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Synthesis of 5-Amino-1-aryl-4-(4-aryl-1,3-thiazol-2-yl)-2,3-dihydro-1*H*-pyrrol-3-ones*

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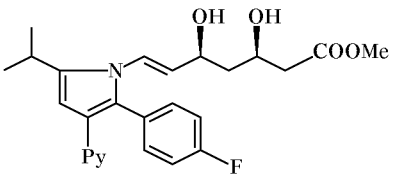
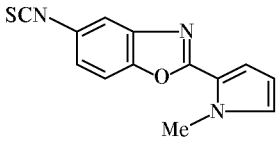
Abstract—Reactions of 2-(4-aryl-1,3-thiazol-2-yl)-3-oxo-4-chlorobutyronitriles with primary aromatic amines result in nucleophilic substitution of the chlorine atom by amino group, followed by intramolecular addition of the secondary amino group to the cyano group. The products are 5-amino-1-aryl-4-(4-aryl-1,3-thiazol-2-yl)-2,3-dihydro-1*H*-pyrrol-3-ones which are structurally related to the known antiischemic drugs.

In the recent years, a number of compounds possessing high biological activity of various kinds were found among heteryl-substituted pyrroles. For example, pyridyl derivatives **Ia** and **Ib** (Scheme 1) inhibit biosynthesis of cholesterol, and they can be used for prevention and treatment of atherosclerosis [1]; benzoxazolyl-substituted pyrrole **II** exhibits antihelmintic properties [2], and tetrazolyl derivatives **IIIa**–**IIId** show antihypertensive activity [3]. Imidazolyl and thiazolyl derivatives **IVa**–**IVc** inhibit thrombosis and were recommended as antiischemic remedies [4]. In particular, compound **IVc** is by a factor of 3500 more potent than aspirin (as test compound) *in vitro* and 200 times more potent *ex vivo* [4].

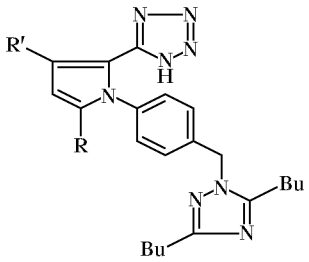
Scheme 1.



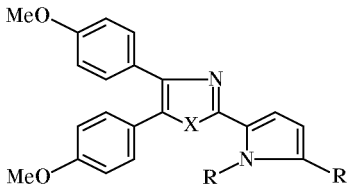
Ia, Ib



II



IIIa–IIId



IVa–IVc

I, R = 2-pyridyl (**a**), 4-pyridyl (**b**); **III**, R = R′ = H (**a**); R = H, R′ = Cl (**b**); R = CF_3, R′ = H (**c**); R = F, R′ = H (**d**); **IV**, X = NH, R = H (**a**); X = S, R = H (**b**); X = S, R = CH_3 (**c**).

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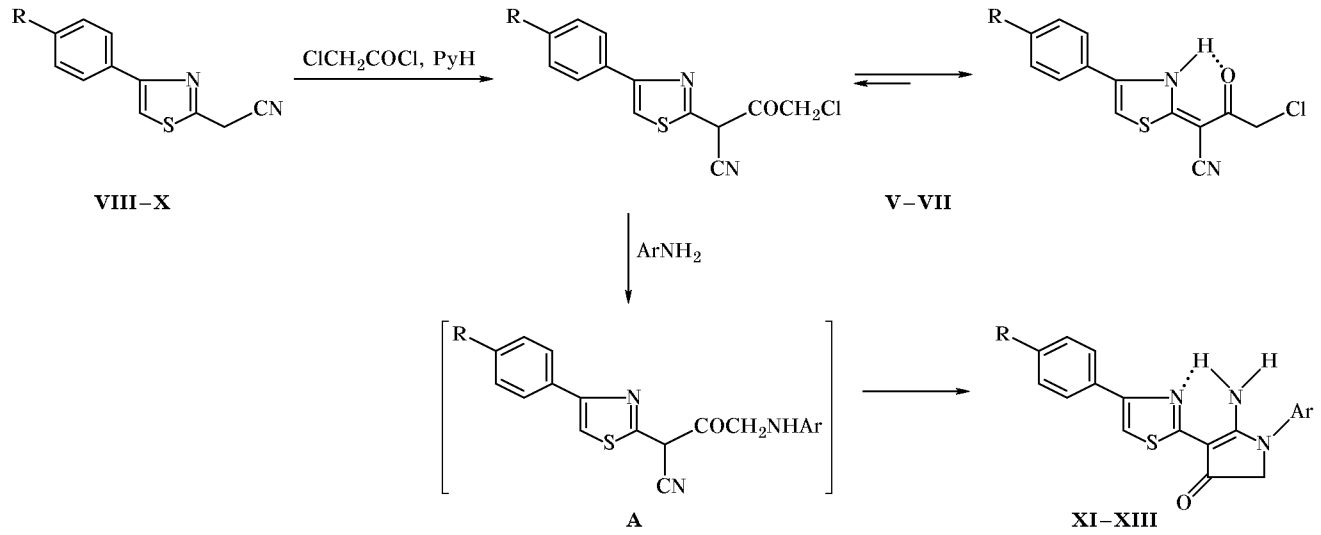
Scheme 2.



V, **VIII**, **XI**, R = H; **VI**, **IX**, **XII**, R = Cl; **VII**, **X**, **XIII**, R = Br; Ar = Ph (**a**), 2-MeC_6H_4 (**b**), 3-MeC_6H_4 (**c**), 4-MeC_6H_4 (**d**), 2-$MeOC_6H_4$ (**e**), 3-$MeOC_6H_4$ (**f**), 4-$MeOC_6H_4$ (**g**), 2,4-$F_2C_6H_3$ (**h**), 2-FC_6H_4 (**i**), 4-*i*-PrC_6H_4 (**j**), 2-$F_3COC_6H_4$ (**k**), 3-$F_3CC_6H_4$ (**l**), 4-piperidinophenyl (**m**), 4-$PhOC_6H_4$ (**n**), 4-$EtOCOCH_2C_6H_4$ (**o**), 3,4-$(CH_2O)_2C_6H_3$ (**p**), 1-$C_{10}H_7$ (**q**), 2-$C_{10}H_7$ (**r**), 4-morpholinophenyl (**s**), 2,3-dihydro-1,4-benzodioxin-6-yl (**t**), 4-$Me_2NC_6H_4$ (**u**), 4-ClC_6H_4 (**v**), 4-$HOCOC_6H_4$ (**w**), 4-Cl-2-MeC_6H_3 (**x**).

Taking the above into account, increasing interest in heteryl-substituted pyrroles becomes clearly understood. 2-Hetarylpyrroles were studied in sufficient detail, while the information on their 3-substituted analogs is much more scanty. The reason lies in different strategies of the synthesis of 2- and 3-hetaryl derivatives. 2-Hetarylpyrroles are usually obtained from readily accessible functionally substituted pyrroles, and heterocyclic fragment is built up on the basis of functional substituent in position *2* [2–4]. By contrast, 3-hetarylpyrroles are synthesized by building up pyrrole ring from acyclic precursor having a heterocyclic moiety in the desired position [1]. Such precursors are much more difficultly accessible than 2-functionalized pyrroles.

For many years, synthesis of 3-hetarylpyrroles was the subject for study in our laboratory: we have synthesized pyrrole derivatives containing pyridyl [5, 6], benzimidazolyl [5–9], and benzothiazolyl groups [8, 9] in position *3*. The present work continues the research in this line; it was aimed at synthesizing 3-(2-thiazolyl)-substituted pyrroles since just thiazolyl derivatives **IV** exhibit the strongest biological activity among the known pyrrole compounds.

The target compounds were synthesized following the above strategy according to which the pyrrole ring was built up on the basis of acyclic precursors. The required starting compounds, 2-(4-arylthiazol-2-yl)-3-oxo-4-chlorobutyronitriles **V**–**VII** were obtained by us previously [10] via C-acylation of accessible 4-arylthiazol-2-ylacetonitriles **VIII**–**X** [11–13] with chloroacetyl chloride in the presence of pyridine (Scheme 2). Halogen-substituted nitriles **V**–**VII** were found to react with aromatic amines, affording 5-amino-1-aryl-4-(4-aryl-1,3-thiazol-2-yl)-2,3-dihydro-1*H*-pyrrol-3-ones **XIb**–**XId**, **XIh**–**XIj**, **XIm**–**XIo**, **XIIa**–**XIIh**, **XIIj**, **XIIk**, **XIIm**–**XIIp**, **XIIr**, **XIIs**, **XIIIa**–**XIIIf**, and **XIIIk**–**XIIIx**. The reaction scheme includes alkylation of aromatic amine with formation of intermediate **A** which undergoes heterocyclization via intramolecular addition of the secondary amino group to cyano group. Analogs of intermediates **A** were reported in [9].

The structure of thiazolylpyrroles **XI**–**XIII** was confirmed by spectral data and elemental analyses. The IR spectra of **XI**–**XIII** lack absorption in the region 2180–2200 cm^{-1}, which is typical of initial halonitriles **V**–**VII** [10]. Instead, two absorption bands appear at 3300–3340 and 3100–3150 cm^{-1} due to stretching vibrations of the primary amino group. It should be emphasized that we observed no carbonyl absorption in the IR spectra of compounds **XI**–**XIII**. This is typical of β-enaminoketone fragment and is consistent with the known data [7–9, 14] for 5-amino-2,3-dihydropyrrol-3-ones.

The ^1H NMR spectra of thiazolyl derivatives **XI**–**XIII**, recorded in DMSO-d_6, contain a two-proton singlet from the methylene group at δ 4.1–4.5 ppm

Table 1. Yields, melting points, and elemental analyses of 5-amino-1-aryl-4-(4-aryl-1,3-thiazol-2-yl)-2,3-dihydropyrrol-3-ones **XIb**–**XId**, **XIh**–**XIj**, **XIm**–**XIo**, **XIIa**–**XIIh**, **XIIj**, **XIIk**, **XIIm**–**XIIp**, **XIIr**, **XIIs**, **XIIIa**–**XIIIf**, and **XIIIk**–**XIIx**

Comp. no.	Yield, %	mp, °C	Found, %		Formula	Calculated, %	
			N	S		N	S
XIb	52	268	12.00	9.18	$C_{20}H_{17}N_3OS$	12.09	9.23
XIc	59	208	12.12	9.09	$C_{20}H_{17}N_3OS$	12.09	9.23
XId	64	291	12.20	9.31	$C_{20}H_{17}N_3OS$	12.09	9.23
XIh	56	219	11.29	8.61	$C_{19}H_{13}F_2N_3OS$	11.38	8.68
XIi	54	221	12.06	9.00	$C_{19}H_{14}FN_3OS$	11.96	9.12
XIj	50	273	11.05	8.69	$C_{22}H_{21}N_3OS$	11.19	8.54
XIm	61	310	13.39	7.84	$C_{24}H_{24}N_4OS$	13.45	7.70
XIn	58	257	9.94	7.62	$C_{25}H_{19}N_3O_2S$	9.88	7.54
XIo	49	198	9.98	7.45	$C_{23}H_{21}N_3O_3S$	10.02	7.64
XIIa	65	294	11.36	8.84	$C_{19}H_{14}ClN_3OS$	11.42	8.72
XIIb	62	307	10.89	8.46	$C_{20}H_{16}ClN_3OS$	11.00	8.40
XIIc	68	252	11.14	8.42	$C_2OH_{16}ClN_3OS$	11.00	8.40
XIId	64	302	10.94	8.35	$C_{20}H_{16}ClN_3OS$	11.00	8.40
XIIe	60	294	10.42	8.14	$C_{20}H_{16}ClN_3O_2S$	10.56	8.06
XIIf	59	234	10.59	8.20	$C_{20}H_{16}ClN_3O_2S$	10.56	8.06
XIIg	64	303	10.61	8.12	$C_{20}H_{16}ClN_3O_2S$	10.56	8.06
XIIh	57	>300	10.35	8.10	$C_{19}H_{12}ClF_2N_3OS$	10.41	7.94
XIIj	49	284	10.26	8.74	$C_{22}H_{20}ClN_3OS$	10.25	7.82
XIIk	61	>300	9.13	6.95	$C_{20}H_{13}ClF_3N_3O_2S$	9.30	7.10
XIIm	69	>300	12.39	7.19	$C_{24}H_{23}ClN_4OS$	12.42	7.11
XIIn	59	298	9.03	7.00	$C_{25}H_{18}ClN_3O_2S$	9.14	6.97
XIIo	59	227	9.37	6.97	$C_{23}H_{20}ClN_3O_3S$	9.26	7.06
XIIp	64	282	10.08	7.84	$C_{20}H_{14}ClN_3O_3S$	10.20	7.78
XIIr	60	>300	9.96	7.58	$C_{23}H_{16}ClN_3OS$	10.05	7.67
XIIs	64	>300	12.26	6.99	$C_{23}H_{21}ClN_4O_2S$	12.37	7.08
XIIIa	50	296	10.08	7.71	$C_{19}H_{14}BrN_3OS$	10.19	7.78
XIIIb	56	>300	9.76	7.46	$C_{20}H_{16}BrN_3OS$	9.86	7.52
XIIIc	58	249	9.94	7.41	$C_{20}H_{16}BrN_3OS$	9.86	7.52
XIIId	51	298	10.01	7.39	$C_{20}H_{16}BrN_3OS$	9.86	7.52
XIIIe	62	288	9.53	7.19	$C_{20}H_{16}BrN_3O_2S$	9.50	7.25
XIIIf	53	239	9.54	7.33	$C_{20}H_{16}BrN_3O_2S$	9.50	7.25
XIIIk	61	>300	8.32	6.42	$C_{20}H_{13}BrF_3N_3O_2S$	8.47	6.46
XIIIl	64	>300	8.77	6.74	$C_{20}H_{13}BrF_3N_3OS$	8.75	6.68
XIIIm	53	>300	11.50	6.44	$C_{24}H_{23}BrN_4OS$	11.31	6.47
XIIIn	54	294	8.21	6.47	$C_{25}H_{18}BrN_3O_2S$	8.33	6.36
XIIIo	59	241	8.39	6.32	$C_{23}H_{20}BrN_3O_3S$	8.43	6.43
XIIIp	48	296	9.04	6.89	$C_{20}H_{14}BrN_3O_3S$	9.21	7.03
XIIIq	57	>300	9.11	7.04	$C_{23}H_{16}BrN_3OS$	9.09	6.93
XIIIr	50	>300	8.94	6.99	$C_{23}H_{16}BrN_3OS$	9.09	6.93
XIIIs	46	>300	11.14	6.41	$C_{23}H_{21}BrN_4O_2S$	11.26	6.45
XIIIt	59	>300	8.99	6.78	$C_{21}H_{16}BrN_3O_3S$	8.93	6.82
XIIIu	51	>300	12.27	6.98	$C_{21}H_{19}BrN_4OS$	12.30	7.04
XIIIv	59	227	9.46	7.16	$C_{19}H_{13}BrClN_3OS$	9.41	7.18
XIIIw	42	>300	9.17	7.06	$C_{20}H_{14}BrN_3O_3S$	9.21	7.03
XIIIx	48	291	9.09	6.89	$C_{20}H_{15}BrClN_3OS$	9.12	6.96

Table 2. ^{1}H NMR spectra of 5-amino-1-aryl-4-(4-aryl-1,3-thiazol-2-yl)-2,3-dihydropyrrol-3-ones **XIb**–**XId**, **XIh**–**XIj**, **XIm**–**XIo**, **XIIa**–**XIIh**, **XIIj**, **XIIk**, **XIIm**–**XIIp**, **XIIr**, **XIIs**, **XIIIa**–**XIIIf**, and **XIIIk**–**XIIx**[a]

Comp. no.	Chemical shifts δ, ppm
XIb	2.26 s (3H, CH_3), 4.16 s (2H, CH_2), 7.39 m (7H, 3-H, 4-H, 5-H, H_{arom}), 7.67 s (1H, SCH), 7.92 d.d (2H, 2-H, 6-H, *J* = 7.0, 1.0 Hz), 8.30 br.s (2H, NH_2)
XIc	2.36 s (3H, CH_3), 4.31 s (2H, CH_2), 7.36 m (7H, 3-H, 4-H, 5-H, H_{arom}), 7.70 s (1H, SCH), 7.93 d.d (2H, 2-H, 6-H, *J* = 7.5, 1.5 Hz), 8.20 br.s (2H, NH_2)
XId	2.36 s (3H, CH_3), 4.25 s (2H, CH_2), 7.40 m (7H, 3-H, 4-H, 5-H, H_{arom}), 7.65 s (1H, SCH), 7.92 d.d (2H, 2-H, 6-H, *J* = 8.0, 2.0 Hz), 8.20 br.s (2H, NH_2)
XIh	4.47 s (2H, CH_2), 7.48–7.51 m (6H, 3-H, 4-H, 5-H, H_{arom}), 7.75 m (5H, NH_2, 2-H, 6-H, SCH)
XIi	4.48 s (2H, CH_2), 6.80 br.s (2H, NH_2), 7.50 m (8H, 3-H, 4-H, 5-H, SCH, H_{arom}), 7.78 d.d (2H, 2-H, 6-H, *J* = 7.0, 2.0 Hz)
XIj	1.23 d (6H, CH_3, *J* = 10.0 Hz), 2.96 m (1H, HC), 4.25 s (2H, CH_2), 7.41 m (7H, 3-H, 4-H, 5-H, H_{arom}), 7.63 s (1H, SCH), 7.91 d.d (2H, 2-H, 6-H, *J* = 7.5, 1.5 Hz), 8.25 br.s (2H, NH_2)
XIm	1.61 m (6H, $CH_2CH_2CH_2$), 3.17 t (4H, CH_2NCH_2, *J* = 6.0 Hz), 4.17 s (2H, CH_2), 7.00 d (2H, 3-H, 5-H, *J* = 9.0 Hz), 7.36 m (5H, 3-H, 4-H, 5-H, 2-H, 6-H, *J* = 9.0 Hz), 7.64 s (1H, SCH), 7.90 d.d (2H, 2-H, 6-H, *J* = 8.0, 1.5 Hz), 8.06 br.s (2H, NH_2)
XIn	4.29 s (2H, CH_2), 7.11 m (5H, OPh), 7.41 d (2H, 3-H, 5-H, *J* = 9.0 Hz), 7.48 m (3H, 3-H, 4-H, 5-H), 7.51 d (2H, 2-H, 6-H, *J* = 9.0 Hz), 7.70 s (1H, SCH), 7.92 d.d (2H, 2-H, 6-H, *J* = 8.0, 1.5 Hz), 8.32 br.s (2H, NH_2)
XIo	1.21 t (3H, CH_3, *J* = 11.0 Hz), 3.72 s (2H, ArCH_2CO_2Et), 4.09 q (2H, OCH_2, *J* = 11.0 Hz), 4.31 s (2H, NCH_2CO), 7.43 m (7H, 3-H, 4-H, 5-H, H_{arom}), 7.70 s (1H, SCH), 7.93 d.d (2H, 2-H, 6-H, *J* = 7.0, 1.0 Hz), 8.40 br.s (2H, NH_2)
XIIa	4.33 s (2H, CH_2), 7.53 m (5H, H_{arom}), 7.69 s (1H, SCH), 7.71 d (2H, 3-H, 5-H, *J* = 9.0 Hz), 7.92 d (2H, 2-H, 6-H, *J* = 9.0 Hz), 8.29 s (2H, NH_2)
XIIb	2.26 s (3H, CH_3), 4.14 s (2H, CH_2), 7.39 s (4H, H_{arom}), 7.60 d (2H, 3-H, 5-H, *J* = 9.0 Hz), 7.73 s (1H, SCH), 7.90 d (2H, 2-H, 6-H, *J* = 9.0 Hz), 8.30 s (2H, NH_2)
XIIc	2.37 s (3H, CH_3), 4.29 s (2H, CH_2), 7.11–7.41 m (4H, H_{arom}), 7.62 d (2H, 3-H, 5-H, *J* = 9.0 Hz), 7.76 s (1H, SCH), 7.91 d (2H, 2-H, 6-H, *J* = 9.0 Hz), 8.30 s (2H, NH_2)
XIId	2.36 s (3H, CH_3), 4.25 s (2H, CH_2), 7.34 s (4H, H_{arom}), 7.60 d (2H, 3-H, 5-H, *J* = 9.0 Hz), 7.72 s (1H, SCH), 7.89 d (2H, 2-H, 6-H, *J* = 9.0 Hz), 8.15 s (2H, NH_2)
XIIe	3.84 s (3H, OCH_3), 4.12 s (2H, CH_2), 7.08 t.d (1H, 5-H_{arom}, *J* = 7.0, 1.5 Hz), 7.22 d (1H, 3-H_{arom}, *J* = 7.0 Hz), 7.45 m (2H, 4-H, 6-H, *J* = 7.0, 1.5 Hz), 7.61 d (2H, 3-H, 5-H, *J* = 8.5 Hz), 7.77 s (1H, SCH), 7.90 d (2H, 2-H, 6-H, *J* = 8.5 Hz), 8.30 s (1H, HN), 9.00 s (1H, NH···N)
XIIf	3.84 s (3H, OCH_3), 4.33 s (2H, CH_2), 6.97 m (2H, 4-H, 6-H), 7.10 d (1H, 2-H, *J* = 1.5 Hz), 7.44 t (1H, 5-H, *J* = 8.5 Hz), 7.63 d (2H, 3-H, 5-H, *J* = 8.5 Hz), 7.76 s (1H, SCH), 7.92 d (2H, 2-H, 6-H, *J* = 8.5 Hz), 8.33 s (2H, NH_2)
XIIg	3.81 s (3H, OCH_3), 4.21 s (2H, CH_2), 7.05 d (2H, 3-H, 5-H, *J* = 9.5 Hz), 7.41 d (2H, 2-H, 6-H, *J* = 9.5 Hz), 7.60 d (2H, 3-H, 5-H, *J* = 8.5 Hz), 7.70 s (1H, SCH), 7.88 d (2H, 2-H, 6-H, *J* = 8.5 Hz), 8.10 s (2H, NH_2)
XIIh	4.20 s (2H, CH_2), 7.20–7.52 m (3H, H_{arom}), 7.62 d (2H, 3-H, 5-H, *J* = 8.5 Hz), 7.78 s (1H, SCH), 7.94 d (2H, 2-H, 6-H, *J* = 8.5 Hz), 8.30 s (2H, NH_2)
XIIj	1.25 d (6H, CH_3, *J* = 10.0 Hz), 2.95 m (1H, HC), 4.30 s (2H, CH_2), 7.40 s (4H, H_{arom}), 7.63 d (2H, 3-H, 5-H, *J* = 9.0 Hz), 7.77 s (1H, SCH), 7.91 d (2H, 2-H, 6-H, *J* = 9.0 Hz), 8.27 s (2H, NH_2)
XIIk	4.35 s (2H, CH_2), 7.61 m (6H, 3-H, 5-H, H_{arom}), 7.76 s (1H, SCH), 7.93 d (2H, 2-H, 6-H, *J* = 9.0 Hz), 8.43 s (2H, NH_2)
XIIm	1.61 m (6H, $CH_2CH_2CH_2$), 3.18 t (4H, CH_2NCH_2, *J* = 6.0 Hz), 4.17 s (2H, CH_2), 7.00 d (2H, 3-H, 5-H, *J* = 9.5 Hz), 7.30 d (2H, 2-H, 6-H, *J* = 9.5 Hz), 7.61 d (2H, 3-H, 5-H, *J* = 9.0 Hz), 7.70 s (1H, SCH), 7.89 d (2H, 2-H, 6-H, *J* = 9.0 Hz), 7.98 s (1H, NH_2)

Table 2. (Contd.)

Comp. no.	Chemical shifts δ, ppm
XIIn	4.26 s (2H, CH_2), 7.02–7.24 m (5H, OPh), 7.41 d (2H, 3-H, 5-H, *J* = 9.5 Hz), 7.50 d (2H, 2-H, 6-H, *J* = 9.5 Hz), 7.60 d (2H, 3-H, 5-H, *J* = 9.0 Hz), 7.72 s (1H, SCH), 7.89 d (2H, 2-H, 6-H, *J* = 9.0 Hz), 8.20 s (2H, NH_2)
XIIo	1.21 t (3H, CH_3, *J* = 11.0 Hz), 3.71 s (2H, ArC**H**$_2$$CO_2$Et), 4.17 q (2H, OCH_2, *J* = 11.0 Hz), 4.28 s (2H, NCH_2CO), 7.42 s (4H, H_{arom}), 7.61 d (2H, 3-H, 5-H, *J* = 8.5 Hz), 7.72 s (1H, SCH), 7.90 d (2H, 2-H, 6-H, *J* = 8.5 Hz), 8.30 s (2H, NH_2)
XIIp	4.21 s (2H, CH_2), 6.09 s (2H, OCH_2O), 6.99 m (2H, 5-H, 6-H), 7.12 d (1H, 2-H, *J* = 1.5 Hz), 7.62 d (2H, 3-H, 5-H, *J* = 9.0 Hz), 7.73 s (1H, SCH), 7.90 d (2H, 2-H, 6-H, *J* = 9.0 Hz), 8.15 s (2H, NH_2)
XIIr	4.39 s (2H, CH_2), 7.41–7.64 m (6H, 3-H, 5-H; SCH; 3-H, 6-H, 7-H_{arom}), 7.88–8.10 m (6H, 2-H, 6-H; 1-H, 4-H, 5-H, 8-H_{arom}), 8.45 s (2H, NH_2)
XIIs	3.33 t (4H, CH_2NCH_2, *J* = 7.0 Hz), 3.75 t (4H, CH_2OCH_2, *J* = 7.0 Hz), 4.19 s (2H, CH_2), 7.05 d (2H, 3-H, 5-H, *J* = 9.5 Hz), 7.34 d (2H, 2-H, 6-H, *J* = 9.5 Hz), 7.61 d (2H, 3-H, 5-H, *J* = 9.0 Hz), 7.70 s (1H, SCH), 7.88 d (2H, 2-H, 6-H, *J* = 9.0 Hz), 8.20 s (1H, NH), 8.91 s (1H, NH···N)
XIIIa	4.30 s (2H, CH_2), 7.48 m (7H, 3-H, 5-H, H_{arom}), 7.70 s (1H, SCH), 7.94 d (2H, 2-H, 6-H, *J* = 9.0 Hz), 8.26 s (2H, NH_2)
XIIIb	2.26 s (3H, CH_3), 4.13 s (2H, CH_2), 7.39 s (4H, H_{arom}), 7.47 d (2H, 3-H, 5-H, *J* = 9.0 Hz), 7.70 s (1H, SCH), 7.93 d (2H, 2-H, 6-H, *J* = 9.0 Hz), 8.30 s (2H, NH_2)
XIIIc	2.37 s (3H, CH_3), 4.30 s (2H, CH_2), 7.20 m (3H, 4-H, 5-H, 6-H_{arom}), 7.33 s (2H, 2-H_{arom}), 7.50 d (2H, 3-H, 5-H, *J* = 9.0 Hz), 7.75 s (1H, SCH), 7.98 d (2H, 2-H, 6-H, *J* = 9.0 Hz), 8.31 s (2H, NH_2)
XIIId	2.35 s (3H, CH_3), 4.25 s (2H, CH_2), 7.35 s (4H, H_{arom}), 7.48 d (2H, 3-H, 5-H, *J* = 9.0 Hz), 7.71 s (1H, SCH), 7.95 d (2H, 2-H, 6-H, *J* = 9.0 Hz), 8.17 s (2H, NH_2)
XIIIe	3.84 s (3H, OCH_3), 4.10 s (2H, CH_2), 7.07 t.d (1H, 5-H_{arom}, *J* = 7.0, 1.5 Hz), 7.20 d.d (1H, 3-H_{arom}, *J* = 7.0, 1.5 Hz), 7.40 d.d (1H, 6-H_{arom}, *J* = 7.0, 1.5 Hz), 7.43 t.d (1H, 4-H_{arom}, *J* = 7.0, 1.5 Hz), 7.48 d (2H, 3-H, 5-H, *J* = 8.5 Hz), 7.70 s (1H, SCH), 7.94 d (2H, 2-H, 6-H, *J* = 8.5 Hz), 8.30 s (1H, NH), 9.00 s (1H, NH···N)
XIIIf	3.82 s (3H, OCH_3), 4.33 s (2H, CH_2), 6.96 m (2H, 4-H, 5-H_{arom}), 7.10 d (1H, 2-H_{arom}, *J* = 1.0 Hz), 7.49 d (1H, 6-H_{arom}, *J* = 9.0 Hz), 7.50 d (2H, 3-H, 5-H, *J* = 9.0 Hz), 7.78 s (1H, SCH), 7.98 d (2H, 2-H, 6-H, *J* = 9.0 Hz), 8.40 s (2H, NH_2)
XIIIk	4.31 s (2H, CH_2), 7.52 m (6H, 3-H, 5-H, H_{arom}), 7.73 s (1H, SCH), 7.97 d (2H, 2-H, 6-H, *J* = 9.0 Hz), 8.38 s (2H, NH_2)
XIIIl	4.39 s (2H, CH_2), 7.50 d (2H, 3-H, 5-H, *J* = 9.0 Hz), 7.72 m (3H, 4-H, 5-H, 6-H_{arom}), 7.80 s (1H, SCH), 7.88 s (1H, 2-H_{arom}), 8.00 d (2H, 2-H, 6-H, *J* = 9.0 Hz), 8.52 s (2H, NH_2)
XIIIm	1.60 m (6H, $CH_2CH_2CH_2$), 3.20 t (4H, CH_2NCH_2, *J* = 5.0 Hz), 4.18 s (2H, CH_2), 7.01 d (2H, 3-H, 5-H, *J* = 9.5 Hz), 7.30 d (2H, 2-H, 6-H_{arom}, *J* = 9.5 Hz), 7.48 d (2H, 3-H, 5-H, *J* = 9.0 Hz), 7.70 s (1H, SCH), 7.94 d (2H, 2-H, 6-H, *J* = 9.0 Hz), 8.30 s (2H, NH_2)
XIIIn	4.27 s (2H, CH_2), 7.13–7.35 m (5H, OPh), 7.41 d (2H, 3-H, 5-H, *J* = 10.0 Hz), 7.48 d (2H, 3-H, 5-H, *J* = 9.0 Hz), 7.50 d (2H, 2-H, 6-H_{arom}, *J* = 10.0 Hz), 7.72 s (1H, SCH), 7.96 d (2H, 2-H, 6-H, *J* = 9.0 Hz), 8.20 s (2H, NH_2)
XIIIo	1.21 t (3H, CH_3, *J* = 10.0 Hz), 3.72 s (2H, ArC**H**$_2$$CO_2$Et), 4.17 q (2H, OCH_2, *J* = 10.0 Hz), 4.31 s (2H, NCH_2CO), 7.43 s (4H, H_{arom}), 7.50 d (2H, 3-H, 5-H, *J* = 9.0 Hz), 7.78 s (1H, SCH), 7.97 d (2H, 2-H, 6-H, *J* = 9.0 Hz), 8.35 s (2H, NH_2)
XIIIp	4.20 s (2H, CH_2), 6.09 s (2H, OCH_2O), 6.98 m (2H, 5-H, 6-H_{arom}), 7.11 d (1H, 2-H_{arom}, *J* = 0.5 Hz), 7.48 d (2H, 3-H, 5-H, *J* = 9.0 Hz), 7.70 s (1H, SCH), 7.94 d (2H, 2-H, 6-H, *J* = 9.0 Hz), 8.12 s (2H, NH_2)
XIIIq	4.29 s (2H, CH_2), 7.46 d (2H, 3-H, 5-H, *J* = 9.0 Hz), 7.58–7.79 m (5H, SCH, 2-H, 3-H, 6-H, 7-H_{arom}), 7.96 d (2H, 2-H, 6-H, *J* = 9.0 Hz), 8.01 m (3H, 4-H, 5-H, 8-H_{arom}), 8.14 s (2H, NH_2)

Table 2. (Contd.)

Comp. no.	Chemical shifts δ, ppm
XIIIr	4.40 s (2H, CH_2), 7.49 d (2H, 3-H, 5-H, *J* = 8.5 Hz), 7.57–7.73 m (4H, SCH, 3-H, 6-H, 7-H_{arom}), 7.90–8.10 m (6H, 2-H, 6-H; 1-H, 4-H, 5-H, 8-H_{arom}), 8.39 s (2H, NH_2)
XIIIs	3.17 t (4H, CH_2NCH_2, *J* = 7.0 Hz), 3.77 t (4H, CH_2OCH_2, *J* = 7.0 Hz), 4.20 s (2H, NCH_2O), 7.05 d (2H, 3-H, 5-H, *J* = 9.5 Hz), 7.35 d (2H, 2-H, 6-H_{arom}, *J* = 9.5 Hz), 7.49 d (2H, 3-H, 5-H, *J* = 9.0 Hz), 7.70 s (1H, SCH), 7.95 d (2H, 2-H, 6-H, *J* = 9.0 Hz), 8.20 s (1H, NH), 8.91 s (1H, NH···N)
XIIIt	4.22 s (4H, OCH_2CH_2O), 4.28 s (2H, NCH_2CO), 6.95 m (3H, H_{arom}), 7.47 d (2H, 3-H, 5-H, *J* = 9.0 Hz), 7.69 s (1H, SCH), 7.94 d (2H, 2-H, 6-H, *J* = 9.0 Hz), 8.20 s (2H, NH_2)
XIIIu	2.95 s (6H, NCH_3), 4.15 s (2H, CH_2), 6.81 d (2H, 3-H, 5-H, *J* = 9.5 Hz), 7.28 d (2H, 2-H, 6-H_{arom}, *J* = 9.5 Hz), 7.47 d (2H, 3-H, 5-H, *J* = 8.5 Hz), 7.67 s (1H, SCH), 7.93 d (2H, 2-H, 6-H, *J* = 8.5 Hz), 8.20 s (2H, NH_2)
XIIIv	4.28 s (2H, CH_2), 7.50 m (6H, 3-H, 5-H, H_{arom}), 7.67 s (1H, SCH), 7.94 d (2H, 2-H, 6-H, *J* = 8.0 Hz), 8.20 s (2H, NH_2)
XIIIw	4.37 s (2H, CH_2), 7.49 m (4H, 3-H, 5-H, 2-H, 6-H_{arom}), 7.70 s (1H, SCH), 7.95 m (4H, 2-H, 6-H, 3-H, 5-H), 8.50 s (2H, NH_2), 11.23 s (1H, OH)
XIIIx	2.25 s (3H, CH_3), 4.16 s (2H, CH_2), 7.49 m (2H, 3-H, 5-H, H_{arom}), 7.79 s (1H, SCH), 8.00 d (2H, 2-H, 6-H, *J* = 9.0 Hz), 8.08 s (2H, NH_2)

[a] Protons of the Ar substituent are denoted as H_{arom}; the other numbers refer to the RC_6H_4 ring.

and a one-proton singlet in the region δ 7.6–7.8 ppm; the latter belongs to proton in position *5* of the thiazole ring. The amino group gives a signal in the region δ 8.0–9.0 ppm; it appears as either two broadened one-proton singlets (due to nonequivalence of the NH_2 protons, one of which is involved in intramolecular hydrogen bond) or one broadened two-proton singlet. In both cases these signals disappear on addition of D_2O. Proton signals of the aryl substituents on the nitrogen atom of the pyrrole ring and in position *4* of the thiazole ring are located as usually. Thus, according to the spectral data, thiazolylpyrroles **XI**–**XIII** exist as enaminoketone tautomers.

The yields, melting points, and elemental analyses of compounds **XI**–**XIII** are given in Table 1, and Table 2 contains their ^{1}H NMR spectral parameters.

EXPERIMENTAL

The progress of reactions was monitored by TLC on Silufol UV-254 plates using chloroform–methanol (9:1) as eluent. The IR spectra were recorded on a Pye Unicam SP3-300 spectrometer from samples pelleted with KBr. The ^{1}H NMR spectra were obtained on a Bruker WP-100SY instrument (100 MHz).

5-Amino-1-aryl-4-(4-aryl-1,3-thiazol-2-yl)-2,3-dihydro-1*H*-pyrrol-3-ones XIb–**XId, XIh**–**XIj, XIm**–**XIo, XIIa**–**XIIh, XIIj, XIIk, XIIm**–**XIIp, XIIr, XIIs, XIIIa**–**XIIIf, and XIIIk**–**XIIIx (***general procedure***).** Appropriate aromatic amine, 0.003 mol, was added to a solution of 0.003 mol of 2-(4-arylthiazol-2-yl)-3-oxo-4-chlorobutyronitrile **V**–**VII** and 0.4 ml (0.003 mol) of triethylamine in 10–15 ml of dioxane, heated to the boiling point. The mixture was refluxed for 3 h until initial compound **V**–**VII** disappeared (according to the TLC data). The mixture was cooled, and the precipitate was filtered off, thoroughly washed with water, dried, and recrystallized from 1-butanol (compounds **XIh**, **XIo**, **XIId**, **XIIj**, **XIIk**, **XIIIa**, **XIIIf**, **XIIIk**, **XIIIs**, and **XIIIx**) or dioxane (**XIb**–**XId**, **XIi**, **XIj**, **XIm**, **XIn**, **XIIa**–**XIIc**, **XIIe**–**XIIh**, **XIIm**–**XIIp**, **XIIr**, **XIIs**, **XIIIb**–**XIIIe**, **XIIIl**–**XIIIr**, and **XIIIt**–**XIIIw**). The yields of products **XI**–**XIII** are given in Table 1.

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