5814 *J. Am. Chem. Soc.* **2001,** *123,* 5814−5815

Generation and Reaction of Metal-Containing Carbonyl Ylides: Tandem [3+2]-Cycloaddition−Carbene Insertion Leading to Novel Polycyclic Compounds

Nobuharu Iwasawa,* Masahide Shido,† and Hiroyuki Kusama

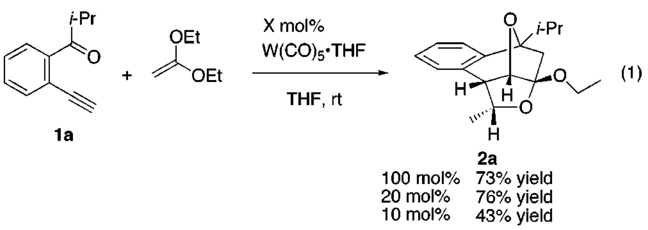
Department of Chemistry, Tokyo Institute of Technology
O-okayama, Meguro-ku, Tokyo 152−8551, Japan
Department of Chemistry, Graduate School of Science
The University of Tokyo, Hongo, Bunkyo-ku
Tokyo 113-0033, Japan

Received February 22, 2001

In this paper, we report the generation of novel metal-containing carbonyl ylides by the reaction of *o*-ethynylphenyl ketones with $W(CO)_5$·THF, and the reaction of these ylides with electron-rich alkenes to give polycyclic compounds through a [3+2]-cycloaddition, followed by insertion of the resulting tungsten carbene moiety into a neighboring C−H bond.

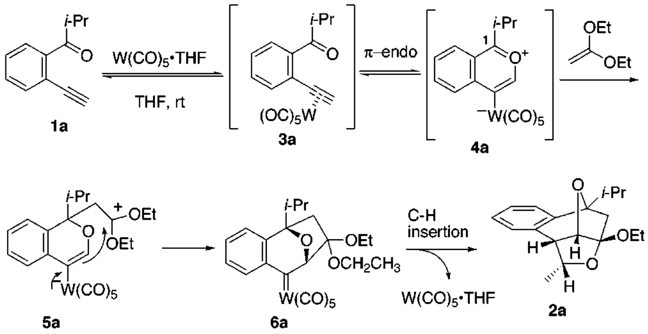
We have previously reported that benzopyranylidene complexes can be prepared by the treatment of *o*-ethynylphenyl ketone derivatives with $W(CO)_5$·THF through the electrocyclization of vinylidene intermediates (see Scheme 2, path iii), and that these complexes undergo Diels−Alder reaction with electron-rich alkenes such as alkenyl ethers, ketene acetals, and enamines to give substituted naphthalenes in good yield.[1] To carry out this reaction by a one-pot procedure, we examined the same complexation reaction *in the presence of* a ketene acetal, which led us to the discovery of the novel reaction pathways described below.

When *o*-ethynylphenyl isopropyl ketone **1a** was treated with a stoichiometric amount of $W(CO)_5$·THF *in the presence of* 4 equiv of 1,1-diethoxyethylene, the starting material was consumed within 2 h at room temperature. To our great surprise, purification of the crude product revealed that the expected 3-ethoxy-1-isopropylnaphthalene[1] had not been formed at all, but rather that a novel polycyclic compound **2a** had been obtained in 73% yield as a single stereoisomer. Furthermore, the same product was also obtained in nearly the same yield even with 20 mol % of $W(CO)_5$·THF. The structure, including the relative stereochemistry, of this compound was confirmed to be as shown in eq 1 by X-ray analysis.



The mechanism of formation of this compound is thought to be as follows (Scheme 1). Treatment of $W(CO)_5$·THF with *o*-ethynylphenyl ketone **1a** gives a metal-containing carbonyl ylide **4a**[2,3] through the endo-mode of attack of the carbonyl oxygen onto the $W(CO)_5$-π-complexed alkynyl part of the molecule.[4,5] Then, the ketene acetal attacks the C1 carbon of this complex followed by intramolecular nucleophilic attack by the resulting vinyltungsten species **5a** to give a formal [3+2]-cycloaddition product, an unstable carbene complex **6a**.[6] Finally, the $W(CO)_5$-carbene moiety thus generated inserts into a C−H bond of the neighboring ethoxy group[7] to give the product **2a** while regenerating $W(CO)_5$·THF. This result is quite interesting because a benzopyranylidene complex is produced when the same reaction is carried out *in the absence of* the ketene acetal, suggesting the presence of an equilibrium between the π-complex **3a**[8] and the metal-containing 1,3-dipole **4a**.

Scheme 1



The generality of this reaction was examined employing several *o*-ethynylphenyl ketone derivatives and electron-rich alkenes. As summarized in Table 1, both vinyl ethers and ketene acetals can be employed as the electron-rich alkene component to give the corresponding polycyclic products in good yield with 10 or 20 mol % of $W(CO)_5$·THF. Several kinds of aryl ketone including an aryl aldehyde can also be employed in this reaction. In most cases, a single diastereomer is obtained, whose relative stereochemistry is assigned to be the same as that of **2a** based on the similarity of the coupling constants in its ^{1}H NMR spectrum.

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* Address correspondence to this author at the Tokyo Institute of Technology.

† The University of Tokyo.

(1) Iwasawa, N.; Shido, M.; Maeyama, K.; Kusama, H. *J. Am. Chem. Soc.* **2000**, *122*, 10226. See also: Ohe, K.; Miki, K.; Yokoi, T.; Nishino, F.; Uemura, S. *Organometallics* **2000**, *19*, 5525.

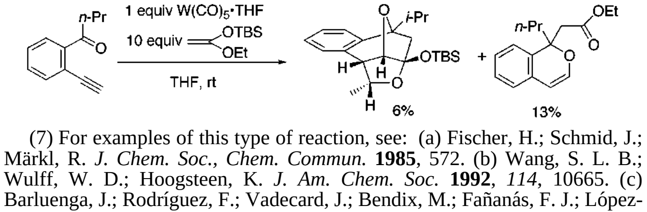
(2) For reviews on the carbonyl ylides, see: (a) Padwa, A.; Weingarten, M. D. *Chem. Rev.* **1996**, *96*, 223. (b) Dörwald, F. Z. *Metal Carbenes in Organic Synthesis*; Wiley-VCH: Weinheim, 1999; p 206. For some recent examples, see: (c) Pirrung, M. C.; Kaliappan, K. P. *Org. Lett.* **2000**, *2*, 353. (d) Kitagaki, S.; Anada, M.; Kataoka, O.; Matsuno, K.; Umeda, C.; Watanabe, N.; Hashimoto, S. *J. Am. Chem. Soc.* **1999**, *121*, 1417.

(3) We have not yet been successful in confirming the presence of metal-containing carbonyl ylides such as **4**. Direct observation of a mixture of *o*-ethynylphenylbutyrophenone **1c** and $W(CO)_5$·THF-d_8 in THF-d_8 by NMR revealed the appearance of small amounts of two kinds of unknown species, one of which could be the carbonyl ylide **4c**. They disappear gradually along with the formation of the benzopyranylidene complex **12c**. We are currently investigating to determine the exact structure of these two species.

(4) For the attack of oxygen nucleophile onto a π-complexed alkyne, see: Hegedus, L. S. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon Press: Oxford, England, 1991; Vol. 4, p 551.

(5) No reaction occurred when a mixture of acetophenone and 1,1-diethoxyethylene was treated with a stoichiometric amount of $W(CO)_5$·THF.

(6) We are not certain whether the reaction proceeds in a stepwise or a concerted manner. In the reaction with the ketene silyl acetal, we observed the formation of the product derived from the first addition step as shown below. (Yields were not optimized.)



(7) For examples of this type of reaction, see: (a) Fischer, H.; Schmid, J.; Märkl, R. *J. Chem. Soc., Chem. Commun.* **1985**, 572. (b) Wang, S. L. B.; Wulff, W. D.; Hoogsteen, K. *J. Am. Chem. Soc.* **1992**, *114*, 10665. (c) Barluenga, J.; Rodríguez, F.; Vadecard, J.; Bendix, M.; Fañanás, F. J.; López-Ortiz, F.; Rodríguez, M. A. *J. Am. Chem. Soc.* **1999**, *121*, 8776. (d) Takeda, K.; Okamoto, Y.; Nakajima, A.; Yoshii, E.; Koizumi, T. *Synlett* **1997**, 1181. (e) Barluenga, J.; Aznar, F.; Fernández, M. *Chem. Eur. J.* **1997**, *3*, 1629. See also: Sulikowski, G. A.; Cha, K. L.; Sulikowski, M. M. *Tetrahedron: Asymmetry* **1998**, *9*, 3145.

(8) For a review of π-complexes of group 6 metals, see: Whiteley, M. W. In *Comprehensive Organometallic Chemistry II*; Abel, E. W., Stone, F. G. A., Wilkinson, G., Eds.; Pergamon: Oxford, 1995; Vol. 5, p 331.

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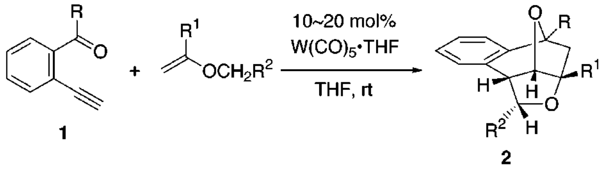


(2)

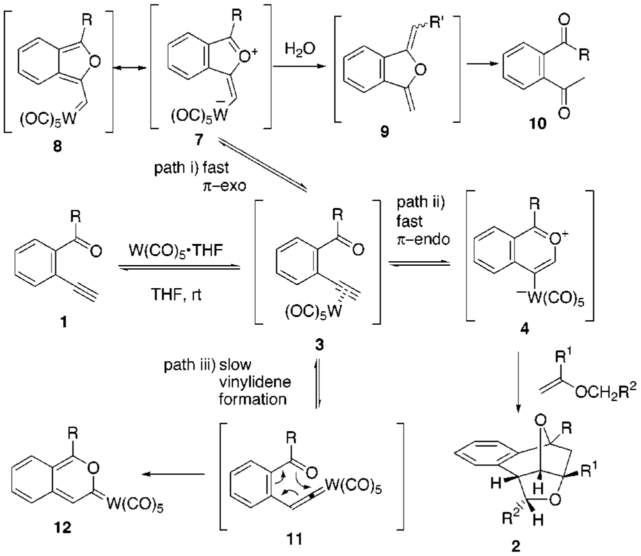
Table 1. Reaction of Various *o*-Ethynylphenyl Ketones with Electron-Rich Alkenes

R =	$R^1 = OC_2H_5$, $R^2 = CH_3$[a]	$R^1 = H$, $R^2 = n\text{-}C_3H_7$[b]
i-Pr (**1a**)	76 (**2a**)	50 (**2d**)
Me (**1b**)	78 (**2b**)	74 (**2e**)
n-Pr (**1c**)	75 (**2c**)	74 (**2f**)
H (**1d**)		94[c] (**2g**)

[a] 20 mol % of $W(CO)_5$·THF and about 5 equiv of the ketene acetal were employed. [b] 10 mol % of $W(CO)_5$·THF and about 10 equiv of the vinyl ether were employed. [c] Including about 5% yield of an isomeric product.

Furthermore, when *o*-ethynylphenyl methyl ketone **1b** (R = Me) was treated with $W(CO)_5$·THF in the presence of 5 equiv of water, *o*-acetylacetophenone **10b** (R = Me) was obtained in about 50% yield. Direct observation of the reaction mixture in THF-d_8 clearly showed the formation of a methyleneisobenzofuran derivative **9b** (R′ = H) at room temperature. This compound is produced by the exo-mode of attack of the carbonyl oxygen onto the $W(CO)_5$-π-complexed alkyne to give **7b** (R = Me), followed by protonation of the C−W bond and deprotonation from the methyl group (see Scheme 2). To account for the various phenomena observed, we propose the following overall picture of the dynamic equilibria involved in this reaction, which can be partially controlled by the order of addition of the reagents.

Scheme 2



The reaction of *o*-ethynylphenyl ketones and $W(CO)_5$·THF can proceed through the following three pathways: (i) exo-attack of the carbonyl oxygen to the π-complexed alkyne to give **7**, which might be in equilibrium with its tautomer **8**,[9] (ii) endo-attack of the carbonyl oxygen to the π-complexed alkyne to give carbonyl ylide **4**, and (iii) 1,2-H shift to give vinylidene complex **11**, which then undergoes irreversible electrocyclization to give pyranylidene complex **12**. We currently suppose that reactions i and ii are faster than reaction iii, but that pathways i and ii are under rapid equilibrium. Thus, in the presence of a reagent capable of trapping intermediate **4** or **7** such as H_2O or electron-rich alkenes, the reaction proceeds through either pathway i or ii to give the corresponding hydrolysis product **10** (path i) or [3+2]-cycloaddition product **2** (path ii).[10] However, in the absence of such trapping reagents, an equilibrium exists between **4**, **7**, and the π-complex **3**, and formation of the vinylidene complex **11** occurs as a relatively slower process,[11] which gives benzopyranylidene complex **12** through an irreversible unimolecular electrocyclization.

In conclusion we have developed a novel method for the generation of metal-containing carbonyl ylides and their [3+2]-cycloaddition followed by carbene insertion for the construction of complex cyclic carbon frameworks. The dynamic equilibrium of the system has also been clarified.

Acknowledgment. This research was partly supported by the Toray Science Foundation and a Grant-in-Aid for Scientific Research from the Ministry of Education, Science, Sports and Culture of Japan. We would like to thank Ms. Sachiyo Kubo for performing X-ray analysis.

Supporting Information Available: Preparative methods and spectral and analytical data of compounds **2** and X-ray data for **2a** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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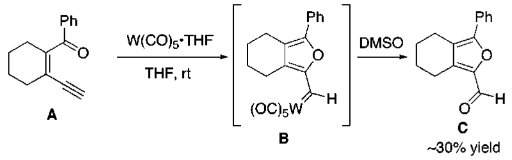
[9] When we examined the reaction of cyclohexene derivative **A** with $W(CO)_5$·THF, formation of a rather unstable, blue-colored complex was observed by TLC. We suppose this complex to be **B**, as DMSO oxidation of the mixture gave an aldehyde **C** in moderate yield. Isolation of the complex **B** and its oxidation to the aldehyde **C** were also presented by Ohe, Uemura, and their co-workers (Kyoto University) at the 79th Annual Meeting of the Chemical Society of Japan, Kobe, March 31, 2001. We thank them for informing us of their unpublished results.



[10] The reason for the difference in the reaction pathways between H_2O and electron-rich alkenes is not obvious.

[11] It is not certain whether there is an equilibrium between the π-complex and the vinylidene complex, although it is generally accepted that there is. For a review of vinylidene complexes, see: (a) McDonald, F. E. *Chem. Eur. J.* **1999**, *5*, 3103. (b) Bruneau, C.; Dixneuf, P. H. *Acc. Chem. Res.* **1999**, *32*, 311. (c) Bruce, M. I. *Chem. Rev.* **1991**, *91*, 197. (d) Bruce, M. I.; Swincer, A. G. *Adv. Organomet. Chem.* **1983**, *22*, 59.