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Rhodium-Catalyzed Direct C–H Phosphorylation of (Hetero)-arenes Suitable for Late-Stage Functionalization

Minsik Min,[a,b] Dahye Kang,[a,b] Sungwoo Jung,[a,b] and Sungwoo Hong[a,b,*]

[a] Department of Chemistry, Korea Advanced Institute of Science and Technology, Daejeon, 305-701, Korea
Fax: (+82)-42-350-2810; Phone: (+82)-42-350-2811; e-mail: hongorg@kaist.ac.kr
[b] Center for Catalytic Hydrocarbon Functionalization, Institute for Basic Science (IBS), Daejeon, 305-701, Korea

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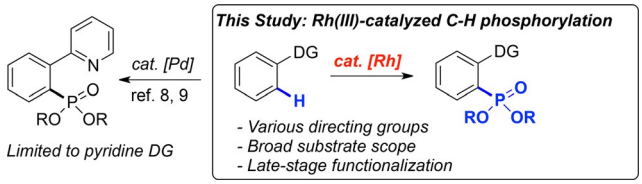
Abstract: Efficient rhodium-catalyzed direct C–H phosphorylation of (hetero)arenes was developed. Various directing groups and a wide range of substrates, including heterocycles, can be utilized in this C–H phosphorylation process, allowing for the rapid installation of the phosphonate group into medicinally and biologically important privileged scaffolds. The efficient and straightforward method could serve as a new tool to streamline late-stage C–H functionalization for preparing aryl phosphonates, which are important structural motif in synthetic and medicinal chemistry.

Keywords: catalyst; C–H activation; late-stage modification; phosphorylation; rhodium

Introduction

Arylphosphonate derivatives have been extensively investigated in the field of medicinal chemistry,[1] material chemistry,[2] catalysis and ligand chemistry.[3] Since the development of the Hirao reaction,[4] Pd-catalyzed carbon−phosphorus bond formation has provided an efficient route to synthesize arylphosphonate derivatives.[5] Despite the significant progress in the area of Pd-catalyzed C–H functionalization,[6] direct C−P bond formation via directed C–H activation poses challenges because of the strong coordination ability of the phosphorus reagent to transition metals.[7] In 2013, the Yu group reported on pyridine directed C–H phosphorylation using a Pd catalyst and by slowly adding a phosphorus reagent using a syringe pump.[8] The Murakami group successfully explored Pd-catalyzed C–H phosphorylation, employing α-hydroxylalkylphosphonate as the masked phosphonating agent to prevent catalyst deactivation (Scheme 1).[9]



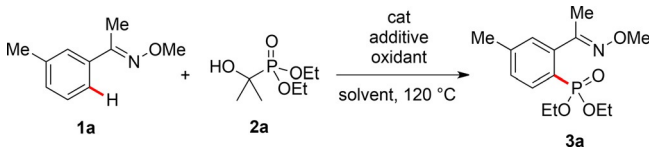
Scheme 1. Direct C–H phosphorylation

Although these methods remarkably improved the efficiency of direct C–H phosphorylation, the precedent examples were limited to substrates bearing non-removable, pyridine-based directing groups. As a result, synthetic applications for rapidly exploring structure-activity relationships (SAR) of a variety of biologically active molecules are not feasible. In this regard, the development of new catalytic systems is highly desirable for expanding the scope and utility of C–H phosphorylation. Herein, we describe the first example of Rh^{III}-catalyzed, C−P bond formation of (hetero)arenes (Scheme 1). Significantly, various directing groups (oxime, pyridine, anilide, amide, and imine) could be applied in this new C–H phosphorylation reaction, which would be suitable for late-stage functionalization of complex bioactive small molecules.

Results and Discussion

We commenced our study by investigating the reactivity of diethyl phosphonate with substrate **1a** bearing *O*-methyl oxime group which is easily removable or transformable into other functional groups. The feasibility of this process was tested with a Cp^*Rh^{III} catalyst that has been widely used in many bond-forming reactions.[10,11] When **1a** was subjected to conditions using $[RhCp^*Cl_2]_2$ as a catalyst, only negligible reac-

Table 1. Optimization of the reaction conditions[a]



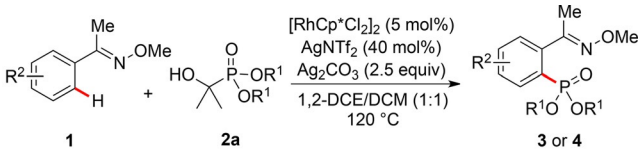
Entry	Cat. (5 mol%)	Additive	Oxidant	Solvent	Yield (%)[b]
1[c]	$[RhCp^*Cl_2]_2$	$AgNTf_2$	Ag_2CO_3	1,2-DCE	trace
2	$[RhCp^*Cl_2]_2$	$AgNTf_2$	Ag_2CO_3	dioxane	11
3	$[RhCp^*Cl_2]_2$	$AgNTf_2$	Ag_2CO_3	DCM	20
4	$[RhCp^*Cl_2]_2$	$AgNTf_2$	Ag_2CO_3	1,2-DCE	54
5	$[RhCp^*(CH_3CN)_3](SbF_6)_2$	–	Ag_2CO_3	1,2-DCE	39
6	$[RhCp^*Cl_2]_2$	$AgNTf_2$	AgOAc	1,2-DCE	trace
7	$[RhCp^*Cl_2]_2$	$AgSbF_6$	Ag_2CO_3	1,2-DCE	44
8	$[RhCp^*Cl_2]_2$	$AgPF_6$	Ag_2CO_3	1,2-DCE	41
9[d]	$[RhCp^*Cl_2]_2$	$AgNTf_2$	Ag_2CO_3	1,2-DCE	70
10[d]	$[RhCp^*Cl_2]_2$	$AgNTf_2$	Ag_2CO_3	1,2-DCE/DCM (1:1)	87
11[e]	$Pd(OAc)_2$	NMMI	AgOAc	*t*BuOH	15

[a] Reactions were performed by using **1a** (0.1 mmol), **2a** (1.4 equiv), catalyst, additive (0.4 equiv), oxidant (2.5 equiv) and solvent (1.0 mL) at 120 °C for 8 h.
[b] Yields were determined by ^1H NMR.
[c] Diethyl phosphonate (1.4 equiv) was used instead of **2a**.
[d] Additive (40 mol%) was used.
[e] $Pd(OAc)_2$ (0.1 equiv), NMMI (0.4 equiv) and K_2HPO_4 (4.5 equiv) were added. NMMI = *N*-Methylmaleimide

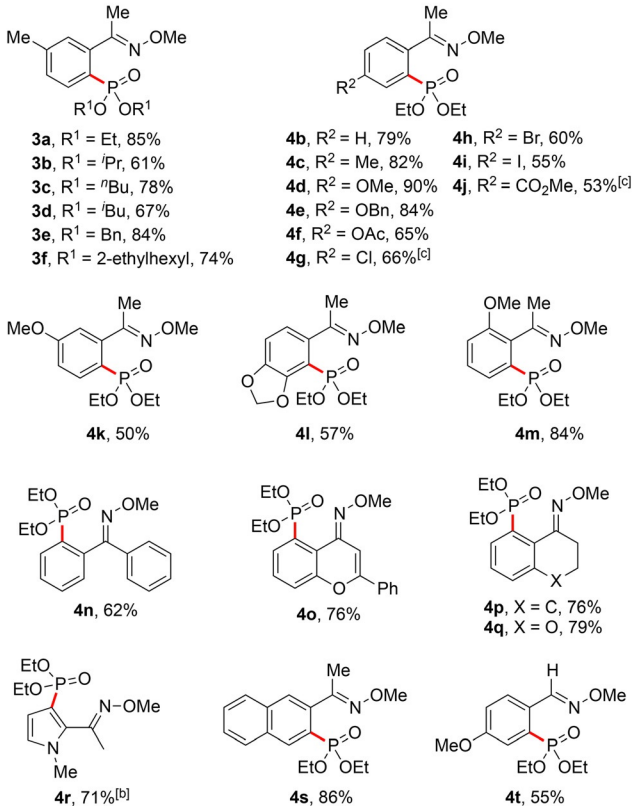
tivity was observed (Table 1, entry 1). Inspired by Murakami's recent work, we turned our attention to α-hydroxylalkylphosphonate as a phosphorylating agent to prevent poisoning of Rh catalyst. To our delight, the use of α-hydroxylalkylphosphonate (**2a**) was found to initiate the phosphorylation reaction and provided the desired product **3a**, albeit only in 11% yield (entry 2). After extensive screenings, 1,2-DCE was found to be the optimal solvent, and the product yield dramatically increased to 54% (entry 4). The reaction only occurred at the sterically more accessible C–H bond, generating a monophosphorylated product. The catalyst $[RhCp^*(CH_3CN)_3](SbF_6)_2$ gave a lower yield (entry 5). The oxidizing agent was also critical to the efficiency of the transformation, and no detectable desired product was obtained with the use of AgOAc or $Cu(OAc)_2$ (entry 6 and see the Supporting Information). Changing the silver additive to $AgSbF_6$ or $AgPF_6$ slightly diminished the reaction efficiency (entries 7 and 8). Pd^{II} catalytic systems which are known to facilitate C–H phosphorylation reactions of arylpyridines, were considerably less effective in the C–P bond formation of oxime substrate (entry 11). Other catalytic systems, including $[Ru(p\text{-cymene})Cl_2]_2$ and $[IrCp^*Cl_2]_2$, were not operative (see SI). Further optimization studies revealed that the best result was obtained when the reaction was performed in a 1:1 mixture of 1,2-DCE and DCM as the co-solvent (entry 10). Under the optimized reaction conditions, the C–H phosphorylation process of **1a** with **2a** (1.4 equiv) in the presence of $[RhCp^*Cl_2]_2$ (5 mol%), $AgNTf_2$ (40 mol%), and Ag_2CO_3 (2.5 equiv) in 1,2-DCE/DCM at 120 °C generated product **3a** in an 87% yield. A control experiment in the absence of $[RhCp^*Cl_2]_2$ catalyst was carried out, and no desired product was obtained (see SI).

With the optimized conditions in hand, we next investigated the scope of both oxime substrates and phosphorylation reagents (Table 2). Various moieties of phosphonates, such as ethyl, isopropyl, butyl, isobutyl, benzyl, and 2-ethylhexyl groups, were surveyed under the optimized conditions and showed similar efficiency. The phosphorylation reaction, however, was not operative with diaryl phosphine oxides. Oxime derivatives bearing either electron-rich (**4c**, **4d**, **4e**, **4f**, **4k**, **4l**, and **4m**) or electron-deficient groups (**4g**, **4h**, **4i**, and **4j**) are compatible to the C–H phosphorylation reaction to provide the desired coupling products in moderate to good yields. Consistent with the previous observation, only monophosphorylated products were observed. In addition, the reaction showed high functional group tolerance, including ethers (**4d**, **4e**, **4k**, **4m**, and **4t**), halides (**4g**, **4h**, and **4i**), acetate (**4f**), and ester (**4j**). Notably, bromo and iodo groups were intact under the reaction conditions, enabling further functionalization at these positions. When *meta*-substituted oximes were used, most of the phosphorylation occurred selectively at the sterically more accessible position (**3a**–**3f**, **4k**, and **4s**). In contrast, for the reaction of 3,4-(methylenedioxy)ketoxime (**1l**) with **2a**, phosphorylation takes place site-selectively at a sterically more hindered po-

Table 2. Substrate scope studies[a]



1 2a 3 or 4

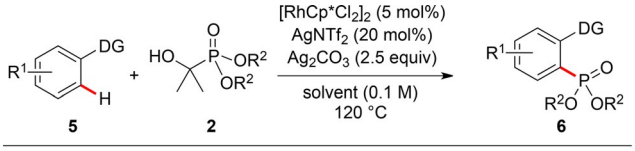


[a] Reactions were carried out by using **1** (0.2 mmol), **2a** (1.4 equiv), $[RhCp^*Cl_2]_2$ (5 mol%), $AgNTf_2$ (40 mol%), Ag_2CO_3 (2.5 equiv) and 1,2-DCE/DCM (1 mL : 1 mL) at 120 °C for 8 h.

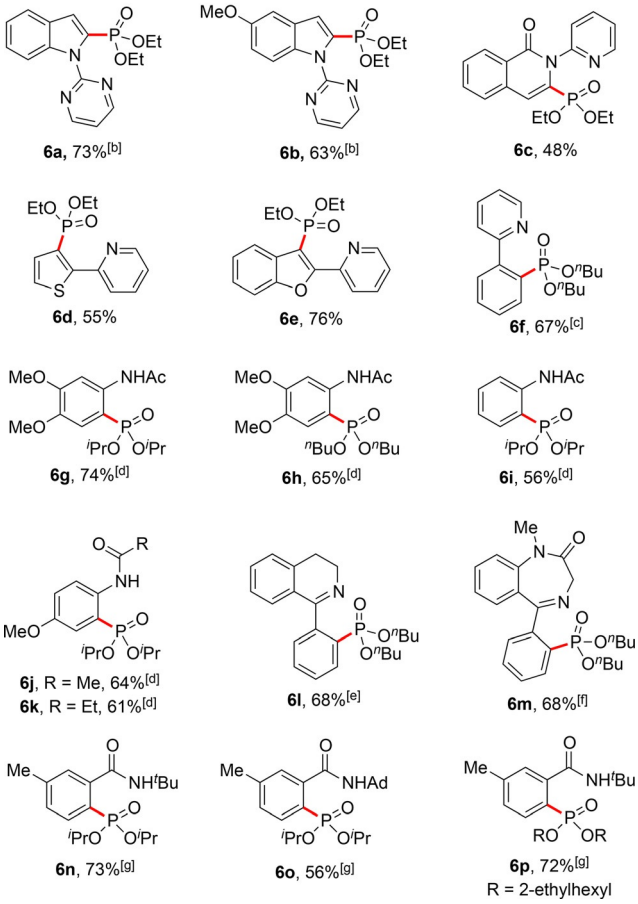
[b] Reactions were carried out by using 1,2-DCE (2 mL) at 120 °C for 2 h.

[c] 8 mol% of $[RhCp^*Cl_2]_2$ was used. Isolated yields are shown.

Table 3. Substrate scope of directing groups[a]



5 2 6



[a] Reactions were carried out by using **5** (0.1 mmol), **2** (1.4 equiv), $[RhCp^*Cl_2]_2$ (5.0 mol%), $AgNTf_2$ (20 mol%), Ag_2CO_3 (2.5 equiv) and DCE (1 mL) at 120 °C for 8 h.

[b] $[RhCp^*Cl_2]_2$ (2.5 mol%), and $AgNTf_2$ (10 mol%) were used.

[c] THF (1 mL) was used.

[d] $[RhCp^*Cl_2]_2$ (8 mol%), $AgNTf_2$ (40 mol%) and iPrOAc (1 mL) were used.

[e] iPrOAc (1 mL) was used.

[f] $PhCF_3$ (1 mL) was used.

[g] $[RhCp^*Cl_2]_2$ (8 mol%), and $AgBF_4$ (40 mol%) were used. Isolated yields are shown.

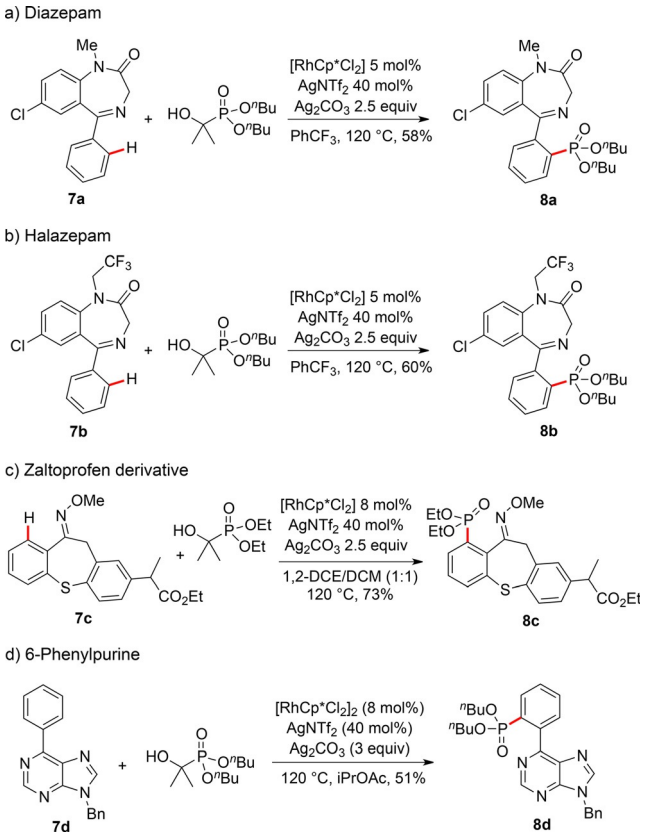
sition, affording **4l**. In addition, the use of *ortho*-substituted ketoxime (**1m**) provided the phosphorylated product **4m** in a yield of 84%. The scope of this transformation with respect to heteroarene substrates was next evaluated, and the desired products were obtained in good yields (**4o**, **4p**, **4q**, and **4r**). Naphthyl substrate was also suitable for this transformation, generating the desired product in an 86% yield (**4s**). Oxime substrate derived from aldehyde was also compatible to the reaction condition to afford the phosphorylated product **4t**.

For broad utility, the scope of other directing groups was investigated (Table 3). Considering the frequency of heterocyclic moieties within biologically active molecules, we subsequently explored heteroarene substrates, and the utility of the present method was broadened by the phosphorylation of prominent structural motifs, including indole, isoquinolone, thiophene, and benzofuran. We further investigated additional directing groups and were pleased to observe that Rh-catalyzed phosphorylation of anilides (**6g–k**) and amides (**6n–p**) worked well in the optimized

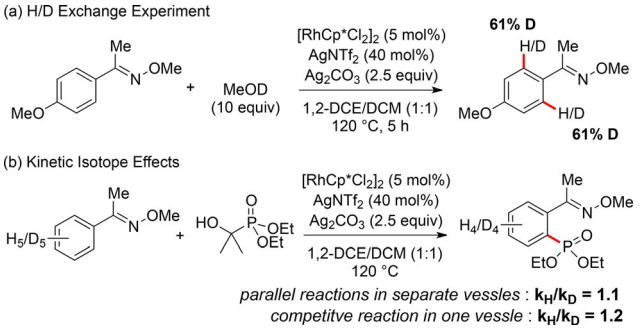
system to produce the desired products. In a similar fashion, imines underwent phosphorylation reactions without difficulty, generating the corresponding products (**6l**, and **6m**).

The utility of the direct C–H phosphorylation reaction as a tool for late-stage functionalization of complex molecules is significant. Therefore, we next assessed the potential that our method for C–H bond phosphorylation could be applied to bioactive complex molecules containing several functional groups. To our delight, the phosphorylation of diazepam **7a** (tranquilizer) and halazepam **7b** (anti-anxiety drug) site-selectively took place under the present catalytic system to yield desired products (Scheme 2a, 2b). Ketoxime **7c** that was derived from zaltoprofen (anti-inflammatory drug) was subjected to phosphorylation conditions to afford the corresponding product **8c** (Scheme 2c). In addition, the phosphorylation of 6-arylpurine **7d** proceeded with excellent *ortho*-selectivity to produce **8d** (Scheme 2d).

To elucidate the mechanism of the phosphorylation process, preliminary experiments were carried out by means of H/D exchange experiments (Scheme 3). A significant level of H/D exchange was observed by the rhodium catalytic system in the presence of CD_3OD, indicating that the C–H activation step



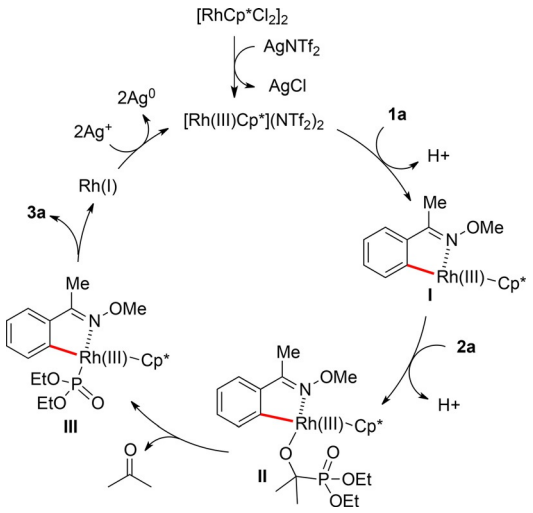
Scheme 2. Late-stage C–H bond phosphorylation.



Scheme 3. Preliminary mechanistic studies.

would be reversible. In addition, kinetic isotope effect (KIE) experiments were performed under the optimized conditions (Scheme 3b). A low values of intermolecular kinetic isotope effect were observed in both parallel reactions ($k_H/k_D = 1.1$) and competitive reaction ($k_H/k_D = 1.2$), implying that the C–H bond cleavage may not be involved in the rate-limiting step.[12]

A plausible mechanism for the Rh-catalyzed phosphorylation process is shown in Scheme 4. The activated cationic Rh^{III} species is generated in situ by the $[RhCp^*Cl_2]_2/AgNTf_2$ catalytic system. Subsequently, Cp^*Rh^{III} catalyst reacts with the *O*-methyl oxime **1a** via C–H activation, providing the five-membered rhodacycle complex **I** with one accessible vacant site.[13] Then, α-hydroxylalkylphosphonate (**2a**) would occupy the vacant site of the metal center to generate complex **II**. Next, β-phosphonate elimination,[14] with the concomitant release of acetone, leads to the formation of complex **III**, which undergoes reductive elimination to afford the desired phosphorylation product. The oxidation of Rh^I by Ag^I regenerates the Rh^{III} species to complete the catalytic cycle.



Scheme 4. Proposed Rh-catalyzed phosphorylation pathway.

Conclusions

In summary, we developed an efficient Rh^{III}-catalyzed C–H phosphorylation reaction, which broadens the utility and its substrate scope. Various directing groups were applicable in the process, providing an efficient and straightforward route for preparing aryl phosphonate derivatives that have high synthetic utility. The present strategy has been verified in late-stage functionalization for the rapid derivatization of medicinally important molecules. Further application to the late-stage drug modification and bioevaluation are currently ongoing.

Experimental Section

General procedure for Rh^{III}-catalyzed phosphorylation

Caution in required because of the internal pressure at 120 °C. The reactions were conducted in Ace pressure tubes (Aldrich). *O*-methyl oxime (0.2 mmol), diethyl (2-hydroxypropan-2-yl)phosphonate (1.4 equiv), $[RhCp^*Cl_2]_2$ (5 mol %), $AgNTf_2$ (40 mol %) and Ag_2CO_3 (2.5 equiv) were combined in 1,2-DCE/DCM (1.0 mL/1.0 mL). The reaction mixture was stirred at 120 °C for 8 h. The reaction mixture was monitored by TLC using 50% EtOAc and 50% *n*-hexane as the mobile phase. After disappearance of starting material, the reaction mixture was diluted and filtered through Celite with DCM. The organic layer was dried over $MgSO_4$. After removal of solvent, the residue was purified by flash chromatography on silica gel to give desired product. Full characterization data and copies of relevant spectra are provided in the Supporting Information.

General procedure for H/D exchange experiment

Caution in required because of the internal pressure at 120 °C. The reactions were conducted in Ace pressure tubes (Aldrich). *O*-methyl oxime **(1d)** (0.1 mmol), $[RhCp^*Cl_2]_2$ (5 mol %), $AgNTf_2$ (40 mol %), Ag_2CO_3 (2.5 equiv) and CD_3OD (10 equiv) were combined in 1,2-DCE/DCM (0.5 mL/0.5 mL). The reaction mixture was stirred at 120 °C for 5 h. The reaction mixture was diluted and filtered through Celite with DCM. The residue was concentrated, and evaporated to dryness under high vacuum. The extent of H/D exchange was determined by integration of ^{1}H NMR.

General procedure for kinetic isotope effect study

a) Parallel experiments: *O*-methyl oxime (**1b**) (0.1 mmol) or *O*-methyl oxime (**[D5]-1a**) (0.1 mmol) were added to two separate screw cap test tubes with diethyl (2-hydroxypropan-2-yl)phosphonate (1.4 equiv), $[RhCp^*Cl_2]_2$ (5 mol %), $AgNTf_2$ (40 mol %), Ag_2CO_3 (2.5 equiv) and 1,2-DCE/DCM (0.5 mL/0.5 mL). The reaction mixture was stirred at 120 °C for 1 h. The reaction mixture was diluted and filtered through Celite with DCM. The residue was concentrated, and evaporated to dryness under high vacuum. The residue was analyzed by integration of ^{1}H NMR using internal standard. Product yield of **4b** was 36% and that of **[D4]-4b** was 33%, leading to KIE value of 1.1.

b) Competitive experiment: *O*-methyl oxime (**1b**) (0.05 mmol) and *O*-methyl oxime (**[D_5]-1a**) (0.05 mmol) were added to same screw cap test tube with diethyl (2-hydroxypropan-2-yl)phosphonate (1.4 equiv), $[RhCp^*Cl_2]_2$ (5 mol %), $AgNTf_2$ (40 mol %), Ag_2CO_3 (2.5 equiv) and 1,2-DCE/DCM (0.5 mL/0.5 mL). The reaction mixture was stirred at 120 °C for 1 h. The reaction mixture was diluted and filtered through Celite with DCM. The residue was concentrated, and evaporated to dryness under high vacuum. The ratio of **4b/[D_4]–4b** was analyzed by integration of ^{1}H NMR to give a KIE value of 1.2.

Acknowledgements

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References

[1] a) M. Sawa, T. Kiyoi, K. Kurokawa, H. Kumihara, M. Yamamoto, T. Miyasaka, Y. Ito, R. Hirayama, T. Inoue, Y. Kirii, E. Nishiwaki, H. Ohmoto, Y. Maeda, E. Ishibushi, Y. Inoue, K. Yoshino, H. Kondo, *J. Med. Chem.* **2002**, *45*, 919; b) S. Sivendran, V. Jones, D. Sun, Y. Wang, A. E. Grzegorzewicz, M. S. Scherman, A. D. Napper, J. A. McCammon, R. E. Lee, S. L. Diamond, M. McNeil, *Bioorg. Med. Chem.* **2010**, *18*, 896; c) Q. Dang, Y. Liu, D. K. Cashion, S. R. Kasibhatla, T. Jiang, F. Taplin, J. D. Jacintho, H. Li, Z. Sun, Y. Fan, J. DaRe, F. Tian, W. Li, T. Gibson, R. Lemus, P. D. van Poelje, S. C. Potter, M. D. Erion, *J. Med. Chem.* **2011**, *54*, 153; d) X. Chen, D. J. Kopecky, J. Mihalic, S. Jeffries, X. Min, J. Heath, J. Deignan, S. Lai, Z. Fu, C. Guimaraes, S. Shen, S. Li, S. Johnstone, S. Thibault, H. Xu, M. Cardozo, W. Shen, N. Walker, F. Kayser, Z. Wang, *J. Med. Chem.* **2012**, *55*, 3837.

[2] a) H. R. Allcock, M. A. Hofmann, C. M. Ambler, R. V. Morford, *Macromolecules* **2002**, *35*, 3484; b) H. Onouchi, T. Miyagawa, A. Furuko, K. Maeda, E. Yashima, *J. Am. Chem. Soc.* **2005**, *127*, 2960; c) C. Queffélec, M. Petit, P. Janvier, D. A. Knight, B. Bujoli, *Chem. Rev.* **2012**, *112*, 3777.

[3] a) G. Helmchen, A. Pfaltz, *Acc. Chem. Res.* **2000**, *33*, 336; b) W. Tang, X. Zhang, *Chem. Rev.* **2003**, *103*, 3029; c) D. S. Surry, S. L. Buchwald, *Angew. Chem.* **2008**, *120*, 6438; *Angew. Chem. Int. Ed.* **2008**, *47*, 6338; d) Y. Guo, H. Fu, H. Chen, X. Li, *Catal. Commun.* **2008**, *9*, 1842; e) Y. Li, L.-Q. Lu, S. Das, S. Pisiewicz, K. Junge, M. Beller, *J. Am. Chem. Soc.* **2012**, *134*, 18325; f) J. M. Bayne, D. W. Stephan, *Chem. Soc. Rev.* **2016**, 45, 765–774.

[4] T. Hirao, T. Masunaga, Y. Ohshiro, T. Agawa, *Synthesis* **1981**, 56.

[5] a) E. L. Deal, C. Petit, J.-L. Montchamp, *Org. Lett.* **2011**, *13*, 3270; b) O. Berger, C. Petit, E. L. Deal, J.-L.

Montchamp, *Adv. Synth. Catal.* **2013**, *355*, 1361; c) K. Xu, H. Hu, F. Yang, Y. Wu, *Eur. J. Org. Chem.* **2013**, *2013*, 319; d) M. Kalek, M. Jezowska, J. Stawinski, *Adv. Synth. Catal.* **2009**, *351*, 3207; e) Y. Belabassi, S. Alzghari, J.-L. Montchamp, *J. Organomet. Chem.* **2008**, *693*, 3171; f) M. Kalek, A. Ziadi, J. Stawinski, *Org. Lett.* **2008**, *10*, 4637; g) W. C. Fu, C. M. So, F. Y. Kwong, *Org. Lett.* **2015**, *17*, 5906.

[6] For Selected reviews, see: a) T. Satoh, M. Miura, *Chem. Lett.* **2007**, *36*, 200; b) I. V. Seregin, V. Gevorgyan, *Chem. Soc. Rev.* **2007**, *36*, 1173; c) O. Daugulis, H.-Q. Do, D. Shabashov, *Acc. Chem. Res.* **2009**, *42*, 1074; d) T. W. Lyons, M. S. Sanford, *Chem. Rev.* **2010**, *110*, 1147; e) C. S. Yeung, V. M. Dong, *Chem. Rev.* **2011**, *111*, 1215; f) D.-G. Yu, B.-J. Li, Z.-J. Shi, *Tetrahedron* **2012**, *68*, 5130; g) K. M. Engle, T.-S. Mei, M. Wasa, J.-Q. Yu, *Acc. Chem. Res.* **2012**, *45*, 788; h) S. H. Cho, J. Y. Kim, J. Kwak, S. Chang, *Chem. Soc. Rev.* **2011**, *40*, 5068; i) Y. N. Wu, J. Wang, F. Mao, F. Y. Kwong, *Chem. Asian J.* **2014**, *9*, 26; j) C. Liu, J. Yuan, M. Gao, S. Tang, W. Li, R. Shi, A. Lei, *Chem. Rev.* **2015**, *115*, 12138.

[7] a) N. V. Dubroviba, A. Börner, *Angew. Chem.* **2004**, *116*, 6007; *Angew. Chem. Int. Ed.* **2004**, *43*, 5883; b) W. B. Beaulieu, T. B. Rauchfuss, D. M. Roundhill, *Inorg. Chem.* **1975**, *14*, 1732; c) L. Ackermann, R. Born, J. H. Spatz, A. Althammer, G. Gschrei, *Pure Appl. Chem.* **2006**, *78*, 209.

[8] C.-G. Feng, M. Ye, K.-J. Xiao, S. Li, J.-Q. Yu, *J. Am. Chem. Soc.* **2013**, *135*, 9322.

[9] C. Li, T. Yano, N. Ishida, M. Murakami, *Angew. Chem.* **2013**, *125*, 9983; *Angew. Chem. Int. Ed.* **2013**, *52*, 9801.

[10] For selected reviews, see: a) D. A. Colby, R. G. Bergman, J. A. Ellman, *Chem. Rev.* **2010**, *110*, 624; b) N. Kuhl, N. Schröder, F. Glorius, *Adv. Synth. Catal.* **2014**, *356*, 1443; c) G. Song, F. Wang, X. Li, *Chem. Soc. Rev.* **2012**, *41*, 3651; d) T. Satoh, M. Miura, *Chem. Eur. J.* **2010**, *16*, 11212; e) J. Yamaguchi, A. D. Yamaguchi, K. Itami, *Angew. Chem.* **2012**, *124*, 9092; *Angew. Chem. Int. Ed.* **2012**, *51*, 8960; f) B. Ye, N. Cramer, *Acc. Chem. Res.* **2015**, *48*, 1308; g) G. Song, X. Li, *Acc. Chem. Res.* **2015**, *48*, 1007.

[11] For selected examples, see: a) T. Satoh, K. Ueura, M. Miura, *Pure Appl. Chem.* **2008**, *80*, 1127; b) P. Zhao, F. Wang, K. Han, X. Li, *Org. Lett.* **2012**, *14*, 3400; c) Y. Lian, R. G. Bergman, L. D. Lavis, J. A. Ellman, *J. Am. Chem. Soc.* **2013**, *135*, 7122; d) J. Y. Kim, S. H. Park, J. Ryu, S. H. Cho, S. H. Kim, S. Chang, *J. Am. Chem. Soc.* **2012**, *134*, 9110; e) J. Chen, G. Song, C.-L. Pan, X. Li, *Org. Lett.* **2010**, *12*, 5426; f) Y. Chen, F. Wang, W. Zhen, X. Li, *Adv. Synth. Catal.* **2013**, *355*, 353; g) N. Guimond, C. Gouliaras, K. Fagnou, *J. Am. Chem. Soc.* **2010**, *132*, 6908; h) X. Zhang, D. Chen, M. Zhao, J. Zhao, A. Jia, X. Li, *Adv. Synth. Catal.* **2011**, *353*, 719; i) Z. Qi, M. Wang, X. Li, *Chem. Commun.* **2014**, *50*, 9776; j) F. Xie, Z. Qi, S. Yu, X. Li, *J. Am. Chem. Soc.* **2014**, *136*, 4780; k) S. Yu, X. Li, *Org. Lett.* **2014**, *16*, 1200; l) K. D. Collins, F. Lied, F. Glorius, *Chem. Commun.* **2014**, *50*, 4459; m) Y. Park, K. T. Park, J. G. Kim, S. Chang, *J. Am. Chem. Soc.* **2015**, *137*, 4534; n) Y. Moon, Y. Jeong, D. Kook, S. Hong, *Org. Biomol. Chem.* **2015**, *13*, 3918; o) D. Kang, S. Hong, *Org. Lett.* **2015**, *17*, 1938; p) Y. Kim, S. Hong, *Chem. Commun.* **2015**, *51*, 11202.

[12] E. M. Simmons, J. F. Hartwig, *Angew. Chem.* **2012**, *124*, 3120; *Angew. Chem. Int. Ed.* **2012**, *51*, 3066.

[13] a) L. Li, W. W. Brennessel, W. D. Jones, *J. Am. Chem. Soc.* **2008**, *130*, 12414; b) L. Li, W. Brennessel, W. D. Jones, *Organometallics* **2009**, *28*, 3492; c) M. Brasse, J. Cámpora, J. A. Ellman, R. G. Bergman, *J. Am. Chem. Soc.* **2013**, *135*, 6427.

[14] a) H. Zhao, A. Afiafard, Z. Lin, *Organometallics* **2006**, *25*, 812; b) L. Zhou, Y. Liu, Y. Zhang, J. Wang, *Chem. Commun.* **2011**, *47*, 3622; c) S. Pan, X. Ma, D. Zhong, W. Chen, M. Liu, H. Wu, *Adv. Synth. Catal.* **2015**, *357*, 3052; d) J. Le Bras, J. Muzart, *Tetrahedron* **2012**, *68*, 10065; e) E. Ozkal, B. Cacherat, B. Morandi, *ACS Catal.* **2015**, *5*, 6458.

