Palladium/Norbornene-Catalyzed Decarbonylative Difunctionalization of Thioesters

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ABSTRACT: The transition-metal-catalyzed decarboxylation of aryl carboxylic acids has drawn significant attention as an efficient and practical tool for the synthesis of substituted arenes. However, the decarboxylative construction of polysubstituted arenes with different contiguous substituents has not been widely reported. Herein, we describe a novel decarbonylative Catellani reaction via palladium-catalyzed, norbornene (NBE)-mediated polyfunctionalization of aromatic thioesters, which serve as readily available carboxylic acid derivatives. A variety of alkyl, aryl, and sulfur moieties could be conveniently introduced into the ipso-positions of the aromatic thioesters. By combining carbonyl-directed C–H functionalization and the classical Catellani reaction, our protocol allows for the construction of 1,2,3-trisubstituted and 1,2,3,4-tetrasubstituted arenes from simple aromatic acids. Furthermore, the late-stage functionalization of a series of drug molecules highlights the potential utility of the reaction.

KEYWORDS: aryl thioester, decarbonylative Catellani reaction, multifunctionalization, cross-coupling, C–H activation

Polysubstituted arenes are prevalent in natural products, pharmaceuticals, and organic materials (Figure 1a). 1,2 Among various methods to construct polysubstituted arenes, the Pd/NBE catalyzed Catellani-type reactions offer distinct access to multisubstituted arenes (Figure 1b). 3–8 The high ring strain of the [2.2.1] bicyclic scaffold together with its structural rigidity enables the norbornene (NBE) to function as a transient mediator to create intermolecular carbopalladation and final extrusion. 9,10 In 1997, Catellani and co-workers disclosed the first cooperative Pd/NBE-catalyzed reaction using aryl iodides, allowing for the expeditious synthesis of ipso-ortho bifunctionalized arenes. 11–13 Following this initial breakthrough, Lautens, Dong, and others have greatly enriched this chemistry in the past few years, making this methodology a reliable route for the synthesis of complex arenes. 14–28 It is noteworthy that the Dong group recently synthesized tetrasubstituted alkenes via a palladium/NBE catalyzed alkenyl Catellani reaction. 29 Furthermore, Pd(II)-initiated Catellani-type reactions with arylboron species have also been reported by Zhou, Zhang, Dong, and co-workers recently. 30–32 With NBE as a transient mediator, Bach first developed a Pd(II)-initiated 2-functionalization of indoles and pyrroles. 33–35 In 2015, Yu and Dong independently reported the meta-selective C–H alkylation and arylation of arene by combining the chelation directed ortho C–H activation and Pd/NBE chemistry. 36,37 Subsequently, this norbornene relay approach has been extensively applied in meta- and para-C–H activations. 38–41 Recently, the Dong group reported a distal alkyl C–H functionalization through this directed Pd/NBE cooperative catalysis. 42

The benign syntheses and structural diversities enable the carboxylic acids to play an important role in organic chemistry. 43–46 Over the past few years, transition-metal-catalyzed transformations of aryl carboxylic acids into new C–C and C–heteroatom bonds have drawn significant attention as an alternative to traditional cross-coupling procedures. In 2002, Myers et al. disclosed a Pd-catalyzed decarboxylative Heck-type olefination of aromatic acids. 47 Subsequently, Gooßen et al. reported a Pd/Cu-cocatalyzed decarboxylative coupling between aromatic acids and aryl halides to form biaryl skeletons. 48 Since these seminal works, tremendous progress has been made in the area of decarboxylative cross-coupling reactions of aromatic acids. 49–51 Moreover, carboxyl groups are efficient directing groups in C–H functionalization. 52–55 Carbonyl-directed ortho-C–H functionalization and subsequent ipso-decarboxylation is a promising approach for the construction of polysubstituted arenes. 56–59 However, these...
reactions mainly focus on decarboxylative protonation. Thus, the development and validation of a general approach to achieve decarboxylative bis- and even polyfunctionalization of broadly available aromatic acids is still a challenge.60 Thioesters are common intermediates in both organic synthesis and biochemical processes.61 Compared with other carboxylic acid derivatives, thioesters are stable but reactive and could undergo the oxidative addition of ArC(O)− to low-valent transition-metal species, generating the ArC(O)−M−S.62−64 In connection with our interest in thioester and norbornene chemistry, we envision that a combination of Pd(0)/NBE and aromatic thioesters could afford the 1,2-disubstituted arenes via decarbonylation of the thioester and subsequent NBE-mediated ortho-C–H and ipso-C–Pd functionalizations (Figure 1c). Many challenges will have to be faced, including direct acylation of the nucleophile,65,66 decarboxylative coupling or decarboxylative thioetherification,67−74 and protodepalladation of the ArPd intermediate.75 Herein, we report a cooperative palladium-catalyzed, NBE-mediated decarboxylative disubstitution of (hetero)aromatic thioesters. The potential applications of this protocol were demonstrated by the late-stage bifunctionalization of some commercial drugs and construction of polysubstituted arenes from aromatic acids.

We began our investigation by choosing S-(p-tolyl)naphthalene-1-carbothioate 1a as the model substrate, ethyl acrylate 2a as the nucleophile, and benzyl bromide 3a as the electrophile. Inspired by the reported classical Catellani reaction conditions,14−22 after screening of various reaction parameters, the desired product 4a was obtained in 68% yield in the presence of Pd(OAc)2 (10 mol %), TFP (25 mol %), norbornene (NBE) (1.5 equiv), and Cu2O (1.5 equiv) at 120 °C (Table 1, entry 1). Control experiments indicated that the palladium, phosphine ligand (TFP), NBE, and Cu2O were all essential for the reaction (Table 1, entries 2−5). Other palladium catalysts could also afford the desired product, albeit in lower yields (Table 1, entry 6). In Catellani-type reactions, the addition of an exogenous base is often required.3−8 Surprisingly, our protocol proceeded smoothly without the addition of Catellani-type reaction commonly used bases, and diminished yields were observed in the presence of bases such as Cs2CO3 and NaOAc (Table 1, entries 7, 8). Among the various phosphine ligands (Table S3), TFP delivered the best yields (Table 1, entries 9, 10). Copper salts are often required as activators to accelerate the C(O)−S cleavage.66 After screening of various copper salts, we found the Cu3O was the
To further enhance the reactivity, a series of modified NBEs were prepared and examined. Compared to simple NBE, succinimide-containing NBEs with relatively bulkier substituents at the N-position were found to be more efficient (NBE-1−4). In contrast, the N-methyl substituted NBE (NBE-5) was inferior, and the unprotected succinimide-derived NBE (NBE-7) was completely ineffectiv. To our delight, N-benzyl substituted NBE (NBE-6) delivered the best yield (85%). C5 amide-substituted NBEs (NBE-8−10) were less effective. Both S-cyano substituted NBE (NBE-11) and 2-methyl ester substituted NBE (NBE-12) afforded trace amounts of desired products.

With the above optimal reaction conditions in hand, we first examined the thioester scope (Table 2). Polycyclic substrates containing a naphthyl or pyrenyl moiety afforded moderate to good yields (4a−4c, 4w). ortho-Substituted thioesters (1d−1s) bearing both electron-donating and electron-withdrawing substituents were all compatible with the reaction conditions, and a variety of tri- and tetrasubstituted arenes were obtained in yields of 30−87% (4d−4s). Aryl bromides, which are

| Scope of aryl thiol esters | NBE-6 |
|--------------------------|-------|
| 4a, R = H, 82%           |       |
| 4b, R = Me, 70%          |       |
| 4c, R = OMe, 58%         |       |
| 4d, R = Me, 79%          |       |
| 4e, R = Ph, 81%          |       |
| 4f, R = Ph, 83%          |       |
| 4g, R = OMe, 30%         |       |
| 4h, R = OPh, 80%         |       |
| 4i, R = CO2Me, 52%       |       |
| 4j, R = 3-Me, 86%        |       |
| 4k, R = 3-F, 87%         |       |
| 4l, R = 4-Me, 71%        |       |
| 4m, R = 4-Cl, 40%        |       |
| 4n, R = 4-CF3, 68%       |       |
| 4o, R = 4-CO2Me, 65%     |       |
| 4p, R = 4-CN, 49%        |       |
| 4q, R = 4-Br, 62%        |       |

**Table 2. Scope of Aryl Thioesters, Olefins, and Electrophiles**

| Reaction conditions: 1 (0.1 mmol), 2 (0.15 mmol), 3 (0.3 mmol), Pd(OAc)2 (0.01 mmol), TFP (0.025 mmol), NBE-6 (0.15 mmol), Cu2O (0.15 mmol), MeCN (2 mL), 120 °C, 12 h. Isolated yields were reported and were calculated based on aryl thioesters. 4Derivatives of benzyl bromide were used as electrophiles for products 4ap−4aw; 4-(chloromethyl)-3,5-dimethylisoxazole was used as the electrophile for product 4ax; derivatives of alkyl iodide were used as electrophiles for products 4ay−4aae. 5NBE-2 was used instead of NBE-6, 2.0 equiv of Na2CO3 was added, and the loading of 3 was reduced to 0.15 mmol.

**Best (Table 1, entries 11, 12).** To further enhance the reactivity, a series of modified NBEs were prepared and examined. Compared to simple NBE, succinimide-containing NBEs with relatively bulkier substituents at the N-position were found to be more efficient (NBE-1−4). In contrast, the N-methyl substituted NBE (NBE-5) was inferior, and the unprotected succinimide-derived NBE (NBE-7) was completely ineffective. To our delight, N-benzyl substituted NBE (NBE-6) delivered the best yield (85%). C5 amide-substituted NBEs (NBE-8−10) were less effective. Both S-cyano substituted NBE (NBE-11) and 2-methyl ester substituted NBE (NBE-12) afforded trace amounts of desired products.

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| Scope of olefin | Triflusal derivative |
|-----------------|---------------------|
| 4ag, R = Me, 88%|                     |
| 4ah, R = F, 62% |                     |
| 4ai, R = CF3, 78%|                    |
| 4aj, R = OMe, 83%|                    |
| 4ak, R = H, 91% |                     |

| Scope of R-X | Aspirin derivative |
|--------------|-------------------|
| 4ap, R = CF3, 62%|                |
| 4aq, R = F, 62% |                   |
| 4ar, R = Cl, 67%|                    |
| 4as, R = Br, 67%|                    |
| 4at, R = CH3, 80%|                  |

| Scope of R-X | Mefenamic Acid derivative |
|--------------|---------------------------|
| 4au, 47%    |                            |
| 4av, 52%    |                            |
| 4aw, 40%    |                            |
| 4ax, 41%    |                            |

| Scope of R-X | Repaglinide derivative |
|--------------|-------------------------|
| 4ay, 42%    |                          |
| 4az, R = n-Propyl, 40%|               |
| 4abb, 43%   |                          |
| 4aac, 40%   |                          |
| 4aad, 39%   |                          |
| 4aae, 35%   |                          |
commonly employed as aryl electrophiles in transition metal-catalyzed cross-couplings, were well tolerated, providing a handle for further functionalization. For ortho-unsubstituted aryl thioesters, dibenzylated products were obtained (4t−4v). Polysubstituted heteroarenes could also be constructed from corresponding aryl heterocyclic thioesters. The coordinative pyridyl thioester gave the product 4y in 42% yield. Continuous trisubstituted thiophene (4x) was synthesized without obstacle. Substrates bearing indole groups provided the desired products in moderate yields (4z−4ab). It should be noted that the type of the nitrogen protecting group of indoles was crucial to the efficiency of the reaction; a phenyl protecting group gave higher yield (4z and 4aa). The synthetic utility of our protocol was further showcased by the diversification of commercial pharmaceuticals, including aspirin, triflusal, mefenamic acid, and repaglinide, furnishing the corresponding products (4ac−4af) in acceptable yields. The scope with respect to the olefin terminating reagents was next investigated. In addition to ethyl acrylate, other electron-deficient olefins, such as acrylonitrile (4am), 2-vinylpyridine (4al), and especially methyl methacrylate (4ao) could be smoothly introduced at the ipso-position. Gratifyingly, styrene and its derivatives, irrespective of bearing electron-donating or electron-withdrawing groups, could serve as effective terminating reagents (4ag−4ak). Intriguingly, when the electron rich and less reactive cyclohexyl vinyl ether was subjected to the reaction conditions, compound 4an bearing branched alkenyl ethers was isolated in 53% yield. Regarding the scope of the electrophiles, benzyl bromides containing trifluoromethyl (4ap), fluorine (4aq), chlorine (4ar), bromine (4as), and methyl (4at) functionalities were all suitable substrates. When pyrrole, furan modified benzyl bromides, and even 6-(bromomethyl)-2-methylquinoline were used as electrophiles, corresponding products 4au−4aw were obtained in moderate yields. Notably, an isoxazole unit was successfully introduced into the ortho-position via methylene with 4-(chloromethyl)-3,5-dimethylisoxazole as the electrophile, and product 4ax was obtained in 41% yield. Then, the range of alkyl iodides as electrophiles was investigated (Table 2, 4ay−4aaa). Alkylation with 1-iodopropane (4az), 1-iodo-2-methylpropane (4aa), as well as the cyclopropyl- and cyclopentyl- substituted iodomethane (4aab and 4aac) gave the desired products in acceptable yields (34−43%). Iodo-

Table 3. Scope of Boronic Acids, Alkenyl Alcohols, and Thiols

| Nu | R2 = p-Toluene | Reaction conditions: | Isolated yields |
|----|----------------|---------------------|----------------|
| 5a | R = Me, 61%    | 1 (0.1 mmol), Nu (0.15 mmol), benzyl bromide (0.3 mmol), Pd(OAc)2 (0.01 mmol), TFP (0.025 mmol), NBE-6 (0.15 mmol), Cu2O (0.15 mmol), MeCN (2 mL), 120 °C, 12 h. | 61% |
| 5b | R = COOEt, 68% | But-3-en-1-ol was used as Nu. | 68% |
| 5c | R = Cl, 70%    | Decarboxylative thiolation reactions: 1 (0.1 mmol), benzyl bromide (0.3 mmol), Pd(OAc)2 (0.01 mmol), (p-MePh)3P (0.025 mmol), NBE-8 (0.15 mmol), CuCl (0.15 mmol), K2CO3 (0.2 mmol), THF (2 mL), 120 °C, 12 h. | 70% |
| 5d | R = F, 62%     | Isolated yields are reported. | 62% |
| 5e | R = Br, 63%    | | 63% |
| 5f | R = CF3, 63%   | | 63% |
| 5g | R = OMe, 55%   | | 55% |
| 5h | R = TMS, 76%   | | 76% |
| 5i | R = H, 55%     | | 55% |

Scheme 1. Gram-Scale One-Pot Synthesis

2-phenyl-benzoic acid (5.05 mmol, 1.0 g) (1) Thioesterification (2) Catellani-type Di-functionalization 5f 52% yield, 0.90 g
methane was also compatible with this protocol and delivered a methylated product \((4ay)\) in 42% yield. Iodides containing functional groups, including acetoxyl \((4aad)\) and a protected amine \((4aae)\), could also serve as effective electrophiles.

To further illustrate the feasibility of this protocol, an ortho-benzylination/ipso-Suzuki cascade of aryl thioesters was carried out (Table 3). By employing thioester 1a, benzyl bromide 3a, and arylboronic acids as the substrates, ipso-arylation occurred smoothly with moderate to good yields \((5a−5q)\). Aryl boronic acids containing ester \((5b)\), chloro \((5c)\), bromo \((5e)\), trimethylsilyl \((5h)\), and nitro \((5k)\) groups were well tolerated, offering additional opportunity for further structural elaboration. When ortho-substituted aryl thioesters were subjected to the reaction conditions, multisubstituted biaryl skeletons were obtained \((5r, 5s)\). \(\text{ipso}\)-Methylation product \((5t)\) was synthesized in 36% yield using methylboronic acid as the terminating reagent. Subsequently, we employed allylic alcohol as the terminating nucleophile. A variety of ketone and aldehyde products were obtained via chain-walking strategies \((5u−5aa)\).

Furthermore, we found that one-pot reaction could be performed smoothly. Take 2-phenyl-benzoic acid as an example, a gram-scale one-pot operation was performed to give the desired product \(4f\) in an yield of 52% (Scheme 1).

The synthetic utility of this methodology was further demonstrated in the late-stage diversification of thioesters 1al derived from 3-methylflavone-8-carboxylic acid, a drug used for the treatment of coronary heart disease (Figure 2a). \(\text{ortho}\)-Benzylation and subsequent \(\text{ipso}\)-Heck or Suzuki cascade of aryl thioester 1al gave the products 6a and 6b in 44% and 50% yields, respectively. When pent-1-en-3-ol was used as a terminating nucleophile, \(\text{ipso}\)-alkylated product 6c was synthesized in 49% yield. In addition, thiolation terminated derivative 6d was isolated in 31% yield. The carboxylate functionality is a practical directing group in transition metal-catalyzed C–H bond functionalization. Thus, by a combination of \(\text{ortho}\) C–H functionalization, the Catellani reaction, and Pd/NBE catalyzed \(\text{ipso}\)-alkenylation/\(\text{ortho}\)-benzylation, 1,2,3-trisubstituted arene \(4f\) and 1,2,3,4-tetrasubstituted arene \(7d\) were readily synthesized from benzoic acid in 55% total yield and 42% total yield, respectively (Figure 2b).

In summary, we have developed a decarbonylative Catellani reaction for the construction of polysubstituted arenes via a domino process involving the decarbonylation of the thioester and subsequent NBE-mediated \(\text{ortho}\)-C–H and \(\text{ipso}\)-C–Pd functionalizations. This protocol utilizes widely available aryl carboxylic acids as feedstocks and features redox-neutral and base-free reaction conditions. The termination step is flexible, as demonstrated by the use of Heck reactions, Suzuki
couplings, alkyllations, and thiolations. The synthetic utility of this protocol is further highlighted by the late-stage diversification of several pharmaceutical drugs. Carboxyl-directed ortho C–H iodination and subsequent Pd(0)/NBE catalyzed Catellani-type reactions of aryl halides and thioesters allowed for the rapid construction of trisubstituted and tetrasubstituted arenes from benzoic acid.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/jacsau.1c00328.

Experimental procedures and compound characterization data (PDF)

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Notes

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REFERENCES

(1) He, J.; Qiu, D.; Li, Y. Strategies toward Aryne Multifunctionalization via 1,2-Benzdiyne and Benzyne. Acc. Chem. Res. 2020, 53, 508–519.

(2) Davison, E. K.; Sperry, J. Natural Products with Heteroatom-Rich Ring Systems. J. Nat. Prod. 2017, 80, 3060–3079.

(3) Catellani, M. Novel methods of aromatic functionalization using palladium and norbornene as a unique catalytic system. Top. Organomet. Chem. 2005, 14, 21–53.

(4) Martins, A.; Mariampillai, B.; Lautens, M. Synthesis in the key of catellani: norbornene-mediated ortho C–H functionalization. Top. Curr. Chem. 2009, 292, 1–33.

(5) Ye, J.; Lautens, M. Palladium-catalyzed norbornene-mediated C–H functionalization of arenes. Nat. Chem. 2015, 7, 863–870.

(6) Della Ca’, N.; Fontana, M.; Motti, E.; Catellani, M. Pd/norbornene: A winning combination for selective aromatic functionalization via C–H bond activation. Acc. Chem. Res. 2016, 49, 1389–1400.

(7) Cheng, H.-G.; Chen, S.-Q.; Chen, R.-M.; Zhou, Q.-H. The Pd(II)-initiated catellani-type reactions. Angew. Chem., Int. Ed. 2019, 58, 5832–5844.

(8) Wang, J.-C.; Dong, G.-B. Palladium/norbornene cooperative catalysis. Chem. Rev. 2019, 119, 7478–7528.

(9) Khoury, P. R.; Goddard, J. D.; Tam, W. Ring strain energies: substituted rings, norbornanes, norbornenes and norbornadienes. Tetrahedron 2004, 60, 8103–8112.

(10) Li, R.-H.; Dong, G.-B. Structurally modified norbornenes: a key factor to modulate reaction selectivity in the palladium/norbornene cooperative catalysis. J. Am. Chem. Soc. 2020, 142, 17859–17875.

(11) Catellani, M.; Frignani, F.; Rangoni, A. A complex catalytic cycle leading to a regioselective synthesis of o,o’-disubstituted vinylarenes. Angew. Chem., Int. Ed. Engl. 1997, 36, 119–122.

(12) Catellani, M.; Cugini, F. A catalytic process based on sequential ortho-alkylation and vinylation of ortho-alkylaryl iodides via palladacycles. Tetrahedron 1999, 55, 6595–6602.

(13) Catellani, M.; Motti, E.; Minari, M. Symmetrical and unsymmetrical 2,6-dialkyl-1,1′-biaryls by combined catalysis of

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aromatic alkylation via palladacycles and Suzuki-type coupling. Chem.
Commun. 2000, 157–158.

(14) Lautens, M.; Piquet, S. A new route to fused aromatic compounds by using a palladium-catalyzed alkylation–alkenylation sequence. Angew. Chem., Int. Ed. 2000, 39, 1045–1046.

(15) Bressy, C.; Alberico, D.; Lautens, M. A route to annulated indoles via a palladium-catalyzed tandem alkylation/direct arylation reaction. J. Am. Chem. Soc. 2005, 127, 13148–13149.

(16) Candito, D. A.; Lautens, M. Palladium-catalyzed domino direct arylation/n-arylation: convenient synthesis of phenanthridines. Angew. Chem., Int. Ed. 2009, 48, 6713–6716.

(17) Candito, D. A.; Lautens, M. Exploiting the chemistry of strained rings: synthesis of indoles via domino reaction of aryl iodides with 2H-azirines. Org. Lett. 2010, 12, 3312–3315.

(18) Martins, A.; Candito, D. A.; Lautens, M. Palladium-catalyzed reductive ortho-arylation: evidence for the decomposition of 1,2-dimethoxystyrene and subsequent arylpalladium(II) reduction. Org. Lett. 2010, 12, 5186–5188.

(19) Chai, D. I.; Thansandote, P.; Lautens, M. Mechanistic studies of Pd-catalyzed regioselective aroyl C−H bond functionalization with strained alkenes: origin of regioselectivity. Chem. – Eur. J. 2011, 17, 8175–8188.

(20) Larrauñiga, M.-H.; Maestri, G.; Beume, A.; Derat, E.; Ollivier, C.; Fensterbank, L.; Courillon, C.; Lacote, E.; Catellani, M.; Malacria, M. Exception to the ortho effect in palladium/norbornene catalysis. Angew. Chem., Int. Ed. 2011, 50, 12253–12256.

(21) Liu, H.; El-Saffarî, M.; Chai, D. I.; Auffret, J.; Lautens, M. Modular and stereoselective synthesis of tetrasubstituted helical alkenes via a palladium-catalyzed domino reaction. Org. Lett. 2012, 14, 3648–3651.

(22) Liu, H.; El-Saffarî, M.; Lautens, M. Expedient synthesis of tetrasubstituted helical alkenes by a cascade of palladium-catalyzed C−H activations. Angew. Chem., Int. Ed. 2012, 51, 9846–9850.

(23) Dong, Z.; Dong, G.-B. ortho vs ipso: Site-selective Pd and norbornene-catalyzed arene C-H amination using aryl halides. J. Am. Chem. Soc. 2013, 135, 18350–18353.

(24) Sun, F.; Li, M.; He, C.; Wang, B.; Li, B.; Sui, X.-W.; Gu, Z.-H. Cleavage of the C(O)−S bond of thioesters by palladium/norbornene/copper cooperative catalysis: an efficient synthesis of 2-(arythio)aryl ketones. J. Am. Chem. Soc. 2016, 138, 7456–7459.

(25) Wang, J.-C.; Li, R.-H.; Dong, Z.; Liu, P.; Dong, G.-B. Complementary site-selectivity in arene functionalization enabled by overcoming the ortho constraint in palladium/norbornene catalysis. Nat. Chem. 2018, 10, 866–872.

(26) Lv, W.-W.; Chen, Y.-H.; Wen, S.; Ba, D.; Cheng, G.-L. Modular and stereoselective synthesis of C-aryl glycosides via catellani reaction. J. Am. Chem. Soc. 2020, 142, 14864–14870.

(27) Liu, Z.-S.; Hua, Y.; Gao, Q.-W.; Ma, Y.-Y.; Tang, H.; Shang, Y.; Cheng, H.-G.; Zhou, Q.-H. Construction of axial chirality via palladium/chiral norbornene cooperative catalysis. Nat. Catal. 2020, 3, 727–733.

(28) Wang, J.; Qin, C.; Lumb, J.-P.; Luan, X.-J. Regioselective synthesis of polyfunctional arenes by a 4-component catellani reaction. Chem 2020, 6, 2097–2109.

(29) Wang, J.-C.; Dong, Z.; Yang, C.; Dong, G.-B. Modular and regioselective synthesis of all-carbon tetrasubstituted olefins enabled by an alkyl catellani reaction. Nat. Chem. 2019, 11, 1106–1112.

(30) Chen, S.-Q.; Liu, Z.-S.;Yang, T.; Hua, Y.; Zhou, Z.-Y.; Cheng, H.-G.; Zhou, Q.-H. The discovery of a palladium(II)-initiated borono-catellani reaction. Angew. Chem., Int. Ed. 2018, 57, 7161–7165.

(31) Shi, G.-F.; Shao, C.-D.; Ma, X.-T.; Gu, Y.-C.; Zhang, Y.-H. Pd(II)-catalyzed catellani-type domino reaction utilizing arylboronic acids as substrates. ACS Catal. 2018, 8, 3775–3779.

(32) Li, R.-H.; Liu, F.-P.; Dong, G.-B. Redox-neutral ortho functionalization of aryl boroxines via palladium/norbornene cooperative catalysis. Chem. 2019, S, 929–939.
(56) Font, M.; Quibell, J. M.; Perry, G. J. P.; Larrosa, I. The use of carboxylic acids as traceless directing groups for regioselective C–H bond functionalization. Chem. Commun. 2017, 53, 5584–5597.

(57) Cornella, J.; Righi, M.; Larrosa, I. Carboxylic acids as traceless directing groups for formal meta-selective direct arylation. Angew. Chem., Int. Ed. 2011, 50, 9429–9432.

(58) Biafora, A.; Krause, T.; Hackenberger, D.; Belitz, F.; Goosfen, L. J. ortho-C–H Arylation of benzoic acids with aryl bromides and chlorides catalyzed by ruthenium. Angew. Chem., Int. Ed. 2016, 55, 14752–14755.

(59) Just-Baringo, X.; Shin, Y.; Panigrahi, A.; Zarattini, M.; Nagyte, V.; Zhao, L.; Kostarelos, K.; Casiraghi, C.; Larrosa, I. Palladium catalysed C–H arylation of pyrenes: access to a new class of exfoliating agents for water-based graphene dispersions. Chem. Sci. 2020, 11, 2472–2478.

(60) Koch, E.; Studer, A. Regioselective threefold aromatic substitution of benzoic acid derivatives by dearomatization, regioselective functionalization, and rearomatization. Angew. Chem., Int. Ed. 2013, 52, 4933–4936.

(61) Corey, E. J.; Nicolaou, K. C. Efficient and mild lactonization method for the synthesis of macrolides. J. Am. Chem. Soc. 1974, 96, 5614–5616.

(62) Hirschbeck, V.; Gehrtz, P. H.; Fleischer, I. Metal-catalyzed synthesis and use of thioesters: recent developments. Chem. - Eur. J. 2018, 24, 7092–7107.

(63) Prokopcová, H.; Kappe, C. O. The Liebeskind-Srogl C–C cross-coupling reaction. Angew. Chem., Int. Ed. 2009, 48, 2276–2286.

(64) Cheng, H.-G.; Chen, H.; Liu, Y.; Zhou, Q.-H. The Liebeskind-Srogl cross-coupling reaction and its synthetic applications. Asian J. Org. Chem. 2018, 7, 490–508.

(65) Tokuyama, H.; Yokoshima, S.; Yamashita, T.; Fukuyama, T. A novel ketone synthesis by a palladium-catalyzed reaction of thiol esters and organozinc reagents. Tetrahedron Lett. 1998, 39, 3189–3192.

(66) Liebeskind, L. S.; Srogl, J. Thiol ester-boronic acid coupling. A mechanistically unprecedented and general ketone synthesis. J. Am. Chem. Soc. 2000, 122, 11260–11261.

(67) Lu, H.; Yu, T.-Y.; Xu, P.-F.; Wei, H. Selective decarbonylation via transition-metal-catalyzed carbon–carbon bond cleavage. Chem. Rev. 2021, 121, 365–411.

(68) Ochiai, H.; Uetake, Y.; Niwa, T.; Hosoya, T. Rhodium-catalyzed decarbonylative borylation of aromatic thioesters for facile diversification of aromatic carboxylic acids. Angew. Chem., Int. Ed. 2017, 56, 2482–2486.

(69) Osakada, K.; Yamamoto, T.; Yamamoto, A. Decarbonylation of thiol esters to give sulfides promoted by transition metal complexes. Tetrahedron Lett. 1998, 28, 6321–6324.

(70) Ichishii, N.; Malapit, C. A.; Wozniak, L.; Sanford, M. S. Palladium- and nickel-catalyzed decarbonylative C–S coupling to convert thioesters to thioethers. Org. Lett. 2018, 20, 44–47.

(71) Brigham, C. E.; Malapit, C. A.; Laloo, N.; Sanford, M. S. Nickel-Catalyzed Decarbonylative Synthesis of Fluoroalkyl Thioethers. ACS Catal. 2020, 10, 8315–8320.

(72) Kato, T.; Kuniyasu, H.; Kajiura, T.; Minami, Y.; Ohtaka, A.; Kinamoto, M.; Terao, J.; Kurosawa, H.; Kambe, K. β-cis-SAr effect on Decarbonylation from α,β-Unsaturated Acyl and Aroyl Complexes. Chem. Commun. 2006, 868–870.

(73) Malapit, C. A.; Bour, J. R.; Brigham, C. E.; Sanford, M. S. Base-free nickel-catalysed decarbonylative Suzuki–Miyaura coupling of acid fluorides. Nature 2018, 563, 100–104.

(74) O’Dull, M. L.; Engle, K. M. Protodepalladation as a Strategic Elementary Step in Catalysis. Synthesis 2018, 50, 4699–4714.

(75) Uma, R.; Crévisy, C.; Grée, R. Transposition of allylic alcohols into carbonyl compounds mediated by transition metal complexes. Chem. Rev. 2003, 103, 27–51.

(76) Vasseur, A.; Bruffaerts, J.; Marek, I. Remote functionalization through alkene isomerization. Nat. Chem. 2016, 8, 209–219.

(77) Werner, E. W.; Mei, T.-S.; Burckle, A. J.; Sigman, M. S. Enantioselective Heck Arylations of Acyclic Alkenyl Alcohols Using a Redox-Relay Strategy. Science 2012, 338, 1455–1458.

(78) Zhu, C.-L.; Zhang, Y.-F.; Kan, J.; Zhao, H.-Q.; Su, W.-P. Ambient-temperature ortho C–H arylation of benzoic acids with aryl iodides with ligand-supported palladium catalyst. Org. Lett. 2015, 17, 3418–3421.

(79) Weis, E.; Johansson, M. J.; Martin-Matute, B. IrIII-catalyzed selective ortho-monooiodination of benzoic acids with unbiased C–H bonds. Chem. - Eur. J. 2020, 26, 10185–10190.

(80) Ye, C.-Q.; Zhu, H.; Chen, Z.-Y. Synthesis of biaryl tertiary amines through Pd/norbornene joint catalysis in a remote C–H amination/Suzuki coupling reaction. J. Org. Chem. 2014, 79, 8900–8905.