Rh(II)-Catalyzed Monocyclopropanation of Pyrroles and its Application to the Synthesis Pharmaceutically Relevant Compounds

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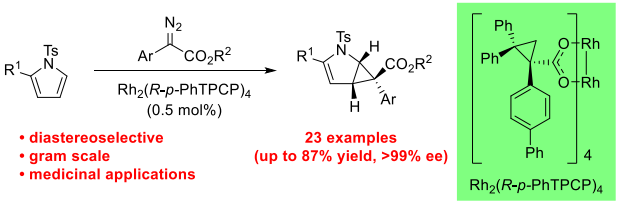
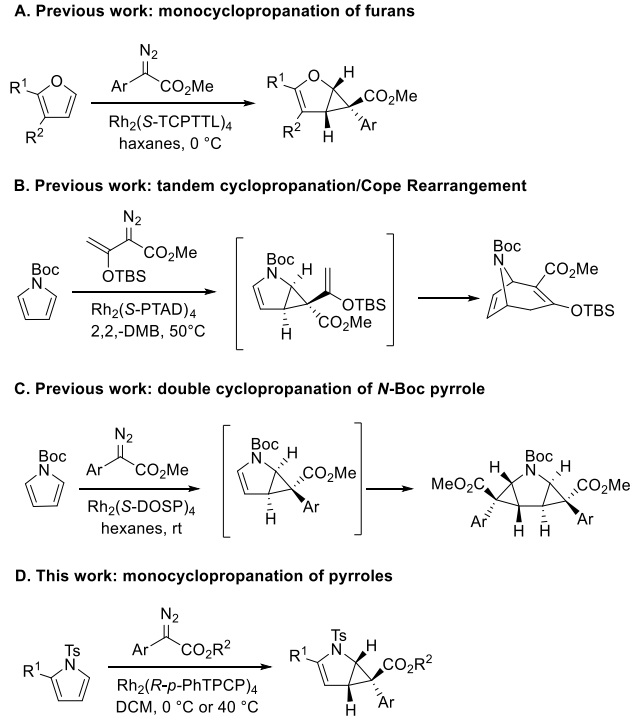
Supporting Information Placeholder

ABSTRACT: Here we report Rh(II)-catalyzed monocyclopropanation reactions on pyrroles in the presence of aryldiazoacetates, providing the corresponding dearomatized products with high levels of enantioselectivity (up to >99% ee). Under the catalysis of Rh_2(*R*-*p*-PhTPCP)$_4$, a broad range of pyrrole substrates and aryldiazoacetates are shown to be compatible. Utilizing these valuable chiral building blocks, we further demonstrate the application of this transformation by synthesizing a homo-β-proline analog and a β-aminocarboxylic acid (β-ACC) derivative from the monocyclopropanated product.



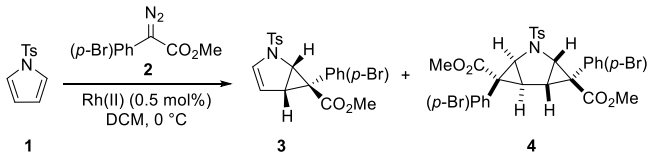
Metal-catalyzed reactions of carbenes with electron-rich heterocycles such as furan and pyrroles are synthetically useful transformations.[1] When protected pyrroles are used as substrates, the outcomes of the reaction usually depend on the electronic nature of the heterocycle. With *N*-H or *N*-alkyl derivatives the common transformation is alkylation at either the C-2 or C-3 position *via* a zwitterionic pathway.[2] However, *N*-acylation causes the pyrrole to be less electron rich and cyclopropane intermediates are typically generated.[2c, 3] Recently, the Reiser group described the asymmetric cyclopropanation of furans and pyrroles catalyzed by Cu(I)-bis(oxazoline) with acceptor-only carbenes derived from alkyl diazoacetates[4], and Davies and Reiser reported the asymmetric monocyclopropanation of furans with donor/acceptor carbenes (Scheme 1A).[5] In addition, the Davies group has shown that cyclopropanes generated from rhodium-catalyzed reactions of donor/acceptor carbenes with *N*-Boc-pyrroles tended to react further under the reaction conditions. Two established reactions involving such reactive intermediates are the tandem cyclopropanation/Cope Rearrangement to form tropane derivatives (Scheme 1B),[6] and double cyclopropanation of protected pyrroles to generate products with six new stereogenic centers (Scheme 1C).[7] Even though the monocyclopropane intermediates derived from donor/acceptor carbenes are implicated in these reactions, their isolation was only possible when the substrate was used as the solvent (in large excess) and still double cyclopropanation was a competing reaction.[7] In this manuscript, we describe conditions for the monocyclopropanation of pyrroles and demonstrate the products can be applied to the syntheses of a homo-β-proline analog as well as a β-aminocarboxylic acid derivative, highlighting the potential medicinal relevance of our strategy (Scheme 1D).

Scheme 1. Rh(II)-catalyzed reactions of donor/acceptor diazo compounds with furans and *N*-protected pyrroles



Recently we reported that Rh_2(*S*-TCPTTL)$_4$ is an exceptional catalyst for the asymmetric monocyclopropanation of furans.[5] However, applying this catalyst to *N*-protected pyrroles was not effective. When *N*-Boc pyrrole was used as the substrate, the reaction yielded the undesired double cyclopropanated product in only trace amount, whereas the reaction of *N*-tosyl pyrrole (**1**) and methyl *p*-bromophenyldiazoacetate (**2**) gave some of the monocyclopropanated product **3**, but also a considerable amount of the double cyclopropanated product **4** (Table 1, entry 1). In order to obtain a higher yield and more selective monocyclopropanation reaction, a systematic catalyst screening was conducted using a wide variety of chiral dirhodium catalysts that have been developed for the reactions of donor/acceptor carbenes. A series of related phthalimido catalysts were examined (entries 1-4, Figure 1). Rh_2(*S*-TCPTAD)$_4$ gave a cleaner monocyclopropanation reaction, but low enantioselectivity. Rh_2(*R*-PTAD)$_4$ and Rh_2(*R*-PTTL)$_4$ resulted in high enantioselectivity, but still the undesired side product **4** was formed. The naphthalimido catalyst Rh_2(*S*-NTTL)$_4$ gave clean monocyclopropana

Table 1. Catalyst optimization of *N*-tosyl pyrrole monocyclopropanation

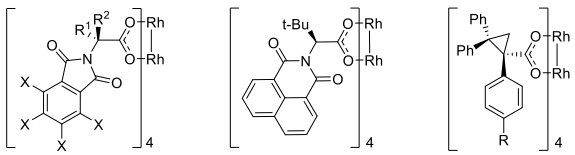


1 3 4

Entry	Catalyst	**3**:**4**[a]	**3**, yield (%)[b]	**3**, ee, (%)[c]
1	Rh_2(*S*-TCPTTL)$_4$	1.4:1	33	66
2	Rh_2(*R*-TCPTAD)$_4$	3.1:1	39	-70
3	Rh_2(*R*-PTAD)$_4$	6.7:1	54	-97
4	Rh_2(*R*-PTTL)$_4$	22.7:1	59	-95
5	Rh_2(*S*-NTTL)$_4$	>30:1	60	85
6	Rh_2(*R*-*p*-BrTPCP)$_4$	>30:1	59	82
7	**Rh_2(R-*p*-PhTPCP)$_4$**	**>30:1**	**56**	**91**
8[d]	Rh_2(R-*p*-PhTPCP)$_4$	>30:1	64	88

*Reaction conditions: **2** (0.3 mmol) in 2.5 mL DCM was added over 90 min to a solution of the pyrrole substrate (0.6 mmol, 2.0 equiv.) and catalyst (0.5 mol%) in 2.5 mL DCM at 0 °C. The reaction was allowed to stir for an additional 30 min. [a]Ratios were determined by reaction crude ^{1}H NMR spectra. [b]All yields are isolated yields. [c]The enantioselectivity was determined by chiral HPLC analysis of the isolated product. [d]The reaction was conducted at reflux (40 °C).*

Figure 1. Structures of rhodium catalysts used in the study



Rh_2(*S*-TCPTTL)$_4$: X = Cl, R^1 = H, R^2 = *t*Bu
Rh_2(*R*-TCPTAD)$_4$: X = Cl, R^1 = adamantyl, R^2 = H
Rh_2(*R*-PTAD)$_4$: X = H, R^1 = adamantyl, R^2 = H
Rh_2(*R*-PTTL)$_4$: X = H, R^1 = *t*Bu, R^2 = H

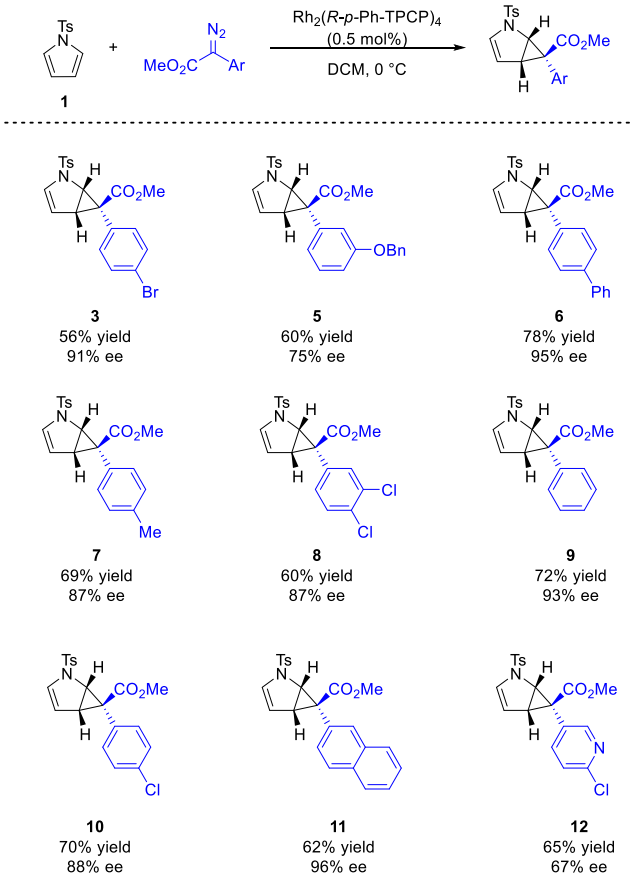
Rh_2(*S*-NTTL)$_4$

Rh_2(*R*-*p*-BrTPCP)$_4$: R = Br
Rh_2(*R*-*p*-PhTPCP)$_4$: R = Ph

tion and 3 was formed in 85% ee (entry 5). The triarylcyclopropane carboxylate catalyst Rh_2(*R*-*p*-BrTPCP)$_4$ also gave cleanly the monocyclopropanated product (entry 6), but Rh_2(*R*-*p*-PhTPCP)$_4$ produced 3 in higher ee (91% ee, entry 7). In an attempt to enhance yield, the reaction was performed at 40 °C (reflux), but a lower enantioselectivity was observed with marginal improvement in yield (entry 8).

With the optimized conditions in hand, the reaction of a series of aryldiazoacetates with *N*-tosyl pyrrole was examined. As shown in Scheme 2, many aryldiazoacetates are compatible with this chemistry, and the desired pyrrolocyclopropanes 3, 5-11 were obtained in good yields and with moderate to high levels of enantioselectivity (75-96% ee). Modifications of the electronic factors and substitution patterns on the aryl ring do not have a major influence on the outcome of the reaction. However, when the aryldiazoacetate contains a pyridine functionality, the pyrrolocyclopropane 12 was formed with a marked drop in enantioselectivity (67% ee).

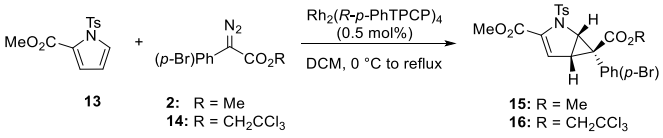
Scheme 2. Scope of monocyclopropanation of *N*-tosylpyrrole



Extension of the optimized conditions to functionalized pyrroles did not lead to good results. For example, reaction with the 2-methoxycarbonyl derivative **13** with the methyl aryldiazoacetate **2** gave low yield of the pyrrolocyclopropane **15** (34%) (Table 2, entry 1), even though the level of enantioselectivity remained high (96% ee). We reasoned that this may be due to inefficient trapping of the carbene by the substrate under these conditions based on the crude ^{1}H NMR. Previously, we had found in our C–H functionalization studies that in reactions of carbenes with unactivated C–H bonds, the yields

tended to be higher when a trichloroethyl ester of the carbene is used instead of the methyl ester.[8] Hence, the reaction was re-optimized for **13** using trichloroethyl *p*-bromophenyldiazoacetate **14**. The initial study was conducted at 0 °C, which gave even lower yield of the desired product **16** (entry 2), but when the reaction was conducted at reflux, the yield was much higher (87%, entry 3) and the enantioselectivity remained high (97% ee). Due to the presence of the electron withdrawing group on the pyrrole, no double cyclopropanation was observed. In addition, the reaction could be conducted with a 0.1 mol% catalyst loading, and the same level of enantioselectivity could be obtained, but the yield was slightly decreased (entry 4).

Table 2. Optimization of reaction with methyl *N*-tosylpyrrole-2-carboxylate



13

2: R = Me
14: R = CH_2CCl_3

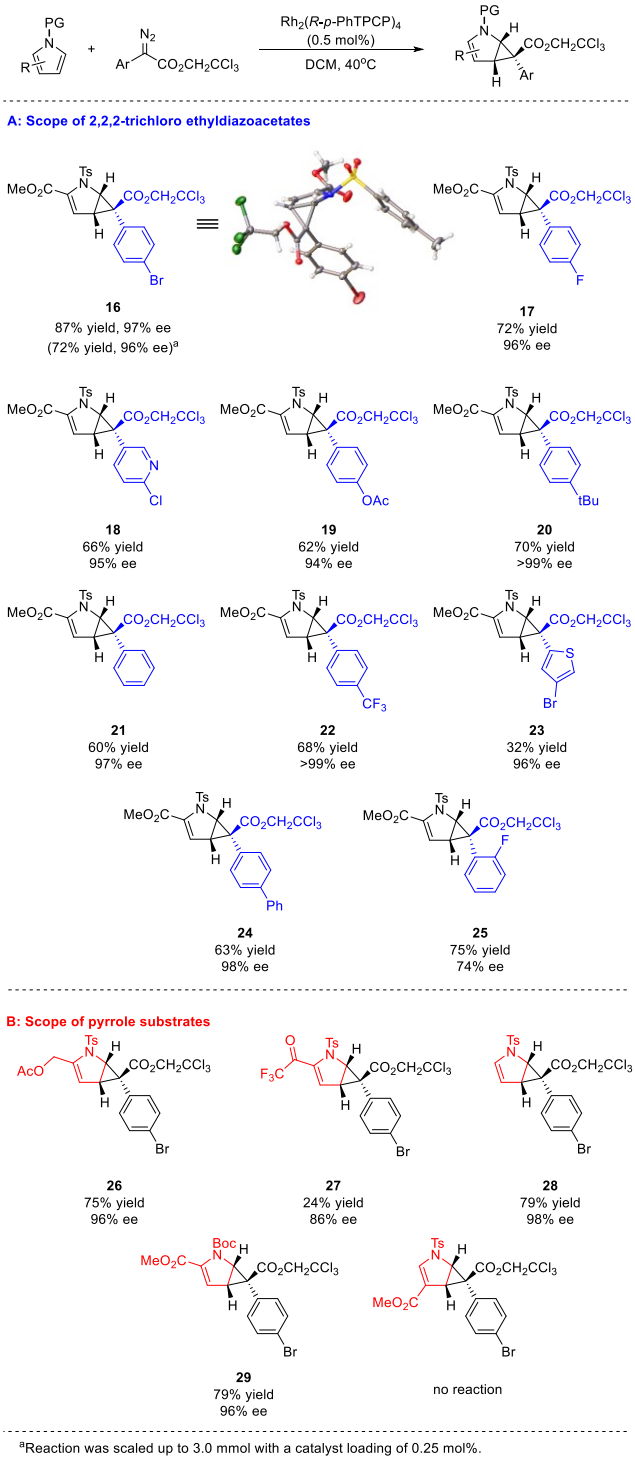
15: R = Me
16: R = CH_2CCl_3

Entry	R	temp (°C)	yield[a] (%)	ee[b] (%)
1	Me	0	34	96
2	CH_2CCl_3	0	15	98
3	CH_2CCl_3	**40**	**87**	**97**
4[c]	CH_2CCl_3	40	69	97

*Reaction conditions: **2** (0.3 mmol) in 2.5 mL DCM was added over 90 min to a solution of the pyrrole substrate (0.6 mmol, 2.0 equiv.) and catalyst (0.5 mol%) in 2.5 mL DCM. The reaction was allowed to stir for an additional 30 min. [a]All yields are isolated yields. [b]The enantioselectivity was determined by chiral HPLC analysis of the isolated product. [c]Reaction conducted with 0.1 mol % of catalyst. The absolute stereochemistry of **16** was assigned by X-ray crystallography study and used for analogy for other compounds.*

The reaction of *N*-tosylpyrroles with a range of trichloroethyl aryldiazoacetates was examined and the results are summarized in Scheme 3. The reaction with **13** gave very high enantioselectivity for pyrrolocyclopropanes **17**-**24** with virtually every aryldiazoacetate (94 to >99% ee) including the pyridine and thiophene derivatives **18** and **23**. Notably, the scalability of the reaction was demonstrated with **16** at 3 mmol (10-fold increase), where the product was produced in 72% yield and 96% ee at gram scale, even at a lowered catalyst loading of 0.25 mol%. The only product that did not give exceptionally high enantioselectivity was the *o*-fluorophenyl derivative **25** (74% ee). The reaction also gave high enantioselectivity with other 2-substituted pyrroles to form **26** and **27** in 96% and 86% ee, respectively. The low yield of the trifluroacetyl derivative **27** (24% yield) is presumably because the pyrrole is now too deactivated for effective trapping of the carbene. Good yields and high levels of enantioselectivity of the monocyclopropanated product were obtained with the unsubstituted pyrrole to form **28** and with the *N*-Boc protected 2-methoxycarbonyl pyrrole to form **29**. However, compound **28** was prone to decomposition even at room temperature within a few hours. The methyl ester version, **3**, nonetheless, was stable. While 2-substituted pyrroles are well tolerated, placing the carboxylate group at the 3-position resulted in no product formation. Instead, substantial dimerization of the diazo compound was observed. This result contrasts with the reactions with furans as 3-methoxycarbonylfuran is an exceptional substrate for cyclopropanation.[5]

Scheme 3. Scope of monocyclopropanation of pyrroles with 2,2,2-trichloroethyl aryldiazoacetates

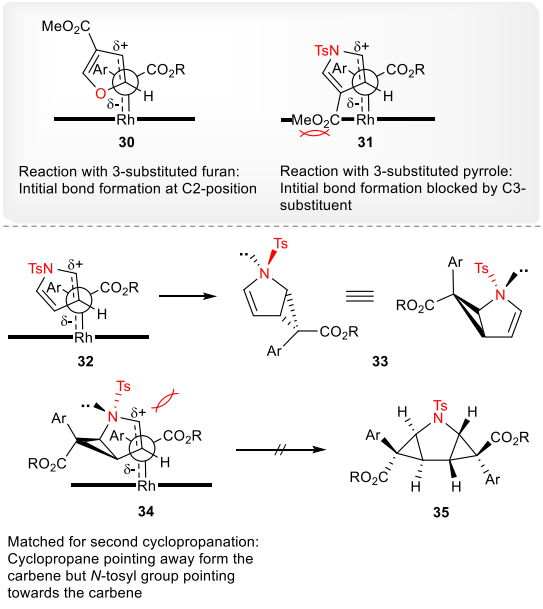


[a]Reaction was scaled up to 3.0 mmol with a catalyst loading of 0.25 mol%.

The asymmetric cyclopropanation of pyrrole displayed some distinctive trends. Unlike the case with furan, the unsubstituted pyrrole system is prone to double cyclopropanation

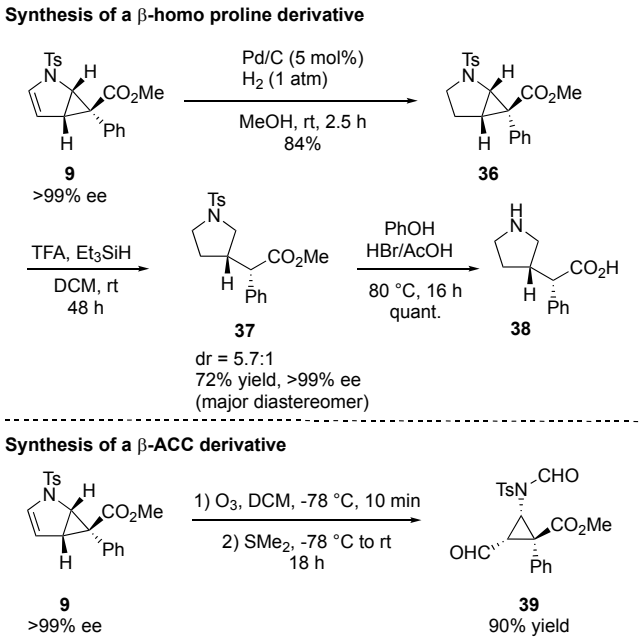
when donor/acceptor carbenes are used. However, this can be controlled by using an *N*-tosyl group with an appropriate, bulky catalyst. 2-Substited pyrroles are effective, yet less reactive substrates, but the reaction fails with 3-substituted pyrroles. These trends are consistent with the general mechanisms for the rhodium-catalyzed reactions of donor/acceptor carbenes with electron rich heterocycles as illustrated in Figure 2.[2c] It is well established that even when the approach of the heterocycle occurs toward a single face of the carbene, either enantiomer of the product can be generated depending on which position of the heterocycle is preferentially attacked. In the case of furans, the concerted asynchronous cyclopropanation initiates at C2, to ensure greater delocalization of the positive charge build up, as shown in transition state (TS) **30**. However, in the case of an *N*-protected pyrrole, attack is preferred at C3 to avoid a steric clash between the protecting group and the catalyst.[2c] Consequently, a C3 substituent is easily accommodated for the cyclopropanation of a furan but it is sterically unfavored for an *N*-protected pyrrole, as illustrated for TS renditions **30** and **31** (Figure 2). The greater tendency of the pyrrole to undergo double cyclopropanation can also be explained by the initial trajectory of the attack during the cyclopropanation. Assuming the attack at the carbene preferentially occurs at the *Re* face as illustrated in structure **32**, the formed enantiomer **33** is the "matched" enantiomer for the second cyclopropanation, since the cyclopropane moiety in **33** is now pointing away from the carbene as illustrated TS **34**. The tendency of the *N*-tosyl group to favor the monocyclopropanation compared to the *N*-Boc group can also be explained because the *N*-sulfonyl nitrogen is closer to be sp^3 hybridized, whereas the *N*-Boc is sp^2 hybridized.[9] Consequently, the tosyl group will reside out of the plane of the dihydropyrrole ring (bond angle approx. 157 °, see Supporting Information) and be on the opposite face to the cyclopropane. This arrangement can be seen in the X-ray structure of **16** (Scheme 3). The tosyl group would then be partially shielding the pyrrolocyclopropane from undergoing the second cyclopropanation.

Figure 2. Model for Rh(II)-catalyzed cyclopropanations with substituted furan and pyrrole substrates



Monocyclopropanated pyrroles have been shown to be readily transformed to enantiomerically pure building blocks such as β-aminocyclopropane carboxylic acids,[10] pyrrolidones[11] or piperidines,[12] being of great value in medicinal chemistry. The utility of the cyclopropane product was demonstrated with the synthesis of a chiral homo-β-proline derivative, a cyclic, strained analog of GABA-16 and several structurally related derivatives that display useful pharmacological activity.[13] Starting from the enantioenriched monocyclopropane **9**, its homo-β-proline analog can be synthesized in a two-step sequence,[4f] featuring a hydrogenation followed by an acid-catalyzed ring opening, which gave rise to a pyrrolidine **37** as the major diastereomer in 72% yield and >99% ee (Scheme 4). The absolute configuration of **37** was unambiguously established by X-ray crystallography. Lastly, the global deprotection was achieved by treatment with HBr in acetic acid in the presence of phenol to reveal the free amino acid **38**.[14] Furthermore, a β-ACC analog was synthesized by subjecting **9** to ozonolysis conditions giving rise to highly substituted cyclopropane **39** in 90% yield with retention of all stereogenic centers, which can be further transformed by known literature procedures.[15] Such amino acids are of great interest due to their intriguing structural properties in peptides.[10]

Scheme 4. Synthetic applications of monocyclopropanated pyrroles



In conclusion, we have developed a highly enantioselective monocyclopropanation procedure for pyrrole substrates using donor/acceptor carbenes. The ability to isolate the monocyclopropane intermediate also represents an advancement in the field of dirhodium catalyst development, as previously this non-isolable intermediate would immediately undergo a second cyclopropanation. With the choice of an appropriate catalyst, monocyclopropanated pyrroles can now be isolated in good yields and high enantioselectivity. The utility of this transformation is also showcased through the synthesis of biologically relevant compounds.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website.
Complete experimental procedures and compound characterization are available in the Supporting Information. (PDF)
CIF file for **16** (CCDC 1936964)
CIF file for **37** (CCDC 1936965)

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Author Contributions

‡ JF and NW contributed equally to the work.

Notes

HMLD is a named inventor on a patent entitled, Dirhodium Catalyst Compositions and Synthetic Processes Related Thereto (US 8,974,428, issued March 10, 2015). The other authors have no competing financial interests.

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DEDICATION

This paper is dedicated to our mentor (OR) and good friend Armin de Meijere on the occasion of his 80th birthday

REFERENCES

(1) For general reviews, see: (a) Schneider, T. F.; Kaschel, J.; Werz, D. B. *Angew. Chem. Int. Ed.* **2014**, *53*, 5504. (b) Reissig, H.-U.; Zimmer, R. *Chem. Rev.* **2003**, *103*, 1151. (c) Davies, H. M. L.; Henley, S. *J. Chem. Soc. Rev.* **2007**, *36*, 1109. (d) Davies, H. M. L.; Spangler, J. E., Reactions of Indoles with Metal-Bound Carbenoids. In *Advances in Heterocyclic Chemistry,* Katritzky, A. R., Ed. 2013; Vol. 110, pp 43-72.

(2) (a) Davies, H. M. L.; Matasi, J. J.; Hodges, L. M.; Huby, N. J. S.; Thornley, C.; Kong, N.; Houser, J. H. *J. Org. Chem*. **1997**, *62*, 1095. (b) Schinnerl, M.; Böhm, C.; Seitz, M.; Reiser, O. *Tetrahedron: Asymmetry* **2003**, *14*, 765. (c) Hedley, S. J.; Ventura, D. L.; Dominiak, P. M.; Nygren, C. L.; Davies, H. M. L. *J. Org. Chem*. **2006**, *71*, 5349. (e) Harrar, K.; Reiser, O. *Chem. Commun*. **2012**, *48*, 3457.

(3) Tanny, S. R.; Grossman, J.; Fowler, F. W. *J. Am. Chem. Soc.* **1972**, *94*, 6495.

(4) (a) Böhm, C.; Schinnerl, M.; Bubert, C.; Zabel, M.; Labahn, T.; Parisini, E.; Reiser, O. *Eur. J. Org. Chem.* **2000**, 2955. (b) Böhm, C.; Reiser, O. *Org. Lett.* **2001**, *3*, 1315. (c) Beumer, R.; Bubert, C.; Cabrele, C.; Vielhauer, O.; Pietzsch, M.; Reiser, O. *J. Org. Chem.* **2000**, *65*, 8960. (d) Schinnerl, M.; Böhm, C.; Seitz, M.; Reiser, O. *Tetrahedron: Asymmetry* **2003**, *14*, 765. (e) Harrar, K.; Reiser, O. *Chem. Commun.* **2012**, *48*, 3457. (f) Pilsl, L. K. A.; Ertl, T.; Reiser, O. *Org. Lett.* **2017**, *19*, 2754.

(5) Lehner, V.; Davies, H. M. L.; Reiser, O. *Org. Lett.* **2017**, *19*, 4722.

(6) Reddy, R. P.; Davies, H. M. L. *J. Am. Chem. Soc.* **2007**, *129*, 10312.

(7) Davies, H. M. L.; Bruzinski, P. R.; Lake, D. H.; Kong, N.; Fall, M. J. *J. Am. Chem. Soc.* **1996**, *118*, 6897.

(8) Guptill, D. M.; Davies, H. M. L. *J. Am. Chem. Soc.* **2014**, *136*, 17718.

(9) Brameld, K. A.; Kuhn, B.; Reuter, D. C.; Stahl, M. *J. Chem. Inf. Model.* **2008,** *48*, 1.

(10) For applications of β-ACCs, see: (a) Koglin, N.; Zorn, C.; Beumer, R.; Cabrele, C.; Bubert, C.; Sewald, N.; Reiser, O.; BeckSickinger, A. G. *Angew. Chem. Int. Ed.* **2003**, *42*, 202. (b) Lang, M.; Bufe, B.; De Pol, S.; Reiser, O.; Meyerhof, W.; Beck-Sickinger, A. G. *J. Pept. Sci.* **2006**, *12*, 258. (c) Urman, S.; Gaus, K.; Yang, Y.; Strijowski, U.; Sewald, N.; De Pol, S.; Reiser, O. *Angew. Chem. Int. Ed.* **2007**, *46*, 3976. (d) De Pol, S.; Zorn, C.; Klein, C. D.; Zerbe, O.; Reiser, O. *Angew. Chem. Int. Ed.* **2004**, *43*, 511. (e) D'Elia, V.; Zwicknagl, H.; Reiser, O. *J. Org. Chem.* **2008**, *73*, 3262. (f) Schmid, M. B.; Fleischmann, M.; D'Elia, V.; Reiser, O.; Gronwald, W.; Gschwind, R. M. *ChemBioChem* **2009**, *10*, 440.

(11) (a) Gheorghe, A.; Schulte, M.; Reiser, O. *J. Org. Chem.* **2006**, *71*, 2173. (b) Roy, S.; Reiser, O. *Angew. Chem. Int. Ed.* **2012**, *51*, 4722.

(12) (a) Watson, P. S.; Jiang, B.; Scott, B. *Org. Lett.* **2000**, *2*, *3679.* (b) Zhang, A.; Neumeyer, J. L.; Baldessarini, R. J. *Chem. Rev.* **2007**, *107*, 274. (c) Zhou, Y.; Gregor, V. E.; Ayida, B. K.; Winters, G. C.; Sun, Z., Murphy; D., Haley, G.; Bailey. D.; Froelich, J. M.; Fish, S.; Webber, S. E.; Hermann, T.; Wall, D. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 1206. (d) J. Yedoyan, N. Wurzer, U. Klimczak, T. Ertl, O. Reiser, *Angew. Chem. Int. Ed.* **2019**, *58*, 3594.

(13) (a) Larsson, O. M.; Thorbek, P.; Krogsgaard-Larsen, P.; Schousboe, A. *J. Neurochem.* **1981**, *37*, 1509. (b) Nielsen, L.; Brehm, L.; Krogsgaard-Larsen, P. *J. Med. Chem.* **1990**, *33*, 71. (c) Crites, G. J.; Malizia, L. A.; Tunnicliff, G. J. *J. Basic Clin. Physiol. Pharmacol.* **2002**, *13*, 179. (d) Yunger, L. M.; Fowler, P. J.; Zarevics, P.; Setler, P. E. *J. Pharmacol. Exp. Ther.* **1984**, *228*, 109. (e) Ali, F. E.; Bondinell, W. E.; Dandridge, P. A.; Frazee, J. S.; Garvey, E.; Girard, G. R.; Kaiser, C.; Ku, T. W.; Lafferty, J. J.; Moonsammy, G. I.; Oh, H.-J.; Rush, J. A.; Setler, P. E.; Stringer, O. D.; Venslavsky, J. W.; Volpe, B. W.; Yunger, L. M.; Zirkle, C. L. *J. Med. Chem.* **1985**, *28*, 653. (f) Falch, E.; Jacobsen, P.; Krogsgaard-Larsen, P.; Curtis, D. R. *J. Neurochem.* **1985**, *44*, 68. (g) Bonanno, G.; Raiteri, M. Br. *J. Pharmacol.* **1987**, *91*, 237. (h) N'Goka, V.; Schlewer, G.; Linget, J. M.; Chambon, J. P.; Wermuth, C. G. *J. Med. Chem.* **1991**, *34*, 2547. (i) Andersen, K. E.; Sørensen, J. L.; Lau, J.; Lundt, B. F.; Petersen, H.; Huusfeldt, P. O.; Suzdak, P. D.; Swedberg, M. D. B. *J. Med. Chem.* **2001**, *44*, 2152. (j) Wein, T.; Petrera, M.; Allmendinger, L.; Hoefner, G.; Pabel, J.; Wanner, K. T. *ChemMedChem* **2016**, *11*, 509.

(14) (a) Li, G.; Sharpless, K. B. *Acta. Chem. Scand.* **1996**, *50*, 649–651. (b) Ohle, H.; Friedeberg, H.; Haeseler, G. *Ber. dtsch. Chem. Ges.* **1936**, *B69*, 2311.

(15) (a) Bubert, C.; Cabrele, C.; Reiser, O. *Synlett* **1997**, 827. (b) Beumer, R.; Bubert, C.; Cabrele, C.; Vielhauer, O.; Pietzsch, M.; Reiser, O. *J. Org. Chem.* **2000**, *65*, 8960. (c) Beumer, R.; Reiser, O. *Tetrahedron* **2001**, *57*, 6497. (d) Koglin, N.; Zorn, C.; Beumer, R.; Cabrele, C.; Bubert, C.; Sewald, N; Reiser, O.; Beck-Sickinger, A. G. *Angew. Chem. Int. Ed.* **2003**, *42*, 202. (e) Boddaert, T.; Taylor, J. E.; Bull, S. D.; Aitken, D. J. *Org. Lett.* **2019**, *21*, 100. (f) Porcu, S.; Luridiana, A.; Martis, A.; Frongia, A.; Sarais, G.; Aitken, D. J.; Boddaert, T.; Guillot, R.; Secci, F. *Chem. Comm.* **2018**, *54*, 13547. (g) Godier-Marc, E.; Aitken, D. J.; Husson, H. P. *Tetrahedron Lett.* **1997**, *38*, 4065.