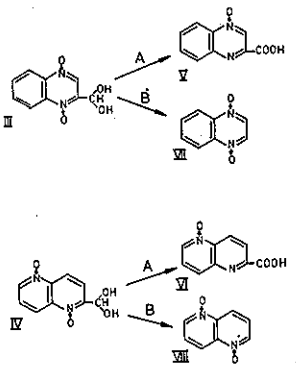

action A to form 2-carboxyquinoxaline 4-N-oxide (V) or 2-carboxy-1,5-naphthyridine 5-N-oxide (VI) respectively and reaction B to form di-N-oxides of unsubstituted quinoxaline or 1,5-naphthyridine (VII and VII).

Quinoxaline-2-aldehyde isolated in the form of a carbonyl compound mainly undergoes reaction B changing to quinoxaline-di-N-oxide.

The optimum pH ranges for reactions A and B were investigated and a possibility of these reactions proceeding simultaneously shown.

The differences in the behavior of quinoxaline and 1,5-naphthyridine di-N-oxides derivatives were revealed.

The transformations of diethylacetal quinoxaline-2-aldehyde di-N-oxide proceeding in the presence of alkaline reagents were studied.

REFERENCES

1) A. S. Elina, I. S. Musatova, G. P. Syrova „Chemistry of the Heterocyclic Compounds", 1972, 9, 1275—1280.

PO 44

POLAROGRAPHIC REDUCTION OF ISOXAZOLES AND THEIR AZAANALOGS IN ANHYDROUS DIMETHYLFORMAMIDE

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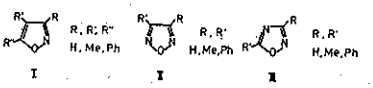
The polarographic behavior of substituted isoxazoles (I) and their azaanalogs (II, III)



was studied in anhydrous dimethylformamide against the background of quarternary ammonium salts. It was shown that the phenyl substituted compounds I possess polarographic activity and the first irreversible two-electron wave corresponds to N-O-bond rupture to form the dianion which is capable of being reduced only in a more negative potential range. In an accessible potential range, four-electron reduction of the derivatives I is likely, with the $E_{1/2}$ value of the second wave depending on the cation nature of the background. Complete saturation of multiple bonds after N-O-bond rupture requiring six electrons can be realized in excess proton donors(benzoic acid).

While reducing the derivatives II and III the first stage also involves two-electron irreversible rupture of N-O-bond. Isoxazole analogs are reduced substantially easier in all cases. The reduction depth of oxadiazoles studied is determined by their structure and protonation rate of intervening particles formed. In the accessible potential region oxadiazol III(R = R' = Me) is capable of accepting two electrons, oxadiazoles II(R = R' = Me), III(R = R' = Ph), III(R = Ph, R' = Me) and III(R = Me, R' = Ph) — four electrons. Complete molecular reduction involving eigth electrons takes place only in the case of oxadiazole II(R = R' = Ph).

In the series of isoxazole I and oxadiazole II and III derivatives greater conjugation of the phenyl ring in the fifth position facilitates the reduction as compared to the corresponding 3-substituted compounds. The replacement of methyl substituents by phenyl ones in disubstituted oxadiazoles III leads to facilitating the reduction/$\Delta E^{1/2}$ of the first waves — 970 mV whereas the analogous effect for oxadiazoles II is 540 mV which is determined by partially broken conjugation due to space interaction of benzene rings in case of 3,4-diphenyl-1,2,5-oxadiazole.

PO 45

SYNTHESIS AND REACTIONS OF ARYLOXYFURAN DERIVATIVES

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A general method of preparing aryloxyfuran derivatives has been developed.

The aryloxyfuron formulation according to the method of Vilsmeier yields 5-aryloxyfurfurals, which were further transformed to 5-aryloxy-2-methylfurans by the Kishner-Wolff reduction.

The corresponding amides were obtained on the basis of the aryl esters of 5-aryloxypyromucic acids and then turned into 2-aminomethyl-5-aryloxyfyrans by the reduction with $LiAlH_4$.

The aryl esters of aryloxypyromucic acids reacted with hydrazine-hydrate to give aryloxypyromucic hydrazides, which formed isopropylidene derivatives by the reaction with acetone.

The hermistatic activity of the compounds synthesized has been investigated

PO 46

THE REACTION OF ARYL- AND ARYLOXYFURANS WITH DIMETHYL ACETYLENEDICARBOXYLATE

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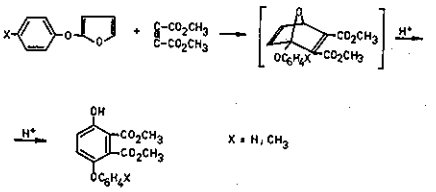
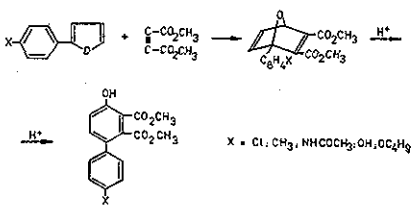
The diene synthesis of aryl- and aryloxyfurans with dimethyl acetylenedicarboxylate has been studied.

The interaction of arylfurans with acetylenedicarboxylic ester yields adducts, which undergo aromatization leading to the esters of hydroxybiphenyldicarboxylic acids.



The presence of electron-donating substituents in the benzene ring of arylfuran favourably affects the above mentioned reaction.

Aryloxyfurans undergo the Diels-Alder reaction with dimethyl acetylenedicarboxylate, giving adducts, which can be transformed by the action of acids to 1-hydroxy-4-phenyloxydicarboxylic acids.



Thus, the synthesis of not readily available esters of hydroxycarboxylic acids of the biphenyl and diphenyloxide series has been realized.

PO 47

SYNTHESIS AND TRANSFORMATION OF THE DERIVATIVES OF PYRROLO(3,2-d)PYRIMIDINE-7-ALDEHYDE

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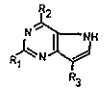
The method of preparing pyrrolo(3,2-d)pyrimidine derivatives based on using of Vilsmeier reagent for pyrrolo cyclization in 5-amino-6-methylpyrimidines, has been found. 4-oxopyrrolo(3,2-d)pyrimidine-7-aldehyde (I), prepared in such a way from 4-oxo-5-amino-6-methylpyrimidine, was transformed to 4-chlorpyrrolo(3,2-d)pyrimidine (II).

In similar conditions during the cyclization of 2-phenyl-4-oxo-5-amino-6-methylpyrimidine the substitution of the oxo-group by chlorine to form 2-phenyl-4-chlorpyrrolo(3,2-d)pyrimidine-7-aldehyde (III) simultaneously proceeds. The nitril (IV) from the aldehyde (III) has been received.

The reaction of the nucleophilic substitution of the chlorine atom in compounds II and IV was investigated.



I. R_1 = H, R_2 = O, R_3 = CHO

II. R_1 = R_3 = H, R_2 = Cl

III. R_1 = C_6H_5, R_2 = Cl, R_3 = CHO

IV. R_1 = C_6H_5, R_2 = Cl, R_3 = C≡N

PO 48

NOVEL 2-BENZENESULFONAMIDO-4-AMINO-5-BENZYLPYRIMIDINES AND SOME OF THEIR REACTIONS

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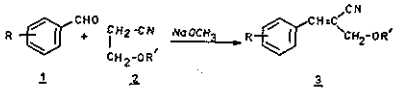
In the EGYT *Pharmacochemical Works* purposeful research has been continuing for years on the field of chemotherapy. One of these important trends is to produce compounds having antibacterial activity. It is well-known, that in the therapy Trimethoprim (2,4-diamino-5-[3',4',5'-trimethoxybenzyl]-pyrimidine) shows synergism with sulfonamides.

We wanted to synthesize modified pyrimidine compounds including the sulfonamide-part on the pyrimidine-ring.

In the present work, the synthesis and several reactions of the new pyrimidine derivatives (**5—7**) are studied. Thus the suitable compounds were produced by the following synthesis route:



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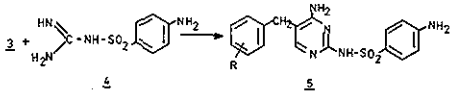
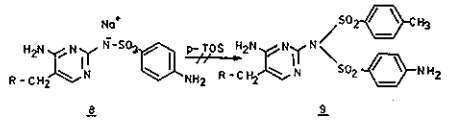


3 4 5

5 R = 3,4,5-MeO; **6** R = 3,4-MeO; **7** R = 3,4-methylenedioxy R' = alkyl

Substituted benzaldehydes (**1**) were condensed with 3-ethoxypropionitril (**2**) in presence of sodium-methoxide during 12 hours, at reflux temperature and gave 2-(subst.-benzylidene)-3-methoxypropionitril (**3**). **3** was cyclized with sulfoguanidin (**4**) in presence of sodium-methoxide, in an autoclave during 16 hours at 100 °C. In this way we obtained N1-(2-(4-amino-5-subst.benzyl)-pyrimidil)-p-aminobenzenesulfonamid (**5—7**).

The proton-activity of sulfonamid-NH- of our materials was studied. After preparing sodium salts of **5,6,7**, we live them reacted with p-toluenesulfonyl chloride (p-TOS) in organic solvents.



8 9

8a R = 3,4,5-trimethoxyphenyl; **8b** R = 3,4-dimethoxyphenyl; **8c** R = 3,4-methylenedioxyphenyl;

But the received sodium-salts (**8a,b,c**) were not able to react with p-TOS. The sodium-salts of **5,6,7** reacted *in situ with* acylation agents and so acyl-derivatives were prepared with lower yield enough.

The demethylation of Trimethoprim by 48% Hydrogen bromid is known from the literature (U.S.P. 3,684,810). This method was applied at **5—7** but we prepared only the starting materials.

The bacteriostatic mechanisms of sulfonamido-Trimethoprim combinations were examined. (Tóth-Martinez, B. Biochem. Pharm. Vol. 26. p.p. 451—456.) Our compounds have antibacterial activity and there are pure competitive inhibitors against p-aminobenzoylglutamate and quasi-irreversible competitive inhibitors against dihydrofolatreductase.