176. Structures and Chemistry of Methanofullerenes: A Versatile Route into *N*-[(Methanofullerene)carbonyl]-Substituted Amino Acids

by **Lyle Isaacs** and **François Diederich***

Laboratorium für Organische Chemie, ETH-Zentrum, Universitätstrasse 16, CH-8092 Zürich

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The reaction of C_{60} with oxadiazole **13** afforded the dimethoxymethanofullerene **7** in 32% yield as a 6-6-ring-bridged isomer with a closed transannular bond. A literature survey showed that all 6-6-ring-bridged methanofullerenes are σ-homoaromatic with a closed transannular bond (6-6-closed) and all 6-5-ring-bridged are π-homoaromatic with an open transannular bond (6-5-open). The preference for 6-6-closed and 6-5-open structures is not due to substituent effects but is best explained with the conservation in these isomers of the favorable bonding seen in C_{60} with higher double-bond character at 6-6 bonds and higher single-bond character at 6-5 bonds. Reaction of C_{60} with diazo diester **15** gave the fullerene diester **14** which was hydrolyzed with BBr_3 in benzene to the methanofullerenecarboxylic acid **10**, a versatile synthon for the preparation of amphiphilic fullerene derivatives. Treatment of **10** with alcohols and amino acid esters under DCC coupling conditions afforded the esters **5** and **17** and the amino-acid derivatives **11** and **12**, respectively.

1. Introduction. – Among the various methods for functionalization of buckminsterfullerene that were developed during the past two years [1] [2], the addition of diazo compounds [3] and diazirines [4] rapidly attracted particular interest as a result of the interesting electronic structures of the produced methanofullerenes [5–8]. Methano-bridging in C_{60} occurs both at the 6-6- and the 6-5-ring junctions, in contrast to bridging by four- [9], five- [10], and six-membered rings [11], which apparently only occurs at the 6-6-ring junction. In addition, similar to the 1,6-methano[10]annulenes [12], methano-bridged fullerenes can adopt a π-homoaromatic structure with an open transannular bond or a σ-homoaromatic structure with a closed transannular bond and experimentally, the 6-6-closed and 6-5-open geometries have been found (*Fig. 1*). In a previous paper, we showed that the addition of diazo acetates to C_{60} in refluxing toluene initially led to kinetic mixtures of 6-5-open (**1**/**3** and **2**/**4**, resp.) and 6-6-closed products (**5** and **6**, resp.), and that further heating of the mixtures led exclusively to the thermodynamic products **5** or **6**, respectively [6]. The assignment of 6-6-closed and 6-5-open structures relied on the evaluation of the ^{13}C-NMR chemical shifts of the bridgehead C-atoms and the coupling constants ^1J(C,H) in the methano bridges, two sensitive indicators for σ/π-homoaromaticity in the analysis of the bonding structure in methanoannulenes [12] [13].

With reliable methods for structural assignment in hand, it was of interest to investigate the effect of substituents in the methano bridge on the position of the valence-isomerization equilibrium between σ- and π-homoaromatic methanofullerenes. Such effects are well established in the 1,6-methano[10]annulenes, where an electron-withdrawing substituent like the CN group at the bridging C-atom favors a closed transannular bond, whereas electron-donating substituents like the Me group favor an open transannular

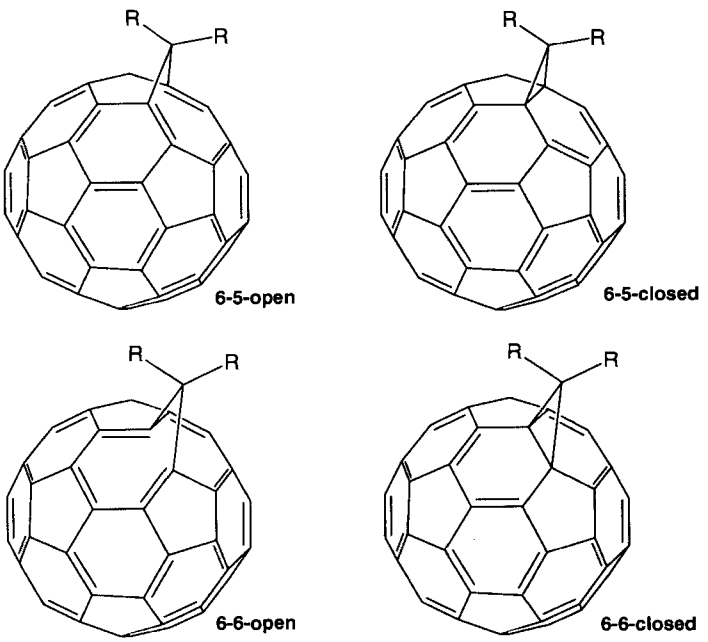
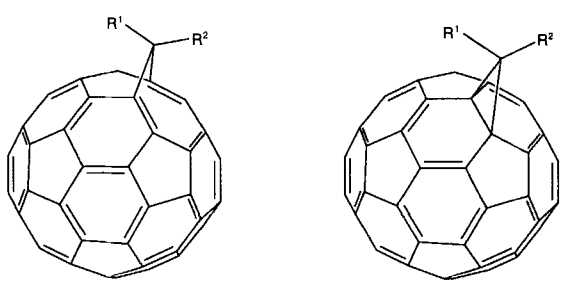
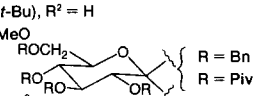


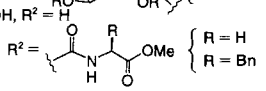
Fig. 1. *The four possible isomeric methanofullerenes.* The labels indicate whether the transannular bonds at the 6-6- and 6-5-ring junctions are open (π-homoaromatic) or closed (σ-homoaromatic) and are used in the text to describe these geometries.

bond or an electronic structure somewhere between the two extreme valence isomers [13] [14]. In this paper, an analysis of previous work combined with new data on dimethoxymethanofullerene **7** shows conclusively that, in contrast to the chemistry of methanoannulenes, the bonding in the bridged C-spheres rather than substituent effects determines the experimentally observed position of the valence-isomerization equilibria in methanofullerenes.



1 $R^1 = H$, $R^2 = COOEt$
2 $R^1 = H$, $R^2 = COO(t\text{-}Bu)$
3 $R^1 = COOEt$, $R^2 = H$
4 $R^1 = COO(t\text{-}Bu)$, $R^2 = H$

5 $R^1 = COOEt$, $R^2 = H$
6 $R^1 = COO(t\text{-}Bu)$, $R^2 = H$
7 $R^1 = R^2 = MeO$
8, **9** $R^1, R^2 =$ 

R = Bn
R = Piv
10 $R^1 = COOH$, $R^2 = H$
11, **12** $R^1 = H$, $R^2 =$ 

R = H
R = Bn

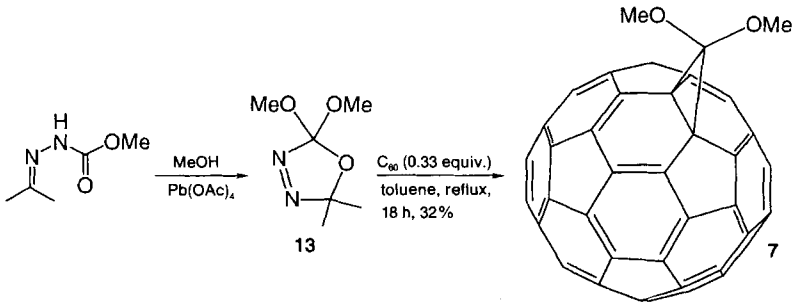
Versatile methods for fullerene functionalization are desirable for the preparation of amphiphilic derivatives that show enhanced solubility in polar solvents and may form interesting mono- and multilayer films on surfaces or at interfaces [11f] [15]. Of particular interest is the preparation of fullerene-substituted amino acids and peptides which, like the methanofullerene-substituted sugar derivatives **8** and **9** [4], could potentially have interesting biological properties. With the methanofullerenecarboxylic acid **10**, we report a versatile new synthon for the preparation of amphiphilic fullerene derivatives and illustrate its utility by the preparation of the amino-acid derivatives **11** and **12**.

2. Substituent Effects in Methanofullerenes. – Recently, we showed that the same type of analysis used to determine the position of valence-isomer equilibria in 1,6-methano[10]annulenes can also be applied to methanofullerenes [6]. In π-homoaromatic methanoannulenes, the bridged C-atoms resonate between 110 and 120 ppm in the ^{13}C-NMR spectrum, while in the σ-homoaromatic structures, these C-atoms are sp^3-hybridized, and their resonances appear around 50–60 ppm [12] [13]. A second spectral criterion used to discriminate between the two structural extremes is the coupling constant ^1J(C,H) of a proton on the methano bridge. In the π-homoaromatic ('open') form, this quantity is typically 140–145 Hz, while in the σ-homoaromatic ('closed') form, its value is typical of a cyclopropane ring (165–170 Hz). The structures of methanofullerenes were assigned in a similar way. In the 6-5-open (π-homoaromatic) derivatives **1–4** as well as in the parent compound with a CH_2-bridge across a 6-5-ring junction [5], the bridgehead C-atoms resonate above 130 ppm, and ^1J(C,H) in the bridge adopts values between 140–145 Hz. In the 6-6-closed (σ-homoaromatic) derivatives **5**/**6** and **9**/**10**, the bridgehead ^{13}C-NMR resonance appears between 70 and 80 ppm, and ^1J(C,H) is 165–170 Hz.

At the start of this study, considerable confusion existed with regard to influences of methano-bridge substituents on the valence isomerization in methanofullerenes. Ester groups at C(61) led to the formation of both 6-5-open (**1–4**) and 6-6-closed isomers (**5**/**6**) [6], and similar findings were now reported for the parent methanofullerene (CH_2-bridge) [5] [7]. The 6-6-open structures were assigned by *Wudl* and coworkers to 6-6-ring-bridged 61-monophenyl- and 61,61-diphenylmethanofullerene derivatives [3] [16]. On the other hand, the sugar derivatives **9**/**10** are clearly 6-6-closed [4]. Apparently, the electron-donating Ph and sugar substituents lead to opposite isomeric preferences. Since we rationalized that the bulky fullerene might have locked the sugar ring into a conformation where it could not stabilize electronically a π-homoaromatic structure, we wanted to prepare a derivative in which both substituents at C(61) were strongly electron-donating and not constrained by a ring in exerting their electronic effects on the valence-isomerization equilibrium. Thus, the dimethoxymethanofullerene **7** was prepared following a recent report by *Warkentin* and coworkers [17] on oxadiazole **13** as a convenient source for dimethoxycarbene (*Scheme 1*).

When the product of the reaction of C_{60} and **13** with the R_f value closest to the faster eluting C_{60} was isolated by flash chromatography (SiO_2, hexane/toluene gradient), its ^{1}H-NMR spectrum showed only a single Me resonance at 4.03 ppm, in accord with structure **7** and establishing that bridging had occurred at the 6-6-ring junction. The ^{13}C-NMR spectrum of **7** showed 16 peaks in the fullerene region above 135 ppm along with a peak at 84.59 ppm for a total of 17 fullerene resonances, as expected for the depicted C_{2v}-symmetry of **7** (the remaining resonances at 97.09 and 55.01 belong to the ketal and MeO C-atoms, resp.). We assigned the peak at 84.59 to the bridgehead C-atoms

Scheme 1



and concluded from its chemical shift that **7** is σ-homoaromatic. In the series **5**–**9**, the ^{13}C-NMR chemical shifts of the bridgehead C-atoms showed a downfield trend from *ca.* 70 (**5**/**6**) to 79 (**8**/**9**) to 85 ppm (**7**). By adding O-atoms to the methano bridge, the ^{13}C-NMR resonances move downfield due to the inductive effect. We clearly prefer this explanation over invoking an increase in the degree of sp^2-character of the bridgehead C-atoms in the series as a result of an increasing substituent-induced preference for a π-homoaromatic structure. This immediately called into question the validity of the assignment of an open structure to 6-6-ring-bridged mono- and diphenylmethanofullerenes by *Wudl* and coworkers [3] [16]. It was not obvious why MeO groups would lead to a closed and Ph groups to an open transannular bond at a 6-6-ring junction. Indeed, since the time of our observation, *Wudl* and coworkers reformulated their original structural assignments of 61-monophenyl- and 61,61-diphenylmethanofullerenes to σ-homoaromatic ones [18]. Similarly, a closed structure was also assigned by *Akasaka et al.* to 6-6-ring-bridged 61,61-bis(2,6-diisopropylphenyl)silanofullerene[60] [19]. Thus, all known 6-6-ring-bridged methanofullerenes possess a closed transannular bond.

3. A Simple Rational for the Preferred Formation of 6-6-Closed and 6-5-Open Methanofullerenes. – Not only do all methanofullerenes that are bridged at the 6-6-ring junction have a closed transannular bond (6-6-closed), but a literature survey also shows that all derivatives that are bridged at the 6-5-ring junction possess an open transannular bond (6-5-open) [5] [6] [20]. We propose a simple structural model that explains why the 6-6-closed and 6-5-open isomers are strongly preferred over the 6-6-open and 6-5-closed geometries, respectively.

In a first approximation, the electronic structure of C_{60} is best described in terms of 1,3,5-cyclohexatriene and [5]radialene (= pentakis(methylidene)cyclopentane) substructures [2] [21] [22]. In X-ray crystal structures of C_{60} derivatives [11a] [11b] [11f] [23], the bonds at the 6-6-ring junctions ('6-6 bonds') are found to be shorter (*ca.* 1.40 Å) than the bonds at the 6-5-ring junctions ('6-5 bonds'; *ca.* 1.45 Å). According to our model, those methanofullerene isomers are formed which preserve best the bonding seen in C_{60}.

Firstly, the bridges in the experimentally produced 6-6-closed and 6-5-open forms provide a better geometric fit than in the unobserved 6-6-open and 6-5-closed forms. It is energetically more favorable to bridge the shorter 6-6-ring junction in a σ-homoaromatic way, which positions the bridgehead C-atoms at closer distance, and to bridge the longer 6-5-ring junction in a π-homoaromatic way, which leads to a larger transannular distance.

More importantly, in a 6-6-closed methanofullerene, all double bonds are localized in 1,3,5-cyclohexatriene and [5]radialene substructures, which corresponds to the favorable bonding situation in C_{60}. In contrast, a consideration of the resonance structures in the 6-6-open valence isomer shows that three 6-5-ring junctions have reached higher double-bond character whereas two 6-6-ring junctions adopt a higher single-bond character (*Fig. 1*). Overall in this isomer, the bond order has decreased in the 6-6 and increased in the 6-5 bonds. This elongation of 6-6 and shortening of 6-5 bonds is energetically costly relative to a C_{60}-like geometry and, therefore, the 6-6-open is strongly disfavored over the 6-6-closed geometry.

Similar reasoning explains why the 6-5-open isomer is strongly preferred over the 6-5-closed structure. The 6-5-open form preserves C_{60}-like bonding with higher double-bond character at all 6-6-ring junctions and higher single-bond character at all 6-5-ring junctions. In contrast, resonance structures in the valence-isomeric 6-5-closed form possess three elongated 6-6 bonds and two contracted 6-5 bonds (*Fig. 1*) which, again, is energetically very costly.

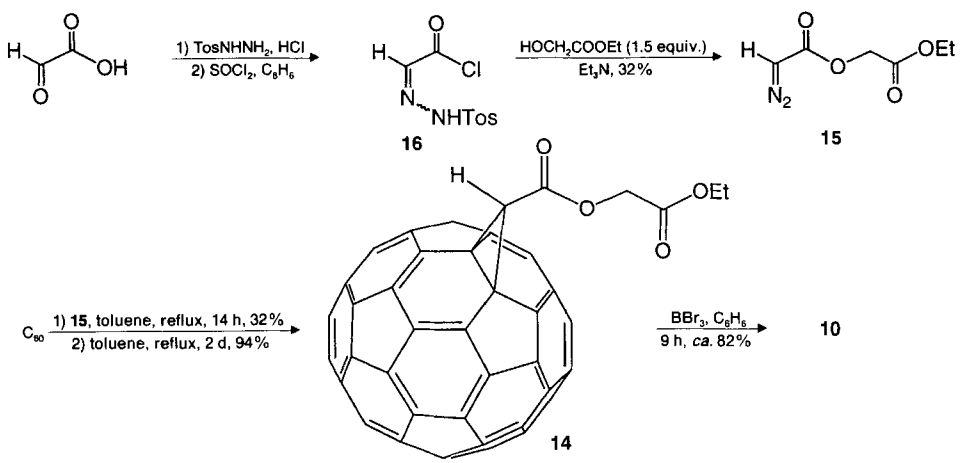
Thus, the preference for 6-6-closed and 6-5-open geometries is due to the conservation in these structures of the C_{60} electronic structure with higher double-bond character at all 6-6-ring junctions and higher single-bond character at all 6-5-ring junctions. Substituent effects, if at all, play a very minor role in determining the valence-isomeric preference.

4. A Methanofullerene-61-carboxylic Acid as a Versatile Synthon for the Preparation of *N*-[(Methanofullerene)carbonyl]-Substituted Amino Acids and Other Amphiphilic Derivatives. – Our initial objective in the elaboration of methanofullerene synthetic chemistry was the preparation of methanofullerenecarboxylic acid **10** from the corresponding ethyl ester **5** and subsequent condensation with amines under formation of *N*-[(methanofullerene)carbonyl]-substituted amino acids and ultimately peptides. However, early attempts to hydrolyze **5** were unsuccessful; presumably the bulky fullerene moiety hinders the approach of nucleophilic reagents on favorable trajectories. Also, model examinations show that nucleophilic attack at the ester carbonyl group in **5** forces the developing oxido anion into the fullerene π-cloud, thus generating an energetically high-lying reaction transition state. Therefore, we changed strategy and prepared the diester **14**, hoping for regioselective hydrolysis of the ethyl-ester moiety, which is located at greater distance from the C_{60} core.

A general route to diazo acetates by *House* and *Blankley* [24] was followed to prepare the diazo diester **15** *via* **16** (*Scheme 2*) which was subsequently reacted with C_{60}. The initially formed mixture of 6-5-open and 6-6-closed isomers was equilibrated to the thermodynamic product **14** by heating in toluene. When **14** was treated with 5 equiv. of BBr_3 in benzene [25], much to our surprise, the methanofullerenecarboxylic acid **10** was readily produced as an insoluble material. In sharp contrast, even extended treatment of **5** with 15 equiv. of BBr_3 resulted in no conversion to acid **10** (TLC analysis). Apparently, chelation of BBr_3 to the terminal ester functionality strongly enhances the rate of hydrolysis by an internal delivery mechanism. Acid **10** could also be prepared in good yield by treatment of the *tert*-butyl ester **6** with toluene-4-sulfonic acid (TosOH) in refluxing benzene. However, the route *via* **14** is preferable since its purification only required one column chromatography in contrast to three for the purification of *tert*-butyl ester **6**.

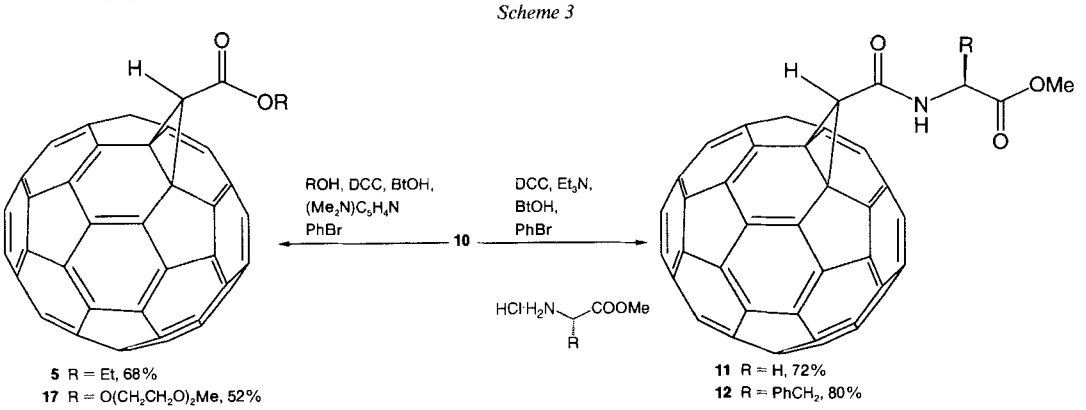
The reactivity of **10** was subsequently explored in DCC-mediated [26] esterification

Scheme 2



and amidation reactions (*Scheme 3*). Reaction of **10** with EtOH in the presence of dicyclohexylcarbodiimide (DCC) and 1*H*-benzotriazol-1-ol (BtOH) in bromobenzene in the presence of a catalytic amount of 4-(dimethylamino)pyridine ($(Me_2N)C_5H_4N$) afforded the known ester **5** in 68% yield. With diethylene glycol monomethyl ether under the same reaction conditions, ester **17** was obtained which is much more soluble in organic solvents than **5** or **6**. The ^{13}C-NMR spectrum of C_s-symmetrical **17** in $CDCl_3$ showed, as expected, 32 well resolved fullerene resonances, which proved to be useful in analyzing the spectrum of C_1-symmetrical **12**.

Scheme 3



Under conditions similar to those of the esterifications, the *N*-[(methanofullerene)-carbonyl]-substituted amino-acid esters **11** and **12** were formed in good yields (*Scheme 3*). The glycine derivative **11** is poorly soluble in pure solvents, and a mixture of CCl_4/$(CD_3)_2SO$ was used to record its ^{13}C-NMR spectrum. The phenylalanine derivative is soluble in $CDCl_3$, and its remarkably resolved 125.6-MHz ^{13}C-NMR spectrum showed 57 of the 60 fullerene resonances expected for a C_1-symmetrical compound. Except for the two bridgehead resonances at 71.29 and 71.21 ppm, all fullerene ^{13}C-NMR signals

appeared in the spectral range between 136 and 149 ppm (*Fig. 2*). Since **12** was prepared from methyl L-phenylalaninate hydrochloride, enantiomerically enriched product formation was expected. Indeed, the circular-dichroism spectrum (*Fig. 3*) showed that one enantiomer, presumably with (*S*)-configuration, was formed predominantly, although the degree of optical purity of **12** remains to be determined.

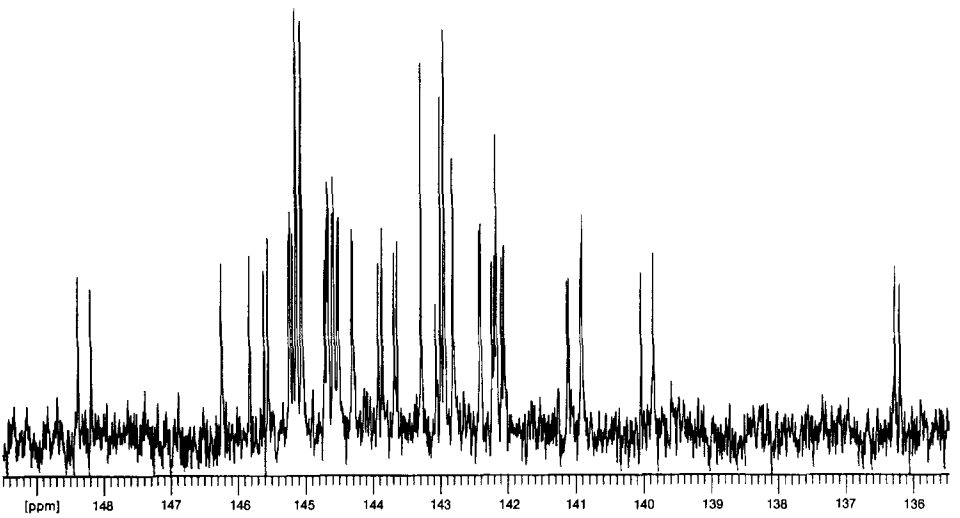


Fig. 2. *Expanded 136–149-ppm region in the* ^{13}C*-NMR spectrum* (125.6 MHz, $CDCl_3$) *of the* C_1*-symmetrical* **12**

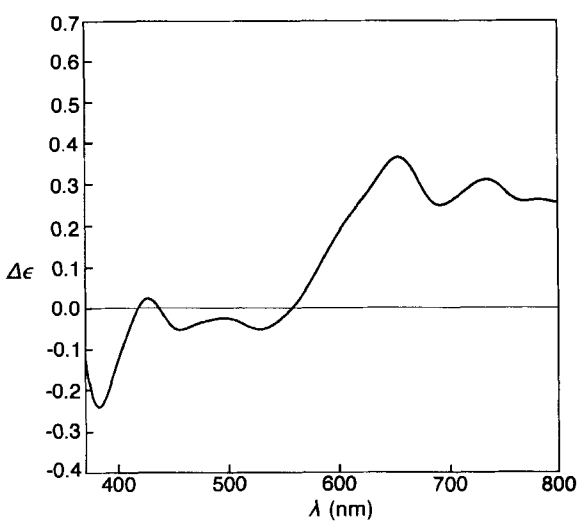


Fig. 3. *CD Spectrum of* **12** ($c = 0.242$ mM) *in* CH_2Cl_2

5. Conclusions. – An analysis of all available data on methanofullerenes, including the newly prepared dimethoxymethanofullerene **7**, showed that all known 6-6-ring-bridged compounds are 6-6-closed (closed transannular bond) and all 6-5-ring-bridged com-

pounds are 6-5-open (open transannular bond). The preference for 6-6-closed and 6-5-open structures is not due to substituent effects. Rather, 6-6-closed and 6-5-open are preferred over 6-6-open and 6-5-closed structures, respectively, since they conserve the bonding seen in C_{60} with higher single-bond character at all 6-5-ring junctions and higher double-bond character at all 6-6-ring junctions. Additionally, π-homoaromatic bridging provides a better steric fit at the longer 6-5-ring junction and, correspondingly, σ-homoaromatic bridging fits better geometrically at the shorter 6-6-ring junction. The question still remains open, under which conditions 6-5-bridged and/or 6-6-bridged compounds are formed and can be isolated. Equilibration studies clearly show that the 6-6-closed structures are the thermodynamic products. It is possible that, in the additions of diazo alkanes and diazo acetates *via* 1,3-dipolar cycloadditions followed by N_2 extrusion or by carbene addition, both 6-5-open and 6-6-closed structures are formed each time, but that the rearrangement to the thermodynamic products occurs at different rates, depending on the substituent. Also, carbene-addition and 1,3-dipolar-cycloaddition mechanisms could show different regioselectivity. With the methanofullerenecarboxylic acid **10**, a versatile synthon is now available for the preparation of amphiphilic and biologically interesting fullerene derivatives like *N*-[(methanofullerene)carbonyl]-substituted amino acids and peptides. The attachment of such *N*-fullerene-substituted amino acids [27] to oligopeptides is now under investigation.

Experimental Part

General. See [6] [11f]. All crystalline fullerene samples include traces of solvents that cannot be removed by drying at 90°/10^{-1} Torr. All melting points of fullerene derivatives are above 275°. UV/VIS: λ_{max} in nm (ε). CD Spectra: *Jasco-J-710* spectrometer. MS: EI = electron ionization; FAB = fast-atom bombardment; LD = laser desorption; *m/z* (%). Elemental analyses are calculated with solvent included.

1,2-Dihydro-61,61-dimethoxy-1,2-methanofullerene[60] (**7**)[1]). A soln. of C_{60} (200 mg, 0.278 mmol) and **13** [17] (133 mg, 0.833 mmol) in toluene (100 ml) was refluxed under N_2 for 18 h at which time TLC analysis (toluene/hexane 1:1) showed very little remaining C_{60}, mono-, di-, and triadducts, in order of decreasing R_f. The crude product was adhered onto silica gel by rotary evaporation and chromatographed. Hexane/toluene 95:5 eluted C_{60} and hexane/toluene 1:1 the pink-red product band (R_f 0.71). Evaporation left a black solid which was washed with Et_2O, dissolved in $CHCl_3$, reprecipitated with Et_2O, and dried (90°/10^{-1} Torr): 70 mg (32%) of **7**. UV/VIS (CH_2Cl_2): 689 (160), 498 (1210), 431 (1740), 404 (sh, 2890), 328 (32560). IR (KBr): 2956*w*, 2926*w*, 1628*w*, 1436*w*, 1426*w*, 1399*s*, 1260*w*, 1247*w*, 1214*w*, 1185*w*, 1138*m*, 1115*m*, 1051*s*, 1014*m*, 954*w*, 861*w*, 596*w*, 576*w*, 554*m*, 524*s*. ^{1}H-NMR (300 MHz, $CDCl_3$): 4.03 (*s*, 6 H). ^{13}C-NMR (125.6 MHz, $CDCl_3$): 145.24; 145.03; 144.93; 144.74 (2 ×); 144.18; 144.16; 143.99; 143.51; 143.34; 143.08; 142.84; 142.43; 142.28; 141.29; 137.63; 97.09; 84.59; 55.01. LD-MS: 794 (M^+), 779, 763, 751, 720. Anal. calc. for $C_{63}H_6O_2 \cdot 0.1\ CHCl_3$ (806.69): C 93.95, H 0.76, O 3.97; found: C 93.97, H 1.12, O 3.96.

(Ethoxycarbonyl)methyl Diazoacetate (**15**). Ethyl glycolate (1.892 g, 1.72 ml, 18.17 mmol) was added under N_2 *via* syringe to a soln. of **16** [24] (3.159 g, 12.11 mmol) in CH_2Cl_2 (45 ml). After dropwise addition of Et_3N (3.065 g, 4.22 ml, 30.29 mmol) over 5 min, the mixture rapidly became dark red and was stirred for 2.5 h. The soln. was washed with 0.1M HCl, sat. aq. $NaHCO_3$, and sat. aq. NaCl soln., dried ($MgSO_4$), and evaporated and the crude product chromatographed (SiO_2, hexane/AcOEt 4:1) and then distilled at 67°/0.5 Torr: **15** (670 mg, 32%). Yellow oil (R_f 0.41). IR (neat): 3114*m*, 2983*m*, 2119*s*, 1758*s*, 1703*s*, 1424*s*, 1386*s*, 1343*s*, 1201*s*, 1171*s*, 1094*s*, 1058*s*, 1029*m*, 943*w*, 918*w*, 861*w*, 843*w*, 739*m*. ^{1}H-NMR (200 MHz, $CDCl_3$): 4.88 (*s*, 1 H); 4.67 (*s*, 2 H); 4.24 (*q*, J = 7.2, 2 H); 1.29 (*t*, J = 7.2, 3 H). ^{13}C-NMR (50 MHz, $CDCl_3$): 168.23; 166.46; 61.62; 60.96; 46.56; 14.17. EI-MS: 172 (4, M^+), 144 (14, $[M - N_2]^+$), 127 (29, $[M - OEt]^+$), 116 (62, $[M - N_2 - CO]^+$), 99 (22, $[M - CO_2Et]^+$), 69 (100, $[CHN_2CO]^+$), 59 (13, $[OCH_2CHO]^+$), 29 (44, $[Et]^+$). HR-MS: 172.0475 (M^+, $C_6H_8N_2O_4$, 172.0484).

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[1]) The most recently proposed numbering system for fullerene[60] was used, see: R. Taylor, *J. Chem. Soc., Perkin Trans. 2* **1993**, 813.

(Ethoxycarbonyl)methyl 1,2-Dihydro-1,2-methanofullerene[60]-61-carboxylate (**14**). A refluxing mixture of C_{60} (1.088 g, 1.51 mmol) and **15** (390 mg, 2.265 mmol) in toluene (1.1 l) was stirred for 18 h. The wine-red soln. was evaporated and the crude product adhered onto silica gel and chromatographed (SiO_2). Residual C_{60} (257 mg, 24%) was eluted with hexane/toluene 1:1 and the purple product band (413 mg, 32%) with pure toluene. After evaporation, the solid was redissolved in toluene (1.1 l) and the soln. refluxed for 46 h and then concentrated to 500 ml and filtered through a plug of SiO_2 using toluene as eluant. The black precipitate obtained upon evaporation of the orange-red product fractions was washed with Et_2O, dissolved in $CHCl_3$, and reprecipitated with Et_2O: 388 mg (94%) of **14**. TLC (hexane/toluene 1:1): R_f 0.69. UV/VIS (CH_2Cl_2): 688 (130), 492 (1060), 427 (1860), 413 (sh, 1690), 401 (sh, 2460), 392 (sh, 3550), 327 (26790). IR (KBr): 2972*w*, 1749*s*, 1629*w*, 1422*m*, 1400*s*, 1385*m*, 1179*m*, 1149*s*, 575*w*, 525*s*. ^{1}H-NMR (300 MHz, $CDCl_3$): 4.98 (*s*, 2 H); 4.91 (*s*, 1 H); 4.34 (*q*, J = 7.2, 2 H); 1.35 (*t*, J = 7.2, 3 H). ^{13}C-NMR (125.6 MHz, $CDCl_3$): 167.11; 165.72; 148.00; 145.53; 145.41; 145.28; 145.24; 145.21; 145.10; 145.04; 144.72 (2 ×); 144.68 (2 ×); 144.65; 144.56; 144.47; 143.96; 143.74; 143.27; 143.08; 143.02; 142.98; 142.96; 142.82; 142.40; 142.21; 142.09; 142.08; 141.16; 140.96; 140.56; 136.50; 70.21; 61.93; 61.91; 38.17; 14.18. FAB-MS: 864 (M^+), 791, 744, 733, 720. Anal. calc. for $C_{66}H_8O_4 \cdot 0.1\ C_7H_8 \cdot 0.1\ CHCl_3$ (864.79): C 90.56, H 1.01, O 7.22; found: C 90.58, H 1.28, O 7.28.

1,2-Dihydro-1,2-methanofullerene[60]-61-carboxylic Acid (**10**). a) *Via* **14**: A total of 0.75 ml (187 mg, 0.746 mmol) of 1M BBr_3 in CH_2Cl_2 was added by syringe under N_2 to a soln. of **14** (129 mg, 0.149 mmol) in benzene (60 ml). After stirring for 9 h, the reaction was quenched by addition of 0.1M HCl, the suspension of **10** in the org. solvent washed with H_2O, and the product suspension in C_6H_6 evaporated. The compound was redissolved in $CHCl_3$/Me_2SO, reprecipitated with hexane and dried overnight at 25°/0.1 Torr: 95 mg (82%) of **10**. Black solid that is quite insoluble in common solvents and only slightly soluble in solvents like bromobenzene and 1,2-dichlorobenzene. IR (KBr): 3442*m*, 3208*w*, 3039*w*, 2922*w*, 1794*s*, 1785*s*, 1706*m*, 1426*s*, 1383*m*, 1315*w*, 1183*m*, 1113*w*, 1090*w*, 1013*s*, 966*m*, 942*m*, 847*s*, 810*s*, 747*m*, 732*m*, 699*s*, 667*m*, 575*m*, 561*w*, 525*s*, 486*m*, 458*w*, 436*w*. ^{1}H-NMR (300 MHz, $CDCl_3$/$(CD_3)_2SO$ 1:1): 5.13 (*s*, 1 H). ^{13}C-NMR ($CDCl_3$/$(CD_3)_2SO$ 1:1): 166.95; 148.76; 146.77; 145.49; 145.04; 144.75; 144.71; 144.67; 144.62; 144.42; 144.38; 144.24; 144.21; 144.10; 143.99; 143.83; 143.52; 143.33; 142.81; 142.67; 142.56; 142.54; 142.51; 142.44; 142.15; 141.82; 141.73; 141.69; 140.61; 140.36; 139.79; 136.15; 71.66; 40.34. FAB-MS: 778 (29, M^+), 733 (48, $[M - COOH]^+$), 720 (100, $[M - CHCOOH]^+$). Anal. calc. for $C_{62}H_2O_2 \cdot 0.5\ Me_2SO$ (817.77): C 92.53, H 0.62; found: C 92.63, H 0.57.

b) *Via* **6**: A mixture of **6** (25 mg, 0.030 mmol) and toluene-4-sulfonic acid (10 mg, 0.058 mmol) in toluene (20 ml) was heated to reflux for 8 h. H_2O (20 ml) was added and stirring continued for 30 min. The H_2O layer was decanted and the toluene layer filtered to give a brown solid which was washed with H_2O and Et_2O, then dried for 12 h at 60°/10^{-1} Torr: 18 mg (77%) of **10**.

Ethyl 1,2-Dihydro-1,2-methanofullerene[60]-61-carboxylate (**5**). To the stirred soln. of **10** (35.7 mg, 0.0458 mmol), EtOH (21.1 mg, 0.458 mmol), and BtOH (31.0 mg, 0.229 mmol) in PhBr (10 ml) were added under N_2 simultaneously by syringe two solns. of DCC (31.0 mg, 0.229 mmol) and 4-(dimethylamino)pyridine (1.12 mg, 0.0092 mmol) in PhBr (0.25 ml each). The reaction was stirred at 20° for 51 h after which the solvent was evaporated to yield a black solid. Column chromatography (SiO_2, toluene) afforded a black powder which was washed exhaustively with Et_2O and hexane and dried at 60°/10^{-1} Torr: 25 mg (68%) of **5**. ^{1}H- and ^{13}C-NMR: identical to those of an authentic sample previously prepared by another method [6].

2-(2-Methoxyethoxy)ethyl 1,2-Dihydro-1,2-methanofullerene[60]-61-carboxylate (**17**). To a stirred soln. of **10** (49 mg, 0.0629 mmol) and BtOH (21.3 mg, 0.157 mmol) in PhBr (10 ml) was added under N_2 diethylene glycol monomethyl ether (75.6 mg, 0.629 mmol) followed by DCC (32.5 mg, 0.157 mmol) and 4-(dimethylamino)pyridine (1.5 mg, 0.0125 mmol). After stirring at 20° for 22 h and evaporation, flash chromatography (SiO_2, $CHCl_3$) gave a pink-red fraction which was evaporated. The black solid was washed on a frit with large amounts of Et_2O, then redissolved in $CHCl_3$, and precipitated by slow diffusion of hexane into the $CHCl_3$ soln. The long black needles were dried for 12 h at 60°/0.1 Torr: 29 mg (52%) of **17**. TLC (toluene): R_f 0.11. UV/VIS (CH_2Cl_2): 689 (160), 491 (1300), 427 (2310), 413 (sh, 2150), 401 (sh, 3080), 393 (sh, 4330), 326 (32130), 258 (107800). IR (KBr): 2919*m*, 2869*m*, 2814*m*, 1740*s*, 1426*m*, 1185*s*, 1157*s*, 1138*m*, 1110*m*, 1028*m*, 901*m*, 728*s*, 706*w*, 688*w*, 574*w*, 525*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 4.85 (*s*, 1 H); 4.64 (*t*, J = 4.6, 2 H); 3.95 (*t*, J = 4.6, 2 H); 3.85–3.75 (*m*, 2 H); 3.7–3.6 (*m*, 2 H); 3.44 (*s*, 3 H). ^{13}C-NMR (125.6 MHz, $CDCl_3$): 166.39; 148.23; 145.67; 145.58; 145.26; 145.21; 145.18; 145.08; 145.06; 144.71; 144.68 (2 ×); 144.66; 144.59; 144.58; 144.42; 143.96; 143.73; 143.27; 143.08; 143.00; 142.96; 142.95; 142.80; 142.43; 142.20; 142.09; 142.07; 141.14; 140.92; 140.61; 136.39; 70.52 (fullerene C-atoms); 71.93; 70.68; 69.03; 65.29; 59.17; 38.85. FAB-MS: 881 (M^+), 778, 733, 720. Anal. calc. for $C_{67}H_{12}O_4 \cdot 0.2\ Et_2O \cdot 0.2\ CHCl_3$ (919.54): C 88.82, H 1.56, O 7.31; found: C 88.76, H 1.52, O 7.43.

Methyl N-*(1,2-Dihydro-1,2-methanofullerene[60]-61-carbonyl)glycinate* (**11**). To a stirred soln. of **10** (56 mg, 0.0719 mmol), methyl glycinate hydrochloride (18.1 mg, 0.144 mmol), and BtOH (19.4 mg, 0.144 mmol) in PhBr

(15 ml) was added at 20° under N_2 *via* syringe Et_3N (14.6 mg, 0.144 mmol), followed by DCC (29.7 mg, 0.144 mmol). After stirring at 20° for 20 h, the mixture was submitted to column chromatography (SiO_2, toluene (removal of PhBr), then $CHCl_3$): pink-red product fraction (R_f 0.58) which gave a dark solid upon evaporation. After exhaustive washing with Et_2O, the solid was redissolved in $CHCl_3$, reprecipitated with Et_2O, and dried for 12 h at 60°/0.1 Torr: 43.5 mg (72%) of **11**. UV/VIS (CH_2Cl_2): 691 (330), 493 (1750), 427 (2930), 414 (sh, 2670), 402 (sh, 3730), 393 (sh, 5100), 326 (35270), 259 (118900). IR (KBr): 3547*w*, 3461*w*, 3414*s*, 3328*s*, 2927*s*, 2849*m*, 1747*m*, 1665*w*, 1625*s*, 1575*m*, 1536*w*, 1432*w*, 1384*w*, 1311*w*, 1243*w*, 1205*w*, 1184*w*, 1087*w*, 575*w*, 525*m*. ^{1}H-NMR (200 MHz, $CS_2/C_6D_6/(CD_3)_2SO$ 12:5:2): 9.24 (br. *s*, 1 H); 5.07 (*s*, 1 H); 4.06 (*d*, J = 5.7, 2 H); 3.53 (*s*, 3 H). ^{13}C-NMR (125.6 MHz, $CCl_4/(CD_3)_2SO$ 2:1; 31 out of 32 fullerene resonances clearly recognizable): 169.67; 164.42; 149.37; 147.38; 145.64; 145.26; 144.69; 144.61; 144.58; 144.51; 144.38; 144.19; 144.16; 143.98; 143.87; 143.65; 143.54; 143.27; 142.84; 142.64; 142.52; 142.50; 142.44; 142.31; 142.19; 141.83; 141.69; 141.67; 140.51; 140.20; 139.93; 135.84; 72.43; 51.71; 41.51; 41.06. FAB-MS: 849 (M^+), 797, 733, 720. Anal. calc. for $C_{65}H_7NO_3 \cdot 0.35\ CHCl_3$ (891.57): C 88.04, H 0.83, N 1.57; found: C 87.90, H 1.00, N 1.65.

Methyl N-*(1,2-Dihydro-1,2-methanofullerene[60]-61-carbonyl)*-L-*phenylalaninate* (**12**). To a stirred soln. of **10** (52 mg, 0.0688 mmol), methyl L-phenylalaninate hydrochloride (28.8 mg, 0.134 mmol), and BtOH (18.0 mg, 0.134 mmol) in PhBr (15 ml) was added at 20° under N_2 DCC (27.6 mg, 0.134 mmol) and Et_3N (13.5 mg, 0.134 mmol) in rapid succession. After stirring for 19 h at 20°, the mixture was submitted to column chromatography (SiO_2, toluene (removal of PhBr), then $CHCl_3$): pink-red product fraction. Evaporation yielded a black solid which was washed with generous quantities of Et_2O, dissolved in $CHCl_3$, reprecipitated with hexane, and dried for 12 h at 60°/0.1 Torr: 50.0 mg (80%) of **12**. UV/VIS (CH_2Cl_2): 497 (1550), 428 (2740), 414 (sh, 2440), 401 (3600), 393 (sh, 5150), 327 (39210), 259 (130400). IR (KBr): 3406*m*, 3294*m*, 3022*w*, 2996*w*, 2940*w*, 2922*w*, 2849*w*, 1740*s*, 1686*m*, 1663*s*, 1536*m*, 1496*m*, 1428*s*, 1203*m*, 1185*s*, 751*m*, 699*m*, 575*m*, 526*s*. ^{1}H-NMR (300 MHz, $CDCl_3$): 7.40–7.20 (*m*, 5 H); 6.85 (*d*, J = 7.8, 1 H); 5.20 (*dt*, J = 7.8, 5.9, 1 H); 4.69 (*s*, 1 H); 3.86 (*s*, 3 H); 3.41 (*dd*, J = 5.9, 14.0, 1 H); 3.31 (*dd*, J = 5.9, 14.0, 1 H). ^{13}C-NMR (125.6 MHz, $CDCl_3$; 57 out of 60 fullerene resonances clearly visible): 171.71; 164.15; 148.38; 148.19; 146.24; 145.82; 145.61; 145.56; 145.23; 145.19; 145.14 (2 ×); 145.12; 145.06 (2 ×); 145.05; 144.71; 144.69; 144.68; 144.66 (2 ×); 144.60; 144.59; 144.57; 144.52; 144.50; 144.31; 144.30; 143.92; 143.86; 143.69; 143.64; 143.28 (2 ×); 143.07; 143.00 (2 ×); 142.94 (2 ×); 142.81 (2 ×); 142.42; 142.40; 142.23; 142.20; 142.17 (2 ×); 142.09; 142.05; 141.13; 141.10; 140.92; 140.91; 140.04; 139.86; 136.27; 136.20; 135.34; 129.38; 128.82; 127.49; 71.29; 71.21; 53.75; 52.71; 41.28; 37.85. FAB-MS: 940 (M^+), 733, 720. Anal. calc. for $C_{72}H_{13}NO_3 \cdot 0.5\ Et_2O$ (980.68): C 90.98, H 1.86, N 1.43; found: C 90.56, H 1.60, N 1.54.

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