

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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Contract/grant sponsor: Grant Agency of the Czech Republic; contract/grant number: 522/99/1465;

Contract/grant sponsor: Framework of the agreement concerning scientific–technical co-operation between Federal Republic of Germany and the Czech Republic; contract/grant number: X.244.2

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*Received 2 April 2001
Revised 4 June 2001
Accepted 12 June 2001*

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 ÚVVR (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.

Acknowledgements

The research was supported via Grant No. 522/99/1465 of the Grant Agency of the Czech Republic. Support was also provided in the

framework of the agreement concerning scientific–technical cooperation between Federal Republic of Germany and the Czech Republic, Project No. X.244.2 ‘Isotopically labelled compounds in the investigations of biotransformations of important xenobiotics’ and is gratefully acknowledged.

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