Short Note

2,2-Bis(phenylselanyl)-1-(*p*-tolyl)vinyl 2-Oxo-2-(*p*-tolyl)acetate

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Abstract: 2,2-Bis(phenylselanyl)-1-(*p*-tolyl)vinyl 2-oxo-2-(*p*-tolyl)acetate was synthesized via the
reaction of *p*-tolylacetylene with diphenyl diselenide and benzoyl peroxide in benzene under at-
mospheric conditions. The molecular structure of the synthesized compound was evaluated using
single-crystal X-ray analysis and spectral analyses. The process reported here provides a rare ex-
ample of the direct and selective transformation of a terminal alkyne to the corresponding geminal
diseleno-substituted alkene.

Keywords: alkyne; benzoyl peroxide; diselenide; addition reaction; oxidation reaction

1. Introduction

Atomically efficient and selective addition reaction of heteroatom compounds to
carbon−carbon unsaturated bonds is one of the most valuable synthetic reactions [1–12].
The addition of heteroatom compounds to alkynes affords the corresponding alkenyl
heteroatoms, which are typically present not only in synthetic intermediates but also in a
variety of natural products and functional molecules [13–18].

During the course of our study on the simultaneous introduction of different het-
eroatom groups into alkynes [19–26], we successfully developed a binary system composed
of benzoyl peroxide [(PhCOO)$_2$; BPO] and diphenyl diselenide [(PhSe)$_2$] for the selective
selenation of alkynes [26]. Specifically, in the case of internal alkynes, the stereoselective
benzoyloxyselenation reaction yielded the corresponding β-(benzyloxy)alkenyl selenides,
whereas terminal alkynes were converted to alkynyl selenides via a C(sp)–H substitution
reaction with (PhSe)$_2$ (Scheme 1). Herein, we report a unique multi-coupling reaction of a
terminal alkyne (*p*-tolylacetylene, **1a**), BPO, and (PhSe)$_2$ to produce a novel 1,2-diketone
compound (**2a**) containing a geminal diseleno-substituted alkene moiety (see, Scheme 2).
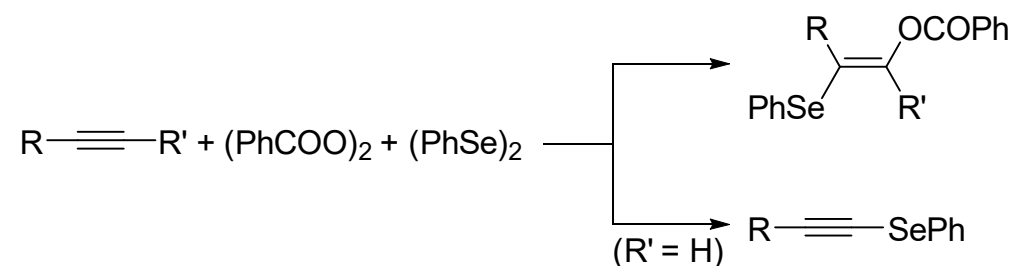
Scheme 1. Selective selenation of alkynes based on a BPO/(PhSe)$_2$ binary system.
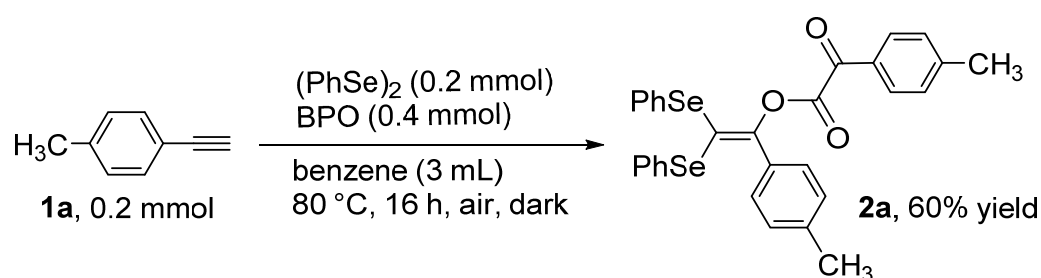
Scheme 2. Synthesis of **2a** through the reaction of **1a** with (PhSe)$_2$ and BPO.

2. Results and Discussion

During the reaction of *p*-tolylacetylene (**1a**) with (PhSe)$_2$ (1 equiv) and BPO (2 equiv) in benzene, the title coupling product, **2a**, was formed in 60% yield. The structure of this product was determined using X-ray diffraction (Scheme 2 and Figure 1) and several spectral analyses (the ^{1}H, ^{13}C{^{1}H} and ^{77}Se{^{1}H} NMR spectra of **2a** are included in the Supplementary Materials). As indicated in Scheme 2, the molecular structure of **2a** consists of one molecule of (PhSe)$_2$ and two molecules of the terminal alkyne **1a**.
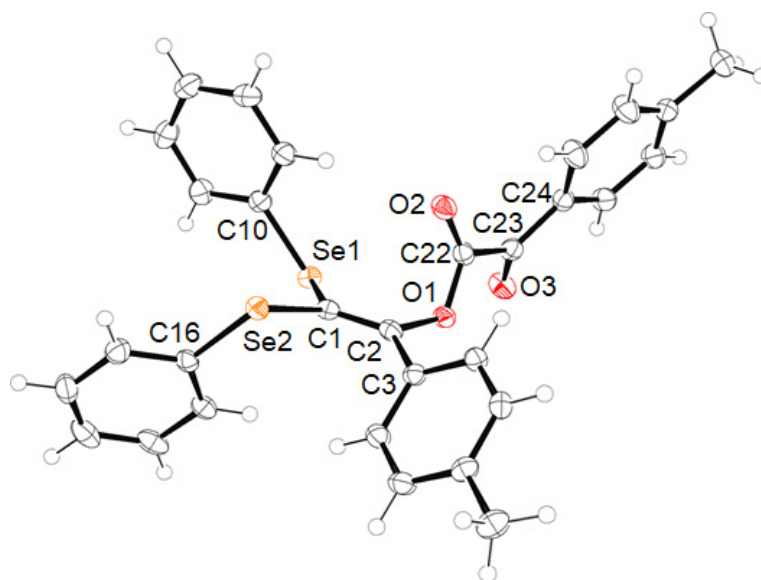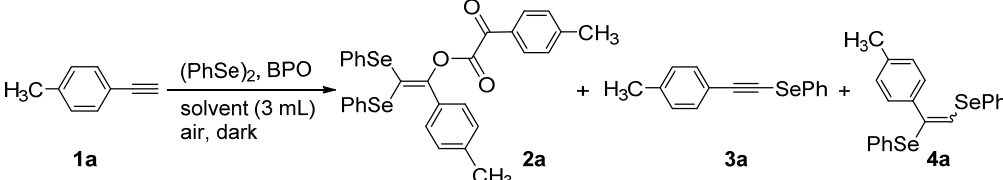

Figure 1. Crystal structure of **2a** with numbered atoms. Ellipsoids are shown at the 50% probability level. Selected interatomic distances (Å) and angles (deg): Se1−C1, 1.9178(17); Se1−C10, 1.916(2); Se2−C1, 1.9021(19); Se2−C16, 1.9188(19); O1−C2, 1.420(2); O1−C22, 1.360(2); O2−C22, 1.195(2); O3−C23, 1.215(2); C1−C2, 1.338(3); C2−C3, 1.482(3); C22−C23, 1.546(3); C23−C24, 1.478(3); C1−Se1−C10, 99.28(8); C1−Se2−C16, 101.23(8); C2−O1−C22, 116.88(14); Se1−C1−Se2, 120.61(10); Se1−C1−C2, 120.87(14); Se2−C1−C2, 118.38(13); O1−C2−C1, 119.30(16); O1−C2−C3, 111.41(15); C1−C2−C3, 129.04(17); O1−C22−O2, 125.80(17); O1−C22−C23, 109.00(15); O2−C22−C23, 125.14(17); O3−C23−C22, 117.29(16); O3−C23−C24, 123.59(17); C22−C23−C24, 119.09(16).

The multi-coupling reaction of **1a**, BPO, and (PhSe)$_2$ was further evaluated under various reaction conditions (Table 1). Increasing the amount of (PhSe)$_2$ did not induce a significant increase in the yield of **2a**, whereas byproducts **3a** and **4a** were formed (entry 1 vs. entry 2). Prolonging the reaction time was also ineffective in improving the yield of **2a** (entry 1 vs. entry 3). When the amount of (PhSe)$_2$ was reduced to 0.10 mmol and an excess amount (0.60 mmol) of BPO was introduced, **3a** was formed as the primary reaction product (entry 4). Among the solvents used, benzene produced the most encouraging results (entry 1 vs. entries 5−7). The yield of **2a** was slightly improved by reducing the amount of the benzene solvent used (entry 8). When the reaction was conducted using

concentrated benzene solvent (heated at 80 °C without cooling water), the yield of **2a** was improved to 63% (entry 9). However, a further increase in the reaction temperature to 100 °C decreased the yield of **2a** (entries 10 and 11).

**Table 1.** Optimization of the reaction conditions for the synthesis of **2a**.

Entry	1a/(PhSe)₂/BPO (mmol)	Solvent	Condition	Yields (%) [a]		
				2a	**3a**	**4a**
1	0.20/0.20/0.40	Benzene	80 °C, 16 h	48	–	–
2	0.20/0.40/0.40	Benzene	80 °C, 16 h	43	25	5
3	0.20/0.2/0.40	Benzene	80 °C, 24 h	40	23	2
4	0.30/0.10/0.60	Benzene	80 °C, 24 h	Trace	48	–
5 [b,c]	0.20/0.20/0.40	Et₂O	80 °C, 16 h	22	7	21
6	0.20/0.20/0.40	Toluene	80 °C, 16 h	9	–	–
7	0.20/0.20/0.40	THF	80 °C, 16 h	N.D.	11	16
8	0.20/0.20/0.40	Benzene (1 mL)	80 °C, 16 h	51	N.D.	6
9 [b,c]	0.20/0.20/0.40	Benzene (1 mL)	80 °C, 16 h	63	N.D.	6
10	0.20/0.20/0.40	Benzene	100 °C, 16 h	6	43	Trace
11	0.20/0.20/0.40	Benzene (1 mL)	100 °C, 16 h	27	N.D.	7

[a] Determined by ¹H-NMR; [b] no cooling water used; [c] majority of the solvent was distilled out during the initial stages of the reaction, and the reaction proceeded under essentially neat conditions.

To evaluate the formation mechanism of **2a**, the reaction of alkynyl selenide **3a** was attempted using equimolar amounts of (PhSe)₂ and BPO to produce the coupling product **2a** in a 61% yield (Scheme 3). The result suggests that alkynyl selenide **3a** acts as an intermediate during the formation of **2a**. It should be noted that **2a** possesses an α-keto ester moiety, which may be formed during the oxidation of the alkynyl ether moiety using molecular oxygen (O₂). Wille et al. previously reported the oxidation of alkynes (e.g., PhC≡CPh) to produce 1,2-diketones (e.g., PhC(=O)–C(=O)Ph) in the presence of O₂, in a process initiated by the thiyl radical (PhS•). More specifically, the thiylperoxyl radical (PhSOO•), derived from PhS• and O₂, acted as an initiator during the oxidation reaction [27]. Therefore, we assume that the C≡C triple bond in the alkynyl ether intermediate **6a** (or **4a**), a precursor to **2a**, underwent oxidation with O₂ in the presence of the selenoperoxyl radical PhSeOO•, which acts as an initiator. Although this process has several potential reaction routes, one of the most promising is given in Scheme 4. The thermal decomposition of BPO generates a benzoyloxy radical, which attacks **3a** to produce alkynyl benzoate, **4a**. The subsequent electrophilic reaction of **3a** with **4a** in the presence of **5a** produced **6a** along with benzoic acid anhydride. Notably, this reaction provides a rare example of the direct and selective transformation of a terminal alkyne to the corresponding geminal diseleno-substituted alkene [28–30].
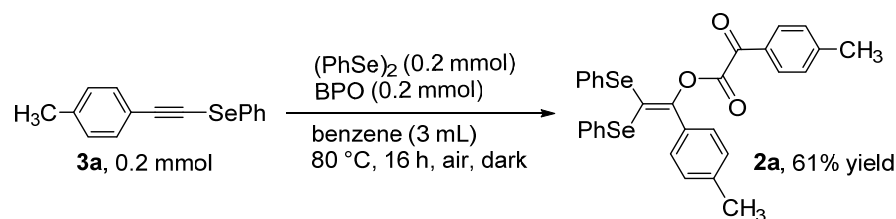
Scheme 3. Synthesis of **2a** via the reaction of **3a** with (PhSe)₂ and BPO.
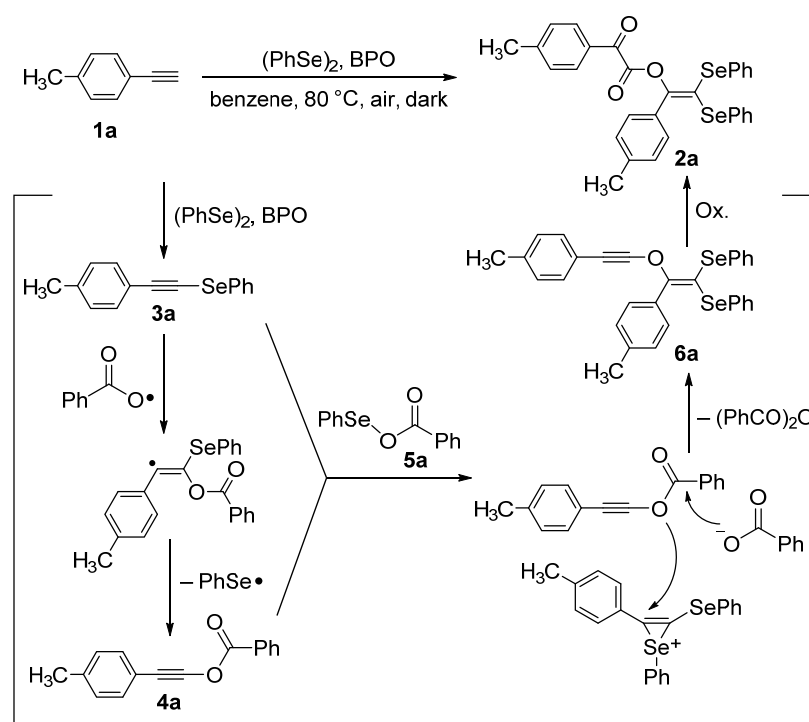
Scheme 4. Possible pathway for the multi-coupling reaction.

3. Experimental

3.1. General

^{1}H-NMR spectra were obtained using a JEOL JMN-ECX400 (400 MHz) FT NMR system (JEOL, Tokyo, Japan), in which CDCl$_3$ was employed as the deuterated solvent and Me$_4$Si was used as an internal standard. ^{13}C{^{1}H} NMR spectra were obtained using a JEOL JNM-ECX400 (100 MHz) FT NMR system (JEOL, Tokyo, Japan). The ^{77}Se{^{1}H} NMR spectrum was obtained using a JEOL JNM-ECX400 (76 MHz) FT NMR system (JEOL, Tokyo, Japan). Unless otherwise stated, all reagents and solvents were purchased from chemical companies and used without further purification.

3.2. Synthesis of 2,2-Bis(phenylselanyl)-1-(p-tolyl)Vinyl 2-Oxo-2-(p-tolyl)Acetate (2a)

Initially, BPO (0.20 mmol), (PhSe)$_2$ (0.20 mmol), *p*-tolylacetylene (**1a**) (0.20 mmol), and benzene (3 mL) were added to a 10 mL round-bottomed flask. The resultant mixture was then heated at 80 °C for 16 h in the dark, under atmospheric conditions. Once the reaction was complete, the reaction mixture was treated with saturated aqueous sodium thiosulfate. The product was then extracted using ethyl acetate, and the resultant combined organic layer was washed using saturated aqueous sodium bicarbonate. The organic layer was neutralized with aqueous HCl (0.1 N). Subsequently, the combined extracts were dried using MgSO$_4$. Filtration and concentration in vacuo yielded the crude product, which was subsequently purified using GPC (eluent CHCl$_3$) to obtain **2a** (35.4 mg, 60% yield) as a pale-yellow solid. Mp 65.0–66.0 °C; ^{1}H-NMR (CDCl$_3$) δ 7.97 (d, *J* = 8.2 Hz, 2H), 7.52 (d, *J* = 7.8 Hz, 2H), 7.37 (dd, *J* = 8.5, 1.1 Hz, 2H), 7.27–7.17 (m, 12H), 2.41 (s, 3H), 2.36 (s, 3H); ^{13}C{^{1}H} NMR (CDCl$_3$) δ 184.4, 160.9, 150.8, 146.4, 139.9, 134.8, 132.3, 131.4, 131.1, 130.5, 130.0, 129.9, 129.6, 129.2, 128.81, 128.77, 128.7, 128.0, 127.3, 113.7, 21.9, 21.5; ^{77}Se{^{1}H} NMR (CDCl$_3$) δ 452, 431; IR (KBr, cm^{-1}): 2360, 2331, 1748, 1683, 1604, 1577, 1475, 1438, 1151, 954, 735; MS (FAB): *m/z* = 592 [M]$^+$. HRMS (ESI) analysis of **2a** also showed *m/z* 468.9585 attributed to the sodium ion adduct of (PhSe)$_2$CHC(=O)(C$_6$H$_4$-*p*-CH$_3$) (calcd *m/z*: 468.9586) generated via decomposition of the thermally unstable 1,2-diketone moiety of **2a** during the analysis, which supports the identification of **2a**.

3.3. X-ray Diffraction Studies

An X-ray crystallographic measurement was carried out on a Rigaku RAXIS-RAPID diffractometer with Mo-Kα radiation at 123 K. Of 39479 reflections collected, 5743 were unique (R_{int} = 0.0465). An empirical absorption correction was applied, which resulted in transmission factors ranging from 0.513 to 0.942. The data were corrected for Lorentz and polarization effects. The structure of **2a** was solved by direct methods and expanded using Fourier techniques. The non-hydrogen atoms were refined anisotropically, and hydrogen atoms were refined using the riding model. All calculations were performed with the *CrystalStructure* [31] crystallographic software package except for refinements, which was performed using SHELXL Version 2014/7 [32].

Crystallographic data: formula weight = 590.44; monoclinic; space group $P2_1/n$; a = 9.62321(17) Å, b = 5.73648(10) Å, c = 45.1254(8) Å; V = 2490.50(8) Å^3; Z = 4; ρ_{calcd} = 1.575 g cm^{-3}; total reflections collected = 39479; GOF = 1.054; R_1 = 0.0264; wR_2 = 0.0672. Crystallographic data have been deposited with Cambridge Crystallographic Data Centre (CCDC-2104238). These data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html (accessed date: 19 August 2021) (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: +44 1223 336033; E-mail: deposit@ccdc.cam.ac.uk).

4. Conclusions

A unique multi-coupling reaction of the terminal alkyne **1a**, (PhSe)$_2$, and BPO was observed, the mechanism of which was based on an oxidation process. We believe that the results presented here provide a novel and facile route for the synthesis of geminal diseleno-substituted alkenes.

Supplementary Materials: The following are available: Figure S1. ^{1}H-NMR spectrum (CDCl$_3$, 400 MHz) of compound **2a**. Figure S2. ^{13}C{^{1}H} NMR spectrum (CDCl$_3$, 100 MHz) of compound **2a**. Figure S3. ^{77}Se{^{1}H} NMR spectrum (CDCl$_3$, 76 MHz) of compound **2a**.

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