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Research Article

A facile preparation of (2,4,6-^{14}C)-cyanuric acid under solvent-free conditions

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Summary

(2,4,6-^{14}C)-Cyanuric acid was prepared from ^{14}C-urea by the heterocyclization of the latter in the presence of ammonium chloride. This procedure involves solvent-free fusing of the reactants in a vacuum sealed glass tube. The product was purified by ion-exchange column chromatography using Sephadex SE C-25. A radiochemical yield of 60.5% was obtained based on ^{14}C-urea and the product had a specific activity of 19.06 mCi/mmol. Copyright © 2002 John Wiley & Sons, Ltd.

Key Words: ^{14}C-urea; (2,4,6-^{14}C)-cyanuric acid; ammonium chloride fusion under vacuum

Introduction

Cyanuric acid is a key intermediate for the synthesis of a variety of organic compounds, which include herbicides and antitumour agents,[1] etc. The importance of this synthon prompted us to prepare the radiolabelled form for bioactive studies. Our aim was to prepare the (2,4,6-^{14}C)-cyanuric acid in a higher yield than previously reported[1,2]

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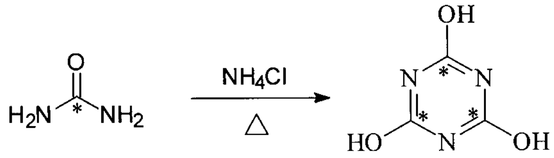
and also to make use of it for the synthesis of carbon-14 labelled herbicides such as prometryn, ametryn, etc.

In our approach, we have utilized the heterocyclization of urea, a procedure which was patented[3] in 1950. However, we have optimized the synthesis of (2,4,6-^{14}C)-cyanuric acid on a millimolar scale. The optimized conditions involve the fusion of radiolabelled urea in the presence of ammonium chloride at 250°C under vacuum.

In our cold synthesis, urea was cyclized to cyanuric acid under solvent free conditions in the presence of ammonium chloride under vacuum in a sealed glass tube at 250°C for a period of 20 min. The reaction product obtained was identified as cyanuric acid from its R_f value by comparison with the authentic sample.† The pure product was obtained by ion-exchange chromatography using Sephadex SE C-25. Further confirmation was also obtained by superimposable IR and UV spectra with an authentic sample. Likewise ^{14}C-urea was cyclized to give (2,4,6-^{14}C)-cyanuric acid (Scheme 1).



Scheme 1.

Experimental

The optimized reaction conditions were used for the synthesis of (2,4,6-^{14}C)-cyanuric acid.

(2,4,6-^{14}C)-Cyanuric acid

Vacuum dried 180 mg (3 mmol) of ^{14}C urea (20 mCi, specific activity 6.66 mCi/mmol) and 160.5 mg (3 mmol) of powdered ammonium chloride were introduced into a pyrex glass tube (dimensions 15 mm OD and 20 cm long). The contents were thoroughly mixed, the tube evacuated and flame sealed. The mixture was fused at 250°C for 20 min

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† Authentic sample obtained from Fluka.

in a muffle furnace. It was then allowed to cool to room temperature before opening. The crude reaction mixture was dissolved in 10 ml of hot distilled water and was filtered through a G-4 sintered funnel. The filtrate was made up to a known volume with distilled water and was assayed for radioactivity. The crude product contained 16.5 mCi. The radiochemical yield was 82.5%. The crude product was then analysed by TLC (silica gel F_{254} obtained from Merck) using the following three different solvent systems, coupled with autoradiography:

(A) *n*-butanol : acetic acid : water (4 : 1 : 1 v/v/v).
(B) *n*-propanol : ammonia solution (4 : 1 v/v).
(C) *n*-butanol : ammonia solution (4 : 1 v/v).

The products were resolved and located as three radioactive spots in the X-ray film and had R_f values as indicated in Table 1.

The major radioactive product was identified as (2,4,6-^{14}C)-cyanuric acid. The other two minor radioactive products were starting material (^{14}C-urea) and an unidentified radioactive by-product.

Purification of (2,4,6-^{14}C)-cyanuric acid

The reaction mixture was dried under vacuum and the product was suspended in 1 ml distilled water. It was loaded on to the Sephadex SE C-25 ion-exchange resin column (15 cm OD and 90 cm height) which was previously treated with 0.1 M hydrochloric acid solution and washed with water until neutral. The eluent was monitored using a GM counter for radioactivity. The products were then eluted with water and the fractions were collected. The radioactive fractions were analysed by TLC coupled with autoradiography. Fractions corresponding to (2,4,6-^{14}C)-cyanuric acid were pooled. The radioactivity of the pure product of known weight was assayed using a liquid scintillation counter (Packard Tri Carb 4530 liquid scintillation counter with

Table 1

Product	R_f value		
	Solvent system		
	A	B	C
^{14}C-Urea	0.639	0.597	0.477
(2,4,6-^{14}C)-Cyanuric acid	0.727	0.465	0.153
Unidentified ^{14}C impurity	0.532	0.682	0.586

scintillation cocktail containing dioxane (1000 ml), naphthalene (100 g), PPO (5 g), POPOP (0.5 g) per litre). Radioactivity: 12.1 mCi and specific activity: 19.6 mCi/mmol. Radiochemical yield: 60%.

Results and discussion

The optimized conditions were determined by varying the amount of ammonium chloride and carrying out the reaction under vacuum for different times. Thus, the use of equimolar quantities of ammonium chloride and urea and the fusion temperature of 250°C for 20 min under vacuum ($\sim$1 mm) were found to be the best for maximizing the yield. The salient feature of our simple approach for heterocyclization is a solvent-free condition. This novel approach for the preparation of (2,4,6-^{14}C)-cyanuric acid resulted in higher radioactive yield[2] than had been previously reported.

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References

1. Nam NH, Hoellinger H, Pichat L, *J Label Compd Radiopharm* 1976; **12**: 517–521.
2. Murray III A, Williams DL. Organic syntheses with isotopes, Part I. *Compound of Isotopic Carbon*, Interscience Publishers, Inc.: New York, 1958; 795.
3. Mackay J. U.S. 2,527,316, 1950.