

Cycloaddition

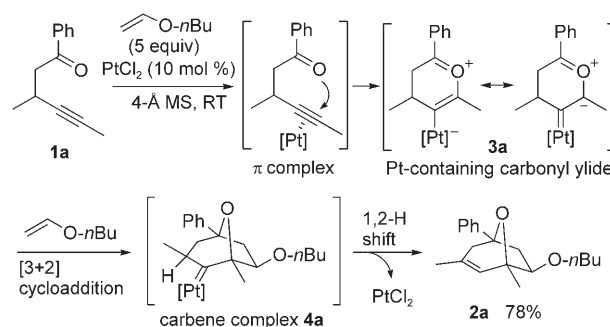
Platinum(II)-Catalyzed Reaction of γ,δ -Ynones with Alkenes for the Construction of 8-Oxabicyclo[3.2.1]octane Skeletons: Generation of Platinum-Containing Carbonyl Ylides from Acyclic Precursors**

Hiroyuki Kusama, Kento Ishida, Hideaki Funami, and Nobuharu Iwasawa*

Transition-metal-containing zwitterionic intermediates generated through the electrophilic activation of alkynes toward nucleophilic attack by a carbonyl oxygen atom or imino nitrogen atom can be used in addition reactions with nucleophiles or cycloaddition reactions with alkenes or alkynes to prepare synthetically useful heterocyclic compounds.^[1–5] However, in almost all cases, it is necessary to employ rigid aromatic substrates for the effective generation of the zwitterionic species. Herein, we report a catalytic method for the generation of nonconjugated platinum(II)-containing carbonyl ylides from acyclic γ,δ -ynones and the [3+2] cycloaddition of such ylides with electron-rich alkenes to give synthetically useful 8-oxabicyclo[3.2.1]octane derivatives in good yield.

First, we examined the reaction of the acyclic γ,δ -ynone **1a**, which contains a methyl substituent at the propargylic position, with *n*-butyl vinyl ether in the presence of a catalytic amount of various electrophilic transition-metal complexes. Although several typical complexes, such as $[\text{W}(\text{CO})_5(\text{thf})]$, $[\text{ReCl}(\text{CO})_5]/h\nu$, $[\text{IrCl}(\text{cod})_2]$, AuCl_3 , and $[\text{AuClPPH}_3]/\text{AgSbF}_6$, caused either no reaction or hydration of the alkyne moiety, PtCl_2 ^[6] was found to be very effective. Thus, the treatment of **1a** with platinum(II) chloride (10 mol %) in the presence of *n*-butyl vinyl ether at room temperature gave the 8-oxabicyclo[3.2.1]octane derivative **2a** in 78% yield as a single diastereoisomer with the butoxy substituent in an *exo* orientation.

We propose the following mechanism for the formation of **2a**: The electrophilic activation of the alkyne moiety in **1a** by platinum(II) chloride induces the attack of the carbonyl oxygen atom onto the alkyne in a 6-*endo* manner to generate the platinum-containing carbonyl ylide **3a**, which then undergoes a [3+2] cycloaddition reaction with *n*-butyl vinyl ether to give the nonstabilized carbene complex **4a**. Finally, a 1,2-hydrogen-atom shift to the carbene carbon atom gives the product **2a** with regeneration of the catalyst (Scheme 1).



Scheme 1. Generation and reaction of the platinum-containing carbonyl ylide **3a** derived from the acyclic γ,δ -ynone **1a**.

Examination of the reaction with several electron-rich alkenes revealed that unsubstituted vinyl ethers, such as *p*-methoxybenzyl vinyl ether, could be used as cycloaddition partners (Table 1, entry 1). Furthermore, the desired product

Table 1: Reaction of various acyclic γ,δ -ynones that contain a substituent at the propargylic position.

Entry	R ¹	R ²	R ³	R ⁴	<i>t</i>	Yield [%]
1	Ph	Me	Me	OPMB	27 h	76
2	Ph	Me	Me	Ph	5 days	43
3	Ph	EtO	Me	<i>n</i> BuO	8 h	84
4	Et	Me	<i>n</i> -pentyl	<i>n</i> BuO	5 days	77

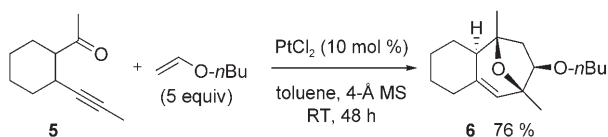
was formed in moderate yield when styrene was used (Table 1, entry 2). Acyclic γ,δ -ynones with an alkyl or alkoxy group at the propargylic position were used successfully as substrates to give synthetically useful 8-oxabicyclo[3.2.1]octane derivatives in good yield (Table 1, entries 3 and 4). The cyclohexane derivative **5** also underwent the desired transformation with *n*-butyl vinyl ether to give the tricyclic compound **6** in 76% yield (Scheme 2). In all cases, the reaction afforded the corresponding *exo* product stereoselectively.

The use of γ,δ -ynone substrates **7** with no substituent at the propargylic position led to interesting results. The reaction of **7a** with *n*-butyl vinyl ether under the reaction conditions used for the transformation of ynones **1** proceeded smoothly at room temperature. However, careful analysis of

[*] Dr. H. Kusama, K. Ishida, Dr. H. Funami, Prof. Dr. N. Iwasawa
Department of Chemistry
Tokyo Institute of Technology
O-okayama, Meguro-ku, Tokyo 152-8551 (Japan)
Fax: (+81) 3-5734-2931
E-mail: niwasawa@chem.titech.ac.jp

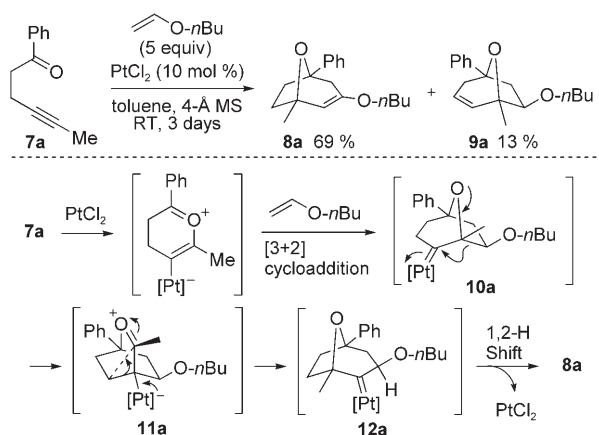
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Scheme 2. Reaction of the cyclohexane derivative **5**.

the products obtained revealed that the major product was the 8-oxabicyclo[3.2.1]octane derivative **8a**, rather than **9a**, which might have been expected to form as the major product on the basis of the results observed with ynones **1**. Compound **9a** was obtained as a minor product (Scheme 3).



Scheme 3. Platinum-catalyzed reaction of acyclic γ,δ -ynones with no substituent at the propargylic position.

The formation of this new type of product **8a** could be explained as follows (Scheme 3): The nonstabilized intermediate carbene complex **10a** is produced from **7a** in a similar manner to the formation of **4a** from **1a**. Instead of the 1,2-hydrogen-atom shift observed for substrates with a substituent at the propargylic position, **10a** undergoes 1,2-alkyl migration^[1c,f,h,2k,7] to generate the oxonium intermediate **11a**.^[8] A further alkyl-group migration to the oxonium moiety produces another nonstabilized carbene intermediate **12a**, which undergoes a 1,2-hydrogen-atom shift to give product **8a**.^[9]

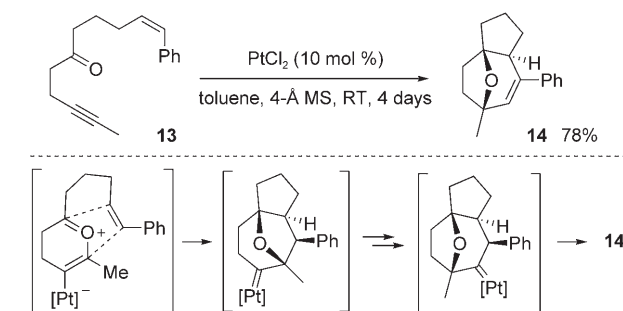
The generality of the reaction of this type of substrate is summarized in Table 2. 8-Oxabicyclo[3.2.1]octane derivatives **8** were obtained as the major product in all reactions of acyclic γ,δ -ynones with no substituent at the propargylic position. Even an active-methyne compound underwent this reaction to give the desired 8-oxabicyclo[3.2.1]octane derivative in good yield (Table 2, entry 6).

Finally, we attempted an intramolecular version of this reaction. Thus, treatment of the acyclic γ,δ -ynone **13**, which contains a styrene moiety, with a catalytic amount of platinum(II) chloride gave the desired product of intramolecular cyclization, the useful polycyclic compound **14**, in good yield (Scheme 4).

Table 2: Reaction of various acyclic γ,δ -ynones with no substituent at the propargylic position.

Entry	R ¹	R ²	R ³	R ⁴	R ⁵	t	Yield [%]
1	Ph	H	H	Me	OEt	39 h	68
2	Ph	H	H	Me	OPMB	31 h	84
3	Ph	H	H	<i>n</i> Bu	<i>n</i> BuO	5 days	67
4 ^[a]	Ph(CH ₂) ₂	H	H	Me	<i>n</i> BuO	4 days	55
5 ^[b]	Ph	Me	Me	Me	<i>n</i> BuO	4 days	52
6 ^[c]	Ph	CO ₂ Et	H	Me	<i>n</i> BuO	6 days	55

[a] [PtCl₂(CH₂CH₂)₂]₂ (5 mol %) was used as the catalyst. [b] The product was obtained as a ketone. [c] PtCl₂: 30 mol %.



Scheme 4. Intramolecular reaction.

In conclusion, we have demonstrated the generation of bifunctional reactive species, platinum(II)-containing carbonyl ylides, from acyclic γ,δ -ynones and the reaction of these intermediates with electron-rich olefins to give synthetically useful 8-oxabicyclo[3.2.1]octane derivatives.^[10] The presence or absence of a substituent at the propargylic position of the ynone substrate determines the course of the reaction after the formation of an intermediate carbene complex, so that two types of 8-oxabicyclo[3.2.1]octane derivatives can be formed selectively.

Experimental Section

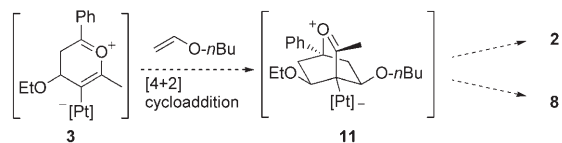
General procedure: An alkene (0.5–1.0 mmol) was added to a mixture of an acyclic γ,δ -ynone (0.1 mmol), PtCl₂ (0.01 mmol), and molecular sieves (4 Å; 100 mg) in toluene (1.0 mL) at room temperature, and the resulting mixture was stirred at room temperature until TLC showed the complete disappearance of the γ,δ -ynone. The reaction was then quenched with saturated, aqueous NaHCO₃, and the reaction mixture was filtered through a short pad of celite. The aqueous layer was extracted with ethyl acetate three times, and the combined organic layers were washed with brine, then dried over MgSO₄. The solvent was removed under reduced pressure, and the residue was purified by chromatography on silica gel to afford the corresponding 8-oxabicyclo[3.2.1]octane derivative.

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- [8] Another possible reaction pathway is the [4+2] cycloaddition^[4b] of a platinum-containing zwitterionic intermediate **3** with *n*-butyl vinyl ether to give the oxonium intermediate **11** directly. However, at present, we believe the [3+2] cycloaddition pathway to be the most plausible pathway in the present reaction on the basis of the experimental result shown in Table 1, entry 3. If the reaction proceeds through a [4+2] cycloaddition, a mixture of **2** and **8** should form from the oxonium intermediate **11** owing to the pseudosymmetric structure of **11**. We are currently carrying out calculations of the reaction pathways to obtain further information on the exact mechanism of this reaction. For a discussion, see: B. F. Straub, *Chem. Commun.* **2004**, 1726–1728.



- [9] It is likely that the 1,2-hydrogen-atom shift to the electron-deficient carbene carbon atom has a hydride-shift character, and that the electron-donating effect of the substituent at the propargylic position of substrates **1** (or the *n*BuO substituent in **12a**) promotes the 1,2-hydrogen-atom shift.
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