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Synthesis and Identification of Quercetin Benzyl Ethers

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Abstract—We have studied the effects of the benzylating agent character, the reactants ratio, and the solvent nature on the composition of the products of quercetin benzylation. The structure of the products has been confirmed by IR, UV, ^{1}H NMR, ^{13}C NMR, and mass spectra.

Keywords: quercetin, benzyl ether, synthesis, NMR spectroscopy

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Flavonoids form one of most numerous groups of naturally occurring polyphenols playing an important part in vital functions of higher plants. These compounds are among plant pigments, they protect the plant tissues from harmful UV radiation, participate in photosynthesis as well as in oxidation phosphorylation, and control the auxins (plant growth hormones) transport; plant flavonoids are known for different kinds of biological and pharmacological activities and the low toxicity [1, 2].

Several bioflavonoid drugs showing P-vitamin activity are industrially produced in Russia. The major flavonoid products are rutin and quercetin **I**, both used for treatment and prevention of different diseases resulting from brittleness and permeability failure of capillaries; these drugs are also used as antioxidants, hepato- and radioprotectors, antiinflammatory and antiulcer agents [3–5]. Flavonoids are also known for antitumor, antimicrobial, antiviral, and antithrombotic action [1, 6–10]. Quercetin and other flavonoids are potential inhibitors of nucleotide phosphodiesterases found in the cellular cytosol [11]. Recent studies have revealed quercetin activity towards HIV-1 reverse transcriptase and integrase along with inhibiting action on herpesvirus [12, 13].

The presence of several hydroxy groups, two aromatic rings, and a pyrone cycle in the quercetin molecule allows for its chemical modification to give a series of biologically active derivatives promising for medical applications. It has been shown that *O*-alkylation of the phenol hydroxyls of quercetin with excess of alkyl halides in DMSO in the presence of alkali yields the penta-*O*-substituted alkyl ethers, whereas the treatment with 3–5 equivalents of the alkyl halides gives the products of incomplete *O*-alkylation [14]. However, the studies involved exclusively UV spectroscopy characterization of the products.

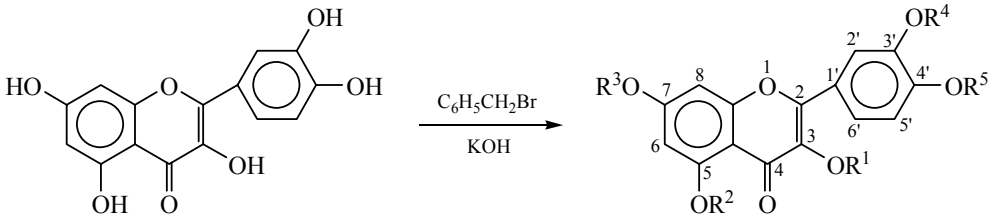
In this work we filled in the gap by preparation and identification of benzyl ethers of quercetin. These partially benzylated quercetin derivatives are suitable substrates for further chemical modifications, because the benzyl groups can be easily cleaved via the catalytic hydrogenolysis under mild conditions.

Quercetin was benzylated with benzyl bromide in the presence of powder KOH, using different ratios of the benzylating agent to the substrate. The products were isolated via column chromatography.

Benzylation of quercetin with excess of benzyl bromide in DMSO in the presence of KOH at 20–22°C during 4 h at the substrate to $C_6H_5CH_2Br$ ratio 1 : 10 yielded a mixture of quercetin penta-*O*-benzyl ether **II** and quercetin tetra-*O*-benzyl ether **III**. Ether **II** was isolated in 77.3% yield via recrystallization from the chloroform–ethanol mixture (Scheme 1).

Absorption bands due to vibrations of free phenol OH groups were not observed in IR spectrum of ether **II**, whereas strong bands assigned to stretching vibrations of C–C bonds in the aromatic rings were found at

Scheme 1.



I **II–VI**

II, $R^1 = R^2 = R^3 = R^4 = R^5 = C_6H_5CH_2$; **III**, $R^1 = R^3 = R^4 = R^5 = C_6H_5CH_2$, $R^2 = H$; **IV**, $R^1 = R^3 = R^5 = C_6H_5CH_2$, $R^2 = R^4 = H$; **V**, $R^1 = R^4 = = R^5 = C_6H_5CH_2$, $R^2 = R^3 = H$; **VI**, $R^1 = R^3 = R^5 = C_6H_5CH_2$, $R^2 = R^4 = Ac$; **VII**, $R^1 = R^4 = R^5 = C_6H_5CH_2$, $R^2 = R^3 = Ac$.

1630–1500 cm^{-1}, along with the C–O–C ether bonds stretching vibrations bands at 1270–1100 cm^{-1}. UV spectrum of ether **II** in ethanol contained strong absorption maxima at 253 and 347 nm. ^1H NMR spectrum of compound **II** contained the signals of five CH_2 groups of the benzyl fragments (at 4.98, 5.10, 5.14, 5.25, and 5.28 ppm) and those of the aromatic protons (6.98–7.70 ppm). ^{13}C NMR spectrum of the compound contained downfield signals of aromatic carbon atoms (126.6–128.8 and 135.7–137.0 ppm) and the signals of benzyl CH_2 groups (70.4–74.1 ppm), absent in the quercetin spectrum. The mass spectrum recorded in the chemical ionization mode contained the molecular ion signals, $[M + H]^+$ (m/z = 753) and $[M - H]^-$ (m/z = 751), corresponding with the $C_{50}H_{40}O_7$ formula.

The chromatographic separation of the mother liquor on silica gel allowed isolation of 22.7% of quercetin 3,3',4',7-tetra-*O*-benzyl ether **III**, its spatially hindered C^5OH group retained. ^1H NMR spectrum (500 MHz) of compound **III** contained the proton signals of four benzyl CH_2 groups (4.99, 5.05, 5.13, and 5.25 ppm). Signals of carbon atoms of those four CH_2 groups were observed in the ^{13}C NMR spectrum as well (70.4, 70.9, 71.2, and 74.3 ppm), along with the downfield signals of the aromatic carbon atoms (127.2–128.8 and 135.9–137.0 ppm). UV spectrum of compounds **III** in ethanol did not change upon addition of 0.01% of NaOEt and NaOAc evidencing the modification of the $C^{3'}OH$ and $C^{4'}OH$ groups [15]. The molecular ion peak observed in the mass spectrum of compound **III**, $[M + H]^+$ (m/z = 663), corresponded to the $C_{43}H_{34}O_7$ formula.

Benzylation of quercetin with benzyl chloride (1 : 10) in a mixture of DMSO and DMF yielded a mixture of benzyl ethers of the substrate that was further separated via the column chromatography. The major reaction product was the tetra-*O*-benzyl ether of quercetin **III** (R_f = 0.82, yield 17.5%).

The less mobile fraction (R_f = 0.75) was identified as 3,4',7-tri-*O*-benzyl quercetin ether **IV** (yield 7.6%). IR spectrum of compound **IV** contained the phenol OH stretching vibrations band (maximum at 3255 cm^{-1}). ^1H NMR spectrum of compound **IV** contained the signals of protons of the three CH_2 benzyl groups (5.03, 5.05, and 5.17 ppm), along with the signals of aromatic protons at 6.5–7.6 ppm. The ^{13}C NMR spectrum contained the signals of carbon atoms of the three benzyl CH_2 groups at 70.2, 70.9, and 74.0 ppm. Chemical shifts of the C^5 and $C^{3'}$ atoms in the spectra of ether **IV** were close to those in the parent quercetin [16].

In order to confirm the benzyl groups location, we recorded UV spectra of ethanol solutions of pure compound **IV** and of compound **IV** in the presence of 0.01% of sodium acetate. The UV spectrum remained almost unchanged in the presence of the weak base pointing at the benzylation of the $C^{4'}OH$ group in compound **IV** [15]. Indeed, the unmodified $C^{4'}OH$ group is more acidic than the $C^{3'}OH$ group, and the long-wavelength absorbance band should have been changed in the presence of the weak base if the $C^{4'}OH$ group was not benzylated [15]. Thus the isolated compound has the structure of 3,4',7-tri-*O*-benzyl ether **IV**. Acylation of the ether **IV** with acetic anhydride in the presence of anhydrous sodium acetate at reflux (see the procedure in [18]) yielded the di-*O*-acetate **VI** in 78% yield. ^1H NMR spectrum of the diacetate contained the signals of the two $COC\underline{H}_3$ groups at 2.29 and 2.52 ppm.

The more polar fraction found in the reaction mixture (R_f = 0.65) was identified as quercetin 3,3',4'-

tri-*O*-benzyl ether **V** (yield 6.9%). Indeed, UV spectra of compound **V** in ethanol and that in the presence of a weak base (C_2H_5OH + 0.01% of NaOAc) were practically identical, confirming the absence of the unmodified $C^{4'}OH$ group. The UV spectrum was not changed in the 0.01 wt % ethanol solution of $AlCl_3$ either; hence, the C^3OH group was modified as well [18]. In the case of compound **V** solution in a strong base (C_2H_5OH + 0.01% of $NaOC_2H_5$), a slight red shift of the first absorption band (by 21 nm) was observed; hence, the C^7OH group was not benzylated [15, 18]. Thus this compound is 3.3',4'-tri-*O*-benzyl ether of quercetin **V**. Acylation of ether **V** gave the di-*O*-acetate **VII** in 76% yield. ^1H NMR spectrum of the product (500 MHz) contained two singlet signals of the acetyl fragments at 2.35 and 2.50 ppm; the ^{13}C NMR signals of the C^5 and C^7 atoms of the product were shifted upfield by 9–10 ppm.

Similarly to the above, the benzylation of quercetin in DMSO at the ratio of the substrate to $C_6H_5CH_2Br$ of 1 : 5 at 20–22°C during 4 h gave a mixture of benzyl ethers with relatively low yields. Chromatographic separation of the mixture allowed isolation of the two major products: quercetin tetra-*O*-benzyl ether **III** (R_f = 0.82 and yield 18.2%) and the tri-*O*-benzyl ether **IV** (R_f = 0.75 and yield 20.9%).

At the similar ratio of the substrate to the benzylating agent, the benzylation of quercetin with benzyl chloride in DMF gave a mixture of benzyl ethers, the major product isolated by chromatography being the tri-*O*-benzyl ether **IV** (yield 17.5%).

To conclude, the benzylation of quercetin in DMSO or DMF in the presence of KOH at 20–22°C led to the formation of either fully or partially benzylated ethers, depending on the substrate to the benzylating agent ratio. The highest yield of the benzyl ethers was observed when using benzyl bromide as the benzylating agent and DMSO as the solvent.

With benzyl bromide taken in excess (1 : 10) and DMSO used as the solvent, a mixture of penta- and tetra-*O*-substituted quercetin benzyl ethers (**II** and **III**) was formed with total yield of 98.5%. At the same reagents ratio, benzylation of quercetin with benzyl chloride in the DMSO–DMF mixture yielded a mixture of the 3,3',4',7-tetra-, 3,4',7-tri-, and 3,3',4'-tri-*O*-benzyl ethers.

Finally, benzylation of quercetin with benzyl bromide taken in the 1 : 5 ratio with respect to the substrate yielded the following major products: the 3,3',4',7-tetra- and 3,4',7-tri-*O*-benzyl ethers (DMSO as solvent) or the 3,4',7-tri-*O*-benzyl ether (DMF as solvent).

EXPERIMENTAL

^1H and ^{13}C NMR spectra of the solutions in $CDCl_3$ were recorded using the Bruker Avance-III (500.13 MHz, ^1H) and Bruker AMX-300 (300 MHz, ^1H and 75.5 MHz, ^{13}C) spectrometers using tetramethylsilane as internal reference.

IR spectra of the suspensions in mineral oil were recorded using the IR Prestige-21 spectrometer (Shimadzu). UV spectra were registered using the UF-400 spectrophotometer (Carl Zeiss) (ethanol solution of the pure compounds, and the ethanol solutions in the presence of 0.01 wt % of 0.01% NaOAc, $NaOC_2H_5$, or $AlCl_3$).

Mass spectral analysis was performed by LC-MS technique using the Shimadzu LCMS-2010 chromato-mass spectrometer (chemical ionization of the solutions in methanol or acetonitrile at atmospheric pressure).

Melting points were measured using the Boëtius heating block.

Silica gel KSK (the 50–150 fraction, Sorbpolimer) was used for column chromatography separation. Thin-layer chromatography was performed using the Sorbfil plates (Sorbpolimer), 50 : 1 benzene–ethanol (A) and 20:1 benzene–ethanol (B) mixtures were used as eluents. The plates were developed with 5 wt % aqueous H_2SO_4 followed by heating at 110–120°C during 2–3 min.

The solvents were purified by common procedures [17]. Compendial quercetin (Ufavita) was used.

Quercetin benzylation with excess (1 : 10) of benzyl bromide in DMSO. 0.56 g (10 mmol) of KOH powder was added to 0.3 g (1 mmol) of quercetin in 10 mL of DMSO, and the mixture was stirred during 20 min. Then 1.2 mL (10 mmol) of $C_6H_5CH_2Br$ was added, and the mixture was stirred during 4 h at 20–22°C. The obtained solution was poured into water acidified with HCl to pH 2–3; the formed viscous red syrup was washed with water via decantation till neutral pH and dried (1.04 g). The recrystallization from the chloroform–ethanol mixture yielded 0.58 g (77.3%) of quercetin penta-*O*-benzyl ether **II**. The mother liquor was separated by chromatography (silica gel, elution with the 300 : 1 v/v benzene–methanol

mixture) to give 0.14 g (21.2%) of quercetin tetra-*O*-benzyl ether **III**.

Quercetin benzylation with excess (1 : 10) of benzyl chloride in DMSO–DMF mixture. 0.56 g (10 mmol) of KOH powder was added to 1.5 g (5 mmol) of quercetin in a mixture of 15 mL of DMSO and 35 mL of DMF, and the mixture was stirred during 30 min. Then, 6 mL (50 mmol) of $C_6H_5CH_2Cl$ was added, and the mixture was stirred during 4 h at 20–22°C; the reaction course was monitored with TLC. After the reaction was completed, the obtained solution was poured into water acidified with HCl to pH 2–3; the formed precipitate was filtered off and dried. The residue was separated via the column chromatography (silica gel; elution with 1 : 0, 300 : 1, 200 : 1, and 100 : 1 v/v benzene–methanol). The isolated products were tetra-*O*-benzyl ether **III** (0.58 g, 17.5%), tri-*O*-benzyl ether **IV** (0.22 g, 7.6%), and tri-*O*-benzyl ether **V** (0.20 g, 6.9%).

Quercetin 3,3',4',5,7-penta-*O*-benzyl ether (II). mp 115–118°C ($CHCl_3$–C_2H_5OH), R_f 0.90 (A). IR spectrum, ν, cm^{-1}: 1654, 1605, 1591, 1512, 1273, 1180, 1171, 1126. ^1H NMR spectrum (300 MHz), δ, ppm: 4.98 s, 5.10 s, 5.14 s, 5.25 s, 5.28 s (10H, CH_2); 6.47 s (1H, H^8), 6.54 s (1H, H^6), 6.98 d (1H, $H^{5'}$, *J* 9 Hz), 7.27 s (1H, $H^{6'}$), 7.30–7.70 m (25H, C_6H_5), 7.78 s (1H, $H^{2'}$). ^{13}C NMR spectrum (75.5 MHz), δ_C, ppm: 173.5 (C^4), 162.7 (C^7), 159.8 (C^5), 158.6 (C^9), 153.0 (C^2), 150.5 ($C^{4'}$), 148.3 ($C^{3'}$), 139.8 (C^3); 137.0–135.7, 128.8–126.6 (C_6H_5); 124.0 ($C^{1'}$), 122.5 ($C^{6'}$), 115.3 ($C^{5'}$), 113.8 ($C^{2'}$), 110.1 (C^{10}), 98.1 (C^6), 93.9 (C^8); 74.1, 72.1, 71.1, 70.9, 70.4 (CH_2). UV spectrum (C_2H_5OH), λ_{max}, nm (log ε): 253 (5.56), 347 (5.35). Mass spectrum: *m/z* 753 $[M + H]^+$, 751 $[M - H]^-$. Found, %: C 79.62; H 6.74. $C_{50}H_{40}O_7$. Calculated, %: C 79.77; H 6.71. *M* 752.9.

Quercetin 3,3',4',7-tetra-*O*-benzyl ether (III). mp 126–128°C ($CHCl_3$–C_2H_5OH), R_f 0.82 (A). IR spectrum, ν, cm^{-1}: 3292 (OH), 1670, 1589, 1277, 1253, 1196, 1169. ^1H NMR spectrum (500 MHz), δ, ppm: 4.99 s, 5.05 s, 5.13 s, 5.25 s (8H, CH_2); 6.44 d (1H, H^8, *J* 12 Hz), 6.98 d (1H, H^6, *J* 8 Hz), 7.24–7.57 m (22H, C_6H_5, $H^{6'}$, $H^{5'}$), 7.73 s (1H, $H^{2'}$). ^{13}C NMR spectrum (75.5 MHz), δ_C, ppm: 178.8 (C^4), 164.5 (C^7), 162.1 (C^5), 156.7 (C^9), 156.6 (C^2), 148.4 ($C^{4'}$), 148.3 ($C^{3'}$); 137.5 (C^3), 137.0–135.9, 128.8–127.2 (C_6H_5); 123.6 ($C^{1'}$), 122.7 ($C^{6'}$), 115.5 ($C^{5'}$), 113.9 ($C^{2'}$), 106.2 (C^{10}), 98.5 (C^6), 93.0 (C^8); 74.3, 71.2, 70.9, 70.4 (CH_2). UV spectrum (C_2H_5OH), λ_{max}, nm (log ε): 260 (5.47), 353 (5.22). Mass spectrum: *m/z* 663 $[M + H]^+$. Found, %: C 77.68; H 5.21. $C_{43}H_{34}O_7$. Calculated, %: C 77.93; H 5.17. *M* 662.7.

Quercetin 3,4',7-tri-*O*-benzyl ether (IV). mp 153–155°C ($CHCl_3$–C_2H_5OH), R_f 0.75–0.77 (A). IR spectrum, ν, cm^{-1}: 3256, 1650, 1600, 1508, 1278, 1252, 1194. ^1H NMR spectrum (300 MHz), δ, ppm: 5.03 s, 5.06 s, 5.17 s (6H, CH_2); 6.43 s (1H, H^8), 6.48 s (1H, H^6), 6.92 d (1H, $H^{5'}$, *J* 9 Hz), 7.24–7.60 m (16H, C_6H_5, $H^{6'}$), 7.63 s (1H, $H^{2'}$). ^{13}C NMR spectrum (75.5 MHz), δ_C, ppm: 178.6 (C^4), 164.3 (C^7), 161.7 (C^5), 156.5 (C^9), 156.3 (C^2), 147.8 ($C^{4'}$), 145.5 ($C^{3'}$), 137.5 (C^3); 136.8–135.6, 128.6–127.0 (C_6H_5); 123.3 ($C^{1'}$), 121.7 ($C^{6'}$), 114.8 ($C^{5'}$), 111.5 ($C^{2'}$), 106.0 (C^{10}), 98.5 (C^6), 92.8 (C^8); 74.0, 70.9, 70.2 (CH_2). UV spectrum (C_2H_5OH), λ_{max}, nm (log ε): ethanol, 258 (5.6), 356 (5.3); C_2H_5OH + 0.01% NaOAc, 258 (5.2), 356 (5.0). Mass spectrum: *m/z* 573 $[M + H]^+$. Found, %: C 75.41; H 4.89. $C_{36}H_{28}O_7$. Calculated, %: C 75.51; H 4.93. *M* 572.6

Quercetin 3,3',4'-tri-*O*-benzyl ether (V). R_f 0.65 (B). IR spectrum, ν, cm^{-1}: 3255 (OH), 1655, 1600, 1505, 1273, 1247, 1197. ^1H NMR spectrum (300 MHz), δ, ppm: 4.71 s, 4.78 s, 4.98 s (6H, CH_2); 6.05 s (1H, H^8), 6.12 s (1H, H^6), 6.75 d (1H, $H^{5'}$, *J* 7 Hz), 6.95–7.45 m (16 H, C_6H_5, $H^{6'}$), 7.48 s (1H, $H^{2'}$). ^{13}C NMR spectrum (75.5 MHz), δ_C, ppm: 178.3 (C^4), 164.2 (C^7), 161.7 (C^5), 156.6 (C^9), 155.5 (C^2), 150.8 ($C^{4'}$), 147.9 ($C^{3'}$), 136.9 (C^3); 136.6–136.3, 128.4–127.1 (C_6H_5); 123.2 ($C^{1'}$), 122.4 ($C^{6'}$), 114.9 ($C^{5'}$), 113.5 ($C^{2'}$), 104.7 (C^{10}), 98.9 (C^6), 93.8 (C^8); 73.9, 70.8, 70.5 (CH_2). UV spectrum, λ_{max}, nm (log ε): ethanol, 258 (5.5), 352 (5.3); C_2H_5OH + 0.01% $NaOCOCH_3$, 252 (5.5), 351 (5.3); C_2H_5OH + 0.01% $AlCl_3$, 258 (5.5); 351 (5.4); C_2H_5OH + 0.01% C_2H_5ONa, 279 (5.5). Mass spectrum: *m/z* 573 $[M + H]^+$. Found, %: C 75.42; H 4.89. $C_{36}H_{28}O_7$. Calculated, %: C 75.51; H 4.93. *M* 572.6.

3',5-Di-*O*-acetyl-3,4',7-tri-*O*-benzylquercetin (VI) [18]**.** 0.15 g of anhydrous sodium acetate was added to a solution of 0.15 g of compound **IV** in 10 mL of acetic anhydride. The mixture was refluxed during 2 h avoiding contact with air moisture. Then the mixture was diluted with cold water; the precipitate was filtered off, washed with water, dried, and recrystallized from the $CHCl_3$–CH_3OH mixture. Yield 78%, mp 158–160°C {mp 161–163°C (benzene–hexane) [15]}. IR spectrum, ν, cm^{-1}: 1772, 1720, 1665, 1605, 1273, 1196, 1163. ^1H NMR spectrum (300 MHz), δ,

ppm: 2.29 s, 2.52 s (6H, CH_3CO); 5.06 s, 5.14 s, 5.16 s (6H, CH_2); 6.69 s (1H, H^8), 6.88 s (1H, H^6), 6.98 d (1H, $H^{5'}$, *J* 8.3 Hz), 7.27–7.50 m (17H, C_6H_5, $H^{6'}$, $H^{2'}$). ^{13}C NMR spectrum (75.5 MHz), δ_C, ppm: 173.2 (C^4); 169.7, 168.8 (C=O); 162.4 (C^7), 157.7 (C^9), 153.8 (C^2), 152.0 (C^5), 150.6 ($C^{4'}$), 139.8 ($C^{3'}$), 139.5 (C^3); 136.4–135.4, 129.1–127.1 (C_6H_5); 123.3 ($C^{1'}$), 122.3 ($C^{6'}$), 113.2 ($C^{5'}$), 112.0 ($C^{2'}$), 108.8 (C^{10}), 99.5 (C^6); 74.2, 70.7, 70.5 (CH_2); 29.7, 20.6 (CH_3).

5,7-Di-*O*-acetyl-3,3',4'-tri-*O*-benzylquercetin (VII) was prepared similarly. Yield 76%, mp 196–198°C ($CHCl_3$–CH_3OH), R_f 0.86 (B). IR spectrum, ν, cm^{-1}: 1769, 1636, 1609, 1595, 1566, 1514, 1278, 1221, 1198, 1144. ^1H NMR spectrum (500 MHz), δ, ppm: 2.35 s, 2.50 s (6H, CH_3CO); 4.97 s, 5.00 s, 5.24 s (6H, CH_2); 6.82 s (1H, H^8), 6.93 d (1H, $H^{5'}$, *J* 8 Hz), 7.20–7.50 m (16H, C_6H_5, $H^{6'}$), 7.65 s (1H, $H^{2'}$). ^{13}C NMR spectrum (75.5 MHz), δ_C, ppm: 173.1 (C^4); 169.3, 167.9 (C=O); 156.5 (C^9), 155.1 (C^7), 153.5 (C^2), 151.0 (C^5), 150.2 ($C^{4'}$), 148.2 ($C^{3'}$), 139.6 (C^3); 136.9–136.5, 128.8–127.2 (C_6H_5); 123.3 ($C^{1'}$), 122.5 ($C^{6'}$), 115.4 ($C^{5'}$), 115.1 (C^6), 113.8 ($C^{2'}$), 113.0 (C^8), 108.7 (C^{10}); 74.0, 71.1, 70.9 (CH_2); 21.1, 21.0 (CH_3). Found, %: C 73.06; H 4.82. $C_{40}H_{32}O_9$. Calculated, %: C 73.16; H 4.91. *M* 656.7.

Quercetin benzylation with 1 : 5 of benzyl bromide. 0.28 g (5 mmol) of KOH powder was added to a solution of 0.3 g (1 mmol) of quercetin in 10 mL of DMSO. After 20 min, 0.6 mL (5 mmol) of $C_6H_5CH_2Br$ was added, and the mixture was stirred during 4 h at 20–22°C, the reaction course being monitored with TLC. After the reaction was complete, the so obtained solution was poured into HCl-acidified water (pH 2–3). The precipitate was filtered off, washed with water, and dried (0.47 g). After chromatographic separation, 0.12 g (18.2%) of compound **III** (R_f = 0.82) and 0.12 g (20.9%) of compound **IV** (R_f = 0.75) were isolated.

Quercetin benzylation with 1 : 5 of benzyl chloride. 0.28 g (5 mmol) of KOH powder was added to a solution of 0.3 g (1 mmol) of quercetin in 10 mL of DMF. After 20 min, 0.6 mL (5 mmol) of $C_6H_5CH_2Cl$ was added, and the mixture was stirred during 4 h at 20–22°C, the reaction course being monitored with TLC. After the reaction was complete, the so obtained solution was poured into HCl-acidified water (pH 2–3). The precipitate was filtered off, washed with water, and dried (0.38 g). After chromatographic separation, 0.10 g (17.5%) of compound **IV** was isolated.

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