Covalent binding of fullerene C_{60} to pharmacologically important compounds

A. R. Tuktarov, L. L. Khuzina, and U. M. Dzhemilev*

Institute of Petrochemistry and Catalysis, Russian Academy of Sciences,
141 prosp. Oktyabrya, 450075 Ufa, Russian Federation.
Fax: +7 (347 2) 84 2750. E-mail: ink@anrb.ru

The cycloaddition of diazo compounds derived from α-tocopherol, betulinic acid, ursolic acid, and Trolox methyl esters to fullerene C_{60} in the presence of a $Pd(acac)_2$—PPh_3—Et_3Al catalytic system was performed. The reactions of the diazo compounds derived from the above-mentioned pharmacologically important compounds with fullerene C_{60} in the presence of the $Pd(acac)_2$—PPh_3—Et_3Al system (1 : 2 : 4) afford predominantly the previously inaccessible pyrazolinofullerenes. A change in the component ratio of the $Pd(acac)_2$—PPh_3—Et_3Al catalyst from 1 : 2 : 4 to 1 : 4 : 4 favors the formation of methanofullerenes exclusively.

Key words: metal complex catalysis, fullerene C_{60}, diazo compounds, cycloaddition, α-tocopherol, betulinic acid, ursolic acid, Trolox, pyrazolinofullerenes, methanofullerenes.

First evidence that fullerenes and their derivatives offer promise as medicinal agents has appeared immediately after the preparation of these compounds in macroamounts. In the last 5—10 years, pyrrolidinofullerenes and methanofullerenes were considered as fullerene derivatives that are in most demand for the design of a new-generation drugs. These compounds can be synthesized by the Prato and Bingel—Hirsch reactions. The above-mentioned fullerene derivatives have unique properties, such as the inhibitory activity against HIV enzymes,[1—6] bactericidal[7—9] and antiviral[10,11] properties. Biological activity data for fullerenes and their derivatives are adequately covered in a monograph.[12] Taking into account the world-wide and our own experience, we hypothesized that the covalent binding of fullerene C_{60} to pharmacologically important compounds would lead to the design of a new generation of biologically active compounds, in which the fullerene moiety will serve as a transport component for the delivery of active substances to damaged cells due to the ability of carbon clusters to efficiently penetrate cell membranes.

The method developed in the present study for the binding of pharmacologically important compounds to fullerene C_{60} is based on the cycloaddition reaction of diazoacetates with carbon clusters catalyzed by the $Pd(acac)_2$—PPh_3—Et_3Al system. This reaction has been performed earlier in our laboratory.[13—16] α-Tocopherol, 20,29-dihydrobetulinic acid, ursolic acid, and Trolox methyl esters exhibiting antioxidant, antitumor, and antiviral properties were used as the initial compounds for investigation.

Results and Discussion

Earlier,[14,15] it has been shown that the reaction of fullerene C_{60} with diazoacetates in the presence of the $Pd(acac)_2$—PPh_3—Et_3Al catalytic system with a component ratio of 1 : 4 : 4 affords methanofullerenes as the only products.

The reaction of the diazoacetyl derivative of α-tocopherol with fullerene C_{60} (in a molar ratio of 5 : 1) in the presence of 20 mol.% of the three-component catalyst $Pd(acac)_2$—PPh_3—Et_3Al (a component ratio is 1 : 4 : 4) in 1,2-dichlorobenzene (*o*-DCB) at 80 °C selectively gives the corresponding methanofullerene **1** in ~75% yield within 1 h (Scheme 1). Similar results were obtained in reactions with diazoacetyl derivatives of 20,29-dihydrobetulinic acid, ursolic acid, and Trolox methyl esters.

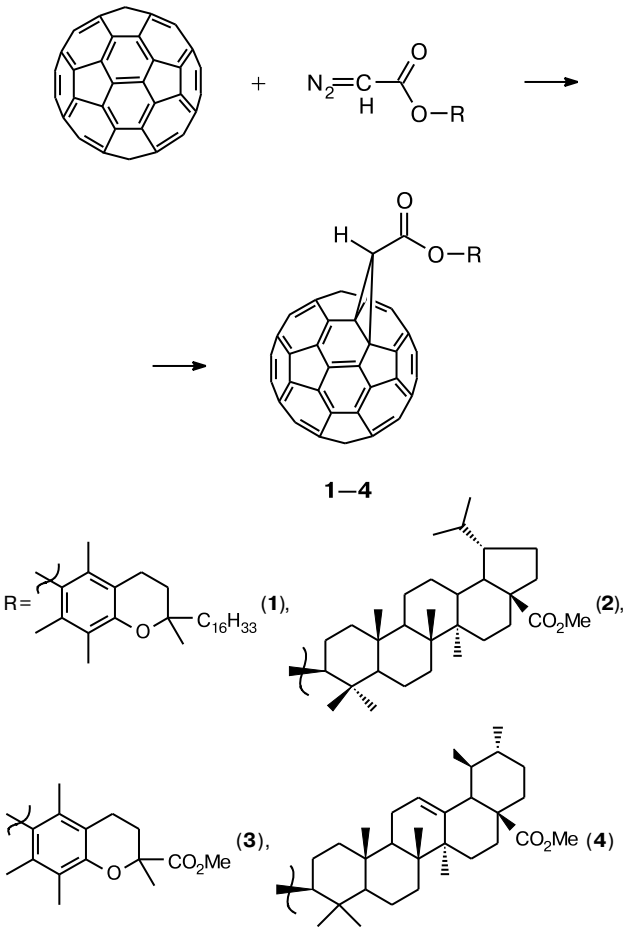
Unconsumed fullerene C_{60} was separated from the target methanofullerenes **1—4** by semi-preparative HPLC. The structures of individual compounds **1—4** were determined by one-dimensional (^1H and ^{13}C) and two-dimensional (HHCOSY, HSQC, HMBC) NMR experiments and MALDI TOF mass spectrometry.

According to the MALDI TOF mass spectrometric data obtained with S_8 as the matrix, compound **1** is characterized by an intense peak of the fragment ion $[M - H] =$ $= 1190.810$ (calculated for $C_{91}H_{50}O_3$, 1191.369).

The ^1H and ^{13}C NMR spectra of individual cycloadduct **1** show all signals characteristic of the fullerene cage (δ_C 136—148) and α-tocopherol attached to the C_{60} molecule through the ester group (δ_C 164.25), whose carbonyl group resides on the cyclopropane methine carbon atom (δ_C 39.09). Meanwhile, the signals for the sp^3-hybridized carbon atoms of the fullerene cage at δ_C 70.54 in the ^{13}C NMR spectrum and the signal for the hydrogen atom of the methine group at δ_H 4.74 in the ^1H NMR spectrum, which correlates with the *trans*-carbon atoms of C_{60} (δ_C 148.17), explicitly indicate the formation of the cyclopropane unit of methanofullerene **1**. Remotness of

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 4, pp. 648—652, April, 2011.

Scheme 1



Reagents and conditions: 80 °C, 1 h, $Pd(acac)_2$—PPh_3—Et_3Al (1 : 4 : 4).

the chiral center in cycloadduct **1** at a distance of eight single bonds eliminates its anisotropic effect on the chemical shifts of the fullerene cage of the molecule as opposed to compounds containing closely spaced chiral centers, which we have studied earlier.[17]

Taking into account that the cycloaddition reaction of diazoacetates with fullerene C_{60} in the presence of the $Pd(acac)_2$—PPh_3—Et_3Al catalytic system (1 : 2 : 4) affords mainly 5,6-open cycloadducts, we made an attempt to perform the reaction of the above-mentioned diazo pharmacons with C_{60} under these conditions in the hope of preparing the corresponding homofullerenes.

However, the reactions of fullerene C_{60} with diazoacetyl derivatives of α-tocopherol and 20,29-dihydrobetulinic acid methyl ester in the presence of the $Pd(acac)_2$—PPh_3—Et_3Al catalyst (1 : 2 : 4; 80 °C, 1 h) gave methanofullerenes **1** and **2** and the corresponding pyrazoline derivatives of C_{60} **6** and **7** in total yields of 58 and 65% in a ratio of ~1 : 1 (Scheme 2, Fig. 1, *a*) instead of the expected homofullerenes. A decrease in the reaction temperature to 60 °C results in the predominant formation of pyrazolinofullerenes **6** and **7** in 35 and 41% yields, respectively (Fig. 1, *b*). In the case of the diazoacetyl derivative of Trolox and ursolic acid methyl esters, we failed to synthesize the corresponding pyrazoline derivatives of fullerene C_{60} in satisfactory yields. In all these experiments, the corresponding methanofullerenes **3** and **4** were obtained; the content of the corresponding [2+3] cycloadducts was at most 5%.

Individual pyrazolinofullerenes **5** and **6** were isolated by semi-preparative HPLC.

The negative-ion MALDI TOF mass spectrum of compound **5** contains an intense molecular ion peak at *m/z* 1218.871 equal to [M] of molecule **5**. The one-dimensional (^1H and ^{13}C) and two-dimensional (COSY, HSQC, HMBC) NMR experiments for compound **5** also confirm the presence of the pyrazoline ring conjugated to the carbonyl group in molecule **5**. We did not detect isomer **5**′ among the reaction products.

Compound **5** exhibits the effect of π-conjugation of the C=N bond to the carbonyl group of the ester moiety, resulting in its high-field shielding (δ_C (C=O) 160.34), unlike the position of the signal of the nonconjugated carbonyl group, for example, in compound **1** (δ_C (C=O) 164.25). The signals for two sp^3-hybridized carbon atoms (δ_C 77.44 and 88.84) and the low-field signal for a hydrogen atom (δ_H (NH) 8.39) unambiguously characterize the structure of compound **5**.

It should be noted that the similar stabilization of the pyrazoline ring has been observed earlier,[18] where stable pyrazolinofullerene was synthesized only by the solid-state reaction.

Extensive pharmacological studies of biological activities of compounds **1—6** are underway at the Research

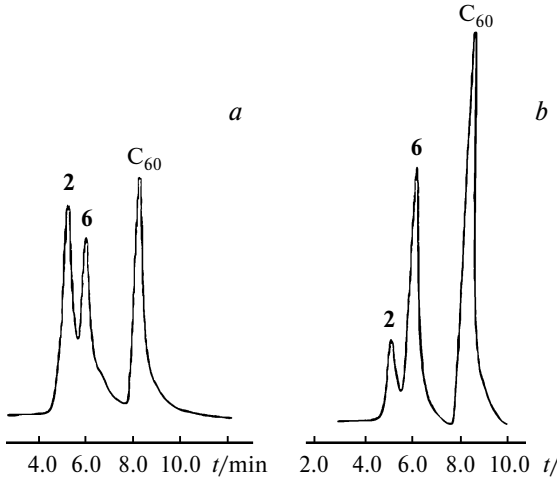
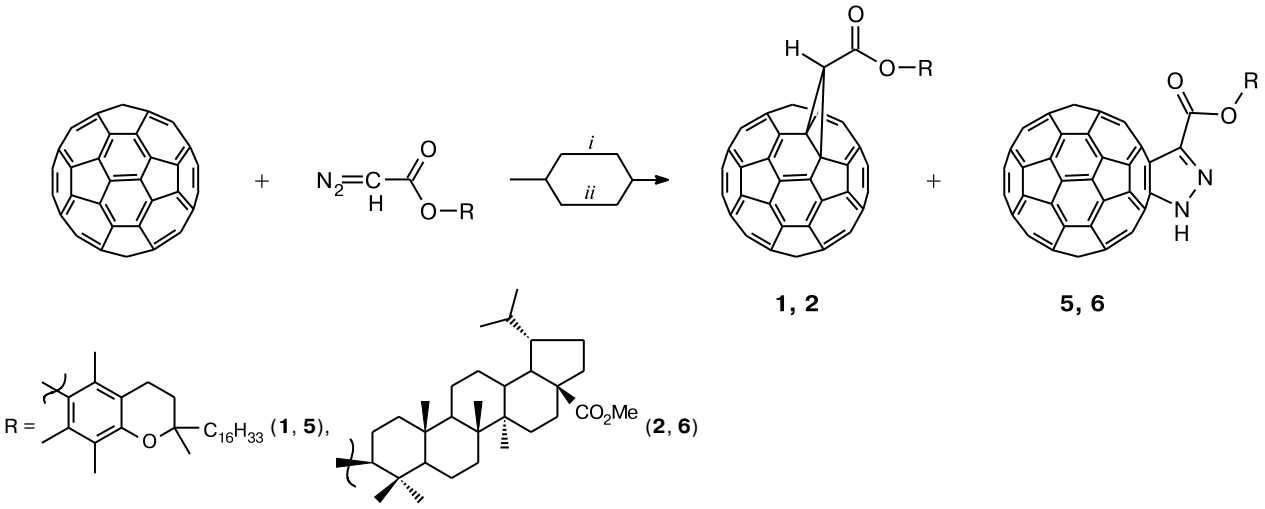
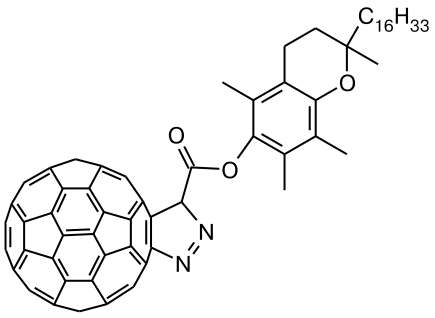


Fig. 1. Composition of the reaction products of the diazoacetyl derivative of 20,29-dihydrobetulinic acid methyl ester with fullerene C_{60} at 80 (*a*) and 60 °C (*b*) based on HPLC data.

Scheme 2



Reagents and conditions: *i*. 60 °C, 1 h, $Pd(acac)_2$—PPh_3—Et_3Al (1 : 4 : 4) ; *ii*. 80 °C, 1 h, $Pd(acac)_2$—PPh_3—Et_3Al (1 : 2 : 4).



5′

Institute of Pharmacology of the Tomsk Scientific Center of the Russian Academy of Medical Sciences.

In conclusion, we developed an efficient method for the covalent binding of pharmacologically important compounds to fullerene C_{60} based on the reaction of the latter with diazoacetyl derivatives of biologically active compounds in the presence of the $Pd(acac)_2$—PPh_3—Et_3Al catalytic system. Individual methanofullerenes were synthesized at a component ratio of the catalyst equal to 1 : 4 : 4. The change in the component ratio from 1 : 4 : 4 to 1 : 2 : 4 allows one to synthesize the previously inaccessible pyrazolinofullerenes in fairly high yields.

Experimental

Experiments were carried out with commercially available [60]fullerene with 99.5% purity (G. A. Razuvaev Institute of Organometallic Chemistry, Russian Academy of Sciences, Nizhny Novgorod). The reaction products were analyzed by HPLC on an Altex Model 330 chromatograph (USA) equipped with an UV detector at a wavelength of 340 nm. Components of the mixture were separated on a Cosmosil Buckyprep Waters metal column (250×10 mm) at room temperature; toluene was used as the mobile phase; the flow rate was 2.0 mL min^{-1}. The IR spectra were recorded on a Bruker VERTEX 70V Fourier-transform infrared spectrometer in KBr pellets. The UV spectra were measured on a Perkin Elmer LAMBDA 750 spectrophotometer. The ^1H and ^{13}C NMR spectra were recorded on a Bruker Avance-400 spectrometer (400.13 and 100.62 MHz, respectively) with a mixture of $CDCl_3$ and CS_2 (1 : 5) as the solvent. The mass spectra were obtained on a MALDI TOF/TOF Autoflex-III Bruker instrument with S_8 as the matrix in the linear negative-ion mode. For deposition on a metal target, the samples were dissolved in toluene.

Cycloaddition of diazo compounds to fullerene C_{60} (general procedure). A solution containing $Pd(acac)_2$ (0.84 mg, 0.00278 mmol) in *o*-DCB (0.4 mL) and PPh_3 (1.46 mg, 0.00556 mmol or 2.92 mg 0.01112 mmol) in *o*-DCB (0.42 mL) was placed in a glass reactor. A solution of Et_3Al (0.01112 mmol) in toluene (0.1 mL) was added with stirring under a stream of dry argon at −5 °C, which was accompanied by a change in the color from pale yellow to pale brown. A solution of C_{60} (10 mg, 0.0139 mmol) in *o*-DCB (1 mL) was added to the resulting catalyst at room temperature, after which the solution turned dark green. The reaction mixture was heated to 60 or 80 °C, and a solution of a diazoacetate (0.0695 mmol) in *o*-DCB (0.5 mL) was added dropwise during 5 min. The mixture was stirred at the corresponding temperature for 1 h, cooled to room temperature, and mixed with aqueous HCl. Then toluene (7 mL) was added, and the organic layer was passed through a column with a small amount of silica gel. Reaction products **1—6** and C_{60} were separated by semi-preparative HPLC using toluene as the eluent.

[2″,5″,7″,8″-Tetramethyl-2″-(4‴,8‴,12‴-trimethyltridecyl)-3″,4″-dihydro-2″*H*-chromen-6″-yl] cyclopropa[1,9](C_{60}-I_h)-fullerene-3′-carboxylate (1). IR, ν/cm^{-1}: 527, 756, 1142, 1378, 1452, 1760. UV ($CHCl_3$), λ_{max}/nm: 260, 326, 426. ^1H NMR, δ: 0.89—0.93 (m, 12 H, Me(4‴), Me(8‴), Me(12‴), H(13‴)); 1.12—2.05 (m, 23 H, CH_2, CH in the tocopherol residue); 1.32 (s, 3 H, MeC(2″)); 2.17, 2.20, and 2.26 (all s, 3 H each, MeAr);

2.69 (t, 2 H, H(4″), J = 6 Hz); 5.08 (s, 1 H, H(1′)). ^{13}C NMR, δ: 12.15, 12.82, 13.64 (MeAr); 19.97, 20.00, 20.06 (MeC(4‴), MeC(8‴) and MeC(12‴)); 21.01 (C(4″)); 21.37 (C(2‴)); 22.92 (C(13‴)); 24.01 (MeC(2″) and C(10‴)); 24.85 (C(6‴)); 28.37 (C(12‴)); 31.52 (C(3″)); 33.13 (C(3‴)); 37.64 (C(9‴)); 37.75 (C(7‴)); 37.85 (C(5‴)); 39.09 (C(1′)); 39.67 (C(11‴)); 39.70 (C(4‴) and C(8‴)); 40.34 (C(1‴)); 70.54 (C(2′) and C(3′)); 75.06 (C(2″)); 117.56 (C(5″)); 123.52 (C(7″)); 124.96 (C(8″)); 126.75 (C(4″a)); 136.57, 137.97, 138.62, 140.84 (C(6″)), 140.89, 141.05, 141.29, 141.88, 142.11, 142.18, 142.52, 142.90, 143.07, 143.12, 143.17, 143.33, 143.39, 143.77, 143.82, 144.03, 144.54, 144.66, 144.76, 145.17, 145.28, 145.33, 145.50, 145.52, 148.17, 149.88 (C(8″a)); 164.25 (CO_2). MS (MALDI-TOF), m/z (I_{rel} (%)): 1190 $[M - H]^-$ (100).

(28″-Methoxycarbonyllupan-3″β-yl) cyclopropa[1,9](C_{60}-I_h)-fullerene-3′-carboxylate (2). IR, ν/cm^{-1}: 524, 756, 1140, 1380, 1460, 1762. UV ($CHCl_3$), λ_{max}/nm: 261, 328, 426. ^{1}H NMR, δ: 0.80 and 0.90 (both d, 3 H each, H(29″), H(30″), J = 7 Hz); 0.91, 0.98, 1.09, 1.12, and 1.29 (all s, 3 H each, H(23′), H(24′), H(25′), H(26′), H(27′)); 0.93—2.27 (m, 24 H, CH_2, CH in the betulinic acid residue); 3.67 (s, 3 H, $MeCO_2$); 4.80 (s, H(1′)); 4.87 (dd, H (3″), J = 5 Hz, J = 9 Hz). ^{13}C NMR, δ: 14.81 (MeC(14″)); 14.89 (MeC(20″)); 16.19 (MeC(10″)); 16.39 (MeC(8″)); 17.13 (MeC(4″)); 18.51 (C(6″)); 21.23 (C(11″)); 23.01 (C(15″)); 23.17 (MeC(20″)); 27.14 (C(12″)); 28.43 (MeC(4″)); 29.92 (C(20″)); 29.95 (C(21″)); 30.05 (C(2″)); 32.24 (C(16″)); 34.57 (C(7″)); 37.28 (C(22″)); 37.50 (C(10″)); 38.10 (C(13″)); 38.79 (C(1″)); 39.73 (C(1′)); 40.84 (C(4″) and C(8″)); 42.66 (C(14″)); 44.31 (C(19″)); 48.99 (C(18″)); 50.40 (C(9″)); 51.03 ($MeCO_2$); 55.71 (C(17″)); 56.94 (C(5″)); 70.90 (C(2′) and C(3′)); 83.79 (C(3″)); 136.44, 140.55, 140.59, 140.99, 141.09, 141.21, 142.10, 142.15, 142.49, 142.88, 142.96, 143.03, 143.08, 143.15, 143.36, 143.37, 144.00, 144.47, 144.64, 144.68, 144.72, 144.83, 145.13, 145.16, 145.21, 145.27, 145.29, 145.62, 145.81, 145.88, 148.36, 148.40, 165.60 (CO_2C(1′)); 176.34 (CO_2C(17″)). MS (MALDI-TOF), m/z (I_{rel} (%)): 1233 $[M]^-$ (100).

(2″-Methoxycarbonyl-2″,5″,7″,8″-tetramethyl-3″,4″-dihydro-2″*H*-chromen-6″-yl) cyclopropa[1,9](C_{60}-I_h)fullerene-3′-carboxylate (3). IR, ν/cm^{-1}: 520, 760, 1180, 1340, 1450, 1730. UV ($CHCl_3$), λ_{max}/nm: 261, 328, 427. ^{1}H NMR, δ: 1.68 (s, 3 H, MeC(2″)); 2.19, 2.24, and 2.28 (all s, 3 H each, MeAr); 2.59—2.71 (m, 4 H, 2 H(3″) and 2 H(4″)); 3.72 (s, 3 H, $MeCO_2$); 5.08 (s, 1 H, H(1′)). ^{13}C NMR, δ: 12.19, 12.78, 13.65 (MeAr); 21.17 (C(4″)); 25.59 (MeC(2″)); 30.47 (C(3″)); 39.00 (C(1′)); 52.18 ($MeCO_2$); 70.48 (C(2′) and C(3′)); 77.00 (C(2″)); 117.33 (C(5″)); 123.56 (C(7″)); 125.02 (C(8″)); 127.12 (C(4″a)); 136.58 (C(6″)); 140.32, 140.83, 141.06, 141.30, 141.35, 141.55, 141.88, 142.00, 142.10, 142.18, 142.31, 142.51, 142.76, 142.81, 142.91, 142.98, 143.07, 143.12, 143.17, 143.38, 143.47, 143.55, 143.71, 143.74, 143.82, 144.02, 144.55, 144.65, 144.77, 144.90, 145.14, 145.18, 145.29, 145.33, 145.43, 145.50, 148.11, 149.77 (C(8″a)), 164.17 (CO_2C(1′)); 173.46 (CO_2C(2″)). MS (MALDI-TOF), m/z (I_{rel} (%)): 1024 $[M]^-$ (100).

(17″-Methoxycarbonylursol)-3″β-yl) cyclopropa[1,9](C_{60}-I_h)-fullerene-3′-carboxylate (4). IR, ν/cm^{-1}: 527, 723, 1143, 1181, 1737. UV ($CHCl_3$), λ_{max}/nm: 261, 327, 426. ^{1}H NMR, δ: 0.81, 1.07, 1.11, 1.14, and 1.15, (all s, 3 H each, Me(4″), Me(4″), Me(8″), Me(10″), Me(14″)); 0.93 and 1.00 (both d, 3 H each, Me(19″), Me(20″), J = 6.0 Hz); 0.98—2.04 (m, 22 H, CH_2, CH in the ursolic acid residue); 2.27 (d, H (18″), J = 11.2 Hz); 3.63 (s, 3 H, $MeCO_2$); 4.81 (s, H (1′)); 4.91 (dd, H (3″), J = 10.8 Hz, J = 6.0 Hz); 5.28 (t, H (12″)). ^{13}C NMR, δ: 15.74 (MeC(10″)); 17.06 (MeC(8″)); 17.29 (MeC(19″)); 17.36 (MeC(4″)); 18.51 (C(6″)); 21.41 (MeC(20″)); 23.56 (C(11″)); 23.77 (C(16″)); 24.10 (MeC(14″)); 28.23 (C(15″)); 28.55 (MeC(4″); C(2″)); 30.91 (C(21″)); 33.10 (C(7″)); 36.81 (C(22″)); 37.06 (C(10″)); 37.99 (C(4″)); 38.61 (C(1″)); 39.14 (C(20″)); 39.20 (C(19″)); 39.65 (C(8″)); 39.71 (C(1′)); 42.07 (C(14″)); 47.64 (C(9″)); 48.06 (C(17″)); 51.35 ($MeCO_2$); 52.96 (C(18″)); 55.59 (C(5″)); 70.88 (C(2′) and C(3′)); 83.79 (C(3″)); 125.47 (C(12″)); 136.40, 138.28 (C(13″)); 140.44, 140.58, 140.96, 141.00, 141.21, 142.10, 142.12, 142.15, 142.29, 142.49, 142.88, 143.03, 143.08, 143.15, 143.35, 143.77, 144.00, 144.47, 144.64, 144.68, 144.72, 144.82, 145.13, 145.16, 145.22, 145.27, 145.30, 145.62, 145.63, 145.83, 145.86, 148.36, 148.40, 165.64 (CO_2C(1′)); 177.61 (CO_2C(17″)). MS (MALDI-TOF), m/z (I_{rel} (%)): 1230 $[M - H]^-$ (100).

[2″,5″,7″,8″-Tetramethyl-2″-(4‴,8‴,12‴-trimethyltridecyl)-3″,4″-dihydro-2″*H*-chromen-6″-yl] 2-pyrazolino-[3′,4′:1,9](C_{60}-I_h)fullerene-3′-carboxylate (5). IR, ν/cm^{-1}: 527, 756, 1140, 1170, 1245, 1378, 1461, 1527, 1715, 3320. UV ($CHCl_3$), λ_{max}/nm: 260, 316, 424. ^{1}H NMR, δ: 0.88—0.94 (m, 12 H, Me(4‴), Me(8‴), Me(12‴), H(13‴)); 1.17—1.82 (m, 23 H, CH_2, CH in the tocopherol residue); 1.28 (s, 3 H, MeC(2″)); 2.12 and 2.16 (both s, 9 H, 3 MeAr); 2.64 (t, 2 H, H(4″), J = 6.8 Hz); 8.39 (s, 1 H, NH). ^{13}C NMR, δ: 12.04, 12.57, 13.40 (MeAr); 19.83, 19.97, 22.84, 22.93 (MeC(4‴), MeC(8‴), MeC(12‴), C(13‴)); 20.87 (C(4″)); 21.28 (C(2‴)); 23.99 (MeC(2″)); 24.75 (C(10‴)); 25.11 (C(6‴)); 28.27 (C(12‴)); 31.37 (C(3″)); 33.05 (C(3‴)); 37.56 (C(9‴)); 37.67 (C(7‴)); 37.71 (C(5‴)); 37.84 (C(11‴)); 39.62 (C(4‴) and C(8‴)); 40.33 (C(1‴)); 77.44 (C(4′)); 88.84 (C(3′)); 75.00 (C(2″)); 117.43 (C(5″)); 123.29 (C(7″)); 125.09 (C(8″)); 126.88 (C(4″a)); 135.89 (C(5′)); 136.40, 140.21, 140.39 (C(6″)), 141.87, 142.22, 142.33, 142.37, 142.59, 142.81, 142.90, 143.06, 143.16, 143.68, 144.10, 144.12, 144.37, 145.20, 145.25, 145.52, 145.71, 145.96, 145.97, 146.05, 146.27, 146.34, 147.48, 147.66, 149.71 (C(8″a)); 160.34 (CO_2). MS (MALDI-TOF), m/z (I_{rel} (%)): 1218 $[M - H]^-$ (30), 720 $[C_{60}]^-$ (100).

(28″-Methoxycarbonyllupan-3″β-yl) 2-pyrazolino[3′,4′:1,9]-(C_{60}-I_h)fullerene-3′-carboxylate (6). IR, ν/cm^{-1}: 580, 770, 1180, 1200, 1420, 1480, 1660, 1760. UV ($CHCl_3$), λ_{max}/nm: 257, 310, 426. ^{1}H NMR, δ: 0.80 and 0.91 (both d, 3 H each, H(29″), H(30″), J = 7 Hz); 0.91, 0.95, 1.05, 1.06, and 1.30 (all s, 3 H each, H(23′), H(24′), H(25′), H(26′), H(27′)); 0.76—2.28 (m, 24 H, CH_2, CH in the betulinic acid residue); 3.66 (s, 3 H, $MeCO_2$); 4.84 (t, H (3″), J = 8 Hz); 8.26 (s, 1 H, NH). ^{13}C NMR, δ: 14.81 (MeC(14″)); 14.91 (MeC(20″)); 16.20 (MeC(10″)); 16.39 (MeC(8″)); 17.05 (MeC(4″)); 18.53 (C(6″)); 21.24 (C(11″)); 23.07 (C(15″)); 23.19 (MeC(20″)); 27.17 (C(12″)); 28.41 (MeC(4″)); 29.93 (C(20″)); 29.96 (C(21″)); 30.08 (C(2″)); 32.26 (C(16″)); 34.60 (C(7″)); 37.24 (C(22″)); 37.53 (C(10″)); 38.10 (C(13″)); 38.83 (C(1″)); 40.84 (C(4″) and C(8″)); 42.66 (C(14″)); 44.32 (C(19″)); 48.98 (C(18″)); 50.39 (C(9″)); 51.00 ($MeCO_2$); 55.70 (C(17″)); 56.92 (C(5″)); 77.28 (C(4′)); 82.80 (C(3″)); 88.41 (C(3′)); 135.86 (C(5′)); 140.16, 140.34, 141.83, 141.86, 142.20, 142.24, 142.35, 142.60, 142.79, 142.89, 143.06, 143.16, 144.11, 144.17, 144.21, 144.40, 144.47, 145.18, 145.21, 145.69, 145.53, 145.74, 145.89, 145.94, 146.02, 146.25, 146.30, 147.14, 147.63, 161.66 (CO_2C(5′)); 176.25 (CO_2C(17″)). MS (MALDI-TOF), m/z (I_{rel} (%)): 1260 $[M - H]^-$ (100).

This study was financially supported by the Program of the Presidium of the Russian Academy of Sciences "Basic Sciences to Medicine" and the Federal Target Program "Scientific and Scientific-Pedagogical Personnel of the Innovative Russia" (Government Contract Nos P1218 and 14.740.11.0014).

References

1. R. Sijbesma, G. Srdanov, F. Wudl, J. A. Castoro, C. Wilkins, S. H. Friedman, D. L. DeCamp, G. L. Kenyon, *J. Am. Chem. Soc.*, 1993, **115**, 6510.
2. S. H. Friedman, D. L. DeCamp, R. Sijbesma, G. Srdanov, F. Wudl, G. L. Kenyon, *J. Am. Chem. Soc.*, 1993, **115**, 6506.
3. R. F. Schinazi, R. Sijbesma, G. Srdanov, C. L. Hill, F. Wudl, *Antimicrob. Agents Chemother*, 1993, **37**, 1707.
4. Z. Zhu, D. I. Schuster, M. E. Tuckerman, *Biochemistry*, 2003, **42**, 1326.
5. T. Da Ros, G. Spalluto, M. Prato, *Croatica Chemica Acta*, 2001, **74**, 743.
6. T. Mashino, K. Shimotohno, N. Ikegami, D. Nishikawa, K. Okuda, K. Takahashi, S. Nakamura, M. Mochizuki, *Bioorg. Med. Chem. Lett.*, 2005, **15**, 1107.
7. N. Tsao, T. Y. Luh, C. K. Chou, T. Y. Chang, J. J. Wu, C. C. Liu, H. Y. Lei, *J. Antimicrobal Chemother*, 2002, **49**, 641.
8. S. Bosi, T. Da Ros, S. Castellano, E. Banfi, M. Prato, *Bioorg. Med. Chem. Lett.*, 2000, **10**, 1043.
9. S. Bosi, L. Feruglio, T. Da Ros, G. Spalluto, B. Gregoretti, M. Terdoslavich, G. Decorti, S. Passamonti, S. Moro, M. Prato, *J. Med. Chem.*, 2004, **47**, 6711.
10. L. L. Dugan, D. M. Turetsky, C. Du, D. Lobner, M. Wheeler, C. R. Almli, C. K.-F. Shen, T.-Y. Luh, D. W. Choi, T.-S. Lin, *Proc. Natl. Acad. Sci. USA*, 1997, **94**, 9434.
11. Y. L. Huang, C. K. Shen, T. Y. Luh, H. C. Yang, K. C. Hwang, C. K.Chou, *Eur. J. Biochem.*, 1998, **254**, 38.
12. L. B. Piotrovskii, O. I. Kiselev, *Fullereny v biologii* [*Fullerens in Biology*], Izd-vo Rostok, 2006, 336 pp. (in Russian).
13. A. R. Tuktarov, A. R. Akhmetov, R. F. Kamalov, L. M. Khalilov, M. Pudas, A. G. Ibragimov, U. M. Dzhemilev, *Zh. Org. Khim.*, 2009, **45**, 1180 [*Russ. J. Org. Chem.* (*Engl. Transl.*), 2009, **45**].
14. A. R. Tuktarov, A. R. Akhmetov, D. Sh. Sabirov, L. M. Khalilov, A. G. Ibragimov, U. M. Dzhemilev, *Izv. Akad. Nauk, Ser. Khim.*, 2009, 1671 [*Russ. Chem. Bull., Int. Ed.*, 2009, **58**, 1724].
15. A. R. Tuktarov, A. R. Akhmetov, L. L. Khasanova, L. M. Khalilov, U. M. Dzhemilev, *Izv. Akad. Nauk, Ser. Khim.*, 2010, 1909 [*Russ. Chem. Bull., Int. Ed.*, 2010, **59**, 1959].
16. A. R. Tuktarov, A. R. Akhmetov, V. V. Korolev, A. A. Khuzin, L. L. Khasanova, N. R. Popod´ko, L. M. Khalilov, *Arkivoc*, 2011, (**viii**), 54.
17. A. R. Tuktarov, V. V. Korolev, A. R. Tulyabaev, N. R. Popod´ko, L. M. Khalilov, U. M. Dzhemilev, *Tetrahedron Lett.*, 2011, **52**, 834.
18. G.-W. Wang, Y.-J. Li, R.-F. Peng, Z.-H. Liang, Y.-C. Liu, *Tetrahedron*, 2004, **60**, 3921.

Received March 14, 2011;
in revised form April 7, 2011