(IJIRSE) International Journal of Innovative Research in Science & Engineering
ISSN (Online) 2347-3207

Preparation of MnO_2 nanoparticles and application in the Synthesis of 2,2'-arylmethylene bis(3-hydroxy-5,5-dimethyl-2-cyclohexene-1-one)

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***Abstract* — Highly stable MnO_2 nano particles catalyst has been prepared by environmentally benign method and characterized by using Raman, XRD, FESEM, and EDAX techniques. The catalytic behaviour of nano crystalline MnO_2 has been demonstrated for the synthesis 2,2'-arylmethylene bis(3-hydroxy-5,5-dimethyl-2-cyclohexene-1-one) via Knoevenagel condensation of aromatic aldehydes and 5,5-dimethyl-1,3-cyclohexanedione under solvent-free conditions. Recyclability, high yield, short reaction time and easy workup are the advantages of the present catalyst.**

Keywords- MnO_2 Nano Particles, aryl aldehydes, 2,2'-arylmethylene bis(3-hydroxy-5,5-dimethyl-2-cyclohexene-1-one)

I. INTRODUCTION

2,2′-Arylmethylene bis(3-hydroxy-5,5-dimethyl-2-cyclohexene-1-one) compounds and their derivatives are significant bio-active compounds and have been assessed as tyrosinase inhibitors[1]. These compounds are key synthons for the synthesis of xanthenes that exhibit significant biological and therapeutic activities such as antioxidants, lipoxygenase inhibitors, antibacterial and antiviral activities [2], besides they are also used in laser technology [3]. Several methods have been reported for the syntheses of 2,2'-arylmethylene bis(3-hydroxy-5,5-dimethyl-2-cyclohexene-1-one) using a number of catalysts [4-11]. Development of newer synthetic methods based on green chemistry processes is increasingly of interest in organic synthesis due to economic and environmental concerns. Solvent free heterogeneous catalysis makes organic synthesis simple, saves energy, and prevents wastage of solvent, chemical hazards and toxicity [12]. In general, MnO_2 is used as an oxidizing agent [13] in organic synthesis. However, to the best of our knowledge, MnO_2 nano particles (NPs) catalysed synthesis of xanthene derivatives via a multicomponent reaction under solvent-free condition unknown. Thus, highly stable and environmentally benign MnO_2 NPs have been synthesised by hydrothermal method and characterized by using Raman, XRD, FESEM, and EDAX techniques. The catalytic behaviour of MnO_2 NPs has been demonstrated for the synthesis 2,2'-arylmethylene bis(3-hydroxy-5,5-dimethyl-2-cyclohexene-1-one) via Knoevenagel condensation of aromatic aldehydes and 5,5-dimethyl-1,3-cyclohexanedione under solvent-free conditions. The detail of the work is presented in this manuscript.

II. MATERIALS AND METHODS

A. Characterization

Melting points were determined in open capillaries and are uncorrected. Chromatography purification was conducted by column chromatography using silica gel. Solvents used for purification were of commercial grade and were purified before use. ^1H and ^{13}C NMR spectra were recorded on a Bruker ultra shield spectrometer (300 and 75 MHz) or a JEOL-500MHz spectrometer (500 and 125 MHz) in $CDCl_3$ solvent using TMS as internal standard. FESEM/EDAX analyses were carried out on a HITACHI S-3400N microscope. The phase composition and crystalline nature of the catalyst was analyzed using PXRD. Bruker D8 ADVANCE MODEL diffractometer was used for recording PXRD data between 2 theta values ranging from 20 and 70 deg using CuK_α as source operating at 40 kV and 30 mA. Raman spectra were recorded using a BRUKER RFS 27: Stand-alone FT-Raman Spectrometer equipped with Nd: YAG 1064 nm as excitation source.

B. Preparation of the MnO_2 NPs Catalyst

MnO_2 NPs has been prepared from commercially available MnO_2 (2g) powder was treated with 25 mL of 10 M NaOH and pH =11was maintained. The mixture was then transferred into a Teflon-lined stainless autoclave at 180 °C for 48 h. After the reaction, the mixture was cooled to RT. The resulted precipitate was washed with distilled water and filtered and further washed three times with 50 mL of 10N HCl. After HCl washing, the precipitate was further washed with distilled water and dried at 120°C for 6 hours and finally calcined at 400 °C for 24 hours. The resulted MnO_2 NPs catalyst was crushed, powdered and used for reactions.

*C. Procedure for the synthesis of 2,2'-arylmethylene bis(3-hydroxy-5,5-dimethyl-2-cyclohexen-1-one (**3**)*

To a 25 mL RB flask, a 2:1 mixture of 5, 5-dimethylcyclohexane-1,3-dione **2** (2 mmol) and arylaldehyde **1** (1 mmol) without any solvent was mixed with MnO_2 NPs (10 mol%). The mixture was heated at 100 °C for the appropriate period of time. After the completion of reaction (TLC monitoring), the reaction mixture was cooled to RT and EtOAc was added, and the catalyst was filtered off. The filtrate was evaporated to dryness, and the solid obtained was further purified by column chromatography on silica gel (100–200 mesh) using a mixture of petroleum ether and ethyl acetate (petroleum ether/ethyl acetate = 3/1, V/V) and/or recrystallization from ethanol to get pure products. The spectral data's of selective compounds are presented below:

*2,2'-Phenylmethylene bis(3-hydroxy-5,5-dimethyl-2-cyclohexene-1-one) (**3a**).*[8]

White crystalline solid; m.p. 184–186 °C; FT-IR (KBr) ν_{max}: 3388, 2962, 1588, 1370, 1254, 1156, 1098, 1031, 811, 577, 486 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$/TMS) δ_H: 11.84 (s, 1H, OH), 7.22-7.01 (m, 5H, ArH), 5.47 (s, 1H, CH), 2.37-2.27 (m, 8H, 4(CH_2), 1.16 (s, 6H, 2CH_3), 1.03 (s, 6H, 2CH_3); ^{13}C NMR (75 MHz, $CDCl_3$/TMS) δ_C: 189.4, 188.4, 137.1, 127.2, 125.8, 124.8, 114.6, 46.1, 45.4, 31.7, 30.4, 28.6, 26.4.

*2,2'-[(4-Methylphenyl)methylene]bis(3-hydroxy-5,5-dimethylcyclohex-2-enone) (**3c**).*[8]

White solid; m.p. 132-134 ℃; FT-IR (KBr) ν_{max}: 2958, 2871, 1714, 1596, 1511, 1450, 1372, 1305, 1041, 813 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$/TMS) δ_H: 11.84 (s, 1H, OH), 7.01-6.99 (m, 2H, ArH), 6.91-6.89 (m, 2H, ArH), 5.42 (s, 1H, CH), 2.40-2.21 (m, 11H, 4(CH_2), CH_3), 1.15 (s, 6H, 2CH_3), 1.02 (s, 6H, 2(CH_3); ^{13}C NMR (125 MHz, $CDCl_3$/TMS) δ_C: 189.4, 188.3, 134.2, 133.8, 127.9, 125.6, 114.6, 46.0, 45.3, 31.3, 30.7, 28.6, 26.3, 19.8.

*2,2'-[(4-Chlorophenyl)methylene]bis(3-hydroxy-5,5-dimethylcyclohex-2-enone) (**3e**).*[8]

White solid; m.p. 139-141 ℃, FT-IR (KBr) ν_{max}: 3435, 2958, 2872, 1595, 1490, 1468, 1374, 1304, 1253, 830 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$/TMS) δ_H: 11.87 (s, 1H, OH), 7.23-7.22 (m, 2H, ArH), 7.02-7.00 (m, 2H, ArH), 5.47 (s, 1H, CH), 2.48-2.28 (m, 8H, 4(CH_2), 1.22 (s, 6H, 2(CH_3), 1.09 (s, 6H, 2(CH_3); ^{13}C NMR (125 MHz, $CDCl_3$/TMS) δ_C: 190.7, 189.4, 136.7, 131.5, 128.3, 128.2, 115.3, 47.0, 46.4, 32.4, 31.4, 29.6, 27.4.

*2,2'-[(4-Bromophenyl)methylene]bis(3-hydroxy-5,5-dimethylcyclohex-2-enone) (**3g**).*[8]

White solid; m.p. 158-160 ℃; FT-IR (KBr) ν_{max}: 3447, 2955, 2869, 1597, 1471, 1419, 1377, 788, 725 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$/TMS) δ_H: 11.87 (s, 1H, OH), 7.39-7.37 (m, 2H, ArH), 6.96-6.95 (m, 2H, ArH), 5.47 (s, 1H, CH), 2.48-2.28 (m, 8H, 4(CH_2), 1.21 (s, 6H, 2(CH_3), 1.09 (s, 6H, 2(CH_3); ^{13}C NMR (125 MHz, $CDCl_3$/TMS) δ_C: 190.7, 189.4, 137.3, 131.3, 128.6, 119.6, 115.2, 47.0, 46.4, 32.4, 31.4, 29.5, 27.4.

*2,2'-[(4-Nitrophenyl)methylene]bis(3-hydroxy-5,5-dimethylcyclohex-2-enone) (**3i**).*[8]

Yellow solid; m.p. 190-192 ℃; FT-IR (KBr) ν_{max}: 3437, 2957, 2868, 1589, 1510, 1458, 1375, 1342, 1252, 1167, 1153, 1044, 851, 733, 588, 492 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$/TMS) δ_H: 11.80 (s, 1H, OH), 8.14-8.12 (m, 2H, ArH), 7.25-7.23 (m, 2H, ArH), 5.54 (s, 1H, CH), 2.51-2.31 (m, 8H, 4(CH_2), 1.24 (s, 6H, 2(CH_3), 1.11 (s, 6H, 2(CH_3); ^{13}C NMR (125 MHz, $CDCl_3$/TMS) δ_C: 190.9, 189.6, 146.5, 146.1, 127.6, 123.5, 114.9, 46.9, 46.4, 33.3, 31.5, 29.5, 27.5.

III. RESULT AND DISCUSSIONS

The MnO_2 NPs synthesised by hydrothermal method has been characterised as follows. Initially, a Raman spectrum was recorded. A strong Raman band at 646 cm^{-1} of MnO_2 NPs can be attributed to the symmetric stretching vibration (Mn–O) of the MnO_2 (Fig. 1a). The X-ray powder pattern of the MnO_2 NPs showed peaks at $2\theta = 28.75, 37.53$ and 41.01^o confirming the presence of β-MnO_2 NPs [JCPDS# 81-2261] and the crystalline size of MnO_2 NPs was found to be 40.26 nm (Fig. 1b). The FESEM images showed the well-defined nano crystals nature of synthesised MnO_2 NPs. The particle size of MnO_2 NPs was estimated to be about 100 nm (Fig. 1c). The EDAX analysis confirms the presence of MnO_2 (Fig. 1d).

The catalytic behavior of the MnO_2 NPs catalyst was examined for the synthesis of 2,2'- phenylmethylenebis (3-hydroxy-5,5-dimethyl-2-cyclohexene-1-one) derivatives. Thus, initially a mixture of benzaldehyde **1a**, and 5, 5-dimethyl-1,3-cyclohexanedione **2** under solvent and catalyst free conditions for the synthesis of 2,2'-phenylmethylenebis (3-hydroxy-5,5-dimethyl-2-cyclohexene-1-one) (Table I, entry 1). However, the reaction afforded only 2,2'- phenylmethylenebis (3-hydroxy-5,5-dimethyl-2-cyclohexene-1-one) **3a** in 40% yield. Interestingly, the use of MnO_2 NPs as heterogeneous catalyst under solvent-free condition afforded 2,2'-phenylmethylene bis (3-hydroxy-5,5-dimethyl-2-cyclohexene-1-one) **3a** in 94-96% yield (Table I, entry 4 and 5). On the other hand, the reaction with different amounts of MnO_2 NPs catalyst under solvent-free conditions at 80°C provided the desired compound 3a in 65% yield (Table 1, entry 2 and 3). When reaction was carried out at 100°C the desired compound 3a was obtained in good yield and the results are summarized in Table I. It has been found that 10 mol % of MnO_2 NPs is the optimum amount of catalyst (Table 1, entry 5). Increasing mol %

of catalyst beyond 10% did not alter the yield (Table I, entry 6), while reducing the mol % of catalyst decreased the yield (Table I, entry 7).

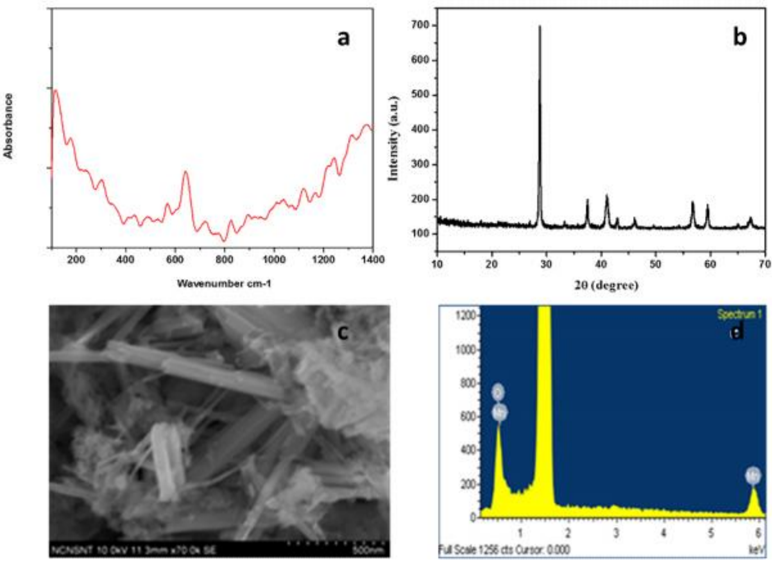
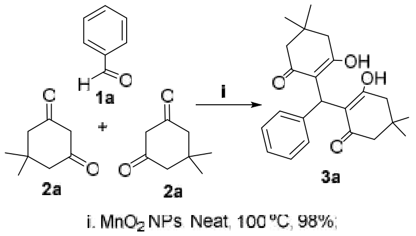


Figure 1. (a) Raman spectra; (b) PXRD; (c) FESEM and (d) EDAX of MnO_2 NPs



Scheme 1

TABLE I. OPTIMIZATION OF MnO_2 NPS CATALYST FOR THE ONE-POT CONDENSATION OF DIMEDONE **2A** WITH BENZALDEHYDE **1A**

Entry	MnO_2 NPs **(mol %)**	**Temperature (°C)**	**Time (min)**	**Product**	**Yield[a] (%)**
1	-	100	20	**3a**	40
2	10	80	20	**3a**	65
3	15	80	20	**3a**	65
4	10	100	10	**3a**	94
5	**10**	**100**	**20**	**3a**	**96**
6	15	100	20	**3a**	96
7	5	100	30	**3a**	75

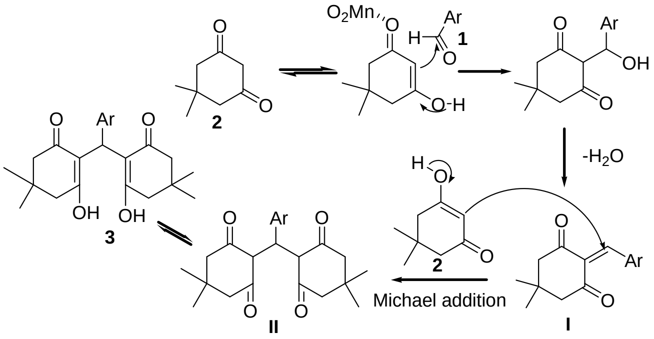
[a] Reaction condition: benzaldehyde: 5, 5-dimethyl-1,3-cyclohexanedione 1:2, at different temperature

Encouraged by the preliminary results and in order to demonstrate the method is general, under the optimized condition, we have used various aryl aldehydes **1a-k** were reacted with **2** and the reactions preceded well to afford bis (3-hydroxy-5,5-dimethyl-2-cyclohexene-1-one) **3a-k** in excellent yields (Table II). From the experimental results, it is observed that, the substitution at the 4-position of the aromatic aldehyde had no significant effect and aldehydes with either electron-donating group or electron-withdrawing group did not alter the yields of the products significantly. Demonstrating the diversity of the aldehydes, heterocyclic aldehyde such as 2-thiophene aldehyde **1k** afforded the desired product **3k** in excellent yield (Table II, entry 11). It should be noted that the present catalyst has advantages over other catalysts in terms of high yield, short reaction time, relative non-toxicity, easy workup and ability to perform reactions under solvent free conditions. Recycling of catalyst was achieved for three times without loss of activity. All the compounds were characterized by spectroscopic data (FTIR, ^{1}H NMR and ^{13}C NMR).

TABLE II. Synthesis of 1,8-Dioxo-octahydro-xanthenes **5a-j**

Entry	Ar-CHO	Diketone	Time (min)	Product	Yield (%)[a]
1	C_6H_5, **1a**	**2**	15	**3a**	98
2	3-H_3C-C_6H_4, **1b**	**2**	25	**3b**	92
3	4-H_3C-C_6H_4 **1c**	**2**	20	**3c**	92
4	3-Cl-C_6H_4, **1d**	**2**	25	**3d**	93
5	4-Cl-C_6H_4, **1e**	**2**	20	**3e**	96
6	3-Br-C_6H_4, **1f**	**2**	20	**3f**	88
7	4-Br-C_6H_4, **1g**	**2**	20	**3g**	90
8	3-NO_2-C_6H_4, **1h**	**2**	20	**3h**	94
9	4-NO_2-C_6H_4, **1i**	**2**	15	**3i**	94
10	4-HO-C_6H_4, **1j**	**2**	45	**3j**	92
11	2-Thienyl, **1k**	**2**	45	**3k**	90

The formation of compound **3** can be explained by the mechanism that presented in Scheme 2. The reaction sequence is one-pot Knoevenagel condensation, Michael addition and tautomerization. Xanthene derivative **3** was believed to be formed via an initial Knoevenagel condensation of 5,5-dimethyl-1,3-cyclohexanedione **2** with benzaldehyde **1a** to afford intermediate **I**. Then the active methylene of 5,5-dimethyl-1,3-cyclohexanedione **2** reacts with intermediate **I** via a conjugate Michael addition to generate the intermediate **II**, which upon tautomerization gives compound **3**.



Scheme 2. Proposed mechanism for the synthesis **3**

In summary, a highly stable and environmentally benign MnO_2 NPs catalyst was prepared and thoroughly characterized by Raman, XRD, FESEM and EDAX techniques. The catalytic activity of MnO_2 NPs has been demonstrated for the synthesis of 2,2’-arylmethylene bis(3-hydroxy-5,5-dimethyl-2-cyclohexene-1-one) under solvent free conditions. The catalyst was found to be recyclable without loss of activity. Further work utilizing the catalysts for other synthetic transformations is in progress in this laboratory.

Acknowledgments

Authors thanks to University of Madras for providing infrastructure facilities, Director, National Center for Nanoscience and Nanotechnology (NCNSNT), University of Madras for Raman, and FE-SEM/EDAX measurements and Department of Chemistry, St. Joseph College, Bangalore, for XRD measurements.

References

[1] K.M. Khan, G.M. Maharvi, M.T.H. Khan, A.J. Shaikh, S. Perveen, S.B. Mild, M.I. Choudhary, Tetraketones: a new class of tyrosinase inhibitors, Bioorg. Med. Chem., 14 (2006), pp. 344–351.

[2] G.M. Maharvi, S. Ali, N. Riaz, N. Afza, A. Malik, M. Ashraf, L. Iqbal, M. Lateef, Mild and efficient synthesis of new tetraketones as lipoxygenase inhibitors and antioxidants, J. Enzyme Inhib. Med. Chem., 23 (2008), pp. 62–69.

[3] O. Sirkecioglu, N. Talinli, A. Akar, Synthesis of 14-alkyl-14H-dibenzo [a,j]xanthenes, J. Chem. Res. (1995), p. 502.

[4] T.S. Jin, A.Q. Wang, H. Ma, J.S. Zhang, T.S. Li, “The reaction of aromatic aldehydes and 5,5-dimethyl-1,3-cyclohexanedione under solvent-free grinding conditions,” Indian J. Chem. Vol. 45B, 2006, pp. 470-474.

[5] T.S. Jin, J.S. Zhang, A.Q. Wang, T.S. Li, “Solid-state condensation reactions between aldehydes and 5,5-dimethyl-1,3-cyclohexanedione by grinding at room temperature,” Synth. Commun. Vol. 35, 2005, pp. 2339-2345.

[6] L.B. Liu, T.S. Jin, L.S. Han, M. Li, N. Qi, T.S. Li, “The reaction of aromatic aldehydes and 1,3-cyclohexanedione in aqueous media,” E-J. Chem. Vol. 3, 2006, pp. 117-121.

[7] S. Kantevari, R. Bantu, L. Nagarapu, “$HClO_4$-SiO_2 and PPA-SiO_2 catalyzed efficient one-pot Knoevenagel condensation, Michael addition and cyclo-dehydration of dimedone and aldehydes in acetonitrile, aqueous and solvent free conditions: Scope and limitations,” J. Mol. Catal. A: Chem. Vol. 269, 2007, pp. 53-57.

[8] M. Bayat, H. Imanieh, S.H. Hossieni, “Synthesis of 2,2’-arylmethylene bis (3-hydroxy-5,5-dimethyl-2-cyclohexeane-1-one) in aqueous medium at room temperature,” Chin. Chem. Lett. Vol. 20, 2009, pp. 656-659.

[9] (a) D.Q. Shi, J. Chen, Q.Y. Zhuang, X.S. Wang, H.W. Hu, “The condensation of aromatic aldehydes with acidic methylene compounds in water,” Chin. Chem. Lett. Vol. 14, 2003, pp. 1242-1245; (b) D.Q. Shi, Q.Y. Zhuang, J. Chen, X.S. Wang, S.J. Tu, H.W. Hu, “Reaction of aromatic aldehydes with 5,5-dimethyl-1,3-cyclohexandione in water,” Chin. J. Org. Chem. 23, 2003, pp. 684–696.

[10] X.S. Fan, Y.Z. Li, X.Y. Zhang, X.Y. Hu, J.J. Wang, $FeCl_3.6H_2O$ catalyzed condensation of aromatic aldehydes with 5,5-dimethyl-1,3-cyclohexanedione in ionic liquids, Chin. Chem. Lett. Vol. 16, 2005, pp. 897-899.

[11] Najmedin Azizi, Sahar Dezfooli, Mohammad Mahmoudi Hashemi, Chemoselective synthesis of xanthenes and tetraketones in a choline chloride-based deep eutectic solvent,” C. R. Chimie Vol. 16, 2013, pp. 997-1001.

[12] K.Tanaka, Solvent-free Organic Synthesis, Wiley-VCH, GmbH and KGaA, Wein-heim, 2004.

[13] G. Cahiez, M. Alami, R. J. K. Taylor, M. Reid, J. S. Foot, "Manganese Dioxide", in Paquette, Leo A., Encyclopedia of reagents for organic synthesis, New York: J. Wiley & Sons, 2004.