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Synthesis of Stable Seleno[3,4-*b*]quinoxaline Derivatives

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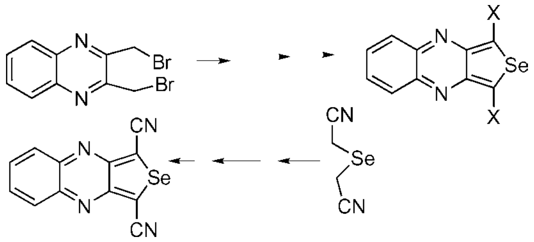
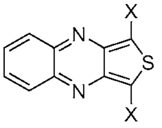
ABSTRACT

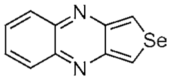


The unstable seleno[2,3-*b*]quinoxoline was generated and functionalized in situ to give the stable dialdehyde and diester derivatives. The dicyano compound was made in several steps from biscyanomethyl selenide and was found to be very stable.

The highly reactive thieno[3,4-*b*]quinoxaline (**1**) has been the object of chemical investigation for about two and half decades.[1] Theoretical analysis indicates that polymers derived from the parent **1** should exhibit an exceptionally small band gap,[2] making this heterocycle attractive in the field of conducting π-conjugated polymers. In earlier studies, the transient formation of **1** was shown by trapping experiments with *N*-phenylmaleimide.[3] Recently, we reported the synthesis of **1** by a base-catalyzed Pummerer reaction.[4] Compound **1** was obtained as acid-sensitive crystals which, when protected from light and oxygen, were stable for several days. Moreover, we have found that thieno[3,4-*b*]quinoxaline bearing carboxaldehyde on the thiophene ring (**2**) is highly stable.[4] The selenium analogue of compound **1**, seleno[3,4-*b*]quinoxaline (**3**), as well as substituted products have hitherto remained unknown. The synthesis of stable seleno[3,4-*b*]quinoxaline derivatives is of undoubted interest in view of the possible comparison of their chemical and physical properties with the analogous sulfur heterocycles. Moreover, studies aiming at the synthesis of this type of novel compound should afford a valuable addition to the scant synthetic methodology of selenophene chemistry. In continuation of our efforts in the study of heteroaromatic *o*-quinonoid molecular systems, we report in this paper the synthesis of seleno[3,4-*b*]quinoxalines as well as further chemistry of the selenoquinoxaline system. The electrochemical properties of the new electron deficient heterocycles are also presented.



1: X=H
2: X=CHO



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Our goal in seleno[3,4-*b*]quinoxalines was the synthesis of derivatives bearing small substituents with electron-acceptor properties. Our objective was the synthesis of 1,3-dicyanoseleno[3,4-*b*]quinoxaline (**4**), which we believe should be stable to air and oligomerization. The multistep synthesis of **4** is outlined in Scheme 1. Reaction of chloroacetonitrile with sodium selenide generated in situ furnished the previ-

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[1] For a review on isomeric thienoquinoxaline, see: Moustafa, O. S.; Yamada Y. J. *Heterocycl. Chem.* **2001**, *38*, 809.

[2] Nayak, K.; Marynick, D. S. *Macromolecules* **1990**, *23*, 2237.

[3] (a) MacDowell D. W. H.; Jeffries, A. T.; Meyers, M. B. *J. Org. Chem.* **1971**, *36*, 1416. (b) Roland, M. M.; Anderson, R. C. *J. Heterocycl. Chem.* **1977**, *14*, 541.

[4] Pohmer, J.; Lakshmikantham, M. V.; Cava, M. P., *J. Org. Chem.* **1995**, *60*, 8283.

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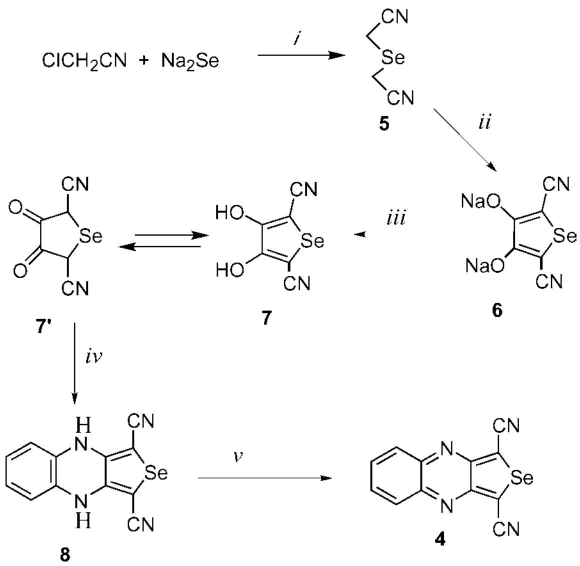
Scheme 1[a]

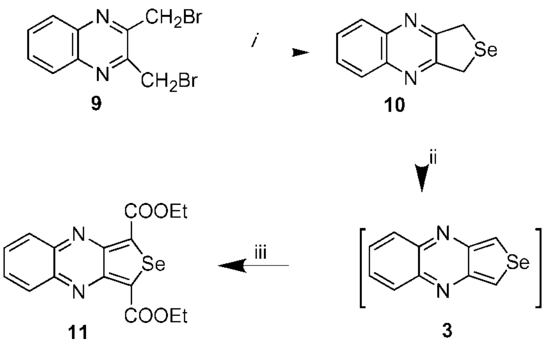


[a] Key: (i) Na_2Se was generated in situ from elemental selenium and $NaBH_4$ in water under N_2; (ii) diethyl oxalate, C_2H_5ONa/EtOH, room temperature, 15 h; (iii) H_2SO_4 35% at 0 °C; (iv) *O*-phenylenediamine, AcOH, reflux 30 min; (*v*) iodobenzene diacetate, CH_2CI_2, room temperature, 4 h (60%).

ously unknown bis(cyanomethyl) selenide **5** in high yield. The condensation of **5** with diethyl oxalate in the presence of excess of sodium ethoxide leads to the formation of the disodium salt of 2,5-dicyano-3,4-dihydroxyselenophene (**6**) in moderate yield. Best results were obtained when the reaction was carried out at room temperature for 15 h. The disodium salt **6** is highly hygroscopic and was converted to the corresponding dihydroxy derivative **7** immediately after its filtration from the reaction mixture. We also noted that the acidification of **6** was best achieved with aqueous solution of 35% sulfuric acid at 0 °C. The overall yield of **7** under these conditions was 35%−40%. In preliminary experiments, we found that **7** reacts with *o*-phenylenediamine in refluxing ethanol to give **8** in very low yield (12%). In the search for better reaction conditions, we found that refluxing equimolar amounts of **7** and *o*-phenylenediamine in acetic acid for 30 min increases the yield up to 80%. Compound **8** prepared under these conditions crystallized as red-orange crystals upon cooling the reaction mixture. The formation of this product indicates the presence to some extent of the diketo tatumeric form **7′** under the reaction conditions. The dihydrodinitrile derivative **8** oxidized smoothly with iodobenzene diacetate to the corresponding o-quinonoid derivative **4.** Similar oxidative aromatization of dihydrobenzo[*c*]selenophene derivative was reported by us recently.[5] Compound **4** forms red stable microcrystals. The stability of **4** is due exclusively to the electron-withdrawing effect of the nitrile groups.

The synthesis of the parent **3** was accomplished as outlined in Scheme 2. The synthesis of the starting material 1,3-dihydroseleno[3,4-b]quinoxaline (**10**) was achieved by an alternate route.[6] Thus, reaction of 2,3-bis(bromomethyl)-quinoxaline (**9**) with sodium selenide generated in situ furnished the dihydro derivative **10**. Best results were obtained when the dibromide **9** was added very slowly to a dilute solution of a selenium reagent. Treatment of the dihydro derivative with iodobenzene diacetate in THF generates the fully aromatic quinoxaline derivative **3**. Attempts to isolate **3** under an inert atmosphere using aqueous workup and solvent extraction yield only a dark solid. However, the generation of **3** under anhydrous conditions in an inert atmosphere made its functionalization more feasible. Thus, in situ dilithiation of the generated **3** with excess *n*-butyllithium and subsequent reaction of the corresponding dianion with ethyl chloroformate gave the diester derivative **11** as yellow microcrystals. Interestingly enough, the monosubstituted derivative was not formed in this reaction. Similar to the dicyano derivative **4**, compound **11** was found to be very stable.

Scheme 2[a]



[a] Key: (i) Na_2Se/THF, 3 h (55%); (ii) iodobenzene diacetate, THF, room temperature, 2.5 h; (iii) 2.2 equiv of *n*-BuLi at −78 °C then addition of 2 equiv of ClCOOEt and stirring at room temperature, overnight (28%).

The selenide **10** treated under Vilsmeier conditions (DMF, $POCl_3$ in methylene chloride), afforded the diformyl compound **12** (Scheme 3). The formation of this product implies that the tautomeric form of **10** in which the selenophene ring is aromatic (**10′**) must be present to some extent under the reaction conditions, since this tautomer can react in a Vilsmeier reaction. Related behavior has been observed in the case of 1,3-dihydrothieno[3,4-*b*]quinoxaline[4] and 2,3-dimethylquinoxaline;[7] the latter reacts in its tautomeric form in a Diels−Alder reaction with maleic anhydride and *p*-benzquinone. The dialdehyde **12** was oxidized smoothly with iodobenzene diacetate to the corresponding *o*-quinonoid dialdehyde **13**, which forms stable orange red crystals. Similar to derivatives **4** and **11**, the stability of **13** is exclusively attributed to electronic effects.

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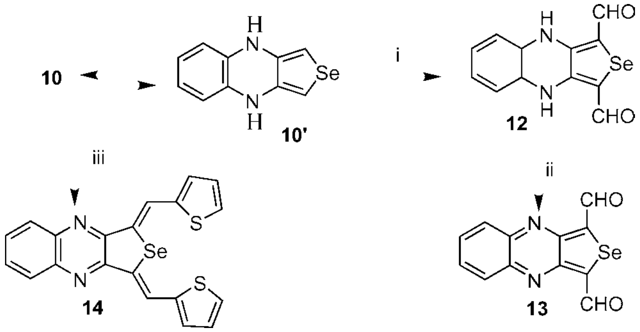
(5) Aqad, E.; Lakshmikantham, M. V.; Cava, M. P., Broker, G. A., Rogers, R. D. *Org. Lett.* **2003**, *5*, 2519

(6) Compound **10** was prepared previously, via the reaction of 2,3-bis-(bromomethyl)quinoxaline with elemental selenium in the presence of a large excess of sodium iodide and subsequent reduction of the corresponding diiodoselenide. Abid, K. Y.; McWhinnie W. R. *J. Organomet. Chem.* **1987**, *330*, 337.

(7) Schönberg, A., Mostafa, A. *J. Chem. Soc.* **1943**, 654.

Scheme 3[a]



[a] Key: (i) $POCl_3/DMF/CH_2Cl_2$, (46%); (ii) iodobenzene diacetate, CH_2Cl_2, room temperature 3 h, (56%); (iii) 2-thiophenecarboxaldehyde, *t*-BuOK/Et_2O, room temperature, overnight.

The similar reactivity of the selenide **10** and 2,3-dimethylquinoxaline suggests that the methylene protons in **10** should be readily deprotonated with the strong base potassium amide, as shown by alkylation to give 2,3-dipropylquinoxaline.[8] In the present case, we found that compound **10** reacts with 2-thiophenecarboxaldehyde in a Knovenagel reaction with the formation of the unsaturated condensation product **14**. Several different approaches were studied, but best results (65−70%) were obtained under basic conditions (potassium *tert*-butoxide/diethyl ether). The *Z*,*Z*-configuration for the condensation product based on NMR spectroscopy is described for analogous products.[9]

The electron-accepting properties of the stable thieno[3,4-*b*]quinoxaline derivatives **4**, **11**, and **13** were studied by cyclic voltammetry (CV). The voltammograms of the three derivatives exhibit two reversible one-electron reduction waves corresponding to the generation of the anion radical and the dianion, respectively (Scheme 4). A representative voltammogram is shown in Figure 1. Judging from the first reduction potential (Table 1), derivative **4**, bearing cyano groups, is the strongest electron acceptor in this series. As expected, the weakest acceptor is derivative **13** incorporating carbethoxy groups in the selenophene ring. The reversibility of the two reduction processes indicates the stability of the anion radical and dianion under the CV experimental conditions. The relatively large differences of potentials between the first and second reduction potential Δ*E* value for compound **4** is similar to the Δ*E* value for tetracyanoquinodimethane (TCNQ) under the same experimental conditions. The large Δ*E* in the case of **4** suggests enhanced stability of its derived dianion **16**. Formally, the dianion **16** could be presented in more than one mesomeric structure. The mesomeric structure **16′** incorporating the aromatic pyrazine moiety and two negative charges adjanced to electron-withdrawing groups describes better the nature of bonding of the dianion and explains its enhanced stability.

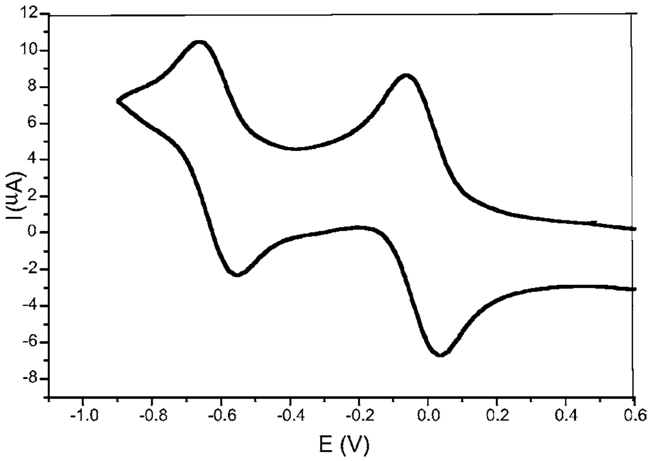
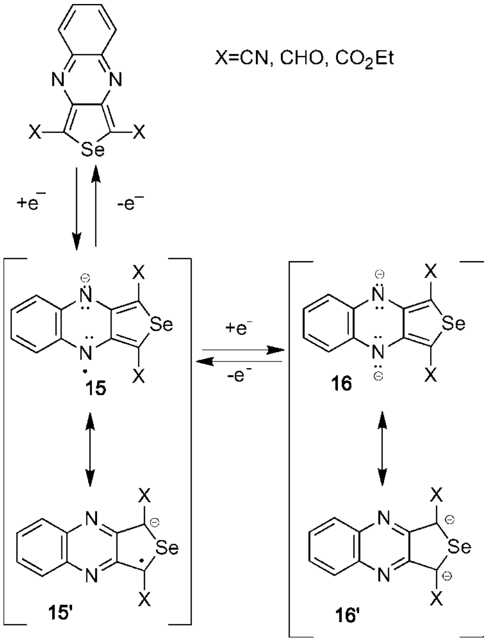


Figure 1. Cyclic voltammetry of **4** (5×10^{-4} M in acetonitrile).

Scheme 4



The strong electron-accepting ability of derivative **4** is similar to that of 2,2-biindanylidene-1,3,1′,3′-tetraone,[10] chloranil, and other strong electron acceptors derived from the *p*-benzoquinone parent system. The latter class of acceptors was widely employed in the synthesis of donor−acceptor charge-transfer complexes.[11] Compound **4** can be thus considered as a parent for a new series of reversible two-stage one-electron systems with strong electron-accepting abilities and is a promising candidate as an acceptor component of conducting donor−acceptor complexes.

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(9) Hieber, G.; Hanak, M.; Wurst, K.; Strahle, J. *Chem. Ber.* **1991**, *124*, 1597.

(10) Khodorkovsky, V.; Ellern, A.; Neilands, O. *Tetrahedron Lett.* **1994**, *35*, 2955.

(11) Khodorkovsky, V.; Becker Y. J. In *Organic Conductors, Fundamentals and Applications*; Farges, J. P., Ed.; Marcel Dekker: New York, 1994; Chapter 3, p 75.

Table 1. Electrochemical[a] Data for **4**, **11**, **13**, and TCNQ

compd	E1 red (V)	E2 red (V)	Δ*E* (V)
4	−0.05	−0.66	0.61
11	−0.22	−0.78	0.56
13	−0.31	−0.80	0.49
TCNQ	0.27	−0.31	0.58

[a] 5×10^{-4} M in acetonitrile, Bu_4NPF_6 supporting elecrolyte, SCE reference electrode, Pt working electrode, 100 m V/s scan rate.

In conclusion, the first synthesis of seleno[3,4-*b*]quinoxaline derivatives has been achieved, and seleno[3,4-*b*]quinoxalines bearing electron-withdrawing groups are stable and exhibit strong electron-accepting abilities. Effort aimed at the use of these electron-deficient and electroactive compounds in the fabrication of new materials is underway.

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Supporting Information Available: Experimental details. This material is available free of charge via the Internet at http://pubs.acs.org.

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