Highly Selective Three-Component Coupling of Ethyl Propiolate, Alkenes, and Diphenyl Diselenide under Visible-Light Irradiation**

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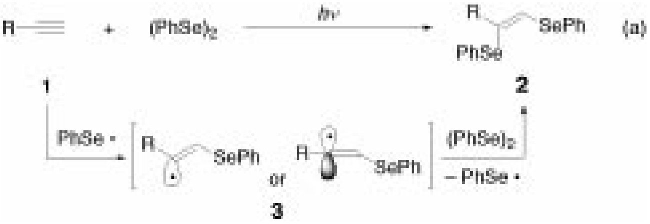
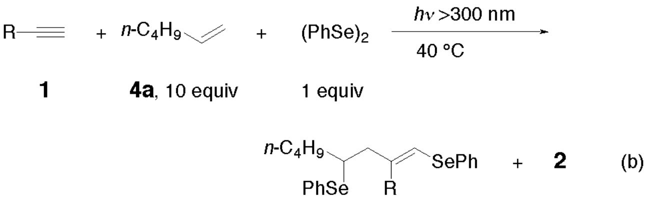
Diphenyl diselenide has its absorption maximum in the near-UV region, and therefore irradiation with light of wavelength greater than 300 nm induces homolytic cleavage of the selenium–selenium bond to generate a phenylseleno radical as a labile species.[1] Compared with the corresponding thiyl radical, the reactivity of the phenylseleno radical toward unsaturated carbon–carbon bonds is lower by a factor of 10–50.[2] However, $(PhSe)_2$ is an excellent trap for carbon radicals and is about 160 times more effective than $(PhS)_2$.[3] Owing to the lower reactivity of PhSe$^\bullet$, the free-radical addition of $(PhSe)_2$ to alkenes does not proceed efficiently.[4] Recently, we found that $(PhSe)_2$ smoothly adds to alkynes with high efficiency at a high initial concentration of the reactants [Eq. (a)].[5] In this reaction, β-(phenylseleno)vinylic radicals **3** appear to be formed as a key intermediate, so if the photoinitiated reaction of $(PhSe)_2$ with alkynes is performed in the presence of alkenes, the sequential addition of the vinylic radical intermediate **3** to alkenes can be expected. The intramolecular coupling reaction between an alkyne, an alkene, and a radical precursor (tin hydride, thiol, sulfonyl chloride, etc.) is well documented;[6] however, their selective intermolecular coupling has remained largely unexplored.[7]

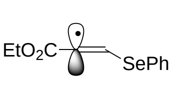


We began our study of this sequential addition reaction by examining the combination of alkyne and alkene. With 1-hexene as standard alkene, three alkynes were tested for the sequential addition of $(PhSe)_2$ [Eq. (b)]. Neither 1-octyne nor phenylacetylene, which generate vinylic σ and π radicals,[8] respectively, by the attack of PhSe$^\bullet$ at the terminal carbon atom, provided the desired alkyne–alkene coupling products **5**. Instead, 1,2-bis(phenylseleno)-1-alkenes (**2**) were obtained as the major products. When the electron-deficient acetylene ethyl propiolate[9] was employed, however, the desired three-component coupling reaction with 1-hexene and $(PhSe)_2$ took place and gave 1,4-bis(phenylseleno)-2-(ethoxycarbonyl)-1-octene (**5**; $R = EtO_2C$, $E/Z = 21/79$) in moderate yield with good selectivity. Accordingly, the reaction proceeds via a vinylic radical **3a**, which is formed by selective attack of PhSe$^\bullet$ on the alkyne,[10] and subsequent addition of **3a** to 1-hexene to generate the homoallylic radical **6a**. These results suggest that a combination of radicals bearing an electron-withdrawing substituent at the radical center and alkenes with an electron-donating substituent is favorable for diselenide-mediated sequential addition to alkynes and alkenes.

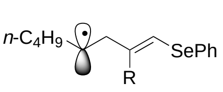


5

R =	5	2
n-C_6H_{13}	trace	46%
Ph	ca. 0%	66%
EtO_2C	38%	7%



3a



6a

Table 1 lists the results of the addition of $(PhSe)_2$ to ethyl propiolate and various alkenes. As expected, increasing the electron density of the alkene dramatically improved the yield of the sequential addition product **5** (entries 1–3). In the case of butyl vinyl ether (**4b**), for example, the desired three-component coupling product **5b** was obtained in 89% yield, and the formation of ethyl 2,3-bis(phenylseleno)acrylate (**2**, $R = EtO_2C$) was suppressed to 2–3% (entry 1). The sequential addition products **5a–g** were obtained as mixtures of stereoisomers with a predominance of the *Z* isomers. With 2,3-dihydrofuran (**4d**), the stereochemistry at the furan ring of the product **5d** was exclusively *trans* (entry 3). Similar reactions can be performed with the enol silyl ether **4e**, allyl alcohol (**4f**), and the acetal **4g**, which give the corresponding coupling products **5e–g** in good yields (entries 4–6). Furthermore, sequential alkyne–diene coupling was demonstrated (entries 7 and 8). In both cases, conjugate addition products **5h**, **5i**, and **5i′** were obtained selectively.

The coupling products have two kinds of seleno group, that is, an alkylseleno group and a vinylseleno group, and are potentially useful synthetic intermediates. The alkylseleno group can be removed reductively,[11] whereas oxidation of the alkylseleno group can lead to olefin formation by *syn* elimination of selenoxide.[12] Furthermore, vinylic selenides are regarded as both carbonyl equivalents (by hydrolysis)[13] and vinyl-transfer reagents (by transition metal catalyzed cross-coupling reactions).[14] We investigated the alkylation of the sequential addition products with organocopper re-

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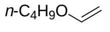
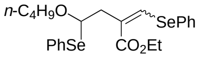
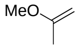
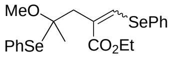
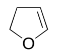
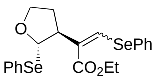
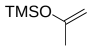
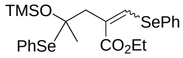
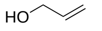
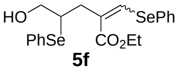
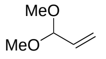
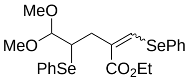
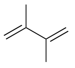
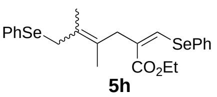
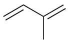
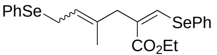
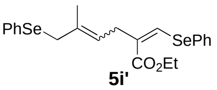
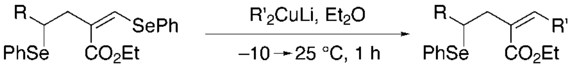
Table 1. Three-component coupling of ethyl propiolate, alkenes, and $(PhSe)_2$.[a]

Entry	Alkene	Product	Yield [%][b]	E/Z
1	 **4b**	 **5b**	89	10:90
2	 **4c**	 **5c**	78	7:93
3	 **4d**	 **5d**[c]	70	15:85
4[d]	 **4e**	 **5e**	71	6:94
5	 **4f**	 **5f**	59	12:88
6	 **4g**	 **5g**	57	8:92
7[f]	 **4h**	 **5h**	56 (72)	67:33[e]
8[f]	 **4i**	 **5i**	55	94:6[e]
		 **5i'**	23	84:16[e]

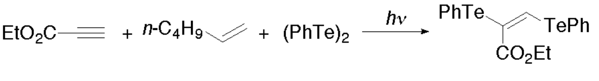
[a] Reaction conditions: ethyl propiolate (0.16 mmol), alkene (15 equiv), $(PhSe)_2$ (1 equiv, added over 1.5 h in several portions), 15 °C, 2 h, $h\nu >$ 300 nm (tungsten lamp, 500 W, Pyrex). [b] Yield of isolated product (NMR). [c] The stereochemistry at the furan ring is exclusively *trans*. [d] Enol silyl ether **4e** (40 equiv). [e] *4E*/*4Z* ratio; *1E*/*1Z* = 0/100. [f] Diene (6 equiv).

agents.[15] Treatment of the coupling product **5j** with lithium dimethylcuprate led to chemoselective methylation to give **7j** with retention of stereochemistry [Eq. (c)]. Similarly, **5b** underwent site-selective butylation on treatment with $n\mathrm{Bu_2CuLi}$. The introduction of a secondary alkyl group such as *sec*-butyl requires the use of an excess of $s\mathrm{Bu_2Cu(CN)Li_2}$ (5 equiv) in the presence of $BF_3\cdot Et_2O$ (THF, −78 to ca. 25 °C, 12 h).[16] =



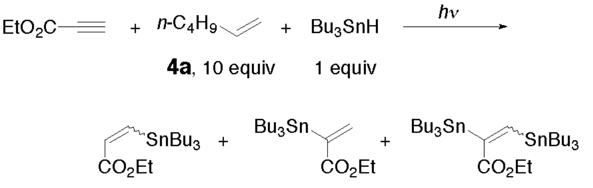
5j, R = *t*BuMe$_2$SiOCH$_2$ R' = Me **7j**, 73%
5b, R = *n*-C$_4$H$_9$O R' = *n*-C$_4$H$_9$ **7b**, 84%
5b, R = *n*-C$_4$H$_9$O R' = *sec*-C$_4$H$_9$ **7b'**, 58%
(c)

In summary, we have developed a highly selective sequential addition of $(PhSe)_2$ to ethyl propiolate and alkenes. Note that the use of diphenyl disulfide instead of $(PhSe)_2$ for the sequential addition reaction resulted in the polymerization of the unsaturated compounds and no formation of the desired three-component coupling products. This is most probably because the ability of $(PhS)_2$ to capture carbon radicals was insufficient to suppress the polymerization reaction.[17] In contrast, the attempted sequential reaction with diphenyl ditelluride resulted only in the formation of the product of $(PhTe)_2$ addition to the alkyne, **8a**, probably due to effective trapping of the carbon radicals [Eq. (d)].[17]



4a, 10 equiv. 1 equiv. **8a**, 19% (d)

Although modern, radical-based synthetic methods often utilize tin hydrides,[18] the attempted tin hydride mediated reaction of ethyl propiolate with 1-hexene under similar reaction conditions gave only the products of addition to the alkyne, **9a**, **10a**, and **11a** [Eq. (e)]. These observations suggest that the present sequential three-component coupling reaction with $(PhSe)_2$ is a kinetically controlled system in which $(PhSe)_2$ facilitates selective sequential addition and inhibits the polymerization of the unsaturated compounds.



4a, 10 equiv 1 equiv (e)

9a, 47% **10a**, 10% **11a**, 7%

Experimental Section

5b: In a Pyrex glass tube (5 mm × 18 cm) under argon atmosphere, ethyl propiolate (30.2 mg, 0.3 mmol), *n*-butyl vinyl ether (760 mg, 7.6 mmol), and diphenyl diselenide (9.4 mg, 0.03 mmol) were irradiated with a tungsten lamp (500 W) at 15 °C. During irradiation, diphenyl diselenide (84.3 mg, 0.27 mmol) was added in nine portions over 1.5 h. After the reaction was complete, the volatile materials were evaporated, and the residue was purified by recycling preparative HPLC (Japan Analytical Industry, Model LC-908), equipped with JAIGEL-1H and -2H columns (GPC) with $CHCl_3$ as eluent to give 136.3 mg (89%) of **5b** as a mixture of stereoisomers (E/Z = 10/90). The stereochemistry of the products was determined by NOE experiments.

5b: Pale yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): Z isomer: $\delta = 0.87$ (t, $^3J(H,H) = 7.3$ Hz, 3 H, $CH_3(CH_2)_3$), 1.28 (t, $^3J(H,H) = 7.1$ Hz, 3 H, CH_3CH_2O), 1.25–1.38 (m, 2 H, $CH_3CH_2(CH_2)_2$), 1.51 (quint, $^3J(H,H) = 7.0$ Hz, 2 H, $CH_3CH_2CH_2CH_2$), 2.85 (dd, $^3J(H,H) = 7.8$, $^2J(H,H) = 14.6$ Hz, 1 H, $CH_2C{=}C$), 2.98 (dd, $^3J(H,H) = 4.9$, $^2J(H,H) = 14.6$ Hz, 1 H, $CH_2C{=}C$), 3.31 (dt, $^3J(H,H) = 6.5$, $^2J(H,H) = 9.3$ Hz, 1 H, CH_2CH_2O), 3.88 (dt, $^3J(H,H) = 6.4$, $^2J(H,H) = 9.3$ Hz, 1 H, CH_2CH_2O), 4.23 (q, $^3J(H,H) = 7.2$ Hz, 2 H, CH_3CH_2O), 5.07 (dd, $^3J(H,H) = 4.9$, 8.3 Hz, 1 H, CH–SePh), 7.43 (s, 1 H, $CH{=}C$), 7.19–7.64 (m, 10 H, Ph); E isomer: $\delta = 0.89$ (t, $^3J(H,H) = 7.3$ Hz, 3 H, $CH_3(CH_2)_3$), 1.23 (t, $^3J(H,H) = 7.1$ Hz, 3 H, CH_3CH_2O), 1.25–1.38 (m, 2 H, $CH_3CH_2(CH_2)_2$), 1.55 (quint, $^3J(H,H) = 7.0$ Hz, 2 H, $CH_3CH_2CH_2CH_2$), 3.01 (dd, $^3J(H,H) = 7.8$, $^2J(H,H) = 14.6$ Hz, 1 H, $CH_2C{=}C$), 3.10 (dd, $^3J(H,H) = 4.9$, $^2J(H,H) = 14.6$ Hz, 1 H, $CH_2C{=}C$), 3.31 (m, 1 H, CH_2CH_2O), 3.87 (m, 1 H, CH_2CH_2O), 4.15 (q, $^3J(H,H) =$

6.6 Hz, 2 H, CH$_3$C*H*$_2$O), 5.21 (dd, ^3J(H,H) = 4.8, 8.4 Hz, 1 H, C*H*–SePh), 7.19–7.64 (m, 10 H, Ph), 8.05 (s, 1 H, C*H*=C); ^{13}C NMR (100 MHz, CDCl$_3$): *Z* isomer: δ = 13.77, 14.17, 19.26, 31.17, 39.68, 60.62, 69.79, 85.91, 124.32, 127.46, 127.95, 128.77, 129.15, 133.24, 135.39, 147.51, 167.03; *E* isomer: δ = 12.93, 14.24, 19.29, 31.10, 41.69, 60.78, 69.72, 86.38, 127.39, 127.95, 128.54, 129.33, 132.93, 133.20, 135.26, 143.39, 164.79; IR (NaCl): $\tilde{\nu}$ = 1694 (C=O), 1574 cm^{-1} (C=C); MS (CI): *m*/*z* (%): 439 (7.0) [$M^+ - \mathrm{BuO}$] or [$M^+ - \mathrm{CO_2Et}$]; elemental analysis calcd for $C_{23}H_{28}O_3Se_2$: C 54.13, H 5.53; found: C 54.24, H 5.66.

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Keywords: alkenes · alkynes · C–C coupling · radical reactions · selenium

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[1] U. Schmidt, A. Müller, K. Markau, *Chem. Ber.* **1964**, *97*, 405–414.

[2] PhS$^\bullet$ is relatively reactive toward carbon–carbon double bonds compared with PhSe$^\bullet$ [$k_{\mathrm{PhS}^\bullet}/k_{\mathrm{PhSe}^\bullet} = 10-50$]: O. Ito, *J. Am. Chem. Soc.* **1983**, *105*, 850–853, and references therein.

[3] (PhSe)$_2$ is more reactive toward alkyl radicals than (PhS)$_2$ [$k_{(\mathrm{PhSe})_2}/k_{(\mathrm{PhS})_2} \approx 160$]: a) G. A. Russell, H. Tashtoush, *J. Am. Chem. Soc.* **1983**, *105*, 1398–1399; b) M. J. Perkins, E. S. Turner, *J. Chem. Soc. Chem. Commun.* **1981**, 139–140; c) G. A. Russell, P. Ngoviwatchai, H. I. Tashtoush, A. Pla-Dalmau, R. K. Khanna, *J. Am. Chem. Soc.* **1988**, *110*, 3530–3538.

[4] For example, the photoinduced reaction of (PhSe)$_2$ with 1-hexene provided only 9% of the corresponding bis-selenide adduct on irradiation for 30 h: A. Ogawa, H. Tanaka, H. Yokoyama, R. Obayashi, K. Yokoyama, N. Sonoda, *J. Org. Chem.* **1992**, *57*, 111–115.

[5] a) A. Ogawa, H. Yokoyama, K. Yokoyama, T. Masawaki, N. Kambe, N. Sonoda, *J. Org. Chem.* **1991**, *56*, 5721–5723; b) T. G. Back, M. V. Krishna, *J. Org. Chem.* **1988**, *53*, 2533–2536; c) A. Ogawa, N. Takami, M. Sekiguchi, H. Yokoyama, H. Kuniyasu, I. Ryu, N. Sonoda, *Chem. Lett.* **1991**, 2241–2242.

[6] a) G. Stork, R. Mook, Jr., *Tetrahedron Lett.* **1986**, *27*, 4529–4532; b) G. Stork, R. Mook, Jr., *J. Am. Chem. Soc.* **1987**, *109*, 2829–2831; c) K. Nozaki, K. Oshima, K. Utimoto, *J. Am. Chem. Soc.* **1987**, *109*, 2547–2549; d) J. E. Brumwell, N. S. Simpkins, N. K. Terrett, *Tetrahedron* **1994**, *50*, 13533–13552; e) C. A. Broka, D. E. C. Reichert, *Tetrahedron Lett.* **1987**, *28*, 1503–1506; f) T. Kataoka, M. Yoshimatsu, Y. Noda, T. Sato, H. Shimizu, M. Hori, *J. Chem. Soc. Perkin Trans. 1* **1993**, 121–129.

[7] E. Lee, C. U. Hur, *Tetrahedron Lett.* **1991**, *32*, 5101–5102.

[8] In general, vinyl radicals are believed to be a mixture of stereoisomeric σ radicals, and a fast equilibrium is present between the stereoisomers: a) R. W. Fessenden, R. H. Schuler, *J. Chem. Phys.* **1963**, *39*, 2147–2195. In contrast, α-aryl-substituted vinylic radicals are assumed to be π radicals: b) L. A. Singer, J. Chen, *Tetrahedron Lett.* **1969**, 4849–4854.

[9] Ethyl propiolate is assumed to generate a vinylic π radical: a) C. Galli, A. Guarnieri, H. Koch, P. Mencarelli, Z. Rappoport, *J. Org. Chem.* **1997**, *62*, 4072–4077; b) H. Rubin, H. Fischer, *Helv. Chim. Acta* **1996**, *79*, 1670–1682; c) J. O. Metzger, M. Blumenstein, *Chem. Ber.* **1993**, *126*, 2493–2499.

[10] Although PhSe$^\bullet$ can also add to alkenes, the reverse reaction from β-selenoalkyl radicals to give the starting alkenes and PhSe$^\bullet$ is probably much faster than that of β-selenoalkenyl radicals to give the starting alkynes and PhSe$^\bullet$.

[11] a) M. Sevrin, D. Van Ende, A. Krief, *Tetrahedron Lett.* **1976**, 2643–2646; b) J. Lucchetti, A. Krief, *Tetrahedron Lett.* **1981**, *22*, 1623–1626; c) D. L. J. Clive, G. Chittattu, C. K. Wong, *J. Chem. Soc. Chem. Commun.* **1978**, 41–42; d) D. L. J. Clive, G. J. Chittattu, V. Farina, W. A. Kiel, S. M. Menchen, C. G. Russell, A. Singh, C. K. Wong, N. J. Curtis, *J. Am. Chem. Soc.* **1980**, *102*, 4438–4447; e) K. C. Nicolaou, *Tetrahedron* **1981**, *37*, 4097–4109; f) T. G. Back, *J. Chem. Soc. Chem. Commun.* **1984**, 1417–1418; g) C. Chatgilialoglu, M. Guerra, A. Guerrini, G. Seconi, K. B. Clark, D. Grillen, J. Kanabus-Kaminska, J. A. Martinho-Simões, *J. Org. Chem.* **1992**, *57*, 2427–2433.

[12] H. J. Reich, S. Wollowitz, *Org. React.* **1993**, *44*, 1–296, and references therein.

[13] J. V. Comasseto, *J. Organomet. Chem.* **1983**, *253*, 131–181.

[14] H. Okamura, M. Miura, K. Kosugi, H. Takei, *Tetrahedron Lett.* **1980**, *21*, 87–90.

[15] a) A. Ogawa, Y. Tsuboi, R. Obayashi, K. Yokoyama, I. Ryu, N. Sonoda, *J. Org. Chem.* **1994**, *59*, 1600–1601; b) J. V. Comasseto, L. W. Ling, N. Petragnani, H. A. Stefani, *Synthesis* **1997**, 373–403.

[16] The *E*/*Z* ratio of the product reflects that of the vinylic selenide starting material: **5b** *E*/*Z* = 10/90, **5j** *E*/*Z* = 7/93, **7b** *E*/*Z* = 7/93, **7b'** *E*/*Z* = 16/84, **7j** *E*/*Z* = 8/92.

[17] The relative rate of dichalcogenides for capturing carbon radicals is as follows: $k_{\mathrm{PhSSPh}}:k_{\mathrm{PhSeSePh}}:k_{\mathrm{PhTeTePh}} = 1{:}160{:}630$.[3a]

[18] a) D. P. Curran in *Comprehensive Organic Synthesis*, *Vol. 4* (Eds.: B. M. Trost, I. Fleming, M. F. Semmelhock), Pergamon, Oxford, **1991**, pp. 779–831; b) D. P. Curran, *Synthesis* **1988**, 417–439; D. P. Curran, *Synthesis* **1988**, 489–513; c) D. P. Curran, N. A. Porter, B. Giese, *Stereochemistry of Radical Reactions*, VCH, Weinheim, **1996**; d) J. Fossey, D. Lefort, J. Sorba, *Free Radicals in Organic Chemistry*, Masson, Paris, **1995**; e) B. Giese, B. Kopping, T. Göbel, J. Dickhaut, G. Thoma, K. J. Kulicke, F. Trach, *Org. React.* **1996**, *48*, 301–856.

The First Determination of Eu–H Distances by Neutron Diffraction on the Novel Hydrides $EuMg_2H_6$ and $EuMgH_4$**

Holger Kohlmann,* Franz Gingl, Thomas Hansen, and Klaus Yvon

The complete crystal structure analysis of metal hydrides usually requires neutron diffraction data. Some elements, however, show excessively high absorption cross sections, σ_a, for neutrons, thus making this technique seemingly impractical. Natural europium (^{nat}Eu) consists of nearly equal amounts of the isotopes ^{151}Eu and ^{153}Eu. Its absorption cross section for thermal neutrons (σ_a = 4530 barns at λ = 179.8 pm) is higher than that of the shielding material cadmium.[1] Pure ^{153}Eu has a lower σ_a but is extremely expensive. Thus no complete, refined crystal structure data are known for europium hydrides, that is no reliable value exists for the distance Eu–H.[2]

Fortunately, the neutron absorption cross section of natural europium is strongly wavelength dependent and shows a minimum at λ = 72 pm (Figure 1). This prompted us to perform the first neutron diffraction experiment at this

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