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Synthesis of a new chiral nitrogen containing diselenide as a precursor for selenium electrophiles

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Abstract

The synthesis of a new chiral nitrogen containing diselenide is described starting from (1*S*,2*S*)-1,2-diphenylethylendiamine. The electrophilic selenium species generated from this diselenide have been used for methoxyselenenylation reactions at room temperature with good yields and high diasteroselectivities. © 1998 Elsevier Science Ltd. All rights reserved.

Efficient and simple routes for the synthesis of chiral nonracemic diselenides have been developed recently.[1] Nitrogen containing diselenides such as **1** can be employed in stereoselective oxyselenenylation–elimination[2] reactions using peroxodisulfates to generate the electrophilic selenium species.[3]

Chiral diselenides have also been described as useful ligands in various transformations such as diethylzinc additions to aldehydes[4] as well as asymmetric hydrosilylation[5] and transfer hydrogenation reactions.[6]

In order to understand the role of the different reaction components on the yield and on the stereoselectivity, investigations on the alkoxyselenenylation step with stoichiometric quantities of the electrophilic selenium species have been carried out. The screening of various oxidizing agents using diselenide **1** as a precursor for stereoselective methoxyselenenylations of styrene leading to the addition product **2** clearly show that the counter ion of the selenium electrophile plays an important role in determining the stereoselectivity as well as the rate of the reaction. Ammonium peroxodisulfate gave the highest diastereomeric ratios with good yields after 72 h.[7] Although the reaction time could be lowered with some other oxidizing agents, the stereoselectivities decreased dramatically (Table 1).

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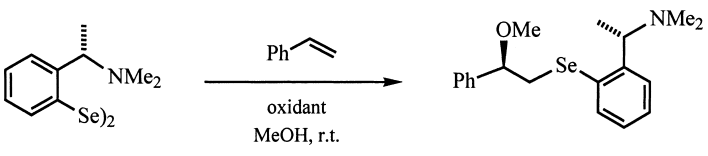
Table 1
Use of different oxidants in the methoxyselenenylation of styrene with diselenide **1** at rt[8,9]

Oxidant	Reaction time	Yield	*de*
Br_2	72 h	94 %	38 %[a]
Br_2, AgOTf	8 h	65 %	35 %[b]
$(NH_4)_2S_2O_8$	72 h	83 %	61 %[b]
$K_2S_2O_8$	72 h	83 %	53 %[a]
$Ce(NH_4)_2(NO_3)_6$	24 h	87 %	30 %[a]
DDQ[8]	72 h	70 %	25 %[a]
$PhI(OAc)_2$[9]	72 h	50 %	25 %[b]

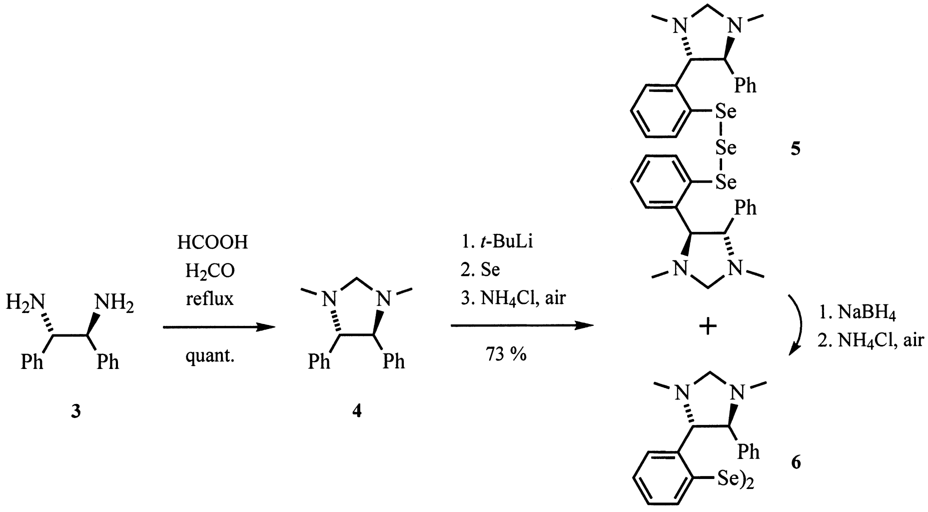
a) Determined by ^{13}C NMR. b) Determined by GC after cleavage of the Ar*Se-moiety.



1 **2**

The conditions for the generation of aryl selenium triflates of oxygen containing diselenides[10] could not be applied to nitrogen containing diselenides like **1** because of the low solubility of the aryl selenium triflates under the reaction conditions (−100°C). However, they can be employed in methoxyselenenylations at room temperature to afford the addition product **2** in only 35% *de*.

Therefore, we designed a more rigid diselenide which was assumed to give better selectivities and shorter reaction times. The easily accessible[11] and even commercially available chiral diamine **3** can be converted to the aminal **4** in quantitative yield by heating at reflux with formic acid and formaldehyde.[12] Compound **4** was then converted into a mixture of triselenide **5**[13] and diselenide **6** (≈1:2.5) by treatment with t-BuLi and elemental selenium. Reduction of this mixture with $NaBH_4$ was followed by reoxidation in ammonium chloride solution to convert **5** into **6**. The reaction mixture was purified by flash chromatography and crystallization from methanol to afford diselenide **6** in 73% overall yield.[14]



3 **4** **5** **6**

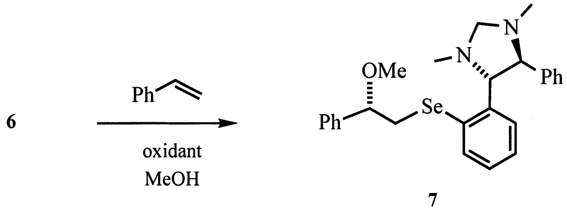
Table 2
Methoxyselenenylation of styrene with diselenide **6**

Entry	Oxidant	Temperature	Reaction time	Yield	*de*[a]
1	Br_2, AgOTf	–100 °C	4 h	98 %	86 %
2	$(NH_4)_2S_2O_8$[b]	25 °C	2 h	95 %	76 %
3	$(NH_4)_2S_2O_8$[b]	–15 °C	12 h	74 %	86 %

a) Determined by ^1H and ^{13}C NMR. b) A catalytic amount of CF_3SO_3H is necessary.

Diselenide **6** was subsequently used for the methoxyselenenylation of styrene. The aryl selenium triflate derived from **6** by reaction with bromine and silver triflate is soluble in a mixture of diethyl ether and methanol at −100°C. After reaction with styrene the addition product **7** is obtained in 98% yield with 86% *de* (Table 2, entry 1).

With ammonium peroxodisulfate in the presence of a catalytic amount of trifluoromethanesulfonic acid it is possible to generate from **6** the corresponding aryl selenium sulfate at room temperature.[15] Addition to styrene yields **7** with a comparable yield and selectivity to that obtained by the triflate (Table 2, entry 2) also when the reaction is carried out at −15°C (Table 2, entry 3). The absolute configuration of the newly generated stereocenter in **7** was assigned by HPLC analysis of 1-methoxy-1-phenylethane formed after reductive deselenenylation of **7**.



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In conclusion, we have prepared a new chiral nitrogen containing diselenide containing an imidazolidine moiety in a few steps. This now facilitates methoxyselenenylations of styrene with high yields and stereoselectivities, even at room temperature.

Alkoxyselenenylations of other alkenes and selenocyclization reactions, as well as the application of diselenide **6** in catalytic oxyselenenylation–elimination sequences are currently under investigation.

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13. Triselenide **5** was identified by FAB-MS analysis and ^{1}H NMR: δ 8.00 (dd, 1H, *J*=1.2, 7.9 Hz), 7.30–6.80 (m, 7H), 6.40 (dd, 1H, *J*=1.5, 7.4 Hz), 4.10 (d, 1H, *J*=5.5 Hz), 3.90 (d, 1H, *J*=5.5 Hz), 3.74 (d, 1H, *J*=9.1 Hz) 3.60 (d, 1H, *J*=9.1 Hz), 2.30 (s, 3H), 2.20 (s, 3H).
14. Selected spectroscopic data of diselenide **6**: ^{1}H-NMR: δ 7.80 (dd, 1H, *J*=1.2, 7.9 Hz), 7.30–7.20 (m, 3H), 7.20–7.10 (m, 2H), 7.05 (ddd, 1H, *J*=1.5, 7.5, 7.9 Hz), 6.94 (ddd, 1H, *J*=1.2, 7.5, 7.9 Hz), 6.67 (dd, 1H, *J*=1.5, 7.5 Hz), 4.14 (d, 1H, *J*=5.4 Hz), 4.00 (d, 1H, *J*=5.4 Hz), 3.85 (d, 1H, *J*=9.0 Hz) 3.80 (d, 1H, *J*=9.0 Hz), 2.42 (s, 3H), 2.32 (s, 3H). ^{13}C NMR: δ 138.9, 137.6, 131.2, 130.6, 129.4, 128.3, 128.2, 128.1, 127.6, 125.5, 79.6, 78.1, 75.8, 40.1, 39.1. ^{77}Se NMR: δ 445.8.
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