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Cucurbit[6]uril-OSO_3H: A Novel Acidic Nanocatalyst for the one-pot preparation of 14-aryl-14*H*-dibenzo[*a,j*]xanthenes and 1,8-dioxo-octahydro-xanthenes

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Abstract: Cucurbit[6]uril-OSO_3H (CB[6]-OSO_3H) has been prepared and used as an efficient acidic nanocatalyst for the one-pot preparation of 14-aryl-14*H*-dibenzo[*a,j*]xanthenes and 1,8-dioxo-octahydro-xanthenes. The nanocatalyst was characterized by FT-IR, AFM, TEM, and TGA analyses. This greener protocol is catalyzed by CB[6]-OSO_3H, and proceeds efficiently in the absence of any organic solvent under optimized, mild, green and environmentally benign reaction conditions in high yields and within short reaction time.

Keywords: Xanthenes, Nanocatalyst, Dimedone, *β*-naphthol, Solvent-free, Cucurbit[6]uril-OSO_3H

1. Introduction

Quite recently chemists have been interested by cucurbit[n]urils (CBn) as new molecular hosts and also nanovessels, while their first report in the literature goes back to 1905. CBn have been the subject of extensive research by supramolecular chemists. Due to the great growth of this field of research, several review articles have been published recently [1-6]. Most recently, the synthesis of functionalized derivatives has progressed, and among the manifold applications, cucurbituril-catalyzed reactions are receiving increasing attention [1].

Meanwhile cucurbit[6]uril, (CB[6]) is a hexameric macrocyclic compound self-assembled from an acid-catalyzed condensation reaction of glycoluril and formaldehyde. Although its synthesis first appeared in the literature in 1905 by Behrend, its chemical nature and structure had been unknown until 1981, when full characterization was reported by Mock and co-workers. The rigid structure and capability of forming stable complexes with molecules and

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ions also make CB[6] attractive as a building block for the construction of supramolecular architectures [2].

Due to xanthenes' applicability such as antibacterial [7], antiviral [8], and anti-inflammatory [9] activities, utilization as leuco-dyes [10], application in laser technology [11], and also as sensitizers in photodynamic therapy [12]; their synthesis is of great importance in organic synthesis. Although many catalysts have been developed for the preparation of biologically important 14-aryl-14*H*-dibenzo[*a,j*]xanthenes [13-17] and 1,8-dioxo-octahydro-xanthene [18-24] derivatives, However, most of these methods show varying degrees of success as well as limitations such as unsatisfactory yields, expensive catalysts, prolonged reaction times, toxic organic solvents, and harsh reaction conditions. Thus the development of an alternate milder procedure is highly demanding which could overcome those limitations.

In continuation of our previous works on the applications of reusable acid catalysts in organic synthesis [25,26] we decided to investigate the synthesis of 14-aryl-14*H*-dibenzo[*a,j*]xanthenes and 1,8-dioxo-octahydro-xanthenes in the presence of CB[6]-OSO_3H under solvent free conditions (Scheme 1).

<Scheme 1>

2. Results and Discussion

In the first step CB[6]$(OH)_{12}$ was prepared according to literature [27]. In the second step CB[6]-OSO_3H was prepared with dropwise addition of $ClSO_3H$ to CB[6]$(OH)_{12}$. (Scheme 2).

<Scheme 2>

To be qualified as a nanocatalyst, CB[6]-OSO_3H was characterized by FT-IR, AFM, TEM, and TGA analyses. In order to confirm the successful functionalization of the CB[6]$(OH)_{12}$ with $ClSO_3H$, FT-IR was employed. The FT-IR spectra of Glycoluril, CB[6], CB[6]$(OH)_{12}$, and CB[6]-OSO_3H has been shown in Fig 1. The stretching vibration of C=O group was found at 1680 and 1760 cm^{-1} for CB[6] and at 1701 and 1766 cm^{-1} for CB[6]$(OH)_{12}$. It should be notified that the stretching vibration of C=O group for CB[6]-OSO_3H was found at 1664 and 1770 cm^{-1} and also a broad peak around 3400 cm^{-1} which is attributed to absorbed water. CB[6]-OSO_3H, shows peaks at 1020 and 1200 cm^{-1} corresponding to S=O stretching vibrations of $-SO_3H$ groups (Fig 1, d).

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<Fig 1>

To ensure the particle size of the catalyst, TEM image was applied. It can be recognized that the particles are under 25 nm in size (Fig 2). This finding is also supported by AFM image.

<Fig 2>

AFM was utilized to view the particle size as well as size distribution of the nanoparticles. As it can be seen in Fig 3, the mean size of the particles in a 5 μm × 5 μm square is 17.8 nm.

<Fig 3>

Heat stability of CB[6]-OSO_3H was evaluated via TGA analysis. TGA diagram of the catalyst indicates that decomposition occurs at 300°C. Thus CB[6]-OSO_3H can be utilized in the reaction, under 300°C without any danger of decomposition.

<Fig 4>

In order to evaluate the catalytic activity of CB[6]-OSO_3H in the preparation of 14-aryl-14*H*-dibenzo[*a,j*]xanthenes derivatives, the reaction of 2 mmol of *β*-naphthol and 1 mmol of benzaldehyde under solvent-free conditions at 110°C in the absence and presence of CB[6]-OSO_3H were examined. It was found that in the absence of solid acid catalyst only trace amount of the desired product was produced even after 5 h of heating (Table 1). When the reaction was performed in the presence of CB[6]-OSO_3H, we were fortunate to obtain the desired product.

<Table 1>

In order to evaluate the appropriate catalyst loading, a model reaction was carried out using 0.01 to 0.03 g of the catalyst, at different temperatures under solvent-free conditions (Table 1). It was found that 0.02 g of the catalyst shows maximum yield in minimum time. Higher percentage of loading of the catalyst (0.03 g) lowers the conversion time but the product's yield is also decreased.

Delighted with these results, we decided to investigate the feasibility of this synthetic procedure for the synthesis of xanthene derivatives. We extended the reaction of *β*-naphthol with a range of aromatic aldehydes under optimized reaction conditions. The respective 14-aryl-14*H*-dibenzo[*a,j*]xanthenes derivatives in high to excellent yields were isolated. The optimized results are summarized in Table 2. This method has the ability to tolerate a variety

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of functional groups such as chloro, nitro, methoxy and methyl. The products were characterized by FT-IR, ^{1}H & ^{13}C NMR. Physical and spectral data of known compounds are in agreement with those reported in the literature.

<Table 2>

As seen from Table 2, electron withdrawing as well as electron donating substituents have the same effect on the reaction rate. It seems steric effects are dominated more than electronic effects.

After the success of CB[6]-OSO_3H in the preparation of 14- aryl-14*H*-dibenzo[*a,j*]xanthenes, we decided to explore the catalytic activity of CB[6]-OSO_3H in the preparation of 1,8-dioxo-octahydro-xanthenes. Subsequently, the condensation of various aromatic aldehydes with dimedone was carried out using CB[6]-OSO_3H as the solid acid catalyst under the above optimized reaction conditions (Scheme 1, Table 3).

<Table 3>

A postulated mechanism is outlined in scheme 3. In the first step, the nucleophilic attack of β-naphthol or dimedone takes place on the carbonyl carbon of aromatic aldehyde in a Knoevenagel condensation manner. In the second step, a Michael addition occurs. In the last step, acid catalyzed cyclization happens with the subsequent dehydration to prepare 14-aryl-14H-dibenzo[a,j]xanthene or 1,8-dioxo-octahydro-xanthene derivatives.

<Scheme 3>

According to increasing interest in human health and environmental concerns, more attention is being paid to green chemistry. With this view we studied the recyclability and reusability of the catalyst. After completion of the reaction the separated CB[6]-OSO_3H was washed with hot ethanol and dichloromethane and dried. The catalyst was used for two more subsequent cycles. To our surprise consistent performance of the catalyst is observed in all the cycles Fig 5.

<Fig 5>

3. Experimental

3.1 General

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All commercially available chemicals were purchased from Merck company and used without further purification. CB[6] and CB[6](OH)$_{12}$ was prepared according to literature [27]. IR spectra were recorded on a BOMEM MB-Series 1998 FT-IR spectrophotometer using KBr pellets for the samples and the catalyst in the range of 4000–400 cm^{-1}. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ on a Bruker Advanced DPX 400 MHz spectrometer using TMS as internal standard. Reaction monitoring was accomplished by TLC on silica gel polygram SILG/UV 254 plates. Thermal stability of the supported catalyst was examined by BÄHR, SPA 503 Thermo-gravimetric Analyzer (TGA) at heating rate of 10 °C min^{-1} over the temperature range of 40–600 °C.

3.2 Typical procedure for the preparation of CB[6]-OSO$_3$H

A 50 mL RBF was equipped with a constant pressure dropping funnel. The gas outlet was connected to a vacuum system through an adsorbing solution of alkali trap. CB[6](OH)$_{12}$ (1 g, 0.84 mmol) together with 20 ml of CH_2Cl_2 was added to the flask and sonicated for 30 minutes. Chlorosulfonic acid (*ca.* 0.7 mL, 10.1 mmol) in CH_2Cl_2 (10 mL) was added dropwise over a period of 30 min at room temperature. After completion of the addition, the mixture was stirred for 2 h, while the residual HCl was eliminated by suction. Then the mixture was washed with excess CH_2Cl_2. Finally, a white solid powder was obtained.

3.3 Typical procedure for the preparation of 14-aryl-14H-dibenzo[a,j]xanthenes/1,8-dioxo-octahydro-xanthenes derivatives

In a test tube, aromatic aldehyde (1.0 mmol), *β*-naphthol or dimedone (2.0 mmol), and CB[6]-OSO$_3$H (0.02 g) was heated at 110^{o}C. Completion of the reaction was indicated by TLC [TLC ethyl acetate/n-hexane (2:5)]. After completion of the reaction (According to Table 2 and 3) the insoluble crude product was dissolved in hot ethanol or CH_2Cl_2 and CB[6]-OSO$_3$H was filtered. The filtrate was concentrated to dryness, and the crude product was recrystallized in ethanol.

3.4 Determination of the acidity of CB[6]-OSO$_3$H

For evaluation of acidity of the catalyst, in a 25 mL aqueous solution of NaCl (1 M, pH = 6.35), CB[6]-OSO$_3$H (40 mg) was added and the resulted mixture was stirred for 2 hours and the pH of solution decreased to 2.18. This is equal to 4.13 mmol H^+/g of the catalyst.

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4. Conclusion

Cucurbit[6]uril-OSO_3H (CB[6]-OSO_3H) has been prepared and used as an efficient acidic nanocatalyst for the one-pot preparation of 14-aryl-14*H*-dibenzo[*a,j*]xanthenes and 1,8-dioxo-octahydro-xanthenes. This greener protocol is catalyzed by CB[6]-OSO_3H, and proceeds efficiently in the absence of any organic solvent under optimized, mild, green and environmentally benign reaction conditions in high yields and within short reaction time.

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References

[1] K. I. Assaf, and W. M. Nau, *Chem. Soc. Rev*., 2015, **44**, 394.
[2] J. W. Lee, S. Samal, N. Selvapalam, H.-J. Kim, and K. Kim, *Acc. Chem. Res*., 2003, **36**, 621.
[3] J. Lagona, P. Mukhopadhyay, S. Chakrabarti, and L. Isaacs, *Angew. Chem. Int. Ed*., 2005, **44**, 4844.
[4] E. Masson, X. Ling, R. Joseph, L. Kyeremeh-Mensah, and X. Lu, *RSC Adv*., 2012, **2**, 1213.
[5] X.-L. Ni, X. Xiao, H. Cong, Q.-J. Zhu, S.-F. Xue, and Z. Tao, *Acc. Chem. Res*., 2014, **47**, 1386.
[6] L. Isaacs, *Acc. Chem. Res*., 2014, **47**, 2052.
[7] T. Hideu, JP 56005480 (1981) (CA **95** 80922b).
[8] R.W. Lamberk, J. A. Martin, J. H. Merrett, K. E. B. Parkes, and G. J. Thomas, PCT Int. Appl. WO 9706178 (1997) (CA **126** P212377y).
[9] J. P. Poupelin, G. Saint-Rut, O. Fussard-Blanpin, G. Narcisse, G. Uchida-Ernouf, and R. Lakroix, *Eur. J. Med. Chem*., 1978, **13**, 67.
[10] A. Banerjee, and A. K. Mukherjee, *Stain. Technol*., 1981, **56**, 83.
[11] O. Sirkecioglu, N. Tulinli, and A. Akar, *J. Chem. Res. Synop*., 1995, 502.
[12] R. M. Ion, D. Frackowiak, A. Planner, and K. Wiktorowicz, *Acta Biochim. Pol*. 1998, **45**, 833.
[13] R. J. Sarma, and J. B. Baruah, *Dyes Pigm*. 2005, **64**, 91.
[14]. P. S. Kumara, B. S. Kumara, B. Rajithaa, P. N. Reddya, N. Sreenivasulua, and Y. T. Reddy, *Arkivoc*, 2006, **xii**, 46.
[15]. M. A. Bigdeli, M. M. Heravi, and G. H. Mahdavinia, *Catal. Commun*., 2007, **8**, 1595.

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DOI: 10.1039/C6RA02255C

[16]. M. Hong, and C. Cai, *J. Fluorine Chem*., 2009, **130**, 989.

[17]. B. Das, B. Ravikanth, R. Ramu, K. Laxminarayana, and B. V. Rao, *J. Mol. Catal. A: Chem*., 2006, **255**, 74.

[18] H. N. Karade, M. Sathe, and M. P. Kaushik, *Arkivoc*, 2007, **xiii**, 252.

[19] S. Kantevari, R. Bantu, and L. Nagarapu, *J. Mol. Catal. A: Chem*., 2007, **269**, 53.

[20] P. Srihari, S.S. Mandal, J.S.S. Reddy, R. Srinivasa Rao, and J.S. Yadav, *Chin. Chem. Lett*., 2008, **19**, 771.

[21] D. Fang , K. Gong, and Z. Liu, *Catal. Lett*., 2009, **127**, 291.

[22] G. Karthikeyana, and A. Pandurangan, *J. Mol. Catal. A: Chem*., 2009, **311**, 36.

[23] G. H. Mahdavinia , M. M. Ghanbari, H. Sepehrian, and F. Kooti, *J. Iran. Chem. Res*., 2010, **3**, 117.

[24] Z. H. Zhang, and Y. H. Liu, *Catal. Commun*., 2008, **9**, 1715.

[25] A. R. Kiasat, A. Mouradezadegun, and S. J. Saghanezhad, *J. Serb. Chem. Soc*., 2013, **78** (4), 469.

[26] A. R. Kiasat, A. Mouradzadegun, and S. J. Saghanezhad, *Chin. J. Catal*., 2013, **34**, 1861.

[27] S. Y. Jon, N. Selvapalam, D. H. Oh, J.-K. Kang, S.-Y. Kim, Y. J. Jeon, J. W. Lee, and K. Kim, *J. Am. Chem. Soc*., 2003, **125**, 10186.

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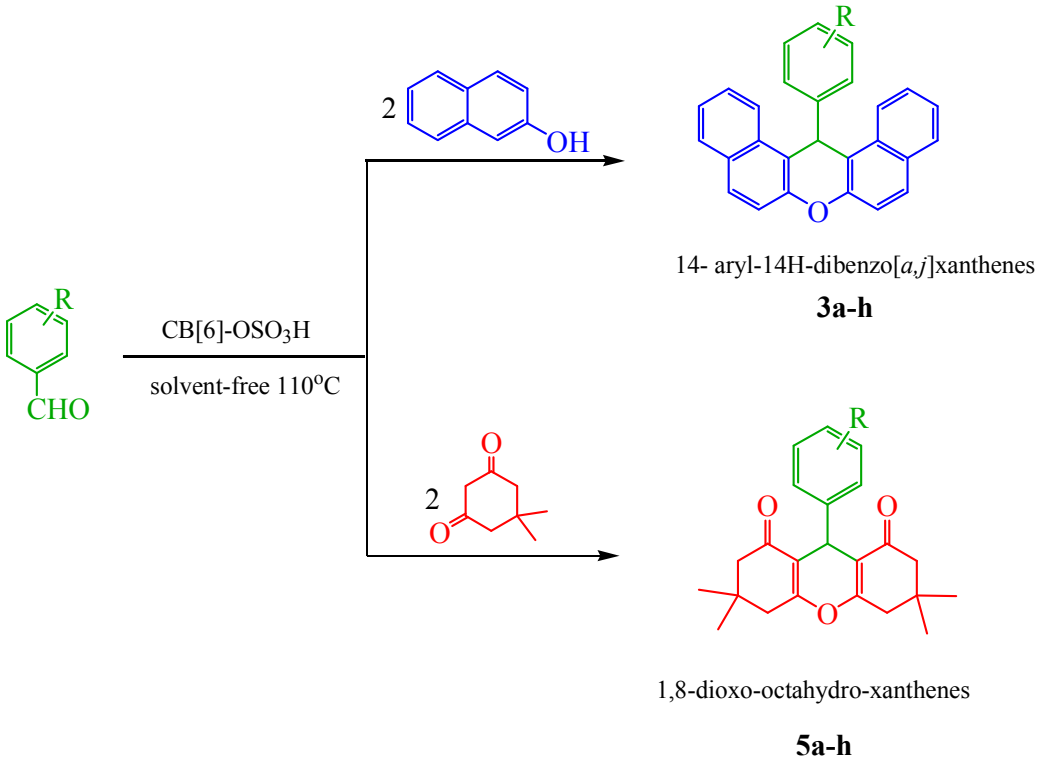

Scheme 1. One-pot preparation of 14- aryl-14*H*-dibenzo[*a,j*]xanthenes (**3a-h**) and 1,8-dioxo-octahydro-xanthenes (**5a-h**)

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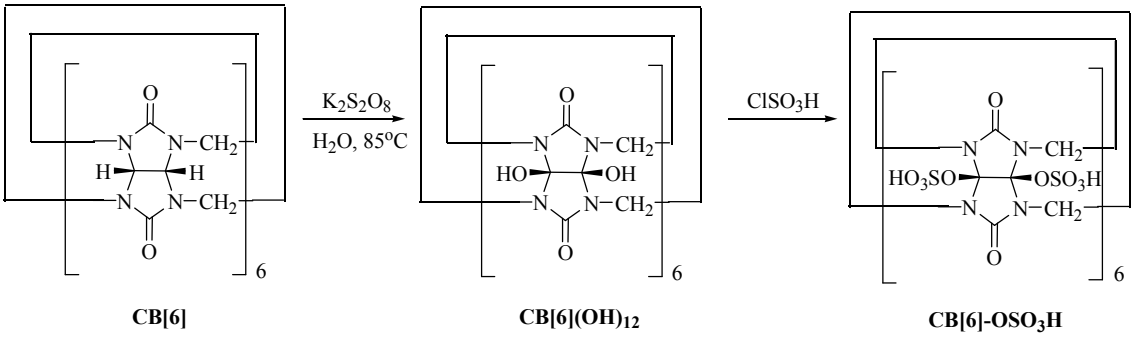

Scheme 2. Preparation of CB[6]-OSO_3H

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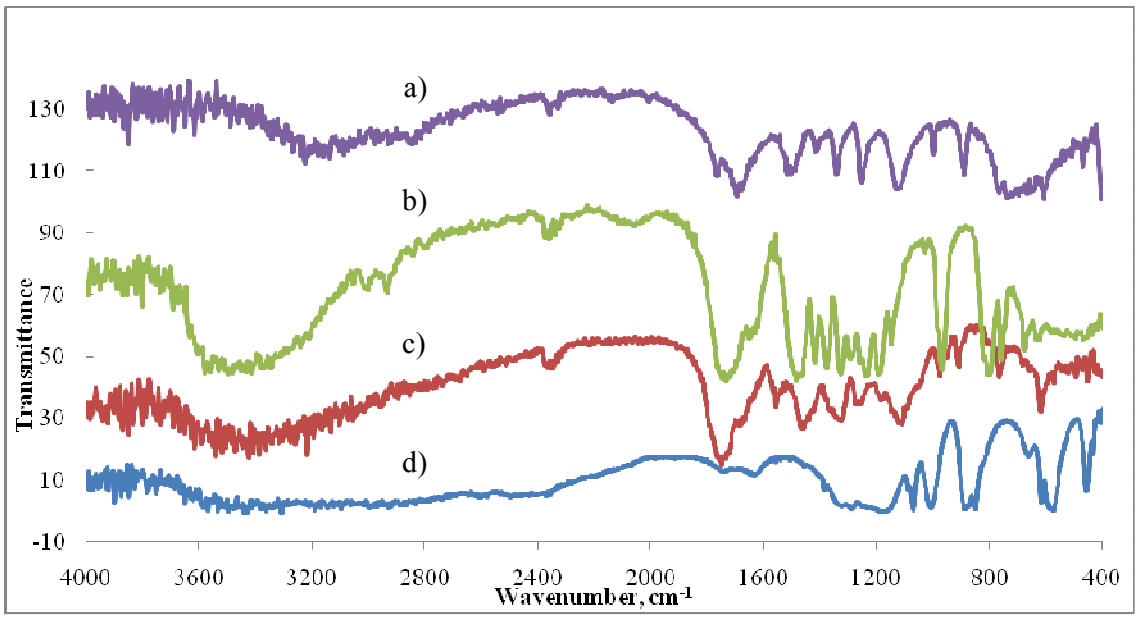

Fig 1. IR spectra of a) Glycoluril, b) CB[6], c) CB[6](OH)$_{12}$, d) CB[6]-OSO$_3$H

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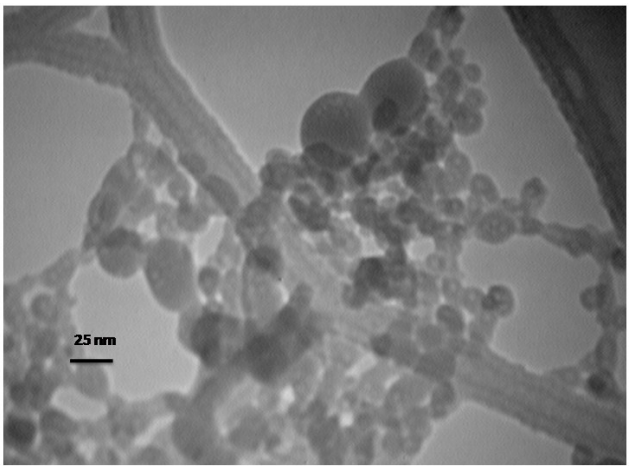

Fig 2. TEM of CB[6]-OSO_3H

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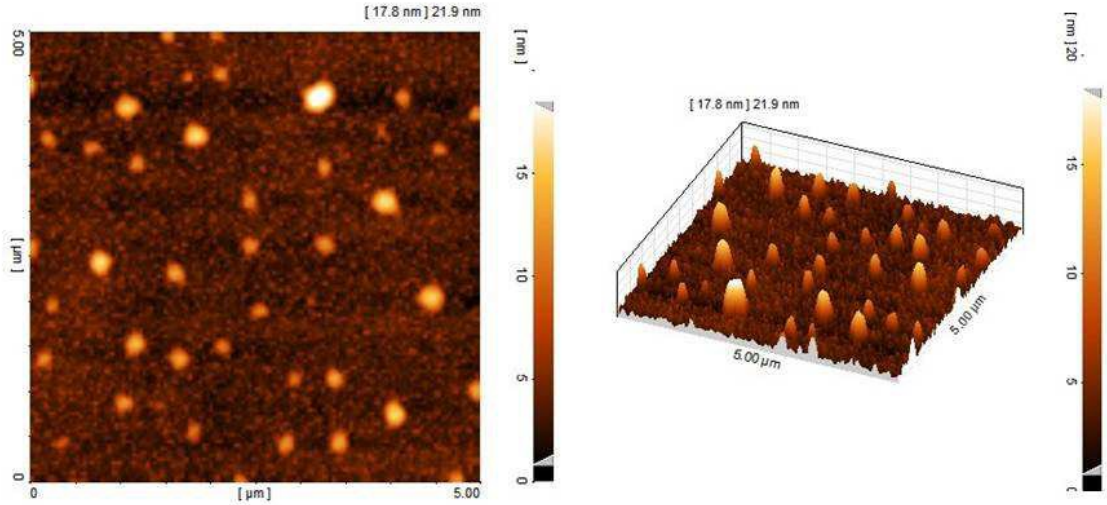

Fig 3. AFM image of CB[6]-OSO_3H

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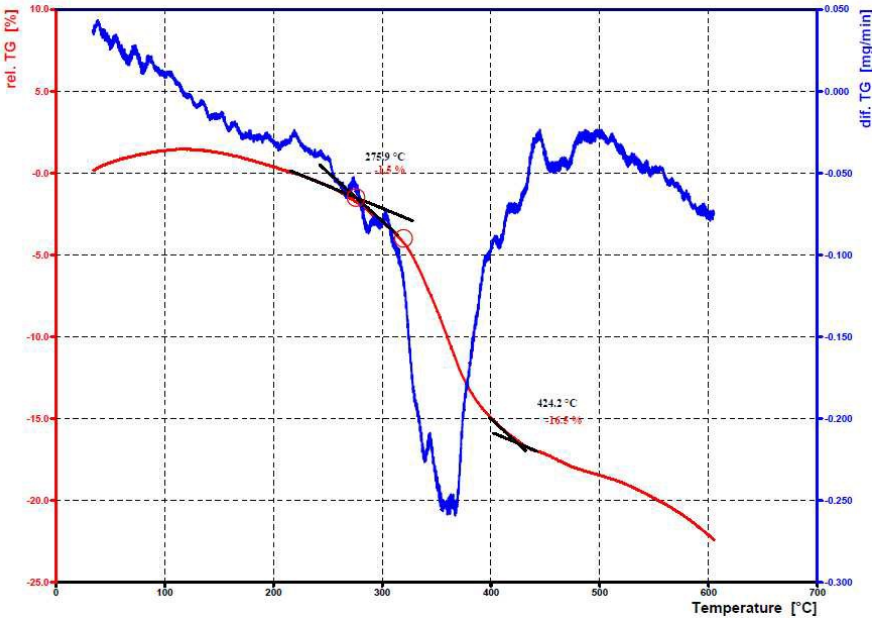

Fig 4. TGA of CB[6]-OSO_3H

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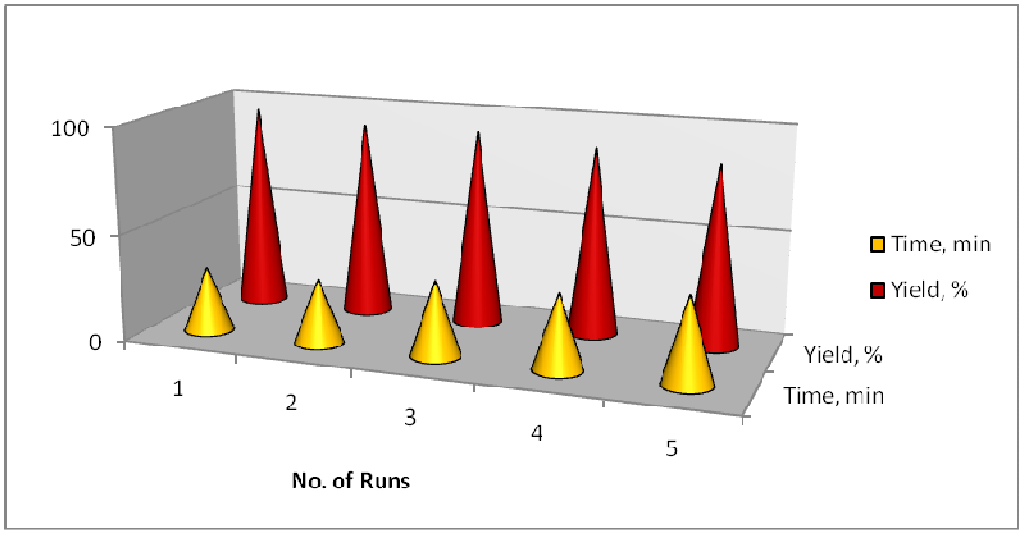

Fig 5. The reusability of CB[6]-OSO_3H in reaction of β-naphthol (2 mmol) and benzaldehyde (1.0 mmol)

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Table 1. Optimum conditions for the reaction of *β*-naphthol (2 mmol) and benzaldehyde (1.0 mmol) under thermal solvent-free conditions.

Entry	Catalyst (g)	Temp.(°C)	Time(min)	Yield(%)
1	0	80	300	<10
2	0	110	300	<10
3	0.01	100	55	45
4	0.01	110	45	52
5	0.02	110	35	96
6	0.03	110	30	95
7	0.05	110	30	83

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Table 2. One-pot preparation of 14- aryl-14*H*-dibenzo[*a,j*]xanthenes promoted by CB[6]-OSO_3H under solvent-free conditions at 110˚C.

Entry	R	Product	Time (min)	Yield (%)
1	H	**3a**	30	96
2	4-NO_2	**3b**	35	92
3	3-NO_2	**3c**	35	94
4	2-Cl	**3d**	45	95
5	4-CH_3	**3e**	30	89
6	4-Cl	**3f**	30	92
7	2-NO_2	**3g**	45	87
8	4-OMe	**3h**	40	82

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Table 3. One-pot preparation of 1,8-dioxo-octahydro-xanthenes promoted by CB[6]-OSO_3H under solvent-free conditions at 110˚C.

Entry	R	Product	Time (min)	Yield (%)
1	H	**5a**	20	98
2	4-NO_2	**5b**	25	92
3	3-NO_2	**5c**	25	93
4	2-NO_2	**5d**	40	95
5	4-CH_3	**5e**	25	90
6	4-OMe	**5f**	30	88
7	2-Cl	**5g**	20	91
8	4-CN	**5h**	35	92

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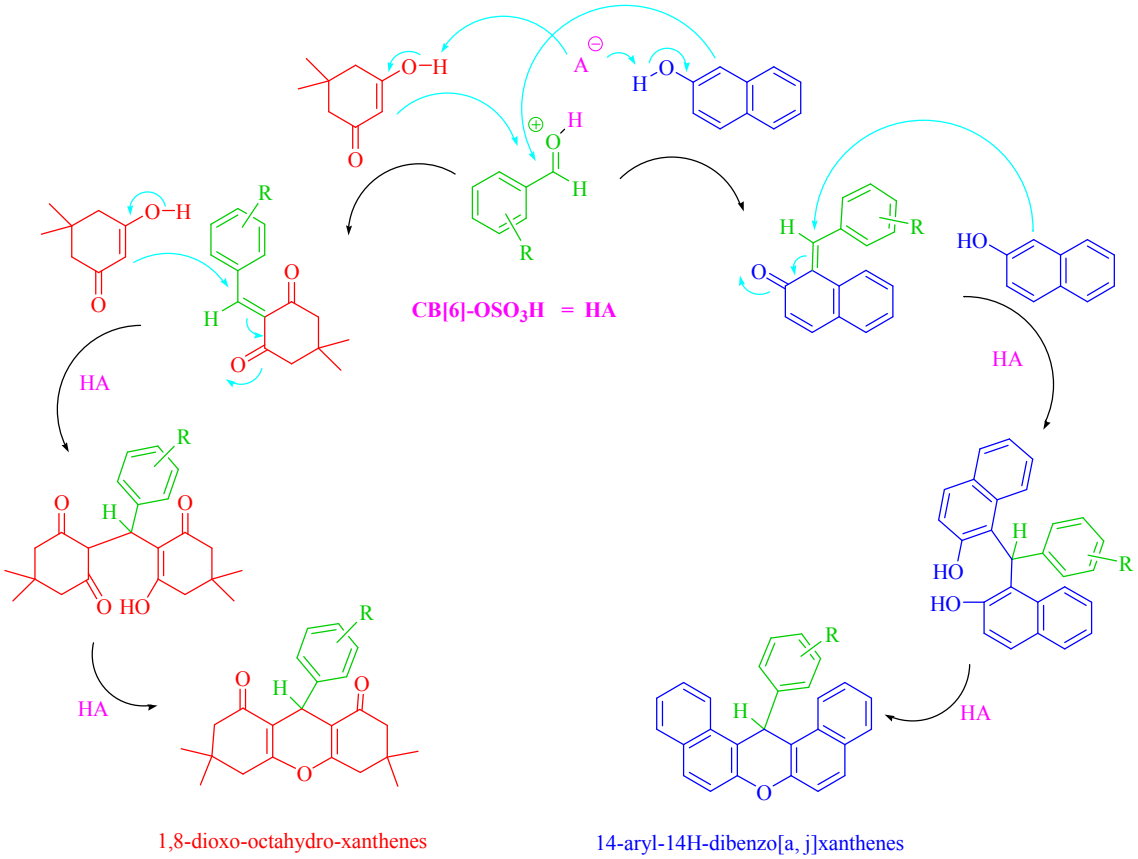

Scheme 3. The postulated mechanism for the CB[6]-OSO_3H catalyzed preparation of xanthenes

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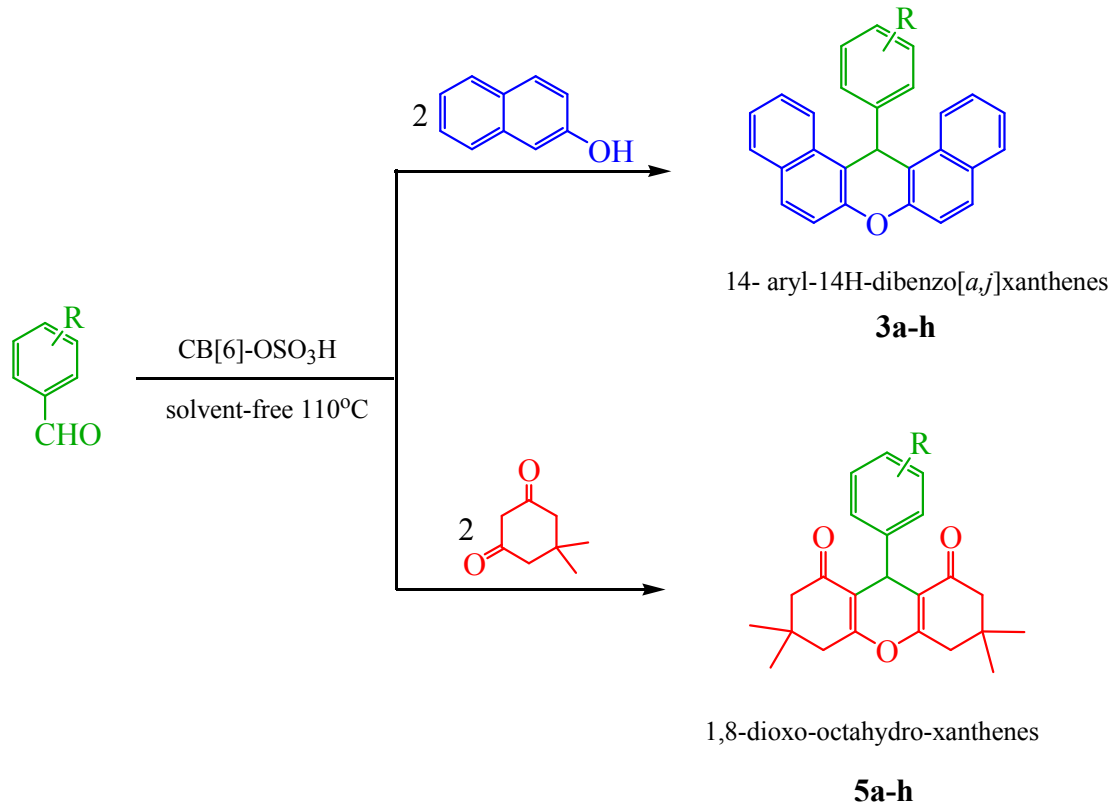

One-pot preparation of 14- aryl-14*H*-dibenzo[*a,j*]xanthenes (**3a-h**) and 1,8-dioxo-octahydro-xanthenes (**5a-h**)