Heterocycle Synthesis

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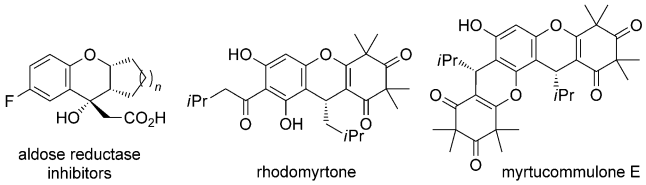
Annulation of Alkynyl Aryl Ethers with Allyl Pivalates To Give 2,3-Bismethylenechromanes through Double C–H Bond Cleavage

Yasunori Minami, Megumi Sakai, Tomohiro Anami, and Tamejiro Hiyama**

Abstract: *The treatment of silylethynyloxyarenes with allylic pivalates in the presence of a palladium catalyst led to efficient C–H bond cleavage in both substrates and a novel annulation reaction to give 2,3-bismethylenechromanes. When ortho-allylated silylethynyloxybenzenes were used as the substrates, the same products were obtained. This result shows that site-selective intramolecular hydrovinylation is involved in the annulation reaction. The synthetic utility of the products was demonstrated by the construction of condensed polycycles.*

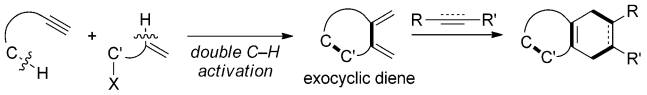
Condensed polycyclic compounds are long-standing important and challenging targets in synthetic chemistry.[1] For example, pyran-based tricycles are the core structure of many natural products and biologically active agents (Scheme 1).[2]



Scheme 1. Selected examples of pharmacologically active chromanes.

The construction of such condensed cycles is straightforward by the Diels–Alder reaction of conjugated exocyclic dienes.[3] Various methods for the preparation of such exocyclic dienes have been reported.[4] As a typical example, Wender and co-workers took advantage of sequential Diels–Alder reactions of 2,3-bismethylene-4-trimethylsilylbutan-1-ol, whereby the initially constructed exocyclic diene intermediates underwent a second Diels–Alder reaction.[5] Although the utility of exocyclic dienes is evident, synthetic methodology for their synthesis has been limited. Previously, we reported that sequential insertion reactions of alkynyl aryl ethers with allenes gave chromane derivatives containing 2,3-exomethylene moieties for the formation of pyran-based condensed cycles.[6c,7,8] However, allenes are unsuitable for mass production: their instability issue imposed a limitation on synthetic diversity. Thus, a more facile preparative method has been required.

At present, catalytic C–H activation followed by a C–C bond-forming reaction is regarded as a powerful synthetic strategy for the preparation of simple and complex molecules. Double C–H activation has been applied to straightforward annulation reactions, thus allowing the rapid synthesis of cyclic compounds.[8b,d,9,10] On the basis of this idea, we set out to invent an annulation reaction through double C–H bond cleavage in two substrates to form exocyclic dienes directly (Scheme 2). We merged the alkynoxy-group strategy[6] with



Scheme 2. Strategy for the straightforward construction of condensed cycles by double C–H bond-cleaving site-selective C–C bond formation.

C–H bond-cleaving allylation with a stable allylic reaction partner that can be readily prepared.[11] Herein, we report the palladium-catalyzed annulation of aryl silylethynyl ethers with allylic electrophiles through cleavage of the *ortho*-C–H bond in the aryl silylethynyl ether and the β-alkenyl C–H bond in the allylic reaction partner. The total transformation produces chromane derivatives with conjugated bismethylene moieties. These compounds are useful for the synthesis of pyran-based polycyclic compounds.

First, we attempted a reaction of *p*-anisyl triisopropylsilylethynyl ether (**1a**) with cinnamyl bromide in the presence of a palladium catalyst and a base. However, this combination led to a complex mixture without any allylation products. We screened various cinnamyl substrates and reaction conditions[12] and found cinnamyl pivalate (**2a**) to be effective for the reaction with **1a**. Thus, the reaction of **1a** with **2a** took place in the presence of $[Pd(dba)_2]$ (5 mol%), PCy_3 (10 mol%), and Cs_2CO_3 (1.1 equiv) at 140 °C in toluene to give the exocyclic product **3a** in 83% yield through cleavage of the *ortho*-C–H bond in **1a** and the β-C–H bond in **2a** (Scheme 3). A simply *ortho*-allylated aryl silylethynyl ether was not observed at all. A catalytic amount of Cs_2CO_3 also gave **3a** in moderate yield, thus suggesting that the coproduced pivalic acid does not hamper the reaction. *t*BuPh$_2$Si, *t*BuMe$_2$Si, and *t*Bu groups in the place of TIPS were not effective. Both 1-TIPS-3-arylpropyne and TIPS-ethynyl aryl ketone were ineffective substrates, thus suggesting that the alkynyl ether moiety is essential for this transformation. We

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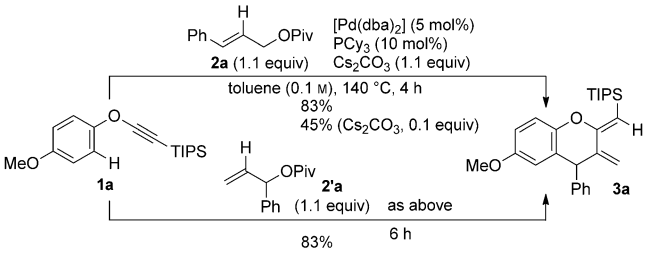
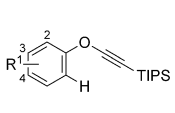
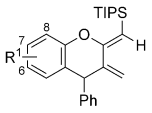
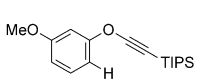
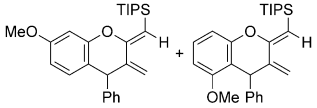
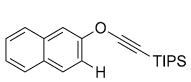
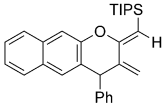


Scheme 3. Palladium-catalyzed double C–H bond-cleaving annulation. Cy = cyclohexyl, dba = dibenzylideneacetone, Piv = pivaloyl.

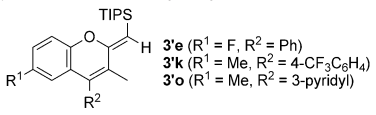
examined the reaction of **1a** with 1-phenyl-2-propenyl pivalate (**2′a**) and also obtained the 4-phenylated product **3a** in a yield similar to that observed in the case with **2a**. This result clearly suggests that a π-allyl palladium intermediate is involved in the present annulation.

The scope of the reaction of **2a** with various aryl silylethynyl ethers was briefly surveyed (Table 1). Substrates **1** in which the aryl group was an unsubstituted phenyl group or had a methyl, phenyl, or fluorine group at the *para* position underwent the desired reaction to give the corresponding products in good to excellent yields (Table 1, entries 1–4).

Table 1: Reaction of **1** with cinnamyl pivalate (**2a**).[a]

Entry	**1**	**3**, Yield [%][b]
		
1[c]	**1b**, R^1 = 4-Me	**3b**, R^1 = 6-Me, 81
2	**1c**, R^1 = H	**3c**, R^1 = H, 80
3	**1d**, R^1 = 4-Ph	**3d**, R^1 = 6-Ph, 72
4	**1e**, R^1 = 4-F	**3e**, R^1 = 6-F, 66[d]
5	**1f**, R^1 = 3-Me	**3f**, R^1 = 7-Me, 80
6	**1g**, R^1 = 2-Me	**3g**, R^1 = 8-Me, 77
7		
	1h	**3h**, 76 (85:15)
8		
	1i	**3i**, 62[e]

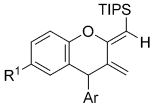
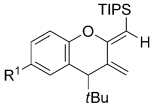
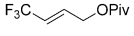
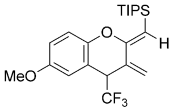
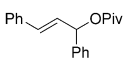
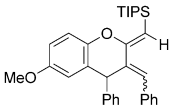
[a] Unless otherwise noted, a mixture of **1** (0.3 mmol), **2a** (0.33 mmol), [Pd(dba)$_2$] (0.015 mmol), PCy_3 (0.03 mmol), Cs_2CO_3 (0.33 mmol), and toluene (3.0 mL) was heated at 140 °C for 4 h. [b] Yield of the isolated product. [c] A mixture of **1b** (1.0 mmol), **2a** (1.1 mmol), [Pd(dba)$_2$] (0.05 mmol), PCy_3 (0.1 mmol), Cs_2CO_3 (1.1 mmol), and toluene (10 mL) was heated at 140 °C for 4 h. [d] Total yield of **3e** and **3′e** (97:3). [e] Total yield of **3i** and **3′i** (98:2).



These results suggest that electron-rich aryl groups in **1** are preferred for the reaction. In fact, an electron-withdrawing CF_3 group at the *para* position was not effective for the reaction. Substrates **1f** and **1g** with a *meta*- or *ortho*-tolyl group gave **3f** and **3g** in 80 and 77% yield, respectively (Table 1, entries 5 and 6). In the case of **1f**, the less-hindered position selectively participated in the reaction. On the other hand, the reaction of the *meta*-methoxy-substituted phenyl ether **1h** gave a mixture of products with a methoxy group at the C7 and C5 positions (85:15) in 76% combined yield (Table 1, entry 7). The 2-naphthyl alkynyl ether **1i** reacted to give **3i** through C–H cleavage at C3 (Table 1, entry 8). In the cases of **1e** and **1i**, conjugated dienes **3′e** and **3′i** were produced, probably as a result of the acceleration of isomerization by the electron-deficient aryl groups.

We next investigated the scope of the reaction with respect to the allyl pivalate (Table 2). Allyl pivalates with phenyl groups with an electron-donating or electron-withdrawing group at the 2- or 4-position or a 2-naphthyl group underwent the desired reaction (Table 2, entries 1–5). α-(3-Pyridyl)allyl pivalate (**2′g**) also participated in the reaction to give product **3o** (Table 2, entry 6). When α-*tert*-butylallyl pivalate (**2′h**) was used, the corresponding products **3p** and **3q** were obtained in high yields (Table 2, entries 7 and 8). To prepare a trifluoromethylated chromane structure,[13] we examined the reaction with 4,4,4-trifluoro-2-butenyl pivalate

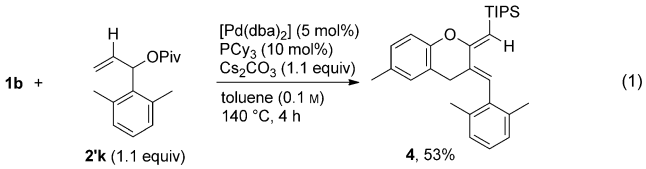
Table 2: Scope of the reaction with respect to **2**.[a]

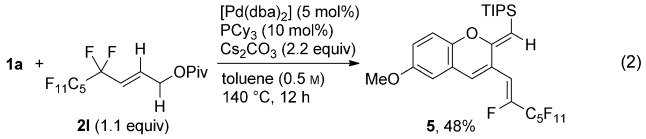
Entry	**1**	**2**	**3**, Yield [%][b]
			
1	**1c**	**2′b** (Ar = 4-OMeC$_6$H$_4$)	**3j** (R^1 = H, Ar = 4-OMeC$_6$H$_4$), 59
2	**1b**	**2′c** (Ar = 4-CF$_3$C$_6$H$_4$)	**3k** (R^1 = Me, Ar = 4-CF$_3$C$_6$H$_4$), 75[c]
3	**1b**	**2′d** (Ar = 2-MeC$_6$H$_4$)	**3l** (R^1 = Me, Ar = 2-MeC$_6$H$_4$), 66
4	**1b**	**2′e** (Ar = 2-PhC$_6$H$_4$)	**3m** (R^1 = Me, Ar = 2-PhC$_6$H$_4$), 71
5	**1b**	**2′f** (Ar = 2-naphthyl)	**3n** (R^1 = Me, Ar = 2-naphthyl), 74
6	**1b**	**2′g** (Ar = 3-pyridyl)	**3o** (R^1 = Me, Ar = 3-pyridyl), 74[d]
		 **2′h**	
7[e]	**1a**		**3p** (R^1 = OMe), 87
8	**1b**		**3q** (R^1 = Me), 83
9	**1a**	 **2i**	 **3r**, 34
10[f]	**1a**	 **2j**	 **3s**, 92[g]

[a] Unless otherwise noted, a mixture of **1** (0.3 mmol), **2** (0.33 mmol), [Pd(dba)$_2$] (0.015 mmol), PCy_3 (0.03 mmol), Cs_2CO_3 (0.33 mmol), and toluene (3.0 mL) was heated at 140 °C for 4 h. [b] Yields of the isolated product. [c] Total yield of **3k** and **3′k** (81:19). [d] Total yield of **3o** and **3′o** (85:15). [e] Reaction time: 16 h. [f] The reaction mixture was heated in toluene (0.8 mL) for 3 h. [g] The product was isolated as an inseparable mixture of stereoisomers (96:4) at the C3 methylidene moiety.

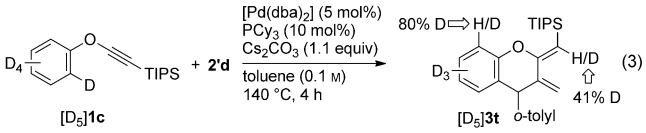
(**2i**) and obtained **3r** successfully, albeit in low yield (Table 2, entry 9). The substrate *trans*-1,3-diphenylallyl pivalate (**2j**) reacted with **1a** to give **3s**, which contains two phenyl groups at the 3-methylidene and C4 positions, in excellent yield (Table 2, entry 10). In contrast, unsubstituted allyl pivalate did not give any annulation product.

The reaction of **1b** with **2′k**, which contains a bulky 2,6-dimethylphenyl (xylyl) group, occurred with different regioselectivity to give **4** with the xylyl group at the C3-methylidene position [Eq. (1)]. In contrast to the reaction of substrate **2i** with a CF_3 group, the perfluoroalkylated allyl pivalate **2l** reacted through sequential regioselective annulation/elimination of HF to form chromene **5** with a *Z* perfluoroalkylated methylidene group at the C3 position [Eq. (2)]. These results indicate that the regioselectivity of the transformation is controlled by steric effects.

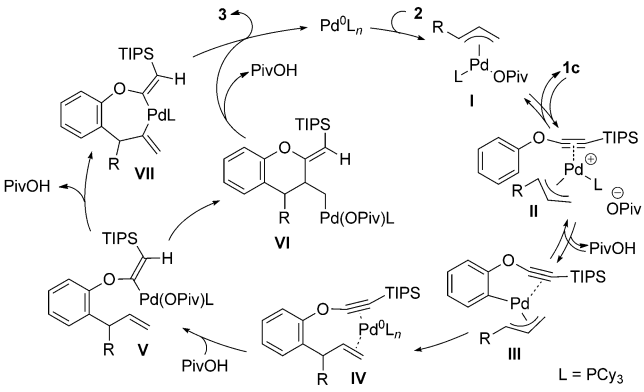




To gain insight into the C–H cleaving event, we used the deuterated substrate [D_5]**1c** for the annulation with **2′d** and obtained [D_5]**3t** with moderate deuteration at the 2-methylidene carbon atom and loss of deuterium at the C8 position [Eq. (3)]. This observation suggests that the *ortho*-C–H bond is cleaved reversibly, and that the C2-methylidene hydrogen atom in **3t** is partially derived from the *ortho*-hydrogen atom in **1**.



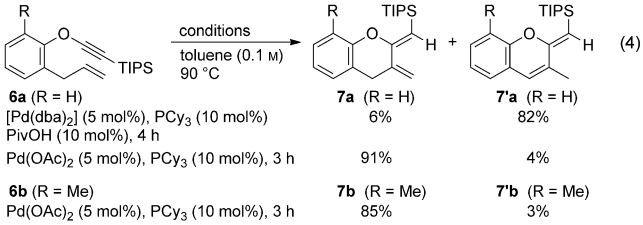
On the basis of the aforementioned results, we propose the reaction mechanism shown in Scheme 4. The ligation of **1** to π-allyl palladium species **I**[14] forms a cationic allylpalladium species **II**, which participates in reversible C–H cleavage through nucleophilic attack by the *ortho*-carbon atom to give allyl aryl palladium complex **III**. Reductive elimination then forms *ortho*-allylic intermediate **IV**. Next, intramolecular hydrovinylation proceeds via vinylpalladium pivalate **V**,[4c,d,e,15] which undergoes intramolecular carbopalladation to form **VI**. Subsequent β-H elimination produces **3**. An alternative pathway is internal C–H bond cleavage through concerted metalation–deprotonation to give **VII**,

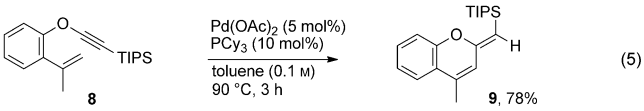


Scheme 4. Proposed mechanism.

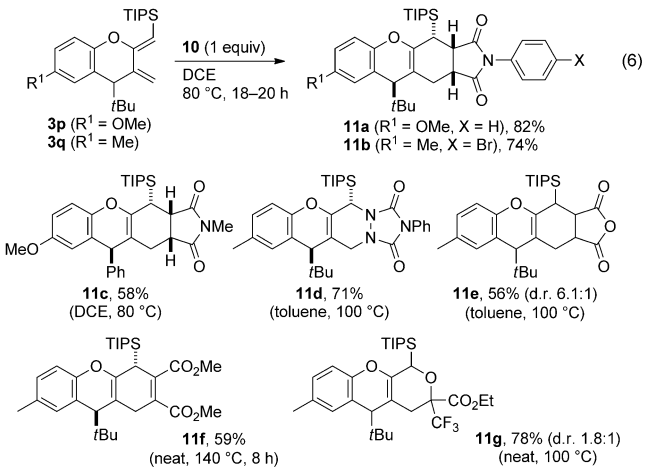
which undergoes reductive elimination to give **3**. The observed regioselectivity may be attributed to steric repulsion between the R group in the π-allylpalladium fragment and the TIPS group in the step from **III** to **IV**. On the other hand, bulky groups in **2**, such as 2,6-xylyl, led to the opposite regioselectivity to avoid the severe steric repulsion of the aryl groups in **1**.

This mechanism suggests that an intramolecular hydrovinylation may be feasible. Indeed, *ortho*-allylated **6a** was converted in the presence of $Pd(OAc)_2$/PCy_3/PivOH at 140 °C into 2,3-bismethylidenechromane **7a** and its isomer **7′a** in 6 and 82 % yield, respectively, possibly through exclusive cleavage of the internal vinyl C–H bond [Eq. (4)]. This observation supports the mechanism in Scheme 4 and clearly appears to compensate the failure of **1** to react with simple allyl pivalate. After optimization, **7a** was obtained in 91 % yield with $Pd(OAc)_2$ and PCy_3 at 90 °C.[16] The use of [$Pd(PCy_3)_2$] instead of $Pd(OAc)_2$ and PCy_3 resulted in no reaction, thus indicating that the hydrovinylation proceeds by a route which does not involve a palladacycle derived from the oxidative cyclization of **6** with the palladium(0) complex.[17,18] 2-Allyl-6-methylphenyl alkynyl ether **6b** was also converted into **7b** (85 %) and **7′b** (3 %) in the presence of $Pd(OAc)_2$/PCy_3 without cleavage of the benzylic C–H bond.[6b] The *ortho*-isopropenyl substrate **8** underwent successful cyclization to form **9** through cleavage of the β-vinyl C–H bond [Eq. (5)].



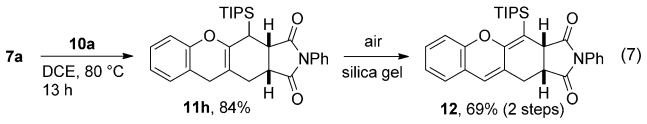


Products **3** and **7** are versatile precursors of linearly condensed polycycles. For example, **3p** underwent the Diels–Alder reaction with *N*-phenylmaleimide (**10a**) to give tetracycle **11a** [Eq. (6); DCE = 1,2-dichloroethane].[19] The C4-



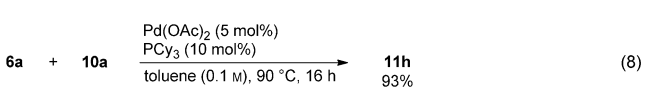
(6)

phenylated diene **3a** and dienophiles such as *N*-(*p*-bromophenyl)- and *N*-methylmaleimide (**10b** and **10c**), 4-phenyl-1,2,4-triazoline-3,5-dione (**10d**), maleic anhydride (**10e**), and dimethyl acetylenedicarboxylate (**10f**) were employed without any problems to give the condensed polycycles **11b–f**. Ethyl 3,3,3-trifluoropyruvate (**10g**) could be used to form the benzopyranopyran derivative **11g** regioselectively. In the reaction leading to **11e** and **11g**, single diastereomers were produced. The reaction of **7a** with *N*-phenylmaleimide (**10a**) gave tetracycle **11h** (84% yield by NMR analysis), which, upon attempted isolation by open-air silica-gel column chromatography, was converted into **12** in 69% yield over two steps, possibly through aerobic oxidation during the purification [Eq. (7)].[20] The tandem hydrovinylation/Diels–



(7)

Alder reaction of **6a** under palladium catalysis was possible in a single operation to give **11h** directly in 93% yield [Eq. (8)].



(8)

In conclusion, the present study has demonstrated two palladium-catalyzed annulation reactions for the synthesis of 2,3-bismethylenechromanes: an intermolecular reaction of alkynyl aryl ethers with allyl pivalates through C–H bond cleavage in each substrate and intramolecular hydrovinylation through vinylic C–H bond cleavage. In the former case, reactions with α- or γ-substituted allyl pivalates produced the same products, thus suggesting that this reaction takes place via π-allyl palladium intermediates. The bis(exomethylene) cyclic products serve as a building block for the synthesis of linear polycycles by the Diels–Alder reaction with various dienophiles.

Acknowledgements

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Keywords: alkynes · allyl substrates · annulation · C–C coupling · C–H activation

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[1] For examples, see: a) K. C. Nicolaou, J. S. Chen, D. J. Edmonds, A. A. Estrada, *Angew. Chem. Int. Ed.* **2009**, *48*, 660; *Angew. Chem.* **2009**, *121*, 670; b) A. Takada, Y. Hashimoto, H. Takikawa, K. Hikita, K. Suzuki, *Angew. Chem. Int. Ed.* **2011**, *50*, 2297; *Angew. Chem.* **2011**, *123*, 2345.

[2] a) C. A. Lipinski, C. E. Aldinger, T. A. Beyer, J. Bordner, D. F. Burdi, D. L. Bussolotti, P. B. Inskeep, T. W. Siegel, *J. Med. Chem.* **1992**, *35*, 2169; b) D. Salni, M. V. Sargent, B. W. Skelton, I. Soediro, M. Sutisna, A. H. White, E. Yulinah, *Aust. J. Chem.* **2002**, *55*, 229; c) F. Shaheen, M. Ahmad, S. N. Khan, S. S. Hussain, S. Anjum, B. Tashkhodjaev, K. Turgunov, M. N. Sultankhodzhaev, M. I. Choudhary, Atta-ur-Rahman, *Eur. J. Org. Chem.* **2006**, 2371; for a recent example of the synthesis of dibenzochromanes, see: d) C.-C. Hsiao, H.-H. Liao, M. Rueping, *Angew. Chem. Int. Ed.* **2014**, *53*, 13258; *Angew. Chem.* **2014**, *126*, 13474.

[3] a) C. C. Nawrat, C. J. Moody, *Angew. Chem. Int. Ed.* **2014**, *53*, 2056; *Angew. Chem.* **2014**, *126*, 2086; b) V. Eschenbrenner-Lux, K. Kumar, H. Waldmann, *Angew. Chem. Int. Ed.* **2014**, *53*, 11146; *Angew. Chem.* **2014**, *126*, 11326.

[4] For examples of the formation of conjugated exocyclic dienes, see: a) W. J. Bailey, H. R. Golden, *J. Am. Chem. Soc.* **1953**, *75*, 4780; b) B. M. Trost, J. M. Tour, *J. Am. Chem. Soc.* **1987**, *109*, 5268; c) B. M. Trost, M. Lautens, C. Chan, D. J. Jebaratnam, T. Mueller, *J. Am. Chem. Soc.* **1991**, *113*, 636; d) B. M. Trost, Y. Shi, *J. Am. Chem. Soc.* **1993**, *115*, 9421; e) B. M. Trost, D. L. Romero, F. Rise, *J. Am. Chem. Soc.* **1994**, *116*, 4268; f) M. Nishida, N. Adachi, K. Onozuka, H. Matsumura, M. Mori, *J. Org. Chem.* **1998**, *63*, 9158; g) M. Mori, Y. Kozawa, M. Nishida, M. Kanamaru, K. Onozuka, M. Takimoto, *Org. Lett.* **2000**, *2*, 3245; h) R. J. K. Richard, G. Casy, *Ramberg–Bäcklund Reaction*, Wiley-VCH, Hoboken, **2003**; i) H.-Y. Jang, M. J. Krische, *J. Am. Chem. Soc.* **2004**, *126*, 7875; j) S. Kezuka, T. Okado, E. Niou, R. Takeuchi, *Org. Lett.* **2005**, *7*, 1711; k) S. Ikeda, N. Daimon, R. Sanuki, K. Odashima, *Chem. Eur. J.* **2006**, *12*, 1797; l) A. Hercouet, F. Berrée, C. H. Lin, L. Toupet, B. Carboni, *Org. Lett.* **2007**, *9*, 1717; m) P. Lu, S. Ma, *Org. Lett.* **2007**, *9*, 5319; n) P. Garcia, Y. Harrak, L. Diab, P. Cordier, C. Ollivier, V. Gandon, M. Malacria, L. Fensterbank, C. Aubert, *Org. Lett.* **2011**, *13*, 2952; o) A. T. Brusoe, E. J. Alexanian, *Angew. Chem. Int. Ed.*

2011, *50*, 6596; *Angew. Chem.* **2011**, *123*, 6726; p) A. T. Brusoe, R. V. Edwankar, E. J. Alexanian, *Org. Lett.* **2012**, *14*, 6096; q) S. Y. Yun, K.-P. Wang, M. Kim, D. Lee, *J. Am. Chem. Soc.* **2012**, *134*, 10783; r) X. Hong, M. C. Stevens, P. Liu, P. A. Wender, K. N. Houk, *J. Am. Chem. Soc.* **2014**, *136*, 17273; s) L. Zhou, B. Xu, J. Zhang, *Angew. Chem. Int. Ed.* **2015**, *54*, 9092; *Angew. Chem.* **2015**, *127*, 9220.

[5] a) P. A. Wender, D. N. Fournogerakis, M. S. Jeffreys, R. V. Quiroz, F. Inagaki, M. Pfaffenbach, *Nat. Chem.* **2014**, *6*, 448; b) P. A. Wender, M. S. Jeffreys, A. G. Raub, *J. Am. Chem. Soc.* **2015**, *137*, 9088.

[6] a) Y. Minami, Y. Shiraishi, K. Yamada, T. Hiyama, *J. Am. Chem. Soc.* **2012**, *134*, 6124; b) Y. Minami, K. Yamada, T. Hiyama, *Angew. Chem. Int. Ed.* **2013**, *52*, 10611; *Angew. Chem.* **2013**, *125*, 10805; c) Y. Minami, M. Kanda, T. Hiyama, *Chem. Lett.* **2014**, *43*, 181; d) Y. Minami, T. Anami, T. Hiyama, *Chem. Lett.* **2014**, *43*, 1791; e) Y. Minami, M. Kanda, M. Sakai, T. Hiyama, *Tetrahedron* **2015**, *71*, 4522; f) Y. Minami, Y. Shiraishi, T. Kodama, M. Kanda, K. Yamada, T. Anami, T. Hiyama, *Bull. Chem. Soc. Jpn.* **2015**, *88*, 1388; g) Y. Minami, T. Kodama, T. Hiyama, *Angew. Chem. Int. Ed.* **2015**, *54*, 11813; *Angew. Chem.* **2015**, *127*, 11979; h) Y. Minami, T. Hiyama, *Acc. Chem. Res.* **2016**, *49*, 67.

[7] For selected examples of reactions of alkynyl ethers, see: a) A. S. K. Hashmi, M. Rudolph, J. Huck, W. Frey, J. W. Bats, M. Hamzić, *Angew. Chem. Int. Ed.* **2009**, *48*, 5848; *Angew. Chem.* **2009**, *121*, 5962; b) Y. Miyauchi, M. Kobayashi, K. Tanaka, *Angew. Chem. Int. Ed.* **2011**, *50*, 10922; *Angew. Chem.* **2011**, *123*, 11114; c) W. Zhao, Z. Wang, J. Sun, *Angew. Chem. Int. Ed.* **2012**, *51*, 6209; *Angew. Chem.* **2012**, *124*, 6313; d) J. R. Cabrera-Pardo, D. I. Chai, S. Liu, M. Mrksich, S. A. Kozmin, *Nat. Chem.* **2013**, *5*, 423; e) J. R. Cabrera-Pardo, D. I. Chai, S. A. Kozmin, *Adv. Synth. Catal.* **2013**, *355*, 2495; f) Y. Bai, J. Yin, W. Kong, M. Mao, G. Zhu, *Chem. Commun.* **2013**, *49*, 7650; g) K. Graf, C. L. Rühl, M. Rudolph, F. Rominger, A. S. K. Hashmi, *Angew. Chem. Int. Ed.* **2013**, *52*, 12727; *Angew. Chem.* **2013**, *125*, 12960; h) W. Cui, J. Yin, R. Zheng, C. Cheng, Y. Bai, G. Zhu, *J. Org. Chem.* **2014**, *79*, 3487; i) J. S. Alford, H. M. L. Davies, *J. Am. Chem. Soc.* **2014**, *136*, 10266; j) J. Yin, Y. Bai, M. Mao, G. Zhu, *J. Org. Chem.* **2014**, *79*, 9179; k) M. Hari Babu, V. Dwivedi, R. Kant, M. S. Reddy, *Angew. Chem. Int. Ed.* **2015**, *54*, 3783; *Angew. Chem.* **2015**, *127*, 3854.

[8] For a review of C–C unsaturated-bond-directed C–H bond activation, see: a) P. Gandeepan, C.-H. Cheng, *Chem. Asian J.* **2015**, *10*, 824; for recent examples, see: b) T. Maekawa, Y. Segawa, K. Itami, *Chem. Sci.* **2013**, *4*, 2369; c) T. Iitsuka, K. Hirano, T. Satoh, M. Miura, *Chem. Eur. J.* **2014**, *20*, 385; d) J. Zhao, N. Asao, Y. Yamamoto, T. Jin, *J. Am. Chem. Soc.* **2014**, *136*, 9540; e) L. Li, Y. Chu, L. Gao, Z. Song, *Chem. Commun.* **2015**, *51*, 15546; f) D. Y. Li, H. J. Chen, P. N. Liu, *Angew. Chem. Int. Ed.* **2016**, *55*, 373; *Angew. Chem.* **2016**, *128*, 381.

[9] For examples of annulation reactions through the cleavage of two C–H bonds in one substrate, see: a) Y.-T. Wu, K.-H. Huang, C.-C. Shin, T.-C. Wu, *Chem. Eur. J.* **2008**, *14*, 6697; b) N. Umeda, K. Hirano, T. Satoh, N. Shibata, H. Sato, M. Miura, *J. Org. Chem.* **2011**, *76*, 13; c) M. Nishino, K. Hirano, T. Satoh, M. Miura, *J. Org. Chem.* **2011**, *76*, 6447; d) Y. Nakao, E. Morita, H. Idei, T. Hiyama, *J. Am. Chem. Soc.* **2011**, *133*, 3264; e) S. Reddy Chidipudi, I. Khan, H. W. Lam, *Angew. Chem. Int. Ed.* **2012**, *51*, 12115; *Angew. Chem.* **2012**, *124*, 12281; f) S. Peng, L. Wang, J. Wang, *Chem. Eur. J.* **2013**, *19*, 13322; g) J. D. Dooley, S. R. Chidipudi, H. W. Lam, *J. Am. Chem. Soc.* **2013**, *135*, 10829; h) M. V. Pham, N. Cramer, *Angew. Chem. Int. Ed.* **2014**, *53*, 3484; *Angew. Chem.* **2014**, *126*, 3552; i) S. P. Cooper, K. I. Booker-Milburn, *Angew. Chem. Int. Ed.* **2015**, *54*, 6496; *Angew. Chem.* **2015**, *127*, 6596; j) G. Naresh, R. Kant, T. Narender, *Org. Lett.* **2015**, *17*, 3446; k) Y. Yang, M.-B. Zhou, X.-H. Ouyang, R. Pi, R.-J. Song, J.-H. Li, *Angew. Chem. Int. Ed.* **2015**, *54*, 6595; *Angew. Chem.* **2015**, *127*, 6695; l) D. J. Burns, D. Best, M. D. Wieczysty, H. W. Lam, *Angew. Chem. Int. Ed.* **2015**, *54*, 9958; *Angew. Chem.* **2015**, *127*, 10096.

[10] M. Cheng, J. Yan, F. Hu, H. Chen, Y. Hu, *Chem. Sci.* **2013**, *4*, 526.

[11] For recent examples of C–H allylation with allylic substrates, see: a) T. Yao, K. Hirano, T. Satoh, M. Miura, *Angew. Chem. Int. Ed.* **2011**, *50*, 2990; *Angew. Chem.* **2011**, *123*, 3046; b) S. Fan, F. Chen, X. Zhang, *Angew. Chem. Int. Ed.* **2011**, *50*, 5918; *Angew. Chem.* **2011**, *123*, 6040; c) Y. Kuninobu, K. Ohta, K. Takai, *Chem. Commun.* **2011**, *47*, 10791; d) Y. Makida, H. Ohmiya, M. Sawamura, *Angew. Chem. Int. Ed.* **2012**, *51*, 4122; *Angew. Chem.* **2012**, *124*, 4198; e) H. Wang, N. Schröder, F. Glorius, *Angew. Chem. Int. Ed.* **2013**, *52*, 5386; *Angew. Chem.* **2013**, *125*, 5495; f) S. Asako, L. Ilies, E. Nakamura, *J. Am. Chem. Soc.* **2013**, *135*, 17755; g) C.-H. Ying, W.-L. Duan, *Org. Chem. Front.* **2014**, *1*, 546; h) M. Kim, S. Sharma, N. K. Mishra, S. Han, J. Park, M. Kim, Y. Shin, J. H. Kwak, S. H. Han, I. S. Kim, *Chem. Commun.* **2014**, *50*, 11303; i) A. Harada, Y. Makida, T. Sato, H. Ohmiya, M. Sawamura, *J. Am. Chem. Soc.* **2014**, *136*, 13932; j) J. Xuan, T.-T. Zeng, Z.-J. Feng, Q.-H. Deng, J.-R. Chen, L.-Q. Lu, W.-J. Xiao, H. Alper, *Angew. Chem. Int. Ed.* **2015**, *54*, 1625; *Angew. Chem.* **2015**, *127*, 1645; k) M. Moselage, N. Sauermann, J. Koeller, W. Liu, D. Gelman, L. Ackermann, *Synlett* **2015**, 1596; l) Y. Suzuki, B. Sun, K. Sakata, T. Yoshino, S. Matsunaga, M. Kanai, *Angew. Chem. Int. Ed.* **2015**, *54*, 9944; *Angew. Chem.* **2015**, *127*, 10082; m) G. Cera, T. Haven, L. Ackermann, *Angew. Chem. Int. Ed.* **2016**, *55*, 1484; *Angew. Chem.* **2016**, *128*, 1506; n) W. Xie, S. Chang, *Angew. Chem. Int. Ed.* **2016**, *55*, 1876; *Angew. Chem.* **2016**, *128*, 1908.

[12] Other cinnamyl substrates (e.g., cinnamyl acetate, phenoxycarbonyloxy, and diethylphosphonate), ligands (e.g., P*t*Bu_3, $PPhCy_2$, PPh_2Cy, PBu_3, and $Cy_2PCH_2CH_2PCy_2$), and salts (e.g., K_2CO_3, Na_2CO_3, K_3PO_4, and no base) gave **3a** in lower yields or not at all. Notably, when cesium pivalate was added to the reaction with cinnamyl bromide under the catalysis of [Pd(dba)$_2$]/PCy_3/Cs_2CO_3, **3a** was formed in 56% yield.

[13] For examples, see: a) S. Trofimenko, B. C. Auman, *Macromolecules* **1994**, *27*, 1136; b) T. Matsuda, A. Okuda, Y. Watanabe, T. Miura, H. Ozawa, A. Tosaka, K. Yamazaki, Y. Yamaguchi, S. Kurobuchi, M. Koura, K. Shibuya, *Bioorg. Med. Chem. Lett.* **2015**, *25*, 1274.

[14] T. Yamamoto, M. Akimoto, O. Saito, A. Yamamoto, *Organometallics* **1986**, *5*, 1559.

[15] a) B. M. Trost, *Chem. Eur. J.* **1998**, *4*, 2405; b) R. Shen, T. Chen, Y. Zhao, R. Qiu, Y. Zhou, S. Yin, X. Wang, M. Goto, L.-B. Han, *J. Am. Chem. Soc.* **2011**, *133*, 17037.

[16] The treatment of **7a** in the presence of Pd(OAc)$_2$/PCy_3 induced isomerization to **7′a** at 90 °C through a hydrogen shift, whereas in the absence of the palladium catalyst, **7a** remained intact.

[17] A mechanism of hydrovinylation in the presence of Pd(OAc)$_2$ and PCy_3 is suggested to be similar to the hydroarylation reaction in Ref. [6d].

[18] Similar reaction conditions for hydrovinylation can be found in Refs. [4c–e,k].

[19] The structure of **11** was determined by NMR analysis in comparison with previously reported compounds (Ref. [6c]).

[20] Similar dehydrogenation was reported previously: G. W. Fischer, W. Schroth, *Tetrahedron* **1976**, *32*, 2225.

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