Palladium-Catalyzed Thioesterification of Alkynes with *O*-Methyl *S*-Phenyl Thiocarbonate

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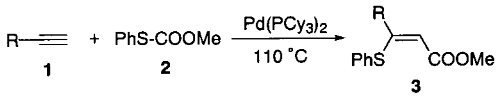
The sulfur-to-carbon bond cleavage by metal complexes[1−3] is a research subject of considerable scrutiny. The majority of the research, however, is related to either the mechanism of desulfurization of oil[2] or the cross-coupling reaction with nucleophiles such as Grignard reagents.[3] We wish to disclose that terminal acetylenes (**1**) undergo an addition reaction with the S−C bond in PhSCOOMe (**2**) (Table 1), an entirely new entry to the addition reactions of heteroatom-containing bonds.[4,5] The reaction furnishes alkenyl sulfide linkages of versatile synthetic applicability.[3] 3-Organothio-2-alkenoic acid esters in particular have been involved as key intermediates in synthetic sequences of biologically important molecules.[6]

When **2** (202.0 mg, 1.2 mmol) was added to a suspension of $Pd(PCy_3)_2$ (27.0 mg, 0.04 mmol) in octane (2 mL), the mixture immediately became a pale-red homogeneous solution. 1-Octyne (**1a**, 147 μL, 1.0 mmol) was then added and the resulting mixture was stirred at 110 °C over 20 h under N_2. GC-MS and GC analyses of the reaction mixture revealed the formation of methyl (*Z*)-3-phenylthio-2-nonenoate (**3a**)[7] in 86% (based on **1a**; 98% regio- and stereoselectivity),[8] (*Z*)-1,2-bis(phenylthio)-1-octene (**4a**; 2%, based on **1a**),[9] PhSMe (4%, based on **2** used), and dimethyl carbonate (2%, based on **1a**). Evaporation followed by column chromatography on silica gel with hexane as eluent led to isolation of **3a** (71%) as a colorless oil.

Table 1. Phenylthioesterification of Terminal Alkynes[a]



R	product	% yield[b]	selectivity[b]
n-C_6H_{13}[c]	**3a**	86	98
n-C_4H_9[c]	**3b**	96	94
CH_3[c,d]	**3c**	32	98
t-C_4H_9	**3d**	41	95
t-$BuMe_2Si(CH_2)_4$[c]	**3e**	86	94
$MeOCH_2$[c]	**3f**	73	84
$(HO)Me_2C$	**3g**	73	100
$Cl(CH_2)_3$	**3h**	62	98
$NC(CH_2)_3$	**3i**	81	62
$C_6H_5CH_2$	**3j** (+**3j′**)[e]	35 (+63)	
C_6H_5	**3k**	62	97
p-$MeOC_6H_4$	**3l**	63	97
p-FC_6H_4	**3m**	55	94

[a] The reactions were carried out at 110 °C for 20 h by using 1.0 mmol of alkynes, 1.2 mmol of methyl phenylthiocarbonate **2**, and 0.04 mmol of $Pd(PCy_3)_2$ in a mixture solvent of 0.5 mL of toluene and 1.5 mL of *n*-octane. [b] GC yield based on the alkynes used, with the selectivity determined by GC. [c] The reaction was performed in *n*-octane. [d] Propyne: 1 atm, yield based on **2** used. [e] **3j′** = methyl 3-phenylthio-4-phenyl-3-butenoate.

The formation of PhSMe is due most likely to the phosphine-catalyzed decarboxylation.[10] On the other hand, byproduct **4a** appears to have come from $(PhS)_2Pd$ species, generation of which presumably is relevant to the dimethyl carbonate formation (vide infra). In practice, careful GC and GC-MS analyses of a $PdMe_2[Ph_2P(CH_2)_4PPh_2]$-catalyzed reaction,[11] which formed a relatively large quantity of **4a** (21% yield, 0.21 mmol), revealed that nearly the same quantity of dimethyl carbonate (0.23 mmol) was also formed.

Use of a polar solvent resulted in a lower yield of **3a** to reveal the following trends: hexane (87% yield of **3a**) ≈ octane (86%) > toluene (67%) ≥ dioxane (62%) > dimethoxyethane (52%) > CH_3CN (23%) ≈ DMF (21%).[11] The solvent effect appears to be associated mainly with the decarboxylation of **2**, which proceeds more readily in polar solvents.[10] Indeed, the extent of the PhSMe formation increased as follows: hexane (6%) ≈ octane (4%) ≈ toluene (7%) < dimethoxyethane (38%) ≤ dioxane (43%) ≈ CH_3CN (43%) < DMF (69%).

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(3) For reviews on metal-assisted transformations of the C−S bond, see: (a) Luh, T.-Y. *Acc. Chem. Res.* **1991**, *24*, 257. (b) Luh, T.-Y.; Leung, M.-K.; Wong, K.-T. *Chem. Rev.* **2000**, *100*, 3187. See also: (c) Kobayashi, S.; Takei, H.; Mukaiyama, T. *Chem. Lett.* **1973**, 1097. (d) Okamura, H.; Miura, M.; Takei, H. *Tetrahedron Lett.* **1979**, *20*, 43. (e) Okamura, H.; Takei, H. *Tetrahedron Lett.* **1979**, 3425. (f) Wenkert, E.; Ferreira, T. W.; Michelotti, E. T. *J. Chem. Soc., Chem. Commun.* **1979**, 637. (g) Trost, B. M.; Ornstein, P. L. *Tetrahedron Lett.* **1981**, *22*, 3463. (h) Fiandanese, V.; Marchese, G.; Naso, F.; Ronzini, L. *J. Chem. Soc., Chem. Commun.* **1982**, 647. (i) Trost B. M.; Lavoie, A. C. *J. Am. Chem. Soc.* **1983**, *105*, 5075. (j) Sugimura, H.; Takei, H. *Chem. Lett.* **1984**, 1505. (k) Fiandanese, V.; Marchese, G.; Naso, F.; Ronzini, L. *J. Chem. Soc., Parkin Trans. 1* **1985**, 1115. (l) Fiandanese, V.; Marchese, G.; Naso, F.; Ronzini, L. *J. Organomet. Chem.* **1986**, *312*, 343. (m) Fiandanese, V.; Marchese, G.; Naso, F.; Ronzini, L. *Synthesis* **1987**, 1034. (n) Fiandanese, V.; Marchese, G.; Mascolo, G.; Naso, F.; Ronzini, L. *Tetrahedron Lett.* **1988**, *29*, 3705. (o) Carpita, A.; Rossi, R.; Scamuzzi, B. *Tetrahedron Lett.* **1989**, *30*, 2699. (p) Babudri, F.; Fiandanese, V.; Mazzone, L.; Naso, F. *Tetrahedron Lett.* **1994,** *35*, 8847.

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(7) The structures of **3a** and **3j′** were further confirmed by reduction to the corresponding alcohols **3a-ol** and **3j′-ol**.

(8) The cis addition was confirmed by an NOE experiment. Irradiation of the triplet at 1.96 ppm due to the allylic protons resulted in an 8% enhancement of the olefinic proton signal at 5.97 ppm.

(9) Compound **4a** was identified with a separately prepared authentic sample. See: Kuniyasu, H.; Ogawa, A.; Miyazaki, S.-I.; Ryu, I.; Kambe, N.; Sonoda, N. *J. Am. Chem. Soc.* **1991**, *113*, 9796.

(10) Jones, F. N. *J. Org. Chem.* **1968**, *33*, 4290.

(11) See Supporting Information for the details.

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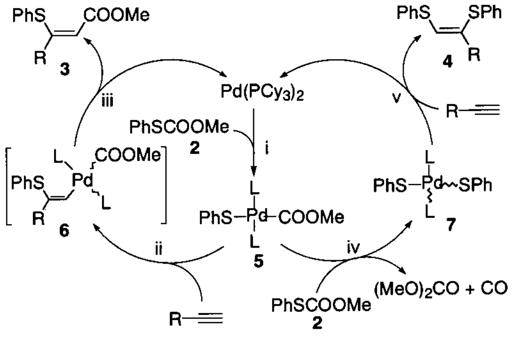
Scheme 1



(L = PCy$_3$)

Other palladium complexes having either less basic or sterically less demanding ligands, such as PPh$_3$, PMe$_2$Ph, Ph$_2$P(CH$_2$)$_4$PPh$_2$, Cy$_2$P(CH$_2$)$_2$PCy$_2$, and PMe$_3$, exerted inferior performance (36−6% yields of **3a**) in the addition reaction of **2** to **1a** in toluene.[11] RhCl(PPh$_3$)$_3$ and RhCl(cod)(PPh$_3$) also catalyzed the addition reaction to give **3a** in 11−15%.

The Pd(PCy$_3$)$_2$-catalyzed thioesterification is readily applicable to various alkynes (Table 1). Besides linear terminal alkynes, sterically congested 3,3-dimethylbutyne also reacted, albeit slowly, resulting in selective formation of **3d**. An exception was the reaction of propyne, which accompanied extensive oligomerization. Functionalities such as siloxy, methoxy, hydroxy, chloro, and cyano groups bound to aliphatic alkynes were tolerated. However, the reaction of 5-hexynonitrile was less selective to give a mixture of isomers, among which the selectivity to **3i** was only 62%.[12] Worth noting in this respect is that a catalyst system generated with a mixture of Pd(PCy$_3$)$_2$ and (η^5-C$_5$H$_5$)(η^3-C$_3$H$_5$)-Pd in a 1:1 ratio (i.e. Pd:PCy$_3$ = 1:1) promoted the reaction of 5-hexynonitrile faster and more selectively (in 10 h, 73% yield with 93% selectivity; in 20 h, 80% yield with 90% selectivity). The reaction of 3-phenyl-1-propyne was also less selective, which was mainly because of **3j** undergoing double bond migration to form its isomer **3j′**.[7] The reaction of aromatic alkynes was somewhat slow, but proceeded with high regio- and stereoselectivity. Under the same reaction conditions, the reactivity of internal alkynes and *S*-alkyl (rather than aryl) *O*-alkyl thiocarbonate was very low. For instance, 4-octyne gave only a trace of the corresponding adduct (<5%).[13] Dimethyl acetylenedicarboxylate was totally unreactive. The reaction of 1-octyne with *S*-ethyl *O*-methyl thiocarbonate resulted in the recovery of the thiocarbonate.

The catalysis appears to involve the elemental processes shown in Scheme 1. The oxidative addition (process i) indeed proceeded at room temperature nearly instantaneously upon mixing Pd(PCy$_3$)$_2$ and **2** (1.5 equiv) in hexane to afford *trans*-Pd(SPh)(COOMe)(PCy$_3$)$_2$ (**5**). Its structure was fully characterized by spectroscopy and confirmed by X-ray crystallography (Figure 1).[14] Heating a toluene-d_8 solution of **5** and 1-octyne (5 equiv) at 110 °C for 2 h, although extensive thermal decomposition of **5** took place, afforded **3a** in 26% yield, which verifies the processes ii + iii.[15] As expected, the reaction of 1-octyne with **2** was smoothly catalyzed by **5** (4 mol %) to give **3a** in 85% yield (94% selectivity) under the standard conditions.

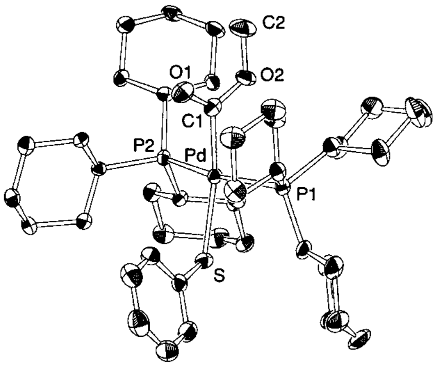


Figure 1. Molecular structure of *trans*-Pd(SPh)(COOMe)(PCy$_3$)$_2$ (**5**). Hydrogen atoms and solvated CH$_2$Cl$_2$ are omitted for clarity.

To look into the provenance of **4a**, we heated a mixture of **5** (0.025 mmol) and **2** (5 equiv) in toluene-d_8 (0.4 mL) at 110 °C for 10 h (process iv). ^{1}H NMR spectroscopy revealed the formation of Pd(SPh)$_2$(PCy$_3$)$_2$ (**7**; 72% based on **5**), a large quantity of PhSMe (0.094 mmol, 75% based on **2**), and dimethyl carbonate (53% based on **5**). ^{31}P NMR spectroscopy also displayed a singlet at 19.8 ppm assignable to **7**.[17] If decarbonylation incidentally occurs at an intermediate stage leading to **7**,[18] one can expect the extrusion of dimethyl carbonate, which indeed was observed. Accordingly we can safely conclude that complex **7**, which can be generated under the catalytic conditions, intercepts 1-octyne (process v) to form **4a** as an undesired side product.[9]

In conclusion, we have developed a simple and efficient addition reaction of PhSCOOMe to alkynes. The process offers a synthetically useful method to simultaneously introduce phenylthio and ester functionalities, both of which can be elaborated on in numerous applications.

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Supporting Information Available: Experimental details, characterization data of **3a-m**, **3a-ol**, **3j′-ol**, **5**, and **7**, and full X-ray structural details for **5**$\cdot$CH$_2$Cl$_2$ (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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[12] Formation of other regio-and stereoisomers was suggested by GC-MS analysis, but we could not confirm their structures by NMR spectroscopy.

[13] Although 4-octyne was mostly recovered unchanged, **2** had completely been converted to PhSMe.

[14] Crystals for X-ray diffraction analysis were obtained by recrystallization from a mixture of CH$_2$Cl$_2$ and CH$_3$OH at −20 °C. Crystal data for **5**$\cdot$CH$_2$Cl$_2$: pale yellow crystals, monoclinic, space group $P2_1/a$, a = 20.329(3) Å, b = 10.066(2) Å, c = 23.082(1) Å, b = 92.610(7)°, V = 4718(1) Å^3, Z = 4, D(calcd) = 1.296 g/cm^3, fw = 920.41, μ(Mo Kα) = 6.53 cm^{-1}. R_1= 0.044, wR_2 = 0.064. GOF = 1.11.

[15] Although insertion to the S−Pd bond (thio-palladation) appears more likely in view of the successful catalytic disulfide addition to alkynes (ref 9), we are unable to exclude the alternative possibility that involves alkoxycarbonyl-palladation. Treatment of **5** with methyl propynoate, a highly reactive alkyne in insertion chemistry (ref 16), to clarify this aspect resulted in only oligomerization even at room temperature.

[16] Onozawa, S-y.; Hatanaka, Y.; Sakakura, T.; Shimada, S.; Tanaka, M. *Organometallics* **1996**, *15*, 5450.

[17] Other signals were also observed at 9.8 ppm arising from free PCy$_3$ and at 38.0 ppm due presumably to [Pd(SPh)(μ-SPh)(PCy$_3$)]$_2$. The conversion of **5** to **7**, however, did not proceed in the thermolysis of **5** alone.

[18] M−COOR species (M = Ni, Pd) are known to decarbonylate. Otsuka, S.; Nakamura, A.; Yoshida, T.; Naruto, M.; Ataka, K. *J. Am. Chem. Soc.* **1973**, *95*, 3180. For relevant reactivities of Pd−COOR species associated with palladium-catalyzed oxalate synthesis and other oxidative carbonylaitons, see: Uchiumi, S.-I.; Ataka, K.; Matsuzaki, T. *J. Organomet. Chem.* **1999**, *576*, 279 and the references therein.