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Synthesis and Some Transformations of *N*,2,2-Trimethyltetrahydro-2*H*-pyran-4-amine

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Abstract—Reaction of 2,2-dimethyltetrahydro-2*H*-pyran-4-one with aqueous methanamine, followed by reduction of the Schiff base thus obtained with sodium tetrahydridoborate gave *N*,2,2-trimethyltetrahydro-2*H*-pyran-4-amine which was subjected to cyanoethylation with acrylonitrile. The resulting 3-(2,2-dimethyltetrahydro-2*H*-pyran-4-ylmethylamino)propanenitrile was reduced with lithium tetrahydridoaluminate to *N*-(2,2-dimethyltetrahydro-2*H*-pyran-4-yl)-*N*-methylpropane-1,3-diamine, and some chemical transformations of the latter were studied.

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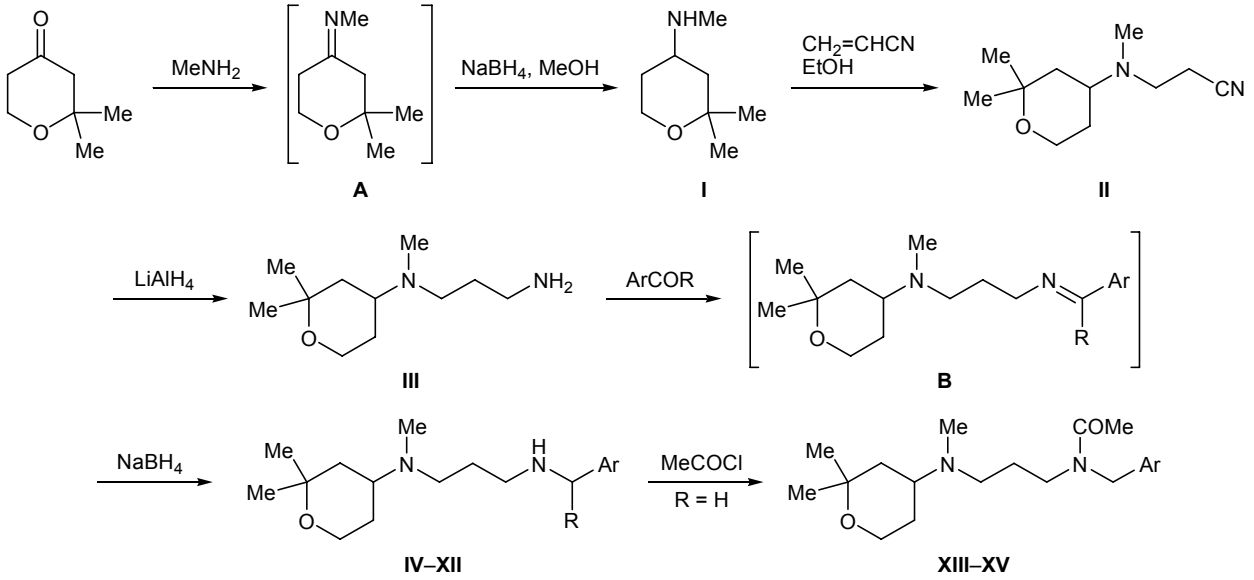
We previously synthesized 4-amino-substituted tetrahydropyrans which showed biological activity [1]. Some substituted diamines having a 3-aminopropylamino group in position *4* of the tetrahydro-2*H*-pyran ring may be valuable starting compounds for subsequent transformations.

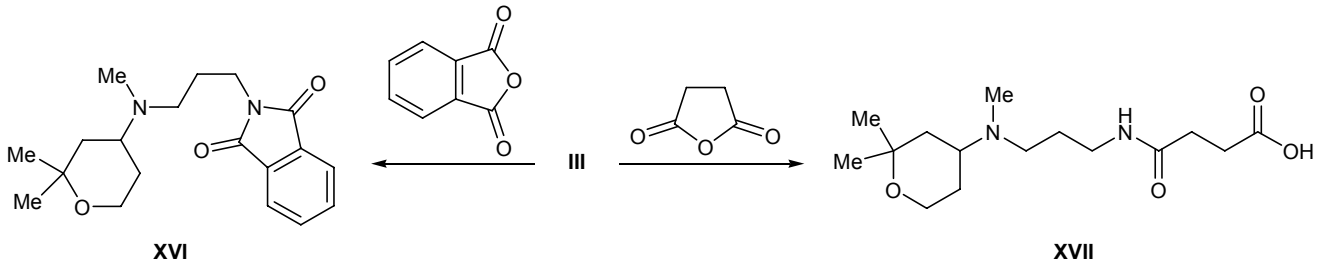
Schiff base **A** generated from 2,2-dimethyltetrahydro-2*H*-pyran-4-one and 25% aqueous methylamine was reduced with sodium tetrahydridoborate to *N*,2,2-trimethyltetrahydro-2*H*-pyran-4-amine (**I**). Compound **I** reacted with acrylonitrile to afford the corresponding cyanoethylation product, 3-(2,2-dimethyl-

Scheme 1.



IV–**X**, R = H; **XI**, **XII**, R = Me; **IV**, **XIV**, Ar = 4-$MeOC_6H_4$; **V**, **XII**, **XV**, Ar = 4-ClC_6H_4; **VI**, Ar = 3,4-$(MeO)_2C_6H_3$; **VII**, Ar = 2-FC_6H_4; **VIII**, Ar = 1,3-benzodioxol-5-yl; **IX**, **XIII**, Ar = furan-2-yl; **X**, Ar = thiophen-2-yl; **XI**, Ar = Ph.

Scheme 2.



XVI **XVII**

tetrahydro-2*H*-pyran-4-ylmethylamino)propanenitrile (**II**). Reduction of **II** with lithium tetrahydridoaluminate gave *N*-(2,2-dimethyltetrahydro-2*H*-pyran-4-yl)-*N*-methylpropane-1,3-diamine (**III**). Diamine **III** was brought into condensation with various aromatic aldehydes and ketones, and Schiff bases **B** thus formed were reduced (without isolation) with sodium tetrahydridoborate to the corresponding trimethylenediamines **IV**–**XII**. Amides **XIII**–**XV** were synthesized by treatment of amines **IV**, **V**, and **IX**, respectively, with acetyl chloride (Scheme 1). The reaction of **III** with phthalic anhydride led to the formation of 2-{3-[(2,2-dimethyltetrahydro-2*H*-pyran-4-yl)methylamino]-propyl}isoindole-1,3-dione (**XVI**), and 4-amino-*N*-[3-(2,2-dimethyltetrahydro-2*H*-pyran-4-ylmethylamino)-propyl]-4-oxobutanoic acid (**XVII**) was formed in the reaction of **III** with succinic anhydride (Scheme 2).

EXPERIMENTAL

The IR spectra were recorded on a Nicolet Avatar 330 FT-IR spectrometer. The ^{1}H NMR spectra were obtained on a Mercury VX-300 instrument at 300 MHz from solutions in DMSO-d_6, using tetramethylsilane as internal reference. 2,2-Dimethyltetrahydro-2*H*-pyran-4-one was synthesized according to the procedures described in [2, 3].

***N*,2,2-Trimethyltetrahydro-2*H*-pyran-4-amine (I).** A flask was charged with 64 g (0.5 mol) of 2,2-dimethyltetrahydro-2*H*-pyran-4-one, 75 ml of 25% aqueous methanamine was added over a period of 10 min, the flask was hermetically capped, and the mixture was stirred (the reaction was accompanied by heat evolution) and left overnight. The solution was then saturated with sodium chloride and extracted with ether, the extract was dried and evaporated, and the residue [yield of crude Schiff base **A** 54 g (76%)] was subjected to reduction. For this purpose, 0.38 mol of Schiff base **A** was dissolved in 250 ml of anhydrous methanol, and 14.4 g (0.8 mol) of sodium tetrahydridoborate was added in portions under stirring and cooling with ice water so that the temperature did not exceed 20°C. The mixture was stirred for 1 h at room temperature and left overnight, the solvent was distilled off, the residue was treated with a 20% solution of sodium hydroxide, the product was extracted into diethyl ether, and the extract was acidified with concentrated hydrochloric acid on cooling with ice water. The aqueous phase was extracted with diethyl ether to remove neutral impurities, neutralized with potassium carbonate, and extracted with diethyl ether. The extract was dried and evaporated, and the residue was distilled under reduced pressure. Yield 39.5 g (73%), bp 84°C (22 mm). IR spectrum: ν 3310 cm^{-1} (NH). ^{1}H NMR spectrum, δ, ppm: 1.20 br.s (1H, NH), 1.08 d.d (1H, 3-H, J = 12.7, 11.4 Hz), 1.17 s and 1.20 s (3H each, 2-CH_3), 1.18 m (1H, 5-H), 1.72 d.d.d (1H, 5-H, J = 12.7, 4.0, 2.0 Hz), 1.80 m (1H, 3-H), 2.39 s (3H, NCH_3), 2.65 t.t (1H, 4-H, J = 11.8, 4.0 Hz), 3.59 d.t.d (1H, 6-H, J = 12.5, 12.0, 2.3 Hz), 3.74 d.d.d (1H, 6-H, J = 12.0, 5.1, 1.9 Hz). Found, %: C 67.15; H 12.00; N 9.83. $C_8H_{17}NO$. Calculated, %: C 67.09; H 11.96; N 9.78.

3-(2,2-Dimethyltetrahydro-2*H*-pyran-4-ylmethylamino)propanenitrile (II). A mixture of 30 g (0.21 mol) of amine **I**, 22 g (0.41 mol) of freshly distilled acrylonitrile, and 170 ml of 96% ethanol was stirred and was then left to stand for three days at room temperature. The solvent and excess acrylonitrile were distilled off, and the residue was distilled under reduced pressure. Yield 32.8 g (80%), bp 132–135°C (4 mm). IR spectrum: ν 2245 cm^{-1} (C≡N). ^{1}H NMR spectrum, δ, ppm: 1.16 s (6H, CH_3), 1.24 t (1H, J = 12.2 Hz), 1.37 t.d (1H, C**H**$_2$CH$_2$CN, J = 12.2, 5.1 Hz), 1.60 m (2H, CH_2CN), 2.26 s (3H, NCH_3), 2.47 t (2H, J = 6.8 Hz), 2.70 t (2H, 3-H, 5-H, J = 6.8 Hz), 2.73 t.t (1H, CH, J = 12.2, 3.9 Hz), 3.52 t.d (1H, OCH_2, J = 12.0, 2.4 Hz), 3.67 d.d.d (1H, OCH_2, J = 12.0, 5.1, 1.9 Hz). Found, %: C 67.25; H 10.21; N 14.32. $C_{11}H_{20}N_2O$. Calculated, %: C 67.31; H 10.27; N 14.27.

***N*^{1}-(2,2-Dimethyltetrahydro-2*H*-pyran-4-yl)-*N*^{1}-methylpropane-1,3-diamine (III).** A solution of 21 g

(0.1 mol) of nitrile **II** in 100 ml of anhydrous diethyl ether was added dropwise under stirring and cooling to a solution of 8 g (0.21 mol) of lithium tetrahydridoaluminate in 250 ml of anhydrous diethyl ether, maintaining the temperature at 0±2°C. The mixture was stirred for 1 h at that temperature and cooled to –10°C with an ice–salt bath, 8 ml of water, 8 ml of a 15% solution of sodium hydroxide and 24 ml of water were added dropwise in succession, the inorganic material was filtered off and washed with diethyl ether, the filtrate was dried and evaporated, and the residue was distilled under reduced pressure. Yield 18 g (84%), bp 106°C (2 mm). IR spectrum, ν, cm^{-1}: 3362, 3300 (NH_2). ^1H NMR spectrum, δ, ppm: 1.15 s (6H, CH_3), 1.23 d.d (1H, 3-H, *J* = 12.8, 11.9 Hz), 1.35 q.d (1H, 5-H, *J* = 12.2 , 5.0 Hz), 1.50 q (2H, NCHC**H**$_2$, *J* = 6.8 Hz), 1.51–1.57 m (2H, 3-H, 5-H), 2.16 s (3H, NCH_3), 2.41 t (2H, NCH_2, *J* = 6.8 Hz), 2.65 t.t (1H, 4-H, *J* = 11.9, 3.8 Hz), 2.65 br (2H, NH_2), 2.98 m (2H, NCH_2), 3.51 t.d (1H, 6-H, *J* = 12.1, 2.4 Hz), 3.65 d.d.d (1H, 6-H, *J* = 11.8, 7.0, 1.9 Hz). Found, %: C 66.02; H 12.02; N 14.04. $C_{11}H_{24}N_2O$. Calculated, %: C 65.95; H 12.08; N 13.98.

Diamines IV–XII (*general procedure***).** A mixture of equimolar amounts of the corresponding aromatic aldehyde (or ketone) and amine **III** in benzene (or xylene in the reactions with aromatic ketones) was heated for 4 h under reflux in a flask equipped with a Dean–Stark trap until water no longer separated. The solvent was removed, the residue was dissolved in methanol (40 ml of methanol per 0.1 mol of Schiff base), and an equimolar amount of sodium tetrahydridoborate was added in portions under stirring and cooling with ice water so that the temperature did not exceed 20°C. The mixture was stirred for 1 h at room temperature, the solvent was distilled off, the residue was treated with a 20% solution of sodium hydroxide, the product was extracted into diethyl ether, the extract was dried and evaporated, and the residue was distilled under reduced pressure.

***N*^{1}-(2,2-Dimethyltetrahydro-2*H*-pyran-4-yl)-*N*^{3}-(4-methoxybenzyl)-*N*^{1}-methylpropane-1,3-diamine (IV).** Yield 78%, bp 200–205°C (3 mm). IR spectrum, ν, cm^{-1}: 1580, 1613 (C=C_{arom}); 3291 (NH). ^1H NMR spectrum, δ, ppm: 1.15 s (6H, CH_3), 1.23 d.d (1H, 3-H, *J* = 12.7, 12.0 Hz), 1.34 q.d (1H, 3-H, *J* = 12.7, 12.0 Hz), 1.34 q.d (1H, 5-H, *J* = 12.1, 5.1 Hz), 1.49–1.59 m (2H, 3-H, 5-H), 1.55 m (2H, NCH_2C**H**$_2$), 2.04 br.s (1H, NH), 2.16 s (3H, NCH_3), 4.42 t (2H, NCH_2, *J* = 7.0 Hz), 2.54 t (2H, NCH_2, *J* = 6.7 Hz), 2.64 t.t (1H, 4-H, *J* = 12.0, 3.8 Hz), 3.50 t.d (1H, 6-H, *J* = 12.1, 2.3 Hz), 3.62 s (2H, C**H**$_2$$C_6H_4$), 3.66 d.d.d (1H, 6-H, *J* = 11.8, 5.1, 1.9 Hz), 3.76 s (3H, OCH_3), 6.77 m and 7.17 m (2H each, C_6H_4). Found, %: C 71.40; H 10.16; N 8.54. $C_{19}H_{32}N_2O_2$. Calculated, %: C 71.21; H 10.06; N 8.74.

***N*^{3}-(4-Chlorobenzyl)-*N*^{1}-(2,2-dimethyltetrahydro-2*H*-pyran-4-yl)-*N*^{1}-methylpropane-1,3-diamine (V).** Yield 76%, bp 200–203°C (4 mm). IR spectrum, ν, cm^{-1}: 1597, 1600 (C=C_{arom}); 3290 (NH). ^1H NMR spectrum, δ, ppm: 1.14 s and 1.15 s (3H each, 2-CH_3), 1.22 d.d (1H, 3-H, *J* = 12.7, 12.0 Hz), 1.33 q.d (1H, 5-H, *J* = 12.1, 5.1 Hz), 1.48–1.58 m (2H, 3-H, 5-H), 1.55 m (2H, NCH_2C**H**$_2$), 1.66 br (1H, NH), 2.16 s (3H, NCH_3), 2.42 t (2H, CH_3NC**H**$_2$, *J* = 6.9 Hz), 2.54 t (2H, $HNCH_2$, *J* = 6.7 Hz), 2.64 t.t (1H, 4-H, *J* = 12.0, 3.8 Hz), 3.50 t.d (1H, 6-H, *J* = 12.1, 2.4 Hz), 3.65 d.d.d (1H, 6-H, *J* = 12.1, 5.1, 1.9 Hz), 3.68 s (2H, C**H**$_2$$C_6H_4$), 7.22–7.29 m (4H, C_6H_4). Found, %: C 66.45; H 8.92; N 8.53. $C_{18}H_{29}ClN_2O$. Calculated, %: C 66.54; H 9.00; N 8.62.

***N*^{3}-(3,4-Dimethoxybenzyl)-*N*^{1}-(2,2-dimethyltetrahydro-2*H*-pyran-4-yl)-*N*^{1}-methylpropane-1,3-diamine (VI).** Yield 68%, bp 210–215°C (1 mm). IR spectrum, ν, cm^{-1}: 1575, 1610 (C=C_{arom}); 3302 (NH). ^1H NMR spectrum, δ, ppm: 1.15 s (6H, 2-CH_3), 1.22 d.d (1H, 3-H, *J* = 12.8, 12.0 Hz), 1.34 q.d (1H, 5-H, *J* = 12.0, 5.0 Hz), 1.49–1.59 m (2H, 3-H, 5-H), 1.54 br (1H, NH), 1.55 q (2H, NCH_2C**H**$_2$, *J* = 6.8 Hz), 2.16 s (3H, NCH_3), 2.43 t (2H, NCH_2, *J* = 6.8 Hz), 2.54 t (2H, NCH_2, *J* = 6.8 Hz), 2.64 t.t (1H, 4-H, *J* = 12.0, 3.8 Hz), 3.50 t.d (1H, 6-H, *J* = 12.1, 2.4 Hz), 3.61 s (2H, C**H**$_2$$C_6H_3$), 3.65 d.d.d (1H, 6-H, *J* = 12.1, 5.2, 2.0 Hz), 3.77 s and 3.80 s (3H each, OCH_3), 6.74 d (2H, 5′-H, 6′-H, *J* = 1.2 Hz), 6.85 t (1H, 2′-H, *J* = 1.2 Hz). Found, %: C 68.60; H 9.81; N 7.95. $C_{20}H_{34}N_2O_3$. Calculated, %: C 68.54; H 9.78; N 7.99.

***N*^{1}-(2,2-Dimethyltetrahydro-2*H*-pyran-4-yl)-*N*^{3}-(2-fluorobenzyl)-*N*^{1}-methylpropane-1,3-diamine (VII).** Yield 76%, bp 170–173°C (2 mm). IR spectrum, ν, cm^{-1}: 1585, 1643 (C=C_{arom}); 3310 (NH). ^1H NMR spectrum, δ, ppm: 1.14 s (6H, CH_3), 1.22 t (1H, CH_2, pyran, *J* = 12.3 Hz), 1.35 q.d (1H, CH_2, pyran, *J* = 12.3, 5.1 Hz), 1.50 m and 1.53 m (1H each, CH_2, pyran), 1.56 m (2H, NCH_2C**H**$_2$), 1.58 br.s (1H, NH), 2.16 s (3H, NCH_3), 2.43 t (2H, NCH_2, *J* = 6.9 Hz), 2.56 t (2H, NCH_2, *J* = 6.5 Hz), 2.63 t.t (1H, 4-H, *J* = 12.0, 3.8 Hz), 3.50 t.d (1H, 6-H, *J* = 12.0, 2.1 Hz), 3.65 d.d.d (1H, 6-H, *J* = 12.0, 5.1, 1.9 Hz), 3.73 s (2H, C**H**$_2$$C_6H_4$); 6.98 m, 7.07 m, 7.18 m, and 7.37 m (1H each, C_6H_4). Found, %: C 70.15; H 9.44; N 9.03. $C_{18}H_{29}FN_2O$. Calculated, %: C 70.09; H 9.48; N 9. 08.

***N*^{3}-(1,3-Benzodioxol-5-ylmethyl)-*N*^{1}-(2,2-dimethyltetrahydro-2*H*-pyran-4-yl)-*N*^{1}-methylpropane-1,3-diamine (VIII).** Yield 75%, bp 205°C (2 mm). IR spectrum, ν, cm^{-1}: 1609, 1640 (C=C$_{arom}$); 3293 (NH). ^{1}H NMR spectrum, δ, ppm: 1.14 s (6H, CH_3), 1.22 t (1H, CH_2, pyran, J = 12.4 Hz), 1.35 t.d (1H, CH_2, pyran, J = 12.4, 5.1 Hz), 1.54 m (4H, CH_2, pyran, $NCH_2C\mathbf{H}_2$), 1.55 br (1H, NH), 2.15 s (3H, NCH_3), 2.42 t (2H, NCH_2, J = 6.9 Hz), 2.52 t (2H, NCH_2, J = 6.7 Hz), 2.64 t.t (1H, 4-H, J = 12.0, 3.8 Hz), 3.50 t.d (1H, 6-H, J = 12.1, 2.3 Hz), 3.59 s (2H, 5′-CH_2), 3.65 d.d.d (1H, 6-H, J = 11.7, 5.1, 1.7 Hz), 5.92 s (2H, OCH_2O), 6.65–6.71 m (2H, C_6H_3), 6.80 br (1H, C_6H_3). Found, %: C 68.28; H 9.10; N 8.43. $C_{19}H_{30}N_2O_3$. Calculated, %: C 68.23; H 9.04; N 8.38.

***N*^{1}-(2,2-Dimethyltetrahydro-2*H*-pyran-4-yl)-*N*^{3}-(furan-2-ylmethyl)-*N*^{1}-methylpropane-1,3-diamine (IX).** Yield 73%, bp 155–160°C (1.5 mm). IR spectrum, ν, cm^{-1}: 1600, 1650 (C=C$_{arom}$); 3390 (NH). ^{1}H NMR spectrum, δ, ppm: 1.14 s and 1.15 s (3H each, CH_3), 1.22 t (1H, 5-H, J = 12.4 Hz), 1.35 t.d (1H, 5-H, J = 12.4, 5.00 Hz), 1.48–1.60 m (2H, 3-H), 1.53 m (2H, $NCH_2C\mathbf{H}_2$), 1.57 br (1H, NH), 2.15 s (3H, NCH_3), 2.41 t (2H, $HNC\mathbf{H}_2$, J = 6.9 Hz), 2.54 t (2H, $CH_3NC\mathbf{H}_2$, J = 6.6 Hz), 2.63 t.t (1H, 4-H, J = 11.9, 3.8 Hz), 3.50 t.d (1H, 6-H, J = 12.0, 2.4 Hz), 3.65 d.d.d (1H, 6-H, J = 12.0, 5.1, 1.9 Hz), 3.65 s (2H, 2′-CH_2), 6.10 d.d (1H, 3′-H, J = 3.2, 0.8 Hz), 6.26 d.d (1H, 4′-H, J = 3.2, 1.8 Hz), 7.32 d.d (1H, 5′-H, J = 1.8, 0.8 Hz). ^{13}C NMR spectrum, δ_C, ppm: 21.7 (CH_3), 27.2 (CH_2), 28.0 (CH_2), 31.5 (CH_3), 36.7 (NCH_3), 38.6 (CH_2), 45.6 (CH_2), 46.9 (CH_2), 51.0 (CH_2), 55.9 (NCH), 60.0 (CH_2), 71.3 (C^2), 105.7 (=CH), 109.5 (=CH), 140.5 (=CH), 154.2 (=C). Found, %: C 68.59; H 10.10; N 10.04. $C_{16}H_{28}N_2O_2$. Calculated, %: C 68.53; H 10.06; N 9.99.

***N*^{1}-(2,2-Dimethyltetrahydro-2*H*-pyran-4-yl)-*N*^{1}-methyl-*N*^{3}-(thiophen-2-ylmethyl)propane-1,3-diamine (X).** Yield 74%, bp 168–170°C (2 mm). IR spectrum, ν, cm^{-1}: 1600, 1655 (C=C$_{arom}$); 3290 (NH). ^{1}H NMR spectrum, δ, ppm: 1.14 s (6H, 2-CH_3), 1.22 t (1H, J = 12.4 Hz), 1.34 d.t.d (1H, CH_2, pyran, J = 12.4, 12.0, 5.1 Hz), 1.49–1.60 m (4H, $NCH_2C\mathbf{H}_2$, CH_2, pyran), 1.73 br.s (1H, NH), 2.16 s (3H, NCH_3), 2.43 t (2H, $CH_3NC\mathbf{H}_2$, J = 6.9 Hz), 2.60 t (2H, $NHC\mathbf{H}_2$, J = 6.6 Hz), 2.64 t.t (1H, 4-H, J = 12.0, 3.8 Hz), 3.50 t.d (1H, 6-H, J = 12.0, 2.3 Hz), 3.65 d.d.d (1H, 6-H, J = 12.0, 5.1, 1.9 Hz), 3.88 s (2H, 2′-CH_2), 6.84–6.88 m (2H, 3′-H, 4′-H), 7.15 d.d (1H, 5′-H, J = 4.9, 1.4 Hz). Found, %: C 64.90; H 9.60; N 9.60. $C_{16}H_{28}N_2OS$. Calculated, %: C 64.82; H 9.52; N 9.45.

***N*^{1}-(2,2-Dimethyltetrahydro-2*H*-pyran-4-yl)-*N*^{1}-methyl-*N*^{3}-(1-phenylethyl)propane-1,3-diamine (XI).** Yield 70%, bp 193°C (3 mm). IR spectrum, ν, cm^{-1}: 1600, 1660 (C=C$_{arom}$); 3297 (NH). ^{1}H NMR spectrum, δ, ppm: 1.14 s (6H, CH_3), 1.21 t (1H, J = 12.3 Hz), 1.34 d (1H, CH_2, pyran, J = 12.3, 5.0 Hz), 1.27 d (3H, $C\mathbf{H}_3CH$, J = 6.6 Hz), 1.50 m (2H, $NCH_2C\mathbf{H}_2$), 1.48–1.57 m (2H, CH_2, pyran), 1.53 br.s (1H, NH), 2.13 s and 2.14 s (1.5H each, NCH_3), 2.31–2.48 m (4H, NCH_2), 2.62 t.t (1H, 4-H, J = 12.0, 3.7 Hz), 3.49 t.d (1H, 6-H, J = 12.0, 2.1 Hz), 3.65 m (1H, 6-H), 3.65 q (1H, $C\mathbf{H}CH_3$, J = 6.6 Hz), 7.10–7.26 m (5H, Ph). Found, %: C 74.90; H 10.65; N 9.14. $C_{19}H_{32}N_2O$. Calculated, %: C 74.95; H 10.59; N 9.20.

***N*^{3}-[1-(4-Chlorophenyl)ethyl]-*N*^{1}-(2,2-dimethyltetrahydro-2*H*-pyran-4-yl)-*N*^{1}-methylpropane-1,3-diamine (XII).** Yield 71%, bp 185–187°C (2 mm). IR spectrum, ν, cm^{-1}: 1594, 1651 (C=C$_{arom}$); 3279 (NH). ^{1}H NMR spectrum, δ, ppm: 1.14 s and 1.14 s (3H each, 2-CH_3), 1.21 d.d (1H, 3-H, J = 12.7, 12.0 Hz), 1.25 d (3H, $C\mathbf{H}_3CH$, J = 6.5 Hz), 1.32 q.d (1H, 5-H, J = 12.1, 5.1 Hz), 1.45–1.57 m (4H, 3-H, 5-H, $NCH_2C\mathbf{H}_2$), 1.60 br.s (1H, NH), 2.14 s (3H, NCH_3), 2.28–2.46 m (4H, CH_2NCH_2), 2.62 t.t (1H, 4-H, J = 12.0, 3.8 Hz), 3.49 t.d (1H, 6-H, J = 12.1, 2.4 Hz), 3.65 m (1H, 6-H), 3.65 q (1H, $C\mathbf{H}CH_3$, J = 6.5 Hz), 7.21–7.28 m (4H, C_6H_4). Found, %: C 67.25; H 9.18; N 8.40. $C_{19}H_{31}ClN_2O$. Calculated, %: C 67.33; H 9.22; N 8.27.

Amides XIII–XV (*general procedure*). A solution of 0.01 mol of acetyl chloride in 20 ml of anhydrous benzene was added dropwise to a mixture of 0.01 mol of amine **IV**, **V**, or **IX** and 0.01 mol of triethylamine in 50 ml of anhydrous benzene. The mixture was heated for 3 h under reflux, cooled, washed with water, and dried, the solvent was distilled off, and the residue was distilled under reduced pressure.

***N*-{3-[(2,2-Dimethyltetrahydro-2*H*-pyran-4-yl)-(methyl)amino]propyl}-*N*-(furan-2-ylmethyl)acetamide (XIII).** Yield 66%, bp 185–190°C (2 mm). IR spectrum, ν, cm^{-1}: 1600, 1650 (C=O). ^{1}H NMR spectrum (two stereoisomers at a ratio of 50:50), δ, ppm: 1.14 s and 1.15 s (3H each, CH_3), 1.23 m and 1.36 m (1H each, CH_2, pyran), 1.45–1.65 m (4H, $NCH_2C\mathbf{H}_2$ and CH_2, pyran), 2.04 s and 2.10 s (1.5H each, $COCH_3$), 2.14 br and 2.15 br (1.5H each, NCH_3), 2.35 m (2H, NCH_2), 2.64 m (1H, 4-H), 3.21–3.31 m (2H, NCH_2), 3.50 m and 3.62–3.70 m (1H each, 6-H), 4.44 s and 4.46 s (1H each, 2′-CH_2), 6.19 m and 6.23 m (0.5H each, 3′-H), 6.29 d.d and 6.32 d.d (0.5H each, 4′-H, J = 3.1, 1.9 Hz), 7.36 d.d (0.5H, 5′-H, J =

1.9, 0.8 Hz), 7.42 d.d (0.5H, 5′-H, J = 1.9, 0.8 Hz). Found, %: C 67.10; H 9.34; N 8.73. $C_{18}H_{30}N_2O_3$. Calculated, %: C 67.05; H 9.38; N 8.69.

***N*-{3-[(2,2-Dimethyltetrahydro-2*H*-pyran-4-yl)-(methyl)amino]propyl}-*N*-(4-methoxybenzyl)acetamide (XIV).** Yield 70%, bp 235–240°C (3 mm). IR spectrum, ν, cm^{-1}: 1610, 1650 (C=C_{arom}); 1690 (C=O). ^{1}H NMR spectrum (two stereoisomers at a ratio of 57:43), δ, ppm: 1.12 s and 1.14 s (3H each, 2-CH_3), 1.21 d.d (1H, 3-H, J = 12.7, 12.0 Hz), 1.32 q.d (1H, 5-H, J = 12.1, 5.0 Hz), 1.44–1.57 m (2H, 3-H, 5-H), 1.59 m (2H, $NCH_2C\mathbf{H}_2$), 2.01 s (1.3H) and 2.06 s (1.7H) (CH_3CO), 2.11 s (1.3H) and 2.12 s (1.7H) (NCH_3), 2.32 t (1.1H, J = 6.5 Hz) and 2.33 t (0.9H, J = 6.9 Hz) ($CH_3NC\mathbf{H}_2$), 2.62 t.t (0.6H) and 2.63 t.t (0.4H) (4-H, J = 12.1, 3.8 Hz), 3.20 m (2H, $NC\mathbf{H}_2CH_2$), 3.48 t.d (1H, 6-H, J = 12.0, 2.3 Hz), 3.64 m (1H, 6-H), 3.75 s (1.7H) and 3.76 s (1.3H) (OCH_3), 4.41 s (1.1H) and 4.43 s (0.9H) ($C\mathbf{H}_2C_6H_4$), 6.75–6.86 m and 7.04–7.14 m (2H each, C_6H_4). Found, %: C 69.50; H 9.50; N 7.80. $C_{21}H_{34}N_2O_3$. Calculated, %: C 69.58; H 9.45; N 7.73.

***N*-(4-Chlorobenzyl)-*N*-{3-[(2,2-dimethyltetrahydro-2*H*-pyran-4-yl)(methyl)amino]propyl}acetamide (XV).** Yield 71%, bp 225–230°C (3 mm). IR spectrum, ν, cm^{-1}: 1690 (C=O); 1580, 1650 (C=C_{arom}). ^{1}H NMR spectrum (two stereoisomers at a ratio of 65:35), δ, ppm: 1.13 s and 1.15 s (3H each, CH_3), 1.22 m (1H, 3-H), 1.33 m (1H, 5-H), 1.44–1.66 m (4H, 3-H, 5-H, $NCH_2C\mathbf{H}_2$), 2.00 s (1H) and 2.09 s (2H) (CH_3CO), 2.12 s (1H) and 2.13 s (2H) (NCH_3), 2.34 m (2H, $CH_3NC\mathbf{H}_2$), 2.63 m (1H, 4-H), 3.23 m (2H, $NC\mathbf{H}_2CH_2$), 3.49 t.d (1H, 6-H, J = 12.0, 2.3 Hz), 3.65 d.d.d (1H, 6-H, J = 12.0, 5.1, 1.9 Hz), 4.47 s (1.3H) and 4.51 s (0.7H) ($C\mathbf{H}_2C_6H_4$), 7.16–7.34 m (4H, C_6H_4). Found, %: C 65.53; H 8.60; N 7.70. $C_{20}H_{31}ClN_2O_2$. Calculated, %: C 65.47; H 8.52; N 7.63.

Compounds XVI and XVII (*general procedure*). A mixture of equimolar amounts of diamine **III** and phthalic or succinic anhydride in benzene was heated for 10 h under reflux in a flask equipped with a Dean–Stark trap until water no longer separated. The solvent was removed, and the residue was distilled under reduced pressure or recrystallized from ethanol).

2-{3-[(2,2-Dimethyltetrahydro-2*H*-pyran-4-yl)-(methyl)amino]propyl}-2,3-dihydro-1*H*-isoindole-1,3-dione (XVI). Yield 70%, bp 208–210°C (2 mm). IR spectrum, ν, cm^{-1}: 1540, 1570 (C=C_{arom}); 1620, 1670 (C=O). ^{1}H NMR spectrum, δ, ppm: 1.13 s and 1.14 s (3H each, CH_3), 1.21 t (1H, J = 12.4 Hz) and 1.33 d.t.d (1H, J = 12.4, 12.0, 5.0 Hz) (CH_2, pyran), 1.50 m (2H, CH_2, pyran), 1.75 m (2H, $NCH_2C\mathbf{H}_2$), 2.16 s (3H, NCH_3), 2.48 t (2H, $CH_3NC\mathbf{H}_2$, J = 6.7 Hz), 2.69 t.t (1H, 4-H, J = 12.0, 3.8 Hz), 3.50 t.d (1H, 6-H, J = 12.0, 2.4 Hz), 3.64 m (1H, 6-H), 3.65 m (2H, NCH_2), 7.74–7.84 m (4H, C_6H_4). Found, %: C 69.00; H 8.00; N 8.54. $C_{19}H_{26}N_2O_3$. Calculated, %: C 69.06; H 7.93; N 8.48.

4-{3-[(2,2-Dimethyltetrahydro-2*H*-pyran-4-yl)-(methyl)amino]propylamino}-4-oxobutanoic acid (XVII). Yield 72%, mp 152°C. IR spectrum, ν, cm^{-1}: 1660 (C=O, amide), 3232–3500 (OH). ^{1}H NMR spectrum, δ, ppm: 1.15 s (6H, CH_3), 1.24 t (1H, J = 12.4 Hz) and 1.35 d.t.d (1H, J = 12.4, 12.0, 5.1 Hz) (CH_2, pyran), 1.49–1.62 m (4H, $NCH_2C\mathbf{H}_2$ and CH_2, pyran), 2.17 s (3H, NCH_3), 2.29 m (2H, $CH_3NC\mathbf{H}_2$), 2.38–2.45 m [4H, $C(O)CH_2CH_2C(O)$], 2.68 t.t (1H, 4-H, J = 12.0, 3.7 Hz), 3.07 t.d (2H, $HNC\mathbf{H}_2$, J = 6.8, 5.8 Hz), 3.51 t.d (1H, J = 12.0, 2.3 Hz) and 3.66 d.d.d (1H, J = 12.0, 5.2, 1.9 Hz) (6-H), 4.95 br (1H, COOH), 7.51 t (1H, NH, J = 5.8 Hz). Found, %: C 60.00; H 9.65; N 9.45. $C_{15}H_{28}N_2O_4$. Calculated, %: C 59.98; H 9.40; N 9.33.

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