Synthesis and Characteristic of 5,6-Dinitro and 5,6-Diaminobenzimidazolone-2

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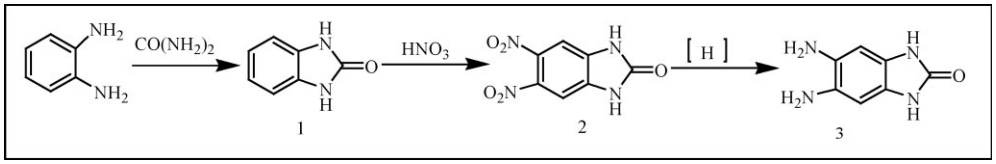

5,6-Dinitro and 5,6-diaminobenzimidazolone-2 can be synthesized at a sufficiently high purity and yield to permit its large scale production in an economically feasible manner. The results of our studies derived optimum conditions for the nitration process necessary to obtain pure 5,6-dinitriobenzimidazolone-2.

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INTRODUCTION

Connected mostly with their ability to form strong hydrogen bonds, benzimidazolone-2 and its derivatives have invoked considerable interest, and they are useful chemicals mainly as the intermediates in production of pharmaceuticals, pesticides, and pigment. 5,6-Dinitrobenzimidazolone-2 possess a variety of biological activities [1] and is explored for corrosion inhibitor [2]. 5,6-diaminobenzimidazolone-2 is widely used in diverse applications such as organic pigments and pharmaceuticals [3].

According to the refs. 4 and 5,5,6-dinitriobenzimidazolone-2 can be obtained by nitration of benzimidazolone-2 or 5-nitrobenzimidazolone-2, and 5,6-diaminobenzimidazolone-2 can be synthesized by reduction of 5,6-dinitriobenzimidazolone (Scheme 1). If pure compounds can obtain by the first method, it has a remarkable advantage in terms of cost.

Although there are some references to the synthesis of two compounds in the literature, very few data were reported. Moreover, the results of our investigations show their purity should be important, since impurities in the substrates can cause a substantial deterioration of the properties of the pigments.

In this article, we provide a process for preparing 5,6-dinitro and 5,6-diaminobenzimidazolone-2 and study the optimum conditions for the nitration reaction. The results indicate two compounds can be synthesized with high purity and yield, which permit a large scale production in an economically feasible manner.

RESULTS AND DISCUSSION

The nitration of bezimidazolone-2 is a key process in the overall reaction, since impure 5,6-dinitrobenzimidazolone-2 can cause a substantial deterioration of the properties of following products. In this article, our special concern is the optimum conditions for the nitric process.

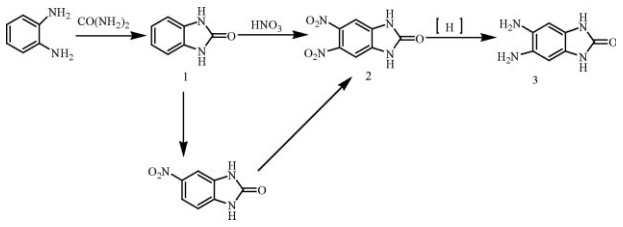
In the nitration reaction, the concentration and the dosage of nitric acid were two important factors. The by-product, 5-nitrobenzimidazolone-2, could be formed when the concentration of nitric acid was lower than 80%. It was found that the preferred concentration of nitric acid was 90% (fuming) [6], and pure 5,6-dinitriobenzimidazolone could be obtained by nitration of benzimidazolone-2 using a excess of fuming nitric acid (1.07:1–1.20:1).

Furthermore, bezimidazolone-2 is soluble in 98% sulfuric acid, and there is a disadvantage of being able to sulfonate starting material. The disadvantage is rarely serious, for nitration is generally a more rapid process than sulfonation, and pure 5,6-dinirtobezimidazolone-2 can be obtained by purified.

To obtain the optimal conditions of the nitration reaction, we designed the L_3^3 orthogonal test, and selected values of D.V.S (Dehydrating value of sulfuric acid), reaction temperature, and reaction time were chosen. The results are shown in Table 1.

The nitrating mixture employed can be characterized by the D.V.S. value. The D.V.S. value is defined as the actual sulfuric acid divided by the total water present

Scheme 1. Synthesis of 5,6-dinitro and 5,6-diaminobenzimidazolone-2.



when nitration is completed, both values being on a weight basis. Hence, water introduced with the reactants-mixed acid and formed in the reaction are both accounted for in the D.V.S. The relationship can be calculated from the equations:

$$\text{D.V.S.} = \frac{\text{Wt. of } H_2SO_4 \text{ used}}{\text{Wt. of } H_2O \text{ at end of reaction}} = \frac{m_{H_2SO_4}}{m_{H_2O}}$$

The results listed in Table 1 show that the higher D.V.S. is, the higher yield is obtained. A 73.75% yield is corresponding to D.V.S. 20. Intuitively, it would seem that the rate of reaction could be increased by increasing concentration sulfuric acid, since an increase in sulfuric acid concentration generates a corresponding increase in nitronium ion activity. Whereas using a significant excess of strong acid would raise the cost of the method, since the acid should be regenerated and purified. Otherwise, the presence of more water in the mixed acid can affect the reaction by (a) increasing the NO_x produced, which increases reaction instability and (b) decreasing the nitrating strength of the acid which, in turn, lowers product yield. Moreover, the results listed in Figure 1 has shown that if D.V.S. exceed 15, the product is low in other by-product impurities without 5-nitrobenzimidazolone-2 and can gain 97% or greater based on HPLC (Fig. 1) by purification. So, this value should be in the range 16–20, more preferably about 20.

Table 1

Parameters and results of the nitration reaction of benzimidazolone-2.[a]

D.V.S.	98% of H_2SO_4 (g)	90% of HNO_3 (g)	Reaction temperature (°C)	Reaction time (h)	Yield[b] (%)
20	44.82	4.02	0–5	2	73.75
20	44.82	4.02	5–10	5	67.35
20	44.82	4.02	10–15	8	66.30
18	37.74	4.02	0–5	5	71.38
18	37.74	4.02	5–10	8	65.13
18	37.74	4.02	10–15	2	69.22
16	31.51	4.02	0–5	8	65.19
16	31.51	4.02	5–10	2	74.05
16	31.51	4.02	10–15	5	60.94

[a] Reaction conditions: benzimidazolone-2, 3.35 g (dissolved in 22.5 g 98% sulfuric acid); the mole ratio of actual nitric acid to theoretical acid, 1.15.
[b] Isolated yield.

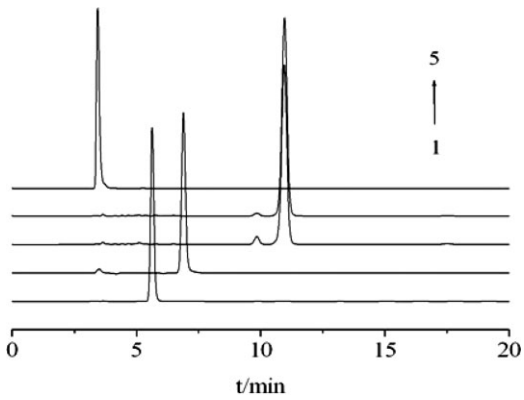


Figure 1. The chromatograms of (1) benzimidazolone-2 (R_f = 5.62, ≥99%); (2) 5-nitrobenzimidazolone-2 (R_f = 6.88, ≥99%, purchased from Aldrich); (3) 5,6-dinitrobenzimidazolone-2 (crude, R_f = 10.95, ≥93%); (4) 5,6-dinitrobenzimidazolone-2 (pure, R_f = 10.95, ≥97%); (5) 5,6-diaminobenzimidazolone-2 (R_f = 3.42, ≥98%).

As the nitration reaction is highly exothermic, it is necessary by using cooling techniques. As regards reaction temperature, pure product by further recrystallization can be obtained below 15°C, and the reaction temperature preferably being in the range of from about 0 to about 5°C. Eventually, it could be shown from Figure 1 that two by-product impurities (R_f = 9.84 and R_f = 17.50) were formed and have a certain relation. When the reaction time is extended, the product (R_f = 9.84) is slowly decreased, and another is increased. Both of them are inevitably formed, however, the total will be less below 5°C. Preferably, the reaction temperature is below 5°C by means of controlling the dropping rate. Immediately after the addition of the mixed acid was complete, the cold solution was poured into ice-water.

The results of our investigations indicated the purity of 5,6-dinitriobenzimidazolone-2 did not affect its reduction process. 5,6-Diaminobenzimidazolone-2 was easily oxidized by oxygen, so the reduction of 5,6-dinitriobenzimidazolone-2 should be under nitrogen, and the light yellow 5,6-diaminobenzimidazolone-2(HPLC 98%) could be obtained.

EXPERIMENTAL

All the reagents were reagent grade and were used without further purification unless otherwise noted. Melting points were determined on a SPSIC WRS-1B digital melting point apparatus which is uncorrected. Infrared spectra were recorded as KBr pellets for all the samples on a Perkin Elmer FT-IR instrument. Nuclear Magnetic Resonance spectra were

recorded as indicated on a Varian INOVA600 spectrometer operating at 600 MHz for ^{1}H nuclei and 150 MHz for ^{13}C nuclei. Chemical shifts are reported downfield from TMS, and coupling constants are given in hertz. Mass spectra were obtained on Perkin Elmer Mass Spectrometer. The elemental analysis was carried out using Flashea 1112Series CHNS-O Analyzer and the METTLER TOLEDO MX5 (Max5.1 g d = 1 μg) weighting device. Quantitative analyses were carried out over a Shimadzu LC−20A HPLC (Column: Ultimate XB-C18 150 × 4.6 mm, 5 μm).

Benzimidazolone-2 (1). Following a literature procedure, a mixture of 54 g (0.5 mol) *o*-phenylenediamine, 34 g (0.57 mol) urea, and 95 mL glycol were stirring under nitrogen for 1 h at 130–140°C, and then heated in an oil bath at a maximum temperature of 170°C for 7 h [7]. The solution was cooled down to 40–50°C, and ∼35 mL of 95% ethanol were added with stirring for 10 min, then ∼100 mL of water were added. The precipitate was recovered by suction filtration and slurried with successive batches of water and 95% ethanol. The residue was dried at 100°C to give 60.2 g of white benzimidazolone-2 (1). Yield 89.9%. M.P.: 317.7–318.6°C; HPLC ≥ 99%, IR: 3128.74, 3021.52, 1741.41, 1484.26, 736.67 cm^{-1}; ^{1}H NMR (DMSO, 600 MHz): δ 6.87(s, 4H), 10.54 (s, 2H); ^{13}C NMR (DMSO, 150 MHz): δ 109.133, 121.060, 130.311, 155.934. Anal. calc. for $C_7H_6ON_2$: C 62.69, H 4.48, N 20.90; found: C 62.79, H 4.60, N 20.59.

5,6-Dinitrobenzimidazolone-2 (2). According to a variation of the method of literature, 5,6-dinitrobenzimidazolone-2 was prepared. Benzimidazolone-2 (67 g, 0.50 mol) was dissolved in 450 g 98% sulfuric acid. The colorless solution was cooled to 0–5°C in an ice bath and 80 g (1.14 mol) of 90% fuming nitric acid in 470 g 98% sulfuric acid was added dropwise to the cooled, stirred solution. The reaction temperature was not allowed to go above 5°C during the addition. After the addition of the nitric acid was complete, the cold solution was poured onto 3 kg of ice rapidly. The yellow precipitate was collected *via* filtration and washed thoroughly four times with 1-L portions of cold water. After drying at 100°C, 101.6 g yellow 5,6-dinitrobenzimidazolone-2 was obtained (HPLC 93%). Yield 90.7%. The crude 2 was recrystallized from 60% aqueous acetone to afford 80 g pure 2. M.P. > 300°C, HPLC ≥ 97%, IR: 3289.9, 3073.67, 1721.95, 1629.54, 1537.29, 1332.22, 883.59 cm^{-1}; ^{1}H NMR (DMSO, 600MHz): δ 7.65 (s, 2H), 11.78 (s, 2H); ^{13}C NMR (DMSO, 150 MHz): δ 105.560, 133.255, 137.810, 156.120; MS: 224. Anal. calc. for $C_7H_4O_5N_4$: C 37.50, H 1.79, N 35.71; found: C 37.65, H 2.00, N 35.62.

5,6-Diaminobenzimidazolone-2 (3). A mixture of 112 g (0.5 mol) of crude 2, 224 g (4 mol) of iron dust, and 1.2 L of 85% ethanol were heated to boiling on an oil bath, the stirrer was started, and a solution of 75 mL concentrated hydrochloric acid in 300 mL 85% ethanol was added dropwise. The mixture was refluxed for 5 h beyond the final addition of hydrochloric acid, and then the hot mixture was made just alkaline to pH paper by the addition of potassium hydroxide pellets. Without allowing the mixture to cool, the iron was removed by filtration and the hot ethanol was used to wash the iron residue. Hydrochloric acid (15%) was added until the filtrate was 4–5 to pH paper, and then the mixture was chilled to 0°C for 12 h. The resulting precipitate was filtered, washed with water, and dried for about 24 h under vacuum with slight nitrogen flow at 80°C to give 75 g (91.4%) of tan 5,6-diaminobenzimidazolone-2 (3). The crude 3 was purified to afford 72 g (87.8%) of light yellow pure 3. M.P.: > 300°C; HPLC ≥ 98%; IR: 3407.18, 3366.27, 3106.60, 1682.70, 850.39 cm^{-1}; ^{1}H NMR (DMSO, 600 MHz): δ 4.07 (s, 2H), 6.23 (s, 2H), 9.81(s, 2H); ^{13}C NMR (DMSO, 150 MHz): δ 96.910, 121.410, 129.550, 155.440; MS: 164. Anal. calc. for $C_7H_8ON_4$: C 51.22, H 4.88, N 34.15; found: C 50.40, H 5.67, N 33.44.

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[6] The nitrating mixture consisting of fuming nitric acid and sulfuric acid was added with care to the solution, and the temperature was kept at 0–5°C in an ice bath. Some nitrogen oxides were released during the addition process. Therefore, operations should be conducted in an efficient fume hood.

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