

## Directed Intermolecular [4 + 2] Cycloaddition of Unactivated 1,3-Diene Substrates with High Regio- and Stereoselectivities

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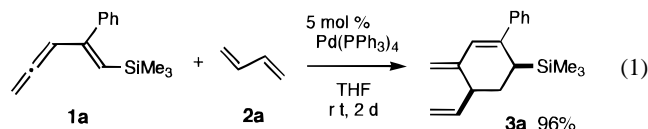
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The [4 + 2], *i.e.*, Diels–Alder type cycloaddition reaction is widely used to construct six-membered carbon skeletons.<sup>1</sup> Whereas numerous modifications of reaction conditions to promote the [4 + 2] cycloaddition reaction are known, they are mostly confined to the combination of electronically dissimilar unsaturated substrates and typically use an electron-deficient dienophile. More forcing conditions have been required for the combination of 1,3-dienes and dienophiles lacking electron-withdrawing or -releasing substituents, which limits the range of their synthetic utilization. Transition metals are potential driving gear for unactivated substrates and have found application to certain inter-<sup>2</sup> and intramolecular<sup>3</sup> reactions. For example, Mandai and Tsuji reported a palladium-catalyzed intramolecular [4 + 2] cycloaddition of an *in-situ*-formed alkenyl-substituted vinylallene.<sup>3c</sup> In this paper, we report the palladium-catalyzed intermolecular *directed* [4 + 2] cycloaddition reaction between a vinylallene<sup>4–8</sup> and an ordinary 1,3-

diene, wherein high regio- and stereoselectivities are achieved under mild conditions without the aid of electron-withdrawing or -releasing substituents.

A vinylallene (**1a**) was treated with 1,3-butadiene (**2a**, 10 equiv) in the presence of 5 mol % of Pd(PPh<sub>3</sub>)<sub>4</sub> in THF at room temperature for 2 days. A [4 + 2] cycloaddition reaction took place to afford a cyclohexene derivative (**3a**) which was isolated in 96% yield by chromatography (eq 1).<sup>9</sup> The vinylallene

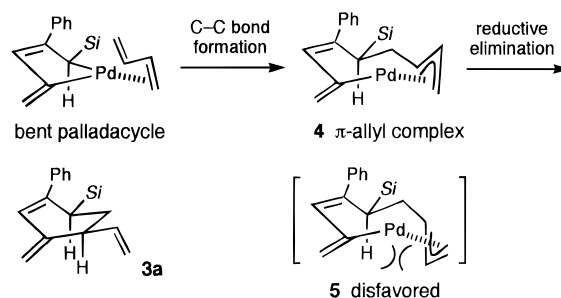


contributed a four-carbon unit to the six-membered ring, with 1,3-butadiene acting as a dienophile to provide a two-carbon complement in a regioselective manner. Only one diastereomer was observed by <sup>1</sup>H and <sup>13</sup>C NMR spectra (300 and 75 MHz, respectively), and the *cis* stereochemistry was assigned on the basis of extensive NOE experiments.

The selective production of **3a** can be explained by assuming the following mechanism (Scheme 1). A five-membered bent palladacycle having the trimethylsilyl group in a pseudoequatorial orientation is initially formed by way of  $\eta^4$ -coordination of **1a** to palladium(0), which is reasonably postulated on the basis of the superior binding aptitude of vinylallenes as exemplified previously by reactions with rhodium(I)<sup>10</sup> and iron(0)<sup>11</sup> complexes. Then, 1,3-butadiene in an *s-trans* form coordinates to palladium. The concurrent binding of **1a** and 1,3-butadiene leads to a directed carbon–carbon bond formation, thereby giving a  $\pi$ -allyl complex (**4**).<sup>12</sup> The observed regio- and stereochemical outcome can be regarded as a consequence of the selective formation of **4**.<sup>13</sup> A pathway leading to a  $\pi$ -allyl complex of the alternative stereochemistry (**5**) is disfavored because of a repulsive steric interaction between the pseudoaxial vinyl group and the pseudoaxial hydrogen atom. Finally, reductive elimination accomplishes [4 + 2] cycloaddition to give rise to **3a**.

Next, an analogous reaction using a vinylallene (**1b**), the geometric isomer of **1a**, was carried out in order to study the relationship between the vinylallene geometries and the cycloadduct stereostructures. The regioselective [4 + 2] cycloaddition also occurred to furnish a cyclohexene derivative (**3b**) in

### Scheme 1



(1) For reviews, see: (a) Lautens, M.; Klute, W.; Tam, W. *Chem. Rev.* **1996**, *96*, 49–92. (b) Oppolzer, W. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Paquette, L. A., Eds.; Pergamon: Oxford, 1991; Vol. 5, pp 315–399. (c) Carruthers, W. *Cycloaddition Reactions in Organic Synthesis*; Pergamon: Oxford, 1990; pp 1–208.

(2) (a) Carbonaro, A.; Greco, A.; Dall'Asta, G. *J. Org. Chem.* **1968**, *33*, 3948–3950. (b) Kohnle, J. F.; Slauch, L. H.; Nakamaye, K. L. *J. Am. Chem. Soc.* **1969**, *91*, 5904–5905. (c) Buchholz, H.; Heimbach, P.; Hey, H.-J.; Selbeck, H.; Wiese, W. *Coord. Chem. Rev.* **1972**, *8*, 129–138. (d) Garratt, P. J.; Wyatt, M. *J. Chem. Soc., Chem. Commun.* **1974**, 251. (e) Siegel, H.; Hopf, H.; Germer, A.; Binger, P. *Chem. Ber.* **1978**, *111*, 3112–3118. (f) tom Dieke, H.; Diercks, R. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 778–779. (g) Matsuda, I.; Shibata, M.; Sato, S.; Izumi, Y. *Tetrahedron Lett.* **1987**, *28*, 3361–3362. (h) Saito, S.; Salter, M. M.; Gevorgyan, V.; Tsuboya, N.; Tando, K.; Yamamoto, Y. *J. Am. Chem. Soc.* **1996**, *118*, 3970–3971.

(3) (a) Wender, P. A.; Jenkins, T. E. *J. Am. Chem. Soc.* **1989**, *111*, 6432–6434. (b) Jolly, R. S.; Luedtke, G.; Sheehan, D.; Livinghouse, T. *J. Am. Chem. Soc.* **1990**, *112*, 4965–4966. (c) Mandai, T.; Suzuki, S.; Ikawa, A.; Murakami, T.; Kawada, M.; Tsuji, J. *Tetrahedron Lett.* **1991**, *32*, 7687–7688. (d) McKinsty, L.; Livinghouse, T. *Tetrahedron* **1994**, *50*, 6145–6154. (e) Wender, P. A.; Jenkins, T. E.; Suzuki, S. *J. Am. Chem. Soc.* **1995**, *117*, 1843–1844.

(4) Thermal Diels–Alder reactions of vinylallenes have been reported in intermolecular cases using activated dienophiles such as  $\alpha,\beta$ -unsaturated carbonyl compounds<sup>5</sup> and in intramolecular cases.<sup>6</sup>

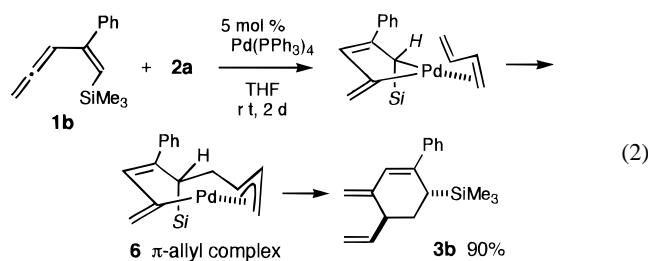
(5) (a) Jones, E. R. H.; Lee, H. H.; Whiting, M. C. *J. Chem. Soc.* **1960**, 341–346. (b) Bertrand, M.; Grimaldi, J.; Waegell, B. *Bull. Soc. Chim. Fr.* **1971**, 962–973. (c) Bross, H.; Schneider, R.; Hopf, H. *Tetrahedron Lett.* **1979**, 2129–2132. (d) Schneider, R.; Siegel, H.; Hopf, H. *Liebigs Ann. Chem.* **1981**, 1812–1825. (e) Yoshida, K.; Grieco, P. A. *Chem. Lett.* **1985**, 155–158. (f) Reich, H. J.; Eisenhart, E. K.; Whipple, W. L.; Kelly, M. J. *J. Am. Chem. Soc.* **1988**, *110*, 6432–6442. (g) Wang, K. K.; Andemichael, Y. W.; Dhumrongvaraporn, S. *Tetrahedron Lett.* **1989**, *30*, 1311–1314. (h) Mondeshka, D.; Tancheva, C.; Angelov, C. *Chem. Ber.* **1990**, *123*, 1381–1386. (i) Koop, U.; Handke, G.; Krause, N. *Liebigs Ann.* **1996**, 1487–1499 and references cited therein.

(6) (a) Deusch, E. A.; Snider, B. B. *Tetrahedron Lett.* **1983**, *24*, 3701–3704. (b) Keck, G. E.; Kachensky, D. F. *J. Org. Chem.* **1986**, *51*, 2487–2493. (c) Reich, H. J.; Eisenhart, E. K.; Olson, R. E.; Kelly, M. J. *J. Am. Chem. Soc.* **1986**, *108*, 7791–7800. (d) Gibbs, R. A.; Bartels, K.; Lee, R. W. K.; Okamura, W. H. *J. Am. Chem. Soc.* **1989**, *111*, 3717–3725. (e) Schlindwein, H.-J.; Himbert, G. *Chem. Ber.* **1989**, *122*, 2331–2339. (f) Okamura, W. H.; Curtin, M. L. *Synlett* **1990**, 1–9. (g) Dulcere, J. P.; Agati, V.; Faure, R. *J. Chem. Soc., Chem. Commun.* **1993**, 270–271 and references cited therein.

(7) Hopf and Binger reported the palladium-catalyzed homodimerization of vinylallene giving a [4 + 2] adduct.<sup>2c</sup>

(8) For thermal Diels–Alder reactions wherein allene is used as a dienophile, see: (a) Fink, M.; Gaier, H.; Gerlach, H. *Helv. Chim. Acta* **1982**, *65*, 2563–2569. (b) Hayakawa, K.; Nishiyama, H.; Kanematsu, K. *J. Org. Chem.* **1985**, *50*, 512–517. (c) Cauwberghs, S. G.; De Clercq, P. *J. Tetrahedron Lett.* **1988**, *29*, 6501–6504. (d) Block, E.; Putman, D. *J. Am. Chem. Soc.* **1990**, *112*, 4072–4074. (e) Padwa, A.; Bullock, W. H.; Norman, B. H.; Perumattam, J. *J. Org. Chem.* **1991**, *56*, 4252–4259. (f) Metz, P.; Betels, S.; Fröhlich, R. *J. Am. Chem. Soc.* **1993**, *115*, 12595–12596. (g) Ikeda, I.; Honda, K.; Osawa, E.; Shiro, M.; Aso, M.; Kanematsu, K. *J. Org. Chem.* **1996**, *61*, 2031–2037 and references cited therein.

90% isolated yield (eq 2). Of note was that the cycloadduct



was again diastereomerically pure within the limits of NMR detection of the trimethylsilyl signal (>99:1), having a *trans* stereostructure. Similarly to the case with **1a**, a bent palladacycle having the silyl group in a pseudoaxial orientation would be initially produced from **1b** on the analogy of the complexation to rhodium(0).<sup>10a</sup> Preferred formation of a  $\pi$ -allyl complex (**6**) from the axially oriented complex accounts for the *trans* selectivity. The presumed 1,3-pseudodiaxial interaction could be more important for **6** than for **4**. We have recently found that a  $\eta^4$ -vinylallene–rhodium complex undergoes ring flipping isomerization through a planar  $\sigma^2$ -bonded rhodacyclopentene.<sup>10a,b</sup> The excellent stereospecificity, however, observed with the two geometric isomers **1a** and **1b** indicates that each bent palladacyclopentene intermediate directly coupled with 1,3-diene in preference to isomerization to the other bent form through a planar palladacycle.

Listed in Table 1 are other examples of the palladium-catalyzed [4 + 2] cycloaddition reactions. Regio- and stereochemical features are quite general with vinylallenes of various substitution patterns, which include a vinylallene equipped with an ester group (**1g**) as well as several unactivated hydrocarbon vinylallenes. From **1g** with an unsymmetrically substituted allenyl group, one stereoisomer (**3g**) with regard to the exocyclic double bond was obtained. Face-selective binding to the metal from the less-hindered side of the vinylallene in an *s-cis* form accounts for this stereoselectivity.<sup>10a,11a,14</sup> For the 2-substituted 1,3-dienes **2b** and **2c**, incorporation of the more substituted carbon–carbon double bond was favored to afford **3h**<sup>15</sup> and **3i** as the exclusive or predominant products. This trend agrees with binding of a substituted 1,3-diene at the less-steric-demanding site and subsequent coupling at the other site.<sup>13</sup>

(9) A cationic rhodium(I) complex, which efficiently catalyzed the [4 + 1] cycloaddition of vinylallenes with carbon monoxide,<sup>10a</sup> failed to promote the [4 + 2] cycloaddition.

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(11) (a) Sigman, M. S.; Kerr, C. E.; Eaton, B. E. *Organometallics* **1995**, *14*, 269–273. (b) Trifonov, L. S.; Orhovats, A. S.; Trewo, R.; Heimgartner, H. *Helv. Chim. Acta* **1988**, *71*, 551–561. (c) Arecas, P.; Jeganathan, S.; Okamura, W. H. *Anal. Quim.* **1993**, *89*, 101–104.

(12) Palladium-catalyzed reactions under comparable conditions using ordinary alkenes or alkynes instead of 1,3-dienes, wherein  $\pi$ -allyl intermediates could not be expected, produced only a trace amount of the corresponding [4 + 2] cycloadducts.

(13) Complexes of the similar geometry have been assumed in dimerization of 1,3-butadiene catalyzed by Ni(0)<sup>2c</sup> and Pt(0): (a) Brown, J. M.; Golding, B. T.; Smith, M. J. *J. Chem. Soc., Chem. Commun.* **1971**, 1240–1241. (b) Barker, G. K.; Green, M.; Howard, J. A. K.; Spencer, J. L.; Stone, F. G. A. *J. Am. Chem. Soc.* **1976**, *98*, 3373–3374.

(14) Similar facial selectivities have been observed in [4 + 1] cycloaddition reactions: (a) Sigman, M. S.; Eaton, B. E. *J. Am. Chem. Soc.* **1996**, *118*, 11783–11788. (b) Mandai, T.; Tsuji, J.; Tsujiguchi, Y. *J. Am. Chem. Soc.* **1993**, *115*, 5865–5866. (c) Darcel, C.; Bruneau, C.; Dixneuf, P. H. *Synlett* **1996**, 218–220.

**Table 1.** Palladium-catalyzed Directed [4+2] Cycloaddition of Vinylallenes (**1**) with 1,3-Dienes (**2**)<sup>a</sup>

vinylallene ( <b>1</b> )	1,3-diene ( <b>2</b> )	product ( <b>3</b> )	isolated yield, % stereochemistry
			93
			—
			98
			92 cis <sup>b,c</sup>
			92 cis <sup>c,d</sup>
			92 cis <sup>c,d</sup>
			87 cis <sup>b,c</sup>
			85
			85
		<b>3i</b> : <b>3j</b> = 71 : 29	97

<sup>a</sup> The reaction was carried out using 5 mol % of Pd(PPh<sub>3</sub>)<sub>4</sub> in THF at room temperature. <sup>b</sup> Determined by <sup>1</sup>H NMR NOE studies. <sup>c</sup> The other diastereomer was not detected by <sup>1</sup>H and <sup>13</sup>C NMR (300 and 75 MHz, respectively). <sup>d</sup> The *cis* stereochemistry was assigned by analogy with other examples.

In summary, intermolecular directed [4 + 2] cycloaddition of vinylallenes with 1,3-dienes is successfully mediated by palladium(0). It should be noted that high regio- and stereoselectivities are generally manifested with a variety of substrates irrespective of the presence of heteroatom functionalities. This study would augment the existing repertoire of synthetic tools for construction of six-membered rings from poor reactants.

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**Supporting Information Available:** Experimental details and characterization for **3** (4 pages). See any current masthead page for ordering and Internet access instructions.

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(15) The uncatalyzed thermal reaction of **1h** and **2b** at 110 °C produced ca. 9% of **3h** in 24 h together with a significant amount of intractable materials derived from **1h** and dimers of **2b**.