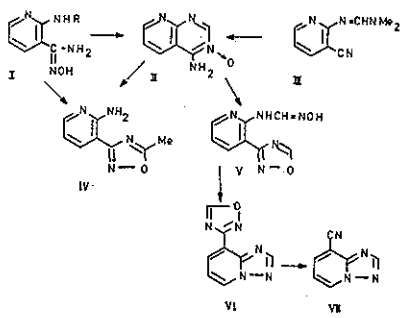

The structures of compounds follow from analytical, spectroscopic and X-ray data. Some other transformations, such as reduction, deoxygenation and cyclizations will be presented.

LE II 12

VILSMEIER-HAACK REACTION OF 5-AMINO-PYRAZOLE DERIVATIVES

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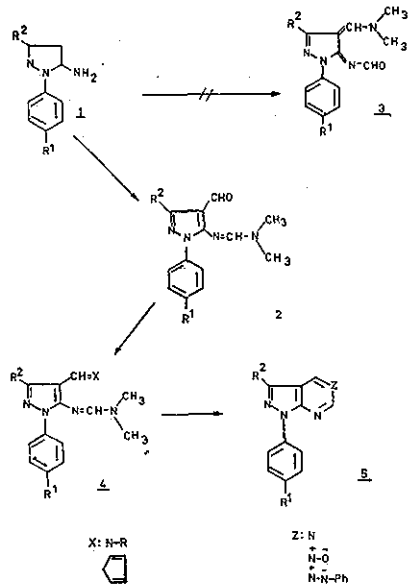
Vilsmeier-Haack reaction of some 1-substituted 5-amino-pyrazoles (1) has been reported by several groups of authors. The products of the reaction have been characterised either by structure 2 (1,2) or 3 (3).

In order to elucidate the above mentioned structural problem we reinvestigated the reactions of 1-substituted and 1,3-disubstituted 5-amino-pyrazoles with dimethyl-formamide — phosphoryl-chloride reagent.

We have found that reactions of 1 and DMF-$POCl_3$ result in the formation of compounds 2 only, independently of the character of R_1 and R_2 substituents. No protection of the 5-amino group could be achieved by acylation. Vilsmeier-Haack reaction of 5-acylaminopyrazoles is accompanied by acyl-splitting and also in these cases compounds 2 are obtained.



Structure 2 was proved by the spectral and chemical properties of the products. The formyl group of 2 could be selectively condensed with nitrogen bases (i. e. phenyl-hydrazine etc.) and CH- acid compounds, leading to pyrazole derivatives 4. Certain representatives of compounds 4 (X = NR) could be cyclized and pyrazolo[3,4-d]pyrimidines (5) were obtained. In some cases spontaneous second-step cyclisation was observed.

The mechanism of the reactions mentioned above will also be discussed.

REFERENCES

1) US Patents 3,544,585; 3,686,171; C. A. 74 76414 (1971); 77 140058 (1972)
2) Ger. Patent 2,008,677; C. A. 76 3850 (1972)
3) Kvitko, I. J., Loginova, T. M.: Zh. Obshch. Khim. 10 1088 (1974)

LE II 13

SYNTHESIS OF PYRROLO[3,2-d]SELENAZOLE AND PYRROLO [3,2-d]THIAZOLE. TWO NOVEL HETEROCYCLES

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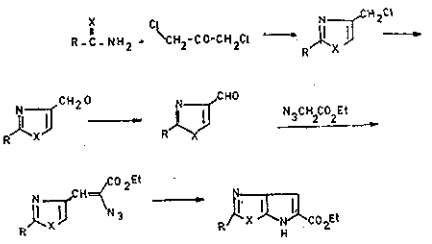
As a part of a program designed to expand the chemistry of fused pyrrole heterocycles, a method was developed for the synthesis of pyrrolo [3,2-d]selenazoles and pyrrolo [3,2-d]thiazoles as it is shown bellow.



R = H, CH_3, C_6H_5; X = S
R = C_6H_5, p-ClC_6H_4-, p-BrC_6H_4-, p-MeC_6H_4-, p-$CH_3OC_6H_4$-, C_4H_3S-; X = Se

The chemistry and structure elucidation of these new heterocycles will be discussed.

LE II 14

THE SYNTHESIS OF 3-SUBSTITUTED AND 3,5-DISUBSTITUTED DERIVATIVES OF 1,2,4-TRIAZOLE

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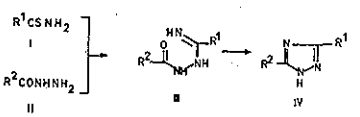
Thermal condensation of thioamides I with acylhydrazides II affords N^1-acylamidrazones III which cyclize to triazoles IV on heating above their melting point. The reaction can be carried out in one step, without the isolation of the intermediate III.



The extent of use of this reaction is illustrated by the preparation of derivatives in which the substituents R^1 and R^2 are hydrogen, methyl, phenyl and ethoxycarbonyl group. The methyl and the phenyl groups can be introduced starting from any of the parent compounds I or II. For monosubstituted derivatives (IV, R^2 = H) formylhydrazine (II, R^2 = H) serves as starting compound; as for the derivatives of 1,2,4-triazole-3-carboxylic acid their preparation from the esters of thioxamic acid (I, R^1 = = COOR) is more convenient because the hydrazide of methoxatic acid (II, R^2 = $COOC_2H_5$) gives low yields.

LE II 15

SYNTHESIS OF 1,3-SELENAZOLIDINE-2-THIONES AND 1,3,5--OXADIAZINE-4-THIONES FROM ISOTHIOCYANATES

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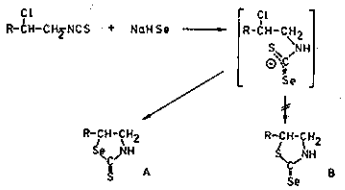
By using the reaction of 2-halogen-ethyl isothyocyanates with ethanolic solution of NaHSe, a simple universal method was elaborated for the preparation of 1,3-selenazolidine-2-thiones. The intermediary selenothiocarbamate is able to undergo intramolecular substitution to give either selenazolidine-2-thione A or thiazolidine-2-selenone B.

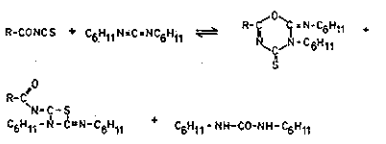


R = H, CH_3, C_6H_5, 4-CH_3-C_6H_4, 4-Cl-C_6H_4

Scheme 1

The structure of the products obtained was proved on the basis of the Raman, IR and mass spectra of selenazolidine-2-thiones and their sulphur analogs, i. e. thiazolidine-2-thiones. These compound were prepared in an analogous way by using the reaction of 2-halogen-ethyl isothiocyanates with NaHS.

The 4-substituded benzoyl isothiocyanates react with dicyclohexylcarbodiimide in [4+2] cycloaddition to yield 1,3,5-oxadiazine-4-thiones. In case of benzoyl isothiocyanate also the [2+2] cycloadduct, i. e. 2-benzoylimino-3-cyclohexyl-4-cyclohexylimino-1,3-thiazetidine, is to be isolated from the reaction mixture after a shorter reaction time.



R = C_6H_5, 4-CH_3-C_6H_4, 4-Cl-C_6H_4, 4-C_6H_5-C_6H_4

Scheme 2

The structure of both cycloadducts was proved by IR and mass spectra.

However, benzoyl isothiocyanates react with diphenylcarbodiimide to give the corresponding substituted benzoylanilides.

LE II 16

PRODUCT OF A REACTION OF 4-CHLORONITROBENZENE WITH 2-CHLOROPHENYLACETONITRILE IN METHANOLIC SOLUTIONS OF ALKALI HYDROXIDES

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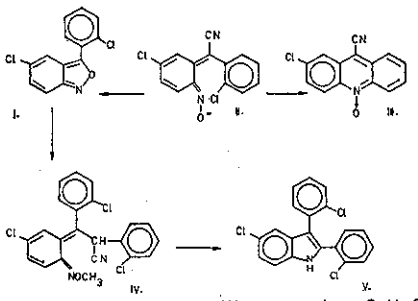
Whereas the reaction of 4-chloronitrobenzene with phenylacetonitrile in a methanolic solution of NaOH (or KOH) at 20—30 °C and in the presence of a small amount of water affords almost exclusively 5-chloro-2,1-benzisoxazole and thus opens a preparatively advantageous approach to 2-amino-5--chlorobenzophenone and the psychotropic 5-phenyl-7-chloro--1,3-dihydro-1,4-benzodiazepin-2-ones, a similar reaction of 4--chloronitrobenzene with 2-chlorophenylacetonitrile has not yet been described. It has ben established now that this reaction leads to a mixture of products from which five crystalline compounds were isolated. Their empirical formulae were determined by analyses and mass spectra and the products were further characeterized by the ^{1}H-NMR, UV and IR spectra, as well as by some chemical reactions.

The desired 2,1-benzisoxazole I ($C_{13}H_7Cl_2NO$) was obtained in a yield of only 12%. It is apparently formed by cyclization of the non-isolated alkaline salt of the oxime II, representing a type postulated in analogous reactions as the primary product. Reduction of compound I with iron and acetic acid yielded 2--amino-5,2'-dichlorobenzophenone.

A yellow substance $C_{14}H_7ClN_2O$ was isolated in a yield of 20%. According to the spectra, it is a condensed aromatic compound containing the N-oxide and nitrile groups. Structure III was assigned which is compatible with the hypothesis that this compound is also formed by cyclization of the intermediate II. Its reduction with $LiAlH_4$ resulted in a mixture of 2-chloro-9-(aminomethyl)acridan and 2-chloroacridan. The alkaline hydrolysis of compound III gave also two products identified as 2-chloroacridine-9-carboxamide (containing the corresponding N-oxide) and 2-chloro-10-hydroxyacridanone.



A further isolated compound (15%) corresponds to $C_{22}H_{15}Cl_3N_2O$. The spectra indicate the presence of OCH_3, C = N — O (oxime) and CN groups. As the most probable, the structure IV is considered and it is assumed that the compound is formed from I by the action of methoxide anion and a further molecule of 2-chlorophenylacetonitrile.

The main product (25%) is a compound $C_{20}H_{12}Cl_3N$ for which the structure of the indole derivative V was suggested on the basis of spectral evidence and confirmed by synthesis: it was obtained by Fischer reaction from 4-chlorophenylhydrazone of 2,2'-dichlorodeoxybenzoin. In our reaction, it could be formed via compound IV.

A minor product (5%) $C_{13}H_8ClNO_3$ was identified by spectra to be 2-chloro-4'-nitrobenzophenone.