Tritium Nuclear Magnetic Resonance Studies of the Specificity in Platinum-catalysed Hydrogen Isotope Exchange of Nitrogen Heterocyclic Compounds

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The orientation of platinum-metal catalysed exchange between tritiated water and pyridine, the picolines, 2,6-lutidine, and the quinolines has been carefully studied by ^3H n.m.r. Exchange at 130 °C occurs preferentially at a position adjacent to the nitrogen atom unless a methyl substituent on C-2 hinders exchange, when a position remote from the methyl substituent is preferred as in alkylaromatic exchange. The results are interpreted in terms of previously proposed π-complex exchange mechanisms.

^3H NUCLEAR magnetic resonance spectroscopy is of use in catalytic hydrogen isotope exchange studies for the quantitative measurement of the distribution of isotope at various sites within the labelled molecule.[1,2] The advantages of the technique over the more conventional analytical methods involving mass spectrometry, ^1H n.m.r., and i.r. spectroscopic analysis of deuteriated materials have recently been illustrated.[3] However, one important aspect of tritium exchange studies coupled with ^3H n.m.r. analysis, is the possibility of studying the exchange pattern early in the exchange cycle, that is, well before scrambling of incorporated isotope becomes significant as previously observed during deuterium exchange over heterogeneous Group VIII transition metals.[4]

^3H N.m.r. spectra may readily be obtained on samples with activities of a few millicuries, and since it is convenient to use an isotope source of several 10s of millicuries the exchange may be studied when only a small part of the available isotope has been incorporated. In this way, the *initial* exchange rates at sites within the molecule may be independently estimated, and it is this information which is of paramount importance in postulating exchange mechanisms. Furthermore, isotope abundance within the labelled molecule remains very low throughout the exchange cycle and any isotope effects by virtue of substantial substitution within the molecule are minimised. Thus the changes in exchange rates noted in some circumstances in the past [5] where molecules became substantially substituted in deuterium are avoided.

A recent report by Elvidge *et al.*[6] of tritium exchange patterns within some nitrogen heterocycles led its authors to conclude that neither simple electronic considerations, nor minor steric factors, can reliably be invoked to account for or predict the exchange results. In this work the authors were careful to allow exchange to proceed to equilibrium, since the emphasis was on the production of highly tritiated materials. Thus the orientations they observed need not represent relative initial exchange rates since scrambling of incorporated isotope is well known over heterogeneous catalysts such as platinum.

Since deuterium exchange patterns in compounds such as pyridine and the quinolines [7] were important in the development of π-complex exchange mechanisms on metal surfaces [8] and relative exchange rates were interpreted by us in terms of steric and electronic effects, we have re-investigated tritium exchange in these compounds, utilising ^3H n.m.r. carefully to monitor the orientation of exchange well before equilibrium was established. The results reported here are rationalised in terms of the original π-complex mechanisms proposed from deuterium exchange studies.

EXPERIMENTAL

Platinum metal was prepared by sodium borohydride reduction of platinum dioxide as previously described.[7] The organic compound (0.1 ml) was placed in a reaction tube along with the prepared catalyst [from PtO_2 (50 mg)] and tritiated water (0.1 ml of 5 Ci ml^{-1}) added. The reaction mixture was degassed by three freeze–thaw cycles under vacuum (10^{-3} Torr) and the reaction ampoule flame-sealed and heated to the required temperature in an oven in a well ventilated fumehood. Samples were analysed by radio-g.l.c. and ^3H n.m.r. as described elsewhere.[1] Peaks in the n.m.r. spectrum were assigned on the basis of previously published chemical shift data.[6]

RESULTS

The results of exchange of pyridine, its methyl derivatives, and the quinolines with tritiated water catalysed by heterogeneous platinum are reported in the Table. The samples for which tritium distributions are quoted were selected at a stage in the exchange cycle where the initial orientation of the exchange was clearly apparent, but late enough such that exchange within the less active sites of the molecule was measurable. To achieve this objective it was necessary to choose a reaction temperature of 60 °C for most compounds, that is substantially below the 125 °C selected by the Surrey group for their study.[6] For completeness some results at higher temperatures are included in the Table.

The exchange patterns in these nitrogen heterocycles is dominated by a preference for exchange in positions adjacent to the nitrogen atom of the ring except where a methyl substituent is also adjacent to the nitrogen atom as in 2-picoline. In pyridine itself, the percentage of tritium per position is higher at C-4 than at C-2 and -6 but when allowance is made for the equivalence of two hydrogen atoms adjacent to nitrogen it is apparent that a tritium atom

TABLE

Platinum-catalysed tritium exchange in nitrogen heterocycles

Compound	Time (h)	Temp. (°C)	% Approach to equilibrium	% Incorporated tritium per site C(1)	C(2)	C(3)	C(4)	C(5)	C(6)	C(7)	C(8)	Me
Pyridine	3.5	60	22.4		21.8	11.3	33.8	11.3	21.8			
2-Picoline	6	60	17.8			<0.1	55.9	29.2	14.9			<0.1
3-Picoline	6	60	14.0		32.2		6.1	14.0	47.6			<0.1
4-Picoline	6	60	12.8		48.9	1.1		1.1	48.9			<0.1
2,6-Lutidine	6	60	21.0			21.8	56.5	21.8				<0.1
Pyridine	24	120	30.0		25.2	16.2	17.2	16.2	25.2			
2-Picoline	2	130	39.8			10.3	17.0	21.1	19.2			10.8
3-Picoline	2	130	24.8		24.1		21.1	23.9	29.6			0.4
4-Picoline	1.5	130	26.7		35.9	11.5		11.5	35.9			1.7
2,6-Lutidine	1.5	130	46.1			15.4	14.4	15.4				9.1
Quinoline	3	130	19.0		31.2	26.3	6.9	2.5	20.4	5.0	7.7	
Isoquinoline	6	130	19.6	41.2		45.0	2.6	3.2	2.8	<0.1	5.3	

is more likely to enter a pyridine molecule at C-2 or -6 than at C-4.

Consideration of the tritium orientation in the picolines and 2,6-lutidine shows distinctly the marked deactivation of ring positions adjacent to methyl substituents. This steric '*ortho*'-deactivation by bulky substituents is well documented in reports of deuterium exchange of alkylbenzenes[9] and more recently in tritium n.m.r. studies of exchange in halogenobenzenes as well as alkylbenzenes over a variety of heterogeneous and homogeneous Group VIII metal catalysts.[3]

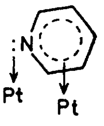
Further features of the results reported in the Table include, first, at 60 °C a preference within the single-ring compounds for exchange at C-4 (*i.e. para* to nitrogen) except where influenced by an adjacent methyl substituent, and secondly, the complete absence of exchange within the methyl substituents themselves at 60 °C. Elevation of the reaction temperature of the single-ring compounds from 60 to *ca.* 130 °C has the effect of considerably diminishing the apparent differences in exchange rates within the ring and of promoting slight exchange within methyl substituents. Thus, for example in 3-picoline, even at only 25% approach to equilibrium, tritium orientation is close to random within the ring.

DISCUSSION

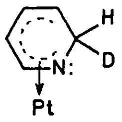
The results are in general agreement with the earlier deuterium exchange study[7] where, for platinum metal, the orientation observed at 130 °C was only slightly different to that from random exchange, while quinoline and isoquinoline exhibited a marked preference for exchange adjacent to the heteroatom. The problem of resolution of ^1H n.m.r. and the requirement of substantial isotopic abundance of deuterium precluded studies of pyridine at lower temperatures and the measurement of the deuterium orientations within the exchanged picolines in this earlier study.[7]

The present results support the theory previously proposed that, with a noble metal surface such as platinum adsorption of a nitrogen heterocyclic aromatic compound involves charge transfer of not only the nitrogen lone pair electrons but also the π-electrons of the ring [species (1)] and exchange may occur by either the associative intermediate [species (2)] or the dissociative intermediate [species (3)].

The function of the nitrogen lone pair is to increase the interaction between the organic compound and the catalyst surface such that the hydrogen atoms adjacent to the nitrogen atom are favourably placed for exchange. On this basis the dissociative mechanism is preferred. However, from the present results it appears that where a methyl substituent is adjacent to the nitrogen atom on the ring, the nitrogen lone pair interaction may be considerably diminished in favour of interaction with the π-electrons of the ring with preferred formation of a dissociative species at a site remote from the nitrogen atom [species (4)]. This steric effect is similar to that proposed previously[9,10] to explain the pronounced '*ortho*-deactivation' within the alkyl- and halogenobenzenes. The recent tritium n.m.r. study[3] of the halogenobenzene systems showed distinctly that the effect was dominantly steric in nature rather than electronic.



(1)



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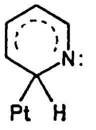

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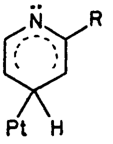

(4)

Thus it is concluded that, while an electronic effect appears to play a part in determining overall exchange patterns in heterocyclic compounds in so far as the lone pair of the nitrogen is thought to influence the position favoured for exchange, even a methyl substituent on the ring may lead to dominant steric effects.

The present results are not in disagreement with those of Elvidge *et al.*[6] since their results for most compounds represent tritiation patterns when exchange is allowed to proceed close to equilibrium. But a comparison of the two studies shows that it is necessary, before observations of exchange patterns are attributed directly to relative exchange rates, and mechanistic interpretations deduced therefrom, that it be established that neither exchange equilibrium nor concurrent randomisation reactions complicate the isotope distributions.

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