

NOTE

[HSO₃-pmim][CH₃SO₃] as an Efficient Catalyst for the Synthesis of Xanthenedione Derivatives

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Xanthenedione derivatives were prepared through the condensation reaction of aromatic aldehydes with 5,5-dimethyl-1,3-cyclohexanedione promoted by 1-methyl-3-(3-sulfopropyl)imidazolium methyl sulphate, the reaction time was 20-40 min with the yields between 83.0-95.1 %. It is shown that the proposed method is fast, high efficient and environmentally benign.

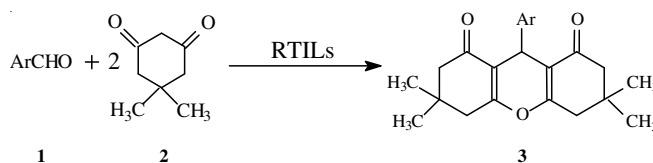
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Xanthenedione derivatives have attracted considerable attention owing to their unique biological activity¹ and they were valuable intermediates because of the inherent activity of the inbuilt pyran ring². The conventional synthetic methods of xanthenedione derivatives were carried out in organic solvent³. As an improvement, the condensation reaction of aromatic aldehydes with 5,5-dimethyl-1,3-cyclohexanedione were proceeded in water for 6 h using NH₂SO₃H and SDS as catalyst⁴. Microwave irradiation has also been used to promoted the condensation reaction⁵. Recently, Fan *et al.*⁶ reported that the synthesis of xanthenedione derivatives could be proceeded in ionic liquid [bmim]BF₄ catalyzed by Lewis acid InCl₃⁶ and FeCl₃·6H₂O⁷, respectively, the reaction time was between 4 to 10 h. However, some of these methods have not been entirely satisfactory, associating with disadvantages such as longer reaction time, using volatile and toxic organic solvent, using catalyst that can not be recycled and so on.

Room temperature ionic liquids (RTILs) have received increasingly attention as potential "greener" alternatives to volatile organic solvent and they have been investigated extensively as a solvent or catalyst for many important organic reactions because of their special properties such as their negligible vapor pressure, tunable polarity, high thermal stability, good solvating ability, ease of recyclability and their potential to enhance reaction rates and selectivity⁸. They have also been referred as "designer solvents," as their properties can be altered by the fine-tuning of parameters such as the choice of organic cation, inorganic anion and alkyl chain

attached to the organic cation. These structural variations offer flexibility to the chemist to devise the most idealized solvent and catalyst, catering for the needs of a particular process⁹.

In continuing our endeavor in green synthesis and using ionic liquids as a recyclable reaction medium to enhance rates and selectivity¹⁰, we report herein a mild and efficient protocol for the preparation of xanthenedione and their derivatives by (1-methyl-3-(3-sulfopropyl)-imidazolium methyl sulphate ([HSO₃-pmim][CH₃SO₃])) as an efficient catalyst (**Scheme-I**).



Scheme-I

Melting points were recorded on an Electrothermal (Shanghai XRC-1) apparatus and are uncorrected. ¹H NMR (300 MHz) and ¹³C NMR (50 MHz) spectra were determined with Bruker AVANCE 300 spectrometer (CDCl₃-d₆) using TMS as internal standard. Mass spectra were recorded on a Finnigan Mat 8230MSr operating 70 eV. IR spectra (cm⁻¹) were measured with a Braic WQF-510 spectrometer. [HSO₃-pmim][CH₃SO₃] was synthesized according to the literature¹¹.

Effects of reaction temperature on the yields of the product were also studied by processing the condensation reaction at

room temperature, 80 °C and 95-100 °C, respectively (Entries 3,8,9). The results shown that the higher of the reaction temperature, the reaction could proceed more efficiently.

General procedure: A mixture of aromatic aldehydes **1** (1 mmol), 5,5-dimethyl-1,3-cyclohexanedione (**2**) (2 mmol), [HSO₃-pmim][CH₃SO₃] (1 mL) were stirred at 95-100 °C for a certain period of time as required to complete the reaction (monitored by TLC), the products was separated by filtering and washing with water, the obtained solid were recrystallized from 80 % ethanol. Then the desired products 3,3,6,6-tetramethyl-9-aryl-1,8-dioxo-1,2,3,4,5,6,7,8-octahydroxanthene (**3a-l**) were obtained.

A variety of substituted aromatic aldehydes were subjected to the condensation reaction to study the substituted effects on the reactivity of them. The results were summarized in Table-1. For most of the substrates, the reaction could be completed in 20-40 min with high yields, whether the substrates having electron-donating groups or with electron-withdrawing groups, however, when the aromatic aldehydes with a bigger *ortho*-position substituent, such as 2-nitrobenzaldehyde and 2,4-dinitrobenzaldehyde, the reaction could not take place owing to the steric factors. 9-Arthenone and acetophenone also could not reacted with compound **2** under the above conditions.

TABLE-1
SYNTHESIS OF XANTHENEDIONE
DERIVATIVES IN [HSO₃-pmim][CH₃SO₃]

Entry	Ar	Time (min)	m.p. (lit) (°C)	Yield (%)
3a	4-(CH ₃) ₂ NC ₆ H ₄	35	220-221 (220-222) ³	89.7
3b	4-ClC ₆ H ₄	20	236-238 (237-239) ⁶	95.1
3c	2- ClC ₆ H ₄	20	226-227 (225-227) ⁶	94.1
3d	4-HOC ₆ H ₄	25	247-248 (246-248) ⁶	93.5
3e	4-CH ₃ OC ₆ H ₄	20	243-245 (242-244) ⁶	93.6
3f	3,4-(OCH ₂ O)C ₆ H ₃	30	220-221 (218.5-220) ³	93.9
3g	C ₆ H ₅	25	200-202 (199-201) ⁶	91.9
3h	4-BrC ₆ H ₄	25	238-240 (234-236) ⁶	92.2
3i	4-CH ₃ C ₆ H ₄	20	210-211 (210-212) ⁶	88.7
3j	3-NO ₂ C ₆ H ₄	40	153-154 (145-147) ⁶	83.0
3k	C ₆ H ₅ CH=CH	30	175-177 (175-177) ⁴	91.0
3l	4-HO-3-CH ₃ OC ₆ H ₃	25	227-228 (226-228) ³	92.8

The reusability and recycling of [HSO₃-pmim][CH₃SO₃] was also investigating. For the condensation reaction of 4-chlorobenzaldehyde and 5,5-dimethyl cyclohexanedione, the product was separated by directly filtering from the reaction mixture the remainder of the ionic liquid [HSO₃-pmim][CH₃SO₃] was extracted with diethyl ether for elimination of unreacted reactant and then dried under vacuum at 90 °C for 2 h to eliminate any water, the recycled [HSO₃-pmim][CH₃SO₃] was reused for subsequent reaction. The catalytic activity of [HSO₃-pmim][CH₃SO₃] did not show any

significant decrease even after five runs. The results were shown in Table-2.

TABLE-2
STUDIES ON THE REUSE OF THE [HSO₃-pmim]
[CH₃SO₃] FOR THE PREPARATION OF **3b**

Round	1	2	3	4	5
Yield (%)	95	95	92	90	89

Conclusion

The present synthetic method is a simple, efficient and green synthesis of 3,3,6,6-tetramethyl-9-aryl-1,8-dioxo-1,2,3,4,5,6,7,8-octahydroxanthene derivatives. The method offers marked improvements with regard to operational simplicity, reaction time, general applicability, high yields of products and greenness of procedure, avoiding hazardous organic solvents and toxic catalysts, so it provides a practical alternative to the existing procedures. The application of the task-specific ionic liquids for other reactions is in progress.

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REFERENCES

1. J.P. Poupelin, G. Saint-Rut, O. Foussard-Blanpin, G. Narcisse, G. Uchida-Ernouf and R. Lacroix, *Eur. J. Med. Chem.*, **13**, 67 (1978).
2. C. O'Callaghan and T.B.H.N. McMurry, *J. Chem. Res. (s)*, 214 (1995).
3. E.C. Horning and M.G. Horning, *J. Org. Chem.*, **11**, 95 (1946).
4. T.S. Jin, J.S. Zhang, A.Q. Wang and F.S. Zhang, *Chin. J. Org. Chem.*, **25**, 335 (2005).
5. S.J. Tu, Y. Gao, X.H. Liu, S.F. Tang and X.J. Qiu, *Chin. J. Org. Chem.*, **21**, 1164 (2001).
6. X.Y. Hu, X.S. Fan and X.Y. Zhang, *Chin. Chem. Lett.*, **16**, 293 (2005).
7. X.S. Fan, Y.Z. Li, X.Y. Zhang, X.Y. Hu and J.J. Wang, *Chin. J. Org. Chem.*, **25**, 1482 (2005).
8. (a) T. Welton, *Chem. Rev.*, **99**, 2071 (1999); (b) J. Dupont, R.F. de Souza and P.A. Z. Suarez, *Chem. Rev.*, **102**, 3667 (2002); (c) N. Jain, A. Kumar, S. Chauhan and S.M.S. Chauhan, *Tetrahedron*, **61**, 1015 (2005); (d) S. Chowdhury, R.S. Mohan and J.L. Scott, *Tetrahedron*, **63**, 2363 (2007).
9. (a) S.G. Lee, *Chem. Commun.*, **10**, 1049 (2006); (b) B.C. Ranu and S. Banerjee, *Org. Lett.*, **7**, 3049 (2005); (c) A.L. Zhu, T. Jiang, D. Wang, B.X. Han, L. Liu, J. Huang, J.C. Zhang and D.H. Sun, *Green Chem.*, **7**, 514 (2005).
10. (a) J.J. Ma, X. Zhou, X.H. Zang, C. Wang, Z. Wang, J.C. Li and Q. Li, *Aust. J. Chem.*, **60**, 146 (2007); (b) J.J. Ma, S.T. Gao, Z. Li, R.X. Tang, H.Y. Liu, C. Wang and Y. Gao, *Chin. J. Org. Chem.*, **28**, 339 (2008); (c) J.J. Ma, X.H. Zang, X. Zhou, C. Wang, J.C. Li and Q. Li, *Indian J. Chem.*, **46B**, 2045 (2007); (d) C. Wang, J.J. Ma, X. Zhou, X.H. Zang, Z. Wang, Y.J. Gao and P.L. Cui, *Synth. Commun.*, **35**, 2759 (2005).
11. L. Zhang, M. Xian, Y.C. He, L.Z. Li, J.M. Yang, S.T. Yu and X. Xu, *Bioresour. Technol.*, **100**, 4368 (2009).