Selenocarbonyl synthesis using Woollins reagent

Pravat Bhattacharyya and J. Derek Woollins*

School of Chemistry, University of St. Andrews, St. Andrews, Fife KY16 9ST, UK

Received 6 June 2001; accepted 21 June 2001

Abstract—[PhP(Se)(μ-Se)]₄ selenates secondary and tertiary amides to the corresponding selenoamides in 30–70% yields at 130°C in toluene and indolizine-3-aldehydes to selenoaldehydes in 40–59% yield at 25°C. © 2001 Published by Elsevier Science Ltd.

The utility of selenocarbonyl compounds as intermediates in heterocycle synthesis and increasing interest in the bioactivity of organoselenium compounds necessitates the development of new techniques for the introduction of selenium into organic molecules. One popular modus operandi is selenation, the exchange of a carbonyl oxygen atom for selenium.

In 1997 Hill and co-workers reported the use of ‘Woollins reagent’, obtained from (PhP)₅ and elemental selenium (P:Se ratio 1:2), for converting tungsten(V) and molybdenum(V) ketenyl complexes to their selenoketenyl counterparts, speculating upon the identity of Woollins reagent as 2,4-bis(phenyl)-1,3-diselenadiphosphetane-2,4-diselenide [PhP(Se)(μ-Se)]₂ 1. Our subsequent crystallographic analysis confirmed 1 to be isostructural with the thionation agent [(p-MeOC₆H₄)P(S)(μ-S)]₂ (Lawesson’s reagent). Although 1 has not received further attention as a selenation reagent, we have recently found this compound to be active towards a range of unsaturated organic substrates to give several unusual phosphorus containing heterocycles. We communicate here our usage of 1 for the selenation of amides and aldehydes.

Compound 1, available in 60–70% yield upon oxidation of (PhP)₅ with 10 equiv. of selenium, was heated together with 3 equiv. of amide in toluene at 130°C. The resulting orange solution was cooled to room temperature, the solvent was removed in vacuo and the selenoamide purified by column chromatography on silica (dichloromethane). Physical data for 1–VII were in accord with literature values. For the indolizine-3-aldehydes the reactions were performed at 25°C on a similar scale to the amides, the products VIII–X being purified by column chromatography on alumina (9:1 v/v toluene/diethyl ether).

Table 1. Selenation using 1a

<table>
<thead>
<tr>
<th>Product</th>
<th>Reaction time (h)</th>
<th>Isolated yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>1</td>
<td>72</td>
</tr>
<tr>
<td>II</td>
<td>2</td>
<td>70</td>
</tr>
<tr>
<td>III</td>
<td>7</td>
<td>30</td>
</tr>
<tr>
<td>IV</td>
<td>1</td>
<td>13</td>
</tr>
<tr>
<td>V</td>
<td>21</td>
<td>38</td>
</tr>
<tr>
<td>VI</td>
<td>2</td>
<td>44</td>
</tr>
<tr>
<td>VII</td>
<td>2</td>
<td>47</td>
</tr>
<tr>
<td>VIII</td>
<td>2</td>
<td>53</td>
</tr>
<tr>
<td>IX</td>
<td>2</td>
<td>59</td>
</tr>
<tr>
<td>X</td>
<td>2</td>
<td>40</td>
</tr>
</tbody>
</table>

*a Reactions were conducted under dinitrogen, subsequent operations were performed in air. For I–VII, a mixture of 1 (0.2 mmol) and the substrate (0.6 mmol) in anhydrous toluene (2 cm³) was heated at 130°C. The resulting orange solution was cooled to room temperature, the solvent was removed in vacuo and the selenoamide purified by column chromatography on silica (dichloromethane). Physical data for I–VII were in accord with literature values. For the indolizine-3-aldehydes the reactions were performed at 25°C on a similar scale to the amides, the products VIII–X being purified by column chromatography on alumina (9:1 v/v toluene/diethyl ether).
precipitation of minor quantities of selenium; while I is appreciably more soluble in pyridine than toluene at elevated temperatures, no enhancements in yield are noted when this solvent is used. Chromatographic purification of I–VII (Fig. 2) on silica removed all phosphorus(V) by-products, characterisation being performed using $^1$H and $^{13}$C($^1$H) NMR, IR and mass spectroscopies. The 72% yield of PhC(Se)NMe$_2$ from PhC(O)NMe$_2$ compares favourably with the selenation of 3-CH$_3$C$_6$H$_4$C(O)NEt$_2$ by PhP(Se)Cl$_2$ (61% yield after 5 h at 90°C) and the 50% yield after 220 h at 90°C using (RP)$_2$Se. ($R_2=2,4’$-Bu$_2$(6-OMe)C$_6$H$_2$)$_2$.

Notably only a 38% yield of PhC(Se)NMe$_2$ using I is obtained after 1 h when selenation is carried out in pyridine. Secondary amides are readily converted to selenoamides by I; in our hands neither PhC(O)NHMe nor $\varepsilon$-caprolactam were selenated satisfactorily using PhP(Se)Cl$_2$, transformations which I effects in 70 and 44% yields, respectively. The slow conversion for PhC(O)NH$\cdot$Bu reflects retardation due to the bulky Bu substituent. Tetramethoxamidate is converted to the selenoxamidate Me$_2$NC(Se)C(O)NMe$_2$ in 38% yield after 21 h, with minor quantities (typically 2–3%) of the diselenoxamidate formed. While $N,N’$-diethyliurea is converted to (EtNH)$_2$CSe in moderate yield, $N,N’$-diphenylurea does not give (PhNH)$_2$CSe but an (as yet) uncharacterised phosphorus compound ($\delta_p$ 47.0, $J_{PSe}$ 853 Hz). I also converts indolizine-3-aldehydes to the selenoaldehydes VIII–X at 25°C in yields of 40–59% after 2 h, cf. 62–81% after 10 min at room temperature using PhP(Se)Cl$_2$. Benzamide is reluctant to undergo selenation using I, yields of PhC(Se)NH$_2$ struggle to reach double figures; we are unable to convert nicotinamide to pyC(Se)NH$_2$ under any conditions.

The stability (shelf life of several months in air, indefinitely under nitrogen), ease of preparation and handling of I contrasts markedly with reagents such as NaHSe, H$_2$Se, (Bu$_3$Al)$_2$Se, (Me$_3$Si)$_2$Se and bis(1,5-cyclooctadienyli)borselenide, which are either air/moisture sensitive or require fresh preparation prior to use. Additionally, substrates containing NH groups can be satisfactorily selenated by I, which does not appear to be the situation for PhP(Se)Cl$_2$. Facile purification of the selenocarboxyls allied to its moderate tolerance towards amine protons makes I stand out as a selenating reagent of great promise. We are currently investigating the latitude of the reactivity of Woollins reagent towards a range of carbonyl containing substrates.

**Acknowledgements**

We are grateful to the EPSRC (P.B.) for funding.

**References**

17. Selected data for Me2NC(O)C(Se)NMe2: \(\delta_H (\text{CDCl}_3, 300.0 \text{ MHz}) : 3.45 (s, 3\text{H}), 3.15 (s, 3\text{H}), 3.00 (s, 3\text{H}), 2.95 (s, 3\text{H}). \delta_C (75.3 \text{ MHz}) : 197.9 (C=Se), 168.0 (C=O), 44.0, 43.7, 37.9, 34.6 (CH3). \) Found (calcd for C18H12N2OSe): C 35.8 (34.8), H 6.0 (5.8), N 13.4 (13.5)\%. EI: \(m/z\) 207, \(M^+\).