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Ir(III)-Catalyzed Aromatic C−H Bond Functionalization via Metal Carbene Migratory Insertion

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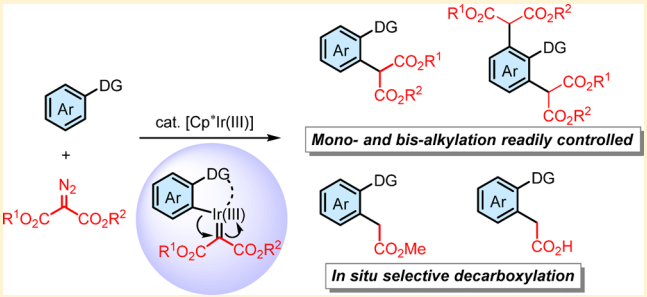
Supporting Information

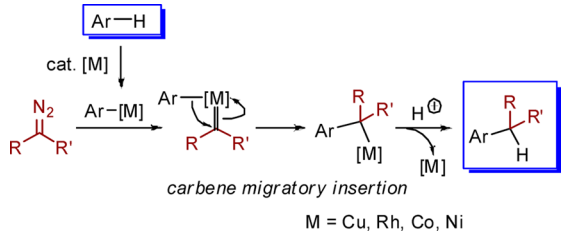
ABSTRACT: Ir(III)-catalyzed coupling of aromatic C−H bonds with diazomalonates has been achieved successfully via a metal carbene migratory insertion process. With different types of carbamoyl directing groups, a wide range of arenes, including heteroarenes, can be used as substrates in this Ir(III)-catalyzed C−H functionalization reaction. Mono- and bisfunctionalized products can be obtained selectively simply by changing the number of equivalents of the diazo substrate. Moreover, when diazomalonates bearing one or two *tert*-butyl groups are used as the substrates, the C−H bond functionalization is followed by decarboxyation, leading to products with a $-CH_2CO_2Me$ or $-CH_2CO_2H$ moiety at the position *ortho* to the directing group. This reaction demonstrates that direct C−H activation and the metal carbene migratory insertion can be merged into one catalytic cycle with an Ir(III) complex as the catalyst.



INTRODUCTION

Transition-metal-catalyzed C−H functionalization with metal carbene species, namely, C−H bond insertion of the metal carbene, is a unique and practical method in organic synthesis.[1] In classic Rh(II) carbene C(sp^3)−H bond insertion reactions, the Rh(II) carbene species is first formed from a carbene precursor, most commonly an α-diazocarbonyl compound. This is followed by a concerted direct C−H insertion mechanism, while the corresponding aromatic C(sp^2)−H bond insertion is proposed as an electrophilic aromatic substitution.[2] In both cases, electron-rich C−H bonds show higher reactivity toward the electron-deficient metal carbene than electron-poor ones. Recently, a new approach toward C(sp^2)−H functionalization has appeared that is proposed to involve a different reaction mode of the metal carbene.[3] The transformation consists of C−H bond metalation followed by metal carbene formation and migratory insertion (Scheme 1).[4]

Scheme 1. Formal Aromatic C(sp^2)−H Bond Insertion



In 2011, we reported an example of this type of aromatic C(sp^2)−H bond insertion in the Cu-catalyzed C−H bond functionalization of 1,3-azoles with *N*-tosylhydrazones (Scheme 2a).[5] In this transformation, the copper carbene precursor of

Scheme 2. Aromatic C(sp^2)−H Bond Functionalization with *N*-Tosylhydrazones or Diazo Compounds

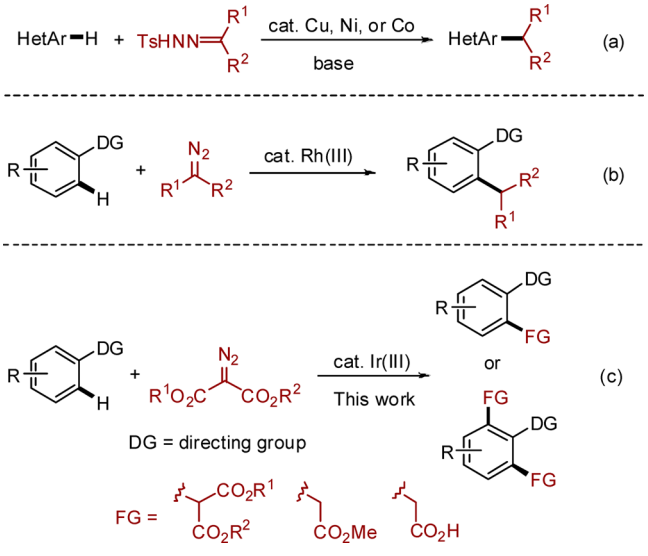


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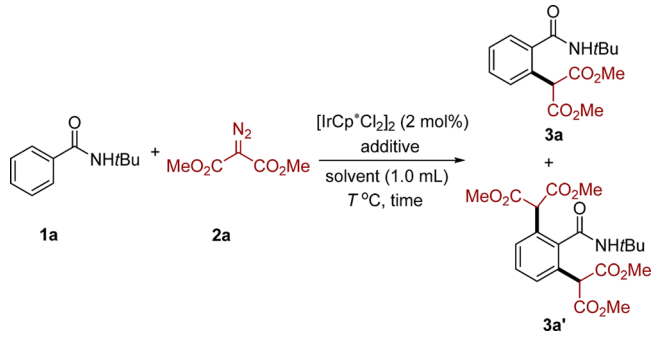
Table 1. Optimization Experiments with the Ir(III)-Catalyzed Reaction of 1a and 2a[a]



entry	additive (mol %)	solvent	t (h)	T (°C)	yield (%)[b]	3a:3a′[c]
1	AgOAc (8)	DCE	24	70	0	–
2	$AgSbF_6$ (8)	DCE	24	70	<1[d]	–
3	$AgNTf_2$ (8)	DCE	24	70	<10	0.6:1
4	$AgNTf_2$ (8)/AgOAc (4)	DCE	24	70	23	15:1
5	$AgNTf_2$(8)/AgOAc(4)	MeCN	24	70	<1[d]	–
6	$AgNTf_2$ (8)/AgOAc (4)	MeOH	24	70	<1[d]	–
7	$AgNTf_2$ (8)/AgOAc (4)	dioxane	24	70	<1[d]	–
8	$AgNTf_2$ (8)/AgOAc (4)	DCE	24	90	38	8:1
9	$AgNTf_2$ (8)/AgOAc (4)	DCE	24	110	30	5:1
10	$AgNTf_2$ (8)/AgOAc (4)	DCE	24	90	25[e]	4:1
11	$AgNTf_2$ (8)/AgOAc (4)	DCE	12	90	86[f]	>30:1
12	$AgNTf_2$ (8)/AgOAc (4)	DCE	10	90	88[g]	>30:1

[a]The reactions carried out with **1a** (0.20 mmol) and **2a** (0.24 mmol) in the presence of 2 mol % Ir(III) catalyst in 1.0 mL of solvent for the indicated times. [b]Yields refer to products isolated by column chromatography. [c]The ratio was estimated by GC–MS analysis of the reaction mixture. [d]Only a trace amount of the product was detected by GC–MS analysis of the reaction mixture. [e]**1a**:**2a** = 1:2. [f]**2a** was dissolved in 0.6 mL of DCE and added via peristaltic pump for 10 h. [g]**2a** was dissolved in 0.6 mL of DCE and added via syringe pump for 5 h.

the diazo substrate is generated in situ from the *N*-tosylhydrazone through a Bamford–Stevens reaction.[6] Hirano and Miura later expanded the substrate scope by replacing Cu(I) with Ni(II) and Co(II) catalysts in similar transformations.[7] In 2012, significant progress was made by Yu and co-workers, who demonstrated that non-heteroarenes bearing a directing group could react with diazo compounds to give an *ortho*-C–H alkylated product under catalysis of a Rh(III) complex.[8,9] Subsequently, the groups of Rovis,[10] Glorius,[11] Li,[12] Cui,[13] Wang,[14] Yi,[15] and Chang[16] as well as our group[17] have demonstrated the successful exploration of diazo compounds as cross-coupling partners in Rh(III)-catalyzed *ortho*-C–H bond functionalization with a directing group (Scheme 2b). Very recently, an asymmetric catalytic version of such a reaction was achieved by Cramer's group using a chiral Rh(III) complex.[18]

Although significant progress has been made in this type of aromatic C(sp^2)–H bond functionalization, it is still in its infancy compared with the traditional C–H insertion of Rh(II) carbene species. New catalysts and versatile reaction types still wait to be explored. In this context, we have noticed that iridium complexes have attracted significant attention in the area of direct C–H functionalizations because of their excellent performance in C–H bond activation.[19−21] For example, Chang and co-workers reported a series of Ir(III)-catalyzed direct C–H bond amination reactions in which organoazides are the most common amino sources.[22] Very recently, the direct C–H alkynylation of arenes was achieved by Li and co-workers using an Ir(III) catalyst, which gives complementary results compared with a Rh(III) catalyst.[23] Inspired by these accomplishments and also in connection to our own interest in cross-coupling reactions involving carbene species,[24] we have conceived that Ir(III)-catalyzed direct C–H bond functionalization of arenes with diazo compounds may be feasible. Herein we report the first chelation-assisted Ir(III)-catalyzed *ortho*-C–H functionalization of aromatic C–H bonds with diazomalonates.[25] This reaction shows a broad scope of aromatic C–H bonds with easy control of the mono- and bis-C–H functionalization (Scheme 2c). Moreover, the directing groups reported in this study, namely, alkyl carbamoyl groups, are different from those previously reported for Rh(III)-catalyzed reactions.[10−18] Mechanistically, an Ir(III) carbene migratory insertion process is proposed as the key step involved in this transformation.

RESULTS AND DISCUSSION

Optimization of the Reaction Conditions. At the outset of this investigation, *N*-*tert*-butylbenzamide (**1a**) and dimethyl diazomalonate (**2a**) were used as the substrates to optimize the reaction conditions (Table 1). The dimeric (pentamethylcyclopentadienyl)iridium complex [Ir(III)-Cp*Cl_2]$_2$, which is the most widely used Ir(III) catalyst precursor in direct C–H functionalization reactions,[22,23] was employed as the catalyst in this reaction. A series of Ag(I) additives, which are required for the formation of a cationic Ir(III) species by chloride abstraction, were first investigated under reaction conditions of 70 °C in DCE for 24 h. However, none or only a trace amount of the expected *ortho*-functionalized product **3a** was observed by GC–MS analysis when AgOAc or $AgSbF_6$ was used as an additive (entries 1 and 2). The strongly cationic $AgNTf_2$ was more efficient than the other Ag(I) additives, but the bisfunctionalized product **3a′** was also formed in significant amount (entry 3). When AgOAc was added together with $AgNTf_2$ as a coadditive,[22e] both the yield

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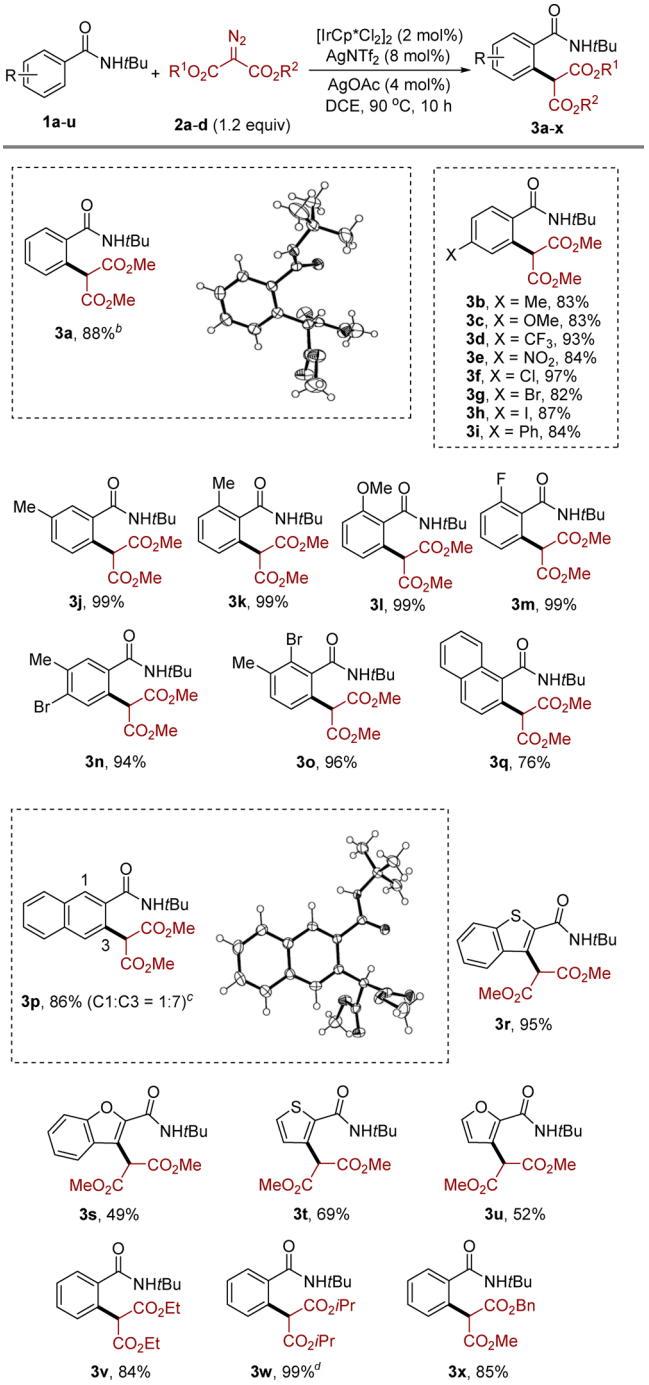
and the ratio of mono- to bisfunctionalized product were improved, and **3a** was isolated in 23% yield (entry 4). The effect of the solvent was then screened, and it was found that no solvent was superior to the non-coordinative solvent DCE (entries 5−7). High reaction temperature could facilitate the transformation; however, the selectivity for the monofunctionalized product over the bisfunctionalized product declined (entries 8 and 9). Increasing the amount of the diazo substrate **2a** did not improve the yield or the selectivity (entry 10). This experiment indicates that low concentration of the diazo substrate may be beneficial for the reaction. Indeed, both the yield and the selectivity improved when the diazo substrate was added slowly (entries 11 and 12). With slow addition of the diazo substrate over 5 h, the product **3a** was isolated in 88% yield with excellent monoalkylation selectivity (entry 12).[26]

Substrate Scope. Having established the optimized reaction conditions, we then explored the scope of this reaction system. A series of substituted aryl amides were first investigated. The reaction with diazomalonates proceeded smoothly to afford the *ortho*-alkylated products in 49−99% yield (Scheme 3). The structure of **3a** was confirmed unambiguously by X-ray crystallography. The electronic properties of the substituents on benzamides showed little influence on this transformation. Benzamides bearing either electron-donating (**3b** and **3c**) or electron-withdrawing (**3d−i**) substituents at the *para* position afforded the corresponding products in excellent yields. The *meta*- and *ortho*-substituted benzamides gave almost quantitative yields in this reaction (**3j−m**). For the *meta*-substituted benzamide **1j**, only one product was observed, and the C−H functionalization occurred regioselectively at the sterically more accessible position (**3j**).[22a] Some multisubstituted benzamides were also subjected to this reaction and afforded the corresponding C−H bond-functionalized products in excellent yields (**3n** and **3o**). It is noteworthy that this reaction fully tolerates halogen substituents, providing the possibility for further transformation via cross-coupling reactions (**3f−h**, **3n**, and **3o**). Naphthamides were also suitable substrates for this reaction, and the C−H-alkylated products were obtained in good yields (**3p** and **3q**). Moderate regioselectivity was observed when 2-naphthamide (**2p**) was used as the substrate, and again the C−H functionalization took place at sterically less hindered site. The structure of the 3-alkylated major product (**3p**) was confirmed through X-ray crystallography. Additionally, this Ir(III)-catalyzed C−H functionalization also tolerated heteroaryl amides, as furan- and thiophene-derived amides were also converted to the corresponding products in moderate to good yields (**3r−u**).

Some other diazomalonate esters were also explored to react with benzamide **1a**, all of which afforded results comparable to those for dimethyl diazomalonate **2a** (**3v−x**). It is again worthwhile to mention that all of these examples gave excellent monoalkylation selectivity under the current reaction conditions, and none or only a trace amount of the bisalkylated products could be detected by GC−MS analysis of the reaction mixture.

We next explored the scope of the directing group on the aromatic substrate of this reaction (Scheme 4). The N substituent on the benzamide can be varied from a *tert*-butyl group to cyclohexyl, isopropyl, propyl, and adamantyl groups, although the less sterically hindered propyl group led to only a moderate yield (**5a−d**). An interesting observation is that the NH moiety is not essential to this transformation, as the reaction still works well with *N*,*N*-disubstituted benzamides (**5e−g**). Again, the steric hindrance of the directing group has an influence on this reaction to some extent (**5e−g**). Apart from benzamides, simple aryl ketones were also suitable substrates for this Ir(III)-catalyzed C−H functionalization reaction, although the corresponding products were obtained in diminished yields (**5h−j**). It should be noted that the

Scheme 3. Scope of the Benzamides in the Ir(III)-Catalyzed C−H Functionalization[a]



[a]The reaction conditions are described in entry 12 of Table 1. [b]Isolated yields with column chromatography. [c]The regioselectivity was determined by ^{1}H NMR spectroscopy. [d]This product was isolated as an isomeric mixture (2.5:1), as a result of the hindered rotation of the amide C−N bond.

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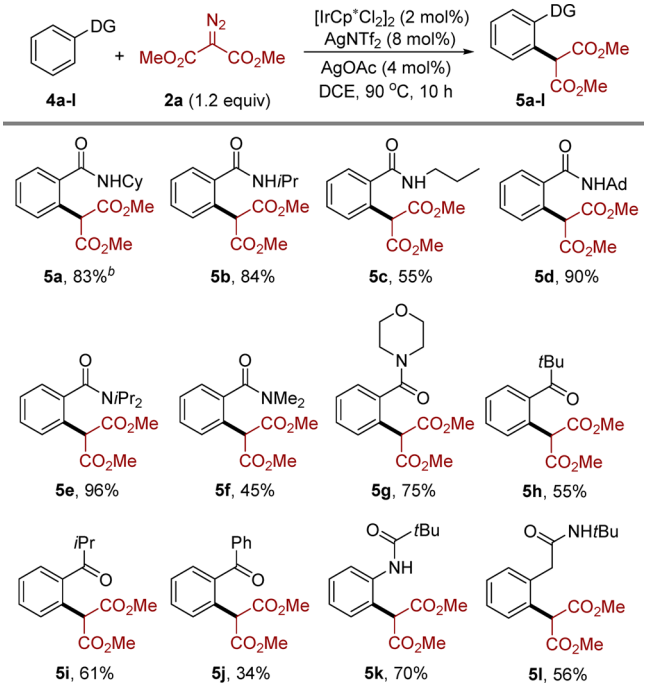
Scheme 4. Scope of the Directing Group in Ir(III)-Catalyzed C−H Functionalization[a]



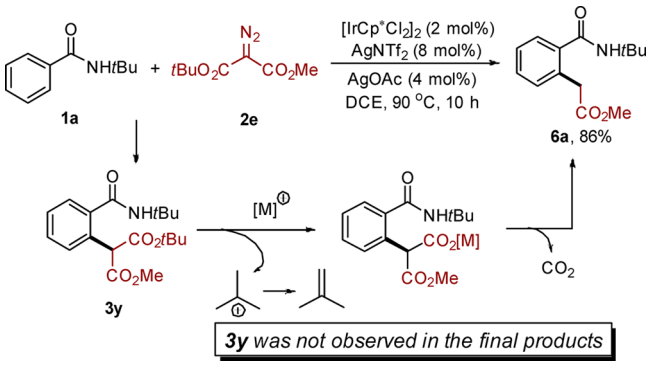
[a]The reaction conditions are described in entry 12 of Table 1. [b]Isolated yields with column chromatography.

bulkiness of the directing group is essential to this C−H functionalization, as the simplest substrates, *N*-methylbenzamide and acetophenone, did not afford the desired products, and the starting materials largely remained. To our delight, this Ir(III)-catalyzed reaction system could be expanded to *N*-pivaloyl-protected aniline in good yield (**5k**). Finally, an analogue of benzamide **1a** enlarged by one carbon between the arene moiety and the directing moiety, was less effective in this reaction, indicating that the size of the iridacycle formed in the C−H activation step has a significant influence on the efficiency of this transformation (**5l**).

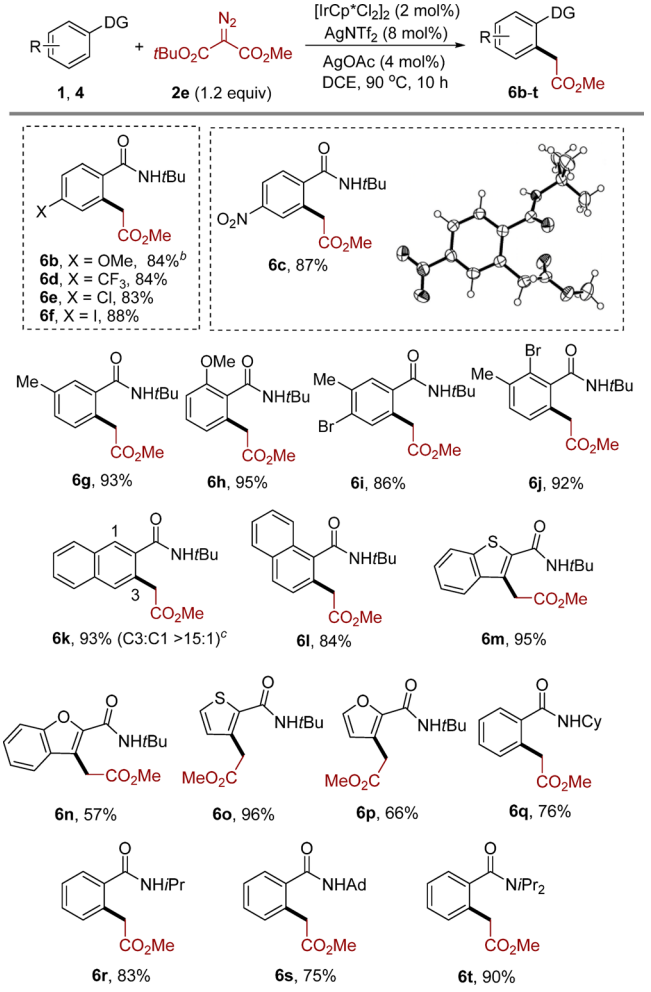
When 1-*tert*-butyl 3-methyl 2-diazomalonate (**2e**) was employed as the carbene precursor to react with benzamide **1a** under the optimized reaction conditions, the anticipated product **3y** was not observed. Instead, monoester product **6a** was obtained in 86% isolated yield. We speculate that the formation of **6a** occurs because the *tert*-butyl ester moiety is liable to hydrolysis under the acidic conditions. Thus, the normal coupling product **3y** is generated first and then undergoes hydrolysis with the assistance of a Lewis acidic Ir(III) or Ag(I) complex. The metal malonate is formed with the release of *tert*-butyl cation, which gives isobutene. Finally, a decarboxylation process occurs, leading to the observed product **6a** (Scheme 5). From the viewpoint of synthesis, this Ir(III)-catalyzed C−H alkylation/C−C bond cleavage sequence affords a method for *ortho*-C−H functionalization with a CH_2CO_2Me moiety.[12,15] Notably, this transformation also shows excellent monoalkylation selectivity.

This Ir(III)-catalyzed C−H alkylation/C−C bond cleavage sequence was then investigated by testing a wide range of arenes (Scheme 6). Similar to the reaction of dimethyl diazomalonate **2a**, this reaction also shows a wide substrate scope with high efficiency and excellent monoalkylation

Scheme 5. Ir(III)-Catalyzed Reaction of Benzamide 1a and Diazomalonate 2e: C−H Alkylation/C−C Bond Cleavage Sequence



Scheme 6. Scope of the Ir(III)-Catalyzed C−H Alkylation/C−C Bond Cleavage Sequence[a]



[a]The reaction conditions are described in entry 12 of Table 1. [b]Isolated yields with column chromatography. [c]The regioselectivity was determined by ^{1}H NMR spectroscopy.

selectivity. Benzamides bearing different types of substituents worked well in this reaction (**6b−j**). The structure of product **6c** was confirmed unambiguously by X-ray crystallography. Compared with the reaction with **2a**, the reaction of 2-naphthamide afforded a better regioselective C−H alkylation

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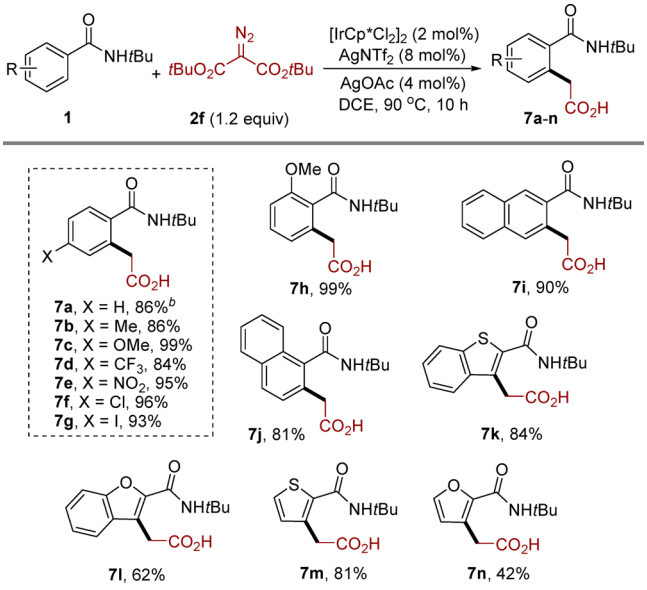
(**6k**), and the reaction of 1-naphthamide showed a similar result (**6l**). Notably, this reaction can also be applied to the functionalization of heteroarenes, affording the corresponding products in moderate to excellent yields (**6m–p**). Other directing groups were also explored under the same reaction conditions, and results comparable to those for the reactions with **2a** were obtained (**6q–t**).

Subsequently, we proceeded to investigate this Ir(III)-catalyzed reaction with di-*tert*-butyl diazomalonate (**2f**), which bears two CO_2tBu moieties, as the carbene precursor. Interestingly, under the identical conditions, one of the two CO_2tBu moieties vanished in the reaction but the other one was only hydrolyzed, affording a free carboxylic acid moiety (Scheme 7, **7a**). To the best of our knowledge, direct

Scheme 7. Scope of the Ir(III)-Catalyzed C–H Alkylation/C–C/C–O Bond Cleavage Sequence[a]

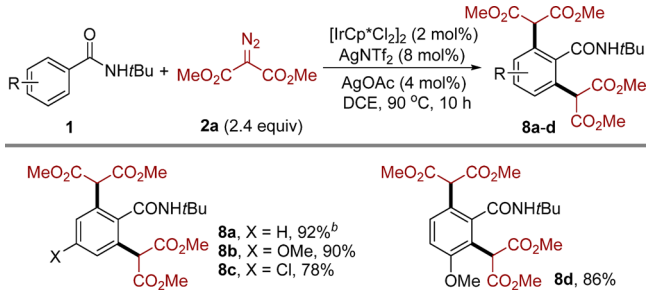


[a]The reaction conditions are described in entry 12 of Table 1. [b]Isolated yields with column chromatography.

transition-metal-catalyzed C–H functionalization with a CH_2CO_2H moiety has not been reported previously. The efficiency of this transformation was then tested using a number of aryl amides, and the corresponding aryl acetic acids were obtained in 42–99% yield (Scheme 7). Benzamides containing electron-donating or electron-withdrawing substituents all reacted smoothly to afford the C–H-functionalized product with a CH_2CO_2H moiety (**7b–h**). Naphthamides were converted to the corresponding products with high efficiency and excellent regioselectivity (**7i–j**). The C–H-functionalized product in the reaction of 2-naphthamide was not observed in the ^1H NMR analysis, demonstrating that the regioselectivity is higher than that of the corresponding reaction of diazomalonate **2a** or **2e**. Heteroaryl amides were also suitable substrates for this transformation, although diminished yields were obtained for the furan-containing heterocycles (**7k–n**). It should be noted again that this type of reaction also shows excellent monoalkylation selectivity.

As shown by the results reported above, the selectivity for mono- versus bisfunctionalization is excellent under the current reaction conditions. However, the bisfunctionalized product was observed in GC–MS analysis during the optimization of the reaction conditions, suggesting the possibility to achieve double C–H bond functionalization in a single operation. This was indeed the case. When 2.4 equiv of dimethyl 2-diazomalonate **2a** was used to react with benzamide **1a** under reaction conditions otherwise identical to those described in entry 12 of Table 1, the bisalkylated product **8a** was obtained cleanly in 92% isolated yield (Scheme 8, **8a**). The substrates

Scheme 8. Scope of the Ir(III)-Catalyzed Double C–H Alkylation Reaction with Diazo Compound 2a[a]

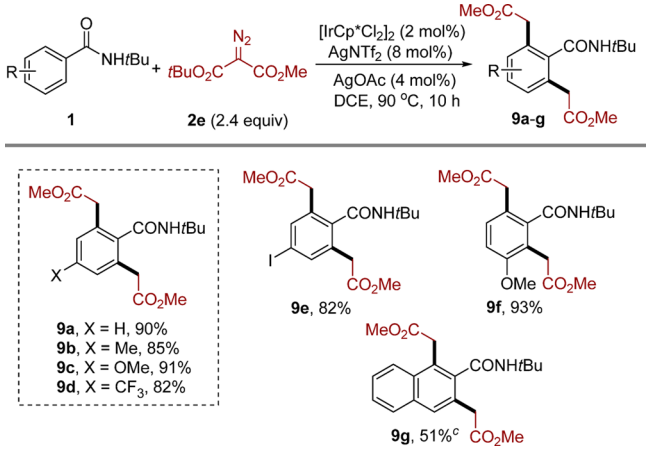


[a]The reaction conditions are described in entry 12 of Table 1, except that the amount of diazo compound **2a** was 0.48 mmol. [b]Isolated yields with column chromatography.

with an electron-donating or electron-withdrawing group at the *para* position or with methoxy at the *meta* position were all tolerated well under the reaction conditions, affording the bisalkylated products in good to excellent yields (Scheme 8, **8b–d**). Therefore, the selectivity for mono- or bisfunctionalized products could be controlled by varying the number of equivalents of the diazo compound used for the reaction.

Similarly, 1-*tert*-butyl 3-methyl 2-diazomalonate **2e** was also suitable substrate for this Ir(III)-catalyzed bisalkylation reaction, and a series of aryl amides were smoothly converted to the bisfunctionalized products with a CH_2CO_2Me moiety (Scheme 9). Benzamides bearing various substituents showed high efficiency in this transformation, affording the corresponding products in 82–93% yield (**9a–f**). 2-Naphthamide could

Scheme 9. Scope of the Ir(III)-Catalyzed Double C–H Alkylation Reaction with Diazo Compound 2e[a]



[a]The reaction conditions are described in entry 12 of Table 1, except that the amount of diazo compound **2e** was 0.48 mmol. [b]Isolated yields with column chromatography. [c]The monoalkylated product **6k** was isolated in 47% yield.

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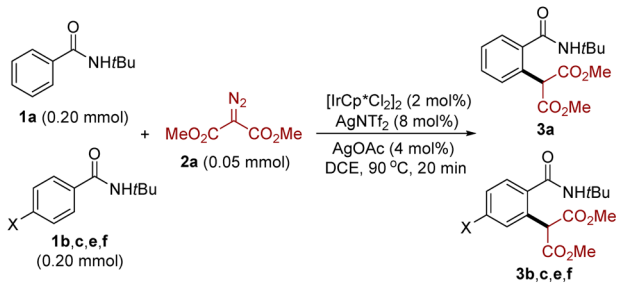
not be fully transformed to the corresponding bisalkylated product, which was isolated in only 51% yield under the same conditions. The monoalkylated product **6k** was also isolated in 47% yield. This result might be attributable to the steric effect, which hindered the second alkylation process (**9g**).

Mechanistic Studies. Preliminary mechanistic studies were then carried out in order to gain insights into the mechanism of this Ir(III)-catalyzed C−H alkylation (Scheme 10).[27] First,

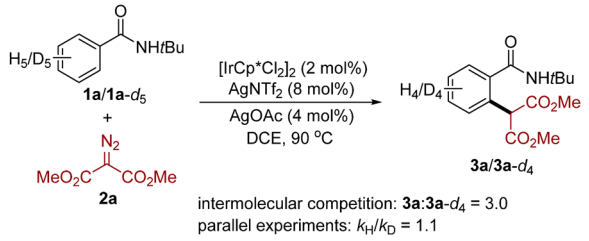
Scheme 10. Experiments for Mechanistic Studies

(a) Electronic effects

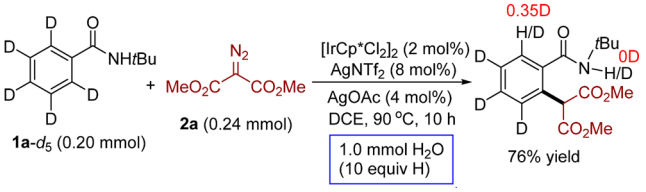


substrate	3c	3b	3f	3e
X	OMe	Me	Cl	NO_2
(3x:3a)	2.0	1.7	0.50	0.11

(b) Kinetic isotope effect (KIE)



(c) Reaction in the presence of excess H_2O



amide competition experiments were performed to study the electronic preference of the reaction. Thus, equimolar mixtures of unsubstituted amide **1a** and *para*-substituted benzamides **1b**, **1c**, **1e**, and **1f** were subjected to the competition reaction. The results from these experiments show a significant electronic effect on the reaction. The ratios of the observed products for substituted benzamides to the product for unsubstituted amide **1a** were 2.0, 1.7, 0.50, 0.11 for OMe, Me, Cl, and NO_2 substituents, respectively (Scheme 10a). We can thus conclude that this Ir(III)-catalyzed C−H functionalization is more favorable for benzamides bearing an electron-donating substituent, indicating that an electrophilic C−H activation is involved in the reaction mechanism of this reaction.[8]

Next, an intermolecular competition experiment using equimolar amounts of **1a** and **1a**-d_5 was carried out (Scheme 10b). Three runs of this reaction for 5, 10, and 20 min afforded similar results, in which the small amount of diazo compound **2a** was consumed completely in all cases. ^{1}H NMR analysis of the product mixture gave an average **3a**:**3a**-d_4 ratio of 3.0. It is noteworthy that the deuterium cleaved from **1a**-d_5 was not incorporated into the malonate moiety of the products, indicating fast H/D exchange with the rather acidic position. Interestingly, the deuterium was partially merged into the amide NH moiety, and the deuterated ratio increased to some extent as the reaction time was prolonged. Another observation is that H/D scrambling did not occur, which indicates that the C−H functionalization is rather faster than the *ortho*-H/D exchange. Meanwhile, two separate reactions of **1a** or **1a**-d_5 under the standard conditions were conducted. The reactions were stopped within 20 min to keep a low conversion (less than 10%). The observed reaction rates of **1a** and **1a**-d_5 were almost the same (k_H/k_D = 1.1). These results suggest that the cleavage of the C−H bond is not involved in the rate-limiting step. The results are in accordance with the aforementioned argument that the reaction may involve an electrophilic C−H metalation pathway. Moreover, the difference of these two KIE values indicates that the rate-limiting step should occur before the cleavage of the C−H bond,[28] and presumably the electrophilic metalation is involved in the rate-limiting step.

Then the reaction of benzamide **1a**-d_5 with diazo compound **2a** was carried out with an additional 5 equiv of H_2O under the standard conditions. The target product was isolated in 76% yield, indicating that water has a marginal effect on the Ir(III)-catalyzed C−H alkylation. Besides, the *ortho*-D was retained in a considerable ratio even in the presence of a large excess amount of H source (10 equiv), again suggesting that the C−H alkylation is faster than the *ortho*-H/D exchange (Scheme 10c). These results indicate that this Ir(III)-catalyzed C−H activation is largely irreversible on the time scale of the reaction, which is in accordance with the previous reports.[22]

Since Ir(III) complexes also catalyze traditional carbene transfer reactions with diazo compounds,[25] some control experiments with traditional carbene acceptors were then carried out in order to gain further insights into the reaction (Scheme 11). When 3 equiv of cyclohexene was added to the standard reaction mixture, cyclopropanation or allylic C−H insertion of the cyclohexene was not observed. Interestingly, the formation of **3a** was completely inhibited, and **1a** and **2a** were recovered in 92% and 48% yield, respectively. This is probably due to the weaker electrophilic nature of the iridium center upon ligation to the alkene (Scheme 11a). When cyclohexene was treated with **2a** in the absence of **1a** under the standard conditions, the cyclopropanation or allylic C−H insertion also did not occur (Scheme 11b).

Similar experiments were then performed by replacing cyclohexene with anisole. In contrast to the experiment with cyclohexene, the C−H alkylation was not affected by the added anisole, and **3a** was obtained in 85% yield. In this reaction, the C−H insertion product of the reaction of the electron-rich anisole with diazo compound **2a** was not observed (Scheme 11c), and the same result was obtained in the absence of **1a** (Scheme 11d). Notably, the experiments also indicated that the diazo compound was consumed slowly in the absence of arene substrate, suggesting that this reaction is largely different from the traditional metal carbene reactions, in which the metal catalyst and the arene substrate interact antecedent to metal carbene formation. Moreover, the directing group was found to be essential for the electrophilic C−H activation, as the simple electron-rich arene anisole did not undergo C−H functionalization under the same conditions.

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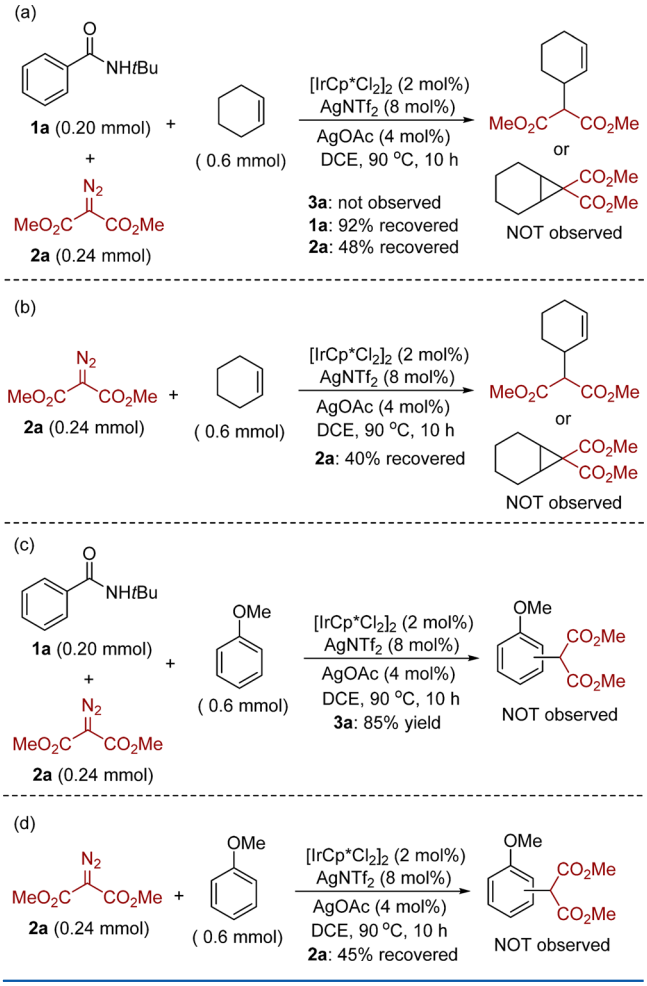
Scheme 11. Control Experiments with Traditional Carbene Acceptors

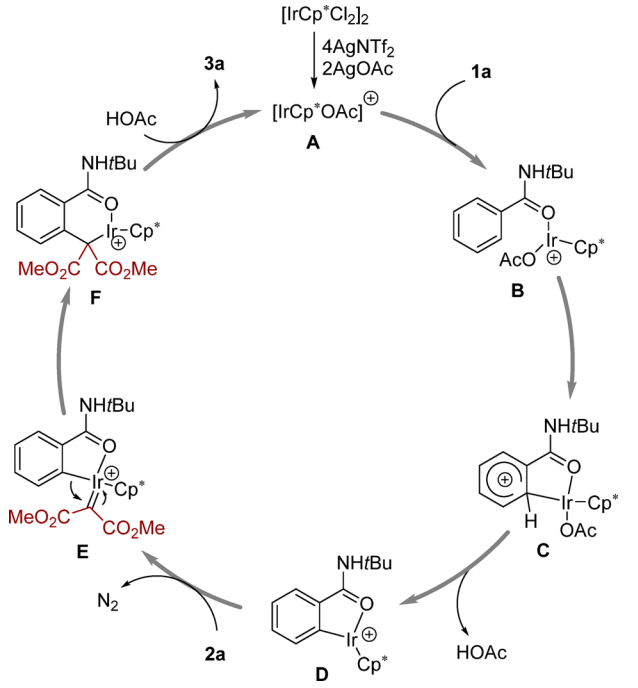


On the basis of these experimental observations and literature precedents,[19−23] a mechanism for the present Ir(III)-catalyzed C−H alkylation reaction is proposed as shown in Scheme 12. First, the active cationic Ir(III) species **A** is generated with the assistance of the Ag salts.[22e] This electrophilic Ir(III) species coordinates to the carbonyl oxygen of the amide to generate iridium complex **B**.[22i] At this point, an intramolecular electrophilic metalation may occur to form intermediate **C**, from which HOAc is eliminated to produce iridacyclic intermediate **D**. The metalation step might be the rate-limiting step according to the above experimental observations. The iridacyclic complex **D** reacts with the diazo compound to form a cyclic Ir(III) carbene species with the extrusion of N_2.[29] Subsequent migratory insertion of Ir(III) carbene species **E** takes place, leading to the formation of intermediate **F**, similar to the Rh(III)-catalyzed C−H functionalization.[8−18] Finally, protonation of **E** produces the desired alkylated product with regeneration of the active Ir(III) catalyst.

CONCLUSION

In summary, we have developed a versatile Ir(III)-catalyzed aromatic *ortho*-C−H alkylation reaction with diazomalonates. This methodology shows the advantages of high efficiency, excellent compatibility of a series of functional groups, and good regioselectivity. In addition to the formal carbene

Scheme 12. Proposed Reaction Mechanism



aromatic C(sp^2)−H bond insertions, C−H functionalization with a CH_2CO_2Me or CH_2CO_2H moiety can be achieved through in situ de-esterification. Additionally, the mono- and bisfunctionalized reaction modes can be readily controlled by varying the amount of diazomalonate used in the reaction. From a mechanistic point of view, this catalytic reaction demonstrates that the well-developed C−H activation process by the Ir(III) complex can be successfully incorporated with the Ir(III) carbene migratory insertion process to achieve highly efficient aromatic C−H bond alkylation. This may open up new possibilities to further develop novel Ir(III)-catalyzed C−H bond transformations.

EXPERIMENTAL SECTION

General Methods. All of the solvents were distilled under a nitrogen atmosphere prior to use. Dioxane was dried over Na with benzophenone ketyl intermediate as the indicator. MeCN, MeOH, and DCE were dried over CaH_2. Aryl amides were prepared according to the literature procedure,[22a] and unless otherwise specified, the catalysts were used directly as received from commercial sources without further purification. For chromatography, 200−300 mesh silica gel (Qingdao, China) was employed. Chemical shifts for ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra are reported relative to tetramethylsilane (TMS). IR spectra are reported in wavenumbers (cm^{-1}). For HRMS measurements, the mass analyzer was FT-ICR.

General Procedure for Ir(III)-Catalyzed Monoalkylation. Under atmospheric conditions, arene **1** or **4** (0.2 mmol), $[IrCp^*Cl_2]_2$ (3.2 mg, 0.004 mmol, 2 mol %), $AgNTf_2$ (6.2 mg, 0.016 mmol, 8 mol %), and AgOAc (1.3 mg, 0.008 mmol, 4 mol %) were successively added to a 10 mL Schlenk tube. The reaction tube was degassed three times with nitrogen gas, and dry DCE (1.0 mL) was added using a syringe. It should be noted that the arene in a liquid form was added to the reaction tube by syringe after addition of the solvent. The reaction tube was immersed in a 90 °C oil bath with stirring, and then diazo compound **2** (0.24 mmol dissolved in 0.6 mL of DCE) was added via peristaltic pump for 5 h. After another 5 h of stirring, the reaction mixture was cooled to room temperature and filtered through a short plug of silica gel (petroleum ether (PE):ethyl acetate (EA) = 1:1, 15 mL). The solvent was then removed in vacuo to leave a crude mixture,

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which was purified by silica gel column chromatography to afford pure product **3a−x**, **5a−l**, **6a−t**, or **7a−n**. For products **3a−x**, **5a−l**, and **6a−t**, PE:EA = 5:1 to 3:1 was generally used as the solvent for column chromatography. For acid products **7a−n**, the reaction mixture was filtered through a short plug of Celite (PE:EA = 1:1, 15 mL) after the reaction was finished, and CH_2Cl_2:MeOH = 75:1 was used as the solvent for column chromatography.

General Procedure for Ir(III)-Catalyzed Bisalkylation. Under atmospheric conditions, arene **1** (0.2 mmol), $[IrCp^*Cl_2]_2$ (3.2 mg, 0.004 mmol, 2 mol %), $AgNTf_2$ (6.2 mg, 0.016 mmol, 8 mol %), and AgOAc (1.3 mg, 0.008 mmol, 4 mol %) were successively added to a 10 mL Schlenk tube. The reaction tube was degassed three times with nitrogen gas, and dry DCE (1.0 mL) was added using a syringe. The reaction tube was immersed in a 90 °C oil bath with stirring, and then diazo compound **2a** or **2e** (0.48 mmol dissolved in 0.6 mL of DCE) was added via peristaltic pump for 5 h. After another 5 h of stirring, the reaction mixture was cooled to room temperature and filtered through a short plug of silica gel (PE:EA = 1:1, 15 mL). The solvent was then removed in vacuo to leave a crude mixture, which was purified by silica gel column chromatography to afford pure product **8a−d** or **9a−g** using PE:EA = 5:1 to 3:1 as the solvent.

*Dimethyl 2-(2-(tert-Butylcarbamoyl)phenyl)malonate (**3a**).* Yield 88% (54 mg); white solid, mp 113−115 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50−7.48 (m, 1H), 7.44−7.40 (m, 2H), 7.36−7.32 (m, 1H), 5.98 (s, 1H), 5.38 (s, 1H), 3.76 (s, 6H), 1.45 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.8, 168.4, 137.9, 130.4, 129.9, 129.7, 128.2, 127.2, 53.6, 52.8, 52.0, 28.6; HRMS (ESI, *m*/*z*) calcd for $C_{16}H_{22}NO_5$ $[M + H]^+$ 308.1492, found 308.1495; IR (film) 735, 1148, 1220, 1528, 1655, 1737, 2917, 3388 cm^{-1}.

*Dimethyl 2-(2-(tert-Butylcarbamoyl)-5-methylphenyl)malonate (**3b**).* Yield 83% (53 mg); white solid, mp 84−85 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (d, *J* = 7.8 Hz, 1H), 7.28 (s, 1H), 7.14 (d, *J* = 7.6 Hz, 1H), 5.97 (s, 1H), 5.40 (s, 1H), 3.76 (s, 6H), 2.36 (s, 3H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.0, 168.4, 140.1, 135.0, 130.3, 130.2, 128.9, 127.2, 53.4, 52.8, 51.8, 28.6, 21.3; HRMS (ESI, *m*/*z*) calcd for $C_{17}H_{24}NO_5$ $[M + H]^+$ 322.1649, found 322.1652; IR (film) 732, 1148, 1237, 1308, 1654, 1737, 2964, 3386 cm^{-1}.

*Dimethyl 2-(2-(tert-Butylcarbamoyl)-5-methoxyphenyl)malonate (**3c**).* Yield 83% (56 mg); white solid, mp 127−128 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (d, *J* = 8.5 Hz, 1H), 7.02 (d, *J* = 2.4 Hz, 1H), 6.84 (dd, *J* = 2.4, 8.5 Hz, 1H), 5.93 (s, 1H), 5.48 (s, 1H), 3.82 (s, 3H), 3.77 (s, 6H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.8, 168.3, 160.5, 132.4, 130.3, 128.8, 115.4, 113.4, 55.4, 53.5, 52.8, 51.8, 28.7; HRMS (ESI, *m*/*z*) calcd for $C_{17}H_{24}NO_6$ $[M + H]^+$ 338.1598, found 338.1602; IR (film) 680, 1147, 1242, 1549, 1622, 1746, 2955, 3296 cm^{-1}.

*Dimethyl 2-(2-(tert-Butylcarbamoyl)-5-(trifluoromethyl)phenyl)-malonate (**3d**).* Yield 93% (70 mg); white solid, mp 123−125 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (s, 1H), 7.62−7.55 (m, 2H), 6.08 (s, 1H), 5.34 (s, 1H), 3.79 (s, 6H), 1.45 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.1, 167.1, 141.2, 131.8 (q, *J* = 32.9 Hz), 131.2, 127.8, 126.9 (q, *J* = 3.7 Hz), 125.2 (q, *J* = 3.5 Hz), 123.4 (q, *J* = 272.6 Hz), 53.5, 53.1, 52.4, 28.5; HRMS (ESI, *m*/*z*) calcd for $C_{17}H_{21}F_3NO_5$ $[M + H]^+$ 376.1366, found 376.1371; IR (film) 688, 1151, 1222, 1331, 1639, 1736, 2917, 3301 cm^{-1}.

*Dimethyl 2-(2-(tert-Butylcarbamoyl)-5-nitrophenyl)malonate (**3e**).* Yield 84% (59 mg); yellow solid, mp 117−119 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (d, *J* = 2.0 Hz, 1H), 8.17 (dd, *J* = 2.0, 8.4 Hz, 1H), 7.60 (d, *J* = 8.4 Hz, 1H), 6.15 (s, 1H), 5.33 (s, 1H), 3.81 (s, 6H), 1.46 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.8, 166.4, 148.2, 143.5, 132.2, 128.4, 125.2, 123.2, 53.4, 53.3, 52.6, 28.5; HRMS (ESI, *m*/*z*) calcd for $C_{16}H_{21}N_2O_7$ $[M + H]^+$ 353.1343, found 353.1353; IR (film) 734, 1150, 1221, 1350, 1656, 1739, 2958, 3311 cm^{-1}.

*Dimethyl 2-(2-(tert-Butylcarbamoyl)-5-chlorophenyl)malonate (**3f**).* Yield 97% (66 mg); white solid, mp 102−104 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, *J* = 1.9 Hz, 1H), 7.38 (d, *J* = 8.2 Hz, 1H), 7.31 (dd, *J* = 1.9, 8.2 Hz, 1H), 6.03 (s, 1H), 5.34 (s, 1H), 3.78 (s, 6H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.2, 167.4, 136.2, 135.8, 132.2, 129.9, 128.6, 128.4, 53.3, 53.0, 52.1, 28.5; HRMS (ESI, *m*/*z*) calcd for $C_{16}H_{21}ClNO_5$ $[M + H]^+$ 342.1103, found 342.1112, calcd for $C_{16}H_{20}ClNNaO_5$ $[M + Na]^+$ 364.0922, found 364.0924; IR (film) 733, 1150, 1219, 1531, 1650, 1739, 2962, 3305 cm^{-1}.

*Dimethyl 2-(5-Bromo-2-(tert-butylcarbamoyl)phenyl)malonate (**3g**).* Yield 82% (63 mg); white solid, mp 110−111 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 1.7 Hz, 1H), 7.48 (dd, *J* = 1.7, 8.2 Hz, 1H), 7.31 (d, *J* = 8.2 Hz, 1H), 6.00 (s, 1H), 5.32 (s, 1H), 3.78 (s, 6H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.3, 167.5, 136.8, 132.8, 132.3, 131.4, 128.8, 124.0, 53.3, 53.0, 52.2, 28.6; HRMS (ESI, *m*/*z*) calcd for $C_{16}H_{21}{}^{79}BrNO_5$ $[M + H]^+$ 386.0598, found 386.0606; IR (film) 733, 1150, 1218, 1530, 1650, 1738, 2959, 3311 cm^{-1}.

*Dimethyl 2-(2-(tert-Butylcarbamoyl)-5-iodophenyl)malonate (**3h**).* Yield 87% (75 mg); white solid, mp 122−124 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 1.4 Hz, 1H), 7.68 (dd, *J* = 1.4, 8.1 Hz, 1H), 7.16 (d, *J* = 8.1 Hz, 1H), 6.03 (s, 1H), 5.28 (s, 1H), 3.78 (s, 6H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.3, 167.6, 138.6, 137.3, 137.3, 132.1, 128.8, 95.9, 53.2, 53.0, 52.1, 28.5; HRMS (ESI, *m*/*z*) calcd for $C_{16}H_{21}INO_5$ $[M + H]^+$ 434.0459, found 434.0465; IR (film) 731, 910, 1150, 1217, 1652, 1737, 2917, 3317 cm^{-1}.

*Dimethyl 2-(4-(tert-Butylcarbamoyl)-[1,1′-biphenyl]-3-yl)-malonate (**3i**).* Yield 84% (64 mg); white solid, mp 112−113 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (s, 1H), 7.58−7.40 (m, 4H), 7.46−7.42 (m, 2H), 7.38−7.35 (m, 1H), 6.07 (s, 1H), 5.46 (s, 1H), 3.78 (s, 6H), 1.46 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.8, 168.2, 142.8, 139.8, 136.6, 130.8, 128.8, 128.6, 127.9, 127.8, 127.2, 126.8, 53.6, 52.9, 52.0, 28.6; HRMS (ESI, *m*/*z*) calcd for $C_{22}H_{26}NO_5$ $[M + H]^+$ 384.1806, found 384.1812; IR (film) 732, 1148, 1217, 1305, 1652, 1736, 2957, 3378 cm^{-1}.

*Dimethyl 2-(2-(tert-Butylcarbamoyl)-4-methylphenyl)malonate (**3j**).* Yield 99% (64 mg); white solid, mp 127−130 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (d, *J* = 7.9 Hz, 1H), 7.27−7.22 (m, 2H), 5.99 (s, 1H), 5.30 (s, 1H), 3.76 (s, 6H), 2.35 (s, 3H), 1.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.0, 168.5, 138.2, 137.8, 130.6, 129.6, 127.9, 127.2, 53.3, 52.8, 51.9, 28.6, 20.9; HRMS (ESI, *m*/*z*) calcd for $C_{17}H_{24}NO_5$ $[M + H]^+$ 322.1649, found 322.1655; IR (film) 734, 1029, 1254, 1541, 1630, 1750, 2926, 3288 cm^{-1}.

*Dimethyl 2-(2-(tert-Butylcarbamoyl)-3-methylphenyl)malonate (**3k**).* Yield 99% (64 mg); white solid, mp 128−131 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (d, *J* = 7.7 Hz, 1H), 7.29−7.25 (m, 1H), 7.17 (d, *J* = 7.4 Hz, 1H), 5.72 (s, 1H), 4.89 (s, 1H), 3.75 (s, 6H), 2.36 (s, 3H), 1.45 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.6, 168.0, 138.7, 134.7, 130.2, 128.7, 126.2, 54.0, 52.8, 52.0, 28.6, 19.2; HRMS (ESI, *m*/*z*) calcd for $C_{17}H_{24}NO_5$ $[M + H]^+$ 322.1649, found 322.1647; IR (film) 732, 910, 1135, 1248, 1628, 1737, 2917, 3256 cm^{-1}.

*Dimethyl 2-(2-(tert-Butylcarbamoyl)-3-methoxyphenyl)malonate (**3l**).* Yield 99% (67 mg); white solid, mp 93−95 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (t, *J* = 8.1 Hz, 1H), 7.08 (d, *J* = 7.8 Hz, 1H), 6.90 (d, *J* = 8.3 Hz, 1H), 5.79 (s, 1H), 5.05 (s, 1H), 3.83 (s, 3H), 3.75 (s, 6H), 1.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.6, 165.7, 156.0, 131.4, 130.0, 128.0, 121.2, 111.0, 55.9, 53.7, 52.8, 51.9, 28.7; HRMS (ESI, *m*/*z*) calcd for $C_{17}H_{24}NO_6$ $[M + H]^+$ 338.1598, found 338.1605; IR (film) 732, 1148, 1264, 1471, 1660, 1737, 2958, 3373 cm^{-1}.

*Dimethyl 2-(2-(tert-Butylcarbamoyl)-3-fluorophenyl)malonate (**3m**).* Yield 99% (64 mg); white solid, mp 150−153 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39−7.28 (m, 2H), 7.08 (t, *J* = 8.7 Hz, 1H), 5.88 (s, 1H), 5.16 (s, 1H), 3.77 (s, 6H), 1.45 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.3, 163.0, 158.9 (d, *J* = 247.1 Hz), 132.6 (d, *J* = 3.4 Hz), 130.6 (d, *J* = 8.8 Hz), 126.2 (d, *J* = 18.5 Hz), 125.1 (d, *J* = 3.3 Hz), 115.7 (d, *J* = 22.5 Hz), 53.4, 52.9, 52.3, 28.6; HRMS (ESI, *m*/*z*) calcd for $C_{16}H_{21}FNO_5$ $[M + H]^+$ 326.1398, found 326.1400; IR (film) 736, 1146, 1244, 1552, 1640, 1734, 2925, 3269 cm^{-1}.

*Dimethyl 2-(5-Bromo-2-(tert-butylcarbamoyl)-4-methylphenyl)-malonate (**3n**).* Yield 94% (75 mg); white solid, mp 138−140 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (s, 1H), 7.31 (s, 1H), 6.04 (s, 1H), 5.26 (s, 1H), 3.78 (s, 6H), 2.39 (s, 3H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.5, 167.6, 138.4, 137.0, 133.5, 129.4, 129.2,

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126.4, 53.0, 53.0, 52.1, 28.6, 22.5; HRMS (ESI, m/z) calcd for $C_{17}H_{23}{}^{79}BrNO_5$ $[M + H]^+$ 400.0754, found 400.0762; IR (film) 733, 1024, 1219, 1435, 1651, 1739, 2955, 3314 cm^{-1}.

*Dimethyl 2-(3-Bromo-2-(tert-butylcarbamoyl)-4-methylphenyl)-malonate (**3o**).* Yield 96% (77 mg); white solid, mp 179−180 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, J = 8.0 Hz, 1H), 7.26 (d, J = 8.0 Hz, 1H), 5.61 (s, 1H), 4.87 (s, 1H), 3.76 (s, 6H), 2.41 (s, 3H), 1.46 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.3, 166.3, 140.2, 139.0, 130.9, 128.6, 127.8, 121.9, 53.9, 53.0, 52.4, 28.5, 23.2; HRMS (ESI, m/z) calcd for $C_{17}H_{23}{}^{79}BrNO_5$ $[M + H]^+$ 400.0754, found 400.0760; IR (film) 731, 1140, 1203, 1434, 1634, 1738, 2951, 3248 cm^{-1}.

*Dimethyl 2-(3-(tert-Butylcarbamoyl)naphthalen-2-yl)malonate (**3p**).* C1:C3 = 1:7, total yield 86% (61 mg). Data for the major product (C3-alkylated): white solid, mp 129−131 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.92 (s, 2H), 7.84−7.82 (m, 2H), 7.55−7.50 (m, 2H), 6.06 (s, 1H), 5.57 (s, 1H), 3.79 (s, 6H), 1.48 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 168.7, 135.3, 133.4, 132.1, 129.3, 128.1, 127.8, 127.7, 127.4, 127.1, 127.0, 53.7, 52.8, 52.0, 28.7; HRMS (ESI, m/z) calcd for $C_{20}H_{24}NO_5$ $[M + H]^+$ 358.1649, found 358.1655; IR (film) 757, 1147, 1220, 1529, 1653, 1736, 2954, 3310 cm^{-1}.

*Dimethyl 2-(1-(tert-Butylcarbamoyl)naphthalen-2-yl)malonate (**3q**).* Yield 76% (54 mg); white solid, mp 165−168 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.97−7.95 (m, 1H), 7.88−7.83 (m, 2H), 7.62 (d, J = 8.7 Hz, 1H), 7.56−7.50 (m, 2H), 5.93 (s, 1H), 5.10 (s, 1H), 3.77 (s, 6H), 1.54 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.6, 136.5, 132.9, 129.8, 129.2, 128.0, 127.2, 126.8, 126.3, 125.6, 125.3, 54.2, 53.0, 52.4, 28.7; HRMS (ESI, m/z) calcd for $C_{20}H_{24}NO_5$ $[M + H]^+$ 358.1649, found 358.1653; IR (film) 758, 1138, 1215, 1434, 1655, 1736, 2955, 3363 cm^{-1}.

*Dimethyl 2-(2-(tert-Butylcarbamoyl)benzo[b]thiophen-3-yl)-malonate (**3r**).* Yield 95% (69 mg); white solid, mp 126−127 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.83−7.78 (m, 2H), 7.42−7.40 (m, 2H), 7.24 (s, 1H), 5.78 (s, 1H), 3.78 (s, 6H), 1.46 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.4, 161.6, 138.7, 138.6, 138.3, 126.0, 125.7, 124.9, 123.0, 122.6, 53.1, 52.4, 50.2, 28.5; HRMS (ESI, m/z) calcd for $C_{18}H_{22}NO_5S$ $[M + H]^+$ 364.1213, found 364.1208; IR (film) 728, 1157, 1297, 1541, 1653, 1746, 2958, 3307 cm^{-1}.

*Dimethyl 2-(2-(tert-Butylcarbamoyl)benzofuran-3-yl)malonate (**3s**).* Yield 49% (34 mg); white solid, mp 164−167 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 7.9 Hz, 1H), 7.46 (d, J = 8.3 Hz, 1H), 7.42−7.38 (m, 1H), 7.30−7.27 (m, 1H), 6.59 (s, 1H), 6.43 (s, 1H), 3.76 (s, 6H), 1.50 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.1, 158.8, 153.1, 144.4, 127.3, 127.0, 123.7, 123.0, 116.9, 111.4, 52.8, 51.8, 47.6, 28.9; HRMS (ESI, m/z) calcd for $C_{18}H_{22}NO_6$ $[M + H]^+$ 348.1442, found 348.1444; IR (film) 751, 1030, 1154, 1276, 1637, 1741, 2922, 3331 cm^{-1}.

*Dimethyl 2-(2-(tert-Butylcarbamoyl)thiophen-3-yl)malonate (**3t**).* Yield 69% (43 mg); white solid, mp 84−85 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.30 (d, J = 5.1 Hz, 1H), 7.18 (d, J = 5.1 Hz, 1H), 6.30 (s, 1H), 5.70 (s, 1H), 3.77 (s, 6H), 1.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.4, 161.5, 136.0, 133.6, 130.0, 125.9, 52.9, 52.2, 51.0, 28.7; HRMS (ESI, m/z) calcd for $C_{14}H_{20}NO_5S$ $[M + H]^+$ 314.1057, found 314.1056; IR (film) 742, 1152, 1214, 1543, 1648, 1736, 2954, 3367 cm^{-1}.

*Dimethyl 2-(2-(tert-Butylcarbamoyl)furan-3-yl)malonate (**3u**).* Yield 52% (31 mg); white solid, mp 164−166 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.34 (d, J = 1.7 Hz, 1H), 6.69 (d, J = 1.7 Hz, 1H), 6.24 (s, 1H), 5.94 (s, 1H), 3.76 (s, 6H), 1.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.2, 158.2, 143.8, 142.0, 122.0, 113.7, 52.8, 51.5, 47.9, 28.9; HRMS (ESI, m/z) calcd for $C_{14}H_{20}NO_6$ $[M + H]^+$ 298.1285, found 298.1282; IR (film) 761, 1151, 1276, 1543, 1638, 1756, 2931, 3357 cm^{-1}.

*Diethyl 2-(2-(tert-Butylcarbamoyl)phenyl)malonate (**3v**).* Yield 84% (56 mg); white solid, mp 47−48 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.52−7.50 (m, 1H), 7.44−7.39 (m, 2H), 7.36−7.32 (m, 1H), 6.00 (s, 1H), 5.32 (s, 1H), 4.30−4.16 (m, 4H), 1.45 (s, 9H), 1.27 (t, J = 7.1 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.5, 168.4, 138.0, 130.4, 129.8, 129.6, 128.1, 127.2, 61.8, 54.0, 51.9, 28.6, 14.0; HRMS (ESI, m/z) calcd for $C_{18}H_{26}NO_5$ $[M + H]^+$ 336.1806, found 336.1810; IR (film) 739, 1031, 1218, 1526, 1658, 1732, 2977, 3374 cm^{-1}.

*Diisopropyl 2-(2-(tert-Butylcarbamoyl)phenyl)malonate (**3w**).* Yield 99% (72 mg) (2.5:1 for the amide bond); white solid, mp 71−73 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.55−7.51 (m, 1.19H), 7.44−7.38 (m, 1.82H), 7.35−7.31 (m, 0.84H), 6.03 (s, 0.74H), 5.93 (s, 0.19H), 5.24 (s, 0.70H), 5.11−5.05 (m, 2.09H), 4.82 (s, 0.33H), 1.45 (s, 9H), 1.28−1.24 (m, 12H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.5, 168.0, (167.0), (139.2), 138.2, 130.5, (129.8), 129.6, 129.5, (128.8), (128.8), 128.0, 127.3, 69.4, (54.6), (54.2), 51.9, 28.6, (28.4), 21.5; HRMS (ESI, m/z) calcd for $C_{20}H_{30}NO_5$ $[M + H]^+$ 364.2118, found 364.2129; IR (film) 738, 1101, 1180, 1220, 1660, 1729, 2982, 3361 cm^{-1}.

*1-Benzyl 3-Methyl 2-(2-(tert-Butylcarbamoyl)phenyl)malonate (**3x**).* Yield 85% (65 mg); colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 7.48−7.30 (m, 9H), 5.93 (s, 1H), 5.43 (s, 1H), 5.19 (AB quart, J = 4.7 Hz, 2H), 3.72 (s, 3H), 1.40 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.7, 168.4, 168.2, 137.8, 135.2, 130.3, 129.8, 129.7, 128.4, 128.2, 128.1, 128.0, 127.1, 67.4, 53.8, 52.7, 51.9, 28.5; HRMS (ESI, m/z) calcd for $C_{22}H_{26}NO_5$ $[M + H]^+$ 384.1806, found 384.1809; IR (film) 736, 1145, 1217, 1307, 1657, 1735, 2964, 3378 cm^{-1}.

*Dimethyl 2-(2-(Cyclohexylcarbamoyl)phenyl)malonate (**5a**).* Yield 83% (55 mg); white solid, mp 137−139 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.52−7.42 (m, 3H), 7.38−7.34 (m, 1H), 6.10 (d, J = 6.8 Hz, 1H), 5.35 (s, 1H), 3.98−3.90 (m, 1H), 3.76 (s, 6H), 2.00 (br, 1H), 1.76−1.73 (m, 2H), 1.66−1.63 (m, 1H), 1.46−1.37 (m, 2H), 1.27−1.18 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.8, 167.9, 136.9, 130.7, 130.2, 129.9, 128.2, 127.3, 53.8, 52.8, 48.7, 32.9, 25.4, 24.8; HRMS (ESI, m/z) calcd for $C_{18}H_{24}NO_5$ $[M + H]^+$ 334.1649, found 334.1642; IR (film) 731, 910, 1149, 1258, 1636, 1751, 2933, 3370 cm^{-1}.

*Dimethyl 2-(2-(Isopropylcarbamoyl)phenyl)malonate (**5b**).* Yield 84% (49 mg); white solid, mp 151−153 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.51−7.42 (m, 3H), 7.37−7.33 (m, 1H), 6.12 (d, J = 6.8 Hz, 1H), 5.36 (s, 1H), 4.26−4.18 (m, 1H), 3.76 (s, 6H), 1.23 (d, J = 6.6 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.8, 167.9, 136.7, 130.8, 130.2, 129.8, 128.2, 127.3, 53.8, 52.8, 41.9, 22.5; HRMS (ESI, m/z) calcd for $C_{15}H_{20}NO_5$ $[M + H]^+$ 294.1336, found 294.1333; IR (film) 706, 1147, 1260, 1546, 1629, 1749, 2955, 3266 cm^{-1}.

*Dimethyl 2-(2-(Propylcarbamoyl)phenyl)malonate (**5c**).* Yield 55% (32 mg); white solid, mp 98−100 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.51−7.42 (m, 3H), 7.38−7.34 (m, 1H), 6.34 (br, 1H), 5.37 (s, 1H), 3.76 (s, 6H), 3.37 (q, J = 6.8 Hz, 2H), 1.66−1.51 (m, 2H), 0.98 (t, J = 7.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.9, 168.7, 136.6, 130.9, 130.3, 130.0, 128.3, 127.4, 53.9, 52.8, 41.6, 22.7, 11.3; HRMS (ESI, m/z) calcd for $C_{15}H_{20}NO_5$ $[M + H]^+$ 294.1336, found 294.1335; IR (film) 741, 1148, 1261, 1435, 1640, 1736, 2961, 3302 cm^{-1}.

*Dimethyl 2-(2-(Adamantan-1-ylcarbamoyl)phenyl)malonate (**5d**).* Yield 90% (69 mg); white solid, mp 144−145 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.51−7.49 (m, 1H), 7.45−7.39 (m, 2H), 7.36−7.32 (m, 1H), 5.83 (s, 1H), 5.39 (s, 1H), 3.76 (s, 6H), 2.11 (s, 9H), 1.72 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.8, 168.1, 138.0, 130.2, 129.8, 129.7, 128.2, 127.2, 53.5, 52.8, 52.7, 41.4, 36.2, 29.4; HRMS (ESI, m/z) calcd for $C_{22}H_{28}NO_5$ $[M + H]^+$ 386.1962, found 386.1960; IR (film) 729, 1148, 1306, 1524, 1652, 1736, 2907, 3365 cm^{-1}.

*Dimethyl 2-(2-(Diisopropylcarbamoyl)phenyl)malonate (**5e**).* Yield 96% (64 mg); white solid, mp 94−96 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, J = 7.6 Hz, 1H), 7.41−7.36 (m, 1H), 7.35−7.31 (m, 1H), 7.17 (d, J = 7.4 Hz, 1H), 4.92 (s, 1H), 3.75 (s, 3H), 3.74 (s, 3H), 3.72−3.67 (m, 1H), 3.56−3.45 (m, 1H), 1.57 (t, J = 7.6 Hz, 6H), 1.12 (d, J = 6.6 Hz, 3H), 1.07 (d, J = 6.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.2, 168.8, 168.2, 138.6, 129.8, 129.4, 128.6, 128.0, 124.8, 53.7, 52.9, 52.8, 50.9, 45.9, 20.6, 20.5, 20.5, 20.3; HRMS (ESI, m/z) calcd for $C_{18}H_{26}NO_5$ $[M + H]^+$ 336.1806, found 336.1802; IR (film) 731, 1032, 1147, 1341, 1436, 1626, 1738, 2936 cm^{-1}.

*Dimethyl 2-(2-(Dimethylcarbamoyl)phenyl)malonate (**5f**).* Yield 45% (64 mg); colorless oil; ^1H NMR (400 MHz, $CDCl_3$) δ 7.60−7.58 (m, 1H), 7.44−7.40 (m, 1H), 7.38−7.34 (m, 1H), 7.24−7.22 (m, 1H),

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4.88 (s, 1H), 3.75 (s, 6H), 3.12 (s, 3H), 2.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.2, 168.4, 136.8, 129.8, 129.2, 128.1, 126.2, 53.8, 52.9, 39.0, 34.8; HRMS (ESI, m/z) calcd for $C_{14}H_{18}NO_5$ $[M + H]^+$ 280.1180, found 280.1177; IR (film) 731, 915, 1195, 1266, 1436, 1629, 1737, 2919 cm^{-1}.

*Dimethyl 2-(2-(Morpholine-4-carbonyl)phenyl)malonate (**5g**).* Yield 75% (48 mg); white solid, mp 99−100 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, J = 7.8 Hz, 1H), 7.45−7.42 (m, 1H), 7.39−7.35 (m, 1H), 7.22 (d, J = 7.5 Hz, 1H), 4.94 (s, 1H), 3.94−3.57 (m, 12H), 3.26 (br, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.8, 135.8, 130.1, 129.8, 129.5, 128.1, 126.1, 66.8, 66.7, 53.6, 52.9, 47.7, 42.1; HRMS (ESI, m/z) calcd for $C_{16}H_{20}NO_6$ $[M + H]^+$ 322.1285, found 322.1280; IR (film) 731, 1019, 1114, 1280, 1432, 1632, 1736, 2954 cm^{-1}.

*Dimethyl 2-(2-Pivaloylphenyl)malonate (**5h**).* Yield 55% (32 mg); colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, J = 8.0 Hz, 1H), 7.45−7.41 (m, 1H), 7.37−7.31 (m, 2H), 4.63 (s, 1H), 3.75 (s, 6H), 1.28 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 213.1, 168.4, 140.6, 130.3, 129.7, 129.4, 127.1, 125.2, 54.1, 52.9, 45.0, 27.6; HRMS (ESI, m/z) calcd for $C_{16}H_{21}O_5$ $[M + H]^+$ 293.1384, found 293.1380; IR (film) 746, 965, 1147, 1276, 1435, 1682, 1739, 2956 cm^{-1}.

*Dimethyl 2-(2-Isobutyrylphenyl)malonate (**5i**).* Yield 61% (34 mg); yellow solid, mp 51−54 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, J = 7.6 Hz, 1H), 7.54−7.48 (m, 2H), 7.45−7.41 (m, 1H), 5.25 (s, 1H), 3.77 (s, 6H), 3.50−3.40 (m, 1H), 1.18 (d, J = 6.9 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 207.9, 168.9, 137.5, 132.5, 131.6, 130.5, 128.2, 128.0, 54.2, 52.7, 38.0, 18.6; HRMS (ESI, m/z) calcd for $C_{15}H_{19}O_5$ $[M + H]^+$ 279.1227, found 279.1224, calcd for $C_{15}H_{18}NaO_5$ $[M + Na]^+$ 301.1046, found 301.1045; IR (film) 732, 979, 1148, 1228, 1435, 1682, 1738, 2923 cm^{-1}.

*Dimethyl 2-(2-Benzoylphenyl)malonate (**5j**).* Yield 34% (21 mg); yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (d, J = 8.3 Hz, 2H), 7.62−7.56 (m, 3H), 7.48−7.40 (m, 4H), 5.14 (s, 1H), 3.73 (s, 6H), 3.50−3.40 (m, 1H), 1.18 (d, J = 6.9 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.5, 168.6, 138.1, 137.5, 133.2, 132.4, 131.1, 130.4, 130.3, 130.0, 128.4, 127.4, 54.0, 52.8; HRMS (ESI, m/z) calcd for $C_{18}H_{17}O_5$ $[M + H]^+$ 313.1070, found 313.1067; IR (film) 717, 1022, 1151, 1257, 1435, 1662, 1739, 2925 cm^{-1}.

*Dimethyl 2-(2-Pivalamidophenyl)malonate (**5k**).* Yield 70% (43 mg); white solid, mp 79−81 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.03 (s, 1H), 7.79 (d, J = 8.1 Hz, 1H), 7.38−7.34 (m, 1H), 7.22−7.20 (m, 1H), 7.15−7.11 (m, 1H), 4.66 (s, 1H), 3.74 (s, 6H), 1.30 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.2, 169.4, 137.0, 131.5, 129.2, 126.5, 125.7, 125.2, 56.8, 53.1, 39.5, 27.4; HRMS (ESI, m/z) calcd for $C_{16}H_{22}NO_5$ $[M + H]^+$ 308.1492, found 308.1490; IR (film) 749, 1155, 1300, 1441, 1680, 1726, 2958, 3353 cm^{-1}.

*Dimethyl 2-(2-(2-(tert-Butylamino)-2-oxoethyl)phenyl)malonate (**5l**).* Yield 56% (36 mg); white solid, mp 87−89 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48−7.46 (m, 1H), 7.35−7.27 (m, 3H), 5.34 (s, 1H), 4.90 (s, 1H), 3.76 (s, 6H), 3.54 (s, 2H), 1.24 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.2, 168.6, 134.2, 131.8, 130.9, 130.2, 128.9, 128.0, 53.8, 52.9, 51.2, 42.5, 28.4; HRMS (ESI, m/z) calcd for $C_{17}H_{24}NO_5$ $[M + H]^+$ 322.1649, found 322.1642; IR (film) 735, 1148, 1224, 1434, 1651, 1737, 2958, 3321 cm^{-1}.

*Methyl 2-(2-(tert-Butylcarbamoyl)phenyl)acetate (**6a**).* Yield 86% (43 mg); colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46−7.44 (m, 1H), 7.36−7.27 (m, 2H), 7.22−7.20 (m, 1H), 6.26 (s, 1H), 3.86 (s, 2H), 3.70 (s, 3H), 1.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.5, 168.9, 138.1, 131.4, 130.8, 129.7, 127.5, 127.4, 52.0, 51.7, 38.6, 28.6; HRMS (ESI, m/z) calcd for $C_{14}H_{20}NO_3$ $[M + H]^+$ 250.1438, found 250.1440; IR (film) 732, 1165, 1220, 1530, 1655, 1738, 2965, 3336 cm^{-1}.

*Methyl 2-(2-(tert-Butylcarbamoyl)-5-methoxyphenyl)acetate (**6b**).* Yield 84% (47 mg); white solid, mp 64−65 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (d, J = 8.5 Hz, 1H), 6.80 (dd, J = 2.5, 8.5 Hz, 1H), 6.73 (d, J = 2.5 Hz, 1H), 6.23 (s, 1H), 3.86 (s, 2H), 3.80 (s, 3H), 3.71 (s, 3H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 168.7, 160.4, 133.5, 130.6, 129.3, 116.4, 112.4, 55.2, 52.1, 51.6, 38.9, 28.7; HRMS (ESI, m/z) calcd for $C_{15}H_{22}NO_4$ $[M + H]^+$ 280.1543, found 280.1545; IR (film) 727, 1163, 1250, 1497, 1648, 1737, 2960, 3338 cm^{-1}.

*Methyl 2-(2-(tert-Butylcarbamoyl)-5-nitrophenyl)acetate (**6c**).* Yield 87% (51 mg); white solid, mp 86−88 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (dd, J = 2.1, 8.4 Hz, 1H), 8.09 (d, J = 2.1 Hz, 1H), 7.61 (d, J = 8.4 Hz, 1H), 6.31 (s, 1H), 3.94 (s, 2H), 3.75 (s, 3H), 1.45 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 166.9, 148.0, 143.8, 133.4, 128.7, 125.9, 122.5, 52.4, 52.3, 38.4, 28.5; HRMS (ESI, m/z) calcd for $C_{14}H_{19}N_2O_5$ $[M + H]^+$ 295.1288, found 295.1292; IR (film) 734, 1220, 1348, 1525, 1648, 1739, 2966, 3303 cm^{-1}.

*Methyl 2-(2-(tert-Butylcarbamoyl)-5-(trifluoromethyl)phenyl)acetate (**6d**).* Yield 84% (53 mg); white solid, mp 75−77 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (s, 2H), 7.48 (s, 1H), 6.27 (s, 1H), 3.91 (s, 2H), 3.73 (s, 3H), 1.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.9, 167.7, 141.5, 132.4, 131.7 (q, J = 32.6 Hz), 128.2, 127.8 (q, J = 3.7 Hz), 124.5 (q, J = 3.7 Hz), 123.5 (q, J = 272.6 Hz), 52.3, 52.1, 38.5, 28.6; HRMS (ESI, m/z) calcd for $C_{15}H_{19}F_3NO_3$ $[M + H]^+$ 318.1312, found 318.1313; IR (film) 842, 1127, 1218, 1330, 1538, 1647, 1741, 3313 cm^{-1}.

*Methyl 2-(2-(tert-Butylcarbamoyl)-5-chlorophenyl)acetate (**6e**).* Yield 83% (47 mg); white solid, mp 73−75 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (d, J = 8.2 Hz, 1H), 7.26 (dd, J = 2.0, 8.2 Hz, 1H), 7.21 (d, J = 2.0 Hz, 1H), 6.27 (s, 1H), 3.83 (s, 2H), 3.72 (s, 3H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.0, 167.9, 136.5, 135.4, 133.4, 130.8, 129.0, 127.6, 52.2, 51.9, 38.4, 28.6; HRMS (ESI, m/z) calcd for $C_{14}H_{19}ClNO_3$ $[M + H]^+$ 284.1048, found 284.1048; IR (film) 830, 1167, 1220, 1538, 1645, 1739, 2965, 3303 cm^{-1}.

*Methyl 2-(2-(tert-Butylcarbamoyl)-5-iodophenyl)acetate (**6f**).* Yield 88% (66 mg); colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (dd, J = 1.4, 8.1 Hz, 1H), 7.58 (d, J = 1.4 Hz, 1H), 7.18 (d, J = 8.1 Hz, 1H), 6.26 (s, 1H), 3.79 (s, 2H), 3.72 (s, 3H), 1.42 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.0, 168.0, 139.6, 137.6, 136.5, 133.5, 129.1, 95.7, 52.2, 51.9, 38.1, 28.6; HRMS (ESI, m/z) calcd for $C_{14}H_{19}INO_3$ $[M + H]^+$ 376.0404, found 376.0403; IR (film) 882, 1167, 1219, 1533, 1644, 1738, 2968, 3320 cm^{-1}.

*Methyl 2-(2-(tert-Butylcarbamoyl)-4-methylphenyl)acetate (**6g**).* Yield 93% (49 mg); white solid, mp 69−70 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.27 (s, 1H), 7.12 (AB quart, J = 7.8 Hz, 2H), 6.28 (s, 1H), 3.80 (s, 2H), 3.70 (s, 3H), 2.34 (s, 3H), 1.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.8, 169.0, 138.0, 137.2, 130.7, 130.4, 128.2, 128.2, 52.0, 51.6, 38.2, 28.6, 20.9; HRMS (ESI, m/z) calcd for $C_{15}H_{22}NO_3$ $[M + H]^+$ 264.1594, found 264.1596; IR (film) 822, 1163, 1221, 1530, 1651, 1739, 2969, 3321 cm^{-1}.

*Methyl 2-(2-(tert-Butylcarbamoyl)-3-methoxyphenyl)acetate (**6h**).* Yield 95% (53 mg); white solid, mp 92−93 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28−7.24 (m, 1H), 6.85−6.81 (m, 2H), 5.97 (s, 1H), 3.83 (s, 3H), 3.73 (s, 2H), 3.70 (s, 3H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.3, 166.4, 156.3, 132.6, 129.8, 128.1, 122.7, 110.2, 55.9, 52.0, 51.7, 38.3, 28.7; HRMS (ESI, m/z) calcd for $C_{15}H_{22}NO_4$ $[M + H]^+$ 280.1543, found 280.1546; IR (film) 764, 1078, 1263, 1470, 1660, 1736, 2962, 3376 cm^{-1}.

*Methyl 2-(5-Bromo-2-(tert-butylcarbamoyl)-4-methylphenyl)-acetate (**6i**).* Yield 86% (59 mg); white solid, mp 97−99 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39 (s, 1H), 7.32 (s, 1H), 6.30 (s, 1H), 3.78 (s, 2H), 3.72 (s, 3H), 2.38 (s, 3H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.3, 168.0, 137.3, 137.2, 134.4, 130.4, 129.8, 126.0, 52.2, 51.8, 37.8, 28.6, 22.3; HRMS (ESI, m/z) calcd for $C_{15}H_{21}{}^{79}BrNO_3$ $[M + H]^+$ 342.0699, found 342.0698; IR (film) 733, 1165, 1220, 1553, 1644, 1739, 2969, 3327 cm^{-1}.

*Methyl 2-(3-Bromo-2-(tert-butylcarbamoyl)-4-methylphenyl)-acetate (**6j**).* Yield 92% (63 mg); white solid, mp 111−114 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.18 (d, J = 7.8 Hz, 1H), 7.08 (d, J = 7.8 Hz, 1H), 5.81 (s, 1H), 3.71 (s, 3H), 3.68 (s, 2H), 2.39 (s, 3H), 1.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.1, 166.9, 140.4, 137.9, 130.7, 129.6, 129.0, 122.2, 52.1, 52.1, 38.2, 28.5, 23.1; HRMS (ESI, m/z) calcd for $C_{15}H_{21}{}^{79}BrNO_3$ $[M + H]^+$ 342.0699, found 342.0700; IR (film) 731, 1170, 1221, 1529, 1655, 1737, 2964, 3307 cm^{-1}.

*Methyl 2-(3-(tert-Butylcarbamoyl)naphthalen-2-yl)acetate (**6k**).* C3:C1 > 15:1, total yield 93% (56 mg); white solid, mp 139−140 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (s, 1H), 7.84−7.76 (m, 2H), 7.66

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(s, 1H), 7.50−7.47 (m, 2H), 6.19 (s, 1H), 4.06 (s, 2H), 3.71 (s, 3H), 1.48 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.6, 169.2, 135.9, 133.6, 131.9, 130.2, 129.2, 127.9, 127.4, 127.2, 127.1, 126.5, 52.0, 51.8, 38.8, 28.6; HRMS (ESI, m/z) calcd for $C_{18}H_{22}NO_3$ $[M + H]^+$ 300.1594, found 300.1596; IR (film) 759, 1165, 1253, 1536, 1659, 1713, 2969, 3310 cm^{-1}.

*Methyl 2-(1-(tert-Butylcarbamoyl)naphthalen-2-yl)acetate (**6l**).* Yield 84% (50 mg); yellow solid, mp 99−101 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, J = 8.4 Hz, 1H), 7.82−7.78 (m, 2H), 7.55−7.46 (m, 2H), 7.30 (d, J = 8.4 Hz, 1H), 6.28 (s, 1H), 3.90 (br, 2H), 3.72 (s, 3H), 1.52 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 168.2, 136.1, 132.5, 130.2, 129.1, 127.9, 127.3, 127.0, 126.2, 125.2, 52.2, 52.1, 38.8, 28.7; HRMS (ESI, m/z) calcd for $C_{18}H_{22}NO_3$ $[M + H]^+$ 300.1594, found 300.1597; IR (film) 732, 1163, 1221, 1526, 1656, 1735, 2968, 3349 cm^{-1}.

*Methyl 2-(2-(tert-Butylcarbamoyl)benzo[b]thiophen-3-yl)acetate (**6m**).* Yield 95% (58 mg); white solid, mp 111−113 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82−7.79 (m, 2H), 7.43−7.38 (m, 2H), 7.32 (br, 1H), 4.12 (s, 2H), 3.74 (s, 3H), 1.50 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 162.1, 139.2, 138.8, 138.2, 127.2, 126.0, 124.7, 122.7, 122.6, 52.6, 52.3, 33.0, 28.8; HRMS (ESI, m/z) calcd for $C_{16}H_{20}NO_3S$ $[M + H]^+$ 306.1158, found 306.1159; IR (film) 757, 1219, 1298, 1541, 1652, 1719, 2966, 3321 cm^{-1}.

*Methyl 2-(2-(tert-Butylcarbamoyl)benzofuran-3-yl)acetate (**6n**).* Yield 57% (33 mg); colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (d, J = 7.8 Hz, 1H), 747−7.38 (m, 2H), 7.30−7.26 (m, 1H), 6.56 (s, 1H), 4.28 (s, 2H), 3.71 (s, 3H), 1.49 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.9, 159.1, 153.0, 144.34, 128.7, 126.9, 123.4, 121.0, 117.8, 111.5, 52.1, 51.6, 29.4, 28.9; HRMS (ESI, m/z) calcd for $C_{16}H_{20}NO_4$ $[M + H]^+$ 290.1387, found 290.1388; IR (film) 748, 1165, 1449, 1517, 1663, 1741, 2968, 3434 cm^{-1}.

*Methyl 2-(2-(tert-Butylcarbamoyl)thiophen-3-yl)acetate (**6o**).* Yield 96% (49 mg); white solid, mp 56−58 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (d, J = 5.0 Hz, 1H), 6.92 (d, J = 5.0 Hz, 1H), 6.85 (br, 1H), 3.90 (s, 2H), 3.73 (s, 3H), 1.45 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.0, 161.8, 136.9, 133.6, 130.3, 126.7, 52.4, 52.0, 34.8, 28.8; HRMS (ESI, m/z) calcd for $C_{12}H_{18}NO_3S$ $[M + H]^+$ 256.1002, found 256.1004; IR (film) 720, 1219, 1299, 1545, 1649, 1736, 2964, 3313 cm^{-1}.

*Methyl 2-(2-(tert-Butylcarbamoyl)furan-3-yl)acetate (**6p**).* Yield 66% (32 mg); colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (d, J = 1.7 Hz, 1H), 6.50 (d, J = 1.7 Hz, 1H), 6.23 (br, 1H), 4.02 (s, 2H), 3.71 (s, 3H), 1.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 158.7, 143.5, 141.9, 122.9, 114.5, 51.9, 51.3, 30.7, 29.0; HRMS (ESI, m/z) calcd for $C_{12}H_{18}NO_4$ $[M + H]^+$ 240.1230, found 240.1230, calcd for $C_{12}H_{17}NNaO_4$ $[M + Na]^+$ 262.1050, found 262.1055; IR (film) 748, 852, 1171, 1525, 1658, 1741, 2921, 3439 cm^{-1}.

*Methyl 2-(2-(Cyclohexylcarbamoyl)phenyl)acetate (**6q**).* Yield 76% (42 mg); white solid, mp 135−136 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, J = 7.4 Hz, 1H), 7.38−7.27 (m, 2H), 7.24 (d, J = 7.4 Hz, 1H), 6.45 (d, J = 5.2 Hz, 1H), 3.95−3.93 (m, 1H), 3.85 (s, 2H), 3.71 (s, 3H), 2.02−1.99 (m, 2H), 1.76−1.62 (m, 3H), 1.46−1.37 (m, 2H), 1.26−1.18 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.7, 168.3, 137.3, 131.6, 130.9, 129.9, 127.8, 127.5, 52.2, 48.6, 38.7, 32.9, 25.5, 24.8; HRMS (ESI, m/z) calcd for $C_{16}H_{22}NO_3$ $[M + H]^+$ 276.1594, found 276.1594, calcd for $C_{16}H_{21}NNaO_3$ $[M + Na]^+$ 298.1414, found 298.1421; IR (film) 732, 909, 1247, 1541, 1628, 1730, 2933, 3284 cm^{-1}.

*Methyl 2-(2-(Isopropylcarbamoyl)phenyl)acetate (**6r**).* Yield 83% (39 mg); white solid, mp 81−83 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, J = 7.4 Hz, 1H), 7.38−7.28 (m, 2H), 7.23 (d, J = 7.4 Hz, 1H), 6.43 (s, 1H), 4.28−4.19 (m, 1H), 3.85 (s, 2H), 3.70 (s, 3H), 1.23 (d, J = 6.5 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.6, 168.4, 137.2, 131.6, 131.0, 130.0, 127.7, 127.4, 52.1, 41.8, 38.6, 22.6; HRMS (ESI, m/z) calcd for $C_{13}H_{18}NO_3$ $[M + H]^+$ 236.1281, found 236.1284, calcd for $C_{13}H_{17}NNaO_3$ $[M + Na]^+$ 258.1101, found 258.1101; IR (film) 731, 1170, 1259, 1533, 1638, 1736, 2970, 3292 cm^{-1}.

*Methyl 2-(2-(Adamantan-1-ylcarbamoyl)phenyl)acetate (**6s**).* Yield 75% (49 mg); white solid, mp 90−91 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (dd, J = 1.3, 7.5 Hz, 1H), 7.36−7.28 (m, 2H), 7.21 (dd, J = 1.3, 7.5 Hz, 1H), 6.09 (s, 1H), 3.87 (s, 2H), 3.72 (s, 3H), 2.10 (s, 9H), 1.71 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.5, 168.6, 138.2, 131.4, 130.8, 129.7, 127.6, 127.4, 52.5, 52.1, 41.4, 38.6, 36.3, 29.4; HRMS (ESI, m/z) calcd for $C_{20}H_{26}NO_3$ $[M + H]^+$ 328.1907, found 328.1909; IR (film) 729, 1162, 1306, 1527, 1649, 1738, 2906, 3362 cm^{-1}.

*Methyl 2-(2-(Diisopropylcarbamoyl)phenyl)acetate (**6t**).* Yield 90% (50 mg); colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32−7.24 (m, 3H), 7.15 (d, J = 7.2 Hz, 1H), 3.86−3.73 (m, 2H), 3.68 (s, 3H), 3.53−3.47 (m, 2H), 1.56 (d, J = 6.8 Hz, 6H), 1.13−1.09 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.8, 169.8, 138.4, 130.8, 130.7, 128.4, 126.9, 125.0, 51.9, 50.8, 45.8, 37.7, 20.7, 20.6, 20.5, 20.4; HRMS (ESI, m/z) calcd for $C_{16}H_{24}NO_3$ $[M + H]^+$ 278.1757, found 278.1755; IR (film) 731, 1162, 1213, 1338, 1436, 1628, 1739, 2966 cm^{-1}.

*2-(2-tert-Butylcarbamoyl)phenyl)acetic Acid (**7a**).* Yield 86% (40 mg); yellow solid, mp 146−148 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.47 (br, 1H), 7.46−7.39 (m, 3H), 7.32−7.28 (m, 1H), 6.37 (br, 1H), 3.68 (s, 2H), 1.49 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.7, 171.1, 135.3, 133.1, 131.6, 131.4, 127.7, 127.4, 53.0, 42.0, 28.5; HRMS (ESI, m/z) calcd for $C_{13}H_{18}NO_3$ $[M + H]^+$ 236.1281, found 236.1280; IR (film) 731, 1219, 1454, 1556, 1590, 1731, 2972, 3290 cm^{-1}.

*2-(2-(tert-Butylcarbamoyl)-5-methylphenyl)acetic Acid (**7b**).* Yield 86% (43 mg); yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.96 (br, 1H), 7.34 (d, J = 7.8 Hz, 1H), 7.21 (s, 1H), 7.10 (d, J = 7.8 Hz, 1H), 6.31 (br, 1H), 3.65 (s, 2H), 2.34 (s, 3H), 1.48 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.8, 171.2, 142.0, 133.2, 132.3, 128.3, 127.4, 52.9, 42.0, 28.5, 21.1; HRMS (ESI, m/z) calcd for $C_{14}H_{20}NO_3$ $[M + H]^+$ 250.1438, found 250.1439; IR (film) 732, 911, 1220, 1455, 1595, 1731, 2972, 3309 cm^{-1}.

*2-(2-(tert-Butylcarbamoyl)-5-methoxyphenyl)acetic Acid (**7c**).* Yield 99% (53 mg); yellow solid, mp 116−118 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.07 (br, 1H), 7.38 (d, J = 8.6 Hz, 1H), 6.92 (d, J = 2.5 Hz, 1H), 6.81 (dd, J = 2.5, 8.6 Hz, 1H), 6.09 (br, 1H), 3.82 (s, 3H), 3.69 (s, 3H), 1.48 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.0, 161.8, 135.7, 129.0, 127.3, 116.4, 113.7, 113.6, 55.5, 52.9, 42.5, 28.6; HRMS (ESI, m/z) calcd for $C_{14}H_{20}NO_4$ $[M + H]^+$ 266.1387, found 266.1385; IR (film) 732, 1251, 1456, 1548, 1603, 1731, 2972, 3307 cm^{-1}.

*2-(2-(tert-Butylcarbamoyl)-5-(trifluoromethyl)phenyl)acetic Acid (**7d**).* Yield 84% (51 mg); yellow solid, mp 132−135 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.83 (br, 1H), 7.59−7.52 (m, 3H), 6.63 (s, 1H), 3.74 (s, 2H), 1.47 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.9, 169.5, 139.2, 133.6, 132.8 (q, J = 33.0 Hz), 128.2, 128.1 (q, J = 3.6 Hz), 124.6 (q, J = 3.5 Hz), 123.2 (q, J = 272.7 Hz), 53.2, 41.0, 28.4; HRMS (ESI, m/z) calcd for $C_{14}H_{17}F_3NO_3$ $[M + H]^+$ 304.1155, found 304.1158; IR (film) 669, 730, 907, 1136, 1332, 1550, 1605, 1732 cm^{-1}.

*2-(2-(tert-Butylcarbamoyl)-5-nitrophenyl)acetic Acid (**7e**).* Yield 95% (53 mg); brown solid, mp 140−143 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.74 (br, 1H), 8.16 (d, J = 2.1 Hz, 1H), 8.10 (dd, J = 2.1, 8.4 Hz, 1H), 7.63 (d, J = 8.4 Hz, 1H), 6.54 (br, 1H), 3.83 (s, 2H), 1.48 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.0, 168.4, 148.6, 141.9, 134.4, 128.8, 126.1, 122.6, 53.3, 40.5, 28.4; HRMS (ESI, m/z) calcd for $C_{13}H_{17}N_2O_5$ $[M + H]^+$ 281.1132, found 281.1137; IR (film) 733, 913, 1222, 1349, 1522, 1655, 2963, 3300 cm^{-1}.

*2-(2-(tert-Butylcarbamoyl)-5-chlorophenyl)acetic Acid (**7f**).* Yield 96% (52 mg); brown solid, mp 158−161 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.83 (br, 1H), 7.40 (d, J = 8.3 Hz, 1H), 7.36 (s, 1H), 7.26 (d, J = 8.3 Hz, 1H), 6.48 (s, 1H), 3.66 (s, 2H), 1.48 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.4, 170.0, 137.2, 134.8, 133.9, 131.4, 128.9, 127.8, 53.1, 41.4, 28.4; HRMS (ESI, m/z) calcd for $C_{13}H_{17}ClNO_3$ $[M + H]^+$ 270.0892, found 270.0893; IR (film) 731, 907, 1220, 1458, 1584, 1721, 2928, 3252 cm^{-1}.

*2-(2-(tert-Butylcarbamoyl)-5-iodophenyl)acetic Acid (**7g**).* Yield 93% (67 mg); gray solid, mp 125−129 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.07 (br, 1H), 7.72 (s, 1H), 7.62 (d, J = 8.1 Hz, 1H), 7.18 (d, J = 8.1 Hz, 1H), 6.56 (s, 1H), 3.61 (s, 2H), 1.47 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6, 170.1, 140.1, 136.7, 134.9, 134.7, 129.0,

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97.7, 53.1, 41.1, 28.4; HRMS (ESI, *m*/*z*) calcd for $C_{13}H_{17}INO_3$ [M + H]$^+$ 362.0248, found 362.0252; IR (film) 733, 894, 1218, 1455, 1580, 1727, 2966, 3291 cm^{-1}.

*2-(2-(tert-Butylcarbamoyl)-3-methoxyphenyl)acetic Acid (**7h**).* Yield 99% (53 mg); yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (t, *J* = 8.0 Hz, 1H), 7.02 (d, *J* = 7.7 Hz, 1H), 6.88 (d, *J* = 8.3 Hz, 1H), 6.45 (s, 1H), 3.87 (s, 3H), 3.63 (s, 2H), 1.48 (s, 9H), acid proton was not found; ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6, 168.0, 156.4, 135.0, 131.5, 124.5, 123.6, 110.6, 56.1, 52.8, 42.1, 28.6; HRMS (ESI, *m*/*z*) calcd for $C_{14}H_{20}NO_4$ [M + H]$^+$ 266.1387, found 266.1388; IR (film) 733, 911, 1081, 1264, 1470, 1596, 1730, 2974 cm^{-1}.

*2-(3-(tert-Butylcarbamoyl)naphthalen-2-yl)acetic Acid (**7i**).* Yield 90% (52 mg); yellow solid, mp 168−171 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 13.76 (br, 1H), 7.92 (s, 1H), 7.80 (d, *J* = 8.0 Hz, 1H), 7.77 (s, 1H), 7.72 (d, *J* = 7.9 Hz, 1H), 7.54−7.45 (m, 2H), 6.55 (s, 1H), 3.78 (s, 2H), 1.53 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.0, 171.3, 134.1, 133.2, 131.5, 130.7, 129.1, 128.1, 127.9, 127.8, 127.5, 127.0, 53.1, 41.8, 28.5; HRMS (ESI, *m*/*z*) calcd for $C_{17}H_{20}NO_3$ [M + H]$^+$ 286.1438, found 286.1442; IR (film) 733, 1166, 1218, 1449, 1527, 1611, 1739, 2969 cm^{-1}.

*2-(1-(tert-Butylcarbamoyl)naphthalen-2-yl)acetic Acid (**7j**).* Yield 81% (43 mg); yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, *J* = 8.4 Hz, 1H), 7.83−7.78 (m, 2H), 7.56−7.47 (m, 2H), 7.34 (d, *J* = 8.4 Hz, 1H), 6.29 (s, 1H), 3.73 (s, 2H), 1.52 (s, 9H), acid proton was not found; ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.9, 169.7, 134.2, 132.6, 130.0, 129.8, 129.0, 128.3, 127.4, 126.4, 124.5, 53.0, 40.9, 28.6; HRMS (ESI, *m*/*z*) calcd for $C_{17}H_{20}NO_3$ [M + H]$^+$ 286.1438, found 286.1445; IR (film) 733, 1220, 1366, 1534, 1611, 1723, 2956, 3316 cm^{-1}.

*2-(2-(tert-Butylcarbamoyl)benzo[b]thiophen-3-yl)acetic Acid (**7k**).* Yield 84% (49 mg); yellow solid, mp 129−132 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.89 (br, 1H), 7.99−7.97 (m, 1H), 7.79−7.77 (m, 1H), 7.48−7.44 (m, 2H), 6.42 (s, 1H), 4.04 (s, 2H), 1.50 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.4, 164.3, 139.1, 138.2, 132.6, 132.3, 127.3, 125.6, 123.6, 122.5, 53.4, 35.6, 28.6; HRMS (ESI, *m*/*z*) calcd for $C_{15}H_{18}NO_3S$ [M + H]$^+$ 292.1002, found 292.1005, calcd for $C_{15}H_{17}NNaO_3S$ [M + Na]$^+$ 314.0821, found 314.0828; IR (film) 729, 909, 1218, 1305, 1547, 1596, 1716, 2972 cm^{-1}.

*2-(2-(tert-Butylcarbamoyl)benzofuran-3-yl)acetic Acid (**7l**).* Yield 62% (34 mg); yellow oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.78 (br, 1H), 7.73 (d, *J* = 7.8 Hz, 1H), 7.50−7.46 (m, 2H), 7.36−7.27 (m, 1H), 6.72 (s, 1H), 4.04 (s, 2H), 1.53 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.6, 160.8, 153.4, 143.64, 128.0, 128.0, 124.0, 121.0, 119.2, 111.7, 52.8, 31.9, 28.7; HRMS (ESI, *m*/*z*) calcd for $C_{15}H_{18}NO_4$ [M + H]$^+$ 276.1230, found 276.1236; IR (film) 732, 1221, 1366, 1453, 1555, 1724, 2965, 3258 cm^{-1}.

*2-(2-(tert-Butylcarbamoyl)thiophen-3-yl)acetic Acid (**7m**).* Yield 81% (39 mg); brown solid, mp 134−137 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.57 (br, 1H), 7.35 (d, *J* = 5.0 Hz, 1H), 7.05 (d, *J* = 5.0 Hz, 1H), 6.18 (s, 1H), 3.86 (s, 2H), 1.48 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 164.0, 138.1, 132.1, 131.6, 127.5, 53.2, 37.8, 28.6; HRMS (ESI, *m*/*z*) calcd for $C_{11}H_{16}NO_3S$ [M + H]$^+$ 242.0845, found 242.0850; IR (film) 732, 909, 1216, 1366, 1422, 1548, 1723, 2970 cm^{-1}.

*2-(2-(tert-Butylcarbamoyl)furan-3-yl)acetic Acid (**7n**).* Yield 42% (20 mg); brown oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.91 (br, 1H), 7.39 (d, *J* = 1.0 Hz, 1H), 6.50 (d, *J* = 1.0 Hz, 1H), 6.41 (br, 1H), 3.77 (s, 2H), 1.48 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.1, 160.3, 143.4, 143.0, 124.3, 115.4, 52.5, 34.0, 28.8; HRMS (ESI, *m*/*z*) calcd for $C_{11}H_{16}NO_4$ [M + H]$^+$ 226.1074, found 226.1072; IR (film) 767, 1188, 1406, 1533, 1611, 1655, 1735, 2970 cm^{-1}.

*Tetramethyl 2,2′-(2-(tert-Butylcarbamoyl)-1,3-phenylene)-dimalonate (**8a**).* Yield 92% (80 mg); yellow solid, mp 119−121 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56−7.54 (m, 2H), 7.44−7.40 (m, 1H), 5.91 (s, 1H), 4.93 (s, 2H), 3.76 (s, 12H), 1.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.7, 168.0, 166.8, 139.1, 129.4, 129.2, 53.9, 53.0, 52.4, 28.4; HRMS (ESI, *m*/*z*) calcd for $C_{21}H_{28}NO_9$ [M + H]$^+$ 438.1759, found 438.1764; IR (film) 731, 1147, 1201, 1311, 1663, 1736, 2959, 3362 cm^{-1}.

*Tetramethyl 2,2′-(2-(tert-Butylcarbamoyl)-5-methoxy-1,3-phenylene)dimalonate (**8b**).* Yield 90% (84 mg); white solid, mp 135−136 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.08 (s, 2H), 5.91 (s, 1H), 4.94 (s, 2H), 3.81 (s, 3H), 3.76 (s, 12H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.5, 166.8, 159.5, 132.0, 130.8, 114.7, 55.4, 53.8, 52.9, 52.2, 28.4; HRMS (ESI, *m*/*z*) calcd for $C_{22}H_{30}NO_{10}$ [M + H]$^+$ 468.1864, found 468.1862; IR (film) 732, 1147, 1309, 1436, 1660, 1737, 2953, 3368 cm^{-1}.

*Tetramethyl 2,2′-(2-(tert-Butylcarbamoyl)-5-chloro-1,3-phenylene)dimalonate (**8c**).* Yield 78% (74 mg); white solid, mp 141−143 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (s, 2H), 5.94 (s, 1H), 4.89 (s, 2H), 3.78 (s, 12H), 1.43 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.2, 165.9, 137.5, 135.1, 131.1, 129.4, 53.6, 53.1, 52.5, 28.4; HRMS (ESI, *m*/*z*) calcd for $C_{21}H_{27}ClNO_9$ [M + H]$^+$ 472.1369, found 472.1370; IR (film) 734, 1020, 1145, 1223, 1658, 1737, 2957, 3350 cm^{-1}.

*Tetramethyl 2,2′-(2-(tert-Butylcarbamoyl)-4-methoxy-1,3-phenylene)dimalonate (**8d**).* Yield 78% (73 mg); white solid, mp 163−165 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, *J* = 8.7 Hz, 1H), 6.97 (d, *J* = 8.7 Hz, 1H), 6.01 (s, 1H), 4.90 (s, 1H), 4.87 (s, 1H), 3.81 (s, 3H), 3.76−1.73 (m, 12H), 1.40 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.9, 168.4, 168.3, 166.5, 157.5, 140.3, 130.6, 121.4, 119.4, 112.2, 56.1, 53.1, 52.8, 52.5, 52.3, 51.2, 28.3; HRMS (ESI, *m*/*z*) calcd for $C_{22}H_{30}NO_{10}$ [M + H]$^+$ 468.1864, found 468.1861; IR (film) 731, 912, 1150, 1263, 1662, 1737, 2955, 3356 cm^{-1}.

*Dimethyl 2,2′-(2-(tert-Butylcarbamoyl)-1,3-phenylene)diacetate (**9a**).* Yield 90% (58 mg); white solid, mp 62−64 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30−7.26 (m, 1H), 7.19−7.17 (m, 2H), 6.27 (s, 1H), 3.71 (s, 10H), 1.42 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.1, 167.8, 139.1, 130.9, 129.4, 128.9, 52.0, 51.8, 38.4, 28.4; HRMS (ESI, *m*/*z*) calcd for $C_{17}H_{24}NO_5$ [M + H]$^+$ 322.1649, found 322.1647; IR (film) 779, 1019, 1162, 1526, 1661, 1736, 2953, 3352 cm^{-1}.

*Dimethyl 2,2′-(2-(tert-Butylcarbamoyl)-5-methyl-1,3-phenylene)-diacetate (**9b**).* Yield 85% (57 mg); white solid, mp 95−97 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.98 (s, 2H), 6.26 (s, 1H), 3.71 (s, 6H), 3.68 (s, 4H), 2.31 (s, 3H), 1.41 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.3, 168.1, 138.8, 136.5, 130.8, 130.1, 52.0, 51.8, 38.4, 28.4, 21.0; HRMS (ESI, *m*/*z*) calcd for $C_{18}H_{26}NO_5$ [M + H]$^+$ 336.1806, found 336.1802; IR (film) 860, 1164, 1222, 1528, 1659, 1736, 2956, 3361 cm^{-1}.

*Dimethyl 2,2′-(2-(tert-Butylcarbamoyl)-5-methoxy-1,3-phenylene)diacetate (**9c**).* Yield 91% (64 mg); white solid, mp 115−117 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.70 (s, 2H), 6.27 (s, 1H), 3.78 (s, 3H), 3.71 (s, 6H), 3.69 (s, 4H), 1.41 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.1, 167.9, 159.4, 132.6, 132.1, 114.8, 55.2, 52.1, 51.7, 38.7, 28.4; HRMS (ESI, *m*/*z*) calcd for $C_{18}H_{26}NO_6$ [M + H]$^+$ 352.1755, found 352.1749; IR (film) 734, 1167, 1320, 1525, 1655, 1731, 2966, 3376 cm^{-1}.

*Dimethyl 2,2′-(2-(tert-Butylcarbamoyl)-5-(trifluoromethyl)-1,3-phenylene)diacetate (**9d**).* Yield 82% (64 mg); white solid, mp 108−110 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (s, 2H), 6.28 (s, 1H), 3.77 (s, 4H), 3.74 (s, 6H), 1.42 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.5, 166.7, 142.3, 132.1, 131.1 (q, *J* = 32.7 Hz), 126.4 (q, *J* = 3.7 Hz), 123.4 (q, *J* = 272.6 Hz), 52.3, 38.4, 28.4; HRMS (ESI, *m*/*z*) calcd for $C_{18}H_{23}F_3NO_5$ [M + H]$^+$ 390.1523, found 390.1526; IR (film) 734, 906, 1156, 1222, 1630, 1739, 2960, 3255 cm^{-1}.

*Dimethyl 2,2′-(2-(tert-Butylcarbamoyl)-5-iodo-1,3-phenylene)-diacetate (**9e**).* Yield 82% (73 mg); white solid, mp 112−115 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (s, 2H), 6.28 (s, 1H), 3.72 (s, 6H), 3.65 (s, 4H), 1.40 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.6, 167.0, 138.7, 138.2, 132.8, 94.5, 52.2, 52.0, 38.0, 28.4; HRMS (ESI, *m*/*z*) calcd for $C_{17}H_{23}INO_5$ [M + H]$^+$ 448.0615, found 448.0651; calcd for $C_{17}H_{22}INNaO_5$ [M + Na]$^+$ 470.0435, found 470.0442; IR (film) 701, 744, 1228, 1566, 1677, 2925 cm^{-1}.

*Dimethyl 2,2′-(2-(tert-Butylcarbamoyl)-4-methoxy-1,3-phenylene)diacetate (**9f**).* Yield 93% (65 mg); white solid, mp 69−71 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (d, *J* = 8.5 Hz, 1H), 6.83 (d, *J* = 8.7 Hz, 1H), 6.20 (s, 1H), 3.80 (s, 3H), 3.71−3.70 (m, 10H), 1.40 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.5, 172.4, 167.8, 156.8, 140.4, 130.5, 122.5, 119.8, 110.8, 55.7, 52.0, 51.8, 37.7, 32.8, 28.5; HRMS (ESI, *m*/*z*) calcd for $C_{18}H_{26}NO_6$ [M + H]$^+$ 352.1755, found 352.1748; IR (film) 731, 1072, 1160, 1268, 1662, 1736, 2956, 3396 cm^{-1}.

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*Dimethyl 2,2′-(2-(tert-Butylcarbamoyl)naphthalene-1,3-diyl)-diacetate (**9g**).* Yield 51% (38 mg) [the monoalkylated product (**6k**) was isolated in 47% yield (28 mg)], white solid, mp 147−149 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, J = 8.0 Hz, 1H), 7.80 (d, J = 7.4 Hz, 1H), 7.70 (s, 1H), 7.55−7.47 (m, 2H), 6.41 (s, 1H), 4.19−3.97 (m, 4H), 3.73−3.72 (m, 6H), 1.45 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.2, 172.1, 168.4, 137.8, 133.3, 131.2, 129.8, 128.5, 128.1, 127.0, 126.8, 126.6, 123.7, 52.3, 52.0, 52.0, 38.7, 35.6, 28.5; HRMS (ESI, m/z) calcd for $C_{21}H_{26}NO_5$ $[M + H]^+$ 372.1806, found 372.1809; IR (film) 730, 1163, 1220, 1525, 1659, 1736, 2955, 3370 cm^{-1}.

■ ASSOCIATED CONTENT

Supporting Information

Experiments for mechanistic studies, copies of ^{1}H and ^{13}C NMR spectra, and X-ray crystallographic data (CIF) for products **3a**, **3p**, and **6c**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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