



## Editorial Chiral Auxiliaries and Chirogenesis II

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Chirality is an inevitable property of our Universe, having an enormous impact in different fields, ranging from nuclear physics and astronomy to living organisms and human beings. Furthermore, chirality has important applications in various technological processes, including in pharmaceutical and agrochemical manufactories. Therefore, in order to highlight importance of this phenomenon in chemical science, the first Special Issue on "Chiral Auxiliaries and Chirogenesis" was launched in 2017 [1]. Upon completion, this Special Issue has attracted much attention in the scientific community, resulting in a high scientific impact according to the articles' access statistics and citation index (with up to 26 citations as of 26 June 2021 [2]).

This success prompted us to initiate the subsequent Special Issue entitled "Chiral Auxiliaries and Chirogenesis II" on the same subject, in 2019, which was completed in 2021. The aim of this second Special Issue, consisting of one review paper and six research articles, was to address some particular aspects of chiral auxiliary and chirogenesis, which were not covered by the first Special Issue.

In particular, Trubitsõn and Kanger in their review [3] describe new methodologies for the synthesis of chiral N-functionalized indoles. The synthesis of enantioenriched indole derivatives is of great importance in organic chemistry, especially in light of their potential application in the pharmaceutical industry. The review illustrates the efficient application of organocatalytic and organometallic strategies for the construction of chiral  $\alpha$ -N-branched indoles. Both the direct functionalization of the indole core and indirect methods based on asymmetric N-alkylation of indolines, isatins, and 4,7-dihydroindoles are discussed.

Another important class of chiral molecules is macrocycle compounds. Recently, the chirality of a novel emerging host molecule, pillar[n]arenes, has attracted increased attention due to their potential applications for chiral induction, molecular recognition, and asymmetric catalysis. In their research communication [4], Xiao et al. report the synthesis and successful resolution of planar ( $P_R$ )- and ( $P_S$ )-enantiomeric Boc-protected pillar[4]arene[1]diaminobenzene. Their racemization kinetics are studied. It is shown that hexane and CH<sub>2</sub>Cl<sub>2</sub> can maintain the enantiomeric forms for long periods, because of the complexation of the solvent molecules with the cavity of pillar[4]arene[1]diaminobenzene. The racemization process is accelerated by increasing the temperature or using solvents that cannot thread into the cavity of these molecules or can destroy the intramolecular hydrogen bond. This study provides, for the first time, thermodynamic parameters of the pillararenes in different solvents that will serve as an important guideline in studying the conformational properties of pillar[n]arenes.

A crucial problem of self-induced diastereomeric anisochronism (SIDA) in NMR is addressed by Baumann et al. in their feature article [5]. This phenomenon may occur when chiral molecules that associate in solution in a dynamic equilibrium that is fast on the NMR timescale exhibit significant condition-dependent NMR chemical shifts. This study is carried out using alcohol and ester derivatives and highlights the potential problems that SIDA can cause. Furthermore, scalemic samples of both the alcohol and ester compounds are first reported to exhibit the phenomenon of self-disproportionation of enantiomers by preparative TLC.



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**Copyright:** © 2021 by the author. Licensee MDPI, Basel, Switzerland. This article is an open access article distributed under the terms and conditions of the Creative Commons Attribution (CC BY) license (https:// creativecommons.org/licenses/by/ 4.0/). Chiral porphyrinoids have important implementations in the fields of chiral sensors, biomimetic functions, asymmetric catalysis, and other applications. Setsune et al. [6] describe the synthesis and magnetic properties of linear trinuclear Cu<sup>II</sup> and Ni<sup>II</sup> complexes of porphyrin analogues embedded with chiral binaphthol units. It is found that the observed paramagnetic shifts in the pyrrolic ligand and the binaphthyl ligand could be used to estimate spin delocalization from the terminal metal and the central metal, respectively, and these paramagnetic <sup>1</sup>H NMR data are consistent with the spin densities calculated. Furthermore, the strong antiferromagnetic coupling observed for both Cu<sup>II</sup><sub>3</sub> and Ni<sup>II</sup><sub>3</sub> complexes could be ascribed to the unique coordination geometry that is also responsible for the reversible ligation of butylamine only at the central metal ion, without decomposi-

multinuclear complexes. Further expansion of supramolecular chirogenesis is considered by Osadchuk et al. in [7]. In particular, a comprehensive study on the complexation of ethane-bridged bis(zinc octaethylporphyrin), as a host, with a chiral guanidine derivative, as a guest, is carried out by means of ultraviolet-visible and circular dichroism absorption spectroscopies, single crystal X-ray diffraction, and computational simulation. The formation of a 1:2 host-guest complex is established by X-ray diffraction and spectroscopic titration studies. Such supramolecular organization of the complex results in a screw arrangement of the two porphyrin subunits, inducing a strong circular dichroism signal in the porphyrin Soret band region. The corresponding computational studies are in good agreement with the experimental results. This study is one of the rare examples of comprehensive circular dichroism analysis of chirality induction in bis-porphyrins caused by external chiral ligands, which can be a benchmark approach for the rationalization of supramolecular chirogenesis in bis-porphyrins. Furthermore, the obtained results demonstrate the necessity of careful consideration of all external and internal factors that influence the supramolecular organization of complex to attain the best match between experimental and simulated circular dichroism spectra.

tion of the trinuclear core. The reported multinuclear complexes of an enantiomerically pure helical porphyrin analogue are expected to lead to further exploration of the helical

In a related chirogenic study, Mądry et al. present a new, sensitive stereodynamic reporter for primary amines operating on the basis of the point-to-axial chirality mechanism [8]. The through-space inductor–reporter interactions force a change in the chromophore conformation toward one of the diastereomeric forms. The structure of the reporter, with the terminal flipping biphenyl groups, leads to the generation of Cotton effects in both lower- and higher-energy regions of the circular dichroism spectrum. The reporter system appears to be sensitive to subtle differences in the inductor structure. Despite the size of the chiral substituent, the molecular structure of the inductor–reporter systems in the solid-state shows many similarities. The most important one is the tendency of the core part of the molecules to adapt to the pseudocentrosymmetric conformation. Supported by weak dispersion and Van der Waals interactions, the face-to-face and edge-to-face interactions between the  $\pi$ -electron systems present in the molecule are found to be responsible for the molecular arrangement in the crystal.

The last article in this Special Issue, by Fujiki et al., is devoted to one of the most fundamental questions of chirogenesis [9]. In particular, it is known that non-charged, semi-flexible, and rod-like helical copolymers and  $\pi$ - $\pi$  molecular stacks reveal sergeantsand-soldiers (Ser-Sol) and majority-rule (Maj) effects in dilute solutions and as a suspension in fluidic liquids. However, a question remains unanswered as to whether the Ser-Sol and Maj effects between non-charged, rod-like helical polysilane copolymers and non-charged, non-helical  $\pi$ -conjugated homopolymers occur when these polysilane copolymers encounter the  $\pi$ -polymer in the co-colloidal systems. Based on different types of chiral polysilane copolymers and detailed analyses of circular dichroism and circularly polarized luminescence results, this paper discusses the origins of noticeable non-mirror-symmetrical Ser-Sol and Maj effects in terms of macroscopic parity violation that differs from the rigorous criteria of the molecular parity violation hypothesis. The comprehensive helicity/chirality transfer experiments in the artificial helical/non-helical polymer co-colloids in the tuned refractive index optofluidic media may suggest possible answers to several unresolved questions in the realms of molecular biology, stereochemistry, supramolecular chemistry, and polymer chemistry, including (i) whether mirror symmetry on macroscopic levels is rigorously conserved and (ii) why Nature chose L-amino acids and five-membered D-furanose (not six-membered D-pyranose) in DNA/RNA.

While this Special Issue has only recently been completed, the scientific interest is strong, as demonstrated by the articles' statistics (with two articles reaching four citations as of 26 June 2021 [10,11]). This may result in a new Special Issue of *Symmetry* covering additional chirality topics, to be launched in the near future.

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## References

- Special Issue "Chiral Auxiliaries and Chirogenesis". Available online: https://www.mdpi.com/journal/symmetry/special\_ issues/chirogenesis (accessed on 26 June 2021).
- Helicene-Based Chiral Auxiliaries and Chirogenesis. Available online: https://www.mdpi.com/2073-8994/10/1/10 (accessed on 26 June 2021).
- 3. Trubitsõn, D.; Kanger, T. Enantioselective Catalytic Synthesis of N-alkylated Indoles. Symmetry 2020, 12, 1184. [CrossRef]
- 4. Xiao, C.; Liang, W.; Wu, W.; Kanagaraj, K.; Yang, Y.; Wen, K.; Yang, C. Resolution and Racemization of a Planar-Chiral A1/A2-Disubstituted Pillar[5]arene. *Symmetry* **2019**, *11*, 773. [CrossRef]
- Baumann, A.; Wzorek, A.; Soloshonok, V.A.; Klika, K.D.; Miller, A.K. Potentially Mistaking Enantiomers for Different Compounds Due to the Self-Induced Diastereomeric Anisochronism (SIDA) Phenomenon. *Symmetry* 2020, 12, 1106. [CrossRef]
- Setsune, J.-I.; Omae, S.; Tsujimura, Y.; Mochida, T.; Sakurai, T.; Ohta, H. Synthesis, Structure, and Magnetic Properties of Linear Trinuclear CuII and NiII Complexes of Porphyrin Analogues Embedded with Binaphthol Units. *Symmetry* 2020, *12*, 1610. [CrossRef]
- Osadchuk, I.; Konrad, N.; Truong, K.-N.; Rissanen, K.; Clot, E.; Aav, R.; Kananovich, D.; Borovkov, V. Supramolecular Chirogenesis in Bis-Porphyrin: Crystallographic Structure and CD Spectra for a Complex with a Chiral Guanidine Derivative. *Symmetry* 2021, 13, 275. [CrossRef]
- 8. Mądry, T.; Czapik, A.; Kwit, M. "Double-Twist"-Based Dynamic Induction of Optical Activity in Multichromophoric System. *Symmetry* **2021**, *13*, 325. [CrossRef]
- Fujiki, M.; Okazaki, S.; Rahim, N.A.A.; Yamada, T.; Nomura, K. Synchronization in Non-Mirror-Symmetrical Chirogenesis: Non-Helical π–Conjugated Polymers with Helical Polysilane Copolymers in Co-Colloids. *Symmetry* 2021, 13, 594. [CrossRef]
- Resolution and Racemization of a Planar-Chiral A1/A2-Disubstituted Pillar[5]arene. Available online: https://www.mdpi.com/ 2073-8994/11/6/773 (accessed on 26 June 2021).
- Enantioselective Catalytic Synthesis of N-alkylated Indoles. Available online: https://www.mdpi.com/2073-8994/12/7/1184 (accessed on 26 June 2021).