Notice

DESCRIPTION CN115784964A

Synthetic methods for 3,3′-diindolomethane

3，3′-二吲哚甲烷的合成方法

[0001]

Technical Field

技术领域

[n0001]

This invention relates to the field of organic synthesis technology, and more specifically, to a method for synthesizing 3,3'-diindolemethane.

本发明涉及有机合成技术领域，具体而言，涉及3,3'-二吲哚甲烷的合成方法。

[0003]

Background Technology

背景技术

[n0002]

3,3′-Diindolemethane is a white or off-white crystalline powder that is widely found in natural plants of the Brassicaceae family. It has important biological and pharmacological activities and is widely used in the fields of medicine and health products. In clinical medicine, it can be used to treat various cancers and tumors.

3,3′二吲哚甲烷为白色或类白色结晶性粉末，广泛存在于十字花科的天然植物中，具有重要的生物活性和药理活性，在医药和保健品领域应用广泛，在临床医学上可用来治疗多种癌症和肿瘤。

[n0003]

There are several methods for synthesizing 3,3′-diindolemethane, some using indole and aldehyde as the main raw materials, others using indole-3-methanol as the main raw material, and still others using indole and N-hydroxymethylacrylamide as the main raw materials.

3,3′二吲哚甲烷的合成方法中有以吲哚和醛为主要原料的，也有以吲哚-3-甲醇为主要原料的，也有以吲哚和N-羟甲基丙烯酰胺为主要原料的。

Among them, the preparation of 3,3′-diindolemethane using indole and aldehydes as raw materials has been reported in many cases.

其中，以吲哚和醛类为原料制备3,3′二吲哚甲烷多有报道。

[n0004]

The existing technology for preparing 3,3′-diindolemethane using indole and aldehydes as raw materials has the following main problems: (1) A large amount of ethanol is used in the solvent, resulting in high production costs; (2) Protective gases such as nitrogen are required during the synthesis process, which is not suitable for industrial production; (3) The synthesis method using water as a solvent relies on reaction conditions such as ultrasonic radiation, which are harsh and the yield is very low (only 45%).

现有技术中以吲哚和醛类为原料制备3,3′二吲哚甲烷主要存在以下问题：(1)溶剂中多采用了大量乙醇，生产成本较高；(2)合成过程中需要氮气等保护气，不适合工业化生产；(2)以水为溶剂的合成方法，多借助超声波辐射等反应条件，反应条件苛刻，收率也很低(仅为45%)。

[n0005]

In view of this, the present invention is proposed.

鉴于此，特提出本发明。

[0008]

Summary of the Invention

发明内容

[n0006]

The purpose of this invention is to provide a method for synthesizing 3,3'-diindolemethane, which aims to achieve the synthesis of 3,3'-diindolemethane using water as a solvent without harsh conditions, while maintaining high product yield and purity.

本发明的目的在于提供一种3,3'-二吲哚甲烷的合成方法，旨在没有苛刻条件的前提下，实现以水为溶剂合成3,3′二吲哚甲烷，且能够保持较高的产品收率和纯度。

[n0007]

This invention is implemented as follows:

本发明是这样实现的：

[n0008]

This invention proposes a method for synthesizing 3,3'-diindolemethane, in which indole, formaldehyde and water are mixed and reacted in the presence of a catalyst, and the mixture is cooled to crystallize after the reaction is complete.

本发明提出了一种3,3'-二吲哚甲烷的合成方法，在催化剂存在的条件下，将吲哚、甲醛和水混合反应，反应完成后降温析晶；

[n0009]

The catalysts include 4-dimethylaminopyridine and phase transfer catalysts.

其中，催化剂包括4-二甲氨基吡啶和相转移催化剂。

[n0010]

The present invention has the following beneficial effects: The present invention uses indole and formaldehyde as raw materials, and synthesizes the target product 3,3'-diindolemethane in the presence of a phase transfer catalyst and a catalyst 4-dimethylaminopyridine, with water as the reaction solvent.

本发明具有以下有益效果：本发明以吲哚和甲醛为原料，在相转移催化剂和催化剂4-二甲氨基吡啶的作用下，以水为反应溶剂合成目标产物3,3'-二吲哚甲烷。

The reaction route provided by this invention has a fast reaction rate, avoids the use of organic solvents, and does not require harsh reaction conditions such as ultrasound, making it a green organic synthesis technology; the final product has a high yield and purity, which is conducive to industrialization.

本发明提供的反应路线反应速率快，避免使用有机溶剂，且不需要超声波等比较苛刻的反应条件，是一种绿色的有机合成技术；最终得到的产品的收率和纯度都比较高，利于产业化。

[0014]

Attached Figure Description

附图说明

[n0011]

To more clearly illustrate the technical solutions of the embodiments of the present invention, the accompanying drawings used in the embodiments will be briefly introduced below. It should be understood that the following drawings only show some embodiments of the present invention and should not be regarded as a limitation on the scope. For those

skilled in the art, other related drawings can be obtained based on these drawings without creative effort.

为了更清楚地说明本发明实施例的技术方案，下面将对实施例中所需要使用的附图作简单地介绍，应当理解，以下附图仅示出了本发明的某些实施例，因此不应被看作是对范围的限定，对于本领域普通技术人员来讲，在不付出创造性劳动的前提下，还可以根据这些附图获得其他相关的附图。

[n0012]

Figure 1 is a flowchart of the synthesis method provided in an embodiment of the present invention;

图1为本发明实施例提供的合成方法的流程图；

[n0013]

Figure 2 shows the test results of the product prepared in Example 1.

图2为实施例1中制备得到产品的测试结果图。

[0018]

Detailed Implementation

具体实施方式

[n0014]

To make the objectives, technical solutions, and advantages of the embodiments of the present invention clearer, the technical solutions in the embodiments of the present invention will be clearly and completely described below.

为使本发明实施例的目的、技术方案和优点更加清楚，下面将对本发明实施例中的技术方案进行清楚、完整地描述。

Unless otherwise specified in the examples, the conditions shall be performed according to the standard conditions or the conditions recommended by the manufacturer.

实施例中未注明具体条件者，按照常规条件或制造商建议的条件进行。

If the manufacturers of the reagents or instruments used are not specified, they are all conventional products that can be purchased commercially.

所用试剂或仪器未注明生产厂商者，均为可以通过市售购买获得的常规产品。

[n0015]

Referring to Figure 1, this embodiment of the invention provides a method for synthesizing 3,3'-diindolemethane. In the presence of a catalyst, indole, formaldehyde, and water are mixed and reacted. After the reaction is completed, the mixture is cooled to crystallize. The catalyst includes 4-dimethylaminopyridine (DMAP) and a phase transfer catalyst.

请参照图1，本发明实施例提供一种3,3'-二吲哚甲烷的合成方法，在催化剂存在的条件下，将吲哚、甲醛和水混合反应，反应完成后降温析晶；其中，催化剂包括4-二甲氨基吡啶(DMAP)和相转移催化剂。

[n0016]

The inventors have creatively utilized 4-dimethylaminopyridine and a phase transfer catalyst for the synthesis of 3,3'-diindolemethane. The reaction can be completed using only water as a solvent, avoiding the use of large amounts of ethanol solvent and reducing reaction costs.

The reaction can be completed without harsh reaction conditions such as ultrasound, which is conducive to industrial application.

发明人创造性地利用4-二甲氨基吡啶和相转移催化剂用于3,3'-二吲哚甲烷的合成，可以在仅采用水为溶剂的条件下完成反应，避免了大量使用乙醇溶剂，降低的反应成本；不需要超声波等比较苛刻的反应条件就能完成反应，有利于实现工业化应用。

More importantly, the embodiments of the present invention can further improve the yield and purity of the product through catalyst optimization.

更为重要的是，本发明实施例通过催化剂的优化能够进一步提升产品的收率和纯度。

[n0017]

In a preferred embodiment of the present invention, the phase transfer catalyst is tetrabutylammonium bromide (TBAB), and the specific principle is as follows:

在本发明优选的实施例中，相转移催化剂为四丁基溴化铵(TBAB)，具体原理如下：

[n0019]

Using tetrabutylammonium bromide as a phase transfer catalyst, the product yield and purity can be maintained at a high level, providing conditions for the industrial application of the process.

采用四丁基溴化铵为相转移催化剂，产品的收率和纯度均能够保持在较高水平，为工艺的工业化应用提供了条件。

Replacing the phase transfer catalyst with tetraethylammonium bromide will significantly reduce product yield and purity.

若将相转移催化剂替换为四乙基溴化铵，将会很大程度上降低产品收率和纯度。

[n0020]

Furthermore, the reaction temperature is 50-80°C, preferably 50-70°C.

进一步地，反应温度为50-80°C，优选为50-70°C。

The reaction time is 6.5-10.5 h; preferably 7.5-10.5 h.

反应时间为6.5-10.5h；优选为7.5-10.5h。

If the reaction temperature is too low, the raw materials cannot dissolve. The reaction temperature needs to be above 50°C, and the reaction efficiency increases accordingly with the increase of reaction temperature. If the reaction temperature is too high, the energy consumption increases significantly, but the reaction rate is not significantly improved.

反应温度过低原料不能溶解，反应温度需要在50°C以上，并且随着反应温度的升高反应效率也相应增加；反应温度过高则能耗显著增加，但是反应速率并没有显著改善。

The inventors discovered that the optimal reaction temperature is 50-70°C and the optimal reaction time is 7.5-10.5h.

发明人发现，反应温度在50-70°C，反应时间在7.5-10.5h为宜。

[n0021]

Specifically, the reaction temperature can be 50°C, 55°C, 60°C, 65°C, 70°C, 75°C, or 80°C; preferably 50°C, 55°C, 60°C, 65°C, or 70°C, but can also be any value between two adjacent values.

具体地，反应温度可以为50°C、55°C、60°C、65°C、70°C、75°C、80°C；优选为50°C、55°C、60°C、65°C、70°C，也可以为相邻两个数值之间的任意取值。

The reaction time depends on the reaction temperature to ensure a complete reaction; the lower the reaction temperature, the longer the reaction time should be.

反应时间根据反应温度而定，以充分反应完全，反应温度越低反应时间相应要更高。

[n0022]

In a preferred embodiment of the present invention, the cooling crystallization is carried out by cooling the temperature by 20-25°C after the reaction is completed and allowing crystallization for 0.5-1.5 hours, so that the product is fully precipitated.

在本发明优选的实施例中，降温析晶是在反应结束之后降温20-25℃，并析晶0.5-1.5h，以使产品充分析出。

Specifically, the temperature reduction can be 20°C, 21°C, 22°C, 23°C, 24°C, or 25°C, or it can be any value between two adjacent values.

具体地，降温可以是降低20°C、21°C、22°C、23°C、24°C、25°C，也可以是相邻两个数值之间的任意取值。

Crystallization is an approximate time. Filtration can be carried out after the crystals have completely precipitated. The crystallization time is approximately 1 hour.

析晶是一个大致时间，待晶体析出完全之后即可进行过滤，大概析晶的时间为1h。

[n0023]

In some embodiments, the process further includes filtering, rinsing, filtering again, and drying the filter cake after cooling and crystallization.

在一些实施例中，还包括在降温析晶之后进行过滤、漂洗，然后进行再次过滤并将滤饼干燥。

The product is separated by filtration, and then unreacted raw materials remaining on the crystal surface are removed by rinsing. A product with higher purity is obtained by filtration and drying again.

通过过滤将产品分离出来，再通过漂洗去除晶体表面残留的未反应原料，通过再次过滤和干燥得到纯度更高的产品。

Specifically, rinsing can be done with ethanol or other organic reagents, which will not be listed here.

具体地，漂洗可以采用乙醇进行漂洗，也可以采用其他有机试剂，在此不进行一一列举。

[n0024]

To further increase the reaction yield, the inventors further optimized the amount of each raw material:

为进一步增加反应的收率，发明人对各原料的用量做了进一步优化：

[n0025]

The molar ratio of formaldehyde to indole is 1:1.8-2.3; preferably 1:2-2.2.

甲醛和吲哚的摩尔比为1:1.8-2.3；优选为1:2-2.2。

The ratio of formaldehyde to indole has a certain impact on the product yield. It is advisable to control the ratio of formaldehyde to indole at 1:2-2.2. Too high or too low a ratio will not help improve the yield.

甲醛和吲哚的用量比对产品的收率有一定影响，将甲醛和吲哚的用量比控制在1:2-2.2为宜，过大过小均不利于提高收率。

[n0026]

The amount of water used is 2-5 times the mass of indole, preferably 3-4 times.

水的用量为吲哚质量的2-5倍，优选为3-4倍。

The amount of water used should be 3-4 times the amount of indole to ensure that formaldehyde and indole are fully dissolved.

水的用量是保证能够充分溶解甲醛和吲哚，水的用量为吲哚用量的3-4倍为宜。

[n0027]

Furthermore, the mass ratio of tetrabutylammonium bromide to formaldehyde is 1.5-5:100; preferably 2.5-4:100.

进一步地，四丁基溴化铵与甲醛的质量比为1.5-5:100；优选为2.5-4:100。

The yield of the product increases with the increase of the amount of tetrabutylammonium bromide used, but the yield tends to stabilize when it reaches 2.5-4:100. It is advisable to control it at 2.5-4:100.

随着四丁基溴化铵用量的增加产品的收率随之增加，但是达到2.5-4:100时收率趋于平稳，控制在2.5-4:100为宜。

[n0028]

Furthermore, the mass ratio of 4-dimethylaminopyridine to formaldehyde is 1-5:100; preferably 2-4:100.

进一步地，4-二甲氨基吡啶与甲醛的质量比为1-5:100；优选为2-4:100。

The mass ratio of 4-dimethylaminopyridine to formaldehyde should be controlled at 2-4:100. If the dosage is too low, the yield will be unsatisfactory, and if the dosage is increased, the yield will not be significantly improved.

4-二甲氨基吡啶与甲醛的质量比控制在2-4:100为宜，用量过低则收率不理想，用量再增加收率也没有显著提高。

[n0029]

The features and performance of the present invention will be further described in detail below with reference to embodiments.

以下结合实施例对本发明的特征和性能作进一步的详细描述。

[n0030]

Example 1

实施例1

[n0031]

This embodiment provides a method for synthesizing 3,3'-diindolemethane, comprising: adding 468g of indole and 60g of formaldehyde to 1500mL of water, heating to 60°C and stirring to dissolve the raw materials, adding 1.8g of tetrabutylammonium bromide, and then adding 1.8g of 4-dimethylaminopyridine, reacting for 7h under central liquid-phase control, cooling to 20°C after the reaction is completed, during which product gradually precipitates,

crystallizing for 1h, filtering, washing the filter cake once with ethanol, drying under vacuum, and drying the filter cake to obtain 427g of product 3,3'-diindolemethane with a purity of 99.5% and a yield of 86.8%.

本实施例提供一种3,3'-二吲哚甲烷的合成方法，包括：取468g吲哚和60g甲醛加入到1500mL水中，加热到60°C搅拌，原料溶解，加入1.8g四丁基溴化铵，再加入1.8g的4-二甲氨基吡啶，反应7h，液相中控，反应结束后降温20°C，降温过程中逐渐有产品析出，结晶1h，过滤，滤饼使用乙醇漂洗一次，抽干，滤饼干燥，得到产品3,3'-二吲哚甲烷427g，纯度99.5%，收率86.8%。

[n0032]

In this embodiment, the molar ratio of formaldehyde to indole is 1:2, the mass ratio of formaldehyde to 4-dimethylaminopyridine is 100:3.0, and the mass ratio of formaldehyde to tetrabutylammonium bromide is 100:3.0.

本实施例中甲醛与吲哚的摩尔比为1:2，甲醛与4-二甲氨基吡啶质量比为100:3.0，甲醛与四丁基溴化铵质量比为100:3.0。

[n0033]

Examples 2-5

实施例2-5

[n0034]

This embodiment provides a method for synthesizing 3,3'-diindolemethane, which differs from Example 1 only in that the molar ratio of formaldehyde and indole is changed.

本实施例提供一种3,3'-二吲哚甲烷的合成方法，与实施例1不同之处仅在于：改变甲醛和吲哚的摩尔比。

[n0035]

In Examples 2-5, the molar ratio of formaldehyde to indole was controlled to be 1:1.8, 1:2.1, 1:2.2, and 1:2.3, respectively.

实施例2-5中分别控制甲醛和吲哚的摩尔比为1:1.8、1:2.1、1:2.2、1:2.3。

[n0036]

Examples 6-11

实施例6-11

[n0037]

This embodiment provides a method for synthesizing 3,3'-diindolemethane, which differs from Example 1 only in that the amount of tetrabutylammonium bromide is changed.

本实施例提供一种3,3'-二吲哚甲烷的合成方法，与实施例1不同之处仅在于：改变四丁基溴化铵的用量。

[n0038]

Examples 6-11 control the mass ratio of formaldehyde to tetrabutylammonium bromide to be 100:1.5, 100:2.0, 100:2.5, 100:3.5, 100:4.0, and 100:5.0, respectively.

实施例6-11分别控制甲醛与四丁基溴化铵质量比为100:1.5、100:2.0、100:2.5、100:3.5、100:4.0、100:5.0。

[n0039]

Examples 12-15

实施例12-15

[n0040]

This embodiment provides a method for synthesizing 3,3'-diindolemethane, which differs from Example 1 only in that the amount of 4-dimethylaminopyridine is changed.

本实施例提供一种3,3'-二吲哚甲烷的合成方法，与实施例1不同之处仅在于：改变4-二甲氨基吡啶的用量。

[n0041]

In Examples 12-15, the mass ratio of formaldehyde to 4-dimethylaminopyridine was controlled to be 100:1.0, 100:2.0, 100:4.0, and 100:5.0, respectively.

实施例12-15分别控制甲醛与4-二甲氨基吡啶质量比为100:1.0、100:2.0、100:4.0、100:5.0。

[n0042]

Examples 16-19

实施例16-19

[n0043]

This embodiment provides a method for synthesizing 3,3'-diindolemethane, which differs from Example 1 only in that the reaction temperature and reaction end time are changed.

本实施例提供一种3,3'-二吲哚甲烷的合成方法，与实施例1不同之处仅在于：改变反应温度和反应结束时间。

[n0044]

In Example 16, the reaction temperature was 50°C and the reaction time was 10.5 hours.

实施例16反应温度为50°C，反应结束时间为10.5h；

[n0045]

In Example 17, the reaction temperature was 70°C and the reaction time was 7.5 hours.

实施例17反应温度为70°C，反应结束时间为7.5h；

[n0046]

In Example 18, the reaction temperature was 80°C and the reaction time was 6.5 hours.

实施例18反应温度为80°C，反应结束时间为6.5h；

[n0047]

In Example 19, the reaction temperature was 90°C and the reaction time was 6.5 h.

实施例19反应温度为90℃，反应结束时间为6.5h。

[n0048]

Comparative Example 1

对比例1

[n0049]

This comparative example provides a method for synthesizing 3,3'-diindolemethane, which differs from Example 1 only in that tetrabutylammonium bromide is replaced with tetraethylammonium bromide (TEAB).

本对比例提供一种3,3'-二吲哚甲烷的合成方法，与实施例1不同之处仅在于：将四丁基溴化铵替换为四乙基溴化铵(TEAB)。

[n0050]

Comparative Example 2

对比例2

[n0051]

This comparative example provides a method for synthesizing 3,3'-diindolemethane, which differs from Example 1 only in that tetrabutylammonium bromide is replaced with tetrabutylammonium chloride (TBACl).

本对比例提供一种3,3'-二吲哚甲烷的合成方法，与实施例1不同之处仅在于：将四丁基溴化铵替换为四丁基氯化铵(TBACl)。

[n0052]

Comparative Example 3

对比例3

[n0053]

This comparative example provides a method for synthesizing 3,3'-diindolemethane, which differs from Example 1 only in that tetrabutylammonium bromide is replaced with tetrabutylammonium iodide (TBAI).

本对比例提供一种3,3'-二吲哚甲烷的合成方法，与实施例1不同之处仅在于：将四丁基溴化铵替换为四丁基碘化铵(TBAI)。

[n0054]

Comparative Example 4

对比例4

[n0055]

This comparative example provides a method for synthesizing 3,3'-diindolemethane, which differs from Example 1 only in that 4-dimethylaminopyridine is replaced with 1-hydroxybenzotriazole (HOBT).

本对比例提供一种3,3'-二吲哚甲烷的合成方法，与实施例1不同之处仅在于：将4-二甲氨基吡啶替换为1-羟基苯并三唑(HOBT)。

[n0056]

Comparative Example 5

对比例5

[n0057]

This comparative example provides a method for synthesizing 3,3'-diindolemethane, which differs from Example 1 only in that 4-dimethylaminopyridine is replaced with 4-pyrrolidinylpyridine (4-PPY).

本对比例提供一种3,3'-二吲哚甲烷的合成方法，与实施例1不同之处仅在于：将4-二甲氨基吡啶替换为4-吡咯烷基吡啶(4-PPY)。

[n0058]

Experimental Example 1

试验例1

[n0059]

The liquid chromatogram of the product obtained in Test Example 1 is shown in Figure 2.

测试实施例1中得到产品的液相色谱图，结果见图2。

As shown in Figure 2, the product prepared in the embodiment of the present invention has a very high purity.

由图2可知，本发明实施例制备得到的产品的纯度很高。

[n0060]

Experimental Example 2

试验例2

[n0061]

The yield and purity of each example were tested using conventional methods. The data for Examples 1-5 are shown in Table 1:

采用常规的方法测试各实施例的收率和纯度，实施例1-5的数据如表1：

[n0062]

Table 1. Effect of formaldehyde to indole molar ratio

表1甲醛与吲哚摩尔比的影响

[n0063]

Examples Formaldehyde to Indole Molar Ratio Yield % Purity % Example 1 1:2 86.8 99.5

Example 2 1:1.8 77.2 98.7 Example 3 1:2.1 87.6 99.4 Example 4 1:2.2 88.5 99.7 Example 5 1:2.3

87.8 99.6

实施例 甲醛和吲哚摩尔比 收率% 纯度% 实施例1 1：2 86.8 99.5 实施例2 1：1.8 77.2 98.7 实施例3 1：2.1 87.6 99.4 实施例4 1：2.2 88.5 99.7 实施例5 1：2.3 87.8 99.6

[n0064]

As can be seen from Table 1, the reaction of the raw materials is incomplete when the molar ratio of formaldehyde to indole is less than 1:2, while the yield can reach more than 85% when the ratio is greater than 1:2.

从表1可以看出，甲醛和吲哚摩尔比低于1：2时原料反应不完全，处于1：2以上时收率可以达到85%以上。

To avoid wasting raw materials, a ratio of 1:2-2.2 is more appropriate.

为避免原料浪费，将比例定为1：2-2.2较为合适。

[n0065]

Experimental Example 3

试验例3

[n0066]

The yield and purity of each example were tested using conventional methods. Data for Example 1 and Examples 6-11 are shown in Table 2.

采用常规的方法测试各实施例的收率和纯度，实施例1和实施例6-11的数据如表2：

[n0067]

Table 2 Effect of tetrabutylammonium bromide dosage

表2四丁基溴化铵用量的影响

[n0068]

Example Formaldehyde to TBAB mass ratio Yield % Purity % Example 1 100:3.0 86.8 99.5 Example 6 100:1.5 79.8 97.4 Example 7 100:2.0 83.5 98.8 Example 8 100:2.5 85.7 99.4 Example 9 100:3.5 87.1 99.5 Example 10 100:4.0 86.8 99.7 Example 11 100:5.0 86.6 99.7

实施例 甲醛和TBAB质量比 收率% 纯度% 实施例1 100：3.0 86.8 99.5 实施例6 100：1.5 79.8 97.4 实施例7 100：2.0 83.5 98.8 实施例8 100：2.5 85.7 99.4 实施例9 100：3.5 87.1 99.5 实施例10 100：4.0 86.8 99.7 实施例11 100：5.0 86.6 99.7

[n0069]

As can be seen from Table 2, the yield increases with the increase of catalyst, but the yield tends to stabilize when it reaches 2.5%-4% (i.e., 100: 2.5-4.0). Therefore, the amount of TBAB used is more suitable at 2.5-4%.

从表2可以看出，随着催化剂的增加收率随之增加，但达到2.5%-4%(即100：2.5-4.0)时，收率趋于平稳，因此TBAB的用量在2.5-4%较为适宜。

[n0070]

Test Example 4

试验例4

[n0071]

The yield and purity of each example were tested using conventional methods. Data from Examples 1 and 12-15 are shown in Table 3.

采用常规的方法测试各实施例的收率和纯度，实施例1和实施例12-15的数据如表3：

[n0072]

Table 34 - Effect of Dimethylaminopyridine Dosage

表34-二甲氨基吡啶用量的影响

[n0073]

Examples Formaldehyde to DMAP mass ratio Yield % Purity % Example 1 100:3.0 86.8 99.5

Example 12 100:1.0 74.3 97.8 Example 13 100:2.0 85.7 98.5 Example 14 100:4.0 86.5 99.8

Example 15 100:5.0 86.7 99.7

实施例 甲醛和DMAP质量比 收率% 纯度% 实施例1 100：3.0 86.8 99.5 实施例12 100：1.0 74.3 97.8

实施例13 100：2.0 85.7 98.5 实施例14 100：4.0 86.5 99.8 实施例15 100：5.0 86.7 99.7

[n0074]

As can be seen from Table 3, the yield remains at a high level when the DMAP dosage is above 2%, but there is no significant change when it is above 4%. Therefore, it is advisable to

determine the dosage to be 2-4%, that is, to control the mass ratio of formaldehyde to DMAP to be 100:2-4.

从表3可以看出，随着DMAP用量在2%以上时，收率保持较高的水准，大于4%时，并无明显变化，所以用量确定为2-4%为宜，即控制甲醛和DMAP的质量比为100：2-4。

[n0075]

Experimental Example 5

试验例5

[n0076]

The yield and purity of each example were tested using conventional methods. Data from Example 1 and Examples 16-19 are shown in Table 4.

采用常规的方法测试各实施例的收率和纯度，实施例1和实施例16-19的数据如表4：

[n0077]

Table 4 Effect of reaction temperature

表4反应温度的影响

[n0080]

The raw materials cannot dissolve well when the reaction temperature is below 40°C, so the reaction temperature is set above 50°C.

反应温度在40°C以下时，原料不能很好的溶解，所以反应温度定在50°C以上。

As can be seen from Table 4, the reaction efficiency increases with increasing reaction temperature. When the temperature reaches above 80°C, the reaction rate changes, but tends to stabilize.

从表4可以看出，随着反应温度增加，反应效率也变快，温度达到80°C以上时，反应速率虽然也有所变化，但已趋于平稳。

Therefore, setting the reaction temperature to 50-70°C can maintain a relatively fast reaction rate, and the mild reaction temperature is also more conducive to production, making it more suitable.

因此，反应温度设为50-70°C既能保持较快的反应速率，而且温和的反应温度也更利于生产，较为适宜。

[n0081]

Experimental Example 6

试验例6

[n0082]

The yield and purity of each example were tested using conventional methods. The data for Example 1 and Comparative Examples 1-6 are shown in Table 5.

采用常规的方法测试各实施例的收率和纯度，实施例1和对比例1-6的数据如表5：

[n0083]

Table 5 Effect of Catalyst

表5催化剂的影响

[n0085]

As can be seen from the test data in Table 5, using TBAB in combination with DMAP as a reaction catalyst is more suitable for the reaction system provided in the embodiments of the present invention, and the yield and purity of the product are both ideal.

从表5的测试数据可知，采用TBAB配合DMAP作为反应催化剂，更适合于本发明实施例提供的反应体系，产品的收率和纯度都较为理想。

[n0086]

In summary, this invention uses indole and formaldehyde as raw materials, and synthesizes the target product 3,3'-diindolemethane in the presence of a phase transfer catalyst and the catalyst 4-dimethylaminopyridine, with water as the reaction solvent.

综上所述，本发明以吲哚和甲醛为原料，在相转移催化剂和催化剂4-二甲氨基吡啶的作用下，以水为反应溶剂合成目标产物3,3'-二吲哚甲烷。

The reaction route provided by this invention has a fast reaction rate, avoids the use of organic solvents, and does not require harsh reaction conditions such as ultrasound, making it a green organic synthesis technology; the final product has a high yield and purity, which is conducive to industrialization.

本发明提供的反应路线反应速率快，避免使用有机溶剂，且不需要超声波等比较苛刻的反应条件，是一种绿色的有机合成技术；最终得到的产品的收率和纯度都比较高，利于产业化。

[n0087]

The above are merely preferred embodiments of the present invention and are not intended to limit the present invention. For those skilled in the art, the present invention can have various modifications and variations.

以上仅为本发明的优选实施例而已，并不用于限制本发明，对于本领域的技术人员来说，本发明可以有各种更改和变化。

Any modifications, equivalent substitutions, improvements, etc., made within the spirit and principles of this invention shall be included within the scope of protection of this invention.

凡在本发明的精神和原则之内，所作的任何修改、等同替换、改进等，均应包含在本发明的保护范围之内。