A Journal of the Gesellschaft Deutscher Chemiker

Angewandte International Edition GDCh Chemie

www.angewandte.org

## Accepted Article

**Title:** Palladium-Catalyzed Decarbonylative Borylation of Carboxylic Acids: Tuning Reaction Selectivity by Computation

**Authors:** Chengwei Liu, Chong-Lei Ji, Xin Hong, and Michal Szostak



**To be cited as:** *Angew. Chem. Int. Ed.* 10.1002/anie.201810145
*Angew. Chem.* 10.1002/ange.201810145

**Link to VoR:** http://dx.doi.org/10.1002/anie.201810145
http://dx.doi.org/10.1002/ange.201810145

WILEY-VCH

10.1002/anie.201810145


WILEY-VCH

# Palladium-Catalyzed Decarbonylative Borylation of Carboxylic Acids: Tuning Reaction Selectivity by Computation

Chengwei Liu, Chong-Lei Ji, Xin Hong* and Michal Szostak*

**Abstract:** *Decarbonylative borylation of carboxylic acids is reported. Carbon electrophiles are generated directly after reagent-enabled decarbonylation of the in situ accessible sterically-hindered acyl derivative of a carboxylic acid under catalyst controlled conditions. The scope and the potential impact of this method are demonstrated in the selective borylation of a variety of aromatics (>50 examples). This strategy was used in the late-stage derivatization of pharmaceuticals and natural products. Computations reveal the mechanistic details of the unprecedented C–O bond activation of carboxylic acids. By circumventing the challenging decarboxylation, this strategy provides a general synthetic platform to access arylpalladium species for a wide array of bond formations from abundant carboxylic acids. The study shows a powerful combination of experiment and computation to predict decarbonylation selectivity.*

Carboxylic acids are considered as ideal substrates for organic synthesis.[1–3] Transition-metal-catalyzed cross-coupling reactions of carboxylic acids proceed via decarboxylative or decarbonylative pathways.[4,5] While decarboxylative cross-coupling reactions have been utilized to great extent to generate aryl nucleophiles,[6] the development of decarbonylative reactions to provide aryl electrophiles has met with limited success (Figure 1).[7,8] In contrast to decarboxylative cross-couplings which typically generate aryl nucleophiles or are performed under oxidative conditions, decarbonylative manifold proceeds under redox-neutral conditions and employs readily accessible activated carboxylic acid derivatives that permit selective oxidative addition of a carboxylic acid to a low valent metal center.[4,8] While several activators have been employed in the past (e.g. acid chlorides, anhydrides, esters, amides), all of these reagents are limited by stability to the reaction conditions, selectivity of the oxidative insertion step, and ease of preparation from carboxylic acids, typically necessitating a separate step involving chromatographic purification[9] which hinders the broad applicability of these methods.

The control of decarbonylation (vs. more straightforward acyl-coupling)[10–12] has remained an enduring challenge to the development of direct redox-neutral cross-coupling reactions of common carboxylic acids in the cross-coupling arena.[4–8] Given the widespread availability and the tremendous potential of the direct cross-coupling of carboxylic acids, we envisioned that the overall net decarbonylative-like process could be achieved by

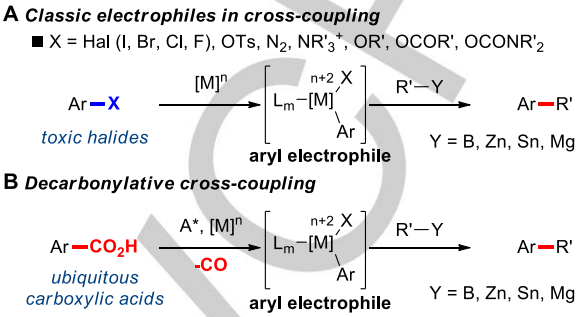



***Figure 1.*** Cross-coupling of aryl halides and carboxylic acids.

sequential C(acyl)–O bond activation and controlled decarbonylation, which engages carboxylic acids in a modular decarbonylative cross-coupling platform.[4,5] This strategy will furnish carbon–heteroatom bonds via the classical oxidative addition mechanism[13] under redox-neutral conditions, with the goal of providing an effective solution to the routine application of carboxylic acids as ubiquitous cross-coupling partners in chemical synthesis (Figure 1).

We first targeted decarbonylative borylation of carboxylic acids because of the key importance of aryl–boron bonds in diverse areas of chemical science (Figure 2).[14] Previous studies have shown that decarbonylative borylation of esters and amides with Ni and Rh catalysis is feasible;[15] however, no method for either the versatile Pd-catalyzed borylation[16] of these substrates or much more broadly applicable borylation of carboxylic acids[1,2,10–12] in any form are currently available, which underscores the challenge that these substrates present to decarbonylative processes.

The proposed coupling was examined using benzoic acid and $B_2pin_2$ as model substrates. To our delight, we found that the combination of $Pd(OAc)_2$ (5 mol%) and dppb (10 mol%) in the presence of $piv_2O$ (1.5 equiv), and $Et_3N$ (1.5 equiv) as base delivered the desired coupling product in 95% yield on a gram scale.[17] A summary of key optimization results is presented in the SI. In all cases examined, formation of acyl products was not detected in crude reaction mixtures, consistent with high capability of the metal catalyst to facilitate decarbonylation.

Having identified the optimal conditions, we next examined the scope of this new aryl–B forming reaction using common carboxylic acids substrates (Figure 2A). As shown, the scope of the reaction is very broad and tolerates an extensive array of carboxylic acids, including simple (**2a-d**) and sterically-hindered carboxylic acids (**2e-h**, **2x**), as well as those bearing diverse neutral, electron-donating and electron-withdrawing substituents (**2d-w**). Perhaps the most notable feature of new method is the capacity to tolerate a broad palette of functional groups that are poised for further manipulation or form key components in synthetic campaigns across all research settings, including halides (**2l**, **2v-w**), nitriles (**2m**, **2q**), esters (**2n**, **2r**, **2am**, **2an**), ketones (**2o**, **2s**, **2at**), aldehydes (**2p**, **2t**), amides (**2ap**, **2ar**), phenols (**2ak**), anilines (**2u**, **2ao**, **2aq**, **2as**), nitrogen- (**2y**, **2aa**,

[*] C. Liu, Prof. Dr. M. Szostak
Department of Chemistry, Rutgers University
73 Warren Street, Newark, NJ 07102 (United States)
E-mail: michal.szostak@rutgers.edu

C. L. Ji, Prof. Dr. X. Hong
Department of Chemistry, Zhejiang University
Hangzhou, 310027 (China)
E-mail: hxchem@zju.edu.cn

Supporting information for this article is given via a link at the end of the document.

10.1002/anie.201810145



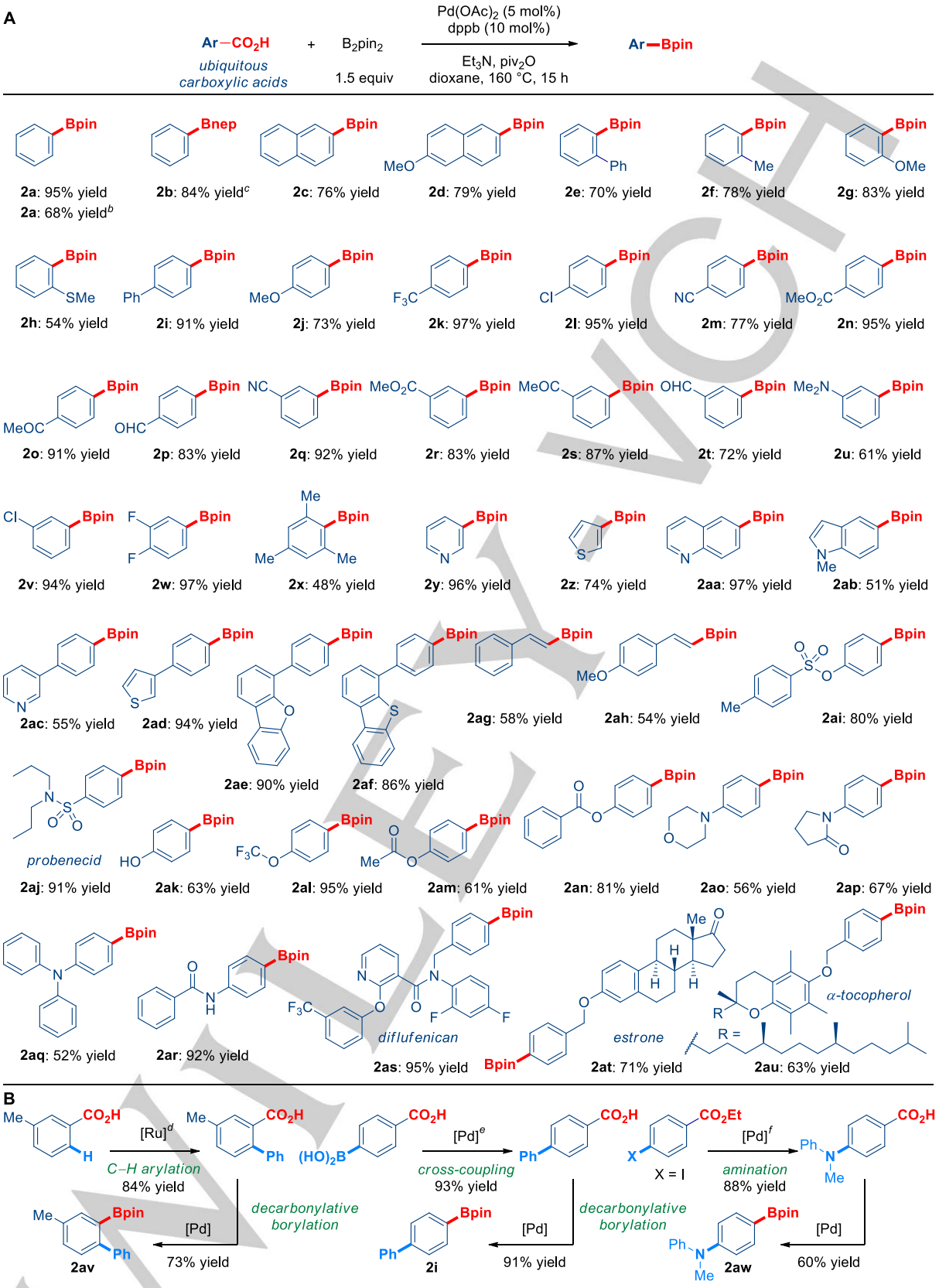




***Figure 2.*** Scope of decarbonylative borylation. [a] Carboxylic acid (1.0 equiv), $Pd(OAc)_2$ (5 mol%), dppb (10 mol%), $B_2pin_2$ (1.5 equiv), $Et_3N$ (1.5 equiv), $piv_2O$ (1.5 equiv), dioxane, 160 °C, 15 h. [b] Performed using $PhCOCO_2H$. [c] Performed using $B_2nep_2$. [d] PhI (1.5 equiv), $[Ru(p\text{-cym})Cl_2]_2$ (4 mol%), $PCy_3HBF4$ (8 mol%), $K_2CO_3$ (1.0 equiv), NMP, 100 °C, 15 h. [e] PhBr (1.2 equiv), $Pd(OAc)_2$ (3 mol%), $Na_2CO_3$ (2.0 equiv), $EtOH/H_2O$, 100 °C, 15 h. [f] PhNHMe (1.0 equiv), $Pd_2(dba)_3$ (1 mol%), Xphos (5 mol%, $K_2CO_3$ (2.0 equiv), *t*-BuOH, 110 °C, 15 h. See SI for experimental details.

10.1002/anie.201810145



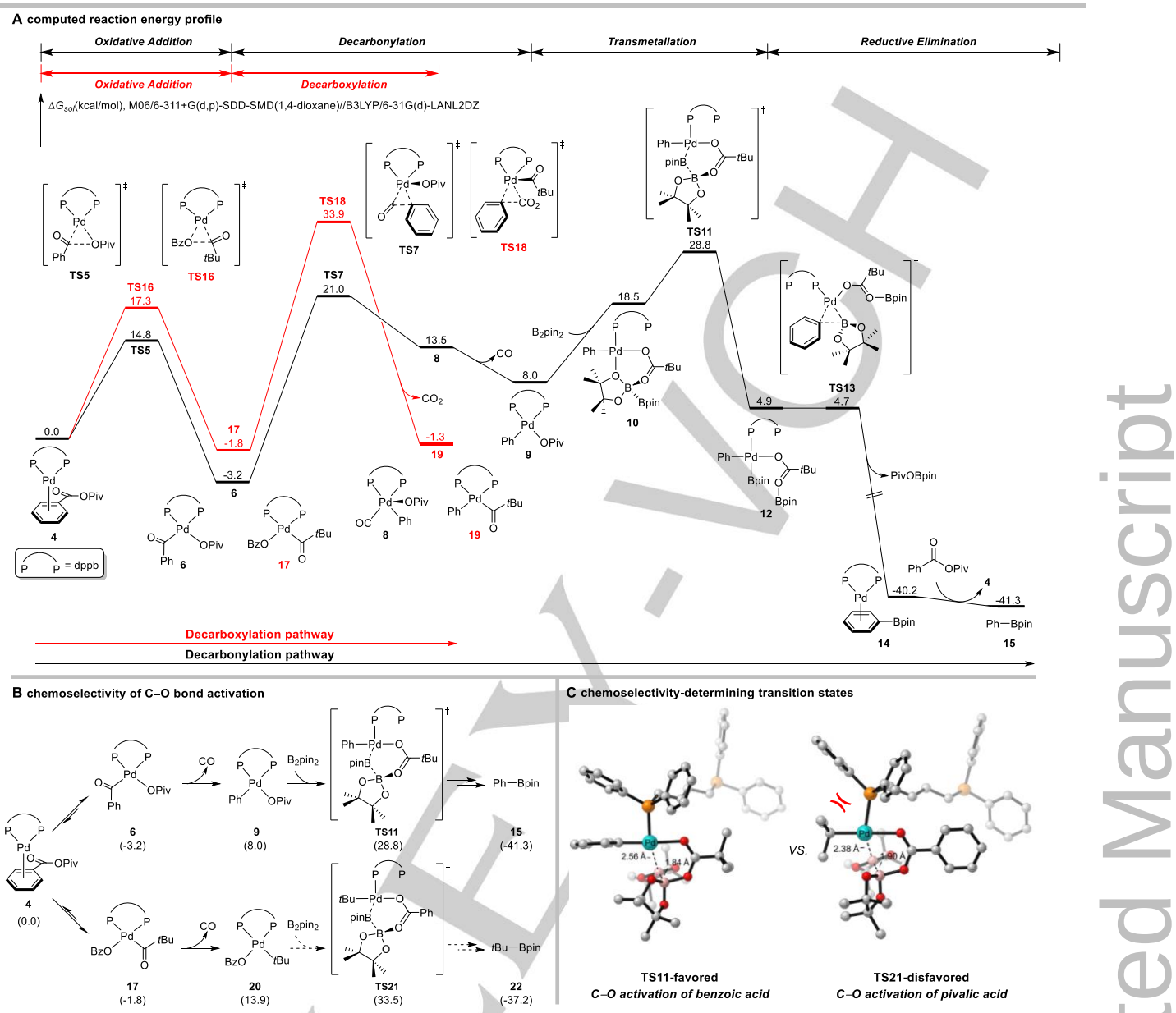




***Figure 3.*** DFT-calculated reaction energy profile and chemoselectivity of C–O bond activation of [Pd(dppb)]-catalyzed decarbonylative borylation of benzoic pivalic anhydride. See SI for computational details.

**2ab**, **2ac**, **2as**), sulfur- (**2z**, **2ad**, **2af**) and oxygen-heterocycles (**2ae**, **2ao**), amines (**2u**, **2ao**), lactams (**2ap**), sulfonate esters (**2ai**), sulfonamides (**2aj**), trifluoromethyl ethers (**2al**). It is particularly noteworthy that this protocol provides direct access to late-stage derivatization of drugs (probenecid, **2aj**), pesticides (diflufenican, **2as**), bioactive probes (estrone, **2at**) and natural products (tocopherol, **2au**). *Clearly, these reactions are enabled by the direct utilization of the carboxylic acid functional handle, and further illustrate the outstanding functional group tolerance of the protocol.*

As a further evidence of the synthetic utility of this new aryl–B forming method, we demonstrated illustrative protocols for sequential cross-coupling exploiting orthogonal properties of carboxylic acids to provide high-value traceless mode of reactivity, including C–H arylation/borylation (**2av**),[18] Suzuki-Miyaura cross-coupling/borylation (**2i**),[19] and amination/borylation (**2aw**)[20] according to the Buchwald protocol (Figure 2B). We note that, at present, aliphatic carboxylic acids are not tolerated due to facile beta-hydride elimination. The reaction tolerates the presence of Bpin residues.

Recent advances in computational studies render DFT calculations a reliable tool in predicting mechanisms of catalytic cross-coupling reactions.[21,22] To gain insight into the proposed Pd(0)/(II) decarbonylative cross-coupling platform, density functional theory (DFT) calculations were performed elucidating the mechanistic details and origins of chemoselectivity of the C–O bond activation (Figure 3). The computed free energy profile of the overall catalytic cycle of decarbonylative borylation is shown in Figure 3A. The C–O bond activations of carboxylic acid anhydride via **TS5** and **TS16** are facile and reversible, leading to two acylpalladium species **6** and **17** in equilibrium.[23] Subsequent decarbonylation via **TS7** is significantly more favorable than the decarboxylation via **TS18**, which corroborates the proposed decarbonylative strategy to activate carboxylic acid.[24] The arylpalladium intermediate **9** then undergoes the transmetallation[25] and reductive elimination[26] to produce the

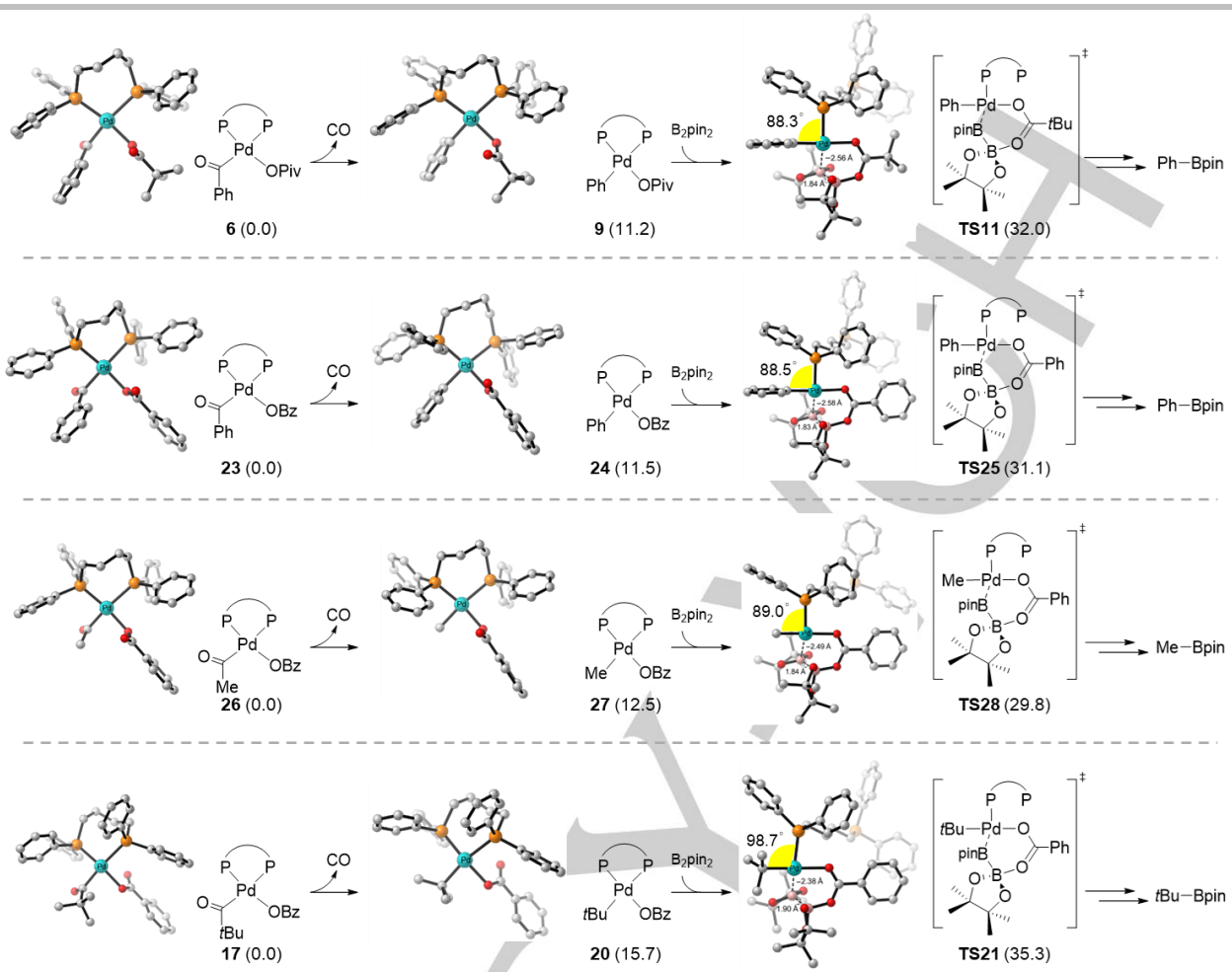



***Figure 4.*** DFT-calculated free energy changes of decarbonylative borylation of acylpalladium. Free energies in kcal/mol are in parenthesis.

decarbonylative borylation product **15**. The computations suggest that the acylpalladium intermediate **6** is the resting state of the catalytic cycle, and that the transmetallation step via **TS11** is the rate-determining step with an overall barrier of 32.0 kcal/mol (**6** to **TS11**).[27] We also attempted to locate the four-membered ring transmetallation transition state.[25a,28] However, all the computations led back to the six-membered ring **TS11**.

The substituent of carboxylic acid anhydride controls the chemoselectivity of C–O bond activation and functionalization by steric effects. Figure 3B shows the free energy changes of the two competing C–O bond activation pathways. Both transformations have the transmetallation step determines the overall catalytic efficiency, and the C–O bond activation of benzoic acid is more favorable by 4.7 kcal/mol (**TS11** vs. **TS21,** Figure 3C). *This is consistent with the experimental observations that only the C–O bond of benzoic acid is cleaved.* The detailed free energy changes of the reaction pathway involving C–O bond activation of pivalic acid are included in the Supporting Information (Figure S1).

To understand the origins of the chemoselectivities of C–O bond activation, the decarbonylative borylation of a series of acylpalladium species were studied (Figure 4). From the LPd(COPh)(OPiv) intermediate **6**, the decarbonylative borylation **TS11** is 32.0 kcal/mol higher in free energy. Changing the pivalate group to benzoate group barely affects the overall barrier, the corresponding transmetallation barrier is 31.1 kcal/mol (**23** to **TS25**). In addition, the comparisons between **23** and **26** suggest that the benzoylpalladium and acetylpalladium intermediates have similar transmetallation barriers. Only with the pivaloylpalladium species **17**, the decarbonylative borylation barrier increases to 35.3 kcal/mol, which clearly suggests that the steric repulsions of the *t*Bu group lead to the high barrier of decarbonylative borylation and shut down the corresponding C–O bond cleavage pathway. The steric effects of the *t*Bu group are reflected by the highlighted angle in the transmetallation transition states; the angle of **TS21** is significantly larger than those of the other transmetallation transition states (**TS11**, **TS25** and **TS28**). These results highlight the importance of anhydride design to achieve the desired C–O bond cleavage of carboxylic acid. The calculations revealed the mechanistic details of the unprecedented C–O bond activation of carboxylic acids. By circumventing the challenging decarboxylation, this strategy provides a general synthetic platform to access arylpalladium species for a wide array of C–X bond formations from abundant carboxylic acids.

In conclusion, this work demonstrates that a combination of experiment and computations serves as a powerful tool to navigate selectivity of decarbonylative processes of carboxylic acids. With all the benefits that carboxylic acids bring to chemical science, this approach will greatly expand the pursuit of a wide variety of cross-coupling reactions.

## Acknowledgements

We thank Rutgers University (M.S.), the NSF (CAREER CHE-1650766, M.S.), NSFC (21702182, X. H.), the Chinese "Thousand Youth Talents Plan" (X. H.), and Zhejiang University (X. H.) for generous financial support. The Bruker 500 MHz spectrometer used in this study was supported by the NSF-MRI grant (CHE-1229030). Calculations were performed on the high-performance computing system at the Department of Chemistry, Zhejiang University.

**Keywords:** decarbonylation • carboxylic acids • transition-metal-catalysis • computational chemistry • regioselectivity

[1] a) L. J. Gooßen, N. Rodriguez, K. Gooßen, *Angew. Chem. Int. Ed.* **2008***, 47*, 3100; b) M. Pichette Drapeau, L. J. Gooßen, *Chem. Eur. J.* **2016**, *22*, 18654.

[2] T. Patra, D. Maiti, *Chem. Eur. J.* **2017**, *23*, 7382.

[3] B. M. Trost, I. Fleming, *Comprehensive Organic Synthesis*, Pergamon Press, **1991**.

[4] a) W. Dzik, P. Lange, L. Gooßen, *Chem. Sci.* **2012**, *3*, 2671; b) N. Rodriguez, L. Gooßen, *Chem. Soc. Rev.* **2011**, *40*, 5030.

[5] For general reviews on cross-coupling, see: a) A. de Meijere, S. Bräse, M. Oestreich, *Metal-Catalyzed Cross-Coupling Reactions and More*, Wiley, **2014**; b) G. Molander, J. P. Wolfe, M. Larhed, *Science of Synthesis: Cross-Coupling and Heck-Type Reactions*, Thieme, **2013**

[6] For seminal studies, see: a) L. J. Gooßen, G. Dong, L. M. Levy, *Science* **2006**, *313*, 662; b) L. J. Gooßen, N. Rodriguez, B. Melzer, C. Linder, G. Deng, L. M. Levy, *J. Am. Chem. Soc.* **2007**, *129*, 4824; For oxidative Heck cross-coupling, see: c) A. G. Myers, D. Tanaka, M. R. Mannion, *J. Am. Chem. Soc.* **2002**, *124*, 11250; For decarbonylative cross-coupling of anhydrides, see: d) E. M. O'Brien, E. A. Bercot, T. Rovis, *J. Am. Chem. Soc.* **2003**, *125*, 10498.

[7] For selected recent examples of decarbonylative and decarboxylative cross-coupling reactions, see: a) S. T. Keaveney, F. Schoenebeck, *Angew. Chem.* **2018**, *130*, 4137; *Angew. Chem. Int. Ed.* **2018**, *57*, 4073; b) A. Chatupheeraphat, H. H. Liao, W. Srimontree, L. Guo, Y. Minenkov, A. Poater, L. Cavallo, M. Rueping, *J. Am. Chem. Soc.* **2018**, *140*, 3724; c) K. Muto, J. Yamaguchi, D. G. Musaev, K. Itami, *Nat. Commun.* **2015**, *6*, 7508; d) A. N. Desnoyer, F. W. Friese, W. Chiu, M. W. Drover, B. O. Patrick, J. A. Love, J. A. *Chem. Eur. J.* **2016**, *22*, 4070; e) A. N. Desnoyer, J. A. Love, *Chem. Soc. Rev.* **2017**, *46*, 197; f) C. Liu, M. Szostak, *Chem. Commun.* **2018**, *54*, 2130; g) Z. Zuo, D. T. Ahneman, L. Chu, J. A. Terrett, A. G. Doyle, D. W. C. MacMillan, *Science* **2014**, *345*, 437; h) D. C. Behenna, Y. Liu, T. Yurino, J. Kim, D. E. White, S. C. Virgil, B. M. Stoltz, *Nat. Chem.* **2012**, *4*, 130; i) D. V. Gribkov, S. J. Pastine, M. Schnürch, D. Sames, *J. Am. Chem. Soc.* **2007**, *129*, 11750.

[8] For a review, see: a) A. Dermenci, G. Dong, *Sci. China Chem.* **2013**, *56*, 685; For recent developments, see: b) L. Guo, M. Rueping, *Acc. Chem. Res.* **2018**, *5*, 1185; For selected mechanistic studies, see: c) Fristrup, P.; Kreis, M.; Palmelund, A.; Norrby, P. O.; Madsen, R. *J. Am. Chem. Soc.* **2008**, *130*, 5206; d) Cavell, K. J. *Coord. Chem. Rev.* **1996**, *155*, 209; e) M. De La Higuera Macias, B. A. Arndtsen, *J. Am. Chem. Soc.* **2018**, *140*, 10140.

[9] For reviews on atom-economy, see: a) C. J. Li, B. M. Trost, *Proc. Natl. Acad. Sci.* **2008**, *105*, 13197; b) Y. Hayashi, *Chem. Sci.* **2016**, *7*, 866; c) B. M. Trost, *Acc. Chem. Res.* **2002**, *35*, 695.

[10] For leading examples of acyl-cross coupling (retention of CO) of carboxylic acid derivatives, see: a) L. J. Gooßen, K. Ghosh, *Angew. Chem.* **2001**, *113*, 3566; *Angew. Chem. Int. Ed.* **2001**, *40*, 3458; b) A. Zapf, *Angew. Chem.* **2003**, *115*, 5552*; Angew. Chem. Int. Ed.* **2003**, *42*, 5394; For recent developments, see: c) G. Meng, M. Szostak, *Org. Lett.* **2015**, *17*, 4364.

[11] For a mechanistic DFT study of the acyl-Suzuki cross-coupling of carboxylic anhydrides, see: L. Gooßen, D. Koley, H. L. Hermann, W. Thiel, *J. Am. Chem. Soc.* **2005**, *127*, 11102.

[12] For decarbonylative Heck cross-coupling of carboxylic acid derivatives, see: a) L. J. Gooßen, J. Paetzold, *Angew. Chem.* **2002**, *114*, 1285; *Angew. Chem. Int. Ed.* **2002**, *41*, 1237; b) J. G. de Vries, *Angew. Chem.* **1998**, *110*, 688; *Angew. Chem. Int. Ed.* **1998**, *37*, 662; c) For Rh-catalyzed decarbonylative Suzuki cross-coupling of benzoic anhydrides, see: L. J. Gooßen, J. Paetzold, *Adv. Synth. Catal.* **2004**, *346*, 1665.

[13] a) R. H. Crabtree, *The Organometallic Chemistry of the Transition Metals*, Wiley, **2014**; b) T. Colacot, *New Trends in Cross-Coupling: Theory and Applications*, RSC, **2015**.

[14] a) N. Miyaura, A. Suzuki, *Chem. Rev.* **1995**, *95*, 2457; b) A. J. J. Lennox, G. C. Lloyd-Jones, *Chem. Soc. Rev.* **2014**, *43*, 412.

[15] a) L. Guo, M. Rueping, *Chem. Eur. J.* **2016**, *22*, 16787; b) J. Hu, Y. Zhao, J. Liu, Y. Zhang, Z. Shi, *Angew. Chem.* **2016**, *128*, 8860; *Angew. Chem. Int. Ed.* **2016**, *55*, 8718; c) H. Ochiai, Y. Uetake, T. Niwa, T. Hosoya, *Angew. Chem.* **2017**, *129*, 2522; *Angew. Chem. Int. Ed.* **2017**, *56*, 2482; For selected examples of decarboxylative borylation, see: d) C. Li, J. Wang, L. M. Barton, S. Yu, M. Tian, D. S. Peters, M. Kumar, A. W. Yu, K. A. Johnson, A. K. Chatterjee, M. Yan, P. S. Baran, *Science* **2017**, *356*, 7355; e) A. Fawcett, J. Pradeilles, Y. Wang, T. Mutsuga, E. L. Myers, V. K. Aggarwal, *Science* **2017**, *357*, 283; f) L. Candish, M. Teders, F. Glorius, *J. Am. Chem. Soc.* **2017**, *139*, 7440; For Pd-catalyzed decarbonylative dehydration, see: g) Y. Liu, S. C. Virgil, R. H. Grubbs, B. M. Stoltz, *Angew. Chem. Int. Ed.* **2015**, *54*, 11800; h) Y. Liu, K. E. Kim, M. B. Herbert, A. Fedorov, R. H. Grubbs, B. M. Stoltz, *Adv. Synth. Catal.* **2014**, *356*, 130; For Ni-catalyzed decarbonylative reactions, see: i) X. Pu, J. Hu, Y. Zhao, Z. Shi, *ACS Catal.* **2016**, *6*, 6692; j) J. Hu, M. Wang, X. Pu, Z. Shi, *Nat. Commun.* **2017**, *8*, 14993.

[16] a) T. Ishiyama, M. Murata, N. Miyaura, *J. Org. Chem.* **1995**, *60*, 7508; b) G. A. Molander, S. L. J. Trice, S. M. Kennedy, S. D. Dreher, M. T. Tudge, *J. Am. Chem. Soc.* **2012**, *134*, 11667.

[17] For selected decarbonylative cross-couplings from our groups, see: a) G. Meng, M. Szostak, *Angew. Chem.* **2015**, *127*, 14726; *Angew. Chem. Int. Ed.* **2015**, *54*, 14518; b) S. Shi, G. Meng, M. Szostak, *Angew. Chem.* **2016**, *128*, 7073; *Angew. Chem. Int. Ed.* **2016**, *55*, 6959; c) G. Meng, M. Szostak, *Org. Lett.* **2016**, *18*, 796; d) C. Liu, M. Szostak, *Angew. Chem.* **2017**, *129*, 12892; *Angew. Chem. Int. Ed.* **2017**, *56*, 12718; e) C. L. Ji, X. Hong, *J. Am. Chem. Soc.* **2017**, *139*, 15522.

[18] a) L. Huang, D. J. Weix, *Org. Lett.* **2016**, *18*, 5432; b) A. Biafora, T. Krause, D. Hackenberger, F. Belitz, L. J. Gooßen, *Angew. Chem.* **2016**, *128*, 14972; *Angew. Chem. Int. Ed.* **2016**, *55*, 14752.

[19] I. Hussain, J. Capricho, M. A. Yawer, *Adv. Synth. Catal.* **2016**, *358*, 3320.

[20] X. Huang, K. W. Anderson, D. Zim, L. Jiang, A. Klapars, S. L. Buchwald, *J. Am. Chem. Soc.* **2003**, *125*, 6653.

[21] a) T. Sperger, I. A. Sanhueza, I. Kalvet, F. Schoenebeck, *Chem. Rev.* **2015**, *115*, 9532; b) C. Poree, F. Schoenebeck, *Acc. Chem. Res.* **2017**, *50*, 605; c) T. Sperger, H. C. Fisher, F. Schoenebeck, *WIREs Comput. Mol. Sci.* **2016**, *6*, 226; d) M. Garcia-Melchor, A. A. C. Braga, A. Lledos, G. Ujaque, F. Maseras, F. *Acc. Chem. Res.* **2013**, *46*, 2626; e) D. Balcells, A. Nova, *ACS Catal.* **2018**, *8*, 3499.

[22] For an excellent perspective on the role of computations to predict mechanisms of organometallic reactions, see: T. Sperger, I. A. Sanhueza, F. Schoenebeck, *Acc. Chem. Res.* **2016**, *49*, 1311.

[23] For selected computational studies of oxidative addition with palladium catalysis, see: a) L. J. Gooßen, D. Koley, H. Hermann, W. Thiel, *Organometallics* **2005**, *24*, 2398; b) M. Ahlquist, P. Fristrup, D. Tanner, P. Norrby, *Organometallics* **2006**, *25*, 2066; c) M. Ahlquist, P. Norrby, *Organometallics* **2007**, *26*, 550; d) K. C. Lam, T. B. Marder, Z. Lin, *Organometallics* **2007**, *26*, 758; e) T. E. Barder, M. R. Biscoe, S. L. Buchwald, *Organometallics* **2007**, *26*, 2183; f) F. Schoenebeck, K. N. Houk, *J. Am. Chem. Soc.* **2010**, *132*, 2496.

[24] For a computational study of decarbonylation with palladium catalysis, see: M. Lesslie, Y. Yang, A. J. Canty, E. Piacentino, F. Berthias, P. Maitre, V. Ryzhov, R. A. J. O'Hair, *Chem. Commun.* **2018**, *54*, 346.

[25] For selected computational studies of transmetallation with palladium catalysis, see: a) M. Sumimoto, N. Iwane, T. Takahama, S. Sakaki, *J. Am. Chem. Soc.* **2004**, *126*, 10457; b) A. A. C. Braga, N. H. Morgon, G. Ujaque, F. Maseras, *J. Am. Chem. Soc.* **2005**, *127*, 9298; c) K. C. Lam, T. B. Marder, Z. Lin, *Organometallics* **2010**, *29*, 1849; d) B. Fuentes, M. Garca-Melchor, A. Lleds, F. Maseras, J. A. Casares, G. Ujaque, P. Espinet, *Chem. Eur. J.* **2010**, *16*, 8596.

[26] For a computational study of reductive elimination with palladium catalysis, see: M. Pérez-Rodríguez, A. A. C. Braga, M. Garcia-Melchor, M. H. Pérez-Temprano, J. A. Casares, G. Ujaque, A. R. de Lera, R. Álvarez, F. Maseras, P. Espinet, *J. Am. Chem. Soc.* **2009**, *131*, 3650.

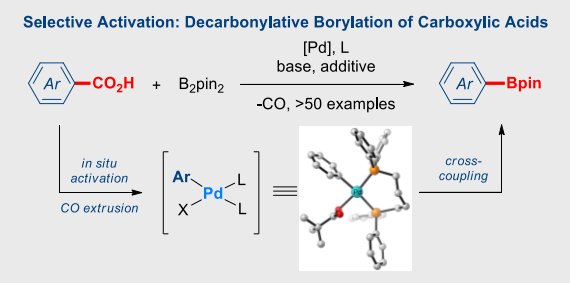
[27] The overall barrier is 27.8 kcal/mol with the M11-computed single point energies. The same trend is also observed with the B3LYP-D3(BJ) optimized geometries. Related details are included in the Supporting Information.

[28] Y. Takeda, A. Kuroda, W. M. C. Sameera, K. Morokuma, S. Minakata, *Chem. Sci.* **2016**, *7*, 6141.

10.1002/anie.201810145



WILEY-VCH




Decarbonylative borylation of carboxylic acids is reported. By circumventing the challenging decarboxylation, this strategy provides a general synthetic platform to access arylpalladium species for a wide array of bond formations from abundant carboxylic acids. Computations illustrate the origin of activation selectivity.

*Chengwei Liu, Chong-Lei Ji, Xin Hong* and Michal Szostak**

***Page No. – Page No.***

**Palladium-Catalyzed Decarbonylative Borylation of Carboxylic Acids: Tuning Reaction Selectivity by Computation**