



Green Synthesis of Arylmethylene[Bis(5,5-Dimethyl-3-Hydroxy-2-Cyclohexene-1-Ones)] from 5,5-Dimethylcyclohexane-1,3-Dione And Arylaldehydes in Aqueous Medium in Presence of Benzyltriethylammoniumchloride (Tebac)

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ABSTRACT

A simple and ecofriendly method has been developed for the synthesis of arylmethylene[bis(5,5-dimethyl-3-hydroxy-2-cyclohexene-1-ones)], from 5,5-Dimethylcyclohexane-1,3-dione and aromatic aldehydes using benzyltriethylammoniumchloride (TEBAC) as a catalyst in an aqueous medium at room temperature. The products were obtained in good to excellent yields.

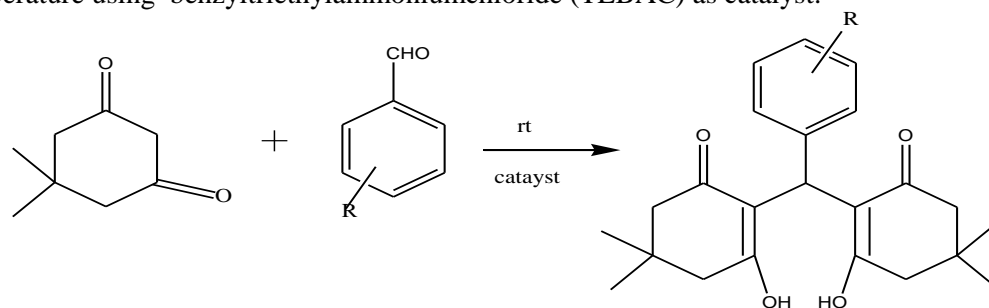
Keywords: Organic synthesis, 5,5-Dimethylcyclohexane-1,3-dione, Arylmethylene[bis(5,5-dimethyl-3-hydroxy-2-cyclohexene-1-ones)], TEBAC.

INTRODUCTION

Now a days, the main goal of researchers, both academic and industrial is to develop environmentally benign synthetic procedures in organic synthesis. C-C bond formation via condensation of active methylene containing compounds with aromatic aldehydes is a reaction of great significance in organic synthesis. Further, there is a great demand these days on carrying out organic synthesis under environmentally benign reaction conditions and that is why great emphasis is being laid on doing away, whenever possible, with the use of volatile and toxic organic solvents[1-3]. The use of environmentally benign solvents represents a very useful and powerful green chemistry technological procedure. In fact, it would be much better, if feasible, to switch from organic solvents to water as a reaction medium in organic reactions[4-7]. The choice of aqueous medium for carrying out organic reactions assumes great significance as water is a non-flammable, inexpensive and readily available green solvent. Further, the use of aqueous medium is advantageous in organic reactions due to its high polarity and the consequent immiscibility with organic solvents. Very few Knoevenagel condensations using water have been reported[8,9]. However, most of them involve harsh reaction conditions, high temperature, long reaction times tedious work ups, use of harmful organic solvents. Tetraketones are important structural precursors for synthesis of many natural products and organic compounds such as acridiediones, xanthenedione and thiaxanthenes derivatives which are reported to show antioxidant properties, lipoxygenase inhibition activity and also act as potential remedial source for inflammation and asthma[10].

Many of the reported methods for the formation of tetraketones have employed various catalysts such as $\text{In}(\text{OTf})_3$, $\text{Yb}(\text{OTf})_3\text{-SiO}_2$, L-hystidine in ionic liquid, proline[11] etc. Many of these involve traditional

thermal heating or microwave irradiation and but they suffer from many limitations. To overcome these disadvantages, we report herein a very simple, economic and green method for synthesis of arylmethylene[bis(5,5-dimethyl-3-hydroxy-2-cyclohexene-1-ones)] tetraketones in an aqueous medium at room temperature using benzyltriethylammoniumchloride (TEBAC) as catalyst.



Scheme-1

MATERIALS AND METHODS

Melting points were measured on a Perfit melting point apparatus and are uncorrected. $^1\text{H-NMR}$ and $^{13}\text{C-NMR}$ spectra were recorded on a Bruker Avance-400 MHz spectrometer in CDCl_3 as solvent and with TMS as internal standard. Chemicals were purchased from CDH and Fluka. Confirmation of product was done by comparing with authentic samples.

General procedure for synthesis of 2, 2'-(arylmethylene)bis(3-hydroxy-5,5-dimethyl-2-cyclohexene-1-one) : Mixture of 5,5-Dimethylcyclohexane-1,3-dione (2mmol), p-chlorobenzaldehyde (1 mmol) and TEBAC (100 mg) in water (5 ml) was taken in a 10 mL Borosil beaker and stirred on a magnetic stirrer for 45 minutes. The reaction was monitored with the help of TLC. The white color product was isolated by filtration, washed with water and dried. The product was pure enough and recrystallised with pure ethanol and obtained in 92% yield.

Spectroscopic data of the products

2,2'-(4-chlorophenylmethylene)bis(3-hydroxy-5,5-dimethyl-2-cyclohexene-1-one) (3a) : Mp: 139-141 $^\circ\text{C}$. $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 1.06 (s, 6H, 2 x CH_3), 1.58 (s, 6H, 2 x CH_3), 2.30–2.50 (m, 8H, 4 x CH_2), 5.48 (s, 1H, CH), 7.00 (d, $J = 8.4$ Hz, 2H, Ar), 7.20 (d, $J = 8.4$ Hz, 2H, Ar), 11.90 (s, 1H, OH).

2,2'-(2,4-dichlorophenylmethylene)bis(3-hydroxy-5,5-dimethyl-2-cyclohexene-1-one) (3b) : Mp: 169-171 $^\circ\text{C}$. $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 0.89 (s, 6H, 2 x CH_3), 1.70 (s, 6H, 2 x CH_3), 2.02–2.31 (m, 8H, 4 x CH_2), 5.65 (s, 1H, CH), 4.33 (s, 1H, Ar), 6.61 (d, $J = 8.4$ Hz, 2H, Ar), 7.09 (d, $J = 8.4$ Hz, 2H, Ar), 11.80 (s, 1H, OH).

2,2'-(4-methylphenylmethylene)bis(3-hydroxy-5,5-dimethyl-2-cyclohexene-1-one) (3c): Mp: 128-130 $^\circ\text{C}$. $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 1.09 (s, 6H, 2 x CH_3), 1.25 (s, 6H, 2 x CH_3), 2.29 (s, 3H, CH_3), 2.32–2.47 (m, 8H, 4 x CH_2), 5.49 (s, 1H, CH), 6.98 (d, $J = 8.0$ Hz, 2H, Ar), 7.26 (d, $J = 8.0$ Hz, 2H, Ar), 11.91 (s, 1H, OH).

2,2'-(4-methoxyphenylmethylene)bis(3-hydroxy-5,5-dimethyl-2-cyclohexene-1-one) (3d): Mp: 146-148 $^\circ\text{C}$. $^1\text{H NMR}$ (400 MHz, CDCl_3): δ 1.09 (s, 6H, 2 x CH_3), 1.22 (s, 6H, 2 x CH_3), 2.28–2.47 (m, 8H, 4 x CH_2), 3.77 (s, 3H, OCH_3), 5.48 (s, 1H, CH), 6.82 (d, $J = 8.8$ Hz, 2H, Ar), 6.79 (d, $J = 8.0$ Hz, 2H, Ar), 11.55, 11.92 (s, 1H, OH).

2,2'-(4-bromophenylmethylene)bis(3-hydroxy-5,5-dimethyl-2-cyclohexene-1-one) (3e): Mp: 161-163 °C. ¹H NMR (400 MHz, CDCl₃): δ 1.09 (s, 6H, 2 x CH₃), 1.21 (s, 6H, 2 x CH₃), 2.28–2.48 (m, 8H, 4 x CH₂), 5.44 (s, 1H, CH), 6.38 (d, *J* = 10.4 Hz, 2H, Ar), 7.94 (d, *J* = 8.8 Hz, 2H, Ar), 11.88 (s, 1H, OH).

2,2'-(4-nitrophenylmethylene)bis(3-hydroxy-5,5-dimethyl-2-cyclohexene-1-one) (3f): Mp: 177-179 °C. ¹H NMR (400 MHz, CDCl₃): δ 1.11 (s, 6H, 2 x CH₃), 1.23 (s, 6H, 2 x CH₃), 2.31–2.51 (m, 8H, 4 x CH₂), 5.54 (s, 1H, CH), 7.24-8.41 (m, 4H, Ar), 11.81 (s, 1H, OH). White solid; m.p. 177-179. IR(KBr): 2969, 2958, 1594, 1513, 1468, 1451, 1375, 1345, 1252, 1154, 1044 and 852 cm⁻¹.

2,2'-(3-nitrophenylmethylene)bis(3-hydroxy-5,5-dimethyl-2-cyclohexene-1-one) (3g): Mp: 183-185 °C. ¹H NMR (400 MHz, CDCl₃): δ 1.05 (s, 6H, 2 x CH₃), 1.20 (s, 6H, 2 x CH₃), 2.24–2.45 (m, 8H, 4 x CH₂), 5.47 (s, 1H, CH), 7.32–7.98 (m, 4H, Ar), 11.79 (s, 1H, OH).

2,2'-(2-nitrophenylmethylene)bis(3-hydroxy-5,5-dimethyl-2-cyclohexene-1-one) (3h): Mp: 189-191 °C. ¹H NMR (400 MHz, CDCl₃): δ 1.01 (s, 6H, 2 x CH₃), 1.15 (s, 6H, 2 x CH₃), 2.17–2.47 (m, 8H, 4 x CH₂), 6.03 (s, 1H, CH), 7.23–7.55 (m, 4H, Ar), 11.58 (s, 1H, OH).

2,2'-(4-hydroxy-3-methoxyphenylmethylene)bis(3-hydroxy-5,5-dimethyl-2-cyclohexene-1-one) (3i): Mp: 193-195 °C. ¹H NMR (400 MHz, CDCl₃): δ 1.03 (s, 6H, 2 x CH₃), 1.16 (s, 6H, 2 x CH₃), 2.22–2.39 (m, 8H, 4 x CH₂), 3.69 (s, 3H, OCH₃), 5.42 (s, 1H, CH), 6.49–6.74 (m, 3H, Ar), 11.90 (s, 1H, OH).

2,2'-(2-hydroxyphenylmethylene)bis(3-hydroxy-5,5-dimethyl-2-cyclohexene-1-one) (3j): Mp: 187-189 °C. ¹H NMR (400 MHz, CDCl₃): δ 1.91 (s, 6H, 2 x CH₃), 2.01 (s, 6H, 2 x CH₃), 2.28–2.61 (m, 8H, 4 x CH₂), 4.67 (s, 1H, CH), 7.17 (d, *J* = 8 Hz, 2H, Ar), 6.84 (d, *J* = 8.4 Hz, 2H, Ar), 10.48 (s, 1H, OH).

2,2'-(3,4-dimethoxyphenylmethylene)bis(3-hydroxy-5,5-dimethyl-2-cyclohexene-1-one) (3k): Mp: 178-180 °C. ¹H NMR (400 MHz, CDCl₃): δ 1.22 (s, 12H, 4 x CH₃), 2.55 (s, 8H, 4 x CH₂), 3.64-3.87 (6H, 2 x OCH₃), 5.70 (s, 1H, CH), 6.69–7.51 (m, 3H, Ar), 9.81.

RESULTS AND DISCUSSION

The present study started with the reaction between 5,5-dimethyl cyclohexane-1,3-dione and p-chloro-benzaldehyde (molar ratio 2:1). Mixture of the reactants with TEBAC as a catalyst in aqueous medium was stirred on a magnetic stirrer at room temperature, and progress of the reaction monitored with the help of TLC. The target compound (3a) was obtained in 92 % yield after 25 min.

Replacing p-chloro-benzaldehyde (2a) with a variety of other aromatic aldehydes containing electron-donating and electron attracting groups, viz., 2,4-dichlorobenzaldehyde (2b), 4-methylbenzaldehyde (2c), 4-methoxybenzaldehyde (2d), 4-bromobenzaldehyde (2e), 3-nitrobenzaldehyde (2f), 4-nitrobenzaldehyde (2g), 2-nitrobenzaldehyde (2h), vanillin (2i), salicylaldehyde (2j), 2,4-dimethoxybenzaldehyde (2k), 3,4-dimethoxybenzaldehyde (2l), gave corresponding products as shown in table 1. As can be noticed from (Table-1) the products (3a-1) were obtained in good yield regardless of various electron donating and releasing groups present in the aromatic aldehyde.

| Entry | RCHO (2) | Product (3) | Time (min) | Yield (%) |
|-------|----------|-------------|------------|-----------|
| | | | | 992 |

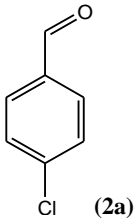
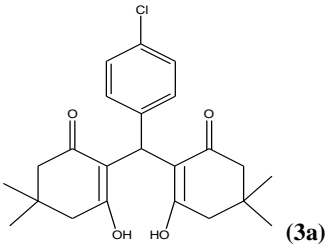
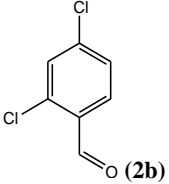
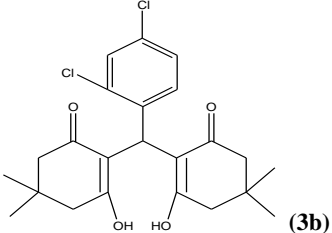
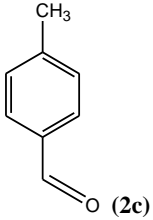
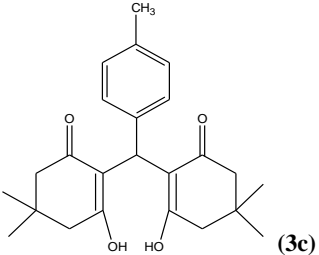
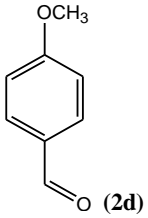
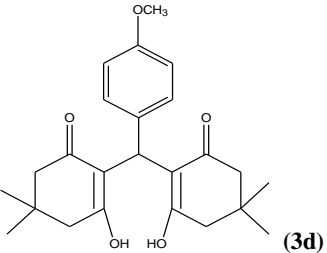
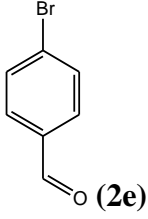
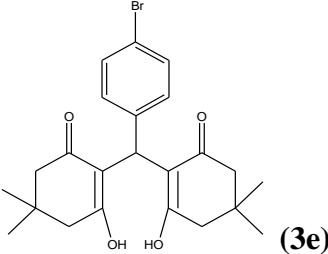
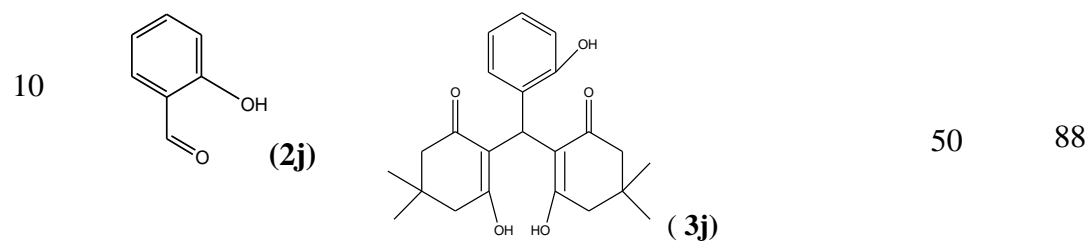
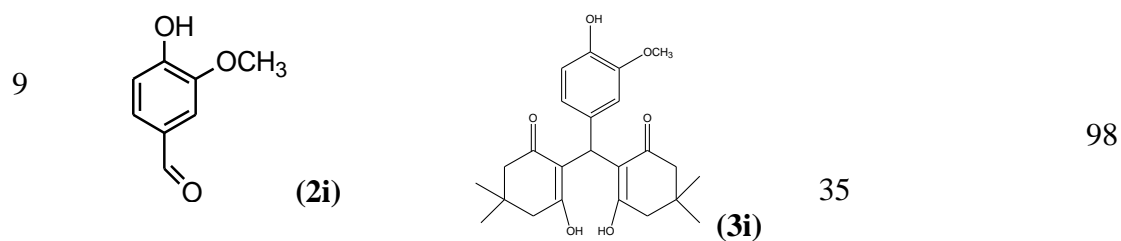
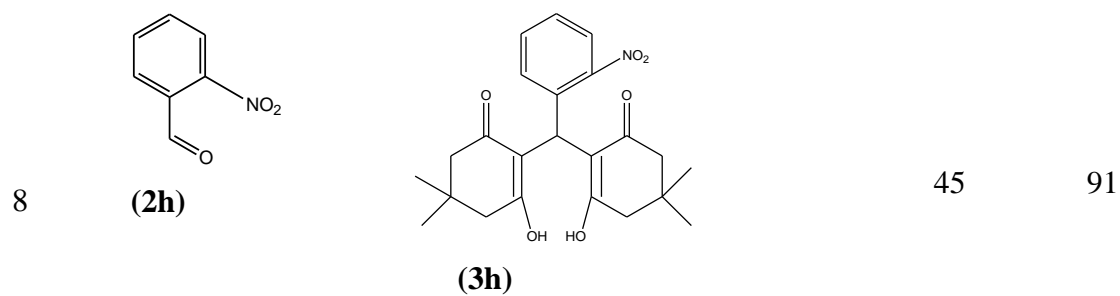
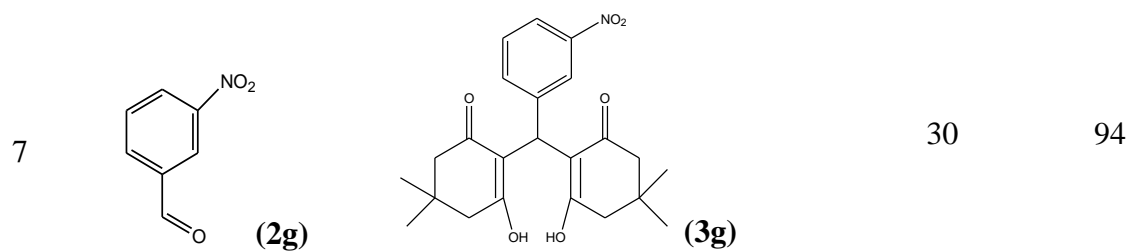
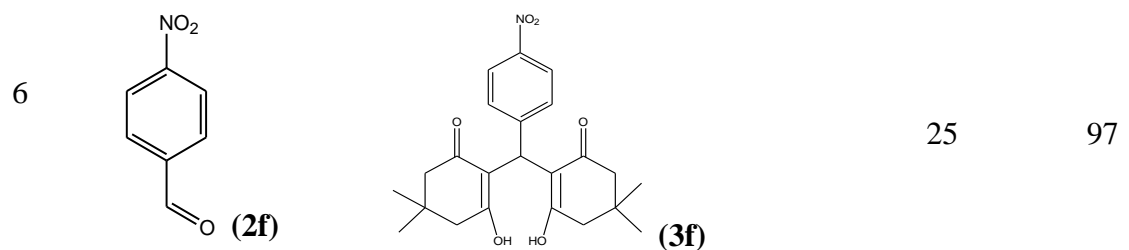
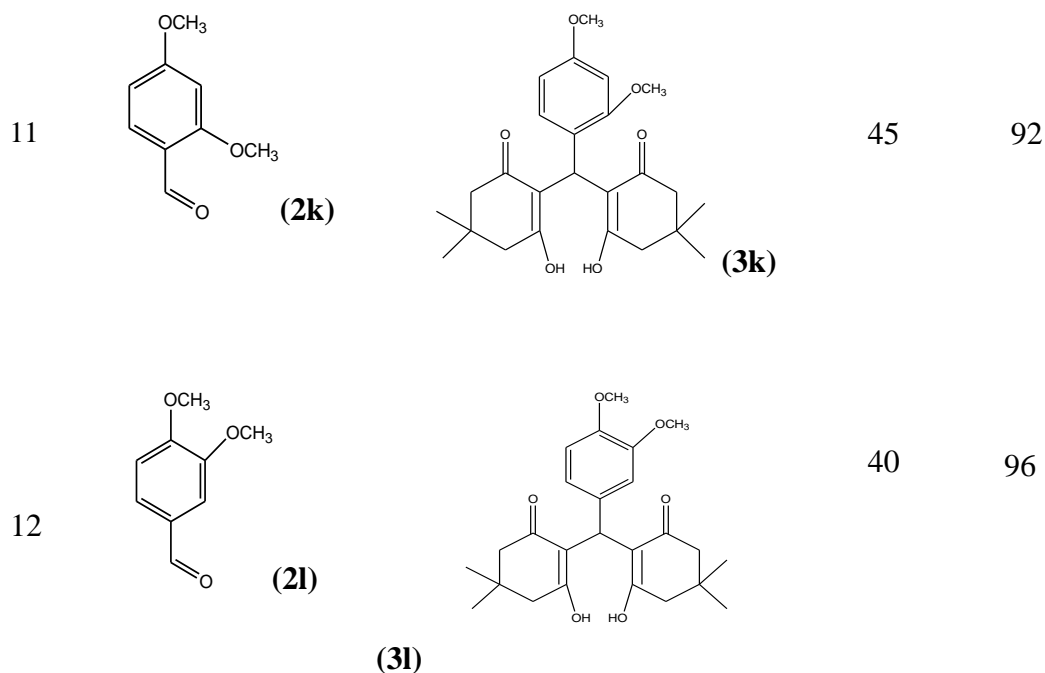
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|---|--|--|----|----|
| 1 |  (2a) |  (3a) | 25 | 92 |
| 2 |  (2b) |  (3b) | 30 | 98 |
| 3 |  (2c) |  (3c) | 40 | 87 |
| 4 |  (2d) |  (3d) | 45 | 89 |

Table 1: Synthesis of arylmethylene[bis(3-hydroxy-2-cyclohexene-1-ones)] via condensation of 5,5-Dimethylcyclohexane-1,3-dione and arylaldehydes in presence of TEBA

| | | | | |
|---|--|--|----|----|
| 5 |  (2e) |  (3e) | 20 | 94 |
|---|--|--|----|----|





APPLICATIONS

The compounds synthesized are important structural precursors for synthesis of many natural products and organic compounds such as acridiediones, xanthenedione and thiaxanthenes derivatives which are reported to show antioxidant properties, lipoxygenase inhibition activity and also act as potential remedial source for inflammation and asthma[10] .

CONCLUSIONS

To conclude, a simple and ecofriendly method has been developed for the synthesis of arylmethylene[bis(5,5-dimethyl-3-hydroxy-2-cyclohexene-1-ones)], from 5,5-Dimethylcyclohexane-1,3-dione and aromatic aldehydes using alanine as a catalyst in an aqueous medium at room temperature.

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REFERENCES

- [1] K. Tanaka, F. Toda, *Chem. Rev.* **2000**, 100, 1025.
- [2] A. Loupy, *Top Cur. Chem.*, **1999**, 206, 153.
- [3] P. Anastas, Warner, *J.Green Chemistry: Theory and practice*, Oxford university press, New York, **1998**.
- [4] (a) P. A. Grieco, *Organic Synthesis in Water*, Thomson Science, London, **1998**, 1–278. (b) C. J. Li, *Chem. Rev.* **2005**, 105, 3095–3165.

- [5] C. J. Li, Chan, T-H. *Reactions in Aqueous Media*, John Wiley & Sons: New York, **1997**.
- [6] A. Lubineau, Auge, J. *Top Cur. Chem.*, **1999**, 206, 1.
- [7] G. Baccolini, C. Boga, Delpivo and G. Micheletti, *Tetrahedron Lett.* **2011**, 52, 1713.
- [8] Firouzeh, N. Hossein, Kiani; *Chin. J. Chem.* **2011**, 29, 2407-2410.
- [9] Adam. McCluskey, Philip J. Robinson, Tim Hill, Janet L. Scott and J. Kate Edwards, *J. Tetrahedron let.*, **2002**, 43, 3117–3120.
- [10] T. Josephrajan & V. T. Ramakrishnan, *Can. J. Chem*, **2007**, 85, 572.
- [11] D. B. Ramachary, M. Kishor, *J. org. Chem*, **2007**, 72, 5056.