

SYNTHESIS OF SUBSTITUTED FURO[2',3':4,5]PYRROLO[1,2-*d*]-[1,2,4]TRIAZOLO[3,4-*f*][1,2,4]TRIAZINES

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In continuation of our previous studies in the synthesis of furocondensed N-heterocycles¹⁻⁵ the preparation of new substituted furo[2',3':4,5]pyrrolo[1,2-*d*][1,2,4]triazolo[3,4-*f*]-[1,2,4]triazines (*IVa* – *IVh*) from 2-methyl and 2,3-dimethyl-4*H*-furo[3,2-*b*]pyrrole-5-carboxhydrazides is described. The synthesis and the synthetic utilization of substituted 4*H*-furo[3,2-*b*]pyrrole-5-carboxhydrazides was the subject of our previous papers¹⁻⁵. Some of these hydrazides were already used in the synthesis¹⁻⁴.

Characteristic data of the synthesized compounds are given in Table I. Their structure has been confirmed by ¹H NMR, UV and IR spectroscopy (Table II).

EXPERIMENTAL

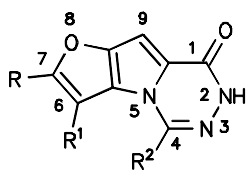
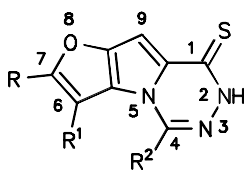
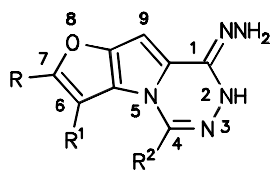
Melting points were determined on a Kofler hot plate apparatus and are uncorrected. Proton NMR spectra were recorded on a Tesla BS 587 (80 MHz) instrument (HMDS as internal standard, (CD₃)₂SO as solvent, δ values in ppm), IR spectra were recorded on FTIR PU 9802/25 (Philips) spectrophotometer using KBr technique (ν in cm⁻¹), and UV spectra were measured on an M-40 (Zeiss, Jena) spectrophotometer in ethanol (λ_{max}/log ε; λ_{max} in nm, ε in m² mol⁻¹).

The starting carboxhydrazides were prepared according to refs^{5,6}.

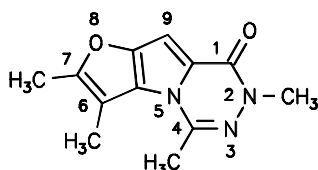
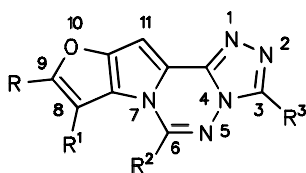
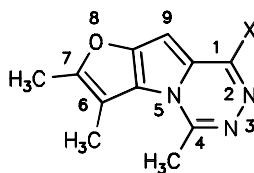
Methylation of *Id* gave rise to derivative *V*. The similar IR and UV spectra of both compounds *Id* and *V* give evidence of the triazinone form of *Id* which is supported by the observations in refs^{7,8}. On the other hand, compound *VIb* exhibits the typical aromatic character in contrast to the parent thione *IId* that shows the hypsochromic shift of 36 nm in the UV spectra and ν_{max} at 1 472 cm⁻¹ in the IR spectra in comparison with refs^{7,8}. The values are comparable with those for the aromatic chloro derivative *VI*, which was prepared by reaction of *Id* with phosphorus oxychloride.

1,2-Dihydrofuro[2',3':4,5]pyrrolo[1,2-*d*][1,2,4]triazin-1-ones (*Ia* – *Id*)

2-Methylfuro[3,2-*b*]pyrrole-5-carboxhydrazide or 2,3-dimethylfuro[3,2-*b*]pyrrole-5-carboxhydrazide (10 mmol) and triethyl orthoformate or triethyl orthoacetate (13.5 mmol) were refluxed in dimethylformamide (5 ml) for 7 h. After cooling, the precipitate was filtered off. Yields and characteristic values are given in Table I.

*I**II**III*

<i>I - III</i>	R	R ¹	R ²
<i>a</i>	CH ₃	H	H
<i>b</i>	CH ₃	H	CH ₃
<i>c</i>	CH ₃	CH ₃	H
<i>d</i>	CH ₃	CH ₃	CH ₃

*V**IV**VI*

<i>IV</i>	R	R ¹	R ²	R ³
<i>a</i>	CH ₃	H	H	H
<i>b</i>	CH ₃	H	H	CH ₃
<i>c</i>	CH ₃	H	CH ₃	H
<i>d</i>	CH ₃	H	CH ₃	CH ₃
<i>e</i>	CH ₃	CH ₃	H	H
<i>f</i>	CH ₃	CH ₃	H	CH ₃
<i>g</i>	CH ₃	CH ₃	CH ₃	H
<i>h</i>	CH ₃	CH ₃	CH ₃	CH ₃

a, X = Cl*b*, X = SCH₃

TABLE I
Characteristic data of the compounds synthesized

Compound	Formula (M.w.)	M.p., °C Yield, %	Calculated/Found			
			% C	% H	% N	% S
<i>Ia</i>	C ₉ H ₇ N ₃ O ₂	281 – 284 ^{a,b}	57.14	3.73	22.21	
	(189.2)	71	57.03	3.88	22.30	
<i>Ib</i>	C ₁₀ H ₉ N ₃ O ₂	271 – 272 ^b	59.10	4.46	20.68	
	(203.2)	78	58.98	4.51	20.59	
<i>Ic</i>	C ₁₀ H ₉ N ₃ O ₂	327 – 328 ^b	59.10	4.46	20.68	
	(203.2)	74	59.00	4.53	20.58	
<i>Id</i>	C ₁₁ H ₁₁ N ₃ O ₂	331 – 333 ^b	60.82	5.11	19.34	
	(217.2)	65	60.73	5.17	19.21	
<i>Ila</i>	C ₉ H ₇ N ₃ OS	259 – 260 ^c	52.67	3.44	20.47	15.59
	(205.2)	64	52.54	3.50	20.49	15.38
<i>Ilb</i>	C ₁₀ H ₉ N ₃ OS	290 – 291 ^{a,c}	54.78	4.14	19.17	14.62
	(219.3)	70	54.62	4.21	19.06	14.51
<i>Ilc</i>	C ₁₀ H ₉ N ₃ OS	336 – 338 ^c	54.78	4.14	19.17	14.62
	(219.3)	89	54.69	4.18	19.10	14.49
<i>Ild</i>	C ₁₁ H ₁₁ N ₃ OS	>360 ^c	56.63	4.75	18.01	13.74
	(233.3)	79	56.49	4.81	17.89	13.80
<i>IIla</i>	C ₉ H ₉ N ₅ O	287 – 288 ^c	53.11	4.46	34.47	
	(203.2)	43	53.07	4.49	34.35	
<i>IIlb</i>	C ₁₀ H ₁₁ N ₅ O	>360 ^c	55.29	5.11	32.24	
	(217.2)	60	55.18	5.19	32.30	
<i>IIlc</i>	C ₁₀ H ₁₁ N ₅ O	232 – 233 ^{a,c}	55.29	5.11	32.24	
	(217.2)	33	55.19	5.15	32.20	
<i>IIId</i>	C ₁₁ H ₁₃ N ₅ O	290 – 291 ^{a,c}	57.13	5.66	30.29	
	(231.3)	34	57.06	5.71	30.19	
<i>IVa</i>	C ₁₀ H ₇ N ₅ O	293 – 294 ^{a,b}	56.33	3.31	32.85	
	(213.2)	73	56.27	3.40	32.92	
<i>IVb</i>	C ₁₁ H ₉ N ₅ O	301 – 303 ^b	58.14	3.99	30.82	
	(227.2)	68	58.02	4.07	30.93	
<i>IVc</i>	C ₁₁ H ₉ N ₅ O	283 – 284 ^{a,b}	58.14	3.99	30.82	
	(227.2)	56	58.06	4.02	30.73	

TABLE I
(Continued)

Compound	Formula (M.w.)	M.p., °C Yield, %	Calculated/Found			
			% C	% H	% N	% S
<i>IVd</i>	C ₁₂ H ₁₁ N ₅ O	318 – 319 ^{a,b}	59.74	4.60	29.03	
	(241.3)	48	59.80	4.68	28.89	
<i>IVe</i>	C ₁₁ H ₉ N ₅ O	280 – 281 ^{a,b}	58.14	3.99	30.82	
	(227.2)	58	58.01	4.10	30.71	
<i>IVf</i>	C ₁₂ H ₁₁ N ₅ O	320 – 321 ^{a,b}	59.74	4.60	29.03	
	(241.3)	63	59.63	4.68	28.94	
<i>IVg</i>	C ₁₂ H ₁₁ N ₅ O	283 – 284 ^{a,b}	59.74	4.60	29.03	
	(241.3)	62	59.68	4.57	29.15	
<i>IVh</i>	C ₁₃ H ₁₃ N ₅ O	343 – 345 ^{a,b}	61.16	5.13	27.44	
	(255.3)	57	61.07	5.24	27.31	
<i>V</i>	C ₁₂ H ₁₃ N ₃ O ₂	235 – 236 ^d	62.32	5.67	18.17	
	(231.2)	76	62.24	5.73	18.30	
<i>VIa</i>	C ₁₁ H ₁₀ ClN ₃ O	172 – 174 ^d	56.05	4.28	17.18	15.04 ^e
	(235.7)	42	55.91	4.34	17.72	14.89 ^e
<i>VIb</i>	C ₁₂ H ₁₃ N ₃ OS	236 – 237 ^d	58.28	5.30	16.99	12.96
	(247.3)	64	58.19	5.36	16.88	12.81

^a Decomposition; crystallized from ^b dimethylformamide, ^c dioxane, ^d ethanol; ^e % Cl.

1,2-Dihydrofuro[2',3':4,5]pyrrolo[1,2-*d*][1,2,4]triazine-1-thiones (*IIa* – *IId*)

Compounds *Ia* – *Id* (10 mmol) and phosphorus pentasulfide (2.3 g, 10 mmol) in dry pyridine (10 ml) were refluxed with stirring for 4 h. The mixture was poured into hot water (70 ml) and the precipitate was filtered off.

1,2-Dihydrofuro[2',3':4,5]pyrrolo[1,2-*d*][1,2,4]triazine-1-hydrazones (*IIIa* – *IIId*)

Compounds *IIa* – *IId* (10 mmol) and hydrazine hydrate 95% (10 ml) were stirred and heated at 110 °C for 6 h. After cooling, the precipitate was filtered off and washed with water.

Furo[2',3':4,5]pyrrolo[1,2-*d*][1,2,4]triazolo[3,4-*f*][1,2,4]triazines (*IVa* – *IVh*)

A mixture of hydrazone *IIIa* – *IIId* (5 mmol) and triethyl orthoformate or triethyl orthoacetate (10 mmol) in dry dimethyl sulfoxide (5 ml) was heated at 170 °C for 3 h. After cooling, the crystals were filtered off and washed with ethanol.

TABLE II
Spectral data of the compounds synthesized

Compound	¹ H NMR spectra, δ, ppm					UV spectra		IR spectra ν, cm ⁻¹
	R s	R ¹ s	R ² s	H-9 s	other signals	λ _{max} nm	logε	
<i>Ia</i>	2.42	6.66	8.63	6.98	11.66 bs (NH)	305	3.17	1 655 ^a
<i>Ib</i>	2.36	6.71	2.48	6.98	11.51 bs (NH)	304	3.28	1 653 ^a
<i>Ic</i>	2.37	2.28	8.56	6.96	11.65 bs (NH)	309	3.11	1 657 ^a
<i>Id</i>	2.36	2.21	2.59	7.00	11.52 bs (NH)	306	3.23	1 654 ^a
<i>IIa</i>	2.44	6.73	9.03	7.16	13.07 bs (NH)	369	3.30	1 555 ^b
<i>IIb</i>	2.43	6.80	2.60	7.14	13.01 bs (NH)	366	332	1 554 ^b
<i>IIc</i>	2.33	2.23	8.88	7.09	13.05 bs (NH)	373	3.10	1 557 ^b
<i>IId</i>	2.43	2.27	2.71	7.24	13.11 bs (NH)	369	3.09	1 553 ^b
<i>IIIa</i>	2.31	6.17	8.27	6.78	11.57 bs (NH) 6.17 bs (NH ₂)	306	3.54	1 630 ^c
<i>IIIb</i>	2.27	6.16	2.30	6.77	11.05 bs (NH) 5.91 bs (NH ₂)	306	3.48	1 637 ^c
<i>IIIc</i>	2.22	2.01	8.26	6.75	11.21 bs (NH) 6.14 bs (NH ₂)	309	3.45	1 645 ^c
<i>IIId</i>	2.28	2.06	2.33	6.81	11.21 bs (NH) 5.93 bs (NH ₂)	309	3.46	1 639 ^c
<i>IVa</i>	2.43	6.74	9.13	7.02 ^d	9.13 s (H-3)	311 251	3.25 3.56	–
<i>IVb</i>	2.42	6.82	9.14	7.24 ^d	2.71 s (C-3–CH ₃)	308 244	3.20 3.57	–
<i>IVc</i>	2.44	6.77	2.53	7.20 ^d	9.16 s (H-3)	307 252	3.38 3.41	–
<i>IVd</i>	2.43	6.88	2.51	7.18 ^d	2.73 s (C-3–CH ₃)	309 246	3.30 3.57	–
<i>IVe</i>	2.31	2.24	8.94	7.17 ^d	9.18 s (H-3)	314 253	3.24 3.48	–
<i>IVf</i>	2.36	2.24	9.09	7.24 ^d	2.79 s (C-3–CH ₃)	309 246	3.30 3.56	–
<i>IVg</i>	2.34	2.27	2.53	7.16 ^d	8.96 s (H-3)	315 255	3.22 3.47	–
<i>IVh</i>	2.37	2.26	2.51	7.17 ^d	2.81 s (C-3–CH ₃)	314 248	3.25 3.54	–
<i>V</i>	2.40	2.25	2.65	7.01	3.51 s (N–CH ₃)	308	3.19	1 645 ^a
<i>VIa</i>	2.38	2.23	2.77	6.95	–	345	3.19	–
<i>VIb</i>	2.44	2.32	2.68	6.83	2.84 s (S–CH ₃)	333	2.78	–

^a ν(C=O); ^b ν(C=S); ^c ν(C=N); ^d H-11.

2,4,6,7-Tetramethyl-1,2-dihydrofuro[2',3':4,5]pyrrolo[1,2-*d*][1,2,4]triazin-1-one (V)

Triazinone *Id* (0.43 g, 2 mmol) was suspended in dry dimethylformamide (4 ml) and NaH (80%; 0.12 g, 4 mmol) was added under stirring. After 15 min, methyl iodide (0.57 g, 4 mmol) was added dropwise and stirring was continued for 1 h. The mixture was then poured into ice water, the precipitate was collected by filtration and crystallized.

1-Chloro-4,6,7-trimethylfuro[2',3':4,5]pyrrolo[1,2-*d*][1,2,4]triazine (VIa)

Triazinone *Id* (0.65 g, 3 mmol) in phosphorus oxychloride (3.5 ml) was refluxed for 3 h. The reaction mixture was poured on ice and neutralized with dilute aqueous ammonia solution. The precipitate was filtered off, washed with water and dried. The crude product was purified by chromatography on a silica gel column in chloroform.

1-Methylthio-4,6,7-trimethylfuro[2',3':4,5]pyrrolo[1,2-*d*][1,2,4]triazine (VIb)

Triazinethione *IId* (0.47 g, 2 mmol) was suspended in dry dimethylformamide (4 ml) and NaH (80%; 0.12 g, 4 mmol) was added under stirring. After 15 min, methyl iodide (0.57 g, 4 mmol) was added dropwise and stirring was continued for 1 h. The mixture was worked up as described above and the crude product was crystallized.

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