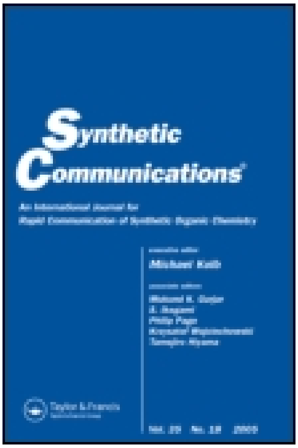


Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry

Publication details, including instructions for authors and subscription information:
http://www.tandfonline.com/loi/lsyc20

Solid-State Condensation Reactions Between Aldehydes and 5,5-Dimethyl-1,3-cyclohexanedion by Grinding at Room Temperature

Tong-Shou Jin [a] , Jian-She Zhang [a] , Ai-Qing Wang [a] & Tong-Shuang Li [a]

[a] Department of Chemistry, College of Chemistry and Environmental Science, Hebei University, Baoding, Hebei Province, China

To cite this article: Tong-Shou Jin, Jian-She Zhang, Ai-Qing Wang & Tong-Shuang Li (2005): Solid-State Condensation Reactions Between Aldehydes and 5,5-Dimethyl-1,3-cyclohexanedione by Grinding at Room Temperature, Synthetic Communications: An International Journal for Rapid Communication of Synthetic Organic Chemistry, 35:17, 2339-2345

To link to this article: http://dx.doi.org/10.1080/00397910500187282

Synthetic Communications®, 35: 2339–2345, 2005
Copyright © Taylor & Francis, Inc.
ISSN 0039-7911 print/1532-2432 online
DOI: 10.1080/00397910500187282

Solid-State Condensation Reactions Between Aldehydes and 5,5-Dimethyl-1,3-cyclohexanedione by Grinding at Room Temperature

Tong-Shou Jin, Jian-She Zhang, Ai-Qing Wang, and Tong-Shuang Li
Department of Chemistry, College of Chemistry and Environmental Science, Hebei University, Baoding, Hebei Province, China

Abstract: An efficient and convenient approach to the synthesis of the two different products from aldehydes and 5,5-dimethyl-1,3-cyclohexanedione in the solid state by grinding is described. This method provides several advantages such as environmental friendliness, high yields, and simple workup procedure.

Keywords: Aldehydes, cyclohexanedione, grinding, solid state, synthesis

INTRODUCTION

The grinding method has increasingly been used in organic synthesis in recent years. Compared with traditional methods, many organic reactions occur more efficiently in the solid state than in solution and in many cases even more selectively, because molecules in the crystals are arranged tightly and regularly.[1] Furthermore, the solid-state reaction has many advantages: little pollution, low cost, and simplicity in progress and handling. A large

Received in Japan February 28, 2005

Address correspondence to Tong-Shou Jin, Department of Chemistry, College of Chemistry and Environmental Science, Hebei University, No. 88 Hezuo Road, Baoding 071002, Hebei Province, China. E-mail: orgsyn@mail.hbu.edu.cn

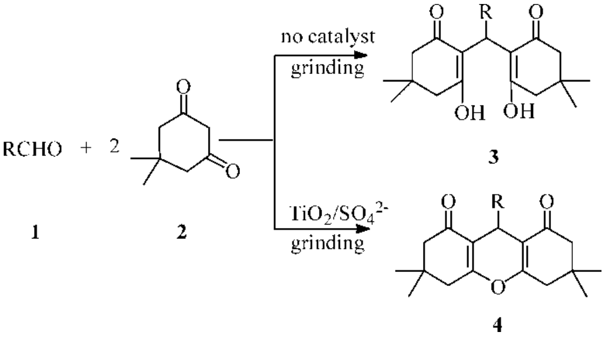
number of organic reactions can be carried out simply and in high yield under mild conditions by this method.[2]

It has been reported that the reaction of aromatic aldehyde and 5,5-dimethyl-1,3-cyclo-hexanedione can obtain 2,2′-arylmethylene bis(3-hydroxy-5,5-dimethyl-2-cyclohexene-1-one) and 1, 8-dioxo-octahydroxanthene and their derivatives in many methods.[3] However, no catalyst or the use of TiO_2/SO_4^{2-} solid superacid as the catalysts in the solid state for the synthesis of the 2,2′-arylmethylene bis(3-hydroxy-5,5-dimethyl-2-cyclohexene-1-one) or 1,8-dioxooctahydroxanthene and their derivatives have not been reported. In this article, we report a general and highly efficient route for the synthesis of these two products and their derivatives with no catalyst or using an inexpensive and commercially available TiO_2/SO_4^{2-} solid superacid as the catalyst. This is an efficient synthesis in solid state, which not only preserves the simplicity but also consistently gives the corresponding products in good to excellent yields (Scheme 1).

A series of examples illustrating this method for the synthesis **3** and **4** were studied. The reaction proceeded smoothly by grinding to give the corresponding products in good to excellent yields. The results are summarized in Table 1 and Table 2.

It was found that different products were obtained using no catalyst or TiO_2/SO_4^{2-} in the reaction (Scheme 1). The reaction in absence of catalyst afforded the product **3** in good yield, but addition of a catalytic amount of TiO_2/SO_4^{2-} resulted in the product **4**. The result showed that the TiO_2/SO_4^{2-} solid superacid had catalytic effect on the synthesis of **4**. From this fact, we suggest that the acid is essential for producing **4**.

The reaction of aromatic aldehyde or aliphatic aldehyde and 5,5-dimethyl-1,3-cyclohexanedione gave different experimental results. Table 1 shows that aromatic aldehyde gives better results than aliphatic aldehyde. For instance, 4-chlorobenzaldehyde and 4-nitrobenzaldehyde reacted with 5,5-dimethyl-1,3-cyclohexanedione in grinding and gave



Scheme 1.

Table 1. Synthesis of **3** with no catalyst in solid state by grinding

Entry	R	Product	Yield[a] (%)	Mp (°C) Found	Mp (°C) Reported[3a]
1	C_6H_5 **1a**	**3a**	86	193–194	194–195
2	4-ClC_6H_4 **1b**	**3b**	90	143–145	141–143[3c]
3	3-ClC_6H_4 **1c**	**3c**	89	188–190	
4	2-ClC_6H_4 **1d**	**3d**	90	203–204	205
5	2,4-$Cl_2C_6H_3$ **1e**	**3e**	85	203–204	
6	4-$O_2NC_6H_4$ **1f**	**3f**	89	190–191	188–190
7	3-$O_2NC_6H_4$ **1g**	**3g**	88	198–199	197–198
8	4-$CH_3C_6H_4$ **1h**	**3h**	89	141–142	
9	4-$CH_3OC_6H_4$ **1i**	**3i**	87	144–145	142–143
10	4-$(CH_3)_2NC_6H_4$ **1j**	**3j**	89	195–196	194.5–195.5
11	4-HOC_6H_4 **1k**	**3k**	90	187–189	188–190
12	2-HOC_6H_4 **1l**	**3l**	86	205–206	205–206
13	3,4-$(OCH_2O)C_6H_3$ **1m**	**3m**	89	176–177	175.5–177
14	$C_6H_5CH{=}CH$ **1n**	**3n**	87	215–216	215–217
15	4-HO-3-$CH_3OC_6H_3$ **1o**	**3o**	86	196–197	195.5–196.5
16	3-BrC_6H_4 **1p**	**3p**	89	203–204	
17	$C_6H_5CH_2$ **1q**	**3q**	65	165–166	164–165
18	H **1r**	**3r**	86	192–193	191–191.5
19	CH_3 **1s**	**3s**	39	182–184	
20	COOH **1t**	**3t**	38	241–242	239
21	i-C_3H_7 **1u**	**3u**	46	153–154	153–154.5
22	CHO **1v**	**3v**	56	232–234	228

[a] Isolated yield.

yields of **3b** (90%) and **3f** (89%) respectively. When acetaldehyde and *i*-butylraldehyde were treated with 5,5-dimethyl-1,3-cyclohexanedione under the same conditions, they gave isolated yields of **3s** (39%) and **3u** (46%) respectively. But, aliphatic aldehyde cannot give the corresponding compounds for the synthesis of **4**. The reason is that instability of aliphatic aldehyde makes the reaction difficult.

The catalyst TiO_2/SO_4^{2-} solid superacid was easily regenerated by filtering the reaction mixture, washing it with hot ethanol, and drying it at 120°C for 2 h. The catalyst could be reused six times for the synthesis of **4b** without significant loss of activity. The results are summarized in Table 3. In addition, it must be pointed out that all of the products were characterized by Mp, IR, ^1H NMR, and elemental analyses.

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 in

Table 2. Synthesis of **4** catalyzed by TiO_2/SO_4^{2-} in solid state by grinding

Entry	Ar	Product	Yield[a] (%)	Mp (°C) Found	Mp (°C) Reported[3a]
1	C_6H_5 **1a**	**4a**	88	204–205	204–205
2	4-ClC_6H_4 **1b**	**4b**	92	229–231	230–231[3d]
3	3-ClC_6H_4 **1c**	**4c**	91	184–186	
4	2-ClC_6H_4 **1d**	**4d**	92	225–226	224–226
5	2,4-$Cl_2C_6H_3$ **1e**	**4e**	89	250–252	253–254[3e]
6	4-$NO_2C_6H_4$ **1f**	**4f**	90	222–223	222
7	3-$NO_2C_6H_4$ **1g**	**4g**	89	170–172	171.5–172.5
8	2-$NO_2C_6H_4$ **1h**	**4h**	90	246–248	246–248[3d]
9	4-HOC_6H_4 **1i**	**4i**	91	246–247	246
10	4-$CH_3OC_6H_4$ **1j**	**4j**	87	242–243	241–243[3d]
11	4-$Me_2NC_6H_4$ **1k**	**4k**	88	221–222	220–222
12	4-$CH_3C_6H_4$ **1l**	**4l**	89	218–219	217–218[3e]
13	4-HO-3-$CH_3OC_6H_3$ **1m**	**4m**	90	227–228	226–228
14	3,4-$(OCH_2O)C_6H_3$ **1n**	**4n**	89	217–218	218.5–220
15	$C_6H_5CH{=}CH$ **1o**	**4o**	89	176–178	175–177[3e]

[a] Isolated yields.

the solid state by grinding. In addition, the reaction in the solid state by grinding methods is less expensive and less toxic than reactions using organic solvents. Moreover, the procedure offers several advantages including high yields, operational simplicity, cleaner reactions, and minimal environmental impact, which make it a useful and attractive process for the synthesis of these compounds.

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

Table 3. Reuse of the catalyst for syntheses of **4b** in solid state by grinding

Entry	Yield (%)
1	92
2	91
3	90
4	88
5	89
6	88

measured on an AVAVCE-400 spectrometer using TMS as internal standard and $CDCl_3$ as solvent. Elemental analysis was measured on a HERAEUS (CHN, Rapid) analyzer.

Preparation of the Catalyst TiO_2/SO_4^{2-} Solid Superacid

The catalyst TiO_2/SO_4^{2-} solid superacid was prepared as follows. $Ti(OH)_4$ was obtained by hydrolyzing $TiCl_4$ with aqueous ammonium hydroxide, washing the precipitates, drying them at 120°C for 4 h, and powdering the precipitates below a 100 mesh. The hydroxide was treated with 2 N H_2SO_4 for 4 h, filtrated, dried, and calcined in furnace at 475°C for 4 h, and finally stored in a desiccator until use.

General Procedure for the Preparation of 3

Aldehyde **1** (2 mmol) and 5,5-dimethyl-1,3-cyclohexanedione **2** (4 mmol) were added to a mortar. The mixture was ground by mortar and pestle at room temperature for 40 min and was kept at room temperature for 48 h. The product was extracted with dichloromethane; the solvent was evaporated under reduced pressure and the crude products were obtained. The crude products **3** were purified by recrystallization from ethanol (95%).

General Procedure for the Preparation of 4

Aromatic aldehyde **1** (2 mmol), 5,5-dimethyl-1,3-cyclohexanedione **2** (4 mmol), and TiO_2/SO_4^{2-} solid superacid (100 mg) were added to a mortar. The mixture was ground by mortar and pestle at room temperature for 30 min and kept at room temperature for 24 h. It was monitored by TLC. After completion of the reaction, the product was extracted with dichloromethane and the catalyst TiO_2/SO_4^{2-} was filtered off and recycled, the solvent was evaporated under reduced pressure, and the crude products **4** were obtained. The crude products were purified by recrystallization from ethanol (95%).

Data of some compounds are shown here:

3c. IR (KBr): $\nu_{max} = 3424, 3058, 2954, 2868, 2634, 1596, 1468, 1418, 1375, 1248, 1151, 974, 890, 870, 789\,cm^{-1}$. ^1H NMR ($CDCl_3$, 400 MHz): $\delta = 1.12$ (s, 6H, $2 \times CH_3$), 1.25 (s, 6H, $2 \times CH_3$), 2.31–2.51 (m, 8H, $4 \times CH_2$), 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 $C_{23}H_{27}ClO_4$: C, 68.56; H, 6.25. Found: C, 68.76; H, 6.14.

3e. IR (KBr): $\nu_{max} = 3425, 3060, 2950, 2865, 2630, 1601, 1470, 1417, 1379, 1250, 1152, 1135, 889, 790\,cm^{-1}$. ^1H NMR ($CDCl_3$, 400 MHz):

$\delta = 1.13$ (s, 6H, 2 × CH_3), 1.25 (s, 6H, 2 × CH_3), 2.30–2.52 (m, 8H, 4 × 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 $C_{23}H_{26}Cl_2O_4$: C, 63.16; H, 5.99. Found: C, 63.02; H, 5.84.

3h. IR (KBr): $\nu_{max} = 3424$, 3061, 2960, 2870, 2628, 1605, 1471, 1380, 1170, 1000, 890, 715 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): $\delta = 1.12$ (s, 6H, 2 × CH_3), 1.24 (s, 6H, 2 × CH_3), 2.31–2.51 (m, 8H, 4 × 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 $C_{24}H_{30}O_4$: C, 73.36; H, 7.91. Found: C, 73.58; H, 7.68.

3n. IR (KBr): $\nu_{max} = 3443$, 3073, 2960, 2870, 1610, 1500, 1494, 1425, 1365, 1298, 1215, 875, 743 cm^{-1}.^1H NMR ($CDCl_3$, 400 MHz): $\delta = 1.12$ (s, 6H, 2 × CH_3), 1.25 (s, 6H, 2 × CH_3), 2.31–2.51 (m, 8H, 4 × CH_2), 2.48 (s, 1H, CH), 6.25–6.33 (m, 2H, —CH═CH—), 6.85–7.01 (m, 5H, ArH), 11.58 (br, s, 1H, OH), 11.92 (br, s, 1H, OH). Anal. calcd. for $C_{25}H_{30}O_4$: C, 76.89; H, 7.74, Found: C, 76.78; H, 7.93.

3o. IR (KBr): $\nu_{max} = 3425$, 3065, 2955, 2870, 1605, 1466, 1418, 1374, 1270, 1195, 995, 870, 710 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): $\delta = 1.16$ (s, 6H, 2 × CH_3), 1.25 (s, 6H, 2 × CH_3), 6.95–7.24 (m, 8H, 4 × CH_2), 3.75 (s, 3H, OCH_3), 5.45 (s, 1H, CH), 6.89–7.16 (m, 3H, ArH), 11.55 (s, 1H, OH), 11.93 (s, 1H, OH). Anal. calcd. for $C_{24}H_{30}O_6$: C, 69.54; H, 7.29. Found: C, 69.75; H, 7.03.

3p. IR (KBr): $\nu_{max} = 3422$, 3060, 2955, 2868, 1594, 1466, 1414, 1374, 1248, 1151, 974, 866, 749 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): $\delta = 1.12$ (s, 6H, 2 × CH_3), 1.25 (s, 6H, 2 × CH_3), 2.31–2.51 (m, 8H, 4 × 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 $C_{23}H_{27}BrO_4$: C, 61.75; H, 6.08. Found: C, 61.98; H, 5.92.

3s. IR (KBr): $\nu_{max} = 3365$, 3025, 2980, 2850, 1665, 1587, 1548, 1505, 1375, 1240, 1196, 850, 756 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): $\delta = 1.12$ (s, 12H, 4 × CH_3), 1.14 (d, 3H, $J = 6.4$ Hz, CH_3), 2.29–2.37 (m, 8H, 4 × 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 $C_{18}H_{26}O_4$: C, 70.56; H, 8.55; Found: C, 70.78; H, 8.32.

3v. IR (KBr): $\nu_{max} = 3425$, 3080, 2970, 2930, 2840, 1640, 1560, 1495, 1440, 1385, 1275, 1045, 935, 790 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): $\delta = 1.14$ (s, 6H, 2 × CH_3), 1.18 (s, 6H, 2 × CH_3), 2.28 (s, 2H, CH_2), 2.42 (s, 2H, CH_2), 2.55 (s, 2H, CH_2), 2.81 (s, 2H, CH_2), 7.28 (d, 1H, $J = 5.3$ Hz, CH), 8.74 (d, 1H, $J = 5.3$ Hz, CHO), 11.64 (br, s, 1H, OH), 11.98 (br, s, 1H, OH). Anal. calcd. for $C_{18}H_{24}O_5$: C, 67.48; H, 7.55. Found: C, 67.69; H, 7.36.

4c. IR (KBr): $\nu_{max} = 3030$, 2980, 1685, 1660, 1620, 1490, 1365, 1200, 1135, 1000, 850, 840 cm^{-1}. ^1H NMR ($CDCl_3$): $\delta = 1.00$ (s, 6H, 2 × CH_3), 1.13 (s, 6H, 2 × CH_3), 2.31 (dd, 4H, $J = 1.6$ Hz, $J = 3.2$ Hz, 2 × CH_2, H-4, 5), 2.47 (s, 4H, 4 × CH_2, H-2, 7), 4.78 (s, 1H, H-9), 7.13–7.25 (m, 4H, ArH). Anal. calcd. for $C_{23}H_{25}ClO_3$: C, 71.77; H, 6.54. Found: C, 71.89; H, 6.45.

4n. IR (KBr): $\nu_{max} = 3030$, 2980, 1725, 1680, 1560, 1510, 1495, 1383, 1275, 1045, 945, 790 cm^{-1}. ^1H NMR ($CDCl_3$): $\delta = 0.98$ (s, 6H, 2 × CH_3), 1.11 (s, 6H, 2 × CH_3), 2.18 (dd, 4H, $J = 1.6$, $J = 2.4$, 2 × CH_2, H-4, 5), 2.45 (s, 4H, 2 × CH_2, H-2, 7), 4.56 (s, 1H, H-9), 5.86 (s, 2H, OCH_2O), 6.77–6.86 (m, 3H, ArH). Anal. calcd. for $C_{24}H_{26}O_5$: C, 73.07; H, 6.64. Found: C, 73.13; H, 6.71.

ACKNOWLEDGMENTS

This project was supported by the National Natural Science Foundation of China (Nos. 29872011 and 29572039); Educational Ministry of China, Educational Department of Hebei Province (990104); and Science and Technology Commission of Hebei Province.

REFERENCES

1. Tanaka, K.; Toda, F. Solvent-free organic synthesis. *Chem. Rev.* **2000**, *100*, 1025.
2. (a) Klingensmith, L. M.; Leadbeater, N. E. Ligand-free palladium catalysis of aryl coupling reactions facilitated by grinding. *Tetrehedron Lett.* **2003**, *44*, 756; (b) Koshima, H.; Matsushige, D.; Miyauchi, M.; Fujita, J. Solid-state photoreaction in two-component molecular crystals of thienylacetic acids and aza aromatic compounds. *Tetrahedron* **2000**, *56*, 6845; (c) Shimo, T.; Uezono, T.; Obata, T.; Yasutake, M.; Shinmyozu, T.; Somekawa, K. X-Ray and MO analysis of highly stereoselective solid-state photocycloadditions of 2-pyrones with maleimide. *Tetrahedron* **2002**, *58*, 6111; (d) Ren, Z. J.; Cao, W. G.; Tong, W. Q. The Kenoevenagel condensation reaction of aromatic aldehydes with malononitrile by grinding in the absence of solvents and catalysts. *Synth. Commun.* **2002**, *32*, 3475.
3. (a) Horning, E. C.; Horing, M. G. Methone derivatives of aldehydes. *J. Org. Chem.* **1946**, *11*, 95; (b) Nagarajan, K.; Shenony, S. J. Chemistry of dimethone—structures of aldehyde–dimethone adducts. *Indian J. Chem.* **1992**, *31B*, 73; (c) Tu, S. J.; Gao, Y.; Liu, X. H.; Tang, S. F.; Qiu, X. J. Microwave-induced reaction of aromatic aldehyde with 5,5-dimethyl-1,3-cyclohexandione in solid or liquid phase. *Chin. J. Org. Chem.* **2001**, *21*, 1164; (d) Tu, S. J.; Zhou, J. F.; Lu, Z. S.; Deng, X.; Shi, D. Q.; Wang, S. H. Condensation of aromatic aldehydes with 5,5-dimethyl-1,3-hexandione without catalyst. *Synth. Commun.* **2002**, *32*, 3063; (e) Jin, T. S.; Zhang, J. S.; Xiao, J. C.; Wang, A. Q.; Li, T. S. Clean synthesis of 1,8-dioxo-octahydroxanthene derivatives catalyzed by *p*-dodecylbenzenesulfonic acid in aqueous media. *Synlett* **2004**, 866.