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SYNTHESIS OF N^1, N^2- ARYL-, ARYLALKYL- AND HETERYLALKYL-SUBSTITUTED OXALIC ACID DIAMIDE

S.O. VARDANYAN, A.B. SARGSYAN, A.S. AVAGYAN*, N.H.PAHUTYAN, H.V.GASPARYAN, A.A. AGHEKYAN

The Scienctific Technological Centre of Organic and Pharmaceutical Chemistry NAS RA,
0014, Republic of Armenia, Yerevan, av. Azatutyan, 26
*E-mail: avagal@mail.ru

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Based on monoethyl esters of oxalic acid amides obtained earlier by the reaction of arylcyclopentylmethyl-, aryltetrahydropyranylmethyl-, isochromanyl-1-methyl-, (1,4-benzodioxan-2-yl)-methyl- and 1-(1,4-benzodioxan-2- yl)-ethyl amines with oxalic acid diethyl ester, by the action of various primary amines, target substituted oxalic acid diamides were synthesized. For the synthesis of diamides containing anilide fragments, ethyl esters of substituted oxalic acid N-arylamides were used, which were reacted with the above arylalkyl- and heterylalkylamines. The antioxidant activity of the synthesized compounds has been studied.

References 10.

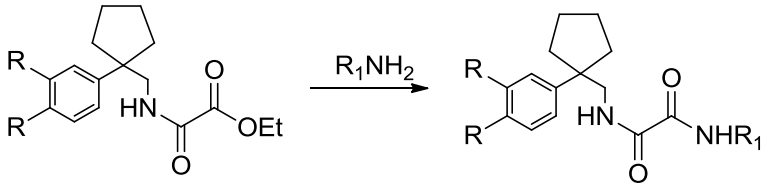
Key words: diamides, oxalic acid, 1,4-benzodioxane-2-ylalkylamines, isochromanylmethylamine, arylcyclopentylmethylamine, diethyloxalate, antioxidant activity.

Compounds with potential biological activity, as a rule, include pharmacophore fragments that are part of the structure of drugs widely used in medical practice. For example, it is known that various derivatives of arylcyclopentylmethylamines and aryltetrahydropyranmethylamines have a wide spectrum of biological activity [1,2]. Isochromane derivatives, as well as 1,4-benzodioxane, containing various substituents in the heterocyclic ring, exhibit adrenolytic, antiarrhythmic, antibacterial, and other properties [3].Since it was shown that mono- and diamides of dicarboxylic acids have low toxicity and exhibit high pharmacological activity [4], we previously

carried out the synthesis of substituted oxaldiamides. Among them, compounds with pronounced antihypoxic activity were identified [5].

In this work, we present a targeted synthesis of new diamide derivatives of oxalic acid containing arylcycloalkane, aryltetrahydropyrane, isochromane, and 1,4-benzodioxane fragments.

The target diamides **3-6** were obtained by the reaction of previously synthesized monoamides of arylcyclopentylmethylamines (**1,2**)[6,7] with various primary amines.



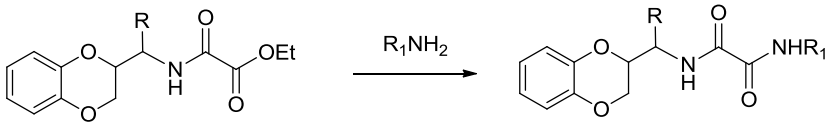
1, 2 **3-6**

R=H (**1**) , CH_3O(**2**)

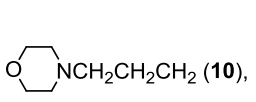
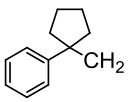
R=H, R_1= $(CH_2)_3OH$ (**3**), $(CH_2)_2N(CH_2CH_2)_2O$ (**4**)

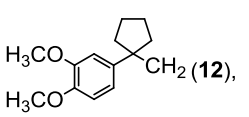
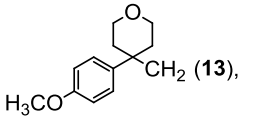
R= CH_3O, R_1= CH_3 (**5**), $CH_2C_6H_5$ (**6**)

To compare biological properties, we also synthesized compounds in which arylalkyl radicals were replaced by heterylalkyl fragments - 1,4-benzodioxane-2-alkyl and 1-isochromanylmethyl. For this, we used the previously obtained 1,4-benzodioxanylalkyl- and isochromanylmethylmonoamidoesters of oxalic acid **7, 8,18** [5], which were converted into the target diamides **9-17** and **19, 20** by the action of primary amines.

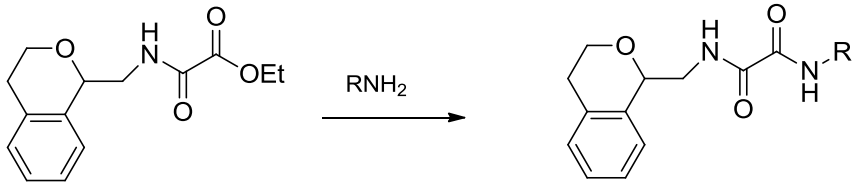


7.R=H, **8**.R=CH_3 **9-17**

R=H: R_1= $(CH_3O)_2C_6H_3CH_2CH_2$(**9**),  (**10**),  (**11**),

 (**12**),  (**13**),  (**14**).

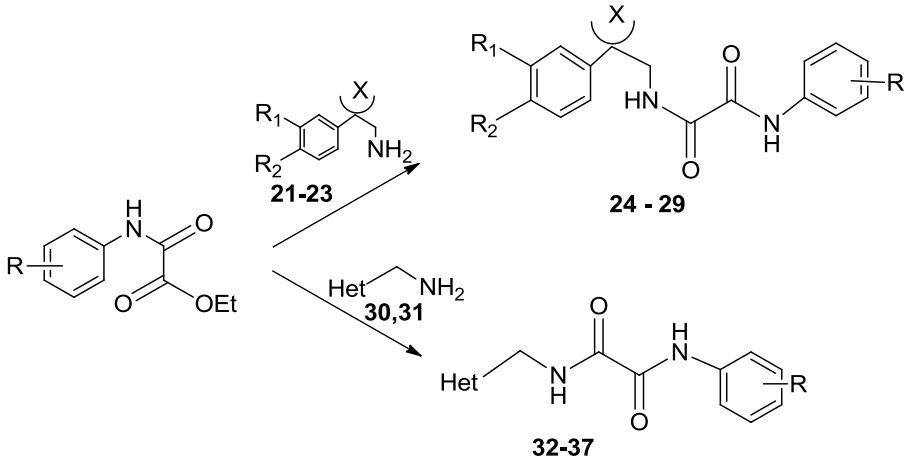
R=CH_3: R_1= $(CH_3)_2CHCH_2$ (**15**), $C_6H_5CH_2$ (**16**), $(CH_3O)_2C_6H_3CH_2CH_2$ (**17**)



18 **19, 20**

R=C_6H_{11} (**19**), $C_4H_3OCH_2$ (**20**)

Diamide derivatives with a substituted aniline fragment were synthesized by the interaction of the above mentioned arylalkylamines **21-23** [6-8], 1-isochromanylmethylamine **30** and (1,4-benzodioxan-2-yl)methylamine **31** [5] with the previously known anilidoethers obtained by us, since substituted aromatic amines practically do not react with the monoester of substituted oxalic acid amide, while they react relatively easily with diethyl ester of oxalic acid, forming anilidoesters. The synthesis was carried out according to the scheme:



X=$(CH_2)_4$: R_1=R_2=H, R=2,4-$(OCH_3)_2$(**24**); R_1=R_2=OCH_3, R=4-OCH_3 (**25**), 2-CH_3,5-OCH_3 (**26**).

X=$(CH_2CH_2)_2O$: R_1=H, R_2=OCH_3, R=3,4-$(CH_3)_2$ (**27**), R=3-CF_3 (**28**), R=3-Cl,4-CH_3 (**29**) .

Het= isochroman-1-yl-methyl: R=3,4-$(CH_3)_2$ (**32**), R=3-CF_3 (**33**), R=3-Cl,4-CH_3 (**34**).

Het=1,4-benzodioxanyl-2-ylmethyl: R=3-Cl,4-CH_3 (**35**), R=3,4-$(CH_3)_2$ (**36**), R=3-CF_3 (**37**).

The structure and purity of the synthesized compounds were confirmed by physicochemical methods and thin layer chromatography.

The antioxidant activity of synthesized compounds in rat brain and liver homogenates was studied in experiments in vitro [9,10]. The antioxidant activity was judged by the percentage changes in the amount of malondialdehyde (MDA) in the experimental samples compared to the control. Compounds were studied at a concentration of 10^{-3} M . A sample was used as a control, where a solvent was added instead of compounds.

The results of the studies showed that all compounds exhibit an antioxidant effect to varying degrees. Some compounds are strong antioxidants that reduce the intensity of oxidative processes in the body. The percentage difference from control in the brain for these compounds is: **3** (70.32%), **4** (89.21%), **6** (89.03%), **9** (83.79%), **10** (79.74%), **14** (90.89%), **28** (87.84 %), and in the liver: **3** (70.32%), **4** (86.21%), **6** (75.68%), **9** (75.05%), **10** (80.42%), **14** (87.16%), **28** (82.1%). The other compounds exhibit a moderate inhibitory effect.

Experimental part

The IR spectra of the compounds were taken on a Nicolet Avatar 330 FT-IR spectrometer in vaseline oil, ^{1}H and ^{13}C NMR spectra - on a Varian Mercury-300 instrument with a frequency of 300.8 and 75.46*MHz*, respectively, solvent: DMSO/CCl4 - 1:3, internal standard - TMS.Melting points were determined on a Boetius microheater. TLC was carried out on Silufol UV-254 plates (eluent, benzene-acetone, 3:1; developer, iodine vapour).

Oxalamides 3-6, 9-17, 19, 20 (general procedure). A mixture of 5*mmol* of amidoesters **1,2, 7, 8, 18** and 5 *mmol* of the corresponding amine in 30*mL* of ethanol was refluxed for 8 *h* (in the reaction with methylamine, the mixture was kept for 18*h* at room temperature). The solvent was distilled off, the residue was treated with hexane, and the precipitate was filtered off and recrystallized from ethanol.

N^1-(3-Hydroxypropyl)-N^2-((1-phenylcyclopentyl)methyl)oxalamide (**3**). Yield 83%, m.p.105-106℃ R_f 0.40. IR spectrum, ν, cm^{-1}: 3258 (NH-amide), 1669 (C=O). ^{1}H NMR spectrum, δ, ppm, Hz: 1.58 – 1.67 m (2H, CH_2CH_2OH); 1.59–2.02 m (8H, 4 CH_2, C_5H_8), 3.25 t.d (2H, J = 6.8 and 6.0, $NC\underline{H}_2$ CH_2CH_2OH); 3.35 d (2H, J=6.5, NCH_2); 3.46 t.d (2H, J = 5.9 and 5.6, OCH_2); 4.15 t (1H, J = 5.6, OH); 7.13 - 7.22 m (1H) and 7.24 - 7.33 m (4H, C_6H_5); 7.47 br.t (1H, J = 6.5, $HNCH_2$); 8.46 br. t (1H, J = 6.0, $HNCH_2CH_2$). ^{13}C NMR spectrum, δ, ppm: 22.9 (2 CH_2), 31.3(CH_2), 34.8 (2 CH_2), 36.2 (NCH_2), 47.4 (NCH_2), 51.4 (C), 58.3 (OCH_2), 125.6 (CH),

126.3(2CH), 127.8(2CH), 145.9, 159.2(CO), 159.4(CO). Found, *%*: C 67.33; H 8.24; N 9.48. $C_{17}H_{24}N_2O_3$. Calculated, *%*: C 67.08; H 7.95; N 9.20.

N^1-(2-Morpholinoethyl)-N^2-((1-phenylcyclopentyl)methyl)oxalamide (4). Yield 77*%*, m.p.118-120 ^oC, R_f 0.43. IR spectrum, ν, cm^{-1}: 3259 (NH-amide), 1665 (C=O). ^{1}H NMR spectrum, δ, ppm, Hz: 1.63 – 2.02 m (8H, 4 CH_2, C_5H_8), 2.39 – 2.43 m (4H, $N(CH_2)_2$ morph.); 2.43 t (2H, J=6.6, NCH_2); 3.25t.d (2H, J = 6.6 and 6.0, $HNCH_2$); 3.35 d (2H, J=6.5, $HNCH_2$); 3.56 – 3.60 m (4H, $O(CH_2)_2$ morph.); 7.13 - 7.22 m (1H) and 7.23 - 7.33 m (4H, C_6H_5); 7.44 br.t (1H, J = 6.5, $HNCH_2$); 8.31 br. t (1H, J = 6.0, $HNCH_2CH_2$). ^{13}C NMR spectrum, δ, ppm: 22.8 (2 CH_2), 34.7 (2 CH_2), 35.6 (NCH_2), 47.3 (NCH_2), 51.4 (C), 52.9 ($N(CH_2)_2$ morph), 56.5 (NCH_2), 65.9 ($O(CH_2)_2$ morph), 125.5 (CH), 126.2(2 CH), 127.7 (2 CH), 145.8, 159.0 (CO), 159.2 (CO). Found, *%*: C 67.13; H 8.34, N 11.92 $C_{20}H_{29}N_3O_3$. Calculated, *%*: C 66.83, H 8.13, N 11.69.

N^1-((1-(3,4-Dimethoxyphenyl)cyclopentyl)methyl)-N^2-methyloxalamide (5). Yield 72*%*, m.p. 125-127 ^oC, R_f 0.50. IR spectrum, ν, cm^{-1}: 3245 (NH-amide), 1665 (C=O). ^{1}H NMR spectrum, δ, ppm, Hz: 1.65 – 2.02 m (8H, 4 CH_2); 3.38 d (2H, J=6.5, NCH_2); 3.77 s (3H, OCH_3); 3.79 s (3H, OCH_3); 6.78 – 6.85 m (3H, C_6H_3); 7.65 br.t (1H, J = 6.5, HN); 8.45br. t (1H, J=5.0, NH). Found, *%*: C 63.99; H 7.80; N 8.51. $C_{17}H_{24}N_2O_4$. Calculated, *%*: C 63.73; H 7.55; N 8.74.

N^1-Benzyl-N^2-((1-(3,4-Dimethoxyphenyl)cyclopentyl)methyl)oxalamide (6). Yield 78*%*, m.p.126-128 ^oC, R_f 0.52. IR spectrum, ν, cm^{-1}: 3250 (NH-amide), 1650 (C=O). ^{1}H NMR spectrum, δ, ppm, Hz: 1.66 – 2.01 m (8H, 4 CH_2 C_5H_8), 3.34d (2H, J = 6.5, NCH_2); 3.79 s (3H, OCH_3); 3.80 s (3H, OCH_3); 4.35 d (2H, J = 6.5, CH_2Ph); 6.75 - 6.83m (3H, C_6H_3); 7.17 - 7.30 m (5H, C_6H_5)7.56 br.t (1H, J = 6.5, $HNCH_2$); 9.02 br. t (1H, , J =6.5, $HNCH_2Ph$). ^{13}C NMR spectrum, δ, ppm: 22.9 (2 CH_2), 35.0 (2 CH_2), 42.5 (CH_2), 47.4 (CH_2), 51.1 (C), 55.2 (2 OCH_3), 111.1 (CH), 111.5 (CH), 118.4 (CH), 126.4 (CH), 127.3(2 CH), 127.7 (2 CH), 138.2, 138.4, 147.3, 148.6, 159.3, 159.4. Found, *%*: C 69.92; H 7.41; N 6.89. $C_{23}H_{28}N_2O_4$. Calculated, *%*: C 69.67; H 7.12; N 7.07.

N^1-(1,4-Benzodioxan-2-yl)methyl)-N^2-(3,4-dimethoxyphenethyl)oxalamide (9). Yield 70*%*, m.p.144-146 ^oC, R_f 0.47. IR spectrum, ν, cm^{-1}: 3252 (NH-amide), 1657 (C=O). ^{1}H NMR spectrum, δ, ppm, Hz: 2.75 t (2H, J = 7.1, NCH_2); 3.38 d (2H, J=6.5, NCH_2); 3.45 t.d (2H, J = 7.1, 5.7, NCH_2); 3.77 s (3H, OCH_3); 3.80 s (3H, OCH_3); 3.88 d.d (1H, J = 11.9 and 7.8, OCH_2); 4.28 -4.33 m (2H, OCH_2 and OCH); 6.71 – 6.82 m (7H, Ar); 8.53 br.t (1H, J = 5.7, NH); 8.80 br.t (1H, J = 6.5, NH). Found, *%*: C 63.22; H 6.39; N 7.30. $C_{21}H_{24}N_2O_6$. Calculated, *%*: C 62.99; H 6.04; N 7.00.

N^1-(1,4-Benzodioxan-2-yl)methyl)-N^2-(3-morpholinopropyl)oxalamide(10). Yield 73*%*, m.p.156-157 ^oC, R_f 0.43. IR spectrum, ν, cm^{-1}: 3258

(NH-amide), 1669 (C=O). ^{1}H NMR spectrum, δ, ppm, Hz: 1.68 m (2H, CH_2); 2.36 – 2.42 m (6H, $N(CH_2)_3$); 3.27 t.d (2H, J = 6.8 and 5.9, NCH_2CH_2); 3.43d.t (1H, J = 13.6 and 6.5, NCH_2 CHO); 3.54 d.t (1H, J = 13.6 and 5.9, NCH_2 CHO); 3.60 – 3.65 m (4H, $O(CH_2)_2$); 3.89 d.d (1H, J = 11.9 and 7.9, OCH_2); NCH_2CH); 4.23 - 4.31 m (2H, OCH_2 and OCH); 6.70–6.82 m (4H, C_6H_4); 8.77 br.t (1H, J = 6.5, NH); 8.82 br.t (1H, J = 5.9, NH).^{13}C NMR spectrum, δ, ppm: 24.7(CH_2), 38.0(NCH_2), 39.1(NCH_2), 53.1 ($N(CH_2)_2$), 56.6 (NCH_2), 65.5 (OCH_2), 65.8 ($O(CH_2)_2$), 70.9 (OCH), 116.4(CH), 116.7(CH), 120.5 (CH), 120.7 (CH), 142.5, 142.7, 158.9, 160.2. Found, %: C 59.81; H 6.70; N 11.79. $C_{18}H_{25}N_3O_5$. Calculated, %: C 59.49; H 6.93; N 11.56.

N^1-(1,4-Benzodioxan-2-yl)methyl)-N^2-((1-phenylcyclopentyl)-methyl)oxalamide (11). Yield 71%, m.p.102-104 ^oC, R_f 0.48. IR spectrum, ν, cm^{-1}: 3260 (NH-amide), 1667 (C=O). ^{1}H NMR spectrum, δ, ppm, Hz: 1.64 – 2.05 m (8H, 4 CH_2 C_5H_8), 3.35 d (2H, J = 6.5, NCH_2); 3.40 d.t (1H, J = 13.7 and 6.6, NCH_2); 3.49 d.t (1H, J = 13.7 and 6.0, NCH_2); 3.85 d.d (1H, J = 11.9 and 7.8, OCH_2); 4.25 -4.32 m (2H, OCH_2 and OCH); 6.72 - 6.80 m (4H, C_6H_4); 7.15-7.24 m (1H) and 7.26-7.36 m (4H, C_6H_5); 7.51 br.t (1H, J = 6.5, NH); 8.82 br.t (1H, J = 6.3, NH). Found, %: C 70.34; H 6.87; N 7.41. $C_{23}H_{26}N_2O_4$. Calculated, %: C 70.03; H 6.64; N 7.10.

N^1-(1,4-Benzodioxan-2-yl)methyl)-N^2-((1-(3,4-dimethoxyphenyl)cyclopentyl)-methyl)-oxalamide (12). Yield 69%, m.p.98-100 ^oC, R_f 0.46. IR spectrum, ν, cm^{-1}: 3258 (NH-amide), 1663 (C=O). ^{1}H NMR spectrum, δ, ppm, Hz: 1.64 – 2.00 m (8H, 4 CH_2 C_5H_8), 3.32d (2H, J = 6.5, NCH_2); 3.40 d.t (1H, J = 13.7 and 6.6, NCH_2); 3.49 d.t (1H, J = 13.7 and 6.0, NCH_2); 3.77 s (3H, OCH_3); 3.80 s (3H, OCH_3); 3.86 d.d (1H, J = 11.9 and 7.8, OCH_2); 4.20 -4.28 m (2H, OCH_2 and OCH); 6.72 - 6.81 m (7H, Ar); 7.53 br.t (1H, J = 6.3, NH); 8.82 br.t (1H, J = 6.5, NH). ^{13}C NMR spectrum, δ, ppm: 22.8 (2 CH_2), 35.0 (2 CH_2), 39.2(NCH_2), 47.4 (NCH_2), 51.1 (C), 55.1 (OCH_3), 55.2 (OCH_3), 65.4 (OCH_2), 70.9 (OCH) 111.1(CH), 111.4 (CH), 116.4(CH), 116.7(CH), 118.3(CH), 120.5 (CH), 120.7 (CH), 138.4, 142.5,142.7, 147.3, 148.5, 158.9, 159.9. Found, %: C 66.31; H 6.89; N 6.35. $C_{25}H_{30}N_2O_6$. Calculated, %: C 66.06; H 6.65; N 6.16.

N^1-(1,4-Benzodioxan-2-yl)methyl)-N^2-((4-(4-methoxyphenyl)tetra-hydro-2*H*-pyran-4-yl)-methyl)oxalamide (13). Yield 68%, m.p.106-108 ^oC, R_f 0.50. IR spectrum, ν, cm^{-1}: 3264 (NH-amide), 1672 (C=O). ^{1}H NMR spectrum, δ, ppm, Hz: 1.82 d.d.d (2H, J = 14.0, 8.9 and 3.6, CH_2); - 2.03 br.d (2H, J = 14.0, CH_2); 3.34d (2H, J = 6.5, NCH_2); 3.34 – 3.54 m (4H,$O(CH_2)_2$); 3.66 – 3.76 m (2H, NCH_2CH); 3.78 s (3H, OCH_3); 3.87 d.d (1H, J = 11.9 and 7.8, OCH_2); 4.19 - 4.28 m (2H, OCH_2 and OCH); 6.71–6.81 m (4H, C_6H_4); 6.84 – 6.89 m (2H, C_6H_4OMe); 7.20 - 7.25 m (2H, C_6H_4OMe); 7.68 br.t (1H, J = 6.1, NH); 8.82 br.t (1H, J = 6.5, NH). ^{13}C

NMR spectrum, δ, ppm: 33.0 (2 CH_2), 39.2 (CH_2), 39.7(C), 49.0(NCH_2), 54.4 (OCH_3), 63.0 ($O(CH_2)_2$), 65.4 (OCH_2) , 70.9 (OCH), 113.5(2CH), 116.4(CH), 116.6(CH), 120.5(CH), 120.7(CH), 127.3(2CH), 134.3, 142.5,142.7, 157.4, 159.1, 159.8. Found, *%*: C 65.87; H 6.77; N 6.70. $C_{24}H_{28}N_2O_6$. Calculated, *%*: C 65.44; H 6.41; N 6.36.

N^1-(1,4-Benzodioxan-2-yl)methyl)-N^2-(1,3,4-thiadiazol-2-yl)oxalamide (14). Yield 64*%*, m.p. 196-198 ^oC, R_f 0.42. IR spectrum, ν, cm^{-1}: 3272 (NH-amide), 1667 (C=O). ^{1}H NMR spectrum, δ, ppm, Hz: 3.41 d.t (1H, J = 13.7 and 6.6, NCH_2); 3.50d.t (1H, J = 13.7 and 6.0, NCH_2); 3.86 d.d (1H, J = 11.9 and 7.5, CH_2O); 4.25 - 4.40 m (2H, OCH_2 and OCH); 6.75–6.84 m (4H, C_6H_4); 9.11 s (1H, =CH); 9.28 br.t (1H, J = 6.3, N<u>H</u>CH_2); 12.81 br.s (1H, NH). Found, *%*: C 48.96; H 4.00; N 17.72. $C_{13}H_{12}N_4O_4S$. Calculated, *%*: C 48.74; H 3.78; N 17.49.

N^1-(1-(1,4-Benzodioxan-2-yl)ethyl)-N^2-isobutyloxalamide (15). Yield 68*%*, m.p.148-150 ^oC, R_f 0.49. IR spectrum, ν, cm^{-1}: 3263 (NH-amide), 1671 (C=O). ^{1}H NMR spectrum, δ, ppm, Hz: two diastereoisomers 60/40%: 0.91 d (2.4H, J = 6.6) and 0.92 d (3.6H, J = 6.6 $(CH_3)_2$); - 1.33 d (1.2H, J = 6.6) and 1.34 d (1.8H , J = 6.6, CH_3); 1.79 – 1.93 m (1H, $CH(Me)_2$); 2.98 -3.05 m (2H, NCH_2); 3.84 m (1H) and 4.01–4.34 m (3H, CH, OCH, OCH_2); 6.70–6.84 m (4H, C_6H_4); 8.35–8.46 m (1.4 H) and 8.72 br.l (0.6 H, J = 9.0, 2 NH). ^{13}C NMR spectrum, δ, ppm: 15.7 and 16.0(CH_3), 19.8 (($CH_3)_2$), 27.7 ($CH(Me)_2$), 44.6 and 44.8 (CHN), 46.2(CH_2), 64.8 and 64.9 (OCH_2), 74.1 and 74.2 (OCH), 116.3 and 116.4 (CH), 116.6 and 116.8(CH), 120.5 (CH), 120.6 (CH), 142.5, 142.80, 142.84 and 142.9 (2 CO), 159.1, 159.2 and 159.4 (2 CO). Found, *%*: C 62.96; H 7.50; N 9.47. $C_{16}H_{22}N_2O_4$. Calculated, *%*: C 62.73; H 7.24; N 9.14.

N^1-Benzyl -N^2-(1-(1,4-benzodioxan-2-yl)ethyl)oxalamide(16). Yield 73*%*, m.p.165-166 ^oC, R_f 0.51. IR spectrum, ν, cm^{-1}: 3246 (NH-amide), 1660 (C=O). Two diastereoisomers, 60:40. ^{1}H NMR spectrum, δ, ppm, Hz: 1.33d (1.8H, J = 6.5) and 1.34 (1.2 H, J = 6.5, CH_3); 3.85-3.93 m (1H) and 4.02-4.35 m (3H, CH, OCH, OCH_2); 4.38 – 4.43 m (2H, CH_2N); 6.67 - 6.73 m (4H, C_6H_4); 7.15-7.31 m (5H, C_6H_5); 8.45 d (0.4H, J = 8.7) and 8.78 d (0.6H, J = 9.0, NH); 9.05 br.t (1H, J = 6.2, NH). Found, *%*: C 67.34; H 6.28; N 8.50. $C_{19}H_{20}N_2O_4$. Calculated, *%*: C 67.05; H 5.92; N 8.23.

N^1-(1-(1,4-Benzodioxan-2-yl)ethyl)-N^2-(3,4-dimethoxyphenethyl)oxalamide (17). Yield 71*%*, m.p.183-185 ^oC, R_f 0.46. IR spectrum, ν, cm^{-1}: 3257 (NH-amide), 1668 (C=O). ^{1}H NMR spectrum, δ, ppm, Hz: 1.33d (3H, J = 6.5, CH_3); -2.75 t (2H, J = 7.1, CH_2); 3.40 t.d (2H, J = 7.1 and 5.7, NCH_2); 3.76 s (3H, CH_3O), 3.79 s (3H, CH_3O), 3.87 d.d (1H, J = 11.2 and 7.1, OCH_2); 4.00–4.09 m (1H, CH_3CH); 4.12 - 4.22 m (2H, OCH_2 and OCH); 6.67 - 6.82 m (7H, Ar); 8.52 br.t (1H, J = 5.7, $NHCH_2$); 8.72 br.d (1H, J = 9.0, <u>NH</u>CH). ^{13}C NMR spectrum, δ, ppm: 16.0 (CH_3), 34.3(CH_2), 40.3 (NCH_2),

44.6 (NCH), 55.1 (OCH_3), 55.2 (OCH_3), 64.9 (OCH_2), 74.2 (OCH), 111.8(CH), 112.6(CH), 116.4(CH), 116.6(CH), 120.3(CH), 120.5(CH), 120.6(CH), 131.3, 142.5, 142.9, 147.4, 148.7, 159.1, 159.3. Found, %: C 63.95; H 6.70; N 7.01. $C_{22}H_{26}N_2O_6$. Calculated, %: C 63.76; H 6.32; N 6.76.

N^1-(Isochroman-1-ylmethyl)-N^2-(cyclohexyl)oxalamide(19). Yield 62%, m.p. 196-197 ^oC, R_f 0.48. IR spectrum, ν, cm^{-1}: 3244 (NH-amide), 1665 (C=O). ^{1}H NMR spectrum, δ, ppm, Hz: 1.25-1.87 m (10H, 5 CH_2); ¬2.68-2.73 m (1H, CHN); 2.74 d.d.d (1H, J = 16.3, 5.4, 3.6, CH_2), 2.89 d.d.d (1H, J = 16.3, 7.5, 4.9, CH_2); 3.50 d.d.d (1H, J = 13.7, 8.8 and 6.0, NCH_2); 3.68 dd (1H, J = 13.7, 6.0 and 3.0, NCH_2); 3.76 d.d.d (1H, J = 11.4, 7.7 and 4.4, CH_2O); 4.15 d.d.d (1H, J = 11.4, 5.4 and 4.4, CH_2O); 4.84 d.d (1H, J = 8.8 and 3.0, OCH); 7.05 – 7.20 m (4H, C_6H_4); 8.08 br.t (1H, J = 6.1, NH); 8.28 br.t (1H, J = 6.0, NH). Found, %: C 68.61; H 7.88; N 9.15. $C_{18}H_{24}N_2O_3$. Calculated, %: C 68.33; H 7.65; N 8.85.

N^1-(Furan-2-ylmethyl)-N^2-(isochroman-1-ylmethyl)oxalamide (20). Yield 69%, m.p. 137-138 ^oC, R_f 0.37. IR spectrum, ν, cm^{-1}: 3234 (NH-amide), 1645 (C=O). ^{1}H NMR spectrum, δ, ppm, Hz: 2.74 d.d.d (1H, J = 16.3, 5.4 and 3.6, CH_2); 2.89 d.d.d (1H, J = 16.3, 7.5 and 4.9, CH_2); 3.49d.d.d (1H, J = 13.7, 8.8 and 6.0, NCH_2); 3.68 d.d (1H, J = 13.7, 6.0 and 3.0, NCH_2); 3.75 d.d.d (1H, J = 11.4, 7.7 and 4.4, OCH_2); 4.12 d.d.d (1H, J = 11.4, 5.4 and 4.4, OCH_2); 4.37 d (2H, J = 6.2 CH_2 furan); 4.85 d.d (1H, J = 8.8 and 3.0, OCH); 6.21 br.d (1H, J = 3.1, H-3 furan); 6.29 d.d (1H, J = 3.1 and 1.8, H-4 furan); 7.05 – 7.18 m (4H, C_6H_4); 7.37 br.d (1H, *J* = 1.8, H-5 furan); 8.30 br.t (1H, J = 6.0, NH); 8.84 br.t (1H, J = 6.2, NH). ^{13}C NMR spectrum, δ, ppm: 28.3 (CH_2), 35.6 (CH_2 fur.), 43.3 (NCH_2), 61.3 (OCH_2), 73.4 (OCH), 106.8 (CH), 109.8 (CH), 124.5 (CH), 125.6 (CH), 126.1 (CH), 128.4 (CH), 133.5, 134.7, 141.1(CH), 151.1, 159.2, 159.3. Found, %: C 65.28; H 5.98; N 8.59. $C_{17}H_{18}N_2O_4$. Calculated, %: C 64.96; H 5.77; N 8.91.

Oxalamides 24-29, 32-37 (general procedure). A mixture of 5 *mmol* of amine **21-23**, **30**, **31** and 5 *mmol* of corresponding anilidoester was heated for 5 h at 120–125 °*C*. The resulting solid was treated with hexane, and the precipitation was filtered off, washed with water, 10% aqueous HCl, and water again, dried in air, and recrystallized from ethanol.

N^1-(2,4-Dimethoxyphenyl)-N^2-((1-phenylcyclopentyl)methyl)oxalamide (24). Yield 80%, m.p.120-122 ^oC, R_f 0.47. IR spectrum, ν, cm^{-1}: 3244 (NH-amide), 1678 (C=O). ^{1}H NMR spectrum, δ, ppm, Hz: 1.64 – 2.06 m (8H, 4 CH_2 C_5H_8), 3.42d (2H, J = 6.6, NCH_2); 3.78 s (3H, OCH_3); 3.93 s (3H, OCH_3); 6.43 d.d (1H, J = 8.8 and 2.6, H-5 C_6H_3); 6.53 d (1H, J = 2.6, H-3 C_6H_3); 7.14 - 7.23 m (1H) and 7.26 - 7.34 m (4H, C_6H_5); 7.68 br.t (1H, J = 6.6, $HNCH_2$); 8.12 d(1H, J = 8.8, H-6 C_6H_3); 9.48 br. s (1H, NH). ^{13}C NMR spectrum, δ, ppm: 22.8 (2 CH_2), 34.8 (2 CH_2), 47.7 (NCH_2), 51.5 (C), 54.7 (OCH_3), 55.4 (OCH_3), 98.1(CH), 103.5 (CH), 119.2, 119.5 (CH), 125.6

(CH), 126.3 (2 CH), 127.8 (2 CH), 145.8, 149.3, 156.0,156.6, 159.3. Found, %: C 69.28; H 7.04; N 7.05. $C_{22}H_{26}N_2O_4$. Calculated, %: C 69.09; H 6.85; N 7.32.

N^1-((1-(3,4-Dimethoxyphenyl)cyclopentyl)methyl)-N^2-(4-methoxyphenyl)oxalamide (25). Yield 72%, m.p.106-108 ^oC, R_f 0.45. IR spectrum, ν, cm^{-1}: 3250 (NH-amide), 1663 (C=O). ^{1}H NMR spectrum, δ, ppm, Hz: 1.65 – 2.00 m (8H, 4 CH_2 C_5H_8); 3.38 d (2H, J=6.5, NCH_2); 3.76 s (3H, OCH_3); 3.78 s (3H, OCH_3); 3.80 s (3H, OCH_3); 6.75–6.88 m (5H, Ar); 7.65 br.t (1H, J = 6.5, HN); 7.70-7.80 m (2H, Ar); 10.22 br. s (1H, NH). Found, %: C 67.11; H 7.20; N 6.89. $C_{23}H_{28}N_2O_5$. Calculated, %: C 66.97; H 6.84; N 6.79.

N^1-((1-(3,4-Dimethoxyphenyl)cyclopentyl)methyl)-N^2-(2-methoxy-5-methylphenyl)oxalamide (26). Yield 74%, m.p.112-114 ^oC, R_f 0.48. IR spectrum, ν, cm^{-1}: 3255 (NH-amide), 1665 (C=O). ^{1}H NMR spectrum, δ, ppm, Hz: 1.66 – 2.01 m (8H, 4 CH_2 C_5H_8), 2.30 s (3H, CH_3); 3.39d (2H, J = 6.5, NCH_2); 3.80 s (3H, OCH_3); 3.82 s (3H, OCH_3); 3.91 s (3H, OCH_3); 6.75 - 6.88 m (5H, Ar); 7.65 br.t (1H, J = 6.5, $HNCH_2$); 8.06 br. s (1H, H-6 C_6H_3); 9.63 br. s (1H, NH). ^{13}C NMR spectrum, δ, ppm: 20.04 (CH_3), 22.8 (2 CH_2), 34.9(2 CH_2), 47.7 (NCH_2), 51.1 (C), 55.1 (OCH_3), 55.2 (OCH_3), 55.3(OCH_3), 109.7 (CH), 111.0 (CH), 111.4(CH), 118.3 (CH), 119.4 (CH), 124.4 (CH), 125.4, 129.1, 138.3, 146.0, 147.3, 148.6, 156.4, 159.1. Found, %: C 67.78; H 7.31; N 6.79. $C_{24}H_{30}N_2O_5$. Calculated, %: C 67.59; H 7.09; N 6.57.

N^1-(3,4-Dimethylphenyl)-N^2-((4-(4-methoxyphenyl)tetrahydro-2*H*-pyran-4-yl)-methyl)-oxalamide (27). Yield 73, m.p.200-202 ^oC, R_f 0.50. IR spectrum, ν, cm^{-1}: 3253 (NH-amide), 1664 (C=O). ^{1}H NMR spectrum, δ, ppm, Hz: 1.81–1.91 m (2H) and 2.00–2.10 m (2H, 2 CH_2); 2.22 s (3H, CH_3); 2.24 s (3H, CH_3); 3.40 d (2H, J=6.6, NCH_2); 3.41 – 3.49 m (2H, OCH_2); 3.68 – 3.76 m (2H, OCH_2); 3.79 s (3H, OCH_3); 6.85 -6.90 m (2H, H-3, 3' C_6H_4OMe); 7.01-8.1 m (1H, H-5 C_6H_3); 7.22 - 7.27 m (2H, H-2.2' C_6H_4OMe); 7.52d.d (1H, J = 8.1, 2.0, H-6 C_6H_3); 7.56 d (1H, J = 2.0, H-2 C_6H_3); 7.80 br.t (1H, J = 6.6, $\underline{HN}CH_2$); 10.08 br. s (1H, NH). Found, %: C 69.90; H 7.38; N 7.32. $C_{23}H_{28}N_2O_4$. Calculated, %: C 69.67; H 7.12; N 7.07.

N^1-((4-(4-Methoxyphenyl)tetrahydro-2*H*-pyran-4-yl)methyl)-N^2-(3-(trifluoromethyl)phenyl)oxalamide (28). Yield 73%, m.p. 114-116 ^oC, R_f 0.49. IR spectrum, ν, cm^{-1}: 3247 (NH-amide), 1674 (C=O). ^{1}H NMR spectrum, δ, ppm, Hz: 1.81–1.91 m (2H) and 2.00–2.10 m (2H, $2CH_2$); 3.42d (2H, J = 6.6, NCH_2); 3.41 – 3.49 m (2H, OCH_2); 3.68 – 3.76 m (2H, OCH_2); 3.79 s (3H, OCH_3); 6.85 -6.90 m (2H, H-3, 3' C_6H_4OMe); 7.21 - 7.26 m (2H, H-2.2' C_6H_4OMe); 7.33 br.d (1H, J = 7.7, H-4 $C_6H_4CF_3$); 7.44 d.d.t (1H, J = 8.2, 7.7, H-5 $C_6H_4CF_3$); 7.86 br.t (1H, J = 6.6, $\underline{HN}CH_2$); 8.05 br. d (1H, J = 8.2, H-6 $C_6H_4CF_3$); 8.28 t (1H, J = 1.7, H-2 $C_6H_4CF_3$); 10.81 s

(1H, NH). ^{13}C NMR spectrum, δ, ppm: 33.1 (2 CH_2), 39.8 (C), 49.2 (NCH_2), 54.4 (OCH_3), 63.0 ($O(CH_2)_2$), 113.6(2 CH), 116.6 k (CH, $J_{C,F}$ = 4.0), 120.0 k (CH, $J_{C,F}$ = 3.9), 123.3(CH), 123.5(CF_3 $J_{C,F}$= 272.0), 127.3 (2 CH), 128.6 (CH), 129.8 q (C CF_3 $J_{C,F}$ = 32.1), 134.3, 138.2, 157.5, 158.1, 159.1. Found, *%*: C 60.85; H 5.63; N 6.70. $C_{22}H_{23}F_3N_2O4$. Calculated, *%*: C 60.55; H 5.31; N 6.42

N^1-(3-Chloro-4-methylphenyl)-N^2-((4-(4-methoxyphenyl)tetrahydro-2*H*-pyran-4-yl)-methyl)-oxalamide (29). Yield 76%, m.p.188-190 ^oC, R_f 0.51. IR spectrum, ν, cm^{-1}: 3245 (NH-amide), 1668 (C=O). ^{1}H NMR spectrum, δ, ppm, Hz: 1.82–1.92 m (2H) and 2.01–2.11 m (2H, $2CH_2$); 2.35 s (3H, CH_3); 3.44 d (2H, J=6.6, NCH_2); 3.45 – 3.52 m (2H, CH_2); 3.70 – 3.78 m (2H, OCH_2); 3.80 s (3H, OCH_3); 6.84 -6.89m (2H, H-3, 3' C_6H_4OMe); 7.16 d (1H, J = 8.3, H-5 C_6H_3); 7.21-7.26 m (2H, H-2.2' C_6H_4OMe); 7.60 d.d (1H, J = 8.3, 2.1, H-6 C_6H_3); 7.80 d (1H, J = 2.1, H-2 C_6H_3); 7.95 br.t (1H, J = 6.2, $HNCH_2$); 10.45 br. s (1H, NH). Found, *%*: C 63.59; H 6.31; N 6.98. $C_{22}H_{25}ClN_2O_4$. Calculated, *%*: C 63.38; H 6.04; N 6.72.

N^1-(3,4-Dimethylphenyl)-N^2-(isochroman-1-ylmethyl)oxalamide (32). Yield 75%, m.p.176-178 ^oC, R_f 0.48. IR spectrum, ν, cm^{-1}: 3270 (NH-amide), 1680 (C=O). ^{1}H NMR spectrum, δ, ppm, Hz: 2.22 s(3H, CH_3); 2.25 s (3H, CH_3); ¬ 2.76 d.t (1H, J = 16.1 and 4.8) and 2.86 – 2.96 m (1H, CH_2); 3.58d.d.d (1H, J = 13.7, 8.7 and 6.2, NCH_2); 3.72 d.d.d (1H, J = 13.7, 5.9 and 3.0, NCH_2); 3.77 d.d.d (1H, J = 11.5, 7.7 and 4.3, CH_2O); 4.14 d.d.d (1H, J = 11.5, 5.5 and 4.8, CH_2O); 4.89d.d (1H, J = 8.7 and 3.0, OCH); 7.01 d (1H, J = 8.1, H-5 C_6H_3); 7.07 – 7.20 m (4H, C_6H_4); 7.50 d.d (1H, J = 8.1 and 2.0, H-6 C_6H_3); 7.53d (1H, J = 2.0, H-2 C_6H_3); 8.43 br.t (1H, J = 5.9, NHCH_2); 10.04 br.s (1H, NH). ^{13}C NMR spectrum, δ, ppm: 18.6 (CH_3), 19.3(CH_3), 28.2(CH_2), 43.5 (NCH_2), 61.5 (OCH_2), 73.4 (OCH), 117.3(CH), 120.9(CH) , 124.4 (CH), 125.6 (CH), 126.1 (CH), 128.3 (CH), 129.0 (CH), 131.5, 133.5, 134.6,134.9, 135.6, 157.2, 159.5. Found, *%*: C 71.25; H 6.79; N 8.58. $C_{20}H_{22}N_2O_3$. Calculated, *%*: C 70.99; H 6.55; N 8.28.

N^1-(Isochroman-1-ylmethyl)-N^2-(3-(trifluoromethyl)phenyl)oxalamide (33). Yield 78%, m.p. 168-169 ^oC, R_f 0.52. IR spectrum, ν, cm^{-1}: 3244 (NH-amide), 1665 (C=O). ^{1}H NMR spectrum, δ, ppm, Hz: 2.75 d.d.d (1H, J = 16.3, 5.4, 3.6) and 2.90 d.d.d (1H, J = 16.3, 7.5, 4.9, CH_2); 3.52 d.d.d (1H, J = 13.7, 8.8 and 6.0) and 3.71 d.d.d (1H, J = 13.7, 6.0 and 3.0, NCH_2); 3.76 d.d.d (1H, J = 11.4, 7.7 and 4.4) and 4.13 d.d.d (1H, J = 11.4, 5.4 and 4.4, CH_2O); 4.88 d.d (1H, J = 8.8 and 3.0, OCH); 7.04-7.17 m (4H, C_6H_4); 7.34 br.d (1H, J = 7.7, H-4), 7.48 d.d (1H, J = 8.2, 7.7, H-5), 8.10 br.d (1H, J = 8.2, H-6) and 8.30 t (1H, J = 1.7, H-2, $C_6H_4CF_3$); 8.51 br.t (1H, J = 6.2, NH); 10.82br.s (1H, NH). Found, *%*: C 60.60; H 4.78; N 7.71. $C_{19}H_{17}F_3N_2O_3$. Calculated, *%*: C 60.32; H 4.53; N 7.40.

N^1-(3-Chloro-4-methylphenyl)-N^2-(isochroman-1-ylmethyl)oxalamide (34). Yield 71%, m.p.182-183 ^oC, R_f 0.53. IR spectrum, ν, cm^{-1}: 3239 (NH-amide), 1678 (C=O). ^{1}H NMR spectrum, δ, ppm, Hz: 2.33 s (3H, CH_3); 2.72d.d.d (1H, J = 16.3, 5.4, 3.6, CH_2), 2.87 d.d.d (1H, J = 16.3, 7.5, 4.9, CH_2); 3.51 d.d.d (1H, J = 13.7, 8.8 and 6.0, NCH_2); 3.62 d.d.d (1H, J = 13.7, 6.0 and 3.0, NCH_2); 3.77 d.d.d (1H, J = 11.4, 7.7 and 4.4, CH_2O); 4.15 d.d.d (1H, J = 11.4, 5.4 and 4.4, CH_2O); 4.89 d.d (1H, J = 8.8 and 3.0, OCH); 7.07 – 7.20 m (4H, C_6H_4); 7.21 d (1H, J = 8.3, H-5 C_6H_3); 7.65 d.d (1H, J = 8.3 and 2.1, H-6 C_6H_3); 7.95 d (1H, J = 2.1, H-2 C_6H_3); 8.47 br.t (1H, J = 6.2, NHCH_2); 10.48 br.s (1H, NH). Found, %: C 63.84; H 5.61; N 8.05. $C_{19}H_{19}ClN_2O_3$. Calculated, %: C 63.60; H 5.34; N 7.81.

N^1-(1,4-Benzodioxan-2-yl)methyl)-N^2-(3-chloro-4-methylphenyl)oxalamide (35). Yield 73%, m.p.176-178 ^oC, R_f 0.50. IR spectrum, ν, cm^{-1}: 3250 (NH-amide), 1673 (C=O). ^{1}H NMR spectrum, δ, ppm, Hz: 2.33 s (3H, CH_3); 3.49 d.t (1H, J = 13.7 and 6.5, NCH_2); 3.60 d.t (1H, J = 13.7 and 6.0, NCH_2); 3.93 d.d (1H, J = 11.8 and 7.6, CH_2O); 4.26 - 4.36 m (2H, OCH_2 and OCH); 6.71–6.83 m (4H, C_6H_4); 7.16 d (1H, J = 8.3, H-5 C_6H_3); 7.64 d.d (1H, J = 8.3 and 2.1, H-6 C_6H_3); 7.94 d (1H, J = 2.1, H-2 C_6H_3); 9.05 br.t (1H, J = 6.2, NHCH_2); 10.54 br.s (1H, NH). ^{13}C NMR spectrum, δ, ppm: 18.9 (CH_3), 39.3(CH_2), 65.5 (OCH_2), 70.9 (OCH), 116.5(CH), 116.7(CH), 118.5 (CH), 120.3 (CH) , 120.6 (CH), 120.8 (CH), 130.2 (CH), 130.6, 133.1, 136.5, 142.5, 142.7, 157.6, 160.0. Found, %: C 60.25; H 4.92; N 7.99. $C_{18}H_{17}ClN_2O_4$. Calculated, %: C 59.92; H 4.75; N 7.76.

N^1-(1,4-Benzodioxan-2-yl)methyl)-N^2-(3,4-dimethylphenyl)oxalamide (36). Yield 70%, m.p.136-138 ^oC, R_f 0.52. IR spectrum, ν, cm^{-1}: 3263 (NH-amide), 1661 (C=O). ^{1}H NMR spectrum, δ, ppm, Hz: 2.22 s (3H, CH_3), 2.25 s (3H, CH_3); ¬ 3.47 d.t (1H, J = 13.7 and 6.5, NCH_2); 3.58 d.t (1H, J = 13.7 and 6.0, NCH_2); 3.93 d.d (1H, J = 11.8 and 7.6, CH_2O); 4.25 - 4.35 m (2H, OCH_2 and OCH); 6.70–6.82 m (4H, C_6H_4); 7.01 d (1H, J = 8.1, H-5 C_6H_3); 7.52 d.d (1H, J = 8.1 and 2.0, H-6 C_6H_3); 7.54 d (1H, J = 2.0, H-2 C_6H_3); 9.01 br.t (1H, J = 6.2, NHCH_2); 10.08 br.s (1H, NH). Found, %: C 67.31; H 6.12; N 8.49. $C_{19}H_{20}N_2O_4$. Calculated, %: C 67.05; H 5.92; N 8.23.

N^1-(1,4-Benzodioxan-2-yl)methyl)-N^2-(3-trifluoromethylphenyl)oxalamide (37). Yield 74%, m.p.156-157 ^oC, R_f 0.48. IR spectrum, ν, cm^{-1}: 3259 (NH-amide), 1670 (C=O). ^{1}H NMR spectrum, δ, ppm, Hz 3.45 d.t (1H, J = 13.7 and 6.5, NCH_2); 3.55 d.t (1H, J = 13.7 and 6.0, NCH_2); 3.91 d.d (1H, J = 11.8 and 7.6, CH_2O); 4.24 - 4.34 m (2H, OCH_2 and OCH); 6.72–6.84 m (4H, C_6H_4); 7.35 br.d (1H, J = 7.7, H-4), 7.50 d.d (1H, J = 8.2, 7.7, H-5), 8.11 br.d (1H, J = 8.2, H-6) and 8.32 t (1H, J = 1.7, H-2, $C_6H_4CF_3$); 9.03 br.t (1H, J = 6.2, NHCH_2); 10.80 br.s (1H, NH). Found, %: C 57.02; H 4.12; N 7.60. $C_{18}H_{15}F_3N_2O_4$. Calculated, %: C 56.85; H 3.98; N 7.37.

N^1, N^2- ԱՐԻԼ-, ԱՐԻԼԱԼԿԻԼ- ԵՎ ՀԵՏԵՐԻԼԱԼԿԻԼ-ՏԵՂԱԿԱԼՎԱԾ ԹՐԹՆՋԿԱԹԹՎԻ ԴԻԱՄԻԴՆԵՐԻ ՍԻՆԹԵԶ

Ս.Հ. ՎԱՐԴԱՆՅԱՆ, Ա.Բ. ՍԱՐԳՍՅԱՆ, Ա.Ս. ԱՎԱԳՅԱՆ*, Ն.Հ. ՊԱՀՈՒԹՅԱՆ,
Հ.Վ. ԳԱՍՊԱՐՅԱՆ, Ա.Ա. ԱՂԵԿՅԱՆ

Թրթնջկաթթվի ամիդների մոնոէթիլային մի շարք եթերներ, որոնք ստացվել են ավելի վաղ արիլցիկլոպենտիլմեթիլ-, արիլտետրահիդրոպիրանիլմեթիլ-, իզոխրոմանիլմեթիլ-, (1,4-բենզոդիօքսան-2-իլ)-մեթիլ- և 1-(1,4-բենզոդիօքսան-2-իլ)-էթիլամինների և դիէթիլօքսալատի ռեակցիայի արդյունքում, փոխազդեցության մեջ են դրվել տարբեր առաջնային ամինների հետ՝ առաջացնելով նոր համապատասխան դիամիդներ: Սինթեզվել են տեղակալված անիլիդների ֆրագմենտներ պարունակող օքսալաթթվի դիամիդներ անիլիդոէթերների և վերը նշված արիլալկիլ- և հետերիլալկիլամինների փոխազդեցությամբ: Հետազոտվել են սինթեզված միացությունների հակաօքսիդանտ հատկությունները:

СИНТЕЗ N^1, N^2- АРИЛ-, АРИЛАЛКИЛ- И ГЕТЕРИЛАЛКИЛЗАМЕЩЕННЫХ ДИАМИДОВ ЩАВЕЛЕВОЙ КИСЛОТЫ

С.О. ВАРТАНЯН, А.Б. САРГСЯН, А.С. АВАКЯН*, Н.А.ПАГУТЯН, Г.В. ГАСПАРЯН, А.А. АГЕКЯН

Научно-технологический центр органической и фармацевтической химии
НАН Республики Армения
Армения, 0014, Ереван, пр. Азатутян, 26
E-mail: aaghekyan@mail.ru

На основе моноэтиловых эфиров амидов щавелевой кислоты, полученных ранее реакцией арилциклопентилметил-, арилтетрагидропиранилметил-, изохроманил-1-метил-, (1,4-бензодиоксан-2-ил)-метил- и 1-(1,4-бензодиоксан-2-ил)-этил аминов с диэтиловым эфиром щавелевой кислоты, действием разнообразных первичных аминов синтезированы целевые замещенные диамиды щавелевой кислоты. Для синтеза диамидов, содержащих фрагменты анилидов, использованы этиловые эфиры замещенных N-ариламидов щавелевой кислоты, которые поставлены во взаимодействие с вышеуказанными арилалкил- и гетерилалкиламинами. Исследована антиоксидантная активность синтезированных соединений.

References

[1] *Агекян А.А., Мкрян Г.Г., Цатинян А.С., Норавян О.С., Гукасян Т.Г., Ширинян Э.А., Маркарян Э.А.* - Синтез новых N-замещенных 1-фенил-1-циклопентилметиламинов. // Хим. ж. Арм., 2011, т.64, №4, с. 531-537.

[2] *Агекян А.А., Мкрян Г.Г., Цатинян А.С., Норавян О.С., Гаспарян Г.В.*- Синтез и биологическая активность арилоксиаминопропанолов на основе замещенных *п*-толилалкиламинов // ЖОрХ, 2016, т.52, вып.2, с.226-230.

[3] The use of stems in the selection of International Nonprietary Names (INN) for pharmaceutical substance s 2018, WHO.

[4] *Козьминых В.О.* - Синтез и биологическая активность замещенных амидов и гидразидов 1,4-дикарбоновых кислот. // Фарм.- хим. ж., 2006, т.40, №1, с. 8-.

[5] *Вартанян С.О., Авакян А.С., Саркисян А.Б., Маркарян Э.А., Арутюнян С.А., Ширинян Э.А., Хачатрян А.Г.* - Синтез и антигипоксическая активность N-1,4-бензодиоксанилметил-, 1,4-бензодиоксанилэтил- и изохроманилметил-замещенных диамидов щавелевой кислоты // Вестник МАНЭБ, 2005, т.10, № 6, с. 198-201.

[6] *Агекян А.А., Маркарян Э.А.* - Исследования в области синтеза N-3,4-диметоксифенилциклопентилметил- N'-замещенных диамидов щавелевой кислоты. //Хим. журнал Армении, 2013, т.66, № 4, с.628-635.

[7] *Агекян А.А., Паносян Г.А., Маркарян Э.А.* - Синтез N-(1-фенилциклопентилметил)-N'-замещенных диамидов щавелевой кислоты.// ЖОрХ,, 2013, т.49, вып.7, с.1097-1100.

[8] *Агекян А.А., Мкрян Г.Г., Мурадян Р.Е., Тумаджян А.Е.* - Синтез амидов и диамидов дикарбоновых кислот на основе (4-(4-метоксифенил)тетрагидро-2*H*-пиран-4-ил)метиламина. // ЖОрХ, 2018, т.54, №6, с .884-889.

[9] *Арутюнян А.В., Дубинина Е.Е., Зыбина Н.А.* - Методы оценки свободнорадикального окисления и антиоксидантной системы организма // СПб, 2000, с. 90.

[10] *Чеснокова Н.П., Моррисон В.В., Понукалина Е.В., Афанасьева Г.А., Бизенкова М,.Н Барсуков В.Ю., Морозова О.Л., Полутова Н.В., Жевак Т.Н.* -О роли активации свободнорадикального окисления в структурной и функциональной дезорганизации биосистем в условиях патологии. //М.,Фундаментальные исследования, 2009, №5, с.122.