Tetrahedron Letters 54 (2013) 6251–6257

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

The di-*t*-butylsilylene protecting group as a bridging unit in linear and macrocyclic bis-malonates for the regioselective multifunctionalization of C_{60}

Sebastiano Guerra, Thi Minh Nguyet Trinh, Franck Schillinger, Lucie Muhlberger, David Sigwalt, Michel Holler, Jean-François Nierengarten *

Laboratoire de Chimie des Matériaux Moléculaires, Université de Strasbourg et CNRS (UMR 7509), Ecole Européenne de Chimie, Polymères et Matériaux (ECPM), 25 rue Becquerel, 67087 Strasbourg Cedex 2, France

ARTICLE INFO

Article history:
Received 29 July 2013
Revised 3 September 2013
Accepted 9 September 2013
Available online 16 September 2013

Keywords:
*t*Butylsilylene
Fullerene
Malonate
Macrocycle
Regioselectivity

ABSTRACT

Fullerene *equatorial* bis-adducts have been prepared with high regioselectivity by a double Bingel reaction between [60]fullerene and di-*t*-butylsilylene-tethered bis-malonates. Macrocyclic bis-malonates incorporating di-*t*-butylsilylene moieties have also been prepared and used to functionalize C_{60} in multiple Bingel cyclopropanations. Fullerene bis-adducts with a *cis-2* addition pattern and tris-adducts with an *e,e,e* addition pattern have been thus obtained. Finally, the bridging di-*t*-butylsilylene is not only a directing group for the cyclization step, it is also a protecting group that can be readily cleaved to afford the corresponding acyclic fullerene polyols.

Fullerene chemistry has generated unprecedented stereochemical problems[1] and the regioselective polyfunctionalization of C_{60} through multiple addition reactions remains a major challenge. Actually, mono-functionalized C_{60} derivatives possess nine different 6–6 bonds (bonds at the junction between two six-membered rings, see Fig. 1) and mixtures of regioisomers are obtained by successive reactions at the C_{60} core.[2,3] The synthesis of fullerene tris-adducts is even more challenging as 46 isomers differing by the relative position of the three addends on the carbon sphere are theoretically possible. The first efficient methodologies allowing the regioselective preparation of C_{60} multi-adducts have been reported by Diederich and co-workers and are based on cyclization reactions on the fullerene scaffold.[4] These seminal contributions have inspired most of the research efforts devoted toward the preparation of fullerene multi-adducts with a well-defined stereochemistry.[5–8] As part of this research, we have recently developed an expeditious synthesis of fullerene tris-adducts based on a threefold Bingel reaction between C_{60} and *t*-butyl(trialkoxy)silane derivatives bearing three malonate substituents.[8] The silane unit is at the same time a directing group allowing the control of the stereochemistry of the tris-addition on the C_{60} sphere during the cyclization step and a protecting group that can be readily cleaved to generate the corresponding acyclic fullerene derivatives. Based on this finding, we became interested in using the di-*t*-butylsilylene protecting group as a bridging unit in linear and macrocyclic bis-malonates for the regioselective bis-functionalization of C_{60}. Upon cyclization, a desilylation reaction provides the corresponding acyclic polyol derivatives. The possibility to easily open the bridging unit upon cyclization is a clear advantage to generate new fullerene building blocks with a controlled distribution of functional groups on their surfaces.

As shown in Scheme 1, the preparation of bis-malonates **2a**–**b** was first achieved from **1a**–**b**[8b] to validate the possibility of using di-*t*-butylsilylene bridged bis-malonates for the regioselective bis-functionalization of C_{60}. Treatment of compounds **1a**–**b** (2 equiv) with di-*t*-butylsilyl bis(trifluoromethanesulfonate) ($tBu_2Si(OTf)_2$, 1 equiv) in DMF in the presence of pyridine (pyr) gave the corresponding bis-malonates **2a**–**b**. Fullerene derivatives **3a**–**b** were then prepared by taking advantage of the versatile regioselective reaction developed in the group of Diederich,[5a] which led to macrocyclic bis-adducts of C_{60} by a cyclization reaction at the C sphere with bis-malonate derivatives in a double Bingel[9] cyclopropanation. Reaction of **2a** with C_{60}, I_2, and 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) in toluene afforded the corresponding cyclization product **3a** in 23% yield. Similarly, compound **3b** was obtained in 48% yield from bis-malonate **2b** and C_{60} under the same conditions.

* Corresponding author. Tel.: +33 368 852 763; fax: +33 368 852 774.
E-mail address: nierengarten@unistra.fr (J.-F. Nierengarten).

0040-4039/$ - see front matter © 2013 Elsevier Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.tetlet.2013.09.024

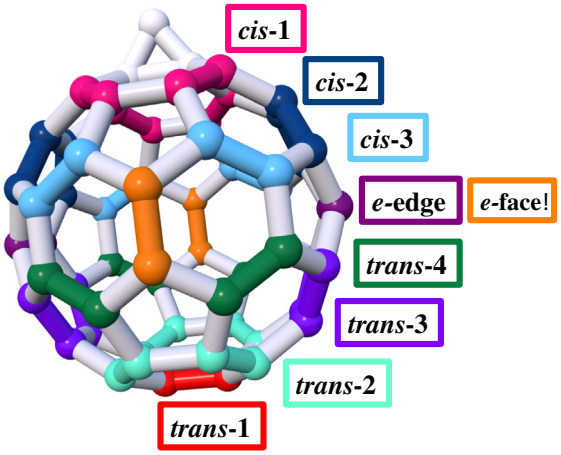
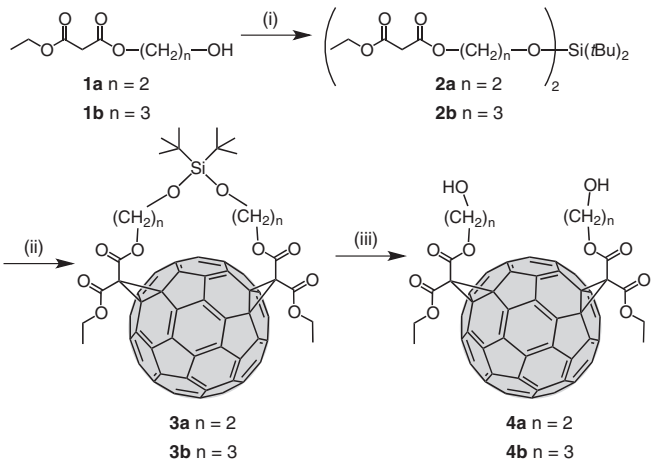


Figure 1. Addition of a second addend to a C_{2v}-symmetrical C_{60} mono-adduct can in principle lead to nine different regioisomeric bis-adducts. Relative to the first addend, the second one can be located either in the same hemisphere (*cis*), in the opposite hemisphere (*trans*) or on the equatorial belt (*e*). For identical addends, a second attack onto the *e*-edge or *e*-face positions leads to identical products.

Fullerene bis-adducts **3a**–**b** were characterized by ^{1}H and ^{13}C NMR, UV–vis, and IR spectroscopies.[10] In addition, their structure was confirmed by MALDI-TOF mass spectrometry showing the expected pseudo-molecular ion peaks at *m*/*z* 1210.2 for **3a** ($[M+H]^+$, calcd for $C_{82}H_{37}O_{10}Si$: 1210.3) and 1237.3 for **3b** ($[M+H]^+$, calcd for $C_{84}H_{41}O_{10}Si$: 1237.3). For both **3a** and **3b**, the molecular symmetry (C_1) deduced from the ^{1}H and ^{13}C NMR spectra suggests an *equatorial* addition pattern. This is also consistent with molecular modeling studies (see ESI). For fullerene derivatives bearing two malonate addends, the relative position of the two cyclopropane rings on the C_{60} core suggested by the molecular symmetry is conveniently confirmed by UV/vis spectroscopy. Effectively, the absorption spectra of C_{60} bis-adducts are highly dependent on the addition pattern and characteristic for each of the regioisomers.[5] The absorption spectra of bis-adducts **3a** and **3b** are similar thus showing that the relative position of the two cyclopropane rings on the fullerene core is identical for both compounds. As shown in Figure 2, the absorption spectrum recorded in CH_2Cl_2 for compound **3b** is broad in the visible region with two shoulders (398 and 410 nm) and a quite sharp band at ca. 420 nm. Indeed, the UV/vis spectrum of **3b** clearly reveals the diagnostic features



Scheme 1. Reagents and conditions: (i) $tBu_2Si(OTf)_2$, DMF, pyr, rt, 12 h (**2a**: 43%; **2b**: 52%); (ii) C_{60}, DBU, I_2, PhMe, −15 °C, 1 h (**3a**: 23%, **3b**: 48%); (iii) $BF_3{\cdot}Et_2O$, CH_2Cl_2, CH_3CN, rt 12 h (**4a**: 91%; **4b**: 74%).

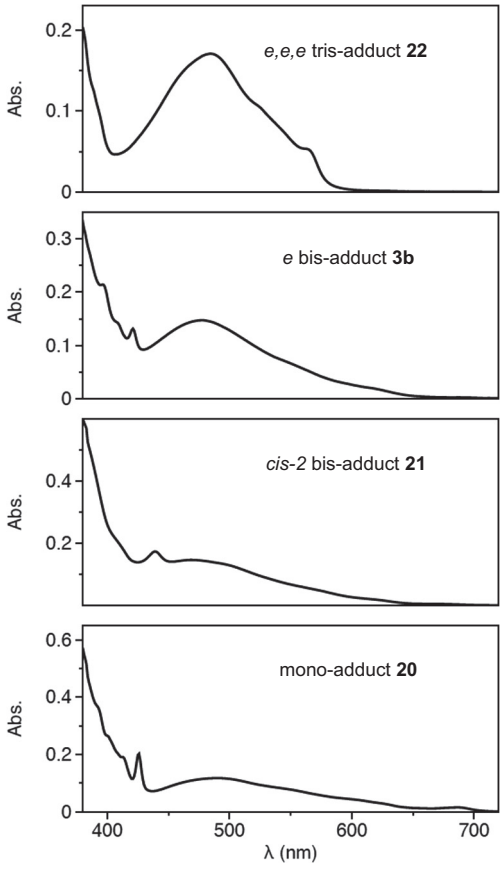
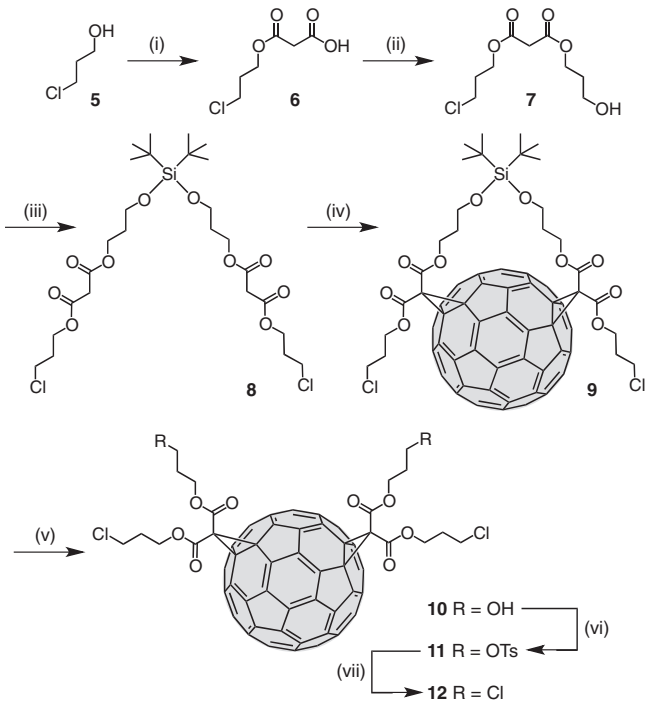


Figure 2. Absorption spectra (CH_2Cl_2) of fullerene derivatives **3b**, **20**, **21**, and **22** showing significant differences as a function of the number of addends. In the case of bis-adducts **3b** and **21**, characteristic features of *e* (**3b**) and *cis-2* (**21**) bis-addition patterns are clearly observed.

previously reported for analogous *equatorial* C_{60} bis-adducts.[5] Therefore, in addition to the C_1 symmetry deduced from their ^{1}H and ^{13}C NMR spectra, the absorption spectra of **3a** and **3b** allowed us to definitively elucidate their stereochemistry. It is worth noting that the *equatorial* addition pattern is C_s symmetric but owing to the macrocyclic structure of compounds **3a**–**b**, the symmetry is reduced.

Finally, different reaction conditions for the cleavage of the connecting di-*t*-butylsilylene protecting group in **3a**–**b** were tested (Scheme 1). Reaction of **3a**–**b** with HF-pyridine in THF gave diols **4a**–**b** in good yields (80–90%). Desilylation conditions using an excess of $BF_3{\cdot}Et_2O$ (20 equiv) in CH_2Cl_2/CH_3CN were also found to be effective for the preparation of **4a**–**b** from **3a**–**b**.[11] From a practical point of view, the use of $BF_3{\cdot}Et_2O$ is by far more convenient as these conditions do not require HF-resistant equipment. Furthermore, traces of pyridine were particularly difficult to remove in samples of **4a**–**b** prepared by treatment of **3a**–**b** with HF.pyridine.

Following the successful preparation of *equatorial* C_{60} bis-adducts from silylene-tethered bis-malonates, a similar synthetic strategy was used for the preparation of an *equatorial* fullerene bis-adducts substituted with two symmetrically substituted malonate addends (Scheme 2). Compound **6** was obtained in an almost quantitative yield by heating 3-chloro-1-propanol (**5**) at 120 °C in the presence of 2,2-dimethyl-1,3-dioxane-4,6-dione (Meldrum's acid). Treatment of **6** (1 equiv) with an excess of 1,3-propanediol (4 equiv) under esterification conditions using *N*-(3-dimethylaminopropyl)-*N*′-ethylcarbodiimide hydrochloride (EDC) and 4-dimethylaminopyridinium tosylate (DPTS) afforded **7** in 50% yield. Subsequent treatment with $tBu_2Si(OTf)_2$/pyr in DMF provided bis-malonate **8** in 51% yield. The C_1-symmetrical macrocyclic



Scheme 2. Reagents and conditions: (i) Meldrum's acid, 120 °C, 3 h (99%); (ii) 1,3-propanediol, EDC, DPTS, CH_2Cl_2, 0 °C to rt, 12 h (50%); (iii) tBu$_2$Si(OTf)$_2$, DMF, pyr, rt, 4 h (51%); (iv) C_{60}, DBU, I_2, PhMe, −15 °C, 1 h (40%); (v) BF_3.Et$_2$O, CH_2Cl_2, CH_3CN, rt 12 h (95%); (vi) TsCl, pyr, CH_2Cl_2, 0 °C to rt, 48 h (77%); (vii) nBu$_4$NCl, THF, rt, 4 h (95%).

fullerene *e*-bis-adduct **9** was then obtained in 40% yield by reaction of **8** with C_{60} in the presence of DBU and I_2. Desilylation with BF_3·Et$_2$O followed by reaction of the resulting **10** with *p*-toluenesulfonyl chloride (TsCl) in the presence of pyridine gave **11**. Finally, treatment of bis-tosylate **11** with an excess of tetra-*n*-butylammonium chloride (nBu$_4$NCl) in THF yielded **12** in 95% yield.

The *equatorial* addition pattern of fullerene bis-adducts **9**–**12** was confirmed by both their absorption spectra and their symmetry deduced from their ^{1}H and ^{13}C NMR spectra. Whereas derivatives **9**, **10**, and **11** bearing unsymmetrically substituted malonate addends are all C_1-symmetrical compounds, bis-adduct **12** with its two C(CO$_2$(CH$_2$)$_3$Cl)$_2$ subunits is C_s symmetric as deduced from a careful analysis of its ^{13}C NMR spectrum (Fig. 3). Out of the 32 expected fullerene resonances, three are observed at δ = 70.1, 71.3, and 71.4 ppm (sp^3 C atoms) and 28 between δ = 138.7 and 147.4 ppm (sp^2 C atoms). It is also worth noting that two of the resonances seen in the sp^2 region show half intensity as well as two of the three resonances observed for the fullerene sp^3 C atoms. Actually, the latter observations are unambiguous proofs for the C_s symmetry of compound **12**. Effectively, for such a fullerene derivative, there are 28 pairs of equivalent C atoms and four unique ones. Furthermore, out of the three possible C_s-symmetrical addition patterns (*cis-2*, *e* and *trans-4*), the only one for which 3 resonances are expected for the sp^3 fullerene C atoms is the *equatorial* bis-adduct. This is further confirmed by the observation of three resonances for the carbonyl C atoms (δ = 163.4, 163.35 and 163.25 ppm). Therefore, the preparation of compound **12** provided definitive and non-ambiguous conclusions about the stereochemistry of fullerene derivatives **9**, **10**, and **11**. With their *e* fullerene addition pattern, these compounds are ideally suited for the preparation of fullerene hexa-adducts with an octahedral addition pattern.[12] This new methodology will be therefore very useful to produce new fullerene scaffolds bearing different malonate addends in a 4:2 ratio.

The concept of using cleavable di-*t*-butylsilylene-tethered bis-malonates for the regioselective functionalization of C_{60} was then extended to cyclo-oligomalonates (Scheme 3). The selective mono-protection of 1,3-propanediol (**13**) was carried out by treatment with Ag_2O and *p*-methoxybenzyl chloride (PMBCl) according to the conditions reported by Bouzide and Sauvé.[13] Treatment of the resulting mono-protected derivative **14** with tBu$_2$Si(OTf)$_2$ and imidazole in DMF provided **15** in 68% yield. The PMB protecting groups in **15** were conveniently removed by treatment with

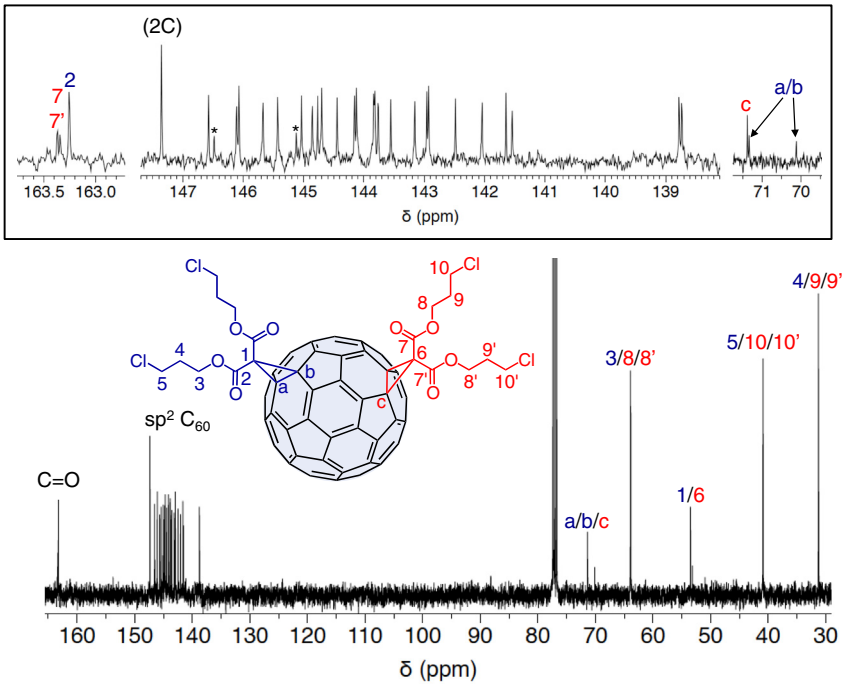
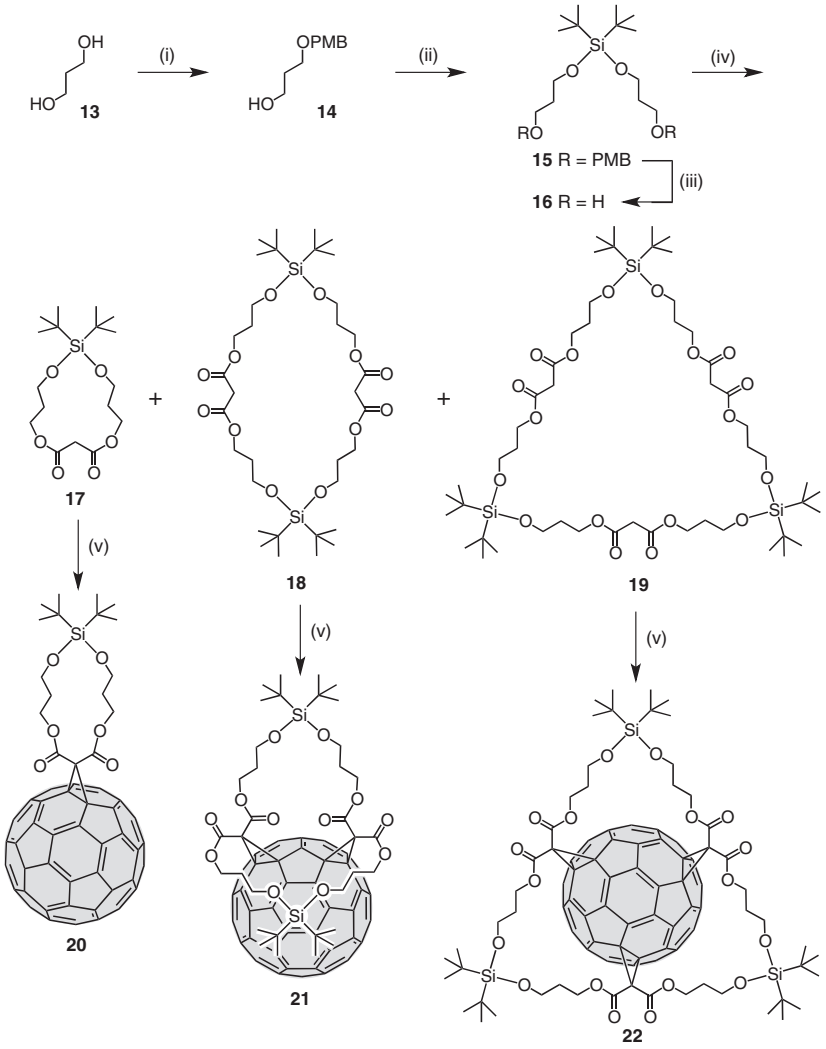


Figure 3. ^{13}C NMR spectrum (CDCl$_3$, 100 MHz) of compound **12**. Inset: detailed views showing the resonances of the carbonyl groups (left), the fullerene sp^2 C atoms (center) and the fullerene sp^3 C atoms (right); * indicates the two sp^2 fullerene C atoms showing half intensity signals.

2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) in CH_2Cl_2 containing a small amount of water. The di-*t*-butylsilylene remained unchanged and key building block **16** was thus obtained in good yields (86%). Reaction of diol **16** with malonyl chloride in the presence of 4-dimethylaminopyridine (DMAP) under pseudo high dilution conditions afforded a mixture of cyclooligomers and polymers. Macrocycles **17**, **18**, and **19** were isolated in a pure form in 24%, 15%, and 3% yield, respectively, by repeated chromatographic separations.[14] While the ^1H and ^{13}C NMR spectra of **17**, **18**, and **19** were in full agreement with their cyclooligomeric structures, it was not possible to conclude about their ring-size based on the NMR data. In the case of **18** and **19**, the proposed structures were confirmed by MALDI-TOF mass spectrometry. For the smallest member, high level of fragmentation prevented the detection of the molecular ion peak. However, based on the elution order of the compounds and on their relative yields, compound **17** is likely the cyclomonomeric derivative. To gain further evidence about the proposed structure for **17**, a Bingel reaction was performed to generate the C_{2v} symmetrical fullerene mono-adduct **20**. The structure of **20** was confirmed by MALDI-TOF mass spectrometry as well as by ^1H and ^{13}C NMR, IR, and UV/vis (Fig. 2) spectroscopies thus showing that compound **17** was effectively the cyclomonomalonate.

Reaction of the 28-membered ring macrocyclic bis-malonate **18** with C_{60} in the presence of iodine and DBU gave the *cis-2* C_{60} bis-adduct **21** with an excellent regioselectivity.[15] Indeed, the only isolable by-product was a bis-fullerene derivative resulting from the reaction of **18** with two molecules of C_{60} but no regioisomeric bis-adducts of **21** could be isolated from the reaction mixture. The ^{13}C NMR spectrum of compound **21** is shown in Figure 4. As discussed in the case of **12**, the presence of half intensity signals for some of the resonances of the fullerene C atoms seen in the sp^2 region is an unambiguous signature for a C_s symmetrical structure. In addition, the presence of only two resonances for the fullerene sp^3 C atoms suggests that this bis-adduct **21** could be either a *cis-2* or a *trans-4* regioisomer. The UV–vis spectrum of **21** is indeed fully consistent with a *cis-2* C_{60} bis-adduct (Fig. 2). The stereochemistry of compound **21** was thus elucidated. To further support this structural assignment, computational studies were also performed. The molecular geometry of the various regioisomers (*cis-2*, *cis-3*, *e*, *trans-3* and *trans-4*) was optimized with *Spartan'10* Macintosh Parallel Edition (Wavefunction Inc., USA) at the AM1 semi-empirical level. The *cis-2* isomer was effectively found to be noticeably lower in energy when compared to all the other regioisomers (ΔE >75 kJ/mol).

The reaction of the cyclo-tris-malonate **19** with C_{60} was also carried out. The reaction was highly regioselective and only the fullerene tris-adduct with an *e*,*e*,*e*-addition pattern was thus obtained. Compound **22** was isolated with a remarkable 61% yield. The relative



Scheme 3. Reagents and conditions: (i) PMBCl, Ag_2O, CH_2Cl_2, 48 h (80%); (ii) tBu$_2$Si(OTf)$_2$, DMF, imidazole, rt, 12 h (68%); (iii) DDQ, CH_2Cl_2, H_2O, rt, 6 h (86%); (iv) malonyl chloride, DMAP, CH_2Cl_2, rt, 48 h (**17**: 24%; **18**: 15%; **19**: 3%); (v) C_{60}, DBU, I_2, PhMe, rt, 1 h (**20**: 46%; **21**: 27%; **22**: 61%).

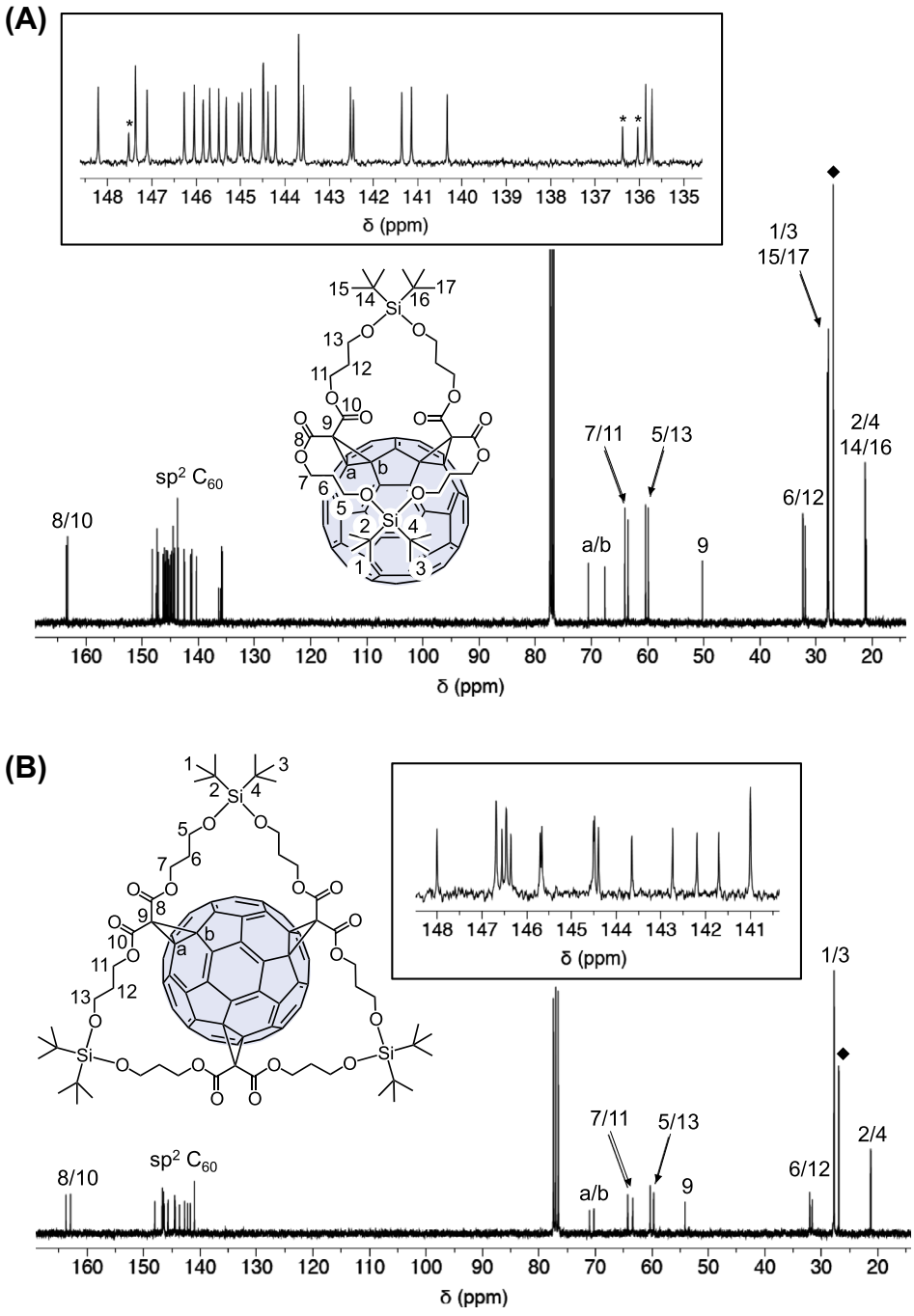
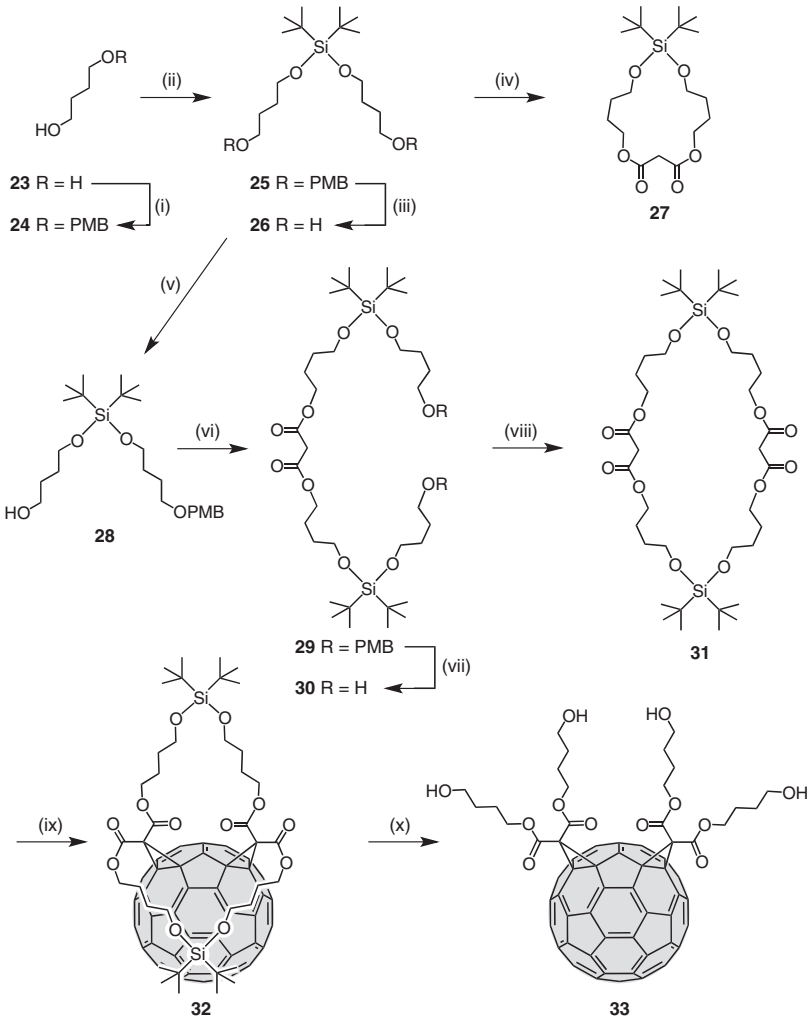


Figure 4. (A) ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of compound **21** (♦: cyclohexane); inset: detailed view showing the resonances of the fullerene sp^2 C atoms; * indicates the sp^2 fullerene C atoms showing half intensity signals. (B) ^{13}C NMR spectrum ($CDCl_3$, 100 MHz) of compound **22** showing its threefold symmetry (♦: cyclohexane); inset: detailed view showing the resonances of the fullerene sp^2 C atoms.

position of the three cyclopropane rings on the C_{60} core were determined based on the symmetry (C_3) deduced from the ^1H and ^{13}C NMR spectra.[16] As shown in Figure 4, the number of resonances observed in the ^{13}C NMR spectrum of **22** is fully consistent with a threefold symmetrical compound. The cherry-red color and the UV/vis spectrum of **22** (Fig. 2) are also in complete agreement with the proposed *e*,*e*,*e*-addition pattern for compound **22**.[8]

As shown in Scheme 4, the preparation of macrocylic oligo-malonates was also carried out from 1,4-butanediol (**23**) by following the synthetic route developed for the preparation of compounds **17**–**19**. Mono-protection of **23** by treatment with Ag_2O/PMBCl followed by silylation ($tBu_2Si(OTf)_2$/imidazole) and deprotection (DDQ) afforded diol **26**. Reaction of **26** with malonyl chloride in the presence of DMAP gave the cyclomonomalonate **27** as the main product. Its structure was confirmed by MALDI-TOF mass spectrometry. Higher cyclooligomers were also obtained but in very low yields. This result prompted us to develop a stepwise synthetic route that will prevent the formation of cyclomonomalonates (Scheme 4). Treatment of **25** with 1 equiv of DDQ provided the mono-protected derivative **28** in 47% yield. Subsequent reaction with malonyl chloride in the presence of DMAP gave malonate **29**. The choice of the appropriate protecting groups for the two terminal alcohol functions of **29** was the key to this synthesis. The deprotection conditions must not be acidic to preserve the bridging di-*t*-butylsilylene groups and may not be basic to preserve the ester functions.[17] The PMB protecting groups being removed under



Scheme 4. Reagents and conditions: (i) PMBCl, Ag_2O, CH_2Cl_2, 48 h (95%); (ii) tBu$_2$Si(OTf)$_2$, DMF, imidazole, rt, 12 h (60%); (iii) DDQ, CH_2Cl_2, H_2O, rt, 6 h (91%); (iv) malonyl chloride, DMAP, CH_2Cl_2, rt, 48 h (51%); (v) DDQ (1 equiv), CH_2Cl_2, H_2O, rt, 6 h (from **25**: 47%); (vi) malonyl chloride, DMAP, CH_2Cl_2, rt, 12 h (67%); (vii) DDQ, CH_2Cl_2, rt, 2 h (68%); (viii) malonyl chloride, DMAP, CH_2Cl_2, rt, 48 h (51%); (ix) C_{60}, DBU, I_2, PhMe, rt, 1 h (39%); (x) $BF_3{\cdot}Et_2O$, CH_2Cl_2, CH_3CN, rt, 12 h (88%).

neutral conditions by treatment with DDQ, both the ester functions and the di-*t*-butylsilylene groups remained effectively intact and diol **30** was obtained in a good yield (68%). Reaction of **30** with malonyl chloride under pseudo high dilution conditions gave cyclobismalonate **31** in 51% yield. Macrocycle **31**, which has a ring size of 32 atoms, was characterized by NMR spectroscopy and mass spectrometry.

Reaction of C_{60} with macrocyclic bis-malonate **31**, I_2, and DBU afforded **32** in 39% yield. As discussed for **21**, the relative position of the two cyclopropane rings on the fullerene core was determined based on the C_s molecular symmetry deduced from the NMR spectra[15] and on the diagnostic features of a *cis-2* bis-addition pattern seen in the absorption spectrum of **32**. Finally, treatment of compound **32** with an excess of $BF_3.Et_2O$ gave the C_s-symmetrical fullerene *cis-2* bis-adduct **33** in 88% yield. With its four alcohol functions, compound **33** is a valuable building block for further chemical modifications.

In conclusion, the reaction of linear and macrocyclic di-*t*-butylsilylene-tethered bis-malonate with C_{60} gave access to fullerene bis-adducts with an excellent regioselectivity. The bridging di-*t*-butylsilylene is not only a directing group during the cyclization step, it is also a protecting group that can be readily cleaved to afford the corresponding acyclic fullerene polyols. By systematically changing the length and the rigidity of the spacer units linking the malonate subunits to the di-*t*-butylsilylene moieties, fullerene bis-adducts with different addition patterns should become easily accessible thus opening new perspectives in the chemistry of multifunctionalized fullerene derivatives.

Acknowledgments

This research was supported by the CNRS, the University of Strasbourg, and the *Agence Nationale de la Recherche* (ANR, *Programme Blanc 2011*, Sweet60s). S.G. gratefully thanks the Swiss National Science Foundation and TMNT the University of Strasbourg (IdEx 2013) for their post-doctoral fellowships. We further thank M. Schmitt for the high field NMR measurements.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.tetlet.2013.09.024.

References and notes

1. (a) Diederich, F.; Kessinger, R. *Acc. Chem. Res.* **1999**, *32*, 537–545; (b) Thilgen, C.; Diederich, F. *Chem. Rev.* **2006**, *106*, 5049–5135; (c) Thilgen, C.; Diederich, F. C. R.

Chimie **2006**, *9*, 868–880; (d) Chronakis, N.; Hirsch, A. C. R. *Chimie* **2006**, *9*, 862–867.
2. Hirsch, A.; Lamparth, I.; Karfunkel, H. R. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 437–438.
3. For representative examples, see: (a) Nakamura, Y.; Takano, N.; Nishimura, T.; Yashima, E.; Sato, M.; Kudo, T.; Nishimura, J. *Org. Lett.* **2001**, *3*, 1193–1196; (b) Kordatos, K.; Bosi, S.; Da Ros, T.; Zambon, A.; Lucchini, V.; Prato, M. *J. Org. Chem.* **2001**, *66*, 2802–2808.
4. (a) Isaacs, L.; Haldiman, R. F.; Diederich, F. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2339–2342; (b) Boudon, C.; Gisselbrecht, J.-P.; Gross, M.; Isaacs, L.; Anderson, H. L.; Faust, R.; Diederich, F. *Helv. Chim. Acta* **1995**, *78*, 1334–1344; (c) Isaacs, L.; Seiler, P.; Diederich, F. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 1466–1469.
5. For examples of regioselective preparations of fullerene bis-adducts based on cyclization reactions, see: (a) Nierengarten, J.-F.; Gramlich, V.; Cardullo, F.; Diederich, F. *Angew. Chem., Int. Ed.* **1996**, *35*, 2101–2103; (b) Nierengarten, J.-F.; Habicher, T.; Kessinger, R.; Cardullo, F.; Diederich, F.; Gramlich, V.; Gisselbrecht, J.-P.; Boudon, C.; Gross, M. *Helv. Chim. Acta* **1997**, *80*, 2238–2276; (c) Ashton, P. R.; Diederich, F.; Gómez-López, M.; Nierengarten, J.-F.; Preece, J. A.; Raymo, F. M.; Stoddart, J. F. *Angew. Chem., Int. Ed.* **1997**, *36*, 1448–1451; (d) Isobe, H.; Tokuyama, H.; Sawamura, M.; Nakamura, E. *J. Org. Chem.* **1997**, *62*, 5034–5041; (e) Nierengarten, J.-F.; Schall, C.; Nicoud, J.-F.; Heinrich, B.; Guillon, D. *Tetrahedron Lett.* **1998**, *39*, 5747–5750; (f) Nierengarten, J.-F.; Felder, D.; Nicoud, J.-F. *Tetrahedron Lett.* **1998**, *39*, 2747–2750; (g) Dietel, E.; Hirsch, A.; Eichhorn, E.; Rieker, A.; Hackbarth, S.; Röder, B. *Chem. Commun.* **1998**, 1981–1982; (h) Schick, G.; Jarrosson, T.; Rubin, Y. *Angew. Chem., Int. Ed.* **1999**, *38*, 2360–2363; (i) Quian, W.; Rubin, Y. *Angew. Chem., Int. Ed.* **1999**, *38*, 2356–2360; (j) Nakamura, Y.; Asami, A.; Inokuma, S.; Ogawa, T.; Kikuyama, M.; Nishimura, J. *Tetrahedron Lett.* **2000**, *41*, 2193–2197; (k) Da Ros, T.; Prato, M.; Lucchini, V. *J. Org. Chem.* **2000**, *65*, 4289–4297; (l) Zhang, S.; Rio, Y.; Cardinali, F.; Bourgogne, C.; Gallani, J.-L.; Nierengarten, J.-F. *J. Org. Chem.* **2003**, *68*, 9787–9797; (m) Chaker, L.; Ball, G. E.; Williams, J. R.; Burley, G. A.; Hawkins, B. C.; Keller, P. A.; Pyne, S. G. *Eur. J. Org. Chem.* **2005**, 5158–5162; (n) Sergeyev, S.; Shär, M.; Seiler, P.; Lukoyanova, O.; Echegoyen, L.; Diederich, F. *Chem. Eur. J.* **2005**, *11*, 2284–2294; (o) Figueira-Duarte, T. M.; Gégout, A.; Olivier, J.; Cardinali, F.; Nierengarten, J.-F. *Eur. J. Org. Chem.* **2009**, 3879–3884.
6. For examples of regioselective synthesis of bis- and tris-adducts from macrocyclic oligomalonates, see: (a) Reuther, U.; Brandmüller, T.; Donaubauer, W.; Hampel, F.; Hirsch, A. *Chem. Eur. J.* **2002**, *8*, 2261–2273; (b) Chronakis, N.; Hirsch, A. *Chem. Commun.* **2005**, 3709–3711; (c) Riala, M.; Chronakis, N. *Org. Lett.* **2011**, *13*, 2844–2847; (d) Sigwalt, D.; Holler, M.; Nierengarten, J.-F. *Tetrahedron Lett.* **2013**, *54*, 3160–3163.
7. For examples of regioselective synthesis of fullerene tris-adducts, see: (a) Rapenne, G.; Crassous, J.; Collet, A.; Echegoyen, L.; Diederich, F. *Chem. Commun.* **1999**, 1121–1122; (b) Beuerle, F.; Chronakis, N.; Hirsch, A. *Chem. Commun.* **2005**, 3676–3678; (c) Beuerle, F.; Hirsch, A. *Chem. Eur. J.* **2009**, *15*, 7434–7446; (d) Gmehling, A.; Donaubauer, W.; Hampel, F.; Heinemann, F. W.; Hirsch, A. *Angew. Chem., Int. Ed.* **2013**, *52*, 3521–3524.
8. (a) Guerra, S.; Schillinger, F.; Sigwalt, D.; Holler, M.; Nierengarten, J.-F. *Chem. Commun.* **2013**, *49*, 4752–4954; (b) Sigwalt, D.; Schillinger, F.; Guerra, S.; Holler, M.; Berville, M.; Nierengarten, J.-F. *Tetrahedron Lett.* **2013**, *54*, 4241–4244.
9. Bingel, C. *Chem. Ber.* **1993**, *126*, 1957–1959.
10. DBU (5 equiv) was added to a solution of C_{60} (1 equiv), appropriate bis-malonate (**2a** or **2b**; 1 equiv) and I_2 (2.5 equiv) in toluene (2 mL/mg of C_{60}) at −15 °C. After 1 h at −15 °C, the resulting mixture was directly filtered on a plug of SiO_2 (first eluted with toluene to eliminate the unreacted C_{60} then with CH_2Cl_2) and concentrated. Column chromatography (SiO_2, CH_2Cl_2/cyclohexane 3:2) gave the corresponding fullerene bis-adduct (**3a** or **3b**). Compound **3a** (59 mg, 23%): dark brown solid; IR (neat): 1744 (C=O); UV/vis (CH_2Cl_2): 310 (sh, 34800), 368 (sh, 9900), 398 (sh, 3900), 410 (sh, 2500), 421 (2400), 479 (2700); ^{1}H NMR (300 MHz, $CDCl_3$): 4.77 (m, 1H), 4.58–3.99 (m, 10H), 3.89 (m, 1H), 1.44 (t, *J* = 7 Hz, 6H), 1.09 (s, 9H) 0.94 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): 164.0, 163.6, 163.5, 163.1, 148.7, 147.4, 146.6, 146.5, 146.4, 146.3, 146.2, 145.8, 145.6, 145.5, 145.4, 145.3, 145.1, 145.0, 144.9, 144.8, 144.7, 144.6, 144.4, 144.2, 144.1, 143.9, 143.8, 143.7, 143.6, 143.5, 143.2, 143.1, 142.2, 142.1, 142.0, 141.8, 141.6, 141.5, 140.6, 140.4, 140.0, 139.8, 139.0, 138.6, 71.1, 70.4, 68.1, 66.7, 63.6, 63.5, 62.4, 60.8, 53.8, 51.2, 28.1, 27.7, 21.8, 21.4, 14.3; MALDI-TOF-MS: 1210.2 (100%, $[M+H]^+$, calcd for $C_{82}H_{37}O_{10}Si$: 1210.3), 1164.7 (21%, $[M-OEt]^+$, calcd for $C_{80}H_{32}O_9Si$: 1165.2). Compound **3b** (332 mg, 48%): dark brown solid; IR (neat): 1751 (C=O); UV/vis (CH_2Cl_2): 310 (sh, 38670), 361 (sh, 13450), 398 (sh, 3850), 409 (sh, 2410), 421 (2260), 479 (sh, 2740); ^{1}H NMR (300 MHz, CD_2Cl_2): 4.81–4.71 (m, 2H), 4.57–4.36 (m, 6H), 3.98–3.84 (m, 4H), 2.06–1.96 (m, 4H), 1.44 (t, *J* = 7 Hz, 6H), 1.06 (s, 9H), 0.94 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$): 164.1, 163.6, 163.3 (2C), 148.8, 147.3, 147.0, 146.5, 146.4, 146.2, 146.1, 145.8, 145.5, 145.4, 145.3, 145.2, 145.1, 145.0, 144.9, 144.8, 144.7, 144.6, 144.5, 144.3, 144.1, 143.9, 143.7, 143.6, 143.5, 143.2, 143.1, 142.5, 142.0, 141.9, 141.8, 141.7, 141.5, 141.2, 140.5, 139.7, 138.8, 138.6, 71.7, 70.5, 64.2, 63.5, 63.4, 63.3, 60.4, 59.8, 54.0, 51.6, 32.2, 31.7, 27.8, 27.0, 21.3, 14.3; MALDI-TOF-MS: 1237.3 ($[M+H]^+$, calcd for $C_{84}H_{41}O_{10}Si$: 1237.3).
11. $BF_3{\cdot}Et_2O$ (20 equiv) was added to a solution of the appropriate fullerene derivative (**3a–b**; 1 equiv) in CH_2Cl_2/CH_3CN (2:1) at room temperature. The resulting mixture was stirred overnight at room temperature. A saturated $NaHCO_3$ aqueous solution was added and the aqueous layer extracted with CH_2Cl_2. The organic layer was washed with water, dried ($MgSO_4$) and concentrated. Column chromatography (SiO_2, CH_2Cl_2/MeOH 96:4) gave **4a–b**. Compound **4a** (36 mg, 91%): brown solid; IR (neat): 3443 (br, OH), 1737 (C=O); UV/vis (CH_2Cl_2): 251 (20040), 309 (sh, 7600), 399 (1300), 410 (sh, 830), 422 (790), 479 (980); ^{1}H NMR (400 MHz, $CDCl_3$): 4.60–4.49 (m, 8H), 3.97 (m, 4H), 2.26 (br s, 1H), 2.09 (br s, 1H), 1.47 (t, *J* = 7 Hz, 6H). MALDI-TOF-MS: 1091.5 (8%, $[M+Na]^+$, calcd for $C_{74}H_{20}O_{10}Na$: 1091.1), 1068.5 (100%, $[M]^+$, calcd for $C_{74}H_{20}O_{10}$: 1068.1). Compound **4b** (61 mg, 74%): brown solid; IR (neat): 3450 (br, OH), 1740 (C=O). UV/vis (CH_2Cl_2): 306 (sh, 21900), 331 (sh, 7400), 397 (sh, 2350), 409 (sh, 1550), 421 (1450), 478 (sh, 1600). ^{1}H NMR (400 MHz, $CDCl_3$): 4.61–4.48 (m, 8H), 3.80 (m, 4H), 2.04 (m, 4H), 1.94 (br s, 2H), 1.46 (t, *J* = 7 Hz, 3H), 1.45 (t, *J* = 7 Hz, 3H); MALDI-TOF-MS: 1096.1 ($[M]^+$, calcd for $C_{76}H_{24}O_{10}$: 1096.1).
12. (a) Iehl, J.; Pereira de Freitas, R.; Delavaux-Nico, B.; Nierengarten, J.-F. *Chem. Commun.* **2008**, 2450–2452; (b) Iehl, J.; Nierengarten, J.-F. *Chem. Eur. J.* **2009**, *15*, 7306–7309; (c) Iehl, J.; Nierengarten, J.-F. *Chem. Commun.* **2010**, *46*, 4160–4162; (d) Nierengarten, J.-F.; Iehl, J.; Oerthel, V.; Holler, M.; Illescas, B. M.; Muñoz, A.; Martín, N.; Rojo, J.; Sánchez-Navarro, M.; Cecioni, S.; Vidal, S.; Buffet, K.; Durka, M.; Vincent, S. P. *Chem. Commun.* **2010**, *46*, 3860–3862; (e) Sigwalt, D.; Holler, M.; Iehl, J.; Nierengarten, J.-F.; Nothisen, M.; Morin, E.; Remy, J.-S. *Chem. Commun.* **2011**, *47*, 4640–4642; (f) Fortgang, P.; Maisonhaute, E.; Amatore, C.; Delavaux-Nicot, B.; Iehl, J.; Nierengarten, J.-F. *Angew. Chem., Int. Ed.* **2011**, *50*, 2364–2367; (g) Iehl, J.; Nierengarten, J.-F.; Harriman, A.; Bura, T.; Ziessel, R. *J. Am. Chem. Soc.* **2012**, *134*, 988–998; (h) Iehl, J.; Frasconi, M.; Jacquot de Rouville, H.-P.; Renaud, N.; Dyar, S. M.; Strutt, N. L.; Carmieli, R.; Wasielewski, M. R.; Ratner, M. A.; Nierengarten, J.-F.; Stoddart, J. F. *Chem. Sci.* **2013**, *4*, 1462–1469.
13. Bouzide, A.; Sauvé, G. *Tetrahedron Lett.* **1997**, *38*, 5945–5948.
14. A solution of DMAP (1.42 g, 11.60 mmol) in anhydrous CH_2Cl_2 (100 mL) was added dropwise within 3 h to a stirred solution of **16** (1.56 g, 5.30 mmol) and malonyl chloride (0.57 mL, 5.83 mmol) in anhydrous CH_2Cl_2 (480 mL). After 18 h, the mixture was filtered on a plug of SiO_2 (CH_2Cl_2) and evaporated. Column chromatography (SiO_2, CH_2Cl_2/cyclohexane 80:20 to CH_2Cl_2) gave **17** (450 mg, 24%), **18** (290 mg, 15%) and **19** (60 mg, 3%). Compound **17**: colorless oil; IR (neat): 1735 (C=O); ^{1}H NMR (400 MHz, $CDCl_3$): 4.29 (t, *J* = 6 Hz, 4H), 3.86 (t, *J* = 6 Hz, 4H), 3.37 (s, 2H), 1.91 (m, 4H), 1.01 (s, 18H); ^{13}C NMR (100 MHz, $CDCl_3$): 166.2, 61.6, 59.3, 42.5, 31.7, 27.8, 20.8. Compound **18**: colorless oil; IR (neat): 1736 (C=O); ^{1}H NMR (400 MHz, $CDCl_3$): 4.29 (t, *J* = 6 Hz, 8H), 3.90 (t, *J* = 6 Hz, 8H), 3.37 (s, 4H), 1.89 (m, 8H), 1.00 (s, 36H); ^{13}C NMR (100 MHz, $CDCl_3$): 166.6, 62.4, 60.0, 41.6, 31.7, 27.8, 21.1; MALDI-TOF-MS: 720.9 ($[M]^+$, calcd for $C_{34}H_{64}O_{12}Si_2$: 720.4). Compound **19**: colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$): 4.22 (m, 12H), 3.84 (t, *J* = 6 Hz, 12H), 3.30 (s, 6H), 1.83 (m, 12H), 0.93 (s, 54H); ^{13}C NMR (100 MHz, $CDCl_3$): 166.6, 62.5, 60.1, 41.5, 31.7, 27.8, 21.1; MALDI-TOF-MS: 1103.5 (100%, $[M+Na]^+$, calcd for $C_{51}H_{96}O_{18}Si_3Na$: 1103.6), 1081.5 (47%, $[M+H]^+$, calcd for $C_{51}H_{97}O_{18}Si_3$: 1081.6).
15. DBU (5 equiv) was added to a solution of C_{60} (1 equiv), appropriate bis-malonate (**18** or **31**, 1 equiv), and I_2 (2.5 equiv) in toluene (2 mL/mg of C_{60}). After 1 h at room temperature, the resulting mixture was directly filtered on a plug of SiO_2 (toluene then CH_2Cl_2) and concentrated. Column chromatography (SiO_2, CH_2Cl_2/cyclohexane 50:50 to CH_2Cl_2) gave the corresponding fullerene bis-adduct (**21** or **32**). Compound **21** (115 mg, 27%): brown glassy solid; IR (neat): 1748 (C=O); UV/vis (CH_2Cl_2): 259 (84200), 323 (sh, 24700), 439 (2500), 476 (2100), 622 (sh, 250); ^{1}H NMR (400 MHz, $CDCl_3$): 4.71–4.62 (m, 4H), 4.50–4.41 (m, 4H), 4.03 (m, 4H), 3.88 (m, 4H), 2.10 (m, 4H), 1.98 (m, 4H), 1.11 (s, 9H), 1.04 (s, 18H), 0.87 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): see Figure 4. MALDI-TOF-MS: 1438.4 ($[M+H]^+$, calcd for $C_{94}H_{61}O_{12}Si_2$: 1438.4). Compound **32** (212 mg, 39%): brown glassy solid; IR (neat): 1743 (C=O); UV/vis (CH_2Cl_2): 259 (88000), 323 (sh, 26200), 439 (2700), 476 (1300), 622 (sh, 280); ^{1}H NMR (400 MHz, $CDCl_3$): 4.57 (m, 2H), 4.50 (m, 2H), 4.39 (m, 2H), 4.26 (m, 2H), 1.99 (m, 4H), 1.84 (m, 4H), 1.75 (m, 4H), 1.63 (m, 4H), 1.07 (s, 9H), 1.04 (s, 9H), 1.03 (s, 9H), 0.95 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): 146.3, 146.1, 145.8, 145.7, 145.5, 145.3, 145.0 (2C), 144.7, 144.6, 144.4 (2C), 144.2, 143.6 (2C), 143.5 (2C), 142.4, 141.3, 141.1, 140.1, 137.2, 136.4, 136.1, 135.7, 70.6, 67.7, 66.7, 63.2, 62.8, 50.3, 28.8, 28.5, 27.9, 27.8, 26.9, 25.5, 25.0, 21.4. MALDI-TOF-MS: 1493.3 ($[M+H]^+$, calcd for $C_{98}H_{69}O_{12}Si_2$: 1493.4).
16. DBU (0.15 mL, 1.00 mmol) was added to a solution of C_{60} (108 mg, 0.15 mmol), **19** (58 mg, 0.15 mmol), and I_2 (131 mg, 0.52 mmol) in toluene (400 mL). After 1 h at room temperature, the resulting mixture was filtered on a plug of SiO_2 (toluene then CH_2Cl_2) and concentrated. Column chromatography (SiO_2, CH_2Cl_2/cyclohexane 50:50 to CH_2Cl_2) gave **22** (55 mg, 61%) as a cherry-red glassy solid; IR (neat): 1751 (C=O); UV/vis (CH_2Cl_2): 252 (169115), 281 (107581), 304 (sh, 86077), 482 (6208), 564 (sh, 1819); ^{1}H NMR (400 MHz, $CDCl_3$): 4.70 (m, 3H), 4.60 (m, 3H), 4.36 (m, 6H), 3.95–3.77 (m, 12H), 1.94 (m, 12H), 0.98 (s, 36H), 0.90 (s, 36H); ^{13}C NMR (100 MHz, $CDCl_3$): see Figure 4; MALDI-TOF-MS: 1797.0 ($[M+H]^+$, calcd for $C_{111}H_{91}O_{18}Si_3$: 1796.5).
17. (a) Nierengarten, J.-F.; Felder, D.; Nicoud, J.-F. *Tetrahedron Lett.* **2000**, *41*, 41–44; (b) Felder, D.; Nierengarten, H.; Gisselbrecht, J.-P.; Boudon, C.; Leize, E.; Nicoud, J.-F.; Gross, M.; Van Dorsselaer, A.; Nierengarten, J.-F. *J. New Chem.* **2000**, *24*, 687–695.