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A facile halogenation of some hydroxyheterocycles using triphenylphosphine and *N*-halosuccinimide

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Abstract

Some hydroxyheterocycles were halogenated to give the corresponding haloheterocycles using triphenylphosphine and *N*-halosuccinimide. In comparison with the usual method using phosphorus oxyhalide, the haloheterocycles were easily isolated. © 1999 Elsevier Science Ltd. All rights reserved.

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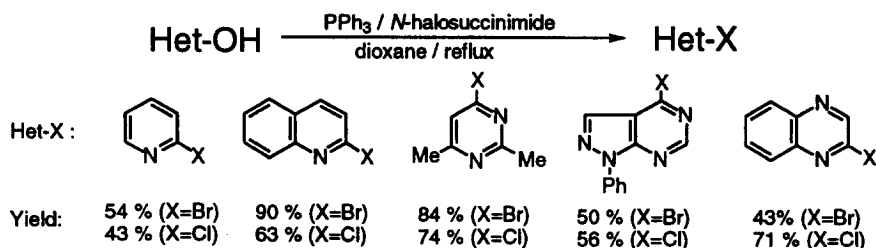
The halogeno-substituted π -deficient heterocycles are very useful intermediates in organic synthesis. They react with nucleophiles such as amines or alkoxides to give the corresponding substituted products, and are lithiated to introduce electrophiles via a halogen–lithium exchange reaction¹ or a tellurium–lithium exchange reaction.^{2,3} It is well known that hydroxyheterocyclic compounds are chlorinated to give chloroheterocyclic compounds^{4–7} using phosphorus oxychloride. Similarly, bromoheterocyclic compounds can be obtained using phosphorus oxybromide.^{7–9} These reagents are, however, very unwieldy on account of their moisture-sensitive nature. Furthermore, phosphorus oxybromide is too expensive for synthetic use. Thus, the development of new modes of halogenation without using a halogenating reagent such as phosphorus oxyhalide would be advantageous for many chemists.

Although the halogenation of alcohol using triphenylphosphine and *N*-halosuccinimide^{10–13} was accomplished 30 years ago, this reaction has not been applied to other substrates. Recently, Frøyen reported the halogenation of carboxylic acid using a combination of triphenylphosphine and *N*-bromosuccinimide.¹⁴ Thus, we speculated that this method could be applied to the bromination of hydroxyheterocyclic compounds. According to Frøyen's paper,¹⁴ a carboxylic acid is brominated to give the corresponding acyl bromide using triphenylphosphine and *N*-bromosuccinimide by heating for a few minutes. We tried the bromination of 2(1*H*)-quinolone using this method.

The experiment proceeded as follows: In a round-bottomed flask, *N*-bromosuccinimide (10 mmol) was added to a solution of triphenylphosphine (10 mmol) in dioxane (100 ml), and stirred at room temperature

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Table 1
Halogenation of some hydroxyheterocycles



for 30 min. A solution of 2(1*H*)-quinolone (2 mmol) was added to the suspension and the reaction mixture was heated to reflux for 4 h. Dioxane was removed under reduced pressure, and the residue was dissolved in dichloromethane and basified with triethylamine. The crude product was purified with SiO₂ chromatography (eluted with hexane:dichloromethane, 1:1) to give 2-bromoquinoline in 90% yield. Because this brominating reagent is inert to water, it does not require quenching with water. When one equivalent of triphenylphosphine and *N*-bromosuccinimide was used, 2-bromoquinoline was obtained only in 39% yield.

Next, we tried bromination or chlorination of some hydroxyheterocycles using this method. Some hydroxyheterocycles shown in Table 1 were converted into haloheterocycles.

To carry out this halogenation in good yield, it is necessary to use 2 to 5 equivalents of the halogenating reagent.

In this study, we have developed a facile halogenation of some heterocycles.

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