

REARRANGEMENT OF N-SUBSTITUTED 1-THIOCARBAMYLAZETIDINES
INTO DERIVATIVES OF 2-IMINO-3,4,5,6-TETRAHYDRO-1,3-THIAZINE

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THE rearrangement of N-substituted 1-thiocarbamylaziridines into derivatives of 2-amino-2-thiazoline is well known.^{1,2,3} It was of interest to prepare some hitherto unknown related compounds with four-membered rings and to investigate their behaviour under conditions applied for rearrangement of three-membered rings.

The N-substituted (mainly aryl) 1-thiocarbamylazetidines (I) were prepared from azetidine⁴ and the corresponding isothiocyanates. Thus the following substances (I) were prepared: R: phenyl-, m.p. 112° (lit.⁴ gives m.p. 110°), R: p-tolyl-, m.p. 144-5°, R: 2',4'-dimethylphenyl-, m.p. 167°, R: p-ethoxyphenyl-, m.p. 120°, R: m-chlorophenyl-, m.p. 112° and R: p-chlorophenyl-, m.p. 146-7°.

These compounds, when heated for 15 min with excess conc. hydrochloric

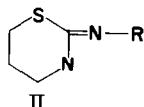
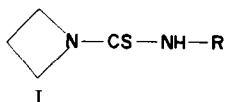
¹ S. Gabriel and R. Stelzner, Ber. 28, 2929 (1895).

² A. S. Deutsch and P. E. Fanta, J. Org. Chem. 21, 892 (1956).

³ M. Tišler, Arch. Pharm. 291/63, 457 (1958).

⁴ C. C. Howard and W. Marckwald, Ber. 32, 2031 (1899).

acid, were almost quantitatively transformed into derivatives of 2-imino-3,4,5,6-tetrahydro-1,3-thiazine (II).

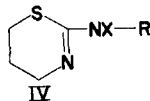
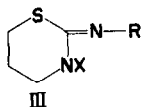


It is well known that the relatively unstable azetidine and its derivatives readily open the ring when treated with acids giving rise to derivatives of n-propylamines or γ -hydroxypropylamines, the last reaction taking place preferentially in dilute acid solution.

Through rearrangement the following compounds (II) were obtained: R: phenyl, m.p. 127^o, R: p-tolyl-, m.p. 140^o, R: p-ethoxyphenyl-, m.p. 132^o, R: m-chlorophenyl-, m.p. 150^o, and R: p-chlorophenyl-, m.p. 156-7^o. However, the synthesis of these compounds can be performed in a much simpler way, e.g. the corresponding isothiocyanates were condensed in alcoholic solution with 3-aminopropanol-(1) and the resulting condensation products, without being isolated, were thereafter cyclized with hot conc. hydrochloric acid. Compounds, obtained by this procedure, showed no depression in m.p. with those obtained through rearrangement. Accordingly, besides the above compounds the following new ones were prepared: II, R: o-tolyl-, m.p. 121^o, R: m-tolyl-, m.p. 90-1^o, R: p-methoxyphenyl-, m.p. 144^o, R: o-methoxyphenyl-, m.p. 127^o and R: cyclohexyl-, m.p. 113^o.

Monosubstituted 2-imino-3,4,5,6-tetrahydro-1,3-thiazines are capable

to exist in two forms, e.g. in the imino form as III (X: H) or in the amino form as IV (X: H).



With closely related substances some authors formulated them in the imine form^{5,6} but many of them prefer the amino form.^{7,8,9,10} The formulation as III is obvious if X in the imino group in the ring is other than hydrogen as in the case of 3-alkyl- or 3-aryl-analogues.^{11,12} On the basis of infra-red spectra of II (R: phenyl-), its N-methyl derivative (III, X: CH₃) (b.p. 175-180°/12 mm) and its N-phenyl derivative (III, X: C₆H₅-)^{11,13} the

⁵ S. Gabriel and T. Posner, Ber. 28, 1029 (1895).

⁶ S. Gabriel and W. E. Lauer, Ber. 23, 87 (1890).

⁷ N. Ghosh, J. Indian Chem. Soc. 11, 23 (1934).

⁸ A. Luchmann, Ber. 29, 1420 (1896).

⁹ G.W. Raiziss, L. W. Clemence and M. Freifelder, J. Amer. Chem. Soc. 63, 2739 (1941).

¹⁰ M. Fränkel, Ber. 30, 2497 (1897).

¹¹ F. B. Dains, R. Q. Brewster, J. S. Blair and W. C. Thompson, J. Amer. Chem. Soc. 44, 2637 (1922).

¹² G. Noah, Ber. 23, 2195 (1890).

¹³ F. Foerster, Ber. 21, 1857 (1888).

structure III seems the most probable also for the monosubstituted compounds (III, X: H).

All m.p. were determined with Kofler's heating microscope and all analyses were in agreement with data, calculated for the above mentioned compounds. A more detailed description of these and related experiments will be reported elsewhere. The author thanks Prof. D. Hadži for measurement of the infra-red spectra.