Table 5. Comparison of the results of Nano SiO_2-OSO_3H with those of other catalysts reported in the literature in the synthesis of 2-substituted aryl (indolyl) kojic acid derivatives.

Entry	Catalyst	Conditions	Time (min)	Yield (%)	Ref.
1	Nano SiO_2-OSO_3H	EtOH/ Reflux	40-75	80-98	This work
2	FAU-Zeolite	Solvent free/110ºC	45-85	82-97	[13]
3	$InCl_3$	Solvent free/120ºC	55-85	75-90	[12]

benzaldehyde and 2-naphthaldehyde under the same reaction conditions, a higher yield of the 2-substituted aryl (indolyl) kojic acid obtained in shorter times (Table 4, entries 10, 11).

Similarly when 5-chloro and 5-bromo indole were treated with 4-methoxy benzaldehyde and kojic acid in the presence of nano silica sulfuric acid (0.003 g), a good yield of the corresponding products were obtained (Table 4, entries 12, 13).

An interesting feature of this method is that the reagent can be regenerated at the end of the reaction and can be used several times without losing its activity. To recover the catalyst, after completion of the reaction, the mixture was filtered, and catalyst was washed with EtOH, and then the solid residue dries. This process was repeated for two cycles, and the yield of product **4a** did not change significantly (Table 1, entries 10, 11).

However, in order to show the merits and drawbacks of this catalyst, our results were compared with two catalysts reported in literature. As shown in Table 5, Nano SiO_2-OSO_3H can act as an effective catalyst with respect to reaction times, yields and conditions.

4. Conclusions

In summary, we have developed one-pot synthesis for the preparation of 2-substituted aryl (indolyl) kojic acid derivatives through three-component reactions of kojic acid with indoles and aryl aldehydes in the presence of a catalytic amount of nano silica sulfuric acid in EtOH. By incorporating two biologically potential moieties in a single molecule the biological activity of these compounds may be enhanced. Also we employed nano silica sulfuric acid as an easily available and less costly, less toxic, and operable under environmentally friendly conditions catalyst in this reaction and obtained desired products with high yields. Therefore, this method is green, simple, efficient and convenient for formation of a wide range of 2-substituted aryl (indolyl) kojic acid derivatives.

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References

[1] (a) R.W. Armstrong, A.P. Combs, P.A. Tempest, S.D. Brown, T.A. Keating, Acc. Chem. Res. 29 (1996) 123-131. (b) N.K. Terret, M. Gardner, D.W. Gordon, R.J. Kobylecki, J. Steel, Tetrahedron 51 (1995) 8135-8173. (c) A. Domling, Chem. Rev. 106 (2006) 17-89.

[2] G.W. Gribble, J. Chem. Soc. Perkin Trans 1. (2000) 1045-1076.

[3] W.N. Xiong, C.G. Yang, B. Jiang, Bioorg. Med. Chem. 9 (2001) 1773-1780.

[4] S. Zhu, S. Ji, X. Su, C. Sun, Y. Liu, Tetrahedron Lett. 49 (2008) 1777-1781.

[5] S.S. El-Nakkady, S.E.S. Abbas, H.M. Roaiah, I.H. Ali, Global. J. Pharm. 6 (2012) 166-177.

[6] L.H. Franco, E.B.K. Joffe, L. Puricelly, M. Tatian, A.M. Seldes, J.A. Palermo, J. Nat. Prod. 61 (1998) 1130-1132.

[7] S. Zhu, S. Ji, K. Zhao, Y. Liu, Tetrahedron Lett. 49 (2008) 2578-2582.

[8] M.P. Zhu, I. Kimiaki, Tetrahedron Lett. 38 (1997) 5301-5302.

[9] X. Xiong, M.C. Pirrung, Org. Lett. 10 (2008) 1151-1154.

[10] (a) M. Sefkow, H. Kaatz, Tetrahedron Lett. 40 (1999) 6561-6562. (b) H.N. Barham, G.N. Reed, J. Am. Chem. Soc. 60 (1938) 1541-1545.

[11] (a) Y. Kobayashi, H. Kayahara, K. Tadasa, H. Tanaka, Bioorg. Med. Chem. Lett. 6 (1996) 1303-1308. (b) R.C. Fox, P.D. Taylor, Synth. Commun. 28 (1998) 1575-1583. (c) A.A. Shestopalov, L.A. Rodinovskaya, A.M. Shestopalov, V.P. Litvinov, Russ. Chem. Bull. 53 (2004) 724-725.

[12] B.V.S. Reddy, M.R. Reddy, Ch. Madan, K.P. Kumar, M.S. Rao, Bioorg. Med. Chem. Lett. 20 (2010) 7507-7511.

[13] B. Sadeghi, Z. Lasemi, F. Amiri Tavasoli, S. Hashemian, H. Zahedi, Syn. React. Inorg. Met. 44 (2014) 1497-1503.

[14] B. Sadeghi, A. Hassanabadi, S. Bidaki, J. Chem. Res. 35 (2011) 666-668. (b) B. Sadeghi, T. Ziya, J. Chem. (2013) Article ID 179013, 5 pages

[15] (a) B. Sadeghi, P.F. Nezhad, S. Hashemian, J. Chem. Res. 38 (2014) 54-57. (b) B. Sadeghi, M. Ghasemi Pirbaluti, P. Farokhi Nezhad, R. Abbasi Nezhad, Res. Chem. Intermed. 41 (2013) 4047-4055.