Pergamon

Tetrahedron Letters 42 (2001) 2317–2319

TETRAHEDRON
LETTERS

Selective sequential addition of diphenyl diselenide to ethyl propiolate and isocyanides upon irradiation with near-UV light

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Received 20 September 2000; revised 15 January 2001; accepted 19 January 2001

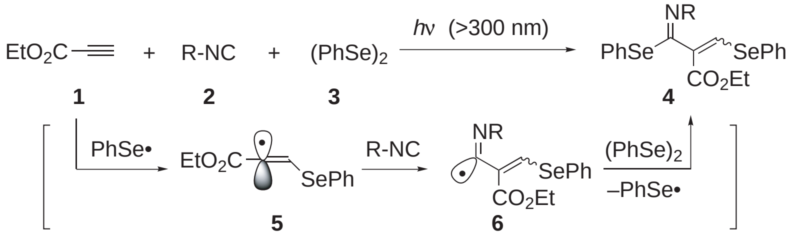
Abstract—Upon irradiation through Pyrex with a tungsten lamp (*hν*>300 nm), diphenyl diselenide adds to electron-deficient alkynes such as ethyl propiolate and isocyanides sequentially to provide the corresponding three-component coupling products in moderate to high yields selectively. The appropriate strength of carbon-radical trapping by diphenyl diselenide facilitates its selective three-component coupling with ethyl propiolate and isocyanides. © 2001 Elsevier Science Ltd. All rights reserved.

In view of the growing interest in selective carbon–carbon bond forming reactions with simultaneous introduction of heteroatom functions, we have investigated the sequential addition of heteroatom compounds to two (or more) unsaturated compounds under radical conditions. To accomplish such radical addition reactions of heteroatom compounds accompanied by selective bond-connection between unsaturated compounds, both the reactivity of heteroatom-centered radicals toward unsaturated bonds and the capturing ability of radical precursors toward carbon radicals are of great importance. For example, the lower radical trapping ability may cause polymerization of unsaturated compounds, whereas the higher one might inhibit the bond-connection between unsaturated compounds.

Recently, we have suggested that diphenyl diselenide[1] is a promising candidate for heteroatom compounds to work its selective three-component coupling with an electron-poor alkyne and an electron-rich alkene.[2] Herein, we wish to report a highly selective sequential addition of diphenyl diselenide to ethyl propiolate and isocyanides,[3] providing the corresponding three-component coupling products bearing both vinyl and imidoyl selenide functions, regioselectively (Eq. (1)).

Upon irradiation with a tungsten lamp (500 W) through Pyrex (*hν*>300 nm), the reaction of ethyl propiolate (**1**, 0.16 mmol) with benzylisocyanide (**2a**, 4.60 mmol)[4] and $(PhSe)_2$ (**3**, 0.16 mmol) in the absence of solvent was conducted at 15°C for 6 h by the addition of $(PhSe)_2$ separately eight times, which afforded the corresponding three-component coupling product (**4a**) in 85% yield after purification by a recycling preparative HPLC (GPC, $CHCl_3$) (entry 1 in Table 1).[5,6]

Similar conditions can be employed with cyclohexylisocyanide (**2b**) and 2,6-xylylisocyanide (**2c**), giving the corresponding three-component coupling products (**4b** and **4c**) selectively (entries 2,3). Functionalities such as $P(O)(OEt)_2$, and ester groups are tolerant toward the selective sequential addition reaction (entries 4,5). On the other hand, a complex mixture is formed in the case of *t*-butylisocyanide, probably due to the decomposition of the imydoyl radical intermediate to *t*-butyl radical.[31]



(1)

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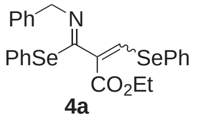
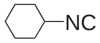
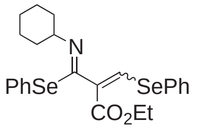
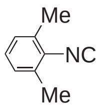
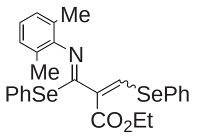
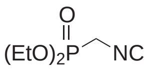
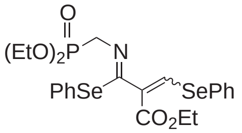
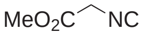
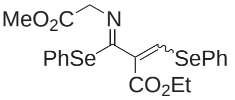
PII: S0040-4039(01)00123-X

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

Entry	Substrate	Product	Yield, %[b]	*E/Z*
1	 **2a**	 **4a**	85	51/49
2	 **2b**	 **2b**	72	35/65
3	 **2c**	 **4c**	59	52/48
4	 **2d**	 **4d**	58	45/55
5	 **2e**	 **4e**	58	55/45

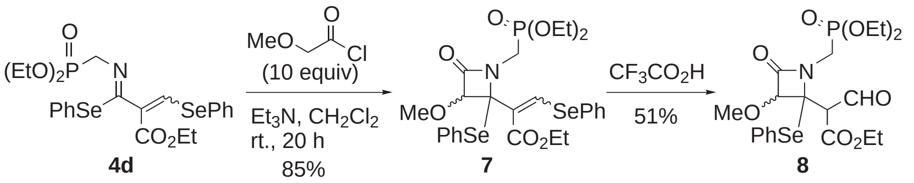
[a] Reaction conditions: ethyl propiolate (0.16 mmol), $(PhSe)_2$ (1 equiv.), isocyanide (20–30 equiv.), 15°C, *hν*: tungsten lamp (500 W, Pyrex).

[b] Isolated yield.

We next examined the sequential addition of $(PhSe)_2$ to several acetylenes in the presence of cyclohexylisocyanide under controlled conditions. Terminal alkynes bearing a carbonyl group such as ethyl propiolate, methyl propiolate, and 1-butyne-3-one undergo the desired sequential addition successfully to give the corresponding three-component coupling products in 59, 70, and 40% yields, respectively. With inner alkynes bearing electron-withdrawing groups such as diethyl acetylenedicarboxylate, the sequential addition proceeds slowly giving 18% of the desired three-component coupling product. In contrast, when 1-octyne, phenylacetylene, and trimethylsilylacetylene are used in place of ethyl propiolate, bisselenation[7] of the alkynes takes place in preference to the desired three-component coupling. These results suggest that electron-deficient alkynes are suitable for this three-component coupling reaction.

A possible mechanistic pathway may include the following (see Eq. (1)): (i) upon irradiation with near-UV light, diphenyl diselenide ($\lambda_{max}=330$ nm) undergoes homolytic dissociation to generate $PhSe^{\bullet}$, which adds to ethyl propiolate selectively, forming β-seleno-substituted vinylic radical (**5**); (ii) the vinylic radical (**5**) reacts with isocyanides to produce imidoyl radical intermediate (**6**), which is trapped with $(PhSe)_2$ yielding the three-component coupling product (**4**) with regeneration of $PhSe^{\bullet}$.

The obtained three-component coupling products, which have several hetero-functions, are expected to work as a promising building block for the synthesis of useful heterocyclic compounds. For example, the reaction of the three-component coupling product (**4d**) with α-methoxyacetyl chloride in the presence of triethylamine successfully provides the corresponding β-lactam (**7**) in good yield, as indicated in Eq. (2). The following treatment of the β-lactam (**7**) with trifluoroacetic acid leads to chemoselective removal of the vinylic selenium function of **7** giving the corresponding aldehyde (**8**) as a precursor for the construction of carbapenem framework.



(2)

In summary, $(PhSe)_2$ is revealed to add to ethyl propiolate and isocyanides sequentially giving the three-component coupling products with high regioselectivity. Further study along these lines is now in progress.

Acknowledgements

This research was supported partly by a Grant-in-Aid for Scientific Research on Priority Areas (12020233) from the Ministry of Education, Science and Culture, Japan.

References

1. The rate constant for the S_H2 reaction of 5-hexenyl radical with $(PhSe)_2$ is 1.2×10^7 M^{-1} s^{-1}, see: Russell, G. A.; Tashtoush, H. *J. Am. Chem. Soc.* **1983**, *105*, 1398–1399.
2. (a) Ogawa, A.; Doi, M.; Ogawa, I.; Hirao, T. *Angew. Chem., Int. Ed.* **1999**, *38*, 2027–2029; (b) Ogawa, A.; Ogawa, I.; Sonoda, N. *J. Org. Chem.* **2000**, *65*, 7682–7685.
3. For radical reactions of isocyanides, see for example: (a) Saegusa, T.; Kobayashi, S.; Ito, Y.; Yasuda, N. *J. Am. Chem. Soc.* **1968**, *90*, 4182; (b) Saegusa, T.; Kobayashi, S.; Ito, Y. *J. Org. Chem.* **1970**, *35*, 2118–2121; (c) Barton, D. H. R.; Ozbalik, N.; Vacher, B. *Tetrahedron* **1988**, *44*, 3501–3512; (d) Chatgilialoglu, C.; Giese, B.; Kopping, B. *Tetrahedron Lett.* **1990**, *31*, 6013–6016; (e) Curran, D. P.; Liu, H. *J. Am. Chem. Soc.* **1991**, *113*, 2127–2132; (f) Curran, D. P.; Liu, H. *J. Am. Chem. Soc.* **1992**, *114*, 5863–5864; (g) Fukuyama, T.; Chen, X.; Peng, G. *J. Am. Chem. Soc.* **1994**, *116*, 3127–3128; (h) Bachi, M. D.; Balanov, A.; Bar-Ner, N. *J. Org. Chem.* **1994**, *59*, 7752–7758; (i) Nanni, D.; Pareschi, P.; Rizzoli, C.; Sgarabotto, P.; Tundo, A. *Tetrahedron* **1995**, *51*, 9045–9062; (j) Ryu, I.; Sonoda N.; Curran, D. P. *Chem. Rev.* **1996**, *96*, 177–194; (k) Yamago, S.; Miyazoe, H.; Goto, R.; Yoshida, J. *Tetrahedron Lett.* **1999**, *40*, 2347–2350; (l) Leardini, R.; Nanni, D.; Zanardi, G. *J. Org. Chem.* **2000**, *65*, 2763–2772.
4. The present three-component coupling between ethyl propiolate (**1**), isocyanides (**2**), and $(PhSe)_2$ requires the use of excess amounts of isocyanides. When the molar ratio of **2**/**1** was diminished, the yield of the three-component coupling product decreased and instead the $(PhSe)_2$ adduct to **1** was formed as a byproduct.
5. The spectral and analytical data for the three-component coupling product, e.g., **4d** is as follows: a yellow oil (obtained as a stereoisomeric mixture ($E/Z=45/55$); ^{1}H NMR (600 MHz, $CDCl_3$) [(E)-**4d**]: δ 1.28 (t, $J=7.2$ Hz, 3 H), 1.32 (t, $J=7.2$ Hz, 6 H), 4.05 (d, $J=16.2$ Hz, 2 H), 4.08 (q, $J=7.2$ Hz, 4 H), 4.18 (quint. like, $J=7.2$ Hz, 4 H), 7.25–7.57 (m, 10 H), 7.65 (s, 1 H). [(Z)-**4d**] δ 1.16 (t, $J=7.2$ Hz, 3 H), 1.38 (t, $J=7.2$ Hz, 6 H), 3.98 (q, $J=7.2$ Hz, 4 H), 4.12 (d, $J=16.2$ Hz, 2 H), 4.24 (quint. like, $J=7.2$ Hz, 4 H), 7.25–7.57 (m, 10 H), 7.98 (s, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) [(E)-**4d**]: δ 14.16, 16.45 (d, $J=3.8$ Hz), 53.45 (d, $J=107.6$ Hz), 61.08, 62.57 (d, $J=4.6$ Hz), 126.89, 128.41, 128.92, 129.10, 129.30, 132.40, 133.37, 136.79, 152.21, 164.46. [(Z)-**4d**] δ 14.09, 16.54 (d, $J=3.8$ Hz), 53.18 (d, $J=107.6$ Hz), 60.90, 62.67 (d, $J=4.6$ Hz), 126.74, 128.30, 128.95, 129.04, 129.44, 130.87, 132.90, 136.24, 147.85, 162.35; IR (NaCl) 3056, 2981, 1709, 1621, 1309, 1225, 1028, 968, 742, 692 cm^{-1}; MS (CI), $m/z=590$ ($M^{+}+1$, 81.1); anal. calcd for $C_{23}H_{28}NO_5PSe_2$: C, 47.03; H, 4.80; N, 2.38. Found: C, 47.10; H, 4.89; N, 2.46.
6. The *syn*- and *anti*-isomers, concerning C–N double bonds, of the three-component coupling products are in rapid equilibrium with each other at ambient temperature, and, as the result, the ^{1}H NMR spectra of the three-component coupling products indicate averaged signals of both isomers.
7. (a) Back, T. G.; Krishna, M. V. *J. Org. Chem.* **1988**, *53*, 2533–2536; (b) Ogawa, A.; Yokoyama, H.; Yokoyama, K.; Masawaki, T.; Kambe, N.; Sonoda, N. *J. Org. Chem.* **1991**, *56*, 5721–5723.