Electronic supporting information

Cross-coupling of [^{11}C]CH_3Li for ^{11}C-labelled PET tracer synthesis

Hugo Helbert[a,b], Ines Farinha Antunes[b], Gert Luurtsema[b], Wiktor Szymanski[c], Ben L. Feringa*[a] and Philip H. Elsinga*[b]

[a] Stratingh Institute for Chemistry, University of Groningen, Nijenborgh 4, 9747 AG, Groningen, The Netherlands.

[b] Department of Nuclear Medicine and Molecular Imaging, University of Groningen, University Medical Center Groningen, Hanzeplein 1, 9713 GZ Groningen, The Netherlands.

[c] Department of Radiology, University of Groningen, University Medical Center Groningen, Hanzeplein 1, 9713 GZ Groningen, The Netherlands.

Contents

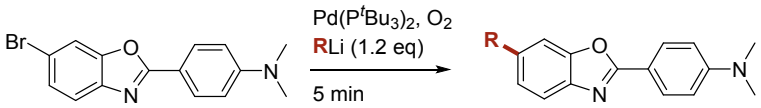
General methods

All reactions were carried out under a nitrogen atmosphere using flame dried glassware and standard Schlenk techniques unless noted otherwise. Column chromatography: Grace-Reveleris purification system with Büchi silica cartridges. TLC: Merck silica gel 60, 0.25 mm. Components were visualized by UV (254 nm, 365 nm) and potassium permanganate staining. Progress of the reaction and conversion were determined by GC-MS (GC, HP6890: MS HP5973) with an HP1 or HP5 column (Agilent Technologies, Palo Alto, CA). Mass spectra were recorded on an AEI-MS-902 mass spectrometer (EI+) or a LTQ Orbitrap XL (ESI+, ESI-, APCI+). ^{1}H-, ^{13}C-NMR were recorded on Bruker 600 MHz (600 MHz and 151 MHz, respectively) or a Varian AMX400 (400 and 100.59, respectively) or 300 MHz (300, 75 MHz, respectively for ^{1}H- and ^{13}C-NMR) using $CDCl_3$ or DMSO-*d6* as solvent. Chemical shift values are reported in ppm with the solvent resonance as the internal standard ($CHCl_3$: δ 7.26 for ^{1}H, δ 77.16 for ^{13}C). Data are reported as follows: chemical shifts, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet), coupling constants (Hz), and integration. FT-IR spectra were recorded on a Nicolet Nexus FT-IR fitted with a Thermo Scientific Smart iTR sampler. All reactions were carried out under a dry air atmosphere using dried glassware and using standard Schlenk techniques unless noted otherwise. Toluene was dried by a MRBAUN solvent purification system (SPS). $Pd(P^tBu_3)_2$ was purchased from Sigma Aldrich or Strem, *n*-BuLi (1.6 M solution in hexanes) and MeLi (1.6 M solution in Et_2O) was purchased from Acros. $[^{11}C]CH_4$ was produced by nuclear reaction $^{14}N(p,\alpha)^{11}C$ on an IBA Cyclone 18/18 cyclotron and subsequently converted into $[^{11}C]CH_3I$ by ''gas phase'' method.[1]

Safety note: Organolithium reagents are highly reactive (pyrophoric) and should be handled by trained experts only. Personal protective equipment should be worn at all times.

Solvent optimization

Supplementary table 1 : influence of the choice of solvent for the organolithium reagent in the cross-coupling reaction



Entry	Organolithium reagent	Solution of RLi (0.2 M)	Conversion[a] (%)
1	*n*-BuLi	THF	0
2	*n*-BuLi	Toluene	77
3	*n*-BuLi	Toluene/THF (9/1)	6
4	MeLi (*n*-BuLi + MeI)	Toluene/Et_2O (9/1)	23
5	MeLi (*n*-BuLi + MeI)	Toluene/Et_2O (8/2)	10
6	MeLi (*n*-BuLi + MeI)	Toluene	70
7	MeLi (*n*-BuLi + MeI)[b]	Toluene	45

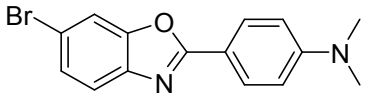
Reaction conditions: To a solution of aryl bromide (0.02 mmol) in toluene (0.1 mL) was added 5 mol % of pre-oxidized catalyst added as a 10 mg/mL solution in toluene. Organolithium reagent was further diluted with the mentioned solvent to reach a 0.2 M solution and was added over 5 min, followed by quenching with MeOH. a) Conversion obtained from GC-MS analysis. b) Cross-coupling performed at 60 °C.

Trapping of the $[^{11}C]$MeLi

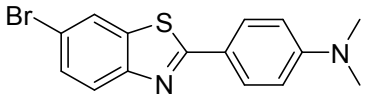
Trapping of $[^{11}C]$MeI and formation of $[^{11}C]$MeLi by Li-halogen exchange with *n*-BuLi was proven efficient in Toluene at rt. Indeed when the trapping vial was quenched with MeOH after trapping, we observed a rapid and complete loss of activity associated with $[^{11}C]$MeLi being quenched into $[^{11}C]$Methane, explaining the loss in activity. Moreover, we did not detected residual $[^{11}C]$MeI by HPLC.

[1] For synthesis of $[^{11}C]CH_3I$ see: P. Larsen, J. Ulin, K. Dahlstrøm and M. Jensen *Appl. Radiat. Isot.* **1997**, *48* (2), 153-157.

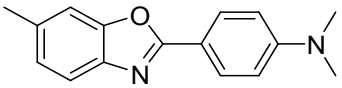
Experimental procedures for the synthesis of precursors and non-radiolabelled reference compounds



4-(6-bromobenzo[d]oxazol-2-yl)-*N,N*-dimethylaniline (1) : 2-amino-5-bromophenol (0.30 g, 1.6 mmol, 1.0 eq) and 4-(dimethylamino)benzoic acid (0.26 g, 1.6 mmol, 1.0 eq) were stirred with 15 mL of PPA (115% H_3PO_4 basis) and heated with an alloy liquid metal bath at 180 °C for 4h. After cooling down to rt, the reaction mixture was slowly transferred into an aq. sol. of K_2CO_3. This solution was then extracted with 3x50 mL of EtOAc and the combined organic layers were washed with 50 mL of H_2O. The organic layer was dried over Na_2SO_4, filtered and the solvent was evaporated to give **1** as a red solid (0.50 g, 98% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 9.0 Hz, 2H), 7.67 (d, *J* = 1.8 Hz, 1H), 7.53 (d, *J* = 8.4 Hz, 1H), 7.41 (dd, *J* = 8.5, 1.8 Hz, 1H), 6.76 (d, *J* = 9.0 Hz, 2H), 3.08 (s, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 164.9, 152.7, 151.2, 142.0, 129.3, 127.6, 120.1, 116.6, 113.7, 113.6, 111.7, 40.2. FT-IR (neat, cm^{-1}): 2897, 2821, 1604, 1507, 810. HR-MS (ESI+), m/z: $[M+H]^+$ Calcd for $C_{15}H_{14}BrN_2O^+$: 317.0284 ; found : 317.0284.



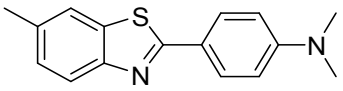
4-(6-bromobenzo[d]thiazol-2-yl)-*N,N*-dimethylaniline (2) : 2-amino-5-bromobenzenethiol (0.25 g, 1.2 mmol, 1.0 eq) and 4-(dimethylamino)benzoic acid (0.20 g, 1.2 mmol, 1.0 eq) were stirred with 15 mL of PPA (115% H_3PO_4 basis) and heated with an alloy liquid metal bath at 180°C for 4 h. After cooling down to rt the reaction mixture was slowly transferred into an aq. sol. of K_2CO_3. The green precipitate was filtered and dried before being purified by column chromatography (EtOAc/Pentane : 10 to 100%) to afford **2** as a green solid (0.26 g, 65% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06 – 7.85 (m, 3H), 7.81 (d, *J* = 8.7 Hz, 1H), 7.52 (d, *J* = 8.7 Hz, 1H), 6.74 (d, *J* = 8.5 Hz, 2H), 3.06 (s, 6H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 169.5, 153.5, 152.5, 136.4, 129.5, 129.1, 124.0, 123.4, 121.0, 117.5, 111.8, 40.3. Data in accordance with the literature.[2] HR-MS (ESI+), m/z: $[M+H]^+$ Calcd for $C_{15}H_{14}BrN_2S^+$: 333.0056 ; found : 333.0055.



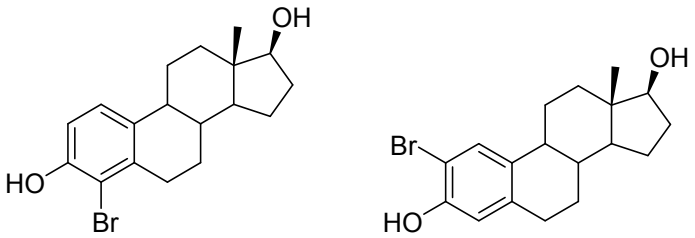
***N,N*-dimethyl-4-(6-methylbenzo[d]oxazol-2-yl)aniline (3) :** In a dry Schlenk flask, $Pd(P^tBu_3)_2$ (5 mol%, 5 µmol, 2.6 mg) was dissolved in 1 mL of dry toluene, 10 mL of pure oxygen was bubbled through the solution and stirred 24 h to achieve full oxidation of the catalyst.[3] 4-(6-Bromobenzo[d]oxazol-2-yl)-*N,N*-dimethylaniline (**1**) (32 mg, 0.10 mmol, 1.00 eq) was added to the catalyst solution. A 1.6 M solution of MeLi (94 µL, 0.15 mmol, 1.5 eq) in Et_2O was diluted with toluene to give a 1 mL solution and was added at r.t. over 5 min. by the use of a syringe pump. After the addition was completed, the reaction was quenched with 0.5 mL of MeOH, and Celite was added to the reaction mixture. The solvent was evaporated under reduced pressure to afford the crude product on Celite which was purified by column chromatography (Pentane/EtOAc : 95/5) to afford **3** (20.7 mg, 87% yield) as a pink solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, *J* = 9.0 Hz, 2H), 7.56 (d, *J* = 8.1 Hz, 1H), 7.32 (s, 1H), 7.11 (d, *J* = 7.9 Hz, 1H), 6.76 (d, *J* = 9.0 Hz, 2H), 3.06 (s, 6H), 2.48 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 163.8, 152.4, 150.9, 134.4, 129.1, 125.5, 118.5, 111.8, 111.7, 110.6, 40.3, 21.9. FT-IR (neat, cm^{-1}): 2908, 2822, 1605, 1508, 1374, 1183, 808. HR-MS (ESI+), m/z: $[M+H]^+$ Calcd for $C_{16}H_{17}N_2O^+$: 253.1335 ; found : 253.1335.

[2] B. C. Lee et al. *Bioorg. Med. Chem.* **2011**, *19*, 2980–2990

[3] For details on catalyst preparation, see also: D. Heijnen et al. *Angew. Chem. Int. Ed.* **2017**, *56*, 3354–3359



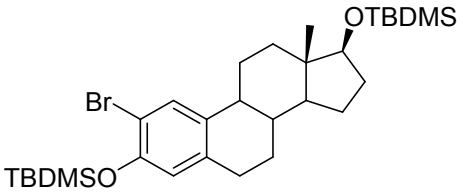
***N,N*-dimethyl-4-(6-methylbenzo[d]thiazol-2-yl)aniline (4):** 4-(6-bromobenzo[d]thiazol-2-yl)-*N,N*-dimethylaniline (**3**) (33 mg, 0.10 mmol, 1.0 eq) was loaded in a dry Schlenk flask followed by the addition of $BF_3{\cdot}Et_2O$ (12 µL, 0.10 mmol, 1.0 eq). The reaction mixture was stirred for 5 min at rt before $Pd(P^tBu_3)_2$ (10 mol%, 10 µmol, 5.6 mg) was added. A 1.6 M solution of MeLi (94 µL, 0.15 mmol, 1.5 eq) in Et_2O was diluted with toluene to give a 1 mL solution and was added at rt over 5 min by the use of a syringe pump. After the addition was completed, the reaction was quenched with 0.5 mL of MeOH, and Celite was added to the reaction mixture. The solvent was evaporated under reduced pressure to afford the crude product on Celite which was purified by column chromatography (Pentane/EtOAc : 95/5) to afford **4** (21 mg, 79% yield) as a yellow solid. ^{1}H NMR (400 MHz, DMSO-*d6*) δ 7.91 – 7.75 (m, 4H), 7.28 (d, J = 8.9 Hz, 1H), 6.81 (d, J = 8.9 Hz, 2H), 3.02 (s, 6H), 2.43 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 168.0, 152.3, 134.6, 134.5, 128.9, 127.7, 121.8, 121.3, 111.9, 40.4, 21.6. Data in accordance with the literature.[4] HR-MS (ESI+), m/z: $[M+H]^+$ Calcd for $C_{16}H_{17}N_2S^+$: 269.1107 ; found : 269.1106.



4-bromoestradiol and 2-bromoestradiol (5a): To a 50 mL solution of estradiol (700 mg, 2.56 mmol, 1.00 eq) in $CHCl_3$ was added dropwise a 30 mL solution of *N*-Bromosuccinimide (480 mg, 2.69 mmol, 1.05 eq) in $CHCl_3$. The reaction mixture was stirred and heated with an oil bath at reflux for 2.5h. The solvent was evaporated and the residue was dissolved in minimal amount of MeOH, addition of H_2O caused the formation of a precipitate which was filtered and washed with cold H_2O. The solid was dried *in vacuo*. EtOH was added, the precipitate filtered and dried to afford 4-bromoestradiol as a white solid (0.40 g, 45% yield). The liquid fraction was evaporated and the residue was recrystallized from hexane/acetone mixture to afford 2-bromoestradiol as a white solid (0.32 g, 36% yield).

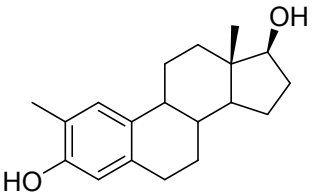
Spectral data for 4-bromoestradiol : ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.79 (s, 1H), 7.09 (d, *J* = 8.5 Hz, 1H), 6.73 (d, *J* = 8.4 Hz, 1H), 4.47 (d, *J* = 4.8 Hz, 1H), 3.55 – 3.45 (m, 2H), 2.85 – 2.74 (m, 1H), 2,60 – 2,51 (m, 1H), 2.27 – 2.18 (m, 1H), 2.15 – 2.04 (m, 1H), 1.92 – 1.78 (m, 3H), 1.57 (q, *J* = 11.5, 9.8 Hz, 1H), 1.45 – 1.00 (m, 7H), 0.63 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 154.9, 139.5, 135.9, 128.1, 116.3, 115.6, 83.1, 52.5, 46.8, 45.8, 40.8, 39.6, 34.0, 33.0, 30.1, 29.4, 25.8, 14.3. Data in accordance with the literature[5]

Spectral data for 2-bromoestradiol (**5a**): ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.78 (s, 1H), 7.24 (s, 1H), 6.60 (s, 1H), 4.47 (s, 1H), 3.57 – 3.43 (m, 1H), 2.68 – 2.62 (m, 2H), 2.23 – 2.13 (m, 1H), 2.09 – 1.99 (m, 1H), 1.91 – 1.70 (m, 1H), 1.62 – 1.49 (m, 1H), 1.41 – 1.00 (m, 1H), 0.63 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ 154.6, 140.0, 135.8, 132.4, 119.2, 109.5, 83.1, 52.5, 46.3, 45.9, 41.4, 39.6, 33.0, 31.7, 29.8, 29.1, 25.9, 14.3. Data in accordance with the literature[6]

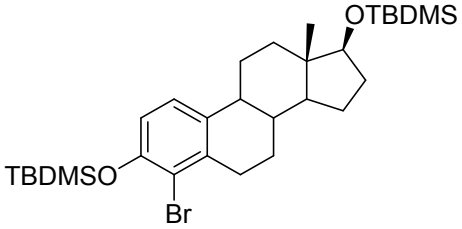


[4] A. Dey and A. Hajra *Org. Lett.* **2019**, *21* (6), 1686–1689
[5] I. Damljanovic et al. *Bull. Chem. Soc. Jpn.* **2007**, *80* (2), 407–409
[6] I. Damljanovic et al. *Bull. Chem. Soc. Jpn.* **2007**, *80* (2), 407–409

bis(tert-butyldimethylsilane protected 2-bromoestradiol (5b): 2-Bromoestradiol (**5a**) (50 mg, 0.14 mmol, 1.0 eq) and imidazole (0.12 mg, 1.7 mmol, 12 eq) were dissolved in 1 mL of DMF, TBDMSCl (0.15 g, 1.0 mmol, 7.0 eq) was added portion-wise and the reaction mixture was stirred overnight at rt. The reaction was quenched by addition of brine and the mixture extracted with 3x30 mL of Et_2O. The combined organic layer was dried over Na_2SO_4, filtered and the solvent was evaporated. The crude compound was purified by column chromatography (100% pentane) to afford **5b** as a white powder (78 mg, 94% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (s, 1H), 6.56 (s, 1H), 3.63 (t, *J* = 8.3 Hz, 1H), 2.79 – 2.71 (m, 2H), 2.27 – 2.07 (m, 2H), 1.99 – 1.81 (m, 3H), 1.71 – 1.59 (m, 1H), 1.53 – 1.07 (m, 7H), 1.03 (s, 9H), 0.89 (m, 9H), 0.74 (s, 3H), 0.23 (s, 6H), 0.04 (s, 3H), 0.02 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.4, 137.9, 135.3, 124.7, 118.7, 116.8, 81.9, 49.8, 44.5, 43.6, 38.1, 37.3, 31.7, 31.1, 27.7, 26.8, 26.0, 26.0, 25.9, 23.4, 18.5, 18.3, 11.5, -4.0, -4.3, -4.6. FT-IR (neat, cm^{-1}): 2926, 2855, 1471, 1249. HR-MS (ESI+), m/z: $[M+H]^+$ Calcd for $C_{30}H_{52}BrO_2Si_2^+$: 579.2684 ; found : 579.2675.



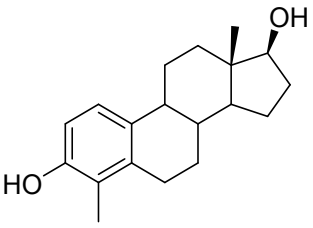
2-methylestradiol (6a): Bis(tert-butyldimethylsilane protected 2-bromoestradiol (**5b**) (50 mg, 86 µmol, 1.0 eq) was loaded in a dry Schlenk flask, followed by the addition of fully oxidized $Pd(P^tBu_3)_2$ (5 mol%, 4.3 µmol, 2.4 mg) as a 0.25 mL solution in toluene. A 1.6 M solution of MeLi (81 µL, 0.13 mmol, 1.5 eq) in Et_2O was diluted with toluene to give a 1 mL solution and was added at rt over 3 min by the use of a syringe pump. After the addition was completed, the reaction was quenched with 1 mL of a 4 M HCl solution in MeOH, and stirred another 2 min to achieve full deprotection. Celite was added to the reaction mixture. The solvent was evaporated under reduced pressure to afford the crude product on Celite which was purified by column chromatography (Pentane/EtOAc : 80/20) to afford **6** (22 mg, 90% yield) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.04 (s, 1H), 6.51 (s, 1H), 3.74 (t, *J* = 8.5 Hz, 1H), 2.78 (dt, *J* = 7.0, 3.0 Hz, 2H), 2.37 – 2.26 (m, 1H), 2.21 (s, 3H), 2.19 – 2.07 (m, 2H), 1.95 (dt, *J* = 12.6, 3.1 Hz, 1H), 1.91 – 1.81 (m, 1H), 1.75 – 1.63 (m, 1H), 1.56 – 1.14 (m, 9H), 0.78 (s, 3H). ^{13}C NMR (75 MHz, $cdcl_3$) δ 151.6, 135.6, 132.5, 127.9, 120.8, 114.9, 82.0, 50.0, 43.9, 43.2, 38.9, 36.7, 30.6, 29.2, 27.3, 26.4, 23.1, 15.6, 11.1. Data in accordance with the literature[7].



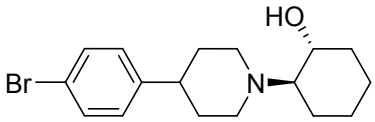
bis(tert-butyldimethylsilane protected 4-bromoestradiol: 4-Bromoestradiol (0.50 g, 1.4 mmol, 1.0 eq) and Imidazole (1.16 g, 17 mmol, 12 eq) were dissolved in 10 mL of DMF, TBDMSCl (1.50 g, 10 mmol, 7.0 eq) was added portion-wise and the reaction mixture was stirred at rt for 4 h. The reaction was quenched by addition of brine followed by 200 mL of H_2O and the mixture extracted with 3x50 mL of Et_2O. The combined organic layer was dried over Na_2SO_4, filtered and the solvent was evaporated. The crude compound was purified by column chromatography (100% pentane) to afford the title compound as a white powder (0.75 g, 91% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.11 (d, *J* = 8.5 Hz, 1H), 6.69 (d, *J* = 8.5 Hz, 1H), 3.64 (t, *J* = 8.3 Hz, 1H), 2.95 (dd, *J* = 18.0, 6.1 Hz, 1H), 2.76 – 2.61 (m, 1H), 2.33 – 2.10 (m, 2H), 2.01 – 1.82 (m, 3H), 1.66 (q, *J* = 10.9, 9.6 Hz, 1H), 1.52 – 1.08 (m, 7H), 1.04 (s, 9H), 0.89 (s, 9H), 0.73 (s, 3H), 0.24 (s, 6H), 0.03 (s, 3H), 0.02 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 153.0, 140.4, 137.8, 127.2, 119.3, 84.4, 52.3, 47.0, 46.1, 40.6, 39.8, 34.2, 33.7, 30.2, 29.3, 28.5, 28.5, 28.4, 25.9,

[7] Bubert et al. *J. Med. Chem.* **2007**, *50*, 4431–4443

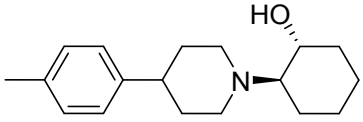
21.0, 20.8, 14.0, -0.3, -1.5, -1.8, -2.1. HR-MS (APCI+), m/z: $[M+H]^+$ Calcd for $C_{30}H_{52}BrO_2Si_2^+$: 579.2684 ; found : 579.2680.



4-methylestradiol: Bis(tert-butyldimethylsilane protected 4-bromoestradiol (0.12 g, 0.20 mmol, 1.0 eq) was loaded in a dry Schlenk flask, followed by the addition of fully oxidized $Pd(P^tBu_3)_2$ (5 mol%, 10 µmol, 5.2 mg) as a 0.5 mL solution in toluene. A 1.6 M solution of MeLi (0.19 mL, 0.30 mmol, 1.5 eq) in Et_2O was diluted with toluene to give a 1 mL solution and was added at rt over 3 min by the use of a syringe pump. After the addition was completed, the reaction was quenched with 1 mL of a 4 M HCl solution in MeOH, and the mixture stirred another 2 min to achieve full deprotection. Celite was added to the reaction mixture. The solvent was evaporated under reduced pressure to afford the crude product on Celite which was purified by column chromatography (Pentane/EtOAc : 80/20) to afford the title compound (36 mg, 63 % yield) as a white solid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.06 (d, *J* = 8.5 Hz, 1H), 6.63 (d, *J* = 8.4 Hz, 1H), 4.57 (s, 1H), 3.73 (t, *J* = 8.5 Hz, 1H), 2.79 (dd, *J* = 17.4, 6.0 Hz, 1H), 2.71 – 2.56 (m, 1H), 2.31 (dd, *J* = 13.3, 3.6 Hz, 1H), 2.25 – 2.06 (m, 5H), 2.04 – 1.88 (m, 2H), 1.80 – 1.65 (m, 1H), 1.46 – 1.15 (m, 7H), 0.77 (s, 3H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 151.5, 136.8, 133.0, 123.5, 122.0, 112.4, 82.1, 50.2, 44.4, 43.3, 38.2, 36.9, 30.8, 27.8, 27.6, 26.7, 23.3, 11.3, 11.2. FT-IR (neat, cm^{-1}): 3300, 2920, 2861, 1277, 1071, 1051, 1010. HR-MS (ESI+), m/z: $[M+H]^+$ Calcd for $C_{19}H_{27}O_2^+$: 287.2006 ; found : 287.2006.

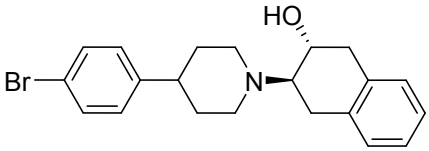


(+/-)-2-(4-(4-bromophenyl)piperidin-1-yl)cyclohexan-1-ol (7): To a solution of 4-(4-bromophenyl)piperidine (2.0 g, 8.3 mmol, 1.0 eq) in 20 mL of EtOH was added dropwise cyclohexene oxide (1.8 mL, 18 mmol, 2.1 eq). The reaction mixture was stirred and heated with an oil bath at reflux for 2 d before being cooled to 0 °C. The precipitate was filtered and washed with cold EtOH to afford, after drying, **7** as white crystals (2.51 g, 89% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (d, *J* = 8.4 Hz, 2H), 7.09 (d, *J* = 8.6 Hz, 2H), 4.06 (s, 1H), 3.39 (td, *J* = 9.8, 4.5 Hz, 1H), 2.93 (d, *J* = 11.3 Hz, 1H), 2.82 – 2.65 (m, 2H), 2.45 (tt, *J* = 12.1, 3.9 Hz, 1H), 2.29 – 2.06 (m, 3H), 1.91 – 1.53 (m, 7H), 1.34 – 1.11 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.9, 134.1, 131.3, 122.4, 73.3, 71.3, 56.0, 48.0, 45.1, 36.9, 36.5, 35.9, 28.3, 26.8, 24.9. FT-IR (neat, cm^{-1}): 3471, 2929, 2854, 2808, 1076. HR-MS (ESI+), m/z: $[M+H]^+$ Calcd for $C_{17}H_{25}BrNO^+$: 338.1114 ; found : 338.1109.

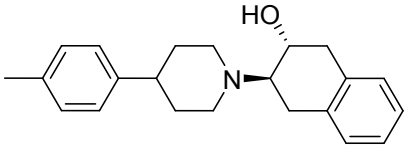


(+/-)-2-(4-(*p*-tolyl)piperidin-1-yl)cyclohexan-1-ol (8): In a dry Schlenk flask, was dissolved (+/-)-2-(4-(4-bromophenyl)piperidin-1-yl)cyclohexan-1-ol (**7**) (67 mg, 0.20 mmol, 1.0 eq) in 1 mL of dry toluene. A solution in 0.5 mL toluene of fully oxidized $Pd(P^tBu_3)_2$ (5 mol%, 10 µmol, 5.6 mg) was added. A 1.6 M solution of MeLi (0.31 mL, 0.5 mmol, 2.5 eq) in Et_2O was diluted with toluene to give a 1 mL solution and was added at rt over 5 min by the use of a syringe pump. After the addition was completed, the reaction was quenched with 0.5 mL of MeOH, and Celite was added to the reaction mixture. The solvent was evaporated under reduced pressure to afford the crude product on Celite which was purified by column chromatography (DCM/MeOH : 95/5 to 90/10) to afford **8** (46 mg, 85% yield) as a yellow solid.). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 – 6.97 (m, 4H), 3.40 (t, J = 9.3 Hz, 1H), 2.94 (d, J = 11.1 Hz, 1H), 2.87 – 2.67 (m, 2H), 2.46 (t, J = 11.9 Hz, 1H), 2.32 (s, 3H), 2.25 (d, J = 9.6 Hz, 2H), 2.14 (d, J = 8.5 Hz, 1H), 1.91 – 1.62 (m, 7H), 1.31 – 1.16 (m, 4H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 135.8, 129.2, 126.7, 70.8,

68.8, 53.4, 45.9, 42.3, 33.9, 33.5, 29.1, 25.5, 24.1, 22.6, 21.0. Data in accordance with the literature[8]. HR-MS (ESI+), m/z: $[M+H]^+$ Calcd for $C_{18}H_{28}NO^+$: 274.2165 ; found : 274.2168.



(+/-)-3-(4-(4-bromophenyl)piperidin-1-yl)-1,2,3,4-tetrahydronaphthalen-2-ol: To a solution of (+/-)4-(4-bromophenyl)piperidine (0.74 g, 3.1 mmol, 1.0 eq.) in 20 mL of EtOH was added dropwise a solution of 2,3-epoxy-1,2,3,4-tetrahydronaphthalene (0.68 g, 4.6 mmol, 1.5 eq) in 5 mL of EtOH. The reaction mixture was stirred and heated with an oil bath at reflux for 2 d before being cooled to 0 °C. The precipitate was filtered and washed with cold EtOH, dried in air, to afford the title compound as white crystals (0.90 g, 75% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, *J* = 8.3 Hz, 2H), 7.17 – 7.03 (m, 6H), 4.34 (s, 1H), 3.97 – 3.81 (m, 1H), 3.32 (dd, *J* = 16.1, 5.9 Hz, 1H), 3.08 – 2.95 (m, 1H), 2.95 – 2.75 (m, 6H), 2.53 (tt, *J* = 12.0, 3.9 Hz, 1H), 2.39 (t, *J* = 11.5 Hz, 1H), 1.99 – 1.57 (m, 4H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 144.9, 134.7, 134.1, 131.7, 129.4, 129.2, 128.7, 126.4, 126.2, 120.1, 66.8, 65.9, 53.6, 45.3, 42.4, 38.0, 34.1, 33.7, 26.4. FT-IR (neat, cm^{-1}): 3160, 2937, 2914, 2844, 1086. HR-MS (ESI+), m/z: $[M+H]^+$ Calcd for $C_{21}H_{25}BrNO^+$: 386.1114 ; found : 386.1112.

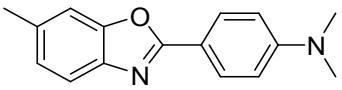


(+/-)-3-(4-(*p*-tolyl)piperidin-1-yl)-1,2,3,4-tetrahydronaphthalen-2-ol: In a dry Schlenk flask, was dissolved (+/-)-3-(4-(4-bromophenyl)piperidin-1-yl)-1,2,3,4-tetrahydronaphthalen-2-ol (0.20 g, 0.50 mmol , 1.0 eq) in 1 mL of dry toluene. A solution in 0.5 mL toluene of fully oxidized $Pd(P^tBu_3)_2$ (5 mol%, 25 µmol, 14 mg) was added. A 1.6 M solution of MeLi (0.78 mL, 1.3 mmol, 2.5 eq) in Et_2O was diluted with toluene to give a 2 mL solution and was added at rt over 5 min by the use of a syringe pump. After the addition was completed, the reaction was quenched with 0.5 mL of MeOH, and Celite was added to the reaction mixture. The solvent was evaporated under reduced pressure to afford the crude product on Celite which was purified by column chromatography (DCM/MeOH : 95/5) to afford the title compound (128 mg, 80% yield) as an off-white solid. ^{1}H NMR (400 MHz, , $CDCl_3$) δ 7.20 – 7.01 (m, 8H), 4.40 (s, 1H), 3.90 (q, *J* = 9.7 Hz, 1H), 3.33 (dd, *J* = 16.1, 5.8 Hz, 1H), 3.08 – 2.75 (m, 7H), 2.53 (t, *J* = 12.1 Hz, 1H), 2.39 (t, *J* = 11.8 Hz, 1H), 2.34 (s, 3H), 1.98 – 1.68 (m, 4H). ^{13}C NMR (151 MHz, $CDCl_3$) δ 142.9, 135.8, 134.7, 134.0, 129.3, 129.2, 129.1, 126.7, 126.2, 126.1, 66.6, 65.8, 53.6, 45.3, 42.4, 37.9, 34.2, 33.8, 26.2, 21.0. Data in accordance with the literature[9]. HR-MS (ESI+), m/z: $[M+H]^+$ Calcd for $C_{22}H_{28}NO^+$: 322.2165 ; found : 322.2168.

[8] K. Shiba et al. *Bioorg. Med. Chem.* **2006**, *14*, 2620–2626

[9] A. Sharma, J. Agarwal and R. K. Peddinti *Org. Biomol. Chem.* **2017**, *15*, 1913–1920

Cross-coupling procedure on a 1 mmol scale



_N,N_-dimethyl-4-(6-methylbenzo[d]oxazol-2-yl)aniline (3)

In a dry Schlenk flask, $Pd(P^tBu_3)_2$ (5 mol%, 50 µmol, 26 mg) was dissolved in 5 mL of dry toluene, 10 mL of pure oxygen was bubbled through the solution and stirred 24 h to achieve full oxidation of the catalyst. 4-(6-Bromobenzo[d]oxazol-2-yl)-*N,N*-dimethylaniline (**1**) (318 mg, 1.00 mmol, 1.00 eq) was added to the catalyst solution. A 1.6 M solution of MeLi (0.94 mL, 1.5 mmol, 1.5 eq) in Et_2O was diluted with toluene to give a 5 mL solution and was added at r.t. over 5 min. by the use of a syringe pump. After the addition was completed, the reaction was quenched with 0.5 mL of MeOH, and Celite was added to the reaction mixture. The solvent was evaporated under reduced pressure to afford the crude product on Celite which was purified by column chromatography (Pentane/EtOAc : 95/5) to afford **3** (191 mg, 76% yield) as a pink solid. ^{1}H-NMR Spectra corresponded to the one described above for compound **3**.

Radiolabeling procedures and purifications

Production of [^{11}C]CH_3I

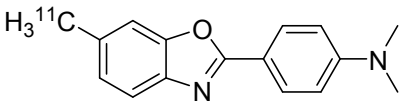
[^{11}C]CH_4 was generated in an IBA Cyclone 18/18 cyclotron by irradiation of a N_2/H_2 (95/5 ratio) gas mixture. The radioactive gas was trapped in a Carboxen® 1000, 60/80 mesh (Sigma Aldrich) at -196 ºC, released by warming up to room temperature and allowed to react with iodine at 720 ºC to form [^{11}C]CH_3I in a gas circulating process (circulating for 260 sec). [^{11}C]CH_3I was selectively retained in a PoraPak™ N 100/120 (Waters Co.) at room temperature, while unreacted [^{11}C]CH_4 was recirculated. At the end of the process, the PoraPak™ trap was heated at 200 ºC and [^{11}C]CH_3I was distilled under continuous helium flow (20 mL/min). The gas stream was passed through a trap containing phosphorous pentoxide and Ascarite II® (20-30 mesh) before being bubbled into the trapping vial. Typically, the formation [^{11}C]CH_3I from [^{11}C]CH_4 proceeds in 30 to 50% RCY. The labelling procedure was performed starting with 3 - 10 GBq of [^{11}C]CH_3I.

General procedure for manual labeling

To an oven-dried, argon-purged 4 mL vial, containing the aryl bromide (0.2 mmol) in 0.5 mL of dry toluene, was added fully pre-oxidized Pd(P^tBu_3)$_2$ in toluene (0.5 mL, 0.01 mmol). In another oven-dried, [^{11}C]MeI was bubbled into an argon-purged 4 mL vial, containing a solution of *n*-BuLi (0.125 mL, 0.20 mmol, 1.6 M in hexanes) in 0.87 mL of dry toluene for 4 min with a flow rate of 20 mL/min. This solution was then taken up into a syringe and added at room temperature over 3 min *via* syringe pump into the reaction mixture with catalyst. After additional 2 min of stirring, the reaction was quenched by addition of 0.5 mL of MeOH. A sample was taken from the reaction mixture and the solvent was evaporated at 50 °C under argon flow. The residue was dissolved in 1 mL of the eluent used for HPLC (solvent system described for each compound below) and injected on HPLC. The product was collected in a 20 mL vial and its activity was measured to access the radiochemical yields. A small amount of non-radiolabelled reference compound was added to this vial and injected on HPLC to confirm the identity of the labelled product. Radiochemical yields and molar activities are reported in accordance with radiochemistry guidelines.[10]

Procedures, HPLC conditions, and chromatogram of the purification of the labelled products

_N,N_-dimethyl-4-(6-([^{11}C]-methyl)benzo[d]oxazol-2-yl)aniline (9)



9: Compound **9** was synthesized according to the general procedure, starting from 4-(6-bromobenzo[d]oxazol-2-yl)-*N,N*-dimethylaniline (**1**) and using 5 mol% of fully pre-oxidized Pd(P^tBu_3)$_2$. No additive were used. The product **9** was collected after HPLC purification in 44% RCY, n = 2. (An aliquot was taken for HPLC analysis and isolation of the final compound, which was extrapolated to the complete reaction mixture to assess the radiochemical yield).

HPLC conditions :

- Column : Phenomenex Luna 5µm C18(2) 100Å 10x250 mm
- Eluent : MeCN/H_2O/Formic acid (80/20/1)
- Flow : 5 mL/min
- Retention time : 6.5 min

[10] For consensus on nomenclature for radiochemistry see: H. H. Coenen et al. *Nucl. Med. Biol.* **2017**, *55*, v–xi

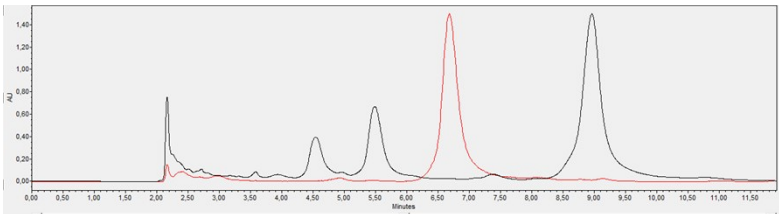


Figure S1: Chromatogram from the injection of the crude reaction mixture on HPLC (radioactive signal in red) – UV detector set at 254 nm

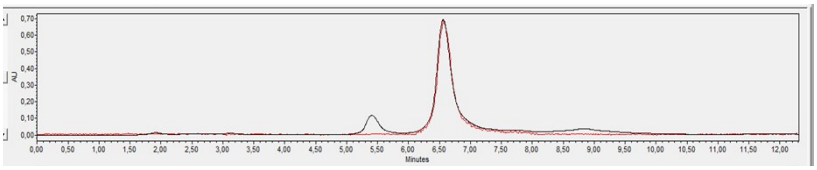
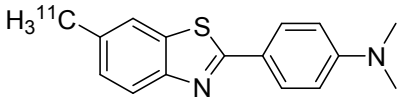


Figure S2: Chromatogram of the spike injection with non-radiolabelled reference compound HPLC (radioactive signal in red) – UV detector set at 254 nm

_N,N_-dimethyl-4-(6-[^{11}C]methylbenzo[d]thiazol-2-yl)aniline (10)



10: Compound **10** was synthesized according to the general procedure, starting from 4-(6-bromobenzo[d]thiazol-2-yl)-*N,N*-dimethylaniline (**2**) and using 10 mol% of fully pre-oxidized Pd(P^tBu_3)$_2$. 1.5 eq. of BF_3.Et_2O (37 µL, 0.30 mmol) was used as additive and added before addition of the catalyst. The product **10** was collected after HPLC purification in 33 – 35% RCY, n = 2. (An aliquot was taken for HPLC analysis and isolation of the final compound, which was extrapolated to the complete reaction mixture to assess the radiochemical yield).

HPLC conditions :

- Column : Phenomenex Luna 5µm C18(2) 100Å 10x250 mm
- Eluent : MeCN/H_2O/Formic acid (80/20/1)
- Flow : 5 mL/min
- Retention time : 8.6 min

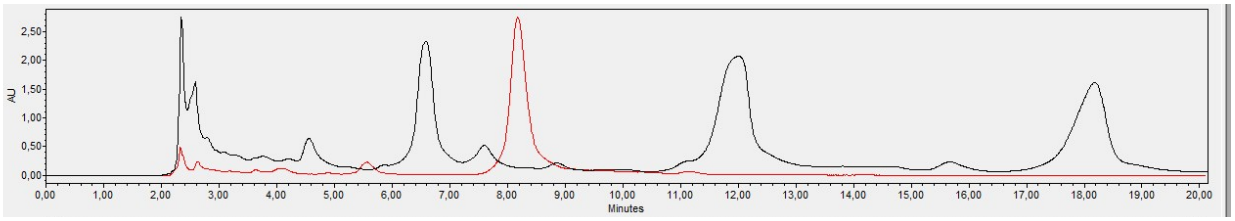


Figure S3: Chromatogram from the injection of the crude reaction mixture on HPLC (radioactive signal in red) – UV detector set at 254 nm

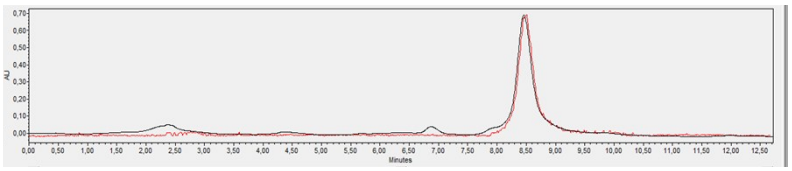
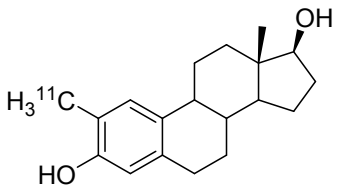


Figure S4: Chromatogram of the spike injection with non-radiolabelled reference compound HPLC (radioactive signal in red) – UV detector set at 254 nm

2-[^{11}C]methylestradiol (11)



11: Compound **11** was synthesized according to the general procedure, starting from bis(tert-butyldimethylsilane protected 2-bromoestradiol (**5b**) and using 5 mol% of fully pre-oxidized Pd(P^tBu_3)$_2$. At the end of the addition of [^{11}C]MeLi, the reaction mixture was directly quenched by addition of 1 mL of 4 M HCl solution in MeOH, and stirred for an additional 2 min at rt. The product **11** was collected after HPLC purification in 51% RCY, n = 2. (An aliquot was taken for HPLC analysis and isolation of the final compound, which was extrapolated to the complete reaction mixture to assess the radiochemical yield).

HPLC conditions :

- Column : SymmetryPrep C18 7µm 125Å 7.8x300 mm
- Eluent : MeOH/H_2O with 0.1% Formic acid (70/30)
- Flow : 5 mL/min
- Retention time : 7.3 min

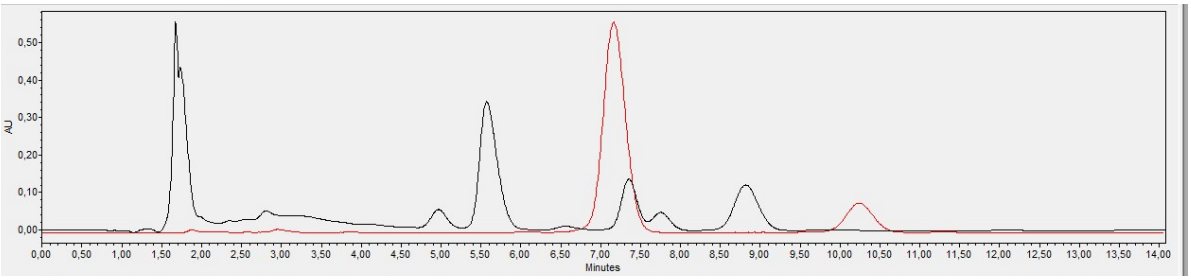


Figure S5: Chromatogram from injection of the crude reaction mixture on HPLC (radioactive signal in red) – UV detector set at 254 nm

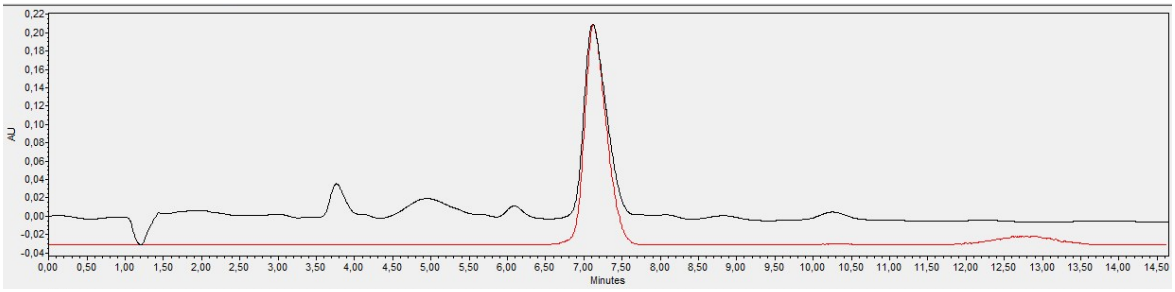
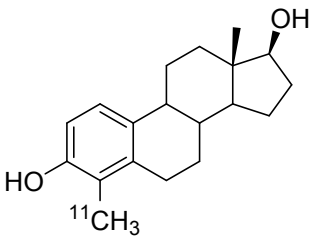


Figure S6: Chromatogram of the spike injection with non-radiolabelled reference compound HPLC (radioactive signal in red) – UV detector set at 254 nm

4-[^{11}C]methylestradiol (12)



12: Compound **12** was synthesized according to the general procedure, starting from bis(tert-butyldimethylsilane protected 4-bromoestradiol and using 5 mol% of fully pre-oxidized Pd(P^tBu_3)$_2$. At the end of the addition of [^{11}C]MeLi, the reaction mixture was directly quenched by addition of 1 mL of 4 M HCl solution in MeOH, and stirred for an additional 2 min at rt. The product **12** was collected after HPLC purification in 55 - 57% RCY, n = 2. (An aliquot was taken for HPLC analysis and isolation of the final compound, which was extrapolated to the complete reaction mixture to assess the radiochemical yield).

HPLC conditions :

- Column : SymmetryPrep C18 7µm 125Å 7.8x300 mm
- Eluent : MeOH/H_2O with 0.1% Formic acid (70/30)
- Flow : 5 mL/min
- Retention time : 10.5 min

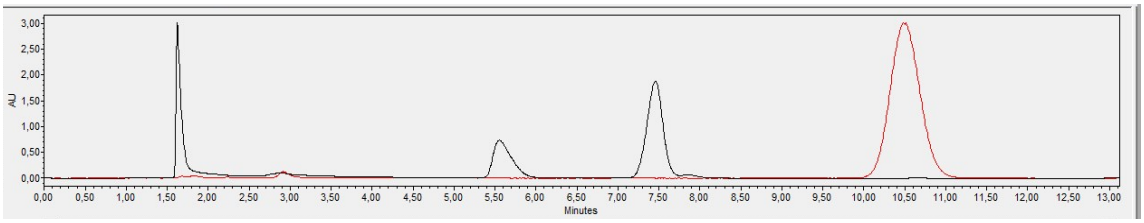


Figure S7: Chromatogram from injection of the crude reaction mixture on HPLC (radioactive signal in red) – UV detector set at 254 nm

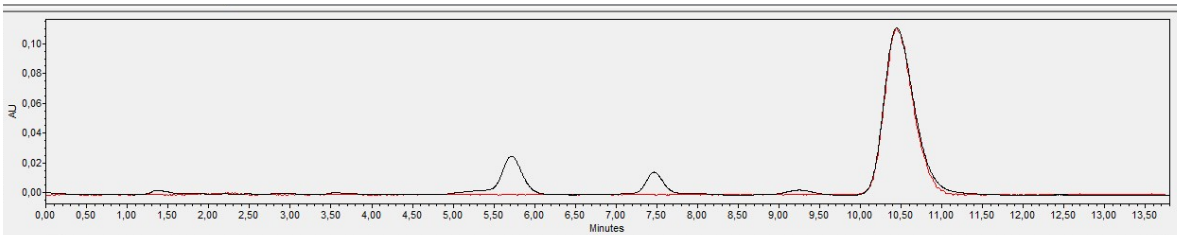
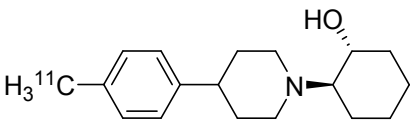


Figure S8: Chromatogram of the spike injection with non-radiolabelled reference compound HPLC (radioactive signal in red) – UV detector set at 254 nm

(+/-)-2-(4-(*p*-[^{11}C]tolyl)piperidin-1-yl)cyclohexan-1-ol (13)



trans-**13:** Compound **13** was synthesized according to the general procedure, starting from (+/-)-2-(4-(4-bromophenyl)piperidin-1-yl)cyclohexan-1-ol (**7**) and using 5 mol% of fully pre-oxidized Pd(P^tBu_3)$_2$. 1.0 eq. of *n*-BuLi (0.125 mL, 0.20 mmol, 1.6 M in hexanes) was used to ensure complete deprotonation and added before the

addition of the catalyst. The product **13** was collected after HPLC purification in 45 ± 5% RCY, n = 4. (An aliquot was taken for HPLC analysis and isolation of the final compound, which was extrapolated to the complete reaction mixture to assess the radiochemical yield).

HPLC conditions :

- Column : SymmetryPrep C18 7µm 125Å 7.8x300 mm
- Eluent : MeOH/H_2O with 0.1% Formic acid (gradient from 70/30 to 50/50 in 15 min.)
- Flow : 5 mL/min
- Retention time : 6.9 min

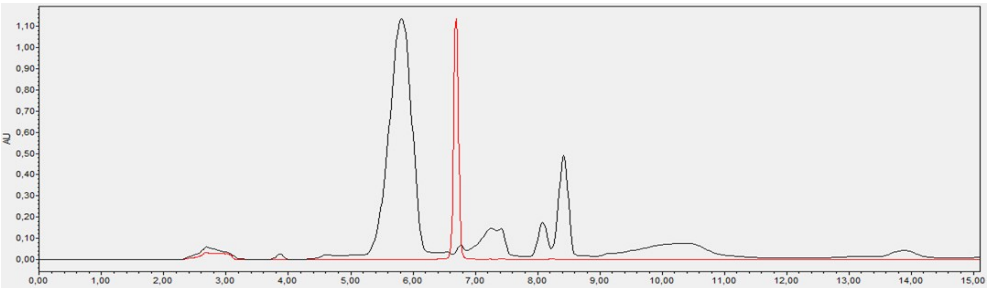


Figure S9: Chromatogram from the injection of the crude reaction mixture on HPLC (radioactive signal in red) – UV detector set at 254 nm

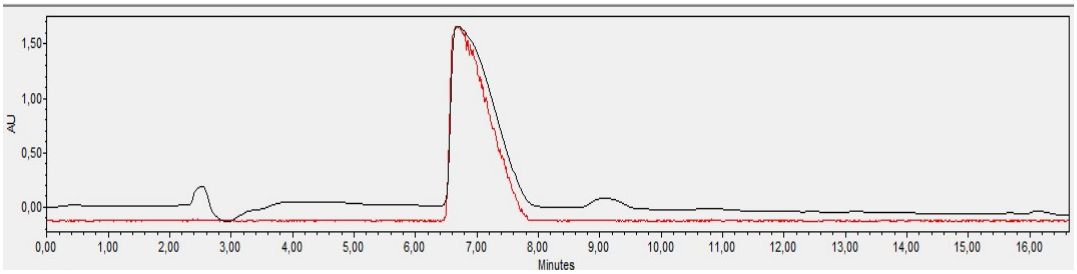
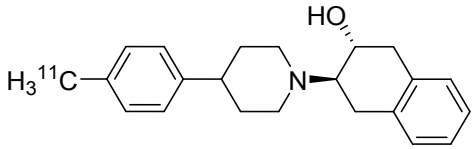


Figure S10: Chromatogram of the spike injection with non-radiolabelled reference compound HPLC (radioactive signal in red) – UV detector set at 212 nm

(+/-)-3-(4-(*p*-[^{11}C]tolyl)piperidin-1-yl)-1,2,3,4-tetrahydronaphthalen-2-ol (14)



trans-**14:** Compound **14** was synthesized according to the general procedure, starting from (+/-)-3-(4-(4-bromophenyl)piperidin-1-yl)-1,2,3,4-tetrahydronaphthalen-2-ol and using 5 mol% of fully pre-oxidized Pd(P^tBu_3)$_2$. 1.0 eq. of *n*-BuLi (0.125 mL, 0.20 mmol, 1.6 M in hexanes) was used to ensure complete deprotonation and added before the addition of the catalyst. The product **13** was collected after HPLC purification in 55 ± 9% RCY, n = 4. (An aliquot was taken for HPLC analysis and isolation of the final compound, which was extrapolated to the complete reaction mixture to assess the radiochemical yield).

HPLC conditions :

- Column : SymmetryPrep C18 7µm 125Å 7.8x300 mm
- Eluent : MeOH/H_2O with 0.1% Formic acid (gradient from 70/30 to 50/50 in 15 min.)
- Flow : 5 mL/min
- Retention time : 8.2 min

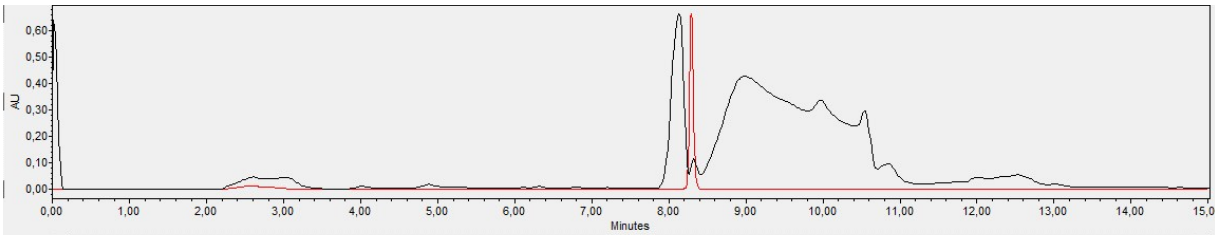


Figure S11: Chromatogram from injection of the crude reaction mixture on HPLC (radioactive signal in red) – UV detector set at 254 nm.

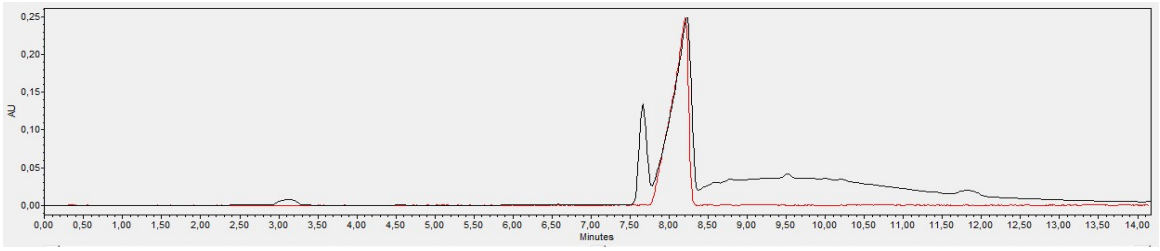
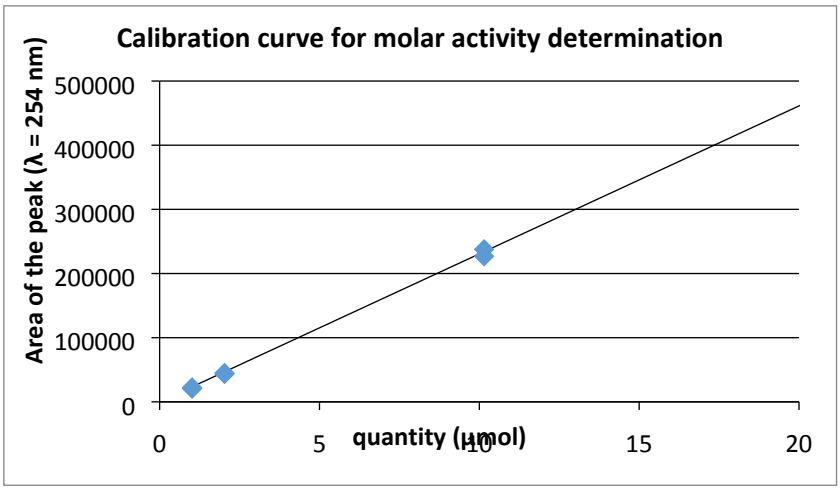


Figure S12: Chromatogram of the spike injection with non-radiolabelled reference compound HPLC (radioactive signal in red) – UV detector set at 254 nm.

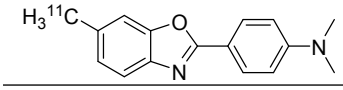
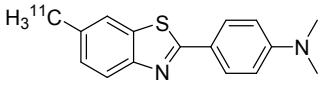
Molar activity determination

The calibration was obtained by injecting different concentration of *N,N*-dimethyl-4-(6-methylbenzo[d]oxazol-2-yl)aniline (**3**) solutions.

amount (µmol)	Peak area
20,3	470823
20,3	466647
10,15	237708
10,15	226915
2,03	43523
2,03	44937
1,015	22364
1,015	20521



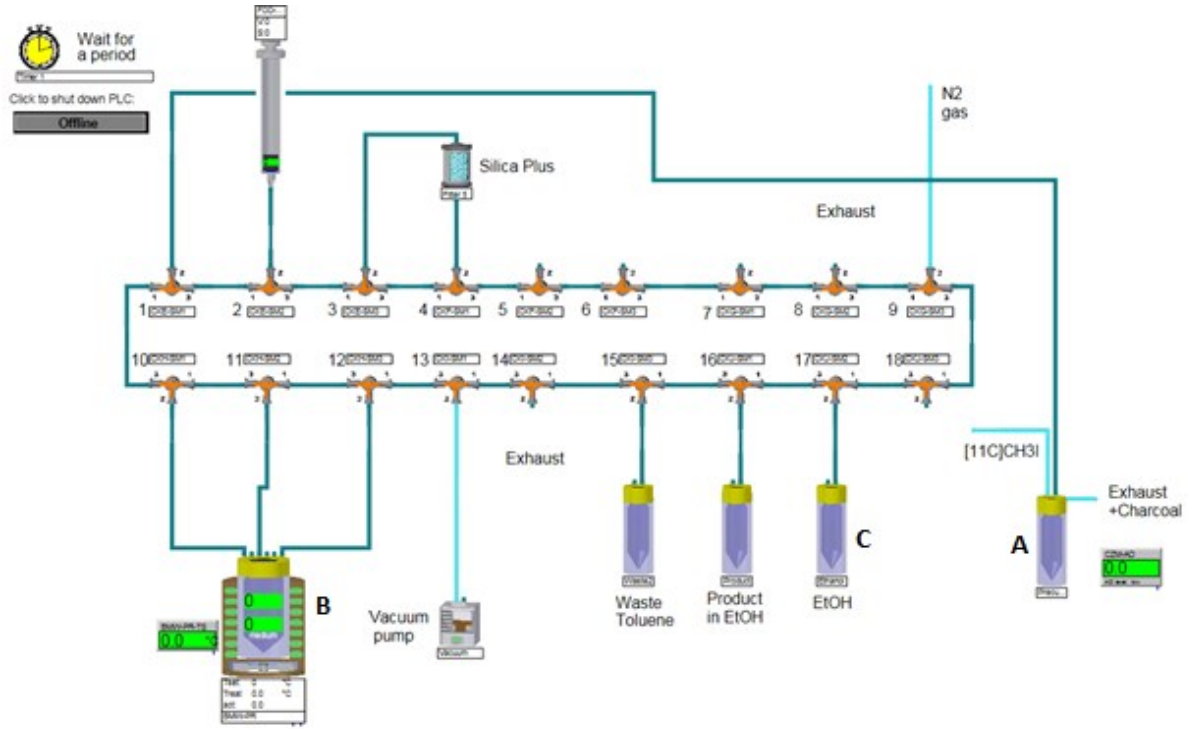
Sample used for molar activity determination

Product	Peak area	activity (MBq)	amount (µmol)	Molar activity (GBq/µmol)
	34180	4,9	1,48	**3.3**
	78492	3,4	3,41	**1.0**
	67516	6,8	2,93	**2.3**

Automated procedure on a commercially available cassette-based module

Brand: **Eckert & Ziegler**
Module: **Modular-Lab PharmTracer**

Scheme of automation:



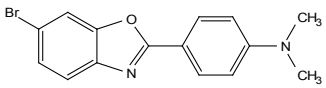
Detailed steps:

Preparation: in vial **A** was added 0.87 mL of dry toluene and *n*-BuLi (0.125 mL, 0.20 mmol, 1.6 M in hexanes). In vial **B** was added the aryl bromide (0.2 mmol) in 0.5 mL of dry toluene, an additive when necessary and finally a solution of fully pre-oxidized $Pd(P^tBu_3)_2$ in toluene (0.5 mL, 0.01 mmol). In vial **C** was added 3 mL of EtOH. The other vials were positioned empty at the locations indicated in the scheme. The cartridge (Sep-Pak Silica Plus Long Cartridge, 690 mg Sorbent per Cartridge, 55 - 105 µm (WAT020520)) was placed as indicated in the scheme, after pre-conditioning with toluene. A 10 mL syringe was positioned as indicated in the scheme. The system was purged with N_2 gas before starting the synthesis.
Reaction: $[^{11}C]CH_3I$ was bubbled into vial **A** for 4 min. At the end of the trapping, the solution was taken up by the syringe and the content of the syringe was added to vial **B** over 5 min, while vial **B** was being stirred at rt. At the end of the addition, the line was purged with N_2 to ensure complete transfer of the $[^{11}C]CH_3Li$ solution to vial **B**.
Cartridge pre-purification: The reaction mixture was taken from vial **B** to the syringe and loaded on the Sep-Pak Silica Plus Cartridge by emptying the syringe, collecting the eluted solvent in the ''waste toluene'' vial. The cartridge was further dried by passing N_2 through it. Then the EtOH from vial **C** was taken by the syringe and used to elute the Sep-Pak Silica Plus Cartridge, the eluted fraction was collected in the ''product in EtOH'' vial. The cartridge was further purged with N_2 to ensure complete elution and the ''product in EtOH'' vial was taken out of the module to proceed to HPLC purification following the conditions as described for the manual synthesis.

Synthesis of **13** was performed on the automated module affording 48 - 50% RCY, n = 2. (An aliquot was taken for HPLC analysis and isolation of the final compound, which was extrapolated to the complete reaction mixture to assess the radiochemical yield).

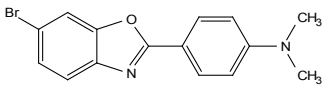
^{1}H- and ^{13}C-NMR spectra

^{1}H-NMR (400 MHz, $CDCl_3$)



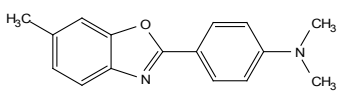
1

^{13}C-NMR (75 MHz, $CDCl_3$)



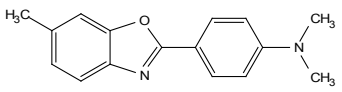
1

^{1}H-NMR (400 MHz, $CDCl_3$)



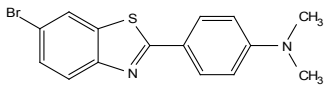
3

^{13}C-NMR (151 MHz, $CDCl_3$)



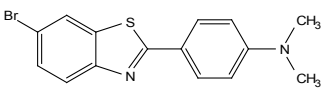
3

^{1}H-NMR (400 MHz, $CDCl_3$)



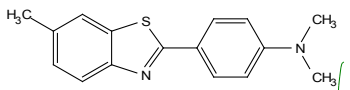
2

^{13}C-NMR (151 MHz, $CDCl_3$)



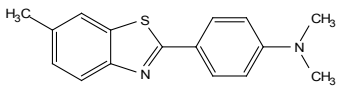
2

^{1}H-NMR (400 MHz, DMSO-d_6)



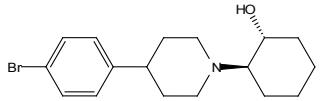
4

^{13}C-NMR (151 MHz, $CDCl_3$)



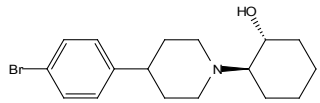
4

^{1}H-NMR (400 MHz, $CDCl_3$)



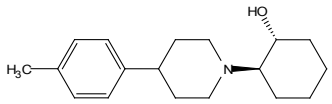
7

^{13}C-NMR (101 MHz, $CDCl_3$)



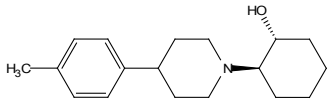
7

^{1}H-NMR (400 MHz, $CDCl_3$)



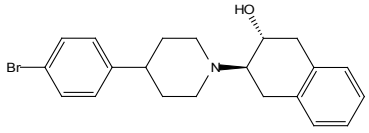
8

^{13}C-NMR (151 MHz, $CDCl_3$)

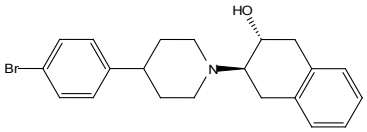


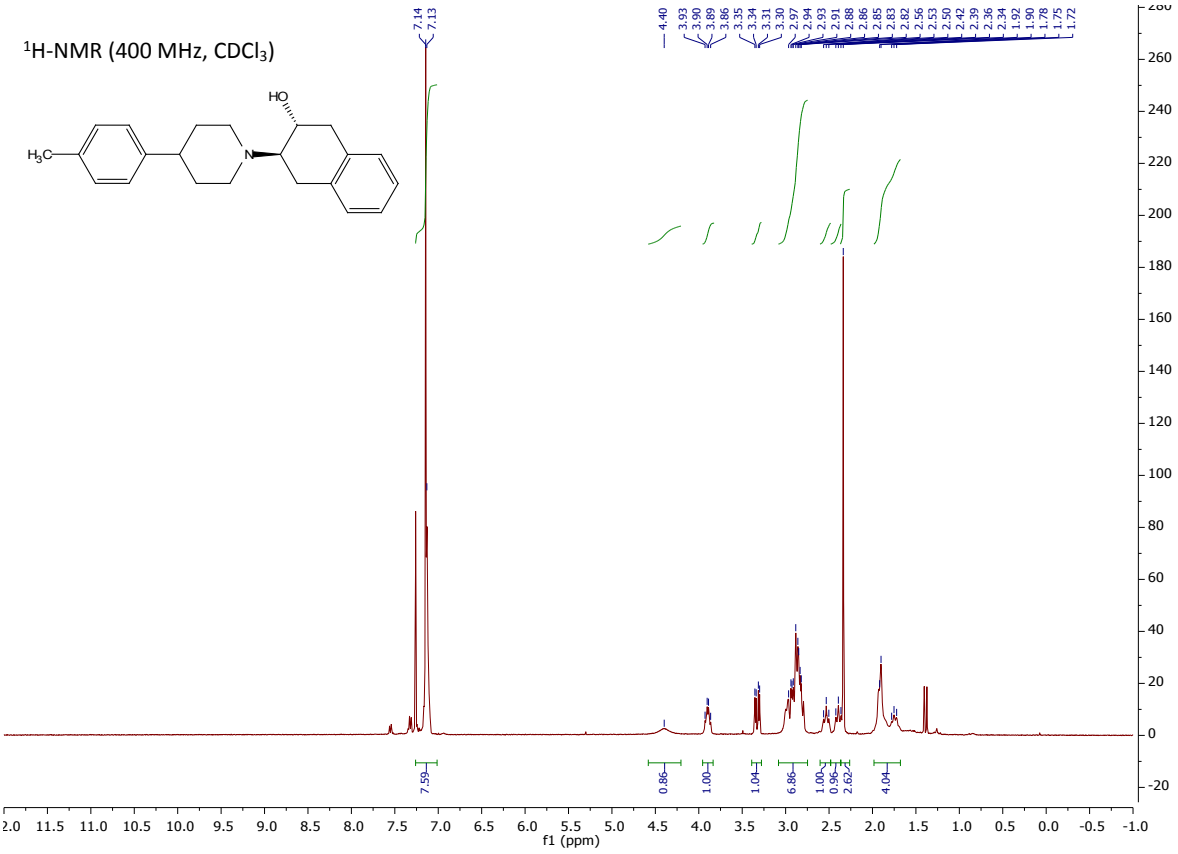
8

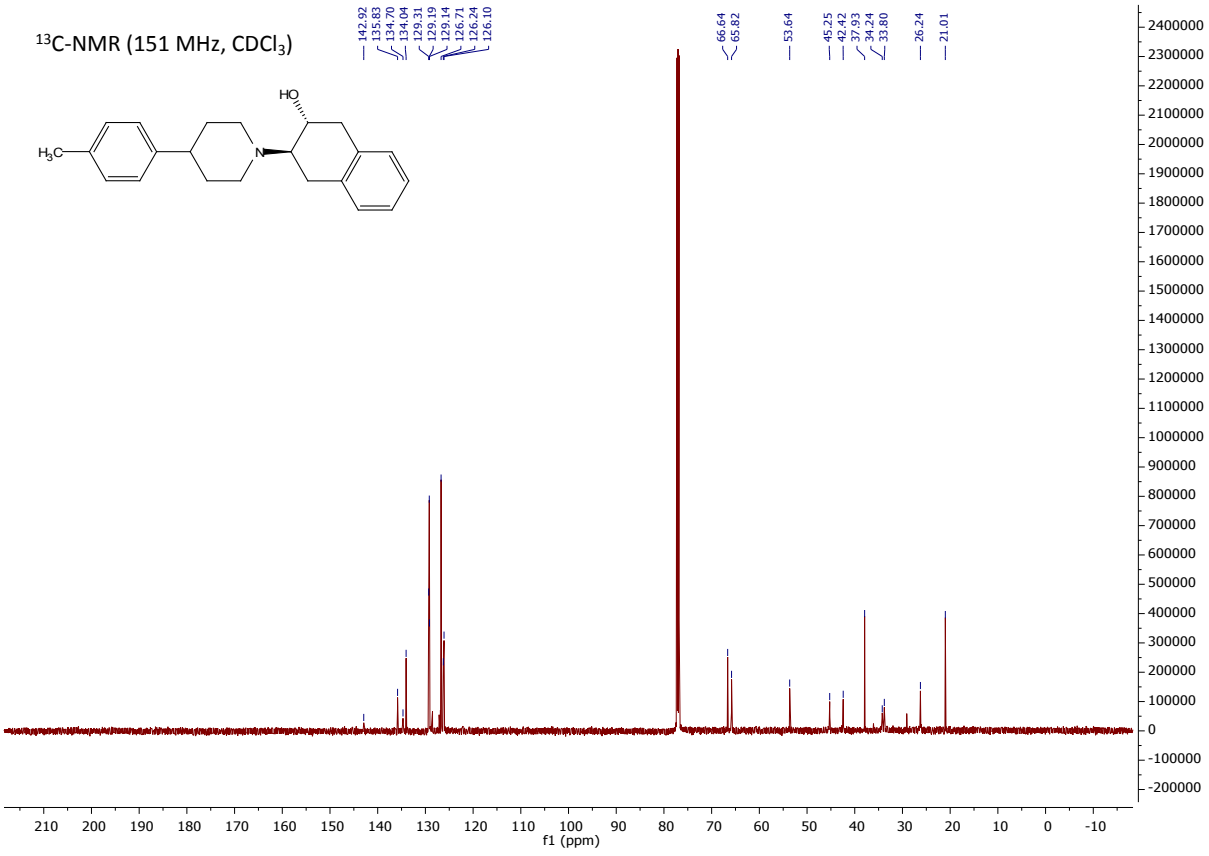
^{1}H-NMR (400 MHz, $CDCl_3$)



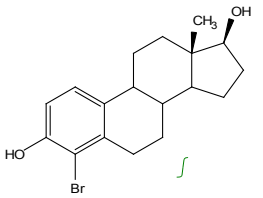
^{13}C-NMR (151 MHz, $CDCl_3$)



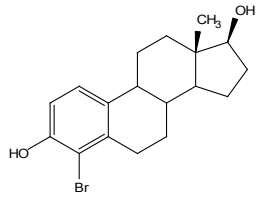

^{1}H-NMR (400 MHz, $CDCl_3$)
HO
H_3C
N
7.14
7.13
4.40
3.93
3.90
3.89
3.86
3.35
3.34
3.31
3.30
2.97
2.94
2.93
2.91
2.88
2.86
2.85
2.83
2.82
2.56
2.53
2.50
2.42
2.39
2.36
2.34
1.92
1.90
1.78
1.75
1.72
7.59
0.86
1.00
1.04
6.86
1.00
0.96
2.62
4.04
f1 (ppm)


^{13}C-NMR (151 MHz, $CDCl_3$)
HO
H_3C
N
142.92
135.83
134.70
134.04
129.31
129.19
129.14
126.71
126.24
126.10
66.64
65.82
53.64
45.25
42.42
37.93
34.24
33.80
26.24
21.01
f1 (ppm)

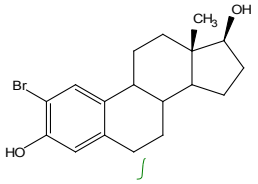
^{1}H-NMR (400 MHz, DMSO-d_6)



^{13}C-NMR (101 MHz, DMSO-d_6)

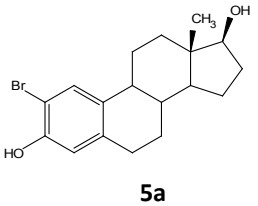


^{1}H-NMR (400 MHz, DMSO-d_6)

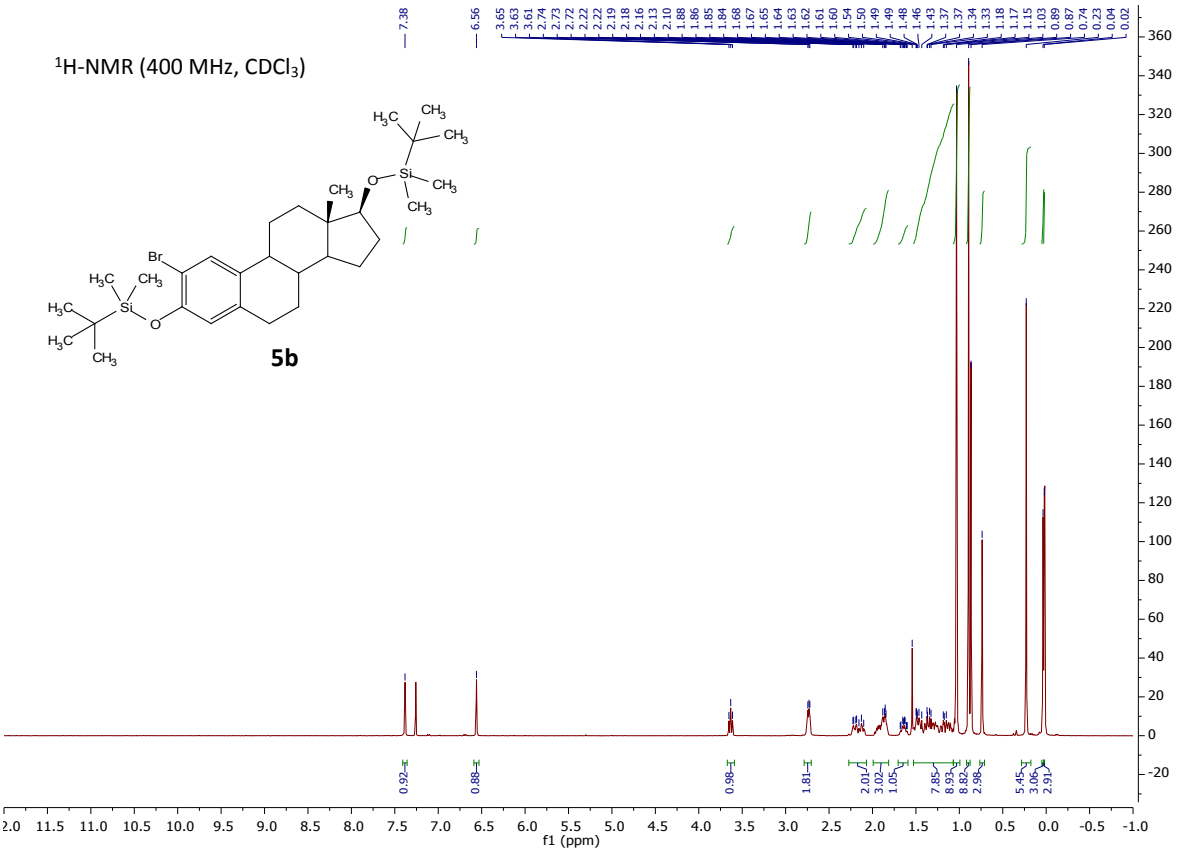


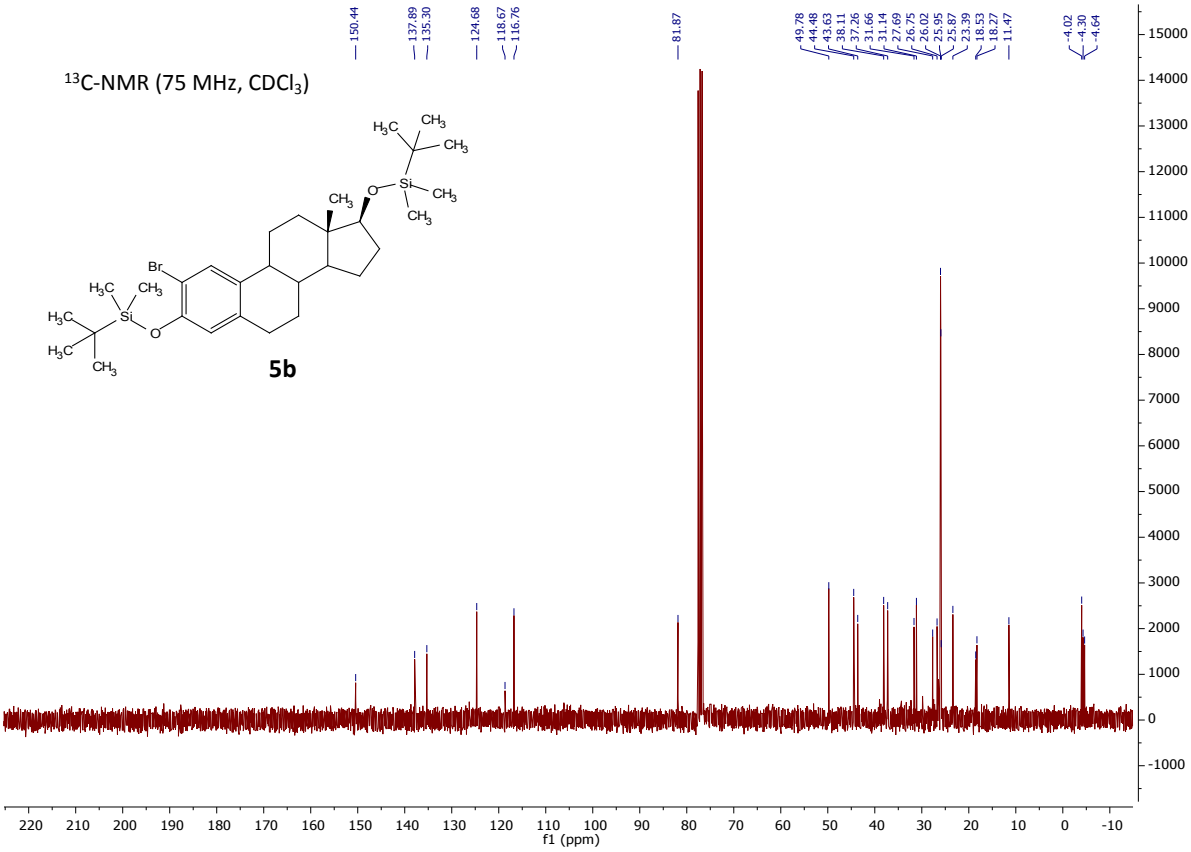
5a

^{13}C-NMR (101 MHz, DMSO-d_6)

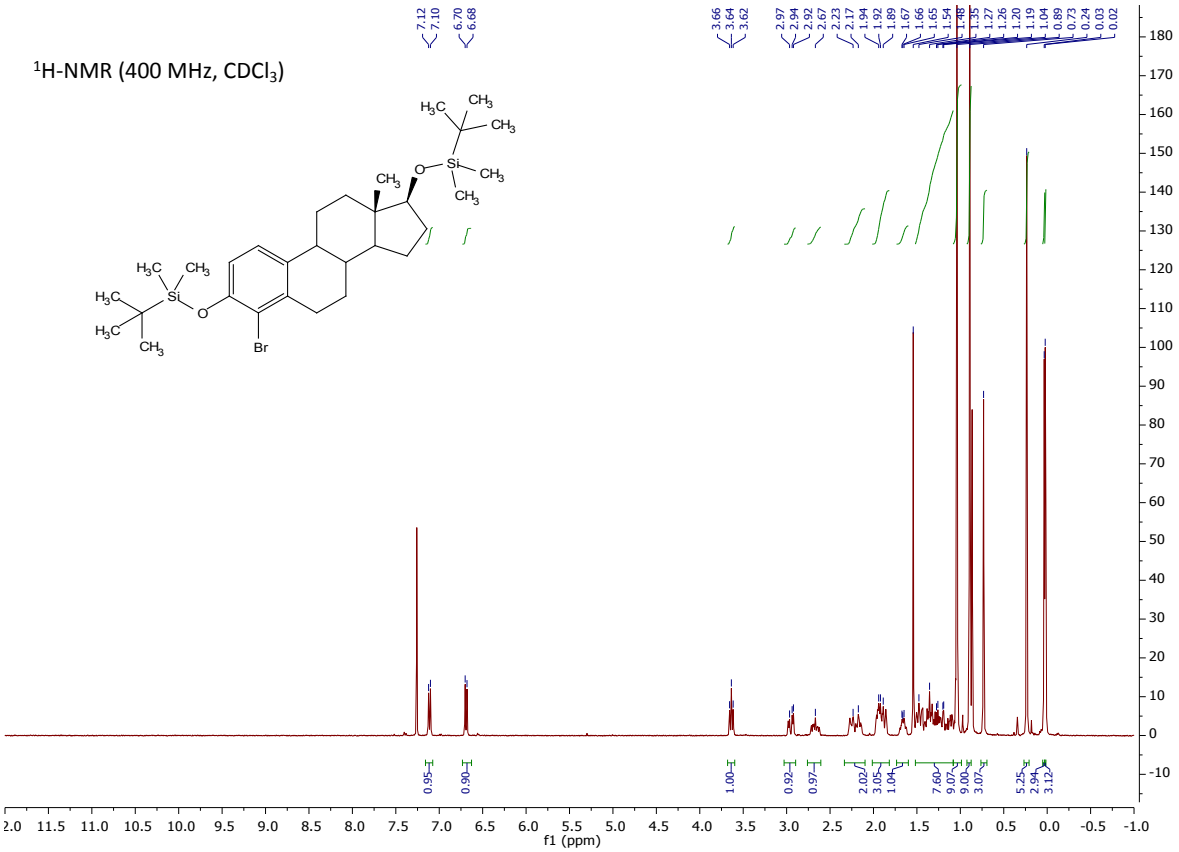


5a

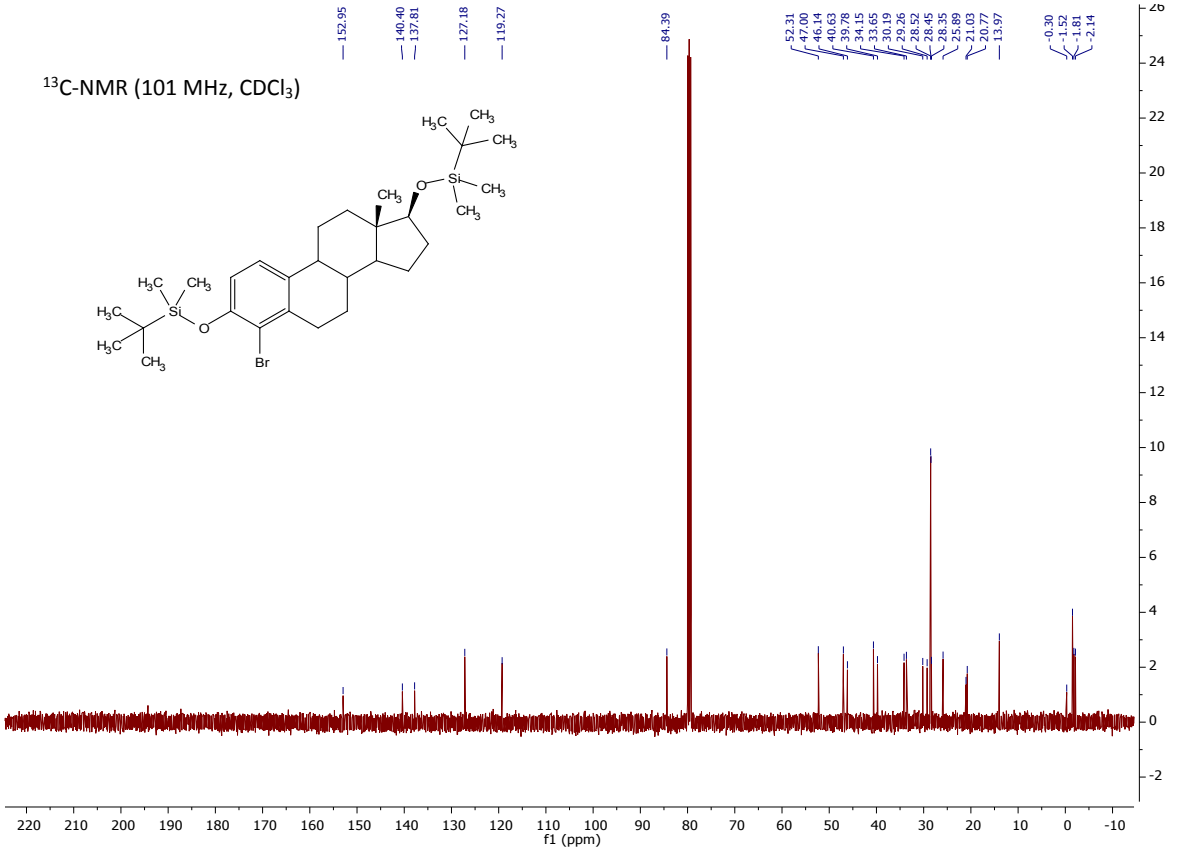

^{1}H-NMR (400 MHz, $CDCl_3$)
5b


^{13}C-NMR (75 MHz, $CDCl_3$)
5b

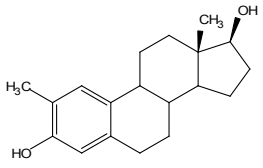
^{1}H-NMR (400 MHz, $CDCl_3$)



^{13}C-NMR (101 MHz, $CDCl_3$)

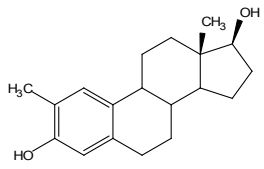


^{1}H-NMR (400 MHz, $CDCl_3$)



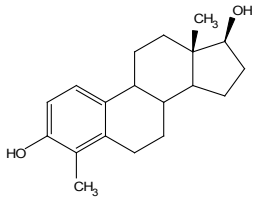
6

^{13}C-NMR (75 MHz, $CDCl_3$)



6

^{1}H-NMR (400 MHz, $CDCl_3$)



^{13}C-NMR (151 MHz, $CDCl_3$)