Furan derivatives
CXCVI. Synthesis and reactions of 3,4-dichlorophenyl-substituted furocondensed derivatives

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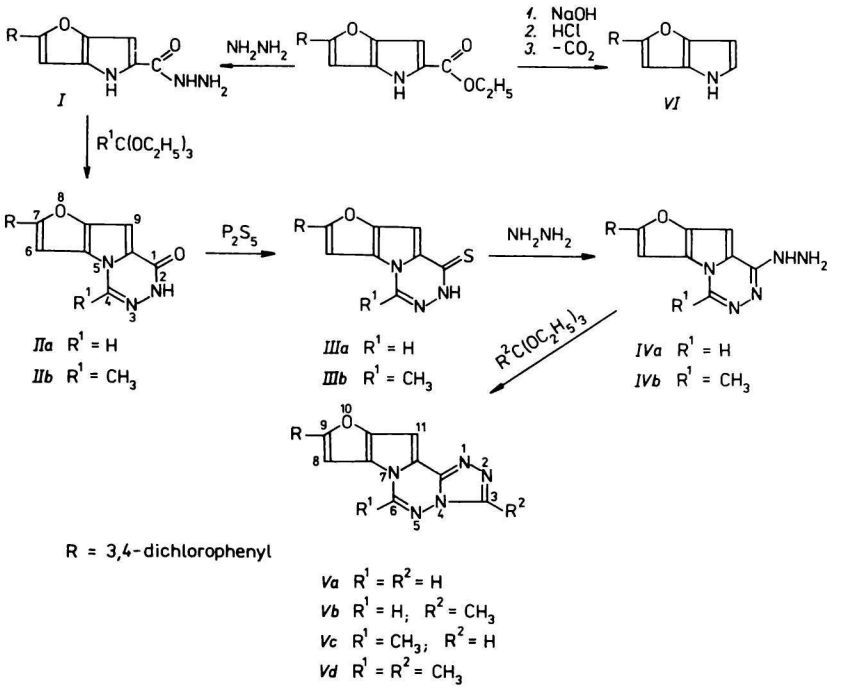
Received 22 July 1983

The preparation of new 9-(3,4-dichlorophenyl)-furo[2′,3′:4,5]pyrrolo-[1,2-*d*]-1,2,4-triazolo[3″,4″-*f*]-1,2,4-triazines is described. Reaction of 2-(3,4-dichlorophenyl)-4*H*-furo[3,2-*b*]pyrrole-2-carboxhydrazide with triethyl orthoformate or orthoacetate afforded 1,2-dihydro-7-(3,4-dichlorophenyl)-furo[2′,3′:4,5]pyrrolo[1,2-*d*]-1,2,4-triazine-1-one or its 4-methyl analogue giving with phosphorus pentasulfide thiones, reacting with hydrazine to the corresponding hydrazino derivatives. The last ones with triethyl orthoformate or orthoacetate underwent cyclization reactions.

Описано получение новых 9-(3,4-дихлорфенил)-фуро[2′,3′:4,5]пирроло[1,2-*d*]-1,2,4-триазоло-[3″,4″-*f*]-1,2,4-триазинов. Реакция 2-(3,4-дихлорфенил)-4*H*-фуро[3,2-*b*]пиррол-2-карбоксигидразида с триэтилортоформиатом или ортоацетатом вела к 1,2-дигидро-7-(3,4-дихлорфенил)-фуро[2′,3′:4,5]пирроло[1,2-*d*]-1,2,4-триазин-1-ону или его 4-метильному аналогу, дающими с пентасульфидом фосфора тионы, которые взаимодействуют с гидразином с образованием соответствующих гидразин-производных. Последние под действием триэтилортоформиата или ортоацетата подвергаются циклизации.

This paper describes study on the synthesis of new 9-(3,4-dichlorophenyl)-furo-[2′,3′:4,5]pyrrolo[1,2-*d*]-1,2,4-triazolo[3″,4″-*f*]-1,2,4-triazines. In the last few years, considerable attention has been drawn to the synthesis of condensed heterocyclic system derived from triazine [1—5], because some of these compounds are biologically effective [6, 7]. The present paper is a continuation of our preceding works [8, 9] on benzo-[*b*]furo analogues. The starting 2-(3,4-dichlorophenyl)-4*H*-furo[3,2-*b*]pyrrole-5-carboxhydrazide (*I*, Scheme 1), which was prepared from the corresponding ester [10], presents a compound with two reaction centres enabling to obtain with triethyl orthoformate or orthoacetate



Scheme 1

condensed systems with a fused 1,2,4-triazine ring. The thus obtained 7-(3,4-dichlorophenyl)-furo[2′,3′:4,5]pyrrolo[1,2-*d*]-1,2,4-triazine-1-ones (*II*) by reacting with phosphorus pentasulfide furnished thiones (*III*). Pyridine was found to be an excellent solvent. The successful reaction course was subject to a high purity of the solvent, high concentration of both reactants, and vigorous stirring.

7-(3,4-Dichlorophenyl)-furo[2′,3′:4,5]pyrrolo[1,2-*d*]-1,2,4-triazine-1-thiones (*III*) yield with hydrazine hydrate 7-(3,4-dichlorophenyl)-1-hydrazino[2′,3′:4,5]pyrrolo[1,2-*d*]-1,2,4-triazines (*IV*) having two new reaction centres. Reaction with triethyl orthoformate, or orthoacetate gave 9-(3,4-dichlorophenyl)-furo[2′,3′:4,5]pyrrolo[1,2-*d*]-1,2,4-triazolo[3″,4″-*f*]-1,2,4-triazines and 3-,6-methyl, as well as 3,6-dimethyl derivatives, respectively. The last reaction requires a water-free reaction medium, the suitable solvent being dimethylformamide (Scheme 1).

In our preceding paper we published [11,12] results obtained during the study of decarboxylation reaction of acids containing furo[3,2-*b*]pyrrole system. The method described was successfully applied to decarboxylation reaction of 2-(3,4-dichlorophenyl)-furo[3,2-*b*]pyrrole-5-carboxylic acid leading to 2-(3,4-dichlorophenyl)-4*H*-furo[3,2-*b*]pyrrole (*VI*). This reaction affords only low yield of the

desired product, which might be due to a low stability of the furo[3,2-*b*]pyrrole system. Compounds *II*—*V* are relatively insoluble, which might be explained by the presence of 3,4-dichlorophenyl residue in furo[3,2-*b*]pyrrole structure.

The IR spectra of *VI* revealed characteristic band $\tilde{\nu}(C=C_{arom})$ at about 1600 cm^{-1}. This band of acid and ester is overlapped by substantially more intense band of C=O group. The IR spectra of *Va*—*Vd* showed absorption bands of C=N vibrations of triazole and triazine rings at 1630 cm^{-1} and 1580 cm^{-1}, the band at the lower wavenumber being more intense. Bands of the same wavelengths were also found in the spectra of compound *IV*. These revealed $\tilde{\nu}$(C—H) at 2963—2995 cm^{-1} and $\tilde{\nu}(C-H)_{arom}$ at 3300—3060 cm^{-1}. Wavenumbers of N—H bonds in the spectra of compounds taken in KBr were at 3350—3160 cm^{-1}.

The UV spectra of all these systems display an intense absorption band at 328—389 nm ($\log\{\varepsilon\} = 3.21$—$3.63$) and a series of weaker bands at 200—300 nm, corresponding to $\pi \rightarrow \pi^*$ electronic transitions.

The ^{1}H NMR spectra evidenced the structure of these compounds. Proton signals of the starting carboxhydrazide *I* were attributed according to a characteristic interaction of the furopyrrole protons. Structure of 1,2,4-triazine derivatives *II*—*IV* was confirmed by the presence of C-4—H or C-4—CH_3 proton signals. Replacement of oxygen atom in *II* by sulfur atom in substance *III* results in a downfield shift of furopyrrole C-6—H, C-9—H proton signals by 0.15 ppm; the C-4—H proton chemical shift value was shifted by 0.41 ppm. The structure of compounds *V* was corroborated by the presence of C-3—H, or C-3—CH_3 proton signals analogously as reported [6, 13]. Long-range coupling constant between H-3 and H-6, H-3 and H-11 in all compounds investigated was found to be $J = 0.8$ Hz.

Experimental

The IR spectra were measured with Specord 71 IR (Zeiss, Jena), the electronic spectra with Specord UV VIS (Zeiss, Jena) spectrometers. Measuring range 200—800 nm, concentration 1×10^{-5}—5×10^{-5} mol dm^{-3} in methanol. The ^{1}H NMR spectra were recorded with a Tesla BS 487 C apparatus operating at 80 MHz. Hexamethyldisiloxane was used as internal reference.

2-(3,4-Dichlorophenyl)-4H-furo[3,2-b]pyrrole-5-carboxhydrazide (I)

80 % Hydrazine hydrate (3.5 g) was added to a solution of ethyl 2-(3,4-dichlorophenyl)-4*H*-furo[3,2-*b*]pyrrole-5-carboxylate (3.24 g; 0.01 mol) in ethanol (50 cm^3), the mixture was refluxed for 6 h and the separated crystals were filtered off after cooling. Yield 2.57 g (83 %), m.p. = 232 °C (ethanol). For $C_{13}H_9Cl_2N_3O_5$ ($M_r = 310.1$) w_i(calcu-

lated): 13.55 % N, 22.86 % Cl; w_i(found): 13.79 % N, 22.57 % Cl. IR spectrum (KBr) $\tilde{\nu}$/cm^{-1}: 1623 (C=O). UV spectrum (dioxan), λ_{max}/nm (log {ε}): 348 (3.63), 281 (2.94). ^{1}H NMR, δ_r/ppm (DMSO-d$_6$): 7.28 (1H, d, C-3—H), 6.84 (1H, dd, C-6—H), 7.67—7.99 (3H, m, H_{arom}), $J_{3,6}$ = 0.8 Hz.

1,2-Dihydro-7-(3,4-dichlorophenyl)-furo[2',3':4,5]pyrrolo-[1,2-d]-1,2,4-triazine-1-one (IIa)

Hydrazide (*I*) (3.1 g; 0.01 mol) and triethyl orthoformate (2 g; 0.012 mol) in dimethylformamide (8 cm^3) were refluxed for 4 h and the crystals were filtered off after cooling. Yield 1.7 g (53 %), m.p. = 296 °C (dimethylformamide). For $C_{14}H_7Cl_2N_3O_2$ (M_r = 320.1) w_i(calculated): 13.13 % N, 22.14 % Cl; w_i(found): 13.36 % N, 21.94 % Cl. IR spectrum (KBr), $\tilde{\nu}$/cm^{-1}: 1639 (C=O). UV spectrum (dioxan), λ_{max}/nm (log {ε}): 340 (3.56), 265 (2.88). ^{1}H NMR, δ_r/ppm (DMSO-d$_6$): 8.62 (1H, s, C-4—H), 7.11 (1H, d, C-9—H), 6.78 (1H, d, C-6—H), 7.69—7.99 (3H, m, H_{arom}), $J_{6,9}$ = 0.8 Hz.

1,2-Dihydro-7-(3,4-dichlorophenyl)-4-methylfuro[2',3': 4,5]-pyrrolo[1,2-d]-1,2,4-triazine-1-one (IIb)

The compound was obtained analogously. Yield 59 %, m.p. = 306 °C (dimethylformamide). For $C_{15}H_9Cl_2N_3O_2$ (M_r = 334.2) w_i(calculated): 12.57 % N, 21.22 % Cl; w_i(found): 12.85 % N, 20.96 % Cl. IR spectrum (KBr), $\tilde{\nu}$/cm^{-1}: 1639 (C=O). UV spectrum (dioxan), λ_{max}/nm (log {ε}): 341 (3.59), 269 (2.98). ^{1}H NMR, δ_r/ppm (DMSO-d$_6$): 7.09 (1H, d, C-9—H), 6.76 (1H, d, C-6—H), 7.73—8.08 (3H, m, H_{arom}), 3.06 (3H, s, C-4—CH_3), $J_{6,9}$ = 0.8 Hz.

1,2-Dihydro-7-(3,4-dichlorophenyl)-furo[2',3':4,5]-pyrrolo[1,2-d]-1,2,4-triazine-1-thione (IIIa)

A mixture of *IIa* (3.2 g; 0.01 mol) and phosphorus pentasulfide (4 g; 0.018 mol) was refluxed in pyridine (10 cm^3) for 6 h while stirred and poured into hot water. The separated precipitate was filtered off; yield 1.90 g (37 %), m.p. = 322 °C (dimethylformamide). For $C_{14}H_7Cl_2N_3OS$ (M_r = 336.2) w_i(calculated): 12.50 % N, 21.09 % Cl, 9.54 % S; w_i(found): 12.34 % N, 20.83 % Cl, 9.27 % S. IR spectrum (KBr), $\tilde{\nu}$/cm^{-1}: 1550 (C=S). UV spectrum (dioxan), λ_{max}/nm (log {ε}): 389 (3.42), 290 (3.22). ^{1}H NMR, δ_r/ppm (DMSO-d$_6$): 9.03 (1H, s, C-4—H), 7.27 (1H, d, C-9—H), 6.96 (1H, d, C-6—H), 7.63—8.01 (3H, m, H_{arom}), $J_{3,6}$ = 0.8 Hz.

1,2-Dihydro-7-(3,4-dichlorophenyl)-4-methylfuro[2',3': 4,5]-pyrrolo[1,2-d]-1,2,4-triazine-1-thione (IIIb)

This compound was prepared similarly as *IIIa*. Yield 69 %, m.p. = 328 °C (dimethylformamide). For $C_{18}H_9Cl_2N_3OS$ ($M_r = 350.2$) w_i(calculated): 12.00 % N, 20.25 % Cl, 9.16 % S; w_i(found): 12.16 % N, 19.92 % Cl, 8.95 % S. IR spectrum (KBr), $\bar{\nu}/cm^{-1}$: 1550 (C=S). UV spectrum (dioxan), λ_{max}/nm (log {ε}): 387 (3.40), 292 (3.29). ^{1}H NMR, δ_r/ppm (DMSO-d_6): 7.28 (1H, d, C-9—H), 6.98 (1H, d, C-4—H), 7.65—8.09 (3H, m, H_{arom}), $J_{3,6} = 0.8$ Hz.

7-(3,4-Dichlorophenyl)-1-hydrazinofuro[2',3': 4,5]-pyrrolo[1,2-d]-1,2,4-triazine (IVa)

Compound *IIIa* (3.36 g; 0.01 mol) and 94 % hydrazine hydrate (15 cm^3) were heated at 80 °C for 6 h, cooled, the separated substance was filtered off and washed with ether. Yield 1.97 g (59 %), m.p. = 318 °C (dioxan). For $C_{14}H_9Cl_2N_5O$ ($M_r = 334.1$) w_i(calculated): 20.96 % N, 21.22 % Cl; w_i(found): 20.70 % N, 21.04 % Cl. UV spectrum (dioxan), λ_{max}/nm (log {ε}): 358 (3.61), 272 (2.79). ^{1}H NMR, δ_r/ppm (DMSO-d_6): 8.31 (1H, s, C-4—H), 7.22 (1H, d, C-9—H), 7.55—7.93 (3H, m, H_{arom}), $J_{3,6} = 0.8$ Hz.

Similarly was prepared the next compound.

7-(3,4-Dichlorophenyl)-1-hydrazino-4-methylfuro[2',3': 4,5]-pyrrolo[1,2-d]-1,2,4-triazine (IVb)

Yield 64 %, m.p. = 316 °C (dioxan). For $C_{15}H_{11}Cl_2N_5O$ ($M_r = 348.2$) w_i(calculated): 20.11 % N, 20.36 % Cl; w_i(found): 19.95 % N, 20.02 % Cl. UV spectrum (dioxan), λ_{max}/nm (log {ε}): 362 (3.56), 276 (2.87). ^{1}H NMR, δ_r/ppm (DMSO-d_6): 7.2 (1H, d, C-9—H), 6.93 (1H, d, C-6—H), 7.53—7.94 (3H, m, H_{arom}), 3.07 (3H, s, C-4—CH_3), $J_{6,9} = 0.8$ Hz.

9-(3,4-Dichlorophenyl)-furo[2',3':4,5]pyrrolo[1,2-d]--1,2,4-triazolo[3",4"-f]-1,2,4-triazine (Va)

Compound *IVa* (3.34 g; 0.01 mol) and triethyl orthoformate (8 g; 0.056 mol) in dimethylformamide (40 cm^3) were refluxed for 4 h, cooled and the separated crystals were filtered off. Yield 62 %, m.p. = 339 °C (dimethylformamide). For $C_{15}H_7Cl_2NO$ ($M_r = 344.1$) w_i(calculated): 20.34 % N, 20.60 % Cl; w_i(found): 20.01 % N, 20.28 % Cl. UV spectrum (dioxan), λ_{max}/nm (log {ε}): 355 (3.28), 258 (2.79). ^{1}H NMR, δ_r/ppm (DMSO-d_6): 9.15 (1H, s, C-3—H), 9.13 (1H, s, C-6—H), 7.34 (1H, d, C-11—H), 7.07 (1H, d, C-8—H), 7.58—7.95 (3H, m, H_{arom}), $J_{8,11} = 0.8$ Hz.

The same procedure was employed for preparation of the following three substances:

9-(3,4-Dichlorophenyl)-3-methylfuro[2',3': 4,5]pyrrolo-[1,2-d]-1,2,4-triazolo[3",4"-f]-1,2,4-triazine (Vb)

Yield 54 %, m.p. = 345 °C (dimethylformamide). For $C_{16}H_9Cl_2N_5O$ ($M_r = 358.2$) w_i(calculated): 19.56 % N, 19.80 % Cl; w_i(found): 19.48 % N, 19.61 % Cl. ^{1}H NMR, δ_r/ppm (DMSO-d_6): 9.11 (1H, s, C-6—H), 7.36 (1H, d, C-11—H), 7.09 (1H, d, C-8—H), 3.00 (3H, s, C-3—CH_3), $J_{8,11} = 0.8$ Hz.

9-(3,4-Dichlorophenyl)-6-methylfuro[2',3': 4,5]pyrrolo-[1,2-d]-1,2,4-triazolo[3",4"-f]-1,2,4-triazine (Vc)

Yield 58 %, m.p. = 342 °C (dimethylformamide). For $C_{16}H_9Cl_2N_5O$ ($M_r = 358.2$) w_i(calculated): 19.56 % N, 19.80 % Cl; w_i(found): 19.48 % N, 19.60 % Cl. UV spectrum (dioxan), λ_{max}/nm (log {ε}): 353 (3.21), 264 (2.81). ^{1}H NMR, δ_r/ppm (DMSO-d_6): 9.14 (1H, s, C-3—H), 7.31 (1H, d, C-11—H), 7.13 (1H, d, C-8—H), 7.68—8.04 (3H, m, H_{arom}), 3.00 (3H, s, C-6—CH_3), $J_{8,11} = 0.8$ Hz.

9-(3,4-Dichlorophenyl)-3,6-dimethylfuro[2',3': 4,5]pyrrolo-[1,2-d]-1,2,4-triazolo[3",4"-f]-1,2,4-triazine (Vd)

Yield 52 %, m.p. = 349 °C (dimethylformamide). For $C_{17}H_{11}Cl_2N_5O$ ($M_r = 372.2$) w_i(calculated): 18.81 % N, 19.04 % Cl; w_i(found): 18.59 % N, 18.62 % Cl. UV spectrum (dioxan), λ_{max}/nm (log {ε}): 354 (3.24), 262 (2.87). ^{1}H NMR, δ_r/ppm (DMSO-d_6): 7.3 (1H, d, C-11—H), 7.08 (1H, d, C-8—H), 3.03 (3H, s, C-3—CH_3), 3.09 (3H, s, C-3—CH_3), $J_{8,11} = 0.8$ Hz.

2-(3,4-Dichlorophenyl)-4H-furo[3,2-b]pyrrole (VI)

The mixture of 2-(3,4-dichlorophenyl)-4*H*-furo[3,2-*b*]pyrrole-5-carboxylic acid (2.96 g; 0.01 mol), copper chromite barium promoted (0.64 g), and quinoline (20 cm^3) was stirred under nitrogen. The temperature was kept 170—175 °C until the evolution of carbon dioxide ceased. The mixture was then cooled to 0 °C, ether added and ethereal solution washed with 1 M-HCl until the quinoline was removed (consumption *ca.* 3000 cm^3), and water. The organic layer was dried with Na_2SO_4, and ether was distilled *in vacuo*. Yield 18 %, m.p. = 104 °C (ether—n-hexane volume ratio = 1 : 1). For $C_{12}H_7Cl_2NO$ ($M_r = 252.1$) w_i(calculated): 5.71 % N, 28.12 % Cl; w_i(found): 5.77 % N, 27.82 % Cl. UV spectrum (dioxan), λ_{max}/nm (log {ε}): 328 (3.52), 245 (2.81). ^{1}H NMR, δ_r/ppm (DMSO-d_6): 6.81 (1H, d, C-5—H), 6.68 (1H, d, C-3—H), 6.19 (1H, m, C-6—H), 7.25—7.80 (3H, m, H_{arom}), $J_{3,6} = 0.8$ Hz.

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Translated by A. Krutošíková