ISSN 1070-4280, Russian Journal of Organic Chemistry, 2011, Vol. 47, No. 9, pp. 1318–1322. © Pleiades Publishing, Ltd., 2011.
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Spirocyclohexadienones: XII.* Dienone–Phenol Rearrangement of 1-Substituted 2-Azaspiro[4.5]undeca-1,6,9-trienes and Their Analogs

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Received February 11, 2011

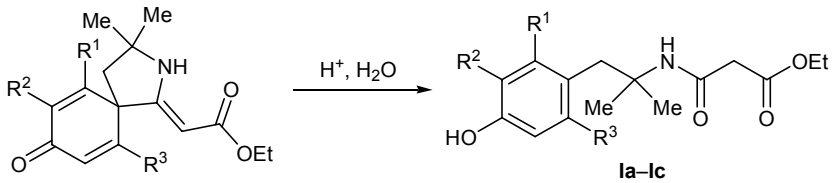
Abstract—Hydrolytic cleavage of 1-substituted 2-azaspiro[4.5]undeca-1,6,9-trienes in acid medium is accompanied by dienone–phenole rearrangement with formation of substituted *N*-[2-(*p*-hydroxyphenyl)ethyl] carboxylic acid amides. 1,2-Dimethoxy-3-oxo-15-phenyl-14-azadispiro[5.1.5.2]pentadeca-1,4,14-triene and 2′-R-7a′-methyl-3a′,4′,5′,6′,7′,7a′-hexahydrospiro[cyclohexa[2,5]diene-1,3′-indol]-4-ones undergo analogous cleavage.

DOI: 10.1134/S1070428011090107

It is known that three-component condensation of anisole derivatives with isobutyraldehyde and nitriles leads to the formation of substituted 2-azaspiro[4.5]-undeca-1,6,9-trienes [1, 2]. Analogous reaction with cyclohexanecarbaldehyde yields dispiro compounds [3]. 1- and 2-Methoxynaphthalenes behave in a similar way [4], whereas 2-methyl-1-(*p*-methoxyphenyl)-cyclohexan-1-ol gives rise to 2′-substituted 7a′-methyl-3a′,4′,5′,6′,7′,7a′-hexahydrospiro[cyclohexa[2,5]diene-1,3′-indol]-4-ones [5]. The above listed spiro compounds characteristically undergo hydrolytic cleavage in acid medium, which is accompanied by dienone–phenol rearrangement with formation of substituted *N*-[2-(*p*-hydroxyphenyl)ethyl] carboxylic acid amides [6]. Such rearrangement of spiro cyclohexadienone derivatives having no substituents in the cyclohexane ring was studied by us previously, and its mechanism was analyzed by quantum-chemical calculations [6, 7].

The goal of the present work was to study dienone–phenol rearrangement of substituted 2-azaspiro[4.5]-undeca-1,6,9-trienes and structurally related 2′-R-7a′-methyl-3a′,4′,5′,6′,7′,7a′-hexahydrospiro-[cyclohexa[2,5]diene-1,3′-indol]-4-ones. The reactions were carried out by heating the initial spiro compound for a short time (0.5 h) in aqueous ethanol containing concentrated sulfuric acid. The presence of methoxy groups in the cyclohexadiene ring of 2-azaspiro[4.5]-undeca-6,9-dienes and 2-azaspiro[4.5]undeca-1,6,9-trienes did not affect the reaction course, and the process occurred in a way similar to hydrolytic cleavage of spiro compounds derived from anisole which had no substituents in the cyclohexadiene ring [6] (Scheme 1).

Scheme 1.

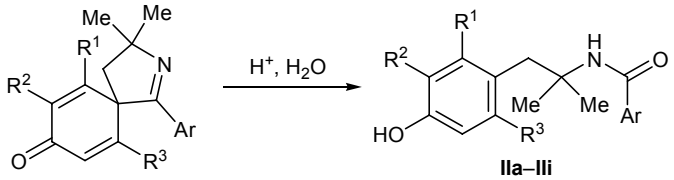


Ia–Ic

$R^1 = R^2 = MeO$, $R^3 = H$ (**a**); $R^1 = H$, $R^2 = R^3 = MeO$ (**b**); $R^1 = R^3 = MeO$, $R^2 = H$ (**c**).

* For communication XI, see [1].

Scheme 2.



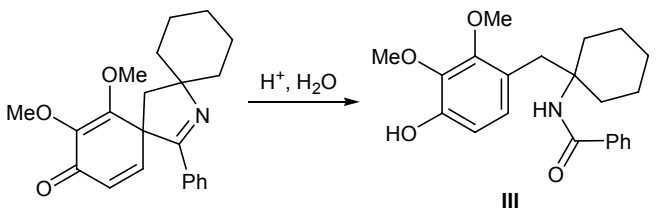
IIa–IIi

$R^1 = R^2 = MeO$, $R^3 = H$, Ar = 4-$MeOC_6H_4$ (**a**); $R^1 = R^2 = MeO$, $R^3 = H$, Ar = 3,4-$(MeO)_2C_6H_3$ (**b**); $R^1 = H$, $R^2 = R^3 = MeO$, Ar = Ph (**c**); $R^1 = H$, $R^2 = R^3 = MeO$, Ar = 3,4-$(MeO)_2C_6H_3$ (**d**); $R^1 = H$, $R^2 = R^3 = MeO$, Ar = 4-BrC_6H_4 (**e**); $R^1 = R^3 = MeO$, $R^2 = H$, Ar = Ph (**f**); $R^1 = R^3 = OMe$, $R^2 = H$, Ar = 4-$MeOC_6H_4$ (**g**); $R^1 = R^3 = MeO$, $R^2 = H$, Ar = 3,4-$(MeO)_2C_6H_3$ (**h**); $R^1 = R^3 = MeO$, $R^2 = H$, Ar = 4-BrC_6H_4 (**i**).

The structure of amides **Ia**–**Ic** thus obtained was confirmed by their IR and ^1H NMR spectra. Crystalline samples of **Ia**–**Ic** displayed in the IR spectra a broad absorption band at ~3330–3340 cm^{-1} due to stretching vibrations of the phenolic hydroxy group and amide NH group and strong absorption bands at 1736–1742 and 1652–1660 cm^{-1}, belonging to stretching vibrations of the ester and amide carbonyl groups, respectively. Ring opening in unsymmetrically substituted 6,7-dimethoxy-2-azaspiro[4.5]undeca-6,9-dien-8-one (Scheme 1, $R^1 = R^2 = MeO$) with formation of compound **Ia** was accompanied by transformation of the doublet from diastereotopic protons on C^4 (δ 1.99 and 2.40 ppm) into a singlet at δ 2.82 ppm and of two signals from nonequivalent methyl groups on C^3 (δ 1.42 and 1.43 ppm) into one singlet at δ 1.35 ppm.

1-Aryl-2-azaspiro[4.5]undeca-1,6,9-trienes [1] reacted in a similar way (Scheme 2), and the yields of amides **IIa**–**IIi** were 44–86%. In the IR spectra of **IIa**–**IIi** (crystalline samples), broadened absorption bands due to stretching vivrations of the phenolic hydroxy group (3348–3579 cm^{-1}) and amide NH group (3215–3414 cm^{-1}) were observed together with strong absorption band belonging to the amide carbonyl group (1645–1650 cm^{-1}). As in the previous case, doublets from diastereotopic protons on C^4 in the ^1H NMR spectra of unsymmetrically substituted initial compounds were converted into singlets at δ 2.79–2.84 ppm (**IIa**–**IIe**), and two singlets from geminal methyl groups on C^3 were transformed into one singlet at δ 1.50–1.52 ppm.

Scheme 3.

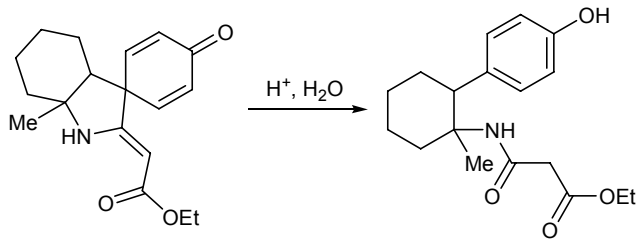


III

Hydrolysis of dispiro compounds, e.g., of 1,2-dimethoxy-15-phenyl-14-azadispiro[5.1.5.2]pentadeca-1,4,14-trien-3-one [3]) involved opening of the central pyrrole ring (Scheme 3). Fusion of a benzene ring to the cyclohexadiene fragment increases stability of the spirocyclic system. Benzo-fused 2-azaspiro[4.5]undeca-6,9-dienes and -1,6,9-trienes obtained from 1- and 2-methoxynaphthalenes [4] did not undergo rearrangement under analogous conditions; their hydrolysis required more sever conditions and was not selective.

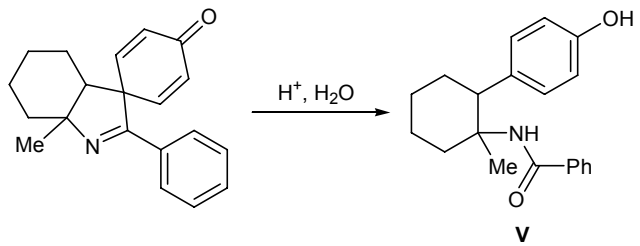
Substituted spiro[cyclohexa[2,5]diene-1,3′-indol]-4-ones have recently attracted researchers' attention [8]. Rearrangement of one of these compounds, ethyl (*Z*)-2-{7a′-methyl-4-oxo-3a′,4′,5′,6′,7′,7a′-hexahydrospiro[cyclohexa[2,5]diene-1,3′-indol]-2′(1′*H*)-ylidene}-acetate synthesized by us previously [5], followed a similar pattern and produced N-substituted malonamic acid ester **IV** (Scheme 4). Likewise, hydrolysis of 7a′-methyl-2′-phenyl-3a′,4′,5′,6′,7′,7a′-hexahydro-

Scheme 4.



IV

Scheme 5.



V

spiro[cyclohexa[2,5]diene-1,3′-indole]-4-one afforded substituted benzamide **V** (Scheme 5).

Biological assay of compounds **Ib** and **IIf**–**IIh** revealed their weak antimicrobial activity against *S. aureus* R 209 (the minimal inhibitory concentration of compound **Ib** was 125 μg/ml, and of **IIf**–**IIh**, ~500–1000 μg/ml) and *E. coli* (500 μg/ml for **Ib**, and 1000 μg/ml for **IIf**–**IIh**); compound **IIi** showed no antimicrobial activity.

EXPERIMENTAL

The IR spectra were recorded on a Bruker IFS 66ps spectrometer with Fourier transform from samples dispersed in mineral oil or thin films obtained by evaporation of a solution in chloroform. The ^{1}H NMR spectra were measured on a Varian Mercury 300 instrument at 300 MHz from solutions in $CDCl_3$; the chemical shifts were determined relative to hexamethyldisiloxane (δ 0.055 ppm). The mass spectra (electron impact, 70 eV) were obtained on an Agilent GC–MS system consisting of an HP 6890N gas chromatograph coupled with an HP 5975B mass-selective detector. The elemental compositions were determined on a Leco CHNS 9321P analyzer. The R_f values were measured on Sorbfil plates (silica gel) using chloroform–acetone (9 : 1) as eluent; spots were visualized under UV light or by treatment with a 2% solution of tetrachloro-1,4-benzoquinone in toluene and subsequent heating. Column chromatography was performed using Silica gel 60 (220–440 Mesh, Alfa Aesar). Commercial 1,2,3-, 1,2,4-, and 1,3,5-trimethoxybenzenes and isobutyraldehyde (Alfa Aesar, Lancaster) were used.

General procedure for the hydrolysis of spirocyclic compounds. The corresponding substrate, 1 mmol, was dissolved in a mixture of 15 ml of alcohol, 5 ml of water, and 1 ml of concentrated sulfuric acid, and the mixture was heated for 0.5 h under reflux and poured into 50 ml of a saturated solution of sodium hydrogen carbonate (until pH ~7). If a solid separated, it was filtered off, dried, and recrystallized from hexane–ethyl acetate. Oily compounds **Ia**, **IId**, and **IIe** were extracted into 50 ml of CH_2Cl_2, the extract was dried over $MgSO_4$ and evaporated, and the residue was purified by chromatography on silica gel using petroleum ether (bp 40–70°C)–ethyl acetate (5 : 1) as eluent.

Ethyl *N*-[2-(4-hydroxy-2,3-dimethoxyphenyl)-1,1-dimethylethyl]malonamate hydrate (Ia). Yield 80%, light yellow oily substance, R_f 0.40. IR spectrum, ν, cm^{-1} (film): 3339 (OH, NH), 3089, 2976, 2937, 2833, 1738 (C=O), 1660 (C=O), 1551, 1495 (C=S), 1467, 1422, 1367, 1340, 1301, 1195, 1173, 1067, 1031, 756. ^{1}H NMR spectrum, δ, ppm: 1.24 t (3H, C**H**$_3$CH$_2$, J = 7.2 Hz), 1.35 s (6H, Me), 2.82 s (2H, C**H**$_2$Ar), 3.17 s (2H, COCH$_2$), 3.84 s and 3.89 s (3H each, OMe), 4.14 q (2H, OCH$_2$, J = 7.2 Hz), 5.96 s (1H, NH), 6.64 d (1H, 5-H, J = 8.4 Hz), 6.73 d (1H, 6-H, J = 8.4 Hz), 7.04 br.s (1H, OH). Found, %: C 53.60; H 6.95; N 3.48. $C_{17}H_{25}NO_6 \cdot 2.5H_2O$. Calculated, %: C 53.11; H 7.86; N 3.64.

Ethyl *N*-[2-(4-hydroxy-2,5-dimethoxyphenyl)-1,1-dimethylethyl]malonamate (Ib). Yield 67%, colorless crystals, mp 124–125°C, R_f 0.44. IR spectrum, ν, cm^{-1} (mineral oil): 3332 (NH), 3111 br (OH), 1742 (C=O, ester), 1652 (C=O, amide), 1606 w, 1573, 1523, 1318, 1208, 1170, 1041, 967 w, 864. ^{1}H NMR spectrum, δ, ppm: 1.17 t (3H, C**H**$_3$CH$_2$, J = 7.2 Hz), 1.31 s (6H, Me), 2.78 s (2H, C**H**$_2$Ar), 3.10 s (2H, COCH$_2$), 3.71 s and 3.76 s (3H each, OMe), 4.04 q (2H, OCH$_2$, J = 7.2 Hz), 5.76 s (1H, NH), 6.51 s (1H, 3-H), 6.57 s (1H, 6-H), 7.21 br.s (1H, OH). Found, %: C 59.98; H 7.40; N 4.09. $C_{17}H_{25}NO_6$. Calculated, %: C 60.16; H 7.42; N 4.13.

Ethyl *N*-[2-(4-hydroxy-2,6-dimethoxyphenyl)-1,1-dimethylethyl]malonamate (Ic). Yield 24%, light yellow oily substance, R_f 0.20. IR spectrum, ν, cm^{-1} (film): 3337 (OH, NH), 2977, 2937, 2842, 1736 (C=O), 1666 (C=O), 1596 (C=C), 1558, 1472, 1373, 1308, 1208, 1152, 1103, 1038, 1000, 819. ^{1}H NMR spectrum, δ, ppm: 1.24 t (3H, C**H**$_3$CH$_2$, J = 7.2 Hz), 1.39 s (6H, Me), 2.77 s (2H, C**H**$_2$Ar), 3.10 s (2H, COCH$_2$), 3.75 s and 3.80 s (3H each, OMe), 4.15 q (2H, OCH$_2$, J = 7.2 Hz), 6.15 s (2H, 3-H, 5-H), 7.38 br.s (1H, NH), 7.54 br.s (1H, OH). Found, %: C 59.97; H 7.36; N 4.04. $C_{17}H_{25}NO_6$. Calculated, %: C 60.16; H 7.42; N 4.13.

***N*-[2-(4-Hydroxy-2,3-dimethoxyphenyl)-1,1-dimethylethyl]-4-methoxybenzamide (IIa).** Yield 88%, mp 135–136°C. IR spectrum, ν, cm^{-1}: 3395 (OH), 3318 (NH), 1645 (C=O), 1609 (C=C), 1572, 1540, 1499, 1303, 1280, 1257, 1184, 1129, 1065, 1029, 933, 846, 823, 764, 695. ^{1}H NMR spectrum, δ, ppm: 1.50 s (6H, Me), 2.79 s (2H, CH$_2$), 3.81 s (3H, OMe), 3.90 s (3H, OMe), 3.93 s (3H, OMe), 6.06 br.s (1H, NH), 6.68 d (1H, 5′-H, J = 8.4 Hz), 6.78 d (1H, 6′-H, J = 8.4 Hz), 6.84 d (2H, 3-H, 5-H, J = 9 Hz), 7.26 br.s (1H, OH), 7.74 d (2H, 2-H, 6-H, J = 9 Hz). Found, %: C 66.87; H 6.88; N 3.84. $C_{20}H_{25}NO_5$. Calculated, %: C 66.84; H 7.01; N 3.90.

***N*-[2-(4-Hydroxy-2,3-dimethoxyphenyl)-1,1-dimethylethyl]-3,4-dimethoxybenzamide hydrate (IIb).** Yield 76%, mp 97–100°C. IR spectrum, ν, cm^{-1}: 3551 (OH), 3377 (NH), 1645 (C=O), 1604 (C=C), 1586, 1545, 1504, 1307, 1266, 1230, 1193, 1184, 1134, 1115, 1070, 1038, 1024, 960, 864, 818, 759. ^{1}H NMR spectrum, δ, ppm: 1.51 s (6H, Me), 2.80 s (2H, CH_2), 3.89 s (6H, OMe), 3.91 s (3H, OMe), 3.94 s (3H, OMe), 6.02 br.s (1H, NH), 6.68 d (1H, 5′-H, J = 8.1 Hz), 6.77 m (2H, 5-H, 6′-H), 7.28 m (2H, 6-H, OH), 7.46 d (1H, 2-H, J = 2.4 Hz). Found, %: C 62.06; H 6.83; N 3.84. $C_{21}H_{27}NO_6 \cdot H_2O$. Calculated, %: C 61.90; H 7.17; N 3.44.

***N*-[2-(4-Hydroxy-2,5-dimethoxyphenyl)-1,1-dimethylethyl]benzamide (IIc).** Yield 14%, mp 156–157°C. ^{1}H NMR spectrum, δ, ppm: 1.52 s (6H, Me), 2.87 s (2H, CH_2), 3.74 s and 3.78 s (3H each, OMe), 5.70 br.s (1H, NH), 6.60 s (1H, 3′-H), 6.63 s (1H, 6′-H), 7.13 s (1H, OH), 7.39 m (3H, 3-H, 4-H, 5-H), 7.64 m (2H, 2-H, 6-H). Found, %: C 69.17; H 6.64; N 4.20. $C_{19}H_{23}NO_4$. Calculated, %: C 69.28; H 7.04; N 4.25.

***N*-[2-(4-Hydroxy-2,5-dimethoxyphenyl)-1,1-dimethylethyl]-3,4-dimethoxybenzamide (IId).** Yield 75%, light yellow oily substance. ^{1}H NMR spectrum, δ, ppm: 1.52 s (6H, Me), 2.88 s (2H, CH_2), 3.74 s (3H, OMe), 3.80 s (3H, OMe), 3.90 s (6H, OMe), 5.69 br.s (1H, NH), 6.61 s (1H, 3′-H), 6.64 s (1H, 6′-H), 6.79 d (1H, 5-H, ^3J = 8.4 Hz), 7.02 s (1H, OH), 7.14 d.d (1H, 6-H, ^3J = 8.4, ^4J = 1.8 Hz), 7.40 d (1H, 2-H, ^4J = 1.8 Hz). Found, %: C 64.68; H 7.05; N 3.52. $C_{21}H_{27}NO_6$. Calculated, %: C 64.77; H 6.99; N 3.60.

4-Bromo-*N*-[2-(4-hydroxy-2,5-dimethoxyphenyl)-1,1-dimethylethyl]benzamide (IIe). Yield 81%, light yellow oily substance. ^{1}H NMR spectrum, δ, ppm: 1.52 s (6H, Me), 2.84 s (2H, CH_2), 3.76 s and 3.78 s (3H each, OMe), 5.89 br.s (1H, NH), 6.61 s (1H, 3′-H), 6.62 s (1H, 6′-H), 7.25 s (1H, OH), 7.53 m (4H, H_{arom}). Found, %: C 55.69; H 5.65; N 3.42. $C_{19}H_{22}BrNO_4$. Calculated, %: C 55.89; H 5.43; N 3.43.

***N*-[2-(4-Hydroxy-2,6-dimethoxyphenyl)-1,1-dimethylethyl]benzamide (IIf).** Yield 86%, mp 177–179°C. IR spectrum, ν, cm^{-1}: 3348 (OH), 3215 (NH), 1646 (C=O), 1617 (C=C), 1584, 1284, 1232, 1210, 1181, 1158, 1141, 1101, 1064, 997, 937, 853, 777, 715. ^{1}H NMR spectrum, δ, ppm: 1.46 s (6H, Me), 2.29 s (2H, CH_2), 3.65 s (6H, OMe), 5.55 s (2H, 3′-H, 5′-H), 7.28 m (3H, 3-H, 4-H, 5-H), 7.66 m (2H, 2-H, 6-H); NH and OH signals were not observed because of fast proton exchange. Found, %: C 69.20; H 6.95; N 4.19. $C_{19}H_{23}NO_4$. Calculated, %: C 69.28; H 7.04; N 4.25.

***N*-[2-(4-Hydroxy-2,6-dimethoxyphenyl)-1,1-dimethylethyl]-4-methoxybenzamide (IIg).** Yield 86%, mp 174–175°C. IR spectrum, ν, cm^{-1}: 3450 (OH), 3414 (NH), 1649 (C=O), 1624 (C=C), 1606, 1592, 1513, 1314, 1285, 1262, 1238, 1217, 1183, 1171, 1158, 1029, 942, 873, 838. ^{1}H NMR spectrum, δ, ppm: 1.48 s (6H, Me), 2.27 s (2H, CH_2), 3.64 s (6H, OMe), 3.78 s (3H, OMe), 5.55 s (2H, 3′-H, 5′-H), 6.75 s (1H, 3-H), 6.76 s (1H, 5-H), 6.77 s (1H, 2-H), 6.78 s (1H, 6-H), 7.63 d (2H, 3-H, 5-H, ^4J = 2.1 Hz), 7.65 d (2H, 2-H, 6-H, J = 1.8 Hz); NH and OH signals were not observed because of fast proton exchange. Found, %: C 67.04; H 6.77; N 3.94. $C_{20}H_{25}NO_5$. Calculated, %: C 66.84; H 7.01; N 3.90.

***N*-[2-(4-Hydroxy-2,6-dimethoxyphenyl)-1,1-dimethylethyl]-3,4-dimethoxybenzamide (IIh).** Yield 67%, mp 157–159°C. IR spectrum, ν, cm^{-1}: 3579 (OH), 3407 (NH), 1650 (C=O), 1624 (C=C), 1586, 1522, 1418, 1319, 1269, 1239, 1225, 1170, 1156, 1064, 1026, 848. ^{1}H NMR spectrum, δ, ppm: 1.46 s (6H, Me), 2.28 s (2H, CH_2), 3.65 s (6H, OMe), 3,84 s (3H, OMe), 3.85 s (3H, OMe), 5.56 s (2H, 3′-H, 5′-H), 6.69 d (1H, 2-H, ^3J = 8.4 Hz), 7.18 d.d (1H, 6-H, ^3J = 8.4, ^4J = 2.1 Hz), 7.42 d (1H, 5-H, ^4J = 2.1 Hz); NH and OH signals were not observed because of fast proton exchange. Found, %: C 64.59; H 6.96; N 3.62. $C_{21}H_{27}NO_6$. Calculated, %: C 64.77; H 6.99; N 3.60.

4-Bromo-*N*-[2-(4-hydroxy-2,6-dimethoxyphenyl)-1,1-dimethylethyl]benzamide (IIi). Yield 66%, mp 136–140°C. IR spectrum, ν, cm^{-1}: 3361 br (NH, OH), 1649 (C=O), 1626 (C=C), 1592, 1285, 1238, 1215, 1158, 1069, 1005, 856, 834, 737, 719. ^{1}H NMR spectrum, δ, ppm: 1.45 s (6H, Me), 2.29 s (2H, CH_2), 3.65 s (6H, OMe), 5.55 s (2H, 3′-H, 5′-H), 7.39 d (2H, 3-H, 5-H, J = 9.0 Hz), 7.55 d (2H, 2-H, 6-H, J = 9.0 Hz); NH and OH signals were not observed because of fast proton exchange. Found, %: C 56.05; H 5.46; N 3.36. $C_{19}H_{22}BrNO_4$. Calculated, %: C 55.89; H 5.43; N 3.43.

***N*-[1-(4-Hydroxy-2,3-dimethoxybenzyl)cyclohexyl]benzamide (III).** Yield 82%, colorless crystals, mp 61–65°C, R_f 0.52. IR spectrum, ν, cm^{-1} (film): 3352 br (NH, OH), 3060, 3005, 2932, 2856, 1649 (C=O), 1602 (C=C), 1578 w, 1534, 1493, 1447, 1423, 1350, 1334, 1289, 1198, 1091, 1062, 1025, 755. ^{1}H NMR spectrum, δ, ppm: 1.37–1.59 m (8H, CH_2), 2.37 m (2H, CH_2), 3.05 s (2H, ArC**H**$_2$), 3.82 s and 3.83 s (3H each, OMe), 5.78 s (1H, NH), 6.00 br.s (1H, OH), 6.58 d (1H, 5′-H, J = 7.8 Hz), 6.74 d (1H, 6′-H, J = 7.8 Hz), 7.34–7.47 m (3H, 3-H, 4-H, 5-H), 7.71 d.d

(2H, 2-H, 6-H, ^3J = 8.4, ^4J = 1.8 Hz). Found, %: C 71.48; H 7.44; N 3.65. $C_{22}H_{27}NO_4$. Calculated, %: C 71.52; H 7.37; N 3.79.

Ethyl *N*-[2-(4-hydroxyphenyl)-1-methylcyclohexyl]malonamate hemihydrate (IV). Yield 64%, light yellow crystals, mp 99–103°C, R_f 0.34. IR spectrum, ν, cm^{-1} (film): 3348 br (NH, OH), 2979, 2931, 2858, 1723 (C=O, ester), 1659 (C=O, amide), 1614 (C=C), 1592 w, 1537, 1480, 1446, 1372, 1336, 1234, 1180, 1032, 832, 757. ^{1}H NMR spectrum, δ, ppm: 1.27 t (1.5H, Me, ^3J = 6.9 Hz), 1.28 t (1.5H, Me, ^3J = 6.9 Hz), 1.32–2.03 m (7H, cyclohexane), 2.47 m (1H, cyclohexane), 2.86 m (1H, ArC**H**), 3.21 s (1H, CH_2), 3.22 s (1H, CH_2), 4.21 q (2H, OCH_2, ^3J = 6.9 Hz), 6.05 s (1H, NH), 6.79 d (2H, 3′-H, 5′-H, ^3J = 8.7 Hz), 7.13 d (2H, 2′-H, 6′-H, ^3J = 8.7 Hz), 7.29 br.s (1H, OH). Found, %: C 66.58; H 7.69; N 4.05. $C_{18}H_{25}NO_4 \cdot 0.5H_2O$. Calculated, %: C 66.03; H 7.94; N 4.28.

***N*-[2-(4-Hydroxyphenyl)-1-methylcyclohexyl]-benzamide (V).** Yield 48%, colorless crystals, mp 102–104°C (decomp.; from hexane–CH_2Cl_2), R_f 0.44. IR spectrum, ν, cm^{-1} (film): 3287 br (NH, OH), 3015, 2975, 2930, 2856, 1650 (C=O), 1613 (C=C), 1578 w, 1514, 1486, 1443, 1372, 1314, 1273, 1235, 1177, 832, 756, 711. ^{1}H NMR spectrum, δ, ppm: 1.36 s (3H, Me), 1.38–2.06 m (7H, cyclohexane), 2.61 m (1H, cyclohexane), 3.20 m (1H, ArC**H**), 5.49 s (1H, NH), 6.09 br.s (1H, OH), 6.85 d (2H, 3′-H, 5′-H, ^3J = 8.4 Hz), 7.13 d (2H, 2′-H, 6′-H, ^3J = 8.4 Hz), 7.36–7.47 m (3H, 3-H, 4-H, 5-H), 7.65 d.d (2H, 2-H, 6-H, ^3J = 8.4 Hz, ^4J = 1.8 Hz). Found, %: C 77.35; H 7.20; N 4.41. $C_{20}H_{23}NO_2$. Calculated, %: C 77.64; H 7.49; N 4.53.

The authors thank V.I. Karmanov and I.A. Borisova for recording the IR spectra, O.A. Maiorova for recording the NMR spectra, and E.V. Baigacheva for performing elemental analysis. This study was performed under financial support by the Presidium of the Russian Academy of Sciences (program no. 21) and by a joint program of the Ural and Siberian Divisions of the Russian Academy of Sciences.

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