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Aluminacyclopentanes in the Synthesis of Ethyl 1-Hydroxycyclopentanecarboxylates

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Abstract—A one-pot procedure has been developed for the synthesis of ethyl 1-hydroxycyclopentanecarboxylates. The procedure includes cycloalumination of terminal olefins with triethylaluminum in the presence of Cp_2ZrCl_2, reaction of alkyl-substituted aluminacyclopentanes formed *in situ* with diethyl oxalate in the presence of a catalytic amount of copper salt, and acid hydrolysis.

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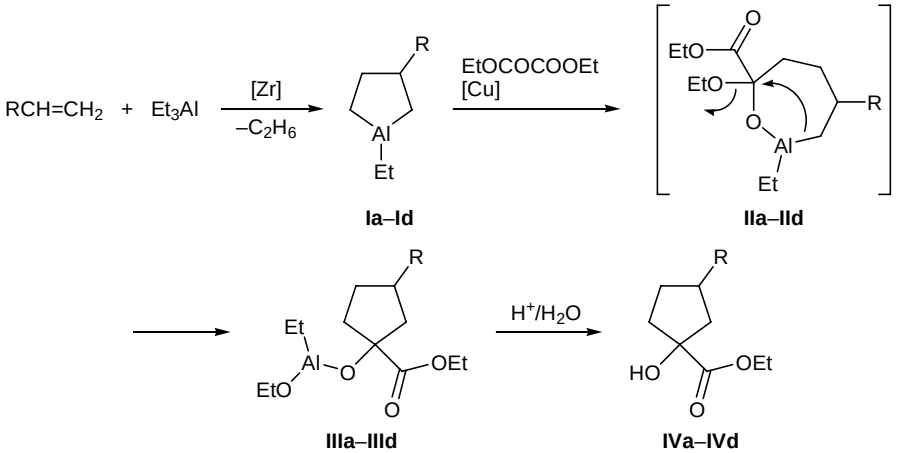
Aluminacyclopentanes **I** available through catalytic cycloalumination of olefins, allenes, and acetylenes with trialkylaluminums or alkylaluminum halides [1, 2] are promising reagents for selective synthesis of five-membered carbo- and heterocyclic compounds, including silacyclopentanes [3], phospholanes [3], tetrahydrothiophenes, and tetrahydroselenophenes [4], as well as butane-1,4-diols [5]. We recently reported on the synthesis of cyclopentanols by CuCl-catalyzed reaction of aluminacyclopentanes with ethyl formate [6].

With a view to extend the scope of application of catalytic cycloalumination and develop one-pot procedures for the synthesis of practically important 1-hydroxycyclopentanecarboxylic acid esters, in the present work we examined reactions of compounds **I** with α,ω-dicarboxylic acid esters in the presence of copper-containing catalysts. Derivatives of cyclopentanecarboxylic acids attract interest as synthons for prostaglandins, fragrant substances, and medicines [7, 8].

The substrates were various 3-substituted aluminacyclopentanes, including that having a fused fullerene fragment, and oxalic, malonic, succinic, and adipic acid esters. Compounds **Ia**–**Id** were synthesized by reaction of the corresponding terminal olefins or fullerene C_{60} with Et_3Al in the presence of Cp_2ZrCl_2 as catalyst [1, 2].

Scheme 1.



[Cu] = CuCl, CuBr, CuI; [Zr] = Cp_2ZrCl_2; R = C_5H_{11} (**a**), C_7H_{15} (**b**), cyclohex-3-en-1-yl (**c**), $PhCH_2$ (**d**).

1-Ethyl-3-pentyl-1-aluminacyclopentane (**Ia**) prepared by reaction of hept-1-ene with an equimolar amount of Et_3Al in the presence of Cp_2ZrCl_2 (5 mol %) [1] was then brought without isolation into reaction with diethyl oxalate in the presence of 15 mol % of CuCl (20°C, 8 h). After hydrolysis of the reaction mixture, we isolated 80% of ethyl 1-hydroxy-3-pentylcyclopentanecarboxylate (**IVa**) (Scheme 1). Some signals in the ^{13}C NMR spectrum of **IVa** were doubled due to formation of *cis* and *trans* stereoisomers at a ratio of about 1:1. The carbonyl carbon atom in the carboxy group gave two signals at δ_C 176.80 and 177.12 ppm; and the C^1 signal appeared at δ_C 81.01/81.23 ppm. The other ring carbon atoms C^2–C^5 also resonated as doublets at δ_C 31.61/31.81, 38.26/38.44, 39.46/39.72, and 45.42/45.91 ppm.

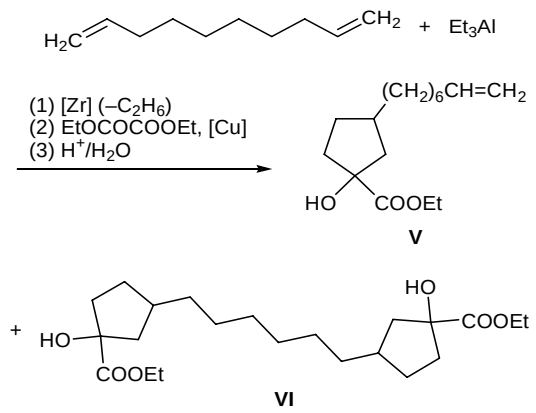
When CuCl was replaced by CuBr or CuI, the yield of **IVa** in the reaction of **Ia** with diethyl oxalate decreased to ~75 and 70%, respectively. No reaction occurred in the absence of catalyst. The reactions with malonic, succinic, and adipic esters instead of diethyl oxalate were characterized by appreciably lower yields of cyclopentanecarboxylic acids and reduced selectivity. Therefore, we used diethyl oxalate in further experiments with aluminacyclopentanes.

The overall yield of 1-hydroxycyclopentanecarboxylates depended on the initial terminal olefin. The yield of compounds **IVa**–**IVd** decreased from 80 to 60% in going from hept-1-ene to non-1-ene and then to 4-vinylcyclohex-1-ene and allylbenzene, i.e., as the size of the substituent on C^3 in compounds **I** increased.

Taking into account published data and our results (by analogy with reactions of cyclic organoaluminum [6] and organomagnesium compounds [9, 10] with carboxylic acid esters), we presumed that 3-substituted aluminacyclopentanes **I** react with diethyl oxalate at the labile Al–C bond to form cyclic semiacetals **II** as primary products. Skeletal transformations of **II** lead to the corresponding 3-substituted ethyl 1-[ethoxy(ethyl)-aluminiooxy]cyclopentanecarboxylates **III**, and hydrolysis of the latter yields 1-hydroxycyclopentanecarboxylates **IV** (Scheme 1).

α,ω-Alkadienes can also be involved in analogous reactions. Thus, the reaction of deca-1,9-diene with 3 equiv of Et_3Al, followed by treatment with diethyl oxalate gave a mixture of ethyl 1-hydroxy-3-(oct-7-en-1-yl)cyclohexane-1-carboxylate (**V**) and diethyl 3,3'-hexamethylenedi(1-hydroxycyclopentanecarboxylate) (**VI**) at a ratio of 5:8 with an overall yield of ~80% (Scheme 2).

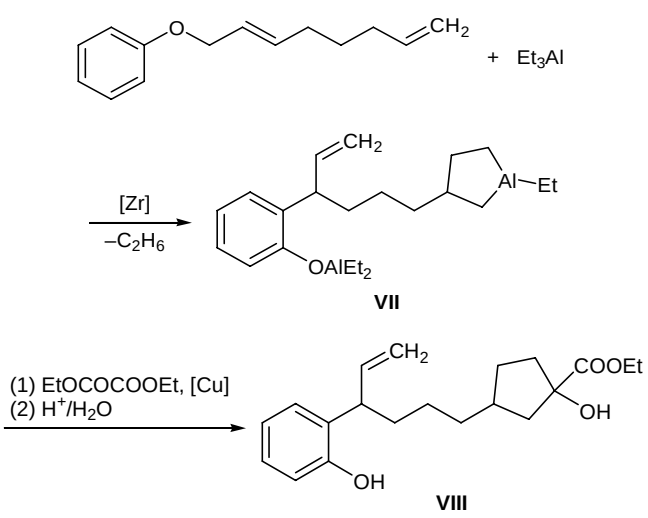
Scheme 2.



[Zr] = Cp_2ZrCl_2, [Cu] = CuCl, CuBr, CuI.

Under the above conditions, 8-phenoxyocta-1,6-diene underwent Claisen rearrangement with formation of 3-substituted aluminacyclopentane **VII** [11] which reacted with diethyl oxalate in the presence of CuCl to afford (after hydrolysis) 70% of ethyl-1-hydroxy-3-[4-(2-hydroxyphenyl)hex-5-en-1-yl]cyclopentanecarboxylate (**VIII**) (Scheme 3). An analogous rearrangement was observed in the carboalumination of allyl phenyl ether with Me_3Al in the presence of a zirconium catalyst [12].

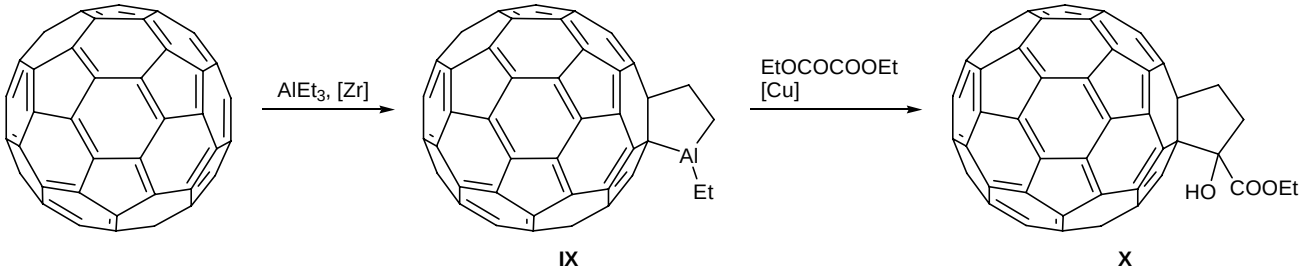
Scheme 3.



[Zr] = Cp_2ZrCl_2, [Cu] = CuCl, CuBr, CuI.

According to our previous data [13], cycloalumination of norbornene and cyclopentadiene dimer with Et_3Al in the presence of Cp_2ZrCl_2 leads to the formation of tri- and tetracyclic organoaluminum compounds with *exo*-oriented aluminacyclopentane fragments. However, we failed to involve such polycyclic com-

Scheme 4.



IX **X**

[Zr] = Cp_2ZrCl_2, [Cu] = CuCl (15 mol %).

pounds in reaction with diethyl oxalate. Presumably, the Al–C bonds therein are sterically shielded by bridgehead carbon atoms, thus preventing them from reacting with diethyl oxalate. On the other hand, unlike aluminacyclopentanes derived from norbornenes, compound **IX** [14] having a fused fullerene C_{60} moiety that shields only one Al–C bond in the aluminacyclopentane fragment reacted with diethyl oxalate in toluene at 20°C (reaction time 8 h) to form ethyl 1'-hydroxycyclopentafullerene-1'-carboxylate (**X**) in ~65% yield (Scheme 4).

Initial fullerene C_{60} and product **X** were separated by column chromatography on silica gel (toluene–ethanol, 4:1, R_f 0.68). The UV spectrum of **X** contains an absorption band with its maximum at λ 443 nm which is typical of closed [6,6]-adducts [15, 16]. Signals at δ_C 124.49–157.73 ppm in the ^{13}C NMR spectrum of **X** were assigned to sp^2-carbon atoms in the fullerene fragment, while fullerene sp^3-carbons resonated at δ_C 66.39 and 72.66 ppm. The C^1 signal of **X** was located at δ_C 96.31 ppm. Its downfield position relative to the corresponding signals of 3-substituted 1-hydroxycyclopentanecarboxylates **IV** is explained by the effect of the fullerene sphere. The carbonyl carbon signal appears at δ_C 170.60 ppm. These data support the structure of **X** as fullerene-fused cyclopentanecarboxylate.

Thus the developed procedure makes it possible to synthesize 1-hydroxycyclopentanecarboxylic acid esters via catalytic cycloalumination of terminal olefins with Et_3Al, followed by reaction of intermediate aluminacyclopentanes with diethyl oxalate in the presence of copper(I)-containing catalysts.

EXPERIMENTAL

Chromatographic analysis was performed on a Chrom-5 chromatograph equipped with a 1200×3-mm column packed with 5% of SE-30 on Chromaton N-AW-HMDS (0.125–0.160 mm); carrier gas helium, flow rate 47 ml/min; oven temperature programming from 50 to 250°C at a rate of 8 deg/min. The IR spectra were recorded on a UR-75 spectrometer from samples prepared as KBr pellets or thin films. The ^1H and ^{13}C NMR spectra were measured from solutions in $CDCl_3$ on a Jeol FX-90Q instrument at 89.55 and 22.5 MHz, respectively; tetramethylsilane was used as reference. The yields were determined by GLC, and the purity of the products was checked by thin-layer chromatography on Silufol UV-254 plates (development with iodine vapor). Reactions with organometallic compounds were carried out in a stream of dry argon. The solvents were dried and distilled prior to use. Triethylaluminum was a commercial product containing 95% of the main substance.

Ethyl 1-hydroxy-3-R-cyclopentanecarboxylates IVa–IVd (*general procedure***).** A glass reactor was charged at 0°C under dry argon with 0.5 mmol of Cp_2ZrCl_2, 3 ml of hexane, 10 mmol of the corresponding olefin, and 12 mmol of Et_3Al. The mixture was allowed to warm up to room temperature and was stirred for 12 h. It was then cooled to –15°C, 1.5 mmol of CuCl was added, and 12 mmol of diethyl oxalate was slowly added. The mixture allowed to warm up to room temperature (20–21°C), stirred for 8 h, treated with 8% hydrochloric acid, and extracted with diethyl ether. The extract was dried over calcium chloride, the solvent was removed, and the product was isolated by chromatography on silica gel.

Ethyl 1-hydroxy-3-pentylcyclopentanecarboxylate (IVa) (a mixture of *cis* and *trans* isomers, ~1:1**).** Yield 80%. Eluent hexane–diethyl ether (1:1), R_f 0.83. IR spectrum, ν, cm^{-1}: 3430, 2960, 2920, 2845, 1720, 1410, 1390, 1190, 1100, 1020, 880, 760 w, 730 w. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 0.87 t (3H, CH_3, ^3J = 6.0 Hz), 1.10–2.35 m (18H, CH, CH_2, CH_3), 4.25 q (2H, CH_2O, ^3J = 7.0 Hz). ^{13}C NMR spectrum

($CDCl_3$), δ_C, ppm: 13.50 (CH_3), 13.60 (CH_3), 22.17 (CH_2), 27.83 (CH_2), 31.06 (CH_2), 31.61 and 31.81 (C^4), 35.12 and 36.65 (CH_2), 38.26 and 38.44 (C^5), 39.46 and 39.72 (C^3), 45.42 and 45.91 (C^2), 60.92 (OCH_2), 81.01 and 81.23 (C^1), 176.80 and 177.12 (COO). Found, %: C 67.79; H 10.18. $C_{13}H_{24}O_3$. Calculated, %: C 68.38; H 10.60.

Ethyl 3-heptyl-1-hydroxycyclopentanecarboxylate (IVb) (a mixture of *cis* and *trans* isomers, ~1:1**).** Yield 78%. Eluent hexane–diethyl ether (1:1), R_f 0.80. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.87 t (3H, CH_3, ^3J = 6.0 Hz), 1.10–2.35 m (20H, CH, CH_2, CH_3), 4.25 q (2H, CH_2O, ^3J = 7.0 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 13.68 (CH_3), 13.82 (CH_3), 22.68 (CH_2), 24.60 (CH_2), 28.95 (CH_2), 27.85 (CH_2), 30.26 (CH_2), 31.74 and 31.92 (C^4), 34.38 and 34.85 (CH_2), 38.48 and 38.63 (C^5), 39.89 and 40.17 (C^3), 45.54 and 46.02 (C^2), 60.96 and 61.21 (OCH_2), 81.15 and 81.37 (C^1), 176.89 and 177.15 (COO). Found, %: C 69.74; H 10.59. $C_{15}H_{28}O_3$. Calculated, %: C 70.27; H 11.01.

Ethyl 3-(cyclohex-3-en-1-yl)-1-hydroxycyclopentanecarboxylate (IVc) (a mixture of *cis* and *trans* isomers, ~1:1**).** Yield 71%. Eluent hexane–diethyl ether (1:2), R_f 0.47. IR spectrum, ν, cm^{-1}: 3450, 3010, 2910, 2850, 2830, 1720, 1430, 1280, 1180, 1100, 1040, 910, 730, 660. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.31 t (3H, CH_3, ^3J = 7.0 Hz), 1.55–2.40 m (14H, CH, CH_2), 4.28 q (2H, CH_2O, ^3J = 7.0 Hz), 5.58–5.91 m (2H, CH=CH). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 14.00 (CH_3), 25.10 (CH_2), 27.46 and 27.67 (C^4), 29.20 (CH_2), 30.53 (CH_2), 32.01 and 32.13 (CH), 38.46 and 38.59 (C^5), 38.93 and 39.06 (C^3), 44.21 and 44.33 (C^2), 61.38 and 61.54 (OCH_2), 81.09 and 81.31 (C^1), 126.25 (=CH), 126.83 (=CH), 177.13 and 177.35 (COO). Found, %: C 69.95; H 8.96. $C_{14}H_{22}O_3$. Calculated, %: C 70.55; H 9.31.

Ethyl 3-benzyl-1-hydroxycyclopentanecarboxylate (IVd) (a mixture of *cis* and *trans* isomers, ~1:1**).** Yield 60%. Eluent hexane–diethyl ether (1:1), R_f 0.39. IR spectrum, ν, cm^{-1}: 3450, 3080 w, 3050 w, 3010 m, 2950, 2930, 2870, 1610, 1720, 1495, 1455, 1380, 1180, 1100, 1020, 910, 880 w, 770 m, 740 m, 705. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.10–2.85 m (12H, CH_3, CH_2, CH), 4.25 q (2H, CH_2O, ^3J = 7.0 Hz), 6.98–7.50 m (5H, H_{arom}). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 14.09 (CH_3), 31.68 and 31.85 (C^4), 33.32 and 33.56 (C^5), 34.05 and 34.31 (C^3), 39.67 (CH_2), 44.16 and 44.52 (C^2), 61.48 and 61.82 (OCH_2), 81.37 and 81.58 (C^1), 125.90 (C_{arom}), 126.98 (2C, C_{arom}), 128.16 (2C, C_{arom}), 145.66 and 146.78 (C_{arom}), 175.11 and 175.57 (COO). Found, %: C 72.09; H 7.7. $C_{15}H_{20}O_3$. Calculated, %: C 72.55; H 8.12.

Ethyl 1-hydroxy-3-(oct-7-en-1-yl)cyclopentanecarboxylate (V) (a mixture of *cis* and *trans* isomers, ~1:1**).** Yield 31%. Eluent hexane–diethyl ether (2:1), R_f 0.38. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.15–2.50 m (22H, CH, CH_2, CH_3), 4.27 q (2H, CH_2O, ^3J = 7.0 Hz), 4.45 d (2H, $=CH_2$, J = 7.0 Hz), 5.51–5.98 m (1H, CH=). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 13.64 (CH_3), 28.16 (CH_2), 28.88 (CH_2), 29.03 (CH_2), 29.39 (CH_2), 31.09 and 31.48 (C^4), 33.92 (CH_2), 35.68 and 35.78 (CH_2), 38.29 and 38.45 (C^5), 39.46 and 39.69 (C^3), 45.42 and 45.90 (C^2), 61.01 and 60.78 (OCH_2), 81.04 and 81.26 (C^1), 113.84 (CH_2=), 138.61 (CH=), 176.80 and 177.08 (COO). Found, %: C 70.51; H 10.02. $C_{16}H_{28}O_3$. Calculated, %: C 71.60; H 10.51.

Diethyl 3,3'-hexamethylenedi(1-hydroxycyclopentanecarboxylate) (VI) (a mixture of *cis* and *trans* isomers, ~1:1**).** Yield 49%. Eluent hexane–diethyl ether (2:1), R_f 0.60. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.13–2.48 m (32H, CH, CH_2, CH_3), 4.26 q (4H, CH_2O, ^3J = 7.0 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 13.24 (CH_3), 28.26 (CH_2), 29.46 (CH_2), 31.69 and 31.88 (C^4), 36.20 and 36.50 (CH_2), 38.29 and 38.53 (C^5), 39.51 and 39.77 (C^3), 45.51 and 45.96 (C^2), 60.21 and 60.98 (OCH_2), 81.14 and 81.32 (C^1), 175.40 and 177.32 (COO). Found, %: C 65.82; H 9.11. $C_{22}H_{38}O_6$. Calculated, %: C 66.30; H 9.61.

Ethyl 1-hydroxy-3-[4-(2-hydroxyphenyl)hex-5-en-1-yl]cyclopentanecarboxylate (VIII). Yield 70%. Eluent hexane–diethyl ether (1:10), R_f = 0.75. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.12–2.46 m (16H, CH, CH_2, CH_3), 3.10–3.30 m (1H, C**H**Ph), 4.20 q (2H, CH_2O, ^3J = 7 Hz), 5.0 d (2H, CH_2=, ^3J = 7 Hz), 5.20–6.30 m (1H, CH_2=C**H**), 6.70–7.30 m (4H, H_{arom}). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 13.87 (CH_3), 28.15 (CH_2), 31.09 (31.48) (C^4), 34.02 (CH_2), 35.26 (CH_2), 35.68 and 36.20 (C^5), 38.54 and 38.65 (C^3), 39.71 and 39.82 (C^2), 42.45 (CH), 61.58 and 61.66 (CH_2O), 81.65 and 81.91 (C^1), 113.92 (CH_2=), 115.08 (C_{arom}), 120.31 and 126.85 (C_{arom}), 128.05 (C_{arom}), 130.30 (C_{arom}), 140.81 and 141.73 (=CH), 153.71 and 154.17 (HOC_{arom}), 175.40 and 177.32 (COO). Found, %: C 71.82; H 8.03. $C_{20}H_{28}O_4$. Calculated, %: C 72.26; H 8.49.

Ethyl 3'-hydroxycyclopenta[1,9](C_{60}-I_h)[5,6]-fullerene-3'-carboxylate (X). A glass reactor was charged under argon with 0.025 mmol of fullerene C_{60} and 30 ml of toluene, the mixture was stirred until it became homogeneous, 0.0025 mmol (10 mol %) of

Cp_2ZrCl_2 and 0.75 mmol of $AlEt_3$ were added, the mixture was stirred for 12 h and cooled to –15°C, 0.01 mmol (40 mol %) of CuCl was added, and 0.75 mmol of diethyl oxalate was slowly added. The mixture was allowed to warm up to room temperature, stirred for 6–8 h, and treated with HCl/Et_2O. The product was isolated by column chromatography on silica gel L (180–250 μm) using toluene–ethanol (4:1) as eluent. Yield 65%, R_f 0.68 (toluene–ethanol, 8:2). UV spectrum, λ_{max}, nm: 260, 332, 443. IR spectrum, ν, cm^{-1}: 3400, 2950, 2870, 1700, 1610, 1460, 1380, 1310, 1180, 1100, 730, 700, 570, 530. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.0–1.24 (7H, CH_2, CH_3), 4.26 q (2H, CH_2O, ^3J = 7 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 13.83, 33.18, 38.01, 59.41, 66.39, 72.66 (sp^3-carbon atoms in C_{60}), 96.31, 170.60; signals from sp^2-carbon atoms of the fullerene sphere were located in the region δ_C 124.49–157.73 ppm.

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