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Tungsten Carbonyl-Induced Cyclizations of Alkynyl Alcohols to Dihydropyranylidene Carbenes and α-Stannyl Dihydropyrans

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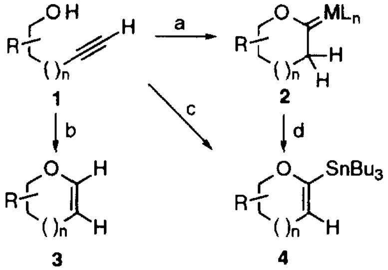
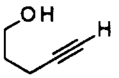
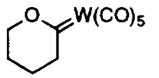
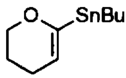
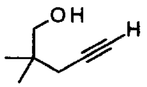
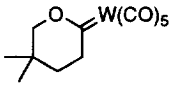
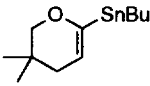
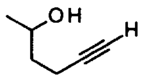
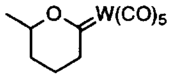
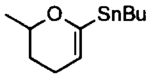
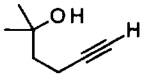
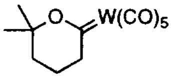
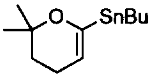
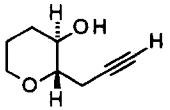
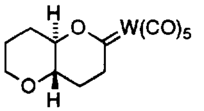
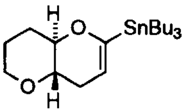
Abstract: Reaction of 1-alkyn-5-ols with tetrahydrofuran-tungsten pentacarbonyl induces cyclization to the corresponding tungsten dihydropyranylidene carbenes. These carbenes can be converted into α-stannyl dihydropyrans upon reaction with tributyltin triflate and triethylamine. This strategy provides the first general preparation of six-membered ring oxacarbenes of the group VI metals, and a novel synthesis of α-stannyl dihydropyrans from acyclic compounds. Copyright © 1996 Elsevier Science Ltd

In 1972 Chisholm and Clark discovered the reaction of 1-alkyn-4-ols (**1**, n = 0) with transition metal complexes to give cyclic oxacarbenes **2** (n = 0, M = Pt; path a).[1] This concept has since been extended to the preparation of five-membered ring oxacarbenes of many other middle- and late-transition metals.[2,3] We have recently developed a mechanistically related single-step transformation of acyclic terminal alkynyl alcohols into isomeric endocyclic enol ethers (**1** → **3**, path b), which is catalyzed by $Et_3N{:}Mo(CO)_5$.[4] In the presence of trialkyltin electrophiles, this same reaction affords a simple and novel route to α-stannyl vinyl ethers **4** (path c).[5] However, these molybdenum-catalyzed cyclizations are apparently limited to formation of five-membered ring compounds (n = 0); 1-alkyn-5-ols **1** (n = 1) are recovered essentially unchanged upon reaction with $Et_3N{:}Mo(CO)_5$.[6] We now report that preformed tungsten pentacarbonyl - tetrahydrofuran complex[7] induces cyclization of 1-alkyn-5-ols **1** (n = 1) into dihydropyranylidene carbenes **2** (ML_n = $W(CO)_5$, n = 1), providing the first general preparation of six-membered cyclic oxacarbenes of the group VI metals.[8] Each of these tungsten oxacarbenes **2** can be converted into the corresponding α-stannyl dihydropyrans **4** (path d, n = 1).[5]



Primary, secondary, and tertiary alkynols **5** - **9** [9] undergo the cyclization to give the corresponding tungsten oxacarbenes **10** - **14** in moderate yields. Tetrahydrofuran and acetone are the best solvents for alkynol cyclization to the six-membered ring tungsten oxacarbenes. Diethyl ether[2g] and dichloromethane[2f] do not form stable complexes with tungsten pentacarbonyl and are suitable solvents for cyclization to six-membered ring oxacarbenes only when tungsten hexacarbonyl is irradiated in the presence of the alkynol substrate. Basic solvents or additives such as tertiary amines and acetonitrile form a stable tungsten pentacarbonyl complex, but these ligands are not effectively displaced by alkyne substrates so that cyclization is not observed in the presence of these solvents. The crystalline carbene products **10** - **11** and **13** are stable for several weeks at room temperature, but rapidly decompose in the oily state (i.e. **12**). The purified carbene intermediates **10** - **14** can be subsequently converted into the corresponding α-stannyl dihydropyrans **15** - **19** in excellent yield by reaction with triethylamine and tributyltin triflate in ether at room temperature.[10]

Table 1. Carbene formation and conversion to α-stannyl dihydrofurans

alkynol	dihydropyranylidene carbene[a] (isolated yield)	α-stannyl dihydropyran[b] (isolated yield)
 **5**	 **10** (42%)	 **15** (84%)
 **6**	 **11** (41%)	 **16** (85%)
 **7**	 **12** (34%)	 **17** (78%)
 **8**	 **13** (35%)	 **18** (100%)
 **9**	 **14** (36%)	 **19** (83%)

Representative procedures: [a] W(CO)$_6$ (3 mmol) was placed in a 100 mL airfree reaction tube (Pyrex) fitted with a reflux condenser and purged with N$_2$. Freshly distilled THF (50 mL) was added and the solid dissolved with stirring. The reaction mixture was then irradiated (350 nm, Rayonet photoreactor) for 2 h under N$_2$ with stirring. The reaction vessel was removed from the light source, alkynols **5** - **9** (1 mmol) in THF (4 mL) were added, and the reaction mixture was stirred for 18 h. Tungsten oxacarbenes **10** - **14** were isolated by solvent evaporation under reduced pressure at 10° C followed by silica gel flash chromatography (pentane / Et$_2$O).

[b] α-Stannyl dihydropyrans were prepared from the corresponding tungsten oxacarbenes, by dissolving compounds **10** - **14** (0.20 mmol) in freshly distilled Et$_2$O (10 mL), and addition of freshly distilled *n*-Bu$_3$SnOTf (0.4 mmol) in Et$_2$O (3 mL) followed by freshly distilled Et$_3$N (1 mL). The reaction mixture was stirred for 6 h. α-Stannyl dihydropyran products **15** - **19** were isolated by flash chromatography on silica gel (pentane / 2% Et$_2$NH). Traces of W(CO)$_6$ were removed under high vacuum.

The direct conversion of alkynol to α-stannyl dihydropyran can also be accomplished in one pot without isolating the tungsten oxacarbene, by generating the carbene in a mixture of diethyl ether and tetrahydrofuran (10 : 1) and then adding tributyltin triflate and triethylamine to the solution containing the carbene intermediate. The overall yields for this one-pot procedure (**5** → **15**, 25% yield; **8** → **18**, 30% yield) are roughly comparable to the yields obtained by isolating the carbene intermediate followed by reaction with tributyltin triflate in a separate step.[11] Note that the carbon-tin bond can be used for a variety of synthetically valuable transformations,[12] and our methodology permits introduction of the trialkyltin moiety under relatively mild reaction conditions.

In conclusion, the novel but conceptually straightforward endocyclization of alkynyl alcohols to six-membered ring products can be achieved for the first time by the use of tungsten carbonyl-induced cyclization. In attaining six-membered ring products, we have significantly enhanced the scope of the alkynol cyclization process. Studies on the generality and functional group compatibility of this transformation and applications to the synthesis of bioactive organic compounds are in progress.

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6. Although both five- and six-membered ring ruthenium oxacarbenes (**2**, ML_n = $RuCp(PPh_3)_2$, n = 0, 1) can be readily formed from the corresponding alkynol precursors (ref. 2c), these ruthenium carbenes proved stable to a number of basic and oxidative reaction conditions and could not be converted into enol

ethers **3** or **4**. The formation of a six-membered ring carbene **2** ($ML_n = Cr(CO)_5$, n = 1) from 4-pentyn-1-ol has been reported with chromium pentacarbonyl - ether complex (ref. 2g), but this procedure requires low temperature photolysis of chromium hexacarbonyl in ether solvent in the presence of alkynol substrate, and in our hands has not proven reproducible for synthesis of six-membered ring oxacarbenes.

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8. Six-membered ring oxacarbenes of group VI metals can also be formed by radical (ref. 8a) or anionic (ref. 8b) additions to α,β-unsaturated metal oxacarbenes. (a) Merlic, C. A.; Xu, D. *J. Am. Chem. Soc.* **1991**, *113*, 9855. (b) Aoki, S.; Fujimura, T.; Nakamura, E. *J. Am. Chem. Soc.* **1992**, *114*, 2985.
9. (a) Compound **6**: Magnus, P.; Slater, M. J.; Principe, L. M. *J. Org. Chem.* **1989**, *54*, 5148. (b) Compounds **7** and **8** were prepared from 1-hexyn-5-one (Sammes, P. G.; Greenberg, S. G.; Davies, L. B. *J. Chem. Soc., Perkin Trans. I* **1981**, 1909) by lithium aluminum hydride reduction (**7**, 67% yield) or methylmagnesium bromide addition (**8**, 50%). (c) Compound **9** was prepared in five steps from 2,3-dihydropyran: (1) *t*-BuLi, THF, -78°C to 0°C; then -78°C, CuI (Kocienski, P.; Yeates, C. *Tetrahedron Lett.* **1983**, *24*, 3905); then $TsOCH_2C{\equiv}CTMS$ (49%); (2) $Co_2(CO)_8$, Et_2O; (3) BH_3-THF, THF, 0°C; then NaOH, H_2O_2; (4) $(NH_4)_2Ce(NO_3)_6$, acetone; (5) 50% aq. NaOH, cat. $PhCH_2NEt_3Cl$, MeCN / CH_2Cl_2, 0°C (11% yield, four steps).
10. Representative spectral data: **9**: colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.00-3.93 (1H, m), 3.58-3.51 (1H, m), 3.43-3.33 (1H, m), 3.23-3.16 (1H, m), 2.71-2.53 (2H, m), 2.18-2.06 (1H, m), 2.07 (1H, t, *J* = 2.7 Hz), 1.83-1.37 (3H, m). ^{13}C NMR (75 MHz, $CDCl_3$) δ 80.8, 79.9, 70.2, 69.6, 67.9, 32.6, 25.3, 22.3. IR (film, $CDCl_3$) 3410, 3294, 2941, 2858, 2120, 1658, 1427, 1343, 1279, 1208, 1099, 1035, 984, 946, 862 cm^{-1}. MS (5.8 v, EI) 140 (M^+, 1), 101 (100), 83 (9), 71 (14), 57 (13), 44 (61). HRMS calcd for $C_8H_{12}O_2$ 140.0837, found 140.0842. **14**: yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.05-3.92 (3H, m), 3.53-3.45 (1H, m), 3.20 (1H, dt, *J* = 7.4, 9.3 Hz), 2.93 (1H, ddd, *J* = 6.1, 9.8, 18.4 Hz), 2.65-2.57 (1H, m), 2.00-1.80 (3H, m), 1.63-1.50 (2H, m). ^{13}C NMR (75 MHz, $CDCl_3$) δ 326.1, 204.7, 197.6, 83.5, 74.3, 55.3, 67.9, 28.6, 25.2, 24.0. IR (film, $CDCl_3$) 2936, 2859, 2069, 1917, 1655, 1458, 1311, 1247, 1190, 1082, 1030, 954, 903 cm^{-1}. **19**: colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.68 (1H, dd, *J* = 2.2, 5.2 Hz), 3.96-3.89 (1H, m), 3.45 (1H, dt, *J* = 3.0, 11.5 Hz), 3.37-3.30 (2H, m), 2.3-2.19 (1H, m), 2.13-1.99 (2H, m), 1.88-1.66 (3H, m), 1.61-0.80 (27H, m). ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.1, 109.4, 75.4, 74.8, 67.8, 29.3, 28.9, 28.8, 27.2, 25.7, 13.7, 9.6. IR (film, $CDCl_3$) 2960, 2928, 2851, 1599, 1471, 1381, 1343, 1260, 1221, 1176, 1157, 1106, 1060, 997, 951 cm^{-1}. MS (3.2 v, EI) 428 (M^+, ^{118}Sn, 8), 373 (100), 317 (66), 261 (48), 177 (10), 139 (9), 71 (11). HRMS calcd for $C_{16}H_{29}O_2{}^{116}Sn$ (M^+-C_4H_9) 369.1184, found 369.1164.
11. At this time we cannot account for the relatively low (ca. 40%) isolated yields of carbene products. Experiments in which the reaction course is followed by ^{1}H NMR (d_8-THF) indicate that organic products such as the corresponding lactones (arising from oxidation) or cyclic enol ethers (from base-induced demetallation) are not formed.
12. For representative synthesis applications of α-stannyl dihydropyrans, see: (a) Hanessian, S.; Martin, M.; Desai. R. C. *J. Chem. Soc., Chem. Commun.* **1986**, 926. (b) Lesimple, P.; Beau, J.-M.; Jaurand, G.; Sinaÿ, P. *Tetrahedron Lett.* **1986**, *27*, 6201. (c) Paquette, L. A.; Oplinger, J. A. *Tetrahedron* **1989**, *45*, 107. (d) Friesen, R. W.; Sturino, C. F. *J. Org. Chem.* **1990**, *55*, 5808. (e) MacLeod, D.; Moorcroft, D.; Quayle, P.; Dorrity, M. R. J.; Malone, J. F.; Davies, G. M. *Tetrahedron Lett.* **1990**, *31*, 6077. (f) Boeckman, R. K.; Charette, A. B.; Asberom, T.; Johnston, B. H. *J. Am. Chem. Soc.* **1991**, *113*, 5337. (g) Grondin, R.; Leblanc, Y.; Hoogsteen, K. *Tetrahedron Lett.* **1991**, *32*, 5021. (h) Dubois, E.; Beau, J.-M. *Carbohydr. Res.* **1992**, *223*, 157. (i) Lesimple, P.; Beau, J.-M. *Bioorg. Med. Chem.* **1994**, *2*, 1319. (j) Bearder, J. R.; Dewis, M. L.; Whiting, D. A. *J. Chem. Soc., Perkin Trans. I* **1995**, 227. (k) Ashworth, P.; Broadbelt, B.; Jankowski, P.; Kocienski, P.; Pimm, A.; Bell, R. *Synthesis* **1995**, 199.

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