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HETEROAROMATICITY. 6. THE EFFECT OF MOLECULAR DISTORTION ON AROMATICITY

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Abstract - The application of a recently described aromaticity index is shown to provide a convenient means of assessing the extent of change in aromaticity of a benzenoid or heterocyclic ring occasioned by steric overcrowding or restrictive ring bridging.

While planarity of benzenoid and heterocyclic rings provides the optimum geometry for conjugation and ensuing aromatic character there is a growing number of such compounds which are not planar. The effect is usually engendered either by steric overcrowding of substituents, or by restrictive trans-ring bridges. The intentional imposition of such distortions has attracted much attention as it offers the possibility of causing bond fixation so that benzene, for example, might tend towards a cyclohexatriene structure. In practice much of the molecular strain resulting from the imposed distortion is accommodated by deformation of bonds and bond angles external to the ring and it is difficult to assess that portion specifically associated with the ring itself. The purpose of this paper is to demonstrate that application of the recently introduced[1] energetically based aromaticity index provides at least a semiquantitative solution to this problem.

The aromaticity index (I_A) is based upon a statistical evaluation of the extent of variation of ring bond order as given by the expression $I_A = 100F(1 - V/V_K)$ where $V = 100/\bar{N} \sqrt{(N - \bar{N})^2/n}$ and $\bar{N}$ is the arithmetic mean of the n various ring bond orders, N. V_K is the value of V for the corresponding non-delocalised Kekule form and F is a scaling factor with values of 1.235, 1, 2.085 and 1.84 for five-membered, six-membered, fused five-six and fused six-six membered ring systems. On this scale benzene, with a resonance energy of 2β, has an I_A of 100 so that a unitary increment on the I_A scale corresponds to 0.02β ie. ca. 0.36 Kcals/mole if we assume the commonly used value of 18Kcals/mole for β

A theoretical study[2] of the effects of different modes of ring deformation of benzene on its resonance energy indicates that a boat conformation, cf. Fig. I, is preferable in this respect to a half-boat or chair conformation. The angle α between the planes $C_1C_2C_3$ and $C_1C_3C_4C_6$ is a convenient indication of the extent of distortion. An angle α of 10° corresponds to a displacement of about 0.13 Å and 30° to one of ca. 0.36 Å. In many situations (vide infra) different α's are observed at the bowsprit and stern.

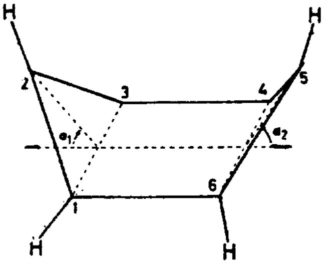
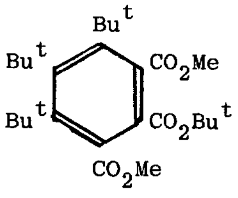
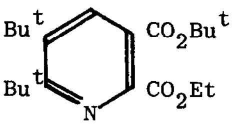


FIGURE I. Boat conformation of deformed benzene ring.

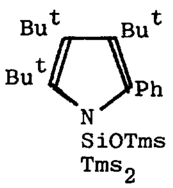
Despite its less favourable energetic status the flattened chair conformation is adopted by hexakis(trifluoromethyl)[3], hexakis(trimethylgermyl)[4] and hexakis(trimethylsilyl)benzene[5] with deviations of 0.024, 0.073 and 0.106 Å respectively from the mean plane. The corresponding I_A's are 93, 92 and 79 respectively relative to 100 for benzene. It should be noted that although the trimethylgermyl group is larger than its silicon counterpart the longer carbon-germanium bond keeps the groups further apart thus



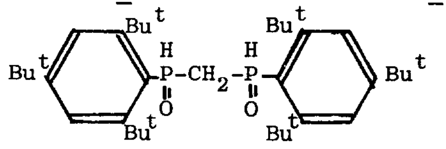
(1)



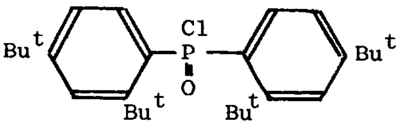
(2)



(5)



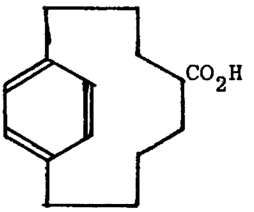
(3)



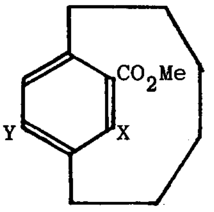
(4)

greatly reducing the distortion. Surprisingly, 1,2,4,5-tetra-t-butylbenzene (I_a = 88) is planar[6] whereas 3,4-di-t-butylbenzoic acid (I_A = 81) adopts a flattened twist boat conformation[7]. The hexasubstituted benzene (1), α = 30.1 and 11.6°, and the penta-substituted pyridine (2), α = 25.5 and 12.9°, provide[8] an interesting comparison. Both adopt an almost identical boat-like conformation with the central t-butyl group bearing carbon displaced by ca. 0.35 Å and the opposite carbon by ca. 0.145 Å, but while (1), I_A = 88, suffers an appreciable loss of aromaticity the pyridine (2) has an I_A

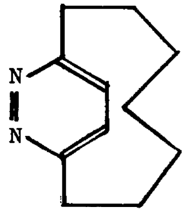
value identical to that of pyridine. Clearly in the latter case the modification of bond lengths compensates for loss of planarity. The benzene rings in (3)[9], $\alpha = 10-15^\circ$, $4.3-7.3^\circ$, also are forced into a boat-like conformation leading to an I_A of 82, and large distortions are also reported for (4)[10] but no bond lengths are as yet available. 2,3-Di-t-butylquinoxaline[11] $I_A = 134$ only experiences a slight increase relative to the parent quinoxaline, $I_A = 132$. The potential role of peri-substituents in bicyclic systems is indicated by the case of 1,3,6,8-tetra-t-butylnaphthalene[12], $I_A = 136$, relative to 142 for naphthalene, in which the rings adopt a flattened half-chair conformation with C1 and C8 displaced 0.29 Å above and below the mean plane.



(6)



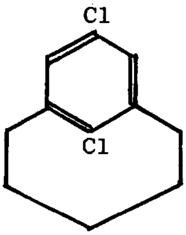
(7) $X = CO_2Me$, $Y = H$
(8) $X = H$, $Y = CO_2Me$



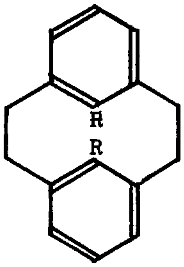
(9)

Information on effects of structural overcrowding on five-membered heterocycles is more limited. The vicinal positioning of the two bulky groups in 3,4-di-t-butylthiophene[13] results in marked lengthening of the C3 - C4 bond to 1.66 from 1.423 Å, and a consequent lowering of I_A to 16 compared to 81.5 for thiophene. However, judicious bond lengthening can also serve to increase aromaticity as in the case of 4,5-di-t-butylimidazole[14] with $I_A = 83$ compared to 79 for imidazole. While the two preceding examples retain ring planarity the pyrrole (5) assumes an envelope conformation ($\alpha = 10.4^\circ$) with the phenyl bearing carbon displaced from the plane of the remaining ring atoms. This results in a substantial lowering of I_A to 65.5 from the value of 85 for pyrrole.

1,4-Bridging of six-membered rings by a sufficiently shortened methylene chain results in the ring adopting a boat conformation. As would be expected the shorter the methylene chain the greater the distortion and this is well borne out by the compounds (6)[16] $I_A = 95$, (7)[17] $I_A = 90$ and (8)[18] $I_A = 91$ with $\alpha = 9.23$, 19.5 and 19.4° respectively. Surprisingly the effect is rather less pronounced for the bridged pyridazine (9)[19] with $I_A = 76.5$ versus 79 for pyridazine. In contrast to the symmetrically distorted boat conformation observed for the foregoing compounds 1,3-bridging, as in (10)[20] $\alpha = 26.8$ and 12° $I_A = 96$, results in the C2 atom being much more displaced from the ring plane than is C5. Similar distortion is

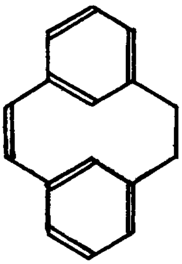


(10)

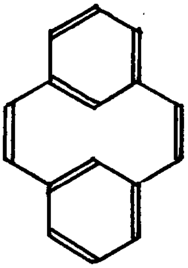


(11) R = H

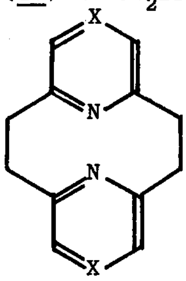
(14) R = CH$_2$Br



(12)

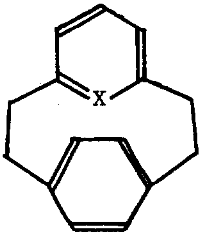


(13)



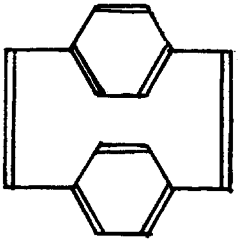
(15) X = CH

(16) X = N

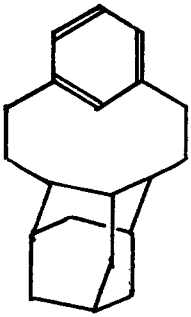


(17) X = CH

(18) X = N



(19)



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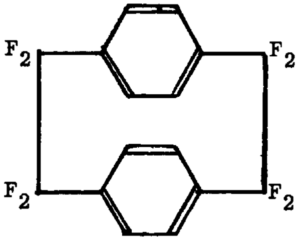

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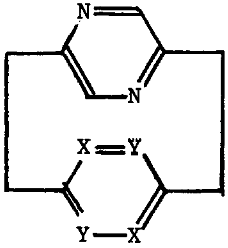
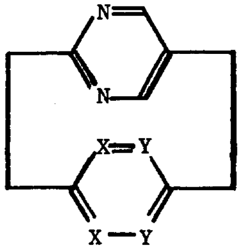


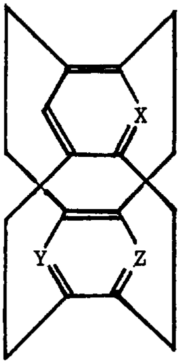
(22) X = CH, Y = N

(23) X = N, Y = CH



(24) X = N, Y = CH

(25) X = CH, Y = N

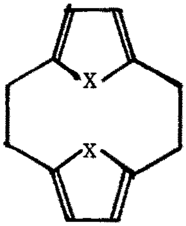


(26) X = Y = CH

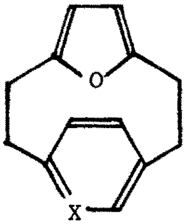
(27) X = Y = N, Z = CH

(28) X = Z = N, Y = CH

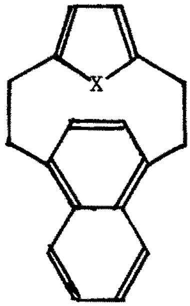
observed in metacyclophanes where the derivatives (11)[21] $I_A = 98$, (12)[22] $I_A = 96$, and (13)[23] $I_A = 92.5$ provide an interesting illustration of the effect of increasing rigidity on displacement of the C2 ring atom and hence the lowering of aromaticity. It should be noted that, as in other systems considered later, the double bonds are essentially orthogonal to the benzene rings. The bulky C2 substituents in (14)[24] increase the deformation even more markedly. The effects are more marked in the pyridinophane (15)[25] $I_A = 78$ versus 86 for pyridine, and the pyrazinophane (16)[26] $I_A = 84.5$ versus 89 for pyrazine possibly due to electrostatic repulsions between the transannular nitrogen atoms. Diminution of aromaticity is even more marked in the meta-bridged rings of the metaparacyclophanes (17)[27] $I_A = 87$ versus 100, and (18)[28] $I_A = 75$ versus 86. However, the I_A of 90 observed for the para bridged benzene rings,α ca. 18°, of (17) and (18) is not so low as would have been anticipated from the value of 77 for the paracyclophane (19)[29] with $\alpha = 13.7°$. By far the largest decrease in aromaticity occasioned by meta-bridging is encountered in the adamantophane (20)[30] with an I_A for the benzenoid ring of 76.6.



(29) X = NH
(30) X = S
(31) X = O



(32) X = CH
(33) X = N

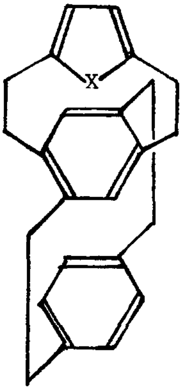


(34) X = O
(35) X = S

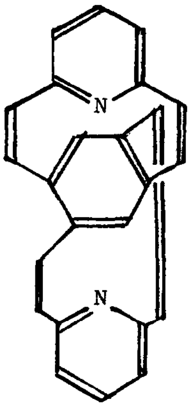
The parent [2.2]paracyclophane (21)[31], $I_A = 93$, with a symmetrical boat-like conformation of the benzene ring, $\alpha = 12.6°$, suffers a modest lowering in aromaticity as is also observed for the pyrazines (22) and and (23)[26], with I_A's of 84.5 and 86 versus 89 for pyrazine itself, and the pyrimidines (24) and (25)[32], with I_A's of 79.5 and 80 relative to 84 for pyrimidine, having α's of 14 to 15°.

Introduction of additional bridges as in the [2.2.2.2]cyclophanes (26)[33], $I_A = 94$, (27)[34] $I_A = 82$ v. 86, and (28)[35] $I_A = 81.5$ v. 86, causes a more subtle change in that the unsubstituted carbon ring atoms are now displaced from the plane of the other four carbons with α's ca. 12°.

The five-membered heterocyclic cyclophanes (29)[36] $I_A = 80.5$ v. 85, (30)[37] $I_A = 72.5$ v. 81.5, and (31)[38] $I_A = 33.5$ v. 53 are a particularly interesting family. The heterocyclic rings are anti-parallel in all three cases but, whereas the pyrrole rings in (29) are planar, the heteroatoms in (30) and (31) are displaced by 0.196 and 0.085 Å respectively leading to envelope conformations. This effect results in a very marked decrease in ring aromaticity, being most prominent for the furanophane (31). The particular sensitivity of the furan ring is further illustrated by the cyclophanes (32)[36], (33)[38], and (34)[39] with I_A's of 42.5, 36 and 44 respectively. In the case of (32) and (34) the furan ring is essentially planar but the oxygen atom is displaced by 0.055 Å out of plane in (33). The thiophene ring in (35)[36] with $I_A = 74$ *v.* 81.5 is also planar. It is noteworthy that the naphthalene moiety in (34)[39] $I_A = 138.5$ and (35)[36] $I_A = 140.5$ *v.* 142 with α *ca.* 14° appears to suffer little loss of aromaticity while the benzene ring in (32) $I_A = 89.5$ $\alpha = 13.2°$ is much less aromatic, as is the pyridine ring in (33) $I_A = 67$ *v.* 86 with $\alpha = 13°$.



(36) X = O
(37) X = S



(38)

Several interesting features emerge from the triple-layer cyclophanes (36)[40], (37)[40] and (38)[41]. Again both the furan and thiophene rings adopt envelope-like conformations. The more marked decrease in the I_A for the furan ring of (36) to 28 from 53, relative to that of 71.5 from 81.5 in the case of the thiophene counterpart (37) is in line with preceeding observations. The exaltation of the aromaticity of the planar pyridine rings of (38) to $I_A = 92$ from 86 is noteworthy. In contrast to the situation in the preceeding systems the planes of the pyridine rings in (38) are perpendicular to the benzenoid one. The outer benzenoid rings of (36) and (37) with I_A's of 96 and 92.5 have similar aromaticity to the benzene rings in paracyclophane.The central benzenoid rings in (36), (37) and (38) with I_A's of 92.5, 87.5 and 89.5 respectively adopt twist boat conformations.

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REFERENCES

1. Bird, C.W., Tetrahedron, 1992, *48*, 335.
2. Iwamura, H., Kihara, H., Misumi, S., Sakata, Y., and Umemoto, T., *Tetrahedron*, 1978, *34*, 3427.
3. Couldwell, M.H., and Penfold, B.R., *J. Cryst. Mol. Struct.*, 1976, *6*, 59.
4. Weissensteiner, W., Schuster, I.I., Blount, J.F., and Mislow, K., *J. Amer. Chem. Soc.*, 1986, *108*, 6664.
5. Sakurai, H., Ebata, K., Kabuto, C., and Sekiguchi, A., *J. Amer. Chem. Soc.*, 1990, *112*, 1799.
6. Stam, C.H., *Acta Cryst.*, 1972, *28*, 2715.
7. Hambley, T.W., Sternhell, S., and Tansey, C.W., *Aust. J. Chem.*, 1990, *43*, 807.
8. Maas, G., Fink, J., Wingert, H., Blatter, K., and Regitz, M., *Chem. Ber.*, 1987, *120*, 819.
9. Muller, G., Reber, G., Karsch, H.H., and Reisacher, H.-U., *Acta Cryst.* 1986, *C42*, 1375.
10. Yoshifuji, M., Shima, I., Inamoto, N., Hirotsu, K., and Higuchi, T., *Angew. Chem. Int. Edn. Engl.*, 1980, *19*, 399.
11. Visser, G.J., and Vos, A., *Acta Cryst.*, 1971, B27, 1793.
12. Handal, J., White, J.G., Franck, R.W., Yuh, Y.H., and Allinger, N.L., *J. Amer. Chem. Soc.*, 1977, *99*, 3345.
13. Bakkers, G., Duisenberg, A.J.M., Kroon, J., and Brandsma, L., *Chem. Struct. Commun.*, 1981, *10*, 361.
14. Visser, G.J., and Vos, A., *Acta Cryst.*, 1971, *B27*, 1802.
15. Richter, H., Arenz, S., Michels, G., Schneider, J., Wagner, O., and Regitz, M., *Chem. Ber.*, 1988, *121*, 1363.
16. Newton, M.G., Walter, T.J., and Allinger, N.L., *J. Amer. Chem. Soc.*, 1973, *95*, 5652.
17. Liebe, J., Wolff, C., Krieger, C., Weiss, J., and Tochtermann, W., *Chem. Ber.*, 1985, 118, 4144.
18. Tobe, Y., Nakayama, A., Kakiuchi, K., Odaira, Y., Kai, Y., and Kasai, N., *J. Org. Chem.*, 1987, *52*, 2639.
19. Gassman, P.G., and Boardman, G.S., *Tetrahedron Lett.*, 1989, 4649.
20. Jenneskens, L.W., Klamer, J.C., de Boer, H.J.R., de Wolf, W.H., Bickelhaupt, F., and Stam, C.W., *Angew. Chem. Int. Edn. Engl.*, 1984, *23*, 238.

21. Kai, Y., Yasuoka, N., and Kasai, N., Acta Cryst., 1977, B33, 754.
22. Taylor, D., Aust. J. Chem., 1978, 31, 1235.
23. Hanson, A.W., and Rohrl, M., Acta Cryst., 1972, B28, 2032.
24. Mathew, M., Acta Cryst., 1968, B24, 530.
25. Pahor, N.B., Calligaris, M., and Pandaccio, L., JCS Perkin 2, 1978, 38.
26. Eiermann, U., Krieger, C., Neugebauer, F.A., and Staab, H.A., Chem. Ber., 1990, 123, 523.
27. Hanson, A.W., Acta Cryst., 1971, B27, 197.
28. Weaver, L.H., and Matthews, B.W., J. Amer. Chem. Soc., 1974, 96, 1581.
29. Coulter, C.L., and Trueblood, K.N., Acta Cryst., 1963, 16, 667.
30. Vogtle, F., Dohm, J., and Rissanen, K., Angew. Chem. Int. Edn. Engl., 1990, 29, 902.
31. Hope, H., Bernstein, J., and Trueblood, K.N., Acta Cryst., 1972,B28, 1733. (The parent paracyclophane displays molecular disordering and the bond lengths are of lower accuracy).
32. Eiermann, U., Krieger, C., and Neugebauer, F.A., Chem. Ber., 1990, 123, 1885.
33. Hanson, A.W., Acta Cryst., 1977, B33, 2003.
34. Hanson, A.W., Cryst. Struct. Commun., 1981, 10, 313.
35. Hanson, A.W., Cryst. Struct. Commun., 1981, 10, 751.
36. Keehn, P., private communication.
37. Pahor, N.B., Calligaris, M., and Randaccio, L., JCS Perkin 2, 1978,42.
38. Atwood, J.L., Hunter, W.E., Wong, C., and Paudler, W.W., J. Het. Chem., 1975, 12, 433.
39. Corson, M., Foxman, B.M., and Keehn, P.M., Tetrahedron, 1978, 34 ,1641
40. Kai, Y., Watanabe, J., Yasuoka, N., and Kasai, N., Acta Cryst., 1980, B36, 2276.
41. Hanson, A.W., Acta Cryst., 1977, B33, 2657