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XANTHONES FROM *Halenia corniculata*. SYNTHESIS AND CHOLAGOGIC ACTION OF CERTAIN DERIVATIVES

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Xanthones containing acetoxy, allyloxy, and aminohydroxyalkyloxy substituents at the C-1 position that are of interest as potential biologically active agents were prepared. The cholegogic action of 1-hydroxy-, 1-acetoxy-, and 1-allyloxy-substituted xanthones was investigated.

Key words: xanthones, alkylation, acetylation, epichlorohydrin, aminolysis, cholagogic action.

Halenia corniculata (L.) Cornaz (Gentianaceae) is an annual plant that grows in wet and swampy habitats in Russia, Mongolia, and Manchuria [1, 2]. Significant populations of *H. corniculata* are concentrated east of Lake Baikal.

The aerial part of this plant is used in Tibetan medicine as a replacement for "ser-tig" for treatment of "bile fever and infection" [3]. Decoction and tincture of *H. corniculata* in vodka are recommended in Siberian folk medicine as an appetite stimulant and digestion regulator and are indicated for gastritis, intestinal and stomach pain, liver diseases, colitis, and enterocolitis [4]. The herb is widely used in traditional medicine in East-Asian countries for liver diseases (hepatitis and cholecystitis) [5]. A polyphenol complex from *H. corniculata* possesses antioxidant and hepatoprotective action [6].

Research on the chemical composition of plants of the *Halenia* genus showed that they are sources of xanthone aglycons and their glycosides [7-9].

We previously described a rational method for isolating 1-hydroxy-2,3,5-trimethoxy- (**1**) and 1-hydroxy-2,3,4,5-tetramethoxyxanthones (**2**) from the aerial part of *H. corniculata* [10]. In the present article, we report the preparation of derivatives of these xanthones that contain various substituents at the C-1 position.

Acetylation of **1** and **2** under standard conditions (pyridine—Ac_2O) formed acetates **3** and **4** in yields of 88.6 and 90.4%, respectively.

Alkylation of **1** and **2** by allylbromide in acetone in the presence of K_2CO_3 [11] produced 1-allyloxy-2,3,5-trimethoxyxanthone (**5**, 95.5%) and 1-allyloxy-2,3,4,5-tetramethoxyxanthone (**6**, 92.8%).

It was previously found that aromatic compounds in which the hydroxyl is esterified by 3-aminopropan-1,2-diol exhibit β-adrenoblocking properties with antihypotensive and antiarhythmic action. Aryl- and hetaryloxypropanolamines were prepared and studied [12]. We alkylated **1** and **2** with (chloromethyl)oxirane to synthesize analogs of this type of preparation, athenolol and anaprilin [13]. We found that **1** and **2** react with epichlorohydrin on brief heating in the presence of an interphase catalyst (0.1 eq) [14]. The reaction produces a mixture of diastereomeric epoxides (*S*)-**7a**,**8a** and (*R*)-**7b**,**8b** in overall yield 67-69% with predominance (2:1) of the (*S*)-diastereomers **7a**,**8a**. Aminolysis of **7a**,**b** with benzylamine by the literature method [15] gives pure 1-(3-benzylamino-2-hydroxy)-propoxy-2,3,5-trimethoxyxanthone (**9**).

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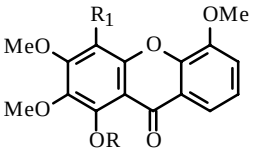
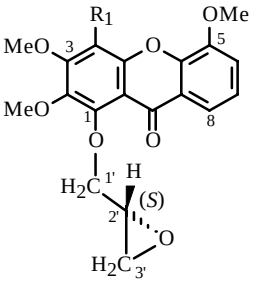


1 - 6

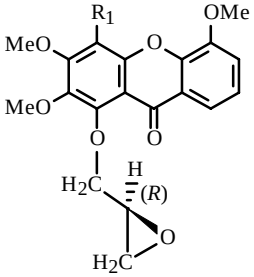
1: R = R_1 = H
2: R = H, R_1 = OMe
3: R = Ac, R_1 = H
4: R = Ac, R_1 = OMe
5: R = All, R_1 = H
6: R = All, R_1 = OMe

1, 2 →



7a, 8a

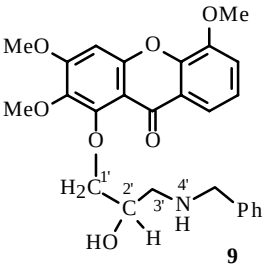
+



7b, 8b

R_1 = H (**7**), OMe (**8**)

7a, b →



9

The oxirane ring can theoretically be opened by the action of the amines in two ways: according to the Krasusky rule for the α-C atom of the three-membered ring and in violation of the rule with formation of the isomeric reaction product. Oligomerization is also possible [16]. It is known [17] that a substituent with a negative inductive effect on the oxirane ring causes the reaction between a nucleophilic reagent and the α-oxide to give only the product with the normal structure. Our results confirmed this. The heterocycle opens exclusively according to the Krasusky rule to form a single isomeric reaction product.

Spectral data established the structures of the prepared compounds. NMR spectra indicated that mixtures of diasteromeric epoxides **7a**,**b** and **8a**,**b** formed. Thus, the PMR spectrum of **7a**,**b** contains a set of 1H multiplets for H-1′ and H-2′ with centers at 3.55, 4.16, and 4.30 ppm for the 2′-(*S*)-diastereomer and 3.73, 4.33, and 4.56 ppm for the 2′-(*R*)-diastereomer. The ratio of diastereomers in the reaction products was determined from the ratio of the integrated intensities of the signals for these protons. The ^{13}C NMR spectrum exhibits doubled signals for C atoms of the xanthone core. The largest differences ($\Delta\delta$ > 1.0 ppm) occur for C-9 (δ 176.25, 174.99 ppm) and C-8a (δ 110.46, 109.20 ppm) (for **7a**,**b**).

The PMR spectrum of the pure product from opening of the epoxide ring of **9** shows signals from benzene protons. The C-1′ protons are magnetically unequivalent and located at 4.51 ppm (dd, J = 4.8 Hz, J = 1.2 Hz) and 4.14 (dd, J = 4.8 Hz, J = 8.6 Hz). The C-2′ proton resonates as a multiplet at 4.17 ppm. Protons of the C-3′ and C-4′ CH_2-groups are narrow multiplets at 2.88 and 3.90 ppm, respectively.

Natural xanthones and their synthetic derivatives have a wide spectrum of pharmacologic action: antidepressants, anti-inflammatories, antimicrobials, cardiotonics, diuretics, antivirals, cholegogics, and psychotropics. Stimulatory action of amino-substituted xanthone derivatives on the CNS was also found in addition to antituberculosis, anti-ulcer, and antitumor activities [18, 19]. We investigated the cholagogic action of **1**-**6** upon administration at doses of 10 and 50 mg/kg in white rats. The degree of cholagogic activity was determined from the increased rate of bile secretion, the total amount of bile isolated during 2-4 h, concentration of bile acids, and the amount of cholesterol and bilirubin isolated in each timed portion.

The results showed that natural xanthones **1** and **2** and their derivatives **3**-**6** have cholagogic activity that is more evident at a dose of 50 mg/kg. Compound **5** has the greatest cholagogic acivity. Thus, single administration at a dose of 50 mg/kg increased the rate of bile secretion over that in control rats by 47, 37, and 18% (for 2, 3, and 4 h, respectively).

However, administration of **1** increased the rate of bile secretion by 30, 16, and 12%, respectively. Administration of **6** to rats at a dose of 50 mg/kg also stimulated a choleretic reaction. The rate of bile secretion increased by 39, 37, and 41% (for 2, 3, and 4 h, respectively); for rats given **2**, by 42, 26, and 32%, respectively. Acetyl-substituted derivatives had poorer cholagogic activity than allyl derivatives. However, administration of **3** increased cholesterol secretion. Administration of **4** facilitated primarily secretion of bile acids.

Thus, acetylation, allylation, and alkylation of natural xanthones was achieved. The newly synthesized xanthone derivatives had distinct cholagogic activity.

EXPERIMENTAL

Freshly distilled solvents and pure reagents were used. Melting points were determined on a Kofler micro-heating stage. Elemental analyses were obtained on a CHN-analyzer (1106 Model, Carlo Erba). IR spectra were recorded on a Vector 22 spectrometer in KBr disks; UV absorption spectra, on an HP 8453 UV—Vis spectrometer in ethanol ($C = 10^{-4}$ M). Moleclar weights and elemental compositions were determined using a high-resolution mass spectrometer (Finnigan MAT 8200). NMR spectra were obtained on a Bruker AC 200 spectrometer (working frequency 200.13 MHz for ^{1}H; 50.32 MHz for ^{13}C) in $CDCl_3$. Signals in PMR spectra of **7-9** were assigned using COSY H—H correlation spectroscopy. Multiplicities of signals in ^{13}C NMR spectra were established using standard methods for recording spectra with J-modulation (JMOD). Xanthones were separated by chromatography over a silica-gel column (L 100/400) with elution by a hexane:ethylacetate mixture (7:3). The separation of compounds and the course of reactions were monitored using TLC on Silufol plates and the same solvent system. The purities of **1** and **2** were determined by HPLC using a Milichrom A-02 liquid chromatography microcolumn [20]. The chromatography conditions were: column 2×75 mm, ProntoSIL-120-5-C-18 AQ sorbent (number 0322, 5 μm), 35°C temperature, 3.2 MPa pressure, 150 μL/min elution rate, UV detection at 244, 260, and 320 nm. The eluent was 0.1% TFA in MeOH.

The aerial part of *H. corniculata* was collected in August 2001 during flowering in Kabansk and Ivolginsk regions (Republic of Buryatia).

Isolation of 1 and 2 from Plant Material. The air-dried and ground aerial part of *H. corniculata* was extracted five times with ethanol (70%) at a 1:12 material:solvent ratio (18-20°C, 72 h). The combined extracts were concentrated in vacuum to an aqueous residue (0.5 L) that was treated successively in a separatory funnel with $CHCl_3$ (25×200 mL) and ethylacetate (25×300 mL).

The $CHCl_3$ extract was concentrated to dryness in a rotary evaporator to afford dry extract (99.8 g, 6.6%). According to HPLC, the principal components were xanthones **1** and **2** and 1-hydroxy-2,3,7-trimethoxyxanthone [7] (1:2:1 ratio). Xanthones were isolated by column chromatography and recrystallization of the fractions from ethanol to give **1** (1.24 g, 0.24%) and **2** (0.65 g, 0.12%) of 96.87 and 95.22% purity.

The ethylacetate extract (53.1 g) contained according to HPLC less than 1-3% of xanthones **1** and **2**. Column chromatography of the ethylacetate extract isolated luteolin (1.6% yield of the air-dried material mass).

1-Acetoxy-2,3,5-trimethoxyxanthone (3). Xanthone **1** (0.25 g) was refluxed in acetic anhydride (2 mL) with pyridine (one drop) for 10 h. The reaction mixture was cooled and treated with distilled water (3 mL). The resulting precipitate was filtered off, washed with ether, and recrystallized from ethylacetate to afford **3** (0.24 g, 88.6%), mp 168-169°C.

IR spectrum (ν, cm^{-1}): 721, 752, 791, 988 (Ar); 1567, 1595, 1610, 1622 (C=C); 1650, 1760 (C=O). UV spectrum (λ_{max}, nm, log ε): 222 (4.09), 248 (4.75), 267 (4.21), 300 (3.45), 343 (3.24). PMR spectrum ($CDCl_3$, δ, ppm, J/Hz): 2.51 (3H, s, $C\underline{H}_3CO$), 3.84 (3H, s, $OC\underline{H}_3$), 3.96 (3H, s, $OC\underline{H}_3$), 3.98 (3H, s, $OC\underline{H}_3$), 6.95 (1H, s, H-4), 7.20 (2H, m, H-6, H-7), 7.77 (1H, dd, J = 7.5, J = 1.5, H-8).

^{13}C NMR spectrum (δ_C, ppm): 20.90 (CH_3), 56.29 (OCH_3), 56.33 (OCH_3), 61.37 (OCH_3), 98.26 (C-4), 109.08 (C-8a), 114.78 (C-6), 117.25 (C-7), 122.79 (C-10a), 123.32 (C-8), 138.80 (C-4a), 142.69 (C-3), 145.53 (C-9a), 148.05 (C-5), 153.82 (C-2), 158.53 (C-1), 169.27 (C=O), 174.79 (C-9).

Mass spectrum (*m*/*z*, %): 344 (6.83), 302 (100), 287 (92.95), 273 (17.26), 259 (40.72), 216 (13.48), 151 (13.14), 93 (17.84), 43 (20.62), 28 (25.34). $C_{18}H_{16}O_7$. Calc. *m*/*z*, 344.08959; exp. *m*/*z*, 344.08804.

This method produced 2,3,4,5-tetramethoxyxanthone **(4)**, 90.4% yield, mp 139-141°C.

IR spectrum (ν, cm^{-1}): 736, 752, 877, 985, 1500, 1596 (C=C); 1654, 1771 (C=O). UV spectrum (λ_{max}, nm, log ε): 240 (4.18), 252 (4.56), 289 (4.08), 355 (3.62).

PMR spectrum ($CDCl_3$, δ, ppm, J/Hz): 2.49 (3H, s, C$\underline{H}_3$CO), 3.86 (3H, s, OC$\underline{H}_3$), 3.99 (3H, s, OC$\underline{H}_3$), 4.10 (3H, s, OC$\underline{H}_3$), 4.12 (3H, s, OC$\underline{H}_3$), 7.17 (1H, dd, J = 7.8, J = 1.5, H-6), 7.23 (1H, dd, J = 7.8, J = 7.5, H-7), 7.77 (1H, dd, J = 7.5, J = 1.5, H-8).

^{13}C NMR spectrum (δ_C, ppm): 20.82 (CH_3), 56.35 (OCH_3), 61.47 (OCH_3), 61.66 (OCH_3), 61.72 (OCH_3), 95.76 (C-4), 106.05 (C-8a), 115.16 (C-6), 117.04 (C-7), 122.50 (C-10a), 123.46 (C-8), 138.00 (C-4a), 139.34 (C-3), 142.05 (C-9a), 145.51 (C-5), 147.40 (C-2), 151.89 (C-1), 169.49 (C=O), 175.11 (C-9).

Mass spectrum (*m*/*z*, %): 374 (5.17), 362 (25.39), 347 (27.95), 332 (93), 317 (100), 43 (19.57). $C_{19}H_{18}O_8$. Calc. *m*/*z*, 374.10016; exp. *m*/*z*, 374.09640.

1-Allyloxy-2,3,5-trimethoxyxanthone (5). A mixture of xanthone **1** (0.5 g), allylbromide (1 mL), and K_2CO_3 (2.5 g) was refluxed in dry acetone (65 mL) for 12 h. The salt was filtered off and washed with acetone. The combined mother liquors were evaporated. The solid was crystallized from ethanol and filtered off after cooling to give **5** (0.54 g, 95.5%), mp 154-156°C.

IR spectrum (ν, cm^{-1}): 735, 790, 993 (Ar); 1567, 1604, 1619 (C=C); 1655 (C=O). UV spectrum (λ_{max}, nm, log ε): 222 (4.12), 249 (4.44), 270 sh (3.69), 285 (4.32), 344 (3.68).

PMR spectrum ($CDCl_3$, δ, ppm, J/Hz): 3.87 (3H, s, OC$\underline{H}_3$), 3.94 (3H, s, OC$\underline{H}_3$), 4.09 (3H, s, OC$\underline{H}_3$), 4.66 (2H, m, C$\underline{H}_2$), 5.22 (1H, m, CH_2=), 5.40 (1H, m, CH_2=), 6.15-6.34 (1H, m, CH=), 6.38 (1H, s, H-4), 7.13 (1H, dd, J = 7.5, J = 1.8, H-6), 7.22 (1H, t, J = 7.5, H-7), 7.83 (1H, dd, J = 7.5, J = 1.8, H-8).

^{13}C NMR spectrum (δ_C, ppm): 56.22 (OCH_3), 56.27 (OCH_3), 61.29 (OCH_3), 75.47 (CH_2), 96.36 (C-4), 110.85 (C-8a), 114.37 (C-6), 117.47 (C-7), 117.76 (CH_2=), 123.11 (C-8), 123.21 (C-10a), 134.18 (CH=), 139.76 (C-4a), 145.29 (C-9a), 147.91 (C-5), 151.86 (C-3), 154.15 (C-2), 158.45 (C-1), 175.06 (C-9).

Mass spectrum (*m*/*z*, %): 342 (16.79), 327 (100), 311 (22.78), 299 (44.55), 285 (29.25), 122 (14.41), 107 (12.22), 93 (46.93), 77 (17.45), 41 (41.60), 28 (37.31). $C_{19}H_{18}O_6$. Calc. *m*/*z*, 342.11033; exp. *m*/*z*, 342.10978.

This method produced from **2** (0.5 g) 1-allyloxy-2,3,4,5-tetramethoxyxanthone **(6)** (0.56 g, 92.8%), mp 118-120°C.

IR spectrum (ν, cm^{-1}): 723, 747, 780, 895, 927, 986, 1500, 1586, 1600 (C=C); 1658 (C=O). UV spectrum (λ_{max}, nm, log ε): 240 (4.12), 253 (4.35), 293 (3.83), 356 (3.36).

PMR spectrum ($CDCl_3$, δ, ppm, J/Hz): 3.91 (3H, s, OC$\underline{H}_3$), 4.00 (3H, s, OC$\underline{H}_3$), 4.06 (3H, s, OC$\underline{H}_3$), 4.10 (3H, s, OC$\underline{H}_3$), 4.62 (2H, d, J = 6.0, C$\underline{H}_2$), 5.23 (1H, m, CH_2=), 5.42 (1H, m, CH_2=), 6.15-6.33 (1H, m, CH=), 7.17 (1H, dd, J = 7.8, J = 1.5, H-6), 7.23 (1H, t, J = 7.8, H-7), 7.84 (1H, dd, J = 7.8, J = 1.5, H-8).

^{13}C NMR spectrum (δ_C, ppm): 56.34 (OCH_3), 61.46 (OCH_3), 61.66 (OCH_3), 61.57 (OCH_3), 96.06 (C-4), 75.52 (CH_2), 105.68 (C-8a), 114.84 (C-6), 117.29 (C-7), 117.61 (CH_2=), 123.97 (C-10a), 123.21 (C-8), 134.23 (CH=), 137.61 (C-4a), 147.54 (C-9a), 148.44 (C-5), 149.48 (C-3), 151.97 (C-2), 155.79 (C-1), 175.37 (C-9).

Mass spectrum (*m*/*z*, %): 372 (36.38), 357 (100), 343 (19.60), 331 (63.26), 329 (17.01), 303 (37.11), 275 (15.49), 273 (17.99), 260 (12.74), 245 (34.25), 41 (16.46). $C_{20}H_{20}O_7$. Calc. *m*/*z*, 372.12089; exp. *m*/*z*, 372.11934.

(2*S*)- and (2*R*)-1-(2,3-Epoxypropoxy)-2,3,5-trimethoxyxanthones (7a,b). A mixture of **1** (0.2 g) and epichlorohydrin (1 mL) was boiled with benzyltrimethylammonium chloride (0.02 g) for 1 h. The reaction mixture was cooled, treated with distilled water (1 mL), vigorously shaken, and treated with methylenechloride (5 mL). The organic layer was separated. The aqueous layer was extracted with methylenechloride (3×5 mL). The combined organic extracts were washed with distilled water and dried over $MgSO_4$. The solvent was removed in a rotary evaporator. The solid was dissolved in ether. Crystals formed upon cooling and were filtered off to afford a mixture of epoxides **7a**,**b** (0.16 g, 67.5%, 2:1 ratio), mp 147-149°C.

PMR spectrum ($CDCl_3$, δ, ppm, J/Hz): 2.72 (1H, m, J_{gem} = 10.3, H-3), 2.85 (1H, m, J_{gem} = 10.3, H-3), 3.55 (1H, m, H-2′ for **7a**), 3.73 (1H, m, H-2′ for **7b**), 3.86, 3.96, 3.99 (three s, 3H each, OC$\underline{H}_3$ for **7b**), 3.90, 3.95, 3.99 (three s, 3H each, OC$\underline{H}_3$ for **7a**), 4.16 and 4.30 (2H, m, H-1′ for **7a**), 4.33 and 4.56 (2H, m, H-1′ for **7b**), 6.85 (1H, s, H-4), 7.22 (2H, m, H-6, H-7), 7.88 (1H, dd, J = 7.8, J = 1.8, H-8).

^{13}C NMR spectrum (δ_C, ppm): for (*S*)-**7**: 44.51 (C-3′), 50.39 (C-2′), 56.20 (OCH_3), 56.27 (OCH_3), 61.33 (OCH_3), 75.49 (C-1′), 96.59 (C-4), 110.46 (C-8a), 114.41 (C-6), 117.28 (C-7), 123.06 (C-10a), 123.13 (C-8), 139.64 (C-4a), 145.25 (C-9a), 147.90 (C5), 151.66 (C-3), 154.09 (C-2), 158.47 (C-1), 174.99 (C-9); for (*R*)-**7**: 43.83 (C-3′), 50.39 (C-2′), 56.27 (OCH_3), 60.91 (OCH_3), 61.33 (OCH_3), 75.44 (C-1'), 96.24 (C-4), 109.20 (C-8a), 114.72 (C-6), 117.51 (C-7), 122.76 (C-10a), 123.30 (C-8), 138.94 (C-4a), 145.25 (C-9a), 147.80 (C-5), 152.20 (C-3), 154.28 (C-2), 158.93 (C-1), 176.25 (C-9).

The above method produced from **2** (0.35 g) 1-(2,3-epoxypropoxy)-2,3,4,5-tetramethoxyxanthone **(8a**,**b)** (0.28 g, 68.5%), mp 101-103°C.

IR spectrum (ν, cm^{-1}): 747, 911, 1500, 1592, 1610 (C=C); 856, 989, 1057, 1096, 1275 (C–O–C); 1657 (C=O). UV spectrum (λ_{max}, nm, log ε): 245 sh (4.06), 254 (4.18), 292 (3.75), 357 (3.82).

PMR spectrum ($CDCl_3$, δ, ppm, J/Hz): 2.73 (1H, m, J_{gem} = 10.5, H-3), 2.87 (1H, m, J_{gem} = 10.5, H-3), 3.55 (1H, m, H-2′ for **8a**), 3.73 (1H, m, H-2′ for **8b**), 3.89, 3.94, 4.04, 4.11 (four s, 3H each, $OC\underline{H}_3$ for **8b**), 3.92, 3.98, 4.05, 4.09 (four s, 3H each, $OC\underline{H}_3$ for **8a**), 4.10 and 4.28 (2H, m, H-1′ for **8a**), 4.30 and 4.50 (2H, m, H-1′ for **8b**), 7.20 (2H, m, H-6, H-7), 7.80 (1H, dd, J = 7.8, J = 1.8, H-8).

^{13}C NMR spectrum (δ_C, ppm): for (*S*)-**8**: 44.52 (C-3′), 50.45 (C-2′), 56.34 (OCH_3), 61.54 (OCH_3), 61.74 (OCH_3), 75.66 (C-1′), 96.65 (C-4), 112.43 (C-8a), 114.86 (C-6), 117.39 (C-7), 122.87 (C-10a), 123.34 (C-8), 137.85 (C-4a), 143.09 (C-9a), 145.37 (C-5), 147.39 (C-3), 148.47 (C-2), 152.04 (C-1), 175.47 (C-9); for (*R*)-**8**: 43.85 (C-3′), 50.45 (C-2′), 55.69 (OCH_3), 61.36 (OCH_3), 61.74 (OCH_3), 75.66 (C-1′), 95.86 (C-4), 111.98 (C-8a), 115.16 (C-6), 117.43 (C-7), 122.59 (C-10a), 123.53 (C-8), 137.85 (C-4a), 143.09 (C-9a), 145.37 (C-5), 147.48 (C-3), 147.96 (C-2), 151.64 (C-1), 175.07 (C-9).

Mass spectrum (*m*/*z*, %): 388 (31), 371 (43), 347 (31), 341 (22), 332 (55), 327 (20), 317 (100), 287 (13), 259 (14), 245 (19). $C_{20}H_{20}O_8$. Calc. *m*/*z*, 388.11580; exp. *m*/*z*, 388.11527.

1-(3-Benzylamino-2-hydroxy)-proproxy-2,3,5-trimethoxyxanthone (9). A solution of epoxides **7a**,**b** (0.14 g) in THF (1 mL) and benzylamine (1 mL) was refluxed for 6 h, cooled, treated with water:ethylacetate:acetic acid (2:1:0.2) with vigorous shaking, and neutralized to pH 7 with dilute acetic acid. The organic layer was removed. The aqueous layer was made basic (pH 9) with ammonia and extracted with methylenechloride (5×3 mL). The combined extracts were concentrated in a rotary evaporator. The solid was recrystallized from ethylacetate, cooled, and filtered off to afford **9** (0.06 g, 33.33%), mp 116-118°C.

IR spectrum (ν, cm^{-1}): 701, 752, 792, 898, 981, 1500, 1599, 1635 (C=C); 1097 (C–O–C); 1660 (C=O); 1563, 1635, 3200, 3320 (C–NH–C); 3441, 3538 (OH). UV spectrum (λ_{max}, nm, log ε): 225 sh (4.16), 250 (4.81), 289 (4.04), 346 (3.64).

PMR spectrum ($CDCl_3$, δ, ppm, J/Hz): 2.88 (2H, m, H-3′), 3.85 (3H, s, $OC\underline{H}_3$), 3.90 (2H, m, CH_2Ph), 3.94 (2H, m, NH, OH), 3.95 (3H, s, $OC\underline{H}_3$), 4.01 (3H, s, $OC\underline{H}_3$), 4.14 (1H, dd, J = 4.8, J = 8.6, H-1′), 4.17 (1H, m, H-2′), 4.51 (1H, dd, J = 4.8, J = 1.2, H-1′), 6.85 (1H, s, H-4), 7.17-7.40 (7H, m, H-6, H-7 and Ph), 7.83 (1H, dd, J = 7.8, J = 1.8, H-8).

^{13}C NMR spectrum (δ_C, ppm): 51.07 (C-5′), 53.65 (C-3′), 56.31 (OCH_3), 56.31 (OCH_3), 61.04 (OCH_3), 68.66 (C-2′), 77.91 (C-1′), 96.24 (C-4), 109.83 (C-8a), 114.83 (C-6), 117.68 (C-7), 122.95 (C-10a), 123.32 (C-8), 126.99 (CH, C-4′), 128.27 (CH, C-5′,6′), 128.31 (CH, C-2′,3′), 139.09 (CH, C-1′), 139.14 (C-4a), 145.41 (C-9a), 147.93 (C-5), 152.34 (C-3), 154.39 (C-2), 158.99 (C-1), 176.28 (C-9).

Mass spectrum (*m*/*z*, %): 345 (30.44) $[M - PhCH_2NCH_2]^+$, 303 (37.09), 302 (100), 287 (63.67), 259 (18.50), 91 (53.93). Found, %: C 64.51, H 5.81, N 3.12. $C_{26}H_{27}O_8H$. Calc., %: C 64.86, H 5.61, N 2.91.

Biological Activity. The cholagogic activity was determined in experiments on Wistar white rats of both sexes and mass 180-200 g. Bile was obtained by acute experiments using the common method [21]. Xanthones were administrated once to animals anesthetized with hexenal at doses of 10 and 50 mg/kg as an aqueous solution to the duodenum. Control rats received purified water of an equivalent volume. The degree of cholagogic activity was estimated from the increase in the excretion rate and the total amount of excreted bile and from the content in it of the principal ingredients: bile acids, cholesterol [22], and bilirubin [23]. Results were treated statistically using the Student criteria.

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