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Phosphates of bridgehead alcohols as putative inositol monophosphatase inhibitors: molecular design and synthetic approach

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Experimental

Column chromatography was performed on silica gel Acros (40-60 μm). Reaction control was carried out by thin-layer chromatography on Silufol plates. ^{1}H, ^{13}C and ^{31}P NMR spectra were recorded in $CDCl_3$ or D_2O at 400, 100 and 162 MHz, respectively. Spectra are referenced to residual $CHCl_3$ (δ 7.26 ppm ^{1}H; δ 77.0 ppm ^{13}C). The signals in ^{31}P are referenced to 85% phosphoric acid. Chemical shifts are given in ppm (δ); multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quadruplet), m (multiplet).

Elemental analysis of synthesized compounds was performed on CNH analyzer Carlo-Erba ER-20. IR spectra were recorded on a Thermo Nicolet IR200 apparatus in KBr plates and reported in cm^{-1}.

Electrospray (ESI) mass spectra data were recorded on an Agilent LC/MSD 1100 SL mass spectrometer [electrospray ionization at atmosphere pressure, positive ion mode, ion trap mass analyzer, solution flow rate of 10 μl min^{-1}, drying gas (N_2) temperature 120 ^{0}C, nebulizer voltage of 5500 V, capillary voltage of 0–300 V]. HPLC-ESIMS spectra were registered on a Water Acquity UPLC System with PDA and TQD detectors (column: Acquity UPLC BEH C18, 50x2.1 mm, 1.7 μm; temperature 35 ^{0}C, mobile phase: 10% acetonitrile in water and 20 mM formic acid; 0.5 ml/min flow rate; MS conditions: negative electrospray mode).

General procedure for the synthesis of o-*hydroxyphenyl adamantlyl phosphate triethylammonium salts.* The solution of *o*-phenylenephosphorochloridate **6** in dry THF was added to the solution of equivalent amounts of corresponding adamantanol and triethylamine in THF. The mixture was stirred at room temperature under inert atmosphere during 12 h. The precipitated solid was filtered off and washed with THF. The filtrate was evaporated under reduced pressure, mixed with triethylamine and water and stirred overnight. The volatile components were evaporated and the product was purified by recrystallization or by column chromatography.

Triethylammonium o-*hydroxyphenyl 1-hydroxy-2-adamantyl phosphate* **7** was prepared according to the general method from adamantanediol **5** (1.12 g, 6.6 mmol), *o*-phenylenephorosphochloridate **6** (1.252 g, 6.6 mmol) and triethylamine (0.92 ml, 6.6 mmol). Recrystallized from ethyl acetate to give 1.49 g of **7** (51% yield).

^{1}H NMR (δ, ppm $CDCl_3$): 1.27 (t, 9H, ^3J = 7.3 Hz, $CH_2C\underline{H}_3$); 1.30-1.33 (m, 1H, adam.); 1.47-150 (m, 1H, adam.); 1.58-1.72 (m, 5H, adam.); 1.78-1.82 (1H, adam.); 1.95-2.05 (m, 4H, adam.); 2.13-2.16 (m, 1H, adam.); 2.97-3.02 (q, 6H, J_{vic} = 7.3 Hz, J_{gem} = 14.6 Hz, $NC\underline{H}_2Me$); 4.34-4.36 (dd, 1H, $^3J_{23}$ = 3.3 Hz, $^3J_{HP}$ = 7.6 Hz, CHOP); 2.67-2.97 (br s, 1H, OH); 6.75-6.79 (dd, 1H, $^3J_{56}$ = 8.1 Hz, $^3J_{54}$ = 6.6 Hz, H^5 arom.); 6.92-6.96 (m, 2H, $^3J_{45}$ = 6.6 Hz, $^3J_{34}$ = 7.5 Hz, H^3 + H^4 arom.); 7.03 (d, 1H, $^3J_{65}$ = 8.1 Hz, H^6 arom.); 11.67 (br s, 1H, NH^+).

^{13}C NMR (δ, ppm $CDCl_3$): 8.48 ($\underline{C}H_3CH_2$); 29.91 ($^3J_{CP}$ = 4.4 Hz, $\underline{C}$HCOP); 30.06; 35.67 ($^3J_{CP}$ = 4.4 Hz, C^3 adam.); 35.82; 36.14; 39.60; 43.66; 45.73 ($CH_3\underline{C}H_2N$); 71.65 ($^3J_{CP}$ = 4.4 Hz, COH adam.); 83.55 ($^2J_{CP}$ = 6.6 Hz, CHOP); 118.93; 119.83; 122.61; 125.01; 142.15 (COP arom.); 149.86 (COH arom.).

^{31}P NMR (δ, ppm $CDCl_3$): 0.54.

Found, %: C 59.67; H 8.36; N 3.28. Calc. for $C_{22}H_{36}NO_6P$, %: C 59.85; H 8.22; N 3.17.

Triethylammonium o-*hydroxyphenyl 2-benzyloxy-1-adamantyl phosphate* **11** was prepared according to the general method from 2-benzyloxyadamantan-1-ol (**10**) (0.7 g, 2.7 mmol), *o*-phenylenephosphorochloridate **6** (0.5 g, 2.7 mmol) and triethylamine (0.38 ml, 2.7 mmol). Column chromatography (chloroform – methanol 15:1) gave 0.7 g of product **11** (49% yield).

^{1}H NMR (δ, ppm $CDCl_3$): 1.05 (t, 9H ^3J = 7.1 Hz., $CH_2C\underline{H}_3$,); 1.28 -1.30 (m, 1H, adam.);1.52-2.63 (m, 4H, adam.); 1.98-2.16 (m, 6H, adam.); 2.31-2.39 (m, 2H, adam.); 2.83 (q, 6H, J_{vic} = 7.1 Hz, $^2J_{gem}$ = 14.1 Hz, $NC\underline{H}_2CH_3$); 3.79 (br s,1H, CHOBn); 4.56 (d, 2H, $^2J_{gem}$ = 11.6 Hz, CH_2Ph); 4.69 (d, 1H, ^2J = 11.6 Hz, CH_2Ph); 6.63 (dd, 1H, $^3J_{56}$ = 8.3 Hz, $^3J_{54}$ = 6.7 Hz, H^5 arom.); 6.88 (m, 2H, $^3J_{45}$ = 6.7 Hz, $^3J_{34}$ = 7.8 Hz, H^3 + H^4 arom.); 7.07 (d, 1H, $^3J_{65}$ = 8.3 Hz, H^6 arom.); 7.17-7.31 (m, 5H, arom.); 11.70 (br s,1H, NH^+).

^{13}C NMR (δ, ppm $CDCl_3$): 8.32 ($CH_2\underline{C}H_3$); 30.20; 30.34; 30.42; 34.42; 35.42; 35.88; 37.64; 42.00; 45.38 ($N\underline{C}H_2CH_3$); 71.72 (CH_2Ph); 80.80 ($^2J_{CP}$ = 7.8 Hz, COP); 83.44 ($^3J_{CP}$ = 5.1 Hz, CHOBn) 119.65; 122.61; 124.56; 126.86; 127.28; 127.46; 128.00; 140.01 ($\underline{C}OCH_2$ arom.); 140.72 ($^2J_{CP}$ = 8.1 Hz, COP arom.); 149.11 (COH arom.).

^{31}P NMR (δ, ppm $CDCl_3$): –5.49.

Triethylammonium o-*hydroxyphenyl 4-benzyloxy-1-adamantyl phosphate* **16** was prepared according to the general method from 4-benzyloxyadamantan-1-ol (**15**) (1.6 g, 6 mmol), *o*-phenylenephosphorochloridate **6** (1.16 g, 6 mmol) and triethylamine (0.85 ml, 6

mmol). Column chromatography (chloroform – methanol 15:1) gave 2.38 g of compound **16** (74% yield).

^{1}H NMR (δ, ppm $CDCl_3$, diastereomeric mixture): 1.19 (t, 9H ^3J = 7.3 Hz., $CH_2C\underline{H}_3$,); 1.39-1.52 (m, 2H, adam.); 1.73-1.76 (m, 1H, adam.); 1.93-2.04 (m, 2H, adam.); 2.09-2.18 (m, 5H, adam.); 2.24-2.43 (m, 3H, adam.); 2.88 (q, 6H, J_{vic} = 7.1 Hz, J_{gem} = 13.5 Hz, $NC\underline{H}_2CH_3$); 3.39 and 3,57 (m, 2x0.5H, CHOBn); 4.51 (br s, 2H, CH_2Ph); 6.75 (dd, 1H, $^3J_{56}$ = 7.6 Hz, $^3J_{54}$ = 6.1 Hz, H^5 arom.); 6.93-6.96 (m, 2H, $^3J_{45}$ = 6.1 Hz, $^3J_{34}$ = 7.6 Hz, H^3 + H^4 arom.); 7.04 (d, 1H, $^3J_{65}$ = 7.6 Hz, H^6 arom.); 7.26-7.37 (m, 5H, Bn); 12.17 (br s,1H, NH^+).

^{13}C NMR (δ, ppm $CDCl_3$ diastereomeric mixture): 8.38 ($CH_2\underline{C}H_3$); 30.12; 30.20; 33.75; 34.70; 34.79; 37.57 ($^3J_{CP}$ = 3.7 Hz, C^8 and C^9 adam.); 41.53 ($^3J_{CP}$ = 2.9 Hz, C^2 adam.); 42.87 and 43.39; 45.36 ($N\underline{C}H_2CH_3$); 69.15 and 69.53 (CH_2Ph); 77.26 (COP); 79.20 and 79.77 (CHOBn); 118.77; 119.64 and 119.68; 122.96; 124.61 and 124.72; 127.17 and 127.25; 127.29 and 127.33; 128.24 and 128.28; 139.28 ($\underline{C}CH_2O$ arom.); 140.88 ($^2J_{CP}$ = 8.05 Hz, COP arom.); 149.51 (COH arom.).

^{31}P NMR (δ, ppm $CDCl_3$, diastereomeric mixture): –3.73 and –3.53.

Triethylammonium o-*hydroxyphenyl 2-hydroxy-1-adamantyl phosphate* **12.** The mixture of compound **11** (0.7g, 0.8 mmol) and 5% palladium on carbon in methanol was treated with hydrogen gas during 5 h. The catalyst was filtered off and the residue was evaporated under reduced pressure to give **12** (0.54 g, yield 93%).

^{1}H NMR (δ, ppm $CDCl_3$): 1.20 (t, 9H ^3J = 7.3 Hz., $CH_2C\underline{H}_3$,); 1.23 -1.34 (m, 2H, adam.); 1.56-2.75 (m, 5H, adam.); 1.92-2.13 (m, 5H, adam.); 2.48-2.51 (m, 1H, adam.); 2.83 (q, 6H, J_{vic} = 7.1 Hz, J_{gem} = 13.9 Hz, $NC\underline{H}_2CH_3$); 4.12 (br s,1H, CHOH); 6.74 (dd, 1H, $^3J_{56}$ = 8.3 Hz, $^3J_{54}$ = 6.6 Hz, H^5 arom.); 6.93 (m, 2H, $^3J_{45}$ = 6.6 Hz, $^3J_{34}$ = 7.6 Hz, H^3 + H^4 arom.); 7.11 (d, 1H, $^3J_{65}$ = 8.3 Hz, H^6 arom.); 11.42 (br s,1H, NH^+).

^{13}C NMR (δ, ppm $CDCl_3$): 8.40 ($CH_2\underline{C}H_3$); 29.73; 30.40; 30.57; 35.45; 36.00; 36.29; 37.15 ($^3J_{CP}$ = 4.3 Hz); 42.40; 45.64 ($N\underline{C}H_2CH_3$); 75.99 (CHOH); 82.38 ($^2J_{CP}$ = 9.5 Hz, COP); 118.20; 119.81; 122.10; 124.83; 140.37 ($^2J_{CP}$ = 6.6 Hz, COP arom.); 148.78.

^{31}P NMR (δ, ppm $CDCl_3$): –4.67.

Triethylammonium o-*hydroxyphenyl 4-hydroxy-1-adamantyl phosphate* **17** was synthesized as analogous to **12** from compound **16** (2.38 g, 4 mmol) and 5% palladium on carbon (0.15 g) to give 1.65 g **17** (84% yield).

^{1}H NMR (δ, ppm $CDCl_3$, diastereomeric mixture): 1.25 (t, 9H ^3J = 7.2 Hz., $CH_2C\underline{H}_3$,); 1.32-1.35 (m, 1H, adam.); 1.50-1.53 (m, 1H, adam.); 1.63-1.66 (m, 1H, adam.); 1.77-1.80 (m, 1H, adam.); 1.96-2.13 (m, 8H, adam.); 2.49-2.51 (m, 1H, adam.); 2.88 (q, 6H, J_{vic} = 7.0 Hz, J_{gem} = 13.3 Hz, $NC\underline{H}_2CH_3$); 3.67 and 3,87 (m, 2x0.5H, CHOH); 6.75 (dd, 1H, $^3J_{56}$ = 8.3 Hz, $^3J_{54}$ = 6.6 Hz, H^5

arom.); 6.93-6.96 (m, 2H, $^3J_{45}$ = 6.6 Hz, $^3J_{34}$ = 8.1 Hz, H^3 + H^4 arom.); 7.04 (d, 1H, $^3J_{65}$ = 8.1 Hz, H^6 arom.); 11.10 (br s,1H, NH^+).

^{13}C NMR (δ, ppm $CDCl_3$, diastereomeric mixture): 8.51 ($\underline{C}H_3CH_2$); 29.36; 29.80 and 30.28; 34.62; 36.36; 36.69; 37.36; 41.43; 43.38; 45.82 ($CH_3\underline{C}H_2N$); 72.14 and 72.60 (CHOH); 80.21 and 80.69 ($^2J_{CP}$= 8.05 Hz, COP); 117.77 and 117.86; 119.84; 121.28; 125.05; 139.77 (COP, arom.); 148.09 and 148.20 (COH, arom.).

^{31}P NMR (δ, ppm $CDCl_3$, diastereomeric mixture): –8.68 and –8.21.

General procedure for the synthesis of adamantyl phosphate barium salts. To the triethylammonium salt in 2M solution of barium acetate (150 ml) the 2% bromine water (180 ml, 22.5 mol) was added. In 15 min the precipitated sediment was filtered, the filtrate was washed with ether and water solution was evaporated up to 80 ml under reduced pressure at 35-40^{0}C. The solution was mixed with activated carbon and stirred at room temperature until it became colorless. Then carbon was filtered off and the filtrate was evaporated to the volume of ~40 ml. Addition of acetone or ethanol to this solution gave a precipitate which was filtered, washed with small amounts of water and dried.

Barium 1-hydroxy-2-adamantyl phosphate **8** was prepared from **7** (0.50 g, 1.1 mmol), barium acetate (78 ml) and bromine water (93 ml). The yield was 0.23 g (52%).

^{1}H NMR (δ, ppm D_2O): 1.34-1.43 (m, 2H, adam.); 1.55-1.70 (m, 6H, adam.); 1.88-2.17 (m, 5H, adam.); 3.37-3.52 (br s,1H, OH); 4.01 (m, 1H, H^2).

^{31}P NMR (δ, ppm D_2O): 3.69.

Found, %: C 28.90; H 4.25. $C_{10}H_{15}BaO_5P\times2H_2O$. After additional drying at 50^{0}C (14 mmHg) found, %: C 28.87; H 4.38. Calc. for $C_{10}H_{15}BaO_5P\times2H_2O$: %: C 28.63; H 4.56.

Barium 2-hydroxy-1-adamantyl phosphate **13** was prepared from **12** (0.445 g, 1 mmol), barium acetate (70 ml) and bromine water (90 ml). The yield was 0.161 g (42%).

^{1}H NMR (δ, ppm D_2O): 1.34-1.37 (m, 1H, adam.); 1.55-1.80 (m, 6H, adam.); 1.91-1.99 (m, 5H, adam.); 2.16-2.21 (m, 1H, adam.); 3.93 (m, 1H, H^2).

^{31}P NMR (δ, ppm D_2O): –0.99.

Found, %: C 28.88; H 4.29. $C_{10}H_{15}BaO_5P\times2H_2O$. After additional drying at 50^{0}C (14 mmHg) found, %: C 28.79; H 4.31. Calc. for $C_{10}H_{15}BaO_5P\times2H_2O$, %: C 28.63; H 4.56.

Barium 4-hydroxy-1-adamantyl phosphate **18** was prepared from **17** (1.65 g, 4 mmol), barium acetate (260 ml) and bromine water (333 ml). The yield was 0.67 g (46%).

^{1}H NMR (δ, ppm D_2O, diastereomeric mixture): 1.33-1.37 (m, 1H, adam.); 1.47-1.50 (m, 1H, adam.); 1.62-1.81 (m, 3H, adam.); 1.87-2.09 (m, 7H, adam.); 2.16-2.23 (m, 1H, adam.); 3.65 and 3.85 (m, 2x0.5H, H^4).

^{13}C NMR (δ, ppm D_2O, diastereomeric mixture): 29.05; 29.29; 29.59; 29,65; 34.43; 35.51; 36.61; 36.79; 38.25; 41.43; 42.94; 43.28; 47.26; 72.97 (C^4); 73.38 (C^1).

^{31}P NMR (δ, ppm D_2O): 0.0

Found, %: C 28.87; H 4.38. $C_{10}H_{15}BaO_5P\times2H_2O$. After additional drying at 50^{0}C (14 mmHg) found, %: C 28.82; H 4.40. Calc. for $C_{10}H_{15}BaO_5P\times2H_2O$, %: C 28.63; H 4.56.

General procedure for the synthesis of adamantyl sodium phosphates. The aqueous suspension of barium salt was stirred with equivalent amount of sodium sulfate at room temperature for 2 days. The precipitate was filtered off and the solution was evaporated to give pure product as a white solid.

Disodium 1-hydroxy-2-adamantylphosphate **9** was synthesized from **8** (147 mg, 0.38 mmol). The yield was 112 mg (100%).

^{1}H NMR (δ, ppm D_2O): 1.25-1.33 (m, 2H, adam.); 1.43-1.64 (m, 6H, adam.); 1.80-2.02 (m, 4H, adam.), 2.08 (m, 1H, H^3), 3.92 (m, 1H, H^2).

^{13}C NMR (δ, ppm D_2O): 29.40; 29.59; 29.68; 35.11; 35.45; 38.59; 42.74; 70.60 ($^2J_{CP}$ = 6.9 Hz, C^2); 79.95 ($^3J_{CP}$ = 3.7 Hz, C^1).

^{31}P NMR (δ, ppm D_2O): 3.96.

IR: 3300 (COH), 1092 (P=O), 975 (POC), 825 (POC).

Found, %: C 34.20; H 5.50. $C_{10}H_{15}Na_2O_5P\times3H_2O$. After additional drying at 50^{0}C (14 mmHg) found, %: C 34.22; H 5.51. Calc. for $C_{10}H_{15}Na_2O_5P\times3H_2O$, %: C 34.69; H 6.11.

ESIMS, *m/z*: 292 (M^+), 314 (M^+Na).

Disodium 2-hydroxy-1-adamantylphosphate **3** was synthesized from **13** (100 mg, 0.17 mmol). The yield was 76 mg (100%).

^{1}H NMR (δ, ppm D_2O): 1.33-1.36 (m, 1H, adam.); 1.54-1.67 (m, 5H, adam.); 1.76-1.97 (m, 6H, adam.); 2.17-2.19 (m, 1H, adam.); 3.94 (m, 1H, H^2).

^{13}C NMR (δ, ppm D_2O): 29.34; 29.87; 30.14; 35.05; 35.50; 36.98; 38.32; 42.21; 76.77 ($^3J_{CP}$ = 3.8 Hz, C^2); 80.62 (C^1).

^{31}P NMR (δ, ppm D_2O): –0.34.

Found, %: C 34.27; H 5.67. $C_{10}H_{15}Na_2O_5P\times3H_2O$. After additional drying at 50^{0}C (14 mmHg) found, %: C 34.33; H 5.70. Calc. for $C_{10}H_{15}Na_2O_5P\times3H_2O$. %: C 34.68; H 6.07.

Disodium 4-hydroxy-1-adamantylphosphate **4** was synthesized from **18** (99 mg, 0.27 mmol). The yield was 75 mg (100%).

^{1}H NMR (δ, ppm D_2O, diastereomeric mixture): 1.29-1.32 (m, 1H, adam.); 1.42-1.45 (m, 1H, adam.); 1.57-1.77 (m, 3H, adam.); 1.81-2.04 (m, 7H, adam.); 2.11-2.17 (m, 1H, adam.); 3.60 and 3.80 (m, 2x0.5H, H^4).

^{13}C NMR (δ, ppm D_2O, diastereomeric mixture): 29.03; 29.26; 29.56; 29,63; 34.42; 35.48; 36.58; 36.76; 38.23; 41.41; 42.94; 43.14; 47.26; 72.96 (C^4); 73.35 (C^1).

^{31}P NMR (δ, ppm D_2O, diastereomeric mixture): –0.1.

Found, %: C 34.25; H 5.47. $C_{10}H_{15}Na_2O_5P\times3H_2O$. After additional drying at 50^{0}C (14 mmHg) found, %: C 34.28; H 5.42. Calc. for $C_{10}H_{15}Na_2O_5P\times3H_2O$, %: C 34.69; H 6.07.

2-Benzyloxyadamantan-1-ol **10** was prepared by standard method from adamantane-1,2-diol (**5**) (1 g, 6 mmol), sodium hydride (60% in mineral oil 0.23 g, 6 mmol) and benzyl chloride (0.68 ml, 6 mmol) in solution of DMF. The reaction mixture was purified by column chromatography to yield 1.13 g (74%) of benzylated product.

^{1}H NMR (δ, ppm $CDCl_3$): 1.41-1.56 (m, 2H, adam.); 1.63-1.83 (m, 6H, adam.); 1.92-1.95 (m, 1H, adam.); 2.07-2.16 (m, 3H, adam.); 2.33-2.34 (m, 1H, adam.); 3.47 (d, 1H, ^3J = 3.5 Hz, C<u>H</u>OBn); 4.49 (d, 1H, ^2J = 11.4 Hz, CH_2Ph); 4.72 (d, 1H, ^2J = 11.4 Hz, CH_2Ph); 7.27-7.40 (m, 5H, arom.).

^{13}C NMR (δ, ppm $CDCl_3$): 29.78; 29.92; 30.02; 31.89; 35.68; 36.18; 40.28; 42.51; 69.56 (COH); 70.52 (CH_2Ph); 85.57 (CHOBn); 127.49; 127.52; 128.41; 138.97.

Found, %: C 65.50; H 7.77; N 2.54. Calc. for $C_{29}H_{42}NO_6P$, %: C 65.52; H 7.96; N 2.63.

4-Benzyloxyadamantan-1-ol **15** was prepared by standard method from adamantane-1,4-diol **14** (2.8 g, 17 mmol), sodium hydride (60% in mineral oil 0.66 g, 17 mmol) and benzyl chloride (1.94 ml, 17 mmol) in solution of DMF. The reaction mixture was purified by column chromatography to yield 3.1 g (72%) of benzylated product.

^{1}H NMR (δ, ppm $CDCl_3$, diastereomeric mixture): 1.38-1.58 (m, 4H, adam.); 1.70-1.77 (m, 4H, adam.); 2.08-2.15 (m, 3H, adam.); 2.26-2.36 (m, 2H, adam.); 3.43 and 3.57 (t, 2x0.5H, ^3J = 3.16 Hz and ^3J = 3.03 Hz, CHOBn); 4.56 (br s,2H, CH_2Ph); 7.28-7.40 (m, 5H, arom.).

^{13}C NMR (δ, ppm $CDCl_3$, diastereomeric mixture): 29.83 and 29.91; 30.20; 33.48; 34.42; 34.90; 39.55; 43.52; 44.93 and 45.39; 67.73 and 68.01 (COH); 69.32 and 69.72 (CH_2Ph); 79.16 and 79.94; 127.07; 127.33; 128.33; 139.17.

The Bayer−Villiger oxidation of 2-oxoadamantan-1-ol. Trifluoroacetic anhydride (13 ml) and 30% aqueous hydrogen peroxide (2.5 ml, 20.9 mmol) were sequentially added to the solution of 2-oxoadamantan-1-ol **19** (0.25 g, 1.5 mmol) in CH_2Cl_2. After stirring at 0^{0}C for 2 h the solvent was evaporated and the residue was subjected to column chromatography on silica gel (ethyl acetate–light petroleum, gradient from 1:3 to 2:1, the chloroform–methanol 10:1).

The major fraction (0.28 g, Rf ~ 0.1 in chloroform–methanol 10:1) was the mixture of diastereomeric cyclohexyldicarboxylic acids **22**.

HPLC-ESIMS m/z 214 $[M-2H]^+$

^{13}C NMR (δ, ppm, acetone-d_6): 25.92, 26.70, 34.39, 35.56, 36.45, 36.96, 41.97 ($\underline{C}HCO_2H$), 68.32 (CH_2OH), 173.77 (C=O), 182.35 (C=O).

The treatment of this fraction with ether solution of diazomethane gave the corresponding dimethyl ester: ^1H NMR (δ, ppm, $CDCl_3$): 1.09-1.18 (m, 1H), 1.52-162 (m, 2H), 1.73-2.32 (m, 8H), 3.65-3.75 (m + s, 8H, CH_2OH + OMe);

^{13}C NMR (δ, ppm $CDCl_3$): 25.43, 25.73, 34.21, 34.87, 35.54, 36.30, 40.53, 51.60, 51.71, 67.95, 171.01, 172.88.

Among other products of the Bayer−Villiger oxidation of ketol **19** bicyclic keto acid **20** was isolated (21 mg, 8%).

HPLC-ESIMS m/z 181 $[M-H]^+$

^1H NMR (δ, ppm, $CDCl_3$): 1.72-1.93 (m, 6H), 2.36-2.38 (m, 4H), 2.52-2.58 (m, 3H), 9.90 (br s, 1H); ^{13}C NMR (δ, ppm $CDCl_3$): 26.32, 30.80, 31.93, 34.84, 46.80 ($\underline{C}HCO_2H$), 180.62 (CO_2H), 214.08 (C=O).

In one of the fractions obtained the minor product with molecular mass (HPLC-ESIMS m/z 197 $[M-H]^+$) was also detected, which corresponds to lactone **21**.

1-Benzyloxyadamantan-2-one was prepared by standard method from adamantane-1,4-diol (**19**) (0.25 g, 1.5 mmol), sodium hydride (60% in mineral oil 0.0.072 g, 1.5 mmol) and benzyl chloride (0.175 ml, 1.5 mmol) in solution of DMF. The reaction mixture was purified by column chromatography to yield 0.12 g (31%) of benzylated product.

^1H NMR (δ, ppm, $CDCl_3$): 1.71-1.80 (m, 2H), 1.84-1.92 (m, 4H), 1.96-2.0 (m, 2H), 2.15-2.21 (m, 4H), 2.52-2.56 (m, 2H), 2.64 (m, 1H, H^3), 4.62 (br s, 2H, CH_2Ph), 7.17 (m, 1H), 7.24 (m, 2H); 7.35 (d, 2H); ^{13}C NMR (δ, ppm $CDCl_3$): 21.60, 29.02, 29.70, 32.72, 38.62, 64.40, 73.39, 128.23, 128.56, 129.75, 137.19, 216.11 (C=O).

The Bayer−Villiger oxidation of 1-benzyloxyadamantan-2-one was carried out as analogous to the reaction for 1-hydroxyadamantan-2-one. The mixture of hardly separated products was resulted herein.