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# Ambiphilic Vinylcarbenoid Reactivity of (α-(Tributylstannyl)-π-allyl)palladium(II) Species

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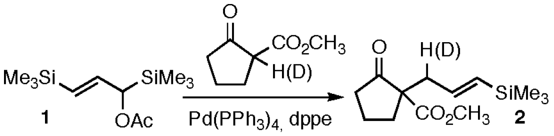
*Summary: The ambiphilic vinylcarbenoid reactivity of (α-(tributylstannyl)-π-allyl)palladium(II) species is demonstrated by the reaction of acetoxystannanes with $Pd(dba)_2$, which promotes electrophilic metal−carbene reactions such as dimerization and cyclopropanation of strained alkenes. On the other hand, $Pd(PPh_3)_4$ and dppe revealed the nucleophilic nature of the dimetallic intermediates through sequential reactions of the carbon−metal bonds with dimethyl malonate.*

(π-Allyl)palladium species are versatile synthetic intermediates that have been abundantly exploited for forming carbon−carbon bonds.[1] The electrophilic nature of (π-allyl)palladium intermediates allows for the addition of various carbon nucleophiles. Contrastingly, bis(π-allyl)palladium compounds undergo nucleophilic addition to aldehydes and imines.[2]

Trost reported the atypical reactivity of α-silylated (π-allyl)-palladium species.[3] In undisclosed yield, allylic substitution of acetoxysilane **1** with 2-(methoxycarbonyl)cyclopentanone provided the monodesilylated compound **2** (eq 1). Labeling studies showed that deuterodesilylation (protodesilylation) and alkylation occurred specifically at the same carbon in the (π-allyl)-palladium intermediate. The authors postulated that α-elimination of acetoxytrimethylsilane from the (π-allyl)palladium species led to a Pd-complexed vinylcarbene. The failure of the transient palladium species to undergo reactions typical of carbenes, as well as labeling studies, suggested a nucleophilic carbene behavior.



(eq 1)

Our group has provided evidence for the carbenoid reactivity of sp$^3$-*gem*-dimetallic iodopalladio(II)−trialkylstannylalkane complexes.[4,5] These electrophilic intermediates dimerize and cyclopropanate strained olefins. Palladium carbenoids have been postulated in a number of carbon−carbon bond forming events.[6] However, few studies have aimed at defining the elusive reactivity of these species. The discrepancy between our work and Trost's observations was an incentive to revisit and expand his initial report to pinpoint the nature of Pd-based carbenoids derived from *gem*-dimetallics. Herein, the ambiphilic vinylcarbenoid reactivity of (α-(tributylstannyl)-π-allyl)palladium(II) species is described. Electrophilic metal−carbene behavior is confirmed by dimerization and cyclopropanation reactions, while a nucleophilic nature is supported by the basicity of the species in the presence of Brønsted acids.

**Scheme 1. Reaction of 1-(Tributylstannyl)alkenyl Acetates with Malonate**

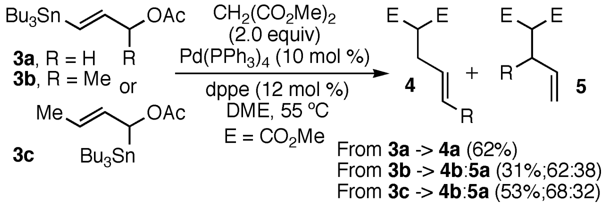
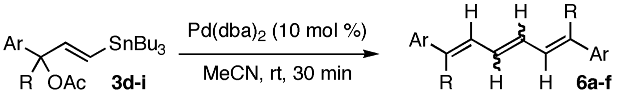


**Table 1. Pd-Catalyzed Allyl Acetate Dimerization**



| entry | Ar | R | yield[a] (%) |
|---|---|---|---|
| 1 | Ph (**3d**) | H | 64 (**6a**) |
| 2 | 3,5-MeO$C_6H_3$ (**3e**) | H | 78 (**6b**) |
| 3 | 3,5-MeO$C_6H_3$ (**3f**) | Me | 92 (**6c**) |
| 4 | 4-F$C_6H_4$ (**3g**) | H | 22 (**6d**) |
| 5 | 4-Me$C_6H_4$ (**3h**) | H | 26 (**6e**) |
| 6 | 2-(allyl)-3-MeO$C_6H_3$ (**3i**) | H | 66 (**6f**)[b] |

[a] Isolated yield of double-bond isomers. [b] Reaction was run at 60 °C.

Propenyl acetate **3a** was initially studied using Trost's conditions. Upon treating **3a** at 55 °C in DME with 2 equiv of dimethyl malonate, $Pd(PPh_3)_4$ (10 mol %), and 1,2-(diphenylphosphino)ethane (dppe; 12 mol %), the malonate adduct **4a** was obtained in 62% yield (Scheme 1). Under the same conditions, stannane **3b** gave a 62:38 ratio of regioisomeric products **4b**:**5a**, in 31% yield.[7] (*E*)-1-(Tributylstannyl)-2-butenyl

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(1) Trost, B. M. *J. Org. Chem.* **2004**, *69*, 5813−5837 and references therein.

(2) Yamamoto, Y.; Nakamura, I. *Top. Organomet. Chem.* **2005**, *14*, 211−239.

(3) Trost, B. M.; Self, C. R. *J. Am. Chem. Soc.* **1983**, *105*, 5942−5944.

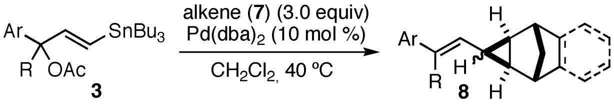
(4) Fillion, E.; Taylor, N. J. *J. Am. Chem. Soc.* **2003**, *125*, 12700−12701.

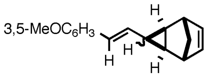
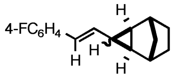
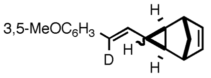
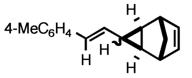
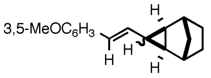
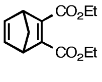
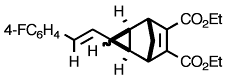
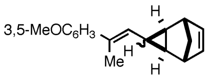
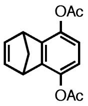
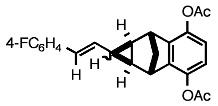
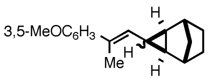
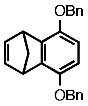
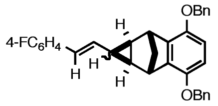
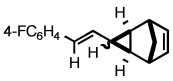
(5) (a) Farina, V.; Hossain, M. A. *Tetrahedron Lett.* **1996**, *37*, 6997−7000. (b) Busacca, C. A.; Swestock, J.; Johnson, R. E.; Bailey, T. R.; Musza, L.; Rodger, C. A. *J. Org. Chem.* **1994**, *59*, 7553−7556.

(6) (a) Gómez-Gallego, M.; Mancheño, M. J.; Sierra, M. A. *Acc. Chem. Res.* **2005**, *38*, 44−53. (b) Bigeault, J.; Giordano, L.; Buono, G. *Angew. Chem., Int. Ed.* **2005**, *44*, 4753−4757. (c) Ohno, H.; Takeoka, Y.; Miyamura, K.; Kadoh, Y.; Tanaka, T. *Org. Lett.* **2003**, *5*, 4763−4766. (d) Nakamura, I.; Bajracharya, G. B.; Mizushima, Y.; Yamamoto, Y. *Angew. Chem., Int. Ed.* **2002**, *41*, 4328−4331. (e) Schweizer, S.; Song, Z.-Z.; Meyer, F. E.; Parsons, P. J.; de Meijere, A. *Angew. Chem., Int. Ed.* **1999**, *38*, 1452−1454. (f) Monterio, N.; Goré, J.; van Hemelryck, B.; Balme, G. *Synlett* **1994**, 447−449. (g) Ogoshi, S.; Morimoto, T.; Nishio, K.; Ohe, K.; Murai, S. *J. Org. Chem.* **1993**, *58*, 9−10. (h) Tomilov, Yu V.; Dokichev, V. A.; Dzhemilev, U. M.; Nefedov, O. M. *Russ. Chem. Rev.* **1993**, *62*, 799−838. (i) Hoye, T. R.; Dinsmore, C. J.; Johnson, D. S.; Korkowski, P. F. *J. Org. Chem.* **1990**, *55*, 4518−4520. (j) Mitsudo, T.; Kadokura, M.; Watanabe, Y. *Tetrahedron Lett.* **1985**, *26*, 3697−3698. (k) Matsumoto, M.; Watanabe, N.; Kobayashi, H. *Heterocycles* **1987**, *26*, 1479−1482. (l) Chakraborti, A. K.; Ray, J. K.; Kundu, K. K.; Chakrabarty, S.; Mukherjee, D.; Ghatak, U. R. *J. Chem. Soc., Perkin Trans. 1* **1984**, 261−273. (m) Anciaux, A. J.; Hubert, A. J.; Noels, A. F.; Petiniot, N.; Teyssié, P. *J. Org. Chem.* **1980**, *45*, 695−702.

10.1021/om0609416 CCC: $37.00

**Table 2. Pd-Catalyzed Cyclopropanation**



| entry | 3 | 7 | 8 (dr)[a] | yield[b] (%) | entry | 3 | 7 | 8 (dr)[a] | yield[b] (%) |
|---|---|---|---|---|---|---|---|---|---|
| 1 | **3e** | **7a** | <br>**8a** (71:29) | 55 | 7 | **3g** | **7b** | <br>**8f** (80:20) | 85 |
| 2 | $d_1$-**3e** | **7a** | <br>$d_1$-**8a** (79:21) | 69 | 8 | **3h** | **7a** | <br>**8g** (66:34) | 59 |
| 3 | **3e** | **7b** | <br>**8b** (94:6) | 48[c] | 9 | **3g** | <br>**7c** | <br>**8h** (90:10) | 21 |
| 4 | **3f** | **7a** | <br>**8c** (73:27) | 58 | 10 | **3g** | <br>**7d** | <br>**8i** (91:9) | 56 |
| 5 | **3f** | **7b** | <br>**8d** (68:32) | 67 | 11 | **3g** | <br>**7e** | <br>**8j** (85:15) | 51 |
| 6 | **3g** | **7a** | <br>**8e** (75:25) | 79 | | | | | |

[a] Determined by $^1$H NMR of the crude mixture. [b] Combined yield of diastereomers. [c] In MeCN at 55 °C, **8b** was formed in 91% yield and 84:16 ratio.

acetate (**3c**) furnished a comparable mixture of allylated malonates **4b** and **5a** (68:32) in a 53% combined yield. Modest yields were due to competing dimerization to 2,4,6-octatrienes, as evidenced by GCMS of the crude mixture.

Palladium-catalyzed dimerization using substrates **3d**–**i** was then investigated. Under Trost's malonate trapping conditions, dimerization was sluggish.[8] Gratifyingly, dimerization to linear trienes **6** proceeded at room temperature for a variety of substrates with Pd(dba)$_2$ (10 mol %) in MeCN (Table 1).[9] The yield was augmented by increasing substitution on the propenyl acetate moiety (entry 2 versus 3). Electronic factors appeared to influence the dimerization efficiency (entries 4 and 5). Initial attempts to intercept the carbenoid via intramolecular cyclopropanation failed. Alkenyl-tethered **3i** reacted solely by dimerization, and no cyclopropane was detected (entry 6). Nonetheless, dimerization was indicative of an electrophilic carbenoid character, which was further probed by intermolecular reactions with strained alkenes.

In MeCN at 40 °C, using stannane **3e** and 10 equiv of norbornadiene (**7a**), a 87:13 mixture of diastereomeric cyclopropanes **8a** was obtained, albeit in a low 27% yield.[10,11] *anti*- and *syn*-Cyclopropanes **8a** were formed, *anti* being the major species, as cyclopropanation occurred solely on the *exo* face of the bicyclic diene.[12] The yield was mainly affected by competing dimerization, which was eliminated by appropriate solvent selection. Tricycle **8a** was obtained in 44% yield (79:21) in (CH$_2$Cl)$_2$ and in 21% yield (56:44) in PhMe. A 71:29 mixture of **8a** was isolated in 55% yield using CH$_2$Cl$_2$ and 3.0 equiv of **7a**without detectable dimer **6b** (Table 2, entry 1).[13]

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(7) Using **3b** in DME, no trapping was observed at room temperature, and at 40 °C, the malonate adducts **4b** and **5a** (61:39) were isolated in 6% yield.

(8) From **3e**, **6b** was formed in 53% yield after 14 h.

(9) From **3b**, malonate trapping using Pd(dba)$_2$ was inefficient, leading solely to dimerization as determined by GCMS.

(10) No dimerization or cyclopropanation took place in the absence of a palladium catalyst. Starting material was quantitatively recovered.

(11) No cyclopropanation was observed under Trost's conditions.

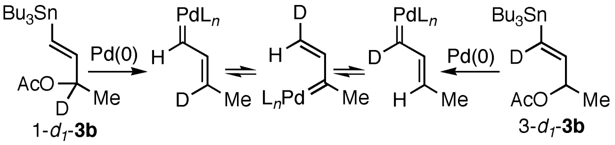
(12) Determined by NOE experiments (see the Supporting Information).

(13) Slow addition of the substrate did not improve the yields.

The scope of the vinylcyclopropanation reaction was then delineated.[14] Using **7a** and norbornene (**7b**) as olefins, the diastereoselectivity ranged from 66:34 to 94:6 (entries 1−8) and isolated yields from 48 to 91%. Labeled *d*-**3e** did not undergo scrambling, providing exclusively cyclopropanes *d*-**8a** (entry 2). Diester **7c** gave a limited 21% yield (entry 9). The aryl ester **7d** and ether **7e** furnished cyclopropanes **8i**,**j** in 56% and 51% yields, respectively (entries 10 and 11), with good diastereoselectivities.[15]

Insights into the nature of the reactive species were gathered through reaction of deuterium-labeled 1-*d*-**3b** and 3-*d*-**3b** with dimethyl malonate. Carbenoid insertion into the malonate C−H bond, and an ensuing [1,3]-carbene shift, should lead to common deuterated products (Scheme 2).[16]

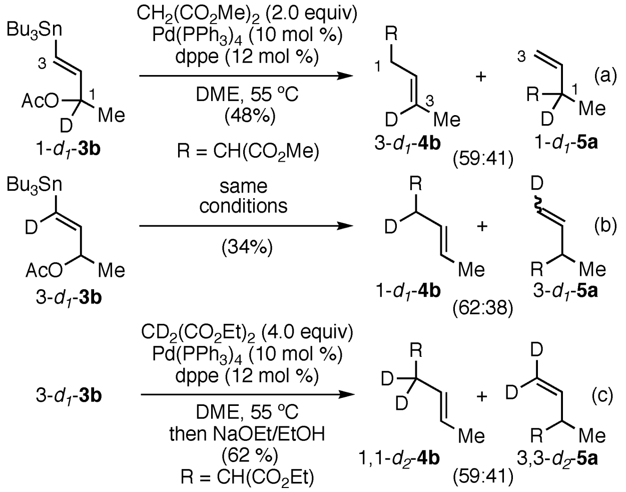
**Scheme 2. [1,3]-Pd−Carbene Shift**



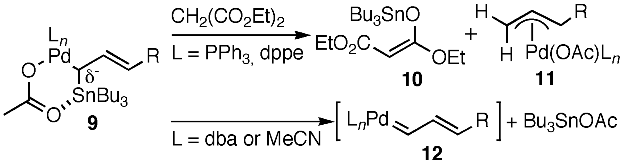
From deuterium-labeled 1-*d*-**3b** and 3-*d*-**3b**, distinct mixtures of linear to branched composition were isolated (Scheme 3a,b),[17] and the carbenoid insertion mechanism was therefore ruled out.

A sequential protodestannylation/($\pi$-allyl)palladium interception mechanism was established by reacting $d_2$-diethyl malonate (98% atom % D) with 3-*d*-**3b**. The *gem*-dideuterio compounds 1,1-$d_2$-**4b** (86% D incorporation) and 3,3-$d_2$-**5a** (89% D incorporation) were formed exclusively in a combined 62% yield (Scheme 3c). Protodestannylation is conceivably facilitated by complexation with the acetate group in *gem*-dimetallic **9** (Scheme 4). The resulting ($\pi$-allyl)palladium(II) complex **11** then undergoes addition with the stannylketene acetal **10**. The dimetallic Brønsted base character is enhanced by electron-rich ligands (PPh$_3$/dppe), and the electrophilic carbenoid reactivity is promoted by Pd(dba)$_2$. In the absence of acidic protons, dimetallic **9** or Pd carbene **12**, formed by elimination of Bu$_3$SnOAc, display electrophilic metal−carbenoid character.

**Scheme 3. Reactions with Deuterium-Labeled Substrates**



**Scheme 4. Proposed Reaction Pathways for Dimetallic 9**



In summary, the ambiphilic vinylcarbenoid nature of ($\alpha$-(tributylstannyl)-$\pi$-allyl)palladium(II) species was established. Mechanistic studies support a *gem*-dimetallic carbenoid whose carbon−metal bonds are sequentially functionalized or further collapse to a Pd carbene. Further efforts to expand the synthetic scope of these species are underway.

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**Supporting Information Available:** Text and tables giving experimental procedures, characterization data, and NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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[14] Recent vinylcyclopropanation methods: (a) Tseng, N.-W.; Mancuso, J.; Lautens, M. *J. Am. Chem. Soc.* **2006**, *128*, 5338−5339. (b) Tenaglia, A.; Marc, S. *J. Org. Chem.* **2006**, *71*, 3569−3575. (c) Miura, T.; Sasaki, T.; Harumashi, T.; Murakami, M. *J. Am. Chem. Soc.* **2006**, *128*, 2516−2517. (d) Kim, B. G.; Snapper, M. L. *J. Am. Chem. Soc.* **2006**, *128*, 52−53. (e) Johansson, M. J.; Gorin, D. J.; Staben, S. T.; Toste, F. D. *J. Am. Chem. Soc.* **2005**, *127*, 18002−18003.

[15] Repeated chromatography was required to separate the starting alkene from the [2 + 1] cycloadduct, thus limiting the isolated yield of pure product.

[16] [1,3]-Ru−carbene shift: (a) Ohe, K.; Fujita, M.; Matsumoto, H.; Tai, Y.; Miki, K. *J. Am. Chem. Soc.* **2006**, *128*, 9270−9271. (b) Kim, M.; Miller, R. L.; Lee, D. *J. Am. Chem. Soc.* **2005**, *127*, 12818−12819. (c) Kamikawa, K.; Tachibana, A.; Shimizu, Y.; Uchida, K.; Furusho, M.; Uemura, M. *Org. Lett.* **2004**, *6*, 4307−4310. [1,3]-Re−carbene shift: (d) Casey, C. P.; Kraft, S.; Powell, D. R. *Organometallics*, **2001**, *20*, 2651−2653.

[17] All products had >98% deuterium incorporation and were one stereoisomer, except for 3-*d*-**5a**, isolated as a 1:1 (*E*:*Z*) mixture.