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Note

The mechanism of saccharide osotriazole formation

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Abstract

The first step in the proposed mechanism is the formation of an osazone–Cu(II) complex that undergoes a one-electron shift from the nitrogen of the ligand to the metal in the complex which is reduced to Cu(I). This complex decomposes with the liberation of $\mathrm{Cu(I)}^{+}$, a ligand radical which undergoes a set of one-electron shifts to form a phenylimine radical $(\mathrm{Ph{-}NH})^{\bullet}$ and the triazole. The $\mathrm{Cu(I)}^{+}$ produced is converted to $\mathrm{Cu(II)}^{2+}$ and Cu^{0} by disproportionation. © 1998 Elsevier Science Ltd. All rights reserved.

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Saccharide phenylosotriazoles were first prepared by C.S. Hudson and co-workers [1] by refluxing a suspension of the corresponding phenylosazone (**1**) in aqueous copper(II) sulfate. Later, numerous saccharide osotriazoles were prepared in the same manner and used to characterize monosaccharide osazones [1–12] disaccharide osazones [13–19] and anhydro-osazones [20–25]. Although more than 50 years have passed since the first saccharide osotriazoles were prepared, no mechanism for their formation has been presented that can explain all the observations made on the reaction during this early time period. These facts are summarized in the following.

(1) Hudson's team [1] observed that the formation of osotriazoles was accompanied by the formation of aniline and preceded by the appearance of an intense red coloration in the reaction mixture, which was attributed to the formation of an osazone–copper complex precursor. These authors were able to study the copper complexes of more the soluble osazones in solution, but could not determine their exact structures since when they tried to isolate them they were quickly converted into osotriazoles and aniline. From their observations they concluded that the role of copper sulfate in the reaction was that of "...a promoter that forms an unstable complex with the osazone and thereby opens a path for a speedy formation of the highly stable triazole ring and the splitting of aniline from the osazone."

(2) The present author's team [26] found that osotriazole formation necessitated the presence of oxidizing agents. Thus, apart from copper(II) sulfate and chloride, which are reduced to metallic copper during the conversion to triazoles, the reaction can be carried out with such oxidizing metal salts, as mercury(II) acetate and iron(III) sulfate and chloride [26]. The same metal salts in their lower states of valency and salts of metals that do not readily accept electrons, such as the chlo-

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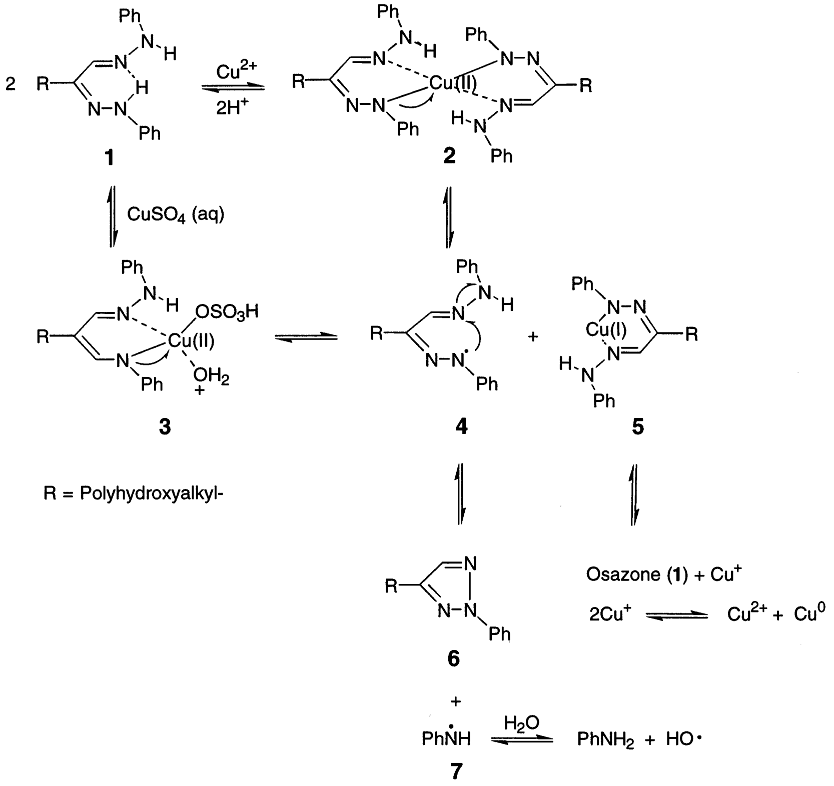

Scheme 1.

rides and sulfates of Na, K, Mg, Ca, Al, etc., do not react with osazones to form osotriazoles [26]. In addition, nonmetallic oxidants such chlorine and bromine in water [27–29], as well as nitrososulfonates [30], can readily achieve the conversion to osotriazoles.

(3) The conversion of osazones to osotriazoles with Cu(II) salts results in the precipitation of about 0.5 mol of metallic copper per mole of osazone. The Hudson team [1] attributed the small amount of copper to side reactions, but the present author's team [26] regarded it as evidence of an oxidation by the Cu(II) ions. Some years ago, a mechanism was offered by the author [31] to explain how osazones could be converted to triazoles without the need for oxidants, i.e., according to Hudson's views [1]. It was suggested that the chelated ring of the osazone acted as a template that facilitates a 1,5-sigmatropic rearrangement that shifts the imino proton attached to the phenylhydrazone residue on C-2 to the nitrogen of the C=N– group attached to C-1 of the osazone. Cyclization of the rearranged molecule, followed by elimination of Ph–NH–, would then afford the osotriazole and aniline. Of course this mechanism did not account for the reduction of Cu(II) into Cu^0, nor did it explain why oxidizing agents are needed for the reaction.

A more plausible scheme is proposed here, which can account for the three observations listed above, i.e., explain why the reaction requires oxidizing agents; why the formation of an osazone–Cu(II) complex precedes triazole formation; how aniline is eliminated to form a triazole and how $Cu(II)^{2+}$ is converted to Cu^0. In the mechanism proposed, Hudson's copper complex is not a promoter, but nonetheless plays a key role. It undergoes an intramolecular oxidation-reduction, namely an oxidation of the ligand to form the osotriazole and aniline and a reduction of Cu(II) to Cu(I), which ultimately yields Cu^0.

The first step in the proposed mechanism is the reaction of the osazone (**1**) with Cu(II) ions to form an osazone–Cu(II) complex such as **2**, which then undergoes a one-electron shift from the nitrogen of the ligand to the metal in the complex (see Scheme 1). The metal is thus reduced from Cu(II) to Cu(I) and the ligand has been oxidized since it has lost an electron. It should be noted that a dimeric complex is not essential for the oxidation–reduction, as a monomeric complex such as the ozasone–Cu(II)–hydrogensulfate complex **3** can achieve the same results. In either case the intramolecular oxidation–reduction will result in the formation of a less stable Cu(I)–ligand complex, which decomposes with the liberation a ligand radical **4**. This product undergoes a set of one-electron shifts to form the triazole (**6**) by way of eliminating a phenylimine radical $(Ph{-}NH)^\bullet$ (**7**), which is quickly converted in water to aniline.

The Cu(I) complex **4** obtained from the dimer **2** will decompose to regenerate a mole of osazone and $Cu(I)^+$, whereas the Cu(I) complex from the monomer **3** will yield the triazole, aniline and $Cu(I)^+$. The $Cu(I)^+$ produced in either way will be converted to $Cu(II)^{2+}$ and Cu^0 by disproportionation. This is a well-known reaction of Cu(I) ions [32], which undergo disproportionation upon boiling in acidified water to give $Cu(II)^{2+}$ and Cu^0. In the present mechanism, the $Cu(II)^{2+}$ formed is recycled and Cu^0 is precipitated in approximately the observed amount (0.5 mol). It should be noted that the amount of copper precipitated depends on the ratio of at least two competing reactions, triazole formation and hydrolysis to the osulose [33]. The role of Cu(II) complexes in triazole formation is to facilitate the oxidation by bringing the electron-rich part of ligand (the nitrogen) next to the oxidant. To explain why stronger oxidising agents such as chlorine or bromine in water can directly convert osazones to osotriazoles without any need for Cu(II) ions [26], whereas weaker oxidants such Cu(II) salts require metal–complex intermediates of the type **3** or **4**, it is suggested that the first are able to attack the stable hydrogen-bonded chelated ring of osazones while the second are not. In conclusion, the ideas proposed herein shed light on the role of metal complexes in the conversion of saccharide osazones to osotriazoles with copper(II) sulfate and explain why the reaction with stronger oxidants does not require any metal complex precursors.

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