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Synthesis of Schiff Base Derived from *p*-Aminobenzoic Acid by Solvent-Free Reaction Using Jet Milling

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A novel synthesis method on solvent-free reaction using jet milling was described. Synthesis of three Schiff bases derived from *p*-aminobenzoic acid had been achieved by this solvent-free reaction using jet milling and the structures of these compounds had been characterized by Fourier transform infrared spectroscopy, ^{1}H NMR techniques and mass spectrometry. This solvent-free reaction using jet milling not only involved mild conditions, a simple operation and short reaction time, but also gave high yield without waste producing work-up procedures. Simultaneously, the investigation also showed this reaction method was feasible and of benefit to environment.

Key Words: Solvent-free reaction, Jet milling, Schiff base, *p*-Aminobenzoic acid.

INTRODUCTION

With the increasing public attention to energy problems and environmental pollution, the research of green chemistry has gained considerable momentum in recent years[1-4]. A solvent-free reaction at low temperature, *viz.* from room temperature to 100 ºC, has particular advantages such as simple manipulation, high selectivity and productivity, low cost, *etc.*[5]. Therefore, this method is used widely as a green chemistry method. An important goal of green chemistry is to develop high yield reactions that do not require workup for removal of catalysts, supports, solvents or other auxiliaries[6]. Thus, the up-scaling of quantitative solvent-free reaction using jet milling is of technical importance. Schiff base attracted great and growing interest in biology and chemistry for many years due to their facile synthesis and wide applications[7-9]. Schiff base and its metal complexes have been shown to exhibit a variety of interesting biological actions, including antibacterial[10], antimicrobial[11], antitubercular[12] and antifungal activities[13]. The previous synthesis of Schiff base was achieved by liquid reaction[14], grinding[15] and high energy ball mill[6]. In this paper, we reported a novel solid-state reaction method on the solvent-free reaction using jet milling and synthesis of three Schiff bases derived from *p*-aminobenzoic acid had been achieved by this reaction method.

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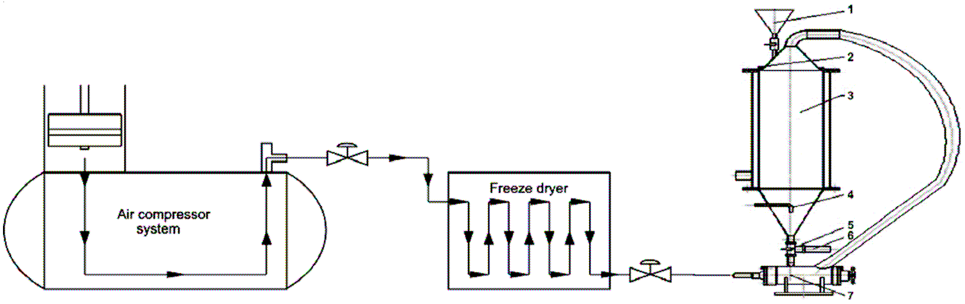
EXPERIMENTAL

Materials and processing route: All materials used in this study were of analytical grade(AR). *p*-Nitrobenzaldehyde, *p*-dimethylamino benzaldehyde and *p*-hydroxy benzaldehyde were purchased from Chengdu Kelong Chemical Reagents Company (Sichuan Province, China) and *p*-aminobenzoic acid was purchased from Beijing Chemical Reagents Company (Beijing, China).

The development of many different milling technologies led to the appearance of the jet mills. Usually, the jet milling was used to produce powder-materials with new and in so far interesting properties. The processing route of jet milling is simple. The powder particles are fed into the flat cylindrical milling chamber tangentially through a venturi system by pressurized air. The particles are accelerated in a spiral movement inside the milling chamber by nozzles, the micronizing effect takes place by the collision between the incoming particles and fixed target. In fact, present reaction equipment (Fig. 1), is based on jet milling. Reactant particles are accelerated to the velocity of sound by the high pressure airflow and sprayed on to the fixed target at high speed. Particle collisions at the fixed target lead to their fracture and their activation and subsequent reaction through an intense energy exchange between the fixed target and themselves.



1-Loading hopper; 2-delivery valve; 3-circulation collecting system; 4-adjustable jet pipeline; 5-tee globe valve; 6-outlet port; 7-reaction zone

Fig. 1. Schematic drawing of the reaction

Synthesis of three Schiff bases: Schiff base was prepared as follows: *p*-aminobenzoic acid and fragrant aldehyde (*p*-hydroxy benzaldehyde, *p*-dimethylamino benzaldehyde and *p*-nitro benzaldehyde), in a 1:1 molar ratio, were mixed and the specific reaction process have described in our previous paper[16]. The product was collected after quantitative reaction (DTA experiments indicated 100 % conversion) and dried in a vacuum at 90 ºC.

Schiff base tests (attribute): The infrared spectra were measured on Nicolet 380 FT-IR spectrometer (KBr pellet), in the range 4000-400 cm^{-1}. The ^1H NMR were recorded on Brucker AVANCE 300 spectrometers. The mass spectra were measured on Brucker Biflex-III Maldi-TOF spectrometer. Differential thermal analysis (DTA) curves were recorded on a WCR-1B analyzer at a heating rate of 10 ºC/min, atmosphere and the reference α-Al_2O_3.

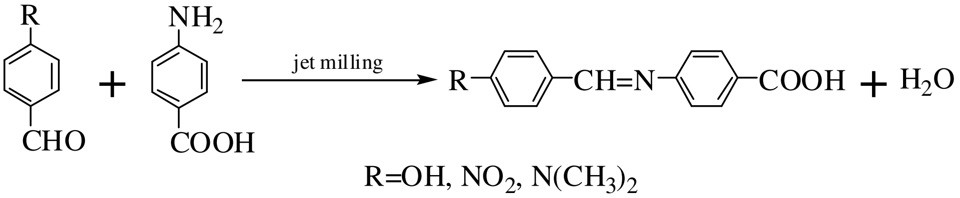


Fig. 2. Synthesis of three Schiff bases

RESULTS AND DISCUSSION

Schiff base derived from *p*-hydroxy benzaldehyde and *p*-aminobenzoic acid (compound A): IR (KBr, ν_{max}, cm^{-1}): 3420, 1683, 1623, 1601, 1570, 1513, 1443, 1165, 831, 773; ^{1}H NMR (DMSO, 300 MHz, ppm) δ: 8.47(s, 1H, CH=N), 10.23(s, 1H, Ar-OH), 12.78 (s, 1H, COOH), 6.88-7.96 (m, 8H, Ar); MS (Maidi-Tof) m/z: 240.1 ([M - 1]$^+$), 196.1 ([M-COOH]$^+$).

Schiff base derived from *p*-nitro benzaldehyde and *p*-aminobenzoic acid (compound B): IR (KBr, ν_{max}, cm^{-1}): 3425, 1681, 1629, 1601, 1589, 1572, 1515, 1424, 1343, 856, 775; ^{1}H NMR (DMSO, 300 MHz, ppm) δ: 8.82 (s, 1H, CH=N), 12.78(s, 1H, COOH), 7.38-8.39 (m, 8H, Ar); MS (Maidi-Tof) m/z: 270.2 ([M]$^+$), m/z 269.2 ([M - 1]$^+$).

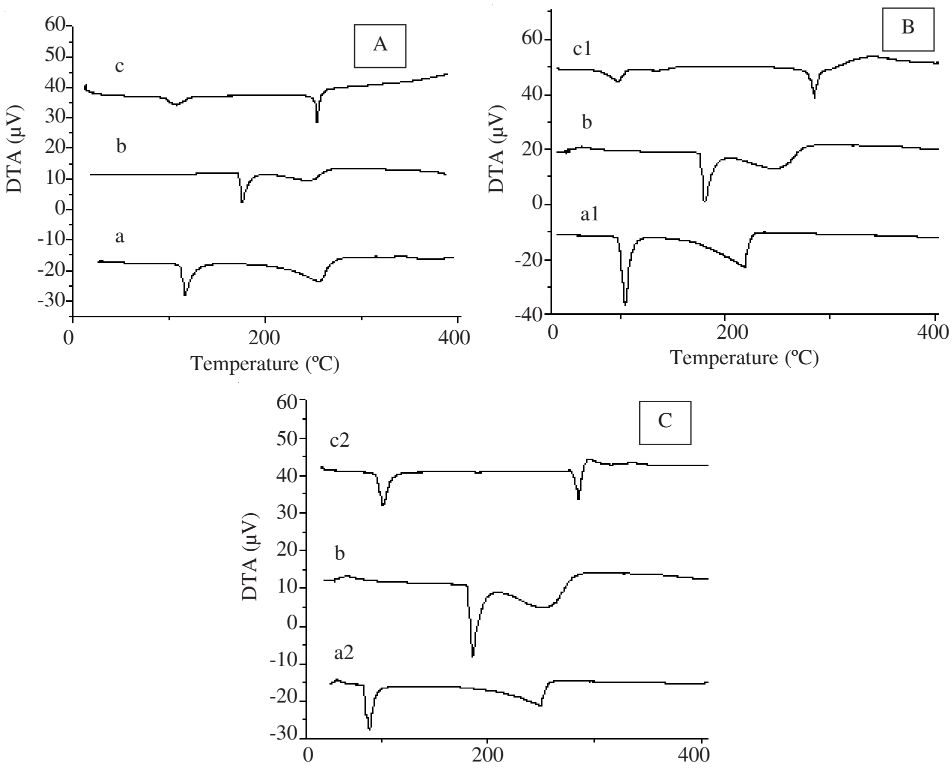
Schiff base derived from *p*-dimethylamino benzaldehyde and *p*-aminobenzoic acid (compound C): IR (KBr, ν_{max}, cm^{-1}): 3425, 2852, 2798, 1679, 1626, 1602, 1584, 1526, 852, 778; ^{1}H NMR (DMSO, 300 MHz, ppm) δ: 8.41 (s, 1H, CH=N), 12.73 (s, 1H, COOH), 6.76-7.96 (m, 8H, Ar), 3.02, 3.00 (s, 6H, -N(CH$_3$)$_2$); MS (Maidi-Top) m/z: 269.1 ([M + 1]$^+$).

DTA and theoretical analysis of reaction process: The influence of the reaction pressure and reaction time to the yields of product were investigated. The relevant reaction conditions and product yield were indicated in Table-1.

TABLE-1
RELEVANT REACTION CONDITIONS AND YIELDS OF FINAL PRODUCTS

Compound	Reaction press (Mpa)	Reaction time (min)	Yield (%)
A	0.2	6	91.1
B	0.2	4	91.8
C	0.4	7	92.5

Simultaneously, in order to comfirm 100 % conversion, DTA experiments were used to detect the reaction process. Fig. 3 showed the DTA experiments of three reaction system at different reaction time. From the DTA spectra of figure A, After 6 min with 0.2 MPa of reaction press, the melting peak of *p*-hydroxy benzaldehyde and *p*-aminobenzoic acid disappeared and raw materials melting endothermic peaks were replaced by the peaks for both water at 100 ºC and productat 245 ºC according to the melting point reported by the literature[6], which showed that the reaction was thus complete after the 6 min. This favourable solvent-free technical procedure was remarkable, as the previous synthesis of the compound **A** required 12 h boiling in ethanol and no yield was reported[14] or required 15 min by high energy ball mill[6]. The DTA spectra did reveal the quantitative reaction of the reactant, but the practical yield was 91.1 % (theoretical yield: 93.1 %), resulting from product's adsorption in the reactor wall. As far as compound **B** and compound **C** are concerned, DTA experiments also indicated 100 % conversion (compound B, reaction time: 4 min, press: 0.2 MPa; compound C, reaction time: 7 min, press: 0.4 MPa) as shown in Figs. B and C.



(a) *p*-Hydroxy benzaldehyde a1: *p*-Nitro benzaldehyde a2: *p*-Dimethylamino benzaldehyde;
b: *p*-Aminobenzoic acid c: product (6 min) c1: product (4 min) c2: product (7 min)

Fig. 3. DTA Patterns of the raw materials and product at differenet reaction time

In order to discuss the consistency between theoretical and practical reaction, we calculated the HOMO and LUMO energy levels for the reactants employed. Calculations were performed with the program VAMP using the semiempirical method PM3. Frontier molecular orbital theory indicated that the reactivity model was based upon the interaction between the HOMO of *p*-aminobenzoic acid and the LUMO of fragrant aldehyde. The possibility of the reaction was related to the

LUMO (fragrant aldehyde)-HOMO (*p*-aminobenzoic acid) energy gap ΔE (Fig. 4). The calculation results were summarized in Table-2. The energy gap ΔE between *p*-nitro benzaldehyde and *p*-aminobenzoic acid was the smallest, consequently, the reaction condition was easiest as shown in Table-1. The energy gap ΔE between *p*-aminobenzoic acid and *p*-dimethylamino benzaldehyde was 8.604 eV which was biggest, so the highest reaction condition was required. The calculation results explained practical reaction conditions of solvent-free reaction using jet milling.

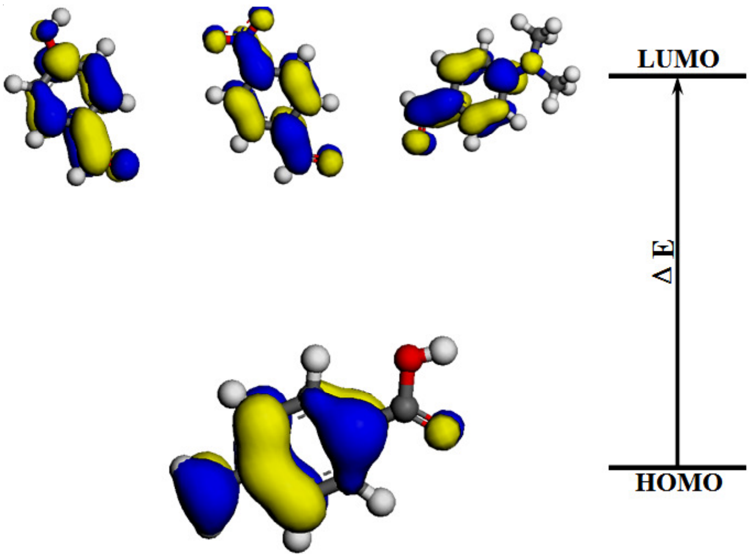


Fig. 4. Energy gap ΔE between LUMO of fragrant aldehyde and HOMO of *p*-aminobenzoic acid

TABLE-2
LUMO AND HOMO LEVELS OF RAW MATERIALS CALCULATED WITH PM3

Compound	E_{HOMO} (eV)	E_{LUMO} (eV)	ΔE (eV)
p-Aminobenzoic acid	-8.969	-0.450	–
p-Hydroxybenzaldehyde	-9.492	-0.452	8.517
p-Nitrobenzaldehyde	-10.824	-1.687	7.282
p-Dimethylaminobenzaldehyde	-8.702	-0.365	8.604

Conclusion

In this paper, we developed a novel Schiff base synthesis method on solvent-free reaction using jet milling. Three Schiff bases derived from *p*-aminobenzoic acid were successfully synthesized by this solvent-free reaction using jet milling. We investigated influence of the reaction pressure and reaction time to the yields of product and calculation results explained practical reaction conditions of solvent-free reaction using jet milling.

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