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Chinese Chemical Letters 23 (2012) 1254–1258
CHINESE CHEMICAL LETTERS
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Insights on the mechanism for synthesis of methylenedianiline from aniline and formaldehyde through HPLC–MS and isotope tracer studies

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Received 29 May 2012
Available online 24 October 2012

Abstract

The mechanism for synthesis of 4,4-methylenedianiline (MDA) *via* condensation reaction of aniline with formaldehyde has been studied extensively in this paper. The intermediate and by-products were isolated and identified. The combination of isotope labeling and HPLC–MS characterizations disclosed that the reaction proceeded through an S_N2 reaction mechanism. Moreover, the effect of aniline/formaldehyde molar ratio on the formation of MDA was investigated. This work would be of significance to understand the reaction mechanism deeply and provide valuable information for further improving the yield of desired product.
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Keywords: 4,4-Methylenedianiline; Condensation reaction; Mechanism; HPLC–MS; Isotopic tracer

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Methylenedianiline (MDA) has been widely used as starting material for the production of 4,4-methylene diphenylene diisocyanate (MDI), which is an important precursor for the manufacture of polyurethanes. A variety of methods have been reported for the synthesis of MDA [1–3]. Ongoing efforts were devoted to developing new catalysts [4–6] or optimizing reaction conditions [7,8]. Industrially, MDA is obtained from the reaction of aniline with formaldehyde in the presence of liquid acid catalysts. Nevertheless, few reports have dealt with the research on the formation process of the intermediate and by-products. Therefore, it is necessary to use appropriate characterization methods, thus giving insights on the mechanism for the MDA synthesis.

In this work, MDA was synthesized by the condensation reaction of aniline and formaldehyde in the presence of HCl. The intermediate and major by-products were isolated and characterized, and DCl was used as a probe to study the deuterium distribution in products. Using high performance liquid chromatography–electrospray tandem mass spectrometry (HPLC–MS) analysis, the structures of products can be confirmed, and the related mechanism of MDA synthesis from aniline and formaldehyde *via* multistep reactions is discussed. Additionally, the effect of aniline/formaldehyde molar ratio on the formation MDA was also studied.

It should be mentioned that Kishore [9] proposed the condensation process consisting of a series of rearrangement reactions in previous literature as shown in Scheme 1. Firstly, aniline first reacts with formaldehyde to provide

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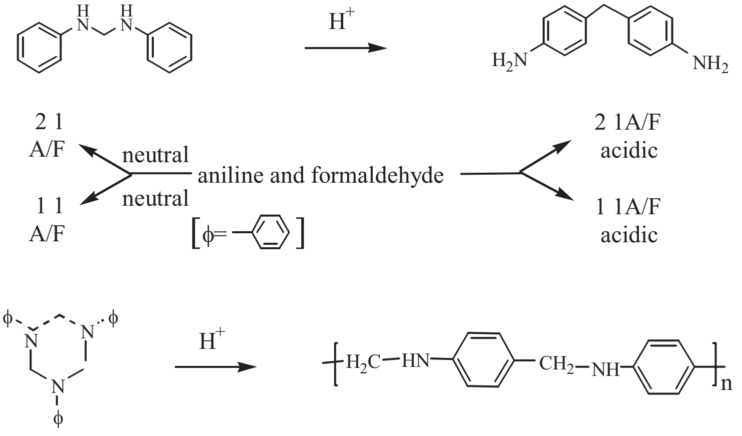
http://dx.doi.org/10.1016/j.cclet.2012.10.001

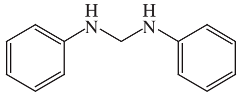
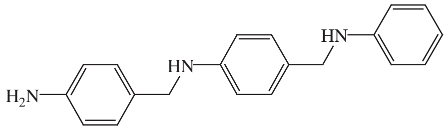
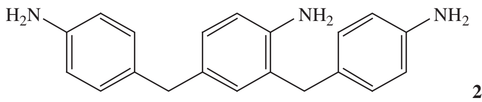
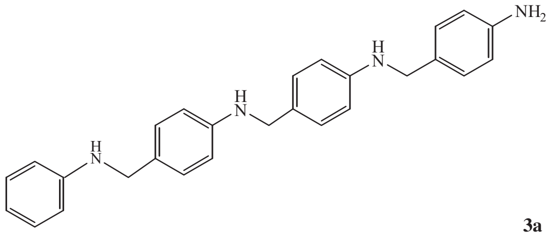
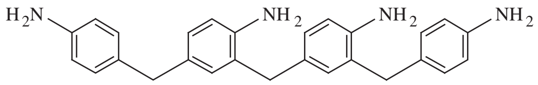


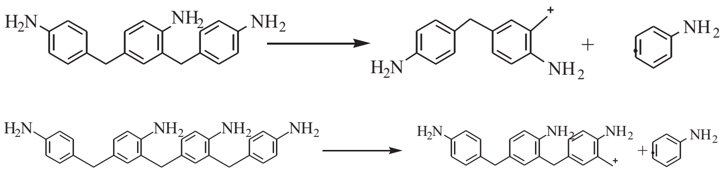
Scheme 1. Mechanism of HCl-catalyzed alternating condensation of aniline and formaldehyde.

N,*N*-methylene diphenylamine (aminal). Subsequently, the aminal formed reacts with HCl and produces MDA. Finally, MDA would be partially converted to oligomers with functionalities of 3 and 4 (*tri*-MDA and *tetra*-MDA) in the presence of acid catalyst.

The intermediate and by-products of *tri*-MDA and *tetra*-MDA formed during the reaction were labeled as **1**, **2** and **3**, respectively. Their configurations were first sketched by excluding other imagination structures based on the molecular weights measured by MS[1], as shown in Table 1.

Table 1
The molecular weights and structures of **1**, **2** and **3**.

Compounds	*m/z* (M+1)$^+$	Molecule weights	Possible structures	Actual structures
1	199.12	198.12	 **1a**	**1a**
2	304.18	303.18	 **2a**  **2b**	**2b**
3	409.30	408.30	 **3a**  **3b**	**3b**

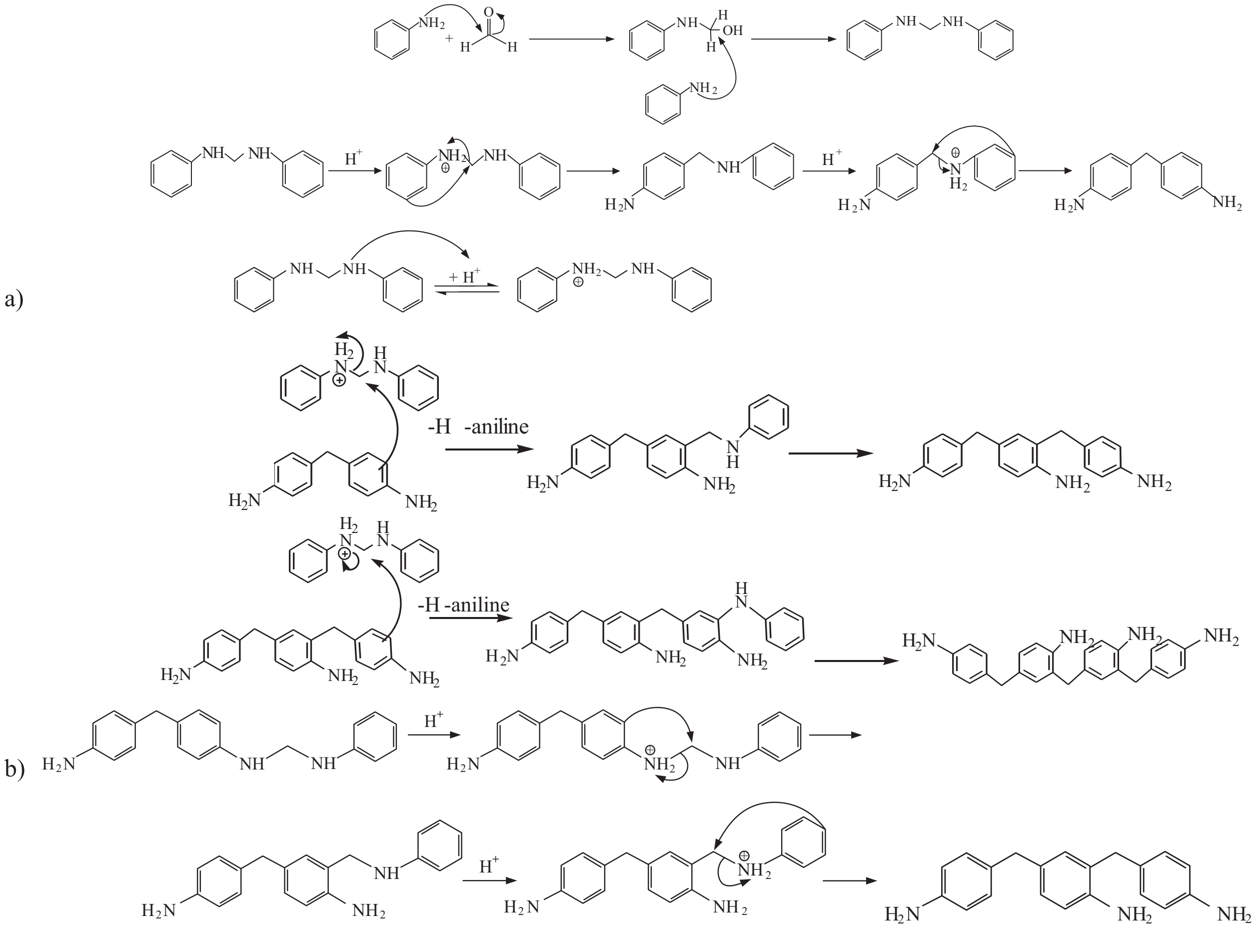


Scheme 2. Proposed cleavage pathways of *tri*-MDA and *tetra*-MDA by HPLC–MS.

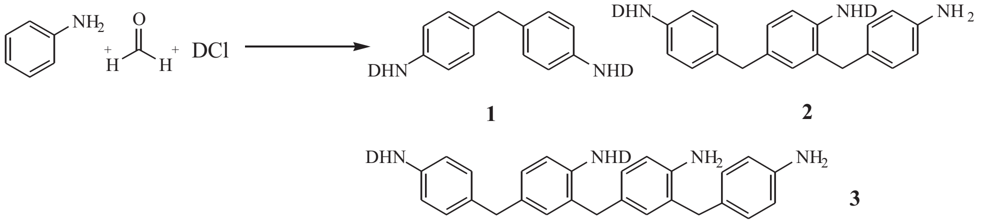
The intermediate **1** could be confirmed by this method. However, it is not enough to confirm the by-products **2** and **3** due to the existing of isomers. The fragments in the MS^2 were therefore used for this purpose.

The proposed pathways of *tri*-MDA and *tetra*-MDA were analyzed by HPLC–MS and shown in Scheme 2. The formation of the fragment ion at *m/z* 211.16 was ascribed to the structure of **2b**, because **2a** could not generate a free radical with such *m/z* value. Thus, by-product **2** was testified to be **2b**. Similarly, by-product **3** was testified as **3b** due to the formation of the fragment ion at *m/z* 316.26, which is impossibly produced from **3a**.

Based on the structures of products confirmed, the mechanism on the formation of MDA, as well as intermediate and by-products could be represented in Scheme 3. The reaction might occur through the nucleophilic addition of adjacent phenyl groups to the cationic carbon atom of formaldehyde. This is the fastest step in this reaction, and can be occurred at room temperature without any acid catalyst. As it is well accepted that free carbonium ions are difficult to stabilize, it suggests that the substrate undergoes an S_N2 type nucleophilic substitution reaction. When the



Scheme 3. Possible mechanism of HCl-catalyzed condensation of aniline and formaldehyde. (a) Proposed mechanism for chain reaction. (b) Further transformation of MDA to downstream derivates might occur under appropriate conditions.



Scheme 4. Expected deuterium enrichment in the reaction of aniline, formaldehyde and DCl.

intermediate is interacted with a Brønsted acid site of the catalyst, the positive partial charge on the C-atom between two benzene rings makes it susceptible to a nucleophilic attack by the free electron pair of the amino function or the phenyl ring of aniline.

The protonation of the secondary amine function is readily achieved by acid catalysis as revealed in Scheme 3(a). This reaction mechanism also provides an explanation for the formation of *tri*-MDA and *tetra*-MDA. *Tri*-MDA and *tetra*-MDA are stable end products of this reaction, and they are both the products of the nucleophilic attack between MDA or *tri*-MDA with aminal molecule. A similar mechanism has been suggested by theoretical speculation as shown in Scheme 3(b).

If the nucleophilic attack occurred on the nitrogen of MDA instead of phenyl ring, MDA-aminal would be formed. Because it contains a methylene bridged biphenyl unit like MDA as well as the secondary amine, it was labeled as MDA-aminal. The molecule is still reactive and can be further converted to *tri*-MDA due to this secondary amino function.

The desired product of MDA and by-products of *tri*-MDA and *tetra*-MDA formed by the reaction were indentified by HPLC–MS. By ion selective mass spectra calibration, the mass peaks at *m/z* 200, 305 and 410 could be assigned to MDA, *tri*-MDA and *tetra*-MDA based on the analysis of corresponding molecular mass, respectively. The results indicated that the distribution of deuterium was the same as the structures in Scheme 4. With respect to the analysis for the reaction, it can be concluded that the mechanism of aniline and formaldehyde complied *via* the pathway of Scheme 3(a).

In this reaction, aniline serves as reactant and solvent. Fig. 1 revealed the dependence of MDA yield on aniline/formaldehyde molar ratio. When aniline/formaldehyde was lower than 2, aminal was easily formed *via* the reaction of aniline and formaldehyde due to the higher concentration of formaldehyde. According to the mechanism discussed above, *tri*-MDA and *tetra*-MDA of polycondensation reactions are easily formed when the aminal concentration is high. The concentration of formaldehyde in the reaction system became lower with the increase of aniline/formaldehyde molar ratio, resulting in too low concentration of condensation reagent to conduct further polymerization. The molar ratio of aniline/formaldehyde at 3 is suitable for obtaining higher MDA yield.

The formation of intermediate and by-products in the condensation reaction of aniline with formaldehyde over HCl catalyst was studied in this work. When DCl was used as probe, there was H/D exchange during the production of MDA and its by-products. HPLC–MS was used to character the distribution of D. Importantly, based on these results,

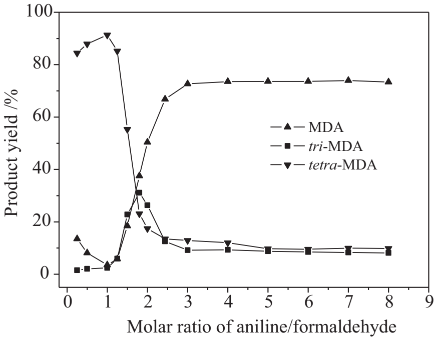


Fig. 1. The effect of molar ratio of aniline/formaldehyde on the formation of MDA and by-products ($T = 100$ °C, $t = 90$ min, HCl/aniline = 1.5).

the condensation reaction is proposed to be occurred through S_N2 reaction mechanism. The results revealed that the amount of aminal can evidently influence the formation of *tri*-MDA and *tetra*-MDA. The experimental results also precisely illustrated this point.

Acknowledgment

This work was supported by the Knowledge Innovation Program of the Chinese Academy of Sciences (No. KGCX2-YW-215).

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