ISSN 1070-4280, Russian Journal of Organic Chemistry, 2011, Vol. 47, No. 2, pp. 239–244. © Pleiades Publishing, Ltd., 2011.
Original Russian Text © Yu.V. Shklyaev, A.A. Smolyak, A.A. Gorbunov, 2011, published in Zhurnal Organicheskoi Khimii, 2011, Vol. 47, No. 2, pp. 247–252.

Eugenol and Its Methyl Ether in the Synthesis of 3-Methyl Derivatives of 3,4-Dihydroisoquinoline

Yu. V. Shklyaev, A. A. Smolyak, and A. A. Gorbunov

Institute of Engineering Chemistry, Ural Division, Russian Academy of Sciences
Perm', 614013 Russia; e-mail: yushka@newmail.ru

Received June 1, 2010

Abstract—3-Methyl derivatives of 1-substituted 3,4-dihydroisoquinoline were obtained proceeding from eugenol and its methyl ether. The propylene oxide in a three-component reaction with veratrol and ethyl cycnoacetate provided the reaction products in a low yield. The isoeugenol in a linear synthesis also gives a low yield of the target compounds.

DOI: 10.1134/S1070428011020138

Quite a number of studies deals with the syntheses of 3-substituted 3,4-dihydroisoquinoline since the latter and the easily obtained therefrom 1,2,3,4-tetrahydro derivatives exhibit a wide range of the biological action. 1,3-Dimethyl-3,4-dihydroisoquinoline induces the Parkinson's syndrome [1], 7-substituted 1,3-dimethyl-1,2,3,4-tetrahydroisoquinolines are inhibitors of the phenylethanolamine-N-methyltransferase [2], 7-hydroxy-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid is the inhibitor of NS3 protease of hepatitis C virus [3].

The majority of the preparation methods of 3-methyl derivatives of 3,4-dihydroisoquinoline is underlain by the reaction of Bischler–Napieralski. N-(2-Chlorobenzoyl) amphetamide undergoes the cyclization into 3-methyl-1-(2-chlorophenyl)-3,4-dihydroisoquinoline at heating in the presence of $POCl_3$ in 37% yield [4], and 1-phenyl-3,4-dihydroisoquinoline forms in 13% yield [5]. A series of 1-hetaryl-substituted 3-methyl-3,4-dihydroisoquinolines was obtained by heating the eugenol methyl ether with hetarylamides or hetarylaldoximes in $POCl_3$ in 16–35% yields [6]. (*S*)-3-Methyl-3,4-dihydroisoquinoline was prepared from the corresponding N-phenethylformamide in polyphosphoric acid in 65% yield [7]. The application of Ritter reaction to the preparation of 3-methyl derivatives of this class compounds would extend the range of reqagents involved and make it possible to obtain compounds close in the structure to the naturally occurring substances. The use of the butyric aldehyde in the three-component synthesis of 3,4-dihydroisoquinoline derivatives resulted only in the preparation of the corresponding 9,10-diethylanthracene [8], whereas the eugenol methyl ether reacted with veratronitrile in sulfuric acid to give 1-arylsubstituted 3-methyl-6,7-dimethoxy-3,4-dihydroisoquinoline [9], but a plausible yield (53%) was obtained only with 3,4-dimethoxybenzonitrile whereas with the anisonitrile the yield of isoquinoline was only 15%, and with 3,4-diethoxybenzonitrile, less than 1%. The reaction of safrole with 3,4,5-trimethoxybenzonitrile in 48% HBF_4 gave the corresponding 3,4-dihydroisoquinoline in 17% yield whereas in the sulfuric acid only tar was obtained [10]. Inasmuch as the carbocation character arising in the protonation of both safrole and eugenol methyl ether should be the same at the use of the propylene oxide we used in the first stage of the research two procedures: *a*, a three-component synthesis from veratrol, propylene oxide, and nitriles, and *b*, from the methyl ether of eugenol and nitriles.

The reaction of veratrol, propylene oxide, and ethyl cycnoacetate brought simultaneously into concn. sulfuric acid led to the formation in a low yield of ethyl (2*Z*)-6,7-dimethoxy-3-methyl-3,4-dihydroisoquinolin-1(2*H*)-ylideneacetate (**I**), and as a side product formed di(3,4-dimethoxyphenyl)propane. At the use of the eugenol methyl ether and ethyl cycnoacetate compound **I** was obtained in 22% yield (Scheme 1).

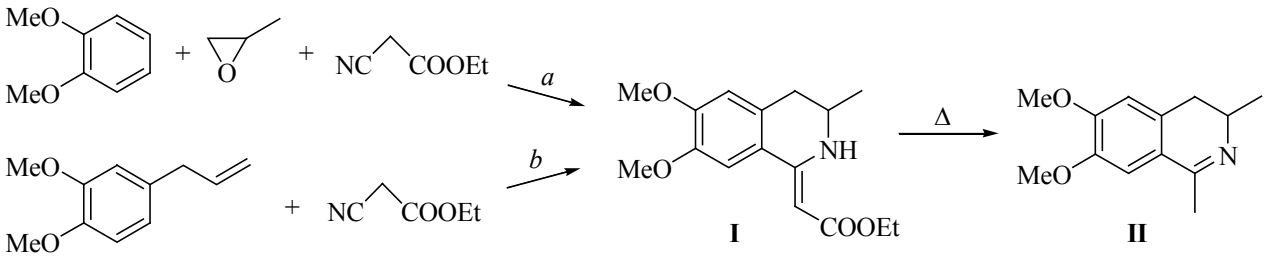
The GC-MS investigation of compound **I** showed

that under the experimental conditions (vaporizer temperature 290°C) ester **I** suffered a thermolysis [11], and only the peak of 1,3-dimethyl-6,7-dimethoxy-3,4-dihydroisoquinoline (**II**), $[M]^{+\bullet}$ 219 (100) was detected, the peak of ester **I** was absent. Analogous pattern was observed with the (2*Z*)-(6,7-dimethoxy-3-methyl-3,4-dihydroisoquinolidene-1-acetamide (**III**) that similarly to the previously observed transformation of substituted amides [12] at the temperature exceeding 100°C dissociated into compound **II** and isocyanic acid (Scheme 2). To confirm this pattern of the reaction course we carried out the reaction between the eugenol methyl ether and acetonitrile that provided compound **II** whose behavior at the GC-MS analysis was identical to the above described.

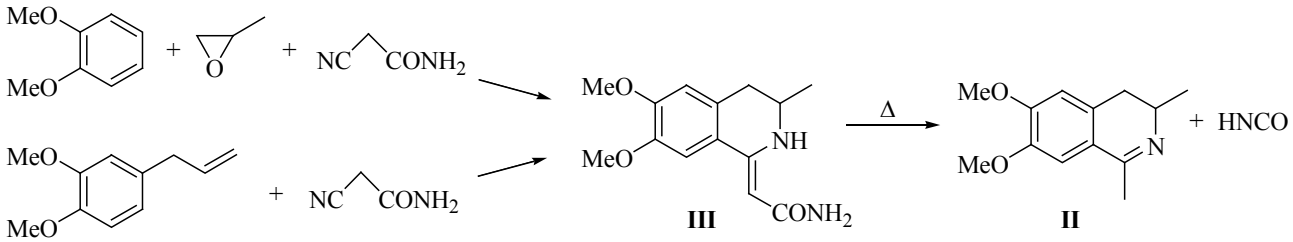
In a similar way the eugenol methyl ether reacted with methyl thiocycnate and with 3,4-dimethoxyphenylacetonitrile giving respectively thiolatim ether **IV** and ketone **VI** formed due to the oxidation of compound **V** at the isolation [13] (Scheme 3).

As shown in [14] the formation of the 3,4-dihydroisoquinoline system under the conditions of Ritter reaction

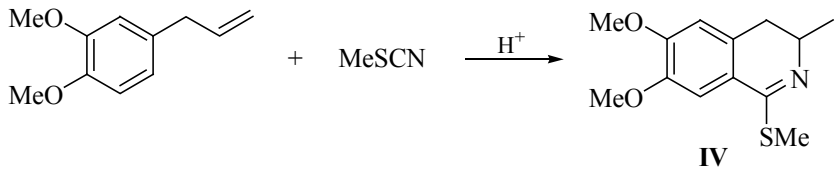
Scheme 1.

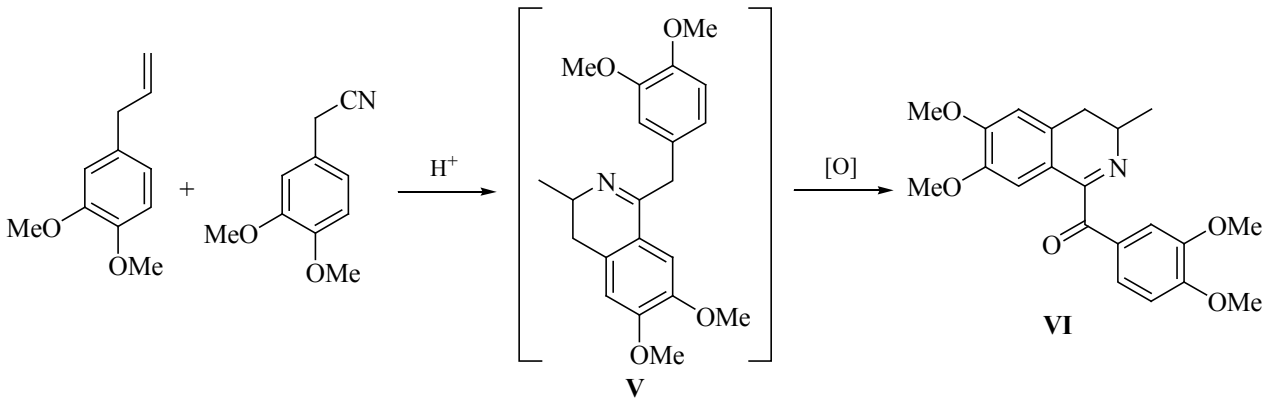


Scheme 2.



Scheme 3.





was possible even in the presence of a free phenol hydroxy group in the initial arene. Inasmuch as the use of the propylene oxide (the synthetic equivalent of the propionic aldehyde) in the three-component synthesis with *O*-methoxyphenol and nitriles leads to the formation of oligomers, it is clear that in this case only the application of eugenol or isougenol is possible.

It is presumable that the reactions of eugenol **A** and isoeugenol **B** would result in different yields for in the protonated eugenol the carbocation center would arise in the β-position with respect to arene, whereas in the isougenol would prevail the α-carbocation much less reactive in Ritter reaction (Scheme 4) [8, 15].

Actually, in the reactions of eugenol and isoeugenol with nitriles the yields of products are essentially different. From the eugenol isoquinolines **VII–XI** were obtained with a free hydroxy group, but their yield in the concn. sulfuric acid was relatively small. The reaction in the methanesulfonic acid improved the yield of the target products approximately twice (Scheme 5).

The same reactions with isoeugenol resulted mainly in oligpmers, the isoquinolines were detected only by the chromatography.

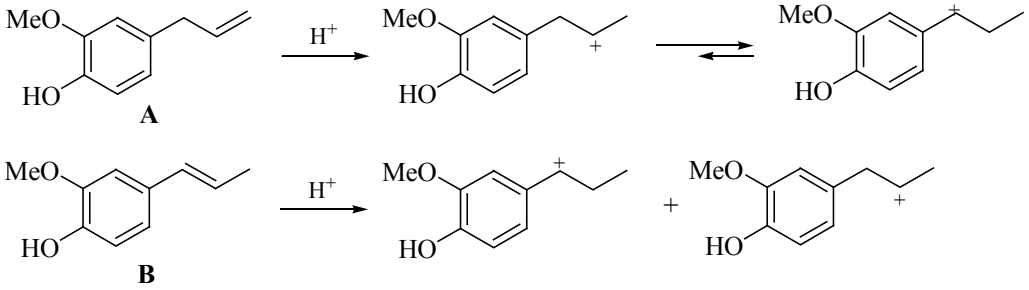
The characteristic feature of compounds **VI** and **XI** is their easy dehydration into the aromatic isoquinolines in the vaporizer of the GC-MS instrument (290°C): alongside the dihydroisoquinolines the corresponding aromatic derivatives always are observed in the ratio ~ 1:2, although the ^{1}H NMR spectra prove the exclusive formation in the synthesis of 3,4-dihydroisoquinolines.

EXPERIMENTAL

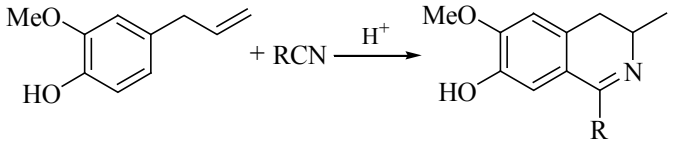
IR spectra were recorded on a spectrophotometer Bruker from mulls in mineral oil. ^{1}H NMR spectra were registered on a spectrometer MercuryPlus-300 (300 MHz) in $CDCl_3$, internal reference HMDS. Mass spectra were measured on GC-MS instrument Agilent Technologies 6890N/5975B (EI, 70 eV). The monitoring of the reaction progress and checking the purity of compounds obtained was performed by TLC on Sorbfil plates, eluent chloroform–acetone, 9:1, development with 0.5% chloranil solution in toluene. Elemental analysis was carried out on an analyzer CHNS-932 Leco Corporation.

Ethyl (2*Z*)-(6,7-dimethoxy-3-methyl-3,4-dihydroisoquinolin-1(2*H*)-ylidene)acetate (I). *a.* A mixture of 1.78 g (0.01 mol) of eugenol methyl ether and 1.13 g (0.01 mol) of ethyl cyanoacetate was added dropwise at vigorous stirring to 2 ml of 94% sulfuric acid while cooling with an ice bath. On completing the addition the reaction mixture was stirred without cooling for 15 min, poured into 200 ml of water, and was neutralized with dry Na_2CO_3 till pH 8–9. The products were extracted into 50 ml of chloroform. The organic layer was washed with water (2×50 ml), dried with $MgSO_4$, chloroform was distilled off on a rotary evaporator. The residue was dissolved in diethyl ether, and the dry HBr was passed till the formation of transparent solution. The precipitate was filtered off and recrystallized from acetonitrile. The hydrobromide was dissolved in 50 ml of water, neutralized with 10% aqueous KOH, the separated precipitate was filtered off

Scheme 4.



Scheme 5.



VII–XI

and recrystallized from hexane. Yield 0.63 g (22%), mp 88–90°C. ^{1}H NMR spectrum, δ, ppm: 1.31 d (3H, 3-CH_3, *J* 12 Hz), 1.29 t (3H, $OCH_2\underline{CH_3}$, *J* 7.5 Hz), 2.67 m (2H, C^4H_2), 3.58 m (1H, H^3), 3.87 s (3H, 6-OCH_3), 3.88 s (3H, 7-OCH_3), 4.16 q (2H, OCH_2, *J* 7.5 Hz), 5.04 c (1H, H_{vinyl}), 6.61 s (1H, H^5), 7.10 c (1H, H^8), 8.88 br.s (1H, NH). Found, %: C 65.81; H 7.39; N 4.68. $C_{16}H_{21}NO_4$. Calculated, %: C 65.96; H 7.27; N 4.81.

b. From a mixture of 1.38 g (0.01 mol) of veratrol, 0.58 g (0.01 mol) propylene oxide, and 1.13 g (0.01 mol) of ethyl cyanoacetate by procedure *a* was obtained 0.15 g (5%) of compound **I**.

1,3-Dimethyl-6,7-dimethoxy-3,4-dihydroisoquinoline (II) was obtained by procedure *a* from a mixture of 1.78 g (0.01 mol) of eugenol methyl ether and 0.41 g (0.01 mol) of acetonitrile. After distilling off the solvent the residue was dissolved in a minimum amount of diethyl ether, and a saturated solution of salicylic acid in the same solvent was added. The precipitate formed in 1–2 min was separated and recrystallized from acetonitrile. The salicylate (mp 149–151°C) was dissolved in 50 ml of water, neutralized with 10% aqueous KOH, the separated precipitate was filtered off and recrystallized from hexane. Yield 0.7 g (32%), mp 74–76°C.

b. Ethyl ester **I** was dissolved in 35 ml of 10% H_2SO_4 and the solution was heated for 2 h. Afterwards it was poured into 200 ml of water, neutralized with dry sodium carbonate to pH 8–9. The products were extracted into 50 ml of chloroform, the solvent was removed on a rotary evaporator. The residue was worked up as described in procedure *a*. Yield of the salicylate of compound **II** 1.13 g (32%), mp 149–151°C. ^{1}H NMR spectrum, δ, ppm: 1.47 d (3H, 3-CH_3, *J* 7 Hz), 2.88 d.d (1H, H^4_A, J_1 16.8, J_2 9.6 Hz), 2.98 s (3H, 1-CH_3), 3.16 d.d (1H, H^4_B, J_1 16.8, J_2 6.3 Hz), 3.97 s (3H, OCH_3), 4.01 s (3H, OCH_3), 4.14 m (1H, H^3), 6.71 s (1H, H^5), 6.74 d (1H, $H^5_{salicyl}$, *J* 8 Hz), 6.80 d (1H, $H^5_{salicyl}$, *J* 8 Hz), 7.08 C (1H, H^8), 7.23 m (1H, $H^4_{salicyl}$), 7.88 d.d (1H, $H^6_{salicyl}$, J_1 8, J_2 1.5 Hz), 14.95 br.s (1H, OH). Mass spectrum, *m/z* (I_{rel}, %): 218 $[M]^+$ (100), 203 $[M - Me]^+$ (80). Hydrochloride, mp 110–112°C. Found, %: C 61.11; H 6.93; N 5.33. $C_{13}H_{17}NO_2 \cdot HCl$. Calculated, %: C 61.05; H 7.09; N 5.48.

(2*Z*)-(6,7-Dimethoxy-3-methyl-3,4-dihydroisoquinolin-1(2*H*)-ylidene)ethanamide (III) was obtained by procedure *a* from a solution of 0.84 g (0.01 mol) of cyanacetamide in 2 ml of cold 94% sulfuric acid and 1.78 g (0.01 mol) of eugenol methyl ether. After distilling off the solvent the residue was crystallized from acetonitrile. Yield 1.21 g (46%), yellow crystals, mp 154–156°C, R_f 0.45 (chloroform–acetone, 9:1). ^{1}H NMR spectrum, δ, ppm: 1.29 d (3H, 3-CH_3, *J* 6.6 Hz), 2.57 d.d (1H, H^4_A, J_1 15, J_2 11.1 Hz), 2.71 d.d (1H, H^4_C, J_1 15, J_2 4.2 Hz), 3.54 m (1H, H^3), 3.87 s (3H, OCH_3), 3.88 s (3H, OCH_3), 4.96 s (1H, H_{vinyl}), 5.10 br.s (2H, NH_2), 6.60 s (1H, H^5), 7.06 s (1H, H^8), 9.47 (1H, NH). Found, %: C 64.25; H 6.80; N 10.84. $C_{14}H_{18}N_2O_3$. Calculated, %: C 64.11; H 6.92; N 10.68.

3-Methyl-1-(methylsulfanyl)-6,7-dimethoxy-3,4-dihydroisoquinoline (IV) was obtained by procedure *a* from a mixture of 1.78 r (0.01 mol) of eugenol methyl ether and 0.73 g (0.01 mol) of methyl thiocyanate. After distilling off the solvent the residue was crystallized from hexane. Yield 1.54 g (61%), mp 92–96°C. ^{1}H NMR spectrum, δ, ppm: 1.33 d (3H, 3-CH_3, *J* 6.6 Hz), 2.42 d.d (1H, H^4_A, J_1 18, J_2 11.7 Hz), 2.43 s (3H, SCH_3), 2.69 d.d (1H, H^4_C, J_1 16, J_2 5.1 Hz), 3.66 m (1H, H^3), 3.88 s (3H, OCH_3), 3.88 s (3H, OCH_3), 6.64 s (1H, H^5), 7.15 s (1H, H^8). Mass spectrum, *m/z* (I_{rel}, %): 251 $[M]^+$ (56), 236 $[M - Me]^+$ (100). Found, %: C 62.18; H 6.81; N 5.49; S 12.88. $C_{13}H_{17}NO_2S$. Calculated, %: C 62.12; H 6.82; N 5.57; S 12.76.

(3-Methyl-6,7-dimethoxy-3,4-dihydroisoquinolin-1-yl)(3,4-dimethoxyphenyl)methanone (VI) was obtained by procedure *a* from a mixture of 1.78 g (0.01 mol) of eugenol methyl ether and 1.77 g (0.01 mol) of 3,4-dimethoxyphenylacetonitrile in 5 ml of dichloromethane. After distilling off the solvent the residue was treated with 2 ml of concn. HCl, and the mixture was left standing for evaporation over 48 h. The residue was extracted with 5 ml of boiling acetone, the insoluble residue was separated and crystallized from ethanol. Yield 1.54 g (38%) of compound **VI** hydrochlide, mp 182–184°C. 1 g of the hydrochloride was dissolved in water, aqueous ammonia was added, the base was extracted with 50 ml of chloroform, the extract was dried, the solvent was removed on the rotary evaporator. Yield 0.82 h (90%), R_f 0.6 (hexane–ethyl acetate, 5 : 1), mp 115–117°C (hexane). ^{1}H NMR spectrum, δ, ppm: 1.44 d (3H, 3-CH_3, *J* 7.1 Hz), 2.61 d.d (1H, H^4_A, J_1 15.6, J_2 11.4 Hz), 2.86 d.d (1H, H^4_C, J_1 15.9, J_2 5.4 Hz), 3.76 s (3H, 6-OCH_3), 3.85 m (1H, H^3), 3.91 s (3H, 7-OCH_3), 3.92 C (3H, 4'-OCH_3), 3.93 C (3H, 3'-OCH_3), 6.73 s (1H, H^5), 6.87 d (1H, H^5, *J* 3 Hz), 6.88 s (1H, H^8), 7.60 d.d (1H, H^6, J_1 8.25, J_2 1.8 Hz), 7.67 d (1H, $H^{2'}$, *J* 1.8 Hz). Mass spectrum, *m/z* (I_{rel}, %): 369 $[M]^+$ (20), 354 $[M - Me]^+$ (8), 165 [3,4-dimethoxyphenylcarbonyl]$^+$

(80). Found, %: C 68.12; H 6.39; N 3.73. $C_{21}H_{23}NO_5$. Calculated, %: C 68.28; H 6.28; N 3.79.

Ethyl (2*Z*)-(7-hydroxy-6-methoxy-3-methyl-3,4-dihydroisoquinolin-1(2*H*)-ylidene)ethanoate (hydrochloride) (VII). A mixture of 1.64 g (0.01 mol) of eugenol and 1.13 g (0.01 mol) of ethyl cyanoacetate was added dropwise at vigorous stirring and cooling with ice to 5 ml of methanesulfonic acid. On completion of the addition the reaction mixture was stirred without cooling for 15 min, then it was poured into 200 ml of water and neutralized with dry sodium carbonate to pH 8–9. The products were extracted into 50 ml of chloroform. The organic layer was washed with water (2×50 ml), dried, chloroform was distilled off on a rotary evaporator. The residue was dissolved in diethyl ether, and the dry HCl was passed till the formation of transparent solution. The precipitate was filtered off, dried, and crystallized from acetonitrile. Yield 1.08 g (34%), mp 166–168°C, R_f 0.7 (ethyl acetate–hexane, 2:1). ^{1}H NMR spectrum, δ, ppm: 1.21 t (3H, $OCH_2\underline{CH_3}$, *J* 7.2 Hz), 1.57 d (3H, 3-CH_3, *J* 6.6 Hz), 2.87 d.d (1H, H^4_A, J_1 15.5, J_2 9.9 Hz), 3.15 d.d (1H, H^4_C, J_1 8.3, J_2 6.3 Hz), 4.00 s (3H, OMe), 4.15 m (1H, H^3), 4.42 q (2H, OCH_2, *J* 7.2 Hz), 6.82 s (2H, C^1H_2), 7.29 d (1H, H^5, *J* 2.1 Hz), 7.43 d (1H, H^8, *J* 3.9 Hz), 7.87 br.s (1H, NH), 14.15 br.s (1H, OH). Found, %: C 57.50; H 6.39; N 4.47. $C_{15}H_{19}NO_4$·HCl. Calculated, %: C 57.42; H 6.42; N 4.46.

Compounds **VIII** and **IX** were similarly obtained.

7-Hydroxy-1,3-dimethyl-6-methoxy-3,4-dihydroisoquinoline (hydrochloride) (VIII) was obtained from the mixture of 0.02 mol of eugenol and 0.02 mol of acetonitrile. After removing the solvent the residue was dissolved in diethyl ether, and the dry HCl was passed, the precipitate was separated and recrystallized first from acetone and then from ethanol. Light-brown crystals. Yield 1.30 g (26%), mp 119–121°C. ^{1}H NMR spectrum, δ, ppm: 1.41 d (3H, 3-CH_3, *J* 6.6 Hz), 2.73 s (3H, 1-CH_3), 2.82 d.d (1H, 4H, J_1 16.5, J_2 10.8 Hz), 3.09 d.d (1H, 4H, J_1 16.5, J_2 6.3 Hz), 3.92 s (3H, OMe), 4.06 m (1H, H^3), 7.05 s (1H, H^5), 7.42 d (1H, H^8, *J* 0.6 Hz), 9.84 s (1H, OH), 13.34 br.s (1H, NH). Mass spectrum, *m/z* (I_{rel}, %): 205 $[M]^{+\bullet}$ (100), 190 $[M-Me]^+$ (100). Found, %: C 59.49; H 6.54; N 5.89. $C_{12}H_{15}NO_2$·HCl. Calculated, %: C 59.63; H 6.67; N 5.79.

7-Hydroxy-3-methyl-1-(methylsulfanyl)-6-methoxy-3,4-dihydroisoquinoline (hydrochloride) (IX) was obtained from the mixture of 0.01 mol of eugenol and 0.01 mol of methyl thiocyanate. After removing the solvent the residue was dissolved in diethyl ether, and the dry HCl was passed, the precipitate was separated and recrystallized first from acetone and then from acetonitrile. Yield 1.8 g (66%), light-brown needle crystals, mp 193–195°C, R_f 0.7 (chloroform–acetone, 9 : 1). ^{1}H NMR spectrum, δ, ppm: 1.36 d (3H, 3-CH_3, *J* 6.6 Hz), 2.76 d.d (1H, H^4_A, J_1 16.8, J_2 2.4 Hz), 3.06 s (3H, SMe), 3.27 d.d (1H, H^4_C, J_1 16.7, J_2 3.3 Hz), 4.00 s (3H, OMe), 4.60 m (1H, H^3), 6.76 s (1H, OH), 7.26 d (1H, H^5, *J* 4.8 Hz), 7.64 d (1H, H^8, *J* 4.8 Hz), 12.89 C (1H, HCl). Mass spectrum, *m/z* (I_{rel}, %): 237 $[M]^{+\bullet}$ (63), 236 $[M-H]^+$ (80), 221 $[M-Me]^+$ (100). Found, %: C 52.54; H 5.99; N 5.31; S 11.57. $C_{12}H_{15}NO_2S$·HCl. Calculated, %: C 52.65; H 5.89; N 5.12; S 11.71.

(2*Z*)-(7-Hydroxy-3-methyl-6-methoxy-3,4-dihydroisoquinolin-1(2*H*)-ylidene)ethanamide (X). To a solution of 0.01 mol of cyanacetamide in 2 ml of 94% sulfuric acid at vigorous stirring and cooling with ice was added dropwise 0.01 mol of eugenol. Further workup was performed as in the preparation of compound **I**. After removing the solvent the residue was crystallized from ethanol. Yield 1.21 g (46%), yellow crystals, mp 197–199°C. ^{1}H NMR spectrum, δ, ppm: 1.27 d (3H, 3-CH_3, *J* 6.3 Hz), 2.62 m (1H, H^4_A), 2.71 m (1H, H^4_C), 3.51 m (1H, H^3), 3.87 s (3H, OCH_3), 4.99 C (1H, H_{vinyl}), 5.61 br.s (2H, NH_2), 6.62 s (1H, H^5), 7.13 s (1H, H^8), 8.48 s (1H, OH), 9.39 s (1H, NH). Mass spectrum, *m/z* (I_{rel}, %): 237 $[M]^{+\bullet}$ (63), 236 $[M-H]^+$ (80), 221 $[M-Me]^+$ (100). Found, %: C 54.66; H 6.14; N 9.72. $C_{13}H_{16}N_2O_3$. Calculated, %: C 54.84; H 6.02; N 9.84.

(7-Hydroxy-3-methyl-6-methoxy-3,4-dihydroisoquinolin-1-yl)(3,4-dimethoxyphenyl)methanone (hydrochloride) (XI) was obtained like compound **VII** from the mixture of 0.01 mol of eugenol and 0.01 mol of 3,4-dimethoxyphenylacetonitrile in 5 ml of dichloromethane. After distilling off the solvent the residue was treated with 2 ml of concn. HCl, and the mixture was left standing for evaporation over 48 h. The residue was extracted with 5 ml of boiling acetone, the insoluble residue was filtered off, dried, and crystallized from acetonitrile. Yield 1.20 g (31%), light-yellow crystals, mp 209–210°C. ^{1}H NMR spectrum, δ, ppm: 1.41 d (3H, 3-CH_3, *J* 5.7 Hz), 2.58 m (1H, H^4_A), 2.82 d.d (1H, H^4_C, J_1 16, J_2 4.8 Hz), 3.83 m (1H, H^3), 3.90 m (12H, OMe), 5.80 br.s (1H, OH), 6.67 s (1H, H^5), 6.81 d (1H, H^5, *J* 5 Hz), 6.83 s (1H, H^8), 7.52 d (1H, $H^{2'}$, *J* 8.4 Hz), 7.63 s (1H, $H^{6'}$). Mass spectrum, *m/z* (I_{rel}, %): 355 $[M]^+$ (24), 340 $[M-Me]^+$ (9), 336 $[M-OH]^+$ (100), 165 [eugenol + H]$^+$ (100). Found, %:

C 61.19; H 5.73; N 3.39. $C_{20}H_{21}NO_5$·HCl. Calculated, %: C 61.30; H 5.66; N 3.57.

ACKNOWLEDGMENTS

The study was carried out under the financial support of the program of the Presidium of the Russian Academy of Sciences no. 18.

REFERENCES

1. Toda, J., Matsumoto, S., Saitoh, T., and Sano, T., *Chem. Pharm. Bull. Jpn.,* 2000, vol. 48, p. 91.
2. Grunewald, G.L., Caldwell, T.M., Li, Q., and Criscione, K.R., *Bioorg. Med. Chem.,* 1999, vol. 7, p. 869.
3. Chen, K.X., Njoroge, F.G., Pichardo, J., Prongay, A., Butkiewicz, N., Yao, N., Madison, V., and Girijavallabhan, V., *Tetrahedron,* 2000, vol. 56, p. 581.
4. Janin, Y.L., Roulland, E., Beurdeley-Thomas, A., Decaudin, D., Monneret, C., and Poupond, M.-F., *J. Chem. Soc*., *Perkin, Trans. 1*, 2002, p. 529.
5. Bermejo, A., Andreu, I., Suvire, F., Leonce, S., Caignard, D.H., Renard, P., Pierre, A., Enriz, R.D., Kortes, D., and Cabedo, N., *J. Med. Chem*., 2002, vol. 45, p. 5058.
6. Kametani, T., Otsuki, K., and Fukui, M., *Pharm. Soc. Jpn.,* 1955, vol. 3, p. 266.
7. Fecik, R.A., Devasthale, P., Pillai, S., Keschavarz-Shokri, A., Shen, L., and Mitscher, L.A., *J. Med. Chem*., 2005, vol. 48, p. 1229.
8. Shklyaev, Yu.V. and Nifontov, Yu.V., *Izv. Akad. Nauk, Ser. Khim*., 2002, p. 780.
9. Ritter, J.J. and Murphy, F.X., *J. Am. Chem. Soc.,* 1952, vol. 74, p. 763.
10. Janin, Y.L., Decaudinb, D., Monneretc, C., and Poupond, M.-F., *Tetrahedron,* 2004, vol. 60, p. 5481.
11. Shklyaev, V.S., Gavrilov, M.S., and Aleksandrov, B.B., *Khim. Geterotsikl. Soedin*., 1986, p. 282.
12. Gorbunov, A.A., *Cand. Sci. (Chem.) Dissertation,* Perm', 1998.
13. Shklyaev, Yu.V., Eltsov, M.A., Rozhkova, Yu.S., Tolstikov, A.G., and Demditsky, V.M., *Heteroatom. Chem.,* 2004, vol. 15, p. 481.
14. Shklyaev, Yu.V., Vshivkova, T.S., and Tolstikov, A.G., *Khim. Geterotsikl. Soedin*., 2009, p. 421.
15. Bishop, R., *Comprehensive Organic Synthesis,* Trost, B.M., Fleming, I., and Winterfeld, E., Oxford: Pergamon Press, 1991, vol. 6, p. 261.