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DESCRIPTION CN113880748A

A green preparation process for 3,3-diindolemethane

一种3,3-二吲哚甲烷的绿色制备工艺

[0001]

Technical Field

技术领域

[n0001]

This invention relates to the field of organic chemical synthesis technology, specifically to a green preparation process for 3,3-diindolemethane.

本发明涉及有机化学合成技术领域，具体涉及一种3,3-二吲哚甲烷的绿色制备工艺。

[0003]

Background Technology

背景技术

[n0002]

3,3-Diindolemethane is widely found in natural products and has many pharmacological and physiological activities.

3,3-二吲哚甲烷广泛存在于天然产物中，并且具有许多药理和生理活性。

For example, it can promote the metabolism of estrogen in the human body and regulate the hormone metabolites secreted by certain cancer cells, making it an effective anti-cancer drug.

比如它能促进人体内雌性激素的新陈代谢，能够调节某些癌细胞分泌的激素代谢物，是一种有效的抗癌药物。

Therefore, the synthesis of 3,3-diindolemethane has attracted widespread attention.

因此，3,3-二吲哚甲烷的合成已经引起了人们的广泛关注。

[n0003]

Currently, most of these compounds are prepared in traditional organic solvents, such as methanol, ethanol, and ethyl acetate. However, these methods have drawbacks, including long reaction times, low yields, and severe environmental pollution.

目前该类化合物大多数的制备主要是在传统的有机溶剂中进行，通常要用到甲醇、乙醇、乙酸乙酯，同时存在反应时间长、产率低、环境污染严重等缺点。

[0006]

Summary of the Invention

发明内容

[n0004]

To address the aforementioned problems, the present invention aims to provide a low-cost, high-yield, simple, and environmentally friendly method for synthesizing 3,3-

diindolemethane. Compared with methods using traditional catalysts, the method of the present invention has the advantages of mild reaction conditions, low catalyst dosage, and reusable solvent.

为解决上述问题，本发明的目的在于提供一种成本低、产率高、工艺简单且环境友好的3,3-二吲哚甲烷的合成方法，与使用传统的催化剂的方法比较，本发明的方法具有反应条件温和，催化剂用量很少且溶剂可重复利用的优点。

[n0005]

To achieve the above objectives, the technical solution of the present invention is as follows.

为实现上述目的，本发明的技术方案如下。

[n0006]

A green preparation process for 3,3-diindolemethane includes the following steps:

一种3,3-二吲哚甲烷的绿色制备工艺，包括以下步骤：

[n0007]

S1. Using indole and formaldehyde as raw materials and cyanuric acid as a catalyst, acetone is added to react and crude 3,3-diindolemethane is prepared.

S1、以吲哚和甲醛为原料，以三聚氰酸作为催化剂，加入丙酮中发生反应，制备得到3,3-二吲哚甲烷粗品；

[n0008]

S2. The crude 3,3-diindolemethane prepared in S1 is recrystallized from ethanol to obtain purified 3,3-diindolemethane.

S2、将S1制备的3,3-二吲哚甲烷粗品，用乙醇重结晶，得到纯化的3,3-二吲哚甲烷。

[n0009]

Furthermore, in S1, the molar ratio of indole to formaldehyde is 2 to 3:1.

进一步，S1中，吲哚与甲醛的摩尔比为2~3：1。

[n0010]

Furthermore, in S1, the amount of cyanuric acid used is 0.5% to 1% of indole by mass percentage.

进一步，S1中，以质量百分比计，三聚氰酸的用量是吲哚的0.5%~1%。

[n0011]

Furthermore, in S1, the mass ratio of indole to acetone is 1:1 to 2.

进一步，S1中，吲哚与丙酮的质量比为1：1~2。

[n0012]

Furthermore, in S1, the reaction temperature is 20–30°C and the reaction time is 1 hour.

进一步，S1中，反应温度为20～30°C，反应时间为1h。

[n0013]

The beneficial effects of this invention are:

本发明的有益效果：

[n0014]

1. This invention uses cyanuric acid as a catalyst. The catalyst has high acidity, good catalytic activity, short reaction time, and high yield.

1、本发明是以三聚氰酸作为催化剂，催化剂的酸度高，催化活性好，反应用时少，产率高。

[n0015]

2. The catalyst of the present invention can be recycled, and its catalytic activity remains almost unchanged during recycling.

2、本发明的催化剂可以循环使用，且在循环使用过程中催化活性几乎保持不变。

[n0016]

3. The catalyst used in this invention is inexpensive and requires only a small amount. The production process generates no waste and has low energy consumption, which conforms to green production technology.

3、本发明使用的催化剂的价格低，且用量少，生产过程无三废产生且能耗低，符合绿色生产工艺。

[n0017]

4. This invention uses acetone as a reaction solvent, which can reduce the environmental pollution caused by the use of organic solvents; and it eliminates the need for repeated crystallization, resulting in a significant improvement in product quality and yield.

4、本发明使用丙酮作为反应溶剂，可减轻因使用有机溶剂而带来的环境污染问题；并且不用重复结晶，产品质量和收率都有很大的提高。

[0021]

Attached Figure Description

附图说明

[n0018]

Figure 1 is a synthetic route diagram of the green preparation process of 3,3-diindolemethane provided by the present invention.

图1是本发明提供的3,3-二吲哚甲烷的绿色制备工艺的合成路线图。

[n0019]

Figure 2 is a purity analysis report of 3,3-diindolemethane prepared in Example 1 of this invention.

图2是本发明实施例1制备的3,3-二吲哚甲烷的纯度分析报告。

[0024]

Detailed Implementation

具体实施方式

[n0020]

To make the objectives, technical solutions, and advantages of this invention clearer, the invention will be further described in detail below with reference to the accompanying drawings and embodiments.

为了使本发明的目的、技术方案及优点更加清楚明白，以下结合附图及实施例，对本发明进行进一步详细说明。

It should be understood that the specific embodiments described herein are merely illustrative of the invention and are not intended to limit the invention.

应当理解，此处所描述的具体实施例仅仅用以解释本发明，并不用于限定本发明。

[n0021]

Based on the embodiments of the present invention, all other embodiments obtained by those skilled in the art without creative effort are within the scope of protection of the present invention.

基于本发明中的实施例，本领域普通技术人员在没有做出创造性劳动前提下所获得的所有其他实施例，都属于本发明保护的范围。

[n0022]

Unless otherwise specified, the experimental methods described in the following embodiments are conventional methods; unless otherwise specified, the reagents and materials are commercially available.

下述各实施例中所述实验方法如无特殊说明，均为常规方法；所述试剂和材料，如无特殊说明，均可在市场上购买得到。

[n0023]

Example 1

实施例1

[n0024]

A green preparation process for 3,3-diindolemethane includes the following steps:

一种3,3-二吲哚甲烷的绿色制备工艺，包括以下步骤：

[n0025]

Take 200g (1.71mol) of indole, 25.5g (0.85mol) of formaldehyde, 1g of cyanuric acid and 200g of acetone, add them to a 500mL three-necked flask equipped with a mechanical stirrer, stir at 20°C, monitor by HPLC, the reaction time is 60min, and the reaction pressure is atmospheric pressure.

取吲哚200g(1.71mol)、甲醛25.5g(0.85mol)、三聚氰酸1g和丙酮200g，加入到500mL带有机机械搅拌的三口瓶中，在20°C下搅拌，HPLC跟踪检测，反应时间60min，反应压力为常压。

After the reaction was completed, the residue was filtered and recrystallized with anhydrous ethanol. After drying, purified 3,3-diindolemethane was obtained with a yield of 94.2% and a purity of >99.5%. The purity analysis results are shown in Figure 2.

反应结束后抽滤，所得滤渣用无水乙醇重结晶，干燥后得到纯化的3,3-二吲哚甲烷，产率为94.2%，产物纯度>99.5%，其纯度分析结果见图2。

[n0026]

The filtrate can be used directly in the next reaction without any treatment.

滤液无需任何处理可直接用于下一次反应。

[n0027]

Example 2

实施例2

[n0028]

A green preparation process for 3,3-diindolemethane includes the following steps:

一种3,3-二吲哚甲烷的绿色制备工艺，包括以下步骤：

[n0029]

Take 200g (1.71mol) of indole, 25.5g (0.85mol) of formaldehyde, 1.6g of cyanuric acid and 200g of acetone, add them to a 500mL three-necked flask equipped with a mechanical stirrer, stir at 20°C, monitor by HPLC, the reaction time is 60min, and the reaction pressure is atmospheric pressure.

取吲哚200g(1.71mol)、甲醛25.5g(0.85mol)、三聚氰酸1.6g和丙酮200g，加入到500mL带有机机械搅拌的三口瓶中，在20°C下搅拌，HPLC跟踪检测，反应时间60min，反应压力为常压。

After the reaction was completed, the mixture was filtered, and the resulting residue was

recrystallized with anhydrous ethanol. After drying, purified 3,3-diindolemethane was obtained with a yield of 95.6% and a product purity of >99.5%.

反应结束后抽滤，所得滤渣用无水乙醇重结晶，干燥后得到纯化的3,3-二吲哚甲烷，产率为95.6%，产物纯度>99.5%。

[n0030]

The filtrate can be used directly in the next reaction without any treatment.

滤液无需任何处理可直接用于下一次反应。

[n0031]

Example 3

实施例3

[n0032]

A green preparation process for 3,3-diindolemethane includes the following steps:

一种3,3-二吲哚甲烷的绿色制备工艺，包括以下步骤：

[n0033]

Take 200g (1.71mol) of indole, 25.5g (0.85mol) of formaldehyde, 2g of cyanuric acid and 200g

of acetone, add them to a 500mL three-necked flask equipped with a mechanical stirrer, stir at 20°C, monitor by HPLC, the reaction time is 60min, and the reaction pressure is atmospheric pressure.

取吡啶200g(1.71mol)、甲醛25.5g(0.85mol)、三聚氰酸2g和丙酮200g，加入到500mL带有机机械搅拌的三口瓶中，在20°C下搅拌，HPLC跟踪检测，反应时间60min，反应压力为常压。

After the reaction was completed, the mixture was filtered, and the resulting residue was recrystallized with anhydrous ethanol. After drying, purified 3,3-diindolemethane was obtained with a yield of 95.0% and a product purity of >99.5%.

反应结束后抽滤，所得滤渣用无水乙醇重结晶，干燥后得到纯化的3,3-二吡啶甲烷，产率为95.0%，产物纯度>99.5%。

[n0034]

The filtrate can be used directly in the next reaction without any treatment.

滤液无需任何处理可直接用于下一次反应。

[n0035]

Example 4

实施例4

[n0036]

A green preparation process for 3,3-diindolemethane includes the following steps:

一种3,3-二吲哚甲烷的绿色制备工艺，包括以下步骤：

[n0037]

Take 200g (1.71mol) of indole, 21g (0.70mol) of formaldehyde, 1.6g of cyanuric acid and 250g of acetone, add them to a 500mL three-necked flask equipped with a mechanical stirrer, stir at 25°C, monitor by HPLC, the reaction time is 60min, and the reaction pressure is atmospheric pressure.

取吲哚200g(1.71mol)、甲醛21g(0.70mol)、三聚氰酸1.6g和丙酮250g，加入到500mL带有机机械搅拌的三口瓶中，在25°C下搅拌，HPLC跟踪检测，反应时间60min，反应压力为常压。

After the reaction was completed, the mixture was filtered, and the resulting residue was recrystallized with anhydrous ethanol. After drying, purified 3,3-diindolemethane was obtained with a yield of 95.7% and a product purity of >99.5%.

反应结束后抽滤，所得滤渣用无水乙醇重结晶，干燥后得到纯化的3,3-二吲哚甲烷，产率为95.7%，产物纯度>99.5%。

[n0038]

The filtrate can be used directly in the next reaction without any treatment.

滤液无需任何处理可直接用于下一次反应。

[n0039]

Example 5

实施例5

[n0040]

A green preparation process for 3,3-diindolemethane includes the following steps:

一种3,3-二吲哚甲烷的绿色制备工艺，包括以下步骤：

[n0041]

Take 200g (1.71mol) of indole, 17g (0.57mol) of formaldehyde, 2g of cyanuric acid and 400g of acetone, add them to a 500mL three-necked flask equipped with a mechanical stirrer, stir at 30°C, monitor by HPLC, the reaction time is 60min, and the reaction pressure is atmospheric pressure.

取吡啶200g(1.71mol)、甲醛17g(0.57mol)、三聚氰酸2g和丙酮400g，加入到500mL带有机机械搅拌的三口瓶中，在30°C下搅拌，HPLC跟踪检测，反应时间60min，反应压力为常压。

After the reaction was completed, the mixture was filtered, and the resulting residue was recrystallized with anhydrous ethanol. After drying, purified 3,3-diindolemethane was obtained with a yield of 93.5% and a product purity of >99.5%.

反应结束后抽滤，所得滤渣用无水乙醇重结晶，干燥后得到纯化的3,3-二吡啶甲烷，产率为93.5%，产物纯度>99.5%。

[n0042]

The filtrate can be used directly in the next reaction without any treatment.

滤液无需任何处理可直接用于下一次反应。

[n0043]

Example 6

实施例6

[n0044]

A green preparation process for 3,3-diindolemethane includes the following steps:

一种3,3-二吲哚甲烷的绿色制备工艺，包括以下步骤：

[n0045]

Take 200g (1.71mol) of indole, 25.5g (0.85mol) of formaldehyde and the filtrate after filtration in Example 1, add them to a 500mL three-necked flask equipped with a mechanical stirrer, stir at 20°C, monitor by HPLC, the reaction time is 60min, and the reaction pressure is atmospheric pressure.

取吲哚200g(1.71mol)、甲醛25.5g(0.85mol)以及实施例1抽滤后的滤液，加入到500mL带有机械搅拌的三口瓶中，在20°C下搅拌，HPLC跟踪检测，反应时间60min，反应压力为常压。

After the reaction was completed, the mixture was filtered, and the resulting residue was recrystallized with anhydrous ethanol. After drying, purified 3,3-diindolemethane was obtained with a yield of 94.0% and a product purity of >99.5%.

反应结束后抽滤，所得滤渣用无水乙醇重结晶，干燥后得到纯化的3,3-二吲哚甲烷，产率为94.0%，产物纯度>99.5%。

[n0046]

Example 7

实施例7

[n0047]

A green preparation process for 3,3-diindolemethane is basically the same as that in Example 6, except that the filtrate after filtration in the previous step (Example 6 and the next reaction) is used directly for the reaction, and after being reused 10 times, the yield is basically maintained between 93.5% and 94.1%, and the product purity is >99.5%.

一种3,3-二吲哚甲烷的绿色制备工艺，与实施例6的方法基本相同，其不同之处在于，采用上一步(实施例6以及下一次的反应)抽滤后的滤液直接进行反应，且重复使用10次后，产率基本维持在93.5~94.1之间，产物纯度>99.5%。

[n0048]

As can be seen from the preparation reactions in Examples 6 and 7, the catalyst contained in the filtrate after filtration can be used directly in the next reaction without any treatment and can be reused multiple times, and the catalytic efficiency of the catalyst does not decrease significantly.

由实施例6和7的制备反应可以得出，抽滤后滤液中含有的催化剂无需任何处理直接用于下一次反应，可以重复使用多次，催化剂的催化效率未有明显下降。

[n0049]

The feed amount and yield results of Examples 1 to 5 are shown in Table 1.

实施例1～5的投料量以及产率结果如表1所示。

[n0050]

Table 1. Feed quantity and yield results for Examples 1-5

表1实施例1～5的投料量以及产率结果

[n0051]

Example	Indole	Formaldehyde	Catalyst	Yield	1	200g	25.5g	1g	94.2%	2	200g	25.5g	1.6g	95.6%	3
						200g	25.5g	2g	95.0%	4	200g	21g	1.6g	95.7%	5
						200g	17g	2g	93.5%						

实施例 吡啶 甲醛 催化剂 产率 1 200g 25.5g 1g 94.2% 2 200g 25.5g 1.6g 95.6% 3 200g 25.5g 2g 95.0% 4 200g 21g 1.6g 95.7% 5 200g 17g 2g 93.5%

[n0052]

As can be seen from Table 1 and the preparation processes of Examples 1-5, the preparation of 3,3-diindolemethane in Examples 1-5 of this invention mainly uses cyanuric acid as a catalyst. The catalyst has high acidity, good catalytic activity, short reaction time, and high yield.

结合表1以及实施例1～5的制备工艺可以看出，本发明实施例1～5的3,3-二吡啶甲烷的制备主要是以三聚氰酸作为催化剂，催化剂的酸度高，催化活性好，反应用时少，产率高。

As illustrated by the preparation process in Examples 6 and 7 of this invention, the catalyst can be recycled, and its catalytic activity remains almost unchanged during recycling.

由本发明实施例6~7的制备工艺说明，催化剂可以循环使用，且在循环使用过程中催化活性几乎保持不变。

[n0053]

The above are merely preferred embodiments of the present invention and are not intended to limit the present invention. Any modifications, equivalent substitutions, and improvements made within the spirit and principles of the present invention should be included within the protection scope of the present invention.

以上仅为本发明的较佳实施例而已，并不用以限制本发明，凡在本发明的精神和原则之内所作的任何修改、等同替换和改进等，均应包含在本发明的保护范围之内。