



Supplementary Material

1. Syntheses and analytical data of the intermediates 3–6

1.1. 3-(Dimethylamino)-1-(furan-2-yl)prop-2-en-1-one (3)

To 16 mL (120.8 mmol) *N,N*-dimethylformamide dimethyl acetal were added 10 g of acetyl furane (90.82 mmol) and the mixture was refluxed for 5.5 h. After cooling to room temperature the solvent was removed under reduced pressure. The residue was dissolved in diethyl ether and the desired product was precipitated by adding 150 mL *n*-hexane. The precipitate was filtered off and washed with 50 mL diethyl ether/*n*-hexane (1:1, *v/v*). After drying under reduced pressure, 13.5 g (81.9 mmol, 90%) of crude product **3** was obtained, which was used without further purification for the following reactions.

^1H NMR (DMSO- d_6 , 300 MHz) δ : 7.79 (dd, $J = 1.8, 0.8$ Hz, 1 H), 7.69 (d, $J = 12.4$ Hz, 1 H), 7.10 (dd, $J = 3.4, 0.8$ Hz, 1H), 6.60 (dd, $J = 3.4$ Hz, 1 H), 5.65 (d, $J = 12.4$ Hz, 1 H), 3.13 (s, 3 H), 2.88 (s, 3 H) ppm. ^{13}C NMR (DMSO- d_6 , 100 MHz) δ : 175.9, 155.0, 153.7, 145.3, 113.5, 112.3, 91.1, 44.9, 37.5 ppm. HRMS (ESI+) m/z calcd. for $\text{C}_9\text{H}_{12}\text{O}_2\text{N}^+$ $[\text{M}+\text{H}]^+$ 166.08626, $\text{C}_9\text{H}_{11}\text{O}_2\text{NNa}^+$ $[\text{M}+\text{Na}]^+$ 188.06820, found 166.08521, 188.06683.

1.2. 2-Cyanoethanimidic acid methyl ester hydrochloride (4)

A mixture of malononitrile (24.8 g, 0.37 mol) and 15.2 mL methanol in 500 mL diethyl ether was cooled to 0 °C and a slight stream of dry HCl gas was added over 2.5 h. Afterwards, 500 mL CH_2Cl_2 was added, the formed precipitate was filtered off, washed with 250 mL CH_2Cl_2 /diethyl ether (1:1) and dried under vacuum. Compound **4** was obtained as an off-white powder with a yield of 54 % (27.0 g, 0.20 mol). Melting point: 103–106 °C.

1.3. 2-Amino-6-(furan-2-yl)nicotinonitrile (5)

Compound **5** was synthesized with slight modifications according to the reported procedure of Troschütz et al. [1].

Compound **4** (1.6 g, 12.1 mmol) and ammoniumacetate (3.3 g, 42.4 mmol) were dissolved in 50 mL MeOH and refluxed for 15 min. Then, the furan **3** (2.0 g, 12.1 mmol) was added and the mixture refluxed for further 3.5 hours. After removing the solvent under reduced pressure, the residue was quenched with 100 mL water, the precipitate filtered off, washed with 50 mL water and dried in a vacuum desiccator (over calcium chloride) to obtain 1.6 g (8.5 mmol, 70 %) of the crude product **5**.

^1H NMR (DMSO- d_6 , 300 MHz) δ : 6.64 (dd, $J = 3.4, 1.7$ Hz, 1 H), 6.91 (bs, 2 H), 6.98 (d, $J = 8.1$ Hz, 1 H), 7.10 (dd, $J = 3.5, 0.8$ Hz, 1 H), 7.84 (dd, $J = 1.8, 0.8$ Hz, 1 H), 7.88 (d, $J = 8.0$ Hz, 1H) ppm. ^{13}C NMR (DMSO- d_6 , 75 MHz) δ : 88.0, 107.2, 111.8, 113.0, 117.7, 143.5, 145.7, 151.2, 152.7, 160.1 ppm. HRMS (ESI+) m/z calcd. for $\text{C}_{10}\text{H}_8\text{ON}_3^+$ $[\text{M}+\text{H}]^+$ 186.06619, found 186.06757.

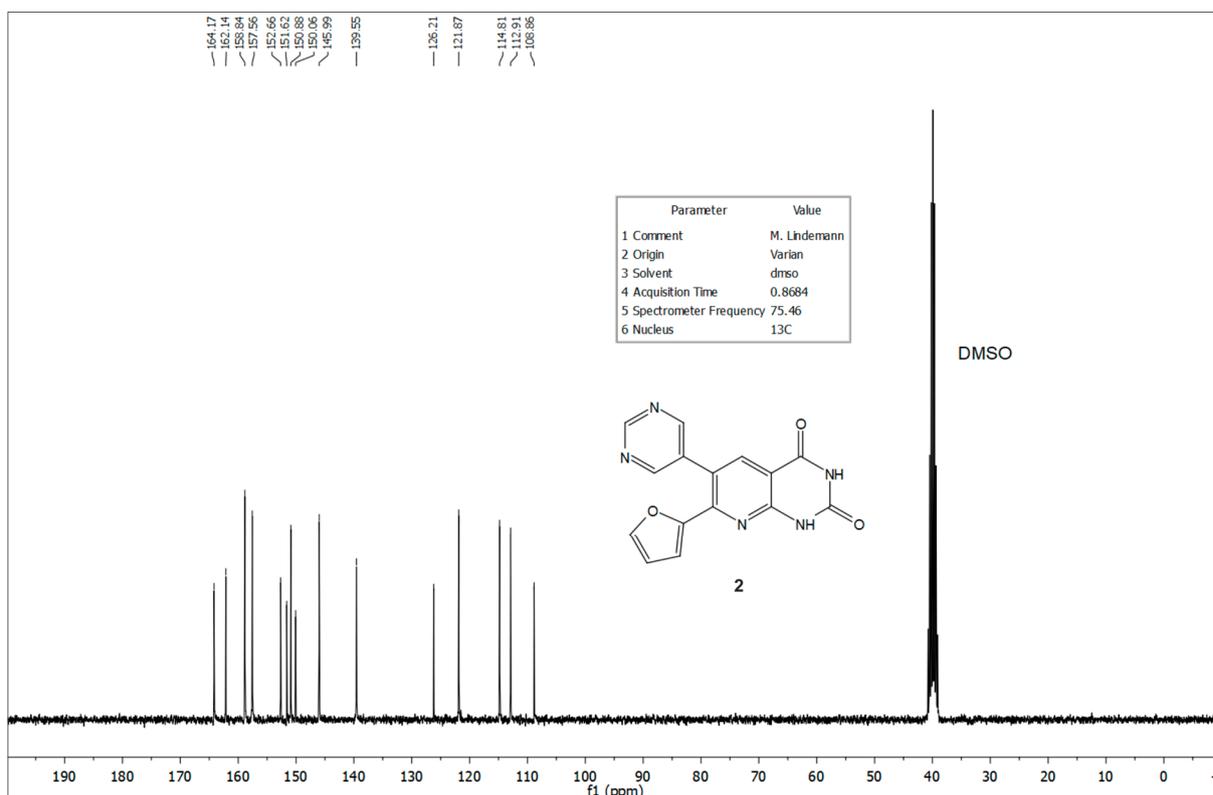
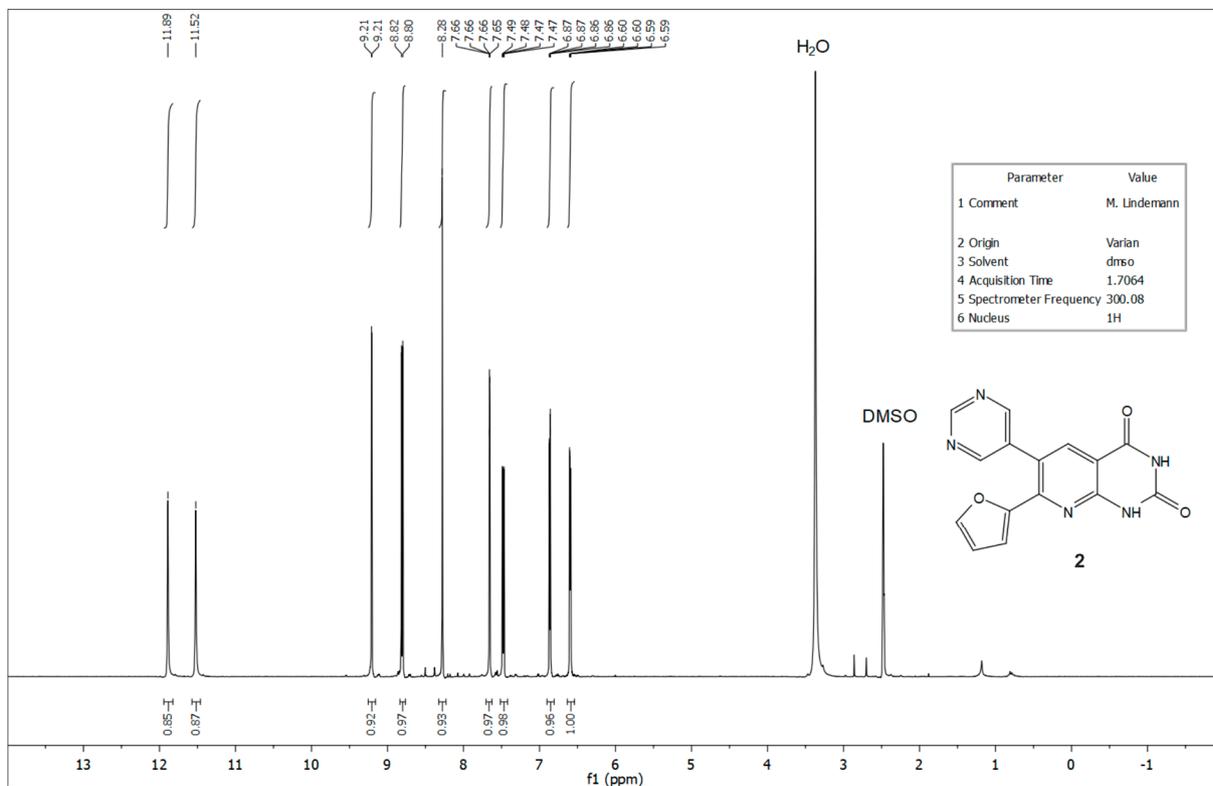
1.4 2-Amino-5-bromo-6-(furan-2-yl)nicotinonitrile (6)

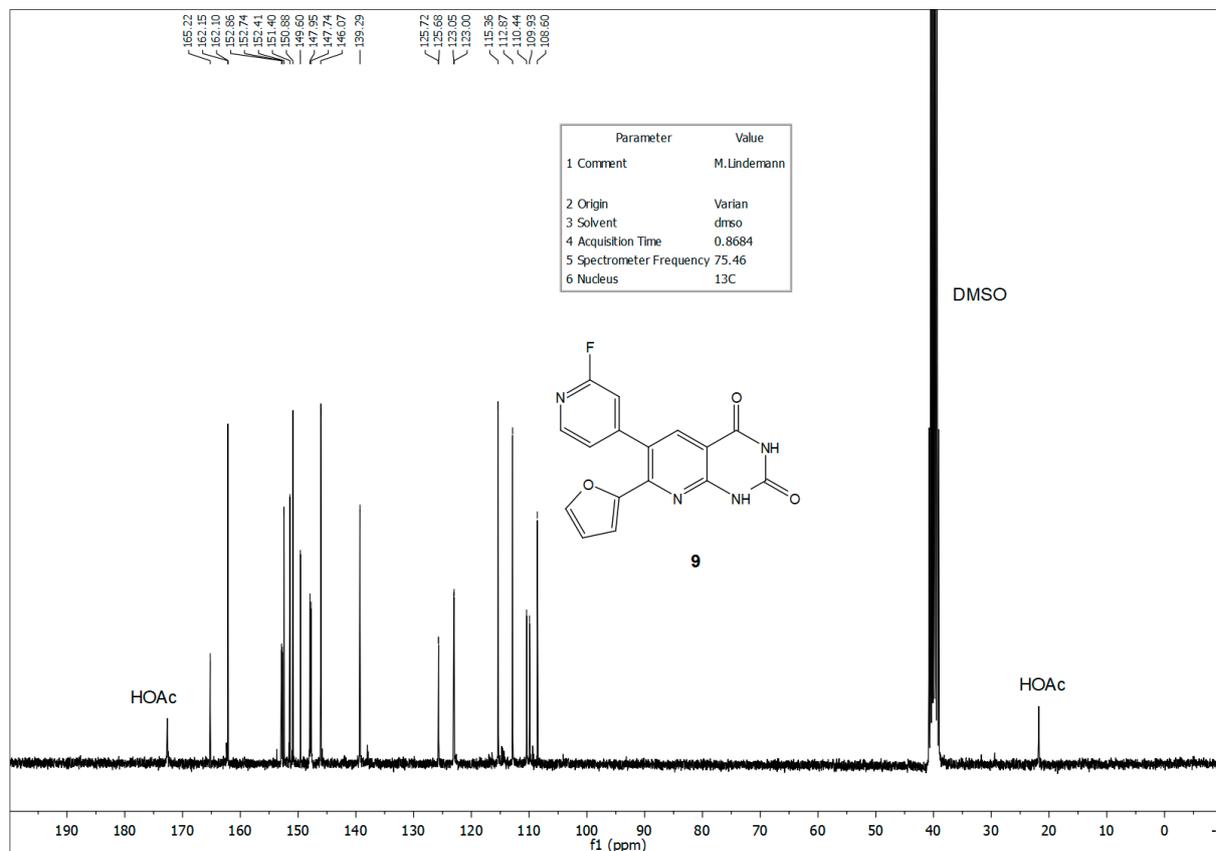
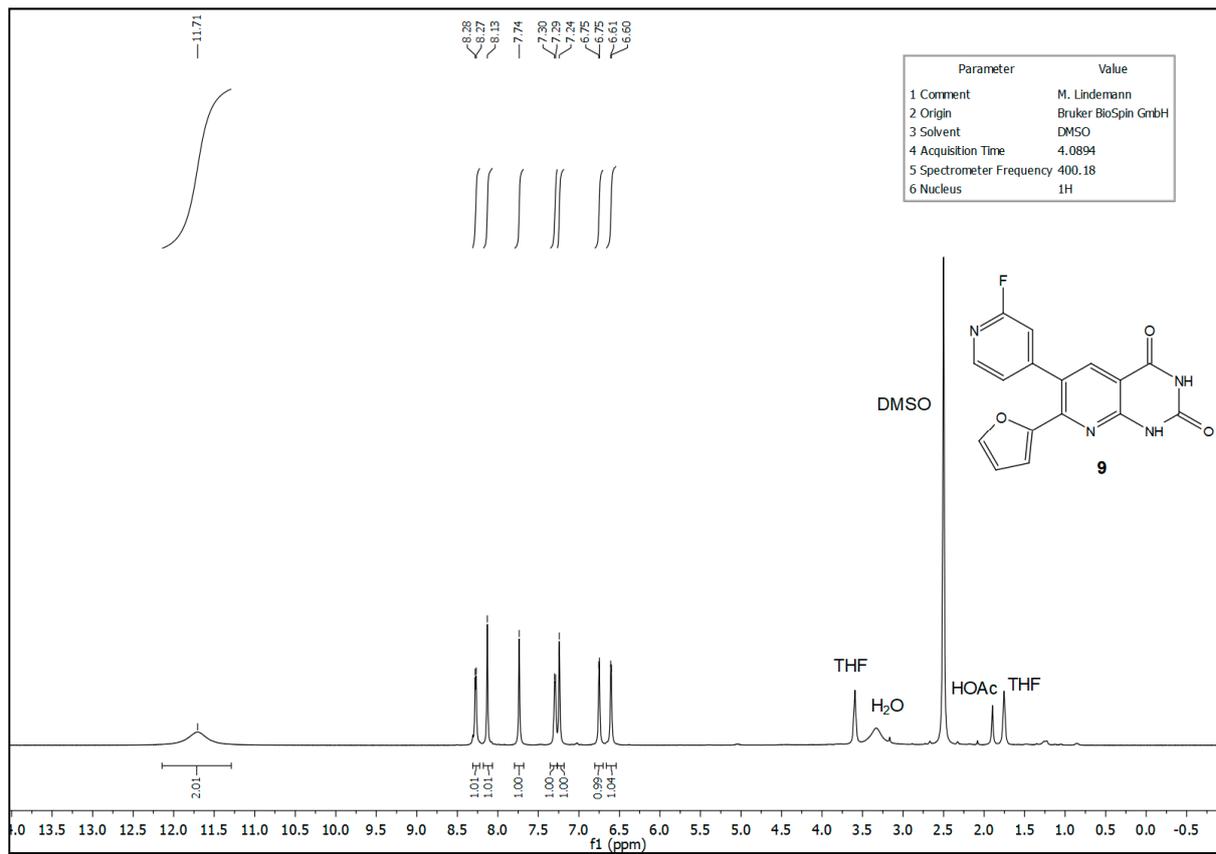
Compound **6** was synthesized with slight modifications according to the reported procedure of Harada et al. [2].

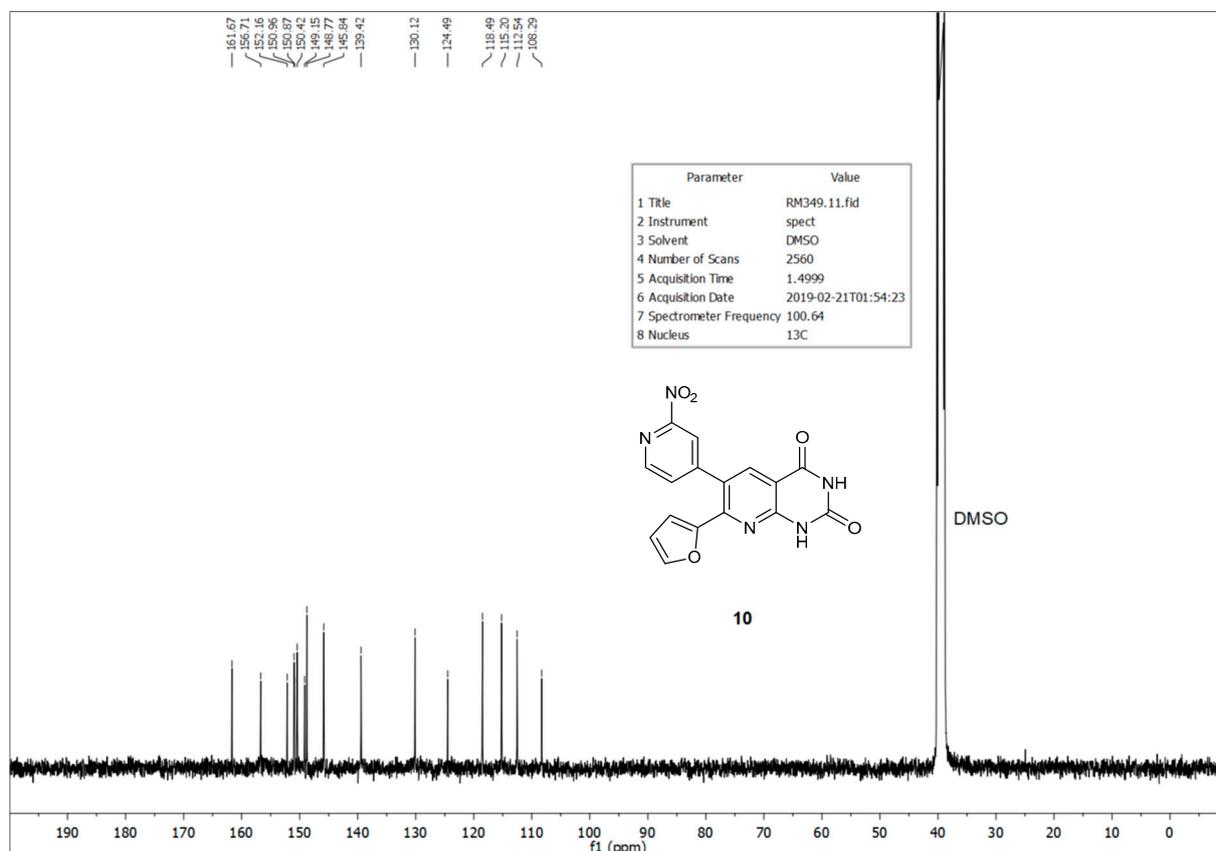
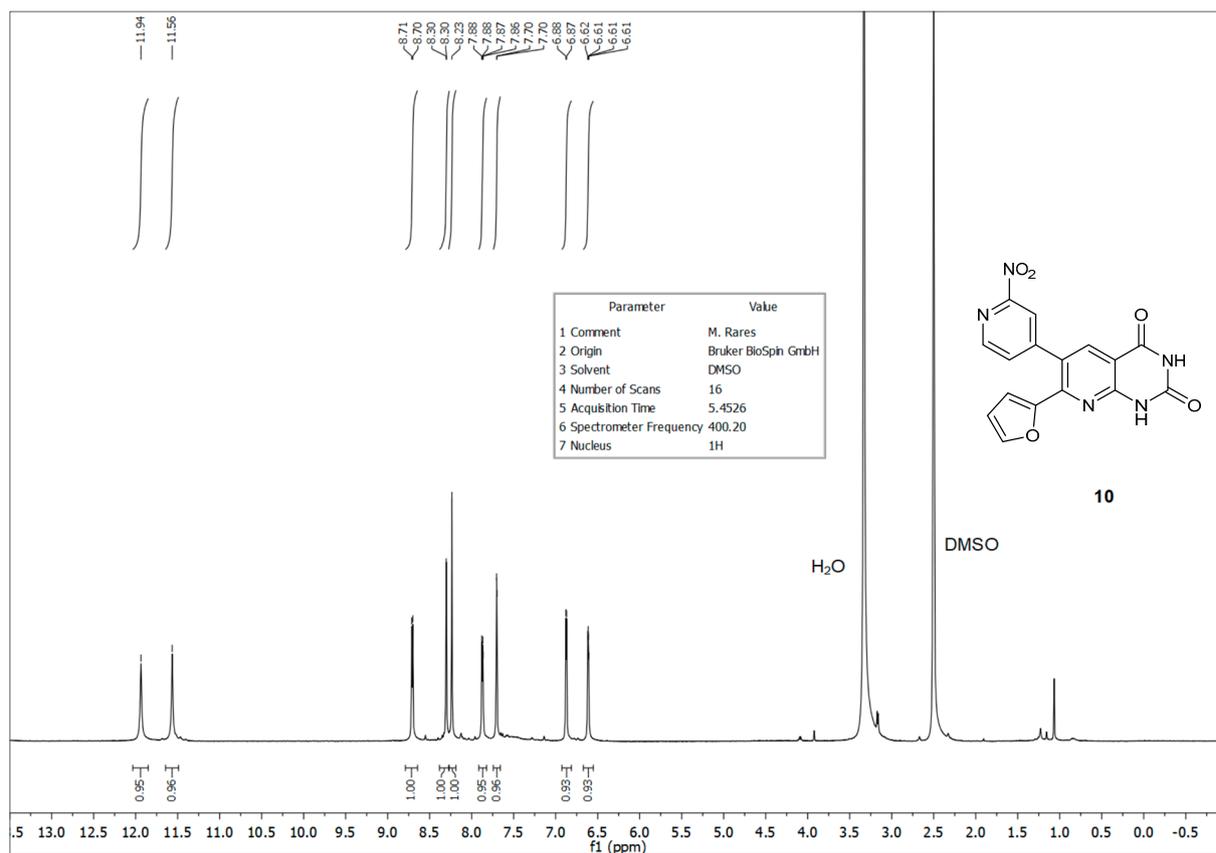
Compound **5** (1.4 g, 7.56 mmol) and 2.5 g (14.04 mmol) of *N*-bromosuccinimide were dissolved in 30 mL DMF and stirred for 12 hours at room temperature. The solution was then poured into 200 mL ethyl acetate and extracted with saturated aqueous sodium carbonate solution (2 x 500 mL) and with 250 mL brine. The combined organic layers were dried over sodium sulfate, filtered and the solvent was evaporated under reduced pressure. The crude material was purified by column chromatography (silica gel, ethyl acetate/*n*-hexane 1:2 *v/v*) to give 1.5 g (5.80 mmol, 77%) of compound **6**.

R_f: 0.45 (ethyl acetate/*n*-hexane 1 : 2 *v/v*, silica gel). ¹H NMR (DMSO-d₆, 400 MHz) δ: 6.72 (dd, *J* = 3.5, 1.7 Hz, 1 H), 7.17 (s, 2 H), 7.44 (dd, *J* = 3.5, 0.8 Hz, 1 H), 7.95 (dd, *J* = 1.7, 0.8 Hz, 1 H), 8.26 (s, 1 H) ppm. ¹³C NMR (DMSO-d₆, 100 MHz) δ: 90.2, 100.1, 112.6, 116.0, 116.1, 145.8, 147.6, 148.6, 150.5, 158.2 ppm. HRMS (ESI+) *m/z* calcd. for C₁₀H₇ON₃⁷⁹Br⁺ [M+H]⁺ 263.97670, found 263.97864.

2. ¹H and ¹³C NMR Spectra of Compounds 2, 9 and 10







3. Representative Radio- and UV-HPLC Chromatograms of the Radiosynthesis of [^{18}F]9

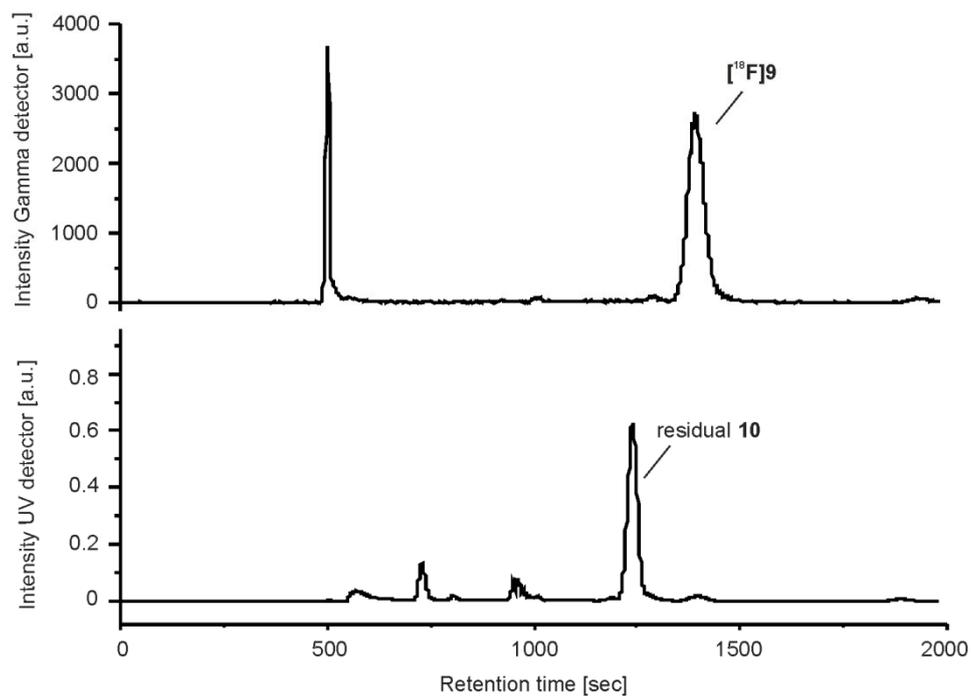


Figure S1. Semi-preparative radio- and UV-HPLC chromatograms of [^{18}F]9 (conditions: Reprosil-Pur C18 AQ, 250 x 20 mm, 60% MeOH/aqu. 20 mM NH_4OAc , 8.0 mL/min).

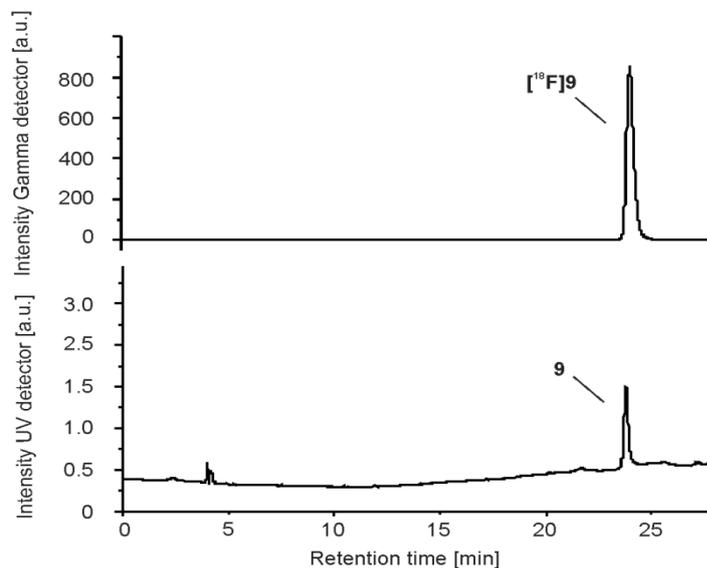


Figure S2. Analytical radio- and UV-HPLC chromatograms of the final product of [^{18}F]9 spiked with the non-radioactive reference 9 (conditions: Reprosil-Pur C18-AQ, 250 x 4.6 mm, gradient with an eluent mixture of ACN/aqu. 20 mM NH_4OAc , 1.0 mL/min).

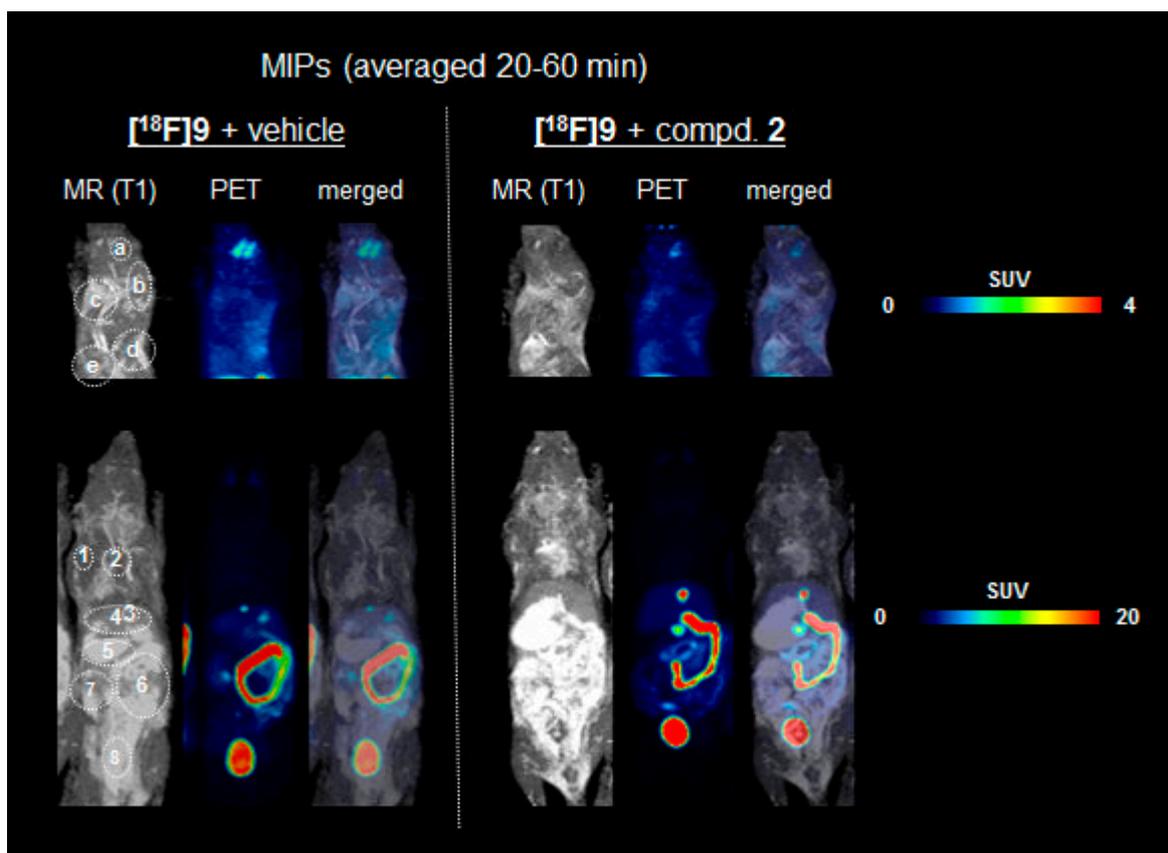
4. PET/MR images of [¹⁸F]9 in healthy mice

Figure S3. Maximum intensity projections (MIPs) of mice treated with vehicle (control group, left) and compound 2 (right) coinjected with [¹⁸F]9. a) Harderian glands, b) brain, c) glandula mandibularis, d) brown adipose tissue, e) heart, 1) muscle, 2) thymus, 3) gall bladder, 4) liver, 5) stomach, 6) intestine, 7) left kidney, 8) bladder.

References

1. Troschütz, R.; Dennstedt, T. Synthesis of Substituted 2-Aminonicotinonitriles. *Arch. Pharm.* **1994**, *327*, 33-40.
2. Harada, H.; Asano, O.; Miyazawa, S.; Ueda, M.; Yasuda, M.; Yasuda, N. Aminopyridine compounds and use thereof as drugs. US 2004/0006082 A1 2004.