Palladium-Catalyzed Alkoxycarbonylation of (Z)-2-En-4-yn Carbonates Leading to 2,3,5-Trienoates
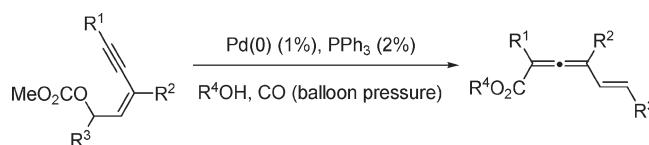
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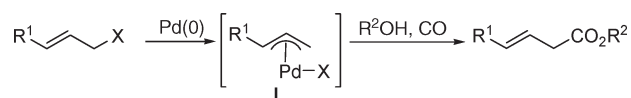
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ABSTRACT

Pd(0)-catalyzed carbonylation of (Z)-2-en-4-yn carbonates in the presence of a balloon pressure of CO in an alcohol donates vinylallenyl esters with an exclusively E-configuration and in high yields. The fact that no such reactivity could be observed with E-configured enyne carbonates may indicate that the reaction is promoted via the cooperative coordination of palladium with both alkynyl and carbonate moieties.

As a part of our initiated systematic studies involving the transition metal catalyzed reactions of conjugated enynes with a leaving group in the allylic position we have conducted Pd(0)-catalyzed carbonylation reactions of 2-en-4-yn carbonate reagents in the presence of an alcohol (alkoxycarbonylation). It is well-known that the Pd(0)-catalyzed alkoxycarbonylation of allylic compounds usually leads to β,γ-unsaturated esters through the involvement of a π-allylpalladium complex (**I**) (Scheme 1).[1]

Scheme 1. Alkoxycarbonylation of Allylic Compounds

On the other hand, the analogous reaction of alkynes containing a leaving group in the propargylic position proceeds via a σ-allenylpalladium[2] (**II**) as an intermediate to produce allenic esters (Scheme 2).[3]
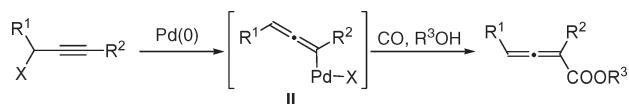
Interestingly however, the analogous experiments with Z-configured enyne carbonates revealed that, even though these conjugated enynes bear the leaving group on the allylic carbon atom, they act in a similar way as the propargylic reagents do, with their Pd(0)-catalyzed reactions proceeding through a 1,5-substitution to afford ester functionalized vinylallene structures.

(1) (a) Kiji, J.; Okano, T.; Higashimae, Y.; Fukui, Y. *Bull. Chem. Soc. Jpn.* **1996**, *69*, 1029. (b) Tsuji, J.; Sato, K.; Okumoto, H. *J. Org. Chem.* **1984**, *49*, 1341. (c) El Houssame, S.; El Firdoussi, L.; Allaoud, S.; Karim, A.; Castanet, Y.; Mortreux, A. *J. Mol. Catal. A* **2001**, *168*, 15. (d) Shimizu, I.; Maruyama, T.; Makuta, T.; Yamamoto, A. *Tetrahedron Lett.* **1993**, *34*, 2135.

(2) σ-Allenylpalladium complexes were isolated and characterized: (a) Elsevier, C. J.; Kleijn, H.; Ruitenberg, K.; Vermeer, P. *J. Chem. Soc., Chem. Commun.* **1983**, 1529. (b) Elsevier, C. J.; Kleijn, H.; Boersma, J.; Vermeer, P. *Organometallics* **1986**, *5*, 716.
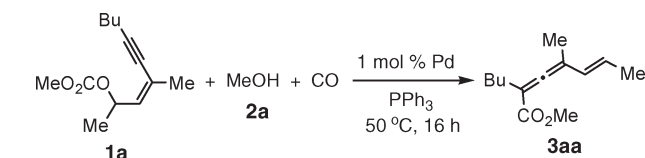
(3) (a) Tsuji, J.; Sugiura, T.; Minami, I. *Tetrahedron Lett.* **1986**, *27*, 731. (b) Tsuji, J.; Mandai, T. *J. Organomet. Chem.* **1993**, *451*, 15 and references therein. (c) Arzoumanian, H.; Choukrad, M.; Nuel, D. *J. Mol. Catal.* **1993**, *85*, 287. (d) Marshall, J. A.; Wolf, M. A.; Wallace, E. M. *J. Org. Chem.* **1997**, *62*, 367. (e) Marshall, J. A.; Wolf, M. A. *J. Org. Chem.* **1996**, *61*, 3238. (f) Trieu, N. D.; Elsevier, C. J.; Vrieze, K. *J. Organomet. Chem.* **1987**, *325*, C23. (g) Imada, Y.; Alper, H. *J. Org. Chem.* **1996**, *61*, 6766. (h) Tsuji, J.; Mandai, T. *Angew. Chem., Int. Ed.* **1995**, *34*, 2589. (i) Ma, S. *Eur. J. Org. Chem.* **2004**, 1175 and references therein. (j) Knight, J. G.; Ainge, S. W.; Baxter, C. A.; Eastman, T. P.; Harwood, S. J. *J. Chem. Soc., Perkin Trans. 1* **2000**, 3188. (k) Piotti, M. E.; Alper, H. *J. Org. Chem.* **1997**, *62*, 8484.

Scheme 2. Alkoxycarbonylation of Propargylic Compounds

The reaction of the (Z)-2-en-4-yn **1a** with MeOH at just 50 °C under a balloon pressure of CO in the presence of 1 mol % Pd(PPh$_3$)$_4$ yielded exclusively the related E-configured vinylallenyl ester molecule (**3aa**) with high yield (Table 1, entry 1). The separate addition of a PPh$_3$ ligand and palladium in the form of Pd$_2$(dba)$_3$-CHCl$_3$ or Pd-(OAc)$_2$ with a respective ligand to palladium ratio of 4/1 afforded lower yields (entries 2 and 3). Nevertheless, lowering the ligand-to-Pd ratio to 2/1 provided the optimal catalyst activity (entries 4−6). However, the conversion of **1a** could not proceed to completion when performing the reaction at room temperature even at prolonged reaction times (entry 7).

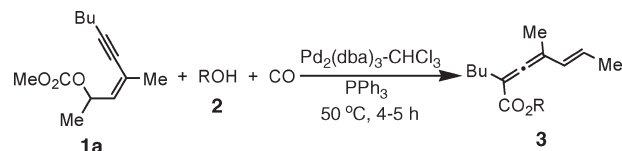**Table 1.** Optimization of Methoxycarbonylation Reaction of Enyne Carbonate **1a**[a]

entry	Pd	PPh$_3$ (%)	yield (%)[b]
1	Pd(PPh$_3$)$_4$	−	85
2	Pd$_2$(dba)$_3$−CHCl$_3$	4	74
3	Pd(OAc)$_2$	4	67
4	Pd$_2$(dba)$_3$−CHCl$_3$	2	89
5	Pd(OAc)$_2$	2	83
6	Pd(OAc)$_2$	1	76
7[d]	Pd$_2$(dba)$_3$−CHCl$_3$	2	74 (22)[c]
8	Pd(PPh$_3$)$_2$Cl$_2$	−	0

[a] **1a**, 0.3 mmol; MeOH, 5 mL; CO, balloon pressure. [b] Determined by ^{1}H NMR using dimethyl sulfoxide as an internal standard. [c] Unreacted reactant. [d] Rt, 30 h.

The compound Pd(PPh$_3$)$_2$Cl$_2$ displayed no catalytic activity; when present, the enyne **1a** was recovered unchanged at the end of the reaction (entry 8).

The carbonylative reaction of **1a** with MeOH, EtOH, or primary saturated C$_3$ and C$_4$ alcohols, under the optimal reaction conditions, that is at 50 °C, a balloon pressure of CO, in 5 mL of alcohol, used in combination with Pd$_2$-(dba)$_3$−CHCl$_3$ (1 mol %)/PPh$_3$ (2 mol %) gave rise to the corresponding 2,3,5-trienoate products (**3aa**−**3ad**) just within 4−5 h in the range of 85−91% isolated yields (Table 2, entries 1−4). A high yield of 2,3,5-trienoate product **3ae** could also be obtained with a bulky alcohol, isopropyl alcohol, albeit at a prolonged reaction time (16 h) (entry 5). In contrast *tert*-butyl alcohol appears to be

Table 2. Alkoxycarbonylation of Enyne Carbonate **1a**[a]

entry	ROH	isolated yield (%)
1	MeOH	90 (**3aa**)
2	EtOH	85 (**3ab**)
3	PrOH	91 (**3ac**)
4	BuOH	85 (**3ad**)
5[b]	*i*-PrOH	91 (**3ae**)
6	*t*-BuOH	0 (**3af**)

[a] **1a**, 0.3 mmol; ROH, 5 mL; CO, balloon pressure; 1 mol % Pd, 2 mol % PPh$_3$. [b] 16 h.

unsuitable because the enyne **1a** was recovered as unreacted when it was carbonylated in *tert*-butyl alcohol (entry 6).

The scope of the carbonylation method was also surveyed for a range of (Z)-2-en-4-yn carbonates.[4] The method is fully suitable for enynes bearing a methyl, secondary alkyl, cyclohexyl, or phenyl group on the alkynyl moiety (R^1) thereby providing the corresponding 2,3,5-trienoate products **3ba**−**3da** in high yields when carbonylated in methanol for 4 h under the established conditions (Table 3, entries 1−3).

The presence of a highly bulky *tert*-butyl group on the alkynyl terminus, however, required a relatively longer reaction period (20 h) for complete conversion and gave rise to the product **3ea** in a moderate yield (64%) (entry 4). The methodology also tolerated well the enyne carbonates of which the R^2 position is occupied by a H, butyl, or phenyl group, affording the desired products **3fa**−**3ha** in around 80−82% yields (entries 5−7).

It appears that the enyne reactivity is more severely influenced by the size of the R^3 group. Varying the R^3 group from methyl to butyl reduced the reactivity of the enyne carbonate remarkably; it took nearly 16 h for complete conversion of **1i** and to produce the corresponding vinylallenyl ester **3ia** at a yield of 81% (entry 8). An even more drastic effect could be observed with the substrate in which R^3 was the isopropyl group; the reaction of **1j** was highly sluggish, and its conversion was incomplete when the reaction temperature employed was 50 °C (entry 9). Nevertheless, elevation of the reaction temperature to 65 °C shortened the reaction period for the complete conversion of **1j** to give the product **3ja** at a yield of 71%.

The methoxycarbonylation of an enyne carbonate of a primary alcohol **1k** interestingly resulted in the formation of a nonseparable mixture of an ester functionalized 2-en-4-yn (**4ka**) byproduct and the desired vinylallene product **3ka** (entry 10).

(4) The preparation of Z-enyne carbonates, such as the one containing a phenyl group in the R^3 position, or in the case where two methyl groups are on the allylic carbon (enyne carbonate of a tertiary alcohol), failed owing to their decomposition in the course of modification of the hydroxyl group to the carbonate.

Table 3. Methoxycarbonylation of 2-En-4-yne Carbonates[a]

Reaction scheme: **1** + MeOH + CO, with Pd₂(dba)₃CHCl₃, PPh₃, 50 °C, **2a** → **3**

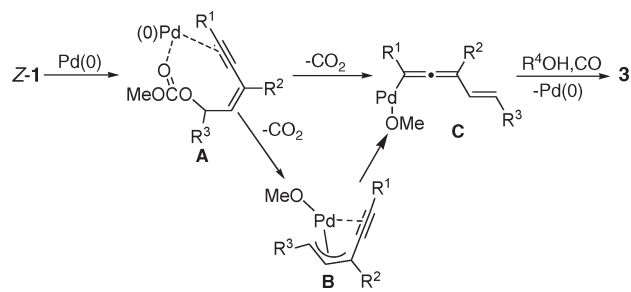| entry	enyne carbonate	time	product (yield)[b]
1	**1b**	4 h	**3ba** (87%)
2	**1c**	4 h	**3ca** (84%)
3	**1d**	4 h	**3da** (85%)
4	**1e**	20 h	**3ea** (64%)
5	**1f**	4 h	**3fa** (81%)
6	**1g**	4 h	**3ga** (80%)
7	**1h**	2 h	**3ha** (82%)
8	**1i**	16 h	**3ia** (81%)
9	**1j**	22 h[c], 8 h[d]	**3ja** (58%, 71%[d])
10	**1k**	24 h[c]	**3ka** (49%) + **4ka** (33%)

[a] **1a**, 0.3 mmol; MeOH, 5 mL; CO, balloon pressure; 1 mol % Pd, 2 mol % PPh₃. [b] Isolated yield. [c] Incomplete conversion. [d] 65 °C.

Evidently, the method would be successful only if the enyne carbonate substrate had a *Z*-configuration, because an *E*-configured enyne carbonate *E*-**1l** led to a complex mixture (containing only small amounts of the desired vinylallenes) when subjected to the Pd(0)-catalyzed methoxycarbonylation reaction as determined by ^{1}H NMR analysis (Scheme 3).

When comparing the results from the reactions of *E*- and *Z*-configured enyne carbonates, it can be considered that the dual coordination of Pd species to a triple bond and the

Scheme 3. Methoxycarbonylation of *E*-Enyne Carbonate **1l**

E-**1l** (Complete conversion) → [Pd(0)/PPh₃, CO, MeOH, Conditions of Table 2] → product, 20% Complex mixture

carbonate functionality (**A**) should facilitate the initiation of the reaction cycle (Scheme 4). As analogy to the Pd(0)-catalyzed reactions of propargylic reagents, the Pd(0)-catalyzed alkoxycarbonylation of *Z*-enyne carbonates should involve the formation of a σ-allenylpalladium(II) complex (**C**) by elimination of the leaving group and double bond migration.[5]

Scheme 4. Reaction Mechanism of Pd(0)-Catalyzed Alkoxycarbonylation of *Z*-2-En-4-yn Carbonates

Z-**1** → Pd(0) → **A** → (−CO₂) → **C** → R⁴OH, CO, −Pd(0) → **3**; **A** → (−CO₂) → **B**

The formation of the σ-allenylpalladium intermediate from propargylic reagents has been based on two unverified paths: (1) the oxidative addition of Pd(0) species and the subsequent shift of Pd to the far alkynyl carbon, or (2) via S_N2' substitution by the attack of the Pd(0) species to the alkynyl carbon.[2,6] Also for our case, it is uncertain whether the oxidative pathway or 1,5-S_N2'' type Pd(0)-substitution is responsible for the formation of the vinylallenylpalladium (**C**) intermediate. Nonetheless, the marked effect on reactivity observed here for the *Z*-enyne carbonates with respect to the size of their allylic cosubstituent (R³) may imply the former. It should also be noted that the formation of (*Z*)-methyl 4-methyldec-3-en-5-ynoate (**4ka**) from the methoxycarbonylation of **1k** can be ascribed to an allylpalladium(II) intermediate.[1]

The reaction cycle should finalize by the reaction of the intermediate **C** with CO and alcohol to generate the product **3** and a catalytically active Pd(0) species.

No center-to-axis chirality transfer selectivity was demonstrated with the our established method; the respective methoxycarbonylation of a nonracemic enyne

(5) The isolation of the vinylallenylpalladium species by adopting the methods applied for propargylic reagents (see ref 2) resulted in decomposition in all our attempts.

(6) (a) Keinan, E.; Bosch, E. *J. Org. Chem.* **1986**, *51*, 4006. (b) Mandai, T.; Yoshikazu, T.; Matsuoka, S.; Tsuji, J. *Tetrahedron Lett.* **1993**, *34*, 7615. (c) Mandai, T.; Matsumoto, T.; Tsujiguchi, Y.; Matsuoka, S.; Tsuji, J. *J. Organomet. Chem.* **1994**, *473*, 343.

carbonate (*R,Z*)-**1b** (94.5% *ee*) led to a racemic mixture of the product.

In summary we have revealed for the first time that the Pd(0)-catalyzed carbonylation of (*Z*)-2-en-4-yn carbonates in an alcohol medium lead to high yields of vinylallenyl esters. *Z*-Conjugated enyne reagents with a leaving group in the allylic position seem to reveal similar characteristic reactivities toward transition metal catalyzed reactions with respect to the propargylic reagents. The studies involving the synthesis of enantioenriched vinylallenes, and the application of *Z*-enynes with different types of leaving groups toward various transition metal catalyzed reactions are currently underway.

Supporting Information Available. Detailed experimental procedures, and compound characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.