Perfluorinated resin-sulfonic acid (Nafion-H): an efficient, environment friendly and recyclable heterogeneous catalyst for the one-pot synthesis of 1,8-dioxo-octahydroxanthenes

S. Mohammad Sajadi[1,*], Mehdi Maham[2], Bayan Omar Ahmad[3]

1. Department of Petrolium Geoscience, Faculty of Science, Soran University, PO box 624, Soran, Kurdistan Regional Government, Iraq

2. Department of Chemistry, Aliabad Katoul Branch, Islamic Azad University, Aliabad Katoul, Iran

3. Department of Chemistry, Faculty of Science, Soran University, PO box 624, Soran, Kurdistan Regional Government, Iraq

*Corresponding author: smohammad.sajadi@gmail.com, mohammad.s@soranu.com

Abstract

A novel, efficient and one-pot method for preparation of 1, 8-dioxo-octahydroxanthene derivatives is reported using Nafion-H as an effective heterogeneous catalyst under thermal and solvent-free conditions. This method has the advantages of high yields, a cleaner reaction, simple methodology, easy work-up and greener conditions. The catalyst is easily prepared, stable, reusable and efficient under the reaction conditions.

Keywords: 1,8-Dioxo-octahydroxanthene,   5,5-Dimethyl-1,3-cyclohexanedione,

Nafion-H, Solvent-free, Heterogeneous catalyst

1. Introduction

The synthesis of xanthene derivatives has been of considerable interest to chemists because of their wide range of biological and pharmaceutical properties such as antiviral, antibacterial (Hideo 1981), and anti-inflammatory activities (Lambert 1997). Furthermore, these compounds can be used as dyes, in laser technology, pH-sensitive fluorescent materials for the visualization of biomolecular assemblies (Knight 1989). In particularly, xanthenediones constitute a structural unit in a number of natural products and have been used as versatile synthons because of the inherent reactivity of the inbuilt pyran ring (OøCallaghan 1999).

There are several reports in the literature for the synthesis of 1,8-dioxo-octahydroxanthene derivatives employing aromatic aldehydes and 5,5-dimethyl-1,3-cyclohexanedione, these include $InCl_3.4H_2O$ in ionic liquid (Fan 2005), solid-state condensation by grinding at room temperature (Jin 2005), NH_2SO_3H in aqueous media (Jin 2005) and microwave-induced synthesis in solid or liquid phase (Tu 2001). However, these methodologies suffer from one or more disadvantages such as low yield, side reactions of aldehydes, lack of easy availability or preparation of the starting materials, prolonged reaction time (16 h to 5 days), use of toxic organic solvents, requirement of excess of reagents or catalysts, special apparatus and harsh reaction conditions. Therefore, it is

desirable to develop a more efficient and convenient method for the synthesis of 1,8-dioxo-octahydroxanthenes. Recently, Jin et al. reported a convenient procedure for the synthesis of 1,8-dioxo-octahydroxanthenes using p-dodecylbenzenesulfonic acid in aqueous media (Jin 2004). Singh et al. (Singh 1996) reported another method for the preparation of 1,8-dioxo-octahydroxanthenes through carbon transfer reactions of 1,3-oxazinanes and oxazolidines with carbon nucleophiles. Many other catalysts such as Fe^{3+}-montmorilonite (Song 2007), $NaHSO_4$-SiO_2 or silica chloride (Das 2007), amberlyst-15 (Das 2006), polyaniline-p-toluenesulfonate salt (John 2006), PPA-SiO_2 (Kantevari 2007) and TMSCl (Kantevari 2006), have been reported for the synthesis xanthenedione derivatives.

One of the most important objectives now is to adapt classical processes so that pollution effects are kept to a minimum, with both a reduction in energy and consumption of raw materials. Solid acid catalysts play a prominent role in organic synthesis under heterogeneous conditions. In recent years, the use of solid acidic catalysts has offered important advantages in organic synthesis, for example, operational simplicity, environmental compatibility, nontoxic, reusability, low cost, and ease of isolation. A tremendous upsurge of interest in various chemical transformations processes by catalysts under heterogeneous conditions has occurred (Habibi 2010; Habibi 2011; Modarresi-Alam 2007; Modarresi-Alam 2008; Mohammadi 2010, Nasrollahzadeh 2009). One of those heterogeneous catalysts is perfluorinated resin-sulfonic acid (Nafion-H)

(Olah 1986).[26] It makes reaction processes convenient, more economic, and environmentally benign. Perfluorinated resin sulfonic acid (Nafion-H) an acid catalyst extensively used for the acylation (Olah 1978), nitration (Olah 1978), acetal synthesis (Olah 1981), -acetamido ketone synthesis (Yakaiah 2007) and in Diels-Alder reaction (Olah 1979). Additionally, the catalyst displays a high activity and thermal stability (up to 201 $^{\circ}$C) and it can be easily recovered and reused.

In continuation of our recent work on the heterocycles (Nasrollahzadeh 2011; Sajadi 2011) we herein report a new protocol for preparation of 1,8-dioxo-octahydroxanthenes from a wide variety of aromatic aldehydes using Nafion-H as a recyclable catalyst (Fig. 1).

2. Materials and Methods

2.1. General

All reagents were purchased from Merck and Aldrich and used without further purification. NMR spectra were recorded on Brucker, 100, 300 and 500 MHz using TMS as an internal standard. Chemical shifts are reported in ppm, and coupling constants are reported in Hz. IR spectra were recorded on a Shimadzu 470 spectrophotometer. Melting points were taken in open capillary tubes with a BUCHI 510 melting point apparatus and were uncorrected. The elemental analysis was performed using Heraeus CHN-O-Rapid analyzer. TLC was performed on Merck-precoated silica gel 60-F254 plates.

2.2. General Procedure for the synthesis of 1,8-dioxo-dodecahydroxanthenes

A mixture of 5,5-dimethyl-1,3-cyclohexanedione (2 mmol), aldehyde (1 mmol) and Nafion-H (485 mg) was heated at 125 $^{\circ}$C for 12 h. After cooling, the reaction mixture was washed with CHCl$_3$ (10 ml). The solvent was evaporated and the crude product recrystallized from EtOH to afford the pure product. The desired pure product(s) were characterized by comparison of their physical data with those of known compounds. The spectral data of some representative 1,8-dioxo-dodecahydroxanthenes are given:

3,3,6,6-Tetramethyl-9-(2-chlorophenyl)-1,8-dioxooctahydroxanthene (3b):

^{1}H NMR (100 MHz, CDCl$_3$) 0.96 (6H, s), 1.04 (6H, s), 2.12 (4H, s), 2.39 (4H, s), 4.83 (1H, s), 7.03-7.34 (4H, m).

3,3,6,6-Tetramethyl-9-(3-nitrophenyl)-1,8-dioxooctahydroxanthene (3e):

^{1}H NMR (100 MHz, CDCl$_3$) 0.92 (6H, s), 1.04 (6H, s), 2.15 (4H, s), 2.45 (4H, s), 4.78 (1H, s), 7.21-7.95 (4H, m).

3,3,6,6-Tetramethyl-9-(4-nitrophenyl)-1,8-dioxooctahydroxanthene (3f):

^{1}H NMR (300 MHz, CDCl$_3$) 0.1 (6H, s), 1.14 (6H, s), 2.15-2.30 (4H, J = 16.4 Hz, q), 2.52 (4H, s), 4.84 (1H, s), 7.49 (2H, J = 8.7 Hz, d), 7.11 (2H, J = 8.7 Hz, d).

3,3,6,6-Tetramethyl-9-(4-N,N-dimethylphenyl)-1,8-dioxooctahydroxanthene (3i):

^{1}H NMR (300 MHz, CDCl$_3$) 1.02 (6H, s), 1.11 (6H, s), 2.15-2.28 (4H, J = 16.3 Hz, q), 2.47 (4H, s), 2.89 (6H, s), 4.68 (1H, s), 6.64-7.15 (4H, m).

3,3,6,6-Tetramethyl-9-(3,4-dimetoxyphenyl)-1,8-dioxooctahydroxanthene (3m):

IR (KBr): 3008, 2959, 1665, 1464, 1361, 1199, 1167, 856 cm^{-1}. ^{1}H NMR (100 MHz, CDCl$_3$) 0.93 (6H, s), 1.03 (6H, s), 2.13 (4H, s), 2.39 (4H, s), 3.71 (3H, s), 3.77 (3H, s), 4.62 (1H, s), 6.66-6.82 (3H, m). Anal. Calcd for C$_{25}$H$_{29}$O$_5$: C, 73.33; H, 7.14. Found: C, 73.40; H, 7.18.

3,3,6,6-Tetramethyl-9-(4-methylphenyl)-1,8-dioxooctahydroxanthene (3n):

^{1}H NMR (100 MHz, CDCl$_3$) 0.96 (6H, s), 1.03 (6H, s), 2.12 (4H, s), 2.23 (4H, s), 2.38 (1H, s), 4.67 (1H, s), 6.98-7.20 (4H, m).

3,3,6,6-Tetramethyl-9-(2-chloro-6-flourophenyl)-1,8-dioxooctahydroxanthene (3o):

IR (KBr): 3070, 2957, 1703, 1653, 1452, 1376, 1240, 1186, 787 cm^{-1}. ^{1}H NMR (100 MHz, CDCl$_3$) 0.92 (6H, s), 1.04 (6H, s), 2.26 (4H, s), 2.46 (4H, s), 4.85 (1H, s), 6.54-7.19 (3H, m). Anal. Calcd for C$_{23}$H$_{23}$O$_3$ClF: C, 68.74; H, 5.77. Found: C, 68.80; H, 5.80.

3,3,6,6-Tetramethyl-9-(1-naphthyl)-1,8-dioxooctahydroxanthene (3q):

IR (KBr): 3049, 2955, 2870, 1667, 1628, 1508, 1467, 1357, 1195, 1166, 1142, 1007, 768, 568, 459 cm^{-1}. ^{1}H NMR (500 MHz, CDCl$_3$) 0.97 (6H, s), 1.11 (6H, s), 2.12 (2H, J = 16.4 Hz, d), 2.20 (2H, J = 16.4 Hz, d), 2.54 (4H, s), 2.58 (1H, s), 7.24-7.33 (1H, m), 7.34 (1H, J = 7.3 Hz, t), 7.48 (1H, J = 7.2 Hz, t), 7.61-7.71 (2H, m), 7.78 (1H, J = 8.0 Hz, d), 8.80-8.98 (1H, m). Anal. Calcd for C$_{27}$H$_{27}$O$_3$: C, 81.17; H, 6.81. Found: C, 81.74; H, 6.87.

3. Result and Discussion

In the first set of experiment, we optimized the amount of Nafion-H as catalyst in the reaction between aldehyde and 5,5-dimethyl-1,3-cyclohexanedione. The amount of Nafion-H was chosen to be 485 mg. Thus, we continued preparation of 1,8-dioxo-octahydroxanthenes in an optimum model experiment: aldehydes (1 mmol), 5,5-dimethyl-1,3-cyclohexanedione (2 mmol) in the presence of Nafion-H (485 mg) (Fig. 1, Table 1) under thermal and solvent-free conditions. As shown in Table 1, benzaldehyde and other aromatic aldehhydes containing electron-withdrawing groups (such as nitro, halide group) or electron-donating groups (such as alkoxyl group) were employed and gave the corresponding 1,8-dioxo-octahydroxanthene. This is a new method for the synthesis of these compounds and in all cases the reaction gives the products in good yields (91–74%) and prevents problems which many associate with solvent use such as cost, handling, safety and pollution. Nafion-H works under heterogeneous conditions. It is an inexpensive and non-hazardous solid acid catalyst. It can easily be handled and removed from the reaction mixture by simple filtration. The recovered catalyst was reused consecutive three times with a minimum variation of the yields of the product.

4. Conclusion

In conclusion, we have developed a novel and highly efficient method for the synthesis of various 1,8-dioxo-octahydroxanthenes by treatment of aromatic aldehydes with 5,5-dimethyl-1,3-cyclohexanedione in the presence of Nafion-H as a heterogeneous catalyst. The significant advantages of this methodology are high yields, mild reaction

conditions, simple work-up procedure, cleaner reaction and easy preparation and handling of the catalyst. The catalyst can be recovered by simple filtration and reused without loss of activity.

5. Acknowledgement

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Table 1: Synthesis of 9-aryl substituted 1,8-dioxo-octahydroxanthenes using Nafion-H

| Entry	Ar	Product	Yield [%][a]	Mp (^{o}C)	Mp (^{o}C) (Literature)
1	C_6H_5	**3a**	80	203-204	204-205 (Horning 1946)
2	2-ClC$_6$H$_4$	**3b**	91	227-229	228-230 (Jin 2004)
3	4-ClC$_6$H$_4$	**3c**	88	229-230	228-230 (Jin 2004)
4	2,4-(Cl)$_2$C$_6$H$_3$	**3d**	89	252-254	253-254 (Jin 2004)
5	3-NO$_2$C$_6$H$_4$	**3e**	75	169-171	168-170 (Jin 2004)
6	4-NO$_2$C$_6$H$_4$	**3f**	78	226-228	226-228 (Jin 2004)
7	3-BrC$_6$H$_4$	**3g**	74	190-192	190-192 (Venkatesan 2008)
8	4-BrC$_6$H$_4$	**3h**	76	234-236	234-236 (Jin 2004)
9	4-N(Me)$_2$C$_6$H$_5$	**3i**	82	225-226	222-225 (Kantevari 2007)
10	2-OCH$_3$C$_6$H$_4$	**3j**	80	186-188	190-191 (Venkatesan 2008)
11	3-OCH$_3$C$_6$H$_4$	**3k**	82	179-180	177-180 (Venkatesan 2008)
12	4-OCH$_3$C$_6$H$_4$	**3l**	85	240-242	241-243 (Horning 1946)
13	3,4-(OCH$_3$)$_2$C$_6$H$_3$	**3m**	83	184-186	-
14	4-CH$_3$C$_6$H$_4$	**3n**	84	217-219	217-218 (Jin 2004)
15	2-Cl-6-F-C$_6$H$_3$	**3o**	87	117-119	-
16	C$_6$H$_5$CH=CH	**3p**	78	176-178	175-177 (Jin 2004)
17	C$_{10}$H$_7$	**3q**	84	237-238	-

[a]Yield refer to the pure isolated products.
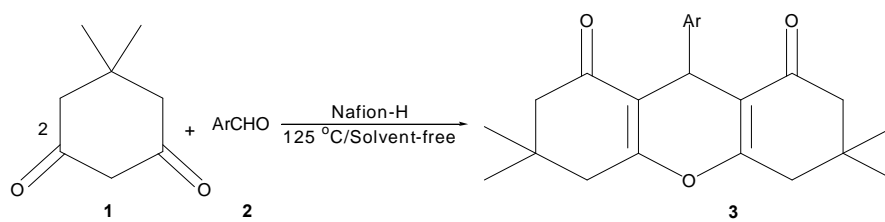
Figure 1. 1,8-dioxo-octahydroxanthenes from a wide variety of aromatic aldehydes using

Nafion-H as a recyclable catalyst