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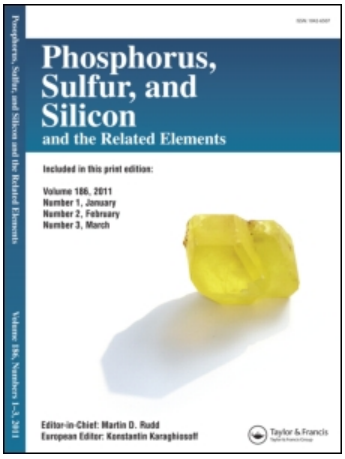

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A CONVENIENT METHOD FOR THE SYNTHESIS OF 6-SELENOPURINE RIBOSIDES

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A CONVENIENT METHOD FOR THE SYNTHESIS OF 6-SELENOPURINE RIBOSIDES

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A convenient method for the synthesis of 6-selenopurine ribosides by nucleophilic displacement of chloride by sodium hydrogen selenide from the corresponding 6-chloropurine ribosides is described. This method provides a useful improvement in yield while significantly simplifying the literature procedures.

Key words: 6-selenoinosine; 6-selenoguanosine; sodium hydrogen selenide; nucleophilic displacement reaction; convenient synthesis.

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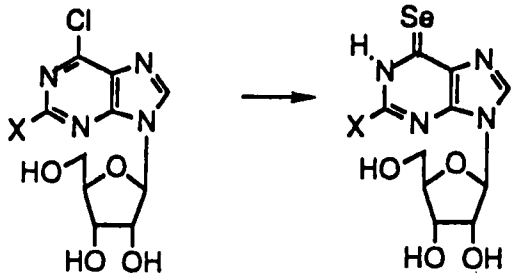
Purine ribosides substituted by selenium in the 6-position (**2**) are of considerable interest due to their antitumor properties.[1-3] The displacement of chloride from the reactive 6-chloropurine riboside (**1**) by a nucleophilic selenium atom has provided an attractive entre into this class of compounds (cf. Scheme 1).

A variety of selenium nucleophiles, such as potassium selenosulfate,[4] selenourea,[5] and sodium hydrogen selenide,[6a-c] have been utilized to effect the insertion of selenium. In earlier procedures, sodium hydrogen selenide was prepared by bubbling hydrogen selenide gas through a solution of sodium hydroxide under an inert atmosphere. A more convenient method for the preparation of sodium hydrogen selenide was described by Klayman and Griffin.[7] They observed that the reaction of sodium borohydride with elemental selenium in either water or ethanol proceeds vigorously with the evolution of hydrogen gas and the formation of the requisite sodium hydrogen selenide. We find that when this reaction is performed in a small vessel with a minimum volume of solvent, the hydrogen evolution is sufficient to degass the solvent and initially provides an inert atmosphere under which one may conduct the subsequent displacement reaction.



1a, X=H **2a, X=H**

1b, X=NH$_2$ **2b, X=NH$_2$**

SCHEME 1

Glass serum bottles provide a convenient medium for carrying out this reaction: elemental selenium and an excess of sodium borohydride in a serum bottle are treated with water, and the bottle loosely capped to allow the expulsion of air by the evolving hydrogen gas. At the completion of the vigorous reaction, a clear colorless solution of sodium hydrogen selenide is obtained. Reaction of this solution with the appropriate 6-chloropurine ribosides (**1**) affords the desired 6-selenopurine ribosides (**2**). The detailed procedures for the preparation and purification of 6-selenoinosine (**2a**) and 6-selenoguanosine (**2b**) are provided below. This method provides a useful improvement in yield while significantly simplifying the literature procedures.[6a-c]

EXPERIMENTAL

6-Selenoinosine (**2a**). In a 100 ml serum bottle, a solution of sodium hydrogen selenide is prepared by treating 320 mg of sodium borohydride (85 mmol) and 302 mg of selenium (38 mmol) with 20 mL of water. A vigorous reaction ensues with the evolution of hydrogen. The bottle is loosely capped with a septum in order to allow the evolved hydrogen to displace the atmosphere. Within minutes the reaction is completed and a clear, colorless solution is obtained. 6-Chloropurine riboside **1a** (1.00 g, 35 mmol) is added in a single portion, the bottle firmly capped and flushed with argon. The solution is heated at 70°C for 10 minutes, chilled to ice bath temperature, and treated with 2 mL of glacial acetic acid. A yellow precipate forms. The solid is collected, washed with methanol, and dried under vacuum. The solid is recrystallized from degassed water (under argon) to afford 760 mg (66%) of glittering yellow plates of 6-selenoinosine **2a**, mp 209–211°C dec (Lit[6a]: 212–214°C).

6-Selenoguanosine (**2b**). A solution of sodium hydrogen selenide in 20 mL of water is prepared from 262 mg (33 mmol) of selenium and 320 mg (85 mmol) of sodium borohydride as described in **2a** above. 2-Amino-6-chloropurine riboside **1b** (1.00 g, 33 mmol) is added and the bottle is firmly capped and flushed with argon. The reaction mixture is heated at 75°C for 1.5 hour and then chilled to ice bath temperature and treated with 1 mL of glacial acetic acid. The solution is chilled for 48 hours and the yellow crystals which separate are collected. The product is dissolved in a hot, degassed solution of sodium carbonate (100 mL water and 200 mg of anhydrous sodium carbonate), filtered, and acidified with glacial acetic acid (2 mL). The solution is chilled and the crystals which separate are collected, washed with water, and dried. This affords 1.09 g (95%) of glittering yellow plates of 6-selenoguanosine **2b**, mp 204–206°C (Lit[6b]: 206–208°C)

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