

Research Article

Synthesis of [1,2-¹⁴C]trichloroacetic acid

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Summary

A growing interest in the phytotoxic effects of trichloroacetic acid (TCA) has led us to develop a small-scale (<1 mmol) one-pot synthesis of [1,2-¹⁴C]TCA with >70% yield and specific activity of 3.7 GBq/mmol. Copyright © 2001 John Wiley & Sons, Ltd.

Key Words: [1,2-¹⁴C]trichloroacetic acid; one-pot synthesis

Introduction

Trichloroacetic acid (TCA) – a secondary air pollutant formed in the atmosphere by photooxidation of C₂-chlorocarbons – is considered to be an important phytotoxic stress factor which influences the health status of forests. Radioindicator techniques using [1,2-¹⁴C]TCA have often been employed to study the behaviour of TCA in the soil and its effects on conifers.^{1–3} However, [1,2-¹⁴C]TCA of high specific activity is not commercially available and the methods described in the literature^{4–6}

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do not lend themselves to small (<1 mmol) scale synthesis at high specific activity.

The described synthetic methods^{4,5} are multistep syntheses starting from [¹⁴C]acetate, [¹⁴C]acetylene or [¹⁴C]acetaldehyde or they only involve mono-¹⁴C-substitution.⁶ Blanchard⁷ used photochlorination of [2-¹⁴C]acetic acid of low specific activity with subsequent ion-exchange chromatographic purification.

Using the publications of Sonia *et al.*⁸ and Abrams *et al.*⁹ as base and building upon our own experience in synthesizing [¹⁴C]bromoacetic acid by direct halogenation of sodium [¹⁴C]acetate in the presence of sulphur¹⁰, we have developed¹² a method for the small-scale synthesis of [1,2-¹⁴C]TCA. Potassium or sodium [1,2-¹⁴C]acetate of maximum specific activity reacts almost quantitatively with gaseous chlorine to produce [1,2-¹⁴C]TCA in the presence of sulphur, red phosphorus and potassium iodide in a closed system.

Experimental

Chemicals: Potassium [1,2-¹⁴C]acetate of 3.7 GBq/mmol was obtained from ÚVVVR (Prague, Czech Republic). Elemental chlorine was synthesized from KMnO₄ and HCl. Other chemicals and solvents of analytical grade quality were obtained from Merck (Darmstadt, Germany) and Fluka (Deisenhoven, Germany).

Apparatus for the synthesis: The synthesis was performed using the standard vacuum line¹¹ and a thick-walled reaction tube (ampoule).

Analytical methods and separation techniques: The radioactivity was measured with the LS 6500 liquid scintillation counter (Beckman, USA). For purification of the product preparative HPLC was carried out on a 250 × 8 mm polymer IEX column (8 μm) in H⁺ form (Watrex, Praha, Czech Republic) with 0.02 M H₃PO₄ as the eluent. The radiochemical purity was checked by a modified TLC method.¹³ Thin-layer chromatograms were developed on cellulose F (Merck, Darmstadt, Germany) with *n*-butanol–ammonia–water (84–1–14) and measured with the Linear Analyzer LB-283 (Laboratorium Berthold, Wildbad, Germany). [1,2-¹⁴C]TCA was analysed by GC-MS using the Finnigan MAT ITD 800 (San Jose, USA) mass spectrometer in connection with the gas chromatograph Varian 3400 (Walnut Creek, USA) equipped with a DB-5 capillary column (30 m × 0.25 mm ID, film thickness *d_f* 0.25 μm, J&W, Folsom, USA).³

Table 1. Synthesis of [1,2-¹⁴C]TCA from 0.1 mmol potassium [1,2-¹⁴C]acetate

No.	Reaction condition				Product composition	
	Catalyst	Cl ₂ (mmol)	T (°C)	Time (h)	DCA [†] (%)	TCA [‡] (%)
1	S	1.0	<180	2 × 6	<50	<30
2	S	2.06	>180	2 × 7.5	>30	>50
3	P/S	2.0	<180	3 × 6	50	30
4	KI/P/S	2.2	117	22	<5	≤5
5	KI/P/S	2.0	>180	4	50	50
6	KI/P/S	2.0	180	18	<5	>95
7	KI/P/S/I ₂	2.2	180	23	<2	>98

[†][1, 2-¹⁴C]dichloroacetic acid.

[‡][1, 2-¹⁴C]trichloroacetic acid.

Synthetic procedure: A 30 ml thick-walled glass ampoule was charged with 0.1 mmol potassium [1,2-¹⁴C]acetate in 1 ml methanol, 0.1 mg red phosphorus, 0.1 mg potassium iodide and a solution of 2 mg sulphur in 2 ml benzene. The solvents were removed by lyophilization, resulting in a very fine, homogeneous mixture of the reaction components. Water-free elemental chlorine (3 mmol) was added via the vacuum line and the ampoule was sealed. The reaction was performed by heating the mixture at 180°C in a bath of boiling diethylene glycol diethylether for 24 h. The non-reacted chlorine and hydrochloric acid were separated from the reaction mixture by lyophilization at -80°C. The residue was dissolved in 2 ml water and distilled on the vacuum line. [1,2-¹⁴C]TCA was separated from the aqueous solution by HPLC. The concentration of [1,2-¹⁴C]TCA was 2 µmol/ml (7.4 MBq/ml). The average yield was >70%, the radiochemical purity >98%.

Results

The results of the experiments with varying catalyst composition, reaction temperatures, and reaction times are shown in Table 1. Experiment No. 7 offers the optimal conditions for the synthesis of [1,2-¹⁴C]TCA with maximum specific activity on the µmol-scale.

The self-decomposition of [1,2-¹⁴C]TCA in aqueous solution is negligible. This has been shown by re-analysis after 1 year of storage in refrigerator several times.

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