

Reaction of Aldehydes and 5,5-Dimethyl-1,3-cyclohexanedione in the Presence of Surfactants in Water

XIN-YING QIN, TONG-SHOU JIN*, JIAN-SHE ZHANG and TONG-SHUANG LI
College of Chemistry and Environmental Science, Hebei University, Baoding 071002, P.R. China
E-mail: jintongshou@yahoo.com.cn

An efficient and convenient approach to the synthesis of the two different products from aldehydes and 5,5-dimethyl-1,3-cyclohexanedione using two kinds of surfactant catalysts sodium dodecyl sulfate (SDS) and dodecanesulfonic acid (DSA) (10 mol %) is described. This method provides several advantages such as environment friendliness, high yields and simple work-up procedure. In addition, water was chosen as a green solvent.

Key Words: 5,5-Dimethyl-1,3-cyclohexanedione, Aromatic aldehyde, Surfactant, Clean synthesis.

INTRODUCTION

Most chemical reactions of organic substances conducted in the laboratory as well as in industry need organic solvents as reaction media, although water is safe, benign, environmentally friendly and cheap compared with organic solvents. Since 1980, Breslow had discovered that Diels-Alder reaction performed in water can be subjected to huge accelerations¹. The observation led to increased interest from synthetic organic chemists in organic reactions in water. Soon it was discovered that other organic reactions, like the Claisen rearrangement², the aldol condensation³, Diels-Alder reaction⁴, benzoin condensation⁵, Mannich reaction⁶ and Michael reaction⁷ exhibit rate enhancements in water. To date, many more organic transformations have been carried out in water⁸.

Although environmental consciousness imposes the use of water as a solvent in both industrial and academic chemists, but organic solvents are still used instead of water for most of the organic substances which are insoluble in water and many reactive substrates, reagents and catalysts are decomposed or deactivated by water. The surfactant used in water can make organic materials solubility or form colloidal dispersions⁹ and is stable in water, so it can solve the two drawbacks of the reactions in water. It has been used in a number of organic reactions as a good catalyst¹⁰. It was reported in literature that 2,2'-alkylmethylene bis(3-hydroxy-5,5-dimethyl-2-cyclohexene-1-one) and 1,8-dioxo-octahydroanthene and their derivatives have been synthesized in many methods¹¹. However, the use of sodium dodecyl sulfate (SDS) and dodecanesulfonic acid (DSA) as the catalysts in aqueous media for the synthesis of the 2,2'-alkylmethylene bis(3-hydroxy-5,5-dimethyl-2-cyclohexene-

1-one) and 1,8-dioxo-octahydroxanthene and their derivatives has not been reported. In this manuscript, we wish to report a general and highly efficient route for the synthesis of (**3**) 2,2'-alkylmethylene *bis*(3-hydroxy-5,5-di-methyl-2-cyclohexene-1-one) and 1,8-dioxo-octahydroxanthene (**4**) and their derivatives using an inexpensive and commercially available SDS and SDA as catalysts. This is an efficient synthesis in aqueous media, not only preserves the simplicity but also consistently gives the corresponding products in good yields.

EXPERIMENTAL

Liquid aldehydes were purified by distillation before use. IR spectra were recorded on a Bio-rad FIS-40 spectrometer (KBr). ^1H NMR spectra were measured on an AVAVCE-400 (400 MHz) spectrometer using TMS as internal standard and CDCl_3 as solvent. Elemental analysis measured on a HERAEUS (CHN, Rapid) analyzer.

General procedure for the preparation of 3 and 4: A mixture of an aromatic aldehyde (2.0 mmol), 5,5-dimethyl-1,3-cyclohexanedione (2.0 mmol) and SDS or DSA (10 mol %) in water (20 mL) was stirred at refluxing water for 6 h. The progress of the reaction was monitored by thin layer chromatograph. After completion of the reactions, the mixture was cooled to room temperature and solid was filtered off and washed with H_2O (40 mL) and the crude products were got. The crude products were purified by recrystallization from ethanol (95 %). Data of some compounds are shown below:

3b: IR (KBr, ν_{max} , cm^{-1}): 3425, 3060, 2954, 2870, 2633, 1598, 1468, 1419, 1375, 1248, 1149, 1066, 974, 870, 789; ^1H NMR: δ 1.12 (s, 6H, $2 \times \text{CH}_3$), 1.24 (s, 6H, $2 \times \text{CH}_3$), 2.30-2.51 (m, 8H, $4 \times \text{CH}_2$), 5.49 (s, 1H, CH), 6.96-7.28 (m, 4H, Ar-H), 11.55 (br, s, 1H, OH), 11.94 (br, s, 1H, OH); Anal. calcd. for $\text{C}_{23}\text{H}_{27}\text{O}_4\text{Cl}$: C, 68.56; H, 6.25. Found: C, 68.78; H, 6.09 %.

3c: IR (KBr, ν_{max} , cm^{-1}): 3424, 3058, 2954, 2868, 2634, 1596, 1468, 1418, 1375, 1307, 1248, 1151, 1066, 974, 890, 870, 789; ^1H NMR: δ 1.12 (s, 6H, $2 \times \text{CH}_3$), 1.25 (s, 6H, $2 \times \text{CH}_3$), 2.31-2.51 (m, 8H, $4 \times \text{CH}_2$), 5.50 (s, 1H, CH), 6.98-7.28 (m, 4H, Ar-H), 11.57 (br, s, 1H, OH), 11.91 (br, s, 1H, OH); Anal. calcd. for $\text{C}_{23}\text{H}_{27}\text{O}_4\text{Cl}$: C, 68.56; H, 6.25. Found: C, 68.78; H, 6.12 %.

3e: IR (KBr, ν_{max} , cm^{-1}): 3425, 3060, 2950, 2865, 2630, 1601, 1470, 1417, 1379, 1250, 1152, 1135, 975, 889, 790; ^1H NMR: δ 1.13 (s, 6H, $2 \times \text{CH}_3$), 1.25 (s, 6H, $2 \times \text{CH}_3$), 2.30-2.52 (m, 8H, $4 \times \text{CH}_2$), 5.51 (s, 1H, CH), 6.98-7.23 (m, 3H, Ar-H), 11.57 (br, s, 1H, OH), 11.93 (br, s, 1H, OH); Anal. calcd. for $\text{C}_{23}\text{H}_{26}\text{O}_4\text{Cl}_2$: C, 63.16; H, 5.99. Found: C, 63.01; H, 5.86 %.

3h: IR (KBr, ν_{max} , cm^{-1}): 3424, 3061, 2960, 2870, 2628, 1605, 1471, 1414, 1380, 1252, 1170, 1140, 1000, 890, 840, 790, 750, 715; ^1H NMR: δ 1.12 (s, 6H, $2 \times \text{CH}_3$), 1.24 (s, 6H, $2 \times \text{CH}_3$), 2.31-2.51 (m, 8H, $4 \times \text{CH}_2$), 5.47 (s, 1H, CH), 2.78 (s, 3H, CH_3Ar), 6.92-7.21 (m, 3H, ArH), 11.57 (br, s, 1H, OH), 11.91 (br, s, 1H, OH); Anal. calcd. for $\text{C}_{24}\text{H}_{30}\text{O}_4$: C, 73.36; H, 7.91. Found: C, 73.58; H, 7.68 %.

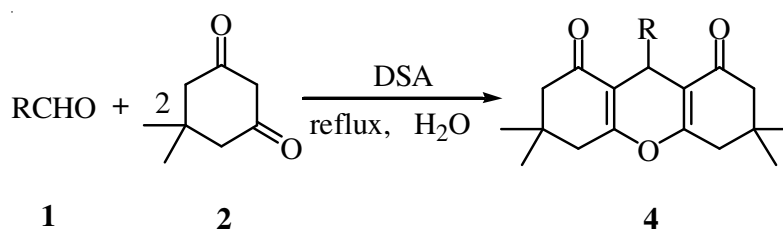
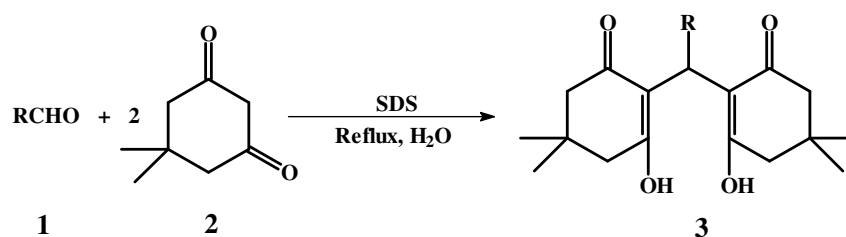
3p: IR (KBr, ν_{\max} , cm^{-1}): 3422, 3060, 2955, 2868, 1594, 1466, 1414, 1374, 1307, 1248, 1151, 1123, 1067, 994, 974, 866, 787, 749; $^1\text{H NMR}$: δ 1.12 (s, 6H, $2 \times \text{CH}_3$), 1.25 (s, 6H, $2 \times \text{CH}_3$), 2.31-2.51 (m, 8H, $4 \times \text{CH}_2$), 5.51 (s, 1H, CH), 7.03-7.33 (m, 4H, ArH), 11.67 (br, s, 1H, OH), 11.92 (br, s, 1H, OH); Anal. calcd. for $\text{C}_{23}\text{H}_{27}\text{BrO}_4$: C, 61.75; H, 6.08. Found: C, 61.98; H, 5.92 %.

3s: IR (KBr, ν_{\max} , cm^{-1}): 3365, 3025, 2980, 2850, 1665, 1587, 1548, 1505, 1375, 1310, 1240, 1200, 1196, 850, 843, 756; $^1\text{H NMR}$: δ 1.12 (s, 12H, $4 \times \text{CH}_3$), 1.14 (d, 3H, $J = 6.4$ Hz, CH_3), 2.29-2.37 (m, 8H, $4 \times \text{CH}_2$), 3.67 (q, 1H, $J = 6.4$ Hz, CH), 11.65 (br, s, 1H, OH), 11.95 (br, s, 1H, OH); Anal. calcd. for $\text{C}_{18}\text{H}_{26}\text{O}_4$: C, 70.56; H, 8.55. Found: C, 70.78; H, 8.32 %.

4o: IR (KBr, ν_{\max} , cm^{-1}): 3035, 2980, 1710, 1670, 1600, 1580, 1500, 1454, 1400, 1375, 1310, 1264, 1040, 970, 740, 700; $^1\text{H NMR}$: δ 1.12 (s, 12H, $4 \times \text{CH}_3$), 2.30 (s, 4H, $4 \times \text{CH}_2$), 2.44 (s, 4H, $4 \times \text{CH}_2$), 4.46 (s, 1H, H-9), 6.26-6.35 (m, 2H, $-\text{CH}=\text{CH}-$), 7.16-7.28 (m, 5H, ArH); Anal. calcd. for $\text{C}_{25}\text{H}_{28}\text{O}_3$: C, 79.79; H, 7.45. Found: C, 79.93; H, 7.34 %.

RESULTS AND DISCUSSION

It was found from **Schemes I** and **II** that different products were got using different catalysts in the reaction. The reaction in presence of SDS alone afforded the product **3**, but addition of a catalytic amount of HCl will result in the product **4**. The result suggests that the combination of a bronsted acid and an anionic surfactant leads to an effect catalyst for synthesis of **4**. Then we tested dodecanesulfonic acid (DSA), which was expected to behave both as a bronsted acid and a surfactant. Indeed DSA (10 mol %) was found to be a good catalyst for producing **4**. From the fact it was suggest that the acidity is essential for producing **4**.



To study the generality of this process, several examples illustrating this method for the synthesis **3** and **4** were studied. The results are summarized in Tables 1 and 2. The effect of electron and the nature of substituents on the aromatic ring did not show strongly obvious effects in terms of yields under this reaction conditions. The reaction proceeded smoothly under refluxing water to give the corresponding products **3** and **4** in good to excellent yields.

TABLE-1
SYNTHESES OF **3** CATALYZED BY SDS IN AQUEOUS MEDIA

Entry	R	Product	Time (h)	Yield (%)	m.p. (°C)	
					Found	Reported ¹¹
1	C ₆ H ₅ 1a	3a	6	86	192-94	194-95
2	4-ClC ₆ H ₄ 1b	3b	6	94	145-47	–
3	3-ClC ₆ H ₄ 1c	3c	6	93	188-90	–
4	2-ClC ₆ H ₄ 1d	3d	6	93	203-04	205
5	2,4-Cl ₂ C ₆ H ₃ 1e	3e	6	90	203-05	–
6	4-O ₂ NC ₆ H ₄ 1f	3f	6	94	188-90	188-89
7	3-O ₂ NC ₆ H ₄ 1g	3g	6	95	198-00	197-98
8	4-CH ₃ C ₆ H ₄ 1h	3h	6	88	141-43	–
9	4-CH ₃ OC ₆ H ₄ 1i	3i	6	87	143-45	142-43
10	4-(CH ₃) ₂ NC ₆ H ₄ 1j	3j	6	86	195-97	194.5-95.5
11	4-HOC ₆ H ₄ 1k	3k	6	87	187-89	188-90
12	2-HOC ₆ H ₄ 1l	3l	6	91	205-07	205-06
13	3,4-(OCH ₂ O)C ₆ H ₃ 1m	3m	6	89	174-76	175.5-77
14	C ₆ H ₄ CH=CH 1n	3n	6	91	215-16	215-17
15	4-HO-3-CH ₃ OC ₆ H ₃ 1o	3o	6	86	195-97	195.5-96.5
16	3-BrC ₆ H ₄ 1p	3p	6	89	203-04	–
17	C ₆ H ₅ CH ₂ 1q	3q	6	65	165-67	164-65
18	H 1r	3r	6	86	190-92	191-91.5
19	H ₃ C 1s	3s	6	39	182-84	–
20	HOOC 1t	3t	6	38	240-42	239
21	<i>i</i> -C ₃ H ₇ 1u	3u	6	46	155-57	153-54.5
22	OHC 1v	3v	6	57	230-32	228

The reaction of aromatic aldehyde or aliphatic aldehyde and 5,5-dimethyl-1,3-cyclohexanedione gave different experimental results catalyzed by SDS. From Table-1, we get the information that the aromatic aldehyde gives better results than that of aliphatic aldehyde. For instance, 4-chlorobenzaldehyde and 4-nitrobenzaldehyde reacted with 5,5-dimethyl-1,3-cyclohexanedione in the refluxing water and gave yields of **3b** (94 %) and **3f** (94 %), respectively. While acetaldehyde and *i*-butyraldehyde were treated with 5,5-dimethyl-1,3-cyclohexanedione under the same condition, it was given the isolated yields of the corresponding compounds **3s** (39 %) and **3u** (46 %). But aliphatic aldehyde can not give the corresponding compounds for the synthesis of **4**. Therefore, it is concluded that aromatic aldehyde exhibits higher reactivity than aliphatic aldehyde.

TABLE-2
 SYNTHESIS OF **4** CATALYZED BY DSA IN AQUEOUS MEDIA

Entry	R	Product	Time (h)	Yield (%)	m.p. (°C)	
					Found	Reported ¹¹
1	C ₆ H ₅ 1a	4a	6	87	202-03	204-05
2	4-ClC ₆ H ₄ 1b	4b	6	93	229-31	230-31
3	3-ClC ₆ H ₄ 1c	4c	6	91	185-86	183-84
4	2-ClC ₆ H ₄ 1d	4d	6	92	224-26	224-26
5	2,4-Cl ₂ C ₆ H ₃ 1e	4e	6	94	252-54	253-54
6	2-NO ₂ C ₆ H ₄ 1f	4f	6	94	247-48	246-48
7	3-NO ₂ C ₆ H ₄ 1g	4g	6	92	170-72	171.5-72.5
8	4-NO ₂ C ₆ H ₄ 1h	4h	6	95	223-25	222
9	4-HOC ₆ H ₄ 1i	4i	6	88	245-47	246
10	4-CH ₃ OC ₆ H ₄ 1j	4j	6	87	242-44	241-43
11	4-Me ₂ NC ₆ H ₄ 1k	4k	6	86	221-23	220-22
12	4-CH ₃ C ₆ H ₄ 1l	4l	6	90	216-18	217-18
13	4-HO-3-CH ₃ OC ₆ H ₃ 1m	4m	6	86	227-29	226-28
14	3,4-OCH ₂ OC ₆ H ₃ 1n	4n	6	87	220-22	218.5-20
15	C ₆ H ₅ CH=CH 1o	4o	6	88	176-78	–

The catalyst plays an important role in the success of the reaction in terms of the rates and the yields. For example, 4-chlorobenzaldehyde reacted with 5,5-dimethyl-1,3-cyclohexanedione in the presence of 1 mol% SDS or DSA to give the product **3b** or **4b** in modest yield (55 or 46 %) in refluxing water after 6 h of reaction time. The catalyst increased to 5, 10 and 15 mol % results in accelerating the reaction yields to 86, 94 and 94 % or 74, 93 and 93 %, respectively. Use of just 10 mol % SDS or DSA in refluxing water is sufficient to push the reaction forward. Higher amounts of the catalyst did not improve the results to a greater extent. The reaction could be carried out in the absence of SDS at equal time (6 h) when the same reaction mixture (**1b** and 5,5-dimethyl-1,3-cyclohexanedione) was subjected to heating in refluxing water. The yield of this run was 26 %. But it cannot give the corresponding products **4b** in the absence of DSA. Under the identical condition, the rate of the reaction was affected by the presence of SDS and the yields of **3b** were 72, 94 and 94 % after different time intervals (3, 6 and 9 h) and if the reaction was in the presence of the catalyst of DSA the yields of **4b** were 68, 93 and 93 %, respectively after the same time intervals. Thus, 10 mol % SDS or DSA was chosen as a quantitative catalyst for these reactions and 6 h was chosen as the reaction time.

In conclusion, we have described a general and highly efficient procedure for the preparation of 2,2'-alkylmethylene bis(3-hydroxy-5,5-dimethyl-2-cyclohexene-1-one) or 1,8-dioxo-octahydroxanthene and their derivatives catalyzed by SDS or DSA in the refluxing water. In addition, it is possible to apply the tenets of green chemistry to the generation of interesting products using aqueous media methods

that are less expensive and less toxic than those with organic solvents. Moreover, the procedure offers several advantages including high yields, operational simplicity, cleaner reactions, minimal environmental impact which makes it a useful and attractive process for the synthesis of these compounds.

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