Nickel-Catalyzed Carbonylative Synthesis of Functionalized Alkyl Iodides

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

xiao-feng.wu@catalysis.de

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

non-noble metal catalysis
ether as the nucleophile
CO-free carbonylation
functionalized alkyl iodides
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; Diduk 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 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...
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 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, other bpy-based N-ligands including phenanthroline and terpyridine failed to catalyze this transformation (see details in Table S3).

### Table 1. Optimization of the Reaction Conditions

| Entry | [Ni]  | Ligand | Solvent | Temperature °C | Yield (%) a,b |
|-------|-------|--------|---------|----------------|---------------|
| 1     | NiCl₂ | dtbbpy | Toluene | 120            | 52            |
| 2     | NiCl₂ | dtbbpy | Toluene | 130            | 45            |
| 3     | NiCl₂ | dtbbpy | Toluene | 140            | 29            |
| 4     | NiBr₂ | 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 | PCy₃  | Toluene | 120            | 48            |
| 9     | Ni(OTf)₂ | PPh₃  | Toluene | 120            | 30            |
| 10    | Ni(OTf)₂ | dtbbpy | Toluene | 120            | 64            |
| 11    | Ni(OTf)₂ | dtbbpy | Xylene  | 120            | 57            |
| 12    | Ni(OTf)₂ | dtbbpy | Chlorobenzene | 120 | 89 |
| 13    | Ni(OTf)₂ | dtbbpy | Cyclohexane | 120 | 42 |
| 14    | Ni(OTf)₂ | dtbbpy | Chlorobenzene | 120 | 95 (93) |
| 15    | Ni(OTf)₂ | dtbbpy | Chlorobenzene | 120 | 32 |
| 16    | Ni(OTf)₂ | dtbbpy | Chlorobenzene | 120 | 41 |

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 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 carbylonylation 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 carbenes 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 Mo(CO)$_6$ revealed that 0.5 equivalent of Mo(CO)$_6$ is optimal and the product 3ab was produced in 64% yield (Table 1, entry 10). Increasing the amount of Mo(CO)$_6$ leads to lower yields, which might be caused by the formation of catalytically nonactive Ni(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 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 Mo(CO)$_6$, other transition metal carbonyl complexes such as Fe$_3$(CO)$_{12}$ and Cr(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 Mo(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 3ob, 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, 3mb). 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 C(sp$^3$)-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.
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,
$$\text{Ni(OTf)}_2 (5 \text{ mol } \%) \quad \text{dtbbpy (5 mol \%)}$$
$$\text{Mo(CO)}_6 (0.5 \text{ equiv})$$
$$\text{PhCl (2 mL), } 120^\circ \text{C, } 16 \text{ h}$$

**1** + **2** \to **3**

- **cyclic ether**
  - **2a**
  - **3ha (21%)**
  - **3ha' (41%)**
  - **2c**
  - **3ac (68%)**
  - **2d**
  - **3hd (68%)**
  - **2e**
  - **3ae (37%)**
  - **2f**
  - **3af (80%)**
  - **3af' (9%)**
  - **2g**
  - **3ag (45%)**
  - **3ag' (23%)**

- **acyclic ether**
  - **2h**
  - **3ah (65%)**
  - **2i**
  - **3ai (48%)**
  - **2j**
  - **3aj (62%)**
  - **2k**
  - **3ak (44%)**
  - **2l**
  - **3al (24%)**
  - **2k**
  - **3ak' (26%)**
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 benzyl 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.
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.

ACKNOWLEDGMENTS
The authors thank financial supports from NSFC (21472174, 21772177) and Zhejiang Natural Science Fund for Distinguished Young Scholars (LR16B020002). The publication of this article was funded by the Open Access Fund of the Leibniz Association.

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.

Received: September 3, 2018
Revised: September 22, 2018
Accepted: September 27, 2018
Published: October 26, 2018

REFERENCES
Christensen, S.H., Holm, T., and Madsen, R. (2014). Ring-opening of cyclic ethers with carbon–carbon bond formation by Grignard reagents. Tetrahedron 70, 4942–4946.

DeGraw, J.I., Colwell, W.T., Crase, J., Smith, R.L., Piper, J.R., Waud, W.R., and Sirotnak, F.M. (1997). Analogues of methotrexate in rheumatoid arthritis. 1. Effects of 10-deazaaminopterin analogues on type II collagen-induced arthritis in mice. J. Med. Chem. 40, 370–377.

Didiuk, M.T., Johannes, C.W., Morken, J.P., and Hoveyda, A.H. (1999). Enantio-, diastereo-, and regioselective zirconium-catalyzed carbomagnesation of cyclic ethers with higher alkyls of magnesium: utility in synthesis and mechanistic implications. J. Am. Chem. Soc. 117, 7097–7104.

Frei, P., Jones, D.H., Kay, S.T., McLellan, J.A., Johnston, B.F., Kennedy, A.R., and Tomkinson, N.C.O. (2018). Regioselective reaction of heterocyclic N-oxides, an acyl chloride, and cyclic thiocarbonyls. J. Org. Chem. 83, 1510–1517.

Gabriele, B., Mancuso, R., and Salerno, G. (2012). Oxidative carbonylation as a powerful tool for the direct synthesis of carbonylated heterocycles. Eur. J. Org. Chem. 2012, 6825–6839.

Getzler, Y.D.Y.L., Kundnani, V., Lobkovsky, E.B., and Coates, G.W. (2004). Catalytic carbonylation of ß-lactones to succinic anhydrides. J. Am. Chem. Soc. 126, 6842–6843.

Jones, D.H., Kay, S.T., McLellan, J.A., Kennedy, A.R., and Tomkinson, N.C.O. (2017). Regioselective three-component reaction of pyridine N-oxides, acyl chlorides, and cyclic ethers. Org. Lett. 19, 3512–3515.
Kinney, R.G., Tjutrins, J., Torres, G.M., Liu, N.J., Kulkarni, O., and Arndtsen, B.A. (2018). A general approach to intermolecular carbonylation of arene C-H bonds to ketones through catalytic aryl triflate formation. Nat. Chem. 10, 193–199.

Kumbhalkar, M.D., Buchanan, J.S., Huber, G.W., and Dumesic, J.A. (2017). Ring opening of biomass-derived cyclic ethers to dienes over silica/alumina. ACS Catal. 7, 5248–5256.

Liu, H., Wei, J., Qiao, Z., Fu, Y., and Jiang, X. (2014). Palladium-catalyzed intramolecular reductive cross-coupling of Csp2–Csp3 bond formation. Chem. Eur. J. 20, 8308–8313.

Lübcke, M., Yuan, W., and Szabó, K.J. (2017). Trifluoromethylthiolation-based bifunctionalization of diazocarbonyl compounds by rhodium catalysis. Org. Lett. 19, 4548–4551.

Morimoto, T., and Kako, K. (2004). Evolution of carbonylation catalysis: no need for carbon monoxide. Angew. Chem. Int. Ed. 43, 5580–5588.

Mukherjee, D., Osseili, H., Truong, K.-N., Spaniol, T.P., and Okuda, J. (2017). Ring-opening of cyclic ethers by aluminum hydridotriphenylborate. Chem. Commun. (Camb.) 53, 3493–3496.

Ohshita, J., Izumi, Y., Lu, Z., Ikadai, J., and Kunai, A. (2006). Ring-opening reactions of cyclic ethers with diodo- and dibromodimethylsilane equivalents. J. Organomet. Chem. 691, 1907–1911.

Peng, J.-B., and Wu, X.-F. (2018). Ligand- and solvent-controlled regio- and chemodivergent carbonylative reactions. Angew. Chem. Int. Ed. 57, 1152–1160.

Peng, J.-B., Qi, X., and Wu, X.-F. (2017). Recent achievements in carbonylation reactions: a personal account. Synlett 28, 175–194.

Quesnel, J.S., and Arndtsen, B.A. (2013). A palladium-catalyzed carbonylation approach to acid chloride synthesis. J. Am. Chem. Soc. 135, 16841–16844.

Seki, Y., Murai, S., Yamamoto, I., and Sonoda, N. (1977). Co2(CO)8 catalyzed reactions of cyclic ethers with hydrosilanes and carbon monoxide. Angew. Chem. Int. Ed. 16, 789.

Tjutrins, J., and Arndtsen, B.A. (2016). A palladium-catalyzed synthesis of (hetero)aryl-substituted imidazoles from aryl halides, imines and carbon monoxide. Chem. Sci. 8, 1002–1007.

Torres, G.M., Quesnel, J.S., Bijou, D., and Arndtsen, B.A. (2016). From aryl iodides to 1,3-dipoles: design and mechanism of a palladium catalyzed multicomponent synthesis of pyrroles. J. Am. Chem. Soc. 138, 7315–7324.

Trewick, S.C., Henshaw, T.F., Hausinger, R.P., Lindahl, T., and Sedgwick, B. (2002). Oxidative demethylation by Escherichia coli AkrB directly reverts DNA base damage. Nature 419, 174–178.

Tsui, Y., Kobayashi, M., Okuda, F., and Watanabe, Y. (1989). Cobalt catalysed ring-opening carbonylation of cyclic ethers using N-(trimethylsilyl)amines. J. Chem. Soc. Chem. Commun. 1253–1254.

Watanabe, Y., Nishiyama, K., Zhang, K., Okuda, F., Kondo, T., and Tsui, Y. (1994). Co2(CO)8 catalyzed ring-opening carbonylation of cyclic ethers using N-silylamines. Bull. Chem. Soc. Jpn. 67, 879–882.

Wu, X.-F. (2016). Palladium-catalyzed carbonylative transformation of aryl chlorides and aryl tosylates. RSC Adv. 6, 83831–83837.

Wu, F.-P., Peng, J.-B., Meng, L.-S., Qi, X., and Wu, X.-F. (2017). Palladium-catalyzed ligand-controlled selective synthesis of aldehydes and acids from aryl halides and formic acid. ChemCatChem 9, 3121–3124.

Wuts, P.G.M., and Greene, T.W. (2014). Greene’s Protective Groups in Organic Synthesis, Fifth Edition (John Wiley & Sons Inc).
Supplemental Information

Nickel-Catalyzed Carbonylative Synthesis
of Functionalized Alkyl Iodides

Jin-Bao Peng, Fu-Peng Wu, Cong Xu, Xinxin Qi, Jun Ying, and Xiao-Feng Wu
Table S1. Screening of the temperature, related to Table 1.

![Chemical structure]

| 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\textsubscript{2} (5 mol%), dtbbpy (5 mol%), Mo(CO)\textsubscript{6} (1 equiv), toluene (2 mL), x °C, 16 h.

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

| Entry | Catal.      | Yield (%) |
|-------|-------------|-----------|
| 1     | NiCl\textsubscript{2} | 52        |
| 2     | NiBr\textsubscript{2} | 57        |
| 3     | NiI\textsubscript{2} | 33        |
| 4     | NiCl\textsubscript{2}•glyme | 57        |
| 5     | Ni(acac)\textsubscript{2} | 30        |
| 6     | Ni(OTf)\textsubscript{2} | 58        |
| 7     | without Ni | 0         |

[a] Reaction conditions: Iodobenzene (0.5 mmol), THF (2 equiv), [Ni] (5 mol%), dtbbpy (5 mol%), Mo(CO)\textsubscript{6} (1 equiv), toluene (2 mL), 120 °C, 16 h.
Table S3. Screening of the ligands, related to Table 1.

| Entry | Ligand      | Yield (%) |
|-------|-------------|-----------|
| 1     | PCy₃        | 48        |
| 2     | dppp        | 0         |
| 3     | BuPAd₂      | 14        |
| 4     | IPr•HCl     | 29        |
| 5     | PPh₃        | 30        |
| 6     | (4-Tolyl)₃P | 47        |
| 7     | t′Bu₃P•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     | Toluene | 60        |
| 4     | 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 (%)<sup>[a]</sup> |
|-------|-----------|-----------------|
| 1     | Mo(CO)<sub>6</sub> | 95              |
| 2     | Fe<sub>3</sub>(CO)<sub>12</sub> | 32              |
| 3     | Co<sub>2</sub>(CO)<sub>8</sub> | 0               |
| 4     | Cr(CO)<sub>6</sub> | 41              |
| 5     | W(CO)<sub>6</sub> | 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)<sub>2</sub> (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)<sub>2</sub> (5 mol%), dtbbpy (5 mol%), Mo(CO)<sub>6</sub> (0.5 equiv.), chlorobenzene (2 mL), 120 °C, 16 h.
Copy of $^1$H and $^{13}$C NMR Spectra of Products

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

Figure S2. $^{13}$C NMR spectrum of 3ab, related to Figure 1.
Figure S3. $^1$H NMR spectrum of 3bb, related to Figure 1.

Figure S4. $^{13}$C NMR spectrum of 3bb, related to Figure 1.
Figure S5. $^1$H NMR spectrum of 3cb, related to Figure 1.

Figure S6. $^{13}$C NMR spectrum of 3cb, related to Figure 1.
Figure S7. $^1$H NMR spectrum of 3db, related to Figure 1.

Figure S8. $^{13}$C NMR spectrum of 3db, related to Figure 1.
Figure S9. $^1$H NMR spectrum of 3eb, related to Figure 1.

Figure S10. $^{13}$C NMR spectrum of 3eb, related to Figure 1.
Figure S11. $^1$H NMR spectrum of 3fb, related to Figure 1.

Figure S12. $^{13}$C NMR spectrum of 3fb, related to Figure 1.
Figure S13. $^1$H NMR spectrum of 3gb, related to Figure 1.

Figure S14. $^{13}$C NMR spectrum of 3gb, related to Figure 1.
Figure S15. $^1$H NMR spectrum of 3hb, related to Figure 1.

Figure S16. $^{13}$C NMR spectrum of 3hb, related to Figure 1.
Figure S17. $^1$H NMR spectrum of 3ib, related to Figure 1.

Figure S18. $^{13}$C NMR spectrum of 3ib, related to Figure 1.
Figure S19. $^1$H NMR spectrum of 3jb, related to Figure 1.

Figure S20. $^{13}$C NMR spectrum of 3jb, related to Figure 1.
Figure S21. $^1$H NMR spectrum of 3kb, related to Figure 1.

Figure S22. $^{13}$C NMR spectrum of 3kb, related to Figure 1.
Figure S23. $^1$H NMR spectrum of 3lb, related to Figure 1.

Figure S24. $^{13}$C NMR spectrum of 3lb, related to Figure 1.
Figure S25. $^1$H NMR spectrum of 3mb, related to Figure 1.

Figure S26. $^{13}$C NMR spectrum of 3mb, related to Figure 1.
Figure S27. $^1$H NMR spectrum of 3nb, related to Figure 1.

Figure S28. $^{13}$C NMR spectrum of 3nb, related to Figure 1.
Figure S29. $^1$H NMR spectrum of 3pb, related to Figure 1.

Figure S30. $^{13}$C NMR spectrum of 3pb, related to Figure 1.
Figure S31. $^1$H NMR spectrum of 3qb, related to Figure 1.

Figure S32. $^{13}$C NMR spectrum of 3qb, related to Figure 1.
Figure S33. $^1$H NMR spectrum of 3rb, related to Figure 1.

Figure S34. $^{13}$C NMR spectrum of 3rb, related to Figure 1.
Figure S35. $^1$H NMR spectrum of 3sb, related to Figure 1.

Figure S36. $^{13}$C NMR spectrum of 3sb, related to Figure 1.
Figure S37. $^1$H NMR spectrum of 3ha, related to Figure 2.

Figure S38. $^{13}$C NMR spectrum of 3ha, related to Figure 2.
Figure S39. $^1$H NMR spectrum of 3ac, related to Figure 2.

Figure S40. $^{13}$C NMR spectrum of 3ac, related to Figure 2.
Figure S41. $^1$H NMR spectrum of 3hd, related to Figure 2.

Figure S42. $^{13}$C NMR spectrum of 3hd, related to Figure 2.
Figure S43. $^1$H NMR spectrum of 3ae, related to Figure 2.

Figure S44. $^{13}$C NMR spectrum of 3ae, related to Figure 2.
Figure S45. $^1$H NMR spectrum of 3af + 3af', related to Figure 2.

Figure S46. $^{13}$C NMR spectrum of 3af + 3af', related to Figure 2.
Figure S47. $^1$H NMR spectrum of 3ag + 3ag’, related to Figure 2.

Figure S48. $^{13}$C NMR spectrum of 3ag + 3ag’, related to Figure 2.
Figure S49. $^1$H NMR spectrum of 3ah, related to Figure 2.

Figure S50. $^{13}$C NMR spectrum of 3ah, related to Figure 2.
Figure S51. $^1$H NMR spectrum of 3ai, related to Figure 2.

Figure S52. $^{13}$C NMR spectrum of 3ai, related to Figure 2.
Figure S53. $^1$H NMR spectrum of 3aj, related to Figure 2.

Figure S54. $^{13}$C NMR spectrum of 3aj, related to Figure 2.
Figure S55. $^1$H NMR spectrum of 3ak + 3ak', related to Figure 2.

Figure S56. $^{13}$C NMR spectrum of 3ak + 3ak', related to Figure 2.
Figure S57. $^1$H NMR spectrum of 3al, related to Figure 2.

Figure S58. $^{13}$C NMR spectrum of 3al, related to Figure 2.
Figure S59. $^1$H 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. $^1$H 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$_3$ ($^1$H NMR $\delta$ 7.26, $^{13}$C NMR $\delta$ 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

Ni(OTf)$_2$ (8.9 mg 5 mol%), dtbbpy (6.7 mg, 5 mol%) and Mo(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 $\mu$L, 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, Rf = 0.25) the desired compound was isolated as a colorless oil (142.8 mg, 93%).

1H NMR (400 MHz, CDCl3) 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).

13C NMR (101 MHz, CDCl3) 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, Rf = 0.25) the desired compound was isolated as a colorless oil (111.9 mg, 70%).

1H NMR (400 MHz, CDCl3) 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).

13C NMR (101 MHz, CDCl3) 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+): C12H15IO2 [M+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, Rf = 0.25) the desired compound was isolated as a colorless oil (139.0 mg, 88%).

1H NMR (400 MHz, CDCl3) δ 7.91 (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).

13C NMR (101 MHz, CDCl3) 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+): C12H15IO2 [M+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, Rf = 0.25) the desired compound was isolated as a colorless oil (113.9 mg, 72%).

1H NMR (400 MHz, CDCl3) 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).

13C NMR (101 MHz, CDCl3) δ 166.61, 143.65, 129.58, 129.10, 127.45, 63.57, 30.13, 29.70, 21.68, 6.03.

HRMS (ESI+): C13H17IO2 [M+H]+ found 333.0342, requires 333.0346 (1.2 ppm).

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, Rf = 0.25) the desired compound was isolated as a colorless oil (136.9 mg, 83%).

1H NMR (400 MHz, CDCl3) 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), 1.94 – 1.83 (m, 2H).

13C NMR (101 MHz, CDCl3) 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+): C13H17IO2 [M+H]+ found 333.0342, requires 333.0346 (1.2 ppm).
**4-Iodobutyl 4-(tert-butyl)benzoate (3b)**
Prepared from 1-(tert-butyl)-4-iodobenzene (91 μL, 0.5 mmol) and tetrahydrofuran (122 μL, 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%).

$^1$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).

$^{13}$C NMR (101 MHz, CDCl$_3$) δ 166.40, 165.60, 140.27, 131.57, 122.58, 113.62, 63.45, 55.45, 30.15, 29.72, 6.14.

**HRMS (ESI+):** $C_{13}H_{21}O_2$ [M+Na]$^+$ found 355.0165, requires 355.0156 (2.5 ppm).

**4-Iodobutyl 3,4-dimethylbenzoate (3gb)**
Prepared from 4-ido-1,2-dimethylbenzene (71 μL, 0.5 mmol) and tetrahydrofuran (122 μL, 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, 77%).

$^1$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), 1.89 (dq, J = 12.2, 6.1 Hz, 2H).

$^{13}$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+):** $C_{13}H_{21}O_2$ [M+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 μL, 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%).

$^1$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).

$^{13}$C NMR (101 MHz, CDCl$_3$) δ 167.90, 167.01, 145.72, 139.99, 130.09, 128.94, 128.17, 127.28, 127.08, 113.62, 63.45, 55.45, 30.15, 29.72, 6.14.

**HRMS (ESI+):** $C_{17}H_{17}O_3$ [M+Na]$^+$ found 403.0158, requires 403.0165 (1.7 ppm).

**4-Iodobutyl [1,1’-biphenyl]-4-carboxylate (3ib)**
Prepared from 4-iodo-1,1'-biphenyl (142.9 mg, 0.5 mmol) and tetrahydrofuran (122 μL, 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%).

$^1$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).

$^{13}$C NMR (101 MHz, CDCl$_3$) δ 166.41, 145.72, 139.99, 130.09, 128.94, 128.17, 127.28, 127.08, 113.62, 63.45, 55.45, 30.15, 29.73, 5.92.

**HRMS (ESI+):** $C_{17}H_{17}O_2$ [M+Na]$^+$ found 403.0158, requires 403.0165 (1.7 ppm).

**4-Iodobutyl 4-acetylenzoate (3jb)**
Prepared from 1-(4-iodophenylethan-1-one (123.0 mg, 0.5 mmol) and tetrahydrofuran (122 μL, 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%).

$^1$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).

$^{13}$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+):** $C_{17}H_{17}O_2$ [M+Na]$^+$ 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 μL, 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%).

\[ \text{H NMR} (400 MHz, CDCl}_3 \delta 8.13 – 8.07 (m, 4H), 4.37 (t, J = 6.1 Hz, 2H), 3.95 (s, 3H), 3.26 (t, J = 6.6 Hz, 2H), 2.03 – 1.88 (m, 4H). \]

\[ \text{C NMR} (101 MHz, CDCl}_3 \delta 166.26, 165.73, 133.99, 129.58, 129.53, 64.22, 52.45, 30.03, 29.61, 5.73. \]

\[ \text{HRMS (ESI+): C}_{13}H_{15}IO_4 [M+Na]^+ \text{ found 384.9917, requires 384.9907 (−0.9 ppm).} \]}

4-Iodobutyl 4-fluorobenzoate (3lb)
Prepared from 1-fluoro-4-iodobenzene (59 μL, 0.5 mmol) and tetrahydrofuran (122 μL, 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%).

\[ \text{H NMR} (400 MHz, CDCl}_3 \delta 8.09 – 8.02 (m, 2H), 7.15 – 7.08 (m, 2H), 4.34 (t, J = 6.2 Hz, 2H), 3.26 (t, J = 6.7 Hz, 2H), 1.99 (ddd, J = 13.3, 7.4, 3.9 Hz, 2H), 1.94 – 1.86 (m, 2H). \]

\[ \text{C NMR} (101 MHz, CDCl}_3 \delta 166.31 (d, J = 150.5 Hz), 164.53, 132.10 (d, J = 9.1 Hz), 126.46, 115.53 (d, J = 22.2 Hz), 63.89, 30.08, 29.66, 5.73. \]

\[ \text{HRMS (ESI+): C}_{11}H_{12}FIO_2 [M+Na]^+ \text{ found 344.9755, requires 344.9758 (−0.9 ppm).} \]

4-Iodobutyl 4-chlorobenzoate (3mb)
Prepared from 1-chloro-4-iodobenzene (119.0 mg, 0.5 mmol) and tetrahydrofuran (122 μL, 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%).

\[ \text{H NMR} (400 MHz, CDCl}_3 \delta 8.00 – 7.94 (m, 2H), 7.45 – 7.40 (m, 2H), 4.35 (t, J = 6.2 Hz, 2H), 3.25 (t, J = 6.7 Hz, 2H), 2.04 – 1.95 (m, 2H), 1.91 (ddd, J = 9.3, 7.9, 5.0 Hz, 2H). \]

\[ \text{C NMR} (101 MHz, CDCl}_3 \delta 165.66, 139.45, 130.95, 128.74, 128.64, 64.01, 30.05, 29.62, 5.74. \]

4-Iodobutyl 3-chlorobenzoate (3nb)
Prepared from 1-chloro-3-iodobenzene (62 μL, 0.5 mmol) and tetrahydrofuran (122 μL, 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%).

\[ \text{H NMR} (400 MHz, CDCl}_3 \delta 8.01 (s, 1H), 7.92 (d, J = 7.7 Hz, 1H), 7.54 (d, J = 8.0 Hz, 1H), 7.39 (t, J = 7.9 Hz, 1H), 4.36 (t, J = 6.2 Hz, 2H), 3.26 (t, J = 6.6 Hz, 2H), 2.02 – 1.88 (m, 4H). \]

\[ \text{C NMR} (101 MHz, CDCl}_3 \delta 165.33, 134.56, 133.03, 131.91, 129.73, 129.65, 127.70, 64.19, 29.99, 29.60, 5.80. \]

4-Iodobutyl 4-bromobenzoate (3pb)
Prepared from 1-bromo-4-iodobenzene (141.4 mg, 0.5 mmol) and tetrahydrofuran (122 μL, 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%).

\[ \text{H NMR} (400 MHz, CDCl}_3 \delta 7.89 (d, J = 8.5 Hz, 2H), 7.59 (d, J = 8.5 Hz, 2H), 4.35 (dt, J = 10.1, 5.1 Hz, 2H), 3.48 (t, J = 6.4 Hz, 2H), 3.25 (t, J = 6.6 Hz, 2H), 2.04 – 1.83 (m, 2H). \]

\[ \text{C NMR} (101 MHz, CDCl}_3 \delta 165.80, 137.76, 131.75, 131.09, 131.00, 64.03, 30.05, 29.62, 5.73. \]

\[ \text{HRMS (ESI+): C}_{11}H_{12}BrIO_2 [M+Na]^+ \text{ found 404.8956, requires 404.8958 (−0.5 ppm).} \]}

\[ \text{GC-MS (EI, 70 ev): m/z (%) = 381.9 ([M]+, 0), 255.1 (58), 257.1 (58), 183.0 (100), 185.0 (98), 155.0 (35), 157.0 (34), 55.1 (63).} \]
Iodobutyl 4-iodobenzoate (3pb)

\[ \text{H NMR (400 MHz, CDCl}_3 \text{)} \delta 7.81 (d, J = 8.4 Hz, 1H), 7.74 (d, J = 8.5 Hz, 1H), 4.35 (dt, J = 10.1, 5.1 Hz, 5H), 3.48 (t, J = 6.4 Hz, 2H), 3.25 (t, J = 6.6 Hz, 2H), 2.04 - 1.83 (m, 9H). \]

GC-MS (EI, 70 ev): m/z (%) = 429.8 ([M]+, 0), 303.1 (68), 248.0 (32), 231.0 (100), 128.0 (35), 127.0 (31).

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, Rf = 0.25) the desired compound was isolated as a colorless oil (78.0 mg, 42%).

\[ \text{H NMR (400 MHz, CDCl}_3 \text{)} \delta 8.15 (d, J = 8.1 Hz, 2H), 7.71 (d, J = 8.3 Hz, 2H), 4.39 (t, J = 6.1 Hz, 2H), 3.26 (t, J = 6.6 Hz, 2H), 2.03 - 1.88 (m, 4H). \]

\[ 1\text{C NMR (101 MHz, CDCl}_3 \text{)} \delta 165.32, 134.68, 134.36, 133.41, 129.98, 125.45 (d, J = 4.0 Hz), 124.97, 64.35, 30.02, 29.59, 5.64. \]

HRMS (ESI+): \[ C_{11}H_{12}F_3IO_2 \text{[M+H]+} \text{found 372.9891, requires 372.9907} \text{ (−1.1 ppm)}. \]

\[ \text{GC-MS (EI, 70 ev): m/z (%) = 371.9 ([M]+, 0), 245.2 (62), 173.1 (100), 145.1 (55), 55.1 (45).} \]

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, Rf = 0.25) the desired compound was isolated as a white solid (136.2 mg, 77%).

\[ \text{H NMR (400 MHz, CDCl}_3 \text{)} \delta 8.61 (s, 1H), 8.06 (dd, J = 8.6, 1.3 Hz, 1H), 7.97 (d, J = 8.0 Hz, 1H), 7.89 (d, J = 8.6 Hz, 2H), 7.58 (dd, J = 18.1, 10.9, 3.8 Hz, 2H), 4.41 (t, J = 6.1 Hz, 2H), 3.29 (t, J = 6.7 Hz, 2H), 2.08 - 1.93 (m, 4H). \]

\[ 1\text{C NMR (101 MHz, CDCl}_3 \text{)} \delta 166.71, 135.54, 132.48, 131.07, 129.37, 128.29, 128.20, 127.78, 127.42, 126.69, 125.19, 63.94, 30.14, 29.72, 6.06. \]

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, Rf = 0.25) the desired compound was isolated as a red-brown oil (125.4 mg, 72%).

\[ \text{H NMR (400 MHz, CDCl}_3 \text{)} \delta 8.91 (d, J = 8.6 Hz, 1H), 8.18 (d, J = 7.2 Hz, 1H), 8.03 (d, J = 8.2 Hz, 1H), 7.89 (d, J = 8.1 Hz, 1H), 7.63 (dd, J = 11.2, 4.2 Hz, 1H), 7.57 - 7.48 (m, 2H), 4.45 (t, J = 6.1 Hz, 2H), 3.28 (t, J = 6.6 Hz, 2H), 2.08 - 2.01 (m, 2H), 2.00 - 1.93 (m, 2H). \]

\[ 1\text{C NMR (101 MHz, CDCl}_3 \text{)} \delta 167.48, 133.85, 133.43, 131.35, 130.16, 128.57, 128.17, 127.09, 126.24, 125.75, 124.50, 63.84, 30.18, 29.74, 5.99. \]

HRMS (ESI+): \[ C_{15}H_{15}IO_2 \text{[M+Na] + found 355.0172, requires 355.0189} \text{ (−4.8 ppm)}. \]

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, Rf = 0.25) the desired compound was isolated as a colorless oil (90.7 mg, 62%).

\[ \text{H NMR (400 MHz, CDCl}_3 \text{)} \delta 8.12 - 8.08 (m, 1H), 7.51 (d, J = 5.0 Hz, 1H), 7.30 (dd, J = 5.0, 3.1 Hz, 1H), 4.29 (t, J = 6.2 Hz, 2H), 3.24 (t, J = 6.7 Hz, 2H), 2.01 - 1.93 (m, 2H), 1.86 (dq, J = 12.3, 6.1 Hz, 2H). \]

\[ 1\text{C NMR (101 MHz, CDCl}_3 \text{)} \delta 162.66, 133.64, 132.70, 127.87, 126.07, 63.47, 30.10, 29.67, 5.93. \]

HRMS (ESI+): \[ C_{16}H_{13}IO_2 \text{[M+Na] + found 332.9419, requires 332.9417} \text{ (−2.0 ppm)}. \]
3-Iodopropyl 4-methoxybenzoate (3ha)
Prepared from 1-iodo-4-methoxybenzene (117.0 mg, 0.5 mmol) and oxetane (98 μL, 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%).

$^1$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).

$^{13}$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 μL, 0.5 mmol) and tetrahydro-2H-pyran (147 μL, 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%).

$^1$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).

$^{13}$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, 16.47. GC-MS (EI, 70 ev): m/z (%) = 318.0 ([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 μL, 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%).

$^1$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).

$^{13}$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+): C$_{14}$H$_{17}$IO$_3$ [M+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 μL, 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 (70.3 mg, 37%).

$^1$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).

$^{13}$C NMR (101 MHz, CDCl$_3$) δ 165.70, 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+): C$_{16}$H$_{15}$I$_3$O$_3$ [M+H]$^+$ found 383.0143, requires 383.0139 (−1.0 ppm).

4-Iodopentyl benzoate (3af)
Prepared from iodobenzene (57 μL, 0.5 mmol) and 2-methyltetrahydrofuran (150 μL, 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%).

$^1$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). $^{13}$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, Rf = 0.25) the desired compound was isolated as a colorless oil (108.9 mg, 68%).

\[ ^1H \text{ NMR (400 MHz, CDCl}_3 \] 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).

\[ ^13C \text{ NMR (101 MHz, CDCl}_3 \] δ 166.48, 132.97, 130.23, 129.56, 128.40, 68.65, 37.44, 33.78, 16.15, 3.86.

HRMS (ESI+): C\textsubscript{12}H\textsubscript{15}IO\textsubscript{2} [M+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, Rf = 0.25) the desired compound was isolated as a colorless oil (48.6 mg, 65%).

\[ ^1H \text{ NMR (400 MHz, CDCl}_3 \] 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).

\[ ^13C \text{ NMR (101 MHz, CDCl}_3 \] 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, Rf = 0.25) the desired compound was isolated as a colorless oil (42.8 mg, 48%).

\[ ^1H \text{ NMR (400 MHz, CDCl}_3 \] δ 8.13 – 8.05 (m, 2H), 7.59 (dd, J = 10.5, 4.2 Hz, 2H), 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).

\[ ^13C \text{ NMR (101 MHz, CDCl}_3 \] 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-isoproxypropane (202 μL, 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 (51.1 mg, 62%).

\[ ^1H \text{ NMR (400 MHz, CDCl}_3 \] 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).

\[ ^13C \text{ NMR (101 MHz, CDCl}_3 \] 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, Rf = 0.25) the desired compound was isolated as a colorless oil (16.6 mg, 24%).

\[ ^1H \text{ NMR (400 MHz, CDCl}_3 \] 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).

\[ ^13C \text{ NMR (101 MHz, CDCl}_3 \] δ 167.10, 132.89, 130.18, 129.57, 128.35, 52.08.
Ethane-1,2-diyl dibenzoate

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.14 – 8.02 (m, 2H), 7.61 – 7.51 (m, 1H), 7.44 (t, $J = 7.7$ Hz, 2H), 4.67 (s, 2H).

$^{13}$C NMR (101 MHz, CDCl$_3$) $\delta$ 166.38, 133.14, 129.83, 129.71, 128.41, 62.74.