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LETTERS

[1,5]SIGMATROPIC SHIFT OF HYDROGEN IN AMINATION OF 3-PYRROLIDINO-1,2,4-TRIAZINE 4-OXIDE[†]

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Abstract: The reaction of 3-pyrrolidino-1,2,4-triazine 4-oxide with ammonia leads to the product of *tele*-substitution of pyrrolidine - 5-amino-1,2,4-triazine 4-oxide. Sigmatropic shift of hydrogen postulated for such reactions has been proved by isolation of key intermediates.

Nucleophilic attack on an azine ring is often accompanied by cleavage of the C-C bond resulting in open-chain or ring-transformation products.[1] This can be illustrated by some classical examples, such as the formation of glutaconic aldehyde derivatives in the reactions of pyridinium or quinolinium cations with a variety of nucleophilies,[2] nucleophilic substitution reactions in pyrimidines according to the ANRORC (Addition of Nucleophile, Ring Opening, Ring Closing) mechanism,[3] or the formation of 3-aminopyridazine as a result of the ring transformation of 3-chloro-6-phenyl-1,2,4-triazine by action of the phenylacetonitrile anion.[4] Often, ring-opening is observed in aromatic N-oxides, as exemplified by hydrolysis of 1,2,4-triazine-4-oxides,[5] by reactions of pyridine N-oxides [6] and 1,2,4-triazine-4-oxides [7] with amines, as well as by the reactions of pyrimidine N-oxides [8] and 1,2,4-triazine-4-oxides [5] with active methylene compounds, etc.

Continuing our studies on nucleophilic substitution reactions in 1,2,4-triazine 4-oxides, we have found that heating 3-pyrrolidino-6-phenyl-1,2,4-triazine-4-oxide **1** with ethanolic ammonia leads to 5-amino-6-phenyl-1,2,4-triazine-4-oxide **2** in 70% yield. The melting point and spectral data for the oxide **2** proved to be identical to those for the compound obtained by amination of 6-phenyl-1,2,4-triazine-4-oxide in liquid ammonia in the presence of potassium permanganate.[9] Obviously in this case, we deal with *tele*-substitution of the pyrrolidino group, as an example of the so-called odd *tele*-substitution (an odd number of atoms lie between the position of nucleophilic attack and that from which a nucleofuge departs). In accordance with the mechanism postulated for such reactions,[10] the [1,5]-sigmatropic shift of hydrogen is a crucial step in conversion of the adduct **A** resulting from the addition of ammonia at C^5 of the 1,2,4-triazine-4-oxide **1** into the 3,4-dihydro intermediate **B**. This is aromatized into the *tele*-substitution product **2** by elimination of pyrrolidine.

In this paper we present new experimental evidence for the generally accepted mechanism mentioned above by isolation of key intermediates. Indeed, the reaction of 1,2,4-triazine-4-oxide **1** with ammonia, dimethylamine or cycloalkylamines has unexpectedly been found to lead under the mild conditions (room temperature) to 6-pyrrolidino-2-amino-1-hydroxy-3-phenyl-1,4,5-triazahexatrienes **3a-d**.

[†] Dedicated to Professor H.C. van der Plas on the occasion of his 70-th birthday

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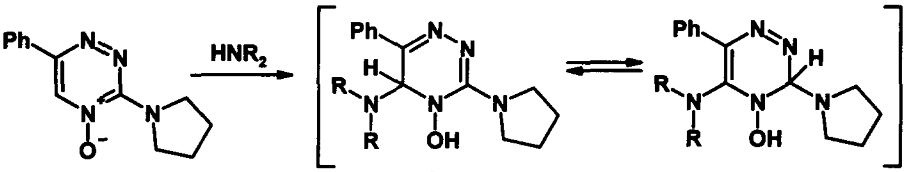
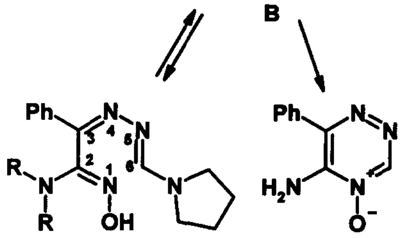
The structures of products **3a-d** are in good agreement with NMR spectral data, and for 1-hydroxy-2,6-dipyrrolidino-3-phenyl-1,4,5-triazahexatriene **3b** was confirmed by X-ray diffraction. In their ^1H NMR spectra chemical shifts of the phenyl protons and H^6 (8.2-8.3 ppm) are identical to those for 1-hydroxy-6-dialkylamino-3-phenyl-1,4,5-triazahexatrienes.[7]



1 **A** **B**

	NR₂	%yield	mp.
3a	amino	68	228-230
3b	pyrrolidino	93	184-186
3c	piperidino	81	154-156
3d	dimethylamino	84	169-171



3a-d **2**

Refluxing triazahexatriene **3a** in ethanol leads to its full conversion into 5-amino-1,2,4-triazine 4-oxide **2**. Taking into account that open-chain 1-hydroxy-1,4,5-triazahexatrienes **3** exist in equilibrium with the cyclic 3,4-dihydro-4-hydroxy-1,2,4-triazines [11] one can see that compounds **3a-d** are just open-chain forms of σ^H-adducts **B**. The location of the substituents and protons in the compounds **3** confirms the conversion of **A** into **B** through the [1,5]-sigmatropic shift of hydrogen.

Thus, a reversible opening of the 1,2,4-triazine ring in the reaction of 3-pyrrolidino-1,2,4-triazine 4-oxide with amines removes the intermediates **B** from the reaction. It allows a study in detail of their structure. The conclusion resulting from this structure is undoubtedly that the odd *tele*-substitution proceeds through the [1,5]-sigmatropic shift of hydrogen.

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