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CONFORMATIONAL DEPENDENCE OF SOLVENT AND LANTHANIDE INDUCED SHIFTS IN ORTHO-SUBSTITUTED N-BENZYLPYRIDINIUM IONS.

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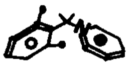
Substituted N-benzylpyridinium salts have been used as model compounds in studies on intramolecular charge-transfer interaction[1,2] and on the NAD^+/NADH redox system[3,4].

Their conformational properties have recently been shown[5] to depend critically on the number and location of substituents in analogy with the behaviour of more extensively studied bridged aromatic compounds such as diphenylmethanes[6,7] and diphenyl (thio)-ethers[8,9]. In non-, mono-, and di-*ortho*-substituted cases a helical conformation (A) prevails, while tri-*ortho*-substitution leads to the adoption of a nearly perpendicular conformation (B), as evident from 'H-NMR spectroscopy.



A

B

In conformation B H-2 is below the central region of the plane of the phenyl ring and is therefore expected to be strongly shielded. Upfield shifts for H-2 in tri-*ortho*-substituted compounds (**4**, **6**) relative to di-*ortho*-substituted compounds (**3**, **5**) of 0.6 - 0.7 ppm (in D_2O at 60 MHz) have been reported[5].

The remarkable solubility of some of the N-benzylpyridinium chlorides in chloroform and the troublesome signal assignment for the pyridinium ring protons in 4 and 6 at 60 MHz in D_2O, prompted us to investigate their 'H-NMR spectra in $CDCl_3$ both in the presence and in the absence of lanthanide shift reagents.

The results of these measurements are compiled in the Table.

'H-NMR data both in D_2O and in $CDCl_3$ show the expected strong upfield shift of H-2 in 4 and 6 relative to 3 and 5, in accordance with the perpendicular conformation claimed previously[5] for 4 and 6.

The upfield shifts in $CDCl_3$(1.1 - 1.4 ppm) appear to be much larger than in D_2O (~ 0.8 ppm). The difference originates from the fact that a rather large downfield shift (0.4-0.6 ppm) of H-2 an H-6 (which are close to the positive nitrogen atom) in $CDCl_3$ relative to D_2O is generally observed, while this solvent effect is absent for H-2 in 4 and 6. This observation seems indicative for a solvent inaccessible position of H-2 in such tri-ortho-substituted compounds.

Addition of lanthanide shift reagents to the $CDCl_3$ solutions leads to remarkable lanthanide induced shifts (LIS).

This seems rather unexpected since the shifts are observed for a cation containing no functional groups capable of complexation with the lanthanide ion.

However it has recently been suggested[10] that in such cases complexation of the lanthanide with the anion (i.e. Cl^-) takes place. The LIS observed thus originates from ion pairs between the cation and the lanthanide-complexed-anion.

Such shifts are expected to be a function of the cation-anion orientation.

It is therefore very interesting to note that in most compounds the largest LIS are observed for protons (H-2,6 and CH_2) closest to the positive nitrogen atom, the probable center for complexation with the anion.

Ortho-substitution in the phenyl ring (3 and especially 5) apparently hinders approach of the anion to the nitrogen atom as indicated by the decreased LIS for CH_2 and H-2,6 and the increased LIS for H-3,4,5.

Tri-ortho-substitution (e.g. 4 and 6) dramatically diminished the LIS of the remaining ortho-pyridinium proton (H-2). The largest shifts now being observed for H-4.

In conclusion the present study shows that the ortho-substitution pattern has a large influence on the solvent and anion accessibility of the pyridinium system in N-benzylpyridinium ions and that LIS can be used for studying cation-(complexed)anion interactions in solution.

The possible consequences of the conformationally controlled accessibility

Table 1 - 'H-NMR and Lanthanide Induced Shift[a] data on N-Benzylpyridinium ions

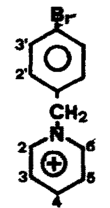
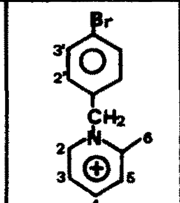
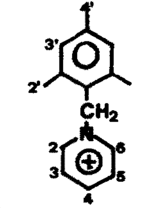
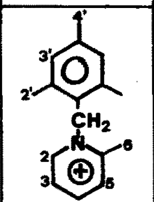
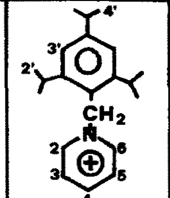
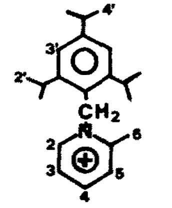
1 Chemical Shifts (ppm) measured at 100 MHz in D_2O (relative to DSS)

2 Chemical Shifts (ppm) measured at 100 MHz in $CDCl_3$ (relative to TMS)

3 Lanthanide Induced Shifts by $Pr(fod)_3$ in $CDCl_3$ (LIS-Pr; all upfield)

4 Lanthanide Induced Shifts by $Eu(fod)_3$ in $CDCl_3$(LIS-Eu;all downfield)

1	3
2	4

COMP	1	2	3	4	5	6
						
2	9.10 14.13 9.77 6.70	9.03 13.92 9.67 7.12	8.81 10.43 9.15 4.83	7.98 4.89 7.99 2.64	0.07 9.43 9.30 5.11	8.01 3.53 7.90 2.07
3	8.37 7.29 8.00 4.68	8.13 7.24 7.98 4.19	8.22 9.61 8.10 5.37	7.80 8.79 7.85 4.05	8.33 9.23 8.33 5.39	7.82 7.42 7.90 4.90
4	8.78 6.08 8.43 3.85	8.62 6.78 8.43 3.35	8.75 9.23 8.63 5.37	8.52 10.42 8.50 5.84	8.87 8.63 8.75 4.47	8.60 10.43 8.52 8.16
5	8.37 7.29 8.00 4.68	8.13 7.29 7.98 4.19	8.22 9.61 8.20 5.37	8.15 10.42 8.25 5.68	8.33 9.23 8.33 5.35	8.26 10.43 8.22 6.31
6	9.10 14.13 9.77 6.70	2.93 6.23 3.00 3.14	8.81 10.43 9.15 4.83	3.12 6.75 3.25 3.75	8.87 9.43 9.30 5.11	3.23 5.87 3.31 3.37
2'	7.70 4.44 7.47 2.31	7.43 4.96 7.27 ~	2.37 2.55 2.25 1.27	2.26 2.88 2.22 1.33	1.23 1.29 1.12 0.71	1.23 1.25 1.14 ~
3'	7.70 0.99 7.47 ~	7.43 0.81 7.27 ~	7.03 0.96 6.93 ~	7.06 0.83 6.90 ~	7.26 0.78 7.17 ~	7.32 0.63 7.13 ~
4'	- - - -	- - - -	2.33 0.37 2.28 ~	2.35 0.38 2.30 ~	1.42 0.39 1.28 ~	1.43 0.25 1.27 ~
CH_2	6.02 10.73 6.38 5.44	6.03 10.54 6.28 5.34	6.05 6.66 6.22 3.28	5.71 5.89 5.93 3.17	6.28 5.25 6.33 2.84	5.88 3.83 5.85 2.01
¢H a	- - - -	- - - -	- - - -	- - - -	3.30 2.85 (3.00) ~	(3.00) 2.87 (2.83) ~
¢H b	- - - -	- - - -	- - - -	- - - -	3.05 0.33 (3.00) ~	(3.00) 0.00 (2.83) ~

[a] The LIS indicated represent those calculated for one mole equivalent of shift reagent from linear extrapolation of the shifts observed for 0 - 0.1 mole equivalents of shift reagent (cf. ref.II for experimental details).

on the reactivity of the pyridinium system should be apparent, and this will be the subject of future investigation.

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