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A simple and stereoselective synthesis of (*Z*)-1,2-bis-arylselanyl alkenes from alkynes using KF/Al_2O_3

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ABSTRACT

The title compounds were synthesized by a one-pot reaction of diaryl diselenides with terminal alkynes avoiding the previous preparation of arylselanyl alkynes. The reactions were performed under mild conditions with a range of terminal alkynes using KF/Al_2O_3 and PEG-400 as solvent. The addition of diaryl diselenides to alkynes occurred stereoselectively to give exclusively (*Z*)-1,2-bis-arylselanyl alkenes in good yields. The reaction time was reduced to a few minutes using microwave irradiation and the KF/Al_2O_3/PEG-400 system can be reused one time without previous treatment with comparable activity.

1. Introduction

In recent years, organoselenium compounds were received great attention in chemical science because they are attractive as key intermediate in organic synthesis[1,2] and because their interesting fluorescent properties[3] and biological activities.[4] Beside, the versatility and applicability of organoselenium compounds in chemical sciences are well described in a great number of reviews[1] and books.[2] Between the organoselenium compounds, 1,2-bis-chalcogenyl alkenes are of special interest, because they can be used as a versatile precursor to enediynes and other functionalized olefins.[5]

1,2-Bis-organylselanyl alkenes have been obtained by the Se–Se bond addition to alkynes catalyzed by palladium,[6] palladium and microwave irradiation,[7] platinum,[6c] rhodium complex,[8] under photochemical[9] or using Ti(*i*-PrO)$_4$/*i*-PrMgCl and electrophilic selenium species.[10] These protocols afford selectively (*Z*)-1,2-bis-organylselanyl alkenes or, in some cases, a mixture of *Z* and *E* isomers and other side products. On the other hand, (*E*)-1,2-bis-arylselanyl styrenes were selectively prepared starting from phenylacetylene and diaryl diselenides under solvent-free,[11] glycerol[12] or in ionic liquid[13] using $NaBH_4$ to generate the nucleophilic selenium species. Recently, the in situ addition of diorganyl diselenides to propargylic alcohols using *n*-BuLi to afford bis-phenylselanyl alkenes in good yields and high stereoselectivity was described.[14] The authors observed that the presence of the acidic hydrogen from hydroxyl group is crucial for the selectivity control in the addition. However, to our knowledge, reaction under basic conditions of terminal alkynes with diorganyl diselenide, avoiding the previous preparation of organylselanyl alkynes to afford (*Z*)-bis-organylselanyl alkenes remains a challenge in organic chemistry.[15]

The development of environmentally benign and clean synthetic protocols using solvents alternative to Volatile Organic Compounds (VOC's), such as water, ionic liquids (ILs) and polyethylene glycol (PEG) has increased.[16] Despite several advantages, the use of water is limited due the low solubility of most of organic substrates, while ILs are expensive and can release hazardous inorganic residues during recycling. To resolve these inconvenients, PEG has been proved a promising media for organic synthesis,[17] including Heck[17a] and Mannich[17b] reactions, cross-coupling,[17c,f] N-arylation[17g] and cycloaddition reactions.[17h]

On other hand, the use of potassium fluoride supported on alumina (KF/Al_2O_3) as a green catalytic system for a number of transformations has been increased.[18] By using KF/Al_2O_3, the products can be easily isolated by filtration and the generation of large amounts of salts at the end of the synthesis, as well as the use

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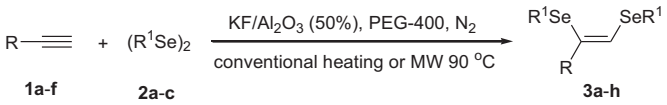
of stoichiometric strong bases, can be avoided. In this sense, KF/Al_2O_3 has been employed by our group[19] and others[20] in various organic transformations. In this way, as a continuation of our studies, we report herein the results of the addition of the diorganyl diselenides to alkynes using KF/Al_2O_3 for the selective synthesis of (*Z*)-1,2-bis-organylselanyl alkenes (Scheme 1).

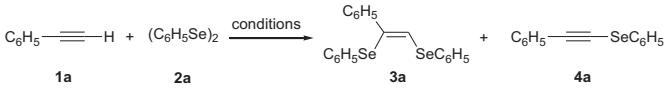


Scheme 1. General scheme of the reaction.

2. Results and discussion

Initially, we chose phenylacetylene **1a** (1.0 mmol) and diphenyl diselenide **2a** (1.0 mmol) as standard starting materials to establish the best reaction conditions for the synthesis of *Z*-1,2-bis-organylselanyl alkenes **3** under N_2 atmosphere (Table 1). We examined the influence of solvent, temperature, amount of KF/Al_2O_3 (50% m/m), as well as the heating source (oil bath and the use of focused microwave irradiation). It was found that using 0.04 g of KF/Al_2O_3 and PEG-400 (2.0 mL) at room temperature, unsatisfactory yield of the product **3a** was obtained and a great amount of diphenyl diselenide was recovered (Table 1, entry 1). When the reaction was performed at 60 °C, a mixture of (*Z*)- and (*E*)-1,2-bis-phenylselanylstyrene **3a** and 1-phenylselanyl-2-phenylethyne **4a** was obtained (Table 1, entry 2). Increasing the temperature to 90 °C, the reaction proceeds smoothly and the desired product **3a** was obtained exclusively in 60% yield (Table 1, entry 3). To our satisfaction, increasing the amount of KF/Al_2O_3 to 0.08 g, the desired product **3a** was obtained in 83% yield (Table 1, entry 4).

Table 1
Investigation of the best conditions to synthesis of **3a**[a]



Entry	KF/Al_2O_3 50% (g)	Solvent	Temperature (°C)	Yield of **3a** (%)	Ratio (*Z*-**3a**/*E*-**3a**)
1	0.04	PEG-400	25	Traces	—
2	0.04	PEG-400	60	61	[b]
3	0.04	PEG-400	90	60	97:3
4	0.08	PEG-400	90	83	97:3
5	0.08	Glycerol	90	62	15:85
6	0.08	None	25	80	12:88
7	0.08	THF	Reflux	n.d.	—
8	None	PEG-400	90	n.d.	—

[a] Reactions performed using **1a** (1 mmol), **2a** (1 mmol), and solvent (2.0 mL) under N_2 atmosphere for 6 h.
[b] It was observed a mixture of the products **3a**/**4a** in a 57:43 ratio.

In other experiment, we studied the influence of the solvent. Thus, it was observed that using glycerol instead PEG-400 (Table 1, entry 5) or under solvent-free conditions (Table 1, entry 6) good yields of **3a** were obtained, but with the preferential formation of the (*E*)-isomer. When THF was used as solvent (Table 1, entry 7), formation of desired product **3a** was not detected and the starting materials were recovered. Similarly, the reaction failed completely in the absence of KF/Al_2O_3 (Table 1, entry 8).

Since the best conditions were established, we explored our method extending the reaction to other terminal alkynes and diaryl diselenides (Scheme 1, Table 2, Method A). As can be seen in Table 2, a range of terminal alkynes worked well and with high stereoselectivity giving exclusively the (*Z*)-alkenes. Beside, differently to the observed when *n*-BuLi was employed,[14] under our conditions the presence of a hydroxyl group at the terminal alkyne is not essential to the formation exclusively of 1,2-bis-arylselanyl alkenes, which were obtained even starting from aromatic and aliphatic alkynes. Thus, propargylic alcohol **1b** reacted under our conditions with diphenyl diselenide **2a** to afford exclusively (*Z*)-1,2-bis-(phenylselanyl)prop-2-en-1-ol **3b** in 72% yield (Table 2, entry 3). Similarly, hex-1-yne **1f** gave 1,2-bis(phenylselanyl)hex-1-ene **3h**, in 32% yield (Table 2, entry 15). In general, our results showed that the reactions between diaryl diselenides and alkynes gave the respective vinyl selenides in good yields. Thus, diaryl diselenides containing electron-withdrawing (−Cl) or electron-donating groups ($-CH_3$) at the aromatic ring gave good yields of products **3c**,**d** (Table 2, entries 5–8).

However, when dimesityl diselenide **2c** was used, the desired 1,2-bis-(mesitylselanyl)alkene was obtained in reaction just with propargylic alcohol **1b**, which afforded **3d** in 90% yield (Table 2; entry 7). Surprisingly, phenylacetylene **1a** reacted smoothly with **2c** to afford the corresponding 1-mesitylselanyl alkynes **4b** in 72% yield (Scheme 2).

In order to obtain an efficient protocol in terms of energy efficience, we performed these reactions under focused microwave irradiation (MW) at the same temperature (90 °C). Thus, the mixture of phenylacetylene **1a** (1.0 mmol), diphenyl diselenide **2a** (1.0 mmol), KF/Al_2O_3 (0.08 g) and PEG-400 (2.0 mL) was irradiated under stirring and fortunately, after 30 min, the product **3a** was selectively obtained in 77% yield (Table 2, entry 2, Method B). To extend the scope of Method B, other terminal alkynes and diaryl diselenides were irradiated with MW and the corresponding products **3b**–**h** were obtained in comparable yields after 30 min. As can be seen in Table 2, Method A (conventional heating in an oil bath) is most suitable for phenylacetylene **1a** and hex-1-yne **1f**. When alkynyl alcohols **1b**–**e** were used, however, Method B (MW heating) provided better yields.

A reuse study of the KF/Al_2O_3/PEG-400 system was carried out for the reaction of **1a** with **2a** to obtain **3a** using MW at 90 °C during 30 min (Method B). After this time, the reaction mixture was diluted with hexane/ethyl acetate (90:10). The upper organic phase was removed and the product was isolated. The remaining KF/Al_2O_3/PEG-400 mixture was directly reused for further reactions. It was observed that a good level of efficiency was maintained in the second reaction (68% yield of **3a**). However, the yield dropped drastically in the third cycle, with **3a** being isolated in only 26% yield.

Following, we study the reaction of diphenyl ditelluride **5** with terminal alkynes under our conditions (Scheme 3). Similarly to the observed with dimesityl diselenide **2c**, the reaction of **5** with phenylacetylene **1a** gave the corresponding 1-phenyltellanyl alkyne **6** in good yield (Scheme 3). When alkynyl alcohols were used, the starting alkynes and ditelluride were recovered.

A plausible mechanism for the reactions of alkynes with diaryl diselenides using PEG-400 as solvent for formation of (*Z*)-1,2-bis-organylselanyl alkenes is depicted on Scheme 4. Initially, the experimental evidence supports that occurs the formation of the 1-organylselanyl-2-organylethyne **4** and selenolate anion.[21] In a second step, the mechanism is similar to the reaction using ethanol and the intermediate **7** could be involved in the formation of **3**. When the reaction was performed using internal diphenyl alkyne, no product was observed, being recovered the starting materials. Besides, in contrast with our findings, under radical conditions, the preferential formation of adducts with *E*-configuration is observed.[9c]