Analytical Chemistry: A Journal (2023)
Clausius Scientific Press, Canada

DOI: 10.23977/analc.2023.020105
ISSN 2616-1958 Vol. 2 Num. 1

Improvement of Synthesis Process of 4-Amino-1, 8 Naphthalene Anhydride

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Keywords: Acenaphthene; 4-amino-1, 8 naphthalene anhydride, nitration, oxidation, gradient elutio

Abstract: Objective: By optimizing the reaction conditions for synthesizing 4-amino-1, 8 naphthalene anhydride compound through three steps of nitration, oxidation and reduction based on the raw material acenaphthene, the yield is improved and the synthesis cost is reduced, so that it can be used for large-scale preparation in the laboratory. Methods: The single variable method was used to explore the effect of temperature conditions on the yield of nitration reaction; to explore the effect of the amount of oxidant, heating and refluxing time, and product post-treatment on the yield of the oxidation reaction; to explore the effect of the amount of absolute ethanol and concentrated hydrochloric acid on the yield of the reduction reaction influences. After the reduction reaction, the gradient elution method of dichloromethane:methanol = 120:1~50:1 was adopted to separate and obtain pure 4-amino-1,8 naphthalene anhydride. Results: The yield of nitration reaction is up to 92.16%, the yield of oxidation reaction is up to 59.49%, and the yield of reduction reaction is up to 77.47%. The purified reduction products are analyzed by 1H-NMR, 13C-NMR and MS (ESI) and the structure was confirmed. Conclusion: The synthesis reaction conditions of 4-amino-1, 8 naphthalene anhydride were optimized, which was helpful for its large-scale preparation in the laboratory, and accumulated important basic experimental data for the industrial production of this compound.

1. Introduction

The 1, 8-naphthalimides have a very wide range of applications [1-2] and are often reported extensively as fluorescent dyes, probes and antitumour agents [3-10]. Both the imide site and the naphthalene ring of this class of compounds can be structurally modified and derivatised to obtain new derivatives, showing structural diversity. The properties of this class of compounds are closely related to their structures, so that naphthalimide derivatives with different structures often have a wide range of pharmaceutical activities, as well as widely varying spectral properties [11]. As an important intermediate in the synthesis of naphthalimide fluorescent dyes [12], 4-amino-1, 8-naphthalic anhydride is of great importance for the development of fluorescent dyes [13]. In recent years, as naphthalimide fluorescent materials have a wide range of applications in the fields of medicine, chemistry and biology [14], they can be used for the detection of organic small molecules and trace element ions in vitro and in vivo by virtue of their high sensitivity, strong

anti-interference and low detection limits [15] [16], especially in the field of medicine, which has a good application prospect and development potential to help diagnose diseases, such as cancer [17], thus improving the cure rate of certain diseases.

However, the development of its application in various fields is hindered by its high market price and complex synthesis process, therefore, the synthesis process improvement and performance study of 4-amino-1, 8-naphthalic anhydride is indispensable. In this project, it is proposed to produce 4-amino-1, 8-naphthalic anhydride by a three-step laboratory reaction of nitration, oxidation and reduction using acenaphthene as the starting material [18-20], and the synthetic route is shown in Figure 1. The reaction conditions of each step were also optimised to improve the yield [21-22], which is expected to reduce the cost of synthesis of 4-amino-1, 8 naphthalic anhydride and facilitate its synthesis in the laboratory in large quantities.

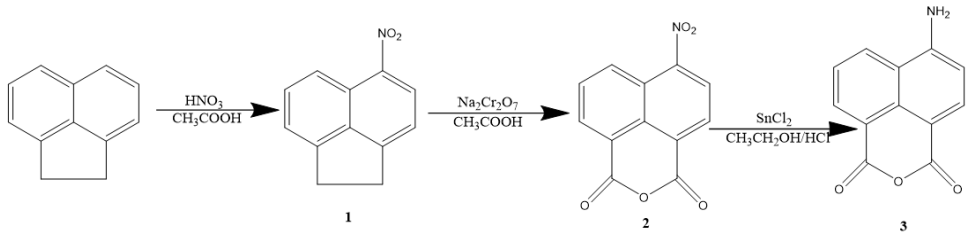

Figure 1: Synthesis of 4-amino-1, 8 naphthalic anhydride

2. Materials and methods

2.1 Apparatus and reagents

2.1.1 Apparatus

SZCL-2 Digital Display Intelligent Temperature Control Magnetic Stirrer (Shanghai Xingchuang Scientific Instruments Co., Ltd.), SHZ-Three Circulating Water Vacuum Pump (Shanghai Yarong Biochemical Instrument Factory), UV-1 Triple UV Analyzer (Hangzhou Qiwei Instrument Co., Ltd.), RE-52AA Rotary Evaporator (Shanghai Yarong Biochemical Instrument Factory), Bruker 400 MHz Nuclear Magnetic Resonance Spectrometer (Bruker Ltd.), BS110 electronic balance (Sartorius, Germany), vacuum drying oven, three-neck flask, thermometer, beaker (50 mL, 100 mL, 500 mL, 1000 mL), extraction flask (100 mL, 500 mL), cloth funnel, vacuum drying oven, measuring cylinder (5 mL, 20 mL, 25 mL, 200 mL).

2.1.2 Reagents

Acenaphthene, concentrated nitric acid, sodium dichromate, glacial acetic acid, SnCl2-2H2O, concentrated hydrochloric acid, anhydrous ethanol, column chromatography silica gel G (200-300 mesh), petroleum ether, ethyl acetate, dichloromethane, methanol, all reagents used are domestic analytical pure reagents.

2.2 Synthesis of 4-amino-1,8 naphthalenhydride (3)

2.2.1 Synthesis of 4-nitroacenaphthene (1) and 2-nitroacenaphthene (1′)

Add 40 mL of glacial acetic acid and 3.00 g (19.48 mmoL) of acenaphthene to a 250 mL three-necked flask fitted with stirring, react at a lower temperature, stir to dissolve for 1 h and then slowly add dropwise 14 mL (Vnitric acid: Vglacial acetic acid = 1:1, mnitric acid = 9.80 g, nnitric acid = 100.80 mmoL) of a mixture of nitric acid and glacial acetic acid for 30 min, dosing Finish.

The reaction was maintained at a certain temperature for 1 h and then filtered and the precipitate was washed with water to neutral. After natural drying, the mixture was purified by silica gel column chromatography using petroleum ether-ethyl acetate (40:1, V/V) as eluent to give a bright yellow solid mixture of 1 and 1′. The reaction formula is shown in Figure 2.

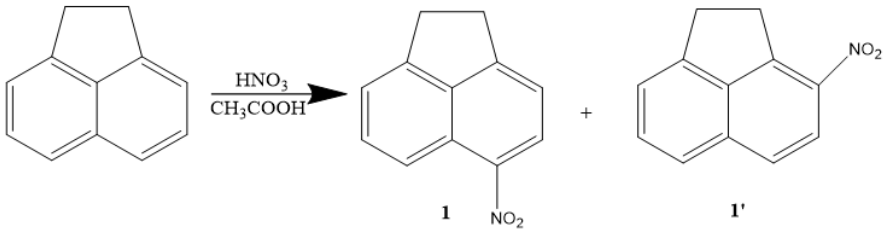

Figure 2: Synthesis of 4-nitroacenaphthene (1) and 2-nitroacenaphthene (1′)

2.2.2 Synthesis of 4-nitro-1,8 naphthalic anhydride (2) and 2-nitro-1,8 naphthalic anhydride (2′)

A 250 mL three-necked flask with stirring was charged with 100 mL of glacial acetic acid, a quantity of sodium dichromate and 3.00 g (15.07 mmoL) of compounds 1 and 1′ and heated to reflux (during which time the reaction solution turned dark green). 5 h later the reaction was terminated and the reaction solution was slowly poured into ice water in an external ice salt bath, stirred and then filtered and the filter cake was washed with water to neutral to give a golden yellow solid mixture of 2 and 2′. . The reaction equation is shown in Figure 3.

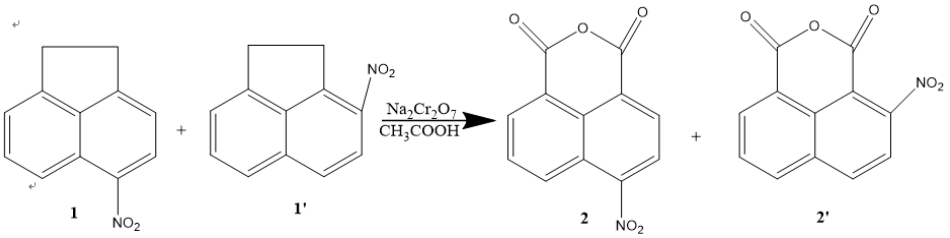

Figure 3: Synthesis of 4-nitro-1, 8 naphthalic anhydride (2) and 2-nitro-1, 8 naphthalic anhydride (2′)

2.2.3 Synthesis of 4-amino-1, 8 naphthalic anhydride (3) and 2-amino-1, 8 naphthalic anhydride (3′)

Add 5 mL of anhydrous ethanol and 0.67 g (2.75 mmoL) of compounds 2 and 2′ to a 50 mL three-necked flask equipped with stirring; add 2 mL (2.36 g, 24.00 mmoL) of concentrated HCl to a 50 mL beaker and 3.10 g (13.74 mmoL) of SnCl2-2H2O with glass rod stirring, dissolve thoroughly and within 10 min The precipitate was washed with water, alcohol and acetone in turn to give an orange-yellow solid mixture of 3 and 3′. The synthetic route is shown in Figure 4.

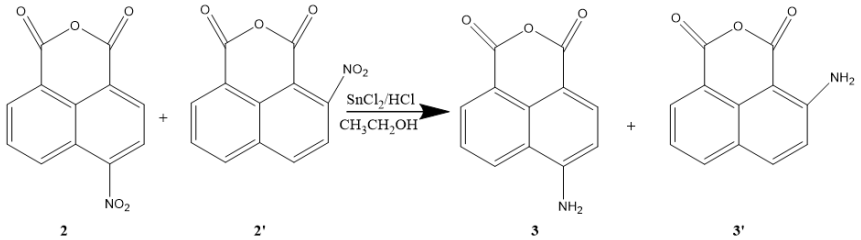

Figure 4: Synthesis of 4-amino-1, 8 naphthalic anhydride (3) and 2-amino-1,8 naphthalic anhydride (3′)

2.2.4 Separation of 4-amino-1, 8 naphthalic anhydride (3) and 2-amino-1, 8 naphthalic anhydride (3′)

A mixture of 3.52 g of compound 3 with 3′ was mixed with 3.52 g of column chromatography silica. The 20.14 g of column chromatography silica was loaded wet onto the column with 50 mL of dichloromethane and the sample was loaded dry. The gradient elution was carried out with dichloromethane: methanol 120:1 (240 mL), 100:1 (100 mL), 90:1 (90 mL), 80:1 (80 mL), 70:1 (70 mL), 60:1 (60 mL) and 50:1 (180 mL) (1 drop of glacial acetic acid and 1 drop of triethylamine for every 10 mL of eluent), and the 50:1 eluate was collected. The solvent was recovered to give a dark yellow oily solid compound 3.

Compound 3: 1H-NMR (400 MHz, DMSO-d6) δ: 8.69 (d, J = 8.4 Hz, 1H, Ph-H-2), 8.43 (d, J = 7.2 Hz, 1H, Ph-H-6), 8.19 (d, J = 8.5 Hz, 1H, Ph-H-8), 7.79 (s, 2H, NH2), 7.69 (t, J = 7.8 Hz, 1H, Ph-H-1), 6.88 (d, J = 8.5 Hz, 1H, Ph-H-9), (as shown in Figure 5).13C-NMR (100 MHz, DMSO-d6) δ: 102.7224 (Ph-C-9), 109.2146 (Ph-C-7), 118.7631 (Ph-C-1), 119.7997 (Ph-C-3), 124.8795 (Ph-C-6), 131.1805 (Ph-C-4), 133.0769 (Ph-C-5), 133.5076 (Ph-C-2), 136.3857 (Ph-C-8), 154.4012 (Ph-C-10), 160.8137 (Ph-C-12), 162.4957 (Ph-C-13) (as shown in Figure 6). Ms (ESI): Calculated for C12H6NO3 [M-H]- 212.0342, found for C12H6NO3[M-H]- 212.0348 (as shown in Figure 7).

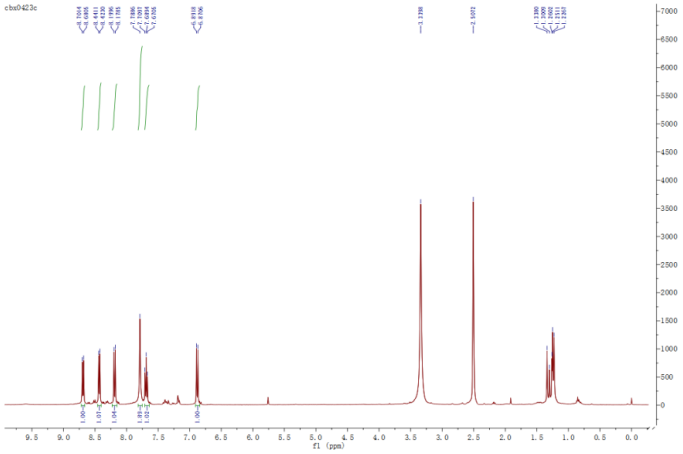

Figure 5: 1H-NMR (400 MHz, DMSO-d6) spectrum of 4-amino-1,8 naphthalic anhydride

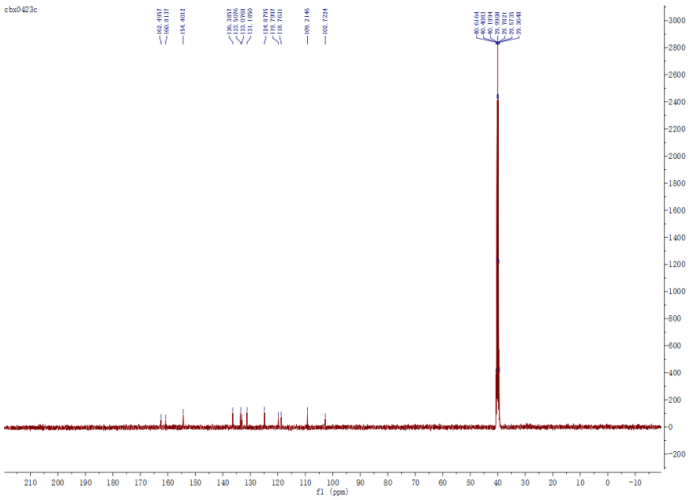

Figure 6: 13C-NMR (101 MHz, DMSO-d6) spectrum of 4-amino-1,8 naphthalic anhydride

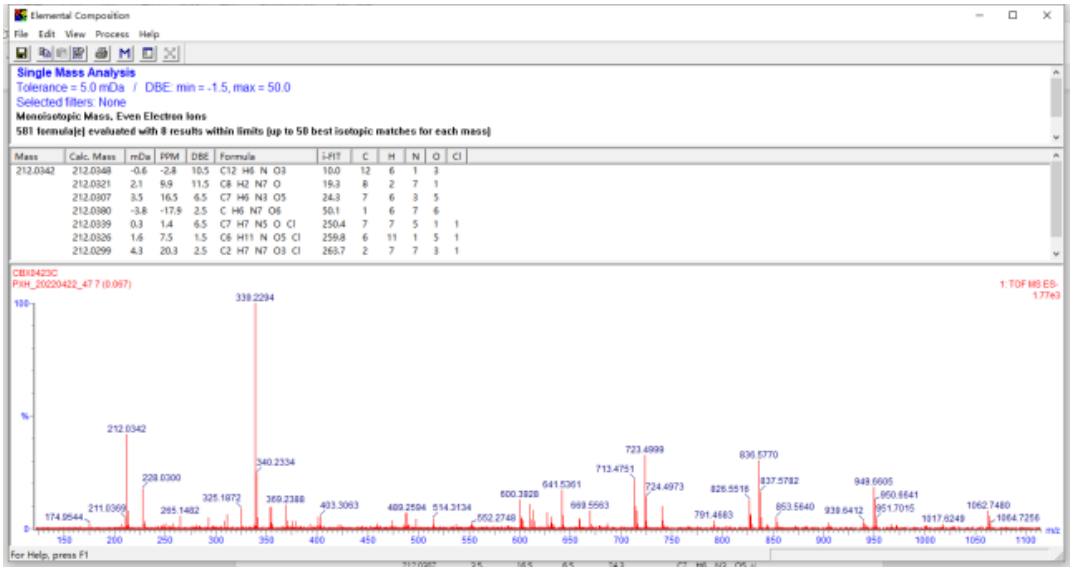

Figure 7: MS (ESI) spectra of 4-amino-1, 8-naphthalene anhydride

3. Results

3.1 Optimisation of conditions for the nitrification reaction

3.1.1 Effect of reaction temperature on the yield of nitrification reaction

In a 250 mL three-necked flask equipped with stirring, 40 mL of glacial acetic acid and 3.00 g (19.48 mmoL) of acenaphthene were added and dissolved with stirring for 1 h. A mixture of nitric acid and glacial acetic acid was slowly added dropwise to 14 mL ($V_{\text{nitric acid}}$: $V_{\text{glacial acetic acid}}$ = 1:1) over 0.5 h. The reaction temperature was varied and the reaction yields were found to vary at different temperatures.

Table 1: Effect of reaction temperature on the yield of nitrification reaction

Reaction temperature	Reaction yield	Product colour
Room temperature, 24~34℃	85.58%	Bright yellow, orange, dark yellow
Ice water bath, 14~16℃	77.12%	Bright yellow, orange, dark yellow
Cold water bath, 24~25℃	88.90%	Bright yellow, orange, dark yellow
Ice salt bath, 8~9℃	92.16%	Bright yellow, orange

As shown in Table 1, changing the reaction temperature had some effect on the yields of compounds 1 and 1′. At lower temperatures, a transient crystallization of glacial acetic acid occurred, but after continuous dropwise addition of the mixed acid solution, the crystallization of glacial acetic acid disappeared and did not affect the reaction yield much. At higher temperatures, the yield was reduced, but the reduction was not significant. Therefore, in summary, the reaction temperature was maintained at 8~9℃, and the reaction effect was better.

3.1.2 Column chromatographic purification of 4-nitroacenaphthene (1) and 2-nitroacenaphthene (1′)

A mixture of 1.08 g of compound 1 and 1′ was mixed with 1.08 g of column chromatography

silica gel. The 30 g of column chromatography silica was loaded wet with 75 mL of petroleum ether: ethyl acetate 30:1 and the sample was loaded dry. The solvent was recovered by bulk elution with petroleum ether:ethyl acetate 30:1 and the 30:1 eluate was collected to give 0.74 g of bright yellow solid compound 1 with 1′. A mixture of 2.74 g of Compound 1 with 1′ was mixed with 2.74 g of column chromatography silica. 30.02 g of column chromatography silica was loaded wet with 75 mL of petroleum ether:ethyl acetate 40:1 and the sample was loaded dry. The solvent was recovered by bulk elution with petroleum ether:ethyl acetate 40:1 and the 40:1 eluate was collected to give 2.52 g of bright yellow solid compound 1 with 1′.

3.1.3 Attempted thin layer identification of 4-nitroacenaphthene (1) and 2-nitroacenaphthene (1′) unfolders

Thin layer chromatography of ethyl acetate solution of raw acenaphthene (a), unspun second extraction product of nitroacenaphthene reaction (b) and spun second extraction product of nitroacenaphthene reaction (c) were carried out. Using petroleum ether: ethyl acetate (40:1) as the unfolding agent, the spots of b and c did not show the main product and by-product spots. Using petroleum ether: ethyl acetate (50:1) as the unfolding agent, the separation of b and c was not good. With petroleum ether: ethyl acetate (100:1) as the unfolding agent, and the separation of b and c was not good with trailing phenomenon. With petroleum ether: ethyl acetate (10:1) as the unfolding agent, the separation of b and c was good. And the main product and by-product could be clearly distinguished.

Using dichloromethane:methanol (60:1, 70:1, 80:1 and 100:1) as the unfolding agent, the separation of b from c was poor, with only single spots and higher Rf values than the combination of petroleum ether and ethyl acetate unfolding agents. Therefore, the combination of dichloromethane and methanol was not suitable for the separation of compounds 1 and 1′. Although petroleum ether: ethyl acetate (30:1) was used as the unfolding agent for the separation of the samples, the difference in Rf values between the main product and by-product spots was less than 0.10, which was not suitable for the separation of compounds 1 and 1′ by column chromatography.

In order to purify the crude product of compound 1 and to separate the main product from the by-products in an attempt to obtain pure compound 1, a large number of unfolding agent attempts were made. Since the separation was better with petroleum ether:ethyl acetate = 10:1, on this basis, glacial acetic acid was added to the unfolding agent dropwise to increase the polarity of the unfolding agent in order to further optimise the separation, this is shown in Table 2. It can be concluded from the data in Table 2 that the Rf value of the product point increased with the addition of ice acetic acid dropwise, but with the increase of the number of ice acetic acid drops, the Rf value of the product point decreased at 20-25 drops. In addition, combined with the spacing of the primary and secondary product points, it can be seen that the petroleum ether:ethyl acetate=10:1 unfolding agent is not suitable for use as an eluent for the post-column chromatography treatment of the nitration reaction products.

From the data in Table 3, it can be seen that by increasing the polarity of the unfolding agent, the main and by-product points could continue to be separated, but the difference between the Rf values of the two points became smaller and smaller, while the Rf value of the main product point was greater than 0.5, which was not suitable as an eluent for the post-treatment of the nitrated product column chromatography. At dichloromethane: petroleum ether=5:1, the main and by-product points were not separated and the Rf value was 0.79. Subsequently, petroleum ether: dichloromethane=10:1 was tried and failed to separate the main and by-product points and there was only a single point with a low Rf value of 0.11. Therefore, the combination of petroleum ether and dichloromethane unfolders was not effective.

Table 2: Results of spotting of petroleum ether: ethyl acetate = 10:1 unfolding agent dropwise with glacial acetic acid

Ice acetic acid	Main product R_f value	By-product R_f values	Are the primary and secondary products separated and if so what is the difference in R_f values
0 drops	0.52	0.63	0.11
5 drops	0.56	0.65	Cannot be separated, two points adjacent to each other
10 drops	0.54	0.63	0.09
15 drops	0.55	0.63	0.08
20 drops	0.63	0.72	0.09
25 drops	0.59	0.68	0.09

Table 3: Results of spot sampling for petroleum ether: ethyl acetate = 10:1 - 2.5:1

Petroleum ether: ethyl acetate	Primary product point R_f value	By-product point R_f value	Whether primary and secondary products are separated
10:1	0.49	0.61	Yes
7:1	0.78	0.91	Yes
6:1	0.67	0.82	Yes
5:1	0.64	0.71	Yes
4:1	0.71	0.79	Yes
3:1	0.81	0.87	Yes
2.5:1	0.64	0.69	Yes

3.2 Optimisation of conditions for the oxidation reaction

3.2.1 Effect of heating reflux length on the yield of the oxidation reaction

In a 250 mL three-necked flask with stirring, 15 mL of glacial acetic acid, 6.00 g of sodium dichromate and 1.00 g (5.02 mmoL) of compounds 1 and 1′ were dissolved with stirring and then heated to reflux (during which the reaction solution turned dark green). The heating reflux length was varied, and the heating reflux length was found to have an effect on the yields of compounds 2 and 2′ as shown in Table 4. Therefore, a heating reflux time of 5.0 h is preferred.

Table 4: Effect of heating reflux duration on the yield of the oxidation reaction

Compound 1 with 1’	Sodium dichromate	$n_{\text{Compound 1 with 1'}}$:$n_{\text{sodium dichromate}}$	Heating reflux time	Yield
1.00 g	6.00 g	1:4	4 h	16.80%
1.05 g	6.00 g	1:4	5 h	32.30%
1.00 g	6.00 g	1:4	6 h	26.70%
0.47 g	2.81 g	1:4	7 h	11.04%

3.2.2 Effect of oxidant dosage on the yield of the oxidation reaction

A 250 mL three-necked flask equipped with stirring was charged with 15 mL of glacial acetic acid, a quantity of sodium dichromate and 1.00 g (5.02 mmoL) of compounds 1 and 1′, stirred to dissolve and heated to reflux (during which time the reaction solution turned dark green). The

reaction was terminated after 5 h. Varying $n_{compound\ 1}$ with 1′: $n_{sodium\ dichromate}$ gives different yields of the oxidation reaction. The results are shown in Table 5.

Table 5: Effect of oxidant dosage on the yield of the oxidation reaction

Compound 1 with 1’	Sodium dichromate	$n_{Compound\ 1\ with\ 1'}$:$n_{sodium\ dichromate}$	Yield
1.01 g	4.52 g	1:3	24.60%
1.05 g	6.00 g	1:4	32.30%
0.50 g	3.50 g	1:4.5	30.10%
1.01 g	7.47 g	1:5	28.60%
0.52 g	4.50 g	1:6	21.40%

As seen from Table 5, when the amount of oxidant was low, the reaction was incomplete and the yield was low; when the amount of oxidant was elevated, side reactions occurred, the colour of the product deepened and the yield decreased. In summary, the best yield was obtained when ncompound 1 was 1:4 with 1′: nsodium dichromate.

3.2.3 Effect of post-treatment of oxidation products on the yield of the oxidation reaction

Table 6: Effect of oxidation product post-treatment method on the yield of the oxidation reaction

Compound 1 with 1’	Sodium dichromate	Post-processing methods	Yield
1.06 g	6.00 g	Crystallisation of glacial acetic acid solution at room temperature	32.30%
1.07 g	6.07 g	Hot glacial acetic acid solution (50 ℃) dissolved, cooled and crystallised	23.90%
1.07 g	6.03 g	Dissolve in saturated sodium bicarbonate solution, adjust pH to 1~2 with concentrated hydrochloric acid and filter by extraction	26.70%
0.46 g	2.72 g	Ice salt bath	57.10%

A 250 mL three-necked flask equipped with stirring was charged with 15 mL of glacial acetic acid, 6.00 g of sodium dichromate and 1.00 g (5.02 mmoL) of compounds 1 and 1′, stirred to dissolve and heated to reflux (during which time the reaction solution turned dark green). The reaction was terminated after 5 h. Different yields of the oxidation reaction are obtained by post-treatment of the oxidation products in different ways. The results are shown in Table 6. From the data in Table 6 it can be seen that the ice salt bath post-treatment gave the best results with yields in excess of 50%.

3.2.4 Validation and results of the modified reaction conditions for the oxidation reaction

Table 7: Validation and results of the improved reaction conditions for the oxidation reaction

Compound 1 with 1’	Sodium dichromate	Iceacetic acid	$n_{Compound\ 1}$:$n_{sodium\ dichromate}$	Heating reflux length	Post-treatment method	Yield
5.04 g	30.38 g	150 mL	1:4	5 h	Ice salt bath	49.83%
4.08 g	24.84 g	120 mL	1:4	5 h	Ice salt bath	58.72%
2.38 g	14.58 g	80 mL	1:4	5 h	Ice salt bath	49.28%
3.11 g	19.21 g	100 mL	1:4	5 h	Ice salt bath	59.49%

From the data in Table 7, it can be concluded that after optimising the reaction conditions, the yield is close to 50% at the minimum and is expected to reach 60% at the maximum. The overall yield was higher than the 49.73% reported in the literature.

3.3 Optimisation of conditions for the reduction reaction

3.3.1 Effect of the volume ratio of anhydrous ethanol to concentrated HCl on the yield of the reduction reaction

As can be seen from the data in Table 8, if the amount of anhydrous ethanol is kept constant, increasing the amount of concentrated HCl will reduce the yield. Keeping the amount of concentrated HCl constant, increasing the amount of anhydrous ethanol will also reduce the yield, so $V_{\text{anhydrous ethanol}}$: V_{HCl} of 2.5:1 is most suitable.

Table 8: Effect of the volume ratio of anhydrous ethanol to concentrated HCl on the yield of the reduction reaction

Compound 2 with 2’	Stannous chloride	Anhydrous ethanol	Concentrated HCl	$V_{\text{anhydrous ethanol}}$:V_{HCl}	Yield
0.67 g	3.14 g	5. mL	2 mL	2.5:1	77.47%
0.66 g	3.10 g	13.5 mL	2.5 mL	5.4:1	73.23%
0.31 g	1.53 g	6 mL	2 mL	3:1	56.63%
0.38 g	1.63 g	6 mL	4 mL	3:2	36.04%

3.3.2 Thin layer identification of 4-amino-1,8 naphthalic anhydride (3) and 2-amino-1,8 naphthalic anhydride (3′)

Four separate 0.05 g reductions of the crude products 3 & 3′ were taken and dissolved in 0.50 mL of Microtubes with ethyl acetate. As silica gel adsorbs compounds containing amino and carboxyl groups, and compounds 3 and 3′ have amino and anhydride groups, ammonia or triethylamine was added to the spreaders to reduce or even inhibit their dragging when spotting. To inhibit the dissociation of its anhydride group and protonate it, thus increasing the molecular polarity of the compound and allowing the primary and secondary product spots to be more easily separated, glacial acetic acid is also added to the unfolding agent accordingly.

Firstly, using petroleum ether: ethyl acetate (1:1 and 2:1) as the unfolding agent, the reduction product spot was a trailing strip with an R_f value of 0.18 per 10 mL of petroleum ether: ethyl acetate unfolding agent without the addition of any acid or alkali; when 2-3 drops of ammonia were added experimentally, the reduction product spot still did not run as a single, long strip with an R_f value of 0.28. In the case of 3 drops of triethylamine, the spotting result was the same as the previous one, with an R_f value of 0.29.

The unfolding agent was replaced with a combination of dichloromethane and methanol and the results are shown in Table 9.

When a single unfolding agent was tried, it was found that when the unfolding agent was polarized, no single point was produced for the reduced product spots at petroleum ether:ethyl acetate = 1:1 or 2:1, and there was serious trailing. In the dichloromethane:methanol 50:1-100:1 condition, there were few cases where a single spot could be run, and the main and by-product spots were not separated, and in most cases there was still no single spot and the trailing was serious. Subsequently, a second unfolding of the spotting results was carried out on the basis of dichloromethane: methanol = 50:1 with 30:1 and 100:1 unfolding agents respectively, and it was

found that the previous trailing phenomenon was reduced and a single spot of product appeared. At 30:1, the R_f value of the reduced product single spot increased further from the previous 0.30-0.35 to 0.70. At 100:1, a single spot of product appeared within the strip with an R_f value of 0.37.

Table 9: Exploration of unfolding agents for dichloromethane and methanol systems

Dichloromethane: Methanol	Whether acid or base is added dropwise per 10mL of spreading agent	Does a single point occur and if so what is the R_f value	Is there any trailing
50:1	None	Yes, 0.30 to 0.35	Yes
50:1	2 drops of glacial acetic acid	Yes, 0.85	Yes
50:1	1 drop of ammonia	No	Yes
50:1	3 drops of ammonia	No	Yes
70:1	None	None	Yes
100:1	None	Yes, 0.10	Yes

In summary, as a single ratio of unfolding agent was not sufficient to separate the main and by-products, a column chromatographic gradient elution method of dichloromethane: methanol = 120:1 - 50:1 was attempted to try to obtain relatively pure compound 3.

3.3.3 Thin layer identification of the purer 4-amino-1,8 naphthalic anhydride (3)

As the first column chromatography gradient eluted and the product obtained after spin evaporation was small and adhered to the walls of the vessel, 1 mL of ethyl acetate was added to dissolve some of the product and the solution was transferred to 0.50 mL of Microtubes. One drop of glacial acetic acid and one drop of triethylamine were added to each 10 mL of solution for the unfolding agent used. At dichloromethane: methanol = 10:1, the main product spot was very obvious, a yellow fluorescent spot visible to the naked eye with an Rf value of 0.77. At violet 365 nm, a light green fluorescent spot appeared at an Rf value of 0.65, the by-product spot, where impurities or pigmented spots were difficult to see and not easily identified and the Rf value calculated.

At dichloromethane: methanol = 20:1, a closer look at the single spot with an Rf value of 0.38 showed a light green fluorescence and was not obvious, in contrast to the main product spot at an Rf value of 0.60, which was more significantly coloured and a side indication that the 4-amino-1,8 naphthalic anhydride was pure in this spinout. At dichloromethane: methanol = 30:1 and 50:1, the separation and analysis of the results were the same as before, except that the Rf values were different from those described above, so I will not repeat them.

4. Conclusions

The optimum experimental conditions for the nitration reaction were: 40 mL of glacial acetic acid and 3.00 g of acenaphthene (19.48 mmoL) were added to a 250 mL three-necked flask equipped with stirring at a reaction temperature of 8-9 ℃ for 1 h. After 1 h, a mixture of nitric acid and glacial acetic acid was slowly added dropwise to 14 mL (Vnitric acid: Vglacial acetic acid = 1:1) over a period of 0.5 h. After 1 h of reaction, the mixture was withdrawn and filtered to give a bright yellow solid mixture of 1 and 1 ′, the yield of which was up to 92.16%. The optimum experimental conditions for the oxidation reaction were: 100 mL of glacial acetic acid, ncompound 1:nsodium dichromate = 1:4, heated at reflux for 5 h to give a golden yellow solid mixture 2 and 2′. The yield was up to 59.49%. The optimum experimental conditions for the reduction reaction were: 5 mL of anhydrous ethanol and 0.67 g (2.75 mmoL) of compounds 2 and 2′ in a 50 mL three-necked flask equipped with stirring; 2 mL (2.36 g, 24.00 mmoL) of concentrated HCl in a 50 mL beaker with a

glass rod stirred with 3.10 g (13.74 mmoL) of SnCl2- 2H2O, fully dissolved, and slowly added dropwise to a three-necked flask with a rubber-tipped dropper within 10 min, with V anhydrous ethanol:V concentrated HCl = 2.5:1 in the reaction solution, yielding an orange-yellow solid mixture of 3 with 3′ after 2 h of reaction. The reduced crude product was eluted by gradient column chromatography using dichloromethane-methanol = 120:1 to 50:1 to give a relatively pure compound 3. The synthesis process of compound 3 was improved, and some experience and data were accumulated for the preparation of this compound in large quantities.

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