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Transformation of a wobble 2-thiouridine to 2-selenouridine via S-geranyl-2thiouridine as a possible cellular pathway

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Abstract

The newly discovered S-geranylated 2-thiouridines (geS2U) (Dumelin et al, Nat. Chem. Biol. 2012) and 2-selenouridines (Se2U) were recently shown to be synthesized by a single enzyme (selenouridine synthase, SelU) through two distinct pathways using the same 2-thiouridine substrate (S2U); however, no clear catalytic mechanism was proposed. We suggest that S-geranyl-2-thiouridine is an intermediate of the SelU-catalyzed conversion of S2U to Se2U. The successful chemical transformation of S2U \rightarrow geS2U \rightarrow Se2U is demonstrated here as an initial approximation of the intracellular pathway. The structure of Se2U was confirmed by spectroscopic methods, which included, for the first time, ⁷⁷Se NMR data (δ 354 ppm).

Keywords: 2-thiouridine, 2-selenouridine, S-geranyl-2-thiouridine, selenouridine synthase, SelU, Salkylation, selenium chemical shift, 77Se NMR

1. Introduction

Transfer RNAs (tRNAs) are unique among natural RNAs because of their substantial content of modified nucleosides, including 5-substituted uridines (x5U, 1) and their analogs containing either a sulfur (2-thiouridines, x5S2U, 2) or selenium atom (2-selenouridines, x5Se2U, 3) in the nucleobase C2

position. These hypermodified nucleosides are located in the wobble position of the anticodon (position 34) of tRNAs specific for glutamine, glutamic acid and lysine [1,2]. Their structural features play a fundamental role in the tuning of codon reading and the efficiency of the translation process [3]. Ten type **2** 2-thiouridines and five type **3** 2-selenouridines are known; the substituents at C5 (X) are shown in Fig. 1.



Figure 1. Structures of the known 5-substituted uridines (x5U, 1), 2-thiouridines (x5S2U, 2), 2-selenouridines (x5Se2U, 3) and S-geranyl-2-thiouridines (x5geS2U, 4).

Two hydrophobic 5-substituted-2-thiouridines in which the sulfur atom is functionalized with a geranyl residue (mnm5geS2U, **4d** and cmnm5geS2U, **4e**) were recently identified in several bacterial strains at position 34 of tRNAs specific for lysine, glutamine and glutamic acid [4]. tRNA geranylation is induced by cellular stress and occurs in less than 7% of the cell population. The geranylation of the wobble S2U nucleoside affects the codon preference and frame shifting during translation. Although the exact mechanism of this effect is unknown, the superior recognition of the G-ending over the A-ending codons by geranylated tRNA^{Lys} is observed.

Selenouridine synthase SelU is the enzyme responsible for selenoation of 2-thiouridine in *E. coli* [5], and Liu and co-workers have demonstrated that this enzyme is also involved in the geranylation of 2-thiouridine [4]. These two chemically disparate processes employ the same 2-thiouridine substrate. For selenoation, the sulfur atom in 2-thiouracil must be converted into a leaving group and further substituted by a selenium nucleophile originating from selenophosphate. By contrast, for geranylation, the same sulfur atom acts as a nucleophile and accepts the geranyl substituent from geranyl diphosphate. It is unclear how these two mechanistically different reactions are mediated by the same catalyst. Moreover, the potential relationship between the two distinct products, Se2U and geS2U, formed from the same precursor is also of interest.

The literature suggests that the chemical transformation of S2U to various C2-substituted uridines might occur through the respective S-alkylated derivatives. For example, S-alkylation of 2-thiouridine yielded a series of 2-alkyl(aryl)aminouridines [6]. In addition, S-methylated 2'-deoxy-2-thiouridine was successfully transformed (via a hydrazino derivative) into a 2-azidonucleoside [7]. Huang et al. demonstrated that S-methylated 2-thiouridine is efficiently transformed to 2-selenouridine upon nucleophilic attack of the hydroselenide ion (HSe⁻) on the partially electropositive C2 center [8]. Accordingly, we hypothesized that the newly discovered S-geranyl-2-thiouridine is an intermediate formed during the transformation of 2-thiouridine (embedded in a tRNA chain) to 2-selenouridine. We therefore attempted the chemical transformation S2U \rightarrow geS2U \rightarrow Se2U as an initial approximation of the intracellular mechanism.

2. Results

The S-geranylated 5'-O-DMT-2-thiouridine substrate (6) was obtained from 2-thiouridine (2a) either through its geranylated form 4a [4] via subsequent dimethoxytritylation at the 5'-OH function or via 5'-OH protection with a DMT group, yielding compound 5, and subsequent geranylation of the sulfur residue (Scheme 1). The structure of S-geranyl-2-thiouridine 2a was confirmed by ¹H and ¹³C NMR and FAB-MS spectral analysis (for numbering, see Supplementary Material Fig. S2; for spectral analysis, see Fig. S3 - S5). The 5'-DMT protection of 4a was accomplished using standard protocols to give pure 6. A similar approach was used for geranylation prior to 5'-OH protection ($2a \rightarrow 5 \rightarrow 6$) (see the Supplementary Material for preparative procedures and ¹H NMR spectral data of 5, Fig. S6, S7 for). The efficiencies of the first and second synthetic approaches were similar and produced pure derivative 6 in 66 and 46% yield, respectively. The structure of 6 was confirmed by ¹H and ¹³C NMR and FAB mass spectrometry (Fig. S8 - S13). The DMT group improved the solubility of 4a in organic solvents, thus facilitating the subsequent selenoation.



Scheme 1. Transformation of S2U 2a to Se2U 3a via an intermediate geS2U 6.

The sodium hydroselenide (NaHSe) required for the subsequent reaction was prepared according to the published procedure [8] by reduction of elemental selenium with NaBH₄ in absolute ethanol under an inert atmosphere. Importantly, the selenium used in the experiment contained 22 at.% of the NMR-active ⁷⁷Se isotope, in contrast to the natural abundance of ⁷⁷Se isotope, which is approximately 7.6%. A solution of ⁷⁷Se-enriched hydroselenide was added to **6**, and the mixture was stirred for 6 h under an inert atmosphere. After aqueous work up, silica gel flash chromatography furnished **7** as a yellow solid in 30% yield.

The structure of **7** was confirmed by ¹H and ¹³C NMR and by FAB mass spectrometry (Fig. S14 - S17). The 22% abundance of ⁷⁷Se retained in **7** was documented by an extended FAB MS spectrum (Fig. 2, m/z 606.5). The resonance line of ⁷⁷Se in the labeled uridine (Fig. 3A, ⁷⁷Se NMR, δ 407.4 ppm) was located downfield of the signal for ⁷⁷Se-selenourea (δ 195 ppm) [9]. ⁷⁷Se enrichment permitted the

acquisition of a 2D HMBC spectrum (Fig. 3B), in which the signal for H1' at δ 6.5 ppm was correlated with the ⁷⁷Se signal at δ 407.4 ppm.

Compound **7** was then detritylated with aqueous acetic acid (50%) for 1 h at room temperature. The resulting product **3a** (Se2U) was isolated by RP-HPLC and characterized by UV (λ_{max} 301 nm), ¹H and ¹³C NMR (in D₂O), and FAB MS (Fig. S18 – S23). The ⁷⁷Se isotope contents in **3a** and **6** were identical (Fig. 2 and S24). The ⁷⁷Se NMR resonance signal for **3a** was observed at δ 353.7 ppm (Fig. S25), i.e., it was shifted approximately 54 ppm upfield from the ⁷⁷Se resonance of **7**.



Figure 2. FAB MS spectrum for **7**. Signals at m/z 609.3 and m/z 606.5 correspond to the molecules containing the most abundant ⁸⁰Se isotope and to those artificially enriched in ⁷⁷Se isotope, respectively.



Figure 3. The ⁷⁷Se NMR spectrum of 5'-*O*-DMT-2-selenouridine **7** (A); The two-dimensional HMBC spectrum showing a cross-peak between H1' at $\delta 6.5$ ppm and ⁷⁷Se signals at δ (B); ⁷⁷Se NMR ($\delta 407.4$ ppm) for spectrum taken with Ph-Se-Se-Ph reference ($\delta 463$ ppm) in CDCl₃.

3. Discussion

In this study, we demonstrated that the chemical transformation of S2U to Se2U proceeds easily *via* the S-geranylated S2U intermediate, in which substitution at the C2 position with nucleophilic selenide occurs, accompanied by the departure of the thioalkyl moiety. Under cellular conditions, this reaction is strictly dependent on the concentration of the selenium donor. At low selenium concentrations (< 10 nM), the geranylated tRNA form is predominant over the seleno-tRNA form; however, selenoation occurs at the expense of the formation of geranylated tRNA at selenium concentrations exceeding 10 nM [4]. Thus, this transformation seems to occur in the cell in a linear manner via $S2U \rightarrow geS2U \rightarrow Se2U$ (Scheme 2) rather than in a parallel manner in which the two individual reactions $S2U \rightarrow Se2U$ and $S2U \rightarrow geS2U$ occur independently, possibly in different catalytic centers [4, 5].



Scheme 2. Scheme of a possible cellular pathway of S2U-tRNA to Se2U-tRNA transformation undergoing through the geS2U-tRNA intermediate (Geranyl-pp – geranyl diphosphate, Se-p – selenophosphate).

The source of selenium in the S2U to Se2U enzymatic transformation is a selenophosphate (SePO $_3^{3-}$), which is the product of the conversion of selenide (HSe) by selenophosphate synthetase (SelD) [10,11]. The reaction utilizes ATP and yields SePO₃³⁻, orthophosphate and AMP. Selenophosphate is also an essential substrate for the generation of selenocysteine (Sec), which is now considered a 21st amino acid. However, selenocysteine is not formed by the direct exchange of sulfur with selenium in cysteine but from Ser-tRNA^{sec} charged with serine [12,13]. The biosynthesis of Sec begins with phosphorylation of the serine moiety catalyzed by phosphoseryl-tRNA kinase (PSTK) and yields Ophosphoseryl-tRNA^{sec} [14]. Activated in this way, the hydroxyl group of serine is replaced by selenium from selenophosphate to afford Sec-tRNA^{sec}. This process supports our hypothesis because attack by the selenium donor is accompanied by the departure of a negatively charged phosphate. From the other the naturally occurring rare nucleoside S-methyl-2-thioadenosine (2side, methylthioadenosine, mS2A) is not the product of consecutive sulfuration and methylation of adenosine molety but of a direct transfer of the methylthio group from SAM [15]. In contrast to the discussed modification there is no any adenosine derivative which would be formed by a nucleophilic attack at C2 of adenine ring of mS2A with subsequent departure of thiomethyl leaving group. Thus, more advanced biological studies are required to evaluate the hypothesis that the transformation of 2-thiouridine to 2-selenouridine follows the linear process $S2U \rightarrow geS2U \rightarrow Se2U$.

4. Conclusions

The successful chemical synthesis of Se2U from S2U via S-geranyl-2-thiouridine presented in this study suggests a possible mechanism of SelU enzyme action in which geS2U serves as an intermediate product of the cellular transformation of S2U to Se2U.

5. Experimental

5. 1. Synthesis of S-geranyl-2-thiouridine (geS2U, 4a) [4]

2-Thiouridine (260.0 mg, 1 mmol) was dissolved in methanol (10 ml). To the solution geranyl bromide (570 μl, 3 mmol) and *N*,*N*-diisopropylethylamine (522 μl, 3 mmol) were added. After stirring at 25°C for 30 minutes the reaction mixture was concentrated *in vacuo*. The residue was dissolved in ethyl acetate and washed with water. The organic layer was dried over anhydrous MgSO₄, concentrated *in vacuo* and subjected to silica gel chromatography (0-5% methanol in ethyl acetate) to yield a white solid (355.0 mg, 0.89 mmol, 89% yield): TLC *R*f = 0.10 (1/9 MeOH/EtOAc (v/v)); ¹H NMR (700 MHz, CDCl₃) δ 8.21 (d, *J* = 7.6 Hz, 1H), 5.96 (d, *J* = 7.6 Hz, 1H), 5.91 (d, *J* = 5.7 Hz, 1H), 5.28 (t, *J* = 8.1Hz, 1H), 5.06 (t, *J* = 7.0 Hz, 1H), 4.45 (q, *J* = 5.2 Hz, 1H), 4.36 (dd, *J* = 5.2, 2.5 Hz, 1H), 4.19 (q, *J* = 2.5 Hz, 1H), 3.93 (m, 2H), 3.87 – 3.81 (m, 2H), 2.10 (m, 2H), 2.02 (m, 2H), 1.73 (s, 3H), 1.69 (s, 3H), 1.60 (s, 3H). ¹³C NMR (176 MHz, DMSO-d6) δ 166.6, 161.9, 141.1, 139.4, 131.0, 123.7, 117.4, 108.9, 91.3, 85.9, 74.6, 69.9, 60.7, 29.5, 25.9, 25.4, 17.6, 16.1. MS-FAB (*m/z*): 397.3 [M+H]⁺, MW: 396.5.

5.2. Synthesis of 5'-O-dimetoxytrityl-S-geranyl-2-thiouridine (6) from 4a

A solution of S-geranyl-2-thiouridine **4a** (355.0 mg, 0.89 mmol) and 4,4 -dimethoxytrityl chloride (603.0 mg, 1.78 mmol) in pyridine (4 ml) was stirred at 25 °C for 20 hours. To the resulting reaction mixture, 10 ml water was added and extracted with CH_2CI_2 . Organic layer was dried over anhydrous MgSO₄, concentrated *in vacuo* and subjected to silica gel chromatography (0-2% methanol in methylene chloride with 0,5 % Py). A white solid (470.0 mg, 0.67 mmol, 75% yield) of **6** was obtained after column chromatography: TLC *R*f = 0.67 (1/9 MeOH/CHCl₃ (v/v)); ¹H NMR (700 MHz, CDCl₃) δ 7.84 (d, J = 7.7 Hz, 1H), 7.43 (dd, J = 8.3, 1.4 Hz, 2H), 7.38 – 7.16 (m, 13H), 6.91 – 6.86 (m, 4H), 5.92 (d, J = 6.3 Hz, 1H), 5.57 (d, J = 7.7 Hz, 1H), 5.32 (m, 1H), 5.09 (m, 1H), 4.66 (q, J = 5.6 Hz, 1H), 4.43 (m, 1H), 4.26 (q, J = 2.6 Hz, 1H), 3.98 (dd, J = 12.8, 8.0 Hz, 1H), 3.87 (dd, J = 12.8, 8.0 Hz, 1H), 3.79 (s, 6H), 3.45 (t, J = 2.8 Hz, 2H), 2.18 – 2.08 (m, 2H), 2.09 – 1.98 (m, 2H), 1.76 (s, 3H), 1.71 (s, 3H), 1.63 (s, 3H); ¹³C NMR (176 MHz, CDCl₃) δ 171.20, 166.70, 161.08, 146.69, 145,40, 142.29, 137.46, 134.26, 132.54, 131.41, 130.61, 129.45, 127.68, 126.07, 118.44, 115.75, 111.14, 93.98, 89.53, 87.10, 77.10, 74.25, 65.91, 57.58, 42.05, 34.15, 28.79, 28.08, 20.11, 18.91. MS-FAB (*m*/*z*): 699.50 [M+H]⁺, MW: 698.88.

5.3. Synthesis of 5'-O-dimetoxytrityl-2-selenouridine (7) [8]

Nucleoside **6** (80 mg), NaBH₄ and Se were dried overnight under reduced pressure. A solution of NaSeH was generated by addition of absolute ethanol (5 ml) to selenium (110 mg of selenium of natural abundance and 23 mg of ⁷⁷Se) and sodium borohydride (NaBH₄, 94 mg) at 0°C. The reaction

was completed in 1h and clear solution was formed. The ethanolic solution was added to **6** (80 mg) and the mixture was stirred for 3h under argon. The reaction mixture was concentrated under reduced pressure and chloroform (5 ml) was added to the residue. The organic layer was washed twice with water (2x3 ml), and then dried over anhydrous magnesium sulfate. Purification was performed by flash chromatography (4% methanol in methylene chloride) and the light yellow compound **7** was obtained (30% yield). TLC *R*f = 0.60 (1/9 MeOH/CHCl₃ (v/v)); ¹H NMR (500 MHz, CDCl₃) δ 8.61 (s, 1H), 8.26 (d, *J* = 8.1 Hz, 1H), 7.67 (t, *J* = 7.6 Hz, 1H), 7.38 – 7.31 (m, 2H), 7.31 – 7.16 (m, 10H), 6.85 – 6.76 (m, 4H), 6.55 (d, J = 1.5 Hz, 1H), 5.58 (d, *J* = 8.1 Hz, 1H), 4.49 (dd, *J* = 7.7, 5.3 Hz, 1H), 4.44 (dd, *J* = 5.3, 1.5 Hz, 1H), 4.19 (dt, *J* = 7.7, 2.3 Hz, 1H), 3.76 (d, *J* = 1.9 Hz, 13H), 3.56 (qd, *J* = 11.3, 2.3 Hz, 2H), 1.29 – 1.16 (m, 5H). ¹³C NMR (126 MHz, Chloroform-d) δ 175.64, 159.40, 158.72, 149.50, 144.29, 140.73, 136.43, 135.22, 134.97, 130.14, 128.10, 127.24, 123.94, 113.35, 108.14, 96.64, 87.13, 84.05, 68.81, 61.03, 55.29. ⁷⁷Se NMR (95 MHz, CDCl₃) δ 407.45. MS-FAB (*m*/*z*): 609.30 [M+H]⁺, MW: 608.53.

5.4. Synthesis of 2-selenouridine (3a)

2-Selenouridine (**3a**) was prepared through detritylation of 5'-*O*-dimethoxytrityl-2-selenouridine (5 mg, 0.008 mmol) by acid treatment (1h, room temperature) (quantitative removal of DMT group). Then the reaction mixture was concentrated under reduced pressure (SpeedVac) and the remaining crude 2-selenouridine was purified by RP-HPLC. The product elution was performed with a gradient of buffer A (20 mM triethylammonium acetate TEAAc, pH 7.1 in water) to buffer B (20mM triethylammonium acetate TEAAc, pH=7.1 in 50 % acetonitrile) on a Kinetex C18 column (5 µm, 4.6 mm x 250 mm, Phenomenex) at a constant flow rate of 1.0 ml/min (0 \rightarrow 15 min from 0 to 25% of B; 15 \rightarrow 20 min from 25 to 100 % of B). Yield 1.95 mg (ca. 80%). ¹H NMR (600 MHz, D₂O) δ 8.03 (dd, *J* = 8.1, 1.3 Hz, 1H), 6.61 (d, *J* = 2.5 Hz, 1H), 6.14 (d, *J* = 8.1 Hz, 1H), 4.29 (q, *J* = 2.5 Hz, 1H), 4.07 (m, 2H), 3.88 (dd, *J* = 13.1, 1.6 Hz, 1H), 3.73 (dd, *J* = 13.1, 2.5 Hz, 1H). ¹³C NMR (151 MHz, D₂O) δ 175.58, 162.83, 141.52, 108.04, 95.86, 83.97, 74.92, 68.33, 59.74. ⁷⁷Se NMR (95 MHz, D₂O) δ 353.79. MS-FAB (*m/z*): 307.2 [M+H]⁺, MW: 306.16.

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References

[1] http://mods.rna.albany.edu/

[2] http://modomics.genesilico.pl/

[3] E.M. Gustilo, F.A Vendeix, P.F. Agris, tRNA's modifications bring order to gene expression, Curr.Opin. Microbiol. 11 (2008) 134-140.

[4] C.E. Dumelin, Y. Chen, A.M. Leconte, Y.G. Chen, D.R. Liu, Discovery and biological characterization of geranylated RNA in bacteria, Nat. Chem. Biol. 8 (2012) 913-919.

[5] M.D. Wolfe, F. Ahmed, G.M. Lacourciere, C.T. Lauhon, T.C. Stadtman, T.J. Larson, Functional diversity of the rhodanese homology domain: the Escherichia coli ybbB gene encodes a selenophosphate-dependent tRNA 2-selenouridine synthase, J. Biol. Chem. 279 (2004) 1801-1809.

[6] A. El-Tayeb, A. Qi, R.A. Nicholas, Ch.E. Muller, Structural modifications of UMP, UDP, and UTP leading to subtype-selective agonists for p2y2, p2y4, and p2y6 receptors, J. Med. Chem. 54 (2011) 2878-2890.

[7] S. Gourdain, C. Petermann, A. Martinez, D. Harakat, P. Clivio, Synthesis and photochemical behavior of the tetrazolo tautomer of 2-azido-4-pyrimidinone-2 -deoxyriboside, J. Org. Chem. 76 (2011) 1906–1909.

[8] H. Sun, J. Sheng, A. Hassan, S. Jiang, J. Gan, Z. Huang, Novel RNA base pair with higher specificity using single selenium atom, Nucleic Acids Res. 40 (2012) 5171-5179.

[9] http://www.chem.wisc.edu/areas/reich/handouts/nmr/se-data.html

[10] A. Ehrenreich, K. Forchhammer, P. Tormay, B. Veprek, A. Böck, Selenoprotein synthesis in *E. coli*. Purification and characterisation of the enzyme catalysing selenium activation, Eur. J. Biochem. 206 (1992) 767-773.

[11] Z. Veres, I. Y. Kim, T. D. Scholz, T. C. Stadtman, Selenophosphate synthetase. Enzyme properties and catalytic reaction, J. Biol. Chem. 269 (1994) 10597-10603.

[12] W. Leinfelder, E. Zehelein, M. A. Mandrand-Berthelot, A. Böck, Gene for a novel tRNA species that accepts L-serine and cotranslationally inserts selenocysteine, Nature 331 (1988) 723-725.

[13] J. Yuan, S. Palioura, J. C. Salazar, D. Su, P. O'Donoghue, M. J. Hohn, A. M. Cardoso, W. B. Whitman, D. Söll, RNA-dependent conversion of phosphoserine forms selenocysteine in eukaryotes and archaea, Proc. Natl. Acad. Sci. U. S. A. 103 (2006) 18923-18927.

[14] B. A. Carlson, X. M. Xu, G. V. Kryukov, M. Rao, M. J. Berry, V. N. Gladyshev, D. L. Hatfield, Identification and characterization of phosphoseryl-tRNA[Ser]Sec kinase, Proc. Natl. Acad. Sci. U. S. A. 101 (2004) 12848-12853.

[15] B. Esberg, H. C. Leung, H. C. Tsui, G. R. Björk, M. E. Winkler, Identification of the miaB gene, involved in methylthiolation of isopentenylated A37 derivatives in the tRNA of Salmonella typhimurium and Escherichia coli, J. Bacteriol. 181 (1999) 7256-7265.





Graphical abstract

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Highlights

- 2-Thiouridine is chemically transformed to 2-selenouridine via S-geranyl 2-thiouridine
- This pathway is proposed to be possible in the cell •
- Acceleration It is suggested that SelU may produce geS2U as an intermediate from S2U to Se2U •

14