OL Organic Letters

Letter

Cite This: Org. Lett. XXXX, XXX, XXX−XXX

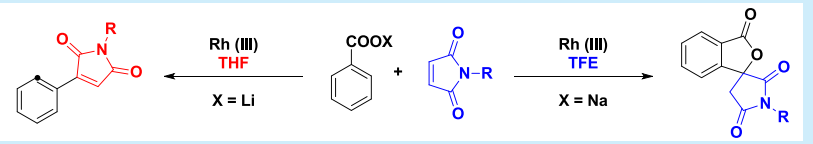
pubs.acs.org/OrgLett

Weak Coordinating Carboxylate Directed Rhodium(III)-Catalyzed C−H Activation: Switchable Decarboxylative Heck-Type and [4 + 1] Annulation Reactions with Maleimides

Mahadev Sharanappa Sherikar and Kandikere Ramaiah Prabhu*

Department of Organic Chemistry, Indian Institute of Science, Bangalore 560 012, Karnataka, India

Supporting Information



ABSTRACT: A weakly coordinating carboxylate directing group assisted C−H activation with maleimides leading to novel and switchable decarboxylative Heck-type and [4 + 1] annulation products catalyzed by Rh(III) has been reported. In these reactions, solvents play a vital role in switching the selectivity. An aprotic solvent, THF, leads to the decarboxylative Heck-type product while the protic solvent, TFE, results in the [4 + 1] annulation product. The methodology shows high functional group tolerance.

Transition-metal-catalyzed directed functionalization for the construction of carbocyclic and heterocyclic molecules is gaining much attention in organic synthesis.[1] Maleimide, succinimide, and spirocyclic pyrrolidine motifs are an important class of compounds, which are present in various natural products and biologically active molecules and have high utility in pharmaceuticals.[2] Several potent drug molecules, such as antimicrobials, anticonvulsants, and inhibitors, contain the maleimide ring as a core feature (Figure 1).[3] One of the great advantages of maleimide and succinimide

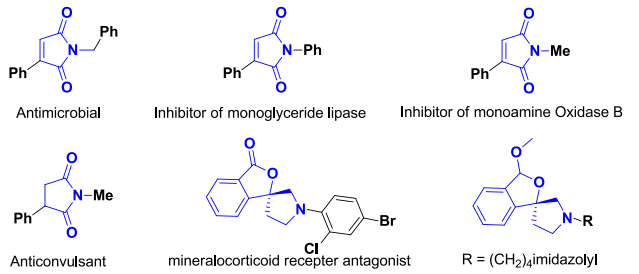
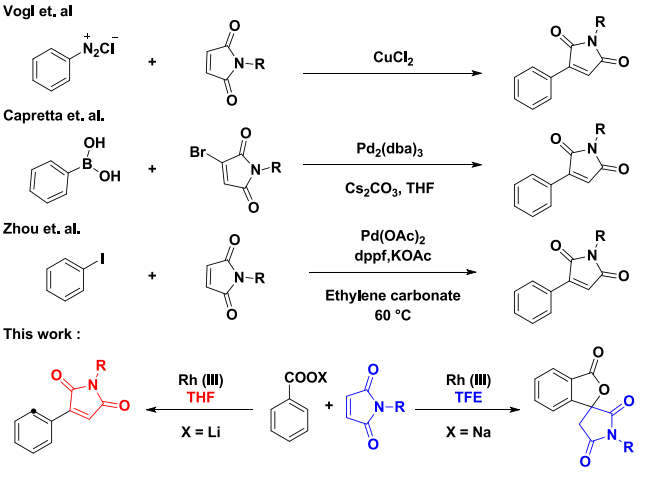


Figure 1. Molecules containing maleimide ring.

rings is that they can be easily converted into heterocyclic compounds such as pyrrolidines and γ-lactams.[4] In C−H activation, generally, maleimide undergoes 1,4-addition reaction due to a rigid bicyclic intermediate of the succinimide ring, which is lacking a β-hydrogen that is synperiplanar. Consequently, succinimide cannot undergo β-hydride elimination.[5] Therefore, a vast majority of reports are on the 1,4-addition reaction of maleimide with aromatic compounds using different directing groups and transition metal catalysts.[4d,6,7] Maleimide is also known to undergo 1,1-type,[8] [3 + 2],[9] and [4 + 2][10] annulation reactions. Generally, substituted maleimides are prepared by reacting an amine with maleic anhydride, whereas obtaining 3-substituted maleimide derivatives by employing the C−H activation strategy is not easy and rare.[5,11] One of the early syntheses of 3-substituted maleimides was reported by Vogl in 1955 using arene diazonium salt and a Cu(II)-catalyst.[12a] Later in 2011, Capretta reported a Suzuki coupling reaction of 3-bromomaleimide with phenylboronic acid.[12b] In 2015, Zhou reported coupling of maleimide with aryl iodide under Pd-catalysis (Scheme 1).[12c] The carboxylic acid is known as a weak coordinating directing group for various synthetic trans-

Scheme 1. Comparison with Previous Work



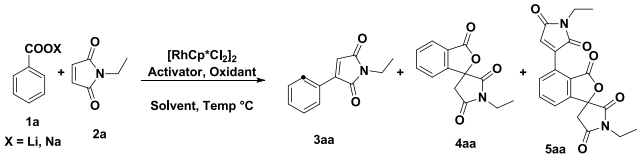
Received: April 23, 2019

DOI: 10.1021/acs.orglett.9b01412
Org. Lett. XXXX, XXX, XXX−XXX

formations under C−H activation conditions.[13,14] The transition-metal-catalyzed decarboxylative hydroarylation of maleimide using acid as a directing group is known under Rh(III)- and Ru(II)-catalysis.[15] However, decarboxylative Heck-type and 1,1-type annulation reactions of maleimide with benzoic acid are not known. We considered using a base in the reaction can avoid the quenching of the metallacycle and thereby the formation of the corresponding Heck-type product can be facilitated. If this idea is successful, the reaction can be fine-tuned to obtain a [4 + 1] annulation product, without undergoing the decarboxylation.

To achieve the decarboxylative Heck-type product, the optimization study began with the reaction of benzoic acid with *N*-ethyl maleimide (**2a**) in the presence of a Rh(III)-catalyst (5 mol %), $AgBF_4$ (20 mol %) as an activator, and $Cu(OAc)_2{\cdot}H_2O$ (1 equiv) as an oxidant in THF at 120 °C (entry 1, Table 1). However, this reaction was futile, and the starting materials were intact during the reaction conditions. To increase the reactivity of the acid in the reaction, K_2CO_3 has been used as a base, as the corresponding carboxylate ion can bind with the metals more effectively. As expected, this reaction using K_2CO_3 (1 equiv) resulted in the formation of decarboxylative Heck-type product **3aa** in 33% yield (entry 2, Table 1). Our attempts to improve the yield of the desired decarboxylative Heck-type product **3aa** were not successful. Thus, we thought it would be beneficial to use the salt of benzoic acid to improve the yield of the desired decarboxylative Heck-type product.

Table 1. Optimization Studies



				yield		
entry	X	$Cu(OAc)_2{\cdot}H_2O$ (equiv)	solvent	**3aa**	**4aa**	**5aa**
1	H	1	THF	–	–	–
2[c]	H	1	THF	33	–	–
3	Na	1	THF	60	–	–
4	K	1	THF	40	–	–
5	Li	1	THF	66	–	–
6	Li	0.75	THF	70	–	–
7	Li	0.50	THF	62	–	–
8[d]	**Li**	**0.75**	**THF**	**79**	–	–
9[e]	Li	0.75	THF	74	–	–
10	Li	0.75	TFE	07	18	–
11	Li	0.75	DCE	21	–	–
12	Li	AgOAc (0.75)	THF	54	–	–
13	Li	$CuCO_3$ (0.75)	THF	57	–	–
14	Li	0.75	TFE	05	25	–
15	Na	0.75	TFE	04	47	10
16[f]	Na	0.75	TFE	07	50	–
17[g]	**Na**	**0.75**	**TFE**	**13**	**67**	–
18[d]	Na	0.75	TFE	11	57	–
19	Na	0.75	HFIP	–	44	–
20	Na	0.75	MeOH	08	30	–

[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.3 mmol) $[RhCp^*Cl_2]_2$ (5 mol %), $AgBF_4$ (4 times the amount of catalyst) and X = Li (for entries 1−9), $AgSbF_6$ (4 times the amount of catalyst) and X = Na (for entries 10−15), temp (120 °C and 100 °C for entries 1−13 and 14−20, respectively). [b]Yields based on ^1H NMR using trimethoxybenzene as an internal standard. [c]K_2CO_3 (1 equiv) used. [d]$[RhCp^*Cl_2]_2$ (7.5 mol %). [e]$[RhCp^*Cl_2]_2$ (10 mol %). [f]**1a** (0.3 mmol) and **2a** (0.2 mmol). [g]**1a** (0.4 mmol), **2a** (0.2 mmol).

On the basis of this, reactions of sodium, potassium, and lithium salts of benzoic acid (**1a**) with *N*-ethyl maleimide (**2a**) and 5 mol % of a Rh(III)-catalyst, $AgBF_4$ as an activator, and $Cu(OAc)_2{\cdot}H_2O$ (1 equiv) as an oxidant in THF at 120 °C (entries 3−5, Table 1) were performed. These reactions resulted in the formation of decarboxylative Heck-type product **3aa** in 60%, 40%, and 66% yields, respectively (entries 3−5, Table 1). As the Li salt of benzoic acid furnished a better yield, further optimizations were carried out using the Li salt of the acid. Decreasing the amount of $Cu(OAc)_2{\cdot}H_2O$ to 0.75 equiv resulted in the formation of **3aa** in 70% NMR yield (entry 6), whereas further lowering the amount of $Cu(OAc)_2{\cdot}H_2O$ furnished **3aa** (62%, entry 7). The yield of **3aa** was enhanced to 79% by loading of the Rh(III)-catalyst to 7.5 mol % (entry 8). A further increase in catalyst loading to 10 mol % furnished the product **3aa** in 74% yield (entry 9). Changing the solvent from THF to a protic solvent, TFE, furnished **3aa** in 7% yield along with [4 + 1] annulation product **4aa** in 18% yield (entry 10). A similar reaction in DCE as a solvent afforded the product **3aa** in 21% yield (entry 11). Employing AgOAc and $CuCO_3$ as oxidants instead of $Cu(OAc)_2{\cdot}H_2O$ led to the formation of **3aa** in 54% and 57% yields, respectively (entries 12 and 13). Among these conditions, we observed that the combination of $Cu(OAc)_2{\cdot}H_2O$ and THF solvent was ideal for affording decarboxylative Heck-type product **3aa** in good yield (79%, entry 8).

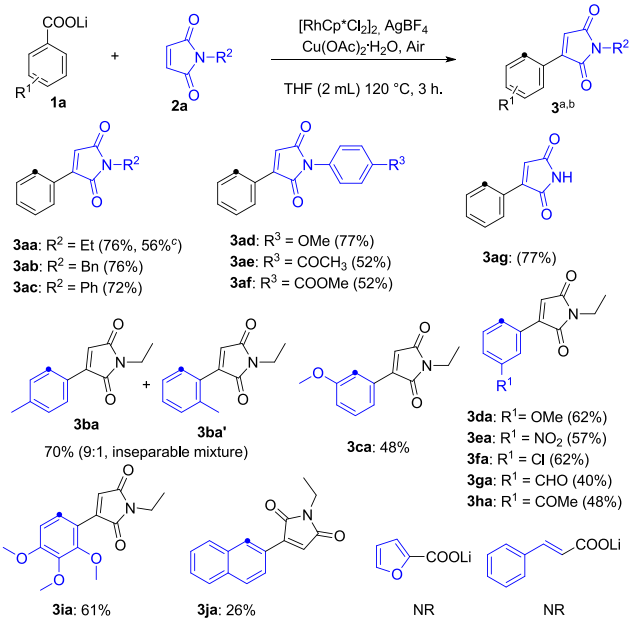
As seen in entry 10, the reaction in a protic solvent (TFE) furnished the corresponding [4 + 1] annulated product **4aa** in 18% yield. Therefore, we directed our optimization efforts toward obtaining the annulated product exclusively. Thus, the reaction of lithium benzoate (**1a**) and *N*-ethyl maleimide (**2a**), with 5 mol % of a Rh(III)-catalyst, $AgSbF_6$, and $Cu(OAc)_2{\cdot}H_2O$ in TFE at 100 °C was performed, which furnished the annulated product **4aa** in 25% yield along with the Heck-type product **3aa** in 5% yield (entry 14, Table 1). Sodium benzoate under the same reaction conditions furnished the annulated **4aa** product in 47% yield along with the Heck-type product **3aa** in 4% yield (entry 15). Quite interestingly, this reaction also led to a double C−H activation of benzoic acid furnishing alkenylation as well as annulation of the benzoic acid forming the product **5aa** in 10% yield. To obtain the annulated product **4aa**, exclusively, the stoichiometry of the reaction had been altered. Therefore, 1.5 equiv of sodium benzoate **1a** was reacted with 1 equiv of maleimide **2a**. This reaction led to the formation of the annulated product **4aa** in 50% yield (entry 16). To our delight, when 2 equiv of sodium benzoate was used, the reaction proceeded well furnishing the annulated product **4aa** in 67% yield along with a minor amount of the Heck-type product **3aa** (13%, entry 17). By increasing the catalyst loading to 7.5 mol %, a mixture of annulated product **4aa** and the Heck-type product **3aa** was obtained in 57% and 11% yields, respectively (entry 18). The reaction in HFIP, a more polar and acidic solvent as compared to TFE, afforded the corresponding annulated product **4aa** exclusively, albeit in low yield (44%, entry 19). The reaction in methanol was not helpful (entry 20, see the Supporting Information for detailed screening studies).

DOI: 10.1021/acs.orglett.9b01412
Org. Lett. XXXX, XXX, XXX−XXX

With these optimization studies, the scopes of the Heck-type, as well as the annulation reactions, were studied using the conditions noted in entries 8 and 17 (Table 1), respectively.

The reactions of lithium benzoate **1a** with *N*-ethyl, benzyl, phenyl, and *N*-(4-methoxy) phenyl substituted maleimide derivatives were facile furnishing the corresponding decarboxylative Heck-type products **3aa**−**3ad** in 72−77% yields (Scheme 2). Similarly, the reaction of lithium benzoate **1a**

Scheme 2. Substrate Scope for Heck-Type Reaction[a]

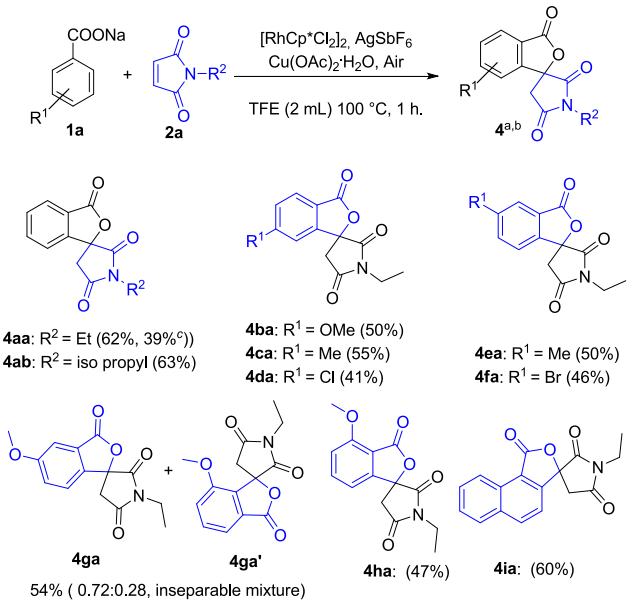


[a]Reaction conditions: Air, **1a** (0.2 mmol), **2a** (0.3 mmol), $[RhCp^*Cl_2]_2$ (7.5 mol %), $AgBF_4$ (30 mol %), $Cu(OAc)_2{\cdot}H_2O$ (0.75 equiv), THF (2 mL), temp 120 °C, time 3 h. [b]Isolated yields. [c]8 mmol scale reaction.

with *N*-(4-acetyl) phenyl and *N*-(methyl-4-benzoate) substituted maleimide furnished the corresponding Heck-type products **3ae** and **3af** in moderate yields (52% and 52%, respectively). The reaction of unsubstituted maleimide with lithium benzoate **1a** afforded the corresponding decarboxylative Heck-type product **3ag** in 77% good yield. The decarboxylative Heck-type reaction of *N*-ethyl maleimide **2a** with the Li salt of *m*-toluic acid occurred at both the *ortho*- and *para*- positions forming the corresponding regioisomers **3ba** and **3ba′** in a 9:1 ratio as an inseparable mixture in 70% yield. The reaction of the lithium salt of 2-methoxybenzoic acid with **2a** gave the corresponding decarboxylative Heck-product **3ca** in 48% yield. The reaction of **2a** with acid salts having electron-donating groups such as OMe and an electron-withdrawing group such as NO_2 and Cl on the phenyl ring of the acid furnished the products **3da**−**3fa** in 57−62% yield. Likewise, the reactions of **2a** with carboxylic acid salts that have −CHO and $COCH_3$ groups at the *para*-position of the phenyl ring of the acid afforded the products **3ga** and **3ha** in 40% and 48% yields, respectively. The reaction of **2a** with a 3,4,5-trimethoxy substituted acid salt derivative displayed good reactivity forming **3ia** in 61% yield. However, the reaction of **2a** with 1-naphthoic acid salt rendered the product **3ja** in 26% yield. The Li salt of 2-fumaric acid and cinnamic acid failed to furnish the corresponding decarboxylative Heck-type product.

After exploring the scope of decarboxylative Heck-type products, the substrate scope for the [4 + 1] annulation reaction was investigated (Scheme 3). The reaction of *N*-ethyl

Scheme 3. Substrate Scope for [4 + 1] Annulation Reaction[a]



[a]Reaction conditions: Air, **1a** (0.4 mmol), **2a** (0.2 mmol), $[RhCp^*Cl_2]_2$ (5 mol %), $AgSbF_6$ (20 mol %), $Cu(OAc)_2{\cdot}H_2O$ (75 mol %), TFE (2 mL), temp 100 °C, time 1 h. [b]Isolated yields. [c]8 mmol scale reaction.

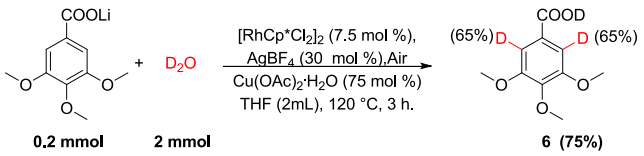
and *N*-isopropyl substituted maleimides with sodium benzoate (**1a**) produced the corresponding [4 + 1] annulation products **4aa** and **4ab** in 62% and 63% yields, respectively. *N*-Ethyl maleimide **2a** reacted well with sodium salts of 4-methoxybenzoic acid, 4-methylbenzoic acid, and 4-chlorobenzoic acid furnishing the corresponding annulated products **4ba**, **4ca**, and **4da** in 50%, 55%, and 41% yields, respectively. The reaction of **2a** with acid salts of *m*-methyl and *m*-bromo benzoic acids afforded the corresponding annulated products **4ea** and **4fa** in 50% and 46% yields, respectively. The reaction of **2a** with *m*-methoxy benzoic acids salt led to the annulations at both *ortho*-positions and furnished a regioisomeric mixture of annulated products **4ga** and **4ga′** in a ratio of 72:28 as an inseparable mixture in 54% yield. Sterically hindered acid salts such as *ortho*-anisic acid salt underwent a smooth annulation with **2a** forming the product **4ha** in 47% yield along with decarboxylative Heck-type product **3ca** (see in Scheme 2) in 25% isolated yield. 1-Naphthoic acid salt also furnished the corresponding annulated product **4ia** in 60% yield.[16]

Interestingly, the Heck-type reaction of lithium benzoate with *N*-benzyl maleimide and *N*-phenyl maleimide furnished biologically active molecules. As seen in Figure 1, compounds **3ab** and **3ac** are a potent antimicrobial and inhibitor of monoglyceride lipase, respectively. The scale-up reaction (8 mmol scale) of the Heck-type reaction of *N*-ethyl maleimide with lithium benzoate furnished the Heck-product **3aa** in 56% yield (Scheme 2). Similarly, the reaction of sodium benzoate with *N*-ethyl maleimide under annulation conditions afforded the corresponding annulated product **4aa** in 39% yield (Scheme 3).

DOI: 10.1021/acs.orglett.9b01412
Org. Lett. XXXX, XXX, XXX−XXX

The D_2O labeling experiment has been performed to gain insight into the reaction mechanism (Scheme 4). The reaction

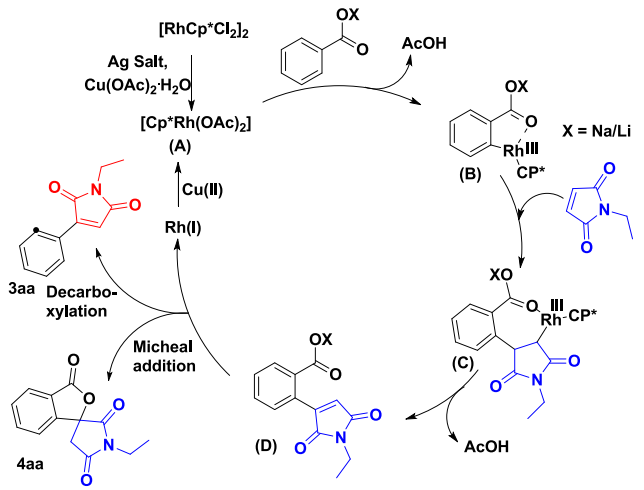
Scheme 4. Deuteration Study



of the Li salt of 3,4,5-trimethoxy benzoic acid with D_2O in the absence of maleimide under decarboxylative Heck-type reaction conditions furnished dideuterated product **6** in 75% yield with deuterium incorporation of 65% at both *ortho*-positions of the acid derivative. This deuterium labeling experiment indicates that the C−H activation step may be reversible.

Based on the literature precedence,[5,8c] a plausible reaction mechanism is shown in Scheme 5. The $[RhCp^*Cl_2]_2$ generates

Scheme 5. Plausible Mechanism



an active intermediate **A** in the presence of Ag-salt and $Cu(OAc)_2{\cdot}H_2O$, which undergoes C−H metalation with aromatic acid salt forming a five-membered rhodacycle **B**. In the next step, maleimide inserts into the five-membered metallacycle leading to a rigid bicyclic intermediate **C**, followed by an E_2 elimination, giving the intermediate **D**, which undergoes decarboxylation to form a decarboxylative Heck-type product as well as [4 + 1] annulation product **3aa** and **4aa**, respectively. In switching the selectivity, solvents play a crucial role. The decarboxylation of the intermediate **D** is avoided in a protic solvent such as TFE, which converts the benzoic acid salt to its corresponding acid derivative. Further, this intermediate instantaneously forms the corresponding spiro-products. On the other hand, in an aprotic solvent, the intermediate **D** is undergoing decarboxylation due to the lack of a proton source, which leads to Heck-type product.

In conclusion, we demonstrated the ability of a weakly coordinating carboxylate group in directing group chemistry. Thus, Rh-catalyzed functionalization of the salts of carboxylic acids with maleimide led to a switchable reaction to obtain either a decarboxylative Heck-type product or [4 + 1] annulation product. Solvents control the desired selectivity. To the best of our knowledge, this is the first report of decarboxylative Heck-type and 1,1-type annulation reactions of maleimide with benzoic acid. Some products obtained by Heck-type reactions are also biologically active molecules.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.9b01412.

Experimental procedures, characterization data, and spectra for all compounds (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: prabhu@iisc.ac.in.

ORCID

Kandikere Ramaiah Prabhu: 0000-0002-8342-1534

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was supported by SERB (EMR/2016/006358), New-Delhi, Indian Institute of Science, and R. L. Fine Chem. We thank Dr. A. R. Ramesha (R. L. Fine Chem) for useful discussions.

■ REFERENCES

(1) (a) Rouquet, G.; Chatani, N. Catalytic Functionalization of $C(sp^2)$-H and $C(sp^3)$-H Bonds by Using Bidentate Directing Groups. *Angew. Chem., Int. Ed.* **2013**, *52*, 11726−11743. (b) Ackermann, L. Carboxylate-Assisted Ruthenium-Catalyzed Alkyne Annulations by C−H/Het−H Bond Functionalizations. *Acc. Chem. Res.* **2014**, *47*, 281−295. (c) Chen, Z.; Wang, B.; Zhang, J.; Yu, W.; Liu, Z.; Zhang, Y. Transition metal-catalyzed C−H bond functionalizations by the use of diverse directing groups. *Org. Chem. Front.* **2015**, *2*, 1107−1295. (d) Yu, D.-G.; Suri, M.; Glorius, F. RhIII/CuII-Cocatalyzed Synthesis of 1H-Indazoles through C−H Amidation and N−N Bond Formation. *J. Am. Chem. Soc.* **2013**, *135*, 8802−8805.

(2) (a) Porter, R. J.; Penry, J. K.; Lacy, J. R.; Newmark, M. E.; Kupferberg, H. J. Plasma concentrations of phensuximide, methsuximide, and their metabolites in relation to clinical efficacy. *Neurology* **1979**, *29*, 1509−1513. (b) Chien, S. C.; Chen, M. L.; Kuo, H. T.; Tsai, T. C.; Lin, B. F.; Kuo, Y. H. Anti-inflammatory activities of new succinic and maleic derivatives from the fruiting body of antrodia camphorate. *J. Agric. Food Chem.* **2008**, *56*, 7017−7022. (c) Geethangili, M.; Tzeng, Y. Review of pharmacological effects of antrodia camphorata and its bioactive compounds. *eCAM* **2009**, *2011*, 212641−212658. (d) Garad, D. N.; Tanpure, S. D.; Mhaske, S. B. Radical-mediated dehydrative preparation of cyclic imides using $(NH_4)_2S_2O_8$-DMSO: application to the synthesis of vernakalant. *Beilstein J. Org. Chem.* **2015**, *11*, 1008−1016. (e) Han, Z.; Li, P.; Zhang, Z.; Chen, C.; Wang, Q.; Dong, X.; Zhang, X. Highly enantioselective synthesis of chiral succinimides via Rh/bisphosphine-thiourea-catalyzed asymmetric hydrogenation. *ACS Catal.* **2016**, *6*, 6214−6218. (f) Kavitha, K.; Praveena, K. S. S.; Ramarao, E. V. V. S.; Murthy, N. Y. S.; Pal, S. Chemistry of cyclic imides: an overview on the past, present and future. *Curr. Org. Chem.* **2016**, *20*, 1955−2001.

(3) (a) Stewart, S. G.; Ho, L. A.; Polomska, M. E.; Percival, A.; Yeoh, G. C. T. Rapid evaluation of antrodia camphorata natural products and derivatives in tumourigenic liver progenitor cells with a novel cell proliferation assay. *ChemMedChem* **2009**, *4*, 1657−1667. (b) Guan, Q.; Zuo, D.; Jiang, N.; Qi, H.; Zhai, Y.; Bai, Z.; Feng, D.; Yang, L.; Jiang, M.; Bao, K.; Li, C.; Wu, Y.; Zhang, W. Microwave-assisted

DOI: 10.1021/acs.orglett.9b01412
Org. Lett. XXXX, XXX, XXX−XXX

synthesis and biological evaluation of 3,4-diaryl maleic anhydride/*N*-substituted maleimide derivatives as combretastatin A-4 analogues. *Bioorg. Med. Chem. Lett.* **2015**, *25*, 631−634.

(4) (a) Hubert, J. C.; Wijnberg, J. B. P. A.; Speckamp, W. N. $NaBH_4$ reduction of cyclic imides. *Tetrahedron* **1975**, *31*, 1437−1441. (b) Wijnberg, J. B. P. A.; Schoemaker, H. E.; Speckamp, W. N. A regioselective reduction of gem-disubstituted succinimides. *Tetrahedron* **1978**, *34*, 179−183. (c) Shintani, R.; Duan, W.; Nagano, T.; Okada, A.; Hayashi, T. Chiral phosphine−olefin bidentate ligands in asymmetric catalysis: Rhodium-catalyzed asymmetric 1,4-addition of aryl boronic acids to maleimides. *Angew. Chem., Int. Ed.* **2005**, *44*, 4611−4614. (d) Lanke, V.; Bettadapur, K. R.; Prabhu, K. R. Site-selective addition of maleimide to indole at the C-2 Position: Ru(II)-catalyzed C−H activation. *Org. Lett.* **2015**, *17*, 4662−4665. (e) Tamizmani, M.; Gouranga, N.; Jeganmohan, M. Rhodium(III)-catalyzed ortho-alkenylation of anilides with maleimides. *Chemistry Select* **2019**, *4*, 2976−2981.

(5) (a) Bettadapur, K. R.; Sherikar, M. S.; Lanke, V.; Prabhu, K. R. Rh(III) catalyzed C-H activation: Mizoroki−Heck-type reaction of maleimides. *Asian J. Org. Chem.* **2018**, *7*, 1338−1342. (b) Sherikar, M. S.; Kapanaiah, R.; Lanke, V.; Prabhu, K. R. Rhodium(III)-catalyzed C−H activation at the C4-position of indole: switchable hydroarylation and oxidative Heck-type reactions of maleimides. *Chem. Commun.* **2018**, *54*, 11200−11204.

(6) (a) Bettadapur, K. R.; Lanke, V.; Prabhu, K. R. Ru (II)-catalyzed C−H activation: ketone-directed novel 1,4-addition of ortho C−H bond to maleimides. *Org. Lett.* **2015**, *17*, 4658−4661. (b) Keshri, P.; Bettadapur, K. R.; Lanke, V.; Prabhu, K. R. Ru(II)-catalyzed C−H activation: amide-directed 1,4-addition of the ortho C−H bond to maleimides. *J. Org. Chem.* **2016**, *81*, 6056−6065. (c) Muniraj, N.; Prabhu, K. R. Co(III)-catalyzed C−H activation: a site-selective conjugate addition of maleimide to indole at the C-2 position. *ACS Omega* **2017**, *2*, 4470−4479. (d) Muniraj, N.; Prabhu, K. R. Cobalt(III)-catalyzed C−H activation: azo directed selective 1,4-addition of ortho C−H bond to maleimides. *J. Org. Chem.* **2017**, *82*, 6913−6921. (e) Zhang, Z.; Han, S.; Tang, M.; Ackermann, L.; Li, J. C−H alkylations of (hetero)arenes by maleimides and maleate esters through cobalt(III) catalysis. *Org. Lett.* **2017**, *19*, 3315−3318. (f) Liu, S. L.; Li, Y.; Guo, J. R.; Yang, G. C.; Li, X. H.; Gong, J. F.; Song, M. P. An approach to 3-(indol-2-yl) succinimide derivatives by manganese-catalyzed C−H activation. *Org. Lett.* **2017**, *19*, 4042−4045. (g) He, Q.; Yamaguchi, T.; Chatani, N. Rh(I)-catalyzed alkylation of ortho-C−H bonds in aromatic amides with maleimides. *Org. Lett.* **2017**, *19*, 4544−4547.

(7) (a) Han, S. H.; Kim, S.; De, U.; Mishra, N. K.; Park, J.; Sharma, S.; Kwak, J. H.; Han, S.; Kim, H. S.; Kim, I. S. Synthesis of succinimide-containing chromones, naphthoquinones and xanthones under Rh(III) catalysis: evaluation of anticancer activity. *J. Org. Chem.* **2016**, *81*, 12416−12425. (b) Han, S.; Park, J.; Kim, S.; Lee, S. H.; Sharma, S.; Mishra, N. K.; Jung, Y. H.; Kim, I. S. Rhodium(III)-catalyzed C(sp^3)−H alkylation of 8-methylquinolines with maleimides. *Org. Lett.* **2016**, *18*, 4666−4669. (c) Han, S. H.; Mishra, N. K.; Jo, H.; Oh, Y.; Jeon, M.; Kim, S.; Kim, W. J.; Lee, J. S.; Kim, H. S.; Kim, I. S. One-pot synthesis of oxindoles through C−H alkylation and intramolecular cyclization of azobenzenes with internal olefins. *Adv. Synth. Catal.* **2017**, *359*, 2396−2401. (d) Chen, X.; Ren, J.; Xie, H.; Sun, W.; Sun, M.; Wu, B. Cobalt(III)-catalyzed 1,4-addition of C−H bonds of oximes to maleimides. *Org. Chem. Front.* **2018**, *5*, 184−188. (e) Reddy, K. N.; Krishna Rao, M. V.; Sridhar, B.; Reddy, B. V. S. Ru(II)-catalyzed hydroarylation of maleimides with cyclic *N*-sulfonylKetimines through ortho C-H bond activation. *Chemistry Select* **2018**, *3*, 5062−5065. (f) Li, F.; Zhou, Y.; Yang, H.; Liu, D.; Sun, B.; Zhang, F. L. Assembly of diverse spirocyclic pyrrolidines via transient directing group enabled ortho-C(sp^2)−H alkylation of benzaldehydes. *Org. Lett.* **2018**, *20*, 146−149.

(8) (a) Miura, W.; Hirano, K.; Miura, M. Copper-mediated oxidative coupling of benzamides with maleimides via directed C−H cleavage. *Org. Lett.* **2015**, *17*, 4034−4038. (b) Lv, N.; Liu, Y.; Xiong, C.; Liu, Z.; Zhang, Y. Cobalt catalyzed oxidant-free spirocycle synthesis by liberation of hydrogen. *Org. Lett.* **2017**, *19*, 4640−4644. (c) Manoharan, R.; Jeganmohan, M. Cobalt-catalyzed oxidative cyclization of benzamides with maleimides: synthesis of isoindolone spirosuccinimides. *Org. Lett.* **2017**, *19*, 5884−5888. (d) Han, S. H.; Mishra, N. K.; Jeon, M.; Kim, S.; Kim, H. S.; Jung, S.-Y.; Jung, Y. H.; Ku, J.- M.; Kim, I. S. Rhodium(III)-catalyzed diastereoselective synthesis of 1-aminoindanes via C-H activation. *Adv. Synth. Catal.* **2017**, *359*, 3900−3904. (e) Jeganmohan, M.; Manoharan, R. Alkylation, annulation and alkenylation of organic molecules with maleimides via transition-metal-catalyzed C−H bond activation. *Asian J. Org. Chem.*, **2019**, DOI: 10.1002/ajoc.201900054. (f) Ramesh, B.; Tamizmani, M.; Jeganmohan, M. Rhodium(III)-Catalyzed Redox-Neutral 1,1-Cyclization of N-Methoxy Benzamides with Maleimides via C−H/N−H/N−O Activation: Detailed Mechanistic Investigation. *J. Org. Chem.* **2019**, *84*, 4058−4071.

(9) (a) Sharma, S.; Oh, Y.; Mishra, N. K.; De, U.; Jo, H.; Sachan, R.; Kim, H. S.; Jung, Y. H.; Kim, I. S. Rhodium-catalyzed [3 + 2] annulation of cyclic *N*-acyl ketimines with activated olefins: anticancer activity of spiroisoindolinones. *J. Org. Chem.* **2017**, *82*, 3359−3367. (b) Tamizmani, M.; Ramesh, B.; Jeganmohan, M. Ruthenium- (II)-catalyzed redox-free [3 + 2] cycloaddition of *N*-sulfonyl aromatic aldimines with maleimides. *J. Org. Chem.* **2018**, *83*, 3746−3755.

(10) Muniraj, N.; Prabhu, K. R. Cobalt(III)-catalyzed [4 + 2] annulation of *N*-chlorobenzamides with maleimides. *Org. Lett.* **2019**, *21*, 1068−1072.

(11) Jambu, S.; Sivasakthikumaran, R.; Jeganmohan, M. Aerobic oxidative alkenylation of weak O-coordinating arylacetamides with alkenes via a Rh(III)-catalyzed C−H activation. *Org. Lett.* **2019**, *21*, 1320−1324.

(12) (a) Rondestvedt, C. S.; Vogl, O. Arylation of unsaturated systems by free radicals. II. arylation of maleimide by diazonium salts. *J. Am. Chem. Soc.* **1955**, *77*, 2313−2315. (b) Awuah, E.; Capretta, A. Development of methods for the synthesis of libraries of substituted maleimides and α,β-unsaturated-γ-butyrolactams. *J. Org. Chem.* **2011**, *76*, 3122−3130. (c) Lim, L. H.; Zhou, J. A challenging heck reaction of maleimides. *Org. Chem. Front.* **2015**, *2*, 775−777.

(13) (a) Ueura, K.; Satoh, T.; Miura, M. An Efficient Waste-Free Oxidative Coupling via Regioselective C-H Bond Cleavage: Rh/Cu-Catalyzed Reaction of Benzoic Acids with Alkynes and Acrylates under Air. *Org. Lett.* **2007**, *9*, 1407−1409. (b) Wang, D. H.; Mei, T. S.; Yu, J. Q. Versatile Pd(II)-Catalyzed C-H Activation/Aryl-Aryl Coupling of Benzoic and Phenyl Acetic Acids. *J. Am. Chem. Soc.* **2008**, *130*, 17676−17677. (c) Mei, T. S.; Giri, R.; Maugel, N.; Yu, J. Q. PdII-Catalyzed Monoselective ortho Halogenation of C_H Bonds Assisted by Counter Cations: A Complementary Method to Directed ortho Lithiation. *Angew. Chem., Int. Ed.* **2008**, *47*, 5215−5219. (d) Zhang, Y. H.; Yu, J. Q. Pd(II)-Catalyzed Hydroxylation of Arenes with 1 atm of O^2 or Air. *J. Am. Chem. Soc.* **2009**, *131*, 14654−14655. (e) Zhang, Y. H.; Shi, B. F.; Yu, J. Q. Palladium(II)-Catalyzed ortho Alkylation of Benzoic Acids with Alkyl Halides. *Angew. Chem., Int. Ed.* **2009**, *48*, 6097−6100. (f) Mochida, S.; Hirano, K.; Satoh, T.; Miura, M. Synthesis of Stilbene and Distyrylbenzene Derivatives through Rhodium-Catalyzed *Ortho*-Olefination and Decarboxylation of Benzoic Acids. *Org. Lett.* **2010**, *12*, 5776−5779.

(14) (a) Engle, K. M.; Mei, T. S.; Wasa, M.; Yu, J. Q. Weak Coordination as a Powerful Means for Developing Broadly Useful C-H Functionalization Reactions. *Acc. Chem. Res.* **2012**, *45*, 788−802. (b) Thuy-Boun, P. S.; Villa, G.; Dang, D.; Richardson, P.; Su, S.; Yu, J. Q. Ligand-Accelerated ortho-C−H Alkylation of Arylcarboxylic Acids using Alkyl Boron Reagents. *J. Am. Chem. Soc.* **2013**, *135*, 17508−17513. (c) Cheng, G.; Li, T. J.; Yu, J. Q. Practical Pd(II)-Catalyzed C−H Alkylation with Epoxides: One-Step Syntheses of 3,4-Dihydroisocoumarins. *J. Am. Chem. Soc.* **2015**, *137*, 10950−10953. (d) Lu, Y.; Wang, H. W.; Spangler, J. E.; Chen, K.; Cui, P. P.; Zhao, Y.; Sun, W. Y.; Yu, J. Q. Rh(III)-catalyzed C−H olefination of Npentafluoroaryl benzamides using air as the sole oxidant. *Chem. Sci.* **2015**, *6*, 1923−1927. (e) Wang, H. W.; Cui, P. P.; Lu, Y.; Sun, W. Y.; Yu, J. Q. Ligand-Promoted Rh(III)-Catalyzed Coupling of Aryl C−H Bonds with Arylboron Reagents. *J. Org. Chem.* **2016**, *81*, 3416−3422.

DOI: 10.1021/acs.orglett.9b01412
Org. Lett. XXXX, XXX, XXX−XXX

(f) Wang, H. W.; Lu, Y.; Zhang, B.; He, J.; Xu, H. J.; Kang, Y. S.; Sun, W. Y.; Yu, J. Q. Ligand-Promoted Rhodium(III)-Catalyzed ortho-C-H Amination with Free Amines. *Angew. Chem., Int. Ed.* **2017**, *56*, 7449−7453.

(15) (a) Bettadapur, K. R.; Lanke, V.; Prabhu, K. R. A deciduous directing group approach for the addition of aryl and vinyl nucleophiles to maleimides. *Chem. Commun.* **2017**, *53*, 6251−6255. (b) Mandal, A.; Sahoo, H.; Dana, S.; Baidya, M. Ruthenium(II)-catalyzed hydroarylation of maleimides using carboxylic acids as a traceless directing group. *Org. Lett.* **2017**, *19*, 4138−414. (c) Kumar, N. Y. P.; Rogge, T.; Yetra, S. R.; Bechtoldt, A.; Clot, E.; Ackermann, L. Mild decarboxylative C−H alkylation: computational insights for solvent-robust Ruthenium(II) domino manifold. *Chem. - Eur. J.* **2017**, *23*, 17449−17453.

(16) During the substrate scope investigation of the [4 + 1] annulation reaction, 5−10% of the corresponding decarboxylative Heck-type product was observed in most of the reactions.

DOI: 10.1021/acs.orglett.9b01412
Org. Lett. XXXX, XXX, XXX−XXX