PERKIN 2 COMMUNICATION

Absolute configuration of chiral fullerenes and covalent derivatives from their calculated circular dichroism spectra

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The theoretical circular dichroism (CD) spectra of optically active C_{60} and C_{70} bis-adducts with chiral functionalization patterns and of the enantiomers of inherently chiral D_2-C_{76} and its mono-adducts were calculated by the π-electron SCF-CI-DV MO method. By comparison with the experimental CD spectra, the absolute configurations of these compounds were assigned.

Although the number of optically resolved inherently chiral fullerenes and derivatives of achiral fullerenes with a chiral functionalization pattern is growing rapidly,[1] the absolute configuration of these compounds has not yet been clearly addressed. Straightforward experimental methods for assigning these absolute configurations are currently not available, and efforts to obtain X-ray quality crystals of the compounds have failed. For the time being, the determination of the absolute configuration relies exclusively on the theoretical calculation of the circular dichroism (CD) spectrum for one enantiomer and comparison with the experimental CD data. Therefore, we have calculated the CD spectra of the enantiomeric C_2-symmetrical *cis*-3 bis-adducts (${}^{f}A$)-**1** and (${}^{f}C$)-**1**,[1a,b,2] the diastereoisomeric C_2-symmetrical bis-adducts of C_{70} ($S,S,S,S,{}^{f}A$)-**2** and ($S,S,S,S,{}^{f}C$)-**3** with chiral addition patterns,[1c] the inherently chiral D_2-symmetrical fullerene enantiomers (${}^{f}A$)-C_{76} and (${}^{f}C$)-C_{76},[3] and the diastereoisomeric C_2-symmetrical C_{76} mono-adducts ($S,S,{}^{f}A$)-**4** and ($S,S,{}^{f}C$)-**5**[4] using the π-electron SCF-CI-DV MO (self consistent field-configuration interaction-dipole velocity molecular orbital) method.[5–7] Here, we assign the absolute configurations of these compounds by comparing their experimental CD spectra to the ones calculated for specific optical isomers. Also, the absolute configurations of the enantiomeric C_2-symmetrical C_{60} bis-adducts ($R,R,{}^{f}A$)-**6** and ($S,S,{}^{f}C$)-**6** and the diastereoisomeric C_1-symmetrical C_{76} mono-adducts ($S,S,{}^{f}A$)-**7** and ($S,S,{}^{f}C$)-**8**[4] are derived by chemical correlation.

In the calculations, the expressions for the rotational strength R_{ba} and dipole strength D_{ba} are given in eqns. (1) and (2), where

$$R_{ba} = 2(\varphi_a|\nabla|\varphi_b)(\varphi_a|\boldsymbol{r} \times \nabla|\varphi_b)\beta_M{}^2/(\pi\sigma_{ba}) \qquad (1)$$

$$D_{ba} = 2(\varphi_a|\nabla|\varphi_b)^2\beta_M{}^2/(\pi\sigma_{ba})^2 \qquad (2)$$

∇ is the del operator, $\boldsymbol{r}$ a distance vector, β_M the Bohr magneton, and σ_{ba} the excitation wavenumber of the transition a→b.[5–7] The atomic coordinates were obtained from AM1 calculations (MOPAC 93),[8] and the final CD and UV–VIS bands were approximated by the Gaussian distribution, eqns. (3) and (4),

$$\Delta\varepsilon(\sigma) = \Sigma\Delta\varepsilon_k \exp\{-[(\sigma - \sigma_k)/\Delta\sigma]^2\} \qquad (3)$$

$$\varepsilon(\sigma) = \Sigma\varepsilon_k \exp\{-[(\sigma - \sigma_k)/\Delta\sigma]^2\} \qquad (4)$$

where $2\Delta\sigma$ is the 1/e width of bands. The $\Delta\sigma$ value of 2300 cm^{-1} was adopted as a standard value. Detailed protocols of the calculations had been published previously.[5–7]

The fact that fullerenes and their covalent derivatives display a multitude of nearly indistinguishable π–π* transitions makes the calculation of their chiroptical properties difficult compared to other π-systems.[6,7] Considering that the fullerenes are distorted, non-planar π-systems, the resonance integral β needed to be adjusted and a value of $k = 0.5$ for $\beta = k\beta_0$ (where β_0 is the resonance integral of a regular aromatic C-atom) was finally found to provide the best fit to the experimental CD and UV–VIS spectra. There remains, however, still a discrepancy between the observed and theoretical absolute wavelengths, with the latter values being slightly lower. This shift to higher energy may come from the fact that only π–π* transitions are taken into account by the SCF-CI-DV MO method. Disagreement between experimental and theoretical transition energies had already been observed by Mason and co-workers in the case of other non-planar π-systems, the hexahelicenes, when they compared the π-SCF method,[5] a similar calculation to ours, with INDO calculations.[9] Comparatively, the INDO[10] method introduces also σ–π* transitions. However, our calculations using the SCF-CI-DV MO method reproduce well the shapes of the CD spectra and, as will be discussed below for C_{76}, give the same results as INDO calculations.

The experimental CD spectra of the two enantiomers (${}^{f}A$)-**1** and (${}^{f}C$)-**1**, which had been prepared by a highly diastereoselective [>97% diastereoisomeric excess (de)] tether-directed bis-cyclopropanation, followed by transesterification (Scheme 1),[1a,b] are displayed in Fig. 1. The CD spectrum was calculated (Fig. 2) for the enantiomer (${}^{f}C$)-**1a** bearing two dimethyl instead of diethyl malonate addends.† The calculated UV–VIS spectrum is also shown. Two regions can be distinguished in the calculated CD spectrum, one from 350 to 800 nm in which the signs of the CD bands together with the transition wavelengths correspond well to the experimental ones, and the other one from 200 to 350 where one band around 310 nm does not have the correct sign. Despite this incorrect band, considering the overall CD spectrum, the absolute configurations [CD(−)488]-(${}^{f}A$)-**1** and [CD(+)490]-(${}^{f}C$)-**1** can be proposed.[11] According to these stereochemical assignments, the enantiomer of **6** obtained by double Bingel addition of (R,R)-**9** to C_{60} (Scheme 1) has the absolute configuration [CD(−)487]-($R,R,{}^{f}A$).[1a]

The diastereoisomeric C_2-symmetrical bis-adducts of C_{70} ($S,S,S,S,{}^{f}A$)-**2** and ($S,S,S,S,{}^{f}C$)-**3** (Fig. 3) with chiral functionalization patterns had been obtained by double Bingel addition of an optically pure malonate derivative, derived from (S)-phenylbutanol, followed by HPLC purification.[1c] As shown in Fig. 3, the CD spectra of the two diastereoisomers are mirror-image shaped. This is due to the dominance of the chiroptical properties of the fullerene cores which display enantiomeric

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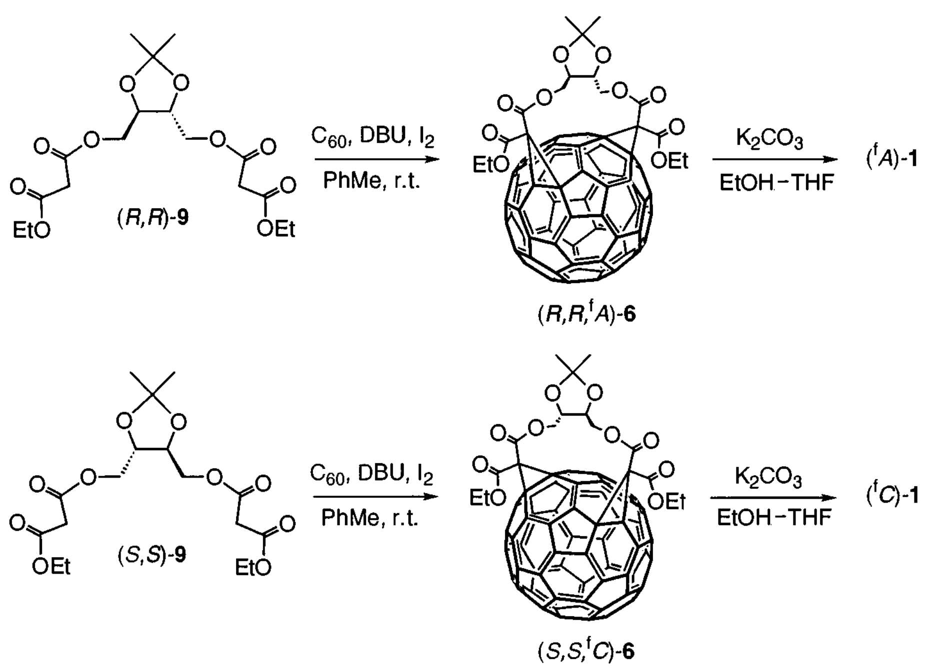
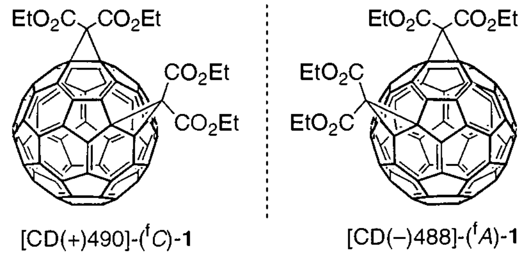
† Dimethyl malonate adducts were considered in all calculations, and the CD and UV–VIS bands were predicted for the wavelength range between 200–800 nm. Experimentally, the choice of CH_2Cl_2 as the solvent (for solubility reasons) prevented the recording of the CD and UV–VIS spectra in wavelength ranges below 250 nm.



Scheme 1 Synthesis of [CD(−)488]-(^{f}*A*)-**1** and [CD(+)490]-(^{f}*C*)-**1** by diastereoselective tether-directed bis-cyclopropanation of C_{60}, followed by transesterification[1a,b]



[CD(+)490]-(^{f}*C*)-**1** [CD(−)488]-(^{f}*A*)-**1**

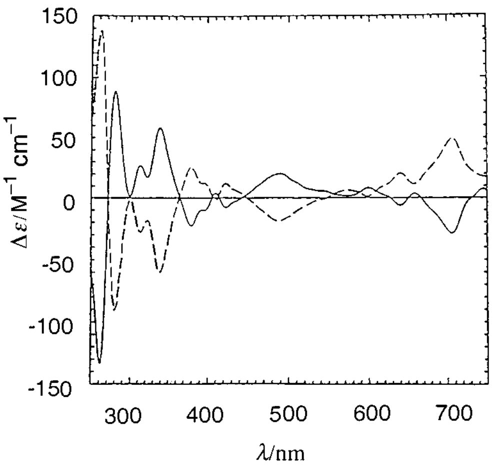


Fig. 1 Experimental CD spectra in CH_2Cl_2 of [CD(−)488]-(^{f}*A*)-**1** and [CD(+)490]-(^{f}*C*)-**1**[1b]

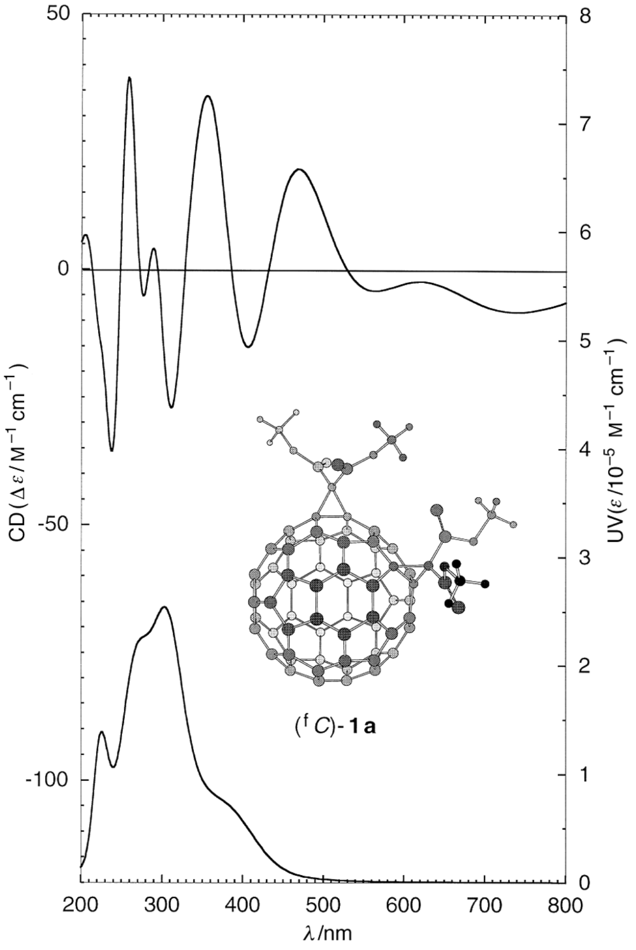
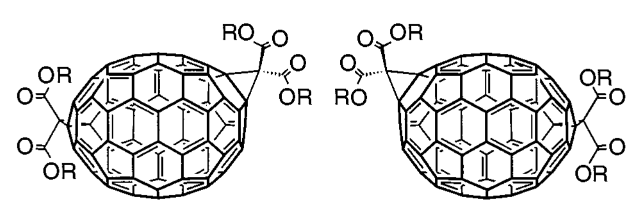


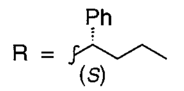
Fig. 2 CD and UV–VIS spectra of (^{f}*C*)-**1a** calculated by the SCF-CI-DV MO method. The AM1-optimized structure is shown.

functionalization patterns in the two compounds. The chiroptical contributions from the optically active malonate addends are negligible. Consequently, the CD calculations were performed for enantiomer (^{f}*C*)-**3a**, with two dimethyl instead of bis[(*S*)-1-phenylbutyl] malonate addends. The resulting calculated CD and UV–VIS spectra are displayed in Fig. 4. In this case, the correspondence between calculated and experimental CD spectra is very good, both for the transition wavelengths and the signs of the bands. Therefore the stereochemical assignments were made with a high degree of confidence as [CD(−)317]-(*S*,*S*,*S*,*S*,^{f}*A*)-**2** and [CD(+)318]-(*S*,*S*,*S*,*S*,^{f}*C*)-**3**.

The D_2-symmetrical higher fullerene C_{76} is the smallest known chiral carbon allotrope (Fig. 5).[3b] In 1993, Hawkins and Meyer reported its first kinetic resolution by asymmetric osmylation.[3c] Very recently, we prepared enantiomerically pure C_{76} by performing an electrochemical retro-Bingel reaction[3a] on the previously reported[4] optically pure diastereoisomers



[CD(−)317]-($S,S,S,S,^{\mathrm{f}}A$)-**2** [CD(+)318]-($S,S,S,S,^{\mathrm{f}}C$)-**3**



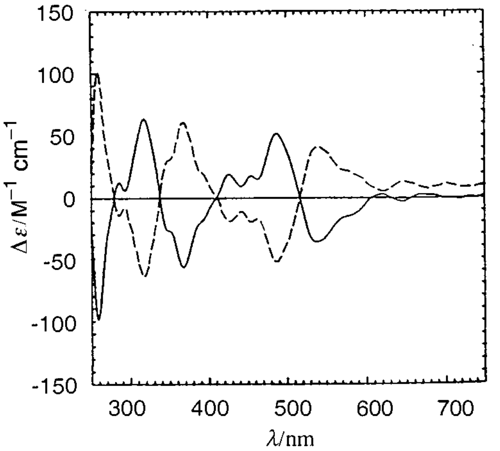


Fig. 3 Experimental CD spectra in CH_2Cl_2 of [CD(−)317]-($S,S,S,S,^{\mathrm{f}}A$)-**2** and [CD(+)318]-($S,S,S,S,^{\mathrm{f}}C$)-**3**[1c]

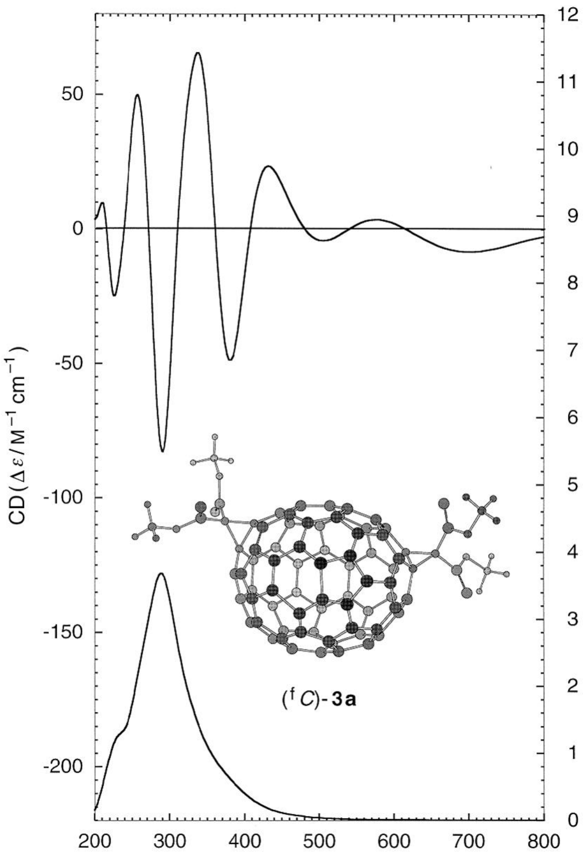
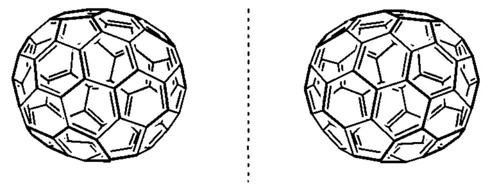


Fig. 4 CD and UV–VIS spectra of ($^{\mathrm{f}}C$)-**3a** calculated by the SCF-CI-DV MO method. The AM1-optimized structure is shown.



[CD(−)282]-($^{\mathrm{f}}A$)-C_{76} [CD(+)281]-($^{\mathrm{f}}C$)-C_{76}

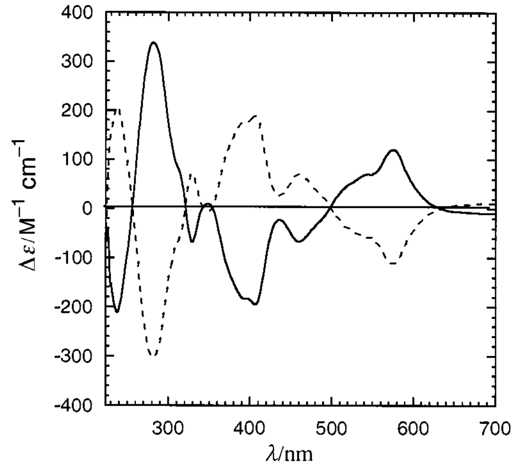
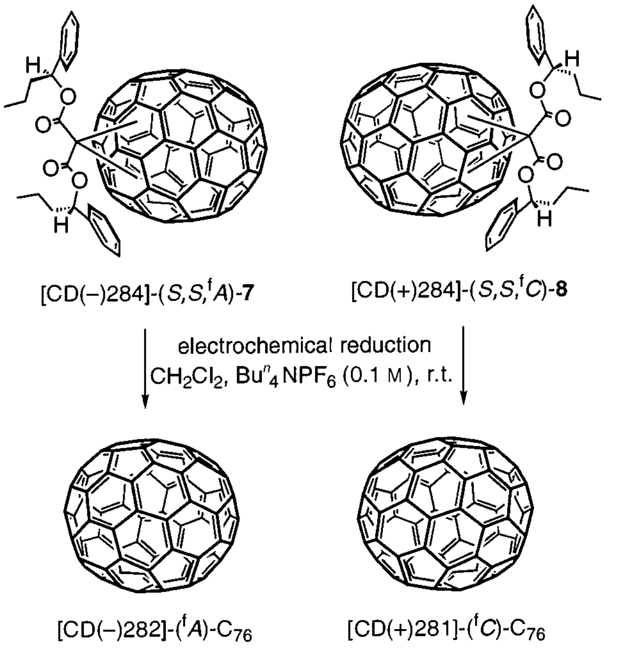


Fig. 5 Experimental CD spectra in CH_2Cl_2 of [CD(−)282]-($^{\mathrm{f}}A$)-C_{76} and [CD(+)281]-($^{\mathrm{f}}C$)-C_{76}[3a]



Scheme 2 Synthesis of [CD(−)282]-($^{\mathrm{f}}A$)-C_{76} and [CD(+)281]-($^{\mathrm{f}}C$)-C_{76} by the retro-Bingel reaction,[3a] performed on C_1-symmetrical [CD(−)284]-($S,S,^{\mathrm{f}}A$)-**7** and [CD(+)284]-($S,S,^{\mathrm{f}}C$)-**8** respectively. The location of the malonate addends on the C-sphere is not exactly known although constitutional assignments have been tentatively made.[3a]

($S,S,^{\mathrm{f}}A$)-**7** and ($S,S,^{\mathrm{f}}C$)-**8** (Scheme 2). Our CD spectra of the pure C_{76} enantiomers are shown in Fig. 5.[3a] They display the expected mirror-image shapes with band positions in full agreement with those reported by Hawkins and Meyer.[3c] In contrast, however, the Cotton effects in our spectra are almost a full order of magnitude larger than those previously reported: it is possible that the enantiomeric purity of the samples obtained by kinetic resolution[3c] was not very high or the concentrations were not accurately determined.

We calculated the CD and UV–VIS spectra of the ($^{\mathrm{f}}C$) enantiomer of C_{76} by the SCF-CI-DV MO method. The theoretical CD spectrum (Fig. 6) shows good agreement with the experimental one, especially in the range between 200–400 nm in which the strongest absorption bands appear. The absolute configuration ($^{\mathrm{f}}C$) can therefore be assigned to the enantiomer having an experimental $\Delta\varepsilon$ value of +338 M^{-1} cm^{-1} at 281 nm.

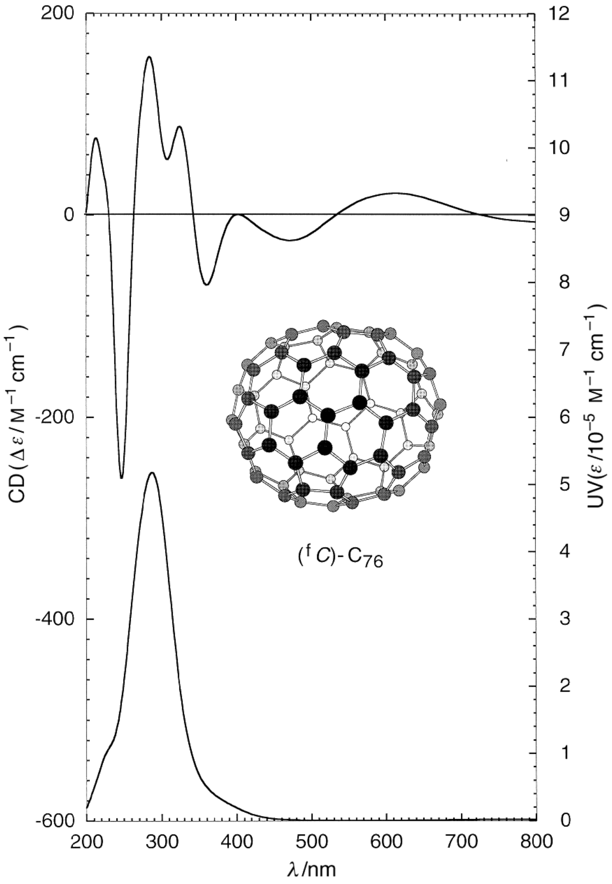
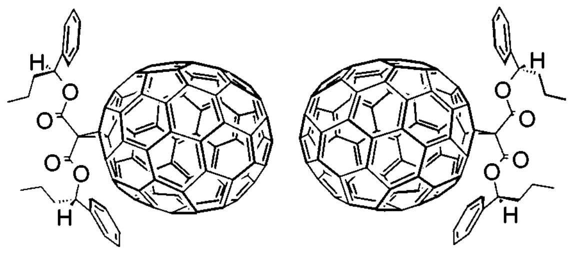


Fig. 6 CD and UV–VIS spectra of (^{f}C)-C_{76} calculated by the SCF-CI-DV MO method. The AM1-optimized structure is shown.

The CNDO (complete neglect of differential overlap)[12a] and INDO (intermediate neglect of differential overlap)[12b] methods have previously been applied by Zerbetto and co-workers to calculate the CD spectra of C_{76} enantiomers.[13] In these calculations, the experimental CD spectra were better reproduced in the higher than in the lower wavelength range. Most importantly, the same absolute configurational assignment can be independently derived from the calculations by Zerbetto and co-workers and from those presented here. Consequently, the absolute configurations [CD(−)282]-(^{f}A)-C_{76} and [CD(+)281]-(^{f}C)-C_{76} are assigned with confidence.

The experimental CD spectra of several C_{76} mono-adducts such as the C_2-symmetrical (S,S,^{f}A)-**4** and (S,S,^{f}C)-**5** (Fig. 7)[4] were also reproduced by the SCF-CI-DV MO method. The spectrum calculated for the (^{f}C)-**5a** enantiomer, with two dimethyl malonate addends, displayed a strong positive Cotton effect around 300 nm (Fig. 8), which corresponds to the strong experimental band around 280 nm. This comparison suggests the assignment of the absolute configurations as [CD(−)281]-(S,S,^{f}A)-**4** and [CD(+)281]-(S,S,^{f}C)-**5**. We propose that the sign of the strong band around 280 nm, which appears in the CD spectra of both enantiomerically pure C_{76} and its mono-adducts, represents a stereochemical fingerprint from which the absolute configuration of other, related derivatives of this inherently chiral fullerene can easily be derived in future work.

Following these stereochemical assignments from CD calculations, the absolute configurations of the diastereoisomerically pure precursors in the retro-Bingel reaction (which takes place with retention of configuration) leading to the pure C_{76} enantiomers (Scheme 2) could be derived by chemical correlation as [CD(−)284]-(S,S,^{f}A)-**7** and [CD(+)284]-(S,S,^{f}C)-**8**. Again, the negative sign of the strong band at 284 appears as a fingerprint for the (^{f}A) configuration of the C_{76} fullerene core.



[CD(−)281]-(S,S,^{f}A)-**4**   [CD(+)281]-(S,S,^{f}C)-**5**

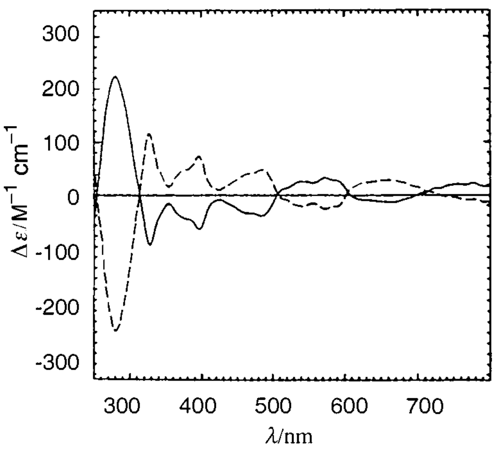


Fig. 7 Experimental CD spectra in CH_2Cl_2 of [CD(−)281]-(S,S,^{f}A)-**4** and [CD(+)281]-(S,S,^{f}C)-**5**[4]

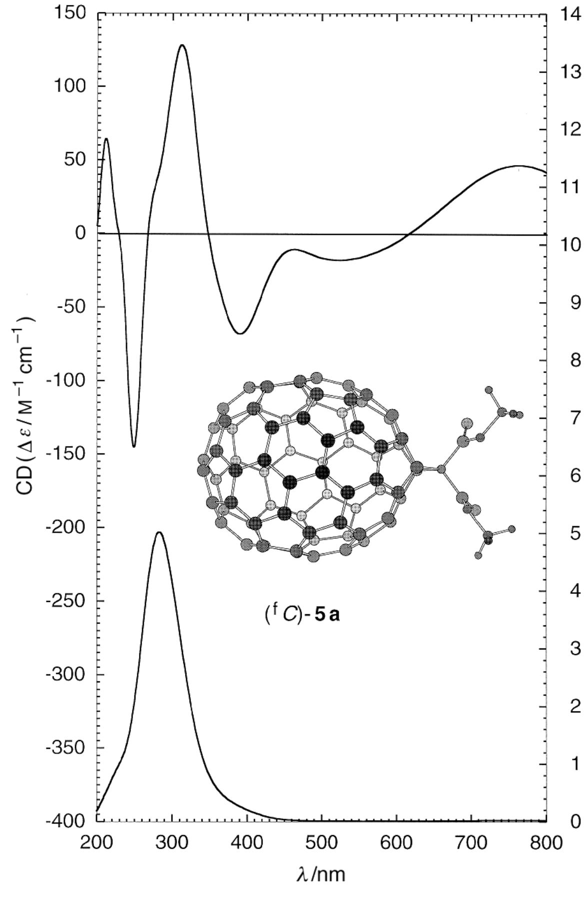


Fig. 8 CD and UV spectra of (^{f}C)-**5a** calculated by the SCF-CI-DV MO method. The AM1-optimized structure is shown.

In summary, we have shown that the CD spectra of enantiomers of inherently chiral C_{76} and its mono-adducts as well as of antipodes of covalent derivatives of achiral fullerenes (C_{60}, C_{70}) with chiral functionalization patterns can be calculated using the SCF-CI-DV MO method. The transition wavelengths and the signs of the Cotton effects in the experimental and calculated spectra are in good agreement, and absolute configurations can be assigned by comparison. This method should find wide future application in view of the increasing number of C_{60} and C_{70} derivatives with chiral functionalization patterns that are currently prepared. It should also be useful in the configurational assignment of other inherently chiral higher fullerenes such as D_3-C_{78} or D_2-C_{84}[14] and their derivatives. In analogy to the diagnostic intense band around 280 nm in the CD spectra of the enantiomers of D_2-C_{76} and its mono-adducts, other CD bands will be identified as stereochemical fingerprints for various families of fullerene derivatives which should facilitate future assignments of absolute configurations.[15]

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