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Photoreactivity of monofluorinated 2-azidobenzimidazoles towards carboxylic acids

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Abstract: Aiming at the development of new photolabeling agents, the synthesis and photoreactivity of all monofluorinated derivatives of 2-azido-1-methylbenzimidazole are described. In the case of 4-, 5-, or 7-fluorination, irradiation in the presence of carboxylic acids (300 nm, Rayonet) afforded the monofluorinated 2-amino-6-acyloxybenzimidazoles in a regioselective manner, presumably after conversion of the initially formed nitrene to the *N*-cyanodiazaxylylene. Incorporation of chloride was also possible, and yields were comparable to those observed for the nonfluorinated parent compound. When blocking the reactive 6-position by a fluoro substituent, the title reaction was not possible. The analysis of the ^{19}F NMR chemical shifts of the 5- and 7-monofluorinated products allowed the distinction between carboxylates and other nucleophiles.

Keywords: arylation; azido compounds; heterocycles; nitrenes; photochemistry.

Dedicated to: Professor Gerhard Erker on the occasion of his 70th birthday.

1 Introduction

Heterocyclic azido compounds are of interest in the field of photoaffinity labeling, a technique used in Chemical Biology. On irradiation, nitrenes are formed, which may link covalently to protein target structures. In particular, 8-azidoadenine derivatives have been investigated experimentally and theoretically [1, 2]. Recently, we discovered the photoarylation of carboxylic acids with 2-azidobenzimidazole derivatives (**1**, Scheme 1), which afforded 2-amino-6-acyloxybenzimidazoles [3]. We were able to photochemically arylate Boc-protected proteinogenic amino acids either at the C-terminus or at the carboxy group of the side chain. The reaction was also applied to small peptides in the presence of water [4]. Earlier, 2-azido-1-methylbenzimidazole had been 6-acetoxylated under thermal conditions [5]. There is also a study on the photoreactivity of 2-azidobenzothiazoles resulting in the aziridination of alkenyl ethers [6].

Probably, a singlet nitrene is formed after loss of dinitrogen, which is converted to the protonated *N*-cyanodiazaxylylene (**2**). This activates the β-position of the α,β-unsaturated iminium partial structure **2** towards nucleophilic attack of an anion (X^-), which is followed by ring closure to the imidazole ring and re-aromatization via a formal hydrogen shift (**3**).

A photochemically triggered, efficient photoarylation might be conducted inside the cell. The analysis and perhaps even identification of covalent drug protein adducts would be facilitated, if normally absent heteroatoms were incorporated, such as fluorine. In this communication, we report on the synthesis and photoreactivity of all monofluorinated 2-azido-*N*-methylbenzimidazoles (**4**, Fig. 1). We were also interested in the ^{19}F NMR chemical shifts of the adducts, which might indicate the type of reaction partner.

2 Synthesis of monofluorinated 2-azido-1-methylbenzimidazoles

The 2-azido group was to be introduced by 2-deprotonation of the corresponding benzimidazole precursors and quenching with tosyl azide. Among the respective monofluorobenzimidazoles, only 5-fluoro-*N*-methylbenzimidazole was known, but its synthesis has not been detailed [7]. Initially, we attempted to synthesize the desired *N*-methylated fluorobenzimidazoles pairwise (**5**/**6**, **7**/**8**) by *N*-methylation of 4(7)-(**9**) and 5(6)-fluorobenzimidazole (**10**), respectively, to be followed by the separation of the fluorinated regioisomers and 2-azidation. However, only the 4-fluorinated 2-azidobenzimidazole **11** proved to be accessible in sufficient quantity by that route (Scheme 2). Methylation of 4(7)-fluorobenzimidazole (**9**) afforded a mixture of *N*-methylated derivatives (**5**:**6** 5:2) favoring the 4-fluoro regioisomer. Separation of the regioisomers by chromatography was not possible, but possible on the level of the corresponding 2-azidobenzimidazoles **11** and **12**, which were obtained via 2-lithiation and

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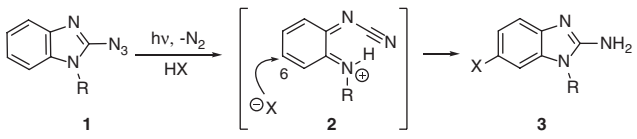


Scheme 1: Possible mechanism of the photoarylation of Brønsted acids with 2-azidobenzimidazole derivatives (**1**).

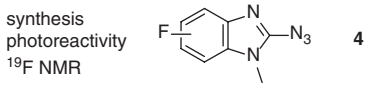


Fig. 1: Subject of the study.

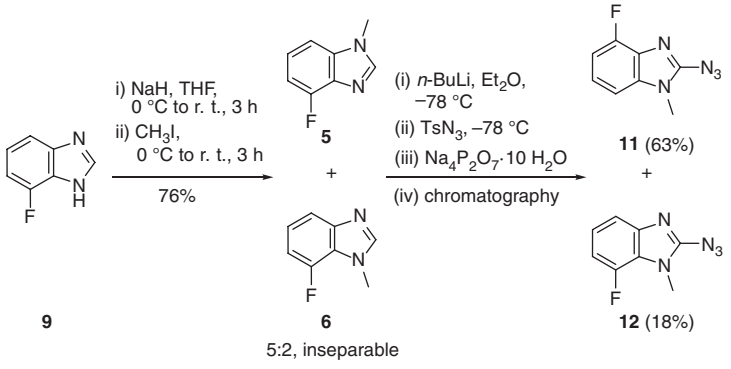
quenching with TsN_3 in Et_2O. The precipitated lithium benzimidazolyl tosyl triazenides were fragmented with aqueous pyrophosphate [8] affording the desired products **11** (63%) and **12** (18%) after chromatography. The analogous sequence was possible starting from 5(6)-fluorobenzimidazole, in turn obtained from 1,2-diamino-4-fluorobenzene. However, the mixture of *N*-methylated 5-fluoro and 6-fluoro regioisomers (1:1) could not be separated on a preparative scale, even after 2-azidation.

Although the methylation/separation approach did provide 2-azido-4-fluoro-1-methyl-1*H*-benzo[*d*]imidazole (**11**) in sufficient quantity, higher yields of the 7-fluorinated regioisomer (**12**) required an independent route (Scheme 3).

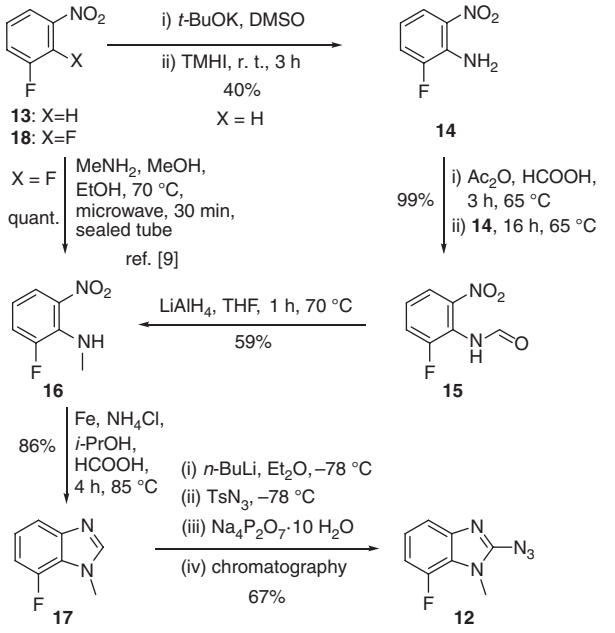
Pagoria et al. had introduced 1,1,1-trimethylhydrazinium iodide (TMHI) for the amination of nitrobenzene derivatives by vicarious nucleophilic substitution [10]. The trimethylammonium group of TMHI acts vicariously as a leaving group, allowing β-elimination of the original hydrogen as part of a trimethylammonium salt. The reaction probably proceeds via an ion radical pair, and the amino group is introduced at the position of the highest spin density of the radical anion [11, 12]. For a recent overview, see reference [13]. Starting from 1-fluoro-3-nitrobenzene (**13**), the desired 2-fluoro-6-nitroaniline (**14**, 40%) was accompanied by a mixture of 2-fluoro-4-nitroaniline and 4-fluoro-2-nitroaniline (40%, 4 : 1 [10], Scheme 3). N-Formylation of **14** to **15** and reduction afforded *N*-methylnitroaniline **16**. Reduction and condensation with formic acid were performed in one step employing iron powder in the presence of NH_4Cl [14]. 2-Azidation of **17** under standard conditions afforded the desired 7-fluorinated 2-azidobenzimidazole **12**. Alternatively, when using the more expensive 1,2-difluoro-3-nitrobenzene (**18**), a quantitative one-step synthesis of 2-fluoro-*N*-methyl-6-nitroaniline (**16**) was possible under microwave conditions by reaction with $MeNH_2$ in MeOH/EtOH in the sealed tube [9].

Mąkosza and Stalewski reported that even 1-fluoro-2,4-dinitrobenzene (Sanger's reagent) can undergo vicarious nucleophilic substitution, leaving the fluoro substituent in place [15]. When using 1,4-difluoro-2-nitrobenzene (**19**) as starting material, formally replacing one nitro substituent of Sanger's reagent by a fluoro substituent, we found that the vicarious and classical S_NAr reactions competed (Scheme 4). On treatment of **19** with *t*-BuOK and TMHI in dimethyl sulfoxide (DMSO), 3,6-difluoro-2-nitroaniline (**20**) was formed in a vicarious S_NAr reaction and obtained as a major product in modest 18% yield, accompanied by the S_NAr product 4-fluoro-2-nitroaniline (**21**, 12%).

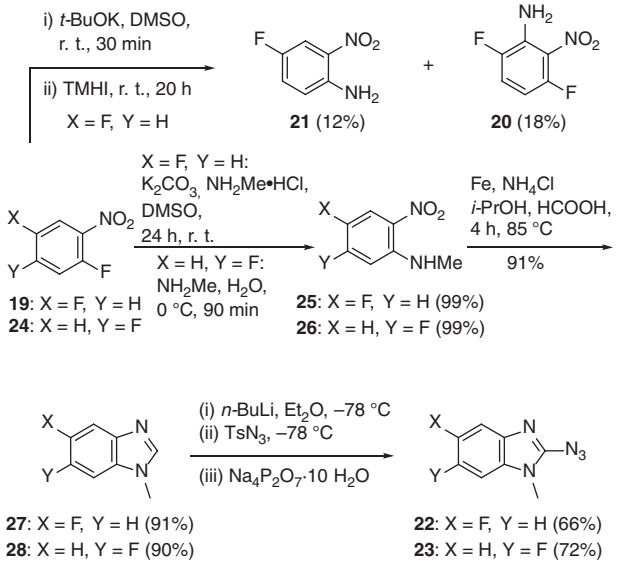
Thus, to make use of 1,4-difluoro-2-nitrobenzene (**19**), classical S_NAr conditions had to be applied. The three-step syntheses of the 5- and 6-fluorinated 2-azidobenzimidazoles **22** and **23** started from 1,4-difluoro-2-nitrobenzene (**19**) and 2,4-difluoro-1-nitrobenzene (**24**), respectively (Scheme 4), which were treated with methylamine affording *N*-methylated fluoronitroanilines **25** and **26**, respectively, in quantitative yields. Nucleophilic substitution of the fluoro by the methylamino group preferably took place *ortho* to the nitro group. Reductive condensation with formic acid afforded compounds **27** and **28** in good yields.



Scheme 2: Synthesis of the 4- and 7-monofluorinated 2-azidobenzimidazoles **11** and **12**.



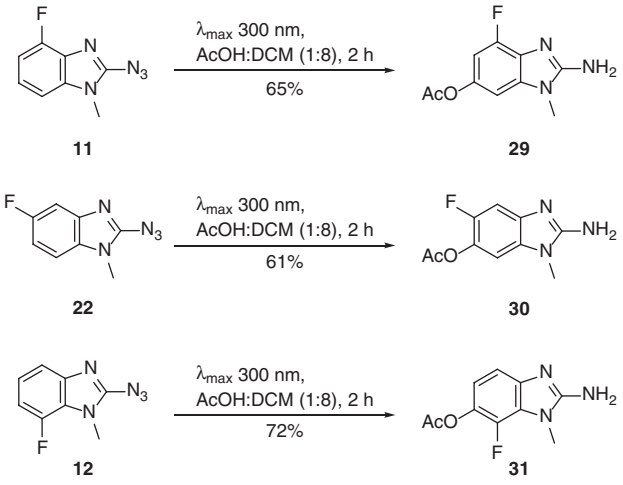
Scheme 3: Routes to 2-azido-7-fluoro-1-methyl-1*H*-benzo[*d*]imidazole (TMHI, trimethylhydrazinium iodide).



Scheme 4: Synthesis of the 5- and 6-monofluorinated 2-azidobenzimidazoles **22** and **23**, and attempted vicarious S_NAr reaction starting from 1,4-difluoro-2-nitrobenzene (**19**).

3 Irradiation experiments

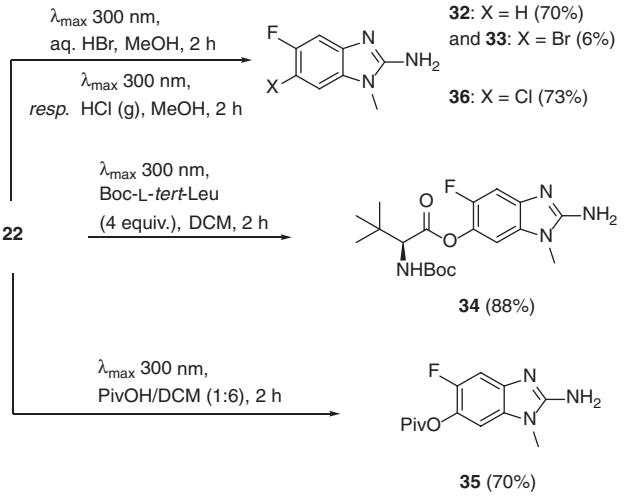
Irradiation of the fluorinated azidobenzimidazoles **11**, **12**, **22**, and **23** was performed in a Rayonet apparatus (RPR 3000, emission maximum 300 nm) in HOAc/dichloromethane (DCM) (1:8) at 12–13 mM concentrations (2 h, Scheme 5). We were pleased to see that, with the exception



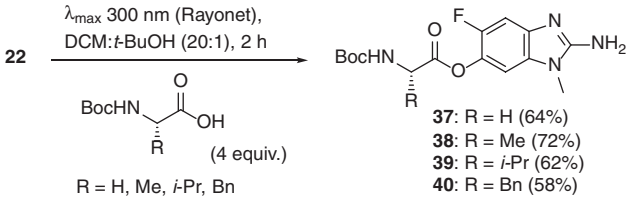
Scheme 5: Irradiation of the fluorinated 2-azidobenzimidazoles **11**, **12**, and **22** in acetic acid/DCM (1:8, Rayonet).

of the 6-fluoro derivative **23**, all compounds behaved in a surprisingly similar, regioselective manner. Always, the 6-position was attacked affording the 6-acetoxy product. Isolated yields varied between 65% (**29**, 4-F), 61% (**30**, 5-F), and 72% (**31**, 7-F). In the case of the 4-fluorinated starting material **11**, trace amounts (< 4%) of isomers were observed in the ^{19}F NMR spectrum. The non-decoupled ^{19}F NMR spectrum of the product mixture showed, besides the doublet ($J = 11.3$ Hz) of the main product **29** (65%), one additional doublet of doublets (0.9%) and one doublet (2.7%), pointing at the 7-acetoxy and 5-acetoxy isomers of **29**, respectively. The 5-fluorinated and 7-fluorinated azidobenzimidazoles **22** and **12** afforded exclusively the 6-acetoxylated products **30** and **31**, respectively. We also irradiated the 6-fluorinated azidobenzimidazole **23**, where the reactive position was blocked by the fluoro substituent. The reaction was far from being clean and provided a mixture of at least six *N*-methylated benzimidazole derivatives. Two of the products were still fluorinated and had incorporated one acetoxy group, according to the ^{19}F NMR and high resolution electrospray ionization (HRESI) mass spectra of the mixture. Separation and structure elucidation are ongoing.

Scheme 6 shows further photoreactions of 2-azido-5-fluorobenzimidazole **22**. With the mineral acids HBr (aq.) and HCl (g) in MeOH, the 6-halogenated products were formed, as observed earlier for the non-fluorinated parent compound. However, the 6-bromo compound was only the minor product (6%), whereas the debrominated product **32** was isolated in good yield (70%). Apparently, protodebromination had occurred, which is a known phenomenon and has been observed, for instance, at bromopyrrole derivatives [16] and at phenyl groups [17].



Scheme 6: Irradiation of 2-azido-5-fluorobenzimidazole **22** in the presence of aqueous HBr, methanolic HCl, Boc-protected *tert*-leucine, and pivalic acid.



Scheme 7: Irradiation of 2-azido-5-fluorobenzimidazole **22** in the presence of Boc-protected proteinogenic amino acids.

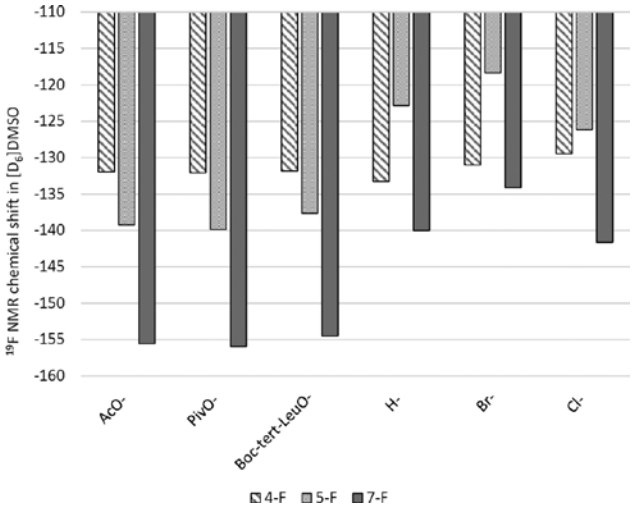


Fig. 2: ^{19}F NMR chemical shifts ([D$_6$]DMSO) of the 6-substituted, monofluorinated 2-aminobenzimidazoles obtained by irradiation of the corresponding 2-azidobenzimidazole derivatives.

Good yields of aryl esters **34** and **35** (88% and 70% yield), formed by reaction with Boc-L-*tert*-leucine and pivalic acid, respectively, were obtained. The reaction with pivalic acid in DCM also led to minor amounts of a non-symmetrical orange diazo compound.

We also conducted a series of irradiation experiments for the 4-fluoro- and 7-fluoro-2-azidobenzimidazoles **11** and **12** (see the Supplementary Information). High yields of irradiation products were also obtained starting from 2-azido-7-fluorobenzimidazole **12** (61%–72%), whereas the 4-fluoro analog **11** afforded yields between 44% and 65%.

Scheme 7 shows the photoarylation of four Boc-protected proteinogenic amino acids (Gly, Ala, Val, Phe) in a 20:1 mixture of DCM and *t*-BuOH, which was used for solubility reasons. Yields between 58% and 72% were isolated, indicating the suitability of 5-fluoro-2-azidobenzimidazole **22** for the photofunctionalization of biologically relevant carboxylic acids. Interestingly, the yields of the photoarylation with fluorinated 2-azidobenzimidazoles were very similar to our earlier examples with no fluorine being in place [3, 4]. Apparently, the fluoro substituents do not exert important electronic influence on the title reaction.

The investigation of fluorinated 2-azidobenzimidazoles was also driven by the question on whether the type of nucleophile attacking at C-6 could be identified simply by analyzing the ^{19}F NMR chemical shift of the adduct. ^{19}F NMR chemical shifts of the parent azidobenzimidazoles **11**, **12**, **22**, and **23** were at δ – 130.15, – 120.45, – 119.61, and – 136.72 ([D$_6$]DMSO), respectively. As shown in Fig. 2, the dispersion of the ^{19}F NMR chemical shifts ([D$_6$]DMSO) of the irradiation products was only small for the 4-fluorinated 2-aminobenzimidazoles, ranging from – 129.45 (6-Cl) to – 133.28 ppm (6-H). In the case of the 5- or 7-fluorinated products, with fluorine in the *o*-position of the 6-substituent, the ^{19}F NMR chemical shifts cover a range of about 13–14 ppm each. Here, it is possible to differentiate between aryl esters and halogenated or unsubstituted products, but it is not possible at this stage to distinguish between aryl esters of different carboxylic acids which exhibit a ^{19}F NMR chemical shift in narrow ranges (2.2 ppm for 5-F, 1.4 ppm for 7-F). Therefore, the synthesis of difluorinated 2-azidobenzimidazoles containing the combination of two ^{19}F NMR probes is encouraged.

4 Experimental section

NMR spectra were taken with a Bruker DRX-400 (400.1 MHz for ^{1}H, 100.6 MHz for ^{13}C, 376.7 for ^{19}F) and a Bruker AV II-600 instrument (600.1 MHz for ^{1}H, 150.9 MHz for ^{13}C) referenced to solvent signal or tetramethylsilane (TMS). Mass spectra were obtained with a ThermoFisher Scientific (LTQ-Orbitrap Velos) spectrometer. For gas chromatograph/mass spectroscopy (GC/MS) measurements, an Agilent

6890 gas chromatograph was equipped with a 30-m analytical column (Phenomenex ZB5-MS, 30 m × 0.25 mm ID, t_f = 0.25 µm). A split injection port at 270°C was used for sample introduction. A JMS-T100GC (GCAccuTOF, JEOL, Japan) time-of-flight mass spectrometer in electron ionization (EI) mode at 70 eV was used. Mass accuracies of equal to or better than 2.5 milli mass units were achieved. A Büchi 530 melting point measurement device was used for determination of the melting points. The values are uncorrected. Thin-layer chromatography (TLC) was performed with silica gel 60 F254 alumina foils from Merck. Zones were detected by fluorescence quenching at 254 nm. For staining, ninhydrin [0.3 g in 100 mL *n*-butanol/HOAc (30:1)] was used. Column chromatography was performed with Merck Geduran silica gel (40–63 µm and 63–200 µm). IR spectra were recorded with a Bruker Tensor 27 spectrometer. UV/Vis spectra were measured with a Varian Cary 100 Bio UV/Vis spectrometer. Optical rotations were measured on a Dr. Kernchen Propol Automatic Polarimeter. The irradiations were carried out in a Rayonet (RPR-200) reactor, equipped with 8 × RPR-3000 Å lamps (300-nm emissions maximum). The jar was made of borosilicate glass. Microwave reactions were performed in a START 1500 reactor (MLS GmbH) with a maximum power of 1200 W. The reactions were performed in a sealed tube at a continuous power of 500 W. Chemicals were purchased from commercial suppliers and used without further purification.

4.1 4-Fluoro-1-methyl-1*H*-benzo[*d*]imidazole (5) and 7-fluoro-1-methyl-1*H*-benzo[*d*]imidazole (6)

To a solution of 4(7)-fluorobenzimidazole (**9**, 0.307 g, 2.3 mmol, 1.0 equiv.) in dry THF (40 mL) was added NaH (60% dispersion in mineral oil, 0.110 g, 2.76 mmol, 1.2 equiv.). After 3 h, iodomethane (0.358 g, 0.16 mL, 2.53 mmol, 1.1 equiv.) was added. After additional 3 h, H_2O was added, followed by aqueous NaOH (10%). The organic layer was collected and the aqueous layer was extracted with EtOAc (3×). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated. Column chromatography [silica, $CHCl_3$/MeOH (20:1)] afforded a 5:2 mixture of regioisomers **5** and **6** (0.270 g, 1.8 mmol, 78%) as an oil. TLC [silica, $CHCl_3$/MeOH (20:1)]: R_f = 0.20. – GC/MS (EI, 70 eV): **5**: t_R = 13.50 min (*m/z* (%) = 150.061 (100, $[M]^+$), calcd. 150.059 for $[C_8H_7FN_2]^+$), **6**: t_R = 15.32 min (*m/z* (%) = 150.061 (100, $[M]^+$), calcd. 150.059 for $[C_8H_7FN_2]^+$). – HRMS ((+)-ESI): *m/z* = 173.04850 (–0.3 ppm, calcd. 173.04855 for $[C_8H_7FN_2+Na]^+$). – IR (diamond ATR): $\tilde{\nu}$ = 3218 cm^{-1} (br. m), 3102 (m), 1598 (s), 1506 (s), 1486 (s), 1464 (m), 1333 (m), 1287 (s), 1273 (m), 1247 (s) 1223 (m), 1191 (m), 1171 (m), 1122 (s), 1082 (m), 1062 (m), 891 (m), 865 (m), 833 (s), 790 (m), 688 (m), 667 (m), 634 (m), 612 (m), 582 (m). – UV (MeOH): λ_{max} (lg ε) = 204 nm (4.35), 248 (3.74), 276 (3.68), 282 (3.67), 287 (3.44). **5**: ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 8.24 (s, 1H, 2-*H*), 7.42 (dd, *J* = 1.0 Hz, *J* = 8.1 Hz, 1H, 7-*H*), 7.25 (ddd, *J* = 4.8 Hz, *J* = 8.1 Hz, *J* = 8.1 Hz, 1H, 6-*H*), 7.03 (ddd, *J* = 0.8 Hz, *J* = 8.0 Hz, *J* = 11.2 Hz, 1H, 5-*H*), 3.86 (s, 3H, NC*H*$_3$). – ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 153.22 (d, J_{CF} = 249.8 Hz, 1C, *C*-4), 145.06 (1C, *C*-2), 137.69 (d, J_{CF} = 9.4 Hz, 1C, *C*-7a), 131.61 (d, J_{CF} = 16.9 Hz, 1C, *C*-3a), 122.82 (d, J_{CF} = 7.4 Hz, 1C, *C*-6), 106.58 (d, J_{CF} = 17.6 Hz, 1C, *C*-5), 106.57 (d, J_{CF} = 3.8 Hz, 1C, *C*-7), 31.02 (1C, N*C*H$_3$). – ^{19}F NMR (376 MHz, [D$_6$]DMSO): δ = –128.66. **6**: ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 8.20 (s, 1H, 2-*H*), 7.48 (ddd, *J* = 0.8 Hz, *J* = 8.1 Hz, *J* = 8.1 Hz, 1H, 4-H), 7.16 (ddd, *J* = 5.0 Hz, *J* = 8.0 Hz, *J* = 8.0 Hz, 1H, 5-H), 7.07 (ddd, *J* = 0.5 Hz, *J* = 8.1 Hz, *J* = 11.7 Hz, 1H, 6-*H*), 3.99 (d, *J* = 1.4 Hz, 3H, NC*H*$_3$). – ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 149.16 (d, J_{CF} = 245.1 Hz, 1C, *C*-7), 147.13 (d, J_{CF} = 4.0 Hz, 1C, *C*-3a), 145.69 (1C, *C*-2), 122.49 (d, J_{CF} = 9.9 Hz, 1C, C-7a), 121.82 (d, J_{CF} = 6.7 Hz, 1C, *C*-5), 115.80 (d, J_{CF} = 4.0 Hz, 1C, *C*-4), 108.01 (d, J_{CF} = 17.1 Hz, 1C, *C*-6), 32.92 (d, J_{CF} = 3.3 Hz, 1C, N*C*H$_3$). – ^{19}F NMR (376 MHz, [D$_6$]DMSO): δ = –135.04.

4.2 2-Azido-4-fluoro-1-methyl-1*H*-benzo[*d*]imidazole (11) and 2-azido-7-fluoro-1-methyl-1*H*-benzo[*d*]imidazole (12)

To a solution of the benzimidazole (0.60 g, 4.0 mmol, 1.0 equiv.) in dry Et_2O (35 mL) under argon was added *n*-BuLi (1.6 M in *n*-hexane, 2.75 mL, 4.4 mmol, 1.1 equiv.) at –78°C. After 2 h, tosyl azide (0.868 g, 4.4 mmol, 1.1 equiv.) was added in one portion. After 3 h at –78°C the mixture was allowed to reach room temperature and stirred for additional 3 h. The reaction was quenched with an aqueous solution of $Na_4P_2O_7 \cdot 10\ H_2O$ (1.963 g, 4.4 mmol, 1.1 equiv., in 30 mL H_2O) and stirred overnight. The organic phase was separated and the aqueous layer was extracted with *t*-BuOMe (3×). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated. Column chromatography [silica, petroleum ether/EtOAc (10:1)] afforded **11** (0.485 g, 2.5 mmol, 63%) and **12** (0.113 g, 0.59 mmol, 18%), separately as yellow solids. 2-Azido-4-fluoro-1-methyl-1*H*-benzo[*d*]imidazole (**11**): TLC [silica, petroleum ether/EtOAc (10:1)]: R_f = 0.21. Mp = 106–108°C. – ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 7.35 (d, *J* = 8.1 Hz, 1H, 7-*H*), 7.21 (ddd, *J* = 4.8 Hz, *J* = 8.1 Hz, *J* = 8.1 Hz, 1H, 6-*H*), 7.05 (dd, *J* = 8.1 Hz, *J* = 11.0 Hz, 1H, 5-*H*), 3.61 (s, 3H, NC*H*$_3$). – ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 151.79 (d, J_{CF} = 248.3 Hz, 1C, *C*-4), 147.94 (C_{qu}., 1C, *C*-2), 138.03 (d, $^3J_{CF}$ = 9.1 Hz, 1C, *C*-7a), 128.95 (d, $^2J_{CF}$ = 17.0 Hz, 1C,

C-3a), 122.23 (d, $^4J_{CF}$ = 7.3 Hz, 1C, *C*-6), 107.75 (d, $^2J_{CF}$ = 17.4 Hz, 1C, *C*-5), 106.56 (d, $^5J_{CF}$ = 3.7 Hz, 1C, *C*-7), 29.46 (1C, N*C*H$_3$). – ^{19}F NMR (376 MHz, [D$_6$]DMSO): δ = –130.15. – HRMS ((+)-ESI): *m*/*z* = 164.06196 (0.67 ppm, calcd. 164.06185 for [C$_8$H$_7$FN$_3$+H]$^+$). – IR (diamond ATR): $\tilde{\nu}$ = 3283–3039 cm^{-1} (br. w), 2165 (m), 2141 (m), 2120 (m), 1635 (m), 1561 (m), 1486 (s), 1433 (s), 1408 (s), 1257 (m), 1232 (m), 1194 (m), 1152 (m), 1049 (m), 1012 (m), 814 (m), 780 (m), 740 (m), 690 (m), 638 (m), 593 (m). – UV (MeOH): λ_{max} (lg ε) = 203 nm (4.16), 233 (3.76), 282 (3.67). 2-Azido-7-fluoro-1-methyl-1*H*-benzo[*d*]imidazole (**12**): TLC [silica, petroleum ether/EtOAc (10:1)]: R_f = 0.37. Mp = 112–114°C. – ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 7.36 (dd, *J* = 0.7 Hz, *J* = 8.1 Hz, 1H, 4-*H*), 7.16 (ddd, *J* = 5.1 Hz, *J* = 8.1 Hz, *J* = 8.1 Hz, 1H, 5-*H*), 7.04 (ddd, *J* = 0.8 Hz, *J* = 8.2 Hz, *J* = 11.7 Hz, 1H, 6-*H*), 3.71 (d, *J* = 1.1 Hz, 1H, NC*H*$_3$). – ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 148.30 (C$_{qu}$., 1C, N*C*N$_3$), 148.25 (d, J_{CF} = 244.5 Hz, 1C, *C*-7), 143.99 (d, J_{CF} = 4.2 Hz, 1C, *C*-3a), 122.67 (d, J_{CF} = 9.3 Hz, 1C, *C*-7a), 122.24 (d, J_{CF} = 7.0 Hz, 1C, *C*-5), 114.06 (d, J_{CF} = 3.7 Hz, 1C, *C*-4), 107.95 (d, J_{CF} = 17.1 Hz, 1C, *C*-6), 31.24 (1C, N*C*H$_3$). – ^{19}F NMR (376 MHz, [D$_6$]DMSO): δ = –136.72. – ^{15}N NMR (by HMBC, [D$_6$]DMSO): δ = –255.7 (*C*NCH$_3$), –162.6 (*C*NCN$_3$). – HRMS ((+)-ESI): *m*/*z* = 164.06196 (0.67 ppm, calcd. 164.06185 for [C$_8$H$_7$FN$_3$+H]$^+$). – IR (diamond ATR): $\tilde{\nu}$ = 3071–2872 cm^{-1} (br. w), 2179 (m), 2134 (m), 1639 (m), 1591 (m), 1483 (s), 1432 (s), 1408 (s), 1289 (m), 1258 (m), 1243 (m), 1166 (m), 1136 (m), 1049 (m), 787 (s), 733 (m), 688 (s), 560 (m). – UV (MeOH): λ_{max} (lg ε) = 204 nm (4.32), 235 (4.03), 282 (3.94).

4.3 2-Fluoro-6-nitroaniline (14)

To a solution of 1-fluoro-3-nitrobenzene (3.00 g, 2.26 mL, 21.3 mmol) in dry DMSO (130 mL) was added TMHI (4.73 g, 23.4 mmol, 1.1 equiv.). After 30 min, KO*t*-Bu (5.74 g, 51.2 mmol, 2.4 equiv.) was added. After 24 h at room temperature, the mixture was poured on ice and acidified to pH 3 by adding 10% HCl. After 30 min, the solution was extracted with EtOAc (3×100 mL) and washed with saturated aqueous NH$_4$Cl (100 mL). The combined organic layers were washed with H$_2$O and dried over MgSO$_4$. Column chromatography [silica, petroleum ether/acetone (9 : 1) to (5 : 1)] afforded 2-fluoro-6-nitroaniline (**14**) as a yellow solid (1.30 g, 8.5 mmol, 40%), in addition to a 4:1 mixture of 2-fluoro-4-nitroaniline and 4-fluoro-2-nitroaniline. TLC [silica, petroleum ether/acetone (9 : 1)]: R_f = 0.26. Mp = 75°C. – ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 7.84 (ddd, *J* = 1.8 Hz, *J* = 8.8 Hz, *J* = 8.8 Hz, 1H, 5-*H*), 7.45 (ddd, *J* = 1.5 Hz, *J* = 7.8 Hz, *J* = 11.5 Hz, 1H, 3-*H*), 7.27 (s, 2H, FCCN*H*$_2$), 6.63 (ddd, *J* = 5.3 Hz, *J* = 7.8 Hz, *J* = 8.8 Hz, 1H, 4-*H*). – ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 151.67 (d, J_{CF} = 242.8 Hz, 1C, *C*-2), 135.97 (d, J_{CF} = 16.6 Hz, 1C, *C*-1), 131.87 (d, J_{CF} = 5.2 Hz, 1C, *C*-6), 121.09 (d, $^4J_{CF}$ = 3.3 Hz, 1C, *C*-5), 119.76 (d, J_{CF} = 18.4 Hz, 1C, *C*-3), 113.48 (d, J_{CF} = 8.0 Hz, 1C, *C*-4). – ^{19}F NMR (376 MHz, [D$_6$]DMSO): δ = –129.32. – HRMS ((+)-ESI): *m*/*z* = 216.06197 (–18.98 ppm, calcd. 216.06607 for [C$_{12}$H$_{10}$NO$_3$]$^+$), 179.02278 (0.28 ppm, calcd. 179.02273 for [C$_6$H$_5$FN$_2$O$_2$+Na$^+$]). – IR (diamond ATR): $\tilde{\nu}$ = 3486 cm^{-1} (br. m), 3364 (br. s), 1638 (s), 1582 (m), 1524 (s), 1440 (s), 1327 (s), 1265 (m), 1251 (m), 1206 (m), 1096 (w), 1068 (m), 843 (m), 789 (m), 737 (s), 710 (m), 559 (m). – UV (MeOH): λ_{max} (lg ε) = 223 nm (4.20), 251 (3.62), 275 (3.70), 394 (3.61).

4.4 *N*-(2-Fluoro-6-nitrophenyl)formamide (15)

A mixture of Ac$_2$O (20 mL) and formic acid (8 mL) was heated at 60°C for 3 h. After cooling the mixture to room temperature, 2-fluoro-6-nitroaniline (**14**, 1.817 g, 11.6 mmol) was added. After 15 h at 60°C the solvent was removed under reduced pressure. The residue was partitioned between saturated NaHCO$_3$ solution and DCM. The aqueous layer was extracted with DCM (3×). The combined organic phases were dried over MgSO$_4$. Column chromatography [silica, CHCl$_3$/MeOH (20:1)] afforded **15** (2.099 g, 11.4 mmol, 98%) as a yellow solid. TLC [silica, CHCl$_3$/MeOH (50:1)]: R_f = 0.05. Mp = 125°C. – ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 10.47 (br. s, 1H, N*H*CHO), 8.30 (d, *J* = 1.3 Hz, 1H, NHC*H*O), 7.84 (ddd, *J* = 1.3 Hz, *J* = 8.3 Hz, *J* = 8.3 Hz 1H, 5-*H*), 7.74 (ddd, *J* = 1.4 Hz, *J* = 8.4 Hz and *J* = 9.8 Hz, 1H, 3-*H*), 7.53 (ddd, *J* = 5.4 Hz, *J* = 8.4 Hz, *J* = 8.4 Hz, 1H, 4-*H*). – ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 160.20 (br. s, 1C, CNH*C*HO), 155.97 (d, J_{CF} = 250.0 Hz, 1C, *C*-2), 145.55 (d, J_{CF} = 1.6 Hz, 1C, *C*-6), 127.44 (d, J_{CF} = 8.8 Hz, 1C, *C*-4), 120.86 (d, J_{CF} = 20.9 Hz, 1C, *C*-3), 120.59 (d, J_{CF} = 3.2 Hz, 1C, *C*-5), 118.49 (d, J_{CF} = 16.6 Hz, 1C, *C*-1). – ^{19}F NMR (376 MHz, [D$_6$]DMSO): δ = –117.41 (br. s, rotamers), –118.36. – GC/MS (EI, 70 eV): t_R = 15.91 min (*m*/*z* (%) = 184.030 (12, [M]$^+$), calcd. 184.028 for [C$_7$H$_5$FON$_2$O$_3$]$^+$). – HRMS ((+)-ESI): *m*/*z* = 207.01765 (–0.05 ppm, calcd. 207.01764 for [C$_7$H$_5$FN$_2$O$_3$+Na]$^+$), 391.04613 (0.17 ppm, calcd. 391.04606 for [C$_{14}$H$_{10}$F$_2$N$_4$O$_6$+Na]$^+$). – IR (diamond ATR): $\tilde{\nu}$ = 1674 cm^{-1} (s), 1614 (m), 1506 (s), 1479 (s), 1445 (m), 1394 (m), 1296 (s), 1271 (s), 1241 (m), 1194 (m), 1164 (m), 1079 (m), 1018 (m), 806 (s), 777 (m), 736 (m), 617 (m), 594 (m). – UV (MeOH): λ_{max} (lg ε) = 202 nm (4.07), 222 (4.15), 253 (3.55), 301 (3.28).

4.5 2-Fluoro-*N*-methyl-6-nitroaniline (16)

From **15**: To a solution of *N*-(2-fluoro-6-nitrophenyl) formamide (**15**, 0.50 g, 2.7 mmol, 1.0 equiv.) in dry THF

(25 mL) under argon at 0°C was slowly added $LiAlH_4$ (0.31 g, 8.1 mmol, 3.0 equiv.). The suspension was stirred at 70°C for 1.5 h and cooled to 0°C. H_2O (1 mL) and 30% NaOH (1 mL) were added, followed by additional H_2O (3×1.5 mL). THF (20 mL) was added, and the mixture was filtered at 70°C. After extraction with THF (3×25 mL), the combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography [silica, $CHCl_3$/MeOH (60:1)] affording an orange solid (0.29 g, 1.7 mmol, 63%). From **18**: To a stirred solution of 1,2-difluoro-3-nitrobenzene (**18**, 0.36 g, 2.3 mmol, 1.0 equiv.) in EtOH (0.30 mL) was added methylamine (40% in MeOH, 0.45 g, 2.3 mmol, 1.0 equiv.). The mixture was then heated in a microwave reactor at 70°C for 45 min. Afterward the mixture was extracted with CH_2Cl_2 (3×30 mL) and the combined organic layers were washed with H_2O (2×75 mL) and brine (60 mL). The organic layer was dried over $MgSO_4$. Concentration under reduced pressure afforded an orange solid (0.391 g, 2.3 mmol, quant.). TLC [silica, $CHCl_3$/MeOH (50:1)]: R_f = 0.20. Mp = 35–37°C. – ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.85 (ddd, J = 1.5 Hz, J = 8.7 Hz, 1H, 5-*H*), 7.75 (br. s, 1H, CN*H*CH$_3$), 7.44 (dddd, J = 0.7 Hz, J = 1.6 Hz, J = 7.9 Hz, J = 9.5 Hz, 1H, 3-*H*), 6.66 (ddd, J = 4.8 Hz, J = 7.9 Hz J = 12.7 Hz, 1H, 4-*H*), 3.12 (dd, J = 5.0 Hz, J = 7.7 Hz, 3H, CNHC*H*$_3$). – ^{13}C NMR (100 MHz, $CDCl_3$): δ = 152.27 (d, J_{CF} = 243.0 Hz, 1C, *C*-2), 136.88 (d, J_{CF} = 11.9 Hz 1C, *C*-1NH), 134.12 (d, J_{CF} = 6.4 Hz, 1C, *C*-6), 122.11 (d, J_{CF} = 3.1 Hz, 1C, *C*-5), 121.87 (d, J_{CF} = 20.9 Hz, 1C, *C*-3), 114.23 (d, J_{CF} = 8.3 Hz, 1C, *C*-4), 32.82 (d, J_{CF} = 12.1 Hz 1C, NH*C*H$_3$). – ^{19}F NMR (376 MHz, $CDCl_3$): δ = –125.45. – GC/MS (EI, 70 eV): t_R = 12.90 min (*m/z* (%) = 170.050 (100, $[M]^+$), calcd. 170.049 for $[C_7H_7FN_2O_2]^+$). – IR (diamond ATR): $\tilde{\nu}$ = 3357 cm^{-1} (m), 1627 (m), 1522 (s), 1427 (m), 1406 (m), 1406 (m), 1335 (m), 1313 (m), 1250 (m), 1180 (s), 1118 (m), 1083 (m), 914 (m), 827 (m), 787 (m), 734 (s), 705 (m), 608 (m), 537 (m). – UV (MeOH): λ_{max} (lg ε) = 223 nm (4.26), 281 (3.66), 422 (3.68).

4.6 7-Fluoro-1-methyl-1*H*-benzo[*d*]imidazole (17)

A suspension of iron powder (1.06 g, 19 mmol, 10 equiv.) in a solution of the starting material (0.33 g, 1.9 mmol, 1.0 equiv.) and NH_4Cl (1.02 g, 19 mmol, 10 equiv.) in *i*-PrOH (20 mL) and formic acid (20 mL) was stirred at 85°C under argon for 3 h. The mixture was diluted with *i*-PrOH (30 mL) and filtered. The filtrate was concentrated to dryness and the resulting residue partitioned between DCM and saturated aqueous $NaHCO_3$. The aqueous layer was extracted with further DCM (5×). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated. Column chromatography [silica, $CHCl_3$/MeOH (20:1) to (1:1)] afforded an ochre solid (0.24 g, 1.6 mmol, 84%). – ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.77 (s, 1H, 2-*H*), 7.60 (d, J = 8.3 Hz, 1H, 4-*H*), 7.16 (ddd, J = 5.0 Hz, J = 8.1 Hz, J = 8.1 Hz, 1H, 5-*H*), 6.96 (ddd, J = 0.5 Hz, J = 8.1 Hz, J = 11.6 Hz, 1H, 6-*H*), 4.01 (d, J = 1.2 Hz, 3H, NC*H*$_3$). – ^{13}C NMR (100 MHz, $CDCl_3$): δ = 149.64 (d, J_{CF} = 246.4 Hz, 1C, *C*-7), 147.29 (d, J_{CF} = 3.8 Hz, 1C, *C*-3a), 144.23 (1C, *C*-2), 122.84 (d, J_{CF} = 10.1 Hz, 1C, *C*-7a), 122.19 (d, J_{CF} = 6.6 Hz, 1C, *C*-5), 116.22 (d, J_{CF} = 4.0 Hz, 1C, *C*-4), 108.55 (d, J_{CF} = 17.1 Hz, 1C, *C*-6), 33.20 (d, J_{CF} = 3.7 Hz, 1C, N*C*H$_3$). – ^{19}F NMR (376 MHz, $CDCl_3$): δ = –136.41. – GC/MS (EI, 70 eV): t_R = 13.44 min (*m/z* (%) = 150.060 (100, $[M]^+$), calcd. 150.059 for $[C_8H_7FN_2]^+$). – IR (diamond ATR): $\tilde{\nu}$ = 3444–3237 cm^{-1} (br. m), 1583 (m), 1493 (m), 1474 (m), 1452 (m), 1351 (m), 1325 (m), 1280 (m), 1243 (m) 1219 (m), 1160 (m), 1120 (m), 1034 (s), 865 (w), 800 (s), 745 (m), 717 (m), 661 (m), 628 (m). – UV (MeOH): λ_{max} (lg ε) = 211 nm (4.65), 246 (4.28), 277 (3.86).

4.7 2-Azido-7-fluoro-1-methyl-1*H*-benzo[*d*]imidazole (12)

To a solution of the benzimidazole (0.20 g, 1.3 mmol, 1.0 equiv.) in dry Et_2O (20 mL) under argon was added *n*-BuLi (1.6 M in *n*-hexane, 0.88 mL, 1.4 mmol, 1.1 equiv.) at –78°C. After 2 h, tosyl azide (0.28 g, 1.4 mmol, 1.1 equiv.) was added in one portion. After 3 h at –78°C, the mixture was allowed to reach room temperature and stirred for additional 3 h. The reaction was quenched with an aqueous solution of $Na_4P_2O_7{\cdot}10\ H_2O$ (0.62 g, 1.4 mmol, 1.1 equiv., in 30 mL H_2O) and stirred overnight. The organic phase was separated and the aqueous layer was extracted with *t*-BuOMe (3×). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated. Column chromatography [silica, petro = leum ether/EtOAc (10:1)] afforded **12** (0.166 g, 0.87 mmol, 67%) as a yellow solid. For characterization data, see above.

4.8 3,6-Difluoro-2-nitroaniline (20) and 4-fluoro-2-nitroaniline (21)

To a solution of 1,4-difluoro-2-nitrobenzene (0.50 g, 3.1 mmol) in dry DMSO (150 mL) was added TMHI (0.69 g, 3.41 mmol, 1.1 equiv.). After 30 min, KO*t*-Bu (0.83 g, 7.44 mmol, 2.4 equiv.) was added. After 24 h at room temperature, the mixture was poured on ice and acidified to pH 3 by adding 10% HCl. After 30 min, the solution was extracted with EtOAc (3×100 mL) and washed with

saturated aqueous NH_4Cl (100 mL). The combined organic layers were washed with H_2O and dried over $MgSO_4$. Column chromatography [silica, $CHCl_3$/MeOH (60:1) to (5:1)] afforded **20** as an orange solid (0.10 g, 0.57 mmol, 18%) and **21** as a yellow solid (0.06 g, 0.38 mmol, 12%). Compound **20**: TLC [silica, $CHCl_3$/MeOH (50:1)]: $R_f = 0.61$. Mp = 79–81°C. – ^{1}H NMR (600 MHz, $CDCl_3$): $\delta = 7.13$ (ddd, $J = 4.3$ Hz, $J = 8.9$ Hz, $J = 13.4$ Hz, 1H, 5-*H*), 6.43 (ddd, $J = 4.2$ Hz, $J = 9.0$ Hz, $J = 13.2$ Hz, 1H, 4-*H*), 5.76 (br. s, 2H, C(N*H*$_2$)). – ^{13}C NMR (150 MHz, $CDCl_3$): $\delta = 153.35$ (dd, $J_{CF} = 3.0$ Hz, $J_{CF} = 258.7$ Hz, 1C, *C*-5), 147.30 (dd, $J_{CF} = 3.8$ Hz, $J_{CF} = 239.4$ Hz, 1C, *C*-3), 134.97 (d, $J_{CF} = 17.0$ Hz, 1C, *C*-1(NH$_2$)), 125.14 (br. s, 1C, *C*-2), 118.35 (dd, $J_{CF} = 10.6$ Hz, $J_{CF} = 20.7$ Hz, 1C, *C*-5), 102.11 (dd, $J_{CF} = 7.4$ Hz, $J_{CF} = 24.1$ Hz, 1C, *C*-4). – ^{19}F NMR (376 MHz, $CDCl_3$): $\delta = -121.77$ (d, $^5J_{FF} = 16.2$ Hz, 1F, C-1*F*, –136.39 (d, $^5J_{FF} = 16.3$ Hz, 1F, C-3*F*)). – GC/MS (EI, 70 eV): $t_R = 12.57$ min (*m/z* (%) = 174.025 (100, [M]$^+$), calcd. 174.024 for [$C_6H_4F_2N_2O_2$]$^+$). – IR (diamond ATR): $\tilde{\nu} = 3502$ cm^{-1} (m), 3395 (m) 1643 (m), 1587 (m), 1527 (s), 1464 (m), 1344 (s), 1268 (s), 1239 (s), 1215 (m) 1120 (m), 1036 (m), 796 (s) 767 (m), 740 (m), 706 (w), 587 (m). – UV (MeOH): λ_{max} (lg ε) = 202 nm (3.98), 226 (4.10), 270 (3.60), 384 (3.47). Compound **21**: TLC [silica, $CHCl_3$/MeOH (50:1)]: $R_f = 0.71$. Mp = 90–91°C. – ^{1}H NMR (400 MHz, [D$_6$]DMSO): $\delta = 7.73$ (ddd, $J = 3.0$ Hz, $J = 9.6$ Hz, 1H, 3-*H*), 7.40 (ddd, $J = 3.0$ Hz, $J = 7.7$ Hz, $J = 10.7$ Hz, 1H, 5-*H*), 7.39 (br. s, 2H, N*H*$_2$), 7.07 (dd, $J = 5.0$ Hz, $J = 9.5$ Hz, 1H, 6-*H*). – ^{13}C NMR (100 MHz, [D$_6$]DMSO): $\delta = 150.41$ (d, $J_{CF} = 236.0$ Hz, 1C, *C*-4), 142.77 (d, $J_{CF} = 5.4$ Hz, 1C, *C*-2), 139.56 (d, $J_{CF} = 2.1$ Hz, 1C, *C*-1), 120.85 (d, $J_{CF} = 28.8$ Hz, 1C, *C*-5), 114.15 (d, $J_{CF} = 28.8$ Hz, 1C, *C*-3), 110.71 (d, $J_{CF} = 7.3$ Hz, 1C, *C*-6). – ^{19}F NMR (376 MHz, [D$_6$]DMSO): $\delta = -127.81$. – GC/MS (EI, 70 eV): $t_R = 13.95$ min (*m/z* (%) = 156.034 (100, [M]$^+$), calcd. 156.034 for [$C_6H_5FN_2O_2$]$^+$).

4.9 4-Fluoro-*N*-methyl-2-nitroaniline (25)

Under argon, 1,4-difluoro-2-nitrobenzene (**19**, 1.00 g, 6.3 mmol, 1.0 equiv.), NH_2Me·HCl (2.13 g, 31.5 mmol, 5.0 equiv.), and K_2CO_3 (4.35 g, 31.5 mmol, 5.0 equiv.) were dissolved in DMSO (15 mL). After 24 h, Et_2O (200 mL) was added, followed by H_2O (3×75 mL) and saturated NaCl (60 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure, affording an orange solid (1.06 g, 6.2 mmol, 98%) with no further workup. TLC [silica, $CHCl_3$/MeOH (50:1)]: $R_f = 0.20$. Mp = 75°C. – ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 8.12$ (br. d, 1H, N*H*CH$_3$), 7.84 (dd, $J = 3.1$ Hz, $J = 9.5$ Hz, 1H, 3-*H*), 7.54 (dddd, $J = 0.5$ Hz, $J = 3.1$ Hz, $J = 7.6$ Hz, $J = 9.4$ Hz, 1H, 5-*H*), 7.04 (dd, $J = 4.8$ Hz, $J = 9.5$ Hz, 1H, 6-*H*), 2.96 (d, $J = 5.0$ Hz, 3H, NHC*H*$_3$). – ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 151.42$ (d, $J_{CF} = 234.9$ Hz, 1C, *C*-4), 143.38 (s, 1C, *C*-1), 129.29 (d, $J_{CF} = 8.7$ Hz, 1C, *C*-2), 125.33 (d, $J_{CF} = 23.8$ Hz, 1C, *C*-5), 116.09 (d, $J_{CF} = 7.4$ Hz, 1C, *C*-6), 110.85 (d, $J_{CF} = 26.2$ Hz, 1C, *C*-3), 29.85 (s, 1C, NH*C*H$_3$). – ^{19}F NMR (376 MHz, $CDCl_3$): $\delta = -128.70$. – GC/MS (EI, 70 eV): **25**: $t_R = 14.65$ min (*m/z* (%) = 170.051 (100, [M]$^+$), calcd. 170.049 for [$C_7H_7FN_2O_2$]$^+$). – IR (diamond ATR): $\tilde{\nu} = 3392$ cm^{-1} (m), 1580 (s), 1510 (s), 1463 (m), 1416 (s), 1404 (s), 1354 (m), 1313 (m), 1279 (m), 1213 (s), 1158 (s), 1107 (m), 1042 (s), 941 (m), 858 (m), 808 (s), 756 (s), 568 (m). – UV (MeOH): λ_{max} (lg ε) = 228 nm (4.30), 273 (3.61), 441 (3.80).

4.10 5-Fluoro-1-methyl-1*H*-benzo[*d*]imidazole (27)

A suspension of iron powder (3.295 g, 59 mmol, 10 equiv.) in a solution of the starting material (1.00 g, 5.9 mmol, 1.0 equiv.) and NH_4Cl (3.16 g, 59 mmol, 10 equiv.) in *i*-PrOH (20 mL) and formic acid (20 mL) was stirred at 85°C for 4 h under argon. The mixture was diluted with *i*-PrOH (30 mL) and filtered. The filtrate was concentrated to dryness and the resulting residue partitioned between DCM and saturated aqueous $NaHCO_3$. The aqueous layer was extracted with further DCM (5×). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated. Column chromatography [silica, $CHCl_3$/MeOH (20:1) to (1:1)] afforded an ochre solid (0.752 g, 5.0 mmol, 85%). TLC [silica, $CHCl_3$/MeOH (20:1)]: $R_f = 0.40$. Mp = 70–72°C. – ^{1}H NMR (400 MHz, [D$_6$]DMSO): $\delta = 8.24$ (s, 1H, 2-*H*), 7.58 (dd, $J = 4.8$ Hz, $J = 8.8$ Hz, 1H, 7-*H*), 7.45 (dd, $J = 2.4$ Hz, $J = 9.9$ Hz, 1H, 4-*H*), 7.14 (ddd, $J = 2.5$ Hz, $J = 9.1$ Hz, $J = 9.7$ Hz, 1H, 6-*H*), 3.85 (s, 3H, NC*H*$_3$). – ^{13}C NMR (100 MHz, [D$_6$]DMSO): $\delta = 158.41$ (d, $J_{CF} = 233.8$ Hz, 1C, *C*-5), 146.16 (1C, *C*-2), 143.61 (d, $J_{CF} = 12.9$ Hz, 1C, *C*-3a), 131.33 (1C, *C*-7a), 110.28 (d, $J_{CF} = 26.0$ Hz, 1C, *C*-6), 109.83 (d, $J_{CF} = 10.5$ Hz, 1C, *C*-7), 104.69 (d, $J_{CF} = 23.7$ Hz, 1C, *C*-4), 30.84 (1C, CN*C*H$_3$). – ^{19}F NMR (376 MHz, [D$_6$]DMSO): $\delta = -121.69$. – GC/MS (EI, 70 eV): $t_R = 14.55$ min (*m/z* (%) = 150.060 (100, [M]$^+$), calcd. 150.059 for [$C_8H_7FN_2$]$^+$). – IR (diamond ATR): $\tilde{\nu} = 1500$ cm^{-1} (s), 1482 (s), 1445 (m), 1424 (m), 1370 (m), 1334 (m), 1249 (m), 1214 (s), 1117 (s), 1097 (m), 949 (m), 895 (m), 875 (m), 849 (m), 829 (m), 795 (s), 633 (s), 610 (m). – UV (MeOH): λ_{max} (lg ε) = 206 nm (4.13), 248 (3.82), 253 (3.81), 280 (3.71), 287 (3.66).

4.11 6-Fluoro-1-methyl-1*H*-benzo[*d*]imidazole (28)

A suspension of iron powder (8.54 g, 153 mmol, 10 equiv.) in a solution of the starting material (2.60 g, 15.3 mmol, 1.0 equiv.) and NH_4Cl (8.18 g, 153 mmol, 10 equiv.) in *i*-PrOH (30 mL) and formic acid (30 mL) was stirred at 85°C for 4 h

under argon. The mixture was diluted with *i*-PrOH (30 mL) and filtered. The filtrate was concentrated to dryness and the resulting residue partitioned between DCM and saturated aqueous $NaHCO_3$. The aqueous layer was extracted with further DCM (5×). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated. Column chromatography [silica, $CHCl_3$/MeOH (20:1) to (1:1)] afforded an ochre solid (2.068 g, 13.8 mmol, 90%). TLC [silica, $CHCl_3$/MeOH (15:1)]: $R_f = 0.41$. Mp = 64–66°C. – ^{1}H NMR (400 MHz, [D_6]DMSO): $\delta = 8.19$ (s, 1H, 2-*H*), 7.64 (dd, $J = 4.8$ Hz, $J = 8.8$ Hz, 1H, 4-*H*), 7.46 (dd, $J = 2.4$ Hz, $J = 9.3$ Hz, 1H, 7-*H*), 7.05 (ddd, $J = 2.6$ Hz, $J = 8.8$ Hz, $J = 11.3$ Hz, 1H, 5-*H*), 3.82 (s, 3H, NCH_3). – ^{13}C NMR (100 MHz, [D_6]DMSO): $\delta = 158.77$ (d, $J_{CF} = 236.1$ Hz, 1C, *C*-6), 145.45 (d, $J_{CF} = 2.7$ Hz 1C, *C*-2), 139.83 (1C, *C*-3a), 134.77 (d, $J_{CF} = 13.9$ Hz, 1C, *C*-7a), 120.16 (d, $J_{CF} = 10.3$ Hz, 1C, *C*-4), 109.48 (d, $J_{CF} = 25.2$ Hz, 1C, *C*-5), 96.87 (d, $J_{CF} = 27.5$ Hz, 1C, *C*-7), 30.76 (1C, CN*C*H$_3$). – ^{19}F NMR (376 MHz, [D_6]DMSO): $\delta = -119.41$. – GC/MS (EI, 70 eV): $t_R = 14.24$ min (*m/z* (%) = 150.060 (100, $[M]^+$), calcd. 150.059 for $[C_8H_7FN_2]^+$). – IR (diamond ATR): $\tilde{\nu} = 1677$ cm^{-1} (m), 1623 (m), 1504 (s), 1459 (s), 1425 (m), 1358 (m), 1327 (w), 1283 (m), 1253 (m), 1194 (m), 1176 (s), 1084 (m), 944 (m), 871 (m), 856 (s), 829 (s), 795 (s), 684 (m), 614 (s), 586 (m). – UV (MeOH): λ_{max} (lg ε) = 206 nm (4.29), 252 (3.73), 272 (3.71), 276 (3.76), 282 (3.74).

4.12 2-Azido-5-fluoro-1-methyl-1*H*-benzo[*d*]imidazole (22)

To a solution of the benzimidazole (**27**, 0.75 g, 5.0 mmol, 1.0 equiv.) in dry Et_2O (40 mL) under argon was added *n*-BuLi (1.6 M in *n*-hexane, 3.44 mL, 5.5 mmol, 1.1 equiv.) at –78°C. After 2 h, tosyl azide (1.085 g, 5.5 mmol, 1.1 equiv.) was added in one portion. After 3 h at –78°C the mixture was allowed to reach room temperature and stirred for additional 3 h. The reaction was quenched with an aqueous solution of $Na_4P_2O_7 \cdot 10\ H_2O$ (2.45 g, 5.5 mmol, 1.1 equiv., in 30 mL H_2O) and the mixture was stirred overnight. The organic phase was separated and the aqueous layer was extracted with *t*-BuOMe (3×). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated. Column chromatography [silica, petroleum ether/EtOAc (10:1)] afforded **22** (0.621 g, 3.3 mmol, 66%) as yellow solid. TLC [silica, petroleum ether/EtOAc (10:1)]: $R_f = 0.17$. Mp = 104–107°C. – ^{1}H NMR (600 MHz, [D_6]DMSO): $\delta = 7.49$ (dd, $J = 4.8$ Hz, $J = 8.8$ Hz, 1H, 7-*H*), 7.35 (ddd, $J = 0.3$ Hz, $J = 2.5$ Hz, $J = 9.7$ Hz, 1H, 4-*H*), 7.07 (ddd, $J = 2.5$ Hz, $J = 8.8$ Hz, $J = 9.9$ Hz, 1H, 6-*H*), 3.58 (s, 3H, NCH_3). – ^{13}C NMR (150 MHz, [D_6]DMSO): $\delta = 158.68$ (d, $J_{CF} = 234.4$ Hz, 1C, *C*-5), 148.82 (C_{qu}., 1C, *C*N$_3$), 141.28 (d, $J_{CF} = 13.2$ Hz, 1C, *C*-3a), 131.87 (1C, *C*-7a), 110.68 (d, $J_{CF} = 10.4$ Hz, 1C, *C*-7), 109.33 (d, $J_{CF} = 25.6$ Hz, 1C, *C*-6), 103.57 (d, $J_{CF} = 24.7$ Hz, 1C, *C*-4), 29.21 (1C, CN*C*H$_3$). – ^{19}F NMR (376 MHz, [D_6]DMSO): $\delta = -120.45$. – HRMS ((+)-ESI): *m/z* = 164.06131 (–3.3 ppm, calcd. 164.06185 for $[C_8H_7FN_3+H]^+$). – IR (diamond ATR): $\tilde{\nu} = 2268$ cm^{-1} (m), 2181 (m), 2135 (m), 1487 (s), 1431 (m), 1407 (m), 1259 (m), 1128 (s), 1093 (m), 955 (m), 855 (m), 792 (s), 689 (m), 671 (m), 639 (m), 612 (m), 548 (m). – UV (MeOH): λ_{max} (lg ε) = 204 nm (4.27), 231 (3.80), 292 (4.01).

4.13 2-Azido-6-fluoro-1-methyl-1*H*-benzo[*d*]imidazole (23)

To a solution of 6-fluoro-1-methyl-1*H*-benzo[*d*]imidazole (**28**, 2.37 g, 15.8 mmol) in dry Et_2O (130 mL) was added *n*-BuLi (1.6 M in *n*-hexane, 10.9 mL, 17.38 mmol, 1.1 equiv.) at –78°C under argon. After 2 h, tosyl azide (3.42 g, 17.38 mmol, 1.1 equiv.) was added in one portion. After 3 h at –78°C the mixture was allowed to reach room temperature and stirred for additional 3 h. The reaction was quenched with an aqueous solution of $Na_4P_2O_7 \cdot 10\ H_2O$ (7.75 g, 17.38 mmol, 1.1 equiv., in 60 mL H_2O) and stirred overnight. The organic phase was separated and the aqueous layer was extracted with *t*-BuOMe (3×). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated. Column chromatography [silica, petroleum ether/EtOAc (10:1)] afforded the product as a yellow solid (2.172 g, 11.38 mmol, 72%). TLC [silica, petroleum ether/EtOAc (10:1)]: $R_f = 0.29$. Mp = 113°C. – ^{1}H NMR (600 MHz, [D_6]DMSO): $\delta = 7.51$ (dd, $J = 4.8$ Hz, $J = 8.8$ Hz, 1H, 4-*H*), 7.42 (dd, $J = 2.5$ Hz, $J = 9.2$ Hz, 1H, 7-*H*), 7.04 (ddd, $J = 2.6$ Hz, $J = 8.8$ Hz, $J = 11.4$ Hz, 1H, 5-*H*), 3.55 (s, 3H, NCH_3). – ^{13}C NMR (150 MHz, [D_6]DMSO): $\delta = 158.27$ (d, $J_{CF} = 235.7$ Hz, 1C, *C*-6), 147.98 (d, $J_{CF} = 2.4$ Hz 1C, *C*-2), 137.35 (1C, *C*-3a), 135.39 (d, $J_{CF} = 13.9$ Hz, 1C, *C*-7a), 118.30 (d, $J_{CF} = 10.0$ Hz, 1C, *C*-4), 109.68 (d, $J_{CF} = 24.8$ Hz, 1C, *C*-5), 97.18 (d, $J_{CF} = 28.3$ Hz, 1C, *C*-7), 29.22 (1C, CN*C*H$_3$). – ^{19}F NMR (376 MHz, [D_6]DMSO): $\delta = -119.61$. – IR (diamond ATR): $\tilde{\nu} = 2170$ cm^{-1} (m), 2130 (s), 1627 (m), 1481 (s), 1438 (s), 1404 (s), 1263 (s), 1173 (s), 1135 (m), 1078 (m), 958 (m), 900 (w), 828 (s), 762 (m), 763 (s), 673 (s), 613 (s), 581 (m). – UV (MeOH): λ_{max} (lg ε) = 204 nm (4.39), 238 (3.96), 292 (4.13).

4.14 6-Chloro-5-fluoro-1-methyl-1*H*-benzo[*d*]imidazole-2-amine (36)

2-Azido-5-fluoro-1-methyl-1*H*-benzo[*d*]imidazole (**22**, 49 mg, 0.26 mmol, 1.0 equiv.) was added to a suspension of NH_4Cl (1.5 g) in MeOH (30 mL) under argon. At room temperature, the reaction mixture was irradiated for 2 h at $\lambda_{max} = 300$ nm (Rayonet apparatus). The solvent was evaporated under

reduced pressure. Saturated aqueous $NaHCO_3$ was added, the organic phase was collected, and the aqueous phase was extracted with EtOAc (3×75 mL). The combined organic phases were washed with brine and dried over $MgSO_4$, filtered, and concentrated. Column chromatography [silica, $CHCl_3$/MeOH (10:1)] afforded **36** as a beige solid (37 mg, 0.19 mmol, 73%). TLC [silica, $CHCl_3$/MeOH (10:1)]: R_f = 0.07. Mp ≥ 250°C. – ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 7.33 (d, J = 6.7 Hz, 1H, 6-*H*), 7.08 (d, ^3J = 10.4 Hz, 1H, 4-*H*), 6.70 (s, 2H, NC(N*H*$_2$)), 3.48 (s, 3H, NC*H*$_3$). – ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 157.25 (1C, N*H*$_2$), 152.84 (d, J_{CF} = 233.8 Hz, 1C, *C*-5), 142.22 (d, J_{CF} = 11.8 Hz, 1C, *C*-3a), 131.95 (1C, *C*-7a), 108.19 (d, J_{CF} = 20.2 Hz, 1C, *C*-6), 107.92 (1C, *C*-7), 101.98 (d, J_{CF} = 24.3 Hz, 1C, *C*-4), 28.67 (1C, N*C*H$_3$). – ^{19}F NMR (376 MHz, [D$_6$]DMSO): δ = –126.15. – ^{15}N NMR (by HMBC, [D$_6$]DMSO): δ = –321.2 (NC*N*H$_2$), –264.7 (C*N*CH$_3$), –187.2 (C*N*CNH$_2$). – HRMS ((+)-ESI): m/z = 222.02044 (–0.14 ppm, calcd. 222.02047 for [C$_8$H$_7$FN$_3$Cl+Na]$^+$). – IR (diamond ATR): $\tilde{\nu}$ = 3300–2800 cm^{-1} (br. w), 1651 (m), 1545 (m), 1489 (m), 1464 (m), 1431 (m), 1414 (m), 1150 (m), 1114 (w), 1094 (w), 1009 (m), 840 (s), 803 (m), 732 (m), 700 (m), 635 (w), 608 (m). – UV (MeOH): λ_{max} (lg ε) = 210 nm (4.47), 255 (3.89), 298 (4.03).

4.15 5-Fluoro-1-methyl-1*H*-benzo[*d*]imidazole-2-amine (32) and 6-bromo-5-fluoro-1-methyl-1*H*-benzo[*d*]imidazole-2-amine (33)

2-Azido-5-fluoro-1-methyl-1*H*-benzo[*d*]imidazole (**22**, 47 mg, 0.25 mmol, 1.0 equiv.) was added to a mixture of MeOH (10 mL) and aqueous HBr (48%, 40 equiv.) under argon. At room temperature, the reaction mixture was irradiated for 2 h at λ_{max} = 300 nm (Rayonet apparatus). After evaporation of the solvent, saturated aqueous $NaHCO_3$ was added until a pH of 8–9 was reached. The organic phase was collected and the aqueous phase was extracted with EtOAc (3×75 mL). The combined organic phases were washed with brine and dried over $MgSO_4$, filtered, and concentrated. Column chromatography [silica, $CHCl_3$/MeOH (10:1)] afforded a mixture of **32** and **33** (12:1, determined by ^{19}F NMR) as a beige solid (38 mg, 0.19 mmol). TLC [silica, $CHCl_3$/MeOH (10:1)]: R_f = 0.20. Mp = 163–166°C. – HRMS ((+)-ESI): m/z = 166.07756 (0.36 ppm, calcd. 166.07750 for [C$_8$H$_8$FN$_3$+H]$^+$), 188.05943 (–0.11 ppm, calcd. 188.05945 for [C$_8$H$_8$FN$_3$+Na]$^+$). – IR (diamond ATR): $\tilde{\nu}$ = 3200–2745 cm^{-1} (br. w), 1655 (m), 1541 (s), 1490 (s), 1478 (s), 1441 (m), 1417 (m), 1379 (m), 1131 (s), 959 (m), 907 (w) 836 (m), 787 (s), 720 (m), 607 (m), 582 (m), 561 (m). – UV (MeOH): λ_{max} (lg ε) = 207 nm (4.48), 250 (3.82), 289 (3.91). Compound **32**: ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 7.11 (dd, J = 4.8 Hz, J = 8.5 Hz, 1H, 7-*H*), 6.92 (dd, J = 2.5 Hz, J = 10.0 Hz, 1H, 4-*H*), 6.75 (s, 2H, NH$_2$), 6.73 (ddd, J = 2.5 Hz, J = 8.5 Hz, J = 11.0 Hz, 1H, 6-*H*), 3.49 (s, 3H, NC*H*$_3$). – ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 158.23 (d, J_{CF} = 231.3 Hz, 1C, *C*-5), 156.14 (1C, N*H*$_2$), 141.98 (d, J_{CF} = 13.9 Hz, 1C, *C*-3a), 131.11 (1C, *C*-7a), 107.57 (d, J_{CF} = 10.4 Hz, 1C, *C*-7), 104.88 (d, J_{CF} = 24.8 Hz, 1C, *C*-6), 100.75 (dd, J_{CF} = 3.3 Hz, J_{CF} = 25.3 Hz, 1C, *C*-4), 28.55 (1C, N*C*H$_3$). – ^{19}F NMR (376 MHz, [D$_6$]DMSO): δ = –122.85. – ^{15}N NMR (by HMBC, [D$_6$]DMSO): δ = –321.2 (NC*N*H$_2$), –265.3 (C*N*CH$_3$), –190.5 (C*N*CNH$_2$). Compound **33**: ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 7.43 (d, J = 6.3 Hz, 1H, 7-*H*), 7.07 (d, J = 10.0 Hz, 1H, 4-*H*), 6.72 (s, 2H, NH$_2$), 3.48 (s, 3H, NC*H*$_3$). – ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 157.67 (1C, N*H*$_2$, 153.67 (d, J_{CF} = 232.6 Hz, 1C, *C*-5), 143.14 (from HMBC 1C, *C*-3a), 131.56 (1C, *C*-7a), 110.39 (from HMBC, 1C, *C*-7), 101.94 (d, J_{CF} = 24.8 Hz, 1C, *C*-6), 95.59 (from HMBC, d, J_{CF} = 24.8 Hz, 1C, *C*-4), 28.65 (1C, N*C*H$_3$). – ^{19}F NMR (376 MHz, [D$_6$]DMSO): δ = –118.34.

4.16 5-Fluoro-*N*-methyl-2-nitroaniline (26)

Aqueous methylamine (40% in H_2O, 3.84 g) was added to 1,5-difluoro-2-nitrobenzene (**24**, 2.501 g, 15.7 mmol, 1.0 equiv.) at 0°C (N_2 atmosphere) over 15 min. The mixture was stirred for 90 min at 0°C and quenched with H_2O (50 mL). The precipitate was filtered affording the yellow product (2.644 g, 15.5 mmol, 99%). TLC [silica, $CHCl_3$/MeOH (15:1)]: R_f = 0.90. Mp = 105°C. – ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.32 (br. s, 1H, C-1N*H*CH$_3$), 8.16 (dd, J = 6.3 Hz, J = 9.5 Hz, 1H, 6-*H*), 6.77 (dd, J = 2.7 Hz, J = 12.3 Hz, 1H, 3-*H*), 6.52 (ddd, J = 2.7 Hz, J = 7.6 Hz, J = 9.5 Hz 1H, 4-*H*), 2.93 (d, J = 5.0 Hz, 3H, NHC*H*$_3$). – ^{13}C NMR (100 MHz, $CDCl_3$): δ = 166.91 (d, J_{CF} = 252.8 Hz, 1C, *C*-5), 148.04 (d, J_{CF} = 13.9 Hz 1C, *C*-1), 129.66 (d, J_{CF} = 12.8 Hz, 1C, *C*-3), 128.16 (s, 1C, *C*-2), 103.27 (d, J_{CF} = 25.2 Hz, 1C, *C*-4), 99.53 (d, J_{CF} = 27.3 Hz, 1C, *C*-6), 29.85 (s, 1C, NH*C*H$_3$). – ^{19}F NMR (376 MHz, $CDCl_3$): δ = – 99.53. – GC/MS (EI, 70 eV): t_R = 14.57 min (m/z (%) = 170.050 (100, [M]$^+$), calcd. 170.049 for [C$_7$H$_7$FN$_2$O$_2$]$^+$). – IR (diamond ATR): $\tilde{\nu}$ = 1632 cm^{-1} (m), 1575 (m), 1512 (m), 1450 (m), 1405 (m), 1343 (m), 1251 (m), 1218 (m), 1159 (m), 1083 (m), 1047 (m), 969 (m), 842 (s), 802 (m), 747 (s), 597 (m), 533 (s). – UV (MeOH): λ_{max} (lg ε) = 231 nm (4.31), 279 (3.64), 406 (3.81).

4.17 Irradiation of monofluorinated 2-azidobenzimidazole derivatives in HOAc/DCM (general procedure)

A solution of the starting material in HOAc/DCM (1:8, 18 mL) was irradiated (λ_{max} = 300 nm, Rayonet apparatus)

under argon for 2 h. Saturated aqueous $NaHCO_3$ was added, until a pH of 8–9 was reached. The organic phase was collected and the aqueous phase was extracted with EtOAc (3×75 mL). The combined organic phases were dried over $MgSO_4$, filtered, and concentrated. The crude product was purified by column chromatography.

4.18 2-Amino-4-fluoro-1-methyl-1*H*-benzo[*d*]imidazole-6-yl-acetate (29)

From 2-azido-4-fluoro-1-methyl-1*H*-benzo[*d*]imidazole (**11**, 58 mg, 0.30 mmol, 1.0 equiv.); column chromatography [silica, $CHCl_3$/MeOH (10:1)] afforded a red solid (45 mg, 0.20 mmol, 67%). TLC [silica, $CHCl_3$/MeOH (10:1)]: R_f = 0.24. Mp = 177–185°C. – ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 6.86 (d, J = 2.0 Hz, 1H, 7-*H*), 6.63 (dd, J = 2.1 Hz, J = 11.3 Hz, 1H, 5-*H*), 6.62 (br. s, 2H, NH_2), 3.48 (s, 3H, NCH_3), 2.25 (s, 3H, OCOCH_3). – ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 169.66 (1C, CO*C*OCH$_3$), 156.09 (1C, *C*-2), 149.37 (d, J_{CF} = 244.7 Hz, 1C, *C*-4), 142.45 (d, J_{CF} = 10.4 Hz, 1C, *C*-6), 137.30 (d, J_{CF} = 12.6 Hz, 1C, *C*-7a), 127.87 (d, J_{CF} = 16.2 Hz, 1C, *C*-3a), 101.47 (d, J_{CF} = 21.5 Hz, 1C, *C*-5), 98.36 (d, J_{CF} = 3.3 Hz, 1C, *C*-7), 28.91 (1C, NCH_3), 20.81 (1C, COCO*C*H$_3$). – ^{19}F NMR (376 MHz, [D$_6$]DMSO): δ = –131.94. MS (EI, 70 eV): m/z (%) = 224.1 (2), 223 (13) [M]$^+$, 182.1 (9), 181.1 (100), 180.1 (44), 153.1 (13), 82.9 (10). – HRMS ((+)-ESI): m/z = 224.08322 (–2.9 ppm, calcd. 224.08298 for [$C_{10}H_{10}FN_3O_2$+H]$^+$), 246.06518 (1.02 ppm, calcd. 246.06493 for [$C_{10}H_{10}FN_3O_2$+Na]$^+$). – IR (diamond ATR): $\tilde{\nu}$ = 3200–2748 cm^{-1} (br. w), 1739 (m), 1661 (m), 1600 (m) 1561 (m), 1487 (m), 1210 (s), 1104 (m), 1024 (m), 985 (m), 907 (m), 838 (m), 720 (m), 647 (m), 588 (m). – UV (MeOH): λ_{max} (lg ε) = 213 nm (4.63), 251 (3.85), 280 (3.72).

4.19 2-Amino-5-fluoro-1-methyl-1*H*-benzo[*d*]imidazol-6-yl-acetate (30)

From 2-azido-5-fluoro-1-methyl-1*H*-benzo[*d*]imidazole (**22**, 53 mg, 0.27 mmol); column chromatography [silica, $CHCl_3$/MeOH (10:1)] afforded an ochre solid (39 mg, 0.17 mmol, 61%). TLC [silica, $CHCl_3$/MeOH (10:1)]: R_f = 0.10. Mp = 170°C. – ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 7.06 (d, J = 7.0 Hz, 1H, 7-*H*), 7.02 (d, J = 11.2 Hz, 1H, 4-*H*), 6.56 (s, 2H, NH_2), 3.46 (s, 3H, NCH_3), 2.30 (s, 3H, OCOCH_3). – ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 169.00 (1C, CO*C*OCH$_3$), 156.92 (1C, *C*-2), 149.29 (d, J_{CF} = 234.2 Hz, 1C, *C*-5), 140.42 (d, J_{CF} = 11.9 Hz, 1C, *C*-3a), 130.77 (1C, C-7a), 129.76 (d, J_{CF} = 15.6 Hz, 1C, *C*-6), 102.20 (1C, *C*-7), 101.45 (d, $^2J_{CF}$ = 21.9 Hz, 1C, *C*-4), 28.61 (1C, NCH_3), 20.27 (1C, COCO*C*H$_3$). – ^{19}F NMR (376 MHz, [D$_6$]DMSO): δ = –139.22. – ^{15}N NMR (by HMBC, [D$_6$]DMSO): δ = –322.4 (NC*N*H$_2$), –264.3 (C*N*CH$_3$), –186.8 (C*N*CNH$_2$). – HRMS ((+)-ESI): m/z = 224.08308 (0.44 ppm, calcd. 224.08298 for [$C_{10}H_{10}FN_3O_2$+H]$^+$), 447.15901 (0.70 ppm, calcd. 447.15869 for [$C_{20}H_{20}F_2N_6O_4$+H]$^+$), 469.14087 (0.51 ppm, calcd. 469.14063 for [$C_{20}H_{20}F_2N_6O_4$+Na]$^+$). – IR (diamond ATR): $\tilde{\nu}$ = 3300–2748 cm^{-1} (br. w), 1750 (m), 1685 (m), 1664 (m), 1552 (m), 1493 (m), 1468 (m), 1369 (m), 1212 (vs), 1177 (s), 1148 (s), 1096 (m), 940 (m), 904 (m), 843 (m), 779 (m), 540 (m). – UV (MeOH): λ_{max} (lg ε) = 207 nm (4.46), 249 (3.78), 293 (3.96).

4.20 2-Amino-7-fluoro-1-methyl-1*H*-benzo[*d*]imidazole-6-yl-acetate (31)

From 2-azido-7-fluoro-1-methyl-1*H*-benzo[*d*]imidazole (**12**, 47 mg, 0.25 mmol); column chromatography [silica, $CHCl_3$/MeOH (8:1)] afforded a brown solid (40 mg, 0.18 mmol, 72%). TLC [silica, $CHCl_3$/MeOH (8:1)]: R_f = 0.38. Mp = 182°C. – ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 6.90 (d, J = 8.4 Hz, 1H, 4-*H*), 7.73 (dd, J = 8.4 Hz, J = 7.5 Hz 1H, 5-*H*), 6.60 (s, 2H, NH_2), 3.64 (s, 3H, NCH_3), 2.30 (s, 3H, OCOCH_3). – ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 168.93 (1C, CO*C*OCH$_3$), 156.41 (1C, *C*-2), 143.50 (d, J_{CF} = 3.8 Hz, 1C, *C*-3a), 139.28 (d, J_{CF} = 244.9 Hz, 1C, *C*-7), 129.68 (d, J_{CF} = 11.1 Hz, 1C, *C*-6), 121.93 (d, J_{CF} = 5.3 Hz, 1C, *C*-7a), 114.57 (1C, *C*-5), 110.02 (d, J_{CF} = 2.7 Hz, 1C, *C*-4), 30.50 (1C, NCH_3), 20.25 (1C, COCO*C*H$_3$). – ^{19}F NMR (376 MHz, [D$_6$]DMSO): δ = –155.56. – ^{15}N NMR (by HMBC, [D$_6$]DMSO): δ = –323.1 (NC*N*H$_2$), –265.5 (C*N*CH$_3$), –185.4 (C*N*CNH$_2$). – HRMS ((+)-ESI): m/z = 224.08319 (0.90 ppm, calcd. 224.08298 for [$C_{10}H_{10}FN_3O_2$+H]$^+$), 447.15899 (0.67 ppm, calcd. 447.15869 for [$C_{20}H_{20}F_2N_6O_4$+H]$^+$), 469.14102 (0.83 ppm, calcd. 469.14063 for [$C_{20}H_{20}F_2N_6O_4$+Na]$^+$). – IR (diamond ATR): $\tilde{\nu}$ = 3326 cm^{-1} (br. w), 3305-2737 (br. w), 1750 (m), 1660 (m), 1556 (m), 1502 (m), 1456 (m), 1367 (m), 1299 (m), 1206 (vs), 1123 (m), 1090 (m), 1054 (m), 1020 (m), 904 (m), 819 (m), 744 (m), 704 (m), 727 (w), 638 (m). – UV (MeOH): λ_{max} (lg ε) = 217 nm (4.36), 250 (3.92), 280 (3.71).

4.21 (*S*)-2-Amino-5-fluoro-1-methyl-1*H*-benzo[*d*]imidazole-6-yl-2-(*tert*-butoxycarbonyl)amino)- 3,3-dimethylbutanoate (34)

A solution of 2-azido-5-fluoro-1-methyl-1*H*-benzo[*d*]imidazole (**22**, 30 mg, 0.16 mmol, 1.0 equiv.) and Boc-L-*tert*-Leu (0.148 g, 0.64 mmol, 4.0 equiv.) in DCM (10 mL) was irradiated (λ_{max} = 300 nm, Rayonet apparatus) under argon for 2 h. The solvent was evaporated and saturated aqueous

$NaHCO_3$ was added. The organic phase was collected and the aqueous phase was extracted with EtOAc (3×75 mL). The combined organic phases were washed with brine, dried over $MgSO_4$, filtered, and concentrated. Column chromatography [silica, $CHCl_3$/MeOH (10:1)] afforded a beige solid (**34**, 57 mg, 0.14 mmol, 88%). TLC [silica, $CHCl_3$/MeOH (10:1)]: R_f = 0.22. Mp = 205°C (decomp.). $[\alpha]_D^{21}$ = +10.2 (*c* 0.57, DMSO). – ^{1}H NMR (600 MHz, [D_6]DMSO): δ = 7.37 (d, *J* = 8.5 Hz, 1H, N*H*COOC(CH_3)$_3$), 7.03 (d, *J* = 11.1 Hz, 1H, 4-*H*), 6.94 (d, *J* = 6.8 Hz, 1H, (CH_3)NCC*H*COCOCH), 6.60 (s, 2H, N*H*$_2$), 4.11 (d, *J* = 8.5 Hz, 1H, (CH_3)$_3$COOCNHC*H*COOCCF), 3.47 (br. s, 3H, NC*H*$_3$), 1.43 (s, 9H, CHNHCOOC(C*H*$_3$)$_3$), 1.07 (s, 9H, FCCOCOCHC(C*H*$_3$)$_3$). – ^{13}C NMR (150 MHz, [D_6]DMSO): δ = 169.98 (1C, FCCO*C*OCHC(CH_3)$_3$), 163.07 (1C, CHNH*C*OOC(CH_3)$_3$), 156.92 (1C, *C*-2), 149.17 (d, J_{CF} = 234.7 Hz, 1C, *C*-5), 140.46 (from HMBC, d, J_{CF} = 6.7 Hz, 1C, *C*-3a), 130.76 (1C, *C*-7a), 129.48 (d, J_{CF} = 16.0 Hz, 1C, *C*-6), 101.85 (1C, *C*-7), 101.53 (d, J_{CF} = 22.0 Hz, 1C, *C*-4), 78.48 (1C, CHNHCOO*C*(CH_3)$_3$), 62.78 (1C, FCC(OCO*C*HC(CH_3)$_3$)), 33.61 (1C, CFC(OCOCH*C*(CH_3)$_3$)), 28.66 (1C, NCH_3), 28.20 (3C, CHNHCOOC(*C*H_3)$_3$), 26.59 (3C, CFC(OCOCHC(*C*H_3)$_3$)). – ^{19}F NMR (376 MHz, [D_6]DMSO): δ = –137.63. – ^{15}N NMR (by HMBC, [D_6]DMSO): δ = –322.2 (NC*N*H$_2$), –293.0 (CH*N*HBoc), –264.3 (C*N*CH$_3$), –187.6 (C*N*CNH$_2$). – HRMS ((+)-ESI): *m*/*z* = 395.20901 (0.25 ppm, calcd. 395.20891 for [$C_{19}H_{27}FN_4O_4$+H]$^+$), 417.19092 (0.17 ppm, calcd. 417.19085 for [$C_{19}H_{27}FN_4O_4$+Na]$^+$), 811.39241 (–0.10 ppm, calcd. 811.39249 for [$C_{38}H_{54}F_2N_8O_8$+Na]$^+$). – IR (diamond ATR): $\tilde{\nu}$ = 3337–3000 cm^{-1} (br. w), 1764 (m), 1695 (m), 1546 (m), 1493 (m), 1466 (m), 1367 (m), 1341 (m), 1245 (m), 1165 (vs), 1061 (m). – UV (MeOH): λ_{max} (lg ε) = 207 nm (4.49), 250 (3.79), 293 (4.01).

4.22 2-Amino-5-fluoro-1-methyl-1*H*-benzo[*d*]imidazole-6-yl-pivalate (35)

A solution of 2-azido-5-fluoro-1-methyl-1*H*-benzo[*d*]imidazole (**22**, 52 mg, 0.27 mmol) and pivalic acid (2 mL, 1.82 g, 17.8 mmol) in DCM (12 mL) was irradiated (λ_{max} = 300 nm, Rayonet apparatus) under argon for 2 h. The solvent was evaporated and saturated aqueous $NaHCO_3$ was added. The organic phase was collected and the aqueous phase was extracted with EtOAc (3×75 mL). The combined organic phases were washed with brine, dried over $MgSO_4$, filtered, and concentrated. The crude product was purified by column chromatography [silica, $CHCl_3$/MeOH (10:1)] affording **35** as a brown solid (68 mg, 0.185 mmol, 70%). TLC [silica, $CHCl_3$/MeOH (10:1)]: R_f = 0.17. Mp = 210–214°C. – ^{1}H NMR (600 MHz, [D_6]DMSO): δ = 7.04 (d, *J* = 7.0 Hz, 1H, 7-*H*), 7.01 (d, *J* = 11.1 Hz, 1H, 4-*H*), 6.56 (s, 2H, N*H*$_2$), 3.47 (s, 3H, NC*H*$_3$), 1.32 (s, 9H, OCOC(C*H*$_3$)$_3$). – ^{13}C NMR (150 MHz, [D_6]DMSO): δ = 176.23 (1C, CO*C*OC(CH_3)$_3$), 156.85 (1C, *C*-2), 149.26 (d, J_{CF} = 254.0 Hz, 1C, *C*-5), 140.32 (d, J_{CF} = 11.8 Hz, 1C, *C*-3a), 130.77 (1C, *C*-7a), 130.05 (d, J_{CF} = 15.6 Hz, 1C, *C*-6), 102.18 (1C, *C*-7), 101.43 (d, J_{CF} = 21.8 Hz, 1C, *C*-4), 38.54 (1C, C(OCO*C*(CH_3)$_3$), 28.64 (1C, NCH_3), 26.82 (3C, C(OCOC(*C*H_3)$_3$). – ^{19}F NMR (376 MHz, [D_6]DMSO): δ = –139.86. – ^{15}N NMR (by HMBC, [D_6]DMSO): δ = –322.6 (NC*N*H$_2$), –264.1 (C*N*CH$_3$), –186.8 (C*N*CNH$_2$). – HRMS ((+)-ESI): *m*/*z* = 266.13009 (0.61 ppm, calcd. 266.12993 for [$C_{13}H_{16}FN_3O_2$+H]$^+$), 288.11187 (0.00 ppm, calcd. 288.11187 for [$C_{13}H_{16}FN_3O_2$+Na]$^+$), 553.23453 (0.00 ppm, calcd. 553.23453 for [$C_{26}H_{32}F_2N_6O_4$+Na]$^+$). – IR (diamond ATR): $\tilde{\nu}$ = 3300–3300 cm^{-1} (br. w), 1751 (m), 1659 (m), 1616 (w), 1554 (m), 1502 (m), 1477 (m), 1278 (m), 1232 (m), 1206 (m), 1175 (m), 1152 (m), 1119 (vs), 1102 (s), 1026 (m), 894 (m), 864 (m), 808 (m), 774 (m), 628 (m), 554 (m). – UV (MeOH): λ_{max} (lg ε) = 207 nm (4.39), 249 (3.71), 293 (3.90).

4.23 Irradiation of 22 in the presence of Boc-protected amino acids (general procedure)

A solution of 2-azido-5-fluoro-1-methyl-1*H*-benzo[*d*]imidazole (**22**, 1.0 equiv.) and the Boc-protected amino acid (4.0 equiv.) in DCM (20 mL) and *t*-BuOH (1 mL) was irradiated (λ_{max} = 300 nm, Rayonet apparatus) under argon for 2 h. The solvent was evaporated and the residue was dissolved in EtOAc. The organic phase was washed with saturated aqueous $NaHCO_3$ (3×) and brine, dried over $MgSO_4$, filtered, and concentrated. The crude product was purified by column chromatography [silica, $CHCl_3$/MeOH (10:1)].

4.24 2-Amino-5-fluoro-1-methyl-1*H*-benzo[*d*]imidazole-6-yl (*tert*-butoxycarbonyl) glycinate (37)

From **22** (47 mg, 0.25 mmol, 1.0 equiv.) and Boc-Gly-OH (0.175 g, 1.00 mmol); beige solid (55 mg, 0.16 mmol, 64%). TLC [silica, $CHCl_3$/MeOH (10:1)]: R_f = 0.15. Mp = 73°C. – ^{1}H NMR (600 MHz, [D_6]DMSO): δ = 7.43 (t, *J* = 6.2 Hz, 1H, COCOCH$_2$-N*H*CO), 7.05 (d, *J* = 7.0 Hz, 1H, 7-*H*), 7.03 (d, *J* = 11.1 Hz, 1H, 4-*H*), 6.58 (s, 2H, N*H*$_2$), 4.00 (d, *J* = 6.2 Hz, 2H, NCCHCOCOC*H*$_2$), 3.46 (s, 3H, NC*H*$_3$), 1.42 (s, 9H, OCOC(C*H*$_3$)$_3$). – ^{13}C NMR (150 MHz, [D_6]DMSO): δ = 169.23 (1C, CO*C*OC(CH_3)$_3$), 156.97 (1C, *C*-2), 155.83 (1C, NH*C*OOC(CH_3)$_3$), 149.15 (d, J_{CF} = 234.7 Hz, 1C, *C*-5), 140.52 (d, J_{CF} = 12.3 Hz, 1C, *C*-3a), 130.76 (1C, *C*-7a), 129.47 (d, J_{CF} = 15.7 Hz, 1C, *C*-6), 102.03 (1C, *C*-7), 101.48 (d, $^2J_{CF}$ = 21.6 Hz, 1C, *C*-4), 78.44 (1C, NHCOO*C*(CH_3)$_3$), 41.69 (1C, NCHCOC-O*C*H$_2$NH), 28.64 (1C, NCH_3), 26.14 (3C, NHCOOC(CH_3)$_3$).

– ^{19}F NMR (376 MHz, [D$_6$]DMSO): δ = –138.95. – ^{15}N NMR (by HMBC, [D$_6$]DMSO): δ = –322.4 (NC*N*H$_2$), –303.1 (CH$_2$*N*HCOO), –264.1 (C*N*CH$_3$), –187.2 (C*N*CNH$_2$). – HRMS ((+)-ESI): m/z = 339.14670 (1.15 ppm, calcd. 339.14631 for [C$_{15}$H$_{19}$FN$_4$O$_4$+H]$^+$), 361.12832 (0.19 ppm, calcd. 361.12825 for [C$_{15}$H$_{19}$FN$_4$O$_4$+Na]$^+$), 699.26731 (0.01 ppm, calcd. 699.26729 for [C$_{30}$H$_{38}$F$_2$N$_8$O$_8$+Na]$^+$). – IR (diamond ATR): $\tilde{\nu}$ = 3300–3200 cm^{-1} (br. w), 1686 (m), 1557 (m), 1493 (m), 1462 (m), 1287 (m), 1256 (m), 1142 (vs), 1052 (m), 1029 (m), 776 (m), 624 (m), 546 (m). – UV (MeOH): λ_{max} (lg ε) = 202 nm (4.39), 241 (3.69), 300 (3.91).

4.25 2-Amino-5-fluoro-1-methyl-1*H*-benzo[*d*]imidazole-6-yl (*tert*-butoxycarbonyl) alaninate (38)

From **22** (48 mg, 0.25 mmol 1.0 equiv.) and Boc-Ala-OH (0.189 g, 1.00 mmol); brown solid (65 mg, 0.18 mmol, 72%). TLC [silica, CHCl$_3$/MeOH (10:1)]: R_f = 0.20. – $[\alpha]_D^{23}$ = –3.8 (*c* 1.40, DMSO). Mp = 119°C. – ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 7.52 (d, *J* = 7.3 Hz, 1H, COCOCHN*H*CO), 7.02 (d, *J* = 11.0 Hz, 1H, 4-*H*), 7.01 (d, *J* = 7.0 Hz, 1H, 7-*H*), 6.58 (s, 2H, N*H*$_2$), 4.30 (qu, ^{3}*J* = 7.3 Hz, 1H, NCCHCOCOC*H*CH$_3$), 3.47 (s, 3H, NC*H*$_3$), 1.43 (s, 3H, CFCOCOCHC*H*$_3$), 1.41 (s, 9H, OCOC(C*H*$_3$)$_3$). – ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 171.97 (1C, CO*C*OC(CH$_3$)$_3$), 156.93 (1C, *C*-2), 155.28 (1C, NH*C*OOC(CH$_3$)$_3$), 149.16 (d, J_{CF} = 235.1 Hz, 1C, *C*-5), 140.45 (d, J_{CF} = 11.7 Hz, 1C, *C*-4), 130.74 (1C, *C*-7a), 129.69 (d, J_{CF} = 15.4 Hz, 1C, NCCH*C*OC-OCH), 101.97 (1C, *C*-7), 101.50 (d, J_{CF} = 21.9 Hz, 1C, *C*-4), 78.36 (1C, NHCOO*C*(CH$_3$)$_3$), 49.02 (1C, NCCHCOCO*C*HNH), 28.65 (1C, NC*H*$_3$), 28.17 (3C, NHCOOC(CH$_3$)$_3$) 16.9 (1C, CFCOC-OCH*C*H$_3$). – ^{19}F NMR (376 MHz, [D$_6$]DMSO): δ = –139.22. – ^{15}N NMR (by HMBC, [D$_6$]DMSO): δ = –322.2 (NC*N*H$_2$), –288.3 (CH*N*HCOO), –264.1 (C*N*CH$_3$), –187.2 (C*N*CNH$_2$). – HRMS ((+)-ESI): m/z = 706.31724 (0.85 ppm, calcd. 706.31664 for [C$_{32}$H$_{42}$F$_2$N$_8$O$_8$+H]$^+$), 727.29861 (0.03 ppm, calcd. 727.29859 for [C$_{32}$H$_{42}$F$_2$N$_8$O$_8$+Na]$^+$). – IR (diamond ATR): $\tilde{\nu}$ = 3300–3200 cm^{-1} (br. w), 1683 (s), 1491 (m), 1462 (m), 1290 (m), 1254 (m), 1144 (s), 1050 (m), 1025 (m), 777 (m), 699 (m). – UV (MeOH): λ_{max} (lg ε) = 203 nm (4.40), 242 (3.68), 299 (3.94).

4.26 2-Amino-5-fluoro-1-methyl-1*H*-benzo[*d*]imidazole-6-yl (*tert*-butoxycarbonyl)-L-valinate (39)

From **22** (49 mg, 0.26 mmol, 1.0 equiv.) and Boc-Val-OH (0.226 g, 1.04 mmol); brown solid (59 mg, 0.16 mmol, 62%). TLC [silica, CHCl$_3$/MeOH (10:1)]: R_f = 0.18. – $[\alpha]_D^{23}$ = –1.1 (*c* 2.3, DMSO). Mp = 63–65°C. – ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 7.42 (d, *J* = 8.2 Hz, 1H, COCOCHN*H*CO), 7.03 (d, *J* = 11.1 Hz, 1H, NCC*H*CF), 6.96 (d, *J* = 6.9 Hz, 1H, 7-*H*), 6.57 (s, 2H, N*H*$_2$), 4.14 (dd, *J* = 6.3 Hz, *J* = 8.1 Hz, 1H, NCCHCOC-OC*H*CH), 3.47 (s, 3H, NC*H*$_3$), 2.16 (m, 1H, C*H*(CH$_3$)$_2$), 1.42 (s, 9H, C(C*H*$_3$)$_3$), 1.01 (d, *J* = 2.7 Hz, 3H, COCOCHC(C*H*$_3$)$_2$), 1.00 (d, *J* = 2.7 Hz, 3H, COCOCHC(C*H*$_3$)$_2$). – ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 170.65 (1C, CO*C*OC(CH$_3$)$_3$), 156.98 (1C, *C*-2), 155.85 (1C, NH*C*OOC(CH$_3$)$_3$), 149.17 (d, J_{CF} = 234.6 Hz, 1C, *C*-5), 140.58 (d, J_{CF} = 11.9 Hz, 1C, *C*-3a), 130.79 (1C, *C*-7a), 129.49 (d, J_{CF} = 15.8 Hz, 1C, *C*-6), 101.90 (1C, *C*-7), 101.52 (d, J_{CF} = 21.8 Hz, 1C, *C*-4), 78.40 (1C, NHCOO*C*(CH$_3$)$_3$), 59.44 (1C, NCCHCOCO*C*HNH), 29.71 (1C, NCCHCOCOCH*C*H(CH$_3$)$_2$), 28.66 (1C, NC*H*$_3$), 28.19 (3C, NHCOOC(C*H*$_3$)$_3$), 18.98 (1C, NCCHCOCOCHCH(C*H*$_3$)$_2$), 18.23 (1C, CH(C*H*$_3$)$_2$). – ^{19}F NMR (376 MHz, [D$_6$]DMSO): δ = –138.48. – ^{15}N NMR (by HMBC, [D$_6$]DMSO): δ = –322.4 (NC*N*H$_2$), –293.5 (CH*N*HCOO), –264.1 (C*N*CH$_3$), –186.8 (C*N*CNH$_2$). – HRMS ((+)-ESI): m/z = 381.19354 (0.73 ppm, calcd. 381.19326 for [C$_{18}$H$_{25}$FN$_4$O$_4$+H]$^+$), 403.17535 (0.37 ppm, calcd. 403.17520 for [C$_{18}$H$_{25}$FN$_4$O$_4$+Na]$^+$), 783.36122 (0.04 ppm, calcd. 783.36119 for [C$_{36}$H$_{50}$F$_2$N$_8$O$_8$+Na]$^+$). – IR (diamond ATR): $\tilde{\nu}$ = 3340–3200 cm^{-1} (br. w), 1685 (s), 1487 (m), 1460 (m), 1294 (m), 1250 (m), 1140 (s), 1048 (m), 1025 (m), 780 (m), 701 (m). – UV (MeOH): λ_{max} (lg ε) = 202 nm (4.50), 247 (3.25), 295 (3.48).

4.27 2-Amino-5-fluoro-1-methyl-1*H*-benzo[*d*]imidazole-6-yl (*tert*-butoxycarbonyl)-L-phenylalaninate (40)

From **22** (46 mg, 0.24 mmol, 1.0 equiv.) and Boc-Phe-OH (0.255 g, 0.96 mmol); red solid (59 mg, 0.14 mmol, 58%). TLC [silica, CHCl$_3$/MeOH (10:1)]: R_f = 0.30. – $[\alpha]_D^{24}$ = +1.9 (*c* 2.6, DMSO). Mp = 81°C. – ^{1}H NMR (600 MHz, [D$_6$]DMSO): δ = 7.57 (d, *J* = 8.1 Hz, 1H, COCOCHN*H*CO), 7.39–7.31 (m, 5H, COC-OCHCH$_2$C$_6$*H*$_5$), 7.04 (d, *J* = 11.0 Hz, 1H, 4-*H*), 6.89 (d, *J* = 6.9 Hz, 1H, 7-*H*), 6.62 (s, 2H, N*H*$_2$), 4.47 (ddd, *J* = 5.0 Hz, *J* = 8.1 Hz, *J* = 13.2 Hz, 1H, NCCHCOCOC*H*CH$_2$), 3.47 (s, 3H, NC*H*$_3$), 3.21 (dd, *J* = 5.0 Hz, *J* = 13.8 Hz, 1H, NCCHCOCOCHC*H*$_2$Ph), 3.04 (dd, *J* = 10.4 Hz, *J* = 13.8 Hz, 1H, NCCHCOCOCHC*H*$_2$Ph), 1.35 (s, 9H, OCOC(C*H*$_3$)$_3$). – ^{13}C NMR (150 MHz, [D$_6$]DMSO): δ = 170.89 (1C, CO*C*OC(CH$_3$)$_3$), 156.90 (1C, *C*-2), 155.50 (1C, NH*C*OOC(CH$_3$)$_3$), 149.20 (d, J_{CF} = 235.1 Hz, 1C, *C*-5), 140.40 (d, J_{CF} = 11.6 Hz, 1C, *C*-3a), 137.36 (1C, CHCOCOCHCH$_2$*C*), 130.70 (1C, *C*-7a), 129.62 (d, J_{CF} = 15.7 Hz, 1C, C-6OCOCH), 129.25 (2C, CHCOCOCHCH$_2$C(CH)$_2$(*C*H)$_2$), 128.29 (2C, CHCOCOCHCH$_2$ C(*C*H)$_2$(CH)$_2$), 126.60 (1C, CHCOCOCHCH$_2$C(CH)$_2$(CH)$_2$*C*H), 101.90 (1C, *C*-7), 101.50 (d, $^2J_{CF}$ = 21.7 Hz, 1C, *C*-4), 78.50 (1C, NHCOO*C*(CH$_3$)$_3$), 55.30 (1C, NCCHCOCO*C*HNH), 36.38 (1C, NCCHCOCOCH*C*H$_2$C), 28.70 (1C, NC*H*$_3$), 28.10 (3C, NHCOOC(*C*H$_3$)$_3$). – ^{19}F NMR (376 MHz, [D$_6$]DMSO): δ = –138.71.

– ^{15}N NMR (by HMBC, [D$_6$]DMSO): $\delta = -322.0$ (NC*N*H$_2$), –291.2 (CH*N*HCOO), –264.3 (C*N*CH$_3$), –187.8 (C*N*CNH$_2$). – HRMS ((+)-ESI): $m/z = 429.19350$ (–1.07 ppm, calcd. 429.19396 for [$C_{22}H_{45}FN_4O_4$+H]$^+$). – IR (diamond ATR): $\tilde{\nu} = 3178–2930$ cm^{-1} (br. w), 1693 (m), 1648 (m), 1546 (m), 1493 (m), 1459 (m), 1145 (s), 1051 (w), 774 (m). – UV (MeOH): λ_{max} (lg ε) = 202 nm (4.64), 245 (3.76), 298 (3.99).

5 Supplementary Information

Irradiation experiments with the 4- and 7-fluorinated 2-azidobenzimidazole derivatives **11** and **12** are described in the Supplementary Information. The ^{1}H, ^{13}C, and ^{19}F NMR spectra of selected compounds are included (available online, DOI: 10.1515/znb-2016-0195).

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