

Oxorhenium(V)-mediated syntheses and structures of oxypyridinium-ammonium zwitterions

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Treatment of *N,N*-bis(2-hydroxybenzyl)-2-(2-aminoethyl)dimethylamine (H₂had) with *trans*-[ReO₂(py)₄]I in acetone affords the iodide salts of the oxypyridinium-ammonium zwitterions *N*¹-(2-hydroxybenzyl)-*N*²,*N*²-dimethyl-*N*¹-((2-oxypyridinium)-1-methyl)ethane-1,2-diamine [Hhpd]⁺ and *N*²,*N*²-dimethyl-*N*¹-bis((2-oxypyridinium)-1-methyl)ethane-1,2-diamine [dod]⁺. The products were characterized by X-ray structure analysis, and NMR and IR spectroscopy.

Key Words: Oxorhenium(V), oxypyridinium-ammonium, zwitterions.

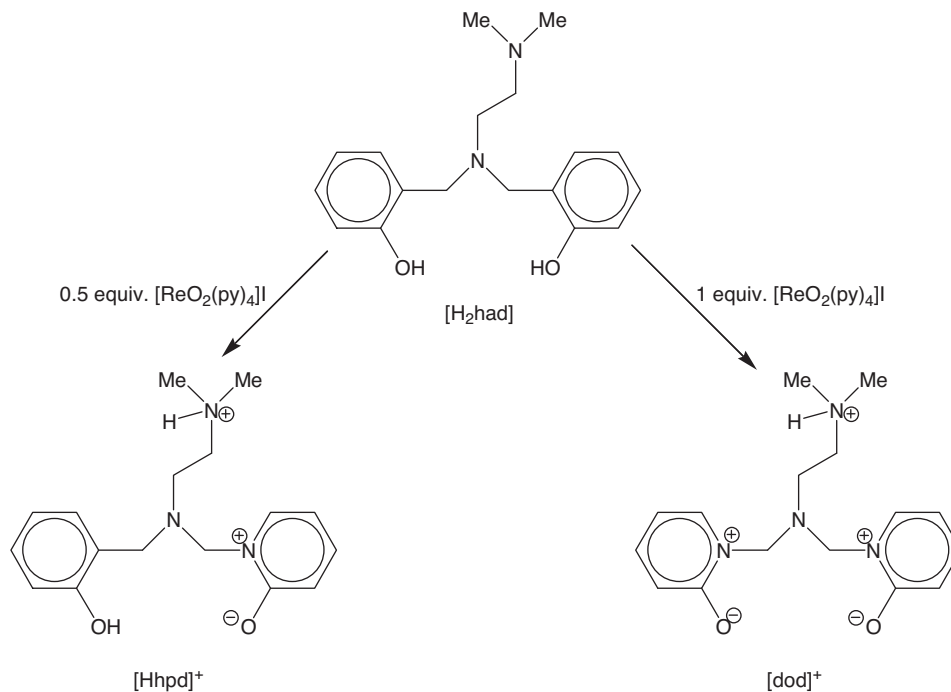
Introduction

There is currently widespread interest in the coordination chemistry of oxorhenium(V) complexes, particularly because some representative compounds of this class show promise as potential therapeutic radiopharmaceuticals¹ and as catalysts for a wide range of transformations of organic compounds.²

We used the “4+1” concept to prepare 6-coordinate oxorhenium(V) complexes by the coordination of dianionic tetradentate N₂O₂-donor chelates. For example, the reaction of *trans*-[ReOCl₃(PPh₃)₂] with *N,N*-bis(2-hydroxybenzyl)-2-(2-aminoethyl)dimethylamine (H₂had)³ in ethanol gave the complex [ReOCl(had)] as the product.⁴ However, by reacting the dioxo starting material *trans*-[ReO₂(py)₄]I with H₂had in acetone,

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the pyridinium zwitterions N^1 -(2-hydroxybenzyl)- N^2,N^2 -dimethyl- N^1 -((2-oxypyridinium)-1-methyl)ethane-1,2-diamine iodide ([Hhpd]I) and N^2,N^2 -dimethyl- N^1 -bis((2-oxypyridinium)-1-methyl)ethane-1,2-diamine iodide ([dod]I) were isolated as products.



Scheme 1. Conversion of H_2had to $[\text{Hhpd}]^+$ and $[\text{dod}]^+$.

Experimental

$\text{trans-}[\text{ReO}_2(\text{py})_4]\text{I}^5$ and H_2had^3 were prepared by literature procedures. Solvents were dried by standard methods, and other chemicals (Aldrich) were used as received after their purity was checked by melting point and NMR. All synthetic procedures were done under a nitrogen atmosphere. IR spectra were recorded for samples in KBr pellets on a Nicolet 20 DXC spectrophotometer in the $4000\text{--}200 \text{ cm}^{-1}$ range. NMR spectra were recorded at 300 MHz on a Bruker AMX-300 spectrometer. All chemical shifts are relative to TMS, with $\text{DMSO-}d_6$ as solvent. Elemental analyses were carried out by the Department of Chemistry at the University of the Western Cape in Cape Town.

Preparation of N^1 -(2-hydroxybenzyl)- N^2,N^2 -dimethyl- N^1 -((2-oxypyridinium)-1-methyl)ethane-1,2-diamine iodide ([Hhpd]I)

A mixture of $\text{trans-}[\text{ReO}_2(\text{py})_4]\text{I}$ (100 mg, 151 μmol) and H_2had (91 mg, 300 μmol) in 15 mL of acetone was heated under reflux for 18 h, with the solution gradually changing colour to green. After heating was stopped, the solution was cooled to room temperature and filtered to give a clear green solution. No precipitate formed. The solvent was removed under vacuum to yield a light green oil, which was dissolved in 10 mL of

dichloromethane, and 3 mL of *n*-heptane was added. After 5 h light green needles of [Hhpd]I.H₂O started to form. Anal. Found (Calcd. For C₁₇H₂₄N₃O₂I.H₂O) C 45.87 (45.65), H 5.58 (5.86), N 9.77 (9.39). Mp 114 °C. IR: 3434m (O-H), 3276m (N-H), 1593s (C=N), 1264s (C-OH), 1233 (C-O⁻). ¹³C-NMR (300 MHz, d⁶-DMSO) δ 43.36 (C9, C10, C11), 47.45 (C8), 53.18 (C7), 55.81 (C12), 116.17 (C2), 120.23 (C4), 123.86 (C6), 124.82 (C16), 129.73 (C3), 131.82 (C14), 132.40 (C5), 132.95 (C13), 134.09 (C17), 150.41 (C15), 156.78 (C1).

Preparation of *N*²,*N*²-dimethyl-*N*¹-bis((2-oxypyridinium)-1-methyl)ethane-1,2-diamine iodide ([dod]I)

A mass of 91 mg of H₂had (302 μmol) was added to a solution of *trans*-[ReO₂(py)₄]I (200 mg, 302 μmol) in 30 mL of acetone, and the mixture was heated under reflux for 18 h, with the solution gradually changing colour to yellow. After cooling to room temperature, the solvent was removed under vacuum to give a solid residue, which was dissolved in a mixture of 10 mL of acetone and 5 mL of *n*-heptane. After standing overnight, light yellow crystals, suitable for X-ray analysis, were collected. Anal. Found (Calcd. For C₁₆H₂₃N₄O₂I.H₂O) C 42.93 (42.87), H 5.47 (5.62), N 12.63 (12.50). Mp 123 °C. IR: 3274m (N-H), 1597s (C=N), 1242s (C-O⁻). ¹³C-NMR (300 MHz, d⁶-DMSO) δ 43.16 (C15, C16), 47.12 (C14), 54.11 (C13), 54.70 (C1, C7), 120.10 (C5, C11), 123.40 (C3, C9), 129.55 (C2, C8), 131.81 (C6, C12), 156.46 (C4, C10). ¹H-NMR δ 2.79 (s, 6H, 2xMe), 3.01 (t, 2H, *J*=6.6, C13H₂), 3.45 (t, 2H, *J*=6.6, C14H₂), 3.83 (s, 4H, C1H₂, C7H₂), 6.84 (t, 2H, *J*=7.4, C4H, C10H), 7.07 (d, 2H, *J*=8.0, C6H, C12H), 7.15 (d, 2H, *J*=6.5, C3H, C9H), 7.20 (t, 2H, *J*=8.0, C5H, C11H).

Crystallography

Diffraction data for H₂had, [Hhpd]I.H₂O, and [dod]I.H₂O were collected on a Nonius Kappa CCD diffractometer with graphite-monochromated Mo K_α radiation (λ = 0.71073 Å). Details of the crystal data, intensity measurements, and data processing are summarized in Table 1. For the structure factors, corrections for Lorentz and polarization effects and absorption were made. The structures were solved by direct methods and refined by full-matrix least-squares procedures using SHELXS97 and SHELXL97.⁶ All H atoms were placed in calculated positions, assigned fixed isotropic displacement parameters 1.2 times the equivalent isotropic *U* value of the attached atom, and allowed to ride on their respective parent atoms. Selected bond lengths and angles are given in Table 2.

Results and discussion

[Hhpd]I and [dod]I were synthesized by the reaction of *trans*-[ReO₂(py)₄]I with 2 equivalents and 1 equivalent, respectively, in acetone. In [Hhpd]I, one of the 2-hydroxyphenyl groups of H₂had is substituted by an oxypyridinium group, and in [dod]I, both 2-hydroxyphenyl groups are converted. Because of the appearance of the pyridinium rings and iodide in the products, these conversions could only have been facilitated by *trans*-[ReO₂(py)₄]I. Although an opinion on the probable mechanism would be highly speculative, it seems obvious that a 6-coordinated intermediate of the type *trans*-[ReO₂(py)₂(H₂had)]⁺, with H₂had coordinated through the 2 nitrogen-donor atoms only, must be formed initially, followed by 2-hydroxyphenyl bond breaking and transfer of a pyridyl group. Previous studies on the reactivity of pyridinium salts revealed that these ring

systems readily react with nucleophiles.⁷ In these transformations the nucleophile attacks the pyridine-carbon atom adjacent to the nitrogen atom to give an intermediate product, which rapidly undergoes solvolysis, for example in methanol, to give pyridones.

Table 1. Crystallographic data.

	H ₂ had	[Hhpd]I.H ₂ O	[dod]I.H ₂ O
Chemical formula	C ₁₈ H ₂₄ N ₂ O ₂	C ₁₇ H ₂₆ N ₃ O ₃ I	C ₁₆ H ₂₅ N ₄ O ₃ I
Formula weight	300.39	447.31	448.30
Crystal system	Monoclinic	Orthorhombic	Orthorhombic
Space group	<i>P</i> 2 ₁ / <i>c</i>	<i>P</i> 2 ₁ 2 ₁ 2 ₁	<i>P</i> 2 ₁ 2 ₁ 2 ₁
Unit cell	<i>a</i> (Å)	9.907(2)	13.9855(3)
	<i>b</i> (Å)	16.480(2)	13.9538(4)
	<i>c</i> (Å)	10.809(4)	10.1854(3)
	β (°)	111.37(2)	
Volume (Å ³)	1643.4(7)	1987.69(9)	1989.13(6)
<i>Z</i>	4	4	4
Density(calc) (Mg.m ⁻³)	1.214	1.495	1.490
Crystal size (mm)	0.05 × 0.17 × 0.29	0.07 × 0.10 × 0.14	0.10 × 0.13 × 0.15
μ (mm ⁻¹)	0.079	1.630	1.630
<i>F</i> (000)	648	904	896
Theta min-max	3.7-26.0	3.3-27.5	3.3-27.5
Observed data [<i>I</i> > 2 σ (<i>I</i>)]	1956	3989	4052
<i>R</i> / <i>R</i> _w	0.0348/0.0748	0.0321/0.0748	0.0339/0.0852
GOF	0.89	1.07	1.04
Min/max resd density (e.Å ⁻³)	-0.21/0.17	-0.62/0.72	-0.70/1.09
CCDC	667,957	667,958	667,959

The X-ray crystal structure determination of the starting material H₂had (Figure 1) shows trigonal pyramidal geometries around N1 [average C-N-C angle = 110.7(1)°] and N2 [average C-N-C angle = 110.0(1)°] with an average C-N bond of 1.472(2) Å (Table 2). The 2 C-OH bonds have an average value of 1.367(2) Å, and the orientation of the pendant arms around N1 is governed by the hydrogen-bonds H(O1)⋯N2, H(O2)⋯O1, H(O2)⋯N1 and H(C15)⋯O1 (see Table 3 and Figure 2).

The X-ray crystal structure analysis for [Hhpd]I revealed the presence of a complex organic pyridinium zwitterion with a dimethylammonium group, a phenolic ring and a pyridinium ring with an oxo group in the 2-position (Figure 3). The geometry around N1 is trigonal-pyramidal with an average C-N-C bond angle of 111.5(3)°, and an average N-C single bond value of 1.475(5) Å. Around N2 the average N-C bond is 1.490(5) Å and the average C-N-C bond angle is 111.9(3)°. The spatial arrangement of the pendant arms around N1 is governed by strong hydrogen bonds. The protonation of N2 is supported by strong intramolecular hydrogen bonds with O1 and N1, in addition to hydrogen bonds between H(O1) and the water of crystallization H₂(O3), and between H(C12) and O2 (Figure 4). The phenolic ring is planar, with the C1-O1 [1.375(4) Å] bond, shorter

than the C13-O2 [1.390(5) Å] bond on the pyridinium ring, and suggests that O2 is present as a singly charged oxo group. The C13-N3 and C17-N3 bonds have an average value of 1.396(6) Å, which differs insignificantly from the average C-C distance of 1.386(6) Å in this ring. Around N3 the average C-N-C bond angle is 120.0(4)°

Table 2. Selected bond lengths (Å) and angles (°).

H ₂ had			
O1-C3	1.363(2)	O2-C10	1.371(2)
C1-N1	1.477(2)	N2-C16	1.468(2)
C1-C2	1.505(2)	C2-C3	1.407(2)
C1-N1-C8	111.2(1)	C16-N2-C17	109.4(1)
N1-C1-C2	113.5(1)	O1-C3-C2	117.0(1)
C2-C7-C6	121.9(1)	C5-C6-C7	119.0(2)
[Hhpd]I.H ₂ O			
C1-O1	1.375(4)	C13-O2	1.390(5)
N1-C12	1.468(5)	C6-C7	1.507(5)
N3-C12	1.509(6)	N2-C10	1.491(5)
N3-C13	1.393(6)	N3-C17	1.398(6)
C7-N1-C8	111.4(3)	C10-N2-C11	110.8(3)
O1-C1-C2	121.8(3)	O2-C13-O3	116.3(4)
C13-N3-C17	118.0(4)	C12-N3-C13	123.4(4)
[dod]I.H ₂ O			
O1-C2	1.375(5)	O2-C8	1.382(5)
C2-N2	1.400(6)	N2-C6	1.395(6)
N3-C7	1.504(6)	C1-N1	1.474(5)
C1-N2	1.503(6)	C14-N4	1.494(5)
C1-N1-C7	110.9(3)	C14-N4-C16	112.5(3)
O1-C2-N2	117.1(4)	O2-C8-N3	117.7(4)
C2-N2-C6	118.3(4)	C7-N3-C8	120.2(4)

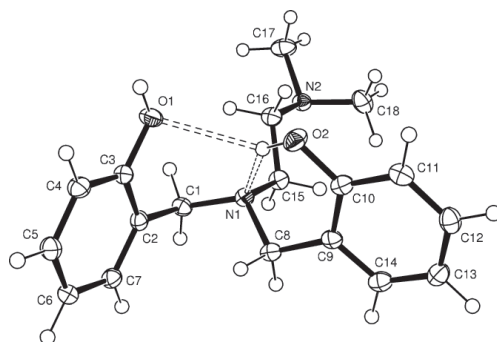


Figure 1. Molecular structure of [H₂had], showing the atom labeling scheme. Intramolecular hydrogen bonds are shown as dashed lines.

and the C12-N3 bond is 1.509(6) Å. The O2-C13-N3 [116.3(4)°] and O2-C13-C14 [122.7(4)°] bond angles are significantly different, due to the O(2)···H(C12) hydrogen bond.

The X-ray crystal structure analysis of [dod]I reveals that both 2-hydroxybenzyl groups of H₂had have been substituted by 2-oxypyridinium groups (Figure 5). The average C-N-C angles around N1 and N4 are 111.6(3)° and 111.7(3)°, respectively. The hydrogen-bonds O2···H(N4), N1···H(N4), O(1)···HA(C1) and N(3)···HB(C1) dictate the spatial arrangement of the arms around N1, and influence the O1-C2-N2 [117.1(4)°]

Table 3. Hydrogen-bond geometry (bond lengths in Å, angles in degrees).

H ₂ had			
D-H***A	H***A	D***A	<DHA
O1-H1***N2	1.77	2.736(2)	167
O2-H2***O1	2.48	3.164(2)	125
O2-H2***N1	1.83	2.710(2)	144
C15-H151***O1	2.52	3.264(2)	129
[Hhpd]I.H ₂ O			
N2-H72***O1	2.19	2.892(4)	141
N2-H72***N1	2.35	2.765(4)	111
O1-H81***3	1.96	2.628(6)	155
O3-H831***I	2.71	3.512(4)	167
C12-H12A***2	2.40	2.841(5)	106
[dod]I.H ₂ O			
N4-H4***2	2.12	2.894(4)	139
N4-H4***N1	2.28	2.764(4)	112
C1-H1***C1-	2.40	2.845(5)	106
H1***N3	2.61	3.028(6)	105

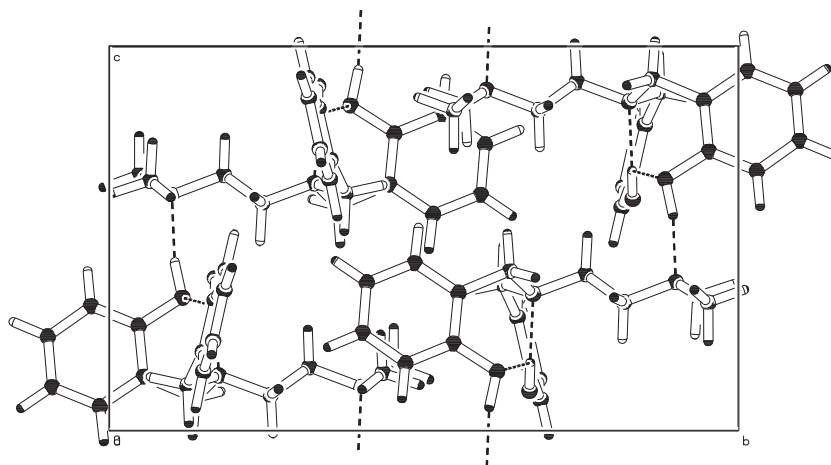


Figure 2. The crystal packing of [H₂had], viewed along the *a* axis. Intermolecular hydrogen bonds are shown as dashed lines.

and O2-C8-N3 [117.7(4)°] bond angles (Figure 6). Both pyridinium rings are planar, with the torsion angles N2-C2-C3-C4 = 0.7(7)° and C8-N3-C12-C11 = 0.2(6)°. The C2-O1 [1.375(5) Å] and C8-O2 [1.382(5) Å] bonds are significantly longer than the C-OH distances in H₂had and suggest the presence of C-O⁻ on the pyridinium rings. The C-C [average 1.383(5) Å] and C-N [average 1.396(6) Å] bonds in the pyridinium rings suggest delocalization. The C2-N2-C6 and C8-N3-C12 bond angles are 118.3(4)° and 117.9(4)°, respectively.

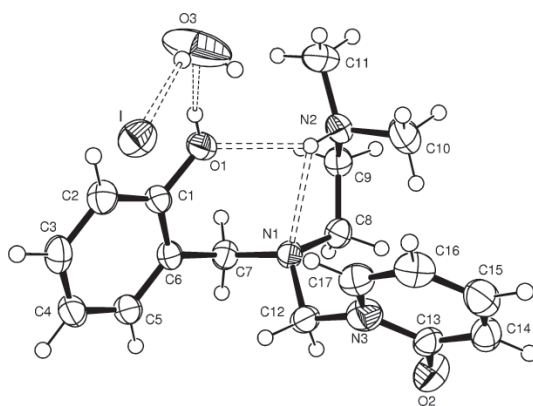


Figure 3. ORTEP drawing of [Hhpd]I.H₂O (50% probability). Intramolecular hydrogen bonds are shown as dashed lines.

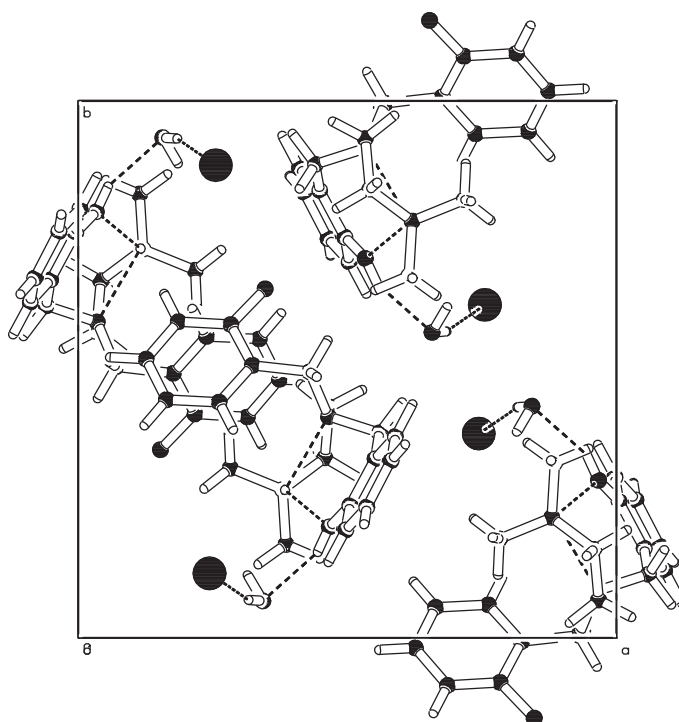


Figure 4. Packing diagram for [Hhpd]I.H₂O, viewed along the *c* axis.

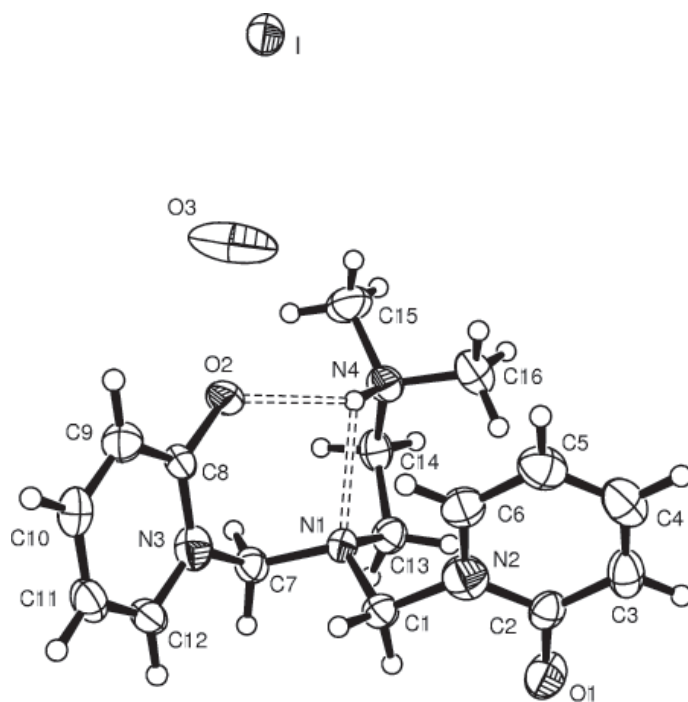


Figure 5. An ORTEP view of [dod]I.H₂O.

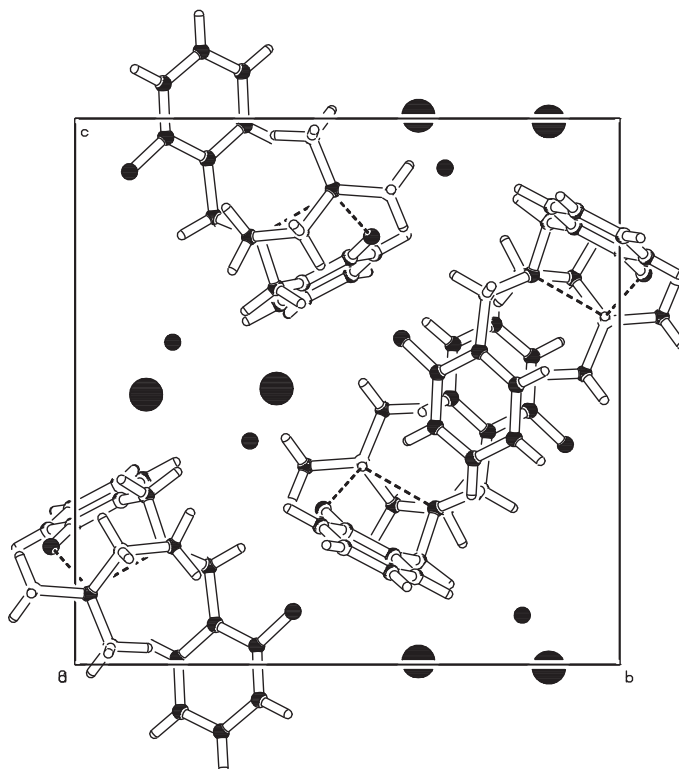
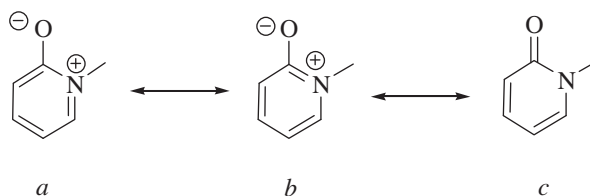


Figure 6. The packing of [dod]I.H₂O in the unit cell, viewed along the *c* axis.

The pyridinium rings can thus be described by the 2 resonance structures *a* and *b*, rather than *c*, in Scheme 2. This is somewhat surprising, since the pyridone form *c* is favoured in polar solvents and in the solid state.^{8,9}



Scheme 2. Possible resonance structures for the pyridinium ring.

In the IR spectra, the protonation of N2 and N4 in [Hhpd]⁺ and [dod]⁺, respectively, to form a dimethylammonium group is confirmed by the characteristic $\nu(\text{N-H})$ bands at 3276 and 3287 cm^{-1} . The $\nu(\text{C=N})$ bands of the pyridinium rings appear as strong peaks at 1593 [Hhpd⁺] and 1597 cm^{-1} [dod⁺]. Two strong absorptions at 1264 and 1233 [Hhpd⁺] and 1 at 1242 cm^{-1} [dod⁺] are assigned to $\nu(\text{C1-O1/C13-O2})$ and $\nu(\text{C2-O1/C8-O2})$, respectively. The ¹³C-NMR spectrum in (CD₃)₂SO is temperature independent and exhibits the expected signals for the 17 and 16 carbon atoms in the structures of [Hhpd]⁺ and [dod]⁺, respectively. The ¹H-NMR spectrum of [Hhpd]⁺ is complex with several overlapping multiplets, which made interpretation difficult and uncertain.

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