Covalent Fullerene Chemistry

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The covalent functionalization of C_{60} has developed vigorously over the past 5 years. Several methods are now available for the formation of C_{60} monoadducts. Regioselective formation of multiple adducts has allowed study of the changes in chemical and physical properties that occur when the conjugated fullerene chromophore is reduced during an increase in functionalization. The systematic development of covalent fullerene chemistry provides an unprecedented diversity of tailor-made three-dimensional building blocks for technologically interesting materials.

The determination of the physical properties of the most abundant soluble fullerenes, C_{60} and C_{70} (*1*), progressed rapidly after the discovery of the bulk preparation method (*2–4*), but similar exploration of their chemical reactivity occurred only after low-priced fullerene soot became commercially available and facile methods for the rapid purification of gram quantities of C_{60} (*5, 6*) and C_{70} (*7*) were discovered. The most facile purification of large quantities of the two fullerenes today involves their flash-chromatographic separation over a mixture of silica gel:activated charcoal 2:1 with toluene (C_{60}) or toluene and *o*-dichlorobenzene (C_{70}) as eluant.

The C_{60} molecule has 12 pentagons, all of which are fully surrounded by hexagons (a total of 20) in a "corannulene-type" fashion (Fig. 1A). Crystal structure determinations by x-ray analysis of transition-metal derivatives (platinum complexes and osmium tetroxide adducts) of C_{60} demonstrate significant bond alternation in the fullerene (*8, 9*). The 30 6-6 bonds (at the junctions between two six-membered rings) have significantly higher double-bond character (bond length ~1.38 Å) than the 60 6-5 bonds [at the junctions between a six- and a five-membered ring (~1.45 Å)]. The electronic structure of C_{60}, with all double bonds exocyclic to the five-membered rings in a [5]radialene fashion (Fig. 1A), is preferentially preserved in stable fullerene derivatives, and the cost of introducing one double bond at a 6-5 ring junction is calculated to be ~8.5 kcal mol^{-1} (*10*). Electrochemical studies showed that C_{60} and C_{70} are very difficult to oxidize but are readily reduced in multiple one-electron reduction steps (*11, 12*), which suggested that fullerenes prefer to react with electron-rich reagents (nucleophiles). Theoretical calculations of the electronic structure of C_{60} in 1986 already predicted an energetically low-lying, threefold-degenerate lowest unoccupied molecular orbital (LUMO), which should readily accept up to six electrons in electrochemical reductions or, in chemical conversions, should be occupied by the electrons transferred by the lone pair of an attacking nucleophile (*13*).

These electrochemical and theoretical findings provided significant guidance to Wudl, Prato, and co-workers, who pioneered much of the early covalent chemistry of the fullerenes (*14, 15*). The development of the covalent chemistry of new compounds also depends on their solubility and stability. The solubility of C_{60} and the higher fullerenes up to ~C_{90} is sufficient in CS_2 and in aromatic or chlorinated hydrocarbons for chemical conversions to occur in homogeneous solution (*16*). Furthermore, fullerene anions, prepared by transfer of electrons or nucleophilic attack, show enhanced solubility in ethereal solvents such as tetrahydrofuran. The high kinetic stability of fullerenes makes them stable starting materials for reactions up to temperatures above 400°C.

The numerous methods for monofunctionalization of C_{60} that have been developed during the past 5 years are illustrated by examples taken from two important classes of derivatives, methanofullerenes and fullerene Diels-Alder adducts. Some of these compounds are of potential interest for biological or materials science applications. For a comprehensive survey of fullerene chemical reactivity, the reader is referred to an excellent recent monograph by Hirsch (*17, 18*). The problem of isomer formation in multiple attacks to C_{60} is described, and it is shown how the tether-directed remote functionalization approach, which had previously been developed for the regioselective functionalization of steroids (*19*), can be applied to regioselective multiple functionalization. Fullerene covalent chemistry is rapidly reaching the capacity for delivering tailor-made intelligent components in molecular and polymeric materials for advanced future technologies.

The Chemical Reactivity of C_{60}

The reactivity of C_{60} is that of a strained, electron-deficient poly-alkene with rather localized double bonds (*20*). It forms adducts readily with radicals, various nucleophiles, and carbenes, participates as the electron-deficient dienophile component in a variety of thermal cycloaddition reactions, and undergoes photochemical cycloadditions (*17*). In addition, C_{60} is readily hydrogenated (*17, 21*) and forms η^2 complexes (coordination to a 6-6 bond) with many transition metals (*10, 17, 22*). All of these additions are exothermic and are presumably driven by the relief of strain in the C_{60} cage that largely results from the pyramidalization of its sp^2 C atoms (*17, 20*). 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 nucleophilic and carbene attacks, hydrogenations, transition-metal complexation, and cycloadditions, 1,2-addition (Fig. 1B) is usually seen, whereas many of the radical additions such as the halogenations (*23*) occur as 1,4-additions across six-membered rings. The 1,4-additions also occur when the fullerene anion, formed by the attack of a nucleophile, is quenched with a bulky electrophile (*24*) (Fig. 1C). With a

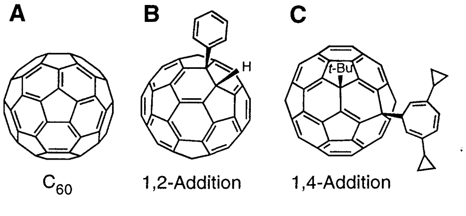

Fig. 1. (**A**) View of I_h-C_{60} showing the isolation of a pentagon in a corannulene-type substructure. Considerable bond alternation and localization is found in x-ray crystal structures. All double bonds are located exocyclic to the pentagons, providing [5]radialene character to the pentagons and cyclohexa-1,3,5-triene character to the hexagons. The length of the short bonds (6-6 bonds) is ~1.38 Å, and that of the long bonds (6-5 bonds) is ~1.45 Å. (**B**) 1,2-Addition to a 6-6 bond in the hydroarylation reaction. The C_{60} is attacked by nucleophilic phenyl magnesium bromide, and the fullerene anion formed is subsequently quenched with a proton as the electrophile. (**C**) 1,4-Addition in a dialkylation reaction. The attack by the large nucleophile *tert*-butyl lithium is followed by quenching with a bulky tropylium cation as the electrophile.

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few notable exceptions, 1,2-additions yield products derived from attack at the 6-6 bonds. In these adducts, the favorable π-electron system of C_{60} is preserved to a large extent, and all double bonds are located exocyclic to the pentagons. In contrast, a 1,4-addition locates one double bond endocyclic to a pentagon. However, this unfavorable electronic effect (~8.5 kcal mol^{-1}) in 1,4-adducts may be compensated by the absence of unfavorable steric (eclipsed) interactions that exist between addends in 1,2-positions. Radical additions are rapid and difficult to control; they usually lead to highly functionalized C_{60}. Up to 34 methyl radicals can be attached to one C_{60}, which acts as a true radical sponge (*25*), and halogenation leads to isomerically pure higher addition products such as $C_{60}Br_6$, $C_{60}Br_8$, and $C_{60}Br_{24}$ (*23*). Most other addition processes yield monoadducts as the main products under appropriate conditions. Although higher additions may occur as side reactions, the control of reagent stoichiometry allows the production of monoadducts in yields between about 50 and 80%. The second addition of nucleophilic reagents occurs more slowly because the electrophilicity of the monoadduct is reduced (*17*).

Besides the many conversions in which C_{60} acts as an electrophile, C_{60} is oxidized with dimethyldioxirane in toluene (*26*) or photochemically by dioxygen in benzene (*27*) to give $C_{60}O$ with an oxirane ring fused to a 6-6 bond. It is also readily osmylated at 6-6 bonds (*8, 28*). Although reactions of fullerenes with electrophiles have been reported, defined homogeneous compounds have so far not been isolated (*17, 29*).

Monoadducts of C_{60}

Methanofullerenes. These compounds represent the most versatile and widely studied class of fullerene adducts (*30*). In theory, there exist four possible isomers: 6-5-open, 6-5-closed, 6-6-open, and 6-6-closed, depending on whether addition takes place at 6-6 or 6-5 bonds and whether the bridgehead C atoms are at nonbonding distance or are connected by a transannular bond (Fig. 2A). Experimentally, the 6-5-closed and the 6-6-open isomers are not observed. Computational studies show that they are energetically disfavored because they contain two (6-5-closed) or three (6-6-open) double bonds located endocyclic to the pentagons (*31*). The 6-5-open isomers are only formed in 1,3-dipolar cycloadditions of diazoalkanes and α-diazocarbonyls to C_{60} (*32*) (Fig. 2, B and C). These reactions produce a 6-6-closed pyrazoline intermediate, which in the case of the addition of diazomethane (CH_2N_2) could be characterized spectroscopically, but in most cases looses N_2 rapidly under formation of 6-5-open and 6-6-closed methano-bridged fullerenes (*6, 30*). The 6-5-open isomers are kinetic products; they contain all double bonds exocyclic to the pentagons, but the location of two double bonds at the bridgehead C atoms causes strain by distorting these double bonds out of planarity (Bredt rule). In most cases, the initially formed 6-5-open adducts, which usually are accompanied by some 6-6-closed adduct, can be rearranged into the thermodynamically more stable 6-6-closed isomers either by heating of the product mixtures (*6, 14, 15*), by photochemical isomerization, presumably through a di-π-methane rearrangement (*33*), or by an electrochemical process (*34*). Interestingly, the parent 6-5-open methanofullerene **1** ($C_{61}H_2$), formed by thermal diazomethane addition and elimination of N_2 (*35*), could not be rearranged into the 6-6-closed isomer **2** by any of the three methods; **2** could only be produced by photochemical irradiation of the intermediate pyrazoline cycloadduct (*36*). The mechanisms for formation of the 6-5-open isomers and their rearrangement into the corresponding 6-6-closed derivatives are still the subject of experimental and theoretical investigations (*31*). Computational and experimental evidence points to the intermediacy of a higher energy 6-5-closed isomer in the 6-5-open to 6-6-closed methanofullerene rearrangement (*31, 37*).

Besides the 1,3-dipolar cycloaddition of diazoalkanes and α-diazocarbonyls followed by N_2 extrusion, a variety of other methods produce methanofullerenes, exclusively in the form of 6-6-closed isomers (*30*) (Fig. 2, D through G). Carbene addition was used to prepare a series of optically active fullerene-sugar conjugates, such as **4**, that could form stable monolayers at an air-water interface (*38, 39*). One of the most versatile reactions in fullerene chemistry is the Bingel cyclopropanation reaction, in which addition of an α-bromomalonate anion is followed by an intramolecular displacement of bromide to yield methanofullerenes such as **5** with two carboxy groups attached to the bridging sp^3 C atom (*40*). By a variant of this reaction, diethynylmethanofullerenes such as **6** were prepared for the construction of fullerene-acetylene molecular scaffolds (*41*); these compounds are also accessible by addition of dialkynylmethylene carbenes prepared from *p*-toluenesulfonylhydrazones (Bamford-Stevens reaction) (*41, 42*). Another general approach to methanofullerenes involves the addition of phosphonium ylides (Wittig reagents) (Fig. 2G) (*43*).

For the transannular bond between the bridgehead C atoms in 6-6-closed methanofullerenes, several high-resolution x-ray crystal structures yielded a length of about 1.57 to 1.61 Å (*44, 45*); in the bis(butadiynyl)methanofullerene **7**, the bridgehead bond length is 1.574 ± 0.003 Å. Similarly accurate structural information is still missing for the transannular distance between the bridgehead C atoms in 6-5-open isomers; computational studies predict values of 2.20 to 2.25 Å for this distance (*31*), in analogy to the transannular distances in the corresponding open 1,6-methano[10]annulenes (*46*).

Methanofullerene monoadducts retain most of the characteristic properties of the unfunctionalized carbon sphere. Many are more soluble than C_{60}, and they usually are quite stable thermally (loss of the methanobridge to regenerate C_{60} does not usually occur below 250°C). The optical absorption spectra of 6-6-closed adducts extend to ~700 nm, with two highly characteristic bands appearing around wavelength maxima $\lambda_{max} = 435$ and 690 nm (*6*). In contrast, the optical absorption spectra of 6-5-open adducts resemble more closely those of pure C_{60}; their conjugated π-chromophore is the least perturbed of all fullerene derivatives compared to C_{60} (*35*).

A variety of methanofullerenes with interesting functions resulting from the combination of the C_{60}-type physical properties of their carbon core and specific properties of the attached groups have been reported (Fig. 3). In CH_2Cl_2 with 0.1 M Bu_4NPF_6 (Bu, *n*-butyl) as electrolyte, the alkynylated derivative **7** (Fig. 2F) undergoes reductive electrochemical polymerization yielding an insoluble, electrically conducting film on the surface of the platinum cathode (*44*). This polymeric film is air stable and can be used as a material in electrodes with a reasonably wide electroactivity range (for example, −0.8 to +0.6 V versus ferrocene in CH_2Cl_2 containing 0.1 M Bu_4NPF_6). The molecular composition corresponds to that of **7**, and no electrolyte is included. In the dendrimer **8**, the dendritic arm dramatically increases the solubility of the fullerene and provides an insulating layer for the C_{60} sphere (*47*). Dendritic encapsulation may provide a useful technique for isolating the C_{60} core and thus changing its physical properties compared to free fullerenes in bulk solid or liquid phase. The ultraviolet-visible spectra and cyclic voltammograms of the soluble polyester **9** were almost identical to those of the monomeric bis(4-hydroxyphenyl)methanofullerene, suggesting that the properties of methanofullerene monomers can be transferred unaltered to polymeric materials (*48*). The soluble rotaxane **10** with two C_{60} stoppers illustrates the introduction of functionalized fullerenes into supramolecular devices (*49*). When **10** reacted with an excess of KCN, the mass spectrum by fast atom bombardment showed that the corresponding copper-free system is a rotaxane: the phenanthroline-crown ether macroring cannot become unthreaded by slipping over the bulky fullerene stoppers.

Biological conjugates. Water-soluble methanofullerenes with biological function are attracting increasing interest. The dicarboxylate **11** was synthesized as a water-soluble inhibitor for the human immunodeficiency virus (HIV) protease. The active site of the protease is complementary in size to a C_{60} molecule (*50*), and **11** inhibits the enzyme with an inhibition constant of 5.3 μM. Starting from the versatile building block **3** (*6, 51*), which is now commercially available (Fluka Chemicals, Buchs, Switzerland), the water-soluble fullerene-peptide conjugate **12** was prepared (*52*). The pentapeptide conjugate corresponds to the hydrophilic residues 4 through 8 of peptide T, which binds to the surface glycoprotein CD_4. In biological assays, **12** showed a remarkable chemotactic potency, and it efficiently stimulated monocyte-directed migration. The water-soluble fullerene-oligonucleotide conjugate **13** is a remarkable agent for the photoinduced sequence-specific cleavage of DNA (*53*). Fullerene monoadducts show an efficiency similar to that of pure C_{60} in sensitizing the photochemical formation of singlet oxygen (*54*), which attacks and cleaves DNA. Photocleavage induced by **13** was studied by complexing the fullerene-oligonucleotide conjugate to linear oligonucleotides (under duplex formation) or to duplexes and hairpin structures (under triple-helix formation) that contained the complementary oligonucleotide sequence. Upon irradiation with $\lambda > 310$ nm, the bound DNA fragments were cleaved in regions expected from the binding of **13**. Interestingly, cleavage occurred with high specificity for guanine residues near the fullerene. These examples only represent a

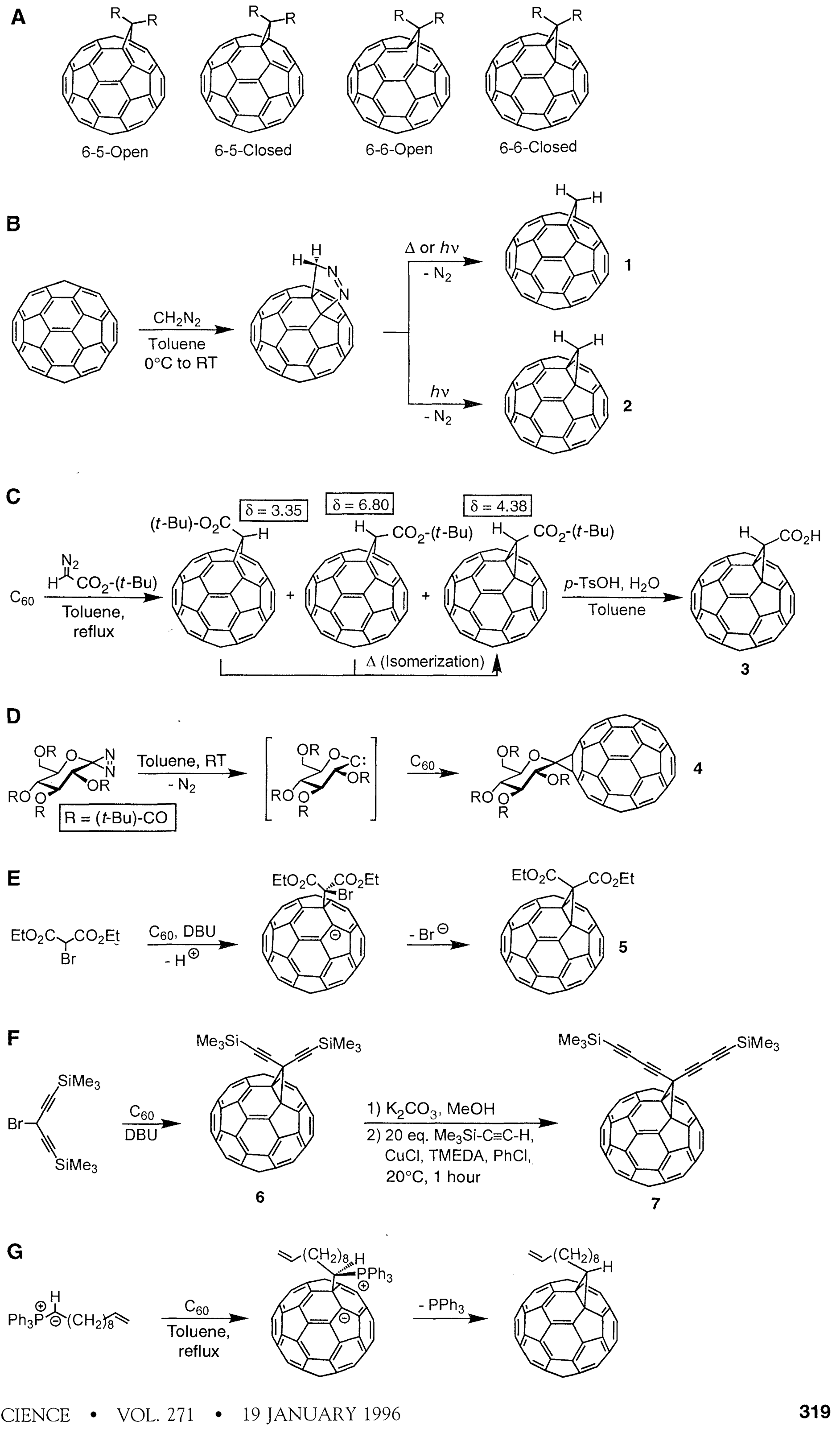

Fig. 2. (**A**) The four theoretically possible isomeric methanofullerenes. Only the 6-5-open and the 6-6-closed isomers are experimentally observed. (**B**) Formation of the parent 6-5-open (**1**) and 6-6-closed (**2**) methanofullerene ($C_{61}H_2$) isomers by 1,3-dipolar cycloaddition of diazomethane to C_{60} to give a 6-6-fused pyrazoline intermediate followed by thermal or photochemical extrusion of N_2 (abbreviations: RT, room temperature; Δ, heat; and *h*ν, light). (**C**) 1,3-Dipolar cycloaddition of *tert*-butyl (*t*-Bu) diazoacetate yields a mixture of two diastereomeric 6-5-open (kinetic) and one 6-6-closed (thermodynamic) products. Shown are the very different ^1H nuclear magnetic resonance (NMR) chemical shifts (δ) of the protons at the bridge C atom in the three isomers as a result of strong anisotropic ring current effects on the fullerene sphere. Prolonged heating converts the 6-5-open isomers into the 6-6-closed isomer. Hydrolysis of the ester yields methanofullerenecarboxylic acid **3** as a versatile building block (*p*-TsOH = *p*-toluenesulfonic acid). (**D**) The optically active fullerene-sugar conjugate **4** is obtained by the attack of a nucleophilic glycosylidene carbene, formed from the corresponding diazirine, to C_{60}; R, alkyl group. (**E**) In the Bingel reaction, α-bromomalonates are deprotonated by a base and react as nucleophiles with C_{60} to give an intermediate anion, which, by displacement of the halide, closes the methano bridge to diesters such as **5** (DBU, 1,8-diazabicyclo[5.4.0]undec-7-ene; Et, ethyl). (**F**) Trimethylsilyl-protected 3-bromopenta-1,4-diyne reacts in the presence of base with C_{60} to give the dialkynylmethanofullerene **6**. Deprotection followed by oxidative acetylenic coupling with trimethylsilylethyne affords **7**, which, upon electrolysis, yields a conducting polymeric film at the cathode (TMEDA, *N,N,N′,N′*-tetramethylethylenediamine; Ph, phenyl; and Me, methyl). (**G**) Formation of methanofullerenes by nucleophilic addition of a phosphonium ylide, a Wittig reagent.

beginning in the exploration of the biological properties of water-soluble tailor-made fullerene derivatives.

Diels-Alder reactions. One of the most widely used reactions in organic chemistry, the [4 + 2] Diels-Alder cycloaddition, has also been applied to the formation of soluble C_{60} monoadducts (*17*). The fullerene reacts as the electron-deficient dienophile with electron-rich 1,3-dienes to form adducts in which a 6-6 bond is fused to a cyclohexene ring. After initial observations by Wudl of the addition of anthracene and other 1,3-dienes to C_{60} (*14*), this reaction was systematically introduced into fullerene chemistry by the groups of Rubin (*55*) and Müllen (*56*) (Fig. 4). Thus, reaction of 2-[(trimethylsilyl)oxy]buta-1,3-diene with C_{60} yielded, after hydrolysis and reduction, alcohol **14**, to which additional functional groups such as α–amino acid derivatives could be attached through esterification (*57*) (Fig. 4A). Besides acyclic 1,3-butadienes (*58*), *o*-quinodimethanes have frequently been used as reactive diene components; they are readily prepared in situ from a variety of precursors (Fig. 4B). Several Diels-Alder monoadducts have been characterized by x-ray crystal structure analysis (*55, 59, 60*).

In general, adducts such as **15** or those formed from acyclic 1,3-dienes are very stable against the retro-Diels-Alder reaction, the thermal cycloreversion reaction leading to the original diene and the free fullerene; most reports describe stabilities up to temperatures above 200°C. In contrast, when the cyclohexene ring in the formed adduct is part of a bicyclic system, the stability decreases significantly, presumably for steric reasons. Thus, the formation of the anthracene adduct **16** (*61*) and of cyclopentadiene adducts such as **17** (*62, 63*) is reversible around 90°C. For the adduct between C_{60} and pure cyclopentadiene, the activation energy for the retro-Diels-Alder reaction is 26.7 kcal mol^{-1} (*63*).

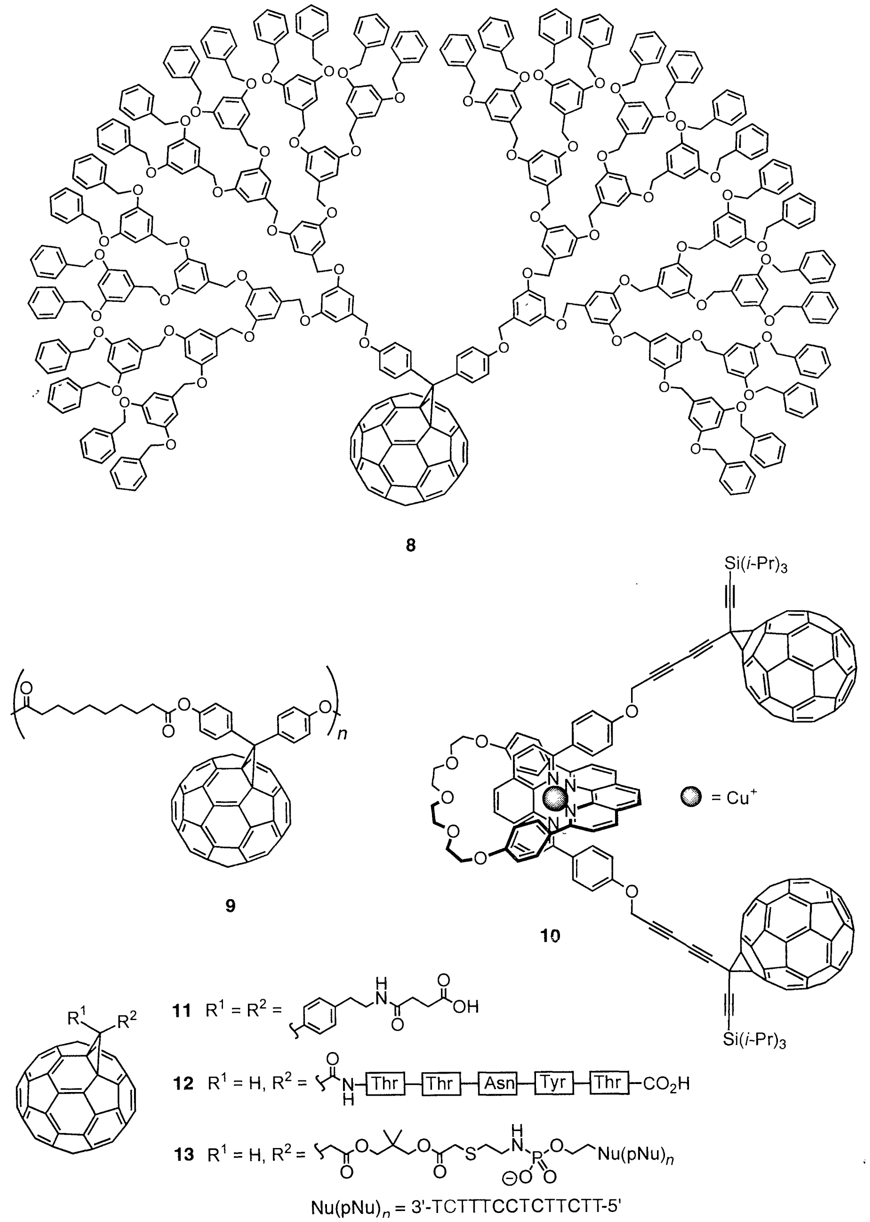

Fig. 3. Methanofullerenes with interesting properties and structures: a fullerene-dendrimer (**8**), a fullerene-polyester polymer (**9**), a fullerene-rotaxane (**10**), a water-soluble inhibitor of HIV protease (**11**), a water-soluble fullerene-peptide conjugate with chemotactic activity (**12**), and a fullerene-nucleotide conjugate as G-selective DNA-cleaving agent (**13**) (Nu, nucleotide).

Interesting functional derivatives have been prepared by Diels-Alder reaction (Fig. 4C). Reversible covalent attachment of C_{60} to give **17** was achieved by a Diels-Alder reaction of the fullerene at room temperature with a polymer support consisting of a Merrifield peptide resin (a styrene-divinylbenzene copolymer) functionalized with cyclopentadiene moieties (*64*). A loading capacity of 23 mg of C_{60} per gram of resin could be obtained. Upon heating, C_{60} was released by cycloreversion, with re-addition to the polymer occurring upon cooling. The crown ether **18** (*59, 65*) was shown to complex K^+ ions in methanol. Monolayers of the K^+ complex of **18** prepared at an air-water interface had a surface requirement of 80 Å^2 per molecule, which is close to the theoretical value for C_{60} (86.6 Å^2 per molecule) (*39, 59*). A green C_{60} adduct (**19**) was obtained in the Diels-Alder addition with a phthalocyanine derivative (*66*). Reduction to produce the monoanion is centered on the fullerene moiety and has a significant effect on the optical properties of the phthalocyanine.

Higher Adducts of C_{60}

Monofunctionalized C_{60} has nine different 6-6 bonds that can react in a second addition (*17*). Therefore, controlling the regiochemistry of the second addition in order to direct the attack to one desired position poses a considerable challenge. Similar problems of isomer formation arise in the addition of a third addend to a purified bis-adduct as well as in the formation of more highly functionalized fullerenes. Multiple regioisomer formation is reduced in reversible reactions, which yield the thermodynamically most stable isomer (*67*) or an isomer that crystallizes out of a reaction mixture (*68*). An example of a higher adduct formed under thermodynamic control is the octahedrally coordinated T_h-symmetrical hexaplatinum complex **20** (*67*).

In contrast, kinetic product distributions were obtained in the bis-osmylation, which yielded five regioisomers (*69*), and in the addition of a second α-bromomalonate in the Bingel reaction, in which seven isomers were formed (*70, 71*). In both conversions, the products were isolated by tedious, scale-limiting high-performance liquid chromatography (HPLC). The most abundant product formed in the bis-osmylation and the double Bingel reaction is an isomer in which both addends are in an equatorial (*e*) relation to each other (Fig. 5A). The preferred formation of this *e*,*e*-isomer can be explained both by steric arguments and by the enhanced orbital coefficients of the LUMO, which accepts the electron density from the incoming nucleophile, in these positions (*71*). The introduction of a third addend in the Bingel reaction also occurs preferentially in the equatorial position (*17, 70*), and starting from the purified *e*,*e*,*e*-isomer, an amazing succession of stepwise *e*-additions, with regard to the previously attached addend (Fig. 5A), leads to hexa-adduct **21** (*71, 72*), with the same octahedral functionalization pattern as in **20**. Presumably by a sequence of similar stepwise *e*-additions, the Diels-Alder reaction of an excess of 2,3-dimethylbuta-1,3-diene with C_{60} afforded directly in 26% yield hexa-adduct **22** (*73*) (Fig. 5B).

Tether-directed remote functionalization. This concept was introduced by Breslow (*19*) for the regioselective functionalization of steroids and long-chain alkanes. The anchor–tether–reactive-group conjugate **23** (Fig. 5C) was designed by semiempirical PM3 calculations (parametric method 3) (*74*) to give, after attachment through a Bingel reaction to C_{60}, tris-adduct **24** regioselectively by Diels-Alder addition at two *e*-positions on opposite sides of the carbon sphere (*75*). Indeed, Bingel addition of **23** to C_{60} in toluene at 20°C with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) as the base followed by heating for 83 hours at 80°C afforded tris-adduct **24** in 60% yield (*76*) with complete regiospecificity. Reaction of **24** with a large excess of α-bromomalonate and DBU in toluene led by sequential *e*-additions in 73% yield to the hexa-adduct **25** (*75, 76*). The overall yield of **25**, starting from C_{60}, was a remarkable 44%, and no tedious regioisomer separation by HPLC was required. The tether-directed remote functionalization method should in the future allow construction of many fullerene derivatives with addition patterns that are accessible by neither thermodynamic nor kinetic control of reactions with free, untethered reagents.

With the use of tether-directed remote functionalization in combination with subsequent *e*-specific additions, an entire series of structurally related mono- through hexa-adducts of C_{60} were prepared. Changes in the physical properties of the carbon sphere as a result of the increasing number of addends are dramatic. The color of toluene solutions changes from purple (C_{60}) to wine-red (mono-), to brown-red (bis- and tris-), to bright red (tetra-), to orange (penta-), and to yellow (hexa-adduct). In hexa-adduct **25**, as in the other octahedrally functionalized derivatives **20** through **22**, the chromophore of the carbon sphere is reduced to the "cubic cyclophane"-type substructure **28**, and the tailing end absorption stops below 460 nm, compared to a cutoff of 560 nm for the lower adducts. The number of one-electron reduction steps decreases with additional addends from six reversible steps in C_{60} (*12*) (first reduction at −0.98 V versus ferrocene) to one irreversible reduction in **25** (at −1.87 V) (*77*). In contrast, oxidation becomes increasingly reversible and facilitated with increasing functionalization, with the hexa-adduct being reversibly oxidized at +0.99 V.

The dialkynylmethanofullerene **26** was prepared and deprotected with $Bu_4N^+F^-$ to give the free diethynyl derivative **27** (*76*). Oxidative cyclization of **27** under Eglinton-Glaser conditions afforded the trimeric and tetrameric macrocycles **29** (32%) and **30** (21%) (Fig. 5D). They are solubilized derivatives of C_{195} and C_{260}, two members of a new class of carbon allotropes (*78*) with the molecular formula $C_{n(60+5)}$ in which the sp^3-hybridized C atoms in acetylenic macrorings are end-capped by three or four C_{60} spheres, respectively.

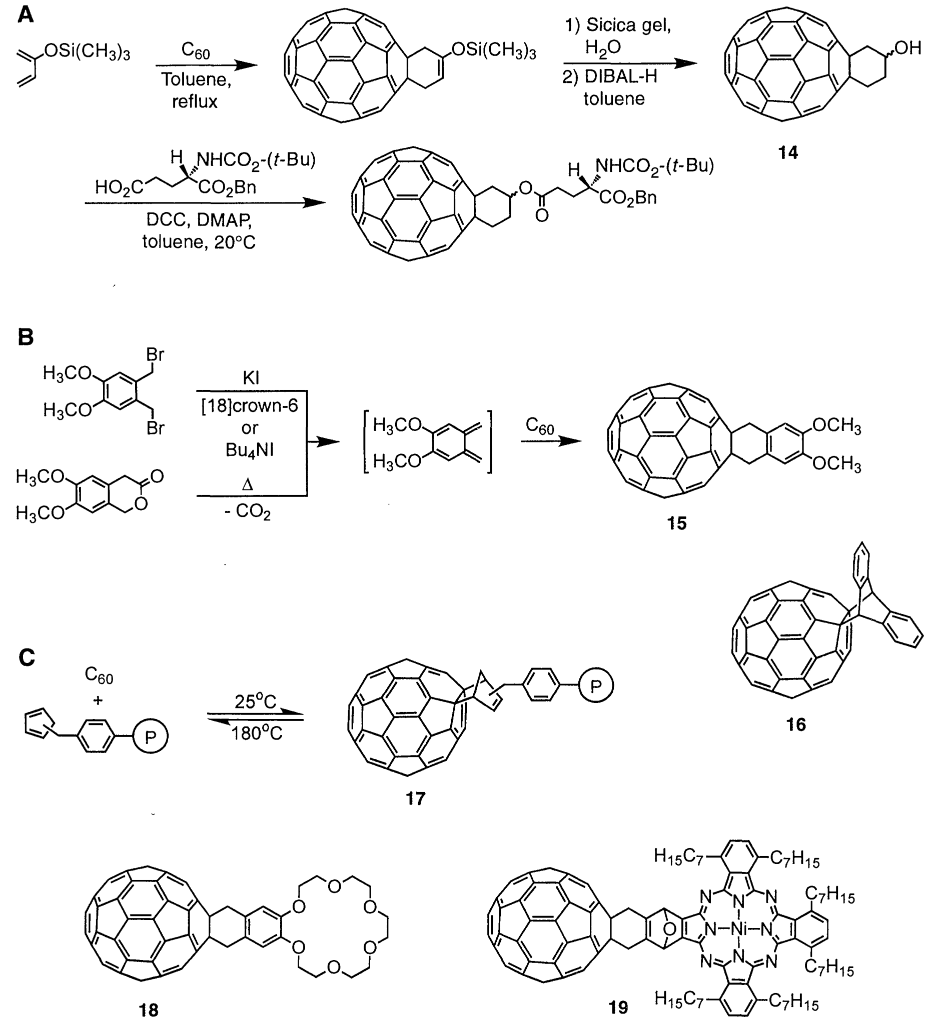

Fig. 4. (**A**) [4 + 2] Diels-Alder cycloaddition to C_{60} yields a cyclohexene derivative, which is transformed into alcohol **14**, a versatile building block, such as for the formation of fullerene–amino acid conjugates [DIBAL-H, diisobutylaluminum hydride; Bn, benzyl; DCC, dicyclohexyl carbodiimide; DMAP, 4-(dimethylamino)pyridine] (**B**) In situ formation of an *o*-quinodimethane, which undergoes Diels-Alder addition to C_{60}. Adducts such as **15** are thermally very stable against cycloreversion by retro-Diels-Alder reaction. In contrast, anthracene (**16**) and cyclopentadiene adducts readily undergo retro-Diels-Alder reactions at ~90°C. (**C**) Diels-Alder adducts with interesting properties and structures: The cyclopentadiene-functionalized Merrifield polymer (P) resin can be loaded with C_{60} at 25°C to give **17**, which releases the fullerene reversibly in a cycloreversion reaction at higher temperature. Fullerene-ionophore **18** forms Langmuir-Blodgett monolayers at the air-water interface. The green fullerene-phthalocyanine conjugate **19** displays redox properties of both fullerene and phthalocyanine moieties.

Outlook

These three-dimensional fullerene derivatives will complement the present repertoire of two-dimensional acetylenic, olefinic, and benzenoid components for the construction of tailor-made molecules and polymers. In materials containing mono- through tris-adducts of C_{60}, the electrochemical (*77, 79*) and photophysical (*80*) characteristics of the free fullerene will almost be fully retained. A variety of predictions for technological applications were made when C_{60} first became available in bulk quantities (*81*), but most of them became disappointments. Today, the failure of these predictions, which were based on the experience with other classes of chemical compounds, is no longer so surprising.

Binary materials such as exohedral salts of functionalized fulleride anions with alkali metal or organic cations remain entirely unexplored and may show conducting, superconducting, or ferromagnetic properties similar to the analogous binary phases formed by free C_{60}. Among the most ambitious challenges in covalent fullerene chemistry are the total synthesis of C_{60} (*82*) and methods allowing the reversible opening and closing of the carbon cage (*83*). Progress in these directions should provide rational ways to the preparation of endohedral complexes (*84*) and heterofullerenes in which C atoms of the carbon shell are replaced by B, N, O, S, P, or other atoms (*17, 85*). Largely unpredictable chemical and physical properties of these compounds await to be discovered.

Although the covalent chemistry of the soluble higher fullerenes (for example, C_{70}, C_{76}, and C_{84}) (*86*) is similar to that of C_{60} in its general principles, the larger number of nonequivalent bonds in these carbon spheres leads to more complex product distributions. Whereas the functionalization of the second-most-abundant soluble fullerene, C_{70}, is increasingly pursued (*17, 87*), a more extensive development of the chemistry of

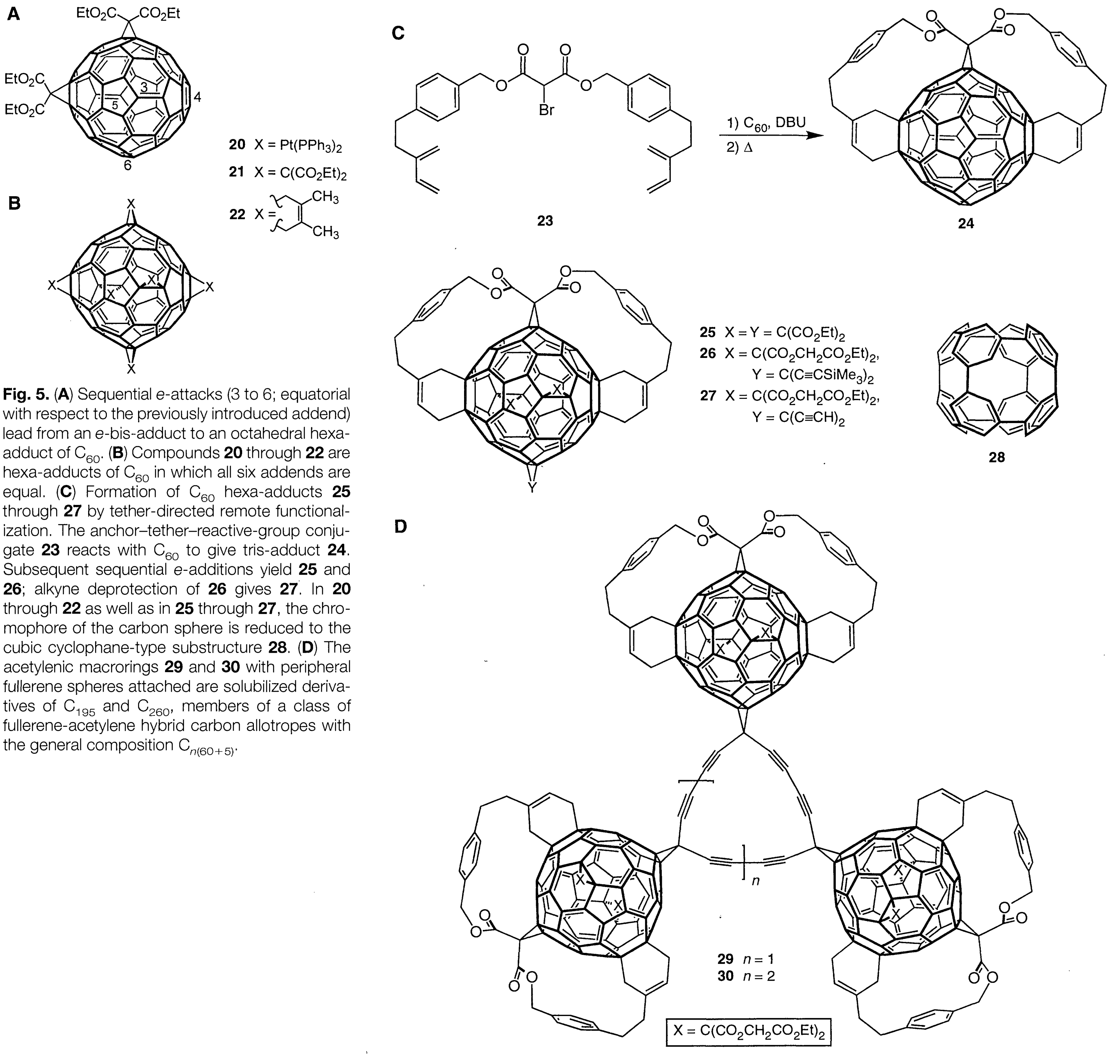

Fig. 5. (**A**) Sequential *e*-attacks (3 to 6; equatorial with respect to the previously introduced addend) lead from an *e*-bis-adduct to an octahedral hexa-adduct of C_{60}. (**B**) Compounds **20** through **22** are hexa-adducts of C_{60} in which all six addends are equal. (**C**) Formation of C_{60} hexa-adducts **25** through **27** by tether-directed remote functionalization. The anchor–tether–reactive-group conjugate **23** reacts with C_{60} to give tris-adduct **24**. Subsequent sequential *e*-additions yield **25** and **26**; alkyne deprotection of **26** gives **27**. In **20** through **22** as well as in **25** through **27**, the chromophore of the carbon sphere is reduced to the cubic cyclophane-type substructure **28**. (**D**) The acetylenic macrorings **29** and **30** with peripheral fullerene spheres attached are solubilized derivatives of C_{195} and C_{260}, members of a class of fullerene-acetylene hybrid carbon allotropes with the general composition $C_{n(60+5)}$.

the larger carbon cages (*87*, *88*) awaits improved methods for both their preparation and purification.

Finally, fullerene research has increased the general interest in new synthetic carbon allotropes (*89*). Already, the comparative analysis of fullerene reactivity to that of extended conjugated carbon-rich materials reveals that facile reversible reduction by multiple one-electron steps and difficult oxidizability may be properties that are common to all unsaturated carbon matter (*90*).

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