

Covalent fullerene chemistry

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Abstract: A brief introduction to the reactivity principles governing the covalent chemistry of fullerenes is provided. The combination of synthetic fullerene and acetylene chemistry gives access to a family of novel molecular carbon allotropes with interesting physical properties. A versatile strategy for the regioselective preparation of specific bis- through hexakis-adducts of C₆₀ based on the tether-directed remote functionalization was developed. Large changes in chemical reactivity and physical properties occur when the conjugated π -chromophore of the fullerene is reduced in size as a result of increasing functionalization. A novel synthesis of enantiomerically pure derivatives of C₆₀ with chiral addition patterns is described.

INTRODUCTION TO FULLERENE REACTIVITY

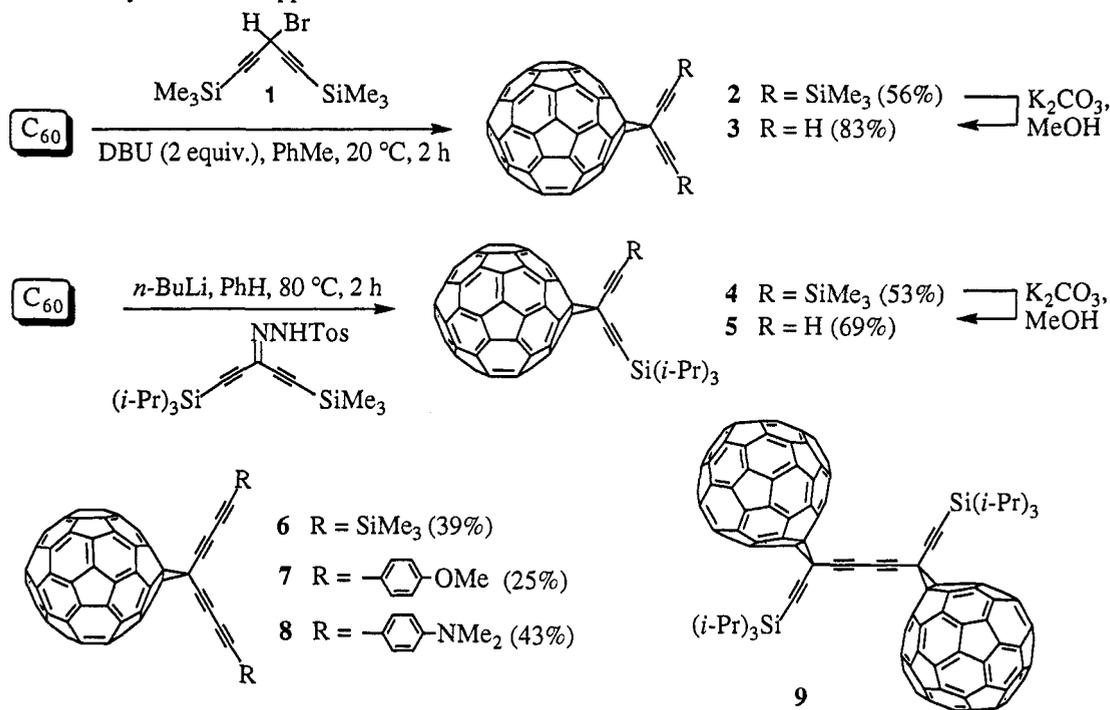
The covalent functionalization of fullerenes (1,2), in particular of the most abundant carbon sphere, buckminsterfullerene C₆₀, has been vigorously developed following the discovery of the bulk preparation method for these carbon allotropes in 1990 (3). A rich variety of methods for the preparation of covalent mono-adducts of C₆₀ are known in which the fullerene reacts as a strained, electron-deficient poly-alkene with rather localized bonds. The molecular carbon allotrope readily adds nucleophiles and carbenes and participates as the electron-deficient dienophile component in many thermal cycloaddition reactions such as the *Diels-Alder* addition. In most of these reactions, 1,2-addition occurs in which the addends add to one of the thirty 6-6 bonds [bonds with high double bond character (bond length ≈ 1.38 Å) at the junction between two six-membered rings]. If both addends in a nucleophilic addition are very bulky, 1,4-addition across a six-membered ring may occur. Thermal 1,3-dipolar cycloadditions of diazoalkanes, α -diazocarbonyls (4), and azides (5,6), followed by elimination of N₂, generate methano- and azafullerenes in which one of the sixty 6-5-bonds [bonds with lower double bond character (bond length ≈ 1.45 Å) at the junction between a six- and a five-membered ring] is bridged. In all mono-adducts formed by 1,2-addition, the fullerene preserves the favorable π -electron system of C₆₀, and all double bonds are located exocyclic to the pentagons, providing [5]radialene character to the pentagons and cyclohexa-1,3,5-triene character to the hexagons. Thus, introduction of a methano bridge at 6-6-bonds produces the 6-6-closed methanofullerene isomer with a transannular bond between the bridgehead C-atoms whereas reaction at 6-5-bonds yields exclusively the 6-5-open isomer in which the two bridgehead C-atoms are at nonbonding distance. The alternative 6-6-open and 6-5-closed isomers are energetically strongly disfavored and do not form because they contain two (6-5-closed) or three (6-6-open) double bonds endocyclic to the pentagons. The 6-6-closed isomer usually is the thermodynamically more stable product, and most 6-5-open methanofullerenes can be converted by thermal, electrochemical, and photochemical methods into the corresponding 6-6-closed derivatives. Most nucleophilic addition processes yield mono-adducts as the main products under appropriate conditions; bis- and higher additions occur more slowly because the electrophilicity of fullerene derivatives becomes increasingly reduced with increasing reduction in the conjugated fullerene π -chromophore. All additions are exothermic and are presumably driven by the relief of strain in the C₆₀ cage that largely results from the pyramidalization of its sp^2 C-atoms. In the adducts, the functionalized fullerene C-atoms change their hybridization from a trigonal sp^2 to a less strained tetrahedral sp^3 state. In this article, the concepts governing fullerene reactivity are illustrated by the formation of methanofullerenes, *Diels-Alder* products, and covalent derivatives resulting from the nucleophilic addition of lithium acetylides to the carbon sphere.

In contrast to the preparation of covalent mono-adducts of C₆₀, the development of selective routes to isomerically pure multiple adducts of the fullerene is still in its infancy (7-10). Monofunctionalized C₆₀

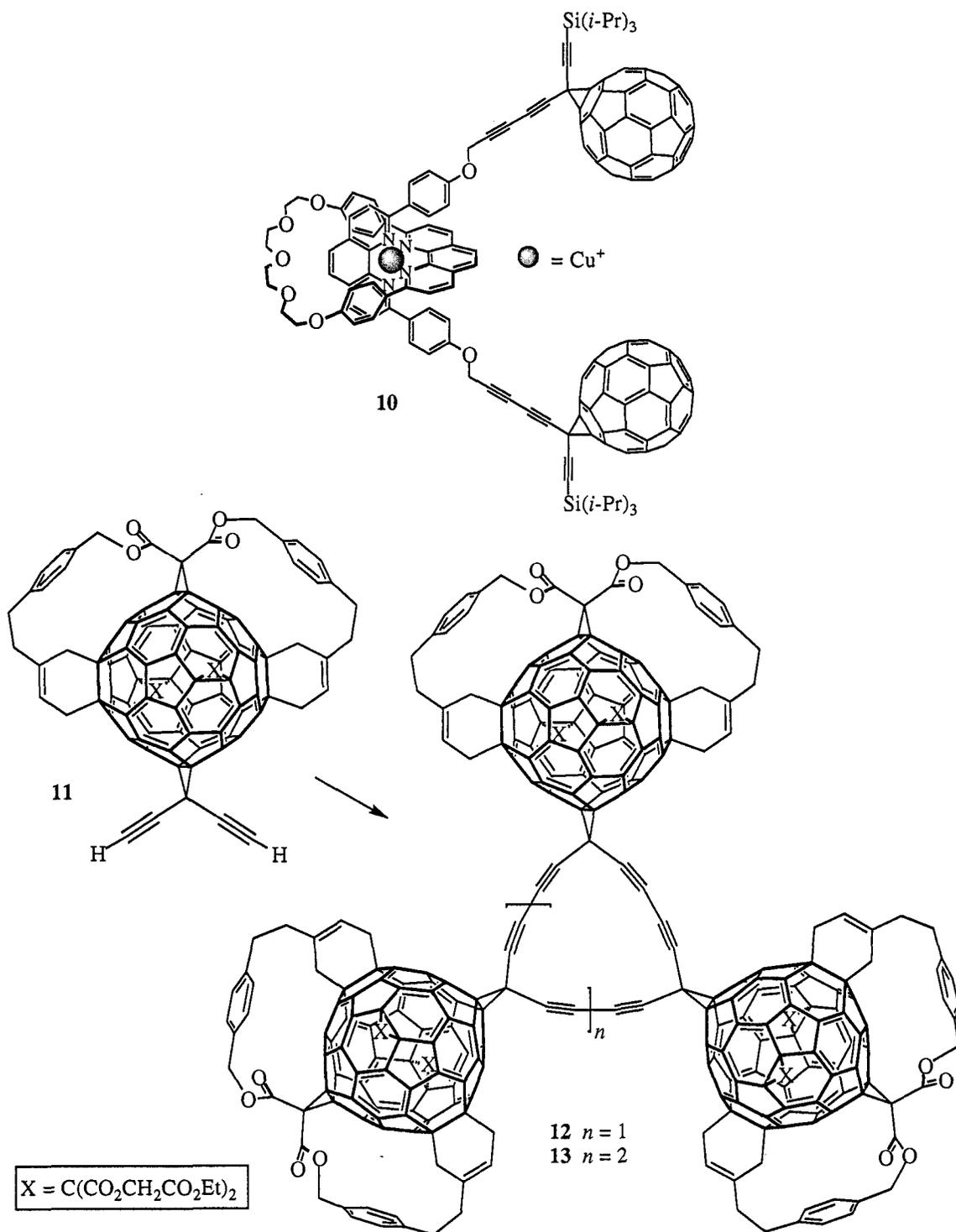
has nine different 6-6-bonds that can react in a second addition, and reactions such as the bis-osmylation (8) or the double *Bingel* cyclopropanation, *i.e.* the addition of bromomalonates in the presence of base (7,11), yielded regioisomeric mixtures of bis-adducts which could only be separated by tedious, scale-limiting high-performance liquid chromatography (HPLC). As illustrated below, we introduced the concept of tether-directed remote functionalization to prepare with high regioselectivity specific bis- through hexakis-adducts of C_{60} (12-15). Since the beginning of bulk scale fullerene chemistry and the isolation and characterization of chiral D_2 -symmetrical C_{76} , prepared from achiral graphite, fullerene chirality has attracted great fascination (16). This article closes with an example for the chiral-tether-mediated enantioselective synthesis of an optically active bis-adduct of C_{60} whose chirality exclusively results from the specific chiral addition pattern (17,18).

FULLERENE-ACETYLENE MOLECULAR SCAFFOLDING

Dialkynylmethanofullerenes are versatile building blocks for molecular construction through oxidative acetylenic coupling. Thus, the parent diethynyl derivative **3** is readily available by treatment of 3-bromo-1,4-pentadiyne **1** with C_{60} in toluene in the presence of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) to give **2**, followed by proto-desilylation (19). Alternatively, the *Bamford-Stevens* reaction was applied to prepare mono-protected **5** *via* **4** (19,20). Starting from **5**, oxidative hetero-coupling yielded compounds **6-8** which, upon electrolysis, all underwent reductive electrochemical polymerization under formation of an insoluble, air-stable, electrically conducting film depositing on the platinum cathode surface (21). Oxidative homo-coupling of **5** led to the dumbbell-shaped dimeric fullerene **9**, which was characterized by X-ray crystallography. The soluble rotaxane **10** with two C_{60} stoppers was also prepared by hetero-coupling starting from **5** (22). When **10** was reacted with an excess of KCN, the fast atom bombardment mass spectrum showed that the phenanthroline-crown ether macrocoring cannot become unthreaded by slipping over the bulky fullerene stoppers.

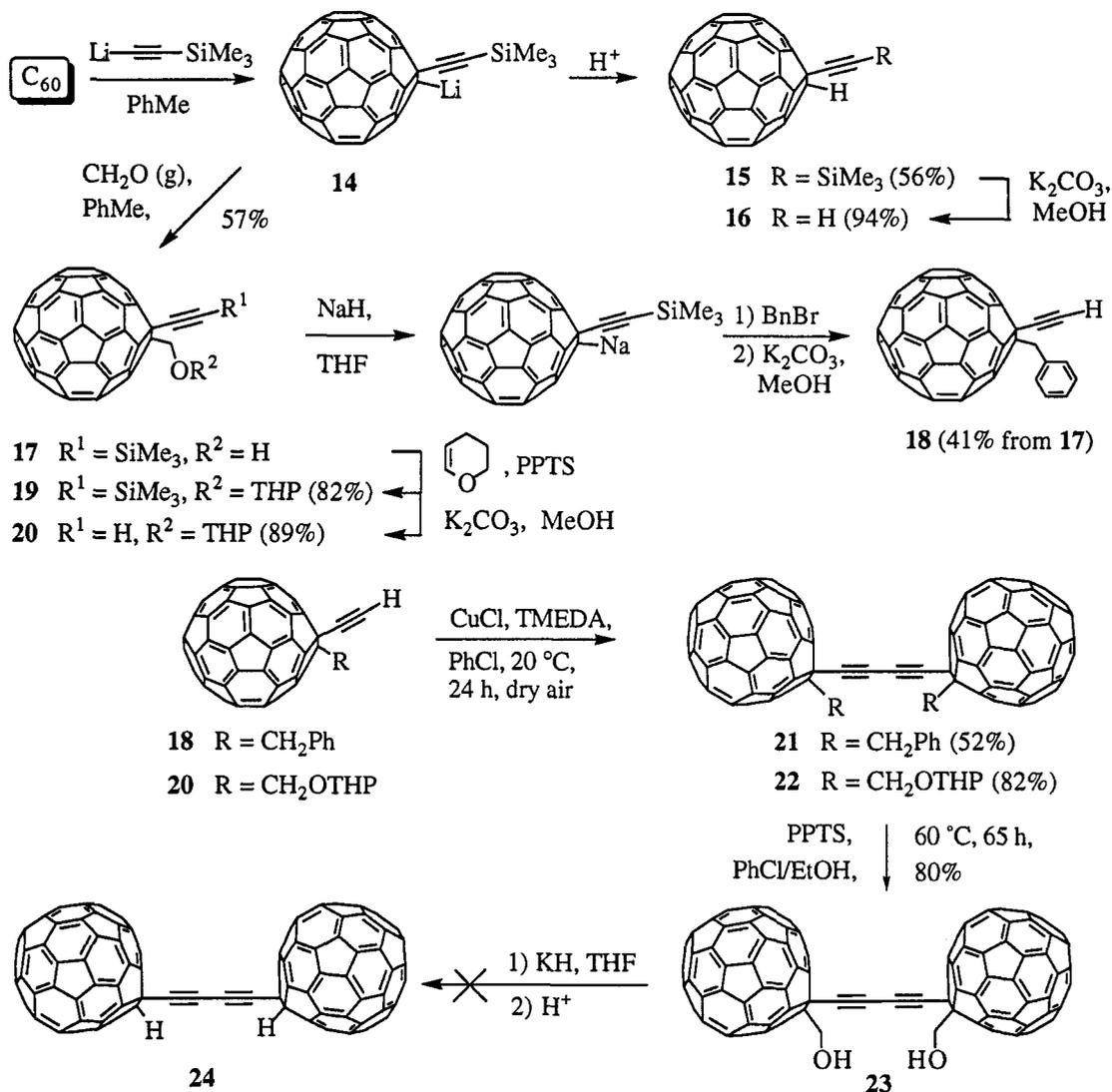


Starting from the diethynylated C_{60} hexakis-adduct **11**, which was prepared by the tether-directed remote functionalization method described below, *Eglinton-Glaser* macrocyclization afforded in a combined yield of 53% trimeric **12** and tetrameric **13** as soluble stable nanomaterials (14). Compounds **12** (MW = 5317 Daltons) and **13** (MW = 7086 Daltons) are solubilized derivatives of C_{195} and C_{260} , members of a new class of molecular carbon allotropes $C_{n(60+5)}$. They can also be viewed as tris- and tetrakis-fullerene adducts of *cyclo*- C_{15} and *cyclo*- C_{20} , respectively; indeed, their MALDI-TOF mass spectra showed as a major fragmentation pattern the sequential loss of the fullerene spheres, which potentially provides a controlled access to the hitherto unknown free cyclocarbons *cyclo*- C_{15} and *cyclo*- C_{20} .



Nucleophilic addition of lithium acetylides provides a method for the direct attachment of alkynyl residues to C₆₀ (19,23). The resulting metallated fullerene **14** can be directly protonated to give **15** and, after protodesilylation, 1-hydro-2-ethynyl[60]fullerene **16**. Quenching the anion with formaldehyde leads to methanol **17** which is unstable under strongly basic conditions and rapidly eliminates formaldehyde. The instability of **17** results from the fact that the fullerene anion is a very good leaving group. As a result of a large polarity difference, methanol **17** is readily separated from unreacted C₆₀. In contrast, larger quantities of

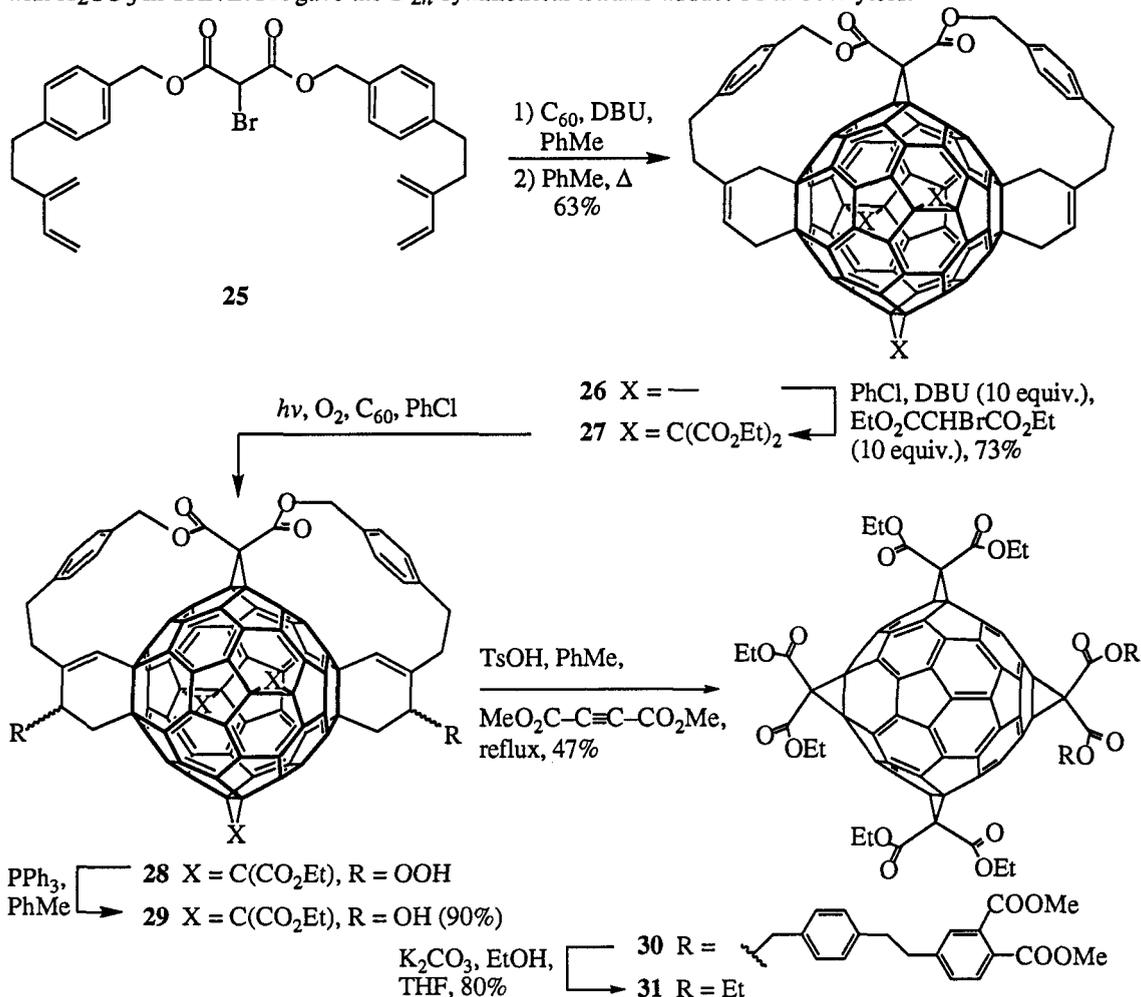
15 or alkylated analogs obtained by quenching **14** with mild alkylating agents are difficult to separate from unreacted fullerene. Therefore, benzylated **18** was best prepared in a one-pot procedure by successive treatment of **17** with NaH in THF, removal of NaH, reflux with benzyl bromide, and finally protodesilylation. Alcohol **17** was transformed into the tetrahydropyranyl ethers **19** and **20**, and oxidative *Hay* coupling starting from **18** or **20** led to the dumbbell-shaped dimeric fullerenes **21** and **22**, respectively (**24**). Cyclic voltammetric measurements revealed that there is no significant electronic communication between the two fullerene spheres in **21** and **22**. Deprotection of **22** yielded the highly insoluble dumbbell **23** with two methanol groups. Attempted conversion of **23** to the all-carbon dianion **24** (C_{124}^{2-}) via base-induced elimination of formaldehyde, however, has not yet been successful and is the subject of further investigations.



HIGHER ADDUCTS OF C₆₀ BY TETHER DIRECTED REMOTE FUNCTIONALIZATION

The tether-directed remote functionalization method allows construction of fullerene derivatives with addition patterns that are accessible by neither thermodynamic nor kinetic control of reactions with free untethered reagents. Thus the anchor-tether-reactive group conjugate **25** gave, after attachment through a *Bingel* reaction to C₆₀, addition at two *e*-positions (*e*, equatorial with respect to the first addend) on opposite sides of the carbon sphere, yielding tris-adduct **26** in 60% yield with complete regioselectivity (12). Reaction of **26** with a large excess of diethyl α -bromomalonate and DBU in toluene led by sequential *e*-additions in 73% yield to the pseudo-octahedrally functionalized hexakis-adduct **27** in which the

conjugated fullerene π -chromophore is reduced to a cubic cyclophane substructure as shown by X-ray crystallography (14). Other higher C_{60} derivatives with unusual addition patterns not accessible by direct synthetic methods become available by removal of the initially introduced tether-reactive group conjugate (15). When a solution of **27** containing C_{60} as 1O_2 sensitizer was irradiated (medium-pressure Hg lamp, Pyrex filter, 25 °C) while a stream of O_2 was bubbled through, the 1O_2 ene-reaction at the two cyclohexene rings yielded after 2 hours a mixture of isomeric allylic hydroperoxides **28** with endocyclic double bonds (25). Reduction of the crude mixture **28** with PPh_3 (10 equiv.) gave an isomeric mixture of allylic alcohols **29** which was transformed into the bis(cyclohexadieno) derivative by acid-catalyzed dehydration. Further reaction with dimethyl acetylenedicarboxylate (10 equiv.) afforded, *via* a *Diels-Alder* retro-*Diels-Alder* sequence, the C_{2v} -symmetrical tetrakis-adduct **30** in 42% overall yield starting from **27**. Treatment of **30** with K_2CO_3 in THF/EtOH gave the D_{2h} -symmetrical tetrakis-adduct **31** in 80% yield.

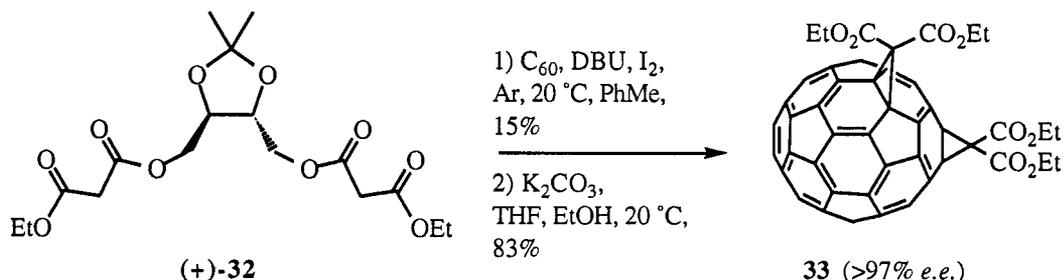


In an extended series of bis- to hexakis-adducts formed by the tether-directed remote functionalization method, the following changes in properties of the fullerene derivatives were observed as a result of the increasing reduction of the π -electron chromophore: a) The higher adducts show reduced reactivity against nucleophilic reagents; thus the Me_3Si alkyne-protecting groups in the precursor to **11** could be readily removed with Bu_4NF , whereas nucleophilic fluoride rapidly attacks the free carbon sphere. b) The colors of the solutions change from purple (C_{60}) to different tones of red and green-yellow (bis- to pentakis-adduct), to yellow (hexakis-adduct **27**). In **27**, the tailing end absorption stops below 460 nm, whereas lower adducts show a cutoff of 560 nm. c) The number of one-electron reduction steps decreases with additional addends from six reversible steps in C_{60} (first reduction at -0.98 V versus ferrocene) to one irreversible reduction in **27** (at -1.87 V) (13). In contrast, oxidation becomes increasingly reversible and facilitated with increasing functionalization, with the hexakis-adduct being reversibly oxidized at $+0.99$ V. The correlation between the degree of functionalization and the changes in redox properties is not entirely

straightforward: the electrochemical properties are not only dependent on the number of addends but also on the regiochemistry of the addition pattern on the surface of the fullerene sphere (13,15).

ENANTIOSELECTIVE SYNTHESIS OF A C₆₀ DERIVATIVE WITH A CHIRAL ADDITION PATTERN

Very recently, we showed that the macrocyclization between C₆₀ and bis-malonate derivatives in a double *Bingel* reaction provides a versatile and simple method for the preparation of covalent bis-adducts of C₆₀ with high regio- and diastereoselectivity (18). Starting from the optically pure bis-malonate derivative **32**, the new bis-functionalization method, followed by transesterification, also permitted the enantioselective preparation of optically active (*cis*-3) bis-adduct **33** whose chirality results exclusively from the addition pattern. With an enantiomeric excess (*e.e.*) higher than 97%, the asymmetric induction in the chirally tethered bis-malonate addition was similarly efficient to that previously reported for the asymmetric *Sharpless* dihydroxylation of C₆₀ (17). The general character of enantioselective multiple functionalizations of fullerenes mediated by optically active, removable tethers is under investigation (26).



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