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# Metal-Catalyzed Bond Reorganization of 1,3-Diynes

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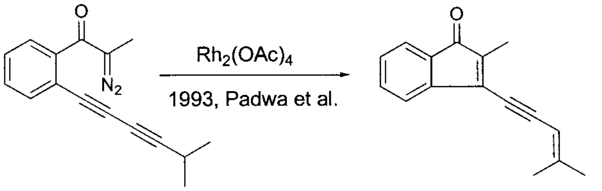
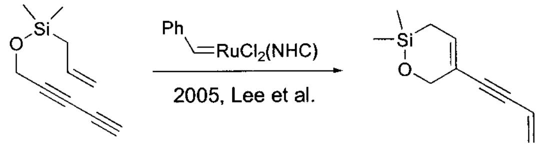
**Keywords:** Rearrangement / 1,3-Diyne / 1,5-Dien-3-yne / Metal carbene / Metallotropic [1,3]-shift

1,3-Diynes possessing propargylic heteroatom substituents provide functionalized 1,5-dien-3-ynes when catalyzed by platinum and gold. This rearrangement implies the involvement of metallotropic [1,3]-shift of the intermediate alkynyl metal carbene species.

The unusual bond reorganization of 1,3-diynes to 1,5-dien-3-ynes mediated by metal carbene species has been reported [Equations (1) and (2)].[1] Considering the frequent presence of this conjugated unsaturated system in many biologically active natural products such as enediynes[2] as well as in non-natural scaffolds possessing important optical and electrical properties like in polydiacetylenes,[3] the efficient method for the synthesis of this functionality should warrant further development.

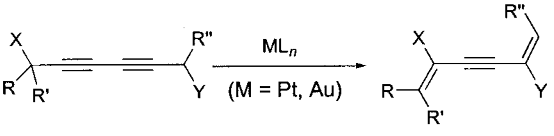


(1)



(2)

To broaden the scope of this novel and potentially powerful bond reorganization, we envisioned the capacity of carbophilic transition metals to generate metal carbene intermediates directly from appropriate alkynes,[4] which might subsequently carry out the expected bond reorganization process. Herein we report an efficient rearrangement of 1,3-diynes possessing propargylic heteroatom substituents to functionalized 1,5-dien-3-ynes [Equation (3)] in the presence of transition metal catalysts.



(3)

First, the general reactivity of diynes toward the bond reorganization was tested with a symmetrical diyne substrate **1** by the use of various metal catalysts (Table 1). Because gold catalysts have shown excellent reactivity toward mono alkyne-containing substrates,[5] several cationic and neutral gold catalysts[6] were tested first. With $(Ph_3P)AuCl/AgBF_4$, low conversion was observed (Entry 1), whereas $(Ph_3P)AuCl/AgSbF_6$ gave incomplete conversion after 12 h and significant decomposition ensued in longer reaction time (Entry 2). Gratifyingly, the reaction with a neutral gold catalyst $AuCl_3$ in dichloroethane at room temperature gave product **2** and **2′** in 65% yield with a 1:6 ratio of the two isomers (Entry 3), but AuCl gave low conversion (Entry 4). The stereochemistry of compound **2** was assigned unambiguously as *E*,*Z* based on the 1:1 ratio of two methyl groups at $\delta$ = 1.85 and 1.67 ppm, whereas the *E*,*E* stereochemistry was assigned for isomer **2′** ($\delta$ = 1.88 ppm) based on spectroscopic evidence. To further improve the efficiency of conversion, other known platinum-based carbophilic catalyst systems were tested.[7] Both $PtCl_2$ (80 °C in toluene) and $PtCl_2(PPh_3)_2$ (100 °C in toluene) gave low conversion (Entries 5 and 6). However, in the presence of atmospheric pressure of carbon monoxide,[8] $PtCl_2$ turned out to be an excellent catalyst, generating **2** and **2′** in 90% yield in a 8:1 ratio (Entry 7). Other metals such as $PdCl_2(PhCN)_2$ were found to be virtually unreactive (Entry 8).[9]

With the two reactive catalyst systems in hand ($AuCl_3$ and $PtCl_2$/CO), we next examined the reactions of diyne substrates containing combinations of different degrees of substitution and acyl groups at the propargylic sites (Table 2).[10] Treatment of **3a** with $PtCl_2$/CO or $AuCl_3$ returned only starting material (Entries 1 and 2). However,

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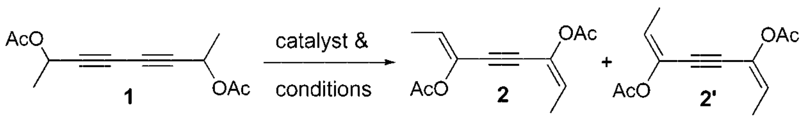
Table 1. Enyne bond reorganization with metal catalysts.[a]



| entry | catalyst / conditions | yield(%)[b] | 2 : 2'[e, f] |
|---|---|---|---|
| 1 | $(Ph_3P)AuCl/AgBF_4$, r.t., $CH_2Cl_2$ | <5[c] | — |
| 2 | $(Ph_3P)AuCl/AgSbF_6$, r.t., $CH_2Cl_2$ | 34[d] | 1 : 6 |
| 3 | $AuCl_3$, r.t., dichloroethane | 65 | 1 : 6 |
| 4 | AuCl, r.t., dichloroethane | 10[c] | — |
| 5 | $PtCl_2$, 80 °C, toluene | 30[c] | — |
| 6 | $(Ph_3P)_2PtCl_2$, 100 °C, toluene | <5[c] | — |
| **7** | **$PtCl_2$/CO, 80 °C, toluene** | **90** | **8 : 1** |
| 8 | $PdCl_2(PhCN)_2$, 70 °C, $CH_3CN$ | <5[c] | — |

[a] With 5 mol-% catalyst loading and 12 h of reaction time. [b] Isolated yields. [c] Low conversion. [d] Low yield due to product decomposition. [e] The ratio was determined by $^1$H NMR spectroscopy. [f] The stereochemistry was assigned by nOe experiment.

under identical conditions, more methyl-substituted substrates **1**, **3b**, and **3c** provided the bond reorganized products **2** (Table 1), **4b**, and **4c** in high yields (Entries 3–6), although the efficiency of the gold catalyst is consistently lower than that of platinum. The stark difference in reactivity of **1** and **3a**–**3d** can be justified on the basis of the sterics and electronics of putative intermediate **5** (Scheme 1).

On electronic grounds, alkyl substituents at the propargylic carbon would stabilize the developing cationic charge character, thereby facilitating the formation of **5** when $R^1$ and/or $R^2$ are methyls. On steric grounds, the increased steric pressure by these substituents at the propargylic carbon would facilitate the rearrangement of **5** to **6**.[11] The reactivity difference observed in **1** and **3a**–**3d** is in line with the formation of ruthenium carbene species in related reactions.[12] Consistent with this rationale, substrate **3d** containing the secondary and primary acetates gave product in only 23% yield with the platinum catalyst, but virtually no reaction with the gold catalyst (Entries 7 and 8).

The reactivity and selectivity trend observed for the reaction of **1** and **3a**–**3d** indicates that the initiation step from which the first vinyl acetate moiety forms is not highly stereoselective (the selectivity ranges from 2:1 to 12:1), but the termination step to form the second vinyl acetate is generally stereoselective (Entries 5 and 6).[13] As such, the total number of isomers are typically two (*E,Z* and *E,E*) instead of three (*E,Z*, *Z,Z*, and *E,E*).

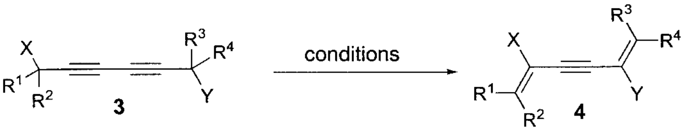
Acyl groups other than acetate such as *p*-nitrobenzoate (NBz) behave similarly in terms of yield but provide *E,Z*-selectivity in a less predictable fashion (Entries 9–11). The reaction of substrate **3f** gave 90% yield of **4f** in a 12:1 ratio (Entry 10) compared to 8:1 for the corresponding acetyl-containing substrate **1** with platinum catalyst, but gave 61% yield of **4f** with only 1.8:1 selectivity with a gold catalyst (Entry11). A symmetrical substrate **3e** provided compound **4e**, which gave a single crystal suitable for X-ray crystallographic analysis,[14] confirming the structural identity of **4e** (Figure 1).

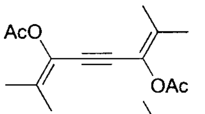
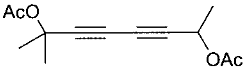
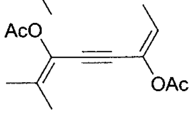
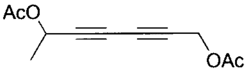
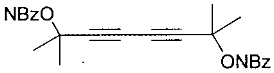
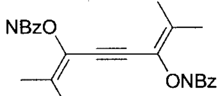
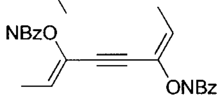
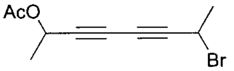
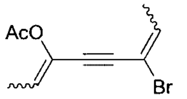
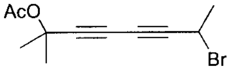
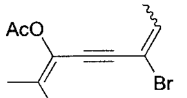
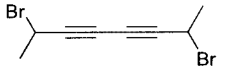
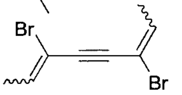
Bromides **3g**–**3i** also participated in the rearrangement reaction with platinum catalyst.[15] Diyne **3g** with a secondary acetate and a secondary bromide gave **4g** in 91% yield with 1.8:1 ratio of two major isomers (Entry 12), however **3g** was recovered unchanged when a gold catalyst was used (Entry 13). Diyne **3h** with a tertiary acetate and a secondary bromide gave 70% yield of **4h** in a 4.3:1 ratio with platinum catalyst (Entry 14). The reaction of dibromo-1,3-diyne **3i** gave 28% of the rearranged product **4i** in a 1.6:1 ratio (Entry 16). This result clearly indicates that a bromide functionality is not a good initiator to form the required carbene intermediate, but it is a suitable terminating group for the rearrangement to provide the observed vinyl bromides **4g**–**4i**.

Although the reaction mechanism for this bond reorganization process is yet to be further elucidated we propose the involvement of the initially formed carbenoid **6** as shown in Scheme 1 followed by its metallotropic [1,3]-shift to **7** (Scheme 2).[16] While **6** and **7** are in equilibrium, a polar functional group such as acyl and bromide would form intermediate **8**, which then undergoes an elimination reaction, delivering the observed product **4**. An alternative reaction mechanism that does not rely on the proposed metallotropic [1,3]-shift would form product **8** via intermediates **9** and **7**.[1a]

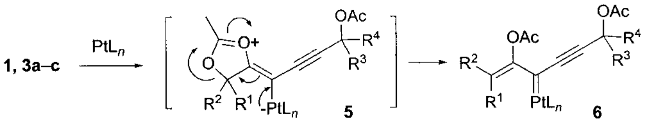
An additional insight into the nature of the intermediates in the rearrangement of 1,3-diynes possessing propargylic heteroatom substituents was obtained when an excess amount of a nucleophile (LiBr) was added to the reaction of **1** and **3c**. Under these modified reaction conditions, **1** and **3c** gave not only the expected products **2** and **4c** but also a bromide-incorporated product **4g** and **4h** in 8.1:1 and 6.5:1 ratios, respectively. The formation of **4g** and **4h** is tentatively rationalized by bromide attack on **10** to generate **11** followed by metal acetate elimination. This, at least, supports the existence of an intermediate **7** although it does not shed light on the involvement of metallotropic shift (Scheme 3).

Table 2. Enyne bond reorganization of diynes possessing acyl groups at the propargylic sites.[a]



| entry | | | condition[b] | | Product | yield (%)[c] | ratio[d] |
|---|---|---|---|---|---|---|---|
| 1 | **3a** |  | **A** | **4a** | — | 0[e] | — |
| 2 | | | **B** | | | 0[e] | — |
| 3 | **3b** |  | **A** | **4b** |  | 93 | — |
| 4 | | | **B** | | | 80 | — |
| 5 | **3c** |  | **A** | **4c** |  | 93 | 15 : 1 (*E*:*Z*) |
| 6 | | | **B** | | | 62 | only *E* |
| 7 | **3d** |  | **A** | **4d** |  | 23 | 2.2 : 1 (*Z*:*E*) |
| 8 | | | **B** | | | <5[e] | — |
| 9 | **3e** |  | **A** | **4e** |  | 91 | — |
| 10 | **3f** |  | **A** | **4f** |  | 90 | 12 : 1 (*ZE*:*EE*) |
| 11 | | | **B** | | | 61 | 1.8 : 1 (*ZE*:*EE*) |
| 12 | **3g** |  | **A** | **4g** |  | 91 | 1.8 : 1[f] |
| 13 | | | **B** | | | <5[e] | — |
| 14 | **3h** |  | **A** | **4h** |  | 70 | 4.3 : 1 (*E*:*Z*) |
| 15 | | | **B** | | | <5 | — |
| 16 | **3i** |  | **A** | **4i** |  | 28 | 1.6 : 1[f] |

[a] With 5 mol-% catalyst loading. [b] **A**: $PtCl_2$/CO, toluene, 80 °C, **B**: $AuCl_3$, dichloroethane, room temp. [c] Isolated yields. [d] The ratio was determined based on $^1H$ NMR spectroscopy. [e] Starting material was recovered. [f] Stereochemistry was not determined.



Scheme 1. Steric and stereoelectronic influence in the formation of alkynyl metal carbene complexes.

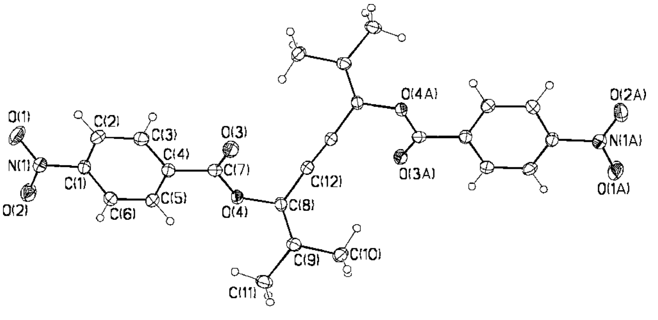
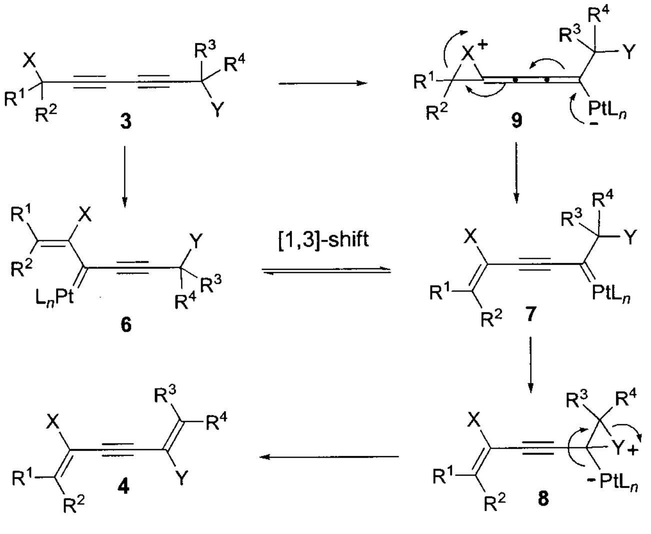
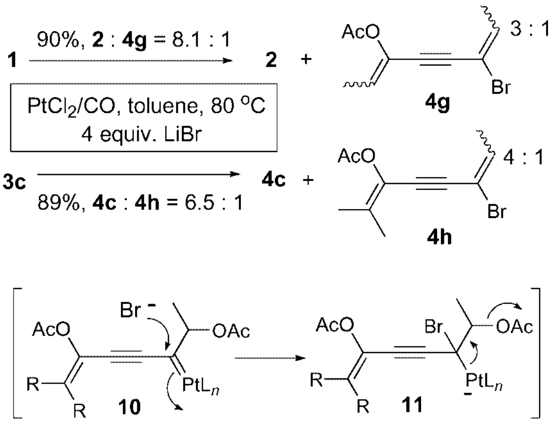


Figure 1. X-ray structures of **4e**.



Scheme 2. Possible reaction mechanisms.



Scheme 3. Reaction with an external nucleophile.

In conclusion, we have demonstrated an efficient rearrangement of 1,3-diynes[17] possessing propargylic heteroatom substituents to functionalized 1,5-dien-3-ynes in the presence of electrophilic transition-metal catalysts. The mechanism of bond reorganization process is most consistent with the involvement of the formation of putative platinum and gold carbene species followed by its metallotropic [1,3]-shift.

**Supporting Information** (see also the footnote on the first page of this article): General procedures for the synthesis of diynes and their metal-catalyzed reactions. Characterization information of represented compounds and selected X-ray structure data of **4e**.

## Acknowledgments

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[8] As pointed out in ref.[7c], carbon monoxide is believed to be a ligand to increase the electrophilicity of Pt due to its strong $\pi$-acceptor capacity. See also J. M. Lutton, R. W. Parry, *J. Am. Chem. Soc.* **1954**, *76*, 4271.

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[10] For the preparation of unsymmetrical diynes, see: J. P. Marino, H. N. Nguyen, *J. Org. Chem.* **2002**, *67*, 6841. Details of substrate preparation are described in the Supporting Information.

[11] In current reactions, formation of an allene was not observed. For examples of an allene formation, see: a) K. Cariou, E. Mainetti, L. Fensterbank, M. Malacria, *Tetrahedron* **2004**, *60*, 9745; b) A. Fürstner, P. Hannen, *Chem. Commun.* **2004**, 2546.

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[13] The stereochemistry was determined by nOe experiment, see Supporting Information.

[14] For selected crystal structure data, see Supporting Information. CCDC-602384 contains the complete crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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