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Cycloaddition

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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**

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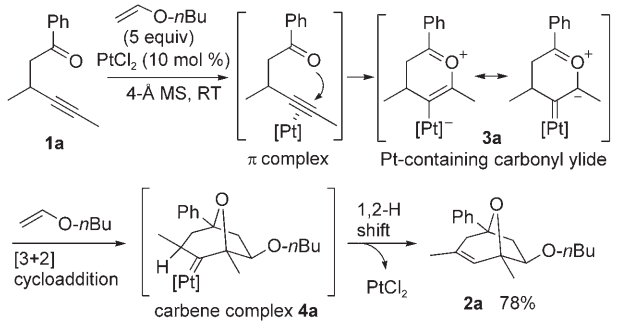
Transition-metal-containing zwitterionic intermediates generated through the electrophilic activation of alkynes toward nucleophilic attack by a carbonyl oxygen atom or imino nitrogen atom can be used in addition reactions with nucleophiles or cycloaddition reactions with alkenes or alkynes to prepare 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 $[W(CO)_5(thf)]$, $[ReCl(CO)_5]/h\nu$, $[\{IrCl(cod)\}_2]$, $AuCl_3$, and $[AuClPPh_3]/AgSbF_6$, 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.

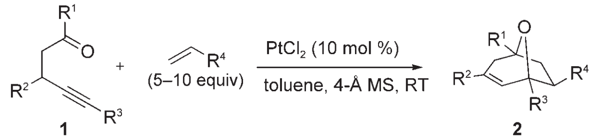
We propose the following mechanism for the formation of **2a**: The electrophilic activation of the alkyne moiety in **1a** by platinum(II) chloride induces the attack of the carbonyl oxygen atom onto the alkyne in a 6-*endo* manner to generate the platinum-containing carbonyl ylide **3a**, which then 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 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.

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	*t*	Yield [%]
1	Ph	Me	Me	OPMB	27 h	76
2	Ph	Me	Me	Ph	5 days	43
3	Ph	EtO	Me	*n*BuO	8 h	84
4	Et	Me	*n*-pentyl	*n*BuO	5 days	77

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

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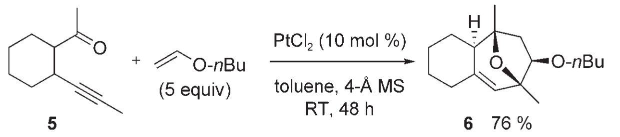
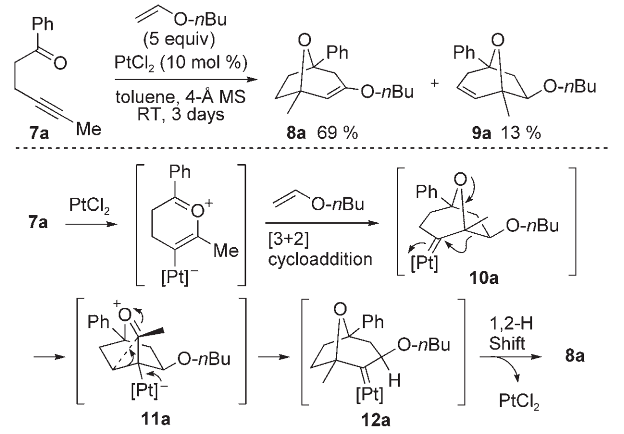


Scheme 2. Reaction of the cyclohexane derivative **5**.

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).



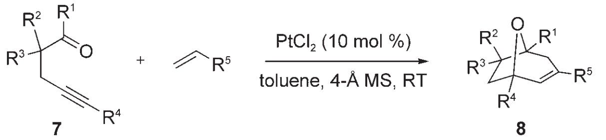
Scheme 3. Platinum-catalyzed reaction of acyclic γ,δ-ynones with no substituent at the propargylic position.

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).

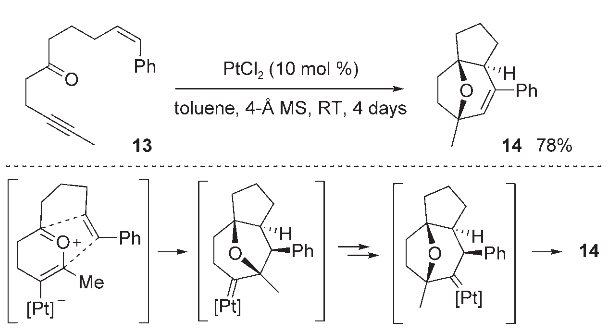
Finally, we attempted an intramolecular version of this reaction. Thus, treatment of the acyclic γ,δ-ynone **13**, which contains a styrene moiety, with a catalytic amount of platinum(II) chloride gave the desired product of intramolecular cyclization, the useful polycyclic compound **14**, in good yield (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	*n*Bu	*n*BuO	5 days	67
4[a]	Ph(CH$_2$)$_2$	H	H	Me	*n*BuO	4 days	55
5[b]	Ph	Me	Me	Me	*n*BuO	4 days	52
6[c]	Ph	CO$_2$Et	H	Me	*n*BuO	6 days	55

[a] [PtCl$_2$(CH$_2$CH$_2$)]$_2$ (5 mol%) was used as the catalyst. [b] The product was obtained as a ketone. [c] PtCl$_2$: 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), PtCl$_2$ (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 NaHCO$_3$, 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 MgSO$_4$. 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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[1] a) N. Iwasawa, M. Shido, H. Kusama, *J. Am. Chem. Soc.* **2001**, *123*, 5814–5815; b) H. Kusama, J. Takaya, N. Iwasawa, *J. Am. Chem. Soc.* **2002**, *124*, 11592–11593; c) H. Kusama, H. Funami, J. Takaya, N. Iwasawa, *Org. Lett.* **2004**, *6*, 605–608; d) J. Takaya, H. Kusama, N. Iwasawa, *Chem. Lett.* **2004**, *33*, 16–17; e) H. Kusama, H. Funami, M. Shido, Y. Hara, J. Takaya, N. Iwasawa, *J. Am. Chem. Soc.* **2005**, *127*, 2709–2716; f) H. Kusama, Y. Miyashita, J. Takaya, N. Iwasawa, *Org. Lett.* **2006**, *8*, 289–292; g) H. Kusama, Y. Suzuki, J. Takaya, N. Iwasawa, *Org. Lett.* **2006**, *8*, 895–897; h) H. Kusama, H. Funami, N. Iwasawa, *Synthesis* **2007**, 2014–2024.

[2] For other examples of the cycloaddition of metal-containing benzopyrylium-type intermediates, see: a) N. Asao, K. Takahashi, S. Lee, T. Kasahara, Y. Yamamoto, *J. Am. Chem. Soc.* **2002**, *124*, 12650–12651; b) N. Asao, T. Nogami, S. Lee, Y. Yamamoto, *J. Am. Chem. Soc.* **2003**, *125*, 10921–10925; c) N. Asao, T. Kasahara, Y. Yamamoto, *Angew. Chem.* **2003**, *115*, 3628–3630; *Angew. Chem. Int. Ed.* **2003**, *42*, 3504–3506; d) N. Asao, H. Aikawa, Y. Yamamoto, *J. Am. Chem. Soc.* **2004**, *126*, 7458–7459; e) N. Asao, K. Sato, Menggenbateer, Y. Yamamoto, *J. Org. Chem.* **2005**, *70*, 3682–3685; f) N. Asao, H. Aikawa, *J. Org. Chem.* **2006**, *71*, 5249–5253; g) N. Asao, K. Sato, *Org. Lett.* **2006**, *8*, 5361–5363; h) S. Shin, A. K. Gupta, C. Y. Rhim, C. H. Oh, *Chem. Commun.* **2005**, 4429–4431; i) N. Kim, Y. Kim, W. Park, D. Sung, A. K. Gupta, C. H. Oh, *Org. Lett.* **2005**, *7*, 5289–5291; j) A. K. Gupta, C. Y. Rhim, C. H. Oh, R. S. Mane, S.-H. Han, *Green Chem.* **2006**, *8*, 25–28; k) G. Dyker, D. Hildebrandt, *J. Org. Chem.* **2005**, *70*, 6093–6096; l) D. Hildebrandt, W. Hüggenberg, M. Kanthak, T. Plöger, I. M. Müller, G. Dyker, *Chem. Commun.* **2006**, 2260–2261; m) C. H. Oh, J. H. Ryu, H. I. Lee, *Synlett* **2007**, 2337–2342; n) J. Zhu, A. R. Germain, J. A. Porco, Jr, *Angew. Chem.* **2004**, *116*, 1259–1263; *Angew. Chem. Int. Ed.* **2004**, *43*, 1239–1243; o) A. B. Beeler, S. Su, C. A. Singleton, J. A. Porco, Jr., *J. Am. Chem. Soc.* **2007**, *129*, 1413–1419.

[3] For recent examples of addition reactions of nucleophiles to metal-containing zwitterionic intermediates, see: a) N. T. Patil, H. Wu, Y. Yamamoto, *J. Org. Chem.* **2005**, *70*, 4531–4534; b) N. Asao, S. Yudha, T. Nogami, Y. Yamamoto, *Angew. Chem.* **2005**, *117*, 5662–5664; *Angew. Chem. Int. Ed.* **2005**, *44*, 5526–5528; c) X. Yao, C.-J. Li, *Org. Lett.* **2006**, *8*, 1953–1955; d) R. Yanada, S. Obika, H. Kono, Y. Takemoto, *Angew. Chem.* **2006**, *118*, 3906–3909; *Angew. Chem. Int. Ed.* **2006**, *45*, 3822–3825; e) J. Zhang, H.-G. Schmalz, *Angew. Chem.* **2006**, *118*, 6856–6859; *Angew. Chem. Int. Ed.* **2006**, *45*, 6704–6707; f) C. H. Oh, R. Reddy, A. Kim, C. Y. Rhim, *Tetrahedron Lett.* **2006**, *47*, 5307–5310; g) Y. Liang, Y.-X. Xie, J.-H. Li, *Synthesis* **2007**, 400–406.

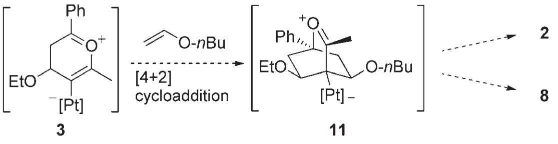
[4] For reviews on cycloaddition reactions of metal-containing zwitterionic intermediates, see: a) H. Kusama, N. Iwasawa, *Chem. Lett.* **2006**, *35*, 1082–1087; b) N. Asao, *Synlett* **2006**, 1645–1656.

[5] Ohe and co-workers studied extensively the synthesis of furylcarbene complexes through the 5-*exo*-dig cyclization of carbonyl enyne compounds; for a review, see: K. Miki, S. Uemura, K. Ohe, *Chem. Lett.* **2005**, *34*, 1068–1073.

[6] For recent reviews on platinum(II)-catalyzed reactions, see: a) C. Nevado, A. M. Echavarren, *Synthesis* **2005**, 167–182; b) C. Bruneau, *Angew. Chem.* **2005**, *117*, 2380–2386; *Angew. Chem. Int. Ed.* **2005**, *44*, 2328–2334; c) C. Nieto-Oberhuber, S. López, E. Jiménez-Núñez, A. M. Echavarren, *Chem. Eur. J.* **2006**, *12*, 5916–5923; d) A. Fürstner, P. W. Davies, *Angew. Chem.* **2007**, *119*, 3478–3519; *Angew. Chem. Int. Ed.* **2007**, *46*, 3410–3449; e) J. Marco-Contelles, E. Soriano, *Chem. Eur. J.* **2007**, *13*, 1350–1357.

[7] For other recent examples of 1,2-alkyl migrations in platinum–carbene intermediates, see: a) J. Sun, M. P. Conley, L. Zhang, S. A. Kozmin, *J. Am. Chem. Soc.* **2006**, *128*, 9705–9710; b) H. Funami, H. Kusama, N. Iwasawa, *Angew. Chem.* **2007**, *119*, 927–929; *Angew. Chem. Int. Ed.* **2007**, *46*, 909–911.

[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.

[10] For reviews on the [3+2] cycloaddition of carbonyl ylide species derived from α-diazoketone derivatives with a Rh catalyst, see: a) G. Mehta, S. Muthusamy, *Tetrahedron* **2002**, *58*, 9477–9504; b) A. Padwa, *Helv. Chim. Acta* **2005**, *88*, 1357–1374.