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A facile synthesis of high specific activity sodium [1-^{14}C] lauryl sulphate under microwave irradiation

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Summary

A highly efficient and optimized synthesis of sodium[1-^{14}C] lauryl sulphate having high specific activity (50 mCi/mmol) is described. Lauric acid was converted to undecyl bromide using a modified Hunsdiecker reaction. This was treated with potassium ^{14}C cyanide (specific activity 50 mCi/mmol) using phase transfer catalysis to yield [1-^{14}C]lauronitrile, which was subsequently hydrolysed with a mixture of concentrated hydrochloric acid:propionic acid (1:2 v/v) under microwave irradiation for 2 min to obtain [1-^{14}C] lauric acid in quantitative yield. The latter on reaction with chlorosulphonic acid and subsequent neutralization with sodium bicarbonate yielded the title compound.

Key Words: [1-^{14}C]lauronitrile; hydrolysis; microwave; [1-^{14}C]lauric acid; sodium [1-^{14}C]lauryl sulphate

Introduction

Sodium [1-^{14}C] lauryl sulphate having high specific activity (50 mCi/mmol) is required for use as a radiotracer in studies related to: (a) the correlation of the inflammatory response associated with skin barrier function damage induced by sodium lauryl sulphate; (b) its skin permeability; and (c) evaluation of the kinetics of its skin reaction. Preparation of higher fatty acids using Grignard carbonation, a synthetic route often employed, requires scrupulously dry conditions and relatively large amounts of substrate for the preparation of the Grignard reagent. Moreover, it can be time consuming. Due to the ease with which a cyano group can be introduced to different moieties by methods such as nucleophilic displacement, addition to carbonyl groups of aldehydes and ketones, hydrocyanation of α, β unsaturated compounds and aromatic substitution into various molecules, the nitrile function is an extremely useful

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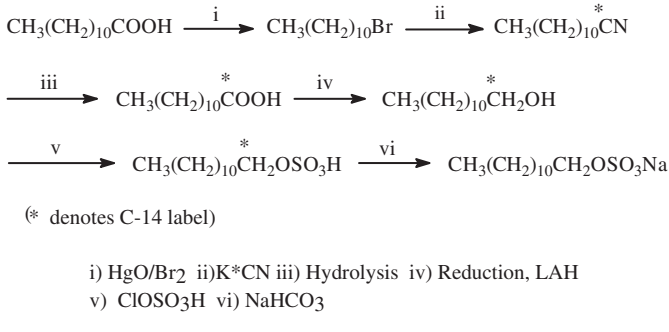
precursor for carboxylic acids. Hence, a preferred route for the preparation of long chain fatty acids is by the hydrolysis of the corresponding nitriles. Various methods are reported in the literature for the hydrolysis of nitriles.[1–10] These methods are generally carried out at high temperatures (100–190°C) and can be time consuming. Hence, these methods, although applicable, are not quite suitable for the preparation of radioisotopically labelled carboxylic acids, as prolonged heating at high temperature can often lead to poor yields due to the radiolytic decomposition. In recent times, microwave technology has taken an undeniable place in chemical laboratory practice as a very effective and non-polluting method of activating reactions.[4] Examples of the use of this technology in organic synthesis are numerous.[11] The use of microwaves provides fast heating of the chemicals above their boiling points thus enhancing the reaction rates and dramatically reducing the reaction times in comparison with conventional heating. Generally degradation reactions do not occur using microwave heating thereby enhancing yields.[12] Chemat has reported the preparation of carboxylic acids from their corresponding nitriles in 30 min by a dry hydrolysis reaction using microwave technology with phthalic acid or anhydride in the absence of water and solvent.[13]

We report here a facile and convenient preparation of sodium [1-^{14}C] lauryl sulphate by hydrolysis of [1-^{14}C] lauronitrile using a hydrochloric acid/propionic acid system under microwave irradiation followed by reaction with chlorosulphonic acid and neutralization with alkali, see Scheme 1.

Lauric acid on decarboxylative bromination with red mercuric oxide and bromine gave undecyl bromide (confirmed by PMR showing a triplet at $\delta = 3.38$, ($J = 5$ Hz) due to the proton of the methylene group next to the bromine). This was also further confirmed by the absence of bands at 3500–3000 and 1710 cm^{-1} corresponding to acid hydroxyl group and acid carbonyl group in the IR spectrum. This was treated with potassium ^{14}C cyanide (specific activity 50 mCi/mmol) using phase transfer catalysis to yield [1-^{14}C]lauronitrile, which was hydrolysed using the hydrochloric acid/



Scheme 1.

propionic acid system under microwave irradiation for 2 min. The formation of the [1-^{14}C] lauric acid was confirmed by TLC followed by autoradiography and IR spectroscopy, by comparison with the data reported in the literature and with an authentic sample. The absence of a band at 2250–2200 cm^{-1} and presence of bands at 3500–3000 cm^{-1} corresponding to the carboxylic acid and 1710 cm^{-1} due to the acid carbonyl group confirmed the formation of the acid. The product was subsequently reacted with chlorosulphonic acid at room temperature followed by neutralization to furnish sodium [1-^{14}C] lauryl sulphate.

Experimental

Undecyl bromide: Bromine (4 g, 1.3 ml, 25 mmol) was added dropwise to a stirred mixture of lauric acid (5 g, 25 mmol) and red mercuric oxide (3.44 g, 5.8 mmol) in carbon tetrachloride (150 ml) over a period of 30 min at room temperature. Thereafter the reaction mixture was slowly heated to reflux and heating is continued for a further period of 2 h. It was cooled to room temperature, filtered and the filter cake washed with carbon tetrachloride. The combined organic layer was washed with water, brine and dried. Removal of solvent and subsequent distillation at 138°C and 18 mm of Hg afforded undecyl bromide (4.7 g, 80%). IR 2960, 1470, 1260 PMR δ 0.9 (br, 3H), 1.2(m, 18H), 3.38(t, 24, $J = 5$ Hz).

[1-^{14}C] lauronitrile: Toluene (2.5 ml) was added to undecyl bromide (0.1 ml, 0.44 mmol), potassium ^{14}C-cyanide (6.0 mCi, specific activity 50 mCi/mmol, 0.12 mmol), tetrabutylammonium bromide (70 mg) and water (0.13 ml). The reaction mixture was heated at reflux for 6 h and extracted with ether (3×15 ml). After removal of the solvent, the residue was purified by column chromatography (silica, 0–15% ethyl acetate in hexane) to yield pure [1-^{14}C]lauronitrile (5.8 mCi, 96%). TLC (silica, 15% ethyl acetate in hexane v/v). R_f for undecylbromide 0.9 and R_f for [1-^{14}C] lauronitrile 0.5.

[1-^{14}C]lauric acid: [1-^{14}C]lauronitrile (0.114 mmol, 5.7 mCi) and a mixture of concentrated hydrochloric acid:propionic acid (1:2 v/v, 300 µl) in a sealed glass ampoule, was heated using a domestic microwave oven, for 2 min. The ampoule was cut open and the reaction mixture was extracted with ether. The product obtained was purified by column chromatography (silica, 15% ethyl acetate in hexane) giving [1-^{14}C] lauric acid in quantitative yield. The formation of [1-^{14}C] lauric acid was confirmed by TLC (silica gel, 15% ethyl acetate in hexane v/v) followed by autoradiography and IR spectroscopy. R_f for [1-^{14}C] lauric acid was 0.2 and R_f for [1-^{14}C]lauronitrile was 0.5. IR 3500–3000, 1710 cm^{-1}.

[1-^{14}C] lauryl alcohol: [1-^{14}C] lauric acid (0.11 mmol, 5.5 mCi, 50 mCi/mmol) in dry ether (10 ml) was added to a solution of $LiAlH_4$ (36 mg) in 25 ml dry ether and heated at reflux for 1 h. The reaction mixture was quenched with

ethyl acetate. The solution was filtered and the organic layer was washed with water, brine, and dried. Removal of the solvent and subsequent purification of the residue by column chromatography (silica, 0–25% ethyl acetate in hexane) gave pure [1-^{14}C] lauryl alcohol (5.3 mCi, 96%). TLC (silica, hexane:ethyl acetate 10:2 (v/v) R_f 0.9).

Sodium [1-^{14}C] lauryl sulphate: [1-^{14}C] Lauryl alcohol (0.1 mmol, 5.1 mCi) in chloroform (10 µl) was treated with chlorosulphonic acid (8 µl, 0.11 mmol) and the mixture was stirred at room temperature for 30 min. The reaction mixture was neutralized with sodium bicarbonate and dried under reduced pressure. The residue was taken up in ethyl acetate and was loaded on to a silica column. The column was washed with ethyl acetate and with methanol to elute pure sodium [1-^{14}C] lauryl sulphate (5 mCi, 98%). The purity was checked by TLC (silica, hexane:ethyl acetate 10:2 (v/v), R_f 0.05).

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