

## Hydrogen-Deuterium Exchange in Some Polyazaindenes

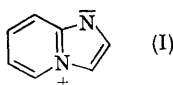
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PYRIDINE exchanges the protons at position-2 and -6 for deuterium only under fairly drastic conditions (10% NaOD at 200°).<sup>1</sup> Pyridine *N*-oxide exchanges at the same positions under somewhat milder conditions (D<sub>2</sub>O at 180°)<sup>1,2</sup> and H-2 and H-6 are readily exchanged in *N*-methylpyridinium salts (D<sub>2</sub>O at 130°).<sup>1,3</sup>

While these deuteration reactions need not necessarily occur by the same mechanisms, the results indicate an increased facility for proton exchange as the positive charge on the nitrogen atom increases.

We have recently indicated that the ground states of many polyazaindenes include considerable contributions due to zwitterionic structures such as (I).<sup>4</sup>



In view of these considerations, we can predict that the polyazaindenes will undergo deuterium exchange under conditions similar to those which are successful in the pyridine series.

\* Deuteration of *s*-triazolo[4,3-*a*]pyridine under neutral conditions results in exchange of H-3 only (ref. 5). Acid-catalyzed exchange studies on some heterocyclic diquaternary salts were reported by Curphy (ref. 6) who concluded that "hydrogen exchange in heterocyclic systems occurs by at least two mechanisms, which operate in some cases with nearly equal facility."

† Two recent Papers (ref. 7) describe the deuteration of some five-membered-ring heterocycles.

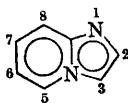
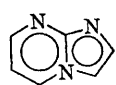
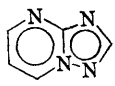
We describe the results of a preliminary study of the deuteration of some polyazaindenes.\* The data for deuterium exchange under acid, as well as base, catalysis are reported in the Table. None of the compounds exchanges deuterium in D<sub>2</sub>O at 100°. The position of substitution was established by n.m.r. spectroscopy, using the n.m.r. analyses previously reported.<sup>4</sup> The exchange reactions were conducted until at least 95% of the exchangeable protons had been exchanged.

*Protons attached to five-membered rings.* †—The proton in position-3 of the imidazo[1,2-*a*]pyridine (II) and of the imidazo[1,2-*a*]pyrimidine (III) exchanges much more readily under both acid and base catalysis than does H-2 in these two ring systems. The acid-catalyzed exchange of H-3 occurs much more readily in the pyridine (II) than in the pyrimidine (III) system; this is consistent with the relative nucleophilicity of position-3 in the two ring systems. This position is also the one involved in electrophilic substitution reactions, as has been shown previously.<sup>4</sup>

The introduction of another nitrogen atom into the ring systems facilitates base-catalyzed removal of some protons, to afford ylid-type intermediates.

TABLE

Deuterium exchange data [ $t_{\frac{1}{2}}$  (hr.)] for some polyazaindenes

Compound <sup>a</sup>	Position of substitution for base catalysis <sup>a</sup> (65°) <sup>b</sup>					Position of substitution for acid catalysis <sup>c</sup> (100°)	
(II) 	H-2 —	H-3 16	H-5 53	H-6 —	H-7 —	H-3 4·5	H-6 —
(III) 	15	2·5 (130)	0·25 (2)	8	—	13	—
(IV) 	10·5	—	>0·05 (0·1)	1·2 (6)	10·5	—	15

<sup>a</sup> 0·5 M-NaOMe in MeOD<sup>b</sup> Numbers in parentheses refer to half-lives at room temperature.<sup>c</sup> 3·0 M-D<sub>2</sub>SO<sub>4</sub><sup>d</sup> The numbering of the positions used is for the sake of clarity in the discussion.

Thus, it is not surprising that H-3 is more readily exchanged in the pyrimidine system (III), and that H-2 is exchangeable in compounds (III) and (IV), while it is not exchangeable (under the conditions cited in the Table) in imidazo[1,2-*a*]pyridine (II).

*Protons attached to six-membered rings.*—The only six-membered-ring proton which is subject to acid-catalyzed deuterium exchange is H-6 of 1,2,4-triazolo[1,5-*a*]pyrimidine (IV). This is also the position which undergoes electrophilic substitution in this ring system.<sup>8</sup>

Under base catalysis, H-5 is exchanged most readily in 1,2,4-triazolo[1,5-*a*]pyrimidine (IV) and least readily in imidazo[1,2-*a*]pyridine (II), an

observation that is again consistent with an ylid-type intermediate. The stabilization of the ylid at position-5 of compounds (III) and (IV) is expected to be much more pronounced than it is in compound (II), where no *para-sp*<sup>2</sup>-nitrogen atom is present. The half-lives reported in the Table are in agreement with these suggestions.

A similar argument can be made to account for the more rapid exchange of H-6 and of H-7 in compound (IV) as compared with compounds (II) and (III).

A Communication published shortly after this manuscript was prepared discusses some further aspects of the deuteration of pyridine compounds.<sup>9</sup>

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<sup>1</sup> Y. Kawazoe, M. Ohnishi, and Y. Yoshioka, *Chem. and Pharm. Bull. (Japan)*, 1964, **12**, 1384.<sup>2</sup> J. A. Zoltewicz and G. M. Kauffman, *Tetrahedron Letters*, 1967, 337.<sup>3</sup> A. R. Katritzky, B. J. Ridgwell, and A. M. White, *Chem. and Ind.*, 1964, 1576; P. Bellingham, C. D. Johnson, and A. R. Katritzky, *ibid.*, 1965, 1384.<sup>4</sup> W. W. Paudler and H. L. Blewitt, *Tetrahedron*, 1965, **21**, 353; *J. Org. Chem.*, 1965, **30**, 4081; W. W. Paudler and J. E. Kuder, *ibid.*, 1966, **31**, 809; *J. Heterocyclic Chem.*, 1966, **3**, 33; W. W. Paudler and L. S. Helmick, *ibid.*, p. 269.<sup>5</sup> K. T. Potts, H. R. Burton, and S. K. Roy, *J. Org. Chem.*, 1966, **31**, 265.<sup>6</sup> T. J. Curphy, *J. Amer. Chem. Soc.*, 1965, **87**, 2063.<sup>7</sup> R. A. Olofsen and J. M. Landesberg, *J. Amer. Chem. Soc.*, 1966, **88**, 4263; R. A. Olofsen, J. M. Landesberg, K. N. Houk, and J. S. Michelman, *ibid.*, p. 4265.<sup>8</sup> Y. Makisumi, *Chem. and Pharm. Bull. (Japan)*, 1961, **9**, 808.<sup>9</sup> R. A. Abramovitch, G. M. Singer, and A. R. Vinutha, *Chem. Comm.*, 1967, 55.