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REARRANGEMENT OF O-VINYL-α-(AMINO-CARBONYL)ACETAMIDOXIMES TO 2-AMINO-PYRROLES AND 2-PYRROLINONES

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Rearrangement and cyclization of O-vinyl-α-(aminocarbonyl)acetamidoximes gives two isomeric 2-aminopyrroles and/or 2-pyrrolinones and this depends on the rearrangement route.

Keywords: 2-aminopyrroles, substituted acetamidoximes, 2-pyrrolinones, rearrangement.

Under Trofimov reaction conditions O-vinyloximes with α-hydrogen atoms are converted to pyrroles. The key stage in the reaction is a [3,3]-sigmatropic rearrangement of the enhydroxylamine tautomer form of the oxime. The imino ketone product cyclizes to a pyrrole [1]. Similarly, O-vinylamidoximes rearrange *via* the tautomeric imino form to amidino aldehydes or ketones which cyclize to form imidazoles [2].

We have studied the thermolysis of the O-vinyl-α-(aminocarbonyl)acetamidoximes **1a-g**. These compounds can potentially react both as oximes (route 1) and as amidoximes (route 2). The thermolysis was carried out in refluxing mesitylene and the reaction products were separated chromatographically.

The main reaction scheme proved to be route 1. The rearrangement product cyclizes *via* either of the nucleophilic nitrogen atoms to give the 2-aminopyrroles **2** or 2-pyrrolinones **3**. With the presence of a secondary amide (R^1 = H) in the molecular fragment nucleophilic attack involving the amide nitrogen atom predominates and this leads principally to the formation of the pyrrolinone **3**. Increasing the bulk of the substituent on the nitrogen atom (compound **1b**) causes an increase in the fraction of the aminopyrrole **2**. When changing to a tertiary amide (compounds **1d,e**) the aminopyrroles **2d,e** become the sole reaction products. They were separated as the ureas **6d,e** after treatment of the reaction mixtures with phenyl isocyanate. We were unable to prepared the pyrroles **2d,e** in the pure state due to their degradation on silica gel. Such a low stability for these compounds gave us grounds to propose that they can undergo tarring in the forcing reaction conditions which can then lead to a low yield of their derivatives. Carrying out the pyrolysis in the presence of refluxing acetylacetone as a "trap" gave the pyrrolopyrimidines **7d,e** in greater yields and this indirectly supports our suggestion.

In several examples the formation of the aminopyrrole **4** was noted. In appears to be obtained by route 2 *via* cyclization of the intermediate involving a nucleophilic carbon atom. We did not identify the formation of the imidazoles **5**.

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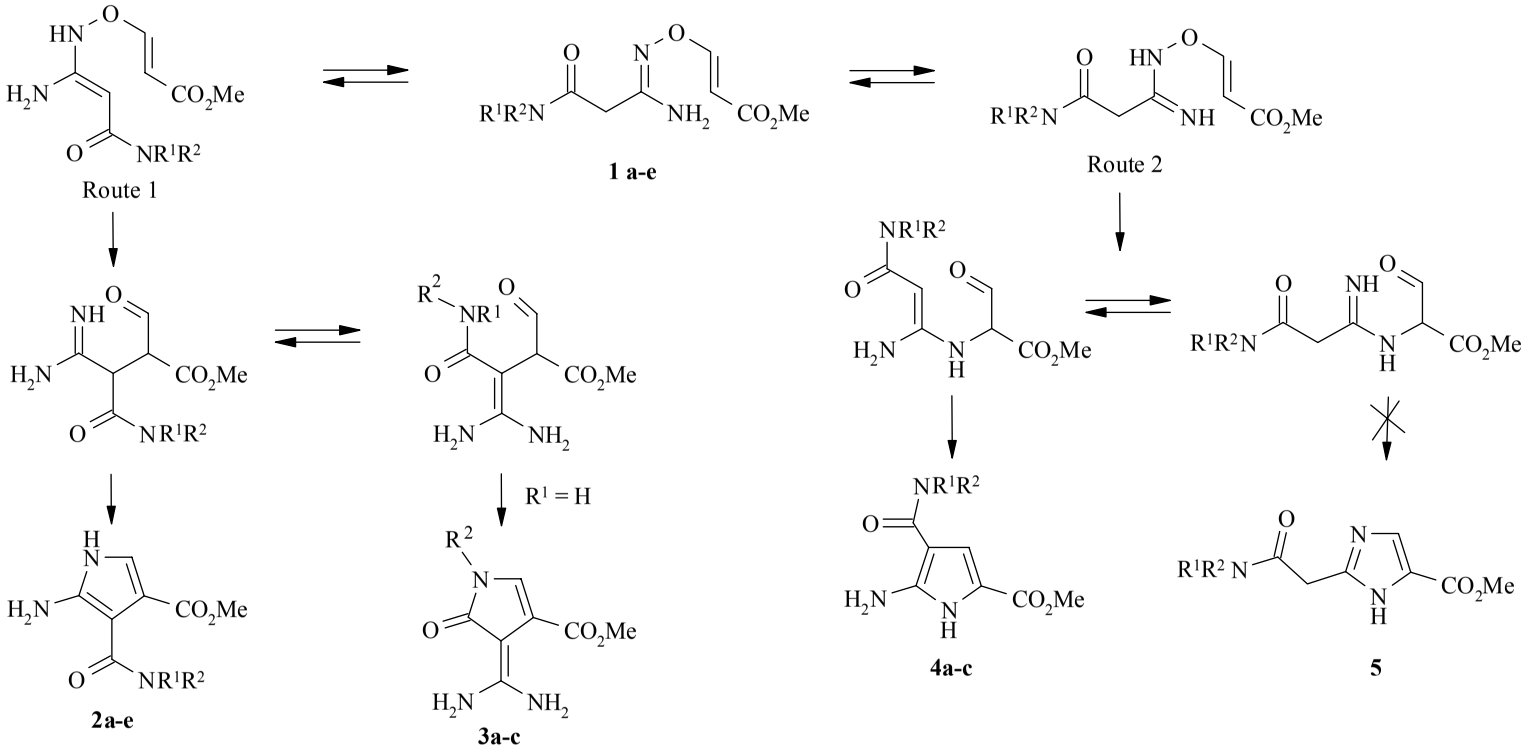

a $R^1 = H$, $R^2 = CH_2CH_2OMe$; **b** $R^1 = H$, $R^2 = c\text{-}C_6H_{11}$; **c** $R^1 = H$, $R^2 = 4\text{-}ClC_6H_4$; **d** $R^1R^2 = (CH_2)_4$; **e** $R^1R^2 = (CH_2)_2O(CH_2)_2$

Yield, %: 7 (**2a**), 19 (**2b**), 10* (**2c**), 23*[2](**2d**), 28*[2] (**2e**); 48 (**3a**), 34 (**3b**), 46 (**3c**); 13 (**4a**), 19 (**4b**), 10* (**4c**).

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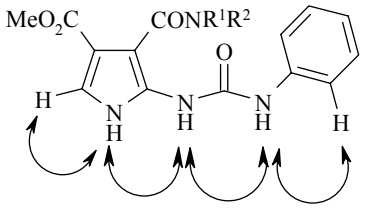
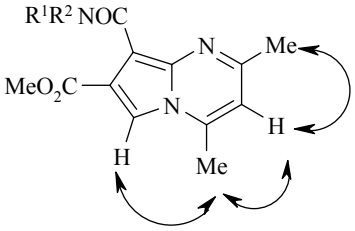
* Overall yield of isomers, theoretically contained in the reaction mixture but not separated, was judged from their ^1H NMR spectra.

*[2] The aminopyrroles **2d,e** were separated as the ureas by treatment with phenylisocyanate.



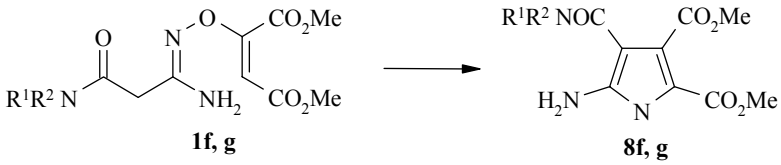
6d, e



7d, e

The structures **2** and **4** were assigned as the corresponding pyrroles on the basis of the direct C–H spin-spin coupling constants for the pyrrole fragment in the NMR spectra. In this case of compound **2** J = 90-196 and for compound **4** J = 172-174 Hz which correspond to the spin-spin couplings for the α- and β- positions of the pyrrole ring respectively [3]. NOESY correlations spectra were also obtained for compounds **6d,e** and **7d,e**. The arrows shown on the scheme indicate the signals for which cross correlations were important in establishing the structure.

Thermolysis of O-vinyl-α-(aminocarbonyl)acetamidoximes **1f,g** in mesitylene gives the dimethyl esters of 5-amino-4-(pyrrrolidin-1-ylcarbonyl)pyrrole-2,3-dicarboxylic acids **8f,g**. In these examples the structure of the aminopyrrole obtained does not permit a conclusion about the route of their formation. Alternatively structured imidazole reaction products were not observed in this case.



1f, g **8f, g**

1, 8 f $R^1,R^2 = (CH_2)_4$; **g** $R^1,R^2 = (CH_2)_2O(CH_2)_2$

EXPERIMENTAL

^{1}H and ^{13}C NMR spectra were recorded on a Bruker DPX 300 (300 and 75 MHz respectively) using DMSO-d_6 as solvent and the residual signals for DMSO-d_6 at 2.50 ppm (for ^{1}H) and 39.52 ppm (for ^{13}C NMR nuclei) were used as internal standards. The spin spin couplings in the proton spectra were measured in first order approximation. Mass spectra were obtained on a Finnigan MAT Incos 50 instrument with EI ionization (70 eV energy). S,H,N analysis was carried out on a Hewlett-Packard HP-185B analyzer. The purity of the products and reaction course were monitored by TLC on ALUGRAM SIL G/UV plates.

O-Vinyl-α-(aminocarbonyl)acetamidoximes 1a-e (General Method). A solution of methyl propiolate (12 mmol) in acetonitrile (5 ml) was added dropwise over 1 h to a refluxing solution of the corresponding amidoxime (10 mmol) and triethylamine (10 mmol) in acetonitrile (25 ml).

Compound 1a. Solvent was evaporated *in vacuo* and the thick, brown oil was flash chromatographed on silica gel using methylene chloride–methanol (20:1) as eluent. Yield 60%. Brown oil. ^{1}H NMR spectrum, δ, ppm (J, Hz): 8.09 (1H, t, J = 5.0, NH); 7.70 (1H, d, J = 12.0, OC<u>H</u>=CH); 6.46 (2H, s, NH_2); 5.45 (1H, d, J = 12.0, OCH=C<u>H</u>); 3.59 (3H, s, CO_2CH_3); 3.37-3.32 (2H, m, $OCH_2C\underline{H}_2NH$); 3.24 (3H, s, $CH_2OC\underline{H}_3$); 3.25-3.20 (2H, m, $OC\underline{H}_2CH_2NH$); 2.95 (2H, s, $C\underline{H}_2C(NH_2)$=NO).

Compound 1b. The solution was treated with activated carbon and solvent removed *in vacuo* to give a thick brown oil which slowly crystallized on standing. Yield 72%. Brown crystals, mp 102-105ºC. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.91 (1H, d, *J* = 7.3, NH); 7.70 (1H, d, *J* = 12.3, OC<u>H</u>=CH); 6.46 (2H, s, NH_2); 5.44 (1H, d, *J* = 12.3, OCH=C<u>H</u>); 3.59 (3H, s, CO_2CH_3); 3.52-3.49 (1H, m, NHC<u>H</u>$(CH_2)_5$); 2.91 (2H, s, C<u>H</u>$_2$C(NH_2)=NO); 1.75-1.52 and 1.32-1.10 (10H, m, cyclohexyl).

Compound 1c. The solution was concentrated *in vacuo*, cooled, and the precipitated crystals were filtered and recrystallized from isopropanol. Yield 48%. Colorless crystals, mp 190-192ºC (with decomp.). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 10.24 (1H, s, NH); 7.72 (1H, d, *J* = 12.0, OC<u>H</u>=CH); 7.61 (2H, d, *J* = 8.0, ArH); 7.37 (2H, d, *J* = 8.0, ArH); 6.58 (2H, s, NH_2); 5.46 (1H, d, *J* = 12.0, OCH=C<u>H</u>); 3.59 (3H, s, CO_2CH_3); 3.18 (2H, s, C<u>H</u>$_2$C(NH_2)=NO).

Compound 1d. Solvent was evaporated *in vacuo* and the thick brown oil was purified by flash chromatography on silica gel using methylene chloride–methanol (20:1) as eluent. Yield 71%. Brown oil, slowly crystallizing to light yellow crystals, mp 93-95ºC. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.70 (1H, d, *J* = 12, OC<u>H</u>=CH); 6.48 (2H, s, NH_2); 5.44 (1H, d, *J* = 12.0, OCH=C<u>H</u>); 3.59 (3H, s, CO_2CH_3); 3.10 (2H, s, C<u>H</u>$_2$C(NH_2)=NO); 3.46-3.41 (2H, m); 3.31-3.26 (2H, m) and 1.92-1.70 (4H, m) (N$(CH_2)_4$).

Compound 1e. Solvent was evaporated *in vacuo* and the thick brown oil was purified by flash chromatography on silica gel using methylene chloride–methanol (30:1) as eluent. Yield 69%. Brown oil. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.70 (1H, d, *J* = 12.0, OC<u>H</u>=CH); 6.48 (2H, s, NH_2); 5.45 (1H, d, *J* = 12.0, OCH=C<u>H</u>); 3.60 (3H, s, CO_2CH_3); 3.60-3.50 (4H, m, morpholine); 3.58-3.40 (4H, m, morpholine); 3.21 (2H, s, C<u>H</u>$_2$C(NH_2)=NO).

O-Vinyl-α-(aminocarbonyl)acetamidoximes 1f,g. A solution of dimethyl acetylenedicarboxylate (12 mmol) in acetonitrile (5 ml) was added dropwise over 15 min to a solution of the corresponding amidoxime (10 mmol) in acetonitrile (25 ml).

Compound 1f. The solution was concentrated by a factor of five at reduced pressure and the precipitate formed on cooling was filtered off, washed with ether, and dried. Yield 49%. Colorless crystals, mp 144-145ºC. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 6.60 (2H, br. s, NH_2); 5.61 (1H, s, C<u>H</u>CO_2CH_3); 3.77 (3H, s, CO_2CH_3); 3.59 (3H, s, CO_2CH_3); 3.46-3.40 (2H, m); 3.32-3.26 (2H, m); 3.12 (2H, s, $CH_2C(NH_2)$=NO), and 1.92-1.70 (4H, m, N$(CH_2)_4$).

Compound 1g. Solvent was removed *in vacuo* to give a thick, brown oil which was purified by flash chromatography on silica gel with methylene chloride–methanol (30:1) as eluent. Yield 60%. Yellow oil. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 6.63 (2H, br. s, NH_2); 5.61 (1H, s, C<u>H</u>CO_2CH_3); 3.77 (3H, s, CO_2CH_3); 3.59 (3H, s, CO_2CH_3); 3.60-3.52 (4H, m, morpholine); 3.48-3.40 (4H, m, morpholine); 3.22 (2H, s, C<u>H</u>$_2$C(NH_2)=NO).

Thermolysis of O-vinyl-α-(aminocarbonyl)acetamidoximes. Compound **1** (2 mmol) was refluxed in mesitylene (4 ml) for 15 min under a nitrogen atmosphere. The mixture was diluted five times with hexane and the precipitate was filtered off and separated by column chromatography on silica gel using methylene chloride–methanol (20:1) as eluent. The yields are given in the Scheme.

Methyl 5-Amino-4-(2-methoxyethylaminocarbonyl)pyrrole-3-carboxylate (2a). Colorless crystals, mp 148-151ºC (ether). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 10.81 (1H, s, H-1); 9.43 (1H, t, *J* = 5.1, NH); 7.05 (1H, d, *J* = 2.9, J_{CH} = 195.0, H-2); 6.19 (2H, s, NH_2); 3.71 (3H, s, CO_2CH_3); 3.43-3.38 (2H, m, OCH$_2$C<u>H</u>$_2$NH); 3.26 (3H, s, CH$_2$OC<u>H</u>$_3$); 3.27-3.21 (2H, m, OC<u>H</u>$_2$CH$_2$NH). ^{13}C NMR spectrum, δ, ppm: 166.8 (<u>C</u>O_2CH_3); 165.6 (CONH); 148.1 (C-5), 121.2 (C-2); 108.7 (C-3); 92.3 (C-4); 71.2 (<u>C</u>H$_2$OCH$_3$); 58.0 (CH$_2$O<u>C</u>H$_3$); 51.4 (CO_2<u>C</u>H$_3$); 38.0 (OCH$_2$<u>C</u>H$_2$N). Mass spectrum, *m/z* (I_{rel}, %); 241 $[M]^+$ (25), 167 $[M–NH(CH_2)_2OCH_3]^+$ (84), 135 $[M\text{-}NH(CH_2)_2OCH_3\text{-}CH_3OH]^+$ (100), 84 (42), 79 (57). Found, %: C 49.35; H 6.14; N 17.48. $C_{10}H_{15}N_3O_4$. Calculated, %: C 49.79; H 6.27; N 17.42.

Methyl 4-(Diaminomethylene)-1-methoxyethyl-5-oxopyrroline-3-carboxylate (3a). Light green crystals, mp 186-188ºC (methylene chloride). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 9.35 (1H, br. s, NH_2) and 8.88 (1H, br. s, NH_2); 7.15 (1H, s, J_{CH} = 192.0, H-2); 6.85 (2H, s, NH_2); 3.74 (2H, t, *J* = 5.1, OCH$_2$C<u>H</u>$_2$NH); 3.69

(3H, s, CO_2CH_3); 3.47 (2H, t, J = 5.1, $OC\underline{H}_2CH_2NH$); 3.22 (3H, s, $CH_2OC\underline{H}_3$). ^{13}C NMR spectrum, δ, ppm: 166.4 ($\underline{C}O_2CH_3$); 164.3 (C-5); 159.0 ($=\underline{C}(NH_2)_2$); 126.0 (C-2); 104.5 (C-3); 81.2 (C-4); 70.4 ($\underline{C}H_2OCH_3$); 57.9 ($CH_2O\underline{C}H_3$); 51.2 ($CO_2\underline{C}H_3$); 41.40 ($OCH_2\underline{C}H_2N$). Mass spectrum, *m/z* (I_{rel}, %): 241 $[M]^+$ (100), 226 (9), 210 $[M–CH_3O]^+$ (8), 196 $[M–CH_2OCH_3]^+$ (20), 183 $[M–CHCH_2OCH_3]^+$ (30), 166 (23), 140 (16), 134 (23), 82 (7). Found, %: C 49.10; H 6.20; N 17.00. $C_{10}H_{15}N_3O_4$. Calculated, %: C 49.79; H 6.27; N 17.42.

Methyl 5-Amino-4-(2-methoxyethylaminocarbonyl)pyrrole-2-carboxylate (4a). Colorless crystals, mp 163-164ºC (methylene chloride). ^1H NMR spectrum, δ, ppm (*J*, Hz): 10.75 (1H, s, H-1); 7.70 (1H, t, J = 5.0, NH); 7.21 (1H, d, J = 2.9, J_{CH} = 173.0, H-2); 5.91 (2H, s, NH_2); 3.69 (3H, s, CO_2CH_3); 3.39-3.35 (2H, m, $OCH_2C\underline{H}_2NH$); 3.32-3.28 (2H, m, $OC\underline{H}_2CH_2NH$); 3.24 (3H, s, $CH_2OC\underline{H}_3$). ^{13}C NMR spectrum, δ, ppm: 165.3 ($\underline{C}O_2CH_3$); 160.6 ($\underline{C}ONH$); 148.0 (C-5); 114.7 (C-2); 112.0 (C-3); 98.3 (C-4); 70.9 ($\underline{C}H_2OCH_3$); 57.9 ($CH_2O\underline{C}H_3$); 50.7 ($CO_2\underline{C}H_3$); 37.9 ($OCH_2\underline{C}H_2N$). Mass spectrum, *m/z* (I_{rel}, %): 241 $[M]^+$ (54), 209 $[M–CH_3OH]^+$ (8), 183 $[M–CHCH_2OCH_3]^+$ (24); 167 $[M–NH(CH_2)_2OCH_3]^+$ (86), 151 $[M–CHCH_2OCH_3–CH_3OH]^+$ (18); 135 $[M–NH(CH_2)_2OCH_3–CH_3OH]^+$ (100), 108 (7), 84 (48), 79 (18). Found, %: C 49.52; H 6.25; N 17.13. $C_{10}H_{15}N_3O_4$. Calculated, %: C 49.79; H 6.27; N 17.42.

Methyl 5-Amino-4-(cyclohexylaminocarbonyl)pyrrole-3-carboxylate (2b). Light gray crystals, mp 237-239ºC (decomp. from methylene chloride). ^1H NMR spectrum, δ, ppm (*J*, Hz): 10.80 (1H, s, H-1); 9.35 (1H, d, J = 7.2, NH); 7.04 (1H, d, J = 2.0, J_{CH} = 192.0, H-2); 6.16 (2H, s, NH_2); 3.71 (3H, s, CO_2CH_3); 3.80-3.60 (1H, m, $NHC\underline{H}(CH_2)_5$); 1.82–1.50 and 1.35-1.19 (10H, m, cyclohexyl). ^{13}C NMR spectrum , δ, ppm: 166.9 ($\underline{C}O_2CH_3$); 164.6 ($\underline{C}ONH$); 147.8 (C-5); 121.1 (C-2); 108.6 (C-3); 92.6 (C-4); 51.4 ($CO_2\underline{C}H_3$); 46.3 (cyclohexyl C-1'); 32.7 (cyclohexyl C-2',6'); 25.4 (cyclohexyl C-4'); 24.2 (cyclohexyl C-3',5'). Mass spectrum, *m/z* (I_{rel}, %): 265 $[M]^+$ (50), 222 (7), 183 $[M+H–c\text{-}C_6H_{11}]^+$ (40), 167 $[M–NH\text{-}c\text{-}C_6H_{11}]^+$ (100), 166 $[M–NH_2\text{-}c\text{-}C_6H_{11}]^+$ (50), 151 (7), 135 $[M–NH\text{-}c\text{-}C_6H_{11}–CH_3\ OH]^+$ (24), 108 (10), 88 (32), 79 (13). Found, %: C 58.67; H 7.20; N 15.76. $C_{13}H_{19}N_3O_3$. Calculated, %: C 58.85; H 7.22; N 15.84.

Methyl 4-(Diaminomethylene)-1-cyclohexyl-5-oxopyrroline-3-carboxylate (3b). Gray crystals, mp 240-245ºC (decomp., from methylene chloride). ^1H NMR spectrum, δ, ppm (*J*, Hz): 9.44 (1H, br. s, NH_2) and 8.81 (1H, br. s, NH_2); 7.17 (1H, s, J_{CH} = 191.0, H-2); 6.83 (2H, s, NH_2); 3.97 (1H, m, $NHC\underline{H}(CH_2)_5$); 3.69 (3H, s, CO_2CH_3); 1.80-1.14 (10H, m, cyclohexyl). ^{13}C NMR spectrum, δ, ppm: 166.3 ($\underline{C}O_2CH_3$); 163.8 (C-5); 159.0 ($=\underline{C}(NH_2)_2$); 122.4 (C-2); 104.7 (C-3); 81.5 (C-4); 51.1 ($CO_2\underline{C}H_3$); 49.9 (cyclohexyl C-1'); 32.3 (cyclohexyl C-2',6'); 25.4 (cyclohexyl C-3',5'); 24.9 (cyclohexyl C-4'). Mass spectrum, *m/z* (I_{rel}, %): 265 $[M]^+$ (100), 249 $[M–NH_2]^+$ (5), 234 $[M–NH_2–CH_3O]^+$ (6), 183 $[M+H–c\text{-}C_6H_{11}]^+$ (66), 166 $[M–NH_2\text{-}c\text{-}C_6H_{11}]^+$ (37), 151 (9), 134 (50), 123 (6), 85 (6), 79 (6). Found, %: C 58.43; H 7.19; N 15.41. $C_{13}H_{19}N_3O_3$. Calculated, %: C 58.85; H 7.22; N 15.84.

Methyl 5-Amino-4-(cyclohexylaminocarbonyl)pyrrole-2-carboxylate (4b). Gray crystals, mp 163-164ºC (from methylene chloride). ^1H NMR spectrum, δ, ppm (*J*, Hz): 10.70 (1H, s, H-1); 7.37 (1H, d, J = 8.0, NH); 7.28 (1H, s, J_{CH} = 172.0, H-2); 5.90 (2H, s, NH_2); 3.80-3.60 (1H, m, $NHC\underline{H}(CH_2)_5$); 3.69 (3H, s, CO_2CH_3); 1.80-1.10 (10H, m, cyclohexyl). ^{13}C NMR spectrum, δ, ppm: 165.6 ($\underline{C}O_2CH_3$); 160.2 ($\underline{C}ONH$); 147.6 (C-5); 114.8 (C-2); 109.9 (C-3); 98.4 (C-4); 51.0 ($CO_2\underline{C}H_3$); 46.2 (cyclohexyl C-1'); 32.4 (cyclohexyl C-2',6'); 25.4 (cyclohexyl C-4'); 24.3 (cyclohexyl C-3',5'). Mass spectrum, *m/z* (I_{rel}, %): 265 $[M]^+$ (83), 234 $[M–CH_3O]^+$ (15), 233 $[M–CH_3OH]^+$ (17), 183 $[M+H–c\text{-}C_6H_{11}]^+$ (44), 167 $[M–NH\text{-}c\text{-}C_6H_{11}]^+$ (75), 166 $[M–NH_2\text{-}c\text{-}C_6H_{11}]^+$ (52), 151 (54), 135 $[M–NH\text{-}c\text{-}C_6H_{11}–CH_3OH]^+$ (100), 140 (31), 135 (100), 107 (27), 98 (48). Found, %: C 59.07; H 7.19; N 15.84. $C_{13}H_{19}N_3O_3$. Calculated, %: C 58.85; H 7.22; N 15.84.

Methyl 5-Amino-4-(4-chloroanilinocarbonyl)pyrrole-3-carboxylate (2c) was isolated as a mixture with the pyrrole **4c** in the ratio ~ 3:2. ^1H NMR spectrum, δ, ppm (*J*, Hz): 11.75 (1H, s, NH); 10.97 (1H, s, H-1); 7.65 (2H, d, J = 8.7, ArH); 7.35 (2H, d, J = 8.7, ArH); 7.16 (1H, d, J = 2.9, J_{CH} = 190.0, H-2,); 6.42 (2H, s, NH_2); 3.80 (3H, s, CO_2CH_3).

Methyl 1-(4-Chlorophenyl)-4-(diaminomethylene)-5-oxopyrrol-2-ine-3-carboxylate (3c). Light yellow crystals, mp 209-210ºC (acetonitrile). ^1H NMR spectrum, δ, ppm (*J*, Hz): 9.20 (1H, br. s, NH_2) and

8.90 (1H, br. s, NH_2); 7.72 (2H, d, J = 8.7, ArH); 7.47 (2H, d, J = 8.7, ArH); 7.45 (1H, s, J_{CH} = 193.0, H-2); 7.04 (2H, s, NH_2); 3.75 (3H, s, CO_2CH_3). ^{13}C NMR spectrum, δ, ppm: 166.4 ($\underline{C}O_2CH_3$); 163.5 (C-5); 159.2 (=$\underline{C}(NH_2)_2$); 136.4 (NHC_6H_4Cl-C-1'); 129.6 (NHC_6H_4Cl-C-4'); 128.7 (NHC_6H_4Cl-C-3',5'); 124.1 (NHC_6H_4Cl-C-4',6'); 122.6 (C-2); 107.6 (C-3); 81.5 (C-4); 51.6 ($CO_2\underline{C}H_3$). Mass spectrum, *m/z* (I_{rel}, %): 293 $[M]^+$ (100), 276 $[M–NH_3]^+$ (15), 244 $[M–NH_3–CH_3OH]^+$ (36), 209 (20), 111 $[C_7H_4Cl]^+$ (20). Found, %: C 51.94; H 4.11; N 12.82. $C_{13}H_{12}ClN_3O_3$. Calculated, %: C 53.16; H 4.12; N 14.31.

Methyl 5-Amino-4-(4-chloroanilinocarbonyl)pyrrole-2-carboxylate (4c) was isolated as a mixture with the pyrrole **2c** in the ratio ~2: 3. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 10.88 (1H, s, H-1); 9.46 (1H, s, NH); 7.76 (2H, d, J = 8.7, ArH); 7.50 (1H, d, J = 2.2, J_{CH} = 174.0, H-2); 7.32 (2H, d, J = 8.7, ArH); 6.08 (2H, s, NH_2); 3.73 (3H, s, CO_2CH_3).

Methyl 5-Amino-4-pyrrolidin-1-ylcarbonyl)pyrrole-3-carboxylate (2d) could not be isolated in an analytically pure state due to its decomposition on silica gel. However, treatment with phenyl isocyanate gave **methyl 4-(pyrrolidin-1-ylcarbonyl)-5-(3-phenylureido)pyrrole-3-carboxylate**. Phenyl isocyanate (0.05 ml) was added to a solution of the unpurified pyrrole **2d** obtained after thermolysis (400 mg) in chloroform (5 ml) and the product was heated to reflux. The solvent was evaporated and the residue was purified by column chromatography on silica gel using methylene chloride–methanol (20:1) as eluent. The urea was separated (165 mg, 23% calculated on compound **1d**). Light gray crystals, mp 203-205ºC (from acetonitrile). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 11.61 (1H, br. s, H-1); 9.29 (1H, br. s, $C_6H_5N\underline{H}$); 8.59 (1H, br. s, $C_6H_5NHCON\underline{H}$); 7.43 (2H, d, J = 8.0, H-3',5'); 7.28 (2H, t, J = 7.6, H-2',6'); 7.10 (1H, d, J = 2.9, J_{CH} = 196.0, H-2); 6.97 (1H, t, J = 7.3, H-4'); 3.68 (3H, s, CO_2CH_3); 3.51-3.39 (2H, m), 3.27-3.15 (2H, m) and 1.88-1.65 (4H, m) ($N(CH_2)_4$). ^{13}C NMR spectrum, δ, ppm: 164.2 ($\underline{C}O_2CH_3$); 163.9 ($\underline{C}ON(CH_2)_4$); 152.5 ($\underline{C}O(NH)_2$); 139.4 (C_6H_5 C-1'); 128.9 (C-5); 128.8 (C_6H_5 C-3',5'); 122.1 (C_6H_5 C-4'); 119.6 (C-2); 118.1 (C_6H_5 C-2',6'); 110.6 (C-3); 105.9 (C-4); 50.8 ($CO_2\underline{C}H_3$); 47.2 and 45.3 ($\underline{C}H_2N\underline{C}H_2$); 24.0 (($\underline{C}H_2)_2$). Mass spectrum, *m/z* (I_{rel}, %): 356 $[M]^+$ (28); 264 $[M–NHC_6H_5]^+$ (100); 237 (17), 232 $[M–NHC_6H_5–CH_3OH]^+$ (28); 193 $[M–NH_2C_6H_5–N(CH_2)_4]^+$ (100); 167 (47), 163 (60), 161 $[M–NH_2C_6H_5–CH_3OH–N(CH_2)_4]^+$ (35); 135 (53), 119 (47), 93 $[NH_2C_6H_5]^+$ (100). Found, %: C 60.53; H 5.64; N 15.49. $C_{18}H_{20}N_4O_4$. Calculated, %: C 60.66; H 5.66; N 15.72.

Methyl 5-Amino-4-(morpholin-1-ylcarbonyl)pyrrole-3-carboxylate (2e) could not be isolated in an analytically pure state due to its decomposition on silica gel. However, treatment with phenyl isocyanate gave **methyl 4-(morpholin-1-ylcarbonyl)-5-(3-phenylureido)pyrrole-3-carboxylate**. Phenyl isocyanate (0.28 ml) was added to a solution of the unpurified pyrrole **2e** obtained after thermolysis (650 mg) in methylene chloride (20 ml) and the product was heated to reflux. The solvent was evaporated and the residue was purified by column chromatography on silica gel using methylene chloride–methanol (30:1) as eluent. The urea was separated (320 mg, 28% calculated on compound **1e**). Light brown crystals, mp 247-248ºC (acetonitrile). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 11.69 (1H, br. s, H-1); 9.17 (1H, br. s, $C_6H_5N\underline{H}$); 8.48 (1H, br. s, $C_6H_5NHCON\underline{H}$); 7.44 (2H, d, J = 8.0, H-3',5'); 7.28 (2H, t, J = 7.6, H-2',6'); 7.15 (1H, d, J = 2.9, J_{CH} = 196.0, H-2); 6.98 (1H, t, J = 7.3, H-4'); 3.68 (3H, s, CO_2CH_3); 3.51-3.39 (2H, m), 3.27-3.15 (2H, m) and 1.88-1.65 (4H, m, $N(CH_2)_4$). ^{13}C NMR spectrum, δ, ppm: 164.4 ($\underline{C}O_2CH_3$); 163.7 ($\underline{C}ON(CH_2)_4$); 152.7 ($\underline{C}O(NH)_2$); 139.4 (C_6H_5 C-1'); 128.9 (C_6H_5 C-3',5'); 128.7 (C-5); 122.2 (C_6H_5 C-4'); 120.1 (C-2); 118.1 (C_6H_5 C-2',6'); 110.9 (C-3); 105.0 (C-4); 66.1 ($\underline{C}H_2O\underline{C}H_2$); 51.0 ($CO_2\underline{C}H_3$); 45.1 ($\underline{C}H_2N\underline{C}H_2$). Mass spectrum, *m/z* (I_{rel}, %): 372 $[M]^+$ (11); 285 $[M–NC_4H_8O]^+$ (5); 280 $[M–NHC_6H_5]^+$ (21); 279 $[M–NH_2C_6H_5]^+$ (11); 253 (5); 193 $[M–NH_2C_6H_5–N(CH_2)_4O]^+$ (53); 167 (22); 163 (18); 161 $[M–NH_2C_6H_5–CH_3OH–N(CH_2)_4O]^+$ (10); 135 (16); 119 (12); 93 $[NH_2C_6H_5]^+$ (100). Found, %: C 57.92; H 5.44; N 14. 97. $C_{18}H_{20}N_4O_5$. Calculated, %: C 58.06; H 5.41; N 15.05.

Dimethyl 5-Amino-4-(pyrrolidin-1-ylcarbonyl)pyrrole-2,3-dicarboxylate (8f). Yield 47%. Light gray crystals, mp 194-196ºC (from acetonitrile). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 11.02 (1H, br. s, H-1); 5.36 (2H, br. s, NH_2); 3.68 (6H, s, $2CO_2CH_3$); 3.45-3.32 (4H, m) and 1.92-1.80 (4H, m) ($N(CH_2)_4$). ^{13}C NMR spectrum, δ, ppm: 165.4 (3-$\underline{C}O_2CH_3$); 163.9 ($\underline{C}ON(CH_2)_4$); 159.6 (2-$\underline{C}O_2CH_3$); 143.1 (C-5); 121.3 (C-2); 110.9 (C-3); 101.3 (C-4); 51.8 ($CO_2\underline{C}H_3$); 51.2 ($CO_2\underline{C}H_3$); 46.3 ($\underline{C}H_2N\underline{C}H_2$); 24.9 (($\underline{C}H_2)_2$). Mass spectrum, *m/z* (I_{rel}, %): 295 $[M]^+$

(22); 264 $[M–CH_3O]^+$ (5); 263 $[M–CH_3OH]^+$ (5), 225 $[M–N(CH_2)_4]^+$ (12); 193 $[M–CH_3OH–N(CH_2)_4]^+$ (43); 163 (8), 135 (5), 108 (6), 70 $[N(CH_2)_4]^+$ (100). Found, %: C 52.78; H 5.66; N 14.11. $C_{13}H_{17}N_3O_5$. Calculated, %: C 52.88; H 5.8; N 14.23.

Dimethyl 5-amino-4-(morpholin-1-ylcarbonyl)pyrrole-2,3-dicarboxylate (8g). Yield 61%. Light gray crystals, mp 163-165ºC (from acetonitrile). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 11.03 (1H, br. s, H-1); 5.32 (2H, br. s, NH_2); 3.69 (6H, s, $2CO_2CH_3$); 3.56-3.52 (4H, m) and 3.45-3.35 (4H, m) (morpholine). ^{13}C NMR spectrum, δ, ppm: 165.0 (3-$\underline{C}O_2CH_3$); 164.6 ($\underline{C}ON(CH_2)_4$); 159.5 (2-$\underline{C}O_2CH_3$); 142.4 (C-5); 122.0 (C-2); 111.2 (C-3); 99.5 C-4); 66.2 ($\underline{C}H_2O\underline{C}H_2$); 51.8 ($CO_2\underline{C}H_3$); 51.2 ($CO_2\underline{C}H_3$); 45.0 ($\underline{C}H_2N\underline{C}H_2$). Mass spectrum, *m/z* (I_{rel}, %): 311 $[M]^+$ (30); 280 $[M–CH_3O]^+$ (8); 279 $[M–CH_3OH]^+$ (15), 225 $[M–N(CH_2)_4O]^+$ (36); 193 $[M–CH_3OH–N(CH_2)_4O]^+$ (100); 163 (15); 86 $[N(CH_2)_4O]^+$ (62). Found, %: C 52.78; H 5.66; N 14.11. $C_{13}H_{17}N_3O_5$. Calculated, %: C 52.88; H 5.8; N 14.23.

Methyl 2,4-dimethyl-8-(pyrrolidin-1-ylcarbonyl)pyrrolo[1,2-*a*]pyrimidine-7-carboxylate (7d). A solution of compound **1d** (0.55 g, 2 mmol) in 2,4-pentanedione (6 ml) was refluxed in a nitrogen atmosphere for 2 h. Solvent was evaporated and the residue was purified using column chromatography on silica gel with methylene chloride–methanol (20:1) as eluent. The product separated as a brown oil (0.34 g, 52%) which slowly crystallized to light brown crystals, mp 186-187ºC (from toluene). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.81 (1H, s, J_{CH} = 196.0, H-6); 6.69 (1H, s, H-3); 3.77 (3H, s, CO_2CH_3); 2.56 (3H, s, 4-CH_3); 2.40 (3H, s, 2-CH_3); 3.52-3.46 (2H, m); 3.14-3.10 (2H, m) and 1.92-1.72 (4H, m) ($N(CH_2)_4$). ^{13}C NMR spectrum, δ, ppm: 163.8 ($\underline{C}O_2CH_3$); 163.2 ($\underline{C}ON(CH_2)_4$); 155.5 (C-2); 142.2 (C-8b); 136.5 (C-4); 117.0 (C-6); 110.5 (C-7); 109.0 (C-3); 108.7 (C-8); 51.5 ($CO_2\underline{C}H_3$); 47.2 and 45.2 ($\underline{C}H_2N\underline{C}H_2$); 25.4 (2-$CH_3$); 24.2 ($(CH_2)_2$); 17.2 (4-$CH_3$). Mass spectrum, *m/z* (I_{rel}, %): 301 $[M]^+$ (36); 231 $[M–N(CH_2)_4]^+$ (100); 201 (17); 173 (29); 146 (17); 70 $[N(CH_2)_4]^+$ (34). Found, %: C 63.62; H 6.45; N 13.46. $C_{16}H_{19}N_3O_3$. Calculated, %: C 63.77; H 6.36; N 13.40.

Methyl 2,4-dimethyl-8-morpholin-1-ylcarbonyl)pyrrolo[1,2-*a*]pyrimidine-7-carboxylate (7e) was prepared similarly to compound **7d**. Yield 53%. Light brown crystals, mp 231-233ºC (toluene). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.86 (1H, s, J_{CH} = 197.0, H-6); 6.71 (1H, s, H-3); 3.80 (3H, s, CO_2CH_3); 2.58 (3H, s, 4-CH_3); 2.41 (3H, s, 2-CH_3); 3.70-3.63 (4H, m), 3.51-3.47 (2H, m) and 3.21-3.17 (2H, m) ($N(CH_2)_4O$). ^{13}C NMR spectrum, δ, ppm: 163.8 ($\underline{C}O_2CH_3$); 163.6 ($\underline{C}ON(CH_2)_4$); 155.9 (C-2); 142.4 (C-8b); 136.7 (C-4); 117.5 (C-6); 110.9 (C-7); 109.1 (C-3); 106.2 (C-8); 66.2 and 66.1 ($\underline{C}H_2O\underline{C}H_2$); 51.5 ($CO_2\underline{C}H_3$); 47.02 and 41.9 ($\underline{C}H_2N\underline{C}H_2$); 24.24 (2-$CH_3$); 17.2 (4-$CH_3$). Mass spectrum, *m/z* (I_{rel}, %): 317 $[M]^+$ (16); 231 $[M–N(CH_2)_4O]^+$ (100); 201 (12); 173 (16); 146 (11); 86 $[N(CH_2)_4O]^+$ (40). Found, %: C 60.51; H 6.12; N 13.02. $C_{16}H_{19}N_3O_4$. Calculated, %: C 60.56; H 6.03; N 13.24.

REFERENCES

1. S. E. Korostova, A. I. Mikhaleva, and B. A. Trofimov, *Usp. Khim.*, **68**, 506 (1999).
2. M. R. Grimmett, *Imidazole and Benzimidazole Synthesis*, Academic Press, London (1997).
3. E. Pretsch, P. Bühlmann, and K. Affolter, *Determination of the Structure of Organic Compounds* [Russian translation], Mir, Moscow (2006).