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Tetraethylammonium Tetraselenotungstate: A Versatile Selenium Transfer Reagent in Organic Synthesis

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Abstract: Organoselenium compounds have attracted intense research owing to their unique biological properties as well as pharmaceutical significance. Progress has been made in developing reagents for incorporation of selenium in an efficient and controlled manner. Herein, we present a review on the recently developed selenium reagent, tetraethylammonium tetraselenotungstate, $[Et_4N]_2WSe_4$ as a versatile selenium transfer reagent in organic synthesis. Tetraselenotungstate has been successfully used for the synthesis of a number of functionalized diselenides, sugar- and nucleoside-derived diselenides, seleno-cystines, selenohomocystines, selenoamides, selenoureas and sugar- and nucleoside-based cyclic-selenide derivatives. Additionally, this reagent has been employed for the ring opening of aziridines to synthesize a variety of β-aminodiselenides. A new selena-aza-Payne type rearrangement of aziridinemethanoltosylates mediated by tetraselenotungstate for the synthesis of allyl amines is also discussed.

Keywords: Aziridines · Diselenides · Selena-aza-Payne and cyclic-diselenides · Selenium · Selenium-transfer reagent · Seleno-cystines · Selenohomocystine · Sugar diselenides · Tetraselenotungstate

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1. Introduction

Selenium was discovered by Berzelius in 1817 and is considered as an essential micro-mineral necessary for cellular function in mammals but toxic at higher levels. The first organo-selenium compound, diethyl selenide, was prepared by Lowig in 1836. In the past decades, organoselenium chemistry has made significant progress starting from the synthesis of simple selenols, selenides and diselenides to the development of organoselenium compounds having therapeutic potential.

Following the discovery of seleno-enzymes, selenium-containing compounds have been studied extensively in recent years because of their interesting reactivity profile,[1] anti-oxidant properties, as enzyme inhibitors, antitumor, anti-infective agents and also for their potential pharmaceutical significance (Fig. 1).[2] Much of the biological activity of selenium is associated with its incorporation into the seleno-cysteine residue of enzymes such as glycine reductase, formatedehydrogenase, hydrogenase, glutathione peroxidase, tetraiodothreonine 5-deiodinase and plasma proteins.[3] Recently, it has been reported that by incorporation of selenium into peptides, it is possible to study the conformational folding preferences of peptides and proteins. Despite the importance of the selenium analogues of amino acids, there are very few synthetic methodologies available for the synthesis of selenium compounds due to difficulties in purification, and relative instability. For example, the synthesis of amino acid, selenocysteine, is difficult because it readily oxidizes to form the diselenide, selenocystine, in the presence of air.

Diselenides are important motifs in selenocystine containing proteins, enzymes and are very good chiral ligands. The most frequently used method for the preparation of organic diselenides is the reaction of alkali metal diselenides with various electrophiles.[4] Generally the metal dis-

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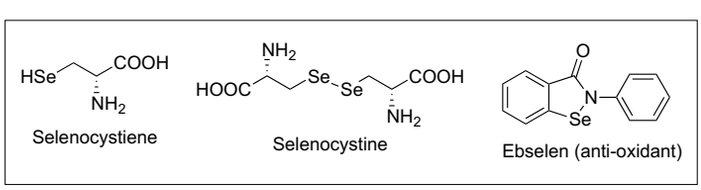
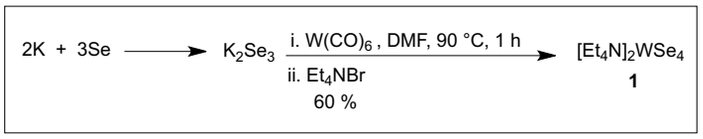
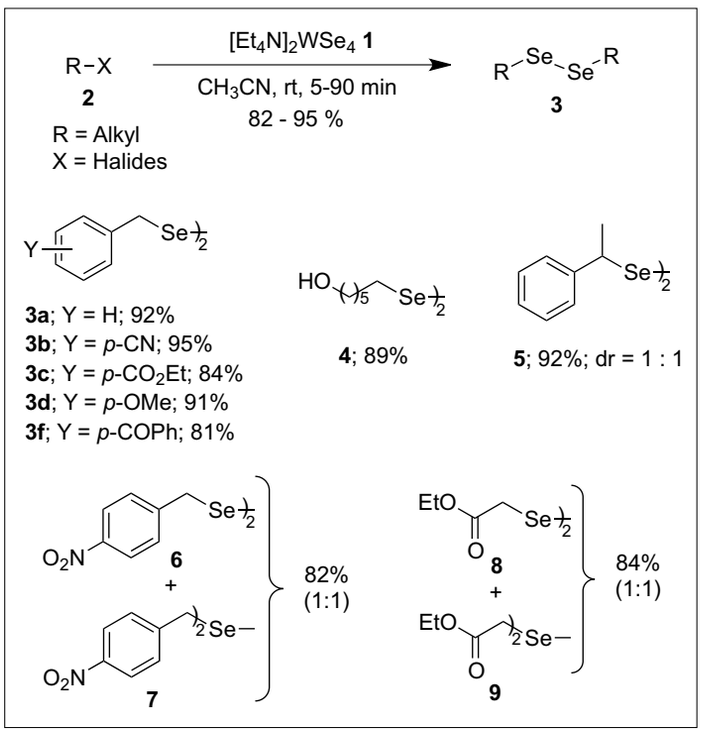


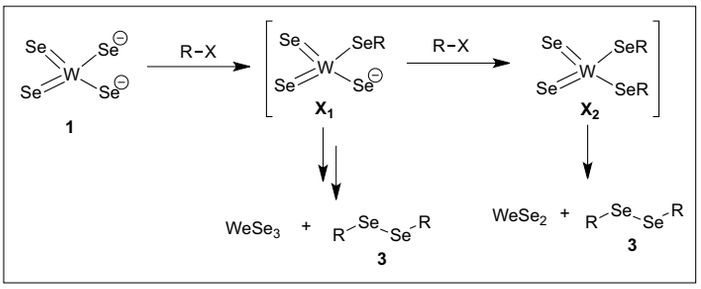
Fig. 1. Biologically active selenium-containing molecules.



Scheme 1. Synthesis of tetraethylammonium tetraselenotungstate (**1**).



Scheme 2. Reaction of tetraselenotungstate **1** with alkyl halides.



Scheme 3. Tentative mechanism of **1** with alkyl halides.

elenides are prepared under strongly basic conditions or using reducing agents such as $NaBH_4$ and $LiEt_3BH$, which are often incompatible with many functional groups. Another drawback is the formation of monoselenides and triselenides as byproducts, which are often very difficult to purify. Furthermore, such procedures require refluxing conditions for the formation of diselenides.

Although several methods are available for the synthesis of organo-selenium compounds,[5] there still exist challenges to develop new versatile selenating reagents, which can perform regio-, and stereo controlled selenium transfer reactions efficiently in a single step. These challenges arise partly because of the relative instability of existing selenating reagents at ambient conditions. Development of practically useful and efficient new selenating reagents is still necessary. Therefore, we have been involved in the development of new selenating reagents in organic synthesis for the last few years. Müller and coworkers first reported tetraselenotungstate in 1981,[6] and since then there have been no comprehensive studies on the use of this selenating reagent. In this review we focus on our work on tetraethylammonium tetraselenotungstate, $[Et_4N]_2WSe_4$ (**1**),[7] and its applications in organic synthesis.

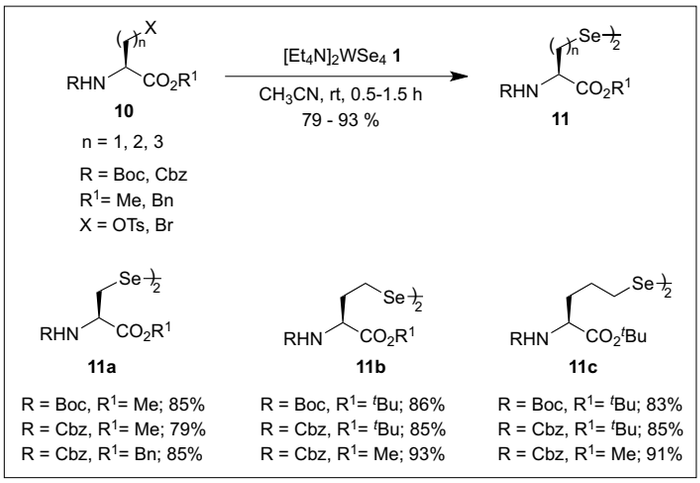
2. Synthesis of Tetraethylammonium Tetraselenotungstate, $[Et_4N]_2WSe_4$

Tetraselenotungstate **1** is prepared by a slight modification of the original procedure reported by Kollis and O'Neal[8] by treatment of K_2Se_3 with $W(CO)_6$ in dry DMF at 90 ºC for 1 hr followed by the addition of Et_4NBr (exchange of potassium counter cation with tetraethylammonium cation makes the reagent more soluble in organic solvents). After filtration, THF is slowly added and the reaction mixture is stored at 4 ºC overnight. This furnishes tetraethylammonium tetraselenotungstate, $[Et_4N]_2WSe_4$ (**1**) as a red crystalline solid in 60% yield (Scheme 1).The reagent can be stored under argon atmosphere for a few months; however it decomposes to the corresponding oxometallic species upon prolonged exposure to air.

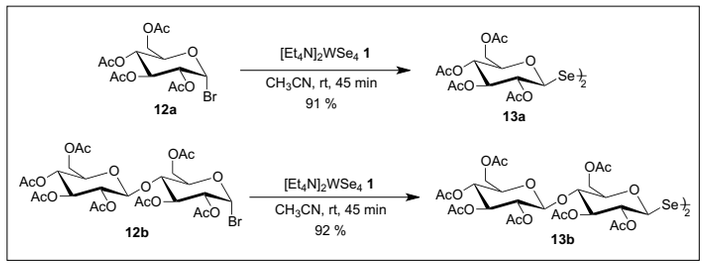
3. Synthesis of Simple Diselenides

Tetraselenotungstate **1** is a highly reactive and soft nucleophile that can transfer selenium to a variety of organic compounds. The study of its chemistry began with the nucleophilic displacement of alkyl halides in an S_N2 fashion to offer alkyl diselenides in a highly pure form. Simple benzyl bromides and its derivatives were easily (5–15 min) converted to the corresponding diselenides using **1** in CH_3CN at ambient temperature (Scheme 2).[9] Generally, the reaction is clean and a simple filter column yields diselenides of high purity and chemical yields (81–95%). Tetraselenotungstate **1**, reacts with the alkyl halides to form the corresponding diselenides chemoselectively without interfering with the easily reducible functional groups such as cyano, ester and keto functionalities. Thus, this reagent has a definite advantage over other procedures involving the use of metal diselenides and reducing agents, which cannot be utilized in some of these cases. Simple long-chain hydroxy alkyl bromides show low reactivity with **1** as compared to benzyl bromides towards the formation of alkyl diselenides. Secondary benzylic bromides are easily transformed into the corresponding diselenides as a diastereomeric mixture. In the case of highly reactive bromides like 4-nitrobenzyl bromide and ethyl bromoacetate, reaction of **1** furnished a mixture of mono- and diselenides in 1 : 1 ratio in reasonable yields without affecting the nitro and ester functionalities (Scheme 2).

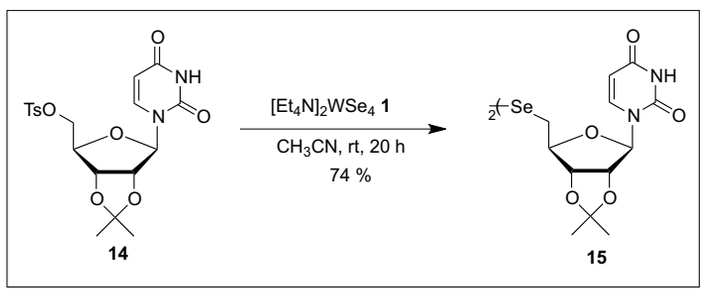
Although reaction of **1** with alkyl halides seems to follow the bimolecular S_N2 substitution pathway, the mechanism of alkylation of selenometallates of this kind has not been completely studied and fully understood. Since reactivity of tetraselenotungstate **1** is similar to tetrathiotungstate, $(WS_4)^{2-}$, a plausible mechanism based on the analogous reaction of tetrathiotungstate with alkyl halides is presented in Scheme 3. In the first step, tetraselenotungstate **1** reacts with alkyl halides by alkylation of selenium to form monoalkylated intermediate $\mathbf{X}_1$ and subsequently the second selenium alkylation forms dialkylated intermediate $\mathbf{X}_2$. The intermediates $\mathbf{X}_1$ and $\mathbf{X}_2$ can undergo induced internal redox reaction with the oxidation of the selenium ligand and concomitant reduction of the metal center to form diselenide **3** along with a mixture of selenotungstates, which could not be purified and characterized.[9]



Scheme 4. Synthesis of selenium-containing amino acid derivatives.



Scheme 5. Synthesis of carbohydrate-derived diselenides from anomeric bromides.



Scheme 6. Synthesis of uridine-derived diselenide **15**.

4. Synthesis of Selenium-containing Amino Acid Derivatives

Selenium-containing amino acids such as selenocystine, selenohomocystine and selenocysteine play a vital role in biology. For example, selenocystine has been used in protein ligation to incorporate selenocysteine in the active site of metalloproteins.[10] A few reports available in the literature for the direct synthesis of selenocystine and selenohomocystine give poor to moderate yields.[11] Using tetraselenotungstate **1** as a selenium transfer reagent, direct synthesis of selenocystine **11a**, selenohomocystine **11b** and selenobishomocystine **11c** derivatives have been achieved starting from the corresponding amino acid derivatives **10** (Scheme 4).[12] This methodology is very useful for the synthesis of selenoamino acid derivatives in small quantities with good chemical yield. In addition, the methodology is highly chemoselective and is compatible with different protecting groups in the molecule.

5. Synthesis of Glycosyl Diselenides

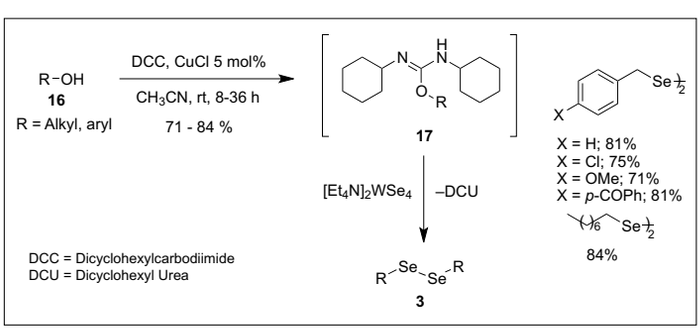
Selenium-containing glycosides are potent antiviral and antitumor compounds in chemical biology. Additionally, selenoglycosides have been used as efficient glycosyl donors in a variety of oligosaccharide synthesis in carbohydrate chemistry. Tetraselenotungstate **1** was successfully utilized for the synthesis of carbohydrate-derived diselenides from the corresponding anomeric bromides. The selenium transfer reaction of **1** with glucose and lactose derived anomeric bromides **12a** and **12b** was efficiently used for the synthesis of β-anomeric diselenides **13a** and **13b** respectively in high chemical yield as shown in Scheme 5.[9]

6. Synthesis of Diselenide Derivatives of Nucleosides

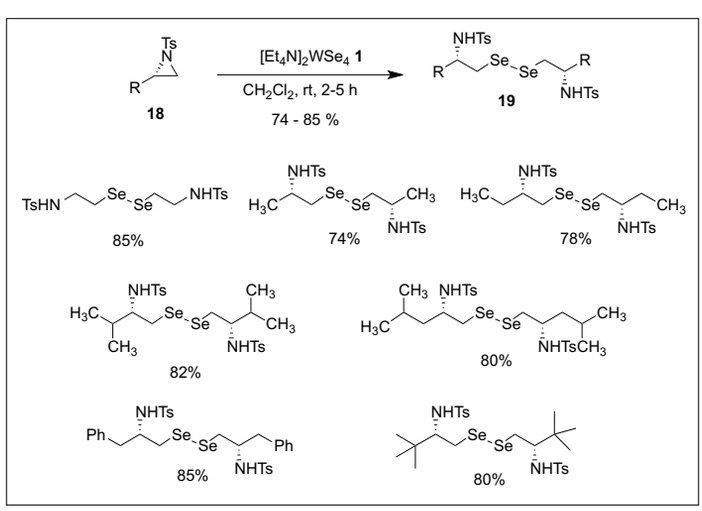
Utilizing **1** as the key reagent, selenonucleoside derivatives can be synthesized from the corresponding nucleoside tosylates as starting materials. The uridine-derived tosylate **14** was subjected to selenium transfer reaction with **1** (1.1 equiv., CH_3CN, rt, 20 h) to furnish the corresponding uridine derived diselenide **15** in 74% yield (Scheme 6).[13] Interestingly, in the case of acetyl-protected thymidine-derived tosylate, an unusual intramolecular reaction with **1** was observed yielding a cyclic diselenide as the only product. This reaction is discussed in detail later in the section on cyclic diselenides.

7. Direct One-pot Conversion of Alcohol to Diselenides

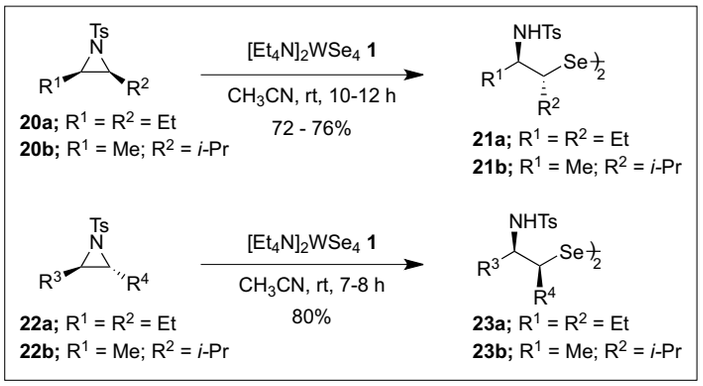
Direct conversion of alcohols to diselenides is an interesting functional group transformation and would lead to environ-



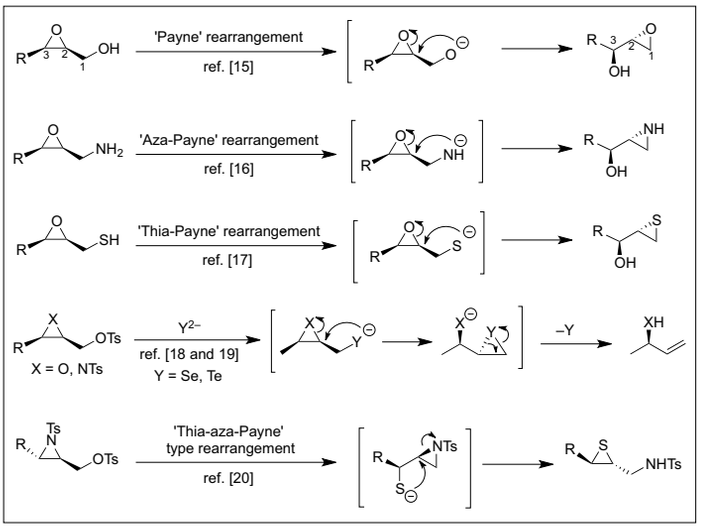
Scheme 7. Direct transformation of alcohols to diselenides using tetraselenotungstate **1**.



Scheme 8. Regiospecific ring opening of mono-substituted aziridines by **1**.



Scheme 9. Regio and stereospecific ring opening of disubstituted aziridines with **1**.



Scheme 10. Different types of Payne rearrangements.

mentally benign methodology in terms of minimal number of steps and waste generated during the reaction. In order to perform the direct transformation, alcohols were activated first using dicyclohexylcarbodiimide and a catalytic amount of CuCl to form activated isourea intermediate **17** *in situ,* which upon reaction with tetraselenotungstate **1** in CH_3CN at room temperature furnished the required diselenides **3** in good yields under mild and neutral reaction conditions (Scheme 7).[9]

8. Aziridine Ring-opening Reactions

Aziridines are very good electrophiles and reactivity of aziridines can be tuned by varying different substituents on the nitrogen atom.[14] For example, simple *N*-alkyl-substituted aziridines are poor electrophiles whereas incorporation of electron-withdrawing groups like Ns, Ts, and acyl make them very reactive electrophiles. Aziridines can be used as substrates for ring-opening reactions with **1**. Simple non-activated aziridines like *N*-alkyl substituted aziridines failed to undergo aziridine ring-opening reactions with **1**. However, activated *N*-tosyl aziridines are good substrates and they underwent smooth ring opening in the presence of **1** without use of any external Lewis acid catalyst. Utilizing this methodology, a number of chirally pure β-amino diselenides were synthesized starting from the corresponding chirally pure mono-substituted *N*-tosyl aziridines using **1** as a selenium transfer reagent. In all cases, regiospecific ring opening took place at the less substituted carbon to furnish chirally pure β-amino diselenides in good yields (Scheme 8).[14b]

Further, this methodology was extended to stereospecific ring-opening reactions of 2,3-disubstituted aziridines. When *meso-N*-tosyl-2,3-diethylaziridine (**20a**) was subjected to ring opening with **1** (1.2 equiv.; CH_3CN, 28 ºC, 10 h) the *anti*-β-aminodiselenide **21a** was obtained in 76% yield. In the case of (±)-*trans-N*-tosyl-2,3-diethylaziridine (**22a**), *syn*-β-aminodiselenide **23a** was obtained exclusively in 80% yield under the same reaction conditions (Scheme 9).

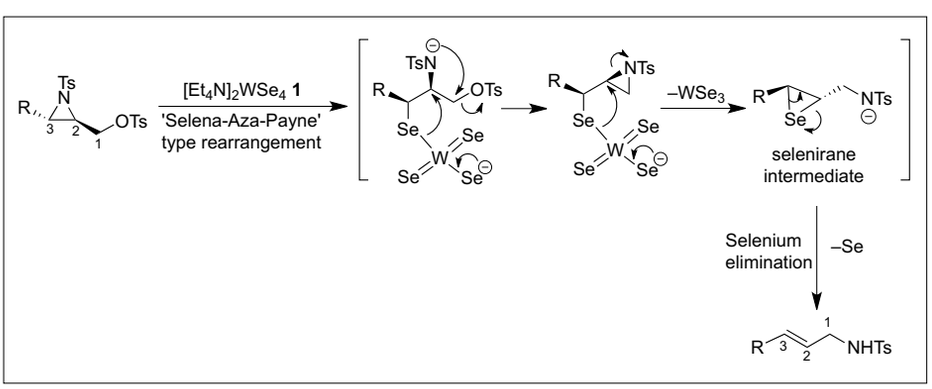
Additionally, regio- and stereospecific ring opening of (±)-*cis-N*-tosyl-1-isopropyl-2-methylaziridine (**20b**) with **1** was reported with the formation of *anti*-β-aminodiselenide **21b** exclusively in good yield. Similarly, in the case of (±)-*trans-N*-tosyl-1-isopropyl-2-methylaziridine (**22b**), the *syn*-β-aminodiselenide **23b** was obtained under similar reaction conditions (Scheme 9). This method provides easy access to a number of β-aminodiselenides in an efficient manner starting from substituted aziridines.[14b]

9. Selena-Aza-Payne-type Rearrangement

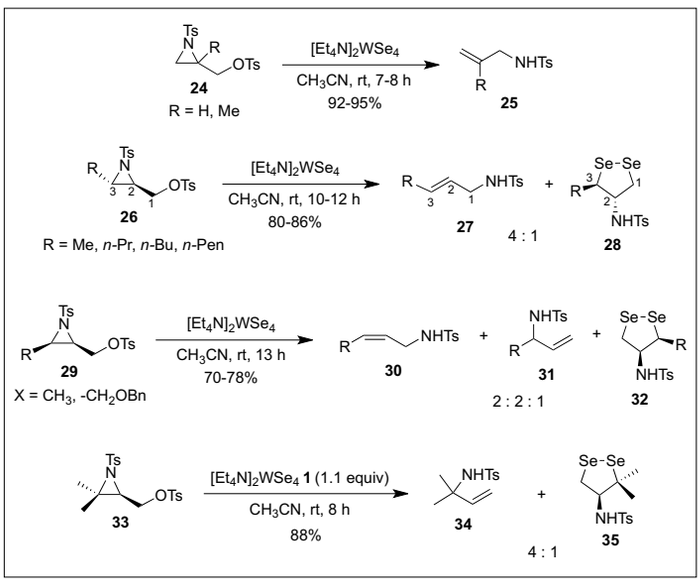
Intramolecular nucleophilic (S_N2) displacement of aziridines/epoxides with oxygen (Payne rearrangement),[15] nitrogen (aza-Payne),[16] sulfur (thia-Payne),[17] selenium[18] and tellurium[19] nucleophiles in the presence of a base is well studied in the literature (Scheme 10). Recently, tetrathiomolybdate mediated thia-aza-Payne-type rearrangement of *N*-tosyl aziridinemethanoltosylates has been reported.[20] During this rearrangement different *N*-tosylaziridinemethanoltosylates were transformed to the corresponding thiirane derivatives.

In a similar fashion, an unusual rearrangement of *N*-tosylaziridinemethanol tosylates was observed with tetraselenotungstate **1**. In this selena-aza-Payne type rearrangement, *N*-tosylaziridinemethanol tosylates were converted to allyl amine derivatives with excellent regio- and stereo control as depicted in Scheme 11.[21] During the rearrangement, the selenirane intermediate underwent spontaneous selenium elimination to yield allyl amine derivatives.

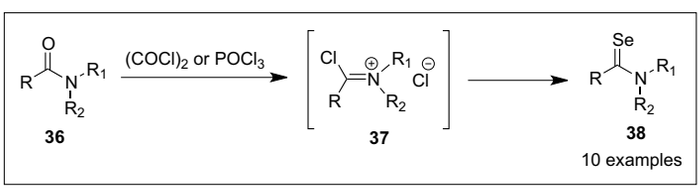
The overall outcome of this rearrangement is nitrogen migration from C(2), C(3) to C(1) carbon to form allyl amine derivatives *via* the formation of selenirane intermediate. This rearrangement is totally different from the well-studied Payne, aza-Payne and thia-Payne and telluride mediated rearrangements reported in the literature so far. In all the previously reported cases, leaving groups such as tosylate or mesylate undergo reaction first followed by aziridine ring opening to give 2-substituted allyl amine or allyl alcohol



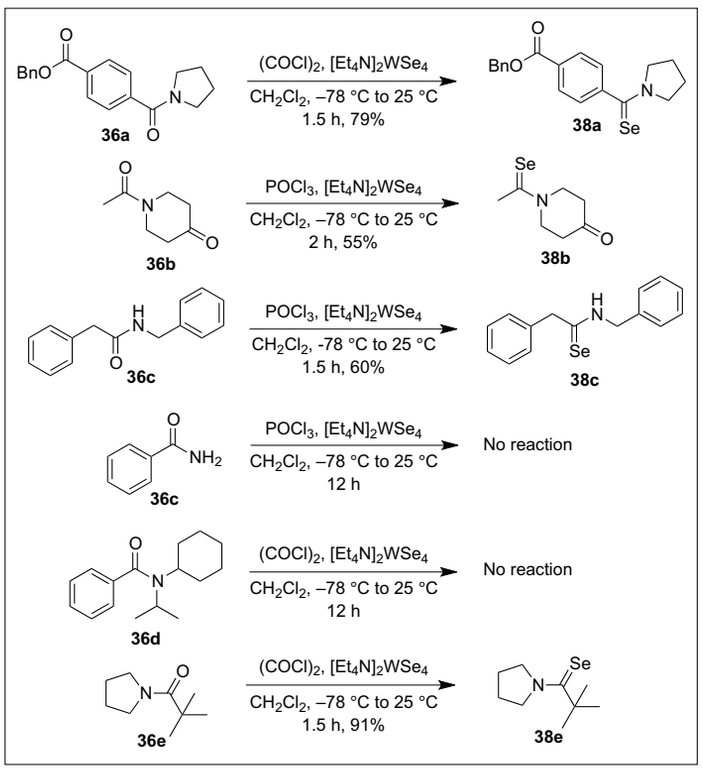
Scheme 11. New selena-aza-Payne-type rearrangement.



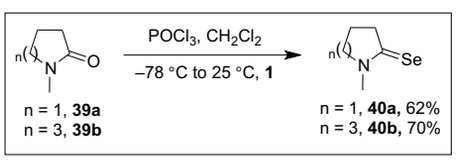
Scheme 12. Selena-aza-Payne-type rearrangement of different aziridinemethanoltosylates.



Scheme 13. Synthesis of selenoamides from the corresponding amides *via* chloroiminium salt.



Scheme 14. Synthesis of various selenoamides.



Scheme 15. Synthesis of *N*-methyl selenolactams.

derivatives, whereas in the present case the ring opening of aziridine takes place first followed by reaction of tosylate to give 2,3-disubstituted allyl amine derivatives as the major product (Scheme 11).

Reaction of simple aziridinemethanoltosylates **24** with **1** furnished exclusively allyl amine derivatives **25** in quantitative yield with excellent regioselectivity. Similarly, the *trans*-aziridinemethanoltosylates **26** gave *trans*-allyl amine derivatives **27** as the major product along with the cyclic diselenides as minor product in 4:1 ratio. In the reaction of *cis*-aziridinemethanoltosylates **29** with **1**, a mixture of regio isomers of allyl amine products **30**, **31** and cyclic diselenides **32** were formed in 2:2:1 ratio. Even 2,3,3-trisubstituted aziridinemethanoltosylate (**33**) underwent rearrangement as expected with **1** and furnished tertiary allyl amine derivative **34** as the major product and the cyclic diselenide **35** (4:1) as the minor product in good yield (Scheme 12).

10. Synthesis of Selenoamides and Selenolactams

Selenoamides are important synthetic precursors for the synthesis of various selenium-containing heterocycles such as selenazole and selenazine derivatives.[22] Unlike amides and thioamides, selenoamides are rather difficult to synthesize owing to the difficulty in preparation and their stability. In general, selenoamides are synthesized by the reaction of amides with various selenating reagents such as $(^tBu_2Al)_2Se$,[5c] $(Me_3Si)_2Se$[23] selenium version of Lawesson's reagent[24] *etc*. Selenoamides are also synthesized from chloroiminium salts by reaction with selenating reagents such as $LiAlSeH_2$[25] and NaSeH.[26] Most of these reactions suffer from lower reaction yields, longer reaction time and harsh reaction conditions.

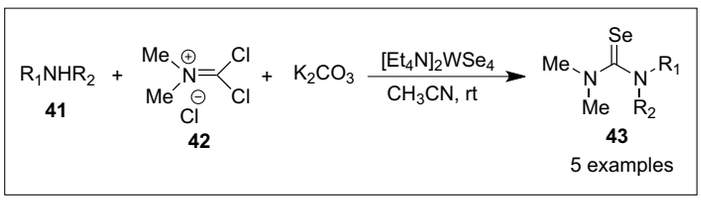
While direct treatment of tetraselenotungstate **1** with amides **36** failed to give the selenoamides, the reaction of amides with oxalyl chloride or $POCl_3$ in CH_2Cl_2 (–78 °C to 25 °C) generated the corresponding chloroiminium salts **37** *in situ* which on treatment with reagent **1**, afforded the corresponding selenoamides **38** in moderate to excellent yields (Scheme 13).[27]

Utilizing this methodology, a number of amides were transformed to the corresponding selenoamides in moderate to good yields without any problem. Additionally, chemoselective transformation could be performed without affecting ester (**36a**) and keto functionality (**36b**). *N*-Mono-substituted amides such as *N*-benzyl phenylacetamide (**36c**) gave very poor yield of the resultant selenoamide when oxalyl chloride was used as the promoter whereas with $POCl_3$ as the promotor, the corresponding selenoamide **38c** was obtained in good yield. On the other hand, benzamide (**36d**, *N*-unsubstituted amide) gave no product under similar reaction conditions. Steric bulk at the nitrogen has a pronounced effect on the reaction yield compared to the steric bulk at the carbonyl carbon. For example, *N*-isopropyl-*N*'-cyclohexylbenzamide (**36d**) did not furnish the corresponding selenoamide whereas *N*-pivaloylpyrrolidine (**36e**) gave the corresponding selenoamide **38e** in 91% yield (Scheme 14).

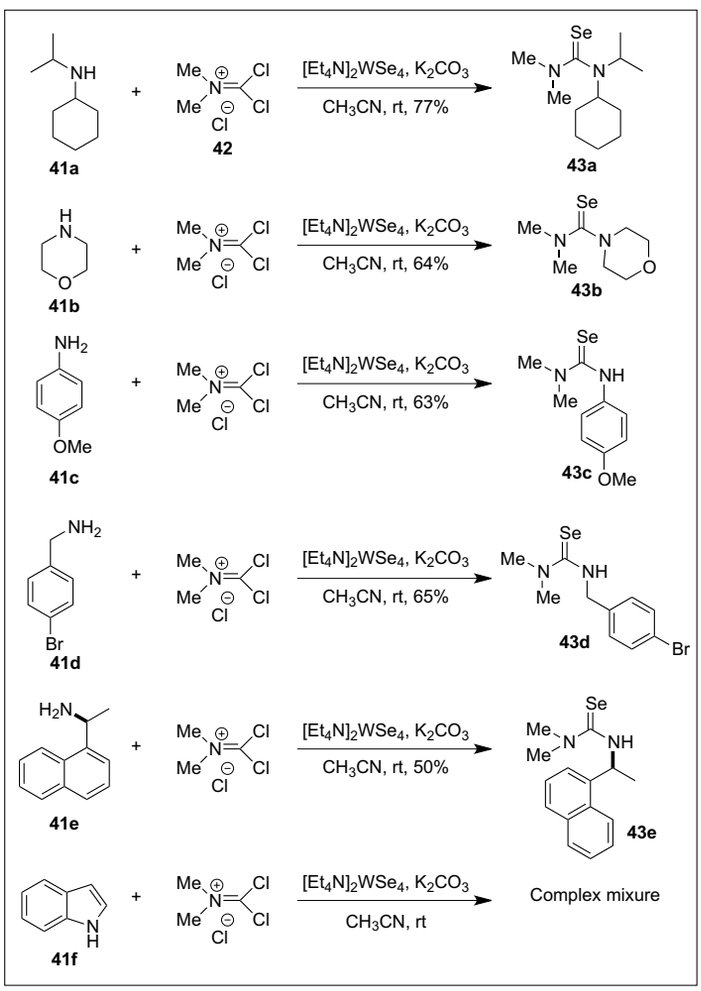
Using the same protocol *N*-methylpyrrolidone (**39a**) and *N*-methyl caprolactam (**39b**) were converted to the corresponding selenolactams **40a** and **40b** in 62% and 70% yields respectively (Scheme 15). The advantages of this methodology are milder reaction conditions and high chemoselectivity compared to other reported methods.

11. Synthesis of Selenoureas

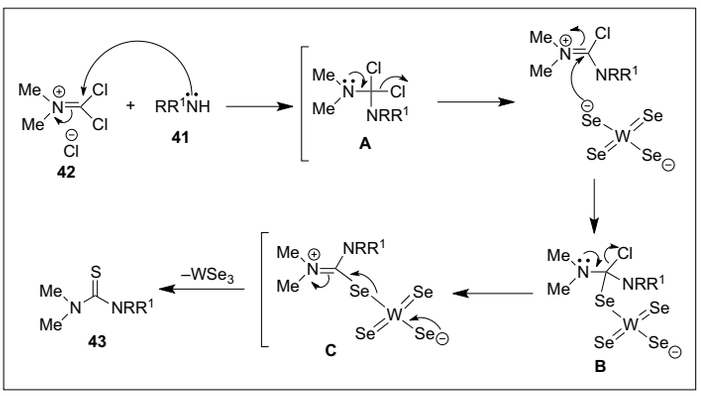
Selenoureas are also one of the key synthetic precursors for the synthesis of many pharmologically important selenium



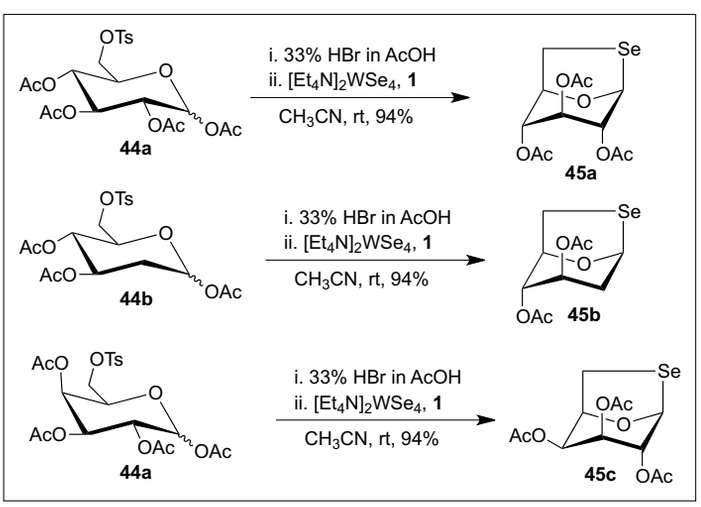
Scheme 16. Synthesis of selenourea derivatives.



Scheme 17. Reaction of various amines with Viehe's iminium salt and reagent **1**.



Scheme 18. Proposed reaction mechanism for the formation of selenourea derivatives.



Scheme 19. Synthesis of 1,6-episeleno sugar derivatives.

heterocycles.[28] In general selenoureas are synthesized from isoselenocynates by reaction with secondary amines.[29] Alternatively they are also synthesized from phosgene iminium chloride, lithium aluminium hydride and elemental selenium.[30] Our group developed a one-pot protocol for the synthesis of selenourea derivatives in good yields under mild conditions by the reaction of primary and secondary amines with Viehe's iminium salt (phosgene iminium chloride) and tetraselenotungstate **1** (Scheme 16). The addition of potassium carbonate increased the chemical yield of the reaction by quenching the hydrochloric acid generated during the reaction.[31] In the absence of potassium carbonate the yields are lower because of partial decomposition of the reagent **1** with hydrochloric acid.

N-Isopropyl cyclohexylamine (**41a**) and morpholine (**41b**) (secondary amines) gave better yields of the resultant selenourea derivatives as compared to other primary amines such as *p*-methoxyaniline (**41c**), *p*-bromobenzylamine (**41d**) and (*S*)-1-(naphthalen-1-yl)ethanamine (**41e**). On the other hand, reaction of indole with Viehe's iminium salt gave a mixture of products, which were difficult to purify because the selenourea derivatives decomposed during purification and were not isolable (Scheme 17).

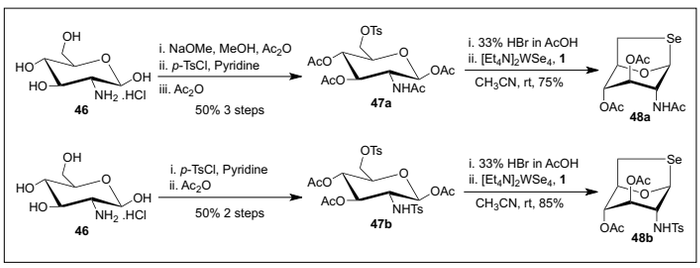
The reaction mechanism involves a simple nucleophilic addition of amine **41** to Viehe's iminium salt **42** to form the corresponding intermediate, **A** which on displacement of one of the chloride ions by the amine followed by reaction with tetraselenotungstate **1** gave intermediate **B**. This intermediate eliminates another chloride ion in a similar fashion to form an iminium intermediate **C**, which then forms the corresponding selenourea derivatives **43** *via* selenium transfer reaction (Scheme 18).

12. Synthesis of Cyclic Selenides

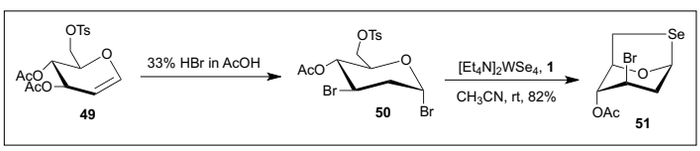
12.1 *Cyclic-monoselenides*

Tetraselenotungstate **1** reacts with a variety of 1,6-diactivated carbohydrate derivatives to furnish the corresponding 1,6-episeleno hexoses *via* selenium transfer at the anomeric carbon.[32] Treatment of 6-*O*-tosyl-1,2,3,4-tetra-*O*-acetyl-α-D-glucopyranoside (**44a)** with HBr in acetic acid gave the corresponding glycosyl bromide**.** The glycosyl bromide was directly treated with tetraselenotungstate **1** (1.2 equiv., CH_3CN, 28 °C, 0.5 h) to give 2,3,4-tri-*O*-acetylselenolevoglucosan (**45a**) in 94% yield. Similarly, 2-deoxy-3,4-di-*O*-acetyselenolevoglucosan (**45b**) and 1,6-episeleno-β-D-galactopyranose (**45c**) were synthesized in excellent yields under similar reactions (Scheme 19).

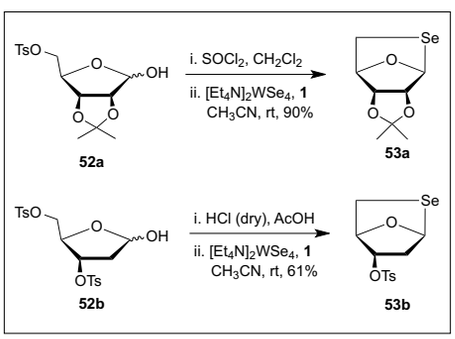
Using the same protocol a number of deoxy amino sugars were synthesized.



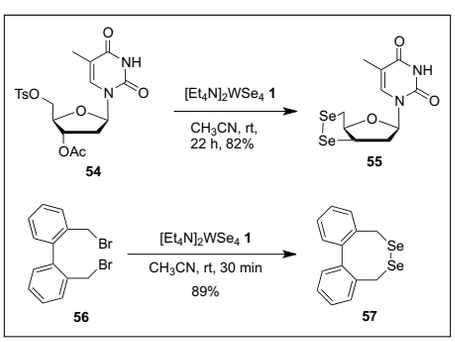
Scheme 20. Synthesis of deoxy amino sugars.



Scheme 21. Synthesis of 2,3,6-trideoxy sugars.



Scheme 22. Synthesis of 1,5-episeleno-pentoses.

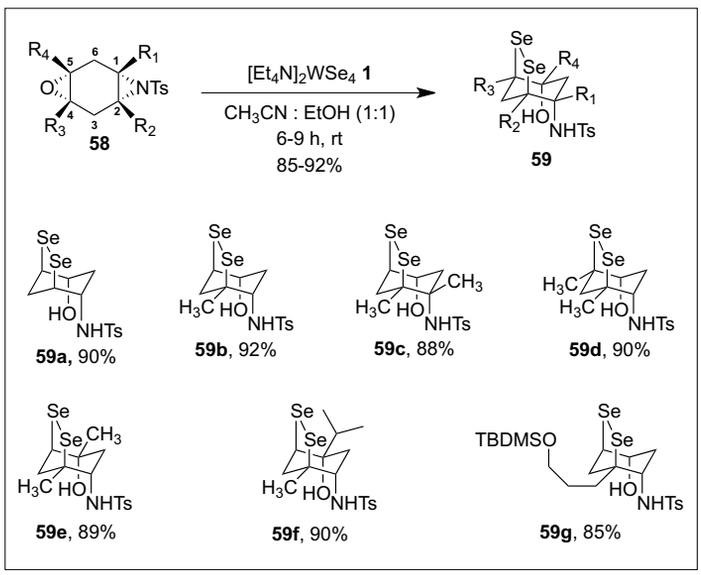


Scheme 23. Synthesis of cyclic diselenides.

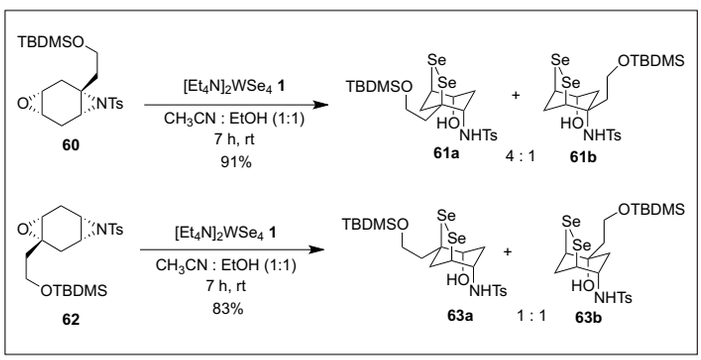
At first 2-acetamido-1,3,4-tri-*O*-acetyl-2-deoxy-6-*O*-*p*-toluenesulfonyl-β-D-glucopyranose (**47a**) was synthesized from glucosamine hydrochloride (**46**) *via* acetylation, tosylation followed by acetylation in moderate yield (50%). Treatment of **47a** with HBr/AcOH followed by treatment with tetraselenotungstate **1** furnished 2-acetamido-3,4-di-*O*-aetyl-2-deoxy-selenolevoglucosan (**48a**). In a similar fashion 2-deoxy-2-tosylamino-3,4-di-*O*-acetyl-1,6-episelenoglucose (**48b**) was synthesized in 85% yield (Scheme 20).

Tetraselenotungstate **1** was also used for the preparation of synthetic precursors of 2,3,6-trideoxy carbohydrate derivatives, as they are present in natural products like aclacinomycin as terminal sugars and are also intermediates in the synthesis of antibiotic, amicetin.[33] Accordingly, 6-*O*-tosyl-3,4-di-*O*-acetyl-D-glucal (**49**) was treated with HBr/acetic acid to give the dibromide **50**, which on treatment with tetraselenotungstate **1** afforded 2,3-dideoxy-3-bromo-4-*O*-acetyl-1,6-episelenoglucopyranose (**51**) in very good yield (Scheme 21).

The reagent **1** has also been successfully used for the synthesis of 1,5-episeleno-pentoses. Treatment of 5-*O*-tosyl-2,3-isopropylidine-D-ribose (**52a**) with $SOCl_2$ in dichloromethane gave the corresponding ribosyl chloride which was immediately treated with **1** to give the corresponding 1,5-episeleno-2,3-isopropylidine-D-ribose (**53a**) in very good yield. Similarly, 2-deoxy-3,5-di-*O*-tosyl-D-erythropentoside (**52b**) on treatment with dry HCl in glacial acetic acid gave the corresponding 2-deoxy-3,5-di-*O*-tosyl-D-erythropentosyl chloride derivative, which upon treatment with **1** afforded 2-deoxy-1,5-episeleno-3-*O*-tosyl-ribose (**53b**) in 61% yield (Scheme 22). These compounds are excellent precursors for the preparation of deoxynucleotides, 2,3-dideoxy-3-thiocytidine (3TC), which are potent anti-human immunodeficiency virus (HIV) active[34] and anti-human hepatitis B virus active.[35]



Scheme 24. Synthesis of cyclic diselenides.

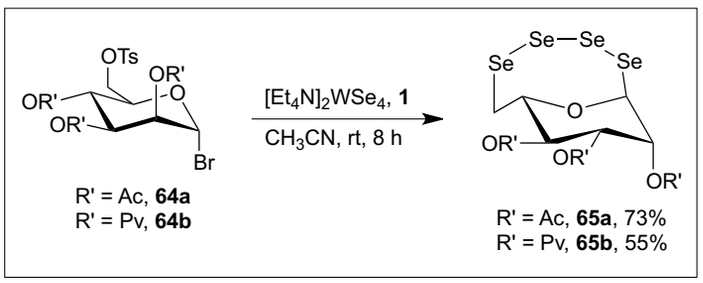


Scheme 25. Synthesis of sterically hindered diselenides.

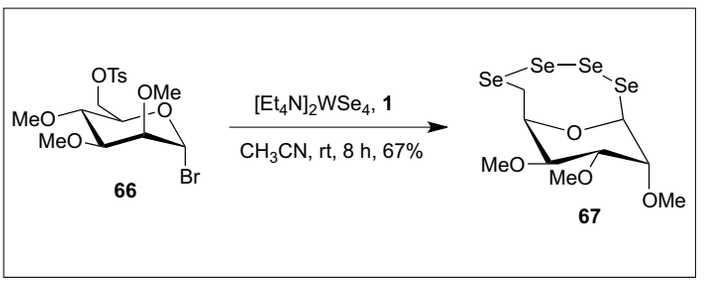
12.2 *Cyclic-diselenides*

Tetraselenotungstate **1** reacts with thymidine-derived tosylate **54** to give an unexpected cyclic diselenide **55** in 82% yield with an inverted configuration at C(3).[13] Although similar diselenides are known, their synthesis involves longer routes and lower yields.[36] In a similar fashion dibromide **56** on treatment with tetraselenotungstate **1** gave the corresponding cyclic diselenide **57** in 89% yield (Scheme 23).[9]

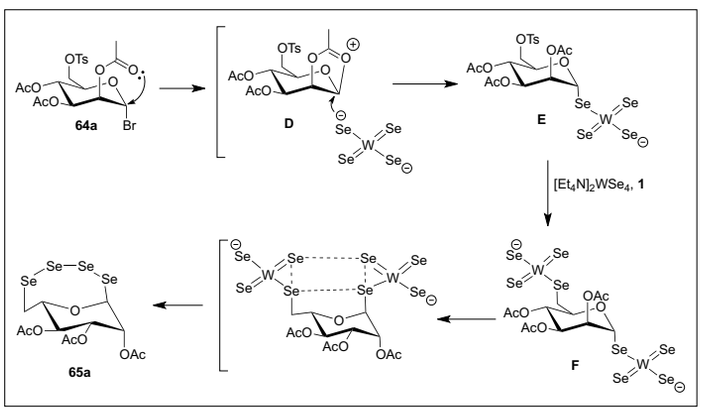
Tetraselenotungstate **1** on reaction with 1,4-*cis*-aziridino epoxides **58**,[37] furnished the corresponding bicyclic diselenides **59** in good to excellent yields.[38] In the case of tri- and tetra-substituted *cis*-aziridino-epoxides, aziridine ring opening always took place at the more substituted carbon atom[39] whereas in case of the epoxide, the ring opening took place both at the less substituted and more substituted carbon atom depending on the substrate. Diselenide **59d** was obtained by ring opening of aziridine from the more hindered carbon and epoxide from the less substituted carbon whereas diselenide **59e** was obtained by the ring opening of aziridine and epoxide from the more substituted carbon centers (Scheme 24).



Scheme 26. Synthesis of cyclic tetraselenides.



Scheme 28. Synthesis of 1,5-*cis*-cyclic tetraselenide.



Scheme 27. Tentative mechanism for the formation of tetraselenide **65a**.

Introduction of a bulky substituent at the aziridine carbon did not change the regioselectivity of aziridine ring opening; aziridino-epoxide **60** on treatment with tetraselenotungstate **1** gave **61a** (obtained by the ring opening of aziridine from the more substituted carbon) as the major product. On the other hand introduction of a bulky substituent at the epoxide carbon showed a pronounced effect on the regioselectivity of ring opening; aziridino-epoxide **62** gave a 1:1 mixture of products **63a** and **63b**, resulting from the ring opening of epoxide from both the possible sites (Scheme 25).

12.3 *Cyclic-tetraselenides*

Tetraselenotungstate **1** on treatment with mannose-derived anomeric bromides **64a** and **64b** furnished novel 1,5-*trans*-substituted cyclic tetraselenides **65a** and **65b** with a carbohydrate backbone, instead of the expected 1,6-episelenide (Scheme 26).[40] The *trans*-stereochemistry of **65a** was confirmed by X-ray crystallography. In order to account for the *trans*-stereochemistry in the formation of tetraselenide **65a** the following tentative mechanism was proposed.

At first, neighboring group participation of the axial acetate group in mannosyl bromide **64a** led to the corresponding oxonium ion intermediate **D**, which on reaction with tetraselenotungstate **1** from the axial side gave the corresponding organoselenium intermediate **E**. Further reaction of **E** with tetraselenotungstate **1** at the C(5) tosylate furnished intermediate **F**, which then through an internal redox process[41] gave the corresponding tetraselenide **65a** (Scheme 27).

On the other hand, reaction of mannosyl bromide **66** (lacking neighboring group participation) with tetraselenotungstate **1** gave exclusively 1,5-*cis*-substituted cyclic tetraselenide **67** in 67% yield (Scheme 28).

13. Conclusion and Outlook

Organoselenium compounds play an important role in biochemical processes and serve to function as antioxidants, anticancer and antiviral agents. Hence, development of new and efficient selenating reagents is becoming more important. In recent years, applicability and utility of tetraselenotungstate as an efficient selenium transfer reagent in organic synthesis has been demonstrated in different areas of organic chemistry, which includes the synthesis of simple diselenides, amino acid-derived diselenides, carbohydrate-based diselenides, selenoamides, selenoureas, cyclic diselenides, mono-selenides and conformationally locked diselenides. Despite these significant advancements, further developments are necessary to broaden the application by making this reagent more versatile and explore the possibility of developing chiral selenium transfer reagents in organic synthesis.

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