Tetrahedron 64 (2008) 10319–10330

Contents lists available at ScienceDirect

Tetrahedron

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

Functionalization of C60 via organometallic reagents

Elise Champeil [a,b], Conor Crean [a], Carlos Larraya [a], Gennaro Pescitelli [c], Gloria Proni [b], Léon Ghosez [a,*]

[a] Institut Européen de Chimie et Biologie-IECB, Univ. Bordeaux 1-CNRS UMR 5248, 2, rue Robert Escarpit, F-33607 Pessac, France
[b] Department of Science, John Jay College of Criminal Justice, 445 west 59th street, New York, NY 10019, United States
[c] Dipartimento di Chimica e Chimica Industriale, Universita di Pisa, Pisa, Italy

ARTICLE INFO

Article history:
Received 7 April 2008
Received in revised form 22 July 2008
Accepted 7 August 2008
Available online 9 August 2008

Keywords:
C60
Nucleophilic addition
Alkylation
Amino acid
Peptide

ABSTRACT

The reaction of [60]fullerene with organolithium and Grignard reagents carrying orthoester, acetal or other end groups yielded adducts **3**–**5** at the 6–6 bond of C60 after quenching with trifluoroacetic acid. The adducts could be easily methylated or benzylated with methyl iodide or benzyl bromide in the presence of potassium *tert*-butoxide to yield exclusively the 1,4-disubstituted C60 **6** and **7a**,**b**. Cleavage of the orthoester, acetal and silylether groups gave the corresponding carboxylic acid **9**, aldehydes **10a**,**b** and **11** and alcohols **12** and **13a**,**b**. The carboxylic acid **9** readily reacted with alanine ethyl ester under standard peptide coupling conditions to give **14** in 55% yield. Attempts to generate a silyl enol ether from the reaction of aldehyde **10b** with TIPSOTf and triethylamine failed. Instead the reaction led to a cyclized ether **16a** (or alcohol **16b** in the absence of silylating agent) resulting from the addition of an initially formed fulleride anion to the aldehyde group. The corresponding acetal **4b** reacted similarly. The reaction of aldehyde **10b** with aniline also gave a cyclized product **19**. Surprisingly, aldehyde **11**, which no longer carried an acidic fullerene proton reacted with aniline to give a product **20** resulting from an intramolecular Diels–Alder reaction followed by aromatization of a primarily formed *N*-phenylimine. Alcohol **13b** could be readily converted to the corresponding bromide using tetramethyl-α-bromoenamine. The bromide was reacted with the carbanion derived from the protected glycine derivative to yield the diastereomeric fullerene amino acid derivatives 1-benzyl-4-[α-propyl-*tert*-butylglycinate benzophenone imine] 1,4-dihydro[60]fullerenes **24a** and **24b**.

1. Introduction

As a result of its unique properties, the all-carbon molecule C60 is a potential source of new materials or chemotherapeutic agents.[1] This has been a stimulus for the study of chemical modifications, which would not significantly modify the properties of the C60 backbone while allowing the introduction of substituents required for a specific application.[2] Some of the most commonly studied reactions of C60 include cycloadditions,[3] cyclopropanations,[4] addition of organometallic reagents,[5] and photo-induced electron transfer reactions.[6] Initial studies on the addition of alkyl lithium and Grignard reagents to C60 have setup the best conditions for the formation of a monoadduct. Thus Hirsch et al. have shown that 12 equiv of the Grignard reagent derived from 2-(2-bromoethyl)-1,3-dioxolane was required to give an optimum yield of 52% of the 1,2-monoadduct 1-[2-(1,3-dioxanyl)ethyl]-2-hydrofullerene[60].[5b] Monoadducts have also been obtained from the reaction of lithium acetylides to C60.[5d] These dihydrofullerene adducts contain an acidic proton allowing the generation of a carbanion centre on the C60 backbone, which can be further reacted with electrophiles.[5f]

In the context of a search of new fullerene-containing chemotherapeutic agents, we needed a series of *C*60-derived building blocks characterized by the presence of functional groups linked to the C60 backbone by a *flexible* tether of variable length. We selected organometallic reagents carrying orthoester, acetal and silylether functional groups as precursors for carboxylic acids, aldehydes and alcohols, respectively. In this paper, we describe our results on the representative additions of functionalized organometallics to C60 as well as some transformations of the resulting adducts.

2. Addition of functionalized organometallics to C60

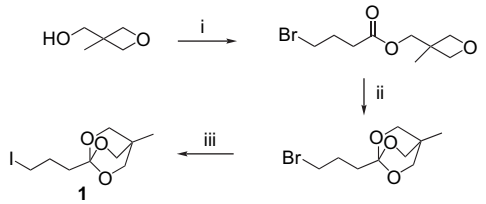
2.1. Synthesis of an organodihydrofullerene orthoester

The reaction of [60]fullerene with organolithium and Grignard reagents[5] had never been exploited to incorporate a protected carboxylic acid functionality onto the C60 sphere. An orthoester was chosen as an equivalent for a carboxylic acid with no acidic α-proton. Since we expected some unstability of the classical methyl or ethyl orthoesters under the conditions of formation of

* Corresponding author. Tel.: +33 5 4000 2217/2223; fax: +33 5 4000 2215.
E-mail address: l.ghosez@iecb.u-bordeaux.fr (L. Ghosez).

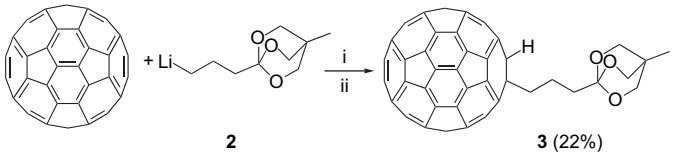
0040-4020/$ – see front matter © 2008 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2008.08.017

the organometallic reagents, we decided to use the more stable bicyclic orthoester prepared by following the general procedure described by Corey (Scheme 1).[7a,b]



Scheme 1. Reagents and conditions: (i) $BrCH_2CH_2CH_2COCl$, pyridine/THF, 0 °C, 1 h; (ii) $BF_3{\cdot}Et_2O$, CH_2Cl_2, 0 °C, 3 h; (iii) NaI, DMF, 100 °C, 2 h.

Compound **1** was transformed into the corresponding organolithium reagent by reaction with *n*-BuLi in THF. Treatment of a toluene solution of [60]fullerene with 1.6 equiv of 1-(2-propyllithium)-4-methyl-2,6,7-trioxabicyclo[2,2,2]-octane **1** gave a black precipitate, which, upon quenching with trifluoroacetic acid, gave 1-hydro-2-[3′-(4″-methyl-2″,6″,7″-trioxabicyclo[2″,2″,2″]-octyl)-propyl]-1,2-dihydro[60]fullerene **3** as a black solid in 20–30% yield (Scheme 2).

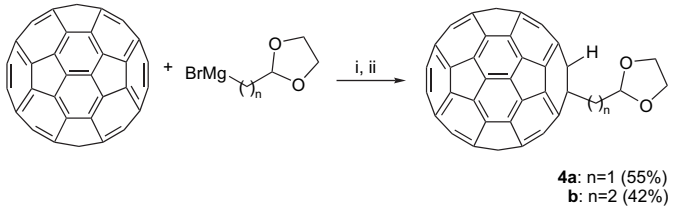


Scheme 2. Reagents and conditions: (i) addition of **2** (prepared from the reaction of *n*-butyl lithium with **1** in 50:50 pentane/diethylether) to C_{60} in toluene at −78 °C, then rt; (ii) excess CF_3COOH.

2.2. Synthesis of organodihydrofullerene acetals

Two commercially available 2-(bromoalkyl)-1,3-dioxolanes were used as precursors of the Grignard reagents for the addition reactions to C60 following the general procedure described by Hirsch et al.[5b] Thus, a molar solution of C60 in toluene was treated with 12 equiv of the Grignard reagents derived from 2-(2-bromoethyl)-1,3-dioxolane and 2-(3-bromopropyl)-1,3-dioxolane. A colour change (purple to dark green/black) immediately occurred suggesting the formation of a fulleride anion. Protonation with trifluoroacetic acid yielded the fullerene acetals **4a** (55%) and **4b** (42%) (Scheme 3).

The UV–vis and NMR spectra of adducts **4a** and **4b** were in agreement with C60 derivatives bearing two organic groups attached at the 1,2-position of the 6,6-junction bond. A singlet at 6.49 ppm was observed in the ^1H NMR spectrum, which is characteristic of a proton attached to the C60 core in a fullerene monoadduct. The ^{13}C NMR showed 27 of the 30 expected sp^2 carbon resonances for a product with a 1,2-addition pattern, with the

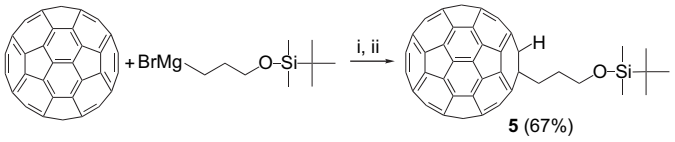


Scheme 3. Reagents and conditions: (i) addition of the Grignard reagent (prepared from the corresponding bromide in THF) to C60 in toluene, rt; (ii) excess CF_3COOH.

associated sp^3 fullerene core carbons at 65.4 and 65.6 ppm. The UV–vis spectra showed an absorption band at 432 nm confirming 1,2-additions of the Grignard reagents. Further characterization was provided by mass spectral data showing molecular ions (M+H) at 824.1 for **4a** and 838.1 for **4b**.

2.3. Synthesis of an organodihydrofullerene *tert*-butyldimethylsilylether

The Grignard reagent[9] obtained from 1-bromo-3-(*tert*-butyldimethylsilyloxy)propane was added to a toluene solution of C60 immediately generating a dark green solution indicative of the formation a the fulleride anion.[10] Quenching with excess trifluoroacetic acid and work-up gave 1-hydro-2-[3′-(*tert*-butyldimethylsiloxy)propyl]-1,2-dihydro[60]fullerene **5** in 67% yield based on consumed C60 (Scheme 4). The separation of adduct **5** from C60 could be effected by flash chromatography using a 10:1 mixture of cyclohexane/toluene. The ^1H NMR spectrum of **5** revealed a singlet at 6.51 ppm characteristic of the proton attached to the fullerene core of a monoadduct. The other NMR signals unambiguously showed the attachment of a *tert*-butyl dimethylsiloxypropyl group. The ^{13}C NMR spectrum showed signals for two sp^3 carbons of the fullerene core at 63 and 64 ppm together with 28 signals in the region 135–156 ppm. The number of signals suggested that the product also resulted from a 1,2-addition. The mass spectrum showed the correct molecular ion (M+H) at 896.1.



Scheme 4. Reagents and conditions: (i) Grignard reagent in THF added to C60 in toluene, rt; (ii) excess CF_3COOH.

3. Alkylation of the 1,2-organodihydrofullerenes

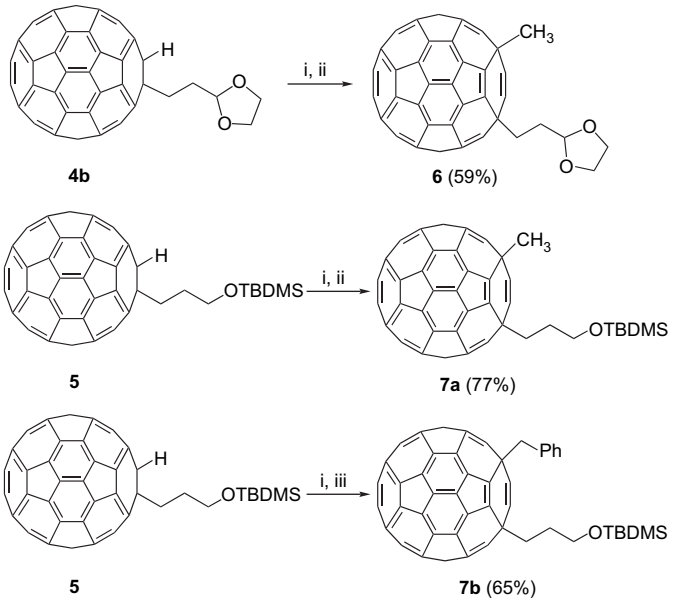
The proton attached to the fullerene core in 1,2-adducts is acidic and its pK_a has been estimated at 5.7 for 1-hydro-2-*tert*-butyl 1,2-dihydro[60]fullerene in dimethylsulfoxide.[5a] This acidity limits the chemistry that could be carried out on such fullerene derivatives and thus we chose to synthesize derivatives where the proton was replaced by a methyl or benzyl group. This substitution should give fullerene derivatives with increased solubility in organic solvents, which would then ease purification by chromatography and also help the investigation of further reactions of the substituted fullerenes.

The addition of organolithium or organomagnesium reagents to C60 followed by protonation of the resulting carbanions has been shown to give 1,2-adducts.[5e] This is an energetically favourable situation (>8 kcal/mol more stable) because the corresponding 1,4-adduct contains a double bond in one of the pentagons. However, the replacement of hydrogen by bulkier substituents could reverse this thermodynamic preference as shown previously in a number of cases.[11]

C60 adducts **4b** and **5** were deprotonated by treatment with 1 equiv of potassium *tert*-butoxide in THF to form green solutions indicative of the formation of the fulleride anion (Scheme 5).

Compounds **6** and **7a** were formed after reaction of the corresponding fulleride anion with 100 equiv of methyl iodide at room temperature for 24 h. Compound **7b** was formed upon treatment with 6 equiv of benzyl bromide for 2 h in refluxing THF.

The 1,4-relationship between the two [60]fullerene substituents was demonstrated by the replacement of the absorption at 436 nm



Scheme 5. Reagents and conditions: (i) potassium *tert*-butoxide, THF, 15 min, rt; (ii) CH_3I, 24 h, rt; (iii) benzyl bromide, 2 h, reflux.

with a broad shoulder at 450 nm.[12] ^{13}C NMR spectra confirmed this assignment: products **6**, **7a** and **7b**, which have no symmetry elements showed the expected 60 signals. The spectra also show the presence of the expected sp^3 hybridized carbon atoms in the C60 core (signals appeared at δ=58.4 and 65.2 for **6**, at δ=59.5 and 63.34 for **7a**, and at δ=60.9 and 63.1 for **7b**). The high resolution mass spectra (HRMS) showed the correct molecular ions for compounds **6**, **7a** and **7b** (837.0897 (M+H) for **6**, 909.1675 (M+H) for **7a** and 985.1994 (M+H) for **7b**). The ^1H NMR spectra of **6** and **7a** revealed singlets at δ=2.86 for **6** and δ=2.83 for **7a** characteristic of methyl protons in the β position of the fullerene core.

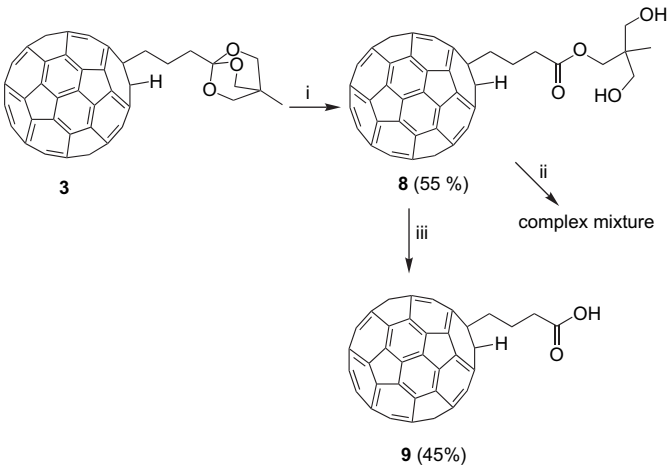
Since the alkylation reaction is irreversible, the preference for substitution at position 4 versus 2 organodihydrofullerene probably resulted from less steric interactions in the linear transition state when the alkyl chain and the incoming electrophile are much further apart.

4. Cleavage of the protecting groups

4.1. Synthesis of organodihydrofullerenecarboxylic acid

Treatment of the fullerene orthoester **3** with trifluoroacetic acid in toluene at room temperature partially cleaved the orthoester to give compound **8** in 55% yield (Scheme 6). This type of ester is known to give the corresponding carboxylic acid upon treatment with base.[12a] However, reactions of **8** with various bases (NaOH, LiOH, K_2CO_3) at room temperature resulted in the formation of an insoluble black powder, which could not be characterized. This was probably due to the high electrophilicity of the fullerene sphere, which makes it more susceptible to nucleophilic attack than the ester group.[2b]

The ester group was eventually cleaved by treatment of **8** in a mixture of trifluoroacetic acid and water in toluene at 80 °C for 16 h. The crude carboxylic acid **9** was washed with methanol, ether and $CHCl_3$. The resulting black powder was taken up in pyridine and insoluble material was filtered off. The product could not be purified by column chromatography. The ^{13}C NMR of the carboxylate salt in deuterated pyridine showed the presence of a carboxylate group with a signal at δ=176.0 for the carbonyl carbon. The ^{13}C NMR spectrum showed signals for two sp^3 hybridized carbons of



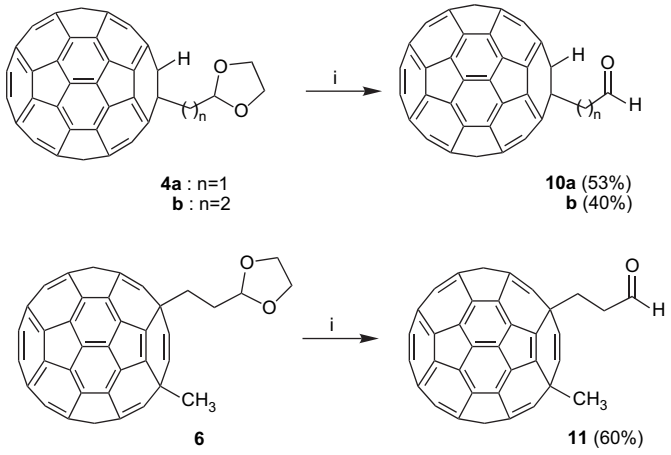
Scheme 6. Reagents and conditions: (i) DCM, trifluoroacetic acid, H_2O, rt; (ii) NaOH or K_2CO_3 or NaH or LiOH in toluene, rt; (iii) trifluoroacetic acid, H_2O, 80 °C.

the fullerene core at δ=59.9 and 65.5 together with 29 signals in the region 136–157 ppm. A singlet at δ=6.65 was observed in the ^1H NMR spectrum, which is characteristic of a proton attached to the C60 core in a fullerene monoadduct. UV–vis spectra showed an absorption band at 432 nm confirming the 1,2-addition pattern. Compound **9** is the first fullerene derivative with a carboxylic acid functionality linked to the C60 sphere via a flexible alkyl chain.

4.2. Synthesis of organodihydrofullerene aldehydes

Despite the fact that a fullerene acetal had been previously synthesized, its transformation into aldehyde had not been reported.[5b] Hydrolysis of acetals **4a**, **4b** and **6** were carried out in refluxing toluene using a trifluoroacetic acid/water mixture to give the organodihydrofullerene aldehydes **10a**, **10b** and **11** in 40–63% yield (Scheme 7).

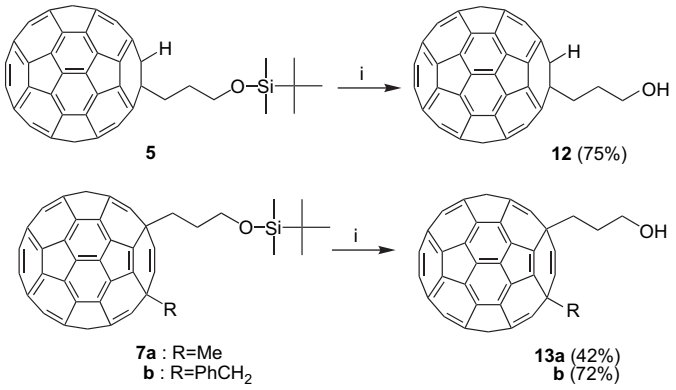
The resulting aldehydes were insoluble in toluene and CS_2 had to be used both for work-up and for NMR analysis. ^1H NMR spectra showed fullerene protons at δ=6.43 (**10a**) or 6.59 (**10b**) and aldehyde protons at δ=10.26 (**10a**), 10.10 (**10b**) and 10.14 (**11**). The methyl group attached to the fullerene sphere (**11**) appeared at δ=2.90. ^{13}C NMR spectra of **10b** and **11** showed two fullerene sp^3 signals at δ=60.1 and 60.3 and δ=54.1 and 62.1, respectively; 26 of the 30 expected core fullerene sp^2 carbons for **10b** and 58 signals for the sp^2 carbon atoms of **11** were also observed.



Scheme 7. Reagents and conditions: (i) toluene, trifluoroacetic acid, H_2O, reflux.

4.3. Synthesis of organodihydrofullerene alcohols

Removal of the *tert*-butyldimethylsilyl protecting group of **5**, **7a** and **7b** was easily performed upon addition of 6 N HCl.[5g] The corresponding alcohols **12**, **13a** and **13b** were obtained in 53–72% yield. Alcohol **12** was insoluble in toluene, and CS_2 was again necessary for purification by chromatography (Scheme 8).



Scheme 8. Reagents and conditions: (i) 6 N HCl, THF, rt.

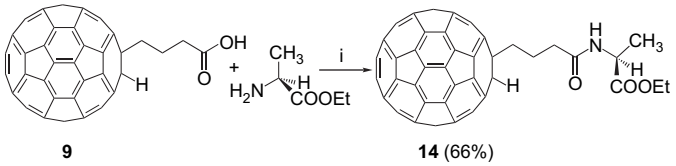
Compound **12** was not sufficiently soluble to obtain a good quality ^{13}C NMR spectrum but the ^{1}H NMR spectrum confirmed the loss of the silyl group and showed a signal at δ=6.51 for the fullerenic proton. The mass spectral data confirmed the structural assignment (molecular ion (M+H) at 782.1).

The fullerene alcohols **13a** and **13b** could be purified by chromatography. They showed higher solubility in toluene and CS_2 as compared to alcohol **12**. The ^{13}C NMR spectrum of **13b** showed two fullerene sp^3 signals at δ=61.0 and 63.1; 52 of the expected 58 fullerene sp^2 signals are also present in the ^{13}C NMR spectrum in the range 136–159 ppm. The ^{1}H NMR spectrum of **13b** showed signals at δ=7.47, 7.55 and 7.67 for the benzyl protons. Compound **13b** also showed characteristic CH_2/CH_3 signals in the range 2–4.5 ppm similar to those of **13a**. (cf. section 7). Compounds **13a** and **13b** were also characterized by mass spectrometry.

5. Selected transformations of 1,2- and 1,4-[60]fullerene adducts

5.1. Coupling of hydro[60]fullerenyl acid 9 with amino acids

C60 carboxylic acid **9** was subjected to standard peptide coupling conditions in the presence of alanine ethyl ester hydrochloride (Scheme 9). In contrast to the acid precursor **9**, the coupling product **14** was easily purified by chromatography and isolated as a brown powder soluble in most common organic solvents. The structure of **14** was established by standard spectroscopic methods. The ^{1}H NMR signal for the fullerenic proton (δ=6.56) shifted downfield compared to that of the acid precursor (δ=6.65). The



Scheme 9. Reagents and conditions: (i) EDC·HCl, HOAt, DCM.

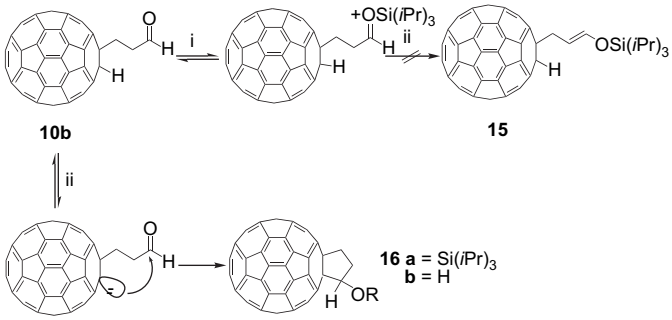
amide proton appeared at δ=6.29 and the ^{13}C NMR spectrum showed signals at δ=171.7 and 173.2 for the two carbonyl groups.

This result showed that standard peptide coupling conditions are compatible with the presence of an acidic proton on the fullerene core.

5.2. Attempt at the formation of a silyl enol ether from aldehyde 4b

Trialkylsilyl enol ethers are useful synthetic intermediates, which allow the introduction of a wide variety of functional groups at the α-position of an aldehyde or a ketone. These reactions are electrophilic additions, which do not require the presence of a base and should therefore be compatible with the presence of an acidic proton on the C60 core.

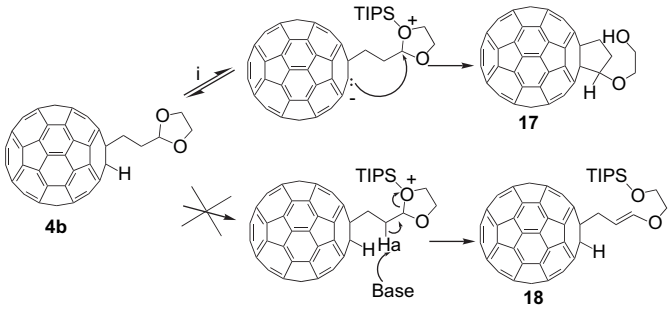
The formation of the silyl enol ether **15** derived from **10b** was attempted by reaction of the aldehyde with a highly electrophilic silylating agent (triisopropylsilyl-trifluoromethanesulfonate) in the presence of a weak base in order to favour reaction at the α-carbon atom of the carbon chain and avoid deprotonation of the fullerene core (Scheme 10). Aldehyde **10b** was stirred at 80 °C in a solution of TIPSOTf and triethylamine in DMF. TLC showed complete disappearance of aldehyde **10b** after 12 h.



Scheme 10. Reagents: (i) Et_3N; (ii) TIPSOTf.

A black powder was isolated after filtration and evaporation of the solvent. This powder had an enhanced solubility compared to aldehyde **10b** and was very soluble in most common organic solvents. The powder was purified by flash chromatography to give compound **16a** in 75% yield. We expected this powder to be the desired silyl enol ether **15**. However, the ^{1}H NMR spectrum revealed that there was no longer a fullerenic proton in this product as no signal around δ=6.5 was observed. Furthermore, signals corresponding to vinyl protons were also absent. The ^{1}H NMR data showed that all alkyl protons were no longer equivalent. Also, a sharp absorption at 431 nm in the UV–vis spectrum was indicative of a C60 derivative with two organic groups attached at the 6,6-junction.[8] The ^{13}C NMR spectrum exhibited signals for two sp^3 carbons in the C60 core (δ 68.4, 69.4) and 58 signals (partially overlapping) for the sp^2 carbons of the C60 core. On the basis of these data, we concluded that a stereogenic centre was attached to the fullerene sphere and that the product was deprived of C_s symmetry. These data were indicative of a cyclic ether probably resulting from deprotonation of **10b** followed by addition of the fullerenyl anion to the aldehyde group. Indeed treatment of **10b** with triethylamine in DMF yielded the simple cyclized product **16b**. Cyclization products had already been observed by Cousseau et al. when they reacted $C60^{2-}$ with diiodo derivatives I–$(CH_2)_n$–I (n=3 and 4).[13] We also decided to examine if an enol ether could be directly formed from acetal **4b**: the oxygen atom of an acetal is indeed more basic than a carbonyl group and silylation should occur more

readily with the net result of increasing the acidity of the α-proton of **4b**, which could then be preferentially removed by the tertiary base. Triisopropylsilyl-trifluoromethanesulfonate was slowly added to a CS_2 solution of **4b** and then *N*,*N*′-diisopropylethylamine was added slowly to the resulting mixture (Scheme 11).

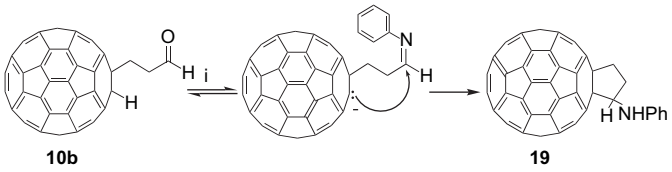


Scheme 11. Reagents and conditions: (i) TIPSOTf in CS_2, 30 °C, 12 h then Hünig's base.

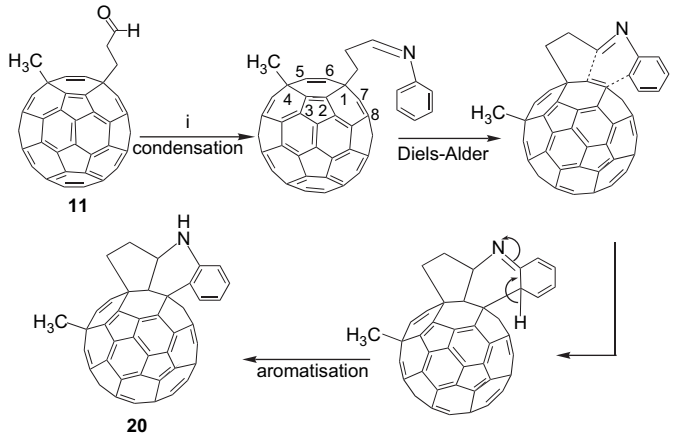
However, these conditions also led to the formation of a cyclized product **17** instead of the expected enol ether **18**. The structure of **17** was determined from analysis of its spectroscopic properties, which were similar to those of compounds **16a** and **16b**. These results suggested that the formation of a silyl enol ether from an aldehyde carried by a side chain attached to C60 would require the replacement of the acidic hydrogen of the fullerene core by a base-insensitive substituent if the length of the tether allows for a cyclization reaction.

5.3. Reaction of 10b and 11 with aniline

The reaction of **10b** with amines was expected to lead to the corresponding imines, which are themselves precursors of amines and amino acids. We selected the reaction of **10b** with aniline as model for this transformation (Scheme 12). A mixture of **10b**, aniline and molecular sieves in benzene yielded a black powder **19**, which could be purified by chromatography on silica gel (yield: 65%). Compound **19** showed enhanced solubility in most common organic solvents compared to aldehyde **10b**. The ^{1}H NMR spectrum of **19** showed no signal in the δ=7.5 region as expected for the proton of the imine group. The absence of a signal at around δ=160 typical for a carbon of an imine bond further confirmed the absence of the expected condensation product. Also no signal was observed at around δ=6.5 indicative that the fullerenic proton was lost during the transformation. As a matter of fact, NMR and UV spectra of **19** were quite similar to those of cyclic ether **16a** or alcohol **16b**. The alkyl protons were now nonhomotopic, the UV–vis spectrum showed a sharp absorption at 430 nm in agreement with a C60 derivative with two organic groups attached at the 6,6-junction bond and the ^{13}C NMR spectrum exhibited signals for two sp^3 carbons in the C60 core (δ=67.2, 70.0) and 58 signals (partially overlapping) for the sp^2 carbons of the C60 core. We concluded that the reaction product was structure **19** resulting from a nucleophilic attack of the fullerenide anion on the imine group. Thus access to an imine from aldehyde **10b** was not possible as a result of the presence of the acidic fullerene proton. We therefore decided to examine the reaction of aniline on the corresponding methylated aldehyde **11** (Scheme 13).



Scheme 12. Reagents and conditions: (i) $C_6H_5NH_2$ (1 equiv), benzene, rt, 72 h.



Scheme 13. Reagents and conditions: (i) aniline (1 equiv), benzene, 4 Å MS, rt, 3 days.

The reaction of **11** with an equimolar amount of aniline was carried out in benzene in the presence of 4 Å MS. The condensation was expected to proceed smoothly as high yields of a fulleroaldimine were previously obtained by Saigo et al. under the same conditions.[14] The reaction was stopped after 16 h and the crude ^{1}H NMR spectrum showed no imine proton.

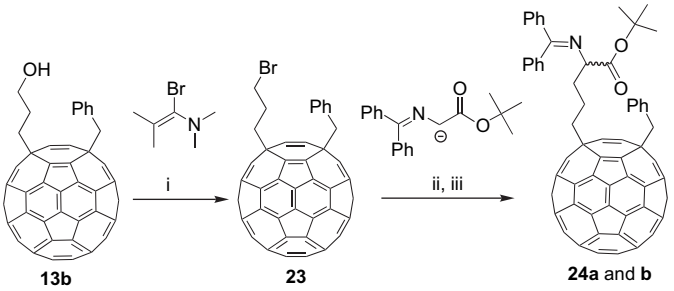
TLC revealed one major spot and compound **20** was isolated by chromatography. The ^{1}H NMR spectrum showed four distinct aromatic protons at δ=7.84, 7.02, 6.69 and 6.57. The proton at the bicyclic ring junction (He) appeared as an octuplet with coupling constants of 2.8, 4.4 and 7.8. The four alkyl protons on the five-membered ring (Ha, Hb, Hc, Hd) were all diastereotopic and appeared between δ=2.30 and 3.01. The protons of the methyl group at the C60 surface gave a sharp singlet at δ=2.35. In the ^{13}C NMR spectrum 53 fullerene sp^2 carbon signals and 1 phenyl ring signal (assigned by HMBC and HMQC experiments) were observed between δ=133 and 159. The remaining five sp^2 carbons of the phenyl ring appeared at δ=129.6, 129.3, 124.0, 120.6 and 116.8. The carbon at the bicyclic junction appeared at δ=65.6 while the proton of the alkyl groups of the five-membered ring appeared at δ=40.7 and 34.1. The signal at δ=27.3 was characteristic of the sp^3 carbon for the protons of the methyl group on the C60 surface. The tetra-addition pattern on C60 was confirmed by the ^{13}C NMR spectrum, which exhibited four sp^3 carbons of the C60 framework at δ=72.1, 60.8, 58.0 and 53.5. Table 1 shows the ^{1}H NMR chemical shifts of compound **20**.

Compound **20** probably resulted from the intermediate imine, which then could have undergone a Diels–Alder reaction between the newly formed C=N bond, the phenyl ring and a C=C bond on the C60 surface. Fullerene derivatives are good dienophiles and readily undergo Diels–Alder reactions. However, in our case, this mechanism implies a rather unusual localization of the electrons in the diene region. Alternatively, the bicyclic compound could be the

Table 1
^{1}H NMR chemical shifts for compound **20**

Protons	Chemical shifts (ppm)
CH_3	2.35
Ha, Hb	2.30, 2.38
Hc, Hd	2.78, 3.01
He	4.27
Hf, Hg, Hh, Hi	7.84, 7.02, 6.69, 6.57

result of an electron transfer reaction mechanism between the phenylimine donor moiety and the fullerene acceptor moiety. The third step would involve the rearomatization of the six-membered ring (Scheme 14). Three double bonds on the surface of C60 (C2–C3, C5–C6, C7–C8) were in close enough proximity to react with the newly formed imine bond and the phenyl ring. Thus three different adducts could in principle be obtained (Fig. 1). The structural assignment of the product was difficult because structures **20**, **21a** and **21b** would be expected to show similar ^{1}H and ^{13}C NMR spectra. HMBC and HMQC experiments were performed but did not provide sufficient indication regarding the addition pattern because of the absence of a fullerenyl proton directly attached to the C60 sphere. Hence, the connectivities of the sp^3 and sp^2 hybridized fullerenyl carbon atoms could not be determined via such NMR experiments. The connectivities of the carbon atoms can be assigned with 2D INADEQUATE or C–C HOHAHA technique but this would have required long experimental time and was not available at the time of the realization of this work. However, a 2D T-ROESY NMR experiment provided information in elucidating the addition pattern of the C60 addend. No NOE correlation between the methyl CH_3 and any of the protons from the bicyclic structure was observed, which was indicative of a 1–4–7–8 addition product (compound **20**) rather than a 1–2–3–4 (compound **21b**) or 1–4–5–6 (compound **21a**) addition. Indeed, in the case of a 1–2–3–4 or a 1–4–5–6 addition, the phenyl protons (Hf, Hg, Hh, Hi) would have been expected to show some NOE correlation with the methyl group on the C60 sphere, as they are located in close proximity.



Scheme 14. Reagents and conditions: (i) DCM, rt, 45 min; (ii) THF, −78 °C, 60 min, warming to rt, then 60 min at rt; (iii) NH_4Cl.

Further evidence for the formation of **20** was obtained from its UV–vis absorption spectrum. It showed remarkable similarity with another compound **22** (Fig. 2) synthesized by Rubin et al., which had an identical addition pattern (1–4–7–8).[15]

Both spectra show considerable reduction in band structure compared to 1–2–3–4 or 1–4–5–6 addition products. Furthermore, the number, position and intensity of the absorption bands of both compounds were extremely similar. Table 2 shows the absorption bands observed by Rubin et al.[15] and by us (compound **20**), and those observed for a 1–2–3–4 addition product. Noteworthy were the absorptions at 406 and 446 nm. They reflected the fact that

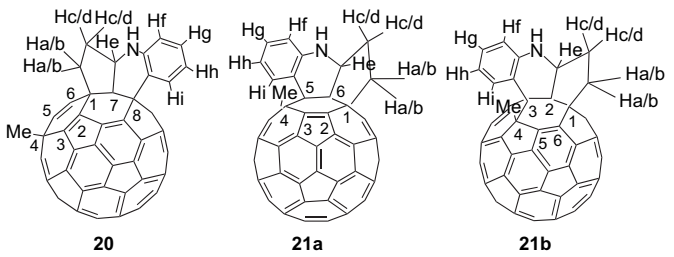


Figure 1. Possible Diels–Alder adducts.

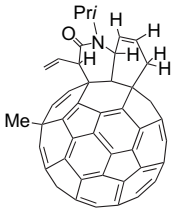


Figure 2. Compound **22** synthesized by Rubin et al.[15]

Table 2
UV–vis absorption bands for compound **20**

Compound	Addition pattern	Absorption bands
20	1–4–7–8	252, 314, 406, 446, 526, 682
Rubin's compound	1–4–7–8	252, 312, 408, 446, 510, 682
Rubin's compound	1–2–3–4	256, 328, 404, 432, 648, 676, 712.

compound **20** retained a C=C double bond at the 5,6-ring junction.

5.4. Synthesis of a protected glycine derivative

The strategy adopted to generate a protected fullerene amino acid derivative from the fullerene alcohol **13b** involved conversion of the alcohol into a fullerene alkyl bromide followed by substitution of the halogen with an anion derived from *N*-(diphenylmethylene)glycine *tert*-butyl ester.[16]

The conversion of the fullerene alcohol to alkyl bromide **23** in 44% yield was rendered possible by the use of (1-bromo-2-methylprop-1-enyl)-*N*,*N*-dimethylamine,[17] a smooth brominating agent, which reacts under neutral conditions (Scheme 14).

The diastereomeric fullerene amino acid derivatives 1-benzyl-4-[α-propyl-*tert*-butylglycinate benzophenone imine] 1,4-dihydro[60]fullerenes (**24a** and **24b**) were generated via the addition of *N*-(diphenylmethylene)glycine *tert*-butyl ester to 1-benzyl-4-[3′-bromopropyl] 1,4-dihydro[60]fullerene (**23**).

Alkylation of *N*-(diphenylmethylene)glycine *tert*-butyl ester has been extensively studied.[16,18,19,20] In general, the *tert*-butyl and diphenylimine protecting groups can be removed under mild conditions. The active methylene group of *N*-(diphenylmethylene)glycine *tert*-butyl ester has been exploited in the syntheses of protected fullerene glycine derivatives obtained via Bingel cyclopropanation reactions. However, deprotection of those protected fullerene glycine derivatives was not successful and was assigned to the electron-withdrawing character of the fullerene sphere making the imine group less susceptible to acidic or basic hydrolysis.[21–24] In our case, we expect molecules **24a** and **24b** to be more easily deprotected due to the presence of the alkyl spacer group between the fullerene and the amino acid group since electron deficiency in the fullerene will not interfere through five σ bonds. Initial alkylation reactions using 50% KOH (aq) as base to generate the active anion were unsuccessful leading to decomposition. It was then decided to generate the anion with LDA and use an excess of *N*-(diphenylmethylene)glycine *tert*-butyl ester anion. The fullerenic anion was formed as shown by the appearance of a green colour but no alkylation product could be identified after quenching. NMR analysis of the black powder suggested the presence of products resulting from multiple additions. When the addition was carried out using exactly 1 equiv of the anion or using a slight excess of the fullerene alkyl bromide a pair of diastereomeric racemic products **24a** and **24b** were isolated and separation of the diastereomers was possible by flash chromatography. The ^{1}H NMR spectra of the two products were practically identical except in the region of benzyl

CH_2 resonances. These two CH_2 protons are diastereotopic and therefore give rise to a pattern of double-doublets typical of an AB system (Fig. 3).

In **24a**, the two signals are almost isochronous and appear as very distorted doublets with J=12.6 Hz. In **24b**, the doublets with J=12.8 Hz are separated by $\Delta\delta$=250 Hz (0.50 ppm at 500 MHz). The chemical shift difference in **24b** could be explained by restricted motion of the benzyl group as a result of an interaction with the diphenylimine group. A similar phenomenon was observed in a series of disubstituted fullerenes, **25a**:$(C_6H_5CH_2)_2$C60, **25b**: $(2\text{-}BrC_6H_5CH_2)_2$C60, **25c**: $(3\text{-}BrC_6H_5CH_2)_2$C60 and **25d**: $(4\text{-}BrC_6H_5\text{-}CH_2)_2$C60, studied by Kadish et al.[25] Their ^{1}H NMR spectra showed two similar AB doublets for the benzyl CH_2 protons of **25a**, **25c** and **25d**; **25b** gave a different pattern, similar to that of **24b** with a much larger $\Delta\delta$ value (0.22 ppm) than the other three compounds (<0.1). This was suggested to be due to a hindered rotation of the phenyl ring in the 2-bromo compound in analogy with studies by Whitesides et al.,[26,27] who showed that the conformation of the phenyl ring with respect to the benzyl CH_2 protons has an effect on the NMR signal. This led us to undertake a molecular modelling study to verify if a similar phenomenon was plausible for compounds **24a** and **24b**.

We deemed that phenyl–phenyl interactions[29] between the benzyl and the diphenylmethylene moieties could play a decisive role in defining the preferential conformations adopted by **24a** and **24b**. Therefore, as a force field for the molecular modelling investigation, we choose OPLS as a result of the correct treatment of intermolecular forces in benzene oligomers[29] and other aromatic π stackings[30] reported with this force field. We built two diastereomeric structures assuming (^{f}*C*)–(α*S*) configuration for **24a** and (^{f}*C*)–(α*R*) for **24b**, as shown in Figure 3 and ran molecular dynamics (MD) and conformational searches (CF) calculations with OPLS.

MD (molecular dynamics) calculations at 300 K showed no substantial difference in the phenyl–CH_2 torsions between the two diastereomers, as the C3′–C2′–C1′–Ha and C3′–C2′–C1′–Hb dihedral angles (see Fig. 4) spanned comparable ranges of values in the simulations. On the contrary, the conformation of the benzyl group as a whole varied somewhat between the two diastereomers: the C2′–C1′–C1–C9 dihedral was almost unrestricted in **24a**, while for **24b** it tended to assume values around −60° and 180°. The restricted motion experienced by the benzyl moiety in

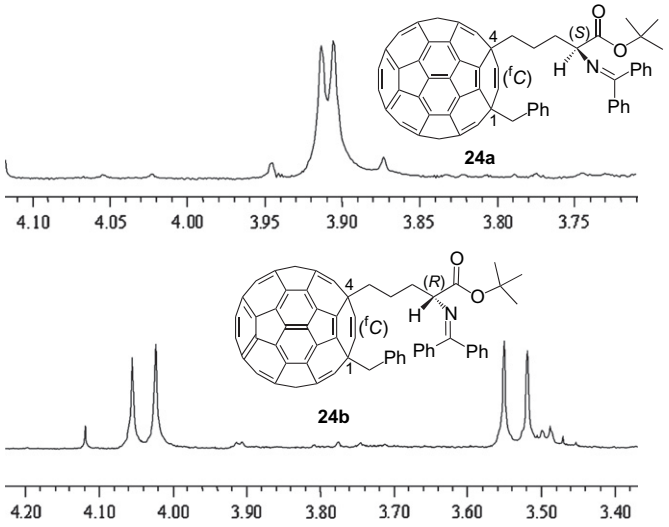


Figure 3. ^{1}H NMR spectra of fullerene amino acid derivatives **24a** and **24b**.

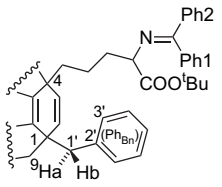


Figure 4.

24b may explain the large anisochrony between Ha (pro-*S*) and Hb (pro-*R*) protons for this diastereomer.

In addition, CS (conformational searches) calculations were run using the procedure described in Section 7.26 to further highlight structural discrepancies between **24a** and **24b**. The two sets of 50 low-energy structures showed in fact significant differences. We were especially interested in structures featuring clear π–π interactions[28] between the benzyl and the diphenylmethylene moieties. For **24b**, several low-energy structures showed interacting phenyl rings, including the absolute minimum (shown as **24b$_{[1]}$** in Fig. 5, right). It exhibited a clear face-to-face π-stacking between the benzyl phenyl Ph_{Bn} and one imino phenyl (Ph1), which was especially close to proton Ha (distance ≈3.3 Å from Ph1 centre) with respect to Hb (≈4.5 Å). In such a situation, Ha is more subjected to the ring current exerted by Ph1, which may help explaining the large chemical shift difference with Hb. For **24a**, on the contrary, only a few low-energy structures showed interacting phenyl rings, including the third most stable conformation (**24a$_{[3]}$**, Fig. 5, left). This exhibited an edge-to-face interaction with much larger distances Ph1–Hb≈5.4 Å and Ph1–Ha≈7.0 Å.

In conclusion, the observed ^{1}H NMR patterns for **24a** and **24b** must be related to a different conformational freedom, possibly associated with the ring current shift exerted by the diphenylmethylene moiety. On this basis, (^{f}*C*)–(α*S*) or (^{f}*A*)–(α*R*) and (^{f}*C*)–(α*R*) or (^{f}*A*)–(α*S*) relative configurations were assigned to **24a** and **24b**, respectively (Fig. 3).

6. Conclusions

This study has confirmed that functional groups carried by a tether can be readily introduced to C60 by addition of functionalized organolithium or Grignard reagents. The resulting orthoesters, acetals or silyl enol ethers can be readily transformed into the parent carboxyl, carbonyl or alcohol functional groups. Preliminary experiments on functional manipulations of these

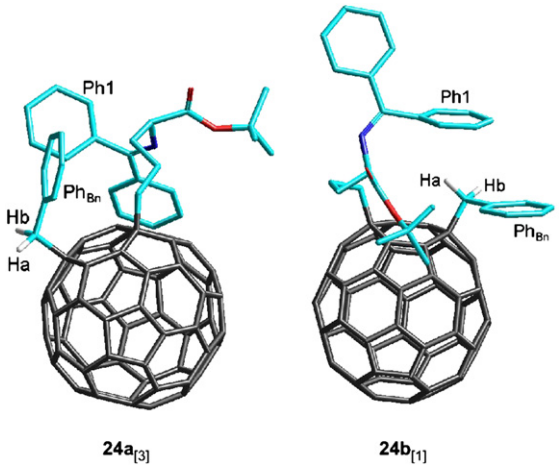


Figure 5. Lowest-energy OPLS structures for **24a** and **24b** exhibiting phenyl–phenyl interactions.

tethered fullerene derivatives showed some limitations in the use of these functionalized [60]fullerenes: thus, while peptide-type coupling could be readily effected with a carboxylic acid derivative, the corresponding aldehyde could not be transformed into an enol ether, cyclization initiated by the formation of a fulleride anion occurred faster than the deprotonation α to the aldehyde. The same was observed with the corresponding acetals or when the aldehyde was reacted with aniline. Replacement of hydrogen by methyl in aldehyde **4b** was expected to allow the formation of an imine by reaction with aniline. This was the case but the imine spontaneously underwent an intramolecular Diels–Alder reaction involving a 6–6 double bond of the fullerene core.

Clearly, further work would be needed to establish the importance of the length of the tether on the functional group manipulation of these tethered fullerenes. It is expected that some reactions will only be possible on derivatives where the acidic fullerene proton is replaced by an inert alkyl group. This should not be a major problem since the properties of the C60 core will not be significantly modified after alkylation.

We have also demonstrated the synthetic use of nucleophilic additions to generate a fullerenyl protected amino acid with a flexible alkyl linker between the fullerene sphere and the amino acid functional group. The two diastereomeric products thus prepared showed different ^{1}H NMR spectra, which were analyzed with the help of molecular modelling. This opens a route to synthetic analogs of phenylalanine carrying a [60]fullerene ring.

7. Experimental

7.1. General

NMR spectra were recorded using a Bruker Avance 400NB spectrometer. UV–vis spectra were recorded using a Varian Cary 300 UV–vis spectrometer. High resolution mass spectrometry was carried out by Cesamo mass spectrometry service, University of Bordeaux 1. C60 was purchased from Aldrich Chemical Company or M.E.R. (Materials and Electrochemical Research company). Solvents were dried by filtration over activated alumina. All reactions were carried out in standard glassware under an inert atmosphere of N_2 or Ar. Organometallic reactions were performed in flame dried Schlenk tubes flushed three times with argon prior to use. Solvents for organometallic reactions were transferred via cannula and deoxygenated twice prior to use. 1-Bromo-3-(*tert*-butyldimethylsiloxy)propane,[9] 2-(3-bromopropyl)-1,3-dioxolane[31] and 1-(2-iodopropyl)-4-methyl-2,6,7-trioxabicyclo[2,2,2]-octane[7b] were synthesized following the published procedures.

7.2. 1-(2-Iodopropyl)-4-methyl-2,6,7-trioxabicyclo[2,2,2]-octane 1

The orthoester was prepared according to the literature procedures.[7b]

^{1}H NMR ($CDCl_3$) 0.78 (s, 6H), 1.75 (t, J=7.4, 2H), 1.98 (m, 2H), 3.19 (t, J=7, 2H), 3.87 (s, 6H); ^{13}C NMR ($CDCl_3$) 6.78, 14.4, 27.6, 30.12, 37.2. HRMS calculated 299.0144, found 299.0148.

7.3. 1-Hydro-2-[3′-(4″-methyl-2″,6″,7″-trioxabicyclo[2″,2″,2″]-octyl)propyl]-1,2-dihydro[60]fullerene 3

2.28 mL (1.6 equiv) of a 0.1 mol/L solution (ether/pentane, 1:1) of 1-(2-iodopropyl)-4-methyl-2,6,7-trioxabicyclo[2,2,2]-octanyl lithium (prepared from the reaction of 1 equivalent of *n*-butyllithium with **1** in 50:50 pentane:diethylether) was added to C60 in toluene at −78 ^{0}C were syringed into toluene solution (100 mL) of fullerene[60] (100 mg, 0.138 mmol). The reaction was quenched with trifluoroacetic acid after 5 min at room temperature. The mixture was filtered off and extracted with water and brine (2×20 mL). The solvent was evaporated and the resulting brown residue was purified by flash chromatography (SiO_2, toluene) to yield 1-hydro-2-[3′-(4″-methyl-2″,6″,7″-trioxabicyclo[2″,2″,2″]-octyl)propyl]-1,2-dihydro[60]fullerene **2** (27 mg, 22% yield) as a black solid: mp >300 °C; ^{1}H NMR (5:1, CS_2:$CDCl_3$) 0.84 (s, 3H), 2.22 (t, J=7.8, 2H), 2.72 (m, 2H), 3.43 (m, 2H), 4.04 (s, 6H), 6.50 (s, 1H); ^{13}C NMR (5:1, CS_2:$CDCl_3$) 14.6, 20.9, 30.4, 37.0, 46.9, 59.6, 65.0, 72.7, 109.0, 135.9, 136.6, 140.0, 141.6, 141.6, 142.0, 142.0, 142.0, 142.0, 142.2, 142.5, 142.5, 143.2, 144.6, 144.7, 145.4, 145.4, 145.9, 146.2, 146.2, 146.3, 146.4, 146.5, 147.2, 147.3, 147.5, 153.9, 156.2; UV–vis ($CHCl_3$) λ_{max} 255 nm, 325, 432. HRMS calculated 893.1177, found 893.1184.

7.4. .1-Hydro-2-[2′-(1″,3″dioxolanyl)ethyl]-1,2-dihydro[60]fullerene 4a

2-(3-Ethylmagnesium bromide)-1,3-dioxolane was prepared from the reaction between 2-(3-bromoethyl)-1,3-dioxolane (1.206 g, 6.66 mmol) and magnesium turnings (24.3 mg, 6.66 mmol) in THF (40 mL) at room temperature using a water bath to control the temperature. The solution of the Grignard reagent was added dropwise via a cannula to a rapidly stirred solution of C60 (400 mg, 0.55 mmol) in toluene (250 mL). An immediate colour change (purple to dark green) was observed. The reaction was quenched with excess trifluoroacetic acid (0.5 mL) and the solvents removed in vacuo. Purification by flash chromatography (SiO_2, toluene) gave 1-hydro-2-[2″-(1″,3″-dioxanyl)ethyl]-1,2-dihydro[60]fullerene **4a** (250 mg, 55%) as a brown solid: mp >300 °C; ^{1}H NMR (5:1, CS_2/$CDCl_3$) 2.95 (m, 2H), 3.58 (m, 2H), 4.08 (m, 2H), 4.21 (m, 2H), 5.40 (t, J=4.2, 1H), 6.48 (s, 1H); ^{13}C NMR (5:1, CS_2/$CDCl_3$) 31.2, 40.4, 59.4, 63.9, 65.2, 103.6, 135.7, 136.2, 139.9, 140.0, 141.3, 141.6, 141.7, 141.7, 141.7, 141.9, 142.3, 142.7, 142.9, 144.3, 144.4, 145.1, 145.2, 145.2, 145.5, 145.8, 145.9, 146.1, 146.7, 147.1, 153.2, 155.2; UV–vis ($CHCl_3$) λ_{max} 254 nm, 325, 405, 433. HRMS calculated 823.0759, found 823.0803.

7.5. 1-Hydro-2-[3′-(1″,3″-dioxolanyl)propyl]-1,2-dihydro[60]fullerene 4b

2-(3-Propylmagnesium bromide)-1,3-dioxolane was prepared from the reaction between 2-(3-bromopropyl)-1,3-dioxolane (151 mg, 0.833 mmol) and magnesium turnings (31 mg, 1.25 mmol) in THF (10 mL) at room temperature using a water bath to prevent excessive reflux. After 2 h, the solution of the Grignard reagent was added dropwise via a cannula to a rapidly stirred solution of C60 (50 mg, 0.069 mmol) in toluene (50 mL). An immediate colour change (purple to dark green) was observed. The reaction was quenched with excess trifluoroacetic acid (0.5 mL) and the solvents were removed in vacuo. Purification by flash chromatography (SiO_2, toluene) gave 1-hydro-2-[3′-(1″,3″-dioxolanyl)propyl]-1,2-dihydro[60]fullerene **4b** (67 mg, 42% yield based on consumed C60) as a brown solid: mp >300 °C; ^{1}H NMR (5:1, CS_2/$CDCl_3$) 2.19 (m, 2H), 2.72 (m, 2H), 3.50 (m, 2H), 3.96 (m, 4H), 5.17 (t, J=4.4, 1H), 6.49 (s, 1H); ^{13}C NMR (5:1, CS_2/$CDCl_3$) 22.1, 34.9, 47.7, 60.2, 65.4, 65.6, 104.7, 136.3, 136.4, 137.0, 140.6, 140.7, 142.1, 142.4, 142.5, 142.5, 142.7, 143.0, 143.7, 145.1, 145.1, 145.8, 145.9, 145.9, 145.9, 146.3, 146.6, 146.7, 146.8, 146.9, 147.5, 154.1, 156.2. HRMS calculated 837.0916, found 837.0923.

7.6. 1-Hydro-2-[3′-(*tert*-butyldimethylsiloxy)propyl]-1,2-dihydro[60]fullerene 5

3-(*tert*-Butyldimethylsiloxy)propyl magnesium bromide was produced from the reaction of magnesium turnings (538 mg, 0.021 mol) and 1-bromo-3-(*tert*-butyldimethylsiloxy)propane

(2.11 g, 8.33 mmol) in THF (10 mL) at room temperature. After 1.5 h, the solution of the Grignard reagent was added dropwise via a cannula to a solution of C60 (0.5 g, 0.69 mmol) in toluene (500 mL). The addition resulted in the immediate formation of a dark green/black solution. The reaction was quenched with 1 mL trifluoroacetic acid and the solvents were removed in vacuo. The solution of the brown residue in 250 mL $CHCl_3$ was washed with 50 mL of brine and water (2×50 mL), and dried over anhydrous $MgSO_4$. Evaporation of the solvents left a brown residue, which was purified by flash chromatography (SiO_2, cyclohexane/toluene, 10:1) to give C60 (25 mg) and 1-hydro-2-[3′-(*tert*-butyldimethylsiloxy)-propyl]-1,2-dihydro[60]fullerene **5** (393 mg, 67% yield based on consumed C60) as a brown solid: mp >300 °C; ^{1}H NMR ($CDCl_3$) 0.23 (s, 6H), 1.04 (s, 9H), 2.80 (m, 2H), 3.50 (m, 2H), 4.15 (t, *J*=6, 2H), 6.51 (s, 1H); ^{13}C NMR ($CDCl_3$) 5.1, 18.5, 26.1, 30.1, 43.6, 59.7, 63.0, 64.8, 135.9, 136.5, 140.1, 140.2, 141.6, 141.7, 141.9, 142.0, 142.1, 142.2, 142.6, 143.1, 143.3, 144.6, 144.7, 145.4, 145.4, 145.9, 146.2, 146.3, 146.4, 146.5, 146.6, 147.1, 147.5, 147.9, 153.4, 156.1. HRMS calculated 895.1518, found 895.1520.

7.7. 1-Methyl-4-[2′-(1″,3″-dioxolanyl)propyl]-1,2-dihydro[60]fullerene 6

A solution of potassium *tert*-butoxide (31 mg, 0.28 mmol) in THF (5 mL) was added to 1-hydro-2-[2′-(1″,3″-dioxanyl)propyl]-1,2-dihydro[60]fullerene **4b** (200 mg, 0.243 mmol) in THF (200 mL) via a cannula. After 15 min, iodomethane (3.4 g, 1.49 mL, 24 mmol) was added dropwise. The reaction was then stirred for 24 h at room temperature. The solvent was removed in vacuo and the residue dissolved in CS_2 (50 mL). The solution was washed with brine (2×25 mL) and water (2×25 mL), and then dried over anhydrous $MgSO_4$. Evaporation of the solvents left a brown residue, which was purified by flash chromatography (SiO_2, CS_2/toluene, 1:1) to give 1-methyl-4-[2′-(1″,3″-dioxanyl)propyl]-1,2-dihydro[60]fullerene **6** (120 mg, 59% yield) as a brown solid: mp >300 °C; ^{1}H NMR (5:1, CS_2/$CDCl_3$) 2.72 (m, 2H), 2.86 (s, 3H), 3.18 (m, 2H), 4.00 (m, 2H), 4.12 (m, 2H), 5.25 (t, *J*=4.35, 1H); ^{13}C NMR (5:1, CS_2/$CDCl_3$) 29.1, 31.5, 36.8, 54.3, 58.4, 65.2, 103.9, 137.4, 137.5, 138.4, 138.7, 138.8, 140.2, 140.8, 141.9, 142.0, 142.2, 142.3, 142.4, 142.5, 142.6, 142.9, 142.9, 143.0, 143.0, 143.1, 143.1, 143.6, 143.7, 143.8, 144.00, 144.1, 144.2, 144.2, 144.2, 144.3, 144.6, 144.6, 144.7, 144.8, 145.0, 145.0, 145.1, 145.4, 145.6, 146.8, 146.8, 146.8, 146.8, 146.9, 147.1, 147.1, 147.2, 147.3, 148.1, 148.5, 148.5, 148.6, 151.4, 152.7, 157.0, 158.7; UV–vis ($CHCl_3$) λ_{max} 257 nm, 364, 450 (br). HRMS calculated 837.0915, found 837.0896.

7.8. 1-Methyl-4-[3′-(*tert*-butyldimethylsiloxy)propyl] 1,4-dihydro[60]fullerene 7a

To 1-hydro-2-[3′-(*tert*-butyldimethylsiloxy)propyl]-1,2-dihydro[60]fullerene **5** (320 mg, 0.36 mmol) in THF (200 mL) was added potassium *tert*-butoxide (44 mg, 0.39 mmol) in THF (15 mL) via a cannula. After 15 min, iodomethane (5.07 g, 0.036 mol) was added dropwise. The reaction was stirred for 24 h at room temperature. The solvent was then removed in vacuo and the residue dissolved in dichloromethane (200 mL). The solution was washed with brine (2×25 mL) and water (2×25 mL), and then dried over anhydrous $MgSO_4$. Evaporation of the solvent left a brown residue, which was purified by flash chromatography (SiO_2, cyclohexane/toluene, 10:1) to give 1-methyl-4-[3′-(*tert*-butyldimethylsiloxy)-propyl] 1,2-dihydro[60]fullerene **7a** (250 mg, 77% yield) as a brown solid: mp >300 °C; ^{1}H NMR ($CDCl_3$) 0.17 (s, 6H), 0.99 (s, 9H), 2.56 (m, 2H), 2.83 (s, 3H), 3.12 (m, 2H), 4.01 (t, *J*=6, 2H); ^{13}C NMR ($CDCl_3$) 4.7, 18.8, 26.4, 29.6, 30.7, 40.03, 54.8, 59.4, 63.3, 138.0, 138.9, 139.1, 139.4, 141.2, 142.3, 142.4, 142.6, 142.9, 142.9, 143.0, 143.0, 143.4, 143.5, 143.6, 144.2, 144.2, 144.3, 144.4, 144.5, 144.6, 144.7, 144.7, 144.5, 144.8, 145.1, 145.2, 145.2, 145.4, 145.4, 145.5, 145.8, 146.6, 147.3, 147.3, 147.4, 147.4, 147.4, 147.5, 147.6, 147.9, 148.7, 149.0, 149.1, 152.3, 153.1, 158.02 159.4. HRMS calculated 909.1675, found 909.1671.

7.9. 1-Benzyl-4-[3′-(*tert*-butyldimethylsiloxy)propyl] 1,4-dihydro[60]fullerene 7b

To 1-hydro-2-[3′-(*tert*-butyldimethylsiloxy)propyl]-1,2-dihydro[60]fullerene **5** (200 mg, 0.223 mmol) in THF (100 mL) was added potassium *tert*-butoxide (50 mg, 0.446 mmol) as a solution in THF (10 mL) via a cannula. After 15 min, benzyl bromide (229 mg, 1.34 mmol) was added dropwise and the reaction mixture was refluxed for 2 h. The solvent was removed in vacuo. The resulting brown residue was purified by flash chromatography (SiO_2, cyclohexane/toluene, 10:1) to give 1-benzyl-4-[3′-(*tert*-butyldimethylsiloxy)propyl] 1,4-dihydro[60]fullerene **7b** (150 mg, 65% yield) as a brown solid: mp >300 °C; ^{1}H NMR ($CDCl_3$) 0.16 (s, 6H), 0.98 (s, 9H), 2.12 (m, 4H), 3.79 (m, 2H), 4.31 (m, 2H), 7.43 (t, *J*=6.8, 1H), 7.51 (t, *J*=7.2, 2H), 7.65 (d, *J*=7.6, 2H); ^{13}C NMR ($CDCl_3$) −4.7, 18.6, 30.5, 38.8, 49.6, 59.5, 60.9, 63.1, 128.0, 128.9, 131.5, 136.8, 138.3, 138.6, 139.1, 139.3, 141.0, 142.4, 142.4, 142.8, 142.9, 142.9, 143.0, 143.0, 143.3, 143.3, 143.5, 143.5, 143.5, 144.1, 144.2, 144.2, 144.3, 144.4, 144.6, 144.6, 144.6, 144.7, 144.8, 145.1, 145.1, 145.2, 145.3, 145.4, 145.4, 145.8, 145.8, 147.3, 147.3, 147.4, 147.6, 147.8, 147.8, 149.0, 149.0, 149.0, 151.1, 153.3, 158.2, 158.3. HRMS calculated 985.1988, found 985.1994.

7.10. 1-Hydro-2-[3′-(2″,2″-bis(hydroxymethyl)propyloxy-carbonyl)propyl]-1,2-dihydro[60]fullerene 8

1-Hydro-2-[3′-(4″-methyl-2″,6″,7″-trioxabicyclo[2″,2″,2″]-octyl)-propyl]-1,2-dihydro[60]fullerene **3** (100 mg, 0.112 mmol) was dissolved in a mixture of dichloromethane (6 mL) and trifluoroacetic acid (6 mL). Two drops of water were added to the solution, which was stirred overnight at room temperature. The solvents were evaporated and the resulting brown residue was washed with methanol and then purified by flash chromatography (SiO_2, toluene) to yield 1-hydro-2-[3′-(2″,2″-bis(hydroxymethyl)propyloxy-carbonyl)propyl]-1,2-dihydro[60]fullerene **8** (56 mg, 55% yield) as a black solid: mp >300 °C; ^{1}H NMR ($CDCl_3$) 1.22 (s, 3H), 2.89 (m, 2H), 2.91 (m, 2H), 3.46 (m, 2H), 4.25 (s, 2H), 4.43 (d, *J*=3.2, 4H), 6.53 (s, 1H); ^{13}C NMR ($CDCl_3$) 16.9, 22.0, 33.7, 38.9, 46.1, 59.6, 64.6, 65.3, 68.6, 135.9, 136.4, 140.1, 140.2, 141.6, 141.6, 141.9, 142.0, 142.1, 142.2, 142.6, 143.2, 144.5, 144.7, 145.4, 145.4, 145.4, 145.86, 146.2, 146.2, 146.4, 146.4, 147.0, 147.3, 147.5, 153.5, 155.3, 156.8, 157.2, 172.6; UV–vis ($CHCl_3$) λ_{max} 256 nm, 325, 433. HRMS calculated 912.1361, found 912.1305.

7.11. 1-Hydro-2-(butanoic acid)-1,2-dihydro[60]fullerene 9

1-Hydro-2-[3′-(2″,2″-bis(hydroxymethyl)propyloxycarbonyl)-propyl]-1,2-dihydro[60]fullerene **8** (100 mg, 0.138 mmol) were dissolved in a mixture of toluene (6 mL) and trifluoroacetic acid (6 mL). Two drops of water were added to the solution, which was stirred overnight at 80 °C. The solvents were evaporated and the resulting brown residue was washed with methanol (3×20 mL) and ether (3×20 mL), dissolved in pyridine, and filtered to afford 1-hydro-2-(butanoic acid)-1,2-dihydro[60]fullerene **9** (40 mg, 45% yield) as a black solid: mp >300 °C; ^{1}H NMR (pyridine-d_5) 2.92 (m, 2H), 3.00 (t, *J*=6.4, 2H), 3.40 (m, 2H), 6.65 (s, 1H); ^{13}C NMR (pyridine-d_5) 23.2, 35.0, 46.4, 59.8, 65.4, 136.3, 136.7, 140.4, 140.4, 140.4, 141.9, 142.3, 142.3, 142.6, 142.8, 143.2, 144.8, 144.9, 145.0, 145.6, 145.6, 145.6, 145.6, 146.2, 146.4, 146.4, 146.6, 146.6, 146.9, 147.5, 147.7, 147.7, 154.9, 156.8, 176.0; UV–vis ($CHCl_3$) λ_{max} 254 nm, 328, 432. HRMS calculated 809.0603, found 809.0612.

7.12. 1-Hydro-2-(2′-ethanal)-1,2-dihydro[60]fullerene 10a

Trifluoroacetic acid (2 mL) and water (0.5 mL) were added to 1-hydro-2-[2″-(1″,3″-dioxolanyl) ethyl]-1,2-dihydro[60]fullerene **4a** (100 mg, 0.121 mmol) dissolved in toluene (50 mL). The reaction mixture was refluxed for 16 h and the solvents were then removed in vacuo. The residue was dissolved in CS_2 (30 mL) and the resulting solution was washed with brine (2×5 mL) and water (2×5 mL), and dried over anhydrous $MgSO_4$. The solvent was removed in vacuo and the residue was purified by flash chromatography (SiO_2, toluene) and washed with ether (3×4 mL) to give 1-hydro-2-(2′-ethanal)-1,2-dihydro[60]fullerene **10a** (50 mg, 53% yield) as a black solid: mp >300 °C; ^{1}H NMR (5:1, CS_2/$CDCl_3$) 2.89 (m, 2H), 3.75 (m, 2H), 3.83 (m, 2H), 6.43 (s, 1H), 10.26 (s, 1H). HRMS calculated 779.0497, found 779.0520.

7.13. 1-Hydro-2-(3′-propanal)-1,2-dihydro[60]fullerene 10b

To 1-hydro-2-[3′-(1″,3″-dioxolanyl) propyl]-1,2-dihydro[60]-fullerene **4b** (40 mg, 0.048 mmol) dissolved in toluene (30 mL) were added trifluoroacetic acid (1 mL) and water (0.5 mL). The reaction mixture was refluxed for 16 h and the solvents were then removed in vacuo. The residue was dissolved in CS_2 (10 mL) and the resulting solution was washed with brine (2×5 mL) and water (2×5 mL), and dried over anhydrous $MgSO_4$. The solvent was removed in vacuo and the residue was purified by flash chromatography (SiO_2, toluene) and washed with pentane (2×2 mL) to give 1-hydro-2-(3′-propanal)-1,2-dihydro[60]fullerene **10b** (15 mg, 40% yield) as a black solid: mp >300 °C; ^{1}H NMR (5:1, CS_2/$CDCl_3$) 2.89 (m, 2H), 3.04 (m, 2H), 3.46 (m, 2H), 6.59 (s, 1H), 10.10 (s, 1H); ^{13}C NMR (5:1, CS_2/$CDCl_3$) 23.4, 32.6, 44.5, 60.1, 60.2, 136.4, 136.8, 140.6, 140.7, 141.1, 142.1, 142.2, 142.3, 142.4, 142.6, 143.0, 143.7, 145.0, 145.8, 145.8, 145.9, 145.9, 146.0, 146.2, 146.6, 146.7, 146.8, 146.8, 147.4, 153.9, 155.8, 200.9. HRMS calculated 793.0653, found 793.0635.

7.14. 1-Methyl-4-(3′-propanal)-1,4-dihydro[60]fullerene 11

Trifluoroacetic acid (2 mL) and water (0.5 mL) were added to 1-methyl-4-[1′-(1′,3′-dioxolanyl) ethyl]-1,4-dihydro[60]fullerene **6** (100 mg, 0.119 mmol) in toluene (50 mL). The reaction mixture was refluxed for 2 h and the solvents were then removed in vacuo. The residue was dissolved in CS_2 (30 mL) and the resulting solution was washed with brine (2×5 mL) and water (2×5 mL), and dried over anhydrous $MgSO_4$. The solvents were removed in vacuo and the residue was purified by flash chromatography (SiO_2, toluene) and washed with ether (3×4 mL) to give 1-methyl-4-(3′-propanal)-1,4-dihydro[60]fullerene **11** (60 mg, 63% yield) as a black solid: mp >300 °C; ^{1}H NMR (5:1, CS_2/$CDCl_3$) 2.90 (s, 3H), 3.40 (dt, *J*=7.8, 14.5, 2H), 3.52 (t, *J*=7.6, 2H), 10.14 (s, 1H); ^{13}C NMR (5:1, CS_2/$CDCl_3$) 29.5, 34.8, 43.8, 54.0, 62.1, 138.3, 138.3, 139.1, 140.1, 140.7, 141.1, 141.2, 141.5, 141.6, 141.7, 141.8, 142.0, 142.1, 142.3, 142.3, 142.7, 142.8, 142.9, 143.2, 143.6, 143.7, 143.9, 144.0, 144.0, 144.0, 144.0, 144.0, 144.3, 144.3, 144.4, 144.5, 144.6, 144.6, 144.8, 144.9, 145.0, 145.1, 145.2, 145.3, 145.6, 145.9, 146.1, 146.2, 146.5, 146.6, 146.8, 146.9, 147.3, 147.3, 147.4, 147.7, 148.10, 148.3, 148.4, 152.3, 154.9, 158.2, 158.48, 197.9. HRMS calculated 793.0653, found 793.0659.

7.15. 1-Hydro-2-(3′-propanol) 1,2-dihydro[60]fullerene 12

To 1-hydro-2-[3′-(*tert*-butyldimethylsiloxy)propyl]-1,2-dihydro[60]fullerene **5** (46 mg, 0.051 mmol) dissolved in THF (5 mL) was added 6 N HCl (1 mL). After stirring the reaction for 2 h at room temperature, the solvent was removed in vacuo and the residue was dissolved in CS_2 (15 mL). The solution was washed with water (2×5 mL), dried over anhydrous $MgSO_4$ and the solvent evaporated to give a brown residue, which was purified by flash chromatography (SiO_2 toluene/ethanol, 4:1) to give 1-hydro-2-(3′-propanol) 1,2-dihydro[60]fullerene **12** (30 mg, 75% yield) as a brown solid: mp >300 °C; ^{1}H NMR (5:2 CS_2/$CDCl_3$) 2.82 (m, 2H), 3.56 (m, 2H), 4.19 (m, 2H), 6.51 (s, 1H). HRMS calculated 781.0653, found 781.0634.

7.16. 1-Methyl 4-(3′-propanol) 1,4-dihydro[60]fullerene 13a

To 1-methyl-4-[3′-(*tert*-butyldimethylsiloxy)propyl] 1,2-dihydro[60]fullerene **7a** (302 mg, 0.33 mmol) in THF (80 mL) was added 6 N HCl (5 mL) dropwise. After stirring the reaction for 2 h at room temperature, the solvent was removed in vacuo and the residue was dissolved in CS_2 (30 mL). The solution was washed with water (2×15 mL), dried over anhydrous $MgSO_4$ and the solvent evaporated to give a brown residue, which was purified by flash chromatography (SiO_2 toluene/ethanol, 10:1) and washed with pentane (3×2 mL) to give 1-methyl 4-(3′-propanol) 1,2-dihydro[60]fullerene **13a** (100 mg, 41.6% yield) as a black solid: mp >300 °C; ^{1}H NMR (5:2 CS_2/$CDCl_3$) 2.62 (m, 2H), 2.87 (s, 3H), 3.13 (m, 2H), 4.25 (m, 2H). HRMS calculated 795.0810, found 795.0811.

7.17. 1-Benzyl-4-(3′-propanol) 1,4-dihydro[60]fullerene 13b

To 1-benzyl-4-[3′-(*tert*-butyldimethylsiloxy)propyl] 1,4-dihydro[60]fullerene **7b** (244 mg, 0.25 mmol) in THF (50 mL) was added 6 N HCl (5 mL). After stirring the reaction for 2 h at room temperature, the solvent was removed in vacuo and the residue was dissolved in $CHCl_3$ (50 mL). The solution was washed successively with brine (2×25 mL) and water (2×25 mL), and dried over anhydrous $MgSO_4$. Following purification by flash chromatography (SiO_2, toluene/ethanol, 4:1), 1-benzyl-4-(3′-propanol) 1,4-dihydro-[60]fullerene **13b** (155 mg, 72% yield) was obtained as a black solid: mp >300 °C; ^{1}H NMR ($CDCl_3$) 2.04 (m, 2H), 2.38 (m, 2H), 3.81 (m, 2H), 4.31 (m, 2H), 7.47 (m, 1H), 7.55 (t, *J*=6.8, 2H), 7.67 (d, *J*=7.2, 2H).^{13}C NMR ($CDCl_3$) 30.6, 38.4, 49.5, 59.3, 61.0, 63.1, 128.0, 129.0, 131.6, 136.9, 138.1, 138.6, 139.2, 139.2, 141.0, 142.3, 142.4, 142.5, 142.8, 142.9, 143.0, 143.0, 143.4, 143.4, 143.5, 143.5, 144.1, 144.2, 144.3, 144.3, 144.4, 144.6, 144.6, 144.7, 144.7, 145.0, 145.1, 145.2, 145.2, 145.3, 145.4, 145.8, 145.9, 147.2, 147.3, 147.3, 147.3, 147.6, 147.6, 147.7, 148.9, 149.0, 149.0, 149.1, 151.0, 153.2, 158.0, 158.5. HRMS calculated 871.1123, found 871.1114.

7.18. 1-Hydro-2-[3′-(L-ALA-OEt) propyl]-1,2-dihydro[60]fullerene 14

1-Hydroxy-7-azabenzotriazole (HOAt) (10.13 mg, 0.0748 mmol) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDC·HCl, 14 mg, 0.07 mmol) were added to a suspension of 1-hydro-2-(butanoic acid)-1,2-dihydro[60]fullerene (40 mg, 0.0498 mmol) **9** in dichloromethane (10 mL). The mixture was stirred at room temperature for 15 min. A solution of HCl·H-L-Ala-OEt (8.36 mg, 0.0548 mmol) and *N*-methyl morpholine (5.8 μL, 5.54 mg, 0.0548 mmol) in 1 mL of dichloromethane was added to the suspension and the resulting mixture was stirred 30 min at room temperature. The solvents were evaporated and the resulting brown residue was purified by flash chromatography (SiO_2, toluene/ethylacetate, 4:1) to yield 1-hydro-2-[3′-(L-Ala-OEt) propyl]-1,2-dihydro[60]fullerene **14** (75 mg, 66% yield) as a black solid: mp >300 °C; ^{1}H NMR ($CDCl_3$) 1.34 (t, *J*=7.2, 3H), 1.54 (d, *J*=6.8, 3H), 2.77 (t, *J*=7, 1H), 2.95 (m, 2H), 3.47 (m, 2H),4.28 (q, *J*=7.2, 2H), 4.75 (m, 1H), 6.29 (d, *J*=6.8, 1H), 6.56 (s, 1H); ^{13}C NMR ($CDCl_3$) 14.1, 18.7, 22.6, 36.0, 46.2, 48.2, 59.5, 61.7, 64.7, 135.9, 136.5, 140.1, 140.2, 141.6, 141.6, 141.9, 142.0, 142.1, 142.2, 142.5, 143.2, 144.6, 144.7, 145.4, 145.4, 145.8, 146.1, 146.2, 146.3, 146.3, 146.4, 147.1, 147.3, 147.4, 153.8, 155.7, 171.6, 173.2; UV–vis ($CHCl_3$) λ_{max} 253 nm, 385, 432. HRMS calculated 908.1287, found 908.1279.

7.19. Cyclopenta-[1,2]-[60]fullerene-3′-triisopropylsilyloxy 16a

Triisopropylsilyl-trifluoromethanesulfonate (0.0476 mL, 54 mg, 0.177 mmol) was added to a suspension of 1-hydro-2-(propanal)-1,2-dihydro[60]fullerene **10b** (106 mg, 0.136 mmol) in DMF (40 mL). After stirring for 30 min at 0 °C, 0.0415 mL (30 mg, 0.297 mmol) of triethylamine was added. The solution was allowed to warm to room temperature and subsequently stirred for 12 h at 80 °C. The mixture was dissolved in CS_2 and washed with ice-cold dilute acid followed by a solution of $NaHCO_3$ and brine. The solution was then dried over anhydrous $MgSO_4$ and the solvent evaporated. The resulting brown residue was purified by flash chromatography (SiO_2, toluene) to yield cyclopentanyl-1,2-[60]fullerene-3′-(triisopropylsilyl)oxy **16a** (95 mg, 75% yield) as a black solid: mp >300 °C; ^{1}H NMR (5:1, CS_2/$CDCl_3$) 1.07 (s, 3H), 1.21 (s, 6H), 1.22 (s, 6H), 1.24 (s, 6H), 2.92 (m, 1H), 3.09 (m, 1H), 3.58 (m, 1H), 3.93 (m, 1H), 5.96 (dd, *J*=4, 4, 1H); ^{13}C NMR (5:1, CS_2/$CDCl_3$) 12.8, 18.0, 18.2, 18.2, 34.1, 39.5, 68.3, 69.4, 83.8, 134.9, 135.6, 135.9, 136.9, 139.3, 139.8, 140.0, 140.1, 141.5, 141.5, 141.6, 141.7, 141.8, 141.9, 141.9, 141.9, 142.0, 142.0, 142.1, 142.3, 142.3, 142.4, 142.4, 142.8, 142.9, 142.9, 144.2, 144.3, 144.3, 144.4, 145.0, 145.0, 145.0, 145.1, 145.1, 145.4, 145.5, 145.5, 145.7, 145.8, 145.8, 145.8, 146.0, 146.3, 146.0, 146.4, 147.1, 147.1, 147.1, 154.5, 155.1, 156.6, 156.9; UV–vis ($CHCl_3$) λ_{max} 253 nm, 327, 404, 431. HRMS calculated 935.1831, found 935.1817.

7.20. Cyclopenta-[1,2]-[60]fullerene-3′-hydroxy 16b

Triethylamine (0.0457 mL, 33 mg, 0.327 mmol) were added to a suspension of 1-hydro-2-(3′-propanal)-1,2-dihydro[60]fullerene **10b** (30 mg, 0.136 mmol) in DMF (40 mL). The solution was stirred for 12 h at 80 °C. The mixture was dissolved in CS_2 and washed with water and brine. The solution was then dried over anhydrous $MgSO_4$ and the solvent evaporated. The resulting brown residue was purified by flash chromatography (SiO_2, CS_2/CH_2Cl_2, 4:1) to afford cyclopentan-3′-ol-1,2-[60]fullerene **16b** (25 mg, 83% yield) as a black solid: mp >300 °C; ^{1}H NMR ($CDCl_3$) 2.72 (d, *J*=4, 1H), 2.93 (m, 1H), 3.15 (m, 1H), 3.63 (m, 1H), 3.97 (m, 1H), 5.83 (m, 1H); ^{13}C NMR ($CDCl_3$) 33.1, 39.7, 69.6, 76.7, 82.7, 134.8, 135.5, 135.7, 138.0, 139.7, 140.0, 140.1, 141.5, 141.6, 141.7, 141.7, 141.8, 141.9, 141.9, 141.9, 142.1, 142.2, 142.4, 142.4, 142.4, 142.9, 144.2, 144.2, 144.3, 144.3, 145.0, 145.0, 145.1, 145.1, 145.1, 145.2, 145.2, 145.3, 145.3, 145.7, 145.8, 145.8, 146.0, 146.0, 146.1, 147.0, 147.1, 152.0, 154.6, 156.4, 156.7; UV–vis ($CHCl_3$) λ_{max} 255 nm, 325, 404, 431. HRMS calculated 779.0497, found 779.0513.

7.21. Cyclopenta-[1,2]-[60]fullerene-3′-oxyethanol 17

Triispropylsilyl-trifluoromethanesulfonate (21.54 μL, 26.44 mg, 0.119 mmol) was added to a suspension of 1-hydro-2-[2′-(1″,3″-dioxolanyl)ethyl]-1,2-dihydro[60]fullerene **4b** (82 mg, 0.099 mmol) in CS_2 (40 mL). After stirring for 30 min at 0 °C, 23.42 μL (17.38 mg, 0.134 mmol) of *N*,*N*′-diisopropylethylamine was added. The solution was allowed to warm to room temperature and subsequently stirred for 12 h at 30 °C. The solvent was evaporated and the resulting brown residue was purified by flash chromatography (SiO_2, CS_2/CH_2Cl_2, 9:1) to afford cyclopentanyl-1,2-[60]fullerene-3′-oxyethanol **17** (72 mg, 88% yield) as a black solid: mp >300 °C; ^{1}H NMR (5:1, CS_2/$CDCl_3$) 2.11 (t, *J*=6.2, 1H), 2.97 (m, 1H), 3.07 (m, 1H), 3.57 (m, 1H), 3.83 (m, 1H), 3.94 (m, 2H), 4.15 (m, 2H), 5.03 (dd, *J*=4.4, 5.6, 1H); ^{13}C NMR (5:1, CS_2/$CDCl_3$) 30.4, 39.3, 62.1, 69.7, 72.4, 73.3, 90.7, 135.0, 135.7, 135.9, 136.9, 139.9, 140.1, 140.2, 140.2, 141.7, 141.9, 142.0, 142.0, 142.0, 142.1, 142.2, 142.2, 142.2, 142.3, 142.5, 142.6, 142.6, 143.0, 143.1, 144.4, 144.5, 144.5, 145.2, 145.3, 145.3, 145.3, 145.6, 145.7, 145.7, 145.8, 146.0, 146.1, 146.2, 146.2, 146.3, 146.7, 147.3, 153.7, 155.2, 156.5, 156.7; UV–vis ($CHCl_3$) λ_{max} 257 nm, 356, 403, 431. HRMS calculated 823.0759, found 823.0733.

7.22. Cyclopenta-[1,2]-[60]fullerene-3′-*N*-phenylamine 19

To a suspension of 1-hydro-2-(3′-propanal)-1,2-dihydro-[60]fullerene **10b** (56 mg, 0.072 mmol) in benzene (40 mL) were added 6.55 μL (6.69 mg, 0.072 mmol) of aniline and 800 mg of molecular sieves (4 Å). After stirring at room temperature for 3 days, the solvent was evaporated. The resulting brown residue was purified by flash chromatography (SiO_2, toluene) to yield cyclopenta-[1,2]-[60]fullerene-3′-*N*-phenylamine **19** (40 mg, 65% yield) as a black solid: mp >300 °C; ^{1}H NMR (5:1, CS_2/$CDCl_3$) 2.95 (m, 1H), 3.11 (m, 1H), 3.69 (m, 1H), 3.74 (m, 1H), 4.50 (d, *J*=8.8, 1H), 5.66 (dt, *J*=5.2, 7.2, 1H), 6.76 (t, *J*=7.4, 1H), 6.94 (d, *J*=8, 2H), 7.22 (t, *J*=8, 2H); ^{13}C NMR (5:1, CS_2/$CDCl_3$) 31.7, 40.0, 67.2, 70.0, 74.6, 113.9, 118.4, 129.4, 134.7, 135.0, 135.1, 135.1, 135.1, 135.2, 136.8, 139.7, 139.7, 140.1, 140.2, 141.4, 141.6, 141.7, 141.8, 141.9, 141.9, 141.9, 142.1, 142.2, 142.4, 142.4, 142.5, 142.8, 144.2, 144.3, 144.3, 144.9, 145.0, 145.0, 145.1, 145.1, 145.1, 145.3, 145.3, 145.4, 145.4, 145.8, 145.8, 145.9, 145.9, 146.0, 146.1, 146.1, 146.3, 146.5, 146.6, 147.0, 147.3, 151.8, 155.7, 155.7, 157.1; UV–vis ($CHCl_3$) λ_{max} 256 nm, 325, 430. HRMS calculated 854.0969, found 854.0963.

7.23. 1,4,7,8-Functionalised fullerene 20

Aniline (16.78 μL, 17.15 mg, 0.184 mmol) and 4 g of molecular sieves (4 Å) were added to a suspension of 1-methyl-4-(3′-propanal)-1,4-dihydro[60]fullerene **10b** (146 mg, 0.184 mmol) in benzene (100 mL). After stirring at room temperature for 3 days, the solvent was evaporated. The resulting brown residue was purified by flash chromatography (SiO_2, toluene) to yield compound **20** (60 mg, 38% yield) as a black solid: mp >300 °C; ^{1}H NMR (5:1, CS_2/$CDCl_3$) 2.30 (m, 1H), 2.35 (s, 3H), 2.48 (m, 1H), 2.78 (m, 1H), 3.01 (m, 1H), 3.81 (d, *J*=2.8, 1H), 4.27 (ddd, *J*=2.8, 4.4, 7.8, 1H), 6.57 (d, *J*=8, 1H), 6.69 (m, 1H), 7.02 (m, 1H), 7.84 (d, *J*=8, 1H); ^{13}C NMR (5:1, CS_2/$CDCl_3$) 27.3, 34.0, 40.6, 53.5, 57.9, 60.8, 65.6, 72.0, 116.8, 120.5, 123.9, 129.3, 129.5, 133.4, 137.0, 137.3, 138.2, 138.3, 140.0, 140.1, 141.2, 141.4, 141.8, 141.8, 142.1, 142.3, 142.4, 142.7, 143.2, 143.5, 143.7, 143.9, 144.3, 144.5, 144.7, 144.8, 144.9, 145.0, 145.1, 145.2, 145.2, 145.3, 146.0, 146.1, 146.3, 146.4, 146.6, 146.8, 146.9, 147.0, 147.0, 147.2, 147.6, 147.6, 147.9, 148.1, 148.3, 148.5, 148.8, 148.9, 149.5, 149.8, 151.6, 151.9, 155.8, 155.9, 158.1; UV–vis ($CHCl_3$) λ_{max} 252 nm, 314, 406, 446, 526, 682. HRMS calculated 868.1126, found 868.1142.

7.24. 1-Benzyl-4-[3′-bromopropyl] 1,4-dihydro[60]fullerene 23

N-(1-Bromo-2-methylprop-1-enyl)-*N*,*N*-dimethylamine (15 mg, 0.084 mmol) was added dropwise to 1-benzyl-4-(3′-propanol) 1,4-dihydro[60]fullerene **13b** (60 mg, 0.069 mmol) in dichloromethane (30 mL). The reaction mixture was then stirred for 45 min at room temperature. Addition of 20 mL of dichloromethane, work-up with brine (2×10 mL) and water (2×10 mL) and drying of the organic layer over anhydrous $MgSO_4$ gave a brown solid after removal of the solvent. Purification by flash chromatography (SiO_2, toluene/ethanol, 4:1) followed by washing with pentane (3×2 mL) gave 1-benzyl-4-[3′-bromopropyl] 1,4-dihydro[60]fullerene **23** (26 mg, 40% yield) as a brown solid: mp >300 °C; ^{1}H NMR ($CDCl_3$) 1.96 (m, 2H), 2.62 (m, 2H), 3.51 (m, 2H), 4.29 (m, 2H), 7.49 (m, 1H), 7.56 (t, *J*=6.8, 2H), 7.67 (d, *J*=7.2, 2H); ^{13}C NMR ($CDCl_3$) 30.4, 33.2, 40.6, 48.9, 49.4, 58.7, 60.9, 127.9, 128.8, 131.5, 136.6, 137.0, 138.1, 139.1, 142.3, 142.8, 142.8, 142.9, 143.0, 143.0, 144.1, 144.3, 144.3, 144.5, 144.6, 144.6, 144.6, 144.7, 144.7, 145.0, 145.1, 145.1, 145.2, 145.3, 145.4, 145.8, 146.5, 146.6, 147.2, 147.3, 147.3, 147.3, 147.5, 147.6, 149.0, 149.0, 149.1, 151.2, 152.8, 152.9, 158.3. HRMS calculated 933.0279, found 933.0250.

7.25. 1-Benzyl-4-[α-propyl-*tert*-butylglycinate benzophenone imine] 1,4-dihydro[60]fullerene 24

Lithium diisopropylamide (0.071 mmol, 35 μL of 2 M stock) was added to THF (2 mL) and cooled to −78 °C. After 15 min, *N*-(diphenylmethylene)glycine *tert*-butyl ester (21 mg, 0.071 mmol) in THF (2 mL) was added via cannula and the solution was maintained at −78 °C for 45 min. After this time, the solution was added dropwise via cannula to 1-benzyl-4-[3′-bromopropyl] 1,4-dihydro[60]fullerene **23** (66 mg, 0.071 mmol) in THF (10 mL) at −78 °C. The solution was maintained at −78 °C for 1 h, and then warmed to room temperature and held at this temperature for a further hour. The reaction was then quenched with saturated NH_4Cl (5 mL), dichloromethane (25 mL) was added and the isolated organic layer was washed successively with brine (2×10 mL) and water (2×10 mL). The solution was then dried over anhydrous $MgSO_4$ and the solvent evaporated. The resulting brown residue was purified by flash chromatography (SiO_2, toluene) to give small amounts (<8 mg) of two products with very similar R_f values (0.51, 0.52).

Compound **24a**: ^{1}H NMR ($CDCl_3$) 1.44 (s, 9H), 2.6 (m, 2H), 2.9 (m, 1H), 3.2 (m, 2H), 3.3 (m, 1H), 3.53–4.02 (A, B, m *J*1=12.4, *J*2=12.8, 2H), 5.24 (s, 1H), 7.1–7.9 (m, 15H); ^{13}C NMR ($CDCl_3$) 28.5, 42.8, 43.8, 47.1, 58.4, 59.9, 65.3, 70.8, 75.2, 127.4, 128.4, 128.6, 129.1, 129.7, 129.9, 130.2, 131.2, 135.2, 135.2, 136.1, 136.6, 139.2, 139.5, 140.6, 141.5, 141.7, 141.8, 142.5, 142.7, 142.9, 143.3, 143.5, 144.1, 144.8, 145.2, 145.3, 145.4, 145.5, 145.6, 145.7, 145.7, 145.9, 145.9, 146.1, 146.8, 146.8, 147.0, 147.1, 147.1, 147.2, 147.8, 148.1, 148.3, 148.6, 148.9, 149.5, 149.9, 150.4, 151.4, 152.6, 154.9, 156.2, 156.3, 161.2, 163.9, 168.3, 172.4. HRMS calculated 1148.2589, found 1148.2637.

Compound **24b**: ^{1}H NMR ($CDCl_3$) 1.52 (s, 9H), 2.5 (m, 2H), 2.9 (m, 1H), 3.01 (m, 2H), 3.4 (m, 1H), 3.87–3.94 (A, B, m, *J*1=12.8, *J*2=12.8, 2H), 5.19 (s, 1H), 7.2–7.7 (m, 15H). HRMS calculated 1148.2589, found 1148.2633.

7.26. Computational studies

Molecular modelling calculations were run using the native OPLS force field in Hyperchem 7.52, Hypercube. Molecular dynamics (MD) simulations were run with the following conditions: simulation run time 10,000 ps, simulation step 1 fs, heat time 100 ps, starting temperature 0 K, simulation temperature 300 K and temperature step 10 K. Simulations were run in vacuo and repeated in duplicate. Conformational searches (CS) on **24a** and **24b** were run with the following procedure: (1) all possible dihedral angles were chosen (eight overall) responsible for different conformations of the benzyl and the propylglycinate moieties; (2) in each step, 1–8 dihedrals were varied randomly; (3) the geometry thus obtained was optimized and retained if passing some post-convergence tests (chirality inversion, duplicate structures); (4) after 1000 steps, all structures within 6 kcal/mol were retained (each of them may be found multiple times in the CS), and the lowest energy 50 structures analyzed.

Ring current shifts were estimated with the classical formula $\Delta\sigma(\text{ppm})=\Delta\chi[(1-3\cos^2\psi)/12\pi r^3]$ valid for a nucleus lying at distance r (in Å) from the centre of the aromatic ring, with the centre-nucleus direction forming an angle ψ with respect to the ring. For the benzene diamagnetic anisotropy, a value $\Delta\chi=1200$ Å^3 was used.

Acknowledgements

Financial support by the European Union *(Plasmabarb: Contract # G5RD-CT-1999-00173)* and IECB is gratefully acknowledged.

References and notes

1. (a) Nakamura, E.; Isobe, H. *Acc. Chem. Res.* **2003**, *36*, 807–815; (b) Yang, J.; Alemany, L. B.; Driver, J.; Hartgerink, J. D.; Barron, A. R. *Chem.—Eur. J.* **2007**, *13*, 2530–2545; (c) Yang, J.; Wang, K.; Driver, J.; Yang, J.; Barron, A. R. *Org. Biomol. Chem.* **2007**, *5*, 260–266; (d) Sofou, P.; Elemes, Y.; Panou-Pomonis, E.; Stavrakoudis, A.; Tsikaris, V.; Sakarellos, C.; Sakarellos-Daitsiotis, M.; Maggini, M.; Formaggio, F.; Toniolo, C. *Tetrahedron* **2004**, *60*, 2823–2828.
2. (a) Taylor, R.; Walton, D. R. M. *Nature* **1993**, *363*, 685–693; (b) Hirsch, A. *The Chemistry of Fullerenes*; Thieme: Stuttgart, New York, NY, 1994; (c) Diederich, F.; Isaacs, L.; Phillip, D. *Chem. Soc. Rev.* **1994**, 243–255; (d) Hirsch, A. *Synthesis* **1995**, 895–913; (e) Hirsch, A. *Top. Curr. Chem.* **1999**, *199*, 1–65; (f) Da Ros, T.; Prato, M. *Chem. Commun.* **1999**, 663–669.
3. (a) Wudl, F. *Acc. Chem. Res.* **1992**, *25*, 157–161; (b) Rubin, Y.; Khan, S.; Freedberg, D. I.; Yeretzian, C. *J. Am. Chem. Soc.* **1992**, *115*, 344–345; (c) Prato, M.; Suzuki, T.; Foroudian, H.; Li, Q.; Khemani, K.; Wudl, F.; Leonetti, J.; Little, R. D.; White, T.; Rickborn, B.; Yamago, S.; Nakamura, E. *J. Am. Chem. Soc.* **1993**, *115*, 1594–1595; (d) An, Y.-Z.; Anderson, H. L.; Rubin, Y. *J. Org. Chem.* **1993**, *58*, 4799–4801; (e) Maggini, M.; Scorrano, G.; Prato, M. *J. Am. Chem. Soc.* **1993**, *115*, 9798–9799.
4. (a) Bingel, C. *Chem. Ber.* **1993**, *126*, 1957–1959; (b) Hirsch, A.; Lamparth, I.; Karfunkel, H. R. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 437–438.
5. (a) Fagan, P. J.; Krusic, P. J.; Evans, D. H.; Lerke, S. A.; Johnston, E. *J. Am. Chem. Soc.* **1992**, *114*, 9697–9699; (b) Hirsch, A.; Grösser, T.; Skiebe, A.; Soi, A. *Chem. Ber.* **1993**, *126*, 1061–1067; (c) Hirsch, A.; Soi, A.; Karfunkel, H. R. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 766–768; (d) Komatsu, K.; Murata, Y.; Takimoto, N.; Mori, S.; Sugita, N.; Wan, T. S. M. *J. Org. Chem.* **1994**, *59*, 6101–6102; (e) Keshavarz, M. K.; Knight, B.; Srdanov, G.; Wudl, F. *J. Am. Chem. Soc.* **1995**, *117*, 11371–11372; (f) Timmerman, P.; Anderson, H. L.; Faust, R.; Nierengarten, J.-F.; Habicher, T.; Seiler, P.; Diederich, F. *Tetrahedron* **1996**, *52*, 4925–4927; (g) Fujiwara, F.; Murata, Y.; Wan, T. S. M.; Komatsu, K. *Tetrahedron* **1998**, *54*, 2049–2058.
6. Mikami, K.; Matsumoto, S.; Ishida, A.; Takamuku, S.; Suenobu, T.; Ukuzumi, S. *J. Am. Chem. Soc.* **1995**, *117*, 11134–11141.
7. (a) Corey, E. J.; Raju, N. *Tetrahedron Lett.* **1983**, *24*, 5571–5574; (b) Keinan, E.; Sinha, S. C.; Singh, S. P. *Tetrahedron* **1991**, *47*, 4631–4638.
8. Kadish, K. M.; Gao, X.; Van Caemelbecke, E.; Suenobu, T.; Fukuzumi, S. *J. Phys. Chem. A* **2000**, *104*, 3878–3883.
9. Maurer, K. W.; Armstrong, R. W. *J. Org. Chem.* **1996**, *61*, 3106–3116.
10. Kitagawa, T.; Takeuchi, K. I. *Bull. Chem. Soc. Jpn.* **2001**, *74*, 785–800.
11. (a) Gonzalez, R.; Wudl, F.; Pole, D. L.; Sharma, P. K.; Warkentin, J. *J. Org. Chem.* **1996**, *61*, 5837–5839; (b) Kitagawa, T.; Tanaka, T.; Murakita, H.; Nishikawa, A.; Takeuchi, K. *Tetrahedron* **2001**, *57*, 3537–3547; (c) Meier, M. S.; Bergosh, R. G.; Gallagher, M. E.; Spielmann, H. P.; Wang, Z. *J. Org. Chem.* **2002**, 5946–5952.
12. (a) See Ref. 8. (b) Murata, Y.; Komatsu, K.; Wan, T. S. M. *Tetrahedron Lett.* **1996**, *37*, 7061–7064; (c) Fukuzumi, S.; Suenobu, T.; Hirasaka, T.; Arakawa, R.; Kadish, K. M. *J. Am. Chem. Soc.* **1998**, *120*, 9220–9227.
13. Allard, E.; Rivière, L.; Delaunay, J.; Dubois, D.; Cousseau, J. *Tetrahedron Lett.* **1999**, *40*, 7223–7226.
14. Hamada, M.; Hino, T.; Kinbara, K.; Saigo, K. *Tetrahedron Lett.* **2001**, *42*, 5069–5071.
15. Rubin, Y.; Ganapathi, P. S.; Franz, A.; An, Y.-Z.; Qian, W.; Neier, R. *Chem.—Eur. J.* **1999**, *5*, 3162–3184.
16. O'Donnell, M. J.; Bennett, W. D.; Wu, S. *J. Am. Chem. Soc.* **1989**, *111*, 2353–2355.
17. Ghosez, L.; Georges-Koch, I.; Patiny, L.; Houtekie, M.; Bovy, P.; Nshimyumukiza, P.; Phan, T. *Tetrahedron* **1998**, *54*, 9207–9222.
18. Lipkowitz, K. B.; Cavanaugh, M. W.; Baker, B.; O'Donnell, M. J. *J. Org. Chem.* **1991**, *56*, 5181–5192.
19. Corey, E. J.; Xu, F.; Noe, M. C. J. *Am. Chem. Soc.* **1997**, *119*, 12414–12415.
20. Lygo, B.; Crosby, J.; Lowdon, T. R.; Peterson, J. A.; Wainwright, P. G. *Tetrahedron* **2001**, *57*, 2403–2409.
21. Burley, G. A.; Keller, P. A.; Pyne, S. G.; Ball, G. E. *Chem. Commun.* **1998**, 2539–2540.
22. Burley, G. A.; Keller, P. A.; Pyne, S. G. *Chem. Commun.* **2000**, 1717–1718.
23. Burley, G. A.; Keller, P. A.; Pyne, S. G.; Ball, G. E. *Chem. Commun.* **2001**, 563–564.
24. Burley, G. A.; Keller, P. A.; Pyne, S. G.; Ball, G. E. *J. Org. Chem.* **2002**, *67*, 8316–8330.
25. Kadish, K. M.; Gao, X.; Caemelbecke, E. V.; Hirasaka, T.; Suenobu, T.; Fukusumi, S. *J. Phys. Chem. A.* **1998**, *102*, 3898–3906.
26. Whitesides, G. M.; Grocki, J. J.; Holtz, J. D.; Steinberg, H.; Roberts, J. D. *J. Am. Chem. Soc.* **1965**, *87*, 1058–1064.
27. Whitesides, G. M.; Holtz, D.; Roberts, J. D. *J. Am. Chem. Soc.* **1964**, *86*, 2628–2634.
28. Anslyn, E. V.; Dougherty, D. A. *Modern Physical Organic Chemistry*; University Science Books: Sausalito, CA, 2006; p. 184 ff.
29. Rusyniak, M. J.; Ibrahim, Y. M.; Wright, D. L.; Khanna, S. N.; El-Shall, M. S. *J. Am. Chem. Soc.* **2003**, *125*, 12001–12013.
30. Hobza, P.; Kabelác, M.; Šponer, J.; Mejzlík, P.; Vondrášek, J. *J. Comput. Chem.* **1997**, *18*, 1136–1150.
31. Wenkert, D.; Ferguson, S. B.; Porter, B.; Qvarnstrom, A.; McPhail, A. T. *J. Org. Chem.* **1985**, *50*, 4114–4119.