Synthesis of 5-substituted 4-aminoalkylpyrazol-3-ones (isoxazol-3-ones) from 3-acyllactams

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Structurally various 3-acyllactams act as 1,3-bielectrophiles in heterocyclization reactions with a variety of hydrazines and hydroxylamines to give aminoalkylpyrazolones and -isoxazolones in high yields.

Key words: 3-acyllactams, pyrazol-3-ones, isoxazol-3-ones, hydrazines, hydroxylamine, heterocyclization.

Reactions of 1,3-dicarbonyl compounds with 1,2-, 1,3-, and 1,4-binucleophiles represent a versatile approach to the syntheses of important nitrogen-containing heterocycles such as pyrazoles, isoxazoles, pyrimidines, *etc*.[1]

3-Acyllactams contain a 1,3-dicarbonyl fragment with the acyl and amide CO groups strongly differing in reactivity. This opens up a promising route to chemo- and regioselective heterocyclization with unsymmetrical binucleophiles. Acyllactams are mainly synthesized by *C*-acylation of *N*-protected lactams with acid anhydrides, acid chlorides,[2] acid fluorides,[3] esters,[4] carboxylic acids,[5] chloroformates,[6] diketene,[7] and pyrrolidin-2-one.[8]

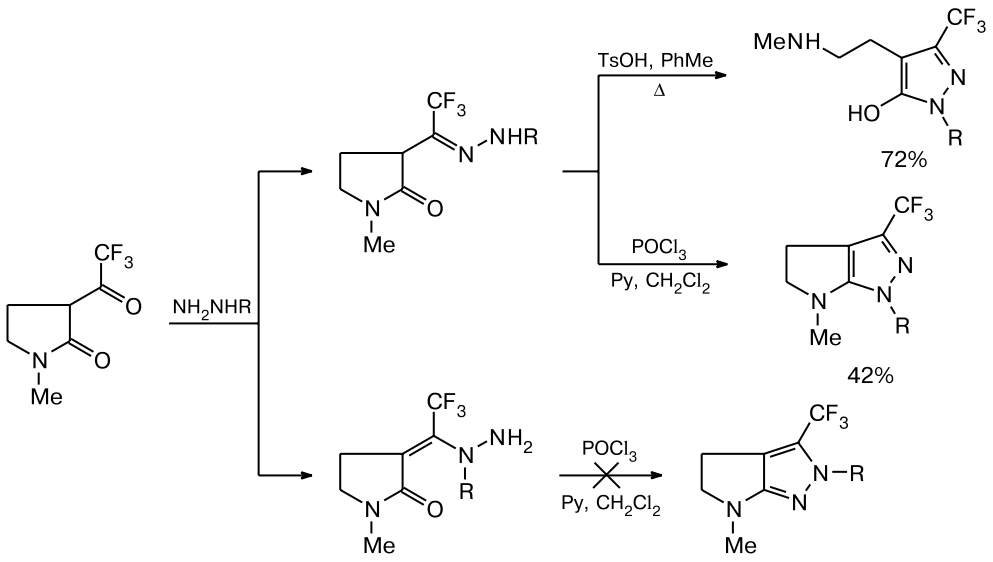
A survey of the literature data revealed that reactions of 3-acyllactams as bielectrophiles with symmetrical and unsymmetrical C,N,S,O-binucleophiles have been studied inadequately.

Single examples of pyrazole formation from 3-acyllactams and hydrazines were reported for the synthesis of trifluoromethylpyrazoles.[9] The reaction products were mixtures of fused or aminoalkyl derivatives of pyrazoles, depending on the hydrazine structure and the cyclization conditions (Scheme 1).

There is only one documented synthesis of isoxazoles by the reaction of 3-acyllactam with hydroxylamine, which was used to obtain analogs of a new fungicidal antibiotic.[10]

For investigation of the properties of *N*-protected 3-acyllactams in reactions with binucleophiles and of the effects of the nature of the acyl and protective groups and

Scheme 1



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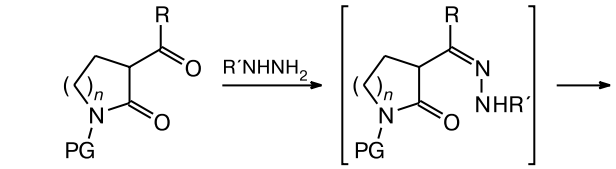
the ring size on heterocyclization, previously we synthesized[11] a wide range of 3-acyllactams containing various substituents (aromatic, heteroaromatic, aliphatic, sterically bulky, framework, and those with the vinyl and diethoxymethyl protective groups).

The goal of the present work was to develop a versatile approach to the syntheses of aminoalkylpyrazoles and -isoxazoles. During the course of the reaction, closure of one heterocycle is accompanied by the opening of the other. The presence of an aminoalkyl fragment in the compounds obtained suggests their potential biological activities.

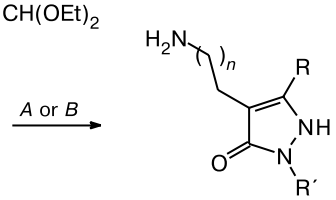
The reactions of 3-acyllactams with hydrazine and its derivatives occur under mild conditions to give 5-substituted 4-aminoalkylpyrazol-3-ones in virtually quantitative yields (Scheme 2). It turned out that heterocyclization into pyrazoles is promoted by 5% solutions of acids (H_2SO_4, HCl, HCO_2H, and AcOH) in ethanol; in the absence of an acid, the reaction is 2 to 3 times slower. The reaction is of general character; the yield and the reaction course do not depend on the nature of the acyl group and the size of the acyllactam ring. In all cases, the *N*-vinyl and *N*-diethoxymethyl protective groups were completely eliminated during the reaction. The developed method is simple and can be easily scaled.

Analogously, *N*-methylated 3-acyllactams react with hydrazine and phenylhydrazine to give substituted *N*-methylpyrazoles (Scheme 3).

Scheme 2



n = 1, 3, PG = CH_2=CH
n = 2, PG = $CH(OEt)_2$



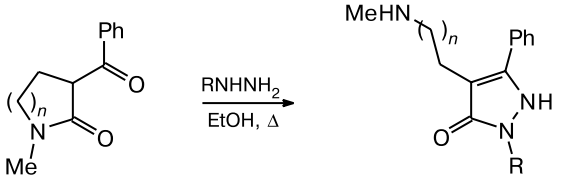
1—22

1—15: n = 1, PG = CH_2=CH;
16—18: n = 2, PG = $CH(OEt)_2$
19—22: n = 3, PG = CH_2=CH

Product	R	R′	Method*	Yield (%)
1	Ph	Ph	*A*	89
2	4-$MeOC_6H_4$	Ph	*A*	93
3	4-$MeOC_6H_4$	4-BrC_6H_4	*A*	90
4	Ph	H	*A*	96
5	Ad	H	*B*	88
6	Bu^t	H	*B*	96
7	4-FC_6H_4	H	*B*	95
8	4-$MeOC_6H_4$	H	*B*	93
9	3-$Me_2NC_6H_4$	H	*B*	91
10	Bn	H	*B*	82
11	$MeSCH_2$	H	*B*	90
12	Me	H	*B*	92
13	Ph	(C=O)NH_2	*B*	88
14	3-ClC_6H_4	(C=S)NH_2	*A*	91
15	Ph	(C=NH)NH_2	*A*	95
16	3-BrC_6H_4	H	*B*	94
17	4-Py	H	*B*	93
18	4-$Me_2NC_6H_4$	H	*B*	87
19	4-Py	H	*B*	90
20	Ph	H	*B*	92
21	4-MeC_6H_4	H	*B*	88
22	*c*-Hexyl	H	*B*	84

* *A*. 4% H_2SO_4, Δ; *B*. EtOH, Δ.

Scheme 3



23: n = 1, R = Ph, 88%
24: n = 2, R = H, 92%

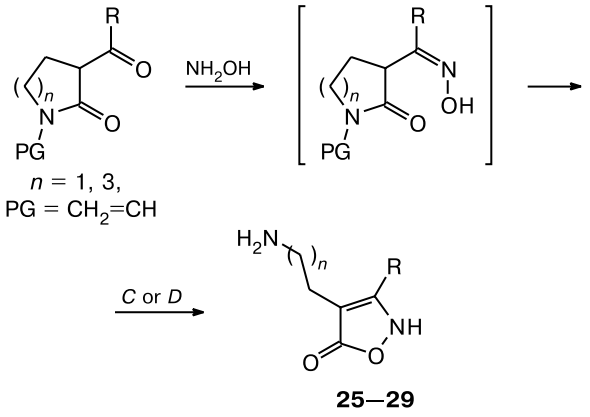
Procedures for the reactions of 3-acyllactams with hydroxylamine leading to isoxazoles should be slightly different, depending on the nature of the acyl group (Scheme 4). For instance, the optimum reaction conditions for 3-acyllactams containing 3- or 4-pyridyl substituents are $NH_2OH \cdot HCl$ (1 equiv.) in boiling ethanol. In the reactions with other 3-acyllactams, a mixture of hydroxylamine (1 equiv.) and its hydrochloride (1 equiv.) in aqueous ethanol was used.

In the case of the 2-pyridyl or pyrazinyl substituents, the heterocyclization conditions were not found: a complex mixture of products was obtained. Neither 3-acyllactams with a N—Me fragment gave isoxazoles because the reaction stopped at the step of oxime formation.

Being 1,3-bielectrophiles, 3-acyllactams could react with unsymmetrical binucleophiles along two pathways. Nevertheless, the heterocyclization is regiospecific because the acyl CO group is substantially more reactive than the amide one and the β-N atom in phenylhydrazine is more nucleophilic than the α-N atom due to the $-I$ effect of the benzene ring. This was additionally confirmed by spectroscopic data: all the pyrazoles obtained contain no isomeric products and their ^1H and ^{13}C NMR spectra are similar. Irradiation of the *ortho*-protons of the phenyl group in compound **23** resulted in no NOE on the rest of the molecule.

Thus, we developed a new general method for the synthesis of 4-aminoalkylpyrazol-3-ones and -isoxazol-3-ones. Various hydrazines and hydroxylamine react with

Scheme 4



Product	*n*	R	Method*	Yield (%)
25	1	Ph	*C*	89
26	1	3-BrC_6H_4	*C*	61
27	1	3-Py	*D*	85
28	1	4-Py	*D*	78
29	3	Ph	*C*	35

* *C*. H_2NOH, $H_2NOH \cdot HCl$, EtOH, H_2O, Δ; *D*. $H_2NOH \cdot HCl$, EtOH, Δ.

3-acyllactams under mild conditions to give the target products in high yields.

Experimental

^1H and ^{13}C NMR spectra were recorded on a Varian VXR-400 spectrometer (400 and 100 MHz, respectively) in $(CD_3)_2SO$ with Me_4Si as the internal standard. Chemical shifts are referenced to Me_4Si with an accuracy of 0.01 ppm. IR spectra were recorded on a UR-20 spectrophotometer (thin film for liquids and Nujol for solids). TLC analysis was performed on Silufol UV-254 plates; spots were visualized in an acidified solution of $KMnO_4$, with a solution of ninhydrin in butanol, in a chamber with the iodine vapor, and with a UV lamp. Preparative column chromatography was carried out on silica gel (63—200 mesh, Merck).

Synthesis of pyrazoles (general procedure). Procedure *A*. Synthesis of pyrazole salts. To a solution of 3-acyllactam (5 mmol) in 25 mL of 4% H_2SO_4, 95% $N_2H_4 \cdot H_2O$ (0.3 mL) was added and the mixture was refluxed for 5 to 10 h. The course of the reaction was monitored by TLC ($MeCN—NH_3$(aq), 95 : 5). Then the reaction mixture was evaporated to dryness and the residue was co-evaporated with water (5 mL) and recrystallized from Pr^iOH. Attempted preparation of free pyrazole bases by alkalization gave thick oils, for which reason we developed another approach to the synthesis of free pyrazoles.

Procedure *B*. Synthesis of free pyrazole bases. To a solution of 3-acyllactam (5 mmol) in 20 mL of EtOH, 95% $N_2H_4 \cdot H_2O$ (2 equiv.) was added and the mixture was refluxed for 10 to 20 h. The course of the reaction was monitored by TLC ($MeCN—NH_3$(aq), 95 : 5). Then the reaction mixture was evaporated to dryness, co-evaporated with water (5 mL), and recrystallized from Pr^iOH.

4-(2-Aminoethyl)-2,5-diphenyl-1,2-dihydro-3*H*-pyrazol-3-one sulfate hydrate (1). Procedure *A*. Yield 89%, m.p. 158—160.5 °C (decomp.). Found (%): C, 51.85; H, 5.24. $C_{17}H_{21}N_3O_6S$. Calculated (%): C, 51.64; H, 5.35. IR, ν/cm^{-1}: 2820—3020. ^1H NMR (400 MHz, $(CD_3)_2SO$), δ: 2.68 (m, 2 H, N—CH_2—C$\underline{H}_2$); 2.92—3.03 (m, 2 H, N—C$\underline{H}_2$—CH_2); 7.04 (t, 1 H, 4-$CH_{Ph—C}$, $^3J_{H,H}$ = 7.3 Hz); 7.22—7.44 (m, 5 H, 3-, 5-$CH_{Ph—C}$, 3-, 4-, 5-$CH_{Ph—N}$); 7.56 (m, 2 H, 2-, 6-$CH_{Ph—N}$); 8.17 (m, 2 H, 2-, 6-$CH_{Ph—C}$). ^{13}C NMR (400 MHz, $(CD_3)_2SO$), δ: 23.26 (N—CH_2—$\underline{C}H_2$); 41.19 (N—$\underline{C}H_2$—CH_2); 92.80 (N—CH_2—CH_2—$\underline{C}$); 118.68 (2-, 6-$CH_{Ph—C}$); 122.52 (4-$CH_{Ph—C}$); 126.68 (4-$CH_{Ph—N}$); 127.51 (2-, 6-$CH_{Ph—N}$); 128.08 (3-, 5-$CH_{Ph—N}$); 128.15 (3-, 5-$CH_{Ph—C}$); 135.92 (1-$C_{Ph—N}$); 141.43 (1-$C_{Ph—C}$); 148.91 (N—C—C=$\underline{C}$—N); 162.29 (N—CO).

4-(2-Aminoethyl)-5-(4-methoxyphenyl)-2-phenyl-1,2-dihydro-3*H*-pyrazol-3-one sulfate trihydrate (2). Procedure *A*. Yield 93%, m.p. 139—141 °C (decomp.). Found (%): C, 46.67; H, 5.73. $C_{18}H_{27}N_3O_9S$. Calculated (%): C, 46.85; H, 5.90. IR, ν/cm^{-1}: 2820—2940. ^1H NMR (400 MHz, $(CD_3)_2SO$), δ: 2.74—2.87 (m, 2 H, N—CH_2—C$\underline{H}_2$); 2.93—3.06 (m, 2 H, N—C$\underline{H}_2$—CH_2); 3.80 (s, 3 H, OMe); 7.07 (d, 2 H, 2-, 6-CH_{Ph}, $^3J_{H,H}$ = 8.0 Hz); 7.25 (t, 1 H, 4-CH_{Ph}, $^3J_{H,H}$ = 7.4 Hz); 7.46 (t, 2 H, 3-, 5-CH_{Ph}, $^3J_{H,H}$ = 7.4 Hz); 7.62 (d, 2 H, 3-, 5-$CH_{C_6H_4}$, $^3J_{H,H}$ = 8.0 Hz); 7.79 (d, 2 H, 2-, 6-$CH_{C_6H_4}$, $^3J_{H,H}$ = 8.0 Hz); 7.92 (br.s, 2 H, N$\underline{H}$—CH_2—CH_2). ^{13}C NMR (400 MHz, $(CD_3)_2SO$), δ: 21.05 (N—CH_2—$\underline{C}H_2$); 38.67 (N—$\underline{C}H_2$—CH_2); 55.32 (OMe); 99.29 (N—CH_2—CH_2—$\underline{C}$); 114.37 (3-, 5-$CH_{C_6H_4}$); 120.61 (2-, 6-CH_{Ph}); 123.33 (1-$C_{C_6H_4}$); 125.57 (4-CH_{Ph}); 128.85 (3-, 5-CH_{Ph}); 129.09 (2-, 6-$CH_{C_6H_4}$); 137.57 (1-C_{Ph}); 148.94 (N—C—C=$\underline{C}$—N); 157.81 (4-$C_{C_6H_4}$); 160.01 (N—CO).

4-(2-Aminoethyl)-2-(4-bromophenyl)-5-(4-methoxyphenyl)-1,2-dihydro-3*H*-pyrazol-3-one sulfate hydrate (3). Procedure *A*. Yield 90%, m.p. 167—169.5 °C (decomp.). Found (%): C, 42.65; H, 4.48. $C_{18}H_{22}BrN_3O_7S$. Calculated (%): C, 42.87; H, 4.40. IR, ν/cm^{-1}: 2820—2960. ^1H NMR (400 MHz, $(CD_3)_2SO$), δ: 2.72—2.82 (m, 2 H, N—CH_2—C$\underline{H}_2$); 2.92—3.02 (m, 2 H, N—C$\underline{H}_2$—CH_2); 3.76 (s, 3 H, OMe); 7.06 (d, 2 H, 3-, 5-CH arom., C_6H_4OMe, $^3J_{H,H}$ = 8.8 Hz); 7.60 (d, 2 H, 2-, 6-CH arom., C_6H_4Br, $^3J_{H,H}$ = 8.7 Hz); 7.64 (d, 2 H, 3-, 5-CH arom., C_6H_4Br, $^3J_{H,H}$ = 8.7 Hz); 7.80 (d, 2 H, 2-, 6-CH arom., C_6H_4OMe, $^3J_{H,H}$ = 8.8 Hz); 7.91 (br.s, 2 H, N$\underline{H}$—CH_2—CH_2). ^{13}C NMR (400 MHz, $(CD_3)_2SO$), δ: 20.97 (N—CH_2—$\underline{C}H_2$); 38.67 (N—$\underline{C}H_2$—CH_2); 55.13 (OMe); 96.32 (HN—C—$\underline{C}$=C—N); 114.07 (3-, 5-CH arom., C_6H_4OMe); 116.82 (4-C arom., C_6H_4Br); 121.49 (3-, 5-CH arom., C_6H_4Br); 128.80 (2-, 6-CH arom., C_6H_4Br); 131.41 (2-, 6-CH arom., C_6H_4OMe); 137.44 (1-C arom., C_6H_4OMe); 143.28 (1-C arom., C_6H_4Br); 146.28 (N—C—C=$\underline{C}$—N); 159.66 (4-C arom., C_6H_4OMe); 163.34 (N—CO).

4-(2-Aminoethyl)-5-phenyl-1,2-dihydro-3*H*-pyrazol-3-one sulfate dihydrate (4). Procedure *A*. Yield 96%, m.p. 143—146 °C (decomp.). Found (%): C, 39.05; H, 5.92. $C_{11}H_{19}N_3O_7S$. Calculated (%): C, 39.16; H, 5.68. IR, ν/cm^{-1}: 2870—3000. ^1H NMR (400 MHz, $(CD_3)_2SO$), δ: 2.69—2.77 (m, 2 H, N—CH_2—C$\underline{H}_2$); 2.86—2.97 (m, 2 H, N—C$\underline{H}_2$—CH_2); 7.35—7.41 (m, 1 H, 4-CH_{Ph}); 7.43—7.53 (m, 4 H, 2-, 3-, 5-, 6-CH_{Ph}). ^{13}C NMR (400 MHz, $(CD_3)_2SO$), δ: 20.78 (N—CH_2—$\underline{C}H_2$); 38.77 (N—$\underline{C}H_2$—CH_2); 96.42 (HN—C—$\underline{C}$=C—N); 127.05 (2-, 6-CH_{Ph}); 128.21

(4-CH_{Ph}); 129.01 (3-, 5-CH_{Ph}); 130.35 (1-C_{Ph}); 140.74 (HN—C—C=C—N); 160.45 (HN—CO).

5-Adamantyl-4-(2-aminoethyl)-1,2-dihydro-3*H*-pyrazol-3-one hydrate (5). Procedure *B*. Yield 88%, m.p. 169—172 °C (decomp.). Found (%): C, 64.73; H, 8.78. $C_{15}H_{25}N_3O_2$. Calculated (%): C, 64.49; H, 9.02. IR, ν/cm^{-1}: 2830—2920. ^{1}H NMR (400 MHz, $(CD_3)_2SO$), δ: 1.68—1.73 (m, 6 H, 4-, 6-, 10-CH_2, Ad); 1.85—1.90 (m, 6 H, 2-, 8-, 9-CH_2, Ad); 1.95—2.02 (m, 3 H, 3-, 5-, 7-CH, Ad); 2.63—2.72 (m, 2 H, N—CH_2—CH_2); 2.76—2.85 (m, 2 H, N—CH_2—CH_2). ^{13}C NMR (400 MHz, $(CD_3)_2SO$), δ: 21.25 (N—CH_2—CH_2); 27.77 (3-, 5-, 7-CH, Ad); 34.07 (1-C, Ad); 35.99 (4-, 6-, 10-CH_2, Ad); 39.28 (N—CH_2—CH_2); 40.53 (2-, 8-, 9-CH_2, Ad); 94.80 (HN—C—C=C—N); 148.91 (HN—C—C=C—N); 160.26 (HN—CO).

4-(2-Aminoethyl)-5-*tert*-butyl-1,2-dihydro-3*H*-pyrazol-3-one (6). Procedure *B*. Yield 96%, m.p. 212—215 °C (decomp.). Found (%): C, 60.17; H, 9.21. $C_9H_{17}N_3O$. Calculated (%): C, 58.99; H, 9.35. IR, ν/cm^{-1}: 2840—3010. ^{1}H NMR (400 MHz, $(CD_3)_2SO$), δ: 1.21 (s, 9 H, CMe_3); 2.51 (t, 2 H, N—CH_2—CH_2, $^3J_{H,H}$ = 5.6 Hz); 2.75 (t, 2 H, N—CH_2—CH_2, $^3J_{H,H}$ = 5.6 Hz). ^{13}C NMR (400 MHz, $(CD_3)_2SO$), δ: 20.78 (N—CH_2—CH_2); 29.75 (CMe_3); 33.66 (CMe_3); 39.15 (N—CH_2—CH_2); 98.38 (HN—C—C=C—N); 155.54 (HN—C—C=C—N); 155.66 (HN—CO).

4-(2-Aminoethyl)-5-(4-fluorophenyl)-1,2-dihydro-3*H*-pyrazol-3-one (7). Procedure *B*. Yield 95%, m.p. 268—272 °C (decomp.). Found (%): C, 59.75; H, 5.41. $C_{11}H_{12}FN_3O$. Calculated (%): C, 59.72; H, 5.47. IR, ν/cm^{-1}: 2870—3010. ^{1}H NMR (400 MHz, $(CD_3)_2SO$), δ: 2.71—2.81 (m, 2 H, N—CH_2—CH_2); 2.90—2.98 (m, 2 H, N—CH_2—CH_2); 7.14—7.23 (m, 2 H, 3-, 5-$CH_{C_6H_4}$); 7.43—7.51 (m, 2 H, 2-, 6-$CH_{C_6H_4}$); 7.55 (br.s, 2 H, HN—CH_2—CH_2). ^{13}C NMR (400 MHz, $(CD_3)_2SO$), δ: 20.64 (N—CH_2—CH_2); 38.60 (N—CH_2—CH_2); 96.29 (HN—C—C=C—N); 115.91 (3-, 5-$CH_{C_6H_4}$); 126.94 (1-$C_{C_6H_4}$); 129.24 (2-, 6-$CH_{C_6H_4}$); 139.72 (HN—C—C=C—N); 160.30 (HN—CO); 160.65 (C—F).

4-(2-Aminoethyl)-5-(4-methoxyphenyl)-1,2-dihydro-3*H*-pyrazol-3-one (8). Procedure *B*. Yield 93%, m.p. 194—197 °C (decomp.). Found (%): C, 61.96; H, 6.29. $C_{12}H_{15}N_3O_2$. Calculated (%): C, 61.79; H, 6.48. IR, ν/cm^{-1}: 2860—3000. ^{1}H NMR (400 MHz, $(CD_3)_2SO$), δ: 2.54 (t, 2 H, N—CH_2—CH_2, $^3J_{H,H}$ = 5.1 Hz); 2.80 (t, 2 H, N—CH_2—CH_2, $^3J_{H,H}$ = 5.1 Hz); 3.76 (s, 3 H, OMe); 6.96 (d, 2 H, 3-, 5-$CH_{C_6H_4}$, $^3J_{H,H}$ = 8.3 Hz); 7.34 (d, 2 H, 2-, 6-$CH_{C_6H_4}$, $^3J_{H,H}$ = 8.3 Hz). ^{13}C NMR (400 MHz, $(CD_3)_2SO$), δ: 20.49 (N—CH_2—CH_2); 38.73 (HN—CH_2—CH_2); 56.51 (OMe); 98.63 (N—C—C=C—N); 115.69 (3-, 5-$CH_{C_6H_4}$); 119.66 (4-$C_{C_6H_4}$); 130.87 (2-, 6-$CH_{C_6H_4}$); 146.45 (HN—C—C=C—N); 156.41 (HN—CO); 161.74 (C—OMe).

4-(2-Aminoethyl)-5-[3-(dimethylamino)phenyl]-1,2-dihydro-3*H*-pyrazol-3-one (9). Procedure *B*. Yield 91%, m.p. 209.5—213 °C (decomp.). Found (%): C, 63.61; H, 7.50. $C_{13}H_{18}N_4O$. Calculated (%): C, 63.39; H, 7.37. IR, ν/cm^{-1}: 2860—2980. ^{1}H NMR (400 MHz, $(CD_3)_2SO$), δ: 2.78—2.91 (m, 4 H, N—CH_2—CH_2); 3.14 (s, 6 H, NMe_2); 7.62—7.73 (m, 2 H, 5-, 6-$CH_{C_6H_4}$); 7.90 (d, 1 H, 4-$CH_{C_6H_4}$, $^3J_{H,H}$ = 7.9 Hz); 7.97 (s, 1 H, 2-$CH_{C_6H_4}$). ^{13}C NMR (400 MHz, $(CD_3)_2SO$), δ: 20.25 (N—CH_2—CH_2); 38.52 (N—CH_2—CH_2); 46.43 (NMe_2); 99.46 (HN—C—C=C—N); 121.77 (4-$CH_{C_6H_4}$); 123.43 (3-$C_{C_6H_4}$); 129.25 (2-$CH_{C_6H_4}$); 130.07 (6-$CH_{C_6H_4}$); 131.93 (5-$CH_{C_6H_4}$); 144.10 (1-$C_{C_6H_4}$); 144.13 (HN—C—C=C—N); 156.63 (HN—C—C=C—N).

4-(2-Aminoethyl)-5-benzyl-1,2-dihydro-3*H*-pyrazol-3-one (10). Procedure *B*. Yield 82%, m.p. 197.5—199 °C (decomp.). Found (%): C, 66.33; H, 6.73. $C_{12}H_{15}N_3O$. Calculated (%): C, 66.34; H, 6.96. IR, ν/cm^{-1}: 2865—2985. ^{1}H NMR (400 MHz, $(CD_3)_2SO$), δ: 2.54—2.64 (m, 2 H, N—CH_2—CH_2); 2.71—2.80 (m, 2 H, N—CH_2—CH_2); 3.91 (s, 2 H, Ph—CH_2); 7.10—7.27 (m, 5 H, Ph). ^{13}C NMR (400 MHz, $(CD_3)_2SO$), δ: 20.32 (N—CH_2—CH_2); 31.84 (Ph—CH_2); 39.65 (N—CH_2—CH_2); 99.81 (HN—C—C=C—N); 129.05 (4-CH_{Ph}); 130.1 (3-, 5-CH_{Ph}); 130.69 (2-, 6-CH_{Ph}); 136.94 (1-C_{Ph}); 149.22 (HN—C—C=C—N); 156.58 (HN—CO).

4-(2-Aminoethyl)-5-[(methylthio)methyl]-1,2-dihydro-3*H*-pyrazol-3-one (11). Procedure *B*. Yield 90%, m.p. 200.5—203 °C (decomp.). Found (%): C, 45.16; H, 7.13. $C_7H_{13}N_3OS$. Calculated (%): C, 44.90; H, 7.00. IR, ν/cm^{-1}: 2845—2980. ^{1}H NMR (400 MHz, $(CD_3)_2SO$), δ: 1.90 (s, 3 H, CH_2—S—Me); 2.63—2.70 (m, 2 H, N—CH_2—CH_2); 2.89—2.97 (m, 2 H, N—CH_2—CH_2); 3.64 (s, 2 H, CH_2—S—Me). ^{13}C NMR (400 MHz, $(CD_3)_2SO$), δ: 16.06 (CH_2—S—Me); 20.07 (N—CH_2—CH_2); 26.99 (CH_2—S—Me); 39.44 (N—CH_2—CH_2); 99.67 (HN—C—C=C—N); 147.05 (HN—C—C=C—N); 156.23 (HN—CO).

4-(2-Aminoethyl)-5-methyl-1,2-dihydro-3*H*-pyrazol-3-one hydrate (12). Procedure *B*. Yield 92%, m.p. 145—147.5 °C (decomp.). Found (%): C, 45.18; H, 8.25. $C_6H_{13}N_3O_2$. Calculated (%): C, 45.27; H, 8.23. IR, ν/cm^{-1}: 2860—2960. ^{1}H NMR (400 MHz, $(CD_3)_2SO$), δ: 2.38 (s, 3 H, Me); 2.84 (t, 2 H, N—CH_2—CH_2, $^3J_{H,H}$ = 7.5 Hz); 3.19 (t, 2 H, N—CH_2—CH_2, $^3J_{H,H}$ = 7.5 Hz). ^{13}C NMR (400 MHz, $(CD_3)_2SO$), δ: 11.06 (Me); 20.10 (N—CH_2—CH_2); 39.69 (N—CH_2—CH_2); 99.59 (HN—C—C=C—N); 147.20 (HN—C—C=C—N); 156.16 (HN—CO).

4-(2-Aminoethyl)-5-oxo-3-phenyl-2,5-dihydro-1*H*-pyrazole-1-carboxamide (13). Procedure *B*. Yield 88%, m.p. 224—227 °C (decomp.). Found (%): C, 58.81; H, 5.55. $C_{12}H_{14}N_4O_2$. Calculated (%): C, 58.53; H, 5.73. IR, ν/cm^{-1}: 2810—3020, 1610. ^{1}H NMR (400 MHz, $(CD_3)_2SO$), δ: 2.69—2.77 (m, 2 H, N—CH_2—CH_2); 2.86—2.96 (m, 2 H, N—CH_2—CH_2); 7.35—7.41 (m, 1 H, 4-CH_{Ph}); 7.43—7.53 (m, 4 H, 2-, 3-, 5-, 6-CH_{Ph}); 7.78 (br.s, 3 H, N—C(=O)—NH_2). ^{13}C NMR (400 MHz, $(CD_3)_2SO$), δ: 20.76 (N—CH_2—CH_2); 38.74 (N—CH_2—CH_2); 96.40 (HN—C—C=C—N); 127.03 (2-, 6-CH_{Ph}); 128.16 (4-CH_{Ph}); 128.95 (3-, 5-CH_{Ph}); 130.34 (1-C_{Ph}); 140.73 (HN—C—C=C—N); 160.38 (HN—C—C=C—N); 203.83 (N—C(=O)—NH_2).

4-(2-Aminoethyl)-3-(3-chlorophenyl)-5-oxo-2,5-dihydro-1*H*-pyrazole-1-carbothioamide sulfate (14). Procedure *B*. Yield 91%, m.p. 141—142 °C (decomp.). Found (%): C, 36.70; H, 3.65. $C_{12}H_{15}ClN_4O_5S_2$. Calculated (%): C, 36.5; H, 3.83. IR, ν/cm^{-1}: 2810—3020, 1480. ^{1}H NMR (400 MHz, $(CD_3)_2SO$), δ: 2.66—2.78 (m, 2 H, NCH_2CH_2); 2.86—2.97 (m, 2 H, NCH_2CH_2); 6.25 (br.s, 3 H, S=C—NH_3^+); 7.40—7.55 (m, 4 H, H arom.); 7.75 (br.s, 3 H, $NH_2^+ \cdot HSO_4^-$). ^{13}C NMR (400 MHz, $(CD_3)_2SO$), δ: 20.67 (N—CH_2—CH_2); 38.57 (N—CH_2—CH_2); 96.80 (HN—C—C=C—N); 125.75, 126.54, 126.57, 127.97, 130.88, 132.50 (C arom.); 133.60 (N—C(=S)—NH_2); 139.32 (HN—C—C=C—N); 160.19 (HN—CO).

4-(2-Aminoethyl)-5-oxo-3-phenyl-2,5-dihydro-1*H*-pyrazole-1-carboximidamide sulfate (15). Procedure *A*. Yield 95%, m.p.

259—260 °C (decomp.). Found (%): C, 49.25; H, 5.21. $C_{24}H_{32}N_{10}O_6S$. Calculated (%): C, 48.97; H, 5.48. IR, ν/cm^{-1}: 2810—3020, 1660. ^{1}H NMR (400 MHz, $(CD_3)_2SO$), δ: 2.59 (t, 2 H, $NCH_2C\underline{H}_2$, $^3J_{H,H}$ = 6.8 Hz); 2.90—2.99 (m, 2 H, $NC\underline{H}_2CH_2$); 7.37—7.47 (m, 3 H, Ph); 7.75—7.58 (m, 2 H, Ph); 7.98—8.06 (br.s, 3 H, NH=C—NH_2); 8.16—8.25 (br.s, 2 H, NH_2^+). ^{13}C NMR (400 MHz, $(CD_3)_2SO$), δ: 21.72 (N—CH_2—$\underline{C}H_2$); 39.66 (N—$\underline{C}H_2$—CH_2); 90.02 (N—C—$\underline{C}$=C—N); 127.75 (4-CH_{Ph}); 128.31 (2-, 6-CH_{Ph}); 128.34 (3-, 5-CH_{Ph}); 133.91 (1-C_{Ph}); 153.28 (H_2N—$\underline{C}$=NH); 155.83 (N—C—C=$\underline{C}$—N); 165.55 (N—CO).

4-(3-Aminopropyl)-5-(3-bromophenyl)-1,2-dihydro-3*H*-pyrazol-3-one (16). Procedure *B*. Yield 94%, m.p. 231—233 °C (decomp.). Found (%): C, 48.78; H, 4.73. $C_{12}H_{14}BrN_3O$. Calculated (%): C, 48.67; H, 4.76. IR, ν/cm^{-1}: 2880—3020. ^{1}H NMR (400 MHz, $(CD_3)_2SO$), δ: 1.66—1.77 (m, 2 H, N—CH_2—$C\underline{H}_2$—CH_2); 2.43—2.51 (m, 2 H, N—$(CH_2)_2$—$C\underline{H}_2$); 2.76—2.85 (t, 2 H, N—$C\underline{H}_2$—$(CH_2)_2$, $^3J_{H,H}$ = 7.7 Hz); 7.33—7.45 (m, 2 H, 2-, 5-$CH_{C_6H_4}$); 7.55—7.66 (m, 2 H, 4-, 6-$CH_{C_6H_4}$). ^{13}C NMR (400 MHz, $(CD_3)_2SO$), δ: 19.30 (N—CH_2—$\underline{C}H_2$—CH_2); 27.92 (N—$(CH_2)_2$—$\underline{C}H_2$); 40.15 (N—$\underline{C}H_2$—$(CH_2)_2$); 103.68 (HN—C—$\underline{C}$=C—N); 124.07 (3-$C_{C_6H_4}$); 128.48 (6-$CH_{C_6H_4}$); 130.20 (1-$C_{C_6H_4}$); 131.96 (2-$CH_{C_6H_4}$); 132.73 (4-$CH_{C_6H_4}$); 135.09 (5-$CH_{C_6H_4}$); 145.70 (N—C—C=$\underline{C}$—N); 157.06 (N—CO).

4-(3-Aminopropyl)-5-pyridin-4-yl-1,2-dihydro-3*H*-pyrazol-3-one (17). Procedure *B*. Yield 93%, m.p. 188—191 °C (decomp.). Found (%): C, 60.73; H, 6.26. $C_{11}H_{14}N_4O$. Calculated (%): C, 60.53; H, 6.47. IR, ν/cm^{-1}: 2870—3040. ^{1}H NMR (400 MHz, $(CD_3)_2SO$), δ: 1.67—1.78 (m, 2 H, N—CH_2—$C\underline{H}_2$—CH_2); 2.55 (t, 2 H, N—$(CH_2)_2$—$C\underline{H}_2$, $^3J_{H,H}$ = 7.8 Hz); 2.82 (t, 2 H, N—$C\underline{H}_2$—$(CH_2)_2$, $^3J_{H,H}$ = 7.8 Hz); 8.06 (d, 2 H, 3-, 5-CH_{Py}, $^3J_{H,H}$ = 6.8 Hz); 8.74 (d, 2 H, 2-, 6-CH_{Py}, $^3J_{H,H}$ = 6.8 Hz). ^{13}C NMR (400 MHz, $(CD_3)_2SO$), δ: 19.77 (N—CH_2—$\underline{C}H_2$—CH_2); 28.08 (N—$(CH_2)_2$—$\underline{C}H_2$); 40.18 (N—$\underline{C}H_2$—$(CH_2)_2$); 106.30 (HN—C—$\underline{C}$=C—N); 126.27 (3-, 5-CH_{Py}); 140.33 (4-C_{Py}); 143.41 (2-, 6-CH_{Py}); 147.33 (HN—C—C=$\underline{C}$—N); 158.37 (HN—CO).

4-(3-Aminopropyl)-5-[4-(dimethylamino)phenyl]-1,2-dihydro-3*H*-pyrazol-3-one (18). Procedure *B*. Yield 87%, m.p. 196.5—198.5 °C (decomp.). Found (%): C, 64.68; H, 7.67. $C_{14}H_{20}N_4O$. Calculated (%): C, 64.59; H, 7.74. IR, ν/cm^{-1}: 2830—2980. ^{1}H NMR (400 MHz, $(CD_3)_2SO$), δ: 1.64—1.75 (m, 2 H, N—CH_2—$C\underline{H}_2$—CH_2); 2.49 (t, 2 H, N—$(CH_2)_2$—$C\underline{H}_2$, $^3J_{H,H}$ = 7.8 Hz); 2.78 (t, 2 H, N—$C\underline{H}_2$—$(CH_2)_2$, $^3J_{H,H}$ = 7.8 Hz); 3.19 (s, 6 H, NMe_2); 7.64—7.73 (m, 4 H, C_6H_4). ^{13}C NMR (400 MHz, $(CD_3)_2SO$), δ: 19.26 (N—CH_2—$\underline{C}H_2$—CH_2); 27.90 (N—$(CH_2)_2$—$\underline{C}H_2$); 40.21 (N—$\underline{C}H_2$—$(CH_2)_2$); 47.88 (NMe_2); 104.12 (HN—C—$\underline{C}$=C—N); 123.26 (3-, 5-$CH_{C_6H_4}$); 130.20 (1-$C_{C_6H_4}$); 131.89 (2-, 6-$CH_{C_6H_4}$); 144.96 (4-$C_{C_6H_4}$); 145.63 (HN-C—C=$\underline{C}$—N); 156.79 (HN—CO).

4-(4-Aminobutyl)-5-pyridine-4-yl-1,2-dihydro-3*H*-pyrazol-3-one hydrate (19). Procedure *B*. Yield 90%, m.p. 179—183.5 °C (decomp.). Found (%): C, 57.72; H, 7.37. $C_{12}H_{18}N_4O_2$. Calculated (%): C, 57.58; H, 7.25. IR, ν/cm^{-1}: 2870—3035. ^{1}H NMR (400 MHz, $(CD_3)_2SO$), δ: 1.36—1.56 (m, 4 H, N—CH_2—$C\underline{H}_2$—$C\underline{H}_2$—CH_2); 2.44—2.53 (m, 2 H, N—$(CH_2)_3$—$C\underline{H}_2$); 2.59—2.66 (m, 2 H, N—CH_2); 7.49—7.55 (m, 2 H, 2-, 6-CH_{Py}); 8.51—8.57 (m, 2 H, 3-, 5-CH_{Py}). ^{13}C NMR (400 MHz, $(CD_3)_2SO$), δ: 22.14 (N—$(CH_2)_2$—$\underline{C}H_2$—CH_2); 27.30 (N—$(CH_2)_3$—$\underline{C}H_2$); 27.80 (N—CH_2—$\underline{C}H_2$—$(CH_2)_2$); 40.61 (N—$\underline{C}H_2$—$(CH_2)_3$); 107.70 (HN—C—$\underline{C}$=C—N); 126.08 (3-, 5-CH_{Py}); 140.21 (4-C_{Py}); 143.34 (2-, 6-CH_{Py}); 147.90 (HN—C—C=$\underline{C}$—N); 158.71 (HN—CO).

4-(4-Aminobutyl)-5-phenyl-1,2-dihydro-3*H*-pyrazol-3-one (20). Procedure *B*. Yield 92%, m.p. 223—227 °C (decomp.). Found (%): C, 67.54; H, 7.24. $C_{13}H_{17}N_3O$. Calculated (%): C, 67.51; H, 7.41. IR, ν/cm^{-1}: 2860—2980. ^{1}H NMR (400 MHz, $(CD_3)_2SO$), δ: 1.27—1.46 (m, 4 H, N—CH_2—$C\underline{H}_2$—$C\underline{H}_2$—CH_2); 2.30—2.36 (m, 2 H, N—$(CH_2)_3$—$C\underline{H}_2$); 2.66—2.74 (m, 2 H, N—CH_2); 7.32—7.42 (m, 5 H, Ph). ^{13}C NMR (400 MHz, $(CD_3)_2SO$), δ: 21.57 (N—$(CH_2)_3$—$\underline{C}H_2$); 27.07 (N—$(CH_2)_2$—$\underline{C}H_2$—CH_2); 27.68 (N—CH_2—$\underline{C}H_2$—$(CH_2)_2$); 40.64 (N—$\underline{C}H_2$—$(CH_2)_3$); 104.48 (HN—C—$\underline{C}$=C—N); 129.51 (2-, 6-CH_{Ph}); 130.74 (1-C_{Ph}); 130.96 (3-, 5-CH_{Ph}); 132.41 (4-CH_{Ph}); 147.58 (HN—C—C=$\underline{C}$—N); 156.30 (HN—CO).

4-(4-Aminobutyl)-5-(4-methylphenyl)-1,2-dihydro-3*H*-pyrazol-3-one (21). Procedure *B*. Yield 88%, m.p. 214—218 °C (decomp.). Found (%): C, 68.50; H, 7.29. $C_{12}H_{18}N_4O_2$. Calculated (%): C, 68.54; H, 7.81. IR, ν/cm^{-1}: 2840—3010. ^{1}H NMR (400 MHz, $(CD_3)_2SO$), δ: 1.26—1.36 (m, 2 H, N—CH_2—$C\underline{H}_2$—$(CH_2)_2$); 1.68—1.77 (m, 2 H, N—$(CH_2)_2$—$C\underline{H}_2$—CH_2); 2.00 (s, 3 H, Me); 2.27—2.39 (m, 2 H, N—$(CH_2)_3$—$C\underline{H}_2$); 2.98—3.04 (m, 2 H, N—$C\underline{H}_2$—$(CH_2)_3$); 6.95—7.04 (m, 4 H, C_6H_4). ^{13}C NMR (400 MHz, $(CD_3)_2SO$), δ: 22.08 (Me); 23.91 (N—$(CH_2)_2$—$\underline{C}H_2$—CH_2); 27.84 (N—CH_2—$\underline{C}H_2$—$(CH_2)_2$); 29.56 (N—$(CH_2)_3$—$\underline{C}H_2$); 49.63 (N—$\underline{C}H_2$—$(CH_2)_3$); 111.24 (HN—C—$\underline{C}$=C—N); 126.17 (1-$C_{C_6H_4}$); 129.34 (2-, 6-$CH_{C_6H_4}$); 131.30 (3-, 5-$CH_{C_6H_4}$); 141.48 (4-$C_{C_6H_4}$); 144.69 (HN—C—C=$\underline{C}$—N); 148.46 (HN—CO).

4-(4-Aminobutyl)-5-cyclohexyl-1,2-dihydro-3*H*-pyrazol-3-one (22). Procedure *B*. Yield 84%, m.p. 152—154 °C (decomp.). Found (%): C, 65.91; H, 7.50. $C_{13}H_{23}N_3O$. Calculated (%): C, 65.79; H, 9.77. IR, ν/cm^{-1}: 2860—2970. ^{1}H NMR (400 MHz, $(CD_3)_2SO$), δ: 0.97—1.38, 1.42—1.69 (m, 14 H, CH_2, cyclohexyl, N—$(CH_2)_2$—$C\underline{H}_2$—$C\underline{H}_2$); 2.22—2.29 (m, 2 H, N—CH_2—$C\underline{H}_2$—$(CH_2)_2$); 2.59—2.65 (m, 1 H, CH, cyclohexyl); 2.69—2.77 (m, 2 H, N—$C\underline{H}_2$—$(CH_2)_3$). ^{13}C NMR (400 MHz, $(CD_3)_2SO$), δ: 21.10 (N—$(CH_2)_2$—$\underline{C}H_2$—CH_2); 26.31 (N—$(CH_2)_3$—$\underline{C}H_2$); 26.81 (3-, 5-CH_2, cyclohexyl); 27.54, 27.65 (4-CH_2, cyclohexyl, N—CH_2—$\underline{C}H_2$); 32.49 (2-, 6-CH_2, cyclohexyl); 35.70 (1-CH, cyclohexyl); 40.18 (N—$\underline{C}H_2$—CH_2); 102.69 (HN—C—$\underline{C}$=C—N); 154.07 (HN—C—C=$\underline{C}$—N); 155.59 (HN—CO).

4-[2-(Methylamino)ethyl]-2,5-diphenyl-1,2-dihydro-3*H*-pyrazol-3-one hydrate (23). Procedure *B*. Yield 88%, m.p. 168—170 °C (decomp.). Found (%): C, 69.52; H, 6.62. $C_{18}H_{21}N_3O_2$. Calculated (%): C, 69.43; H, 6.80. IR, ν/cm^{-1}: 2840—3010. ^{1}H NMR (400 MHz, $(CD_3)_2SO$), δ: 2.53 (s, 3 H, Me); 2.69—2.75 (m, 2 H, N—CH_2—$C\underline{H}_2$); 2.96—3.02 (m, 2 H, N—$C\underline{H}_2$—CH_2); 7.04 (t, 1 H, 4-CH_{Ph-C}, $^3J_{H,H}$ = 7.2 Hz); 7.26—7.42 (m, 5 H, 3-, 5-CH_{Ph-C}, 3-, 4-, 5-CH_{Ph-N}); 7.52 (d, 2 H, 2-, 6-CH_{Ph-N}, $^3J_{H,H}$ = 7.5 Hz); 8.09 (d, 2 H, 2-, 6-CH_{Ph-C}, $^3J_{H,H}$ = 8.1 Hz). ^{13}C NMR (400 MHz, $(CD_3)_2SO$), δ: 21.89 (N—CH_2—$\underline{C}H_2$); 31.99 (Me); 50.21 (N—$\underline{C}H_2$—CH_2); 92.85 (HN—C—$\underline{C}$=C—N); 118.80 (2-, 6-CH_{Ph-N}); 122.79 (4-CH_{Ph-C}); 126.81 (4-CH_{Ph-N});

127.55 (2-, 6-CH_{Ph-C}); 128.13, 128.22 (3-, 5-CH_{Ph-C}, 3-, 5-CH_{Ph-N}); 135.64 (1-C_{Ph-C}); 141.16 (1-C_{Ph-N}); 148.80 (HN—C—C=C—N); 161.40 (HN—CO).

4-[3-(Methylamino)propyl]-5-phenyl-1,2-dihydro-3*H*-pyrazol-3-one (24). Procedure *B*. Yield 92%, m.p. 192—194.5 °C (decomp.). Found (%): C, 67.69; H, 7.26. $C_{13}H_{17}N_3O$. Calculated (%): C, 67.51; H, 7.41. IR, ν/cm^{-1}: 2810—3020. ^{1}H NMR (400 MHz, $(CD_3)_2SO$), δ: 1.63—1.75 (m, 2 H, N—CH_2—C$\underline{H}_2$—CH_2); 2.39—2.47 (m, 5 H, N—$(CH_2)_2$—C$\underline{H}_2$, NMe); 2.73—2.83 (m, 2 H, N—C$\underline{H}_2$—$(CH_2)_2$); 7.40—7.44 (m, 5 H, Ph). ^{13}C NMR (400 MHz, $(CD_3)_2SO$), δ: 19.33 (N—CH_2—C$\underline{H}_2$—CH_2); 26.69 (N—$(CH_2)_2$—C$\underline{H}_2$); 34.08 (NMe); 49.39 (N—C$\underline{H}_2$—$(CH_2)_2$); 102.94 (HN—C—C=C—N); 127.67 (4-CH_{Ph}); 129.34 (2-, 6-CH_{Ph}); 130.91 (3-, 5-CH_{Ph}); 132.28 (1-C_{Ph}); 147.07 (HN—C—C=C—N); 156.31 (HN—CO).

Synthesis of isoxazoles 25, 26, and 29. Procedure *C*. Hydroxylamine hydrochloride (10 mmol) and KOH (5 mmol) in water (5 mL) were added to a solution of 3-acyllactam (5 mmol) in EtOH (15 mL). The reaction mixture was refluxed for 10 to 20 h. The course of the reaction was monitored by TLC (MeCN—NH_3(aq), 95 : 5). The resulting mixture was evaporated to dryness and diluted with cold water (5 mL) and aqueous NH_3 (5 mL) with stirring and cooling; the precipitate was filtered off.

4-(2-Aminoethyl)-3-phenylisoxazol-5(2*H*)-one (25). Yield 89%, m.p. 200.5—201 °C (decomp.). Found (%): C, 64.51; H, 6.07. $C_{11}H_{12}N_2O_2$. Calculated (%): C, 64.69; H, 5.92. IR, ν/cm^{-1}: 1620, 3250. ^{1}H NMR (400 MHz, $(CD_3)_2SO$), δ: 2.46 (t, 2 H, $NCH_2C\underline{H}_2$, $^3J_{H,H}$ = 5.6 Hz); 2.96 (t, 2 H, $NC\underline{H}_2$, $^3J_{H,H}$ = 5.6 Hz); 7.33—7.43 (m, 5 H, Ph); 8.61 (br.s, 2 H, NH_2). ^{13}C NMR (400 MHz, $(CD_3)_2SO$), δ: 21.34 ($NCH_2\underline{C}H_2$); 40.85 ($N\underline{C}H_2CH_2$); 78.71 (O=C—C=C); 127.46 (4-CH_{Ph}); 127.94 (2-, 6-CH_{Ph}); 128.26 (3-, 5-CH_{Ph}); 133.02 (1-C_{Ph}); 162.49 (O=C—C=C); 178.01 (O=C).

4-(2-Aminoethyl)-3-(3-bromophenyl)isoxazol-5(2*H*)-one (26). Yield 69%, m.p. 168—169 °C (decomp.). Found (%): C, 46.82; H, 4.05. $C_{11}H_{11}BrN_2O_2$. Calculated (%): C, 46.66; H, 3.92. IR, ν/cm^{-1}: 1645, 3230. ^{1}H NMR (400 MHz, $(CD_3)_2SO$), δ: 2.45 (t, 2 H, $NCH_2C\underline{H}_2$, $^3J_{H,H}$ = 5.5 Hz); 2.96 (t, 2 H, $NC\underline{H}_2$, $^3J_{H,H}$ = 5.5 Hz); 7.35—7.58 (m, 4 H, C_6H_4); 8.54 (br.s, 2 H, NH_2). ^{13}C NMR (400 MHz, $(CD_3)_2SO$), δ: 21.21 ($NCH_2\underline{C}H_2$); 40.64 ($N\underline{C}H_2CH_2$); 78.56 (O=C—C=C); 121.63 (C—Br); 126.53 (6-$CH_{C_6H_4}$); 129.79 (4-$CH_{C_6H_4}$); 130.56 (2-$CH_{C_6H_4}$); 130.78 (1-$C_{C_6H_4}$); 135.44 (5-$CH_{C_6H_4}$); 161.07 (O=C—C=C); 178.04 (C=O).

4-(4-Aminobutyl)-3-phenylisoxazol-5(2*H*)-one (29). Yield 35%, m.p. 169—170 °C (decomp.). Found (%): C, 67.47; H, 6.71. $C_{13}H_{16}N_2O_2$. Calculated (%): C, 67.22; H, 6.94. IR, ν/cm^{-1}: 1650, 3280. ^{1}H NMR (400 MHz, $(CD_3)_2SO$), δ: 1.42—1.53 (m, 2 H, $NCH_2C\underline{H}_2C\underline{H}_2CH_2$); 2.19 (t, 2 H, $N(CH_2)_3C\underline{H}_2$, $^3J_{H,H}$ = 6.5 Hz); 2.78 (t, 2 H, NCH_2, $^3J_{H,H}$ = 6.5 Hz); 7.30—7.49 (m, 5 H, Ph); 8.06 (br.s, 2 H, NH_2). ^{13}C NMR (400 MHz, $(CD_3)_2SO$), δ: 21.34 ($N(CH_2)_2\underline{C}H_2CH_2$); 25.86 ($N(CH_2)_3\underline{C}H_2$); 27.32 ($NCH_2\underline{C}H_2(CH_2)_2$); 40.13 ($N\underline{C}H_2CH_2$); 80.09 (O=C—C=C); 126.97 (4-CH_{Ph}); 127.71 (2-, 6-CH_{Ph}); 128.25 (3-, 5-CH_{Ph}); 134.01 (1-C_{Ph}); 162.03 (O=C—C=C); 177.70 (C=O).

Synthesis of isoxazoles 27 and 28. Procedure *D*. Hydroxylamine hydrochloride (5 mmol) was added to a solution of 3-acyllactam (5 mmol) in EtOH (10 mL). The reaction mixture was refluxed for 5 to 10 h. The course of the reaction was monitored by TLC (MeCN—NH_3(aq), 95 : 5). The resulting mixture was cooled and the product was filtered off.

4-(2-Aminoethyl)-3-pyridin-3-ylisoxazol-5(2*H*)-one hydrochloride (27). Yield 85%, m.p. 195—198 °C (decomp.). Found (%): C, 49.76; H, 4.71. $C_{10}H_{12}ClN_3O_2$. Calculated (%): C, 49.70; H, 5.00. IR, ν/cm^{-1}: 1630—3270. ^{1}H NMR (400 MHz, $(CD_3)_2SO$), δ: 2.61—2.69 (m, 2 H, N—CH_2—C$\underline{H}_2$); 2.88—2.99 (m, 2 H, N—C$\underline{H}_2$—CH_2); 7.64 (dd, 1 H, 5-CH_{Py}, $^3J_{H,H}$ = 8.0 Hz, $^3J_{H,H}$ = 4.9 Hz); 8.04 (br.s, 2 H, NH_2^+); 8.13 (dt, 1 H, 4-CH_{Py}, $^3J_{H,H}$ = 8.0 Hz, $^4J_{H,H}$ = 2.1 Hz); 8.78 (d, 1 H, 6-CH_{Py}, $^3J_{H,H}$ = 4.9 Hz); 8.84 (d, 1 H, 2-CH_{Py}, $^4J_{H,H}$ = 2.1 Hz). ^{13}C NMR (400 MHz, $(CD_3)_2SO$), δ: 20.06 (N—CH_2—C$\underline{H}_2$); 37.23 (N—C$\underline{H}_2$—CH_2); 92.17 (O=C—C=C—N); 124.06 (3-C_{Py}); 124.28 (5-CH_{Py}); 136.05 (4-CH_{Py}); 147.66 (2-CH_{Py}); 151.11 (6-CH_{Py}); 159.28 (O=C—C=C—N); 171.91 (C=O).

4-(2-Aminoethyl)-3-pyridin-4-ylisoxazol-5(2*H*)-one hydrochloride (28). Yield 78%, m.p. 182—184.5 °C (decomp.). Found (%): C, 49.53; H, 4.88. $C_{10}H_{12}ClN_3O_2$. Calculated (%): C, 49.70; H, 5.00. IR, ν/cm^{-1}: 1650—3240. ^{1}H NMR (400 MHz, $(CD_3)_2SO$), δ: 2.65—2.76 (m, 2 H, N—CH_2—C$\underline{H}_2$); 2.93—3.03 (m, 2 H, N—C$\underline{H}_2$—CH_2); 8.15 (d, 2 H, 3-, 5-CH_{Py}, $^3J_{H,H}$ = 5.8 Hz); 8.85 (d, 2 H, 2-, 6-CH_{Py}, $^3J_{H,H}$ = 5.8 Hz). ^{13}C NMR (400 MHz, $(CD_3)_2SO$), δ: 20.73 (N—CH_2—C$\underline{H}_2$); 38.93 (N—C$\underline{H}_2$—CH_2); 93.61 (O=C—C=C—N); 127.11 (3-, 5-CH_{Py}); 143.65 (2-, 6-CH_{Py}); 146.06 (4-C_{Py}); 159.33 (O=C—C=C—N); 174.47 (C=O).

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