

Aromaticity and Optical Activity

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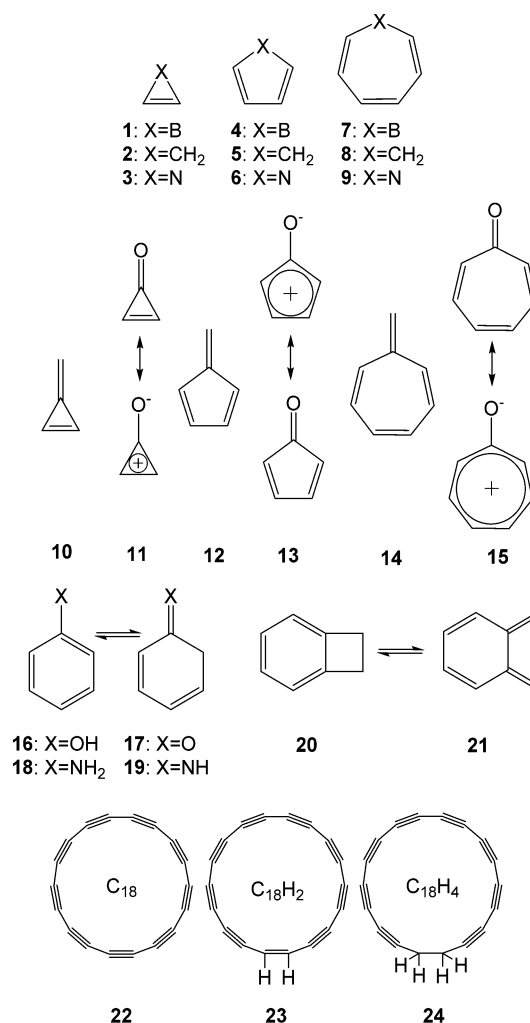
S Supporting Information

ABSTRACT: The relationship between aromaticity and optical activity is investigated in comparisons of heterocycles with $4n + 2$ and $4n$ π -electrons, in cyclic ketones with and without aromatic resonance structure representations, in tautomers and pericyclic reaction partners in which only one compound of each pair is aromatic, and in partially hydrogenated cyclo- C_{18} derivatives with both radial and tangential π -orbitals. In all comparisons, aromaticity is correlated to diminished optical activity. A heuristic explanation of this observation is grounded in the electric dipole–magnetic dipole polarizability contribution to optical activity in which the sense of electric dipoles and magnetic dipoles become uncoupled when electrons can circulate around a ring with either sense. These observations form a basis for making broad structure–optical activity correlations from inspection of molecular structure.

Aromaticity¹ and nonresonant optical activity² are properties of molecules that both depend on, or are characterized by, the circulation of electrons. Moreover, they are subjects of vast, long-standing bodies of research out of which structural organic chemistry emerged in the 19th century. And, yet, these subjects have no intersection because aromaticity has been best evaluated in flat, achiral compounds and optical activity has been analyzed for chiral molecules with only a small number of achiral exceptions.^{3–9} But, we showed that by relaxing the necessity of chirality in the contemplation of optical activity, molecules and their associated wave functions become untwisted while structure–optical activity property relations become transparent.⁹ Here, we aim to establish a relationship between aromaticity and optical activity on the basis of quantum chemical computation evaluated through the prism of qualitative, pedagogical concepts of organic electronic structure.

The relationship between aromaticity and optical activity is made in comparisons of four sets of compounds (Scheme 1) including the following: (1) prototypical aromatic and antiaromatic heterocycles: 1/3, 4/6, and 7/9, as well as their respective nonaromatic, hydrocarbon congeners, 2, 5, and 8; (2) ketones 11, 13, and 15 with strongly dipolar resonance structures that are more aromatic or more antiaromatic than their hydrocarbon congeners 10, 12, and 14, respectively; (3) pairs of compounds in equilibrium (16/17, 18/19, and 20/21) for which only one of each pair is aromatic; and (4) polyynes including the “doubly aromatic” 22, partially reduced *in silico* to singly aromatic 23, and further reduced to nonaromatic 24.

Scheme 1



Long wavelength (1064 nm) optical rotations were calculated for this set of compounds using standard methods described previously,⁹ and more fully in a variety of review articles.¹⁰ All calculations were performed using Gaussian09, version D.01 (see Supporting Information for full citation). Compounds 8 and 9 were constrained as flat (C_{2v}) for comparison. The long wavelength optical rotation was calculated using B3LYP and the aug-cc-pVDZ basis set for

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compounds 1–21 and with 6-311+G** for 22–24. The computed values are summarized in Table 1.

Table 1. Computed Gyration Tensor Elements (atomic units, bohr⁴)

g_{xy} aug-cc-pVDZ, 1064 nm		
aromatic	nonaromatic	antiaromatic
1: -0.7	2: -1.3	3: -14.8
6: -0.3	5: -5.1	4: -16.0
7: -10.6	8: -34.1	9: -74.6
aromatic	nonaromatic	antiaromatic
11: 0	10: -3.1	–
–	12: -7.5	13: -8.0
15: -18.5	14: -34.9	–
g_i^a for 16, 17, 19; g_{xy} for 18, 20–21 aug-cc-pVDZ, 1064 nm		
aromatic	nonaromatic	
16: -2.2	17: -16.2	
18: -4.6	19: -20.1	
20: -2.0	21: -50.6	
g_i^a for 24; g_{xy} for 22–23 6-311+G**, 1064 nm		
doubly ^b aromatic	singly ^c aromatic	nonaromatic
22: 0	23: -161	24: -311 ^d

^a g_i represents the largest eigenvalue for C_s or C_2 symmetric compounds that are aligned in general directions. ^bCyclic radial and tangential π -orbitals. ^cCyclic tangential π -orbitals. ^d24 is chiral and has a small gyration tensor trace. The stereoisomer represented has the largest negative eigenvalue along the approximate xy direction.

Compounds 1–9 are C_{2v} symmetric or constrained to be so. Therefore, they have only one independent, nonzero gyration component, $g_{xy} = -g_{-xy}$. These molecules are in possession of what Efrati and Irvine have described as orientation-dependent handedness.¹¹ The aromatic member (1, 6, and 7) of each ring-size group is less optically active than its antiaromatic partner (3, 4, and 9, respectively). In comparison with the nonaromatic congeners (2, 5, and 8) we can see that *aromaticity reduces optical activity while antiaromaticity enhances optical activity*. The gyration tensor representation surfaces are plotted in Figure 1 for selected compounds. Like other attempts to measure aromaticity, relative comparisons can only be made between sets of compounds with the same ring size.¹²

To understand the deleterious consequences of aromaticity for optical activity, we consider why an oriented D_{6h} symmetric benzene molecule is optically inactive in all directions—it has no nonzero gyration tensor elements—whereas pyridine is optically active along directions $[x,y,0]$ and $[-x,y,0]$. The answer is grounded in the way in which the elements of a second rank pseudo-axial tensor transform under the symmetry operations of a particular point group. The necessary condition for optical activity in solution is chirality. For oriented molecules, the absence of a center of symmetry is requisite, but not sufficient (e.g., C_{nv} where $n > 2$). There are four acentric, nonenantiomorphous point groups that admit optical activity in some directions including D_{2d} , S_4 , C_{2v} , and C_s . There is little in this accounting that is intuitive. Algebra is required to enumerate the chiral groups plus the four others that are optically active in some direction. See appendix of ref 7.

A heuristic explanation focuses on the electric dipole–magnetic dipole coupling contribution to optical activity only (Figure 2). For a given electric dipole generated in the plane of a benzene ring by the light field, charge separation can be

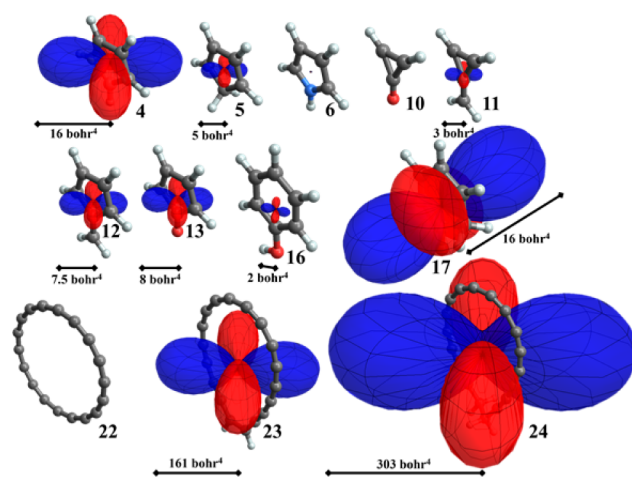


Figure 1. Structures and representation surfaces of the computed gyration tensors for selected compounds in Table 1. Red (Blue) corresponds to a negative (positive) gyration, that, due to a sign change upon conversion to azimuthal rotation, is dextrorotatory (levorotatory).

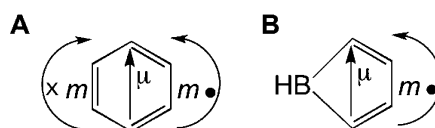


Figure 2. (A) To generate an electric dipole (μ) in benzene with a light field, the charge can circulate around the π -system in a clockwise or counterclockwise direction, thus generating equal and opposite magnetic dipole moments (m). (B) In an antiaromatic system, the directions of μ and m are always fixed relative to one another. z is the polar diad axis or the approximate polar diad axis and y is in the plane of the molecule.

achieved by circulating π -electrons clockwise or counterclockwise, thus producing magnetic dipole moments that cancel one another. However, if we break the cyclic circulation of charge, as in 1H-borole (4), the senses of the associated electric and magnetic dipoles are strictly coupled.

Compounds in the second series are also C_{2v} symmetric with one independent tensor component. Differences among cyclopropenone (11), cyclopentadienone (13), and tropone (15) in comparison with their hydrocarbon congeners, 10, 12, and 14, respectively, are reckoned in terms of the aromaticity of the corresponding resonance structures pictured in Scheme 1. For compounds 11 and 15 that permit representation as dipolar aromatic resonance structures, the optical activities are much smaller than their nonaromatic hydrocarbon reference compounds 10 and 14, whereas the optical activity of 13, whose dipolar resonance structure is antiaromatic with respect to the five-membered ring, has a slightly larger optical activity than 12 (Table 1).

Compounds 16, 17, and 19 have symmetry C_s but still only one independent gyration tensor eigenvalue. Our observations of 1–15 led to predictions for pairs 16/17, 18/19, and 20/21. Aromatic compounds 16, 18, and 20 are in equilibrium with the nonaromatic 17, 19, and 21, respectively. We confirmed our expectation that the members of the latter set will be more optically active than the corresponding aromatic compounds. The optical activities of 17 and 19 are larger than 16 and 18, respectively, by a factor of 4–7. Likewise, the tetraene (21) is

25 times more optically active than its pericyclic reaction partner, benzocyclobutane (**20**).

Lastly, we analyze cyclo- C_{18} with D_{18h} symmetry.¹³ It is optically inactive as required by its symmetry but doubly aromatic with respect to 18 π -electrons in both radial and in tangential π -orbitals. By reducing *in silico* one of the triple bonds to a double bond, symmetry is reduced to C_{2v} , an optically active point group. One of the two conjugated circuits is broken, and the optical activity rises from 0 to -161 bohr^4 for g_{xy} . Further reduction of this double bond breaks the second aromatic circuit, thereby nearly doubling the optical activity to -311 bohr^4 (Figure 2).

In sum, aromaticity causes optical rotation to plummet, all other things being equal. This observation supports broad chiroptical structure-property correlations not heretofore considered. The simplified electronic structures of flat compounds make clear the associated chiroptical response that may otherwise be obscured for chiral compounds with twisted wave functions.

■ ASSOCIATED CONTENT

📄 Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.5b11138.

Complete Gaussian reference, Cartesian coordinates for all structures, and full linear response chiroptical tensors (PDF)

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Notes

The authors declare no competing financial interest.

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