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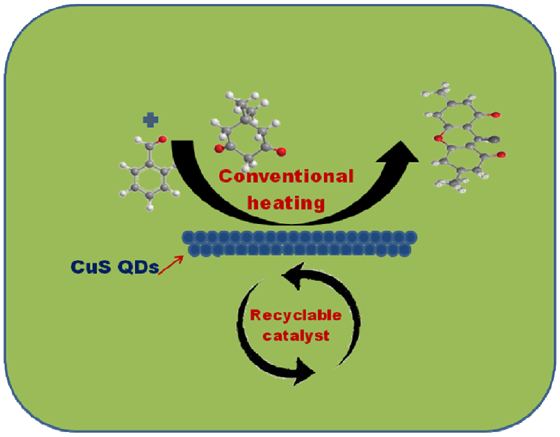
GRAPHICAL ABSTRACT



CuS quantum dots have been proved to be an efficient catalyst in synthesis of xanthenes in terms of high yield, reduction of time and energy consumption under solvent free conditions with easy work up

An efficient and green synthesis of xanthenes derivatives using CuS quantum dots as heterogeneous and reusable catalyst under solvent free condition

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Abstract

Efficient and environmentally friendly syntheses of xanthenes derivatives by using CuS quantum dots (QDs) as a catalyst have been carried out. This catalyst has been recovered by using simple filtration and reused for multiple cycles without much lose of its efficiency. The procedure has several advantages, such as economic availability of catalyst, simple procedure, ease of product isolation, no harmful byproducts, less reaction time and high yields. CuS QDs (2-3 nm) have been proved to be a better catalyst than CuO NPs (18-22 nm) in terms of energy consumption, reaction time, yield of product and amount of catalyst used.

Keywords: CuS quantum dots, heterogeneous catalyst, xanthenes, reusability, solvent free organic reaction

1. Introduction

Catalysis is an important field in chemistry. Most chemical reactions involve a catalyst in at least one of their steps. Because of environmental issues, the selection of catalyst has become most important in chemical reaction. The “Green Chemistry” concept is an interesting approach to reduce negative environmental impacts of organic synthesis. [1] Modern chemistry requires chemical processes designed to reduce waste production, which facilitates efficient reuse and recycling of catalyst. Consequently, chemists are now showing a considerable interest in heterogeneous catalytic processes. [2-6] In heterogeneous catalysis, the reacting molecules adsorb on the catalytically active solid surface. Chemical bonds are broken and formed on the surface and eventually the products are released back into liquid or gaseous phase. [7, 8] This led to the idea that the catalysts having larger surface to volume ratio can act as better heterogeneous catalysts. This very fact lays the basis for the use of nanoparticles (NPs) as heterogeneous catalysts in many reactions. [9, 10] The other major advantages of using NPs as a catalyst are as follows: they are eco-friendly and reusable; they can be used at room temperature under solvent free conditions; and they can be easily separated. Thus, because of all these advantages, they have been employed in a large number of organic reactions.

Synthesis of xanthenes and its derivatives is a useful multicomponent reaction that is gaining importance in organic and pharamaceutical industry. [11, 12] It involves the condensation between aldehyde and dimedone or napthol in the presence of catalysts. Xanthene derivatives possess broad range of useful properties such as antibacterial, anti inflammatory, antiviral, photo dynamic therapy, dyes, laser technology, and pH sensitive fluorescent materials for visualization of biomolecules. [13-19] We have already reported CuO NPs as efficient catalyst in synthesis of xanthenes. [20] Further we are exploring the possibility of other catalysts with enhanced catalytic efficiency. Recently we have also reported synthesis of CuS quantum dots (QDs) and investigated their catalytic activity in Biginelli reaction. [21] As the synthesis of CuS QDs has been carried out in microwave using greener approach and has achieved many advantages such as low energy cost, shorter processing time, less pollution and lower reaction temperature with high yield as compared to other methods. [22-25] CuS QDs in Biginelli reaction acted as a highly efficient catalyst in terms of short reaction time, i.e., 3-4 min, easy work up, excellent yield, enhanced energy efficiency, cost effectiveness and harmlessness of byproducts. Keeping all the advantages in view, we have explored CuS QDs as catalyst in synthesis of xanthenes under solvent free condition. We found that CuS QDs as catalyst in synthesis of xanthenes showed much more better activity than CuO NPs in terms of reaction time, energy consumption, amount of catalyst required, yield of product and cost. [20]

Catalysts involved in synthesis of xanthenes already present in literature have some drawbacks, such as anhydrous condition, high reaction temperature, prolonged reaction time, high cost, harmful and difficult handling of reagents, low yield, difficult work up. [26-29] But in the case of CuS QDs as catalyst all the above problems have been overcome. The advantages of CuS QDS as a catalyst are as follows: short reaction time, i.e., 6-15 min, easy work up, excellent yield, improved energy competence, low cost and no harmful byproducts.

2. Experimental

2.1 General remarks

Dimedone and napthol were supplied by Sigma Aldrich. Copper chloride was obtained from Glaxo laboratory, India, and sodium hydroxide (NaOH) and benzaldehyde were supplied by Qualigens of 98%. p-chlorobenzaldehyde, m-chlorobenzaldehyde, o-anisaldehyde, p-anisaldehyde, o-nitrobenzaldehyde and p-nitrobenzaldehyde, m-nitrobenzaldehyde, p-bromobenzaldehyde, p-cyanobenzaldehyde, p-methyl benzaldehyde were purchased from HiMedia. Ethanol was supplied by Changshu, Yangyuan Chemicals China. All chemicals were used without further purification. Doubly distilled water was used for the synthesis of CuS QDs.

^{1}H and ^{13}C NMR spectra were measured on a model advance II (Bruker) instrument with a frequency 300 MHz for ^{1}H NMR and a frequency of 100 MHz frequency for ^{13}C NMR using TMS as the internal standard and $CDCl_3$ as the solvent. Microwave (MW) with a power of 800 W was used for the synthesis of CuS QDs.

2.2 Synthesis and characterization of CuS QDs

CuS QDs were synthesized via a cost effective and greener approach with a very high yield in 2 min using MW and water as the medium. Detailed procedure is reported earlier. [21] The QDs were characterized by UV-visible spectrometer, XRD, TEM and SAED. The size of QDs was obtained in the range of 2-3 nm by TEM. [21]

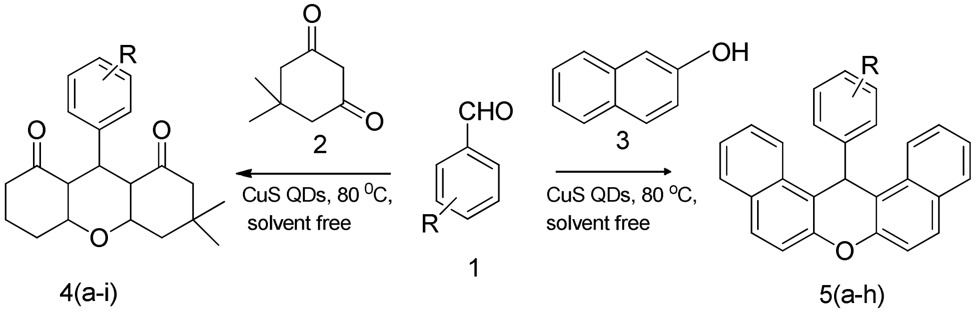
2.3 Synthesis and characterization of xanthenes

A mixture of aldehyde (1 mmol), 2-naphthol (2 mmol) or dimedone (2 mmol) and CuS QDs (0.006 g) was heated with stirring at 80°C in an oil bath. The progress of reaction was monitored by TLC. After cooling, the reaction mixture was dissolved in dichloromethane (DCM) and the mixture was stirred for 5 min. The suspended solution was filtered and then the heterogeneous nanocatalyst was recovered. The DCM was evaporated and the crude product was recrystallized from ethanol to give the pure product. The isolated catalyst was washed with ethanol and dried at room temperature overnight. The catalyst was reused for at least 4 times without an appreciable decrease of yield. All of the pure products were characterized by comparison of their physical (melting point) and spectral data viz ^{1}H and ^{13}C NMR (supplementary data with those of authentic samples). [30-32]

3. Results and Discussion

3.1 Variation of amount of catalyst

For the optimization of the reaction conditions to test the catalytic activity of CuS QDs for the synthesis of xanthenes, we have selected the reaction of napthol and bezaldehyde in a 2:1 ratio as a model substrate in the presence of CuS QDs as heterogeneous catalyst under solvent free conditions at 80°C (Table 1.). The results in Table 1 confirm that the yield of 5a xanthenes increased with increase in the amount of catalyst from 1 mg to 6 mg. Further increase in the amount of catalyst showed no improvement in yield. But in the case of CuO NPs the optimized amount of catalyst was more, i.e., 7 mg. Therefore, CuS QDs are better than CuO NPs in terms of consumption of catalyst. [20]



R= H, Cl, Br, NO_2, CN, OCH_3

Scheme 1. Synthesis of xanthenes using CuS QDs as catalyst.

Table 1. Variation of amount of catalyst for 5a in table 2.

S.No.	Amount of catalyst (mg)	Time (mins)/ % yield[a]
1.	nil	60/0
2.	1	20/66
3.	2	17/70
4.	3	15/78
5.	4	14/83
6.	5	12/88
7.	6	10/96
8.	7	8/89
9.	7	10/96

[a] Yields are related to isolated pure products.

3.2 Synthesis of different xanthenes (Products)

After the optimization of the reaction conditions, we have examined the scope of reaction of β-naphthol or dimedone with various aromatic aldehyde with electron withdrawing and electron releasing group in the presence of CuS QDs according to the general experimental procedure. In all cases, the reaction proceeded smoothly to give corresponding xanthene in excellent yields (Table 2.). Time taken for synthesis of xanthenes was longer and yield of different xanthenes was lower in the case of CuO NPs [20] than in the case of CuS QDs as the catalyst.

Table 2. Synthesis of different xanthenes using CuS QDs.[a]

Product[b]	R	Time (mins)	Yield[c] (%)	Melting point[d] (°C)	Ref.
4a	H	6	95	202-203	32
4b	2-OCH_3	12	90	230-231	32
4c	4-OCH_3	11	88	240-242	30
4d	4-NO_2	4	92	220-221	32
4e	3-Cl	10	90	182-183	30
4f	4-Cl	8	93	231-232	30
4g	4-Br	8	89	242-243	30
4h	4-CN	7	90	260-262	30
4i	4-CH_3	13	88	214-215	30
5a	H	10	96	180-181	30
5b	4-CH_3	15	87	228-229	30
5c	4-OCH_3	14	89	203-204	30
5d	4-NO_2	6	95	311-313	30
5e	3-Cl	9	89	210-211	32
5f	4-Cl	8	87	288-289	30
5g	4-Br	8	89	295-297	30
5h	4-CN	7	94	219-220	30

[a] all the reactions were carried out under solvent free conditions with catalyst amount 6 mg.

[b] all the products are known, characterized by ^1H and ^{13}C NMR spectral analysis and compared with the authentic samples.

[c] Yields are related to isolated pure products.

[d] melting points are compared with reported values.

3.3 Recyclability of catalyst

After completion of the reaction, the reaction mixture was dissolved in DCM and then the catalyst was separated by filteration. The CuS QDs were washed three to four times with

DCM (3 mL) and then dried at 100 °C for 5 h. The separated catalyst was used for 4 cycles with only a slight decrease in activity, as shown in Fig. 1.

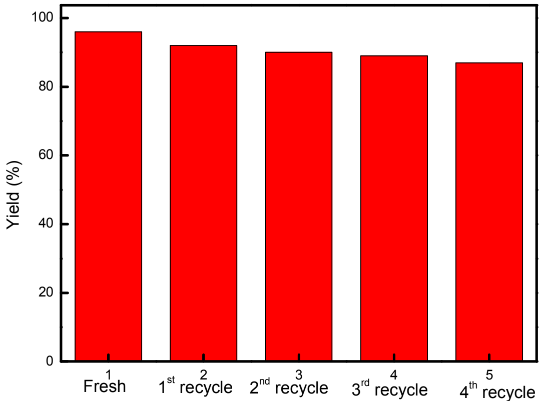


Fig. 1. Recycling ability of CuS QDs for 5a in table 2.

3.4 Comparison with other catalyst present in literature

Earlier work [33-40] carried out for synthesis of xanthenes showed that reactions with different catalysts required either higher amount of catalyst or longer reaction time. [33, 35-40]In some cases reactions were performed in DCM, [37, 39] which results in difficult work up and environmental hazards. A comparative analysis of CuS QDs as catalyst for the synthesis of xanthenes with other reported catalysts [30,10,33-40] (Table 3.) demonstrated that CuS QDs were proved to be an efficient catalyst in terms of relative high yield and time reduction. Although CuO NPs are quite efficient as a catalyst [20], CuS QDs showed enhanced activity. This can be due to the size of particles, as CuS QDs (2-3 nm) have a very small size compared to CuO NPs (18-22 nm). Therefore, the surface to volume ratio is higher and the number of active sites is bigger in CuS QDs, resulting in their higher activity.

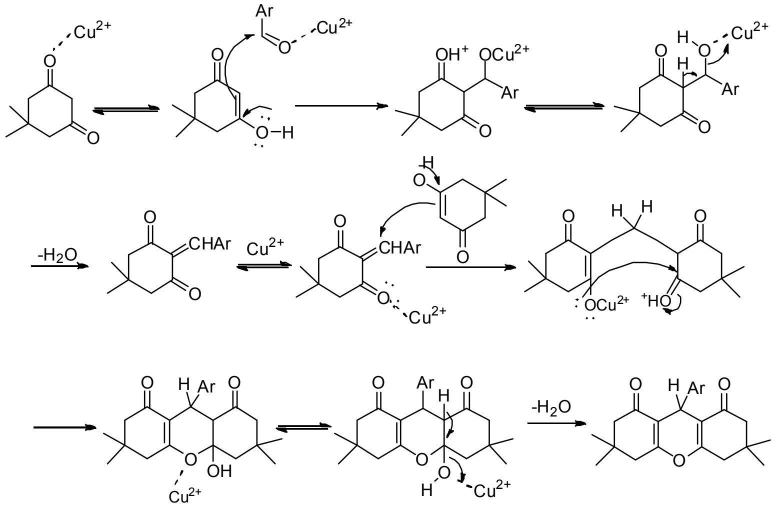
Table 3. Comparison of CuS QDs with other catalyst used in literature.

Name of Catalyst	Amount of Catalyst (mg)	Time/ yield in (%)	Solvent/ condition	Ref.
$K_5CoW_{12}O_{40}.3H_2O$	64	2 (h)/ 91	Solvent free/ 125 ^{0}C	33
Succinimide-N-sulfonic acid	10	35 (mins)/ 92	Solvent free/ 80 ^{0}C	34
Sulfamic acid:	9.7	8 (h)/ 93	Solvent free/ 125 ^{0}C	35

Tungstophosphoric acid/ zirconia composites	50	1 (h)/ 99	Solvent free/ 130 ^{0}C	36
Iodine	25.38	2.5 (h)/ 90	Solvent free/ 90 ^{0}C	37
$Fe(HSO_4)_3$	35	4 (h)/ 85	DCM	38
Amberlyst-15	10	2 (h)/ 94	Solvent free/ 125 ^{0}C	39
Functionalized mesoporous materials	20	6 (h)/ 80	DCM/ 25 ^{0}C	40
ZnO NPs	10	28 (mins)/ 87	Solvent free/ 80 ^{0}C	30
Fe_3O_4 NPs	20	30 (mins)/ 88	Solvent free/ 80 ^{0}C	10
CuO NPs	7	14(mins)/ 89	Solvent free/ 80 ^{0}C	20
CuS QDs	6	10 (mins)/ 96	Solvent free/ 80 ^{0}C	This Work

3.5 Plausible reaction mechanism

Copper moieties in CuS QDs behave as lewis acid, as they have a great tendency to coordinate with different functional group, such as carbonyl (-CO), nitrile (-CN), hydroxyl (-OH), thiol (-SH), etc. Dimedone or aldehyde undergoes chemical adsorption by interaction with acidic surface of metal sites. Because of interaction between the carbonyl group of substrate with CuS QDs, the carbonyl group of aldehyde was activated for nucleophilic attack in the next step, leading to a speedup of the reaction. Finally, the product was obtained and the CuS QDs were released for further reactions. Similar mechanism is in the cases of napthol and aldehyde.



Scheme 2. Plausible mechanism of synthesis of xanthenes.

4. Conclusion

In summary, an efficient, facile and economical method of one pot synthesis of xanthenes and its derivatives from napthol, dimedone and various aldehydes has been developed, using CuS QDs as inexpensive and ecofriendly catalyst under solvent free conditions. Attractive features, such as shorter reaction time, elevated yields, simplicity of product isolation, economic availability of catalyst, easy procedure and solvent free condition combined with easy recovery, harmless byproduct and reuse of this catalyst without much loss in product yield, make CuS QDs one of the best catalysts for synthesis of xanthenes. CuS QDs have been proved to be very efficient as compared to other catalysts that have already been used for the synthesis of xanthenes.

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