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Synthesis, Stability, and Photoreactivity of Diazirinyl-Substituted *N*-Heterocycles Based on Indole, Benzimidazole, and Imidazole

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The synthesis, thermal stability, and photoreactivity of trifluoromethyl diazirines installed at the heterocyclic section of *N*-methylindole, *N*-methylbenzimidazole, and at *N*-methylimidazole were investigated. *N*-Tosyl-3-diazirinylindole and *N*-methyl-2-diazirinylbenzimidazole proved to be thermally stable, whereas the corresponding 2-diazirinylindole was not. The least stable was 2-diazirinylimidazole, which underwent rapid decomposition. Quenching with ethanol indicated that the corresponding carbene was formed. Decomposition is rationalized by exothermic coarctate ring-opening of the carbene. Quantum mechanical calculations [B3LYP/6-311G(2d,2p)] predict singlet ground states of all carbenes. Accordingly, Friedel–Crafts alkylation products were formed on irradiation (350 nm, Rayonet) of the *N*-methylbenzimidazole-based diazirine in the presence of phenol.

Introduction

The photoreactive heterocycle 3*H*-diazirine constitutes a key structural element of tags and building blocks used for photoaffinity labeling (PAL).[1–4] Among diazirine-functionalized amino acids, photophenylalanine had long been the only option.[5] The set of amino acid-derived diazirines was widened by the introduction of L-photoleucine, *rac*-photoisoleucine/*rac*-photo-*allo*-isoleucine, L-photomethionine,[6] L-photolysine,[7] and L-photoproline.[8] However, all of the latter share an α-hydrogen, which can undergo a 1,2-shift after the carbene has been formed, resulting in an unreactive olefin. Diazirinyl substitution of *N*-heterocyclic side chains of proteinogenic amino acids have only recently been investigated and led to the invention of stable photo-tryptophans by Murai et al.[9] and by us,[10] in which a trifluoromethyl-diazirinyl moiety is installed in the 5- or 6-position of the indole ring. Until today, there have been no investigations on the introduction of a diazirinyl unit at the enamine portion of indole. The imidazole ring of histidine has also not been diazirinylated. Studies on heterocycles with (trifluoromethyl)diazirinyl substituents in the α-position of the heteroatom appear to be restricted to thiophene[11] and benzothiophene[12] derivatives. There are also stable β-diazirinylated heterocycles, including thiophene[13] and pyrazole.[14]

We now report the synthesis, thermal stability, and photoreactivity of indoles, *N*-methylbenzimidazole, and *N*-methylimidazole that bear a diazirinyl unit in the 2-position (Figure 1). The synthesis of a 3-diazirinylindole is also included. The stability of the diazirines was investigated and how they reacted under irradiation conditions. DFT calculations were performed to determine the preferred spin ground states.

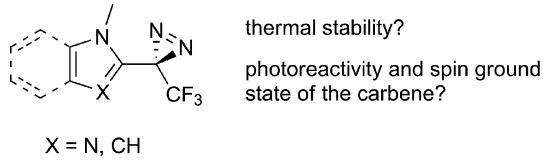

Figure 1. Subject of study.

Results and Discussion

Installation of the (trifluoromethyl)diazirinyl moiety began with trifluoroacetylation of the respective positions of indole, benzimidazole, and imidazole. After conversion to the oxime and *O*-tosylation, the diaziridines were formed, followed by oxidation to the diazirines.

Indole

In the case of indole, the 2-position of *N*-(*tert*-butoxycarbonyl)indole (**1a**) was trifluoroacetylated after *ortho*-lithiation (*t*BuLi) to afford ketone **2a**,[15] followed by deprotection to **2c**[16] and conversion to oxime **3a** (Scheme 1). *O*-Tosylation of **3a** worked, but subsequent treatment with liquid ammonia afforded diaziridine **4a** in only 8% yield,

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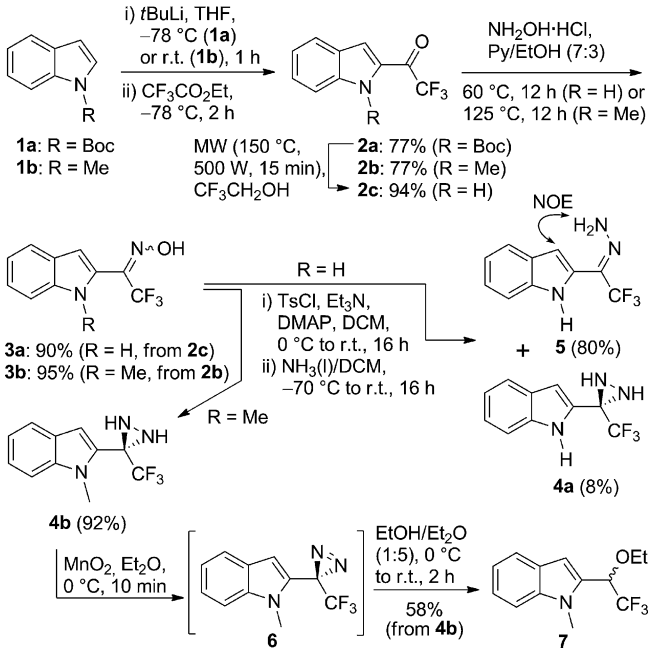
with the main product being the isomeric (*E*)-hydrazone **5** (80%, configuration confirmed by NOE correlation between the NH_2 group and indole 3-H).

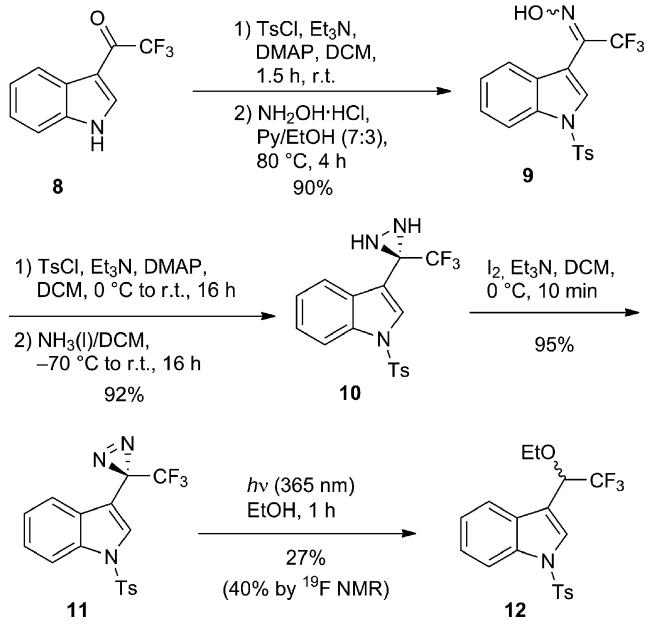


Scheme 1. Synthesis of thermally labile 2-diazirinylindole **6** and its decomposition to ethoxy compound **7**.

Thus, we turned to *N*-methylindole (**1b**) as starting point, which was trifluoroacetylated in the 2-position (**2b**) and reacted to oxime **3b** by treatment with hydroxylamine (Scheme 1). Tosylation of *N*-methylindole-derived oxime **3b** (*E*/*Z*, 95:5) by employing tosylchloride (TsCl)/NEt_3/catalytic 4-(dimethylamino)pyridine (DMAP) was followed by clean conversion to stable diaziridine **4b** with liquid ammonia (–78 °C to room temp.) in CH_2Cl_2 (92% over 2 steps). According to TLC monitoring, oxidation of **4b** to the diazirine with I_2/NEt_3 in CH_2Cl_2 or pyridinium chlorochromate in CH_2Cl_2/pyridine at 0 °C was a spot-to-spot conversion. However, on work-up diazirine **6** started to decompose even at room temperature. Formation of **6** was deduced after immediate quenching of a sample obtained by heterogeneous oxidation of diaziridine **4b** with MnO_2 in Et_2O with EtOH at 0 °C.[9] Stable ethoxy derivative **7** was isolated in 58% yield, referred to diaziridine **4b**.

Scheme 2 shows the synthesis of regioisomeric 1-tosyl-3-diazirinylindole **11**, which was accessible in five steps starting from 3-trifluoroacetylindole (**8**).[17] *N*-Tosylation of **8**, which preceded installation of the oxime unit, afforded intermediate **9**. Diaziridine **10** was obtained after tosylation of **9** and reaction with liquid ammonia (92%).

Irradiation of **11** in EtOH (λ_{max} 365 nm, 1 h) afforded ether **12** in 27% isolated yield (40% of the total ^{19}F NMR integral) aside from decomposed material. Without irradiation, diazirine **11** did not react with EtOH at room temperature even after several days.



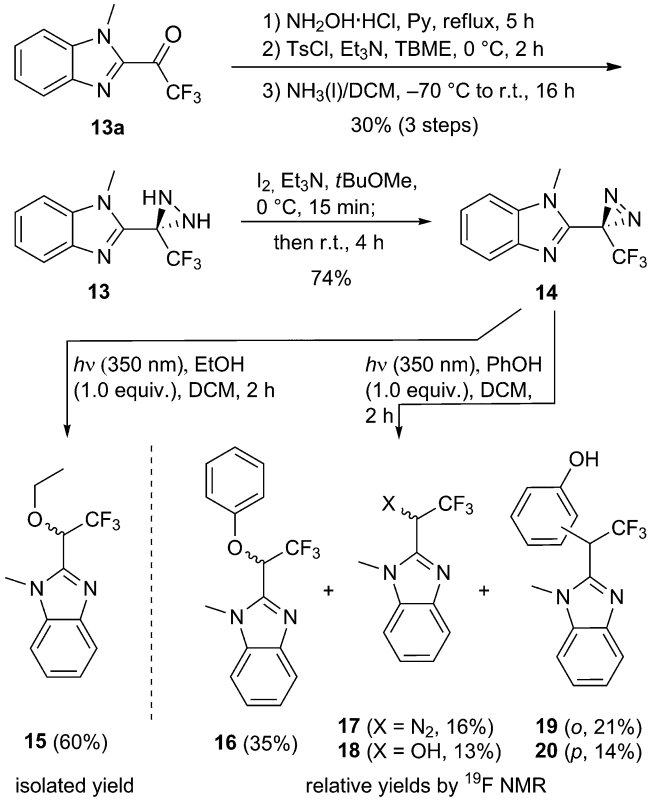
Scheme 2. Synthesis of thermally stable *N*-tosylated 3-diazirinylindole **11** and photoreaction in EtOH.

N-Methylbenzimidazole

We wondered whether replacement of C3 of indole-based diazirine **6** would alter the stability. Thus, diazirinyl benzimidazole **14** was synthesized from the known ketone **13a**[18] in four steps through diaziridine **13** by following the standard protocol (Scheme 3). X-ray analysis of diaziridine **13** revealed that the N–N bond (152 pm) is situated almost parallel to the ring plane of the imidazole section (Figure 2).[19]

In contrast to its indole analog, *N*-methylbenzimidazole-based diazirine **14** proved to be stable up to 88 °C, according to DSC measurements. This put us into the position to investigate the photoreactivity of **14** in more detail. Photoreaction of *N*-methylbenzimidazole-based diazirine **14** in EtOH (350 nm, Rayonet) was slow and ethoxy adduct **15** formed as the only product (46% after 2 h, Scheme 3). Interestingly, the reaction was faster and gave a higher yield (60% isolated yield, **15**) in CH_2Cl_2 (10 mM) in the presence of only one equivalent of EtOH. We observed a similar effect of CH_2Cl_2 in the photoreaction of phototryptophan.[10]

Diazirine **14** was also irradiated in the presence of PhOH (1 equiv., 10 mM) in CH_2Cl_2 to provide a comparison with our recent study on the reactivity of (*p*-methoxyphenyl)trifluoromethyl carbene.[20] We identified five major products (Scheme 3), besides traces of unidentified signals in the ^{19}F NMR spectrum. Aryl ether **16** was dominant (35% relative yield by ^{19}F NMR), followed by *o*- and *p*-alkylated phenol derivatives (**19**, 21%, and **20**, 14%). In addition, we observed hydroxylated product **18** (13% relative yield), which was also synthesized for comparison. Diazo derivative **17** (16% relative yield) gave a characteristic signal at –55.8 ppm (assigned by 2D NMR experiments, see the Supporting Information).



Scheme 3. Synthesis of benzimidazole-based diazirine **14** and photoreactions in the presence of EtOH and PhOH. For compounds **16**–**20**, relative yields are given, obtained by integration of the ^{19}F NMR spectrum. TBME = *tert*-butyl methyl ether.

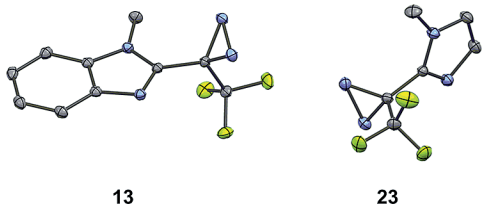
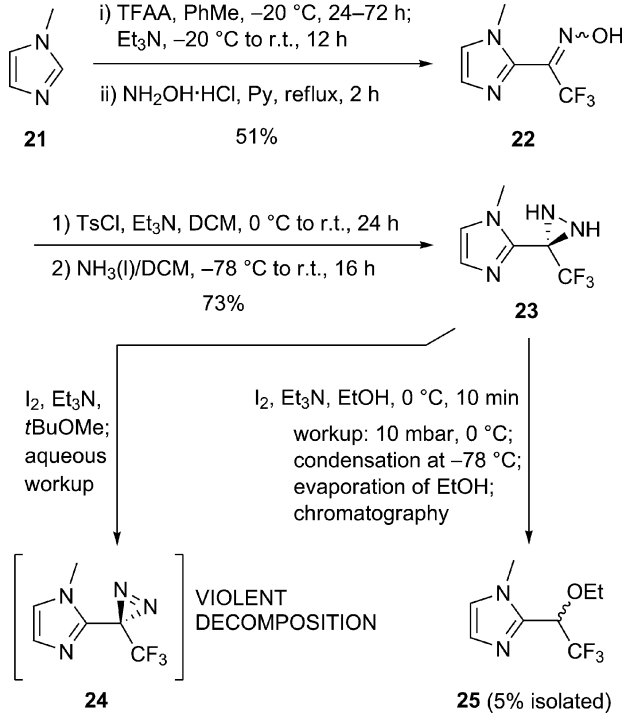


Figure 2. Structures of diaziridines **13** and **23** (one of two independent molecules) in the crystal.[19] Hydrogen atoms have been omitted for clarity.

N-Methylimidazole

In the case of *N*-methylimidazole we were only able to reach diaziridine (**23**, Scheme 4). *N*-Methylimidazole (**21**) was treated with trifluoroacetic anhydride (TFAA)/NEt_3,[18] to avoid 2-lithiation, and the resulting ketone was converted into oxime **22** without prior purification (51%). Tosylation of **22** with TsCl and NEt_3 and treatment with liquid ammonia afforded **23** (73% over 2 steps; X-ray structure,[19] see Figure 2). Compound **23** and benzimidazole-based analog **13** constitute the first diaziridines with two unsubstituted nitrogens for which X-ray analyses have been obtained.[21] CAUTION: After oxidation of diaziridine **23** (I_2/NEt_3, *t*BuOMe, TLC monitoring), extraction of the reaction mixture with aqueous $Na_2S_2O_3$ (0.2 M)/citric acid (0.2 M), and removal of the solvent from the dried organic phase, the resulting crude product underwent violent decomposition with self-ignition. Thus, imidazole-based diazirine **24** will probably not be suitable as a partial structure of a photohistidine.



Scheme 4. Synthesis and oxidation of imidazole diaziridine **23**.

As for *N*-methylindole-derived diazirine **6** (Scheme 1), it was possible to trap *N*-methylimidazole-based diazirine **24** under thermal conditions without irradiation, in much lower yield. We oxidized diaziridine **23** in EtOH instead of *t*BuOMe at 0 °C (I_2/NEt_3, 10 min). The solution was condensed in a cooling trap at –78 °C, warmed to room temperature overnight, and subjected to column chromatography after evaporation of EtOH. The volatile EtOH adduct **25** of the carbene was the only isolable product (5%, δ_F = –75.0 ppm, CF_3; δ_H = 5.03 ppm, q, $^3J_{FH}$ 7.4 Hz, *H*COEt, both in $CDCl_3$). Decay of diazirine **24** in EtOH appears to follow first order kinetics at room temperature (see the Supporting Information). Diaziridine **23** was treated with I_2/NEt_3 in EtOH at 0 °C and, after dilution at 0 °C, UV/Vis spectra were recorded every 5 min at constant 25 °C without prior workup. Figure 3 shows the decay of the long-wave diazirine absorption band at 359 nm and the formation of a new, more intense band with a final maximum at 269 nm. The product mixture generated by the decay of **24** was investigated also by GC/EIMS and by ^{19}F NMR spectroscopy, which indicated formation of ether **25** as the major product (28% by ^{19}F NMR integration). The rising band at 269 nm is not caused by **25** and we were not able to isolate any product corresponding to that band. It might be speculated that the diazo compound, which is isomeric to diazirine **24**, causes the absorption at 269 nm. Diederich had reported absorption bands around 270 nm for aryl(trifluoromethyl)diazomethanes.[22] However, in the

^{19}F NMR spectrum of the mixture formed after decay in EtOH, we did not observe a signal of the diazo compound, which appeared at δ = –56 ppm for benzimidazole-based compound **17**. Another possibility could be the formation of an azine with a ^{19}F NMR chemical shift expected at around –67 ppm,[20] and we indeed observed a signal in the crude mixture. The constantly intense band at λ_{max} 220 nm could be caused by iodide formed by reduction of iodine.

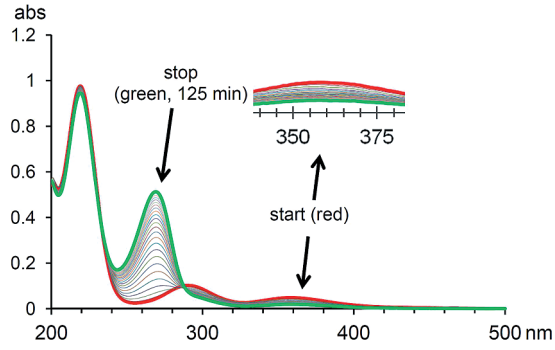


Figure 3. Thermal decay of diazirine **24** in EtOH (32 µm, 25 °C) after oxidation with I_2/NEt_3, monitored by UV/Vis spectroscopy.

DFT Calculations

Interested in the preferred spin states of our carbenes, we performed a DFT study at the B3LYP/6-311G(2d,2p) level of theory (PCM model for solvent effects, Gaussian09[23]). We found that all carbenes derived from diazirines **6**, **14**, and **24** exhibit singlet ground states in the gas phase, in CH_2Cl_2, and MeOH. Relative to the triplet state, the singlet carbenes derived from **6**, **14**, and **24** are stabilized by 7.0, 2.4, and 7.9 kcal/mol in the gas phase, respectively. This makes it likely that the first reaction of any of the above carbenes in the presence of Brønsted acids will be their protonation to the carbenium ion. Earlier, we investigated the reaction of singlet (*p*-methoxyphenyl)(trifluoromethyl)-carbene in the presence of phenol, which involves protonation, followed by nucleophilic attack of phenolate at the resultant carbenium ion, as shown by deuteration experiments.[20] A similar mechanism may lead to the formation of phenol adducts **16**, **19**, and **20**. EtOH is less acidic than phenol, but should still be able to protonate the singlet carbenes derived from **6**, **14**, and **24**, which suggests the mechanism of formation of adducts **7**, **15**, and **25**.

We also employed quantum chemical calculations [B3LYP/6-311G(2d,2p)] for an orienting analysis of the thermal stability of diazirines **6**, **14**, **24**, to address the decay of the diazirine, and possible subsequent reactions of the carbene.

Diazirines react to the carbene either directly or through a diazo intermediate. There is a comprehensive review by Korneev on the matter.[24] For the benzimidazole-based diazo compound **17** high stability can be expected, because we were able to isolate it as a mixture with compound **19**. Although we cannot exclude that diazo compounds derived from diazirines **6** and **24** would show similar stability, we focused on the direct decay of diazirines **6**, **14**, **24** to corresponding carbenes **6b**, **14b**, **24b** (Figure 4). Our calculations [B3LYP/6-311G(2d,2p)] reveal that the relative energy of the resulting singlet carbenes, relative to their parent diazirines, increases following the order **6b** < **24b** < **14b**. Taking into account the formation of one molecule of dinitrogen leads to product combinations showing similar energies as the starting diazirines. The rise in entropy by converting one molecule into two will result in a clearly negative free reaction enthalpy. Transition states **6a**, **14a**, **24a** are passed with activation energies of 19.4, 22.9, and 21.0 kcal/mol, respectively, which indicated that the compounds should barely be isolable at room temperature. The highest barrier was calculated for benzimidazole-based diazirine **14**, which was the most stable in our experiments. The lowest barrier was calculated for indole-based diazirine **6**. All transition states display one elongated C–N bond.

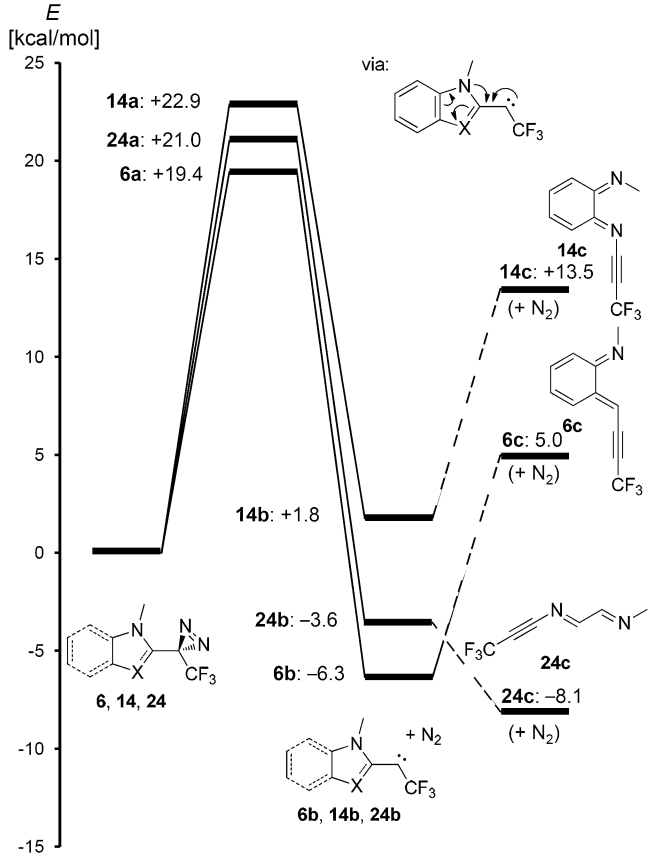


Figure 4. Calculated relative energies at the B3LYP/6-311G(2d,2p) level of theory. The energy of diazirine starting materials **6**, **14**, and **24** was always set to zero. The calculated energies of the **b** and **c** series include the energy of dinitrogen.

Coarctate ring-opening of the carbenes would afford azaxylylene **6c**, diazaxylylene **14c**, and diimine **24c** (Figure 4). That type of reaction is known to proceed through low barriers (3–5 kcal/mol).[25] Sheridan et al. proposed similar open-chain products formed from 2-diazirinyl-benzothiophenes.[12] According to our calculations, only the reaction of carbene **24b** to *transoid* diimine **24c** is exothermic (–4.5 kcal/mol). Coarctate ring-opening of carbenes **6b**

(+11.3 kcal/mol) and **14b** (+11.7 kcal/mol) is endothermic, presumably because the aromatic character of their benzoid systems is lost. We expect diimine **24c** to react exothermically and fuel further thermal decomposition of diazirine **24**. Only in the presence of protic solvents may the cycle be stopped by formation of carbene adducts such as **25**.

Conclusions

We investigated the synthesis, thermal stability, and photoreactivity of diazirinyl-substituted derivatives of the heterocycles indole and imidazole, which occur in the side chains of the amino acids tryptophan and histidine. Before this study, neither diazirinyl-substituted imidazoles were known, nor indoles carrying a trifluoromethyl diazirinyl unit in the enamine portion. Only phototryptophans carrying a trifluoromethyldiazirinyl moiety at the benzene portion of the indole side-chain have been reported recently.[9,10]

We obtained thermally stable diazirines only in two cases: 3-diazirinylated *N*-tosylated indole (**11**) and 2-diazirinylated benzimidazole (**14**). In the case of *N*-unsubstituted 2-diazirinylindole, even the synthesis of precursor diaziridine **4a** proved difficult, and provided mainly hydrazone **5** instead. We would not have predicted the thermal instability of 2-diazirinylated *N*-methylindole (**6**) and *N*-methylimidazole (**24**). In particular, 2-diazirinylimidazole **24** showed violent decomposition on attempts to isolate solid material. At least in the case of the benzimidazole-derived diazirine, isomeric diazo compound **17** proved to be sufficiently thermally stable to be isolated. Based on our experimental study it can be stated that 2- and 3-substituted indoles are expected to be thermally less stable than 5- and 6-(trifluoromethyl)diazirinyl indoles.[9,10]

For all four diazirines, EtOH adducts of the corresponding carbenes were obtained, either thermally at room temperature or after irradiation. We found alkylation of the phenol hydroxy group and the *o*- and *p*-positions, but not the *m*-position on irradiation of **14** in the presence of phenol. This suggests protonation of a singlet carbene to the carbenium ion, followed by Friedel–Crafts alkylation of phenol. We observed this behavior for the singlet (*p*-methoxyphenyl)(trifluoromethyl) carbene.[20] DFT calculations predict that all of carbenes resulting from nitrogen loss prefer a singlet ground state.

The violent decomposition of diazirine **24** can be rationalized by the exothermal, low barrier coarctate ring-opening of carbene **24a** to reactive *N*-alkynyldiazadiene **24c**, as indicated by DFT calculations. Benzimidazole-based diazirine **14**, which is thermally stable up to 80 °C, proved to be the most suitable singlet carbene source, which we will now explore further with respect to photoaffinity labeling.

Experimental Section

General: NMR spectra were recorded with a Bruker DPX-200 (200 MHz for ^{1}H, 188 MHz for ^{19}F), a Bruker AV II-300 (300 MHz for ^{1}H, 75 MHz for ^{13}C), a Bruker DRX 400 or a Bruker AV III-400 (400 MHz for ^{1}H, 100 MHz for ^{13}C, 376 MHz for ^{19}F) and a Bruker AV-II 600 (600 MHz for ^{1}H, 150 MHz for ^{13}C) spectrometer at 299 K. Chemical shifts are given in ppm (δ scale) and referenced to tetramethylsilane or the residual solvent peak. Mass spectra were obtained with a LTQ Orbitrap Velos, a Thermo Finnigan LTQ FT, a Thermo Finnigan MAT95 and a Finnigan MAT 95 XLT. GC–MS was performed with an Agilent Technologies 6890 gas chromatograph by using a Phenomenex ZB5-MS 0.25 μm column (internal diameter: 0.25 mm, length: 30 m) and a JMST100GC (GCAccuTOF, JEOL, Japan) apparatus at 70 eV (EI). IR spectra were recorded with a Bruker Tensor 27 spectrometer. UV/Vis spectra were measured with a Varian Cary 100 Bio UV/Vis spectrometer. Melting points were measured with a Büchi 530 melting point apparatus. Microwave reactions were performed with a MLS START 1500 microwave synthesizer in a sealed tube (max. 20 mL). The instrument consists of a continuous-focus microwave power delivery system with selectable power output from 0–1200 W. The reaction temperature was monitored by an IR sensor. Irradiations were carried out in a Rayonet Photochemical Reactor© (RPR-200), which was equipped with eight RPR-3500 Å lamps (350 nm emission maximum) or eight UV-A lamps (Philips Actinic BL TL 8 W/10 1 FM, 350–400 nm) and an operating fan (temperature approximately 30 °C). The glass jars were made of borosilicate glass, if not stated otherwise. Chemicals were purchased from commercial suppliers and used without further purification. Solvents were dried prior to use by using standard methods, unless otherwise noted. Flash column chromatography was performed on Merck silica gel 60 (40–63 μm) and Merck RP-18 silica gel (40–63 μm). TLC was done on Merck silica gel 60 F_{254} and Merck silica gel 60 RP-18 F_{254S} aluminum sheets. HPLC separations were carried out with a Merck Hitachi intelligent pump, fitted with a Phenomenex Luna C 18(2) 5 μm column.

***tert*-Butyl 2-(2,2,2-Trifluoroacetyl)-1*H*-indole-1-carboxylate (2a):** To a well-stirred solution of 1-Boc-indole (**1a**, 8.48 g, 39.03 mmol) in anhydrous tetrahydrofuran (THF; 100 mL) under Ar at –78 °C was added *t*BuLi (1.9 M in pentane, 23.6 mL, 44.88 mmol, 1.15 equiv.) carefully through a syringe. After being stirred at –78 °C for 1 h ethyl trifluoroacetate (7.43 mL, 62.45 mmol, 1.6 equiv.) was added dropwise through a syringe and the reaction mixture was stirred for further 2 h at the same temperature. The reaction was quenched with NH_4Cl solution (25% aq., 100 mL) and the mixture was extracted with *t*BuOMe (2× 60 mL). The combined organic phase was dried with $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash chromatography (petroleum ether/CH_2Cl_2, 5:1) to obtain compound **2a** as a colorless oil (9.40 g, 77%), which crystallized during storage in a freezer and afforded a colorless solid. R_f = 0.48 (petroleum ether/CH_2Cl_2, 5:1), m.p. 29–30 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.62 (s, 9 H, CH_3 *t*Bu), 7.32 (ddd, J = 8.1, 7.3, 0.9 Hz, 1 H, 5-H), 7.45 (m, 1 H, 3-H), 7.52 (ddd, J = 8.5, 7.2, 1.2 Hz, 1 H, 6-H), 7.69 (ddd, J = 8.0, 0.9 Hz, 1 H, 4-H), 8.09 (dd, J = 8.6, 0.8 Hz, 1 H, 7-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 27.77 (3× CH_3 *t*Bu), 85.97 (C_q *t*Bu), 115.05 (*C*-7), 119.67 (q, $^4J_{CF}$ = 3.1 Hz, *C*-3), 116.36 (q, $^1J_{CF}$ = 290.2 Hz, *C*F$_3$), 123.56 (*C*-4), 124.15 (*C*-5), 127.20 (*C*-3a), 129.35 (*C*-6), 130.96 (*C*-2), 139.34 (*C*-7a), 149.14 (N*C*O$_2$), 174.06 (q, $^2J_{CF}$ = 37.2 Hz, *C*OCF$_3$) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –73.91 (s, CF_3) ppm. IR (ATR): $\tilde{\nu}$ = 3134 (w), 2988 (w), 2937 (w), 1737 (m), 1698 (m), 1612 (w), 1517 (m), 1477 (w), 1455 (w), 1388 (m), 1356 (m), 1315 (s), 1292 (s), 1265 (m), 1226 (m), 1203 (m), 1157 (s), 1128 (s), 1102 (s), 1015 (w), 990 (s), 946 (w), 891 (m), 873 (w), 847 (s), 814 (w), 744 (s), 723 (m), 678 (w), 614 (m), 577 (m), 542 (m) cm^{-1}. UV (MeOH):

λ_{max} (log ε) = 202 nm (4.16), 222 (4.17), 311 (4.15). HRMS (EI): calcd. for $C_{15}H_{14}F_3NO_3$ $[M]^+$ 313.0920; found 313.0923.

2,2,2-Trifluoro-1-(1-methyl-1*H*-indol-2-yl)ethan-1-one (2b): To a well-stirred solution of 1-methylindole (**1b**, 2.40 g, 18.30 mmol) in anhydrous THF (60 mL) under Ar at room temperature was added *t*BuLi (1.9 M in pentane, 11.1 mL, 21.04 mmol, 1.15 equiv.) carefully through a syringe. After being stirred at room temperature for 1 h the mixture was cooled to –78 °C, followed by dropwise addition of ethyl trifluoroacetate (3.5 mL, 29.27 mmol, 1.6 equiv.) through a syringe. The reaction mixture was stirred and warmed to –50 °C within 2 h, then quenched with NH_4Cl solution (25% aq., 60 mL) and extracted with *t*BuOMe (2× 50 mL). The combined organic phase was dried with $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash chromatography (petroleum ether/CH_2Cl_2, 5:1) to obtain title compound **2b** as a light yellow solid (3.20 g, 77%). R_f = 0.53 (petroleum ether/CH_2Cl_2, 5:1), m.p. 84–85 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 4.08 (s, 3 H, NC*H*$_3$), 7.19 (ddd, *J* = 8.0, 6.8, 1.0 Hz, 1 H, 5-H), 7.40 (dd, *J* = 8.6, 0.9 Hz, 1 H, 7-H), 7.44–7.49 (m, 1 H, 6-H), 7.57 (dd, *J* = 1.9, 0.6 Hz, 1 H, 3-H), 7.73 (ddd, *J* = 8.1, 0.9, 0.9 Hz, 1 H, 4-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 32.36 (N*C*H$_3$), 110.55 (*C*-7), 116.74 (q, $^4J_{CF}$ = 4.2 Hz, *C*-3), 116.86 (q, $^1J_{CF}$ = 290.6 Hz, *C*F$_3$), 121.72 (*C*-5), 124.04 (*C*-4), 125.95 (*C*-3a), 128.16 (*C*-2), 128.32 (*C*-6), 141.43 (*C*-7a), 173.23 (q, $^2J_{CF}$ = 35.8 Hz, *C*OCF$_3$) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –71.35 (s, C*F*$_3$) ppm. IR (ATR): $\tilde{\nu}$ = 3135 (w), 3063 (w), 2948 (w), 1673 (s), 1615 (m), 1512 (m), 1463 (m), 1426 (w), 1401 (w), 1359 (m), 1331 (w), 1291 (m), 1241 (w), 1210 (m), 1138 (s), 1120 (s), 1100 (s), 949 (m), 891 (w), 821 (w), 800 (w), 743 (s), 726 (s), 617 (m), 588 (m), 544 (w) cm^{-1}. UV (MeOH): λ_{max} (log ε) = 205 nm (4.34), 238 (3.97), 323 (4.23). HRMS (EI): calcd. for $C_{11}H_8F_3NO$ $[M]^+$ 227.0553; found 227.0550.

2,2,2-Trifluoro-1-(1*H*-indol-2-yl)ethan-1-one (2c): A solution of *N*-Boc protected indole **2a** in trifluoroethanol (15 mL) was heated in a sealed tube under microwave conditions (150 °C, 500 W) for approx. 15 min. After cooling to room temperature, the reaction mixture was evaporated to dryness under reduced pressure. The residue was purified by flash chromatography (petroleum ether/CH_2Cl_2, 1:1) to afford **2c** (3.03 g, 94%) as a yellow solid. R_f = 0.37 (petroleum ether/CH_2Cl_2, 1:1), m.p. 124–125 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.21 (ddd, *J* = 8.1, 4.7, 3.2 Hz, 1 H, 5-H), 7.44–7.47 (m, 2 H, 6-H, 7-H), 7.54 (m, 1 H, 3-H), 7.76 (dd, *J* = 8.2, 0.9 Hz, 1 H, 4-H), 9.26 (br. s, 1 H, 1-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 112.51 (*C*-7), 115.47 (q, $^4J_{CF}$ = 3.4 Hz, *C*-3), 116.88 (q, $^1J_{CF}$ = 288.6 Hz, *C*F$_3$), 122.19 (*C*-5), 124.24 (*C*-4), 127.62 (*C*-3a), 128.70 (*C*-2), 128.96 (*C*-6), 138.94 (*C*-7a), 173.21 (q, $^2J_{CF}$ = 37.1 Hz, *C*OCF$_3$) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –72.47 ppm. IR (ATR): $\tilde{\nu}$ = 3348 (s), 1661 (s), 1620 (m), 1571 (w), 1521 (m), 1502 (m), 1440 (w), 1419 (w), 1353 (w), 1330 (w), 1290 (m), 1225 (m), 1194 (m), 1129 (s), 1024 (s), 945 (w), 906 (m), 822 (m), 770 (m), 747 (s), 726 (s), 629 (s), 602 (m), 578 (s) cm^{-1}. UV (MeOH): λ_{max} (log ε) = 205 nm (4.36), 211 (4.35), 238 (3.78), 272 (3.60), 281 (3.63), 290 (3.64), 324 (4.11). HRMS (EI): calcd. for $C_{10}H_6F_3NO$ $[M]^+$ 213.0396; found 213.0395.

2,2,2-Trifluoro-1-(1*H*-indol-2-yl)ethan-1-one Oxime (3a): To a solution of the 2-trifluoroacetylindole **2c** (3.00 g, 14.07 mmol) in pyridine (60 mL) and EtOH (25 mL) was added hydroxylamine hydrochloride (1.17 g, 16.89 mmol, 1.2 equiv.) and the mixture was stirred at 60 °C for approx. 12 h. After complete conversion of the starting material the reaction mixture was cooled to room temperature and the solvents were removed in vacuo. The residue was treated with *t*BuOMe (50 mL) and washed with water (2× 50 mL) and brine (50 mL), then dried with $MgSO_4$ and concentrated under reduced pressure. Flash chromatography (pure CH_2Cl_2) of the residue gave title compound **3a** (2.90 g, 90%) as a colorless solid. R_f = 0.32 (pure CH_2Cl_2), m.p. 188–192 °C. ^{1}H NMR (400 MHz, [D$_6$]-DMSO): δ = 6.96 (s, 1 H, 3-H), 7.09 (ddd, *J* = 8.0, 7.0, 1.0 Hz, 1 H, 5-H), 7.25 (ddd, *J* = 8.2, 7.0, 1.2 Hz, 1 H, 6-H), 7.64 (d, *J* = 8.3 Hz, 1 H, 7-H), 7.67 (dd, *J* = 8.0, 0.8 Hz, 1 H, 4-H), 11.65 (br. s, 1 H, 1-H), 13.40 (br. s, 1 H, O*H*) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 105.83 (*C*-3), 112.76 (*C*-7), 120.15 (*C*-5), 121.31 (*C*-4), 121.43 (q, $^1J_{CF}$ = 274.1 Hz, *C*F$_3$), 122.89 (*C*-2), 124.08 (*C*-6), 125.88 (*C*-3a), 136.87 (*C*-7a), 137.55 (q, $^2J_{CF}$ = 30.9 Hz, *C*NOH) ppm. ^{19}F NMR (376 MHz, [D$_6$]DMSO): δ = –63.08 (s, C*F*$_3$) ppm. IR (ATR): $\tilde{\nu}$ = 3463 (w), 3202 (w), 3117 (w), 2924 (w), 1651 (w), 1620 (w), 1516 (w), 1455 (w), 1435 (w), 1408 (w), 1344 (m), 1324 (w), 1285 (w), 1223 (m), 1188 (w), 1160 (w), 1131 (s), 1053 (m), 973 (s), 932 (m), 896 (w), 845 (w), 800 (m), 730 (s), 657 (m), 612 (m), 565 (w) cm^{-1}. UV (MeOH): λ_{max} (log ε) = 204 nm (4.35), 227 (4.10), 238 (4.13), 309 (4.33). HRMS (ESI): calcd. for $C_{10}H_7F_3N_2O$ $[M + H]^+$ 229.0583; found 229.0584.

2,2,2-Trifluoro-1-(1-methyl-1*H*-indol-2-yl)ethan-1-one Oxime (3b): To a solution of the 2-trifluoroacetylindole **2b** (2.20 g, 9.68 mmol) in pyridine (35 mL) and EtOH (15 mL) was added hydroxylamine hydrochloride (3.36 g, 48.42 mmol, 5.0 equiv.) and the mixture was heated to reflux for approx. 10 h. After complete conversion of the starting material the reaction mixture was cooled to room temperature and the solvents were removed in vacuo. The residue was treated with *t*BuOMe (50 mL) and washed with water (2× 50 mL) and brine (50 mL), then dried with $MgSO_4$ and concentrated under reduced pressure. Flash chromatography (pure CH_2Cl_2) of the residue gave title compound **3b** (2.23 g, 95%) as a colorless solid. R_f = 0.39 (pure CH_2Cl_2), m.p. 135–138 °C. ^{1}H NMR (400 MHz, $CDCl_3$, *E*/*Z*-isomers): δ = 3.65 and 3.75 ppm (s, 3 H, NC*H*$_3$), 6.75 and 6.84 (d, *J* = 0.8 Hz, 1 H, 3-H), 7.15 and 7.16 (ddd, *J* = 8.0, 6.8, 1.2 Hz, 1 H, 5-H), 7.28–7.34 (m, 1 H, 6-H), 7.32 and 7.36 (dd, *J* = 8.3, 0.9 Hz, 1 H, 7-H), 7.64 and 7.66 (ddd, *J* = 8.0, 0.9, 0.9 Hz, 1 H, 4-H), 8.91 and 8.98 (br. s, 1 H, NO*H*) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, *E*/*Z*-isomers): δ = 31.60 and 31.66 (N*C*H$_3$), 104.79 and 107.37 (*C*-3), 109.88 (*C*-7), 120.20 (q, $^1J_{CF}$ = 273.9 Hz, *C*F$_3$), 120.37 and 120.45 (*C*-5), 121.65 and 121.80 (*C*-4), 123.70 and 123.99 (*C*-6), 123.95 (*C*-2), 126.80 and 127.02 (*C*-3a), 138.23 and 138.77 (*C*-7a), 142.07 and 142.60 (q, $^2J_{CF}$ = 32.0,/34.3 Hz, *C*NOH) ppm. ^{19}F NMR (376 MHz, $CDCl_3$, *E*/*Z*-isomers): δ = –63.70, –68.42 (s, C*F*$_3$) ppm. IR (ATR): $\tilde{\nu}$ = 3241 (w), 2952 (w), 1613 (w), 1516 (w), 1465 (m), 1444 (m), 1398 (m), 1351 (w), 1295 (m), 1238 (w), 1183 (m), 1133 (s), 1008 (m), 956 (s), 843 (w), 805 (m), 728 (s), 650 (m), 614 (w), 582 (w), 564 (w) cm^{-1}. UV (MeOH): λ_{max} (log ε) = 217 nm (4.49), 298 (4.01). HRMS (ESI): calcd. for $C_{11}H_9F_3N_2O$ $[M + H]^+$ 243.0740; found 243.0741.

2-(2,2,2-Trifluoro-1-hydrazonoethyl)-1*H*-indole (5): To a stirred solution of the oxime **3a** (2.75 g, 12.05 mmol) and NEt_3 (2.5 mL, 18.08 mmol, 1.5 equiv.) in CH_2Cl_2 (60 mL) was added tosyl chloride (2.53 g, 13.26 mmol, 1.1 equiv.) portion-wise at 0 °C, followed by DMAP (147 mg, 1.21 mmol, 0.1 equiv.). The reaction mixture was stirred at room temperature for approx. 16 h, then cooled to 0 °C and quenched with water (60 mL). The phases were separated and the aqueous phase was extracted with CH_2Cl_2 (2× 30 mL). The combined organic extracts were dried with $MgSO_4$ and concentrated under reduced pressure to give the crude product, which was used without further purification directly for the next step. An analytical sample was purified by column chromatography (petroleum ether/CH_2Cl_2, 60:40) to confirm the structure of the corresponding tosyl oxime and was a light brown solid. R_f = 0.48 (petroleum ether/ CH_2Cl_2, 1:1). ^{1}H NMR (400 MHz, $CDCl_3$, *E*/*Z*-iso-

mers): δ = 2.44 and 2.47 ppm (s, 3 H, CH_3), 7.10–7.24 (m 2 H, 5-*H*, 3-H), 7.30–7.43 (m, 3 H, 6-H, $H_{m\text{-aryl}}$), 7.49–7.55 (m, 1 H, 7-H), 7.62 and 7.69 (ddd, *J* = 8.1, 0.8 Hz, 1 H, 4-H), 7.93 and 7.97 (ddd, *J* = 8.5, 1.9 Hz, 2 H, $H_{o\text{-aryl}}$), 9.15 and 9.58 (br. s, 1 H, 1-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$, major isomer): δ = 21.80 (*C*H$_3$), 112.09 (*C*-7), 112.78 (q, $^4J_{CF}$ = 2.9 Hz, *C*-3), 120.02 (q, $^1J_{CF}$ = 278.1 Hz, *C*F$_3$), 121.65 (*C*-5), 122.68 (*C*-4), 124.08 (*C*-2), 126.07 (*C*-3a), 127.09 (*C*-6), 129.51 (2 × *C*H$_{o\text{-aryl}}$), 129.93 (2 × *C*H$_{m\text{-aryl}}$), 130.66 ($C_{aryl}SO_3$), 137.85 (*C*-7a), 144.19 (q, $^2J_{CF}$ = 33.0 Hz, *C*NOTos), 146.50 ($C_{p\text{-aryl}}$) ppm. ^{19}F NMR (376 MHz, $CDCl_3$, *E*/*Z*-isomers): δ = –62.50 and –63.91 (s, C*F*$_3$) ppm. IR (ATR): $\tilde{\nu}$ = 3426 (w), 3061 (w), 1672 (w), 1602 (w), 1527 (w), 1508 (w), 1415 (w), 1371 (m), 1325 (w), 1287 (w), 1225 (w), 1197 (m), 1180 (m), 1164 (m), 1137 (s), 1091 (m), 1032 (m), 948 (w), 880 (m), 819 (m), 771 (m), 731 (m), 715 (s), 658 (m), 626 (m), 545 (s) cm^{-1}. UV (MeOH): λ_{max} (log ε) = 202 nm (4.46), 221 (4.27), 323 (4.30). HRMS (ESI): calcd. for $C_{17}H_{13}F_3N_2O_3S$ [M + Na]$^+$ 405.0491; found 405.0493.

To a cooled flask containing liquid ammonia (approx. 180 mL) at –70 °C was added a solution of the crude tosyloxime (obtained in the step before) in CH_2Cl_2 (30 mL) and the mixture was stirred for 8 h at this temperature. The ammonia was then allowed to evaporate allowing the solution to warm to room temperature overnight. The resulting suspension was filtered, the solids were washed with CH_2Cl_2 and the filtrate was concentrated under reduced pressure. Column chromatography (pure CH_2Cl_2) of the residue yielded hydrazone **5** together with diaziridine **4a** as an inseparable mixture (2.41 g, 88% over 2 steps, dark green blue solids) in a ratio of 10:1. R_f = 0.38 (pure CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 5.73 (br. s, 2 H, N*H*$_2$), 6.13 (d, *J* = 1.9 Hz, 1 H, 3-H), 7.07–7.12 (m, 1 H, 5-H), 7.16 (ddd, *J* = 8.1, 7.1, 1.3 Hz, 1 H, 6-H), 7.29 (dd, *J* = 8.0, 0.9 Hz, 1 H, 7-H), 7.53 (dd, *J* = 7.5, 0.7 Hz, 1 H, 4-H), 8.69 (br. s, 1 H, 1-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 90.96 (*C*-3), 110.63 (*C*-7), 118.32 (q, $^1J_{CF}$ = 277.5 Hz, *C*F$_3$), 120.01 (*C*-4), 120.21 (*C*-5), 122.10 (*C*-6), 128.25 (*C*-3a), 133.33 (*C*-7a), 139.99 (*C*-2), 144.99 (q, $^2J_{CF}$ = 36.0 Hz, *C*NCF$_3$) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –73.13 (s, C*F*$_3$) ppm. IR (ATR): $\tilde{\nu}$ = 3514 (w), 3401 (w), 3372 (m), 3108 (w), 3065 (w), 1663 (s), 1588 (m), 1516 (w), 1453 (m), 1423 (m), 1386 (m), 1352 (m), 1338 (m), 1184 (s), 1127 (s), 980 (w), 928 (w), 773 (m), 739 (s), 674 (m), 658 (m), 608 (w), 582 (w) cm^{-1}. UV (MeOH): λ_{max} (log ε) = 204 nm (4.38), 219 (4.35), 313 (4.11). HRMS (ESI): calcd. for $C_{10}H_8F_3N_3$ [M + H]$^+$ 228.0743; found 228.0744.

1-Methyl-2-[3-(trifluoromethyl)diaziridin-3-yl]-1*H*-indole (4b): To a stirred solution of the oxime **3b** (2.20 g, 9.08 mmol) and NEt_3 (2.1 mL, 15.44 mmol, 1.7 equiv.) in CH_2Cl_2 (50 mL) was added tosyl chloride (2.08 g, 10.90 mmol, 1.2 equiv.) portionwise at 0 °C, followed by DMAP (111 mg, 0.91 mmol, 0.1 equiv.). The reaction mixture was stirred at room temperature for approx. 16 h, then cooled to 0 °C and quenched with water (50 mL). The phases were separated and the aqueous phase extracted with CH_2Cl_2 (2 × 25 mL). The combined organic extracts were dried with $MgSO_4$ and concentrated under reduced pressure to give the crude tosyloxime, which was used without further purification directly for the next step. To a cooled flask containing liquid ammonia (approx. 180 mL) at –70 °C was added a solution of the crude tosyloxime in CH_2Cl_2 (20 mL) and the mixture was stirred for 4 h at this temperature. The ammonia was then allowed to evaporate allowing the solution to warm to room temperature overnight. The resulting suspension was filtered, the solids were washed with CH_2Cl_2 and the filtrate was concentrated under reduced pressure. Column chromatography (CH_2Cl_2/petroleum ether, 3:1) of the residue yielded diaziridine **4b** (2.02 g, 92%) as a light yellow solid. R_f = 0.45 (CH_2Cl_2/petroleum ether, 6:1), m.p. 75–76 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.48 (d, *J* = 8.9 Hz, 1 H, N$H_{diaziridine}$), 2.88 (d, *J* = 8.7 Hz, 1 H, N$H_{diaziridine}$), 3.83 (s, 3 H, NCH_3), 6.73 (d, *J* = 0.7 Hz, 1 H, 3-H), 7.15 (ddd, *J* = 8.0, 6.7, 1.3 Hz, 1 H, 5-H), 7.28–7.33 (m, 1 H, 6-H), 7.35 (dd, *J* = 8.2, 0.9 Hz, 1 H, 7-H), 7.62 (ddd, *J* = 7.9, 0.9, 0.9 Hz, 1 H, 4-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 30.94 (N*C*H$_3$), 52.97 (q, $^2J_{CF}$ = 38.1 Hz, $C_{q\text{-diaziridine}}$), 104.98 (*C*-3), 109.65 (*C*-7), 120.37 (*C*-5), 121.35 (*C*-4), 123.07 (q, $^1J_{CF}$ = 278.1 Hz, *C*F$_3$), 123.39 (*C*-6), 126.65 (*C*-3a), 129.97 (*C*-2), 137.75 (*C*-7a) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –76.64 (s, C*F*$_3$) ppm. IR (ATR): $\tilde{\nu}$ = 3226 (w), 3128 (w), 1466 (w), 1443 (w), 1411 (w), 1358 (w), 1319 (w), 1254 (w), 1233 (w), 1149 (s), 1006 (w), 953 (m), 914 (m), 876 (w), 850 (w), 799 (m), 753 (m), 729 (m), 703 (m), 648 (w), 586 (w), 552 (w) cm^{-1}. UV (MeOH): λ_{max} (log ε) = 217 nm (4.60), 270 (3.94), 284 (3.86), 294 (3.69). HRMS (EI): calcd. for $C_{11}H_{10}F_3N_3$ [M]$^+$ 241.0821; found 241.0825.

2-(1-Ethoxy-2,2,2-trifluoroethyl)-1-methyl-1*H*-indole (7): To a stirred solution of diaziridine **4b** (100 mg, 0.42 mmol) in Et_2O (5 mL) was added MnO_2 (180 mg, 2.1 mmol, 5.0 equiv.) at 0 °C and the reaction mixture was stirred at this temperature for approx. 1 h (gave crude diazirine **6**, which is not stable at room temperature; R_f = 0.50 in petroleum ether/ CH_2Cl_2, 6:1). The solid was filtered off, washed with Et_2O (5 mL) and the filtrate was collected in an ice-cooled flask containing EtOH (2 mL) and a stirring bar. The ice-bath was removed and the solution was stirred and warmed to room temperature. After 2 h the solvents were removed in vacuo and the residue was purified by flash chromatography (petroleum ether/ CH_2Cl_2, 5:1, R_f = 0.36) to obtain title compound **7** as a yellowish oil (61 mg, 57%). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.24 (t, *J* = 7.0 Hz, 3 H, CH_3), 3.57–3.66 (m, 2 H, OCH_2), 3.82 (s, 3 H, NCH_3), 4.94 (q, $^3J_{HF}$ = 7.0 Hz, 1 H, C*H*CF$_3$), 6.65 (s, 1 H, 3-H), 7.13 (ddd, *J* = 8.0, 7.0, 1.1 Hz, 1 H, 5-H), 7.27 (ddd, *J* = 8.3, 7.0, 1.2 Hz, 1 H, 6-H), 7.34 (dd, *J* = 8.3, 0.8 Hz, 1 H, 7-H), 7.61 (ddd, *J* = 7.9, 0.9, 0.9 Hz, 1 H, 4-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.97 (*C*H$_3$), 30.73 (N*C*H$_3$), 66.08 (O*C*H$_2$), 74.79 (q, $^2J_{CF}$ = 32.8 Hz, *C*HCF$_3$), 105.09 (*C*-3), 109.46 (*C*-7), 120.00 (*C*-5), 121.06 (*C*-4), 122.68 (*C*-6), 123.68 (q, $^1J_{CF}$ = 282.0 Hz, *C*F$_3$), 126.95 (*C*-3a), 130.32 (*C*-2), 138.63 (*C*-7a) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –75.09 (s, C*F*$_3$) ppm. IR (ATR): $\tilde{\nu}$ = 3058 (w), 2980 (w), 2938 (w), 2891 (w), 1541 (w), 1468 (w), 1404 (w), 1351 (w), 1326 (w), 1269 (m), 1238 (w), 1169 (m), 1126 (s), 1097 (s), 1033 (w), 1012 (w), 913 (w), 870 (w), 846 (w), 790 (m), 750 (m), 735 (m), 704 (m), 646 (w), 584 (w), 554 (w) cm^{-1}. UV (MeOH): λ_{max} (log ε) = 218 nm (4.58), 272 (3.93), 284 (3.86). HRMS (ESI): calcd. for $C_{13}H_{14}F_3NO$ [M + H]$^+$ 258.1100; found 258.1101.

2,2,2-Trifluoro-1-(1*H*-indol-3-yl)ethan-1-one (8):[26] To a stirred solution of indole (2.00 g, 17.07 mmol) in dimethylformamide (30 mL) was added TFAA (4.75 mL, 34.14 mmol, 2.0 equiv.) dropwise at room temperature and the reaction mixture was stirred overnight. The solvent was removed in vacuo and the sticky oil was dissolved in EtOAc (50 mL) and washed with water (50 mL) and $NaHCO_3$ (satd. aq., 50 mL), then dried with $MgSO_4$ and concentrated under reduced pressure. Flash chromatography (petroleum ether/EtOAc, 5:1 to 5:4) of the residue followed by recrystallization (petroleum ether/EtOAc, 5:1) gave the title compound as colorless crystals (3.37 g, 93%). R_f = 0.45 (CH_2Cl_2/petroleum ether, 6:1), m.p. 209 °C. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 7.29–7.38 (m, 2 H, 6-H, 5-H), 7.60 (dd, *J* = 5.8, 1.9 Hz, 1 H, 7-H), 8.20 (d, *J* = 8.1 Hz, 1 H, 4-H), 8.48 (s, 1 H, 2-H), 12.71 (br. s, 1 H, 1-H) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 108.86 (*C*-3), 112.99 (*C*-7), 116.89 (q, $^1J_{CF}$ = 291.6 Hz, *C*F$_3$), 121.09 (*C*-4), 123.40 (*C*-5), 124.32 (*C*-6), 125.75 (*C*-3a), 136.65 (*C*-7a), 137.55 (*C*-2), 173.88 (q, $^2J_{CF}$ = 33.8 Hz, *C*OCF$_3$) ppm. ^{19}F NMR (376 MHz, [D$_6$]DMSO): δ = –70.90 (s, C*F*$_3$) ppm. IR (ATR): $\tilde{\nu}$ = 3224 (w), 3134 (w), 3068

(w), 2937 (w), 2876 (w), 1739 (w), 1634 (m), 1585 (m), 1521 (w), 1492 (w), 1461 (m), 1430 (m), 1391 (m), 1339 (w), 1265 (m), 1233 (m), 1185 (m), 1125 (s), 1088 (m), 1010 (w), 938 (w), 894 (m), 869 (m), 772 (m), 733 (s), 646 (m), 616 (m), 596 (m), 541 (m) cm^{-1}. UV (MeOH): λ_{max} (log ε) = 206 nm (4.43), 247 (4.05), 262 (3.94), 266 (3.93), 312 (4.08). HRMS (ESI): calcd. for $C_{10}H_6F_3NO$ $[M + Na]^+$ 236.0294; found 236.0295.

2,2,2-Trifluoro-1-(1-tosyl-1*H*-indol-3-yl)ethan-1-one (8a): To a stirred solution of ketone **8** (3.15 g, 14.78 mmol) and NEt_3 (3.1 mL, 22.17 mmol, 1.5 equiv.) in CH_2Cl_2 (60 mL) was added tosyl chloride (2.87 g, 15.07 mmol, 1.02 equiv.). The reaction mixture was stirred at room temperature for approx. 1.5 h, then quenched with water (60 mL). The phases were separated and the aqueous phase extracted with CH_2Cl_2 (2 × 30 mL). The combined organic extracts were dried with $MgSO_4$ and concentrated under reduced pressure. The crude product was load on silica and purified by column chromatography (petroleum ether/EtOAc, 10:1) to obtain *N*-tosyl ketone **8a** (5.08 g, 94%) as a colorless solid. R_f = 0.49 (petroleum ether/EtOAc, 8:1), m.p. 126–129 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.38 (s, 3 H, C$H_{3\text{-tosyl}}$), 7.32 (d, J = 8.5 Hz, 2 H, $H_{m\text{-aryl}}$), 7.38–7.47 (m, 2 H, 5-H, 6-H), 7.87 (d, J = 8.5 Hz, 2 H, $H_{o\text{-aryl}}$), 7.97 (dd, J = 7.3, 1.3 Hz, 1 H, 7-H), 8.32 (dd, J = 7.4, 1.9 Hz, 1 H, 4-H), 8.44 (ddd, J = 1.7, 1.6, 1.6 Hz, 1 H, 2-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.66 ($CH_{3\text{-tosyl}}$), 113.28 (*C*-7), 113.74 (*C*-3), 116.35 (q, $^1J_{CF}$ = 290.7 Hz, CF_3), 122.78 (*C*-4), 125.58 (*C*-5), 126.65 (*C*-6), 127.35 (*C*-3a), 127.39 (2 × $CH_{o\text{-aryl}}$), 130.47 (2 × $CH_{m\text{-aryl}}$), 133.94 ($C_{aryl}SO_2$), 134.45 (*C*-7a), 135.00 (q, $^4J_{CF}$ = 5.1 Hz, *C*-2), 146.59 ($C_{p\text{-aryl}}$), 175.97 (q, $^2J_{CF}$ = 36.3 Hz, $COCF_3$) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –73.35 (s, CF_3) ppm. IR (ATR): $\tilde{\nu}$ = 3148 (w), 3112 (w), 2919 (w), 1702 (m), 1596 (w), 1530 (m), 1481 (w), 1445 (m), 1377 (m), 1338 (w), 1316 (w), 1301 (w), 1269 (m), 1239 (w), 1171 (m), 1128 (s), 1100 (s), 1084 (s), 1021 (w), 973 (s), 876 (m), 834 (w), 810 (m), 771 (m), 755 (s), 705 (m), 656 (s), 628 (m), 565 (s), 532 (s) cm^{-1}. UV (MeOH): λ_{max} (log ε) = 202 nm (4.53), 231 (4.15), 246 (4.17), 281 (3.67), 288 (3.65). HRMS (EI): calcd. for $C_{17}H_{12}F_3NO_3S$ $[M]^+$ 367.0485; found 367.0476.

2,2,2-Trifluoro-1-(1-tosyl-1*H*-indol-3-yl)ethan-1-one Oxime (9): To a solution of *N*-tosyl ketone **8a** (4.89 g, 13.31 mmol) in pyridine (70 mL) and EtOH (30 mL) was added hydroxylamine hydrochloride (1.30 g, 18.63 mmol, 1.4 equiv.) and the mixture was stirred at 80 °C for approx. 6 h. After complete conversion of the starting material the reaction mixture was cooled to room temperature and the solvents were removed in vacuo. The residue was treated with *t*BuOMe (70 mL) and washed with water (2 × 50 mL) and brine (50 mL), then dried with $MgSO_4$ and concentrated under reduced pressure. Flash chromatography (petroleum ether/EtOAc, 6:1) of the residue gave the title compound (4.90 g, 96%) as a colorless solid. R_f = 0.30 (petroleum ether/EtOAc, 6:1), m.p. 120–123 °C. ^1H NMR (400 MHz, $CDCl_3$, *E*/*Z*-isomers): δ = 2.34 and 2.35 ppm (s, 3 H, C$H_{3\text{-tosyl}}$), 7.22–7.31 (m, 3 H, $H_{m\text{-aryl}}$, 5-H), 7.37 (ddd, J = 8.4, 7.3, 1.1 Hz, 1 H, 6-H), 7.56 (d, J = 8.0 Hz, 1 H, 4-H), 7.78–7.84 (m, 2 H, $H_{o\text{-aryl}}$), 7.97–8.03 (m, 2 H, 7-H, 2-H), 8.54 and 8.94 (br. s, 1 H, NO*H*). ^{13}C NMR (100 MHz, $CDCl_3$, *E*/*Z*-isomers): δ = 21.59 ($CH_{3\text{-tosyl}}$), 107.82 (*C*-3), 113.37 and 113.46 (*C*-7), 120.68 (q, $^1J_{CF}$ = 274.5 Hz, CF_3), 122.38 and 122.67 (*C*-4), 123.78 and 124.23 (*C*-5), 125.42 and 125.75 (*C*-6), 127.04 and 127.11 (2 × $CH_{o\text{-aryl}}$), 127.73 (*C*-3a), 128.20 (*C*-2), 130.14 and 130.17 (2 × $CH_{m\text{-aryl}}$), 134.19 (*C*-7a), 134.60 and 134.65 ($C_{aryl}SO_2$), 142.14 (q, $^2J_{CF}$ = 33.8 Hz, *C*NOH), 145.67 and 145.76 ($C_{p\text{-aryl}}$) ppm. ^{19}F NMR (376 MHz, $CDCl_3$, *E*/*Z*-isomers): δ = –63.28, –67.45 (s, CF_3) ppm. IR (ATR): $\tilde{\nu}$ = 3433 (w), 3152 (w), 1595 (w), 1552 (w), 1448 (w), 1419 (w), 1372 (w), 1355 (w), 1273 (m), 1162 (s), 1128 (s), 1104 (m), 1084 (m), 1008 (m), 975 (s), 890 (m), 811 (w), 758 (m), 701 (m), 662 (m), 565 (s), 534 (s) cm^{-1}. UV (MeOH): λ_{max} (log ε) = 202 nm (4.51), 275 (4.03), 284 (4.04). HRMS (ESI): calcd. for $C_{17}H_{13}F_3N_2O_3S$ $[M + Na]^+$ 405.0491; found 405.0492.

1-Tosyl-3-[3-(trifluoromethyl)diaziridin-3-yl]-1*H*-indole (10): To a stirred solution of oxime **9** (5.09 g, 13.31 mmol) and NEt_3 (3.7 mL, 26.62 mmol, 2.0 equiv.) in CH_2Cl_2 (70 mL) was added tosyl chloride (3.05 g, 15.97 mmol, 1.2 equiv.) portionwise at 0 °C, followed by DMAP (163 mg, 1.33 mmol, 0.1 equiv.). The reaction mixture was stirred at room temperature for approx. 16 h, then quenched with cold water (100 mL). The phases were separated and the aqueous phase extracted with CH_2Cl_2 (2 × 30 mL). The combined organic extracts were dried with $MgSO_4$ and concentrated under reduced pressure to give the crude tosyloxime, which was used without further purification directly for the next step. To a cooled flask containing liquid ammonia (approx. 200 mL) at –70 °C was added a solution of the crude tosyloxime in CH_2Cl_2 (30 mL) and the mixture was stirred for 4 h at this temperature. The ammonia was then allowed to evaporate allowing the solution to warm to room temperature overnight. The resulting suspension was filtered, the solids were washed with CH_2Cl_2 and the filtrate was concentrated under reduced pressure. Column chromatography (petroleum ether/EtOAc, 3:1) of the residue yielded diaziridine **10** (4.65 g, 92%) as a colorless solid. R_f = 0.36 (petroleum ether/EtOAc, 4:1), m.p. 151 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 2.31 (d, J = 9.0 Hz, 1 H, N$H_{diaziridine}$), 2.35 (s, 3 H, C$H_{3\text{-tosyl}}$), 2.82 (d, J = 9.0 Hz, 1 H, N$H_{diaziridine}$), 7.23–7.30 (m, 3 H, $H_{m\text{-aryl}}$, 5-H), 7.36 (ddd, J = 8.4, 7.3, 1.2 Hz, 1 H, 6-H), 7.76 (d, J = 8.0 Hz, 1 H, 4-H), 7.79 (d, J = 8.4 Hz, 2 H, $H_{o\text{-aryl}}$), 7.89 (s, 1 H, 2-H), 7.98 (ddd, J = 8.4, 0.8, 0.8 Hz, 1 H, 7-H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.57 ($CH_{3\text{-tosyl}}$), 53.69 (q, $^2J_{CF}$ = 38.0 Hz, $C_{q\text{-diaziridine}}$), 113.19 (*C*-3), 113.67 (*C*-7), 120.49 (*C*-4), 123.24 (q, $^1J_{CF}$ = 278.0 Hz, CF_3), 123.90 (*C*-5), 125.51 (*C*-6), 127.00 (2 × $CH_{o\text{-aryl}}$), 127.47 (*C*-2), 127.99 (*C*-3a), 130.10 (2 × $CH_{m\text{-aryl}}$), 134.66 (*C*-7a), 134.77 ($C_{aryl}SO_2$), 145.57 ($C_{p\text{-aryl}}$) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –76.74 (s, CF_3) ppm. IR (ATR): $\tilde{\nu}$ = 3265 (w), 1597 (w), 1447 (w), 1362 (m), 1311 (w), 1264 (w), 1212 (m), 1171 (m), 1151 (s), 1125 (s), 1089 (m), 1024 (w), 972 (m), 903 (w), 844 (w), 813 (w), 742 (m), 714 (w), 704 (w), 685 (s), 654 (m), 584 (s), 570 (s), 535 (s) cm^{-1}. UV (MeOH): λ_{max} (log ε) = 203 nm (4.51), 231 (4.12), 249 (4.16), 281 (3.66), 288 (3.62). HRMS (EI): calcd. for $C_{17}H_{14}F_3N_3O_2S$ $[M]^+$ 381.0753; found 381.0747.

1-Tosyl-3-[3-(trifluoromethyl)-3*H*-diazirin-3-yl]-1*H*-indole (11): To a stirred solution of diaziridine **10** (1.00 g, 2.62 mmol) and NEt_3 (909 µL, 6.56 mmol, 2.5 equiv.) in CH_2Cl_2 (25 mL) was added iodine (998 mg, 3.93 mmol, 1.5 equiv.) at 0 °C. The reaction mixture was stirred at this temperature for 5–10 min, then quenched with $Na_2S_2O_3$ solution (0.5 M, 30 mL). After phase separation the aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL) and the combined organic phase was dried with $MgSO_4$ and the solvents evaporated in vacuo. Purification by column chromatography (petroleum ether/CH_2Cl_2, 5:3) gave diazirine **11** (915 mg, 92%) as a yellowish solid. R_f = 0.59 (petroleum ether/CH_2Cl_2, 5:3). ^1H NMR (300 MHz, $CDCl_3$): δ = 2.35 (s, 3 H, C$H_{3\text{-tosyl}}$), 7.22–7.29 (m, 3 H, $H_{m\text{-aryl}}$, 5-H), 7.32–7.38 (m, 1 H, 6-H), 7.55 (d, J = 8.0 Hz, 1 H, 4-H), 7.78 (d, J = 8.4 Hz, 2 H, $H_{o\text{-aryl}}$), 7.84 (s, 1 H, 2-H), 7.98 (ddd, J = 8.4, 0.9, 0.9 Hz, 1 H, 7-H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 21.58 ($CH_{3\text{-tosyl}}$), 24.63 (q, $^2J_{CF}$ = 42.8 Hz, $C_{q\text{-diazirine}}$), 109.73 (*C*-3), 113.73 (*C*-7), 120.22 (*C*-4), 121.84 (q, $^1J_{CF}$ = 274.2 Hz, CF_3), 123.89 (*C*-5), 125.64 (*C*-6), 127.02 (2 × $CH_{o\text{-aryl}}$), 127.86 (*C*-3a), 128.03 (*C*-2), 130.16 (2 × $CH_{m\text{-aryl}}$), 134.49 (*C*-7a), 134.61 ($C_{aryl}SO_2$), 145.72 ($C_{p\text{-aryl}}$) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –68.06 (s, CF_3) ppm. IR (ATR): $\tilde{\nu}$ = 3154 (w), 2928 (w), 2855 (w),

1609 (w), 1597 (w), 1493 (w), 1449 (m), 1372 (m), 1283 (m), 1237 (w), 1173 (s), 1149 (s), 1131 (s), 1105 (m), 1088 (s), 1026 (w), 980 (s), 877 (m), 816 (m), 799 (m), 755 (m), 740 (s), 704 (m), 687 (s), 656 (s), 608 (w), 568 (s), 534 (s) cm^{-1}. UV (MeOH): λ_{max} (log ε) = 205 nm (4.52), 235 (4.15), 248 (4.16), 282 (3.72). HRMS (ESI): calcd. for $C_{17}H_{12}F_3N_3O_2S$ $[M + Na]^+$ 402.0495; found 402.0495.

3-(1-Ethoxy-2,2,2-trifluoroethyl)-1-tosyl-1*H*-indole (12): A solution of *N*-tosyl diazirine **11** (46 mg, 121 μmol) in EtOH (8 mL) was irradiated for 1 h at λ_{max} = 365 nm (UV-A) in a flask made of borosilicate glass. After evaporation of the solvent, the residue was purified by column chromatography (petroleum ether/CH_2Cl_2, 5:3) to obtain compound **12** as a colorless oil (13 mg, 27%). R_f = 0.36 (petroleum ether/CH_2Cl_2, 5:3). ^{1}H NMR (600 MHz, $CDCl_3$): δ = 1.23 (t, J = 7.0 Hz, 3 H, CH_3), 2.35 (s, 3 H, C$H_{3\text{-tosyl}}$), 3.54–3.64 (m, 2 H, OCH_2), 4.87 (q, $^3J_{HF}$ = 6.7 Hz, 1 H, CHCF_3), 7.22–7.28 (m, 3 H, $H_{m\text{-aryl}}$, 5-H), 7.34 (dd, J = 7.8, 7.8 Hz, 1 H, 6-H), 7.68 (d, J = 7.9 Hz, 1 H, 4-H), 7.71 (s, 1 H, 2-H), 7.77 (d, J = 8.4 Hz, 2 H, $H_{o\text{-aryl}}$), 7.96 (dd, J = 8.4, 0.7 Hz, 1 H, 7-H) ppm. ^{13}C NMR (150 MHz, $CDCl_3$): δ = 15.05 (*C*H$_3$), 21.58 (*C*H$_{3\text{-tosyl}}$), 66.31 (O*C*H$_2$), 74.10 (q, $^2J_{CF}$ = 32.8 Hz, *C*HCF$_3$), 113.56 (*C*-7), 114.82 (*C*-3), 120.82 (*C*-4), 123.59 (*C*-5), 123.92 (q, $^1J_{CF}$ = 282.0 Hz, *C*F$_3$), 125.15 (*C*-6), 126.55 (*C*-2), 126.89 (2 × *C*H$_{o\text{-aryl}}$), 128.73 (*C*-3a), 130.00 (2 × *C*H$_{m\text{-aryl}}$), 134.87 (*C*$_{aryl}$SO$_2$), 135.11 (*C*-7a), 145.31 (*C*$_{p\text{-aryl}}$) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –76.58 (s, CF_3) ppm. IR (ATR): $\tilde{\nu}$ = 2981 (w), 2929 (w), 2884 (w), 1597 (w), 1563 (w), 1447 (w), 1372 (m), 1268 (m), 1171 (s), 1122 (s), 1091 (s), 1020 (w), 975 (m), 906 (w), 812 (m), 796 (w), 747 (m), 714 (m), 676 (m), 656 (m), 630 (m), 572 (s), 536 (s) cm^{-1}. UV (MeOH): λ_{max} (log ε) = 203 nm (4.50), 208 (4.47), 249 (4.16), 281 (3.64), 288 (3.61). HRMS (ESI): calcd. for $C_{19}H_{18}F_3NO_3S$ $[M + Na]^+$ 420.0852; found 420.0854.

2,2,2-Trifluoro-1-(1-methyl-1*H*-benzo[*d*]imidazol-2-yl)ethanone Oxime (13b): To a solution of ketone **13a**[18] (1.50 g, 6.85 mmol, 1.0 equiv.) in pyridine (20 mL) was added hydroxylamine hydrochloride (685 mg, 9.87 mmol, 1.5 equiv.) in one portion and the solution was heated to reflux for 5 h. After cooling to room temp. the solvent was removed under reduced pressure and the residue was dissolved in *t*BuOMe (20 mL) and H_2O (20 mL). The phases were separated and the organic phase was extracted with H_2O (20 mL). Then the combined aqueous layers were extracted with *t*BuOMe (20 mL). The combined organic fractions were washed with aqueous citric acid (0.2 M, 20 mL) and dried with $MgSO_4$. Removal of the solvent under reduced pressure gave oxime **13b** (664 mg, 2.81 mmol, 43%) as a yellowish solid. R_f = 0.4 [petroleum ether/CH_2Cl_2 (2:1)], m.p. 204–207 °C. ^{1}H NMR (400 MHz, [D$_6$]-DMSO): δ = 13.89 (s, 1 H, O-*H*), 7.76–7.74 (m, 1 H, 4-H), 7.68–7.66 (m, 1 H, 7-H), 7.41–7.37 (m, 1 H, 6-H), 7.33–7.29 (m, 1 H, 5-H), 3.73 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 142.3 (1 C, *C*-3a), 140.3 (1 C, *C*-2), 138.2 (q, $^2J_{CF}$ = 34.0 Hz, 1 C, *C*N), 135.3 (1 C, *C*-7a), 123.9 (1 C, *C*-6), 122.6 (1 C, *C*-5), 120.4 (q, $^1J_{CF}$ = 273.3 Hz, 1 H, *C*F$_3$), 119.9 (1 C, *C*-4), 111.1 (1 C, *C*-7), 31.0 (1 C, *C*H$_3$) ppm. ^{19}F NMR (376 MHz, [D$_6$]DMSO): δ = –64.2 (s, CF_3) ppm. IR (ATR): $\tilde{\nu}$ = 3068 (w), 2955 (w), 2559 (w), 2465 (w), 1870 (m), 1648 (m), 1616 (w), 1531 (w), 1480 (m), 1459 (m), 1406 (m), 1319 (m), 1290 (s), 1248 (w), 1184 (m), 1133 (s), 1043 (s), 986 (s), 914 (m), 742 (s),. 632 (m), 566 (m) cm^{-1}. UV/Vis (MeCN): λ_{max} (log ε) = 284.0 nm (3.92), 202.0 (4.60). MS (EI): *m*/*z* (%) = 243 (100), 174 (80), 158 (41). HRMS (EI): calcd. for $C_{10}H_8F_3N_3O$ $[M]^+$ 243.06140; found 243.06191.

2,2,2-Trifluoro-1-(1-methyl-1*H*-benzo[*d*]imidazol-2-yl)ethanone *O*-Tosyl Oxime (13c): Oxime **13b** (390 mg, 1.60 mmol, 1.0 equiv.) was dissolved in *t*BuOMe (10 mL) and cooled to 0 °C. TsCl (335 mg, 1.76 mmol, 1.1 equiv.) and NEt_3 (0.33 mL, 2.41 mmol, 1.5 equiv.) were added and the solution was stirred for 2 h at 0 °C. The solution was washed with H_2O (20 mL) and the aqueous phase was extracted with *t*BuOMe (10 mL). The combined organic phases were dried with $MgSO_4$ and the solvent was removed under reduced pressure. Purification of the crude product by column chromatography gave tosylated oxime **13c** (478 mg, 1.20 mmol, 75%) as a colorless solid. R_f = 0.68 [petroleum ether/EtOAc (2:1)], m.p. 139–142 °C. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 7.98–7.94 (m, 2 H, *o*CH_{tosyl}), 7.83–7.81 (m, 1 H, 4-H),7.78–7.76 (m, 1 H, 7-H), 7.60–7.58 (m, 2 H, *m*CH_{tosyl}), 7.52–7.48 (m, 1 H, 6-H), 7.42–7.38 (m, 1 H, 5-H), 3.76 (s, 3 H, CH_3), 2.48 (s, 3 H, CH_{3tosyl}) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 147.5 (*p,* 1 C*C*H$_{tosyl}$), 146.5 (q, $^2J_{CF}$ = 35.6 Hz, 1 C, *C*N), 142.0 (1 C, *C*-3a), 136.7 (1 C, *C*-2); 135.3 (1 C, *C*-7a), 130.7 (2 C, *m*CH_{tosyl}), 129.3 (1 C, *ipso*CH_{tosyl}), 129.0 (2 C, *m*CH_{tosyl}), 125.1 (1 C, *C*-6), 123.6 (1 C, *C*-5), 120.4 (1 C, *C*-4), 118.5 (q, $^1J_{CF}$ = 277.1 Hz, 1 C, *C*F$_3$), 111.6 (1 C, *C*-7), 31.6 (1 C, *C*H$_3$), 21.3 (1 C, *C*H$_{3tosyl}$) ppm. ^{19}F NMR (376 MHz, [D$_6$]DMSO): δ = –64.6 (s, CF_3) ppm. IR (ATR): $\tilde{\nu}$ = 3172 (w), 3057 (w), 2954 (w), 2922 (w), 1641 (w), 1596 (w), 1575 (w), 1471 (m), 1400 (s), 1324 (m), 1241 (m), 1197 (s), 1177 (s), 1159 (s), 1141 (s), 1096 (m), 1025 (s), 1007 (m), 913 (s), 844 (m), 812 (m), 715 (m), 743 (s), 724 (s), 685 (m), 660 (s), 623 (s), 544 (s) cm^{-1}. UV/Vis (MeOH): λ_{max} (log ε) = 300 nm (3.85), 276 (3.76), 228 (4.21), 203 (4.60). MS (EI): *m*/*z* (%) = 397.0 (41), 227.0 (47), 214.0 (47), 174.0 (72), 158.0 (87). 155.0 (75), 145.0 (55), 81.0 (100). HRMS (EI): calcd. for $C_{17}H_{14}F_3N_3O_3S$ $[M]^+$ 397.07025; found 397.07056.

1-Methyl-2-[3-(trifluoromethyl)diaziridin-3-yl]-1*H*-benzo[*d*]imidazole (13): Tosylated oxime **13c** (467 mg, 1.18 mmol, 1.0 equiv.) was dissolved in CH_2Cl_2 (10 mL) and added dropwise to stirred NH_3 (l, 20 mL) at –78 °C. The reaction mixture was stirred for 2 h at –78 °C and then warmed to room temp. Filtration of the suspension and removal of the solvent under reduced pressure gave diaziridine **13** (262 mg, 1.08 mmol, 92%) as a colorless solid. R_f = 0.45 [petroleum ether/EtOAc (2:1)], m.p. 148 °C. ^{1}H NMR (400 MHz, [D$_6$]DMSO): δ = 7.71–7.69 (m, 1 H, 4-H), 7.65–7.63 (m, 1 H, 7-H), 7.39–7.35 (m, 1 H, 6-H), 7.31–7.27 (m,1 H, 5-H), 4.62–4.60 (m, 1 H, N-*H*), 4.52–4.50 (m, 1 H, N-*H*), 3.89 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, [D$_6$]DMSO): δ = 144.8 (1 C, *C*-3a), 141.5 (1 C, *C*-2), 135.5 (1 C, *C*-7a), 123.8 (1 C, *C*-6), 123.4 (q, $^1J_{CF}$ = 278.3 Hz, 1 C, *C*F$_3$), 122.7 (1 C, *C*-5), 119.7 (1 C, *C*-4), 110.9 (1 C, *C*-7), 52.5 (q, $^2J_{CF}$ = 37.1 Hz, 1 C, *C*N), 30.7 (1 C, *C*H$_3$) ppm. ^{19}F NMR (376 MHz, [D$_6$]DMSO): δ = –73.2 (s, CF_3) ppm. IR (ATR): $\tilde{\nu}$ = 3241 (w), 3077 (m), 2942 (w), 1527 (w), 1476 (m), 1447 (m), 1409 (m), 1336 (m), 1288 (w), 1231 (m), 1151 (s), 1007 (m), 959 (m), 919 (m), 898 (m), 847 (w), 809 (w), 764 (m), 742 (s), 724 (s), 681 (m), 637 (w), 593 (w), 558 (w), 538 (m) cm^{-1}. UV/Vis (MeOH): λ_{max} (log ε) = 284 nm (3.75), 276 (3.83), 269 (3.79), 257 (3.87), 206 (4.49). MS (EI): *m*/*z* (%) = 242.0 (33), 193.0 (33), 158.0 (29), 144.0 (100). HRMS (EI): calcd. for $C_{10}H_9F_3N_4$ $[M]^+$ 242.07738; found 242.07792.

1-Methyl-2-[3-(trifluoromethyl)-3*H*-diazirin-3-yl]-1*H*-benzo[*d*]imidazole (14): Diaziridine **13** (262 mg, 1.08 mmol, 1.0 equiv.) was dissolved in *t*BuOMe (5 mL) and cooled to 0 °C. NEt_3 (0.33 mL, 2.38 mmol, 2.2 equiv.) and iodine (329 mg, 1.29 mmol, 1.2 equiv.) were added and the solution was stirred for 2 h (avoiding light after the addition of I_2). Then the reaction mixture was washed with aqueous $Na_2S_2O_3$ (0.2 M, 5 mL) and aqueous citric acid (0.2 M, 5 mL). The organic phase was dried with $MgSO_4$ and the solvent was removed under reduced pressure. Purification of the crude product by column chromatography gave diazirine **14** (214 mg, 891 μmol, 83%) as a colorless to orange solid. R_f = 0.82 [petroleum ether/EtOAc (2:1)], m.p. 88 °C (decomposition). ^{1}H NMR

(400 MHz, $CDCl_3$): δ = 7.83–7.80 (m, 1 H, 4-H), 7.400–7.397 (m, 1 H, 7-H), 7.390–7.388 (m, 1 H, 6-H), 7.36–7.32 (m, 1 H, 5-H), 4.01 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 142.3 (1 C, *C*-3a), 141.0 (1 C, *C*-2), 135.5 (1 C, *C*-7a), 124.8 (1 C, *C*-6), 123.4 (1 C, *C*-5), 121.1 (1 C, *C*-4), 121.3 (q, $^1J_{CF}$ = 274.9 Hz, 1 C, *C*F_3), 110.0 (1 C, *C*-7), 30.6 (1 C, *C*H_3), 23.5 (q, $^2J_{CF}$ = 44.3 Hz, 1 C, *C*N) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –67.6 (s, CF_3) ppm. IR (ATR): $\tilde{\nu}$ = 3065 (w), 2958 (w), 1635 (w), 1619 (w), 1473 (m), 1403 (m), 1336 (m), 1302 (m), 1247 (m), 1201 (s), 1187 (s), 1154 (s), 1005 (w), 970 (s), 911 (m), 886 (m), 746 (s), 727 (s), 695 (m), 564 (m), 541 (m) cm^{-1}. UV/Vis ($CHCl_3$): λ_{max} (log ε) = 322 nm (2.85), 274 (3.83), 258 (3.89), 234 (3.76). MS (EI): *m*/*z* (%) = 240.0 (5), 212.0 (100). 165.0 (24), 143.0 (40), 102.0 (24). HRMS (ESI): calcd. for $C_{10}H_7F_3N_4$ [M + H]$^+$ 241.06956; found 241.06963.

2-(1-Ethoxy-2,2,2-trifluoroethyl)-1-methyl-1*H*-benzo[*d*]imidazole (15): Protocol A: A solution of diazirine **14** (66 mg, 275 µmol, 1.0 equiv.) in EtOH (0.3 mL) was irradiated for 2 h (λ_{max} = 350 nm, Rayonet). The solvent was removed under reduced pressure. Column chromatography of the product mixture [petroleum ether/EtOAc (10:1)] gave starting material **14** (20 mg, 83 µmol, 30%) and ether **15** (33 mg, 128 µmol, 46%) as colorless solids. **Protocol B:** To a solution of diazirine **14** (100 mg, 417 µmol, 1.0 equiv.) in CH_2Cl_2 (42 mL) was added EtOH (0.024 mL, 417 µmol, 1.0 equiv.) and the solution was irradiated for 2 h (λ_{max} = 350 nm, Rayonet). The solvent was removed under reduced pressure and purification of the crude product by column chromatography [petroleum ether/EtOAc (10:1)] gave ether **15** (64 mg, 60%) as colorless solid. R_f = 0.38 [petroleum ether/EtOAc (10:1)], m.p. 73 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.99–7.80 (m, 1 H, 4-H), 7.43–7.40 (m, 1 H, 7-H), 7.39–7.35 (m, 1 H, 6-H), 7.34–7.30 (m, 1 H, 5-H), 5.24 (q, $^3J_{FH}$ = 7.3 Hz, 1 H, OC*H*), 3.96 (s, 3 H, CH_3), 3.72 (dq, $^3J_{HH}$ = 7.0, $^2J_{HH}$ = 27.4 Hz, 1 H, CH_2), 3.72 (dq, $^3J_{HH}$ = 7.0, $^2J_{HH}$ = 46.1 Hz, 1 H, CH_2), 1.28 (t, $^3J_{HH}$ = 7.0 Hz, 3 H, CH_2CH_3) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): δ = 145.4 (1 C, *C*-2), 142.1 (1 C, *C*-3a), 136.9 (1 C, *C*-7a), 123.8 (1 C, *C*-6), 123.3 (q, $^1J_{CF}$ = 282.5 Hz, 1 C, *C*F_3), 122.7 (1 C, *C*-5), 120.3 (1 C, *C*-4), 109.7 (1 C, *C*-7), 77.0 (q, $^2J_{CF}$ = 33.0 Hz, 1 C, O*C*H), 67.6 (1 C, *C*H_2), 30.9 (q, $^5J_{CF}$ = 2.3 Hz, 1 C, *C*H_3), 14.9 (1 C, CH_2CH_3) ppm. ^{19}F NMR (376 MHz, $CDCl_3$): δ = –74.5 (s, CF_3) ppm. IR (ATR): $\tilde{\nu}$ = 3072 (w), 2970 (w), 2935 (m), 2877 (w), 1636 (m), 1614 (m), 1505 (m), 1478 (m), 1387 (m), 1341 (m), 1319 (m), 1284 (m), 1259 (m), 1174 (m), 1126 (s), 1094 (s), 1059 (s), 1011 (m), 903 (m), 877 (m), 855 (m), 803 (m), 776 (m), 744 (s), 729 (s), 671 (m), 589 (m), 569 (m), 547 (m) cm^{-1}. UV/Vis ($CHCl_3$): λ_{max} (log ε) = 308 nm (3.07), 287 (3.70), 278 (3.75), 270 (3.70), 258 (3.85), 252 (3.84), 235 (3.71), 233 (3.70). HRMS (ESI): calcd. for $C_{12}H_{13}F_3N_2O$ [M + H]$^+$ 259.10527; found 259.10536.

Irradiation of 14 with PhOH: Diazirine **14** (113 mg, 471 µmol, 1.0 equiv.) was dissolved in CH_2Cl_2 (47 mL). PhOH (44 mg, 471 µmol, 1.0 equiv.) was added and the solution was irradiated for 2 h (λ_{max} = 350 nm, Rayonet). The solvent was removed under reduced pressure followed by HPLC analysis [Phenomenex Luna 250 × 10, C18(2), 5 µm, gradient MeOH/H_2O (2:1) to MeOH within 10 min] of the product mixture. HPLC fraction 1 (retention time 5.6 min): mixture of compounds **20** and **18**; HPLC fraction 2 (7.3 min): mixture of compounds **19** and **17**; HPLC Fraction 3 (9.8 min): **16**.

4-[2,2,2-Trifluoro-1-(1-methyl-1*H*-benzo[*d*]imidazol-2-yl)ethyl]phenol (20): ^{1}H NMR (600 MHz, [D$_4$]MeOH): δ = 7.76 (m, 1 H, 4-H), 7.45–7.44 (m, 1 H, 7-H), 7.320–7.29 (m with impurities, 2 H, 5-H, 6-H), 7.262–7.256 (m, 2 H, *m*CH_{phenol}), 6.79–6.77 (m, 2 H, *o*CH_{phenol}), 5.42 (q, $^3J_{FH}$ = 8.8 Hz, 1 H, C*H*CF_3), 3.63 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, [D$_4$]MeOH): δ = 159.4 (1 C, *C*-1$_{phenol}$), 150.0 (1 C, *C*-2), 142.8 (1 C, *C*-3a), 136.6 (1 C, *C*-7a), 132.1 (*m,* 2 C*C*H$_{phenol}$), 126.3 (q, $^1J_{CF}$ = 276.8 Hz, 1 C, *C*F_3), 124.4 (1 C, *C*-6), 123.7 (1 C, *C*-5), 123.1 (1 C, *C*-4$_{phenol}$), 120.0 (1 C, *C*-4), 116.8 (2 C, *o*CH_{phenol}), 111.4 (1 C, *C*-7), 48.3 (q, $^2J_{CF}$ = 29.3 Hz, 1 C, *C*HCF$_3$), 30.3 (1 C, *C*H_3) ppm. ^{19}F NMR (376 MHz, [D$_4$]-MeOH): δ = –67.0 (s, CF_3) ppm. HRMS (ESI): calcd. for $C_{16}H_{13}F_3N_2O$ [M + Na]$^+$ 329.08722; found 329.08741.

2,2,2-Trifluoro-1-(1-methyl-1*H*-benzo[*d*]imidazol-2-yl)ethanol (18): In addition to isolation by HPLC alcohol **18** was synthesized from ketone **13a**. Ketone **13a** (100 mg, 439 µmol, 1.0 equiv.) was dissolved in *i*PrOH (5 mL) and cooled to 0 °C with an ice bath. $NaBH_4$ (33 mg, 872 µmol, 2.0 equiv.) was added. The solution was stirred and slowly warmed to room temp. within 3 h. Aqueous HCl (1 M) was added until gas formation was no longer observed. Saturated aqueous $NaHCO_3$ was then added until pH = 7. The aqueous phase was extracted three times with EtOAc (5 mL) and the combined organic fractions were dried with $MgSO_4$. Removal of the solvent under reduced pressure gave alcohol **18** (77 mg, 335 µmol, 76%) as a colorless solid. R_f = 0.40 [petroleum ether/EtOAc (2:1)], m.p. 192 °C. ^{1}H NMR (600 MHz, [D$_4$]MeOH): δ = 7.69–7.67 (m, 1 H, 4-H), 7.56–7.54 (m, 1 H, 7-H), 7.38–7.35 (m, 1 H, 6-H), 7.32–7.28 (m, 1 H, 5-H), 5.54 (q, $^3J_{FH}$ = 7.3 Hz, 1 H, C*H*CF$_3$), 4.00 (s, 3 H, CH_3) ppm. ^{13}C NMR (100 MHz, [D$_4$]MeOH): δ = 148.8 (1 C, *C*-2), 142.6 (1 C, *C*-3a), 137.6 (1 C, *C*-7a), 125.6 (q, $^1J_{CF}$ = 282.1 Hz, 1 C, *C*F_3), 125.0 (1 C, *C*-6), 124.0 (1 C, *C*-5), 120.2 (1 C, *C*-4), 111.3 (1 C, *C*-7), 69.2 (q, $^2J_{CF}$ = 33.5 Hz, *C*HCF$_3$), 31.4 (1 C, CH_3) ppm. ^{19}F NMR (376 MHz, [D$_4$]MeOH): δ = –76.2 (s, CF_3) ppm. IR (ATR): $\tilde{\nu}$ = 3392 (w, br.), 3065 (w), 2925 (w), 1594 (w), 1494 (m), 1479 (m), 1395 (m), 1337 (m), 1322 (m), 1268 (m), 1224 (s), 1191 (s), 1175 (s), 1143 (s), 1083 (s), 1067 (s), 1005 (m), 915 (m), 857 (m), 737 (m), 688 (m), 672 (m), 618 (w), 594 (w), 561 (w) cm^{-1}. UV/Vis (MeOH): λ_{max} (log ε) = 285 nm (3.67), 276 (3.78), 268 (3.77), 258 (3.81), 206 (4.42). HRMS (ESI): calcd. for $C_{10}H_9F_3N_2O$ [M + H]$^+$ 231.07397; found 231.07402.

2-[2,2,2-Trifluoro-1-(1-methyl-1*H*-benzo[*d*]imidazol-2-yl)ethyl]phenol (19): ^{1}H NMR (600 MHz, [D$_4$]MeOH): δ = 7.72–7.70 (m, 1 H, 4-H), 7.44–7.40 (m, 1 H, 7-H), 7.32–7.30 (m, 1 H, C*H*-3$_{phenol}$), 7.28–7.25 (m, 2 H, 5-H, 6-H), 7.21–7.17 (m, 1 H, C*H*-5$_{phenol}$), 6.93–6.91 (m, 1 H, C*H*-6$_{phenol}$), 6.81–6.77 (m, 1 H, C*H*-4$_{phenol}$), 5.80 (q, $^3J_{FH}$ = 8.9 Hz, 1 H, C*H*CF$_3$), 3.68 (s, 3 H, CH_3) ppm. ^{13}C NMR (150 MHz, [D$_4$]MeOH): δ = 156.5 (1 C, *C*H-1$_{phenol}$), 150.4 (1 C, *C*-2), 142.9 (1 C, *C*-3a), 136.5 (1 C, *C*-7a), 131.2 (1 C, *C*H-5$_{phenol}$), 131.1 (1 C, *C*H-3$_{phenol}$), 126.7 (q, $^1J_{CF}$ = 279.2 Hz, 1 C, *C*F_3), 124.4 (1 C, *C*-6), 123.6 (1 C, *C*-5), 120.9 (1 C, *C*H-4$_{phenol}$), 119.9 (1 C, *C*-4), 119.1 (1 C, *C*H-2$_{phenol}$), 116.5 (1 C, *C*H-6$_{phenol}$), 110.9 (1 C, *C*-7), 41.2 (q, $^2J_{CF}$ = 30.1 Hz, 1 C, *C*HCF$_3$), 30.2 (1 C, *C*H_3) ppm. ^{19}F NMR (376 MHz, [D$_4$]MeOH): δ = –66.4 (s, CF_3) ppm. HRMS (ESI): calcd. for $C_{16}H_{12}DF_3N_2O$ [M + H]$^+$ (D from NMR solvent exchange) 308.11155; found 308.11152.

2-(1-Diazo-2,2,2-trifluoroethyl)-1-methyl-1*H*-benzo[*d*]imidazole (17): ^{1}H NMR (600 MHz, [D$_4$]MeOH): δ = 8.07–8.05 (m, 1 H, 6-*H*), 7.66–7.64 (m, 1 H, 7-H), 7.61–7.57 (m, 1 H, 6-H), 7.44–7.40 (m, 1 H, 5-H), 3.88 (s, 3 H, CH_3) ppm. ^{13}C NMR (150 MHz, [D$_4$]-MeOH): δ = 160.1 (q, $^2J_{CF}$ = 32.0 Hz, 1 C, *C*-2), 142.6 (1 C, *C*-3a), 141.0 (1 C, *C*-2), 139.9 (1 C, *C*-7a), 128.2 (1 C, *C*-6), 123.4 (1 C, *C*-5), 123.2 (q, $^1J_{CF}$ = 279.2 Hz, 1 C, *C*F_3), 113.3 (1 C, *C*-4), 112.8 (1 C, *C*-7), 31.7 (1 C, *C*H_3) ppm. ^{19}F NMR (376 MHz, [D$_4$]-MeOH): δ = –56.3 (s, CF_3) ppm.

1-Methyl-2-(2,2,2-trifluoro-1-phenoxyethyl)-1*H*-benzo[*d*]imidazole (16): ^{1}H NMR (400 MHz, [D$_4$]MeOH): δ = 7.71–7.69 (m, 1 H, 4-H), 7.55–7.53 (m, 1 H, 7-H), 7.39–7.25 (m, 4 H, 5-H, 6-H, *m*CH_{phenol}), 7.04–7.00 (m, 3 H, *o*CH_{phenol}, *p*CH_{phenol}), 6.36 (q, $^3J_{FH}$

= 6.6 Hz, 1C, C*H*CF$_3$), 3.98 (s, 3 H, C*H*$_3$) ppm. ^{13}C NMR (100 MHz, [D$_4$]MeOH): δ = 157.4 (1 C, *ipso*CH_{phenol}), 145.9 (1 C, *C*-2), 142.8 (1 C, *C*-3a), 137.6 (1 C, *C*-7a), 131.0 (2 C, *m*CH_{phenol}), 125.4 (1 C, *C*-6), 124.5 (q, $^1J_{CF}$ = 281.2 Hz, 1 C, *C*F$_3$), 124.4 (1 C, *C*-5), 124.2 (1 C, *p*CH_{phenol}) 120.4 (1 C, *C*-4), 116.8 (2 C, *o*CH_{phenol}), 111.6 (1 C, *C*-7), 74.3 (q, $^2J_{CF}$ = 34.1 Hz, 1 C, *C*HCF$_3$), 31.4 (1 C, *C*H$_3$) ppm. ^{19}F NMR (376 MHz, [D$_4$]MeOH): δ = –74.3 (s, C*F*$_3$) ppm. IR (ATR): $\tilde{\nu}$ = 3385 (w, br.), 3063 (w), 2924 (w), 1595 (m), 1495 (m), 1478 (m), 1441 (m), 1395 (m), 1337 (m), 1321 (m), 1270 (m), 1224 (s), 1190 (s), 1173 (s), 1149 (s), 1084 (s), 1066 (s), 1005 (w), 980 (w), 915 (m), 856 (m), 772 (m), 735 (s), 687 (s), 672 (m), 618 (m), 597 (m), 560 (m) cm^{-1}. UV/Vis (MeOH): λ_{max} (log ε) = 285 nm (3.80), 276 (3.92), 268 (3.91), 258 (3.94), 206 (4.55). HRMS (ESI): calcd. for $C_{16}H_{13}F_3N_2O$ [M + H]$^+$ 307.19527; found 307.10557.

2,2,2-Trifluoro-1-(1-methyl-1*H*-imidazol-2-yl)ethanone Oxime (22): To a solution of 1-methylimidazole (4.0 g, 48.72 mmol, 1.0 equiv.) in toluene (200 mL) at –20 °C was slowly added TFAA (8.24 mL, 58.48 mmol, 1.2 equiv.), followed by the addition of NEt$_3$ (8.14 mL, 58.83 mmol, 1.2 equiv.). The solution was warmed to room temp. overnight and the organic phase was washed with H_2O (100 mL). The aqueous layer was extracted with EtOAc (2×50 mL). The organic layers were combined and the solvent was removed under reduced pressure. Distillation (110 °C, 17 mbar) gave ketone **21a** (6.46 g, 36.29 mmol, 74%) as a colorless solid. To a solution of ketone **21a**[18] (800 mg, 4.49 mmol, 1.0 equiv.) in pyridine (3.5 mL) was added hydroxylamine-HCl (313 mg, 6.74 mmol, 1.5 equiv.) in one portion and the resulting solution was heated to reflux for 2 h. After cooling to room temp. the solvent was removed under reduced pressure. *t*BuOMe (5 mL) was added to the residue and the resulting suspension was extracted twice with citric acid (0.2 M, 5 mL). In the following the aqueous phase was extracted with EtOAc (5 mL). The combined organic phase was dried with $MgSO_4$ and subsequent removal of the solvent gave oxime **22** (600 mg, 3.11 mmol, 69%) as a colorless solid. R_f = 0.7 (EtOAc); M.p. 118–120 °C. ^{1}H NMR (400 MHz, [D$_6$]acetone): δ = 7.346–7.343 (m, 1 H, 4-H), 7.135–7.132 (m, 2 H, 5-H), 3.72 (s, 3 H, C*H*$_3$) ppm. ^{13}C NMR (100 MHz, [D$_6$]acetone): δ = 140.0 (q, $^2J_{CF}$ = 34.2 Hz, 1 C, *C*O), 135.3 (1 C, *C*-2), 129.7 (1 C, *C*-4), 124.3 (1 C, *C*-5), 121.4 (q, $^1J_{CF}$ = 273.0 Hz, 1 C, *C*F$_3$), 34.2 (1 C, *C*H$_3$) ppm. ^{19}F NMR (376 MHz, [D$_6$]acetone): δ = –65.8 (s, C*F*$_3$) ppm. IR (ATR): $\tilde{\nu}$ = 3177 (w), 2653 (m, br.), 2564 (m, br.), 2476 (m, br.), 1851 (m, br.), 1653 (m), 1470 (m), 1442 (m), 1413 (m), 1324 (s), 1283 (w), 1202 (s), 1122 (s), 1055 (m), 1024 (s), 977 (s), 932 (s), 798 (w), 760 (s), 718 (s), 654 (w), 620 (m) cm^{-1}. UV/Vis (MeOH): λ_{max} (log ε) = 262 nm (3.53), 203 (3.91). HRMS (ESI): calcd. for $C_6H_6F_3NO$ [M + H]$^+$ 194.05357; found 194.05314.

2,2,2-Trifluoro-1-(1-methyl-1*H*-imidazol-2-yl)ethanone *O*-Tosyl Oxime (22a): Oxime **22** (581 mg, 3.01 mmol, 1.0 equiv.) was dissolved in CH_2Cl_2 (10 mL) and cooled to 0 °C. NEt$_3$ (0.62 mL, 4.51 mmol, 1.5 equiv.) and TsCl (688 mg, 3.61 mmol, 1.2 equiv.) were added and the resulting solution was stirred and warmed to room temp. overnight. The reaction mixture was extracted with H_2O (10 mL) and the aqueous phase was washed twice with CH_2Cl_2 (10 mL). The combined organic phases were dried with $MgSO_4$. Purification by column chromatography [petroleum ether/EtOAc, 4:1 to 2:1] gave tosylated oxime **22a** (787 mg, 2.47 mmol, 82%) as a yellowish oil. R_f = 0.48 [petroleum ether/EtOAc (2:1)]. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.88–7.85 (m, 2 H, *o*CH), 7.40–7.38 (m, 2 H, *m*C*H*), 7.233–7.230 (m, 1 H, *H*-4$_{imidazole}$), 7.113–7.111 (m, 1 H, *H*-5$_{imidazole}$), 3.68 (s, 3 H, C$H_{3imidazole}$), 2.41 (s, 3 H, C*H*$_3$) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 146.8 (1 C, *p*C q), 145.8 (q, $^2J_{CF}$ = 35.6 Hz, 1 C, *C*O), 132.3 (1 C, *C*-2$_{imidazole}$), 130.9 (1 C, *C*-4$_{imidazole}$), 130.4 (1 C, *ipso*Cq), 130.1 (2 C, *m*CH), 129.4 (2 C, *o*CH), 124.4 (1 C, *C*-5$_{imidazole}$), 118.9 (q, $^1J_{CF}$ = 277.5 Hz, 1 C, *C*F$_3$), 34.6 (1 C, *C*H$_{3,imidazole}$), 21.8 (1 C, *C*H$_3$) ppm. ^{19}F NMR (376 MHz, CDCl$_3$): δ = –67.0 (s, C*F*$_3$) ppm. IR (ATR): $\tilde{\nu}$ = 3146 (w), 3058 (w), 1646 (w), 1592 (m), 1467 (m), 1419 (w), 1371 (m), 1306 (m), 1281 (m), 1198 (s), 1164 (s), 1092 (m), 1046 (w), 996 (m), 917 (m), 885 (s), 787 (m), 768 (s), 743 (m), 708 (s), 681 (s), 652 (m), 628 (m), 613 (s), 546 (s) cm^{-1}. UV/Vis (CHCl$_3$): λ_{max} (log ε) = 292 nm (3.78), 276 (3.73), 239 (3.87). MS (EI): *m*/*z* (%) = 347.0 (33), 155.0 (55), 91.0 (100). HRMS (EI): calcd. for $C_{13}H_{12}F_3N_3O_3S$ [M]$^+$ 347.05460; found 347.05506.

1-Methyl-2-[3-(trifluoromethyl)diaziridin-3-yl]-1*H*-imidazole (23): Tosylated oxime **22a** (733 mg, 2.11 mmol, 1.0 equiv.) was dissolved in CH_2Cl_2 (10 mL) and added to a stirred solution of NH_3 (l) at –78 °C. The suspension was stirred for 2 h at –78 C. Then the solution was warmed to room temp. within 30 min. The reaction mixture was filtered and the filtrate was concentrated under reduced pressure affording diaziridine **23** (326 mg, 1.88 mmol, 89%) as a colorless solid. R_f = 0.5 (EtOAc), m.p. 99–101 °C. ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.05 (m, 1 H, 4-H), 6.93 (m, 1 H, 5-H), 3.79 (s, 3 H, C*H*$_3$), 2.81 (s, 2 H, N-*H*) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 138.8 (1 C, *C*-2), 128.8 (1 C, *C*-4), 123.0 (1 C, *C*-5), 122.8 (q, $^1J_{CF}$ = 278.1 Hz, 1 C, *C*F$_3$), 52.5 (q, $^2J_{CF}$ = 38.7 Hz, 1 C, *C*N), 33.5 (1 C, *C*H$_3$) ppm. ^{19}F NMR (376 MHz, CDCl$_3$): δ = –76.2 (s, C*F*$_3$) ppm. IR (ATR): $\tilde{\nu}$ = 3230 (m), 3068 (w, br.), 2962 (w), 1726 (w), 1667 (w), 1575 (w), 1491 (m), 1468 (w), 1416 (m), 1345 (w), 1281 (m), 1247 (m), 1132 (s), 1082 (m), 957 (m), 929 (m), 874 (m), 763 (s), 700 (m), 680 (m), 618 (w), 558 (w) cm^{-1}. UV/Vis (CHCl$_3$): λ_{max} (log ε) = 300 nm (2.69), 288 (2.69), 239 (3.00), 233 (2.46). MS (EI): *m*/*z* (%) = 192.1 (9), 176.0 (51), 143.0 (45), 94.0 (100). HRMS (EI): calcd. for $C_6H_7F_3N_4$ [M]$^+$ 192.06173; found 192.06217.

2-(1-Ethoxy-2,2,2-trifluoroethyl)-1-methyl-1*H*-imidazole (25): Diaziridine **23** (100 mg, 525 μmol, 1.0 equiv.) was dissolved in EtOH (10 mL) and cooled to 0 °C. NEt$_3$ (0.146 mL, 1.05 mmol, 2.0 equiv.) was added followed by dropwise addition of iodine (133 mg, 525 μmol, 1.0 equiv.), which was dissolved in EtOH (10 mL). After stirring for 5 min at 0 °C the solution was evaporated under high vacuum and condensed in a cooling trap at –78 °C. The reaction mixture was warmed to room temp. overnight. EtOH was removed under reduced pressure (p_{min} = 50 mbar) and ether **25** (5 mg, 24 μmol, 5%) was isolated by column chromatography as a pale yellow oil. R_f = 0.07 (CHCl$_3$). ^{1}H NMR (400 MHz, CDCl$_3$): δ = 7.029–7.026 (m, 1 H, 4-H), 6.918–6.915 (m, 1 H, 5-H), 5.03 (q, $^3J_{FH}$ = 7.4 Hz, 1 H, *H*CCF$_3$), 3.79 (s, 3 H, NC*H*$_3$), 3.71–3.56 (m, 2 H, OC*H*$_2$), 1.25 (t, $^3J_{HH}$ = 7.0 Hz, 3 H, C*H*$_3$) ppm. ^{13}C NMR (100 MHz, CDCl$_3$): δ = 139.2 (m, 1 C, *C*-2), 128.4 (1 C, *C*-4), 124.0 (1 C, *C*-5), 123.4 (q, $^1J_{CF}$ = 282.3 Hz, 1 C, *C*F$_3$), 76.1 (q, $^2J_{CF}$ = 32.9 Hz, 1 C, H*C*CF$_3$), 67.1 (1 C, O*C*H$_2$), 33.7 (m, 1 C, N*C*H$_3$), 14.9 (1 C, *C*H$_3$) ppm. ^{19}F NMR (376 MHz, CDCl$_3$): δ = –75.0 (s, C*F*$_3$) ppm. IR (ATR): $\tilde{\nu}$ = 3267 (w, br.), 3114 (w), 2982 (w), 2938 (w), 2902 (w), 1739 (w), 1670 (m), 1580 (w), 1492 (m), 1447 (w), 1411 (m), 1355 (m), 1299 (m), 1175 (s), 1150 (s), 1124 (s), 1101 (s), 906 (m), 864 (w), 808 (m), 751 (m), 700 (m), 670 (m), 633 (w), 583 (w), 537 (w) cm^{-1}. UV/Vis (CHCl$_3$): λ_{max} (log ε) = 283 nm (3.19), 239 (3.19), 232 (3.05). MS (EI): *m*/*z* (%) = 208.1 (11), 164.0 (100), 144.0 (53), 111.0 (77), 83.0 (17). HRMS (EI): calcd. for $C_8H_{11}F_3N_2O$ [M]$^+$ 208.08180; found 208.08183.

Supporting Information (see footnote on the first page of this article): X-ray structure determination; computational chemistry; ^{1}H, ^{13}C, ^{19}F NMR spectra and supporting images.

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