

Electronic supporting information for

Cleavage of ethers in an ionic liquid. Enhancement, selectivity and
potential application

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General Experimental

Reagents for synthesis (substituted phenols, guaiacol, 1-bromo-2-phenylethane, pyridine and 1-bromobutane) were obtained from commercial sources and purified according to literature procedures prior to use.¹ Phenol was recrystallised from hexane while other reagents were dried over either sodium hydroxide or magnesium sulfate prior to being distilled under reduced pressure. Substituted phenols were used without further purification. All other compounds were used immediately after purification.

Kinetic analyses were carried out on either a Bruker Avance III 400, 500 or 600 spectrometer with a BBFO probe using *ca.* 0.6 mL of reaction mixture in a flame sealed 5 mm NMR tube. The reaction rate was measured at a given temperature (maintained using either a water bath or temperature control in the spectrometer) through monitoring the disappearance of the methyl starting material at $\delta ca.$ 3.5 for the methyl ether cleavage for compounds **5-7** and the relative integration of aliphatic signals due to both the starting material (*ca.* 4.0 ppm) and the product ($\delta ca.$ 3.5) for the phenethyl ether cleavage in compounds **4-10** using ¹H NMR spectroscopy. NMR data was processed using either MestReNova 10.0.2 or Bruker Topspin 3.2 software.

Once each kinetic analysis was complete, coulometric Karl-Fischer analysis was then performed to determine the water content of each reaction mixture using a Metrohm 831 KF Coulometer.

The residual halide content of the ionic liquid used in this work was determined by ion chromatography, using a Metrohm 883 Basic IC Plus with an eluent of aqueous sodium carbonate/sodium hydrogen carbonate buffer (pH *ca.* 6.4), and data processed using MagicIC Net 2.1 software.

Infrared (IR) data was collected using a Nicolet iS5 spectrometer coupled with a iD7 attenuated total reflectance (ATR) accessory with a crystal inset. Intensity abbreviations are abbreviated as very weak (vw), weak (w), medium (m), strong (s) and very strong (vs).

Observed pseudo-first order rate constants were converted to second order rate constants through dividing by the concentration of the nucleophile (in this case, bromide) according to the following equation;

$$k_2 = \frac{k_{\text{obs}}}{[\text{Br}^-]}$$

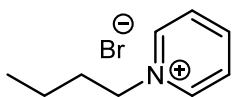
Activation parameters could then be obtained by fitting the second order rate constants to the bimolecular Eyring equation;²

$$\ln\left(\frac{k_2 h}{k_B R T^2}\right) = \frac{\Delta S^\ddagger}{R} - \frac{\Delta H^\ddagger}{RT}$$

Fitting was performed using the Microsoft Excel LINEST function across at least 4 temperatures with a range of at least 30 K.

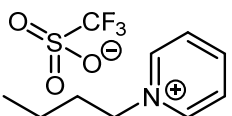
Synthesis of ionic liquids and reagents

N-Butylpyridinium bromide [Bpyr][Br] **3**



Freshly distilled pyridine (34.1 g, 431 mmol) and 1-bromobutane (69.8 g, 509 mmol) were stirred together at room temperature under a nitrogen atmosphere for 7 days. The excess reagents were then decanted off and the remaining crystals were washed with ethyl acetate (150 mL) to give [Bpyr][Br] as white crystals (43.6 g, 47%) which was used without further purification. m.p. 98-101°C (lit. 99°C⁴). ¹H NMR (400 MHz, CDCl₃) δ 9.64 – 9.57 (m, 2H, Ar-H), 8.55 (m, 1H, Ar-H), 8.16 (m, 2H, Ar-H), 5.01 (t, *J* = 7.4 Hz, 2H, NCH₂), 2.10 – 1.97 (m, 2H, NCH₂CH₂), 1.49 – 1.34 (m, 2H, CH₃CH₂), 0.95 (t, *J* = 7.4 Hz, 3H, CH₃).

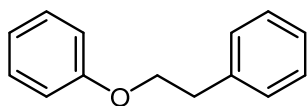
N-Butylpyridinium triflate [Bpyr][OTf] **3**



[Bpyr][Br] (40.3 g, 186 mmol) was dissolved in dichloromethane (100 mL). Triflic acid (28.9 g, 192 mmol) was then added dropwise over 15 min to this solution with stirring; the gas evolved was passed through a saturated aqueous sodium carbonate solution using a flow of dry nitrogen. Once approximately 80% of the dichloromethane had evaporated, more dichloromethane (50 mL) was then added and the procedure was repeated until the dichloromethane solution no longer tested positive for bromide using an aqueous silver nitrate test. The remaining solvent from was then removed *in vacuo* to give [Bpyr][OTf] **3** as a viscous, pale yellow liquid (47.2 g, 89%). ¹H NMR (400 MHz, D₂O) δ 8.77 (d, *J* = 6.1 Hz, 2H, Ar-H), 8.47 (t, *J* = 8.0 Hz, 1H, Ar-H), 8.00 (t, *J* = 7.0 Hz, 2H, Ar-H)ⁱ, 4.54 (t, *J* = 7.4 Hz, 2H, NCH₂), 1.93 (qn, *J* = 7.4 Hz, 2H, NCH₂CH₂), 1.29 (h, *J* = 7.4 Hz, 2H, NCH₂CH₂), 0.87 (t, *J* = 7.4, 3H, CH₃) which matched previously reported data.⁵ Ion chromatography; <0.1 mol% Br.

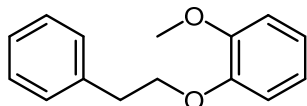
ⁱ The authors acknowledge the unusual coupling constants. However they are consistent with literature and were not further examined.

Phenethoxybenzene **4**



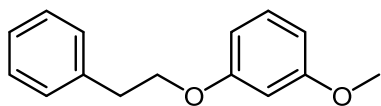
Phenol (1.51 g, 16.0 mmol) was stirred in acetonitrile (25 mL) with potassium carbonate (2.35 g, 17.0 mmol) at room temperature for 2 h. 1-Bromo-2-phenylethane (1.30 mL, 9.55 mmol) was then added dropwise (over 10 min) and the resulting mixture was stirred at reflux under a nitrogen atmosphere overnight. The resulting orange solution was filtered, the solvent was removed from the filtrate *in vacuo* and the residue was purified using column chromatography (5% ethyl acetate in hexane, silica) to give phenethoxybenzene **4** as a colourless liquid (177 mg, 9%). ¹H NMR (400 MHz, CDCl₃) δ 7.41 – 7.21 (m, 6H, Ar-H), 7.01 – 6.88 (m, 4H, Ar-H), 4.21 (t, *J* = 7.1 Hz, 2H, OCH₂CH₂), 3.13 (t, *J* = 7.1 Hz, 2H, CH₂CH₂Ar) which matched previously reported data.⁶

1-Methoxy-2-phenethoxybenzene **5**



Guaiacol (616 mg, 4.96 mmol) was stirred in acetonitrile (25 mL) with potassium carbonate (794 mg, 5.75 mmol) at room temperature for 2 h. 1-Bromo-2-phenylethane (0.30 mL, 2.2 mmol) was then added dropwise (over 10 min) and the resulting mixture was stirred at reflux under a nitrogen atmosphere overnight. The resulting orange solution was filtered, the solvent removed from the filtrate *in vacuo* and the residue purified using column chromatography (5% ethyl acetate in hexane, silica) to give 1-methoxy-2-phenethoxybenzene **5** as a colourless liquid (128 mg, 25%). ¹H NMR (400 MHz, CDCl₃) δ 7.46 – 7.24 (m, 5H, Ar-H), 7.04 – 6.92 (m, 4H, Ar-H), 4.28 (t, *J* = 7.6 Hz, 2H, OCH₂CH₂), 3.92 (s, 3H, CH₃), 3.23 (t, *J* = 7.6 Hz, 2H, CH₂CH₂Ar) which matched previously reported data.⁷

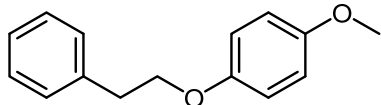
1-Methoxy-3-phenethoxybenzene **6**



m-Methoxyphenol (0.51g, 4.1 mmol) was stirred in acetonitrile (10 mL) with potassium carbonate (0.70 g, 5.1 mmol) at room temperature for 1 h. Bromophenylethane (0.30 mL, 2.2 mmol) was then added dropwise (over 5 min) and the resulting mixture was stirred at 40°C under a nitrogen atmosphere overnight. The resulting solution was filtered, the solvent was removed from the filtrate *in vacuo* and the residue was purified using column

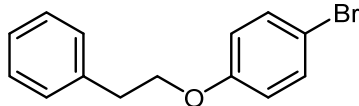
chromatography (10% ethyl acetate in hexane, silica) to give 1-methoxy-3-phenethoxybenzene **6** as a colourless liquid (92.1 mg, 18%). ^1H NMR (400 MHz, CDCl_3) δ 7.44 – 7.20 (m, 6H, Ar-H), 6.62 – 6.49 (m, 3H, Ar-H), 4.23 (t, $J = 7.1$ Hz, 2H, OCH₂CH₂), 3.84 (s, 3H, CH₃), 3.16 (t, $J = 7.1$ Hz, 2H, CH₂CH₂Ar). ^{13}C NMR (151 MHz, CDCl_3) δ 160.84 (Ar), 160.06 (Ar), 138.22 (Ar), 129.87 (Ar), 129.00 (Ar), 128.49 (Ar), 126.50 (Ar), 106.73 (Ar), 106.41 (Ar), 101.03 (Ar), 68.67 (OCH₂CH₂), 55.28 (OCH₃), 35.78 (CH₂CH₂Ar). ATR-IR ν_{max} / cm^{-1} 3086 (vw), 3062 (vw), 3027 (vw), 3001 (vw), 2938 (w br), 2872 (vw), 2834 (vw), 1589 (s), 1491 (s), 1467 (s), 1452 (s), 1386 (w), 1334 (w), 1286 (s), 1264 (s), 1198 (s), 1169 (s), 1146 (vs), 1082 (m), 1043 (s), 993 (w), 948 (w), 929 (w), 834 (s), 751 (s), 698 (s), 685 (s), 605 (m), 566 (m), 549 (m), 494 (m), 458 (m).

1-Methoxy-4-phenethoxybenzene **7**



p -Methoxyphenol (4.52 g, 36.4 mmol) was stirred in acetonitrile (50 mL) with potassium carbonate (5.48 g, 39.7 mmol) at room temperature for 2 h. Bromophenylethane (2.90 mL, 21.6 mmol) was then added dropwise (over 15 min) and the resulting mixture was stirred at 40°C under a nitrogen atmosphere for 7 days. The resulting solution was filtered, the solvent was removed from the filtrate *in vacuo* and the residue was purified using column chromatography (10% ethyl acetate in hexane, silica) to give 1-methoxy-4-phenethoxybenzene **7** as colourless crystals (865 mg, 18%). m.p. 56-58°C (lit. not reported). ^1H NMR (400 MHz, CDCl_3) δ 7.34 – 7.19 (m, 5H, Ar-H), 6.82-6.84 (m, 4H, Ar-H), 4.12 (t, $J = 7.2$ Hz, 2H, OCH₂CH₂), 3.75 (s, 3H, OCH₃), 3.07 (t, $J = 7.2$ Hz, 2H, ArCH₂CH₂) which matched previously reported data.⁸

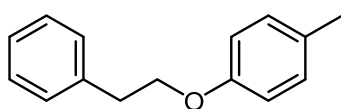
1-Bromo-4-phenethoxybenzene **8**



p -Bromophenol (2.06 g, 11.9 mmol) was stirred in acetonitrile (40 mL) with potassium carbonate (2.02 g, 14.6 mmol) at room temperature for 2 h. Bromophenylethane (1.50 mL, 11.0 mmol) was then added dropwise (over 5 min) and the reaction was stirred at 50°C under a nitrogen atmosphere for 7 days. The resulting orange solution was filtered, the solvent was removed from the filtrate *in vacuo* and the residue was purified using column

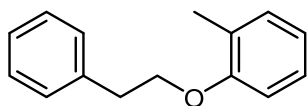
chromatography (hexane graduated to 5% ethyl acetate in hexane, silica) to give 1-bromo-4-phenethoxybenzene **8** as a colourless liquid (170 mg, 6%). ^1H NMR (400 MHz, CDCl_3) δ 7.40 – 7.24 (m, 7H, Ar-H), 7.83 (s, 1H, Ar-H), 7.79 (s, 1H, Ar-H), 4.17 (t, $J = 7.1$ Hz, 2H, OCH₂CH₂), 3.11 (t, $J = 7.1$ Hz, 2H, ArCH₂CH₂). ^{13}C NMR (151 MHz, CDCl_3) δ 157.91 (Ar), 137.99 (Ar), 132.24 (Ar), 128.98 (Ar), 128.53 (Ar), 126.59 (Ar), 116.37 (Ar), 112.87 (Ar), 68.92 (OCH₂CH₂), 35.70 (ArCH₂CH₂). ATR-IR ν_{max} / cm^{-1} 3085 (vw), 3062 (vw), 3027 (vw), 2933 (vw br), 2870 (vw br), 1590 (m), 1577 (w), 1486 (s), 1470 (m), 1453 (m), 1386 (w), 1284 (m), 1233 (vs), 1170 (m), 1101 (w), 1072 (m), 1025 (s), 1001 (m), 910 (vw), 868 (vw), 819 (s), 749 (m), 697 (s), 640 (m), 600 (w), 576 (m), 504 (m), 459 (w).

1-Methyl-4-phenethoxybenzene **9**



p-Cresol (3.11 g, 29.0 mmol) was stirred in acetonitrile (20 mL) with potassium carbonate (5.78 g, 41.8 mmol) at room temperature for 2 h. Bromophenylethane (4.6 g, 24.9 mmol) was then added dropwise (over 5 min) and the resulting mixture was stirred at 60°C under a nitrogen atmosphere for 4 days. The resulting solution was filtered, the solvent was removed from the filtrate *in vacuo* and the residue was purified using column chromatography (2% ethyl acetate in hexane, silica) to give 1-methyl-4-phenethoxybenzene **9** as a colourless liquid (1.17 g, 22%). ^1H NMR (300 MHz, CDCl_3) δ 7.41 – 7.20 (m, 5H, Ar-H), 7.16 – 7.04 (m, 2H, Ar-H), 6.89 – 6.77 (m, 2H, Ar-H), 4.18 (t, $J = 7.2$ Hz, 2H, OCH₂CH₂), 3.12 (t, $J = 7.2$ Hz, 2H, ArCH₂CH₂), 2.31 (s, 3H, CH₃) which matched previously reported data.⁹

1-Methyl-2-phenethoxybenzene **10**¹⁰

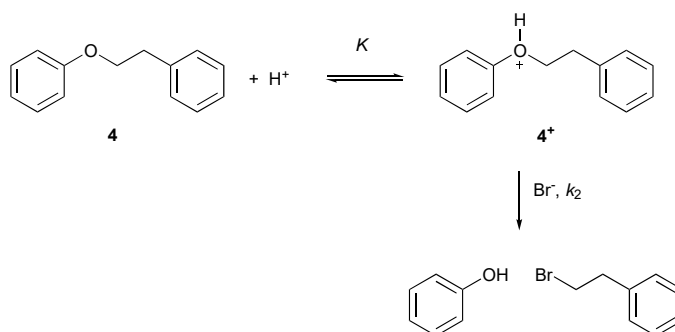


o-Cresol (2.11 g, 19.5 mmol) was stirred in acetonitrile (30 mL) with potassium carbonate (3.08 g, 22.3 mmol) at room temperature for 2 h. Bromophenylethane (2.3 mL, 17 mmol) was then added dropwise (over 15 min) and the resulting mixture was stirred at 60°C under a nitrogen atmosphere for 7 days. The resulting solution was filtered, the solvent was removed from the filtrate *in vacuo* and the residue was purified using column chromatography (10% ethyl acetate in hexane, silica) to give 1-methyl-2-phenethoxybenzene **10** as a colourless liquid (955 mg, 27%). ^1H NMR (300 MHz, CDCl_3) δ 7.39 – 7.21 (m, 5H, Ar-H), 7.19 – 7.09 (m,

2H, Ar-H), 6.92 – 6.78 (m, 2H, Ar-H), 4.21 (t, $J = 6.8$ Hz, 2H, OCH₂CH₂), 3.14 (t, $J = 6.8$ Hz, 2H, ArCH₂CH₂), 2.23 (s, 3H, CH₃) which matched previously reported data.¹⁰

Mathematical expression for the effect of the preequilibrium on the measured activation parameters

The reaction examined in the main text proceeds first *via* a protonation equilibrium then through a S_N2 pathway. An example reaction scheme is shown below for compound **4**. The concentrations of each compound in the pathway can be expressed mathematically which enables an examination into how the position of the preequilibrium may change the activation parameters measured in Figure 1. Note that the assumption that H⁺ and Br⁻ exist as separate ions is made.



Since the initial protonation can be considered as an equilibrium

$$K = \frac{[\mathbf{4}^+]}{[\mathbf{4}][\text{H}^+]}$$

$$[\mathbf{4}^+] = K[\mathbf{4}][\text{H}^+]$$

The rate of formation of the products can be defined as

$$\text{rate} = k_2[\mathbf{4}^+][\text{Br}^-]$$

However, since ¹H NMR analysis was used to monitor the above reaction as it proceeded, the signal monitored is likely the weighted average due to the signal from both compounds **4** and **4**⁺ shown above.

$$\text{rate}_{\text{obs}} = k_{2\text{obs}}[\mathbf{4}_{\text{total}}][\text{Br}^-]$$

Substituting for $[\mathbf{4}^+]$, equating the above relationships and rearrangement gives

$$k_{2\text{obs}} = k_2 K \frac{[\mathbf{4}][\text{H}^+]}{[\mathbf{4}_{\text{total}}]}$$

To evaluate whether the initial equilibrium has any effect on the activation parameters obtained through the Eyring equation, $k_{2\text{obs}}$ needs to be substituted into the bimolecular Eyring equation to determine any effect the value of K may have on the observed value of either ΔH^\ddagger or ΔS^\ddagger .ⁱⁱ This gives the following equations

$$\ln\left(\frac{k_{2\text{obs}}h}{k_{\text{B}}RT^2}\right) = \frac{\Delta S_{\text{obs}}^\ddagger}{R} - \frac{\Delta H_{\text{obs}}^\ddagger}{RT}$$

$$\ln\left(\frac{k_2h}{k_{\text{B}}RT^2} \cdot K \frac{[\mathbf{4}][\text{HBr}]}{[\mathbf{4}_{\text{total}}][\text{Br}^-]}\right) = \frac{\Delta S_{\text{obs}}^\ddagger}{R} - \frac{\Delta H_{\text{obs}}^\ddagger}{RT}$$

$$\ln\left(\frac{k_2h}{k_{\text{B}}RT^2}\right) + \ln\left(K \frac{[\mathbf{4}][\text{HBr}]}{[\mathbf{4}_{\text{total}}][\text{Br}^-]}\right) = \frac{\Delta S_{\text{obs}}^\ddagger}{R} - \frac{\Delta H_{\text{obs}}^\ddagger}{RT}$$

$$\ln\left(\frac{k_2h}{k_{\text{B}}RT^2}\right) = \frac{\Delta S_{\text{obs}}^\ddagger}{R} - \ln\left(K \frac{[\mathbf{4}][\text{H}^+]}{[\mathbf{4}_{\text{total}}]}\right) - \frac{\Delta H_{\text{obs}}^\ddagger}{RT}$$

$$= \frac{\Delta S^\ddagger}{R} - \frac{\Delta H^\ddagger}{RT}$$

ⁱⁱ It is assumed that over the temperature range considered, there is negligible change in the position of the equilibrium. This is not unreasonable given the nature of the process and is supported by the fact that no deviation from linearity is seen in the Eyring plot.

This relationship shows that if the variation of the position of the equilibrium were to affect the activation parameters obtained for different solvent mixtures, it would only cause a change in the entropy of activation. Equating the entropy terms gives

$$\Delta S_{\text{obs}}^{\ddagger} = \Delta S^{\ddagger} + R \ln \left(K \frac{[4][\text{H}^+]}{[4_{\text{total}}]} \right)$$

For the difference in entropy seen experimentally to be caused by the shift in equilibrium;

$$\Delta S_{\text{A}}^{\ddagger} - \Delta S_{\text{B}}^{\ddagger} = R \ln \left(K_{\text{A}} \frac{[4_{\text{A}}][\text{H}^+_{\text{A}}]}{[4_{\text{totalA}}]} \right) - R \ln \left(K_{\text{B}} \frac{[4_{\text{B}}][\text{H}^+_{\text{B}}]}{[4_{\text{totalB}}]} \right)$$

Given the measured change in entropy

$$73.4 = R \ln \left(K_{\text{A}} \frac{[4_{\text{A}}][\text{H}^+_{\text{A}}]}{[4_{\text{totalA}}]} \right) - R \ln \left(K_{\text{B}} \frac{[4_{\text{B}}][\text{H}^+_{\text{B}}]}{[4_{\text{totalB}}]} \right)$$

$$8.83 = \ln \left(K_{\text{A}} \frac{[4_{\text{A}}][\text{H}^+_{\text{A}}]}{[4_{\text{totalA}}]} \right) - \ln \left(K_{\text{B}} \frac{[4_{\text{B}}][\text{H}^+_{\text{B}}]}{[4_{\text{totalB}}]} \right)$$

$$8.83 = \ln \left(\frac{K_{\text{A}} [4_{\text{A}}][\text{H}^+_{\text{A}}][4_{\text{totalB}}]}{K_{\text{B}} [4_{\text{totalA}}][4_{\text{B}}][\text{H}^+_{\text{B}}]} \right)$$

Substituting for K from equation 1 gives;

$$8.83 = \ln \left(\frac{[4^+_{\text{A}}][4_{\text{totalB}}]}{[4_{\text{totalA}}][4^+_{\text{B}}]} \right)$$

$$6836 = \frac{[4^+_{\text{A}}][4_{\text{totalB}}]}{[4_{\text{totalA}}][4^+_{\text{B}}]}$$

Assuming that the total concentration of ether does not change significantly between the two cases being compared, the ratio between the two protonated forms is almost 7000. This seems highly unlikely so even if some change in the entropy of activation is caused by the protonation equilibrium, the majority is due to a shift in organisation around the starting materials or transition state as is described in the main text.

Calculation of the *ortho* Hammett σ Value

Work by Fujita and Nishioka¹¹ describe the experimentally measured value of the σ value of an *ortho* substituent by the following equation; where E_s^{ortho} and F_{ortho} are used to describe the steric and field effects for an *ortho* substituent respectively.

$$\log\left(\frac{k_{2ortho}}{k_{2H}}\right) = \rho\sigma + \delta E_s^{ortho} + fF_{ortho} = \rho\sigma_{ortho}$$

Fujita and Nishioka have calculated and tabulated data for ρ , δ , f , E_s^{ortho} and F_{ortho} across a wide range of reactions. The terms ρ , δ and f are specific to each reaction, while E_s^{ortho} and F_{ortho} are specific to the functional group. This means that we can approximate a σ value for the *ortho* substituents here by substituting in the values for ρ , δ , f , E_s^{ortho} and F_{ortho} from a similar reaction into the following equation.

$$\sigma_{ortho} = \sigma + \frac{1}{\rho}(\delta E_s^{ortho} + fF_{ortho})$$

The issue in this case is that no data is available for the effect of changing substituents on the protonation of an ether, so various other similar reactions were considered for the calculation of the *ortho* σ values. Table S1 shows the reference values used for both E_s^{ortho} and F_{ortho} . Table S2 as well as Figures S1-S4 show a variety of different reactions and their corresponding values for ρ , δ and f that were used to calculate the Hammett σ values for the *o*-Me and *o*-OH used in this work. The variety of fits show that no model reaction could be found which allowed both *ortho* substituents to lie on the trend line in the Hammett plot. Reaction 2 was chosen to calculate the *ortho* values used in the main text since it is an acid dissociation reaction at a positively charged heteroatom α to the aromatic ring, which also provided a reasonable fit for the data.

Table S1. Standard values for E_s^{ortho} and F_{ortho} used in the calculation of the Hammett σ value used in main text.

R	E_s^{ortho}	F_{ortho}
<i>o</i> -OH	-0.55	0.29
<i>o</i> -Me	-1.24	0.04

Table S2. Values for ρ , δ and f for a range of different reactions listed by Fujita and Nishioka as well as the σ_{ortho} values calculated from them.

Reaction number	Reaction	Reaction type	ρ	δ	f	σ_{ortho} (OH)	σ_{ortho} (Me)
1	ArCOOH	Acid dissociation	1	-0.392	1.469	0.272	0.375
2	ArNH ₃ ⁺	Acid dissociation	2.946	-0.534	1.766	-0.096	0.079
3	ArOH	Acid dissociation	2.036	0.167	2.395	-0.074	-0.225
4	ArCOO(CH ₂) ₂ N ⁺ Me ₃	Hydrolysis	1.371	0.458	1.170	-0.306	0.017

Figure S1. Hammett plot for the reaction of a range of ethers with hydrogen bromide. *Ortho* σ values (orange) are based off calculations from Reaction 1 in Table S2.

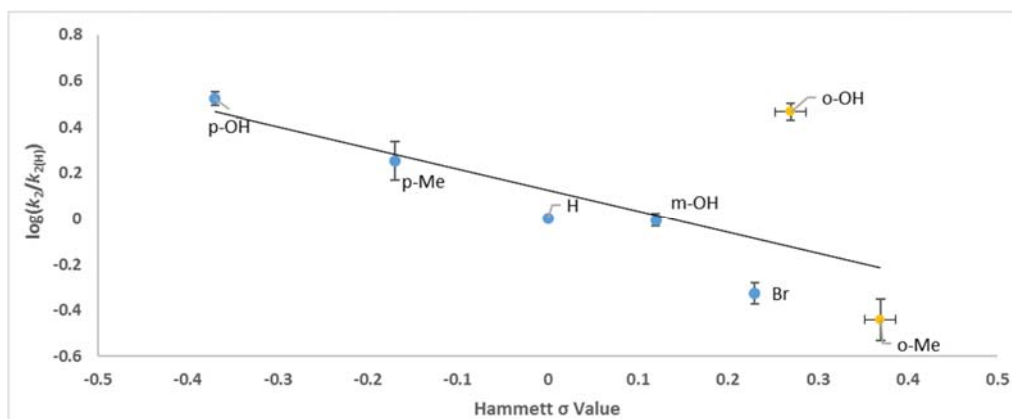


Figure S2. Hammett plot for the reaction of a range of ethers with hydrogen bromide. *Ortho* σ values (orange) are based off calculations from Reaction 2 in Table S2.

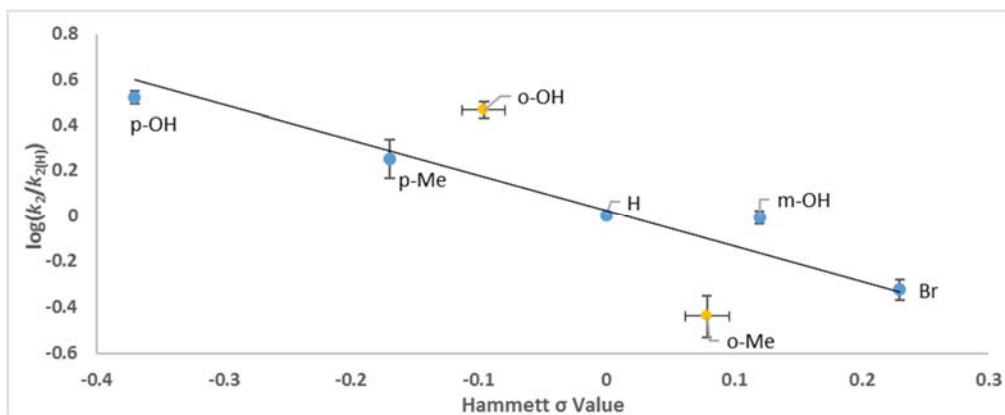


Figure S3. Hammett plot for the reaction of a range of ethers with hydrogen bromide. *Ortho* σ values (orange) are based off calculations from Reaction 3 in Table S2.

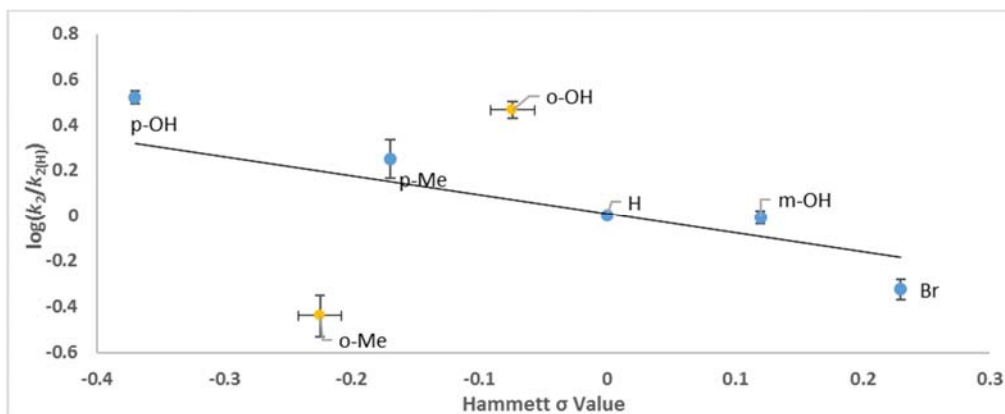
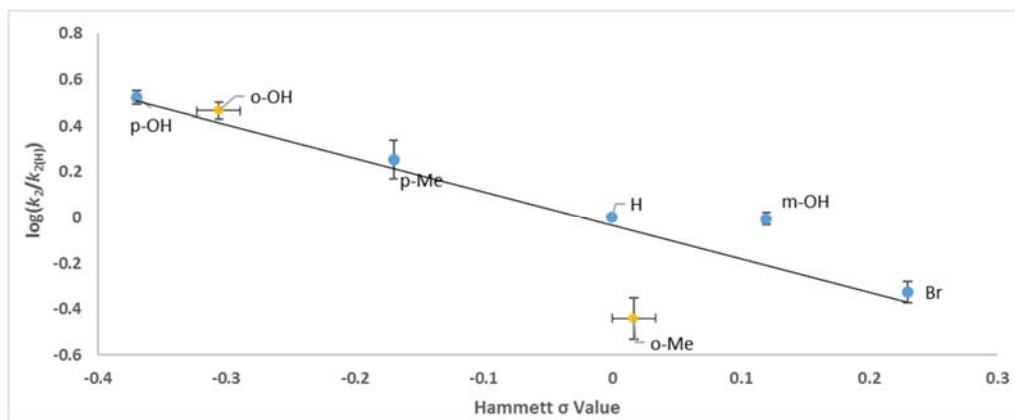


Figure S4. Hammett plot for the reaction of a range of ethers with hydrogen bromide. *Ortho* σ values (orange) are based off calculations from Reaction 4 in Table S2.



Data for figures shown in main text

Data for Figure 1

Figure S5. Eyring plot for the rate of reaction for anisole **1** with hydrogen bromide in [Bpyr][OTf] **3** with *ca.* 23% water shown in the main text in Figure 1.

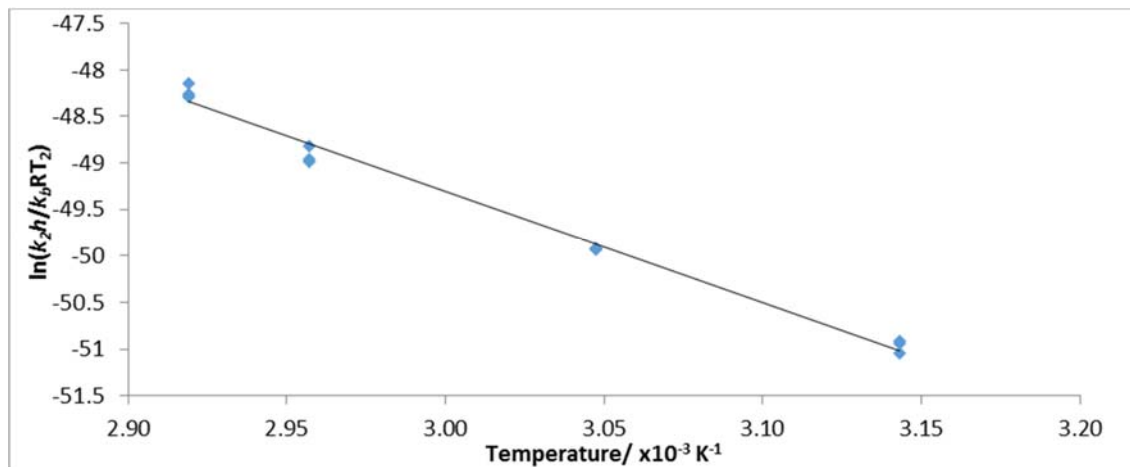


Table S3. Data for the Eyring plot of the rate of reaction for anisole **1** with hydrogen bromide in [Bpyr][OTf] **3** with *ca.* 23% water shown in the main text in Figure 1.

T / K	[Br ⁻] / M	$k_{\text{obs}} / 10^{-6} \text{ s}^{-1}$	$k_2 / 10^{-6} \text{ M}^{-1} \text{ s}^{-1}$
318.2	0.403	0.481	1.19
318.2	0.403	0.534	1.33
318.2	0.403	0.545	1.35
328.2	0.403	1.56	3.86
328.2	0.403	1.58	3.93
328.2	0.403	1.55	3.85
338.2	0.403	4.24	10.5
338.2	0.403	5.02	12.4
338.2	0.403	4.37	10.8
342.6	0.403	9.02	22.4
342.6	0.403	10.1	25.1
342.6	0.403	8.78	21.8
342.6	0.403	8.77	21.8

Table S4. Water content for the reaction of anisole **1** with hydrogen bromide in [Bpyr][OTf] **3** with *ca.* 23% water.

Sample Number	Water content 1 / mol%	Water content 2 / mol%
1	26.6	26.8
2	17.6	26.8
3	26.4	26.0
4	20.0	21.2
5	24.8	21.1
6	26.4	-
7	25.1	26.8
8	18.1	18.4
	Average water content	23.5
	σ of water content	3.50

Figure S6. Eyring plot and data for the rate of reaction for anisole **1** with hydrogen bromide in [Bpyr][OTf] **3** with *ca.* 14% water shown in the main text in Figure 1.

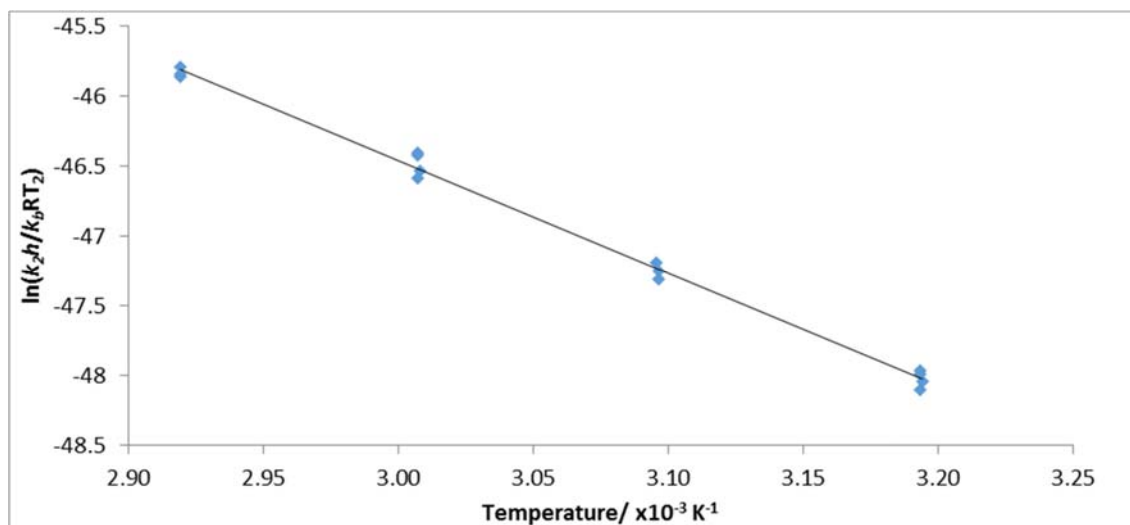


Table S5. Data for the Eyring plot of the rate of reaction for anisole **1** with hydrogen bromide in [Bpyr][OTf] **3** with *ca.* 14% water shown in the main text in Figure 1.

T / K	[Br] / M	$k_{\text{obs}} / 10^{-5} \text{ s}^{-1}$	$k_2 / 10^{-5} \text{ M}^{-1} \text{ s}^{-1}$
313.1	0.585	1.36	2.33
313.2	0.585	1.47	2.51
313.2	0.585	1.43	2.45
313.2	0.585	1.28	2.19
323.0	0.585	3.19	5.45
323.0	0.585	3.02	5.16
323.1	0.585	3.38	5.78
332.5	0.585	6.94	11.9
332.6	0.585	6.58	11.3
332.6	0.585	7.74	13.2
332.6	0.585	7.87	13.5
342.6	0.585	15.5	26.4
342.6	0.585	14.5	24.7
342.6	0.585	14.7	25.2

Table S6. Water content for the reaction of anisole **1** with hydrogen bromide in [Bpyr][OTf] **3** with *ca.* 14% water.

Sample Number	Water content 1 / mol%	Water content 2 / mol%
1	10.2	
2	11.8	
3	14.9	14.5
4	13.8	14.9
5	11.3	
6	15.7	15.7
7	14.9	15.0
8	10.9	
9	12.1	
10	11.7	
Average water content		13.4
σ of water content		1.88

Table S7. Rate data for the reaction of anisole **1** with hydrogen bromide in [Bpyr][OTf] **3** with varying water content as shown in the main text as Figure 1.

Water content / mol%	[Br ⁻] / M	$k_{\text{obs}} / 10^{-5} \text{ s}^{-1}$	$k_2 / 10^{-4} \text{ M}^{-1} \text{ s}^{-1}$
3.72 (0.01)	0.537	25.1	4.66
4.00 (0.02)	0.537	25.6	4.77
4.14 (0.05)	0.537	24.4	4.54
7.11 (0.01)	0.600	22.5	3.75
7.65 (0.01)	0.600	26.8	4.47
8.62 (0.07)	0.600	25.2	4.20
13.4 (1.9)	0.585	15.5	2.64
13.4 (1.9)	0.585	14.5	2.47
13.4 (1.9)	0.585	14.7	2.52
13.9 (0.6)	0.607	21.4	3.52
14.4 (0.1)	0.607	22.8	3.75
14.4 (0.1)	0.607	22.1	3.64
20.7 (0.7)	0.813	22.3	2.75
21.9 (0.1)	0.813	16.1	1.98
21.9 (0.3)	0.813	15.6	1.92
24.1 (3.5)	0.403	0.874	0.217
24.1 (3.5)	0.403	0.618	0.153
24.1 (3.5)	0.403	0.765	0.190

Errors are shown in brackets next to corresponding water content. Errors are calculated as half the range of duplicate measurements, except for *ca.* 14% and *ca.* 23% which are standard deviation.

Data for Figure 2

Table S8. Rate data for the reaction of phenylethyl phenyl ether **4** with hydrogen bromide in [Bpyr][OTf] **3** with varying water content as shown in the main text as Figure 2.

Water content / mol%	[Br ⁻] / M	$k_{\text{obs}} / 10^{-6} \text{ s}^{-1}$	$k_2 / 10^{-6} \text{ M}^{-1} \text{ s}^{-1}$
5.46 (0.08)	0.756	17.54	23.2
5.49 (0.05)	0.756	18.07	23.9
6.21 (0.09)	0.756	17.23	22.8
11.9 (0.2)	0.806	14.45	17.9
12.2 (0.1)	0.806	13.94	17.3
12.7 (0.1)	0.806	14.22	17.7
18.4 (0.1)	0.926	8.95	9.67
19.8 (0.3)	0.926	9.51	10.3
21.8 (0.3)	0.926	9.52	10.3
30.0 (0.1)	1.11	6.24	5.64
30.7 (0.1)	1.11	6.31	5.71
32.8 (0.1)	1.11	6.30	5.70
35.0 (0.6)	1.30	2.73	2.10
45.1 (0.3)	1.30	3.26	2.50
46.7 (0.1)	1.30	3.06	2.35

Errors are shown in brackets next to corresponding water content. Errors are calculated as half the range of duplicate measurements

Data for Figure 3

Table S9. Rate data for the reaction of 1-methoxy-2-phenethoxybenzene **5** with hydrogen bromide in [Bpyr][OTf] **3** with varying water content as shown in the main text as Figure 3.

Water content / mol%	[Br ⁻] / M	$k_{\text{obs}}^{\text{a}} / 10^{-5} \text{ s}^{-1}$	$k_2^{\text{a}} / 10^{-4} \text{ M}^{-1} \text{ s}^{-1}$	$k_{\text{obs}}^{\text{b}} / 10^{-6} \text{ s}^{-1}$	$k_2^{\text{b}} / 10^{-6} \text{ M}^{-1} \text{ s}^{-1}$
3.96 (0.44)	0.190	43.8	23.1	13.0	68.8
4.30 (0.29)	0.190	43.7	23.0	13.1	69.0
4.90 (0.18)	0.190	49.4	26.1	12.5	65.9
11.3 (0.3)	0.244	37.6	15.4	10.4	42.6
11.7 (0.1)	0.244	36.2	14.8	10.8	44.5
12.5 (0.1)	0.244	40.0	16.4	9.83	40.4
16.1 (1.0)	0.267	37.9	14.2	7.73	28.9
18.5 (0.4)	0.267	34.4	12.9	8.20	30.7
18.8 (0.3)	0.267	33.0	12.4	7.99	29.9
53.2 (0.6)	0.519	4.74	0.912	0.963	1.85
53.6 (0.1)	0.519	5.42	1.04	0.963	1.86
54.3 (0.8)	0.519	4.66	0.898	1.17	2.24

^aReaction at the methyl ether site. ^bReaction at the phenethyl ether site.

Errors are shown in brackets next to corresponding water content. Errors are calculated as half the range of duplicate measurements.

Data for compounds 6-10, not shown in main text Figures

Table S10. Rate data for the reaction of 1-methoxy-4-phenethoxybenzene **6** with hydrogen bromide in [Bpyr][OTf] **3** with varying water content.

Water content / mol%	[Br ⁻] / M	$k_{\text{obs}}^{\text{a}} / 10^{-5} \text{ s}^{-1}$	$k_2^{\text{a}} / 10^{-4} \text{ M}^{-1} \text{ s}^{-1}$	$k_{\text{obs}}^{\text{b}} / 10^{-6} \text{ s}^{-1}$	$k_2^{\text{b}} / 10^{-6} \text{ M}^{-1} \text{ s}^{-1}$
4.33(0.20)	0.427	59.5	13.9	33.3	78.0
4.59(0.07)	0.427	58.5	13.7	33.3	78.1
4.65(0.18)	0.427	57.2	13.4	32.5	76.3
16.3(1.7)	0.680	70.7	10.4	58.1	85.4
17.3(0.6)	0.680	72.6	10.7	58.4	85.8
17.3(0.1)	0.680	66.8	9.82	56.6	83.3

^aReaction at the methyl ether site. ^bReaction at the phenethyl ether site.

Errors are shown in brackets next to corresponding water content. Errors are calculated as half the range of duplicate measurements.

Table S11. Rate data for the reaction of 1-methoxy-3-phenethoxybenzene **7** with hydrogen bromide in [Bpyr][OTf] **3** with varying water content.

Water content / mol%	[Br ⁻] / M	$k_{\text{obs}}^{\text{a}} / 10^{-5} \text{ s}^{-1}$	$k_2^{\text{a}} / 10^{-5} \text{ M}^{-1} \text{ s}^{-1}$	$k_{\text{obs}}^{\text{b}} / 10^{-6} \text{ s}^{-1}$	$k_2^{\text{b}} / 10^{-6} \text{ M}^{-1} \text{ s}^{-1}$
8.09(0.22)	0.456	22.5	49.4	10.4	22.8
7.06(0.26)	0.456	21.5	47.2	10.4	22.8
8.04(0.31)	0.456	21.1	46.2	10.6	23.3
21.7(0.4)	0.880	28.9	32.9	15.0	17.1
22.6(0.2)	0.880	29.5	33.5	7.57	8.60
23.2(0.3)	0.880	30.1	34.2	13.8	15.6
29.7(2.3)	0.464	2.51	5.42	1.62	3.49
31.4(0.2)	0.464	2.21	4.77	1.60	3.45
32.2(0.4)	0.464	2.30	4.95	1.58	3.41

^aReaction at the methyl ether site. ^bReaction at the phenethyl ether site.

Errors are shown in brackets next to corresponding water content. Errors are calculated as half the range of duplicate measurements.

Table S12. Rate data for the reaction of 1-bromo-4-phenethoxybenzene **8** with hydrogen bromide in [Bpyr][OTf] **3** with varying water content.

Water content / mol%	[Br ⁻] / M	$k_{\text{obs}} / 10^{-6} \text{ s}^{-1}$	$k_2 / 10^{-6} \text{ M}^{-1} \text{ s}^{-1}$
6.17(0.19)	0.611	6.57	10.8
6.29(0.13)	0.611	6.56	10.8
6.47(0.03)	0.611	7.03	11.5
18.7(1.6)	0.727	5.56	7.65
19.0(0.4)	0.727	5.19	7.14
20.2(0.9)	0.727	5.00	6.88
30.3(0.8)	0.658	1.84	2.81
30.9(0.3)	0.658	1.78	2.70
30.9(0.8)	0.658	1.80	2.73

Errors are shown in brackets next to corresponding water content. Errors are calculated as half the range of duplicate measurements.

Table S13. Rate data for the reaction of 1-methyl-4-phenethoxybenzene **9** with hydrogen bromide in [Bpyr][OTf] **3** with varying water content.

Water content / mol%	[Br ⁻] / M	$k_{\text{obs}} / 10^{-6} \text{ s}^{-1}$	$k_2 / 10^{-6} \text{ M}^{-1} \text{ s}^{-1}$
6.49(0.18)	0.305	13.6	44.7
6.91(0.02)	0.305	12.9	42.4
27.6(0.1) ^a	0.305	11.6	38.1
25.0(0.3)	0.800	18.5	23.1
25.7(0.2)	0.800	18.8	23.4
25.8(0.1)	0.800	18.1	22.7
39.9(0.1)	0.550	1.74	3.17
40.3(0.3)	0.550	1.74	3.16
40.3(0.3)	0.550	1.74	3.16

^aA crack was noticed in the NMR tube upon measurement of the water content. It is believed to have absorbed water after completion of the kinetic studies. For use in the main text, it was assumed to have a water content equal to the average of the other 2 samples prepared with it.

Errors are shown in brackets next to corresponding water content. Errors are calculated as half the range of duplicate measurements.

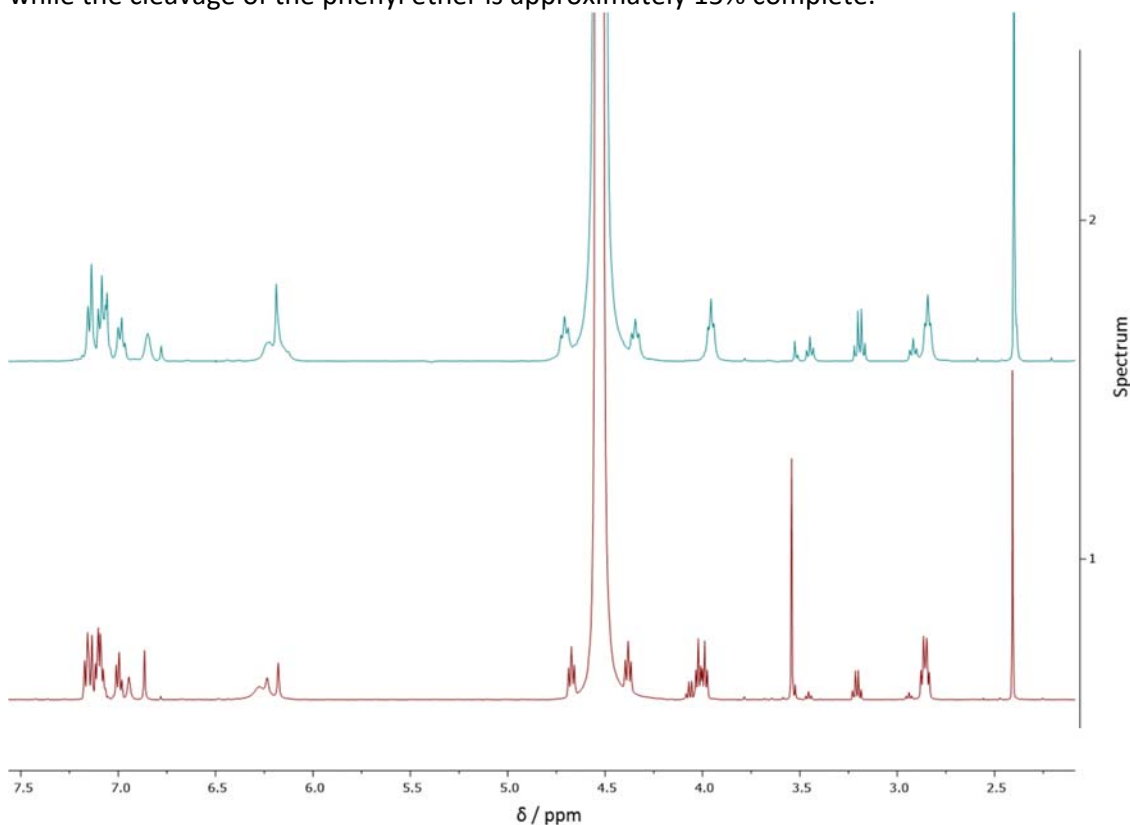
Table S14. Rate data for the reaction of 1-methyl-2-phenethoxybenzene **10** with hydrogen bromide in [Bpyr][OTf] **3** with varying water content.

Water content / mol%	[Br ⁻] / M	$k_{\text{obs}} / 10^{-6} \text{ s}^{-1}$	$k_2 / 10^{-6} \text{ M}^{-1} \text{ s}^{-1}$
5.89(2.15)	0.745	13.8	18.6
6.01(0.09)	0.745	12.0	16.2
6.30(0.59)	0.745	11.9	15.9
20.0(0.6)	0.816	8.30	10.2
19.5(0.4)	0.816	9.97	12.2
20.0(0.4)	0.816	9.82	12.0
31.8(0.1)	0.885	5.23	5.91
31.9(0.2)	0.885	5.14	5.81
32.4(0.1)	0.885	5.42	6.13

Errors are shown in brackets next to corresponding water content. Errors are calculated as half the range of duplicate measurements.

Representative ^1H NMR spectra before and after the methyl ether cleavage demonstrating the formation of the hydroxy intermediate species

Figure S7. ^1H NMR spectra for the demethylation of compound **6** showing the changes in signals over the course of the reaction. The red spectrum was obtained at approximately 60% cleavage of the methyl ether, the blue spectrum is at the completion of the demethylation, while the cleavage of the phenyl ether is approximately 15% complete.



Over the course of the demethylation reaction, changes in the ^1H NMR signals occur. The largest is that the signal due to the methyl protons, which occurs as a singlet at about δ 3.6, decreases and ultimately disappears. Signals due to the alkyl methylene groups (δ 4.0 and 2.9) do not shift significantly (<15 Hz). These data, along with the limited changes in the signals due to the aromatic protons, are consistent with cleavage of the methyl ether. These changes are observed prior to significant changes in signals corresponding to the alkyl methylene groups, indicating that effectively methyl ether cleavage precedes phenyl ether cleavage.

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