



Synthesis and Geometric Structure of N,N,N'-tris(Benzoyl)trimesinic Acid Dihydrazide

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N,N,N'-Tris(benzoyl) trimesinic acid dihydrazide was synthesized from benzoyl hydrazine and trischloride and the structures of N,N,N'-tris(benzoyl) trimesinic acid dihydrazide had been characterized by Fourier transform infrared spectroscopy, ¹H nuclear magnetic resonance techniques. The reaction condition was investigated by orthogonal experiment and the optimized reaction condition by orthogonal experiment is molar ratio of benzoyl hydrazine: trischloride 5:1, reaction time 4 h, reaction temperature 70 °C, the yield is 65.7 %. SEM showed the particles of N,N,N'-tris(benzoyl)trimesinic acid dihydrazide were not completely regular and the average size of the particles was 3-4 μm. At the same time, the optimized geometric structure of N,N,N'-tris(benzoyl)trimesinic acid dihydrazide was carried out by theoretical calculations using the semiempirical method PM3.

Key Words: Trisamides, Benzoyl hydrazine, Trimesinic acid, Orthogonal experiment.

INTRODUCTION

Amides have been widely used in synthetic intermediates¹, material chemistry², drug discovery³, polymer^{4,5} due to their antitumour⁶, antibacterial⁷ and nucleating properties⁸, etc. For example, Du *et al.*⁹ reported that a novel dihydrophilic beatine, N,N-bis[3-(dimethylcarboxymethylammonio)propyl]lauramide was synthesized using lauroyl chloride, tetramethyldipropylene-triamine and sodium chloroacetate as starting materials and surface chemical properties of the product were measured. The result showed that the lowest surface tension was 36.04 mN/m, critical micelle concentration was 1.07×10^{-3} mol/L at 25 °C.

In previous work¹⁰, we had synthesized some bisamides compounds and these bisamides compounds can serve as a nucleating agent of poly(L-lactic acid) for dramatic increasing in crystallization rate and final crystalline content as indicated by isothermal and non-isothermal crystallization measurements. Thus, in this paper, to develop more amides, N,N,N'-tris(benzoyl)-trimesinic acid dihydrazide was synthesized from benzoyl hydrazine and trischloride and the reaction condition, morphology and the optimized geometric structure of N,N,N'-tris(benzoyl)trimesinic acid dihydrazide was investigated.

EXPERIMENTAL

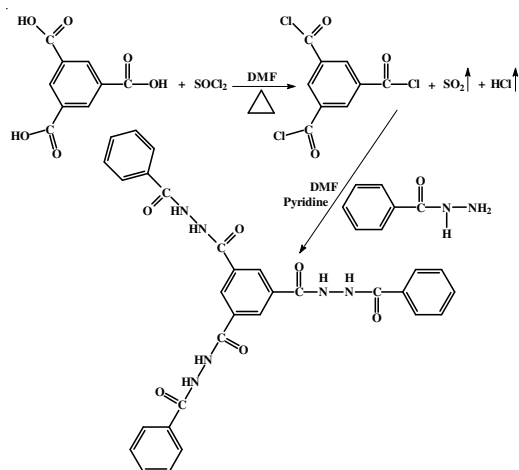
Benzoyl hydrazine, trimesinic acid, thionyl dichloride, N,N-dimethylacetamide and pyridine in this study were of analytical grade (AR).

Synthesis of N,N,N'-tris(benzoyl)trimesinic acid dihydrazide: N,N,N'-tris(Benzoyl)trimesinic acid dihydrazide was prepared as shown in **Scheme-I**: trimesinic acid, thionyl dichloride of 60 mL in the presence of N,N-dimethylacetamide as catalyst was mixed and the mixture was heated up to 80 °C and held at 80 °C for 10 h with stirring. After cooling to room temperature and evaporation of thionyl dichloride in vacuum, the residue was trischloride.

Benzoic hydrazide and N,N-dimethylacetamide of 50 mL were mixed and the mixture was purged under nitrogen atmosphere. Trischloride was added slowly onto the mixture, followed by adding pyridine of 0.06 mol and the mixture was heated up to certain temperature and held for period of time with stirring. Reaction mixture was poured onto water of 300 mL and stirred, followed by filtrating. Obtained crude product was washed four times by water of each 250 mL at room temperature and then washed by methanol of 200 mL at 50 °C to eliminate raw materials and by-products, the resulting product was dried in a vacuum at 45 °C.

Fourier transform infrared spectra were recorded on a Bio-Rad FTS135 spectrophotometer from 4000-400 cm⁻¹. The sample of N,N,N'-tris(benzoyl)trimesinic acid dihydrazide was mixed with KBr powders and pressed into a disk suitable for IR measurement.

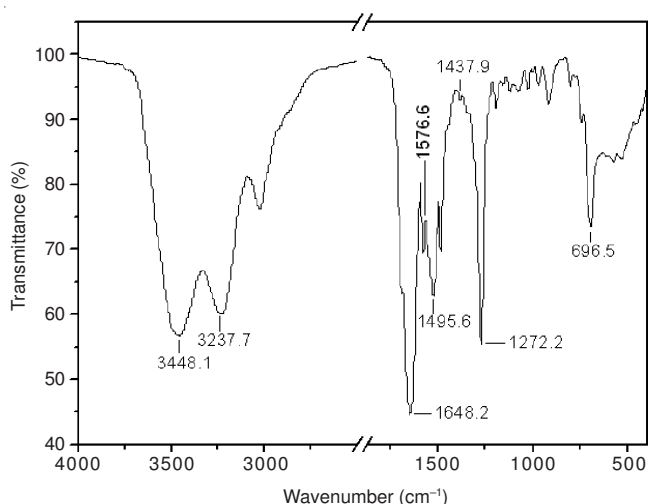
¹H nuclear magnetic resonance of N,N,N'-tris(benzoyl)-trimesinic acid dihydrazide was recorded on Bruker AVANCE 300 spectrometers. The solvent was dimethyl sulphoxide.

Scheme-I: Synthesis of *N,N,N'*-tris(benzoyl)trimesinic acid dihydrazide

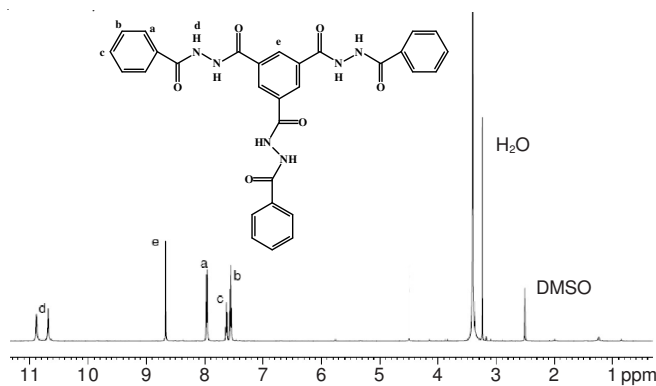
The morphologies of *N,N,N'*-tris(benzoyl)trimesinic acid dihydrazide was examined by XL-30 ESEM FEG, Philips, in 15-20 kV accelerating voltage (Tungsten filament).

RESULTS AND DISCUSSION

Structures of *N,N,N'*-tris(benzoyl)trimesinic acid dihydrazide: FT-IR spectra of *N,N,N'*-tris(benzoyl)trimesinic acid dihydrazide was shown in Fig. 1. In the spectra, the peaks at 3448.1 and 696.5 cm^{-1} contribute to the absorption of N-H stretching vibration and the plane bending vibration; the absorption peak at 3238 cm^{-1} belongs to C-H stretching vibration of benzene; and the absorption peak at 1648 cm^{-1} contribute to C=O stretching vibration of the amide group. Then the absorption peaks at 1577, 1496 and 1438 cm^{-1} proved the existence of a benzene. The absorption peak at 1272 cm^{-1} was mixed peak including C-N stretching vibration and N-H bending vibration absorption.

Fig. 1. FTIR spectra of *N,N,N'*-tris(benzoyl)trimesinic acid dihydrazide

^1H NMR patterns of *N,N,N'*-tris(benzoyl)trimesinic acid dihydrazide is depicted in Fig. 2. The single peak at $\delta_{\text{H}} = 10.88$ and 10.68 are proton resonance peaks of N-H of *N,N,N'*-tris(benzoyl)trimesinic acid dihydrazide, the multiple peaks at $\delta_{\text{H}} = 7.54\text{--}7.97$ are proton resonance peaks of benzene of benzoyl hydrazine. However, the single peaks at $\delta_{\text{H}} = 8.67$

Fig. 2. ^1H NMR spectra of *N,N,N'*-tris(benzoyl)trimesinic acid dihydrazide

belongs to proton resonance peak of benzene of trimesinic acid. Infrared spectrum and ^1H NMR analysis confirms that *N,N,N'*-tris(benzoyl)trimesinic acid dihydrazide was synthesized.

Synthesis conditions of *N,N,N'*-tris(benzoyl)trimesinic acid dihydrazide: The influence of the reaction ratio, reaction time and reaction temperature to the yield of *N,N,N'*-tris(benzoyl)trimesinic acid dihydrazide was investigated by orthogonal experiment. Factors and level of orthogonal experiment are listed in Tables 1 and 2. The influence of reaction time to yield of *N,N,N'*-tris(benzoyl)trimesinic acid dihydrazide is the greatest and the influence of reaction temperature is the weakest. The reason is that the yield of *N,N,N'*-tris(benzoyl)trimesinic acid dihydrazide can be improved with only suitable reaction time due to high reactivity of trischloride and it is also because of the high reactivity of trischloride that the reaction rapid occurs on the condition of room temperature, which result in the weakest influence of reaction temperature.

TABLE-1
FACTORS AND LEVEL OF ORTHOGONAL EXPERIMENT

Level	Factor		
	Reaction time (A) (h)	Reaction ratio ^a (B)	Reaction temperature (°C)
1	2 h	1:3	60
2	4 h	1:4	70
3	6 h	1:5	80

^aTrischloride: Benzoic hydrazide.

TABLE-2
RESULTS OF ORTHOGONAL EXPERIMENT

Run	A	B	C	Scheme	Yield (%)
1	1	1	1	A ₁ B ₁ C ₁	61.80
2	1	2	2	A ₁ B ₂ C ₂	73.16
3	1	3	3	A ₁ B ₃ C ₃	75.98
4	2	1	2	A ₂ B ₁ C ₂	73.37
5	2	2	3	A ₂ B ₂ C ₃	67.70
6	2	3	1	A ₂ B ₃ C ₁	80.29
7	3	1	3	A ₃ B ₁ C ₃	68.96
8	3	2	1	A ₃ B ₂ C ₁	52.35
9	3	3	2	A ₃ B ₃ C ₂	61.31
K ₁	2.11	2.04	1.94	—	—
K ₂	2.21	1.93	2.08	—	—
K ₃	1.83	2.18	2.13	—	—
Extreme difference	0.38	0.25	0.19	—	—
Important factor	A > B > C				
Optimized scheme	A ₂ B ₃ C ₃				

Thus, the optimized reaction condition by orthogonal experiment is molar ratio of benzoyl hydrazine: trischloride 5:1, reaction time 4 h, reaction temperature 70 °C. However, the optimized scheme is not in orthogonal experiment, it is necessary that the experiment should be carried out with the optimized scheme and the result shows that the yield of N,N,N'-tris(benzoyl)trimesinic acid dihydrazide is the highest with optimized condition and the yield is 87.3 %.

Morphology and geometric structure of N,N,N'-tris(benzoyl)trimesinic acid dihydrazide: Morphology of synthesized N,N,N'-tris(benzoyl)trimesinic acid dihydrazide was observed by SEM (B is the partly amplificatory images of A, respectively). As seen in Fig. 3, the particles of N,N,N'-tris(benzoyl)trimesinic acid dihydrazide are not completely regular and there existed large and small particles, resulting form uneven mixing during reaction and purification or van der Waals and coulombic forces between the particles and the average size of the N,N,N'-tris(benzoyl)trimesinic acid dihydrazide particles was 3-4 μm .

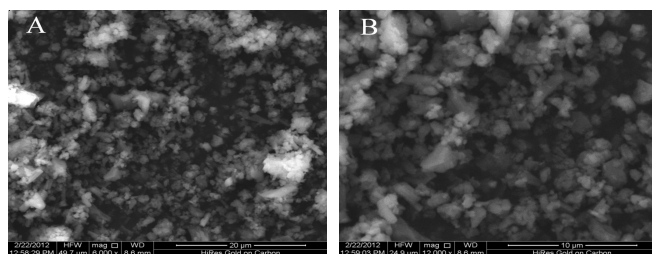


Fig. 3. SEM of N,N,N'-tris(benzoyl)trimesinic acid dihydrazide

The optimized geometric structure of N,N,N'-tris(benzoyl)trimesinic acid dihydrazide was carried out by the theoretical calculation and the calculations were performed using DMol3. The optimized geometry structure of N,N,N'-tris(benzoyl)trimesinic acid dihydrazide is shown in Fig. 4 and the HOMO and LUMO of N,N,N'-tris(benzoyl)trimesinic acid dihydrazide is -0.20778 and -0.107521 eV, respectively.

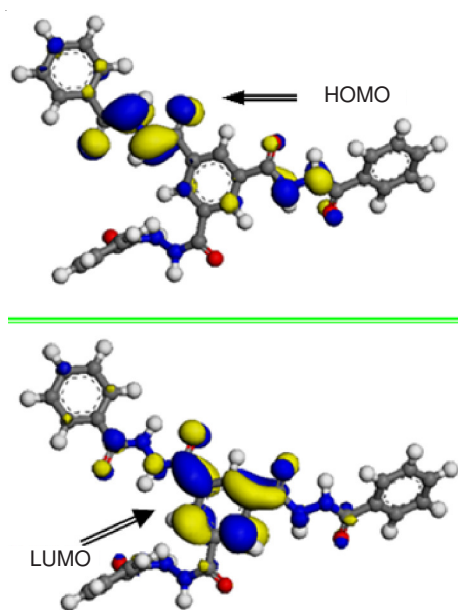


Fig. 4. Optimized geometric structure, HOMO and LUMO of N,N,N'-tris(benzoyl)trimesinic acid dihydrazide

Conclusion

N,N,N'-tris(Benzoyl)trimesinic acid dihydrazide was synthesized from benzoyl hydrazine and trischloride which was deprived from trimesinic acid *via* acylation. The optimized reaction condition was obtained by the orthogonal experiment. Morphology of N,N,N'-tris(benzoyl)trimesinic acid dihydrazide were not completely regular and the average size of the particles was 3-4 μm . The optimized geometric structure of N,N,N'-tris(benzoyl)trimesinic acid dihydrazide was carried out by theoretical calculations using the semi-empirical method PM3.

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