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Gold and Brønsted acid catalyzed isomerization of [3]cumulenols and [3]cumulenones: efficient syntheses of 1,5-dien-3-ynes and furan derivatives

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ABSTRACT

An attractive method for assembling π-conjugated dienynes with high stereoselectivity was achieved by dehydration reaction of TMS-substituted [3]cumulenols catalyzed by TsOH·H_2O. On the other hand, cycloisomerizations of the corresponding [3]cumulenones catalyzed by gold(I) complexes afford vinyl furans through activation of the cumulenic double bond via a π-complex, and during the process, deprotonation from an alkyl group on cumulene terminus takes place to induce the isomerization.

[3]Cumulenes have attracted much attention in recent years since they have potential applications in antitumor drug design[1] and as advanced materials with unique electronic and photonic properties.[2] Cumulenes are also versatile synthetic intermediates in organic synthesis[3], such as in Diels–Alder reaction,[3a] domino Heck/C–H activation,[3b] cycloaddition,[3c] sulfurization,[3d] as ligands for metal complexation[3e–g], and so on. Although much progress has been achieved in this field, the reaction chemistry of functionalized [3]cumulenes has far less been developed, this may be due to the limited synthetic methods that are available for these compounds.[4] Recently, we have shown that zirconocene–ethylene mediated coupling of 1,3-butadiynes with aldehydes or ketones provides an one-pot efficient method for *cis*-[3]cumulenols.[5] We also found the diverse reactivity of zirconacyclocumulenes derived by the coupling of benzynezirconocenes with 1,3-butadiynes toward aldehydes or aroyl cyanides, leading to *cis*-[3]cumulenols and [3]cumulenones, respectively.[6] These results prompted us to explore the synthetic utilization of these oxygen-functionalized [3]cumulenes. Herein we'd like to report the isomerization reactions of tetra-substituted cumulenes under the catalysis of Brønsted acids or gold catalyst. These methods offer the facile syntheses of 1,5-dien-3-ynes and vinylfurans under mild reaction conditions.

Conjugated molecules, such as enynes, enediynes, tetraethynylethenes (TEE, 3,4-diethynylhex-3-ene-1,5-diyne), (*E*)-1,2-diethynylethenes, (DEE, (*E*)-hex-3-ene-1,5-diyne) and 1,5-dien-3-ynes are attractive compounds and versatile building blocks for the construction of π-conjugated polymers and designed nanoarchitectures.[7,8] Especially, due to the high π-electron delocalization behavior in these π-conjugated molecules or polymers, they have shown a wide application in advanced organic materials, such as in molecular wires, electroluminescence, switches, ferromagnetism, nonlinear optics, organic conductors, etc.[7] During the course of our studies on the reactivity of tetra-substituted [3]cumulenols, we found that 1,5-dien-3-ynes[9] could be formed with high stereoselectivity via the Brønsted acid catalyzed dehydration of cumulenols. Dehydration processes mediated by Brønsted acids or Lewis acids are well documented reactions. However, a 1,6-elimination of H_2O in which the leaving group and the hydrogen have intervening π bonds such as in cumulene derivatives is rare. It was found that in the presence of a catalytic amount of TsOH·H_2O (10 mol %), the alcohol **1** was smoothly converted into dienynes **2** with high stereoselectivities (Table 1). (1*E*,5*E*)-isomer of **2** was obtained as major products as determined by the ^1H NMR of the reaction mixtures. The configuration of the dienyne double bond was determined by a spectroscopic method of product **2a** using the NOESY technique. Representative results are given in Table 1. The reaction could be readily applied to TMS-substituted cumulenols. A wide range of aromatic substituents at C-1 bearing electron-donating or electron-withdrawing substituents could be incorporated successfully into the sequence, generating the corresponding dienynes in good selectivity and good yields (74–93%).

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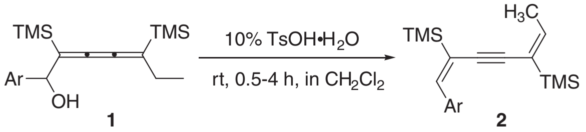
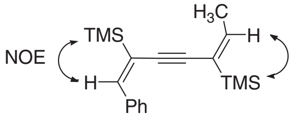
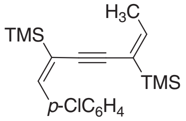
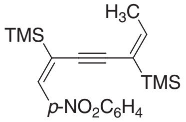
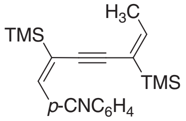
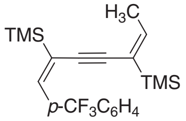
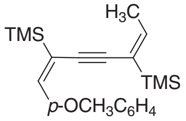
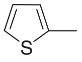
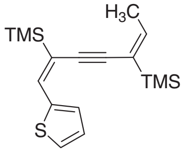
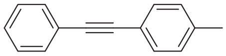
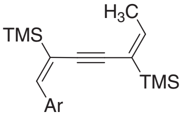
Table 1
Bronsted acids catalyzed synthesis of (1*E*,5*E*)-1,5-dien-3-ynes



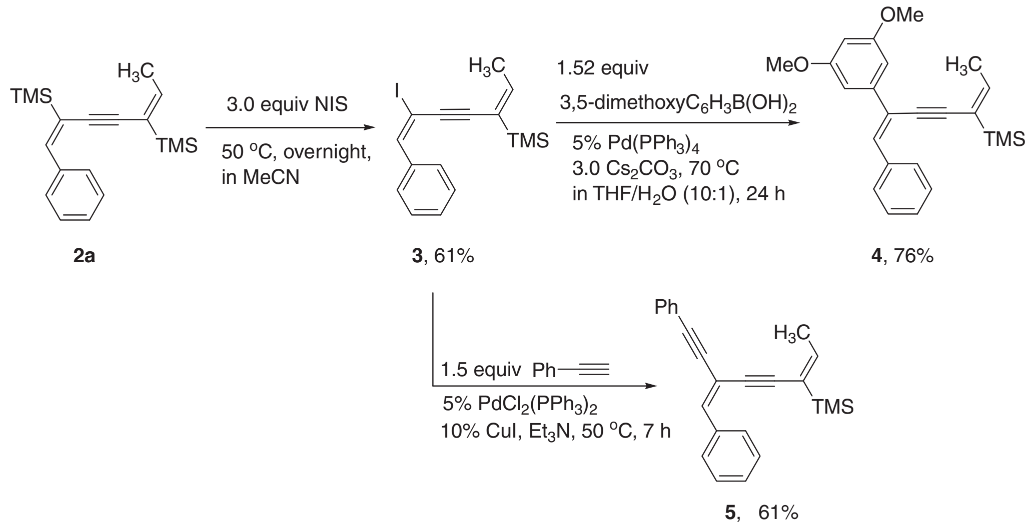
Entry	Ar	Product		Yield[a] (%)	Isomeric purity[b]
1	Ph (**1a**)		**2a**	88	>99:1
2	*p*-ClC_6H_4 (**1b**)		**2b**	74	>99:1
3	*p*-$NO_2C_6H_4$ (**1c**)		**2c**	93[c]	
4	*p*-CNC_6H_4 (**1d**)		**2d**	86	>98:2
5	*p*-$CF_3C_6H_4$ (**1e**)		**2e**	81	>99:1
6	*p*-$OCH_3C_6H_4$ (**1f**)		**2f**	84	97:3
7	 (**1g**)		**2g**	80	98:2
8	 (**1h**)	 Ar= 4-(phenylethynyl)phenyl	**2h**	77	>93:7

[a] Isolated yields of the pure products.
[b] Determined by the ^1H NMR of the crude reaction mixture.
[c] Containing small amount of impurity.

The functionalities of –Cl, –NO_2, –CN, CF_3, –MeO, and phenylalkynyl groups in the aromatic ring were well tolerated during the reaction. A thienyl group at C-1 was also compatible under the reaction conditions, furnishing **2g** in 80% yield (entry 7). The simplicity of this method should make it valuable to stereodefined dienynes as well as poly(enynes), which may find potential utilities in material science.

The utility of TMS-substituted 1,5-dien-3-ynes produced by this chemistry as useful synthetic intermediates for further elaborations was demonstrated through a Si–I exchange reaction followed by a Pd-catalyzed Suzuki coupling[10] reaction (Scheme 1). Treatment of **2a** with 3 equiv of NIS selectively afforded monoiodine compound **3**, which underwent coupling reaction with aryl boronic acid in the presence of Pd catalyst to give the arylated product **4** in 76% yield and coupling with phenylacetylene to furnish the conjugated eneyne product **5** in 61% yield (97% pure). The structure of **3** was confirmed by 2D NMR spectra.

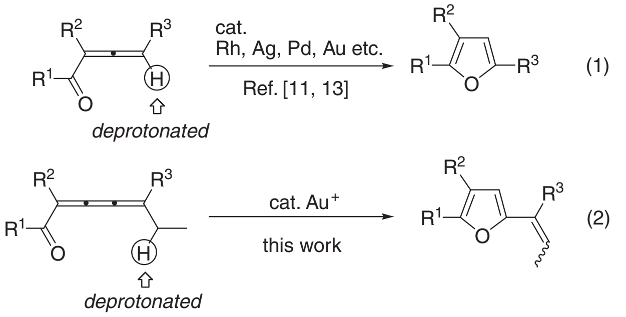
We proceeded to examine the reactivity of TMS-substituted [3]cumulenones, and concentrated on metal-catalyzed cycloisomerization reactions. Although transition-metal-catalyzed cycloisomerizations of allenyl ketones are well known, there is no report for [3]cumulenones. Metal catalyzed cyclization of allenyl ketones are attractive methods for the synthesis of furans. For example, Marshall et al. discovered that allenyl ketones can be rearranged into furans under mild conditions by Rh(I) or Ag(I) catalysts.[11] Hashmi had reported the Pd-catalyzed dimerization of



Scheme 1. Transformation of **2a** to various functionalized dienynes.

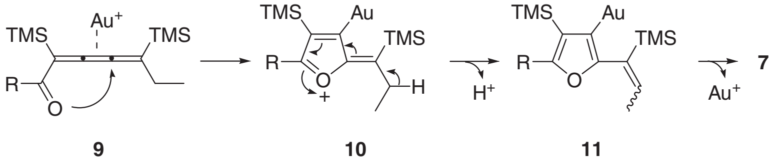
terminal allenyl ketones[12] and Au(III)-catalyzed cyclization of allenyl ketones.[13] A novel 1,2-migration of functional groups, such as halogen, acyloxy, phosphatyloxy groups in allenones was also to be reported by Gevorgyan for the synthesis of furans.[14] Except for 1,2-migration reactions, usually at least one hydrogen substituent in the allenones employed in these studies is required to induce the isomerization (Scheme 2, Eq. 1). [3]Cumulenyl ketones can be viewed as an extension of allenyl ketones by incorporation of a third cumulated π bond, which would represent an important class of suitable substrates for this strategy. Here we found that gold could catalyze the cycloisomerization of cumulenones to substituted vinyl furans, in which deprotonation from an alkyl group on cumulene terminus takes place to induce the isomerization (Scheme 2, Eq. 2).

The requisite cumulenones **6** can be easily obtained by oxidation of the corresponding *cis*-[3]cumulenols by IBX in DMSO in 40–94% yields. However, during the oxidation process, a *Z*–*E* isomerization occurred, thus cumulenone **6** was used as a mixture of *Z*/*E* isomers. After much effort, we found that vinyl furan derivatives **7** or desilylated product **8** can be formed selectively under the catalysis of $(PPh_3)AuCl/AgOTf$ (Table 2). For example, cumulenone **6c** bearing a *p*-$NO_2C_6H_4$ group afforded the corresponding vinyl furan **7c** in 67% yield as a 4.3:1 mixture of *E* and *Z* isomers at room temperature, along with 24% desilylated product **8c** (Table 2, entry 3). Simply increasing the reaction temperature to 80 °C and using dichloroethane as solvent resulted in the formation of desilylated product **8c** in 82% yield as a sole product (entry 4). The formation of **8c** is supposed to be the result of a competitive reaction pathway involving a gold-catalyzed desilylation process. The *E*-configuration of the major isomers in vinyl furan products has been confirmed by NOESY spectra of **7c** and **8c**. We have chosen the following reaction conditions: 2 mol % of $(PPh_3)AuCl/AgOTf$ in $ClCH_2CH_2Cl$ stirred at 80 °C (condition B) for the study of the reaction scope.



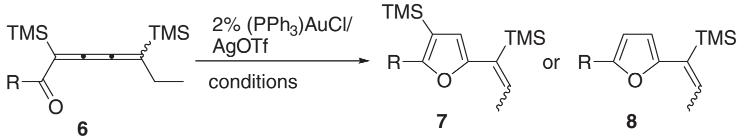
Scheme 2. Metal-catalyzed cycloisomerization reactions of allenones or cumulenones.

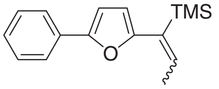
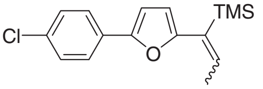
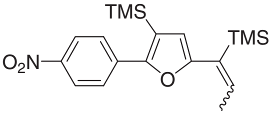
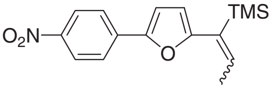
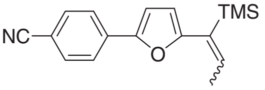
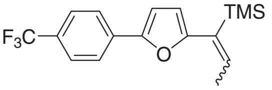
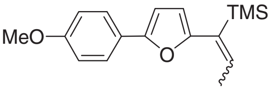
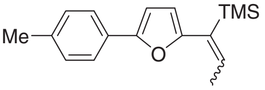
To test the generality of this chemistry, a wide variety of [3]cumulenones have been examined in this cyclization process (Table 2). The aromatic ring at C-1 bearing electron-withdrawing as well as electron-donating substituents all reacted very well to provide the di- or tri-substituted furan products in good to high yields. Cyclization of a *para*-chlorophenyl-substituted **6b** generated the corresponding desilylated furan **8b** in 86% yield (*E*/*Z* = 10.6:1), and only a trace of any byproducts was formed (Table 2, entry 2). The reaction of 4-CNC_6H_4 substituted **6d** resulted in the formation of vinyl furan **8d** in 84% yield with high stereoselectivity (entry 5, 40:1 of *E*/*Z* isomers). Introducing a stronger electron-withdrawing group such as $-CF_3$ does not influence the efficiency of this reaction, the corresponding product **8e** was obtained in 73% yield upon heating at 80 °C (entry 6). The reaction also proceeded smoothly with the substrate bearing electron-donating group at aromatic ring, leading to the products **8f** and **8g** in 60–64% yields (entries 7 and 8). It is interesting to note that in the case of vinyl furan **8g**, a *Z* to *E* isomerization occurs during



Scheme 3. Proposed mechanism for the formation of vinyl furans **7**.

Table 2
Gold-catalyzed cyclization of *cis*-[3]cumulenones to vinyl furans



Entry	R	Conditions[a]	Product	Yield[b] (%)
1	Ph (**6a**)	B, 2 h	 (**8a**)	82(4.6:1)
2	*p*-ClC$_6$H$_4$ (**6b**)	B, 3 h	 (**8b**)	86(10.6:1)
3	*p*-NO$_2$C$_6$H$_4$ (**6c**)	A, 6 h	 (**7c**)	67(4.3:1)[c]
4	(**6c**)	B, 3 h	 (**8c**)	82(5.0:1)
5	*p*-CNC$_6$H$_4$ (**6d**)	B, 3 h	 (**8d**)	84(40:1)
6	*p*-CF$_3$C$_6$H$_4$ (**6e**)	B, 2 h	 (**8e**)	73(2.8:1)
7	*p*-MeOC$_6$H$_4$ (**6f**)	B, 10 h	 (**8f**)	60(6.8:1)
8	*p*-MeC$_6$H$_4$ (**6g**)	B, 2.5 h	 (**8g**)	64(8.5:1)

[a] Condition A: room temperature, in CH$_2$Cl$_2$. Condition B: 80 °C, in ClCH$_2$CH$_2$Cl.
[b] Isolated yields. The ratio of *E*/*Z* isomer is given in parentheses.
[c] Compound **8c** was also isolated in 24% yield as a mixture of two isomers in a ratio of 3:1.

standing in CDCl$_3$ solution at room temperature. For example, a 98:2 mixture of *E*/*Z* isomers was obtained after 7 days.

We propose the following mechanism for this reaction (Scheme 3). In the first step, the activation of cumulenone by forming a π-complex with PPh$_3$Au$^+$ dramatically enhances the electrophilicity of the cumulenic double bond, which facilitates the nucleophilic attack by the carbonyl oxygen. Thus the subsequent 5-*exo-dig* ring closure occurs followed by deprotonation from the ethyl group to afford furanyl gold intermediate **11**. Deauration furnishes the vinyl furan product **7**. The furan derivatives of **8** might be formed by gold-assisted desilylation of **7**.

In summary, we present here a study on the reactivity of tetra-substituted [3]cumulenols or [3]cumulenones with Brønsted acids and gold catalysts. These transformations provide efficient routes to 1,5-dien-3-ynes with high stereoselectivity and vinyl furans under mild reaction conditions, which are of interest in material science and organic synthesis. Further studies to extend the scope and synthetic utility of functionalized cumulenes are in progress in our laboratory.

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2011.02.057.

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