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A facile access to chalcogen and dichalcogen bearing dialkylamines and diols

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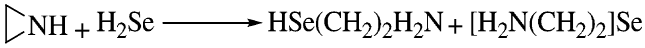
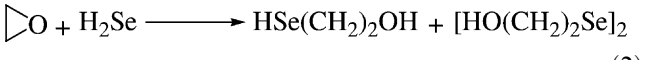
Abstract—A highly practical procedure for the preparation of novel classes of chalcogen bearing diamines [$\{H_2N(CH_2)_n\}_2E$] and diols [$\{HO(CH_2)_n\}_2E$] (n = 2 or 3 and E = Se or Te) by the reaction of disodiumchalcogenide and haloalkylamines or haloalcohols is presented.

Organic diamines and diols represent one of the most extensively studied classes of compounds as synthetic intermediates for the synthesis of a variety of functional molecules. These molecules have significance in analytical and inorganic chemistry as versatile ligands because they can be readily derivatized, thus allowing the introduction of other functional groups. Moreover, their compounds with platinum group metals have also been the targets of intense research due to their inhibition of cell division. For example, *cis*-diamminedichloroplatinum(II) (*cis*-platin), has demonstrated clinical utility in cancer chemotherapy.[1] In continuation of our research interest in the development of multifunctional organochalcogen compounds,[2] we required chalcogen-bearing diamines and diols as precursors. Chalcogen-based methods are now a very important tool in organic synthesis[3] and a few of the β-, γ-, and δ-hydroxyalkylselenides and chiral amino diselenides have shown synthetic utility in organic transformations.[4,5] Additionally, diamino- and dihydroxydialkylchalcogenides and dichalcogenides could be useful sources of precursors for various organic reactions that are based on alcohols and amines. Thus the combination of two different entities in the same molecule may provide an opportunity for their further study where both individual as well as synergistic effects on target molecules can be visualized.

A few reports are available in the literature[6] on the synthesis of β-hydroxyselenides and diamines, however in



(1)



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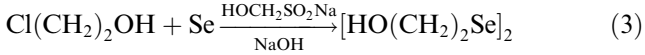

(3)

none of them is an efficient and straightforward synthesis of chalcogen-bearing diamines and diols described. For instance, ethylenimine has been opened by hydrogen selenide to form 2-aminoethylselenol which was immediately converted into bis(2-aminoethyl)selenide[6a] (Eq. 1). Similarly, ethylene oxide reacts with hydrogen selenide to give a low yield of 2-hydroxyethylselenol, which was contaminated with the corresponding diselenide[6b] (Eq. 2). Both methods used toxic hydrogen selenide as a starting material. There are also reports[7] detailing the synthesis of a compound of the form [$\{HO(CH_2)_2\}_2E_2$] (Eq. 3). We followed this method for the synthesis of bis(2-hydroxyethyl)diselenide but the difficulties we encountered included a very high level of oxidizability and volatility, coupled with the particularly aggressive odor of the derivatives formed. These considerations encouraged us to develop a more reliable

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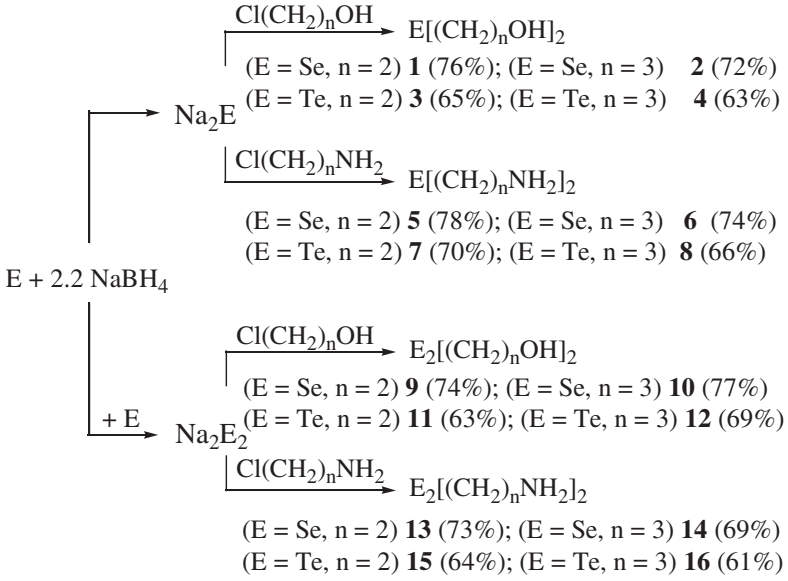
and practical procedure for preparing chalcogen-bearing diamines and diols. The present communication describes an easy access to chalcogen bearing diamines and diols in which the yields exceed 60% and with little or no purification required. Relatively stable chalcogenide and dichalcogenide species (**1**–**16**) were synthesized by the reaction between disodium chalcogenide or disodium dichalcogenide (generated in situ by the reduction of elemental selenium or tellurium with sodium borohydride in aqueous THF) and haloalkyl derivatives (Scheme 1).

Various routes to generate sodium chalcogenides or dichalcogenides are available in the literature.[8] We followed one of the literature procedures for the reduction of elemental selenium[9a] (in ethanol) and tellurium[9b] (in 20% aqueous NaOH) with $NaBH_4$ to generate Na_2E and Na_2E_2 (E = Se or Te) species and their reactions with electrophilic substrates. The yields of the desired species in our case (**5**–**8**) and (**13**–**16**) were found to be satisfactory. However, the isolation of the hydroxy derivatives was tedious and produced emulsions which hindered the usual work-up procedures. Moreover, both chalcogenide and dichalcogenide species (**5**–**8**) and (**13**–**16**) contained ethanol or water, as shown by their respective ^1H NMR spectra, even after several hours of drying under reduced pressure. Since we needed several organochalcogen species, we decided to investigate the feasibility of using Na_2E and Na_2E_2 (E = Se or Te) species generated by $NaBH_4$ in aqueous THF in the presence of NaOH. The reduction of elemental selenium or tellurium in aqueous THF offers a much better solution to generate mono or dichalcogenides, since the reduced species are usually stable enough in solution to be stored and handled without special precautions. Furthermore, the reaction does not produce any undesired amounts of volatile chalcogen species and thus higher yields of the products are obtained. Both dialkylchalcogenide and dichalcogenide species[10–12] (**1**–**16**) were obtained in >60% yields as colorless or pale yellow, semi-viscous liquids and were found to be stable enough to be stored for long periods under nitrogen atmosphere at low temperature (0–10 °C). The physical properties of these derivatives were found to be similar to those of aliphatic alcohols and amines and no serious decomposition or dissociation was observed due to the presence of the chalcogen in their structural units. They were soluble and stable in methanol, ethanol, 2-propanol, acetonitrile, and DMSO under ambient conditions in a dry nitrogen atmosphere and could be recovered without any problem after several days. However, slight oxidation or decomposition was observed at room temperature when they were exposed to air. Our attempts to distil them under reduced pressure not only caused decomposition but also the recovery was poor (23%–30%) after distillation. These compounds were sufficiently pure for further reactions with little or no chromatographic purifications of the final product. The derivatives were analyzed by IR, ^1H, and ^{13}C NMR spectroscopy, ES-MS, and FAB-MS confirming the proposed formulations. The chemical shifts in the ^1H NMR spectra (in $CDCl_3$) for these compounds (**1**–**16**) exhibited signals for hydroxy, amino, and methylene protons with expected multiplicities further confirming the formation of single species. These compounds react like the corresponding organic diamines and alcohols thus offering synthetic applications.

In summary, a new series of aliphatic, amino and hydroxy-containing monoselenide and diselenides was synthesized in an easy, one-step synthesis in which the yields exceeded 60% with no (**1**–**8**) or little purification (**9**–**16**) required by column chromatography. Incorporation of chalcogen into diamine or diol frameworks may result in different binding properties compared to their purely chalcogen or amino and hydroxy counterparts and their combined properties could be realized simultaneously or individually from the same molecule. Research work



Scheme 1.

addressing these issues is already underway in our laboratories together with the development of synthetic routes for chalcogen-containing macrocycles, azacrown and crown ethers using these species as source precursors, and will be reported in due course.

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10. In a representative reaction, sodium selenide was generated by reaction of gray elemental selenium (0.79 g, 10 mmol) and sodium hydroxide (0.88 g, 22 mmol) and $NaBH_4$ (0.84 g, 22 mmol) (exothermic) in aqueous THF (20 mL + 0.2 mL H_2O) under N_2. The colorless sodium selenide solution thus obtained was was allowed to warm to room temperature over 0.5 h then treated with a solution of 3-chloropropanol (1.89 g, 20 mmol) in THF (10 mL) under N_2. The reaction mixture was stirred overnight at room temperature, and concentrated under reduced pressure. The residual mass was diluted with deionized water and extracted with chloroform (3×25 mL). The combined organic fractions were collected, dried over magnesium sulfate, filtered, and the solvent was removed in vacuo yielding a nearly colorless, viscous liquid that was found to be essentially free from diselenide derivatives. In rare cases, where formation of a slight amount of diselenide was observed, it was simply removed by column chromatography ($CHCl_3$:CH_3OH 95:5) on silica gel to afford pure bis(hydroxyalkyl)selenide. Bis(hydroxy)tellurides were also prepared similarly from Na_2Te [generated in an identical way except that the reaction mixture in the case of tellurium was warmed for a short time (55–65 °C) to complete the dissolution of the tellurium (ca. 20 min)] and the corresponding bromo compounds. Satisfactory analyses and spectral data were obtained for all new compounds. ^1H NMR data of some representative compounds are reported as follows: $[HO(CH_2)_2Se(CH_2)_2OH]$ **1**: colorless viscous liquid; NMR ($CDCl_3$): ^1H (300 MHz), δ 3.92 (t, 4H, J(HH) 7 Hz, –OCH_2), 3.1 (t, 4H, J(HH) 6 Hz, –SeCH_2), 2.35 (s, 2H, OH); ^{13}C (75 MHz), δ 61.72 (OCH_2), 20.04 (Se–CH_2). $[HO(CH_2)_3Se(CH_2)_3OH]$ **2**: colorless viscous liquid; NMR ($CDCl_3$): ^1H (300 MHz), δ 3.73 (t, 4H, J(HH) 7 Hz,

–OCH_2), 2.67 (t, 4H, J(HH) 6 Hz, –SeCH_2), 1.93 (m, 4H, J(HH) 6 Hz, –CH_2–), 3.46 (s, 2H, OH); ^{13}C (75 MHz), δ 61.13 (OCH_2), 32.07 (–CH_2–), 19.54 (Se–CH_2). [HO$(CH_2)_2$Te$(CH_2)_2$OH] **3**: pale viscous liquid; NMR ($CDCl_3$): ^{1}H (300 MHz), δ 3.86 (t, 4H, J(HH) 6 Hz, –OCH_2), 2.9 (t, 4H, J(HH) 6.5 Hz, –TeCH_2), 2.31 (s, 2H, OH). [HO$(CH_2)_3$Te$(CH_2)_3$OH] **4** : pale viscous liquid; NMR ($CDCl_3$): ^{1}H (300 MHz), δ 3.68 (t, 4H, J(HH) 6 Hz, –OCH_2), 2.72 (t, 4H, J(HH) 7.4 Hz, –TeCH_2), 1.98 (m, 4H, J(HH) 7 Hz, –CH_2), 3.46 (s, 2H, OH); ^{13}C (75 MHz), δ 60.05 (OCH_2), 30.08 (–CH_2–), 10.02 (Te–CH_2).

11. To a cooled (0 °C) and stirred suspension of elemental selenium (0.79 g, 10 mmol) and sodium hydroxide (0.88 g, 22 mmol) in aqueous THF (20 mL + 0.2 mL H_2O) under N_2, was added $NaBH_4$ (0.84 g, 22 mmol) (exothermic) in small quantities. The pink color of the diselenide was soon generated and then gradually faded to a colorless solution of monoselenide (usually taking only a few minutes). This was allowed to warm to room temperature over 0.5 h. The clear colorless solution thus formed was treated with a solution of 3-chloropropylamine hydrochloride (2.60 g, 20 mmol) in water (20 mL) under N_2. The reaction mixture was stirred for 6 h at room temperature and was then diluted with 0.2 M NaOH solution (50 mL) followed by extraction with chloroform (3 × 25 mL). The combined organic extracts were washed with water and brine and dried over anhydrous $MgSO_4$. The drying agent was removed by filtration, and the filtrate was concentrated to dryness on a rotary evaporator to give analytically pure **6** as a pale colored, viscous liquid. Satisfactory analyses and spectral data were obtained for all new compounds. ^{1}H NMR data of some representative compounds are reported in the following.
[H_2N$(CH_2)_2$Se$(CH_2)_2$NH_2] **5**: pale viscous liquid; NMR ($CDCl_3$): ^{1}H (300 MHz), δ 2.93 (t, 4H, J(HH) 7.2 Hz, –NCH_2), 2.73 (t, 4H, J(HH) 6.7 Hz, –SeCH_2), 1.63 (s, 4H, NH_2); ^{13}C (75 MHz), δ 42.55 (–NCH_2), 27.83 (–SeCH_2). [H_2N$(CH_2)_3$Se$(CH_2)_3$NH_2] **6**: pale viscous liquid; NMR ($CDCl_3$): ^{1}H (300 MHz), δ 2.81 (t, 4H, J(HH) 7 Hz, –NCH_2), 2.63 (t, 4H, J(HH) 6.5 Hz, –SeCH_2), 1.91 (m, 4H, J(HH) 6 Hz, CH_2), 1.45 (s, 4H, NH_2); ^{13}C (75 MHz), δ 41.06 (N–C), 33.09 (C–C), 20.78 (Se–C).
[H_2N$(CH_2)_2$Te$(CH_2)_2$NH_2] **7**: pale viscous liquid; NMR ($CDCl_3$): ^{1}H (300 MHz), δ 2.98 (t, 4H, J (HH) 7.0 Hz, –NCH_2), 2.75 (t, 4H, J (HH) 6.9 Hz, –TeCH_2), 1.53 (m, 4H, C–CH_2–C); ^{13}C (75 MHz), δ 43.60 (N–C), 8.66 (Te–C).
[H_2N$(CH_2)_3$Te$(CH_2)_3$NH_2] **8**: pale viscous liquid; NMR ($CDCl_3$): ^{1}H (300 MHz), δ 2.69 (t, 4H, J (HH) 7.0 Hz, –NCH_2), 2.61 (t, 4H, J (HH) 6.8 Hz, –TeCH_2), 1.85–1.75 (m, 8H, CH_2 and NH_2); ^{13}C (75 MHz), δ 44.29 (N–C), 36.27 (C–C), 9.15 (Te–C).

12. The colorless solution of sodium selenide generated as above (ref. 9) was treated with one equivalent of elemental selenium (0.79 g, 10 mmol) and the reaction solution became purple in color. The reaction mixture was stirred for a further 2–3 h, during this period a complete dissolution of selenium was observed and the brownish-red aqueous solution of Na_2Se_2 thus obtained was cooled to room temperature and treated with a solution of 3-chloropropanol (1.89 g, 20 mmol) in THF (10 mL) under N_2. The reaction mixture was stirred overnight at room temperature, and concentrated under reduced pressure. The residual mass was diluted with deionized water and extracted with chloroform (3 × 25 mL). The combined organic fractions were collected, dried over magnesium sulfate, and filtered, and the solvent was removed in vacuo yielding a nearly colorless, viscous liquid which was found to be essentially free from monoselenide derivatives. In rare cases where formation of a slight amount of monoselenide was observed, it was simply removed by column chromatography ($CHCl_3$:CH_3OH 95:5) on silica gel to afford pure bis(hydroxy)diselenide. Bis(hydroxy)ditelluride were prepared similarly from Na_2Te_2 and the corresponding bromo compounds. Satisfactory analyses and spectral data were obtained for all new compounds. ^{1}H NMR data of some representative compounds are reported as follows:
[HO$(CH_2)_3$Se$_2$$(CH_2)_3$OH] **10**: colorless viscous liquid; ES-MS: m/z 278 for [M^+]. NMR ($CDCl_3$): ^{1}H (300 MHz), δ 3.75 (t, 4H, J(HH) 6 Hz, –OCH_2), 3.01 (t, 4H, J(HH) 7.2 Hz, –SeCH_2), 2.01 (m, 4H, J(HH) 6.4 Hz, –CH_2–), 2.30 (s, 2H, OH); ^{13}C (75 MHz), δ 61.62 (OCH_2), 34.85 (–CH_2–), 26.03 (Se–CH_2). [HO$(CH_2)_3$Te$_2$$(CH_2)_3$OH] **12** : pale viscous liquid; ES-MS: m/z 378 for [M^+]. NMR ($CDCl_3$): ^{1}H (300 MHz), δ 3.71 (t, 4H, J(HH) 5.9 Hz, –OCH_2), 3.18 (t, 4H, J(HH) 7.2 Hz, –TeCH_2), 1.99 (m, 4H, J(HH) 6.4 Hz, –CH_2), 2.11 (s, 2H, OH); ^{13}C (75 MHz), δ 61.31 (OCH_2), 32.35 (–CH_2–), 11.07 (Te–CH_2).