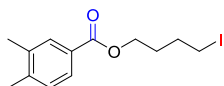
$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.95 (d, J = 8.2 Hz, 2H), 7.27 (d, J = 8.0 Hz, 2H), 4.34 (t, J = 6.2 Hz, 2H), 3.26 (t, J = 6.7 Hz, 2H), 2.71 (d, J = 7.6 Hz, 2H), 2.05 – 1.95 (m, 2H), 1.95 – 1.85 (m, 2H), 1.26 (t, J = 7.6 Hz, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 166.61, 149.85, 129.70, 127.92, 127.66, 63.56, 30.13, 29.70, 28.97, 15.27, 6.03. HRMS (ESI+): $\text{C}_{13}\text{H}_{17}\text{IO}_2$ $[\text{M}+\text{H}]^+$ found 333.0342, requires 333.0346 (1.2 ppm).



4-Iodobutyl 4-(*tert*-butyl)benzoate (3fb)

Prepared from 1-(*tert*-butyl)-4-iodobenzene (91 μ L, 0.5 mmol) and tetrahydrofuran (122 μ L, 1.5 mmol). After purification by column chromatography (petroleum ether/EtOAc = 50:1, Rf = 0.25) the desired compound was isolated as a colorless oil (155.4 mg, 86%).

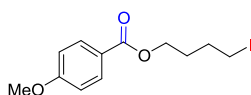
$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.97 (d, J = 8.4 Hz, 2H), 7.46 (d, J = 8.4 Hz, 2H), 4.34 (t, J = 6.2 Hz, 2H), 3.26 (t, J = 6.7 Hz, 2H), 2.06 – 1.95 (m, 2H), 1.95 – 1.84 (m, 2H), 1.34 (s, 9H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 166.56, 156.64, 129.43, 127.39, 125.36, 63.53, 35.09, 31.12, 30.14, 29.71, 6.02. **HRMS (ESI+):** $\text{C}_{15}\text{H}_{21}\text{IO}_2$ $[\text{M}+\text{H}]^+$ found 361.0678, requires 361.0659 (5.2 ppm).



4-Iodobutyl 3,4-dimethylbenzoate (3gb)

Prepared from 4-iodo-1,2-dimethylbenzene (71 μ L, 0.5 mmol) and tetrahydrofuran (122 μ L, 1.5 mmol). After purification by column chromatography (petroleum ether/EtOAc = 50:1, Rf = 0.25) the desired compound was isolated as a colorless solid (140.0 mg, 84%).

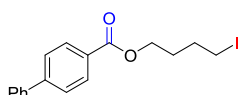
$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.80 (s, 1H), 7.76 (d, J = 7.9 Hz, 1H), 7.19 (d, J = 7.8 Hz, 1H), 4.32 (t, J = 6.2 Hz, 2H), 3.25 (t, J = 6.7 Hz, 2H), 2.31 (s, 6H), 1.99 (dq, J = 11.4, 6.5 Hz, 2H), 1.89 (dq, J = 12.2, 6.1 Hz, 2H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 166.80, 142.32, 136.73, 130.59, 129.67, 128.36, 127.12, 63.51, 30.14, 29.70, 19.99, 19.67, 5.97. **HRMS (ESI+):** $\text{C}_{13}\text{H}_{17}\text{IO}_2$ $[\text{M}+\text{Na}]^+$ found 355.0156, requires 355.0165 (2.5 ppm).



4-Iodobutyl 4-methoxybenzoate (3hb)

Prepared from 1-iodo-4-methoxybenzene (117.0 mg, 0.5 mmol) and tetrahydrofuran (122 μ L, 1.5 mmol). After purification by column chromatography (petroleum ether/EtOAc = 20:1, Rf = 0.20) the desired compound was isolated as a colorless oil (128.2 mg, 77%).

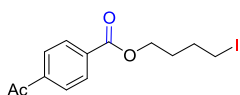
$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.97 (d, J = 8.9 Hz, 2H), 6.90 (d, J = 8.9 Hz, 2H), 4.29 (t, J = 6.2 Hz, 2H), 3.84 (s, 3H), 3.23 (t, J = 6.8 Hz, 2H), 2.01 – 1.81 (m, 4H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 166.25, 163.36, 131.57, 122.58, 113.62, 63.45, 55.45, 30.15, 29.72, 6.14.



4-Iodobutyl [1,1'-biphenyl]-4-carboxylate (3ib)

Prepared from 4-iodo-1,1'-biphenyl (142.9 mg, 0.5 mmol) and tetrahydrofuran (122 μ L, 1.5 mmol). After purification by column chromatography (petroleum ether/EtOAc = 50:1, Rf = 0.20) the desired compound was isolated as a colorless oil (91.7 mg, 49%).

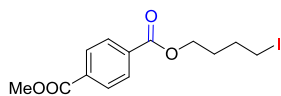
$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.11 (d, J = 8.3 Hz, 2H), 7.65 (dd, J = 16.7, 7.8 Hz, 4H), 7.48 (t, J = 7.5 Hz, 2H), 7.40 (t, J = 7.3 Hz, 1H), 4.38 (t, J = 6.2 Hz, 2H), 3.28 (t, J = 6.7 Hz, 2H), 2.07 – 1.98 (m, 2H), 1.92 (dq, J = 12.8, 6.4 Hz, 2H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 166.41, 145.72, 139.99, 130.09, 128.94, 128.17, 127.28, 127.08, 63.78, 30.15, 29.73, 5.92. **HRMS (ESI+):** $\text{C}_{17}\text{H}_{17}\text{IO}_2$ $[\text{M}+\text{Na}]^+$ found 403.0158, requires 403.0165 (1.7 ppm).



4-Iodobutyl 4-acetylbenzoate (3jb)

Prepared from 1-(4-iodophenyl)ethan-1-one (123.0 mg, 0.5 mmol) and tetrahydrofuran (122 μ L, 1.5 mmol). After purification by column chromatography (petroleum ether/EtOAc = 20:1, Rf = 0.25) the desired compound was isolated as a colorless oil (84.9 mg, 49%).

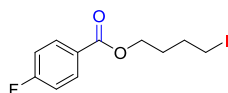
$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.09 (d, J = 8.3 Hz, 2H), 7.98 (d, J = 8.3 Hz, 2H), 4.35 (t, J = 6.2 Hz, 2H), 3.23 (t, J = 6.6 Hz, 2H), 2.62 (s, 3H), 2.00 – 1.84 (m, 4H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 197.40, 165.60, 140.27, 133.91, 129.78, 128.20, 64.23, 30.03, 29.59, 26.86, 5.80. **HRMS (ESI+):** $\text{C}_{13}\text{H}_{15}\text{IO}_3$ $[\text{M}+\text{H}]^+$ found 347.0141, requires 347.0139 (0.6 ppm).



4-Iodobutyl methyl terephthalate (3kb)

Prepared from 1-(4-iodophenyl)ethan-1-one (123.0 mg, 0.5 mmol) and tetrahydrofuran (122 μ L, 1.5 mmol). After purification by column chromatography (petroleum ether/EtOAc =20:1, Rf = 0.20) the desired compound was isolated as a colorless solid (76.0 mg, 42%).

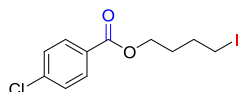
$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.13 – 8.07 (m, 4H), 4.37 (t, J = 6.1 Hz, 2H), 3.95 (s, 3H), 3.26 (t, J = 6.6 Hz, 2H), 2.03 – 1.88 (m, 4H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 166.26, 165.73, 133.99, 129.58, 129.53, 64.22, 52.45, 30.03, 29.61, 5.73. **HRMS (ESI+)**: $\text{C}_{13}\text{H}_{15}\text{IO}_4$ $[\text{M}+\text{Na}]^+$ found 384.9917, requires 384.9907 (–2.6 ppm). **GC-MS (EI, 70 ev)**: m/z (%) = 362.0 ($[\text{M}]^+$, 0), 235.2 (71), 163.1 (100), 149.1 (18), 135.1 (18).



4-Iodobutyl 4-fluorobenzoate (3lb)

Prepared from 1-fluoro-4-iodobenzene (59 μ L, 0.5 mmol) and tetrahydrofuran (122 μ L, 1.5 mmol). After purification by column chromatography (petroleum ether/EtOAc =50:1, Rf = 0.25) the desired compound was isolated as a colorless oil (148.9 mg, 93%).

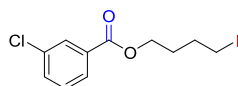
$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.09 – 8.02 (m, 2H), 7.15 – 7.08 (m, 2H), 4.34 (t, J = 6.2 Hz, 2H), 3.26 (t, J = 6.7 Hz, 2H), 1.99 (ddd, J = 13.3, 7.4, 3.9 Hz, 2H), 1.94 – 1.86 (m, 2H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 166.31 (d, J = 150.5 Hz), 164.53, 132.10 (d, J = 9.1 Hz), 126.46, 115.53 (d, J = 22.2 Hz), 63.89, 30.08, 29.66, 5.73. **HRMS (ESI+)**: $\text{C}_{11}\text{H}_{12}\text{FIO}_2$ $[\text{M}+\text{Na}]^+$ found 344.9755, requires 344.9758 (–0.9 ppm).



4-Iodobutyl 4-chlorobenzoate (3mb)

Prepared from 1-chloro-4-iodobenzene (119.0 mg, 0.5 mmol) and tetrahydrofuran (122 μ L, 1.5 mmol). After purification by column chromatography (petroleum ether/EtOAc =50:1, Rf = 0.25) the desired compound was isolated as a colorless oil (128.2 mg, 76%).

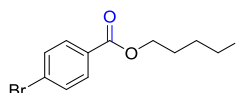
$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.00 – 7.94 (m, 2H), 7.45 – 7.40 (m, 2H), 4.35 (t, J = 6.2 Hz, 2H), 3.25 (t, J = 6.7 Hz, 2H), 2.04 – 1.95 (m, 2H), 1.91 (ddd, J = 9.3, 7.9, 5.0 Hz, 2H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 165.66, 139.45, 130.95, 128.74, 128.64, 64.01, 30.05, 29.62, 5.74.



4-Iodobutyl 3-chlorobenzoate (3nb)

Prepared from 1-chloro-3-iodobenzene (62 μ L, 0.5 mmol) and tetrahydrofuran (122 μ L, 1.5 mmol). After purification by column chromatography (petroleum ether/EtOAc =50:1, Rf = 0.25) the desired compound was isolated as a colorless oil (112.1 mg, 66%).

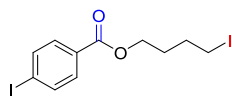
$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.01 (s, 1H), 7.92 (d, J = 7.7 Hz, 1H), 7.54 (d, J = 8.0 Hz, 1H), 7.39 (t, J = 7.9 Hz, 1H), 4.36 (t, J = 6.2 Hz, 2H), 3.26 (t, J = 6.6 Hz, 2H), 2.02 – 1.88 (m, 4H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 165.33, 134.56, 133.03, 131.91, 129.73, 129.65, 127.70, 64.19, 29.99, 29.60, 5.80.



4-Iodobutyl 4-bromobenzoate (3pb)

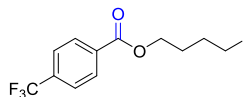
Prepared from 1-bromo-4-iodobenzene (141.4 mg, 0.5 mmol) and tetrahydrofuran (122 μ L, 1.5 mmol). After purification by column chromatography (petroleum ether/EtOAc =50:1, Rf = 0.25) the desired compound was isolated as a colorless oil (67.4 mg, 45%).

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.89 (d, J = 8.5 Hz, 2H), 7.59 (d, J = 8.5 Hz, 2H), 4.35 (dt, J = 10.1, 5.1 Hz, 2H), 3.48 (t, J = 6.4 Hz, 2H), 3.25 (t, J = 6.6 Hz, 2H), 2.04 – 1.83 (m, 2H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 165.80, 137.76, 131.75, 131.09, 131.00, 64.03, 30.05, 29.62, 5.73. **HRMS (ESI+)**: $\text{C}_{11}\text{H}_{12}\text{BrIO}_2$ $[\text{M}+\text{Na}]^+$ found 404.8956, requires 404.8958 (–0.5 ppm). **GC-MS (EI, 70 ev)**: m/z (%) = 381.9 ($[\text{M}]^+$, 0), 255.1 (58), 257.1 (58), 183.0 (100), 185.0 (98), 155.0 (35), 157.0 (34), 55.1 (63).



4-Iodobutyl 4-iodobenzoate (3pb')

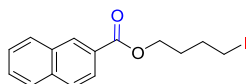
$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.81 (d, $J = 8.4$ Hz, 1H), 7.74 (d, $J = 8.5$ Hz, 1H), 4.35 (dt, $J = 10.1, 5.1$ Hz, 5H), 3.48 (t, $J = 6.4$ Hz, 2H), 3.25 (t, $J = 6.6$ Hz, 2H), 2.04 – 1.83 (m, 9H). **GC-MS (EI, 70 ev):** m/z (%) = 429.8 ($[\text{M}]^+$, 0), 303.1 (68), 248.0 (32), 231.0 (100), 128.0 (35), 127.0 (31).



4-Iodobutyl 4-(trifluoromethyl)benzoate (3qb)

Prepared from 1-iodo-4-(trifluoromethyl)benzene (75 μL , 0.5 mmol) and tetrahydrofuran (122 μL , 1.5 mmol). After purification by column chromatography (petroleum ether/EtOAc =50:1, $R_f = 0.25$) the desired compound was isolated as a colorless oil (78.0 mg, 42%).

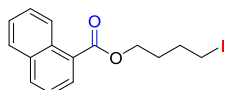
$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.15 (d, $J = 8.1$ Hz, 2H), 7.71 (d, $J = 8.3$ Hz, 2H), 4.39 (t, $J = 6.1$ Hz, 2H), 3.26 (t, $J = 6.6$ Hz, 2H), 2.03 – 1.88 (m, 4H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 165.32, 134.68, 134.36, 133.41, 129.98, 125.45 (d, $J = 4.0$ Hz), 124.97, 64.35, 30.02, 29.59, 5.64. **HRMS (ESI+):** $\text{C}_{11}\text{H}_{12}\text{F}_3\text{IO}_2$ $[\text{M}+\text{H}]^+$ found 372.9891, requires 372.9907 (-1.1 ppm). **GC-MS (EI, 70 ev):** m/z (%) = 371.9 ($[\text{M}]^+$, 0), 245.2 (62), 173.1 (100), 145.1 (55), 55.1 (45).



4-Iodobutyl 2-naphthoate (3rb)

Prepared from 2-iodonaphthalene (127.0 mg, 0.5 mmol) and tetrahydrofuran (122 μL , 1.5 mmol). After purification by column chromatography (petroleum ether/EtOAc =50:1, $R_f = 0.25$) the desired compound was isolated as a white solid (136.2 mg, 77%).

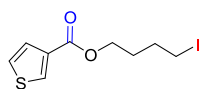
$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.61 (s, 1H), 8.06 (dd, $J = 8.6, 1.3$ Hz, 1H), 7.97 (d, $J = 8.0$ Hz, 1H), 7.89 (d, $J = 8.6$ Hz, 2H), 7.58 (ddd, $J = 18.1, 10.9, 3.8$ Hz, 2H), 4.41 (t, $J = 6.1$ Hz, 2H), 3.29 (t, $J = 6.7$ Hz, 2H), 2.08 – 1.93 (m, 4H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 166.71, 135.54, 132.48, 131.07, 129.37, 128.29, 128.20, 127.78, 127.42, 126.69, 125.19, 63.94, 30.14, 29.72, 6.06.



4-Iodobutyl 1-naphthoate (3sb)

Prepared from 1-iodonaphthalene (75 μL , 0.5 mmol) and tetrahydrofuran (122 μL , 1.5 mmol). After purification by column chromatography (petroleum ether/EtOAc =50:1, $R_f = 0.25$) the desired compound was isolated as a red-brown oil (125.4 mg, 72%).

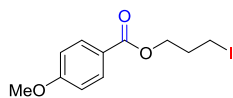
$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.91 (d, $J = 8.6$ Hz, 1H), 8.18 (d, $J = 7.2$ Hz, 1H), 8.03 (d, $J = 8.2$ Hz, 1H), 7.89 (d, $J = 8.1$ Hz, 1H), 7.63 (dd, $J = 11.2, 4.2$ Hz, 1H), 7.57 – 7.48 (m, 2H), 4.45 (t, $J = 6.1$ Hz, 2H), 3.28 (t, $J = 6.6$ Hz, 2H), 2.08 – 2.01 (m, 2H), 2.00 – 1.93 (m, 2H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 167.48, 133.85, 133.43, 131.35, 130.16, 128.57, 127.81, 127.09, 126.24, 125.75, 124.50, 63.84, 30.18, 29.74, 5.99. **HRMS (ESI+):** $\text{C}_{15}\text{H}_{15}\text{IO}_2$ $[\text{M}+\text{H}]^+$ found 355.0172, requires 355.0189 (-4.8 ppm).



4-Iodobutyl thiophene-3-carboxylate (3tb)

Prepared from 3-iodothiophene (52 μL , 0.5 mmol) and tetrahydrofuran (122 μL , 1.5 mmol). After purification by column chromatography (petroleum ether/EtOAc =50:1, $R_f = 0.25$) the desired compound was isolated as a colorless oil (90.7 mg, 62%).

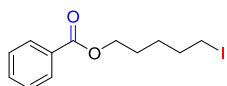
$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.12 – 8.08 (m, 1H), 7.51 (d, $J = 5.0$ Hz, 1H), 7.30 (dd, $J = 5.0, 3.1$ Hz, 1H), 4.29 (t, $J = 6.2$ Hz, 2H), 3.24 (t, $J = 6.7$ Hz, 2H), 2.01 – 1.93 (m, 2H), 1.86 (dq, $J = 12.3, 6.1$ Hz, 2H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 162.66, 133.64, 132.70, 127.87, 126.07, 63.47, 30.10, 29.67, 5.93. $\text{C}_9\text{H}_{11}\text{IO}_2\text{S}$ $[\text{M}+\text{Na}]^+$ found 332.9419, requires 332.9417 (-2.0 ppm).



3-Iodopropyl 4-methoxybenzoate (3ha)

Prepared from 1-iodo-4-methoxybenzene (117.0 mg, 0.5 mmol) and oxetane (98 μ L, 1.5 mmol). After purification by column chromatography (petroleum ether/EtOAc =20:1, Rf = 0.20) the desired compound was isolated as a colorless oil (65.6 mg, 41%).

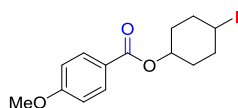
$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 7.99 (d, J = 8.9 Hz, 2H), 6.92 (d, J = 8.8 Hz, 2H), 4.37 (t, J = 6.0 Hz, 2H), 3.86 (s, 3H), 3.30 (t, J = 6.9 Hz, 2H), 2.28 (t, J = 6.4 Hz, 2H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 166.12, 163.46, 131.62, 122.40, 113.65, 64.24, 55.45, 32.62, 1.54.



5-Iodopentyl benzoate (3ac)

Prepared from iodobenzene (57 μ L, 0.5 mmol) and tetrahydro-2H-pyran (147 μ L, 1.5 mmol). After purification by column chromatography (petroleum ether/EtOAc =50:1, Rf = 0.25) the desired compound was isolated as a colorless oil (109.2 mg, 68%).

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.08 – 8.01 (m, 2H), 7.55 (t, J = 7.4 Hz, 1H), 7.44 (t, J = 7.6 Hz, 2H), 4.32 (t, J = 6.5 Hz, 2H), 3.21 (t, J = 6.9 Hz, 2H), 1.94 – 1.85 (m, 2H), 1.83 – 1.75 (m, 2H), 1.62 – 1.51 (m, 2H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 166.55, 132.88, 130.36, 129.54, 128.35, 64.59, 33.02, 27.70, 27.05, 6.47. GC-MS (EI, 70 ev): m/z (%) = 318.0 ($[\text{M}]^+$, 0), 192.2 (21), 123.1 (28), 105.1 (100), 77.1 (33), 69.1 (42).

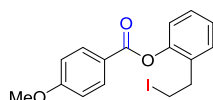


4-Iodocyclohexyl 4-methoxybenzoate (3ad)

Prepared from 1-iodo-4-methoxybenzene (117.0 mg, 0.5 mmol) and (1s,4s)-7-oxabicyclo[2.2.1]heptane (152 μ L, 1.5 mmol). After purification by column chromatography (petroleum ether/EtOAc =20:1, Rf = 0.20) the desired compound was isolated as a colorless oil (123.7 mg, 68%).

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.02 (d, J = 8.9 Hz, 2H), 6.94 (d, J = 8.9 Hz, 2H), 5.17 (tt, J = 5.9, 2.9 Hz, 1H), 4.49 (ddd, J = 11.5, 8.2, 3.2 Hz, 1H), 3.87 (s, 3H), 2.35 – 2.20 (m, 2H), 2.11 – 1.97 (m, 4H), 1.93 – 1.76 (m, 2H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 165.59, 163.40, 131.60, 122.99, 113.63, 69.59, 55.44, 35.03, 32.19, 30.51.

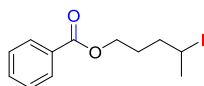
HRMS (ESI+): $\text{C}_{14}\text{H}_{17}\text{IO}_3$ $[\text{M}+\text{H}]^+$ found 361.0306, requires 361.0295 (-3.0 ppm).



2-(2-Iodoethyl)phenyl 4-methoxybenzoate (3ae)

Prepared from 1-iodo-4-methoxybenzene (117.0 mg, 0.5 mmol) and 2,3-dihydrobenzofuran (170 μ L, 1.5 mmol). After purification by column chromatography (petroleum ether/EtOAc =20:1, Rf = 0.15) the desired compound was isolated as a colorless oil (70.3 mg, 37%).

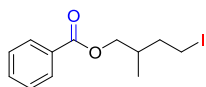
$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.17 (d, J = 8.9 Hz, 2H), 7.33 (ddd, J = 14.4, 8.1, 3.9 Hz, 2H), 7.25 (d, J = 6.9 Hz, 1H), 7.19 (d, J = 8.0 Hz, 1H), 7.01 (d, J = 8.9 Hz, 2H), 3.91 (s, 3H), 3.35 (t, J = 7.8 Hz, 2H), 3.16 (t, J = 7.7 Hz, 2H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 164.70, 164.10, 149.16, 132.67, 132.33, 130.31, 128.23, 126.18, 122.89, 121.42, 114.04, 55.58, 35.12, 3.63. HRMS (ESI+): $\text{C}_{16}\text{H}_{15}\text{IO}_3$ $[\text{M}+\text{H}]^+$ found 383.0143, requires 383.0139 (-1.0 ppm).



4-Iodopentyl benzoate (3af)

Prepared from iodobenzene (57 μ L, 0.5 mmol) and 2-methyltetrahydrofuran (150 μ L, 1.5 mmol). After purification by column chromatography (petroleum ether/EtOAc =50:1, Rf = 0.25) the desired compound was isolated as a colorless oil (141.2 mg, 89%).

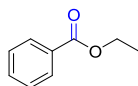
$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.04 (d, J = 7.4 Hz, 2H), 7.57 (t, J = 7.3 Hz, 1H), 7.45 (t, J = 7.7 Hz, 2H), 4.42 – 4.30 (m, 2H), 4.23 (dt, J = 14.7, 6.9 Hz, 1H), 2.14 – 1.74 (m, 7H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 166.54, 132.95, 130.25, 129.56, 128.38, 63.97, 39.37, 29.14, 29.03, 28.97.



4-Iodo-2-methylbutyl benzoate (3ag)

Prepared from iodobenzene (57 μL , 0.5 mmol) and 3-methyltetrahydrofuran (129.0 mg, 1.5 mmol). After purification by column chromatography (petroleum ether/EtOAc =50:1, R_f = 0.25) the desired compound was isolated as a colorless oil (108.9 mg, 68%).

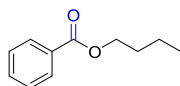
$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.07 – 8.01 (m, 2H), 7.59 – 7.52 (m, 1H), 7.48 – 7.40 (m, 2H), 4.24 – 4.15 (m, 2H), 3.35 – 3.18 (m, 2H), 2.18 – 2.00 (m, 2H), 1.84 – 1.74 (m, 1H), 1.07 (d, J = 6.2 Hz, 1H), 1.04 (d, J = 6.7 Hz, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 166.48, 132.97, 130.23, 129.56, 128.40, 68.65, 37.44, 33.78, 16.15, 3.86. **HRMS (ESI+):** $\text{C}_{12}\text{H}_{15}\text{IO}_2$ [$\text{M}+\text{Na}$] $^+$ found 341.0009, requires 341.0012 (–0.9 ppm).



Methyl benzoate (3ah)

Prepared from iodobenzene (57 μL , 0.5 mmol) and ethoxyethane (78 μL , 1.5 mmol). After purification by column chromatography (petroleum ether/EtOAc =50:1, R_f = 0.25) the desired compound was isolated as a colorless oil (48.6 mg, 65%).

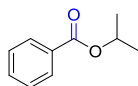
$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.05 (d, J = 7.3 Hz, 2H), 7.55 (t, J = 7.4 Hz, 1H), 7.44 (t, J = 7.6 Hz, 2H), 4.38 (q, J = 7.1 Hz, 2H), 1.40 (t, J = 7.1 Hz, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 166.63, 132.78, 130.52, 129.52, 128.29, 60.93, 14.32.



Butyl benzoate (3ai)

Prepared from iodobenzene (57 μL , 0.5 mmol) and 1-butoxybutane (253 μL , 1.5 mmol). After purification by column chromatography (petroleum ether/EtOAc =50:1, R_f = 0.25) the desired compound was isolated as a colorless oil (42.8 mg, 48%).

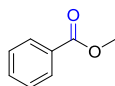
$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.13 – 8.05 (m, 2H), 7.59 (dd, J = 10.5, 4.2 Hz, 1H), 7.47 (dd, J = 10.6, 4.7 Hz, 2H), 4.37 (t, J = 6.6 Hz, 2H), 1.80 (dt, J = 14.5, 6.7 Hz, 2H), 1.58 – 1.47 (m, 2H), 1.02 (dd, J = 9.8, 5.0 Hz, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 166.66, 132.76, 130.54, 129.51, 128.29, 64.80, 30.78, 19.27, 13.74.



Isopropyl benzoate (3aj)

Prepared from iodobenzene (57 μL , 0.5 mmol) and 2-isopropoxypropane (202 μL , 1.5 mmol). After purification by column chromatography (petroleum ether/EtOAc =50:1, R_f = 0.25) the desired compound was isolated as a colorless oil (51.1 mg, 62%).

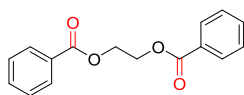
$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.08 (dd, J = 5.2, 3.3 Hz, 2H), 7.62 – 7.56 (m, 1H), 7.47 (dd, J = 10.6, 4.7 Hz, 2H), 5.30 (dt, J = 12.5, 6.3 Hz, 1H), 1.42 (d, J = 6.3 Hz, 6H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 166.11, 132.67, 130.93, 129.49, 128.24, 68.33, 21.95.



Methyl benzoate (3al)

Prepared from iodobenzene (57 μL , 0.5 mmol) and (methoxymethyl)benzene (195 μL , 1.5 mmol). After purification by column chromatography (petroleum ether/EtOAc =50:1, R_f = 0.25) the desired compound was isolated as a colorless oil (16.6 mg, 24%).

$^1\text{H NMR}$ (400 MHz, CDCl_3) δ 8.07 – 8.00 (m, 2H), 7.59 – 7.52 (m, 1H), 7.44 (t, J = 7.7 Hz, 2H), 3.92 (s, 3H). $^{13}\text{C NMR}$ (101 MHz, CDCl_3) δ 167.10, 132.89, 130.18, 129.57, 128.35, 52.08.



Ethane-1,2-diyl dibenzoate

¹H NMR (400 MHz, CDCl₃) δ 8.14 – 8.02 (m, 2H), 7.61 – 7.51 (m, 1H), 7.44 (t, *J* = 7.7 Hz, 2H), 4.67 (s, 2H).

¹³C NMR (101 MHz, CDCl₃) δ 166.38, 133.14, 129.83, 129.71, 128.41, 62.74.