PL 9

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 fastinating 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 derivotives 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 ^{1}H- and ^{13}C-NMR spectroscopic studies and ^{15}N-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 derivotives — is also discussed in detail; special attention will be given to a mechanistic study on this ring contraction with ^{15}N-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 isostructurol 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 Toft constont 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 triol.

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 otom were obtained in the reaction between trimethyl-, dimethylethoxy-, methyldiethoxy- and triethoxy(chloromethyl)silanes and the corresponding (3--chloropropyl)silanes with heterocyclic amines. The γ-organosilicon amines were also prepared by hydrosilylation of 1-heterylalkenes with trialkyl- and triethoxysilanes in the presence of 0,1 M chloroplotinic acid solution in proponol-2.

Heterocyclic organosilicon β-amines were obtained by the addition of pyrrolidine, piperidine and perhydroozepine 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 perhydroozepine (neopentyl compounds) were obtained through reduction of the appropriate trimethylacetic acid amines with $LiAlH_4$.

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-triorganylsilylalkyl- derivatives of pyrrolidine, piperidine and perhydroazepine potentiometric titration with perchloric acid in methanol and determination of $\upsilon C\text{-}D\ldots N$ shifts in IR spectra for associates with deuterochloroform 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 $(p\text{-}d)_\pi$ 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 Me_3Si and Me_3C groups;

(5) the inductive influence of the Me_3Si and Me_3C groups becomes completely attenuated along the chain of three methylene groups, and γ-amines have basicity equal to that of 1-propyl derivotives;

(6) the basic strenght diminishes with successive substitution of methyl groups for ethoxy groups at the silicon atom;

(7) transition from saturated to ethylenic, and further to acetylenic compounds resulted in the reduction of the basic strength by 0.7—0.8 and 2.0—2.2 pK units, respectively, the values consistent with the alteration of the electron-accepting capacity of the substituents;

(8) substitution of hydrogen for trimethylsilyl group in the 1-propargyl derivatives caused a slight increase in the basic strength of the compounds, which was, nevertheless, lower than that of the t-butyl compounds, due to the strong $(p-d)_\pi$ interaction between π electrons of the triple bond with free 3d-orbitals on the silicon atom in the organosilicon acetylenic amines;
(9) trimethylsilylmethyl- and neopentyl derivatives (α-amines) were less basic as compared to β-compounds.

The latter findings were contrasted by the linear correlation between pK_a and the inductive effect of the substituents. Persistent linear relationship between the basic strength of the 1-substituted heterylamines and σ^* was not obtained unless α-amines possessing abnormally low basic strength were excluded from the correlation analysis.

Decrease in the basic strength of organic amines is due to the steric shielding during solvatation of the basicity centre by the neopentyl group (which is also apparent on the molecular models), in the case of organosilicon compounds the reason lies in the intramolecular electronic interaction between the silicon and nitrogen atoms.

Inductive constants calculated for the trimethylsilylmethyl group (—0.17; —0.18; 0.176) on the basis of correlation equations are independent of the steric effect of heterocycles (E_S equals 0.51, 0.79, and 1.1, respectively) and are suggestive that the decrease in the electron-donating properties of the group is electronic in nature.

To investigate the effect of association on the chemical shift of chloroform in NMR spectra, we used dilution with 1-(trimethylsilylalkyl)pyrrolidines. The chemical shift (δ_K) was found to be proportional to the hydrogen bond stability, which was determined in the present case by the basic properties of the nitrogen atom.

Our data showed that electron-donating capacity of the nitrogen atom in α-amine (δ_K = —1.06) was lower not only with respect to β-amine (δ_K = —2.11) but also with respect to 1-propylpyrrolidine (δ_K = —1.54).

Similar results were obtained from ^{13}C and ^{29}Si NMR spectra for organosilicon derivatives of pyrrolidine and from determination of electron-donating capacity of nitrogen in pyrrolidine, piperidine and perhydroazepine derivatives by IR spectroscopy (as evidenced by $\Delta\nu C{-}D\ldots N$ shift of deuterochloroform).

Thus, by the use of various physico-chemical methods it was shown that besides +I-effect of the trialkylsilyl group in organosilicon α-amines exists another electronic effect acting in the opposite direction which is responsible for the decrease in the electron density on the nitrogen atom.

I am very graeful to R. Y. Sturkovich, E. Liepiņš, T. V. Koshik, E. S. Deriglazova, E. I. Kositsyna, and M. Mägi who were engaged in the experiments, and to prof. M. G. Voronkov for the useful discussion.

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PHOTOCHEMISTRY A MODERN TOOL IN HETEROCYCLIC CHEMISTRY — SOME SELECTED EXAMPLES

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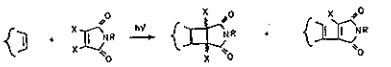
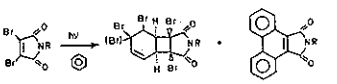
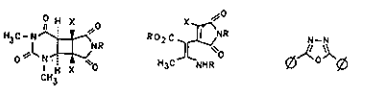
In the first part heterocyclic molecules are compared with aliphatic, olefinic and carbocyclic compounds regarding their reactivity in the excited state. In many cases a similar and parallel behaviour can be stated, due to the fact that frequently excitation occurs selectively to carbonyl groups or olefinic groups of the appropriate heterocyclic ring system.
Then new $\pi 2s + \pi 2s$ — cycloaddition reactions are presented of dihalomaleimides to aromatic compounds (1), enaminoesters and heterocycles (2).



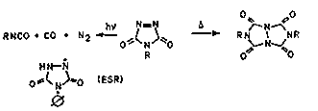
The stereochemistry of the photoadducts, product distribution, side and secondary reactions are discussed in detail. Irradiation of dibromomaleimide in benzene results in a new example of an isolable 2+2-adduct to the benzene molecule:



Besides there is observed also double alkylation reaction and subsequent stilbene-analog photocyclisation to give phenanthra[9, 10-c] = pyrroles. DXMI upon irradiation add also smoothly to uracil (2), while β-aminocrotonates add DXMI at the electron-rich C_β.
Additionally new photoreactions of 2,5-diaryl-1,3,4-oxadiazoles to uracils have been found (3).



The next part deals with photochemical and thermal reactions of 4-substituted 1,2,4-Triazolin-3,5-diones („4-R-TAD") (4,5). Irradiation leads to fragmentation into CO, N_2 and Isocyanates, while thermolysis gives — via a new radical intermediate: 4-phenyl-urazolyl — the Stollé-(6) s-triazolo[1,2-a]s-triazole:



Several other new and versatile addition-, cycloaddition- and decomposition reactions of the R-TAD are described.
The last part is devoted to a new approach towards the problem: electrocyclic photoisomerization of 1,4-thiazepines into bicyclic molecules of the penam structure (7). An improved synthesis of 1,4-thiazepinones is presented as well as transformation reactions of these into suitable model compounds for carrying out photoinduced internal electrocyclic reactions.