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Identification of mesomeric substructures by through-space NMR shieldings (TSNMRS). Trimethine cyanine/merocyanine-like or aromatic π-electron delocalization?

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ABSTRACT

The spatial magnetic properties, through-space NMR shieldings (TSNMRS), of amino-substituted heteroaromatic six-membered ring systems such as pyrylium/thiopyrylium analogues have been calculated using the GIAO perturbation method employing the nucleus independent chemical shift (NICS) concept and visualized as iso-chemical-shielding surfaces (ICSS) of various size and direction. The TSNMRS values were employed to quantify and visualize the existing aromaticity of the studied compounds. Due to strong conjugation of six-membered ring π-electrons and lone pairs of the *exo*-cyclic amino substituents (restricted rotation about partial C,N double bonds) the interplay of *still aromatic* and *already dominating trimethine cyanine/merocyanine-like substructures* can be estimated.

1. Introduction

The shielding at or above the centre of aromatic ring systems and realized by the concept of nucleus independent chemical shielding (NICS)[1] is a parameter that can be used to characterize the aromaticity of organic compounds. NICS values calculated for a grid system surrounding the molecules can also be used to locate the diatropic and paratropic regions of the molecules involved.[2] This kind of through-space NMR shieldings (TSNMRS) have been visualized[3] as iso-chemical-shielding surfaces (ICSS) and employed to quantify the anisotropic effects of functional groups,[3] to determine the stereochemisty of nuclei proximal to functional groups,[3–5] and to visualize and quantify (anti)aromaticity.[6,7] The results obtained so far have been reviewed.[8]

Using our approach,[3,7,8] we found the TSNMRS methodology to be a viable alternative for the identification of benzenoid/quinoid structures if the ^{1}H NMR spectra are too complex or if X-ray structures were unavailable.[9] In another study,[10] we extended our examination to keto–enol tautomers (with benzenoid, quinoid, antiaromatic or pseudoaromatic substructures) and to push-pull structures (which can exist as zwitterionic forms with pseudoaromatic substructures) in order to identify the status of present aromaticity.

Especially because of this latter success, we are going to study in this paper the π-electron distribution of aromatic/heteroaromatic compounds subject to present substituents employing our TSNMRS approach.[3,7,8] Substituents on aromatic moieties, as *e.g.* the amino group are well known for delocalization of its electron lone pair *via* the aromatic π-electron sextet; most evident result proves to be the restricted rotation about the corresponding partial C,N double bond[11] (*cf.* Scheme 1). The corresponding barrier to rotation can be readily determined by dynamic NMR spectroscopy and often yields free energies of activation ($\Delta G^{\#}$) up to 23 kcal/mol which, on the other hand, document large *exo*-cyclic C,N bond orders and, hereby, remarkable contributions of the corresponding mesomeric structures (**1b-d** in Scheme 1) to the ground state structure of the studied aromatic compounds; at least present aromaticity should be lowered to some amount. The magnitude of this contribution, reducing present aromaticity, is unknown but can be theoretically calculated or experimentally detected in terms of the rotational barrier $\Delta G^{\#}$/kcal/mol about the partial C,N double bond.

These rotational barriers prove to be exceptionally high in amino-substituted pyrylium/thiopyrylium salts (*cf.* Scheme 2) in

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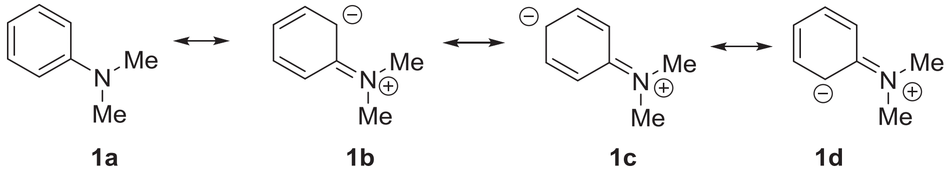
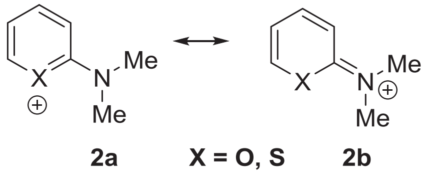


Scheme 1.



Scheme 2.

which the present positive charge is delocalized throughout the whole π-system including amino nitrogen atoms(s). Because the aromaticity of non-substituted pyrylium/thiopyrylium salts is comparable with the one of benzene, particularly large lowering of the aromaticity of these species is expected and was experimentally confirmed by the highest rotational barriers measured so far.[12]

The dynamic behaviour of several amino-substituted pyrylium and thiopyrylium salts was studied and the extremely high barriers to rotation between 18 and 23 kcal/mol were determined.[12] Substructures in these compounds are penta- or trimethine cyanine (*cf.* **3b,c** in Scheme 3) and merocyanine moieties, respectively (*cf.* **4a** in Scheme 3), both well known for distinct n,π-electron delocalization (*cf.* **3b,c** and **4b** in Scheme 3); the stability of the latter substructures was assessed to be high enough to name present compounds *bridged merocyanines* or *penta(tri)methine cyanines*, respectively.[13] Further support comes from the successful nitration of a 1,3,5-*tris*-amino pyrylium salt,[14] which is unknown in traditional pyrylium salt chemistry.[15]

The question arises if this kind of amino-substituted pyrylium and thiopyrylium salts is still aromatic or present aromaticity is crucially lowered by the merocyanine or trimethine cyanine substructures, respectively, and if yes to which amount. An answer will be given on basis of our TSNMRS methodology.[3,7,8]

2. Computational details

The quantum chemical calculations were performed using the Gaussian 09 program package[16] and carried out on LINUX clusters. The studied structures were fully optimized at the MP2/6-311G(*d,p*) level of theory without constraints.[17] The self-consisted reaction field (SCRF) method and the Integral Equation Formalism using Polarized Continuum Model (IEFPCM)[18] were used at the MP2/6-311G(*d,p*) level of theory to consider the solvent. The obtained structures have been confirmed as local minima by performing harmonic frequency calculations at the optimized geometries.

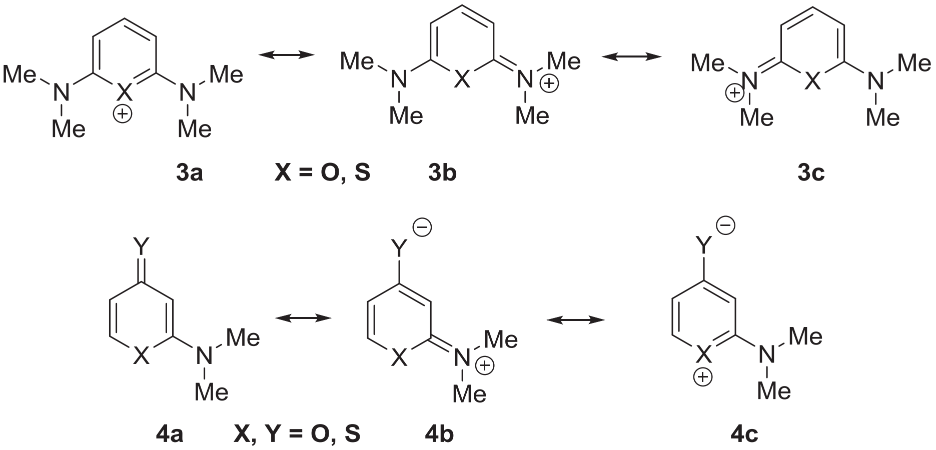
NICS values[19] were computed on the basis of the MP2/6-311G(*d,p*) geometries using the gauge-including atomic orbital (GIAO) method[20,21] at the B3LYP/6-311G(*d,p*)[22] theory level[23]; variation of the basis set was found to be of non-significant influence on the NICS values. To calculate the spatial NICS, ghost atoms were placed on a lattice of −10 Å to +10 Å with a step size of 0.5 Å in the three directions of the Cartesian coordinate system. The zero points of the coordinate system were positioned at the centers of the studied structures. The resulting 68,921 NICS values, thus obtained, were analyzed and visualized by the SYBYL 7.3 molecular modeling software[24]; different iso-chemical-shielding surfaces (ICSS) of −0.1 ppm (red) deshielding, and 6 ppm (white), 5 ppm (blue), 2 ppm (cyan), 1 ppm (greenblue) 0.5 ppm (green) and 0.1 ppm (yellow) shielding were used to visualize the TSNMRS of studied structures in the various figures. ICSS are a quantitative indication of the diatropic ring current effect in ^1H NMR spectroscopy[3,7,8]; the computed shielding(deshielding) ICSS quantify the ring current effect in ^1H NMR spectroscopy subject to distance from the molecular centre of the molecule (in Å).[8]

TSNMRS were computed and appropriately examined herein as the central topic of this paper. Of significant note though, there have been some developments of the NICS index[25] showing that it is not the average NICS, but rather only the NICS$(1)_{zz}$ component that needs to be used to rigorously quantify aromaticity.[26] Single average NICS values have been proved to be unsuitable for the general quantitative evaluation of aromaticity.[27]

3. Results and discussion

3.1. Structures of studied compounds

Computed characteristic geometry parameters (torsional angles



Scheme 3.