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Catalytic [2+1]-Cycloaddition of Ethyl Diazoacetate to Fullerene [60]

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Abstract—Cyclopropanation of C_{60}-fullerene was performed with ethyl diazoacetate in the presence of $Pd(PPh_3)_4$ catalyst. A probable reaction mechanism is suggested.

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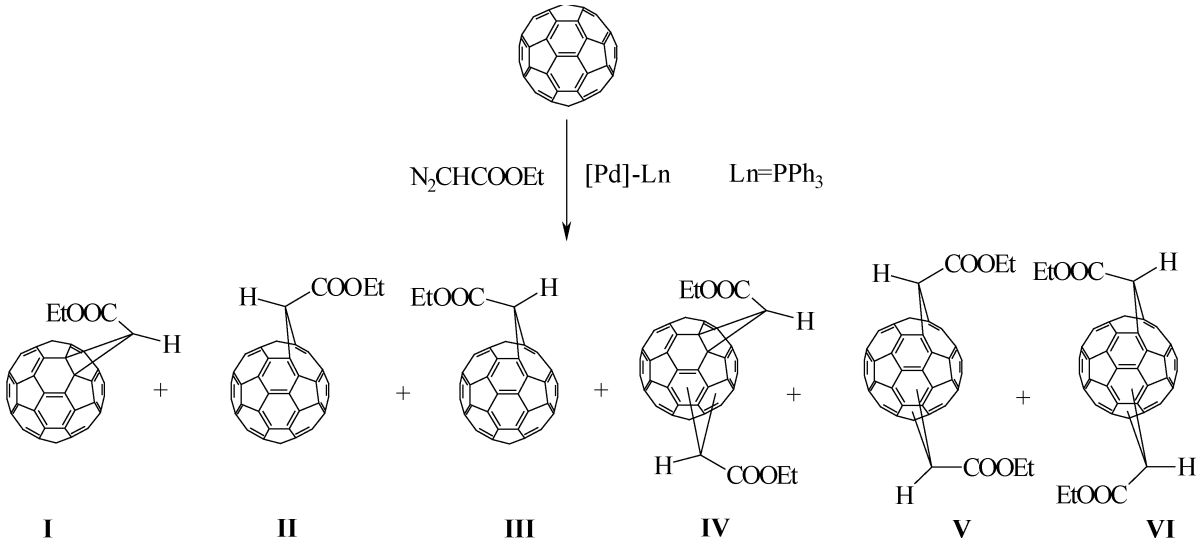
The particular attention to fullerocyclopropanes is due to the opportunities of their applications in medicine [1–7] and also as components of energy-rich fuels. The preparative procedure for fullerocyclopropanes synthesis is the cyclopropanation of fullerene with stabilized α-halocarbanions (Bingel reaction) [8]. Yet among the first reports on the synthesis of fullerocyclopropanes described way the addition of diazo compounds to the fullerene[60] [9]. In 1995 the first example was published of catalytic [2+1]-cycloaddition of diazomethane to C_{60} in the presence of catalytic quantities of $Pd(OAc)_2$ [10] that led to the formation in a low yield of 6,6-closed methanofullerene. A more successful attempt to use transition metal complexes for carbenes generation was published in [2] by an example of the cyclopropanation of C_{60}-fullerene with ethyl diazoacetate in the presence of $Rh_2(OAc)_4$. Unlike the thermal procedure [11] in the catalytic reaction the 6,6-closed fullerocyclopropane formed selectively.

The known methods of ethyl diazoacetate [2+1]-cycloaddition to C_{60}-fullerene possess a number of drawbacks, namely, the low yields of the target cycloaddition products both under the conditions of the thermal reaction [11, 12] and at the application of fairly expensive Rh complexes in the stoichiometric quantity for the cyclopropanation of the C_{60}-carbon cluster [2].

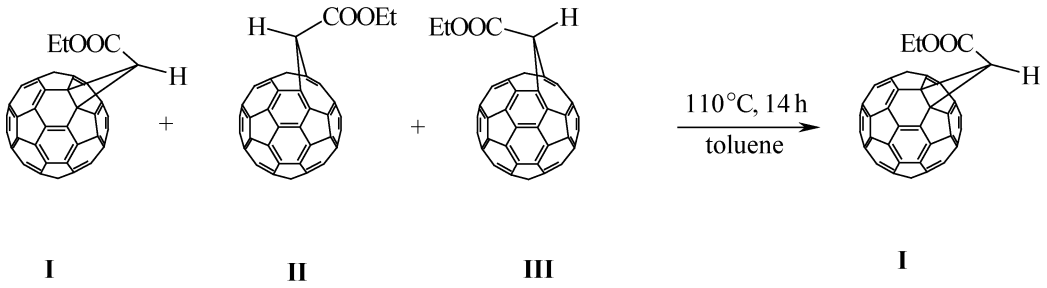
In consideration of the above we attempted in this research to carry out the ethyl diazoacetate [2+1]-cycloaddition to C_{60} in the presence of catalytic quantities of more available Cu and Pd complexes extensively used in the cyclopropanation of unsaturated compounds [13–20]. In some cases we used also Rh compounds for comparison of the catalytic activity of transition metal complexes. Besides in this study the structure of the obtained [2+1]-adducts of fullerene is discussed in more detail.

Among the tested catalysts underlain by salts and compounds of Cu, Pd, and Rh the most active in the reaction of the ethyl diazoacetate [2+1]-cycloaddition to C_{60} proved to be the complex $Pd(PPh_3)_4$ obtained [21] in situ from $Pd(acac)_2$–Ph_3P–Et_3Al, 1 : 4 : 4. The reaction of the ethyl diazoacetate with fullerene C_{60} (molar ratio 5 : 1) in the presence of 10 mol% of catalyst $Pd(PPh_3)_4$ (80°C, 7 h, toluene) provided a mixture of 6,6-closed **I** and 5,6-open adducts **II** and **III**, and also of the corresponding products of bis-addition **IV–VI** in an overall yield 68% at the ratio of mono- and diadducts ~3 : 1. According to [11] the reaction of the ethyl diazoacetate with fullerene C_{60} at heating (110°C, 7 h) occurred with the formation of cycloadducts **I–III** in an overall yield ~35%.

Scheme 1.



Scheme 2.



In performing the reactions of the ethyl diazoacetate with fullerene C_{60} in toluene the deactivation of the forming carbene was observed [2] resulting in a sharp decrease in the cycloadducts yields. Therefore we replaced in this reaction toluene by *o*-dichlorobenzene. As a result we succeeded to carry out the ethyl diazoacetate [2+1]-cycloaddition to fullerene C_{60} at 80°C in 30 min in the presence of 10 mol% of $Pd(PPh_3)_4$, with the formation of adducts **I–VI** in the overall yield ~70% (Scheme 1). The increase in the reaction time to 1 h gave the yield of adducts **I–VI** up to 80%, but the ratio of products of mono- and diaddition changed from ~2:1 to ~1:1. Similar results were obtained on reducing the catalyst amount to 5 mol% simultaneously increasing the reaction time from 30 min to 1 h. The application of $Pd(PPh_3)_4$ in equimolar amount to C_{60} made it possible to reduce the reaction time to 10 min with the overall yield of compounds **I–VI** ~87% [at the ratio of adducts (**I–III**):(**IV–VI**) ≈ 7 : 3). At the longer reaction (up to 30 min) the yield of products **I–VI** did not notably increase.

The mixtures of products of mono- **I–III** and bisaddition **IV–VI** were isolated by preparative HPLC. 1D (^{1}H and ^{13}C NMR, DEPT, 135°C) and 2D (HHCOSY, HSQC, HMBC) experiments demonstrated that compounds **I–III** consisted of a mixture of 6,6-closed and stereoisomers of 5,6-open fullerene monoadducts, and compounds **IV–VI** were a mixture of regioisomers of 6,6-closed and 5,6-open bisadducts.

Individual fullerene cycloadduct **I** was isolated from the mixture of adducts **I–III** by preparative HPLC (Scheme 2). We failed to separate adducts **II** and **III** since their physicochemical constants and polarity at chromatography were too close. In keeping with [11] the boiling of the mixture of adducts **I–III** in toluene for 24 h resulted in isomerization of compounds **II** and **III** with the formation of the individual 6,6-closed isomer **I**. We obtained this result in a shorter time (14 h).

In the ^{13}C NMR spectrum of individual compound **I** obtained at heating (110°C, 14 h) the mixture of

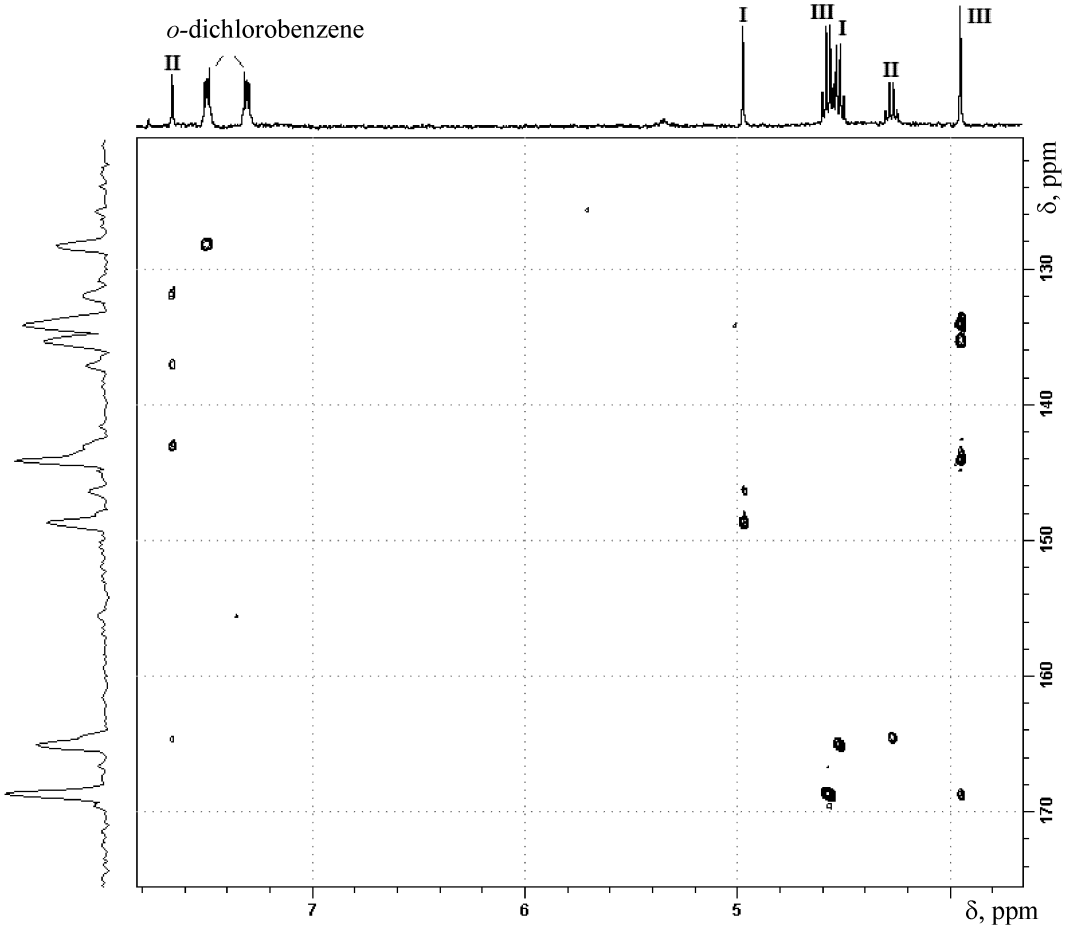
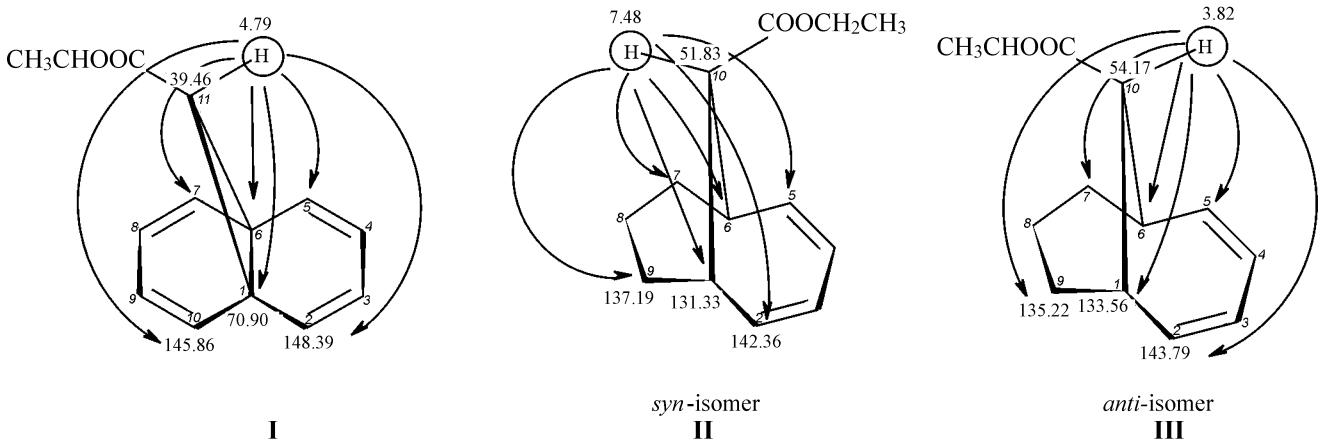


Fig. 1. HMBC experiment on fullerene aducts mixture **I–III** [400.13 (^{1}H), 100.62 MHz (^{13}C), solvent – CS_2–acetone-d_6, 10:1].

cycloadducts **I–III** 25 signals were observed in the fullerene region, δ 136–149 ppm, and three of them had the double intensity. The presence of a symmetry mirror plane in fullerocyclopropane **I** resulted in the appearance of two signals from the cyclopropane. The bridging carbon atom (δ 39.46 ppm) is linked to a hydrogen whose singlet signal is observed at 4.79 ppm confirming the formation of the fused cyclopropane fragment [11] on the 6,6-substituted fullerene framework. The mass spectrum (ES TOF) of fullerocyclopropane **I** contained strong peaks of the molecular ion, *m/z* 806, and the ion $[M - H + Na]^+$, *m/z* 828, confirming the formation of the monocycloadduct.

In the spectrum of the mixture of 6,6- and 5,6-substituted isomers **I–III** (the signals ratio 1:1:3) the prevailing isomer was 5,6-isomer **III**, whose bridging carbon signal was located in a weaker field (δ 54.17 ppm) than in the spectrum of isomer **II** (δ 51.83 ppm) [11]. The methine proton located in the shielded region (δ 3.82 ppm) belonged to isomer **III** in contrast to the strongly deshielded hydrogen atom (δ 7.48 ppm) situated over the plane of the five-membered fragment in molecule **II**.

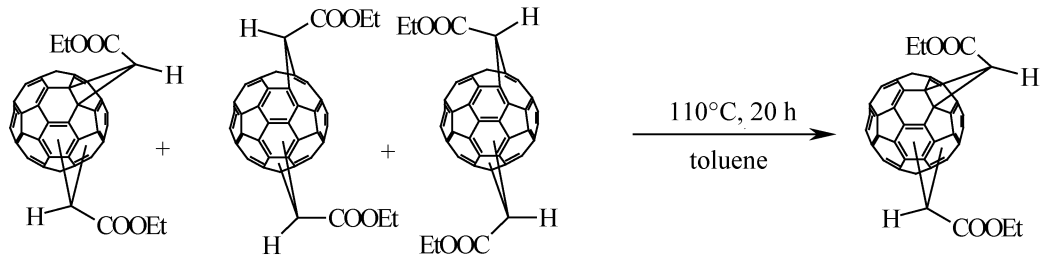
In the HMBC experiments on the mixture of isomers **I–III** (Fig. 1) cross-peaks of hydrogen atoms at the corresponding bridging carbons were observed with the fullerene carbon atoms in the β- and γ-surrounding. The couplings of hydrogen atom (δ 4.79 ppm) with cyclopropane carbon atoms of the fullerene framework $C^{1,6}$ (δ 70.90 ppm) and with equivalent in pairs four sp^2-hybridized carbon atoms (δ 145.86 and 148.39 ppm) in the *syn*- ($C^{7,10}$) and *anti*- ($C^{2,5}$) positions with respect to the ethoxycarbonyl group are characteristic of compound **I**; therewith the cross-peaks of the *syn*-directed atoms $C^{2,5}$ located downfield (δ 148.39 ppm) are of higher intensity compared to the upfield signal of *anti*-atoms $C^{7,10}$ (δ 145.86 ppm) (Fig. 2). The downfield signal of the hydrogen atom attached to the tertiary carbon in compound **II** (δ 7.48 ppm) has three cross-peaks with



I **II** **III**

Fig. 2. Remote couplings of methine hydrogen with the carbon atoms in fullerene framework in HMBC experiments.

Scheme 3.



IV **V** **VI** **IV**

a nodal atom C^{1} (δ 131.33 ppm) and vicinal atoms $C^{7,9}$ (δ 137.19) and $C^{2,5}$ (δ 142.36 ppm) of the fullerene skeleton of the molecule; it is also coupled with the ethoxycarbonyl group (δ 164.25 ppm). Analogous four characteristic cross-peaks are observed also for the upfield proton signal (δ 3.82 ppm) of 6,5-open isomer **III** prevailing in the mixture.

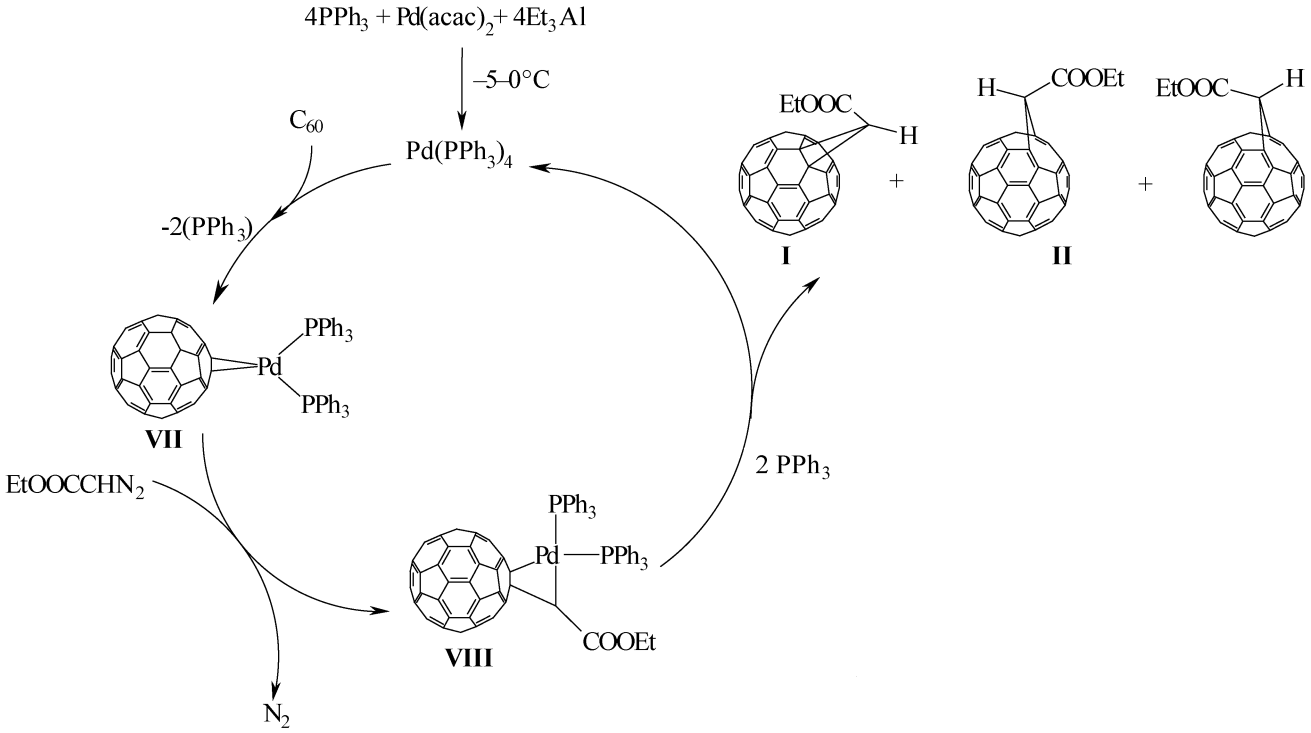
In bisadducts **IV–VI** the number of isomers with respect to substituents position on the fullerene framework of the molecule grows as seen in the increased number of the characteristic signals. The most clearly the splitting is observed on the signal of the ester group, therewith three maxima (δ 164.19, 164.52, 164.65) correspond to fragments of 6,6-closed isomers, and four signals at δ 168.05, 168.28, 168.54, and 168.72 ppm, to 6,5-open isomers. The number of signals in the proton spectra of adducts **IV–VI** also essentially increased corresponding to isomeric addition products. In the spectra of isomers of the 6,6-addition type **IV** three signals of methine protons are observed at 4.70, 4.76, and 5.12 ppm (broadened signal), in the spectra of isomers of 5,6-addition type *anti*-(**V**), at 6.31, 7.05, 7.08 ppm, and the methine protons of isomers **VI** appear at 4.36, 4.37, and 4.49 ppm. Mass spectrum of the obtained mixture of bisadducts **IV–VI** contains strong peaks with *m/z* 914 $[M - H + Na]^+$ and 915 $[M + Na]^+$ confirming the formation of compounds **IV–VI**.

The thermal isomerization of the mixture of fullerene bisadducts **IV–VI** (toluene, 110°C, 20 h) resulted in a considerable decrese in the content of isomers **V** and **VI** (Scheme 3).

In the ^1H NMR spectrum of the products of thermal isomerization of the mixture of bisadducts **IV–VI** considerably increased the intensity of the methine proton signal at 5.12 ppm indicating the growth in the fraction of 6,6-closed isomers **IV**. Regretfully, the ^{13}C NMR spectrum did not permit unambiguous estimation of the position of the second cyclopropane fragment in the molecule **IV**.

The discussion of the probable mechanism of the catalytic action of the Pd complex on the [2+1]-cycloaddition of ethyl diazoacetate to fullerene is based on the results of [22–24]. Proceeding from the published data and our own results we present below the scheme

Scheme 4.



of the mechanism of the ethyl diazoacetate cycloaddition to C_{60} involving the Pd complexes (Scheme 4).

The oxidative fullerene C_{60} addition to $Pd(PPh_3)_4$ occurs with the formation of palladiumcyclopropane complex $C_{60}Pd(PPh_3)_2$ (**VII**) as confirmed by the appearance in the ^{31}P NMR spectrum of a single peak, δ 25.23 ppm, and by the change in the color of the fullerene solution from violet-red to dark green [23, 24]. Further N_2CHCO_2Et reacts with complex **VII** at the polarized bond Pd–C with a simultaneous elimination of N_2 and the formation of intermediate fulleropalladacyclobutane **VIII** that under the reaction conditions transforms into compounds **I–III** with the regeneration of $Pd(PPh_3)_4$.

Hence we developed an efficient method of catalytic [2+1]-cycloaddition of ethyl diazoacetate to C_{60}-fullerene securing high yields of target products, and the most probable mechanism of this reaction was suggested.

EXPERIMENTAL

In experiments we used commercially available fullerene[60] of 99.5% purity from Razuvaev Institute of Organometallic Chemistry, Russian Academy of Sciences, Nizhnii Novgorod. Reaction products were analyzed by HPLC method on a chromatograph Altex-330 (USA) equipped with UV detector on 340 nm wavelength. The components of mixtures were separated on a metal column Cosmosil Buckyprep Waters 250×10 mm at room temperature, mobile phase toluene, flow rate 2.0 ml/min. IR spectra were recorded on a spectrophotometer Specord 75IR (Carl Zeiss Jena) from pellets with KBr. UV spectra were taken on spectrophotometers Specord M-40 and Specord M-80. ^1H and ^{13}C NMR spectra were registered on a spectrometer Bruker Avance-400 (400.13 and 100.62 MHz) from solutions in a mixed acetone-d_6–CS_2, 1:10 v/v. Mass spectra were measured on a mass spectrometer Micromass LCT, TOF Electrospray.

Ethyl diazoacetate [2+1]-cycloaddition to C_{60}-fullerene. Into a glass reactor was charged 0.00139 mmol of $Pd(acac)_2$ in 0.2 ml of *o*-dichlorobenzene, 0.0056 mmol of PPh_3 in 0.21 ml of *o*-dichlorobenzene, and the reactor was cooled to –5–0°C. In a flow of dry argon while stirring was added 0.0056 mmol of Et_3Al in 0.1 ml of toluene, the color of solution changed from light yellow to light brown. To the catalyst obtained at room temperature was added 0.0139 mmol of C_{60}-fullerene in 1 ml of *o*-dichlorobenzene, the mixture was heated at 80°C, and dropwise was added within 5 min 0.0695 mmol of ethyl diazoacetate in 0.5 ml of *o*-dichlorobenzene, the stirring was continued for 1 h at 80°C. The reaction mixtuire

was cooled to room temperature, 8 ml of toluene was added, and the solution was passed throgh a thin bed of silica gel. The reaction products **I–VI** and C_{60}-fullerene were separated by preparative HPLC, eluent toluene.

1'-Ethoxycarbonyl-(C_{60}-I_h)[5,6]fullero[2',3':1,9]-cyclopropane (I). IR spectrum, cm^{-1}: 1660, 1270, 1110, 1040, 820, 540. UV spectrum ($CHCl_3$), λ_{max}, nm: 260, 327, 424. ^1H NMR spectrum, δ, ppm: 1.55 t (3H, CH_3, *J* 7 Hz), 4.50 q (2H, CH_2, *J* 7 Hz), 4.80 s (1H, CH). ^{13}C NMR spectrum, δ, ppm: 14.82, 39.48, 62.28, 70.95 (sp^3), 136.48, 140.84, 140.99, 141.26, 142.06, 142.18, 142.31, 142.52, 142.88, 143.04, 143.11, 143.13, 143.40, 143.79, 144.04, 144.48, 144.67, 144.70, 144.86, 145.12, 145.21, 145.29, 145.62, 145.86, 148.39, 164.83 (COOEt). Mass spectrum ES TOF, *m/z* (I_{rel}, %): 720 (87) $[C_{60}]^+$, 806 (100) $[M]^+$, 828 (100) $[M - H + Na]^+$.

***syn*-1'a-Ethoxycarbonyl-1'a-hydro-1'a(2')-homo-(C_{60}-I_h)[5,6]fullerene (II).** ^1H NMR spectrum, δ, ppm: 1.39 t (3H, CH_3, *J* 7 Hz), 4.25 q (2H, CH_2, *J* 7 Hz), 7.48 s (1H, CH). ^{13}C NMR spectrum, δ, ppm: 14.59, 51.83, 61.96, 131.33, 134.13, 137.19, 138.76, 138.82, 140.82, 142.01, 142.33, 142.36, 142.65, 143.55, 143.92, 144.35, 144.45, 144.73, 144.93, 145.03, 145.64, 147.70, 164.25 (COOEt).

***anti*-1'a-Ethoxycarbonyl-1'a-hydro-1'a(2')-homo-(C_{60}-I_h)[5,6]fullerene (III).** ^1H NMR spectrum, δ, ppm: 1.51 t (3H, CH_3, *J* 7 Hz), 4.55 q (2H, CH_2, *J* 7 Hz), 3.82 sC (1H, CH). ^{13}C NMR spectrum, δ, ppm: 14.77, 54.17, 62.60, 133.56, 134.03, 135.29, 137.90, 138.07, 138.30, 138.52, 138.54, 140.23, 141.82, 142.05, 142.21, 142.45, 142.63, 142.89, 143.03, 143.09, 143.27, 143.31, 143.40, 143.70, 143.79, 144.04, 144.66, 144.72, 144.95, 145.21, 145.27, 147.90, 168.83 (COOEt).

The mixture of stereo- and regioisomeric fullerene bisadducts IV–VI. UV spectrum ($CHCl_3$), λ_{max}, nm: 260, 327, 421. ^1H NMR spectrum, δ, ppm: 0.9–1.50 m, 3.78–4.32 m, 4.36 s, 4.37s, 4.49 s, 4.70 s, 4.76 s, 5.12 s, 6.31 s, 7.05 s, 7.08 s. ^{13}C NMR spectrum, δ, ppm: 14.55, 37.93, 41.88, 44.71, 47.06, 49.45, 51.26, 53.30, 53.68, 59.38, 61.60, 61.76, 61.90, 62.10, 62.23, 62.45, 140–148, 164.19, 164.52, 164.65, 168.05, 168.28, 168.54, 168.72. Mass spectrum ES TOF, *m/z* (I_{rel}, %): 914 (100) $[M - H + Na]$, 915 (80) $[M + Na]$.

Thermal isomerization of open 5,6-adducts of fullerene into the closed 6,6-cycloadduct. In a glass reactor 20 mg of a mixture of compounds **I–III** or **IV–VI** was dissolved in 20 ml of toluene, the solution was refluxed for 14–20 h at the heating bath temperature not exceeding 140°C. Toluene was distilled off on a rotary evaporator, the residue was dried in a vacuum and analyzed by spectral methods.

The mixture of regioisomeric fullerene bisadducts (IV). IR spectrum, cm^{-1}: 1740, 1620, 1170, 1080, 1020, 780, 520. UV spectrum ($CHCl_3$), λ_{max}, nm: 261, 333, 423. ^1H NMR spectrum, δ, ppm: 1.4–1.6 m, 4.25–4.57 m, 4.72 s, 4.80 s, 5.13 s. ^{13}C NMR spectrum, δ, ppm: 14.56, 15.24, 38.21, 42.57, 49.64, 62.17, 62.88, 63.57, 140–148, 164.23, 164.58, 164.80.

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