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Deamination of Some *N*-Amino Nitrogen Heterocycles Using *Preyssler*'s Anion

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Summary. Some *N*-aminotriazines and -triazoles were treated with *Preyssler*'s anion as catalyst in acetic acid to afford the corresponding deaminated triazines and triazoles. The reaction is suggested to proceed *via* formation of *N*-nitrosamines with subsequent N–NO bond cleavage.

Keywords. *N*-Aminotriazines, -triazoles; *N*-Nitrosamines; N–NO bond cleavage; Heteropolyacids.

Introduction

The triazine scaffold is found in compounds presenting a wide spectrum of biological antiproliferative, antitubulin, antiangiogenic, and antidepressive agents or in plant-protection applications, such as the triazine herbicides. Other factors which have contributed to the widespread use of triazine assemblies in drug discovery are the ease of manipulation and the availability of cheap starting materials used to build this class of compounds [1].

It has been found that many 1,2,4-triazoles possess a wide spectrum of activities including antibacterial, antifungal, antiviral, anticonvulsant, antidepressant, antihypertensive, analgesic, and hypoglycemic properties. As an important type of fungicides, triazole compounds are highly efficient, low poisonous, and inward-absorbent. Metal complexes containing triazole ligands may also show biological activity [2]. 1,2,4-Triazoles have attracted great and growing interest in coordination chemistry because of the fact that they can synthesize transition metal coordination polymers with bridging by the two close adjacent nitrogen atoms (N1 and N2) or the 4-positioned one (N4). 1,2,4-Triazoles also exhibit excellent bioactivities making them of particular interest for their multifarious uses in agriculture, medicine, and industry [3, 4]. Glycosylated triazole derivatives, like 1-β-D-ribofuranosyl-1*H*-1,2,4-triazole-3-carboxamide (Virazol) [5] belong to the highly potent drugs against *DNA* and *RNA* viruses [6]. Moreover, this compound shows antitumor activity [7], just as the anomeric 1-(2,3,4,6-tetra-*O*-acetyl-D-glucopyranosyl)-5-nitro-1*H*-1,2,4-triazoles [8].

The catalytic function of heteropolyacids (HPAs) and related polyoxometalate compounds have attracted much attention, particularly in the last two decades [9–11]. The important advantages of this heteropolyacids are, such as: strong *Brønsted* acidity with 14 acidic protons, high thermal stability, high hydrolytic stability (*pH* 0–12), reusability, safety, quantity of waste, separability, corrosiveness, high oxidation potential, and greenness along with an exclusive structure. These have attracted much attention to this catalyst. It has been shown that some heteropolyanions exhibit interesting catalytic properties as green and eco-friendly catalysts for redox and acid–base type reactions in industrial applications [12, 13].

In this paper we wish to report an interesting and unexpected deamination reaction from *N*-aminotria-

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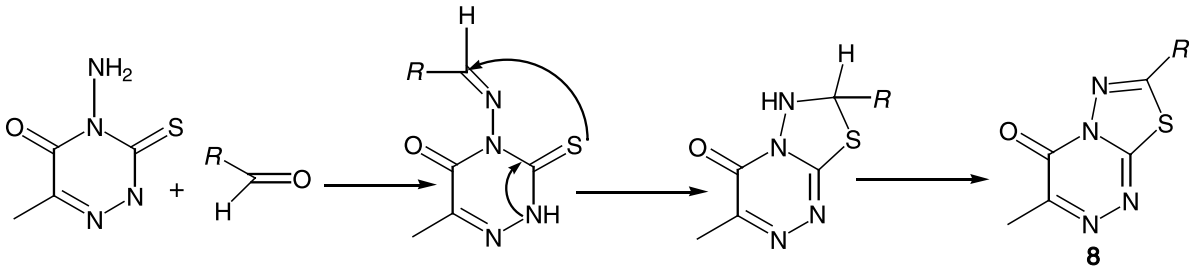


Scheme 1

zines and *N*-aminotriazoles using *Preyssler*'s anion, $H_{14}[NaP_5W_{30}O_{110}]$.

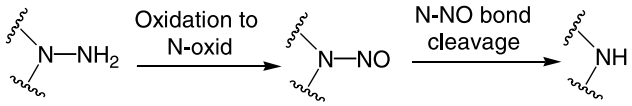
Results and Discussion

Recently, a series of heteropolyacid catalyzed reactions, such as oxidation of aldehydes and alcohols, *N*-oxidation of pyridine, esterification of aliphatic and aromatic carboxylic acids have been reported from our laboratory [14–19]. The application of the *Preyssler* catalyst is mostly limited and only a few demonstrations of catalytic activity have been reported.

We prepared an imine from 6-methyl-4-amino-3-thioxo-1,2,4-trizine (**1**) and benzaldehyde to implement an intramolecular cyclization using heteropolyacids as green and oxidative catalysts in order to obtain thiadiazino[2,3-*c*]-1,2,4-triazine **8** (Scheme 1). The progress of reaction was monitored by TLC. Surprisingly, we found instead of the expected thiadiazino-1,2,4-triazine **8** a mixture of benzaldehyde and 6-methy-3-thioxo-1,2,4-triazine. This means that under this condition the imine became hydrolyzed and the aminotriazine was deaminated. The cyclizations of various imines were then investigated and in all cases the deaminated products were detected. Thus, we prepared a range of various heterocyclic *N*-amines **1**–**7** and refluxed them under the same condition in acetic acid in the presence of *Preyssler*'s anion to investigate the possibility of deamination. The results are shown in Table 1.

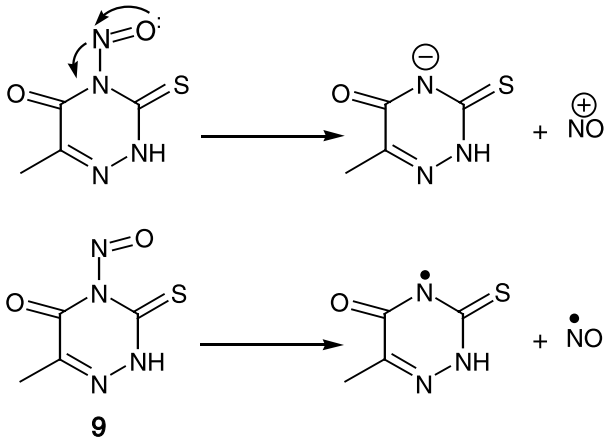
It is noteworthy to mention that the aminotriazoles and aminotriazines **1**–**7** can not be deaminated by just refluxing them in acetic acid even for prolonged time (24 h). Thus, this interesting deamination is only prompted by heteropolyacid catalysis.

It has been shown that some heteropolyanions exhibited interesting catalytic properties for redox and/or acid–base type reactions [15]. Presumably,



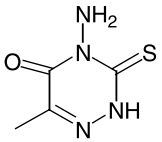
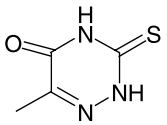
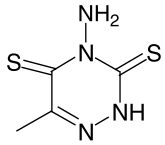
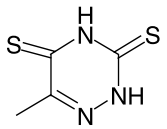
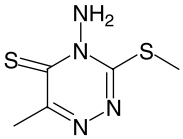
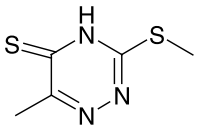
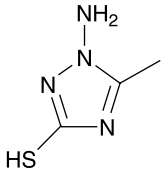
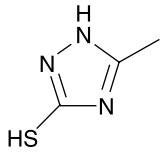
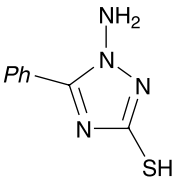
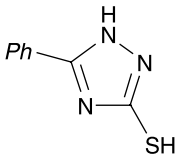
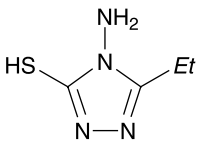
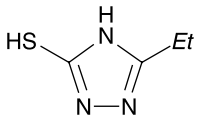
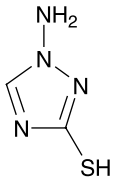
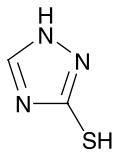
Scheme 2

in the present case, these amines were oxidized to the corresponding *N*-nitrosamines and then an N–NO bond cleavage occurred (Scheme 2). *N*-Nitrosamines can produce NO through a homolytic cleavage of the N–NO bond, and also can form NO^+ through a heterolytic cleavage of the relevant bond (Scheme 3) [20]. The driving force for NO to be transferred from one molecule will largely depend on the bond energy between NO and *Y*, where *Y* is the atom to which the NO group is attached [21]. The N–NO bond of these *N*-nitroso derivatives tends to be weak, and *N*-nitroso derivatives were not stable under the reaction conditions. On the other hand, deamination of the *N*-amines **1**–**7** were carried out *via* *N*-nitroso derivatives as an intermediate and it is conceivable that the heterolytic cleavage is preferred under this condition. Only when we quenched the reactions, small amounts of *N*-nitroso derivatives could be sep-



Scheme 3

Table 1. Deamination of *N*-amino-1,2,4-triazines and *N*-amino-1,2,4-triazoles

	N-Amines	Amines	Yield/%	mp/°C	
				Found	Refs. [22, 23]
1			61	218–220	219–221
2			53	217	215–217
3			44	174–176	178
4			58	114–116	116–118
5			55	259–261	258–260
6			48	245–247	247
7			57	220–222	221–224

arated and detected by GC-MS, FT-IR, and ^{1}H NMR spectroscopy.

In conclusion, we found that the heteropolyacid, *i.e.* the *Preyssler*'s anion, can act as a catalyst for the oxidation of *N*-aminotriazines and -triazoles **1–7** to the corresponding *N*-nitrosamines. The N–NO bond of these *N*-nitroso derivatives tends to be weak, and deamination of the *N*-amines **1–7** occurs by N–NO bond cleavage.

Experimental

Melting points were measured by using the capillary tube method with an electrothermal 9200 apparatus. ^{1}H NMR spectra were recorded on a Bruker AC-80 MHz spectrometer using *TMS* as an internal standard ($CDCl_3$ solution). IR spectra were recorded from KBr disks on the FT-IR Bruker Tensor 27. GC analyst were carried out on a Network GC System-Agilent 5973. All products were known and characterized by comparison of their physical and spectra data with those already reported [22, 23].

Catalyst Preparation

Preyssler's anion, $H_{14}[NaP_5W_{30}O_{110}]$, was prepared by passage of a solution of the potassium salt in water through a column (50 cm × 1 cm) of Dowex50 W × 8 in the H^+ form and evaporation of the elute to dryness under vacuum [18].

Deamination of Amino Heterocycles: General Procedure

A mixture of 10 mmol heterocyclic *N*-amines **1**–**7**, prepared according to Ref. [22], and 0.74 mg *Preyssler*'s anion (0.1 mmol) was refluxed in 10 cm^3 acetic acid for 24 h. After completion of the reaction (monitored by TLC) the mixture was cooled to room temperature and the precipitated products were separated by filtration, washed with cold ethanol, and recrystallized from ethanol. The catalyst could be recycled after evaporation of solvent from the residue solution and washing with dichloroethane, and re-used in another reaction. All products gave satisfactory spectral data in accord with the assigned structures (Table 1).

Acknowledgements

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