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RING TRANSFORMATIONS OF HETEROCYCLES;
A SYNTHETIC TOOL

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In the last decade a vast number of papers have appeared dealing with one of the most fascinating properties of heterocycles i. e. their ability to undergo ring interconversions. The ring interconversions are found to be of synthetic interest since compounds can be prepared by this method, which otherwise are difficult to obtain or even inaccessible.

Our primary interest in this field was concerned with ring transformations which take place by treatment of halogeno derivatives of azines, diazines and triazines with the strong nucleophile potassium amide in liquid ammonia. A review on these reactions has appeared.¹

In this lecture new ring transformations of pyrimidines with different nucleophilic reagents — carbanions, liquid ammonia, amidines, hydrazine and hydroxylamine are presented. We have observed that in order to achieve these ring transformations the heterocyclic ring has to be activated for nucleophilic attack by quaternisation. Therefore as substrates the N-methylpyrimidinium salts, the pyrimidine N-oxides and the N-aminopyrimidinium salts (a new class of compounds) are chosen.

First the conversion of N-methylpyrimidinium salt with pyridines, pyrazoles and isoxazoles will be discussed and the results of ¹H- and ¹³C-NMR spectroscopic studies and ¹⁵N-studies on the mechanism of these conversions.

Special attention will be paid to the conversions of N-methylpyrimidinium salts into substituted pyrimidines by reaction with liquid ammonia and amidines, since these conversions represent interesting examples of a so-called degenerate (ipso) ring transformation.

The reaction of pyrimidine N-oxides with liquid ammonia as well as hydroxylamine — both reactions lead to different isoxazole derivatives — is also discussed in detail; special attention will be given to a mechanistic study on this ring contraction with ¹⁵N-labelled compounds.

Finally a discussion will come up on to the reaction of N-aminopyrimidinium salts with hydrazine (yielding pyrazoles), liquid ammonia (yielding pyrazoles and 1,3-dipolar cycloaddition dimers) and hydroxylamine (giving pyrimidine N-oxides). The last-mentioned reaction is of preparative interest, since it presents the first non-oxidative method for the synthesis of pyrimidine N-oxides.

Attempts will be described to correlate the chemical data on reactivity, especially the positions of attack of the nucleophile in these three different pyrimidines with Frontier Orbital calculations.

1) H. C. van der Plas — Ring Transformations of Heterocycles, vol. 1 and 2, Academic Press, London and New York.
H. C. van der Plas, — Lectures in Heterocyclic Chemistry, vol. II, s. 89.

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ELECTRONIC EFFECTS IN THE HETEROCYCLIC
ORGANOSILICON AMINES

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Organosilicon substituents are known to exert a more distinct positive inductive effect as compared to their isostructural organic substituents, which is due to the fact that the silicon is less electronegative (1.8) than the carbon (2.5). Thus, the σ^+ value for trimethylsilyl group is -0.78 , whereas for t-butyl group it is -0.30 . The ρ constant estimated for trimethylsilylmethyl group on the basis of the inductive effect attenuation equation was -0.26 which is in good agreement with the experimental value calculated from trimethylsilylacetic acid ionization constant, its methyl ester hydrolysis rate constant and the Si-H bond stretching frequency in dimethyl(trimethylsilylmethyl)silane.

We have discovered, however, that some physical and chemical properties of heterocyclic organosilicon amines cannot be explained by the observed inductive effect of trimethylsilyl group and the inductive effect of the substituents in the compounds shows anomalous attenuation along the chain of methylene groups.

To study transmission of electronic effects in organosilicon compounds the corresponding organosilicon derivatives in the pyrrolidine, piperidine and perhydroazepine series were synthesized along with their organic analogues, and physico-chemical properties of the compounds obtained were put to trial.

Organosilicon derivatives of pyrrolidine, piperidine and perhydroazepine which have a nitrogen atom bonded to silicon were synthesized through trialkylchlorosilane interaction with heterocyclic amines.

Organosilicon amines containing amino groups in the α - or γ -position with respect to the carbon atom were obtained in the reaction between trimethyl-, dimethylethoxy-, methyl-diethoxy- and triethoxy(chloromethyl)silanes and the corresponding (3-chloropropyl)silanes with heterocyclic amines. The γ -organosilicon amines were also prepared by hydrosilylation of 1-heteroalkenes with trialkyl- and triethoxysilanes in the presence of 0.1 M chloroplatinic acid solution in propanol-2.

Heterocyclic organosilicon β -amines were obtained by the addition of pyrrolidine, piperidine and perhydroazepine to trimethylvinylsilane in the presence of lithium or butyllithium.

Organosilicon acetylenic amines were synthesized in the reaction between trimethylsilylpropargylchloride and heterocyclic amines or by means of organomagnesium synthesis.

1-Tert-butylpyrrolidine, -piperidine, and -perhydroazepine were synthesized by cyclization of t-butylamine with α,ω -dibromoalkanes in the ether solution. The carbon analogues of trimethylsilylmethyl derivatives of pyrrolidine, piperidine and perhydroazepine (neopentyl compounds) were obtained through reduction of the appropriate trimethylacetic acid amines with LiAlH₄. The carbon-containing analogue of 1-[2-(trimethylsilyl)ethyl]piperidine was prepared by reduction of 3,3-dimethyl-1-piperidino-2-butanone with hydrazine hydrate in triethylene glycol (after Kizhner-Wolff).

To study the basis strength of 1-organyl- and 1-triorganysilyl-alkyl- derivatives of pyrrolidine, piperidine and perhydroazepine potentiometric titration with perchloric acid in methanol and determination of ¹³C-D...N shifts in IR spectra for associates with deuteriochloroform was employed to give the following results:

- (1) the basic strength of organic and organosilicon amines depends on the size of the cycle and diminishes in the following order: perhydroazepine > pyrrolidine > piperidine;
- (2) among the synthesized compounds the highest basicity was exerted by the 1-t-butyl derivatives;
- (3) due to the (p-d)_x interaction between the silicon and nitrogen atoms, the 1-trimethylsilyl compounds showed the weakest basic properties while possessing the highest inductive constant;
- (4) trimethylsilylalkyl derivatives were more basic as compared to the corresponding carbon-containing analogues, the fact consistent with the inductive effects of the Me₃Si and Me₃C groups;
- (5) the inductive influence of the Me₃Si and Me₃C groups becomes completely attenuated along the chain of three methylene groups, and γ -amines have basicity equal to that of 1-propyl derivatives;
- (6) the basic strength diminishes with successive substitution of methyl groups for ethoxy groups at the silicon atom;