A Convenient Synthesis of 14C-Anthralin

Eine einfache Synthese für 14C-Anthralin

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renewed interest in this topic, mostly directed toward the investigation of anthracenediones described by Bhawal et al.11 Hence, the commercially available 14C-source [2-14C]-cyanoacetic acid (1) was esterified with diazomethane to give the required methyl 2-14C-cyanoacetate (2). Ester 2, upon reaction with the arylene obtained from 3-bromoanisole and lithium disopropylamide (LDA), gave [10-14C]-cyano-9-hydroxy-1,8-dimethoxyanthracene (3) directly. - The mechanism of this reaction has been suggested to consist of two pathways: a non-concerted [2 + 2] cycloaddition involving a tandem-addition rearrangement, and an arylene [4 + 2] cycloaddition11. - Oxidation of 3 with hydrogen peroxide in alkaline solution11 gave [10-14C]-1,8-dimethoxy-9,10-anthracenedione (4) in 80% yield. Final reduction of 4 with SnCl₂ in acetic acid/hydrochloric acid proceeded with concomitant ether cleavage and cleanly produced [10-14C]-anthralin (5) in 86% yield.

Experimental Part

Melting points: Büchi 510 melting point apparatus, uncorrected.- EIMS: Varian MAT 311A (70 eV).- Analytical TLC: EM Science precoated TLC plates with silica gel F-254.- Tetrahydrofuran (THF) and disopropylamine were distilled from LiAlH₄ and CaCl₂, respectively. All other organic reagents were distilled before use.- [2-14C]-cyanoacetic acid: American Radio-labeled Chemicals Inc.- n-Butyllithium (n-BuLi) and Diazald: Aldrich Chemical Co.- 3-Bromanisole: Fluka Chemie AG.- All reactions were carried out in flame-dried flasks under N₂. Radioactivity was measured using LSC (Liquid Scintillation Counter) "Quantulus" 1220 (LKB Wallac).

Methyl [2-14C]-cyanoacetate (2)

In a glove box (Atmos Bag, Aldrich) filled with N₂, [2-14C]-cyanoacetic acid (55 mCi/mmol = 23.9 GBq/g) was dissolved in abs. ether and mixed with unlabelled cyanoacetic acid (0.85 g, 10 mmol) in 10 ml of abs. ether. The solution was cooled to 0°C, and a cooled ether solution of diazomethane was added in small portions. After stirring for 1 h, the mixture was dried over Na₂SO₄, distilled, and afforded 0.9 g (91%) of 2, sufficiently pure for the next step.

[10-14C]-10-Cyano-9-hydroxy-1,8-dimethoxyanthracene (3)

To a cooled (~78°C) solution of 2 (0.9 g, 9.1 mmol) in 10 ml of abs. THF, a cold solution of LDA (15 mmol in 30 ml in THF) was added over a period of 20 min, then the solution was stirred at ~78°C for 15 min. Bromoanisole (3.8 g, 20 mmol) in 50 ml of abs. THF was added rapidly, the solution was warmed to ~40°C, and a cooled (~40°C) solution of LDA (30 mmol in 50 ml of abs. THF) was added slowly (ca. 30 min). The solution was stirred for an additional 10 min, then allowed to warm to room temp.,
quenched with 20 ml of satd. NH₄Cl solution, and the solvent was evaporated in vacuo. The residue was dissolved in CH₂Cl₂ (200 ml) and washed with dil. HCl (50 ml), then with a satd. aq. solution of NaCl, dried over Na₂SO₄, and concentrated (rotary evaporator) to afford a sufficiently pure labelled substance, homogeneous by TLC (CH₂Cl₂, Rf: 0.7). Yield 360 mg, mp. 261°C [lit.¹]: 261-262°C.- An experiment using a higher excess of arynes did not increase the incorporation rate of the label but triggered the formation of the pertinent tryptene derivative and non-identified side products (tic).

[10-¹⁴C]-1,8-Dimethoxy-9,10-anthracenedione (4)

To a solution of 3 (360 mg, 1.3 mmol) in 50 ml of ethanol was added in one portion an aqueous solution containing 10% NaOH (10 ml) and 30% H₂O₂ (10 ml). The mixture was stirred for 5 h at 75°C and then at room temp. for 12 h. The mixture was cooled to 0°C, the precipitated anthracenedione was filtered, washed with water, and dried to give a pure product: 280 mg (80%), mp. 223°C [lit.¹²]: 223-224°C.- EIMS (70 eV): m/z 268 (54), 253 (100), 251 (20), 152 (18), 139 (19).

To a refluxing solution of 4 (250 mg, 0.93 mmol) in glacial acetic acid (20 ml) a solution of 40% SnCl₂ in 37% HCl (5.0 ml) was added dropwise over 3 h. The solution was poured into 10 ml of ice water, and the resulting yellow precipitate was collected by filtration. Recrystallization from acetic acid afforded 5: 180 mg (86%), mp. 170°C [lit.¹³]: 169-171°C. EIMS (70 eV): m/z 227 (15), 226 (100), 225 (5), 198 (11), 197 (13), 152 (9), 151 (8).

[10-¹⁴C]-1,8-Dihydroxy-9(10H)-anthracenone (5)

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References


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