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$AlCl_3$-$ZnCl_2$/SiO_2 as an efficient catalyst for the synthesis of 1,8-dioxo-octahydroxanthene under solvent-free condition

Kirti S.Niralwad, Kiran F.Shelke, Bapurao B.Shingate, Murlidhar S.Shingare*

Department of Chemistry, Dr. Babasaheb Ambedkar Marathwada University, Aurangabad - 431 004, (INDIA)

E-mail : msshingare_org@rediffmail.com

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ABSTRACT

A mixture of $AlCl_3$-$ZnCl_2$ supported on silica gel has been found to be a new efficient medium for the synthesis of 1,8-dioxo-octahydroxanthene *via* condensation of aromatic aldehydes and dimedone under solvent-free condition with excellent yields.

KEYWORDS

Aldehyde;
Dimedone;
Heterogeneous catalyst;
Xanthenedione derivatives;
Solvent-free.

INTRODUCTION

Hetrocycles plays an important role in the design and discovery of new physiological/pharmacologically active compound[1]. Chemically 1,8-dioxo-octahydroxanthenes are heterocyclic compound with the xanthene framework. Xanthene derivatives are parent compounds of a large number of naturally occurring and synthetic derivatives and occupy a prominent position in medicinal chemistry[2]. Xanthenes are an important class of organic compounds that find use as dyes[3], fluroscent materials for visualization of biomolecules[4]. In particular, xanthenedione constitute a structural unit in a number of natural products[5] and have been used as versatile synthones because of inherent reactivity of the inbuilt pyran ring[6]. The synthesis of these heterocyclic compounds is of great interest for both organic and medicinal chemistry. These compounds have also been investigated for agricultural bactericidal activity[7], anti-inflammatory effect[8] and anti-viral activity[9]. The synthesis of xanthenediones usually carried out by condensation of active methylene carbonyl compounds with aldehydes catalysed by sulphuric acid or HCl[10]. Recently, many procedures have been reported for the synthesis of 1,8-dioxo-octahydroxanthenes by condensation of dimedone and aldehyde using silica sulphuric acid[11], Dowex-50W[12], $HClO_4$-SiO_2 and PPA-SiO_2[13], silica chloride and $NaHSO_4$-SiO_2[14], p-dodecyl benzenesulphonic acid[15], Fe^{3+}-montmorillonite[16], Amberlite-25[17], diammonium hydrogen phosphate[18], TMSCl[19], tetrabutyl ammonium hydrogen sulphate [20], Ferric hydrogen sulphate[21], $InCl_3.4H_2O$[22], trienthyl benzyl ammonium chloride[23] and Bismuth trichloride[24] as a catalyst. Each of these methods have their own advantages but also suffer from one or more disadvantages such as prolonged reaction time[14,15,17,19], tedious work-up processes, low yield[13] and harsh reaction condition[18]. The major disadvantage of some of the method is that the reaction does not go for completion and stop at open chain structure instead of forming the cyclized compound[18]. Consequently, there is still need to develop a more efficient, simple, milder and high yield protocol for the synthesis of xanthene derivatives.

Recently, some researchers have used the catalyst

$AlCl_3$-$ZnCl_2$/SiO_2 in many organic reactions such as Fries-rearrangement[25], and hetero-fries-rearrangement[26] and Beckmann rearrangement[27].

In continuation of our previous work, we have developed the cheap and eco-friendly materials as catalysts for development of new synthetic methodologies[28]. In this paper, we would like to report a mild and high yielding solvent-free protocol for the synthesis of 1,8-dioxo-octahydroxanthenes via cyclo-condensation of various aldehydes and 1,3-cyclohexenedione by using $AlCl_3$-$ZnCl_2$/SiO_2 as a catalyst.

EXPERIMENTAL

The materials were obtained from commercial suppliers and were used without further purification. The uncorrected melting points of compounds were taken in an open capillary in a paraffin bath. The progress of the reactions was monitored by TLC (Thin Layer Chromatography). 1H NMR spectra were recorded on an 400 MHz FT-NMR spectrometer in $CDCl_3$ as a solvent and chemical shift values are recorded in units δ (ppm) relative to tetramethylsilane (Me_4Si) as an internal standard.

Preparation of catalyst

To 100g of SiO_2 (70-230mesh): $AlCl_3$. $6H_2O$: $ZnCl_2$ (5:2.3:1.28 W/ W/ W) was added in water (150ml) and the product was well mixed to give a gel-like material. The water was evaporated in vacuo and the gel left to stand at 120°C overnight. The resulting solid granules were ground and further activated by heating to 230°C in vacuo. The catalyst was stored under dry conditions.

General procedure

The mixture of aldehyde (1mmol), dimedone (2mmol) and $AlCl_3$-$ZnCl_2$/SiO_2 (15 mol %) were heated at 110°C as the time indicated in TABLE 1. The completion of reaction was monitored by TLC (Hexane: EtOAc 8:2). The reaction mixture was cooled at room temperature and the solid product was extracted with dichloromethane. The catalyst was easily regenerated by filtering the reaction mixture, washing it with hot ethanol and dried at 110°C for 2h. The organic layer was evaporated under reduced pressure and the crude product was obtained. The crude products were purified by recrystallization from ethanol.

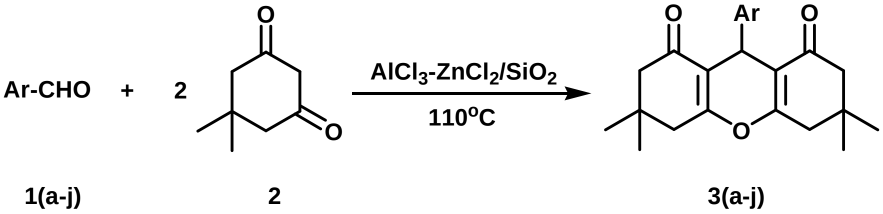
RESULT AND DISCUSSION

Herein, we would like to report a mild and high yielding solvent-free method for the synthesis of 1,8-dioxo-octahydroxanthene derivatives in excellent yield using $AlCl_3$-$ZnCl_2$/SiO_2 as a catalyst.

To optimize the reaction conditions, the 4-chlorobenzaldehyde and dimedone were employed as the model reaction at 110°C in $AlCl_3$-$ZnCl_2$/SiO_2 to compare the catalytic performance as shown in (TABLE 2) and (TABLE 3).

We also observed that, the model reaction was carried out in presence of 5 mol% of catalyst $AlCl_3$-$ZnCl_2$/SiO_2 to give the product (3b) in modest yield (75%) but when the concentration of catalyst have been increased from 10 and 15 mol% results in accelerating the reaction yields to 89% and 90% respectively. Use of 15 mol% of catalyst is sufficient to push the reaction forward. Higher amount of the catalyst did not improve catalyst for this reaction, as shown in (TABLE 2).

To determine the optimization of catalysts, the model reaction was carried out in different catalyst under same condition as shown in (TABLE 3). When $AlCl_3$ was employed, the corresponding product was obtained in 75% yield (TABLE 3, entry 1). However the model reaction was carried out in $ZnCl_2$ and SiO_2 gives 70%



Scheme 1 : $AlCl_3$-$ZnCl_2$/SiO_2 as an Efficient catalyst for the synthesis of 1,8-dioxo-octahydroxanthene under solvent-free condition

TABLE 1 : $AlCl_3$-$ZnCl_2$/SiO_2 mediated synthesis of various 1,8-dioxo-octahydroxanthenes.

Entry	Ar	Product	Time (h)	Yield (%)^a	M.P(°C)	
					Found	Reported
1	C_6H_5	3a	1.3	88	202-203	204-205[20]
2	4-ClC_6H_4	3b	1.00	90	228-230	230-231[20]
3	4-$OCH_3C_6H_4$	3c	1.3	89	238-240	241-243[20]
4	4-OH,3-$OCH_3C_6H_3$	3d	1.45	89	227-228	226-228[15]
5	2-$NO_2C_6H_4$	3e	3.30	82	244-246	246-248[20]
6	4-BrC_6H_4	3f	2.00	85	238-240	240-242[19]
7	4-OHC_6H_4	3g	1.30	88	247-248	246-247[20]
8	4-FC_6H_4	3h	2.00	83	224-226	225-227[21]
9	2-ClC_6H_4	3i	3.30	85	227-229	228-230[15]
10	3-$NO_2C_6H_4$	3j	3.30	85	169-170	171-172[20]

^{a}Isolated yields.

and 65% yield respectively and we have found that $AlCl_3$-$ZnCl_2$/SiO_2 is a better catalyst with respective to reaction time and yield of obtained products.

We have also observed that the aldehyde both with electron withdrawing groups and electron donating groups afforded the corresponding product in good yields. Para and mete substituted substrates reacted almost well. However aldehyde bearing substituent at ortho position turned out to be reluctant to undergo the condensation reaction, the longer reaction time is required for this substrate to get the corresponding product in high yield (TABLE 1, entries 3e, 3i).

Our attention was then directed towards the possibility of recycling the reaction media since the recovery and reuse of catalyst is highly preferable for greener process. The recyclability of the catalyst in the model reaction was checked as shown in (TABLE 4). The separated catalyst can be reused after washing with $CHCl_3$ sand drying at 110°C. The catalyst was removed in excellent yields and catalyst was used in mentioned reaction for five times it shows the same activity such as fresh catalyst without any loss of its activity.

In conclusion, The $AlCl_3$/$ZnCl_2$ supported on silica gel has been shown to be an efficient medium for the synthesis of 1,8-dioxo-octahydroxanyhene under solvent-free condition. This method has advantages such as, the reaction is fast and solvent-free, the catalyst could be reused for several runs and the ease of work-up.

TABLE 2 : Optimization of mol % for model reaction (3b).

Entry	Catalyst (mol %)	Yield (%)^a
1	5	75
2	10	90
3	15	90

^{a}Isolated yields.

TABLE 3 : Synthesis of (3b) using different catalysts under refluxing conditions.

Entry	Catalyst	Time (h)	Yield (%)
1	$AlCl_3$	7	75
2	$ZnCl_2$	6	70
3	SiO_2	9	65
4	$AlCl_3$-$ZnCl_2$/SiO_2	1	90

TABLE 4 : Recyclability of catalyst for the synthesis of (3b).

Cycle	Fresh	First	Second	Third	Fourth
Yield (%)^a	90	90	89	89	88

^{a}Isolated Yields.

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