

Supporting Information

Highly efficient syntheses of [methyl-¹¹C]thymidine and its analogue 4'-[methyl-¹¹C]thiothymidine as nucleoside PET probes for cancer cell proliferation by Pd⁰-mediated rapid C-[¹¹C]methylation

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1. General Information
2. a) HPLC chart for co-injection of **1** (retention time: 10.5 min), b) HPLC chart for co-injection of **4** (retention time: 12.0 min), c) HPLC chart for co-injection of [¹¹C]**1** (retention time: 6.8 min), d) HPLC chart for co-injection of [¹¹C]**4** (retention time: 7.4 min).

3. a) HPLC chart after the rapid [^{11}C]C-methylation of [^{11}C]CH₃I and **6**, giving [^{11}C]**1** (retention time: 12.5 min), and b) HPLC chart after purification of [^{11}C]**1**
4. a) HPLC chart after the rapid [^{11}C]C-methylation of [^{11}C]CH₃I and **5**, giving [^{11}C]**4** (retention time: 12.5 min), and b) HPLC chart after purification of [^{11}C]**4**

1. General information

Instrument: Shimadzu HPLC system with a system controller (SCL-10AVP), a degasser (DGU-12A), a liquid chromatograph (LC-10AT and LC-10ATVP), a column oven (CTO-10AVP), an UV-vis detector (SPD-10A), and software (CLASS-VP); column, SHIM-PACK CLC-ODS (6.0 mm I.D. × 250 mm, SHIMADZU); mobil phase, CH₃CN:100 mM NaH₂PO₄ containing 200 mM NaClO₄ (pH 2) (6:94, v/v); flow rate, 1.0 mL min⁻¹; detection, UV 260 nm; column temperature, 40 °C; retention time, thymidine (**1**), 10.7 min.

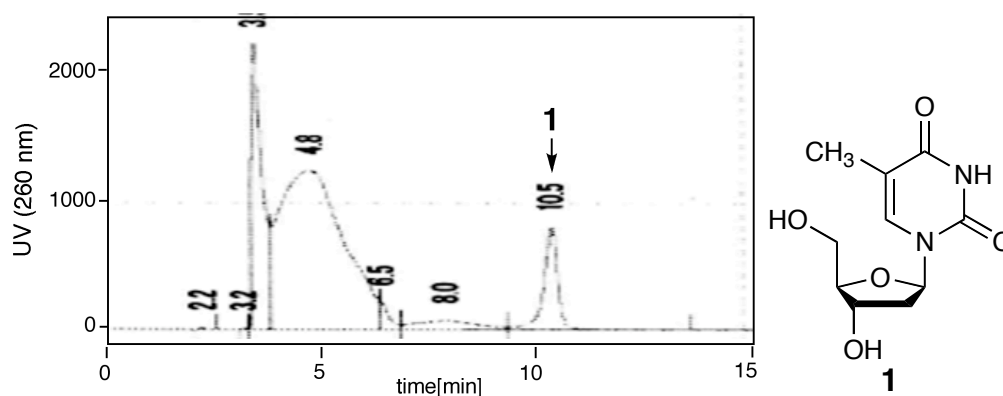
Instrument: JASCO HPLC system with a chromatography interface (LC-Net II/ADC), a quaternary HPLC pump (PU-2089Plus), a diode array detector (MD-2010Plus), a column oven (CO-2065Plus), a recycling valve unit (RV-2080-02), and software (chrom NAV chromatography data system); column, SHIM-PACK CLC-ODS (6.0 mm I.D. × 150 mm, SHIMADZU); mobil phase, CH₃CN:100 mM NaH₂PO₄ containing 200 mM NaClO₄ (pH 2) (6:94, v/v); flow rate, 1.0 mL min⁻¹; detection, UV 260 nm; column temperature, 40 °C; retention time, 4'-thiothymidine (**4**), 12.0 min; 2'-deoxy-4'-thiouridine (**8**), 6.8 min.

Shimadzu HPLC system with a system controller (CBM-20A), an online degasser (DHU-20A₃), a solvent delivery unit (LC-20AD), a column oven (CTO-20AC), a photodiode array detector (SPD-20A), and software (LC solution) and an Aloka radioanalyzer (RLC-700).

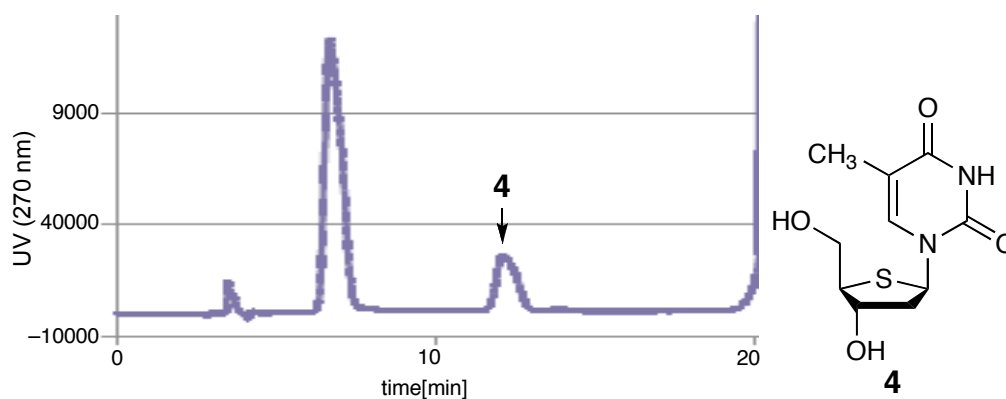
Preparative HPLC conditions: semi-preparative column, Gemini 5 C18 (21.2 mm I.D. × 250 mm, Phenomenex); mobile phase, CH₃CN:100 mM NH₄HCO₃ (pH 7.8) (4:96, v/v); flow rate, 9.9 mL min⁻¹; detection, UV 265 nm; retention time of [methyl-¹¹C]thymidine, 12.5 min; mobile phase, CH₃CN:100 mM NH₄HCO₃ (pH 7.8) (7:93, v/v); flow rate, 9.9 mL min⁻¹; detection, UV 270 nm; retention time of 4'-[methyl-¹¹C]thiothymidine, 12.5 min.

Analytical HPLC conditions for determination of purity: column, Luna 5 C18 (4.6 mm I.D. × 150 mm, Phenomenex); mobile phase, CH₃CN:100 mM NH₄HCO₃ (pH 7.8) (4:97, v/v); flow rate, 1.0 mL min⁻¹; detection, UV 265 nm; retention time of [methyl-¹¹C]thymidine, 6.9 min; mobile phase, CH₃CN:100 mM NH₄HCO₃ (pH 7.8) (8:93, v/v); flow rate, 1.0 mL min⁻¹; detection, UV 270 nm; retention time of 4'-[methyl-¹¹C]thiothymidine, 7.5 min.

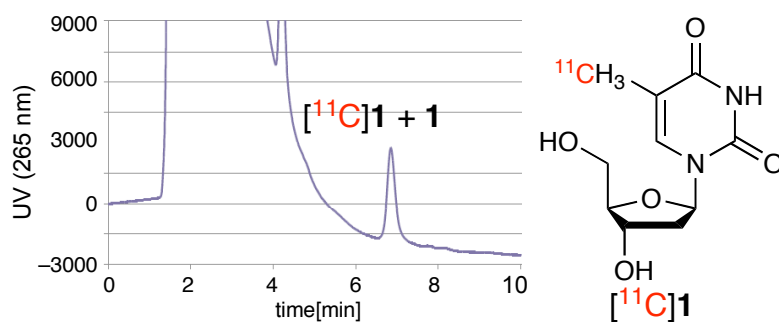
2. a) HPLC chart for co-injection of **1** (retention time: 10.5 min)



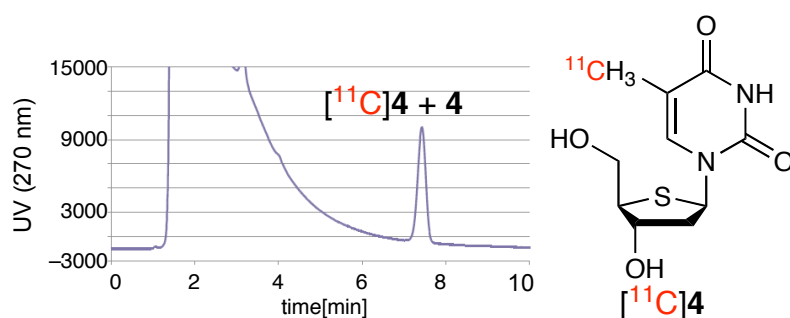
b) HPLC chart for co-injection of **4** (retention time: 12.0 min)



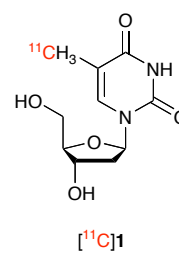
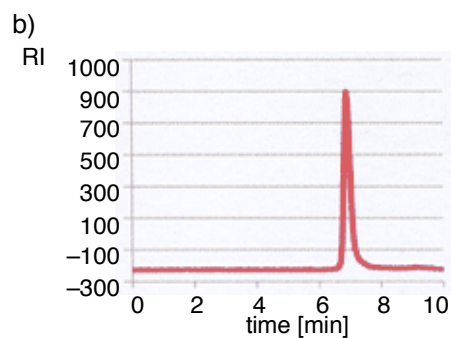
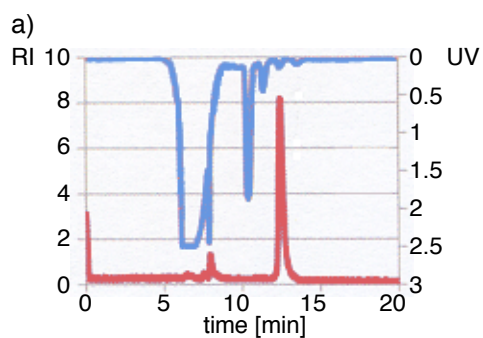
c) HPLC chart for co-injection of [^{11}C]**1** (retention time: 6.8 min)



d) HPLC chart for co-injection of [^{11}C]**4** (retention time: 7.4 min)



3. a) HPLC chart after the rapid [^{11}C]C-methylation of [^{11}C]CH₃I and **6**, giving [^{11}C]**1** (retention time: 12.5 min), and b) HPLC chart after purification of [^{11}C]**1**.



3. a) HPLC chart after the rapid [¹¹C]C-methylation of [¹¹C]CH₃I and **5**, giving [¹¹C]**4** (retention time: 12.5 min), and b) HPLC chart after purification of [¹¹C]**4**

