

Palladium(0)-Catalyzed Cope Rearrangement of Acyclic 1,5-Dienes. Bis(π -allyl)palladium(II) Intermediate

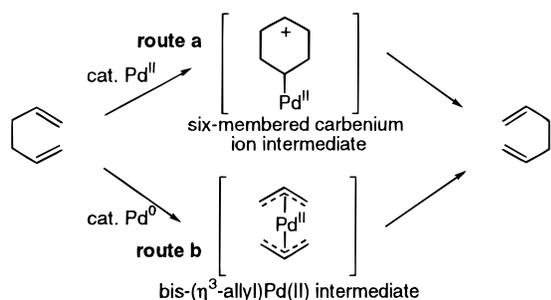
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Since the earlier examples of Pd(II)-mediated Cope rearrangement studied by Jonassen¹ and Heimbach,² and the first Pd(II)-catalyzed version developed by Overman,³ the transition metal catalyzed [3,3]-sigmatropic rearrangement becomes one of the important transformations in modern organic synthesis.⁴ Detailed mechanistic studies on the Pd(II)-catalyzed rearrangements revealed that the reaction proceeds via a palladium-bound six-membered carbenium ion intermediate (route a in Scheme 1).^{3,5}

Scheme 1. Palladium-Catalyzed Cope Rearrangement



As an alternative mechanism, oxidative addition of the allylic C–C bond to form bis(η^3 -allyl)Pd^{IV}Cl₂ was proposed.⁶ This proposal is very interesting from the viewpoint of the present day importance for C–C bond activation,⁷ since the proposed process involves the Pd(II) insertion into a nonstrained and nonfunctionalized C–C bond.^{8,9} However, the proposed mechanism was not operative in the Pd(II)-promoted rearrangement due to the lack of products of [1,3]-rearrangement and to the strict chair topography of the PdCl₂-catalyzed rearrangement of (3*R*,5*E*)-

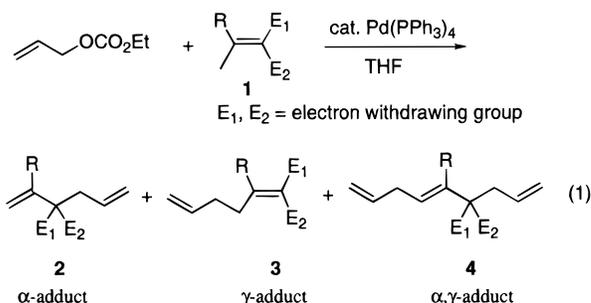
Table 1. Palladium-Catalyzed Allylation of Activated Olefins **1** with Allyl Ethylcarbonate^a

entry	1	temp (°C)	yield (%) ^b	ratio of adducts (2:3:4)
1 ^c	1a	r.t.	82 (11)	68:24:8
2	1a	r.t.	quant	78:0:22
3	1b	r.t.	quant	76:0:24
4	1c	r.t.	quant	72:0:28
5	1d	r.t.	92	86:0:14
6 ^d	1e	r.t.	85	73:13:14
7	1f	r.t.	quant	83:0:17
8	1g	r.t.	88	100:0:0
9	1a	50	76 (10)	0:11:89
10	1b	50	97	0:8:92
11	1c	50	75 (21)	0:16:84

^a Unless otherwise specified, 2.5 equiv of allyl ethyl carbonate were used for the reaction. ^b Isolated yield based on **1**. The recovery yields of **1** are shown in parentheses. ^c One equivalent of allyl ethyl carbonate was used for this experiment. ^d One regioisomer was obtained in each adduct.

2,3-dimethyl-3-phenyl-1,5-heptadiene.^{3b} We now report the first example for the palladium(0)-catalyzed Cope rearrangement of certain 1,5-hexadienes, which proceeds through the bis(η^3 -allyl)-Pd(II) intermediate (route b) formed by the Pd(0) insertion into a nonstrained C–C bond (Scheme 1).

We previously reported the palladium(0)-catalyzed alkoxyallylation of trisubstituted activated olefins with allylic carbonates;¹⁰ in these experiments the two substituents at the β -position of activated olefins were H and aryl, or H and *tert*-butyl.¹¹ On the way to further development of this pronucleophile addition reaction, an interesting C–H activation reaction was found when we used tetra-substituted activated olefins **1** whose β -substituents were aryl and methyl, *tert*-butyl and methyl, or aryl and ethyl. The results are summarized in Table 1 and eq 1. The reaction of



(1) Trebellas, J. C.; Olechowski, J. R.; Jonassen, H. B. *J. Organomet. Chem.* **1966**, *6*, 412.

(2) Heimbach, P.; Molin, M. *J. Organomet. Chem.* **1973**, *49*, 477.

(3) (a) Overman, L. E.; Knoll, F. M. *J. Am. Chem. Soc.* **1980**, *102*, 865.

(b) Overman, L. E.; Jacobsen, E. J. *J. Am. Chem. Soc.* **1982**, *104*, 7225. (c) Bluthé, N.; Malacria, M.; Gore, J. *Tetrahedron Lett.* **1983**, 1157. (d) Overman, L. E.; Renaldo, A. F. *Tetrahedron Lett.* **1983**, 2235. (e) Overman, L. E.; Renaldo, A. F. *Tetrahedron Lett.* **1983**, 3757.

(4) (a) Schenck, T. G.; Bosnich, B. *J. Am. Chem. Soc.* **1985**, *107*, 2058.

(b) Overman, L. E. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 579.

(5) Overman, L. E.; Renaldo, A. F. *J. Am. Chem. Soc.* **1990**, *112*, 3945.

(6) Hamilton, R.; Mitchell, T. R. B.; Rooney, J. J. *Chem. Commun.* **1981**, 456.

(7) Recent reviews: (a) Lutz, R. P. *Chem. Rev.* **1984**, *84*, 205. (b) Crabtree, R. H. *Chem. Rev.* **1985**, *85*, 245. (c) Rybtchinski, B.; Milstein, D. *Angew. Chem., Int. Ed. Engl.* **1999**, *38*, 870.

(8) Catalytic insertion of rhodium complexes into the C–C bond activated by the strained system: (a) Murakami, M.; Amii, H.; Ito, Y. *Nature* **1994**, *370*, 540. (b) Murakami, M.; Amii, H.; Shigetou, K.; Ito, Y. *J. Am. Chem. Soc.* **1996**, *118*, 8285. (c) Murakami, M.; Takahashi, K.; Amii, H.; Ito, Y. *J. Am. Chem. Soc.* **1997**, *119*, 9307. Activated by the adjacent carbonyl group: (d) Jun, C.-H.; Lee, H. *J. Am. Chem. Soc.* **1999**, *121*, 880.

(9) Catalytic insertion of palladium complexes into the C–C bond activated by the strained system: (a) Edelbach, B. L.; Lachicotte, R. J.; Jones, W. D. *J. Am. Chem. Soc.* **1998**, *120*, 2843. Activated by the functionalized system: (b) Nilsson, Y. I. M.; Andersson, P. G.; Bäckvall, J.-E. *J. Am. Chem. Soc.* **1993**, *115*, 6609. (c) Vicart, N.; Goré, J.; Cazes, B. *SYNLETT* **1996**, 850. (d) Trost, B. M.; Bunt, R. C. *J. Am. Chem. Soc.* **1998**, *120*, 70. (e) Nozaki, K.; Sato, N.; Takaya, H. *J. Org. Chem.* **1994**, *59*, 2679.

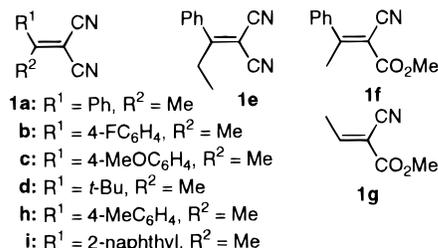
1a with allyl ethyl carbonate (1 equiv) proceeded very smoothly in the presence of Pd(PPh₃)₄ catalyst (5 mol %) at room temperature for 30 min, giving a 68:24:8 mixture of α -adduct **2a**, γ -adduct **3a**, and α,γ -adduct **4a** in 82% yield along with the recovered **1a** (11%) (entry 1). The alkoxyallylation adduct, which was the sole product in the previous cases of trisubstituted olefins, was not obtained at all.¹⁰ The formation of a major product, α -adduct **2a**, can be explained by the γ -proton abstraction–enolate formation–allylation at the α -position.¹² The use of 2.5 equiv of allyl ethyl carbonate increased the chemical yields very much to give a 78:22 mixture of **2a** and **4a** in essentially quantitative yield without formation of the γ -adduct **3a** (entry 2). Under the same

(10) Nakamura, H.; Sekido, M.; Ito, M.; Yamamoto, Y. *J. Am. Chem. Soc.* **1998**, *120*, 6838.

(11) The activated olefin, whose two substituents at the β -position were H and pentyl, underwent the proton absorption at the γ -position followed by allylation at the α -position to give 4,4-dicyano-1,5-decadiene.

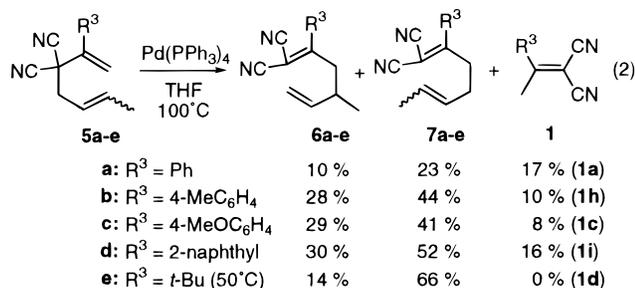
(12) (a) Tsuji, J.; Shimizu, I.; Minami, I.; Ohashi, Y. *Tetrahedron Lett.* **1982**, *23*, 4809. (b) Tsuji, J.; Shimizu, I.; Minami, I.; Ohashi, Y.; Sugiura, T.; Takahashi, K. *J. Org. Chem.* **1985**, *50*, 1523.

reaction conditions, the other aryl olefins **1b–c** and the *tert*-butyl substituted olefin **1d** gave results similar to the above: approximately 7–9:3–1 mixtures of **2b–d** and **4b–d** were obtained in quantitative to very high yields, and no γ -products were produced (entries 3–5). In the case of olefin **1e**, where an ethyl



group was substituted at the β -position instead of a methyl group, a mixture of **2e**, **3e**, and **4e** was produced in a ratio of 73:13:14, respectively (entry 6). Not only the olefins derived from malononitrile (**1a–e**) but also the tetra-substituted olefin **1f**, derived from methyl cyanoacetate, gave an 83:17 mixture of **2f** and **4f** in quantitative yield (entry 7). However, the trisubstituted olefin **1g** produced selectively the α -adduct **2g** in 88% yield without being accompanied by **3g** and **4g** (entry 8).

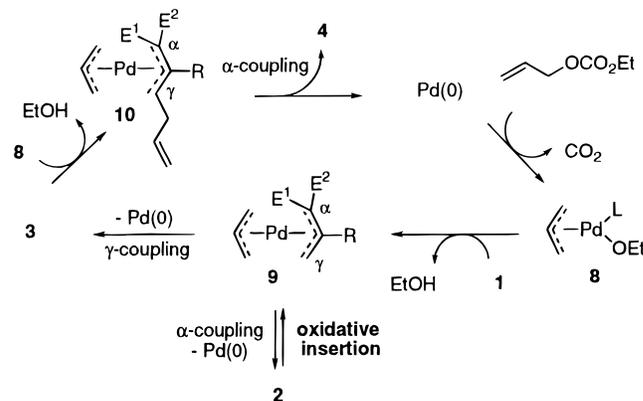
All the above reactions were performed at room temperature. An interesting observation was made when the reaction was carried out at 50 °C (entries 9–11). The α,γ -adducts **4a–c** were obtained as a major product with small amounts of the γ -adducts **3a–c**; the α -adducts **2a–c** were not obtained at all. The results at 50 °C suggested either or both of the following two possibilities: (1) kinetically formed **2a–c** would undergo rearrangement to **3a–c** under the reaction conditions which further would react with allyl carbonate to give **4a–c** and (2) kinetically formed **2a–c** would react further with allyl carbonate to give **4a–c**.¹³ The treatment of isolated α -adduct **2a** with a catalytic amount of Pd(PPh₃)₄ in THF at room temperature for 30 min gave a 3:1:1 mixture of **3a**, **4a**, and **1a** in 24% yield, along with the recovered **2a** (69% yield). No isomerization of **2a** was observed at 50 °C in the absence of Pd(0) catalyst. These results clearly indicate that the α -adducts **2a–c** undergo isomerization to the γ -adducts **3a–c** at 50 °C in the presence of Pd(0) catalyst. To obtain further evidence on the proposed Pd(0)-catalyzed rearrangement, the 1,5-heptadiene derivatives **5a–e** were synthesized and subjected to the Pd(0)-catalyzed reaction (eq 2).¹⁴ The treatment of **5a** with a



catalytic amount of Pd(PPh₃)₄ (2 mol %) in THF at 100 °C for 3 h gave a mixture of the corresponding ordinary Cope rearrangement product **6a** (10%) and the straight chain 1,5-diene **7a** (23%), along with 17% of the deallylated olefin **1a**.¹⁵ The thermal reaction of **5a** at 100 °C without Pd(0) catalyst gave **6a** exclusively. The 2-aryl-substituted 1,5-heptadiene derivatives (**5b–c**), where electron-

donating groups were substituted at the para position of the phenyl group, and the 2-naphthyl-substituted substrate **5d** gave **7b–d** (41–52%) as a major product along with the Cope rearrangement products **6b–d** (28–30%) and the deallylated olefins **1h,c,i** (8–16%).¹⁶ It should be noted that none of **7a–d** were obtained in the absence of Pd(PPh₃)₄ catalyst. In the case of **5e**, where the *tert*-butyl group was substituted at the C-2 carbon of the 1,5-heptadiene, the rearrangement proceeded very smoothly even at 50 °C to give **7e** in 66% yield together with 14% of **6e**: none of **1d** was produced. Now, it is clear that the Pd(0) insertion into a nonstrained C–C bond followed by Cope type rearrangement through bis- π -allylpalladium complexes is operative in the rearrangement of certain 3,3-dicyano-1,5-heptadienes.¹⁷

Scheme 2



A plausible mechanism is shown in Scheme 2. The reaction of palladium(0) with allyl ethyl carbonate would give the π -allylpalladium **8**,¹² which would react with **1** to give the bis(η^3 -allyl)palladium complex **9**.¹⁸ The intermediate **9** would undergo reductive coupling in either an α - or γ -manner to give the α -adduct **2** or γ -adduct **3**, respectively. There is an equilibrium between **2** and **9**, but there is no equilibrium between **3** and **9** under the reaction conditions. Actually the treatment of **3a** with 5 mol % of Pd(PPh₃)₄ in THF at 50 °C for 2 days did not produce any rearranged products but resulted in the recovery of **3a**. The thermodynamically favored **3** would undergo further allylation with **8**, which would give the α,γ -adduct **4** via a bis(η^3 -allyl)-palladium intermediate **10**.

We have presented the first example of a Pd(0)-catalyzed nonordinary Cope rearrangement via a bis(η^3 -allyl)Pd(II) intermediate, which is generated by the oxidative insertion of Pd(0) to a nonstrained carbon–carbon σ -bond. The straight-chain products **7** are not easily available via the previously known Pd(II)-catalyzed or the thermal rearrangement, and therefore the present procedure complements the previously established useful Cope rearrangement. We believe that the present two findings, the Pd(0) insertion into a nonstrained C–C σ -bond and the Pd(0)-catalyzed nonordinary Cope rearrangement, provide a conceptual advance in organic and organometallic chemistry.

Supporting Information Available: Experimental data for compounds **2–7** (PDF). This material is available free of charge via the Internet at <http://pubs.acs.org>.

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(16) It is thought that the fragment leading to the formation of **1a,h,c,i** would be volatile butene, although we did not intend to confirm the formation of it.

(17) We tested 2-substituted 3-cyano-3-ethoxycarbonyl- and 3,3-diethoxycarbonyl-1,5-heptadienes under similar reaction conditions, but the starting materials were recovered.

(18) Recently we have found that a bis- π -allylpalladium complex has nucleophilic character and reacts with aldehydes and imines very smoothly: Nakamura, H.; Iwama, H.; Yamamoto, Y. *J. Am. Chem. Soc.* **1996**, *118*, 6641.

(13) However, this possibility seems to be very small.

(14) The 1,5-heptadiene derivatives **5** were synthesized from the reaction of **1a** with crotyl ethyl carbonate in the presence of palladium(0) catalyst.

(15) In this case, the starting material **5a** was recovered in 32% yield. However, in other cases, the starting materials **5b–e** were consumed completely after 3 h. The reaction at lower temperatures (50–70 °C) was sluggish.