

Accepted Article

Title: Palladium-Catalyzed Cascade C-O Cleavage and C-H Alkenylation of Phosphinyl Allenes: An Expeditious Approach to 3-Alkenyl Benzo[b]phosphole Oxides

Authors: Teng Liu, Xue Sun, and Lei Wu

This manuscript has been accepted after peer review and appears as an Accepted Article online prior to editing, proofing, and formal publication of the final Version of Record (VoR). This work is currently citable by using the Digital Object Identifier (DOI) given below. The VoR will be published online in Early View as soon as possible and may be different to this Accepted Article as a result of editing. Readers should obtain the VoR from the journal website shown below when it is published to ensure accuracy of information. The authors are responsible for the content of this Accepted Article.

To be cited as: Adv. Synth. Catal. 10.1002/adsc.201800103

Link to VoR: http://dx.doi.org/10.1002/adsc.201800103

FULL PAPER

DOI: 10.1002/adsc.201((will be filled in by the editorial staff))

Palladium-Catalyzed Cascade C-O Cleavage and C-H Alkenylation of Phosphinyl Allenes: An Expeditious Approach to 3-Alkenyl Benzo[*b*]phosphole Oxides

Teng Liu,^a Xue Sun,^a and Lei Wu^{a,b,*}

^a Jiangsu Key Laboratory of Pesticide Science and Department of Chemistry, College of Sciences, Nanjing Agricultural University, Nanjing 210095, P. R. China.

[Tel/Fax: +86-25-84395351; E-mail: rickywu@njau.edu.cn]

^b Key Laboratory of Molecular Recognition and Function, Institute of Chemistry, Chinese Academy of Sciences, Beijing 100190, P. R. China.

Received: ((will be filled in by the editorial staff))

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/adsc.201#######.((Please delete if not appropriate))

Abstract. A phosphine oxide-directed intramolecular cyclization of phosphinyl allenes is established for the first time. The palladium-catalyzed intramolecular cyclization provides an unprecedented cascade C-O cleavage and direct C-H alkenylation toward novel 3-alkenyl benzo[*b*]phosphole oxides, along with broad group tolerance and high regioselectivity. Control experiments and mechanistic studies explain the sequential performance of $C(sp^3)$ -OAr cleavage and P=O directed $C(sp^2)$ -H activation.

Keywords: 3-Alkenyl Benzo[*b*]phosphole Oxides, C-O Cleavage, C-H Alkenylation, Phosphinyl Allenes, Palladium Catalysis.

1 Introduction

Organophosphorus chemistry has evolved into a blooming research area over the past decades, benefiting from a fact that phosphorus substituents vitally regulate important biological, medicinal, material, and catalytic functions.^[1] Moreover, the versatile roles in performing as ligands or direct groups to influence the reactivity and selectivity of metal catalysts make them particularly attractive to organic chemists. From this point of view, phosphine oxides (P=O) directed C-H activation and functionalization provide a promising tool in novel phosphine ligands development and organic synthesis owing to their broad substrate scope and high atom economy.^[2] Since 2013, elegant studies on phosphoryl directed C-H functionalization have been independently reported by several leading scientists, including Glorius, Kim, Lee, Yang, Loh, Miura, Shi

and others.^[3] Inherently, these works share a common point in utilizing phosphoryl-containing compounds as directing groups for two-component crosscoupling, in other words, the reaction of in-situ generated metallacyclic intermediates with an extramolecular nucleophile or electrophile (Scheme 1, a). It is predictable that, P=O directed intramolecular cyclization will offer an efficient approach to phosphonic construct diverse heterocyclic compounds. However, as far as we know, this strategy has not been reliably established yet.^[2,4]

Benzo[b]phosphole oxides as representative phosphonic heterocyclic compounds have long been investigated in the development of new classes of optoelectrochemical materials,^[5] together with an emerging direction as asymmetric induction precursors.^[6] *The high value of benzo[b]phosphole oxides necessitates their explorations on structural diverse against classical dibenzo[b]phosphole oxides and synthetic innovations.* Nevertheless, to date, only a handful of catalytic methods were reported, with substrates confined in the annulations of alkynes and phosphorus compounds.^[7] For pioneer studies (**Scheme 1**, b), in 2013, silver or manganesemediated C-H/P-H functionalization reactions of *H*arylphosphine oxides with internal alkynes to access benzo[*b*]phosphole oxides were documented by the groups of Duan,^[7a] Satoh and Miura,^[7b] respectively. Soon after this, Yoshikai described a modular approach to benzo[*b*] phosphole derivatives based on one-pot sequential coupling of arylzinc reagents, alkynes, dichlorophenylphosphines and oxidants, sequentially catalyzed by cobalt and copper.^[7c] Very recently, Lakhdar developed a photoredox catalytic protocol using eosin Y as the catalyst and *N*-ethoxy-2-methylpyridinium tetrafluoroborate as the oxidant.^[7d] Although much progress has been made, the reported strategies on P-ring closure still suffered from several drawbacks, such as stoichiometric transition metals, synthetic oxidants, low yields, poor regioselectivity or limited substrate scope. More importantly, alkenyl benzo[*b*]phosphole oxides, a new family member of benzo[*b*]phosphole oxides possessing promising optoelectrochemical properties, have been underdeveloped within the regime.^[8]





Scheme 1. Representative Studies on Phosphine Oxides-Directed Cross-Couplings (a); Synthesis of Benzo[*b*] phosphole Oxides (b); Classifications of Allylic Fragments (c); Our Previous Work (d); This Work (e).

Since 2015, our group has advanced researches on palladium-catalyzed coupling of phosphinyl allenes

bearing allylic fragments (1) with arylboronic acids, *N*-tosylhydrazones, and conjugated *N*-tosylhydra-

zones, respectively (Scheme 1, c).^[9] The couplings were initiated through a common π -allylpalladium intermediate, generated from the cleavage of α allenylic aryl ether bonds. Intriguingly, an unprecedented palladium-catalyzed cleavage of alkenyl C-P(O) bonds directed by P=O and pyrazole moieties was also discovered by us.^[9c] Note that the cleavage of allyl fragments with electron-rich functionalities (Scheme 1d, XR: X=O, N; R=aryl, alkyl) to generate π -allyl-metal species is challenging but attractive,^[10] this process has been dominantly limited within cross-couplings, though being extended direct C-H functionalization to recently.^[10c,10e] Inspired by the aforementioned studies and our previous works on direct C-H functionalization and organophosphorus chemistry,^[11] we envisioned that, the phosphinyl allenes bearing allylic fragments (1) upon palladium catalysis might form six-membered palladacycles, which then undergo intramolecular cyclization to deliver a novel family of benzo[b]phosphole oxides (2) (Scheme 1, e).

2 Results and Discussion

We initiated the study by examining a palladium dichloride-catalyzed intermolecular cyclization of phosphinyl allenes (1a) in the presence of sodium pivalate and refluxing THF. The usage of sodium pivalate was based on its basicity and facilitation on 10.1002/adsc.201800103

direct C-H functionalization.^[12] For a preliminary result, alkenyl benzo[b]phosphole oxides 2a was isolated in 23% yield along with about 5% yield of 2'a (Table 1, entry 3), which indicated that 2a and 2'a might be an olefin isomerization pair. Systematically screenings of the conditions were performed after then. The cyclization exhibited obvious sensitivity to the solvents used. Toluene, acetonitrile and 1,4-dioxane afforded better yields than of other solvents, offering further optimizations. Alternative palladium catalysts, such as $Pd(OAc)_2$, $Pd(TFA)_2$ and $Pd(PPh_3)_2Cl_2$, improved the yields up to 50% and spontaneously suppressed the formation of 2'a to some extent (entries 9-11). Taking into account that 2'a might be convertible into 2a via isomerization, various bases were tested subsequently. Delightfully, as shown in entry 14, cesium carbonate significantly enhanced the cyclization yields up to 70%, with only trace amount of 2'a detected. In sharp contrast, other bases adversely affected the efficiency, resulting in either no reaction or formation of much more isomer 2'a (entries 13, 15-20). Eventually, the combination of cesium carbonate and sodium pivalate was considered as the best components to enable the reaction (entry 14). The observations together with the control experiments in entries 21-23, strongly suggested that palladium precursor, a base and an additive would synergistically play vital roles in achieving high efficiency and suppressing the unwanted isomer.

Table 1. Palladium-catalyzed Intramolecular Cyclization of Phosphinyl Allenes (1a): Conditions Screening.^[a]



entry	catalyst (5 mol%)	base/solvent/additive	yield (2a/2'a,%) ^[b]
1	PdCl ₂	PivONa/THF/-	trace
2	PdCl ₂	PivONa/CH ₂ Cl ₂ /-	0
3	PdCl ₂	PivONa/Toluene/-	23/<5
4	PdCl ₂	PivONa/H ₂ O/-	20/<5
5	PdCl ₂	PivONa/DME/-	trace
6	PdCl ₂	PivONa/Acetonitrile/-	42/10
7	PdCl ₂	PivONa/DMF(110 °C)/-	trace
8	PdCl ₂	PivONa/dioxane/-	40/10
9	Pd(OAc) ₂	PivONa/dioxane/-	28/15
10	Pd(TFA) ₂	PivONa/dioxane/-	42/10
11	Pd(PPh3)2Cl2	PivONa/dioxane/-	50/29

12	Pd(PPh3)2Cl2	PivOCs/dioxane/-	45/35
13	Pd(PPh3)2Cl2	PivONa/dioxane/K2CO3	39/31
14	Pd(PPh ₃) ₂ Cl ₂	PivONa/dioxane/Cs ₂ CO ₃	70/trace
15	Pd(PPh ₃) ₂ Cl ₂	PivONa/dioxane/t-BuOK	trace
16	Pd(PPh ₃) ₂ Cl ₂	PivONa/dioxane/t-BuOLi	trace/51
17	Pd(PPh ₃) ₂ Cl ₂	PivONa/dioxane/Et ₃ N	42/22
18	Pd(PPh ₃) ₂ Cl ₂	PivONa/dioxane/NaHCO3	29/18
19	Pd(PPh ₃) ₂ Cl ₂	PivONa/dioxane/DBU	trace
20	Pd(PPh ₃) ₂ Cl ₂	PivONa/dioxane/DABCO	49/27
21	Pd(PPh ₃) ₂ Cl ₂	-/dioxane/Cs2CO3	trace
22	Pd(PPh ₃) ₂ Cl ₂	-/dioxane/-	0
23	-	PivONa/dioxane/-	0

^[a] Reaction conditions: phosphinyl allene (**1a**, 0.3 mmol), catalyst (5 mol%), base (0.9 mmol), additive (0.6 mmol) in 3 mL refluxing solvent for 18 hours;

^[b] Isolated yield.

With the optimized conditions in hand, the effect of electron-rich functionalities on ether moiety was investigated firstly. Substrates bearing aromatic substitutions showed comparable reactivities with excellent yields (Table 2, entries 1-4), whereas an alkyl one performed sluggishly under the standard conditions, with only 10% yield of target product formed (entry 5). In terms of substitution-free substrate (α -allenic alcohol, R=H), a dihydrofuranyl derivative (**I**)^[13] was isolated instead of 3-alkenyl benzo[b] phosphole oxides (entry 6), resulting from the nucleophilic attack of hydroxyl group to palladium-allene complex. Notably, most of the purified allene substrates were highly viscous gum, therefore 2,6-dimethylphenyl substituted allenes were chosen for further studies due to their crystalline state and operationally simplicity.

Table2.Palladium-catalyzedIntramolecularCyclization of Phosphinyl Allenes: Ether SubstitutionEffect.

\langle	Ph ₂ P=O PivONa, o dioxane	(PPh ₃)Cl ₂ Cs ₂ CO ₃ , , reflux	CH ₃ O 2b
Entry	R	Product	Isolated Yield (%)
1	2,6-Dimethylphenyl	2b	96
2	Phenyl	2b	95
3	4-Methylphenyl	2b	93
4	2,4-difluorophenyl	2b	89
5	-CH ₂ CH ₂ Ph	2b	10
6	Н		73

Subsequently, we evaluated the substrate scope of various phosphinyl allenes (1a-10) by altering the endmost substitutions of allenes. As depicted in Scheme 2, the cyclization delivered varieties of 3alkenyl benzo[b]phosphole oxides with yields ranged from medium to excellent, depending on the structure and electronic properties of substituents. On one hand, phosphinyl allenes bearing endmost symmetrical alicyclic or alkyl substitutions afforded products 2a-**2e** in good to excellent yields, with cyclopentyl derivative as an exceptional case. An ORTEP drawing of the molecular structure of 2c (CCDC 1574953) was given in Figure 1a.^[14] It is noticed that alkenyl benzo[b]phosphole oxide contains a prochiral center (phosphorus atom),^[15] however, the X-ray structure of **2c** exhibits only *R*-isomer in a crystal cell (see details in S.I.). We deduced that this might be attributed to a spontaneous resolution at molecular level upon recrystallization.^[16] Phosphinyl allenes with terminal heterocycles furnished 2f, 2g/2g'in yields of 57% and 50%, respectively. On the other hand, substrates bearing endmost unsymmetrical substitutions proceeded smoothly to give structurally diverse alkenyl benzo[b]phosphole oxides (2h-2o), with yields ranged from 53-94%. In this part, the cyclization was quite susceptible to the electron effect where substrates with strong electron-donating group (p-methoxy, 1i) and electron-withdrawing group (ptrifluoromethyl, 1k) furnished distinct results (93% vs 65%). When it came to ethyl and propyl derivatives (1m-1o), the cyclization products gave slightly preferences of E-selectivity with ratios of 2.4-4.2:1 over Z-isomers.

Scheme 2. Palladium-catalyzed Intramolecular Cyclization of Phosphinyl Allenes: Substrate Scope on Allenes Moiety.^{[a],[b]}



^[a] Reaction conditions: phosphinyl allene (1, 0.3 mmol), Pd(PPh₃)₂Cl₂ (5 mol%), Cs₂CO₃ (0.9 mmol), sodium pivalate (0.6 mmol), 3 mL 1,4-dioxane, reflux. ^[b] Isolated yield.

^[c] E/Z ratios were determined by ¹H-NMR and HPLC.

The substrate scopes of phosphinyl allenes containing various arylphosphine oxides were evaluated as well (**Scheme 3**). The cyclization was explained as insensitive to steric hindrance, in which the ortho-methyl substituted allene bearing dimethyl

terminals (1p) proceeded quite well to afford 2p with a yield of 84%. Interestingly, the reaction showed excellent regioselectivity once the aryl moieties bearing meta-substitutions. For substrates with metamethyl (1q, 1r) or 1,3-dioxo groups (1s), the reactions cyclized exclusively at the central orthopositions in excellent yields up to 99%, with the regioselectivities determined according to ¹HNMR data (the hydrogen atoms at the hindered positions after cyclization) disappeared and X-rav crystallographic analysis of 2s (CCDC 1574954, Figure 1b).^[14] With respect to *para*-substituents, the cyclization tolerated with chloro, tert-butyl, methoxy and trifluoromethoxy groups, furnishing products 2t-2x in medium to good yields. Although the cyclizations presented insusceptibility to the electron effect of substituents on phosphine oxides, sensitivity was found in the case of changing allene terminals. For instance, para-fluoro, para-chloro-substituted substrates (1u and 1v) substantially impaired the efficiency. To our delight, para-trifluoromethoxy group improved the stereo-preference as well and 62% yield of *E*-isomer (2y-E) was isolated with a ratio of 5.9:1 over Z-isomer. As for polyaromatic systems, β -naphthyl derivated substrate (1aa) gave selective cyclization on α -position, which could also be ascribed to the influence of electron density. In general, considering that the C-H alkenylation occurred directly on the aryl moieties of phosphine oxides, the relative substituents exhibited excellent regiocontrol, along with superior stereo-control than those generated from the endmost of allenes. Moreover, to the best our knowledge, this intramolecular P=O directed strategy affords the bes regioselectivity to build benzo[b]phosphole oxides scaffolds over the previous reports.^[7] As fo. aryl/alkyl-substituted phosphinyl allene (1ab), the reaction pathway was entirely changed, delivering a (E)-1,3-butadiene product (II) in 73% yield, which was produced from the nucleophilic attack of 2,6dimethylphenolate to the π -allyl-palladium species. The distinct result can be rationalized that the alkyl group weakened the polarization of P=O bond, hence preventing the coordination of π -allyl-palladium with P=O moiety from forming a key $C(sp^2)$ -H activation intermediate.



Figure 1. X-ray structures of 2c ([a]) and 2s ([b]).

Scheme 3. Palladium-catalyzed Intramolecular Cyclization of Phosphinyl Allenes (1a): Substrate Scope on Phosphine Oxide Moiety.



^[a] Reaction conditions: phosphinyl allene (1, 0.3 mmol), Pd(PPh₃)₂Cl₂ (5 mol%), Cs₂CO₃ (0.9 mmol), sodium pivalate (0.6 mmol), 3 mL 1,4-dioxane, reflux.
^[b] Isolated yield.

^[c] E/Z ratios were determined by ¹H-NMR, and the major isomers were separated by preparative HPLC.

Control experiments were conducted to determine the reaction mechanism. To confirm the transformation of 2' to final product 2, 2'a was synthesized under standard conditions by replacing cesium carbonate with t-BuOLi. The intermediate could be fully converted into 2a in the presence of cesium carbonate (Scheme 4, eq. a), probably through a 1,5-hydrogen shift process^[17] or baseassisted isomerization. When deuterated 1e was employed, no 1,5-D-atom shift was observed in the final product, with **2e-D**⁵ exclusively formed in 71% yield (eq. b, see details in S.I.). The negative result under base-free conditions in eq. a and the deuteration experiment collectively pointed to the isomerization process instead of 1,5-hydrogen shift. With the consideration of clarifying the P=O directed cyclization, analogues including tosyl-substituted allene (**3**) and benzoyl-substituted allene (**5**) were synthesized and applied to the cyclization conditions (eqs. c and d). However, these allenes decomposed rapidly, without detection of any proposed cyclization products (**4/4'**, **6/6'**).^[18] Finally, an arylether-free analogue, (4-methylpenta-2,3-dien-2-yl)diphenyl phosphine oxide (**7**), was found to be entirely inert under the identical reaction conditions (eq. e), which suggested that the C-H activation as an initial step to form palladium intermediates can be ruled out accordingly.

Scheme 4. Mechanism Studies.



Based on the observed experimental facts, as well as previous reports on palladium-catalyzed allene cyclocarbo-palladation,^[3,11,19] chemistry and plausible mechanism is proposed in Scheme 5. Initially, oxidative addition and cleavage of $C(sp^3)$ -O(Ar) bond lead to the formation of π -allylpalladium species [A]. Subsequent $C(sp^2)$ -H activation and P=O direction in the presence of pivalate should be involved to give the transition state [B], as was strongly supported by the control experiments (Table 1, entries 21-23; Scheme 4, eq. c and d). Afterwards, base removes the pivalic acid to form the sixmembered cyclopalladium intermediate [C], followed by reductive elimination to generate isomer 2', along with the recycle of the Pd(0) catalyst. Eventually, **2'** isomerizes to the final product **2**, with the assistance of cesium carbonate.

Scheme 5. Plausible Mechanism.



3 Conclusion

In conclusion, for the first time, we disclosed a palladium-catalyzed cyclization of phosphinyl allenes toward the synthesis of novel 3-alkenyl benzo[b] phosphole oxides. The intramolecular cyclization was consisted of an unprecedented cascade C-O cleavage and P=O directed C-H alkenylation pathway. Various 3-alkenyl benzo[b]phosphole oxides were obtained with medium to excellent yields, along with broad group tolerance and high regioselectivity. We anticipated that this novel strategy will enrich the C-H activation chemistry and provide new classes of optoelectro-chemical materials.

Experimental Section

Typical Procedures for the Palladium-Catalyzed Intramolecular Cyclization of Phosphinyl Allenes. To a 5 mL two-necked flask equipped with condenser under nitrogen was added phosphinyl allene (1a, 128 mg, 0.3 mmol), Pd(PPh₃)₂Cl₂ (11 mg, 5 mol%), Cs₂CO₃ (293 mg, 0.9 mmol), PivONa (74 mg, 0.6 mmol) and 3 mL degassed 1,4-dioxane. The reaction mixture was then heated to reflux for 18 hours until the complete consuming of 1a as monitored by TLC. After all of the volatiles were removed under vacuum, the crude product was purified on flash chromatography (eluent: 1:1 (v/v) of ethyl acetate/ petroleum ether) to afford product 2a (64 mg, 70% yield) as a viscous yellow liquid. TLC ($R_f = 0.24$, petroleum ether/ethyl acetate = 1:1). ¹**H-NMR** (400 MHz, CDCl₃) δ 7.69-7.64 (m, 2H), 7.60-7.56 (m, 1H), 7.54-7.49 (m, 1H), 7.47-7.41 (m, 3H), 7.35-7.26 (m, 2H), 5.32 (s, 1H), 4.90 (s, 1H), 1.90 (d, J = 12.3 Hz, 3H), 1.67-1.60 (m, 1H), 0.81-0.73 (m, 2H), 0.56-0.47 (m, 2H). ¹³C-NMR (101 MHz, CDCl₃) δ 150.7 (d, J = 21.2 Hz), 144.2 (dd, J = 21.7, 6.7 Hz), 133.0 (d, J = 2.0 Hz), 132.2 (d, J = 2.8 Hz), 131.9 (d, J = 28.5 Hz), 130.9 (d, J = 37.9 Hz), 130.8 (d, J = 10.6 Hz), 129.3 (d, J = 97.3 Hz), 128.9 (d, J = 12.2 Hz), 128.8 (d, J = 9.6 Hz), 128.3 (d, J = 10.5 Hz), 123.1 (d, J = 10.9 Hz), 112.8, 27.3, 16.1, 10.7 (d, J = 11.2 Hz), 7.3 (d, J = 7.3 Hz). ³¹**P-NMR** (162 MHz, CDCl₃) δ 40.4 (s). **HR-MS** (ESI): ([M+H]⁺) Calcd for C₂₀H₂₀OP: 307.1246, Found: 307.1243. **IR** (film) v 3077, 3007, 2909, 2849, 2159, 2029, 1976, 1732, 1627, 1588, 1568, 1481, 1436, 1282, 1198, 1156, 1128, 1023, 776, 693 cm⁻¹.

Acknowledgements

We are grateful for financial support from the Key Laboratory of Molecular Recognition and Function, Institute of Chemistry, Chinese Academy of Sciences (2017LMRF004), and the Fundamental Research Funds for the Central Universities (NJAU, Grant No. KYTZ201604).

References

- For selected books and reviews: a) L. D. Quin, A Guide to Organophosphorus Chemistry, John Wiley & Sons, New York, 2000; b) S. Van der Jeught, C. V. Stevens, Chem. Rev. 2009, 109, 2672; c) C. S. Demmer, N. Krogsgaard-Larsen, L. Bunch, Chem. Rev. 2011, 111, 7981; d) C. Queffélec, M. Petit, P. Janvier, D. A. Knight, B. Bujoli, Chem. Rev. 2012, 112, 3777; e) J. L. Montchamp, Acc. Chem. Rev. 2014, 47, 77.
- [2] a) Y.-N. Ma, S.-X. Li, S.-D. Yang, Acc. Chem. Res.
 2017, 50, 1480; b) Y. Yang, Z. Shi, Chem. Commun
 2018, 54, 1676.
- [3] a) D. Zhao, C. Nimphius, M. Lindale, F. Glorius, Org. Lett. 2013, 15, 4504; b) L. Y. Chan, L. Cheong, S. Kim, Org. Lett. 2013, 15, 2186; c) D. Eom, Y. Jeong, Y. R. Kim, E. Lee, W. Choi, P. H. Lee, Org. Lett. 2013, 15, 5210; d) H.-L. Wang, R.-B. Hu, H. Zhang, A.-X. Zhou, S.-D. Yang, Org. Lett. 2013, 15, 5302; e) Y. Unoh, Y. Hashimoto, D. Takeda, K. Hirano, T. Satoh, M. Miura, Org. Lett. 2013, 15, 3258; f) M. Itoh, Y. Hashimoto, K. Hirano, T. Satoh, M. Miura, J. Org. Chem. 2013, 78, 8098; g) H. Zhang, R.-B. Hu, X.-Y. Zhang, S.-X. Li, S.-D. Yang, Chem. Commun. 2014, 50, 4686; h) K. M. Crawford, T. R. Ramsever, C. J. A. Daley, T. B. Clark, Angew. Chem. Int. Ed. 2014, 53, 7589; i) Y.-N. Ma, H.-Y. Zhang, S.-D. Yang, Org. Lett. 2015, 17, 2034; j) X.-H. Hu, X.-F. Yang, T.-P. Loh, Angew. Chem. Int. Ed. 2015, 54, 15535; k) Y Unoh, T. Satoh, K. Hirano, M. Miura, ACS Catal. 2015, 5, 6634; 1) Z.-J. Du, J. Guan, G.-J. Wu, P. Xu, L.-X. Gao, F.-S. Han, J. Am. Chem. Soc. 2015, 137, 632; m) T. T. Nguyen, L. Grigorjeva, O. Daugulis, ACS Catal. 2016, 6, 551; n) Y. Yang, X. Qiu, Y. Zhao, Y. Mu, Z. Shi, J. Am. Chem. Soc. 2016, 138, 495; o) Y. Yang, R. Li, Y. Zhao, D. Zhao, Z. Shi, J. Am. Chem. Soc. 2016, 138, 8734; p) S.-X. Li, Y.-N. Ma, S.-D. Yang, Org. Lett. 2017, 19, 1842; q) Z. Liu, J.-Q. Wu, S.-D. Yang, Org. Lett. 2017, 19, 5434; r) Y. Sun, N. Cramer, Angew. Chem. Int. Ed. 2017, 56, 364.
- [4] Although Cui et. al. reported a palladium-catalyzed

arylation of *ortho*-bromodiarylphosphine oxides to access dibenzo[b]phosphole oxides, this work was not exemplified as P=O directed process. Moreover, phosphine oxide-free substrates were also applicable, see: a) Y. Cui, L. Fu, J. Cao, Y. Deng, J. Jiang, *Adv. Synth. Catal.* **2014**, *356*, 1217; b) J. Song, Y. Li, W. Sun, C. Yi, H. Wu, H. Wang, K. Ding, K. Xiao, C. Liu, *New. J. Chem.* **2016**, *40*, 9030. For non-P=O directed cyclizations, see: c) Y.-N. Ma, M.-X. Cheng, S.-D. Yang, *Org. Lett.* **2017**, *19*, 600; d) Y.-N. Ma, X. Zhang, S.-D. Yang, *Chem. Eur. J.* **2017**, *23*, 3007.

- [5] For selected reviews, see: a) F. Mathey, Acc. Chem. Res. 2004, 37, 954; b) Y. Matano, H. Imahori, Org. Biomol. Chem. 2009, 7, 1258; c) M. A. Shameem, A. Orthaber, Chem. -Eur. J. 2016, 22, 10718; d) M. P. Duffy, W. Delaunay, P.-A. Bouit, M. Hissler, Chem. Soc. Rev. 2016, 45, 5296.
- [6] M. Gicquel, Y. Zhang, P. Aillard, P. Retailleau, A. Voituriez, A. Marinetti, Angew. Chem. Int. Ed. 2015, 54, 5470.
- [7] a) Y.-R. Chen, W.-L. Duan, J. Am. Chem. Soc. 2013, 135, 16754; b) Y. Unoh, K. Hirano, T. Satoh, M. Miura, Angew. Chem. Int. Ed. 2013, 52, 12975; c) B. Wu, M. Santra, N. Yoshikai, Angew. Chem. Int. Ed. 2014, 53, 7543; d) V. Quint, F. Morlet-Savary, J.-F. Lohier, A.-C. Lalevée, Gaumount, S. Lakhdar, J. Am. Chem. Soc. 2016, 138, 7436; e) Y. Zhou, Z. Gan, B. Su, J. Li, Z. Duan, F. Mathey, Org. Lett. 2015, 17, 5722; f) B. Wu, R. Chopra, N. Yoshikai, Org. Lett. 2015, 17, 5666; g) P. Zhang, Y. Gao, L. Zhang, Z. Li, Y. Liu, G. Tang, Y. Zhao, Adv. Synth. Catal. 2016, 358, 138; h) Y. Zhang, G. Hu, D. Ma, P. Xu, Y. Gao, Y. Zhao, Chem. Commun. 2016, 52, 2815; i) D. Ma, W. Chen, G. Hu, Y. Zhang, Y. Gao, Y. Yin, Y. Zhao, Green Chem. 2016, 18, 3522; j) Y. Unoh, Y. Yokoyama, T. Satoh, K. Hirano, M. Miura, Org. Lett. 2016, 18, 5436; k) W. Ma, L. Ackermann, Synthesis, 2014, 46, 2297.
- [8] Only one case of 2-alkenyl benzo[b]phosphole oxides was reported, which were synthesized via Heck and Stille coupling of 2-bromobenzo[b]phosphole oxides with alkenes or tin reagents, see: Y. Matano, Y. Hayashi, K. Suda, Y. Kimura, H. Imahori, Org. Lett. 2013, 15, 4458.
- [9] a) Y.-Z. Chen, L. Zhang, A.-M. Lu, F. Yang, L. Wu, J. Org. Chem. 2015, 80, 673; b) M. Mao, L. Zhang, Y.-Z. Chen, J. Zhu, L. Wu, ACS Catal. 2017, 7, 181; c) J. Zhu, M. Mao, H.-J. Ji, J.-Y. Xu, L. Wu, Org. Lett. 2017, 19, 1946.
- [10] a) T. Nishikata, B. H. Lipshutz, J. Am. Chem. Soc. 2009, 131, 12103; b) T. Nishikata, B. H. Lipshutz,

Chem. Commun. **2009**, *0*, 6472; c) S. Asako, L. Ilies, E. Nakamura, *J. Am. Chem. Soc.* **2013**, *135*, 17755; d) X. Huo, M. Quan, G. Yang, X. Zhao, D. Liu, Y. Liu, W. Zhang, *Org. Lett.* **2014**, *16*, 1570; e) Y. Minami, M. Sakai, T. Anami, T. Hiyama, *Angew. Chem. Int. Ed.* **2016**, *55*, 8701.

- [11] a) W.-C. Yang, P. Dai, K. Luo, L. Wu, Adv. Synth. Catal. 2016, 358, 3184; b) K. Luo, Y.-Z. Chen, W.-C. Yang, J. Zhu, L. Wu, Org. Lett. 2016, 18, 452; c) K. Luo, Y.-Z. Chen, L.-X. Chen, L. Wu, J. Org. Chem. 2016, 81, 4682; d) L. Zhang, J. Zhu, J. Ma, L. Wu, W.-H. Zhang, Org. Lett. 2017, 19, 6308.
- [12] a) Y. Li, W.-H. Wang, K.-H. He, Z.-J. Shi, Organometallics, 2012, 31, 4397; b) L. Ackermann, Chem. Rev. 2011, 111, 1315.
- [13] For a silver-catalyzed formation of 3-phosphoryl-2,5dihydrofurans, see: V. Ch. Christov, I. E. Ismailov, I. K. Ivanov, *Molecules*, **2015**, *20*, 7263.
- [14] CCDC 1574953 (2c) and CCDC 1574954 (2s), contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/ data_request/cif.
- [15] For the recent studies on P-chiral phosphine oxides, see: a) Z. S. Han, L. Zhang, Y. Xu, J. D. Sieber, *Angew. Chem. Int. Ed.* 2015, 54, 5474; b) R. Beaud, R. J. Phipps, M. J. Gaunt, *J. Am. Chem. Soc.* 2016, *138*, 13183; c) Y. Sun, N. Cramer, *Angew. Chem. Int. Ed.* 2017, 56, 364.
- [16] A similar spontaneous resolution phenomenon of allenyl-bis-phosphine oxides was recently reported by Swamy: G. Gangadhararao, R. N. P. Tulichala, K. C. K. Swamy, *Chem. Commun.* **2015**, *51*, 7168.
- [17] W. von E. Doering, X. Zhao, J. Am. Chem. Soc. 2006, 128, 9080.
- [18] The polarization and coordinative power of directing groups may make a big difference among sulfones, ketones and phosphine oxides for C-H activation herein. As mentioned by Ackermann, those weakly coordinating groups were subtle to several factors, strongly depending on the type of reactions, the nature of the transition metals as well as the exact reaction conditions. See: a) S. De Sarkar, W. Liu, S. I. Kozhushkov, L. Ackermann, Adv. Synth. Catal. 2014, 356, 1461; b) Z. Chen, B. Wang, J. Zhang, W. Yu, Z. Liu, Y. Zhang, Org. Chem. Front. 2015, 2, 1107.
- [19] a) J. Zhao, K. Oniwa, N. Asao, Y. Yamamoto, T. Jin, J. Am. Chem. Soc. 2013, 135, 10222; b) A. J. Mota, A. Dedieu, C. Bour, J. Suffert, J. Am. Chem. Soc. 2005, 127, 7171.

FULL PAPER

Palladium-Catalyzed Cascade C-O Cleavage and C-H Alkenylation of Phosphinyl Allenes: An Expeditious Approach to 3-Alkenyl Benzo[*b*]phosphole Oxides

Adv. Synth. Catal. 2018, Volume, Page - Page

Teng Liu, Xue Sun, and Lei Wu*



R - Meuryi, Euryi, Aliphauc Cyclics, R - Alkyi, Aryi, R - Alkyi, Hali

The first P=O directed intramolecular cyclization of allenes

□ A new member of benzo[b]phosphole family: 3-alkenyl benzo[b]phosphole oxides
 □ Cascade C-O Cleavage and C-H Alkenylation, 28 examples, yields up to 99%