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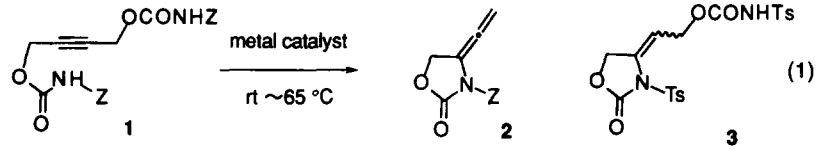
Efficient Synthesis of 4-Ethenylidene-2-oxazolidinones via Palladium-Catalyzed Aminocyclization of 2-Butyn-1,4-diol Biscarbamates

Masanari Kimura, Yoshinori Wakamiya, Yoshikazu Horino, and Yoshinao Tamaru*
Department of Applied Chemistry, Faculty of Engineering, Nagasaki University, 1-14 Bunnkyo, Nagasaki 852, Japan

Abstract: 4-Ethenylidene-2-oxazolidinones **2**, **6**, and **9** are prepared in reasonable yields by the reaction of 2-butyn-1,4-diol biscarbamates in the presence of catalytic amounts of $Pd_2(dba)_3$•$CHCl_3$ (0.005 equiv) and triethylamine (0.1 equiv). The allenic three carbons are not aligned straight, but considerably distorted (173.6°); the enamine double bond is reactive toward unsaturated amides (providing **4**) and methyl vinyl ketone (providing **10**). © 1997 Elsevier Science Ltd.

2-Oxazolidinones constitute an important class of heterocycles that are widely used in the industrial, pharmaceutical, and agricultural fields as well as in organic synthesis. We reported a convenient synthesis of 4-methylene-2-oxazolidinones from propargyl carbamates catalyzed by Cu(I) and Ag(I) salts.[1] 4-Methylene-2-oxazolidinones are of special interest as synthetic intermediates; they are functionalized with enamine and allylic alcohol moieties, by virtue of which, Murai et al.,[2] for example, succeeded in the generation of a so called "azatrimethylenemethane-palladium" intermediate.

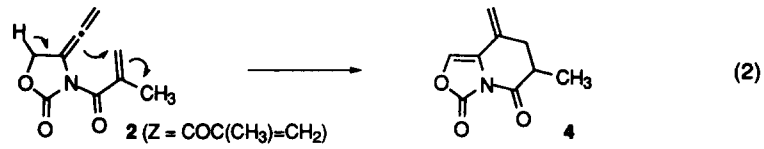


1 **2** **3**

Here we report an efficient synthesis of 4-ethenylidene-2-oxazolidinones **2**, **6**, and **9** from 2-butyn-1,4-diol biscarbamates **1**, **5**, and **8**, respectively (eqs 1,3,4). 2-Butyn-1,4-diol biscarbamates **1** (Z = Ts, Ms, Bz, α-methylacryloyl, Ph), **5**, and **8** were readily prepared in high yields from the corresponding diols and isocyanates (2.2 equiv) [triethylamine (2.2 equiv) in dry THF at rt under N_2, 1~2 h].

As apparently seen from Table 1, the transformation of **1** (Z = Ts, Ms, Bz) to **2** (eq 1) best proceeded in the presence of $Pd_2(dba)_3$•$CHCl_3$ (0.005 equiv, dba = dibenzylideneacetone) and triethylamine (0.1 equiv).[3] These reactions were complete within 12 h at rt (runs 1,7,8). In the absence of triethylamine (run 2), the reaction did not proceed to any appreciable extent at rt; at higher temperature, **1** decomposed to provide an intractable mixture that did not contain **2**. The use of an increased amount of the palladium complex (run 3) facilitated the reaction, but suppressed the yield of **2**. Other palladium complexes showed marginal success (runs 4,5). Copper(I) chloride, as being in accord with the results previously reported from our laboratories,[1] selectively promoted aminocyclization of **1** to provide **3** (run 6, eq 1). In this case, **2** was not formed at all.

The results shown in runs 9 and 10 (Table 1) deserve some comments. When the reaction of **1** (Z = α-methylacryloyl) was conducted at rt, the reaction was rather slow and provided **4** (15%, $R_{f\,4}$ = 0.4, ethyl acetate:hexane = 1:1, v./v.) in addition to the expected **2** (14%, $R_{f\,2}$ = 0.8, $R_{f\,1}$ = 0.1) (eq 2). The former might be formed via a further reaction of the primary product **2** (eq 2), which probably involved an intramolecular ene-type reaction. Indeed, at the elevated temperature, **4** was obtained as the sole product (run 10).



(2)

Table 1. Pd- and Cu-Catalyzed Aminocyclizataion of 2-Butyn-1,4-diol Biscarbamates 1[a]

run	Z of 1	metal catalyst (equiv)	base (equiv)	temp (°C)/time (h)	product: % yield[b]
1	Ts	$Pd_2(dba)_3$•$CHCl_3$ (0.005)	Et_3N (0.1)	rt/7	**2** (Z = Ts): 73
2	Ts	$Pd_2(dba)_3$•$CHCl_3$ (0.005)	none	rt/2 → 65/3	decomposition of **1**[c]
3	Ts	$Pd_2(dba)_3$•$CHCl_3$ (0.1)	Et_3N (0.1)	rt/2	**2** (Z = Ts): 44
4	Ts	$Pd(PPh_3)_4$ (0.1)	Et_3N (0.1)	rt/25 → 65/4	**2** (Z = Ts): 45
5	Ts	$Pd(OAc)_2$ (0.1)	Et_3N (0.1)	rt/4	**2** (Z = Ts): 3
6	Ts	CuCl (0.1)	Et_3N (0.1)	rt/17 → 65/5	**3** (Z = Ts): 54
7	Ms	$Pd_2(dba)_3$•$CHCl_3$ (0.005)	Et_3N (0.1)	rt/12	**2** (Z = Ms): 43
8	Bz	$Pd_2(dba)_3$•$CHCl_3$ (0.002)	Et_3N (0.1)	rt/12	**2** (Z = Bz): 66
9		$Pd_2(dba)_3$•$CHCl_3$ (0.005)	Et_3N (0.1)	rt/47	**2**: 14[d], **4**:15[d]
10		$Pd_2(dba)_3$•$CHCl_3$ (0.005)	Et_3N (0.1)	50/7	**4**: 33[d]
11	Ph	$Pd_2(dba)_3$•$CHCl_3$ (0.005)	Et_3N (0.1)	50/55	no reaction
12	Ph	$Pd_2(dba)_3$•$CHCl_3$ (0.005)	^{t}BuOK (0.1)	50/55	decomposition of **1**[c]

[a] Reactions were performed as follows: **1** (1 mmol), a transition metal complex, and a base (indicated amount) in dry THF (5 ml) under N_2. [b] All products were isolated by means of column chromatography over silica gel. Yields refer to the isolated yields for analytically pure products [except for **2** (Z = Ms), which was rather unstable and could not be purified enough for elemental analysis]. [c] Complex mixture that did not contain the expected products resulted. [d] For the structures of **2** and **4**, see equation 2.

Unfortunately, **1** (Z = Ph) was either unreactive under usual conditions (run 11, Table 1) or decomposed under somewhat different conditions (run 12).

Next, we applied the reaction to C_1-substituted 2-butyn-1,4-diols (eq 3). For the cyclization of **5**, two products (**6** and **7**) are conceivable, the former being formed by nucleophilic addition of the C_1-carbamate to the acetylenic C_2-carbon with concomitant elimination of the C_4-carbamate, and the latter being generated the opposite way round. As apparent from the results summarized in Table 2 (runs 1-6), C_1-monosubstituted **5** provided a mixture of **6** and **7** in a ratio of ca. 2:1, irrespective of the steric and electronic nature of the substituents. C_1-Disubstituted **5** (runs 7,8), on the other hand, furnished **6** almost exclusively.

The successful cyclization of 1,1,4,4-tetrasubstituted biscarbamate **8** (eq 4), together with those discussed above (Tables 1 and 2), clearly indicates that the amidocyclization of 2-butyn-1,4-diol biscarbamates is a versatile and efficient entry to 4-ethenylidene-2-oxazolidinones bearing a wide variety of substituents.

The present palladium-catalyzed novel cyclization reaction may proceed via oxidative addition of Pd(0)

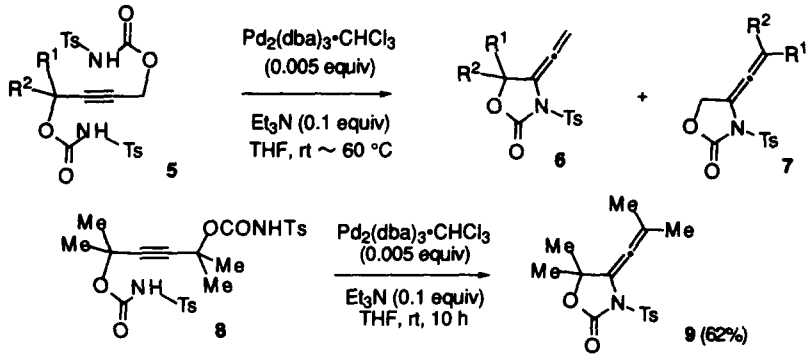


Table 2. Pd-Catalyzed Aminocyclization of 1-Substituted 2-Butyn-1,4-diol Bistosylcarbamates 5[a]

run	5			temp (℃)/time (h)	% yield of 5 and 6[b]	ratio[c]
		R^1	R^2			
1	**5a**	Me	H	rt/6	47	**6a** : **7a** = 2.1 : 1
2	**5b**	Et	H	rt/54	47	**6b** : **7b** = 1.7 : 1
3	**5c**	i-Pr	H	50/20	45	**6c** : **7c** = 2.5 : 1
4	**5d**	c-Hex	H	60/20	40	**6d** : **7d** = 2.5 : 1
5	**5e**	Ph	H	rt/11	58	**6e** : **7e** = 2.1 : 1
6	**5f**	*t*-Bu	H	rt/42 → 40/25	58	**6f** : **7f** = 2.0 : 1
7	**5g**	Me	Me	rt/13	70	**6g** : **7g** = 30 : 1
8	**5h**	-$(CH_2)_5$-		rt/4	56	**6h** : **7h** = 20 : 1

[a] Reactions were performed as follows: **5** (1 mmol), $Pd_2(dba)_3$•$CHCl_3$ (0.005 mmol), Et_3N (0.1 mmol) in dry THF (5 ml) under N_2 (see eq 3). For runs 7 and 8, $Pd_2(dba)_3$•$CHCl_3$ (0.02 mmol) was applied. [b] All products were isolated as mixtures of **6** and **7** by means of column chromatography over silica gel. Yields refer to the isolated yields for analytically pure products. [c] The ratio was determined by ^1H NMR (400 MHz).

species to one of the C-carbamate bonds to provide propargylpalladium(II) **I** and/or allenylpalladium(II) intermediates **II** (Fig. 1).[4] **I** would cyclize in S_N2' fashion and **II**, via **III**, would cyclize via reductive elimination to furnish **2**, **6**, and **9**.

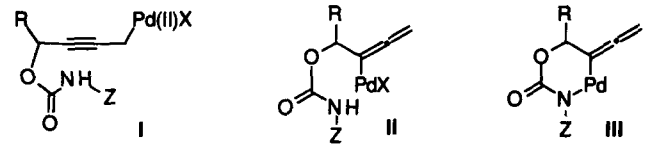


Fig. 1

In Figure 2 is shown the X-ray structure of **6e**, which indicates that the oxazolidinone ring atoms, the allenic central C(7), and the sulfonyl S(10) and O(24) atoms all reside virtually in a plane. Interestingly, the allenic carbons (C_1, C_7, and C_8) are not aligned straight, but C_7 and C_8 are located significantly away from the sulfonyl group ($\angle C_1$-C_7-C_8 = 173.6°, $\angle N_5$-C_1-C_7 = 130.4°, $\angle C_2$-C_1-C_7 = 126.3°).

As suggested by the strained structure of the allene bond, **2** turned out to be extremely reactive toward hetero Diels-Alder reaction (eq 5). When heated with methyl vinyl ketone at 80 ℃, **2** reacted selectively at the

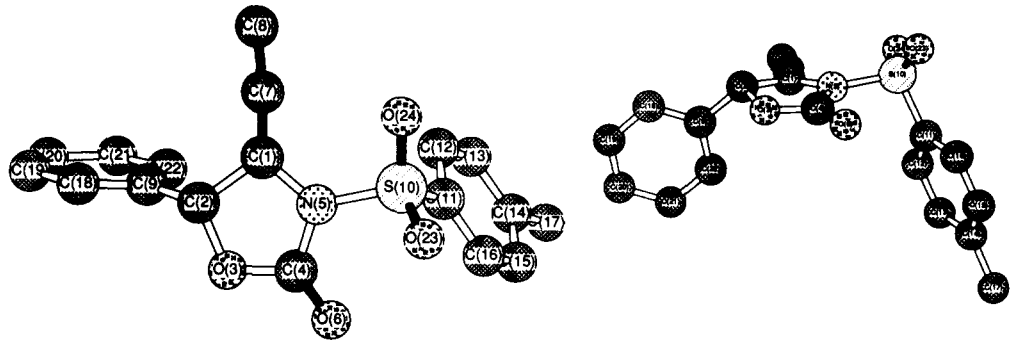
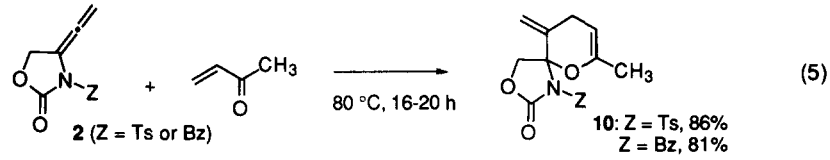


Fig. 2. X-ray structure of 6e. Selected data of bond angles and dihedral angles: C_1-C_7-C_8 173.6°, C_2-C_1-C_7 126.3°, N_5-C_1-C_7 130.4°, C_2-C_1-C_7-C_8 14.5°, N_5-C_1-C_7-C_8 -166.4°.

enamine double bond to furnish spiro adducts **10**.[5] We are currently under extensive study to reveal the full reaction features of the allenic moiety of **2** toward cycloaddition reactions.[6]



(5)

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3. General procedure (run 1, Table 1): To a mixture of **1** (Z = Ts, 480 mg, 1 mmol) and $Pd_2(dba)_3$•$CHCl_3$ (5.2 mg, 0.005 mmol) were added THF (5 ml, dried over Na•benzophenone ketyl) and Et_3N (14 μl, 0.1 mmol) via syringes. The solution was stirred under N_2 for 7 h at ambient temperature and then concentrated *in vacuo*. The residue was chromatographed over silica gel (hexane-ethyl acetate gradient) to afford **2** (Z = Ts) as a solid in 73% yield (193 mg). **2** (Z = Ts): mp 101.5-103.0 ℃ (ethyl acetate/hexane); IR (KBr) 1805 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 2.46 (s, 3 H), 4.86 (t, J = 4.8 Hz, 2 H), 5.71 (t, J = 4.8 Hz, 2 H), 7.36 (d, J = 8.4 Hz, 2 H), 7.93 (d, J = 8.4 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 21.8, 63.9, 92.6, 103.8, 128.3, 129.9, 134.1, 146.1, 150.3, 192.0. Anal: C, H, N, S.
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5. 7-Methyl-10-methylene-1-tosyl-1-aza-3,6-dioxaspiro[4.5]-7-decen-2-one (**10**, Z = Ts): mp 145.0-147.0 ℃ (ethyl acetate/hexane); IR (KBr) 1795 (s), 1690 (w) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.83 (br s, 3 H), 2.45 (s, 3 H), 2.90 (dm, J = 18.0 Hz, 1 H), 3.05 (dm, J = 18.0 Hz, 1 H), 4.12 (d, J = 9.2 Hz, 1 H), 4.33 (d, J = 9.2 Hz, 1 H), 4.74 (m, 1 H), 5.35 (br d, J = 2.6 Hz, 1 H), 5.55 (br d, J = 2.6 Hz, 1 H), 7.34 (d, J = 8.4 Hz, 2 H), 8.04 (d, J = 8.4 Hz, 2 H). Anal: C, H, N, S.
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