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# Investigation of the reaction of dimedone with aromatic aldehydes in the presence of copper oxide nanoparticles

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## Abstract

Variously substituted methylene bis(3-hydroxy-5,5-dimethyl-2-cyclohexene-1-one) derivatives were synthesized in 83–96% yield by the reaction of substituted benzaldehyde with 5, 5-dimethyl-1, 3-cyclohexanedione in the presence of CuO nanoparticles (NPs). Tandem grinding involves Knoevenagel condensation followed by the Michael addition in sequence for the formation of 2, 2'-arylmethylenebis (3-hydroxy-5, 5-dimethyl-2-cyclohexene-1-one) derivatives. Copper oxide NPs were synthesized by sol-gel method. The characterization of CuO NPs was done on the basis of PXRD, FTIR, SEM and TEM techniques. The synthesized derivatives were characterized on the basis of spectral analyses and corresponding melting points reported in the literature.

## Keywords

biscyclohexenone
solvent-free
recyclable
heterogeneous
CuO nanoparticles
Grindstone chemistry

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## Key findings

- This method provides an improved pathway in terms of excellent yield, short reaction time, solvent-free conditions, energy-efficiency, eco-friendliness, and low catalyst loading.
- This method is safe as there is no usage of costly reagents and toxic chemicals.
- The catalyst can be recycled and reused without any significant loss in its catalytic activity.

Supplementary materials

## 1. Introduction

Catalysis plays an important role in any organic transformation. Due to environmental concerns, selection of a catalyst is very crucial. The catalyst selected should be environment-friendly and should meet the principles of "Green chemistry" [1]. Nowadays, nanoparticles (NPs) are regarded as effective heterogeneous catalysts for several organic reactions, as NPs have high surface/volume ratio [2]. Hence, great interest has been shown by organic chemists to heterogeneous catalytic systems rather than homogeneous catalysts, as the former possess active sites on their surface and thus reactants get adsorbed on catalysts, solid surface, and reaction occurs giving product which gets desorbed from the surface. This very fact forms the basis of nanocatalysis [3, 4]. Furthermore, a nanocatalyst can be easily separated from the reaction mix, recovered and recycled without losing its catalytic activity, as was observed in various organic reactions. In the present article, we investigated the reaction of dimedone with differently substituted aromatic aldehydes in the presence of copper oxide nanoparticles (CuO NPs). Among variously synthesized nanoparticles, nanocrystalline copper oxide is one of the extensively used surface materials with profound applications in biomedical field [5], dye degradation [6], supercapacitors [7], food packaging applications [8], electrochemical energy storage [9], biosensors [10], nano fluids [11], solar power plant [12], and it exhibits diverse biological activities [13]. Further, its use as an outstanding catalyst in several organic transformations is well demonstrated [14–19]. Several organic reactions including the aza-Michael reaction [14], A3 coupling reaction [15], azide-olefin cycloaddition [16], hydroboration of alkynes [17], Ullmann coupling reaction [18], and C–N cross-coupling reaction [19], etc., can be conducted in the presence of very small quantity of CuO NPs.

The biological activities of substituted methylene bis (3-hydroxy-5, 5-dimethyl-2-cyclohexene-1-one) derivatives are well demonstrated. These derivatives are well-known for their varied pharmacological activities, such as antimicrobial, antioxidant, and anticancer activity [20]. They are important precursors for preparing xanthenedione derivatives, which act as the potential antibacterial, analgesic, anti-inflammatory and anticancer agents [21–26].

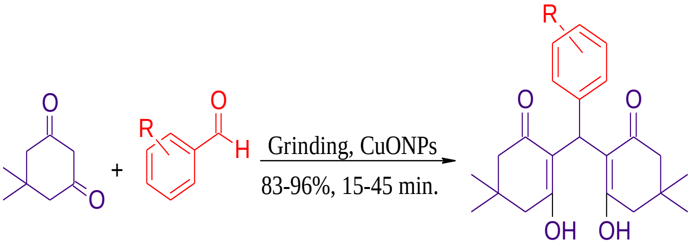
There are reported methods which describe the use of different catalytic systems for producing these compounds. The catalysts employed as of now include urea [27], nano-$ZnAl_2O_4$ [28], KF/$Al_2O_3$ [29], $SmCl_3$ [30], triethylammonium acetate [31], copper octoate [32], TEAOH [33], $MnO_2$ NPs [34], copper(0) nanoparticles onto silica [35], baker's yeast [36], silica-diphenic acid [37], etc. For all we know, there is no report available in the literature which describes the investigation of reaction of aromatic aldehydes with dimedone in the presence of CuO NPs as a catalyst under grinding for the synthesis of substituted methylenebis (3-hydroxy-5,5-dimethyl-2-cyclohexene-1-one)derivatives **(3a–j).** Most of the reported methods require costly reagents and chemicals. Though many reported methods have advantages in terms of good yield yet, some of them are pollution-causing, time-consuming, need long hours of refluxing, tedious work-up procedure, and in some cases, separation of catalyst; hence, recyclability is the biggest challenge. Encouraged by these observations, CuO NPs were explored as heterogeneous catalyst for synthesizing substituted methylene bis (3-hydroxy-5, 5-dimethyl-2-cyclohexene-1-one) derivatives **3a–j** under grinding (Table 1). CuO NPs are safe, non-toxic, cheap and can be easily prepared [38, 39]. Therefore, in continuation to our earlier interest in synthesizing bioactive molecules using nanocatalysts, we now report the synthesis of CuO NPs and their use as heterogeneous catalyst for the synthesis of **3a–j** (Table 1) by the condensation of aromatic aldehydes and dimedone in 1:2 molar ratio under grindstone chemistry technique (Scheme 1). CuO NPs were synthesized by sol-gel method and characterized on the basis of FTIR, UV-VIS, SEM, and TEM techniques. The synthesized compounds were characterized on the basis of reported melting points and spectral studies.

## 2. Materials and Methods

### 2.1. General

All chemicals used for the experimental procedure were obtained from the Sigma Aldrich and Merck and used as received. Melting point apparatus was used for the determination of melting points (MPs) that were uncorrected. TLC was used to check the progress of reaction by using benzene: ethyl acetate (8:2) as an eluent. Nanoparticles were characterized from PXRD performed with PANalytical X'Pert Pro Diffractometer using Cu (Kα) radiation (wavelength: 1.5406 Å), operated at 45 kV and 40 mA at room temperature in the range of 2θ from 20 to 90°. Infra-red spectra were recorded in KBr on a Perkin Elmer Infrared RXI FTIR spectrophotometer.

SEM was recorded on HITACHI, JAPAN, Model SU8010 SERIES. HRTEM was recorded on JEM 2100 plus model. BRUKER AVANCE NEO (500 MHz) spectrometer was used to record $^1H$ and $^{13}C$ NMR spectra in $CDCl_3$ using TMS as internal reference standard. The resulting compounds were identified on the basis of their reported melting points and their spectral ($^1H$ NMR, $^{13}C$ NMR and FTIR) analysis. To prepare copper oxide nanoparticles, deionized water was used.



R=H; 4-$CH_3$; 4-$OCH_3$; 2-Cl; 4-Cl; 2-Br; 4-Br; 2-$NO_2$; 4-$NO_2$; 4-OH; 2-OH

**Scheme 1** Synthesis of aryl substituted methylene bis (3-hydroxy-5, 5-dimethyl-2-cyclohexene-1-one) derivatives.

**Table 1** CuO NPs mediated synthesis of methylene bis (cyclohexenone) derivatives[a] under grinding.

| Entry | R | Catalyst | Yield (%)[b] | Melting points (°C) (found) | Melting points (°C) (reported) | Time (min) |
|---|---|---|---|---|---|---|
| **3a** | H | CuO NPs | 90 | 191–192 | 191–192 [37] | 20 |
| **3b** | 4-$OCH_3$ | CuO NPs | 86 | 143–145 | 143–145 [37] | 25 |
| **3c** | 4-$CH_3$ | CuO NPs | 91 | 135–137 | 135–137 [37] | 30 |
| **3d** | 4-Cl | CuO NPs | 83 | 144–145 | 145 [37] | 35 |
| **3e** | 2-Cl | CuO NPs | 96 | 144–145 | 145 [37] | 45 |
| **3f** | 2-Br | CuO NPs | 90 | 152–154 | 152–154 [37] | 20 |
| **3g** | 4-Br | CuO NPs | 83 | 152–154 | 152–154 [37] | 20 |
| **3h** | 2-OH | CuO NPs | 92 | 195–198 | 205–206 [43] | 20 |
| **3i** | 2-$NO_2$ | CuO NPs | 85 | 180–182 | 188–189 [27] | 25 |
| **3j** | 4-$NO_2$ | CuO NPs | 84 | 181–182 | 188–189 [27] | 20 |
| **3a** | H | no catalyst | traces on tlc | – | – | 60 |

[a] Reaction conditions: aromatic aldehyde (10 mmole), dimedone (20 mmole), and CuO NPs (30 mg), grinding, solvent-free conditions.
[b] Isolated product yield.

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### 2.2. Preparation of copper oxide nanoparticles (CuO NPs)

Sol-gel method was used to prepare copper oxide nanoparticles [40]. For a typical experimental procedure, 0.1 M copper (II) chloride dihydrate solution ($CuCl_2\cdot 2H_2O$) and 2 M NaOH solution was prepared in deionized water. Heating of 100 ml of 0.1 M copper (II) chloride dihydrate solution was carried out at 80 °C along with continuous stirring, and then 1 ml glacial acetic acid was added followed by the gradual (dropwise) addition of NaOH (2M) to the solution. There was an immediate blue to black color change leading to the formation of black precipitate of CuO NPs, which was washed 3–4 times with deionized water, filtered, and dried at 80 °C for 24 h in hot electric oven. Finally, the formed CuO NPs were calcined at 450 °C for 4 h in a muffle furnace.

### 2.3. Method for the synthesis of aryl substituted methylene bis(3-hydroxy-5, 5-dimethyl-2-cyclohexene-1-one)derivatives (3a–j)

A mixture of an aromatic aldehyde (10 mmole), dimedone (20 mmole), and CuO NPs (30 mg) was ground in a mortar with the help of pestle of suitable size at room temperature until the reaction was completed (TLC). As reaction completed, ice cold water was added to the crude product, which was filtered and washed 2–3 times with distilled water. After drying at room temperature, the product was dissolved in hot ethyl alcohol, and the nanocatalyst was recovered simply by filtration. Finally, the solvent was evaporated on a water bath, and the crude product obtained was recrystallized from ethyl alcohol to obtain pure product (Table 1). The synthesized aryl substituted methylene bis (3-hydroxy-5, 5-dimethyl-2-cyclohexene-1-one) derivatives were characterized on the basis of their spectral analysis and by comparing their MPs with the corresponding MPs reported in the literature.

### 2.4. Spectral characterization data

#### 2.4.1. 2,2′-(phenyl)methylenebis(3-hydroxy-5,5-dimethyl-2-cyclohexene-1-one) 3a

Color: crystalline white; m.p. 191–192 °C; IR (KBr cm$^{-1}$): 3740, 3840, 2957, 2876, 1608, 1523, 1472, 1364, 1231, 1146, 979, 834, 708 cm$^{-1}$; $^1$H NMR (500 MHz, $CDCl_3$): $\delta_H$ (ppm): 1.03 (6H, resonated singlet, $2CH_3$), 1.13 (6H, *s*, $2CH_3$), 2.21–2.47 (8H, *m*, $CH_2$ ), 5.50 (1H, *s*, CH), 6.79 (*d*, *J* = 8.7 Hz, 2H, Ar–H), 7.00 (2H, *d*, Ar–H), 10.30 (*br. s*, 1H, OH), 11.92 (*br. s*, 1H, OH) ppm; $^{13}$C NMR (400 MHz, $CDCl_3$): $\delta_C$ (ppm): 27.47, 28.31, 29.73, 31.49, 32.79, 46.51, 47.10, 54.17, 57.39, 76.81, 77.12, 77.45, 115.64, 125.93, 126.84, 128.29, 138.10, 189.58, 190.42, 190.63, 203.85 ppm (supplementary materials) [37].

#### 2.4.2. 2,2′-(4-methoxyphenyl)methylenebis(3-hydroxy-5,5-dimethyl-2-cyclohexene-1-one) 3b

Color: crystalline white; m.p.143–145 °C; IR (KBr cm$^{-1}$): 3740, 3852, 2956, 2882, 1596, 1511, 1455, 1330, 1162, 1034, 822, 660 cm$^{-1}$; $^1$H NMR (500 MHz, $CDCl_3$): $\delta_H$ (ppm): 0.98 (6H, resonated singlet, $CH_3$), 1.07 (6H, *s*, $CH_3$), 2.21–2.47 (8H, *m*, $CH_2$), 3.73 (3H, *s*, $OCH_3$), 5.48 (1H, *s*, CH), 6.78 (*d*, *J* = 8.7 Hz, 2H, Ar–H), 6.98 (*d*, *J* = 8.55 Hz, 2H, Ar–H), 10.30 (*br. s*, 1H, OH), 11.92 (*br. s*, 1H, OH) ppm;$^{13}$C NMR(500 MHz, $CDCl_3$): $\delta_C$ (ppm): 27.42, 29.59, 31.40, 32.03, 46.43, 47.05, 53.97, 55.14, 77.03, 77.29, 77.54, 113.65, 115.75, 127.91, 129.86, 157.60, 189.38, 190.38, 203.78 (supplementary materials).

#### 2.4.3. 2,2′-(4-methylphenyl)methylenebis(3-hydroxy-5,5-dimethyl-2-cyclohexene-1-one) 3c

Color: crystalline white; m.p. 135–137 °C; IR (KBr cm$^{-1}$): 3854, 3741, 2957, 2880, 1596, 1458, 1368, 1246, 1152, 916, 818, 662 cm$^{-1}$; $^1$H NMR (500 MHz, $CDCl_3$); $\delta_H$ (ppm): 0.98 (6H, resonated singlet, $2CH_3$), 1.07 (6H, *s*, $2CH_3$), 2.27–2.50 (8H, *m*, $CH_2$), 2.50 (4H, *s*, $2CH_2$), 3.28 (3H, *s*, $CH_3$), 5.50 (1H, *s*, CH), 6.96 (*d*, *J* = 8.05 Hz 2H, Ar–H) 7.05 (*d*, *J* = 8.05 Hz, 2H, Ar–H), 10.31 (*br. s*, 1H, OH), 11.91 (*br. s*, 1H, OH) ppm. $^{13}$C NMR (500 MHz, $CDCl_3$): $\delta_C$ (ppm): 20.93, 27.45, 28.41, 29.60, 31.44, 32.43, 46.46, 53.98, 57.43, 77.05, 77.31, 77.56, 115.70, 126.72, 129.13, 135.01, 135.17, 189.46, 190.43, 203.80 ppm (supplementary materials) [37].

#### 2.4.4. 2,2′-(4-chlorophenyl) methylene bis (3-hydroxy-5,5-dimethyl-2-cyclohexene-1-one) 3d

Color: crystalline white; m.p. 144–145 °C; IR (KBr cm$^{-1}$): 3278, 2957, 2878, 1721, 1598, 1477, 1373, 1299, 1234, 1166, 1074, 826, 713 cm$^{-1}$; $^1$H NMR(500 MHz, $CDCl_3$); $\delta_H$ (ppm): 1.03 (6H, *s*, $2CH_3$), 1.09 (6H, *s*, $2CH_3$), 2.34–3.09 (8H, *m*, $CH_2$), 5.45 (1H, *s*, CH), 7.17 (*d*, *J* = 9.1 Hz, 2H, *d*, Ar–H), 7.24 (*d*, *J* = 8.55 Hz, 2H, Ar–H), 11.84 (*br. s*, 1H, OH) ppm;$^{13}$C NMR (400 MHz, $CDCl_3$): $\delta_C$ (ppm): 27.48, 29.69, 31.50, 32.46, 46.65, 47.11, 76.78, 77.09, 77.41, 77.75, 115.39, 128.27, 128.43, 129.10, 131.66, 136.76, 189.51, 190.70 ppm (supplementary materials) [37].

#### 2.4.5. 2,2′-(2-chlorophenyl) methylenebis(3-hydroxy-5,5-dimethyl-2-cyclohexene-1-one) 3e

Color: crystalline white; m.p. 144–145 °C; IR (KBr cm$^{-1}$): 3840, 3740, 3383, 3063, 2953, 1721, 1611,1462, 1333, 1145, 1055, 903, 842, 745, 649 cm$^{-1}$; $^1$H NMR (500 MHz, $CDCl_3$); $\delta_H$ (ppm): 1.02 (6H, *s*, $2CH_3$), 1.06 (6H, *s*, $2CH_3$), 2.33–2.51 (8H, *m*, $CH_2$), 5.61 (1H, *s*, CH), 7.18 (2H, *d*, Ar–H), 7.24 (2H, *d*, Ar–H), 11.93 (*br. s*, 1H, OH) ppm; $^{13}$C NMR (400 MHz, $CDCl_3$): $\delta_C$ (ppm): 28.31, 29.34, 31.58, 32.11, 47.02, 54.19, 57.39, 76.80, 77.11, 77.43, 115.75, 128.27, 126.53, 129.45, 130.41, 133.59, 136.68, 189.87, 203.83 ppm (supplementary materials) [37].

#### 2.4.6. 2,2′-(2-bromophenyl)methylenebis(3-hydroxy-5,5-dimethyl-2-cyclohexene-1-one) 3f

Color: crystalline white; m.p. 152–154 °C; IR (KBr cm$^{-1}$): 2958, 2870, 1627, 1612, 1475, 1154, 754, 689 cm$^{-1}$; $^1$H NMR (500 MHz, $CDCl_3$); $\delta_H$ (ppm): 1.01 (6H, *s*, $2CH_3$), 1.07 (6H, *s*, $2CH_3$), 2.34–2.50 (8H, *m*, $CH_2$), 5.46 (1H, *s*, CH), 6.94 (2H, *d*, Ar–H), 7.24 (2H, *d*, Ar–H), 11.86 (*br. s*, 1H, OH) ppm;$^{13}$C

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NMR (400 MHz, $CDCl_3$): $\delta_C$ (ppm): 28.30, 29.34, 31.48, 32.26, 40.89, 46.49, 47.11, 50.74, 54.16, 57.40, 76.83, 77.14, 77.47, 114.83, 115.20, 128.29, 133.65, 136.68, 159.87, 162.30, 189.58, 190.71, 203.86 ppm (supplementary materials) [37].

### 2.4.7. 2,2′-(4-bromophenyl)methylenebis(3-hydroxy-5,5-dimethyl-2-cyclohexene-1-one) 3g

Colour: crystalline white; m.p. 152–154 °C; IR (KBr cm$^{-1}$): 3849, 3740, 2957, 2878, 2581, 1590, 1471, 1371, 1254, 1160, 1066, 898, 819, 583 cm$^{-1}$; $^1$H NMR (500 MHz, $CDCl_3$); $\delta_H$ (ppm): 1.09 (6H, resonated singlet, $2CH_3$), 1.14 (6H, *s*, $2CH_3$), 2.28–2.46 (8H, *m*, $CH_2$), 5.44 (1H, *s*, CH), 6.96 (2H, *d*, Ar–H), 7.38 (2H, *d*, Ar–H), 10.32 (*br. s*, 1H, OH), 11.92 (*br. s*, 1H, OH) ppm;$^{13}$C NMR (400 MHz, $CDCl_3$): $\delta_C$ (ppm): 27.23, 29.54, 31.49, 32.40, 40.77, 46.96, 50.60, 76.67, 76.99, 77.31, 115.18, 119.57, 128.54, 130.12, 137.21, 162.44, 189.40, 190.63, 196.39 ppm (supplementary materials) [37].

### 2.4.8. 2,2′-(2-hydroxyphenyl)methylenebis(3-hydroxy-5,5-dimethyl-2-cyclohexene-1-one) 3h

Color: crystalline white; m.p. 175–178 °C; IR (KBr cm$^{-1}$): 3849, 3740, 2883, 2814, 1646, 1557, 1410, 1167, 768, 695 cm$^{-1}$; $^1$H NMR (500 MHz, $CDCl_3$); $\delta_H$ (ppm): 0.97 (6H, resonated singlet, $2CH_3$), 1.12 (6H, *s*, $2CH_3$), 2.31–2.58 (8H, *m*, $CH_2$), 2.58 (1H, *s*, OH), 4.70 (1H, s, CH), 6.99 (*d*, *J* = 4.9 2H, Ar–H) 7.13 (*J* = 4.75 d, 2H, Ar–H), 10.47 (*br. s*, 1H, OH), ppm;$^{13}$C NMR (500 MHz, $CDCl_3$): $\delta_C$ (ppm): 26.59, 27.08, 29.65, 30.99, 32.20, 43.14, 49.93, 50.46, 77.10, 77.36, 76.84, 110.99, 115.67, 118.29, 124.50, 128.02, 150.89, 168.93, 171.01, 196.86, 200.61 ppm (supplementary materials) [43].

### 2.4.9. 2,2′-(2-nitrophenyl)methylenebis(3-hydroxy-5,5-dimethyl-2-cyclohexene-1-one) 3i

Color: Light Yellow; m.p. 160–162 °C; IR (KBr cm$^{-1}$): 3849, 3740, 3286, 2955, 2881, 1720, 1617, 1524, 1455, 1150, 1072, 986, 749, 689 cm$^{-1}$; $^1$H NMR (500 MHz, $CDCl_3$); $\delta_H$ (ppm): 1.00 (6H, *s*, $2CH_3$), 1.13 (6H, *s*, $2CH_3$), 2.17–2.50 (8H, *m*, $CH_2$), 6.01 (1H, *s*, CH), 7.21–7.53 (4H, *m*, Ar–H), 10.31 (*br. s*, 1H, OH), 11.92 (*br. s*, 1H, OH) ppm;$^{13}$C NMR (400 MHz, $CDCl_3$): $\delta_C$ (ppm): 28.24, 28.59, 31.98, 46.34, 46.92, 76.78, 77.10, 77.42, 114.71, 124.41, 127.25, 131.44, 149.79, 189.52, 190.97 ppm (supplementary materials) [27].

### 2.4.10. 2,2′-(4-nitrophenyl)methylenebis(3-hydroxy-5,5-dimethyl-2-cyclohexene-1-one) 3j

Color: crystalline white; m.p. 160–162 °C; IR (KBr cm$^{-1}$): 3849, 3740, 2954, 2879, 1720, 1609, 1521, 1452, 1153, 1070, 842, 750, 697 cm$^{-1}$; $^1$H NMR (500 MHz, $CDCl_3$); $\delta_H$ (ppm): 1.13 (6H, resonated singlet, $2CH_3$), 1.15 (6H, *s*, $2CH_3$), 2.31–2.50 (8H, *m*, $CH_2$), 5.54 (1H, *s*, CH), 7.25 (*d*, *J* = 8.1Hz, 2H, Ar–H), 8.13 (*d*, *J* = 8.85 Hz, 2H, Ar–H), 11.79 (*br. s*, 1H, OH) ppm;$^{13}$C NMR (500 MHz, $CDCl_3$): $\delta_C$ (ppm): 27.44, 29.47, 31.46, 33.24, 46.38, 46.97, 77.07, 114.88, 123.48, 127.64, 146.55, 189.58, 190.94 ppm (supplementary materials) [27].

## 3. Results and Discussion

At first, we investigated the amount of CuO NPs required for the reaction of benzaldehyde (1 mmole) and dimedone (2 mmole). For this, different amounts of CuO NPs (10 mg, 20 mg and 30 mg) were taken to carry out the reaction. 30 mg (0.03 mol %) of the CuO NPs provided excellent yield of the product (Scheme 1). Therefore, we carried out the reaction of benzaldehyde with dimedone in 1:2 molar ratio using 30 mg CuO NPs by stirring the mixture at 100 °C; the reaction occurred in 60 min with 83% yield of the product. For this reaction, a mixture of dimedone (2 mmol), benzaldehyde (1 mmol) and 30 mg of CuO NPs in $H_2O$ was magnetically stirred at 100 °C till the reaction was completed. After this (as shown by TLC), CuO NPs were separated from the hot reaction mixture simply by filtration. The solid product obtained on evaporating the solvent was filtered, and recrystallized from ethanol. In order to optimize the reaction conditions, a mixture of 1 mmol of benzaldehyde and 2 mmol of dimedone in the presence of CuO NPs (30 mg) was refluxed in ethanol for appropriate time till the reaction was completed, which took around 2–3 h. As soon as the reaction was completed (as indicated by TLC), CuO NPs were separated, the reaction mixture was cooled to room temperature, and the solid product obtained was filtered and recrystallized from ethanol leading to 88% yield. Finally, the reaction was established under grinding in the absence of any solvent to improve the yield. The reaction was carried out successfully within 20 min with excellent product yield (90%). Hence, all the compounds were synthesized by grinding the reactants together using mortar and pestle of suitable size (Table 1, Scheme 1). The reaction occurred under solvent-free conditions by grinding the reactants together for 20 to 45 min in the presence of 30 mg of CuO NPs, and the products were obtained in 83–96% yield. The reaction progress was monitored by TLC. For comparison, the synthesis of 3a was performed in the absence of any catalyst under grinding for 1 h, but only trace amount of the product was obtained on TLC. The compatibility of this reaction was further observed with benzaldehyde substituted with methyl, nitro, methoxy, chloro, bromo, hydroxyl, etc., groups in terms of reaction time and yield. 2, 2'-Aryl methylene bis (3-hydroxy-5,5-dimethyl-2-cyclohexene-1-one) derivatives **(3a–j)** were characterized by comparison of their spectral data and melting points with those reported in the literature. $^1$H NMR spectra of **3a–j** showed the resonated singlet signals in the range δ 0.90–1.34 ppm for $CH_3$ protons, resonated multiplet signals at δ 2.14–2.47 (8H, m, –$CH_2$), 5.48 (1H, s, –CH), two OH protons (–C=C–OH) resonated in the range of 10.30–11.93 ppm. $^{13}$C NMR spectra of **3c** show signals at δ 20.93–53.98 (aliphatic $CH_3$, $CH_2$, CH carbons), 115.70 (–C=C–), 126.72–135.17 (aromatic carbons), 189.46 (=C–OH), 190.43 (C=O) ppm. Advantageous features of present methodology are mild reaction conditions, short reaction time (10–45 min), and higher product yield (83–96%), easy-work up, low catalyst loading, energy-efficiency, and recyclability of the catalyst.

### 3.1. Characterization of CuO NPs

Characterization of nanoparticles is done on the basis of FTIR, XRD, FESEM, and TEM analysis.

Figure 1 shows FTIR spectrum of copper oxide nanoparticles.The absorption band at 3360 cm$^{-1}$ is due to stretching vibration of –OH bond and a small band at 1641 cm$^{-1}$ corresponds to bending vibration of –OH bond due to physically adsorbed water molecules on the CuO NPs [40]. Absorption bands between 500 and 1000 cm$^{-1}$ are assigned to the respective asymmetric and symmetric stretching vibrational frequency of Cu–O–Cu bands [41]. The crystalline or amorphous nature of nanoparticles can be analyzed with the help of X-ray diffraction (XRD). The CuO nanoparticles are crystalline in nature as identified by the well-defined peaks in XRD. XRD analysis of the CuO NPs showed diffraction peaks at 2θ of 32.60, 35.61, 38.85, 48.83, 53.58, 58.40, 61.65, 66.17, 68.13, 72.50, 75.17 corresponding to planes (110), (-111), (111/200), (-202), (020), (202), (-113), (022/-311), (113/220), (311), and (004/222), respectively. This XRD pattern shown in Figure 2 agrees with single phase CuO NPs with a monoclinic structure (JCPDS 72-0629) [42].

We calculated the average crystallite size of the CuO NPs from XRD by applying Debye-Scherrer equation:

$$D = K\frac{\lambda}{\beta\cos\theta} = 0.9\frac{\lambda}{\beta\cos\theta} \quad (1)$$

$$\beta = \frac{\mathrm{FWNM}\cdot 3.14}{180} \quad (2)$$

where $K$ is the Scherrer constant; $D$ is the average crystallite size (nm), λ is the X-ray wavelength, λ = 0.15406 nm and θ = Bragg angle in degrees, half of 2θ, β is the line broadening at FWHM in radians.

The average size of the NPs calcined at 450 °C for 4 h obtained from the peaks at 2θ=32.6090, 35.6108, 38.8579, 48.8395 and 58.4074 in XRD (Figure 2) using the Debye-Scherrer formula is about 21 nm. SEM images (Figure 3A) of CuO NPs before recycling depict show that the CuO NPs are scattered and connected.

Figure 3A shows the formation of regular shaped NPs and well-nanotablet tube (rod-shaped NPs) model. Agglomerated and aggregated crystals are clearly seen in the SEM images. The representation of the grains is regular, and the microstructure consists of many neatly arranged rod shaped particles (nano-tablet tube) [40].

The morphology of CuO NPS was determined by TEM images (Figure 4). Figure 4 shows that CuO NPs consist of a mixture of spherical and elongated particles of similar size.

### 3.2. Probable mechanism of the reaction

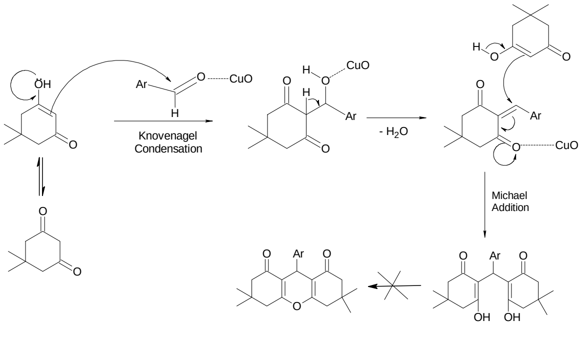
The proposed mechanism for the formation of 2,2’-aryl methylene bis (3-hydroxy-5, 5-dimethyl-2-cyclohexene-1-one) derivatives involves the Knoevenagel condensation between the aromatic aldehyde and 5,5-dimethyl-1,3-cyclohexanedione (1,3-diketone) followed by the Michael addition [28] of the intermediate olefin (α, β-unsaturated carbonyl compound) with another molecule of 5,5-dimethyl-1,3-cyclohexanedione (1,3-diketone) leading to the formation of uncyclized product, 2, 2’-arylmethylenebis(3-hydroxy-5,5-dimethyl-2-cyclohexene-1-one) by using catalytic amount of nano-CuO (Scheme 2). Knoevenagel condensation [28] is facilitated in the presence of Lewis acidic sites (Cu$^{+2}$) coordinated to the oxygen of carbonyl group of 1, 3-diketone and leads to deprotonation of 5,5-dimethyl-1,3-cyclohexanedione (1, 3-diketone) in the presence of Lewis basic sites (O$^{-2}$) of nano-CuO (Scheme 2). Xanthenedione derivatives were not formed under similar reaction conditions. This is confirmed on the basis of spectral analyses and by comparison of their melting points with those taken from the literature.

### 3.3. Recyclability and reusability of the catalyst

After the accomplishment of the reaction (as indicated by TLC using benzene: ethyl acetate (8:2) as eluent), the CuO nanocatalyst was separated from the hot reaction mixture by simple filtration. The separated and recovered nanocatalyst was washed five to six times with ethanol, dried, and reused five times for the same reaction. The results indicated that nanocatalyst showed high efficiency even after five successive runs of recycling, and only a slight yield reduction was observed (Figure 5). From these results, it can be concluded that the nanocatalyst can act as a suitable environ-economic contender from the environmental point of view. Further, in order to assess the integrity of the nanocatalyst, FESEM analysis was conducted after five successive runs of recycling (Figure 3B). FESEM images indicated preserved integrity of the CuO nanocatalyst indistinguishable from FESEM images obtained before recycling (Figure 3A).

## 4. Limitations

We investigated the reaction of dimedone with aromatic aldehydes in the presence of CuO nanocatalyst under grinding so as to synthesize xanthenedione derivatives. These derivatives were not formed; instead, a formation of 2, 2’-aryl methylene bis (3-hydroxy-5,5-dimethyl-2-cyclohexene-1-one) derivatives takes place.



**Scheme 2** Probable mechanism of the reaction.

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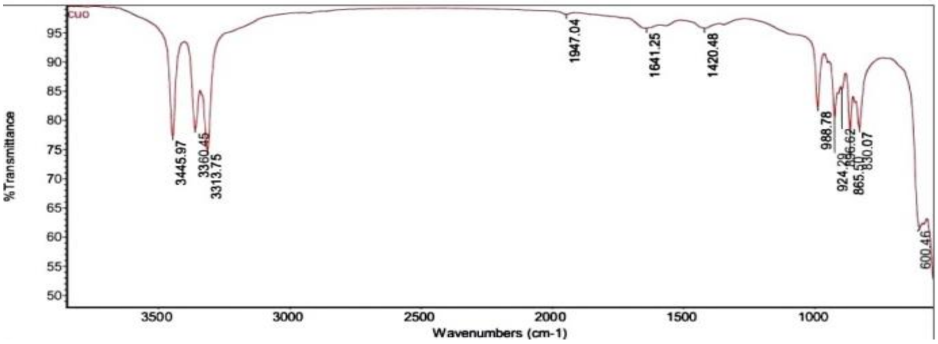

**Figure 1** FTIR spectra of CuO nanoparticles.

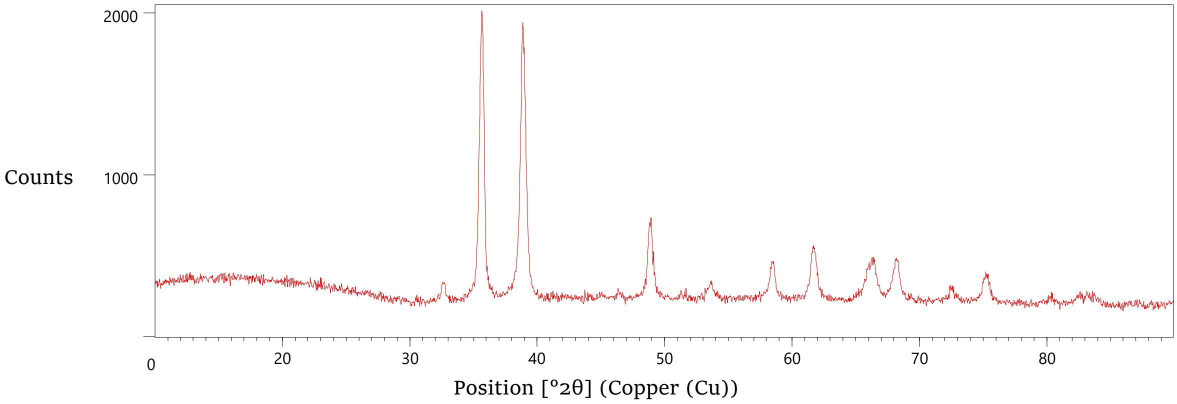

**Figure 2** X-Ray Diffraction of CuO nanoparticles.

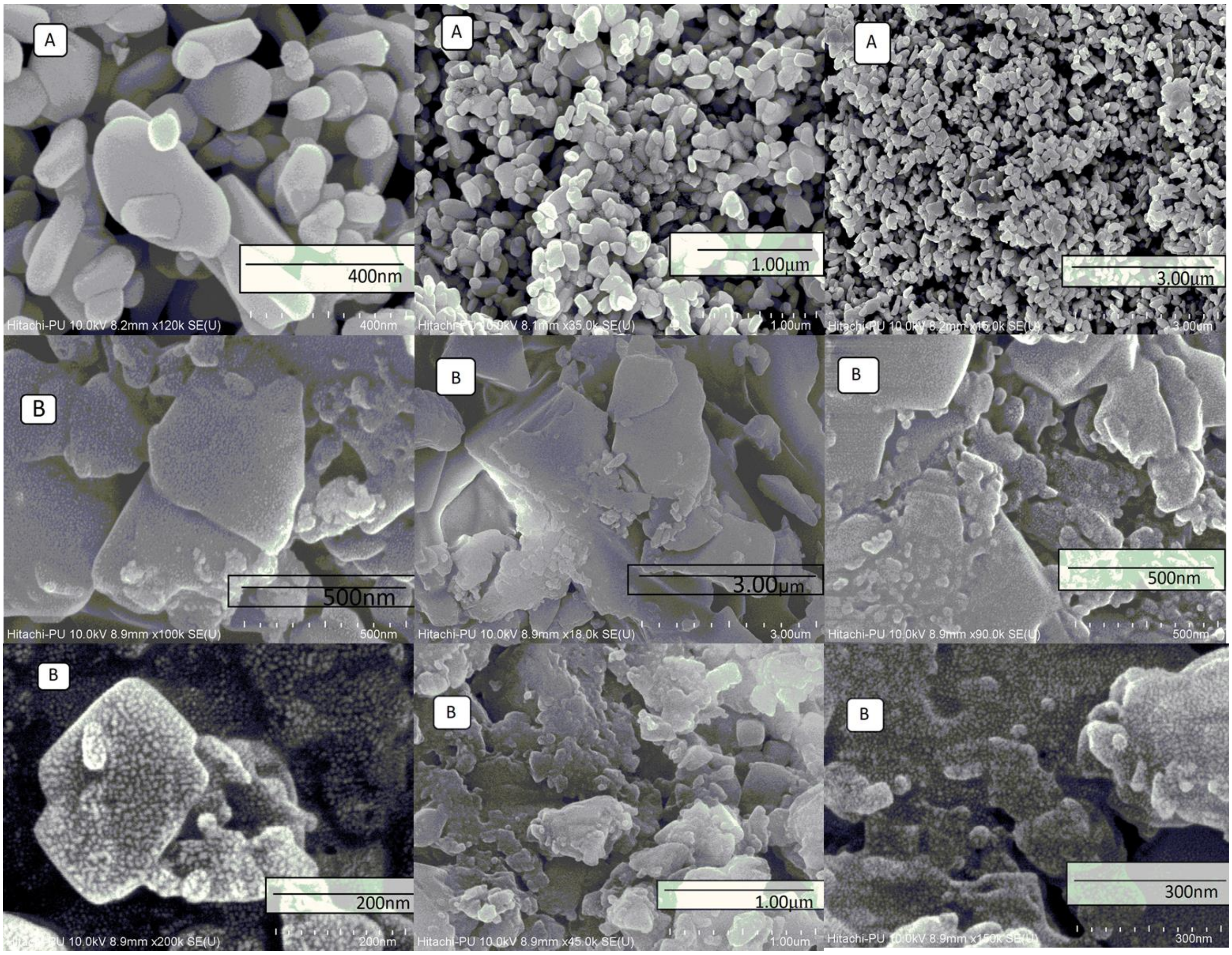

**Figure 3** FESEM images of CuO nanoparticles before (a) and after recycling (b).

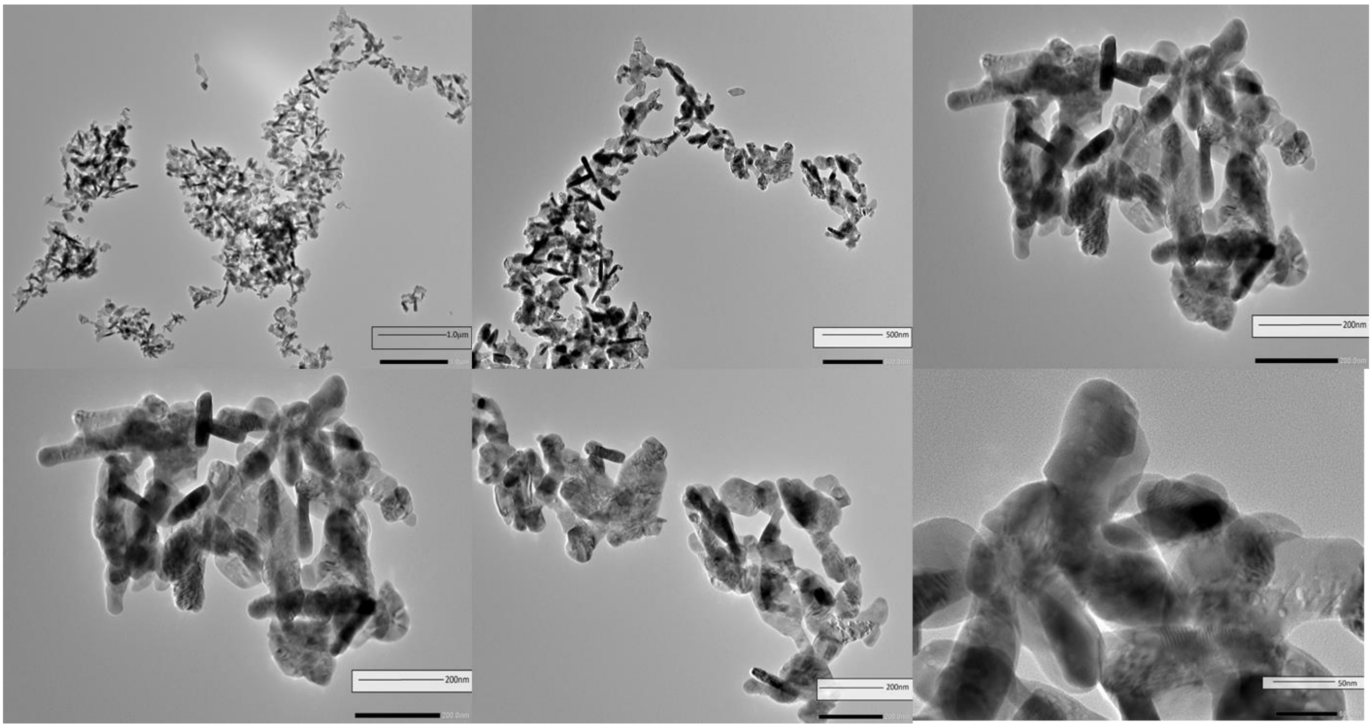

**Figure 4** HRTEM images of CuO nanoparticles.

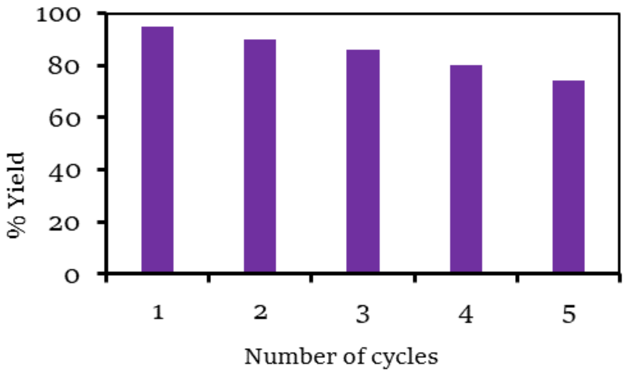

**Figure 5** Recyclability of CuO nano-catalyst.

This may be due to generation of less heat during friction for the cyclization to take place. This method is robust and energy-efficient for the synthesis of substituted methylene bis cyclohexenone derivatives. In the near future, we will try to carry out this reaction by using non-conventional energy source to obtain xanthenedione derivatives in the presence of different heterogeneous catalysts.

## 5. Conclusions

We have developed an eco-friendly approach for the synthesis of 2, 2'-arylmethylene bis (3-hydroxy-5,5-dimethyl-2-cyclohexene-1-one)derivatives under solvent-free conditions by using heterogeneous CuO nanocatalyst. This method provides several advantages in terms of safety, non-toxicity, high product yield, short reaction time, eco-friendliness, energy efficiency and easy separation of catalyst. There is no usage of costly reagents and chemicals. Additionally, the catalyst can be recycled and reused for five successive runs without any significant loss in its catalytic activity.

## • Supplementary materials

This manuscript contains supplementary material, which is available on the corresponding online page.

## • Conflict of interest

The authors declare no conflict of interest.

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