

# 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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Received 24 November 1998

2,3-Dimethylfuro[3,2-*b*]pyrrole-2-carbohydrazide was used in the synthesis of 2,3-dimethyl-7*H*-furo[2',3':4,5]pyrrolo[1,2-*d*][1,2,4]triazin-1-ones. These compounds with phosphorus(V) sulfide afforded 2,3-dimethylfuro[2',3':4,5]pyrrolo[1,2-*d*][1,2,4]triazin-1-thiones, which with hydrazine hydrate yielded 8-hydrazono-2,3-dimethylfuro[2',3':4,5]pyrrolo[1,2-*d*][1,2,4]triazines. By their reactions with orthoesters dimethylfuro[2',3':4,5]pyrrolo[1,2-*d*][1,2,4]triazolo[3,4-*f*][1,2,4]triazines were obtained.

There are seven possible fused 1,2,4-triazines with pyrrole ring; one bicyclic system could be produced from [*b*]-[*f*]-bonds that except [*e*]-bond could form three bicyclic systems [1, 2]. All of them except those on [*e*]-bond incorporate one nitrogen of the triazine ring to form the fused pyrrole ring and are characterized by the presence of that nitrogen as a bridgehead.

A wide variety of methods for the preparation of pyrrolo-fused 1,2,4-triazines [1, 3] have been classified according to starting compounds, *e.g.* syntheses by construction of the second heterocyclic ring on the existing heterocycle by intramolecular cyclization, intramolecular cycloadditions, and syntheses from acyclic precursors. A large number of [1,2,4]-triazines that are fused with one or more heterocycles are well known and wide variety of synthetic methods for their preparations are available [1–3].

We have been interested [4–12] in chemistry of the 1,2,4-triazine ring system fused with furo[3,2-*b*]pyrrole on [*d*]- and 1,2,4-triazole ring on [*f*]-bonds for several years.

The synthesis of the 2,3-dimethyl-4*H*-furo[3,2-*b*]pyrrole-5-carbohydrazide as starting compound for fusion of 1,2,4-triazine moiety was the subject of our previous paper [9]. Two reaction centres in the carbohydrazides *I* enable the formation of fused [1,2,4]triazine by reaction with triethyl orthoesters (Scheme 1). Triazinones *IIa*–*IIc* prepared by such a way were converted to the corresponding thiones *IIIa*–*IIIc* using phosphorus(V) sulfide in dry pyridine. Heating of the thiones *IIIa*–*IIIc* in hydrazine hydrate gave hydrazones *IVa*–*IVc* in moderate yield. The prolonged reaction time as well as the increasing of temperature did not influence the yield.

The broad utility of heterocyclic hydrazines as starting materials for the preparation of several fused

systems containing triazole and tetrazole nuclei has received increasing attention [9–13]. The hydrazone tautomeric form of *IVa*–*IVc* enables the fusion of [1,2,4]triazole ring by the reaction with triethyl orthoformate, triethyl orthoacetate or triethyl orthopropionate giving compounds *Va*–*Ve* (Table 1). *N,N*-Dimethylformamide was found to be a good solvent for this reaction.

The <sup>1</sup>H NMR spectra evidenced the structure of synthesized compounds (Table 2). Formation of 1,2,4-triazine derivative *IIa* from *I* was backed by C-5—C<sub>2</sub>H<sub>5</sub> proton signals. The replacement of oxygen in *IIa* by sulfur in *IIIa* resulted in a downfield shift of H-9 and N—H proton signals. For *IVa* an upfield shift of H-9 was observed in comparison with *IIa* and *IIIa* owing to the effect of hydrazono group at C-8 (Table 2). Formation of the title compounds *Va*–*Ve* was corroborated by the presence of C-3—H and C-3—R<sup>1</sup> substituents, respectively, as well as by the chemical shifts of C-6—H and C-6—R substituents.

## EXPERIMENTAL

Melting points were determined on a Kofler hot-stage apparatus. <sup>1</sup>H NMR spectra were recorded on a Tesla BS 587 spectrometer (80 MHz) in DMSO-*d*<sub>6</sub>. The IR spectra were taken on FTIR PU 9802/25 (Philips) spectrophotometer using KBr technique (0.5 mg in 300 mg of KBr). The syntheses of the compounds *IIb*, *IIc*, *IIIb*, *IIIc*, *IVb*, and *IVc* were described in [9].

### 7,8-Dihydro-5-ethyl-2,3-dimethylfuro[2',3':4,5]-pyrrolo[1,2-*d*][1,2,4]triazin-8-one (*IIa*)

A mixture of *I* (1.93 g; 10 mmol) and triethyl or-

**Table 1.** Characterization and Spectral Data of Synthesized Compounds<sup>a</sup>

Compound	Formula $M_r$	$w_i(\text{calc.})/\%$ $w_i(\text{found})/\%$			Yield/% M.p./°C	IR, $\bar{\nu}/\text{cm}^{-1}$
		C	H	N		
<i>IIa</i>	$\text{C}_{12}\text{H}_{13}\text{N}_3\text{O}_2$	62.33	5.67	18.17	88	3169, 3049,
	231.25	62.48	5.57	18.22	293—295	2920, 1643
<i>IIIa</i> <sup>b</sup>	$\text{C}_{12}\text{H}_{13}\text{N}_3\text{OS}$	58.28	5.30	16.99	92	3107, 2976,
	247.32	58.44	5.26	17.02	298—300	2920, 1265
<i>IVa</i>	$\text{C}_{12}\text{H}_{15}\text{N}_5\text{O}$	58.76	6.16	28.55	54	3351, 2921,
	245.28	58.72	6.12	28.48	241—243	1584, 1509
<i>Va</i>	$\text{C}_{13}\text{H}_{13}\text{N}_5\text{O}$	61.16	5.13	27.43	68	3108, 1591,
	255.28	61.12	5.08	27.47	256—260	1531, 1354
<i>Vb</i>	$\text{C}_{13}\text{H}_{13}\text{N}_5\text{O}$	61.16	5.13	27.43	66	3102, 1593,
	255.28	61.08	5.22	27.56	308—311	1520, 1399
<i>Vc</i>	$\text{C}_{14}\text{H}_{15}\text{N}_5\text{O}$	62.44	5.61	26.01	62	3069, 1586,
	269.30	62.38	5.66	26.20	300—303	1520, 1404
<i>Vd</i>	$\text{C}_{14}\text{H}_{15}\text{N}_5\text{O}$	62.44	5.61	26.01	59	3092, 1587,
	269.30	62.52	5.53	26.24	269—272	1532, 1416
<i>Ve</i>	$\text{C}_{15}\text{H}_{17}\text{N}_5\text{O}$	63.59	6.05	24.72	56	3075, 1588,
	283.33	63.49	6.00	24.84	244—247	1530, 1375

a) Compounds were crystallized from DMF. b)  $w_S(\text{calc.})$ : 12.97 %;  $w_S(\text{found})$ : 13.02 %.

**Table 2.**  $^1\text{H}$  NMR Data of Synthesized Compounds

Compound	$\delta$
<i>IIa</i>	1.28 (t, 3H, $\text{CH}_2\text{CH}_3$ ), 2.26 (s, 3H, C(3)- $\text{CH}_3$ ), 2.40 (s, 3H, C(2)- $\text{CH}_3$ ), 3.01 (q, 2H, $\text{CH}_2\text{CH}_3$ ), 7.04 (s, 1H, H-9), 11.12 (bs, 1H, NH)
<i>IIIa</i>	1.29 (t, 3H, $\text{CH}_2\text{CH}_3$ ), 2.27 (s, 3H, C(3)- $\text{CH}_3$ ), 2.42 (s, 3H, C(2)- $\text{CH}_3$ ), 3.06 (q, 2H, $\text{CH}_2\text{CH}_3$ ), 7.22 (s, 1H, H-9), 13.16 (bs, 1H, NH)
<i>IVa</i>	1.26 (t, 3H, $\text{CH}_2\text{CH}_3$ ), 2.06 (s, 3H, C(3)- $\text{CH}_3$ ), 2.28 (s, H, C(2)- $\text{CH}_3$ ), 2.73 (q, 2H, $\text{CH}_2\text{CH}_3$ ), 5.91 (s, 2H, $\text{NH}_2$ ), 6.80 (s, 1H, H-9), 11.21 (bs, 1H, NH)
<i>Va</i>	1.36 (t, 3H, $\text{CH}_2\text{CH}_3$ ), 2.32 (s, 3H, C(8)- $\text{CH}_3$ ), 2.39 (s, 3H, C(9)- $\text{CH}_3$ ), 2.99 (q, 2H, $\text{CH}_2\text{CH}_3$ ), 7.19 (s, 1H, H-11), 8.99 (s, 1H, H-3)
<i>Vb</i>	1.38 (t, 3H, $\text{CH}_2\text{CH}_3$ ), 2.33 (t, 3H, C(8)- $\text{CH}_3$ ), 2.43 (s, 3H, C(9)- $\text{CH}_3$ ), 3.23 (q, 2H, $\text{CH}_2\text{CH}_3$ ), 7.30 (s, 1H, H-11), 9.20 (s, 1H, H-6)
<i>Vc</i>	1.39 (t, 3H, $\text{CH}_2\text{CH}_3$ ), 2.33 (s, 3H, C(8)- $\text{CH}_3$ ), 2.42 (s, 3H, C(9)- $\text{CH}_3$ ), 2.57 (s, 3H, C(6)- $\text{CH}_3$ ), 3.23 (q, 2H, $\text{CH}_2\text{CH}_3$ ), 7.24 (s, 1H, H-11)
<i>Vd</i>	1.36 (t, 3H, $\text{CH}_2\text{CH}_3$ ), 2.30 (s, 3H, C(8)- $\text{CH}_3$ ), 2.41 (s, 3H, C(9)- $\text{CH}_3$ ), 2.85 (s, 3H, C(3)- $\text{CH}_3$ ), 2.98 (q, 2H, $\text{CH}_2\text{CH}_3$ ), 7.24 (s, 1H, H-11)
<i>Ve</i>	1.37 (t, 3H, $\text{CH}_2\text{CH}_3$ ), 1.39 (t, 3H, $\text{CH}_2\text{CH}_3$ ), 2.32 (t, 3H, C(8)- $\text{CH}_3$ ), 2.42 (s, 3H, C(9)- $\text{CH}_3$ ), 3.00 (q, 2H, $\text{CH}_2\text{CH}_3$ ), 3.22 (q, 2H, $\text{CH}_2\text{CH}_3$ ), 7.24 (s, 1H, H-11)

thiopropionate (2.11 g; 12 mmol) was refluxed in *N,N*-dimethylformamide (10 cm<sup>3</sup>) for 4 h. After cooling, the precipitate was filtered off.

#### 7,8-Dihydro-5-ethyl-2,3-dimethylfuro[2',3':4,5]-pyrrolo[1,2-*d*][1,2,4]triazine-8-thione (*IIIa*)

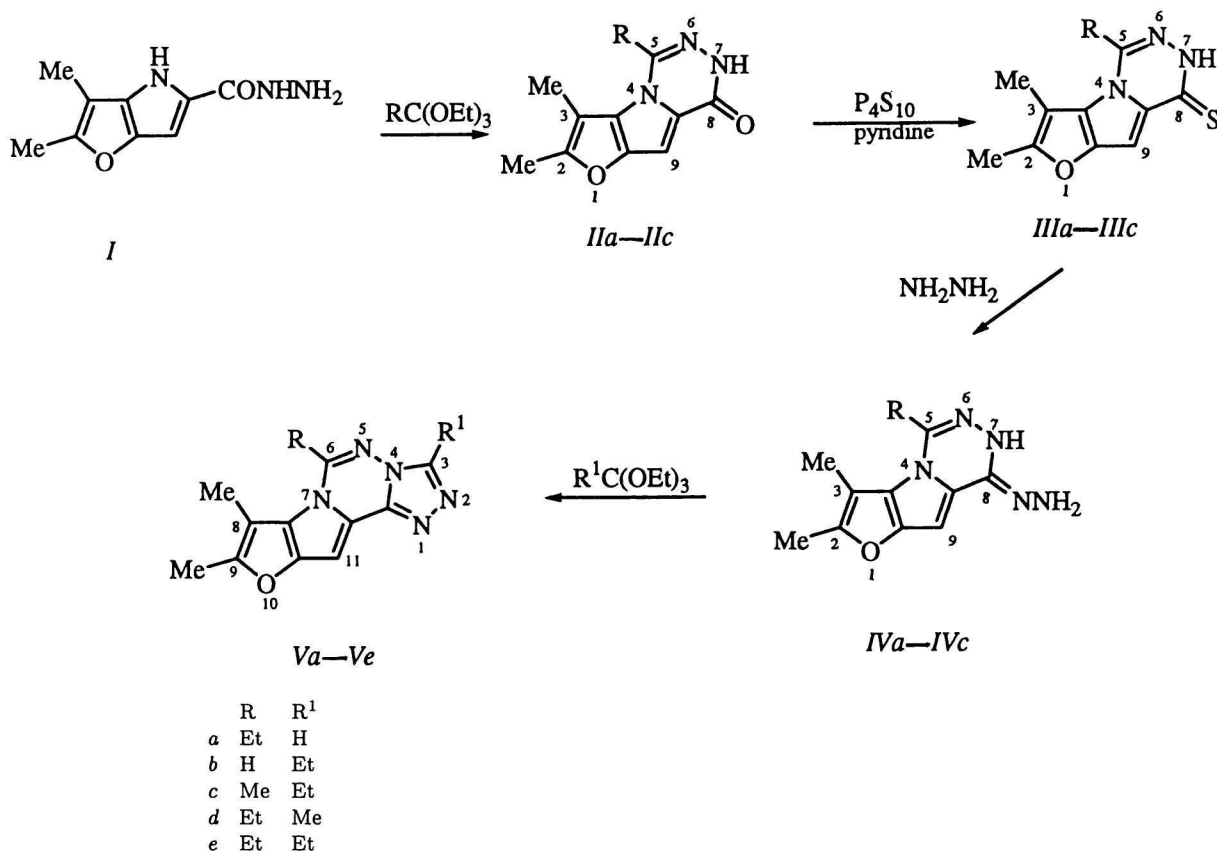
A mixture of compound *IIa* (2.31 g; 10 mmol) and phosphorus pentasulfide (2.3 g; 10 mmol) in dry pyridine (10 cm<sup>3</sup>) was refluxed with stirring for 4 h. The mixture was poured into hot water (70 cm<sup>3</sup>) and the precipitate was filtered off.

#### 7,8-Dihydro-5-ethyl-8-hydrazono-2,3-dimethylfuro[2',3':4,5]pyrrolo[1,2-*d*][1,2,4]triazine (*IVa*)

The compound *IIIa* (2.47 g; 10 mmol) and 97 % hydrazine hydrate were stirred and heated at 110°C for 6 h. After cooling, the precipitate was filtered off and washed with water.

#### 8,9-Dimethylfuro[2',3':4,5]pyrrolo[1,2-*d*][1,2,4]-triazolo[3,4-*f*][1,2,4]triazines (*Va*—*Ve*)

A mixture of hydrazone *IVa* (1.22 g; 5 mmol)



Scheme 1

and triethyl orthoformate, orthoacetate or orthopropionate or those of hydrazones IVb and IVc only with triethyl orthopropionate in dry dimethyl sulfoxide (5 cm<sup>3</sup>) was heated at 170°C for 3 h. After cooling, the crystals were filtered off and washed with ethanol.

**Acknowledgements.** This study was supported by the Grant Agency of the Slovak Ministry of Education (projects 1/4207/97 and 1/6249/99). The authors are indebted to O. Lakatošová for the measurement of IR spectra. The excellent assistance of J. Lehká is gratefully acknowledged.

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