RESEARCH ON 2-ACYL-3-AMINOBENZOFURANS

II.* SYNTHESIS OF HETEROCYCLIC SYSTEMS FROM 2-ACYL-3-AMINOBENZOFURAN DERIVATIVES

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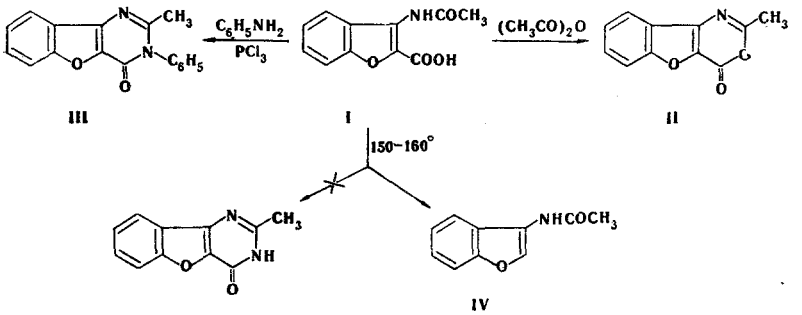
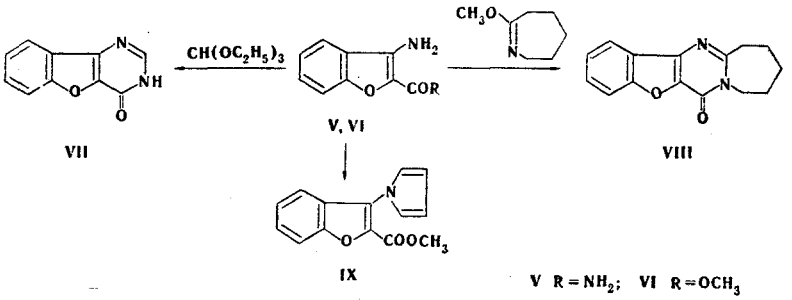
Various condensed heterocyclic systems were obtained from 2-acyl-3-aminobenzofuran derivatives.

Continuing our research on 2-acyl-3-aminobenzofuran derivatives, we have studied the possibility of the preparation of various condensed heterocyclic systems from them in order to make a further investigation of their chemical properties.

When 2-carboxy-3-acylaminobenzofuran (I), which we previously obtained in [1], was heated with acetic anhydride, 2-methyl-4-oxobenzofuro[3,2-d]-1,3-oxazine (II) was formed. Benzofuropyrimidine derivative III was obtained by reaction of I with aniline in the presence of phosphorus trichloride. In an attempt to obtain the pyrimidine derivative by heating I with acetamide at 150-160°C we isolated a decarboxylation product – 3-acetamidobenzofuran (IV) – which we have previously described in [1].



Starting I was isolated when the reaction temperature was lowered. Condensation of the amide (V) and methyl ester (VI) of 3-aminobenzofuran-2-carboxylic acid, respectively, with ethyl orthoformate in acetic anhydride and with caprolactam O-methyl ether gave the corresponding benzofuropyrimidine derivatives VII and VIII.



*See [1] for communication I.

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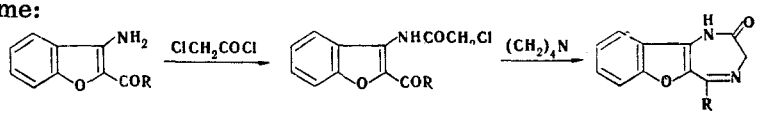
Methyl 3-(1-pyrryl)benzofuran-2-carboxylate (IX) is formed in good yield when VI is refluxed with 2,5-dimethoxytetrahydrofuran in acetic acid. The benzofuro-1,4-diazepine derivative (XII) was synthesized via the following scheme:



X XI XII

X-XII R = C_6H_5

The structures of the compounds obtained in this research were confirmed by IR and PMR spectroscopy.

EXPERIMENTAL

The IR spectra of KBr pellets of the compounds were recorded with a UR-10 spectrometer. The PMR spectra of $CDCl_3$ (II) and trifluoroacetic acid (XII) solutions were recorded with a JNM-4H-100 spectrometer with tetramethylsilane as the internal standard.

2-Methyl-4-oxobenzofuro[3,2-d]-1,3-oxazine (II). A 1.5-g (6.9 mmole) sample of I was refluxed with 4.5 ml of acetic anhydride, after which the mixture was cooled and the resulting crystals were removed by filtration and washed with cold heptane to give 1.2 g (87%) of II with mp 152° (from heptane). Found: C 65.7; H 3.7; N 6.5%. $C_{11}H_7NO_3$. Calculated: C 65.7; H 3.5; N 6.6%. IR spectrum: 1760 and 1800 cm^{-1} (CO). PMR spectrum ($CDCl_3$), ppm: 2.52 (singlet, CH_3) and 7.3-7.9 (aromatic H).

2-Methyl-3-phenyl-4-oxobenzofuro[3,2-d]pyrimidine (III). A solution of 0.45 g of phosphorus trichloride in 5 ml of toluene was added dropwise to a mixture of 1.9 g (9 mmole) of I and 0.85 g (9 mmole) of aniline in 150 ml of toluene, and the mixture was then refluxed for 3 h and allowed to stand overnight. The organic layer was washed with sodium carbonate solution and water, and the toluene was removed by distillation to give 1.3 g (54%) of III with mp 238-240° (from alcohol). Found: C 73.6; H 4.6%. $C_{17}H_{12}N_2O_2$. Calculated: C 73.9; H 4.8%. IR spectrum: 1710 cm^{-1} (C=O).

4-Oxobenzofuro[3,2-d]pyrimidine (VII). A mixture of 2.5 g (14 mmole) of 3-aminobenzofuran-2-carboxamide [1], 22 ml of ethyl orthoformate, and 23 ml of acetic anhydride was refluxed for 2 h, after which the solvent and excess acetic anhydride were removed by vacuum distillation, and the residue was recrystallized from methanol to give 0.4 g (15%) of VII with mp 297-300° (from methanol) (mp 301-304° [2]). Found: C 64.4; H 3.2%. $C_{10}H_6N_2O_2$. Calculated: C 64.5; H 3.2%.

2-Carbomethoxy-3-aminobenzofuran (VI). A 3.8-g (0.02 mole) sample of methyl o-cyanophenoxyacetate was dissolved in 20 ml of a 0.5 M solution of sodium methoxide in methanol, and the mixture was allowed to stand at room temperature for 24 h. The solvent was then evaporated, and the residue was washed with water to give 2.9 g (76%) of VI with mp 82-84° (from benzene). Found: C 63.0; H 4.6%. $C_{10}H_9NO_3$. Calculated: C 62.8; H 4.7%.

9-Oxo-3,4,5,6,7,8-hexahydrobenzofuro[3,2-d]pyrimido[1,2-*a*]azepine (VIII). A mixture of 2.2 g (11 mmole) of 2-carbomethoxy-3-aminobenzofuran and 2.6 g (0.011 mole) of caprolactam O-methyl ether was heated at 160° for 8 h, after which it was cooled, and the resulting oil crystallized slowly on standing. The crystals were removed by filtration and washed with alcohol to give 1 g (35%) of VIII with mp 163-165° (from alcohol). Found: C 70.7; H 5.8%. $C_{15}H_{14}N_2O_2$. Calculated: C 70.9; H 5.5%. IR spectrum: 1700 cm^{-1} (C=O).

2-Carbomethoxy-3-(1-pyrryl)benzofuran (IX). A mixture of 2 g (0.01 mole) of VI and 1.4 g (0.01 mole) of 2,5-dimethoxytetrahydrofuran was refluxed with 20 ml of glacial acetic acid for 1.5 h, after which the solution was evaporated to dryness, and the crystalline residue was washed with alcohol to give 1.7 g (68%) of IX with mp 102-103° (from alcohol). Found: C 69.5; H 4.6%. $C_{14}H_{11}NO_3$. Calculated: C 69.7; H 4.6%. IR spectrum: 1720 cm^{-1} (C=O).

2-Benzoyl-3-[N-(ω-chloroacetamido)]benzofuran (XI). A 2.8-g (25 mmole) sample of chloroacetyl chloride was added dropwise with stirring to a solution of 5.3 g (22 mmole) of 2-benzoyl-3-aminobenzofuran [1] in 100 ml of dry benzene, and the mixture was refluxed for 3.5 h. It was then cooled, and the solvent was removed by distillation to give 5.5 g (79%) of XI with mp 127-128° (from alcohol). Found: C 65.0; H 4.0%. $C_{17}H_{12}ClNO_3$. Calculated: C 65.1; H 4.0%.

5-Phenyl-3,6-dihydro-1,4-diazepino[6,5-b]benzofuran-2(1H)-one (XII). A mixture of 3 g (0.01 mole) of benzofuran XI and 1.4 g (0.01 mole) of urotropin in 50 ml of absolute alcohol was refluxed for 10 h, after which it was cooled and the resulting precipitate was removed by filtration to give 1.5 g of XII. The solvent was removed from the mother liquor by distillation to give another 0.5 g of product with mp 255° (dec., from alcohol). Found: C 73.8; H 4.7%. $C_{17}H_{12}N_2O_2$. Calculated: C 73.9; H 4.3%. IR spectrum, cm^{-1}: 1685 (C=O) and 3080 (N–H). PMR spectrum, ppm: 4.83 (doublet, CH_2) and 7.6-8.0 (aromatic H).

LITERATURE CITED

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2. K. Gewald and H. I. Jänsch, J. prakt. Chem., 315, 779 (1973).

ARYL 2-THIENYL SULFIDES AND ARYL 2-THIENYL SULFONES

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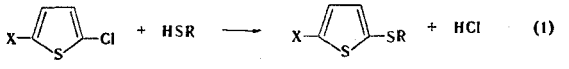
A method was developed for the synthesis of the previously unknown aryl 2-thienyl sulfides; the method is based on the reaction of 2-chlorothiophene and its derivatives with thiophenols in the gas phase at 450-500°C. The synthesized sulfides were oxidized to the corresponding aryl 2-thienyl sulfones, which were also previously unknown. 2,5-Dichlorothiophene reacts with excess thiophenol to give 2,5-bis(phenylthio)thiophene, which is oxidized to the corresponding disulfone.

Up until now, aryl thienyl sulfides have been unknown. We have developed a simple method for the synthesis of aryl 2-thienyl sulfides based on the reaction of thiophenols with 2-chlorothiophene and its derivatives at 450-500°C in an inert gas atmosphere.

2-Chlorothiophene and its derivatives (I) react with thiophenols in a flow system (in an empty quartz tube) to give the corresponding aryl 2-thienyl sulfides (II) in 30-50% yields.

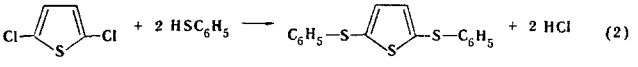


(1)

I II

X = H, C_2H_5, Cl, C_6H_5S; R = C_6H_5, 4-$CH_3C_6H_4$, 1-$C_{10}H_7$

2,5-Bis(phenylthio)thiophene (III) is simultaneously formed from 2,5-dichlorothiophene and thiophenol.



(2)

III

The yield of III increases as the ratio of RSH to RCl is raised (Table 1).

4-Thiocresol does not undergo reaction (2), and 1-thionaphthol does not react at all with 2,5-dichlorothiophene.

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