What Is the Main Feature Distinguishing the Through-Space Interactions in Cyclophanes from Their Aliphatic Analogues?

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ABSTRACT: Classical cyclophanes with two benzene rings have been compared with cyclophanes with one benzene ring replaced with an aliphatic part and aliphatic compounds, which are cyclopane analogues. Analysis of geometry, atomic charges, and aromatic and steric energy and investigation of intramolecular noncovalent interactions and charge mobility show that there is no special feature that distinguishes the classical cyclophanes from aliphatic analogues, so the definition of cyclophanes can be extended to other compounds.

1. INTRODUCTION

Cyclophanes are hydrocarbons of immense structural diversity containing aromatic units (typically benzene rings) and an aliphatic chain that forms a bridge between two non-adjacent positions of the aromatic ring.1−7 Most typical are the cyclophanes having two benzene rings joined by aliphatic bridges between the para and/or meta positions of the aromatic rings. In the other group of cyclophanes, one benzene ring is replaced by an aliphatic part. In \([n]\)cyclophanes (\(n\) is the number of methylene groups), the oligomethylene bridges connect the para or meta positions in benzene; in the so-called "aralipphanes," the ethylene bridges join the aromatic and aliphatic rings. The cyclophanes can be also designed as compounds having an assembly of aromatic rings and aliphatic chains as alternate components of a large ring. In the complex derivatives, multitude aromatic units and bridges form cage-like structures.8

Cyclophanes were intensively investigated due to their physicochemical properties and many applications2−10 resulting from their special structure. Among the most important aspects of cyclophanes are the following: aromaticity of benzene rings, a noncovalent through-space interaction, and a steric strain.

The ability of macrocyclic cyclophanes of defined cavity size to bind guest molecules through noncovalent interactions (host−guest complexation) attracted great interest in view of a possibility of various applications, particularly in biomolecular recognition.11

The aim of our present study is a comparison of the through-space interaction and some through-bond interactions in typical cyclophanes with two benzene rings where one benzene ring is joined with an aliphatic unit, \([n]\)cyclophanes and aralipphanes as well as aliphatic analogues of cyclophanes where both benzene rings have been replaced with alicyclic ones. As the "reference system," we have taken a typical cyclophane, widely investigated \(1\ [2.2]\text{paracyclophane}^{1−24}\) (Scheme 1). The other typical cyclophanes analyzed are II metapara[2.2]cyclophane,24 anti-[2.2]metacyclophanes IIIa and IIIb,12,15,24 and syn-[2.2]metacyclophane IIIc.12 These classical cyclophanes are compared to the \([n]\)cyclophanes (VI,25 VII,25 VIII,26,27 and IX26,27) and aralipphanes (IV, V,28 X,29 XI,30 and XII31). The last group of the investigated compounds, XIII32,33 and XIV34 with two alicyclic rings joined by the ethylene bridges does not belong to the cyclophanes family.

We have undertaken investigation of the geometry, atomic charges, mobility of the electrons in the molecule, energy of the interactions between the benzene ring and aliphatic unit, steric strain, and the attractive and repulsive through-space interactions for compounds presented in Scheme 1. The typical cyclophanes I−III1−24 and \([n]\)cyclophanes VI−IX26,27 were the object of previous investigation, but in order to perform a reliable comparative study of the different groups of cyclophanes, analysis of properties using the same method of calculation seems to be desirable. The crystal structure of compounds V,28 X,28 and XI30 and the derivative of XII31 were known, but the intramolecular interactions have not been an object of investigations up to now.

2. RESULTS

2.1. Geometry of the Investigated Compounds.
Distortion of the aromatic ring from planarity influences the \(\pi\) electron delocalization in the aromatic ring and contributes to the strain of the molecule. Despite the non-planarity of the

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Strain. The torsional strain connected with the ethylene bridges is present in all compounds, except of IIIa, V, VI, and X. The maximal strain \( \beta = 1.776^\circ \) was found for I.

The distance between the benzene rings in typical cyclophanes as well as between the benzene ring and aliphatic part is an important geometrical factor that determines the attractive and, on the other side, the repulsive through-space interactions. The shortest C···C distances \( R_{\text{min}} \) for the investigated cyclophanes are collected in Table 1. For all the cyclophanes, the \( R_{\text{min}} \) values are shorter than the sum of the van der Waals radii \((3.2–3.4 \text{ Å})\). The C···C distance shorter than 2.5 Å was found for I, VI, VII, and VIII.

### 2.2. Atomic Charges

Atomic charges for the investigated molecules have been calculated in the frame of the QTAI approach and are a result of integration of the electron charge over the atomic beta sphere. The atomic charges for investigated compounds are presented in Table 2. For all the investigated compounds, the aromatic ring carbon atoms exhibit the negative charge. Inspection of Table 2 shows that replacement of the second benzene ring with an aliphatic unit for all the cyclophanes except XII results in the increase of the negative charge values on the ipso C\(^1\) atom. The largest negative values on the C\(^1\) atom can be seen for VI, VIII, and XI for which the strong deviation of the benzene ring from planarity is found (Table 1). This is in agreement with the observation of Hernández-Trujillo.\(^{27}\) For XIII, positive charges for the carbon atoms in cycloxyal phthallic rings have been detected. For XIV, positive charges have been found for C\(^1\) and C\(^6\) carbon atoms and negative for other atoms of the 1,4-cyclohexadienyl rings.

### 2.3. AIE and SE Energy

Stability of the cyclophanes is related to the energy of both through-space and through-bond interactions.\(^{12,14,15,19,21,24}\) Discussion performed by Grimme\(^{14,15}\) for para- and metacyclophanes showed that the main attractive forces between the aromatic rings resulted from dispersive and electrostatic interactions. These forces are counterbalanced by the Pauli repulsion. Grimme\(^{17}\) showed that the attractive “overlap-dispersive” interaction plays an important role in cyclophanes. The through-space orbital \( \pi-\pi \) interactions are present only in some cyclophanes.\(^{2,13,22,24,26}\) Therefore, the energy of the through-space interaction in cyclophanes will be dependent on the energy of the attractive (dispersive, electrostatic, and orbital) interaction and repulsive Pauli interaction energy.

### Table 1. Selected Geometrical Parameters for the Investigated Molecules

| compound | \( \alpha [^\circ] \) | \( \beta [^\circ] \) | \( R_{\text{min}} \text{ C···C [Å]} \) |
|----------|----------------|----------------|-----------------|
| I        | 12.822         | 1.776          | 2.1235          |
| II       | 15.652, 9.029  | 37.600, -34.583| 2.7186          |
| IIIa     | 10.337         | 59.460         | 3.0146          |
| IIIb     | 0              | 59.900         | 2.5821          |
| IIIc     | 7.361          | -24.064        | 2.7261          |
| IV       | 14.982         | 62.143, 43.720 | 3.1145          |
| V        | 16.944         | 62.051         | 3.2664          |
| VI       | 29.43          | 63.933         | 2.4347          |
| VII      | 16.376         | 32.613         | 2.499           |
| VIII     | 23.323         | 48.794, -48.815| 2.4746          |
| IX       | 18.151         | -92.252        | 2.4816          |
| X        | 16.320         | 61.291         | 2.8247          |
| XI       | 19.038         | 44.422         | 2.9377          |
| XII      | 11.806         | 40.457         | 2.8992          |
| XIII     | 34.536         | 3.9616         |                |
| XIV      | 143.811        | 2.8242         |                |

\[ \begin{align*}
\text{α} & = 29.43^\circ & \text{β} & = 23.323^\circ & R_{\text{min}} & = 2.5821 \text{ Å} \\
\end{align*} \]
3. Inspection of Table 3 shows that the positive values of the Grimme et al. The strain energy (SE) is associated with CH₂CH₂ group and isolated benzene and aliphatic fragments. XII ring and alicyclic ring or aliphatic chain in cyclophanes energy of the through-space interaction between the benzene molecules. This same procedure was used to calculate the benzene dimer and the energy of individual benzene molecules. A similar method was applied for aliphatic analogues of the cyclophane ethylene linkage does not influence the electronic structure and mutual interaction of the benzene rings. A typical cyclophane molecule was replaced by two aromatic linkages including additional hydrogens from the ethylene group keeps the direction of the removed CC bond and has the CH bonds length of 1.01 Å. The AIE energy of the optimized cyclophane give the SE energy. Similar reference between the energy of the ethylene bridges. The energy of the optimized cyclophane containing the benzene ring and two cyclophane ethylene bridges with complementary hydrogen and subtraction of the obtained energies as well as the energies of the optimized ethylene linkages including additional hydrogens from the energy of the optimized cyclophane give the SE energy. Similar to the AIE calculation, aliphatic cyclophane analogues are treated as typical cyclophanes and two CH₃ groups of the aliphatic chain closest to the ring are used as the ethylene linkages.

Table 2. Net Charge of Atoms [au] for the Investigated Molecules Resulting from Integration over Atomic Basins; Atom Numbering According to Scheme 1

| compound | q₁ | q₂ | Q₃ | q₄ | q₅ | q₆ | A | B | C | D |
|----------|----|----|----|----|----|----|----|----|----|----|
| I        | −0.0025 | −0.0194 | −0.0196 | −0.0025 | −0.0194 | −0.0196 | 0.043 | 0.043 |
| II       | −0.0086 | −0.0291 | −0.0294 | −0.0084 | −0.017 | −0.0175 | 0.0517 | 0.0467 | −0.2591 | −0.159 |
| IIIa     | −0.0086 | −0.0323 | −0.0321 | 0.0324 | −0.0086 | 0.0242 | 0.0482 | 0.0482 |
| IIIb     | −0.0085 | −0.0323 | −0.0232 | −0.0324 | −0.0084 | −0.0244 | 0.0482 | 0.0482 |
| IIIc     | −0.0013 | −0.0227 | −0.0005 | −0.0211 | −0.0153 | −0.0248 | 0.045 | 0.0419 | 0.0422 | 0.0449 |
| IV benzene | −0.0113 | −0.0219 | −0.0102 | −0.0002 | −0.0203 | −0.0343 | 0.05 | 0.0402 | 0.0499 | 0.0429 |
| cyclohexane | 0.0565 | −0.034 | −0.0398 | 0.0568 | −0.0319 | 0.0228 |
| V benzene | −0.0091 | −0.0298 | −0.0315 | −0.0093 | −0.03 | −0.0315 | 0.053 | 0.0531 | 0.037 |
| cyclohexane | 0.0504 | 0.0479 | 0.033 | 0.0505 | 0.0475 | 0.0334 |
| VI       | −0.0145 | −0.0353 | −0.0203 | −0.056 | −0.0141 | −0.0315 | 0.0563 | 0.045 | 0.0557 | 0.0452 |
| VII      | −0.0078 | −0.0325 | −0.0213 | −0.0322 | −0.0094 | −0.0277 | 0.0448 | 0.0448 | 0.053 | 0.0502 |
| VIII     | −0.0163 | −0.0347 | −0.0348 | −0.0163 | −0.0347 | −0.0348 | 0.0605 | 0.0416 |
| IX       | −0.0105 | −0.031 | −0.0315 | −0.0105 | −0.031 | −0.0315 | 0.0555 | 0.0447 |
| X        | −0.0113 | −0.0312 | −0.0217 | −0.0311 | −0.0113 | −0.028 | 0.046 | 0.037 |
| XI       | −0.0175 | −0.0258 | −0.0258 | −0.0175 | −0.0333 | −0.0333 | 0.0488 | 0.0331 |
| XII      | −0.0005 | −0.0262 | −0.0172 | −0.0003 | −0.0262 | −0.0173 | 0.0041 | 0.0519 | 0.0532 | 0.0523 |
| XIII     | 0.0621 | 0.0468 | 0.0372 | 0.0555 | 0.041 | 0.0341 | 0.0394 | 0.0356 | 0.0394 | 0.0356 |
| XIV      | −0.0171 | −0.032 | −0.0324 | −0.0171 | −0.032 | 0.0324 | 0.05 | 0.05 |

Table 3. AIE and SE Energy Interaction between Two Benzene Rings, a Benzene Ring and Aliphatic Chains or Aromatic Ring, and Two Aliphatic Rings for Compounds I–XIV

| compound | AIE [kcal/mol] | SE [kcal/mol] |
|----------|----------------|---------------|
| I        | 12.86296       | 44.00923      |
| II       | 0.158508       | 22.35044      |
| IIIa     | 1.266498       | 13.93807      |
| IIIb     | 11.75422       | 13.93851      |
| IIIc     | 7.236918       | 25.24444      |
| IV       | 26.46061       | 20.05451      |
| V        | 27.89898       | 32.12104      |
| VI       | 39.82094       | 40.07172      |
| VII      | 18.21359       | 26.99707      |
| VIII     | 47.41384       | 58.92427      |
| IX       | 11.75767       | 40.10394      |
| X        | 10.54319       | 38.15395      |
| XI       | 10.88324       | 38.32923      |
| XII      | 7.466021       | 21.9573       |
| XIII     | −3.26846       | 23.37311      |
| XIV      | −0.41303       | 14.74124      |
The QTAIM permits investigation of the hydrogen bond and other noncovalent interactions.\textsuperscript{35,36,38} Methods were used: the quantum theory of atoms in molecules (QTAIM)\textsuperscript{35} to detect and describe the noncovalent interactions in the investigated compounds, two theoretical approaches.\textsuperscript{39,40} This method visualizes very weak hydrogen bonds, van der Waals interactions, dispersion, and steric repulsion by means of the NCI plots and NCI surfaces. The plots of the reduced density gradient versus the electron density multiplied by the sign of the second Hessian of the electron density eigenvalue ($\lambda_2$) are used to investigate the existence of a weak interaction. The spikes at the negative values indicate the attractive non-covalent interactions, while the positive correspond to the steric repulsion. A dispersive interaction usually appears as two spikes symmetrically located around zero in the NCI plot. The spikes in the region between +0.01 to 0 au correspond to a weak attractive dispersion interaction. The noncovalent attractive interaction and steric repulsion may be also visualized as the gradient isosurfaces in the real space for the molecule. The NCI approach traditionally uses color for the isosurfaces: green for attractive interactions, other QTAIM parameters also must be taken into account: the ellipticity of the electron density at the BCP ($\epsilon$) cannot be very high,\textsuperscript{39} and the bond path cannot be very bent. A positive value of the Laplacian of the electron density at BCP indicates the type of interaction. For noncovalent ("closed-shell") interactions, it has to be in the 0.024–0.139 au range.\textsuperscript{38}

In order to investigate very weak dispersive and repulsive interactions, the noncovalent interaction (NCI) approach can be applied.\textsuperscript{39,40} This method visualizes very weak hydrogen bonds, van der Waals interactions, dispersion, and steric repulsion by means of the NCI plots and NCI surfaces. The plots of the reduced density gradient versus the electron density multiplied by the sign of the second Hessian of the electron density eigenvalue ($\lambda_2$) are used to investigate the existence of a weak interaction. The spikes at the negative values indicate the attractive non-covalent interactions, while the positive correspond to the steric repulsion. A dispersive interaction usually appears as two spikes symmetrically located around zero in the NCI plot. The spikes in the region between +0.01 to 0 au correspond to a weak attractive dispersion interaction. The noncovalent attractive interaction and steric repulsion may be also visualized as the gradient isosurfaces in the real space for the molecule. The NCI approach traditionally uses color for the isosurfaces: green for attractive interactions and red for the repulsive interactions.

Both methods, QTAIM and NCI, were applied for the investigation of the through-space interactions in the cyclophanes and their aliphatic analogues under study. QTAIM analysis for [2.2]paracyclophane (I) was performed previously.\textsuperscript{12,13,22–24} The QTAIM plot reveals the presence of C···

\begin{table}[h]
\centering
\caption{Characteristics of the Bond Critical Point (BCP) for the Inter-ring Interactions in the Investigated Compounds}  
\begin{tabular}{|c|c|c|c|c|c|}
\hline
compound & $\rho(r)$ [au] & $V^2(r)$ [au] & $\epsilon(r)$ & bond path length [$\text{Å}$] & nonlinearity of the bond path [$\text{Å}$] & DI \\
\hline
IIIa C--C & 0.0201 & 0.0582 & 0.0000 & 2.6766 & 0.0017 & 0.0964 \\
IIIB C--C & 0.0201 & 0.0582 & 0.0000 & 2.6771 & 0.0017 & 0.0962 \\
IIIc C--C & 0.0181 & 0.0545 & 0.3691 & 2.7286 & 0.0024 & 0.0562 \\
IV CH--H & 0.0208 & 0.0685 & 0.3302 & 1.8683 & 0.0906 & 0.0422 \\
IV CH--C & 0.0138 & 0.0478 & 1.7776 & 2.4756 & 0.0303 & 0.0251 \\
V CH--C & 0.0189 & 0.0570 & 0.2925 & 2.2394 & 0.0138 & 0.0355 \\
V CH--C & 0.0189 & 0.0570 & 0.2925 & 2.2389 & 0.0138 & 0.0355 \\
VI C--C & 0.0143 & 0.0558 & 2.4364 & 2.8855 & 0.0590 & 0.0300 \\
VII H--C & 0.0113 & 0.0435 & 2.5153 & 3.0758 & 0.3843 & 0.0144 \\
IX CH--C & 0.0135 & 0.0420 & 0.6719 & 2.5304 & 0.0617 & 0.0368 \\
IX CH--C & 0.0135 & 0.0420 & 0.6719 & 2.5290 & 0.0617 & 0.0369 \\
$X$ H--H & 0.0100 & 0.0304 & 0.0376 & 2.1592 & 0.0499 & 0.0225 \\
$X$ H--H & 0.0126 & 0.0448 & 0.8029 & 2.2666 & 0.1870 & 0.0247 \\
$X$ H--H & 0.0100 & 0.0304 & 0.0379 & 2.1595 & 0.0499 & 0.0225 \\
$X$ H--H & 0.0126 & 0.0448 & 0.8030 & 2.1870 & 0.0247 \\
$X$ H--C & 0.0302 & 0.1030 & 0.8474 & 2.0627 & 0.0196 & 0.0560 \\
XI H--C & 0.0084 & 0.0250 & 0.5849 & 2.7244 & 0.0449 & 0.0238 \\
XI H--C & 0.0084 & 0.0250 & 0.5842 & 2.7241 & 0.0448 & 0.0238 \\
XI H--C & 0.0259 & 0.0893 & 1.0510 & 2.1160 & 0.0165 & 0.0464 \\
XI H--C & 0.0259 & 0.0894 & 1.0475 & 2.1149 & 0.0165 & 0.0464 \\
XIII H--H & 0.0144 & 0.0487 & 0.3646 & 2.1058 & 0.1281 & 0.0258 \\
XIII H--H & 0.0100 & 0.0376 & 0.9952 & 2.2848 & 0.1424 & 0.0229 \\
XIII H--H & 0.0140 & 0.0487 & 0.3646 & 2.1058 & 0.1281 & 0.0258 \\
XIII H--H & 0.0109 & 0.0376 & 0.9952 & 2.2848 & 0.1424 & 0.0229 \\
XIII H--H & 0.0152 & 0.0528 & 0.4814 & 2.0743 & 0.0791 & 0.0217 \\
XIV C--C & 0.0086 & 0.0253 & 0.1678 & 3.1719 & 0.0355 & 0.0260 \\
XIV C--C & 0.0086 & 0.0253 & 0.1678 & 3.1719 & 0.0355 & 0.0260 \\
\hline
\end{tabular}
\end{table}
C, CH⋯C, and H⋯H bond paths, suggesting the existence of noncovalent through-space interactions between the parts of the investigated molecules. For some compounds, no bond path has been found (Table 4).

Figure 1. NCI plots and gradient isosurfaces for the compounds without bond paths between parts of the molecules: VIII, II, VII, and XII.
Figure 2. Investigated compounds IIIa, IIIc, XIV, and VI with the inter-ring C···C interaction.
Figure 3. Investigated compounds with intermolecular CH···C interactions.
The first group constitutes II, VIII, and XII for which no bond paths in the QTAIM plots are observed (Figure 1). The compound I, which belongs to this group, was investigated in detail using the QTAIM methods and discussed previously.12,13,22,23 The absence of bond paths indicates that there are no through-space orbital interactions between the C atoms in benzene ring and the C atom of another part of the investigated compounds. For VII, the bond path between the aliphatic H atom and C atom belonging to the benzene ring is found, but the high ellipticity of the electron density at BCP, small electron density at BCP,36 and the DI index as well as high nonlinearity of the bond path (d) excludes the possibility of a stable interaction. The presence of dispersive interactions between the benzene ring and other parts of the molecule has been visualized in the NCI diagram for all compounds by the presence of spikes in the region between −0.01 and 0 au (Figure 1). The numerous spikes in the region between 0 and +0.002 au corresponding to repulsive interactions are observed in the NCI diagrams. The spikes at approximately +0.002 au observed in the NCI plots of all compounds correspond to the nonbonding interactions in the center of the benzene ring. The NCI gradient isosurfaces in the real space for the molecule evidence the dispersive interactions by the presence of green planes. The blue color on the green background indicates that the dispersive interaction becomes stronger. For this group of cyclophanes, the main interactions are the attractive through-space interactions with a dispersive character. The repulsive interaction in the barrelene moiety in XII is visualized by the red color.

The second group contains compounds for which the bond paths between the carbon atoms belonging to different rings have been found. The presence of this type of bond path suggests the through-space π−π interaction. The C···C bond paths have been found for anti-[2.2]metacyclophanes IIIa and IIIb of a slightly different geometry (Table) as well as for IIIc syn-[2.2]metacyclophane. Unexpectedly, for XIV, which does not belong to the family of cyclophanes (Table 3 and Figure 2), the C···C bond paths have also been found. The QTAIM analysis showed that, for IIIa and IIIb, the values of the charge density at the BCP are equal to 0.0201 au and the lengths of the bond path are 2.6766 and 2.6771 Å, respectively. The values of the DI index for IIIa and IIIb are the highest among the investigated compounds. Slightly weaker interactions have been suggested for IIIb, taking into account the fact that the charge density at BCP is 0.0108 au and the bond path length is 2.6728 Å. These results are in accordance with the results obtained previously by Caramori and Galembeck12 who showed the existence of the through-space π−π orbital interactions.

For XIV, two bond paths joining the carbon atoms, which are engaged in the double bonds of different cyclohexadiene rings, have been found. A small value of the electron density at the BCP and a length of the bond path of 3.1719 Å suggest that the through-bond interaction cannot be classified as a C−C orbital interaction. For IIIa and IIIc, the C···C interactions are represented by the NCI spike at approximately −0.02 au. For XIV, the respective spike merges in the region of the attractive−dispersive interaction. Comparison of the NCI diagrams for IIIa−c shows a difference in the dispersive interactions. For XIV, the green plane shows that the dispersive interaction covers the entire molecule including the linkage between the rings. For VI, a small value of the electron density and DI at BCP suggest the presence of a weak interaction but high ellipticity and the nonlinearity of the bond path indicates that this C···C interaction cannot be stable (Table 4).

The third group involves cyclophanes with the presence of CH···H and H···H interactions. The through-space noncovalent CH···C interactions have been evidenced by presence of the bond paths joining the hydrogen atom of the aliphatic unit with the carbon atom of the benzene ring. This interaction is characteristic for V, X, and XI.

The CH···π interaction was broadly discussed in the literature, and the criteria of a possibility of a formation of the CH···π hydrogen bond basing on the QTAIM analysis were proposed.41 For V, the presence of two CH···C bond paths referring to the interaction between the aliphatic CH hydrogen atom and aromatic carbon atom with a ρ(r) of 0.0189 au was found. The low ellipticity values and small deviations from linearity evidence the presence of the two CH···π hydrogen bonds.

X is the cyclophane of particular interest because of two bond paths joining one aliphatic hydrogen atom with two ipso carbon atoms of the benzene ring (Figure 3). For both bond paths, the electron density at the BCP is 0.0259 au, which indicates the presence of an exceptional bifurcated CH···π hydrogen bond. However, the high value of ellipticity of the electron density at the BCP suggests potential instability of these interactions. Except the bifurcated CH···π hydrogen bond, also two other very weak CH···π interactions have been evidenced. In XI where the adamantyl moiety is connected via an ethylene bridge to the carbon atom in the para position of the benzene, other noncovalent interactions are present. The CH···π hydrogen bond is the strongest in comparison to other hydrogen bonds in the investigated compounds (ρ = 0.0302 au; Laplacian = +0.1030 au). For this cyclophane, four bifurcated H···H interactions are present, joining the hydrogen atoms of the aliphatic CH groups with these of the benzene ring as well with the H atom of the ethylene bridge.

For the IV cyclophane, the CH···C bond path is found but the high ellipticity value for the electron density at BCP indicates instability of this interaction. At the same time, the presence of a stronger H···H interaction has been shown (ρ = 0.0208, Laplacian = +0.0685). This interaction may be classified as a strong H···H hydrogen bond.36,42

For the aliphatic perhydroparacyclophane XIII, several bifurcated H···H interactions between the hydrogen atom of the ethylene bridges have been found. Nonlinearity of these bond paths and relatively high ellipticity suggest instability of these interactions.

The presence of the CH···π hydrogen bond for three alaraphanes (V, X, and XI) has been visualized in the NCI plots by the presence of spikes in the range of −0.02 to −0.03 au. The H···H hydrogen bond in IV is illustrated by the spike at approximately 0.02 au. The attractive dispersion interactions are evidenced by the spikes in the region below −0.01 au. Numerous spikes in the region from 0 to +0.02 au can be connected with the presence of strong repulsive interactions in the center of the molecules. The green and blue colors in the NCI gradient surfaces are evidence of the attractive dispersive interactions between the rings and the aliphatic parts. For XIII, the NCI diagram and NCI plot indicate the presence of the dispersive attractive interactions between the aliphatic rings.

The QTAIM analysis of the investigated compounds shows that there are no essential differences in the through-space interactions between the cyclophanes and their aliphatic
analogues. The character of the non-covalent through-space interactions, C···C, H···H, or C···H···π, has been determined by the structure of the compounds. The C···C bond paths have been found for typical cyclophanes (IIIa, IIIb, and IIIc) and their aliphatic analogue XIV. However, only for IIIc cyclophanes, the existence of the orbital π···π interaction has been shown.

The NCI approach has evidenced that the attractive dispersion interaction plays an important role for all investigated compounds.

2.5. Induced Current Density (ACID). Despite the fact that the QTAIM method delivers parameters that represent the electron population in the atomic basin and electron delocalization, we have decided to use the induced current density (ACID) approach, as a complementary method to the QTAIM method. The electron population in the atomic basin and electron delocalization, we have decided to use the induced current density (ACID) approach, as a complementary method to the QTAIM method.

According to Figure 4, the mobility of electrons in the aromatic ring is concentrated along the aromatic bonds but not the aromatic ring center, so the repulsive interaction in the aromatic ring found using the NCI approach is confirmed. It can be suggested that the mobility of the electrons in the CH2···CH2 linkage is the highest for cyclophanes I, IIIc, and XIV for which the aromatic or cyclohexadiene rings are located one under the other and close to parallel.

3. CONCLUSIONS

(1) The energy of the through-space interaction is dominated by the repulsive interactions in cyclophanes, while the attractive interaction dominates in their aliphatic analogues.

(2) The analysis of the through-space interactions in the investigated compounds shows that there are no essential differences in the through-space interactions between cyclophanes and their aliphatic analogues.

(3) The QTAIM analysis shows that the C···C, H···C, and H···H bond paths have been found for investigated compounds. The type of the interaction and its strength and stability depend on the geometry of the compound.

(4) The dispersive interactions are the common attractive through-space forces for all the compounds under study.

4. CALCULATION METHOD

The optimization of the investigated [2.2]cyclophanes was performed with the Gaussian 16 program the at DFT B3LYP/6-311++G**-DG3 level of calculation including Grimme dispersion. The wave functions evaluated for optimized molecules were used as an input to the AIMALL program version 17.11.14.

The very weak interactions not very well evident in the frame of the QTAIM method were analyzed with the NCI program. The first derivative of the electron density that describes the deviation from a homologous electron distribution was plotted as a function of the electron density multiplied by the sign of the second Hessian eigenvalue that allows to differentiate repulsive and attractive interactions and indicate the interaction strength. In the frame of the NCI method, also visualization of the gradients isosurfaces in real space for the molecule is possible. Traditionally, a blue isosurface for attractive, red for repulsive, and green for intermediate interactions are used. The gradient isosurfaces were visualized with VMD program for reduced density gradient isosurface of 0.5.

To visualize delocalization of electrons, the ACID program was used. This method is based on the anisotropy of the current-induced density (ACID) and visualizes mobility of the electrons not localized at the nuclei.

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