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RESEARCH ARTICLE

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Research on multiphase synthesis of 1,5-di(*o*-anisidino) anthraquinone

Abstract According to the Ullman reaction mechanism, the synthesis of 1,5-di(*o*-anisidino)anthraquinone was achieved by the multiphase reaction of 1,5-dichloroanthraquinone in xylene and *o*-anisidine in the presence of copper metal powder and potassium acetate. The effects of various factors on the reaction, such as the dosages of xylene and catalyst, molar ratios of raw materials, and reaction times were investigated. When the molar ratio of 1,5-dichloroanthraquinone to *o*-anisidine and potassium acetate is 1:10:2.5 and the catalyst dosage based on 1,5-dichloroanthraquinone is 5.3%, the conversion of 1,5-dichloroanthraquinone is 97.8% and the yield of 1,5-di(*o*-anisidino)anthraquinone is 80.6% after reflux for 10 h. Under these conditions, the recovery of the solvent is 86.0%. The target compound was identified by MS, ^{1}H NMR, IR and DSC.

Keywords 1,5-dichloroanthraquinone, 1,5-di(*o*-anisidino)anthraquinone, multiphase reaction, HPLC

1 Introduction

1,5-Di(*o*-anisidino)anthraquinone is a versatile compound which could be used as a dye in inks [1] and in automatic transmission fluids [2]. After chlorosulfonation, it could copolymerize with monomer to obtain copolymers with excellent color properties [3]. In addition, it also could be used as fluid crystals [4].

The chlorine atom at 1-position of anthraquinone exhibits activity in substitution reactions, which makes 1-chloroanthraquinone, 1,5-dichloroanthraquinone, and 1,8-dichloroanthraquinone be a group of readily available raw materials for the preparation of anthraquinone derivatives [5–7]. X-ray diffraction analysis of a single crystal shows that the chlorine atom at 1-position is obviously repelled by the nearby oxygen atom. Such a repelling force may enhance chlorine's leaving tendency in a substitution reaction [8], so 1-(*o*-anisidino)anthraquinone can be easily obtained as a main product. However, it is difficult to prepare 1,5-di(*o*-anisidino)anthraquinone because of the depressed activity of chlorine atom at 5-position by the electron donating effect of *o*-anisidino group at 1-position. At present, there are two main routes to prepare 1,5-di(*o*-anisidino)anthraquinone. One route is by the reaction of 1,5-dichloroanthraquinone with *o*-anisidine [2], in which the *o*-anisidine acts as the reaction reagent as well as the solvent. An alternative one involves the reaction of 1,5-dichloroanthraquinone and *o*-anisidine in nitrobenzene under reflux [9]. The important features of these two routes include their long reaction times at higher temperatures and toxicity of the solvents, which are difficult to recycle. Therefore, some modifications are needed to prepare 1,5-di(*o*-anisidino)anthraquinone with higher yields and convert raw materials under mild conditions.

To prepare 1,5-di(*o*-anisidino)anthraquinone with higher yields and lower costs under mild conditions, this paper reports the preparation of 1,5-di(*o*-anisidino) anthraquinone in the presence of copper metal powder by the reaction of 1,5-dichloroanthraquinone and *o*-anisidine in xylene, in which the solvent is relatively nontoxic and widely used in industry. During the research, the reaction was monitored by HPLC. In addition, solvent recycling was carried out.

2 Experimental

2.1 Reagents and equipments

1,5-Dichloroanthraquinone (98.3%) was purchased from Shanghai Weile Chemical Technology Co., Ltd (China). *o*-Anisidine, xylene, copper metal powder, potassium acetate and hydrochloric acid were from reagent companies and used directly.

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Agilent 1100 HPLC was used to monitor the reaction. HP 1100 MS, Varian INOVA 400 M NMR, FT/IR-430 Spectrometer and 910s DSC were used to characterize the structure of 1,5-di(*o*-anisidino)anthraquinone.

2.2 Synthesis of 1,5-di(*o*-anisidino)anthraquinone

A 100 mL three-necked flask was charged with 1,5-dichloroanthraquinone (1.41 g, 0.005 mol), *o*-anisidine (5.75 mL, 0.05 mol), anhydrous potassium acetate (1.225 g, 0.012 mol) and copper metal powder (0.075 g). The mixture was refluxed for 10 h. Subsequently, xylene was removed in a vacuum and 21.5 mL of xylene was recycled. After cooled to room temperature, the reaction mixture was added to 200 mL of hydrochloric aqueous solution under stirring. After filtration and drying, 2.45 g of the product was obtained with content of 74.0% (yield 80.6%).

2.3 Measurements of conversions and yields

The external standard method of HPLC was adopted to determine the conversions of 1,5-dichloroanthraquinone and the yields of 1,5-di(*o*-anisidino)anthraquinone. The HPLC was equipped with a Hypersil ODS2 Chromatographic Column (250 mm × 4.6 mm), detector of 335nm and methanol/water as fluent, with flow speed of 1 mL/min.

3 Results and discussion

The reaction of 1,5-dichloroanthraquinone with *o*-anisidine is similar to the Ullman reaction [10], and the mechanism is shown in Fig. 1.

The reaction bears an ionic character. During the reaction, a copper complex forms initially between the chlorine and copper, then the carbon atom linking with the chlorine atom is attacked by dissociative amine molecule to obtain the product. This kind of reaction is often carried out in protic solvents, excessive amines or polar nitrobenzene. However, the de-halogenation of the product usually occurs under a protic environment. On the other hand, when the excessive amine exists, it is easily oxidized, consequently leading to the deactivation of the catalyst and difficulty in the treatment of final products. Nitrobenzene is also used as a solvent in the reaction, but sometimes several side reactions may occur with nitrobenzene as reactant. Therefore, in this paper, 1,5-di(*o*-anisidino)anthraquinone was prepared in xylene, which is an aprotic, nonpolar, relatively nontoxic and inert solvent and is easy to recycle.

According to the reaction mechanism above, the reaction was influenced by factors such as the dosages of catalyst and solvents and the molar ratios of raw materials. The effects of these factors on the reaction were investigated in detail.

3.1 Effect of the dosages of xylene

Not only the concentration of *o*-anisidine, but also the dispersion of 1,5-dichloroanthraquinone depended on the dosage of xylene. Thus, the effect of the dosage of xylene on the yield of 1,5-di(*o*-anisidino)anthraquinone (Y) was investigated under the conditions of $n(C_{14}H_6Cl_2O_2):n(C_7H_9NO):n(CH_3COOK) = 1:6:2.5$, $\omega(Cu) = 3.5\%$ (the mass ratio of copper metal powder to 1,5-dichloro anthraquinone), and reflux for 10 h. The results are shown in Fig. 2.

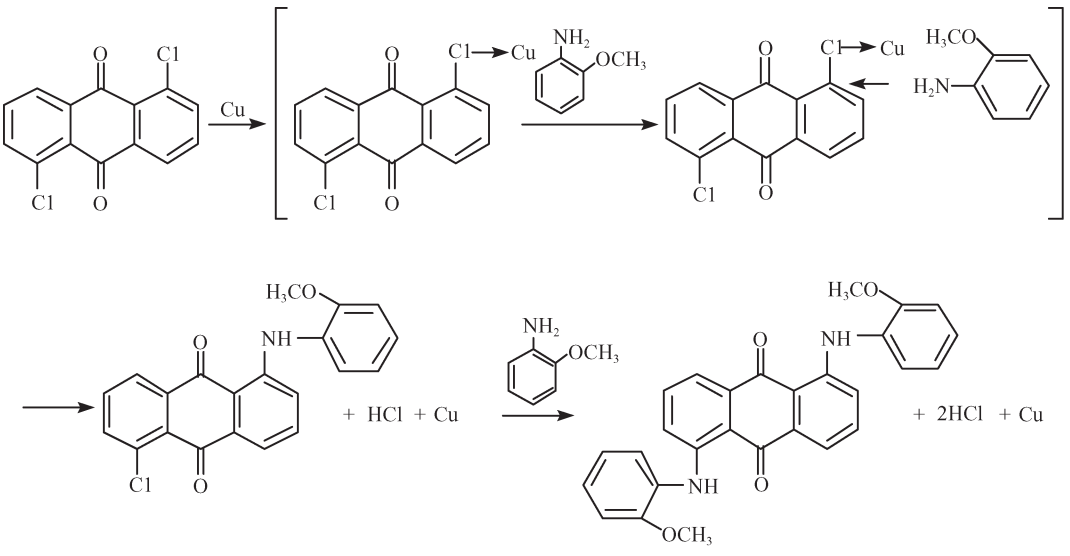

Fig. 1 The reaction mechanism of the synthesis

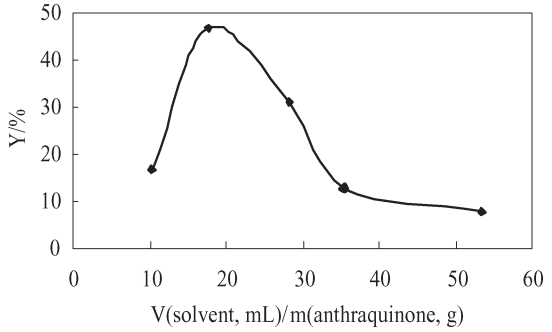

Fig. 2 Effect of xylene on the yields of the target compound

As shown in Fig. 2, the yields of 1,5-dichloroanthraquinone increased with an increase of the ratios of xylene volume (mL) to the mass of 1,5-dichloroanthraquinone (g), then decreased when a maximum appeared at a ratio of 18. With an increase of the dosages of xylene, the reactants could mix and adequately be in contact to obtain the product. However, if the dosages of xylene were too large, the concentrations of *o*-anisidine decreased, consequently reducing the yields. From these two situations, the ratio of 18 was employed in the experiment.

3.2 Effect of acid binding agents

Table 1 shows the effect of acid binding agents on the conversions of 1,5-dichloroanthraquinone (C) under $n(C_{14}H_6Cl_2O_2)$:$n(C_7H_9NO)$:n(alkali) = 1:6:2.5, V(solvent, mL)/$m(C_{14}H_6Cl_2O_2$, g) = 18, ω(Cu) = 3.5%, and reflux for 10 h.

Table 1 Effect of acid binding agents on the conversions of anthraquinone

Acid binding agent	C/%
CH_3COOK	83.2
K_2CO_3	65.2
Na_2CO_3	36.2

Among the acid binding agents, potassium acetate has higher solubility in xylene, while the solubility of sodium carbonate is lower, so the yield of 1,5-di(*o*-anisidino) anthraquinone was higher with potassium acetate as acid binding agent and lower with the sodium carbonate. In addition, when sodium carbonate was used as acid binding agent, the water produced could cause side reactions. Therefore, potassium acetate was used as acid binding agent.

3.3 Effect of the dosages of catalyst

As shown in Table 2, the effect of the dosages of catalyst on the reaction was studied under the conditions of

Table 2 Effect of the dosages of catalyst on the reaction

No.	ω(Cu)/%	Y/%	C/%
1	0	–	22.0
2	1.8	32.7	–
3	3.5	46.5	83.2
4	5.3	60.3	93.8
5	7.1	60.4	91.4

$n(C_{14}H_6Cl_2O_2)$:$n(C_7H_9NO)$:$n(CH_3COOK)$ = 1:6:2.5, V (solvent, mL)/m($C_{14}H_6Cl_2O_2$, g) = 18, and reflux for 10 h. It can be seen that the yields of 1,5-di(*o*-anisidino) anthraquinone and the conversions of 1,5-dichloroanthraquinone increased with increasing dosages of copper metal powder, but the effect of the catalyst was limited when the dosage reached 5.3%.

3.4 Effect of molar ratios of raw materials

Under the conditions of $n(C_{14}H_6C_{12}O_2)$:$n(CH_3COOK)$ = 1:2.5, V(solvent, mL)/$m(C_{14}H_6Cl_2O_2$, g) = 18, ω(Cu) = 5.3% and reflux for 10 h, the results of the yields and conversions with varying molar ratios of raw materials are shown in Fig. 3. When the molar ratios of n(amine)/n (anthraquinone) increased from 4:1 to 10:1, the yields of the product increased because of the higher concentrations of *o*-anisidine. But when the ratio increased further to 16:1, the yields decreased. This might be attributed to the deactivation of the catalyst and acid binding agent, which are wrapped by the black resinoid byproducts because the excessive amines are oxidized at a higher temperature. Under the reaction conditions, the conversions of 1,5-dichloroanthraquinone were maintained at about 98% because the *o*-anisidine was enough during the reaction.

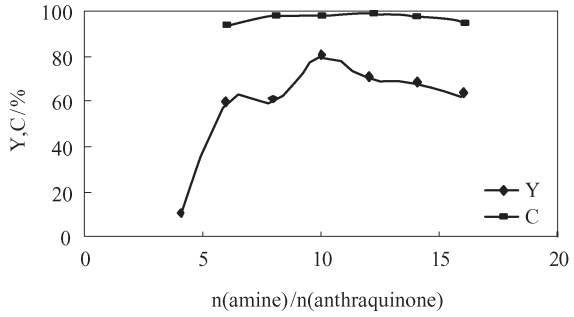

Fig. 3 Effect of molar ratios of the raw materials on the reaction

3.5 Effect of reaction times

Table 3 shows the effect of reaction times (t_r) on the reaction under reflux and the conditions of $n(C_{14}H_6Cl_2O_2)$: $n(C_7H_9NO)$:$n(CH_3COOK)$ = 1:10:2.5, ω(Cu) = 5.3%, V

Table 3 Effect of reaction times on the reaction

No.	t_r/h	Y/%	C/%
1	8	18.3	87.0
2	10	80.6	97.8
3	12	76.0	99.0
4	14	69.1	98.3

(solvent, mL)/$m(C_{14}H_6\ Cl_2\ O_2$, g) = 18. It was found that the yields of the product increased with increasing reaction times; however, it decreased when the reaction times rose up to 10 h. The main factor for this difference is that the dehalogenation of the product occurred to produce mono-substituted anthraquinone at the higher temperature for a longer time. In addition, other byproducts may yield because of the thermal decomposition of *o*-anisidine [11]. On the other hand, the conversions of 1,5-dichloroanthraquinone increased with increasing the reaction time first, but were unchanged after 10 h. Therefore, 10 h was selected as the reaction time.

3.6 Analysis of the reaction compounds

The investigations showed that the yields of 1,5-di(*o*-anisidino)anthraquinone were not high in conditions selected above because of the byproducts, although the conversions of 1,5-dichloroanthraquinone were at a high level. Hence, the reaction compounds were analyzed with HPLC-MS and MS under the conditions of $n(C_{14}H_6C_{l2}O_2)$:n(amine):$n(CH_3COOK)$ = 1:8:2.5, V(solvent, mL)/$m(C_{14}H_6Cl_2O_2$, g) = 18, ω(Cu) = 5.3%, and reflux for 10 h. The results are shown in Table 4. Besides the target compound 1,5-di(*o*-anisidino)anthraquinone, two main byproducts were detected: 1-(*o*-anisidino) anthraquinone byproduct 1 produced from the dehalogenation of 1,5-di(*o*-anisidino)anthraquinone and 1-*o*-anisidino-5-chloro anthraquinone byproduct 2 from the mono-substitution of 1,5-dichloroanthraquinone.

3.7 Structure characterization

The target compound 1,5-di(*o*-anisidino)anthraquinone was characterized by MS, ^{1}H NMR, IR and DSC. In Fig. 4, MS (APCI Positive) spectrum of the target compound gives a correct quasimolecular ion peak (M +H) at m/z 451.0.

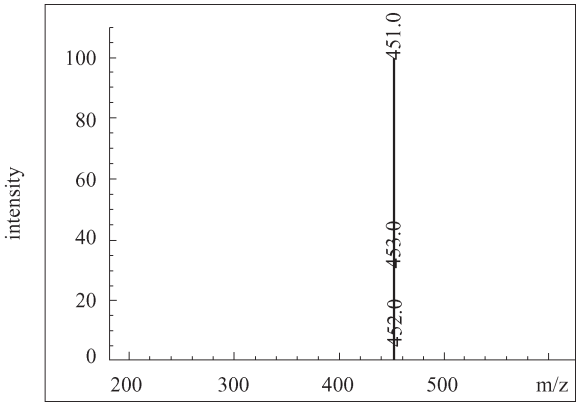

Fig. 4 MS spectrum of the target compound

^{1}H NMR(400M, DMSO-d_6) spectrum of 1,5-di(*o*-anisidino)anthraquinone shows the chemical shifts at δ11.22 (s, 2H, –NH–), δ 7.01–7.67 (m, 14H, Ar-H), and δ 3.88 (s, 6H, $-CH_3$). The chemical shifts of imine groups appear at the much lower field because of the intramolecular hydrogen bonds.

IR spectrum of 1,5-di(*o*-anisidino)anthraquinone exhibits the typical bands of N–H at 3430 cm^{-1}, C–H at 3023 cm^{-1} in the benzene ring, C–H at 2954 cm^{-1} in methyl groups, C=O at 1617 cm^{-1}, C (in benzene ring) – N at 1259 cm^{-1}, C–O–C at 1166 cm^{-1}, and typical absorption of ortho-substituted benzene ring at 750 cm^{-1}.

The melting point of 1,5-di(*o*-anisidino)anthraquinone determined by DSC is 206.3–209.6°C.

4 Conclusions

According to the Ullman reaction mechanism, 1,5-di(*o*-anisidino)anthraquinone was synthesized in xylene, which is an aprotic, nonpolar, and relatively nontoxic solvent and is used to displace the highly toxic nitrobenzene or *o*-anisidine. Structures of the main products were determined. After the detailed investigation of reaction conditions, 1,5-di(*o*-anisidino)anthraquinone was synthesized under mild conditions.

Table 4 Analysis of the reaction compounds

analysis methods	compd.	retention time/min	A/%	MS(m/z) ([M+H]$^+$)	substituent	
					1-position	5-position
HPLC-MS	target compd.	29.18	85.8	451.0	*o*-$NH(C_6H_4)OCH_3$	*o*-$NH(C_6H_4)OCH_3$
HPLC-MS	byproduct 1	20.65	9.0	330.1	*o*-$NH(C_6H_4)OCH_3$	–H
MS	byproduct 2	–	–	364.1	–Cl	*o*-$NH(C_6H_4)OCH_3$

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