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N,N-Chiral Ligands Enabling Palladium-catalyzed Enantioselective Intramolecular Heck-Matsuda Carbonylation Reactions by Sequential Migratory and CO Insertions.

Rafaela C. Carmona,[a] Otto D. Köster[a] and Carlos Roque Duarte Correia*[a]

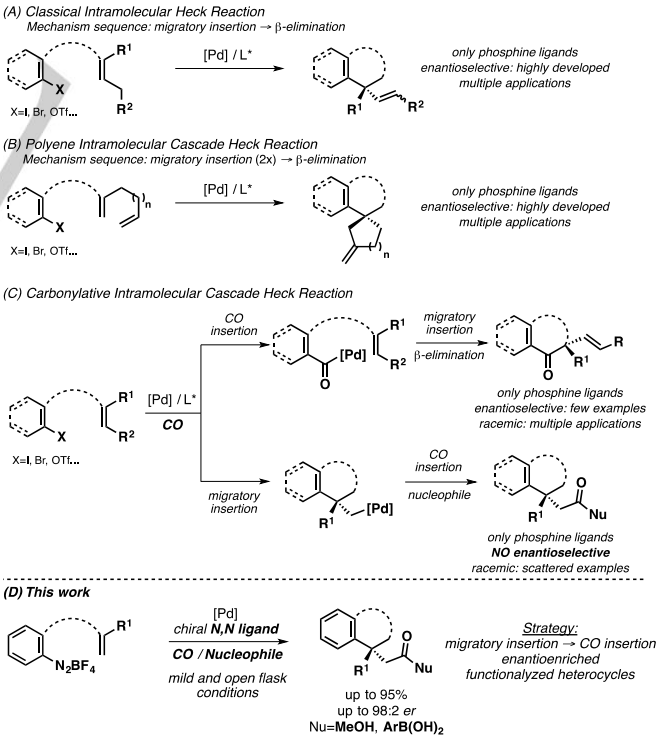
Dedication ((optional))

Abstract: Unprecedented enantioselective intramolecular Heck carbonylation reactions were achieved employing arenediazonium salts and *N*,*N*-chiral ligand. This methodology encompasses the first examples of an enantioselective Heck carbonylation through migratory insertion followed by CO insertion sequence. The enantioenriched functionalized dihydrobenzofurans were obtained in good to high yields and enantiomeric ratios up to 98:2 under mild and operationally simple reaction conditions.

The palladium catalyzed asymmetric Heck reaction is one of the most robust methodologies for efficient formation of C–C bonds and its intramolecular version is widely employed to achieve variable ring sizes.[1] The combination of its tolerance to different functional groups and substitution patterns in the alkene portion together with the development of cascade reactions turned the asymmetric intramolecular Heck reaction into a key method to reach molecular complexity in total synthesis of complex molecules.[2, 3]

The asymmetric intramolecular Heck reaction can be classified into three classes[4] depending on the mechanism sequence involved after oxidative addition (Scheme 1). The key issue to achieve enantioselectivity in these reactions is related to the β-elimination step, which should be controlled to avoid losing the newly formed stereocenter. There are a few different ways to overcome this problem, including directed elimination (Scheme 1A) and cascade reactions by capturing the σ-alkyl-palladium intermediate leading to β-elimination away from the stereogenic center (Schemes 1B and 1C).

After the oxidative addition, the classical intramolecular Heck reaction occurs via migratory insertion followed by the β-elimination step (Scheme 1A). This strategy has been substantially explored and is commonly employed for quaternary stereocenters formation,[5] preventing the β-elimination step to destroy the new stereocenter.[6] Regarding the cascade methodologies, the enantioselective polyene cascade sequence has been extensively developed and was applied in a wide range of natural products total synthesis.[7] This transformation happens fundamentally *via* sequential migratory insertions, trapping the σ-alkyl-palladium intermediate by other alkene moiety, preserving the created stereocenter (Scheme 1B). Additionally, a variety of nucleophiles can be used to react with the Pd^{II} intermediates, such as aromatic, organometallic compounds and CO.[8] Among them, the latter has the advantage to yield an acyl-palladium intermediate prone to further nucleophilic attack, thus leading to a diversity of carbonylated compounds.[3a] These reactions are known as carbonylative Heck reactions and can follow two distinct fates: *i*) an *endocarbonylative* pathway where the insertion of CO happens just after the oxidative addition, followed by the migratory insertion, leading to cyclic ketones (Scheme 1C top);[9] *ii*) an *exocarbonylative* pathway, where the CO insertion occurs after the migratory insertion into the double bond (Scheme 1C bottom).[10] Despite the potential of the intramolecular carbonylative Heck reaction to produce enantioenriched carbonyl compounds, this transformation is underexplored in the literature. To the best of our knowledge, there are only two enantioselective examples for the endocarbonylative pathway[11] and no examples for the exocarbonylation were reported to date.[5l, 12]



Scheme 1. Outline of the Intramolecular Heck Reaction.

Herein, we report the first enantioselective intramolecular exocarbonylative Heck reaction through the combination of

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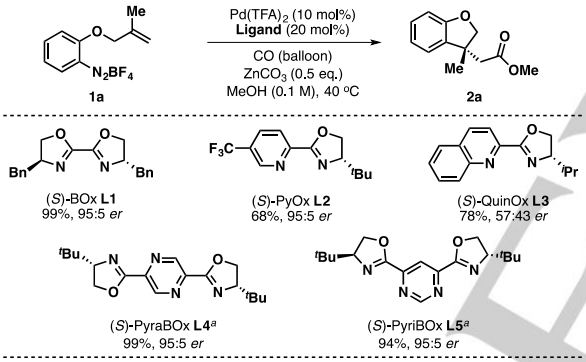
arenediazonium salts and *N,N*-chiral ligands. This catalytic system allowed the synthesis of enantioenriched functionalized dihydrobenzofurans under mild and operationally simple reaction conditions. It is worth pointing out that this is also the first time in which arenediazonium salts were employed intramolecularly in an enantioselective transformation.[13]

The study toward the enantioselective exocarbonylative intramolecular Heck reaction was initiated by the investigation of the catalytic system. The arenediazonium salt **1a** was chosen as the model substrate and after a few experiments, the use of $Pd(TFA)_2$, $ZnCO_3$ and MeOH, under CO atmosphere was found as an ideal condition to evaluate different *N,N*-chiral ligands (Table1). Gratifyingly, the *bis*-oxazoline (*S*)-BOx **L1** furnished the desired product **2a** in quantitative yield and 95:5 enantiomeric ratio (*er*). The pyridine-oxazoline (*S*)-PyOx**L2** also provided the product in good *er*, however in lower yield. In contrast, the use of quinoline-oxazoline (*S*)-QuinOX **L3** yielded the product in very low enantioselectivity. Finally, the pyrazine and pyrimidine *bis*-oxazolines **L4** and **L5**, highly efficient ligands toward asymmetric Heck-Matsuda reaction,[14] were successful in affording the product in excellent yields and enantiomeric ratios.

Table 1. Ligand evaluation.

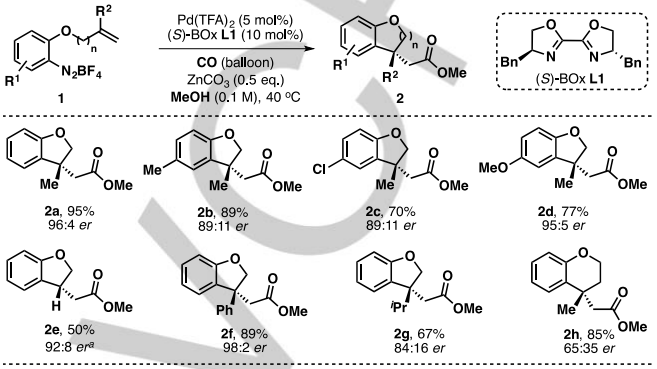


[a] 11 mol% of ligand was employed. Yields were determined by ^1H NMR and enantiomeric ratios were determined by chiral SFC analysis.

Despite the efficiency shown by **L4** and **L5**, ligand **L1** revealed a slightly higher efficiency after some optimization in the reaction conditions involving the amount of catalyst, base and temperature.

With the reaction conditions established, the reaction scope regarding the arenediazonium salt structure was evaluated (Table 2). The use of the arenediazonium salts containing methyl, chlorine or methoxy substituents on the aromatic ring (R^1) furnished the corresponding products **2b**, **2c** and **2d** in good yields and enantioselectivities. The influence of substituents on the double bond (R^2) was also evaluated. Notably, the product **2e** was obtained in 50% yield and good enantioselectivity with the corresponding aromatic benzofuran not being observed (See SI for details). This was an interesting result since the corresponding arenediazonium salt **1e** contains R^2=H on the alkene moiety, which could allow a fast β-elimination and consequent loss of the stereogenic center. Additionally, other substituents on the double bond (R^2) were also tolerated and products **2f** and **2g** containing a phenyl and an isopropyl group were obtained in 89% yield (98:2 *er*) and 67% yield (84:16 *er*) respectively. The feasibility of expanding this methodology to provide 6-membered cycles was also evaluated and the corresponding dihydrobenzopyran **2h** was formed exclusively in 85% yield (65:35 *er*). Regardless of its lower enantioselectivity compared to the 5-membered ones, the exocarbonylative pathway was preferred and no cyclic ketone product from an eventual endocarbonylation was observed.

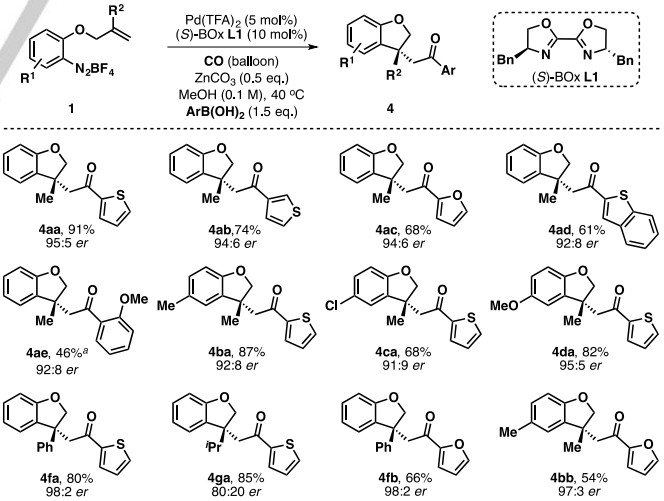
Table 2. Enantioselective intramolecular carbonylative Heck reaction.



[a] 5.5 mol% of ligand (*S*)-PyraBOx **L4** was employed. Isolated yields are shown and enantiomeric ratios were determined by chiral SFC analysis.

These encouraging results prompted the extension of the methodology by using boronic acids as coupling partners (Table 3). The model arenediazonium salt **1a** was submitted to the reaction conditions above together with 2-thienylboronic acid **3a** to furnish the desired product **4aa** in 91% yield and 95:5 *er*. Interestingly, the use of boronic acids bearing heteroatoms surpassed the competitive formation of **2a** by the addition of the methanol, used as the solvent, into the acyl palladium intermediate.

Table 3. Enantioselective intramolecular carbonylative Heck reaction with boronic acids.[a]



[a] Isolated yields are shown and enantiomeric ratios were determined by chiral SFC analysis. [b] 40% of the corresponding methyl ester **2a** was observed.

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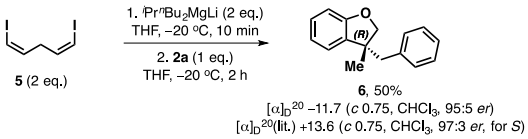
Different heteroaromatic boronic acids were tolerated and the products **4ab**, **4ac** and **4ad** were preferentially formed in good yields and enantioselectivities. The use of 2-methoxyphenylboronic acid **3e** furnished the desired product **4ae** in good enantioselectivity, however the corresponding methoxylated product **2a** was also observed in 1:1 ratio.

The arenediazonium salt structure was evaluated next and the presence of substituents on the aromatic ring (R^1) furnished selectively the corresponding products **4ba**, **4ca**, **4da** and **4bb** in good yields and high enantioselectivities. Moreover, the presence of a phenyl group on the alkene (R^2) did not affect the reaction efficiency affording the products **4fa** and **4gb** in good yields and high enantiomeric ratios. In agreement with the proposed catalytic cycle (see Scheme 3), the ^{i}Pr group leads to a higher steric hindrance with ligand substituent affording the corresponding product **4ga** in 85% yield and lower enantioselectivity.

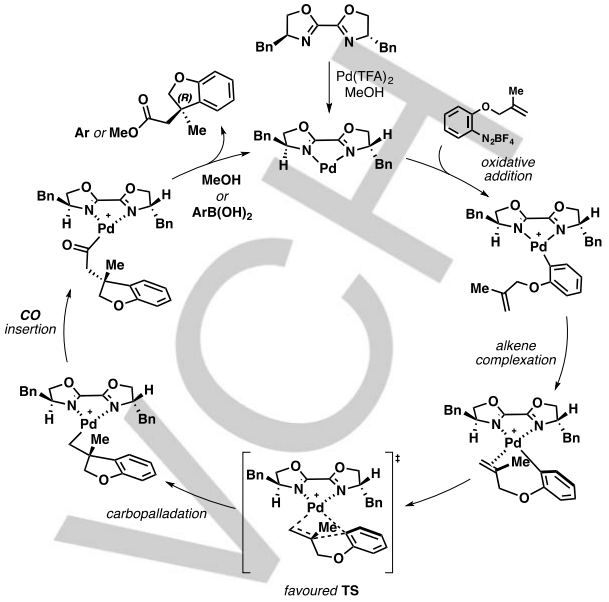
The absolute stereochemistry was determined using the Sparr reaction[15] to transform the carboxylic ester **2a** (Table 2) into the corresponding known[16] arene **6** through a double nucleophilic addition of 1,5-organodimagnesium reagent formed from diiodide **5** (Scheme 2).



Scheme 2. The absolute configuration determination.

Based on the absolute configuration of carboxylic ester **2a,** a catalytic cycle starting from the oxidative addition on the diazonium salt is proposed. Next, the alkene complexation to the cationic palladium succeeds preferentially through the *Si* face of the olefin moiety in the enantiodetermining transition state. In the sequence, the carbopalladation takes place, followed by CO and nucleophile insertions affording the corresponding (*R*)-**2** and (*R*)-**4** products (Scheme 3).

In summary, we have developed the first enantioselective intramolecular exocarbonylative Heck reaction. The unprecedented use of chiral *N*,*N*-ligand in an intramolecular Heck reaction together with the use of arenediazonium salts proved to benefit the formation of the exocarbonyl product. The developed methodology showed efficiency towards the synthesis of enantioenriched and functionalized dihydrobenzofurans. Further investigations to extend the mechanistic understanding and substrate variability are ongoing in our laboratory and will be reported in due course.



Scheme 3. Proposed catalytic cycle.

Experimental Section

A 4 mL vial equipped with a magnetic stir bar was charged with $Pd(CF_3CO_2)_2$ (5 mol%, 0.005 mmol, 1.7 mg), (*S*)-Box **L1** (10 mol%, 0.01 mmol, 3.2 mg), and MeOH (1.0 mL). The vial was capped and the mixture was stirred at 40 °C for 5 minutes to form the precatalyst. Next, the vial was cooled to room temperature and charged with $ZnCO_3$ (0.5 equiv, 0.05 mmol, 6.3 mg) and the appropriate arenediazonium salt **1** (1.0 equiv, 0.10 mmol). The vial was closed with a rubber cap and a CO balloon was attached. The CO was allowed to bubble into the reaction mixture for 30 seconds and then the reaction was stirred at 40 °C, under CO atmosphere, until complete consumption of the arenediazonium salt (β-naphthol test, approx. 10-20 minutes). Next, the solvent was removed in vacuo and the crude solubilized with EtOAc (2 mL). The resulting solution was filtered through a short pad of silica gel and washed with EtOAc (3 x 4 mL). The crude mixture was purified by flash chromatography to afford pure samples of the corresponding Heck products

Acknowledgements

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Keywords: enantioselective Heck reactions • intramolecular Heck reactions• cascade reactions • *N*,*N* ligands • palladium catalysis

[1] a) I. P. Beletskaya, A. V. Cheprakov, *Chem. Rev.* **2000**, *100*, 3009-3066; b) K. Tamao, T. Hiyama, E.-i. Negishi, *J. Organomet. Chem.* **2002**, *653*, 1-4; c) J. T. Link in *Organic Reactions, Vol 60* (Eds.: L. E. Overman), John Wiley & Sons, Inc., Hoboken, **2004**, pp. 157-561; d) F. Alonso, I. P.

10.1002/anie.201805831

Beletskaya, M. Yusa, *Tetrahedron* **2005**, *61,* 11771-11835; e) M. Oestreich, in *The Mizoroki–Heck Reaction*, Wiley, Chichester, **2009**; f) J. G. Taylor, A. V. Moro, C. R. D. Correia, *Eur. J. Org. Chem.* **2011**, *2011*, 1403-1428; g) F.-X. Felpin, L. Nassar-Hardy, F. LeCallonnec, E. Fouquet, *Tetrahedron* **2011**, *67*, 2815-2831.

[2] a) L. E. Overman, *Pure Appl. Chem.* **1994**, *66*, 1423-1430; b) A. B. Dounay, L. E. Overman, *Chem. Rev.* **2003**, *103*, 2945-2964; c) M. Shibasaki, E. M. Vogl, T. Ohshima, *Adv. Synth. Catal.* **2004**, *346*, 1533-1552; d) L. F. Tietze, H. Ila, H. P. Bell, *Chem. Rev.* **2004**, *104*, 3453-3516; e) M. Del Bel, A. R. Abela, J. D. Ng, C. A. Guerrero, *J. Am. Chem. Soc.* **2017**, *139*, 6819-6822; f) S. Chaudhuri, S. Ghosh, S. Bhunia. A. Bisai, *Chem. Commun.* **2018**, *54*, 940-943.

[3] a) E.-i. Negishi, C. Copéret, S. Ma, S.-Y. Liou, F. Liu, *Chem. Rev.* **1996**, *96*, 365-393; b) A. de Meijere, S. Bräse, *J. Organomet. Chem.* **1999**, *576*, 88-110; c) R. Grigg, V. Sridharan, *J. Organomet. Chem.* **1999**, *576*, 65-87; d) C. J. Chapman, C. G. Frost, *Synthesis* **2007**, 1-21; e) L. E. Overman, M. Rosen, *Tetrahedron* **2010**, *66*, 6514-6525; f) H. Clavier, H. Pellissier, *Adv. Synth. Catal.* **2012**, *354*, 3347-3403.

[4] The intramolecular Heck reaction can also occur *via* desymmetrization, see: M. Shibasaki, T. Ohshima, in *The Mizoroki–Heck Reaction*, (Eds.: M. Oestreich), Wiley, Chichester, **2009**, pp. 463-483.

[5] Selected examples: a) A. B. Dounay, K. Hatanaka, J. Kodanko, M. Oestreich, L. E. Overman, L. Pfeifer, M. M. Weiss, *J. Am. Chem. Soc*. **2003**, *125*, 6261-6271; b) A. B. Dounay, L. E. Overman, A. D. Wrobleski, *J. Am. Chem. Soc.* **2005**, *127*, 10186-10187; c) A. B. Dounay, P. G. Humphreys, L. E. Overman, A. D. Wrobleski, *J. Am. Chem Soc.* **2008**, *130*, 5368-5377; d) C. Shen, R.-R. Liu, R.-J. Fan, Y.-L. Li, T.-F. Xu, J.-R. Gao, Y.-X. Jia, *J. Am. Chem. Soc.* **2015**, *137*, 4936-4939. For an oxidative intramolecular Heck example, see: e) K. Akiyama, K. Mikami, *Heterocycles* **2007**, *74*, 827-834. For an aza-Heck example, see: f) N. J. Race, A. Faulkner, G. Fumagalli, T. Yamauchi, J. S. Scott, M. Rydén-Landergren, H. A. Sparkes, J. F. Bower, *Chem. Sci.* **2017**, *8*, 1981-1985.

[6] For tertiary stereocenter formation, see: a) S. Nukui, M. Sodeoka, M. Shibasaki, *Tetrahedron Lett.* **1993**, *34*, 4965-4968; b) K. Kiewel, M. Tallant, G. A. Sulikowski, *Tetrahedron Lett.* **2001**, *42*, 6621-6623; c) L. F. Tietze, R. Schimpf, *Angew. Chem. Int. Ed. Engl.* **1994**, *33*, 1089-1091; d) L. F. Tietze, T. Raschke, *Synlett* **1995**, 597-598; e) L. F. Tietze, T. Raschke, *Liebigs Ann. Chem.* **1996**, 1981-1987; f) L. F. Tietze, A. Modi, *Eur. J. Org. Chem.* **2000**, *2000*, 1959-1964; g) L. F. Tietze, K. Thede, R. Schimpf, F. Sannicolò, *Chem. Commun.* **2000**, 583-584.

[7] For the first example of enantioselective Heck reaction, see: a) N. E. Carpenter, D. J. Kucera, L. E. Overman, *J. Org. Chem.* **1989**, *54*, 5846-5848. For examples of the application of enantioselective polyene cascade Heck reaction in total synthesis, see: b) S. Bräse, A. de Meijere, in *Metal-Catalyzed Cross Coupling Reactions*, *Vol 1* (Eds.: A. de Meijere, F. Dieder-ich), Wiley-VCH, Weinheim, **2004**, pp. 217-296; c) A. B. Dounay, L. E. Overman, in *The Mizoroki–Heck Reaction*, (Eds.: M. Oestreich), Wiley, Chichester, **2009**, pp. 533-569; d) S. P. Maddaford, N. G. Andersen, W. A. Cristofoli, B. A. Keay, *J. Am. Chem. Soc.* **1996**, *118*, 10766-10773; e) D. Lucciola, B. A. Keay, *Synlett* **2011**, 1618-1622; f) S. M. Canhama, B. D. Hafensteinera, A. D. Lebsacka, T. L. May-Dracka, S. Nam, B. A. Stearns, L. E. Overman, *Tetrahedron* **2015**, *71*, 6424-6436; g) E. Coya, N. Sotomayor, E. Lete, *Adv. Synth. Catal.* **2015**, *357*, 3206-3214.

[8] For recent examples on capturing the σ-alkyl-palladium intermediate, see: a) J. Fan, W. Wei, M. Zhou, R. Song, J.-H. Li, *Angew. Chem. Int. Ed.* **2014**, *53*, 6650-6654; b) D. D. Vachhani, H. H. Butani, N. Sharma, U. C. Bhoya, A. K. Shah, E. V. Van der Eycken, *Chem. Commun.* **2015**, *51*, 14862-14865; c) H. Yoon, M. Rölz, F. Landau, M. Lautens, *Angew. Chem. Int. Ed.* **2017**, *56*, 10920-10923; c) M. Pérez-Gómez, S. Hernández-Ponte, D. Bautista, J.-A. García-López, *Chem. Commun.* **2017**, *53*, 2842-2845. Selected reviews: d) J. E. M. N. Klein, R. J. K. Taylor, *Eur. J. Org. Chem.* **2011**, *2011*, 6821-6841; e) H. Pellisier, *Adv. Synth. Catal.* **2016**, *358*, 2194-2259.

[9] Non-enantioselective endocarbonylation selected examples: a) E.-i. Negishi, J. A. Miller, *J. Am. Chem. Soc.* **1983**, *105*, 6761-6763; b) E.-i. Negishi, J. M. Tour, *Tetrahedron Lett.* **1986**, *27*, 4869-4872; c) C. Copéret, S. Ma, E.-i. Negishi, *Angew. Chem Int. Ed. Engl.* **1996**, *35*, 2125-2126; d) X. Wu, P. Nilsson, M. Larhed, *J. Org. Chem.* **2005**, *70*, 346-349; e) K. S. Bloome, E. J. Alexanian, *J. Am. Chem. Soc.* **2010**, *132*, 12823-12825; f) R. Frutos-Pedreño, J.-A. García-López, *Adv. Synth. Catal.* **2016**, *358*, 2692-2700; g) H. A. Dondas, S. Belveren, S. Poyraz, R. Grigg, C. Kilner, M. Ferraándiz-Saperas, E. Selva, J. M. Sansano, *Tetrahedron* **2018**, *74*, 6-11.

[10] Non-enantioselective exocarbonylation selected examples: a) V. K. Aggarwal, P. W. Davies, W. O. Moss, *Chem. Commun.* **2002**, 972-973; b) V. K. Aggarwal, P. W. Davies, A. T. Schmidt, *Chem. Commun.* **2004**, 1232-1233; c) B. Seashore-Ludlow, P. Somfai, *Org. Lett.* **2010**, *12*, 3732-3735; For an aza-Heck example see: d) A. Faulkner, J. S. Scott, J. F. Bower, *J. Am. Chem. Soc.* **2015**, *137*, 7224-7230.

[11] a) T. Suzuki, Y. Uozumi, M. Shibasaki, *J. Chem. Soc., Chem. Commun.* **1991**, 1593-1595; b) T. Hayashi, J. Tang, K. Kato, *Org. Lett.* **1999**, *1*, 1487-1489.

[12] No enantioselective exocarbonylation Heck reaction has been reported to date. Only hydride, cyanide and heteroaryl groups have been successfully reported to capture the σ-alkyl-palladium in an enantioselective Heck reaction. For recent highly enantioselective examples of cascade intramolecular Heck reaction, see: a) M. Minatti, X. Zheng, S. L. Buchwald, *J. Org. Chem.* **2007**, *72*, 9253-9258; b) A. Pinto, Y. Jia, L. Neuville, J. Zhu, *Chem. Eur. J.* **2007**, *13*, 961-967; c) W. Kong, Q. Wang, J. Zhu, *J. Am. Chem. Soc.* **2015**, *137*, 16028-16031. d) G. Yue, K. Lei, H. Hirao, J. Zhou, *Angew. Chem. Int. Ed.* **2015**, *54*, 6531-6535; e) W. Kong, Q. Wang, J. Zhu, *Angew. Chem. Int. Ed.* **2016**, *55*, 9714-9718; f) X.-M. Xu, L. Zhao, J. Zhu, M.-X. Wang, *Angew. Chem. Int. Ed.* **2016**, *55*, 3799-3803; g) W. Kong, Q. Wang, J. Zhu, *Angew. Chem. Int. Ed.* **2017**, *56*, 3987-3991. For an enantioselective cascade aza-Heck example see: h) X. Bao, Q. Wang, J. Zhu, *Angew. Chem. Int. Ed.* **2017**, *56*, 9577-9581.

[13] For racemic intramolecular Heck-Matsuda reaction, see: a) F. A. Siqueira, J. G. Taylor, C. R. D. Correia, *Tetrahedron Lett.* **2010**, *51*, 2102-2105. For the first intermolecular enantioselective Heck-Matsuda reaction, see: b) C. C. Oliveira, A. G. Salles Jr., E. A. F. Santos, C. R. D. Correia, *Tetrahedron Lett.* **2012**, *53*, 3325-3328.

[14] a) C. C. Oliveira, A. Pfaltz, C. R. D. Correia, *Angew. Chem. Int. Ed.* **2015**, *54*, 14036-14039; b) F. de Azambuja, R. C. Carmona, T. H. D. Chorro, G. Heerdt, C. R. D. Correia, *Chem. Eur. J.* **2016**, *22*, 11205-11209; c) I. U. Khan, S. Kattela, A. Hassan, C. R. D. Correia, *Org. Biomol. Chem.* **2016**, *14*, 9476-9480; d) A. R. Silva, E. C. Polo, N. C. Martins, C. R. D. Correia, *Adv. Synth. Catal.* **2018**, *360*, 346-365.

[15] A. Link, C. Fischer, C. Sparr, *Angew. Chem. Int. Ed.* **2015**, *54*,12163-12166.

[16] W. You, M. K. Brown, *J. Am. Chem. Soc.* **2015**, *137*, 14578-14581.

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Layout 2:

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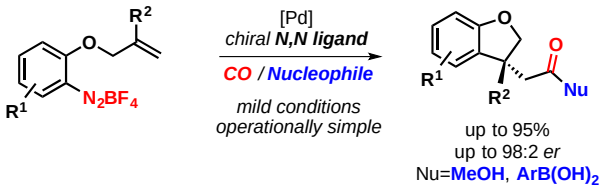

The first enantioselective intramolecular Heck exocarbonylation

*R. C. Carmona, O. D. Köster, C. R. D. Correia**

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N,N-Chiral Ligands Enabling Palladium-catalyzed Enantioselective Intramolecular Heck-Matsuda Carbonylation Reactions by Sequential Migratory and CO Insertions.

Remarkable Enantioselective Exocarbonylations: The first examples of novel enantioselective intramolecular Heck carbonylations are reported employing arenediazonium salts and *N,N*-chiral ligands. Enantioenriched dihydrobenzofurans compounds were obtained through an unprecedented sequence of migratory insertion followed by CO insertion.