Supporting Information

pK_as of the Conjugate Acids of *N*-Heterocyclic Carbenes in Water

Eleanor M. Higgins,[a] Jennifer A. Sherwood,[b] Anita G. Lindsay,[a] James Armstrong,[a] Richard S. Massey,[a] Roger W. Alder[c] and AnnMarie C. O'Donoghue[a]*

[a] *Department of Chemistry, University Science Laboratories, South Road, Durham DH1 3LE, UK. E-mail: annmarie.odonoghue@durham.ac.uk*

[b] *The School of Chemistry and Chemical Biology, University College Dublin, Belfield, Dublin 4, Ireland.*

[c] *The School of Chemistry, University of Bristol, Bristol BS8 1TS, UK.*

Table of Contents

General instrumentation

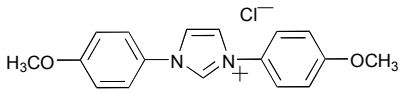
NMR samples were prepared in deuterated chloroform, deuterium oxide and d^6-dimethyl sulfoxide (DMSO). Tetramethylsilane (TMS) was used as an internal reference in deuterated chloroform. NMR spectra were recorded on Oxford Varian Unity Inova 300 and 500 MHz, Varian Unity 300 MHz, and Bruker Ultrashield 400 MHz NMR spectrometers. ^1H and ^{13}C NMR chemical shifts in $CDCl_3$ are reported relative to $CHCl_3$ at 7.27 ppm and 77.0 ppm respectively. In D_2O, ^1H NMR chemical shifts are reported relative to HOD at 4.67 ppm. In d^6-DMSO, ^1H NMR and ^{13}C NMR chemical shifts are reported relative to d^5-DMSO at 2.50 ppm and 39.52 ± 0.06 ppm respectively. Coupling constants (*J*) are reported in Hz. Multiplicities are indicated by: br s (broad singlet), s (singlet), d (doublet), t (triplet), q (quartet) and m (multiplet).

Materials

Deuterium oxide (99.9 % D) was purchased from Apollo Scientific Ltd. Deuterium chloride (35 wt %, 99.5 % D), potassium deuteroxide (40 wt %, 98+ %D), deuterated chloroform (99.8 % D), 1,3-bis(4-chlorophenyl)imidazolium chloride (99%), 1-ethyl-3-methylimidazolium chloride (99%) and tetramethylammonium hydrogensulfate were purchased from Sigma Aldrich. 1,3-Bis(*t*-butyl)imidazolium chloride (99%) and 1,3-bis(adamantyl)imidazolium chloride (99%) were purchased from Strem Chemicals Ltd. 1-Butyl-3-methylimidazolium hexafluorophosphate, 1-hexyl-3-methylimidazolium hexafluorophosphate (99%) and 1-octyl-3-methylimidazolium bromide (99%) were purchased from Solvent Innovation Chemicals Ltd. Samples of 1,3-diethyl-3,4,5,6-tetrahydropyrimidinium hexafluorophosphate, 1,3-di-(*i*-propyl)-3,4,5,6-tetrahydropyrimidinium hexafluorophosphate, and di-*i*-propylaminomethylidene(di-*i*-propyl)ammonium hexafluorophosphate (*N*,*N*,*N*',*N*'-tetra-(*i*-propyl)formamidinium hexafluorophosphate) were generously provided by Prof. Roger Alder at the University of Bristol.[S1] All other chemicals were reagent grade and were used without further purification unless otherwise stated.

Synthesis of Substrates

1,3-Bis(4-methoxyphenyl)imidazolium chloride $1H^+b–Cl^–$

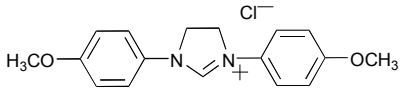


$1H^+b–Cl^–$

Following a modified procedure of Abrams *et al.*,[S2] *p*-anisidine (4.59 g, 37.3 mmol) in *n*-propanol (40 mL) was added to glyoxal (40 wt % aqueous solution, 2.16 g, 18.6 mmol) in H_2O (5 mL). The green-yellow solution was stirred at room temperature for 4 hours after which time the reaction was complete. The mixture was filtered and the precipitate washed with water, and recrystallised from ethyl acetate (30 mL). The product, glyoxal-bis-(4-methoxyphenyl)imine, was formed as large yellow needle like crystals (4.99 g, 67 %) with spectroscopic data (^{1}H NMR) in accordance with the literature.[S2] ***m.p.*** 166-168 °C.

Chloromethylethyl ether (0.330 g, 3.40 mmol) in THF (15 mL) was added to glyoxal-bis(4-methoxyphenyl)imine (10 g, 3.4 mmol) in a large reaction vessel. An extraction thimble (15 × 50 cm) charged with 4 Å molecular sieves was suspended in the reaction flask using copper wire. After 24 hours stirring under nitrogen at room temperature, a black solid precipitated. The solid was collected by suction filtration and purified by column chromatography on a silica column (methanol/dichloromethane 1:9) to yield product **$1H^+b–Cl^–$** as a beige powder (0.980 g, 91 %). ***m.p.*** > 250 ºC; R_f (methanol : dichloromethane = 1 : 9) = 0.32; $\boldsymbol{\nu}_{\mathbf{max}}$ (neat)/cm^{-1} 3332, 1556, 1501, 1281 and 820; $\boldsymbol{\delta}_{\mathbf{H}}$ (400 MHz; $CDCl_3$) 9.98 (1H, s, NCHN), 8.21 (2H, s, C*H*C*H*), 7.60 (4H, d, *J* 9.0, *o*-CH), 6.99 (4H, d, *J* 9.0, *m*-CH) and 3.60 (6H, s, *p*-OCH_3); $\boldsymbol{\delta}_{\mathbf{C}}$ (125 MHz; $CDCl_3$) 162.9, 130.7, 126.6, 125.0, 118.0, and 58.4; ***m/z*** (ESI+) 281.1 (100); HRMS (ESI+) $C_{17}H_{17}N_2O_2$ requires 281.1290, found 281.1284 (-2.1 ppm).

1,3-Bis(4-methoxyphenyl)-4,5-dihydroimidazolium chloride $2H^+b–Cl^–$



$2H^+b–Cl^–$

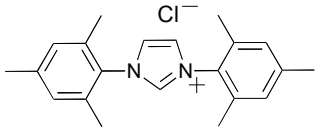
Following a modified procedure of Abrams *et al.*,[S2] glyoxal–bis(4-methoxyphenyl)imine **7** (0.500 g, 1.80 mmol) in methanol (50 mL) and THF (10 mL) was treated at 0 ºC with $NaBH_4$ (0.145 g, 3.70 mmol) dissolved in sodium hydroxide (1.50 mL 1.0 N) and water (10 mL). The solution was refluxed for 1 hour at 80 ºC,

under nitrogen until it turned colourless. A further 10 mL of water was added and the solution was concentrated *in vacuo*. Yellow crystals were observed to precipitate out of solution, which were collected by suction filtration and dried to yield *N*, *N*'-bis-(4-methoxyphenylamino)ethane (4.70 g, 78 %) with spectroscopic data (^{1}H NMR) in accordance with the literature.[S2] ***m.p.*** 117-120 °C.

N, *N*'-Bis(4-methoxyphenylamino)ethane (1.00 g, 3.60 mmol), was added to ammonium tetrafluoroborate (0.380 g, 3.60 mmol) and triethyl orthoformate (10 mL). The mixture was refluxed at 120 ºC for 3 hours. The resulting yellow liquid contained a beige precipitate, which was isolated by suction filtration and dried *in vacuo*. Recrystallization from ethanol yielded 1,3-bis(4-methoxyphenyl)-4,5-dihydroimidazolium tetrafluoroborate (0.35 g, 30 %); R_f(diethyl ether : ethyl acetate = 4 : 3) = 0.18; ***m.p.*** > 250 ºC; δ_H (300 MHz, $CDCl_3$) 9.71 (1H, s, NCHN), 7.55 (4H, d, *J* 3.3, *o*-CH), 7.10 (4H, d, *J* 3.3, *m*-CH), 4.51 (4H, s, CH_2CH_2), 3.80 (6H, s, *p*-OCH_3); δ_C (125 MHz; d_6-DMSO) 158.6, 151.4, 130.0, 120.6, 115.4, 56.2, 49.2.

Dowex® 1×4-50 anion exchange resin in the chloride form (5.00 g), was fully hydrated into a resin – water slurry then packed in a column (5 mL). 1,3-Bis(4-methoxyphenyl)-4,5-dihydroimidazolium tetrafluoroborate (1.00 g 3.10 mmol), was dissolved in methanol (30 mL) and then water was added (10 mL). The solution was run through the column and the resin was washed with water and methanol. The resulting analyte solution was concentrated and dried *in vacuo* to give the chloride product **2H$^+$b–Cl$^-$** (0.35 g, 99 %) with spectroscopic data (^{1}H and ^{13}C NMR) in accordance with the literature.[S3] ***m.p.*** > 250 °C.

1,3-Bis(2,4,6-trimethylphenyl)imidazolium chloride 1H$^+$c–Cl$^-$

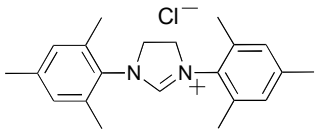


1H$^+$c–Cl$^-$

Following a modified procedure of Arduengo *et al*., chloromethylethyl ether (0.300 g, 3.17 mmol) in THF (1 mL) was added to a solution of glyoxal-bis(2,4,6-trimethylphenyl)imine[S4] (0.900 g, 3.08 mmol) in THF (10 mL). An extraction thimble (15 × 50 mm) charged with 4 Å molecular sieves was suspended in the reaction flask using copper wire. After 30 min stirring under nitrogen at room temperature, a white solid precipitated, which was collected by suction filtration and recrystallized from *n*-

hexane to yield product **1H$^+$c–Cl$^-$** as a white powder (0.49 g, 48 %) with spectroscopic data (^{1}H and ^{13}C NMR) in accordance with the literature.[S4] ***m.p.*** > 250 °C (lit. m.p. 350 - 352 °C[S4]).

1,3-Bis(2,4,6-trimethylphenyl)-4,5-dihydroimidazolium chloride 2H$^+$c–Cl$^-$



2H$^+$c–Cl$^-$

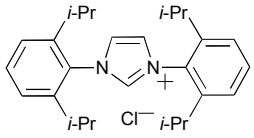
Following a modified procedure of Arduengo *et al.*, glyoxal–bis(2,4,6-trimethylphenyl)imine[S4] (2.95 g, 10.1 mmol), in THF (40 mL) was treated at 0 ºC with $NaBH_4$ (3.00 g, 79.3 mmol) and was stirred for 16 hours at 23 ºC, and subsequently heated to reflux for 3 hours under nitrogen. The reaction mixture was cooled on ice, and a HCl solution (3 M) was slowly added drop-wise to the mixture until effervescence had ceased. H_2O (10 mL) was added, the solution turned cloudy and a white precipitate formed. The precipitate was collected by suction filtration, and recrystallized from ethanol to yield *N*, *N*'-bis-(2,4,6-trimethylphenylamino)ethane dihydrochloride as a white powder (2.72 g, 74 %) with spectroscopic data (^{1}H and ^{13}C NMR) in accordance with the literature.[S4] ***m.p.*** > 250 °C.

Following a modified procedure of Scholl *et al.*,[S5] *N*, *N*'-Bis(2,4,6-trimethylphenylamino)ethane dihydrochloride (1.00 g, 2.71 mmol), was added to ammonium tetrafluoroborate (0.280 g, 2.67 mmol) and triethyl orthoformate (3.00 mL, 3 mmol). The beige liquid obtained yielded a precipitate of similar colour, which was then isolated by suction filtration. Hot ethanol was added to the mother liquor and it was placed in the freezer for three days. The white crystals formed were filtered, washed with hexane, dried *in vacuo* and recrystallized from ethanol to yield 1,3-bis(2,4,6-trimethylphenyl)-4,5-dihydroimidazolium tetrafluoroborate (1.02 g, 96 %) with spectroscopic data (^{1}H and ^{13}C NMR) in accordance with the literature.[S5] ***m.p.*** > 250 °C.

Dowex® 1×4-50 anion exchange resin in the chloride form (5.00 g) was fully hydrated into a resin - water slurry, then packed in a column (10 cm length). 1,3-Bis(2,4,6-trimethylphenyl)-4,5-dihydroimidazolium tetrafluoroborate **2H$^+$c–BF$_4^-$**

(0.150 g, 0.381 mmol), was dissolved in a minimum volume of methanol and water (20 mL) and run through the column. The column was washed several times with water and methanol. The resulting analyte solution was concentrated and dried *in vacuo* to give the chloride product **2H$^+$c–Cl$^-$** as an off-white solid (0.131 g, 92 %). 4,5-Dihydroimidazolium salt **2H$^+$c–Cl$^-$** has been prepared by an alternative method and characterized in the literature previously.[S4] ***m.p.*** >250 ºC; $\boldsymbol{\delta_H}$ (300 MHz; $CDCl_3$) 8.32 (1H, s, NCHN), 6.99 (4H, s, *m*-CH), 4.68 (4H, s, CH_2CH_2), 2.42 (12H, s, *o*-CH_3), 2.31 (6H, s, *p*-CH_3).

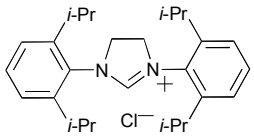
1,3-Bis(2,6-di-(*i*-propyl)phenyl)imidazolium chloride 1H$^+$d–Cl$^-$



1H$^+$d–Cl$^-$

Following a modified procedure of Arduengo *et al.*,[S4] chloromethylethyl ether (0.250 g, 20.7 mmol) in THF (7 mL) was added to glyoxal-bis(2,6-di-(*i*-propyl)phenyl)imine[S4] (1.00 g, 2.70 mmol) in a large reaction vessel. An extraction thimble (15 × 50 mm) charged with 4 Å molecular sieves was suspended in the reaction flask using copper wire. After 24 hours stirring under nitrogen at room temperature, a precipitate appeared out of the dark red solution. The resulting precipitate was collected by suction filtration and dried to yield the product **1H$^+$d–Cl$^-$** as a powder (1.07 g, 94 %) with spectroscopic data (^{1}H and ^{13}C NMR) in accordance with the literature.[S4] ***m.p.*** > 250 °C (lit. m.p. > 255 °C[S4]).

1,3-Bis(2,6-di-(*i*-propyl)phenyl)-4,5-dihydroimidazolium chloride 2H$^+$d–Cl$^-$



2H$^+$d–Cl$^-$

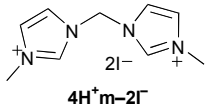
Following a modified procedure of Arduengo *et al.*,[S4] glyoxal–bis(2,6-di-(*i*-propyl)phenyl)imine (1.00 g, 2.70 mmol) in methanol (50mL) and THF (30 mL) was treated at 0 ºC with $NaBH_4$ (0.01 g, 2.70 mmol) dissolved in sodium hydroxide (2 mL 1.0 N) and water (5 mL). The solution was refluxed for 16 hours at 80 ºC under nitrogen, then quenched with HCl (0.5 M) and water (30 mL) was added. The solution was concentrated and a white solid precipitated, which was collected by suction

filtration, and dried *in vacuo* to yield *N*, *N*'-bis(2,6-di-(*i*-propyl)phenylamino)ethane dihydrochloride (1.02 g 100%) with spectroscopic data (^{1}H and ^{13}C NMR) in accordance with the literature.[S4]

N, *N*'-Bis(2,6-di-(*i*-propyl)phenylamino)ethane dihydrochloride (0.067 g, 0.18 mmol), was added to ammonium tetrafluoroborate (0.018 g, 0.18 mmol) and triethyl orthoformate (10 mL). The mixture was refluxed at 120 °C for 24 hours. The resulting yellow liquid contained a crystalline beige precipitate. The solid was isolated and recrystallized from ethanol to yield 1,3-bis(2,6-di-(*i*-propyl)phenyl)-4,5-dihydroimidazolium tetrafluoroborate as a crystalline solid (0.62 g, 54%). 1,3-Bis(2,6-di-(*i*-propyl)phenyl)-4,5-dihydroimidazolium tetrafluoroborate has been prepared by an alternative method and characterized in the literature previously.[S6] ***m.p.*** > 250 °C; $\boldsymbol{\delta_H}$ (300 MHz; d_6-DMSO) 9.43 (1H, s, NCHN), 7.54 (2H, t, *J* 7.5, *p*-CH), 7.42 (4H, d, *J* 7.5, *m*-CH), 4.53 (4H, s, CH_2CH_2), 3.07 (4H, m, C*H*$(CH_3)_2$), 1.34 (12H, d, *J* 7.0, CH(C*H*$_3)_2$), 1.19 (12H, d, *J* 7.0, CH(C*H*$_3)_2$)).

Dowex® 1×4-50 anion exchange resin in the chloride form (5 g), was fully hydrated into a resin- water slurry then packed in a column (10 cm). 1,3-Bis(2,6-di-(*i*-propyl)phenyl)-4,5-dihydroimidazolium tetrafluoroborate (0.08 g, 0.16mmol), was dissolved in methanol, (15 mL) and water (10 mL) and run through the column. The column was then washed with methanol and water. The resulting analyte solution and washings were concentrated and dried *in vacuo* to yield a white solid 1,3-bis(2,6-di-(*i*-propyl)phenyl)-4,5-dihydroimidazolium chloride (0.070 g, 99 %).
4,5-Dihydroimidazolium salt **2H$^+$c–Cl$^-$** has been prepared by an alternative method and characterized in the literature previously.[S4] $\boldsymbol{\delta_H}$ (300 MHz; d_6-DMSO) 9.43 (1H, s, NCHN), 7.54 (2H, t, *J* 7.5, *p*-CH), 7.42 (4H, d, *J* 7.5, *m*-CH), 4.53 (4H, s, CH_2CH_2), 3.07 (4H, m, C*H*$(CH_3)_2$), 1.34 (12H, d, *J* 7.0, CH(C*H*$_3)_2$), 1.19 (12H, d, *J* 7.0, CH(C*H*$_3)_2$)).

1,1'-Dimethyl-3,3'-methylene-diimidazolium diiodide 4H$^+$m–2I$^-$

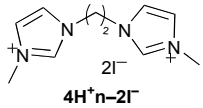


4H$^+$m–2I$^-$

Following a modified procedure of Muehlhofer *at al.*,[S7] *N*-methylimidazole (1.94 mL, 24.2 mmol) was added to dry THF (15 mL) under an argon atmosphere.

Diiodomethane (1.90 mL, 13.4 mmol) was then added and the resulting mixture was stirred at 80 °C for 21 hours. The white precipitate produced after this time was filtered and washed with THF (3 × 5 mL). Three recrystallisations of this precipitate from methanol gave white crystals of diimidazolium salt **4H$^+$m–2I$^-$** (1.01 g, 18%) with spectroscopic data (^{1}H and ^{13}C NMR) in accordance with the literature.[S7] ***m.p.*** > 250 °C.

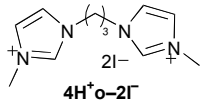
1,1'-Dimethyl-3,3'-(1,2-ethylene)-diimidazolium diiodide 4H$^+$n–2I$^-$



4H$^+$n–2I$^-$

Following a modified procedure of Muehlhofer *et al.*,[S7] 1,2-diiodoethane (3.41 g, 12.1 mmol) was added to *N*-methylimidazole (1.94 mL, 24.2 mmol) under an argon atmosphere. The resulting mixture was stirred at 25 °C for 24 hours to yield a deep purple solution. Water (100 mL) was then added and the purple globules of iodine were removed to leave a yellow solution. Water was removed by rotary evaporation to yield a yellow oil containing a white precipitate. The latter precipitate was filtered and recrystallised from ethanol to give white crystals of diimidazolium salt **4H$^+$n–2I$^-$** (0.048 g, 1%) with spectroscopic data (^{1}H and ^{13}C NMR) in accordance with the literature.[S7]

1,1'-Dimethyl-3,3'-(1,3-propylene)-diimidazolium diiodide 4H$^+$o–2I$^-$

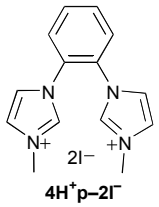


4H$^+$o–2I$^-$

N-Methylimidazole (1.94 mL, 24.2 mmol) was added to dry THF (100 mL) under an argon atmosphere. 1,3-diiodopropane (1.38 mL, 12.1 mmol) was then added and the resulting mixture was stirred at 80 °C for 18 hours under an argon atmosphere. After this time the mixture had separated into two liquid layers: a bottom orange layer and an upper colourless layer. On cooling the orange liquid layer solidified to yield a yellow solid. The solid was collected by filtration, washed with THF (3× 5 mL) and recrystallised twice from ethanol to give diimidazolium salt **4H$^+$o–2I$^-$** as a white powder (2.29 g, 41%); ***m.p.*** 145-146 ºC; ν_{max} (neat)/cm^{-1} 3137, 3075, 1574, 1162, 764, 613; δ_H (500 MHz; d_6-DMSO) 9.18 (2H, s, NCHN), 7.81 (2H, s, CHC*H*), 7.75 (2H, s, C*H*CH), 4.25 (4H, t, *J* 7.0, CH_2CH$_2$CH_2), 3.87 (6H, s, CH$_3$), 2.40 (2H, q, *J* 7.0,

$CH_2CH_2CH_2$); δ_C (125 MHz; d_6-DMSO) 137.5, 124.4, 122.9, 46.4, 36.7, 30.2; ***m/z*** (ESI+) 793.1 (10), 334.4 (8, $M+H^+-I^-$), 333.2 (88, $M-I^-$), 251.1 (10), 205.2 (47, $M-2I^-$), 123.8 (75), 96.0 (100), 82.0 (85); HRMS (ESI+) $C_{11}H_{18}N_4I^+$ requires 333.0576, found 333.0566 (-3.0 ppm).

1,1'-Dimethyl-3,3'-(1,2-phenylene)-diimidazolium diiodide $4H^+p–2I^–$



$4H^+p–2I^–$

Following a modified procedure of Tubaro *et al.*,[S8] 1,1'-(1,2-phenylene)bis(imidazole) (0.60 g, 2.9 mmol) and methyl iodide (0.36 mL, 5.8 mmol) were added to methanol (10 mL) and the resulting solution was stirred at 40 °C for 96 hours. The solid that had precipitated after this time was removed by filtration and was recrystallised from methanol to give diimidazolium diiodide **$4H^+p–2I^–$** (0.18 g, 16 %) with spectroscopic data (^{1}H and ^{13}C NMR) in accordance with the literature.[S8] ***m.p.*** 232-233 °C.

Preparation of Solutions

Stock solutions of potassium deuteroxide and potassium chloride were prepared by dilution and titration of the commercial concentrated solutions. Stock solutions of buffers, K_2DPO_4 and KD_2PO_4, were obtained from potassium phosphate monobasic and dibasic by exchanging the hydrogen atoms for deuterium. This was achieved by dissolving the salts in D_2O, followed by removal of solvent under reduced pressure. The process was repeated five times and the salts were freeze dried. Phosphate buffers were prepared by mixing stock solutions of K_2DPO_4 and KD_2PO_4 in D_2O with addition of KCl to give solutions of buffer at various acid/ base ratios and I=1.0 (KCl).

Stock solutions of quinuclidine-DCl and quinuclidinone-DCl salts in D_2O were obtained from quinuclidine-HCl and quinucidinone-HCl salts respectively by exchanging the hydrogen atoms for deuterium as for the preparation of exchanged phosphate salts. Quinuclidine and quinuclidinone buffers were prepared by mixing stock solutions of exchanged salt and stock solutions of potassium deuteroxide with

the addition of KCl when needed to give solutions of buffer at various acid/base ratios and I=1 (KCl).

Stock solutions of acetate buffers were prepared by mixing stock solutions of potassium acetate and DCl with addition of KCl when needed to give buffer solutions at various acid/base ratios and I=1.0 (KCl).

Kinetic methods

All azolium salts were rigorously dried before use in deuterium exchange experiments. H/D exchange reactions were carried out in 12.5 mL vials which were incubated at 25 ± 0.1 ºC in a thermostated water bath. All reactions were carried out in D_2O with the ionic strength maintained at I = 1.0 with KCl, with the exception of substrates 1,3-bis(4-chlorophenyl)imidazolium chloride **1H$^+$a-Cl$^-$** (I = 0.5), 1,3-bis(4-methoxyphenyl)imidazolium chloride **1H$^+$b-Cl$^-$** (I = 0.5), and 1,3-bis(4-methoxyphenyl)-4,5-dihydroimidazolium chloride **2H$^+$b-Cl$^-$** (I = 0.25). In these cases the poor solubility of the substrate in water required a lower ionic strength. Typically reactions were run on a 5 or 6 mL scale, and were initiated by injection of 500 or 1000 μL of substrate stock solution (50 mM in D_2O) to the KOD or buffer solution, containing internal standard, tetramethylammonium deuteriosulfate. In general, the final substrate and internal standard concentrations in the reaction solutions were 5 - 10 mM and 0.5 - 1 mM, respectively. This ensured an approximately 1:1 ^{1}H NMR integration ratio of the singlet due to relevant acidic hydrogen of substrate and the broad triplet due to the 12 methyl hydrogens of internal standard. In cases where the reaction solution had a final pD of ≤ 7, the substrate was added neat to the reaction solution and dissolved with the aid of sonication when required.

The reaction progress was monitored over time by withdrawing aliquots (~800 μL) at timed intervals. Generally reaction of substrate was followed for at least two halftimes. These aliquots were quenched to pD values 3-4 units below that of the reaction mixture by addition of > 1 M DCl solution. The samples were either analysed immediately or placed in a sealed plastic bag containing calcium chloride and stored in the freezer for analysis at a later time.

The pH values of buffered solutions were determined at 25 ºC using a MeterLab^{TM}

PHM 290 pH-Stat Controller equipped with a radiometer (pH 4 - 7 - 10 @ 25 ºC) combination electrode, that could be standardised between pH 4 - 7 or pH 7 - 10 to encompass the pH of the buffer solution. The pD (± 0.03) was calculated by adding 0.4 to the observed reading of the pH meter.[S9] The deuteroxide concentration (M) was calculated from the equation $[DO^-] = (10^{pD - pKw})/\gamma_{DO}$, where $K_w = 10^{-14.87}$ M^2 is the ion product of D_2O at 25 ºC and γ_{DO} is the apparent activity coefficient of deuteroxide ion under our experimental conditions.[S10] The apparent activity coefficient of deuteroxide ion, γ_{DO}, was determined from the measured pH of solutions of known $[HO^-]$ in water at I = 1.0 (KCl) and 25 °C, with the assumption that $\gamma_{DO} = \gamma_{HO}$. For these measurements, the pH apparatus was standardized at 7.00 and at 12.47 with calcium hydroxide that was saturated at 21 °C.[S11] Due to the relatively short shelf-life of the Radiometer combination electrode, it was necessary to replace the electrode once the sensitivity fell below 96%. Although the same model of electrode was always used, values of γ_{DO} were re-determined with each electrode and were found to vary from 0.73-0.77.

The estimated error on the observed pseudo-first-order rate constant for exchange (k_{ex}, s^{-1}) is ± 10 % based on the error of the ^{1}H NMR measurement. Although the measurements of k_{ex} are single determinations, the calculated error in similar carbon acidity measurements and calculations performed by Richard *et al*[S12-S13] is ± 10 % for k_{ex} and ± 0.5 units for the pK_a.

In general, ^{1}H NMR spectra were acquired with 64 – 128 transients. In the case of 1,3-bis(4-chlorophenyl)imidazolium chloride **1H$^+$a-Cl$^-$**, 1,3-bis(4-methoxyphenyl)imidazolium chloride **1H$^+$b-Cl$^-$**, 1,3-bis(*t*–butyl)imidazolium chloride **1H$^+$h-Cl$^-$**, 1,3-bis(4-methoxyphenyl)4,5-dihydroimidazolium chloride **2H$^+$b-Cl$^-$** and *N*,*N*,*N*',*N*'-tetra-(*i*-propyl)formamidinium hexafluorophosphate **6H$^+$-PF$_6^-$**, ^{1}H NMR spectra were run with 128 – 1056 transients and a total acquisition time of between 1-7 hours. These longer spectral acquisition times were employed where an improved signal/noise ratio was required due to the low solubility of the substrate. ^{1}H NMR spectral baselines were subject to a first – order drift correction before integration of the peak areas. Substrate and product peak areas were compared with the peak of the internal standard that was set to an arbitrary figure of 1000.

Determination of first and second order rate constants for deuteroxide ion catalyzed exchange

Deuterium exchange reactions were monitored in buffered D_2O solutions for which the range of buffers employed depended on the reactivity of the parent azolium salt **5H**$^+$ towards deprotonation by deuteroxide ion. Deuterium exchange resulted in a decrease of the singlet due to the C(2)–H of **5-H**$^+$ relative to the broad triplet at 3.3 ppm due to the methyl hydrogens of internal standard, tetramethylammonium deuteriosulphate.Values of the fraction of remaining substrate **5H**$^+$ could be calculated using [Eq. (s1)] by comparing the integrated areas of the singlet due to the C(2)-H ($A_{C(2)–H}$) with those of the internal standard (A_{IS}). The observed first order rate constant for deuterium exchange, k_{ex} (s^{-1}), could be obtained as the slope of a semilogarithmic plot of the fraction of remaining substrate against time according to [Eq. (s2)].

$$f(s) = \frac{(A_{C(2)–H}/A_{IS})_t}{(A_{C(2)–H}/A_{IS})_0} \qquad (s1)$$

$$\ln f(s) = -k_{ex}t \qquad (s2)$$

As mentioned in the main text, the effect of an increase in total buffer concentration on k_{ex} at fixed pD was investigated for a range of representative azolium salts. In all cases a 2-9–fold increase in the total buffer concentration resulted in no significant change (± 10%) in k_{ex} at 25°C (see p S72 for details of experiments). Thus at the buffer concentrations of these experiments it was concluded that values of k_{ex} may be described by [Eq. (s3)] where only deuteroxide-ion catalysed exchange is significant. The value for deprotonation by solvent water as a base is expected to be much lower than other contributing terms so can also be neglected.[S13] Plots of the first order rate constants k_{ex} against deuteroxide concentration were linear with slopes equivalent to k_{DO}, the second order rate constants for deuteroxide catalysed exchange.

$$k_{ex} = k_{DO}[DO^-] \qquad (s3)$$

For each compound listed in Table 1 of the main paper, the relevant kinetic data used in the determination of k_{ex} and k_{DO} values are given below in addition to representative NMR spectral data of the C2 H/D exchange process in D_2O solution.

1,3-Bis(4-chlorophenyl)imidazolium chloride $1H^+a–Cl^-$

Figure s1: Representative ^1H NMR spectra at 500 MHz of imidazolium salt **$1H^+a–Cl^-$** (0.1 mM, pD 5.97), obtained during exchange of the C2-H (s, 9.69 ppm) for deuterium in 100 mM acetic acid buffer solution (90% f_B) in D_2O at 25 ºC and I = 0.5 (KCl). [Internal standard, tetramethylammonium deuteriosulfate (s, 3.09 ppm)]

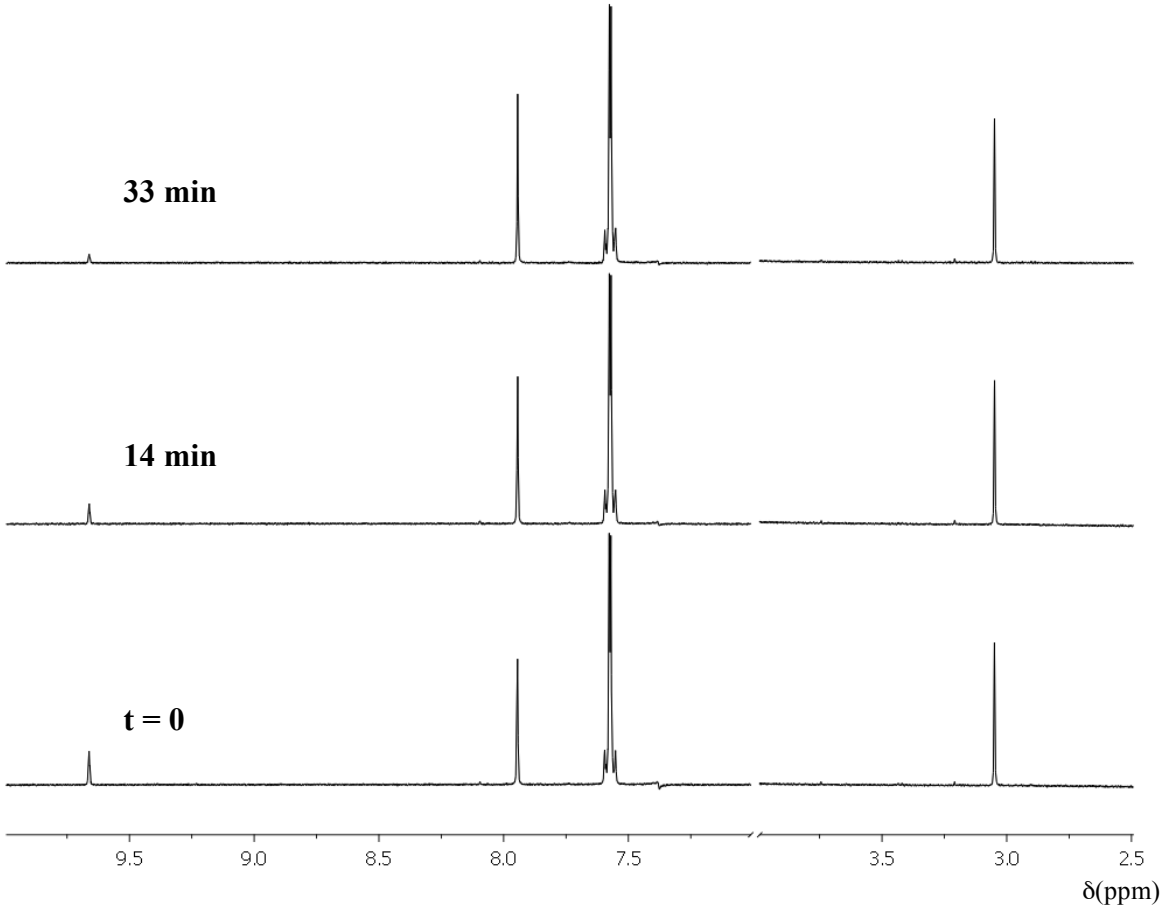


Figure s2. Semilogarithmic plots of the fraction of unexchanged substrate against time for the deuterium exchange reaction of **1H$^+$a–Cl$^-$** in 100 mM acetic acid buffers in D_2O at 25 ºC and I = 0.5 (KCl).

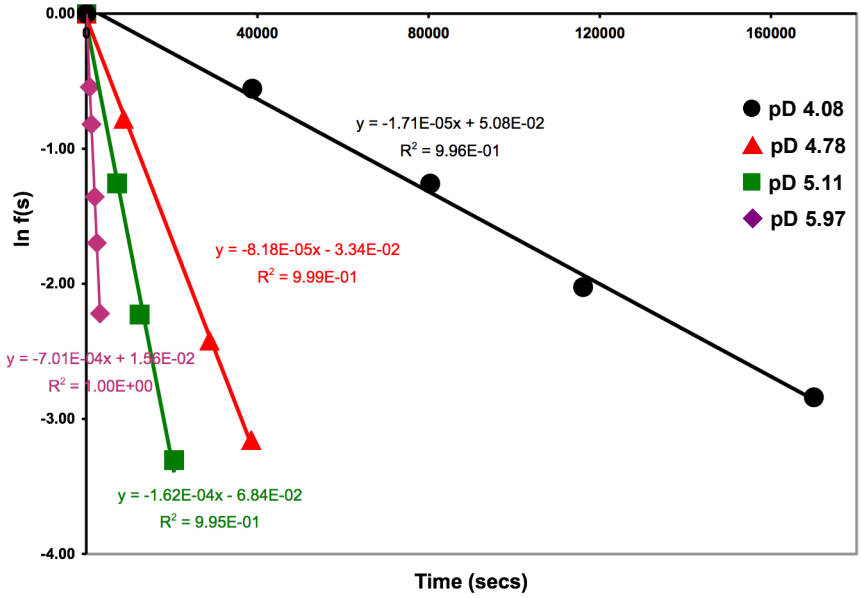


Figure s3: Plot of k_{ex} against [DO$^-$] for the H/D exchange reaction of imidazolium salt **1H$^+$a–Cl$^-$** in 100 mM acetic acid buffers in D_2O at 25 ºC and I = 0.5 (KCl).

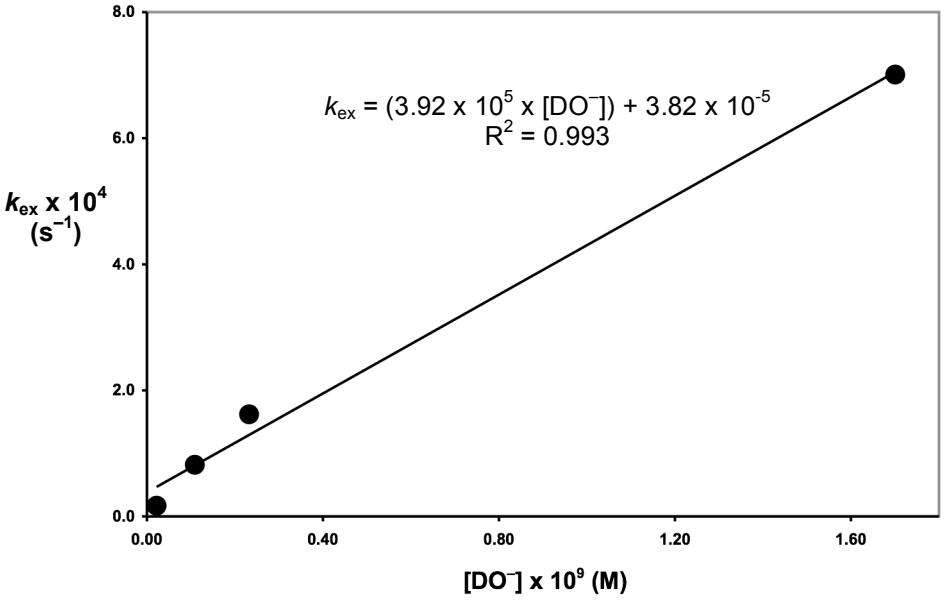


Table s1: First and second-order rate constants for exchange of the C2-H of imidazolium salt **1H$^+$a–Cl$^-$** for deuterium in acetic acid buffers in D_2O at 25 ºC and I = 0.5 (KCl).

[Buffer]$_{total}$, M	**pD**	**[DO$^-$], M**	**k_{ex}, s^{-1}**	**k_{DO}, M^{-1}s^{-1} [a]**
0.1	4.08	2.18×10^{-11}	1.71×10^{-5}	3.92×10^{5}
	4.78	1.09×10^{-10}	8.18×10^{-5}	
	5.11	2.32×10^{-10}	1.62×10^{-4}	
	5.97	1.70×10^{-9}	7.01×10^{-4}	

(a) The second-order rate constant, k_{DO}, was obtained from the slope of the plot of k_{ex} against [DO$^-$] in Figure s3.

1,3-Bis(4-methoxyphenyl)imidazolium chloride $1H^+b–Cl^–$

Figure s4: Representative ^1H NMR spectra at 500 MHz of imidazolium salt **$1H^+b–Cl^–$** (1 mM, pD 4.06), obtained during exchange of the C2-H (s, 9.46 ppm) for deuterium in 100 mM acetic acid buffer solution (10% f_B) in D_2O at 25 ºC and I = 0.5 (KCl). [Internal standard, tetramethylammonium deuteriosulfate (s, 3.08 ppm)]

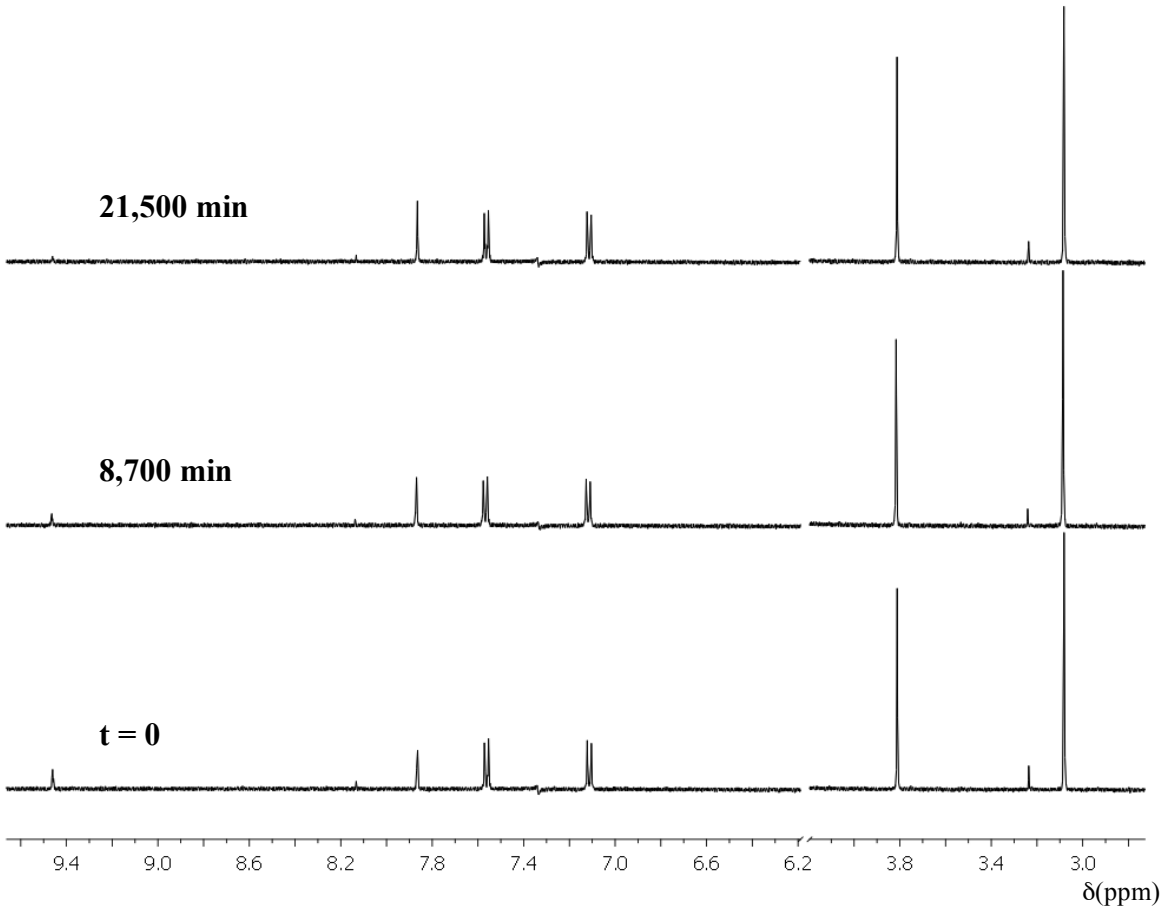


Figure s5. Semilogarithmic plots of the fraction of unexchanged substrate against time for the deuterium exchange reaction of **1H$^+$b–Cl$^-$** in 100 mM acetic acid buffers in D_2O at 25 ºC and I = 0.5 (KCl).

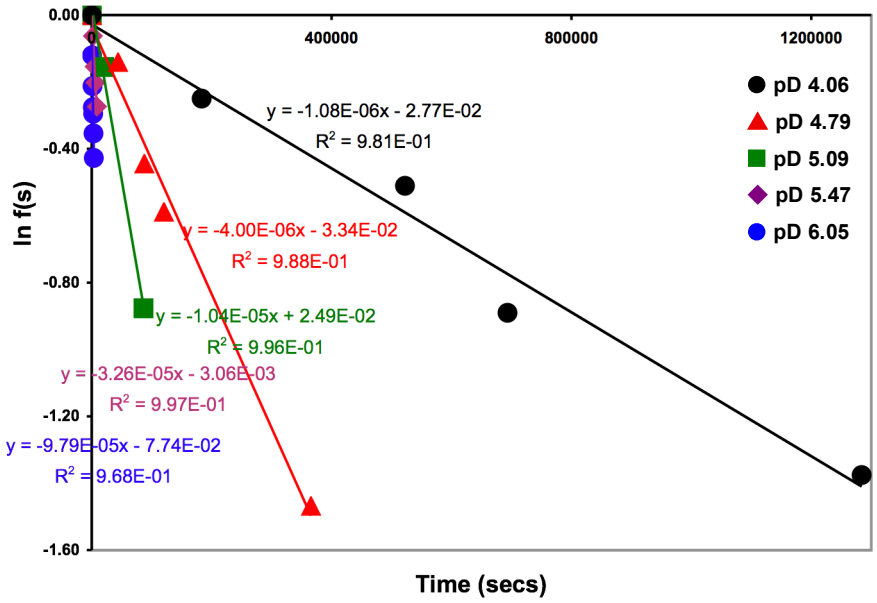


Figure s6: Plot of k_{ex} against [DO^-] for the H/D exchange reaction of imidazolium salt **1H$^+$b–Cl$^-$** in 100 mM acetic acid buffers in D_2O at 25 ºC and I = 0.5 (KCl).

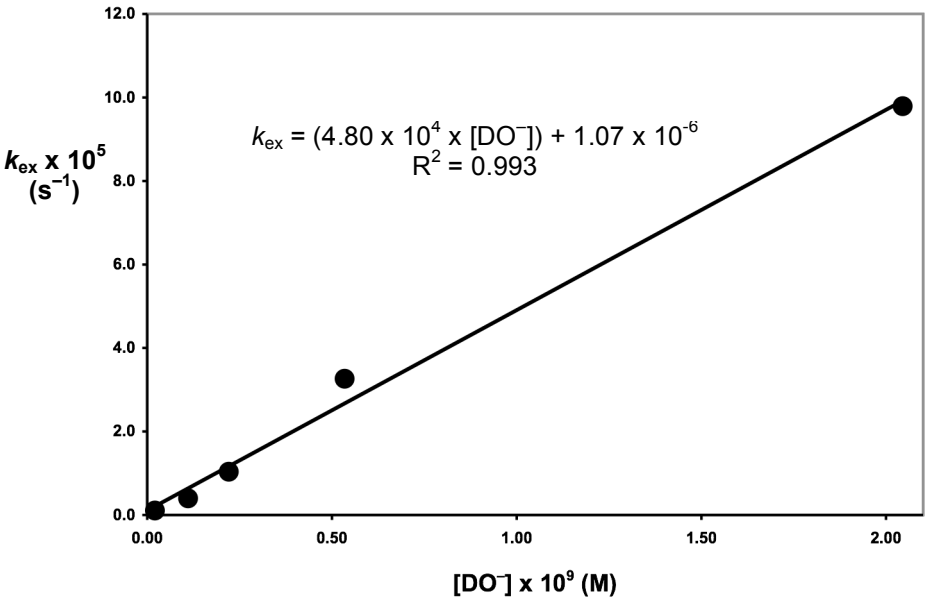


Table s2: First and second-order rate constants for exchange of the C2-H of imidazolium salt **1H$^+$b–Cl$^-$** for deuterium in acetic acid buffers in D_2O at 25 ºC and I = 0.5 (KCl).

[Buffer]$_{total}$, M	**pD**	**[DO$^-$], M**	**k_{ex}, s^{-1}**	**k_{DO}, M^{-1}s^{-1} a**
0.10	4.06	2.09×10^{-11}	1.08×10^{-6}	4.80×10^{4}
	4.79	1.11×10^{-10}	4.00×10^{-6}	
	5.09	2.21×10^{-10}	1.04×10^{-5}	
	5.47	5.34×10^{-10}	3.26×10^{-5}	
	6.06	2.05×10^{-9}	9.79×10^{-5}	

(a) The second-order rate constant, k_{DO}, was obtained from the slope of the plot of k_{ex} against [DO$^-$] in Figure s6.

1,3-Bis(2,4,6-trimethylphenyl)imidazolium chloride $1H^+c–Cl^-$:

Figure s7: Representative ^1H NMR spectra at 500 MHz of imidazolium salt **$1H^+c–Cl^-$** (5 mM, pD 5.99), obtained during exchange of the C2-H (s, 9.10 ppm) for deuterium in 100 mM acetic acid buffer solution (90% f_B) in D_2O at 25 ºC and I = 1.0 (KCl). [Internal standard, tetramethylammonium deuteriosulfate (s, 3.13 ppm)]

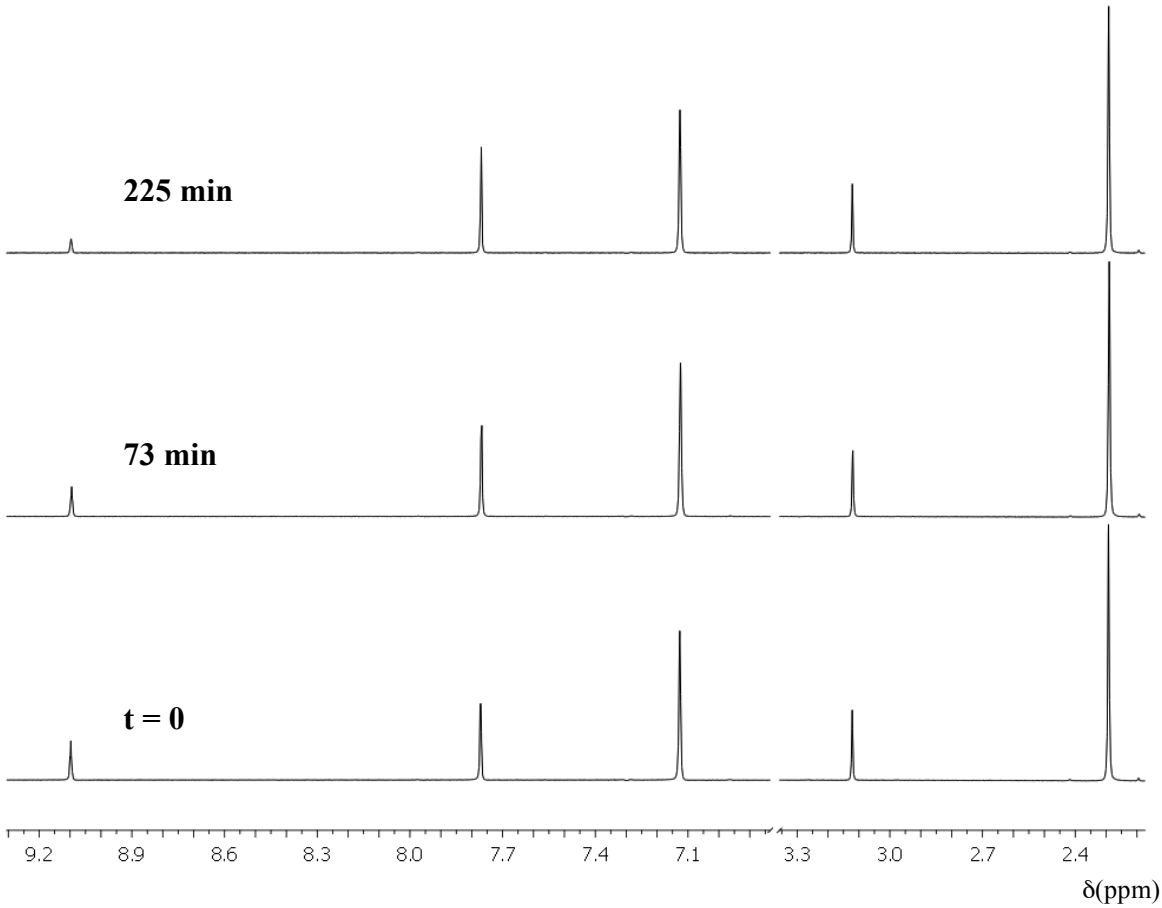


Figure s8. Semilogarithmic plots of the fraction of unexchanged substrate against time for the deuterium exchange reaction of **1H$^+$c–Cl$^-$** in 100 mM acetic acid buffers in D_2O at 25 ºC and I = 1.0 (KCl): (a) pD 4.38, 4.70. (b) pD 5.60, 5.99

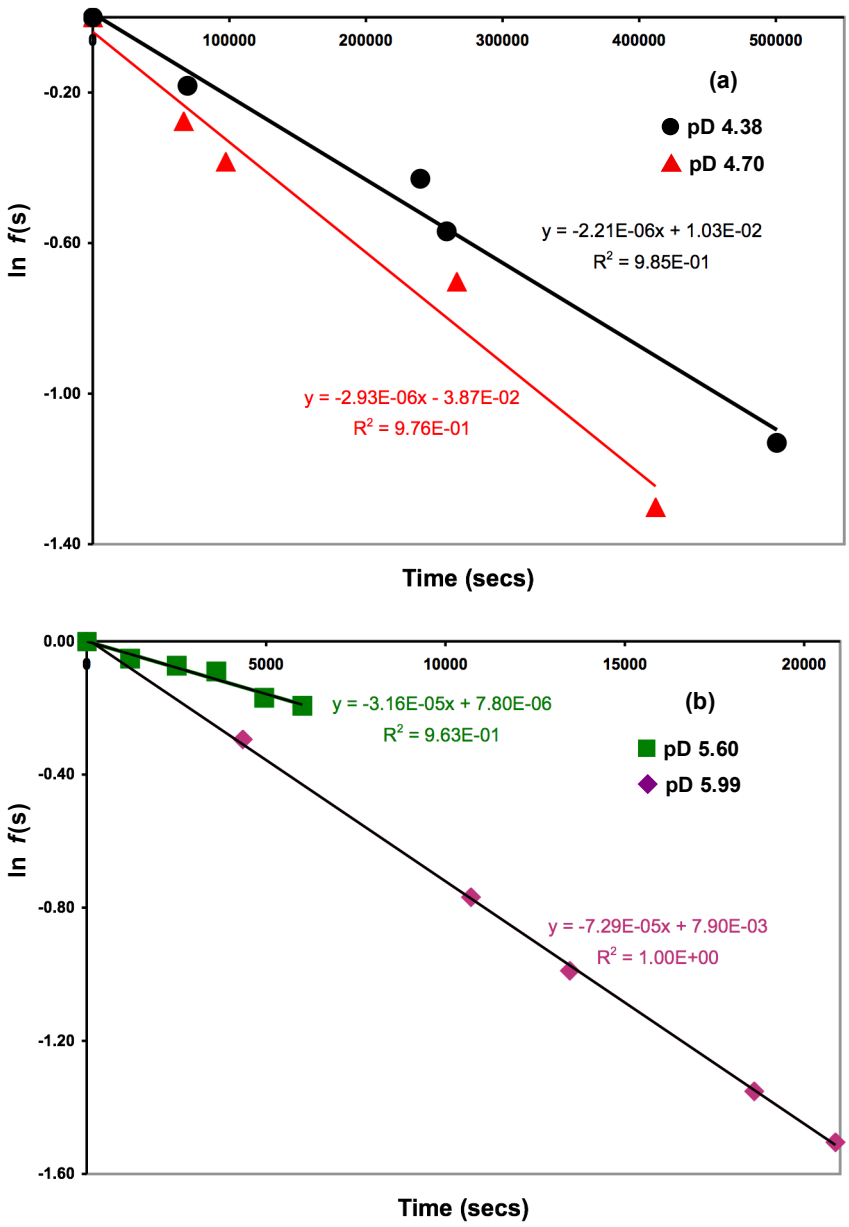


Figure s9: Plot of k_{ex} against [DO^-] for the H/D exchange reaction of imidazolium salt **$1H^+c–Cl^-$** in acetic acid buffers in D_2O at 25 ºC and I = 1.0 (KCl).

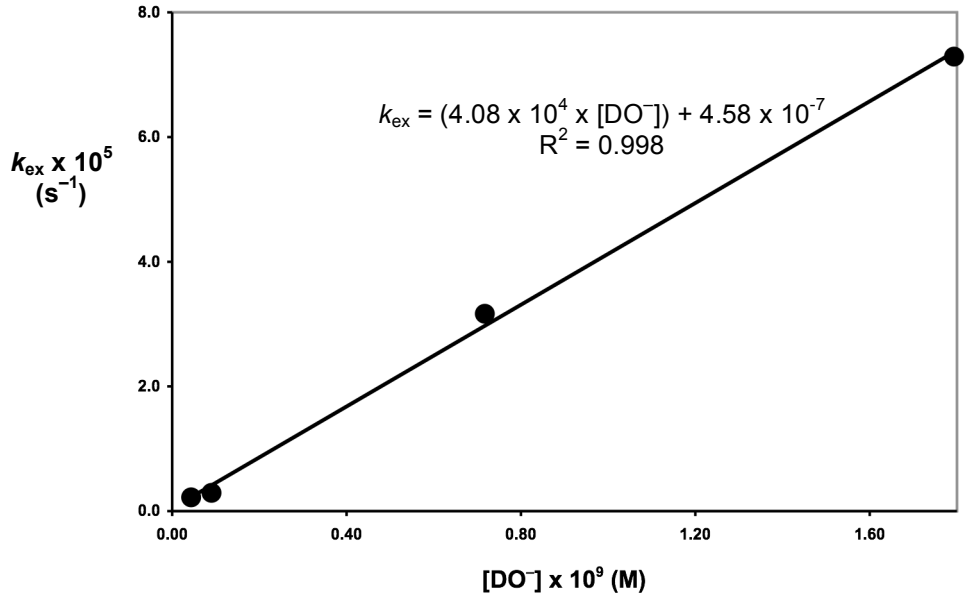


Table s3: First and second-order rate constants for exchange of the C2-H of imidazolium salt **$1H^+c–Cl^-$** for deuterium in acetic acid buffers in D_2O at 25 ºC and I = 1.0 (KCl).

$[Buffer]_{total}$, M	pD	$[DO^-]$, M	k_{ex}, s^{-1}	k_{DO}, $M^{-1}s^{-1}$ [a]
0.1	4.38	4.33×10^{-11}	2.21×10^{-6}	4.08×10^4
	4.70	9.01×10^{-11}	2.93×10^{-6}	
	5.60	7.17×10^{-10}	3.16×10^{-5}	
	5.99	1.79×10^{-9}	7.29×10^{-5}	

(a) The second-order rate constant, (k_{DO}), was obtained from the slope of the plot of k_{ex} against [DO^-] in Figure s9.

1,3-Bis(di-(*i*-propyl)phenyl)imidazolium chloride $1H^+d–Cl^-$

Figure s10: Representative ^{1}H NMR spectra at 500 MHz of imidazolium salt **$1H^+d–Cl^-$** (2.5 mM, pD 5.97), obtained during exchange of the C2-H (s, 9.57 ppm) for deuterium in 100 mM phosphate buffer solution (10% f_B) in D_2O at 25 ºC and I = 1.0 (KCl). [Internal standard, tetramethylammonium deuteriosulfate (s, 3.12 ppm)]

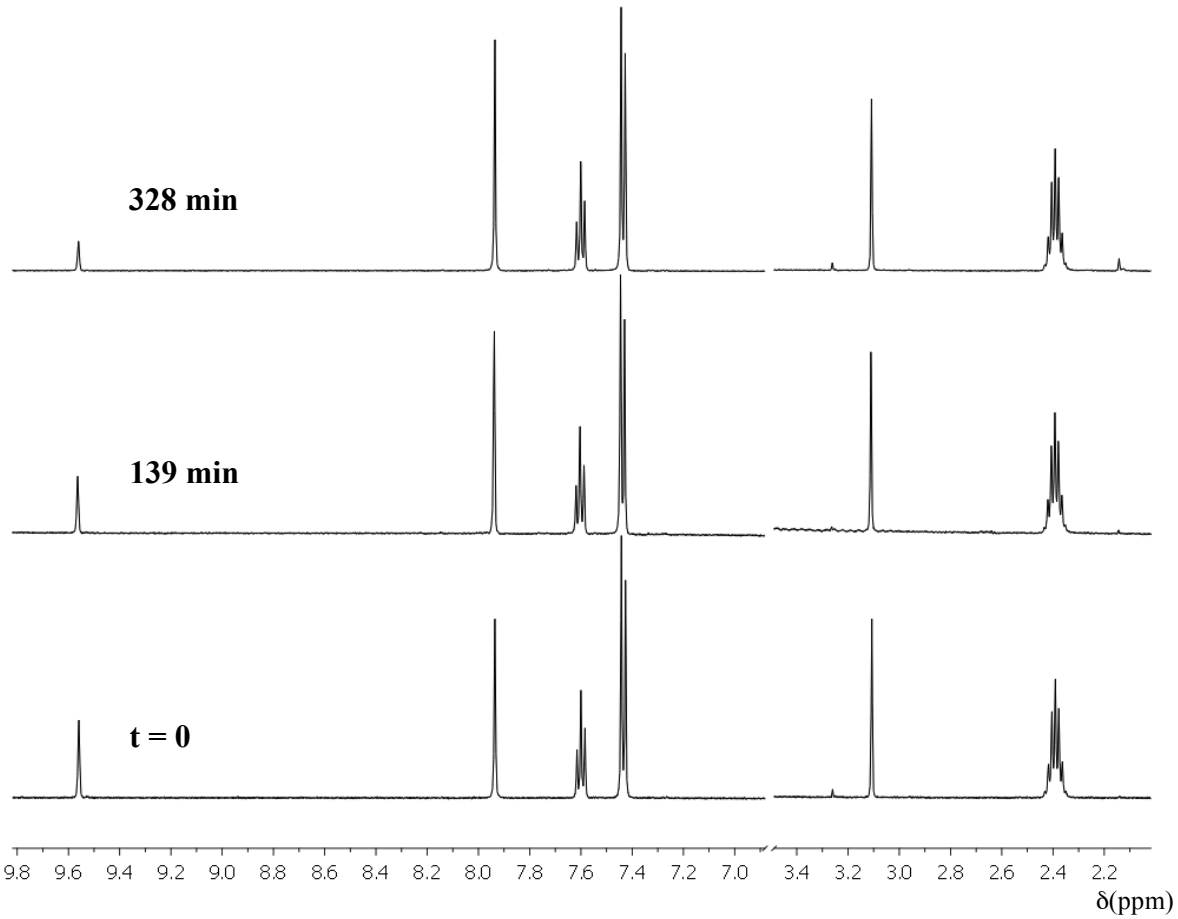


Figure s11. Semilogarithmic plots of the fraction of unexchanged substrate against time for the deuterium exchange reaction of **1H$^+$d–Cl$^-$** in 100 mM phosphate buffers in D_2O at 25 ºC and I = 1.0 (KCl).

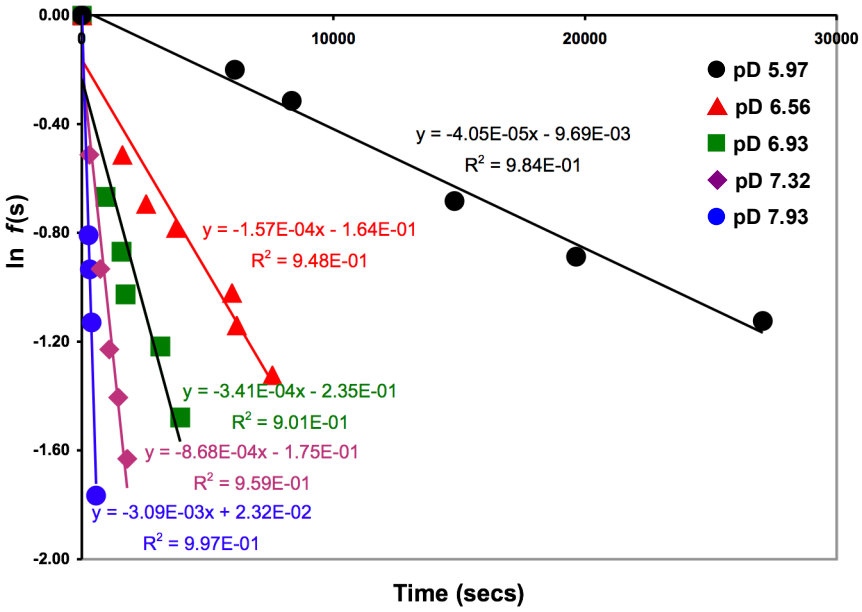


Figure s12: Plot of k_{ex} against [DO$^-$] for the H/D exchange reaction of imidazolium salt **1H$^+$d–Cl$^-$** in 100 mM phosphate buffers in D_2O at 25 ºC and I = 1.0 (KCl).

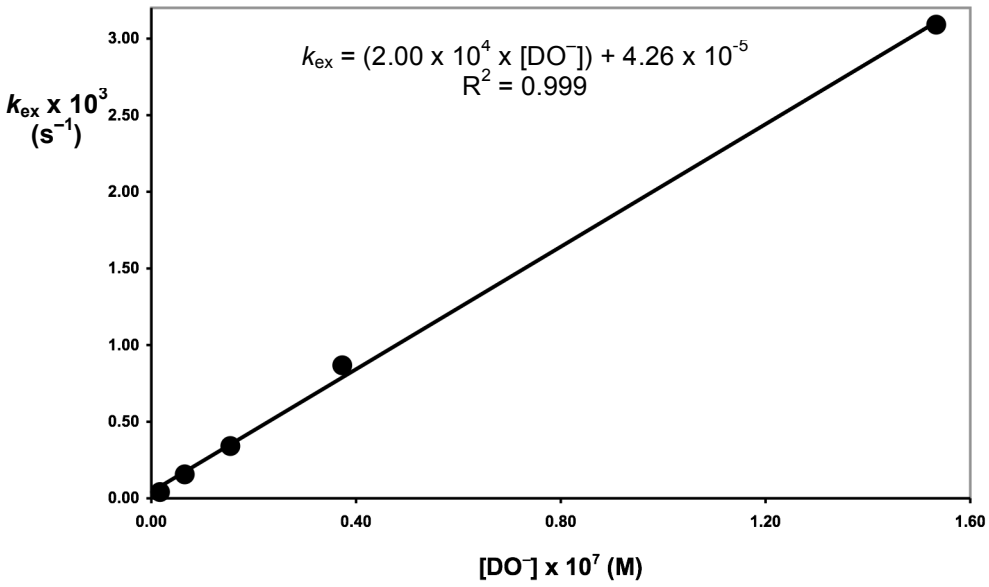


Table s4: First and second-order rate constants for exchange of the C2-H of imidazolium salt **1H$^+$d–Cl$^-$** for deuterium in 100 mM phosphate buffers in D_2O at 25 ºC and I = 1.0 (KCl).

[Buffer]$_{total}$, M	**pD**	**[DO$^-$], M**	**k_{ex}, s^{-1}**	**k_{DO}, M^{-1}s^{-1} [a]**
	5.97	1.69×10^{-9}	4.05×10^{-5}	
	6.56	6.53×10^{-9}	1.57×10^{-4}	
0.1	6.93	1.54×10^{-8}	3.41×10^{-4}	2.00×10^{4}
	7.32	3.73×10^{-8}	8.68×10^{-4}	
	7.93	1.53×10^{-7}	3.09×10^{-3}	

(a) The second-order rate constant, k_{DO}, was obtained from the slope of the plot of k_{ex} against [DO$^-$] in Figure s12.

1-Ethyl-3-methylimidazolium chloride $1H^+e–Cl^-$

Figure s13: Representative ^1H NMR spectra at 300 MHz of imidazolium salt **$1H^+e–Cl^-$** (5 mM, pD 6.94), obtained during exchange of the C2-H (s, 8.64 ppm) for deuterium in 250 mM phosphate buffer solution (50% f_B) in D_2O at 25 ºC and I = 1.0 (KCl). [Internal standard, tetramethylammonium deuteriosulfate (s, 3.13 ppm; CH_3)]

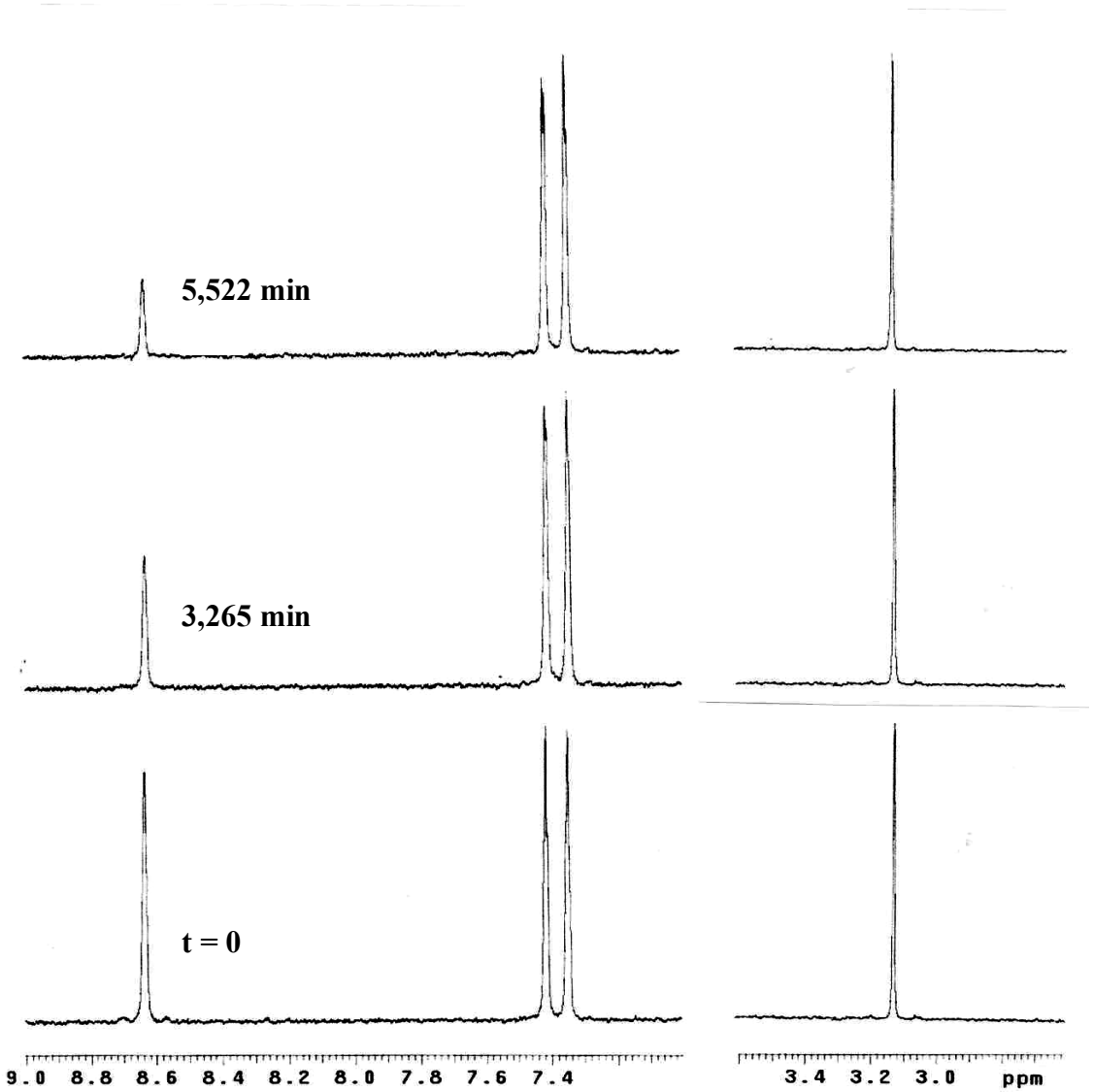


Figure s14. Semilogarithmic plots of the fraction of unexchanged substrate against time for the deuterium exchange reaction of **1H$^+$e–Cl$^-$** in 250 mM phosphate buffers at 25 ºC and I = 1.0 (KCl).

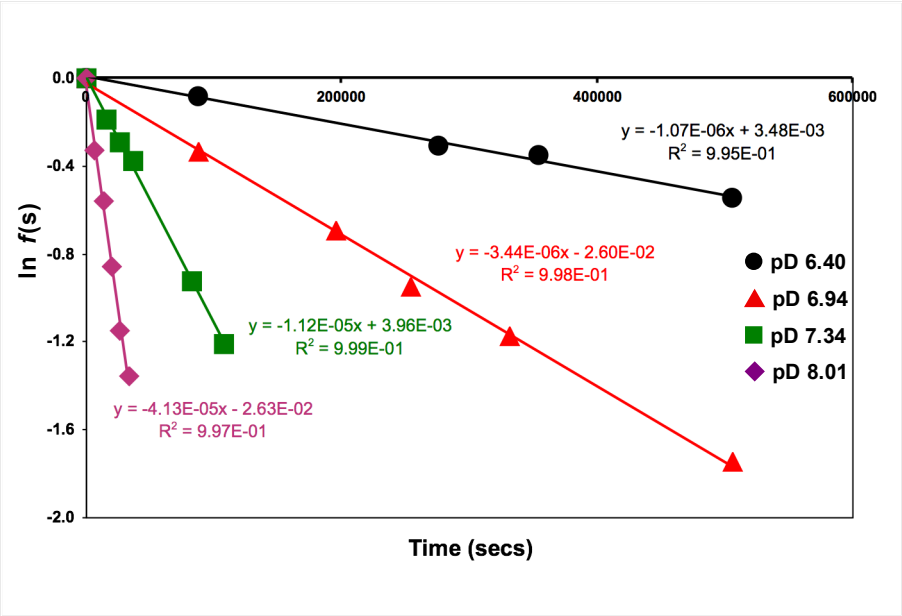


Figure s15: Plot of k_{ex} against [DO$^-$] for the H/D exchange reaction of imidazolium salt **1H$^+$e–Cl$^-$** in D_2O at 25 ºC and I = 1.0 (KCl).

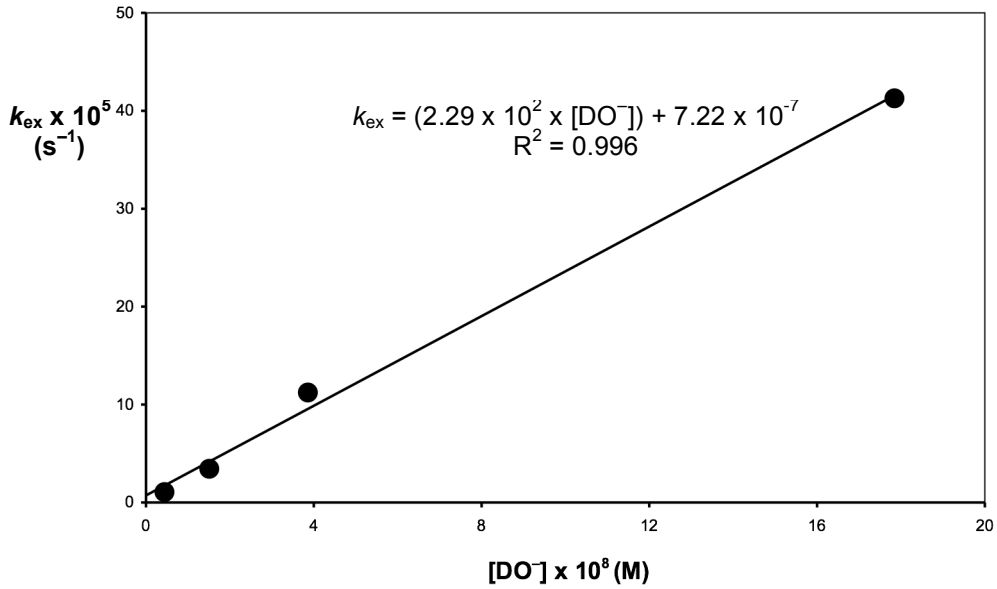


Table s5: First and second-order rate constants for exchange of the C2-H of imidazolium salt **1H$^+$e–Cl$^-$** for deuterium in phosphate buffers in D_2O at 25 ºC and I = 1 (KCl).

[Buffer]$_{total}$, M	**pD**	**[DO$^-$], M**	**k_{ex}, s^{-1}**	**k_{DO}, M^{-1}s^{-1} [a]**
0.25	6.40	4.41×10^{-9}	1.07×10^{-6}	2.29×10^{2}
	6.94	1.51×10^{-8}	3.44×10^{-6}	
	7.34	3.86×10^{-8}	1.12×10^{-5}	
	8.01	1.78×10^{-7}	4.13×10^{-5}	

(a) The second-order rate constant, k_{DO}, was obtained from the slope of the plot of k_{ex} against [DO$^-$] in Figure s15.

1-*n*Butyl-3-methylimidazolium hexafluorophosphate $1H^+f–PF_6^-$

Figure s16: Representative ^1H NMR spectra at 400 MHz of imidazolium salt **$1H^+f–PF_6^-$** (10 mM, pD 8.12), obtained during exchange of the C2-H (s, 8.68 ppm) for deuterium in 250 mM phosphate buffer solution (90% f_B) in D_2O at 25 ºC and I = 1.0 (KCl). [Internal standard, tetramethylammonium deuteriosulfate (s, 3.15 ppm; CH_3)]

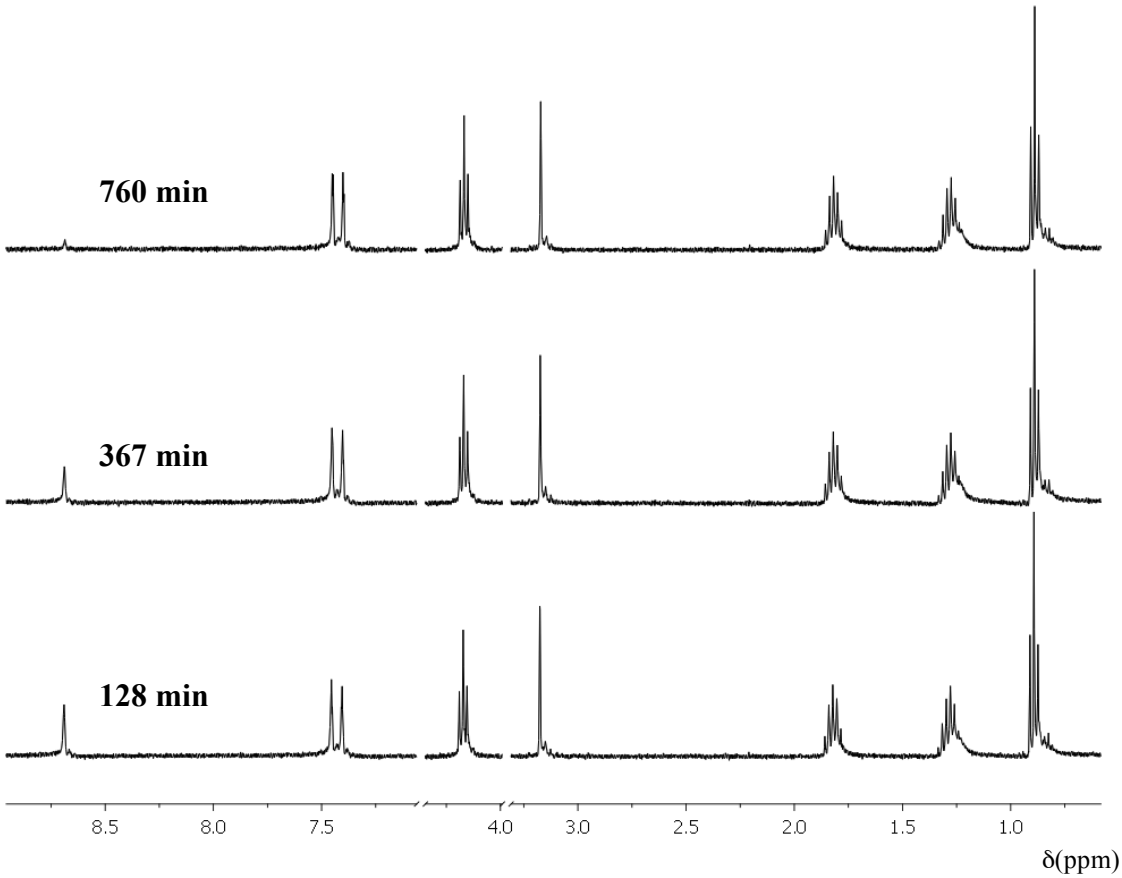


Figure s17. Semilogarithmic plots of the fraction of unexchanged substrate against time for the deuterium exchange reaction of $\mathbf{1H^{+}f–PF_6^{-}}$ in 250 mM phosphate buffers in D_2O at 25 ºC and I = 1.0 (KCl).

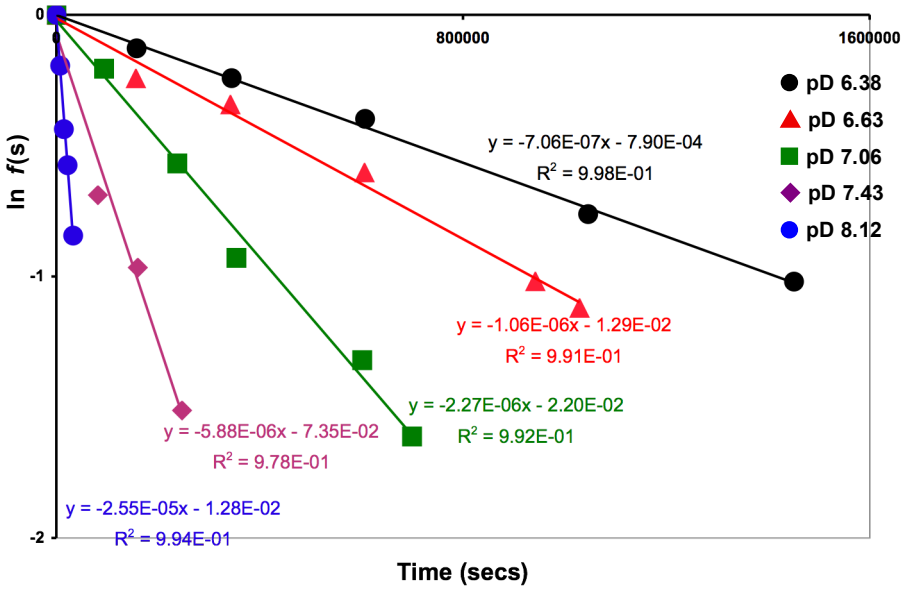


Figure s18: Plot of k_{ex} against $[DO^{-}]$ for the H/D exchange reaction of imidazolium salt $\mathbf{1H^{+}f–PF_6^{-}}$ in D_2O at 25 ºC and I = 1.0 (KCl).

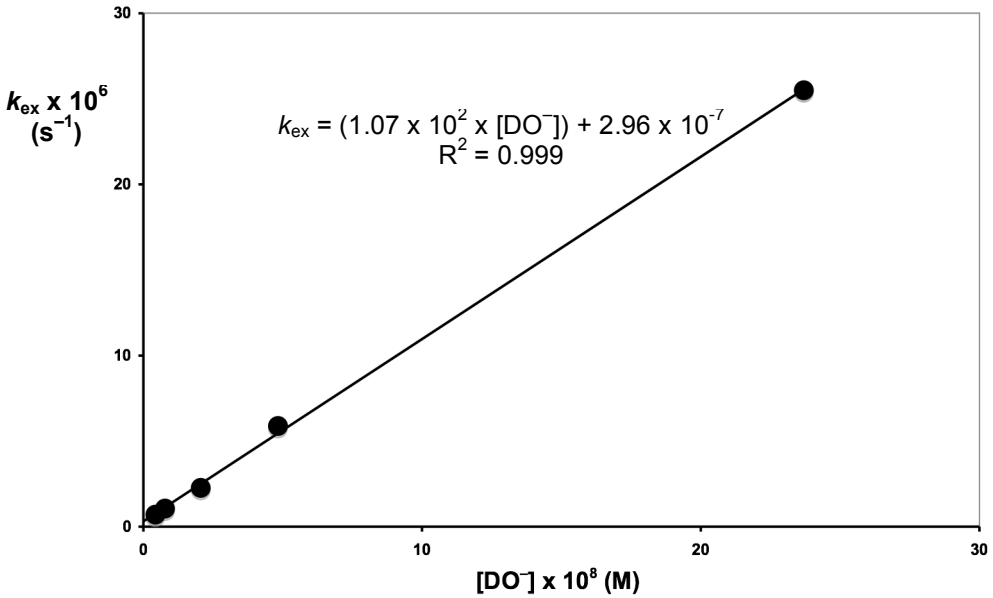


Table s6: First and second-order rate constants for exchange of the C2-H of imidazolium salt $\mathbf{1H^{+}f–PF_6^{-}}$ for deuterium in phosphate buffers in D_2O at 25 ºC and I = 1 (KCl).

$[Buffer]_{total}$, M	pD	$[DO^{-}]$, M	k_{ex}, s^{-1}	k_{DO}, $M^{-1}s^{-1}$ [a]
0.25	6.38	4.30×10^{-9}	7.06×10^{-7}	1.07×10^{2}
	6.63	7.75×10^{-9}	1.06×10^{-6}	
	7.06	2.06×10^{-8}	2.27×10^{-6}	
	7.43	4.83×10^{-8}	5.88×10^{-6}	
	8.12	2.37×10^{-7}	2.55×10^{-5}	

(a) The second-order rate constant, k_{DO}, was obtained from the slope of the plot of k_{ex} against $[DO^{-}]$ in Figure s18.

1-*n*Hexyl-3-methylimidazolium hexafluorophosphate $1H^+g–PF_6^-$

Figure s19: Representative ^1H NMR spectra at 400 MHz of imidazolium salt $\mathbf{1H^+g–PF_6^-}$ (10 mM, pD 8.12), obtained during exchange of the C2-H (s, 8.68 ppm) for deuterium in 250 mM phosphate buffer solution (90% f_B) in D_2O at 25 ºC and I = 1.0 (KCl). [Internal standard, tetramethylammonium deuteriosulfate (s, 3.16 ppm; CH_3)]

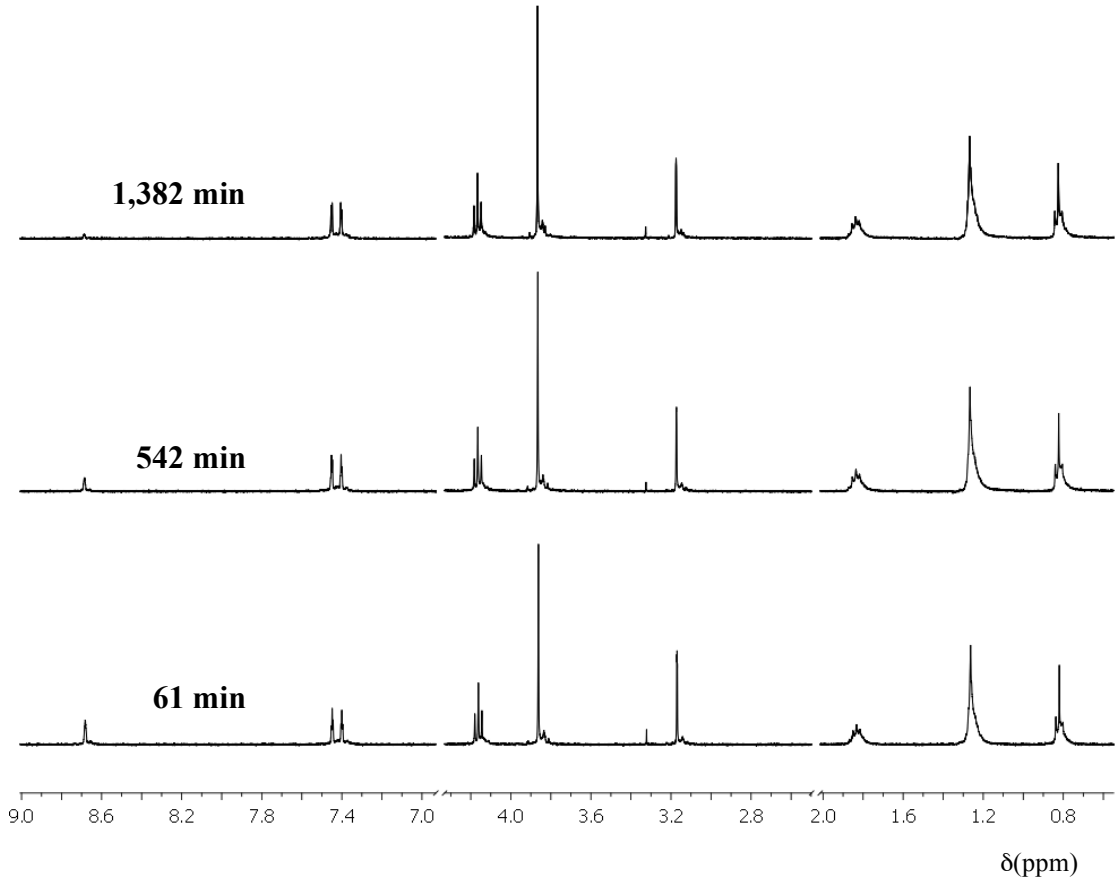


Figure s20. Semilogarithmic plots of the fraction of unexchanged substrate against time for the deuterium exchange reaction of **1H$^+$g–PF$_6^-$** in 250 mM phosphate buffers in D_2O at 25 ºC and I = 1.0 (KCl).

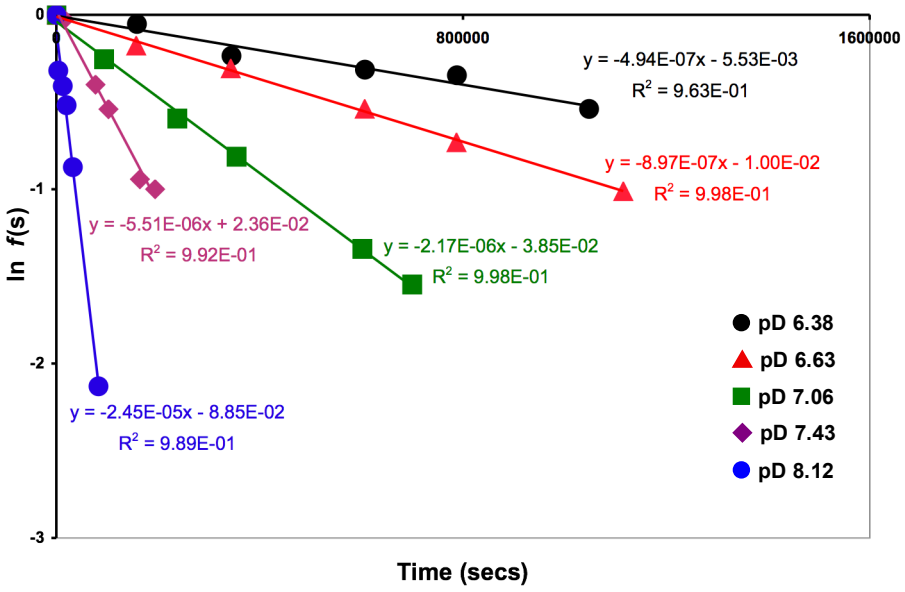


Figure s21: Plot of k_{ex} against [DO$^-$] for the H/D exchange reaction of imidazolium salt **1H$^+$g–PF$_6^-$** in 250 mM phosphate buffers in D_2O at 25 ºC and I = 1.0 (KCl).

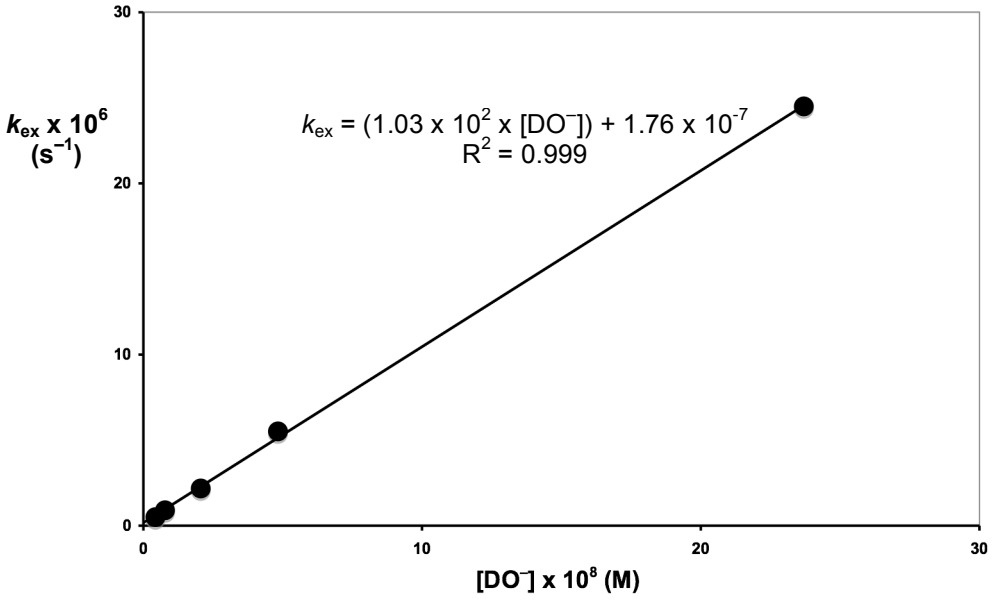


Table s7: First and second-order rate constants for exchange of the C2-H of imidazolium salt $\mathbf{1H^{+}g–PF_6^{-}}$ for deuterium in 250 mM phosphate buffers in D_2O at 25 ºC and I = 1 (KCl).

$[Buffer]_{total}$, M	pD	$[DO^{-}]$, M	k_{ex}, s^{-1}	k_{DO}, $M^{-1}s^{-1}$ [a]
0.25	6.38	4.30×10^{-9}	4.94×10^{-7}	1.03×10^{2}
	6.63	7.75×10^{-9}	8.97×10^{-7}	
	7.06	2.06×10^{-8}	2.17×10^{-6}	
	7.43	4.83×10^{-8}	5.51×10^{-6}	
	8.12	2.37×10^{-7}	2.45×10^{-5}	

(a) The second-order rate constant, k_{DO}, was obtained from the slope of the plot of k_{ex} against $[DO^{-}]$ in Figure s21.

1-*n*Octyl-3-methylimidazolium bromide $1H^+h–Br^–$

Figure s22: Representative ^1H NMR spectra at 400 MHz of imidazolium salt **$1H^+h–Br^–$** (10 mM, pD 7.43), obtained during exchange of the C2-H (s, 8.68 ppm) for deuterium in 250 mM phosphate buffer solution (70% f_B) D_2O at 25 ºC and I = 1.0 (KCl). [Internal standard, tetramethylammonium deuteriosulfate (s, 3.17 ppm; CH_3)]

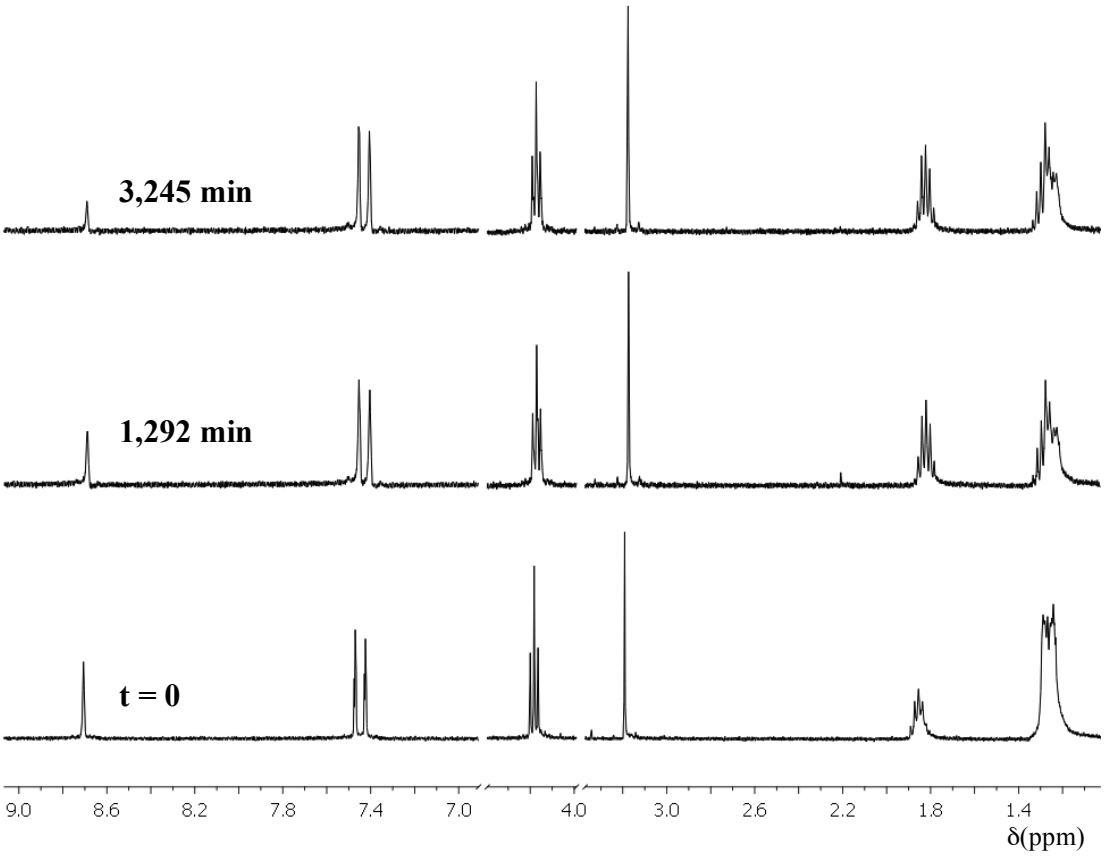


Figure s23. Semilogarithmic plots of the fraction of unexchanged substrate against time for the deuterium exchange reaction of **1H$^+$h–Br$^-$** in 250 mM phosphate buffers in D_2O at 25 ºC and I = 1.0 (KCl).

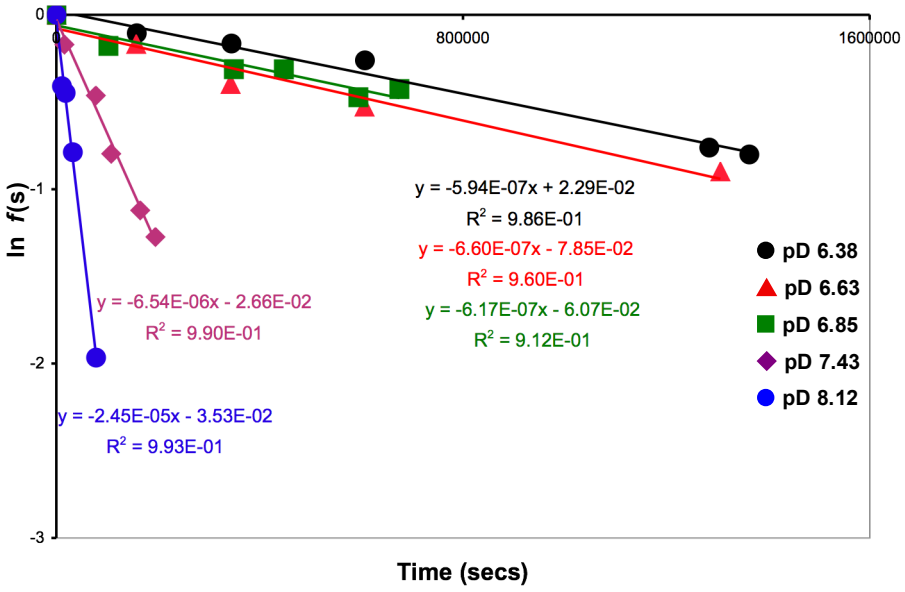


Figure s24: Plot of k_{ex} against [DO$^-$] for the H/D exchange reaction of imidazolium salt **1H$^+$h–Br$^-$** in 250 mM phosphate buffers in D_2O at 25 ºC and I = 1.0 (KCl).

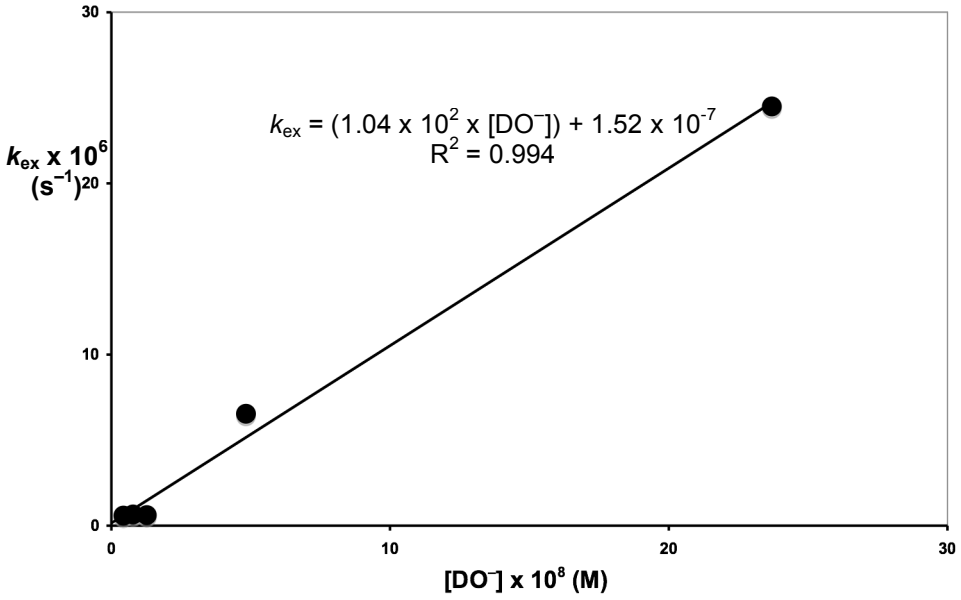


Table s8: First and second-order rate constants for exchange of the C2-H of imidazolium salt **1H$^+$h–Br$^-$** for deuterium in 250 mM phosphate buffers in D_2O at 25 ºC and I = 1 (KCl).

[Buffer]$_{total}$, M	**pD**	**[DO$^-$], M**	**k_{ex}, s^{-1}**	**k_{DO}, M^{-1}s^{-1} [a]**
	6.38	4.30×10^{-9}	5.94×10^{-7}	
	6.63	7.75×10^{-9}	6.60×10^{-7}	
0.25	6.85	1.27×10^{-8}	6.17×10^{-7}	1.04×10^{2}
	7.43	4.83×10^{-8}	6.54×10^{-6}	
	8.12	2.37×10^{-7}	2.45×10^{-5}	

(a) The second-order rate constant, k_{DO}, was obtained from the slope of the plot of k_{ex} against [DO$^-$] in Figure s24.

1,3-Bis(*t*-butyl)imidazolium chloride $1H^+i–Cl^-$

Figure s25: Representative ^1H NMR spectra at 300 MHz of imidazolium salt **$1H^+i–Cl^-$** (5 mM, pD 7.96), obtained during exchange of the C2-H (s, 8.63 ppm) for deuterium in 250 mM phosphate buffer solution (70% f_B) in D_2O at 25 ºC and I = 1.0 (KCl). [Internal standard, tetramethylammonium deuteriosulfate (s, 3.17 ppm)]

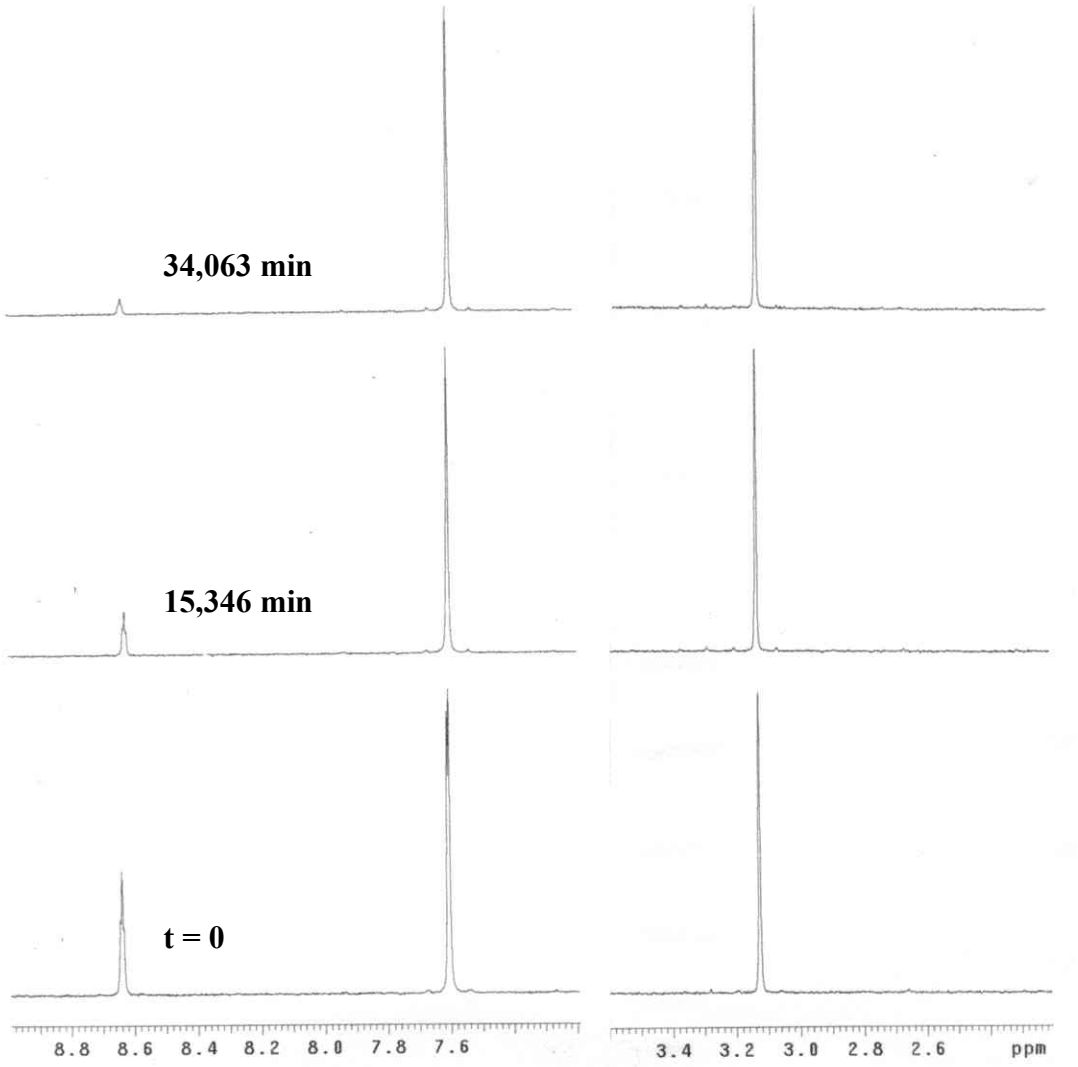


Figure s26. Semilogarithmic plots of the fraction of unexchanged substrate against time for the deuterium exchange reaction of **1H$^+$i–Cl$^-$** in 100 mM quinuclidinone buffers (a) and 250 mM phosphate buffers (b) in D_2O at 25 ºC and I = 1.0 (KCl).

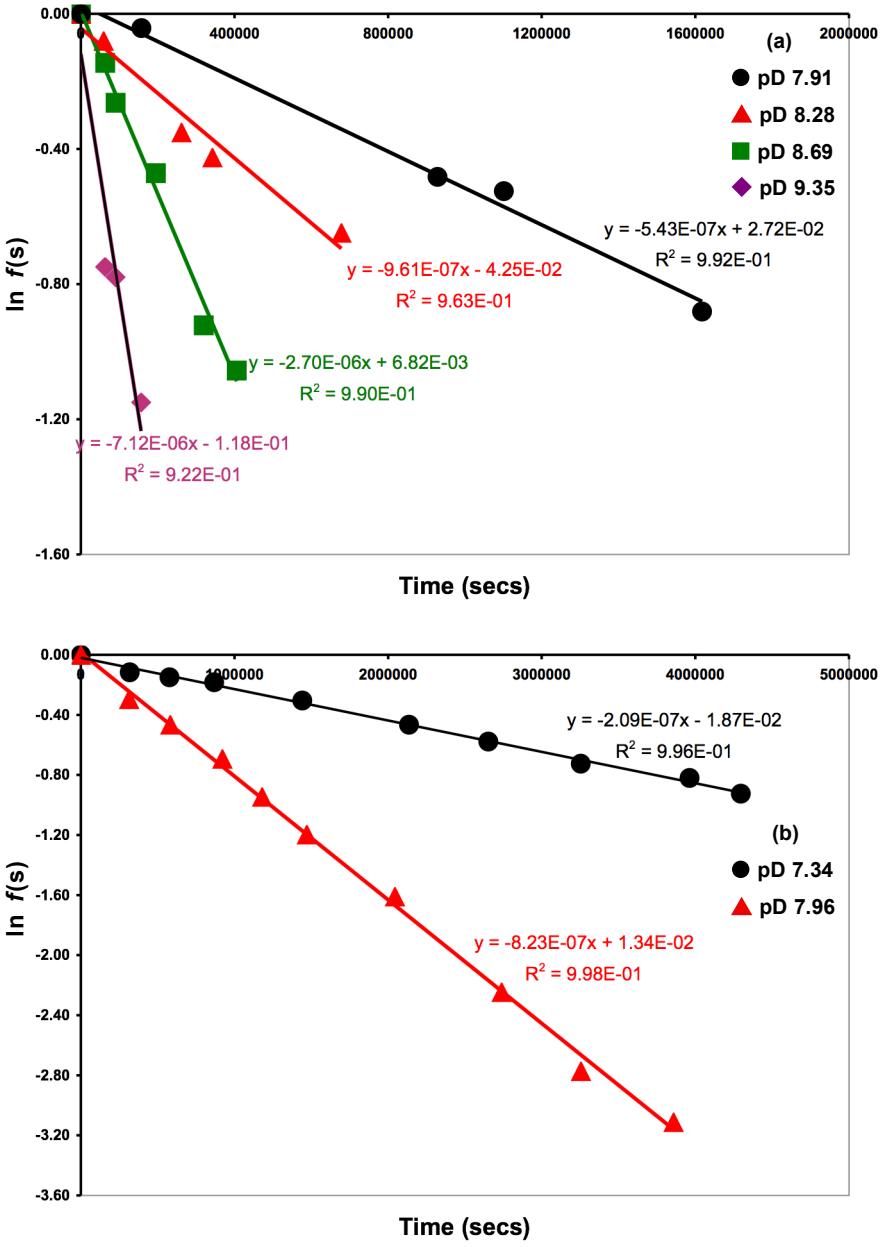


Figure s27: Plot of k_{ex} against [DO^-] for the H/D exchange reaction of imidazolium salt **1H$^+$i–Cl$^-$** in quinuclidinone and phosphate buffers in D_2O at 25 ºC and I = 1.0 (KCl).

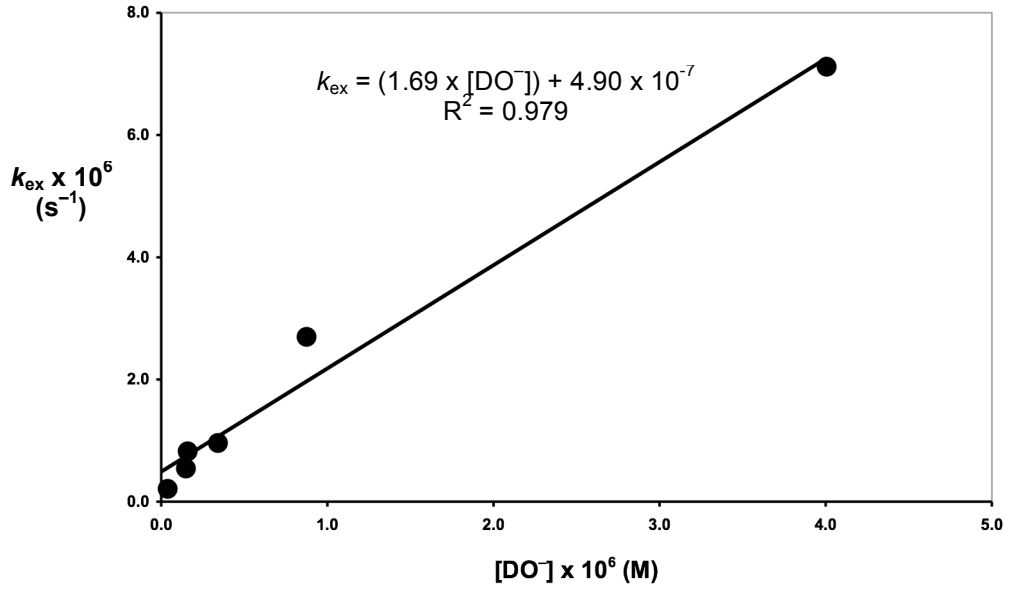


Table s9: First and second-order rate constants for exchange of the C2-H of imidazolium salt **1H$^+$i–Cl$^-$** for deuterium in quinuclidinone and phosphate buffers in D_2O at 25 ºC and I = 1.0 (KCl).

[Buffer]$_{total}$, M	pD	[DO^-], M	k_{ex}, s^{-1}	k_{DO}, $M^{-1}s^{-1}$ [c]
	7.91	1.48×10^{-7}	5.43×10^{-7}	
	8.28	3.42×10^{-7}	9.61×10^{-7}	
0.10 [a]	8.69	8.74×10^{-7}	2.70×10^{-6}	
	9.35	4.01×10^{-6}	7.12×10^{-6}	
				1.69
0.25 [b]	7.34	3.86×10^{-8}	2.09×10^{-7}	
	7.96	1.59×10^{-7}	8.23×10^{-7}	

(a) Quinuclidinone buffer. (b) Phosphate buffer. (c) The second-order rate constant, k_{DO}, was obtained from the slope of the plot of k_{ex} against [DO^-] in Fig s27.

1,3-Bis(adamantyl)imidazolium chloride $1H^+j–Cl^–$

Figure s28: Representative ^1H NMR spectra at 300 MHz of imidazolium salt **$1H^+j–Cl^–$** (5 mM, 4.23×10^{-3} M KOD), obtained during exchange of the C2-H (s, 8.68 ppm) for deuterium in D_2O at 25 ºC and I = 1.0 (KCl). [Internal standard, tetramethylammonium deuteriosulfate (s, 3.18 ppm)]

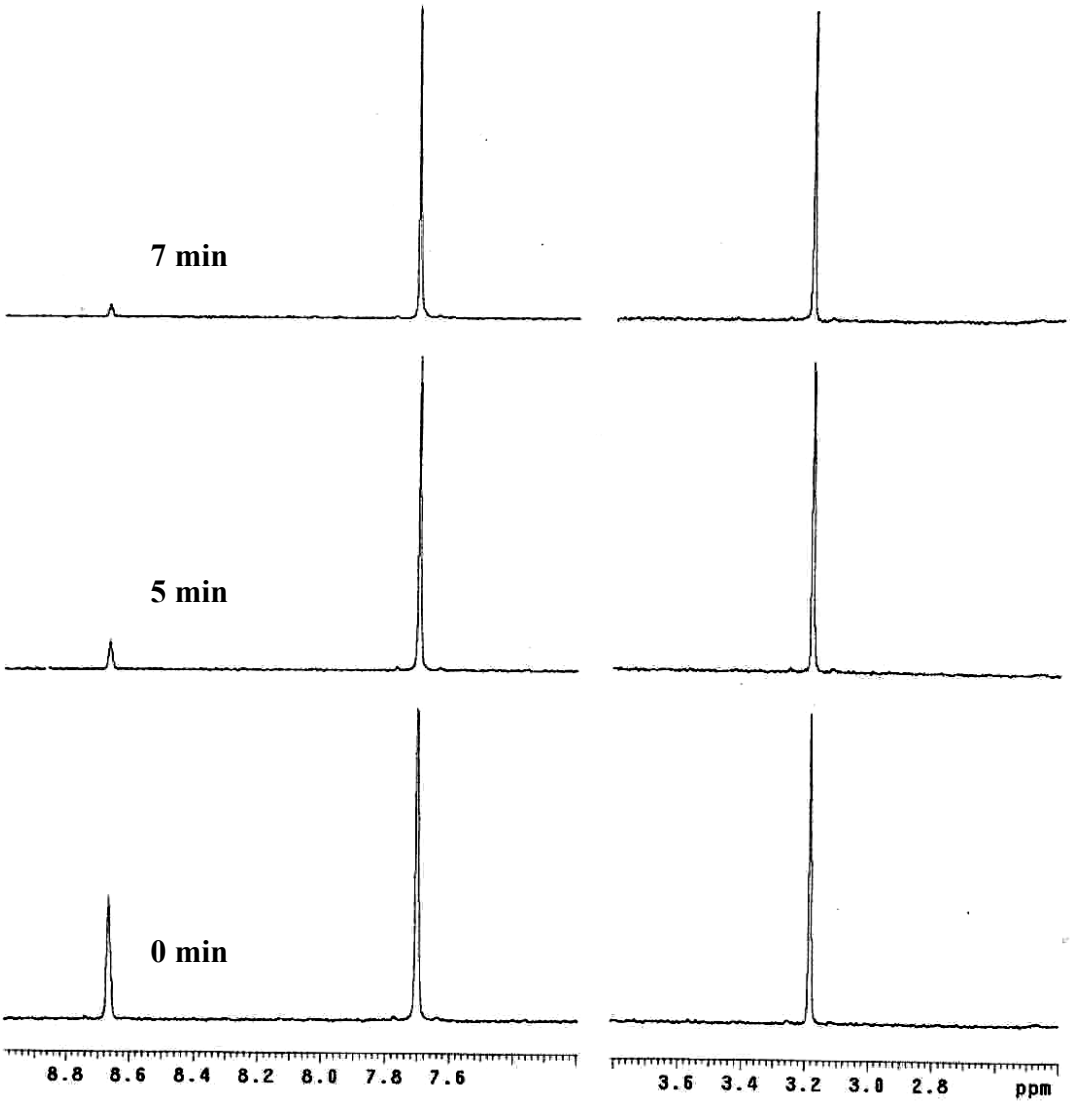


Figure s29. Semilogarithmic plots of the fraction of unexchanged substrate against time for the deuterium exchange reaction of **1H$^+$j–Cl$^-$** in KOD solution (● 2.11×10^{-3} M, ▲ 4.23×10^{-3} M, ■ 8.45×10^{-3} M) in D_2O at 25 ºC and I = 1.0 (KCl).

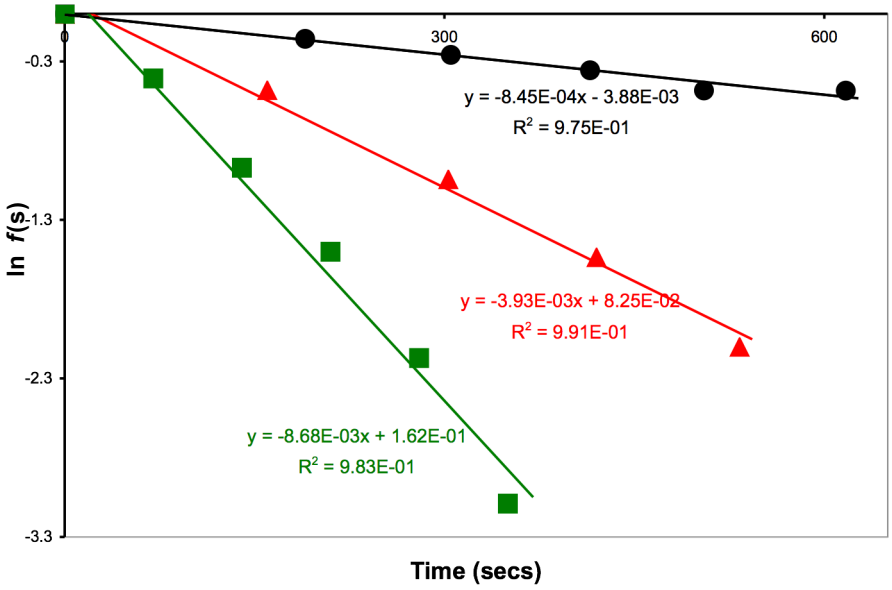


Figure s30 Semilogarithmic plots of the fraction of unexchanged substrate against time for the deuterium exchange reaction of **1H$^+$j–Cl$^-$** in phosphate buffer (pD 7.96) at 25 ºC and I = 1.0 (KCl).

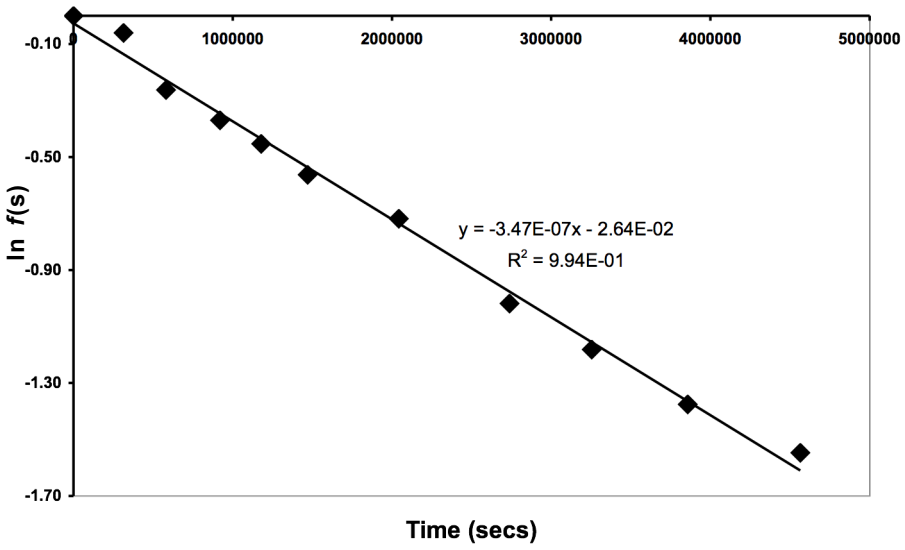


Figure s31: Plot of k_{ex} against [DO^-] for the H/D exchange reaction of imidazolium salt **1H$^+$j–Cl$^-$** in 250 mM phosphate buffer (pD 7.96) and in KOD solution in D_2O at 25 ºC and I = 1.0 (KCl).

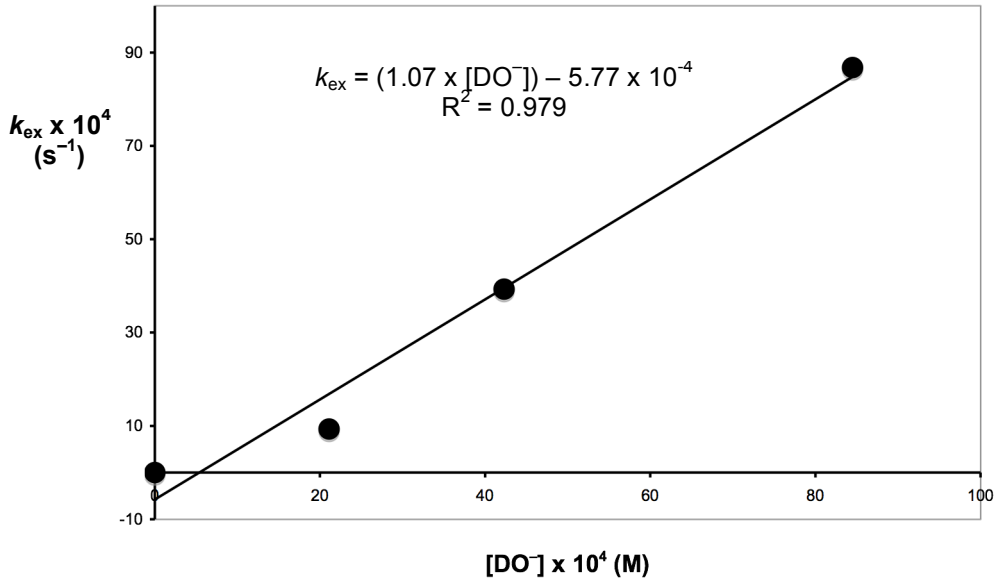


Table s10: First and second-order rate constants for exchange of the C2-H of imidazolium salt **1H$^+$j–Cl$^-$** for deuterium in 250 mM phosphate buffer (pD 7.96) and in KOD solution in D_2O at 25 ºC and I = 1.0 (KCl).

[DO^-],M	k_{ex}, s^{-1}	k_{DO}, $M^{-1}s^{-1}$ [a]
1.59×10^{-7}	3.47×10^{-7}	1.07
2.11×10^{-3}	8.45×10^{-4}	
4.23×10^{-3}	3.93×10^{-3}	
8.45×10^{-3}	8.68×10^{-3}	

(a)The second-order rate constant, k_{DO}, was obtained from the slope of the plot of k_{ex} against [DO^-] in Fig s31.

1,3-Bis(4-methoxyphenyl)-4,5-dihydroimidazolium chloride $2H^+b–Cl^–$

Figure s32: Representative ^1H NMR spectra at 500 MHz of imidazolium salt **$2H^+b–Cl^–$** (0.1 mM, pD 5.41), obtained during exchange of the C2-H (s, 9.14 ppm) for deuterium in 100 mM acetic acid buffer solution (70% f_B) in D_2O at 25 ºC and I = 0.25 (KCl) [Internal standard, tetramethylammonium deuteriosulfate (s, 3.13 ppm; CH_3)]

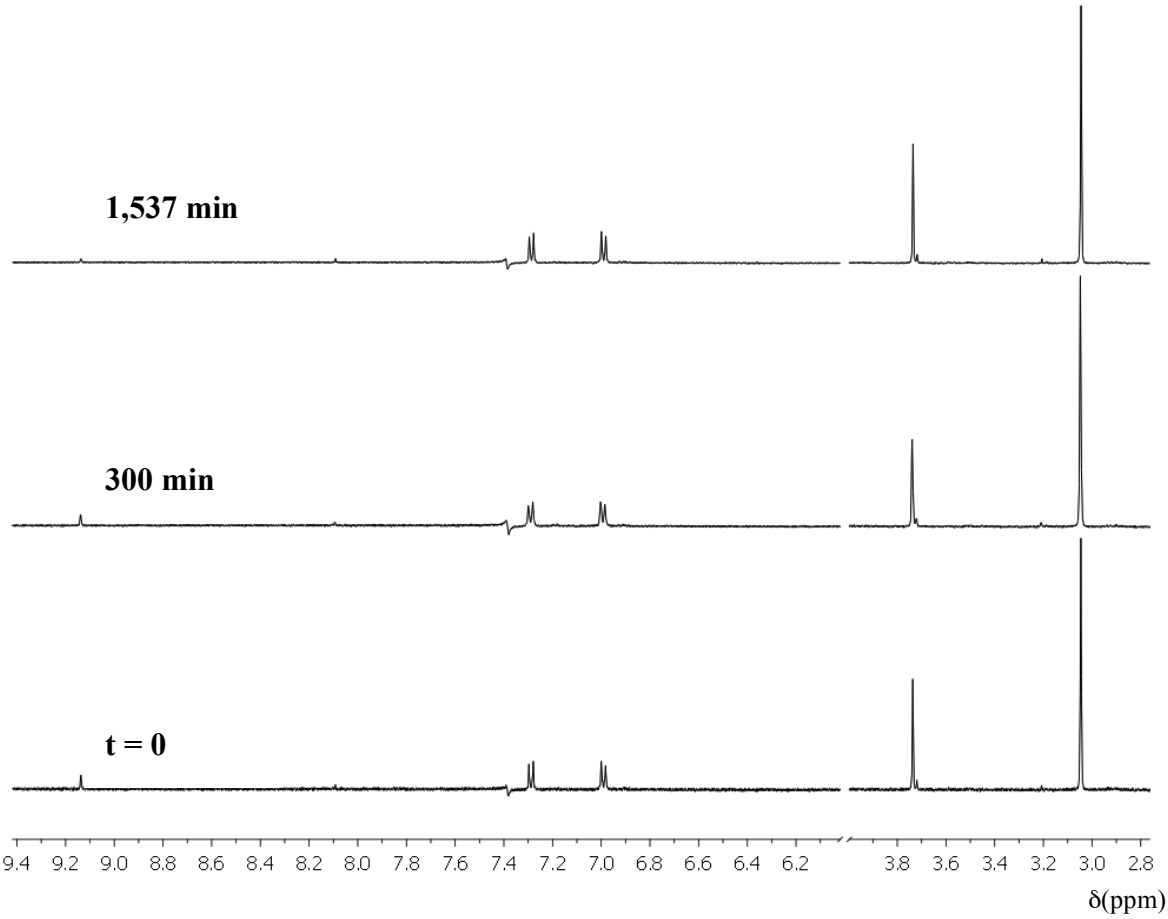


Figure s33. Semilogarithmic plots of the fraction of unexchanged substrate against time for the deuterium exchange reaction of **2H$^+$b–Cl$^-$** in 100 mM acetic acid buffers in D_2O at 25 ºC and I = 0.25 (KCl).

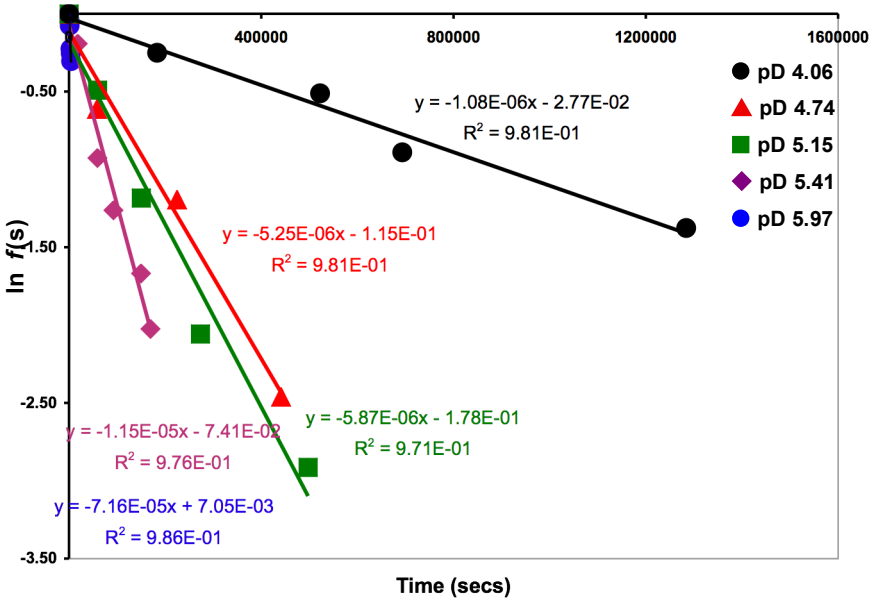


Figure s34: Plot of k_{ex} against [DO^-] for the H/D exchange reaction of imidazolium salt **2H$^+$b–Cl$^-$** in 100 mM acetic acid buffers in D_2O at 25 ºC and I = 0.25 (KCl).

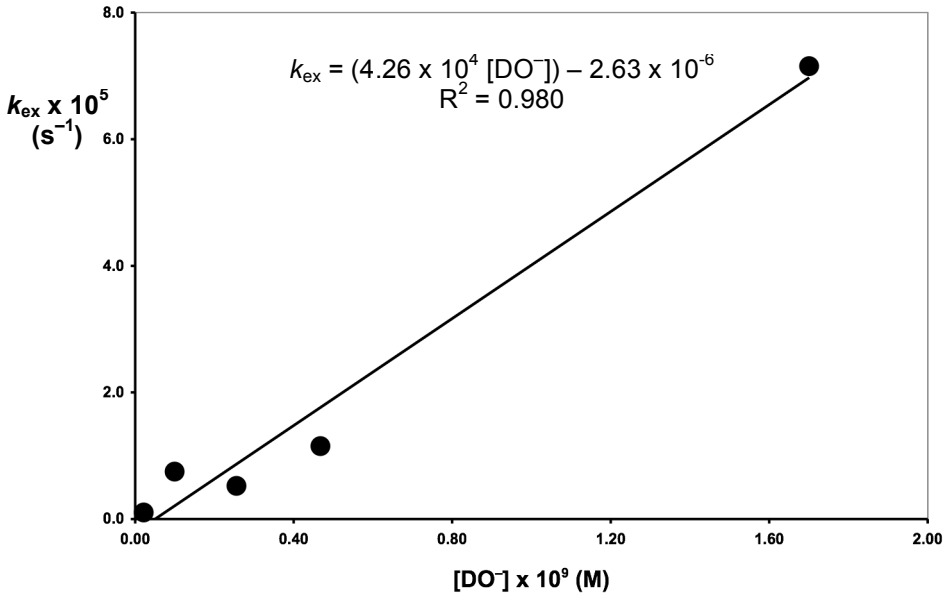


Table s11: First and second-order rate constants for exchange of the C2-H of 4,5-dihydroimidazolium salt **$2H^+$b–Cl–** for deuterium in 100 mM acetic acid buffers in D_2O at 25 ºC and I = 0.25 (KCl).

$[Buffer]_{total}$, M	**pD**	**$[DO^-]$, M**	**k_{ex}, s^{-1}**	**k_{DO}, $M^{-1}s^{-1}$ a**
0.10	4.06	2.09×10^{-11}	1.08×10^{-6}	4.26×10^4
	4.74	9.95×10^{-11}	5.25×10^{-6}	
	5.15	2.56×10^{-10}	5.87×10^{-6}	
	5.41	4.67×10^{-10}	1.15×10^{-5}	
	5.97	1.70×10^{-9}	7.16×10^{-5}	

(a) The second-order rate constant, k_{DO}, was obtained from the slope of the plot of k_{ex} against $[DO^-]$ in Figure s34.

1,3-Bis(2,4,6-trimethylphenyl)-4,5-dihydroimidazolium chloride $2H^+c–Cl^–$

Figure s35: Representative ^1H NMR spectra at 500 MHz of imidazolium salt **$2H^+c–Cl^–$** (5 mM, pD 7.91), obtained during exchange of the C2-H (s, 8.55 ppm) for deuterium in 100 mM phosphate buffer solution (90% f_B) in D_2O at 25 ºC and I = 1.0 (KCl). [Internal standard, tetramethylammonium deuteriosulfate (s, 3.13 ppm; CH_3)]

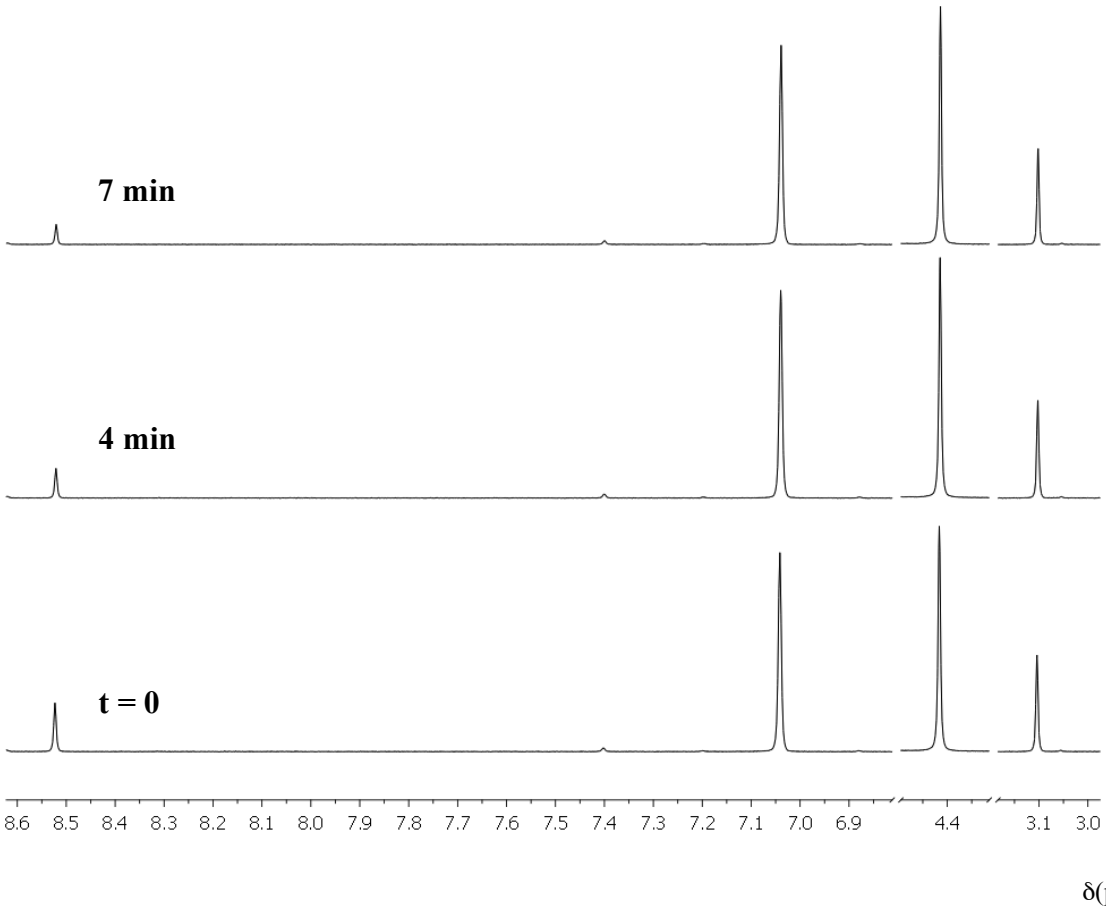


Figure s36. Semilogarithmic plots of the fraction of unexchanged substrate against time for the deuterium exchange reaction of **2H$^+$c–Cl$^-$** in 100 mM phosphate buffers in D_2O at 25 ºC and I = 1.0 (KCl).

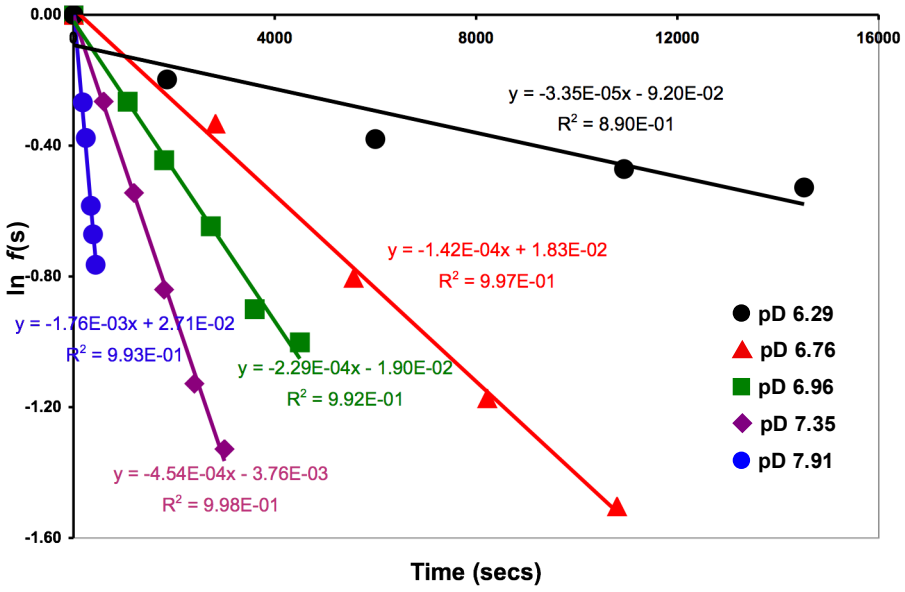


Figure s37: Plot of k_{ex} against [DO$^-$] for the H/D exchange reaction of imidazolium salt **2H$^+$c–Cl$^-$** in 100 mM phosphate buffers in D_2O at 25 ºC and I = 1.0 (KCl).

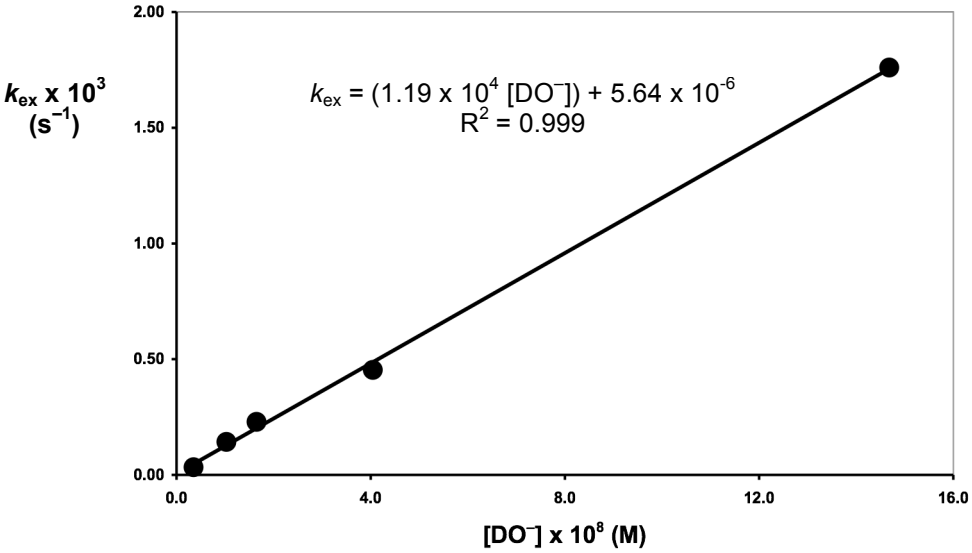


Table s12: First and second-order rate constants for exchange of the C2-H of 4,5-dihydroimidazolium salt **$2H^{+}c–Cl^{-}$** for deuterium in phosphate buffers in D_2O at 25 ºC and I = 1.0 (KCl).

$[Buffer]_{total}$, M	**pD**	**$[DO^{-}]$, M**	**k_{ex} , s^{-1}**	**k_{DO} , $M^{-1}s^{-1}$** [a]
0.10	6.29	1.65×10^{-8}	3.35×10^{-5}	1.19×10^{4}
	6.76	4.08×10^{-8}	1.42×10^{-4}	
	6.96	1.03×10^{-7}	2.29×10^{-4}	
	7.35	1.45×10^{-7}	4.54×10^{-4}	
	7.91	3.51×10^{-7}	1.76×10^{-3}	

(a) The second-order rate constant, k_{DO}, was obtained from the slope of the plot of k_{ex} against $[DO^{-}]$ in Figure s37.

1,3-Bis(di-(*i*-propyl)phenyl)-4,5-dihydroimidazolium chloride $2H^+d–Cl^-$

Figure s38: Representative ^1H NMR spectra at 500 MHz of imidazolium salt **$2H^+d–Cl^-$** (2.5 mM, pD 7.36), obtained during exchange of the C2-H (s, 9.01 ppm) for deuterium in 100 mM phosphate buffer solution (70% f_B) in D_2O at 25 ºC and I = 1.0 (KCl). [Internal standard, tetramethylammonium deuteriosulfate (s, 3.13 ppm; CH_3)]

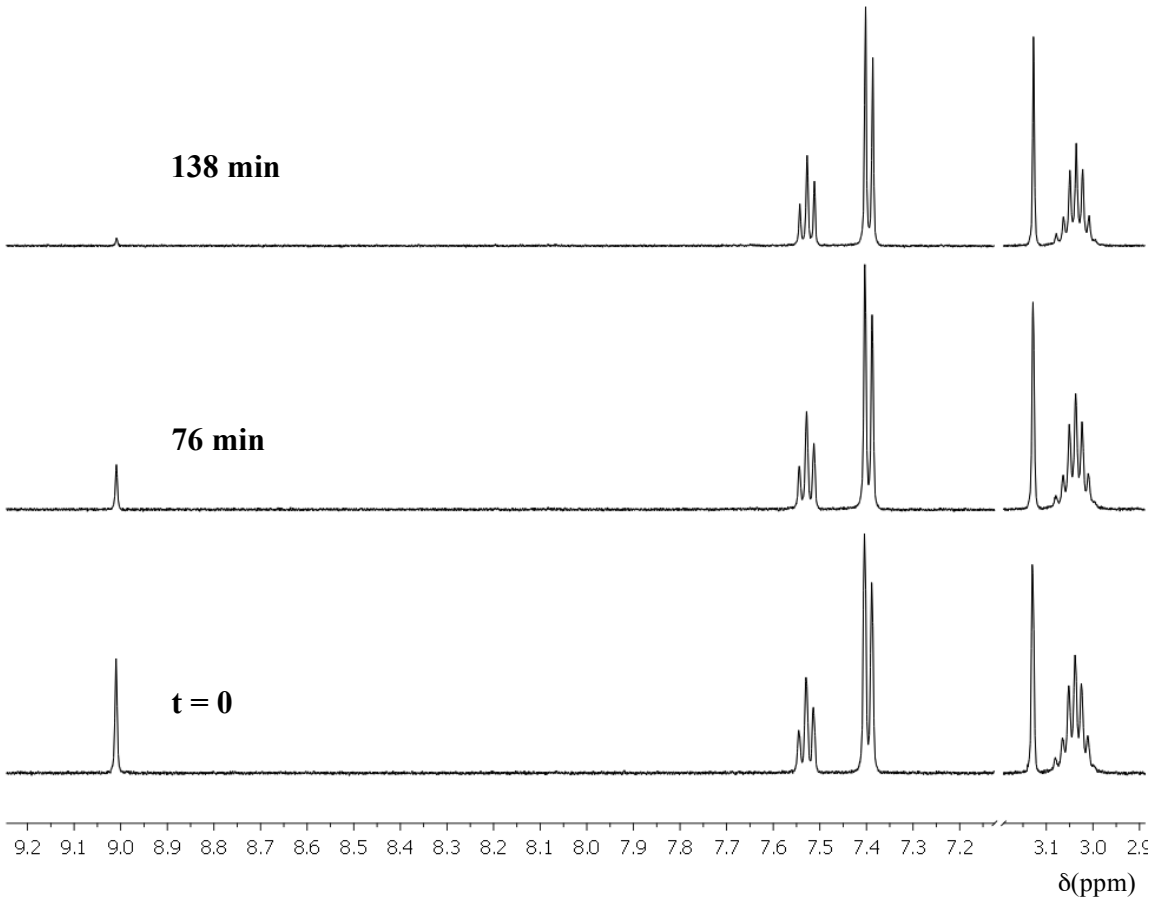


Figure s39. Semilogarithmic plots of the fraction of unexchanged substrate against time for the deuterium exchange reaction of **$2H^+d–Cl^-$** in 100 mM phosphate buffers in D_2O at 25 ºC and I = 1.0 (KCl).

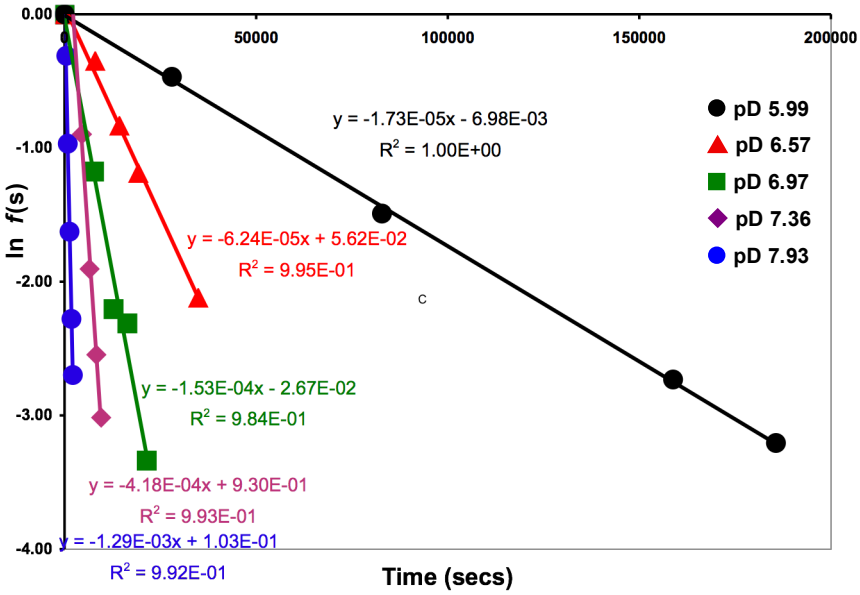


Figure s40: Plot of k_{ex} against [DO^-] for the H/D exchange reaction of imidazolium salt **$2H^+d–Cl^–$** in 100 mM phosphate buffers in D_2O at 25 ºC and I = 1.0 (KCl).

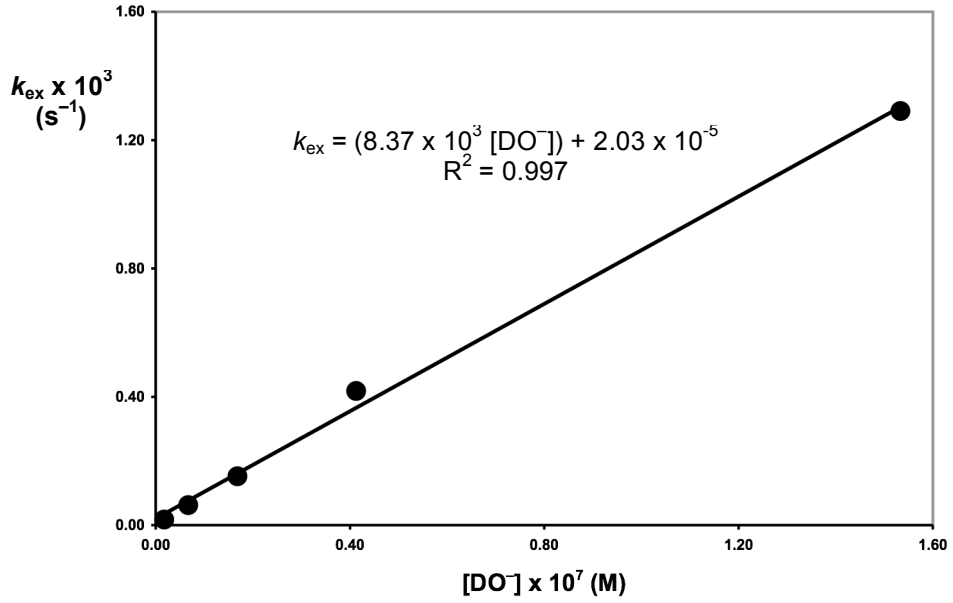


Table s13: First and second-order rate constants for exchange of the C2-H of 4,5-dihydroimidazolium salt **$2H^+d–Cl^–$** for deuterium in 100 mM phosphate buffers in D_2O at 25 ºC and I = 1.0 (KCl).

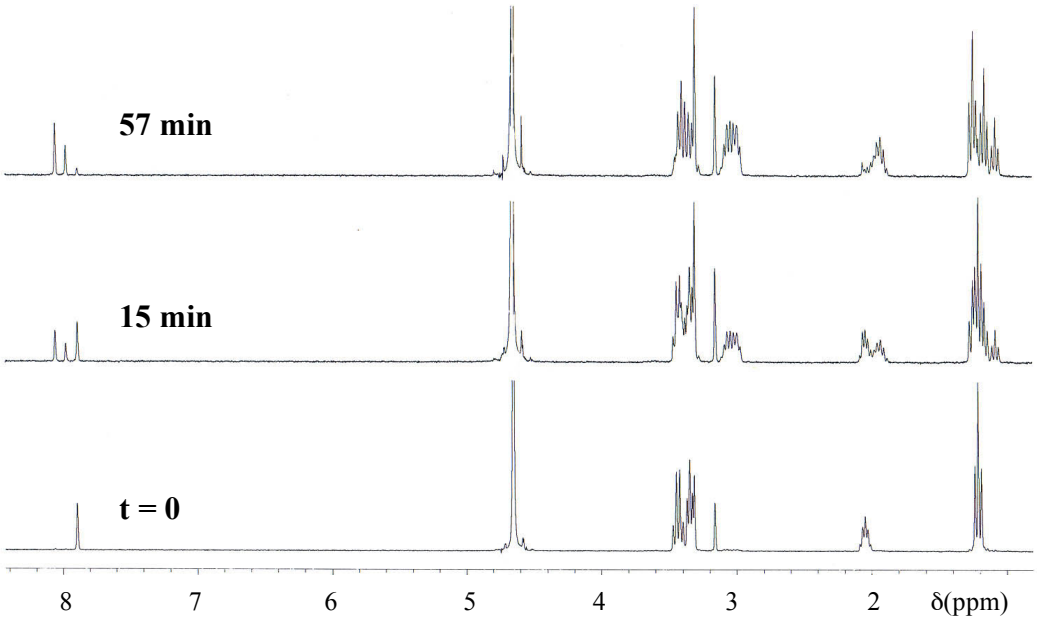
$[Buffer]_{total}$, M	**pD**	**$[DO^-]$, M**	**k_{ex} , s^{-1}**	**k_{DO} , $M^{-1}s^{-1}$** [a]
	5.99	1.75×10^{-9}	1.73×10^{-5}	
	6.57	6.69×10^{-9}	6.24×10^{-5}	
0.1	6.97	1.68×10^{-8}	1.53×10^{-4}	8.37×10^3
	7.36	4.13×10^{-8}	4.18×10^{-4}	
	7.93	1.53×10^{-7}	1.29×10^{-3}	

(a) The second-order rate constant, k_{DO}, was obtained from the slope of the plot of k_{ex} against [DO^-] in Figure s40.

1,3-Diethyl-3,4,5,6-tetrahydropyrimidin-1-ium hexafluorophosphate $3H^+k\text{-}PF_6^-$

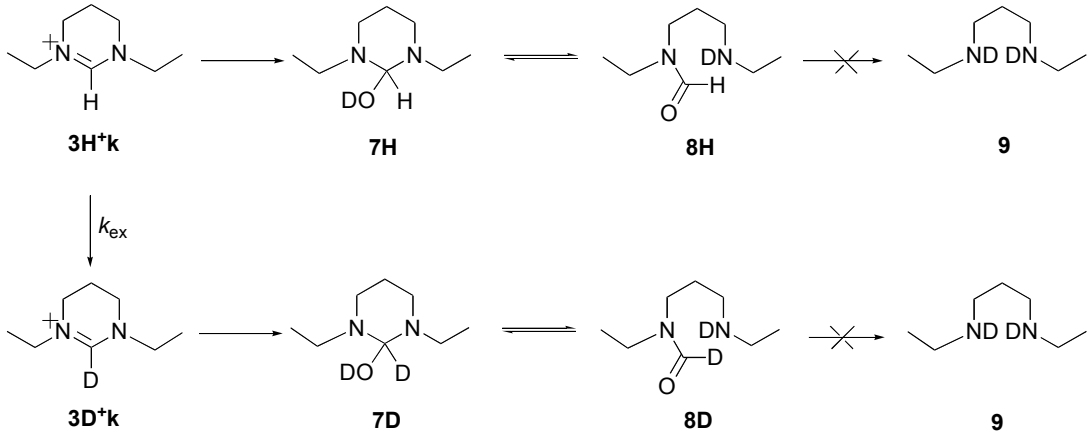
In this case a competing hydrolysis reaction at C2 occurred in parallel with deuterium exchange of the C2-H of tetrahydropyrimidinium salt **$3H^+k\text{-}PF_6^-$** (Figure (s41)). Reaction aliquots were quenched to pD 4 prior to ^{1}H NMR analysis.

Figure s41: Representative ^{1}H NMR spectra at 300 MHz of tetrahydropyrimidinium salt **$3H^+k\text{-}PF_6^-$** (5 mM), obtained during exchange of the C2-H (s, 7.89 ppm) for deuterium and competing hydrolysis in 0.05 M KOD in D_2O at 25 ºC and I = 1.0 (KCl). [Internal standard, tetramethylammonium deuteriosulfate (s, 3.18 ppm; CH_3)]



The peak due to the C2-H of **$3H^+k\text{-}PF_6^-$** appears as a singlet at 7.89 ppm. The signal due to the CH_2 protons of the *N*-ethyl substituents appear as a quartet at 3.41 ppm. The peak due to the C4-H_2 and C6-H_2 appears as a triplet at 3.31 ppm and that due to the C5-H_2 appears as a quintet at 2.05 ppm. Finally, the peak due to the methyl protons of the *N*-ethyl substituents appears as a triplet at 1.20 ppm. Decreases in peak areas due to all substrate hydrogens are observed over time relative to internal standard. Hydrolysis of tetrahydropyrimidinium salt **$3H^+k\text{-}PF_6^-$** and, also potentially, 2-deuterated exchange product **$3D^+k\text{-}PF_6^-$** would result in formation of formamide **(8-H)** and **(8-D)** respectively. H/D-exchange is not expected to occur at C1 of formamide **(8-H)** as exchange of this hydrogen for deuterium is significantly slower than of the C2-H of tetrahydropyrimidinium salt **$3H^+k\text{-}PF_6^-$** under these conditions.

The decay of the singlet at 7.89 ppm is accompanied by the increase in two new singlets at 7.97 and 8.07 ppm. Integration shows that the relative areas of these two new singlets remain constant over the timescale of the reaction. This could be due to the formation of two different products at fixed relative rates. From the NMR spectral changes over time it is clear that further hydrolysis of formamide derivative **(8-H/D)** to formate and diamine **(9)** is not occurring on the timescale of the reaction, and, in any case, this would be a sequential rather than a parallel reaction. The appearance of the two new singlets at at 7.97 and 8.07 ppm is most likely due to the formation of one product which is in rapid equilibrium with a second product over the timescale of the reaction (however slow interconversion on the NMR timescale so that the two species give separate distinct peaks). This is consistent with a hydrolysis reaction to yield an initial hemiaminal adduct **(7-H)** in rapid equilibrium with formamide derivative **(8-H)**. The two new singlets at 7.97 and 8.07 ppm can be assigned to the C2-H of aminal **(7-H)** and the C1-H of formamide derivative **(8-H)**. Another option is a rapid equilibrium between formamide **(8-H)** and a hydrate adduct, however this is unlikely as *N*,*N*-dimethylformamide is unhydrated in D_2O solution.



In order to distinguish the exchange and hydrolysis reactions, it is necessary to determine the area of one hydrogen of H-hydrolysis product only. The chemical shift of the peaks due to ring methylene hydrogens and hydrogens on the *N*-ethyl substituent will not be altered by a switch from H to D at C2 or C1 of either **(7)** or **(8)**. Thus peaks for these hydrogens cannot be used to quantify H-hydrolysis product only. To quantify H-hydrolysis product we assume that the sum of the areas of the two singlets at 7.97 and 8.07 ppm are due to one hydrogen. Addition of the total area of these two new singlets at a given timepoint to the remaining area of the singlet due to

the C2-H of reactant **3H$^+$k-PF$_6^-$** will permit the rate of disappearance of substrate due to exchange only to be estimated.

First order rate constants (k_{obs}, s^{-1}) for the overall disappearance of substrate due to both hydrolysis and exchange ($k_{obs} = k_{hyd} + k_{ex}$) could be determined from the slopes of semilogarithmic plots of the fraction of remaining substrate (f(s)) against time as described by equations (s1) and (s2) [plots not shown] where $A_{C(2)–H}$ is the area of the singlet due to the C2-H of tetrahydropyrimidinium salt **3H$^+$k-PF$_6^-$** at 7.89 ppm. The values for k_{ex} (s^{-1}) were obtained from the slopes of semilogarithmic plots of the fraction of remaining substrate against time with correction for the formation of hydrolysis product in this period (f(s)', equation (s4)). In equation (s4), $A_s^{7.97}$ and $A_s^{8.07}$ are the areas of the two singlets at 7.97 and 8.07 ppm.

$$f(s)' = \frac{(A_{C(2)–H}/A_{IS})_t}{(A_{C(2)–H}/A_{IS})_0} + \frac{(A_s^{7.97} + A_s^{8.07})/A_{IS})_t}{(A_{C(2)–H}/A_{IS})_0} \qquad (s4)$$

The values for k_{hyd} (s^{-1}) shown in Table s14 were calculated by subtraction of the rate constants for exchange only ((k_{ex}, s^{-1}) from those for overall disappearance of substrate (k_{obs}, s^{-1}).

Table s14: First-order rate constants for the C2-deprotonation and hydrolysis reactions of tetrahydropyrimidinium salt **3H$^+$k-PF$_6^-$** in deuteroxide solution in D_2O at 25° C, and ionic strength I = 1.0 (KCl).

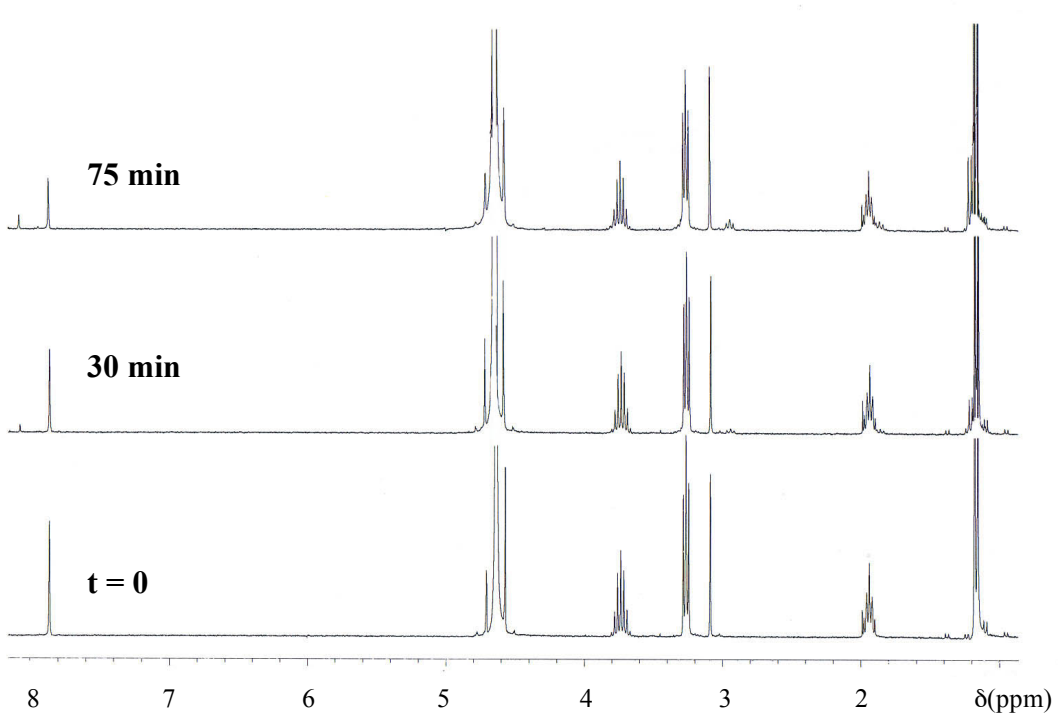
[DO$^-$], M	k_{obs}, s^{-1}	k_{ex}, s^{-1}	k_{hyd}, s^{-1}
0.050	6.73×10^{-4}	3.78×10^{-5}	6.36×10^{-4}
0.060	9.98×10^{-4}	5.62×10^{-5}	9.42×10^{-4}
0.070	1.40×10^{-3}	9.69×10^{-5}	1.31×10^{-3}
0.080	1.72×10^{-3}	1.53×10^{-4}	1.57×10^{-3}
0.090	1.93×10^{-3}	2.40×10^{-4}	1.69×10^{-3}
0.095	2.11×10^{-3}	1.31×10^{-4}	1.98×10^{-3}

Plots of the first order rate constants k_{ex} or k_{hyd}, against deuteroxide concentration were linear with slopes equivalent to k_{DO} and k_{HYD}, the second order rate constants for deuteroxide catalysed exchange and hydrolysis, respectively. Values of $k_{DO} = 3.48 \times 10^{-3}$ ($M^{-1}s^{-1}$) and $k_{HYD} = 2.83 \times 10^{-2}$ ($M^{-1}s^{-1}$) were obtained as the slopes of these linear correlations.

1,3-Di-(*i*-propyl)-3,4,5,6-tetrahydropyrimidinium hexafluorophosphate $3H^+$l-PF_6^-

As for tetrahydropyrimidinium salt **$3H^+$k-PF_6**, a competing hydrolysis reaction was also observed in parallel with C2 H/D exchange in the case of 1,3-Di-(*i*-propyl)-3,4,5,6-tetrahydropyrimidinium hexafluorophosphate **$3H^+$l-PF_6** (Figure s42). In this case the exchange reaction is 6-fold faster than the hydrolysis reaction.

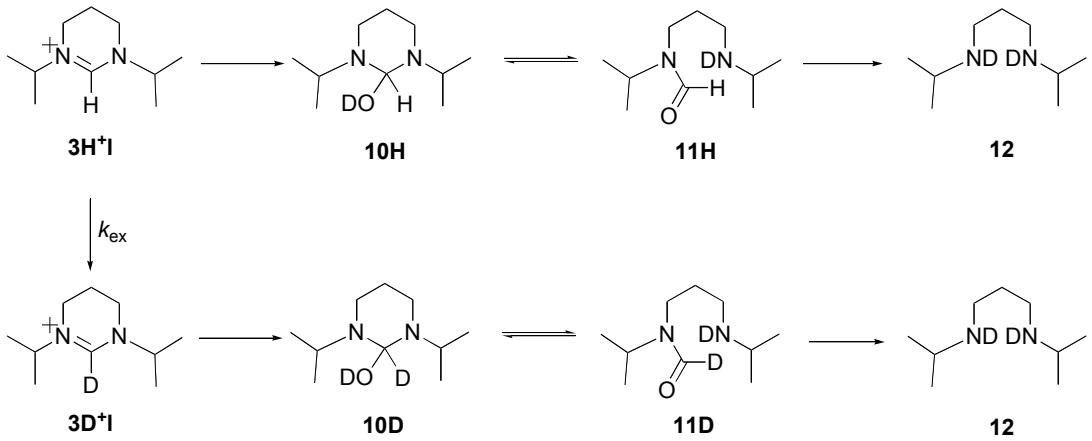
Figure s42: Representative ^{1}H NMR spectra at 300 MHz of tetrahydropyrimidinium salt **$3H^+$l-PF_6^-** (5 mM), obtained during exchange of the C2-H (s, 7.88 ppm) for deuterium and competing hydrolysis in 0.12 M KOD in D_2O at 25 ºC and I = 1.0 (KCl). [Internal standard, tetramethylammonium deuteriosulfate (s, 3.18 ppm; CH_3)]



The peak due to the C2-H of **$3H^+$k-PF_6^-** appears as a singlet at 7.88 ppm. The signal due to the two methinyl hydrogens of the *N*-*i*-propyl substituents appears as a septet at 3.70 ppm. The peak due to the C4-H_2 and C6-H_2 appears as a triplet at 3.27 ppm and that due to the C5-H_2 appears as a quintet at 1.90 ppm. Finally, the peak due to the methyl protons of the *N*-*i*-propyl substituents appears as a doublet at 1.20 ppm. Decreases in peak areas due to all substrate hydrogens are observed over time relative to internal standard.

Reaction aliquots were quenched to pD 4 prior to ^{1}H NMR analysis. Hydrolysis of tetrahydropyrimidinium salt **3H$^+$l-PF$_6^-$** and, also potentially, 2-deuterated exchange product **3D$^+$l-PF$_6^-$** would result in formation of formamide **11-H** and **11-D** respectively. H/D-exchange is not expected to occur at C1 of formamide **(11-H)** as exchange of the C1-H for deuterium is significantly slower than of the C2-H of tetrahydropyrimidinium salt **3H$^+$l-PF$_6^-$**.

The decay of the singlet at 7.88 ppm is accompanied by the increase in a new singlet at 8.10 ppm due to the C1-H of formamide derivative **11-H**, which has been confirmed by mass spectrometry (spectra not shown). From the NMR spectral changes over time it is clear that further hydrolysis of formamide derivative **11-H/D** to formate and diamine **(12)** is not occurring on the timescale of the reaction. Hydrolysis would initially yield a hemiaminal adduct **10-H/D**, however, in this case the equilibrium lies essentially completely towards formamide **11-H/D** likely due to steric hindrance at the hemiaminal by the bulky isopropyl groups.



To quantify H-hydrolysis product we assume that the area of the singlet at 8.10 ppm is due to one hydrogen. Addition of the area of this singlet at a given timepoint to the remaining area of the singlet due to the C2-H of reactant **3H$^+$l-PF$_6^-$** will permit the rate of disappearance of substrate due to exchange only to be estimated.

The reaction data was treated in a similar manner as for tetrahydropyrimidinium salt **3H$^+$k-PF$_6^-$.** First order rate constants (k_{obs}, s^{-1}) for the overall disappearance of substrate due to both hydrolysis and exchange ($k_{obs} = k_{hyd} + k_{ex}$) could be determined from the slopes of semilogarithmic plots of the fraction of remaining substrate (f(s)) against time as described by equations (s1) and (s2) [plots not shown] where $A_{C(2)–H}$ is

the area of the singlet due to the C2-H of trihydropyrimidinium salt **3H$^+$l-PF$_6^-$**. The values for k_{ex} (s^{-1}) were obtained from the slopes of semilogarithmic plots of the fraction of remaining substrate against time with correction for the formation of hydrolysis product in this period (f(s)', equation (s5)). In equation (s5), $A_s^{8.10}$ is the area of the new singlet that appears at 8.10 ppm.

$$f(s)' = \frac{(A_{C(2)-H}/A_{IS})_t}{(A_{C(2)-H}/A_{IS})_0} + \frac{(A_s^{8.10})/A_{IS})_t}{(A_{C(2)-H}/A_{IS})_0} \qquad (s5)$$

The values for k_{hyd} (s^{-1}) shown in Table s15 were calculated by subtraction of the rate constants for exchange only ((k_{ex}, s^{-1}) from those for overall disappearance of substrate (k_{obs}, s^{-1}).

Table s15: First-order rate constants for the C2-deprotonation and hydrolysis reactions of trihydropyrimidinium salt **3H$^+$l-PF$_6$** in deuteroxide solution in D_2O at 25° C, and ionic strength I = 1.0 (KCl).

[DO$^-$], M	**k_{obs}, s^{-1}**	**k_{ex}, s^{-1}**	**k_{hyd}, s^{-1}**
0.060	6.79×10^{-5}	5.11×10^{-5}	1.68×10^{-5}
0.070	7.94×10^{-5}	5.86×10^{-5}	2.07×10^{-5}
0.080	9.53×10^{-5}	6.47×10^{-5}	3.06×10^{-5}
0.090	1.03×10^{-4}	8.92×10^{-5}	1.34×10^{-5}
0.095	1.20×10^{-4}	9.04×10^{-5}	2.97×10^{-5}
0.100	1.44×10^{-4}	1.04×10^{-4}	3.94×10^{-5}
0.120	1.84×10^{-4}	1.32×10^{-4}	5.13×10^{-5}
0.140	2.10×10^{-4}	1.65×10^{-4}	4.56×10^{-5}

Plots of the first order rate constants k_{ex} or k_{hyd}, against deuteroxide concentration were linear with slopes equivalent to k_{DO} and k_{HYD}, the second order rate constants for deuteroxide catalysed exchange and hydrolysis, respectively. Values of $k_{DO} = 1.48 \times 10^{-3}$ ($M^{-1}s^{-1}$) and $k_{HYD} = 2.21 \times 10^{-4}$ ($M^{-1}s^{-1}$) were obtained as the slopes of these linear correlations.

1,1'-Dimethyl-3,3'-methylene-diimidazolium diiodide $4H^+m–2I^–$

Figure s43: Representative ^{1}H NMR spectra at 300 MHz of imidazolium salt **$4H^+m–2I^–$** (10 mM, pD 5.03), obtained during exchange of the C2-H (s, 9.13 ppm) for deuterium in 100 mM acetic acid buffer solution (50% f_B) in D_2O at 25 ºC and I = 1.0 (KCl). [Internal standard, tetramethylammonium deuteriosulfate (s, 3.09 ppm)]

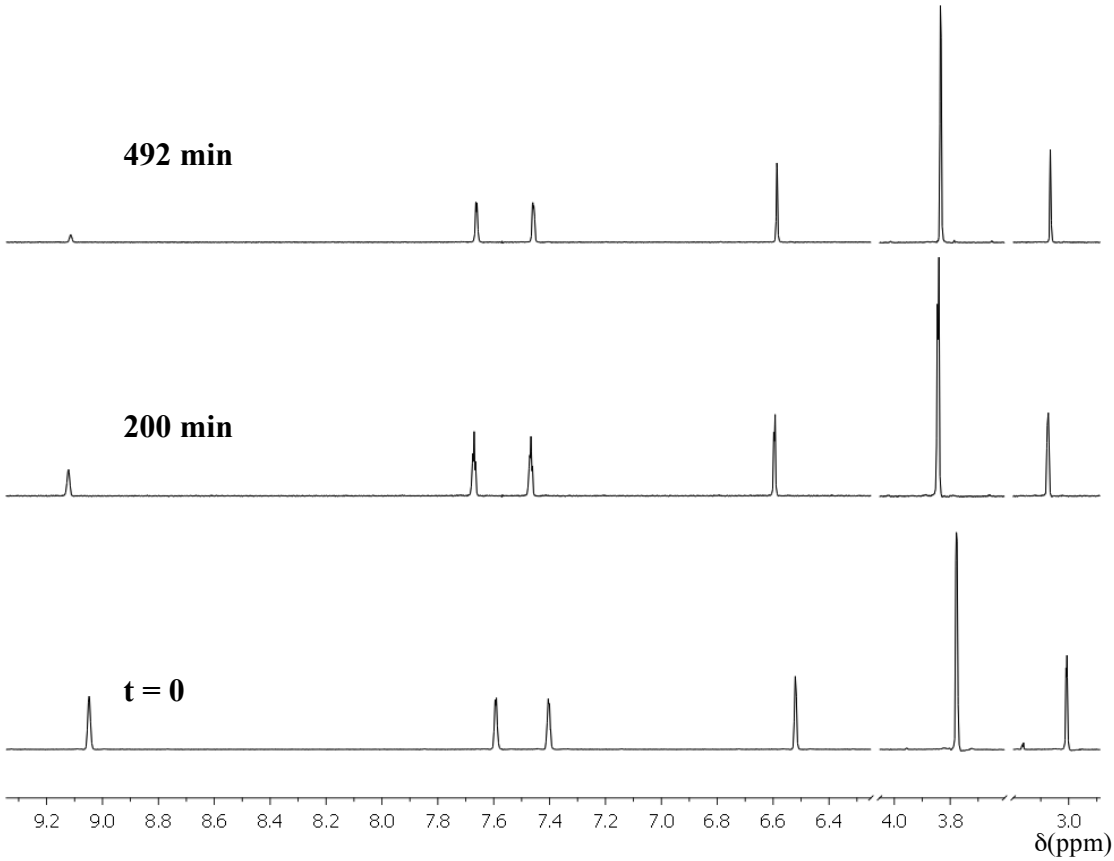


Figure s44: Semilogarithmic plots of the fraction of unexchanged substrate against time for the deuterium exchange reaction of **4H$^+$m–2I$^-$** in 100 mM acetic acid buffers in D_2O at 25 ºC and I = 1.0 (KCl).

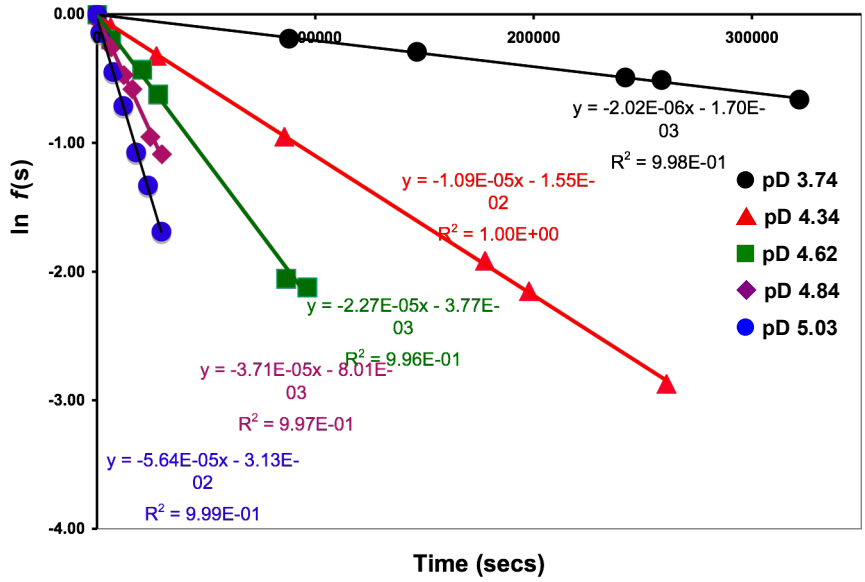


Figure s45: Plot of k_{ex} against [DO^-] for the H/D exchange reaction of imidazolium salt **4H$^+$m–2I$^-$** in 100 mM acetic acid buffers in D_2O at 25 ºC and I = 1.0 (KCl).

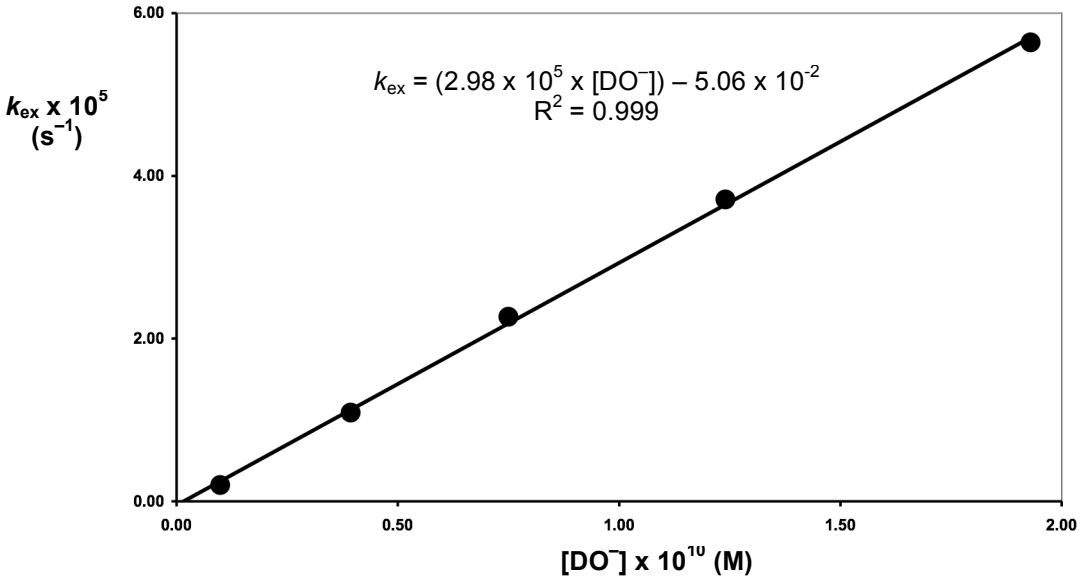


Table s16: First and second-order rate constants for exchange of the C2-H of imidazolium salt **4H$^+$m–2I$^-$** for deuterium in acetic acid buffers in D_2O at 25 ºC and I = 1.0 (KCl).

[Buffer]$_{total}$, M	**pD**	**[DO$^-$], M**	**k_{ex}, s^{-1}**	**k_{DO}, M^{-1}s^{-1} [a]**
	3.74	9.88×10^{-12}	2.02×10^{-6}	
	4.34	3.93×10^{-11}	1.09×10^{-5}	
0.1	4.62	7.50×10^{-11}	2.27×10^{-5}	2.98×10^{5}
	4.84	1.24×10^{-10}	3.71×10^{-5}	
	5.03	1.93×10^{-10}	5.64×10^{-5}	

(a) The second-order rate constant, k_{DO}, was obtained from the slope of the plot of k_{ex} against [DO$^-$] in Figure s45.

1,1'-Dimethyl-3,3'-(1,2-ethylene)-diimidazolium diiodide $4H^+n–2I^–$

Figure s46: Representative ^{1}H NMR spectra at 300 MHz of imidazolium salt **$4H^+n–2I^–$** (10 mM, pD 5.94), obtained during exchange of the C2-H (s, 8.71 ppm) for deuterium in 100 mM acetic acid buffer solution (90% f_B) in D_2O at 25 ºC and I = 1.0 (KCl). [Internal standard, tetramethylammonium deuteriosulfate (s, 3.09 ppm)]

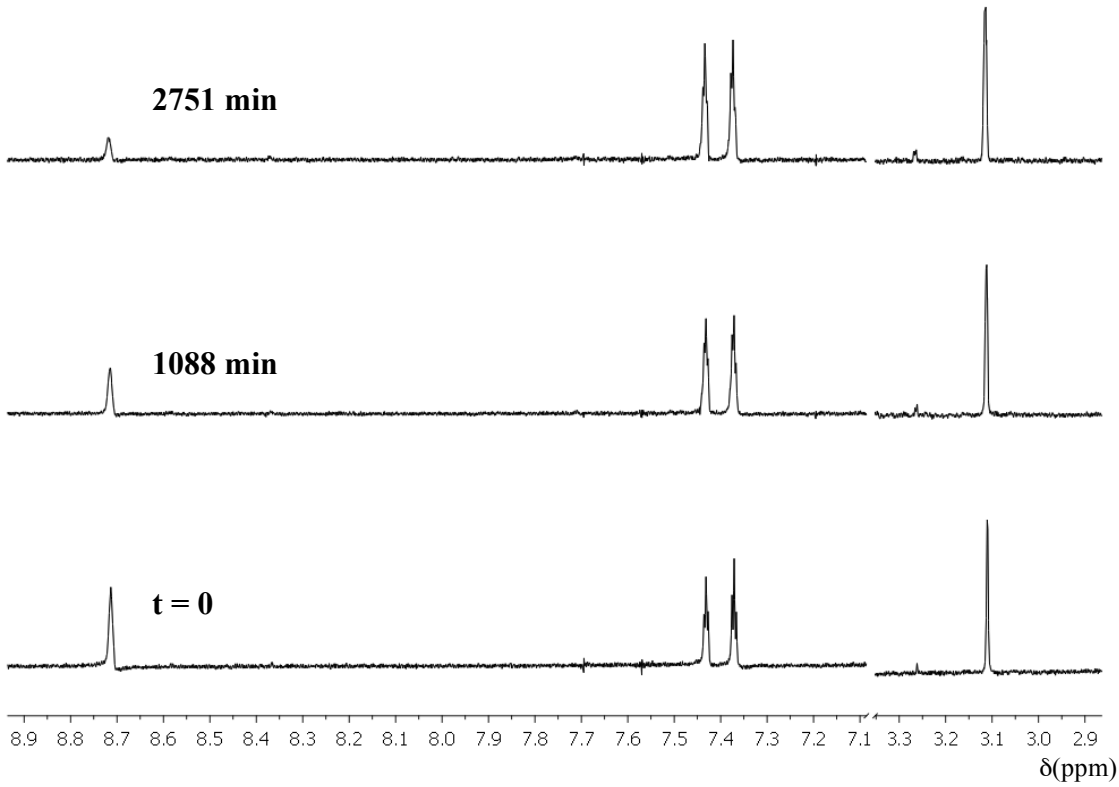
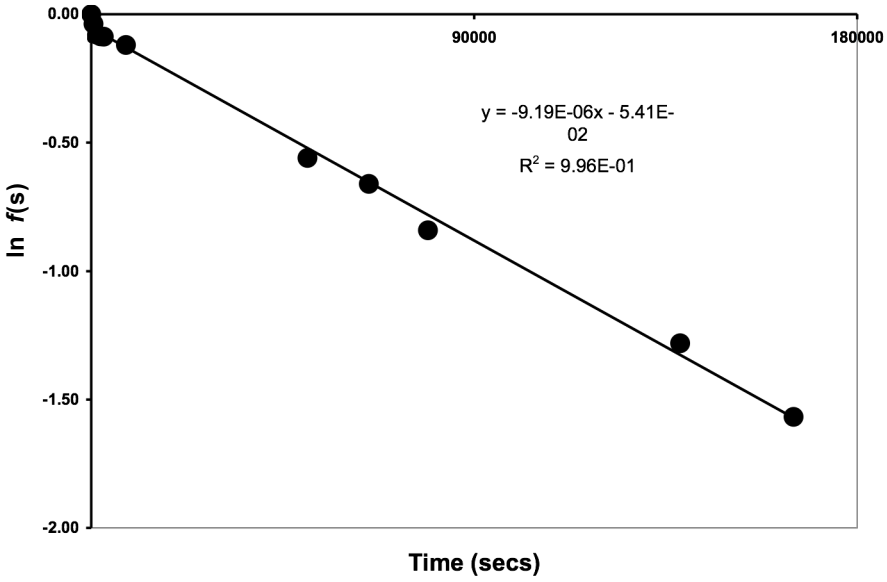


Figure s47: Semilogarithmic plot of the fraction of unexchanged substrate against time for the deuterium exchange reaction of **$4H^{+}n–2I^{-}$** in 100 mM acetic acid buffer (● pD 5.94) in D_2O at 25 ºC and I = 1.0 (KCl).



1,1'-Dimethyl-3,3'-(1,3-propylene)-diimidazolium diiodide $4H^+o–2I^–$

Figure s48: Representative ^{1}H NMR spectra at 300 MHz of imidazolium salt **$4H^+o–2I^–$** (10 mM, pD 6.59), obtained during exchange of the C2-H (s, 8.69 ppm) for deuterium in 100 mM phosphate buffer solution (30% f_B) in D_2O at 25 ºC and I = 1.0 (KCl). [Internal standard, tetramethylammonium deuteriosulfate (s, 3.09 ppm)]

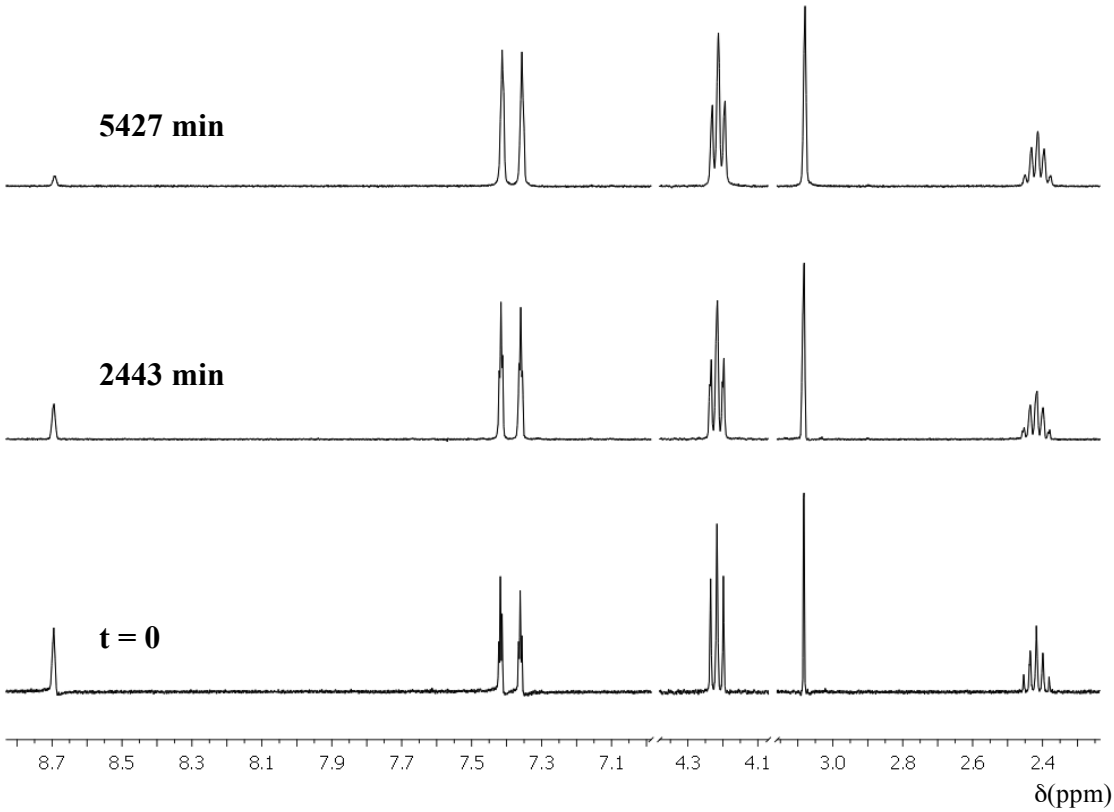


Figure s49: Semilogarithmic plots of the fraction of unexchanged substrate against time for the deuterium exchange reaction of **4H$^+$o–2I$^-$** in 100 mM phosphate buffers in D_2O at 25 ºC and I = 1.0 (KCl).

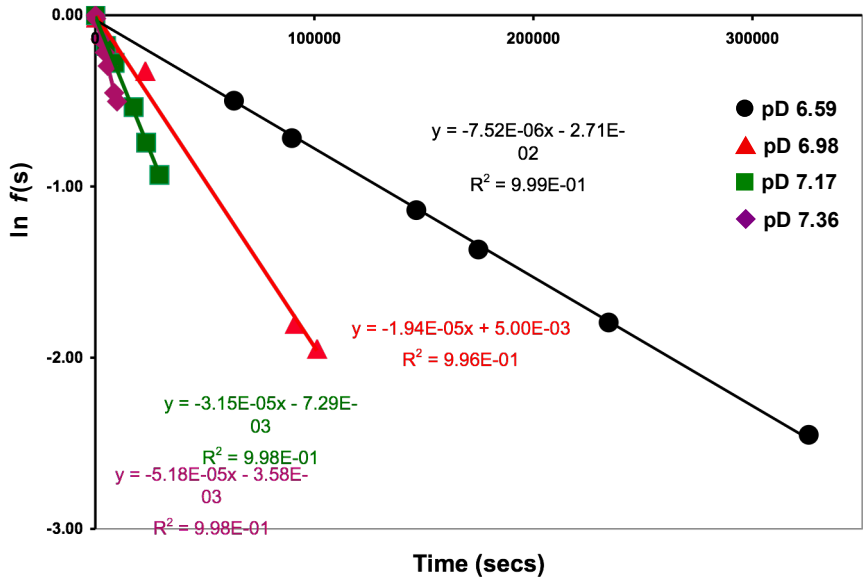


Figure s50: Plot of k_{ex} against [DO$^-$] for the H/D exchange reaction of imidazolium salt **4H$^+$o–2I$^-$** in 100 mM phosphate buffers in D_2O at 25 ºC and I = 1.0 (KCl).

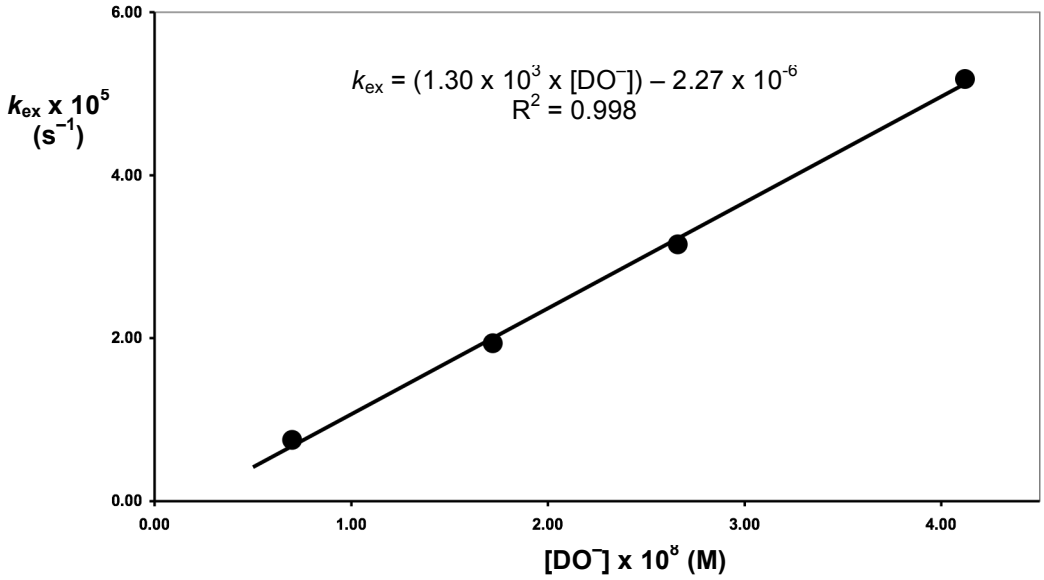


Table s17: First and second-order rate constants for exchange of the C2-H of imidazolium salt **4H$^+$o–2I$^-$** for deuterium in phosphate buffers in D_2O at 25 ºC and I = 1.0 (KCl).

[Buffer]$_{total}$, M	**pD**	**[DO$^-$], M**	**k_{ex}, s^{-1}**	**k_{DO}, M^{-1}s^{-1} [a]**
0.1	6.59	7.00×10^{-9}	7.52×10^{-6}	1.30×10^{3}
	6.98	1.72×10^{-8}	1.94×10^{-5}	
	7.17	2.66×10^{-8}	3.15×10^{-5}	
	7.36	4.12×10^{-8}	5.18×10^{-5}	

(a) The second-order rate constant, k_{DO}, was obtained from the slope of the plot of k_{ex} against [DO$^-$] in Figure s50.

1,1'-Dimethyl-3,3'-(1,2-phenylene)-diimidazolium diiodide $4H^+p–2I^–$

Figure s51: Representative ^1H NMR spectra at 300 MHz of imidazolium salt **$4H^+p–2I^–$** (10 mM, pD 4.73), obtained during exchange of the C2-H (s, 9.05 ppm) for deuterium in 100 mM acetic acid buffer solution (40% f_B) in D_2O at 25 ºC and I = 1.0 (KCl). [Internal standard, tetramethylammonium deuteriosulfate (s, 3.09 ppm)]

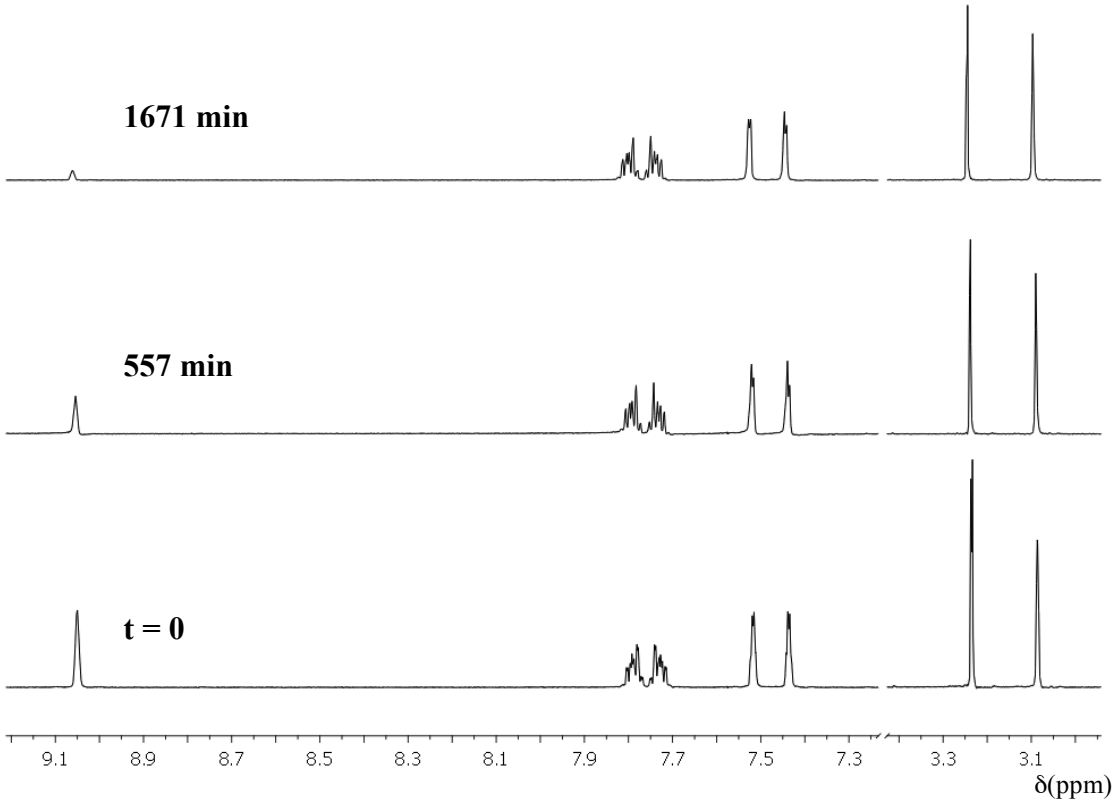


Figure s52: Semilogarithmic plots of the fraction of unexchanged substrate against time for the deuterium exchange reaction of **4H$^+$p–2I$^-$** in 100 mM acetic acid buffer solution in D_2O at 25 ºC and I = 1.0 (KCl).

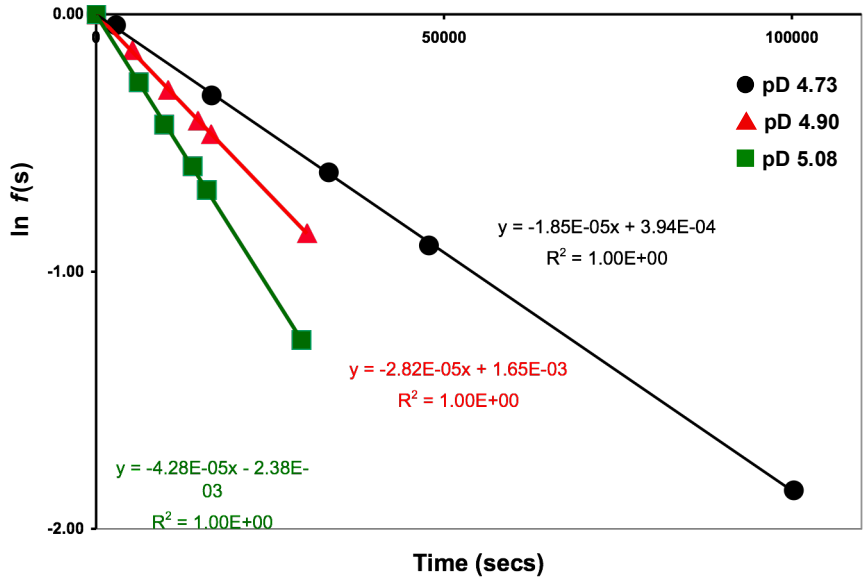


Figure s53: Plot of k_{ex} against [DO^-] for the H/D exchange reaction of imidazolium salt **4H$^+$p–2I$^-$** in 100 mM acetic acid buffer solution in D_2O at 25 ºC and I = 1.0 (KCl).

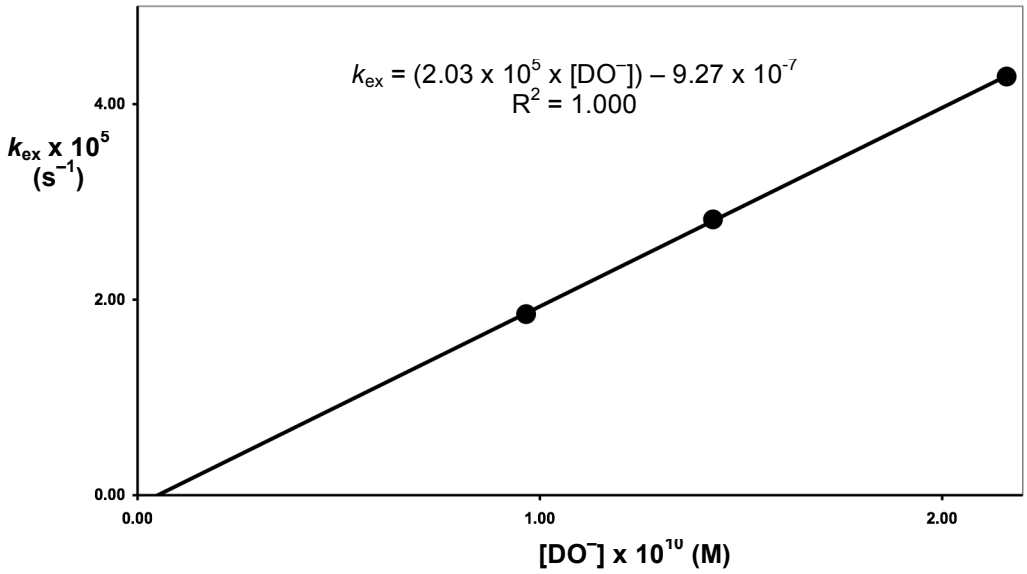


Table s18: First and second-order rate constants for exchange of the C2-H of imidazolium salt **4H$^+$p–2I$^-$** for deuterium in acetic acid buffer solution in D_2O at 25 ºC and I = 1.0 (KCl).

[Buffer]$_{total}$, M	**pD**	**[DO$^-$], M**	**k_{ex}, s^{-1}**	**k_{DO}, M^{-1}s^{-1} [a]**
0.1	4.73	9.66×10^{-11}	1.85×10^{-5}	2.03×10^{5}
	4.90	1.43×10^{-10}	2.82×10^{-5}	
	5.08	2.16×10^{-10}	4.28×10^{-5}	

(a) The second-order rate constant, k_{DO}, was obtained from the slope of the plot of k_{ex} against [DO$^-$] in Figure s53.

N,N'-Bis(di-(*i*-propyl)amino)formamidinium hexafluorophosphate $6H^+–PF_6^-$

The determination of rates of deuteroxide ion-catalysed exchange of the C2-H of acyclic formamidinium ion $\mathbf{6H^+–PF_6^-}$ to form the corresponding deuterated product $\mathbf{6D^+–PF_6^-}$ were attempted in the range pD 12.12 – 13.06 in quinuclidine buffers and deuteroxide solution.

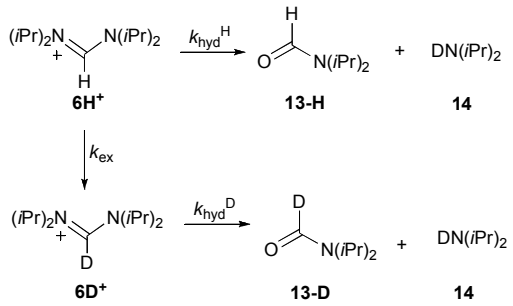
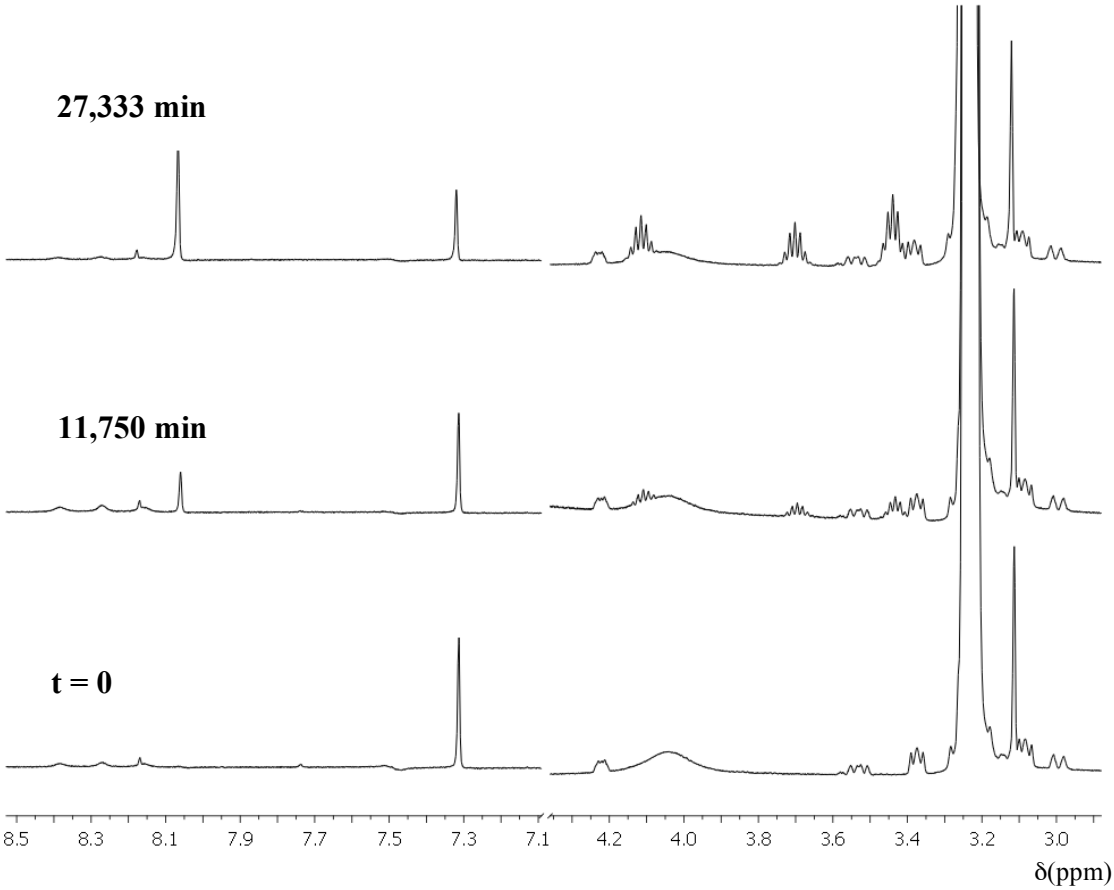


Figure s54 shows representative ^{1}H NMR spectra of formamidinium ion $\mathbf{6H^+–PF_6^-}$ (5 mM, pD 12.12), obtained during the attempted exchange for deuterium of the C2-H in 50% f_B quinuclidine buffer solution in D_2O at 25 °C and ionic strength I = 1.0 (KCl). Reaction aliquots were quenched to pD 4 prior to ^{1}H NMR analysis. The peak due to the C2-H appears as a singlet at 7.36 ppm. The signal due to the four methinyl C-*H*s of the four equivalent isopropyl substituents appears as a broad singlet at 4.06 ppm. The signal due to the twenty four *N*-methyl hydrogens appears as a doublet at 1.37 ppm (not shown). All other peaks in the region 0 – 3.8 ppm in the spectrum are due to hydrogens of quinuclidine buffer and internal standard, tetramethylammonium deuteriosulfate. Under these experimental conditions deuterium exchange does not compete with hydrolysis. The signal due to C2-H at 7.36 ppm decayed over the course of the reaction, and this was matched by the growth of a new singlet at 8.09 ppm due to the C1-H of *N*,*N*'-di-(*i*-propyl)formamide **13-H**. The decay of the broad singlet due to the four N-C*H*s of $\mathbf{6H^+–PF_6^-}$ was matched by the appearance of three new multiplets in the region 3.40-3.45, 3.65-3.70 and 4.05-4.10 ppm due to the N-C*H* protons of both **13-H** and **14**. The decay of the doublet due to the twenty four methyl hydrogens of $\mathbf{6H^+–PF_6^-}$ was matched by the growth of two doublets at 1.25 ppm and 1.20 ppm due to the twelve methyl hydrogens on formamide **13-H** and a doublet at 1.08 ppm due to the twelve methyl hydrogens of amine **14** (not shown). Thus deuterium exchange is not detectible under these experimental conditions and the disappearance of the signal due to the C2-H of formamidinium ion $\mathbf{6H^+–PF_6^-}$ is due entirely to hydrolysis of the substrate.

Figure s54: Representative ^{1}H NMR spectra at 300 MHz of acyclic formamidinium ion **6H^{+}–PF$_6^-$** (5 mM, pD 12.12), obtained during reaction in 100 mM quinuclidine buffer solution (50% f_B) in D_2O at 25 ºC and I = 1.0 (KCl). [Internal standard, tetramethylammonium deuteriosulfate (s, 3.11 ppm)]



The observed first order rate constant for hydrolysis, k_{hyd} (s^{-1}), could be obtained as the slope of a semilogarithmic plot of the fraction of remaining substrate against time according to [Eq. (s2)] (Figure s55). The experimental first-order rate constants for the hydrolysis of formamidinium ion **6H^{+}–PF$_6^-$** (k_{hyd}, s^{-1}) in quinuclidine buffers at different pD values and in deuteroxide solution are shown in Table s19. A plot of the first order rate constants, k_{hyd}, against deuteroxide concentration was linear with slope equivalent to k_{HYD}, the second order rate constant for hydrolysis. A value of k_{HYD} = 3.02×10^{-4} ($M^{-1}s^{-1}$) was obtained as the slope of this linear correlation.

Figure s55. Semilogarithmic plots of the fraction of remaining substrate against time for the hydrolysis reaction of acyclic formamidinium ion **6H$^+$–PF$_6^-$** in quinuclidine buffers and deuteroxide solution in D_2O at 25 ºC and I = 1.0 (KCl).

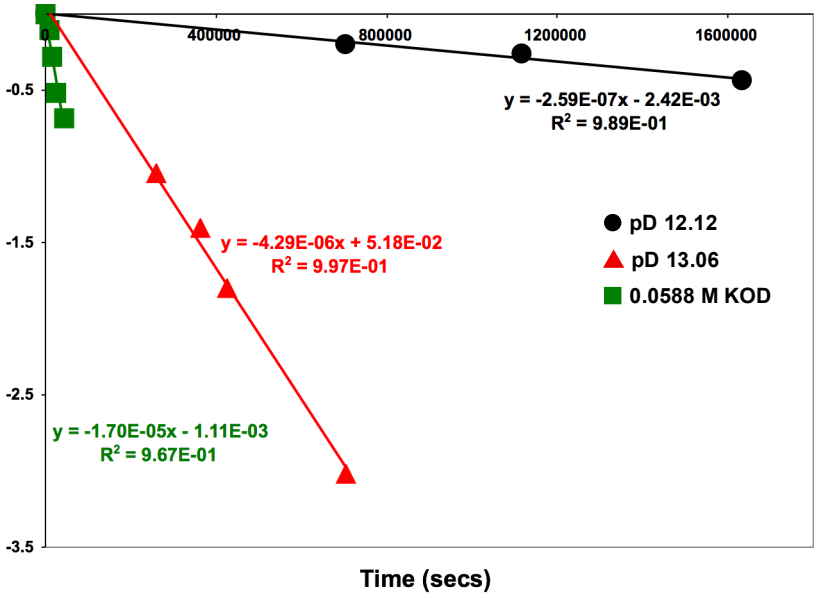


Table s19: First and second-order rate constants for the hydrolysis of acyclic formamidinium ion **6H$^+$–PF$_6^-$** in quinuclidine buffers and deuteroxide solution in D_2O at 25 ºC and I = 1.0 (KCl).

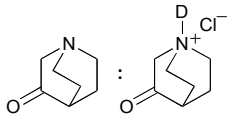
[Buffer]$_{total}$, M	**pD**	**[DO$^-$], M**	**k_{hyd}, s^{-1}**	**k_{HYD}, M^{-1}s^{-1}** [b]
0.1	12.12	2.38×10^{-3}	2.59×10^{-7}	
	13.06	2.08×10^{-2}	4.29×10^{-6}	
				3.02×10^{-4}
		5.88×10^{-2} [a]	1.70×10^{-5}	

(a) Unbuffered titrated deuteroxide ion solution. (b) The second-order rate constant, k_{HYD}, was obtained from the slope of the plot of k_{hyd} against [DO$^-$].

Determination of Contribution of Buffer Catalysis to Rate Constants for Deuterium Exchange

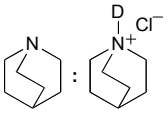
An investigation of the contribution of buffer catalysis to overall rate constants for C(2) H/D exchange was experimentally performed for representative imidazolium, 4,5-dihydroimidazolium and tetrahydropyrimidinium ions. These included 1-ethyl-3-methylimidazolium chloride **1H$^+$e–Cl$^–$**, 1,3-di-(*t*-butyl)imidazolium chloride **1H$^+$i–Cl$^–$**, 1,3-bis(2,4,6-trimethylphenyl)-4,5-dihydroimidazolium chloride **2H$^+$d–Cl$^–$** and 1,3-di-(*i*-propyl)-3,4,5,6-tetrahydropyrimidinium hexafluorophosphate **3H$^+$l–PF$_6^–$**. In these experiments, deuterium exchange was followed in a range of buffer solutions all containing the same percentage of the free base component of the buffer (*i.e.* a constant buffer ratio was maintained). ^{1}H NMR spectral details were exactly as described earlier for each of these azolium ions and the first order rate constants for exchange, k_{ex} (s^{-1}) were determined as described on pS12. Tables s20-23 give the k_{ex} (s^{-1}) values as a function of a change in the total concentration of buffer at fixed buffer ratios. In all cases a 2-9–fold increase in the total buffer concentration resulted in no significant change (± 10%) in k_{ex} at 25°C when corrections have been made for the small changes in pD that occur as a result of dilution at constant ionic strength.

Table s20: First order rate constants, k_{ex} (s^{-1}), for exchange for deuterium of the C(2)-H of 1-ethyl-3-methylimidazolium chloride **1H$^+$e–Cl$^–$** in quinuclidinone buffers (10% free base) in D_2O at 25 ºC and I = 1.0 (KCl).

Buffer	[Buffer]$_{total}$, M [a]	f_B [b]	pD	k_{ex}, s^{-1}
	0.05	0.1	7.25	5.92×10^{-6}
	0.15	0.1	7.26	5.79×10^{-6}
	0.25	0.1	7.25	6.46×10^{-6}
	0.45	0.1	7.24	6.84×10^{-6}

(a) Total concentration of buffer. (b) Fraction of buffer present in the basic form.

Table s21: First order rate constants, k_{ex} (s^{-1}), for exchange for deuterium of the C(2)-H of 1,3-di-(*t*-butyl)imidazolium chloride **1H$^+$i–Cl$^-$** in quinuclidine buffers (10% free base) in D_2O at 25 ºC and I = 1.0 (KCl).

Buffer	[Buffer]$_{total}$, M [a]	f_B [b]	pD	k_{ex}, s^{-1}
	0.15	0.1	11.22	1.02×10^{-3}
	0.25	0.1	11.22	1.07×10^{-3}
	0.35	0.1	11.22	1.09×10^{-3}

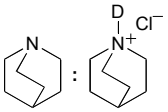
(a) Total concentration of buffer. (b) Fraction of buffer present in the basic form.

Table s22: First order rate constants, k_{ex} (s^{-1}), for exchange for deuterium of the C(2)-H of 1,3-bis(2,4,6-trimethylphenyl)-4,5-dihydroimidazolium chloride **2H$^+$d–Cl$^-$** in phosphate buffers (30% free base) in D_2O at 25 ºC and I = 1.0 (KCl).

Buffer	[Buffer]$_{total}$, M [a]	f_B [b]	pD	k_{ex}, s^{-1}
$D_2PO_4^-/DPO_4^{2-}$	0.10	0.3	6.76	1.43×10^{-4}
	0.20	0.3	6.59	9.10×10^{-5}
	0.40	0.3	6.61	1.03×10^{-4}
	0.50	0.3	6.62	9.24×10^{-5}

(a) Total concentration of buffer. (b) Fraction of buffer present in the basic form.

Table s23: First order rate constants, k_{ex} (s^{-1}), for exchange for deuterium of the C(2)-H of 1,3-di-(*i*-propyl)-3,4,5,6-tetrahydropyrimidinium hexafluorophosphate **3H$^+$I–PF$_6^-$** in quinuclidine buffers (10% free base) in D_2O at 25 ºC and I = 1.0 (KCl).

Buffer	[Buffer]$_{total}$, M [a]	f_B [b]	pD	k_{ex}, s^{-1}
	0.05	0.1	11.13	2.48×10^{-7}
	0.15	0.1	11.20	3.24×10^{-7}
	0.25	0.1	11.17	3.19×10^{-7}

(a) Total concentration of buffer. (b) Fraction of buffer present in the basic form.

References

(S1) 1,3-Diethyl-3,4,5,6-tetrahydropyrimidin-1-ium hexafluorophosphate, and di-*i*-propylaminomethylidene(di-*i*-propyl)ammonium hexafluorophosphate were prepared as described in: (*a*) R. W. Alder, M. E. Blake, S. Bufali, C. P. Butts, A. G. Orpen, J. Schutz and S. J. Williams, *J. Chem. Soc., Perkin Trans. 1*, 2001, 1586-1593. 1,3-Di-(*i*-propyl)-3,4,5,6-tetrahydropyrimidin-1-ium hexafluorophosphate was prepared as described in (*a*) above and in S. Saba, A. Brescia and M. K. Kaloustian, *Tet. Lett.*, 1991, **32**, 5031-5034.

(S2) M. B. Abrams, B. L. Scott and R. T. Baker, *Organometallics*, 2000, **19**, 4944-4956.

(S3) N. Stylianides, A. A. Danopoulos, D. Pugh, F. Hancock and A. Zanotti-Gerosa, *Organometallics*, 2007, **26**, 5627-5635.

(S4) A. J. Arduengo III, R. Krafczyrk and R. Schmutzler, *Tetrahedron*, 1999, **55**, 14523-14534.

(S5) M. Scholl, S. Ding, C. W. Lee and R. H. Grubbs, *Org. Lett.*, 1999, **1**, 953-956.

(S6) M. Iglesias, D. J. Beetstra, J. C. Knight, L. Ooi, A. Stasch, S. Coles, L. Male, M. B. Hursthouse, K. J. Cavell, A. Dervisi, and I. A. Fallis, *Organometallics*, 2008, **27**, 3279-3289.

(S7) M. Muehlhofer, T. Strassner, E. Herdtweck and W. A. Herrmann, *J. Organomet. Chem.*, 2002, **660**, 121-126.

(S8) C. Tubaro, A. Biffis, C. Gonzato, M. Zecca and M. Basato, *J. Mol. Cat. A: Chemical*, 2006, **248**, 93-98.

(S9) P. K. Glasoe and F. A. Long, *J. Phys. Chem.*, 1960, **64**, 188-190.

(S10) A. K. Covington, R. A. Robinson and R. G. Bates, *J. Phys. Chem.*, 1966, **70**, 3820-3824.

(S11) R. G. Bates, V. E. Bower and E. R. Smith, *J. Res. Natl. Bur. Stand.,* 1956, **56**, 305-312.

(S12) J. P. Richard, G. Williams and J. Gao, *J. Am. Chem. Soc.*, 1999, **121**, 715-726.

(S13) T. L. Amyes, S. T. Diver, J. P. Richard, F. M. Rivas and K. Toth, *J. Am. Chem. Soc.*, 2004, **126**, 4366-4374.