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Separation of the Energetic and Geometric Contribution to the Aromaticity. Part IX. Aromaticity of Pyrazoles in Dependence on the Kind of Substitution

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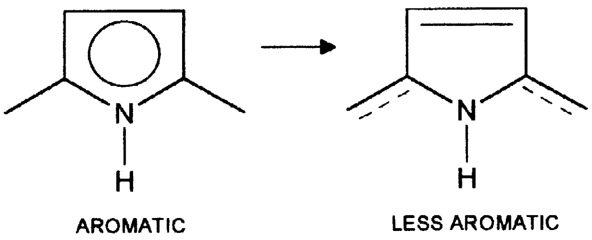
Abstract. Crystal and molecular structures of the 4-(4'-N,N-dimethylaminophenyl)-3,5-dimethyl-1,7-diphenyl-bis-pyrazolo[3,4-b;4',3'-e]pyridine (I) and 3,5-dimethyl-1,4,7-triphenyl-bis-pyrazolo[3,4-b;4',3'-e]pyridine (II) are reported, with R = 0.0505 and 0.0538, respectively. Application of the HOMA model[1] to molecular geometry of the title compounds enriched by the data for pyrazoles retrieved from CSD and from RHF/6-311G** *ab-initio* calculations led to the conclusion formulated as a rule that decrease of aromaticity of pyrazole is caused by an increase of the double bond character of the exo-cyclic bonds with substituents attached to C3 and C4 atoms in the ring.

Introduction

Pyrazoles belong to a group of π-electron systems with a strong aromatic character.[1,2] Aromaticity of nitrogen-containing π-electron cyclic systems is sensitive to structural changes[3-5] and hence these systems have been widely used for studies of multidimensionality of aromaticity.[3,4] Five-membered rings of the title compounds may exhibit this feature even more since one of the two nitrogen atoms shares the electron pair with the π-electron system of the ring and hence the whole system may be more mobile than the six-membered rings. Hence sensitivity of their aromatic character may be observed even in solvent.[6] Recently it has been shown that pyrrole rings in porphyrins lost much of their aromaticity[7] due to the localisation of one of the double bonds forced by nitrogen and 2,5-carbon atoms participating in a macrocylic π-electron system of strongly delocalised π-electrons.

Scheme I



The purpose of this paper is application of the HOMA index[1,8,17] and a magnetic index NICS[9] to discuss the aromaticity of pyrazole rings in dependence on the nature of substitution studied by X-ray diffraction

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structure determination and *ab-initio* calculations.

Experimental

X-ray diffraction. The X-ray measurements of the two crystals, 4-(4'-dimethylaminophenyl)-3,5-dimethyl-1,7-diphenyl-bis-pyrazolo[3,4-b;4',3'-e]pyridine[10] and 3,5-dimethyl-1,4,7-triphenyl-bis-pyrazolo[3,4-b;4',3'-e] pyridine,[11] obtained according ref. 12, were made on a KM-4 KUMA diffractometer with graphite monochromated CuKα radiation. The data were collected at room temperature using ω-2θ scan technique. The intensity of the control reflections varied by less than 3%, and the linear correction factor was applied to account for this effect. The data were also corrected for Lorentz and polarisation effects, but no absorption correction was applied. The structure was solved by direct methods[13] and refined using SHELXL.[14] The refinement was based on F^2 for all reflections except those with very negative F^2. The weighted R factor, wR and all goodness-of-fit S values are based on F^2. The non-hydrogen atoms were refined anisotropically, whereas the H-atoms were placed in the calculated positions and their thermal parameters were refined isotropically. The atomic scattering factors were taken from the International Tables.[15] Table 1 presents the observed selected bond lengths for the two compounds.

Fig. 1. The labelling of atoms in 4-(4'-N,N-dimethylaminophenyl)-3,5-dimethyl-1,7-diphenyl-bis-pyrazolo [3,4-b:4',3'-e]pyridine (molecules I A and B; R= NMe_2) and 3,5-dimethyl-1,4,7-triphenyl-bis-pyrazolo[3,4-b;4',3'-e] pyridine (molecule II; R=H)

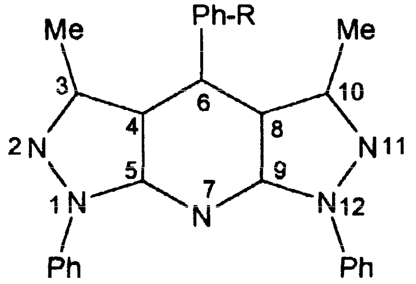


Table 1. Selected bond lengths [A] for 4-(4'DMAP)-3,5-DM-1,7-DP-BPP (molecule I) and the 3,5-DM-1,4,7-TP-BPP (molecule II)

	IA*	IB*	II
N_1-N_2	1.386(2)	1.391(2)	1.370(3)
N_1-C_5	1.364(2)	1.371(2)	1.363(3)
N_2-C_3	1.303(3)	1.301(2)	1.303(3)
C_3-C_4	1.435(3)	1.428(3)	1.423(3)
C_4-C_5	1.413(3)	1.416(3)	1.418(3)
C_4-C_6	1.399(3)	1.403(3)	1.389(3)
N_7-C_5	1.334(2)	1.332(2)	1.316(3)
N_7-C_9	1.334(2)	1.338(2)	1.315(3)
N_{12}-C_9	1.369(2)	1.369(3)	1.363(3)
N_{11}-N_{12}	1.394(2)	1.387(2)	1.371(3)
N_{11}-C_{10}	1.299(3)	1.302(3)	1.299(3)
C_6-C_8	1.397(3)	1.400(3)	1.380(3)
C_8-C_9	1.415(3)	1.410(3)	1.415(3)
C_8-C_{10}	1.440(3)	1.434(3)	1.427(3)

* Two independent molecules in the asymetric unit

Calculation details. *Ab-initio* RHF/6-311G** calculations for molecules and their conformations listed in Table 3 were carried out using Gaussian 94 program.[16] NICS values calculated at HF/6-31+G* level of theory.

Results and discussion

Molecular geometry of I and II (Table 1) permits one to use the aromaticity index HOMA[8] and its components EN and GEO[1] to analyse of the relation between the nature of substitution and the aromatic character of the ring. The GEO term describes the changes in aromaticity (its decrease) due solely to an increase in bond lengths alternation, whereas the EN term reflects the changes in aromatic character due to the lengthening of the mean bond lengths in question.[18] Table 2 presents HOMA, EN and GEO values for pyrazole rings for the title compounds and mean values for three kinds of pyrazole derivatives retrieved from CSD.[19]

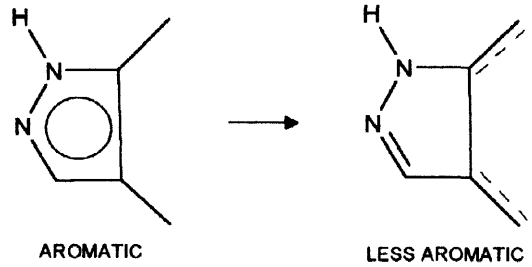
It is immediately clear that pyrazole rings in I and II have a much lower aromatic character than any of the derivatives with non-cyclic substituents. This situation is formally similar to another one observed for pyrrole rings in porphyrins[7] where pyrrole rings have HOMA values ca 0.6 which may be compared with the HOMA value ca 0.9[1] for the case substituted by non-cyclic substituents. The same kind of observation is found for pyrazole rings fused to aromatics (23 entries). The interpretation of the above presented results and observed effects is similar to those found for pyrrole derivatives. It was as follows[7]: substitution of the pyrrole rings in positions 2,5 by substituents with a partly double bond character or inclusion to the macrocylic π-electron system with a considerable π-electron delocalisation leads to a substantial double bond localisation in the ring and in consequence to the decrease of its aromaticity, as it was presented by scheme I. This kind of effect was observed in cases where substituents with partly double bonds were attached to the aromatic ring. A considerable decrease in aromaticity was observed in the study of CH_2^+ substituents interacting with benzenoid hydrocarbons.[20]

Table 2. HOMA, EN and GEO values for the rings in the title compounds and for three kinds of pyrazole: substituted with open substituents, and fused to saturated and aromatic rings.

Kind of pyrazole derivative	n	mean values of HOMA	mean values of EN	mean values of GEO
two pyrazole rings in **IA** (mean values)	2	0.660	0.169	0.172
two pyrazole rings in **IB** (mean values)	2	0.627	0.183	0.191
two pyrazole rings in **II** (mean values)	2	0.753	0.118	0.129
substituted pyrazoles	45	0.919	0.015	0.066
pyrazole fused to a saturated cycle	7	0.933	0.030	0.037
pyrazole fused to aromatic cycles	23	0.851	0.093	0.057

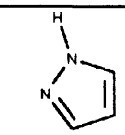
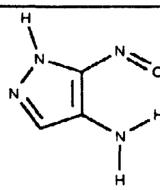
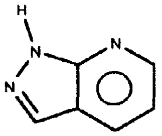
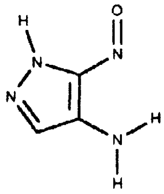
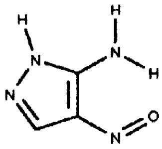
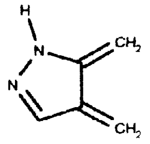
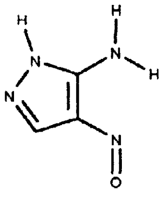
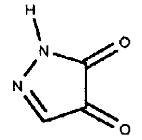
In the present analysis we consider a case of pyrazole rings fused *via* C_4-C_5 or C_8C_9 (Fig. 1) bond to a pyridine ring - a system where the delocalization of π-electrons is very high. The HOMA values for the pyridine ring for three independent rings in I and II are 0.917, 0.922 and 0.933. The mean values of C_5-N_7 (C_9-N_7) bonds and of C_4-C_6 (C_6-C_8) bonds are 1.328 and 1.395A, respectively, and may be compared with the typical single bonds 1.465 (for CN) and 1.467A (for CC) and the optimal ones[8] 1.334 and 1.388A, respectively. Our hypothesis is that inclusion of the pyrazole ring *via* C_4 (C_8) and C_5 (C_9) atoms into a system with an increased double bond character of the exocyclic bonds causes an increase in bond alternation and in consequence a decrease of the aromatic character of the ring in question. Scheme II illustrates this rule.

Scheme II



To support this hypothesis we have carried out *ab-initio* RHF/6-311G** calculations for a few selected derivatives of pyrazole; Table 3 presents the values of aromaticity indices: HOMA, EN, GEO and NICS.

Table 3. Aromaticity indices for pyrazol fragment of model molecules based on RHF/6-311G** geometry

Label	Formula	Aromaticity indices	Label	Formula	Aromaticity indices
1		H=0.900 E=0.000 G=0.100 NICS= -14.7	5		H=0.917 E=0.003 G=0.080 NICS= -14.3
2		H=0.819 E=0.031 G=0.150 NICS= -13.0	6		H=0.904 E=0.002 G=0.094 NICS= -12.9
3		H=0.782 E=0.032 G=0.186 NICS= -11.8	7		H=-0.011 E=0.443 G=0.663 NICS = -0.5
4		H=0.782 E=0.025 G=0.193 NICS= -11.5	8		H=-1.025 E=0.777 G=1.248 NICS= +9.8

Apart from the nonsubstituted pyrazole (**1**) and its derivative (**2**) fused to the pyridine ring there are four derivatives (**3-6**) in which in positions 4 and 5 (labelling see Fig. 1) are attached substituents which may interact *via* a through resonance effect: the nitroso- and amino groups. Finally a molecular geometry of 3,4-dimethylene derivative (**7**) and a diketone is presented (**8**). The picture is clear: high aromaticity for unsubstituted pyrazole (HOMA = 0.90, NICS= -14.7), a decrease of aromaticity in a pyridine derivative (**2**, HOMA = 0.82, NICS= -13.0) and still more in the case of di-methylene (**7**, HOMA = -0.01, NICS= -0.5) and dramatically more in the case of di-ketone (**8**, HOMA =-1.02, NICS= +9.8). In the last two cases a decrease in aromaticity is due almost equally to EN and GEO, the same as in the case of experimental data for I and II. In other cases a decrease in HOMA values is due mostly to the geometric factor. In the case of amino and nitroso derivatives (**3-6**) the situation is more complex. We observe an increase in aromaticity (**5**, **6**) up to HOMA = 0.92 and NICS= -14,3 and a substantial decrease in aromaticity (**3**, **4**) down to HOMA= 0.78 and NICS= -11.5. The difference between those two pairs of conformers is considerable and needs comment. The nitroso group in a direct vicinity of the nitrogen atom with a lone pair is capable of conjugation (NH in the ring) and causes a significant push-pull effect leading to an increase in π-electron delocalisation (**5**, **6**) and in consequence an increase of the aromatic character. An opposite effect operates in (**3**, **4**), where push-pull effect between N=O and NH_2 groups works mainly locally, since the lone pair at N-H hinders extension of the π-electron delocalisation. In all cases a very good agreement between the geometry based index HOMA a magnetic index NICS is observed.

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10. Triclinic, space group P-1, a=9.181 (2) A, b=12.420 (2) A, c=21.357 (4) A, α=87.56 (3) deg., β=83.70 (3) deg., γ=87.65 (3) deg., Z=4; 9142 independent reflections, R=0.0505. Further details of the crystal structure: list of structure factors, anisotropic displacement parameters, H-atom coordinates, complete geometry will be sent to the Cambridge Structural Database.
11. Triclinic, space group P-1, a=8.597 (2), b=10.508 (2) A, c=12.472 (2), α=105.38 (3) deg., β=98.95 (3) deg., γ=101.29 (3) deg., Z=2; 4360 independent reflections, R=0.0538. Further details of the crystal structure: list of structure factors, anisotropic displacement parameters, H-atom coordinates, complete geometry will be sent to the Cambridge Structural Database.
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