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Nickel(0)-Catalyzed Unprecendented Zipper Annulation of Certain Conjugated Enynes

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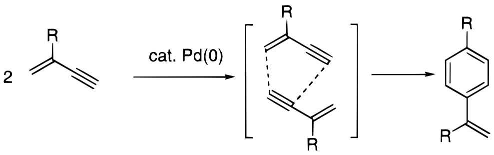
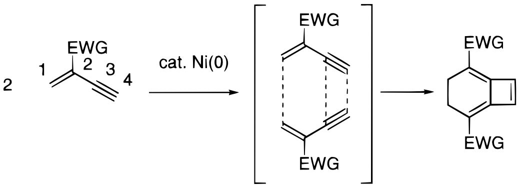
The transition-metal catalyzed cycloaddition reaction between unsaturated hydrocarbons is a powerful synthetic method, and many reactions have been reported in the literature.[1] Recently, we discovered palladium-catalyzed [4+2] *homo*-benzannulation of conjugated enynes[2] (eq 1) and this reaction was further



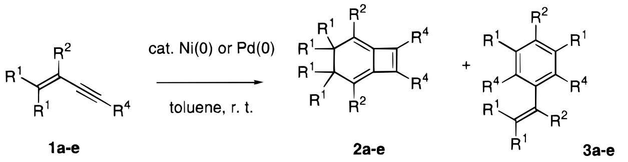
(1)

extended to the [4+2] *cross*-benzannulation of conjugated enynes with diynes,[3] which alleviated significantly the inherent problem associated with the [2+2+2] approach. In contiunation of our interest in understanding the reactivity profile of the [4+2] approach, we undertook an investigation of the reaction of conjugated enynes with electron-withdrawing groups. Quite interestingly, certain enynes **1** having electron-withdrawing groups underwent an unprecedented annulation reaction, which we call "zipper annulation", in the presence of nickel catalysts (eq 2).



(2)

Table 1. Nickel(0)-Catalyzed Zipper Annulation of Conjugated Enynes[a]



	enyne (**1**)					yield (%)	
entry	R^1	R^2	R^4	catalyst[b]	time	**2**	**3**
1	H	*n*-C$_6$F$_{13}$ (**1a**)	H	Ni(PPh$_3$)$_4$[c]	20 min	89	0
2	H	*n*-C$_6$F$_{13}$ (**1a**)	H	Ni(PPh$_3$)$_4$[d]	2 h	79	0
3	H	*n*-C$_6$F$_{13}$ (**1a**)	H	Pd(PPh$_3$)$_4$	5.5 h	33	30
4	H	PhCF$_2$ (**1b**)	H	Ni(PPh$_3$)$_4$	20 min	55	0[g]
5	H	*n*-C$_6$H$_{13}$CF$_2$ (**1c**)	H	Ni(PPh$_3$)$_4$	50 min[e]	52	0[g]
6	F	*n*-C$_9$H$_{19}$ (**1d**)	H	Ni(PPh$_3$)$_4$	20 h	27	0[h]
7	H	CN (**1e**)	*n*-C$_6$H$_{13}$	Pd(PPh$_3$)$_4$[f]	16 h	29	39

[a] To a mixture of Ni(cod)$_2$ (27.5 mg, 0.1 mmol) and PPh$_3$ (105 mg, 0.4 mmol) in dry toluene (0.5 mL) was added a solution of **1a** (1 mmol) in toluene (0.5 mL) at room temperature. For details, see Supporting Information. [b] The reaction was carried out in the presence of 10 mol % of the catalyst, unless otherwise noted. [c] The reaction was carried out in the presence of 5 mol % of the catalyst. [d] The catalyst was prepared by the reaction of NiBr$_2$(PPh$_3$)$_2$ and PPh$_3$ in the presence of Zn dust. See ref 5 [e] A solution of enyne was added dropwise to a solution of the catalyst for 30 min and stirred for 20 min at room temperature. [f] The reaction was carried out in the presence of 2 mol % of the catalyst. [g] Other products were not isolated. [h] A mixture of oligomerized compounds was isolated as a byproduct.

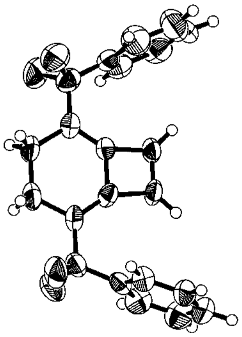


Figure 1. ORTEP drawing of **2b**.

2-Perfluorohexyl-1-butene-3-yne (**1a)** dimerized in a highly regiospecific manner in the presence of a catalytic amount of Ni(PPh$_3$)$_4$ (5 mol %), which was prepared in situ from Ni(cod)$_2$ and PPh$_3$, to give the strained bicyclo[4.2.0]octa-1,3,7-triene (**2a**) in 89% yield (Table 1, entry 1). When Ni(PPh$_3$)$_4$ was generated in situ from (PPh$_3$)$_2$NiBr$_2$, PPh$_3$, and Zn dust, a longer reaction time was required and the yield of **2a** decreased slightly. In entries 1 and 2, none of the usual [4+2] benzannulation product **3a** was produced. To make clear whether the formation of this unexpected product is due either to the substrate or to the Ni catalyst, the reaction of **1a** was carried out in the presence of Pd(PPh$_3$)$_4$ (entry 3). The Pd-catalyzed reaction was slower than the Ni-catalyzed reaction and a nearly 1:1 mixture of **2a** and **3a** was obtained in a lower yield (63% combined yield). Furthermore, the reaction of 2-hexyl-1-butene-3-yne in the presence of Ni(PPh$_3$)$_4$ (10 mol %) gave neither the corresponding zipper annulation product nor the [4+2] benzannulation adduct. Accordingly, it is clear that both the fluorinated substituent at C-2 and Ni(0) catalyst are essential in obtaining the zipper annulation product in high yield. Other catalysts such as CpCo(CO)$_2$[1c] and RhCl(PPh$_3$)$_3$,[4] which are effective catalysts for the cyclotrimerization of alkynes, were tested, but products such as **2** or **3** were not obtained. The reaction of α,α-difluorobenzyl- and 1,1-difluoroheptylenynes (**1b** and **1c**) proceeded smoothly to give the corresponding bicyclic products **2b** and **2c**, respectively, in fair yields (entries 4 and 5). Therefore, the zipper annulation takes place in general for enynes bearing perfluorinated or partially fluorinated C-2 substituents. Even a

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(1) For reviews, see, for example: (a) Lautens, M.; Klute, W.; Tam, W. *Chem. Rev.* **1996**, *96*, 49−92. (b) Schore, N. E. *Chem. Rev.* **1988**, *88*, 1081−1119. (c) Vollhardt, K. P. C. *Angew. Chem., Int. Ed. Engl.* **1984**, *23* (**8**), 539−644.

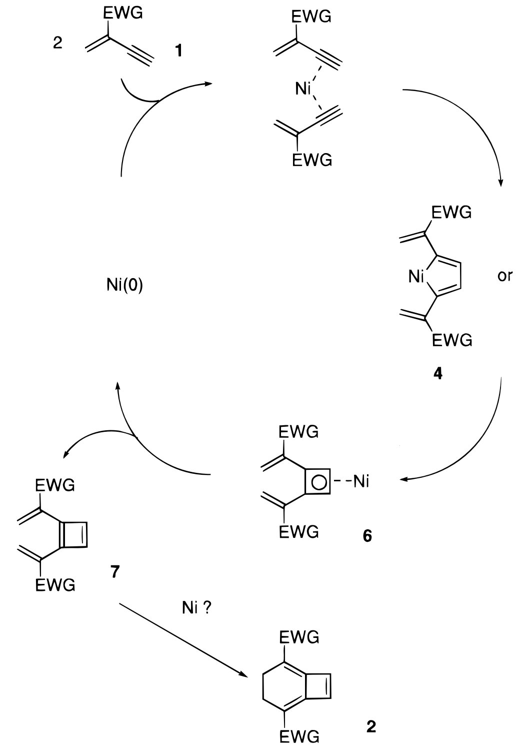
(2) Saito, S.; Salter, M. M.; Gevorgyan, V.; Tsuboya, N.; Tando, K.; Yamamoto, Y. *J. Am. Chem. Soc.* **1996**, *118*, 3970−3971.

(3) (a) Gevorgyan, V.; Takeda, A.; Yamamoto, Y. *J. Am. Chem. Soc.* **1997**, *119*, 11313−11314. (b) Gevorgyan, V.; Takeda, A.; Homma, M.; Sadayori, N.; Radhakrishnan, U.; Yamamoto, Y. *J. Am. Chem. Soc.* **1999**, *121*, 6391−6402. (c) Review: Gevorgyan, V.; Yamamoto, Y. *J. Organomet. Chem.* **1999**, *576*, 232−247.

(4) Neeson, S. J.; Steverson, P. J. *Tetrahedron* **1989**, *45*, 6239−6348 and references therein.

10.1021/ja993861k CCC: $19.00

Scheme 1



1,1-difluoroenyne **1d** having an *n*-nonyl substituent at C-2 underwent zipper annulation to give **2d** although the yield was low (entry 6). 2-Cyanoenyne **1e** reacted in the presence of a Pd(0) catalyst to give a mixture of **2e** and **3e** in 68% combined yield (entry 7), although the nickel-catalyzed reaction afforded a complex mixture of the products.

The structures of the bicyclic products **2a**−**e** were determined unambiguously by spectroscopic methods. Furthermore, the structure of **2b** was confirmed by an X-ray crystallographic analysis, and an ORTEP structure of **2b** is shown in Figure 1.[6] The two rings (four- and six-membered rings) were coplanar, and the distances of the carbon−carbon atoms are within the values expected for the structure of **2b**.[7]

Currently we assume the mechanism of this reaction as shown in Scheme 1. The Ni(0) species would coordinate with the alkyne moiety of the enynes **1** and the nickelacyclopentadiene **4** or bis π-allylnickel **5** would be formed.[8] The reductive elimination of the Ni(0) species from these complexes might proceed through the nickel cyclobutadiene complex **6** or directly give the unstable cyclobutadiene intermediate **7**. The existence of an electron-withdrawing group may be essential for facilitating the reductive elimination to **6** or **7**. A pericyclic reaction of **7** (or **6**) in either the presence or the absence of Ni(0) catalyst would give the bicyclo[4.2.0]triene **2**.

It is not yet clear why an electron-withdrawing group, especially a perfluoroalkyl group, is essential and why the Ni(0) catalyst is more efficient than the Pd(0) catalyst for this unprecedented zipper annulation reaction. Although it is premature to settle the mechanism, the strained bicyclo[4.2.0]trienes are formed from enynes in one step: especially the fluorinated trienes may be useful as a monomer for the synthesis of fluorinated polymers. We are currently investigating such a possibility in addition to the detailed mechanistic study of the zipper reaction.

Acknowledgment. This work was supported in part by the Japan Securities Scholarship Foundation.

Supporting Information Available: Synthetic procedures and characterization data for the compounds **1**−**3**, and the crystallographic data of **2b** (PDF). This material is available free of charge via the Internat at http://pubs.acs.org. See any current masthead page for ordering information and Web access instructions.

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[5] Iyoda, M.; Tanaka, S.; Otani, H.; Nose, M.; Oda, M. *J. Am. Chem. Soc.* **1988**, *110*, 8494−8500.

[6] Crystalographic data for **2b**: MF = $C_{22}H_{16}F_4$, MW = 356.36, orthoronbic; $a = 10.123(3)$ Å, $b = 30.654(4)$ Å, $c = 5.709(3)$ Å, $V = 1771(6)$ Å^3, space group $P2_12_12_1$, $Z = 4$, $D_c = 1.336$ g/cm^3. Data collection was done using Mo Kα radiation ($\mu = 1.06$ cm^{-1}) with a rotating anode diffractometer (50 kV, 120 mA). A total of 2316 reflections was collected, of which 1383 reflections with $I_o > 1\sigma(I_o)$ were used in the refinement. The final R factor was 0.065 ($R_w = 0.059$). The final difference peaks were $\rho_{max} = 0.20$ and $\rho_{min} = -0.20$ e/Å^3. For details, see Supporting Information.

[7] For details, see Supporting Information.

[8] It is widely accepted that the matallacyclopentadiene is an important intermediate in the transition metal catalyzed cyclotrimerization of alkynes. See: *Principles and Applications of Organotransition Metal Chemistry*; Collman, J. P., Hegedus, L. S., Norton, J. R., Finke, R. G., Eds.; University Science Books: Mill Vally, 1987: Section 18.3c, pp 870−879, and ref 1.