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Tetraselenotungstate: an efficient selenating reagent for the synthesis of β-amino diselenides by aziridine ring opening reactions

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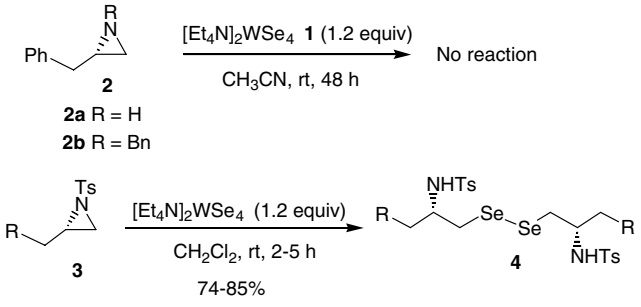
Abstract—Tetraselenotungstate **1** has been shown to be a versatile selenating reagent and has been used successfully for the regio- and stereospecific ring opening of aziridines to afford a number of interesting β-amino diselenides in good yields in a single step under mild reaction conditions without using any Lewis acid.

Following the discovery of seleno-enzymes, selenium-containing compounds have been studied extensively because of their interesting reactivity profile[1] and potential pharmaceutical significance.[2] Although several methods are available for the synthesis of organo-selenium compounds,[3] there still exist challenges to develop new versatile selenating reagents which can perform regio- and stereocontrolled selenium transfer reactions efficiently in a single step. These challenges arise partly because of the relative instability of existing selenating reagents at room temperature. Additionally, conventional selenating reagents generally yield monoselenides and triselenides as by-products.[1] Recently Braga et al. reported the synthesis of β-amino diselenides from aziridines using Li_2Se_2 as a selenating reagent.[4] Importantly, chiral diselenides have been employed as useful ligands and as catalysts in various asymmetric transformations such as diethylzinc addition to aldehydes,[5] asymmetric hydrosilylation,[6] and 1,4-addition of Grignard reagents to enones.[7] Having demonstrated earlier in our laboratory the use of benzyltriethylammonium tetrathiomolybdate as an efficient sulphur transfer reagent in aziridine ring opening reactions,[8] it was of interest to study the reactivity of tetraethylammonium tetraselenotungstate,[9] $[Et_4N]_2WSe_4$ **1** as a selenium transfer reagent in aziridine ring opening reactions. In this letter, we report the results of regio- and stereospecific nucleophilic[10] ring opening of aziridines with **1** to afford a number of β-amino diselenides[4] in good yields.

We began our investigation with a study of the reaction of optically pure non-activated aziridines[11] **2** with **1** (1.2 equiv, CH_3CN, 28 °C, 48 h), but no ring opening took place even under reflux conditions. The aziridine **2a** was then converted into *N*-tosyl aziridines[11c] **3** which on treatment with **1** (1.2 equiv, CH_2Cl_2, 28 °C, 2–5 h) underwent smooth ring opening in a regiospecific manner without using any external Lewis acid to afford β-amino diselenides[10] **4** in very good yields without loss of optical activity[12] (Scheme 1). It can be seen from Table 1 that this methodology is general and that all



Scheme 1. Regiospecific ring opening of mono-substituted aziridines **3**.

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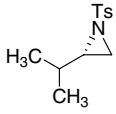
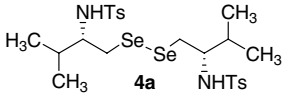
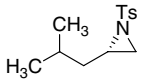
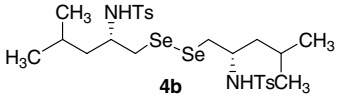
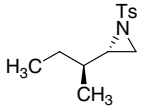
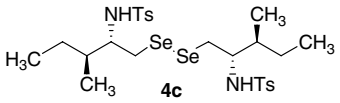
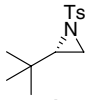
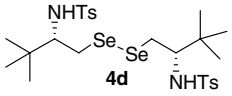
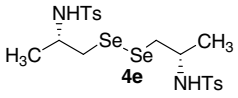
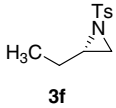
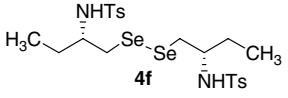
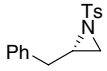
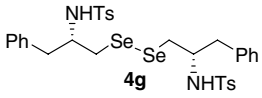
Table 1. Synthesis of enantiopure β-aminodiselenides

Entry	Aziridine	Enantiopure β-aminodiselenide	Time (h)	Yield (%)
1	 **3a**	 **4a**	4	82
2	 **3b**	 **4b**	4	80
3	 **3c**	 **4c**	3	84
4	 **3d**	 **4d**	5	80
5	 **3e**	 **4e**	2	74
6	 **3f**	 **4f**	2	78
7	 **3g**	 **4g**	2	85

the reactions proceeded smoothly under mild reaction conditions to afford the desired β-amino diselenides in good yields. The structure of compound **4c**[13] was confirmed by single crystal X-ray analysis (Fig. 1).

Having successfully demonstrated the ring opening of mono-substituted aziridines **3** with **1**, the stage was set to test the stereospecificity in the ring opening of 2,3-disubstituted aziridines **5** with **1**. Accordingly *meso*-*N*-tosyl-2,3-diethylaziridine **5a**[14] was treated with **1** (1.2 equiv, CH_3CN, 28 °C, 10 h) to afford, exclusively, the *anti*-β-aminodiselenide **6a** in 76% yield. In the case of (±)-*trans*-*N*-tosyl-2,3-diethylaziridine **5b**,[14] *syn*-β-aminodiselenide **6b** was obtained in 80% yield under the same reaction conditions (Scheme 2 and Table 2).

In order to assess the regio- and stereospecificities of aziridine ring opening, (±)-*cis*-*N*-tosyl-1-isopropyl-2-methylaziridine[15] **5c** was treated with **1** (1.2 equiv, CH_3CN, 28 °C, 12 h) to afford exclusively the *anti*-β-aminodiselenide **6c** in 72% yield. Similarly, in the case of (±)-*trans*-*N*-tosyl-1-isopropyl-2-methylaziridine[15] **5d**, the *syn*-β-aminodiselenide **6d** was obtained in 80% yield under the given reaction conditions (Table 2). It is reasonable to visualize the nucleophilic attack of reagent **1** on the aziridine **5** from the less hindered side in a regio- and stereospecific manner followed by opening of a second aziridine ring to form an intermediate **X**. The intermediate **X** can then undergo an internal redox process[16] to form the β-aminodiselenides **6** (Scheme 2).

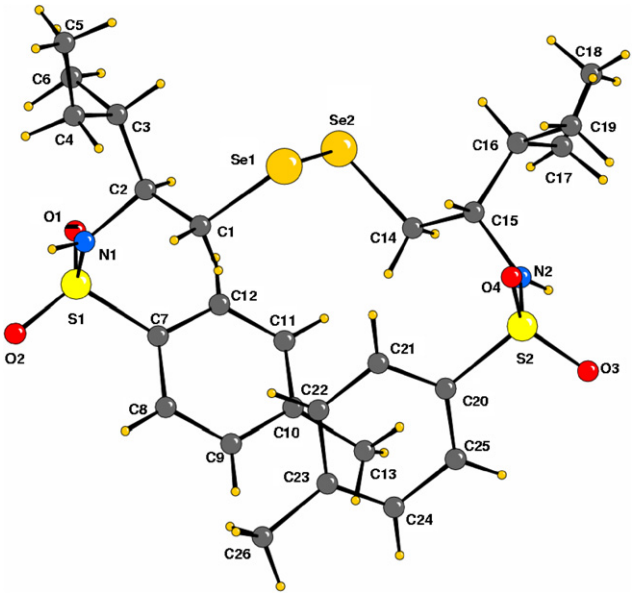
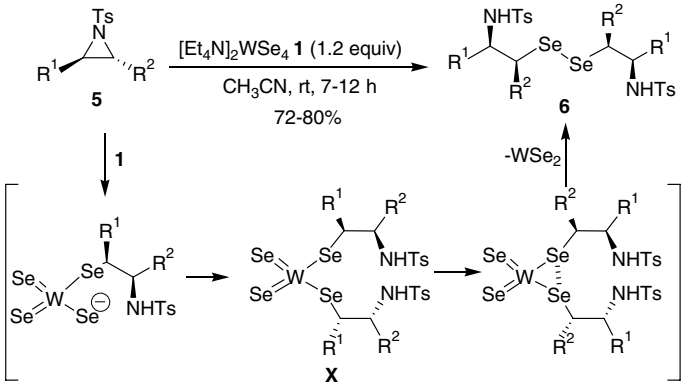
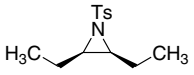
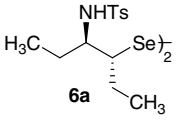
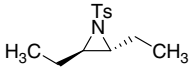
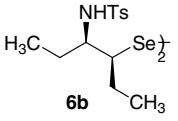
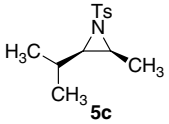
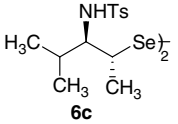
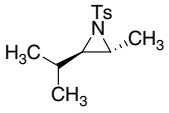
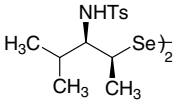


Figure 1. X-ray CAMERON molecular structure of compound **4c.**



Scheme 2. Tentative mechanism for regio- and stereospecific ring opening of aziridines.

Table 2. Synthesis of substituted β-aminodiselenides

Entry	2,3-Disubstituted aziridine	β-Aminodiselenide	Time (h)	Yield (%)
1	 **5a**	 **6a**	10	76
2	 **5b**	 **6b**	8	80
3	 **5c**	 **6c**	12	72
4	 **5d**	 **6d**	7	80

In conclusion, we have demonstrated that tetraethylammonium tetraselenotungstate **1** is an efficient selenium transfer reagent in aziridine ring opening reactions which lead to the synthesis of chirally pure β-aminodiselenides in very good yields without using any Lewis acid or base under neutral and mild reaction conditions. The chiral β-aminodiselenides thus formed will be studied for their efficiency as chiral ligands in diethylzinc addition to aldehydes.

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12. *General procedure for aziridine ring opening with* **1**: To a stirred solution of aziridine **3g** (0.144 g, 0.5 mmol) in CH_2Cl_2 (3 mL), tetraethylammonium tetraselenotungstate **1** (0.455 g, 0.60 mmol) was added at room temperature (28 °C). After completion of the reaction (TLC, 2 h) the solvent was removed in vacuo and the black residue was extracted with CH_2Cl_2–Et_2O (1:4, 5 × 20 mL) and filtered through a Celite pad. The filtrate was concentrated and the crude product was purified by flash column chromatography on silica gel (230-400 mesh, eluting with hexane:ethyl acetate 9:1) to obtain the β-aminodiselenide **4g** as a yellow oil.
Compound **4g**: $R_f = 0.65$ (EtOAc/hexanes, 3:7); Yield: 0.156 g, 85%; $[\alpha]_D^{27}$ −75.22 (*c* 4.6, CH_2Cl_2); IR (neat): 3280, 1333, 1157, 1090, 1035, 814, 667 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 7.61 (d, $J = 8.1$ Hz, 4H), 7.19–7.16 (m, 10H), 6.98–6.95 (m, 4H), 5.13 (d, $J = 7.5$ Hz, 2H), 3.74–3.65 (m, 2H), 3.23 (dd, $J = 12.6$, 4.8 Hz, 2H), 3.01 (dd, $J = 12.6$, 6.6 Hz, 2H), 2.87 (dd, $J = 14.0$, 6.3, 2H), 2.70 (dd, $J = 14.0$, 6.9 Hz, 2H), 2.39 (s, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 143.2, 137.0, 136.4, 129.6, 129.3, 128.6, 126.9, 126.7, 55.4, 39.9, 35.5, 21.5; ^{77}Se NMR (76 MHz, $CDCl_3$): 283.2; HR-ESMS *m*/*z*: Calcd for $C_{32}H_{36}N_2O_4S_2Se_2[M^+ + Na]$: 759.0345. Found: 759.0375.
Compound **6c**: $R_f = 0.60$ (EtOAc/hexanes, 3:7); Yield: 0.120 g, 72%; mp: 121 °C; IR (neat): 3276, 1330, 1160, 816, 670 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, 1:1 mixture of diastereomers): δ 7.78 (d, $J = 8.4$ Hz, 4H), 7.28 (d, $J = 8.4$ Hz, 4H), 5.09 (d, $J = 9.0$ Hz, 1H), 4.85 (d, $J = 9.3$ Hz, 1H), 3.49–3.39 (m, 2H), 3.24–3.17 (m, 2H), 2.41 (s, 6H), 1.94–1.85 (m, 2H), 1.44 (d, $J = 7.2$ Hz, 3H), 1.32 (d, $J = 6.9$ Hz, 1H), 0.84–0.71 (m, 12H); ^{13}C NMR (75 MHz, $CDCl_3$, 1:1 mixture of diastereomers): δ 143.2, 143.1, 137.8, 137.7, 129.5, 129.4, 127.1, 127.0, 65.0, 64.9, 43.8, 31.6, 31.3, 21.5, 21.0, 20.9, 20.8, 19.0, 18.9; ^{77}Se NMR (76 MHz, $CDCl_3$): 284.2; HR-ESMS *m*/*z*: calcd for $C_{26}H_{40}N_2O_4S_2Se_2[M^+ + Na]$: 691.0658. Found: 691.0680.
13. *Crystal data for compound* **4c.** The structure was solved by direct methods (SIR92). Refinement was by full-matrix least-squares procedures on *F*2 by using SHELXL-97. Crystal system: Orthorhombic, space group: $P2_12_12_1$, cell parameters: $a = 13.041(3)$, $b = 14.234(3)$, $c = 18.824(4)$ Å, $\alpha = 90.00$, $\beta = 90.00$, $\gamma = 90.00°$, $V = 3494.32$ Å^3, $Z = 4$, $\rho_{calcd} = 1.27$ g cm^{-3}, $F(000) = 1368$, $\mu = 2.26$ mm^{-1}, $\lambda = 0.71073$ Å. Total number l.s. parameters = 331. $R1 = 0.058$ for 6156 $F_0 > 4\sigma(F_0)$ and 0.095 for all 25,458 data. $wR2 = 0.121$, GOF = 0.984, restrained GOF = 0.984 for all data. (CCDC 610612). Crystallographic data (excluding structure factors) for the structure in this letter have been deposited with the Cambridge Crystallographic Data Centre as a supplementary publication. Copies of these data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk or via www.ccdc.cam.ac.uk/conts/retrieving.html.
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