Tetrahedron Vol. 42, No. 1, pp. 89 to 92, 1986
Printed in Great Britain.

0040-4020/86 $3.00+.00

THE APPLICATION OF A NEW AROMATICITY INDEX TO SIX-MEMBERED RING HETEROCYCLES

C. W. BIRD

Department of Chemistry, King's College London(KQC),
Kensington (Queen Elizabeth) Campus,
Campden Hill, London W8 7AH, England.

(*Received in UK 2 September* 1985)

Abstract-A previously described index of aromatic character has now been applied to six-membered ring heterocycles. Of particular interest is its ability to indicate the extent of aromatic character retained by the amide form of potential hydroxyheterocycles.

An earlier paper[1] introduced a new index of aromatic character based upon a statistical evaluation of the deviations in peripheral bond orders, which can be derived readily from experimentally determined bond lengths. Its utility was initially exemplified with reference to five-membered ring heterocycles. The present paper extends this treatment to their six-membered counterparts.

The aromaticity indices, I_6, calculated for a range of six-membered heterocycles are listed in Table 1. The values were obtained following the procedure described earlier[1] and as before are based wherever possible on the bond lengths recorded for the parent heterocycle.

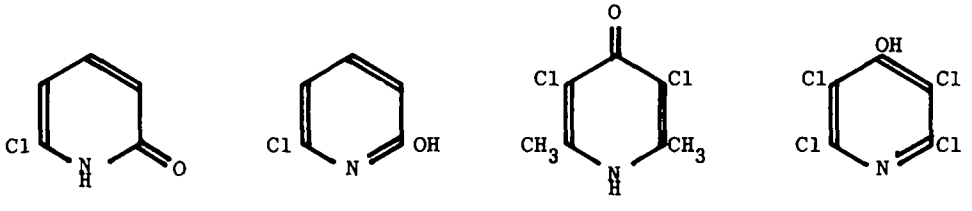
TABLE 1 Aromaticity Indices for Six-membered Heterocycles (I_6)

Heterocycle	I_6	Ref.[a]	Heterocycle	I_6	Ref.[a]
(Benzene	100	)	Pyridazine	78.9	10
Pyridine	85.7	2	Pyrimidine	84.3	11
Pyridinium methiodide	66.7	3	Pyrazine	88.8	12
Pyridine N-oxide	74.4	4	1,2,3-Triazine	76.9	13
Pyridinium dicyano-methylide	70.1	5	1,2,4-Triazine	86.1	14
			1,3,5-Triazine	100	15
Pyridinium N-nitroimine	76.0	6	1,2,4,5-Tetrazine	97.8	16
Phosphorin	74.1	7	Pyran-2-one	32.9	17
Arsenin	66.9	7	Pyran-4-one	37.2	18
Pyrylium cation	65.8	8	Pyran-4-thione	47.9	18
1,3,5-Thiadiazinium cation	53.1	9	1,2,6-Thiadiazin-4-one	54.2	19

[a] Reference to source of bond lengths used for calculation of I_6

In keeping with expectation the indices indicate decreasing aromaticity in the sequence: benzene >pyridine >phosphorin >arsenin~pyrilium cation. Conversion of pyridine into a quaternary salt, the N-oxide or an N-ylide results in a lowering of its aromaticity. The effect of the introduction of additional ring nitrogen atoms depends upon their orientation, thus pyridazine <pyrimidine~ pyridine <pyrazine. This presumably reflects the more even distribution of electronic charge effected by a more symmetrical arrangement of the nitrogen atoms. The effect is perhaps more clearly emphasised in the case of the isomeric triazines where aromaticity increases in the sequence: 1,2,3- <1,2,4- <1,3,5-triazine.

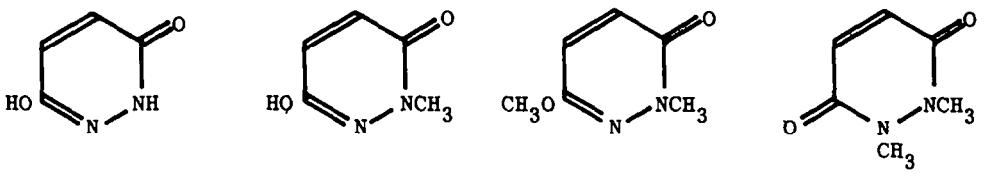
The low aromaticity generally accorded to 2- and 4-pyrones is borne out by the I_6 values of 32.9 and 37.2 respectively. Unfortunately no bond lengths have been recorded for the corresponding thiapyrones, but the I_6 value calculated for thiapyran-4-thione of 40.8 when compared with that of 47.9 for pyran-4-thione suggests that the thiapyrones are less aromatic than their oxygen counterparts. In contrast the corresponding 2- and 4-pyridones still retain much of the aromaticity of the corresponding hydroxypyridine, cf. Figure 1. The slightly lower I_6 values calculated for these hydroxypyridines than the parent heterocycle may arise from the participation of the ring nitrogen in hydrogen bonding in the crystal lattice. Reference has been made above to the effect of involvement of the pyridine nitrogen lone pair in bond formation in lowering the I_6 value. It is of particular interest that these results indicate similar aromaticities for the 2- and 4-pyridone systems. Recent molecular orbital calculations on the changes in resonance energies of cyclic polyenes caused by distortions indicate that the relationship between these aromaticity indices and resonance energies is a non-linear one[20]. However, the differences in the aromaticity indices for the pairs of tautomers would seem to be in reasonable qualitative accord with the estimated resonance energy difference of ca. 30kJ/mole between 2-pyridone and its hydroxy tautomer[21]. Resonance energies in the range 96-134kJ/mole have been attributed to pyridine[22].



59 [24] 81 [24] 61 [25] 81 [26]

FIGURE 1

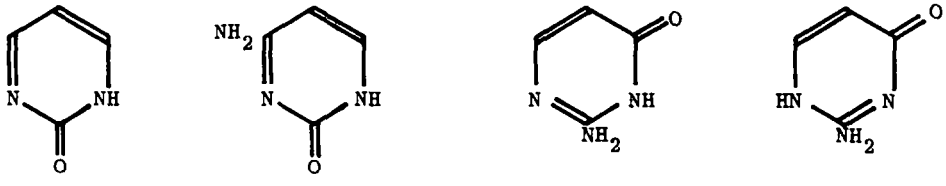
The aromaticity indices obtained for the principal tautomer of 3,6-dihydroxypyridazine (maleic hydrazide) and some of its derivatives are shown in Figure 2. Comparison of these values with that for pyridazine itself, I_6= 78.9, indicates that there is a similar energy difference between 6-hydroxypyridazinone and its dihydroxy tautomer to that observed in the 2-hydroxypyridine/2-pyridone system. While this appears an eminently reasonable conclusion there appears to be no other quantitative information on this topic. There is an even more surprising lack of information on the energetic differences between the tautomeric forms of the hydroxypyrimidines. The aromaticity indices for a range of compounds displayed in Figure 3 provide some useful guidance on this aspect. Comparison of the I_6



63 [27] 62 [28] 60 [29] 49 [30]

FIGURE 2

indices for 2-pyrimidone and cytosine with the value of 84.3 for pyrimidine shows once more a similar difference between the tautomers to that found for the 2-hydroxypyridine/2-pyridone situation suggesting a parallel energy difference. It is noteworthy that a recent[23] ab initio molecular orbital study deduced an energy difference of 29.8kJ/mole between cytosine and its hydroxy tautomer. Another interesting feature of the data in Figure 3 is the higher aromaticity indicated for 3H-isocytosine than its 1H-tautomer, especially in view of the close comparability of 2- and 4-pyridones. It would be particularly interesting to know what effect if any the amino substituent has on the situation. In view of the controversies that have arisen over the comparison of conclusions regarding tautomeric equilibria studied in differing environments it must be emphasised that all of the present data regard molecules in the solid state.



64 [31] 61 [32] 66 [33] 59.5 [33]

FIGURE 3

The foregoing discussion indicates the potential value of this aromaticity index approach for examining aromaticity dependent properties or behaviour of six-membered heterocycles, just as was earlier exemplified for their five-membered counterparts.

REFERENCES

1. C.W. Bird, Tetrahedron, 1985, 41, 1409.
2. F. Mata, M.J. Quintana and G.O. Sørensen, J. Mol. Struct., 1977, 42, 1.
3. R.A. LaLancette, W. Furey, J.N. Costanzo, P.R. Hemmes and F. Jordan, Acta Cryst., Part B, 1978, 34, 2950.
4. O. Snerling, C.J. Nielsen, L. Nygaard, E.J. Pedersen and G.O. Sørensen, J. Mol. Struct., 1975, 27, 205.
5. C. Bugg and R.L. Sass, Acta Cryst., 1965, 18, 591.
6. J. Arriau, J. Deschamps, J.R.C. Duke, J. Epsztajn, A.R. Katritzky, E. Lunt, J.W. Mitchell, S.Q. Abbas Rizvi and G. Roch, Tetrahedron Letters, 1974, 3865.
7. A.J. Ashe III, Acc. Chem. Res., 1978, 11, 153.
8. M.G.B. Drew, G.W.A. Fowles, D.A. Rice, and K.J. Shanton, J. Chem. Soc., Chem. Commun., 1974, 614.
9. G.V. Boyd, P.F. Lindley and G.A. Nicolaou, J. Chem. Soc., Chem. Commun., 1984, 1105.

10. A. Almenningen, G. Bjørnsen, T. Ottersen, R. Seip and T.G. Strand, Acta Chem. Scand., Ser. A, 1977, 31, 63.
11. L. Fernholt and C. Rømming, Acta Chem. Scand., Ser. A, 1978, 32, 271.
12. B.J.M. Bormans, G. De With and F.C. Mijlhoff, J. Mol. Struct., 1977, 42, 121.
13. E. Oeser and L. Schiele, Chem. Ber., 1972, 105, 3704.
14. J.L. Atwood, D.K. Krass and W.W. Paudler, J. Heterocycl. Chem., 1974, 11, 743.
15. G.J. Bullen, D.J. Corney and F.S. Stephens, J. Chem. Soc., Perkin Trans 2, 1972, 642.
16. F. Bertinotti, G. Giacomello and A.M. Liquori, Acta Cryst., 1956, 9, 510.
17. D.J. Chadwick, I.W. Easton and R.A.W. Johnstone, Tetrahedron, 1984, 40, 2451.
18. J.N. Macdonald, S.A. Mackay, J.K. Tyler, A.P. Cox and I.C. Ewart, J. Chem. Soc. Faraday 2, 1981, 77, 79.
19. S. Harkema, Acta Cryst., Ser. B, 1978, 34, 2927.
20. J. Paldus and E. Chin, Int. J. Quantum Chem., 1983, 24, 373; J. Paldus, E.Chin and M.G. Grey, ibid., 1983, 24, 395; R. Pauncz and J. Paldus, ibid., 1983, 24, 411; J. Paldus and M. Takahashi, ibid., 1984, 25, 423.
21. C.D. Johnson, Comprehensive Heterocyclic Chemistry, eds. A.R. Katritzky and C.W. Rees, Pergamon Press, Oxford, 1984, vol. 2, p.99.
22. M.J. Cook, A.R. Katritzky and P. Linda, Adv. Heterocycl. Chem., 1974, 17, 255.
23. M.J. Scanlan and I.H. Hillier, J. Amer. Chem. Soc., 1984, 106, 3737.
24. J. Almlöf, Å. Kvick and O. Olovsson, Acta Cryst., Ser. B, 1971, 27, 1201.
25. F.P. Boer, J.W. Turley and F.P. van Remoortere, J. Chem. Soc., Chem. Commun., 1972, 573.
26. F.P. Boer, Acta Cryst., Ser. B, 1972, 28, 3200.
27. P.D. Cradwick, J. Chem. Soc., Perkin 2, 1976, 1386.
28. T. Ottersen, Acta Chem. Scand., Ser. A, 1974, 28, 661.
29. T. Ottersen, Acta Chem. Scand., Ser. A, 1974, 28, 666.
30. T. Ottersen, Acta Chem. Scand., 1973, 27, 835.
31. S. Furberg and J. Solbakk, Acta Chem. Scand., 1970, 24, 3230.
32. D.L. Barker and R.E. Marsh, Acta Cryst., 1964, 17, 1581.
33. B.D. Sharma and J.F. McConnell, Acta Cryst., 1965, 19, 797.