

Supporting information

Proton Transfer Reactions of a Bridged *Bis*-propyl *Bis*-imidazolium Salt

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General Instrumentation

NMR samples were prepared in deuterated chloroform or deuterium oxide. NMR spectra were recorded on Bruker Ultrashield 400 MHz and Oxford AS500 500 MHz 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.

Infrared spectra were recorded on a Perkin-Elmer Spectrum RX-1 FT-IR spectrometer as KBr discs or thin films between NaCl plates.

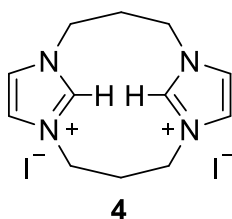
Melting points were determined using a Gallenkamp MPD 350-BM3.5 melting point apparatus and are uncorrected.

Analytical thin layer chromatography (tlc) was carried out on pre-coated 0.20 mm Machery-Nagel Polygram SIL G/UV₂₅₄ silica plates. Visualization was carried out by absorption of ultraviolet light.

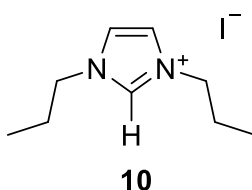
Materials All chemicals used were reagent grade, purchased from Sigma Aldrich and were used with no further purification unless stated in the synthetic method. D_2O (99.9% D) was purchased from Cambridge Isotope Laboratories Inc. Deuteriochloroform (CDCl_3 , 99.8% D) was purchased from Sigma Aldrich.

Synthesis of Substrates

Bis-propyl *bis*-imidazolium di-iodide **4** was prepared according to a literature procedure.^[S1]



1,3-Dipropylimidazolium iodide (**10**)



Based on a procedure by Thieuleux and co-workers,^[S2] a mixture of sodium hydride (6.11 g, 41 mmol) and imidazole (1.0 g, 15 mmol) in dry THF (30 mL) was stirred for 20 min at r.t. under an inert atmosphere. 1-Iodopropane (3.0 mL, 31 mmol) was added dropwise and the solution refluxed for 48 h. The solution was filtered and the precipitate washed with THF. The filtrate was evaporated under reduced pressure, and the residue dissolved in dichloromethane (30 mL) and filtered. The solution was washed with pentane (4 × 30 mL) and solvent removed under reduced pressure to yield the title compound as a brown oil (2.67 g, 64%), with spectroscopic details in accordance with the literature. ¹H NMR (700 MHz, CDCl₃): δ_H 1.01 (6H, t, *J*=7.4 Hz, 2 × CH₃), 2.00 (2H, m, 2 × CH₂), 4.34 (4H, t, *J*=7.3 Hz, 2 × NCH₂), 7.36 (2H, d, *J*=1.6 Hz, 2 × CH), 10.32 (1H, s, NCH(N)); ¹³C NMR (176 MHz, CDCl₃): δ_C 10.9 (2 × CH₃), 23.9 (2 × CH₂), 51.9 (2 × CH₂), 122.1 (2 × CH), 137.1 (NCH(N)).

Kinetic Details

Measurement of pD in D_2O solutions

Calibration: The pH values of buffered solutions were determined at 25 °C using a MeterLab™ PHM 290 pH -Stat Controller equipped with a radiometer (pH 4 - 7 @ 25 °C) combination electrode, that could be standardised between pH 4 - 7 to encompass the pH of the buffer solution.

Determination of $[DO^-]$: The pD (± 0.03) was calculated by adding 0.4 to the observed reading of the pH meter in the D_2O solution.^[S3] The deuteroxide concentration (M) was calculated using Eqn (S1):

$$[DO^-] = (10^{pD - pK_w})/\gamma_{DO} \quad (S1)$$

where $K_w = 10^{-14.87}$ M is the ionic product of D_2O ^[S4] at 25 °C and γ_{DO} is the apparent activity coefficient of deuteroxide ion under our experimental conditions. The apparent activity coefficient of deuteroxide ion, $\gamma_{DO} = 0.73$, 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 solution that was saturated at 21 °C.^[S4] pD values were recorded at the beginning and end of reaction, and were found to be constant (± 0.05).

NMR Parameters

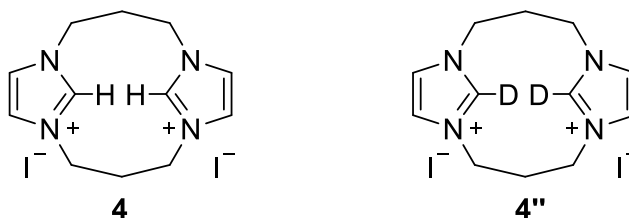
1H NMR spectra of imidazolium salts **4** and **10** were recorded on either Bruker Ultrashield 400 MHz or Oxford AS500 500 MHz NMR spectrometers. Spectra were run with 32 transients and a relaxation delay of 20 seconds, sweep width of 8298.76 Hz, acquisition time of 4 sec and a 90° pulse angle (total running time approximately 13 min). 1H 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.

Deuterium Exchange Reactions in Water

For each imidazolium salt **4** and **10** the following data are included: a representative ^1H NMR overlay of deuterium exchange at one pD value, a semi-logarithmic plot of $f(s)$ as a function of time for all pDs and a second order plot of k_{ex} values against deuterioxide concentration.

Bridged *bis*-propyl *bis*-imidazolium diiodide (**4**)

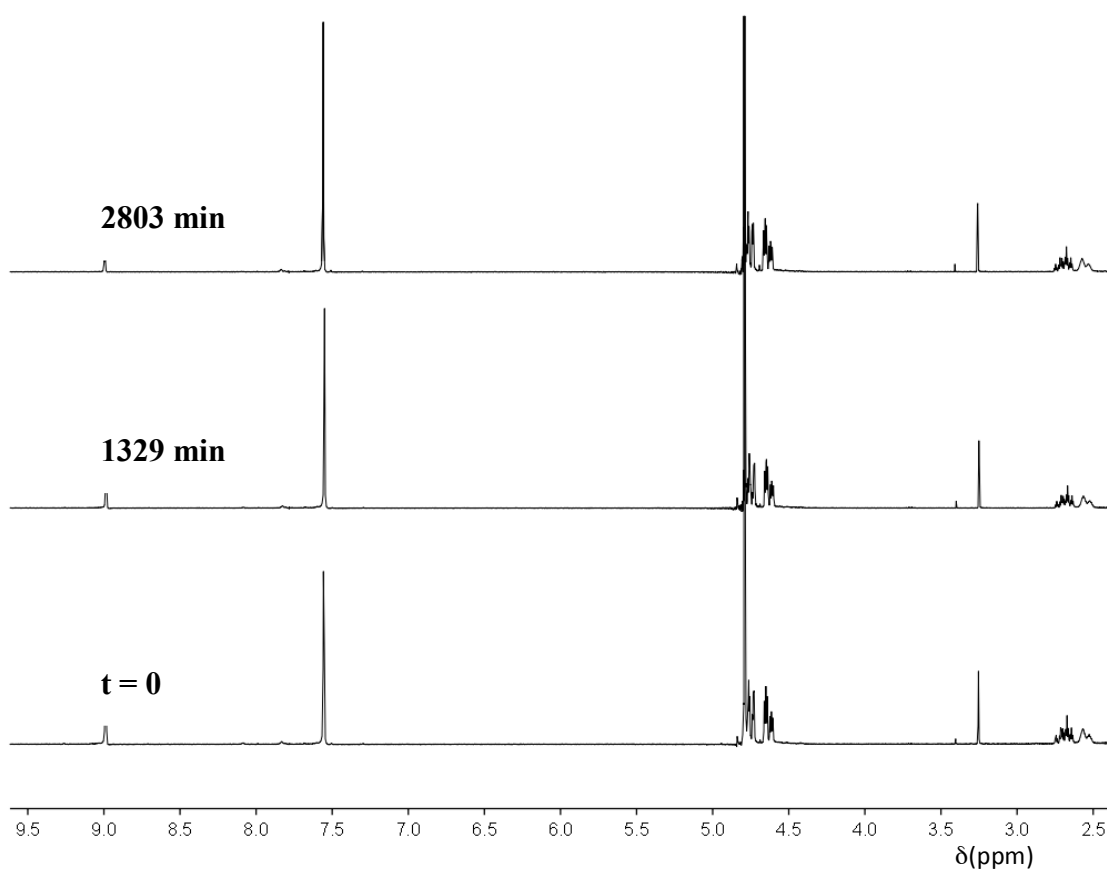


Pseudo-first-order rate constants for the deuterioxide ion-catalysed exchange of the two C(2)-H groups of imidazolium salt **4** to form di-deuterated product **4''** were determined by ^1H NMR spectroscopy (400 MHz).

A representative set of spectra taken at three time points during the reaction in acetic acid buffer at pD 5.46 (70% f_B) is shown in Figure S1. Deuterium exchange at the two C(2)-H positions resulted in the disappearance of the C(2)-H singlet at 8.99 ppm over the course of the reaction. The extent of exchange was measured relative to the 12 equivalent non-exchangeable protons of the internal standard at 3.24 ppm. A singlet corresponding to the four equivalent C(4)-H and C(5)-H protons appears at 7.56 ppm. Signals corresponding to the four CH_2 groups adjacent to the nitrogen atoms on the propyl linkers appear as triplets at 4.77, 4.73, 4.65 and 4.61 ppm. Signals corresponding to the remaining two CH_2 groups on the propyl linkers appear as a set of multiplets at 2.63 – 2.73 ppm. No change was observed in

the integrated area of any other peak relative to the internal standard, indicating that deuterium exchange does not occur at any position other than at C(2)-H under these conditions.

Figure S1: Representative ^1H NMR spectra at 400 MHz of *bis*-imidazolium di-iodide 4 (10 mM, pD 5.46), obtained during exchange of the C(2)-H (s, 8.99 ppm) for deuterium in D_2O at 25 °C and $I = 1.0$ (KCl) [Internal standard, tetramethylammonium deuteriosulfate (s, 3.24 ppm)]



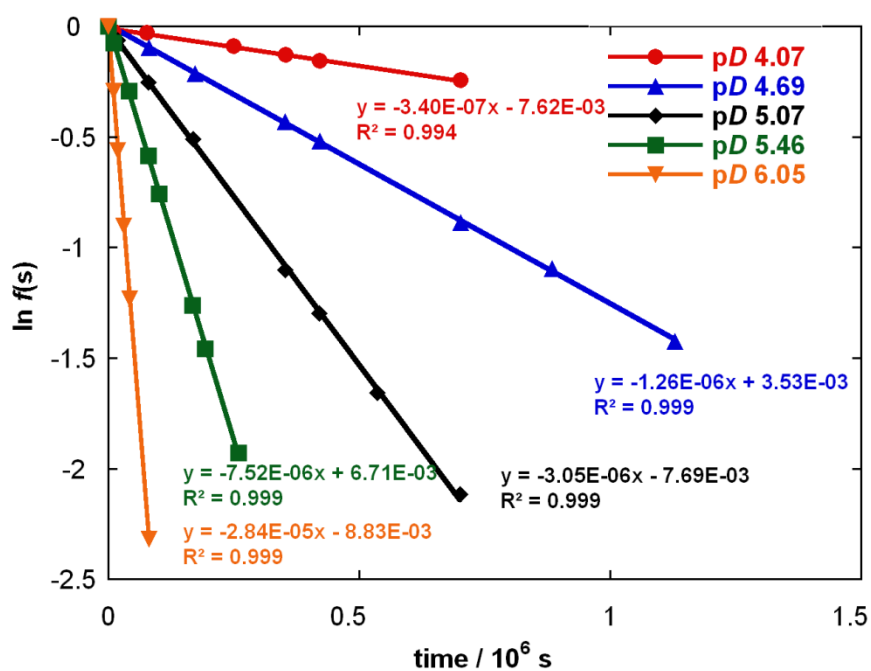
Experimentally observed first-order rate constants for exchange, k_{ex} (s^{-1}), were determined from the slopes of semi-logarithmic plots of $f(s)$ against time at each pD. Reaction data and values of k_{ex} are presented in Table S1 and Figure S2.

Table S1: Reaction data and first-order rate constants for exchange of the two C(2)-H groups of bis-imidazolium di-iodide 4 for deuterium in solutions of acetic acid buffer (250 mM) in D₂O at 25 °C and *I* = 1.0 (KCl).

f_B	$[\text{DO}^-], \text{M}$	time, s	$f(s)$	$\ln f(s)$	$k_{\text{ex}}, \text{s}^{-1}$
10%	2.17×10^{-11} (pD 4.07)	0	1.000	0.000	3.40×10^{-7}
		11100	0.977	-0.023	
		77760	0.971	-0.030	
		250200	0.915	-0.089	
		353400	0.879	-0.128	
		422400	0.855	-0.156	
		702060	0.783	-0.245	
30%	9.05×10^{-11} (pD 4.69)	0	1.000	0.000	1.26×10^{-6}
		80940	0.907	-0.098	
		172620	0.807	-0.214	
		352740	0.650	-0.431	
		421740	0.595	-0.519	
		701760	0.412	-0.887	
		884520	0.334	-1.095	
		1129080	0.241	-1.425	
50%	2.17×10^{-10} (pD 5.07)	0	1.000	0.000	3.05×10^{-6}
		19140	0.938	-0.064	
		80520	0.776	-0.253	
		169200	0.600	-0.511	
		352380	0.333	-1.101	
		421020	0.273	-1.298	
		535860	0.190	-1.658	
		701100	0.121	-2.116	
70%	5.33×10^{-10} (pD 5.46)	0	1.000	0.000	7.52×10^{-6}
		10440	0.928	-0.075	
		41220	0.747	-0.292	
		79740	0.557	-0.585	
		101640	0.468	-0.758	
		168180	0.283	-1.261	
		192900	0.232	-1.459	
		258900	0.145	-1.930	
90%	2.07×10^{-9} (pD 6.05)	0	1.000	0.000	2.84×10^{-5}
		10140	0.746	-0.293	
		19320	0.570	-0.562	
		30780	0.405	-0.903	
		43080	0.292	-1.231	
		81420	0.098	-2.320	

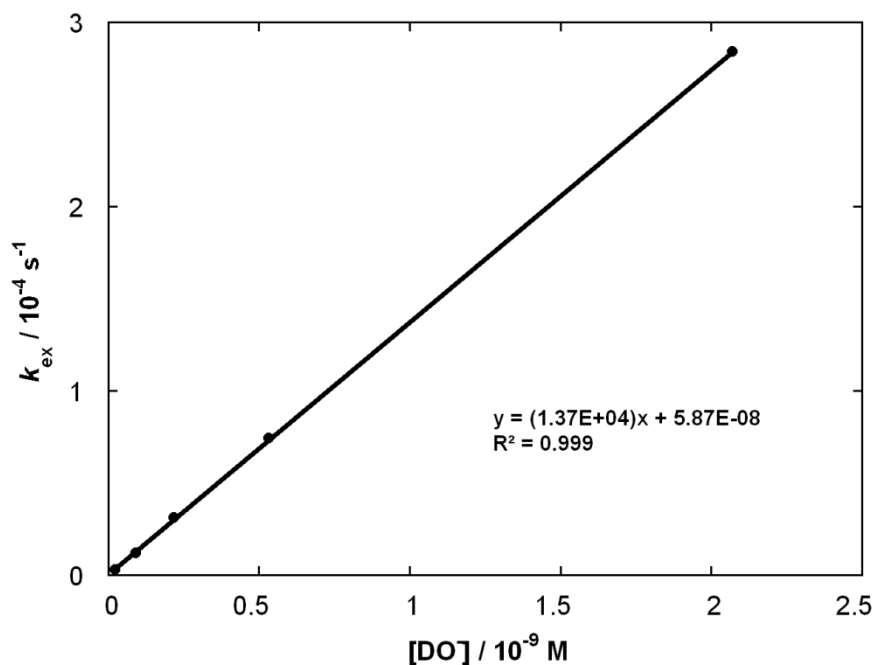
(a) Concentration of deuteroxide ion calculated using Equation S1. (b) Fraction of substrate remaining $f(s)$ calculated using Eqn (1) (main paper). (c) Pseudo-first-order rate constant for exchange, k_{ex} (s^{-1}), obtained from the slope of the plot of $\ln f(s)$ against time in Figure S2.

Figure S2: Semilogarithmic plots of the fraction of unexchanged substrate against time for the deuterium exchange reaction of 4 in solutions of acetic acid buffer (250 mM) in D₂O at 25 °C and *I* = 1.0 (KCl).

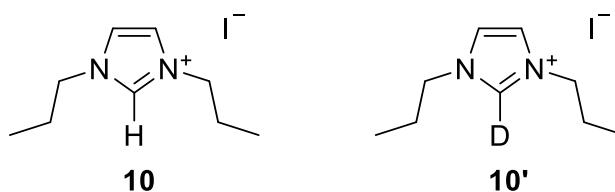


A value of $1.37 \times 10^4 \text{ M}^{-1} \text{ s}^{-1}$ for the second-order rate constant for deuterioxide ion-catalysed exchange, k_{DO} , was obtained from the slope of a plot of k_{ex} against deuterioxide ion concentration (Figure S3).

Figure S3: Plot of k_{ex} against $[\text{DO}^-]$ for the H/D-exchange reaction of *bis*-imidazolium di-iodide **4** in D_2O at 25 °C and $I = 1.0$ (KCl)



1,3-Dipropylimidazolium iodide (**10**)

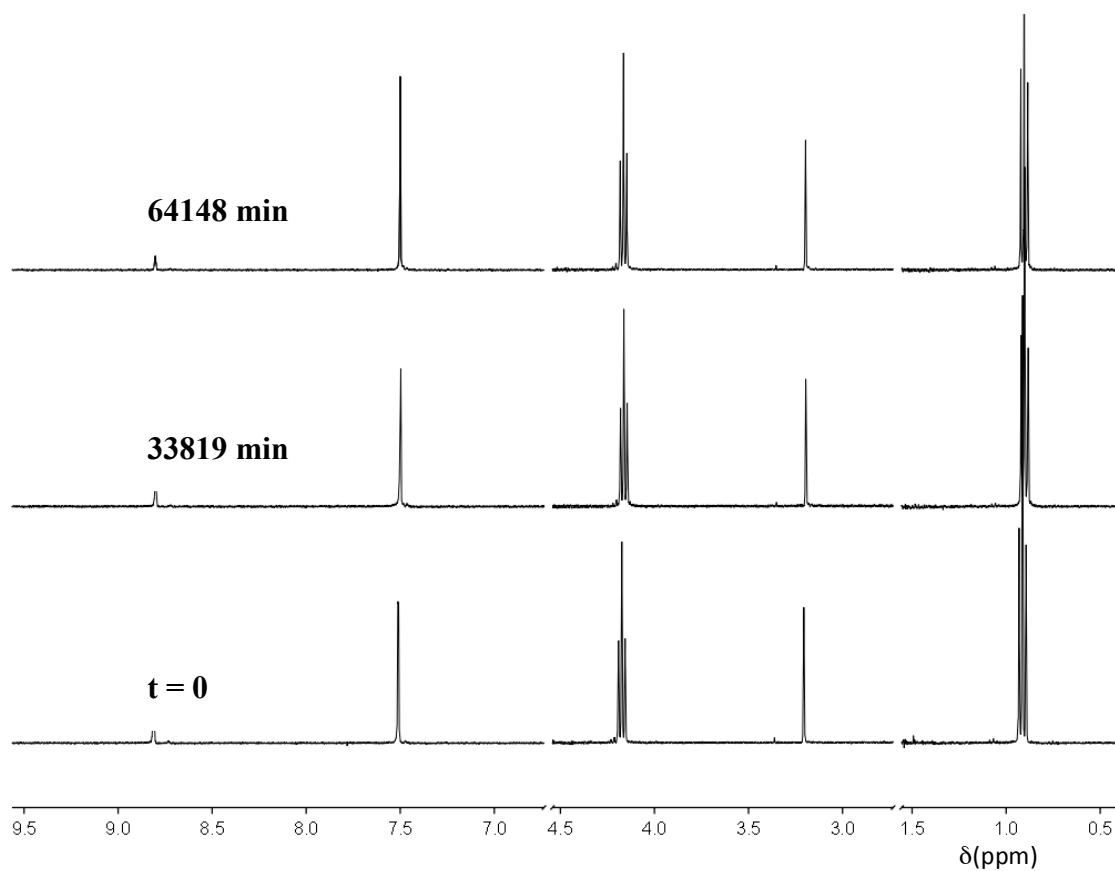


Pseudo-first-order rate constants for the deuterioxide ion-catalysed exchange of the C(2)-H of imidazolium salt **10** to form deuterated product **10'** were obtained by ^1H NMR spectroscopy (400 MHz).

A representative set of spectra taken at three time points during the reaction in acetic acid buffer at pD 4.07 (10% f_{B}) is shown in Figure S4. Deuterium exchange at the C(2)-H position resulted in the disappearance of the C(2)-H singlet at 8.81 ppm over the course of the reaction. The extent of exchange was measured relative to the 12 equivalent non-

exchangeable protons of the internal standard at 3.20 ppm. A singlet corresponding to two equivalent C(4)-H and C(5)-H protons appears at 7.51 ppm. Signals corresponding to the two CH₂ groups on the propyl linker appear as a triplet and multiplet at 4.16 and 1.89 ppm respectively, and the signal corresponding to the CH₃ group appears as a triplet at 0.91 ppm. No change was observed in the integrated area of any other peak relative to the internal standard, indicating that deuterium exchange does not occur at any position other than at C(2)-H under these conditions.

Figure S4: Representative ¹H NMR spectra at 400 MHz of dipropyl imidazolium iodide 10 (10 mM, p*D* 6.05), obtained during exchange of the C(2)-H (s, 8.81 ppm) for deuterium in D₂O at 25 °C and *I* = 1.0 (KCl) [Internal standard, tetramethylammonium deuteriosulfate (s, 3.20 ppm)]



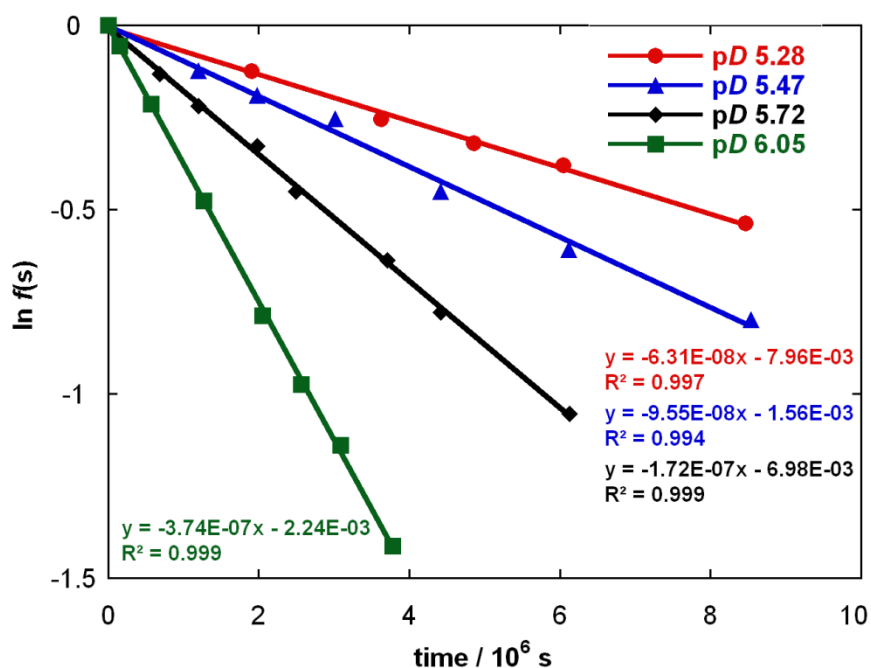
Experimentally observed first-order rate constants for exchange, k_{ex} (s^{-1}), were determined from the slopes of semi-logarithmic plots of $f(s)$ against time at each pD . Reaction data and values of k_{ex} are presented in Table S2 and Figure S5.

Table S2: Reaction data and first-order rate constants for exchange of the C(2)-H of dipropyl imidazolium iodide 10 for deuterium in solutions of acetic acid buffer (250 mM) in D_2O at 25 °C and $I = 1.0$ (KCl).

f_{B}	$[\text{DO}^-], \text{M}$	time, s	$f(s)$	$\ln f(s)$	$k_{\text{ex}}, \text{s}^{-1}$
60%	3.57×10^{-10} (pD 5.28)	0	1.000	0.000	6.31×10^{-8}
		1904760	0.883	-0.124	
		3631020	0.774	-0.256	
		4859460	0.725	-0.321	
		6047400	0.684	-0.380	
		8469840	0.584	-0.538	
70%	5.52×10^{-10} (pD 5.47)	0	1.000	0.000	9.55×10^{-8}
		1198800	0.884	-0.123	
		1977360	0.827	-0.190	
		3014160	0.776	-0.254	
		4413480	0.637	-0.451	
		6120060	0.545	-0.608	
80%	9.82×10^{-10} (pD 5.72)	0	1.000	0.000	1.72×10^{-7}
		684720	0.878	-0.131	
		1199940	0.803	-0.219	
		1977960	0.721	-0.327	
		2491980	0.637	-0.451	
		3708840	0.528	-0.638	
		4419780	0.459	-0.779	
		6124380	0.349	-1.054	
90%	2.10×10^{-9} (pD 6.05)	0	1.000	0.000	3.74×10^{-7}
		152100	0.946	-0.055	
		572700	0.808	-0.213	
		1271340	0.621	-0.476	
		2049120	0.455	-0.787	
		2563380	0.378	-0.974	
		3091080	0.320	-1.140	
		3780180	0.243	-1.413	

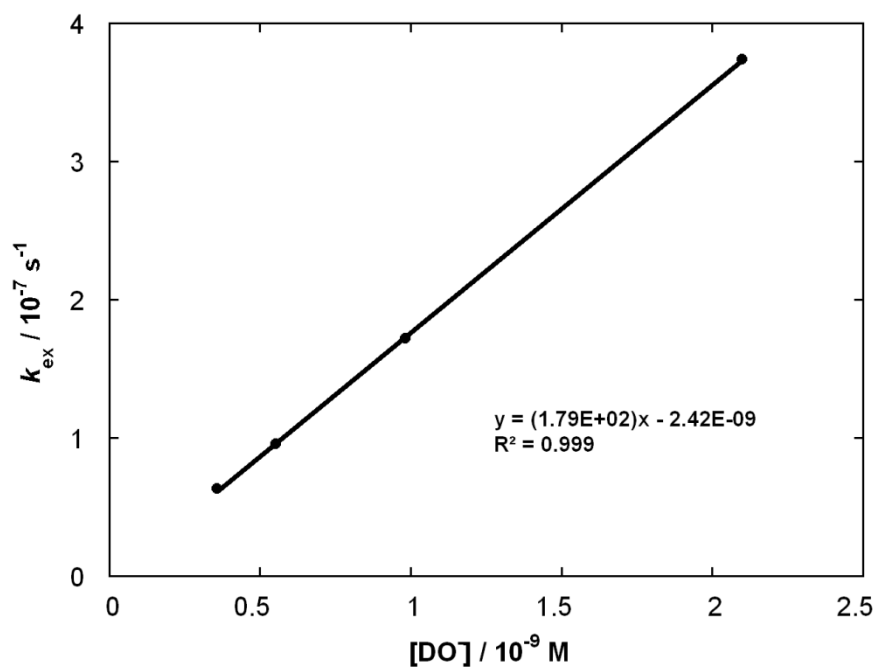
(a) Concentration of deuterioxide ion calculated using Equation S1. (b) Fraction of substrate remaining $f(s)$ calculated using Eqn (1) (main paper). (c) Pseudo-first-order rate constant for exchange, k_{ex} (s^{-1}), obtained from the slope of the plot of $\ln f(s)$ against time in Figure S5Figure S2.

Figure S5: Semilogarithmic plots of the fraction of unexchanged substrate against time for the deuterium exchange reaction of dipropyl imidazolium iodide 10 in solutions of acetic acid buffer (250 mM) in D₂O at 25 °C and *I* = 1.0 (KCl).



A value of $1.79 \times 10^2 \text{ M}^{-1} \text{ s}^{-1}$ for the second-order rate constant for deuterioxide ion-catalysed exchange, k_{DO} , was obtained from the slope of a plot of k_{ex} against deuterioxide ion concentration (Figure S6).

Figure S6: Plot of k_{ex} against $[\text{DO}^-]$ for the H/D-exchange reaction of dipropyl imidazolium iodide 10 in D₂O at 25 °C and *I* = 1.0 (KCl)



References

- [S1] J. A. Murphy, S. Zhou, D. W. Thomson, F. Schoenebeck, M. Mahesh, S. R. Park, T. Tuttle and L. E. A. Berlouis, *Angew. Chem. Int. Ed.* **2007**, *46*, 5178-5183.
- [S2] M. Bouhrara, E. Jeanneau, L. Veyre, C. Copéret and C. Thieuleux, *Dalton Trans.*, 2011, **40**, 2995.
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- [S4] A. K. Covington, R. A. Robinson, R. G. Bates, *J. Phys. Chem.*, 1966, **70**, 3820.