Supporting Information
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Supporting information

Improvements of C-H radio-iodination of N-acylsulfonamides toward implementation in clinics

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2 Formation of 1a-Pd in CD$_3$OD

In a NMR tube were introduced 2-chloro-$N$-tosylbenzamide 1a (10 mg, 32.3 µmol) and CD$_3$OD (0.75 mL). A $^1$H NMR spectrum was recorded ($^1$H NMR t$_0$) and Pd(OAc)$_2$ (7.2 mg, 32.3 µmol) followed by PTSA monohydrate (7.2 mg, 64.6 µmol) and a magnetic stirrer were added. $^1$H NMR spectra were recorded after 30 and 60 min reaction time ($^1$H NMR t$_{30}$ and $^1$H NMR t$_{60}$). $^1$H NMR ratio were calculated based on the integration of the methyl signal respectively at 2.46 ppm for 1a and 2.40 ppm for 1a-Pd.
$^1$H NMR t30

$^1$H NMR t60
3 C-H radio-iodination

3.1 General information

Sodium [$^{125}$I]iodide was purchased from by Perkin Elmer as none carrier added [$^{125}$I]sodium iodide in 1x10⁻⁵ M NaOH. In each case, this was diluted in water prior to use. HPLC analysis were performed with a Waters Alliance HPLC system equipped with an autosampler, a Waters 2996 Photodiode Array UV-detector and LB 500 HERM GAMMA radiodetector. Radiochemical conversions are determined by integration of the observed peaks on the radio-chromatogram. Identity of the radio-iodinated molecules was assessed by comparison of retention times of standards on the UV detector. The activities of [$^{125}$I]radiolabeled samples were determined using a radioisotope dose calibrator CRC-15R (Capintec) and standardized with a calibration source of $^{133}$Ba (9.402 MBq from Eckert & Ziegler).

HPLC gradient A: Water/acetonitrile containing 0.1% of formic acid, 0.8 mL.min⁻¹, Waters XSelect HSS C18 column, 3.5 µm, 4.6 x 100 mm

0-5 minute (5% to 50% MeCN) linear increase
5-11 minute (50% MeCN) isocratic
11-12 minute (50% MeCN to 95% MeCN) linear increase
12-15 minute (95% MeCN)
15-16 minute (95% to 5% MeCN) linear decrease
16-19 minute (5% MeCN) isocratic
3.2 General procedure for the $^{125}$I-radioidination of substituted $N$-Tosylbenzamides

In a V-vial equipped with a stirrer bar, $N$-chlorosuccinimide (0.016 M in methanol, 95 µL) was added to an aqueous solution of $[^{125}]$sodium iodide (5µL, 2-3 MBq). The resulting mixture was stirred for 15 minutes at room temperature. In parallel, in another V-vial, starting $N$-acylsulfonamide (0.16 M in methanol, 40 µL), PTSA (8.8 mM in methanol, 20µL) and palladium acetate (2.5 mM in DCM/MeOH 1/24, 40µL) were mixed together for 15 minutes at room temperature. 50 µL of the obtained mixture was added to the $[^{125}]$NIS solution, along with 20 µL of pure TFA, the resulting mixture was stirred for 15 minutes at room temperature and quenched with a solution of sodium thiosulfate (0.05 M in water, 200 µL) and diluted with water (550 µL) and methanol (550 µL). An aliquot was removed for analysis by radioHPLC (gradient A) to assess the radiochemical conversion.

3.3 Radio HPLC chromatograms

$[^{125}]$-2-Chloro-6-iodo-$N$-(4-methylbenzenesulfonyl)benzenecarboxamide $[^{125}]$ 2a
[\text{[\textsuperscript{125}I]-2-Fluoro-6-iodo-N-(4-methylbenzenesulfonfyl)benzenecarboxamide [\textsuperscript{125}I}\text{2b}}

[\text{[\textsuperscript{125}I]-2-Methyl-6-iodo-N-(4-methylbenzenesulfonfyl)benzenecarboxamide [\textsuperscript{125}I]\text{2c}}]
$[^{125}]I\text{-2-Iodo-}N-(4\text{-methylbenzenesulfonyl})\text{benzenecarboxamide} \quad[^{125}]I2d$

$[^{125}]I\text{-2-Methoxy-6-Iodo-}N-(4\text{-methylbenzenesulfonyl})\text{benzenecarboxamide} \quad[^{125}]I2e$
$[^{125}]^\text{I}-3,6$-Diiodo-$N$-(4-methylbenzenesulfonyl)benzenecarboxamide $[^{125}]^\text{I}2f$

$[^{125}]^\text{I}-3$-(Trifluoromethyl)-6-iodo-$N$-(4-methylbenzenesulfonyl)benzenecarboxamide $[^{125}]^\text{I}2g$
[\textsuperscript{\textit{125}}I]-3-Methyl-6-iodo-\textit{N}-(4-methylbenzenesulfonyl)benzenecarboxamide [\textsuperscript{\textit{125}}I]2h

[\textsuperscript{\textit{125}}I]-4-Bromo-6-iodo-\textit{N}-(4-methylbenzenesulfonyl)benzenecarboxamide [\textsuperscript{\textit{125}}I]2i
$[^{125}I]-2,4$-Dichloro-$6$-iodo-$N$-(benzenesulfonyl)benzenecarboxamide $[^{125}I]2j$

$[^{125}I]-2,4$-Dichloro-$6$-iodo-$N$-[(5-bromo-2-thienyl)sulfonyl]benzenecarboxamide $[^{125}I]2k$