ChemComm

Regioselective one-step synthesis of *trans*-3,*trans*-3,*trans*-3 and *e,e,e* [60]fullerene tris-adducts directed by a C_3-symmetrical cyclotriveratrylene tether

Gwénaël Rapenne,[a] Jeanne Crassous,[b] André Collet,*[b] Luis Echegoyen*[c] and François Diederich*[a]

[a] *Laboratorium für Organische Chemie, ETH-Zentrum, Universitätstrasse 16, CH-8092 Zürich, Switzerland. E-mail: diederich@org.chem.ethz.ch*

[b] *Laboratoire de Stéréochimie et des Interactions Moléculaires, CNRS UMR 5532, Ecole Normale Supérieure de Lyon, 46 Allée d'Italie, 69364 Lyon Cedex 07, France*

[c] *Department of Chemistry, University of Miami, Coral Gables, FL 33124, USA*

Received (in Cambridge, UK) 22nd April 1999, Accepted 12th May 1999

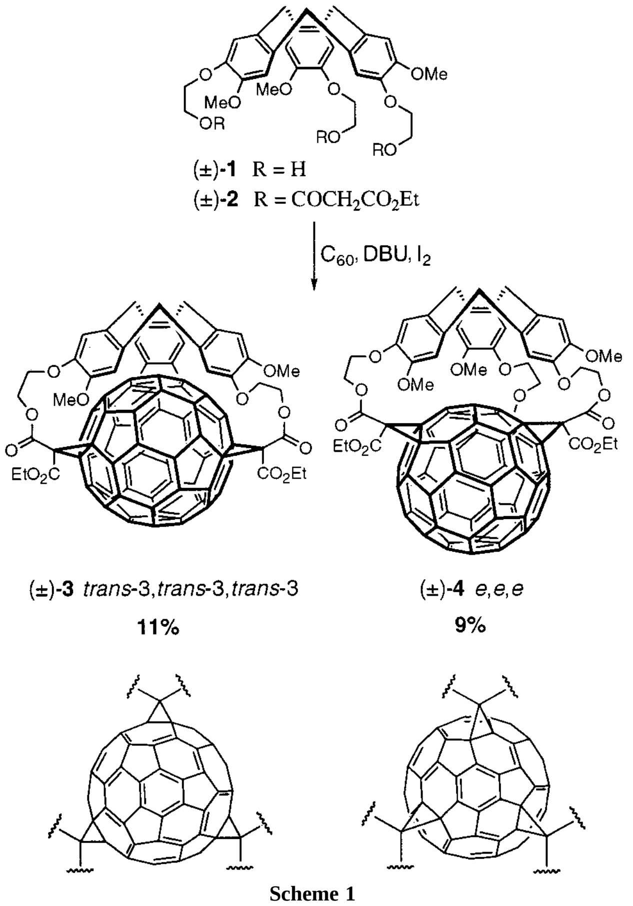
The first covalent cyclotriveratrylene (CTV)–C_{60} adducts were prepared by the tether-directed Bingel reaction, which gave the two C_3-symmetrical *trans*-3,*trans*-3,*trans*-3 and *e,e,e* tris-adducts with a high degree of regioselectivity.

The preparation of higher covalent adducts of buckminsterfullerene (C_{60}) with interesting electrochemical[1] or chiroptical properties[2] is currently under intense investigation. The tether-directed remote functionalisation method developed in the Diederich group for this purpose has proved to be very powerful because of its high regio- and stereoselectivity.[3] This methodology has been used successfully to prepare enantiomerically pure *cis*-3 bis-adducts with inherently chiral functionalisation patterns[2] or cyclophane-type crown ether[4a] and porphyrin[4b,5] conjugates with interesting redox properties, in which the second chromophore is doubly connected to the *trans*-1 positions at the two poles of the carbon sphere. Many functionalisation reactions of C_{60} leading to a variety of mono- and bis-adducts have been reported.[6] In contrast, only a few examples of tris-adducts have been described.[2a,7,8] In theory, bis-adducts of C_{60} derived from Bingel cyclopropanation reactions[9] can exist as eight different regioisomers, seven of which have been detected and isolated.[7a] The number of possible regioisomers increases to 46 in the case of tris-adducts in which three of the thirty 6-6 bonds (bonds between two six-membered rings) have been cyclopropanated.[6b] In 1994, Hirsch and co-workers reported the stepwise preparation of such tris-adducts and eventually obtained the *trans*-3,*trans*-3,*trans*-3 and *e,e,e* regioisomers together with other isomers, after tedious separation and purification.[7a]

Here we report the tether-directed regioselective synthesis of two new C_3-symmetrical tris-adducts having *trans*-3,*trans*-3,*trans*-3 and *e,e,e* structures, respectively, in one step from C_{60}. Cyclotriveratrylene (CTV) is well-suited in size and shape to interact favorably with C_{60}.[10] The affinity between these two molecules, which is reinforced by the electron donor character of CTV and the electron acceptor properties of C_{60}, has been evidenced by the formation of a crystalline complex in which C_{60} adopts a nesting position at van der Waals contact distance above the concave surface of the CTV macrocycle.[10a] These features prompted us to utilize a C_3-symmetric tris-malonate derivative of CTV, such as (±)-**2**, as a template for preparing tris-aducts of C_{60} by the tether-directed Bingel reaction (Scheme 1). The required (±)-**2** was obtained in one step by reacting the C_3-symmetrical CTV derivative (±)-**1**[11] with 3.3 equiv. of ethyl malonyl chloride (room temperature, CH_2Cl_2–pyridine). After column chromatography (SiO_2, $CH_2Cl_2 \rightarrow CH_2Cl_2$–1% MeOH), (±)-**2** was obtained in 77% yield as a colorless solid.

The Bingel reaction of (±)-*2* with C_{60} was carried out in the presence of 9 equiv. of DBU and 3 equiv. of I_2. After 4 h, two products (±)-**3** and (±)-**4** had formed which were separated by column chromatography (SiO_2 H, $CH_2Cl_2 \rightarrow CH_2Cl_2$–2% MeOH) and isolated in 11 and 9% yield, respectively. FAB-MS spectra† of (±)-**3** and (±)-**4** displayed the molecular ions expected for the tris-adducts shown in Scheme 1. This is the first example of tris-adduct formation by a one-step tether-directed Bingel addition.

The C_3-symmetry of the two adducts was established using NMR spectroscopy. The ^{1}H NMR spectra of (±)-**3** and (±)-**4** display the usual features for a C_3-CTV unit, *i.e.* two singlets for the aromatic H-atoms, one singlet for the OMe groups and the characteristic AB quartet for the CH_2 bridges. This means that the adducts must themselves possess a C_3 axis that is common to the CTV and the C_{60} subnits. The ^{13}C NMR spectra (Fig. 1), showing 20 resolved peaks for the fullerene C-atoms of (±)-**3** and 18 for those of (±)-**4**, support this conclusion. Since among all the possible regioisomers only the *trans*-3,*trans*-3,*trans*-3 and *e,e,e* trist-adducts exhibit such a symmetry (the *cis*-1,*cis*-1,*cis*-1 tris-adduct cannot form for steric reasons), the structures



Scheme 1

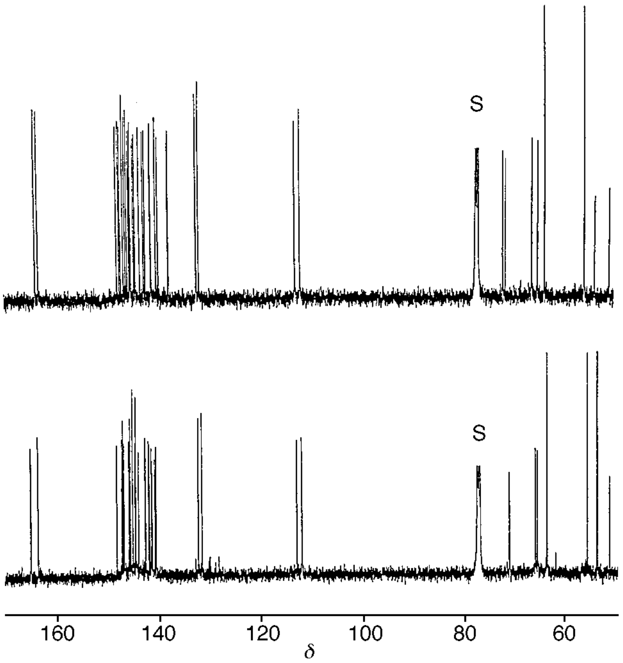


Fig. 1 ^{13}C NMR (125 MHz, $CDCl_3$) spectra of (*a*) tris-adduct (±)-**3** and (*b*) tris-adduct (±)-**4**; S stands for solvent.

of the two new tris-adducts were thus unambiguously established.

Since all attempts at transesterification to give the corresponding known tris(diethyl malonate) adducts[7a] failed, the structures of the two compounds were initially assigned with the help of UV-visible spectroscopy (CH_2Cl_2). Regioisomer (±)-**3** exhibits a cherry-red colour and (±)-**4** an orange–red colour, which are the same as those previously reported for the regioisomeric *trans*-3,*trans*-3,*trans*-3 and *e,e,e* tris(diethyl malonate) adducts, respectively.[7a] This difference is reflected in an additional absorption band at λ_{max} = 422 nm in the UV-visible spectrum of (±)-4.

The assignment of (±)-**3** and (±)-**4** as the *trans*-3,*trans*-3,*trans*-3 and *e,e,e* isomers, respectively, was further supported by a close comparison of their NMR spectra with those of analogous untethered tris-cyclopropanated C_{60} derivatives.[7a,b] The ^{13}C NMR chemical shifts of the bridgehead sp^3-C-atoms in the fullerene shell have been shown to appear at higher field in the *e,e,e* than in the *trans*-3,*trans*-3,*trans*-3 regiosomer, whereas the opposite behaviour has been observed for the methano bridge C-atom. The ^{13}C NMR resonances for the cyclopropane fragments were in fact observed at δ 71.63, 71.11 (bridgehead) and 50.61 (bridge) for (±)-**3** and at δ 70.73, 70.66 (bridgehead) and 51.07 (bridge) for (±)-**4**. The structural assignment was further corroborated by the position of the ^1H NMR resonance of the axial protons in the methylene bridges of the CTV fragment. For the tris-adduct (±)-**4** (δ 4.65), this signal is nearly unaffected with respect to that observed for the free CTV (±)-**2** (δ 4.74) whereas for (±)-**3**, it is significantly downfield shifted to δ 5.33. This indicates a much greater proximity of the CTV fragment to the fullerene core with its deshielding pentagon rings, which is expected for the *trans*-3,*trans*-3,*trans*-3 regioisomer, as shown in Scheme 1.

The total yield of tris-adducts is 20%, with a distribution of 55% of *trans*-3,*trans*-3,*trans*-3 and 45% of *e,e,e* regioisomer. Given the low statistical yield of 0.5% for (±)-**3** and 1% for (±)-**4** (among the 46 possible tris-adduct regioisomers), one can assume that the CTV template is largely responsible for this high degree of regioselectivity.

Since a splitting and doubling of the NMR signals is observed neither for (±)-**3** nor for (±)-**4**, one can expect the triply tethered reaction to be diastereoselective. We are currently investigating the use of optically pure C_3-CTV **2**[12] as starting material in order to confirm this diastereoselectivity, which opens new perspectives in the preparation of optically active derivatives of C_{60} and other fullerenes.

This work was supported by the Swiss National Science Foundation, the CNRS and the US National Science Foundation (CHE-9816503). G. R. is grateful for a Lavoisier postdoctoral fellowship of the French Ministry of Foreign Affairs.

Notes and references

† *Selected data* for (±)-**3**: cherry-red solid; λ_{max}(CH_2Cl_2)/nm (ε/dm^3 mol^{-1} cm^{-1}) 297 (33 100), 316 (25 500), 488 (2810), 570 (1250, sh); δ_H(500 MHz, $CDCl_3$) 6.61 (s, 3 H), 6.55 (s, 3 H), 5.33 [d, *J* 12.5, 3 H, CTV-CH_2(ax)], 4.63 (m, 6 H), 4.45 (m, 6 H), 4.13 (m, 3 H), 4.02 (m, 3 H), 3.63 (s, 9 H), 3.37 [d, *J* 12.5, 3 H, CTV-CH_2(eq)], 1.42 (t, *J* 7.1, 9 H); δ_C(125 MHz, $CDCl_3$) 164.13, 163.55, 148.36, 147.89, 147.59, 147.06, 146.69, 146.31, 145.97, 145.73, 145.68, 145.53, 144.97, 144.67, 143.74, 143.00, 142.66, 141.64, 141.49, 140.60, 140.14, 138.16, 132.67, 132.11, 113.17, 112.15, 71.63, 71.11, 65.80, 64.65, 63.32, 55.42, 53.41, 50.61, 14.10; *m/z* (HR-FAB$^+$-MS) 1596.2839 (M$^+$, calc. 1596.2841). For (±)-**4**: orange–red solid; λ_{max}(CH_2Cl_2)/nm (ε/dm^3 mol^{-1} cm^{-1}) 296 (43 600), 319 (30 000), 422 (2450), 486 (3270), 568 (1550); δ_H(500 MHz, $CDCl_3$) 6.56 (s, 3 H), 6.53 (s, 3 H), 4.93 (m, 3 H), 4.82 (m, 3 H), 4.65 [d, *J* 14.5, 3 H, CTV-CH_2(ax)], 4.47 (m, 6 H), 4.15 (m, 6 H), 3.58 (s, 9 H), 3.38 [d, *J* 14.5, 3 H, CTV-CH_2(eq)], 1.40 (t, 9 H); δ_C (125 MHz, $CDCl_3$) 164.96, 163.57, 148.32, 147.44, 147.34, 147.14, 146.95, 146.02, 145.73, 145.22, 144.78, 144.58, 144.10, 142.69, 142.06, 141.89, 141.55, 141.40, 140.87, 140.62, 132.32, 131.65, 112.93, 111.95, 70.73, 70.66, 65.53, 65.10, 63.30, 55.24, 53.40, 51.07,14.10 *m/z* (HR-FAB$^+$-MS) 1596.2835 (M$^+$, calc. 1596.2841).

1 L. Echegoyen and L. E. Echegoyen, *Acc. Chem. Res.*, 1998, **31**, 593.

2 (*a*) J.-F. Nierengarten, T. Habicher, R. Kessinger, F. Cardullo, F. Diederich, V. Gramlich, J. P. Gisselbrecht, C. Boudon and M. Gross, *Helv. Chim. Acta*, 1997, **80**, 2238; (*b*) M. Taki, Y. Nakamura, H. Uehara, M. Sato and J. Nishimura, *Enantiomer*, 1998, **3**, 231; (*c*) H. Isobe, H. Tokuyama, M. Sawamura and E. Nakamura, *J. Org. Chem.*, 1997, **62**, 5034.

3 F. Diederich and R. Kessinger, *Acc. Chem. Res.*, in the press.

4 (*a*) J.-P. Bourgeois, L. Echegoyen, M. Fibbioli, E. Pretsch and F. Diederich, *Angew. Chem., Int. Ed. Engl.*, 1998, **37**, 2118; (*b*) J.-P. Bourgeois, F. Diederich, L. Echegoyen and J.-F. Nierengarten, *Helv. Chim. Acta*, 1998, **81**, 1835.

5 E. Dietel, A. Hirsch, E. Eichhorn, A. Rieker, S. Hackbarth and B. Röder, *Chem. Commun.*, 1998, 1981.

6 (*a*) A. Hirsch, *Top. Curr. Chem.*, 1999, **199**, 1; (*b*) A. Hirsch, *The Chemistry of the Fullerenes*, Thieme, Stuttgart, 1994.

7 See for example: (*a*) A. Hirsch, I. Lamparth and H. R. Karfunkel, *Angew. Chem., Int. Ed. Engl.*, 1994, **33**, 437; (*b*) F. Djojo and A. Hirsch, *Chem. Eur. J.*, 1998, **4**, 344; (*c*) T. Hamano, K. Okuda, T. Mashino, M. Hirobe, K. Arakane, A. Ryu, S. Mashiko and T. Nagano, *Chem. Commun.*, 1997, 21.

8 For tether-directed preparations of tris-adducts, see: L. Isaacs, F. Diederich and R. F. Haldimann, *Helv. Chim. Acta*, 1997, **80**, 317; F. Cardullo, P. Seiler, L. Isaacs, J.-F. Nierengarten, R. F. Haldimann, F. Diederich, T. Mordasini-Denti, W. Thiel, C. Boudon, J.-P. Gisselbrecht and M. Gross, *Helv. Chim. Acta*, 1997, **80**, 343.

9 C. Bingel, *Chem. Ber.*, 1993, **126**, 1957.

10 (*a*) J. W. Steed, P. C. Junk, J. L. Atwood, M. J. Barnes, C. L. Raston and R. S. Burkhalter, *J. Am. Chem. Soc.*, 1994, **116**, 10 346; (*b*) J. L. Atwood, M. J. Barnes, M. G. Gardiner and C. L. Raston, *Chem. Commun.*, 1996, 1449; (*c*) H. Matsubara, A. Hasegawa, K. shiwaku, K. Asano, M. Uno, S. Takahashi and K. Yamamoto, *Chem. Lett.*, 1998, 923; (*d*) H. Matsubara, T. Shimura, A. Hasegawa, M. Semba, K. Asano and K. Yamamoto, *Chem. Lett.*, 1998, 1099.

11 J. Canceill, J. Gabard and A. Collet, *J. Chem. Soc., Chem. Commun.*, 1983, 122; J. Canceill, J. Gabard and A. Collet, *J. Am. Chem. Soc.*, 1984, **106**, 5997; G. Vériot, J. P. Dutasta, G. Matouzenko and A. Collet, *Tetrahedron*, 1995, **51**, 389.

12 A. Collet, in *Comprehensive Supramolecular Chemistry*, ed. F. Toda, Pergamon, 1996, vol. 6, ch. 9, pp. 281–303.

Communication 9/03226F