

On the oxidation of allylmelamines

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2,4,6-triamino-1,3,5-triazine (melamine) was first prepared in 1834 by Liebig. It has already been used for several decades for the production of melamine-formaldehyde resins and has therefore gained industrial importance. Particularly, during the last years new possibilities for the cross-linking of melamine have been developed to replace harmful formaldehyde. The synthesis of epoxy modified melamine derivatives is one possibility for this purpose. 2-Diallylamino-4,6-bis(dimethylamino)-1,3,5-triazine was chosen as difunctional starting material, whereat solubility in organic solvents is enhanced by the use of the N-alkylated product. Epoxidations of the allyl functionalities were carried out using several common epoxidation agents. Partially, conversion took place forming mainly by-products like substituted hydroxyl amines and hydroxy triazine derivatives. Nevertheless, epoxidation of double bonds took place forming different epoxy containing structures, which may be useful starting materials for further conversions.

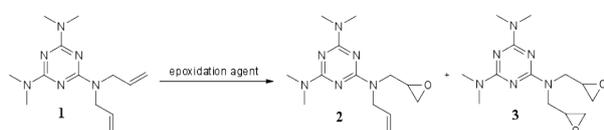
1 Introduction

Justus von Liebig first prepared 2,4,6-triamino-1,3,5-triazine (melamine) in 1834 by heating a mixture of potassium thiocyanate and ammonium chloride [1]. Since the development of melamine-formaldehyde (MF) resins in the 1930s [2], melamine has gained more and more industrial importance. Particularly, during the last years the use of formaldehyde for MF resins was of public interest, as the world health organization (WHO) classified formaldehyde 2006 as suspected carcinogen [3]. Thus, new possibilities for the cross-linking of melamine have been developed to replace formaldehyde. Nevertheless, until now no serious method has been found. An appropriate method to avoid formaldehyde, is the synthesis of melamine derivatives bearing functional groups that can be cross-linked, for example vinyl groups [4] or epoxides. Pedroso et al. [5] already described the preparation of epoxy-modified melamine derivatives using melamine and epichlorohydrin. Thereby only the production of prepolymers was possible. Another approach for the synthesis of epoxides is the epoxidation of double bonds. Applicable starting materials for that purpose are allylmelamines, which are already known since 1948 [6]. By the reaction of cyanuric chloride with various amines, allyl substituted melamine derivatives bearing different functionalities are accessible. Recently, the polymerization of allylmelamines was investigated [7]. Epoxidation of these derivatives may lead to monomers that can be cross-linked by polyaddition forming new polymers. The aim of the presented work is the epoxidation of 2-diallylamino-4,6-bis(dimethylamino)-1,3,5-triazine (**1**) using different epoxidation agents. On the one hand this starting material was chosen because it may lead to difunctional epoxides. Furthermore, the solubility in common organic solvents is increased using N-alkylated compounds. Established epoxidation agents like *m*-chloroperoxybenzoic acid (*m*CPBA), *tert*-butyl hydroperoxide (TBHP), hydrogen peroxide (H₂O₂), and sodium hypochlorite in combination with different catalysts were tested. Some reagents turned out to be too weak epoxidation agents, whereas others led to oxidation at which mainly by-products were formed, that will be presented in this paper.

2 Results and Discussion

The epoxidation of **1** using different epoxidation agents was studied, whereat next to the synthesis of 2-allylglycidylamino-4,6-bis(dimethylamino)-1,3,5-triazine (**2**) especially the preparation of 2-diglycidylamino-4,6-bis(dimethylamino)-1,3,5-triazine (**3**) was desired.

Scheme 1:



First, epoxidation was tested using TBHP. Because of the high selectivity and safety it is often applied in organic oxidations, activated by catalysts like MoO₃ [8,9]. Attempts to epoxidize **1** were carried out in different organic solvents under reflux conditions. TBHP dissolved in water was used as well as anhydrous TBHP in decane (Table 1). Reactions were carried out with and without the addition of catalyst MoO₃ **3** and monitored by electrospray ionisation-mass spectrometry (ESI-MS). Even after reaction times of more than 48 hours no conversion of **1** was detected. Thus, TBHP seems to be an inappropriate epoxidation agent for this purpose.

Table 1: Solvent systems used to epoxidize **1** using TBHP with and without addition of MoO₃ as catalyst

Entry	TBHP	Solvent	Catalyst	Result ¹
1	in water	tetrahydrofuran	no	-
1	in water	tetrahydrofuran	yes	-
2	in water	toluene	no	-
2	in water	toluene	yes	-
3	in water	chloroform	no	-
3	in water	chloroform	yes	-
4	in decane	chloroform	no	-
4	in decane	chloroform	yes	-

¹ ± = positive or negative conversion of starting material

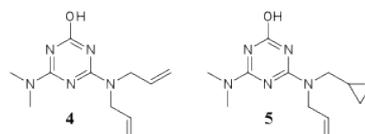


Figure 1: By-products formed in the epoxidation of **1** using *m*CPBA: 2-hydroxy-4-diallylamino-6-dimethylamino-1,3,5-triazine (**4**), 2-hydroxy-4-allylglycidylamino-6-dimethylamino-1,3,5-triazine (**5**)

Epoxidation agents showing higher activities are peracids, like *m*CPBA. Prileschajew employed such compounds already 1909 in epoxidation reactions [10] and they are still used today. Therefore, **1** was reacted in dichloromethane at a temperature of 0 °C by stepwise addition of *m*CPBA. Analyses using ESI-MS showed signals probably referring to **2**, **1**, and by-products generated by hydrolysis of dimethylamino groups (**4**, **5**). Conversion could not be advanced by further addition of peracid.

The oil obtained after workup of the reaction mixture contained next to **1** about 76% mono oxidized product, analyzed by high-pressure liquid chromatography (HPLC-MS). However, NMR measurements showed that the formed product does not contain epoxy functionalities. The only change compared to the spectrum of **1** is the occurrence of two unequal signals of dimethylamino groups at 2.87 and 3.11 ppm (Figure 2).

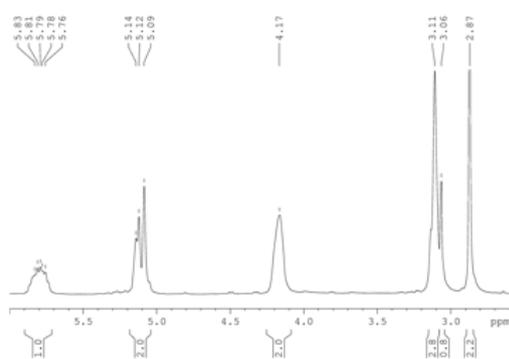


Figure 2: $^1\text{H-NMR}$ spectrum of mono oxidized product. CDCl_3 was used as solvent and internal standard. The signal at 3.06 ppm refers to unreacted starting material

Thus, oxidation occurred on a dimethylamino functionality leading to the formation of an amine oxide. The generation of amine oxides using *m*CPBA is well known [11,12], as well as the Meisenheimer rearrangement that can be performed using such compounds, whereas substituted hydroxylamines are formed [12,13]. Therefore, the formation of two different structures is possible (Scheme 2). Reaction may stop after generation of 2-dimethylamino-4-diallylamino-6-dimethylamino-1,3,5-triazine (**6**) or a further rearrangement to 2-diallylamino-4-dimethylamino-6-(dimethylamino)oxy-1,3,5-triazine (**7**) occurs. Additional 2D NMR correlation experiments indicate the formation of **7**, as no coupling between the protons of the oxidized dimethylamino group and the quaternary carbon atom of the triazine ring system was detected.

Scheme 2:

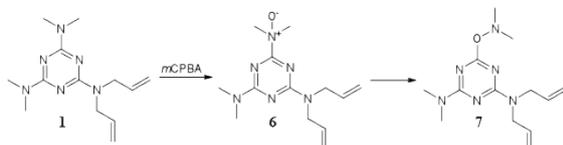


Table 2: Attempts to epoxidize **1** using H_2O_2 , FeCl_3 , H_2pydic , and pyrrolidine

Entry	Solvent	Result ¹
1	isopropyl alcohol	-
2	dichloromethane	-
3	dimethylformamide	-
4	acetonitrile	-

¹ \pm = positive or negative conversion of starting material

Using *m*CPBA the generation of amine oxides is the preferred reaction. Therefore, the application of hydrogen peroxide as epoxidation agent was tested. As an experiment indicated, hydrogen peroxide alone is not able to epoxidize the double bond, but it may be activated using different catalysts. One possibility to activate peroxides is the use of FeCl_3 in combination with pyridine-2,6-dicarboxylic acid (H_2pydic) and pyrrolidine [14,15]. Attempts to epoxidize **1** using this system were carried out at room temperature using different solvents (Table 2). Reactions were monitored by ESI-MS, but even after reactions times of 24 hours only the unchanged starting material was detected.

Another method for the activation of hydrogen peroxide is the application of MoO_3 as catalyst [16]. So, **1** was reacted with hydrogen peroxide and MoO_3 in various solvents at different temperatures. Additionally, a few attempts were done using sodium hydrogen carbonate (NaHCO_3) as promoter (Table 3). Except one experiment, all attempts did not lead to the formation of epoxy groups. Even using an excess of hydrogen peroxide no conversion took place. Only experiment 10 led to an oxidation of the starting material. As just this particular combination of solvent and catalysts is active, it is supposed that reaction follows the mechanism shown in Scheme 3.

Table 3: Solvent systems used to epoxidize **1** using TBHP with and without addition of MoO_3 as catalyst

Entry	Solvent	Temperature	NaHCO_3 ²	Result ³
1	chloroform	r.t. ¹	no	-
2	chloroform	40°C	-	-
3	chloroform	61°C	-	-
4	tetrahydrofuran	40°C	-	-
5	tetrahydrofuran	66°C	-	-
6	tetrahydrofuran	r.t. ¹	+	-
7	H_2O_2	60°C	-	-
8	acetonitrile	40°C	-	-
9	acetonitrile	82°C	-	-
10	acetonitrile	r.t. ¹	+	+
11	dimethylformamide	r.t. ¹	+	-

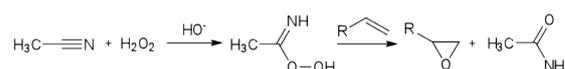
¹ r. t. = room temperature

² \pm = addition/ no addition of NaHCO_3

³ \pm = positive or negative conversion of starting material

Hydrogen peroxide is able to add on nitriles under light basic conditions forming peroxy-carboximidic acids [17], which are stronger epoxidation agents than pure hydrogen peroxide.

Scheme 3:



An additional catalyst like MoO_3 should not be necessary. Therefore, further experiments were done without catalyst using various amounts of hydrogen peroxide and NaHCO_3 . It was found, that conversion is higher when no extra catalyst is used and small doses of base are applied. Furthermore, several additions of small portions of peroxide and base led to better results, whereas beside **2** also **3** is formed.

Table 4: Attempts to epoxidize **1** using H_2O_2 and acetonitrile

Entry	H_2O_2	NaHCO_3	Result ¹
1	2x 10 eq.	1 x 0.25 eq.	+
2	2x 10 eq.	1 x 0.25 eq.	+
3	3x 10 eq.	1 x 0.25 eq.	+
4	2x 5 eq.	1 x 0.25 eq.	+
5	3x 10eq.	3 x 0.25 eq.	+
6	10 eq. + 2x 5 eq.	3 x 0.25 eq.	+

¹ \pm = positive or negative conversion of starting material

The product obtained after workup was analyzed using HPLC-MS and contains next to **2** and **3** also by-products like **7**. Differentiation between these products was done by comparing the fragmentations of the mass signals. However, the main components of the obtained solid are by-products like **5** and **8**, which were isolated using column chromatography. The generation of epoxy functionalities was confirmed by NMR analyses (Figure 4). Furthermore, the mechanism via peroxy-carboximidic acids was approved, as acetamide was isolated from the reaction residue. Epoxidation was successful, but the requested structures **2** and **3** were only formed in minor amounts. Basically, hydrolysis of dimethylamino groups occurred forming **4,5**, and **8**.

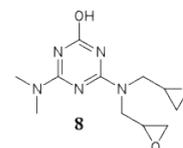


Figure 3: By-product formed in the reaction of **1** with H_2O_2 in acetonitrile. 2-hydroxy-4-diglycidylamino-6-dimethylamino-1,3,5-triazine (**8**)

Acetamide: 0.14 g white solid, mp: 78-79 °C, ¹H-NMR (200 MHz, DMSO-d₆, 30 °C): δ = 7.25 (s, 1H, -NH), 6.64 (s, 1H, -NH), 1.76 (s, 3H, -CH₃) ppm; IR (KBr) ν = 3347, 3187, 2807, 2353, 2320, 1660, 1393, 1348, 1149, 1044, 1001, 873, 825 cm⁻¹

Jacobsen epoxidation

At first a bleach solution is prepared by mixing 8.4 mL (12.5 mmol) sodium hypochlorite solution (10%) and 16.8 mL (0.05 M) of an aqueous disodium hydrogen phosphate solution. pH value is brought to 11.3 by addition of sodium hydroxide. A three-necked round-bottom flask is charged with 0.50 g (1.9 mmol) **1** dissolved in 2 mL dichloromethane, 0.13 g (0.8 mmol) 4-phenylpyridine-N-oxide and 0.08 g (0.1 mmol) **9** under an argon atmosphere. The mixture is cooled to 0 °C and 10.4 mL of the bleach solution are added over a period of 30 minutes. Stirring is continued for 5 hours. Afterwards, dichloromethane and water are added and the organic layer is washed two times with water. The black residue is further worked up using column chromatography (silica gel 60, chloroform:methanol = 30:1). However, neither product nor starting material was detected using ESI-MS and NMR.

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