List of Publications


3. Synthesis of unsymmetrical pyridyl aryl selenides by the reductive cleavage of SeSe bond. K. K. Bhasin; Shivani Doomra; Gurjeet Kaur; Ekta Arora; Neelam Singh; Yogesh Nagpal; Rajeev Kumar; Rishu; T. M. Klapoetke; S. K. Mehta. Phosphorus, Sulfur, Silicon and Related Elements, 2008, 183, 992.


Research Article

Regioselective Synthesis of Bis(2-halo-3-pyridyl) Dichalcogenides (E = S, Se and Te): Directed Ortho-Lithiation of 2-halopyridines

K. K. Bhasin,1 Neelam Singh,2 Shivani Doomra,1 Ekta Arora,1 Ganga Ram,1 Sukhjinder Singh,1 Yogesh Nagpal,1 S. K. Mehta,1 and T. M. Klapotke3

1 Department of Chemistry, Panjab University, Chandigarh 160 014, India
2 Department of Chemistry, Chaudhary Devi Lal University, 125055 Sirsa, Haryana, India
3 Department of Chemistry and Biochemistry, Ludwig-Maximilians University, 81377 Munich, Germany

Received 20 July 2006; Revised 26 December 2006; Accepted 16 January 2007

Recommended by Govindasamy Mugesh

A novel method for the preparation of hitherto unknown symmetrical bis(2-halo-3-pyridyl) dichalcogenides (E = S, Se and Te) by the oxidation of intermediate 2-halo-3-pyridyl chalcogenolate, prepared by lithiation of 2-halo pyridines using lithium diisopropylamine is being reported. All the newly synthesized compounds have been characterized through elemental analysis employing various spectroscopic techniques, namely, NMR (1H, 13C, 77Se), infrared, mass spectrometry, and X-ray crystal structures in representative cases.

Copyright © 2007 K. K. Bhasin et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

1. INTRODUCTION

Organoselenium and organotellurium compounds are finding renewed interest as synthetic reagents in organic synthesis [1, 2]. In addition to their synthetic applications, these compounds are fast gaining contemporary interest due to their indispensable applications in electronic industry [3], as organic conductors [4] and precursors for semiconducting materials [5], in biology [6] and in medical imaging.

It is curious to note that the chemistry of alkyl, aryl, and mixed alkyl aryl chalcogenides has developed rapidly for the last two decades and is of immense interest to organic chemists [7] and biochemists [8], whereas the chemistry of pyridyl derivatives virtually remained neglected, in spite of its greater utility [9]. Recently, the chemistry of pyridyl derivatives has attracted the attention of the scientific community due to their unique properties, which encourage them to the new and exciting applications in organic synthesis. In recognition of its importance, renewed efforts have evolved for the convenient methodologies of their synthesis.

The presence of nitrogen in the aromatic ring brings remarkable changes and has attracted considerable attention of the practicing chemists as precursors in pharmacological compounds [10], for the preparation of liquid crystals [11], in the synthesis of polymers, and as ligands in transition metal complexes.

2. EXPERIMENTAL

All the manipulations were carried under a dry and de-oxygenated nitrogen atmosphere to prevent the oxidation of oxygen-sensitive intermediates. Elemental sulphur, selenium, and tellurium (Sigma-Aldrich, Bangalore, India) were stored in a desiccator prior to use. Tetrahydrofuran (THF) was dried using sodium and benzophenone prior to use. Diisopropylamine (DIA) was distilled using CaE^ and was stored on molecular sieves. 2-halopyridines (Halo = F, Cl, and Br), n-butyl lithium of analytical grade were purchased from Aldrich and used without further purification. 1H, 13C, and 77Se NMR spectra were recorded on a Jeol AL spectrometer operating at 300, 75.432, 57.203, and 94.790 MHz, respectively in CDCl₃, using Me₄Si as an internal standard for 1H and 13C NMR. Me₂Se and Me₂Te were used as an external reference for 77Se and 125Te NMR. IR spectra were obtained between KBr plates.
on a Perkin-Elmer model 1430. C, H, and N analyses were performed on a Perkin-Elmer 2400 CHN analyzer. Mass spectra were obtained on a VG-70S11-250J mass spectrometer. Separation and purifications of compounds were carried out using column chromatography performed on activated silica gel using hexane/ethyl acetate as eluant.

3. SYNTHESIS OF 2-HALO-3-PYRIDYL CHALCOGEN COMPOUNDS (X = F, CL, AND BR)

A 100 mL three-necked round bottom flask was charged with 20 mL dry THF and 3 mL (22 mmol) DIA under nitrogen and was cooled to -20°C. To this solution was added dropwise 17.6 mL (22 mmol, 1.25 M) n-butyl lithium with continuous stirring and the mixture was allowed to stand for 1 hour at 0°C. To this solution of lithium diisopropylamine (LDA) was added slowly a solution of 2-halopyridine (20 mmol) in THF (10 mL) at -50°, -40°, and -78°C in case of fluoro-, chloro-, and bromopyridine, respectively. Stirring was continued for additional one hour after which dry and activated elemental chalcogen (S, Se, and Te) (20 mmol) was added in small portions with continuous stirring. The temperature was raised slowly up to room temperature. It was found that sulphur and selenium takes 20–30 minutes to dissolve completely, while tellurium takes nearly one hour to dissolve, owing to surface oxidation of the metal. The product was hydrolyzed using 5 mL solution of aqueous ammonium chloride and nitrogen supply was discontinued. The reaction was then subjected to aerial oxidation for 10–12 hours in case of selenols and tellurols. Thiols, obtained from the hydrolysis of thiolate, gave a poor yield of disulfides upon aerial oxidation. Therefore, oxidation of thiols was performed using dimethyl sulfoxide (DMSO) at 80–90°C, in which is a mild and successful oxidizing agent for the oxidation of thiols to disulfides. THF was removed on rota-evaporator; the resulting mixture was diluted with water and was extracted in dichloromethane (3 × 40 mL). Inorganic impurities were removed by repeatedly washing the organic layer with brine (3 × 30 mL) followed by distilled water. The organic extract was then dried over anhydrous sodium sulfate and concentrated on rota-evaporator. The product was purified on a silica column using 10% ethyl acetate-hexane as eluant.

4. RESULTS AND DISCUSSION

Mautner et al. [12] were the first to prepare bis(2-pyridyl) diselenide by reacting 2-bromo pyridine with toxic hydrogen selenide (see Scheme 1).

Toshimitsu et al. [13, 14] modified this synthesis circumventing the use of toxic hydrogen selenide by using sodium hydrogen selenide obtained by the reacting elemental selenium with sodium borohydride in 2-ethoxyethanol. Bhasin et al. [15] have optimized the use of this reagent for the synthesis of various substituted methyl- and bromopyridyl selenium and tellurium compounds (see Scheme 2).

Syper and Mlochowski [16] developed a new methodology for the synthesis of bis(2-pyridyl) diselenide by reacting dilithium diselenide with 2-bromopyridine. Various methyl substituted 2-pyridyl diselenides/ditellurides were synthesized by Bhasin and Singh [17] using a mild and easily available reducing agent, hydrazine hydrate (see Scheme 3).
Engman and Cava [18] prepared bis(2-pyridyl) ditelluride through lithium bromine exchange of 2-bromo-pyridine using sterically hindered and highly reactive t-butyl lithium at ~78°C in THF. The preparation of methyl substituted bis(2-pyridyl) diselenides and ditellurides were extended by Bhasin et al. [19] using metal-halogen exchange of methyl-substituted bromopyridines using n-butyl lithium.

Heteroatom-directed aromatic lithiation is a versatile route towards the synthesis of π-deficient heterocycles [20]. The presence of C–X bond in 2-halopyridines, apart from allowing easy and selective metalation at ortho-position, makes it potentially reactive towards nucleophiles, allowing the introduction of other functional groups. Metalation at ortho-position is facilitated owing to the ortho-directing ability of halogen substituent, particularly fluorine and chlorine. Such an intermediate is potentially reactive towards electrophilic selenium and tellurium metals. Therefore, design of new methods allowing metalation of 2-halopyridine for chalcogen incorporation with the retention of C–X bond could be of great synthetic value.

Among the various organolithium reagents, LDA has been known to bring about selective deprotonation as it is a nonnucleophilic base and does not lead to metal-halogen exchange reactions in halogenopyridines, which occur with n-butyl lithium.

In an effort to achieve the synthesis of target compounds, the deprotonation of 2-halopyridines (X= F, Cl, Br) was carried out under cryogenic conditions in THF using LDA as base. Reports from literature indicate that LDA can be used efficiently to induce exclusive lithiation at C-3 position [21] as a consequence of DoM effect (directed ortho-metalation). It was observed that the use of LDA prevented nucleophilic addition of base on C=N bond as well as metal-halogen exchange reactions. The intermediate, 3-lithio-2-halo-pyridine, generated in situ was reacted with elemental chalcogen (S, Se, and Te) at low temperature. The insertion of chalcogen atom into C–Li bond took place readily resulting in the formation of 2-halo-3-pyridylchalcogenolate (Scheme 4). It was found that sulfur and selenium undergo smooth insertion into the C–Li bond while tellurium takes time to undergo insertion. This is possibly due to the metallic character and passive nature of this element. The resulting solution of 2-halo-3-pyridylchalcogenolate was subsequently subjected to hydrolysis. The oxidative coupling of resulting thiols, selenols, and tellurols affords the desired bis(2-halo-3-pyridyl) dichalcogenide in good yield.

Simple aerial oxidation was sufficient to obtain diselenides and ditellurides, but thiols had to be oxidized using DMSO to get a quantitative yield of the desired disulfide (Scheme 5).

In order to ascertain the applicability of this protocol for the synthesis of various 2-halo-3-pyridyl chalcogenides, a series of reactions was set up. The results obtained revealed that the methodology was best applicable to chloro- and fluoro-derivatives. The yield was lowered to less than half in case of bromoderivatives. Insertion of tellurium in 2-bromo-3-lithiopyridine gave a poor result to the extent that even the recovery of a substantial amount of compound, sufficient for characterization, was not possible.

5. SPECTROSCOPIC STUDIES

The compounds prepared (Table 1) were characterized with the help of various spectroscopic techniques, namely, 1H (Table 2), 13C (Table 3), 77Se/125Te NMR (Table 4), IR, UV-Vis spectroscopy, mass spectrometry, and X-ray crystallographic techniques.

6. 1H NMR STUDIES

1H NMR spectra of hitherto unknown bis(2-halo-3-pyridyl) dichalcogenides were obtained in CDCl3 using TMS as internal reference. The NMR characterization of dichalcogenides along with the data has been given in Table 2. It was observed that the 1H NMR spectra for the dichalcogenides display three different sets of protons in aromatic region. In case of bis(2-chloro-3-pyridyl) diselenide, H-6 proton appears most downfield and lies in 8.22–8.24 ppm while the signals corresponding to H-4 and H-5 appear at lower frequencies and
Table 1: Physical properties and analytical data of various 2-halo-3-pyridyl chalcogen compounds.

<table>
<thead>
<tr>
<th>Compound</th>
<th>Physical state</th>
<th>Melting point (°C)</th>
<th>Yield (%)</th>
<th>C</th>
<th>H</th>
<th>N</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bis(2-chloro-3-pyridyl) disulfide</td>
<td>Colorless crystalline solid</td>
<td>160*</td>
<td>52</td>
<td>41.11 (41.52)</td>
<td>1.95 (2.07)</td>
<td>9.25 (9.68)</td>
</tr>
<tr>
<td>Bis(2-chloro-3-pyridyl) diselenide</td>
<td>Yellow diamond-shaped crystals</td>
<td>206-207</td>
<td>54</td>
<td>30.89 (31.16)</td>
<td>1.22 (1.55)</td>
<td>7.02 (7.27)</td>
</tr>
<tr>
<td>Bis(2-chloro-3-pyridyl) ditelluride</td>
<td>Orange-diamond shaped crystals</td>
<td>178-180</td>
<td>50</td>
<td>24.63 (24.74)</td>
<td>1.17 (1.23)</td>
<td>5.38 (5.77)</td>
</tr>
<tr>
<td>Bis(2-fluoro-3-pyridyl) diselenide</td>
<td>Pale yellow diamond-shaped crystals</td>
<td>62-63</td>
<td>65</td>
<td>33.82 (34.09)</td>
<td>1.54 (1.70)</td>
<td>7.49 (7.95)</td>
</tr>
<tr>
<td>Bis(2-fluoro-3-pyridyl) ditelluride</td>
<td>Red crystalline solid</td>
<td>55-59</td>
<td>58</td>
<td>26.13 (26.78)</td>
<td>1.09 (1.32)</td>
<td>6.01 (6.25)</td>
</tr>
<tr>
<td>Bis(2-bromo-3-pyridyl) diselenide</td>
<td>Orange crystalline powder</td>
<td>152-155</td>
<td>35</td>
<td>25.15 (25.31)</td>
<td>1.12 (1.26)</td>
<td>5.75 (5.90)</td>
</tr>
</tbody>
</table>

* Decomposes at 160°C.

Table 2: $^1$H NMR data of various 2-halo-3-pyridyl chalcogen compounds.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Compound</th>
<th>$^1$H NMR (δ, ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>H-4</td>
</tr>
<tr>
<td>1</td>
<td>Bis(2-chloro-3-pyridyl) disulfide</td>
<td>7.83-7.86 (dd, 2H, 7.8, 1.8 Hz)</td>
</tr>
<tr>
<td>2</td>
<td>Bis(2-chloro-3-pyridyl) diselenide</td>
<td>7.88-7.91 (dd, 2H, 7.8, 1.8 Hz)</td>
</tr>
<tr>
<td>3</td>
<td>Bis(2-chloro-3-pyridyl) ditelluride</td>
<td>7.90-7.93 (dd, 2H, 4.5, 7.8 Hz)</td>
</tr>
<tr>
<td>4</td>
<td>Bis(2-fluoro-3-pyridyl) diselenide</td>
<td>7.03-7.08 (m, 2H)</td>
</tr>
<tr>
<td>5</td>
<td>Bis(2-fluoro-3-pyridyl) ditelluride</td>
<td>7.00-7.06 (m, 2H)</td>
</tr>
<tr>
<td>6</td>
<td>Bis(2-bromo-3-pyridyl) diselenide</td>
<td>7.79-7.82 (dd, 2H, 7.8, 1.8 Hz)</td>
</tr>
</tbody>
</table>

Table 3: $^{13}$C NMR data of various 2-halo-3-pyridyl chalcogen compounds.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Compound</th>
<th>$^{13}$C NMR (chemical shift)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>C-2</td>
</tr>
<tr>
<td>1</td>
<td>Bis(2-chloro-3-pyridyl) disulfide</td>
<td>147.59</td>
</tr>
<tr>
<td>2</td>
<td>Bis(2-chloro-3-pyridyl) diselenide</td>
<td>148.93</td>
</tr>
<tr>
<td>3</td>
<td>Bis(2-chloro-3-pyridyl) ditelluride</td>
<td>152.74</td>
</tr>
<tr>
<td>4</td>
<td>Bis(2-fluoro-3-pyridyl) diselenide</td>
<td>162.15</td>
</tr>
<tr>
<td></td>
<td></td>
<td>159.05</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(d, J = −234.05 Hz)</td>
</tr>
<tr>
<td>5</td>
<td>Bis(2-fluoro-3-pyridyl) ditelluride</td>
<td>164.4, 161.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(d, J = −234.05 Hz)</td>
</tr>
<tr>
<td>6</td>
<td>Bis(2-bromo-3-pyridyl) diselenide</td>
<td>148.50</td>
</tr>
</tbody>
</table>
Table 4: 77Se/125Te NMR data of various 2-halo-3-pyridyl chalcogen compounds.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Compound</th>
<th>77Se/125Te (δ, ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Bis(2-chloro-3-pyridyl) diselenide</td>
<td>387.1</td>
</tr>
<tr>
<td>2</td>
<td>Bis(2-fluoro-3-pyridyl) diselenide</td>
<td>370.3</td>
</tr>
<tr>
<td>3</td>
<td>Bis(2-bromo-3-pyridyl) diselenide</td>
<td>407.1</td>
</tr>
<tr>
<td>4</td>
<td>Bis(2-chloro-3-pyridyl) ditelluride</td>
<td>7.5</td>
</tr>
<tr>
<td>5</td>
<td>Bis(2-fluoro-3-pyridyl) ditelluride</td>
<td>419.8</td>
</tr>
</tbody>
</table>

fall in the regions 7.88–7.91 ppm and 7.15–7.19 ppm, respectively. The order of chemical shift values of pyridyl protons follows the order H-6 > H-4 > H-5. To substantiate these predictions further, [1H–1H] COSY studies were performed on the newly synthesized compounds.

7. [1H–1H] COSY (HOMCOR-2D) AND [1H–13C] COSY (HETCOR-2D) STUDIES

2D correlation spectroscopy helps in the assignment of protons and carbon signals in NMR spectrum, besides providing vital information about proton-proton and proton-carbon connectivities. The off-diagonal contours (cross-peaks) allow the identification of proton signals and help in interpreting 13C NMR spectrum. [1H–1H] COSY spectrum clearly shows a correlation of H-5 proton with H-4 and H-6 due to its ortho-position with respect to both. [1H–13C] COSY (HETCOR) correlates the peaks of a proton spectrum with the peaks of 13C spectrum (Figure 1).

The 13C peaks have unequivocally been sorted out with the help of off-diagonal cross-peaks corresponding to 1JCH coupling interactions. Accordingly, the assignments lie in the order of chemical shift as under C-2 > C-6 > C-4 > C-3 > C-5.

8. 13C NMR STUDIES

As evident from the 13C NMR studies of 2-halopyridines, the carbon-13 signals resonate downfield with the increasing electronegativity (F > Cl > Br) of halogen atom. Carbon atom directly bonded to the halogen experiences maximum deshielding due to −1 effect of halogen. However, the inductive effect decreases from fluorine to bromine resonance effect (+R) increases; the carbon atom at para position with respect to halogen (C-5) shows the reverse trend in observed chemical shift values.

It appears that in the newly synthesized bis(2-halo-3-pyridyl) dichalcogenides, due to the opposing nature of inductive and resonance effect of chalcogen and halogen atoms, no such generalizations can be made. The interpretations of [1H–1H] and [1H–13C] COSY (Figure 1) studies and 13C NMR data reveal that in diselenides, C-2 carbon resonates most downfield relative to TMS.

9. 77Se NMR STUDIES

77Se NMR of bis(2-halo-3-pyridyl) diselenides (X = F, Cl, Br) were recorded in CDCl₃ employing Me₂Se as external
Table 5: Mass spectral data of bis(2-chloro-3-pyridyl) diselenide/ditelluride.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Compound</th>
<th>Stands for</th>
<th>Relative intensity</th>
<th>Assignment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Bis(2-chloro-3-pyridyl) diselenide</td>
<td>385</td>
<td>47.1</td>
<td>[M]+</td>
</tr>
<tr>
<td></td>
<td></td>
<td>304</td>
<td>4.6</td>
<td>[(ClPy)$_2$Se]$^+$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>192</td>
<td>100</td>
<td>[ClPy$_2$Se]$^+$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>157</td>
<td>10.6</td>
<td>[Py$_2$Se]$^+$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>77</td>
<td>3.7</td>
<td>[PyH]$^+$</td>
</tr>
<tr>
<td>2</td>
<td>Bis(2-chloro-3-pyridyl) ditelluride</td>
<td>485</td>
<td>23.4</td>
<td>[M]+</td>
</tr>
<tr>
<td></td>
<td></td>
<td>355</td>
<td>11.6</td>
<td>[(ClPy)$_2$Te]$^+$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>242</td>
<td>42.5</td>
<td>(ClPy$_2$Te)$^+$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>207</td>
<td>3.5</td>
<td>[Py$_2$Te]$^+$</td>
</tr>
<tr>
<td></td>
<td></td>
<td>77</td>
<td>100</td>
<td>[PyH]$^+$</td>
</tr>
</tbody>
</table>

It is curious to note that with the increase in the electronegativity of the halogen at C-2 position, an upfield shift is observed. It is also worthwhile to mention that all these compounds exhibit $^{77}$Se resonance at higher frequency relative to bis(2-pyridyl) diselenide. An answer may lie in the existing intermolecular short contacts operating in the molecule as evident from the solid-state structural studies.

10. $^{125}$Te NMR STUDIES

Chemical shifts are cited with respect to neat Me$_2$Te ($\delta = 0$ ppm) as external reference.

11. $^{19}$F NMR STUDIES

The proton-noise decoupled $^{19}$F NMR spectra of the fluorinated derivatives were recorded in deuterated chloroform, CDCl$_3$, using trichlorofluoromethane, CFCI$_3$ (freon-11) as the external reference. The $^{19}$F signals for both compounds, bis(2-fluoro-3-pyridyl) diselenide and bis(2-fluoro-3-pyridyl) ditelluride, were observed as well-defined signals at -50.62 and -59.3 ppm.

12. MASS SPECTROMETRY

The isotopic richness of natural selenium and tellurium helps in the identification of selenium and tellurium containing fragments in the mass spectra of organoselenium and organotellurium compounds. A number of characteristic ions found in the mass spectra have been tabulated in Table 5.

13. IR STUDIES

This technique has been used for the general characterization of the newly prepared pyridyl selenium and tellurium compounds. IR spectra of these compounds were recorded in the range 4000–400 cm$^{-1}$ in compressed transparent pellets made from powdered compounds and dry KBr. IR spectra of various compounds synthesized have been summarized in Table 6.

14. MOLECULAR GEOMETRY AND CRYSTAL STRUCTURE OF BIS(2-CHLORO-3-PYRIDYL) DISELENIDE

To understand the structural details, single crystal X-ray diffraction analysis of bis(2-chloro-3-pyridyl) diselenide was carried out. A perspective view of the structure of this compound is shown in Figure 2. The selected bond parameters are listed in Tables 7 and 8. The molecule crystallizes in monoclinic, P2$_1$/c space group:

\[ a = 11.390(2) \text{ Å}, \quad b = 27.851(5) \text{ Å}, \quad c = 11.849(2) \text{ Å}, \]
\[ \alpha = 90^\circ, \quad \beta = 112.984(3)^\circ, \quad \gamma = 90^\circ. \]
Table 6: Infrared spectral data of various 2-halo-3-pyridyl chalcogen compounds.

<table>
<thead>
<tr>
<th>Entry</th>
<th>Compound</th>
<th>cm⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Bis(2-chloro-3-pyridyl) disulfide</td>
<td>3097.6, 3045.5, 2924.8, 1736.9, 1555.2, 1431.6, 1260.0, 1212.1, 1143.2, 1059.4, 796.0, 750.8, 723.2, 655.9, 517.9, 438.1, 474.0</td>
</tr>
<tr>
<td>2</td>
<td>Bis(2-chloro-3-pyridyl) diselenide</td>
<td>3018.7, 1946.8, 1720.5, 1576.7, 1555.0, 1411.9, 1290.1, 1226.6, 1126.8, 1063.4, 1025.8, 834.1, 792.0, 731.8, 634.8, 502.4</td>
</tr>
<tr>
<td>3</td>
<td>Bis(2-chloro-3-pyridyl) ditelluride</td>
<td>3018.6, 2925.9, 2853.9, 1736.4, 1599.0, 1426.3, 1377.1, 1245.8, 1018.4, 1052.3, 762.0, 668.8, 627.5, 497.2</td>
</tr>
<tr>
<td>4</td>
<td>Bis(2-fluoro-3-pyridyl) diselenide</td>
<td>3036.7, 2925.9, 2853.9, 1736.4, 1599.0, 1426.3, 1377.1, 1245.8, 1018.4, 1052.3, 762.0, 668.8, 627.5, 497.2</td>
</tr>
<tr>
<td>5</td>
<td>Bis(2-fluoro-3-pyridyl) ditelluride</td>
<td>2924.8, 2853.3, 1574.3, 1553.7, 1415.6, 1245.8, 1066.0, 1018.4, 788.1, 646.3, 566.2</td>
</tr>
</tbody>
</table>

Table 7: Important bond lengths [Å] and angles [°] for bis(2-chloro-3-pyridyl) diselenide.

<table>
<thead>
<tr>
<th>Bond</th>
<th>Length [Å]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Se(1A)–C(2A)</td>
<td>1.926(8)</td>
</tr>
<tr>
<td>Se(1A)–Se(2A)</td>
<td>2.973(13)</td>
</tr>
<tr>
<td>Se(1A)–C(7A)</td>
<td>1.912(9)</td>
</tr>
<tr>
<td>Se(1C)–Se(2C)</td>
<td>2.3003(13)</td>
</tr>
<tr>
<td>Se(1C)–Se(2C)</td>
<td>1.898(9)</td>
</tr>
<tr>
<td>C(2A)–Se(1A)–Se(2A)</td>
<td>102.0(2)</td>
</tr>
<tr>
<td>C(2A)–Se(1A)–Se(2C)</td>
<td>101.8(2)</td>
</tr>
<tr>
<td>C(2A)–Se(1A)–Se(2B)</td>
<td>102.3(2)</td>
</tr>
<tr>
<td>C(2B)–Se(1B)–Se(2B)</td>
<td>101.8(2)</td>
</tr>
</tbody>
</table>

Table 8: Important torsion angles [°] for bis(2-chloro-3-pyridyl) diselenide.

<table>
<thead>
<tr>
<th>Torsion</th>
<th>Angle [°]</th>
</tr>
</thead>
<tbody>
<tr>
<td>C(2A)–Se(1A)–C(2A)–C(2B)</td>
<td>83.1(3)</td>
</tr>
<tr>
<td>C(2B)–Se(1B)–C(2B)–C(2C)</td>
<td>-82.7(5)</td>
</tr>
<tr>
<td>C(2C)–Se(1C)–C(2C)–C(2D)</td>
<td>-84.6(4)</td>
</tr>
<tr>
<td>Se(1A)–C(2A)–C(3A)–C(4A)</td>
<td>-177.3(6)</td>
</tr>
<tr>
<td>N(1A)–C(1A)–C(2A)–Se(1A)</td>
<td>178.0(6)</td>
</tr>
</tbody>
</table>

Table 9: Important bond lengths [Å] and angles [°] for bis(2-chloro-3-pyridyl) ditelluride.

<table>
<thead>
<tr>
<th>Bond</th>
<th>Length [Å]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Te–C(2)</td>
<td>2.12(4)</td>
</tr>
<tr>
<td>Te–Te</td>
<td>2.677(4)</td>
</tr>
<tr>
<td>C–Te</td>
<td>1.754(3)</td>
</tr>
<tr>
<td>N–C(1)</td>
<td>1.313(3)</td>
</tr>
<tr>
<td>C(2)–Te–C(1)</td>
<td>99.3(6)</td>
</tr>
<tr>
<td>C(1)–N–C(5)</td>
<td>116.3(2)</td>
</tr>
<tr>
<td>N–C(1)–C(2)</td>
<td>126.4(2)</td>
</tr>
<tr>
<td>C–Te</td>
<td>1.339(4)</td>
</tr>
<tr>
<td>C–C</td>
<td>1.396(3)</td>
</tr>
<tr>
<td>C–C</td>
<td>1.387(3)</td>
</tr>
<tr>
<td>C–C</td>
<td>1.383(3)</td>
</tr>
<tr>
<td>C–Te</td>
<td>115.62(17)</td>
</tr>
<tr>
<td>C–C–Te</td>
<td>118.0(2)</td>
</tr>
<tr>
<td>Te–C–Te</td>
<td>124.30(17)</td>
</tr>
</tbody>
</table>
Table 10: Important torsion angles [°] of bis(2-chloro-3-pyridyl) ditelluride.

<table>
<thead>
<tr>
<th>Bond Configuration</th>
<th>Torsion Angle [-]</th>
</tr>
</thead>
<tbody>
<tr>
<td>C(5) - N - C(1) - C(2)</td>
<td>-0.3(4)</td>
</tr>
<tr>
<td>N - C(1) - C(2) - Te</td>
<td>-174.83(19)</td>
</tr>
<tr>
<td>C(1) - C(2) - Te</td>
<td>4.8(3)</td>
</tr>
<tr>
<td>Te - C(2) - C(3)</td>
<td>174.54(17)</td>
</tr>
<tr>
<td>Te - Te - C(2) - C(3)</td>
<td>-168.01(17)</td>
</tr>
</tbody>
</table>

**15. MOLECULAR STRUCTURE OF BIS(2-CHLORO-3-PYRIDYL) DITELLURIDE**

Beautiful and bright orange colored, diamond-shaped single crystals of bis(2-chloro-3-pyridyl) ditelluride were obtained by a slow evaporation of dichloromethane and hexane (1 : 2). X-ray single crystal analysis of a selected specimen was done on Bruker Smart CCD diffractometer.

The compound crystallizes into monoclinic, C2/c space group:

\[ a = 11.6112(14) \, \text{Å}, \quad b = 9.7812(12) \, \text{Å}, \quad c = 12.0760(14) \, \text{Å}, \quad \alpha = 90^\circ, \quad \beta = 113.717(2)^\circ, \quad \gamma = 90^\circ. \]

The ORTEP diagram of the compound is given in Figure 3 and important bond parameters are given in Tables 9 and 10.

**ACKNOWLEDGMENTS**

The first author is thankful to Department of Science and Technology (DST) and Council of Scientific and Industrial Research (CSIR) for financial assistance vide Sanctions no. SR/SI/IC-02/2003 and no. 01(1865)/03/EMR-II, respectively. The third author is thankful to University Grants Commission (UGC) for Teacher Fellowship. The authors are also thankful to Professor P. Mathur, Indian Institute of Technology, Mumbai (India) for providing X-ray facilities.

**REFERENCES**


A Novel Approach Toward the Synthesis and Characterization of Pyrimidyl Chalcogen Compounds

K. K. Bhasin,1 Ekta Arora,1 Rishu,1 Shivani Doomra,2 Nishima,1 Yogesh Nagpal,1 Rajeev Kumar,1 W. Weigand,3 and S. K. Mehta1

1Department of Chemistry and Centre of Advanced Studies in Chemistry, Panjab University, Chandigarh, India
2Department of Chemistry, D.A.V. College, Chandigarh, India
3Universitaet Jena, Institute fuer Anorganische und Analytische Chemie, Jena, Germany

A variety of hitherto unknown symmetrical and unsymmetrical pyrimidyl chalcogen compounds have been synthesized and characterized by elemental analysis using various spectroscopic techniques viz. NMR 1H, 13C, 77Se and infrared. Two different methodologies were employed. The first method involves the use of hydrazine hydrate as reducing agent to generate dichalcogenide anions followed by reaction with 2, 4-dichloropyrimidine to give the dichalcogenide compounds in good yield. The second method employs chlorine-magnesium exchange of 2,4-dichloropyrimidine using iso propyl magnesium chloride. The synthesis of the mixed phenyl pyrimidyl selenides have been achieved using sodium borohydride in ethanol as a reductive reagent to cleave Se-Se bond followed by alkylation with 2-chloro-4, 6-dimethylpyrimidine and 2, 4-dichloropyrimidine.

Keywords 2,4-dichloropyrimidine; diselenide; pyrimidine; selenium

INTRODUCTION

Heterocycles are major building blocks in many biologically active molecules and their functionalization is an active field of research.1 The pyrimidine moiety is widely found in natural products and its compounds are widely used as inhibitors of human immunodeficiency virus,2 act as effective anti-cancer drugs,3 and as anti-rejection drugs4 in transplantations. It is curious to note, however, that the pyrimidine compounds of sulfur and selenium do not occupy the appropriate

The authors gratefully acknowledge the Department of Science and Technology, New Delhi, for financial support.

Address correspondence to K. K. Bhasin, Department of Chemistry, Panjab University, Chandigarh 160 014, India. E-mail: kkbhasin@pu.ac.in
RESULTS AND DISCUSSION

Jerchel et al.\textsuperscript{5} were the first to explore the chemistry of pyridyl selenium compounds and synthesize bis (4-pyridyl) diselenide and bis (4-pyridyl) selenide by reacting N-pyridyl (4-pyridinium) chloride with hydrogen selenide. We, therefore, felt it necessary to develop a safe and convenient method for its preparation. Subsequently, the method was improved by reducing elemental selenium with sodium borohydride in different solvents by various coworkers.\textsuperscript{6} Different methodologies in the subsequent years explored variations of the published procedures to improve the yield of 2,2'-dipyridyl diselenide. Bhasin et al.\textsuperscript{7} have developed and optimized the conditions for the preparation of stable bis (2-pyridyl) diselenide/ditelluride by lithiation of pyridine using BF\textsubscript{3}-Et\textsubscript{2}O complex followed by insertion of elemental selenium/tellurium and subsequent oxidation.

In pursuance of our work on the synthesis of dipyridyl diselenide, we report herein a convenient, operationally simple and facile synthetic route for the synthesis of hitherto unknown dipyrimidyl dichalcogenide and phenyl pyrimidylselenides (Scheme 2). The starting materials 2-chloro-4, 6-dimethylpyrimidine and 2,4-dichloropyrimidine were prepared by chlorination of 4,6-dimethyl-2-hydroxypyrimidine hydrochloride and 2,4-dihydroxypyrimidine respectively using phosphorus oxychloride.

The synthetic strategy that has been followed to prepare bis [4-dimethylamino-2-pyrimidyl] dichalcogenide employs hydrazine
hydrate as the reducing reagent for chalcogens (S, Se) in dimethylformamide. It has been found that dimethyl formamide acts both as solvent and a nucleophile, leading to nucleophilic substitution of chlorine at fourth position by dimethyl amino group, -NMe₂.

Attempts to prepare the titled dichalcogenides by chlorine-magnesium exchange reaction employing isopropyl magnesium chloride at fourth position was not successful.

To synthesize unsymmetrical pyrimidyl selenides, ethanolic sodium borohydride was used for the reductive cleavage of Se-Se bond in diphenyl diselenide (Scheme 3). Dimethyl formamide (DMF) has been employed as co-solvent in this reaction. It has been found that DMF improves the yield of the desired product by solubilizing the phenylselenolate ion, which is otherwise known to exist as a boron complex possessing diminished nucleophilicity.8 9

SCHEME 3
The disulfide/diselenide and monoselenides thus prepared are stable enough to be purified by column chromatography (silica gel using hexane-ethyl acetate) on a laboratory bench. The compounds are soluble in conventional organic solvents and have a shelf life of several months without any sign of decomposition even at room temperature. The compounds prepared have been fully characterized with the help of various spectroscopic techniques.

**EXPERIMENTAL**

All experiments were carried out in dry oxygen–free nitrogen atmosphere. IR spectra were recorded between KBr plates on a Perkin-Elmer Model 1430 ratio recording spectrometer. $^1$H NMR and $^{13}$C NMR spectra were recorded in $\text{CCl}_3/\text{CDCl}_3$ using tetramethylsilane as an internal standard and $^{77}$Se with dimethylselenide as an external reference on a Jeol 300MHz spectrometer. Carbon, Hydrogen and Nitrogen were estimated micro analytically on a Perkin-Elmer 2400 CHN Elemental analyzer.

**Synthesis of 4, 6-Dimethyl-2-hydroxypyrimidine Hydrochloride**

Urea (12 g) in 100 ml of boiling ethanol (b.pt. 78°C) was treated with acetyl acetone (20 g) and the hot solution was treated with 27 ml of conc. $\text{HCl}$ with stirring. The mixture was refluxed for 24 h after which time 24.0 g (75%) of 4, 6-Dimethyl-2-hydroxypyrimidine hydrochloride was isolated by filtration and subsequent washing with cold ethanol and diethyl ether.

**Synthesis of 4, 6-Dimethyl-2-chloropyrimidine**

The mixture of 4, 6-Dimethyl-2-hydroxypyrimidine hydrochloride (20.0 g, 0.125 mol) and phosphorous oxychloride (110 ml) was refluxed for 10 h, after which time the residual phosphorous oxychloride was removed in vacuo. The residual oil was poured into 50 g of ice and neutralized below 10°C with a concentrated solution of potassium hydroxide. The resulting mixture and 300 ml diethyl ether was vigorously stirred for 10 h. The organic extract was evaporated to dryness. The residual crude product was recrystallized from a minimal amount of petroleum ether (b.pt. 40–70°C) giving 13.8 g (77%) of colorless 4, 6-Dimethyl-2-chloropyrimidine plates. M.pt.37–38°C. $^1$H NMR (CDCl$_3$): $\delta$ 6.89(s, 1H), 2.37(s, 6 H).
Synthesis of Bis [4-dimethylamino-2-pyrimidyl] Diselenide/Disulfide

To a vigorously stirred mixture of powdered sodium hydroxide (3.0 g, 75 mmol), elemental chalcogen (S = 1.6 g or Se = 4.0 g, 50 mmol) and dimethylformamide (30 ml), 100% hydrazine hydrate was added slowly. After stirring for nearly 6 hr. at room temperature, a solution of 4, 6-dimethyl-2-chloropyrimidine (100 mmol) dissolved in 15 ml DMF was added dropwise. The reaction was refluxed for 2–3 h and monitored by TLC. After completion of reaction, it is diluted with about 250 ml of distilled water and extracted in dichloromethane (3 x 50 ml). The organic layer was separated and solvent evaporated to get the crude product in solid form. The product was subjected to purification on a silica column using hexane as eluant.

General Procedure for Synthesis of Unsymmetrical Pyrimidyl Selenides

To a solution of Ar₂Se₂ (Ar = phenyl) in 50 ml of C₂H₅OH-DMF (3:2) was added 0.456 g (12 mmol) of NaBH₄ in parts with continuous stirring at 0–5°C; 10 mmol of alkylating agent (4, 6-dimethyl-2-chloropyrimidine or 2,4-dichloropyrimidine) diluted with equal volume of DMF was added drop wise. Reaction was complete within 1–2 h. Extraction is done in dichloromethane after evaporating ethanol under vacuum. The organic layer was repeatedly washed with distilled water (3 x 40 ml), dried over anhydrous sodium sulfate. Solvent was evaporated on rota evaporator and the product was subjected to purification on a silica column using hexane as eluant.

Bis [4-dimethylamino-2-pyrimidyl] Diselenide

Yield = 65%, Yellow crystalline solid, m.p. = 79–81°C, ¹H NMR; δ 7.9 (d, 1H), 6.83 (d, 1 H), 3.14 (s, 6H); ¹³C NMR; δ161.2, 157.1,154.7,150.4,145.8,140.3,134.0,128.8,55.4; ⁷⁷Se NMR; 431.57; IR (KBr, cm⁻¹): 2924.4, 2853.3, 1566.0, 1521.4, 1458, 1405.3, 1340.4, 1208.3, 790.4, 550.7.

Bis [4-dimethylamino-2-pyrimidyl] Disulfide

Yield = 67%, Yellow crystalline solid, m.p. = 130°C, ¹H NMR; δ 8.50 (d, 1H), 7.45 (d, 1 H), 3.50 (s, 6H); ¹³C NMR; δ160.2, 154.1, 150.4, 101.5, 34.0; IR (KBr, cm⁻¹): 2925.4, 1568.3, 1405.4, 1340.6, 1208.3, 790.4, 550.7.
4-6-Dimethyl-2-pyrimidylselenobenzene
Yield = 75%, White crystalline solid, m.p. = 58-62°C, $^1$H NMR: $\delta$ 7.61(d,2H), 7.31(m,3H), 6.58 (s,1H), 2.28 (s,6 H) ; $^{13}$C NMR: $\delta$ 170.3, 166.9, 136.9, 136.0, 129.6, 128.2, 117.5, 36.8, 23.8; $^{77}$Se NMR: $\delta$ 486.8; IR (KBr, cm$^{-1}$): 2924.0, 1578.0, 1529.0, 1438.0, 1341.0, 783.0, 542.0; Anal. Calcd. for C$_{12}$H$_{12}$N$_2$Se; C, 54.50; H, 4.54, N, 10.60. Found: C, 37.03, H, 3.36, N, 12.38.

2-Phenylseleno-4-chloropyrimidine
Yield = 75%, White crystalline solid, m.p. = 49-51°C, $^1$H NMR: $\delta$ 8.08 (d, 1H), 7.00(d, 2H), 7.45 (m, 3H); $^{13}$C NMR: $\delta$ 162.6, 161.3, 160.8, 159.8, 157.2, 120.0; $^{77}$Se NMR: $\delta$ 500.69; IR (KBr, cm$^{-1}$): 2924.0, 1542.0, 1518.0, 1478.0, 1439.0, 790.0, 592.6; Anal. Calcd. for C$_{10}$ H$_7$Cl N$_2$Se; C, 44.28; H, 2.58, N, 10.33. Found: C, 44.42, H, 1.96, N, 9.71.

In summary, in this present paper, we have proposed a simple and convenient methodology to prepare novel pyrimidine chalcogen compounds in good to excellent yields.

REFERENCES
Synthesis of Unsymmetrical Pyridyl Aryl Selenides by the Reductive Cleavage of Se-Se Bond

K. K. Bhasin,1 Shivani Doomra,2 Gurjeet Kaur,3 Ekta Arora,1 Neelam Singh,1 Yogesh Nagpal,1 Rajeev Kumar,1 Rishu,1 T. M. Klapoetke,4 and S. K. Mehta1

1Department of Chemistry and Centre of Advanced Studies in Chemistry, Panjab University, Chandigarh, India
2Department of Chemistry, D.A.V.College-10, Chandigarh, India
3Department of Chemistry, G.C.G.-11, Chandigarh, India
4Department of Chemistry and Biochemistry, Ludwig Maximilians University, Munich, Germany

An efficient protocol for the synthesis of novel hitherto unknown substituted and unsubstituted phenyl pyridyl selenides from dipyridyldiphenyl diselenides and phenyl/pyridyl halides in the presence of copper catalysed system, Cu2O/Mg/bpy is being presented. All the synthesized selenides are either light yellow coloured liquids or low melting solids. All the newly synthesized compounds have been thoroughly characterized by elemental analysis employing various spectroscopic techniques viz., infrared, multinuclear NMR (1H, 13C, 77Se) and mass spectrometry (in representative cases).

Keywords Copper; phenyl; pyridyl; reductive cleavage; selenide

INTRODUCTION

Chemistry of alkyl, aryl, and mixed alkyl aryl selenides has developed rapidly for the last two decades and find extensive applications in organic synthesis,1 organic superconductors,2 MOCVD,3 and biochemistry.4 It is curious to note that the analogous chemistry of pyridyl derivatives has remained neglected over the years probably due to non-availability of a convenient and efficient synthesis.

Recently, the chemistry of pyridyl derivatives has attracted the attention of the scientific community due to their unique properties, which...
endear them to new and exciting applications in organic synthesis and biochemistry. In recognition of its importance, renewed efforts have evolved for the convenient methodologies of their synthesis. Literature is swamped with several synthetic procedures for the preparation of alkyl, aryl and mixed alkyl aryl selenides. All these methods employ a reducing agent to reduce elemental selenium-to-selenium dianion ($\text{Se}^{2-}$ and $\text{Se}^{4-}$) viz. $\text{NaBH}_4$, $\text{LiAlH}_4$, $\text{R}_4\text{N}^+\text{BH}_4^-$, $\text{LiEt}_4\text{BH}$, $\text{HOCH}_2\text{SO}_3\text{Na}$, $\text{Na/NH}_2$, and so on, followed by quenching with alkyl/aryl halides. Another versatile approach towards the synthesis of unsymmetrical organoselenium compounds involve the formation of intermediate selenolates $\text{RSe}^-$ generated in situ by reductive cleavage of Se-Se bond in diorganyl diselenides. Reductive cleavage of Se-Se bond can be realized with a galaxy of reducing agents such as $\text{N}_2\text{H}_4\cdot\text{H}_2\text{O}$, $\text{R}_4\text{N}^+\text{BH}_4^-$, $\text{NaBH}_4$, $\text{LiEt}_4\text{BH}$, and so on. In recent times, some metals like indium, lanthanum, samarium, and their salts have also been reported to cleave Se–Se bond.

Catalytic procedures are considered more applicable, however, as many functional groups cannot withstand harsh reaction conditions. Various complexes such as $\text{Pd(PPh}_3)_4$, $\text{(bpy)}_2\text{NiBr}_2$, and $\text{RhCl(PPh}_3)_3$ have been successfully exploited to prepare unsymmetrical selenides. A number of selenides have been prepared by the direct nickel (II) and copper (II)-catalyzed coupling of a diselenide with aryl iodides. In this paper, we wish to report a mild, convenient, and economical method for the synthesis of pyridyl phenyl selenides using eco-friendly reagents.

RESULTS AND DISCUSSION

Mautner et al. synthesized 2,2'-dipyridyl diselenide by reacting 2-bromo pyridine with toxic hydrogen selenide. Later, many research groups modified this procedure by developing safe and convenient methods for their preparation by reducing elemental selenium with sodium borohydride in different solvents. Researchers used different methodologies, in the subsequent years, explored variations of the published procedures to improve the yield of 2,2'-dipyridyl diselenide. Bhasin et al. have developed and optimized the conditions for the preparation of stable substituted dipyridyl diselenides by the bromine exchange of 2-bromo methyl substituted pyridine using n-butyl lithium in THF at $-78^\circ\text{C}$ that avoids the use of toxic gases coupled with better yields.

In pursuance of our work on the synthesis of dipyridyl diselenides, we report herein a convenient, operationally simple, and facile synthetic route for the synthesis of hitherto unknown substituted and unsubstituted pyridyl phenyl selenides. The method involves the reductive
cleavage of dipyridyl/diphenyl diselenides in DMF at 110 –120 °C using the catalyzed system Cu$_2$O/Mg/bpy. The intermediate selenolate anion generated in situ by the slow addition of dipyridyl/diphenyl diselenides to the heterogeneous system was followed by quenching with different electrophiles as depicted in Scheme 1.

**SCHEME 1** Synthesis of unsymmetric phenyl pyridyl selenides.

All the reactions were carried out in the presence of oxygen free nitrogen. The mixed pyridyl selenides thus prepared are all stable compounds and can be purified by column chromatography. All the synthesized phenyl pyridyl selenides are light yellow coloured liquids or low melting solids. The compounds dissolve readily in organic solvents and have a shelf life of several months without any sign of decomposition even at room temperature under nitrogen atmosphere.

**EXPERIMENTAL**

All the manipulations were carried out under a dry and deoxygenated nitrogen atmosphere to prevent the oxidation of oxygen sensitive selenium intermediates. Elemental selenium (Himedia) was stored in a desiccator prior to use. Diphenyl and dipyridyl diselenides were prepared by literature methods. DMF was distilled using K$_2$CO$_3$ and stored on molecular sieves. Bromobenzene (Aldrich) and other chemicals were of analytical grade and used without further purification. 2-Bromopyridine and 2,5-dibromopyridine were prepared from the corresponding 2-aminopyridines (Aldrich). $^1$H, $^{13}$C, and $^{77}$Se NMR spectra were recorded on a Jeol AL 300 MHz spectrometer in CDCl$_3$, using Me$_4$Si as an internal standard for $^1$H and $^{13}$C NMR. Me$_2$Se was used as an external reference for $^{77}$Se NMR; Infrared spectra were obtained between KBr plates on a Perkin-Elmer model 1430 spectrophotometer. C, H, and N analysis was performed on a
Synthesis of Unsymmetrical Pyridyl Aryl Selenides

Perkin-Elmer 2400 CHN analyzer. Mass spectra were obtained on a VG 7070H mass spectrometer. Separation and purification of compounds were done by column chromatography performed on activated silica gel using hexane as eluant.

General Procedure for the Synthesis of Unsymmetrical Selenides

In a 50 ml flame dried three necked round bottom flask (200 mg) activated magnesium, (28 mg) cuprous oxide, (62 mg) 2,2'-bipyridyl were taken in 15 ml dried DMF. Diphenyl diselenide (0.62 g, 2 mmol) was added to the above mixture followed by quenching with substituted 2-bromopyridines (4 mmol). The mixture was stirred at 110°C for 15-20 h. The colour of the reaction mixture changed from red to dark brown within 20–25 min. Stirring and refluxing was continued until the completion of the reaction, which is monitored by TLC. After evaporation of the solvent, the residue obtained was dissolved in dichloromethane. Ionic impurities were removed by washing the organic extract repeatedly with distilled water. The combined organic fractions were dried over anhydrous sodium sulphate and the solvent was evaporated on rotavapor. The product thus obtained was purified over silica column using hexane as eluant. Using this methodology, a number of compounds were prepared which were characterized through elemental analysis and various spectroscopic techniques.

Unsymmetrical Pyridyl Phenyl Selenides

2-Pyridyl phenyl selenide, (C_{6}H_{4}NSeC_{6}H_{5}), [1]. Yellow viscous liquid; Yield: 60 %; \(^{1}H\) NMR (CDCl\(_{3}\)/TMS): \(\delta\) 8.29-8.31 (d, 1H, 3.6Hz), 7.56–7.63 (m, 2H), 7.26–7.33 (m, 4H), 6.85–6.9 (m, 2H); \(^{13}C\) NMR (CDCl\(_{3}\)/TMS): \(\delta\) 158.7, 149.53, 136.12, 136.12, 129.12, 128.79, 127.66, 123.8, 119.99; \(^{77}Se\) NMR: \(\delta\) 469.859; I.R. (KBr, cm\(^{-1}\)): 3408.3, 2984.1, 2924.9, 1951.3, 1734.8, 1569.7, 1476.3, 1302.4, 1275.5, 1147.6, 1042.7, 985.3, 840.2, 477.7, 461.3; MS (EI, %): 234 (85), 232 (70), 154 (30), 78 (80); Anal. Calcd.: C, 56.17; H, 3.82; N, 5.95%; Found; C, 56.50; H, 3.53; N, 5.72%.

3-Methyl-2-pyridyl phenyl selenide, (CH_{3}C_{6}H_{4}NSeC_{6}H_{5}), [2]. Yellow viscous liquid; Yield: 70%; \(^{1}H\) NMR (CDCl\(_{3}\)/TMS): \(\delta\) 8.09(s, 1H), 7.50–7.55(m, 2H), 7.17–7.34(m, 4H), 6.84–6.88(q, 1H), 2.26(s, 3H); \(^{13}C\) NMR (CDCl\(_{3}\)/TMS): \(\delta\) 156.3, 147.2, 136.4, 136.3, 135.5, 133.2, 128.9, 128.7, 128.0, 127.8, 120.6, 20.6; I.R. (KBr, cm\(^{-1}\)): 3049.6, 2924.2, 2361.3, 1569.5, 1440.2, 1389.3, 1193.4, 1124.8, 1066.1, 1022.1, 987.6, 786.9, 736.8, 689.1, 661.5, 469.7; Anal. Calcd.: C, 57.83; H, 4.41; N, 5.82%; Found; C, 57.69; H, 4.34; N, 5.54 %.
4-Methyl-2-pyridyl phenyl selenide, \( \text{CH}_3 \text{C}_5 \text{H}_3 \text{NSeC}_6 \text{H}_5 \). Yellow viscous liquid; Yield: 70%; \( ^1 \text{H} \) NMR (CDCl_3/TMS): \( \delta \) 7.99–8.08 (dd, 1H, 26.1 Hz), 7.44–7.54 (m, 2H), 7.07–7.23 (m, 3H), 6.61–6.65 (m, 2H), 2.0 (s, 3H); \( ^13 \text{C} \) NMR (CDCl_3/TMS): \( \delta \) 157.8, 149.0, 146.9, 135.6, 128.8, 128.1, 127.6, 124.2, 121.1, 20.4; \( ^77 \text{Se} \) NMR: \( \delta \) 467.05; I.R. (KBr, cm\(^{-1}\)): 3435.3, 3054.6, 2920.7, 2358.7, 1584.2, 1454.4, 1375.8, 1277.4, 1267.9, 1116.2, 1077.5, 1022.6, 819.6, 741.7, 692.3, 520.3, 471.5; Anal. Calcd.: C, 57.83; H, 4.41; N, 5.62 %; Found: C, 57.53; H, 4.91; N, 5.82 %.

5-Methyl-2-pyridyl phenyl selenide, \( \text{CH}_3 \text{C}_5 \text{H}_3 \text{NSeC}_6 \text{H}_5 \). Yellow viscous liquid; Yield: 70%; \( ^1 \text{H} \) NMR (CDCl_3/TMS): \( \delta \) 8.15 (s, 1H), 7.52–7.61 (m, 2H), 7.17–7.27 (m, 3H), 7.05–7.09 (m, 1H), 6.80–6.84 (m, 1H), 2.13 (s, 3H); \( ^13 \text{C} \) NMR (CDCl_3/TMS): \( \delta \) 154.24, 149.80, 136.96, 135.39, 130.41, 129.54, 128.17, 127.9, 18.89; \( ^77 \text{Se} \) NMR: \( \delta \) 464.11; I.R. (KBr, cm\(^{-1}\)): 2921.2, 1724.4, 1584.2, 1555.9, 1364.6, 1274.6, 1223.2, 1072.7, 1022.8, 999.9, 816.4, 640, 474.6; Anal. Calcd.: C, 57.83; H, 4.41; N, 5.62 %; Found: C, 57.62; H, 4.57; N, 5.75 %.

6-Methyl-2-pyridyl phenyl selenide, \( \text{CH}_3 \text{C}_5 \text{H}_3 \text{NSeC}_6 \text{H}_5 \). Yellow viscous liquid; Yield: 70%; \( ^1 \text{H} \) NMR (CDCl_3/TMS): \( \delta \) 7.56 (s, 2H), 7.23–7.25 (d, 3H, 6Hz), 7.10–7.15 (t, 1H), 6.61–6.73 (dd, 2H), 2.39 (s, 3H); \( ^13 \text{C} \) NMR (CDCl_3/TMS): \( \delta \) 158.5, 158.1, 136.4, 136.0, 129.40, 128.5, 127.9, 120.8, 120.7, 119.8, 119.5, 24.07; I.R. (KBr, cm\(^{-1}\)): 3053.8, 2923.1, 2852.3, 1577.2, 1476.0, 1388.6, 1327.1, 1302.5, 1248.9, 1161.2, 1086.7, 1065.7, 1021.8, 999.1, 842.6, 774.1, 740.4, 61.6, 663.8, 546.9, 474.5; Anal. Calcd.: C, 57.83; H, 4.41; N, 5.62 %; Found: C, 57.62; H, 4.57; N, 5.56 %.

5-Bromo-2-pyridyl phenyl selenide, \( \text{BrC}_5 \text{H}_3 \text{NSeC}_6 \text{H}_5 \). Yellow low melting solid; Yield: 70%; \( ^1 \text{H} \) NMR (CDCl_3/TMS): \( \delta \) 8.45–8.47 (d, 1H, 2.1 Hz), 7.59–7.68 (d, 1H, 1.5 Hz), 7.38–7.56 (m, 5H), 6.83–6.86 (d, 1H, 4.8 Hz); \( ^13 \text{C} \) NMR (CDCl_3/TMS): \( \delta \) 157.3, 150.6, 139.8, 136.2, 129.8, 129.0, 127.4, 124.4, 117.4; \( ^77 \text{Se} \) NMR: \( \delta \) 473.09; I.R. (KBr, cm\(^{-1}\)): 3055.3, 2923.2, 1550.3, 1476.2, 1347.6, 1310.3, 1270.5, 1211.7, 1179.3, 1071.7, 1020, 958.3, 918.2, 767.8, 670.0, 622.9, 591.3, 493.0, 476.0; MS (EI, %) 311 (100), 234 (30), 157 (45), 77 (80); Anal. Calcd.: C, 42.03; H, 2.54; N, 4.45 %; Found: C, 41.89; H, 2.96; N, 4.78 %.

In summary, most of these synthetic protocols in the literature suffer from one or the other disadvantages viz., lengthy synthetic steps, harsh reaction conditions, expensive reducing agents, contamination of desired products with impurities, non-reproducible results and sensitive to aerial oxidation. The present paper takes into account these constraints in developing a mild, more convenient, commercially viable, and efficient reaction for the synthesis of desired phenyl pyridyl selenides under neutral conditions.
REFERENCES


Mixed Surfactant Based Microemulsions as Vehicles for Enhanced Solubilization and Synthesis of Organoselenium Compounds

S. K. Mehta,* Khushwinder Kaur, Ekta Arora, and K. K. Bhasin

Department of Chemistry and Centre of Advanced Studies in Chemistry, Panjab University, Chandigarh, 160 014 India

Received: March 28, 2009; Revised Manuscript Received: May 27, 2009

We exploited the added degree of compositional freedom provided by mixed AOT/lecithin surfactants in reverse isooctane microemulsion to demonstrate that a small amount of added lecithin significantly enhances the solubility of organodiselenides over that in AOT reverse isooctane microemulsions alone. Conductivity results show that the added lecithin significantly increases the solubility of four different organodiselenides and raises the temperature required to induce percolation. FTIR, 1H NMR, and UV-visible techniques were utilized to gain insight into the interactions of organodiselenides, AOT and lecithin headgroups with water in the micellar core. The information obtained from these experiments was used to design a novel synthetic route for preparing 4-chloro-2-(naphthalen-2-ylselanyl) pyrimidine in reverse microemulsion.

Introduction

Microemulsions are stable, transparent solutions of water, oil, and surfactant and have been described as consisting of spherical droplets of dispersed phase separated from a continuous phase by a surfactant film.1-3 The surfactant aggregates in microemulsions are closely packed globules where the polar headgroup of the surfactant molecule occupies the interior of the aggregates and the hydrophobic tail extends in the bulk apolar solvent with water encapsulated in compartments.4-7 Microemulsions as chemical reaction media are interesting subjects of study because these media are macroscopically homogeneous, isotropic, and heterogeneous on a microscopic scale.5 Their structural characteristics offer the opportunity to solubilize and stabilize relatively large and otherwise insoluble molecules in the microemulsion core. The physicochemical properties of such systems are often very different from those of unsolvated molecules or condensed phases being more or less influenced by confinement effects, inhomogeneous distribution, orientation order, and interfacial interactions.8-10 In recent years, various research groups have shown an increased interest in the assimilation of additives in the microemulsion media.11-14

The structure of the surfactant also plays a dramatic role in the properties of microemulsions and the amount of additive hosted by them. The anionic surfactant bis(2-ethylhexyl)sodium sulfosuccinate (AOT) has a surfactant packing parameter, P, of 1.1 and tends to have a spontaneous curvature that is concave toward water.13 The macroscopically single phase water-in-oil microemulsions of AOT can incorporate water typically to water/AOT (φ = [water]/[AOT]) level of 30-40 and sufficient quantities of the additive. The zwitterionic surfactant phosphatidylcholine, i.e., lecithin (LC), has a significantly larger headgroup but a smaller packing parameter of 0.6 compared to AOT.15-17 In aqueous systems, LC tends to form interfaces with minimal curvature. The combination of AOT and LC further leads to a highly rigid gel that can incorporate a significantly high amount of water (φ = 50-70).18,19

Our interest lies in the microemulsion formed by the mixing of AOT and LC in water and isooctane leading to ME-1 (water/AOT/isooctane) and ME-II (water/AOT+LC/isooctane) microemulsions and assimilation of organodiselenides viz., dipyr imidyl derivatives such as, bis(4-dimethylamino-2-pyrimidyl) diselenide (C6H4NH2Se2), bis(4-chloro-2-pyrimidyl) diselenide (C6H4Cl2Se2), dinapthyl diselenide, (Nap2Se2) and bis(diphenyl methyl) diselenide (Ph2CHSe2) in ME-1 and ME-II. In addition, the synthesis of 4-chloro-2-(naphthalen-2-ylselanyl) pyrimidine in microemulsion media employing 2,4-dichloropyrimidine as starting reagent has also been attempted.

Organodiselenides are relatively large molecules and are insoluble in aqueous media. The compound (Ph2CHSe)2 is considered to be a derivative of methyl selenide that lacks the repulsive smell but possesses a good shelf life with interesting chemical behavior. Pyrimidyl, napthyl and phenyl derivatives have been taken into account to make comparative studies between the behaviors of aromatic selenium compounds in microemulsion media. The napthyl moiety consists of fused, planar, and rigid aromatic ring systems with 10π electrons that result in remarkable differences in its properties as compared to the phenyl20 and pyrimidyl analogues. The pyrimidyl moiety is found in natural products and widely used as inhibitors of human immunodeficiency virus, as effective anticancer drugs,22 23 besides being antirejection drugs in transplantations.

Water-in-oil microemulsions exhibit a low electrical conductivity as the layers of surfactant separate water droplets. However, when the temperature, T, increases beyond the critical value (i.e., Tc), the conductivity increases sharply. This sudden rise in conductance has been related to an increase in the attractive interactions between the droplets that facilitate migration of surfactant counterions along connected paths through the microemulsion, leading to the phenomenon of electric percolation.24-26

To date, no data has been reported on the synthesis of organoselenides in microemulsion media (to the best of our knowledge). However, there exists extensive evidence of the ability of microemulsions to influence reaction rates and equilibria, e.g., the hydrolysis of hydroxyacids27-29 and other carboxylic acid derivatives.30 Interesting reports exist in literature.
on the kinetics of chemical reactions on microemulsions. Prediction and interpretation of the kinetic influence of these media are relatively easy when the reagents congregate in the aqueous microdroplets that act as variable size nanoreactors concentrating the reagents.

Experimental Section

Materials. Sodium bis(2-ethylhexyl) sulfosuccinate (AOT; Fluka, purity >95%), lecithin (LC) extracted from soybeans, NaI, Na2SO4 (Fluka, purity >95%), Na2S (Fluka, purity >95%), isooctane (E-Merck, purity >99%), NaI, and Na2SO4 (Fluka, purity >95%), ethanol (Fluka, purity >95%), and DMF (Fluka, purity >99%) were used as received. Organodiselenides including (Nap2Se2, (Ph2CHSe)2, C12N6H16Se2, C8N4H4Se2Cl2, C6N2H5SeCl), and C6N2H5Cl, were synthesized in the laboratory and characterized through various spectroscopic techniques. The structures of AOT, lecithin, and assimilated organodiselenides have been presented in Schemes 1 and 2.

Conductivity Measurements. Electrical conductivity measurements of the samples were carried out with Pico digital conductivity meter operating at 50 Hz from Labindia instruments with an absolute accuracy of ±3% and precision of ±0.1%. The cell constant used was 1.0 cm⁻¹. The temperature was kept constant with the help of RE320 Ecoline thermostat with an accuracy of ±0.01 K.

FTIR Spectroscopy. FTIR spectra were recorded in the spectral region of 4400—650 cm⁻¹ using Perkin-Elmer (RX1) FTIR spectrophotometer with AgCl windows.

UV—Vis Absorption Spectroscopy. UV—vis absorption spectra were obtained in the spectral range of 250—500 nm using Jasco 530 spectrophotometer with precision of ±0.2 nm using quartz cells with a path length of 1 cm⁻¹.

NMR Spectroscopy. ¹H chemical shifts were observed with the help of Bruker AC 400 NMR. Spectral calibration was performed using D₂O or CCl₄—CDCl₃ as internal standard. ¹³C and ³²S chemical shifts were observed with the help of Jeol 300 NMR.

Mass Spectrometry. The mass spectrum was obtained on a Q-TOF micromass spectrometer.

Preparation of Samples. A series of experiments were carried out and [AOT] = 0.784 M and [AOT]:[LC] = 0.747M:0.01 M at w = 30 were found to be most acceptable concentrations to enhance assimilation of organodiselenides. All the samples were transparent and optically clear. For the synthesis of 4-chloro-2-(naphthalen-2-ylselanyl) pyrimidine (C₄N₂H₂Cl₂), wide range of ME compositions w = 2 to 40 have been used in case of both ME-I (water/AOT/ isooctane) and ME-II (water/AOT + LC/isooctane). This allowed us to modify the droplet size (by changing w) and the maximum 2,4-dichloropyrimidine (C₄N₂H₂Cl₂) intake capacity. Variable surfactant concentrations have been tried up to a total surfactant concentration of 0.784 M. However, ME formulated at w = 30 and [AOT:LC] = 0.784 M was found to be the most suitable to work with. The tried lower surfactant concentrations could not assimilate significant quantity of compound for the reaction to take place. ME-I could not be used for synthesis due to similar reasons. Moreover, it did not support 3.5 mL of C₂H₅OH—DMF, and the solution turned turbid. Therefore, ME-II was used to carry out the synthesis of C₆N₂H₅SeCl.

Results and Discussion

Although the basic understanding of the percolation phenomenon in AOT based microemulsion has been fairly studied, however, the knowledge of percolation in AOT/LC mixed microemulsion is limited. Hong et al. have reported that the addition of small amounts of LC to AOT based microemulsions stabilized the micellar interface and the leakage of encapsulated β-galactosidase to the bulk aqueous phase was therefore negligible. They have also tried to relate specific interfacial properties, which affect protein extraction in AOT and lecithin microemulsions. The comparative percolation study of AOT and lecithin microemulsions has also been carried out by Fontanella et al. Percolation phenomenon in branched lecithin microemulsions has also been reported by Aliotta and Fazio. The current percolation study has been undertaken with a view that percolation phenomenon is a sensitive and convenient measure of microinterface of microemulsions solubilizing various organodiselenides which clearly reflects the chalogen-micellar and micellar-micellar interactions. This provides a better insight into the specific interfacial properties, which affect organodiselenide solubilization and behavior in the AOT and AOT—lecithin microemulsions.
The solubilization behavior observed thus opens the gateway for organic synthesis.

**Dependence of Conductivity on Temperature.** Temperature is known to have great influence on the properties and dynamics of MES.$^{11-14}$ The conductance behavior of ME-I and ME-II has been monitored when the temperature was varied under a constant composition. The solubilization increases from 2.5 to 30 mM for ME-I and 5 mM for ME-II at [AOT:LC] = [0.774:0.01] (solid red lines show SBE fitting).

**TABLE 1: Percolation Threshold Temperature for ME-I at Different Organodiselenide Concentrations**

<table>
<thead>
<tr>
<th>organodiselenide</th>
<th>[conc.] (mM)</th>
<th>$n_i$</th>
<th>$n_f$</th>
<th>$\theta_c$ (K)</th>
<th>Differential SBE</th>
</tr>
</thead>
<tbody>
<tr>
<td>without</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$C_7N_7H_5Se_2$</td>
<td>5</td>
<td>-0.60 ± 0.02</td>
<td>3.02 ± 0.03</td>
<td>308.55</td>
<td>307.71</td>
</tr>
<tr>
<td>15</td>
<td>-0.60 ± 0.02</td>
<td>3.50 ± 0.09</td>
<td>313.64</td>
<td>313.64</td>
<td></td>
</tr>
<tr>
<td>$C_6N_6H_6Se_2Cl$</td>
<td>5</td>
<td>-0.52 ± 0.02</td>
<td>3.09 ± 0.05</td>
<td>311.11</td>
<td>309.22</td>
</tr>
<tr>
<td>15</td>
<td>-0.57 ± 0.02</td>
<td>3.09 ± 0.05</td>
<td>311.05</td>
<td>309.22</td>
<td></td>
</tr>
<tr>
<td>$C_6N_6H_6Se_2$</td>
<td>5</td>
<td>-0.52 ± 0.02</td>
<td>3.09 ± 0.05</td>
<td>311.05</td>
<td>309.22</td>
</tr>
<tr>
<td>15</td>
<td>-0.66 ± 0.03</td>
<td>3.19 ± 0.09</td>
<td>312.05</td>
<td>311.44</td>
<td></td>
</tr>
<tr>
<td>(Ph2CHSe)2</td>
<td>5</td>
<td>-0.63 ± 0.01</td>
<td>2.94 ± 0.01</td>
<td>310.00</td>
<td>310.46</td>
</tr>
<tr>
<td>15</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ME-II</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>without</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$C_7N_7H_5Se_2$</td>
<td>2.5</td>
<td>-0.61 ± 0.01</td>
<td>2.88 ± 0.03</td>
<td>318.13</td>
<td>318.88</td>
</tr>
<tr>
<td>5</td>
<td>-0.60 ± 0.02</td>
<td>2.82 ± 0.03</td>
<td>318.63</td>
<td>318.56</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>-0.60 ± 0.02</td>
<td>2.93 ± 0.02</td>
<td>319.15</td>
<td>319.99</td>
<td></td>
</tr>
<tr>
<td>50</td>
<td>-0.57 ± 0.01</td>
<td>3.43 ± 0.05</td>
<td>327.15</td>
<td>326.17</td>
<td></td>
</tr>
<tr>
<td>$C_6N_6H_6Se_2Cl$</td>
<td>5</td>
<td>-0.47 ± 0.02</td>
<td>3.04 ± 0.05</td>
<td>319.15</td>
<td>318.23</td>
</tr>
<tr>
<td>15</td>
<td>-0.48 ± 0.04</td>
<td>3.17 ± 0.01</td>
<td>320.15</td>
<td>320.55</td>
<td></td>
</tr>
<tr>
<td>50</td>
<td>-0.48 ± 0.02</td>
<td>2.96 ± 0.03</td>
<td>323.10</td>
<td>321.80</td>
<td></td>
</tr>
<tr>
<td>$C_6N_6H_6Se_2$</td>
<td>5</td>
<td>-0.65 ± 0.02</td>
<td>3.01 ± 0.03</td>
<td>313.05</td>
<td>311.85</td>
</tr>
<tr>
<td>15</td>
<td>-0.69 ± 0.02</td>
<td>2.94 ± 0.04</td>
<td>314.05</td>
<td>314.49</td>
<td></td>
</tr>
<tr>
<td>50</td>
<td>-0.48 ± 0.03</td>
<td>2.96 ± 0.03</td>
<td>324.07</td>
<td>323.80</td>
<td></td>
</tr>
<tr>
<td>(Ph2CHSe)2</td>
<td>2.5</td>
<td>-0.61 ± 0.01</td>
<td>2.88 ± 0.03</td>
<td>318.63</td>
<td>317.88</td>
</tr>
<tr>
<td>5</td>
<td>-0.60 ± 0.02</td>
<td>2.93 ± 0.02</td>
<td>319.15</td>
<td>319.99</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>-0.48 ± 0.02</td>
<td>3.17 ± 0.01</td>
<td>320.15</td>
<td>320.65</td>
<td></td>
</tr>
</tbody>
</table>

* log $n_i =\text{initial conductance}$, log $n_f =\text{final conductance}$.

where $\theta$ and $\theta_c$ represent conductance and temperature. $\Delta \theta$ is the constant interval of $\theta$ and $\theta_c$ for stand for initial, final, and percolation stages respectively. At constant composition, organodiselenides have been found to delay the percolation process. The delay becomes more pronounced with the increase in concentration of organodiselenide. The value of $\theta_c$ for compositions under study varies as $C_7N_7H_5Se_2Cl > NapSe_2 > (Ph_2CHSe)_2 > C_6N_6H_6Se_2Cl > (Ph_2CHSe)_2 > C_6N_6H_6Se_2 > NapSe_2 > without for ME-I at [organodiselenide] = 5 mM.

Maitra et al.$^{35}$ have reported that in the percolative ME the droplets retain their closed structure although infinite clusters are formed due to inter droplet interactions. The mutual contact and the bridging between the droplets is due to tail of additives either at the interface (e.g., hydrotopes and bile salts)$^{11}$ or in the core of the droplets (e.g., poly (ethylene glycol)s).$^{13}$ The pyrimidyl derivatives have two active N-ends that anchor the droplet surface. This results in the bridging of the nanodroplets and the conduit formation is favored. The pyrimidyl derivative is a rigid nonplanar moiety in which one (pyrimidyl—Se—) unit is bent leaving the central horizontal plane. It contains electronically active —(—Se—Se—)— along with two N-ends. The molecule adheres to the droplet interface resulting in bridging of the nanodroplets. The phenyl and naphthyl derivatives of selenium have no such active sites except for —(—Se—Se—)— and remain in the dispersion medium, resisting the droplet fusion by enhancing the blockening effect and thus delaying the percolation threshold. However, in ME-II even the phenyl and naphthyl derivatives may be restricted to the interface because the introduction of LC in ME-II leads to the immobilization of hydrophobic and hydrophilic regions which allows the formation of extended structures that are organized over multiple length scale.$^{18-36}$

Surfactant molecules solubilized in MES display a large variety of microstructures, which are sensitive to some control parameters such as temperature, size of water pool, effect of external entity, etc. The local geometric constraints and the subtle balance of opposing forces originating from polar head groups, and the hydrophobic tail of the surfactant molecules determine the morphology of self-assembling system. The calculation of thermodynamic parameters of ME-I and ME-II further indicates that the microenvironment of the system without organodiselenide is less organized as compared to the presence of organodiselenides. The higher value of $\theta$ observed in ME-II as compared to ME-I indicates the more organized surroundings of ME-II as compared to ME-I (Supporting Information).

The interactions between the organodiselenide and the MES are best revealed by $^1H$ NMR, FT IR, and UV—vis absorption spectroscopy. The water pool properties of microemulsion have been extensively studied by FT IR and $^1H$ NMR.$^{37-40}$ Typical $^1H$ NMR spectra of ME-I and ME-II with and without organodiselenide reveal a unique peak due to aromatic region in organodiselenide molecules. Table 1 (Supporting Information) shows the comparison of peaks in ME-I and ME-II. The inspection of data reveals that the peaks due to aromatic protons are retained in ME-I and ME-II indicating that the organodiselenide moiety is intact in the ME system and is not subjected to any breakdown. Peaks due to aromatic protons and headgroup protons are downfield in ME-I as compared to ME-II. These findings are consistent with the fact that addition of LC in ME-I involves progressive change in the electron cloud of the protons of the headgroup. The organodiselenide interaction is mainly localized in the proximity of the polar head groups of the
surfactant. This is revealed by the shifts of the headgroup protons in ME-I and ME-II.

The UV–vis absorption spectra of ME-I and ME-II have been characterized using various spectroscopic techniques. vmax/cm−1 for (Ph2CHSe)2; only a broad band is observed. The observed

\[ \text{absorption} = \frac{\text{intensity of absorption bands}}{\text{nature of}} \]

The Amax of organodiselenide OH (cm−1) CO (cm−1) S=O (cm−1) COC (cm−1) are 3325.0, 3343.0, 1702.8, 1706.2, 1044.2, 1046.1, 1225.6, 1228.1. The observed trends in position and intensity of absorption bands depend upon the nature of electronic transition responsible for absorption and can be explained in terms of molecular orbital theory. The spectra of organodiselenide bands have been presented in Figure 2, panels A and B, respectively. The observed trends in position and intensity of absorption bands depend upon the nature of electronic transition responsible for absorption and can be explained in terms of molecular orbital theory. The spectra of organodiselenide depend mainly on the three effects: inductive, hyperconjugative and torsional (steric).

Table 2 depicts the stretching frequencies of various bands in organodiselenide.

<table>
<thead>
<tr>
<th>organodiselenide</th>
<th>OH (cm−1)</th>
<th>CO (cm−1)</th>
<th>S=O (cm−1)</th>
<th>COC (cm−1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ME-I</td>
<td>3323.0, 3343.1</td>
<td>1706.4, 1704.5</td>
<td>1045.2, 1046.1</td>
<td>1225.5, 1225.1</td>
</tr>
<tr>
<td>ME-II</td>
<td>3323.0, 3343.3</td>
<td>1702.8, 1707.3</td>
<td>1045.5, 1045.8</td>
<td>1230.9, 1225.3</td>
</tr>
</tbody>
</table>

The stretching frequency in FT IR reflects the interaction between the surfactant molecules and the organodiselenides. Table 2 depicts the stretching frequencies of various bands in ME-I and ME-II. The state of organodiselenide in ME-I and ME-II can be rationalized in terms of organodiselenide entrapped in the interfacial layer of appropriately oriented AOT/AOT+LC monolayers. A comparison of OH band frequencies of the organodiselenides reveals a shift to higher frequency of around 11.3, 24.8, 28.5, 18, and 20.1 cm−1, respectively, for C2H5N2H4Se2, C6H5N2H4SeCl2, NapSe2, (Ph2CHSe)2, and without ME-II than ME-I. The peak centered at 1706 cm−1, assigned to CO stretching shows a similar trend of shift towards the higher frequency with the incorporation of organodiselenide.

The high frequency values observed in ME-II as compared to ME-I further reveal the entrapping of organodiselenide at the interface. However, a shift of around 1 cm−1 observed for C=O–C and S=O– is modest. A representative spectrum for different absorption regions has been presented in Figure 3.

Preparation and Characterization of 4-Chloro-2-(naphthalen-2-ylselanyl) Pyrimidine C8N4H4Se2Cl2

To a solution of NapSe2 (0.53 mM, 0.022 g) in 3.5 mL of CH2OH-DMF (6:1) was added 0.022 g of NaHBe in parts with continuous stirring at 0–5 °C, and the reaction was maintained under inert atmosphere of nitrogen so as to prevent oxidation of selenide anion. After 5 min of stirring, 152 mM (wt ME) of C6H5N2H4Cl2 in ME-II with [AOT:LC] = 0.774 M:0.01 M, φ = 30 was added dropwise. Completion of the reaction as evidenced by TLC was observed within 30 min. The obtained product was subjected to column chromatography using ethyl acetate as eluant, which gave the desired compound in 45% yield. C6H5N2H4SeCl2 was characterized using various spectroscopic techniques. νmax/cm−1 of CH-Se stretching is 1541.5 and 1390.1(C=C), 791.0(C=Se) and 665.4(C–C); δ(ppm)/1H: 53200 MHz, CDCl3/C6D6, Me2SO) 8.39–8.35 (1H, d, J = 8.1, 5-H), 8.16–8.12 (2H, m, 8-H, 16-H), 8.04–7.98 (2H, m, 9-H,14-H), 7.63–7.59 (3H, m, 11-H, 12-H, 13-H), 6.52–6.50 (1H, d, J = 5.2, 6-H); δ(ppm)/13C(C75 MHz, CDCl3/C6D6, Me2SO) 175.09, 160.63, 157.28, 137.41, 134.56, 134.45, 131.88, 128.97, 128.11, 127.67, 126.25, 124.29, 118.73. δ(ppm)/1S=O75 MHz,
Figure 3. Comparison of infrared stretching band of ME-II at \( \omega = 30 \) in the presence of 10 mM organodiselenide showing different stretching regions (A) OH, (B) CO, (C) S-CH-, and (D) COC ester linkage.

Our interest in the synthesis of \( \text{C}_4\text{N}_2\text{H}_9\text{SeCl} \) originated from the fact that general synthetic procedures employed for the synthesis of organochalcogen compounds are rather complicated as they involve long refluxing, controlled experimental conditions, and high cost. The Bhasin group has synthesized 4-chloro-2-(naphthalen-2-ylselenyl) by a conventional method using sodium borohydride as the reducing agent. The reaction completes in 3 h but involves work up with costly solvents. Therefore, development of a practical, efficient, and quick process is quite desirable. Therefore, the one-pot procedure for the synthesis of \( \text{C}_4\text{N}_2\text{H}_9\text{SeCl} \) in ME media was attempted which involves low reaction time and avoids the use of toxic solvents as compared to conventional methods for synthesis of organochalcogen compounds.

We hereby report the first ever organoselenide synthesis in ME media. Being microheterogeneous, microemulsions are excellent solvents for both lipophilic organic substances and polar reagents, such as inorganic and organic salts. Performing the reaction in a microemulsion is therefore a useful way to overcome the solubility problems that are frequently encountered in organic synthesis. This can be attributed to the large interfacial area and high dynamics of MEs. Many organic compounds have a polar and a nonpolar end. Such molecules will orient at the oil–water interface. Attack by a water-soluble species will then preferentially occur from the water side and vice versa for water insoluble reagents. Since \( \text{C}_4\text{N}_2\text{H}_9\text{Cl} \) is insoluble in water and isooctane, the reaction is expected to take place at the interface. The oil–water interface and the selected

SCHEME 3: Probable Mechanism for the Synthesis of 4-Chloro-2-(naphthalen-2-ylselenyl) Pyrimidine
stoichiometric amounts may induce orientation of reactants in microemulsion system, which might lead to selective nucleophilic substitution of chlorine atom at second position of pyrimidine. The reaction proceeds with the reduction of NapSe2 with NaBH4 to yield NapSe- anion. The C4N2H9Cl is expected to stay at the interface where the electron cloud of the surfactant interface interacts with the electric field produced by the NapSe- ion. The local hydrophobicity of the naphthyl ring drags the NapSe- pyrimidine. The reaction proceeds with the reduction of Nap2Se2 to CSIR for fellowships. K.K. and E.A. are thankful to CSIR for financial assistance. J. Phys. Chem. B, Vol. 113, No. 31, 2009 10691

Figure 4. Representative FTIR spectra of C4N2H9SeCl in various regions (A) 1200–1700 and (B) 500–800 cm⁻¹. The confirm the formation of C4N2H9SeCl. The region from 1300–1600 cm⁻¹ show clear peaks at 1541.5 and 1399.1 cm⁻¹. This has been presented in Figure 4. The peaks at 1541.5 and 1399.1 cm⁻¹ are due to C=C of pyrimidine moiety. For the region 500–800 cm⁻¹, the peaks at 665.4 and 791.0 cm⁻¹ have been assigned to C-Se and C-Cl bonds of the obtained product.

Knowledge of the mixed surfactant systems could have many applications in material synthesis. The expanded range of micellar geometries and functionalities available in mixed surfactant systems not only makes them useful for applications but also provides opportunities for fundamental studies of self-assembly. Surfactant solutions are of significant interest in synthesis of nanostructures and synthetic compounds. The surfactant combinations described here fall in the category of systems in which aqueous phase synthesis may be combined with organic phase synthesis to create new tools for synthetic chemistry. The obtained knowledge of physicochemical parameters provides an easy route for variation of the structural parameters needed for such research efforts. The ability to selectively modify the microstructure through composition or temperature change also benefit in directing the morphological synthesis of materials.

Conclusions

The incorporation of organodiselenides in microemulsion significantly affects the solubilization and electric percolation phenomenon. ME-II serves as a better host for the assimilation of organodiselenides as compared to ME-I. The better behavior of ME-II further provides a gateway for synthesis of C4N2H9SeCl. Conductivity and spectroscopy results indicate the presence of ionic interactions between organodiselenides, AOT, and water molecules. The probing of water pool and interfacial properties reveals that organodiselenide molecules are restricted at the interface in ME-II. This understanding of physical parameters and interactions has implications for the design of surfactant systems for organic synthesis. This finds a way for the first ever attempt for synthesis of C4N2H9SeCl in ME-II media. The synthetic procedure for the synthesis of C4N2H9SeCl reported hitherto is simple, convenient and does not involve troublesome manipulations and use of toxic solvents.

Acknowledgment. S.K.M. and K.K.B. are grateful to DST and CSIR for financial assistance. K.K. and E.A. are thankful to CSIR for fellowships.

Supporting Information Available: 1H NMR, 13C NMR, and mass spectra of 4-chloro-2-(naphthalen-2-ylselenyl) pyri-
midine (C$_4$H$_2$N$_2$SeCl) and experimental details of thermodynamics of droplet clustering. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

(50) Bhasin, K. K.; Avora, E.; Mehta, S. K., unpublished work.
Preparation and characterization of bis[4-dimethylamino-2-pyrimidyl] dichalcogenides (S, Se, Te): X-ray crystal structure of bis[4-dimethylamino-2-pyrimidyl] diselenide and its physicochemical behavior in microemulsion media

K.K. Bhasin, Ekta Arora, Khushwinder Kaur, Sung-Kyu Kang, Michael Gobel, T.M. Klapoetke, S.K. Mehta

Department of Chemistry and Centre of Advanced Studies in Chemistry, Panjab University, Chandigarh 160014, India
Korea Institute of Energy Research, 71-2 Jang-dong, Yuseong-gu, Daejeon, South Korea
Department of Chemistry and Biochemistry, Ludwig Maximilian University, Munich, Germany

ARTICLE INFO
Article history:
Received 7 August 2008
Received in revised form 18 October 2008
Accepted 21 October 2008
Available online 25 October 2008

Abstract
Novel and synthetically important bis[4-dimethylamino-2-pyrimidyl] dichalcogenides (S, Se, Te) have been prepared and characterized with the help of elemental analysis and various spectroscopic techniques. The methodology employs hydrazine hydrate in dimethylformamide to reduce elemental chalcogen to generate the dichalcogenide anions, \( E^2\) (E=S, Se, Te), followed by reaction with 2,4-dichloropyrimidine to afford bis[4-dimethylamino-2-pyrimidyl] dichalcogenides in good yield. It further exploits the additional compositional degree of freedom available in mixed surfactant solution to allow solubilization and stabilization of bis[4-dimethylamino-2-pyrimidyl] diselenide in microemulsion media.

Keywords: Selenium, Tellurium, Pyrimidine, Organochalcogens, Microemulsion

1. Introduction

In the last few decades various organochalcogen (alkyl, aryl, mixed alkylaryl, pyridyl selenium, and tellurium) compounds have been extensively studied owing to their novel and unparallel properties. These compounds find widespread use as convenient intermediates or reagents in organic synthesis, biochemistry, organic superconductors, and semiconducting materials. In an effort to synthesize these compounds various procedures have been explored. Tanji et al. employed the reaction of 2-bromo-pyridine with lithium alkyl tellurolates to obtain alkyl pyridyl tellurides while Bhasin et al. have developed and optimized the conditions for the preparation of stable bis(2-pyridyl) diselenide/ditelluride by lithiating pyridine using BF \(_3\)-Et\(_2\)O complex followed by insertion of elemental selenium/tellurium and subsequent oxidation. Bis(2-pyridyl) diselenide has also been shown to be a potential immuno-stimulant and inducer of interferon gamma and other cytokines in human peripheral blood leukocytes.

Microemulsions are dynamic supramolecular aggregates spontaneously formed by dissolving surfactant in organic media. These aggregates allow molecules of disparate polarities (i.e., diorganodichalcogenides) to be brought into contact with each other. Microemulsions help in solubilization of molecules insoluble in organic and aqueous solvents and can provide useful reaction media for organic synthesis. The physicochemical properties of such systems are often very different from those of naked molecules or condensed phases and are influenced by confinement effects, inhomogeneous distribution, orientation order, and interfacial interactions. Water-in-oil microemulsions exhibit a low electrical conductivity as the layers of surfactant separate water droplets. However, when the temperature increases beyond the critical value \( \theta_c \), the conductivity increases sharply. This sudden rise in conductance has been related to increase in the attractive interactions between the droplets that facilitate migration of surfactant counter ions along connected paths through the microemulsion, leading finally to the phenomenon of electric percolation.

In pursuance of our work on pyridylchalcogen compounds, we wish to report herein, a convenient and facile method for synthesis of some newly designed pyrimidyl chalcogen compounds by employing hydrazine hydrate as a reducing agent for elemental
chalcogen atom in dimethylformamide. This line of approach appears to be potentially useful in view of the many known biologically important compounds,23 which contain the pyrimidyl moiety. Amir et al.25 have provided a broad view of antiinflammatory activity possessed by compounds having a pyrimidine nucleus. 2,4-Diaminopyrimidine derivatives, that have been well established as antiviral agents, now have been modified to antitumor agents23 5-Alkyl- or 5-alkylaryl-substituted pyrimidine derivatives are useful intermediates in the synthesis of antiviral nucleosides. Schinazi et al.24 reported the synthesis and the biological activity of several 5-(phenylselenenyl)-pyrimidine nucleosides as potential antiviral agents. More recently,25,26 a variety of newly synthesized 6-phenylselenenyl acyclic pyrimidines was found to have potent antihumanimmunodeficiency virus type-1 (HIV-1) activity. Bardos27 group synthesized 5-selenium-substituted derivatives (diselenides) of uracil, 2'-deoxyuridine, and 2'-deoxyuridylic acid. Amino- and dimethylamino-substituted dipyrimidyl diselenides have been reported28 by use of UV irradiation. Curiously, these compounds have not been studied extensively compared to the corresponding aromatic and aliphatic derivatives although the pyrimidyl compounds are anticipated to exhibit interesting properties due to presence of two electron withdrawing nitrogen in their skeleton structure. To explore the behavior of studied compounds, an additional study has been carried out by assimilating bis[4-dimethylamino-2-pyrimidyl] diselenide whereas at 36.6 ppm in disulfide. A comparison of 

2. Results and discussion

The synthetic strategy to prepare disubstituted pyrimidyl chalcogen compounds employs 100% hydrazine hydrate in DMF to reduce chalcogens to generate dichalcogenide anions \( \text{E}_2^- \) (E=S, Se, Te) followed by reaction with 2,4-dichloropyrimidine to give 1a-1c in good yield (Scheme 1).

\[
4 \text{E} + \text{N}_2\text{H}_4\cdot\text{H}_2\text{O} + 4\text{NaOH} \xrightarrow{\text{DMF}} 2\text{Na}_2\text{E}_2 + 5\text{H}_2\text{O} + \text{N}_2
\]


The advantage of this methodology is the selective nucleophilic substitution of chlorine atom at second position of 2,4-dichloropyrimidine by dimethylamino group from the solvent dimethylformamide. It is well known that DMF can act as formylating agent,29 however, in these reactions it acts as a nucleophilic reagent leading to replacement of activated chlorine atom in both fields in selenium and tellurium compounds as compared to sulfur one. The aromatic protons in pyrimidyl ring H-3 and H-4 resonate at high δ value in case of diselenide compared to disulfide that can be clearly explained on the basis of decreased electronegativity down the group in chalcogen family. However, the chemical shift is usually upfield in case of disulfide (S<Te<Se) that may be attributed to intramolecular repulsions in this compound. \(^{13}C\) NMR spectroscopic results reveal that the aromatic carbons fall in the region of 100-162 ppm. The chemical shift value of the methyl carbon of dimethylamino group resonate at higher field in selenium and tellurium compounds and have a shelf life of several months without any sign of decomposition even at room temperature.

2.1. Spectroscopic studies

\(^1H\) NMR characterization of dichalcogenide compounds shows an upfield shift of ring protons w.r.t. the protons of 2,4-dichloropyrimidine due to displacement of electronegative chlorine with chalcogen atom. The aliphatic protons of the methyl carbon of dimethylamino group resonate at higher field in selenium and tellurium compounds as compared to sulfur one. The aromatic protons in pyrimidyl ring H-3 and H-4 resonate at high δ value in case of diselenide compared to disulfide that can be clearly explained on the basis of decreased electronegativity down the group in chalcogen family. However, the chemical shift is usually upfield in case of disulfide (S<Te<Se) that may be attributed to intramolecular repulsions in this compound. \(^{13}C\) NMR spectroscopic results reveal that the aromatic carbons fall in the region of 100-162 ppm. The chemical shift value of the methyl carbon of dimethylamino group appear at about 37 ppm in case of diselenide and disulfide whereas at 36.6 ppm in disulfide. A comparison of stretching frequencies, obtained from FTIR results, reveals a regular trend in the variation of absorption values.

As commonly observed in EIMS, extensive dissociation of C-E bond (E=S, Se, Te) occurred and consequently the base peaks did not correspond to molecular ion peaks. In case of bis[4-dimethylamino-2-pyrimidyl] diselenide, the mass spectrum is complicated due to
several isotopes of selenium. The fragment corresponding to 4-N,N-dimethylamino pyrimidyl radical is the most intense and appears at m/e 122 and is assigned as the base value. The fragment ions containing selenium show a highly characteristic and definite pattern of signal intensities depending on the natural abundance of various isotopes of selenium. Bis[4-dimethylamino-2-pyrimidyl] ditelluride shows prominent peak corresponding to [C12H16N6Te]+ (m/e 372) while other low intensity peaks result from [C10H10N5Te]+ (m/e 328) and [C10H6N5Te]+ (m/e 324).

2.2. Crystal structure determination of bis[4-dimethylamino-2-pyrimidyl] diselenide (1)

To have a better understanding of the structural details, single crystal X-ray diffraction of (1) was carried out. A perspective view and atom numbering scheme of (1) is given (Fig. 1). Crystal data for (1): C12H16N6Se2, M=402.23; monoclinic; a=9.2362(11), b=13.2178(13), c=12.7392(16) Å; V=1555.1(3) Å³, T=200 K; 8=1.718 g/cm³; Z=4; 3601 reflections measured, R=0.0665, wR2=0.1450 for 1379 (½2½) unique reflections, which were used in all calculations. The final R indices were R1=0.1027, wR2=0.1696 (all data).

The two pyrimidine rings have an average C-C bond length of 1.319 Å and C-C=C bond angle of 115.7°. The Se-Se bond distance of 2.3162(16) Å relates well with the corresponding distances reported for other diselenides, which ranges from 2.29 to 2.39 Å (Pauling scale).37 The Se-C bond length [Se1-C1 1.905(2) Å] is also in agreement with the value of 1.93 Å suggested by Pauling as a typical value of other diselenides.37

2.3. Assimilation of bis[4-dimethylamino-2-pyrimidyl] diselenide in microemulsion media

Bis[4-dimethylamino-2-pyrimidyl] diselenide, C12H16N6Se2, has been assimilated in microemulsion (water/AOT/isooctane (ME-I) and water/AOT+LC/isooctane (ME-II)) and characterized with the help of conductive and spectroscopic techniques. The conductance behavior of ME-I and ME-II has been monitored when temperature is varied under a constant composition. The solubilization increases from 2.5 to 50 mM for bis[4-dimethylamino-2-pyrimidyl] diselenide. C12H16N6Se2 in ME-II as compared to 15 mM in ME-I. The temperature-conductance profiles of bis[4-dimethylamino-2-pyrimidyl] diselenide, C12H16N6Se2 at different concentrations viz., 5 and 15 mM for ME-I and 5, 15, 30, and 50 mM for ME-II have been depicted (Fig. 2). The percolation parameters for ME-I and ME-II are tabulated in Table 1. The plots have been fitted to Sigmoidal Boltzmann equation.38

\[ \log \frac{\text{log } \gamma}{\text{log } \gamma} = \frac{1}{\text{log } \gamma} \left( \frac{1}{1 + \exp(\theta - \theta_c)} \right) \]

where i, f, and c are the initial, final, and percolative stages. At constant composition, bis[4-dimethylamino-2-pyrimidyl] diselenide 1b has been found to delay the percolation process. The delay becomes more pronounced with the increase in concentration of organodiselenide.

Matra et al.39 have reported that in the percolative ME, the droplets retain their closed structure although infinite clusters are formed due to droplet interactions. The mutual contact and the bridging between the droplets are due to the presence of additives either at the interface or in the core of the droplets. The pyrimidyl derivatives have two active N-sites that anchor the droplet surface. This results in the straight bridging of the droplets and the conduit formation is favored. The pyrimidyl derivative is a rigid non-planer moiety in which one (pyrimidyl-Se-)- unit is bent leaving the central horizontal plane. It contains electronically active (−Se-Se−) moiety along with two N-sites. The molecule adheres to the droplet interface but the configuration results in the eclipsed bridging due to two droplets engulfing the same

![Figure 1. ORTEP diagram showing the conformation for bis(4-dimethylamino-2-pyrimidyl) diselenide (1).](image1)

![Figure 2. Variation of temperature for C12H16N6Se2 for ME-I and ME-II at (AOT) (LC)=0.774:0.01.](image2)

<table>
<thead>
<tr>
<th>Organodiselenide</th>
<th>Concentration (mM)</th>
<th>log f</th>
<th>log i</th>
<th>R2 (K)</th>
<th>Differential SBE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Without</td>
<td>-0.46±0.02</td>
<td>3.02±0.03</td>
<td>309.55</td>
<td>307.77</td>
<td></td>
</tr>
<tr>
<td>C12H16N6Se2 (ME-I)</td>
<td>5</td>
<td>-0.59±0.02</td>
<td>3.30±0.06</td>
<td>309.55</td>
<td>309.68</td>
</tr>
<tr>
<td></td>
<td>15</td>
<td>-0.66±0.02</td>
<td>3.39±0.09</td>
<td>313.64</td>
<td>313.64</td>
</tr>
<tr>
<td>C12H16N6Se2 (ME-II)</td>
<td>2.5</td>
<td>-0.61±0.01</td>
<td>2.88±0.03</td>
<td>316.13</td>
<td>317.88</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>-0.60±0.02</td>
<td>2.82±0.03</td>
<td>318.63</td>
<td>318.56</td>
</tr>
<tr>
<td></td>
<td>15</td>
<td>-0.60±0.02</td>
<td>2.93±0.02</td>
<td>319.15</td>
<td>319.99</td>
</tr>
<tr>
<td></td>
<td>50</td>
<td>-0.57±0.01</td>
<td>3.43±0.05</td>
<td>327.05</td>
<td>326.17</td>
</tr>
</tbody>
</table>

log f—initial conductance, log i—final conductance.
organodiselenide moiety. However, the introduction of LC in ME-II leads to the immobilization of hydrophobic and hydrophilic regions, which allows the formation of extended structures that are organized over multiple length scales and this restricts bis[4-dimethylamino-2-pyrimidyl] diselenide. An inspection of data reveals that the peaks due to aromatic protons are retained in ME-I and ME-II indicating that the organodiselenide moiety is intact in ME system and is not subjected to any breakdown. Peaks due to aromatic protons and head group protons are downfield in ME-I as compared to ME-II. These findings are consistent with the fact that addition of LC in ME-I involves progressive change in the surfactant. This is revealed by the shifts of polar head groups of the surfactant. This is supported by the interpretation of UV-vis spectra of related compounds cited in the literature. A representative spectrum for different absorption regions has been presented (Fig. 3).

The slight red shift observed in ME-I as compared to ME-II suggests that the organodiselenide is more tightly held at the micellar interface in ME-II and, therefore, indicate that ME-II serves as a better host for the assimilation of organodiselenide.

3. Conclusion

The present report constitutes the first successful attempt to synthesize novel bis[4-dimethylamino-2-pyrimidyl] dichalcogenides (S, Se, Te) by simple synthetic methodology. The synthesis involve nucleophilic substitution by dimethylamino group from the solvent dimethylformamide, which otherwise act as a formylating agent. These compounds are anticipated to have potential applications in medicinal field. In addition, the interactions of bis[4-dimethylamino-2-pyrimidyl] diselenide with core water, AOT, and Lecithin head groups in microemulsion media reveal significant enhancement of its solubilization capacity.

4. Experimental section

4.1. Materials and instrumentation

All experiments were carried out in dry oxygen-free nitrogen atmosphere. Hydrazine hydrate (Qualigens India, purity >99%), selenium (Hi-media, purity >99%), elemental sulfur (Hi-media, purity >99%), tellurium (Hi-media, purity >96%), uracil (Hi-media, purity >99%), sodium bis(2-ethylhexyl) sulfosuccinate (AOT) (Fluka, purity >99%), phosphatidylycholine (Lecithin) (LC) (Fluka, purity ~98%), isooctane (E-Merck, purity >99%) were newly purchased and stored in dessicator prior to use.
4.2. Synthesis of 2,4-dichloropyrimidine

In a 500 ml, two-necked, round-bottom flask equipped with a condenser, uracil (3.0 g, 75 mmol), elemental chalcogen (S = 1.6 g, Se = 4.0 g, Te = 6.4 g, 50 mmol), and dimethylformamide (30 ml), 100% hydrazine hydrate (3.50 ml) was added. The solution was refluxed with stirring for 3.5 h at 110 °C. The residual phosphorous oxychloride was removed microanalytically on a Perkin-Elmer 2400 CHN Elemental Analyzer.

4.3. Synthesis of bis[4-dimethylamino-2-pyrimidyl] dichalcogenide

To a vigorously stirred mixture of powdered sodium hydroxide (3.5 g, 75 mmol), elemental chalcogen (S = 10 g, selenium = 10 g, 10 g, 10 g), and dimethylformamide (30 ml), 100% hydrazine hydrate was added slowly. After stirring for nearly 5 h at room temperature, a solution of 2,4-dichloropyrimidine (100 mmol) dissolved in 15 ml DMF was added dropwise. The reaction was monitored by TLC. After completion of reaction, it was diluted with about 250 ml of distilled water and extracted in dichloromethane (3 × 50 ml). The organic layer was decanted and solvent evaporated. The product was subjected to purification on a silica column using hexane as eluant (5:1).

4.3.1. Bis[4-dimethylamino-2-pyrimidyl] disulfide


4.3.2. Bis[4-dimethylamino-2-pyrimidyl] dithiophosphate

Yield = 50%, red crystalline solid, mp = 112–114 °C. [Found: C, 29.83; H, 3.32; N, 16.52. Calcd for C6H12N2P: C, 30.00; H, 3.12; N, 21.01.]

4.3.3. Bis[4-dimethylamino-2-pyrimidyl] dithiophosphate

Yield = 50%, red crystalline solid, mp = 112–114 °C. [Found: C, 29.83; H, 3.32; N, 16.52. Calcd for C6H12N2P: C, 30.00; H, 3.12; N, 21.01.]

4.4. Preparation of microemulsion

A series of experiments were assembled and [AOT] = 0.784 M and [W][TO][O] = 0.774 M were found to be most acceptable concentrations to enhance assimilation of bis[4-dimethylamino-2-pyrimidyl] diselenide, C12H16N6Se2. All the samples were transparent and optically clear. The assimilation of bis[4-dimethylamino-2-pyrimidyl] diselenide, C12H16N6Se2 in ME-II enhanced the solubilization from 2.5 to 50 mM in ME-II as compared to 15 mM in ME-I.

4.5. Physical measurements

IR spectra were recorded between KBr plates on a Perkin-Elmer Model 1430 ratio recording spectrometer. 1H NMR spectra were recorded in D2O using tetramethylsilane as an internal standard using Bruker 400 MHz spectrometer. UV-vis absorption spectra were obtained in the spectral range of 250–500 cm⁻¹ using HITACHI 330 model spectrophotometer with precision of ± 0.2 nm using quartz cells with a path length of 1 cm⁻¹. The electrical conductivity measurements of the samples were carried out with Pico digital conductivity meter operating at 50 Hz using Labinord instruments with an accuracy of ± 0.1%. The cell constant used was 1.0 cm⁻¹. The temperature was kept constant with the help of RE320 Ecoline thermostat with an accuracy of ± 0.01 K. Triple distilled water with conductance less than 3 µs cm⁻¹ was used for the preparation of microemulsions.

4.5.1. Bis[4-dimethylamino-2-pyrimidyl] diselenide

Clear yellow solution in ME-I and ME-II. 1H NMR (400 MHz, CDCl3) δ 8.21–8.20 (1H, d, J = 6.4 Hz, H-6), 7.10–7.09 (1H, d, J = 6.4 Hz, H-5), 4.43–3.60 (12H, s, NMe2), 1.87–0.86 (6H, d, J = 5.2 Hz, H-5), 6.91–6.00 (1H, d, J = 5.2 Hz, H-5), 5.43, 4.15, 3.22, 1.74, 1.42, 1.13, 0.98 (ME-II); UV–vis absorption spectroscopy: λmax/nm 326.61 (ME-I), 321.30 (ME-II); IR (AgCl, cm⁻¹): 1629.0, 1582.6, 1566.6, 1538.0, 1458.0, 1409.0, 1168.6, 1045.8, 1230.9, 1045.8, 1207.3, 1094.5, 1285.5 (ME-I), 3236.3, 1703.7, 1045.8, 1225.3 (ME-II), 3233.0, 1706.4, 1045.2, 1225.5 (pure ME-II) for OH, CO, S, C–O–C.

4.6. X-ray crystallographic studies

Diffraction quality yellow colored single crystals of (1) were obtained by the slow evaporation of dichloromethane/hexane solution of the compound. Suitable crystals were chosen from a crop of crystals, mounted on glass fibers and data collected on VG 7070H diffractometer for the cell determination and intensity data collection. The diffraction data were collected using monochromatic Mo Kα radiation at 200 K. Crystal structure was solved by direct methods (SHELX-97)44 and refined by full matrix least squares method.

Crystallographic data have been deposited with Cambridge Crystallographic Data Centre as supplementary publication number CCDC 697324. Copy of data can be obtained, free of charge, on
application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [lsc 4 0 1223 330635 or e-mail: deposit@ccdc.cam.ac.uk].

Acknowledgements

K.K.B. and S.K.M. are thankful to the CSIR and DST for financial support. The authors are also thankful to Central Instrumentation Laboratories (CIL), Panjab University, Chandigarh, India for providing necessary instrumentation facility.

References and notes


Synthesis and characterization of novel quinoline selenium compounds: X-ray structure of 6-methoxy-3H-[1,2]diselenolo[3,4-b]quinoline

K.K. Bhasin a*, Ekta Arora a, Chee-Hun Kwak b, S.K. Mehta a

a Department of Chemistry and Centre of Advanced Studies in Chemistry, Panjab University, Chandigarh 160 014, India
b Department of Chemistry, Suncheon National University, Suncheon 540-742, South Korea

ARTICLE INFO

Article history:
Received 14 October 2009
Received in revised form 6 January 2010
Accepted 7 January 2010
Available online 14 January 2010

Keywords:
Quinoline
Selenium
Vilsmeier cyclisation
Diselenolo quinoline

1. Introduction

Organic compounds containing selenium are of considerable interest since they exhibit diverse biological activities with numerous therapeutic applications [1,2]. In addition, the presence of a heterocyclic ring as the organic moiety in these compounds alters their properties to a great extent. A pharmacologically active heterocycle is the quinoline ring that occurs in several natural products and displays a broad range of biological activity [3,4] including antitumour, hypoglycemic, antihistamine and anticarcinogenic properties [5], etc. Due to their importance as substructures in a broad range of natural and designed products, significant efforts have been directed into the development of new quinoline based structures [6]. Amongst methodologies reported for the preparation of quinolines, Vilsmeier [7] cyclisation is the most straightforward protocol (Scheme 1). Therefore, for the synthesis of 2-chloro-3-formylquinolines, the present work deals with the corresponding acetamides.

Among potentially attractive new starting materials for the preparation of organic selenium compounds are carbonyl compounds, and their reaction with hydrogen selenide and its salts have been explored under a variety of alkaline and acidic conditions to give low yield of diselenides and selenoaldehyde oligomers, respectively [8]. Margolis and Pittman [9] obtained low yields of aliphatic diselenides when the corresponding ketones were treated with excess hydrogen selenide in the presence of strong hydrochloric acid. The synthesis of various diselenides by an amine catalysed reaction of carbonyl compounds with hydrogen selenide has also been reported [10]. In all these methods, long reaction times are required and the products are found to be invariably contaminated with elemental selenium and oligoselenides. The latter are difficult to remove from the desired diselenides and show decomposition with liberation of elemental selenium upon storage and handling.

An alternative method avoiding the use of hydrogen selenide gas involves the reductive selenation of aromatic and heteroaromatic aldehydes (ArCHO) employing Se/CO/H2O system in DMF [11]. However, this method is less effective in case of aliphatic aldehydes. Consequently, there is a great interest in the synthesis of diselenide derivatives of quinoline by a simple method using reactants containing both carbonyl and halide species.

In continuation of our work on the synthesis of organic selenium compounds [12] and the convenient synthesis of 2-chloro-3-formylquinolines, the present paper deals with the synthesis of quinoline selenium compounds.

2. Result and discussion

The Vilsmeier cyclisation was performed to prepare the precursors for the synthesis of quinoline selenium compounds (Scheme 1). A survey of literature has revealed that compounds containing Se-Se bond, acyclic and cyclic, are potential labilizing agents for lysosomes and mitochondria in vitro [13]. In this work we wish...
to report the synthesis and characterization of a few hitherto unknown derivatives of the titled heterocycles and a viable mechanism for the unusual ring closure involved in the reaction.

The present article reveals the synthesis of 3H-[1,2]diselenolo[3,4-b]quinoline (II a-b) and quinolinyl methyl diselenide (III a-b) systems (Scheme 2) wherein sodium


Scheme 1. Vilsmeier cyclisation.

Scheme 2. Reaction scheme for synthesis of quinoline selenium compounds.

Scheme 3. Mechanistic pathway for diselenolo[3,4-b]quinoline (II a-b) and quinolinyl methyl diselenide (III a-b).
hydrogen selenide (NaHSe) has been used as a nucleophilic reagent for 2-chloro-3-formylquinolines (I-a-b) in the presence of piperidine hydrochloride.

2.1. Spectroscopic studies

It was observed that the \(^1H\) NMR spectra for the diseleneno \([3,4-b]\)quinoline (II a-b) display four different sets of protons in aromatic region and one peak in aliphatic region corresponding to the methylene moiety.

Compounds (II a-b) whose identity has been tentatively predicted on the basis of NMR studies give rise to four distinct set of signals, three of which correspond to quinolinyl ring protons, whereas the remaining one signal in aliphatic region resonate much upfield (\(\delta 3.60\) for II a and \(\delta 3.75\) for II b) as compared to the methylene signal in corresponding cyclised selenium compounds (\(\delta 4.51\) for II a and \(\delta 4.49\) for II b). This indicates that the methylene protons are presumably located on a side chain rather than being in a cyclic structure. The two different environments experienced by the selenium atoms in the compounds II a-b is also confirmed by the appearance of two signals in \(^77Se\) NMR.

In the mass spectrum of 6-methyl-3H-[1,2]diselecteno[3,4-b]quinoline (II a), ([M]+*+1) ion peak appears at m/z value of 316. 1,2-Bis(2-chloro-6-methoxyquinolin-3-yl)methyl diselenide (III b) display the molecular ion peak at m/z value of 573. Mass fragments of II b and II a have also been characterized by mass spectrometry.

A plausible mechanism for the reaction has been demonstrated in Scheme 3. In this sequence, the initial reaction involves the formation of an amine-aldehyde adduct such as hemiaminal or aminal 1 or 2. Nucleophilic displacement by the hydrogen selenide anion on 1 or 2 followed by an intramolecular elimination leads to a short lived selenoaldehyde intermediate 3. In this reaction sequence, two displacement steps, i.e. oxygen by nitrogen, and nitrogen, in turn, by selenium are taking place. Furthermore, it is proposed that the reduction of this selenoaldehyde 3 involves initial selenophilic attack by the hydrogen selenide anion, forming the diselenol anion 4. This diselenol anion then can undergo intramolecular attack by sodium borohydride (Loba, purity > 99.5%), elemental selenium (Hi-media, purity > 99%) and piperidine hydrochloride (Hi-media, purity > 99%) were newly purchased and stored in dessicator prior to use. 2-Chloro-3-formyl quinolines were prepared by reported methods [14]. All the compounds prepared were fully characterized by IR, \(^1H\), and \(^13C\) NMR. Mass fragments of II a-b and III a have also been characterized by mass spectrometry.

2.2. X-ray crystallography studies

Perspective view of the compound II b is shown in Fig. 1 and all other relevant details about crystal structure determination and refinement parameters are given in Table 1.

The Se-Se bond length is 2.354 Å. The most predominant short contact is observed between Se(1) - H(10) as depicted by the interatomic distance of 3.010 Å which is less than the sum of the Vander wall radii (3.100 Å). Nonbonding interactions present in the crystal structure are shown in Fig. 1. The crystal packing also shows that the two molecules facing each other have the selenium atoms in the opposite directions.

3. Experimental

3.1. General

All the experimental manipulations were carried out in dry and deoxygenated nitrogen atmosphere. Absolute ethanol (Fluka, purity > 99.5%) was used as the solvent for the reactions. Sodium borohydride (Loba, purity > 99.5%), elemental selenium (Hi-media, purity > 99.5%) and piperidine hydrochloride (Hi-media, purity > 99%) were newly purchased and stored in dessicator prior to use. 2-Chloro-3-formyl quinolines were prepared by reported methods [14]. All the compounds prepared were fully characterized using elemental analysis on a Perkin-Elmer model 2400 CHN analyzer. \(^1H\), \(^13C\) NMR spectra were recorded on a Jeol AL 300 MHz spectrometer in CDC\(_3\)/CCl\(_4\). Tetramethylsilane (TMS) was used as an internal standard for \(^1H\) NMR and \(^13C\) NMR. Infrared spectra were obtained between KBr plates using CCL\(_4\) as a solvent and stored in dessicator prior to use.

3.2. General procedure for the synthesis of quinoline chalcogen compounds (II a-b, III a-b)

Grey powdered selenium (60 mmol) and sodium borohydride (70.6 mmol) were placed into a 500 mL three necked flask fitted with a ground glass stirrer, a reflux condenser, and a ground glass stopper with a rubber septum. 2-Chloro-3-formyl quinolines were prepared by reported methods [14]. All the compounds prepared were fully characterized by \(^1H\), \(^13C\) NMR and IR spectroscopy.
with a nitrogen inlet, addition funnel, and reflux condenser. The flask was flushed with nitrogen, immersed in an ice bath, and absolute ethanol (100 mL) was added slowly with stirring. Stirring was continued until all selenium had dissolved and a colorless solution resulted. To this solution was added piperedine hydrochloride (50 mmol) followed by aldehyde (47 mmol). The reaction mixture was heated under reflux for 1 h and cooled to room temperature to give red solution. Addition of sodium borohydride (12 mmol) in a test tube resulted. To this solution was added piperidine hydrochloride (5 ppm) 145.4, 137.2, 136.6, 132.0, 130.7, 128.0, 127.5, 126.3, 59.8, 26.2; IR (KBr, v cm⁻¹): 3025.0, 1515.3, 1454.0, 1302.5, 1292.8, 1284.9, 1102.8, 1002.5, 620.8, 552.2, 478.3; ES-MS: m/z (Assignment, R.I.): 301 [{C₇H₇N₆Se₂}⁺, 1, 20]

3.2.4. 1,2-Bis(2-chloro-6-methylquinolim-3-y)methyl diselenide (III a)

Yellow crystalline solid, M.P.: 135–137 °C. Yield, 26%, Anal. Calc. (%) for C₂₂H₁₈N₂Se₂, C, 42.19; H, 3.64; N, 5.19. Found: C, 42.1; H, 3.6; N, 5.2.

Yellow crystalline solid, M.P.: 135–137 °C. Yield, 26%, Anal. Calc. (%) for C₂₂H₁₈N₂Se₂, C, 42.19; H, 3.64; N, 5.19. Found: C, 42.1; H, 3.6; N, 5.2.

Preparation and characterization of symmetrical bis[4-chloro-2-pyrimidyl] dichalcogenide (S, Se, Te) and unsymmetrical 4-chloro-2-(arylchalcogenyl) pyrimidine: X-ray crystal structure of 4-chloro-2-(phenylselanyl) pyrimidine and 2-(p-tolylselanyl)-4-chloropyrimidine

K.K. Bhasin1,∗, Ekta Arora1, S.K. Mehta1, T.M. Kläpoetke1

1 Department of Chemistry and Centre of Advanced Studies in Chemistry, Panjab University, Chandigarh-160014, India
2 Department of Chemistry and Biochemistry, Ludwig Maximilian University, Munich, Germany

ARTICLE INFO

Article history:
Received 25 December 2009
Received in revised form
17 August 2010
Accepted 2 September 2010
Available online 21 September 2010

Keywords:
Selenium
Tellurium
Pyrimidine
Nucleophilic substitution

ABSTRACT

Synthesis of a novel class of multinucleate pyrimidine chalcogen (S/Se/Te) derivatives has been successfully attempted for the first time by the selective substitution of chlorine at the C-2 position of 2,4-dichloropyrimidine with nucleophilic dichalcogenide anion \( \text{E}^- \) (\( \text{E} = \text{S}, \text{Se}, \text{Te} \)) to afford bis[4-chloro-2-pyrimidyl] dichalcogenide. The highly electrophilic nature of 2,4-dichloropyrimidine compared to aryl chlorides has been further exploited to prepare a variety of 4-chloro-2-(arylchalcogenyl) pyrimidine compounds by substituting the chlorine exclusively at the C-2 position of 2,4-dichloropyrimidine with a variety of chalcogen bearing aryl anions \( \text{ArE}^- \) (\( \text{Ar} = \text{phenyl, 1-naphthyl, p-tolyl, 4,6-dimethyl-2-pyrimidyl, 2-pyridyl, 4-methyl-2-pyridyl} \)). All the newly prepared symmetrical and unsymmetrical pyrimidyl chalcogen compounds have been thoroughly characterized with the help of various spectroscopic techniques viz., NMR (\( ^1\text{H}, ^{13}\text{C}, ^{77}\text{Se} \)), FT-IR and mass spectrometry (in representative cases). The crystal structures of 4-chloro-2-(phenylselanyl) pyrimidine and 2-(p-tolylselanyl)-4-chloropyrimidine have been determined by X-ray crystallography.

© 2010 Published by Elsevier B.V.

1. Introduction

Over the last thirty years, many important organic transformations were efficiently achieved using organochalcogen intermedias \([1–5]\) that find extensive application in many diversified areas, such as metallurgy, chemicals, electronic conductors, and so on. A majority of these compounds are no longer considered toxic and some of them are used as antioxidants, enzyme inhibitors, cytotoxic agents for tumor cells and immunomodulators \([6–9]\).

Organochalcogen compounds containing \( \text{E}^- \) (\( \text{E} = \text{S}, \text{Se}, \text{Te} \)) bond display an extremely rich chemistry and are of particular interest since these can (a) act as electrophilic \([10]\) and nucleophile \([11]\) reagents in organic reactions (b) they exert protective effects against reactive oxygen species in the body \([12]\) (c) have applications in ligand chemistry \([13,14]\) and in various metal organic chemical vapor deposition (MOCVD) processes as precursors for the formation of thin films \([15,16]\).

∗ Corresponding author. Tel.: +91 172 2534407; fax: +91 172 2545074; E-mail address: kkbhasin@pu.ac.in (K.K. Bhasin).

A variety of methods for the preparation of symmetrical diorganyl chalcogenides, \( \text{R}_2\text{E} \) and diorganyl dichalcogenides, \( \text{R}_2\text{E}_2 \) (\( \text{E} = \text{S}, \text{Se}, \text{Te} \)) are known. Invariably, these methods are based on the reaction of alkali metal chalcogenides/dichalcogenides with appropriate halalkanes in an aqueous or non-aqueous medium. The only difference in the preparative procedure adopted by various chemists lies in the generation of the alkali metal chalcogenides/dichalcogenides. Alkali metal chalcogenides/dichalcogenides can be prepared in situ by reducing elemental chalcogens by a variety of reducing agents viz. \( \text{LiAlH}_4 \) \([17]\), \( \text{R}_2\text{N}^-\text{BH}_4 \) \([18]\), \( \text{LiEt}_2\text{BH} \) \([19]\), \( \text{HOCH}_2\text{SO}_2\text{Na} \) \([20]\), and \( \text{Na/H}_2 \text{NH} \) (\([21]\). In literature use of some metals like indium \([22]\), lanthanum \([23]\), samarium \([24]\) and their salts \([25]\) have also been reported to cleave chalcogen–chalcogen bond. A number of alkyl aryl selenides have been prepared by the direct nickel \([26,27]\) and copper \([28]\) catalyzed \([27,28]\) coupling of selenide anions with aryl iodides. Different synthetic procedures for the preparation of the pyridyl selenium and tellurium compounds are also documented in the literature. Jerchel et al. \([29]\) were the first to synthesize bis(4-pyridyl) diselenide and bis(4-pyridyl) selenide by reacting N-pyridyl (4-pyridinum) chloride with hydrogen selenide. Tanji et al. \([30]\) reported the formation of alkyl pyridyl telluride by reacting bromopyridine with lithium alkyltellurolate. Recently, Bhasin and Singh
2.1. Bis[4-chloro-2-pyrimidyl] diselenide 1b

Yield: 65%, red crystallized solid. δ = 8.39–8.37 (d, J = 6.0 Hz, 1H).

1H NMR (300 MHz, CDCl3, 25 °C): δ = 8.39–8.37 (d, J = 6.0 Hz, 1H), 7.64–7.82 (d, J = 6.0 Hz, 1H) ppm. 13C NMR: δ = 164.7, 160.0, 149.0, 118.0, C8H14N2SeCl2; calc. δ 163.6, 160.4, 149.0, 118.0. MS-EI: m/e (%): 318.6 ([C10H7N2SeCl]+, 34.5), 231.8 (C10H6N2SeCl, 27.6). IR (KBr): ν = 2924, 1539, 1400, 1330, 1192, 1071, 755, 727 cm⁻¹. MS-EI: m/e [M+H]+: 319.3, 232.4, C10H7N2SeCl: calc. δ 319.4, 232.5; found δ 319.5, 232.4.

2.1.3. Bis[4-chloro-2-pyrimidyl] ditelluride 1c

Yield: 55%, black solid. δ = 8.08–8.06 (d, J = 6.0 Hz, 1H). 1H NMR (300 MHz, CDCl3, 25 °C): δ = 8.08–8.06 (d, J = 6.0 Hz, 1H) ppm. 13C NMR: δ = 162.9, 157.3, 129.8. C15H14N2Te2; calc. δ 162.9, 157.3, 129.8; found δ 162.9, 157.3, 129.8. MS-EI: m/e [M+H]+: 367.1, 280.2, (C15H13N2Te2), 132.5, C15H13N2Te2: calc. δ 367.1, 280.2, 132.5. Curiously, no attempt has been made to synthesize and characterize bis[4-chloro-2-pyrimidyl] ditelluride or bis[4-chloro-2-(aryltelluroyl)] pyrimidine compounds so, we wish to report herein a convenient method for preparation of hitherto unknown titled pyrimidyl chalcogen compounds.

2. Materials and methods

All experiments were carried out in air—oxygen free nitrogen atmosphere. Sodium borohydride (Loba, purity > 95%), elemental selenium (Hi-media, purity > 99%), elemental sulfur (Hi-media, purity > 98%), elemental tellurium (Hi-media, purity > 99.5%) and sodium borohydride (Loba, purity > 99.5%), elemental tellurium (Hi-media, purity > 99.5%) and arylthio (phenylthio, 2,4-dichloropyrimidine [38], diphenyl diselenide [31] and dipicolyl diselenide [31] were prepared by reported methods. IR spectra were recorded between 400–4000 cm⁻¹ using KBr pellets on a Perkin—Elmer Model 1430 ratio recording spectrometer. A variety of newly synthesized 6-phenylselenenyl acyclic pyrimidines [35,36] have recently been found to have potent antihuman immunodeficiency—virus-type-1 (HIV-1) activity. Bardos et al. [37] have synthesized successfully 5-selenium-substituted derivatives of uracil, 2/-deoxyuridine, and 2'-deoxyuridylic acid.

2.2. General procedure for synthesis of unsymmetrical pyrimidyl chalcogen compounds

To a solution of Ar₂E₂ (E = Se, Ar = phenyl, 1-naphthyl, p-tolyl, 4,6-dimethyl-2-pyrimidyl, 2-pyridyl, 4-methyl-2-pyridyl, E = S, Ar = phenyl, 5 mmol) in 50 ml of C₂H₅OH-DMF (3:2) was added NaN₃ (300 mmol) and ethanol (30 ml), sodium borohydride (1.85 g, 50 mmol) in 50 ml. The organic layer was then washed with water, dried (Na₂SO₄) and evaporated to leave the crude product; which was purified by column chromatography over silica gel (hexane—ethyl acetate) to furnish pure product.

2.2.1. 4-Chloro-2-(phenylselenyl) pyrimidine 1a

Yield: 68%, white solid. δ = 8.39–8.37 (d, J = 6.0 Hz, 1H). 1H NMR (300 MHz, CDCl₃, 25 °C): δ = 8.39–8.37 (d, J = 6.0 Hz, 1H), 7.64–7.82 (d, J = 6.0 Hz, 1H) ppm. 13C NMR: δ = 164.7, 160.0, 149.0, 118.0, C₈H₁₄N₂SeCl₂; calc. δ 163.6, 160.4, 149.0, 118.0. MS-EI: m/e (%): 318.6 ([C₁₀H₇N₂SeCl]+, 34.5), 231.8 (C₁₀H₆N₂SeCl, 27.6). IR (KBr): ν = 2924, 1539, 1400, 1330, 1192, 1071, 755, 727 cm⁻¹. "H NMR (300 MHz, CDCl₃, 25 °C): δ = 8.39–8.37 (d, J = 6.0 Hz, 1H), 7.64–7.82 (d, J = 6.0 Hz, 1H).
2.2.4. 2-(p-tolylenethyl)-4-chloropyrimidine 2d

Yield: 76%, light yellow crystalline solid. M.p. 75-78 °C. Rf (10% EtO) (hexane) 0.36. IR (KBr): v = 2924, 1542, 1449, 1401, 1324, 827, 670 cm⁻¹. 1H NMR (300 MHz, CDCl₃, 25 °C): δ = 8.27-8.22 (t, 1H), 8.03-7.99 (m, 2H), 7.73-7.68 (t, 2H), 7.62-7.44 (m, 3H), 7.30-7.25 (d, J = 15.0 Hz, 2H), 6.81-6.74 (d, J = 21.0 Hz, 1H), 2.45 (s, 3H) ppm. 13C NMR: δ = 176.0, 160.6, 157.1, 157.0, 157.1, 157.2, 157.4, 134.5, 134.4, 131.9, 128.9, 128.1, 127.7, 126.2, 124.3, 118.7. 77Se NMR: δ = 428 ppm. MS-EI: m/e (%): 271 ([C₂H₄N₂SeCl]⁺, 100), 236 ([C₂H₄N₂Cl]⁻, 10). C₆H₅N₂SeCl calcd. C 52.41, H 2.80, N 8.73; found C 52.71, H 2.89, N 8.45.

2.2.5. 4-Chloro-2-(naphthalen-2-ylselanyl) pyrimidine 2e

Yield: 57%, yellow crystalline solid. M.p. 130-132 °C. Rf (10% EtO) (hexane) 0.28. IR (KBr, cm⁻¹): 1676, 1573, 1221, 118.23, 23.86. C₆H₅N₂SeCl: calcd. C 52.89, H 2.89, N 8.45.

2.2.6. 2-(4-Methylpyrimidin-2-ylselanyl)-4-chloropyrimidine 2f

Yield: 47%, yellow crystalline solid. M.p. 55-57 °C. Rf (10% EtO) (hexane) 0.36. IR (KBr): v = 2924, 1542, 1449, 1401, 1323, 827, 670 cm⁻¹. 1H NMR (300 MHz, CDCl₃, 25 °C): δ = 8.36-8.34 (d, J = 6.0 Hz, 2H), 8.31-8.29 (d, J = 6.0 Hz, 2H), 6.79 (s, 1H), 2.39 (s, 6H) ppm. 13C NMR: δ = 167.6, 157.3, 122.13, 118.23, 23.86. C₆H₅N₂SeCl: calcd. C 39.93, H 2.49, N 8.37.

2.2.7. 4-Chloro-2-(pyridin-2-ylselanyl) pyrimidine 2g

Yield: 65%, yellow powder. M.p. 144-147 °C. Rf (10% EtO) (hexane) 0.24. IR (KBr): v = 1542, 1449, 1401, 1323, 827, 670 cm⁻¹. 1H NMR (300 MHz, CDCl₃, 25 °C): δ = 8.58-8.56 (d, J = 6.0 Hz, 1H), 8.17-8.15 (d, J = 6.0 Hz, 1H), 7.76-7.61 (m, 2H), 7.23-7.29 (d, J = 9.0 Hz, 1H), 7.27-7.24 (m, 1H) ppm. 13C NMR: δ = 157.3, 150.9, 137.5, 130.3, 120.4, 120.3. MS-EI: m/e (%): 271 ([C₂H₄N₂SeCl]⁺, 100), 236 ([C₂H₄N₂Cl]⁻, 10). C₆H₅N₂SeCl: calcd. C 39.85, H 2.21, N 15.49; found C 39.97, H 2.13, N 15.38.

2.3. X-ray crystallographic studies

Diffraction quality single crystals of 4-chloro-2-(phenylselanyl) pyrimidine (2b) and 2-(p-tolylenethyl)-4-chloropyrimidine (2d) were obtained by the slow evaporation of dichloromethane-hexane solution of the corresponding compounds. Colorless crystals of (2b) and light yellow crystals of (2d) were obtained. Suitable crystals were chosen from a crop of crystals and mounted on glass fibers and data sets were collected on Nonius MACH3 diffractometer for the cell determination and intensity data collection. The diffraction data were collected using monochromatic Mo Kα radiation at 293(2) K and 150 (2) K for (2b) and (2d) respectively. The details of crystal structure determination and refinement parameters for (2b) and (2d) are given in Table 3 and Table 4 respectively.

Crystal structure was solved by direct methods (SHELXS-97) [42] and refined by full matrix least squares method.

3. Results and discussion

The research on the synthesis of the pyrimidine and its analogues has been going on continuously in search of new biologically active molecules. It is anticipated that pyrimidyl chalcogen compounds may also display the redox activity like other selenium derivatives of aniline, pyridine and quinoline. As a result of our ongoing project, we have reported an efficient synthetic route to bis(4-dimethylamino-2-pyrimidyl) dichalcogenides [43] (1a–c) by exploring the reaction of dichalcogenide anion E₂⁻ in dimethylformamide as the solvent. In this case, chlorine atom at C-2 position of 2,4-dichloropyrimidine was substituted by the in situ generated E₂⁻ (E = Se, S, Te) anion. In addition, substitution at C-4 position by dimethylamino group is also facilitated by the dimethylformamide used as a solvent. Thus, it was considered of interest to use another solvent i.e. absolute ethanol instead of DMF that would lead to retention of the chlorine at the C-4 position of 2,4-dichloropyrimidine. The reaction scheme for the

![Scheme 1](image-url)
Step 1

2 NaBH₄ + 3E + 6C₂H₅OH ——> Na₂E₂ + H₂ + 2 B(OEt)₃ + 6H₂

Scheme 3. Mechanism for the synthesis of unsymmetrical chalcogen compounds.

synthesis of the titled compounds uses sodium borohydride to carry out not only the reduction of elemental chalcogens but also for the reductive cleavage of chalcogen—chalcogen bond in diaryl dichalcogen compounds.

In order to solubilize completely the starting dichalcogen compounds as well as its nucleophilic borane complex, [(ArE)₂Na] (OCH₂CH₂)₂, two volumes of DMF were added to three volumes of ethanol. Addition of DMF as a co-solvent improved the yield by solubilizing the diaryl chalcogenolate ion [44]. DMF being a highly polar solvent can be easily removed by simply washing with water. The entire scheme involving sodium borohydride as reducing agent was found effective for the synthesis of symmetrical and unsymmetrical pyrimidyl chalcogen compounds (1a—c, 2a—h) (Scheme 1). The mechanism involved in the reaction is represented by Scheme 2 and Scheme 3. The advantage of this methodology to synthesize unsymmetrical chalcogen compounds is the selective nucleophilic substitution of chlorine atom at C-2 position of 2,4-dichloropyrimidine by arylchalcogenide anion (ArE⁻) resulting in (Scheme 1). The mechanism involved in the reaction is represented by Scheme 2 and Scheme 3. The advantage of this methodology to synthesize unsymmetrical chalcogen compounds is the selective nucleophilic substitution of chlorine atom at C-2 position of 2,4-dichloropyrimidine by arylchalcogenide anion (ArE⁻) resulting in the formation of C(Pym)-E bond.

The bis[4-chloro-2-pyrimidyl] dichalcogen compounds (1a—c) and 4-chloro-2-(arylchalcogenyl) pyrimidine (2a—h) thus prepared are stable enough to be purified by column chromatography (silica gel using hexane—ethyl acetate). The compounds are soluble in conventional organic solvents and have a long shelf life without any sign of decomposition even at room temperature.

3.1 Spectroscopic studies

1H NMR characterization of bis[4-chloro-2-pyrimidyl] dichalcogen compounds (1a—c) shows that the proton at C-5 of bis[4-chloro-2-pyrimidyl] ditelluride (1c) is shifted up field due to greater shielding of protons by tellurium metal as compared to selenium metal in bis[4-chloro-2-pyrimidyl] diselenide (1b). The resonance signals of pyrimidine ring in all of the unsymmetrical selenides show an up field shift for H-5 protons relative to those of the corresponding bis[4-chloro-2-pyrimidyl] diselenide (1b). Nevertheless, the signals appear up field with respect to the protons of 2,4-dichloropyrimidine. 13C NMR spectra of bis[4-chloro-2-pyrimidyl] dichalcogen compounds (1a—c) display 13C signal of the pyrimidyl group in the range of 118.0—167.0 (δ, ppm). The carbon signal of 2-(p-tolylselanyl)-4-chloropyrimidine (2b) shows that the molecular ion peak is observed as base peak at m/z value 284 and 271 respectively. [M + 1] and [M — 1] peaks are observed for 4-chloro-2-(phenylselanyl) pyrimidine (2b). The fragment ions containing selenium show a highly characteristic and definite pattern of signal intensities depending on the natural abundance of various isotopes of selenium.

In IR spectra of these compounds, vibrations due to pyrimidyl and aryl groups can be easily identified. A strong and sharp band at 2900—2930 cm⁻¹ has been assigned to aromatic C—H stretching and is consistent with the values found for C—H stretching vibrations in aromatic compounds. [45,46] An intense band around 1500—1550 cm⁻¹ can be assigned to aromatic C=C stretching vibrations of the aryl rings, whereas a medium to sharp intensity band between 750 and 900 cm⁻¹ has been assigned to νCl deformation mode of aromatic ring. A comparison of νCl (where E = S, Se, Te) stretching bands in pyrimidyl chalcogenides reveals a regular trend in the variation of νCl absorption frequencies. In bis[4-chloro-2-pyrimidyl] dichalcogen compounds (1a—c) and 4-chloro-2-(arylchalcogenyl) pyrimidine (2a—h) a C—Cl band is observed near 620—700 cm⁻¹.

3.2 Solid-state structures: crystal structure determination of 4-chloro-2-(phenylselanyl) pyrimidine (2b) and 2-(p-tolylselanyl)-4-chloropyrimidine (2d)

To have an understanding of the structural details, single crystal X-ray diffraction of 4-chloro-2-(phenylselanyl) pyrimidine (2b) and 2-(p-tolylselanyl)-4-chloropyrimidine (2d) was carried out. A perspective view and atom numbering scheme of (2b) and (2d) are
given (Fig. 1 and Fig. 2 respectively). The important bond parameters for (2b) and (2d) are listed in Table 1 and Table 2 respectively.

The average C—C bond length in the pyrimidine ring in (2b) and (2d) is 1.304 Å and 1.329 Å respectively. The Se—C bond lengths in (2b) are [Se(1)—C(2), 1.904(4) Å], [Se(1)—C(5), 1.914(4) Å] and in (2d) are [Se(1)—C(2), 1.9157(19) Å] and [Se(1)—C(5), 1.9123(18) Å]. The average C—C bond length in phenyl ring in (2b) is 1.372 Å and in tolyl ring in (2d) is 1.390 Å. The observed bond angle C(2)—Se(1)—C(5) and C(2)—Se(1)—C(5) in (2b) and (2d) is 99.88(15) and 98.39(8) respectively. These bond angles indicate the distortion of sp3 carbon from its regular tetrahedral geometry and established the V' shaped geometry about C—Se—C bond. Interestingly, the compound 2-(p-tolylselanyl)-4-chloropyrimidine (2d) has shown hydrogen-bonding interactions between the nitrogen atom of pyrimidyl ring of one crystal unit and hydrogen atom of the other pyrimidyl ring of other crystal unit. However, the compound 4-chloro-2-(phenylselanyl) pyrimidine (2b) displayed N—H intermolecular interactions between nitrogen of pyrimidyl ring and hydrogen of the phenyl ring within the crystal lattice. Also in 4-chloro-2-(phenylselanyl) pyrimidine (2b), short contacts are observed between C-3 of the pyrimidine ring and H-4 of the pyrimidyl ring of the other molecule and another C—H interaction between C-4 of the pyrimidine ring and H-3 of the pyrimidyl ring of the other molecule which is marked from the measured C—H distances which are less than the vander Waals distance (2.90 Å).

Table 1: Selected bond parameters of (2b).

<table>
<thead>
<tr>
<th>Bond length (Å)</th>
<th>Bond angle (°)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Se(1)—C(2)</td>
<td>1.904(4)</td>
</tr>
<tr>
<td>N(1)—C(1)</td>
<td>1.325(5)</td>
</tr>
<tr>
<td>C(10)—Se(1)</td>
<td>1.382(5)</td>
</tr>
<tr>
<td>C(2)—Se(1)</td>
<td>1.390(6)</td>
</tr>
<tr>
<td>C(3)—N(2)—C(2)</td>
<td>117.4(3)</td>
</tr>
</tbody>
</table>

Fig. 2. (a) Diagram showing the conformation and atom numbering scheme (b) and the C—Cl and N—H interactions for 2-(p-tolylselanyl)-4-chloropyrimidine (2d).
4. Conclusion

The present report constitutes the first successful attempt to synthesize novel bis[4-chloro-2-pyrimidyl] dichalcogenide (S, Se, Te) and 4-chloro-2-[arylchalcogenyl] pyrimidine compounds by simple synthetic methodology. These compounds are anticipated to have potential applications in medicinal field.

Acknowledgment

KKB is thankful to DST, New Delhi for research grant (SR/S1/IC-37/2009) and UGC, New Delhi for financial support (37-320/2009, SR). We are thankful to Prof. P. Mathur, Indian Institute of Technology, Mumbai for carrying out X-ray crystallographic studies.

Appendix A. Supplementary material

CCDC 736021 and 736022 contain the supplementary crystallographic data for Compound 2b and 2d. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

References