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Reverse of Regioselectivity in Intramolecular Nucleophilic Substitution of π-Allyl Palladium Species. Highly Selective Formation of Vinylic Cyclopropanes via the Pd(0)-Catalyzed Coupling–Cyclization Reaction of Organic Iodides with 2-(2′,3′-Dienyl)malonates

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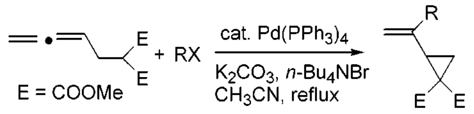
ABSTRACT



Vinylic cyclopropanes were formed highly selectively via the Pd(PPh$_3$)$_4$-catalyzed insertion–intramolecular nucleophilic substitution reaction of aryl or 1-alkenyl iodides with 2-(2′,3′-dienyl)malonates. The regioselectivity observed here is different from what was reported by Cazes et al.

Allenes are a class of compounds with unique reactivity and chirality when properly substituted.[1] Recently much attention has been paid to the chemistry of allenes.[2] Among our efforts toward transition metal-catalyzed chemistry of allenes,[3] we observed the exclusive formation of five-membered butenolides and furans from 2,3-dienoic acids[4] and 1,2-dienyl ketones,[5] respectively. Interestingly, the Pd(0)-catalyzed coupling−cyclization reaction of 2,3-dienols and organic halides afforded three-membered vinylic oxiranes; the formation of the corresponding 2,5-dihydrofurans was not observed, implying that the intramolecular nucleophilic substitution of the π-allyl palladium occurred regiospecifically via path a (Scheme 1).[6]

Cazes et al. studied the Pd(0)-catalyzed coupling cyclization reaction of 2-(2′,3′-dienyl)malonates with organic halides.[7] In most cases the five-membered cyclopentene derivatives were formed as the major products. The regio-

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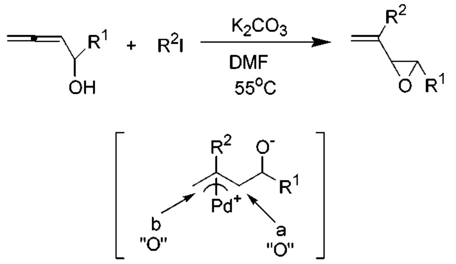
(1) Schuster, H. F.; Coppola, G. M. *Allenes in Organic Synthesis*; John Wiley & Sons: New York, 1988. *The Chemistry of Ketenes, Allenes, and Related Compounds*, Part 1; Patai, S., Ed.; John Wiley & Sons: New York, 1980.

(2) (a) Hashmi, A. S. K. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1581−1583. (b) Ma, S.; Shi, Z.; Yu, Z. *Tetrahedron Lett.* **1999**, *40*, 2393−2396. Ma, S.; Shi, Z.; Yu, Z. *Tetrahedron* **1999**, *55*, 12137−12148.

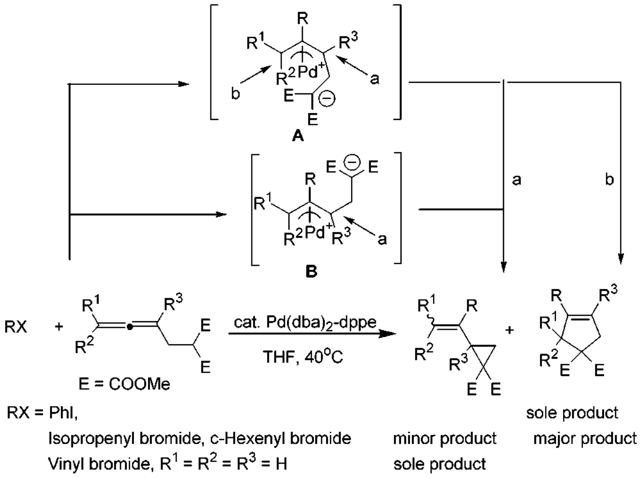
(3) For some examples of Pd-catalyzed reactions see: (a) Shimizu, I.; Tsuji, J. *Chem. Lett.* **1984**, 233. Ahmar, M.; Cazes, B.; Gore, J. *Tetrahedron Lett.* **1984**, *25*, 4505. (b) Larock, R. C.; Berrios-Pena, N. G.; Fried, C. A. *J. Org. Chem.* **1991**, *56*, 2615. (c) Larock, R. C.; Zenner, J. M. *J. Org. Chem.* **1995**, *60*, 482. (d) Okuro, K.; Alper, H. *J. Org. Chem.* **1997**, *62*, 1566. (e) Walkup, R. D.; Guan, L.; Mosher, M. D.; Kim, S. W.; Kim, Y. S. *Synlett* **1993**, 88. (f) Ohno, H.; Toda, A.; Miwa, Y.; Taga, T.; Osawa, E.; Yamaoka, Y.; Fujii, N.; Ibuka, T. *J. Org. Chem.* **1999**, *64*, 2992. (g) Ma, S.; Negishi, E. *J. Org. Chem.* **1994**, *59*, 4730. (h) Grigg, R.; Xu, L. *Tetrahedron Lett.* **1996**, *37*, 4251. (i) Nemoto, H,; Yoshida, M.; Fukumoto, K. *J. Org. Chem.* **1997**, *62*, 6450. Jeong, I.;-Y.; Nagao, Y. *Tetrahedron Lett.* **1998**, *39*, 8677. (j) Grigg, R.; Rasul, R.; Redpath, J.; Wilson, D. *Tetrahedron Lett.* **1996**, *37*, 4609. Oppolzer, W.; Pimm, A.; Stammen, B.; Hume, W. E. *Helv. Chim. Acta* **1997**, *80*, 623.

10.1021/ol006165u CCC: $19.00

Scheme 1



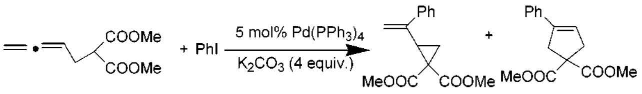
Scheme 2



selectivity is opposite to that of our results with 2,3-allenols[6] and consistent with that observed with 2,3-allenoic acids[4] and 1,2-allenyl ketones.[5] The only case reported for the exclusive formation of 1,5-(bismethoxylcarbonyl)-2-vinyl cyclopropane was the Pd(0)-catalyzed reaction of vinyl bromide with 2-(2′,3′-dienyl)malonates (Scheme 2).[7a,b] In this paper we wish to report our own results on the Pd(0)-catalyzed reaction of 2-(2′,3′-dienyl)malonates with organic halides, in which a completely different regioselectivity was observed.

When we carried out the reaction of dimethyl 2-(2′, 3′-butadienyl)malonate **1** with PhI under the conditions described in ref 6, i.e., $Pd(PPh_3)_4$ as the catalyst, K_2CO_3 as the base, and DMF (or DMSO) as the solvent, we did observe the formation of cyclopropane derivative **3a** together with cyclopentene derivative **4a** (entries 1 and 2, Scheme 3).

Scheme 3



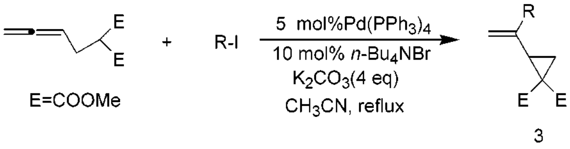
entry	solvent	additive	temp(°C)/time (h)	**3a** (%)	**4a** (%)
1	DMF	-	60/25	65	8
2	DMSO	-	62/22	49	21
3	toluene	-	82/15.5	30	0
4	benzene	-	80/15	40	0
5	CH_3CN^a	-	reflux/21	41	0
6	CH_3CN	-	reflux/19.5	32	0
7	CH_3CN	***n*-Bu$_4$NBr**	reflux/15	80	0
8	CH_3CN^b	-	reflux/22	10	0
9	CH_3CN^b	***n*-Bu$_4$NBr**	reflux/18	29	0

[a] $Pd_2(dba)_3 \cdot CHCl_3$ (2.5 mol%) and dppe (5 mol%) were used as the catalytic system
[b] PhBr was used instead of PhI

However, this reaction did occur in toluene, benzene, or CH_3CN to afford 1,1-(bismethoxycarbonyl)-2-(1′-phenyl)-ethenyl cyclopropane **3a** exclusively, albeit in low yield (30−41%) (entries 3−6, Scheme 3), indicating a nice solvent effect on the regioselectivity of this reaction. Luckily, after some trial and error, we found that *the addition of a catalytic amount of n-Bu$_4$NBr* as the phase transfer catalyst improved the yield of **3a** dramatically, and the formation of the five-membered product, i.e., 1-phenyl-4,4-(bismethoxycarbonyl)-cyclopentene **4a**, was not observed (entry 7, Scheme 3). The addition of a catalytic amount of the phase transfer catalyst, i.e., TBAB, may facilitate oxidative addition, carbopalladation of allene, and the intramolecular nucleophilic substitution reaction while it did not change the regioselectivity of this transformation.[8] For the reaction with phenyl bromide, the yields were lower; however, the effect of TBAB was still obvious (compare entries 8 and 9, Scheme 3).

With this optimized reaction conditions in hand, we studied the $Pd(PPh_3)_4$-catalyzed reaction of aryl halides/1-alkenyl

Table 1. $Pd(PPh_3)_4$-Catalyzed Cyclization of Methyl 2-(2′,3′-Butadienyl)malonate with Organic Iodides



entry	R (**2**)	time (h)	yield (%) of **3**
1	Ph (**2a**)	15	80 (**3a**)
2	(*E*)-1-hexenyl (**2b**)	16	67 (**3b**)
3	*p*-methoxyphenyl (**2c**)	17	69 (**3c**)
4	*p*-methylphenyl (**2d**)	24	82 (**3d**)
5	*p*-methoxycarbonylphenyl (**2e**)	24	58 (**3e**)
6	(*E*)-1-(2′-phenyl)ethenyl (**2f**)	16	46 (**3f**)
7	*p*-bromophenyl (**2g**)	17	83 (**3g**)
8	naphthyl (**2h**)	23	86 (**3h**)

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(4) (a) For the Pd(0)/Ag^+-cocatalyzed cyclization of organic halides with 1,2-allenyl carboxylic acids to afford butenolides, see: Ma, S.; Shi, Z. *J. Org. Chem.* **1998**, *63*, 6387−6389. Ma, S.; Duan, D.; Shi, Z. *Org. Lett.* **2000**, *2*, 1419. (b) For CuX_2 (X = Br, Cl)-mediated cyclization of 1,2-allenyl carboxylic acids to afford *β*-halobutenolides, see: Ma, S.; Wu, S. *J. Org. Chem.* **1999**, *64*, 9314.

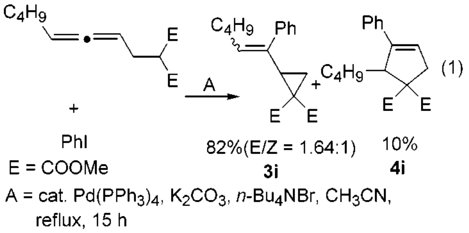
(5) Ma, S.; Zhang, J. *Chem. Commun.* **2000**, 117−118. Ma, S.; Li, L. *Org. Lett.* **2000**, *2*, 941.

(6) Ma, S.; Zhao, S. *J. Am. Chem. Soc.* **1999**, *121*, 7943.

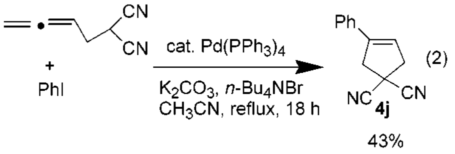
(7) (a) Ahmar, M.; Cazes, B.; Gore, J. *Tetrahedron Lett.* **1985**, *26*, 3795. (b) Ahmar, M.; Cazes, B.; Gore, J. *Tetrahedron* **1987**, *43*, 3453. (c) Besson, L.; Bazin, J.; Gore, J.; Cazes. B. *Tetrahedron Lett.* **1994**, *35*, 2881. (d) Gamez, P.; Ariente, C.; Gore, J.; Cazes, B. *Tetrahedron* **1998**, *54*, 14835.

halides with 2-(2′,3′-butadienyl)malonate; the results are summarized in Table 1. It should be pointed out that for all entries in Table 1 only the vinylic cyclopropane derivatives were formed, aryl iodides with both an electron-donating or electron-withdrawing group can be used (entries 3−5), the reaction afforded 1,3-dienyl cyclopropanes when 1-alkenyl iodides were used (entries 2 and 6), and with *p*-bromophenyl iodide, only the carbon−iodine bond participated in the oxidative addition reaction while the carbon−bromine remained intact (entry 7).

The reaction of methyl 2-(2′,3′-heptadienyl)malonate with PhI under the same reaction conditions afforded a mixture of three-membered and five-membered products with the three-membered product **3i** predominating (eq 1).



However, the unique regioselectivity seems to be limited to maolonate derivatives. The reaction of 2-(2′,3′-butadienyl)-malonitrile with PhI afforded the cyclopentene derivative **4j** as the sole product (eq 2).



In conclusion, we have developed an efficient synthesis of vinylic cyclopropane derivatives. It is obvious that the selectivity is high and different from that observed by Cazes et al.[7] The relative stability of the intermediates **A** and **B** in the reaction process determined the regioselectivity of this reaction, indicating the exclusive formation of a **B**-type intermediate for the reactions shown in Table 1. Further studies on the scope and mechanism, especially the factor controlling the regioselectivity, of this reaction are underway in our laboratory.

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Supporting Information Available: Typical experimental procedure and analytical data for all products. This material is available free of charge via the Internet at http://pubs.acs.org.

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(8) Jeffery, T. *Synthesis* **1987**, 70. Jeffery, T. *Tetrahedron Lett.* **1985**, *26*, 2667. Jeffery, T. *J. Chem. Soc., Chem. Commun.* **1984**, 1287.