

Efficient synthesis of substituted 1, 8-Dioxo-octahydroxanthene using copper silicate as reusable catalyst

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ABSTRACT

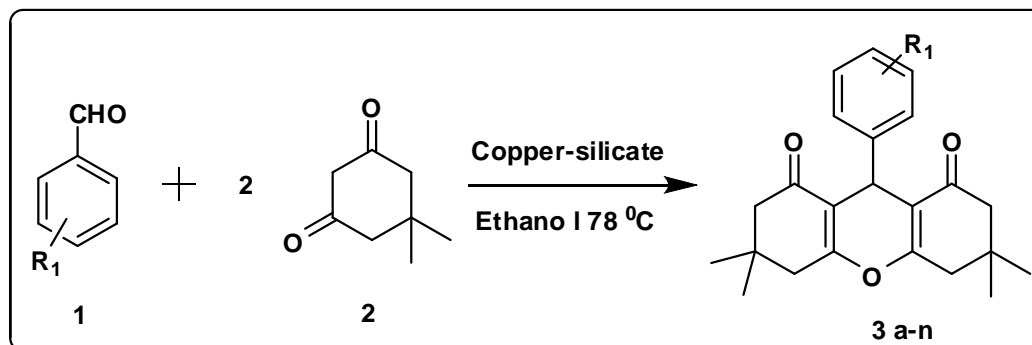
One pot synthesis of substituted 1,8 –dioxo-octahydroxanthene has been developed by the reaction of substituted benzaldehyde with 5,5-dimethylcyclohexane-1,3-dione in ethanol as solvent using copper silicates as heterogeneous catalyst has been recovered and reused. Synthetic protocol has some advantages such as short reaction time and easy workup procedure.

Keywords: Sulphamic Acid, Indazole, Microwave Irradiation, Mild Catalyst

INTRODUCTION

Xanthenes moiety is found to be an important class of oxygen contain heterocyclic compound. These xanthenes derivatives are of interest because, they exhibit a wide-range of biological properties; such as antimicrobial [1], antibacterial [2], antimalarial [3], antiviral [4], anti-inflammatory [5], anticancer [6], antioxidant [7] and analgesic [8]. In addition, they have been used as mGlu 1 receptor enhancers [9].

Numerous reports have been found for the xanthenes synthesis via, aldehydes and 1, 3 dicyclohexanedione catalyzed by various Lewis acid catalysts such as InCl₃ [10], Dowex-50W [11] Fe₃O₄ nanoparticles [12], SmCl₃ [13], Zinc oxide nanoparticles [14], Strontium triflate [15], I₂ [16], Cesium fluoride [17], Triethylbenzylammonium chloride [18], Amberlyst [19], TiO₂/SO₄²⁻ [20], NaHSO₄-SiO₂ [21], Silica chloride [22], CuO nanoparticles [23] also some reports have been found by using acid catalyst such as ascorbic acid [24], PEG-SO₃H [25], *p*-TSA [26], AcOH-H₂SO₄ [27], HClO₄-SiO₂ [28], cellulose sulfuric acid [29]. Recently used TMG-based N, N-disulfonic ionic liquids [30], low melting oxalic acid dehydrate [31]. LPCAS [32]. In previous report there is scope for the development of new methodology because these methods suffered from the use of hazardous catalyst, tedious workup procedures and reactions are time consuming. Herein, we report new method for the synthesis of 1,8 –dioxo-octahydroxanthene from substituted benzaldehyde and 5,5-dimethylcyclohexane-1,3-dione in ethanol as solvent by using copper silicate as catalyst (Scheme 1).



Scheme 1. Synthesis of substituted 1,8 –dioxaoctahydroxanthene

EXPERIMENTAL

All starting materials and chemical reagents were purchased from SD fine chemical company and used without further purification, melting points were determined in open capillaries using electrochemical MK₃ apparatus. IR spectra were recorded using Perkin-Elmer FT-IR spectrometer by using KBr pellets, ¹H & ¹³C NMR spectra were recorded on Bruker 400 MHz NMR spectrometer in DMSO as solvent and chemical shift values were recorded in δ (ppm).

General procedure for synthesis of substituted 1,8 –dioxaoctahydroxanthene

In a 10 mL round bottom flask, mixture of 5,5-dimethylcyclohexane-1,3-dione (1 mmol), 4-fluorobenzaldehyde **1a** (1 mmol) and copper silicate as a catalyst in 5 mL ethanol, resulting reaction mixture refluxed at 78 °C. The reaction was monitored by using TLC after the completion of reaction. The reaction mixture was cooled and filtered to remove insoluble catalyst. The filtrate was poured on ice-cold water to get solid product. The solid product obtained was washed with cold water, dried and recrystallized in ethanol to obtain pure product. The separated catalyst was washed with water and finally ethyl acetate, dried at 70 °C for 15 min and reused.

Spectral data

Compounds (3n)

3m; mp: 226-228 °C; IR (KBr, cm⁻¹) 3077, 2958, 1665, 1559, 1240, 1013.

¹H NMR (400 MHz, DMSO): δ 1.2-1.4 (m, 12 H, CH₃), 2.2 -2.6 (m, 8H CH₂), 5.55 (s, 1H, C-H), 7.24-7.26 (m, 2H, Ar-H), 8.13-8.15 (m, 2H, Ar-H), ¹³C NMR (100 MHz, DMSO): -31.29, 39.51, 101.11, 122.93, 129.9, 166.45, 167.45, 187.21, MS (ESI): 396 [M+1]⁺

3n; mp: 207-210 °C; IR (KBr, cm⁻¹) 2995, 1591, 1507, 1007,

¹H NMR (400 MHz, DMSO): δ 1.13-1.25 (m, 12 H, CH₃), 2.26 -2.42 (m, 8H CH₂), 3.76-3.82 (m, 9H), 5.50 (s, 1H, C-H), 7.35-7.37 (m, 2H, Ar-H), ¹³C NMR (100 MHz, DMSO): -26.75, 46.28, 60.79, 104.14, 115.52, 133.90, 152.79, 189.24, 190.33 MS (ESI): 3441 [M+1]⁺

RESULTS AND DISCUSSION

Synthesis of substituted 1,8 –dioxaoctahydroxanthene was carried out by the reaction of different aromatic 5,5-dimethylcyclohexane-1,3-dione and substituted benzaldehyde. In order to optimize reaction conditions we have carried out a model reaction of 4-NO₂ benzaldehyde and 5,5-dimethylcyclohexane-1,3-dione.

In order to have suitable catalyst for the reaction, we have carried out reaction by using two different heterogeneous catalysts such as ZnCl₂.SiO₂ and copper silicates, in order to compare reactivity, we have also carried out reaction by using homogeneous ionic liquid [Emim]HSO₄ as an

catalyst. We have carried out reaction in different solvents such as methanol, ethanol and acetonitrile. The results obtained are reported in **Table-1**. From the results obtained it is clear that in methanol at room temperature and at 60 °C better yields are obtained by using copper silicate as compare to other two catalysts (Entry No. 10 and 11). Also same is the case with acetonitrile and ethanol. By using copper silicate as catalysts and ethanol as solvent excellent yields were obtained (90 %, entry no 14).

Table 1. Optimization of reaction conditions for the synthesis of (3a-p).

Entry	Solvent	Catalyst	Temp °C	Yield ^a %
1	Methanol	ZnCl ₂ .SiO ₂	rt	50
2	Methanol	ZnCl ₂ .SiO ₂	60	70
3	Acetonitrile	ZnCl ₂ .SiO ₂	rt	72
4	Acetonitrile	ZnCl ₂ .SiO ₂	80	76
5	Ethanol	ZnCl ₂ .SiO ₂	78	84
6	Methanol	[Emim]HSO ₄	rt	60
7	Acetonitrile	[Emim]HSO ₄	80	74
8	Methanol	[Emim]HSO ₄	60	76
9	Acetonitrile	[Emim]HSO ₄	80	78
10	Methanol	Copper silicates	rt	72
11	Methanol	Copper silicates	60	78
12	Acetonitrile	Copper silicates	rt	74
13	Acetonitrile	Copper silicates	80	88
14	Ethanol	Copper silicates	78	90

In order to see the effect of electron withdrawing and donating groups present in benzaldehydes on the synthesis of xanthenes derivatives, we have carried out reaction using various substituted benzaldehydes and remarkable yields of products were obtained. It means this catalytic system of copper silicates in ethanol at 78 °C works well for the synthesis of different derivatives.

Table 2. Reaction of different aromatic 5,5-dimethylcyclohexane-1,3-dione and substituted aldehydes for the preparation of substituted 1,8 –dioxo-octahydroxanthene

Entry	R ₁	Product	Time (m)	Yield ^a %	Mp. ^{ref}
1	4-NO ₂ C ₆ H ₄	3a	55	90	225-226 ¹²
2	4-FC ₆ H ₄	3b	50	85	224-226 ²⁵
3	4-ClC ₆ H ₄	3c	48	84	235-237 ¹²
4	4-BrC ₆ H ₄	3d	46	86	240-241 ¹²
5	C ₆ H ₅	3e	45	88	184-185
6	2-ClC ₆ H ₄	3f	45	89	285-287
7	4-MeC ₆ H ₄	3g	47	91	214-216 ²⁵
8	4-OMeC ₆ H ₄	3h	57	92	242-244 ²⁵
9	2-Br-C ₆ H ₄	3i	45	87	226-227 ³²
10	3,4 di-OMeC ₆ H ₃	3j	48	92	177-179 ²⁵
11	3,4,5 tri-OMe C ₆ H ₂	3k	44	88	209-211 ³²
12	3-NO ₂ C ₆ H ₄	3l	56	86	167-169 ¹²
13	4-NO ₂ C ₆ H ₄	3m	56	80	226-228 ²⁵
14	3,4,5-tri-OMe C ₆ H ₂	3n	40	92	207- 210 ²⁵

Reusability study of copper silicate catalyst was carried out for the standard model reaction, up to the five consecutive runs, the result obtained are given in Table – 3. Up to third cycle result obtained are good but after that yield decreases rapidly this might be because of deactivation off the catalyst.

Table 3. Recycling study of catalyst on the standard model reaction of 4-NO₂ benzaldehyde and 5,5-dimethylcyclohexane-1,3-dione.

Number of cycles	Yield obtained
1	90 %
2	88 %
3	85 %
4	77 %
5	71 %

CONCLUSION

In conclusion, we have successfully synthesized substituted 1,8 –dioxo-octahydroxanthene (3a–n) by the reaction of 5, 5-dimethylcyclohexane-1,3-dione, substituted aldehyde in a ethanol as a solvent and copper silicate as a heterogeneous catalyst, The striking features of the reaction are green method, excellent yields, easy workup procedure, in short time.

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