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配位诱导的硝酸铜与水杨酸甲酯的高选择性自由基硝基化反应

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摘要:硝酸铜与水杨酸酯的硝基化反应得到了高收率的对位产物。电子吸收光谱、循环伏安、电喷雾质谱的研究表明该反应经历的是一个自由基硝基化机理。硝酸铜与水杨酸甲酯的配位促使硝酸根断裂氮氧键产生硝基自由基、氧自由基和配合物自由基。硝基自由基与水杨酸甲酯或配合物反应得到硝基水杨酸甲酯或硝基化配合物。硝基化配合物经过水解将铜离子转化成氧化铜沉淀而生成硝基水杨酸甲酯。

关键词:水杨酸甲酯;硝酸铜;自由基硝基化;配位
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Coordination-Mediated Radical Nitration of Methyl Salicylate by Copper(Ⅱ) Nitrate with High Regioselectivity

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Abstract: High yield and para-selective products were obtained by the nitration of methyl salicylate (MeS) and copper(Ⅱ) nitrate(CuN). The results of electron absorption spectra (EAS), Cyclic Voltammetry(CV) and electrospray ionization mass spectra (ESIMS) reveal that the reaction favors a radical nitration mechanism. It is the coordination of MeS with CuN that promotes the splitting of N-O bonds of nitrate group in CuN, and results in the formation of nitro radicals, oxygen radicals and complex radicals. The nitro radicals can react with MeS or the complexes of MeS to form nitration products. The nitrated complexes immediately turn to methyl nitrosalicylate by Cu(Ⅱ) ions being hydrolyzed to copper(Ⅱ) oxides.

Key words: methyl salicylate; Cu(Ⅱ) nitrate; radical nitration; coordination

0 Introduction

The serious effluent problems, created by nitration processes based on mixed nitric and sulfuric acids, have stimulated the search for alternative procedure[1-8]. Over the past two decades, remarkable progress has been made to improve the nitration procedure and synthesis efficiency[9] by using various nitrating salts[10-17]. The use of metal nitrates has received much study and many developments. However, the nitration of aromatic compounds lacks positional selectivity which mainly gives rise to ortho(o) isomers[18] and the nitration mechanism has not come to a conclusion[19]. So seeking new standpoints for the explanation of nitration reaction process remains an important challenge for chemists.

Nitration is usually considered as an electrophilic aromatic substitution reaction[19]. Pierre Laszlo et al[9]

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proposed a plausible radical mechanism to explain the nitration of phenol by ferric nitrate:

$ArOH+Fe(Ⅲ) \rightarrow ArOH^{+\cdot}+Fe(Ⅱ)$

$(O_3N)_2Fe(Ⅲ)\text{-}O\text{-}NO_2 \rightarrow (O_3N)_2Fe(Ⅲ)\text{-}O\cdot+\cdot NO_2$

$ArOH^{+\cdot}+\cdot NO_2 \rightarrow [Ar(OH)NO_2)^+]$

The authors did not provide any direct evidence for the formation of radical intermediates. The interaction between phenol and ferric nitrate was also not considered. Our present studies aim at improving para region-selectivity and obtaining evidence for the likely radical nitration procedure mediated by the coordination of copper (Ⅱ) nitrate (CuN) and methyl salicylate (MeS) [20]. The complexes or intermediates formed during the nitration process of MeS with copper (Ⅱ) nitrate were monitored by Electric Absorption Spectra (EAS), Cyclic Voltammetry (CV) and Electrospray Ionization Mass Spectra (ESIMS). With these evidences, we proposed a new radical nitration mechanism.

1 Experimental

1.1 General remarks

The IR spectra were recorded on a Bruker VECTOR22 FTIR spectrometer using KBr pellet technique. Themogravimetric analyses were carried out on a Setaram Labsys™TG-DSC16 thermal analyzer. The elemental analysis of C, H, N was performed on a Perkin-Elmer 240C elemental analyzer; ^1H NMR experiments were performed on a Bruker AM 500 spectrometer. The ESIMS were determined on a Finnigan LCD mass spectrometer; the concentration of the samples was about 1 mol dm^{-1}. The diluted solutions were electro-sprayed at a flow rate of 5×10^{-6} $dm^{-3}\cdot min^{-1}$ with a needle voltage of +4.5 kV. The mobile phase was acetonitrile, and the samples run in the positive-ion mode. Cyclic Voltammetry was performed in a three-electrode system of a CHI660 electrochemical workstation. Ethyl acetate and KNO_3 were used as the solvent and the supporting electrolyte, and Pt-C, Ag/AgCl and Pt were used as working electrode, reference electrode, and auxiliary electrode, respectively.

1.2 Experimental procedure for the nitration reaction of MeS and CuN

In a 100 mL flask, a certain amount of $Cu(NO_3)_26H_2O$ (AR) was dissolved in ethyl acetate solution (AR 20 mL), then MeS was added. The mixture solution was heated to reflux under stirring with a magnetic stirrer.

For a certain reaction interval, 0.2 mL reaction solution was taken out and diluted to 10 mL with ethyl acetate for the EAS determination using a Shimadzu UV3100 spectrophotometer. After cooling and filtrating, the formed precipitates were collected as by-products after washing with ethyl acetate and drying in air at room temperature, the filtrate was used to isolate crude products by evaporating ethyl acetate. After washing with water, the crude products were dissolved in ethyl acetate. Two crystalline products with the same molecular weight of 197.15 were obtained by fractional crystallization. One is the yellow grain crystal isolated at the beginning, which is methyl 3-nitrosalicylate (M3NS), another is the pale white needle crystal isolated finally, which is identified to be methyl 5-nitrosalicylate (M5NS).

2 Results and discussion

2.1 Evidence from EAS and the identification of products nitrated by CuN

The color of ethyl acetate solution of copper nitrate and MeS is blue. It becomes green upon refluxing. The broad absorption band (Fig.1) ranging from 600 nm to 800 nm is owing to the $d \rightarrow d^*$ electronic transition of Cu (Ⅱ) which leads to blue color.

The absorption band from 400 nm to 500 nm with maximum at 450 nm leads to teal color, indicating the formation of copper salicylate complexes. After refluxing for 40 min, the intensity of this band is decreased greatly, which means that the complexes are formed before transferring to nitrated products and a teal precipitant is isolated.

The isolated solid is hydroxide copper oxides with some undecomposed complexes [21-22]. From the filtrate, two nitrated products with the same molecular

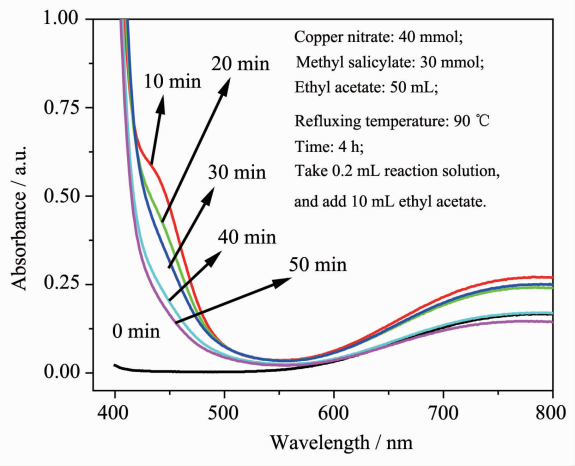


Fig.1　Electron absorption spectra of reaction solution after refluxing for different times

weight of 197.15 are obtained by chromatograph separation over silica gel or recrystallization separation. One is the yellow grain crystal (methyl 3-nitrosalicylate (M3NS)) isolated at the beginning, the other is the pale white needle crystal methyl 5-nitrosalicylate (M5NS) isolated finally[21].

2.2　Region selectivity and total yield of the nitration under different conditions

The region selectivity and total yield of the nitration are listed in Table 1. It is clear that the reaction exhibits a characteristic of para-selective nitration and P/O ratio is around 5 at the highest yield (82.73%). The nitration yield and para-selectivity are higher than that of phenol because of coordination.

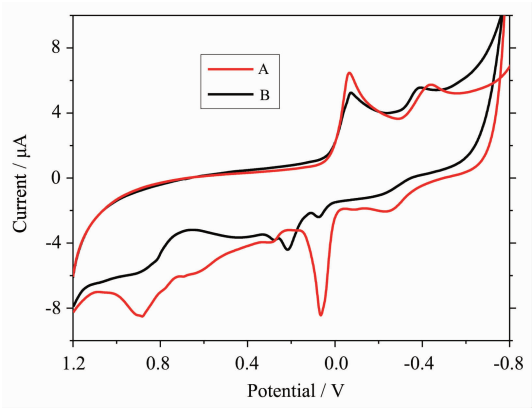
Table 1　Region selectivity and total yield of the nitration under different conditions

No	Synthesis conditions				Results			
	CuN / mmol	MeS or phenol / mmol	T / ℃	t / h	Total yield / %	M3NS / M / %	M5NS / M / %	P / O ratio
1	20	30(MeS)	90	2	48.47	12.19	87.81	7.20
2	20	30(MeS)	90	3	54.60	16.84	83.16	4.94
3	20	30(MeS)	90	4	65.73	14.87	86.13	5.72
4	20	30(MeS)	90	5	63.46	16.78	83.22	5.96
5	10	30(MeS)	90	4	38.94	16.45	83.55	5.08
6	20	30(MeS)	90	4	65.73	14.87	86.13	5.72
7	30	30(MeS)	90	4	80.21	17.22	82.78	4.81
8	40	30(MeS)	90	4	82.73	16.71	83.29	4.99
9	50	30(MeS)	90	4	79.57	17.25	82.75	4.80
10	40	30(phenol)	90	4	71.94	21.74	78.26	3.60

Note: CN: Copper nitrate; MeS: methyl salicylate; T: refluxing temperature; t: reaction time; M=M3NS(g)+M5NS(g)

2.3　Cyclic Voltammetry (CV) of the reaction solution of CuN and MeS

Fig.2 shows the Cyclic Voltammetry of different solution. From the results we know there are two oxidation-reduction peaks of CuN (Fig.2-A) owing to Cu(Ⅱ) oxidation-reduction. Furthermore, two oxidation-reduction peaks emerge in the reaction solution of MeS and CuN (Fig.2-B). The reduction potential is more positive and the oxidation potential is more negative, compared to those of CuN, which is owing to the formation of complexes between MeS and CuN. The oxidation-reduction reaction occurs more easily for the complexes.



A: Solutin of Cu(Ⅱ) nitrate (dissolved by 0.1 mol·L^{-1} KNO_3); B: Reaction solution of MeS and CuN (dissolved in 0.1 mol·L^{-1} KNO_3)

Fig.2　Cyclic Voltammetry of different solutions(scan rate: 0.01 V·s^{-1})

2.4 Evidence for the formation of complexes between CuN and MeS from ESIMS

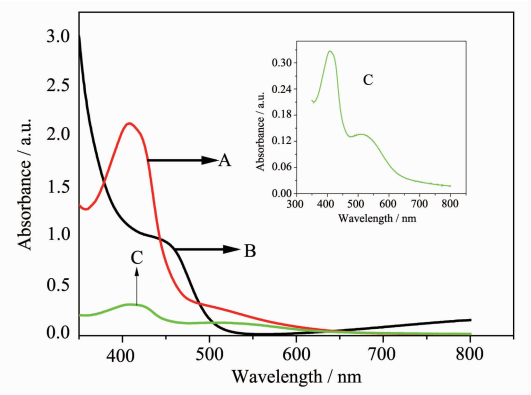
The main species or intermediates formed in the mixing solution of CuN with MeS before and after refluxing were evaluated by ESIMS. The main species are at m/z=145.23 (147.17), 274.91, 279.38, 302.83, 318.72 (320.02), 346.76, 362.72, 374.76, 390.77, 478.55 (480.42, 481.58). The formation of these species can be described as follows.

$[Cu(NO_3)(MS)(CH_3CN)_2(H_2O)_{1.5}]^+(m/z=390.77) \rightarrow$
$[Cu(NO_2)(MeS)(CH_3CN)_2(H_2O)_{1.5}]^+(m/z=374.76)+ \cdot O$
$[Cu(NO_3)(NO_2)(MS)(CH_3CN)]^+(m/z=362.72) \rightarrow$
$[Cu(NO_3)(NO_2)(MeS)(CH_3CN)]^+(m/z=346.76)+ \cdot O$
$\rightarrow[Cu(NO_3)(MeS)(CH_3CN)]^+(m/z=318.72)+ \cdot NO_2$
$\rightarrow[Cu(NO_2)(MeS)(CH_3CN)]^+(m/z=302.83)+ \cdot O$

It is the formed complexes of CuN and MeS that induce the formation of nitro and oxygen radicals.

2.5 Identification of the oxygen radicals

It was reported[23] hydroxylamine oxidation can be used to identify oxygen radicals. The reaction solution of CuN and MeS at 90 ℃ for 20 min is blue and the broad absorption band at 550 ~800 nm is owing to unreacted CuN. As shown in Fig.3, when the solution is added to hydroxylamine hydrochloride, 4-hydroxy benzenesulfonic acid and 1-naphthylamine, there exist two new absorption bands at 405 nm and 520 nm (Fig.3-C). The absorption band at 402 nm is attributed to the addition of 4-hydroxy benzenesulfonic acid and 1-naphthylamine. (Fig.3-B) The absorption band at 520 nm is owing to the oxidation of hydroxylamine hydrochloride by oxygen radicals to nitrite (Fig.3-A) which reacts with 4-hydroxyl benzenesulfonic acid and 1-naphthylamine to form red complex. The results identify the existence of oxygen radicals in the reaction solution of CuN and MeS.



A. add ed hydroxylamine hydrochloride; B. added 4-hydroxyl benzenesulfonic acid and 1-naphthylamine; C. added 4-hydroxyl benzenesulfonic acid, 1-naphthylamine and hydroxylamine hydrochloride

Fig.3 Identification of O radical by hydroxylamine oxidation method

2.6 Nitration mechanism via radicals

As effective nitrating agent, nitro radicals are capable of attaching onto the phenol ring of MeS to induce nitration reaction. When the coordinated MeS is nitrated, it will disassociate because nitrated MeS shows very weak coordination ability towards Cu (Ⅱ) ions. So, the Cu (Ⅱ) ions are hydrolyzed to hydrate copper (Ⅱ) oxide with few of nitrate groups and complexes. Therefore, we propose a radical mechanism in Fig.4 to describe the nitration process:

The mechanism described in Fig.4 includes coordination, activation, radical formation, π-complex formation, σ-complex formation, complex disassociation to nitrated MeS with hydrolysis of Cu (Ⅱ). The complexes of Cu (Ⅱ) with MeS were directly demonstrated by EAS and ESIMS. The activation process is referred to the electron transfer process in inner coordination sphere promoted by heating. The splitting of O-N bonds in activated complexes then results in the liberation of nitro radicals as detected by ESIMS method. Oxygen radicals have been identified by hydroxylamine oxidation method. Nitro radicals show strong affinity toward phenol ring of MeS to form π-complex and σ-complex intermediates. Final nitration products are formed when Cu (Ⅱ) is disassociated from these intermediates through h ydrolysis.

3 Conclusions

High yield and para-selectivity nitration products were obtained by the reaction of CuN and MeS. A series of complexes of CuN with MeS were detected in their mixture solution by EAS, CV and ESIMS. It is the coordination of MeS and Cu(Ⅱ) ion that initiates an electron transfer process from MeS to Cu (Ⅱ) ion and

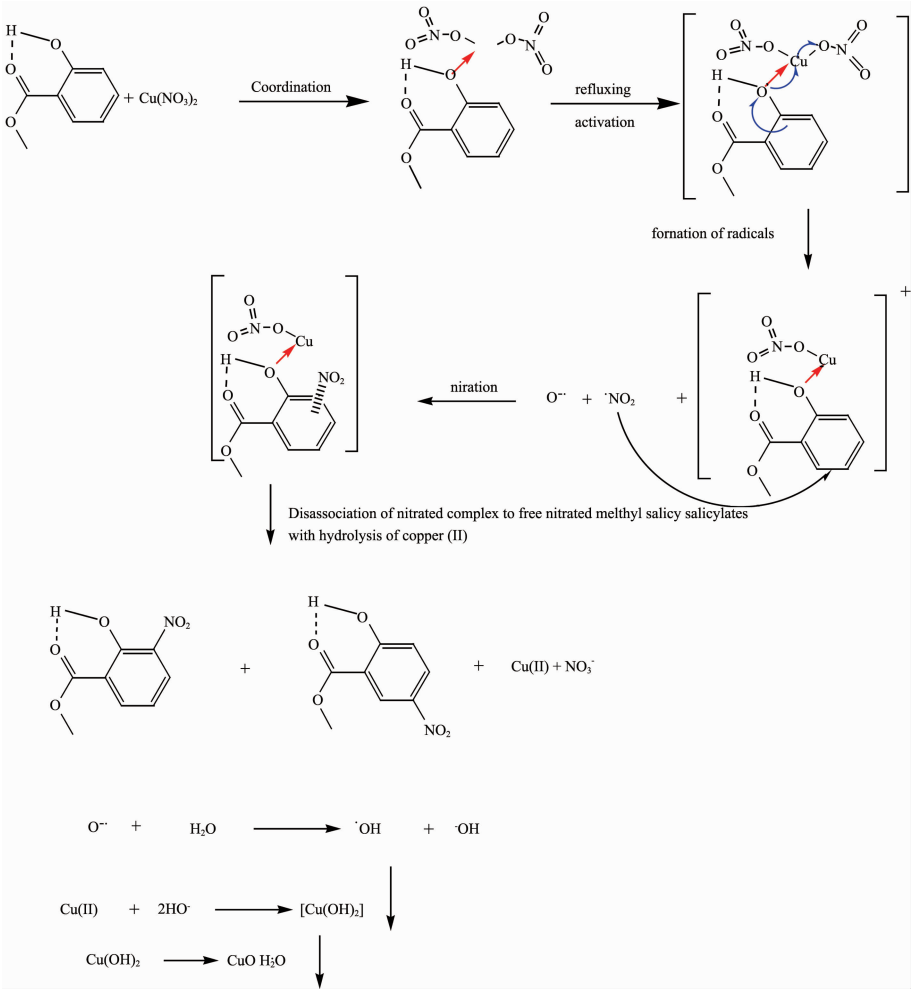


Fig.4　A comprehensive mechanism of nitration reaction of MeS and copper(Ⅱ) nitrate, including coordination, activation, radical formation, nitration and hydrolysis of Cu(Ⅱ), free of nitrated MeS

then to nitrate groups leading to the formation of nitro and oxygen radicals. Nitro radicals react with MeS or the complexes of MeS and CuN through radical nitration substitution reaction. The final nitrated products are obtained as free ligands since the nitrated complexes are disassociated through the hydrolysis of Cu (Ⅱ) to Cu (Ⅱ) oxides. Therefore, a radical nitration mechanism has been proposed to explain the nitration using metal nitrates as nitrating reagents.

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