Synthesis of the Selenium Congener of the Naturally Occurring Nucleoside Guanosine, 6-Selenoguanosine (1)

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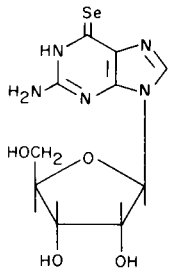
Sir:

We wish to report the synthesis of 6-selenoguanosine (I) and some preliminary data on the chemical reactivity and stability of the exocyclic seleno group. The syntheses of thionucleosides has been investigated (2) in considerable detail due to their observed biological and chemotherapeutic activity. Interest in this area has recently increased as a result of the isolation and characterization of several thionucleosides from naturally occurring sources, *e.g.* methyl 2-thiouridine-5-acetic acid (3), 2-thiocytidine (4), and various other thionucleosides from t-RNA (5). There is an increasing accumulation of reports indicating a definite relationship between well known sulfur metabolites and the corresponding selenium analogs, *e.g.* selenomethionine (6). In fact, it has been established that there is a dietary requirement for selenium, presumably as a seleno-organic compound (6). A number of disorders have been attributed to selenium deficiencies (7) and it has been found that prevention of these disorders can be accomplished much more effectively by seleno compounds than by the sulfur amino acids, on a molar basis (8). These data prompted our synthesis of the selenium congener of 6-thioguanosine and guanosine.

Treatment of 2-amino-6-chloro-9-(β-D-ribofuranosyl)-purine (9) with a methanolic solution of sodium hydrogen selenide (10) at reflux temperature for 15 minutes furnished nucleoside material which was characterized (11) as 6-selenoguanosine (I) in over 50% yield; m.p. 206-208° dec.; UV λ max (*p*H 1), 260 nm (ε = 5,500) and 366 nm (ε = 18,700); λ max (water), 359 nm (ε = 21,200); λ max (*p*H 11), 256 nm (ε = 12,250) and 330 nm (ε = 18,100); pmr revealed a low broad peak in the δ 12-13 region (N1 proton), a sharp singlet at δ 8.3 (C8 proton), a singlet δ 6.8 (exocyclic amino group) and the characteristic pattern for the ribose moiety. In view of the reported (12) instability of 6-selenopurine-9-riboside under neutral and basic conditions, we have conducted a preliminary investigation into the stability of 6-selenoguanosine toward basic conditions. After exposure of 6-selenoguanosine to a 1 *N* sodium hydroxide solution for 2 hours at room temperature, there was observed essentially no decomposition as determined by the ultraviolet spectra of the reaction mixture which revealed a constant ε max at 330 nm. The same results were obtained using 6 *N* sodium hydroxide for 2 hours at room temperature. Exposure of 6-selenoguanosine to 1 *N* sodium hydroxide at reflux temperature for 30 minutes resulted in no decomposition, although after 1 hour there was observed a decrease in the ε max at 330 nm of approximately 15% and the appearance of a small amount of selenium metal. Therefore it appears that the presence of an exocyclic amino group at position two has conferred a significant increase in the stability of 6-selenopurine-9-riboside toward basic conditions.



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Another point of considerable interest was the observation that on treatment of I with Raney nickel in water at room temperature there was observed a complete disappearance of the absorption peak at 359 nm in the UV with the concomitant appearance of an absorption peak at 303 nm (water) within 5 minutes (13). This facile removal of the seleno group appears to proceed at a much faster rate than the removal of the corresponding thio group from 6-thioguanosine. This would indicate that the exocyclic seleno group may possess the potential of becoming a very versatile and important group for further functional group transformations. The synthesis of additional selenonucleosides and the use of the seleno group for functional group transformations are under investigation in our laboratory.

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Received May 27, 1970

Salt Lake City, Utah 84112