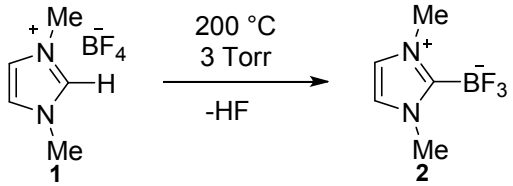
SUPPORTING INFORMATION

Materials and Methods

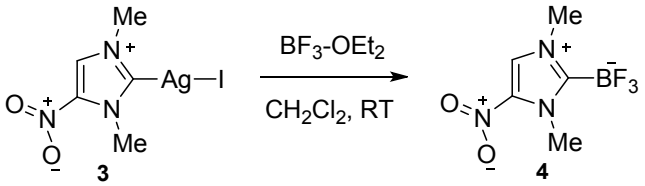
General Consideration. 1, 3-dimethyl-1*H*-imidazolium tetrafluoroborate (**1**),[1] and 1, 3-dimethyl-4-nitroimidazolium silver complex (**3**)[2] were synthesized according to the reported procedure. 1-Methylimidazole, boron trifluoride diethyl etherate (BF_3-OEt_2), methyl iodide (CH_3I), 10% palladium supported carbon, and succinic anhydride were purchased from Alfar Aesar; 4-nitroimidazole was purchased from Tokyo Chemical Industry Co., Ltd; N, N-di-*iso*-propylethylamine (DIEA), and maleic anhydride were purchased from Sigma Aldrich; silver oxide was purchased from Strem chemicals; acetic anhydride was purchased from EM industries, Inc; sodium acetate was purchased from Mallinckrodt. All chemicals were used without further purification. Solvents were dried by passing through an alumina column (CH_2Cl_2), refluxing under N_2 over Na (Et_2O and THF), refluxing under N_2 over CaH_2 (CH_3CN). Electrospray mass spectra were acquired on a MDS Sciex API QStar Pulsar. NMR spectra were recorded on a Varian Unity Inova 400 NMR and an Inova 500B spectrometer at ambient temperature. Chemical shifts are given in ppm, and are referenced to residual ^1H and ^{13}C solvent signals as well as external BF_3-Et_2O (^{11}B NMR and ^{19}F NMR).

Preparation of 1, 3-dimethylimidazolium-2-trifluoroborate (2)



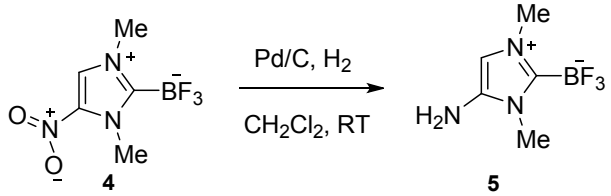
1, 3-Dimethyl-1*H*-imidazolium tetrafluoroborate (0.252 g, 1.37 mmol) was placed into a sublimation apparatus, connected *via* a liquid-N_2-cooled trap to a high-vacuum line. The powder was heated by a heating mantle under reduced pressure to 200 °C at which point compound **2** started condensing on the cold finger. The sublimation was continued for 15 min. Compound **2** (0.196 g, 1.19 mmol) was obtained in a 87 % yield. ^1H NMR (499.4 MHz, CD_3CN): δ 3.85 (s, 6H, -C*H*$_3$), 7.11 (s, 2H, =C*H*). ^{13}C NMR (125.6 MHz, CD_3CN): δ 35.93 (-*C*H$_3$), 122.64 (=*C*H). ^{11}B NMR (128.2 MHz, CD_3CN): δ 0.21 (q, $J_{B\text{-}F}$ = 37.0 Hz). ^{19}F NMR (282.2 MHz, CD_3CN): δ -139.2 (q, $J_{B\text{-}F}$ = 37.0 Hz). HRMS (ESI^+) calcd for $[M\text{-}F]^+$: 145.0748, found: 145.0758.

Preparation of 1, 3-dimethyl-4-nitroimidazolium-2-trifluoroborate (4)



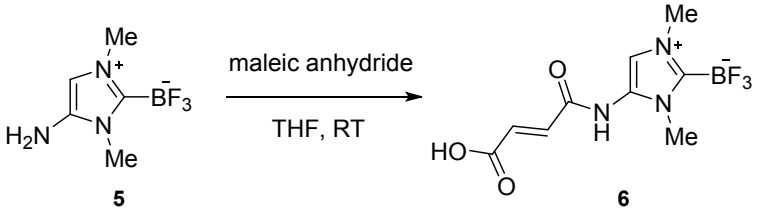
BF_3-OEt_2 (0.34 mL, 2.75 mmol) was added to a suspension of **3** (0.691 g, 0.92 mmol) in CH_2Cl_2 (15 mL) at room temperature. The suspension was stirred for 4 h and filtered. The filtrate was purified by flash chromatography using silica gel as a stationary phase and CH_2Cl_2 as a mobile phase to remove an excess BF_3-OEt_2 and an imidazolium salt impurity. The purified solution was dried in *vacuo* resulting **4** as a white powder (0.160 g) in a 83 % yield. ^{1}H NMR (499.4 MHz, CD_3CN): δ 3.94 (s, 3H, -C*H*$_3$), 4.16 (s, 3H, -C*H*$_3$), 8.21 (s, 1H, =C*H*). ^{13}C NMR (125.6 MHz, CD_3CN): δ 35.84 (*C*H$_3$), 37.61 (*C*H$_3$), 126.04 (=*C*H), 138.55 (=*C*NO$_2$). ^{11}B NMR (128.2 MHz, CD_3CN): δ 0.13 (q, $J_{B\text{-}F}$ = 33.5 Hz). ^{19}F NMR (469.9 MHz, CD_3CN): δ -137.86 (q, $J_{B\text{-}F}$ = 33.5 Hz). HRMS (ESI$^-$) calcd for [M-H]$^-$: 208.0505, found: 208.0517.

Preparation of 1, 3-dimethyl-4-amino-imidazolium-2-trifluoroborate (5)



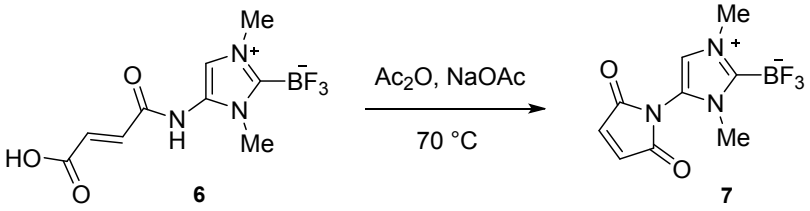
10% palladium on carbon (0.235 g, 0.221 mmol Pd) was added to a solution of **4** (0.461 g, 2.21 mmol) in CH_2Cl_2 (20 mL). Hydrogen gas was bubbled through the solution for 30 min. The mixture was stirred under a hydrogen atmosphere overnight at room temperature. The solution was then filtered over celite and the solvent was removed under vacuum yielding **5** as a white powder (0.307 g) in a 78 % yield. ^{1}H NMR (499.4 MHz, CD_3CN): δ 3.61 (s, 3H, -C*H*$_3$), 3.73 (s, 3H, -C*H*$_3$), 4.02 (s, 2H, -N*H*$_2$), 6.37 (s, 1H, =C*H*). ^{13}C NMR (125.6 MHz, CD_3CN): δ 30.67 (*C*H$_3$), 35.51 (*C*H$_3$), 104.57 (=*C*H), 138.20 (=*C*NH$_2$). ^{11}B NMR (128.2 MHz, CD_3CN): δ 0.27 (q, $J_{B\text{-}F}$ = 37.2 Hz). ^{19}F NMR (375.9 MHz, CD_3CN): δ -138.0 (q, $J_{B\text{-}F}$ = 37.2 Hz). HRMS (ESI$^-$) calcd for [M-H]$^-$: 178.0763, found: 178.0758.

Preparation of 1, 3-dimethyl-4-maleic acid-imidazolium-2-trifluoroborate (6)



Maleic anhydride (0.172 g, 1.76 mmol) was added to a solution of **5** (0.1572g, 0.88 mmol) in THF (8 mL). The reaction mixture was stirred for 20 h at room temperature resulting in a white precipitate. The powder was collected by filtration and then dried in *vacuo* yielding **6** (0.180 g) in a 74 % yield. ^{1}H NMR (399.5 MHz, D_2O): δ 3.46 (s, 3H, -CH_3), 3.61 (s, 3H, -CH_3), 6.22 (d, 1H, =C*H(*CO)), 6.39 (d, 1H, =C*H(*CO)), 7.08 (s, 1H, =C*H*) . ^{13}C NMR (125.6 MHz, CD_3CN): δ 31.64 (*C*H_3), 35.96 (*C*H_3), 116.92 (=*C*H), 126.56 (=*C*N(CO)(CH=CH)COOH), 129.99 (-H*C*=CH-), 131.67 (-HC=*C*H-), 167.35 (*C*=O), 168.71 (*C*=O). ^{11}B NMR (128.2 MHz, D_2O): δ -0.30 (q, $J_{B\text{-}F}$ = 40.0 Hz). ^{19}F NMR (469.9 MHz, D_2O): δ -137.4 (q, $J_{B\text{-}F}$ = 40.0 Hz). HRMS (ESI$^-$) calcd for [M-H]$^-$: 276.0767, found: 276.0748.

Preparation of 1, 3-dimethyl-4-maleimide-imidazolium-2-trifluoroborate (7)



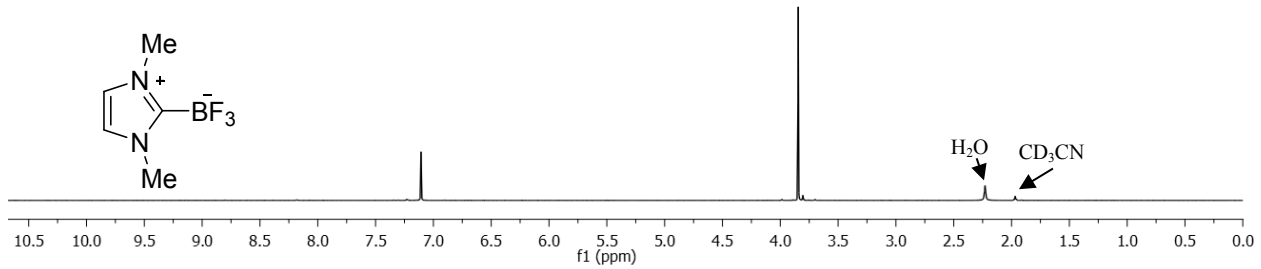
A solution of **6** (0.131 g, 0.47 mmol) and sodium acetate (NaOAc) (0.064 g, 0.47 mmol) in acetic anhydride (Ac_2O) (15 mL) was heated to 70 °C for 3 h. After 3 h, the acetic anhydride was removed in vacuum. The crude product was re-dissolved in CH_2Cl_2 (30 mL) and then, the solution was washed with water (3x30 mL). The organic layer was dried with $MgSO_4$. Finally, the solvent was removed in vacuum yielding **7** (0.088 g) as a white powder in a 72 % yield. ^{1}H NMR (499.4 MHz, CD_3CN): δ 3.65 (s, 3H, -CH_3), 3.91 (s, 3H, -CH_3), 7.08 (s, 2H, maleimide=C*H*), 7.30 (s, 1H, =C*H*). ^{13}C NMR (125.6 MHz, CD_3CN): δ 32.36 (*C*H_3), 36.70 (*C*H_3), 121.33 (=*C*H), 121.52 (=*C*N(C(O)CH)$_2$), 135.86 (maleimide=*C*H), 168.75 (*C*=O). ^{11}B NMR (128.2 MHz, CD_3CN): δ 0.29 (q, $J_{B\text{-}F}$ = 35.6 Hz). ^{19}F NMR (375.9 MHz, CD_3CN): δ -138.5 (q, $J_{B\text{-}F}$ = 35.6 Hz). HRMS (ESI$^-$) calcd for [M+Na]$^-$: 282.0638, found: 282.0650.

Crystallographic Measurements

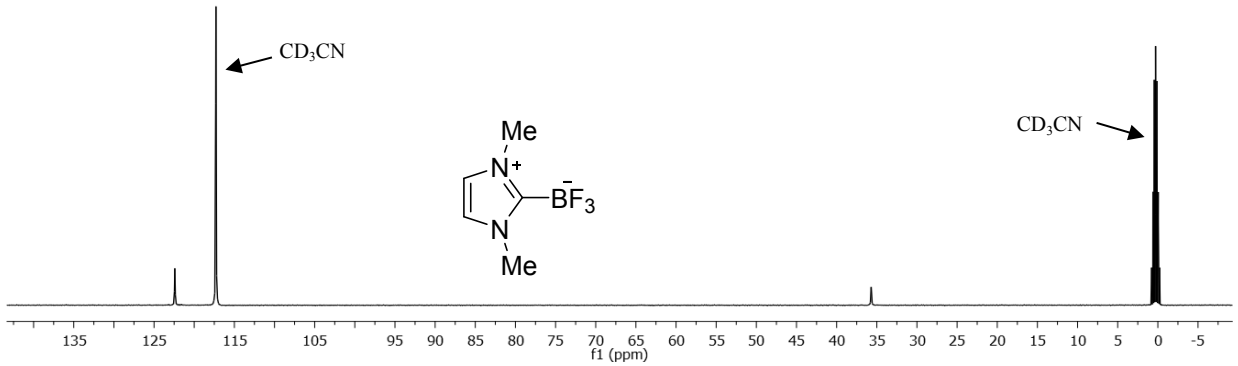
Single crystals of **2** were obtained by slow diffusion of Et_2O into a CH_3CN solution of **2**. Single crystals of **4** and **7** were obtained by slow diffusion of pentane into a THF solution of **4** and **7**, respectively. The crystallographic measurement of **2**, **4**, and **7** were performed using a Bruker APEX-II CCD area detector diffractometer, with graphite-monochromated Mo-K_α radiation (λ = 0.71069 Å). A specimen of suitable size and quality was selected and mounted onto a nylon loop. The semi-empirical method SADABS was applied for absorption correction. The structure was solved by direct methods, and refined by the full-matrix least-square metahod against F^2 with the anisotropic temperature parameters for all non-hydrogen atoms. All H atoms were geometrically placed and refined using the riding model approximations. Data reduction and further calculations were performed using the Bruker SAINT+ and SHELXTL NT program packages. CCDC: 1402916–1402918 contains the supplementary crystallographic data for this paper and can be accessed free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

Figure S1. ^{1}H, ^{13}C, ^{11}B, and ^{19}F NMR spectra of **2** in CD_3CN.

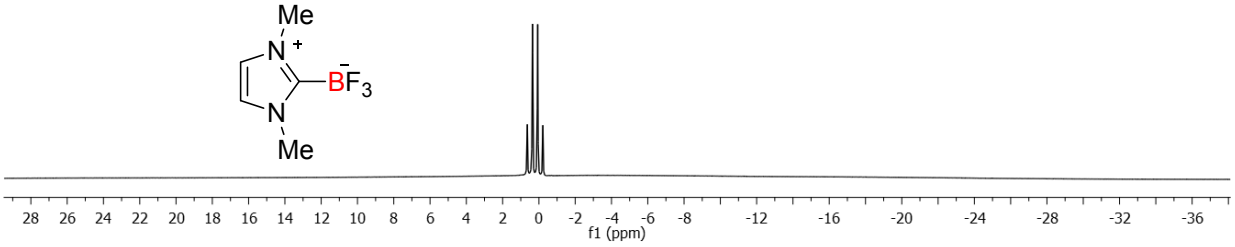
^{1}H NMR



^{13}C NMR



^{11}B NMR



^{19}F NMR

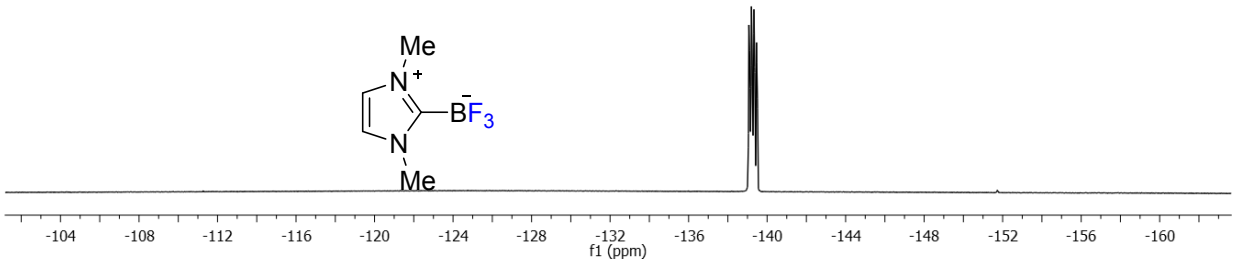
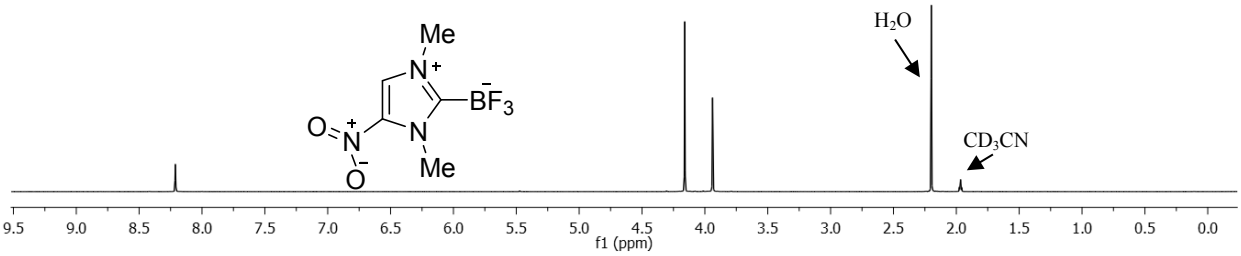
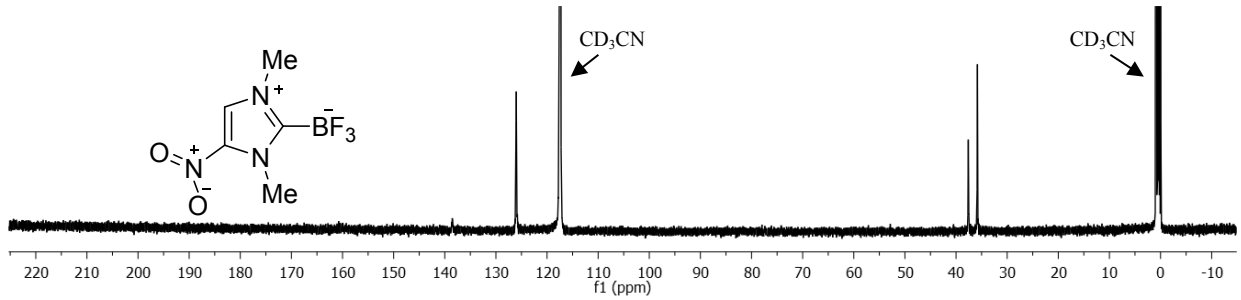


Figure S2. ^{1}H, ^{13}C, ^{11}B, and ^{19}F NMR spectra of **4** in CD_3CN.

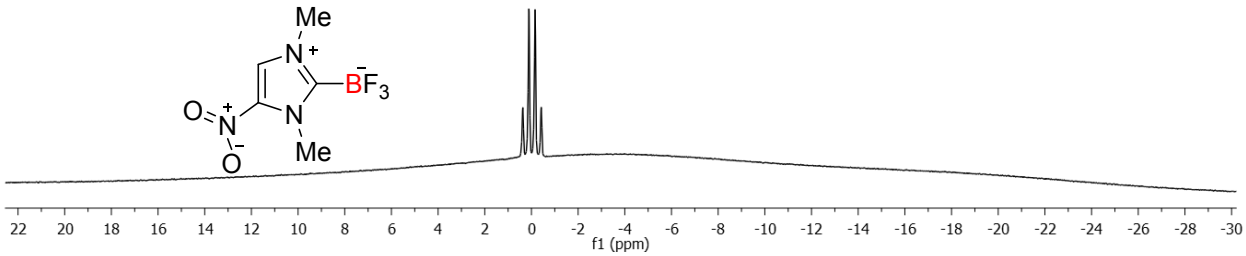
^{1}H NMR



^{13}C NMR



^{11}B NMR



^{19}F NMR

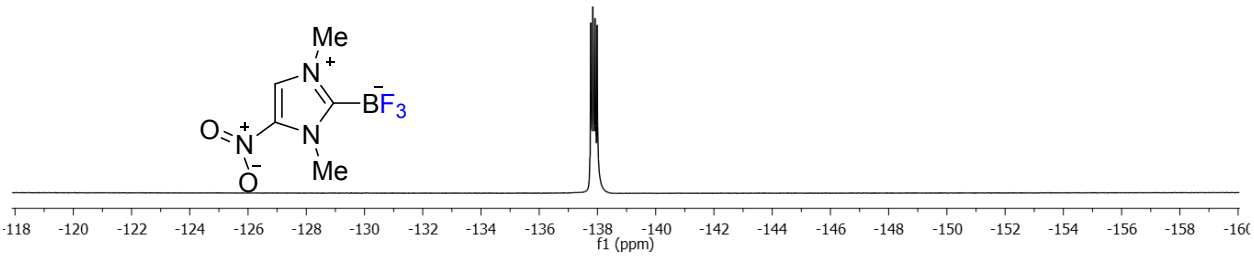
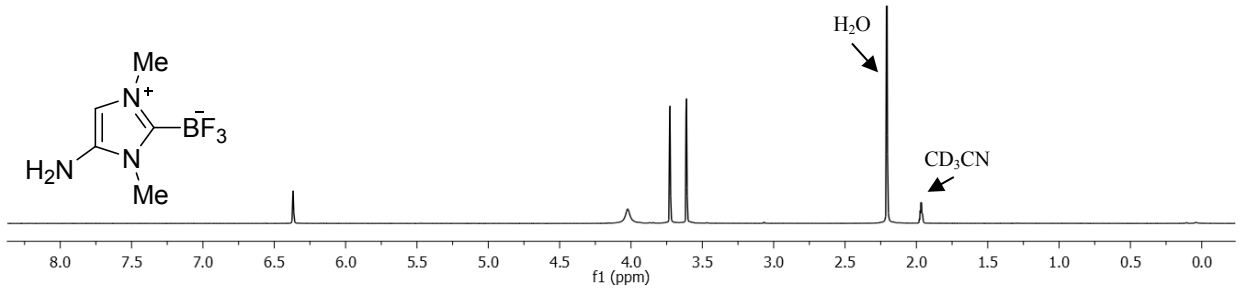
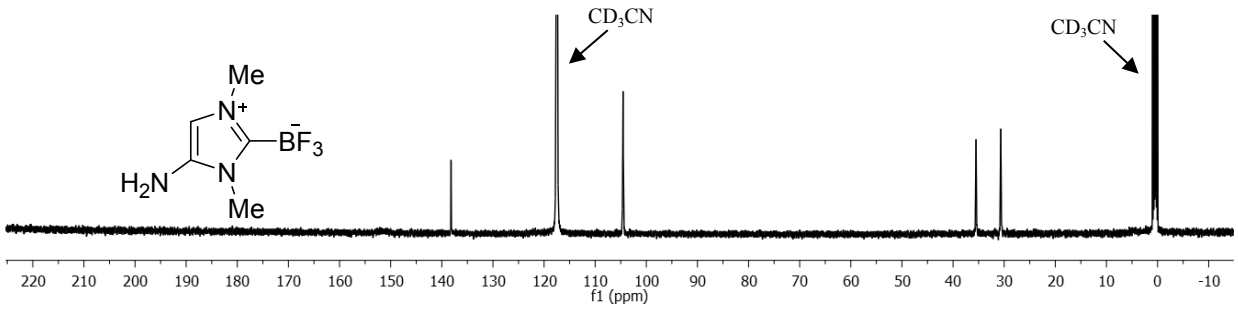


Figure S3. ^{1}H, ^{13}C, ^{11}B, and ^{19}F NMR spectra of **5** in CD_3CN.

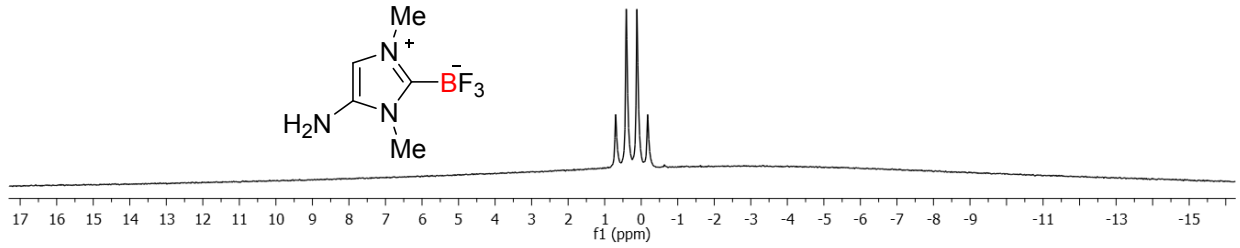
^{1}H NMR



^{13}C NMR



^{11}B NMR



^{19}F NMR

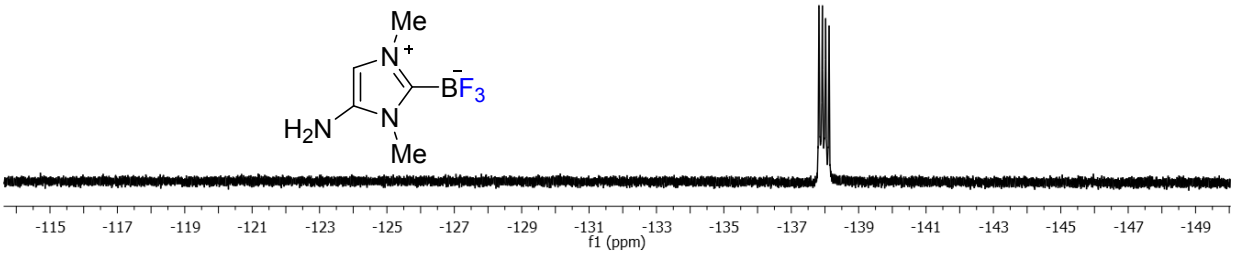
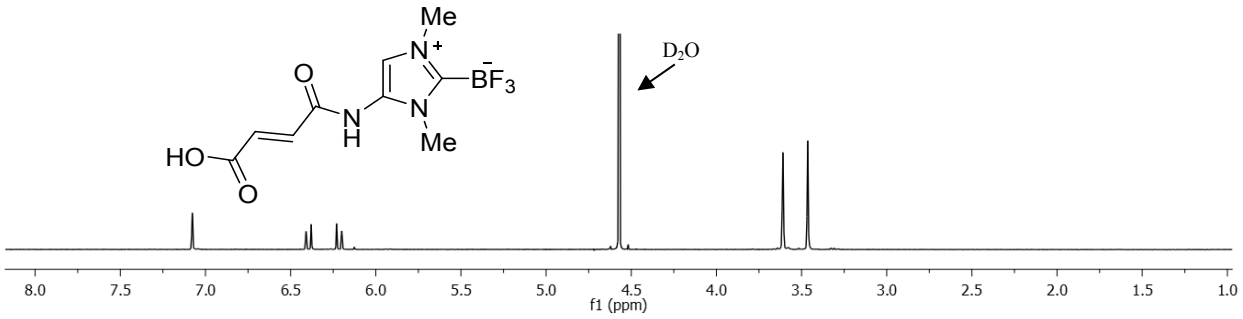
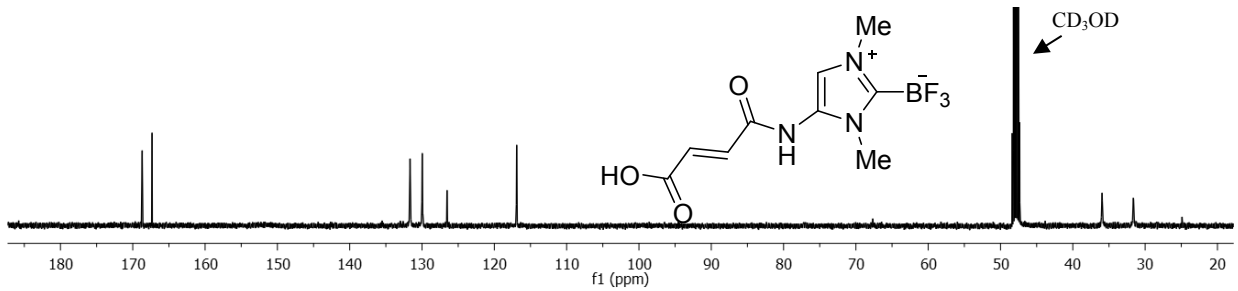


Figure S4. ^{1}H, ^{13}C, ^{11}B, and ^{19}F NMR spectra of **6** in D_2O.

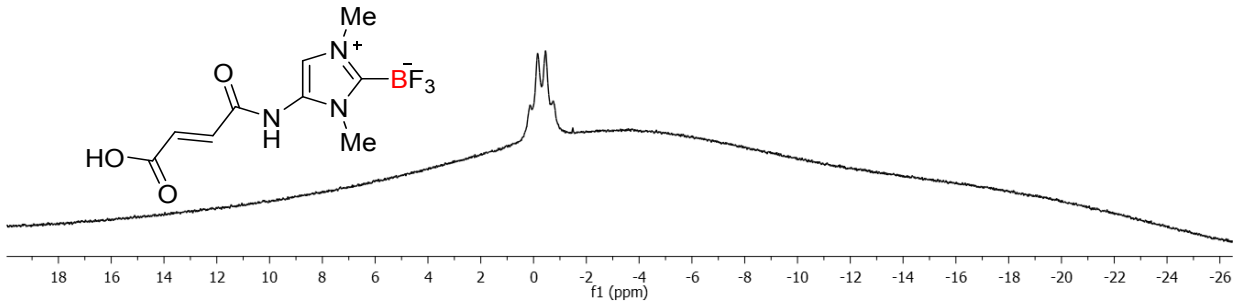
^{1}H NMR



^{13}C NMR



^{11}B NMR



^{19}F NMR

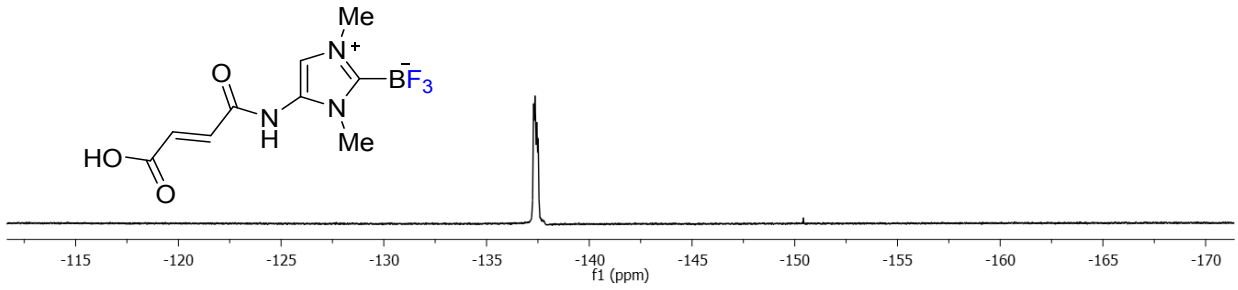
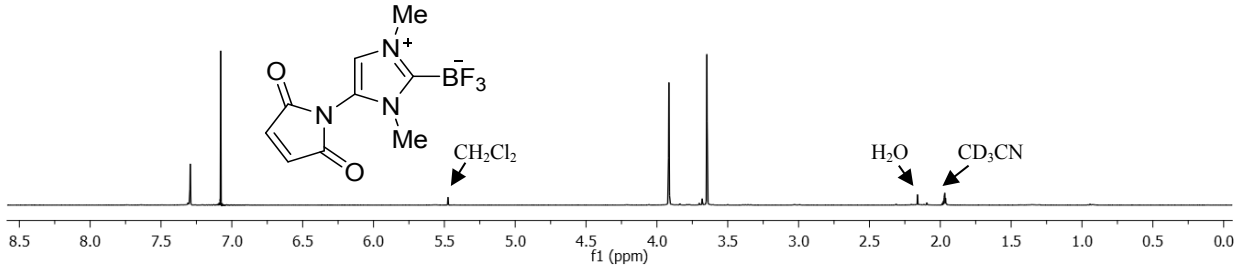
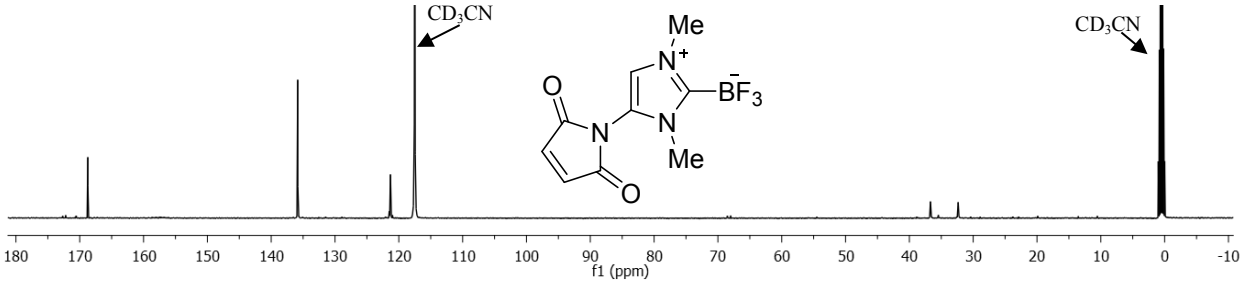


Figure S5. ^{1}H, ^{13}C, ^{11}B, and ^{19}F NMR spectra of **7** in CD_3CN.

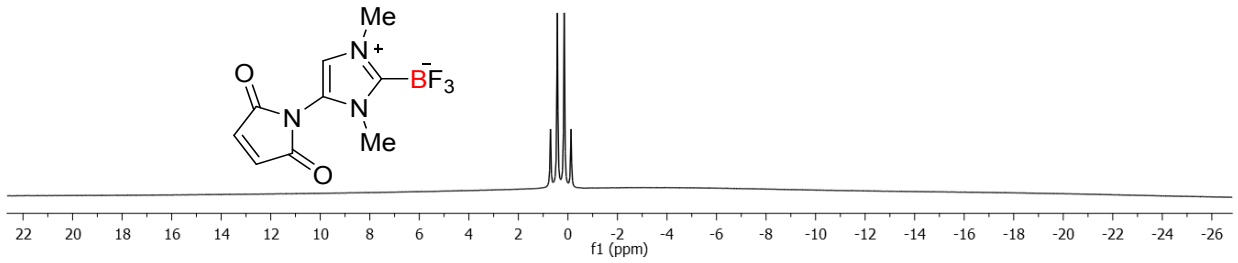
^{1}H NMR



^{13}C NMR



^{11}B NMR



^{19}F NMR

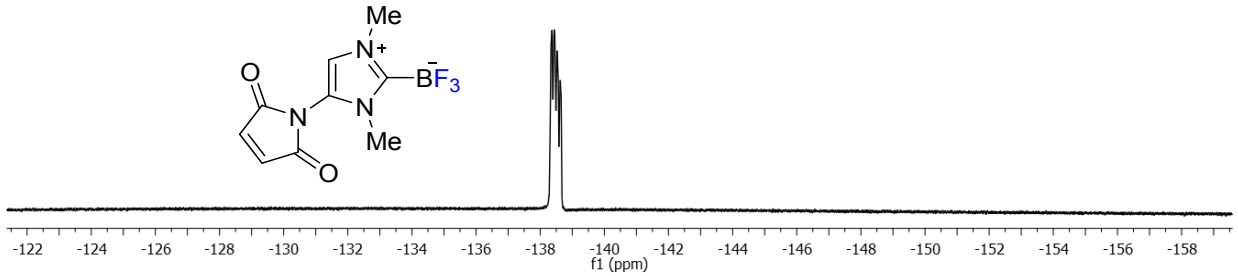


Figure S6. High resolution mass spectrum of **2**

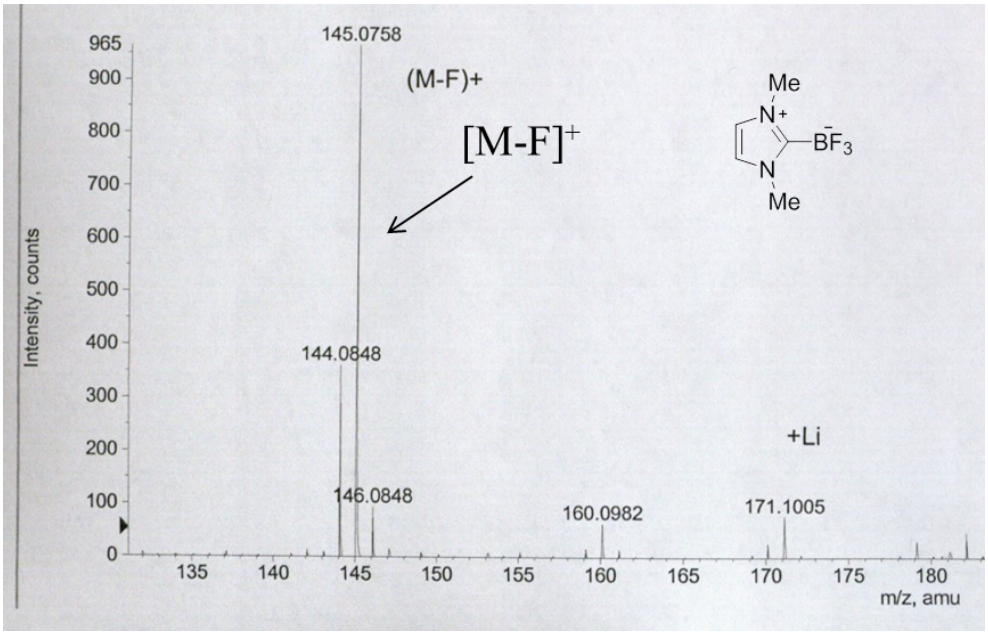


Figure S7. High resolution mass spectrum of **4**

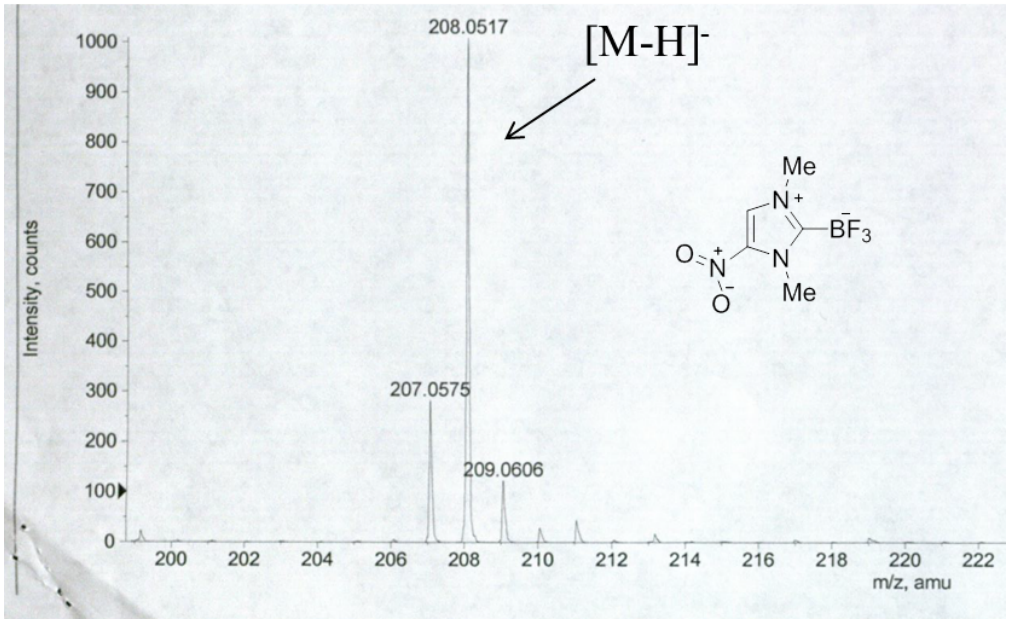


Figure S8. High resolution mass spectrum of **5**

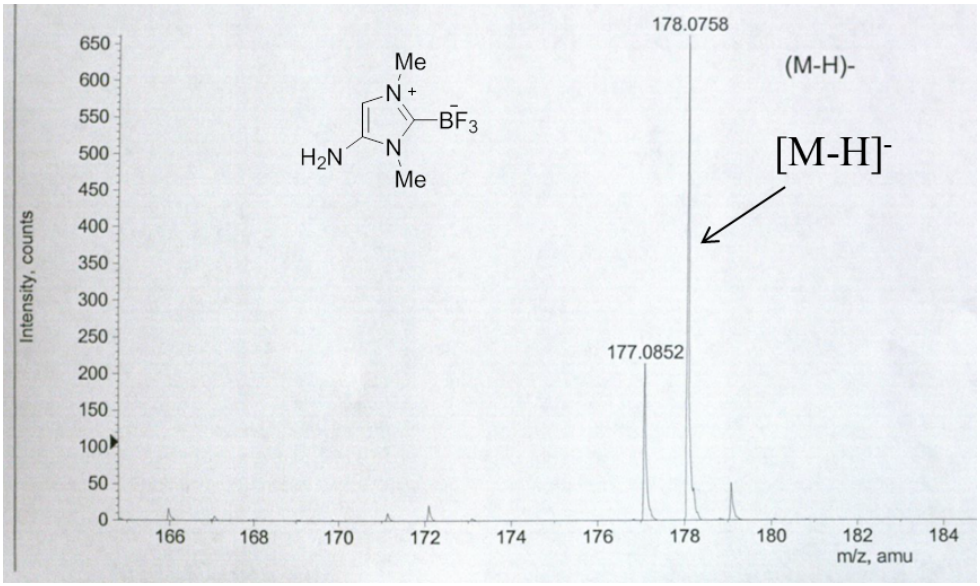


Figure S9. High resolution mass spectrum of **6**

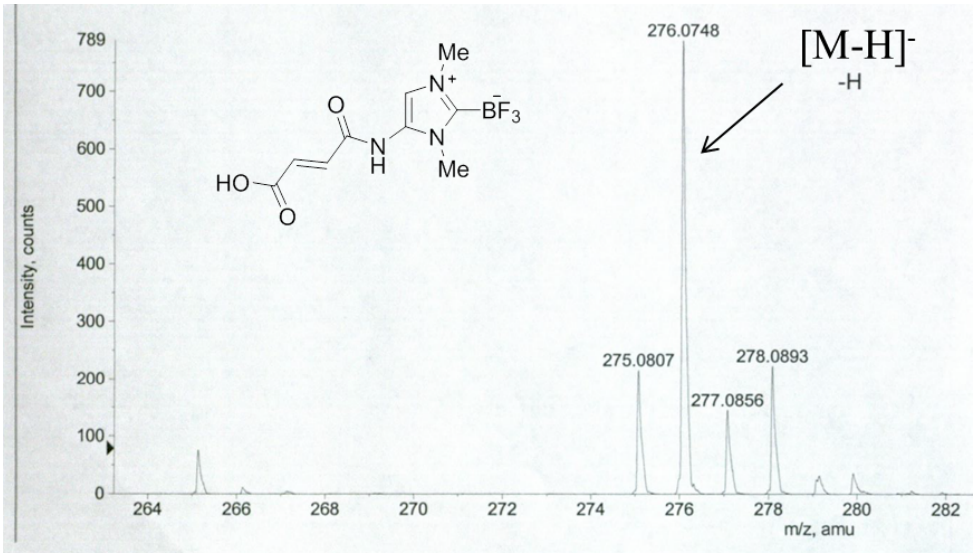
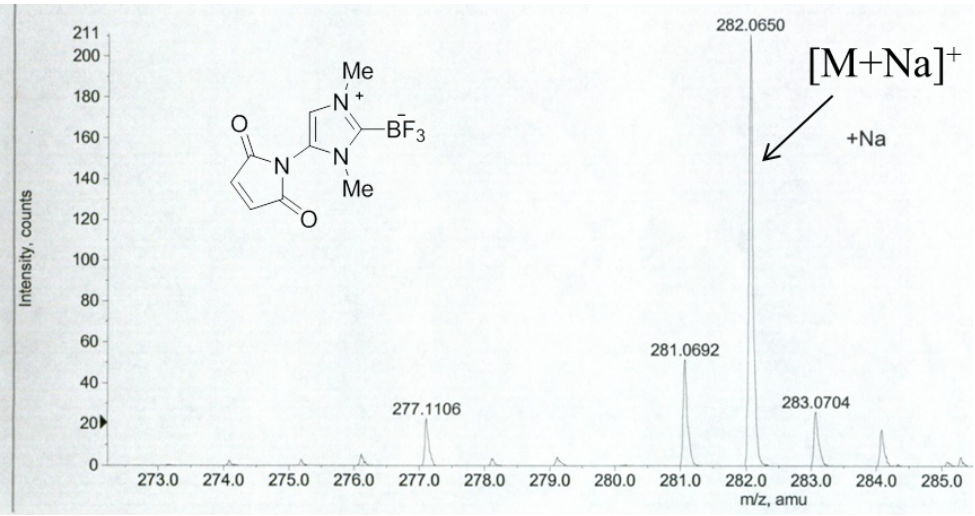


Figure S10. High resolution mass spectrum of **7**



Kinetic studies of the hydrolysis reactions

A sample of **2**, **4**, **5**, and **7** (5 mg) was dissolved in 0.2 mL CD_3CN and 0.8 mL D_2O phosphate buffer (pH 7.5, 500 mM). The ^{19}F NMR spectra of **2**, **4**, **5**, and **7** were collected periodically. The decomposition of aryltrifluoroborate species were monitored by integration of the decreasing aryltrifluoroborate signal in conjunction with the increasing signal corresponding to free F^-. All spectra were processed using the VNMRJ Version 2.2 NMR software. The rate constant, k_{obs}, was calculated using a well-established NMR method reported in the literature.[3] This method is based on the fact that that the concentration in $ArBF_3$ species is proportional to the ^{19}F NMR integration of $ArBF_3$ signal divided by the sum of the integration of $ArBF_3$ signal and the free fluoride signal. For convenience, the value of the $ArBF_3$ integration is arbitrarily set at 100 and the free fluoride integration determined. Based on the ^{19}F NMR results, free F^- NMR signal was only observed in the aqueous solution of **2**, and **5** after a week. The resulting data is provided in Table **S1** and **S2**.

Table S1: Kinetic data for the hydrolysis of **2**. The values provided for F^- and $ArBF_3$ correspond to the integration of the corresponding NMR signal.

		Data for **2**		
				k= 1.2E-6
			exp. Ratio	calc. ratio
Time (min)	[F]	$[BF_3]$	$[BF_3]/([BF_3]+[HF]$	$[BF_3]/([BF_3]+[HF]$
0	0.00	100	1.0000	1.0000
1141	0.34	100	0.9966	0.9986
2594	0.41	100	0.9959	0.9969
4152	0.48	100	0.9953	0.9950
9776	0.76	100	0.9925	0.9882
11000				0.9867
12000				0.9855
13000				0.9843
14000				0.9831
15000				0.9820

Table S2: Kinetic data for the hydrolysis of **5**. The values provided for F^- and $ArBF_3$ correspond to the integration of the corresponding NMR signal.

		Data for **5**		
				k= 1.1E-6
			exp. Ratio	calc. ratio
Time (min)	[F]	$[BF_3]$	$[BF_3]/([BF_3]+[HF]$	$[BF_3]/([BF_3]+[HF]$
0	0.00	100	1.0000	1.0000
1434	0.20	100	0.9980	0.9984
2884	0.31	100	0.9970	0.9968
4563	0.49	100	0.9952	0.9950
10126	0.91	100	0.9910	0.9889
11000				0.9880
12000				0.9869
13000				0.9858
14000				0.9847
15000				0.9837

Radiochemistry Experiment

All chemicals were purchased in analytical grade and used without further purification. Analytical reversed-phase HPLC using a Gemini 5μ C18 column (250 x 4.6mm) was performed on a SPD-M30A photodiode array detector (Shimadzu) and model 105S single-channel radiation detector (Carroll & Ramsey Associates). The flow was set to 1mL/min. The mobile phase stayed at 95% solvent A and 5% solvent B from 0-2min and then changed with a gradient from 95% solvent A 5% solvent B to 95% solvent B and 5% solvent A in 20min. Solvent A is 0.1% TFA in water and solvent B is 0.1% TFA in acetonitrile.

Radiochemistry

The radiolabeling reactions were carried out using the following protocol unless otherwise specified. Compound **2** or **7** (1.2 μmol) was mixed with $SnCl_4$ (5 eq) in MeCN (10 μL). The resulting solution was then combined with a MeCN solution (30 μL) of [^{18}F]fluoride. After shaking at 60°C for 10 min, the reaction was quenched by adding 200 μL of water. The mixture passed through a Sep-Pak cartridge (Sep-Pak Plus tC18) and washed with 3 mL water. The radiofluorinated derivatives [^{18}F]**2** or [^{18}F]**7** was eluted off the cartridge with 1mL MeCN and an aliquot of the MeCN fraction (30 μCi) was used for HPLC analysis. The results are compiled in Tables S3 and S4.

For [^{18}F]**7**, the pH of the solution collected after HPLC purification was adjusted to 7 by addition of 0.1N NaOH. The resulting solution was then mixed with an aqueous solution of H-Cys-Phe-OH (400 μg, 1.5μmol). After shaking for 10 min at room temperature, a portion of the reaction mixture (0.01mCi) was loaded onto HPLC for further analysis and purification. The HPLC containing [^{18}F]**7**-H-Cys-Phe-OH was collected. The HPLC eluent was removed using a rotary evaporator. [^{18}F]**7**-H-Cys-Phe-OH was reconstituted in 1x PBS for stability test and small animal study.

In Vitro Stability

[^{18}F]**7**-H-Cys-Phe-OH was incubated in 1x PBS buffer at 37 °C. An aliquot of the solution (10 μCi) was taken out and loaded on HPLC at 0.5h, 1h and 2h time point for analysis (Figure S14).

Small animal PET Imaging

Animal procedures were performed according to a protocol approved by the UNC institutional Animal Care and Use Committee. PET scans were performed using a small animal PET/CT scanner (Vista eXplore, GE Healthcare, Inc) with a center resolution of 1.2- and 4.6-mm axial field of view. A CT scan was first acquired for subsequent attenuation correction and anatomic registration. A normal nude mouse was anesthetized using 2% isoflurane and injected with 3.1 MBq (86 μCi) of [^{18}F]**7**-H-Cys-Phe-OH via tail vein. At 1, 2, and 4h post injection, static emission scans were acquired for 10-20 min. Raw PET images were reconstructed using 2D ordered subset expectation maximization (OSEM) algorithms with scatter, random and attenuation correction.

Table S3: radiosynthetic results for [^{18}F]**2**

Pre Sep-Pak purification							Post Sep-Pak purification			Post HPLC	
Entry	Starting activity (mCi)	Amount of [**2**] (μmol)	MeCN Volume (μL)	$SnCl_4$ (eq)	Temp (℃)	Time (min)	Amount of [**2**] (μmol)	Activity (mCi)	solution volume (mL)	Amount of [**2**] (μmol)	Activity (mCi)
1	37.2	0.6	40	5	25	10	0.5	14.4	1	0.5	13.2
2	77.2	1.2	40	5	25	10	0.8	35.5	1	0.8	32.5
3	34.5	2.4	40	5	25	10	0.4	17.4	1	0.4	16.3
4	39.3	1.2	40	10	25	10	0.4	20.5	1	0.4	19.0
5	39.7	1.2	40	15	25	10	0.4	20.0	1	0.4	19.1
6	48.4	1.2	40	5	40	10	0.6	29.5	1	0.6	27.3
7	37.1	1.2	40	5	60	10	0.4	21.3	1	0.4	19.8
8	42.9	1.2	40	5	25	20	0.4	23.1	1	0.4	21.4
9	55.4	1.2	40	5	25	30	0.6	23.1	1	0.6	22.1

Table S4: radiosynthetic results for [^{18}F]**7**

Pre Sep-Pak purification							Post Sep-Pak purification			Post HPLC	
Entry	Starting activity (mCi)	Amount of [**7**] (μmol)	MeCN Volume (μL)	$SnCl_4$ (eq)	Temp (℃)	Time (min)	Amount of [**7**] (μmol)	Activity (mCi)	solution volume (mL)	Amount of [**7**] (μmol)	Activity (mCi)
1	38	1.2	40	5	60	10	0.4	21.9	1	0.4	20.5

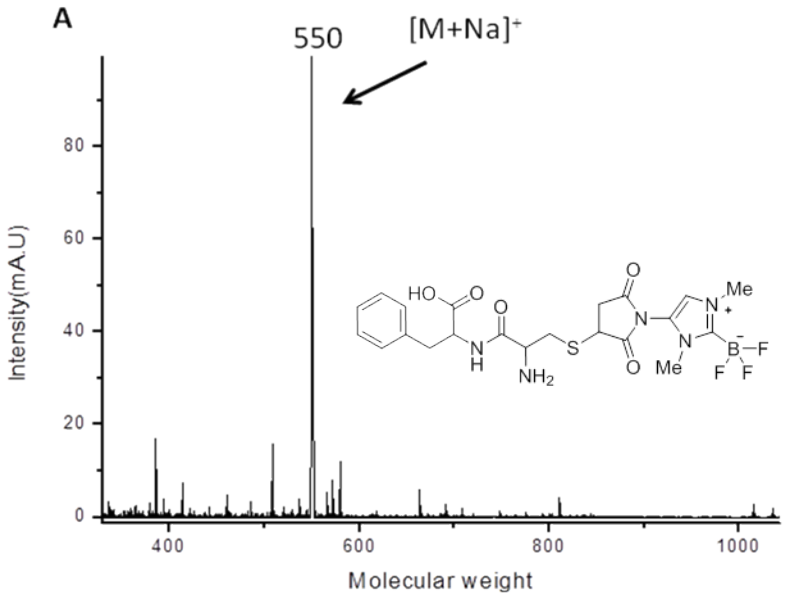


Figure S11. Mass spectrum of **7**-H-Cys-Phe-OH

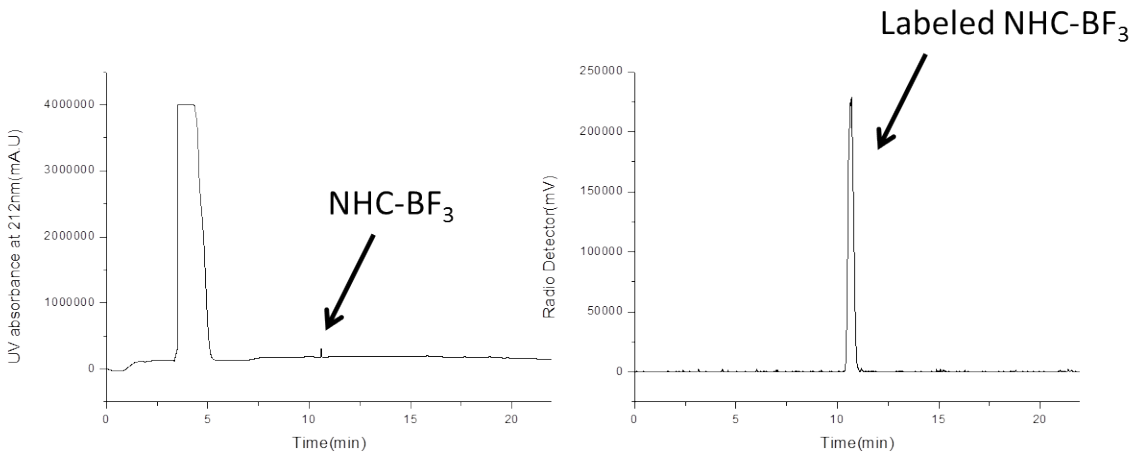


Figure S12. HPLC profiles obtained in the radiofluorination of **2**.
(left) UV signal. (right) Radio signal

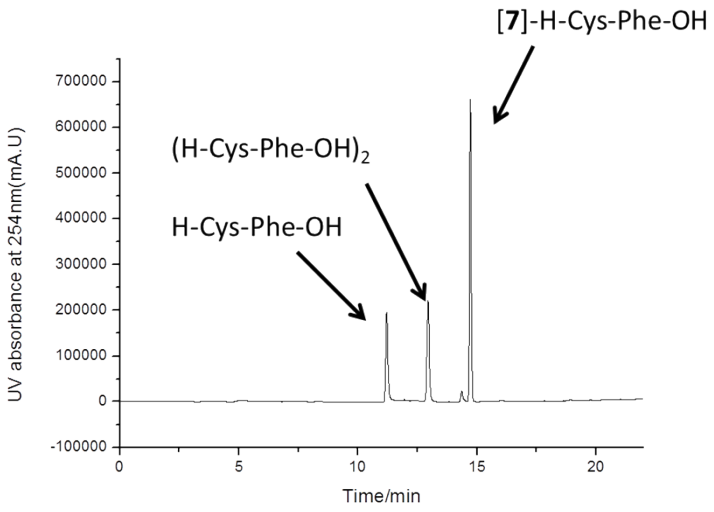


Figure S13. Crude UV-HPLC profile for the ^{18}F-labeling of BF_3-carbene-Cys-Phe

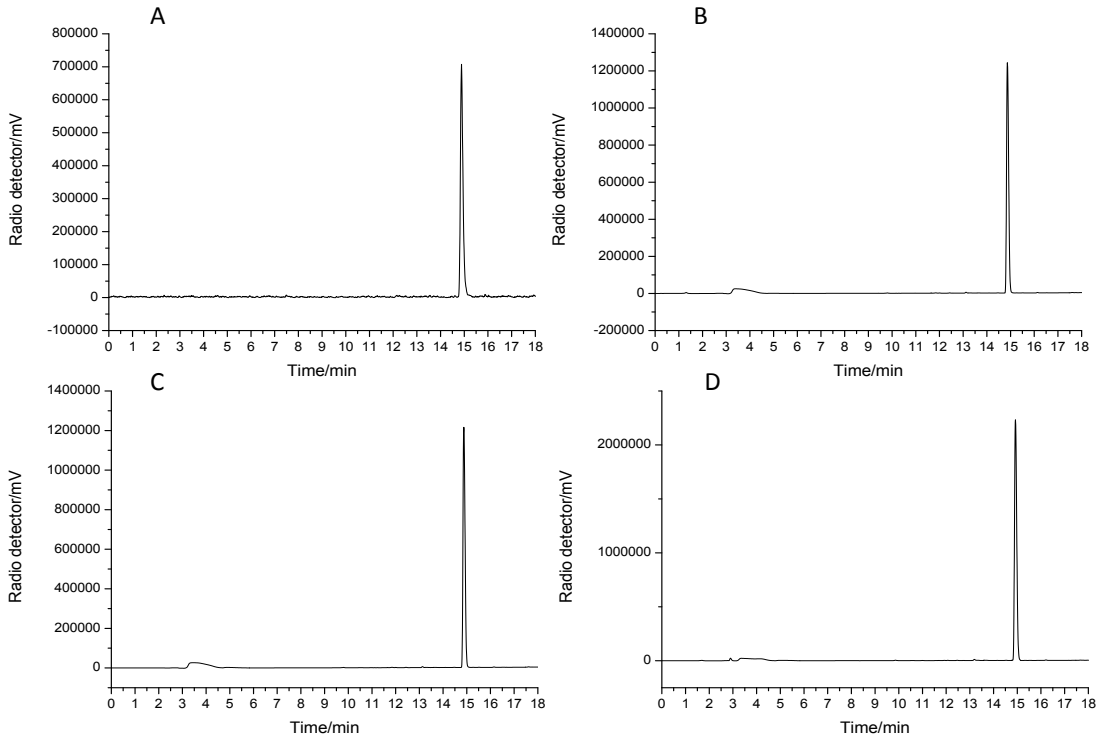


Fig. S14. A: [^{18}F]**7** standard Radio-HPLC profile. B,C,D: [^{18}F]**7** in 1x PBS for 0.5h, 1h and 2h with purity of 96.6%, 93.9%, and 92.5%, respectively.

References

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