Diels–Alder Adduct of C_{60} and 4-Carboxy-*o*-quinodimethane: Synthesis and Chemical Transformations

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The Diels–Alder reaction of *o*-quinodimethanes to buckminsterfullerene C_{60} (**1**) affords thermally stable derivatives. 4-Carboxy-*o*-quinodimethane (**4**) was prepared in situ from 3,4-bis(bromomethyl)-benzoic acid (**3**) and reacted with **1** to give the carboxy-substituted adduct mixture **5**(n). Due to its decreased solubility, **5**(n) was used without further purification for transformations into the corresponding esters and amines. This was achieved by two different methods: (a) via the carboxylic acid chloride **6**(n), whereby the alcohol/amine has to be used in excess, and (2) via the active ester **7**($n = 1$), which allows stoichiometric reactions with amines. All these derivatives are quite soluble in commonly used organic solvents. This enabled us to separate and completly characterize the products.

The unique optical, mechanical, and electronic properties[1] of buckminsterfullerene C_{60} (**1**) make it attractive for incorporation into polymers[2] and for attachment to electron donors[3] or physiologically active compounds.[4] Toward this end, it is necessary to prepare physically stable and, at the same time, chemically reactive C_{60} adducts. The [4 + 2]-cycloaddition reaction of *o*-quinodimethanes with C_{60} is the method of choice for this purpose,[5] because, on the one hand, the adducts are thermally stable and, on the other hand, it is possible to use *o*-quinodimethane as a vehicle for the introduction of a multitude of reactive functional groups (e.g. amino or carboxy). Herein, we report on the synthesis of carboxy-substituted adducts of C_{60} and *o*-quinodimethane and the subsequent reactions of these adducts with alcohols and amines.

NBS bromination of 3,4-dimethylbenzoic acid (**2**) with benzoyl peroxide as radical initiator yields 3,4-bis(bromomethyl)benzoic acid (**3**), which can be transformed into the corresponding carboxy-substituted *o*-quinodimethane **4** by base-induced bromine elimination in boiling toluene.[6] This extremely reactive diene adds to the electron poor C_{60} (**1**) in a [4 + 2]-Diels–Alder cycloaddition reaction to give the adducts **5**(n) (Figure 1) which can be identified by FD mass spectrometry (Figure 2) and ^{1}H-NMR spectroscopy. It appears, however, that the adducts are insoluble in toluene, benzene, or chloroform, sparingly soluble in THF and DMSO, and reasonably soluble only in pyridine and pyrrolidine. This is probably due to the formation of intermolecular hydrogen bonds. Therefore, the product mixture is not separated by chromatography but is used without further purification for the following transformations.

The transformation of **5**(n) into the corresponding amides and esters was achieved by two different routes (Figure 3): (a) preparation of the carboxylic acid chlorides **6**(n) and reaction of these compounds with alcohols or amines and (b) preparation of the 2,4,6-trichlorophenolic active esters **7**(n), separation of the resulting active esters, and reaction of the separated adducts with amines.

(a) Preparation of C_{60} Carboxylic Acid Chlorides 6(n) and Their Reactions. The adduct mixture of **5**(n) was first treated with boiling $SOCl_2$. After evaporation of unreacted $SOCl_2$, the residue was dissolved in chloroform and reacted with a 10-fold excess of methanol at room temperature in the presence of 2 equiv of triethylamine to yield the carboxylic acid esters **8**(n). Due to their good solubility in chloroform, these adducts can be easily isolated by chromatography on a polystyrene gel.[7] The monoadduct **8**($n = 1$), which is the major component of the reaction mixture (53%), can be characterized by FD mass spectrometry and ^{1}H-NMR, ^{13}C-NMR, UV/vis, and IR spectroscopy. The FD mass spectrum shows the corresponding peak of the monoadduct (m/z 882) without fragmentation.[8] The UV/vis spectrum of the monoadduct exhibits a small maximum at ca. 435 nm, which is characteristic for all C_{60} monoadducts and therefore well suited for the detection of the monoadducts during

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(6) In this reaction, KI as base and 18-crown-6 as phase-transfer catalyst are used.

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(8) In FD-mass spectra, all C_{60} adducts can be easily detected and usually no fragmentations are observed.

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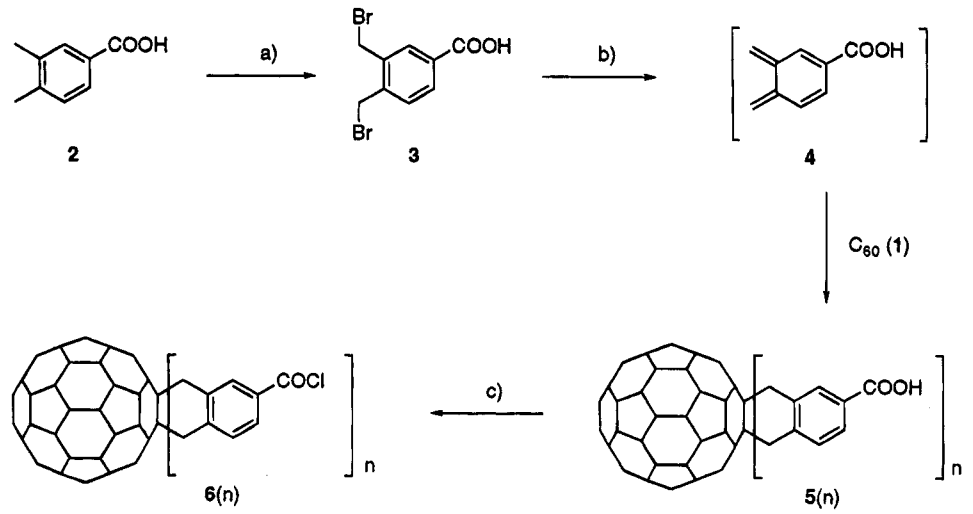

Figure 1. Synthesis of the carboxylic C_{60} adducts **5**(n): (a) CCl_4; NBS (2.4 equiv); dibenzoyl peroxide (0.1 equiv); (b) toluene; KI (4 equiv); 18-crown-6 (3 equiv); (c) $SOCl_2$.

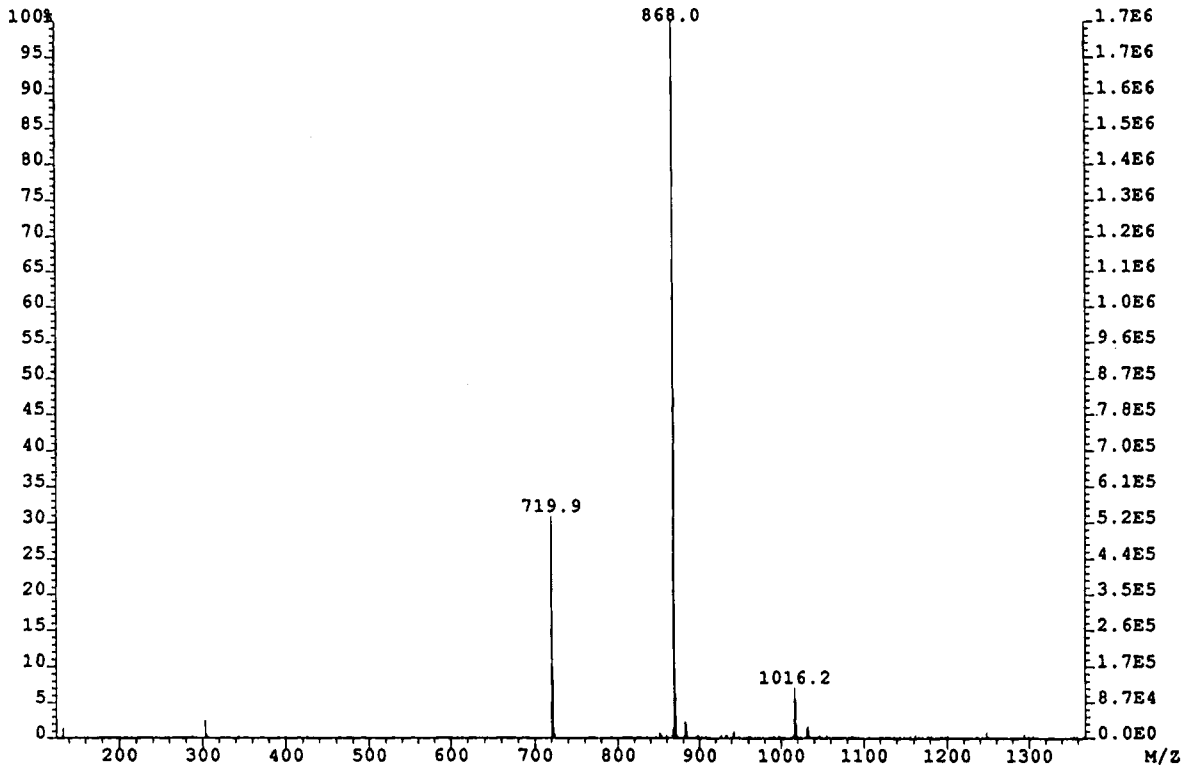

Figure 2. FD-mass spectrum of **5**(n).

chromatography. The ^{1}H-NMR spectrum shows a resonance for the methyl protons of the ester group at δ 4.01. Owing to the cyclohexene ring inversion,[9] the benzylic protons appear as two broadened signals at δ 4.54 and 4.87 and the arene protons resonate at δ 7.76, 8.25, and 8.36. Due to the C_s symmetry, there are 30 peaks arising from quaternary C_{60} carbon atoms and 6 signals for the arene unit between δ 128 and 158 in the ^{13}C-NMR spectrum, two signals for the benzylic carbon atoms at δ 45.1 and 45.3, and two signals for the quaternary aliphatic C_{60} carbon atoms at δ 65.8 and 65.9. The signals for the ester group appear at δ 52.8 for the methyl group and at δ 167 for the carbonyl carbon atom. The IR spectrum shows the typical C=O stretch absorbtion at 1717 cm^{-1}.

To apply the above route for the synthesis of even more complex esters, we used cholesterol to synthesize **9**(n = 1), which should be interesting for the study of C_{60}'s properties in biological systems. The treatment of carboxylic acid chloride mixture **5**(n) with a 5-fold excess of cholesterol yields ester mixture **9**(n) as a brown powder, which is well soluble in chloroform and can be separated by chromatography on polystyrene gel (Figure 4). The monoadduct **9**(n = 1) was characterized by FD mass spectrometry and ^{1}H NMR. The ^{1}H-NMR spectrum shows typical resonances for cholesterol as well as the signals for benzylic protons of **9**(n = 1) at δ 4.5 and 4.8 and resonances of the arene unit at δ 7.75, 8.26, and 8.34. In the FD mass spectrum, two fragments (m/z: 868 and

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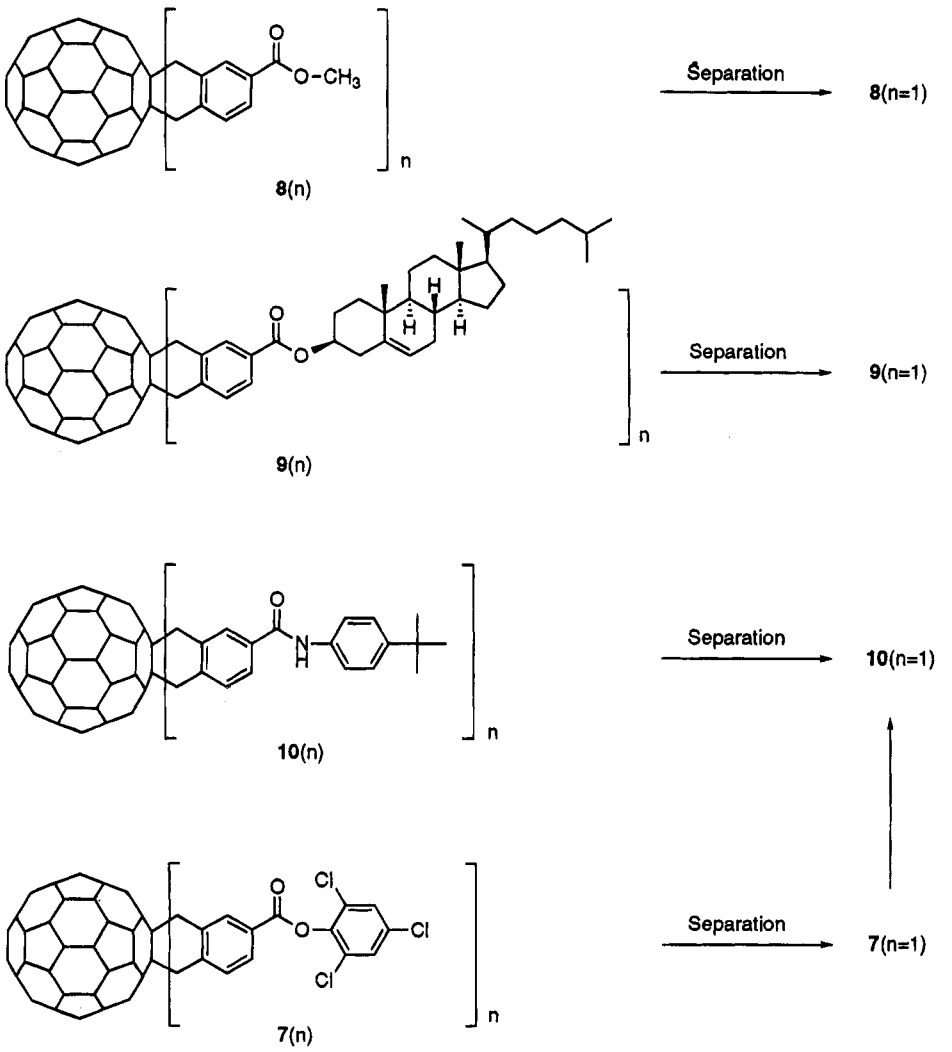

Figure 3. Reaction scheme for the preparation of **6**(*n*), **7**(*n*), **8**(*n*), **9**(*n*), and **10**(*n*).

368) can be observed besides the peak of the monoadduct **9**(n = 1) (*m/z* 1236). Regretfully, this ester does not build up liquid crystalline phases as observed with cholesterol itself.[10]

To demonstrate the versatility of the present approach, amines were also used as reactants. Since aliphatic amines add directly to C_{60} to yield an undefined product mixture,[11] 4-*tert*-butylaniline was used as the reactant. Again, the monoadduct **10**(n = 1), which was isolated by chromatography on polystyrene gel, is the major component of the reaction mixture and has been fully characterized. In the ^{1}H-NMR spectrum, the *tert*-butyl group resonates at δ 1.3 and the amine proton at δ 7.90, and the AA'BB' system of the aniline unit appears at δ 7.37 and 7.57. As expected, the ^{13}C-NMR spectrum shows 40 resonances for the sp^2 carbons of C_{60} and 10 arene carbon atoms and signals of the *tert*-butyl group at δ 31.6 and 34.6. In the IR spectrum, we observe NH stretch absorbtion at 3300 cm^{-1} and amide absorbtions at 1658 and 1518 cm^{-1}, in addition to the common absorbtions of C_{60}.

Although the monoadducts **8**, **9**, and **10** are obtained in good yields, this method has one major drawback, which is the impossibility to perform stoichiometric reactions. To accomplish this, it is necessary to prepare C_{60} active esters which are less reactive than the carboxylic acid chlorides and hence separable by chromatography.

(b) Preparation of the C_{60} Active Esters 7(*n*) and Their Reactions. The 2,4,6-trichlorophenolic active ester, which is well known from peptide chemistry,[12] was selected because these active esters are sufficiently inert to be handled under ambient conditions, yet, at the same time, are reactive enough to react with aliphatic and aromatic amines to afford the corresponding amides.

The monoadduct **7**(n = 1) was prepared by first reacting the carboxylic acid chloride mixture **6**(n) with 2,4,6-trichlorophenol and then separating the resulting mixture by chromatography. The characterization of the monoadduct **7**(n = 1) was achieved by FD mass spectrometry and ^{1}H-NMR, ^{13}C-NMR, and UV/vis spectroscopy. In contrast to the crude carboxylic acid mixture, the monoadduct **7**(n = 1) allows the performance of stochiometric reactions. Though the reactivity of **7**(n = 1) is not great enough to enable the reaction with alcohols (even at higher temperatures no reaction occurs), it is well suited for reactions with amines.

The amidation of **7**(n = 1) with aliphatic amines is very fast and takes place at room temperature, which could

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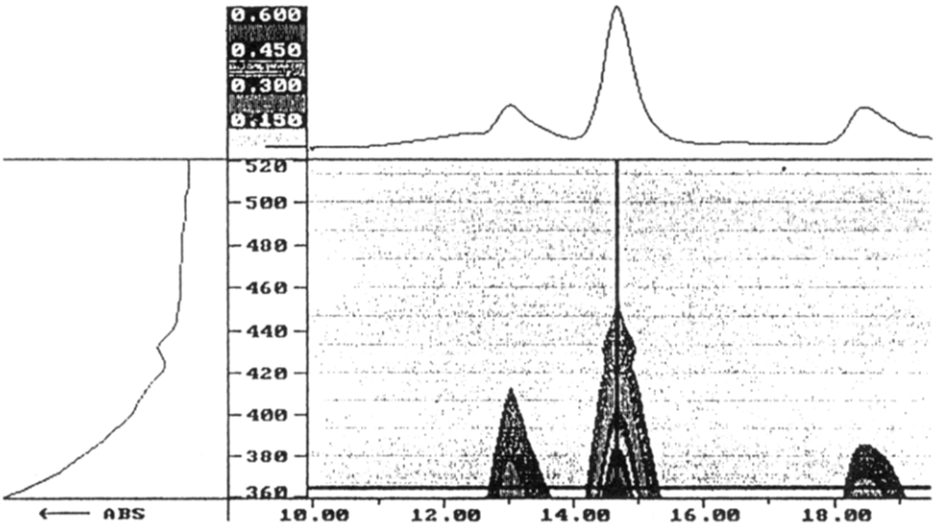

Figure 4. Elugram showing the separation of **8**(n): column, 20 × 600 mm; stationary phase, PSS gel, 5 μm, 100 Å; mobile phase, 7 mL/min, chloroform; injection, 2 mL of a saturated solution; detection, diode array detector (above, elugram at 365 nm; on the left side, UV/vis spectrum of the monoadduct).

be proved in the case of pyrolidine by FD mass spectrometry, but the direct attack of the amine to the C_{60} core as a side reaction cannot be excluded.[11] Due to the reduced nucleophilicity of aromatic amines, the reaction of **7**(n = 1) with these compounds requires several hours, temperatures above 80 °C, and a polar aprotic solvent such as *N*,*N*-dimethylacetamide, in which these reactions are accelerated by a factor of about 100.[13] For example 4-*tert*-butylaniline gives the amide **10**(n = 1), described above, in 90% yield. The structures of the amide compounds were established by FD mass spectrometry and ^{1}H-NMR, ^{13}C-NMR, UV/vis, and IR spectroscopy.

The carboxylic acid derivative of C_{60} is accessible from 3,4-dimethylbenzoic acid in a two-step synthesis. This compound is a versatile building block for the construction of more complex C_{60} adducts because it can easily be converted to more reactive adducts (acid chlorides and 2,4,6-trichlorophenolic active esters) which react with alcohols or amines to give the corresponding esters or amides. This reactivity should enable the incorporation of C_{60} units into main-chain and side-chain polymers and the synthesis of a variety of C_{60} derivatives to study their biological activities and material properties.

Experimental Section

3. A mixture of 4.5 g (30 mmol) of 3,4-dimethylbenzoic acid (**2**), 12.8 g (66 mmol) of NBS, and 0.5 g of benzoyl peroxide was refluxed in 250 mL of CCl_4 for 2 h, and the formed succinimide was removed from the reaction solution by filtration. The solvent was evaporated, and the crude product was allowed to crystallize in methanol at −15 °C to yield 5.7 g (61%) of **3**: mp 180−182 °C.

5(*n*). C_{60} (1 g, 1.39 mmol) (**1**), 0.45 g (1.46 mmol) of **3**, 0.8 g (3 mmol) of 18-crown-6, and 1.7 g (10 mmol) of KI were refluxed in dry toluene for 12 h. After evaporation of the solvent, the residue was washed with methanol and the product was extracted with 2 L of THF. Removal of the solvent afforded 530 mg of the crude product.

General Procedure for the Preparation of Carboxylic Acid Derivatives via the Carboxylic Acid Chloride. The crude product of **5** was refluxed in $SOCl_2$ for 30 min, after which $SOCl_2$ was removed by vacuum distillation and the residue was dissolved in chloroform. The nucleophilic component and triethylamine were added in excess, and the mixture was stirred for several hours at room temperature. The solution was washed successively with 2N HCl and H_2O, and the products were separated by chromatography on polystyrene gel with chloroform as eluent.

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Supplementary Material Available: ^{1}H NMR and mass spectra of **7**−**10** (n = 1) and a full listing of spectroscopic data (7 pages). This material is contained in libraries on microfiche, immediatelly follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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