Electronic Supplementary Information (ESI)

Metal-free α-CH amination of ethers with hypervalent sulfonylimino-λ^3-bromane that acts as an active nitrenoid species at room temperature

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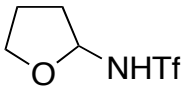
1. Methods

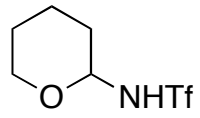
General Information. IR spectra were recorded on JASCO FT/IR-420 spectrometers. ^{1}H NMR and ^{13}C NMR spectra were obtained on either a JEOL JNM-AL300, JNM-AL400, or Bruker AV400 spectrometers. Chemical shifts (δ) are reported in parts per million (ppm) downfield from internal Me_4Si. Mass spectra (MS) were obtained on a Waters LCT Premier, or SHIMADZU Model GCMS-QP 505 spectrometer. Preparative thin-layer chromatography (TLC) was carried out on precoated plates of silica gel (MERCK, silica gel F-254). Kieselgel 60 (Merck, 230-400 mesh) was used for column chromatography. Melting points were determined with a Yanaco micro melting points apparatus and are uncorrected.

Substrates. [*p*-(Trifluoromethyl)phenyl][*N*-(trifluoromethylsulfonyl)imino]-λ^3-bromane (**1**) was synthesized by the reaction of *p*-(trifluoromethyl)phenyl(difluoro)-λ^3-bromane,[S1] prepared from bromine trifluoride by the reaction with [4-(trifluoromethyl)phenyl]trimethylsilane, with trifluoromethanesulfonamide ($TfNH_2$) in a Teflon PFA vessel according to a literature method.[S2] A Teflon PFA vessel was used because of the liberation of hydrogen fluoride in the reaction. The imino-λ^3-bromane **1** is fairly stable in the solid state and can be stored for more than a month without any decomposition in a refrigerator (at 4 °C) under argon. Care should be taken in handling bromine trifluoride, because it will react violently with most organic compounds:[S1] therefore, the reaction of BrF_3 with *p*-$CF_3C_6H_4SiMe_3$ was carried out in a Teflon PFA tube at -78 to -25 °C in dichloromethane under argon in the presence of MeCN (2 equivalents relative to BrF_3), which stabilizes BrF_3 by the coordination to the hypervalent bromine(III) atom. Benzyl *tert*-butyl ethers **4** were prepared according to the reported method.[S3]



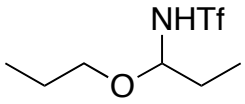
3a

General Procedure for Amination of Ethers with *N*-Triflylimino-λ^3-bromane 1. A Typical Example (Table 1, Entry 1). A solution of imino-λ^3-bromane **1** (20 mg, 0.053 mmol) in THF (0.53 mL) was stirred at room temperature for 1 h under argon. Evaporation under vacuum gave a solid residue. Recrystallization from dichloromethane-hexane at -30 °C gave *N*-(tetrahydrofuran-2-yl)trifluoromethane-sulfonamide (**3a**) (9.9 mg, 85%) as colorless needles; mp 77 °C; IR (KBr) 3117, 2903, 2808, 1467, 1385, 1353, 1234, 1200, 1149, 1122, 996, 613 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.62 (br d, J = 7.9 Hz, 1H), 5.47-5.38 (m, 1H), 4.0 (dt, J = 8.4, 6.6 Hz, 1H), 3.88 (dt, J = 8.4, 6.6 Hz, 1H), 2.38-2.25 (m, 1H), 2.07-1.85 (m, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 119.4 (q, $^{1}J_{CF}$ = 320.7 Hz), 86.0, 68.1, 33.0, 23.9; HRMS (ESI, negative) *m/z* calcd for $C_5H_7F_3NO_3S$ [(M-H)$^-$] 218.0099, found: 218.0098. Anal. Calcd for $C_5H_8F_3NO_3S$: C, 27.40; H, 3.68; N, 6.39. Found: C, 27.13; H, 3.68; N, 6.52. In a separate experiment, ^{1}H NMR yield (93%) of α-amino ether **3a** in a crude reaction mixture was determined using 1,1,2,2-tetrachloroethane as an internal standard. Solid state structure of **3a** is shown in Fig. S2.



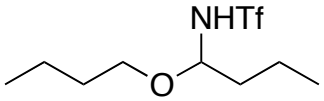
3b

***N*-(Tetrahydropyran-2-yl)trifluoromethanesulfonamide (3b):** repeated trituration with hexane at -30 °C and the subsequent evaporation of the solvent under vacuum gave **3b** (46%) as a colorless oil; IR (neat) 3302, 3134, 2951, 2864, 1454, 1383, 1196, 1146, 1080, 1043, 960, 895, 741, 621 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.54 (br d, *J* = 10.3 Hz, 1H), 4.73 (dt, *J* = 2.9, 10.3 Hz, 1H), 4.04-3.95 (m, 1H), 3.62-3.51 (m, 1H), 1.98-1.84 (m, 2H), 1.70-1.41 (m, 4H); HRMS (ESI, negative) *m/z* calcd for $C_6H_9F_3NO_3S$ [(M-H)$^-$] 232.0255, found: 232.0251. Anal. Calcd for $C_6H_{10}F_3NO_3S$: C, 30.90; H, 4.32; N, 6.01. Found: C, 31.20; H, 4.39; N, 5.90.



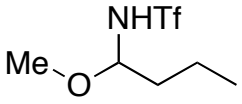
3c

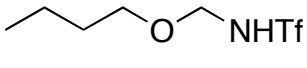
***N*-(1-Propoxypropyl)trifluoromethanesulfonamide (3c):** evaporation of dipropyl ether under vacuum gave **3c** as a colorless oil; IR (neat) 3302, 2974, 2943, 2883, 1439, 1377, 1232, 1198, 1155, 985, 617 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.11 (br d, *J* = 8.8 Hz, 1H), 4.63 (dt, *J* = 8.8, 6.2 Hz, 1H), 3.72 (dt, *J* = 9.4, 6.4 Hz, , 1H), 3.41 (dt, *J* = 9.4, 6.4 Hz, , 1H), 1.88-1.49 (m, 4H), 0.99 (t, *J* = 7.4 Hz, 3H), 0.94 (t, *J* = 7.4 Hz, 3H); HRMS (ESI, negative) *m/z* calcd for $C_7H_{13}F_3NO_3S$ [(M-H)$^-$] 248.0568, found: 248.0564.



3d

***N*-(1-Butoxybutyl)trifluoromethanesulfonamide (3d)**: evaporation of dibutyl ether under vacuum gave **3d** as a colorless oil; IR (neat) 3302, 2964, 2877, 1437, 1379, 1232, 1196, 1155, 980, 619 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.13 (br d, *J* = 9.5 Hz, 1H), 4.67 (ddd, 9.5, 7.6, 4.8 Hz, 1H), 3.75 (dt, *J* = 9.5, 6.5 Hz, 1H), 3.43 (dt, *J* = 9.5, 6.5 Hz, 1H), 1.83-1.30 (m, 8H), 0.96 (t, *J* = 7.2 Hz, 3H), 0.93 (t, *J* = 7.2 Hz, 3H); HRMS (ESI, negative) *m/z* calcd for $C_9H_{17}F_3NO_3S$ [(M-H)$^-$] 276.0881, found: 276.0883.

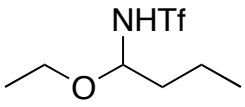


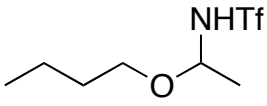
3e and 

3f

A 92:8 mixture of *N*-(1-methoxybutyl)trifluoromethanesulfonamide (3e) and *N*-(butoxymethyl)trifluoromethanesulfonamide (3f): the attempted chromatographic separation of **3e** and **3f** resulted in an extensive decomposition; ^1H NMR (300 MHz, $CDCl_3$) δ 5.82-5.69 (br s, 1H, **3f**), 5.21 (br d, *J* = 9.3 Hz, 1H, **3e**), 4.74 (d, *J* = 6.6 Hz, 2H, **3f**), 4.59 (ddd, *J* = 9.3, 7.1, 4.9 Hz, 1H, **3e**), 3.55 (t, *J* = 6.3 Hz, 2H, **3f**), 3.43 (s, 3H, **3e**), 1.83-1.20 (m, each 4H, **3e** and **3f**), 0.95 (t, *J* = 6.7 Hz, 3H, **3e**), 0.90 (t, *J* = 5.7 Hz, 3H, **3f**); HRMS (ESI, negative) *m/z* calcd for $C_6H_{11}F_3NO_3S$ [(M-H)$^-$] 234.0412, found:

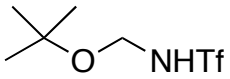
234.0410.



3g and 

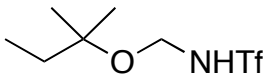
3h

A 46:54 mixture of *N*-(1-ethoxybutyl)trifluoromethanesulfonamide (3g) and *N*-(1-butoxyethyl)trifluoromethanesulfonamide (3h): the attempted chromatographic separation of **3g** and **3h** resulted in an extensive decomposition: a colorless oil; IR (neat) 3302, 2964, 2877, 1439, 1379, 1232, 1198, 1153, 978, 619 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 5.14-4.98 (each 1H, **3g** and **3h**), 4.84 (dq, *J* = 9.4, 5.7 Hz, 1H, **3h**), 4.67 (ddd, *J* = 9.5, 7.4, 4.6 Hz, 1H, **3g**), 3.86-3.63 (each 1H, **3g** and **3h**), 3.58-3.36 (each 1H, **3g** and **3h**), 1.85-1.17 (m, each 7H, **3g** and **3h**), 0.95 (t, *J* = 7.0 Hz, 3H, **3g**), 0.93 (t, *J* = 7.0 Hz, 3H, **3h**); HRMS (ESI, negative) *m/z* calcd for $C_7H_{13}F_3NO_3S$ [(M-H)$^-$] 248.0568, found: 248.0557.



3i

***N*-(*t*-Butoxymethyl)trifluoromethanesulfonamide (3i):** repeated trituration with hexane at room temperature and the subsequent evaporation of the solvent under vacuum gave **3i** (37%) as a colorless oil; IR (neat) 3319, 2981, 2916, 2848, 1439, 1371, 1232, 1198, 1146, 1016, 611 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 5.53 (br s, 1H), 4.73 (d, *J* = 6.7 Hz, 2H), 1.25 (s, 9H); HRMS (ESI, negative) *m/z* calcd for $C_6H_{11}F_3NO_3S$ [(M-H)$^-$] 234.0412, found: 234.0411.



3j

***N*-[(1,1-Dimethylpropoxy)methyl]trifluoromethanesulfonamide (3j):** repeated trituration with hexane at room temperature and the subsequent evaporation of the solvent under vacuum gave labile **3j**, contaminated with a small amount of impurity; ^1H NMR (400 MHz, $CDCl_3$) δ 5.54-5.33 (br s, 1H), 4.71 (d, *J* = 5.8 Hz, 2H), 1.52 (q, *J* = 7.2 Hz, 2H), 1.20 (s, 6H), 0.89 (t, *J* = 7.2 Hz, 3H); HRMS (ESI, negative) *m/z* calcd for $C_7H_{13}F_3NO_3S$ [(M-H)$^-$] 248.0568, found: 248.0570.

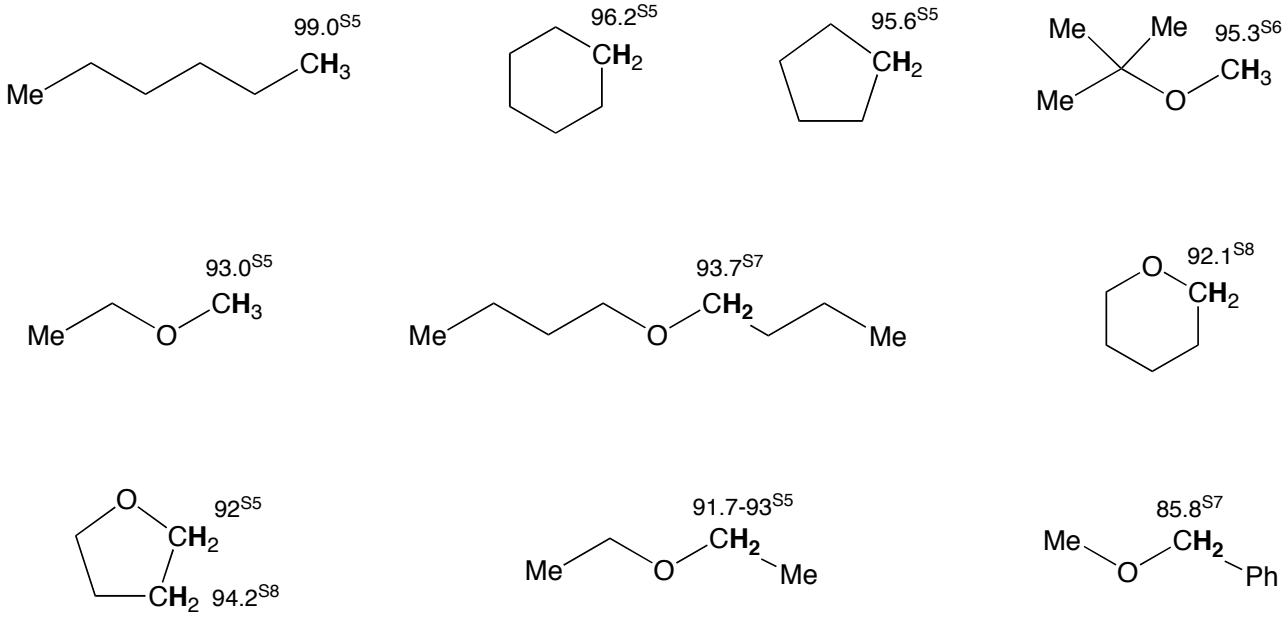
General Procedure for Reaction of Benzyl *tert*-Butyl Ethers 4 with *N*-Triflylimino-λ^3-bromane 1. A Typical Example (Table 3, Entry 2). A solution of imino-λ^3-bromane **1** (11 mg, 0.028 mmol) in benzyl *tert*-butyl ether (**4b**) (0.28 mL) was stirred at room temperature for 1 h under argon. After addition of a 5% aqueous HCl solution (0.1 mL), the mixture was stirred for 2 h. After neutralization with an aqueous $NaHCO_3$ solution and the subsequent addition of NaCl, the yield of benzaldehyde (**5b**, 100%) was determined by capillary GC (FFS ULBON HR-1, 0.25 mm x 50 m, 100 ºC) with undecane as an internal standard.

Conditions for capillary GC analysis; **5a**, FFS ULBON HR-1/100 ºC/undecane; **5c**, FFS ULBON HR-20/100 ºC/tetradecane; **5d**, FFS ULBON HR-1/100 ºC/decane; **5e**, FFS ULBON HR-10/50 ºC/nonane.

Kinetic Measurements (Fig. 1). Rates for C-H amination of THF with imino-λ^3-bromane **1** were measured by monitoring the decrease in absorbance at 240 nm at 30 ± 0.1 °C on Shimadzu UV-160A spectrophotometer.[S4] The reaction temperature was controlled by a CPS S-1700 controller and accurate to within ± 0.1 ºC. A stock solution of imino-λ^3-bromane **1** was prepared by weighting and dissolving in dichloromethane (0.014 M) at room temperature and stored in a refrigerator at -20 ºC. To a solution of THF in 2,2,4,4-tetramethylpentane (3.0 mL) in a quartz cuvette inserted in a cell compartment of the spectrophotometer and equilibrated at the reaction temperature was added 20 μL of the stock solution of imino-λ^3-bromane **1** from a microsyringe. The absorbance change was fed to a computer NEC PC-9821V13 through an interface and processed by a pseudo-first-order kinetics program. The reaction followed pseudo-first-order kinetics for at least 4 half-lives and the pseudo-first-order rate constants k_{obs} were calculated. The values for triplicate runs were averaged.

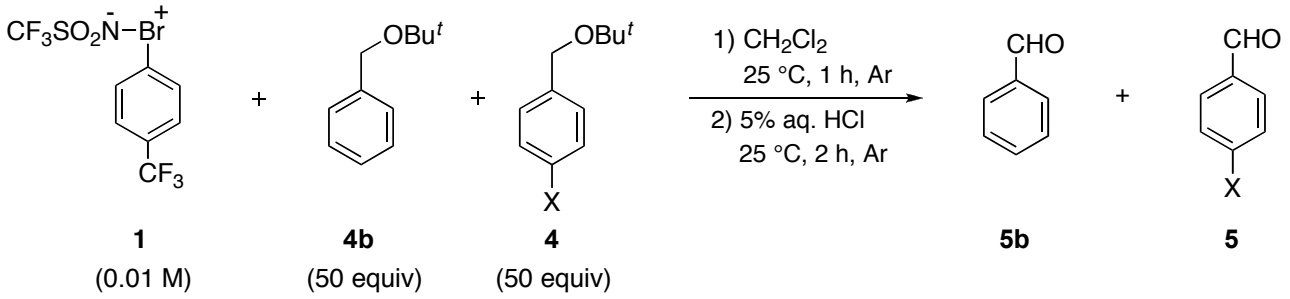
Curve Fittings (Fig. 1). The curve fittings were carried out by a nonlinear least-squares method (Marquardt-Levenberg Algorithm) with use of SigmaPlot (Jandel Scientific, San Rafael, CA) on a personal computer.

2. Bond dissociation energies of ethers and related alkanes



Scheme S1. Bond dissociation energies (kcal mol^{-1}) of ethers and related alkanes. Boldface indicates dissociated hydrogen atom.

3. Substituent effects for benzylic amination of benzyl ethers 4 with iminobromane 1



1 (0.01 M) + **4b** (50 equiv) + **4** (50 equiv) → **5b** + **5**

Relative reactivities k_{rel} of benzyl ethers **4** toward iminobromane **1** at 25 °C

4	X	k_{rel}
4a	Me	1.4
4b	H	1.0
4d	Cl	0.95
4e	CF_3	0.66

Scheme S2 Substituent effects for benzylic amination of benzyl ethers **4** with iminobromane **1.**

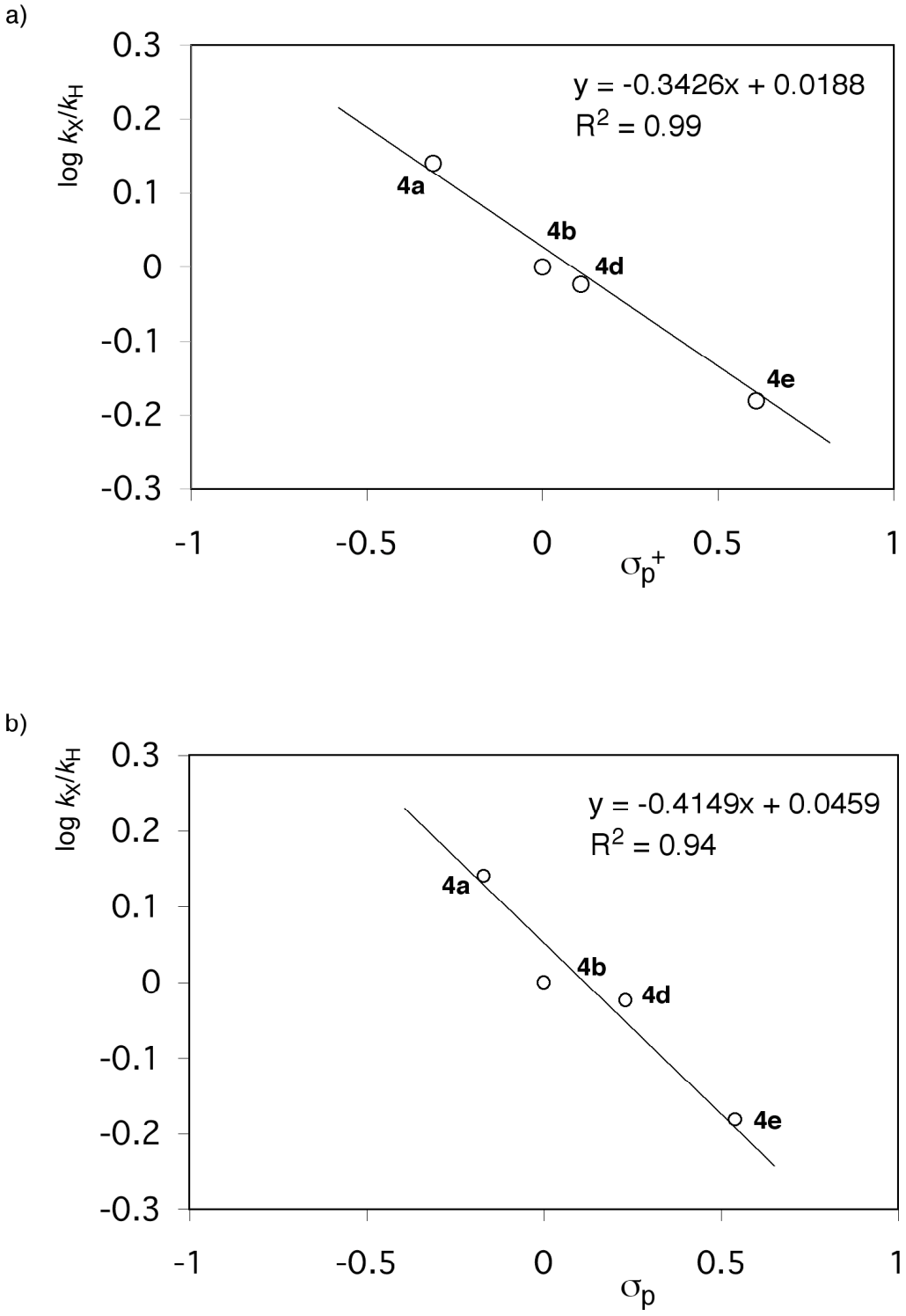
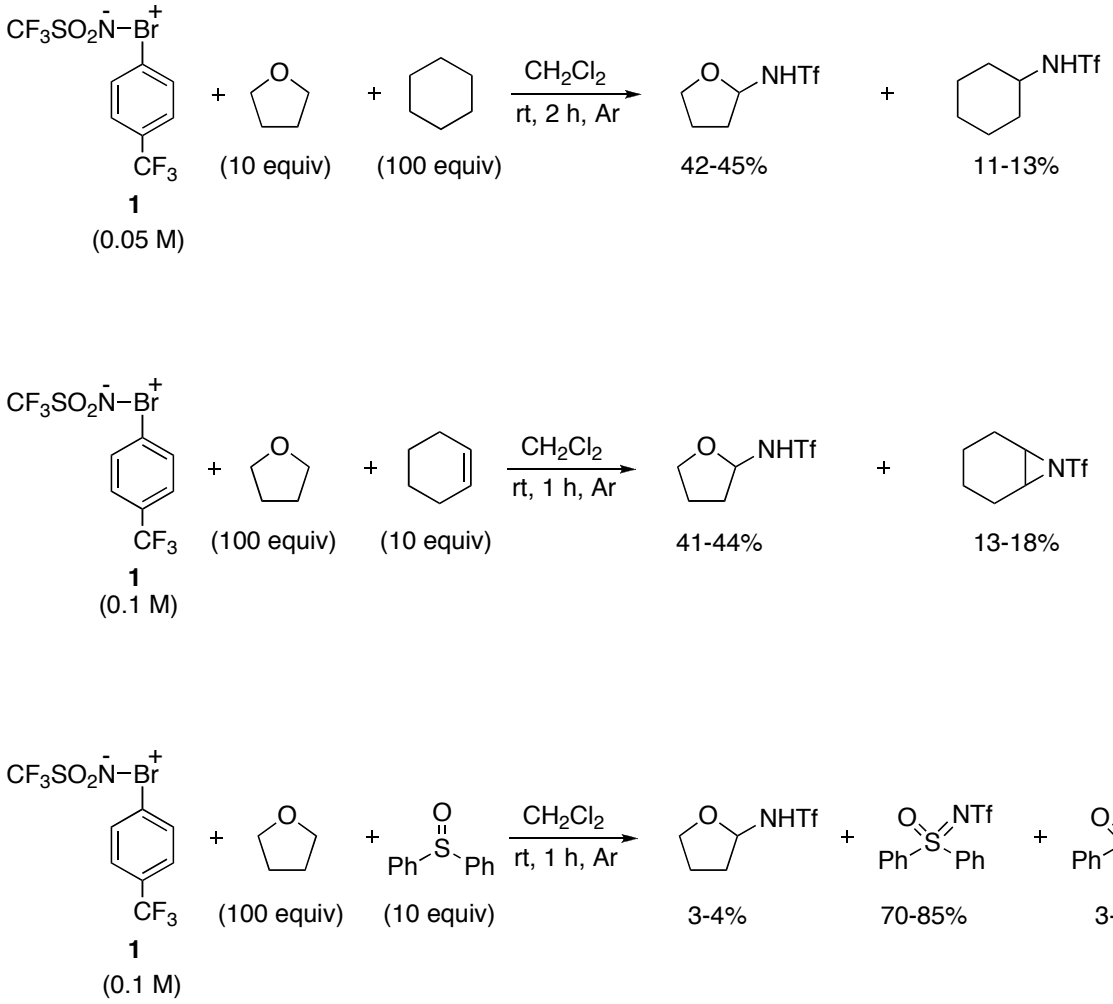


Fig. S1 Hammett plots for competitive reactions of benzyl ethers **4** with imino-λ^3-bromane **1**: (a) σ_p^+. (b) σ_p.

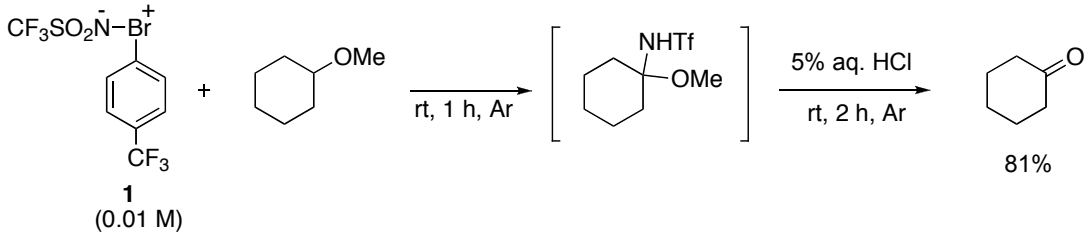
4. Competition experiments between THF and various substrates



Scheme S3 Competition experiments between THF and various substrates: yields for duplicate runs were shown.

5. Oxidative deprotection of methyl ethers of secondary alcohols

Our method might be useful for oxidative deprotection of methyl ethers of secondary alcohols. For instance, Scheme S4 shows that cyclohexyl methyl ether directly affords cyclohexanone in 81% yield by the reaction with imino-λ^3-bromane **1**, after acidic hydrolysis of the reaction mixture.



Scheme S4 Reaction with cyclohexyl methyl ether.

6. ORTEP structure of α-(*N*-triflylamino)tetrahydrofuran (3a)

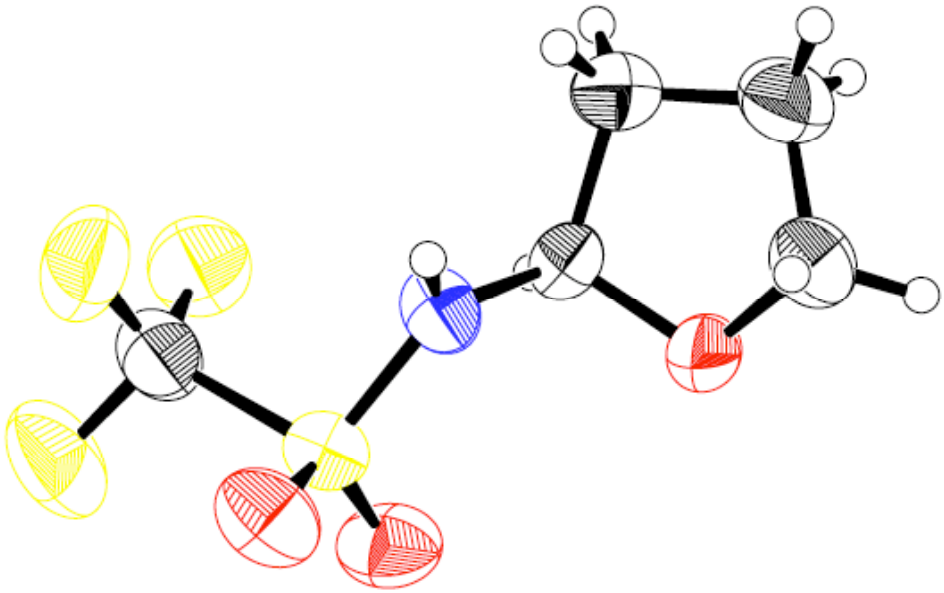


Fig. S2 ORTEP structure of α-(*N*-triflylamino)tetrahydrofuran (**3a**) with 50% thermal ellipsoids.

7. References

S1 M. Ochiai, Y. Nishi, S. Goto, M. Shiro and H. J. Frohn, *J. Am. Chem. Soc.*, 2003, **125**, 15304.

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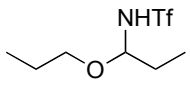
S6 H. Hoshino, K. Sakakibara and K. Watanabe, *Chem. Lett.*, 2008, **37**, 774.

S7 K. R. Przybylak and M. T. D. Cronin, *THEOCHEM*, 2010, **955**, 165.

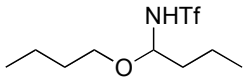
S8 A. B. Shtarev, F. Tian, W. R. Dolbier and B. E. Smart, *J. Am. Chem. Soc.*, 1999, **121**, 7335.

8. Spectra



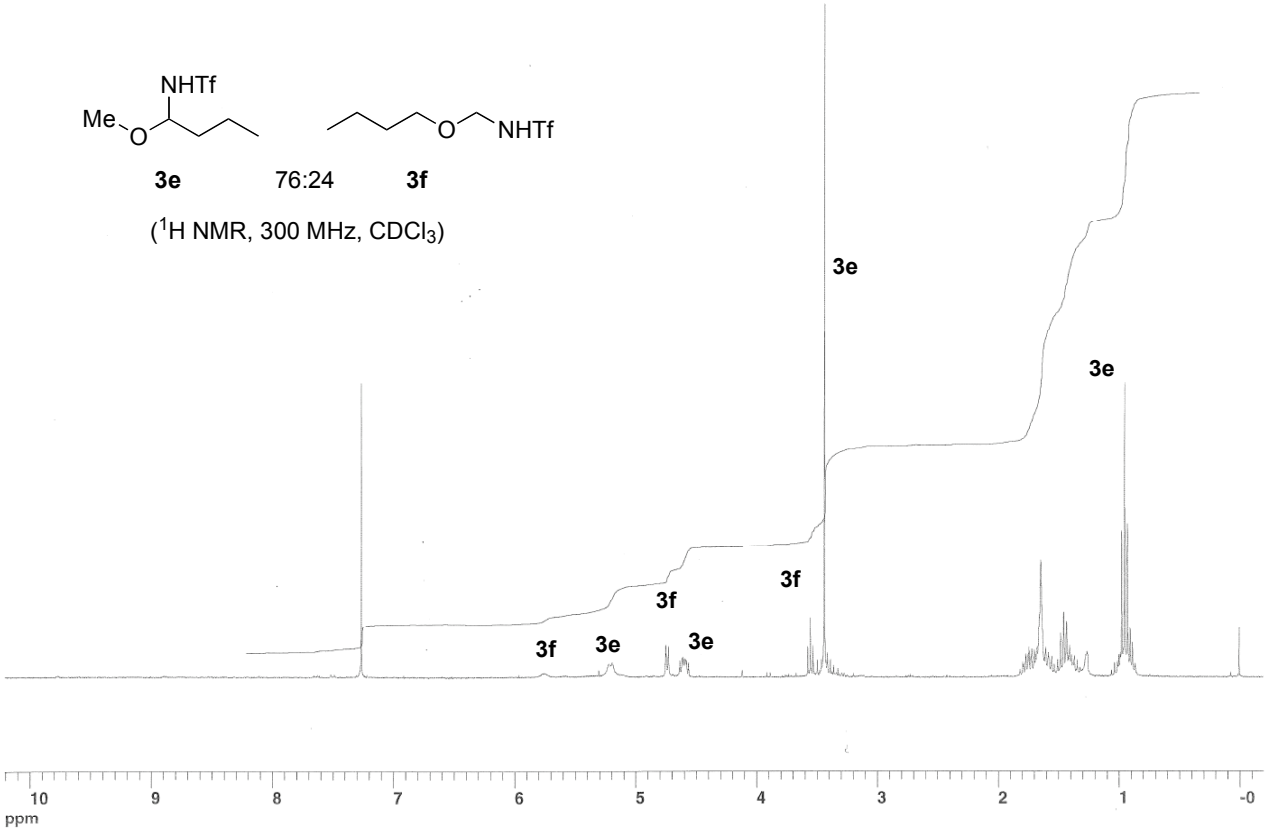
3c

(^{1}H NMR, 300 MHz, $CDCl_3$)



3d

(^{1}H NMR, 300 MHz, $CDCl_3$)


NHTf
Me
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3e
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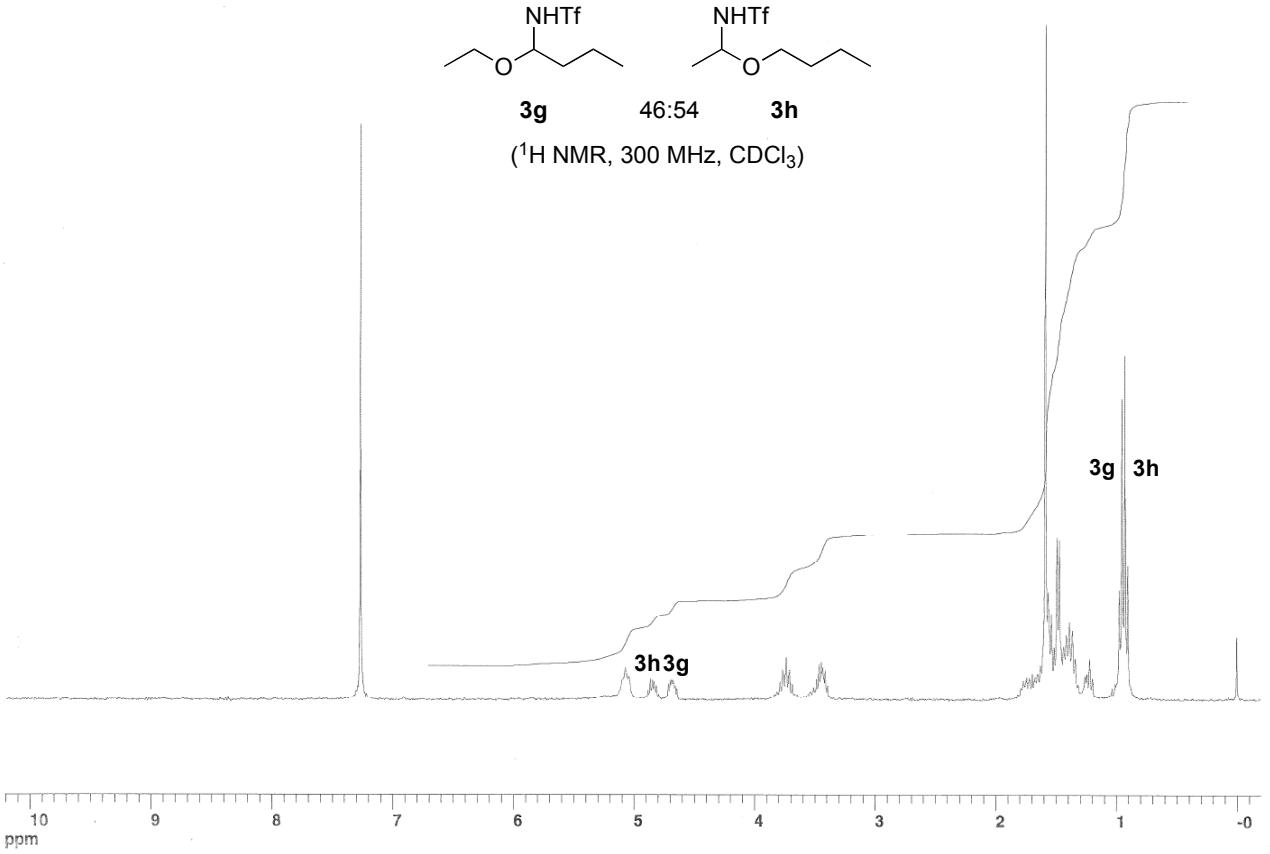
ppm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NHTf
O
3g
46:54
3h
(1H NMR, 300 MHz, CDCl3)
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3h
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2
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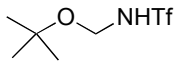
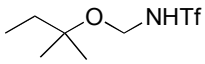


3i

(^{1}H NMR, 400 MHz, $CDCl_3$)



3j

(^{1}H NMR, 400 MHz, $CDCl_3$)