Heteroatom Chemistry
Volume 11, Number 2, 2000

Copper-Catalyzed Cross-Coupling of α-Seleno-Acylzirconocene Chloride with Haloalkynes: Synthesis of α-Seleno-Substituted Vinyl Alkynyl Ketones

Ai-Ming Sun and Xian Huang*

Department of Chemistry, Zhejiang University, Xi-xi Campus, Hangzhou 310028, P. R. China

Received

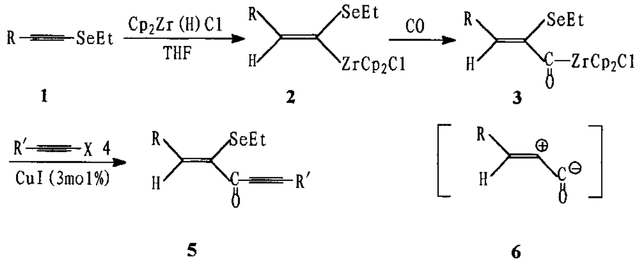
ABSTRACT: *The copper-catalyzed cross-coupling reaction of α-selenoacylzirconocene chloride* 3 *with haloalkynes in the presence of carbon monoxide gives α-seleno-substituted vinyl alkynyl ketones* 5 *in moderate yields. The reaction conditions are neutral and mild enough (room temperature, 1 atm carbon monoxide) that other functional groups in either coupling partner can be brought unaltered into the coupled product. The E geometry in the α-alkylseleno vinylzirconocene reagent is maintained during the coupling reaction.* © 2000 John Wiley & Sons, Inc. Heteroatom Chem 11:91–93, 2000

INTRODUCTION

Vinyl alkynyl ketones are important intermediates in the synthesis of a wide variety of organic compounds. They are Michael acceptors for a diverse range of nucleophiles [1] including organocopper reagents [2]. A number of methods of synthesis of vinyl alkynyl ketones are available [3–5]; they are most often synthesized by the reaction of α,β-unsaturated acid halides with various olefinic reagents. However, to date, there are no reported studies of syntheses of seleno-substituted vinyl alkynyl ketones. Therefore, we now wish to report that α-seleno-substituted vinyl alkynyl ketones could be synthesized by hydrozirconation of internal alkylselenoacetylenes, followed by CuI-catalyzed cross-coupling with haloalkynes in the presence of atmospheric carbon monoxide.

RESULTS AND DISCUSSION

The CuI-catalyzed reaction of haloalkynes with intermediates, α-selenoalkenylzirconocene reagents in tetrahydrofuran (THF), in the presence of carbon monoxide gave good yields of the α-seleno-substituted vinyl alkynyl ketones (Scheme 1, Table 1).

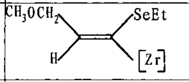
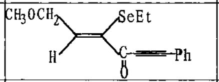
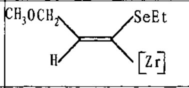
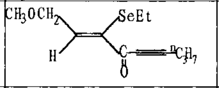
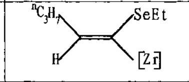
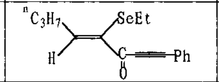
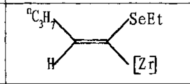
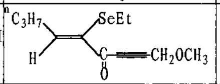
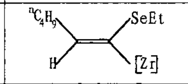
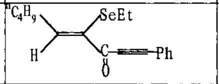
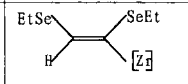
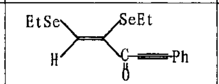
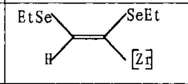
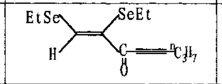
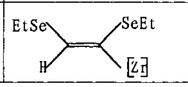
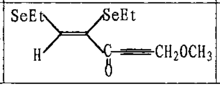


SCHEME 1

Correspondence to: Xian Huang. Fax: 86571 8807077; E-mail: *huangx@mail.hz.zj.cn*

Contract Grant Sponsor: National Natural Science Foundation of China.
Contract Grant Number: 29493800.
Contract Grant Sponsor: National Natural Science Foundation of China.
Contract Grant Number: 29772007.
Contract Grant Sponsor: Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Academia Sinica.

TABLE 1 Copper-Catalyed Carbonylation Coupling of (*E*)-α-Selanylvinylzirconiums with Haloalkynes

Entry	(E)-α-Selanylvinylzirconium	Haloalkynes	Vinyl alkynyl ketones	Yield[a] (%)
5a		$\mathrm{Ph{\equiv}I}$		70
5b		$\mathrm{{}^{n}C_3H_7{\equiv}I}$		65
5c		$\mathrm{Ph{\equiv}Br}$		62
5d		$\mathrm{CH_3OCH_2{\equiv}I}$		58
5e		$\mathrm{Ph{\equiv}I}$		75
5f		$\mathrm{Ph{\equiv}I}$		72
5g		$\mathrm{{}^{n}C_3H_7{\equiv}Br}$		68
5h		$\mathrm{CH_3OCH_2{\equiv}Br}$		70

[a] Isolated yield.
[b] [Zr] = Cp_2ZrCl

Many transition-metal catalyzed coupling reactions of organic halides with organometallic reagents in the presence of carbon monoxide have been shown to give ketones. Nickel catalyzes the carbonylative coupling of bromobenzene with phenylmagnesium bromide to yield benzophenone [6]. Palladium-catalyzed coupling reactions of organic halides with organotin reagents in the presence of carbon monoxide have been reported [7]. In most of these reactions, however, relatively high reaction temperature (120°C) and carbon monoxide pressures (20–30 atm) were utilized [8a–c].

Transmetallation of organic ligands from zirconium to copper has become a very intensely researched process due to the wide application of organocopper reagents in synthetic chemistry [9–10]. A number of features of this reaction make it especially attractive synthetically. The reaction takes place under neutral, mild reaction conditions and at room temperature, with low carbon monoxide and atmospheric pressure. The reaction is highly catalytic, requiring only 3 mol% of CuI catalyst.

In this reaction, the acylzirconocene chloride reacts as an unmasked acyl anion under mild reaction conditions. Disubstituted vinylic selenides, which can be reacted with Grignard reagents [11] or organozinc halides [12] in the presence of $NiCl_2$(dppe), are synthetically equivalent to carbonyl compounds. (*E*)-α-selanylvinylzirconocene chloride **3** thus represents the synthetic equivalent of the cation-anion synthon **6** (Scheme 1).

In summary, copper-catalyzed carbonylative cross-coupling of (*E*)-α-selanylvinylzirconiums with haloalkynes were achieved under extremely mild conditions. The method described herein may afford a way to synthesize unsymmetrical vinyl alkynyl ketones. We are presently exploring the possibilities of extending this procedure for the synthesis of seleno-substituted cyclic ketones.

EXPERIMENTAL

^1H NMR spectra were recorded on an AZ-300 MHz spectrometer with tetramethylsilane (TMS) as an internal standard. Mass spectra were determined using a Finigan 8230 mass spectrometer. IR spectra were obtained by use of neat capillary cells on a Shimadzu IR-408 instrument. The reactions were carried out in predried glassware (150°C, 4 hours) and cooled under a stream of dry nitrogen. All solvents were dried, deoxygenated, and redistilled before use. Zirconium hydride $Cp_2Zr(H)Cl$ and internal alkylselenoacetylenes were prepared according to the methods described previously in the literature, Refs. [13] and [14], respectively.

General Procedure for the Synthesis of α-Seleno-Substituted Vinyl Alkynyl Ketones 5a–h

Under a nitrogen atmosphere, acetylenic selenides **1** (3 mmol) in THF (1.25 mL) were added to a freshly prepared suspension of $Cp_2Zr(H)Cl$ (4 mmol) in THF (15 mL) at room temperature, and the mixture was stirred for 0.5 hours. Then to the resulting clear green mixture was added CuI (0.09 mmol) and haloalkynes **4** (3 mmol) at an atmospheric pressure of CO at room temperature, and the mixture was stirred for 30 minutes at ambient temperature. The reaction mixture was treated with aqueous $NaHCO_3$ and extracted with ether (3 × 15 mL). The combined ethereal extracts were washed with saturated sodium chloride solution, dried over $MgSO_4$, and concentrated under reduced pressure to give a crude oil, which was purified by flash column chromatography (silica gel hexane:EtOAc = 10:1) to give **5a–h**.

Characterization Data of 5a–h

Compound **5a**: ^1H NMR δ 7.10–7.49 (m,5H), 6.30 (t, J = 7.0 Hz, 1H), 3.85 (d,2H), 3.25 (s,3H), 2.61 (q,2H), 1.39 (t,3H). ν_{max} 3110, 2925, 1690, 1495, 1201, 700. MS: *m/z* 307 (M^+). Anal. Calc. for $C_{15}H_{16}SeO_2$: C, 58.64; H, 5.25%. Found: C, 58.23; H, 5.31%.

Compound **5b**: ^{1}H NMR δ 6.01 (t, *J* = 6.4Hz, 1H), 3.88 (d, J = 6.4Hz, 2H), 3.29 (s, 3H), 2.64 (q, 2H), 1.67–1.40 (m, 5H), 0.90–1.11 (m, 5H). ν_{max} 3450, 2933, 1610. MS: *m/z* 273 (M^+). Anal. Calc. for $C_{12}H_{18}SeO_2$: C, 52.77; H, 6.64%. Found: C, 52.43; H, 6.31%.

Compound **5c**: ^{1}H NMR δ 7.10–7.50 (m, 5H), 6.20 (t, *J* = 6.9Hz, 1H), 2.54 (q, 2H), 1.95–2.34 (m, 2H), 1.49 (t, 3H), 1.18–1.47 (m, 2H), 0.75 (t, 3H). ν_{max} 3404, 2912, 1600, 1483, 1190, 662. MS: *m/z* 305 (M^+). Anal. Calc. for $C_{16}H_{18}SeO$: C, 62.96; H, 5.94%. Found: C, 62.84; H, 6.01%.

Compound **5d**: ^{1}H NMR δ 6.30 (t, *J* = 6.9Hz, 1H), 3.90 (s, 2H), 3.22 (s, 3H), 2.52 (q, 2H), 1.97–2.40 (m, 2H), 1.50 (t, 3H), 1.18–1.45 (m, 2H), 0.76 (t, 3H). ν_{max} 3410, 2933, 1610. MS: *m/z* 273 (M^+). Anal. Calc. for $C_{12}H_{18}SeO_2$: C, 52.77; H, 6.64%. Found: C, 52.43; H, 6.31%.

Compound **5e**: ^{1}H NMR δ 7.12–7.53 (m, 5H), 6.19 (t, *J* = 6.8 Hz, 1H), 2.54 (q, 2H), 1.96–2.35 (m, 2H), 1.48 (t, 3H), 1.14–1.49 (m, 4H), 0.81 (t, 3H). ν_{max} 3403, 2922, 1609, 1485, 1192, 701. MS: *m/z* 319 (M^+). Anal. Calc. for $C_{17}H_{20}SeO$: C, 63.95; H, 6.31%. Found: C, 63.74; H, 6.40%.

Compound **5f**: ^{1}H NMR δ 7.09–7.25 (m, 5H), 6.75 (s, 1H), 2.62 (q, 4H), 1.40 (t, 6H). ν_{max} 3420, 2950, 1600, 1420, 1198, 710, 690. MS: *m/z* 370 (M^+) Anal. Calc. for $C_{15}H_{16}Se_2O$: C, 48.67; H, 4.36%. Found: C, 48.45; H, 4.54%.

Compound **5g**: ^{1}H NMR δ 6.02 (s, 1H), 2.64 (q, 4H), 1.68–1.41 (m, 8H), 0.92–1.12 (m, 5H). ν_{max} 3415, 2940, 1605. MS: *m/z* 336 (M^+). Anal. Calc. for $C_{12}H_{18}Se_2O$: C, 52.77; H, 6.64%. Found: C, 58.43; H, 6.31%.

Compound **5h**: ^{1}H NMR 6.25 (s, 1H), 3.95 (s, 2H), 3.23 (s, 3H), 2.65 (q, 4H), 1.42 (t, 6H). ν_{max} 3423, 2952, 1603. MS: *m/z* 338 (M^+). Anal. Calc. for $C_{11}H_{16}Se_2O_2$: C, 39.08; H, 4.77%. Found: C, 39.32; H, 4.59%.

REFERENCES

[1] Bergman, E. D.; Ginsburg, D.; Pappo, R. Org React 1959, 10, 179–555.
[2] Posner, G. H. Org React 1972, 19, 1.
[3] Nielsen, A. T.; Houlihan, W. J.. Org React 1968, 16, 1.
[4] (a) Balban, A.T.; Nenitzecsu, C.D. Friedel-Crafts Related Reactions; John Wiley & Sons, New York, 1964, Part 2, pp. 979–1047; (b) Hacini, S.; Pardo, R.; Santelli, M. Tetrahedron Lett 1979, 4553; (c) Schostarez, H.; Paquette, L. A.. Tetrahedron 1981, 37, 4431.
[5] (a) Fristad, W. E.; Dime, D. S.; Bailey, T. R.; Paquette, L. A. Tetrahedron Lett 1979, 1999; (b) Paquette, L. A.; Fristad, W. E.; Dime, D. S.; Bailey, T. R. J Org Chem 1980, 45, 3017; (c) Cooke, F.; Schwindeman, J.; Magnus, P. Tetrahedron Lett 1979, 1995; (d) Magnus, P.; Quagliato, D. A. Organometallics 1982, 1, 1243.
[6] Collman, J. P.; Hegedus, L. S. Principles and Applications of Organotransition Metal Chemistry; University Sciences Books: Mill Valley, CA, 1980; pp 482–491.
[7] Yamamoto, Y.; Kohara, T.; Yamomto, A. Chem Lett 1976, 1217.
[8] (a) Tanaka, M.. Tetrahedron Lett 1979, 2601; (b) Tanaka, M. Synthesis 1981, 47; (c) Kobayashi, T.; Tanaka, M. J Organomet Chem 1981, 205, C27; (d) Bumagin, N. A.; BuMagina, I. G.; Kashin, N. A.; Beletskaya, I. P. Dokl Akad Nauk SSSR 1981, 261, 1141.
[9] Lipshuz, B. H.; Sengupta, S. Org React 1992, 41, 135.
[10] Wipf, P. Synthesis 1993, 537.
[11] Hercsi, L.; Heimaus, B.; Allard, C. Tetrahedron Lett 1994, 35, 6729.
[12] Yang, D. Y.; Huang, X. Synlett 1997, 891.
[13] Hart, D. W.; Schwartz, J. J Am Chem Soc 1974, 96, 8115.
[14] Comasseto, J. V.; Ferreira, J. T. B.; Petragnani, N. J Organomet Chem 1981, 216, 287.