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A NEW ROUTE TO THE SYNTHESIS OF IMIDAZO [4,5-c] PYRAZOLES

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Summary: A new synthesis of imidazo [4,5-c] pyrazoles, obtained through cyclisation of 4-nitroso-5-alkylamino-pyrazoles, is described.

During our research on the pharmacological and antifungal activity of pyrazole derivatives,[1] we became interested in the synthesis of imidazo[4,5-c] pyrazoles (**1**).

The only reported synthetic approaches to such compounds are: a) the Curtius rearrangement followed by cyclisation of 5-amino-4-pyrazolecarbonyl azides,[2a] b) the cyclisation of 4-nitro-5-benzylamino-pyrazoles,[2b] c) the reaction of 4,5-diamino-pyrazoles with carbon disulfide[2c] and d) the cycloaddition of diazomethane on to the C-C double bond of 5-nitroimidazoles.[2d]

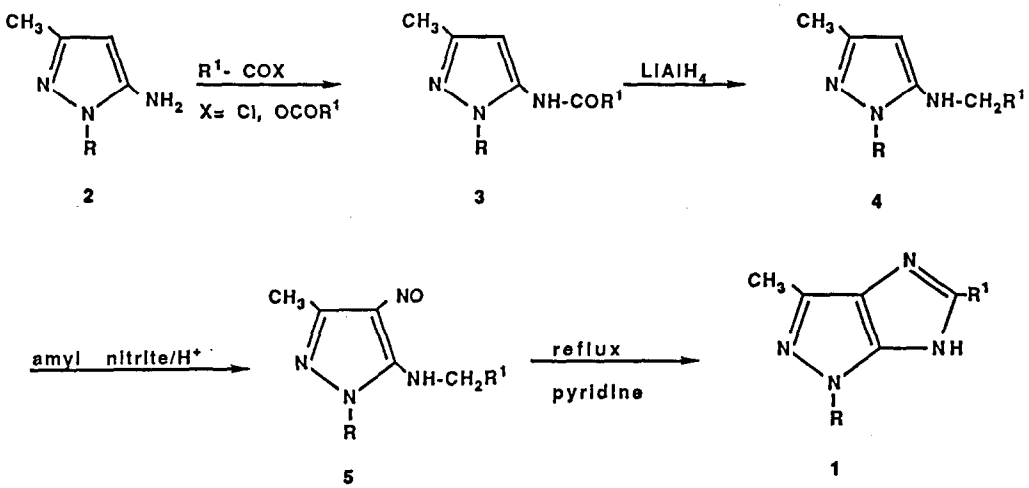
All these reactions have applications limited only to specific derivatives. Thus we decided to investigate a new route of general application for the synthesis of the target compounds (**1**).

On the basis of previously reported studies on the formation of the imidazole ring from α-alkylimino oximes[3] or from α-alkylamino nitroso derivatives,[4] we investigated the new synthetic route, reported in the scheme.

The 5-amino-pyrazoles (**2**) were reacted with benzoyl chloride or with acetic anhydride to give the 5-acylamino-pyrazoles (**3**). The reduction of compounds (**3**) with $LiAlH_4$ afforded the corresponding 5-alkylamino-pyrazoles (**4**). The nitrosation of compounds (**4**) with amyl nitrite gave the 4-nitroso-5-alkyl amino-pyrazoles (**5**). All these reactions provided the pertinent products in good yields.

On heating under reflux in pyridine (10-90 min.) compounds (**5**) cyclized to the expected imidazo[4,5-c]pyrazoles (**1**). Compounds (**1**) were isolated as crystal-

line pure products (yields from 58 to 88%). The spectral data (i.r., ^{1}H-n.m.r.) of compounds (1-5) agree with the reported structures.



2 3 4 5 1

R= CH_3, C_6H_5, 2-ClC_6H_4, 3-ClC_6H_4, 4-ClC_6H_4, 2-FC_6H_4, 3-FC_6H_4, 4-FC_6H_4

R'= CH_3, C_6H_5

Our method, with respect to the previously reported ones, provides a convenient entry into a variety of imidazo[4,5-c]pyrazoles substituted in 1,3,5-positions.

The biological activities of compounds (1) are under investigation.

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