Resolution and circular dichroism of an asymmetrically cage-opened [60]fullerene derivative

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The enantiomers of the first cagewise *inherently* asymmetric C_{60} derivative, *i.e.* *N*-MEM (MEM = 2-methoxyethoxymethyl) keto lactam 1, have been separated by HPLC and their chiroptical properties compared with data obtained from C_{60} derivatives that are dissymmetric or asymmetric due to chiral addends.

N-MEM keto lactam **1** (Fig. 1) is the first example of a well-defined open-cage derivative of C_{60}.[1] It is obtained from C_{60} in two synthetic steps, and (±)-**1** serves as the key intermediate in the synthesis of azafullerenes, *e.g.* $(C_{59}N)_2$,[2] $C_{59}NH$[3] and $K_6C_{59}N$.[4] Stereochemically, **1** is an interesting molecule, because it can be regarded as a (highly symmetrical) sphere with a chiral orifice. A larger version could be envisioned as a chiral selector, operating by enantioselective endohedral complexation.

Various chiral C_{60} derivatives have been prepared thus far.[5,6] Chirality can be introduced into C_{60} derivatives *via* chiral addends, either asymmetric[7,8] or C_2-symmetric,[9] as well as *via* an inherently asymmetric addition or substitution pattern, such as in 2 : 1 adducts with C_2-symmetry.[10,11] Higher fullerenes and carbon nanotubes can be inherently chiral.[12] C_2 C_{76}, D_3 C_{78} and D_2 C_{80} have been obtained in enantiomerically pure form *via* kinetic resolution by asymmetric osmylation, providing optically active forms of carbon.[13] Since keto lactam **1** is the first open-cage C_{60} derivative with an inherently asymmetric cage functionalization pattern, it is of interest to determine a possible resemblance of the chiroptical properties of **1** with those of the chirally modified C_{60} compounds. Here we present the successful resolution of (±)-**1** and the chiroptical properties of the individual enantiomers.

Chromatography of racemic **1**[1] as a 0.3 mg ml^{-1} solution in toluene–1,2-dichlorobenzene (2 : 1 v/v) on an analytical chiral stationary phase HPLC column [Bakerbond Pirkle Type DNBPG 5 μm (4.6 × 250 mm)], using *n*-hexane–$CHCl_3$–Pr^{i}OH (70 : 30 : 1 v/v/v) as the eluent (flow rate 1 ml min^{-1}) and UV detection at λ = 328 nm, gave enough separation to yield the enantiomers in 80 and 92% ee (as inferred from a second HPLC experiment, Fig. 2), respectively. The two fractions were assigned to (+)-**1** and (−)-**1**, respectively, by determining their specific rotations at 589 nm.

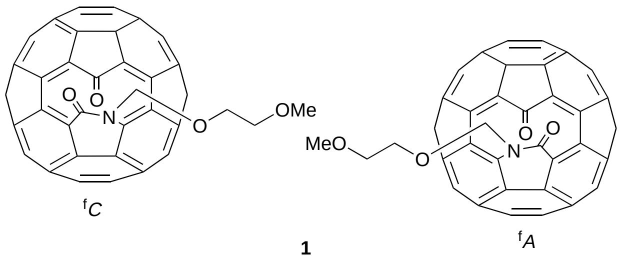

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Fig. 1 Molecular structure of the two enantiomeric forms of **1** with configurational description ^fC and ^fA according to ref. 6

The UV–VIS spectrum of (±)-**1**, the circular dichroism (CD) spectrum and the resulting *g* value ($g = \Delta\varepsilon/\varepsilon \approx \Delta A/A$) of (+)-**1** are shown in Fig. 3. The CD spectrum of (−)-**1** was found to have a mirror image relation to that of (+)-**1**. Similar to the UV–VIS absorption, the CD spectrum of (+)-**1** extends throughout the 200–700 nm spectral range. The strongest Cotton effect is found at λ = 325 nm ($\Delta\varepsilon$ = +29 M^{-1} cm^{-1}), coinciding with the lowest energy dipole-allowed transition of **1** (λ = 328 nm). Comparison with, for example, (+)-hexahelicene, which has a *g* value of +7.0 × 10^{-3} at λ = 325 nm for the π–π* transition, shows however that the *g* value of (+)-**1** (g_{325} = +6.4 × 10^{-4}) is an order of magnitude lower and represents a typical value for a noninherently dissymmetric chromophore.[14] Various chirally modified [6,6]-dihydrofullerene derivatives show a diagnostic CD band at about λ = 430 nm, whose sign has been taken as an indicator for the absolute configuration.[8,15–17] For (+)-**1**, a local extreme in the CD spectrum is found at λ = 426 nm, where the Cotton effect is negative. Tentatively applying the sector rule of Wilson *et al.* to **1** suggests that (+)-**1** corresponds to the ^fA configuration (Fig. 1).[15] The largest *g* values of (+)-**1** are found in the wavelength range λ = 600–700 nm, with a maximum of $g = -1.7 \times 10^{-2}$ at 659 nm, a typical value for a magnetically-allowed dipole-forbidden transition.

In summary, we have separated the two enantiomers of the C_{60} derivative (±)-**1** using chiral HPLC, providing a first example of an open-cage fullerene with a chiral orifice. The inherently chiral functionalization of the eleven-membered ring causes a dissymmetric perturbation on the π system of the fullerene, resulting in optical activity extending over the entire

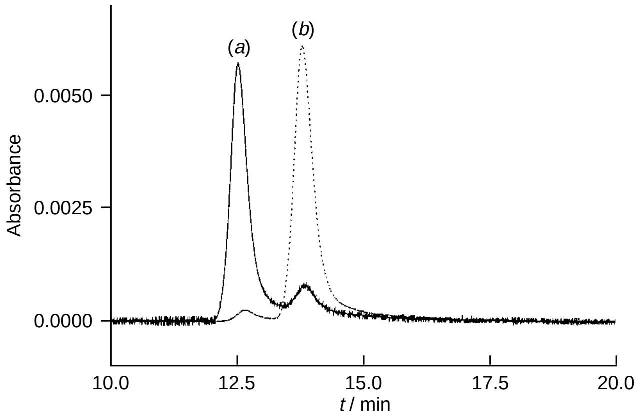

Fig. 2 Chiral HPLC chromatogram of separated samples of (*a*) (+)-**1** and (*b*) (−)-**1** (Bakerbond Pirkle Type DNBPG, eluent: *n*-hexane–$CHCl_3$–Pr^{i}OH (70 : 30 : 1 v/v/v), flow rate 1 ml min^{-1}, UV detection at λ = 328 nm)

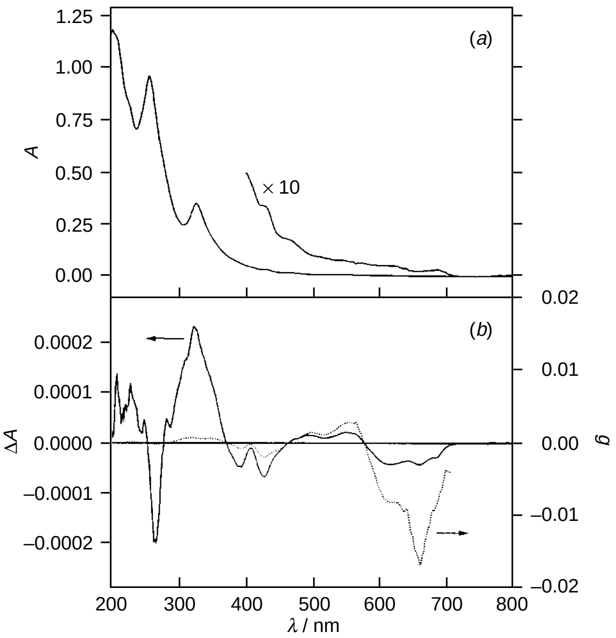

Fig. 3 (*a*) UV–VIS absorption spectrum of (±)-**1** (c = 7.6 × 10^{-6} M) [λ_{max}/nm = 204 (ε = 1.5 × 10^5 M^{-1} cm^{-1}, *n*-hexane), 260 (1.2 × 10^5, $CHCl_3$), 328 (4.5 × 10^4, $CHCl_3$), 428 (4.7 × 10^3, $CHCl_3$) and 688 (4.2 × 10^2, $CHCl_3$)]. (*b*) CD spectra (left axis) and *g* value (right axis) of (+)-**1** (c = 7.6 × 10^{-6} M). The UV–VIS and CD spectra were recorded using a solution in *n*-hexane for the region λ = 200–248 nm and in $CHCl_3$ for the region λ = 248–800 nm. The $CHCl_3$ spectra were recorded at higher concentrations and mathematically scaled to the spectrum in *n*-hexane for representation.

absorption spectrum, with high *g* values in the low-energy region.

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Footnote and References

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1 J. C. Hummelen, M. Prato and F. Wudl, *J. Am. Chem. Soc.*, 1995, **117**, 7003.
2 J. C. Hummelen, B. Knight, J. Pavlovich, R. González and F. Wudl, *Science*, 1995, **269**, 1554.
3 M. Keshavarz-K, R. González, R. G. Hicks, G. Srdanov, V. I. Srdanov, T. G. Collins, J. C. Hummelen, C. Bellavia-Lund, J. Pavlovich, F. Wudl and K. Holczer, *Nature*, 1996, **383**, 147.
4 K. Prassides, M. Keshavarz-K, J. C. Hummelen, W. Andreoni, P. Giannozzi, E. Beer, C. Bellavia, L. Cristofolini, R. González, A. Lappas, Y. Murata, M. Malecky, V. I. Srdanov and F. Wudl, *Science*, 1996, **271**, 1833.
5 F. Diederich, C. Thilgen and A. Herrmann, *Nachr. Chem. Tech. Lab.*, 1996, **44**, 9.
6 C. Thilgen, A. Herrmann and F. Diederich, *Helv. Chim. Acta*, 1997, **80**, 183.
7 A. Vasella, P. Uhlmann, C. A. A. Waldraff, F. Diederich and C. Thilgen, *Angew. Chem.*, 1992, **104**, 1388.
8 A. Bianco, M. Maggini, G. Scorrano, C. Toniolo, G. Marconi, C. Villani and M. Prato, *J. Am. Chem. Soc.*, 1996, **118**, 4072.
9 M. Maggini, G. Scorrano, A. Bianco, C. Toniolo and M. Prato, *Tetrahedron Lett.*, 1995, **36**, 2845.
10 J. M. Hawkins, A. Meyer and M. Nambu, *J. Am. Chem. Soc.*, 1993, **115**, 9844.
11 A. Hirsch, I. Lamparth and H. R. Karfunkel, *Angew. Chem.*, 1994, **106**, 453.
12 F. Diederich and R. L. Whetten, *Acc. Chem. Res.*, 1992, **25**, 119; S. Iijima, *Nature*, 1991, **354**, 56.
13 J. M. Hawkins and A. Meyer, *Science*, 1993, **260**, 1918; J. M. Hawkins, M. Nambu and A. Meyer, *J. Am. Chem. Soc.*, 1994, **116**, 7642.
14 M. S. Newman, R. S. Darlak and L. Tsai, *J. Am. Chem. Soc.*, 1967, **89**, 6191.
15 S. R. Wilson, Q. Lu, J. Cao, Y. Wu, C. J. Welch and D. I. Schuster, *Tetrahedron*, 1996, **52**, 5131.
16 M. Maggini, G. Scorrano, A. Bianco, C. Toniolo, R. P. Sijbesma, F. Wudl and M. Prato, *J. Chem. Soc., Chem. Commun.*, 1994, 305.
17 F. Novello, M. Prato, T. Da Ros, M. De Amici, A. Bianco, C. Toniolo and M. Maggini, *Chem. Commun.*, 1996, 903.

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