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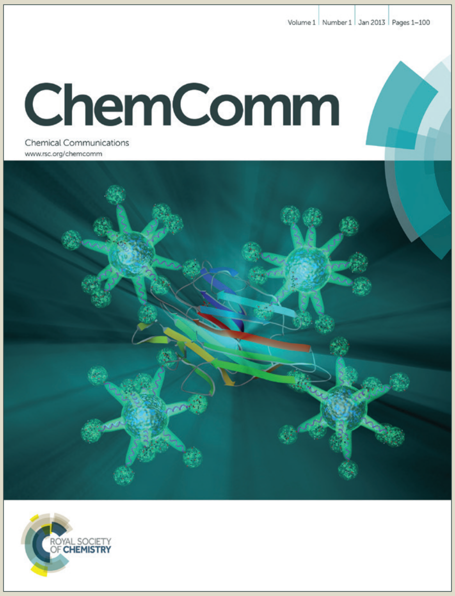

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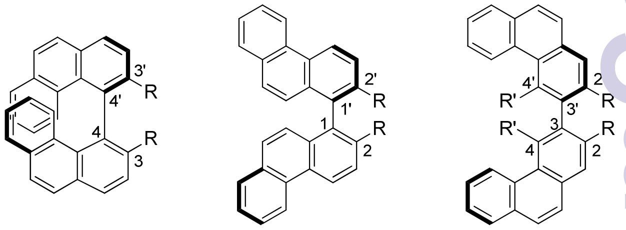
The role of magnetic-electric coupling in exciton-coupled ECD spectra. The case of bis-phenanthrenes.

Sandro Jurinovich,[a] Ciro A. Guido,[a] Torsten Bruhn,[b] Gennaro Pescitelli,*[a] and Benedetta Mennucci*[a]

Apparent exceptions to the exciton chirality method may arise for chromophores underoging transitions which are both electric- and magnetic-dipole allowed, for example bis-phenanthrenes. We present a computational approach to calculate exciton-coupled CD spectra based on a quantum-mechanical description of the excitonic parameters, which also includes the solvent effects.

The exciton chirality method (ECM)[1-3] is the spectroscopic method most used for the absolute configuration assignment of (supra)molecular compounds, in addition to the anomalous scattering effect in X-ray crystallography. The ECM applies to electronic circular dichroism (CD) spectra of compounds containing two or more chromophores endowed with electric-dipole allowed transitions. A typical CD spectrum contains two bands of similar amplitude and opposite signs (a so called couplet). In the standard "visual" application of the ECM, known as the exciton chirality rule, the sign of the couplet (that of its longer-wavelength component) is related to the sense of twist between the two electric-dipole transition moments (EDTM) and hence, if the molecular conformation is known, to the absolute configuration.[1-3] The method also lends itself as a tool for conformational analysis[4] and, most notably, the study of supramolecular systems.[5] The thoroughly demonstrated reliability and wide popularity of the ECM make any possible exception to the exciton chirality rule of great interest. In the past, a few alleged inconsistencies between the EC and X-ray methods were subsequently solved or retracted.[2] Lately, apparent sign reversals in ECD spectra have been attributed to unpredictable molecular conformations.[6] Possible failures of the method may be expected if the relevant electric-dipole allowed transitions are contaminated e.g. by charge-transfer transitions altering their nature.[7] When the molecular conformation is safely established and the involved electronic transitions understood, no exception or failure of the ECM is virtually possible. However, a possible interference in the application of the ECM may arise when the electric-dipole allowed transitions involved in exciton coupling are associated with non-negligible intrinsic magnetic transition dipole moment (MDTM). In such a case, the coupling between the combined electric and magnetic transition moments (the "μm" term) may have opposite sign, and be more intense than, the purely electric/electric coupling (the "μμ" term), thus leading to an apparent exception of the exciton chirality rule.[8] The importance of intrinsic MDTM's is in fact usually neglected in the common application of the ECM, while it is known to be crucial in interpreting CD spectra of compounds endowed with electric-forbidden transitions, including the n-π* amide transition in peptides and proteins.[9]

Here we present a quantum-mechanical (QM) approach based on Time-dependent Density Functional Theory (TDDFT) which simulates the exciton CD spectra using a gauge-independent formulation. Within this framework, all the components of the excitonic matrix, namely site energies, electronic couplings and electric and magnetic moments are calculated in a self-consistent QM approach possibly including the effects of the environment. All the details of the method are reported in the Electronic Supporting Information (ESI).



1 (R=H)
1a (R=SH)

2 (R=H)
2a (R=OCH_3)

3 (R,R'=H)
3a (R=OH,R'=Ph)

Scheme 1 Bis-phenanthrene models and compounds with various linkages. In all cases (a*R*) configuration is shown.

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[a] Dipartimento di Chimica e Chimica Industriale, Università di Pisa
Via G. Moruzzi 3, I-56124 Pisa (Italy). E-mail: gennaro.pescitelli@dcci.unipi.it and benedetta.mennucci@dcci.unipi.it
[b] Institut für Organische Chemie, Universität Würzburg Am Hubland, 97074 Würzburg (Germany).

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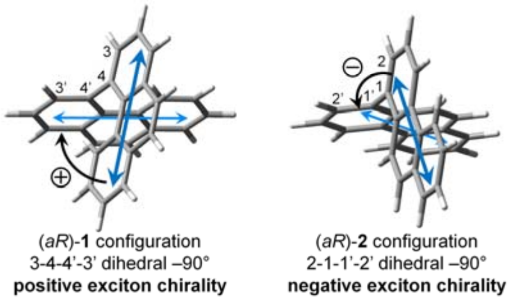
The method is applied here to bis-phenanthrenes, i.e. compounds like **1-3** (Scheme 1) where two phenanthrene rings are directly attached to each other. The interest in this family of compounds is twofold: the bis-phenanthrene motif is, rather surprisingly, found in several natural products, mainly isolated from the plant family of *Orchidaceae*;**[10]** second, like other atropisomeric biaryls such as 1,1'-binaphthyls, they are the basis for very efficient chiral catalysts and auxiliaries, for example VAPOL (**3a**).**[11]** Moreover, while 1,1'-binaphthyls and other biaryls represent a sort of benchmark for stereochemical analysis based on the ECM,**[12]** the applicability of this latter to bis-phenanthrene derivatives has been controversial,**[13-16]** strongly limiting its application to natural products.**[10]** In fact, while Harada and co-workers, based on the results on 1,1'-bisphenanthrene **2a**, claimed that the ECM is "not valid for phenanthrene chromophores",**[15]** Rosini and co-workers reached the opposite conclusion in their analysis of 4,4'-bisphenanthrene **1a**.**[14]** Our results reconcile the above findings and demonstrate that the apparent discrepancy is due to the neglect of the intrinsic magnetic moments.

We discuss 1,1'- and 4,4'-bis(phenanthrene) (**1** and **2**) as model compounds, and **1a** and **2a** as examples of real compounds. CD spectra of bis-phenanthrene compounds are expected to show strong CD couplets in the region of the most intense transitions 3A$_1$ and 3B$_2$ (^{1}B$_a$ and ^{1}B$_b$ in Platt's nomenclature) of phenanthrene.[17] Therefore, it is crucial to reproduce accurately the relative energies and intensities of these two transitions. Excited-state calculations were run with TDDFT using Gaussian'09 package;[18] computational details are reported in the ESI. Because of the complexity of the electronic excitations of phenanthrene, a preliminary screening of functionals was performed. The results are compared with available reference data[19, 20] in Table 1 and in the ESI. Reference calculations found an energy difference in the range 0.17-0.25 eV with an oscillator strength *f* ratio of 0.22 (CASPT2). As seen in Table 1, the functional PBE0-1/3[21] predicts an energy difference of 0.19 eV in agreement with CCSDR(3) calculations, and a reasonable *f* ratio of 0.17. The comparison with experimental values is complicated by the coalescence of the two bands in solution, however stretched film spectra confirm the presence of two bands with the correct polarization and energy order.[22]

Table 1 Calculated and experimental data for the main electronic transitions of phenanthrene.[a]

Trans.[b]	Calculated energy / eV (osc. strength *f* / au)			Exper. ν_{max} / eV, λ_{max} / nm
	CCSDR(3)[c]	CASPT2[d]	PBE0-1/3[e]	(ε_{max} / M^{-1}cm^{-1})[f]
2A$_1$ (^{1}L$_b$)	4.02	3.42 (0)	4.17 (0.002)	3.54, 350 (350)
1B$_2$ (^{1}L$_a$)	4.81	4.37 (0.038)	4.40 (0.006)	4.23, 293 (16000)
3A$_1$ (^{1}B$_a$)	5.27	4.56 (0.268)	5.00 (0.137)	4.94, 251
3B$_2$ (^{1}B$_b$)	5.44	4.81 (1.218)	5.19 (0.810)	(33000) [g]

[a] All calculations in vacuo. [b] Symmetry and Platt's nomenclature; ordering from CCSDR(3) data. [c] From ref. 19. [d] From ref. 20, (14/12) active space. [e] Our results, cc-pVTZ basis set on B3LYP/6-311G(d) optimized geometry. [f] In cyclohexane, from ref. 17. [g] A$_1$ (260 nm) plus B$_2$ transition (250 nm).[22]



Scheme 2 Exciton chirality rule for the coupling of ^{1}B$_b$ ETDMs in model dimers (a*R*)-**1** and (a*R*)-**2**.

Models **1** and **2** were built by connecting two optimized phenanthrene units at the desired positions in an orthogonal arrangement, and re-optimizing only the new C-C bonds while all other internal coordinates were kept frozen. For the strongest long-axis polarized ^{1}B$_b$ transition, the ECM predicts positive couplet for (a*R*)-**1** and a negative couplet for (a*R*)-**2** in the model geometries (Scheme 2).

In the exciton chirality theory the rotational strength of an excitonic state *k*, originating from the coupling of 0→*a,b* transitions at frequencies $\nu_{i0a,b}$ on chromophores *i, j* is:[3]

$$R_k = \mathrm{Im}\left\{\sum_{i,j}^{n}\sum_{a,b}^{m} c_{i0a}^{k}\, c_{j0b}^{k}\left[\boldsymbol{\mu}_{i0a}\cdot\boldsymbol{m}_{j0b} + \frac{i\pi\nu_{j0a}}{c}\boldsymbol{\mu}_{i0a}\cdot\boldsymbol{R}_{ij}\times\boldsymbol{\mu}_{j0b}\right]\right\} \quad (1)$$

where **μ** and ***m*** are the EDTM and intrinsic MDTM, the coefficients c_{i0a} are the eigenvectors obtained from the diagonalization of the exciton Hamiltonian, and $\boldsymbol{R}_{ij}$ is the relative position of the two chromophores. In the "visual" application of the ECM used for the exciton chirality rule (e.g. in Scheme 2), only the second term of the sum in the brackets is taken into account (μμ term). This is because most organic chromophores considered in ECM applications have electric-dipole allowed transitions belonging to totally-symmetric *irrep*'s which are magnetically forbidden. This is not the case of phenanthrene ^{1}B$_b$ transition which belongs to the B$_1$ *irrep* in the C_{2v} group and is both electrically and magnetically allowed. The EDTM is long-axis polarized in the aromatic plane, while the MDTM is oriented perpendicular to the plane and amounts to 1.66 au (PBE0-1/3 calculations). In these conditions, the first term (μm term) of the sum becomes non-negligible. To evaluate the two terms, we have recently developed an EXcitonic Analysis Tool (EXAT),[23] in which the results coming from QM calculations are properly combined to obtain excitonic energies and properties.[24] Here, EXAT is combined with a gauge-independent formulation of the excitonic rotational strength both in length and velocity formalism (see ESI). Within this framework it is possible to calculate the overall (μμ+μμ term) and the μμ term separately, thus disentangling their effects. When this approach is applied to model dimers (a*R*)-**1** and (a*R*)-**2**, the calculated μμ coupling between ^{1}B$_b$ transitions is in agreement with the expectations of the ECM. This coupling is responsible for a strong positive couplet for (a*R*)-**1** and a strong negative couplet for (a*R*)-**2** in the 220-260 nm region (Fig. 1). When the μm coupling is included, however, a difference emerges. For dimer

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(a*R*)-**1**, the overall coupling ("μμ+μm" term) is only slightly more intense than the μμ term alone (Fig. 1a). The μμ and μm couplings have the same sign and define two positive couplets which reinforce each other, yielding an overall positive couplet as predicted by the exciton chirality rule. For dimer (a*R*)-**2**, on the contrary, the overall term has opposite sign to the μμ term and defines a positive couplet (Fig. 1b). This means that the μm coupling is responsible for a very strong positive couplet which overwhelms the μμ negative couplet. For (a*R*)-**2**, the exciton chirality rule predicts the wrong absolute configuration.

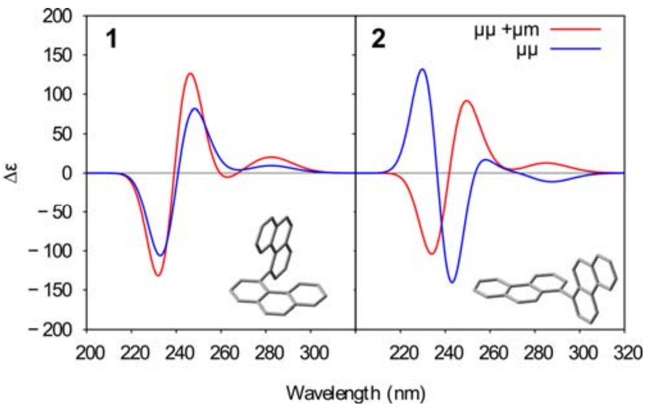

Fig 1 PBE0-1/3/cc-pVTZ excitonic spectra on model dimers (a*R*)-**1** and (a*R*)-**2**, including the first 4 transitions for each chromophore. Here and in other figures a Gaussian bandshape with 0.2 eV width was employed.

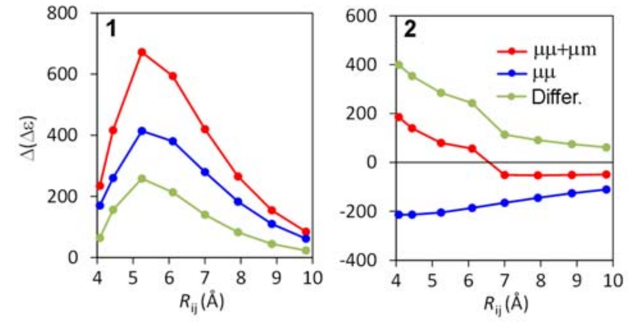

Fig. 2 Couplet amplitude Δ(Δε) (peak-to-trough width) calculated as a function of the interchromophoric distance for detached dimers obtained from (a*R*)-**1** and (a*R*)-**2**. Only ^1B_a and ^1B_b transitions included; R_{ij} is the distance between the centres of mass for the two chromophores.

The relative importance of the two coupling terms may be better estimated by considering the dependence on the interchromophoric distance R_{ij}. Because of the mutual cancellation of exciton CD bands of opposite sign, the amplitude of an exciton CD couplet depends on the product of the rotational strengths and the electronic coupling,[3] which, in its dipolar approximation, depends on R_{ij}^{-3}. The two μμ and μm terms are therefore expected to scale with R_{ij}^{-2} and R_{ij}^{-3}, respectively. As in EXAT calculations the full QM transition densities are employed instead of the point-dipole approximation, the situation is more complicated, still a different dependence on the distance is expected for the two couplings. Thus, we run EXAT calculations on a series of detached dimers in which the 1,1′ (for **2**) or 4,4′ bonds (for **1**) were cut, the C1-C1′ or C4-C4′ distances varied from 1.5 Å to 8.0 Å, and the separated chromophores saturated with a hydrogen atom. In this way, the angular part of the coupling is roughly invariant and the dependence on R_{ij} is highlighted. The results of EXAT calculations are shown in Fig. 2 and in the ESI. For the detached dimers obtained from (a*R*)-1, both the overall (μμ+μm) and μμ couplings maintain the same sign along the series, indicating that the two terms μμ and μm also have the same sign. For the detached dimers obtained from (a*R*)-**2**, on the contrary, the overall coupling changes sign as a result of the faster increasing of the μm term with respect to the μμ term. As a consequence, the μm term (associated with a positive couplet) dominates at shorter distances, while the μμ term (associated with a negative couplet) dominates at larger distances.

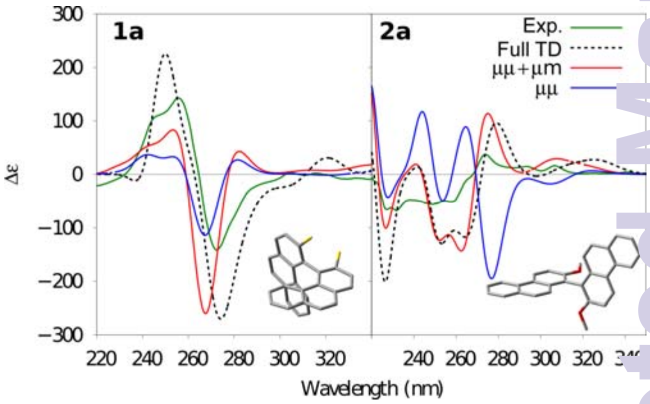

Fig. 3 Full and excitonic (PBE0-1/3/cc-pVTZ) calculated spectra of compounds (a*R*)-**1a** and (a*R*)-**2a**.

Finally, we run calculations on the two real systems **1a** and **2a**. Geometries were optimized at B3LYP/6-311G(d) level and TDDFT calculations were performed at PBE0-1/3/cc-pVTZ level. The Polarizable Continuum Model in its Integral Equation Formalism (IEF-PCM) version[25] was used to include solvent effects. For (a*R*)-**1a** (Fig. 3), all methods predict a strong negative couplet around 250 nm, in agreement with experimental results and ECM prediction (for this compound, the presence of the –SH substituent tilts the direction of the phenanthrene ^1B_b EDTM toward C-3,[26] hence the two ^1B_b EDTM's define a negative chirality for a*R* configuration; see ESI). This result confirms that the ECM is fully applicable to 4,4′- bis(phenanthrenes), regardless of the co-occurrence of ^1B_a and ^1B_b transitions in the crucial region. For (a*R*)-**2a** (Fig. 3), the experimental spectrum does not show a clear couplet but rather a series of weak bands in the 220-280 nm region.[15] Full TDDFT calculations and excitonic (μμ+μm) calculations agree with each other and reproduce – though not perfectly – the experimental spectrum. By contrast, the μμ term is very different from the overall coupling and shows an opposite sign for the ^1B_b couplet. We conclude that for **2a** the CD spectrum is still interpretable in terms of the exciton coupling, but only if the intrinsic magnetic moments are taken into account. Otherwise, the exciton chirality rule fails if based only on the electric moments.

In systems like phenanthrene where a curved π-electron delocalization is present, electronic transitions that are both electrically and magnetically allowed (such as phenanthrene ^1B_b) imply some "curvature" of the transition density (Fig. 4). It

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is interesting to notice that a "curvature of the π-electron delocalization" has been related to the exceptionally strong two-photon CD of VAPOL.[27] The geometry of the biaryl linkage determines the way the two curved transition densities face each other, that is, how the excitonic EDTM and origin-independent MDTM's, resulting from the in-phase and anti-phase combinations of the individual chromophores, combine with each other. For a convex arrangement like in 1,1'-bis(phenanthrenes) (**2** in Fig. 4),[15] the combination yields two terms (μμ and μm) with opposite signs which may lead to an apparent exception of the exciton chirality rule. On the contrary, no exception is expected for a concave arrangement like in 4,4'-bis(phenanthrenes) (**1**).[14] We also notice that it is not necessary to have two "curved" chromophores to observe the exception, because one phenanthrene facing from its convex side a chromophore like naphthalene might be sufficient to get a μm term strong enough to overcome the μμ one.[13,28]

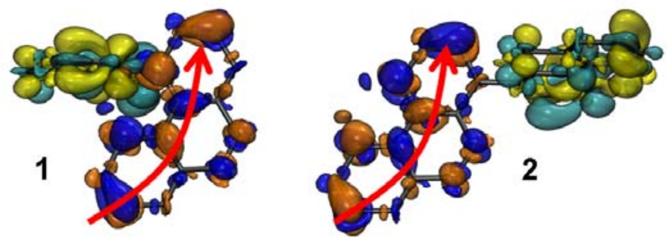

Fig 4 Transition densities computed for phenanthrene at PBE0-1/3/cc-pVTZ level (isovalue 0.0015), plotted in the arrangements corresponding to model dimers **1** and **2**.

In conclusion, we have demonstrated that a reliable prediction of exciton CD spectra of certain (supra)molecular compounds cannot avoid the simultaneous consideration of both electric-electric and electric-magnetic terms. For an accurate QM description of the excitonic properties it is also necessary to include solvent effects. The application to 1,1'-bis-phenanthrenes has clearly shown that cases which have been indicated as exceptions of the ECM, they are not but instead they cannot be described through the straightforward application of the exciton chirality rule.[1-3] Our analysis also demonstrates the crucial role played by the specific interchromophoric arrangement: the impact of magnetic moments is strong only for some geometries, such as the 1,1'-linkage in bis-phenanthrenes, while it is minor for others, such as the 4,4'-linkage in bis-phenanthrenes.

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References

1. N. Berova, N. Harada and K. Nakanishi, in *Encyclopedia of Spectroscopy and Spectrometry*, ed. J. C. Lindon, Elsevier, Oxford, 1999, pp. 470-488.
2. N. Harada and K. Nakanishi, *Circular Dichroic Spectroscopy - Exciton Coupling in Organic Stereochemistry*, University Science Books, Mill Valley, CA, 1983.
3. N. Harada, K. Nakanishi and N. Berova, in *Comprehensive Chiroptical Spectroscopy*, eds. N. Berova, P. L. Polavarapu, K. Nakanishi and R. W. Woody, John Wiley & Sons, Inc., Hoboken (NJ), 2012, pp. 115-166.
4. N. Berova, L. Di Bari and G. Pescitelli, *Chem. Soc. Rev.*, 2007, **36**, 914-931.
5. G. Pescitelli, L. Di Bari and N. Berova, *Chem. Soc. Rev.*, 2014, **43**, 5211-5233.
6. J. D. Chisholm, J. Golik, B. Krishnan, J. A. Matson and D. L. Van Vranken, *J. Am. Chem. Soc.*, 1999, **121**, 3801-3802; D. Gargiulo, F. Derguini, N. Berova, K. Nakanishi and N. Harada, *J. Am. Chem. Soc.*, 1991, **113**, 7046-7047; S. Matile, N. Berova, K. Nakanishi, J. Fleischhauer and R. W. Woody, *J. Am. Chem. Soc.*, 1996, **118**, 5198-5206.
7. T. Furo, T. Mori, T. Wada and Y. Inoue, *J. Am. Chem. Soc.*, 2005, **127**, 8242-8243; J. Joy, R. T. Cheriya, K. Nagarajan, A. Shaji and M. Hariharan, *J. Phys. Chem. C*, 2013, **117**, 17927-17939; G. Pescitelli and L. Di Bari, *J. Phys. Chem. C*, 2014, **118**, 24197-24198.
8. T. Bruhn, G. Pescitelli, S. Jurinovich, A. Schaumlöffel, F. Witterauf, J. Ahrens, M. Bröring and G. Bringmann, *Angew. Chemie Int. Ed.*, 2014, **53**, 14592-14595.
9. R. W. Woody, *Biomed. Spectrosc. Imag.*, 2015, **4**, 5-34; B. M. Bulheller, A. Rodger and J. D. Hirst, *Phys. Chem. Chem. Phys.*, 2007, **9**, 2020-2035.
10. G. Bringmann, C. Günther, M. Ochse, O. Schupp and S. Tasler, in *Fortschritte der Chemie organischer Naturstoffe / Progress in the Chemistry of Organic Natural Products*, eds. W. Herz, H. Falk, G. W. Kirby and R. E. Moore, Springer Vienna, 2001, pp. 1-249.
11. Y. Zhang, Z. Lu and W. D. Wulff, *Synlett*, 2009, **2009**, 2715-2739.
12. S. F. Mason, R. H. Seal and D. R. Roberts, *Tetrahedron*, 1974, **30**, 1671-1682.
13. N. Harada, T. Hattori, T. Suzuki, A. Okamura, H. Ono, S. Miyano and H. Uda, *Tetrahedron Asymm.*, 1993, **4**, 1789-1792.
14. G. Gottarelli, G. Proni, G. P. Spada, D. Fabbri, S. Gladiali and C. Rosini, *J. Org. Chem.*, 1996, **61**, 2013-2019.
15. T. Hattori, K. Sakurai, N. Koike, S. Miyano, H. Goto, F. Ishiya and N. Harada, *J. Am. Chem. Soc.*, 1998, **120**, 9086-9087.
16. A. G. Petrovic, S. E. Vick and P. L. Polavarapu, *Chirality*, 2008, **20**, 501-510.
17. H. H. Jaffé and M. Orchin, *Theory and Applications of Ultraviolet Spectroscopy*, Wiley, New York, 1962.
18. M. J. Frisch, et al., Gaussian, Inc., Wallingford CT, 2013.
19. H. H. Falden, K. R. Falster-Hansen, K. L. Bak, S. Rettrup and S. P. A. Sauer, *J. Phys. Chem. A*, 2009, **113**, 11995-12012.
20. R. González-Luque, L. Serrano-Andrés, M. Merchán and M. P. Fülscher, *Theor. Chem. Acc.*, 2003, **110**, 224-232.
21. C. A. Guido, E. Brémond, C. Adamo and P. Cortona, *J. Chem. Phys.*, 2013, **138**, 021104.
22. E. W. Thulstrup, J. Michl and J. H. Eggers, *J. Phys. Chem.*, 1970, **74**, 3868-3878.
23.EXAT (Excitonic Analysis Tool) S. Jurinovich, C. A. Guido and B. Mennucci, University of Pisa, Italy, 2014, https://www1.dcci.unipi.it/molecolab/tools/.
24. S. Jurinovich, G. Pescitelli, L. Di Bari and B. Mennucci, *Phys. Chem. Chem. Phys.*, 2014, **16**, 16407-16418.
25. B. Mennucci, E. Cances and J. Tomasi, *J. Phys. Chem. B*, 1997, **101**, 10506-10517.
26. L. Di Bari, G. Pescitelli, F. Marchetti and P. Salvadori, *J. Am. Chem. Soc.*, 2000, **122**, 6395-6398.
27. C. Diaz, N. Lin, C. Toro, R. Passier, A. Rizzo and F. E. Hernández, *J. Phys. Chem. Lett.*, 2012, **3**, 1808-1813.
28. A. Solladié-Cavallo, et al., *Eur. J. Org. Chem.*, 2002, **2002**, 1788-1796.

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