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Carbon–Carbon Bond Cleavage of Diynes through the Hydroamination with Transition Metal Catalysts

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Althogh a number of researches on C–C bond cleavage have been carried out,¹ only a few examples on the cleavage of alkynes are known: C–C bond cleavage of alkynes ligated to metal complexes² and oxidative cleavage.³ Furthermore, most of these reactions do not proceed in a catalytic manner, and the use of a stoichiometric amount of reagents is needed.⁴ Recently, Jun et al. reported catalytic C–C triple bond cleavage through the rhodiumcatalyzed hydroiminoacylation.⁵ During our investigation on palladium-catalyzed hydroamination of alkynes using o-aminophenol,⁶ we found that the C–C bond cleavage of diynes 1 with oaminophenols 2 is catalyzed efficiently by Ru and Pd catalysts to give the corresponding 2-substituted benzoxazoles 3 and 4 (eq 1).



The results are summarized in Table 1. The reaction of 1,3-decadiyne **1a** (1.0 equiv) with *o*-aminophenol **2a** ($\mathbb{R}^3 = \mathbb{H}$, 1.5 equiv) in the presence of a catalytic amount of Ru₃(CO)₁₂ and NH₄PF₆, followed by hydrolysis of the products, gave the benzoxazoles 3a and 4a, almost quantitatively, in a ratio of 3:1 (entry 1). Apparently, 3a was obtained through the C-C triple bond cleavage as shown in path a, and 4a was obtained through path b. Since $R^2 = H$, acetone **3a'** must be produced in the same yield as 3a and 2-octanone 4a' in the same yield as 4a. Although detection of acetone was not attempted due to its volatile characteristics, the formation of 2-octanone was detected (see also entry 2, vide infra). We examined a number of reaction conditions and finally found that the highest chemical yield and highest ratio of 3a/4a were obtained under the conditions similar to those of Wakatsuki's hydroamination.⁷ We tested various kinds of d⁸ and d¹⁰ transition metals that exhibit catalytic activities for hydroamination.8 When AuCl₃ and CuCl were used instead of Ru₃(CO)₁₂, a 3:1 mixture of 3a and 4a was obtained almost quantitatively. However, the use of PdCl₂, PtCl₂, and CuI afforded the products in 45-64% yields although the product ratio was again 3:1. The reaction of 1,3tetradecadiyne 1b gave a 4:1 mixture of 3b and 4b in 74% yield along with 2- dodecanone 4b' (11% yield) (entry 2). Cyclohexylsubstituted diyne 1c also gave a mixture of benzoxazoles 3c and 4c in the ratio of 7:1 in 81% yield (entry 3). The sterically bulkier diyne 1c gave higher ratio of 3:4. Interestingly, sterically more hindered benzoxazoles 3a-c, in comparison with 4a-c, were obtained as the major product. The reaction of 1d having 'Bu group as R¹ substituent gave almost exclusively **3d** in 81% yield (entry

Table 1. Ru-Catalyzed Carbon–Carbon Bond Cleavage of Terminal Diynes 1 with 2-Aminophenol $2a^a$

entry	R ¹	R ²	1	reaction time, h	yield, % ^b	3:4
1	"Hex	Н	1a	20	98	3:1
2	ⁿ Dec	Н	1b	36	74^c	4:1
3	Cyclohexyl	Н	1c	20	81	7:1
4	'Bu	Н	1d	20	81	>30:1
5	$Ph(CH_2)_2$	Н	1e	20	77	3:1
6	TIPSO(CH ₂) ₄	Н	1f	20	70	3:1
7	Cl(CH ₂) ₃	Н	1g	20	58	1:1

^{*a*} Reaction conditions: 0.75 mmol 2-aminophenol **2a**, 0.50 mmol diyne, 1 mol % Ru₃(CO)₁₂, 3 mol % NH₄PF₆, methanol (10 M), 80 °C. ^{*b*} Combined isolated yields based on 2-aminophenol. ^{*c*} 2-Dodecanone was obtained in 11% yield. TIPS = tris(triisopropyl)silyl

 Table 2.
 Ru-Catalyzed Carbon-Carbon Bond Cleavage of 1,3-Decadiyne 1a with Substituted Aminophenols 2^a

entry	R ³	2	reaction time, h	yield, % ^b	3:4
1	$4-NO_2$	2b	20	81	3:1
2	4-Cl	2c	20	97	3:1
3	4-Me	2d	20	95	3:1
4	4-OMe	2e	48	70	3:1
5	5-NO ₂	2f	20	68	3:1
6 ^c	5-Me	2g	20	87	3:1
7	3-Me	2h	20	79	4:1

^{*a*} Reaction conditions: 0.75 mmol 2-aminophenol **2**, 0.50 mmol diyne, 1 mol % $Ru_3(CO)_{12}$, 3 mol % NH_4PF_6 , methanol (10 M), 80 °C. ^{*b*} Combined isolated yields based on 2-aminophenols. ^{*c*} Concentration 5 M, due to the insolubility of **2g**.

4). When the phenyl- and siloxy-substituted diynes 1e and 1f were employed, the cleavage reaction also proceeded in good yields (entries 5 and 6). Even the chlorine-substituted diyne 1g gave the C-C bond cleavage products 3g and 4g in 58% yield (entry 7).

Next, we investigated the C–C bond cleavage with substituted aminophenols (Table 2). When a proton at the C-4 position was substituted with an electron-withdrawing NO₂ group (**2b**), the yield of the products became lower than that of **2a** (entry 1 of Table 2 vs entry 1 of Table 1). The chloro- and methyl-substituted aminophenols **2c** and **2d** gave results similar to those for **2a**. The reaction of 4-methoxy-aminophenol **2e**, having a strong electron-donating group, was very sluggish (entry 4). Thus, both a strong EWG and EDG at the C-4 position retarded the C–C bond cleavage. This trend was also observed when the 5-substituted aminophenols **2f** and **2g** were employed (entries 5 and 6).⁹ The sterically hindered aminophenol, 3-methyl-aminophenol **2h**, gave the products in lower yield, but the selectivity for **3** was slightly higher than for the others (entry 7).

The C–C cleavage reaction of internal diynes proceeded smoothly with palladium(II) catalysts. The catalyst $Pd(NO_3)_2$ gave the best result among palladium catalysts.¹⁰ Other catalysts such as Ru and Au did not work at all in the case of internal diynes. Among various solvents, "BuOH was the most efficient.¹¹ The

Table 3. Pd-Catalyzed Carbon-Carbon Bond Cleavage of Internal Diynes 1 with 2-Aminophenol 2a^a

entry	\mathbb{R}^1	R ²	1	reaction time, h	yield, % ^b	3:4
1	ⁿ Bu	ⁿ Bu	1o	4	97	1:1
2	Ph	Ph	1p	24	89	1:3

^{*a*} Reaction conditions: 0.75 mmol 2-aminophenol **2a**, 0.50 mmol diyne, 6 mol % Pd(NO₃)₂, *n*-butanol (10 M), 120 °C. ^{*b*} Combined isolated yields based on 2-aminophenol.

Scheme 1. A Proposed Mechanism for the C–C Bond Cleavage of Divnes



reaction of 5,7-dodecadiyne **1o** (0.50 mmol) with **2a** (0.75 mmol) in the presence of $Pd(NO_3)_2$ gave a 1:1 mixture of **3o** and **4o** in 97% yield (entry 1, Table 3). Here again, 2-heptanone **3o'** and 2-hexanone **4o'** were obtained along with **3o** and **4o**. Very similarly, the reaction of diphenylbutadiyne **1p** produced a 1:3 mixture of **3p** and **4p** in 89% yield together with 1-phenyl-2-pentanone **3p'** and acetophenone **4p'** (entry 2, Table 3).

The catalytic hydroamination of one of the alkyne groups of the divnes 1 to give the enamines 5 is the key step of the C-C bond cleavage (Scheme 1).6-8 Tautomerization of 5 gives the corresponding α,β -unsaturated imines 6. The conjugate addition of aminophenol 2a to 6 provides the β -aminoimines 7 and their tautomers 8. The intramolecular cyclization of the iminophenol groups of 7 and 8 gives the ketals 9 and 10, respectively. The C-C bond cleavage through the retro-Mannich-type reaction produces the benzoxazoles 4 and 3. The selectivity of products is determined by the relative size of R^1 and R^2CH_2 . When sterically hindered terminal divnes are used, the relative size of R¹ is larger than that of R^2CH_2 . Then, formation of 10 becomes more favorable than that of 9; with the bulkier R^1 , steric repulsion between R^1 and Ar of the sp² plane of 9 becomes stronger than that between $R^{2}CH_{2}$ and Ar of 10^{12} In the case of internal divide 1p, the size of R^1 is smaller than that of R²CH₂, and **4p** is selectively obtained.

To obtain supportive data for this mechanism, 2.2 equiv of aniline were treated with **1a** under the reaction conditions of the C–C bond cleavage. As expected, the β -aminoimine **11** was obtained in 62% yield (eq 2). Next, the ketone **12** and aminophenol **2a** were reacted in MeOH at 80 °C, giving the expected oxazole products **13** and **14** in 57% yield in a ratio of 3:1 (eq 3). These results strongly support the proposed mechanism shown in Scheme 1.



Catalytic C–C bond cleavage procedures are not popular in organic chemistry, and no method employing diynes is known. The present method supplies a new pair of scissors for C–C bond cleavage.

Supporting Information Available: Spectroscopic and analytical data of synthesized compounds and information on procedures (PDF). This material is available free of charge via the Internet at http:// pubs.acs.org.

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- (9) The precise reason for this electronic effect of the substituents is not clear, but a smilar effect was also observed in the Pd-catalyzed hydroamination of monoalkynes using *o*-aminophenols (unpublished results).
 (10) The yields of the reaction of 5,7-dodecadiyne **10** with **2a** in the presence
- (10) The yields of the reaction of 5,7-dodecadiyne 10 with 2a in the presence of palladium catalysts (6 mol %) and NH₄PF₆ (12 mol %) are as follows; Pd(NO₃)₂ (97%), PdCl₂(PPh₃)₂ (76%), Na₂PdCl₄ (69%) and PdCl₂ (65%).
- (11) Higher reaction temperature was needed (120 °C); therefore, "BuOH was used instead of MeOH.
- (12) The steric congestion at the quaternary carbon center of the oxazole ring is not so influential on the relative stability of 9 and 10 since the substituent R²CH₂ or R¹ takes an orthogonal direction to the oxazole plane.

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