Parity Violation Energy Difference calculation of atropisomers

Dhanalakshmi Vadivel (dhanalakshmi.vadivel@unipv.it)
University of Pavia
Daniele Dondi
University of Pavia

Research Article

Keywords: Parity violation, Atropisomers, helicenes, cinnabar, homochirality

Posted Date: September 14th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-2005462/v1

Additional Declarations: No competing interests reported.

Version of Record: A version of this preprint was published at Origins of Life and Evolution of Biospheres on June 14th, 2023. See the published version at https://doi.org/10.1007/s11084-023-09639-w.

Abstract

Enantiomers have a different energy due to the parity violation effects. Up to now, these effects are difficult to calculate and their final effect on the choice of one enantiomer in the homochirality issue is still a matter of debate. Nevertheless, many scientists support the role of this tiny energy difference in the triggering of homochirality. In this work, we studied the energy difference in atropisomers, a class of stereoisomers in which the chirality is given by the block of rotation around one bond. Atropisomers might have a low energy barrier for the interconversion and this is interesting for the equilibration of the two enantiomers and the choice of the most stable enantiomer. Moreover, structures might be extended like in the case of polymers or crystals having helical framework and thus giving an additive effect on the parity violation energy of the whole structure. The parity violation energy difference here is discussed with the correlation on the general structure of the final molecule giving a qualitative model to predict the sign of local contributions of atoms.

Introduction

Life consists of macromolecules such as proteins, sugars, DNAs, RNAs and other biopolymers. Surprisingly, the presence of only one enantiomer is almost quantitative (Fujii N 2002). As if it is known that in order to have a useful polymer for the sustaining of life the chirality of its components should be controlled (Green et al. 1999, Wu et al. 2012, Bonner 2000, Klabunovskii 2012), the reason for the preference of one enantiomer with respect to the other is still a matter of debate. Yamagata, in 1966, (Yamagata 1966) was the first scientist that proposed PVED may have determinately selected life's use of the natural L-amino acids rather than their D mirror images. Obviously, some mechanisms of chiral amplification (Green et al. 1999, Hawbaker and Blackmond 2019, Bonner 1996, Blackmond 2006) should have arisen in the past, but still scientists are divided in an initial random choice of chirality (statistical or for some external sources like circularly polarized light (Meierhenrich 2002) or for some other physics laws like parity violation (Macdermott 1995, Hawbaker and Blackmond 2019, Klabunovskii 2012). Parity violation gives a small energy difference between enantiomers and it is caused by the weak neutral current mediated by the Z boson. This total effect gives a Parity Violation Energy Difference (PVED). PVED depends on the atomic masses of elements involved, scaling approximately like Z^n(where n is about 5, where Z is the nuclear charge of the atom). (Laerdahl and Schwerdtfeger 1999, Schwerdtfeger et al. 2003). Furthermore, in accordance with the single-center theorem of Hegstrom (Hegstrom et al. 1980), the substance should contain more than one heavy element (either as ligands or chiral centers).

PVED, for common organic molecules having lighter elements, is in the range of femto- to pico- J/mol (Quack 2002). Even if there are some theoretical works showing that the actual enantiomers present in biomolecules are the most stable, like D-glyceraldehyde in gas-phase (Kikuchi et al. 2002) and in solution (Kitayama et al. 2002) for amino acids it is less evident (Laerdahl 2000, Bergerd and Quack 2000, MacDermott et al. 2009, Lee and Shin 2004, Kitayama et al. 2002B) a complete cause-effect is not clear (Avalos et al. 2000). Our own research group demonstrated that natural alpha amino acids showing higher thermodynamical stability compared to their structural isomers of the rest by investigation on over 100'000 isomers (Crespi et al. 2021).

The same confusion appears when PVED of partial biomolecules are calculated like polypeptides (Faglioni et al. 2005), DNA (Faglioni et al. 2005b), RNA (Faglioni et al. 2006) and proteins secondary structures (Faglioni and Cuesta 2011). This is also due to the fact that the direct measurement of PVED on molecules is still lacking, even if intriguing, for the high-level science involved (Darquié et al. 2010,Tokunaga et al. 2013, Blanchard et al. 2020, Eills et al. 2017). This is true also with indirect measurement of PVED differences, that up to now they were refuted (Viedma 2007, Avalos et al. 2000).

The aim of this work is to put the basis for a theoretical PVED calculation of rigid chiral compounds that are already known in literature and thus their practical synthesis is feasible and the theoretically investigated properties might be experimentally verified. In fact, a reasonable prediction of the effects is lacking (Mason and Tranter 1984), since for complex molecules the PVED effect on atoms might be additive or subtractive. The results may be of general interest for prebiotic chemistry because this allows for a rapid screening of possible structures (e.g. minerals) that may have led to a selection of chirality. The results can in fact be extended based on the shape of the molecule which leads to effects of the same sign.

Experimental section

Geometry optimizations were made with Gaussian 09 by using the B3LYP functional with 6-31G(d) basis set. All the minima are characterized to have no imaginary frequencies. PVED calculations were performed by using a customized version of the Dirac08 program (http://wiki.chem.vu.nl/dirac/index.php/Dirac_Program). A Single point energy was calculated starting from the optimized geometries. Different basis sets were used for PVED calculations. For the case with heavy atoms, zeroth and fourth order relativistic approximation (ZORA) was used. For mercury, Dyall CV2Z (core valence double zeta) basis set (Dyall and Gomes 2009) was used and cc-pVDZ (Dunning 1989) for other atoms.

Results and Discussion

Atropisomers with no heavy elements

The Parity Violation Energy Difference (PVED) depends on the fourth power of Z. In the first part of our work we considered chiral molecules known in literature showing atropisomerism but containing instead no heavy elements. This should facilitate the screening of molecules having the most interesting (larger PVED) backbone structures and in second instance our findings could be applied in the search of similar molecular architectures with heavy elements. Our search starts from helicenes, organic compounds having an exceptionally high optical rotatory power.

Atoms are colored by the PVED contribution of single atoms. Red and green color indicate, respectively, a positive and a negative effect (Figure 1). The total PVED effect is given by the summation of the atomic contributions (Table 1).

Table 1 Total PVED calculated with the different basis set. *:for the compound 3 it was calculated the opposite enantiomer

Molecule	**PVED (Ha)**	
	STO-6G	**cc-pVDZ**
Hexahelicene (1)	-4.5×10^{-20}	/
Heptahelicene (2)	-6.4×10^{-20}	-4.8×10^{-20}
Diazahelicene (3)*	2.6×10^{-20}	1.7×10^{-20}
Paracyclophane (4)	/	-9.1×10^{-21}
Twisted pentacene (5)	-2.4×10^{-19}	-2.2×10^{-19}

The modulus of PVED effect of helicenes 1-3 is inversely proportional to the distance from the center of the molecule. However, the sign changes alternatively leading ultimately to a low value of PVED. Values are almost insensitive by the substitution of carbon with nitrogen (see 3 vs. 1). For diazahelicene, the lower PVED value was due to the conformation change with respect to 1. In fact, as it is visible in figure XC, carbon atoms of the terminal benzene rings give a low effect on PVED. PVED slightly increases with the increase of atoms in the structure (2 vs. 1).

The effect of the basis set was explored with compound 3. Total PVED calculated with STO-6G, 6-31G(d) and cc-pVDZ are, respectively: -6.4×10^{-20}, -4.2×10^{-20} and -4.8×10^{-20} Ha. Unfortunately calculations did not converge on all basis sets. Paracyclophane 4 (figure 2) has a scarcely predictable behavior that depends on the low symmetry. The best molecular structure from the point of view of cooperative PVED effect is the twisted pentacene 5 (Figure 2). This reflects on the highest PVED calculated among molecules 1-5 (see table 1).

The PVED effect of molecules having a phenylene repeating unit (Figure 3) was then investigated. Phenylenes have a low rotation barrier for the conversion between R and S. Usually at ambient temperature the rotation is free. However, ring substitutions might increase the rotational barrier. PVED of phenylenes shows a cooperative effect for atoms lying on the main axis, while the contribution of other atoms is almost negligible (figure 4).

Table 2 Calculated PVED for phenylenes and total value of PVED divided by the number of repeating units (See text)

Molecule	**PVED (Ha)**	**PVED/n (Ha x10^{21})**
Biphenyl (n=2)	$1.7\text{x}10^{-21}$	0.85
Triphenyl (n=3)	$3.4\text{x}10^{-21}$	1.13
Tetraphenyl (n=4)	$5.1\text{x}10^{-21}$	1.28
Pentaphenyl (n=5)	$6.8\text{x}10^{-21}$	1.36

The PVED of (poly)phenylenes is proportional to the number of phenylene repeating units (table 2). As it is visible from the last column of table 2, the total PVED divided by the number of repeating units shows an increment with a value that tends to 1.4.

Cinnabar crystals

Cinnabar (HgS) is a good candidate for the investigation of PVED since it can crystallize giving a helical structure (see figure 5). Calculations were effectuated on portions of HgS chains containing from 1 to 3 mercury atoms. Chains are capped with hydrogen atoms, however, the contribution of hydrogen to the total PVED is negligible. The highest calculated PVED is about 10^{-15} Ha for the HgS_2H_2 fragment. However, the PVED does not increase with the number of mercury atoms (See table 3).

Table 3 Total PVED calculated for cinnabar chains

Formula	Total PVED (Ha)
HgS_2H_2	$-2.09\text{x}10^{-15}$
$Hg_2S_3H_2$	$-7.91\text{x}10^{-16}$
$Hg_3S_4H_2$	$-4.92\text{x}10^{-16}$

Table 4 PVED contribution of single mercury atoms for the cinnabar-like structures calculated

Structure	**Contribution of mercury atom(s) on total PVED (Ha)**		
HgS_2H_2	$-2.09\text{x}10^{-15}$		
$Hg_2S_3H_2$	$-3.93\text{x}10^{-16}$	$-3.93\text{x}10^{-16}$	
$Hg_3S_4H_2$	$-3.57\text{x}10^{-16}$	$2.32\text{x}10^{-16}$	$-3.57\text{x}10^{-16}$

Analyzing more in detail the structures (Fig. 6), it is visible how in the structure having three mercury atoms, one mercury atom has a PVED of a different sign. In table 4 are listed all the values of PVED effect on mercury atoms for the different structures considered.

It seems reasonable to think that the PVED of atoms in these structures might depend on the position of the main inertia axis of the molecule. In fact, for the cinnabar analogue having one mercury atom, the value is high for the mercury (being close to the center of mass of the molecule). For the case with two atoms, the inertia axis runs parallel to the segment connecting the two Hg centers but is shifted towards the SH ends. In this case, the effect is lower since the axis is not close to the atomic centers. In the last case, with 3 mercury atoms, the inertia axis is parallel to the Hg atoms closer to SH ends, but it is shifted toward the central mercury atom. The sign of PVED might change with respect to the distance, as already mentioned by Lazzeretti (Faglioni and Lazzeretti 2001).

Conclusion

In the screw-like molecules considered, it seems to emerge that the PVED absolute value of atoms depends on the distance between atoms and axis of inertia of the molecule. However, the sign of PVED is difficult to predict. Heteroatoms in the structures calculated show less effect on the total value.

Complex molecules containing no heavy elements could provide a useful benchmark for the rapid screening of promising backbone structures. PVED can be calculated for larger systems containing more than one heavy atom.

Chiral crystals of achiral molecules could be promising for detecting PVED effects since their additive effect depends on the number of atoms present in the structure.

Declarations

Conflict of interest **-** The authors declare no conficts of interest.

Ethical Approval and Consent to participate – Not applicable

Human and Animal Ethics - Not applicable

Consent for publication - Not applicable

Availability of supporting data - Not applicable

Competing interests - Not applicable

Funding - Not applicable

Authors' contributions - Dhanalakshmi Vadivel: working, writing and discussion. Daniele Dondi: Principle Investigator, planing and suggestion.

Acknowledgements - CINECA Supercomputer Center, with computer time granted by ISCRA ARCAT project (HP10CXJWQY).

Authors' information - Dhanalakshmi Vadivel (corresponding author: dhanalakshmi.vadivel@unipv.it) and Daniele Dondi (daniele.dondi@unipv.it)

References

1. Avalos M, Babiano R, Cintas P, et al (2000) From parity to chirality: chemical implications revisited. Tetrahedron: Asymmetry 11:2845–2874. https://doi.org/10.1016/S0957-4166(00)00265-2
2. Berger R, Quack M (2000) Electroweak Quantum Chemistry of Alanine: Parity Violation in Gas and Condensed Phases. ChemPhysChem 1:57–60. https://doi.org/10.1002/1439-7641(20000804)1:1<57::AID-CPHC57>3.0.CO;2-J
3. Blanchard JW, King JP, Sjolander TF, et al (2020) Molecular parity nonconservation in nuclear spin couplings. Phys Rev Research 2:023258. https://doi.org/10.1103/PhysRevResearch.2.023258
4. Bonner WA (1996) Enantioselective autocatalysis. IV. Implications for parity violation effects. Origins Life Evol Biosphere 26:27–45. https://doi.org/10.1007/BF01808158,
5. Bonner WA (2000) Parity violation and the evolution of biomolecular homochirality. Chirality 12:114–126. https://doi.org/10.1002/(SICI)1520-636X(2000)12:3<114::AID-CHIR3>3.0.CO;2-N
6. Crespi S, Vadivel D, Bellisario A, Dondi D (2021) Computational Study of the Stability of Natural Amino Acid isomers. Orig Life Evol Biosph 51:287–298. https://doi.org/10.1007/s11084-021-09615-2
7. Darquié B, Stoeffler C, Shelkovnikov A, et al (2010) Progress toward the first observation of parity violation in chiral molecules by high-resolution laser spectroscopy. Chirality 22:870–884. https://doi.org/10.1002/chir.20911
8. Donna G. Blackmond (2006) Nature 441:xi–xi. https://doi.org/10.1038/7093xia
9. Dunning TH (1989) Gaussian basis sets for use in correlated molecular calculations. I. The atoms boron through neon and hydrogen. The Journal of Chemical Physics 90:1007–1023. https://doi.org/10.1063/1.456153
10. Dyall KG, Gomes ASP (2009) Revised relativistic basis sets for the 5d elements Hf–Hg. Theoretical Chemistry Accounts 125:97. https://doi.org/10.1007/s00214-009-0717-7
11. Eills J, Blanchard JW, Bougas L, et al (2017) Measuring molecular parity nonconservation using nuclear-magnetic-resonance spectroscopy. Phys Rev A 96:042119. https://doi.org/10.1103/PhysRevA.96.042119
12. Faglioni F, Lazzeretti P (2001) Understanding parity violation in molecular systems. Phys Rev E 65:011904. https://doi.org/10.1103/PhysRevE.65.011904
13. Faglioni F, Passalacqua A, Lazzeretti P (2005) Parity Violation Energy Of Biomolecules – I: Polypeptides. Orig Life Evol Biosph 35:461–475. https://doi.org/10.1007/s11084-005-3511-0
14. Faglioni F, D’Agostino PS, Cadioli B, Lazzeretti P (2005b) Parity violation energy of biomolecules – II: DNA. Chemical Physics Letters 407:522–526. https://doi.org/10.1016/j.cplett.2005.04.009

15. Faglioni F, Cuesta IG, Lazzeretti P (2006) Parity violation energy of biomolecules – III: RNA. Chemical Physics Letters 432:263–268. https://doi.org/10.1016/j.cplett.2006.10.030
16. Faglioni F, Cuesta IG (2011) Parity-Violation Energy of Biomolecules—IV: Protein Secondary Structure. Orig Life Evol Biosph 41:249–259. https://doi.org/10.1007/s11084-010-9229-7
17. Fujii N (2002) D-Amino Acids in Living Higher Organisms. Origins of life and evolution of the biosphere 32:103–127. https://doi.org/10.1023/A:1016031014871
18. Green MM, Park J-W, Sato T, et al (1999) The Macromolecular Route to Chiral Amplification. Angew Chem Int Ed 38:3138–3154. https://doi.org/10.1002/(SICI)1521-3773(19991102)38:21%3C3138::AID-ANIE3138%3E3.0.CO;2-C
19. Hawbaker NA, Blackmond DG (2019) Energy threshold for chiral symmetry breaking in molecular self-replication. Nat Chem 11:957–962.https://doi.org/10.1038/s41557-019-0321-y
20. Hegstrom RA, Rein DW, Sandars PGH (1980) Calculation of the parity nonconserving energy difference between mirror-image molecules. The Journal of Chemical Physics 73:2329–2341. https://doi.org/10.1063/1.440383
21. Kikuchi O, Kitayama T, Watanabe T, et al (2002) Parity-violating energy of d-glyceraldehyde. Journal of Molecular Structure: THEOCHEM 579:147–150. https://doi.org/10.1016/S0166-1280(01)00725-4
22. Kitayama T, Ushikubo T, Morihashi K, Kikuchi O (2002) Conformation and parity-violating energy of hydrated d-glyceraldehyde in aqueous solution. Journal of Molecular Structure: THEOCHEM 586:1–7. https://doi.org/10.1016/S0166-1280(01)00803-X
23. Kitayama T, Watanabe T, Takahashi O, et al (2002b) Parity-violating energy for the chirality-producing step in Strecker synthesis of l -alanine. Journal of Molecular Structure: THEOCHEM 584:89–94. https://doi.org/10.1016/S0166-1280(02)00023-4
24. Klabunovskii EI (2012) Homochirality and its significance for biosphere and the origin of life theory. Russ J Org Chem 48:881–901. https://doi.org/10.1134/S1070428012070019
25. Laerdahl JK, Schwerdtfeger P (1999) Fully relativistic *ab initio* calculations of the energies of chiral molecules including parity-violating weak interactions. Phys Rev A 60:4439–4453. https://doi.org/10.1103/PhysRevA.60.4439
26. Laerdahl JK, Wesendrup R, Schwerdtfeger P (2000) D- orL-Alanine: That Is the Question. ChemPhysChem 1:60–62. https://doi.org/10.1002/1439-7641(20000804)1:1%3C60::AID-CPHC60%3E3.0.CO;2-M
27. Lee K, Shin S, Ka J (2004) Tunneling dynamics of amino-acid: model for chiral evolution? Journal of Molecular Structure: THEOCHEM 679:59–63. https://doi.org/10.1016/j.theochem.2004.04.004
28. Macdermott AJ (1995) Electro weak enantioselection and the origin of life. Origins Life Evol Biosphere 25:191–199. https://doi.org/10.1007/BF01581582.
29. MacDermott AJ, Fu T, Hyde GO, et al (2009) Electroweak Parity-Violating Energy Shifts of Amino Acids: The "Conformation Problem." Orig Life Evol Biosph 39:407–437. https://doi.org/10.1007/s11084-009-9161-x

30. Mason SF, Tranter GE (1984) The parity-violating energy difference between enantiomeric molecules. Molecular Physics 53:1091–1111. https://doi.org/10.1080/00268978400102881
31. Meierhenrich, U. J., Thiemann, W. H. P., Barbier, B., Brack, A., Alcaraz, C., Nahon, L., & Wolstencroft, R. (2002). Circular polarization of light by planet Mercury and enantiomorphism of its surface minerals. Origins of Life and Evolution of the Biosphere, 32(2), 181-190.
32. Quack M (2002) How Important is Parity Violation for Molecular and Biomolecular Chirality? Angew Chem Int Ed 41:4618–4630. https://doi.org/10.1002/anie.200290005
33. Schwerdtfeger P, Gierlich J, Bollwein T (2003) Large Parity-Violation Effects in Heavy-Metal-Containing Chiral Compounds. Angew Chem Int Ed 42:1293–1296. https://doi.org/10.1002/anie.200390333
34. Tokunaga SK, Stoeffler C, Auguste F, et al (2013) Probing weak force-induced parity violation by high-resolution mid-infrared molecular spectroscopy. Molecular Physics 111:2363–2373. https://doi.org/10.1080/00268976.2013.821186
35. Viedma C (2007) Selective Chiral Symmetry Breaking during Crystallization: Parity Violation or Cryptochiral Environment in Control? Crystal Growth & Design 7:553–556. https://doi.org/10.1021/cg060698d
36. Wu M, Walker SI, Higgs PG (2012) Autocatalytic Replication and Homochirality in Biopolymers: Is Homochirality a Requirement of Life or a Result of It? Astrobiology 12:818–829. https://doi.org/10.1089/ast.2012.0819
37. Yamagata Y (1966) A hypothesis for the asymmetric appearance of biomolecules on earth. Journal of Theoretical Biology 11:495–498. https://doi.org/10.1016/0022-5193(66)90110-X

Figures

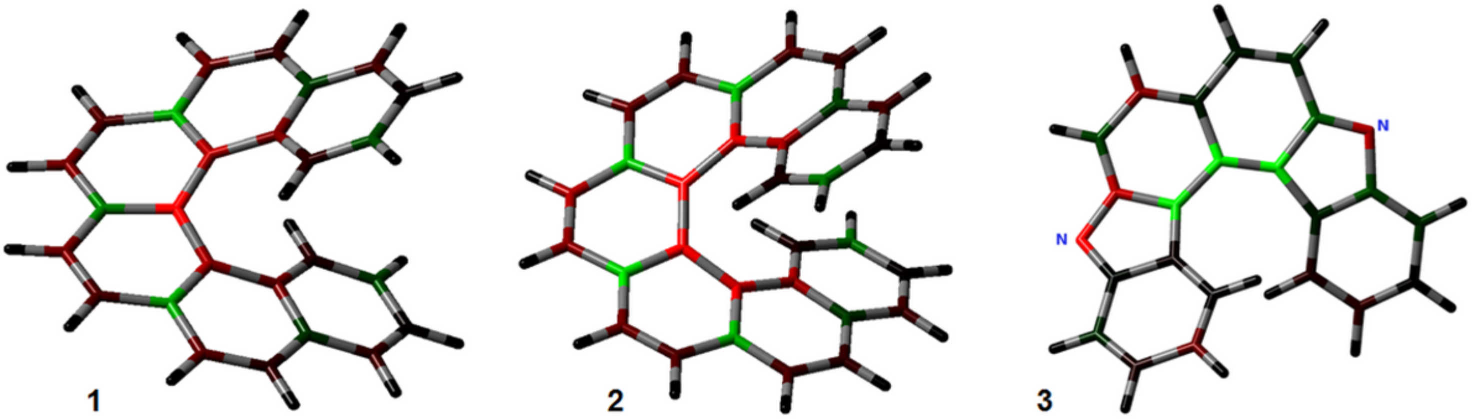

Figure 1

Calculated PVED of atoms shown in color (see text). 1: Hexahelicene, 2:Heptahelicene, 3:Diazahelicene

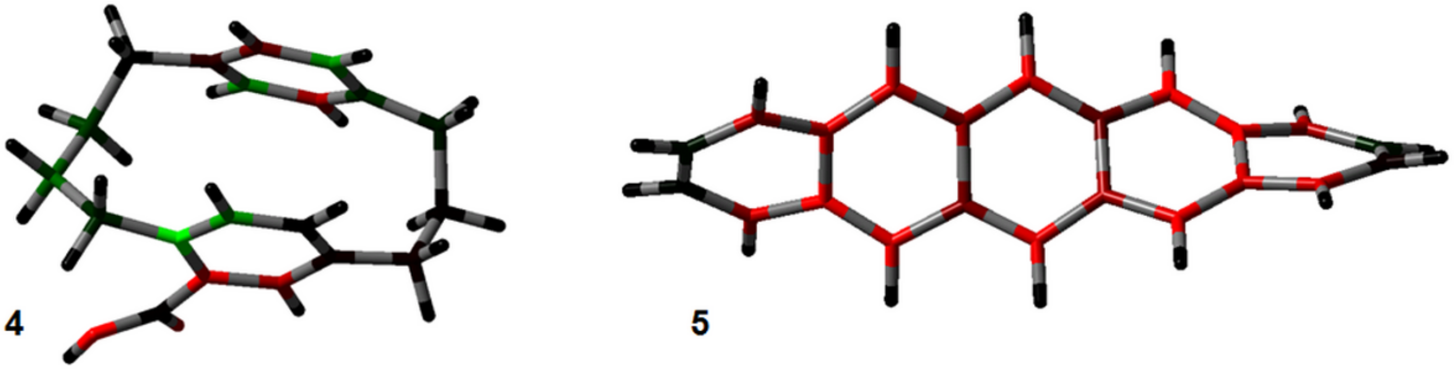

Figure 2

Calculated PVED of atoms shown in color (see text). 4: chiral paracyclophane, 5:twisted pentacene

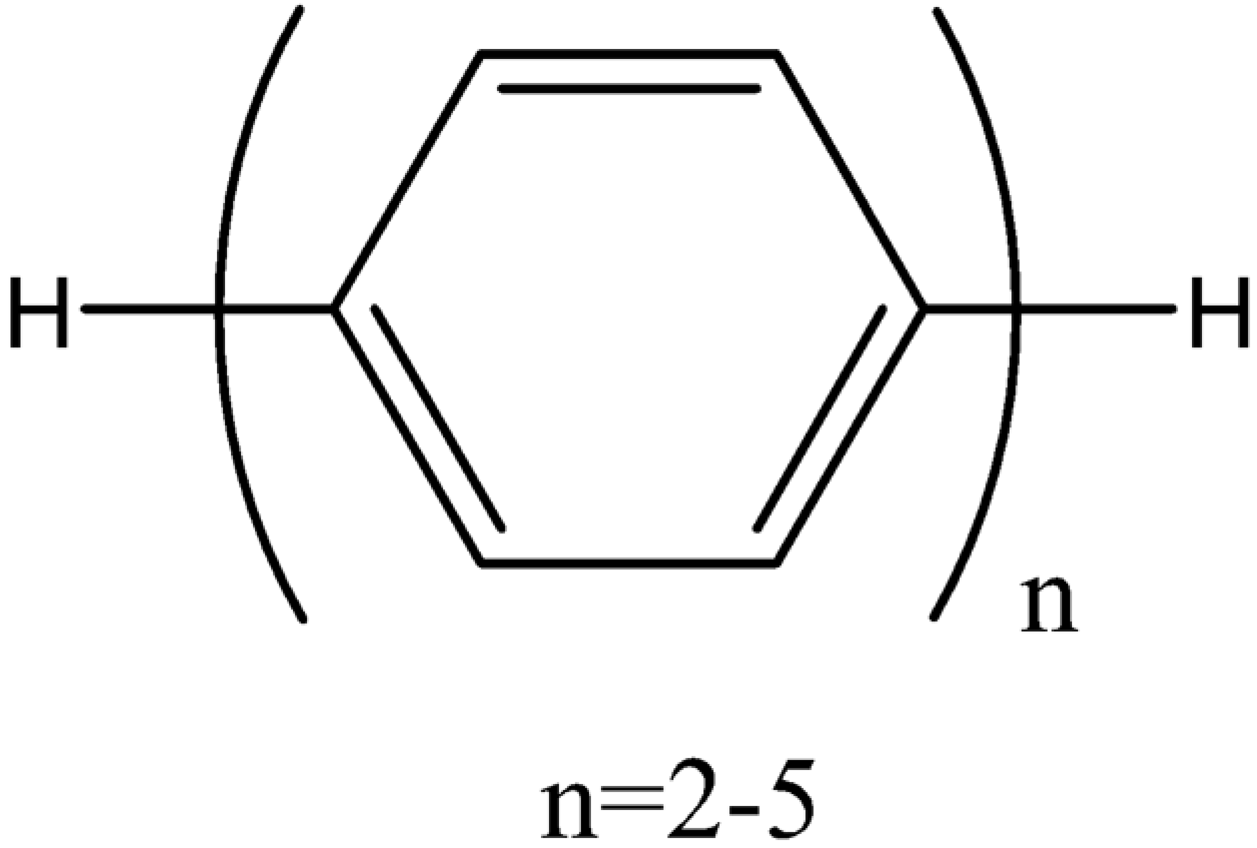

Figure 3

Formula representation of phenylenes objects of this work

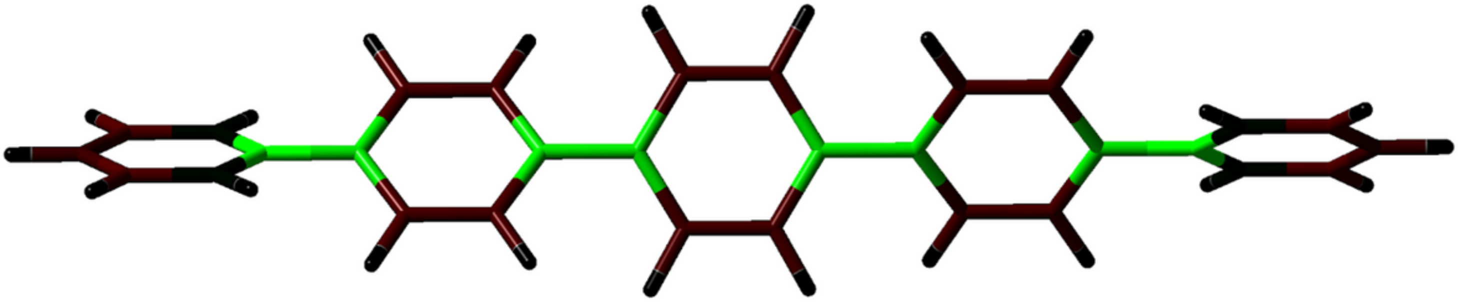

Figure 4

Calculated PVED of pentaphenylene. Atoms color by their PVED contribution (see text)

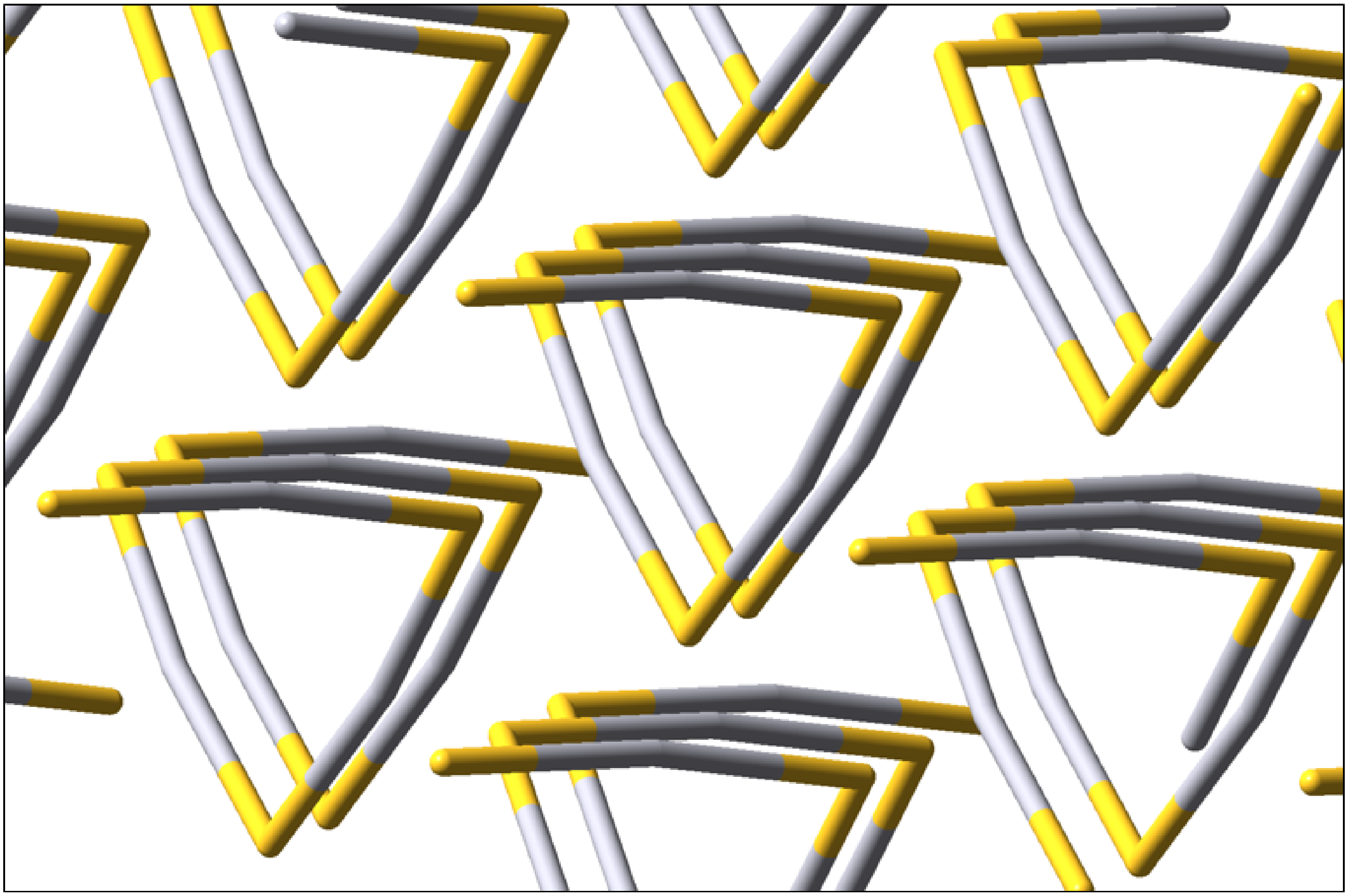

Figure 5

Representation of the cinnabar crystal structure

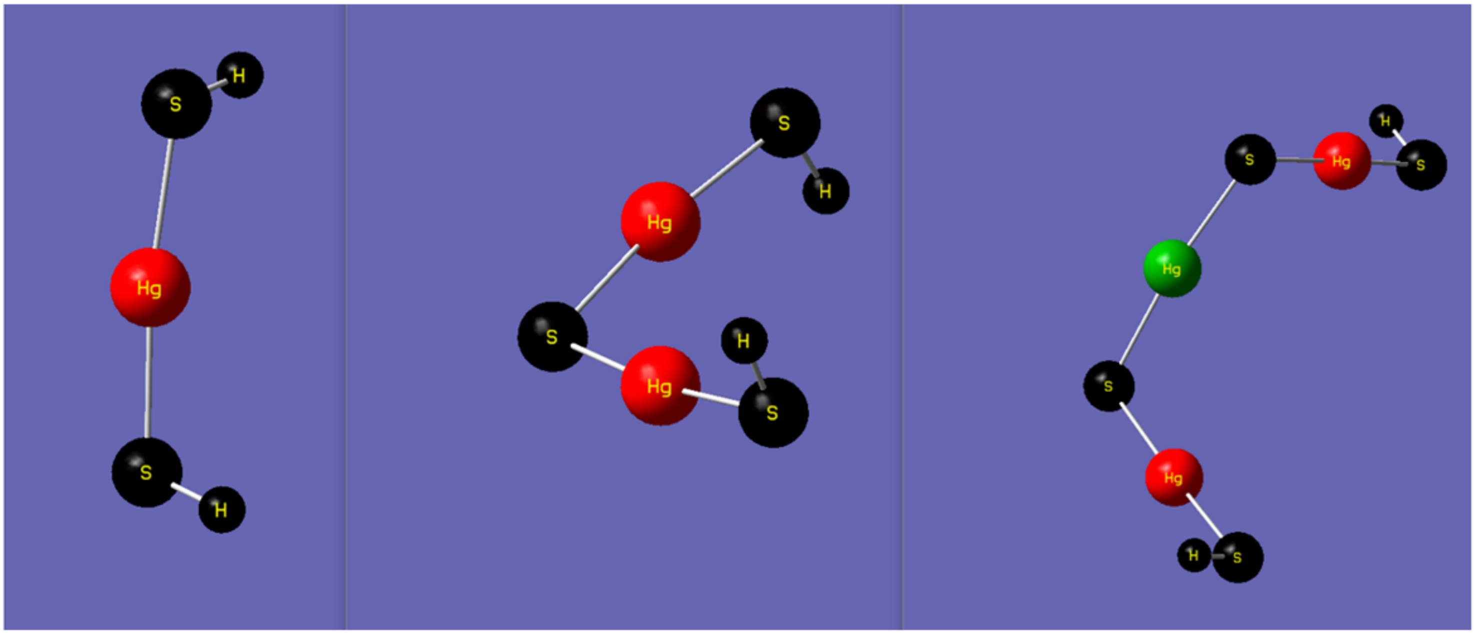

Figure 6

Representation of HgxSyH2molecules calculated. Atom color (red and green) depends on the PVED sign and the intensity of the color is proportional to the absolute value