Synthesis and Identification of SO$_3$H-functionalized Phthalimide (SFP) as an Efficient Catalyst for the Condensation of Dimedone with Arylaldehydes

Abdolkarim Zare[1*], Hakimeh Asvar[1], Fatemeh Zarei[1], Maryam Khalili[1], Zahra Kordrostami[1], Ahmad Reza Moosavi-Zare[2], Vahid Khakyzadeh[3]

[1]Department of Chemistry, Payame Noor University, Tehran, Iran
[2]Department of Chemistry, University of Sayyed Jamaleddin Asadabadi, Asadabad, Iran
[3]Faculty of Chemistry, Bu-Ali Sina University, Hamedan, Iran
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Abstract

A SO$_3$H-containing solid acid namely SO$_3$H-functionalized phthalimide (SFP) was synthesized from phthalimide and chlorosulfonic acid, and identified by studying its FT-IR, ^{1}H and ^{13}C NMR, Mass, XRD, TG and DTG spectra. Afterward, its catalytic activity was examined for the solvent-free condensation of dimedone (5,5-dimethyl-1,3-cyclohexanedione) (2 eq.) with arylaldehydes (1 eq.). The results showed that SFP is a highly efficient catalyst to promote the title reaction for the preparation of 9-aryl-1,8-dioxo-octahydroxanthenes.

Keywords: *SO$_3$H-functionalized phthalimide (SFP), SO$_3$H-containing solid acid, Dimedone (5,5-Dimethyl-1,3-cyclohexanedione), Arylaldehydes, 9-Aryl-1,8-dioxo-octahydroxanthene.*

Introduction

Development of heterogeneous, environmentally benign and easily recyclable catalysts for synthesis of useful organic compounds is of importance [1-8]. Solid acids, as a significant kind of theses catalysts, have been designed, and successfully applied to promote different organic reactions [1-8]. Application of solid acid catalysts in organic transformations are associated with various advantages, such as simple process and product isolation, catalyst efficiency, good agreement with the green chemistry protocols, need for milder conditions, high reaction selectivity, appropriate thermal stability, improvement in atom efficacy, and reduce in volume of waste. Among the different classes of solid acids, SO$_3$H-containing ones have been attracted

Corresponding author: *Dr. Abdolkarim Zare, Department of Chemistry, Payame Noor University, PO BOX 19395-3697, Tehran, Iran. E-mail: abdolkarimzare@pnu.ac.ir.*

much attention by chemists to catalyze a variety of organic transformations [3-8].

It is noteworthy that most of the organic reactions are performed in volatile and toxic organic solvents, and this subject is not environmentally acceptable from green chemistry view point. Solvent-free conditions are the most successful techniques to solve this problem. Moreover, this technique saves energy, makes synthesis simpler, enhances reaction rates, increases yields and selectivity, and prevents solvent waste, hazards, and toxicity [8-12]. The coupling of solvent-free conditions with the use of heterogeneous catalysts represents an appropriate approach toward the so-called ideal synthesis [8-12].

The condensation reaction between dimedone (5,5-dimethyl-1,3-cyclohexanedione) (2 eq.) and arylaldehydes (1 eq.) has been used as a useful route for preparation of 9-aryl-1,8-dioxo-octahydroxanthene [13-22], as biologically [23-27] and industrially [28,29] important compounds. Some biological activities of these xanthene derivatives are anticancer [23], antibacterial [24], anti-inflammatory [25], antiviral [26], and antiplasmodial [27] properties.

In this research, we report the preparation of an attractive member of SO_3H-containing solid acids namely SO_3H-functionalized phthalimide (SFP) via the reaction of phthalimide with chlorosulfonic acid, and its full identification by studying FT-IR, ^1H and ^{13}C NMR, Mass, XRD (X-ray diffraction), TG (thermal gravimetric) and DTG (derivative thermal gravimetric) spectra. Then, we have applied this solid acid as an environmentally benign, heterogeneous, efficient and recyclable catalyst for the condensation of dimedone (5,5-dimethylcyclohexane-1,3-dione) (2 eq.) with arylaldehydes (1 eq.) in the absence of solvent to give 9-aryl-1,8-dioxo-octahydroxanthene derivatives in high yields and in short reaction times.

Experimental

All chemicals were purchased from Merck or Fluka Chemical Companies. All known compounds were identified by comparison of their melting points and spectral data with those reported in the literature. Progress of the reactions was monitored by TLC using silica gel SIL G/UV 254 plates. The ^1H NMR (250 or 500 MHz) and ^{13}C NMR (62.5 or 125 MHz) were run on a Bruker Avance DPX, FT-NMR spectrometer. Thermal gravimetry (TG) and differential thermal gravimetric (DTG) were analyzed by a Perkin Elmer (Model: Pyris 1). Melting points were recorded on a Büchi B-545 apparatus in open capillary tubes.

Procedure for the preparation of SO_3H-functionalized phthalimide (SFP)

To a round-bottomed flask (50 mL) containing phthalimide (0.736 g, 5 mmol), was added chlorosulfonic acid (0.594 g, 5.1 mmol) dropwise at 10 °C. After the addition was

completed, the reaction mixture was stirred at room temperature for 5 h, and then at 70 °C for 3 h. At the end of the process, the residue was washed with CH_2Cl_2 (2×10 mL), and dried to give SFP as a white solid in 98% yield. FT-IR (KBr): 3350-2950, 1718, 1305, 1287, 1182, 1088, 1070 cm^{-1}; ^1H NMR (250 MHz, DMSO-d$_6$, δ/ppm): 7.40-7.55 (m, 4H, aromatic hydrogens), 11.00 (s, 1H, OH of the SO_3H group). ^{13}C NMR (62.5 MHz, DMSO-d$_6$, δ/ppm): 122.6, 132.0, 134.0, 169.0. Mass (*m/z*): 227 (M$^+$), 228 (M$^+$+1), 210 (M$^+$-OH), 146 (M$^+$-SO$_3$H), 132 (M+-NSO$_3$H), 104 (M+-CONSO$_3$H) and 76 (M+-(CO)$_2$ NSO$_3$H).

General procedure for the condensation of dimedone with arylaldehydes using SFP

To a mixture of dimedone (0.28 g, 2 mmol) and aromatic aldehyde (1 mmol) in a test tube, was added SFP (0.045 g, 0.2 mmol). The resulting mixture was firstly stirred magnetically at 80 °C, and after solidification of the reaction mixture, it was vigorously stirred with a small rod at the same temperature. After completion of the reaction, as indicated by TLC, the reaction mixture was cooled to room temperature, EtOAc (5 mL) was added to the reaction mixture, stirred for 2 min and filtered (the product is soluble in EtOAc; but, SFP is insoluble in this solvent). The solvent of the filtrate was evaporated and the resulting solid (crude product) was recrystallized from EtOH (96%) to afford the pure product. The recycled

catalyst was washed with EtOAc (3 mL), dried and reused for the next run. The catalytic activity of SFP was restored for two times recycling.

Selected spectral data of 9-sryl-1,8-dioxo-octahydroxanthenes

*3,3,6,6-Tetramethyl-9-phenyl-1,8-dioxo-octahydroxanthene (**1**)*

^1H NMR (500 MHz, DMSO-d$_6$, δ/ppm): 0.90 (s, 6H), 1.04 (s, 6H), 2.09 (d, 2H, *J* = 16.1 Hz), 2.27 (d, 2H, *J* = 16.2 Hz), 2.53 (d, 2H, *J* = 17.1 Hz), 2.58 (d, 2H, *J* = 17.7 Hz), 4.53 (s, 1H), 7.10 (t, 1H, *J* = 7.0 Hz), 7.18 (d, 2H, *J* = 7.0 Hz), 7.21 (t, 2H, *J* = 7.20 Hz). ^{13}C NMR (75 MHz, CDCl$_3$, δ/ppm): 27.3, 29.3, 31.8, 32.2, 40.9, 50.7, 115.6, 126.4, 128.0, 128.4, 144.1, 162.3, 196.4.

*3,3,6,6-Tetramethyl-9-(3,4,5-trimethoxy-phenyl)-1,8-dioxo-octahydroxanthene (**4**)*

^1H NMR (500 MHz, DMSO-d$_6$, δ/ppm): 0.96 (s, 6H), 1.05 (s, 6H), 2.14 (d, 2H, *J* = 16.2 Hz), 2.29 (d, 2H, *J* = 16.2 Hz), 2.50-2.54 (Distorted AB system, 4H), 3.32 (s, 3H), 3.60 (s, 3H), 3.69 (s, 3H), 4.50 (s, 1H), 6.42 (s, 2H). ^{13}C NMR (75 MHz, CDCl$_3$, δ/ppm): 27.2, 29.4, 31.8, 32.2, 40.9, 50.7, 56.1, 60.7, 105.6, 115.5, 136.5, 139.7, 152.8, 162.4, 196.5.

*3,3,6,6-Tetramethyl-9-(3-nitrophenyl)-1,8-dioxo-octahydroxanthene (**6**)*

^1H NMR (500 MHz, CDCl$_3$, δ/ppm): 1.01 (s,

6H), 1.13 (s, 6H), 2.18 (d, 2H, $J = 16.3$ Hz), 2.27 (d, 2H, $J = 16.3$ Hz), 2.53 (t, 4H, $J = 18.5$ Hz), 4.85 (s, 1H), 7.41 (t, 1H, $J = 7.9$ Hz), 7.81 (d, 1H, $J = 7.5$ Hz), 7.99 (d, 1H, $J = 8.2$ Hz), 8.06 (s, 1H). ^{13}C NMR (125 MHz, CDCl$_3$, δ/ppm): 27.7, 29.6, 32.5, 32.7, 41.2, 51.0, 114,9, 122.0, 123.1, 129.2, 136.0, 146.8, 148.7, 163.5, 196.8.

3,3,6,6-Tetramethyl-9-(4-chlorophenyl)-1,8-dioxo-octahydroxanthene (9)

1H NMR (500 MHz, DMSO-d$_6$, δ/ppm): 0.90 (s, 6H), 1.04 (s, 6H), 2.09 (d, 2H, $J = 16.1$ Hz), 2.27 (d, 2H, $J = 16.1$ Hz), 2.52 (d, 2H), 2.57 (d, 2H, $J = 17.6$ Hz), 4.51 (s, 1H), 7.19 (d, 2H, $J = 8.3$ Hz), 7.29 (d, 2H, $J = 8.2$ Hz). ^{13}C NMR (75 MHz, CDCl$_3$, δ/ppm): 27.3, 29.3, 31.5, 32.2, 40.8, 50.7, 115.2, 128.2, 129.8.2, 131.9, 142.8, 162.5, 196.4.

Results and discussion

Having in mind the unique properties of SO$_3$H-containing solid acidic catalysts, we decided to synthesize solid acid SO$_3$H-functionalized phthalimide (SFP). Thus, phthalimide (1 eq.) was reacted with chlorosulfonic acid (1 eq.) in which SFP was obtained as a white powder (Scheme 1).
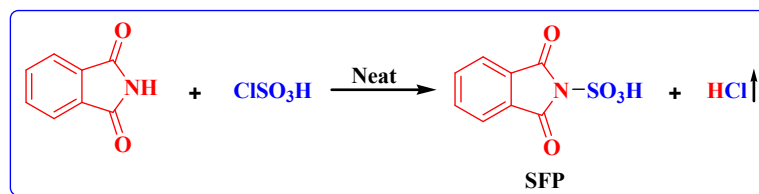
Scheme 1. The synthesis of SFP.

After the production of SFP, it was characterized by studying its FT-IR, ^{1}H and ^{13}C NMR, Mass, XRD, TG and DTG spectra as follow:

In the FT-IR spectrum of SFP, a broad peak was observed at 2950-3350 cm^{-1}; this peak is attributed to the hydroxy of the SO$_3$H group. The strong peak at 1718 cm^{-1} is related to the carbonyl groups of the solid acid. Two peaks observed at 1305 and 1088 cm^{-1} is corresponded to the vibrational modes of N-SO$_2$ bond. The strong absorptions at 1287 and 1182 cm^{-1} are assigned to the asymmetric and symmetric stretching and bending for S-O vibrations of the SO$_3$H. The band viewed at

1070 cm^{-1} is related to the S-OH bend.

In the ^{1}H NMR spectrum of the solid acid (figure 1), a multiplet peak at 7.40-7.55 ppm with integral 4 corresponds to four aromatic hydrogens. The peak observed at 11.00 ppm with integral 1, is related to the acidic hydrogen of SO$_3$H. To confirm that this peak is truly related to the hydrogen of SO$_3$H, the ^{1}H NMR spectra of the starting materials for the preparation of SFP (i.e. phthalimide and chlorosulfonic acid) was also run in DMSO-d$_6$; in these spectra, the acidic hydrogens peaks were viewed at 11.00 (for SFP), 11.31 (for phthalimide) and 13.54 (for ClSO$_3$H) ppm. The difference between the acidic hydrogens

of the solid acid and its reactants verified that phthalimide was effectively reacted with chlorosulfonic acid to afford SFP (in fact, the peak observed at 11.00 ppm of SFP spectrum, is truly related to its SO_3H group, not acidic hydrogens of the unreacted starting materials, i.e. the SO_3H of chlorosulfonic acid or NH of phthalimide).
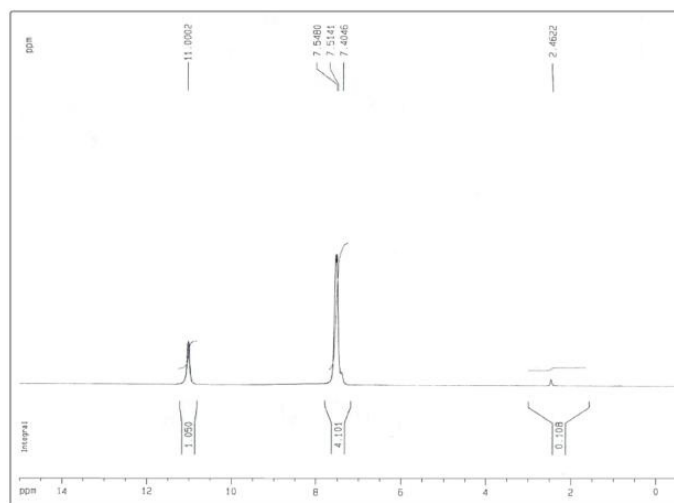

Figure 1. The ^1H NMR spectrum of SFP.

In the ^{13}C NMR spectrum, three peaks 122.6, 132.0, and 134.0 ppm, correspond to the three carbon kinds of the aromatic ring. Furthermore, a peak viewed at 169.0 ppm is attributed to the carbonyl groups. In the mass spectrum of SFP, molecular mass (M^+) and (M^++1) peaks is observed in m/z = 227 and 228, correspondingly. The other peaks which assist to identify the solid acid include 210 (M^+-OH), 146 (M^+-SO_3H), 132 (M^+-NSO3H), 104 (M^+- $CONSO_3H$) and 76 (M^+-$(CO)_2NSO_3H$). The XRD pattern of SFP is shown in figure 2, which displayed four peaks at 2θ = 7.70, 13.90, 15.50 and 23.30. This peak indicates that the solid acid has a crystal form.
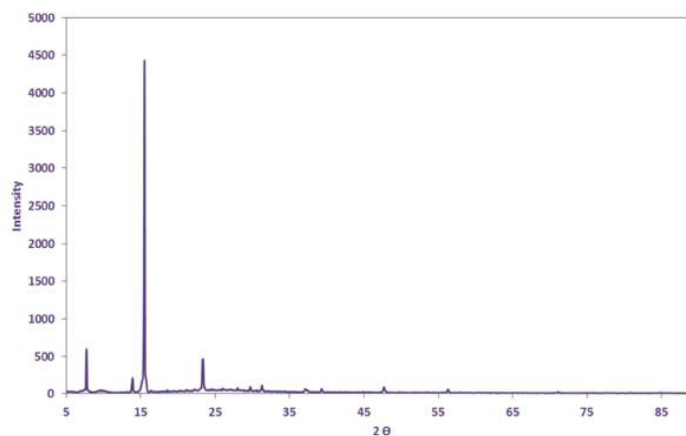

Figure 2. The XRD pattern of SFP.

Thermal gravimetric analysis of SFP was studied at range of 25-500 °C (temperature increase rate of 10 °C.min⁻¹, nitrogen atmosphere). The consequent diagrams are shown in figure 3. The thermal gravimetric (TG) and derivative thermogravimetry (DTG) diagrams indicate weight losses in two steps, at about 150-220 °C, and 275-360 °C.
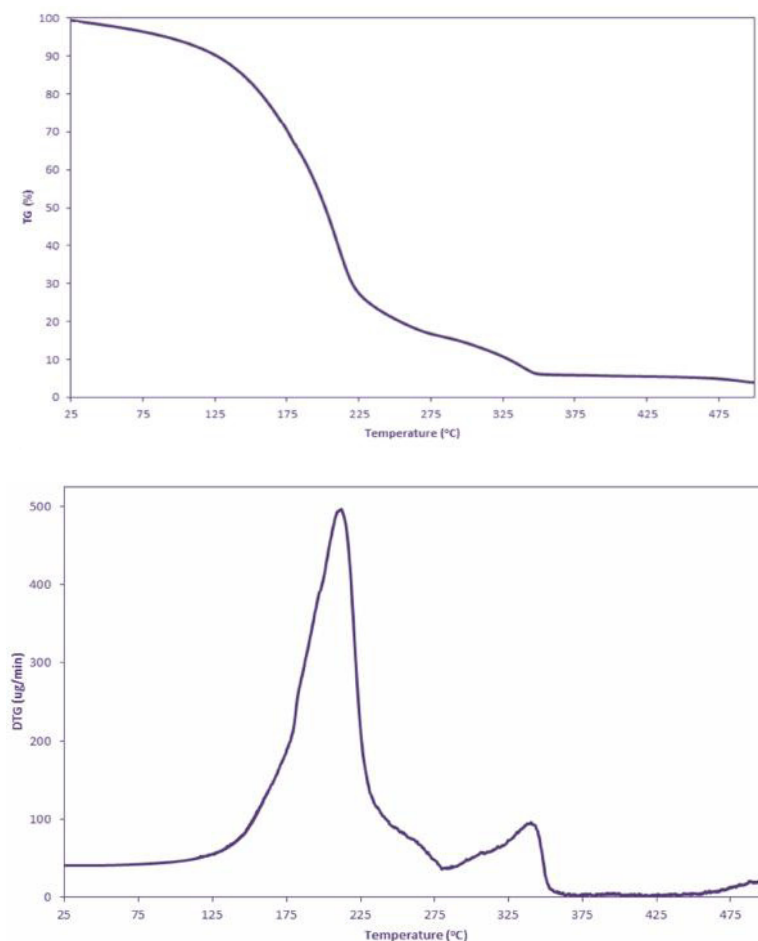

Figure 3. The TG and DTG diagrams of SFP.

After full identification of SFP, its catalytic activity was tested on the reaction of dimedone with arylaldehydes to give 9-aryl-1,8-dioxo-octahydroxanthenes. For this purpose, the reaction of dimedone (2 mmol) with 3-nitrobenzaldehyde (1 mmol) was chosen as a model reaction (Scheme 2), and its behavior was observed in the presence of 10-25 mol% of SFP at range of 60-85 °C. The results showed that 20 mol% of the catalyst and 80 °C were enough to carry out the transformation efficiently; in these conditions, the respective 9-aryl-1,8-dioxo-octahydroxanthene was obtained in 98% yield within 25 min.
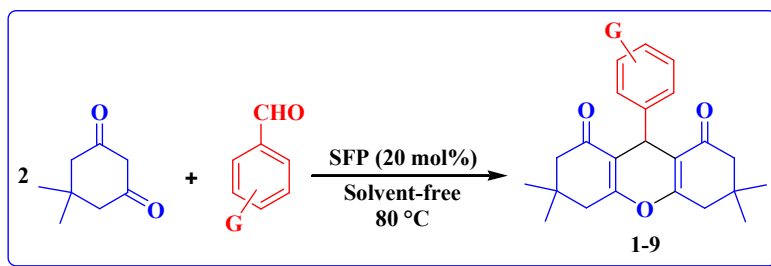
Scheme 2. The production of 9-aryl-1,8-dioxo-octahydroxanthene using SFP.

After the reaction was optimized, different arylaldehydes were reacted with dimedone in the presence of SFP; the related results are indicated in figure 4.
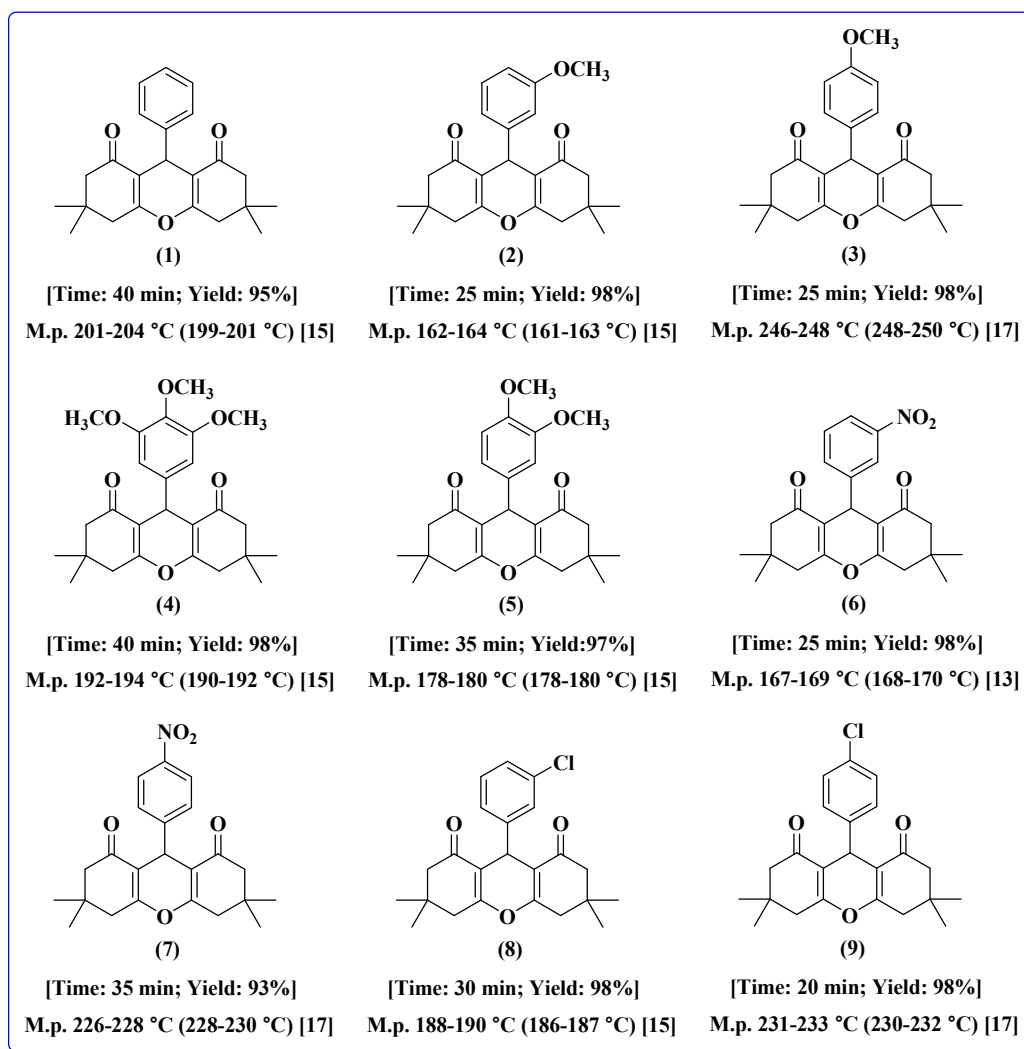

(1)
[Time: 40 min; Yield: 95%]
M.p. 201-204 °C (199-201 °C) [15]

(2)
[Time: 25 min; Yield: 98%]
M.p. 162-164 °C (161-163 °C) [15]

(3)
[Time: 25 min; Yield: 98%]
M.p. 246-248 °C (248-250 °C) [17]

(4)
[Time: 40 min; Yield: 98%]
M.p. 192-194 °C (190-192 °C) [15]

(5)
[Time: 35 min; Yield:97%]
M.p. 178-180 °C (178-180 °C) [15]

(6)
[Time: 25 min; Yield: 98%]
M.p. 167-169 °C (168-170 °C) [13]

(7)
[Time: 35 min; Yield: 93%]
M.p. 226-228 °C (228-230 °C) [17]

(8)
[Time: 30 min; Yield: 98%]
M.p. 188-190 °C (186-187 °C) [15]

(9)
[Time: 20 min; Yield: 98%]
M.p. 231-233 °C (230-232 °C) [17]

Figure 4. The preparation of 9-aryl-1,8-dioxo-octahydroxanthene using SFP.

As it is obvious from this figure, the catalyst was highly efficient and general for the production of 9-aryl-1,8-dioxo-octahydroxanthene derivatives; all substituents on the

arylaldehydes including methoxy, nitro, and chloro in different positions of the aromatic ring afforded the respective products in high yields and in short reaction times.

Conclusion

In summary, we have synthesized, identified and applied an attractive solid acid namely SO$_3$H-functionalized phthalimide to promote a useful organic reaction, i.e. the preparation of 9-aryl-1,8-dioxo-octahydroxanthenes from dimedone and arylaldehydes. The promising points for the presented methodology are short reaction times, high yields, generality, efficiency, cleaner reaction profile, simplicity, ease of the catalyst production and reusability of the catalyst.

Acknowledgements

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