3422 *J. Org. Chem.* **1997,** *62,* 3422−3423

Communications

The First Examples of the Palladium-Catalyzed Thiocarbonylation of Propargylic Alcohols with Thiols and Carbon Monoxide

Wen-Jing Xiao and Howard Alper*

Department of Chemistry, University of Ottawa,
10 Marie Curie, Ottawa, Ontario, Canada K1N 6N5

Received January 23, 1997

The use of transition metal complexes as homogeneous catalysts in reactions involving organosulfur compounds as substrates has been the subject of relatively few investigations,[1] while there are numerous publications concerning the analogous oxo reactants.[2] Perhaps the widespread belief that organosulfur compounds are poisons to catalysts has precluded intensive research in this area.[3] We have now examined the reaction of proparglic alcohols with thiols and carbon monoxide in the presence of palladium-based catalysts. Palladium(0) complexes were found to exhibit excellent catalytic activity toward the thiocarbonylation of propargylic alcohols, affording thiofuranones (**2**), thioesters (**3**), or dithioesters (**4**) as the principal product, depending on the reaction conditions. To our knowledge, these are the first examples of the transition-metal-catalyzed thiocarbonylation of propargylic alcohols with thiols and CO.

The search for new methods for the preparation of thiol esters and sulfur-containing γ-lactones is a topic of current interest.[4,5] Not only do these compounds constitute a group of natural products,[6] but they are also attractive building blocks in the synthesis of complex organic molecules.[7] The reaction described herein (eq 1) represents one of the most straightforward routes to these compounds.

Table 1. Palladium-Catalyzed Reaction of 1a with PhSH and CO with or without *p*-TsOH in THF[a]

entry	catalyst system	isolated yield (%) 2a	3a	4a
1	$Pd(PPh_3)_4$	13	58	7
2	$Pd(PPh_3)_4$ + *p*-TsOH	trace	74	9
3	$Pd(OAc)_2$	23	18	14
4	$Pd(OAc)_2 + PPh_3$	16	56	8
5	$Pd(OAc)_2 + PPh_3$ + *p*-TsOH	trace	82	trace
6	$Pd(OAc)_2$ + dppp	64	16	5
7	$Pd(OAc)_2$ + dppp + *p*-TsOH	12	68	trace
8[b]	$Pd(dba)_2$	36	13	trace
9[c]	$Pd(dba)_2$ + *p*-TsOH	16	29	trace
10	$Pd(dba)_2 + PPh_3$	63	7	5
11[c]	$Pd_2(dba)_3CHCl_3 + PPh_3$ + *p*-TsOH	8	38	5

[a] Reaction conditions: **1a** (2 mmol), cat. (0.06 mmol), ligand PPh_3 (0.24 mmol) or dppp (0.12 mmol), *p*-TsOH (0.1 mmol) (if used), THF (5 mL), 400 psi CO, 100 °C, 48 h. After being cooled to room temperature and releasing CO, the reaction mixture was filtered through Celite with chloroform as an eluant. The crude product was purified by preparative TLC (*n*-hexane:EtOAc = 10:1 as eluant), affording analytically pure products. [b] 14% of substrate was recovered. [c] Some catalyst decomposition was observed.

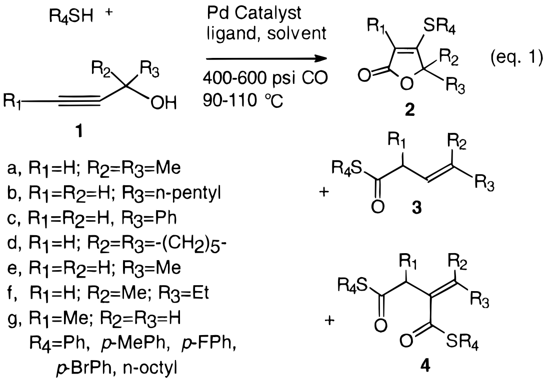

Table 1 shows the results of the carbonylation reaction of 2-methyl-3-butyn-2-ol (**1a**) with thiophenol using several palladium catalysts. Initial catalyst screening indicated that use of palladium(0) or palladium(II) complexes with added phosphine ligands displayed the highest catalytic activity toward the formation of **2a** and **3a** in THF. In particular, the use of 3 mol % palladium acetate with 4 equiv of triphenylphosphine and 5 mol % of *p*-toluenesulfonic acid (*p*-TsOH) was the most effective catalyst system for the selective formation of **3a** in 82% yield (Table 1, entry 5).

$Pd(PPh_3)_4$ is also an excellent catalyst for this reaction (Table 1, entry 2). However, other palladium catalysts, such as $Pd(dba)_2$ (Table 1, entries 8−10), $Pd_2(dba)_3{\cdot}CHCl_3$ (Table1, entry 11), and $Pd(OAc)_2$, without added phosphine ligand (Table 1, entry 3), were less effective for this transformation. Use of $Pd(dba)_2$, with triphenylphosphine, but in the absence of *p*-TsOH, gave **2a** in good yield (Table 1, entry 10). The bidentate phosphine, 1,3-bis(diphenylphosphino)propane (dppp), was also effective as an added ligand for the $Pd(OAc)_2$-catalyzed reaction, and good yields of **2a** and **3a** resulted in the absence and presence of *p*-TsOH (Table 1, entries 6 and 7). In contrast to these palladium catalyst systems, $[Rh(COD)Cl]_2$, which is active for the carbonylation of sulfur-substituted heterocycles,[8] was ineffective for the reaction of **1a** with PhSH and CO. In addition, $Ir_4(CO)_{12}$ and Ru3-

---

[1] (a) Crudden, C. M.; Alper, H. *J. Org. Chem.* **1995**, *60*, 5579. (b) Ogawa, A.; Takeba, M.; Kawakami, J.; Ryu, I.; Kambe, N.; Sonoda, N. *J. Am. Chem. Soc.* **1995**, *117*, 7564. (c) Ogawa, A.; Kawakami, J.; Sonoda, N.; Hirao, T. *J. Org. Chem.* **1996**, *61*, 4161. (d) Shim, S. C.; Antebi, S.; Alper, H. J. *Org. Chem.* **1985**, *50*, 147. (e) Antebi, S.; Alper, H. *Tetrahedron Lett.* **1985**, *26*, 2609. (f) Calet, S.; Alper, H. *Tetrahedron Lett.* **1986**, *27*, 3573. (g) Calet, S.; Alper, H. *Organometallics* **1987**, *6*, 1625. (h) Antebi, S.; Alper, H. *Can. J. Chem.* **1986**, *64*, 2010. (i) Wang, M. D.; Calet, S.; Alper, H. *J. Org. Chem.* **1989**, *54*, 20.

[2] (a) Falbe, J. *New Syntheses with Carbon Monoxide*; Springer-Verlag: Berlin, 1980; p 1. (b) Colquhoun, H. M.; Thompson, D. J.; Twigg, M. V. *Carbonylation*; Plenum Press: New York, 1991. (c) Stille, J. K. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon: Oxford, 1991; Vol. 4, p 913. (d) Tsuji, J.; Mandai, T. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2589.

[3] Hutton, A. T. In *Comprehensive Coordination Chemistry*; Wilkinson, G., Gillard, R. D., McCleverty, J. A., Eds.; Pergamon Press: Oxford, U.K., 1984; Vol. 5, p 1151. Although sulfur is considered to be a potential catalyst poison, there are many examples where sulfur-containing compounds are useful ligands: Frost, C. G.; Williams, J. M. J. *Tetrahedron Lett.* **1993**, *34*, 2015. See also ref 5.

[4] Adamczyk, M.; Fishpaugh, J. R. *Tetrahedron Lett.* **1996**, *37*, 4305.

[5] Oeveren, A. V.; Feringa, B. L. *J. Org. Chem.* **1996**, *61*, 2920.

[6] (a) Halcomb, R. L.; Boyer, S. H.; Wittman, M. D.; Olson, S. H.; Denhart, D. J.; Liu, K. K. C.; Danishefsky, S. J. *J. Am. Chem. Soc.* **1995**, *117*, 5720. (b) Corey, E.; Reichard, G. *J. Am. Chem. Soc.* **1992**, *114*, 10677.

[7] (a) Thuillier, A.; Metzner, P. *Sulfur Reagents in Organic Synthesis*; Academic Press: New York, 1994. (b) Fukuyama, T.; Lin, S.; Li, L. *J. Am. Chem. Soc.* **1990**, *112*, 7050. (c) Penn, J.; Owens, W. *Tetrahedron Lett.* **1992**, *33*, 3737.

[8] Khumtaveeporn, K.; Alper, H. *J. Chem. Soc., Chem. Commun.* **1995**, 917.

S0022-3263(97)00126-6 CCC: $14.00

Table 2. Palladium-Catalyzed Reaction of Propargylic Alcohols with Thiols and CO (400 psi) at 100 °C

entry	**1**	thiol (R_4)	solvent	catalytic system	isolated yield (%)		
					2	**3**	**4**
1	**1a**	Ph	THF	$Pd(PPh_3)_4$ + *p*-TsOH	trace	74	9
2		*p*-$CH_3C_6H_4$	THF	$Pd(PPh_3)_4$ + *p*-TsOH	trace	85	trace
3		*p*-FC_6H_4	THF	$Pd(PPh_3)_4$ + *p*-TsOH	trace	52	18
4		n-octyl	THF	$Pd(OAc)_2$ + PPh_3 + *p*-TsOH	8	68	trace
5[a]	**1b**	Ph	THF	$Pd(PPh_3)_4$ + *p*-TsOH	trace	76	4
6[b]	**1c**	Ph	THF	$Pd(PPh_3)_4$ + *p*-TsOH	6	73	5
7	**1d**	Ph	THF	$Pd(PPh_3)_4$ + *p*-TsOH	13	64	trace
8[c]	**1e**	Ph	THF	$Pd(PPh_3)_4$ + *p*-TsOH	10	72	4
9[d]	**1f**	Ph	THF	$Pd(PPh_3)_4$ + *p*-TsOH	0	63	14
10	**1g**	Ph	THF	$Pd(OAc)_2$ + PPh_3 + *p*-TsOH	trace	72	trace
11[e,f]	**1a**	Ph	THF	$Pd(PPh_3)_4$	0	0	66
12[e,f]		*p*-FC_6H_4	THF	$Pd(PPh_3)_4$	0	0	74
13[f–h]		Ph	toluene	$Pd(PPh_3)_4$ + *p*-TsOH	trace	7	77
14[f–h]	**1e**	Ph	toluene	$Pd(PPh_3)_4$ + *p*-TsOH	trace	4	73
15	**1a**	Ph	DME	$Pd(PPh_3)_4$	67	5	4
16		*p*-BrC_6H_4	DME	$Pd(PPh_3)_4$	73	7	trace
17		n-octyl	DME	$Pd(PPh_3)_4$	74	10	0
18	**1f**	Ph	DME	$Pd(PPh_3)_4$	70	4	4
19	**1e**	Ph	DME	$Pd(PPh_3)_4$	88	trace	trace
20	**1d**	Ph	DME	$Pd(PPh_3)_4$	85	trace	trace
21	**1a**	furanyl	DME	$Pd(PPh_3)_4$	76	trace	0

[a] $E/Z = 1.4{:}1$. [b] $E/Z = 2.3{:}1$. [c] $E/Z = 1.4{:}1$. [d] $E/Z = 1.5{:}1$. [e] Reaction temperature 90 °C. [f] ROH/RSH = 1:2.5. [g] Reaction temperature 110 °C. [h] 600 psi of CO.

$(CO)_{12}$ afforded complicated mixtures of products, none of which were **2a**, **3a**, or **4a**.

The results for the palladium-catalyzed carbonylative coupling reaction of propargylic alcohols with thiols and CO are presented in Table 2. Arenethiols and alkanethiols can be employed successfully in the reaction (Table 2, entries 1–4) together with primary, secondary, and tertiary acyclic propargyl alcohols containing a terminal acetylene (Table 2, entries 1, 5, and 10). In addition, the use of a propargyl alcohol bearing a substituent at the acetylene terminus with benzenethiol under the same conditions gave the thioester (**3a**) as the only product in 72% isolated yield (Table 2, entry 10). We have also found that propargyl alcohols can be thiocarbonylated selectively to give monothioester, dithioester, or sulfur-containing furanones, depending on the reaction conditions. When the reaction is conducted in THF with a catalytic amount of *p*-TsOH and the ratio of propargyl alcohol to thiol is 1:1, the thioester was formed as a major product in 52–85% yield (Table 2, entries 1–10). The reaction was carried out in toluene under more severe conditions (110 °C, 600 psi CO) to afford mainly dithiocarbonylation products (Table 2, entries 13 and 14). Tertiary propargylic mesylates with a terminal triple bond are very reactive and give a high yield of the dithioester under milder conditions (90 °C, 400 psi) (Table 2, entries 11 and 12). The reaction in DME and in the absence of *p*-TsOH selectively afforded the sulfur-substituted furanones **4** in 67–88% yield (Table 2, entries 15–21).

In conclusion, we have developed a palladium-catalyzed carbonylative coupling reaction of propargyl alcohols and thiols. By using different reaction conditions, one can produce monothioesters, dithioesters, or sulfur-containing furanones in good to excellent yield and selectivity. Not only is this methodology attractive for the preparation of thioesters and sulfur-substituted lactones, but it also demonstrates the utility of transition-metal catalysts in the reactions of sulfur compounds. We are currently examining the application of this method to different classes of substrates.

Acknowledgment. We are grateful to the Natural Sciences and Engineering Council of Canada for support of this research.

Supporting Information Available: General experimental procedures and characterization data for all products and ^{1}H-NMR spectra for new compounds (21 pages).

JO970126N