Electronic Supplementary Material (ESI) for ChemComm.

Last-Step ^{18}F-Fluorination of Supported 2-(Aryl-di-*tert*-Butylsilyl)-*N*-Methyl-Imidazoles Conjugates for Applications in Positron Emission Tomography.

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Electronic Supplementary Information

Table of Contents

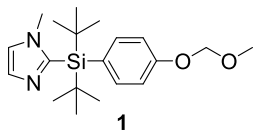
A) Organic syntheses

a) General methods

All commercial materials were used without further purification, unless indicated. ^{1}H NMR and ^{13}C NMR were recorded on BRUKER AVANCE I 300 Mhz (^{1}H: 300MHz, ^{13}C: 75.3MHz, ^{19}F: 282.3 MHz, ^{29}Si: 59.6 MHz), BRUKER AVANCE II 400 Mhz (^{1}H: 400MHz, ^{13}C: 100.2 MHz, ^{19}F: 376.3 MHz, ^{29}Si: 79.5 MHz) or BRUKER AVANCE III 600 Mhz (^{1}H: 600MHz, ^{13}C: 150.3 MHz, ^{19}F: 564.5 MHz, ^{29}Si: 119.2 MHz) spectrometers. The chemical shifts for the NMR spectra are reported in ppm relative to the solvent residual peak. Coupling constants J are reported in hertz (Hz). The following abbreviations are used for the multiplicities: s, singlet; d, doublet; t, triplet; q, quartet; qt, quintet; st, sextet; m, multiplet; br, broad; dd, doublet of doublet. Yields refer to isolated material determined to be pure by NMR spectroscopy and thin-layer chromatography (TLC), unless specified in the text. Analytical TLC was performed on Fluka Silica Gel 60 F254. High resolution mass spectra were performed by the CESAMO (Talence, France) and were recorded on Qq-TOF tandem mass spectrometer (API Q-STAR Pulsari, Applied Biosystems). Experiments under microwave irradiation were performed using a Biotage Initiator 2.5. UPLC coupled with mass were performed on an ACQUITY UPLC® using a Column ACQUITY UPLC® BEH C18 (1.7µm, 2.1 x 50mm) heated at 60°C. Samples were eluted with a flow of 0.5 mL/min using programs (eluent A = H_2O + HCOOH 0.1% and eluent B = MeCN + HCOOH 0.1%). The PDA detector was a SQD and the mass detector was a NOISE NRVP-B (INPUT: DC 12V 500 mA). The mass program was done in ES^+ and ES^-, using m/z: 100-1000 or 200-2000, scan time 0.2, cone voltage 30 V, from 0 to 6 min.

*b) Syntheses of **1-6** and **PS-7***

2-(Di-*tert*-butyl(4-(methoxymethoxy)phenyl)silyl)-1-methyl-1*H*-imidazole 1



1

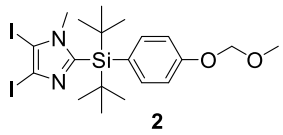
In a first flask (**flask 1**) under nitrogen, 1-methylimidazole (78 mg, 0.95 mmol, 1eq.) was dissolved in dry THF (0.5 mL) and a *n*-butyllithium solution (1.2M in hexane, 0.87 mL, 1.05 mmol, 1.2 mol/L, 1.1 eq.) was added at -80°C. Then, the reaction mixture was stirred at rt for 10 min.

At the same time, 1-bromo-4-(methoxymethoxy)benzene (315 mg, 1.45 mmol, 1.5eq.) was dissolved in dry THF (1 mL) in a second flask under nitrogen (**flask 2**), and a *n*-butyllithium solution (1.2M in hexane, 2.2 mL, 2.64 mmol, 2.7eq.) was added at -80°C. The reaction mixture was stirred at -80°C for 30 min and then 10 min at rt.

In a third flask (**flask 3**) under nitrogen, di-*tert*-butylsilanediyl bis(trifluoromethanesulfonate) (203 mg, 1.56 mmol, 1.7eq.) was dissolved in dry THF (2.5 mL) at room temperature and then cooled to -80°C. The reaction mixture of **flask 1** was slowly added by syringe in **flask 3** at -80°C before adding consecutively the reaction mixture of **flask 2** by syringe into **flask 3** at -80°C. The mixture of **flask 3** was stirred for 16h while being allowed to slowly return to rt. Then, the crude reaction mixture was concentrated under reduced pressure and purified by column chromatography on silica gel (cyclohexane/EtOAc: 90/10; Rf = 0.3) to obtain compound **1** (115 mg, 33%) as a brown powder. ^{1}H NMR analysis was in accordance to the data previously reported:[1] **^{1}H NMR (300 MHz, $CDCl_3$) :** δ (ppm) 7.53 (d, *J* = 8.7 Hz, 2H), 7.32 (d, *J* = 0.8 Hz, 1H), 7.03 (d, *J* = 8.7 Hz, 2H), 6.99 (d, *J* = 1 Hz, 1H), 5.20 (s, 2H), 3.50 (s, 3H), 3.42 (s, 3H), 1.15 (s, 18H).

[1] M. Tisseraud, J. Schulz, D. Vimont, M. Berlande, P. Fernandez, P. Hermange and E. Fouquet, *Chem. Commun.,* 2018, **54**, 5098-5101.

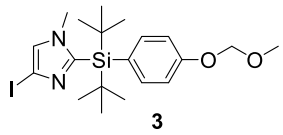
2-(Di-*tert*-butyl(4-(methoxymethoxy)phenyl)silyl)-4,5-diiodo-1-methyl-1*H*-imidazole 2



2

Under nitrogen, **1** (273 mg, 0.76 mmol, 1 eq.,) was dissolved in acetonitrile (3 mL), and *N*-iodosuccinimide (513 mg, 2.28 mmol, 3 eq.,) was added at room temperature. The reaction was stirred for 24h at 60°C. Then, the solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel (cyclohexane/CH_2Cl_2 : 50/50 ; Rf = 0.4) to give **2** (377 mg, 81%) as a yellow powder. **^{1}H NMR (300 MHz, $CDCl_3$) :** δ (ppm) 7.50 (d, *J* = 8.5 Hz, 2H), 7.04 (d, *J* = 8.7 Hz, 2H), 5.21 (s, 2H), 3.51 (s, 3H), 3.41 (s, 3H), 1.13 (s, 18H); **^{13}C NMR (75 MHz, $CDCl_3$) :** δ (ppm) 158.5, 154.6, 137.6 (2C), 126.0, 115.7 (2C), 97.5, 94.3, 86.6, 56.4, 40.2, 29.4 (6C), 20.9 (2C); **^{29}Si NMR (59 MHz, $CDCl_3$) :** δ (ppm) -5.24 ; **HRMS (ESI/TOF$^+$) :** $C_{20}H_{30}N_2O_2SiI_2$ $[M+Na]^+$ calculated 635.0058, found 635.0081.

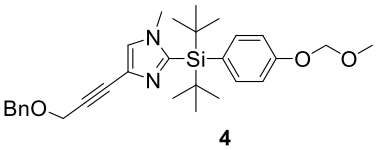
2-(Di-*tert*-butyl(4-(methoxymethoxy)phenyl)silyl)-4-iodo-1-methyl-1*H*-imidazole 3



3

Under nitrogen, **2** (136 mg, 0.22 mmol, 1 eq.,) was dissolved in dry THF (4 mL), a solution of ethylmagnesium bromide in Et_2O (3.0 M, 81µL, 0.24 mmol, 1.1 eq.,) was added at 0°C. The reaction was stirred 30 min at 0°C. Saturated aqueous solution of ammonium chloride (20 mL) was added to quench the reaction and the aqueous layer was extracted three times with ethyl acetate (3x 20 mL). The combined organic layers were washed with brine (20 mL) and dried over sodium sulfate. The solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel (cyclohexane/ CH_2Cl_2 : 50/50 ; Rf = 0.3) to give **3** (102 mg, 95%) as a yellow oil. **^{1}H NMR (300 MHz, $CDCl_3$) :** δ (ppm) 7.50 (d, *J* = 8.7 Hz, 2H), 7.04 (s, 1H), 7.03 (d, *J* = 8.6 Hz, 2H), 5.20 (s, 2H), 3.50 (s, 3H), 3.39 (s, 3H), 1.14 (s, 18H); **^{13}C NMR (75 MHz, $CDCl_3$) :** δ (ppm) 158.4, 151.4, 137.6 (2C), 128.4, 126.5, 115.6 (2C), 94.3, 83.6, 56.3, 36.6, 29.4 (6C), 20.8 (2C); **^{29}Si NMR (59 MHz, $CDCl_3$) :** δ (ppm) -6.83; **HRMS (ESI/TOF$^+$) :** $C_{20}H_{31}N_2O_2SiI$ $[M+Na]^+$ calculated 509.1091, found 509.1108.

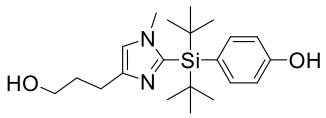
2-(Di-*tert*-butyl(4-(methoxymethoxy)phenyl)silyl)-4--(3-(benzyloxy)prop-1-ynyl)-1-methyl-1*H*-imidazole 4



4

Under nitrogen, $Pd(PPh_3)_4$ (6.9 mg, 6 µmol, 0.05 eq.,), CuI (2.3 mg, 12 µmol, 0.1 eq.,) and **3** (60 mg, 0.12 mmol, 1 eq.,) were dissolved in dry DMF (2.5 mL). Triethylamine (0.6 mmol, 5 eq., 83.6 µL) and 1-(prop-2-ynyloxy)methyl)benzene (52.6 mg, 0.36 mmol, 3 eq.,) were added at room temperature. The reaction mixture was stirred at 80°C for 3h then water (20 mL) was added. The aqueous layer was extracted three times with diethyl ether (3x 20 mL), the combined organic layers were washed with brine (20 mL) and dried over magnesium sulfate. The solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel (cyclohexane/ CH_2Cl_2: 20/80 ; Rf = 0.7) to give **4** (53.3 mg, 88%) as a colourless oil. **^{1}H NMR (300 MHz, $CDCl_3$) :** δ (ppm) 7.51 (d, *J* = 8.4 Hz, 2H), 7.40-7.30 (m, 5H), 7.19 (s, 1H), 7.04 (d, *J* = 8.1 Hz, 2H), 5.21 (s, 2H), 4.68 (s, 2H), 4.42 (s, 2H), 3.50 (s, 3H), 3.38 (s, 3H), 1.16 (s, 18H); **^{13}C NMR (75 MHz, $CDCl_3$) :** δ (ppm) 158.4, 149.3, 137.6 (2C), 128.5 (2C), 128.3 (2C), 127.9, 127.8, 126.6, 124.9, 115.5 (2C), 94.3, 84.9, 81.5, 71.7, 58.4, 56.3, 36.8, 29.4 (6C), 20.7 (2C); **^{29}Si NMR (59 MHz, $CDCl_3$) :** δ (ppm) -6.58; **HRMS (ESI/TOF$^+$) :** $C_{30}H_{40}N_2O_3Si$ $[M+H]^+$ calculated 505.2880, found 505.2896.

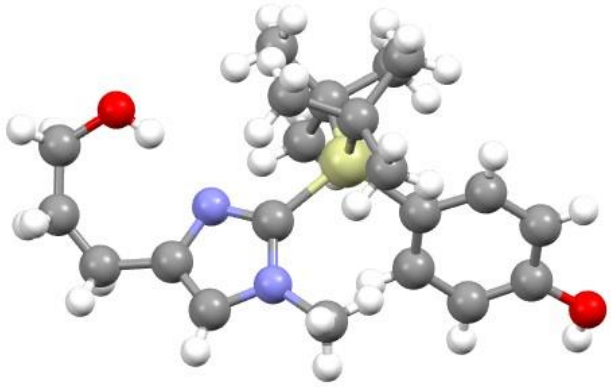
4-(Di-*tert*-butyl(4-(3-hydroxypropyl)-1-methyl-1*H*-imidazol-2-yl)silyl)phenol 5



5

10% Palladium on carbon (69.5 mg, 50% w/w,) and acetic acid (80 µL, 1.4 mmol, 10 eq.) were added to a solution of **4** (69.5 mg, 0.14 mmol, 1 eq.,) in methanol (4 mL). The reaction mixture was placed under hydrogen atmosphere and stirred at room temperature for 16h. The crude reaction was filtered on celite and washed with methanol (20 mL). The solvent was removed under reduced pressure. The residue was dissolved in methanol (4 mL) and an aqueous solution of sulfuric acid (6.2M, 0.22 mL, 1.4 mmol, 10 eq.,) was added, and the reaction mixture was stirred at 50°C for 5h. Then, a saturated aqueous solution of $NaHCO_3$ (40 mL) was added. The mixture was extracted with ethyl acetate (3x 20 mL), the combined layers were dried over magnesium sulfate, the solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel (CH_2Cl_2/MeOH: 95/5) to give **5** (34.8 mg, 66%) as a white amorphous solid. **^{1}H NMR (300 MHz, MeOD) :** δ (ppm) 7.62 (d, *J* = 8.6 Hz, 2H), 7.09 (s, 1H), 7.03 (d, *J* = 8.5 Hz, 2H), 3.84 (t, *J* = 6.2 Hz, 2H), 3.57 (s, 3H), 2.91 (t, *J* = 6.9 Hz, 2H), 2.07 (m, 2H), 1.32 (s, 18H); **^{13}C NMR (75 MHz, MeOD) :** δ (ppm) 159.9, 148.7, 144.2, 138.7 (2C), 124.6, 121.7, 116.0 (2C), 62.8, 37.2, 33.3, 29.9 (6C), 25.5, 21.40 (2C); **^{29}Si NMR (59 MHz, MeOD) :** δ (ppm) -6.66; **HRMS (ESI/TOF$^+$) :** $C_{21}H_{34}O_2N_2Si$ $[M+H]^+$ calculated 375.2462, found 375.2465.

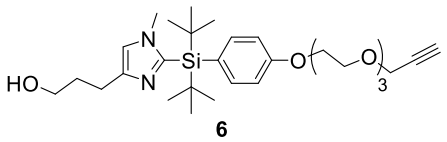
Monocrystals of this compound were obtained by slow evaporation from an AcOEt/toluene mixture. Crystallographic data was acquired at CESAMO (UMR 5255) on a Bruker APEX 2 DUO. A single crystal was mounted and immersed in a stream of nitrogen gas [T = 150(2) K]. Data were collected, using a microfocus sealed tube of Mo K_α radiation (k = 0.71073 Å) on a KappaCCD diffractometer. Data collection and cell refinement were performed using APEX2 2013.10-0 (Bruker AXS Inc.), and SAINT v8.34A (Bruker AXS Inc.). Data reduction was performed using SAINT v8.34A (Bruker AXS Inc.). Correction for absorption was performed using multi-scan integration as included in SADABS V2012/1 (Bruker AXS). Structure solutions were found by charge flipping methods (SUPERFLIP (Palatinus & Chapuis, 2007) EDMA (Palatinus et al., 2012)) and refined with (SHELXL).[2] Crystallographic data for this structure has been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 2169890. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44-(0)1223-336033 or e-mail: deposit@ccdc.cam.ac.uk)



*Mercury drawing of the crystalline structure of **5** obtained by X-Ray diffraction analysis*

[2] G. M. Sheldrick *Acta Crystallographica Section A.* 2008, **64**, 112-122.

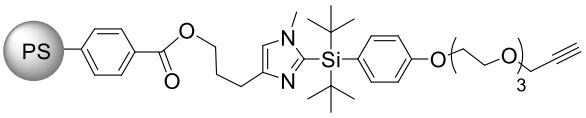
3-(2-((4-(2-(2-(2-(Prop-2-ynyloxy)ethoxy)ethoxy)ethoxy)phenyl)di-t*ert*-butylsilyl)-1-methyl-1*H*-imidazol-4-yl)propan-1-ol 6



6

Potassium *tert*-butoxide (84.2 mg, 0.75 mmol, 1.5 eq.) and a solution of 2-(2-(2-(prop-2-ynyloxy)ethoxy)ethoxy)ethyl 4-methylbenzenesulfonate (257 mg, 0.75 mmol, 1.5 eq.) in dry THF (9 mL) were added to a solution of **5** (0.5 mmol, 161 mg) in dry THF (9 mL) at room temperature. The reaction mixture was stirred at room temperature for 72h. The solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel (CH_2Cl_2/Ethyl Acetate: 80/20) to give **6** as a colorless oil (218 mg, 80 %). **^{1}H NMR (300 MHz, $CDCl_3$) :** δ (ppm) 7.45 (d, *J* = 8.7 Hz, 2H), 6.85 (d, *J* = 8.7 Hz, 2H), 6.65 (s, 1H), 4.13 (d, *J* = 2.3 Hz, 2H), 4.08 (m, 2H), 3.81 (m, 2H), 3.73-3.66 (m, 4H), 3.63 (m, 6H), 3.26 (s, 3H), 2.75 (m, 2H), 2.35 (t, *J* = 2.2 Hz, 1H,), 1.80 (m, 2H), 1.07 (s, 18H); **^{13}C NMR (75 MHz, $CDCl_3$) :** δ (ppm) 159.7, 147.5, 142.7, 137.4 (2C), 125.3, 120.2, 114.0 (2C), 79.6, 74.5, 70.8, 70.7, 70.5, 69.7, 69.1, 67.1, 62.6, 58.4, 36.7, 31.4, 29.3 (6C), 25.6, 20.5 (2C) ; **^{29}Si NMR (59 MHz, $CDCl_3$) :** δ (ppm) -6.78 ; **HRMS (ESI/TOF$^+$) :** $C_{30}H_{47}O_5N_2Si$ $[M+H]^+$ calculated 545.3405, found 545.3418.

Polystrene resin-Imidazole-SiFA-Alcyne PS-7

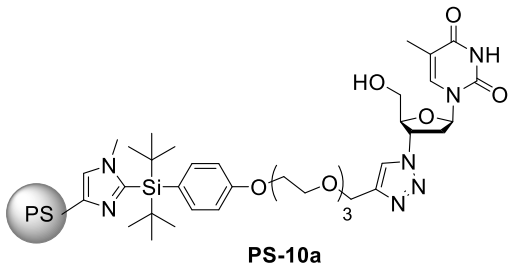


PS-7

In sealed reactor of 10 mL, **6** (19 mg, 34.9 µmol, 1 eq.) was dissolved in toluene (2.5 mL) in the presence of benzoyl chloride polymer bound (2.1mmol/g, 100.3 mg, 150.5 µmol, 5eq). Triethylamine (50 µl, 358.72 µmol, 10 eq) and dimethylaminopyridine (10.3 mg, 84.31 µmol, 2.4 eq) were added to the reaction mixture. The reaction was stirred at 110°C for 3 days and the disappearance in the solution of **6** was monitored by TLC. After allowing the reaction mixture to cool at rt, the polymer was filtered on a sintered glass filter (porosity 4) and washed consecutively with methanol, water, dichloromethane and methanol. After drying under reduced pressure, polymer **PS-7** was recovered (92.7mg) and used without further treatment (theoretical loading: ≈0.36 mmol/g).

*c) Syntheses of **PS-10a**, **PS-10b**, **PS-10c** and **PS-10d***

Polystrene resin-Imidazole-SiFA-Thymidine PS-10a

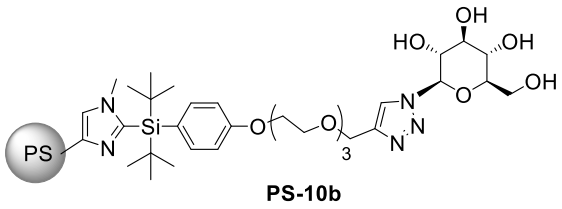


PS-10a

In sealed reactor of 5 mL, **PS-7** (95.6 mg, 36µmol, 1 eq.), [Cu(Cl(TBTA)]Cl·1.5H_2O[3] (33.7 mg, 50.7 µmol, 1.4 eq.) and (+)-sodium L-ascorbate (7 mg, 36 µmol, 1 eq.) were dissolved in DMF (1.5 mL). *N*,*N*-Diisopropylethylamine (60 µL, 345 µmol, 9.6 eq.) and zidovudine (AZT) (82 mg, 307 µmol, 8.5 eq.) were added in the reaction mixture. The reaction was heated at 100°C for 1h using micro-wave irradiation (30 W). After allowing the reaction mixture to cool at rt, the polymer was filtered on a sintered glass filter (porosity 4) and washed consecutively with DMF, water and methanol. After drying under reduced pressure, polymer **PS-10a** was recovered (85 mg) and used without further treatment (theoretical loading: ≈0.34 mmol/g).

[3] P. S. Donelly, S. D. Zanatta, S. C. Zammit, J. M. White and S. J. Williams, *Chem. Commun.*, 2008, 2459-2461

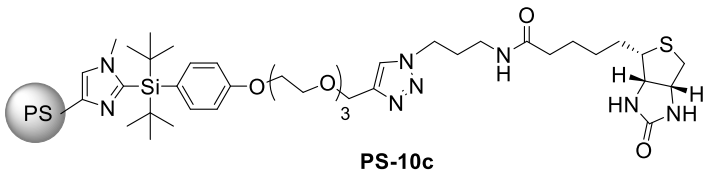
Polystrene resin-Imidazole-SiFA-Glucose PS-10b



PS-10b

In sealed reactor of 5 mL, **PS-7** (201 mg, 71 µmol, 1 eq.), [Cu(Cl(TBTA)]Cl·1.5H_2O[3] (38.7 mg, 58.2 µmol, 0.8eq.) and (+)-sodium L-ascorbate (23.4 mg, 118 µmol, 1.7 eq.) were dissolved in DMF (4.0 mL). *N*,*N*-Diisopropylethylamine (120 µL, 689 µmol, 9.7 eq.) and 1-azido-1-deoxy-*β*-D-glucopyranose (147 mg, 715 µmol, 10 eq.) were added in the reaction mixture. The reaction was heated at 70°C for 48h. After allowing the reaction mixture to cool at rt, the polymer was filtered on a sintered glass filter (porosity 4) and washed consecutively with DMF, water, acetonitrile and methanol. After drying under reduced pressure, polymer **PS-10b** was recovered (208 mg) and used without further treatment (theoretical loading: ≈0.34 mmol/g).

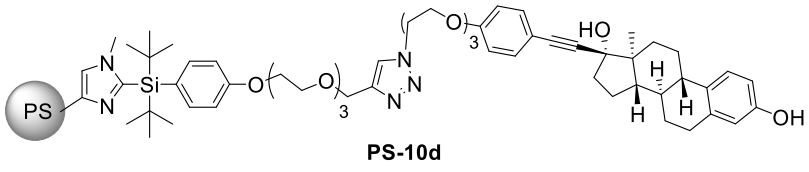
Polystrene resin-Imidazole-SiFA-Biotin PS-10c



PS-10c

In sealed reactor of 5 mL, **PS-7** (180 mg, 64 µmol, 1 eq.), [Cu(Cl(TBTA)]Cl·1.5H_2O[3] (37.3 mg, 56 µmol, 0.8eq.) and (+)-sodium L-ascorbate (48 mg, 242 µmol, 3.7 eq.) were dissolved in DMF (4.0 mL). *N*,*N*-Diisopropylethylamine (120 µL, 689 µmol, 10 eq.) and 1-biotin-3-azidopropylamine (209 mg, 640 µmol, 10 eq.) were added in the reaction mixture. The reaction was heated at 70°C for 48h. After allowing the reaction mixture to cool at rt, the polymer was filtered on a sintered glass filter (porosity 4) and washed consecutively with DMF, water, acetonitrile and methanol. After drying under reduced pressure, polymer **PS-10c** was recovered (188 mg) and used without further treatment (theoretical loading: ≈0.32 mmol/g).

Polystrene resin-Imidazole-SiFA-Estradiol PS-10d



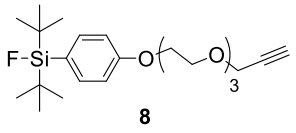
PS-10d

In sealed reactor of 5 mL, **PS-7** (218 mg, 81µmol, 1 eq.), [Cu(Cl(TBTA)]Cl ·1.5H_2O[3] (29.7 mg, 44.7 µmol, 0.55 eq.) and (+)-sodium L-ascorbate (77 mg, 389 µmol, 4.8 eq.) were dissolved in DMF (4.0 mL). *N*,*N*-Diisopropylethylamine (120 µL, 689 µmol, 8.5 eq.) and 2-(2-(2-azidoethoxy)ethoxy)ethyl-4-(ethynylestradiol)-phenolate[4] (308 mg, 564 µmol, 7eq.) were added in the reaction mixture. The reaction was heated at 100°C for 1h using micro-wave irradiation (30 W). After allowing the reaction mixture to cool at rt, the polymer was filtered on a sintered glass filter (porosity 4) and washed consecutively with DMF, water, acetonitrile and methanol. After drying under reduced pressure, polymer **PS-10d** was recovered (220 mg) and used without further treatment (theoretical loading: ≈0.30 mmol/g).

[4] A. Tabey, H. Audrain, E. Fouquet and P. Hermange, *Chem. Commun.,* 2019, **55**, 7587-7590.

*d) ^{19}F-Fluorination of supported precursors **PS-7** and **PS-10a-d***

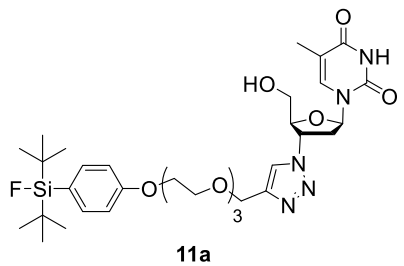
(4-(2-(2-(2-(Prop-2-ynyloxy)ethoxy)ethoxy)ethoxy)phenyl)di-*tert*-butylfluorosilane 8



8

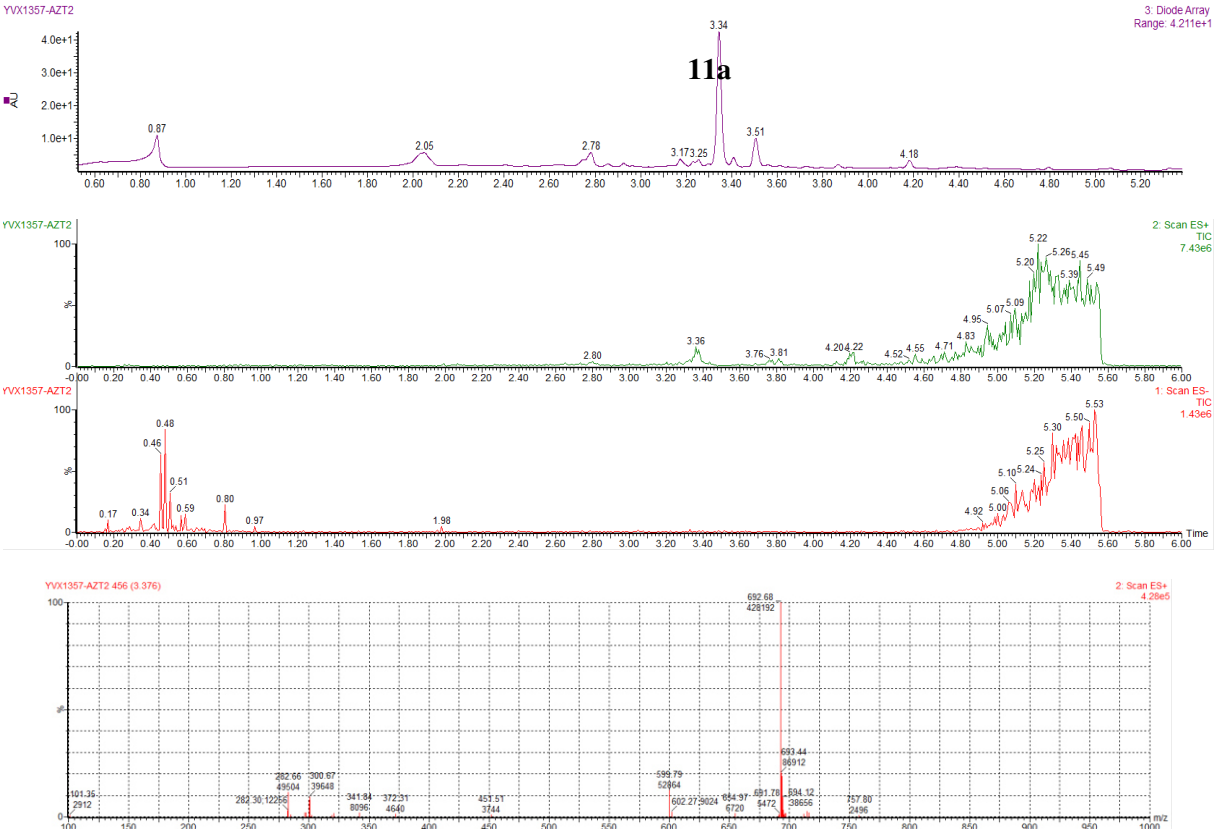
In a sealed reactor of 5 mL, polymer **PS-7** (24.4 mg, ≈8.8 µmol) was suspended in dry THF (0.8 mL) and a solution of aqueous hydrofluoric acid (0.1M, 110 µL, 11 µmol, 1.3 eq.) was added. The mixture was heated at 70°C for 2 h. The resin beads were filtered on a sintered glass filter (porosity 4) and washed with dichloromethane. The combined organic fractions were evaporated under reduced pressure to give **8** (4 mg, 9.43 µmol, quantitative) as a white amorphous solid. **^{1}H NMR (300 MHz, $CDCl_3$) :** δ (ppm) 7.50 (d, *J* = 8.5 Hz, 2H), 6.93 (d, *J* = 8.5 Hz, 2H), 4.20 (m, 2H), 4.15 (m, 2H), 3.87 (m, 2H), 3.77-3.67 (m, 8H), 2.42 (t, *J* = 2.4 Hz, 1H), 1.04 (d, *J* = 1.1 Hz, 18H); **^{13}C NMR (75 MHz, $CDCl_3$) :** δ (ppm) 159.8, 135.9 (2C), 127.1, 113.9 (2C), 74.6, 71.0, 70.8, 70.6, 69.9, 69.3, 67.2, 58.6, 29.8 (6C), 28.2, 20.5 (2C); **^{29}Si NMR (59 MHz, $CDCl_3$) :** δ (ppm) 14.3 (d, *J* = 296 Hz) ; **^{19}F NMR (282 MHz, $CDCl_3$) :** δ (ppm) -188.72 ; **HRMS (ESI/TOF^{+}) :** $C_{23}H_{37}O_4SiF$ $[M+Na]^+$ calculated 447.2337, found 447.2339.

3'-Deoxy-3'-[4-((2-(2-(2-(4-(di-tert-butylfluorosilyl)phenoxy)ethoxy) ethoxy)ethoxy)methyl)-1*H*-1,2,3-triazol-1-yl]-thymidine 11a



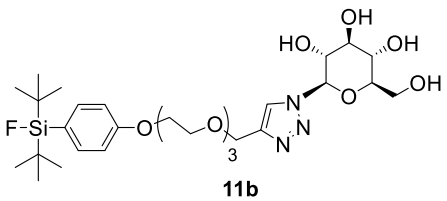
11a

In a sealed reactor of 5 mL, polymer **PS-10a** (16 mg, ≈5.4 µmol) was suspended in dry THF (0.8 mL) and a solution of aqueous hydrofluoric acid (0.1M, 110 µL, 11 µmol, 2.0 eq.) was added. The mixture was heated at 70°C for 2 h. The resin beads were filtered on a sintered glass filter (porosity 4) and washed with dichloromethane. The combined organic fractions were evaporated under reduced pressure to give **11a** (2.0 mg, 2.9 µmol, 54%) as a white amorphous solid. ^{1}H NMR analysis was in accordance to the data previously reported[1] and no traces of **8** was detected in the product. The sample purity was analysed by analytical UPLC/mass: $t_{\mathbf{11a}}$ = 3.34 min, $[M+H]^+$ found = 692.68. (Column ACQUITY UPLC® BEH C18 (1.7µm, 2.1 x 50mm) heated at 60°C with A = H_2O + HCOOH 0.1% and B = MeCN + HCOOH 0.1% as eluents (0.5 mL/min, program: 10% of B (0 min) → 10% of B (0.1 min) → 100% of B (4.5 min) → 100% of B (5 min) → 10% of B (5.2 min) → 10% of B (6 min)); **^{1}H NMR (300 MHz, $CDCl_3$) : δ (ppm)** 8.10 (s, 1H), 7.73 (s, 1H), 7.51 (d, *J* = 8.5 Hz, 2H), 7.37 (s, 1H), 6.92 (d, *J* = 8.6 Hz, 2H), 6.19 (t, *J* = 6.7 Hz, 1H), 5.39 (d, *J* = 6.1, 1H), 4.70 (s, 2H), 4.41 (d, *J* = 5.3 Hz, 1H), 4.15 (t, *J* = 4.8 Hz, 2H), 4.01 (d, *J* = 13.8 Hz, 1H), 3.87 (t, *J* = 4.8 Hz, 2H), 3.76-3.66 (m, 9H), 3.49 (s, 1H), 2.96-2.88 (m, 2H), 1.95 (d, *J* = 0.9 Hz, 3H), 1.03 (d, *J* = 0.9 Hz, 18H).



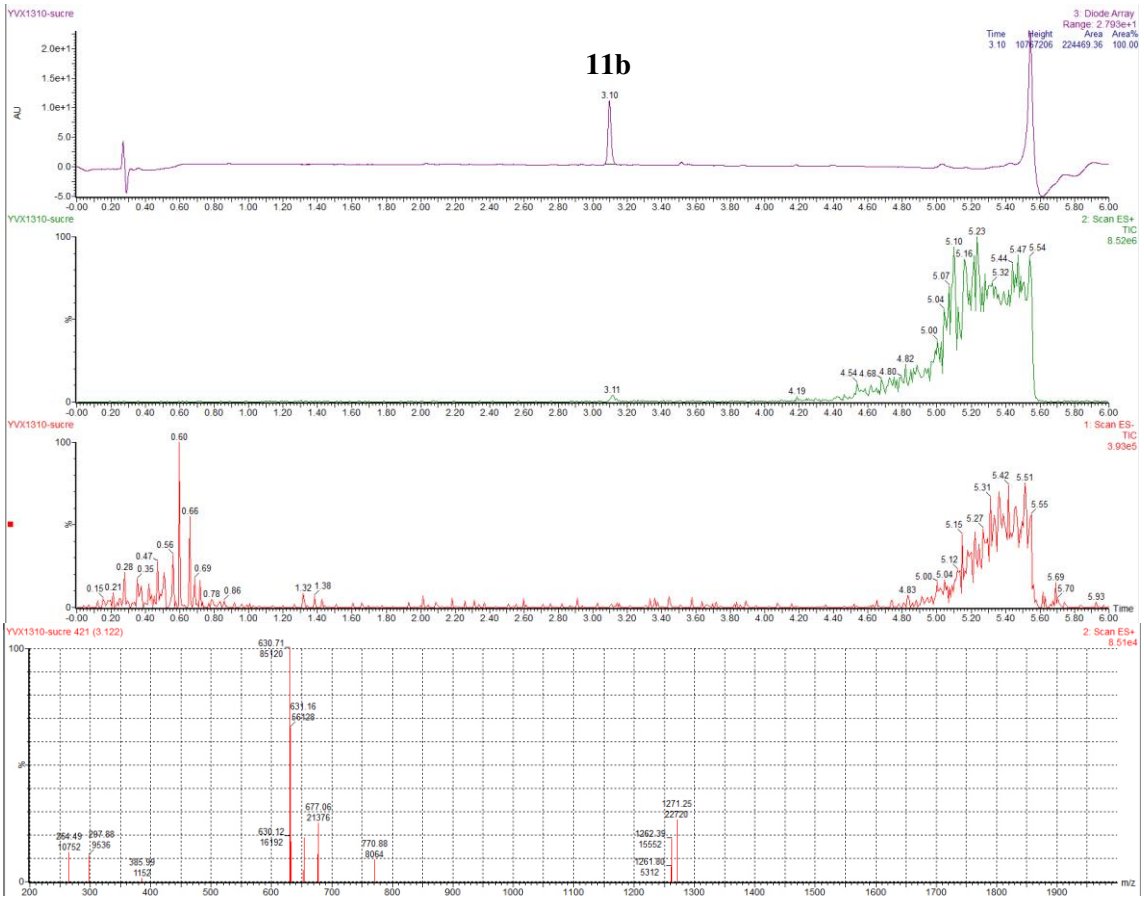
Analytic UPLC/mass chromatograms of 11a

***β*-D-1-Deoxy-1-[4-((2-(2-(2-(4-(di-tert-butylfluorosilyl)phenoxy)ethoxy)ethoxy)ethoxy)methyl)-1*H*-1,2,3-triazol-1-yl]-glucopyranose 11b**



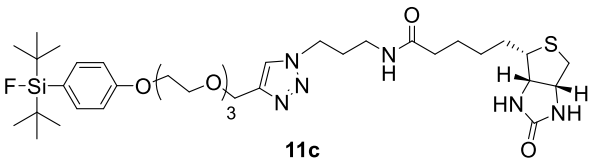
11b

In a sealed reactor of 5 mL, polymer **PS-10b** (31.6 mg, ≈10.7 µmol) was suspended in dry THF (0.5 mL) and a solution of aqueous hydrofluoric acid (0.1M, 200 µL, 20 µmol, 1.9 eq) was added. The mixture was heated at 70°C for 2 h. The resin beads were filtered on a sintered glass filter (porosity 4) and washed with dichloromethane. The combined organic fractions were evaporated under reduced pressure to give **11b** (7.6 mg, 12 µmol, 100%) as a white amorphous solid. ^{1}H NMR analysis was in accordance to the data previously reported[1] and no traces of **8** was detected in the product. The sample purity was analysed by analytical UPLC/mass: $t_{\mathbf{11a}}$ = 3.10 min, $[M+H]^+$ found = 630.71. (Column ACQUITY UPLC® BEH C18 (1.7µm, 2.1 x 50mm) heated at 60°C with A = H_2O + HCOOH 0.1% and B = MeCN + HCOOH 0.1% as eluents (0.5 mL/min, program: 10% of B (0 min) → 10% of B (0.1 min) → 100% of B (4.5 min) → 100% of B (5 min) → 10% of B (5.2 min) → 10% of B (6 min)); **^{1}H NMR (600 MHz, MeOD) :** δ (ppm) 8.18 (s, 1H), 7.52 (d, *J* = 8.5 Hz, 2H), 6.99 (d, *J* = 8.5 Hz, 2H), 5.60 (d, *J* = 9.1 Hz, 1H), 4.65 (s, 2H), 4.16 (t, *J* = 3.0 Hz, 2H), 3.92-3.85 (m, 4H), 3.73-3.64 (m, 8H), 3.56-3.48 (m, 3H), 1.04 (d, *J* = 1.1 Hz, 18H).



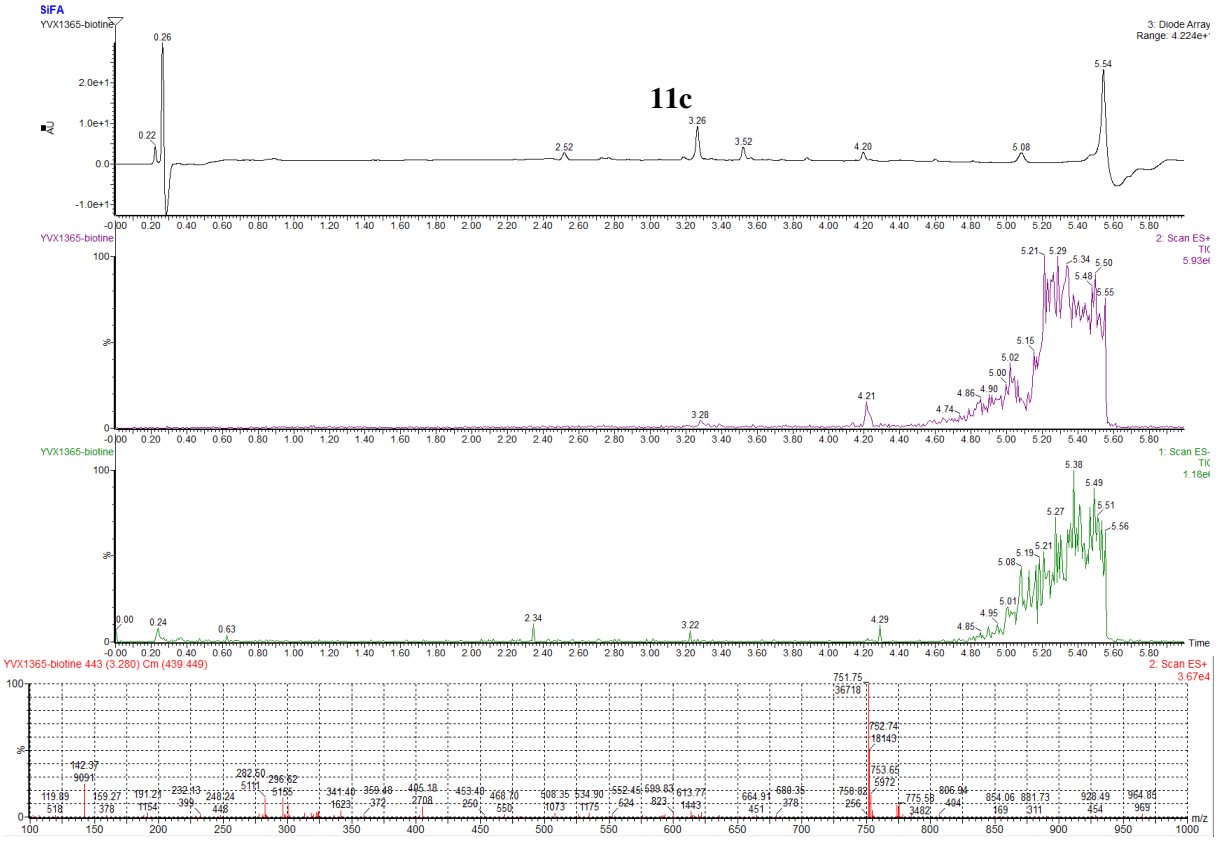
Analytic UPLC/mass chromatograms of 11b

***N*-[3-(4-((2-(2-(2-(4-(di-tert-butylfluorosilyl)phenoxy)ethoxy)ethoxy)ethoxy)methyl)-1*H*-1,2,3-triazol-1-yl)propanyl]-biotinamide 11c**



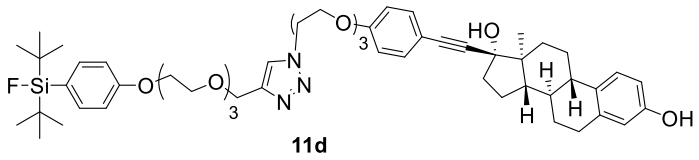
11c

In a sealed reactor of 5 mL, polymer **PS-10c** (19.0 mg, ≈6.1 µmol) was suspended in dry THF (0.5 mL) and a solution of aqueous hydrofluoric acid (0.1M, 200 µL, 20 µmol, 3.3 eq) was added. The mixture was heated at 70°C for 2 h. The resin beads were filtered on a sintered glass filter (porosity 4) and washed with dichloromethane. The combined organic fractions were evaporated under reduced pressure to give **11c** (5.0 mg, 6.6 µmol, 100%) as a white amorphous solid. ^{1}H NMR analysis was in accordance to the data previously reported[1] and no traces of **8** was detected in the product. The sample purity was analysed by analytical UPLC/mass: t_{11a} = 3.26 min, $[M+H]^+$ found = 751.75. (Column ACQUITY UPLC® BEH C18 (1.7µm, 2.1 x 50mm) heated at 60°C with A = H_2O + HCOOH 0.1% and B = MeCN + HCOOH 0.1% as eluents (0.5 mL/min, program: 10% of B (0 min) → 10% of B (0.1 min) → 100% of B (4.5 min) → 100% of B (5 min) → 10% of B (5.2 min) → 10% of B (6 min)); **^{1}H NMR (300 MHz, MeOD) :** 8.04 (s, 1H), 7.52 (d, *J* = 8.5 Hz, 2H), 6.98 (d, *J* = 8.5 Hz, 2H), 4.62 (s, 2H), 4.48 (dd, *J* = 4.6 Hz, *J* = 7.8 Hz, 1H), 4.42 (t, *J* = 6.9 Hz, 2H), 4.30 (dd, *J* = 4.3 Hz, *J* = 7.8 Hz, 1H), 4.16 (t, *J* = 3.1 Hz, 2H), 3.85 (t, *J* = 4.6 Hz, 2H), 3.71-3.66 (m, 8H), 3.20 (t, *J* = 3.9 Hz, 3H), 2.90 (dd, *J* = 12.8 Hz, *J* = 4.9 Hz, 1H), 2.69 (d, *J* = 12.7 Hz, 1H), 2.21 (t, *J* = 7.2 Hz, 2H), 2.09 (qt, *J* = 6.6 Hz, 3H), 1.45 (q, *J* =1.5 Hz, 2H), 1.04 (d, *J* = 1.0 Hz, 18H).



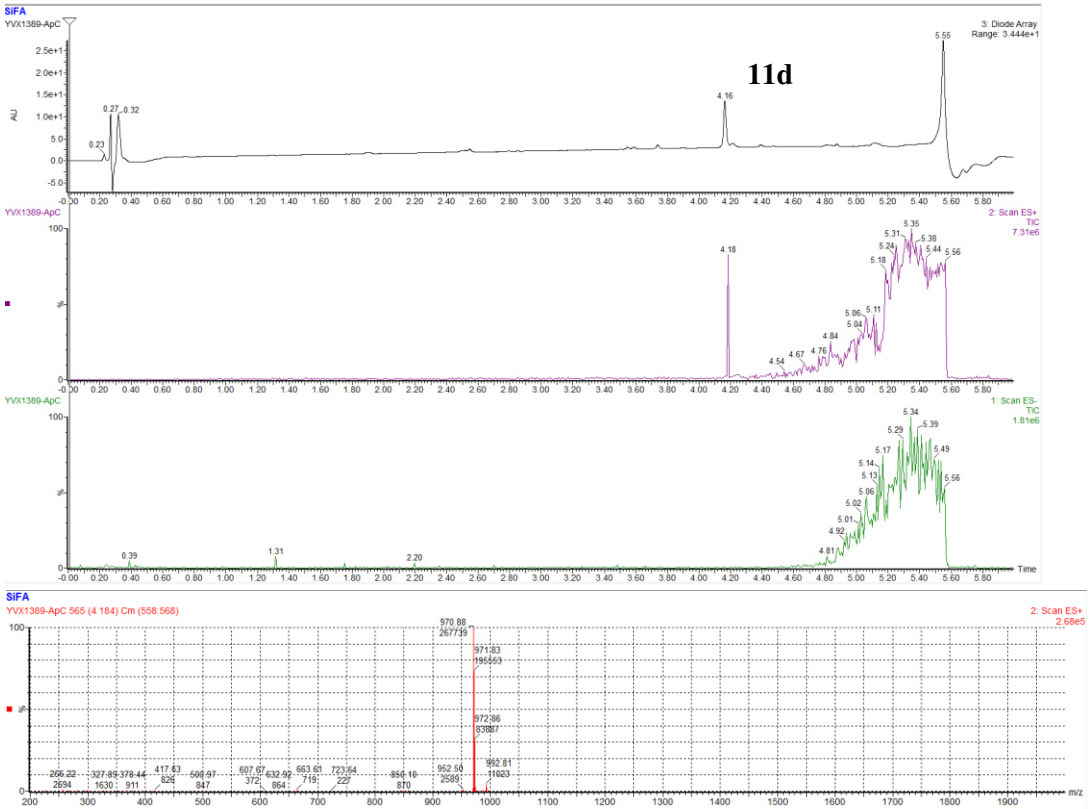
Analytic UPLC/mass chromatograms of 11c

17-(4-((2-(2-(2-(4-(di-tert-butylfluorosilyl)phenoxy)ethoxy)ethoxy)ethoxy)methyl))-1*H*-1,2,3-triazol-1-yl)ethoxy)ethoxy)ethoxy)phenyl)ethynyl)-estradiol 11d



11d

In a sealed reactor of 5 mL, polymer **PS-10d** (38.3 mg, ≈11.5 µmol) was suspended in dry THF (0.5 mL) and a solution of aqueous hydrofluoric acid (0.1M, 200 µL, 20 µmol, 1.7 eq) was added. The mixture was heated at 70°C for 2 h. The resin beads were filtered on a sintered glass filter (porosity 4) and washed with dichloromethane. The combined organic fractions were evaporated under reduced pressure to give **11d** (7.0 mg, 7.2 µmol, 63%) as a colorless oil. No traces of **8** was detected in the product by ^{1}H NMR analysis. The sample purity was analysed by analytical UPLC/mass: t_{11a} = 4.16 min, $[M+H]^+$ found = 970.88. (Column ACQUITY UPLC® BEH C18 (1.7µm, 2.1 x 50mm) heated at 60°C with A = H_2O + HCOOH 0.1% and B = MeCN + HCOOH 0.1% as eluents (0.5 mL/min, program: 10% of B (0 min) → 10% of B (0.1 min) → 100% of B (4.5 min) → 100% of B (5 min) → 10% of B (5.2 min) → 10% of B (6 min)); **^{1}H NMR (600 MHz, $CDCl_3$) :** δ (ppm) 7.49 (d, *J* = 8.1 Hz, 2H), 7.36 (d, *J* = 8.5 Hz, 2H), 7.16 (d, *J* = 8.4 Hz, 1H), 6.91 (d, *J* = 8.2 Hz, 2H), 6.84 (d, *J* = 8.6 Hz, 2H), 6.62 (dd, *J* = 8.3, *J* = 2.4 Hz, 1H), 6.55 (d, *J* = 2.2 Hz, 1H), 4.67 (slarge, 1H), 4.42 (dd, *J* = 10.3 Hz, *J* = 4.2 Hz, 1H), 4.29 (d, *J* = 10.4 Hz, 1H), 4.13-4.10 (m, 4H), 3.87-3.61 (m, 12H), 2.75 (dd, *J* = 17.9 Hz, *J* = 4.20 Hz, 1H), 2.41-2.34 (m, 2H), 2.29-2.18 (m, 1H), 2.10-2.06 (m, 2H), 1.98-1.74 (m, 13H), 1.50-1.41 (m, 3H), 1.36-1.32 (m, 2H), 1.03 (s, 18H), 0.92 (s, 3H) ; **^{13}C NMR (150.3 MHz, $CDCl_3$) :** 159.9, 158.6, 153.3, 138.2, 135.4 (d, J =4.0 Hz, 2C), 133.1(2C), 132.6, 127.8, 126.5, 124.6 (d, J = 12.1 Hz, 2C), 115.4, 115.2, 114.5 (2C), 113.9(2C), 112.7, 91.5, 85.6, 80.3, 75.6, 70.7, 70.6, 70.5, 70.5, 69.8, 69.6, 69.2, 67.6, 67.4, 67.0, 49.7, 47.6, 43.6, 39.4, 39.0, 37.7, 33.0, 29.6, 27.9, 27.3 (6C), 27.2, 26.5, 22.9, 20.3 (d, *J* =12.5 Hz, 2C), 12.9; **^{19}F NMR (282 MHz, $CDCl_3$) :** δ (ppm) 188.66 ; **^{29}Si NMR (59 MHz, $CDCl_3$) :** δ (ppm) 14.39 (d, *J* = 296.6 Hz); **HRMS (ESI/TOF$^-$) :** $C_{55}H_{76}O_9N_3F_1Si_1$ [M+Na] calculated 992.52271 found 992.52420.



Analytic UPLC/mass chromatograms of 11d

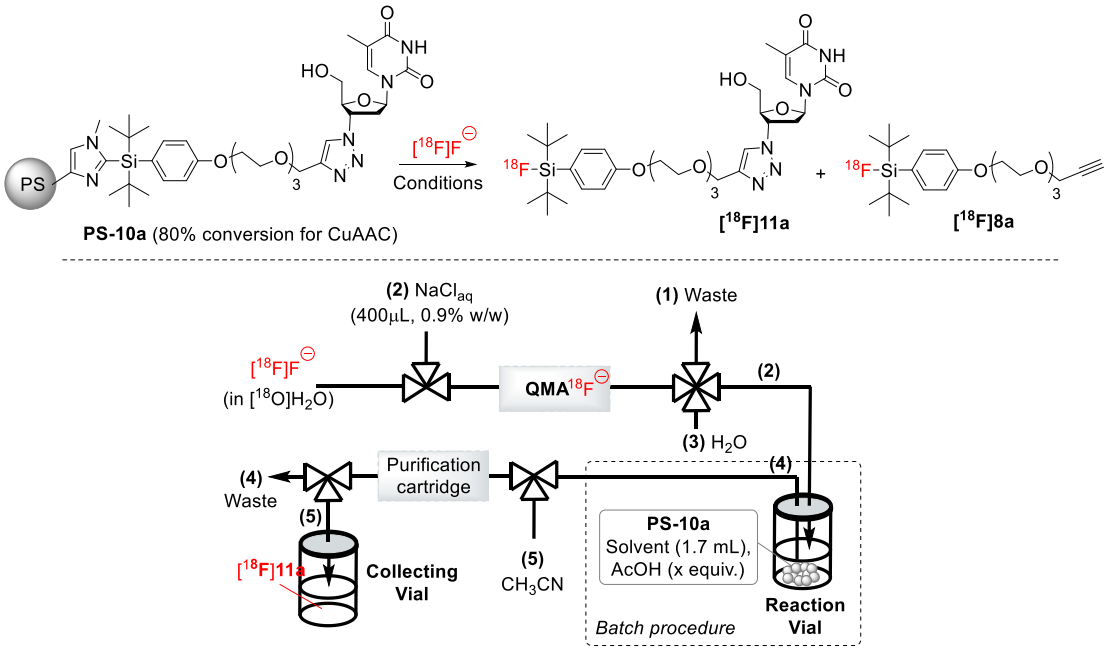
B) Radiosyntheses

a. General methods

No-carrier added [^{18}F]Fluoride was produced by the CEA in Paris via the ^{18}O(p,n)^{18}F nuclear reaction, and directly delivered as a H_2[^{18}O]O solution (2-5mL). All radiosyntheses were performed in a lead-shielded Trasis hotcell® H2000 using an automated TRASIS PET Tracer synthesizer (AllinOne® module with 36 actuators, up to 5 syringe drivers, 2 heaters and a cartridge heater). The pressures of nitrogen and vacuum were monitored in real time. The AllinOne® module is equipped with a built-in HPLC with DAD and radioactivity detectors. The synthesizer was controlled using the Trasis Supervision® software version 2.30. Before each radiosynthesis, careful control of electronics and cassette was performed in order to avoid remote and leak issues. The purification was performed on C18 Sep-Pak cartridge (Waters) pre-conditioned according the following procedure: 100% A->20% B (5mL) -> 20% B (2mL) -> 40% B (2 mL) -> 60% B (2 mL) -> 80% B (2mL)-> 100% B (2 mL) with A = acetonitrile and B = water. The radiochemical purity was determined using an analytical radio-HPLC equipped with a Shimadzu pump (LC-20A), a 20µL injection loop (SIL-20AC) and a Luna C18 column (5µm, 250x4.6mm) inside a column oven (CTO-20AC). The detection was performed using a UV detector with variable wavelength from Shimadzu (SPD-20A) and a gamma detector from Raytest. A Capintech INC CRC® 25PET Dose calibrator was used to measure the activity.

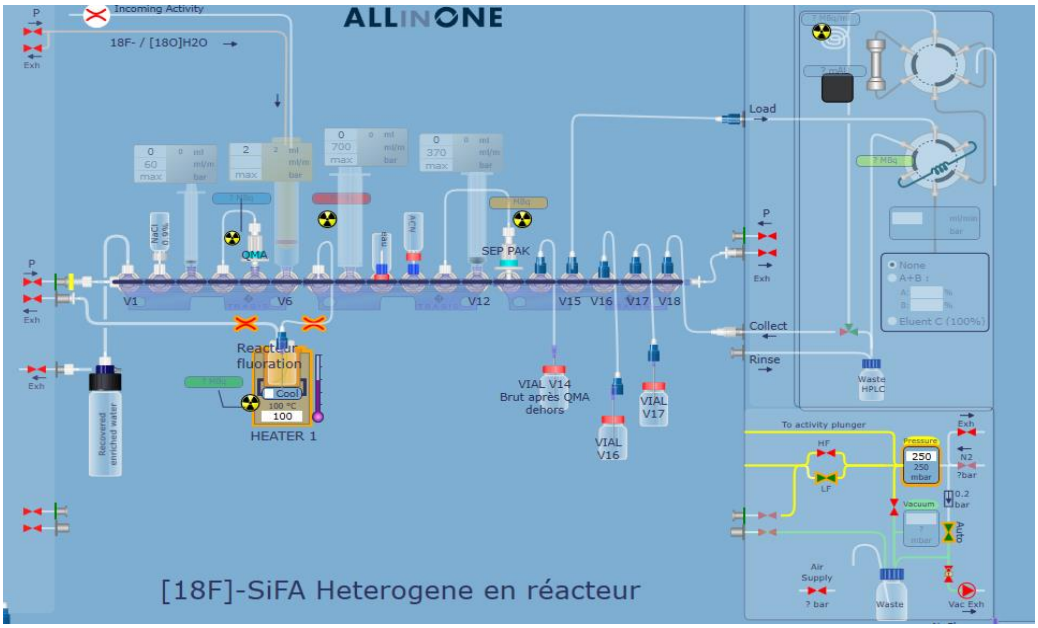
*b. Optimization of the conditions and radiosyntheses of **[^{18}F]11a***

1) Optimisation of the experimental conditions for the "Batch procedure" with **[^{18}F]11a**



Polymer **PS-10a** (5mg or 10mg, ≈0.34 mmol/g ImidSiFA grafted, ≈80% conversion for the CuAAC conjugation step) was added in the reaction vial (reactor R1) with acetic acid (10 eq or 60 eq) in THF or acetonitrile (1.7 mL). Then, [^{18}F]fluoride was automatically transferred into the synthesizer into syringe 2 and trapped by passing the solution through an anion-exchange resin cartridge (Sep-Pak QMA light, Waters). Release of [^{18}F]fluoride from QMA cartridge was achieved by eluting an aqueous solution of NaCl (0.9% w/w, 400 µL) with syringe 1 to the reaction vial R1 previously loaded (only 300µL of this solution could be transferred effectively in R1 due to the dead volume of the system). The pinch of the reactor was closed and the resulting mixture was allowed to react at 100°C for 15 min

to 30 min. The mixture was then cooled at 40°C and homogenized by nitrogen bubbling at low flow for 1 min (400mbar concomitant with a vacuum set at -40 mbar). Then, the reaction mixture was collected with syringe 3. The reactor was washed by adding 2 mL of a 1:1 mixture of acetonitrile and water (using syringe 4). The content was homogenized again by nitrogen bubbling at low flow for 1 min (400mbar concomitant with a vacuum set at -40 mbar) and he content of the vial was collected using syringe 3. The reactor was washed a third time with water (4mL), homogenized under N_2 bubbling for 1 min as previously described and collected using syringe 3. The full content of syringe 3 (containing 66% of water) was passed through a C18 Sep-Pak cartridge at 3mL/min until emptiness. Then, the cartridge was washed with additional water (4mL) at 3mL/min using syringe 4. Finally, the product was eluted at 1mL/min from the C18 Sep-Pak cartridge using acetonitrile (4mL, from syringe 4) to the collecting vial (valve 14) placed outside of the hotcell®. The radiochemical yield (RCY) was calculated from the decay-corrected activity inside the collecting vial divided by activity in the reaction vial R1 before the fluorination (at the time where fluoride-18 was fully eluted from the QMA to R1) and multiplied by the radiochemical purity (RCP). The purity of the fluorinated compound **[^{18}F]11a** was checked from a sample by analytical HPLC at a flow rate of 0.5 or 1mL/min using the following program: 70% of B (8 min) -> 75% of B (4min) -> 75% of B (20min)-> 95% of B (5min) ->95% of B (5min)-> 70% of B (3 min) with A = water + 0,1% of trifluoroacetic acid and B = ACN + 0,1% of trifluoroacetic acid. Compound **[^{18}F]8** (t_R ^{radio} ≈ 30 min or 35 min) was detected in this case along with the desired compound **[^{18}F]11a** (t_R ^{radio} ≈ 10 min or 20 min).



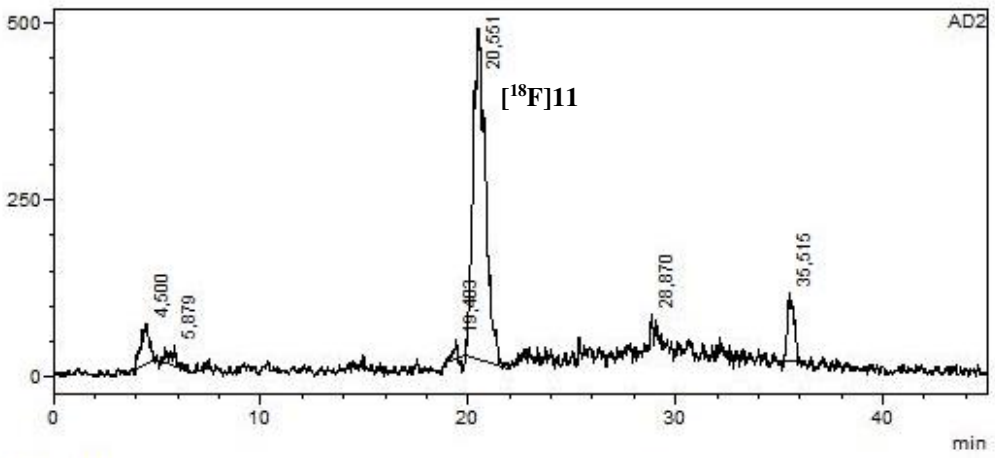
Layout of the cassette for the "Batch procedure"

Results of the optimization experiments are summarized in the following table:

Experiment (nb of runs)	Mass of **PS-10a**	Conditions	RCY of **[^{18}F]11a** (%)	RCP of **[^{18}F]11a** (%)	Final Activity (MBq)
1 (n = 1)	5 mg	THF (1.7 mL), AcOH (10 equiv), 100°C, 15 min	8	81	452
2 (n = 1)	5 mg	**CH_3CN** (1.7 mL), AcOH (10 equiv), 100°C, 15 min	16	67	1254
3 (n = 1)	5 mg	CH_3CN (1.7 mL), AcOH (**60 equiv**), 100°C, 15 min	17	65	755
4 (n = 1)	**10 mg**	CH_3CN (1.7 mL), AcOH (60 equiv), 100°C, 15 min	14	71	880
5 (n = 1)	5 mg	CH_3CN (1.7 mL), AcOH (60 equiv), 100°C, **30 min**	19	76	940

*Experiment 1 (***PS-10a** (5 mg)**,** THF (1.7 mL), AcOH (10 equiv), 100°C, 15 min)

	Analytical code	**YVX1.258**
	Activity fixed on QMA	7.75 GBq
t = 0 min	Activity eluted in R1	7.60 GBq
t = 17 min	Activity in R1 (end of fluorination)	6.32 GBq
t = 60 min	Activity in the collecting vial	452 MBq
	t_R ^{radio} of **[^{18}F]11a**	20.55 min
	Radiochemical purity of **[^{18}F]11a**	81 %
	t_R ^{radio} of **[^{18}F]8**	35.52 min
	Percentage of **[^{18}F]8**	8 %
	Activity Yield	5 %
	RCY (decay corrected)	**8 %**



<Peak Table>

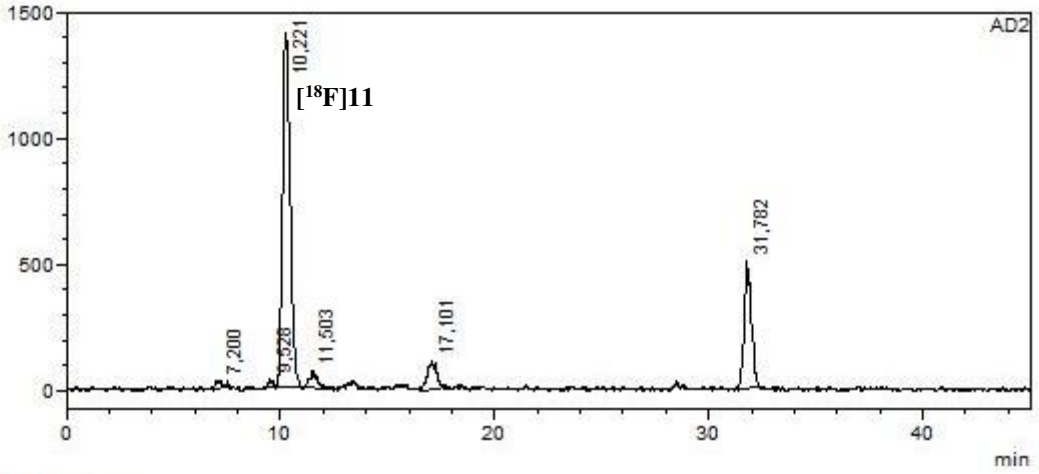
AD2

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	4,500	1579997	55322	6,598		M	
2	5,879	730030	28646	3,049		M	
3	19,403	92754	28430	0,387		M	
4	20,551	19447564	466484	81,211		M	
5	28,870	134283	19156	0,561		M	**[^{18}F]8**
6	35,515	1962270	97150	8,194		M	
Total		23946899	695190				

Analytic Radio HPLC chromatogram of Experiment 1

*Experiment 2 (***PS-10a** (5 mg)**,** CH_3CN (1.7 mL), AcOH (10 equiv), 100°C, 15 min)

	Analytical code	**YVX1.256**
	Activity fixed on QMA	11.56 GBq
t = 0 min	Activity eluted in R1	10.15 GBq
t = 16 min	Activity in R1 (end of fluorination)	9.4 GBq
t = 63 min	Activity in the collecting vial	1.254 GBq
	t_R ^{radio} of **[^{18}F]11a**	10.22 min
	Radiochemical purity of **[^{18}F]11a**	67 %
	t_R ^{radio} of **[^{18}F]8**	31.78 min
	Percentage of **[^{18}F]8**	22 %
	Activity Yield	11%
	RCY (decay corrected)	16 %



<Peak Table>

AD2

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
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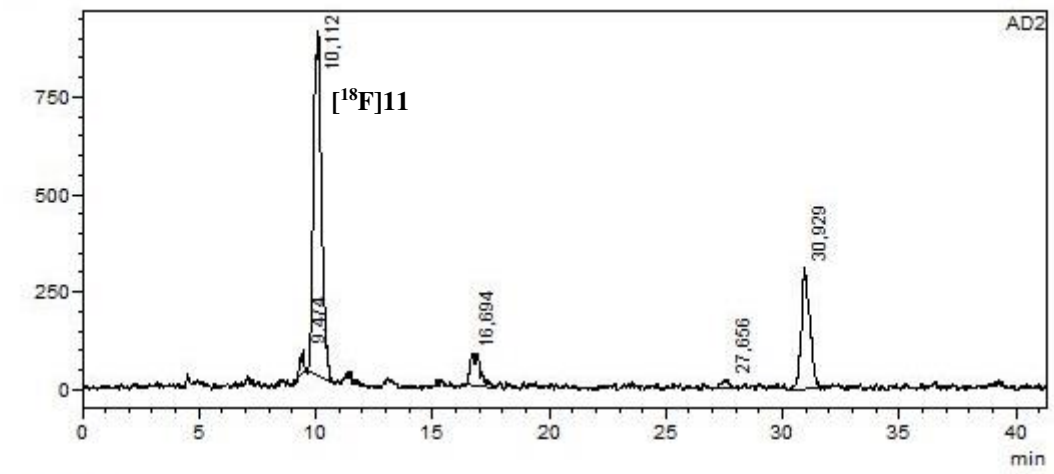
2	9,528	457666	33407	0,885		M	
3	10,221	34594062	1402375	66,921		M	
4	11,503	1344998	63511	2,602		M	**[^{18}F]8**
5	17,101	3257368	113688	6,301		M	
6	31,782	11470336	504477	22,189		M	
Total		51694055	2144830				

Analytic Radio HPLC chromatogram of Experiment 2

*Experiment 3 (***PS-10a** (5 mg)**,** CH_3CN (1.7 mL), AcOH (60 equiv), 100°C, 15 min)

	Analytical code	**YVX1.250**
	Activity fixed on QMA	9.8 GBq
t = 0 min	Activity eluted in R1	7.0 GBq
t = 19 min	Activity in R1 (end of fluorination)	6.2 GBq
t = 72 min	Activity in the collecting vial	755 MBq
	t_R ^{radio} of **[^{18}F]11a**	10.11 min
	Radiochemical purity of **[^{18}F]11a**	65%
	t_R ^{radio} of **[^{18}F]8**	30.93 min
	Percentage of **[^{18}F]8**	24%
	Activity Yield	11%
	RCY (decay corrected)	17%



<Peak Table>

AD2

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
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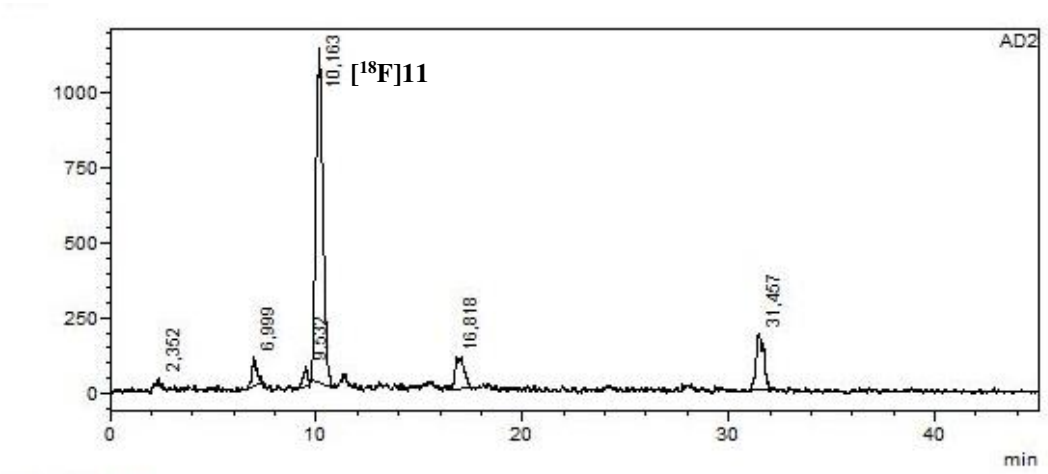
2	10,112	21010062	880894	65,268		M	
3	16,694	2425703	78215	7,535		M	
4	27,656	432498	21712	1,344		M	**[^{18}F]8**
5	30,929	7798383	310902	24,226		M	
Total		32190474	1349374				

Analytic Radio HPLC chromatogram of Experiment 3

*Experiment 4 (***PS-10a** (10 mg)**,** CH_3CN (1.7 mL), AcOH (60 equiv), 100°C, 15 min)

	Analytical code	**YVX1.255**
	Activity fixed on QMA	11.6 GBq
t = 0 min	Activity eluted in R1	10.07 GBq
t = 18 min	Activity in R1 (end of fluorination)	8.9 GBq
t = 61 min	Activity in the collecting vial	1.473 GBq
	t_R ^{radio} of **[^{18}F]11a**	10.16 min
	Radiochemical purity of **[^{18}F]11a**	71 %
	t_R ^{radio} of **[^{18}F]8**	31.46 min
	Percentage of **[^{18}F]8**	13 %
	Activity Yield	12 %
	RCY (decay corrected)	17 %



<Peak Table>

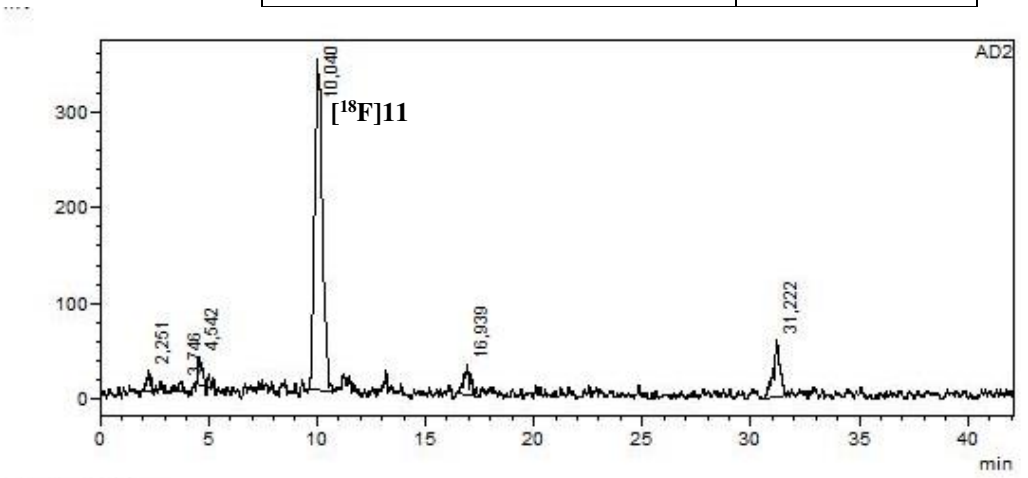
AD2

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	2,352	280397	26818	0,756		M	
2	6,999	1596300	94808	4,303		M	
3	9,532	898161	62193	2,421		M	
4	10,163	26225569	1112539	70,691		M	
5	16,818	3254540	111236	8,773		M	**[^{18}F]8**
6	31,457	4844058	188883	13,057		M	
Total		37099026	1596476				

Analytic Radio HPLC chromatogram of experiment 4

*Experiment 5 (***PS-10a** (5 mg)**,** CH_3CN (1.7 mL), AcOH (60 equiv), 100°C, 30 min)

	Analytical code	**YVX1.251**
	Activity fixed on QMA	8.8 GBq
t = 0 min	Activity eluted in R1	7.39 GBq
t = 24 min	Activity in R1 (end of fluorination)	5.82 GBq
t = 66 min	Activity in the collecting vial	940 MBq
	t_R ^{radio} of **[^{18}F]11a**	10.04 min
	Radiochemical purity of **[^{18}F]11a**	76 %
	t_R ^{radio} of **[^{18}F]8**	31.22 min
	Percentage of **[^{18}F]8**	11 %
	Activity Yield	12 %
	RCY (decay corrected)	19 %



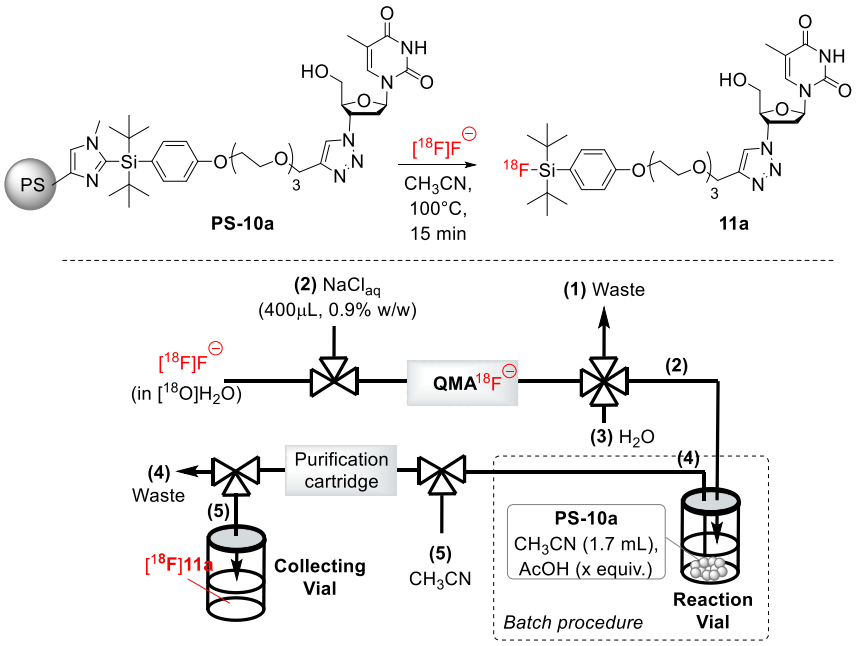
<Peak Table>

AD2

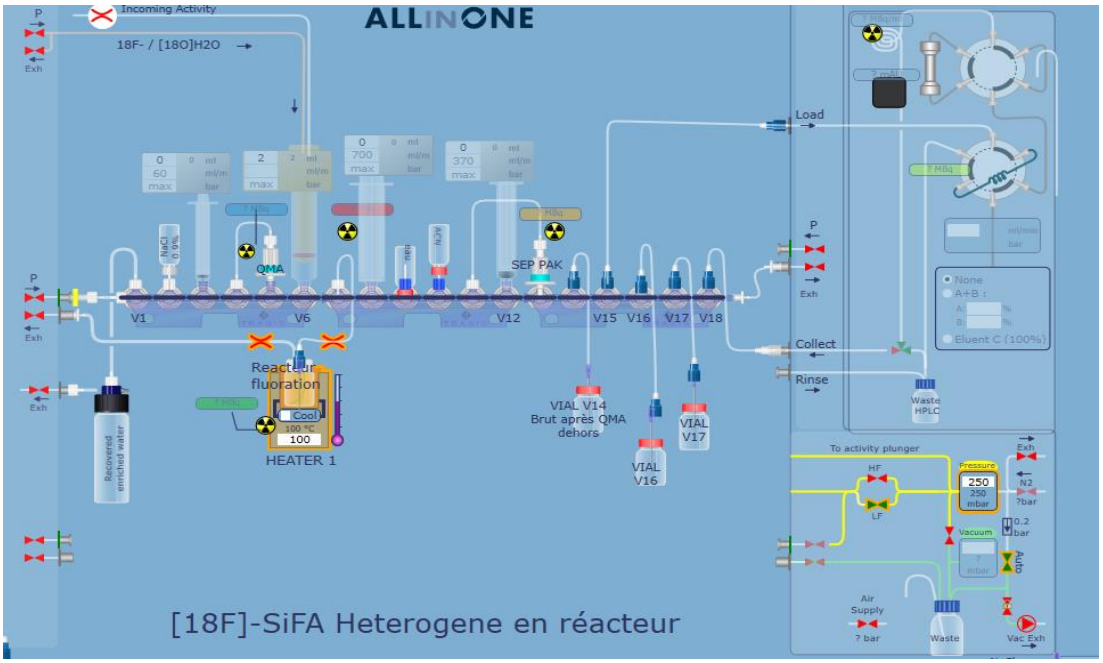
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	2,251	217943	20080	1,961		M	
2	3,746	129655	10124	1,167		M	
3	4,542	441331	28467	3,971		M	
4	10,040	8423774	343554	75,792		M	
5	16,939	630822	31623	5,676		M	[^{18}F]8
6	31,222	1270862	59827	11,434		M	
Total		11114387	493675				

Analytic Radio HPLC chromatogram of experiment 5

2) Synthesis of **[^{18}F]11a** using the "Batch procedure"



Polymer **PS-10a** (5mg, ≈0.34 mmol/g ImidSiFA grafted, 100% conversion for the CuAAC conjugation step) was added in the reaction vial (reactor R1) with acetic acid (10 eq or 60 eq) in acetonitrile (1.7 mL). Then, [^{18}F]fluoride was automatically transferred into the synthesizer into syringe 2 and trapped by passing the solution through an anion-exchange resin cartridge (Sep-Pak QMA light, Waters). Release of [^{18}F]fluoride from QMA cartridge was achieved by eluting an aqueous solution of NaCl (0.9% w/w, 400 µL) with syringe 1 to the reaction vial R1 previously loaded (only 300µL of this solution could be transferred effectively in R1 due to the dead volume of the system). The pinch of the reactor was closed and the resulting mixture was allowed to react at 100°C for 15 min. The mixture was then cooled at 40°C and homogenized by nitrogen bubbling at low flow for 1 min (400mbar concomitant with a vacuum set at -40 mbar). Then, the reaction mixture was collected with syringe 3. The reactor was washed by adding 2 mL of a 1:1 mixture of acetonitrile and water (using syringe 4). The content was homogenized again by nitrogen bubbling at low flow for 1 min (400mbar concomitant with a vacuum set at -40 mbar) and he content of the vial was collected using syringe 3. The reactor was washed a third time with water (4mL), homogenized under N_2 bubbling for 1 min as previously described and collected using syringe 3. The full content of syringe 3 (containing 66% of water) was passed through a C18 Sep-Pak cartridge at 3mL/min until emptiness. Then, the cartridge was washed with additional water (4mL) at 3mL/min using syringe 4. Finally, the product was eluted at 1mL/min from the C18 Sep-Pak cartridge using acetonitrile (4mL, from syringe 4) to the collecting vial (valve 14) placed outside of the hotcell®. The radiochemical yield (RCY) was calculated from the decay-corrected activity inside the collecting vial divided by activity in the reaction vial R1 before the fluorination (at the time where fluoride-18 was fully eluted from the QMA to R1) and multiplied by the radiochemical purity (RCP). The purity of the fluorinated compound **[^{18}F]11a** was checked from a sample by analytical HPLC at a flow rate of 1mL/min using the following program: 70% of B (8 min) -> 75% of B (4min) -> 75% of B (20min)-> 95% of B (5min) ->95% of B (5min)-> 70% of B (3 min) with A = water + 0,1% of trifluoroacetic acid and B = ACN + 0,1% of trifluoroacetic acid. The desired compound **[^{18}F]11a** was detected by radio HPLC (t_R ^{radio} ≈ 10 min).



Layout of the cassette for the synthesis of [^{18}F]11a by the "Batch procedure"

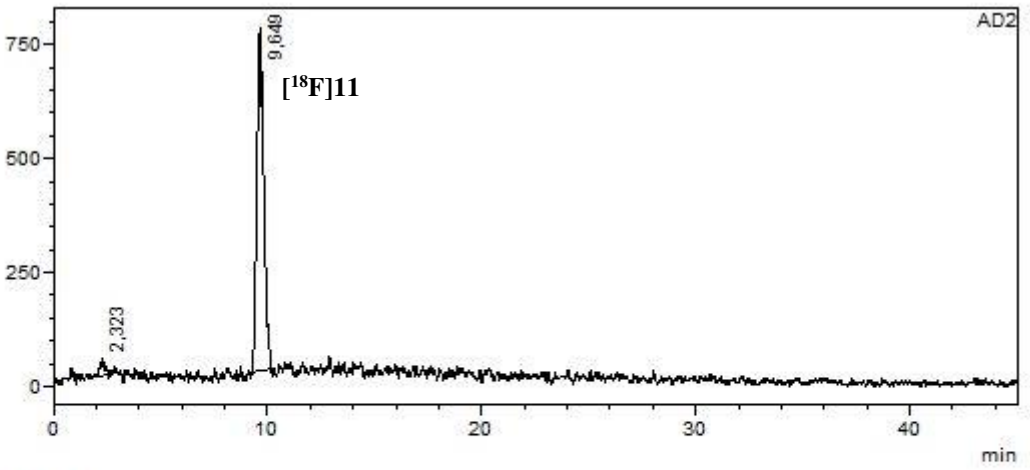
Results of the experiments are summarized in the following table:

Experiment (nb of runs)	Conditions	RCY of [^{18}F]**11a** (%)	RCP of [^{18}F]**11a** (%)	Final Activity (MBq)
6 (*n* = 1)	**PS-10a (5 mg), CH_3CN (1.7 mL), AcOH (60 equiv), 100°C, 15 min**	**12**	**97**	**780**
7 (*n* = 3)	**PS-10a** (5 mg), CH_3CN (1.7 mL), AcOH (10 equiv), 100°C, 15 min	13 ± 3[a]	97 ± 3[a]	-
7-1 (*n* = 1)	**PS-10a** (5 mg), CH_3CN (1.7 mL), AcOH (10 equiv), 100°C, 15 min	15	>98	1181
7-2 (*n* = 1)	**PS-10a** (5 mg), CH_3CN (1.7 mL), AcOH (10 equiv), 100°C, 15 min	10	94	742
7-3 (*n* = 1)	**PS-10a** (5 mg), CH_3CN (1.7 mL), AcOH (10 equiv), 100°C, 15 min	11	97	849

[a] mean ± standard deviation of the 3 experiments

*Experiment 6 (***PS-10a** (5 mg)**,** THF (1.7 mL), AcOH (60 equiv), 100°C, 15 min)

	Analytical code	**YVX1.262**
	Activity fixed on QMA	9.29 GBq
t = 0 min	Activity eluted in R1	8.9 GBq
t = 19 min	Activity in R1 (end of fluorination)	7.8 GBq
t = 54 min	Activity in the collecting vial	780 MBq
	t_R ^{radio} of **[^{18}F]11a**	9.65 min
	Radiochemical purity of **[^{18}F]11a**	97%
	Activity Yield	9%
	RCY (decay corrected)	12%



<Peak Table>

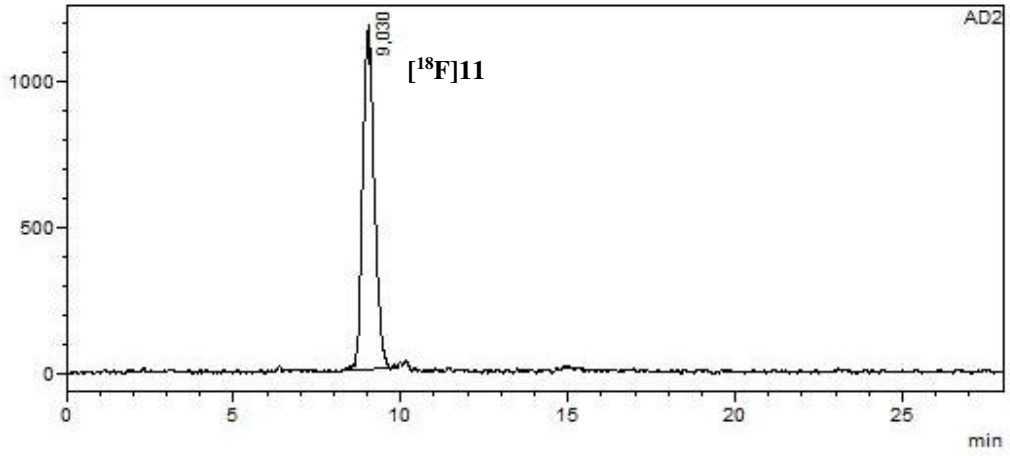
AD2

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	2,323	488299	35838	2,866		M	
2	9,649	16546526	753009	97,134		M	
Total		17034825	788847				

Analytic Radio HPLC chromatogram of experiment 6

*Experiment 7-1 (***PS-10a** (5 mg)**,** THF (1.7 mL), AcOH (10 equiv), 100°C, 15 min)

	Analytical code	**YVX1.276**
	Activity fixed on QMA	11.25 GBq
t = 0 min	Activity eluted in R1	10.4 GBq
t = 17 min	Activity in R1 (end of fluorination)	9.31 GBq
t = 40 min	Activity in the collecting vial	1.181 GBq
	t_R ^{radio} of **[^{18}F]11a**	9.03 min
	Radiochemical purity of **[^{18}F]11a**	>98%
	Activity Yield	11%
	RCY (decay corrected)	**15%**



<Peak Table>

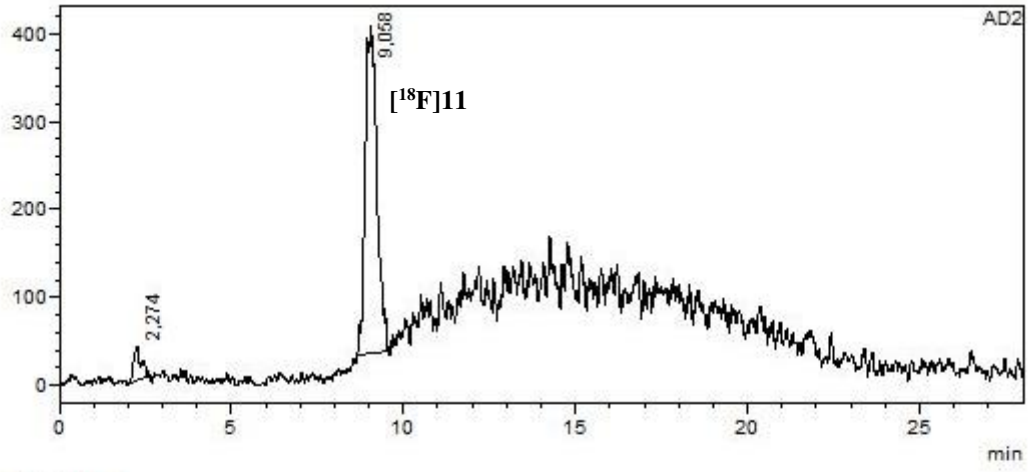
AD2

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	9,030	28231396	1171137	100,000		M	
Total		28231396	1171137				

Analytic Radio HPLC chromatogram of experiment 7-1

*Experiment 7-2 (***PS-10a** (5 mg)**,** THF (1.7 mL), AcOH (10 equiv), 100°C, 15 min)

	Analytical code	**YVX1.277**
	Activity fixed on QMA	10.25 GBq
t = 0 min	Activity eluted in R1	9.6 GBq
t = 17 min	Activity in R1 (end of fluorination)	8.66 GBq
t = 40 min	Activity in the collecting vial	742 MBq
	t_R ^{radio} of **[^{18}F]11a**	9.06 min
	Radiochemical purity of **[^{18}F]11a**	94%
	Activity Yield	8%
	RCY (decay corrected)	**10%**



<Peak Table>

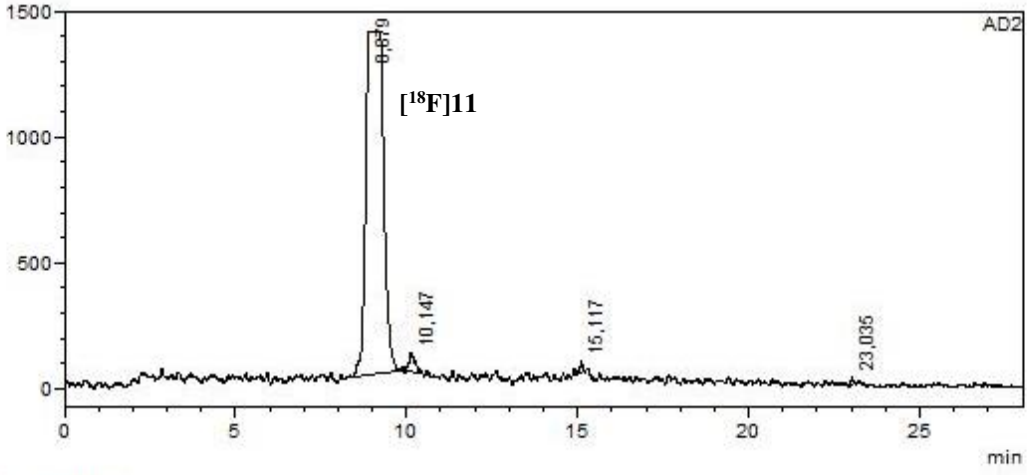
AD2

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	2,274	556692	38132	5,969		M	
2	9,058	8769942	370564	94,031		M	
Total		9326635	408696				

Analytic Radio HPLC chromatogram of experiment 7-2

*Experiment 7-3 (***PS-10a** (5 mg)**,** THF (1.7 mL), AcOH (10 equiv), 100°C, 15 min)

	Analytical code	**YVX1.281**
	Activity fixed on QMA	10.39 GBq
t = 0 min	Activity eluted in R1	9.95 GBq
t = 18 min	Activity in R1 (end of fluorination)	8.7 GBq
t = 41 min	Activity in the collecting vial	849 GBq
	t_R ^{radio} of **[^{18}F]11a**	8.88 min
	Radiochemical purity of **[^{18}F]11a**	97%
	Activity Yield	9%
	RCY (decay corrected)	**11%**



<Peak Table>

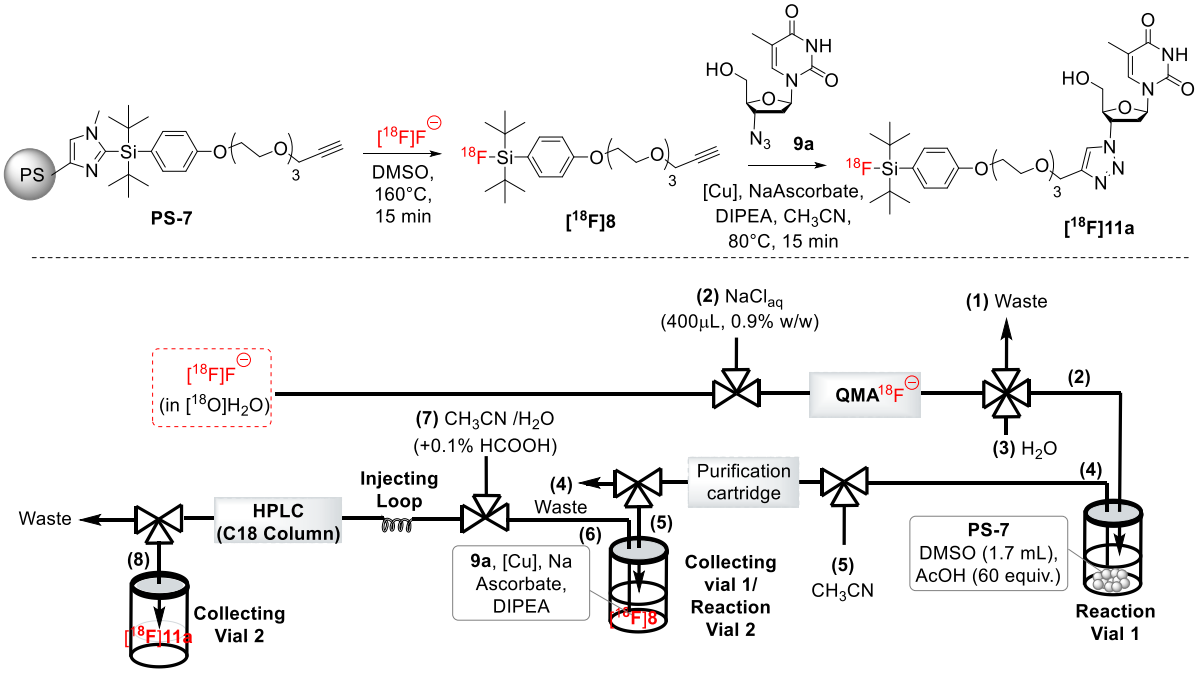
AD2

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	8,879	48558245	1362393	97,433		M	
2	10,147	830266	74103	1,666		M	
3	15,117	339421	48688	0,681		M	
4	23,035	109841	28972	0,220		M	
Total		49837772	1514155				

Analytic Radio HPLC chromatogram of experiment 7-3

3) Indirect synthesis of **[^{18}F]11a**

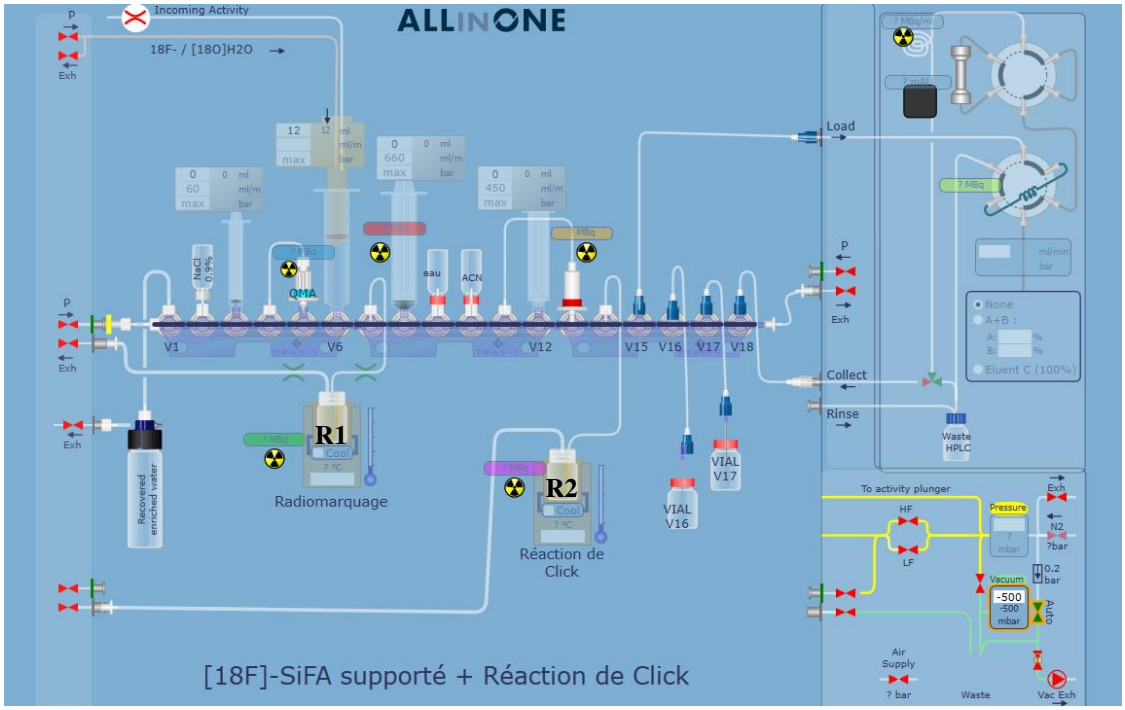
For comparison, an indirect synthesis was performed by radiofluorination of PS-ImidSiFA-Alkyne **PS-7** followed by CuAAC click reaction of the resulting **[^{18}F]8** with AZT.



Polymer **PS-7** (5mg, ≈0.36 mmol/g ImidSiFA grafted) was added in the reaction vial 1(reactor R1) with acetic acid (60 eq) in DMSO (1.7 mL). Then, [^{18}F]fluoride was automatically transferred into the synthesizer into syringe 2 and trapped by passing the solution through an anion-exchange resin cartridge (Sep-Pak QMA light, Waters). Release of [^{18}F]fluoride from QMA cartridge was achieved by eluting an aqueous solution of NaCl (0.9% w/w, 400 µL) with syringe 1 to the reaction vial R1 previously loaded (only 300µL of this solution could be transferred effectively in R1 due to the dead volume of the system). The pinch of the reactor was closed and the resulting mixture was allowed to react at 100°C for 15 min to 30 min. The mixture was then cooled at 40°C and homogenized by nitrogen bubbling at low flow for 1 min (400mbar concomitant with a vacuum set at -40 mbar). Then, the reaction mixture was collected with syringe 3. The reactor was washed by adding 2 mL of a 1:1 mixture of acetonitrile and water (using syringe 4). The content was homogenized again by nitrogen bubbling at low flow for 1 min (400mbar concomitant with a vacuum set at -40 mbar) and he content of the vial was collected using syringe 3. The reactor was washed a third time with water (4mL), homogenized under N_2 bubbling for 1 min as previously described and collected using syringe 3. The full content of syringe 3 (containing 66% of water) was passed through a C18 Sep-Pak cartridge at 3mL/min until emptiness. Then, the cartridge was washed with additional water (4mL) at 3mL/min using syringe 4. Finally, the product was eluted at 1mL/min from the C18 Sep-Pak cartridge using acetonitrile (4mL, from syringe 4) to the collecting vial 1 (C1, valve 16) placed outside of the hotcell® to measure the yield after the first step of radiolabelling.

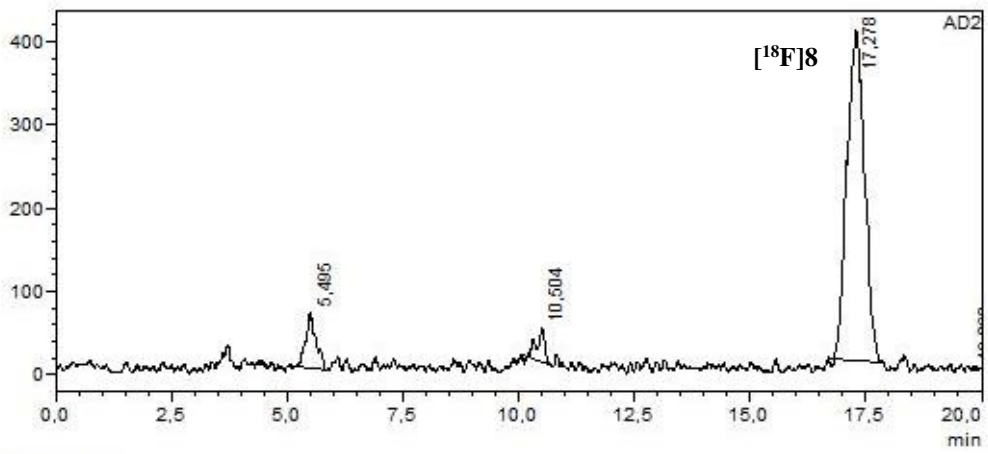
The second step was the CuAAC Click reaction with AZT in reaction vial 2 (R2) loaded before the beginning of the synthesis with AZT (zidovudine) (2 mg, 7.5µmol), sodium ascorbate (2 mg, 10 µmol), [CuCl(TBTA)]Cl (1 mg, 0.35 µmol) and diisopropylethylamine (7µL, 5.2 mg, 40µmol). ^{18}F-Fluorinated compound **[^{18}F]8** in acetonitrile (4 mL) was added to reactor 2 (R2) by using vacuum line from V16 in collecting vial 1 at -500 mbar. The reaction mixture was heated at 80°C for 15 min under low flow nitrogen bubbling (100mbar with a vacuum set at -50 mbar) to stirr the reaction. The content of R2 was collected by using syringe 4. The reactor was washed with acetonitrile (4mL), collected with syringe 4 and transferred to the injection loop at 2 mL/min. The purification of

the final compound **[^{18}F]11a** was performed by the built-in HPLC module using a reverse phase semi-preparative column (Luna C18 (5 µm, 100 Å, 250x10mm) using a mixture of acetonitrile/water (65/35) buffered with 0.1% of formic acid as eluent (isocratic). Two fractions were collected in V17 in two different collecting vial C2 and C3. The first fraction in C2 corresponded to the desired ^{18}F-SiFA-AZT **[^{18}F]11a** (t_R =12 min) and the second fraction in C3 corresponded to the unreacted ^{18}F-SiFA-alkyne **[^{18}F]8** (t_R =19 min). Analytical HPLC of each fraction were performed using at 1mL/min with the following program: 80% of B (13 min) -> 95% of B (2min) -> 95% of B (3min) -> 80% of B (2 min). (A = water + 0,1% of trifluoroacetic acid and B = acetonitrile + 0,1% of trifluoroacetic acid, t_R ^{radio} **[^{18}F]11a** = 6.48 min, t_R ^{radio} **[^{18}F]8** = 17.20 min).



Layout of the cassette for the synthesis of [^{18}F]11a by the "Indirect procedure"

	Experiment	**YVX1.491**	
	Activity fixed on QMA	10.28 GBq	
t = 0 min	Activity eluted in R1	9.18 GBq	Radiolabelling
t = 21 min	Activity in R1 (end of fluorination)	7.8 GBq	
t = 44 min	Activity in collecting vial C1	1037 MBq	
	t_R ^{radio} **[^{18}F]8**	17.23 min	
	Radiochemical purity	88%	
	Activity yield for step 1	11%	
	Radiochemical yield for step 1	15 %	
t = 88 min	Activity collected in C2 (t_R =12 min)	126 MBq	Click reaction
	t_R ^{radio} **[^{18}F]11a**	6.48 min	
	Radiochemical purity	>98%	
	Activity yield for step 1&2	1%	
	Radiochemical yield for step 1&2	**2%**	
t = 99 min	Activity collected in C3 (t_R =19 min)	232 MBq	
	t_R ^{radio} **[^{18}F]8**	17.23 min	
	Radiochemical purity	>98%	

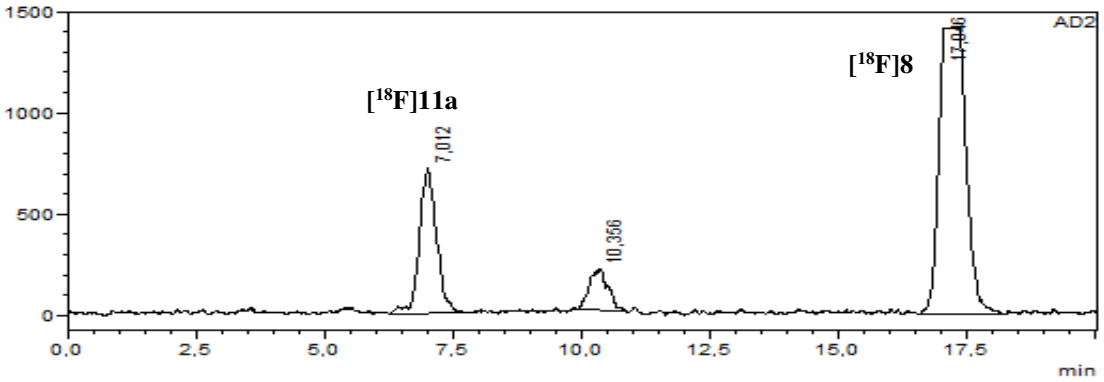


<Peak Table>

AD2

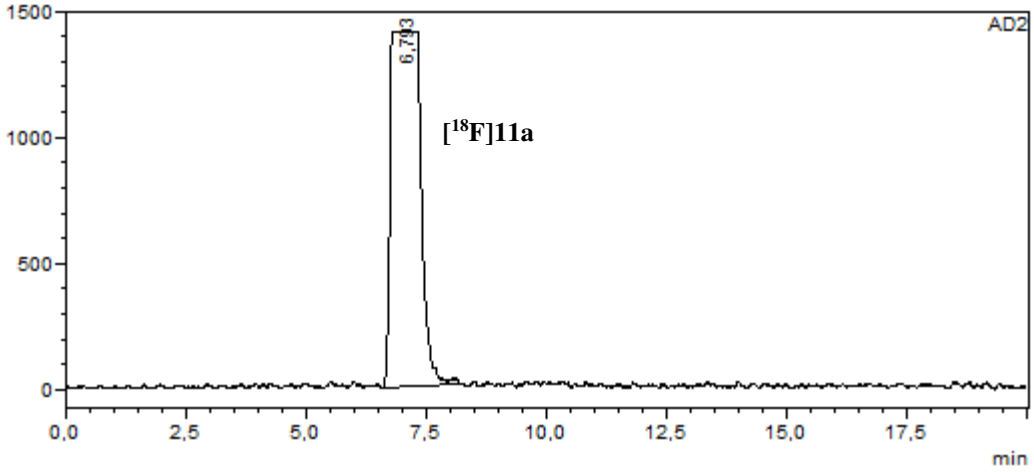
Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	5,495	1002607	65980	8,407		M	
2	10,504	413114	39510	3,464		M	
3	17,278	10491957	396770	87,976		M	
4	19,862	18242	5566	0,153			
Total		11925919	507826				

Analytic Radio HPLC chromatogram of [^{18}F]8 after the first reaction



Peak Start	Peak End	Ret. Time	Height	Area	Area%
6,292	7,783	7,012	715232	16436064	22,577
9,833	10,875	10,356	207691	5220707	7,171
16,542	18,267	17,046	1405411	51144512	70,252
			2328334	72801283	100,000

Analytic Radio HPLC chromatogram of the crude of the Click reaction



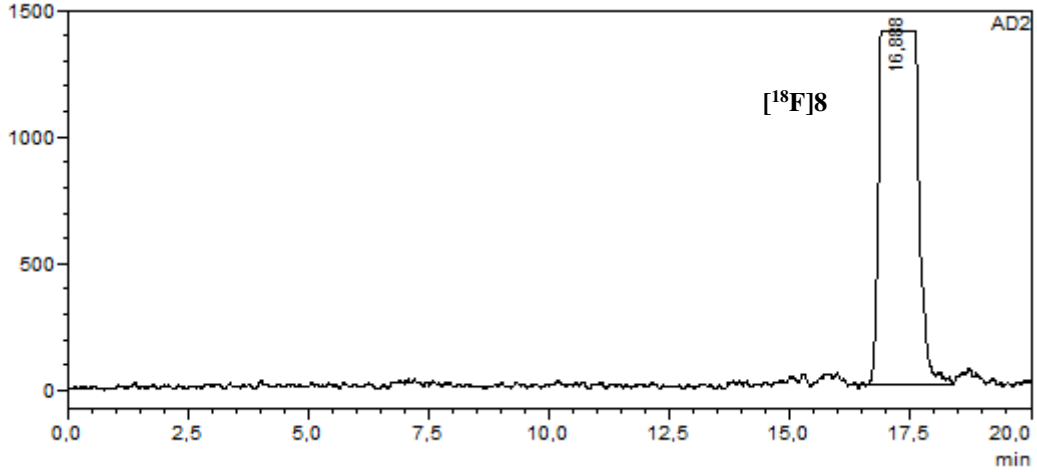
<Peak Table>

AD2

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	6,793	60048603	1404690	100,000		M	

Analytic Radio HPLC chromatogram of [^{18}F]11a after HPLC purification

(t_R PrepHPLC = 12 min)



<Peak Table>

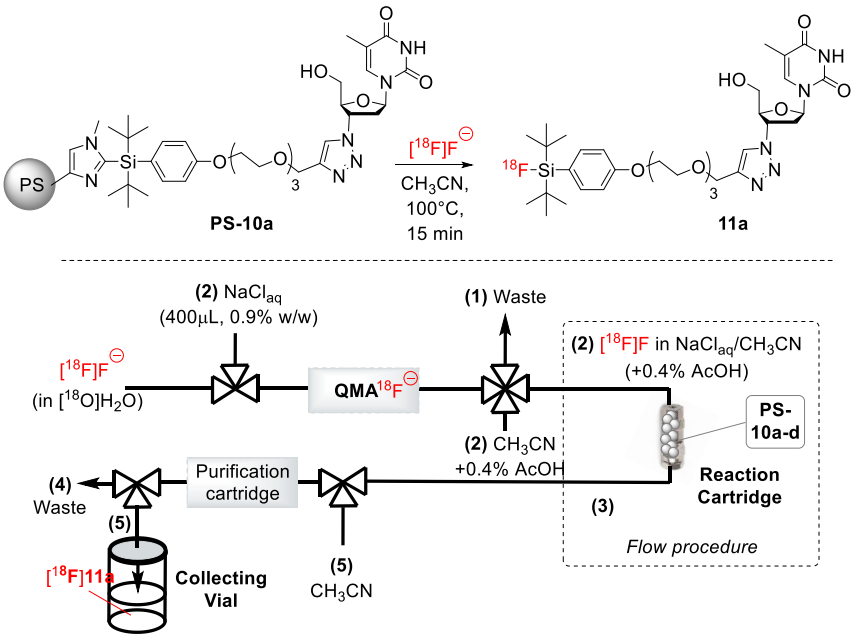
AD2

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	16,888	76079180	1393989	100,000		M	

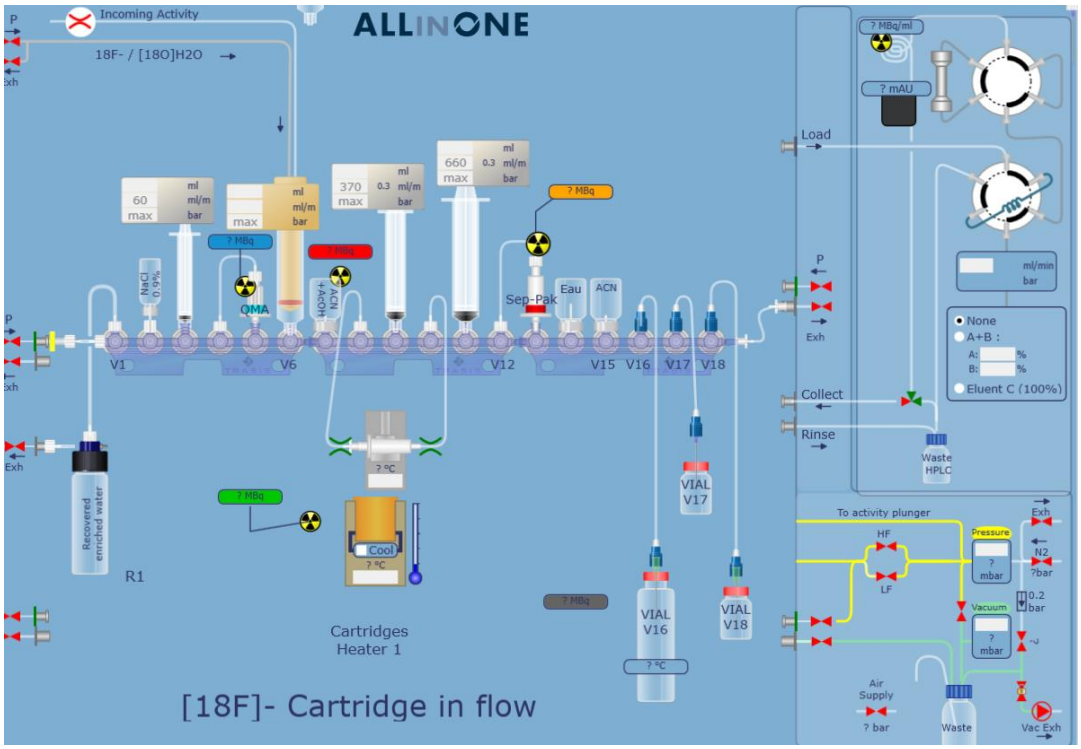
Analytic Radio HPLC chromatogram of [^{18}F]8 after HPLC purification

(t_R PrepHPLC = 19 min)

4) Synthesis of **[^{18}F]11a** with the "Flow procedure"

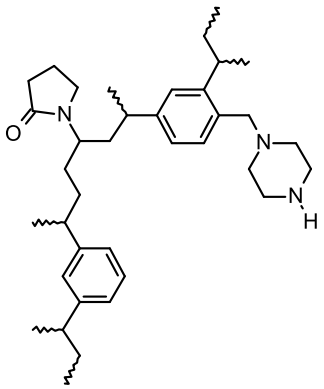


Polymer **PS-10a** (5mg, ≈0.34 mmol/g ImidSiFA grafted, 100% conversion for the CuAAC conjugation step) was mixed with the commercial polymer Oasis WAX (100 mg, 60 µm, 80 Å) and the mixture was packed inside a "metallic cartridge" (Empty stainless steel HPLC column, 20x4mm). A mixture of acetic acid (0.4 mL) in acetonitrile (100 mL) was used to impregnate the cartridge on valve V9 at 1mL/min. The impregnation was performed before closing the hotcell® to check the absence of leaks from the cartridge. The cartridge was pre-heated in advance at 100°C with the cartridge heater. Then, [^{18}F]fluoride was automatically transferred into the synthesizer into syringe 2 and trapped by passing the solution through an anion-exchange resin cartridge (Sep-Pak QMA light, Waters). Release of [^{18}F]fluoride from QMA cartridge was achieved by eluting an aqueous solution of NaCl (0.9% w/w, 400 µL) with syringe 1 to syringe 3, and a mixture at 0.4% of acetic acid in acetonitrile (3.7-4.1 mL) was consecutively retrieved from valve 7 into syringe 3. Firstly, 1.3 mL of the overall content of syringe 3 mixture was pushed into the inlet of the cartridge at 1mL/min (as a dead volume of 1.3 mL was calculated between the cartridge and the syringe). Then, the reaction was performed in flow by transferring the content of syringe 3 at 0.3 mL/min over 15-16 min to syringe 4 through the reaction cartridge until emptiness. After this transfer, the cartridge was washed with acetonitrile containing 0.4% of acetic acid (1mL) from syringe 3 to syringe 4 at 3 mL/min. Water (11 mL) was taken from vial 14 to syringe 4. The content of syringe 4 (containing 68% of water) was eluted on the C18 cartridge at 3mL/min to vial 16. Then, the cartridge was washed with water (4mL) at 3mL/min using syringe 4 collected in vial 16 and finally, product **[^{18}F]11a** was eluted at 1mL/min from the purification cartridge by using acetonitrile (4mL) from syringe 4 to a collecting vial 17 placed outside of the hotcell®. The purity of the fluorinated compound **[^{18}F]11a** was checked from a sample by analytical HPLC at a flow rate of 1mL/min using the following program: 70% of B (11 min) -> 75% of B (4min) ->75% of B (15min)-> 95% of B (5 min) -> 95% of B (5 min) -> 70% of B (1 min) with A = water + 0,1% of trifluoroacetic acid and B = ACN + 0,1% of trifluoroacetic acid. The desired compound **[^{18}F]11a** was detected by radio HPLC (t_R ^{radio} : 9.09min).



Layout of the cassette for the synthesis of [^{18}F]11a by the "Flow procedure"

Metallic cartridge used for the synthesis in cartridge



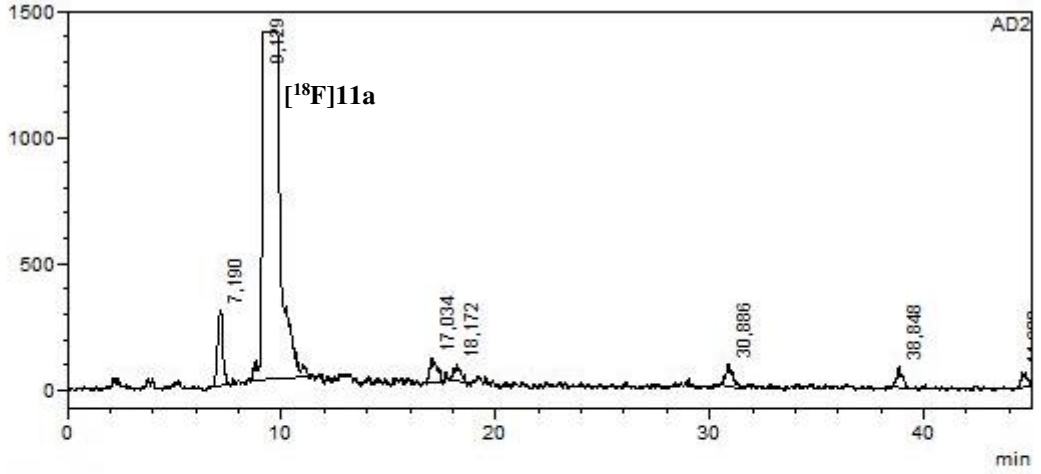
Representative structure of the Oasis WAX Resin mixed with PS-10a in the reaction cartridge

Experiment (nb of runs)	Conditions (Flow procedure)	RCY of [^{18}F]**11a** (%)	RCP of [^{18}F]**11a** (%)	Final Activity (MBq)
8 (*n* = 2)	**PS-10a (5 mg), CH_3CN (1.7 mL), AcOH (60 equiv), 100°C, 16 min**	**7 ± 1**[a]	**87 ± 3**[a]	**-**
8-1 (*n* = 1)	**PS-10a** (5 mg), CH_3CN (1.7 mL), AcOH (10 equiv), 100°C, 16 min	6	85	292
8-2 (*n* = 1)	**PS-10a** (5 mg), CH_3CN (1.7 mL), AcOH (10 equiv), 100°C, 16 min	7	89	504

[a] mean ± standard deviation of the 2 experiments

*Experiment 8-1 (***PS-10a** (5 mg)**,** THF (1.7 mL), AcOH (60 equiv), 100°C, 16 min, flow procedure)

	Analytical code	**YVX1.289**
t = 0 min	Activity fixed on QMA	7.71 GBq
t = 62 min	Activity in the collecting vial	292 MBq
	t_R ^{radio} of **[^{18}F]11a**	9.12 min
	Radiochemical purity of **[^{18}F]11a**	85%
	Activity Yield	4%
	RCY (decay corrected)	6%



<Peak Table>

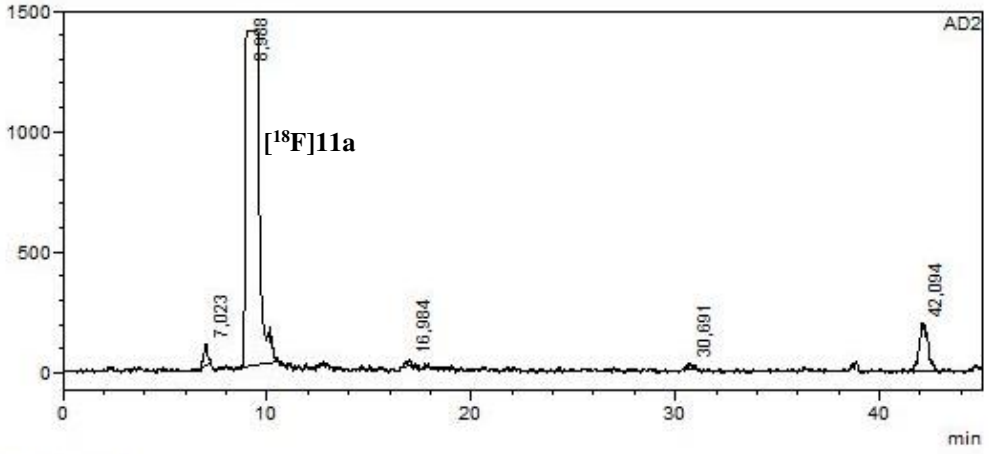
AD2

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7,190	5231744	298828	5,551		M	
2	9,129	80665856	1371793	85,588		M	
3	17,034	2325366	98554	2,467		M	
4	18,172	1493279	69024	1,584		M	
5	30,886	1905728	88062	2,022		M	
6	38,848	1481647	82447	1,572		M	
7	44,608	1145128	60531	1,215		M	
Total		94248748	2069239				

Analytic Radio HPLC chromatogram of experiment 8a

*Experiment 8-2 (***PS-10a** (5 mg)**,** THF (1.7 mL), AcOH (60 equiv), 100°C, 15 min, flow procedure)

	Analytical code	YVX1.294
t = 0 min	Activity fixed on QMA	10.1 GBq
t = 51 min	Activity in the collecting vial	504 MBq
	t_R ^{radio} of **[^{18}F]11a**	8.99 min
	Radiochemical purity of **[^{18}F]11a**	89%
	Activity Yield	5%
	RCY (decay corrected)	7%



<Peak Table>

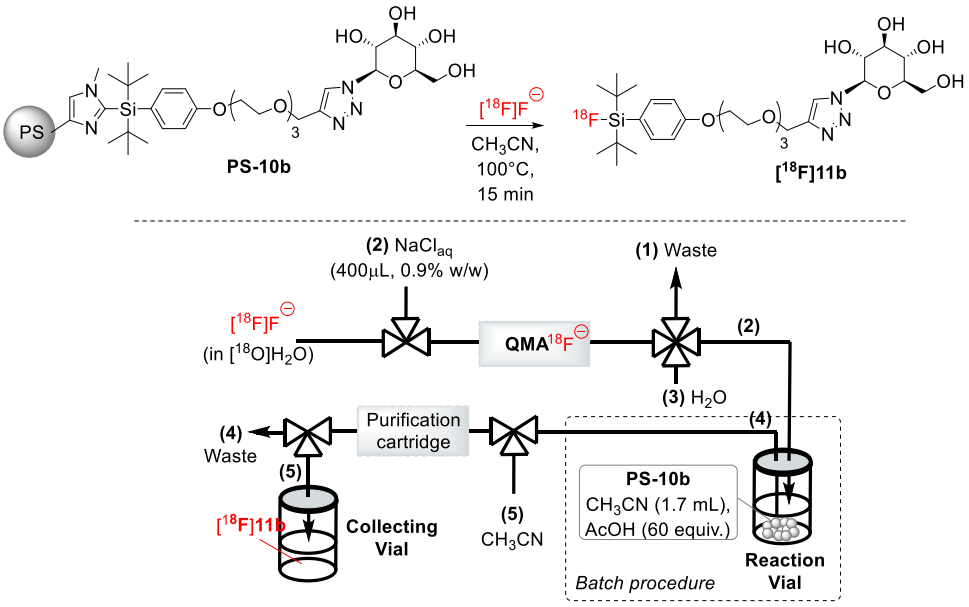
AD2

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7,023	1167049	89489	1,628		M	
2	8,988	64007831	1390166	89,293		M	
3	16,984	353231	27585	0,493		M	
4	30,691	398546	25040	0,556		M	
5	42,094	5756648	196364	8,031		M	
Total		71683304	1728643				

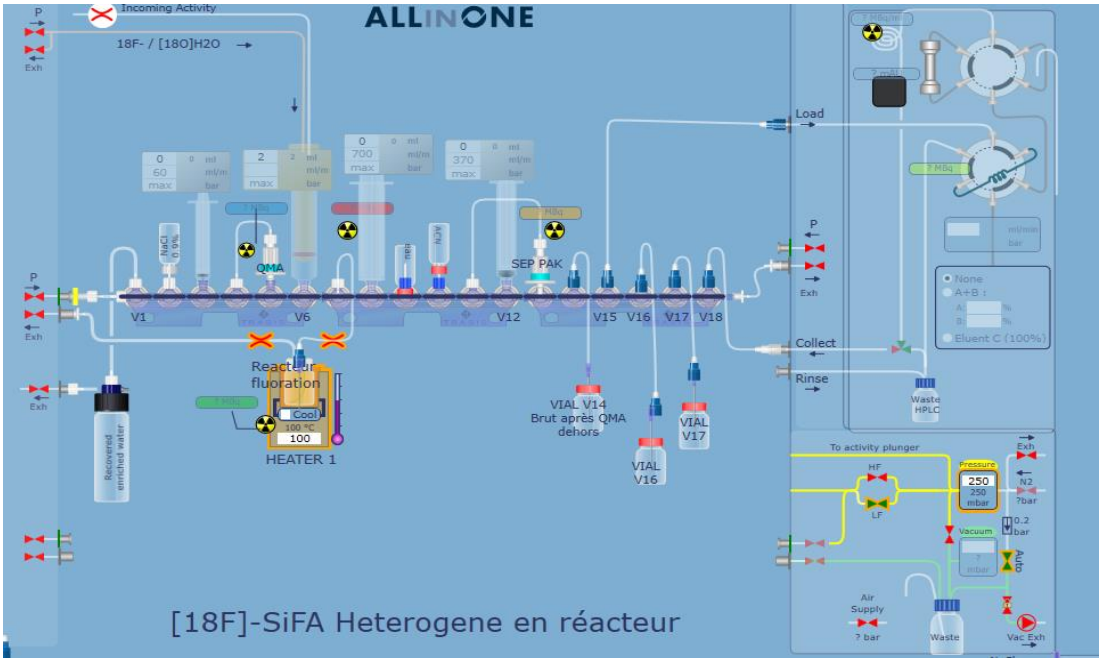
Analytic Radio HPLC chromatogram of Experiment 8b

c. Radiosyntheses of [^{18}F]11b, [^{18}F]11c and [^{18}F]11d

1) Radiosynthesis of **[^{18}F]11b** using the "Batch procedure"



Polymer **PS-10b** (5mg, ≈0.34 mmol/g ImidSiFA grafted, 100% conversion for the CuAAC conjugation step) was added in the reaction vial (reactor R1) with acetic acid (60 eq) in acetonitrile (1.7 mL). Then, [^{18}F]fluoride was automatically transferred into the synthesizer into syringe 2 and trapped by passing the solution through an anion-exchange resin cartridge (Sep-Pak QMA light, Waters). Release of [^{18}F]fluoride from QMA cartridge was achieved by eluting an aqueous solution of NaCl (0.9% w/w, 400 µL) with syringe 1 to the reaction vial R1 previously loaded (only 300µL of this solution could be transferred effectively in R1 due to the dead volume of the system). The pinch of the reactor was closed and the resulting mixture was allowed to react at 100°C for 15 min. The mixture was then cooled at 40°C and homogenized by nitrogen bubbling at low flow for 1 min (400mbar concomitant with a vacuum set at -40 mbar). Then, the reaction mixture was collected with syringe 3. The reactor was washed by adding 2 mL of a 1:1 mixture of acetonitrile and water (using syringe 4). The content was homogenized again by nitrogen bubbling at low flow for 1 min (400mbar concomitant with a vacuum set at -40 mbar) and he content of the vial was collected using syringe 3. The reactor was washed a third time with water (4mL), homogenized under N_2 bubbling for 1 min as previously described and collected using syringe 3. The full content of syringe 3 (containing 66% of water) was passed through a C18 Sep-Pak cartridge at 3mL/min until emptiness. Then, the cartridge was washed with additional water (4mL) at 3mL/min using syringe 4. Finally, the product was eluted at 1mL/min from the C18 Sep-Pak cartridge using acetonitrile (4mL, from syringe 4) to the collecting vial (valve 14) placed outside of the hotcell®. The radiochemical yield (RCY) was calculated from the decay-corrected activity inside the collecting vial divided by activity in the reaction vial R1 before the fluorination (at the time where fluoride-18 was fully eluted from the QMA to R1) and multiplied by the radiochemical purity (RCP). The purity of the fluorinated compound **[^{18}F]11b** was checked from a sample by analytical HPLC at a flow rate of 1mL/min using the following program: 70% of B (8 min) -> 95% of B (5min) ->95% of B (5min)-> 70% of B (3 min) with A = water + 0,1% of formic acid and B = ACN + 0,1% of formic acid. The desired compound **[^{18}F]11b** was detected by radio HPLC (t_R ^{radio} ≈ 6.6 min).



Layout of the cassette for the synthesis of [^{18}F]11b by the "Batch procedure"

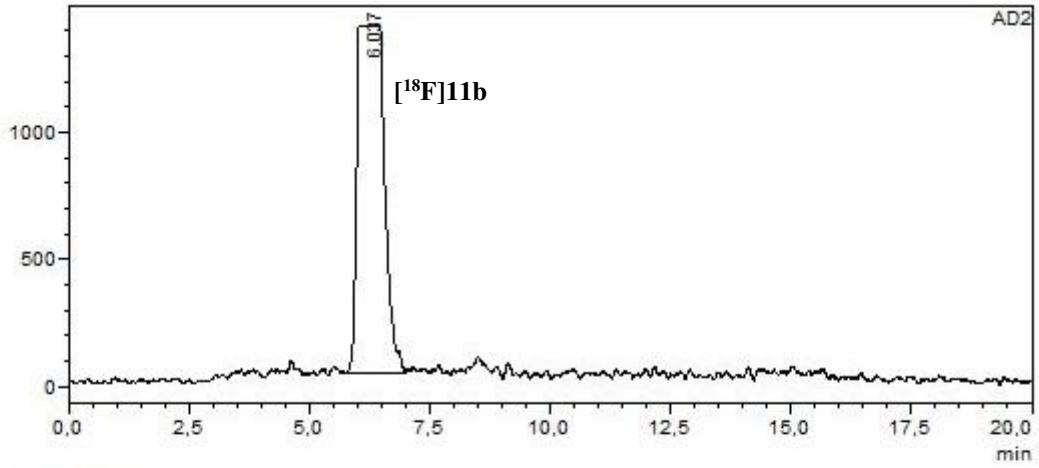
Results of the experiments are summarized in the following table:

Experiment (nb of runs)	Conditions	RCY of **[^{18}F]11b** (%)	RCP of **[^{18}F]11b** (%)	Final Activity (MBq)
9 (*n* = 3)	**PS-10b (5 mg), CH_3CN (1.7 mL), AcOH (60 equiv), 100°C, 15 min**	**12 ± 2**[a]	**>98**	**-**
9-1 (*n* = 1)	**PS-10b** (5 mg), CH_3CN (1.7 mL), AcOH (60 equiv), 100°C, 15 min	17	>98	845
9-2 (*n* = 1)	**PS-10b** (5 mg), CH_3CN (1.7 mL), AcOH (60 equiv), 100°C, 15 min	15	>98	1269
9-3 (*n* = 1)	**PS-10b** (5 mg), CH_3CN (1.7 mL), AcOH (60 equiv), 100°C, 15 min	19	>98	1173

[a] mean ± standard deviation of the 3 experiments

*Experiment 9-1 (***PS-10b** (5 mg)**,** THF (1.7 mL), AcOH (60 equiv), 100°C, 15 min)

	Analytical code	**YVX1.362**
	Activity fixed on QMA	6.61 GBq
t = 0 min	Activity eluted in R1	6.54 GBq
t = 17 min	Activity in R1 (end of fluorination)	5.82 GBq
t = 40 min	Activity in the collecting vial	845 MBq
	t_R ^{radio} of **[^{18}F]11b**	6.04 min
	Radiochemical purity of **[^{18}F]11b**	>98%
	Activity Yield	13 %
	RCY (decay corrected)	**17 %**



<Peak Table>

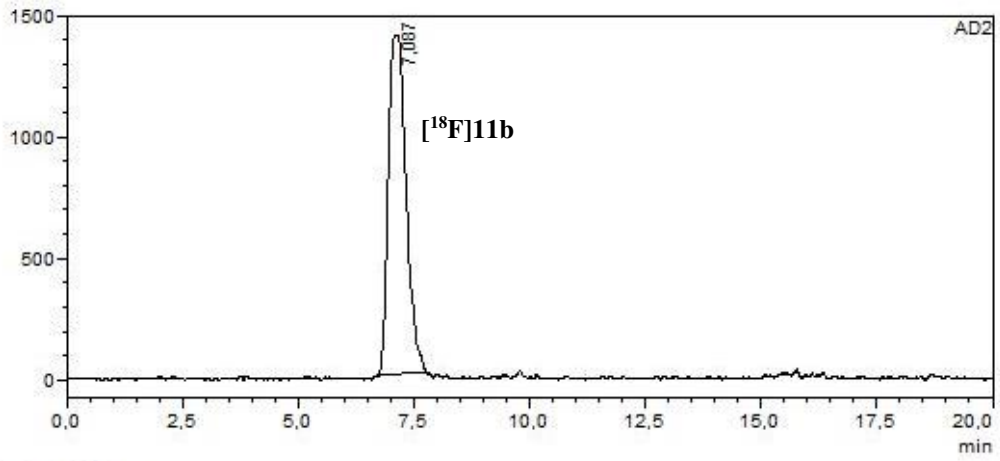
AD2

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	6,037	52856138	1361284	100,000		M	
Total		52856138	1361284				

Analytic Radio HPLC chromatogram of Experiment 9a

*Experiment 9-2 (***PS-10b** (5 mg)**,** THF (1.7 mL), AcOH (60 equiv), 100°C, 15 min)

	Analytical code	**YVX1.363**
	Activity fixed on QMA	11. 26 GBq
t = 0 min	Activity eluted in R1	10.94 GBq
t = 19 min	Activity in R1 (end of fluorination)	9.51 GBq
t = 45 min	Activity in the collecting vial	1269 MBq
	t_R ^{radio} of **[^{18}F]11b**	7.09 min
	Radiochemical purity of **[^{18}F]11b**	>98%
	Activity Yield	12 %
	RCY (decay corrected)	**15 %**



<Peak Table>

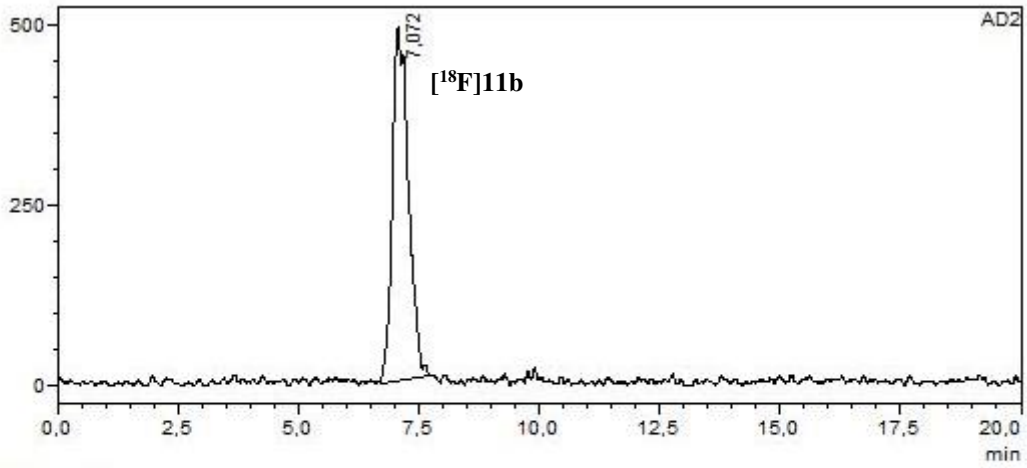
AD2

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7,087	37280902	1390513	100,000		M	
Total		37280902	1390513				

Analytic Radio HPLC chromatogram of Experiment 9b

*Experience 9-3 (***PS-10b** (5 mg)**,** THF (1.7 mL), AcOH (60 equiv), 100°C, 15 min)

	Analytical code	**YVX1.364**
	Activity fixed on QMA	7.75 GBq
t = 0 min	Activity eluted in R1	7.80 GBq
t = 17 min	Activity in R1 (end of fluorination)	7.15 GBq
t = 39 min	Activity in the collecting vial	1173 MBq
	t_R ^{radio} of **[^{18}F]11b**	7.07 min
	Radiochemical purity of **[^{18}F]11b**	>98%
	Activity Yield	15%
	RCY (decay corrected)	**19%**



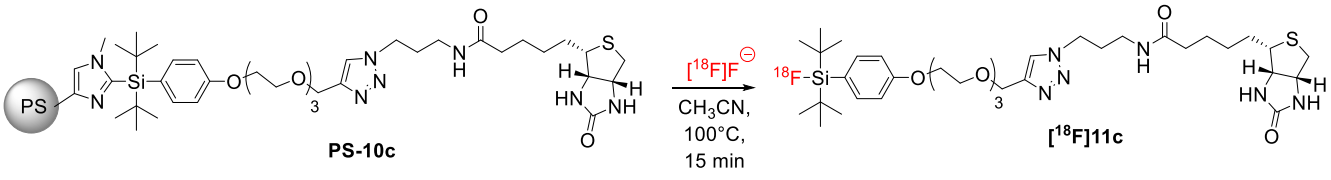
<Peak Table>

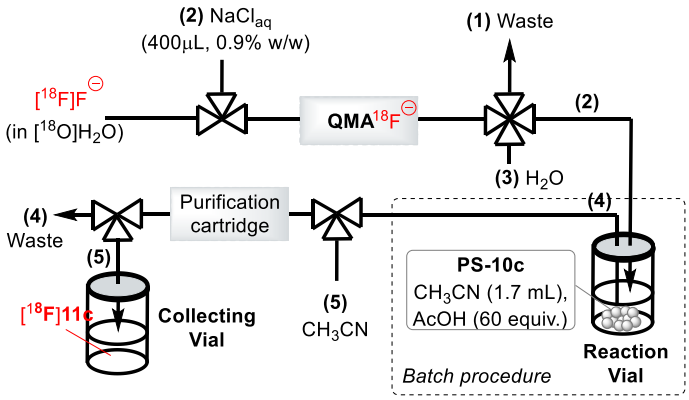
AD2

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	7,072	11419055	488664	100,000		M	
Total		11419055	488664				

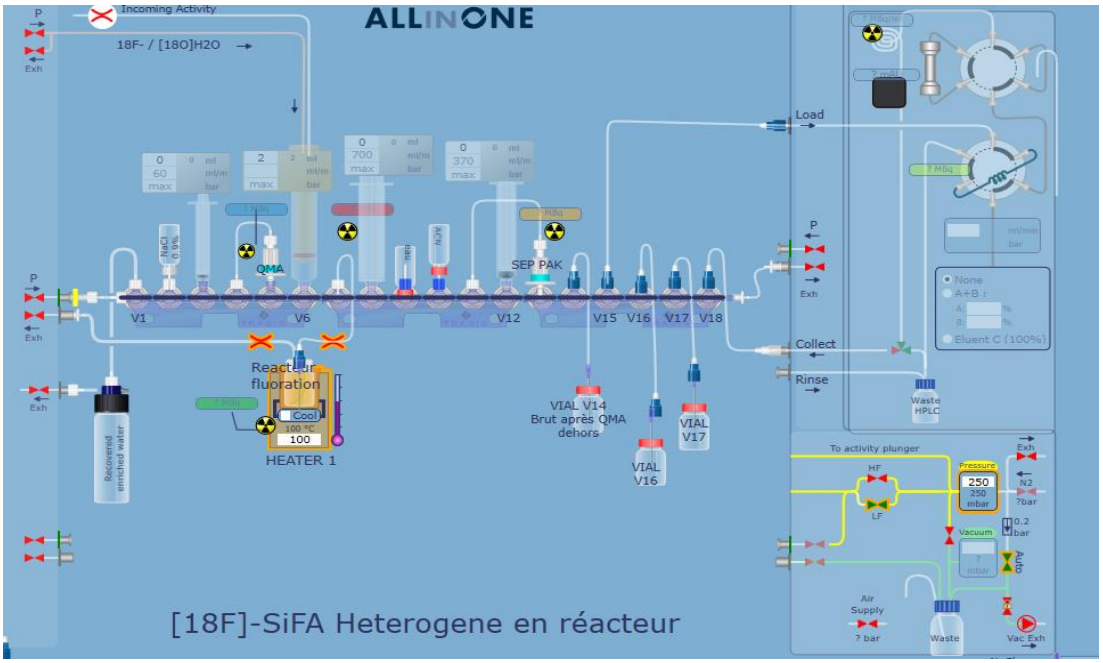
Analytic Radio HPLC chromatogram of Experiment 9c

2) Radiosynthesis of **[^{18}F]11c** using the "Batch procedure"





Polymer **PS-10c** (5mg, ≈0.32 mmol/g ImidSiFA grafted, 100% conversion for the CuAAC conjugation step) was added in the reaction vial (reactor R1) with acetic acid (60 eq) in acetonitrile (1.7 mL). Then, [^{18}F]fluoride was automatically transferred into the synthesizer into syringe 2 and trapped by passing the solution through an anion-exchange resin cartridge (Sep-Pak QMA light, Waters). Release of [^{18}F]fluoride from QMA cartridge was achieved by eluting an aqueous solution of NaCl (0.9% w/w, 400 µL) with syringe 1 to the reaction vial R1 previously loaded (only 300µL of this solution could be transferred effectively in R1 due to the dead volume of the system). The pinch of the reactor was closed and the resulting mixture was allowed to react at 100°C for 15 min. The mixture was then cooled at 40°C and homogenized by nitrogen bubbling at low flow for 1 min (400mbar concomitant with a vacuum set at -40 mbar). Then, the reaction mixture was collected with syringe 3. The reactor was washed by adding 2 mL of a 1:1 mixture of acetonitrile and water (using syringe 4). The content was homogenized again by nitrogen bubbling at low flow for 1 min (400mbar concomitant with a vacuum set at -40 mbar) and he content of the vial was collected using syringe 3. The reactor was washed a third time with water (4mL), homogenized under N_2 bubbling for 1 min as previously described and collected using syringe 3. The full content of syringe 3 (containing 66% of water) was passed through a C18 Sep-Pak cartridge at 3mL/min until emptiness. Then, the cartridge was washed with additional water (4mL) at 3mL/min using syringe 4. Finally, the product was eluted at 1mL/min from the C18 Sep-Pak cartridge using acetonitrile (4mL, from syringe 4) to the collecting vial (valve 14) placed outside of the hotcell®. The radiochemical yield (RCY) was calculated from the decay-corrected activity inside the collecting vial divided by activity in the reaction vial R1 before the fluorination (at the time where fluoride-18 was fully eluted from the QMA to R1) and multiplied by the radiochemical purity (RCP). The purity of the fluorinated compound **[^{18}F]11c** was checked by analytical HPLC at a flow rate of 1mL/min using program 1 (75% of B (8 min) -> 95% of B (5min) ->95% of B (5min)-> 75% of B (3 min)) or program 2 (70% of B (8 min) -> 95% of B (5min) ->95% of B (5min)-> 70% of B (3 min)) with A = water + 0.1% of formic acid and B = CH_3CN + 0.1% of formic acid. The desired compound **[^{18}F]11c** was detected by radio HPLC (t_R ^{radio} ≈ 7.0 min or 8.9 min).



Layout of the cassette for the synthesis of [^{18}F]11c by the "Batch procedure"

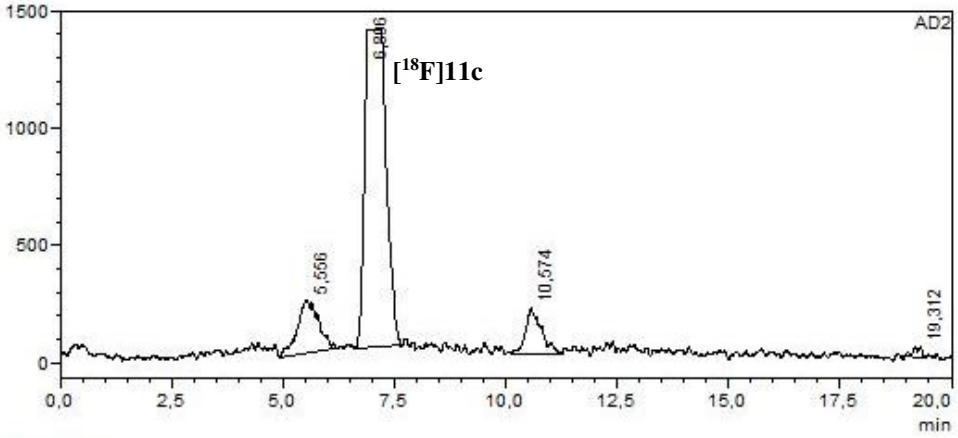
Results of the experiments are summarized in the following table:

Experiment (nb of runs)	Conditions	RCY of **[^{18}F]11c** (%)	RCP of **[^{18}F]11c** (%)	Final Activity (MBq)
10 (*n* = 3)	**PS-10c (5 mg), CH_3CN (1.7 mL), AcOH (60 equiv), 100°C, 15 min**	**13 ± 1**[a]	**86 ± 7**[a]	**-**
10-1 (*n* = 1)	**PS-10c** (5 mg), CH_3CN (1.7 mL), AcOH (60 equiv), 100°C, 15 min	14	78	973
10-2 (*n* = 1)	**PS-10c** (5 mg), CH_3CN (1.7 mL), AcOH (60 equiv), 100°C, 15 min	12	89	752
10-3 (*n* = 1)	**PS-10c** (5 mg), CH_3CN (1.7 mL), AcOH (60 equiv), 100°C, 15 min	13	90	860

[a] mean ± standard deviation of the 3 experiments

*Experiment 10-1 (***PS-10c** (5 mg)**,** THF (1.7 mL), AcOH (60 equiv), 100°C, 15 min)

	Analytical code	**YVX1.377**
	Activity fixed on QMA	10.00 GBq
t = 0 min	Activity eluted in R1	9.20 GBq
t = 17 min	Activity in R1 (end of fluorination)	8.02 GBq
t = 40 min	Activity in the collecting vial	973 MBq
	t_R ^{radio} of **[^{18}F]11c**	6.90 min
	Radiochemical purity of **[^{18}F]11c**	78%
	Activity Yield	11%
	RCY (decay corrected)	**14%**



<Peak Table>

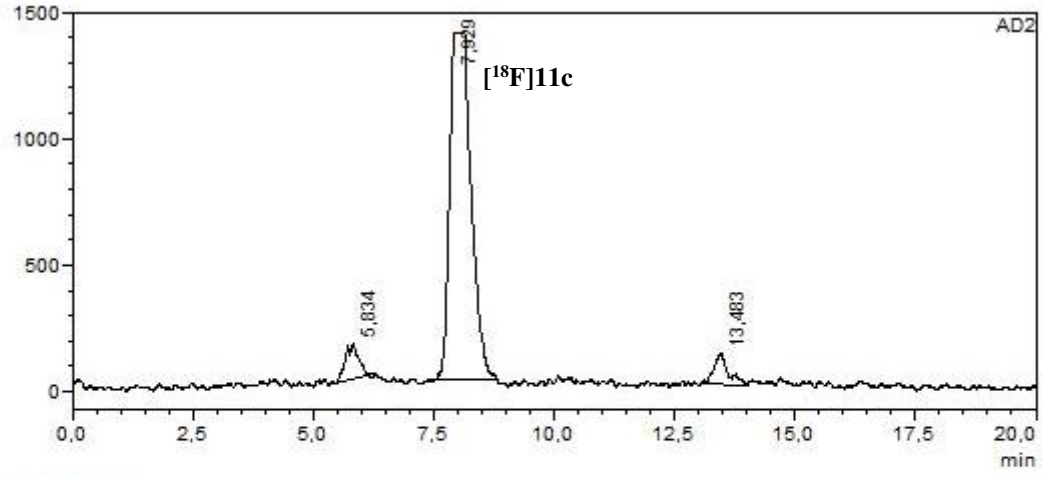
AD2

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	5,556	7519649	222039	13,037		M	
2	6,896	44897722	1350733	77,840		M	
3	10,574	4654771	191779	8,070		M	
4	19,312	607595	49096	1,053		M	
Total		57679737	1813647				

Analytic Radio HPLC chromatogram of experiment 10-1

*Experiment 10-2 (***PS-10c** (5 mg)**,** THF (1.7 mL), AcOH (60 equiv), 100°C, 15 min)

	Analytical code	**YVX1.378**
	Activity fixed on QMA	9.08 GBq
t = 0 min	Activity eluted in R1	8.20 GBq
t = 16 min	Activity in R1 (end of fluorination)	7.2 GBq
t = 42 min	Activity in the collecting vial	752 MBq
	t_R ^{radio} of **[^{18}F]11c**	7. 93 min
	Radiochemical purity of **[^{18}F]11c**	89%
	Activity Yield	9%
	RCY (decay corrected)	12%



<Peak Table>

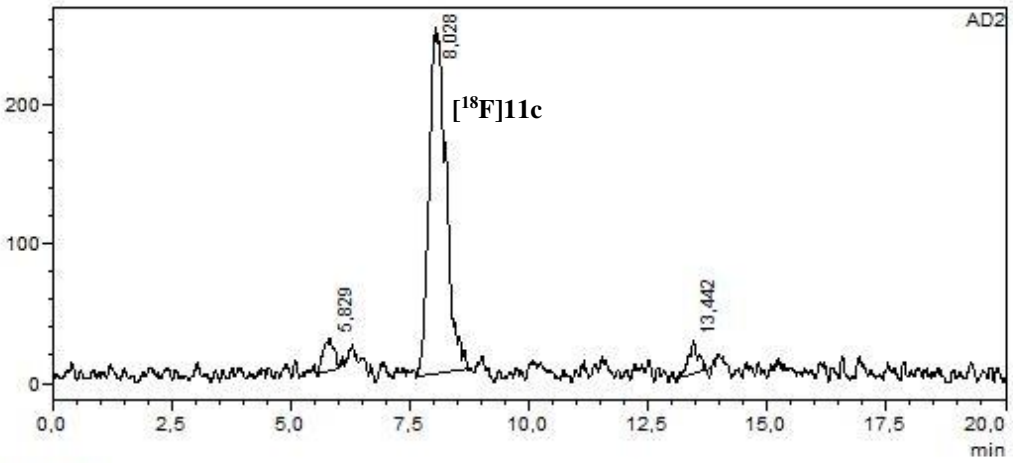
AD2

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	5,834	2684579	142954	5,724		M	
2	7,929	41690838	1368537	88,894		M	
3	13,483	2524014	124909	5,382		M	
Total		46899432	1636400				

Analytic Radio HPLC chromatogram of experiment 10-2

*Experiment 10-3 (***PS-10c** (5 mg)**,** THF (1.7 mL), AcOH (60 equiv), 100°C, 15 min)

	Analytical code	**YVX1.379**
	Activity fixed on QMA	9.3 GBq
t = 0 min	Activity eluted in R1	8.55 GBq
t = 18 min	Activity in R1 (end of fluorination)	7.50 GBq
t = 40 min	Activity in the collecting vial	860 MBq
	t_R ^{radio} of **[^{18}F]11c**	8.02 min
	Radiochemical purity of **[^{18}F]11c**	90%
	Activity Yield	10%
	RCY (decay corrected)	**13%**



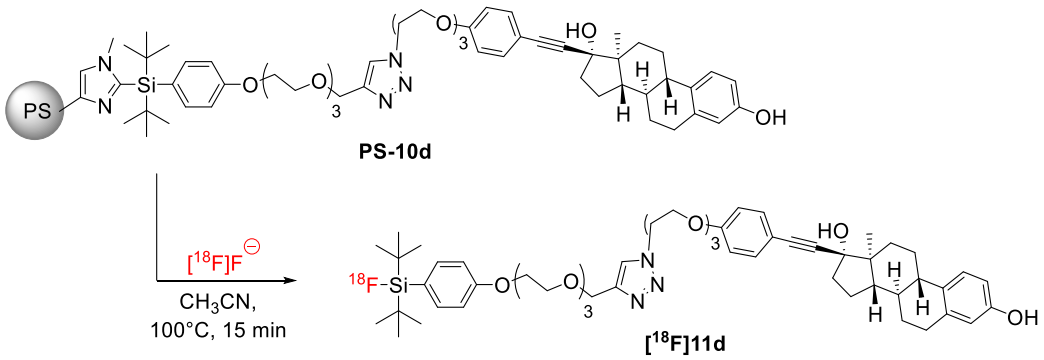
<Peak Table>

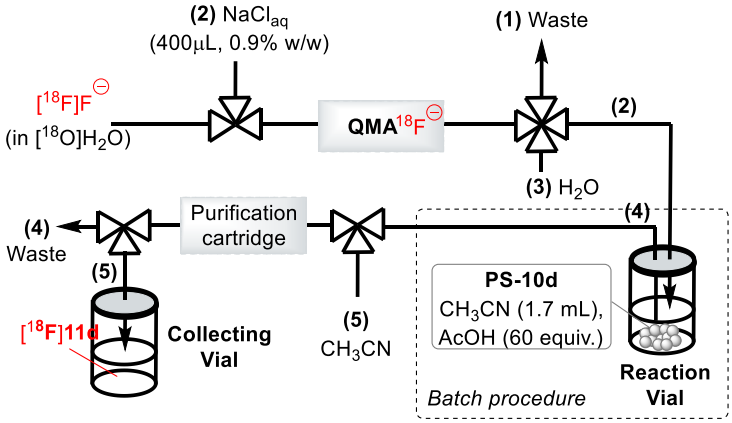
AD2

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	5,829	357165	22115	5,328		M	
2	8,028	6028292	246903	89,932		M	
3	13,442	317685	23898	4,739		M	
Total		6703143	292916				

Analytic Radio HPLC chromatogram of experiment 10-3

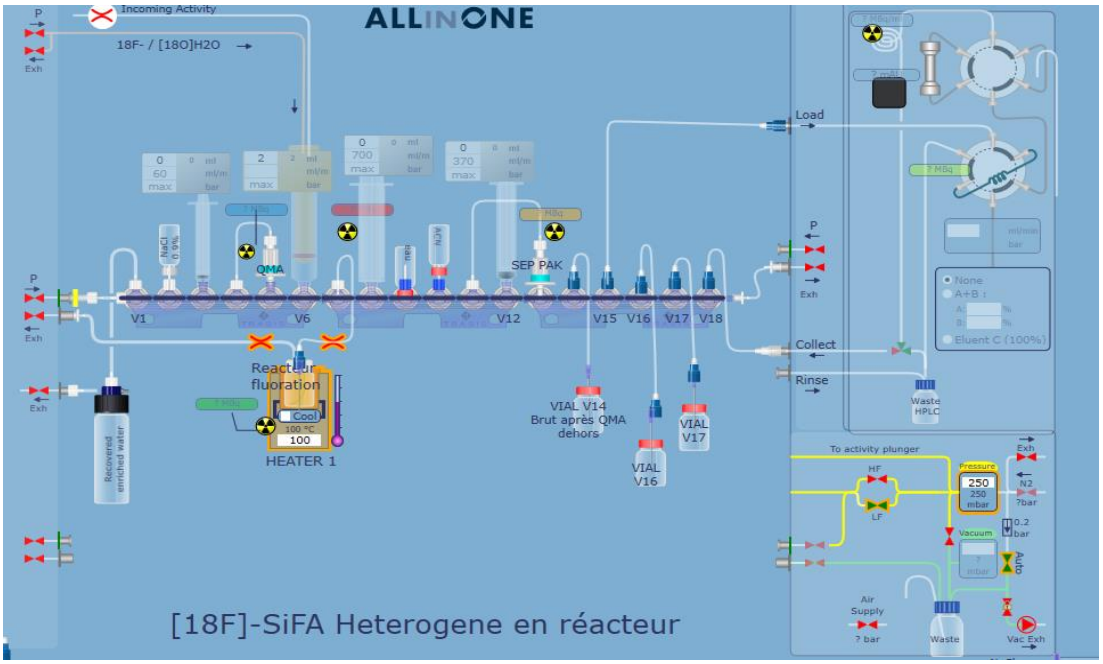
3) Radiosynthesis of **[^{18}F]11d** using the "Batch procedure"





Polymer **PS-10d** (5mg, ≈0.30 mmol/g ImidSiFA grafted, 100% conversion for the CuAAC conjugation step) was added in the reaction vial (reactor R1) with acetic acid (60 eq) in acetonitrile (1.7 mL). Then, [^{18}F]fluoride was automatically transferred into the synthesizer into syringe 2 and trapped by passing the solution through an anion-exchange resin cartridge (Sep-Pak QMA light, Waters). Release of [^{18}F]fluoride from QMA cartridge was achieved by eluting an aqueous solution of NaCl (0.9% w/w, 400 µL) with syringe 1 to the reaction vial R1 previously loaded (only 300µL of this solution could be transferred effectively in R1 due to the dead volume of the system). The pinch of the reactor was closed and the resulting mixture was allowed to react at 100°C for 15 min. The mixture was then cooled at 40°C and homogenized by nitrogen bubbling at low flow for 1 min (400mbar concomitant with a vacuum set at -40 mbar). Then, the reaction mixture was collected with syringe 3. The reactor was washed by adding 2 mL of a 1:1 mixture of acetonitrile and water (using syringe 4). The content was homogenized again by nitrogen bubbling at low flow for 1 min (400mbar concomitant with a vacuum set at -40 mbar) and he content of the vial was collected using syringe 3. The reactor was washed a third time with water (4mL), homogenized under N_2 bubbling for 1 min as previously described and collected using syringe 3. The full content of syringe 3 (containing 66% of water) was passed through a C18 Sep-Pak cartridge at 3mL/min until emptiness. Then, the cartridge was washed with additional water (4mL) at 3mL/min using syringe 4. Finally, the product was eluted at 1mL/min from the C18 Sep-Pak cartridge using acetonitrile (4mL, from syringe 4) to the collecting vial (valve 14) placed outside of the hotcell®. The radiochemical yield (RCY) was calculated from the decay-corrected activity inside the collecting vial divided by activity in the reaction vial R1 before the fluorination (at the time where fluoride-18 was fully eluted from the QMA to R1) and multiplied by the radiochemical purity (RCP). The purity of the fluorinated compound **[^{18}F]11c** was checked by analytical HPLC at a flow rate of 1mL/min using the following program: 90% of B (8 min) -> 95% of

B (5min) ->95% of B (5min)-> 90% of B (3 min) with A = water + 0.1% of formic acid and B = CH_3CN + 0.1% of formic acid. The desired compound **[^{18}F]11d** was detected by radio HPLC (t_R ^{radio} ≈ 10.0 min).



Layout of the cassette for the synthesis of [^{18}F]11d by the "Batch procedure"

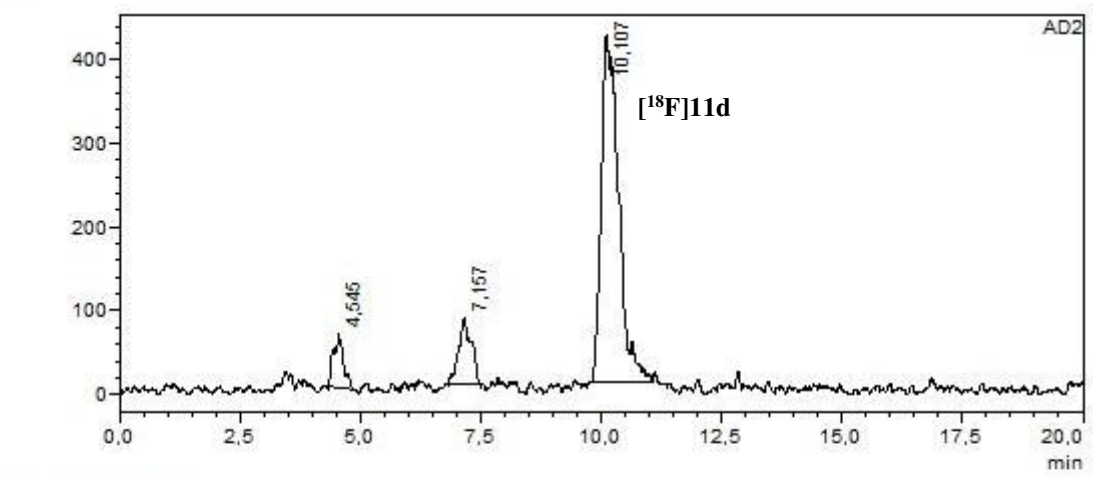
Results of the experiments are summarized in the following table:

Experiment (nb of runs)	Conditions	RCY of **[^{18}F]11d**(%)	RCP of **[^{18}F]11d** (%)	Final Activity (MBq)
11 (*n* = 3)	**PS-10c (5 mg), CH_3CN (1.7 mL), AcOH (60 equiv), 100°C, 15 min**	**9 ± 4**[a]	**71 ± 11**[a]	**-**
11-1 (*n* = 1)	**PS-10c** (5 mg), CH_3CN (1.7 mL), AcOH (60 equiv), 100°C, 15 min	13	81	1183
11-2 (*n* = 1)	**PS-10c** (5 mg), CH_3CN (1.7 mL), AcOH (60 equiv), 100°C, 15 min	9	60	1100
11-3 (*n* = 1)	**PS-10c** (5 mg), CH_3CN (1.7 mL), AcOH (60 equiv), 100°C, 15 min	6	73	524

[a] mean ± standard deviation of the 3 experiments

*Experiment 11-1 (***PS-10d** (5 mg)**,** THF (1.7 mL), AcOH (60 equiv), 100°C, 15 min)

	Analytical code	**YVX1.367**
	Activity fixed on QMA	10.16 GBq
t = 0 min	Activity eluted in R1	9.49 GBq
t = 16 min	Activity in R1 (end of fluorination)	8.24 GBq
t = 43 min	Activity in the collecting vial	1183 MBq
	t_R ^{radio} of **[^{18}F]11d**	10.10 min
	Radiochemical purity of **[^{18}F]11d**	81%
	Activity Yield	10%
	RCY (decay corrected)	**13%**



<Peak Table>

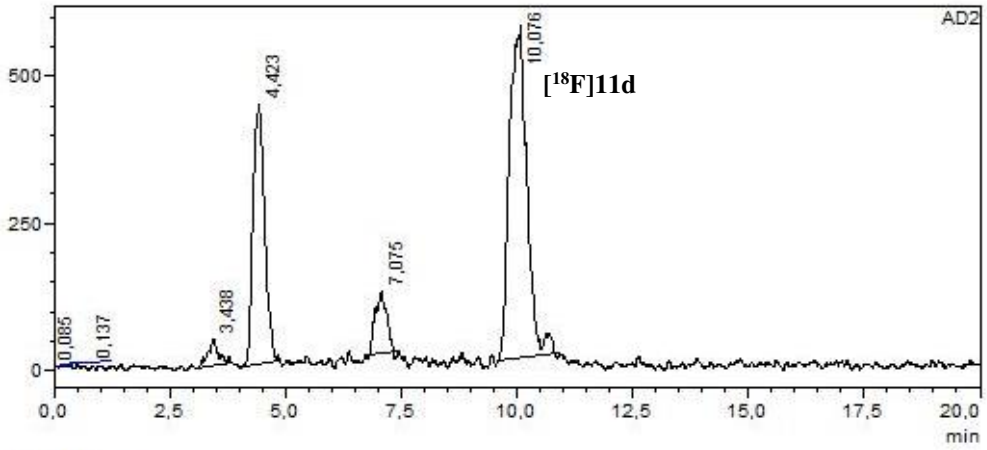
AD2

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	4,545	932668	64233	7,273		M	
2	7,157	1464953	79140	11,424		M	
3	10,107	10426098	414189	81,303		M	
Total		12823719	557562				

Analytic Radio HPLC chromatogram of experiment 11-1

*Experiment 11-2 (***PS-10d** (5 mg)**,** THF (1.7 mL), AcOH (60 equiv), 100°C, 15 min)

	Analytical code	**YVX1.375**
	Activity fixed on QMA	10.81 GBq
t = 0 min	Activity eluted in R1	9.96 GBq
t = 16 min	Activity in R1 (end of fluorination)	8.94 GBq
t = 41 min	Activity in the collecting vial	1100 MBq
	t_R ^{radio} of **[^{18}F]11d**	10.08 min
	Radiochemical purity of **[^{18}F]11d**	60%
	Activity Yield	7%
	RCY (decay corrected)	**9%**



<Peak Table>

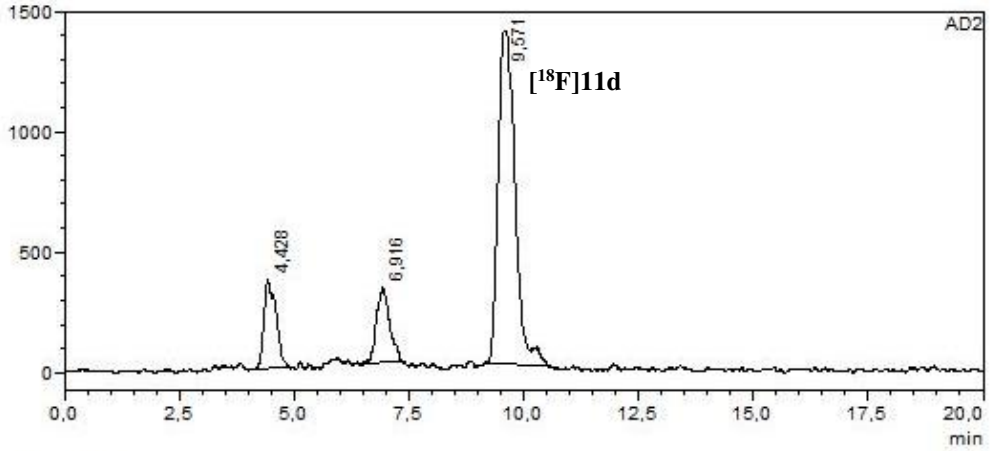
AD2

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	0,085	4529	2255	0,018			
2	0,137	8541	4161	0,034		V	
3	3,438	716337	44614	2,861		M	
4	4,423	7678390	441316	30,670		M	
5	7,075	1715648	103150	6,853		M	
6	10,076	14912429	564389	59,564		M	
Total		25035875	1159885				

Analytic Radio HPLC chromatogram of experiment 11-2

*Experiment 11-3 (***PS-10d** (5 mg)**,** THF (1.7 mL), AcOH (60 equiv), 100°C, 15 min)

	Analytical code	**YVX1.375**
	Activity fixed on QMA	8.69 GBq
t = 0 min	Activity eluted in R1	7.90 GBq
t = 17 min	Activity in R1 (end of fluorination)	7.00 GBq
t = 40 min	Activity in the collecting vial	524 MBq
	t_R ^{radio} of **[^{18}F]11d**	9.57 min
	Radiochemical purity of **[^{18}F]11d**	73%
	Activity Yield	5%
	RCY (decay corrected)	**6%**



<Peak Table>

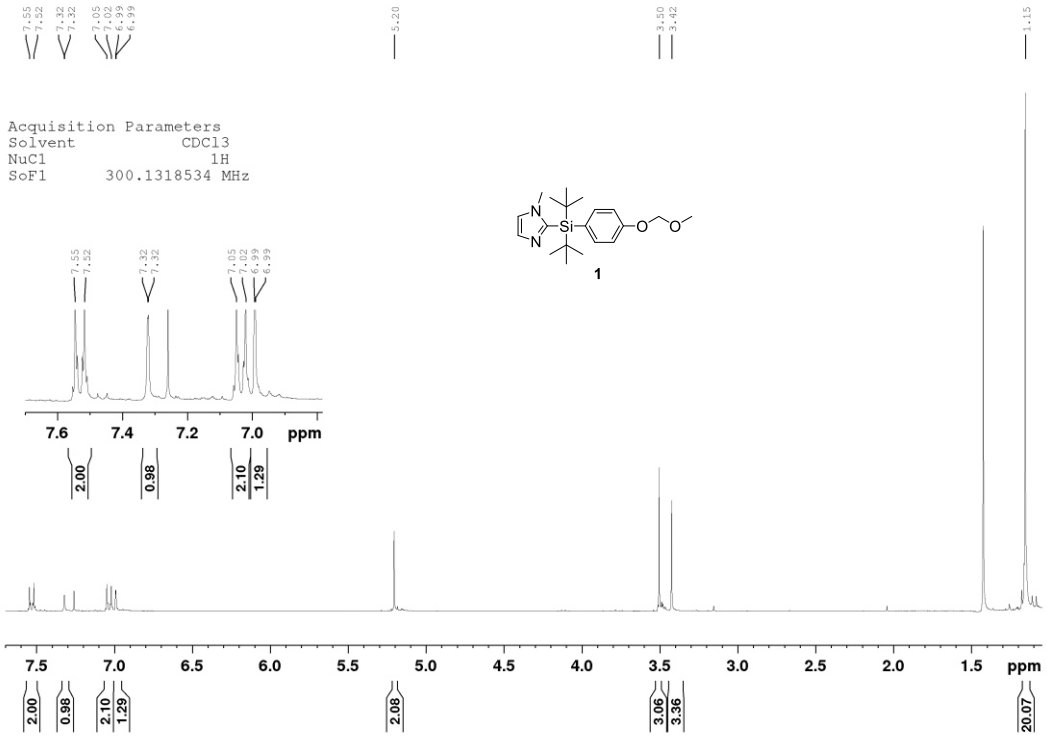
AD2

Peak#	Ret. Time	Area	Height	Conc.	Unit	Mark	Name
1	4,428	6849039	373340	14,171		M	
2	6,916	6280275	313160	12,994		M	
3	9,571	35202362	1374857	72,835		M	
Total		48331676	2061357				

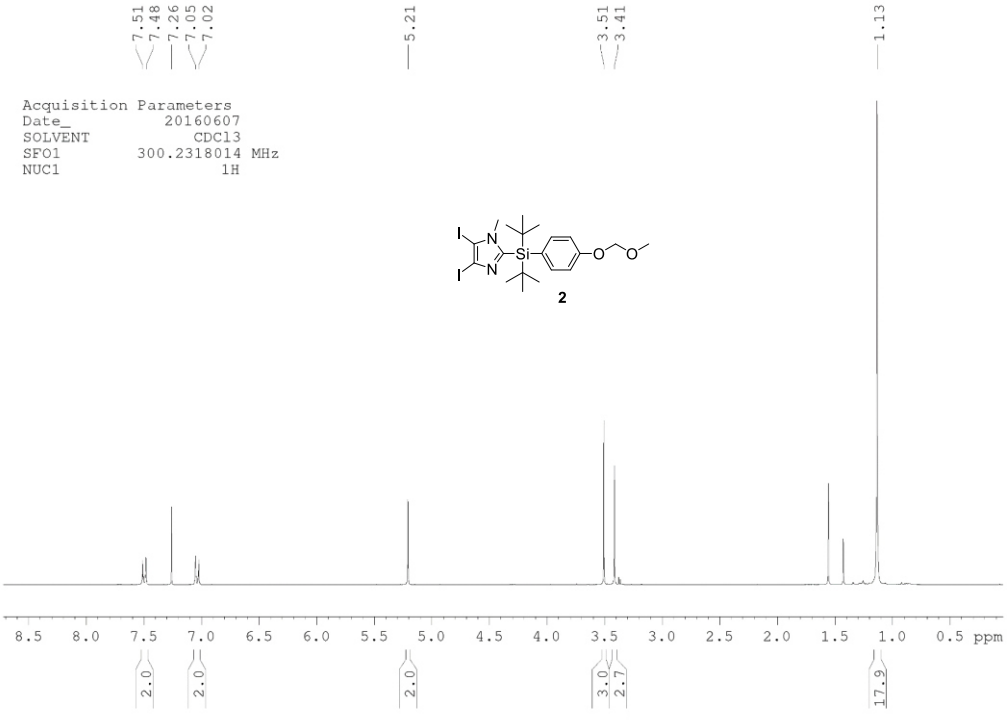
Analytic Radio HPLC chromatogram of experiment 11-3

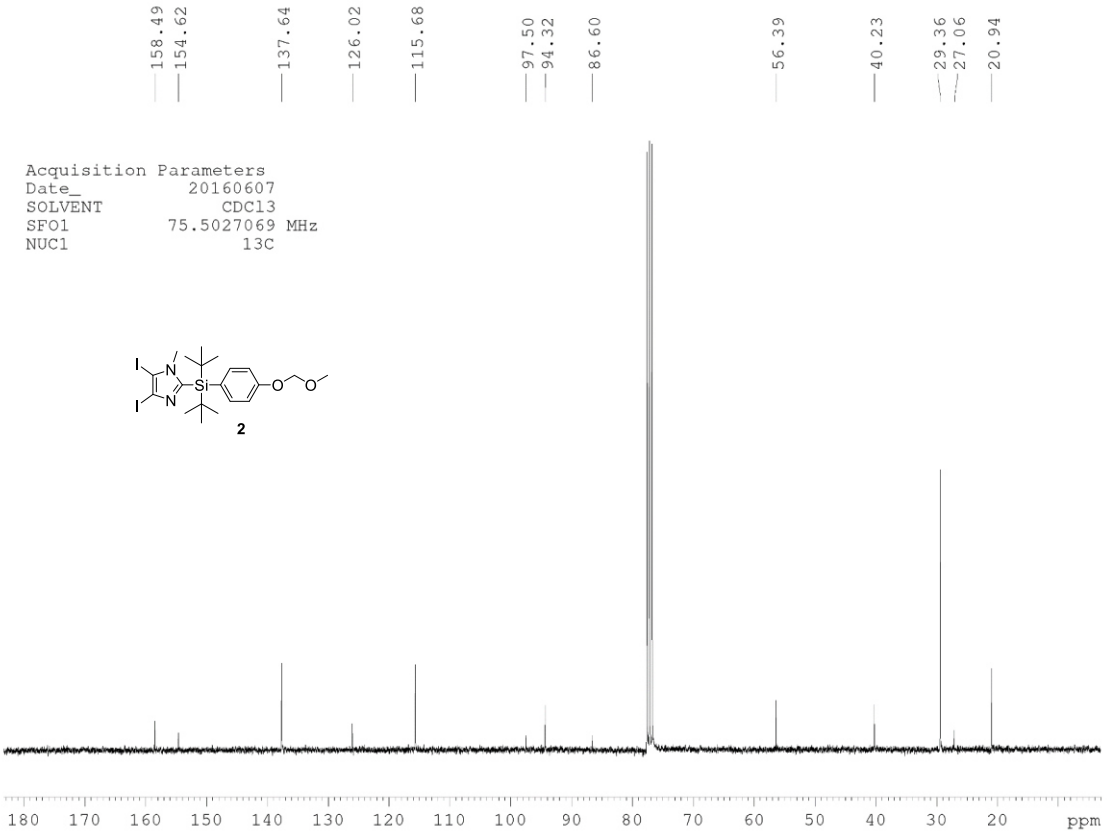
C) ^{1}H, ^{13}C, ^{29} Si and ^{19}F NMR spectra

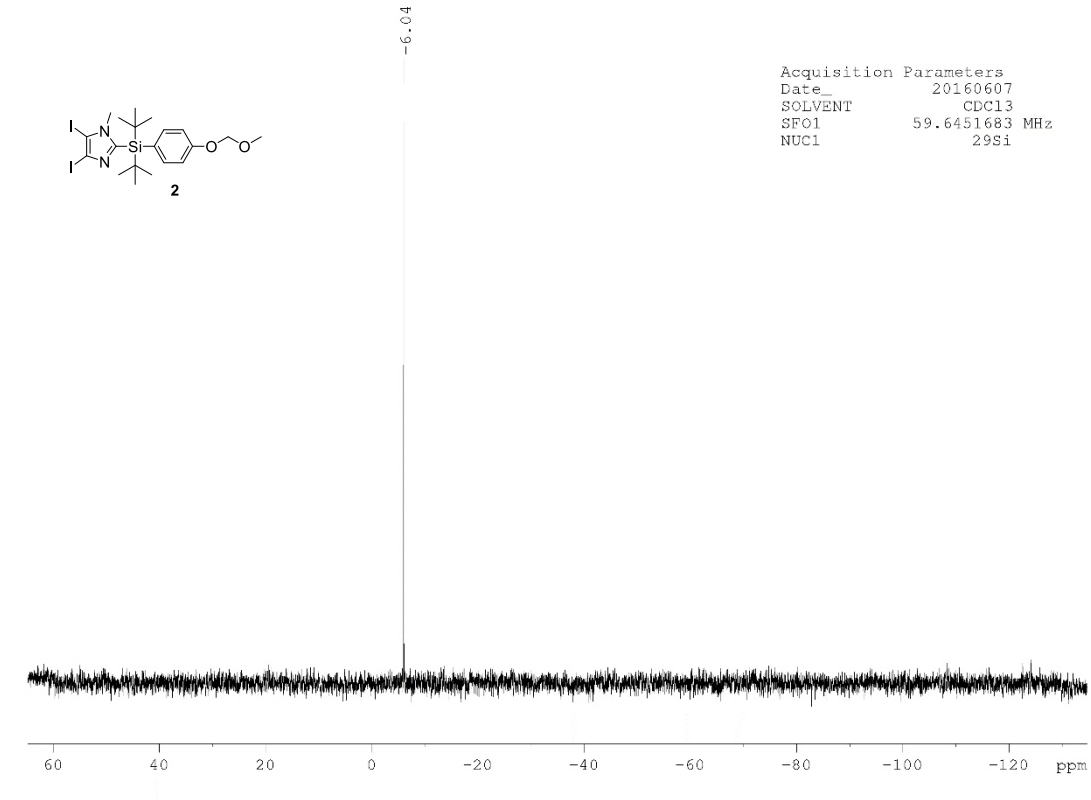
2-(di-*tert*-butyl(4-(methoxymethoxy)phenyl)silyl)-1-methyl-1*H*-imidazole 1



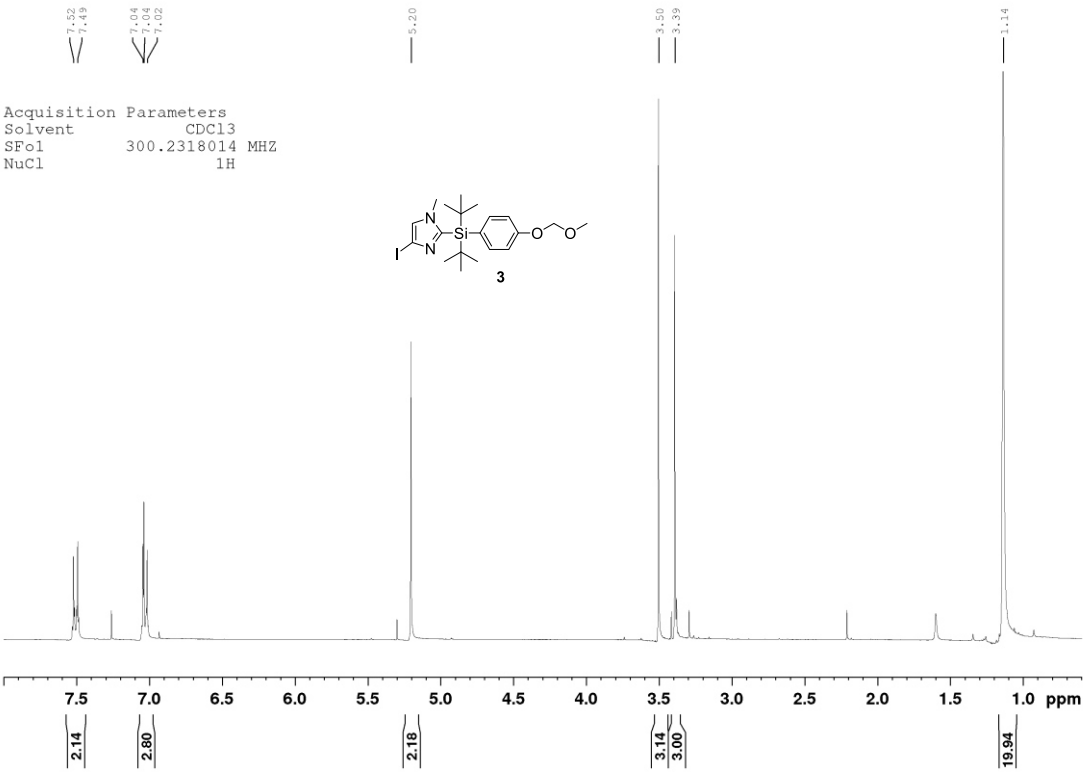
2-(di-*tert*-butyl(4-(methoxymethoxy)phenyl)silyl)-4,5-diiodo-1-methyl-1*H*-imidazole 2

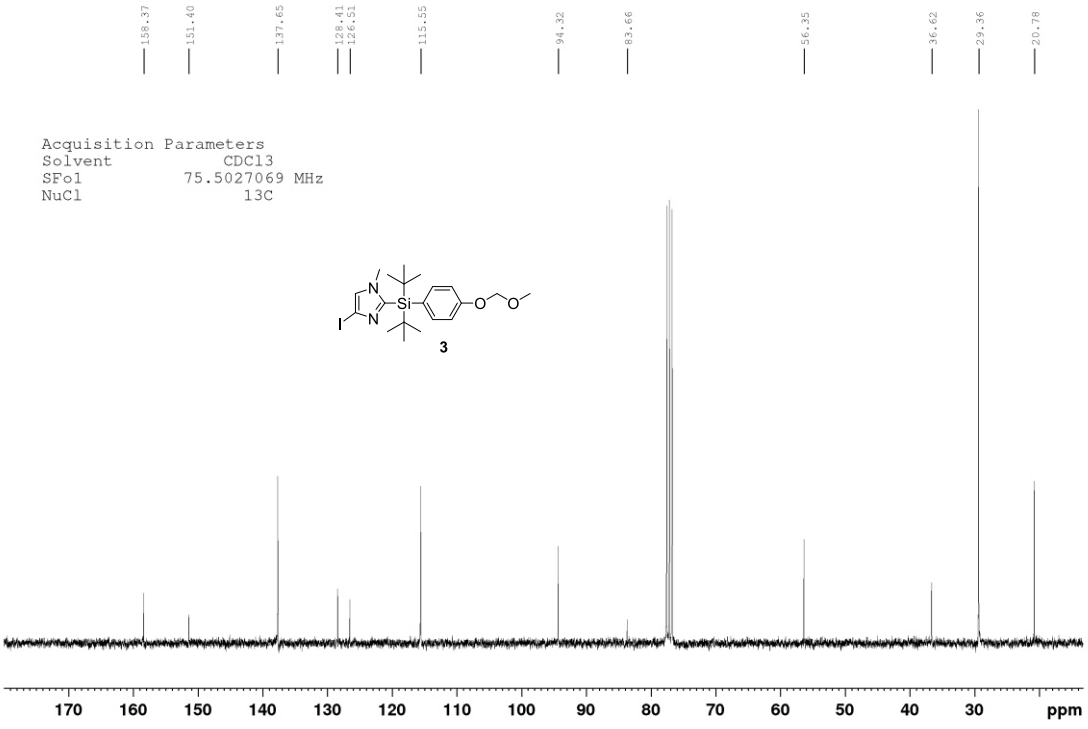


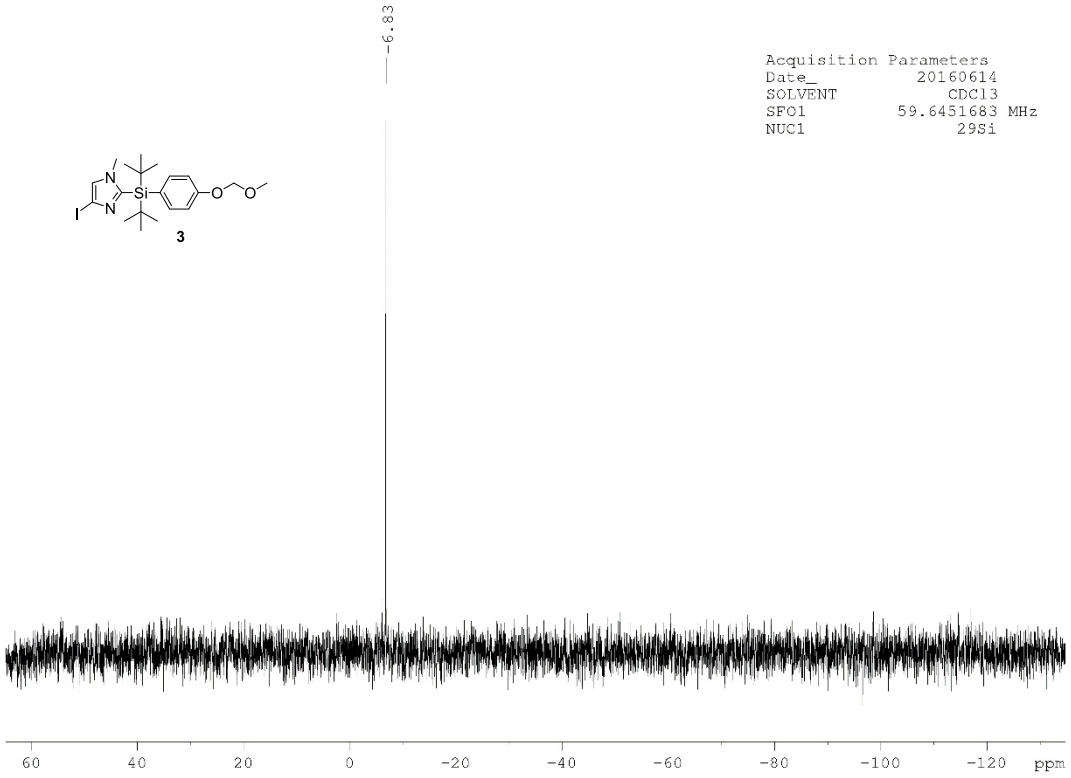

158.49
154.62
137.64
126.02
115.68
97.50
94.32
86.60
56.39
40.23
29.36
27.06
20.94
Acquisition Parameters
Date_ 20160607
SOLVENT CDCl3
SFO1 75.5027069 MHz
NUC1 13C
2
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm


-6.04
Acquisition Parameters
Date_ 20160607
SOLVENT CDCl3
SFO1 59.6451683 MHz
NUC1 29Si
2
60 40 20 0 -20 -40 -60 -80 -100 -120 ppm

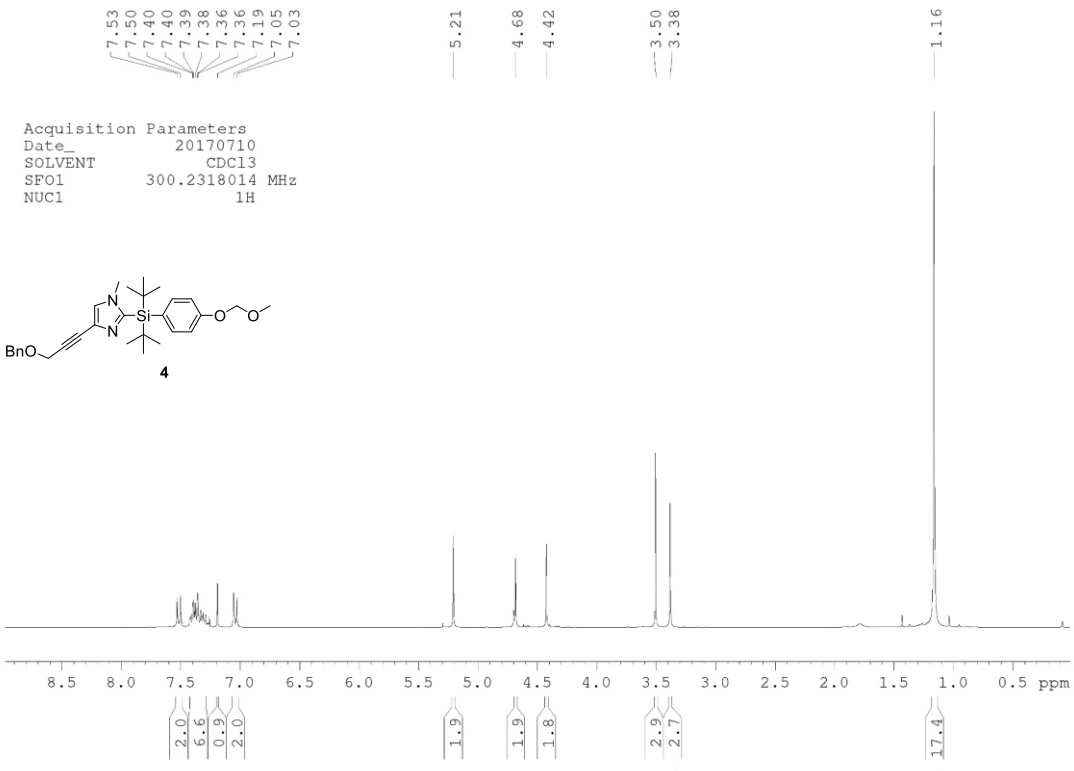
2-(di-*tert*-butyl(4-(methoxymethoxy)phenyl)silyl)-4-iodo-1-methyl-1*H*-imidazole 3

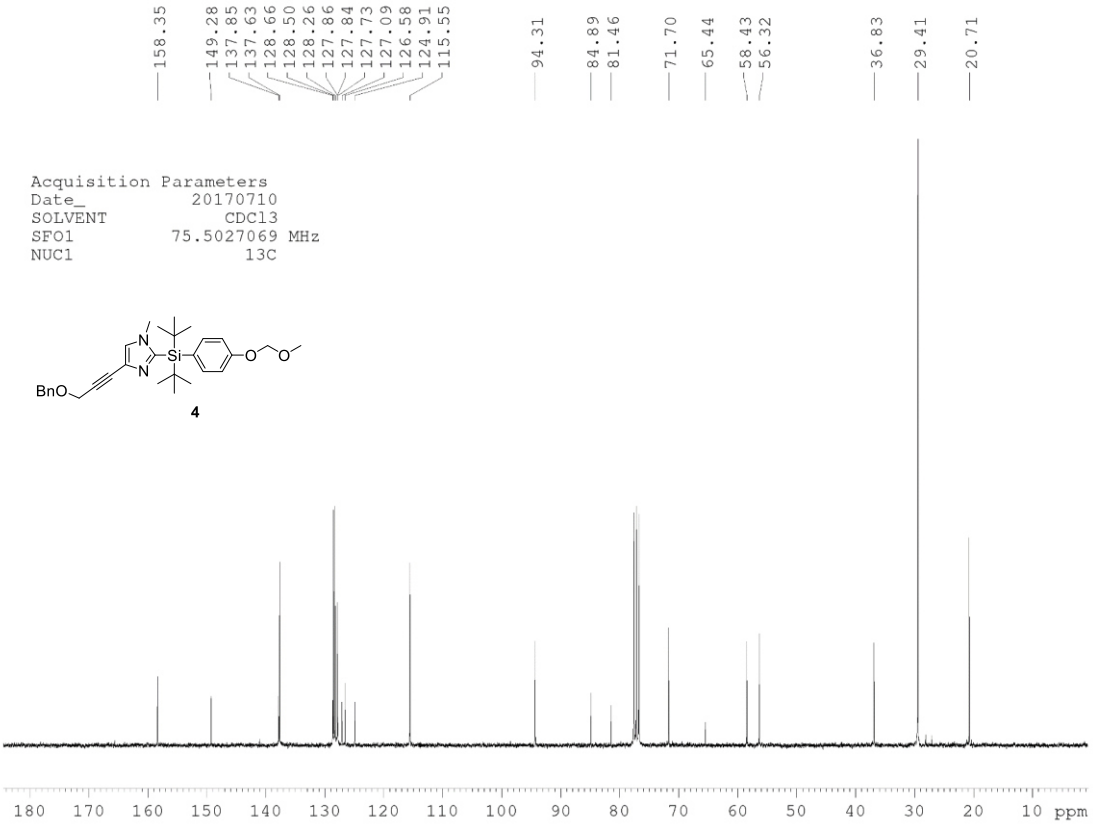


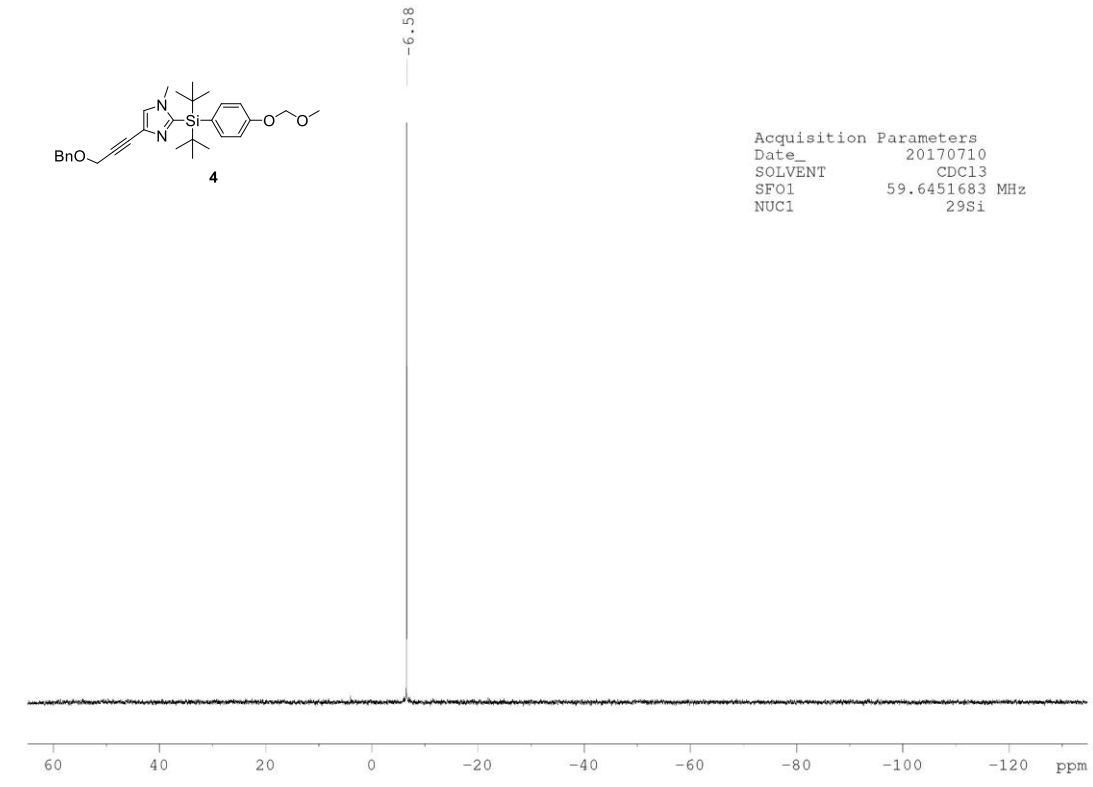




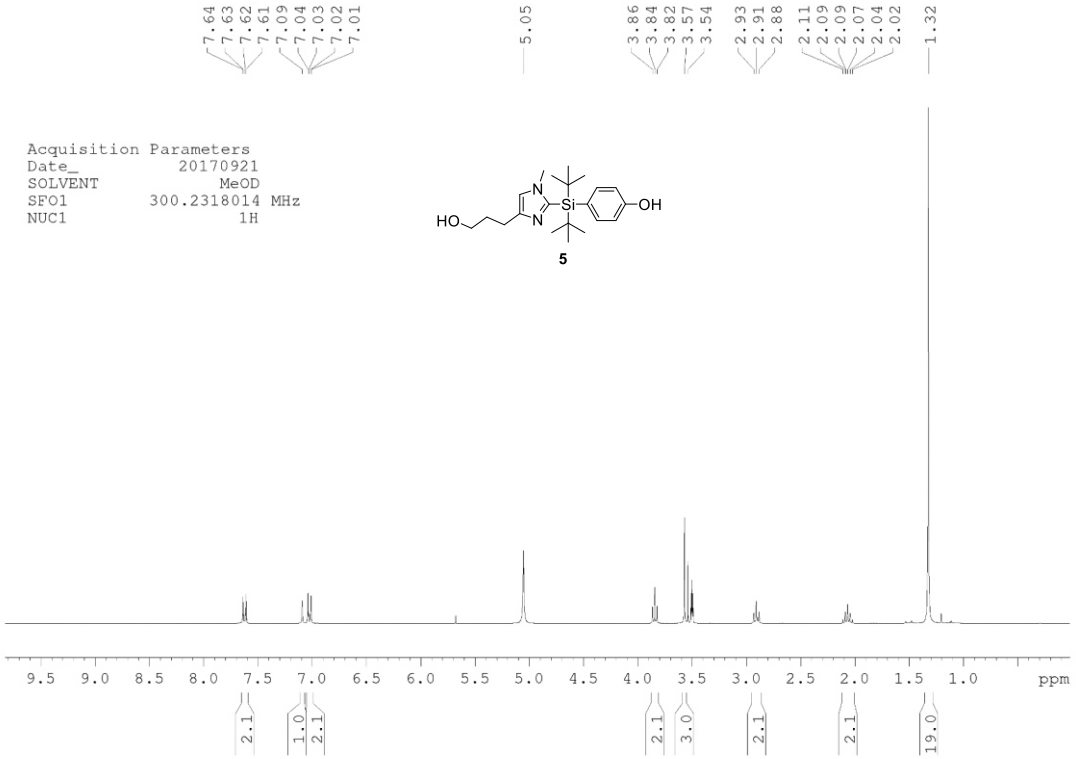
2-(di-*tert*-butyl(4-(methoxymethoxy)phenyl)silyl)-4--(3-(benzyloxy)prop-1-ynyl)-1-methyl-1*H*-imidazole 4

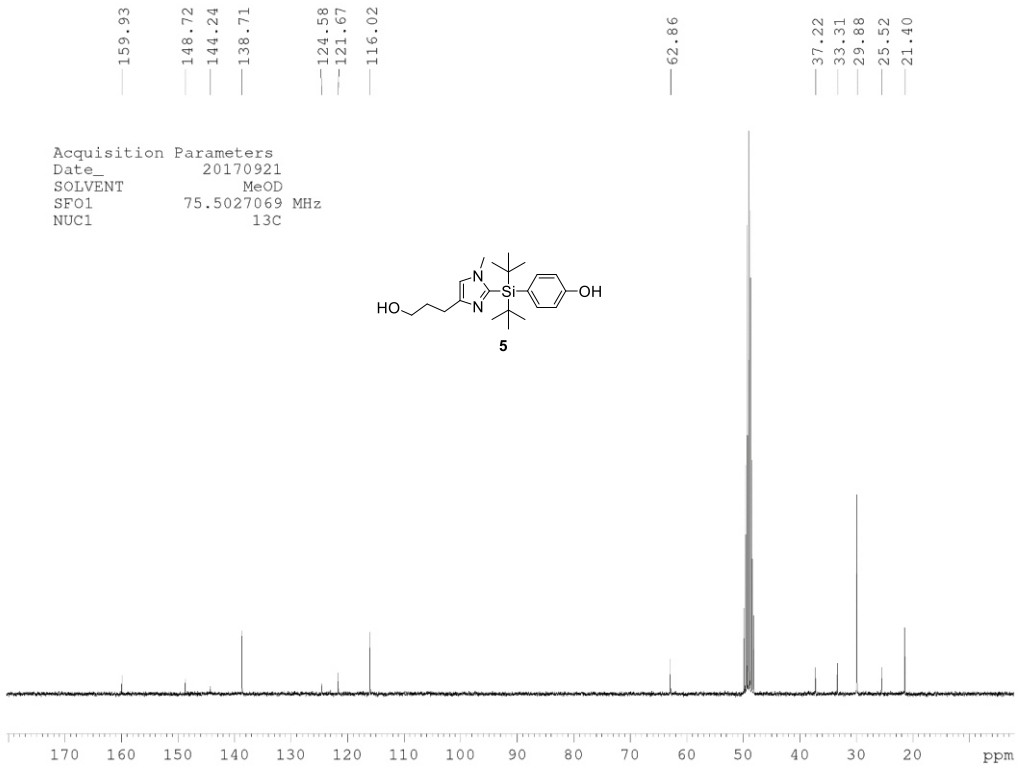


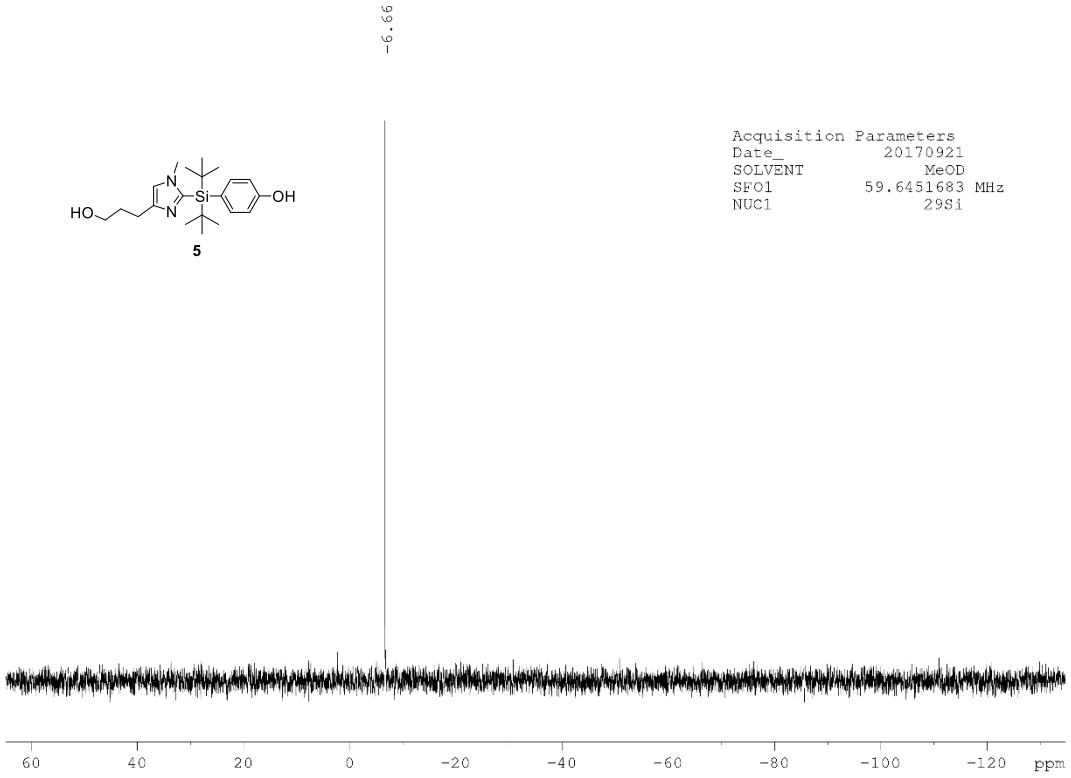

158.35
149.28
137.85
137.63
128.66
128.50
128.26
127.86
127.84
127.73
127.09
126.58
124.91
115.55
94.31
84.89
81.46
71.70
65.44
58.43
56.32
36.83
29.41
20.71
Acquisition Parameters
Date_ 20170710
SOLVENT CDCl3
SFO1 75.5027069 MHz
NUC1 13C
BnO
4
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm


-6.58
BnO
4
Acquisition Parameters
Date_ 20170710
SOLVENT CDCl3
SFO1 59.6451683 MHz
NUC1 29Si
60 40 20 0 -20 -40 -60 -80 -100 -120 ppm

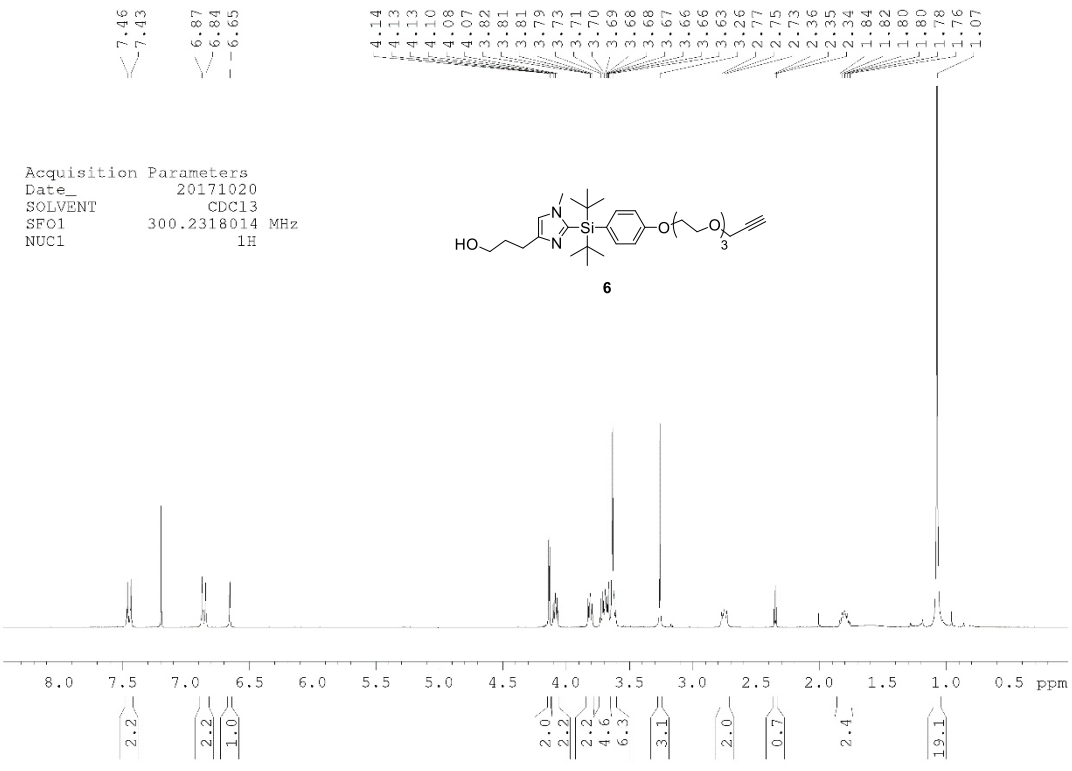
4-(Di-*tert*-butyl(4-(3-hydroxypropyl)-1-methyl-1*H*-imidazol-2-yl)silyl)phenol 4

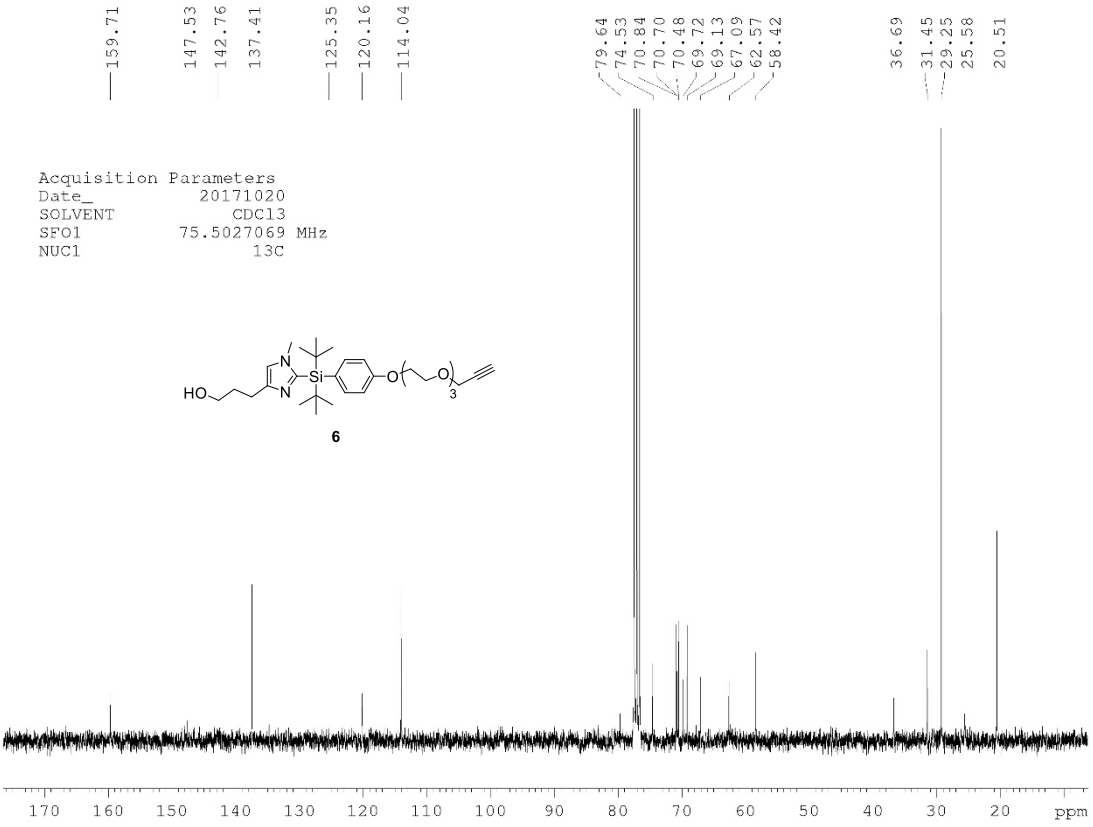


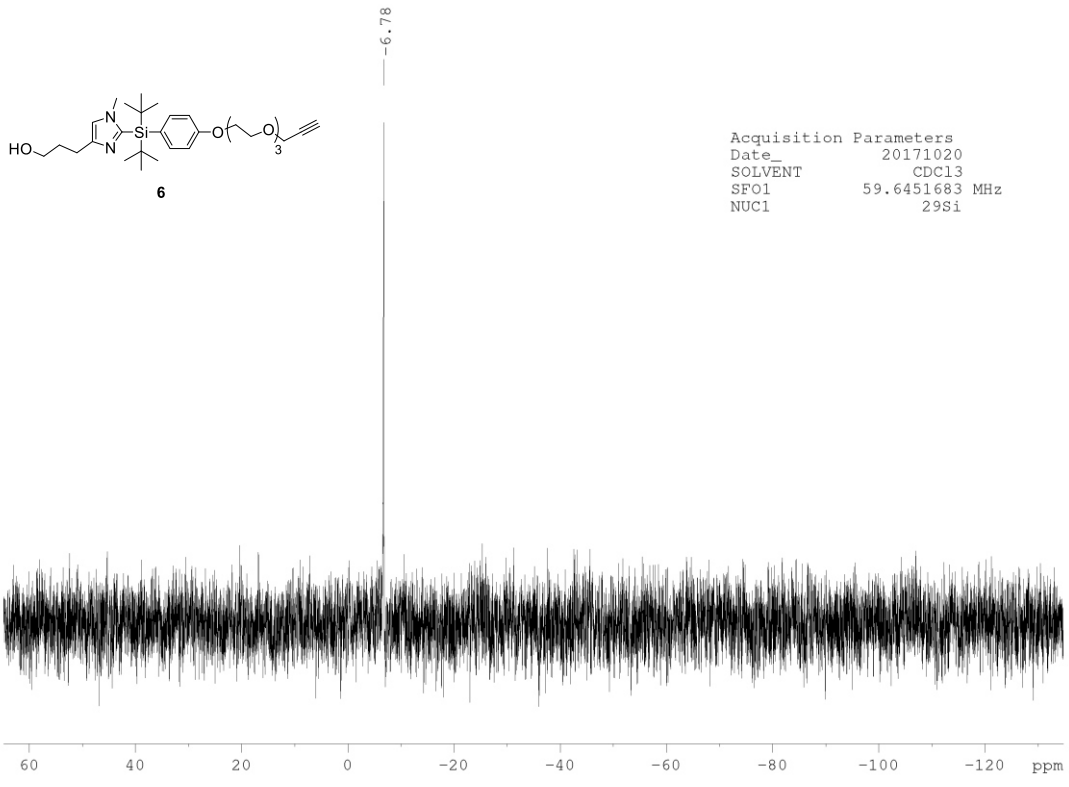




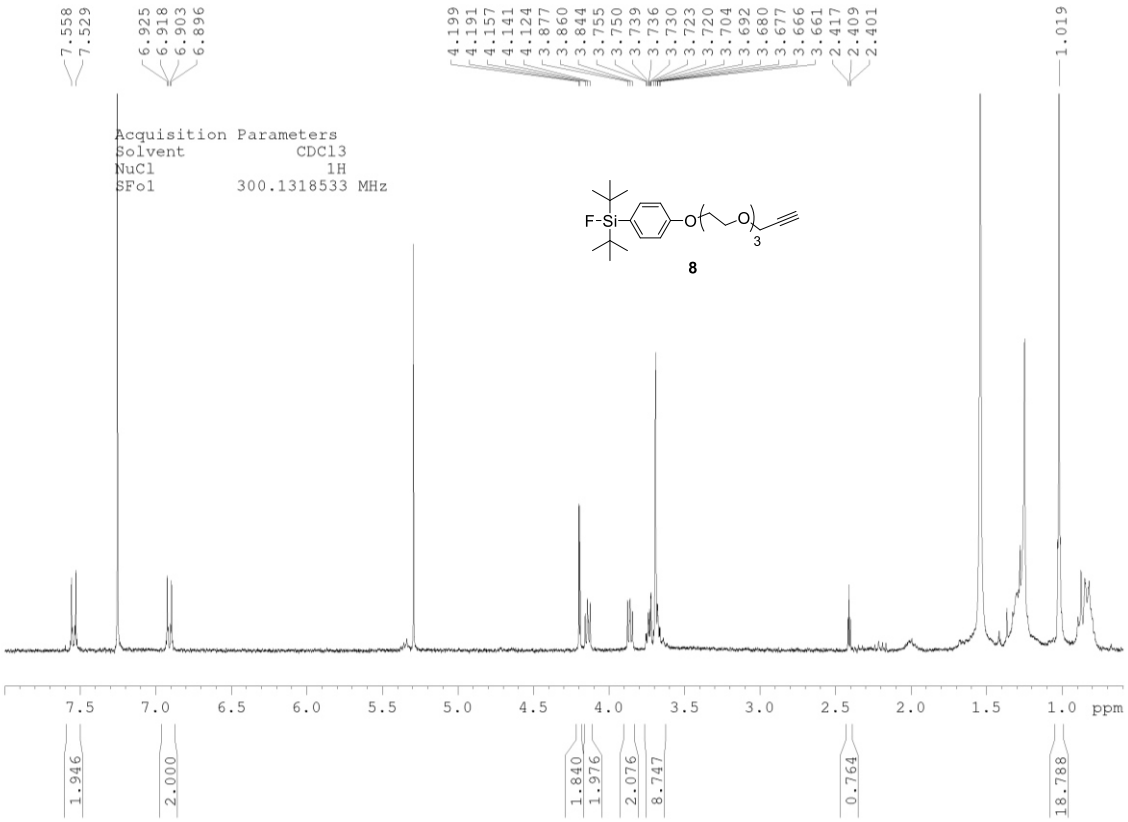
3-(2-((4-(2-(2-(2-(Prop-2-ynyloxy)ethoxy)ethoxy)ethoxy)phenyl)di-t*ert*-butylsilyl)-1-methyl-1*H*-imidazol-4-yl)propan-1-ol 6

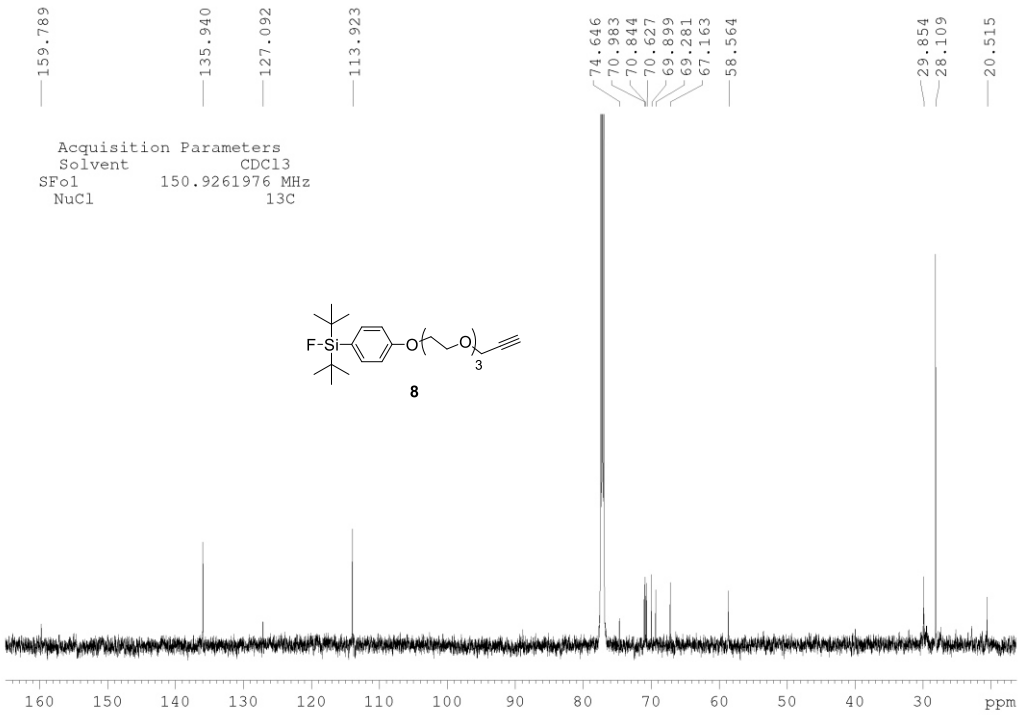


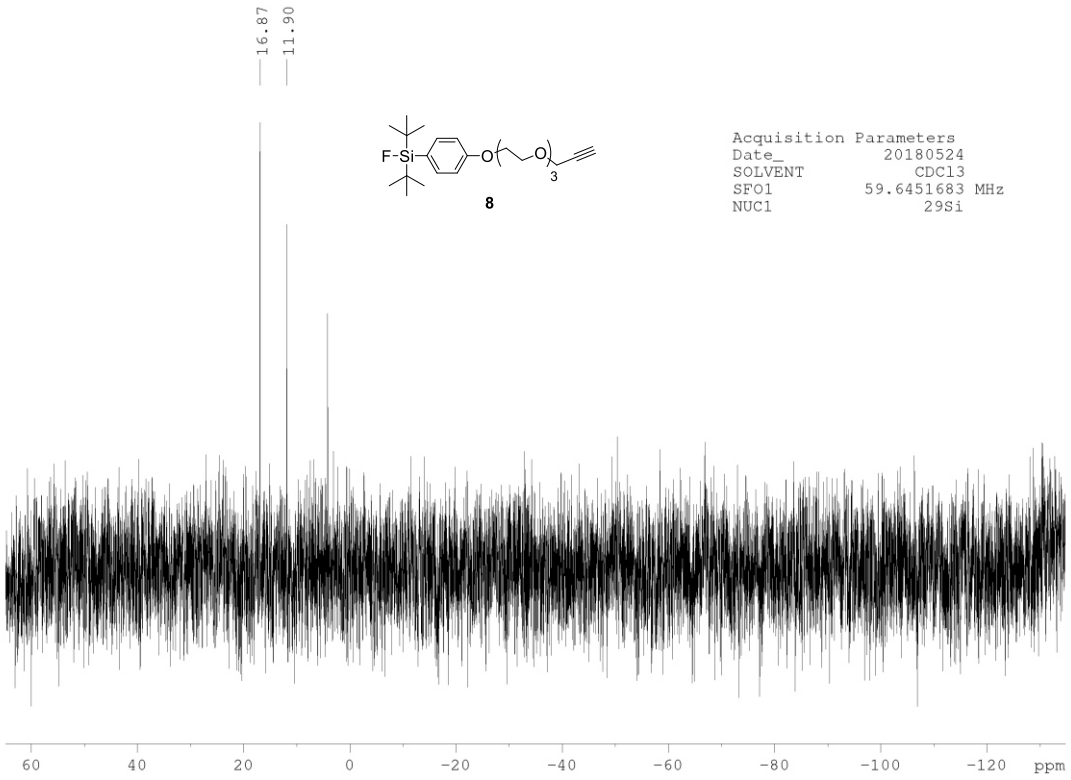

159.71
147.53
142.76
137.41
125.35
120.16
114.04
79.64
74.53
70.84
70.70
70.48
69.72
69.13
67.09
62.57
58.42
36.69
31.45
29.25
25.58
20.51
Acquisition Parameters
Date_ 20171020
SOLVENT CDCl3
SFO1 75.5027069 MHz
NUC1 13C
HO
Si
O
3
6
170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 ppm

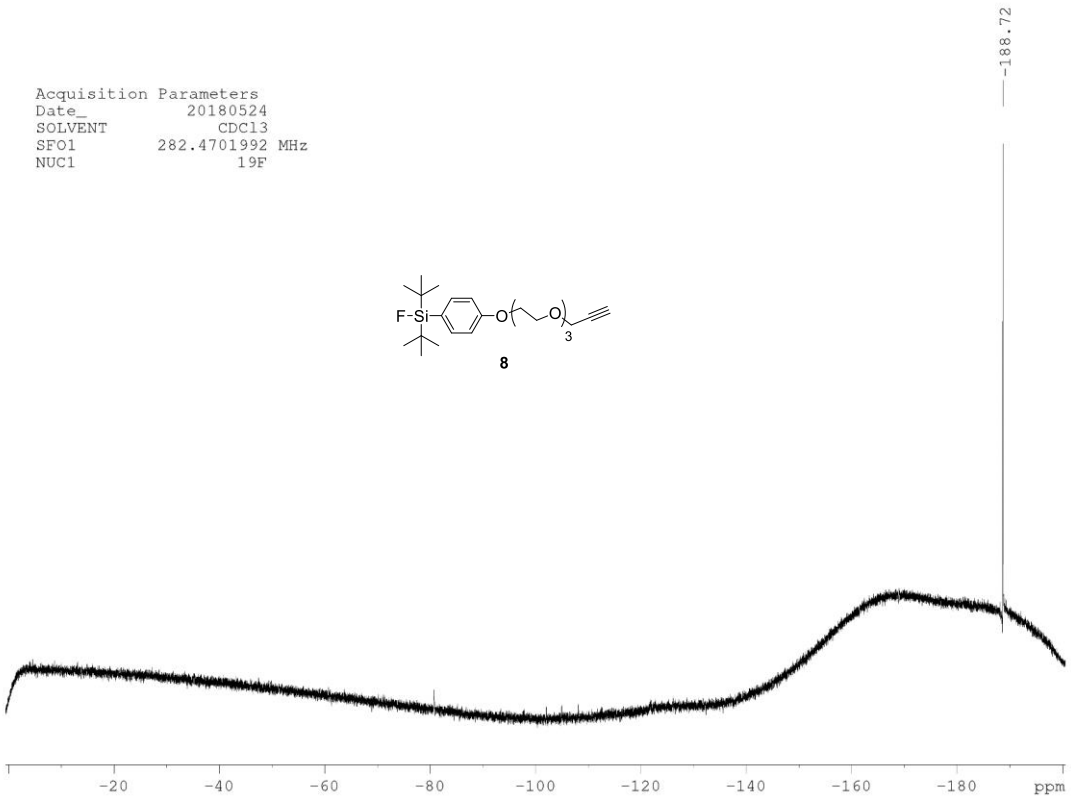

-6.78
HO
Si
O
3
6
Acquisition Parameters
Date_ 20171020
SOLVENT CDCl3
SFO1 59.6451683 MHz
NUC1 29Si
60 40 20 0 -20 -40 -60 -80 -100 -120 ppm

(4-(2-(2-(2-(Prop-2-ynyloxy)ethoxy)ethoxy)ethoxy)phenyl)di-*tert*-butylfluorosilane 8






16.87
11.90
F-Si
O
O
3
8
Acquisition Parameters
Date_ 20180524
SOLVENT CDCl3
SFO1 59.6451683 MHz
NUC1 29Si
60
40
20
0
-20
-40
-60
-80
-100
-120
ppm


-188.72
Acquisition Parameters
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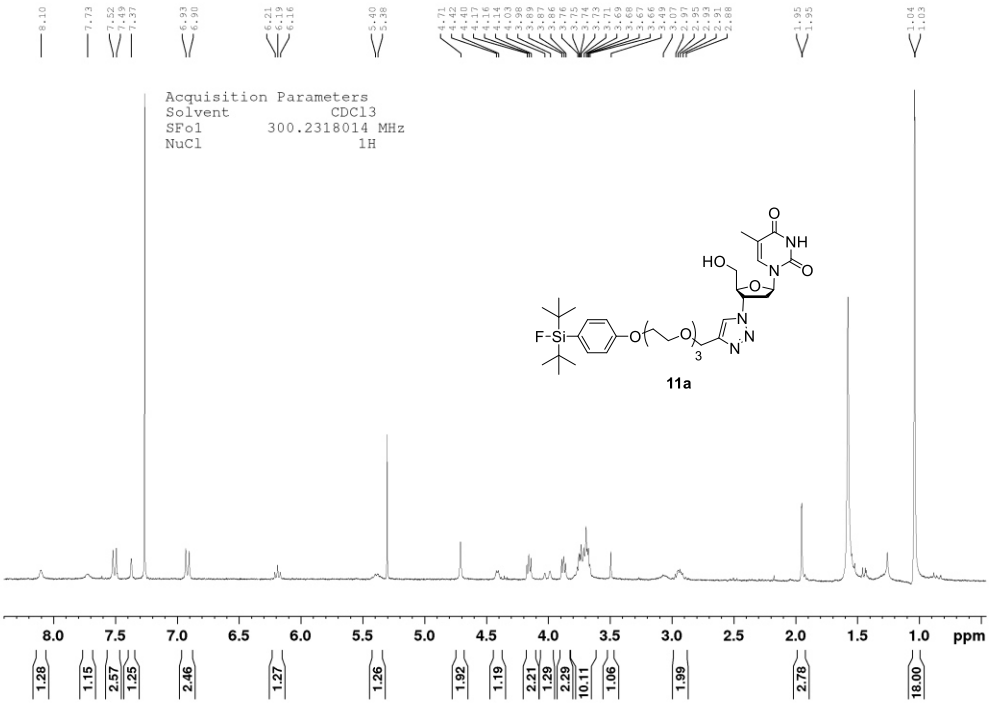
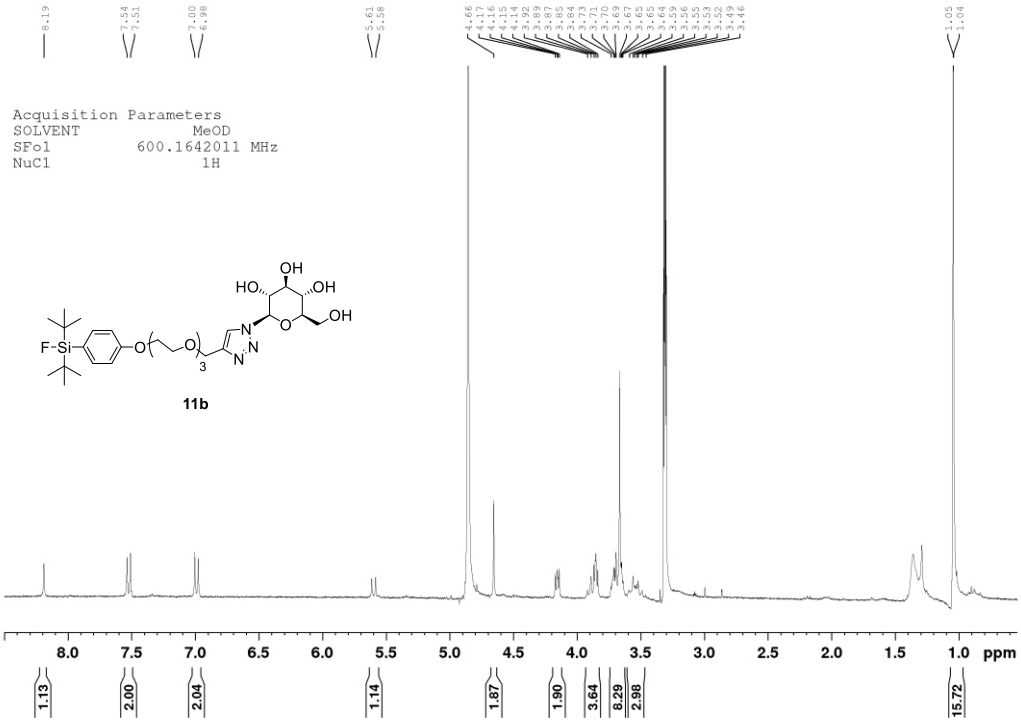
SFO1 282.4701992 MHz
NUC1 19F
F-Si
O
O
3
8
-20
-40
-60
-80
-100
-120
-140
-160
-180
ppm

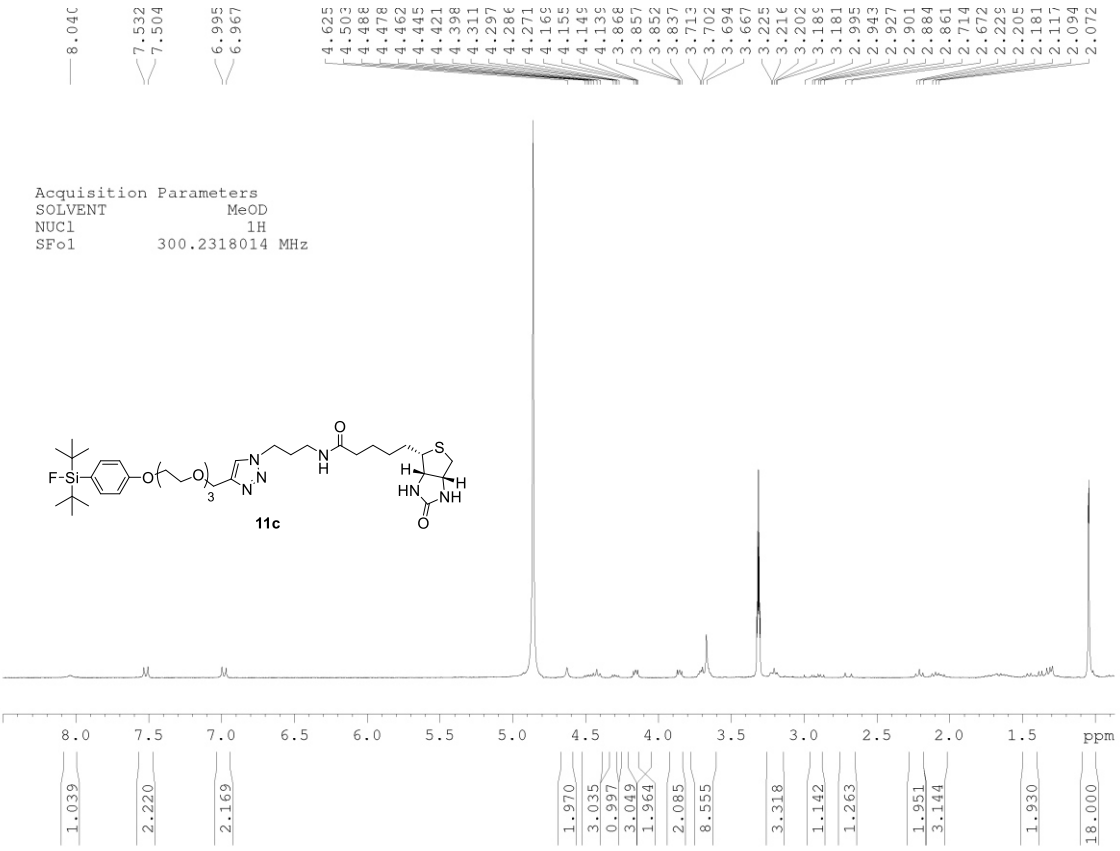
3'-Deoxy-3'-[4-((2-(2-(2-(4-(di-tert-butylfluorosilyl)phenoxy)ethoxy) ethoxy)ethoxy)methyl)-1*H*-1,2,3-triazol-1-yl]-thymidine 11a



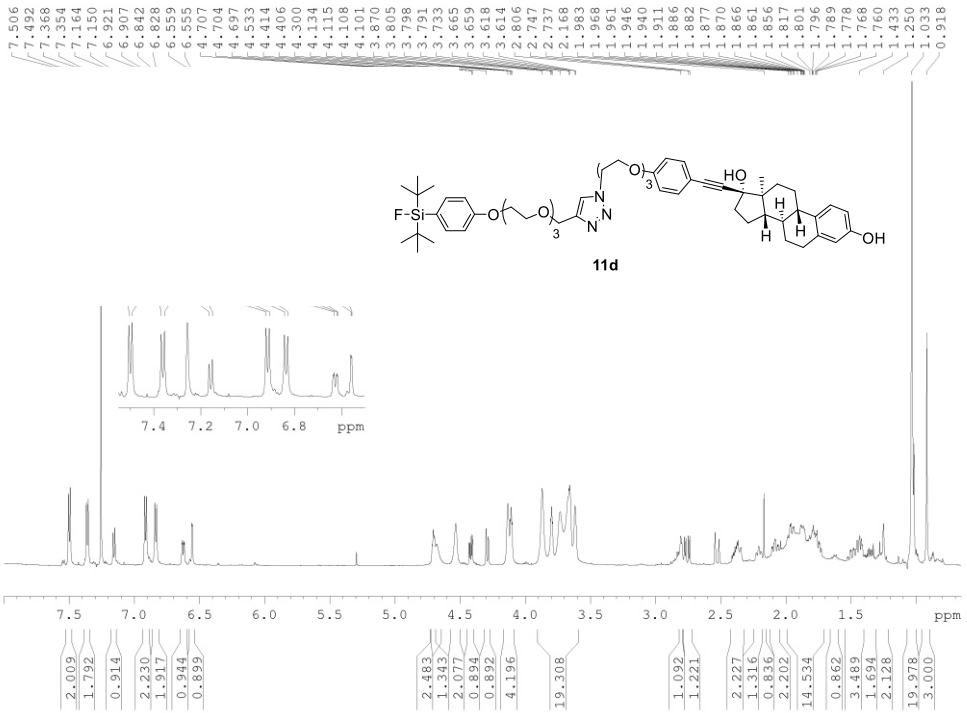
***β*-D-1-Deoxy-1-[4-((2-(2-(2-(4-(di-tert-butylfluorosilyl)phenoxy)ethoxy)ethoxy)ethoxy)methyl)-1*H*-1,2,3-triazol-1-yl]-glucopyranose 11b**

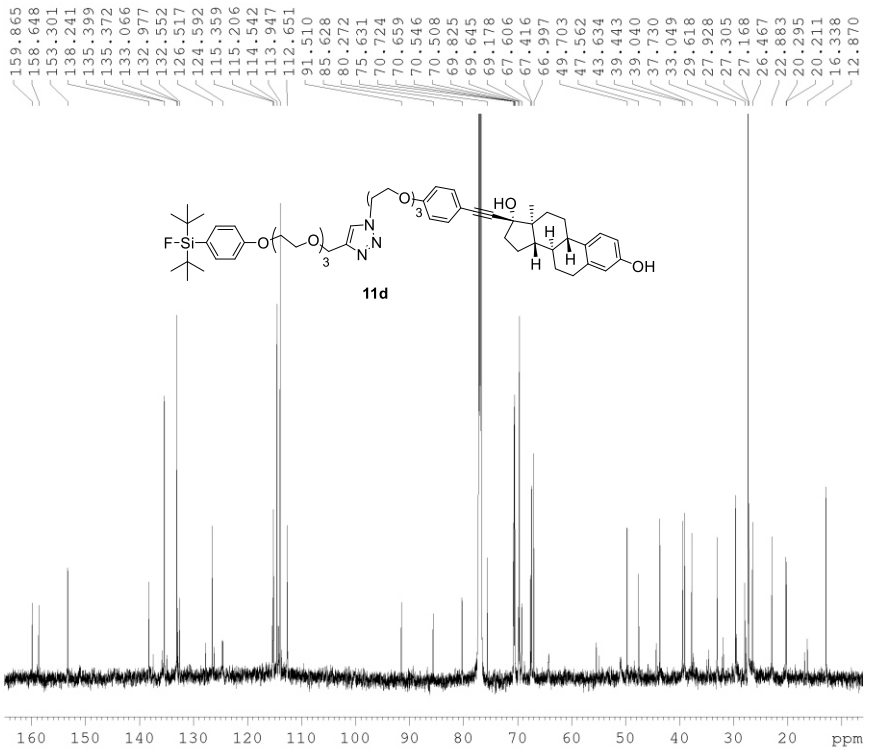


_N_-[3-(4-((2-(2-(2-(4-(di-tert-butylfluorosilyl)phenoxy)ethoxy)ethoxy)ethoxy)methyl)-1_H_-1,2,3-triazol-1-yl)propanyl]-biotinamide 11c



17-(4-((2-(2-(2-(4-(di-tert-butylfluorosilyl)phenoxy)ethoxy)ethoxy)ethoxy)methyl))-1_H_-1,2,3-triazol-1-yl)ethoxy)ethoxy)ethoxy)phenyl)ethynyl)-estradiol 11d



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PROCNO                1

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PULPROG           zgpg
TD               65536
SOLVENT          CDCl3
NS               59219
DS                   4
SWH          37878.789 Hz
FIDRES         1.155969 Hz
AQ             0.8650752 sec
RG                2050
DW              13.200 usec
DE               8.57 usec
TE              298.2 K
D1           3.00000000 sec
D11          0.03000000 sec
TD0                  1
SFO1       150.9261976 MHz
NUC1               13C
P1              16.30 usec
PLW1       115.08000183 W
SFO2       600.1624008 MHz
NUC2               1H
CPDPRG[2       waltz16
PCPD2            70.00 usec
PLW2        12.50000000 W
PLW12        0.16327000 W
PLW13        0.08212100 W

F2 - Processing parameters
SI              131072
SF          150.9103603 MHz
WDW                 EM
SSB       0
LB                2.00 Hz
GB        0
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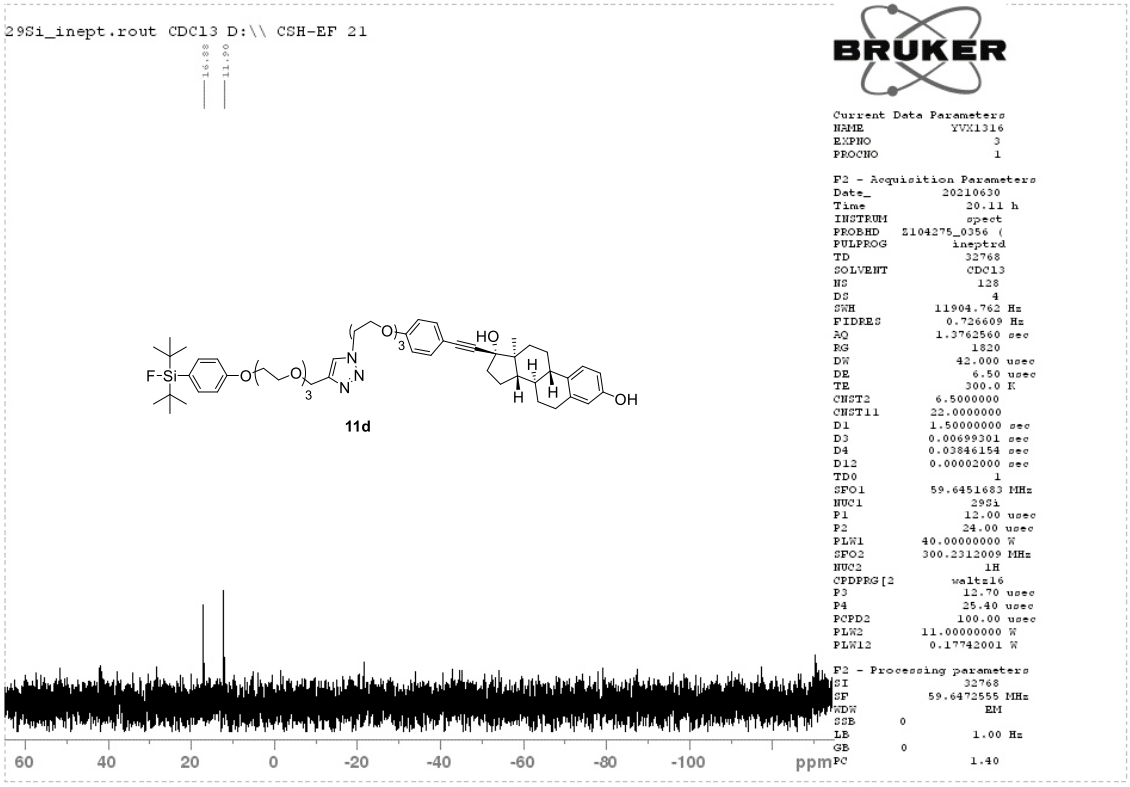

BRUKER

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Current Data Parameters
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EXPNO                  3
PROCNO                 1

F2 - Acquisition Parameters
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Time              20.11 h
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PROBHD   5104275_0356 (
PULPROG        ineptrd
TD                32768
SOLVENT           CDCl3
NS                  128
DS                    4
SWH          11904.762 Hz
FIDRES         0.726609 Hz
AQ             1.3762560 sec
RG                 1820
DW               42.000 usec
DE                6.50 usec
TE               300.0 K
CNST2          6.5000000
CNST11        22.0000000
D1             1.50000000 sec
D3             0.00699301 sec
D4             0.03846154 sec
D12            0.00002000 sec
TD0                   1
SFO1        59.6451683 MHz
NUC1               29Si
P1               12.00 usec
P2               24.00 usec
PLW1        40.00000000 W
SFO2       300.2312009 MHz
NUC2               1H
CPDPRG[2        waltz16
P3               12.70 usec
P4               25.40 usec
PCPD2           100.00 usec
PLW2        11.00000000 W
PLW12        0.17742001 W

F2 - Processing parameters
SI                32768
SF          59.6472555 MHz
WDW                  EM
SSB       0
LB                1.00 Hz
GB        0
PC                1.40
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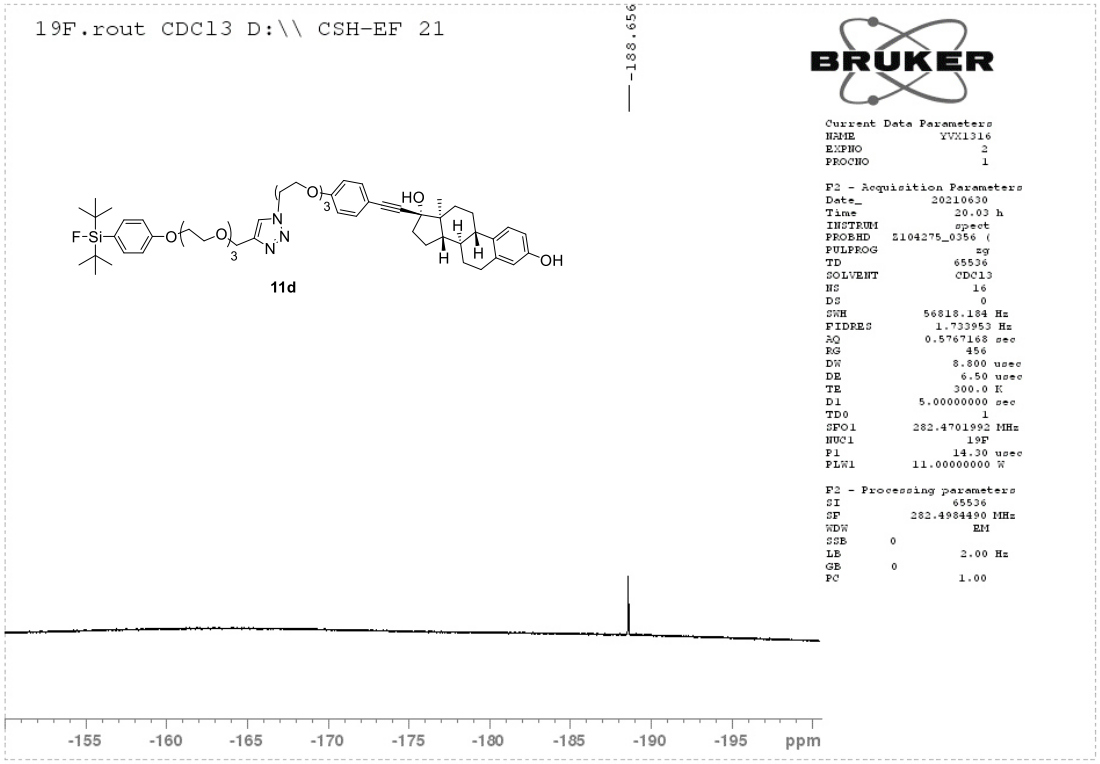
19F.rout CDCl3 D:\\ CSH-EF 21
-188.656
F-Si
O
O
3
N
N
N
O
3
HO
H
H
H
OH
11d
Current Data Parameters
NAME YVK1316
EXPNO 2
PROCNO 1
F2 - Acquisition Parameters
Date_ 20210630
Time 20.03 h
INSTRUM spect
PROBHD 5104275_0356 (
PULPROG zg
TD 65536
SOLVENT CDCl3
NS 16
DS 0
SWH 56818.184 Hz
FIDRES 1.733953 Hz
AQ 0.5767168 sec
RG 456
DW 8.800 usec
DE 6.50 usec
TE 300.0 K
D1 5.00000000 sec
TD0 1
SFO1 282.4701992 MHz
NUC1 19F
P1 14.30 usec
PLW1 11.00000000 W
F2 - Processing parameters
SI 65536
SF 282.4984490 MHz
WDW EM
SSB 0
LB 2.00 Hz
GB 0
PC 1.00
-155
-160
-165
-170
-175
-180
-185
-190
-195
ppm