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Synthesis of Substituted Pyridazin-3-ones, 1,2-Oxazin-3-ones, and Furopyrimidines from (Arylmethylidene)furan-2(3*H*)-ones

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Abstract—Reactions of 5-substituted 3-(arylmethylidene)furan-2(3*H*)-ones with hydrazine hydrate, hydroxylamine, and guanidine involved opening of the furanone ring. Their hydrazinolysis under mild conditions afforded acyclic 4-oxoalkanoic acid hydrazides which underwent heterocyclization to substituted pyridazinones in boiling ethanol. The presence of an alkyl substituent in the 5-position of the initial furanone favored heterocyclization with the formation of pyrazolidinone derivatives. The reactions of 3-(arylmethylidene)furan-2(3*H*)-ones with hydroxylamine and guanidine also produced new six-membered heterocycles, 2*H*-1,2-oxazin-3(4*H*)-ones and 4,6-disubstituted 3,4-dihydrofuro[2,3-*d*]pyrimidin-2-amines, respectively.

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Heterocyclic compounds containing a pyrimidine, pyridazine, or oxazine fragment attract considerable interest due to their potential diverse biological activity. These structural fragments are present in molecules of natural compounds and synthetic drugs exhibiting antitumor, antiviral, antibacterial, and other kinds of activity [1–9].

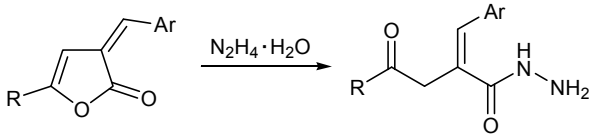
Six-membered heterocycles are most often synthesized on the basis of binucleophiles containing an HNNH, C=N, or CNH_2 moiety, such as guanidine, hydrazine, and hydroxylamine. These nitrogen nucleophiles are characterized by high reactivity and are widely used to construct new nitrogen-containing heterocyclic systems with various combinations of heteroatoms. Readily obtainable 3-arylmethylidenefuran-2(3*H*)-ones are convenient and accessible substrates for the synthesis of various difficultly accessible heterocyclic, spirocyclic, and polycyclic compounds [10–18]. 3-Arylmethylidenefuran-2(3*H*)-ones possess a combination of properties typical of cyclic esters and α,β-unsaturated carbonyl compounds, and they are capable of reacting with compounds having labile hydrogen atoms. In this respect, arylmethylidene derivatives of furan-2(3*H*)-ones can be regarded as suitable building blocks for the synthesis of various heterocyclic compounds with pyrimidine and pyridazine fragments.

In view of the above stated, development of methods for the synthesis of compounds containing pyridine and pyridazine fragments is a promising research line. In the present work we studied reactions of 5-substituted 3-arylmethylidenefuran-2(3*H*)-ones with hydrazine, hydroxylamine, and guanidine.

Furanones **1a**–**1d** reacted with an equimolar amount of hydrazine hydrate in ethanol at room temperature to give 4-oxoalkanoic acid hydrazides **2a**–**2d** (Scheme 1). The ^{1}H NMR spectra of **2a**–**2d** showed singlets due to CH_2 (δ 3.13–3.21 ppm), C=CH (δ 7.08–7.15 ppm), NH (δ 7.85–8.03 ppm), and NH_2 protons (δ 5.18–5.23 ppm), as well as aromatic proton signals at δ 7.03–7.98 ppm. The structure of previously unknown compounds **2a**–**2d** was additionally proved by ^{13}C NMR spectra which contained an upfield signal at δ_C 41.5–47.1 ppm due to methylene carbon atom, downfield signals from two carbonyl carbon atoms at δ_C 164.3–169.4 and 193.1–197.5 ppm, and a number of signals of sp^2-hybridized carbons.

Compounds **2a**–**2d** were formed as a result of opening of the lactone ring of **1a**–**1d** at the C^2–O bond,

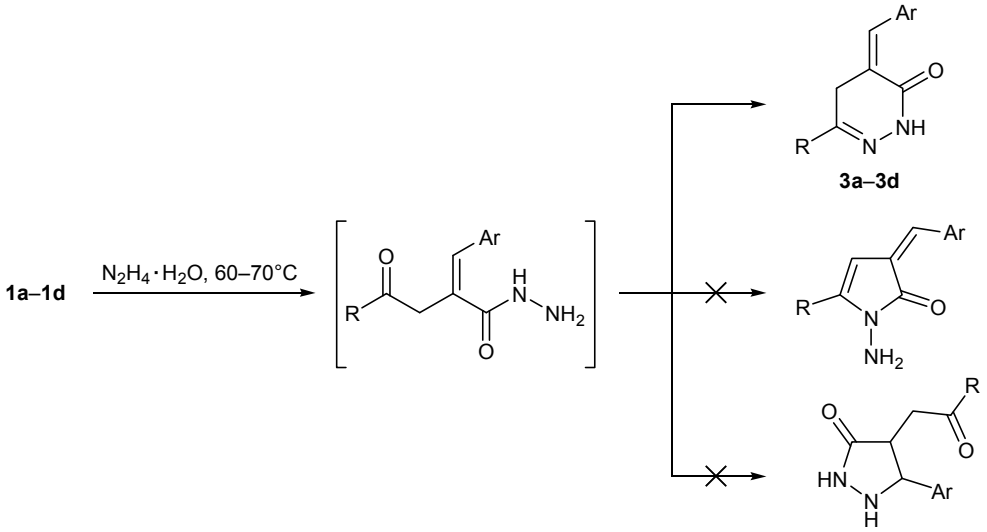
Scheme 1.



1a–1d **2a–2d**

R = Ph, Ar = 2-ClC_6H_4 (**a**), R = 4-MeC_6H_4, Ar = 2-ClC_6H_4 (**b**), 4-$MeOC_6H_4$ (**c**); 3-$O_2NC_6H_4$ (**d**).

Scheme 2.



R = Ph, Ar = 2-ClC_6H_4 (**a**), R = 4-MeC_6H_4, Ar = 2-ClC_6H_4 (**b**), 4-$MeOC_6H_4$ (**c**); 3-$O_2NC_6H_4$ (**d**).

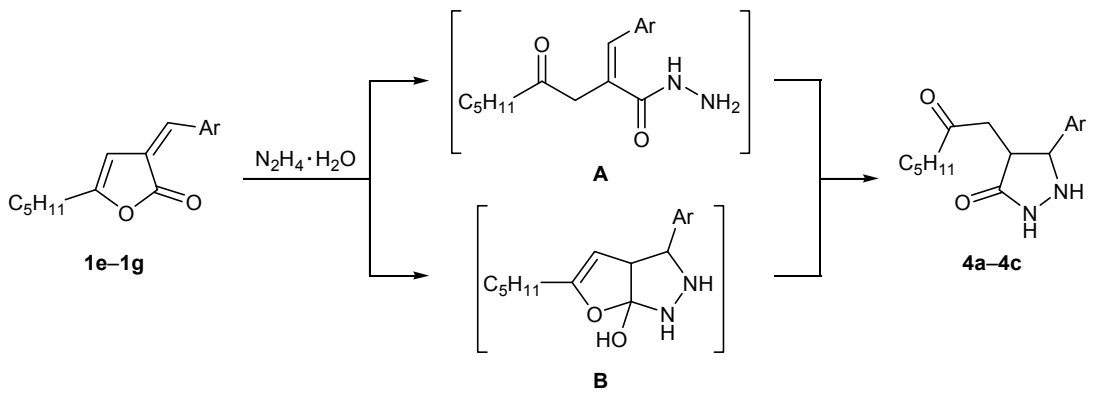
and no further heterocyclization occurred under the given conditions.

When the reaction of **1a**–**1d** with hydrazine hydrate was carried out in boiling ethanol, the products were substituted dihydropyridazin-3(2*H*)-ones **3a**–**3d** (Scheme 2). The ^{1}H NMR spectra of **3a**–**3d** displayed singlets of methylene protons on C^5 of the pyridazine ring (δ 2.15–2.22 ppm), proton on the exocyclic double bond (δ 6.89–7.01 ppm), NH proton (δ 7.02–7.12 ppm), and aromatic protons (δ 7.19–8.05 ppm). In the ^{13}C NMR spectra of **3a**–**3d**, the C^5 signal was observed at δ_C 35.7–41.2 ppm, sp^2-hybridized carbons resonated in the region δ_C 118.6–153.6 ppm, and the carbonyl carbon signal was located at δ_C 166.2–169.4 ppm.

Unlike the reaction at room temperature which stops at the stage of formation of acyclic hydrazide, in boiling ethanol intermediate hydrazide undergoes intramolecular cyclization to pyridazinone derivative via attack by the primary amino group on the ketone carbonyl carbon atom and elimination of water molecule. No alternative reaction paths leading to five-membered heterocycles (dihydropyrrole or pyrazolidine) were observed.

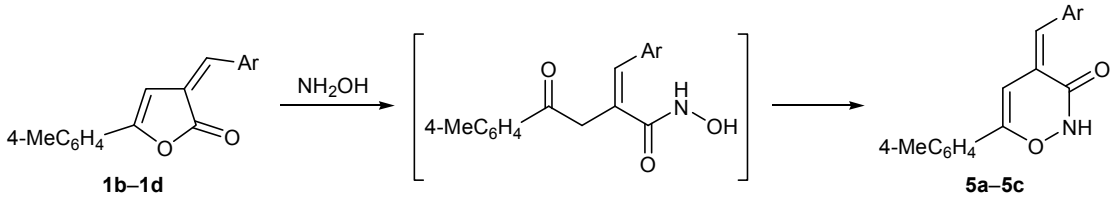
The presence of an alkyl (pentyl) group in the 5-position of initial 3-arylmethylidenefuran-2(3*H*)-ones **1e**–**1g** changed the reactivity, and the reaction of **1e**–**1g** with hydrazine hydrate afforded 68–72% of substituted pyrazolidin-3-ones **4a**–**4c** (Scheme 3). The structure of **4a**–**4c** was proved by spectral methods. In the ^{1}H NMR spectra of **4a**–**4c** we observed a multiplet signal of the alkyl substituent at δ 0.96–2.48 ppm, doublets of doublets of exocyclic methylene protons at δ 2.67–2.74 and 3.42–3.49 ppm, a multiplet of 4-H at δ 3.63–3.77 ppm, a doublet of 3-H at δ 4.22–4.31 ppm,

Scheme 3.



1e, **4a**, Ar = Ph; **1f**, **4b**, Ar = 3-$O_2NC_6H_4$; **1g**, **4c**, Ar = 4-$MeOC_6H_4$.

Scheme 4.



1b–1d **5a–5c**

1b, **5a**, Ar = 2-ClC_6H_4; **1c**, **5b**, Ar = 4-$MeOC_6H_4$; **1d**, **5c**, Ar = 3-$O_2NC_6H_4$.

two broadened NH singlets at δ 6.12–6.16 and 8.31–8.37 ppm, and a set of aromatic proton signals in the region δ 6.76–7.43 ppm. The ^{13}C NMR spectra of **4a**–**4c** contained a series of upfield signals due to sp^3-carbons and two downfield carbonyl carbon signals, as well as other signals.

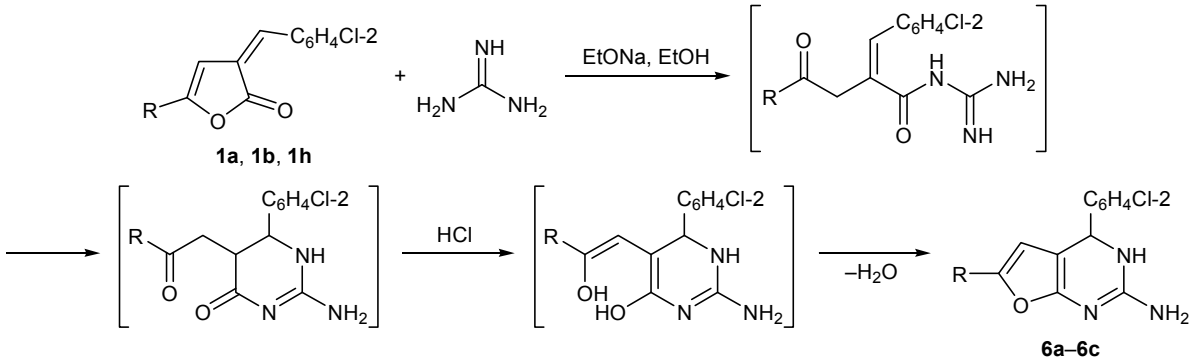
In this case, the reaction path is determined mainly by the activity of different reaction centers in the intermediate. The latter may be either hydrazide **A** or bicyclic structure **B**. Due to the presence of alkyl substituent, the positive charge on the neighboring carbonyl carbon atom of intermediate hydrazide **A** is reduced, so that cyclization to six-membered pyridazinones can be ruled out; on the other hand, the carbon atom of the arylmethylidene fragment remains electron-deficient, which favors formation of pyrazolidine system. Another reaction sequence is also possible, namely the formation of bicyclic system **B** and subsequent opening of the furanone ring to give compounds **4a**–**4c**.

Treatment of furan-2(3*H*)-ones **1b**–**1d** with excess hydroxylamine hydrochloride in the presence of a catalytic amount of pyridine in boiling ethanol for 6–8 h led to the formation of 1,2-oxazin-3(4*H*)-ones **5a**–**5c** (Scheme 4). The ^1H NMR spectra of **5a**–**5c** contained singlets of proton on the exocyclic double bond (δ 7.44–7.58 ppm) and 5-H of the oxazine ring (δ 7.20–7.25 ppm) and downfield signals of the NH proton (δ 8.39–8.51 ppm) and aromatic protons (δ 7.23–8.13 ppm). A series of signals of sp^2-carbon atoms were observed in the ^{13}C NMR spectra of **5a**–**5c** in the region δ_C 103.6–147.2 ppm, and the carbonyl carbon signal was located at δ_C 168.5–174.9 ppm, which provided an additional support to the proposed structure.

Hydroxylamine molecule possesses two nonequivalent nucleophilic centers, among which the nitrogen atom is more nucleophilic. Attack of hydroxylamine on C^2 of the furan ring of **1b**–**1d** gives intermediate hydroxamic acid which undergoes intramolecular cyclization via attack of the NHOH oxygen atom on the ketone carbonyl carbon atom. The cyclization is favored by deficit of electron density on C^4 and high nucleophilicity of the OH oxygen atom. Furthermore, flexibility of the C–N–OH fragment in the hydroxamic acid molecule favors appropriate spatial arrangement of the reaction centers for oxazine ring closure.

The reactions of 5-substituted 3-arylmethylidenefuran-2(3*H*)-ones **1a**, **1b**, and **1h** with guanidine carbonate were carried out by heating the reactants for 5 h in boiling ethanol in the presence of sodium ethoxide. The mixtures were then neutralized with concentrated aqueous HCl. The products were identified as dihydrofuro[2,3-*d*]pyrimidin-2-amines **6a**–**6c** (Scheme 5). Their ^1H NMR spectra displayed singlets of 5-H (δ 6.54–6.82 ppm), 4-H (δ 5.13–5.45 ppm), 3-H (δ 3.10–3.18 ppm), and NH_2 group (δ 0.97–1.13 ppm)

Scheme 5.



1a, **1b**, **1h** **6a–6c**

6, R = Ph (**a**), 4-MeC_6H_4 (**b**), 4-$MeOC_6H_4$ (**c**).

and a set of aromatic proton signals in the region δ 7.06–7.51 ppm. In the ^{13}C NMR spectra of **6a**–**6c**, the C^4 nucleus resonated at δ_C 49.8–52.1 ppm, sp^2-carbon signals were located at δ_C 103.9–146.2 ppm, and the C^2 signal was observed at δ_C 157.4–159.9 ppm.

Taking into account high reactivity of guanidine and the presence of several electrophilic centers in arylmethylidenefuranones **1**, some alternative reaction paths could be expected. However, the product structure suggests the following transformation sequence: initial attack of the amino group of guanidine on the lactone fragment of furan-2-one with opening of the lactone ring, closure of pyrimidine ring via intramolecular attack of the imino group on the C=C double bond, and subsequent enolization and intramolecular dehydration (Scheme 5).

EXPERIMENTAL

The ^1H and ^{13}C NMR spectra were recorded at 20–25°C on a Varian 400 spectrometer (operating frequencies 400 and 100 MHz, respectively) using $CDCl_3$ as solvent and tetramethylsilane as internal standard. Analytical thin-layer chromatography was performed on DC-Fertigfolien ALUGRAM Xtra SIL G/UV-254 plates using hexane–ethyl acetate–chloroform (2:2:1) as eluent; spots were visualized under UV light. The melting points were measured in open capillaries. The elemental analyses were obtained with a Vario Micro cube Elementar CHNS analyzer.

Initial 5-substituted 3-arylmethylidenefuran-2(3*H*)-ones **1a**–**1h** were synthesized according to the procedure described in [19].

4-Oxobutanoic acid hydrazides 2a–2d (*general procedure*). A mixture of 0.02 mol of compound **1a**–**1d** and 0.02 mol of hydrazine hydrate in 12 mL of ethanol was stirred for 30–50 min at 20–25°C. The precipitate was filtered off, washed with water, and recrystallized from ethanol.

2-[(2-Chlorophenyl)methylidene]-4-oxo-4-phenylbutanehydrazide (2a). Yield 84%, mp 129–131°C. ^1H NMR spectrum, δ, ppm: 3.13 s (2H, CH_2), 5.18 s (2H, NH_2), 7.15 s (1H, =CH), 7.34–7.79 m (9H, H_{arom}), 7.85 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 47.1, 119.1, 121.3, 122.8, 124.3, 125.9, 127.9, 129.5, 130.5, 131.7, 132.3, 134.6, 135.9, 136.4, 138.5, 169.4, 194.7. Found, %: C 65.15; H 5.21; N 9.24. $C_{17}H_{15}ClN_2O_2$. Calculated, %: C 64.87; H 4.80; N 8.90.

2-[(2-Chlorophenyl)methylidene]-4-(4-methylphenyl)-4-oxobutanehydrazide (2b). Yield 81%, mp 131–133°C. ^1H NMR spectrum, δ, ppm: 2.45 s (3H, CH_3), 3.17 s (2H, CH_2), 5.23 s (2H, NH_2), 7.08 s (1H, =CH), 7.18 d and 7.32 d (2H each, $MeC_6\mathbf{H}_4$, J = 8.1 Hz), 7.39–7.68 m (4H, H_{arom}), 8.03 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 25.8, 45.4, 121.5, 122.8, 123.2, 125.2, 126.4, 127.7, 126.7, 128.9, 133.2, 133.2, 134.1, 137.1, 164.3, 193.1. Found %: C 66.03; H 4.91; N 8.72. $C_{18}H_{17}ClN_2O_2$. Calculated %: C 65.75; H 5.21; N 8.52.

2-[(4-Methoxyphenyl)methylidene]-4-(4-methylphenyl)-4-oxobutanehydrazide (2c). Yield 76%, mp 123–125°C. ^1H NMR spectrum, δ, ppm: 2.43 s (3H, CH_3), 3.45 s (OCH_3), 3.21 s (2H, CH_2), 5.21 s (2H, NH_2), 7.11 s (1H, =CH), 7.03 d (2H, H_{arom}, J = 8.1 Hz), 7.46 d (2H, H_{arom}, J = 8.1 Hz), 7.28 d and 7.56 d (2H each, $MeC_6\mathbf{H}_4$, J = 8.1 Hz), 7.96 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 22.1, 42.9, 53.2, 118.4, 120.3, 122.2, 124.7, 128.2, 129.1, 130.4, 131.7, 133.8, 158.2, 166.2, 197.5. Found, %: C 70.38; H 6.42; N 9.04. $C_{19}H_{20}N_2O_3$. Calculated, %: C 70.35; H 6.21; N 8.64.

4-(4-Methylphenyl)-2-[(3-nitrophenyl)methylidene]-4-oxobutanehydrazide (2d). Yield 86%, mp 143–145°C. ^1H NMR spectrum, δ, ppm: 2.52 s (3H, CH_3), 3.19 s (2H, CH_2), 5.20 s (2H, NH_2), 7.14 s (1H, =CH), 7.23 d and 7.65 d (2H each, $MeC_6\mathbf{H}_4$, J = 8.1 Hz), 7.74–7.98 m (4H, H_{arom}), 8.01 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 27.4, 41.5, 119.3, 120.2, 121.9, 122.8, 124.1, 125.3, 126.1, 127.4, 128.3, 130.5, 133.5, 137.5, 165.6, 197.3. Found, %: C 64.04; H 5.49; N 12.65. $C_{18}H_{17}N_3O_4$. Calculated, %: C 63.71; H 5.05; N 12.38.

Compounds 3a–3d and 4a–4c (*general procedure*). A mixture of 0.02 mol of compound **1a**–**1g** and 0.06 mol of hydrazine hydrate in 20 mL of ethanol was refluxed with stirring for 50–60 min. After cooling, the precipitate was filtered off, washed with water, and recrystallized from propan-2-ol.

4-[(2-Chlorophenyl)methylidene]-6-phenyl-4,5-dihydropyridazin-3(2*H*)-one (3a). Yield 69%, mp 192–194°C. ^1H NMR spectrum, δ, ppm: 2.15 s (2H, CH_2), 7.01 s (1H, =CH), 7.08 s (1H, NH), 7.19–7.68 m (9H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 38.3, 116.2, 117.4, 118.3, 119.1, 121.9, 122.7, 124.5, 126.1, 127.9, 128.4, 130.2, 131.5, 133.3, 139.3, 142.1, 164.2. Found, %: C 69.11; H 4.73; N 9.76. $C_{17}H_{13}ClN_2O$. Calculated, %: C 68.81; H 4.42; N 9.44.

4-[(2-Chlorophenyl)methylidene]-6-(4-methylphenyl)-4,5-dihydropyridazin-3(2*H*)-one (3b). Yield 73%, mp 201–203°C. ^1H NMR spectrum, δ, ppm:

2.20 s (2H, CH_2), 2.48 s (3H, CH_3), 6.93 s (1H, =CH), 7.02 s (1H, NH), 7.03 d and 7.46 d (2H each, $MeC_6\mathbf{H}_4$, J = 8.1 Hz), 7.67–7.95 m (4H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 24.6, 40.1, 119.8, 120.6, 121.3, 123.7, 125.1, 126.3, 127.5, 129.5, 131.5, 133.1, 134.6, 138.2, 140.3, 162.3. Found, %: C 69.76; H 5.12; N 8.68. $C_{18}H_{15}ClN_2O$. Calculated, %: C 69.57; H 4.86; N 9.01.

4-[(4-Methoxyphenyl)methylidene]-6-(4-methylphenyl)-4,5-dihydropyridazin-3(2*H*)-one (3c). Yield 76%, mp 209–211°C. ^1H NMR spectrum, δ, ppm: 2.16 s (2H, CH_2), 2.45 s (3H, CH_3), 3.53 s (OCH_3), 6.89 s (1H, =CH), 7.05 s (1H, NH), 7.07 d (2H, H_{arom}, J = 8.1 Hz), 7.49 d (2H, H_{arom}, J = 8.1 Hz), 7.21 d and 7.68 d (2H each, $MeC_6\mathbf{H}_4$, J = 8.1 Hz). ^{13}C NMR spectrum, δ_C, ppm: 25.9, 39.5, 54.7, 116.2, 121.4, 122.7, 123.3, 125.6, 128.2, 129.8, 133.2, 135.1, 142.1, 159.3, 163.9. Found, %: C 74.62; H 6.21; N 9.54. $C_{19}H_{18}N_2O_2$. Calculated, %: C 74.49; H 5.92; N 9.14.

6-(4-Methylphenyl)-4-[(3-nitrophenyl)methylidene]-4,5-dihydropyridazin-3(2*H*)-one (3d). Yield 68%, mp 210–212°C. ^1H NMR spectrum, δ, ppm: 2.22 s (2H, CH_2), 2.51 s (3H, CH_3), 6.94 s (1H, =CH), 7.12 s (1H, NH), 7.25 d and 7.71 d (2H each, $MeC_6\mathbf{H}_4$, J = 8.1 Hz), 7.87–8.05 m (4H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 25.2, 38.9, 118.8, 124.7, 125.1, 125.9, 126.3, 127.7, 128.1, 128.9, 129.4, 130.2, 132.1, 133.9, 143.3, 161.2. Found, %: C 66.97; H 5.03; N 13.42. $C_{18}H_{15}N_3O_3$. Calculated, %: C 67.28; H 4.71; N 13.08.

4-(2-Oxoheptyl)-5-phenylpyrazolidin-3-one (4a). Yield 71%, mp 97–99°C. ^1H NMR spectrum, δ, ppm: 0.96–2.35 m (11H, C_5H_{11}), 2.69 d.d (2H, J = 13.2, 4 Hz), 3.46 d.d (2H, CH_2, J = 13.2, 7 Hz), 3.63–3.69 m (1H, 4-H), 4.27 d (1H, 5-H, J = 8.1 Hz), 6.12 s (1H, NH), 8.37 s (1H, NH), 6.76–7.05 m (5H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 12.2, 21.5, 24.9, 29.7, 37.8, 41.4, 46.7, 74.7, 123.8, 124.7, 127.8, 129.1, 132.1, 133.8, 182.9, 209.7. Found, %: C 70.47; H 7.70; N 10.67. $C_{16}H_{22}N_2O_2$. Calculated, %: C 70.04; H 8.08; N 10.21.

5-(3-Nitrophenyl)-4-(2-oxoheptyl)pyrazolidin-3-one (4b). Yield 79%, mp 112–113°C. ^1H NMR spectrum, δ, ppm: 0.99–2.43 m (11H, C_5H_{11}), 2.67 d.d (2H, J = 13.2, 4 Hz), 3.42 d.d (2H, CH_2, J = 13.2, 7 Hz), 3.68–3.72 m (1H, 4-H), 4.31 d (1H, 5-H, J = 8.1 Hz), 6.14 s (1H, NH), 8.31 s (1H, NH), 7.17–7.43 m (4H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 14.7, 22.3, 26.1, 30.4, 36.2, 42.9, 45.9, 75.2, 126.2, 127.3, 129.1, 132.5, 133.6, 135.3, 184.2, 210.5. Found, %: C 60.42; H 6.95; N 12.98. $C_{16}H_{21}N_3O_4$. Calculated, %: C 60.17; H 6.63; N 13.16.

5-(4-Methoxyphenyl)-4-(2-oxoheptyl)pyrazolidin-3-one (4c). Yield 72%, mp 92–93°C. ^1H NMR spectrum, δ, ppm: 1.04–2.48 m (11H, C_5H_{11}), 2.74 d.d (2H, J = 13.2, 4 Hz), 3.49 d.d (2H, CH_2, J = 13.2, 7 Hz), 3.71–3.77 m (1H, 4-H), 3.75 s (3H, OCH_3), 4.22 d (1H, 5-H, J = 8.1 Hz), 6.16 s (1H, NH), 8.35 s (1H, NH), 7.00–7.28 m (4H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 14.7, 22.3, 26.1, 30.4, 36.2, 42.9, 45.9, 75.2, 126.2, 127.3, 129.1, 132.5, 133.6, 135.3, 184.2, 210.5. Found, %: C 67.15; H 8.13; N 9.34. $C_{17}H_{24}N_2O_3$. Calculated, %: C 67.08; H 7.95; N 9.20.

Compounds 5a–5c (*general procedure*). A mixture of 0.01 mol of compound **1b**–**1d**, 0.03 mol of hydroxylamine hydrochloride, and 0.03 mol of pyridine in 30 mL of ethanol was refluxed with stirring for 6–8 h. The mixture was cooled and poured into cold water, and the precipitate was filtered off, washed with water, and recrystallized from propan-2-ol.

4-[(2-Chlorophenyl)methylidene]-6-(4-methylphenyl)-2*H*-1,2-oxazin-3(4*H*)-one (5a). Yield 72%, mp 117–119°C. ^1H NMR spectrum, δ, ppm: 2.45 s (3H, CH_3), 7.20 s (1H, 5-H), 7.44 s (1H, =CH), 7.23 d and 7.39 d (2H each, $MeC_6\mathbf{H}_4$, J = 8.1 Hz), 7.85–8.13 m (4H, H_{arom}), 8.47 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 23.9, 103.6, 125.1, 125.8, 126.2, 127.8, 128.3, 132.6, 133.4, 137.6, 157.4, 168.5. Found, %: C 69.69; H 4.87; N 4.87. $C_{18}H_{14}ClNO_2$. Calculated, %: C 69.35; H 4.53; N 4.49.

4-[(4-Methoxyphenyl)methylidene]-6-(4-methylphenyl)-2*H*-1,2-oxazin-3(4*H*)-one (5b). Yield 69%, mp 115–117°C. ^1H NMR spectrum, δ, ppm: 2.41 s (3H, CH_3), 3.58 s (3H, OCH_3), 7.25 s (1H, 5-H), 7.53 s (1H, =CH), 7.02 d (2H, H_{arom}, J = 8.1 Hz), 7.35 d (2H, H_{arom}, J = 8.1 Hz), 7.12 d and 7.41 d (2H each, $MeC_6\mathbf{H}_4$, J = 8.1 Hz), 8.39 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 25.3, 54.8, 107.5, 117.6, 126.6, 128.3, 127.7, 128.9, 130.4, 132.4, 134.5, 136.2, 159.1, 163.6, 169.8. Found, %: C 73.88; H 5.76; N 4.78. $C_{19}H_{17}NO_3$. Calculated, %: C 74.25; H 5.58; N 4.56.

6-(4-Methylphenyl)-4-[(3-nitrophenyl)methylidene]-2*H*-1,2-oxazin-3(4*H*)-one (5c). Yield 67%, mp 92–94°C. ^1H NMR spectrum, δ, ppm: 2.43 s (3H, CH_3), 7.23 s (1H, 5-H), 7.58 s (1H, =CH), 7.15 d and 7.38 d (2H each, $MeC_6\mathbf{H}_4$, J = 8.1 Hz), 7.78–8.07 m (4H, H_{arom}), 8.51 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 26.7, 108.4, 116.5, 123.8, 125.1, 127.3, 128.7, 129.3, 131.6, 132.4, 135.3, 136.1, 138.4, 147.2, 158.5, 174.9. Found, %: C 66.78; H 4.85; N 8.61. $C_{18}H_{14}N_2O_4$. Calculated, %: C 67.07; H 4.38; N 8.69.

Compounds 6a–6c (*general procedure*). A mixture of 0.01 mol of compound **1a**, **1b**, or **1h** and 0.01 mol of guanidine carbonate in 15 mL of ethanol containing 0.001 mol of sodium ethoxide was refluxed with stirring for 5 h. The mixture was cooled and neutralized with concentrated aqueous HCl, and the precipitate was filtered off, washed with water, and recrystallized from propan-2-ol.

4-(2-Chlorophenyl)-6-phenyl-3,4-dihydrofuro-[2,3-*d*]pyrimidin-2-amine (6a). Yield 67%, mp 176–178°C. ^{1}H NMR spectrum, δ, ppm: 1.13 s (2H, NH_2), 3.13 s (1H, NH), 5.45 s (1H, 4-H), 6.54 s (1H), 7.21–7.43 m (9H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 52.1, 105.1, 119.1, 124.3, 124.9, 125.1, 127.2, 128.1, 128.9, 130.2, 131.8, 132.4, 135.9, 137.3, 143.1, 159.6. Found, %: C 66.35; H 4.13; N 13.34. $C_{18}H_{14}ClN_3O_4$. Calculated, %: C 66.77; H 4.36; N 12.98.

4-(2-Chlorophenyl)-6-(4-methylphenyl)-3,4-dihydrofuro[2,3-*d*]pyrimidin-2-amine (6b). Yield 73%, mp 196–198°C. ^{1}H NMR spectrum, δ, ppm: 1.05 s (2H, NH_2), 2.67 s (3H, CH_3), 3.18 s (1H, NH), 5.13 s (1H, 4-H), 6.68 s (1H), 7.21 d and 7.43 d (2H each, $MeC_6\mathbf{H}_4$, J = 8.1 Hz), 7.25–7.38 m (4H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 25.3, 49.8, 103.9, 121.8, 122.5, 124.5, 125.7, 127.5, 128.1, 128.9, 129.3, 131.6, 133.6, 134.5, 135.2, 145.3, 157.4. Found, %: C 67.87; H 4.93; N 12.82. $C_{19}H_{16}ClN_3O$. Calculated, %: C 67.56; H 4.77; N 12.44.

4-(2-Chlorophenyl)-6-(4-methoxyphenyl)-3,4-dihydrofuro[2,3-*d*]pyrimidin-2-amine (6c). Yield 65%, mp 188–190°C. ^{1}H NMR spectrum, δ, ppm: 0.97 s (2H, NH_2), 3.10 s (1H, NH), 3.65 s (3H, OCH_3), 5.28 s (1H, 4-H), 6.82 s (1H), 7.06 d (2H, H_{arom}, J = 8.1 Hz), 7.51 d (2H, H_{arom}, J = 8.1 Hz), 7.18–7.31 m (4H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 50.2, 54.8, 107.7, 119.6, 122.7, 124.2, 124.9, 125.1, 126.2, 127.8, 128.1, 129.1, 130.2, 131.2, 132.5, 146.2, 159.9. Found, %: C 64.79; H 4.24; N 12.05. $C_{19}H_{16}ClN_3O_2$. Calculated, %: C 64.50; H 4.56; N 11.88.

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