*J. Org. Chem.* **1998,** *63,* 2609−2612

# Highly Regioselective Palladium-Catalyzed Thiocarbonylation of Allenes with Thiols and Carbon Monoxide

Wen-Jing Xiao, Giuseppe Vasapollo,[†] and Howard Alper*

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

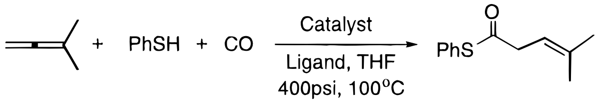
*Received November 19, 1997*

A series of mono- and di-substituted allenes underwent direct thiocarbonylation with thiols and carbon monoxide to form the corresponding $\beta,\gamma$-unsaturated thioesters in 73−94% yields. This reaction requires catalytic quantities of $Pd(OAc)_2$ (3 mol %) and triphenylphosphine (12 mol %) in THF under an atmosphere of CO (400 psi) at 100 °C for 48 h. Other palladium catalyst systems such as $Pd_2(dba)_3{\cdot}CHCl_3{-}PPh_3$, $Pd(PPh_3)_4$, and $Pd(OAc)_2{-}$dppp are also effective for this reaction. The thiocarbonylation reaction is believed to proceed via an allylpalladium intermediate. The reaction exhibits high regioselectivity, in which the thiophenyl group adds to the less substituted double bond of allenes to give $\beta,\gamma$-unsaturated thioesters.

## Introduction

Sulfur-containing compounds have long been known to act as a poison for noble metal catalysts because of their strong coordinating and adsorptive properties, which cause them to block the reactive sites of metals.[1] That is why organic sulfur compounds have been widely employed as the sources of ligands for various transition metals,[2,1a] but there have been relatively few investigations of metal-catalyzed synthetic reactions involving organosulfur compounds as reactants.[3] On the contrary, a variety of transition-metal-catalyzed carbonylation reactions of sulfur-containing compounds,[3a−i] and the thiocarbonylation of thiols to various substrates,[3e,h,j] have been extensively developed during the past decade. For instance, one of us reported that a series of allyl aryl and allyl alkyl sulfides can be carbonylated to the corresponding thioesters catalyzed by both palladium and ruthenium systems.[3i] It was found that even acyclic carbon−heteroatom bonds could be carbonylated using $[Rh(COD)Cl]_2$ as a catalyst,[3r] and this is the first example of the insertion of CO into an acyclic carbon heteroatom bond that did not involve the formation of a $\pi$-allylic intermediate. Recently we reported a palladium-catalyzed carbonylative coupling reaction of propargyl alcohols and thiols[3j] in which we believe an allene species is a possible intermediate. Therefore, we decided to examine the palladium-catalyzed reactions of allenes with thiols and carbon monoxide. We now report our discovery that palladium catalyst systems such as $Pd(OAc)_2{-}PPh_3$ indeed catalyze the carbonylative addition of thiols and CO to allenes, leading to the regioselective formation of $\beta,\gamma$-unsaturated thioesters.

**Table 1. Palladium-Catalyzed Thiocarbonylation of Allene 1a with Thiophenol**[a]



| entry | catalyst | additive | time (h) | isolated yield (%) |
|---|---|---|---|---|
| 1 | none | none | 48 | 0 |
| 2 | $Pd(PPh_3)_4$ | none | 48 | 67 |
| 3 | $Pd(OAc)_2$ | none | 60 | 37 |
| 4 | $Pd(OAc)_2$ | 4 equiv of $PPh_3$ | 48 | 94 |
| 5 | $Pd(OAc)_2$ | 2 equiv of dppp | 48 | 88 |
| 6 | $Pd(OAc)_2$ | 2 equiv of dppb | 48 | 72 |
| 7 | $Pd(dba)_2$ | none | 48 | 52 |
| 8 | $Pd_2(dba)_3{\cdot}CHCl_3$ | none | 48 | 56 |
| 9 | $Pd_2(dba)_3{\cdot}CHCl_3$ | 4 equiv of $PPh_3$ | 48 | 90 |
| 10 | $[RhCl(COD)]_2$ | none | 48 | 13 |
| 11 | $RhCl(PPh_3)_3$ | none | 48 | 5 |
| 12 | $Co_2(CO)_8$ | none | 60 | 3 |
| 13 | $NiCl_2(PPh_3)_2$ | none | 48 | 0 |
| 14 | $RuCl_2(PPh_3)_3$ | 2 equiv of $PPh_3$ | 48 | 21 |

[a] Reaction conditions: 3-methyl-1,2-butadiene (3 mmol), thiophenol (2 mmol), catalyst (0.06 mmol), $PPh_3$ (0.24 mmol, if used), dppp or dppb (0.12 mmol, if used), 400 psi CO, 100 °C, THF (7 mL).

## Results and Discussion

We chose 3-methyl-1,2-butadiene (**1a**) as a model substrate and investigated its reaction with thiols, CO, and catalytic quantities of a variety of metal complexes. The results are summarized in Table 1. Initial catalyst

---

[†] Present address: Department of Material Science, University of Lecce, Lecce, Italy.

(1) (a) Dubois, M. R. *Chem. Rev.* **1989**, *89*, 1. (b) Hegedus, L. L.; McCabe, R. W. *Catalyst Poisoning*; Marcel Dekker: New York, 1984. (c) 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.

(2) (a) Frost, C. G.; Williams, J. M. J. *Tetrahedron Lett.* **1993**, *34*, 2015. (b) Yamamoto, T.; Sekine, Y. *Inorg. Chim. Acta* **1984**, *83*, 47. (c) Canich, J. M.; Cotton, F. A.; Dunbar, K. R.; Falvello, L. R. *Inorg. Chem.* **1988**, *27*, 804. (d) Murray, S. G.; Hartley, F. R. *Chem. Rev.* **1981**, *81*, 365.

(3) (a) Antebi, S.; Alper, H. *Organometallics* **1986**, *5*, 596. (b) Shim, S. C.; Antebi, S.; Alper, H. *J. Org. Chem.* **1985**, *50*, 147. (c) Shim, S. C.; Antebi, S.; Alper, H. *Tetrahedron Lett.* **1985**, *26*, 1935. (d) Wand, M. D.; Calet, S.; Alper, H. *J. Org. Chem.* **1989**, *54*, 20. (e) Antebi, S.; Alper, H. *Can. J. Chem.* **1986**, *64*, 2010. (f) Calet, S.; Alper, H. *Organometallics* **1987**, *6*, 1625. (g) Calet, S.; Alper, H. *Tetrahedron Lett.* **1986**, *27*, 3573. (h) Antebi, S.; Alper, H. *Tetrahedron Lett.* **1985**, *26*, 2609. (i) Crudden, C. M.; Alper, H. *J. Org. Chem.* **1995**, *60*, 5579. (j) Xiao, W.-J.; Alper, H. *J. Org. Chem.* **1997**, *62*, 3422. (k) Ogawa, A.; Takeba, M.; Kawakami, J.; Ryu, I.; Kambe, N.; Sonoda, N. *J. Am. Chem. Soc.* **1995**, *117*, 7564. (l) Ogawa, A.; Kawakami, J.; Sonoda, N.; Hirao, T. *J. Org. Chem.* **1996**, *61*, 4161. (m) Luh, T. Y.; Ni, Z. J. *Synthesis* **1990**, 89. (n) Goux, C.; Lhoste, P.; Sinon, D. *Tetrahedron Lett.* **1992**, *33*, 8099. (o) Kuniyasu, H.; Ogawa, A.; Kambe, N.; Sonoda, N. *J. Am. Chem. Soc.* **1992**, *114*, 5902. (p) Kuniyasu, H.; Ogawa, A.; Miyazaki, S.; Ryu, I.; Kambe, N.; Sonoda, N. *J. Am. Chem. Soc.* **1991**, *113*, 9796. (q) Keim, W.; Herwig, J. *J. Chem. Soc., Chem. Commun.* **1993**, 1592. (r) Khumtaveeporn, K.; Alper, H. *J. Org. Chem.* **1994**, *59*, 1414. (s) Backvall, J. E.; Ericsson, A. *J. Org. Chem.* **1994**, *59*, 5850.

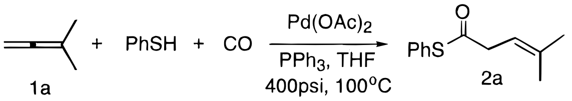
S0022-3263(97)02121-X CCC: $15.00

**Table 2. Solvent Effect for Palladium-Catalyzed Thiocarbonylation of Allene 1a with PhSH**[a]

| entry | solvent | time (h) | isolated yield(%) |
|---|---|---|---|
| 1 | THF | 48 | 94 |
| 2 | DME | 60 | 83 |
| 3 | $CH_2Cl_2$ | 48 | 92 |
| 4 | benzene | 72 | 76 |

[a] Reaction conditions: 3-methyl-1,2-butadiene (3 mmol), thiophenol (2 mmol), $Pd(OAc)_2$ (0.06 mmol), $PPh_3$ (0.24 mmol), 400 psi CO, 100 °C, solvent (7 mL).

screening indicated that use of palladium(0) and palladium(II) complexes with added phosphine ligands displayed the highest catalytic activity toward the formation of **2a** in THF (entries 4–6 and 9 in Table 1). In particular, the use of 3 mol % palladium acetate (relative to thiol) with 4 equiv of triphenylphosphine was the most effective catalyst system for the formation of **2a** in 94% yield (eq 1).



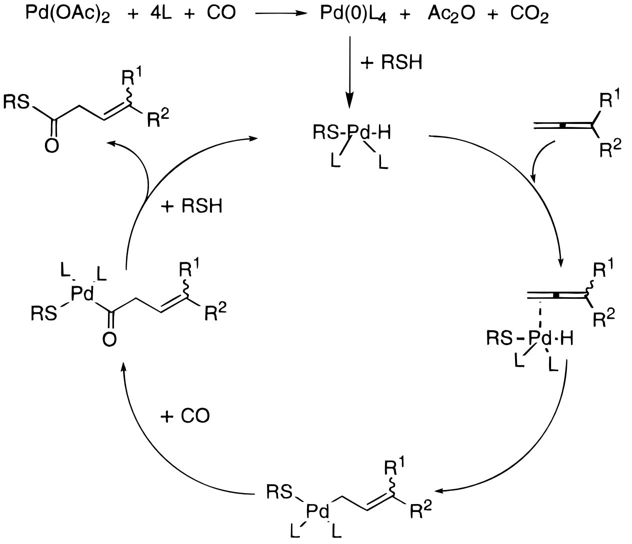
(eq. 1)

$Pd(PPh_3)_4$ is also a good catalyst for this reaction (entry 2 in Table 1). However, other palladium(0) catalysts without added phosphine ligands, such as $Pd(dba)_2$ (entry 7 in Table 1) and $Pd_2(dba)_3{\cdot}CHCl_3$ (entry 8 in Table 1), were less effective for this transformation. Although palladium acetate does catalyze the thiocarbonylation, the reaction afforded **2a** in low yield (entry 3 in Table 1). In addition to triphenylphosphine, the bidentate phosphines, 1,3-bis(diphenylphosphino)propane (dppp) and 1,4-bis(diphenylphosphino)butane (dppb), were also effective as an added ligands for the $Pd(OAc)_2$-catalyzed reactions (entries 5 and 6 in Table 1).

Other metal systems which are known to insert into C–S bonds were also examined. $[Rh(COD)Cl]_2$, which is active for the carbonylation of sulfur-substituted heterocycles,[4a] and $RuCl_2(PPh_3)_3$, which can catalyze the insertion of CO into allylic carbon–sulfur bonds,[2i] were ineffective catalysts for the present carbonylation reaction (entries 10 and 14 in Table 1). $NiCl_2(PPh_3)_2$, which has been reported to catalyze the cross coupling of allyl sulfides and Grignard reagents,[4b] did not promote the thiocarbonylation (entry 13 in Table 1). In addition, $RhCl(PPh_3)_3$ and $Co_2(CO)_8$ were also ineffective in this case even using stoichiometric amounts of the transition-metal complexes (entries 11 and 12 in Table 1). Starting material was recovered when the reaction was performed in the absence of the catalyst (entry 1 in Table 1).

The effect of the solvent in the carbonylative coupling reaction of **1a** with thiophenol and CO was also studied, and the results are illustrated in Table 2. Using the $Pd(OAc)_2$–$PPh_3$ catalyst system, we found that the reaction works well in THF, 1,2-dimethoxyethane (DME), or dichloromethane but less so in benzene (Table 2). Also, CO pressures of 400–800 psi gave **2a** in similar yields. Prolonged heating did not increase the reaction yield (76 h versus 48 h), while a decrease (to 50 °C) or increase (to 150 °C) in the reaction temperature resulted in a reduction of the yield of **2a**.

**Scheme 1**



The carbonylative coupling reaction of a series of allenes (**1a**–**h**) was effected using 1 equiv of thiols or mercaptans, 3 mol % of $Pd(OAc)_2$, and 12 mol % of $PPh_3$, in THF at 400 psi CO for 48 h at 100 °C. The $\beta,\gamma$-unsaturated thioesters were isolated in 73–94% yields (Table 3). The reaction exhibits highly regioselectivity. The 1,1-disubstituted allene, **1a**, and monosustituted allenes, **1b**, **1f**, and **1g**, reacted with thiols and CO affording $\beta,\gamma$-unsaturated thioesters as the sole product, in which the phenylthiocarbonyl group added to the unsubstituted part of the allene (entries 1–7, 11, and 12 in Table 3). The reaction is slower when the allene contains an electron-withdrawing group, but the regioselectivity is unaffected in this case (entry 12 in Table 3). 1,3-Disubstituted unsymmetrical allenes such as **1d** and **1e** undergo thiocarbonylation preferentially at the less bulkier of the two double bonds (entries 9 and 10 in Table 3), while symmetrical internal allenes can, of course, only afford one product (entries 8 and 13 in Table 3). Note that monosubstituted and 1,3-disubstituted allenes react with thiophenol and CO to give a mixture of *E* and *Z* thioesters (entries 7–12 in Table 3) in which the *E* isomers predominate.

A possible pathway for the reaction may include the formation of an H–Pd–SR species via oxidative addition of RSH to Pd(0).[5,6] The mechanism outlined in Scheme 1 merits consideration and comprises the following steps:

(1) formation of Pd(0) as the active catalyst ($Pd(OAc)_2$, which is easy reduced to Pd(0) in the presence of phosphine ligands with CO);[7]

(2) oxidative addition of Pd(0) by RSH to give H–Pd–SR;

(3) coordination of the allene double bond and subsequent insertion into a Pd–H bond to form a $\sigma$-thiopalladium intermediate;

(4) coordination and CO insertion resulting in the formation of a carbonylthio species;

---

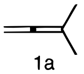
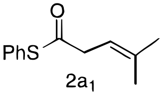
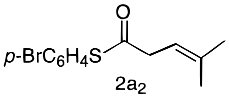
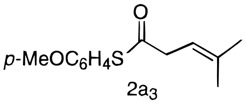
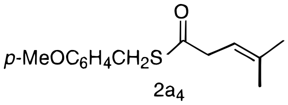
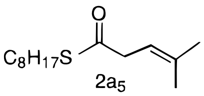
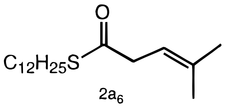
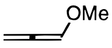
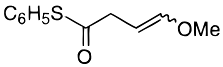
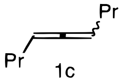
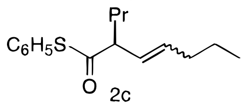
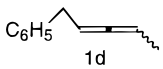
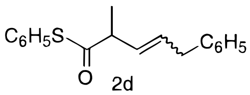
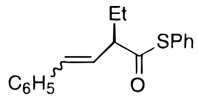
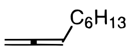
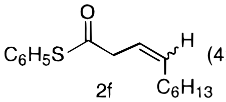
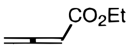
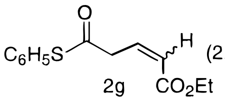
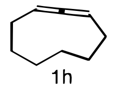
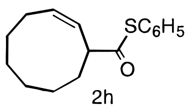
[4] (a) Khumtaveeporn, K.; Alper, H. *J. Chem. Soc., Chem. Commun.* **1995**, 917. (b) Okamura, H.; Miura, M.; Takei, H. *Tetrahedron Lett.* **1979**, 43.

[5] Grushin, V. V. *Chem. Rev.* **1996**, *96*, 2011.

[6] Reppe, W. *Liebigs Ann. Chem.* **1953**, 582, 1. In this paper Reppe reported a similar platinum compound, $HPt(SPh)(PPh_3)_2$.

[7] Tsuji, J. *Palladium Reagents and Catalysts*; John Wiley & Sons: New York, 1995.

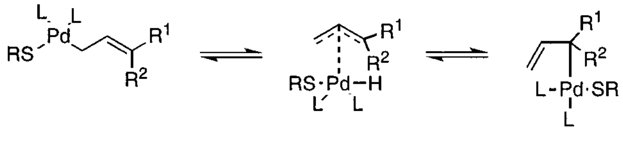
**Table 3. Palladium-catalyzed Thiocarbonylation of Allenes with Thiols**[a]

| entry | Allene | thiol | product ( E/Z ) [b] | yield (%) [c] |
|---|---|---|---|---|
| 1[d] |  1a | $C_6H_5SH$ |  $2a_1$ | 94 |
| 2 | 1a | p-$BrC_6H_4SH$ |  $2a_2$ | 73 |
| 3 | 1a | p-$MeOC_6H_4SH$ |  $2a_3$ | 76 |
| 4 | 1a | p-$MeOC_6H_4CH_2SH$ |  $2a_4$ | 83 |
| 5 | 1a | $C_8H_{17}SH$ |  $2a_5$ | 77 |
| 6 | 1a | $C_{12}H_{25}SH$ |  $2a_6$ | 92 |
| 7 |  1b | $C_6H_5SH$ |  2b (1.8:1) | 83 |
| 8 |  1c | $C_6H_5SH$ |  2c (1.4:1) | 86 |
| 9 |  1d | $C_6H_5SH$ |  2d (2.7:1) | 83 |
| 10 |  1e | $C_6H_5SH$ |  2e (9:1) | 87 |
| 11 |  1f | $C_6H_5SH$ |  2f (4:1) | 80 |
| 12[e] |  1g | $C_6H_5SH$ |  2g (2.2:1) | 88 |
| 13 |  1h | $C_6H_5SH$ |  2h | 92 |

[a] Reaction conditions: allene (2 mmol), thiol (2 mmol), CO 400 psi, $Pd(OAc)_2$ (0.06 mmol), $PPh_3$ (0.24 mmol), THF (7 mL), 100 °C, 48 h. [b] The ratio of E to Z is measured by $^1H$ NMR. [c] Based on the thiophenol employed. [d] The mole ratio of **1a** to PhSH is 3:2. [e] Reaction time: 60 h.

(5) quenching the carbonylthiopalladium complex by RSH and regeneration of a Pd(0) species.

An equilibrium between two σ-allylthiopalladium species (which are formed when the thiocarbonylation takes place to the external or the internal double bond) may occur under the reaction conditions. Other isomers were not observed in the reaction.



## Conclusions

Palladium catalysts such as $Pd(OAc)_2-PPh_3$, $Pd(PPh_3)_4$, and $Pd_2(dba)_3{\cdot}CHCl_3-PPh_3$ are effective for the thiocarbonylation of allenes with thiols and carbon monoxide. The reaction is completely regioselective, in which the thiophenyl group added to the less substituted double bond of the allene to give the β,γ-unsaturated thioester. These reactions further demonstrate the efficacy of palladium catalysts in synthetic reactions of thiols.

The clarification of the precise mechanism of this reaction and the development of new transition-metal-catalyzed reactions of sulfur compounds is now under investigation.

## Experimental Section

**General Methods.** $^{1}$H NMR and $^{13}$C NMR spectra were recorded on Varian Gemini 200 and Bruker AMX 250 spectrometers. Chemical shifts were reported in ppm ($\delta$) relative to tetramethylsilane (TMS), and $J$ values are given in hertz. Chemical shifts in $^{13}$C NMR were measured relative to CDCl$_3$. IR spectra were recorded on a Bomem MB 100-C15 Fourier transform spectrometer and are reported in wavenumbers (cm$^{-1}$). Mass spectra were obtained on a VG 7070E spectrometer. Thin-layer chromatographic (TLC) analyses were performed on silica gel Merck 60 F$_{254}$ plates (250 $\mu$m layer thickness). A Fisher-Johns apparatus was used for melting point determinations. Elemental analyses were performed by the elemental analysis service of the department of chemistry at the University of Ottawa.

THF, DME, and benzene were distilled from sodium benzophenone ketyl prior to use. CH$_2$Cl$_2$ was distilled from CaH$_2$ under N$_2$ prior to use. Thiophenol, 4-bromothiophenol, 4-methoxybenzenethiol, 4-methoxy-α-toluenethiol, 1-octanethiol, and 3-methyl-1,2-butadiene (**1a**) were purchased from Aldrich and were used as received. Methoxyallene (**1b**),[8] 3,4-heptadiene (**1c**),[9] 1-phenyl-1,2-butadiene (**1d**),[9] 1-phenyl-2,3-pentadiene (**1e**),[9] 1,2-nonadiene (**1f**),[10] ethyl 1,2-butadienoate (**1g**),[11] 1,2-cyclononadiene (**1h**),[12] Pd$_2$(dba)$_3$·CHCl$_3$,[13] and [Rh(COD)Cl]$_2$[14] were prepared according to the literature methods.

**General Procedure for the Palladium Thiocarbonylation of Allenes with Thiols.** To a 45 mL Parr autoclave fitted with a glass liner and stirring bar were added Pd(OAc)$_2$ (0.06 mmol), PPh$_3$ (0.24 mmol), allene (2.0 mmol), thiol (2.0 mmol), and dry THF (7 mL). The CO line was flushed three times with CO, the autoclave was fill-vented three times with CO to displace the air, and subseqently the pressure was increased to 400 psi. The mixture was stirred in the autoclave at 100 °C (oil bath temperature) for 48 h. After cooling, the excess CO was released. The reaction mixture was filtered through Florisil, and the solvent was removed by rotary evaporation. The residue was separated by PTLC (silica gel, eluant: *n*-hexane/ethyl acetate 10:1).

**Phenyl 4-methyl-3-pentenethioate (2a$_1$):** oil; IR (neat) 1708 cm$^{-1}$ (C=O); $^{1}$H NMR (200 MHz, CDCl$_3$) $\delta$ 1.70 (s, 3H), 1.78 (s, 3H), 3.35 (d, 2H, $J = 7.4$ Hz), 5.36 (t, 1H, $J = 7.4$ Hz), 7.30−7.49 (m, 5H); $^{13}$C NMR (50 MHz, CDCl$_3$) $\delta$ 18.10, 25.76, 43.10, 115.10, 127.76, 128.68, 129.07, 133.27, 137.82, 196.36; MS (EI) *m/z* 206 (M$^+$); HRMS calcd for C$_{12}$H$_{14}$OS 206.0765, found 206.0790.

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

**Supporting Information Available:** $^{1}$H NMR and $^{13}$C NMR spectra of **2a$_1$**, **2a$_2$**, **2a$_5$**, **2b**, and **2e** and characterization data for all products (17 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO972121W

---

[8] (a) Merz, A. *Angew. Chem., Int. Ed. Engl.* **1973**, 12, 846. (b) Meyer, A.; McCabe, D. J.; Curtis, M. D. *Organometallics* **1987**, *6*, 1491.

[9] Skattebol, L.; Solomon, S. *Organic Syntheses*; Wiley: New York, 1973; Collect. Vol. V, p 306.

[10] Crabbe, P.; Nassim, B.; Robert-Lopes, M.-T. *Organic Syneses*; Wiley: New York, 1990; Collect. Vol. VI, p 276.

[11] Lang, R. W.; Hansen, H.-J. *Helv. Chim. Acta* **1980**, *63*, 438.

[12] (a) Bach, R. D.; Mazur, U.; Brummel, R. N.; Lin, L.-H. *J. Am. Chem. Soc.* **1971**, *93*, 7120. (b) Okude, Y.; Hiyama, T.; Nozaki, H. *Tetrahedron Lett.* **1977**, *43*, 3829.

[13] Ukai, T.; Kawazura, H.; Shii, Y. *J. Organomet. Chem.* **1974**, *65*, 253.

[14] Cramer, R. *Inorg. Synth.* **1974**, *15*, 14.