1,3-THIAZEPINES.

2. REACTION OF 2-IMINOHEXAHYDROTHIAZEPINES WITH PHENYLISOCYANATE AND ISOThIOCYANATES

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We have shown that as a result of reaction of phenylisocyanate with 2-benzyl- and 2-aryliminohexahydrothiazepines, the corresponding N-substituted N-tetrahydroazepinyl-N'-phenylureas are formed. In the case of isothiocyanates, on boiling in different solvents we obtained the products of the exchange reaction; and at room temperature, we also obtained substituted thioureas. We suggest a probable scheme for the process.

Acylation reactions of amino-1,3-thiazepine and its derivatives are represented in the literature by isolated examples. The only descriptions found in the literature are for the reaction of 2-aminotetrahydrothiazepine hydrobromide with ketene [2], the reaction of a few derivatives of 2-aminodihydrobenzothiazepine with diphenylketene [3], and the reaction of 2-phenyliminothiohydrothiazepine with a number of acyl halides [4]. Reactions with isocyanates and isothiocyanates have not been studied in general. Furthermore, ureido- and thioureido-substituted thiazepines and their hydrogenated analogs can serve as convenient synthons in fine organic synthesis, and are potential biologically active substances. Accordingly, we studied the reaction of 2-benzyl- (Ia) and 2-aryliminothiohydrothiazepines (Ib-d) with phenylisocyanate and a number of isothiocyanates.

The reactions of compounds Ia-d with phenylisocyanate both at room temperature in acetone (Procedure A) and with boiling in acetone, chloroform, benzene, or toluene (Procedure B) lead to N-benzyl(aryl)-N-(4,5,6,7-tetrahydro-1,3-thiazepin-2-yl)-N'-phenylureas (IIa-d) in high yields (Table 1).

\[
\text{NR + PhNCO} \rightarrow \text{IIa-d} \\
\text{Ia-d} \quad \text{IIa-d}
\]

\[\text{I, II } a \text{ R} = \text{CH}_2\text{Ph, bR} = \text{Ph, cR} = \text{C}_6\text{H}_4\text{NMe}_2-4, \text{dR} = \text{C}_{10}\text{H}_7-\alpha\]

In contrast to these results, when boiling thiazepines Ia-d with arylisothiocyanates under similar conditions, the corresponding thioureas were not obtained. In the case of thiazepine Ib, after boiling for many hours with phenylisothiocyanate we isolated only the starting reagents, although the formation of an unidentified product was detected chromatographically. When thiazepine Ib was boiled in toluene with p-chlorophenylisothiocyanate and thiazepine Ic was boiled in toluene with phenylisothiocyanate, we obtained compounds which are the result of an exchange reaction: 2-(p-chlorophenylimino) hexahydrothiazepine (Ie) and phenylisothiocyanate in the first case, hexahydrothiazepine Ib and p-(dimethylamino) phenylisothiocyanate in the second case:

*For communication 1, see [1].
We assumed that thioureido derivatives of thiazepine are thermally stable, and carried out the reactions with isothiocyanates at room temperature according to Procedure A. In this case, in fact from amine Ia and phenylisothiocyanate we obtained two substituted thioureas (III and IV). In addition to those compounds, the reaction mixture contained products of the exchange reaction, and also the starting reagents:

\[
\text{Ia} + \text{PhNCS} \to \begin{array}{c}
\text{III} \\
\text{IV}
\end{array} + \text{PhNCS} + \text{Ib} + \text{PhNCS}
\]

A similar pattern was observed when thiazepine Ib was reacted with benzylisothiocyanate. The only product of reaction of amine Ia with benzylisothiocyanate was thiourea III. Analysis of the results obtained allows us to conclude that the reaction of thiazepines Ia-d with isothiocyanates at room temperature occurs according to the following scheme:

\[
\begin{array}{c}
\text{Ia} + \text{PhNCS} \\
\text{PhNCS} + \text{Ib}
\end{array}
\]

In the first step, the exchange process occurs; then the formed and starting thiazepine derivative enter into competing reactions with the formed and starting isothiocyanates, which leads to thioureido derivatives. At higher temperature, the latter decompose and therefore we can isolate only the products of the exchange reaction. The fact that in the reaction of amine Ia with phenylisothiocyanate we isolated only two thioureas III and IV out of the four possible ones is probably connected with the low stability of the other products. From imine Ib of phenylisothiocyanate, we obtained a third possible thiourea (V), which in fact proved to be an unstable compound: it decomposed into the starting reagents when recrystallization was attempted, when repeatedly treated with organic solvents, even in the cold, or during column chromatography. The indicated properties explain its absence in the products of the reactions described above.