Simplified time-dependent density functional theory (sTD-DFT) for molecular optical rotation

Cite as: J. Chem. Phys. **153**, 084116 (2020); https://doi.org/10.1063/5.0020543 Submitted: 01 July 2020 . Accepted: 13 August 2020 . Published Online: 28 August 2020

Marc de Wergifosse 跑, Jakob Seibert 跑, and Stefan Grimme 跑





Lock-in Amplifiers up to 600 MHz





J. Chem. Phys. **153**, 084116 (2020); https://doi.org/10.1063/5.0020543 © 2020 Author(s).

Simplified time-dependent density functional theory (sTD-DFT) for molecular optical rotation

Cite as: J. Chem. Phys. 153, 084116 (2020); doi: 10.1063/5.0020543 Submitted: 1 July 2020 • Accepted: 13 August 2020 • Published Online: 28 August 2020



Marc de Wergifosse, 🐌 🝺 Jakob Seibert, 🕩 and Stefan Grimme 🕩

AFFILIATIONS

Mulliken Center for Theoretical Chemistry, Institut für Physikalische und Theoretische Chemie, Beringstr. 4, 53115 Bonn, Germany

^{a)}Author to whom correspondence should be addressed: mdewergifosse@gmail.com

ABSTRACT

Theoretical methods able to screen large sets (e.g., conformers) of possibly large compounds are needed in many typical quantum chemistry applications. For this purpose, we here extend the well-established simplified time-dependent density functional theory (sTD-DFT) method for the calculation of optical rotation. This new scheme is benchmarked against 42 compounds of the OR45 set as well as thirteen helicene derivatives and one bio-molecular system. The sTD-DFT method yields optical rotations in good quantitative agreement with experiment for compounds with a valence-dominated response, e.g., conjugated π -systems, at a small fraction of the computational cost compared to TD-DFT (1–3 orders of magnitude speed-up). For smaller molecules with a Rydberg state dominated response, the agreement between TD-DFT and the simplified version using standard hybrid functionals is somewhat worse but still reasonable for typical applications. Our new implementation in the stda code enables computations for systems with up to 1000 atoms, e.g., for studying flexible bio-molecules.

Published under license by AIP Publishing. https://doi.org/10.1063/5.0020543

I. INTRODUCTION

Chirality is a universal and fascinating concept present all over in nature and materials. Biological processes can imply biochemical chiral systems such as right-handed α -helix present in proteins or right-handed double stranded DNA.¹ The olefactorial activity of enantiomers can be very different. For example, the (R)limonene presents an orange flavor, while the (L)-enantiomer smells like turpentine.² Molecular carbon nanostructures are a new and interesting area of research in chiral materials.³ In their recent account on this emerging topic, Fernández-García et al.³ stressed out that "controlling chirality in carbon nanostructures currently represents a major challenge for the chemical community." They also showed progress on the synthesis of such materials, including metallofullerenes, endohedral fullerenes, graphene quantum dots, curved nanographenes, and molecular chiral bilayer nanographenes. The latter is a new kind of materials, which has the specificity to have an enantiospecific synthesis, thanks to its enantiopure starting helicene reactant.⁴ This was a particularly important finding since the synthesis of enantiopure nanographenes was only

reports showed that nanographene can be used for applications in photovoltaics^{5,6} and sensing.⁷ "Smaller" chiral π -conjugated organic molecules such as heteroatomic helicenes with their fascinating optical properties and electronic structures have also shown a strong potential for applications as organic light-emitting diodes, organic field-effect transistors, organic photovoltaics, and spintronics.¹ The chemistry of (hetero)helicenes started in 1903 with the synthesis by Meisenheimer and Witte⁸ of two azahelicenes. However, it was only in 1956 that the helicene chemistry started to grow, thanks to the communication of Newman and Lednicer⁹ on the synthesis and resolution of hexahelicene. Since then, a plethora of derivatives containing main-group elements (B, Si, N, P) were proposed,¹ which can drastically change their electronic and optical properties, even presenting some semiconductor-like behaviors. The absolute configuration of helicenes is usually easily assigned because of their strong $\pi \to \pi^*$ transitions in the polycyclic π -conjugated system. At the sodium D-line wavelength (589.3 nm), (P)-helicenes present a dextrorotary optical rotation, while (M)-helicene are levorotary.¹ In this context, theoretical chemistry could play a role in

possible by a chiral chromatography step. Note that the recent

the design of new large helicenes or chiral bilayer nanographenes with enhanced and fine-tuned chiroptical properties or to help to assign the absolute configuration of a chiral compound. For many of such applications, a theoretical method able to screen a large set of compounds providing a good agreement with experiment may be very useful. Because most of these systems are too large to be routinely treated by current standard methods, often truncated structures are used for comparison with experiment, but this could lead to significant errors, in particular, for conjugated molecules.



When linearly polarized light passes through an enantiomerically pure chiral compound, the plane of light rotates in a way that is dependent on the molecular structure and the wavelength of the incident light. This phenomenon is known as the optical rotation (OR) or optical birefringence. In 1929, Rosenfeld¹⁰ presented its theoretical background using time-dependent perturbation theory showing that the variation of the electric dipole moment of a molecule induced by a frequency-dependent electromagnetic field reads

$$\vec{\mu}_{ind.}(t) = \overleftarrow{\alpha}(-\omega;\omega) \cdot \vec{E} + \overleftarrow{G}(-\omega;\omega) \cdot \frac{\partial \vec{B}}{\partial t} + \cdots,$$
(1)

where $\overrightarrow{\alpha}$ is the electric dipole polarizability tensor and G is the electric dipole-magnetic dipole polarizability tensor. The OR is proportional to the trace of G. To determine this quantity, several ab initio methods were implemented in the past, e.g., in the frameworks of the coupled-cluster theory (CC) or the density-functional theory (DFT).¹¹ The former method class, which is dedicated to small systems because of its generally high computational cost, is currently the most reliable one to evaluate the OR of a molecule. Among them, the coupled-cluster singles and doubles (CCSD) approach was first implemented by Ruud et al.^{12,13} This was followed by another implementation by Crawford et al.^{14,15} Kongsted et al. also developed a CC3 implementation.¹⁶ For larger systems, DFT often provides a better balance between cost and accuracy.¹⁷ In 1999, the first time-dependent DFT (TD-DFT) calculations were done by Yabana and Bertsch¹⁸ using the local density approximation (LDA). This formalism was expanded to hybrid exchange-correlation functionals in 2000 by Cheeseman et al.¹⁹ but only for the static case. This was extended to frequency-dependent responses by the same researchers in 2001²⁰ and also by Grimme²¹ using density functional response theory as well as by Autschbach et al.^{22,23} All of these TD-DFT implementations used the length formalism for the electric dipole moment operator implying a gauge-origin invariance problem using a finite basis set. To enforce origin independence, it was first proposed to use gauge-including atomic orbitals (GIAOs) that distribute the gauge origin over the molecule. In 2002, Grimme, Furche, and Ahlrichs²⁶ proposed to use the wellknown velocity form of the electric dipole operator instead of the length form by means of a canonical transformation first described by Goeppert-Mayer.²⁷ Following this, Pedersen et al.²⁸ proposed also to switch from the length representation to the velocity one but they directly plugged in the electronic momentum operator \vec{p} instead of the velocity form of the electric dipole operator. Their computed values at any frequency include unphysical static contributions that were corrected for by subtracting the static value. This approach is commonly known as the modified-velocity representation. In 2011, Autschbach²⁹ also proposed to correct for another type of origin invariance that may arise because of the truncation of the multipole expansion that treats the electromagnetic field.

For larger systems, as those mentioned above, even TD-DFT based OR calculations are computationally not feasible. In this work, we propose to extend the well-known simplified TD-DFT (sTD-DFT) method³⁰⁻³⁵ to the evaluation of the OR in both length and velocity representations for treating large systems. We

describe an extended version of the algorithm used for the evaluation of polarizabilities.³³ The sTD-DFT level of theory was proposed by one of us³⁰⁻³² to treat large systems by approximating two-electron integrals using short-range damped Coulomb interactions of transition density monopoles in the TD-DFT scheme. A tight-binding variant called sTD-DFT-xTB also exists to treat even larger systems.³² We recently extended this scheme to the evaluation of polarizabilities and first hyperpolarizabilities³³ as well as to determine excited-state absorption.³⁴ A spin-flip version also exists.^{35,36}

To benchmark our method, we used the first 42 molecules of the OR45 standard set proposed by Srebro *et al.*³⁸ The three last metal complexes were discarded because their structures are not provided in Ref. 38. This benchmark set (see Fig. 1) encompasses many very small molecules with a dominating diffuse Rydberg state response for which it is expected that the monopole approximation used in the sTD-DFT method will not work well. For larger systems for which the response is dominated by valence transitions, the OR should be better described by sTD-DFT as already shown for related properties.^{30–35} Additionally, we compute ORs for four types of recently synthesized helicenes derivatives by Crassous and co-workers.^{37,39–41} Figure 2 depicts the structure of azabora[n]helicenes (n = 6,8, and 10)³⁹ and the corresponding platina[10]helicene analogue, phospha[n]helicenes (n = 6 and 7),⁴⁰



FIG. 2. Structures of the four azabora[n]helicenes (n = 6, 8, and 10) and the corresponding platina[10]helicene analogue, four phospha[n]helicene oxides ("Men" stands for *I*-menthyl), (P,P)-bis-helicenic 2,2'-bipyridine as well as when coordinated to Zn(OAc)₂, and two chiral cycloiridiated complexes bearing helicenic NHC licands.³⁷

the (P,P)-bis-helicenic 2,2'-bipyridine with and without coordination to Zn(OAc)₂,⁴¹ and two chiral cycloiridiated complexes bearing helicenic NHC ligands.³⁷ Because of the importance of the OR for structural investigations of bio-molecular systems, tryptophan is also investigated.

This article is organized as follows. The sTD-DFT theoretical background to evaluate the OR of a molecule is presented in Sec. II. Section III provides computational details, and Sec. IV discusses the results followed by conclusions in Sec. V.

II. THEORY

In the following, p, q, r, s indices refer to general molecular orbitals, i, j, k, l refer to occupied, and a, b, c, d to unoccupied molecular orbitals. The evaluation of the frequency-dependent OR at the sTD-DFT level of theory derives from the density-matrix-based TD-DFT formalism^{42–48} previously used by us for the evaluation of the linear and quadratic response functions.^{33,34} In this formalism, the linear (electric dipole) response vectors $\mathbf{X}_{\zeta}(\omega)$ and $\mathbf{Y}_{\zeta}(\omega)$ are obtained by solving the standard TD-DFT equation

$$\begin{bmatrix} \begin{pmatrix} \mathbf{A} & \mathbf{B} \\ \mathbf{B} & \mathbf{A} \end{pmatrix} - \omega \begin{pmatrix} 1 & 0 \\ 0 & -1 \end{pmatrix} \end{bmatrix} \begin{pmatrix} \mathbf{X}_{\zeta}(\omega) \\ \mathbf{Y}_{\zeta}(\omega) \end{pmatrix} = - \begin{pmatrix} \mu_{\zeta} \\ \mu_{\zeta} \end{pmatrix},$$
(2)

where $\mu_{\zeta,ai} = \langle \phi_a | \hat{\mu}_{\zeta} | \phi_i \rangle$,

$$A_{ia,jb} = \delta_{ij}\delta_{ab}(\epsilon_a - \epsilon_i) + 2(ia|jb) - a_x(ij|ab) + (1 - a_x)(ia|f_{XC}|jb), (3)$$

and

$$B_{ia,jb} = 2(ia|bj) - a_x(ib|aj) + (1 - a_x)(ia|f_{XC}|bj).$$
(4)

The **A** and **B** matrices are expressed considering a hybrid exchange– correlation functional with a fraction a_x of exact exchange. ϵ_p is the energy of the *p* orbital, (ia|jb), (ia|bj), and (ib|aj) are exchange type integrals in Mulliken notation, (ij|ab) is a Coulomb-type integral, and $(ia|f_{XC}|jb)$ and $(ia|f_{XC}|bj)$ are the response of the exchange– correlation functional. Then, the symmetric response vector reads

$$\mathbf{X}_{\zeta}(\omega) + \mathbf{Y}_{\zeta}(\omega) = \frac{-2\mu_{\zeta}}{(\mathbf{A} + \mathbf{B}) - \omega^2(\mathbf{A} - \mathbf{B})^{-1}}.$$
 (5)

In the sTD-DFT formalism, three simplifications are applied. First, the CI space is truncated by applying a single energy selection threshold as the parameter that accounts for configurations important to describe excitation energies below that value. Second, two-electron integrals are approximated by short-range damped Coulomb interactions of transition density monopoles,

$$(pq|rs)' = \sum_{A}^{N} \sum_{B}^{N} q_{pq}^{A} q_{rs}^{B} \Gamma_{AB}, \qquad (6)$$

where q_{Pq}^{ba} are transition charge densities centered on atom A determined by a Löwdin population analysis. Damping functions Γ_{AB} are different in the case of Coulomb or exchange integrals and are given

by the Mataga–Nishimoto–Ohno–Klopman (MNOK)^{49–51} damped Coulomb operator

$$\Gamma_{AB}^{J} = \left(\frac{1}{(R_{AB})^{y_{f}} + (a_{x}\eta)^{-y_{f}}}\right)^{\frac{1}{y_{f}}},\tag{7}$$

$$\Gamma_{AB}^{K} = \left(\frac{1}{(R_{AB})^{y_{K}} + \eta^{-y_{K}}}\right)^{\frac{1}{y_{K}}},$$
(8)

respectively, where y_J and y_K are parameters and η is the chemical hardness mean of atoms A and B (values taken from Ref. 52). y_J and y_K are linear functions of the amount of exact exchange a_x included into the functional.³⁰ Third, responses of the exchange–correlation functional in (3) and (4) are neglected. In the simplified framework, **A'** and **B'** matrix elements used to evaluate the symmetric response vector $\mathbf{X}'_{\zeta}(\omega) + \mathbf{Y}'_{\zeta}(\omega)$ read

$$A'_{ia,jb} = \delta_{ij}\delta_{ab}(\epsilon_a - \epsilon_i) + 2(ia|jb)'_K - (ij|ab)'_J, \tag{9}$$

$$B'_{ia,jb} = 2(ia|bj)'_{K} - a_{x}(ib|aj)'_{K}.$$
(10)

To evaluate the frequency-dependent OR, one needs to evaluate diagonal elements of the electric dipole–magnetic dipole polarizability tensor,

$$G_{\alpha\alpha}(\omega) = -\omega^{-1} \Im \langle \langle m_{\alpha}; \mu_{\alpha} \rangle \rangle_{\omega}, \qquad (11)$$

which is directly linked to the imaginary part of the electric dipolemagnetic dipole linear response function $\Im\langle\langle m_{\alpha}; \mu_{\alpha} \rangle\rangle_{\omega}$. The sumover-state expression of this quantity reads

$$\Im\langle\langle m_{\alpha};\mu_{\alpha}\rangle\rangle_{\omega} = \Im\sum_{n} \left[\frac{\langle 0|m_{\alpha}|n\rangle\langle n|\mu_{\alpha}|0\rangle}{\omega-\omega_{n}} - \frac{\langle 0|\mu_{\alpha}|n\rangle\langle n|m_{\alpha}|0\rangle}{\omega+\omega_{n}}\right],$$
(12)

where

$$\langle 0|\mu_{\alpha}|n\rangle = \sqrt{2}\sum_{ai}\mu_{ai}^{\alpha}(X_{ia}^{n}+Y_{ia}^{n})$$
(13)

and

$$\langle 0|m_{\alpha}|n\rangle = \sqrt{2}\sum_{ai}m_{ai}^{\alpha}(X_{ia}^{n} - Y_{ia}^{n})$$
(14)

are transition moments between the ground state and an excited state that can be expressed in terms of excitation and deexcitation eigenvectors X_{ia}^n and Y_{ia}^n , respectively. In the length representation, the electric dipole operator takes the form

$$\vec{\mu}^L = -\vec{r},\tag{15}$$

and the magnetic operator reads

$$\vec{m} = \frac{i}{2c} (\vec{r} - \vec{R}) \times \vec{\nabla}.$$
 (16)

J. Chem. Phys. **153**, 084116 (2020); doi: 10.1063/5.0020543 Published under license by AIP Publishing

To recover the electric dipole–magnetic dipole linear response function expression as a function of linear (electric dipole) response vectors $\mathbf{X}_{\alpha}(\omega)$ and $\mathbf{Y}_{\alpha}(\omega)$, we use their sum-over-state expressions,

$$X_{\alpha,ai}(\omega) = \sum_{n} \mu_{ia,\alpha} \left(X_{ia}^{n} + Y_{ia}^{n} \right) \left[\frac{X_{ia}^{n}}{\omega - \omega_{n}} - \frac{Y_{ia}^{n}}{\omega + \omega_{n}} \right], \quad (17)$$

$$Y_{\alpha,ai}(\omega) = \sum_{n} \mu_{ia,\alpha} \left(X_{ia}^{n} + Y_{ia}^{n} \right) \left[\frac{Y_{ia}^{n}}{\omega - \omega_{n}} - \frac{X_{ia}^{n}}{\omega + \omega_{n}} \right], \quad (18)$$

and plug them into Eq. (12), obtaining the following expression:

$$\Im\langle\langle m_{\alpha};\mu_{\alpha}\rangle\rangle_{\omega}=\Im\left(2\sum_{ai}m_{\alpha}(X_{\alpha,ai}(\omega)-Y_{\alpha,ai}(\omega))\right).$$
 (19)

Equation (19) is a function of the anti-symmetric response vector because the magnetic dipole operator is imaginary. This current density matrix can be easily obtained by the transformation of the symmetric response vector

$$X_{\alpha,ai}(\omega) - Y_{\alpha,ai}(\omega) = \sum_{jb} \omega (A - B)_{ia,jb}^{-1} (X_{\alpha,jb}(\omega) + Y_{\alpha,jb}(\omega)).$$
(20)

The final expression for the electric dipole-magnetic dipole linear response function is obtained as a function of the symmetric response vector

$$\Im\langle\langle m_{\alpha};\mu_{\alpha}\rangle\rangle_{\omega} = \Im\left(2\omega\sum_{ia,jb}m_{\alpha}(A-B)^{-1}_{ia,jb}(X_{\alpha,jb}(\omega)+Y_{\alpha,jb}(\omega))\right).$$
(21)

The orientation average

$$\beta(\omega) = -\mathrm{Tr}\frac{\Im\langle\langle m_{\alpha}; \mu_{\alpha} \rangle\rangle_{\omega}}{3\omega}$$
(22)

is directly linked to the measured specific rotation by the following expression:

$$[\alpha]_{\omega} = 1.343 \times 10^{-4} \frac{\tilde{\nu}^2 \beta(\omega)}{M} \gamma_s, \qquad (23)$$

where γ_s is the Lorentz solvent correction factor $[\gamma_s = (n^2 + 2)/3]$, which is considered equal to the one in our study. Autschbach *et al.*^{22,23} noted that neglecting the Lorentz factor usually gave more balanced results with respect to experiment. Another useful quantity that is often used is the molar rotation, given by

$$[\phi]_{\omega} = [\alpha]_{\omega} \frac{M}{100}.$$
 (24)

In the length formalism, the electric dipole–magnetic dipole linear response function is origin dependent. To avoid this drawback, we have also implemented the evaluation of the OR in the velocity representation, following Ref. 26, which used the velocity form of the dipole operator by means of a canonical transformation

$$\vec{\mu}_{ia}^{V} = -\sum_{jb} (A - B)_{ia,jb}^{-1} \vec{\nabla}_{jb}.$$
(25)

For large basis set with diffuse functions (e.g., aug-cc-pVDZ), we obtain not fully rotationally invariant results with the sTD-DFT scheme in both representations. The deviations of the OR for random molecule rotations around the center-of-mass (CMA) are typically less than 1% but may reach up to 30% in problematic cases. The reason for this is not entirely clear, but it seems to be related to the non-rotational invariance of the grid used in the underlying DFT treatment as well as inherent properties of the Löwdin partitioning scheme, as discussed by Mayer.^{53,54} Because the problem practically vanishes for smaller basis sets such as 6-31+G(d), we do not consider it further at this point and suggest to perform OR calculations consistently in CMA coordinates for convenience.

III. COMPUTATIONAL DETAILS

The evaluation of the OR in both length and velocity representations at the sTD-DFT level of theory is implemented in the stda program.⁵⁵ The subroutine previously written to evaluate the polarizability is adapted for this purpose with the extra step that transforms the symmetric response vector into the antisymmetric one. Note that the computation of the velocity representation is slightly more costly than in the length formalism because of the extra canonical transformation [Eq. (25)]. A paragraph on computational times of the simplified method with respect to the full scheme is provided in the Sec. IV for molecules 38–42.

The geometries of the 42 compounds from the OR45 benchmark set were taken from Ref. 38 as well as their experimental molar rotations at the sodium D-line. With Dalton2018.0,^{56,57} we computed reference TD-DFT OR frequency dispersion (from 1900.0 1500.0 nm, 1064.0 nm, 929.0 nm, 794.0 nm, 713.0 nm, 632.8 nm, 589.3 nm, 579.0 nm, 546.0 nm, 436.0 nm, to 365.0 nm) with B3LYP, PBE0, and BHandHLYP exchange-correlation functionals using the aug-cc-pVDZ basis set and compare them to the corresponding sTD-DFT values. The sodium D-line values provided by Srebro et al.38 at the PBE0 level are practically identical to ours. For the second, third, fourth, and fifth test cases, the structures and experimental molar rotations were taken from Refs. 37 and 39-41, respectively. For the structures of this second case study, we took the mirror image of those provided for 1a, 1b, and 1d because they were in (M) instead of (P) configuration. Note that for phosphahelicenes,⁴⁰ the geometries provided are truncated models where *l*-menthyl and *n*-propyl groups are replaced by methyl.

For the sTD-DFT computations, we used the same setup for all compounds considered in this study. First, the SCF step was carried out with Q-Chem 5.1⁵⁸ to obtain Kohn–Sham orbitals and energies. For the first set of molecules, B3LYP, PBE0, and BHandHLYP exchange–correlation functionals were used with the aug-cc-pVDZ basis set. In a few cases, some near linear basis set dependencies were removed using the BASIS_LIN_DEP_THRESH keyword in Q-Chem to enforce SCF convergence. For the four other sets, we used the same basis set [except for compounds (P)-1d1, 3a, and 3b including transition metals for which we used def2-SV(P) as it was used originally^{37,39}] but the CAM-B3LYP exchange–correlation

functional. Note that we also tested B3LYP, PBE0, and BHandHLYP here, but the agreement with experiment is slightly worse than with the long-range corrected CAM-B3LYP functional. Second, OR values were computed with our new implementation in the stda program.⁵⁵ For the first case study, a configuration selection energy threshold of 50 eV was used for the smallest molecules (1–35) and 20 eV for the largest ones (36–42). These thresholds were chosen large enough to converge the absolute OR to a deviation of less than 15% of the full value. The convergence of the OR as a function of this threshold is discussed for molecules 1, 36, and 37 in Sec. IV. For the second, third, and fourth test cases, we used a threshold of 15 eV.

The conformers of tryptophan were generated by the CREST⁵⁹ program at the GFN2-xTB⁶⁰ tight-binding quantum chemistry level. Solvation effects for water were implicitly accounted for by the GBSA^{61,62} continuum model. Second, all conformers within a 6 kcal/mol GFN2-xTB energy window were optimized at the PBEh-3c(COSMO)^{63,64} level of theory. Third, within a 4 kcal/mol PBEh-3c energy window, all remaining structures were used as input for PW6B95/def2-QZVP^{65,66} single point energy calculations. Free energies were computed for the lowest energy conformers by adding solvation free energies with COSMO-RS^{67,68} and thermostatistical contributions at a temperature of 298.15 K within the modified⁶⁹ rigid-rotor harmonic oscillator approximation based on the GFN2-xTB structure an vibrational frequencies ($\Delta G = \Delta E_{PW6B95}$ + $\Delta G_{solv}^{COSMO-RS} + \Delta G_{RRHO}^{GFN2-xTB}$). This is the same protocol we used recently to compute the first hyperpolarizability of tryptophan.⁷⁰ The OR of relevant conformers with a population larger than 1.5% was computed at the sTD-CAM-B3LYP/6-31+G(d) level of theory applying an energy threshold of 14 eV.

All specific OR values $[\alpha]$ are given in $[dm(g/cm^3)]^{-1}$, and molar rotations are given in cm^2 dmol⁻¹ units. The DFT reference calculations were done with Dalton2018.0,^{56,57} while the DFT input for the stda⁵⁵ code was obtained from Q-Chem 5.1.⁵⁸ The TD-DFT computational times were obtained with the very efficient Turbomole code.⁷¹ In the following, we use s "functional name" as the short notation that refers to a sTD-DFT calculation made with this functional (e.g., sB3LYP is the short notation for a sTD-DFT/B3LYP calculation).

IV. RESULTS

Figure 3 compares experimental and theoretical molar rotations at the sodium D-line for the 42 first molecules of the OR45 benchmark set at both sTD-DFT and TD-DFT levels of theory with the B3LYP hybrid functional and the aug-cc-pVDZ basis set. Figure S1 shows results with PBE0 and BHandHLYP functionals, which are not explicitly discussed here because they are very similar to those with B3LYP. We used both length and velocity forms for the sTD-DFT calculations but provide no direct comparison with TD-DFT values in the velocity formulation because Dalton uses a modified-velocity representation, which is not available in the stda code. When comparing to experiment, one has to keep in mind that we did not account for solvent or dynamic structural effects. Figures S2–S8, supplementary material, provide OR frequency dispersion of the 42 compounds computed with both TD-DFT and sTD-DFT schemes. Note that at the sodium D-line (589.3 nm), the OR is usually significantly enhanced compared to perturbations at other commonly used wavelengths, e.g., 1900 nm.

Compounds 1-13 are all substituted three-membered ring molecules. For 1-7, the trends of the OR values compared to experiment are well reproduced by sTD-DFT and slightly better when the velocity formulation is employed. Molecule 6 is an interesting case for which the simplified scheme outperforms the full scheme in reproducing the experimental OR value. The sB3LYP/velocity molar rotation is 48% lower than the experimental one, while the B3LYP underestimates the value by 88%. Figure S2 presents the frequency dispersion of 6 that shows very different results in the simplified scheme compared to TD-DFT. By comparing to the experimental OR value, one can conclude that the non-approximated TD-DFT frequency dispersion is wrong. Tentatively, this could be assigned to the neglected exchange-correlation response in the sTD-DFT framework or because the two-electron integrals in the simplified scheme provide the right 1/R asymptotic decay.

Compounds 7-11 share the same aziridine motif with different substitutions. The experimental OR value of (2R,3R)-2,3dimethylaziridine (7) is particularly well reproduced by all methods. The decrease in the response experimentally observed when adding a chlorine or a bromine in 8 and 9 is reproduced by all schemes, but the decrease in the OR in the sB3LYP treatment is too small to change the sign, as observed in the experiment. B3LYP is performing slightly better but overshooting with respect to experiment. A look at their frequency dispersion is very informative (Fig. S3) because one can see that a negative decrease in the response is missing with the sTD-DFT scheme. Here, a sophisticated multipole approximation for the two-electron integrals and/or a possible reintroduction of the exchange-correlation kernel may improve this. This is currently under investigation. (1S,2R)-1-chloro-2methylaziridine (10) and (1R,2R)-1-chloro-2-methylaziridine (11) are diastereomers. The experimental change of sign and amplitudes between these two are well reproduced at the sB3LYP level, though underestimated. B3LYP is performing better in this case.

For compounds 12 and 13, conformers from different tert-butyl group orientations may contribute. Here, only one structure was used for each molecule as in Ref. 38. This probably explains the discrepancy observed for compound 12 with respect to experiment. For 13, the simplified scheme provides the best agreement with experiment.

For compounds 14–18, the experimental trends are well reproduced by both methods. Note that the frequency dispersion of 16 (Fig. S3) at the sTD-DFT level of theory provides a wrong positive enhancement that flips the sign of the response at small wavelengths.

The polycyclic ketones 19–22, namely, (1R)-norcamphor, (1S)norbornenone, (1R)-camphor, and (1R)-fenchone, are well-studied compounds. Particularly interesting is norbornenone (20) because of its large negative OR compared to the structurally similar norcamphor (19). For norcamphor, all schemes yield consistent results, but none of them can reproduce the negative experimental sign. The large negative enhancement experimentally observed for norbornenone is well-reproduced by both levels of theory with a 18% underestimation at the sB3LYP/velocity level with respect to



FIG. 3. Comparison of experimental and theoretical molar OR values for the 42 first compounds of the OR45 benchmark set obtained at the B3LYP/aug-cc-pVDZ level of theory. Data for the simplified formalism are given in velocity and length representations, while the unmodified TD-DFT results are obtained in the length representation.

experiment, while B3LYP is only 4% larger. For molecules 21 and 22, the sB3LYP method qualitatively reproduces the experimental change of OR sign due to the change of the two methyl group positions in both isomers. B3LYP performs better in this case. Note that

employing a smaller basis set such as 6-31+G(d) with the velocity form yields a better result (see Fig. S15).

Compounds 23–28 share the same 6,8-dioxabicyclo[3.2.1]octane motif with different substituents. sB3LYP molar rotations of these

molecules are systematically underestimated with respect to B3LYP ones.

Experimentally, adding a methyl group to the (1S,5R)-2,7,8trioxabicyclo[3.2.1]octane (29), resulting in compound 30, decreases the OR by 22.9° cm² dmol⁻¹. While the experimental molar rotations of 29 and 30 are underestimated at the sB3LYP/velocity level by 31% and 39%, respectively, this trend is particularly well followed with a 27.8° cm² dmol⁻¹ difference between 29 and 30. With a 16% and 22% underestimation with respect to experiment for 29 and 30, respectively, B3LYP performs only slightly better.

For molecules including 31–34, the results with both methods are of mixed quality. For 31, Fig. S7 shows an inaccurate treatment of the frequency dispersion by the simplified method with respect to the full scheme, leading to a tiny negative OR value at the sodium D-line. For 32, none of the methods can reproduce the experimental OR sign. For 33, the simplified method in both formalisms yields the best agreement with experiment. Note that because of its π -conjugation, the response of 33 is dominated by valence contributions, a situation for which the sTD-DFT method is particularly performing well. In view of the experimental result for 34, a wrong negative contribution is present in the B3LYP frequency dispersion but not in the one obtained with the simplified method.

The experimental OR of trans-cyclooctene (35) is very well reproduced by B3LYP with a deviation of only 0.4%, while sB3LYP underestimates by 56%. The related electronic circular dichrosim of this compound is known to be difficult to describe due to Rydbergvalence mixing of the π - π^* state.⁷² One should also keep in mind that the sTD-DFT method is globally parameterized to reproduce excitation energies but not specifically for OR. Re-adjusting the global parameters is easily possible and can be useful to tackle a specific set of similar compounds, as shown already in Refs. 33 and 70. For example, in compound 35, if the parameter y_1 is set to 1.1 instead of the default 0.566, an sB3LYP/velocity OR value of 461° cm² dmol⁻¹ is obtained at 589.3 nm, which is very close to the experimental one of 458° cm² dmol⁻¹. For 36, the experimental value is also largely underestimated by the simplified scheme. If one uses the same y_1 parameter value of 1.1, the sB3LYP molar rotation is drastically improved to a value of -735° cm² dmol⁻¹ (expt. -718° cm² $dmol^{-1}$).

As already stated in the computational details, we chose an energy threshold of 20 eV to select important configuration state functions for molecules 36–42 and 50 eV for others. Figures S9 and S10 show the convergence of the OR at 589.3 nm as a function of this threshold for molecules 1 and 36, respectively. Clearly, at the recommended default threshold value, the OR is mostly converged. For compound 37, the sB3LYP method in length and velocity representations underestimates both experimental and B3LYP values. As shown in Fig. S11, a threshold of 20 eV is well suited for here, and a value of 50 significantly improves this result (see Fig. S13). Even with a tight threshold of 50 eV, the OR computation takes only 13.5 min on an eight-core desktop computer (Intel core i7-6700, 3.40 GHz), while it took about 9 h to perform the full calculation with Dalton on a 28-core cluster node. Figure S12 shows the dependence of the computation time as a function of the threshold for 37.

The last ensemble of molecules of the OR45 set concerns helicenes (compounds 38–42). It is expected that the sTD-DFT

method will perform better for such systems because their response is valence dominated while others systems of the OR45 benchmark set are more Rydberg state dominated. It is well established that the sTD-DFT method provides a better treatment for valence excitations,^{30–35} which is the case for large π -conjugated organic compounds. For 38-42, the sB3LYP/length OR values are 11%, 12%, 9%, 15%, and 9% lower than B3LYP ones, respectively. With respect to experiment, the sB3LYP/velocity treatment yields the best agreement. While small deviations to experiment with 12%, 10%, 11%, and -3% are observed for 38, 39, 40, and 42, none of the methods (including other exchange-correlation functionals, see Fig. S1) is able to describe the decrease in the OR observed for compound 40. The results provided in the OR45 original publication³⁸ lead to the same conclusion. Other trends such as the intensification of the OR with increasing number of rings in the helicenes or the substitution in the [6]helicene (molecule 39) by bromine are well described. These results are very promising for the application of the simplified method for the design of new helicenes with enhanced optical rotations.

Figure 4 presents results for some typical cases as a function of the energy threshold. Timings for the TD-DFT calculations are also displayed and were obtained with the very efficient Turbomole⁷¹ program. The TD-DFT OR calculations took 2 h 19 min, 5 h 14 min, 6 h 20 min, 5 h 34 min, and 9 h 44 min wall-time on eight cores for 38, 39, 40, 41, and 42, respectively. sTD-DFT results obtained with a threshold of 20 eV are converged to better than 1% deviation finishing within 6.8 min, 13.1 min, 17.0 min, 15.9 min, and 23.0 min, which is less than 5% of the full scheme. This speedup factor of about 20 can be even increased at a lower threshold. With a value of 8 eV, most of the response physics is already recovered, and OR values are converged to about ±5%. At this level, the timings diminish impressively to only 0.07 min, 0.11 min, 0.14 min, 0.11 min, and 0.17 min, respectively, corresponding to a speedup of almost 2000 with respect to the full scheme. For example, to screen new helicene structure motifs, such a threshold is already sufficient to provide the qualitative description needed.

To assess the effect of using a smaller basis set for the evaluation of the OR response at the sTD-DFT level, Figs. S14 and S15 present sB3LYP results with both 6-31+G(d) and aug-cc-pVDZ basis sets in comparison with experiment for compounds 38–42 and 19–22, respectively. For the helicenes, we observe deviations with respect to experiment of 1.2%, -1.6%, 46.8%, -4.1%, and -15.3% with the 6-31+G(d) basis set for compounds 38–42, respectively. This is better than with the aug-cc-pVDZ basis set for which deviations of 11.6%, 9.4%, 78.6%, 11.1%, and -2.9% are observed when compared to the experiment. For compounds 19–22, a similar comparison to experiment yields deviations of -110.7%, -38.9%, -22.0%, and -28.5%using the 6-31+G(d) basis set, while -123.6%, -17.5%, -42.7%, and -75.2% with aug-cc-pVDZ. These results suggest that the 6-31+G(d) basis set represents a reasonably more efficient alternative to treat large systems.

The design of new helicenes with enhanced chiroptical properties such as new chiral bilayer nanographenes⁴ is of timely interest. Theoretical chemistry could play a large role in screening such structures to optimize their design and provide adequate guidelines to experimentalists. Figure 5 presents the comparison between experimental and sCAM-B3LYP/aug-cc-pVDZ[or def2-SV(P) for



FIG. 4. Convergence of OR values and computational times for molecules 38, 39, 40, 41, and 42 as a function of the energy threshold calculated at the sB3LYP/aug-cc-pVDZ on an eight-core desktop computer (Intel core i7-6700, 3.40 GHz). TD-DFT computational times are also provided. They were obtained on eight CPUs (Intel Xeon CPU E5-2660 v4, 3.2 GHz).





1d1, 3a, and 3b] molar rotations for some recently synthesized helicenes, including four azabora[n]helicenes (n = 6, 8, and 10)³⁵ and the corresponding platina[10]helicene analogue, four phospha[n]helicenes (n = 6 and 7),⁴⁰ (P,P)-bis-helicenic 2,2'-bipyridine (un)coordinated to $Zn(OAc)_2$,⁴¹ and two chiral cycloiridiated complexes bearing helicenic NHC ligands.³⁷ Considering that we are not accounting for solvent or temperature-dependent structural effects, the agreement between theory and experiment is striking. For the four azaborahelicenes, the OR trend with increasing number of rings is well-followed by our method. The observed underestimation of 32% with respect to experiment for molecule 1d seems to be related to the choice of the functional, though. For example, the sB3LYP value of 37973° cm² dmol⁻¹ represents an overestimation of 18%. The experimentally observed response enhancement from the azabora[10]helicene molecule to the platina[10]helicene compound is also well-followed by the simplified method.

For the four phosphahelicene oxides, experimental trends are nicely reproduced by the sTD-DFT method showing its predictive power. The inclusion of solvent effects may close the gap between experimental and theoretical values. Note that we used truncated structures as already mentioned in Sec. II. In Ref. 40, the authors also provided the untruncated optimized geometry for [6]-M-endo-2 for which they obtained a deterioration of the agreement between theory and experiment. The same tendency is followed by the simplified method. A value of -12358° cm² dmol⁻¹ is obtained for the untruncated structure, while we have -14758° cm² dmol⁻¹ for the truncated geometry. To improve this treatment, a conformer sampling seems necessary because of the flexible groups attached.

The next two compounds are also well-described. We observe an overestimation with respect to experiment by 37% and 9% for (P,P)-bis-helicenic 2,2'-bipyridine and when coordinated to $Zn(OAc)_2$, respectively. The better value for (P,P)-(+)-1- $Zn(OAc)_2$ may be due to a less flexible structure because of the two additional bonds to Zn, while for the other system, a conformational search should be considered to provide a Boltzmann-weighted value. Note that our intention here is not to provide the best possible comparison to experiment but more to show capabilities of the new method.

The last two molecules are cycloiridiated complexes bearing helicenic NHC ligands. The experimental OR value for 3a was obtained for a mixture of two stereoisomers (P,S_{lr}) - and (M,S_{lr}) -3a in CH₂Cl₂. As it was proposed in the original publication,³⁷ we computed the molar rotation as the Boltzmann-average of (P,S_{lr}) - and (M,S_{lr}) -3a. We obtained a value 207° cm² dmol⁻¹, not far from the experimental value of 230° cm² dmol⁻¹. Concerning 3b, an experimental value of 12 350° cm² dmol⁻¹ was measured for the (P,S_{lr}) -3b enantiomer. The agreement seems worse with a molar rotation of 8732° cm² dmol⁻¹ calculated with the simplified scheme. However, these values refer to gas phase calculations, and including the Lorentz correction factor [Eq. (23)] for dichloromethane, solvent corrected OR values for 3a and 3b of 278° cm² dmol⁻¹ and 11727° cm² dmol⁻¹, respectively, closer to the experimental ones are obtained.

The OR values of the amino acid tryptophan were computed. Previous studies^{70,73} underline the importance of considering a conformer ensemble for the reasonable theoretical simulation of optical properties. An established workflow in this regard is the computation of the desired property on each conformer structure and averaging the values weighted by the respective Boltzmann population.⁷⁰ The significantly populated conformers together with specific OR values computed at the sTD-CAM-B3LYP/6-31G+G(d) level of theory are depicted in Fig. 6. The OR values of the



FIG. 6. Conformer ensemble for tryptophan. Specific rotation at the sodium D-line, population, and relative free energies are given in the plotted structures. α_{calc} denotes the Boltzmann weighted specific rotation for tryptophan. The experimental value is taken from the Ref. 74.

different conformers vary between $-145.8^{\circ}[dm(g/cm^3)]^{-1}$ (conformer 2) and $153.1^{\circ}[dm(g/cm^3)]^{-1}$ (conformer 5). Note that taking only the most contributing conformer (1) with a specific rotation of $-1.2^{\circ}[dm(g/cm^3)]^{-1}$ would result in a bad agreement with the experimental value. Clearly, a single-structure approach where only the energetically lowest conformer is considered seems to be inappropriate for the computation of the OR of conformationally flexible systems. The Boltzmann-weighted specific rotation of the entire conformer ensemble amounts to $-35.8^{\circ}[dm(g/cm^3)]^{-1}$, which agrees well with the experimental value of $-31.5^{\circ}[dm(g/cm^3)]^{-1}$.

V. CONCLUSION

In this contribution, we introduce a new theoretical method to efficiently calculate the optical rotation of large molecular systems in the sTD-DFT framework. While the agreement with respect to experiment or the non-approximated TD-DFT scheme for small systems with Rydberg-dominated response is only semi-quantitative, good results are obtained for large systems at a tiny fraction of the computational cost of a full TD-DFT calculation. In particular, for helicenes, we were able to reproduce various observed trends regarding the number rings or for different substitutions. These results are particularly important for the design of new compounds where the screening of a large number of structures may be necessary and for which normal TD-DFT calculations are unfeasible. We showed that for a small configuration selection energy threshold, trends are still well reproduced while achieving a speedup of about a factor of 2000 with respect to the full scheme. Encouraging results for a bio-molecule example are obtained by considering a proper conformational ensemble. Future projects on optical rotation calculations for biomolecules such as peptides or even entire proteins may include molecular dynamics and will be considered as follow-up to this study. Furthermore, a deeper analysis of the molecular origin of the optical rotation is of timely interest, and a corresponding method-independent framework is currently under development.

SUPPLEMENTARY MATERIAL

See the supplementary material for the comparison between theory and experiment with PBE0 and BHandHLYP for the 42 first molecules of the OR45 benchmark set, as well as their frequency dispersions with B3LYP, BHandHLYP, and PBE0 hybrid exchangecorrelation functionals, convergences of the optical rotation of compound 1, 36, and 37 as a function of the energy threshold, computation time for the optical rotation of compound 37 as a function of the energy threshold, the corrected optical rotation frequency dispersion of 37 using an energy threshold of 50 eV, and comparisons of experimental and theoretical optical rotation for compounds 38–42 and 19–22 obtained at the B3LYP/6-31+g(d) level.

ACKNOWLEDGMENTS

This work was supported by the DFG in the framework of the "Gottfried-Wilhelm-Leibniz" prize.

DATA AVAILABILITY

The data that support the findings of this study are available from the corresponding author upon reasonable request.

REFERENCES

¹K. Dhbaibi, L. Favereau, and J. Crassous, Chem. Rev. 119, 8846 (2019).

²L. Friedman and J. G. Miller, Science 172, 1044 (1971).

³J. M. Fernández-García, P. J. Evans, S. Filippone, M. Á. Herranz, and N. Martín, Acc. Chem. Res. **52**, 1565 (2019).

⁴P. J. Evans, J. Ouyang, L. Favereau, J. Crassous, I. Fernández, J. Perles, and N. Martín, Angew. Chem., Int. Ed. **57**, 6774 (2018).

⁵M.-L. Tsai, W.-C. Tu, L. Tang, T.-C. Wei, W.-R. Wei, S. P. Lau, L.-J. Chen, and J.-H. He, Nano Lett. **16**, 309 (2016).

⁶N. Martín, Adv. Energy Mater. 7, 1601102 (2017).

⁷S. Zhou, H. Xu, W. Gan, and Q. Yuan, RSC Adv. 6, 110775 (2016).

⁸J. Meisenheimer and K. Witte, Ber. Dtsch. Chem. Ges. 36, 4153 (1903).

⁹M. S. Newman and D. Lednicer, J. Am. Chem. Soc. 78, 4765 (1956).

¹⁰L. Rosenfeld, Z. Angew. Phys. **52**, 161 (1929).

¹¹T. D. Crawford, Theor. Chem. Acc. **115**, 227 (2006).

¹²K. Ruud and T. Helgaker, Chem. Phys. Lett. **352**, 533 (2002).

¹³K. Ruud, P. J. Stephens, F. J. Devlin, P. R. Taylor, J. R. Cheeseman, and M. J. Frisch, Chem. Phys. Lett. 373, 606 (2003).

¹⁴M. C. Tam, N. J. Russ, and T. D. Crawford, J. Chem. Phys. **121**, 3550 (2004).

¹⁵T. D. Crawford, L. S. Owens, M. C. Tam, P. R. Schreiner, and H. Koch, J. Am. Chem. Soc. **127**, 1368 (2005).

¹⁶J. Kongsted, T. B. Pedersen, M. Strange, A. Osted, A. E. Hansen, K. V. Mikkelsen, F. Pawlowski, P. Jørgensen, and C. Hättig, Chem. Phys. Lett. 401, 385 (2005).

¹⁷J. Autschbach, L. Nitsch-Velasquez, and M. Rudolph, in *Electronic and Magnetic Properties of Chiral Molecules and Supramolecular Architectures*, edited by R. Naaman, D. N. Beratan, and D. Waldeck (Springer Berlin Heidelberg, Berlin, Heidelberg, 2011), pp. 1–98.

¹⁸K. Yabana and G. F. Bertsch, Phys. Rev. A 60, 1271 (1999).

¹⁹J. R. Cheeseman, M. J. Frisch, F. J. Devlin, and P. J. Stephens, J. Phys. Chem. A 104, 1039 (2000).

²⁰ P. J. Stephens, F. J. Devlin, J. R. Cheeseman, and M. J. Frisch, J. Phys. Chem. A 105, 5356 (2001).

²¹S. Grimme, Chem. Phys. Lett. **339**, 380 (2001).

²²J. Autschbach and T. Ziegler, J. Chem. Phys. **116**, 891 (2002).

²³J. Autschbach, S. Patchkovskii, T. Ziegler, S. J. A. van Gisbergen, and E. Jan Baerends, J. Chem. Phys. **117**, 581 (2002).

²⁴T. Helgaker, K. Ruud, K. L. Bak, P. Jørgensen, and J. Olsen, Faraday Discuss. 99, 165 (1994).

²⁵ M. Krykunov and J. Autschbach, J. Chem. Phys. 123, 114103 (2005).

²⁶S. Grimme, F. Furche, and R. Ahlrichs, Chem. Phys. Lett. **361**, 321 (2002).

²⁷ M. Göppert-Mayer, Ann. Phys. **401**, 273 (1931).

²⁸T. B. Pedersen, H. Koch, L. Boman, and A. M. J. Sánchez de Merás, Chem. Phys. Lett. **393**, 319 (2004).

²⁹J. Autschbach, ChemPhysChem 12, 3224 (2011).

³¹C. Bannwarth and S. Grimme, Comput. Theor. Chem. **1040-1041**, 45 (2014).

³²S. Grimme and C. Bannwarth, J. Chem. Phys. **145**, 054103 (2016).

³³M. de Wergifosse and S. Grimme, J. Chem. Phys. **149**, 024108 (2018).

³⁴M. de Wergifosse and S. Grimme, J. Chem. Phys. **150**, 094112 (2019).

³⁶M. de Wergifosse, J. Seibert, B. Champagne, and S. Grimme, J. Phys. Chem. A 123, 9828 (2019).

³⁷N. Hellou, C. Jahier-Diallo, O. Baslé, M. Srebro-Hooper, L. Toupet, T. Roisnel, E. Caytan, C. Roussel, N. Vanthuyne, J. Autschbach, M. Mauduit, and J. Crassous, Chem. Commun. **52**, 9243 (2016).

³⁰S. Grimme, J. Chem. Phys. **138**, 244104 (2013).

³⁵M. de Wergifosse, C. Bannwarth, and S. Grimme, J. Phys. Chem. A **123**, 5815 (2019).

³⁸M. Srebro, N. Govind, W. A. de Jong, and J. Autschbach, J. Phys. Chem. A **115**, 10930 (2011).

³⁹C. Shen, M. Srebro-Hooper, M. Jean, N. Vanthuyne, L. Toupet, J. A. G. Williams, A. R. Torres, A. J. Riives, G. Muller, J. Autschbach, and J. Crassous, Chem. Eur. J. 23, 407 (2017).

⁴⁰K. Yavari, W. Delaunay, N. De Rycke, T. Reynaldo, P. Aillard, M. Srebro-Hooper, V. Y. Chang, G. Muller, D. Tondelier, B. Geffroy *et al.*, Chem. Eur. J. 25, 5303 (2019).

⁴¹ H. Isla, N. Saleh, J.-K. Ou-Yang, K. Dhbaibi, M. Jean, M. Dziurka, L. Favereau, N. Vanthuyne, L. Toupet, B. Jamoussi, M. Srebro-Hooper, and J. Crassous, J. Org. Chem. 84, 5383 (2019).

⁴²A. Zangwill and P. Soven, Phys. Rev. A 21, 1561 (1980).

43 S. Hirata and M. Head-Gordon, Chem. Phys. Lett. 314, 291 (1999).

⁴⁴F. Furche, J. Chem. Phys. 114, 5982 (2001).

⁴⁵F. Wang, C. Y. Yam, and G. Chen, J. Chem. Phys. **126**, 244102 (2007).

⁴⁶A. J. Thorvaldsen, K. Ruud, K. Kristensen, P. Jørgensen, and S. Coriani, J. Chem. Phys. **129**, 214108 (2008).

⁴⁷F. Zahariev and M. S. Gordon, J. Chem. Phys. 140, 18A523 (2014).

⁴⁸S. M. Parker, D. Rappoport, and F. Furche, J. Chem. Theory Comput. **14**, 807 (2018).

⁴⁹K. Nishimoto and N. Mataga, Z. Phys. Chem. **12**, 335 (1957).

⁵⁰K. Ohno, Theor. Chim. Acta 2, 219 (1964).

⁵¹G. Klopman, J. Am. Chem. Soc. 86, 4550 (1964).

⁵²D. C. Ghosh and N. Islam, Int. J. Quantum Chem. **110**, 1206 (2010).

⁵³I. Mayer, Chem. Phys. Lett. **393**, 209 (2004).

⁵⁴I. Mayer, Struct. Chem. 27, 51 (2016).

⁵⁵See https://github.com/grimme-lab/stda/ for the stda code.

⁵⁶ K. Aidas, C. Angeli, K. L. Bak, V. Bakken, R. Bast, L. Boman, O. Christiansen, R. Cimiraglia, S. Coriani, P. Dahle, E. K. Dalskov, U. Ekström, T. Enevoldsen, J. J. Eriksen, P. Ettenhuber, B. Fernández, L. Ferrighi, H. Fliegl, L. Frediani, K. Hald, A. Halkier, C. Hättig, H. Heiberg, T. Helgaker, A. C. Hennum, H. Hettema, E. Hjertenaes, S. Høst, I.-M. Høyvik, M. F. Iozzi, B. Jansík, H. J. A. Jensen, D. Jonsson, P. Jørgensen, J. Kauczor, S. Kirpekar, T. Kjaergaard, W. Klopper, S. Knecht, R. Kobayashi, H. Koch, J. Kongsted, A. Krapp, K. Kristensen, A. Ligabue, O. B. Lutnaes, J. I. Melo, K. V. Mikkelsen, R. H. Myhre, C. Neiss, C. B. Nielsen, P. Norman, J. Olsen, J. M. H. Olsen, A. Osted, M. J. Packer, F. Pawlowski, T. B. Pedersen, P. F. Provasi, S. Reine, Z. Rinkevicius, T. A. Ruden, K. Ruud, V. V. Rybkin, P. Sałek, C. C. M. Samson, A. S. de Merás, T. Saue, S. P. A. Sauer, B. Schimmelpfennig, K. Sneskov, A. H. Steindal, K. O. Sylvester-Hvid, P. R. Taylor, A. M. Teale, E. I. Tellgren, D. P. Tew, A. J. Thorvaldsen, L. Thøgersen, O. Vahtras, M. A. Watson, D. J. D. Wilson, M. Ziolkowski, and H. Ågren, Wiley Interdiscip. Rev.: Comput. Mol. Sci. 4, 269 (2014).

⁵⁷Dalton, a molecular electronic structure program, release dalton2018.0, 2018, see http://daltonprogram.org.

⁵⁸Y. Shao, Z. Gan, E. Epifanovsky, A. T. B. Gilbert, M. Wormit, J. Kussmann, A. W. Lange, A. Behn, J. Deng, X. Feng, D. Ghosh, M. Goldey, P. R. Horn, L. D. Jacobson, I. Kaliman, R. Z. Khaliullin, T. Kuś, A. Landau, J. Liu, E. I. Proynov, Y. M. Rhee, R. M. Richard, M. A. Rohrdanz, R. P. Steele, E. J. Sundstrom, H. L. Woodcock III, P. M. Zimmerman, D. Zuev, B. Albrecht, E. Alguire, B. Austin, G. J. O. Beran, Y. A. Bernard, E. Berquist, K. Brandhorst, K. B. Bravaya, S. T.

Brown, D. Casanova, C.-M. Chang, Y. Chen, S. H. Chien, K. D. Closser, D. L. Crittenden, M. Diedenhofen, R. A. DiStasio, Jr., H. Do, A. D. Dutoi, R. G. Edgar, S. Fatehi, L. Fusti-Molnar, A. Ghysels, A. Golubeva-Zadorozhnaya, J. Gomes, M. W. D. Hanson-Heine, P. H. P. Harbach, A. W. Hauser, E. G. Hohenstein, Z. C. Holden, T.-C. Jagau, H. Ji, B. Kaduk, K. Khistyaev, J. Kim, J. Kim, R. A. King, P. Klunzinger, D. Kosenkov, T. Kowalczyk, C. M. Krauter, K. U. Lao, A. D. Laurent, K. V. Lawler, S. V. Levchenko, C. Y. Lin, F. Liu, E. Livshits, R. C. Lochan, A. Luenser, P. Manohar, S. F. Manzer, S.-P. Mao, N. Mardirossian, A. V. Marenich, S. A. Maurer, N. J. Mayhall, E. Neuscamman, C. M. Oana, R. Olivares-Amaya, D. P. O'Neill, J. A. Parkhill, T. M. Perrine, R. Peverati, A. Prociuk, D. R. Rehn, E. Rosta, N. J. Russ, S. M. Sharada, S. Sharma, D. W. Small, A. Sodt, T. Stein, D. Stück, Y.-C. Su, A. J. W. Thom, T. Tsuchimochi, V. Vanovschi, L. Vogt, O. Vydrov, T. Wang, M. A. Watson, J. Wenzel, A. White, C. F. Williams, J. Yang, S. Yeganeh, S. R. Yost, Z.-Q. You, I. Y. Zhang, X. Zhang, Y. Zhao, B. R. Brooks, G. K. L. Chan, D. M. Chipman, C. J. Cramer, W. A. Goddard III, M. S. Gordon, W. J. Hehre, A. Klamt, H. F. Schaefer III, M. W. Schmidt, C. D. Sherrill, D. G. Truhlar, A. Warshel, X. Xu, A. Aspuru-Guzik, R. Baer, A. T. Bell, N. A. Besley, J.-D. Chai, A. Dreuw, B. D. Dunietz, T. R. Furlani, S. R. Gwaltney, C.-P. Hsu, Y. Jung, J. Kong, D. S. Lambrecht, W. Liang, C. Ochsenfeld, V. A. Rassolov, L. V. Slipchenko, J. E. Subotnik, T. Van Voorhis, J. M. Herbert, A. I. Krylov, P. M. W. Gill, and M. Head-Gordon, Mol. Phys. 113, 184 (2015).

⁵⁹ P. Pracht, F. Bohle, and S. Grimme, Phys. Chem. Chem. Phys. 22, 7169 (2020).
 ⁶⁰ C. Bannwarth, S. Ehlert, and S. Grimme, J. Chem. Theory Comput. 15, 1652 (2019).

⁶¹S. Grimme, C. Bannwarth, and P. Shushkov, J. Chem. Theory Comput. **13**, 1989 (2017).

⁶²W. C. Still, A. Tempczyk, R. C. Hawley, and T. Hendrickson, J. Am. Chem. Soc. 112, 6127 (1990).

⁶³S. Grimme, J. G. Brandenburg, C. Bannwarth, and A. Hansen, J. Chem. Phys. 143, 054107 (2015).

⁶⁴A. Klamt and G. Schüürmann, J. Chem. Soc., Perkin Trans. 2 1993, 799.

65 Y. Zhao and D. G. Truhlar, J. Phys. Chem. A 109, 5656 (2005).

⁶⁶F. Weigend and R. Ahlrichs, Phys. Chem. Chem. Phys. 7, 3297 (2005).

⁶⁷F. Eckert and A. Klamt, <u>AIChE J.</u> 48, 369 (2002).

⁶⁸COSMOtherm, C3.0, release 1601, COSMOlogic GmbH & Co. KG, http://www. cosmologic.de.

⁶⁹S. Grimme, Chem. - A Eur. J. 18, 9955 (2012).

⁷⁰J. Seibert, B. Champagne, S. Grimme, and M. de Wergifosse, J. Phys. Chem. B 124, 2568 (2020).

⁷¹TURBOMOLE V6.2 2010, a development of University of Karlsruhe and Forschungszentrum Karlsruhe GmbH, 1989-2007, TURBOMOLE GmbH, since 2007; available from http://www.turbomole.com.

⁷²S. Grimme and S. D. Peyerimhoff, "Theoretical study of circular dichroism spectra in the vacuum-ultraviolet," in *The Role of Rydberg States in Spectroscopy and Photochemistry: Low and High Rydberg States*, edited by C. Sándorfy (Springer Netherlands, Dordrecht, 1999), pp. 93–119.

73 M. D. Kundrat and J. Autschbach, J. Phys. Chem. A 110, 12908 (2006).

⁷⁴S. Budavari, P. E. Heckelman, J. F. Kinneary, M. J. O'Neil, and A. Smith, *The Merck Index: An Encyclopedia of Chemicals, Drugs, and Biologicals* (Merck, Whitehouse Station, NJ, 1996).