Electrochemically Induced Retro-Cyclopropanation Reactions

M. Ángeles Herranz,[a] François Diederich,[b] and Luis Echegoyen*[a]

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The efficient removal of methano addends from fullerenes using reductive electrochemistry is a versatile and useful reaction, which was initially called the retro-Bingel reaction since it was observed for the first time on bis(alkoxycarbonyl)methano adducts, commonly known as Bingel adducts. Since its initial discovery, this reaction has been successfully employed in the separation of enantiomers and constitutional isomers of fullerenes, which in some cases were otherwise not accessible. Even more interesting than the retro-Bingel reaction was the electrochemically induced isomerization that bis-methano adducts of C_{60} exhibit, and which was referred to as the "shuffle". The combination of both reactions gave interesting results during the electrolysis of tetrakis-, pentakis-, and hexakis-Bingel adducts of C_{60}. The selective removal of Bingel-type addends, while leaving other addends undisturbed, was also investigated. More recently, it was observed that in addition to bis(alkoxycarbonyl)methano adducts, electrochemical reduction of other methano adducts, such as spiromethanofullerenes, could also result in removal of the methano addends, thus the reaction was more generally denoted as retro-cyclopropanation. In some of the spiromethanofullerenes investigated, and depending on the solvent used, an electrochemically induced intermolecular addend transfer was observed, which provided a regioisomeric distribution that differed significantly from that obtained by a synthetic route. We have recently shown that singly bonded dimers are formed as intermediates during retro-cyclopropanation reactions. In this microreview, we describe the general observations that led to the initiation of these exciting electrochemical investigations, review the differences between the chemical and electrochemical methodologies in retro-cyclopropanation reactions and explore the mechanisms involved during addend removal.
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1. Introduction

Among the various methods used for the functionalization of C_{60}, cyclopropanations have been found to be very efficient for the preparation of fullerene derivatives.[1] Of

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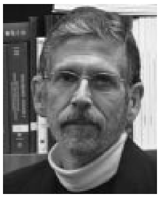
[a] Department of Chemistry, Clemson University
Clemson, SC 29634, USA
Fax: (internat.) + 1-864-656-6613
E-mail: luis@clemson.edu
[b] Laboratorium für Organische Chemie, ETH-Hönggerberg
Wolfgang-Pauli-Strasse 10, 8093 Zürich, Switzerland

Maria Ángeles Herranz was born in Vic (Barcelona), Spain in 1972. She received her B.Sc., M.Sc., and PhD degrees in 1995, 1996 and 2001, respectively, from the Universidad Complutense de Madrid (UCM) for work in the synthesis and study of the properties of donor-acceptor systems based on [60]fullerene and tetrathiafulvalene, under the supervision of Professors Nazario Martín and Carlos Seoane. In March 2001, she joined Professor Echegoyen's research group at the University of Miami, Florida, as a postdoctoral fellow. After a very fruitful nine months stay, she decided to continue her postdoctoral work with Prof. Echegoyen at Clemson University, South Carolina, where she coordinated the design and establishment of the new research laboratories. Her research focuses on the electrochemical and spectroelectrochemical characterization of new dyads derived from cyclooctatetraene and tetrathiafulvalene, and on the characterization of fullerene-derived materials employing electrochemical, ESR, and NMR techniques.

Born in the Grand-Duchy of Luxembourg (1952), François Diederich studied chemistry at the University of Heidelberg (1971−1977). He joined the group of Prof. Heinz A. Staab for his diploma and doctoral thesis which he completed in 1979 with the synthesis of kekulene. Following postdoctoral studies with Prof. Orville L. Chapman at UCLA (1979−1981), investigating arynes in argon matrices, he returned to Heidelberg for his Habilitation at the Max-Planck-Institut für Medizinische Forschung (1981−1985). Subsequently, he joined the faculty in the Department of Chemistry and Biochemistry at UCLA where he moved up the ranks to become Full Professor of Organic and Bioorganic Chemistry in 1989. In 1992, he returned to Europe, joining the Laboratory of Organic Chemistry at the ETH Zürich. Since 2002, he is the Head of the newly founded Department of Chemistry and Applied Biosciences at the ETH. His research interests, documented in more than 420 publications, span from medicinal chemistry, with a focus on molecular recognition studies, to dendritic mimics of globular proteins, and to advanced fullerene- and acetylene-based materials with novel optoelectronic properties.



Luis Echegoyen was born in La Habana, Cuba, in 1951. He obtained both his B.Sc. and Ph.D. degrees from the University of Puerto Rico in Rio Piedras in 1971 and 1974, respectively. After a one-year postdoctoral stay at the University of Wisconsin-Madison, subsequent appointments have included Chemist I, Nuclear Magnetic Resonance Spectroscopist at Union Carbide Corporation, Bound Brook, New Jersey, (1975−1977); Assistant Professor at the University of Puerto Rico, (1977−1980); Associate Professor at the University of Puerto Rico, (1980−1982); Adjunct Associate Professor at the University of Maryland, College Park, Maryland, (1982−1983); Program Officer, Chemical Dynamics Program, National Science Foundation, Washington, D.C., (1982−1983); Associate Professor at the University of Miami, Coral Gables, Florida, (1983−1987); Member of the Chemistry Advisory Committee-NSF (1986−1989); and Professor at the University of Miami, Coral Gables, Florida (1987−2001). In 2002 he was appointed to serve as Chair of the Department of Chemistry at Clemson University, in South Carolina. His research interests cover fullerene chemistry, electrochemistry and supramolecular chemistry, with special emphasis on electrosynthetic routes developed for the preparation of fullerene derivatives, preparation of new materials by electrocrystallization techniques and design of self-assembled, surface-confined, templated monolayer sensors. He is the author or co-author of over 220 research articles.

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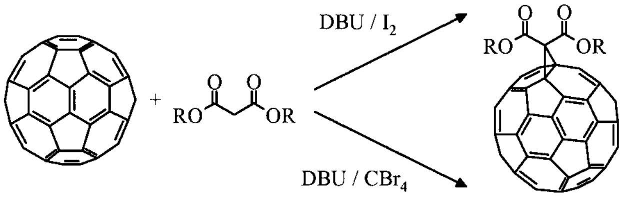
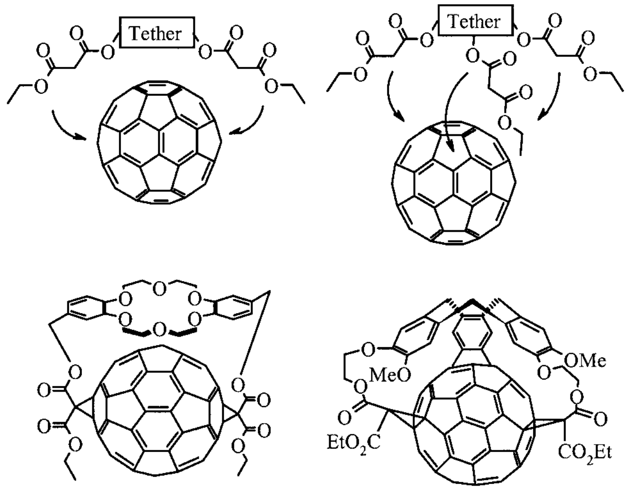
these cyclopropanations, the Bingel reaction probably provides the highest yields of the corresponding methanofullerenes under relatively mild conditions.[2] The Bingel reaction can be carried out starting directly from malonates. In this case, an α-halomalonate is generated in situ, and direct treatment of C_{60} with malonates in the presence of iodine,[3] or CBr_4,[4] and a base results in the formation of a cyclopropane ring fused to the fullerene core at a [6,6]-junction (Scheme 1). Direct treatment of C_{60} with diethyl malonate gives a 57% yield of the corresponding monoadduct, and when diethyl bromomalonate is used instead a 45% yield is obtained.[4]



Scheme 1. The Bingel reaction

A second malonate addition provides a mixture of seven bis-adducts, and although the *equatorial (e)* (15.5% yield) and *trans-3* bis-adducts (12% yield) are favored, the high-yield synthesis of fullerene multi-adducts is hampered by poor regioselectivity.[5] In order to have regioisomeric control of bis- and tris-adduct formation, the group of Diederich et al. introduced the concept of tether-directed remote functionalization (Figure 1).[6,7] Bis-malonates that are connected by a spacer of predetermined length and rigidity enforce a particular regioisomeric bis-addition pattern on the surface of the fullerene. Using this approach, a variety of bis(cyclopropanated) [60]fullerene derivatives have been prepared. For example, employing a dibenzo-18-crown-6 tether, the *trans-1* bis-adduct **1** was prepared in relatively high yields (30% vs. the 0.8−2% obtained from a stepwise Bingel reaction with diethyl 2-bromomalonate),[8,9] and the complex regiochemistry of bis-additions to C_{70} can be controlled as demonstrated in recent contributions.[10−12]

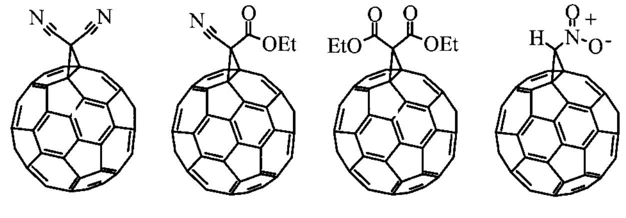


1 **2**

Figure 1. Tether-directed remote functionalization

The number of possible regio- and stereoisomers increases to forty six in the case of tris-adducts in which three of the thirty [6,6]-bonds are cyclopropanated;[13] examples of tether-directed syntheses of tris-adducts directly from C_{60} are still very rare. The first reported example employed a cyclotriveratrylene (CTV) tether, which allowed the synthesis of an approximately 1:1 mixture of (*trans-3, trans-3, trans-3*)-(**2**) and (*e*,*e*,*e*) tris-adducts (overall yield about 20%).[14] More recently, several cyclo-[*n*]-alkylmalonates were synthesized and allowed to react with C_{60} with high regioselectivity by the Hirsch group.[15] The macrocycles containing identical alkyl spacers selectively form bis- and tris-adducts of C_{60} with rotational symmetry. In contrast, when macrocycles with two different alkyl spacer lengths are used, the reaction exclusively yields C_s-symmetric bis-adducts.[15]

The electrochemical properties of all of these bis- and tris-adducts have been studied in reasonable detail.[16,17] One surprising observation was made with bis(methano)-fullerenes with a *cis-2* addition pattern, that exhibited a chemically irreversible, second one-electron reduction: they were found to lose their methano substituent during controlled-potential electrolysis. This particular observation, together with the reported electrochemical instability of the monoanion of 1,2-methano[60]fullerene-61,61-dinitrile (**3**)[18a] and diethyl 1,2-methano-[60]fullerene-61,61-dicarboxylate (**5**)[18b] (Figure 2) led to the initiation of the work summarized here.



3 **4** **5** **6**

Figure 2. Some methanofullerenes reported to be unstable under CV and Osteryoung Square-Wave Voltammetry (OSWV) conditions

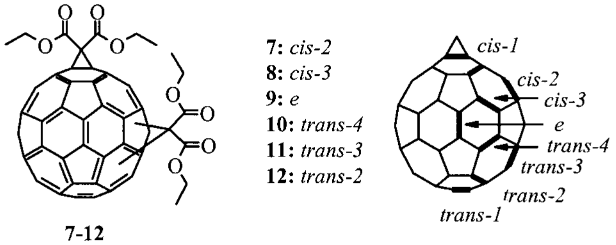
Wudl and co-workers studied the cyclic voltammetric (CV) behavior of derivatives **3**−**6** (Figure 2) at room and low temperatures, and they clearly observed that **3**, **4** and **6** were converted, even at −72 °C, to C_{60}, upon addition of one electron. Compound **5** showed, on the cyclic voltammetric timescale, evidence of a chemical reaction following the fourth reduction wave.

Here we have compiled all of the results obtained from these initial observations, from the discovery of a new electrochemically induced reaction, to its useful applications in fullerene chemistry, including mechanistic details and analysis of the intermediates involved in the course of the reaction.

2. The Discovery of the Retro-Bingel Reaction

2.1. The Methano-Addends can Move on the Surface: "The Shuffle"

As briefly mentioned in the Introduction, a surprising observation during the analysis of the electrochemical behavior of the *cis-2* bis-methanofullerene **7** (Figure 3) marked the beginning of this work. During the course of that investigation, it was discovered that upon controlled-potential electrolysis (CPE) of **7** with one electron per molecule, followed by re-oxidation, the *cis-2* isomer disappeared completely, and a mixture of other bis-isomers was formed.[19]



7-12

Figure 3. C_{60} bis-adducts **7−12** subjected to CPE at the first and second reduction potentials

The initial CV of compound **7** is shown in Figure 4, where the irreversibility of the second reduction process is evident from the voltammogram. However, after CPE at the first reduction potential, the second reduction appeared to be more chemically reversible than in the original CV, and appeared similar to those of the other bis-adducts such as **8** and **9** (Figure 4). Undoubtedly, a chemical reaction occurs following a one-electron electrolysis, which "shuffles" the addends on the fullerene surface. HPLC analysis of the electrolyzed solution showed that the *cis-2* isomer had completely disappeared and the *e* bis-adduct became the predominant isomer in the newly formed product mixture (*e*: 57%; *trans-3*: 31%; *trans-4*: 8%; *cis-3*: 4%). Surprisingly, when similar experiments were conducted with other synthetically available bis-adducts (**7−12**), electrolysis did not produce any changes in the CVs and the starting materials were recovered unaltered. Isomeric conversion upon 1e$^-$ CPE occurred only for the *cis-2* bis-methanofullerene **7**.

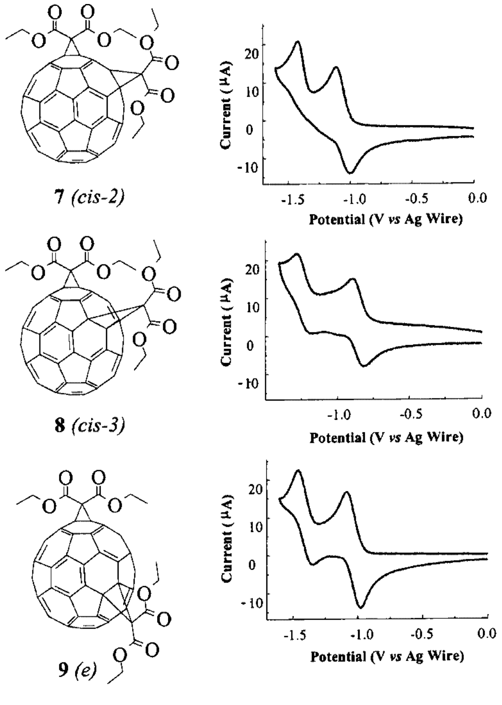


Figure 4. CVs of *cis-2*, *cis-3*, and *e* bis-adducts **7−9** in CH_2Cl_2 (0.1 M Bu_4NPF_6) at a scan rate of 100 mV·s^{-1}

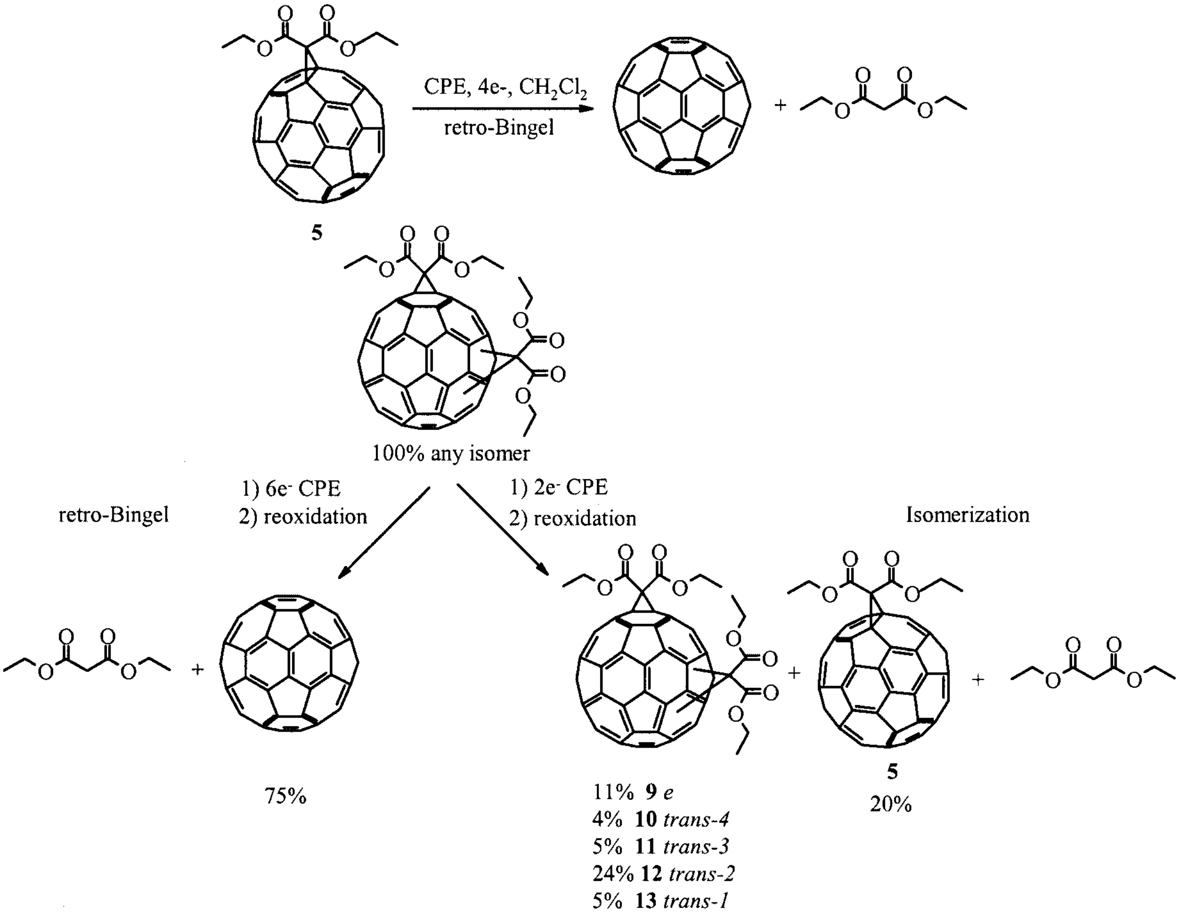
These observations led to the investigation of the behavior of the bis-methanofullerenes **7−12** upon 2e$^-$ CPE. In most of the cases, a substantial amount of current remained after two electrons had been transferred. Stopping the electrolysis at this point, followed by re-oxidation and HPLC analysis of the products, showed practically identical relative product distributions, regardless of which isomer was electrolyzed.[19] These distributions were different from that obtained if a second Bingel addition is conducted on the monoadduct.[5] The product mixtures obtained by electrolysis of the bis-adducts **7−12** did not contain any of the *cis-2* or *cis-3* bis-adducts. The major isomer formed was always the *trans-2* derivative (40−50%), approximately 10% of the *trans-1* bis-adduct was produced in every case, and the *e*-isomer was also formed in a high percentage (ca. 25%).[20,21] The preferred formation of both *e*- and *trans*-isomers could be a consequence of their inherently higher stability, as compared to the *cis* derivatives,[5] and the fact that the same product distribution was observed after 2e$^-$ CPE of individual bis-adducts **7−12** seemed to indicate that the isomerization occurred under thermodynamic control.

Proof that the isomerization occurred *intra*- and not *inter*molecularly was obtained from the 2e$^-$ CPE of a solution containing a 1:1 ratio of the mixture of seven isomers of $(EtOOC)_2C{<}C_{60}{>}C(COOEt)_2$ and seven of $(PrOOC)_2C{<}C_{60}{>}C(COOPr)_2$. Analysis of the final product mixtures by HPLC, as well as by MALDI-TOF mass spectrometry, failed to detect any crossover products.[21]

The other important observation made at that time was that if the electrolysis of bis-adducts **7−12** was not stopped after transferring two electrons, but allowed to proceed to completion so that the currents reached background levels, both addends were removed and pure C_{60} was recovered in 75% yield (see Scheme 2).

2.2. Removal of the Methano-Addends: The Retro-Bingel Reaction

As already mentioned in the previous section, reductive electrolysis of bis(ethoxycarbonyl) methano fullerenes can also result in the removal of the addends. Mono-adduct **5**, when analyzed by CV, exhibited two reversible one-electron waves.[22] Chemical irreversibility of the second reduction was only evident at very low scan rates. When **5** was subjected by CPE to its monoanionic state (−1.2 V vs. Ag wire), the charge transferred corresponded exactly to one electron per molecule, and the resulting anion was very



Scheme 2. Retro-Bingel and isomerization reactions

stable, with no apparent decomposition after thirty minutes. However, when CPE was conducted at approximately the reduction potential for the formation of the dianion, the current did not decrease to background level after four electrons were added. Clear changes in the CV indicated that some chemical reaction took place. Upon re-oxidation and product analysis, an 82% yield of pure C_{60} was obtained, and the new electrochemically induced reaction which efficiently removed the cyclopropane ring adduct was called the retro-Bingel reaction.[21,22]

In order to test the generality of the new electrolytic reaction, in addition to the experiments mentioned with bisadducts **7−12**, a mono bis(ethoxycarbonyl)methano-C_{70} was also investigated following the same electrolysis protocol. Purification of the solution after coulometric reduction (which requires a net charge transfer of four electrons per molecule) followed by oxidation, resulted in a 70% yield of isolated C_{70}. This conversion occurred stepwise as new waves between 0 and −0.5 V vs. Ag started to appear during electrolysis, providing evidence for the formation of intermediates.[22] The nature of these intermediates has been recently determined and will be the subject of discussion in section 6.[23]

2.3. Systematic Application of the Electrochemical Retro-Bingel Reaction to Multiple Malonate Adducts of C_{60}

Additional applications of the retro-Bingel reaction, acting in concert with the isomerization reaction, started to emerge immediately after the discovery of these electrochemical processes. CPE studies of seven different isolated and characterized isomers of tris[bis(ethoxycarbonyl)methano]-[60]fullerene demonstrated that after discharging two electrons per molecule in CH_2Cl_2,[24] a competition between retro-Bingel and isomerization reactions takes place, with preferential loss of one or two addends. Figure 5 shows a series of CVs for the (*e*,*e*,*e*) isomer **14**, as representatives of typical voltammograms for these compounds at room temperature. On the basis of the voltammetric information, the retro-Bingel reaction was evident. Notice the appearance of a small (irreversible) oxidation peak at −1.02 V when the potential is reversed after the second reduction wave. The voltammetric response of compound **14** was also studied at a lower temperature (figure not shown), and improved reversibility of the first and second reductions was observed when the potential was scanned cathodically throughout the potential window of the solvent.[24]

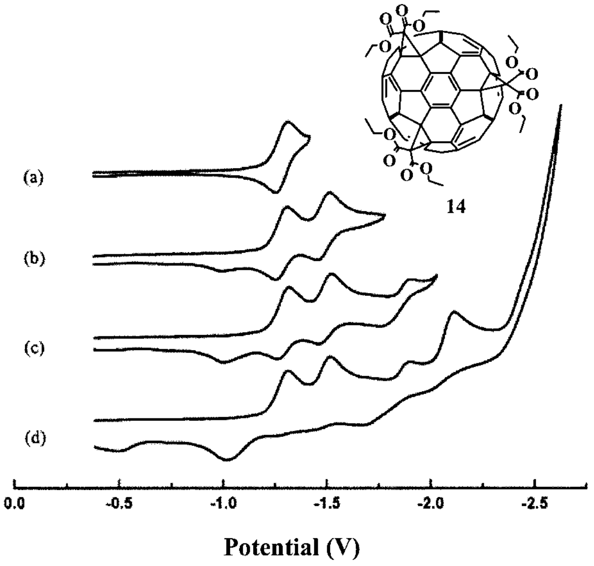


Figure 5. Cyclic voltammograms of (*e*,*e*,*e*) tris-adduct **14** in CH_2Cl_2 (+ 0.1 M Bu_4NPF_6) at a scan rate of 200 $mV{\cdot}s^{-1}$, reversing the scan rate after the (a) first, (b) second, (c) third, and (d) fourth reduction waves

Calculations at the PM3 and AM1 levels revealed that upon two-electron reduction, these tris-adducts exhibit opposite reactivity to when they are in their neutral state. This led to thermodynamic as opposed to kinetic control of product distributions. In agreement with the CV data, it was also observed that lowering the temperature during electrolysis increased the degree of isomerization.[24]

Controlled-potential electrolysis of tetrakis-, pentakis-, and hexakis-Bingel adducts of C_{60} was performed in an attempt to maximize the production of tris-adducts with well-defined regiochemistry,[25] which still remains an important goal in fullerene chemistry. Indeed, easy access to the (*e*,*e*,*e*)-hexaacid derived from **14**[26,27] was most desirable, because it exhibits a high solubility in water and is a very potent antioxidant.[28]

In order to determine the ideal conditions for tris-adduct production, penta-adduct **15** was subjected to CPE transferring 1, 4, 6, and $11.5e^-$, respectively, at room temperature (Figure 6). The retro-Bingel reaction was observed to occur partially, even after the transfer of only $1e^-$, producing predominantly tetrakis adducts. The cyclic voltammograms of **15** after $4e^-$ CPE (see c in Figure 6) showed a positive shift of the first reduction wave and at least two quasi-reversible waves. Product analyses evidenced the presence of tris- (25%), tetrakis- (49%), pentakis- (21%), and in a small percent (4%), bis-adducts. After $6e^-$ CPE, the cyclic voltammogram (e in Figure 6) resembled the one after $4e^-$ CPE and product analyses provided a slightly different adduct distribution (mono: 7%, bis: 12%, tris: 30%, tetrakis: 35%, pentakis: 6%). Finally, the cyclic voltammogram of **15** after $11.5e^-$ CPE (d in Figure 6) exhibited three reversible waves characteristic of the parent C_{60}, which was isolated in a 48% yield after column chromatography.

In general, typical isolated yields of tris-adducts were around 30%, and (*trans-4*, *trans-2*, *e*) and (*trans-3*, *trans-4*, *e*) were the predominant regioisomers. Interestingly, the desired (*e*,*e*,*e*) isomer was detected, but only in very small amounts.[25]

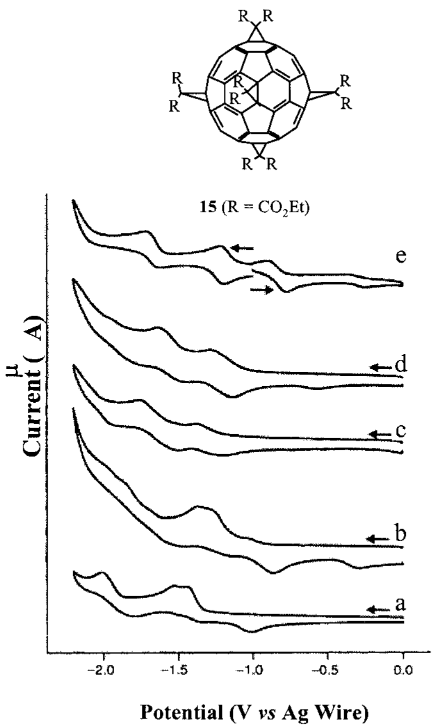


Figure 6. Cyclic voltammograms in CH_2Cl_2 (0.1 M Bu_4NPF_6) under vacuum and at room temperature, scan rate 100 $mV{\cdot}s^{-1}$: (a) pentakis adduct **15**; (b) **15** after $1e^-$ CPE; (c) after $4e^-$ CPE; (d) after $6e^-$ CPE; (e) after $11.5e^-$ CPE

2.4. Selective Electrolytic Removal of Bis(ethoxycarbonyl)methano Addends from C_{60} Bis-Adducts

One of the most important considerations in order to test the utility of these reactions was to show that electrochemical reduction could selectively remove Bingel-type adducts while leaving other adducts unaffected.[29,30]

Regioselective multiple functionalization of fullerenes usually requires the temporary introduction of an addend that can subsequently be removed. In order to achieve this, several protocols have been applied in the past, such as Diels−Alder additions of 9,10-dimethylanthracenes,[31] Diels−Alder addition with buta-1,3-dienes,[17,32,33] or dipolar cycloadditions with formation of isoxazoline rings.[34] The possibility of a chemoselective electrochemical removal of a Bingel addend from the fullerene core in the presence of a different addend was then comprehensively investigated.[29]

A variety of well-characterized mixed bis-adducts of C_{60} were prepared, where one of the addends was always a bis(ethoxycarbonyl)methano group (Figure 7). All of the cases showed that CPE led to the selective removal of the Bingel addend, while the other one was retained. The isolated yields of the corresponding mono-adducts were over 60%, making them synthetically useful in the preparation, through a protective-deprotective protocol, of fullerene derivatives with the desired functionalization scheme.[29]

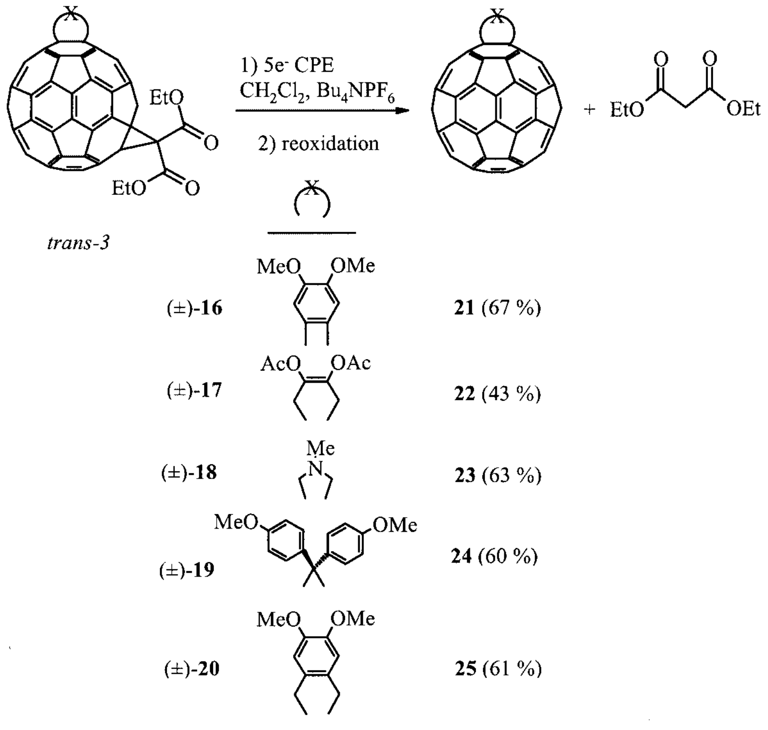


Figure 7. Selective removal of bis(ethoxycarbonyl)methano addends in mixed C_{60} bis-adducts

3. The Scope of the Retro-Cyclopropanation Reaction

The design of novel fullerene derivatives exhibiting better electron-acceptor properties than C_{60} is still a major objective within the context of developing optically and electrochemically active systems for different applications.[35] Wudl and Martín described the electrochemical properties of the methanofullerenes **26** and **30**, which bear quinone-type addends (Figure 8).[36] These compounds exhibit irreversible electrochemistry, most probably resulting from the cleavage of one of the cyclopropane bonds connecting the addend to C_{60} upon reduction.[37,38] These observations, coupled with those of the retro-Bingel reaction, motivated the study of the CPE behavior of compounds **26**−**31** (Figure 8).

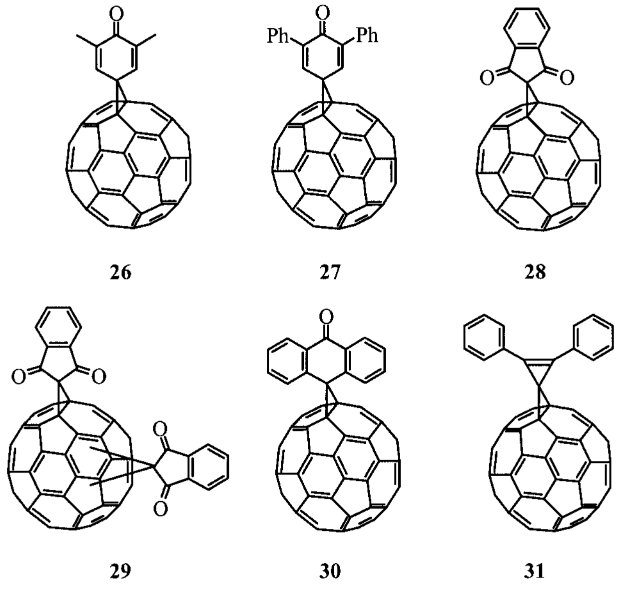


Figure 8. Spiromethanofullerenes that exhibit retro-cyclopropanation reactions under reductive electrochemistry

Experiments with these fullerene adducts were first carried out in dichloromethane solutions (see some of the CVs obtained in Figure 9). The indandione derivative **28** yielded 58% and the anthraquinone compound **30** 65% of recovered C_{60} after 3.7 and 2.3e⁻ CPE, respectively, followed by reoxidation.[39,40]

These observations clearly showed that the retro-Bingel reaction was more general than originally believed and was redefined as a retro-cyclopropanation reaction.

These retro-cyclopropanation reactions were demonstrated to be mechanistically complex processes. The quinoid spiromethanofullerene **26** did not cleave with formation of C_{60}, nor was the starting material recovered, when subjected to the same electrochemical protocol. Additionally, methanofullerene **31** led to the formation of insoluble products after 2.8e⁻ CPE. As mentioned earlier, all retro-cyclopropanation reactions described thus far were performed in CH_2Cl_2, a convenient solvent for fullerene derivative electrochemistry due to solubility considerations. However, the observation of methano adduct formation with C_{84}^{2-} in this solvent, to yield $C_{84}{>}(CH_2)_n$,[41] led to the study of the reactivity between C_{60}^{n-} and CH_2Cl_2.[42] It was determined that the mono- and dianions of C_{60} are stable in CH_2Cl_2, but the trianion resulted in the addition of up to

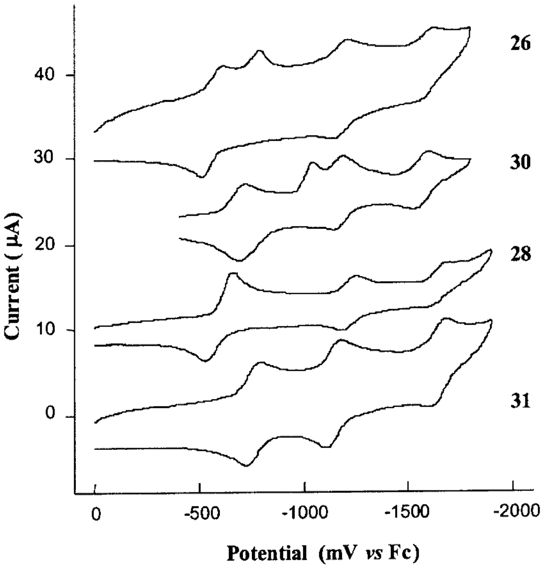


Figure 9. Cyclic voltammograms of spiromethanofullerenes **26**, **28**, **30** and **31** in CH_2Cl_2

three methano bridges to C_{60}, as clearly observed by mass spectrometry.[42] It was consequently decided to change the solvent to THF to test the generality of the retro-cyclopropanation reaction and to avoid unwanted reactions with the solvent. These experiments led to some very interesting results.[43,44]

Compounds **26−30** were subjected to CPE in (+ 0.1 M Bu_4NPF_6) THF and the products were separated and analyzed.[43,44] CPE of **28**, as a representative example, was performed at a more cathodic potential (ca. 100−150 mV) than the first two-electron reduction wave (the CV in THF is very similar to the one of **28** in Figure 9), and 1.8e⁻ per molecule were discharged. Reoxidation and purification yielded 81% of a mixture of fullerene products, consisting of 40% C_{60}, 27% recovered **28**, and a third fraction (14%) with higher polarity. Product analysis showed this fraction to be composed of the bis-adducts: fullerenes with two indandione groups attached (MALDI-TOF: *m*/*z* = 1009). The formation of bis-adducts from the electrolysis of **28** was further proven by comparison with the independently prepared mixture of bis-adducts **29** (Figure 10). The mixture of regioisomeric bis-adducts **29** was separated by preparative HPLC chromatography, and the fractions assigned by ^1H NMR and UV/Vis spectroscopy: *trans-2* 14%, *trans-3* 16%, *e* 41%, *cis-3* 5%, *cis-2*, 19%.[43] The regioisomeric bis-adducts obtained by electrolysis were then assigned using HPLC. The regioisomer distribution obtained was clearly different from that obtained from the regular synthetic route (*trans-2* 6%, *trans-3* 11%, *e* 43%, *cis-3* 37%). The significant formation of the *cis-3* regioisomer was, and still is, unprecedented in covalent fullerene chemistry, except when it is selectively targeted using the tether-directed remote functionalization method.[17]

Based on these results, the proposed mechanism for the formation of bis-adducts during the CPE timescale involves the existence of two distinct pathways. When the reductive

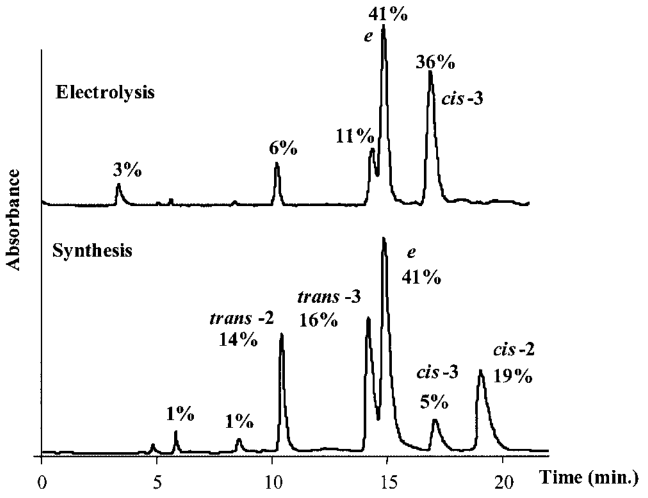


Figure 10. HPLC chromatograms of the regioisomers of bis-adduct **29** obtained electrochemically vs. chemically

electrochemistry leads to the cleavage of one of the two cyclopropane-bridging bonds, the intermediate is capable of either losing the addend from the fullerene cage or of reacting with another molecule. This could lead to the formation of dimers in which the two fullerene cages share one or two addends.[43]

Additionally, CPE of the regioisomeric mixture **29** after the first reduction wave discharged a total of 2e⁻ per molecule. Reoxidation and purification yielded 14% of C_{60}, 33% of monoadduct **28**, as well as 33% of bis-adducts **29**. No tris-adducts were isolated. The regioisomeric distribution of the recovered bis-adducts changed when compared with the starting material, from 5% to 13% of *cis-3*. These derivatives also appear to experience the isomerization reaction previously observed in bis(ethoxycarbonyl)methano fullerenes, but the regioisomeric distributions seem to indicate profound mechanistic differences between the behavior of **29** and **7−12**.

In order to investigate the mechanisms and to characterize the electroreduced intermediates in these retro-cyclopropanation reactions, compounds **32** and **33** were studied as part of a series of compounds incorporating nitrophenyl groups, which, when reduced, exhibit a strong and easily recognizable ESR signal.[45]

The electrochemistry of **32** and **33** was studied by CV (Figure 11) and Osteryoung square-wave voltammetry (OSWV). Compound **32** exhibits three reversible fullerene reductions[46] and one reversible nitrobenzene reduction. Derivative **33** exhibits a higher degree of chemical irreversibility. The electronic differences between the compounds were reflected by the different extent of the retro-cyclopropanation reaction. CPE of **32**, after the third reduction wave, resulted in the formation of 23% C_{60}, while electrolysis of **33** (more "Bingel-like"), after the fourth reduction wave, gave a 52% yield of C_{60}. Furthermore, the formation of bis-adducts was observed in 18% and 11%, respectively.

ESR spectra were recorded after exhaustive electrolysis at the different potentials corresponding to the various

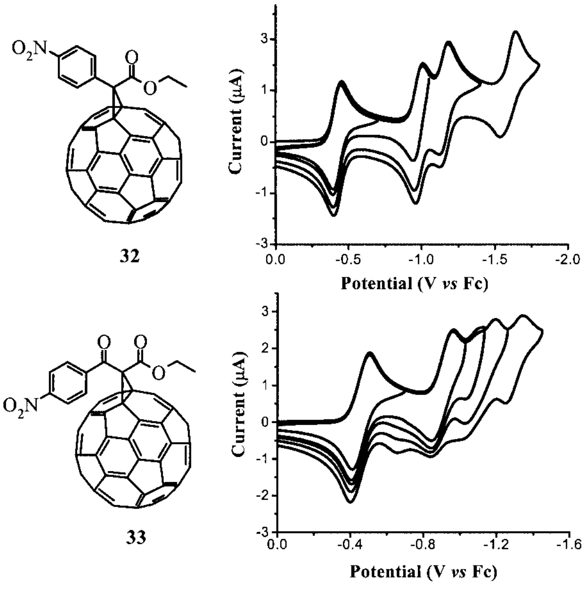


Figure 11. Retro-cyclopropanation reactions of nitrophenyl-methanofullerene derivatives

anionic states. The ESR analysis of compound **33** provided the most complete picture of the series studied, and the spectra, after reductions at 1, 3, and 4e$^-$ CPE, are shown in Figure 12. The ESR spectrum recorded at the first reduction shows a fullerene-based signal, with a g value of 2.00008.[47–49] After a three-electron reduction, the ESR spectrum shows the presence of both nitrophenyl and fullerenyl radicals, with g factors of 2.00471 and 2.00105, respectively. The estimated coupling constants in the p-nitrophenyl-based radical are a_N = 7.35 G, a_o = 2.96 G, and a_m = 0.81 G. The simulated spectrum is shown in Figure 12 (d) and it reproduces exactly the ESR behavior of this p-nitrophenyl-based radical.[45] When the electrolysis was continued for a total of four electrons transferred per molecule, a modified nitrophenyl-based radical dominated the spectrum. It showed four coupling constants, with a_N = 9.18 G, a_o = 3.26 G, a_m = 1.02 G, and an additional doublet splitting of 0.40 G. Why the a_N values change from 7.02 G to 9.18 G is still not understood, but it has been amply documented that this hyperfine coupling constant is very sensitive to solvent and counterion effects.[50,51] The simulated spectrum using these coupling constants is shown in Figure 12 (e), which clearly shows that the radical generated contains a single spin 1/2 nucleus, most probably a proton, which exhibits a hyperfine coupling constant of 0.40 G.

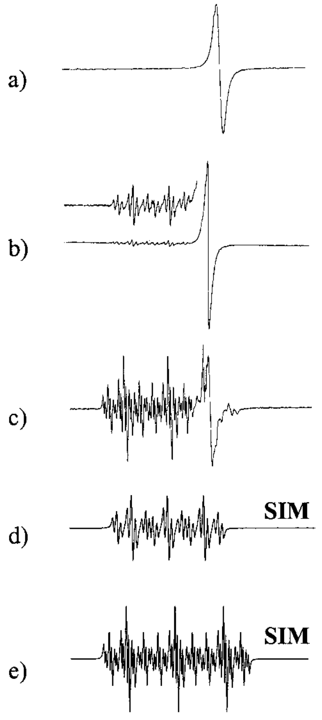


Figure 12. ESR spectra for the reduction of **33** in THF. (a) after one-electron coulometric reduction, (b) after three electrons, (c) four electrons, (d) computer simulation of the p-nitrophenyl-based signal after three-electron reduction, the parameters used for this simulation are: a_N = 7.35 G, a_o = 2.96 G and a_m = 0.81 G, linewidth = 0.30 G, and (e) computer simulation of the p-nitrophenyl-based signal after four-electron reduction; the parameters used for this simulation are: a_N = 9.18 G, a_o = 3.26 G, a_m = 1.02 G and a_H = 0.40 G, linewidth = 0.20 G.

A proposed structure for the radical intermediate was the dicarbonylic radical derivative (with only one proton between both ketone groups) that results from cleavage of the cyclopropane ring. This seemed like a reasonable intermediate based on the previously reported value of a_{Me} = 0.66 G for 4-nitroacetophenone,[50] and was in agreement with the organic intermediates characterized subsequently in retro-cyclopropanation reactions.[52]

4. The Retro-Cyclopropanation Reaction as a Synthetic Tool in the Preparation of Higher Fullerene Isomers

4.1. The Retro-Cyclopropanation Reaction to Prepare Optically Active C_{76} Enantiomers

The first reported useful application of the retro-cyclopropanation reaction was the separation of the enantiomers of C_{76}, using an optically active malonate as a chiral auxiliary.[22] Prior to that work, Hawkins and Meyer performed the kinetic optical resolution of the inherently chiral fullerene D_2-C_{76} by employing the asymmetric Sharpless osmylation reaction.[53] A comparison of the circular dichroism (CD) spectra reported by Hawkins and Meyer for the C_{76} enantiomers[53] with those of a variety of optically active, covalent derivatives of C_{76} prepared by Herrmann and Diederich,[54] revealed a large, unexpected difference in the magnitude of the Cotton effects. Whereas Diederich's covalent C_{76} derivatives displayed bands reaching $\Delta\varepsilon$ values up to 250 $\mathrm{M}^{-1}\cdot\mathrm{cm}^{-1}$, the enantiomerically pure fullerenes reported by Hawkins and Meyer displayed bands with $\Delta\varepsilon$ values up to only 32 $\mathrm{M}^{-1}\cdot\mathrm{cm}^{-1}$.[53,55] In order to reinvestigate the chiroptical properties of C_{76} and to test the power and generality of the retro-cyclopropanation reaction, the pure diastereomeric Bingel-type adducts with (S, S, ^fA) and (S, S,

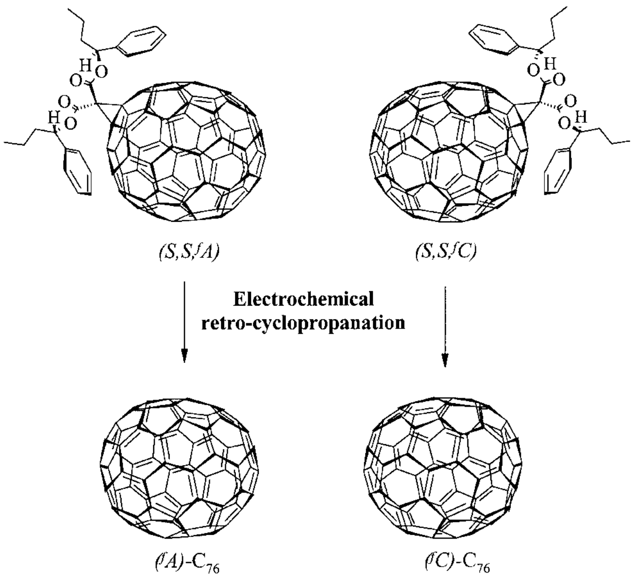


Figure 13. Electrochemically induced retro-cyclopropanation reaction in the preparation of enantiomerically pure C_{76}

^{f}C) configurations (Figure 13) were prepared as previously reported.[56] The general idea was to use a chiral Bingel addend as an auxiliary, to allow separation of the diastereomers followed by removal of the addend via the retro-cyclopropanation reaction, to yield the pure enantiomers of C_{76}.

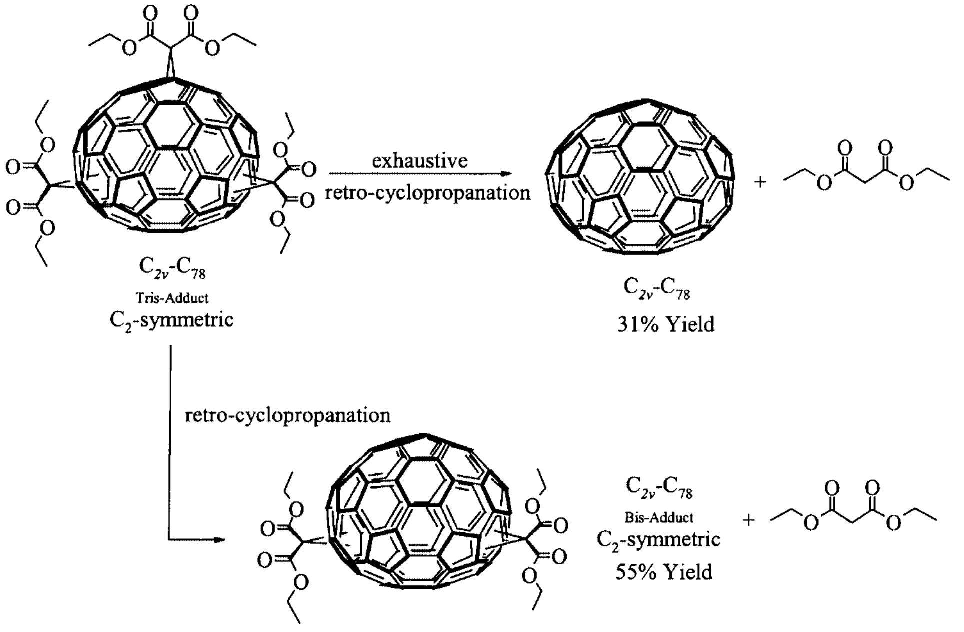
Both diastereoisomers (Figure 13) were independently submitted to CPE and subsequent purification by HPLC. The two enantiomers of C_{76} were obtained in low yields (between 5−10%). So far, it has been impossible to optimize these yields due to the limited availability of the starting diastereoisomers.[56]

The CD spectra of the enantiomers of C_{76} exhibited the expected mirror-image relationship with band positions that were in full agreement with those reported by Hawkins and Meyer.[53,55] In contrast with their results, however, the Cotton effects observed in these spectra were almost a full order of magnitude larger than those previously reported. The $\Delta\varepsilon$ values reached 210 $\text{M}^{-1}\cdot\text{cm}^{-1}$ and were therefore much more in agreement with the values measured previously for optically pure C_{76} derivatives.[55]

4.2. The Retro-Cyclopropanation Reaction to Isolate Pure C_{2v}-C_{78} and a New C_2-Symmetric Bis-Adduct

The retro-cyclopropanation reaction was also applied to a tris-methano adduct of C_{2v}-C_{78} (Scheme 3). During CPE, the tris-adduct was converted cleanly, in 55% yield, to a bis-adduct with C_2 symmetry. Interestingly, this bis-adduct was different from any of the C_{78} bis-adducts that had previously been isolated from the Bingel reaction. Thus, the retro-cyclopropanation reaction was able to afford methanofullerene derivatives that are otherwise not accessible. Continued electrolysis of the C_{78} derivative resulted in the complete removal of the three adducts and the consequent formation of pure C_{2v}-C_{78} in a 31% yield.[21]

Partial electrolysis of other bis-adducts of C_{78}, such as D_3-C_{78}, led to CVs very similar to the ones obtained for the C_{2v}-C_{78} tris-adduct, and to intermediate CVs similar to the ones obtained during its electrolytic reduction. This is probably the result of "shuffling" or isomerization of the addends on the surface of C_{78}.[19]



Scheme 3. Preparation of C_{2v}-C_{78} by retro-cyclopropanation

4.3. The Retro-Cyclopropanation Reaction in the Optical Resolution of D_2-C_{84}

The typical methods used for separating pure constitutional isomers of fullerenes, including those of C_{84}, involve tedious chromatographic separations.[57] Using such methods, a total of nine isomers of C_{84} have been isolated and characterized.[57] By far the most complete electrochemical characterization of C_{84} isomers was provided by Pénicaud and co-workers, who reported electrochemical results for D_2(IV), D_{2d}(II), D_{2d}(I), D_2(II), C_2(IV), and for one of the C_s isomers of C_{84}, tentatively assigned by them as C_s(V).[58] An alternative purification method was possible using the electrochemically induced retro-cyclopropanation reaction, which made use of chiral functionalization of the isomer mixture, followed by HPLC separation and final removal of the functional groups.[41] Since the functional group is chiral, this method offered the advantage of not only providing pure constitutional isomers but also enantiomers after removal of the chiral auxiliary.[41] A conceptually similar approach was recently described by Saunders and co-workers using dimethylanthracene as a reversible derivatization agent to separate seven constitutional isomers of C_{84} in a single stage.[59] Regardless of which separation method was used, electrochemical characterization of the isomers has proven to be revealing.[41,58]

In our approach, a C_{84} fraction of soot enriched in higher fullerenes was treated in *o*-dichlorobenzene at 20 °C with bis[(*S*)-1-phenylbutyl]-2-bromomalonate in the presence of DBU. Subsequent purification by column chromatography yielded four fractions containing (according to mass spectrometry) pure C_{84}, mono-adducts, bis-adducts, and tris-adducts, respectively. The mono-adduct and bis-adduct fractions were further separated by HPLC. The bis-adduct fraction led to six main products. The fourth and fifth fractions corresponded to C_2-symmetrical bis-adducts that gave mirror-image CD spectra with large Cotton effects. With the enantiomerically pure malonate addends, such spectra are characteristic of a pair of diastereoisomeric C_{84} adducts, the CD spectra of which are dominated by the contributions of the enantiomeric π-chromophores of the inherently chiral fullerene cores. The UV/Vis spectra of the two diastereoisomers differed considerably from those of the isolated achiral D_{2d}-C_{84} bis-adduct,[41] which suggested that they are derivatives of the chiral fullerene D_2-C_{84}. This was clearly confirmed after the retro-Bingel reaction and the electrochemical investigations on the parent fullerene enantiomers. CPE of the separated diastereoisomers afforded the pure enantiomers of D_2-C_{84}, and their mirror image CD spectra (Figure 14) corresponded nicely to those reported by Hawkins et al. for samples obtained by kinetic resolution by asymmetric osmylation.[60]

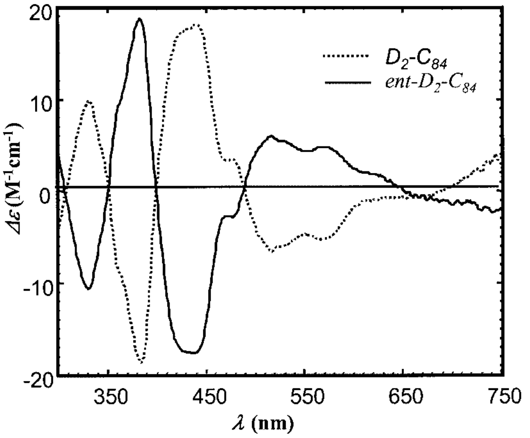
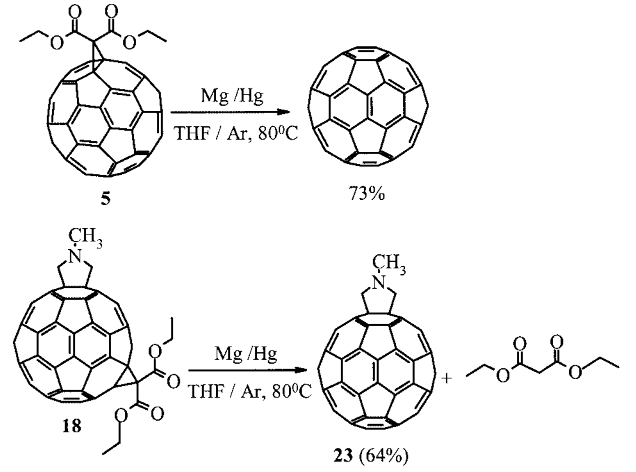


Figure 14. Circular dichroism of D_2-C_{84} enantiomers

5. The Chemical Retro-Cyclopropanation Reaction

The potential of using cyclopropane addends as general protecting-deprotecting groups for fullerene derivative synthesis prompted the investigation of this reaction under chemical reducing conditions.[61] Bis(alkoxycarbonyl)methano addends were removed reasonably efficiently by treatment with amalgamated magnesium powder (10% mercuric bromide) in THF, under reflux for three days. C_{60} was isolated in 73% yield while unchanged starting material was recovered in 23% yield.

The selective removal of the bis(alkoxycarbonyl)methano addend in C_{60} derivatives vs. other addends was also investigated.[61] When **18** (Scheme 4) was allowed to react for three days with amalgamated magnesium (50 equiv.), fulleropyrrolidine **23**[62] was isolated in 64% yield, and the heterocycle was stable under the conditions of the chemical retro-cyclopropanation reaction.



Scheme 4. Chemical retro-cyclopropanation reaction

Another reductive chemical retro-cyclopropanation process was recently reported by Keller, Pyne, et al. They achieved the ring-opening of tethered bis-imino esters of C_{60} upon treatment with five equivalents of boron trifluoride-diethyl ether and 10 equivalents of sodium cyanoborohydride.[63–65] Besides C_{60}, these reactions yielded a new class of 1,2-dihydro[60]fullerenylglycine derivatives, which resulted from the reductive ring-opening of one methanoimino ester moiety and a retro-cyclopropanation reaction of the other.[66]

More recently, these chemical retro-cyclopropanation reactions were carried out in the presence of 18-crown-6 in order to see if there was any effect due to the interactions between the alkaline earth metal cation and the crown macro-ring. The 18-crown-6 was added in a large molar excess (50 mmol) with respect to the fullerene derivative (1 mmol) and this considerably improved the yields obtained and the reproducibility of the reactions.[67,68]

The use of a twofold excess of the highly toxic agent $HgBr_2$ is the main disadvantage of this method when it comes to the development of a large-scale procedure to use methanofullerenes as protective groups in fullerene chemistry. Due to the promising results obtained with the combination $Mg/HgBr_2$/18-crown-6 as the reducing agent, the chemical retro-cyclopropanation reactions were tried for a series of spiromethanofullerenes in the absence of $HgBr_2$ (Figure 15). After the usual workup of the reaction and purification, analysis of the reaction mixture by HPLC and MALDI-TOF showed the formation of the parent C_{60} in 27–52% yield.[68]

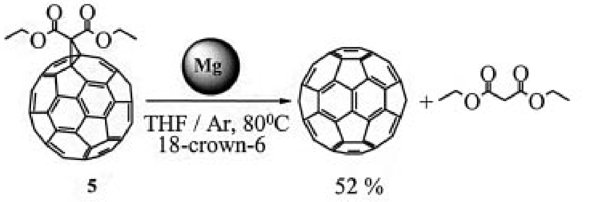


Figure 15. Chemical retro-cyclopropanation reaction in the presence of 18-crown-6

One of the most interesting examples that illustrates the difference between the chemical and electrochemical methodologies involves the *trans-1* conjugate **1**. In this derivative, which possesses a dibenzo-18-crown-6 ether in its structure, the chemical retro-cyclopropanation did not work at all. Interestingly, but not totally unexpectedly, **1** was efficiently converted into C_{60} using the electrochemical retro-cyclopropanation protocol.[67]

The *trans-1* bis-adduct **1** was converted via CPE to its monoanionic state, ca. 100–150 mV cathodically from the first reduction wave. The charge transferred corresponded to one electron per molecule and no changes were observed in the CV. When the CPE was carried out after the second reduction wave, changes in the CV indicated that a chemical transformation had taken place. After 30 minutes of electrolysis, reoxidation of the solution at 0 V (vs. Ag) led to the voltammogram shown in Figure 16 (dashed line) with an anodically shifted first (172 mV) and second reduction (166 mV), compared to the starting fullerenocrown. Purification and analysis of the recovered solution by column chromatography yielded pure C_{60} in 70% yield. In addition, to determine the potential effect of cation complexation on the electroreductive reaction, the CPE of **1** was also carried out in the presence of KPF_6. CPE after the second reduction wave showed a $2e^-$/molecule transfer that was fully reversible; no changes in the cyclic or OSWV voltammograms were observed. The compound was recovered in high yield following reoxidation to its neutral state. Complexation of the DB18-C-6 moiety in **1** by a metal ion seemed to result in pronounced stabilization of the overall structure and inhibition of the retro-cyclopropanation reaction.[67]

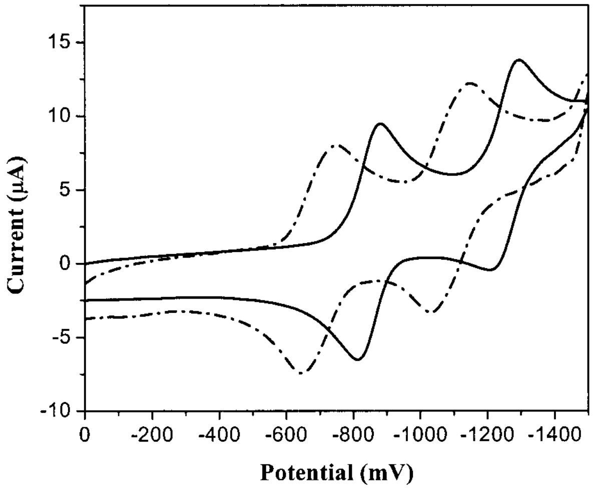


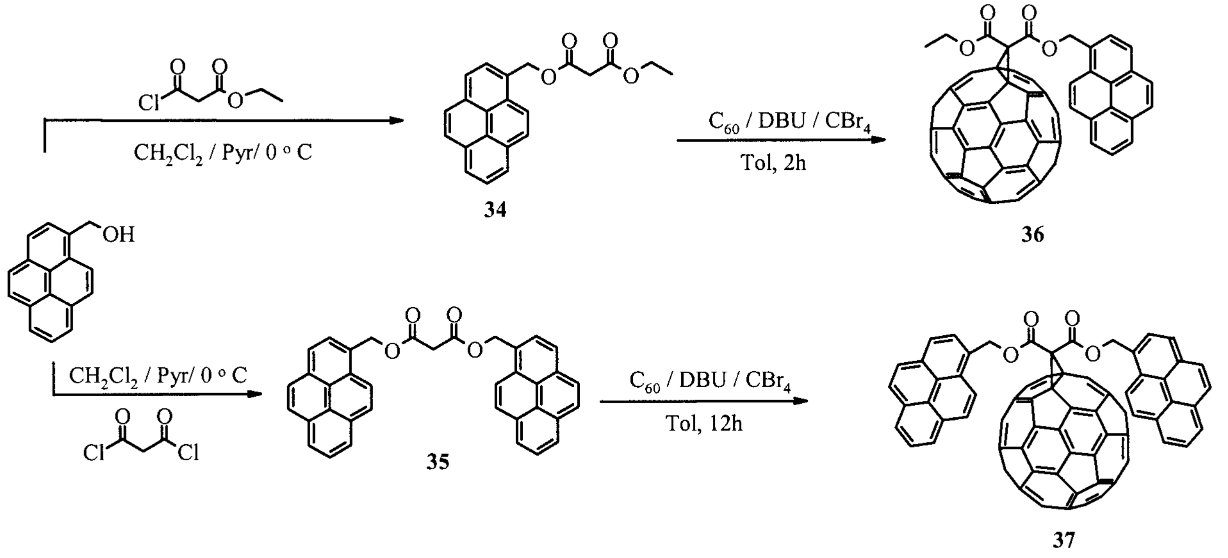
Figure 16. Cyclic voltammograms in CH_2Cl_2 (+ 0.1 M Bu_4NPF_6) at 100 mV·s^{-1} for: (a) (—) *trans-1*-fullerene-dibenzo-18-crown-6 (**1**); (b) (–·–·) same derivative after $2e^-$ CPE and reoxidation

6. Mechanistic Studies on Electrochemically Induced Retro-Cyclopropanation Reactions

While the C_{60} resulting from retro-cyclopropanation reactions was easily identified and purified from the reaction mixtures, it was only recently that other products derived from these reactions were characterized.[52]

Despite several attempts to isolate the intermediates involved in retro-cyclopropanation reactions, the fate of the cyclopropane group was unknown until fluorescent pyrene malonates were prepared and their electrochemical retro-cyclopropanation reactions and corresponding product analyses were performed. Methanofullerenes **36** and **37** were prepared using a synthetic procedure that involves two steps: an esterification reaction of 1-pyrenemethanol with one or two equivalents of ethoxycarbonylacetic acid chloride or malonic acid dichloride to form **34** or **35**, respectively, and Bingel reaction of derivatives **34** and **35**, by direct treatment with C_{60} and CBr_4/DBU in toluene (Scheme 5).

CPE of **36** and **37** performed after the second reduction caused important changes in the voltammograms. After approximately $2.2e^-$ per molecule were transferred, a stable



Scheme 5. Synthesis of the fluorescent methanofullerene derivatives **36** and **37**

intermediate was observed (see below for other details). Analysis of the products obtained after electrolysis of **37** showed a 48% yield of C_{60}, with traces of a compound with similar polarity to that of C_{60}, and a 50% yield of another highly fluorescent product. The major fluorescent fraction was identified after detailed NMR, MALDI-TOF, and UV/Vis studies, as malonate **35**. This was the first time that detailed product analysis after a retro-cyclopropanation reaction showed the presence of the original malonates **34** and **35**, along with C_{60}.[52]

Nuretdinov et al.[70−72] have published several papers in which they studied bis(ethoxycarbonyl)- or bis(ethoxyphosphoryl)fullerene derivatives electrochemically and by ESR spectroscopy. They observed that retro-cyclopropanation occurs, and on the basis of cyclic voltammetry and the number of exchanged electrons, calculated following Nicholson's treatment,[73] they reported rate constants for the chemical processes involved in the retro-cyclopropanation reaction. However, the proposed mechanism, which involves the possibility of a dimerization process, was not supported by simulations or product characterizations.

Digital simulation of the cyclic voltammetric results of some methanofullerenes has also afforded a better understanding of the mechanistic details involved in these electroreductive reactions.[69] The study was conducted with different C_{60} derivatives in which the addends result in different electrochemical responses. They range from the non-electroactive addend in **5** to the electroactive and highly interacting unit in spiromethanofullerene **28**. Electrochemical data obtained at different scan rates for a given potential window were fit with the BAS digital simulation program Digisim. All CV scans were limited to the first three reduction processes in order to focus the attention on the first stages of the electrochemically induced retro-cyclopropanation reaction, which generally occurs after the second reduction process. The proposed mechanism was similar for all the compounds and involved two main chemical reactions in a reversible-square scheme.[69]

Figure 17 (a) shows the CV for a 0.1 mM THF solution of **5**. Three main reduction processes were observed, the first two being reversible and the third one chemically irreversible, in agreement with previous results obtained using other solvents.[22] The small peak between the second and third C_{60}-based reductions was designated II*. This peak became more evident if the scan rate was decreased, indicating that this process was due to some unstable species, arising from chemical reaction. According to these experimental observations, the reaction mechanism proposed and tested by digital simulations was that shown at the top of Figure 17. This scheme accounts for the main features of the recorded CVs. A slow initial chemical reaction was responsible for the smooth peak (II*$_c$) observed in the forward scan (b in Figure 17) and another fast reaction accounted for the irreversibility of the third reduction. Peaks I and II were reversible for all the scan rates recorded. This was in agreement with a reversible chemical reaction, such as the opening of the cyclopropane ring.

Compound **28** showed a more complicated CV behavior, having undergone an initial two-electron reduction followed by another process which was 700 mV more cathodic (see a in Figure 18, solid line). Interestingly, an intermediate irreversible peak was found (II) whose intensity increased with the scan rate relative to the other two peaks. At $V = 3\ V{\cdot}s^{-1}$, the current-function ratios between peaks I, II, and III were evidently different (a in Figure 18, dotted line) from those at $0.5\ V{\cdot}s^{-1}$ (a in Figure 18, solid line). This feature, and the general shape of the curve, was reminiscent of a bi-electronic slow electron-transfer process.[69,74] The simulation shown in Figure 18 (b) was made using the mechanism shown on top of the figure. This diagram was proposed based on the new experiments and the data previously reported.[39−43] The mechanism for **28** involved the

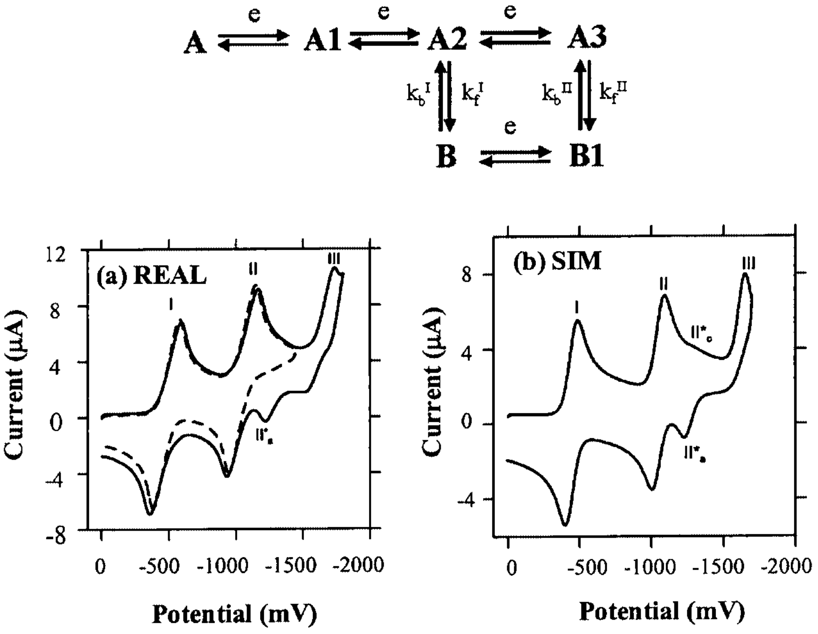


Figure 17. (a) Cyclic voltammetric curves for a 0.1 mM THF solution of **5** at V = 1 V·s^{-1}, Pt as working electrode, Pt-mesh counter electrode and Ag wire as a quasi-reference electrode; (b) best simulated curve for **5**, following the mechanism shown on top of the figure at 0.5 V·s^{-1}

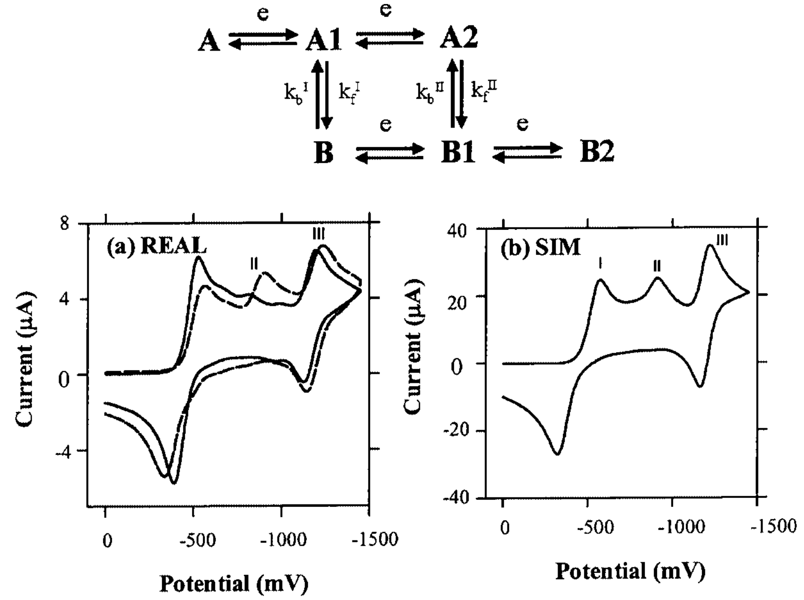


Figure 18. (a) Cyclic voltammetric curves for a 0.5 mM THF solution of **28** at V = 0.5 V·s^{-1} (—) and 3 V·s^{-1} (– – –), Pt as working electrode, Pt-mesh counter electrode and Ag wire as a quasi-reference electrode; (b) best simulated curve for **28**, following the mechanism shown on top of the figure at 3 V·s^{-1}

cleavage of the cyclopropane ring after the first electron reduction. At slower rates, a second electron was transferred at the same potential as the first one. Increasing the scan rate allowed the observation of the increase of the height of the intermediate peak (II), which was due to the original species.

We have considered in this last section the characterization of the products resulting from the electrochemically induced retro-cyclopropanation reactions, as well as the mechanistic evaluation of these processes by means of cyclic voltammetry. However, the ultimate goal in the study of retro-cyclopropanation reactions has been the recent isolation and electrochemical and ESR characterization of the intermediates involved in these processes. The four phosphonate or sulfone methanofullerene derivatives **38**−**41** (Figure 19) were synthesized to probe their stability upon electrolytic reductions. Derivatives **38** and **39** were fairly stable upon electroreduction and did not exhibit retro-cyclopropanation reactions until more than three electrons per C_{60} derivative were transferred. Monoadduct **40** generated C_{60} quantitatively after a 2.8e$^-$ CPE, and **41** showed evidence for the formation of a very stable intermediate that was oxidized at a potential 500 mV more positive than the first fullerene-based reduction of the parent compound.[23]

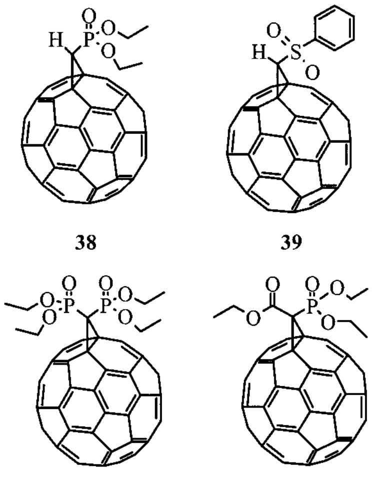


Figure 19. Phosphonate or sulfone methanofullerenes studied by reductive electrochemistry

Controlled-potential electrolyses performed after each reduction step of **41** showed that a chemical reaction occurred when more than 2e$^-$/molecule were transferred, and unexpected changes in the cyclic voltammogram were observed. In Figure 20, the evolution of the electrochemical behavior of the solution was shown as the electrolysis proceeded. The original CV is shown as the solid line in Figure 20 (a) and the CV obtained after the addition of 2.7e$^-$/molecule as the dotted line. Surprisingly and interestingly, the appearance of a new and reversible redox couple (see section marked with a circle), approximately 0.5 V more positive than the first fullerene-based reduction, was clearly observed in the voltammogram. After reoxidation at this stage, the cyclic voltammogram depicted in Figure 20 (see b, solid line) was observed, which corresponded to that of C_{60}. Purification and analysis of the products showed a 57% yield of C_{60} and 33% of recovered starting material. Conversely, if reductive electrochemistry of the intermediate was continued beyond 3e$^-$/C_{60} monoadduct, efficient removal of the cyclopropane ring and formation of C_{60}^{3-} occurred, which immediately reacted with the solvent. Methanofullerenes C_{60}>$(CH_2)_n$ ($n = 1-3$) were recovered after reoxidation.[23]

Komatsu et al.[75] recently reported the isolation of a dimer formed by coupling of monomer radicals with diethoxyphosphorylmethyl groups, and were able to obtain an X-ray crystal structure of it. Other dimeric fullerene derivatives have been generated in different ways[76–82] and similar observations to the ones obtained for **41** — oxidation of a fullerene derivative monoanion followed by a rapid recombination reaction to a neutral singly bonded dimer with 1-octynyl groups on each C_{60} cage — have been reported.[83]

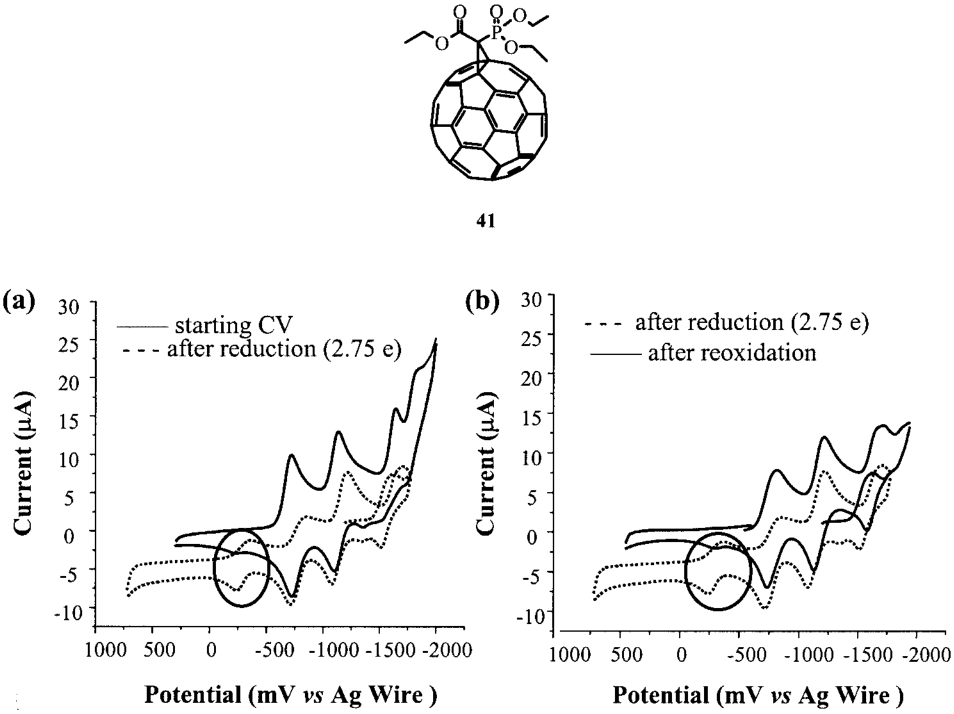


Figure 20. Controlled-potential electrolysis results of **41**; cyclic voltammetric curves for a 0.1 mM CH_2Cl_2 solution of **41** at 100 mV·s^{-1}, GC as working electrode, Pt-mesh counter electrode, and an Ag wire as a quasi-reference electrode

During the study of these derivatives, a relevant article was published by Konarev et al. where a singly bonded C_{70} dimer was characterized by X-ray crystallography.[84] Based on these results, and previous observations that pointed to the formation of intermediates during the electrolysis of a C_{70}-Bingel monoadduct,[22] the electrochemistry of the C_{70} derivative **42** was reinvestigated, paying particular attention to the potential formation of dimeric species.

The electroreduction of **42** was monitored by cyclic voltammetry during controlled-potential electrolysis under high-vacuum conditions using our established protocol. Figure 21 (a) shows that the starting material was electrochemically reduced sequentially by four monoelectronic reduction waves. The reduction steps C_1, C_2, and C_3 were assumed to be fullerene-based, and C_4 was considered to be adduct-based. When potentials were cathodically scanned beyond C_3 and C_4, an intermediate oxidation A_0 could be observed at approximately 500 mV more positive than the first fullerene-based reduction C_1 (see a in Figure 21). Interestingly, this intermediate was also observed when controlled-potential electrolysis was carried out around the first reduction wave, when even fewer than $1e^-/C_{70}$-Bingel monoadduct molecule were discharged. Electrochemical oxidation of the solution led to recovery of the starting material, whereas further reduction resulted in cyclopropane-ring removal.

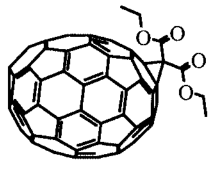
In order to obtain additional information about the intermediates observed, the ESR spectrum (see b in Figure 21) of the electrolysis mixture under vacuum, when less than $1e^-/C_{70}$ adduct were transferred, was recorded. Two main signals were observed: one apparently fullerene-based signal with $g = 1.99995$, and another with $g = 2.00103$. These values were in reasonable agreement with the reported ionic complex of a singly bonded $(C_{70}^{-})_2$ dimer with cyclotriveratrylene[84] and other solid structures previously reported.[23] Additionally, the ESR spectra appeared to be dimer-concentration dependent. These observations were in agreement with the existence of an equilibrium between two C_{70} adduct radical anions, if the negative charge was localized in the fullerene core or in the adduct. Therefore, we proposed that during reductive electrolysis, a dimerization reaction occurred through an $EC_{DIM}E$ scheme, with pre-equilibration.

Several attempts to trap this intermediate for further analysis led to inconclusive results, as the intercage bond was too weak to resist analysis. However, controlled-potential electrolysis of **42** (0.79 e/molecule) followed by quenching with an excess of CH_3I yielded a clear $m/z = 2081$ peak by MALDI mass spectrometry, consistent with dimer formation, with the additional incorporation of two methyl groups, molecular oxygen, and sodium. Multiple experiments provided similar results with mass spectral peaks with m/z ratios that evidenced the formation of dimeric [70]fullerene structures ($m/z > 1700$).[23]

On the basis of the results summarized in this section, we proposed a mechanism for the retro-cyclopropanation reaction that involves the heterolytic opening of the cyclopropane ring leading to charge formation either in the fullerene core or in the addend, and that these interconvert at equilibrium. Dimers can then form between fullerene-based radicals.[23]

Summary and Outlook

The aim of this microreview was to consider the generality and practical utility of the electrochemical retro-cyclo-


42

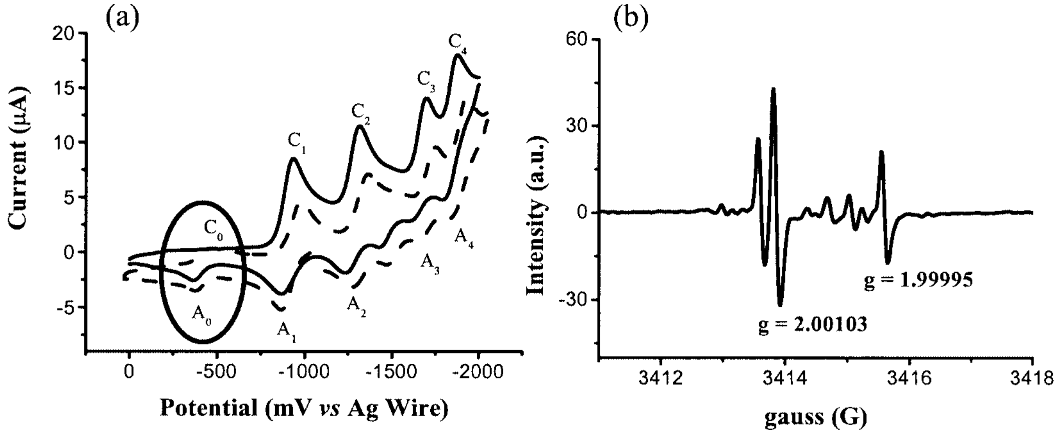


Figure 21. Reductive electrochemistry data for **42**. (a) Solid line: starting CV under high vacuum conditions; dashed line: cyclic voltammogram obtained after 1 e⁻ reduction of **42**, (b) ESR spectrum obtained after 1 e⁻ reduction of **42**

propanation reaction. This process was observed for the first time during controlled-potential electrolysis at the second reduction potential of diethyl 1,2-methano-[60]fullerene-61,61-dicarboxylate (**5**) in CH_2Cl_2, which led to more than 80% of recovered C_{60}. Initially, this reaction was called the retro-Bingel reaction, since it was the reverse of the well-known Bingel addition of malonates to form cyclopropane rings of fullerenes. The first reported useful application of this reaction was in the separation of enantiomers of C_{76}, using an optically active malonate as a chiral auxiliary. As described above, this Bingel/retro-Bingel sequence was also used recently to separate constitutional isomers and enantiomers of C_{84}. Interestingly, partial electrolysis of bis- or tris-Bingel adducts of C_{60} led to isomerization of the adducts. One of the important developments which made these reactions synthetically more useful, was to show that electrochemical reduction could selectively remove Bingel-type adducts while leaving other adducts undisturbed. A variety of well-characterized mixed bis-adducts of C_{60} were prepared, where one of the adducts was always a bis(ethoxycarbonyl)methano group, and the other one ranged from a pyrrolidine to a bis(*p*-methoxyphenyl)methano group. In every case it was shown that controlled-potential electrolysis led to the selective removal of the Bingel adduct, while the other one was retained.

Spiromethanofullerenes were also subjected to CPE processes based on the initial observation of Wudl and co-workers of irreversible electrochemical behavior for some of the compounds, presumably resulting from the cleavage of one of the cyclopropane bonds connecting the addend to C_{60} upon reduction. In fact, CPE in CH_2Cl_2 resulted in the efficient removal of the addend to form the parent C_{60}, confirming the electrochemical process as a retro-cyclopropanation reaction. Exhaustive reductive electrolysis in THF led also to efficient addend removal, but a new reaction pathway was observed: electrochemically induced addend transfer between C_{60}-monoadducts led to bis-adduct formation. This observation was later confirmed in several nitrophenylspiromethanofullerenes with easily recognizable EPR signals.

The chemical version of the retro-cyclopropanation process has also been considered briefly in this microreview. The chemical reaction was initially carried out using a Mg/Hg amalgam as reducing agent and, subsequently, the presence of 18-crown-6 in these reactions proved to increase the efficiency and reproducibility, thus expanding the utility of the cyclopropanation-retro-cyclopropanation strategy as part of a protection-deprotection protocol in the synthesis of non-Bingel type adducts.

More recently digital simulations have helped to elucidate the mechanistic details involved in these reactions and the formation of singly bonded dimers as intermediates during retro-cyclopropanation reactions has been established experimentally.

Future applications in the preparation of unusual derivatives with controlled regiochemistry, particularly for C_{70} and higher fullerenes derivatives, remain unexplored.

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