Full Paper

An investigation of aromaticity in hydroxybenzenes based on the study of magnetically induced current density

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**Abstract**

Hydroxybenzenes are derivatives of benzene in which one or more H atoms are replaced by OH groups. This work considers the effect of such replacement on the aromaticity of the ring, by assessing the aromaticity through the values and patterns of the magnetically induced current density. The results show that aromaticity is quenched and the quenching depends on the number and positions of the substituting OH groups. The isosurfaces of the magnitude of the current density also highlight connections between the donor and acceptor atoms forming an intramolecular hydrogen bond.

**KEYWORDS**

aromaticity, current density, current strength, diatropic, paratropic

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1 | INTRODUCTION

Hydroxybenzenes (HYBs) are derivatives of benzene in which one or more H atoms are replaced by OH groups. They have a variety of biological activities, such as antibacterial,\(^{11}\) antioxidant,\(^{12-14}\) antifungal,\(^{15,16}\) anticarcinogenic.\(^{16,7}\) They are important also as parent compounds of classes of naturally occurring compounds with interesting properties, including biological activities. These classes include flavonoids,\(^{2,8,9}\) (poly)phenolic components found in many plants and important as phytonutrients), resorcinolic lipids,\(^{17}\) (phenolic lipids in which one or more long aliphatic chains are attached to a resorcinol (1,2-dihydroxybenzene) ring), and phloroglucinols\(^{10}\) (derivatives of 1,3,5-trihydroxybenzene, with interesting potentialities as lead drugs for the treatment of degenerative diseases\(^{11}\) as well as malaria, tuberculosis, and other diseases.\(^{10}\) Biological activities depend on the finest details of the molecular structures and properties.\(^{12}\) This has been confirmed for HYBs.\(^{13-15}\) For instance, the radical-scavenging activity is favored by the presence of intramolecular hydrogen bonds (IHBS), making compounds with consecutive OHs the most active,\(^{2}\) and the para position of two OHs corresponds to greater activity than the meta position.\(^{2,22}\) It is therefore interesting to investigate all the molecular properties of HYBs. A previous study\(^{14}\) focused on conformational associated preferences and related properties in vacuo and in solution, including the stabilizing effects and geometrical characteristics (parameters) of IHBS and the consideration of adducts with explicit water molecules to complement the information from the polarisable continuum model\(^{17,18}\) study in water solution.

The current study focuses on the aromaticity of HYBs, considering all the HYBs and all their conformers. Aromaticity is a concept which has been given a variety of definitions.\(^{19}\) The conclusive statement of the review by Schleyer,\(^{20}\) "while ‘benzene-like’ still suffices for some, the ‘cyclic delocalization of mobile electrons’ description now seems paramount.” In the case of benzene derivatives (as the compounds considered in the current work), the reference to the presence of a \(\pi\) system with electron density above and below the plane of the hexagonal benzene ring should suffice; however, the concept of “cyclic delocalization of mobile electrons” has greater affinity with the consideration of induced current.

Aromaticity relates to biological activities and other molecular properties and behavior in various ways. The inclusion of aromatic substituent constants into structure activity correlation studies dates some decades back.\(^{21}\) The number of aromatic rings that can be acceptable in a viable drug has been a crucial question. The influence of aromatic rings on properties such as water solubility, lipophilicity, and bioactivities such as albumin binding or some inhibition properties, suggests that the presence of more than three aromatic rings may not be optimal for viable drugs meant for oral administration.\(^{22}\) The importance of avoiding the risk of mutagenic side-effects on designing a new drug has prompted studies on the mutagenic activity of aromatic compounds. A 1981 study\(^{23}\) reports that aromatic hydrocarbons with 1–4