

Short communication

Amberlyst-15: An efficient reusable heterogeneous catalyst for the synthesis of 1,8-dioxo-octahydroxanthenes and 1,8-dioxo-decahydroacridines[☆]

Biswanath Das^{*}, Ponnaboina Thirupathi, I. Mahender, V. Saidi Reddy, Yerra Koteswara Rao

Organic Chemistry Division-I, Indian Institute of Chemical Technology, Hyderabad 500007, India

Received 5 October 2005; received in revised form 24 November 2005; accepted 24 November 2005

Available online 6 January 2006

This paper is dedicated to Professor M.C. Wang, Chaoyang University of Technology, Taiwan.

Abstract

Amberlyst-15 has been found to be an efficient catalyst for the synthesis of 1,8-dioxo-octahydroxanthenes and 1,8-dioxo-decahydroacridines in excellent yields. The former have been synthesized from aromatic aldehydes and 5,5-dimethyl-1,3-cyclohexanedione while the latter from this mixture along with amines. The method is an easy access to functionalized xanthene and acridine derivatives. The catalyst can be reused.

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Keywords: 1,8-Dioxo-octahydroxanthenes; 1,8-Dioxo-decahydroacridines; Amberlyst-15; Heterogeneous catalyst

In recent years economic and environmental concerns encourage the application of heterogeneous catalyst to carry out various organic transformations. These catalysts make the processes clean, safe, high-yielding and inexpensive. We recently applied several heterogeneous catalysts to discover different novel useful synthetic methodologies [1]. In continuation of the work, we have observed that Amberlyst-15 is an efficient heterogeneous catalyst for the synthesis of 1,8-dioxo-octahydroxanthenes (**1**) and 1,8-dioxo-decahydroacridines (**2**). The former were prepared from a mixture of aromatic aldehydes and 5,5-dimethyl-1,3-cyclohexanedione by heating in CH₃CN under reflux in the presence of the catalyst while the latter from this mixture along with amines under the similar reaction conditions (Scheme 1).

Previously a limited work has been done on the synthesis of **1** and **2**. Compound **1** was prepared earlier using piperidine [2a] or *p*-dodecylbenzenesulfonic acid (DBSA) [2b] as a catalyst, but with piperidine, noncyclization product was also formed. DBSA was also employed [3a] for the preparation of **2** but the products were restricted to *p*-toluidine derivatives. In another approach,

1,8-dioxodecahydroacridines (**2**) derived from *p*-toluidine were prepared by applying microwave irradiation [3b].

A general method has now been developed for the synthesis of both 1,8-dioxo-octahydroxanthenes (**1**) and 1,8-dioxo-decahydroacridines (**2**) utilizing Amberlyst-15 as a heterogeneous catalyst (Table 1). Various functionalized **1** was prepared from different aromatic aldehydes and 5,5-dimethyl-1,3-cyclohexanedione. Electron-donating or electron-withdrawing groups present in the aromatic ring of the aldehydes did not affect the reaction. Cinnamaldehyde also underwent the reaction readily. For the preparation of **2** various structurally diverse aromatic aldehydes and amines were used along with 5,5-dimethyl-1,3-cyclohexanedione. Here also the aromatic aldehydes containing both electron-donating and electron-withdrawing groups afforded the products with high yields. Aromatic as well as aliphatic amines underwent the conversion equally. The structures of the products were established from their spectral (¹H NMR and MS) and analytical data.

Amberlyst-15 works under heterogeneous condition. It is an inexpensive and non-hazardous solid acid catalyst. It can easily be handled and removed from the reaction mixtures by simple filtration. The recovered catalyst was reused consecutive three times with a minimum variation of the yields of the products.

In conclusion, we have developed a novel and efficient method for the synthesis of 1,8-dioxo-octahydroxanthenes and 1,8-dioxo-decahydroacridines in high yields employing

[☆] Part 61 in the series "Studies on novel synthetic methodologies." ICT Communication No. 051114.

^{*} Corresponding author. Tel.: +91 40 27160512; fax: +91 40 27160512.

E-mail address: biswanathdas@yahoo.com (B. Das).

Table 1
Preparation of 1,8-dioxo-octahydroxanthenes (**1**) and 1,8-dioxo-decahydro-acridines (**2**) using Amberlyst-15^a

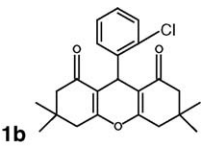
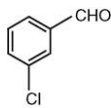
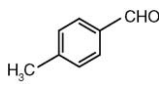
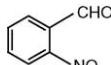
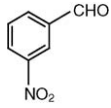
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2		–	 1b	5.0	90
3		–	 1c	5.0	93
4		–	 1d	5.0	94
5		–	 1e	5.0	90
6		–	 1f	5.0	95
7		–	 1g	5.0	93
8		–	 1h	5.0	92

Table 1 (Continued)

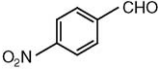
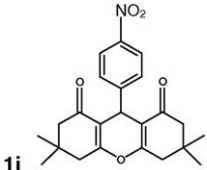
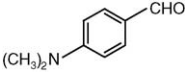
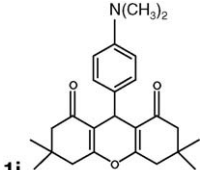
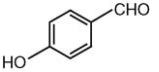
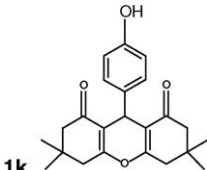
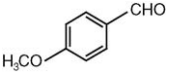
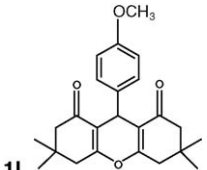
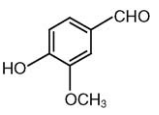
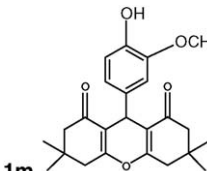
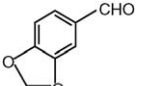
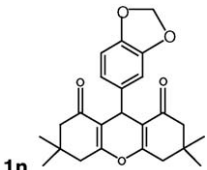
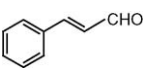
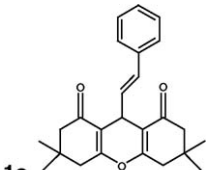
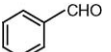
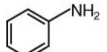
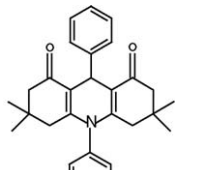
Entry	ArCHO	RNH ₂	Product	Time (h)	Isolated yield (%)
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10		–	 1j	5.0	96
11		–	 1k	5.0	96
12		–	 1l	5.0	94
13		–	 1m	5.0	92
14		–	 1n	5.0	91
15		–	 1o	5.0	90
16			 2a	5.0	81

Table 1 (Continued)

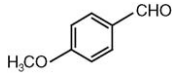

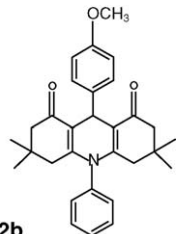
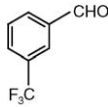

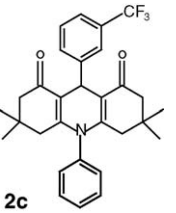
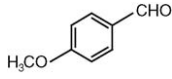
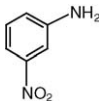
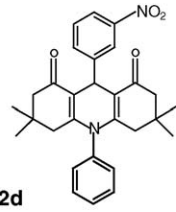
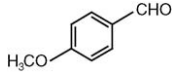
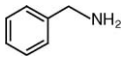
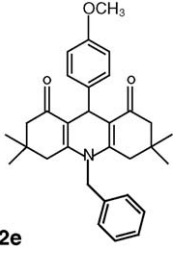
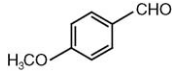
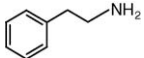
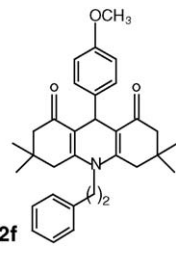
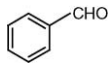
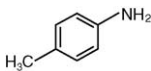
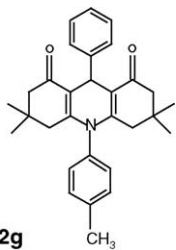
Entry	ArCHO	RNH ₂	Product	Time (h)	Isolated yield (%)
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18			 2c	4.5	89
19			 2d	4.5	95
20			 2e	6.5	82
21			 2f	6.0	85
22			 2g	5.5	82

Table 1 (Continued)

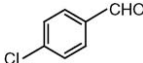
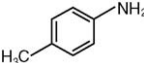
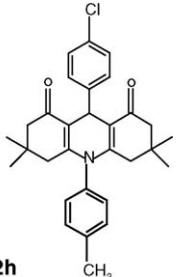
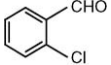
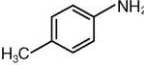
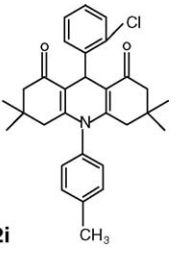
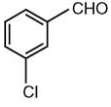
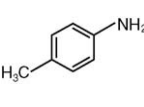
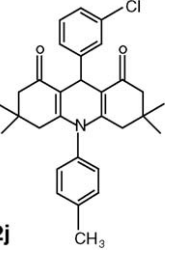
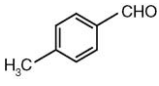
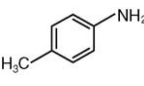
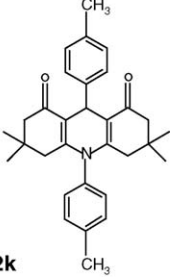
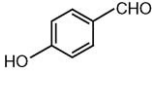
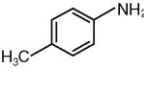
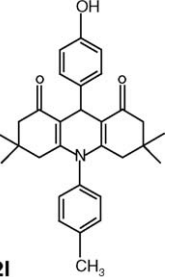
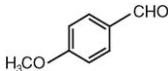
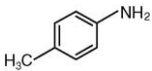
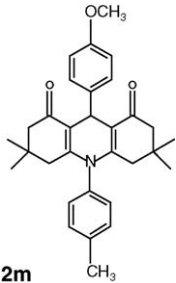
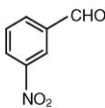
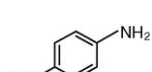
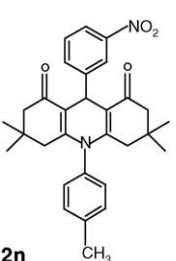
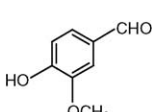
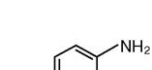
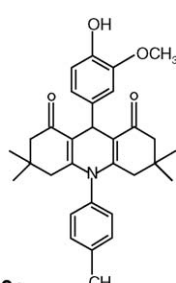
Entry	ArCHO	RNH ₂	Product	Time (h)	Isolated yield (%)
23			 2h	4.5	90
24			 2i	5.0	85
25			 2j	5.0	87
26			 2k	4.5	91
27			 2l	4.5	90

Table 1 (Continued)

Entry	ArCHO	RNH ₂	Product	Time (h)	Isolated yield (%)
28			 2m	4.5	94
29			 2n	5.0	86
30			 2o	5.5	83

^a The structures of the products were established from their spectral (¹H NMR and MS) and analytical data.

Amberlyst-15 as a heterogeneous solid acid. The application of an inexpensive, easily available and reusable catalyst makes this method simple, clean, practical and economically viable. The method is an easy access to functionalized xanthenes and acridines.

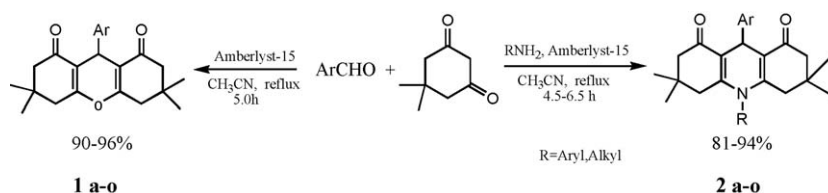
1. Experimental

1.1. General procedure for the preparation of 1,8-dioxo-octahydroxanthenes and 1,8-dioxo-decahydroacridines

To a solution of an aromatic aldehyde (1 mmol) and 5,5-dimethyl-1,3-cyclohexanedione (2 mmol) in CH₃CN (10 ml)

Amberlyst-15 (200 mg) was added. The mixture was refluxed and the reaction was monitored by TLC. After completion of the reaction, the mixture was filtered and the catalyst was recovered to use subsequently. The filtrate was concentrated and the residue was purified by column chromatography over silica gel using EtOAc–hexane (2:3) as eluent to obtain pure 1,8-dioxo-octahydroxanthene derivative.

For the preparation of 1,8-dioxo-decahydroacridine derivative, an amine (1.2 mmol) was mixed with the solution of an aromatic aldehyde (1 mmol) and 5,5-dimethyl-1,3-cyclohexanedione (2 mmol) in CH₃CN (10 ml). Amberlyst-15 (200 mg) was added and the reaction was conducted under the conditions as above. The product was purified by column chromatography over silica gel using EtOAc–hexane



Scheme 1.

(2:3) as eluent to afford pure 1,8-dioxo-decahydroacridine derivative.

The spectral (^1H NMR and MS) and analytical data of the unknown compounds are given below. The spectral properties of the remaining known compounds [2a,2b,3a,3b] matched well with those reported earlier.

2a: White solid, mp 254–256 °C; ^1H NMR (200 MHz, CDCl_3): δ = 7.60–7.49 (m, 3H), 7.38 (dd, J = 8.0, 2.0 Hz, 2H), 7.28–7.19 (m, 4H), 7.06 (dt, J = 8.0, 2.0 Hz, 1H), 5.21 (s, 1H), 2.12 (q, J = 14.0 Hz, 4H), 2.03 (d, J = 16.0 Hz, 2H), 1.78 (d, J = 16.0 Hz, 2H), 0.98 (s, 6H), 0.82 (s, 6H); FABMS: m/z = 426 ($\text{M}^+ + 1$); anal. calcd. for $\text{C}_{29}\text{H}_{31}\text{NO}_2$: C, 81.88; H, 7.29; N, 3.29. Found: C, 81.78; H, 7.20; N, 3.34.

2b: Light yellow solid, mp 220–222 °C; ^1H NMR (200 MHz, CDCl_3): δ = 7.61–7.48 (m, 3H), 7.27–7.18 (m, 4H), 6.73 (d, J = 8.0 Hz, 2H), 5.12 (s, 1H), 3.74 (s, 3H), 2.12 (q, J = 14.0 Hz, 4H), 2.02 (d, J = 16.0 Hz, 2H), 1.73 (d, J = 16.0 Hz, 2H), 0.95 (s, 6H), 0.81 (s, 6H); FABMS: m/z = 456 ($\text{M}^+ + 1$); anal. calcd. for $\text{C}_{30}\text{H}_{33}\text{NO}_3$: C, 79.12; H, 7.25; N, 3.08. Found: C, 79.23; H, 7.28; N, 3.01.

2c: White solid, mp 245–247 °C; ^1H NMR (200 MHz, CDCl_3): δ = 7.82 (dt, J = 8.0, 2.0 Hz, 1H), 7.66–7.54 (m, 4H), 7.46 (d, J = 8.0, 2H), 7.46–7.34 (m, 2H), 5.44 (s, 1H), 2.23 (q, J = 14.0 Hz, 4H), 2.14 (d, J = 16.0 Hz, 2H), 1.79 (d, J = 16.0 Hz, 2H), 0.94 (s, 6H), 0.80 (s, 6H); FABMS: m/z = 494 ($\text{M}^+ + 1$); anal. calcd. for $\text{C}_{30}\text{H}_{30}\text{F}_3\text{NO}_2$: C, 73.02; H, 6.09; N, 2.84. Found: C, 73.18; H, 6.14; N, 2.90.

2d: Yellow solid, mp 276–278 °C; ^1H NMR (200 MHz, CDCl_3): δ = 8.45 (dd, J = 8.0, 2.0 Hz, 1H), 8.14 (d, J = 2.0 Hz, 1H), 7.80 (t, J = 8.0 Hz, 1H), 7.62 (dd, J = 8.0, 2.0 Hz, 1H), 7.27 (d, J = 8.0 Hz, 2H), 6.78 (d, J = 8.0 Hz, 2H), 5.16 (s, 1H), 3.76 (s, 3H), 2.15 (brs, 4H), 2.04 (d, J = 16.0 Hz, 2H), 1.72 (d,

J = 16.0 Hz, 2H), 0.98 (s, 6H), 0.86 (s, 6H); FABMS: m/z = 501 ($\text{M}^+ + 1$); anal. calcd. for $\text{C}_{30}\text{H}_{32}\text{N}_2\text{O}_5$: C, 72.0; H, 6.40; N, 5.60. Found: C, 72.15; H, 6.48; N, 5.51.

2e: Viscous; ^1H NMR (200 MHz, CDCl_3): δ = 7.30–7.18 (m, 5H), 6.92–6.87 (m, 2H), 6.74 (d, J = 8.0 Hz, 2H), 5.27 (s, 1H), 4.88 (s, 2H), 3.78 (s, 3H), 2.31–1.88 (m, 8H), 1.0 (s, 6H), 0.96 (s, 6H); FABMS: m/z = 470 ($\text{M}^+ + 1$); anal. calcd. for $\text{C}_{31}\text{H}_{35}\text{NO}_3$: C, 79.32; H, 7.46; N, 2.99. Found: C, 79.27; H, 7.52; N, 2.92.

2f: Viscous; ^1H NMR (200 MHz, CDCl_3): δ = 7.28–7.16 (m, 5H), 6.99–6.90 (m, 2H), 6.73 (d, J = 8.0 Hz, 2H), 5.38 (s, 1H), 3.78 (s, 3H), 3.58–3.47 (m, 2H), 2.98 (dd, J = 7.0, 2.0 Hz, 2H), 2.42–2.01 (m, 8H), 1.02 (s, 6H), 1.0 (s, 6H); FABMS: m/z = 484 ($\text{M}^+ + 1$); anal. calcd. for $\text{C}_{32}\text{H}_{37}\text{NO}_3$: C, 79.50; H, 7.66; N, 2.90. Found: C, 79.57; H, 7.62; N, 2.96.

Acknowledgement

The authors thank CSIR and UGC, New Delhi for financial assistance.

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