

## Notes

## Conversion of Acid Chlorides to Substituted Acetylenes with Tungsten Alkylidyne

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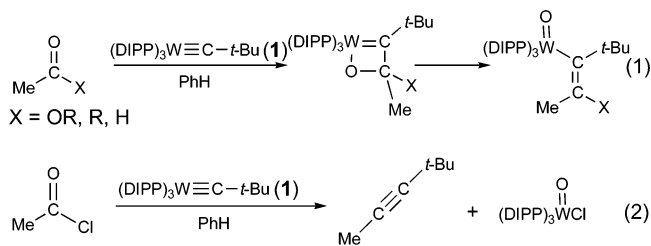
**Summary:** Our investigation into the conversion of acid chlorides to substituted acetylenes using tungsten alkylidyne is presented. Several acid chlorides can be converted to acetylenes in good yields, although a more straightforward synthesis of the required tungsten alkylidyne would be desirable.

## Introduction

Although a number of methods exist for the conversion of aldehydes into olefins, there are a limited number of methods available for converting higher oxidation state carbonyl compounds into acetylenes, and essentially all of these methods require multistep procedures.<sup>1,2</sup> A potentially useful procedure that shows promise for the synthesis of disubstituted acetylenes is the reaction of acid chlorides with well-defined tungsten alkylidyne. A single example of this reaction has been reported, but no investigation of the scope or applicability to typical organic substrates has been conducted.<sup>3</sup> The ready availability of acid chlorides, either commercially or in one step from the corresponding carboxylic acids, should allow for the straightforward synthesis of a wide range of acetylenes that otherwise could not be easily prepared. Hence, the development of such a “Wittig-like” reaction for acid chlorides was undertaken.

## Results and Discussion

The reaction of the 2,6-diisopropylphenoxy (DIPP) alkylidyne **1** with carbonyl functionalities is known to result in the formation of vinyl oxo species (eq 1).<sup>3</sup> This transformation is high yielding with aldehydes, ketones, and formate esters. However, when the carbonyl is an acid chloride, a further reaction can take place, as depicted in eq 2. Elimination of the tungsten chloride across the double bond leads to an acetylene composed of the original substituents from the acid chloride and alkylidyne. The tungsten species that is eliminated presumably ends up as a chlorotrialkoxy species. We undertook an examination of this reaction with the hopes of developing a broadly useful organic transformation.



The synthesis of alkylidyne **1** followed the five-step literature procedure from  $\text{WCl}_4$ , and **1** could be prepared on a multigram scale using standard inert atmosphere techniques.<sup>4</sup> However, we routinely prepared the starting  $\text{WCl}_4$  from  $\text{WCl}_6$ , because in our hands commercial samples of  $\text{WCl}_4$  were not sufficiently pure to allow for a clean, high-yielding synthesis.<sup>5</sup>

The conversion of acetyl chloride to 4,4-dimethyl-2-pentyne after treatment with alkylidyne **1** at room temperature was successful as expected.<sup>3</sup> The reaction of several more complex acid chlorides with alkylidyne **1** also proceeded to give the desired acetylenes, as depicted in Table 1.<sup>6</sup> Most reactions proceeded to give good to excellent yields of the desired product, including the synthesis of an enediyne from fumaroyl dichloride,

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(1) All common techniques require more than one step. Some representative examples: (a) Katritzky, A. R.; Abdel-Fattah, A. A. A.; Wang, M. *J. Org. Chem.* **2002**, *67*, 7526–7529. (b) Katritzky, A. R.; Wang, J.; Karodia, N.; Li, J. *J. Org. Chem.* **1997**, *62*, 4142–4147. (c) Bestmann, H.-J.; Kumar, K.; Schaper, W. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 167–168. (d) Logan, R. T.; Roy, R. G.; Woods, G. F. *J. Chem. Soc., Perkin Trans. 1* **1982**, 1079–1084. (e) Gilbert, J. C. Weerasooriya, U. *J. Org. Chem.* **1979**, *44*, 4997–4998. (f) Lythgoe, B.; Waterhouse, I. *J. Chem. Soc., Perkin Trans. 1* **1979**, 2429–2436. (g) Kano, S.; Yokomatsu, T.; Shibuya, S. *J. Org. Chem.* **1978**, *43*, 4366–4367. (h) Bartlett, P. A.; Green, F. R.; Rose, E. H. *J. Am. Chem. Soc.* **1978**, *100*, 4852–4858.

(2) Unsubstituted acetylenes can be synthesized from aldehydes, but multiple steps are required to obtain substituted acetylenes. For examples, see: (a) Matsumoto, M.; Kuroda, K. *Tetrahedron Lett.* **1980**, *21*, 4021–4024. (b) Miyano, S.; Izumi, Y.; Hashimoto, H. *J. Chem. Soc., Chem. Commun.* **1978**, 446–447. (c) Corey, E. J.; Fuchs, P. L. *Tetrahedron Lett.* **1972**, 3769–3772.

(3) Freudenberg, J. H.; Schrock, R. R. *Organometallics* **1986**, *5*, 398–400.

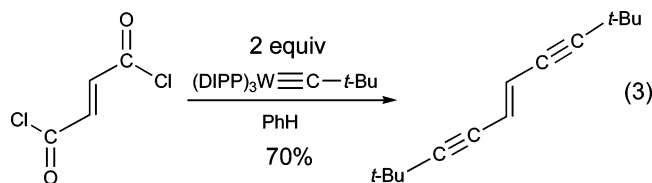
(4) Churchill, M. R.; Ziller, J. W.; Freudenberg, J. H.; Schrock, R. R. *Organometallics* **1984**, *3*, 1554–1562.

(5) Schrock, R. R.; Sturgeooff, L. G.; Sharp, P. R. *Inorg. Chem.* **1983**, *22*, 2801–2806.

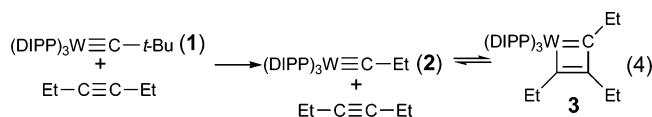
Table 1. Acetylene Synthesis

R	yield
Me-	83%
CH=CHCH <sub>2</sub> CH <sub>2</sub> -	74%
<i>trans</i> -MeCH=CH-	75%
Ph-	70%
4- <i>t</i> -BuC <sub>6</sub> H <sub>4</sub> -	80%
4-MeO-C <sub>6</sub> H <sub>4</sub> -	88%
4-NO <sub>2</sub> -C <sub>6</sub> H <sub>4</sub> -	42%

as shown in eq 3. However, reaction of the electron-deficient *p*-nitrobenzoyl chloride proceeded sluggishly. Although no byproducts were observed, the reaction provided only 42% yield of the desired acetylene after 7 days. The electron-rich *p*-methoxybenzoyl chloride provided the desired acetylene in the highest yield, 88%. We believe that this pattern of reactivity derives from the Lewis acidic nature of the alkyldiyne reagent. The more electron-rich carbonyl species can more easily provide electron density to bind to the tungsten metal center, whereas electron-deficient carbonyls resist this activation.



Having successfully synthesized a range of *tert*-butyl-substituted acetylenes, we sought to further broaden the scope of this transformation through the synthesis of ethyl-substituted acetylenes. A straightforward approach to this goal would be to rely on the known metathesis activity of tungsten alkyldiyne,<sup>7</sup> such that a variety of alkyldiyne substituents could be prepared from a single metal precursor. However, this proposed process is complicated by the fact that the metathesis reaction of alkyldiyne **1** with 3-hexyne proceeds to give the metallacyclobutadiene **3** (eq 4), not the alkyldiyne **2**, by further addition of an additional equivalent of 3-hexyne to the short-lived **2**.<sup>8</sup>

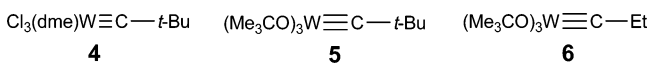


We proceeded to study the reactivity of **3** with a number of acid chlorides, hopeful that a small amount

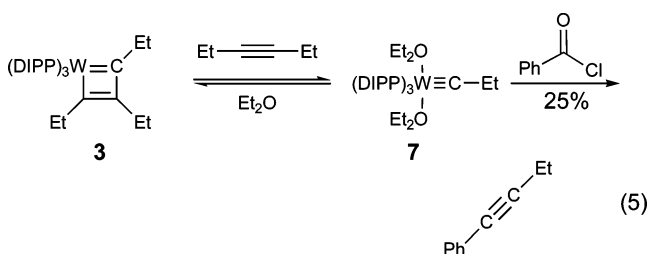
(6) Standard reaction conditions for all acetylene syntheses: Under an atmosphere of argon, 1.1 equiv of tungsten alkyldiyne (0.1 M in benzene) was treated with 1.0 equiv of the indicated acid chloride. After stirring at rt for 2 h, the cloudy reaction mixture was directly filtered through a plug of silica to remove the metal salts and provide the pure acetylene product.

(7) For some reviews of this process, see: (a) Schrock, R. R. In *Handbook of Metathesis*; Grubbs, R. H., Ed.; Wiley-VCH: Weinheim, Germany, 2003; Vol. 1, pp 173–189. (b) Schrock, R. R. *Polyhedron* **1995**, *14*, 3177–3195. (c) Engel, P. F.; Pfeffer, M. *Chem. Rev.* **1995**, *95*, 2281–2309. (d) Mayr, A.; Hoffmeister, H. *Adv. Organomet. Chem.* **1991**, *32*, 227–324. (e) Schrock, R. R. *Acc. Chem. Res.* **1986**, *19*, 342–348.

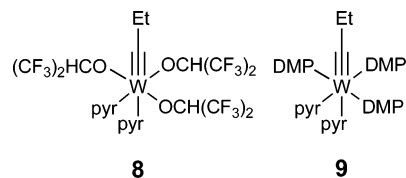
of the reactive **2** would be present in solution and be capable of effecting the desired transformation. Unfortunately, the desired acetylene products were never observed. We examined other alkyldiyne complexes as well, including **4**, **5**, and **6**, all of which failed to participate in the desired transformation.



After significant experimentation, we observed that the reaction of metallacyclobutadiene **3** with benzoyl chloride in the presence of ethyl ether allowed the reaction to proceed, albeit at a slower rate and in lower yield, to give the desired acetylene product (eq 5).



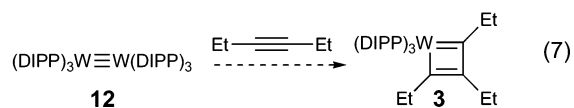
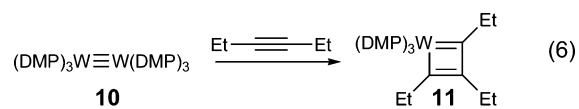
We have been unable to observe any intermediates in this reaction to date. However, we believe that in the presence of a donating solvent such as ethyl ether,<sup>9</sup> an intermediate alkyldiyne such as **7** can be formed in sufficient quantity to react with the acid chloride in solution and produce the desired acetylene (eq 6). Complexes **8**<sup>9</sup> and **9**<sup>9</sup> (DMP = 2,6-dimethylphenoxy), similar to the proposed **7**, but with pyridine ligands in place of the ethers, have been observed previously.



With this information in hand, we attempted to devise a simplified, optimized synthesis of a useful tungsten precursor, so that this transformation could be readily performed in the laboratory without the need for the lengthy, six-step synthesis of alkyldiyne **1**. Because the tungsten dimer W<sub>2</sub>DMP<sub>6</sub> (**10**), possessing six 2,6-dimethylphenoxy ligands, is known to react with acetylenes to produce metallacyclobutadiene complexes **11** (eq 6),<sup>8</sup> we envisioned performing the parallel reaction to generate the DIPP metallacyclobutadiene **3** (eq 7) from dimer W<sub>2</sub>(DIPP)<sub>6</sub>, **12**. Unfortunately, we have not been successful in our efforts to prepare **12**, probably due to its highly hindered nature. In addition, the reaction of **11** with acid chlorides does not parallel that of **3**, providing none of the desired acetylene products. Presumably the steric hindrance derived from the DIPP ligands is responsible for the enhanced reactivity of **3**, as well as the inaccessibility of **12**.

(8) Latham, I. A.; Sita, L. R.; Schrock, R. R. *Organometallics* **1986**, *5*, 1508–1510.

(9) Freudenberger, J. H.; Schrock, R. R.; Churchill, M. R.; Rheingold, A. L.; Ziller, J. W. *Organometallics* **1984**, *3*, 1563–1573.



In conclusion, we have made progress toward a reaction that is capable of generating disubstituted

acetylenes in a single reaction from readily available acid chlorides. The reaction involves the use of a bulky DIPP-substituted tungsten alkylidyne reagent, which can be prepared on large scale.

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