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A Novel Synthesis of Benzo[*b*]selenophenes via Regioselective Intramolecular Transformation of 4-(3-Nitroaryl)-1,2,3-selenadiazoles

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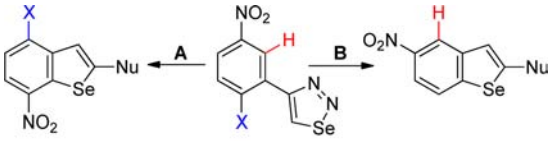
ABSTRACT



Conditions: KOH, NuH (X = H, Cl; NuH = R^1R^2NH)
A: in the presence of oxidant
B: in the absence of oxidant

Base-promoted transformation of 4-(3-nitroaryl)-1,2,3-selenadiazoles *via* intermediate formation of eneselenolates followed by 5-*exo-trig* cyclization is reported. The regiochemistry of the intramolecular cyclization is condition-dependent. In the presence of an oxidant, the oxidative nucleophilic substitution of the hydrogen (ONSH, S_NAr^H) pathway, by oxidative aromatization of the rapidly formed σ^H-adduct, takes place. In the absence of oxidant, the reaction proceeds *via* intermediate formation of the σ^{Cl}-adduct, following nucleophilic aromatic substitution of the halogen (S_NAr^{Cl}) pathway.

4-Substituted 1,2,3-selenadiazoles (**I**) are usually easily decomposed with the liberation of nitrogen and formation of alkyneselenolates (**II**) under the influence of strong bases, such as organolithium reagents, potassium ethoxide, etc.[1] The acetylenic selenolates are widely used in organic chemistry for the synthesis of acetylenic selenides, in 1,3-anionic cycloaddition reactions and in other cyclization reactions or, after protonation, as a source of highly reactive alkyneselenols (**III**) and tautomeric selenoketenes (**IV**, Scheme 1).[2]

W. Dehaen and our previous studies[3] have demonstrated an intramolecular 5-*exo-dig* cyclization reaction of the *in situ* generated *ortho*-hydroxy- and -aminoselenoketenes to be a facile, straightforward, and efficient approach toward benzo[*b*]furans and indoles. These results prompted us to examine the possible synthesis of benzo[*b*]selenophenes by a 5-*exo-trig* cyclization reaction of the *in situ* generated *ortho*-haloselenoketenes with the participation of external nucleophiles (Scheme 2).

It should be mentioned that the synthesis and characterization of benzo[*b*]selenophenes are of current interest

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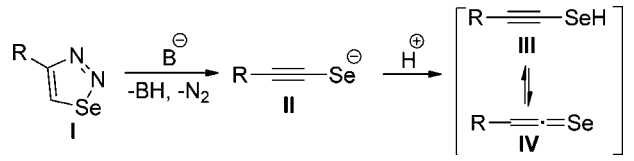
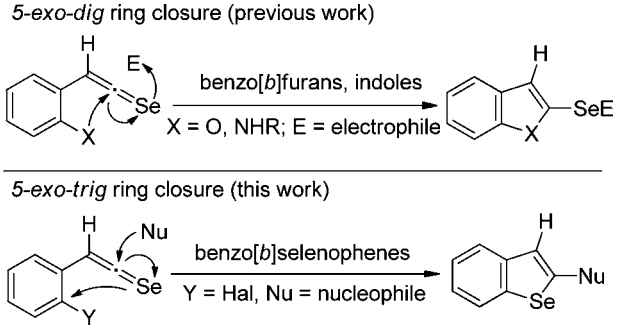
Scheme 1. Base-Promoted Generation of Selenoketens



owing to their potential applications as organic semiconductors for various optoelectronic devices,[4] potent biological activity, and synthetic utility.[5]

Scheme 2. Possible Cyclization Pathways for *ortho*-Substituted Arylselenoketenes



The examples of benzo[*b*]selenophene ring construction are numerous. One of the most versatile and well-developed approaches to the benzo[*b*]selenophenes provided by electrophilic cyclization of various 1-(1-alkynyl)-2-(methylseleno)arenes under the action of Br_2, NBS, I_2, ICl, PhSeCl, PhSeBr, and $Hg(OAc)_2$ was reported by Larock.[6]

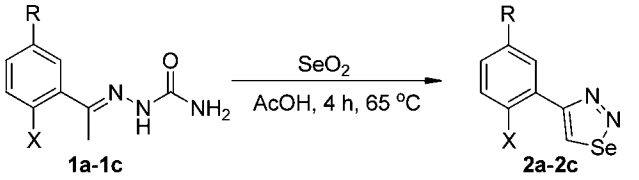
However, the syntheses of benzo[*b*]selenophenes having other than alkyl and aryl substituents at the C(2) position of the selenophene ring are few and nonsystematic.[7]

In particular, the only reported method for the synthesis of 2-aminobenzo[*b*]selenophene was the reduction of 2-nitrobenzo[*b*]selenophene. 2-Aminobenzo[*b*]selenophene was used for the preparation of selenium-containing polymethine dyes.[7a] Beckmann rearrangement of 2-acetyl-3-phenylbenzo[*b*]selenophene oxime promoted by polyphosphoric acid gave 2-acetylamino-3-phenylbenzo[*b*]selenophene.[7b] Another 2-aminobenzo[*b*]selenophene derivative, 2-benzoyl-amino-3-phenylbenzo[*b*]selenophene, was synthesized by a reaction of diphenyldiazomethane with benzoyl isoselenocyanate.[7c]

Herein, we would like to report a convenient two-step regioselective synthesis of a variety of multifunctional benzo[*b*]selenophenes from the readily available semicarbazones of nitroacetophenones. Moreover, the nature and position of the substituents on the benzo[*b*]selenophene ring make them appropriate for further use as building blocks for assembling structurally more complex derivatives. For example, the amino group at the C(2) position of the selenophene ring may be additionaly modified. Meanwhile, the C(3) atom is very susceptible to electrophilic attack, as it is a terminal atom of the enamine moiety and allows smooth attachment of electrophiles. The nitro group on the aryl ring may be reduced to amino, whereas the halogen atom may be used in a variety of cross-coupling reactions.

In order to obtain entry to 1,2,3-selenadiazoles, and hence selenoketenes, we prepared the novel 4-(2-chloroaryl)-l,2,3-selenadiazoles **2a**, **2b** and known[8] 4-(3-nitrophenyl)-l,2,3-selenadiazole **2c**. To this end, the semicarbazones of acetophenones **1a**–**1c** were treated with selenium dioxide in acetic acid to give **2a**–**2c** (Scheme 3).

Scheme 3. Synthesis of 4-Aryl-1,2,3-selenadiazoles



2a, R = H, X = Cl (65%); **2b**, R = NO_2, X = Cl (63%)
2c, R = NO_2, X = H (71%)

We next conducted a base-catalyzed anionic ring opening of selenadiazoles **2a**–**2c** to generate alkyneselenolates **3**. The intermediacy of **3** was confirmed by trapping its methyl derivatives **4a** and **4b** upon addition of iodomethane. In turn, the addition of such a weakly nucleophilic proton donor as H_2O resulted in the immediate formation of alkyneselenol-selenoketene tautomeric species **5** and **6** dimerized to diselenafulvene **7**. Whereas the introduction of more powerful nucleophiles, such as aliphatic amines, led to the competitive addition of the nucleophile to the selenoketene moiety affording eneselenolates **8** which, in the absence of an activating nitro group, underwent no subsequent transformation and formed stable selenoamides **9a**–**9c** upon addition of an acid (Scheme 4).

In the case of eneselenolates **8** having an electron-withdrawing nitro group on the aromatic ring, the reaction progressed further. In addition, when the reaction was carried out under an oxygen-free atmosphere (argon) the exclusive isolated products were the expected benzo[*b*]selenophenes **12a**–**12d**. We noticed that the presence of oxygen dramatically changed the course of the reaction. Thus, decomposition of **2b** in the medium *N*,*N*-diethylamine under an air atmosphere gave the mixture of products **12a**

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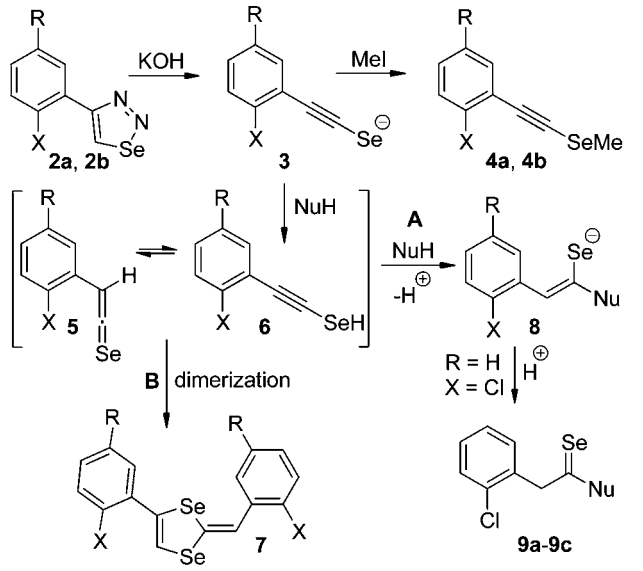
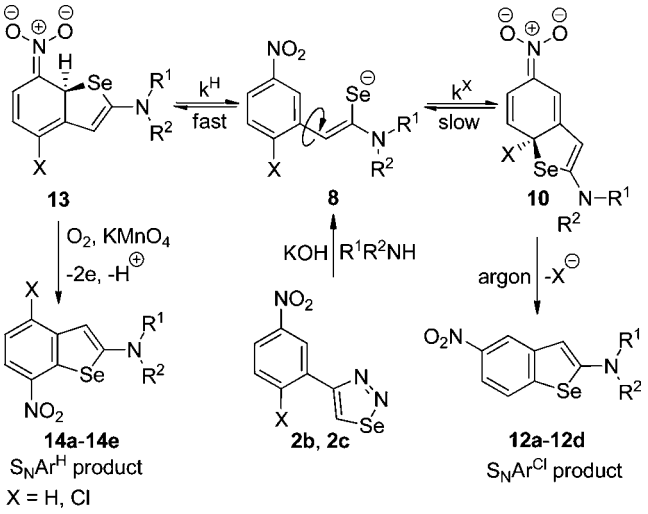
Scheme 4. Transformations of Alkyneselenolates in the Presence of Electrophiles, Good Nucleophiles, and Poor Nucleophiles



A: good nucleophiles (alkylamines), **B**: poor nucleophiles (water)
4a, R = H, X = Cl (64%); **4b**, R = NO_2, X = Cl (72%)
7, R = NO_2, X = Cl (78%)
9a, NuH = $(C_2H_5)_2NH$ (71%); **9b**, $(CH_2)_5NH$ (65%)
9c, $[(CH_2)_2O(CH_2)_2]NH$ (62%)

(8%) and **14a**, (30%). Thereafter, we investigated the influence of a classical oxidant ($KMnO_4$) on the course of the reaction. Benzo[*b*]selenophenes **14a**–**14e** were formed selectively under the oxidative conditions (Scheme 5, Table 1).

Scheme 5. Pathways of Eneselenolates Transformation. Synthesis of Benzo[*b*]selenophenes from 4-(3-Nitroaryl)-1,2,3-selenadiazoles



Obviously, the reaction proceeded through the fast and reversible intramolecular addition of highly nucleophilic eneselenolate species **8** in a position *ortho* occupied with

Table 1. Synthesis of Benzo[*b*]selenophenes

			product (yield, %)		
entry	NuH (solvent)	X	S_NAr^{Cl}	S_NAr^H	cond.[a]
1	$(CH_3CH_2)_2NH$	Cl	**12a** (54)		**A**
2	$(CH_2)_4NH$	Cl	**12b** (79)		**A**
3	$(CH_2)_5NH$	Cl	**12c** (47)		**A**
4	$[(CH_2)O(CH_2)_2]NH$	Cl	**12d** (71)		**A**
5	$(CH_3CH_2)_2NH$	Cl	**12a** (8)	**14a** (30)	**B**
6	$(CH_3CH_2)_2NH$	Cl		**14a** (83)	**C**
7	$(CH(CH_3)_2NH$	Cl		**14b** (74)	**C**
8	$(CH_2)_5NH$	Cl		**14c** (60)	**C**
9	$[(CH_2)O(CH_2)_2]NH$	Cl		**14d** (57)	**C**
10	$(CH_3CH_2)_2NH$	H		**14e** (63)	**C**

[a] **A**: argon atmosphere. **B**: air atmosphere. **C**: air atmosphere, $KMnO_4$.

hydrogen to produce σ^H-adduct **13**. It may indicate the rate of **13** formation is higher than that of the σ^{Cl}-adduct **10** and that oxidation of the former with oxygen is also a relatively fast process.[9] The exclusive oxidative nucleophilic substitution of hydrogen (ONSH) took place in the presence of the stronger oxidant $KMnO_4$. In the absence of the oxidant the σ^H-adduct **13** rearranged to the σ^{Cl}-adduct **10**, which irreversibly transformed to the final substitution product **12** after the departure of chlorine.

The superior regioselectivity of the reaction toward the S_NAr^H product in the presence of oxidant may be rationalized considering the possible method of σ^H-adduct **13** formation depicted in Scheme 6. As it was shown above (Scheme 4) the base-promoted decomposition of selenadiazole **2b** led to the alkyneselenolate **3** which, on protonation, formed the higly reactive selenoketene species **5**. The intermediate **5** may assumedly exist in two rotational conformations **5-I** and **5-II**. In either event, the sequential nucleophilic attack takes place on the side opposite to the position of the bulky aryl ring affording conformeric eneselenolates **8-I** and **8-II**. Despite the relatively higher positive charge on the C-atom *para* to the NO_2 group compared to that of the C-atom *ortho* to the NO_2 group[10] the formation of σ^H-adducts **13** occurs exclucively in the precence of an oxidant. It may be explained considering that the selenolate anion is a "soft" and polarizable

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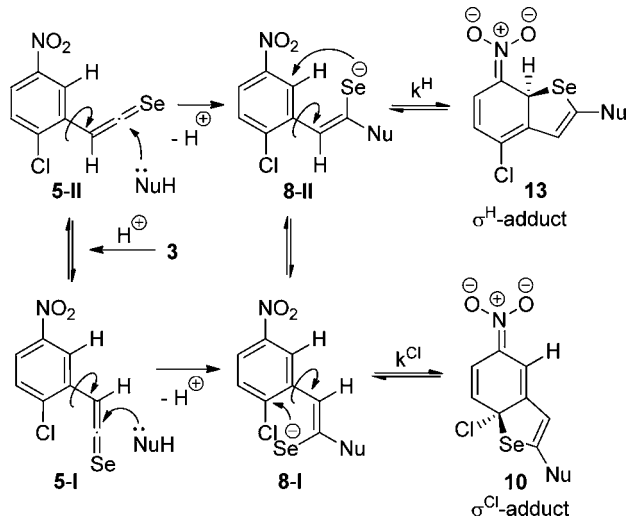
Scheme 6. Formation of σ^H- and σ^{Cl}-Adducts upon Addition of Nucleophile to Selenoketene Moiety



nucleophile enabling an orbitally controlled mode of cyclization. Under the orbital control, the C-atom (*ortho* to NO_2) accommodating the relatively higher electron density, compared to the C-atom *para* to NO_2, provides a better overlap between the HOMO of the nucleophile and the LUMO of the electrophile favoring the formation of the σ^H-adduct **13**. Another factor facilitating the formation of **13** is the lower steric repulsion between the large Se-atom and small H-atom in the transition state on the way from **8-II** to **13** compared to that between the Se-atom and Cl-atom in the transition state on the way from **8-I** to **10**. Additional stabilization of the σ^H-adduct **13** may be achieved through the formation of hydrogen bonding between the O-atom of the NO_2 group and the H-atom at the sp^3 carbon of the σ^H-adduct **13**, which is not the case for the σ^{Cl}-adduct **10**. Rapid accumulation along with the high concentration and stability of the σ^H-adduct **13** due to the previously discussed factors resulted in a substantial predominance of **14a** (30%, S_NAr^H) over **12a** (8%, S_NAr^{Cl}) product even in the presence of such a moderate oxidant as atmospheric oxygen. In the presence of a powerful oxidant such as $KMnO_4$, the formation of **14a** occurs exclusively despite the low solubility of the oxidizing agent in the reaction medium.

It should be noted that numerous examples of the nucleophilic substitution of hydrogen (ONHS) in the reactions of aromatic and heteroaromatic compounds with carbon,[11] nitrogen,[12] phosphorus,[13] and oxygen[14] nucleophiles have been well documented and thoroughly investigated. To our knowledge, we reported the first evidence of the ONHS process with the participation of a selenium nucleophile.

In summary, we have developed a new, convenient, and straightforward approach to benzo[*b*]selenophenes from the readily available 4-(nitroaryl)-l,2,3-selenadiazole. The regioselectivity of the reaction may be easily varied depending on the presence or absence of the oxidating agent in the reaction mixture.

Supporting Information Available. Experimental details and characterization data of new compounds along with copies of ^1H, ^{13}C NMR and mass spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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The authors declare no competing financial interest.