

Synthesis of Dibenzylidene Acetone via Aldol Condensation of Diacetone Alcohol with Substituted Benzaldehydes

Pramod Kulkarni* and Ganesh Totre

Post Graduate Centre in Organic Chemistry and Department of Chemistry, Hutatma Rajguru Mahavidyalaya, Rajgurunagar, Pune-410505, India.

Article history: Received: 17 February 2019; revised: 06 July 2019; accepted: 11 July 2019. Available online: 30 September 2019. DOI: <http://dx.doi.org/10.17807/orbital.v11i5.1388>

Abstract:

Aldol condensation between diacetone alcohol and substituted benzaldehyde using calcium hydroxide as a base was investigated. Reaction of diacetone alcohol with benzaldehyde in the presence of base formed 4-benzylidene-5-hydroxy-5-methyl-1-phenylhex-1-en-3-one, which then converted into dibenzylidene acetone. The advantages of this method include high yield, use of inexpensive catalyst, easy workup, and simple purification process.

Keywords: aldol condensation; aromatic aldehyde; calcium hydroxide; diacetone alcohol; dibenzylidene acetone

1. Introduction

Dibenzylidene acetone possesses an aromatic ketone and an enone moiety and is an important component in a variety of biological compounds. Dibenzylidene acetone is obtained by an aldol condensation of benzaldehyde and acetone in the presence of sodium hydroxide as a catalyst. Dibenzylidene acetones having different substitutions on the aromatic rings are used as a precursor for the synthesis of flavonoids, which are abundant in comestible plants. Majority of the naturally occurring or synthetically obtained dibenzylidene acetone are biologically active and are extensively used in pharmaceutical applications. Dibenzylidene acetone undergoes a variety of chemical reactions and is intermediates in the synthesis of heterocyclic compounds [1] such as isoxazoles, quinolinones, thiadiazines and flavones [2]. They are also key intermediates in addition reaction like cycloaddition, Michael addition due to the presence of enone functionality. The dibenzylidene acetone exhibits a wide range of biological activities [3], such as antifungal [4], antioxidant [5], antimalarial [6], analgesic [7] and

antitumor characteristics [8, 9].

Numerous approaches for synthesis of dibenzylidene acetone based on carbon-carbon bond formation have been reported. Among them, the aldol condensation reaction plays an important role. The prominent way for the synthesis of dibenzylidene acetone is the classical Claisen-Schmidt condensation using sodium hydroxide [10] or barium hydroxide [11]. The other ways to obtain carbon-carbon bonds are by Suzuki reaction [12], Wittig reaction [13], Friedal-crafts acylation with cinnamoyl chloride [14], and Photo-Fries rearrangement of phenyl cinnamates [15]. The synthesis of dibenzylidene acetone requires two steps with the first step being aldol formation and the following being dehydration. The aldol reaction can also be performed in acidic medium [16] as well as in the presence of zirconium chloride [17]. Recently, alternative methods for the synthesis of dibenzylidene acetone has been reported by using SOCl_2 [18] and by using basic alumina in microwave irradiation [19]. However, these methods have disadvantages such as harsh reaction conditions, toxic reagents, strong acidic

*Corresponding author. E-mail: pramodskulkarni3@gmail.com

or basic conditions, longer reaction time, low yield, and selectivity. Hence, it is imperative to develop new methods for synthesis of dibenzylidene acetone.

Calcium hydroxide is a white powder with pH 12.6 that is sparingly soluble in water [20]. Calcium hydroxide has been used in selective C-4 acylation of pyrazolones [21] and in synthesis of benzopyrans [22, 23]. The effect of calcium reagents on aldol reactions of phenolic enolates and acetone with aldehydes is well studied [24-26]. In the present study, aldol condensation between diacetone alcohol and substituted benzaldehydes in the presence of calcium hydroxide to afford dibenzylidene acetone is reported.

2. Results and Discussion

In the preliminary trial, aldol condensation reaction between diacetone alcohol and benzaldehyde with calcium hydroxide as a base was considered as a model reaction. The reaction was monitored by TLC. The product dibenzylidene acetone (**3a**) was isolated by acid work-up, purified by recrystallization from ethanol and characterized by NMR and IR spectroscopic methods. The IR spectra showed no bands beyond 3300 cm^{-1} , typical for alcohol, confirming

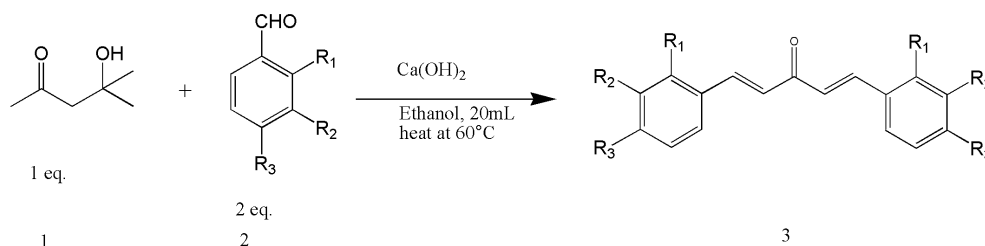
the absence of OH group. The ^1H NMR spectra showed no signals in aliphatic region. Different solvents were screened (**Table 1**), and ethanol was found to be the suitable solvent for this reaction with a yield of 80%.

Table 1. Effect of Solvent on aldol condensation of diacetone alcohol and benzaldehyde using calcium hydroxide as a base.^a

Sr. no	Solvent	Time (hrs)	% Yield ^b
1	MeOH	2	80
2	H ₂ O	5	75
3	DMF	3	20
4	EtOH	1.5	85

^aReaction conditions: 5mmol of diacetone alcohol and 10 mmol of substituted benzaldehyde and 2 equivalent of calcium hydroxide stirring with heat in respective solvent; ^bIsolated yield.

Next we extend the scope of reaction with various substituted benzaldehyde. The substituted groups on benzaldehyde are electron donating and electron withdrawing at *o*-, *m*-, *p*-position. The result are summarized in **Table 2**. The substituent at *para* position is electron withdrawing group increases yield of product with short reaction time and electron donating substituent decreases the yield with long reaction of time. *O*- substituted benzaldehyde gives moderate yield due to steric interaction.



Scheme 1. Aldol condensation between Diacetone alcohol and benzaldehyde using calcium hydroxide in ethanol.

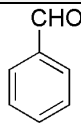
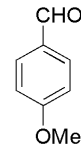
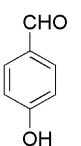
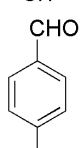
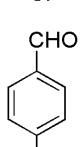
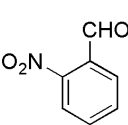
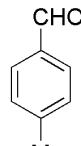
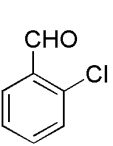
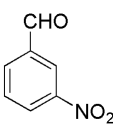
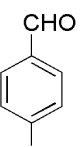
3. Material and Methods

Experimental Section

All the reagents and chemicals were obtained from commercial sources and used without further purification. Yields were calculated from isolated products. Melting points were determined in open capillary tubes and were uncorrected. All compounds were known and characterized by spectroscopic data (FTIR, ^1H NMR, ^{13}C NMR and HRMS). FTIR spectra were

recorded on an Alpha T Burker spectrophotometer. ^1H and ^{13}C NMR spectra were recorded at room temperature on BRUKER AVANCE DRX-500 MHz spectrometers using CDCl_3 as solvent and referenced to tetramethyl silane (internal standard). The purity of synthesized compounds and the development of reactions were monitored by thin layer chromatography (TLC) on Merck pre-coated silica gel 60 F254 aluminium sheets, visualized by UV light.

Table 2: Results of reaction between substituted benzaldehydes and diacetone alcohol to give substituted dibenzylidene acetones^a.

Entry	Aryl Aldehyde	Product(3)	Time sec	%Yield ^b	Melting point °C [Ref]
1.		3a	1.5	85	121-122 [24]
2.		3b	3	76	119-120 [24]
3.		3c	4	53	245-247 [28]
4.		3d	2	86	182-183 [29]
5.		3e	1.20	89	247-248 [30]
6.		3f	7	65	188
7.		3g	3.5	52	170-171 [24]
8.		3h	6	91	115-117 [29]
9.		3i	2	74	234-235 [30]
10.		3j	1.40	87	221-222 [27]

^aReaction conditions: 5mmol of diacetone alcohol and 10 mmol of substituted benzaldehyde and 2 equivalent of calcium hydroxide using ethanol as solvent at 60°C; ^b: Isolated yield.

General procedure for the preparation of dibenzylidene acetone

Diacetone alcohol (5mmol) and aryl aldehydes (10mmol) were added to 20mL ethanol under stirring at 60°C followed by addition of calcium hydroxide (10mmol). The progress of reaction was monitored by TLC using ethyl acetate: petroleum ether (2:8) solvent system. After complete consumption of aldehyde, the reaction mixture was poured into ice cold water in a beaker. The precipitated calcium salt was neutralized by concentrated HCl, at 0-5°C. Dibenzylidene acetone was precipitated as yellow crystal, filtered on Buchner funnel, and purified by recrystallization from ethanol.

Spectral data of synthesized compounds

1,5-diphenyl-1,4-pentadien-3-one (3a): IR (KBr) in cm^{-1} 3056, 3020, 1662, 1628, 1612, 1581, 1563; ^1H NMR (CDCl_3) δ 7.10(d, 2H, $J=15.4$ Hz), 7.52-7.60 (m, 10H), 7.78 (d, 2H, $J=15.4$ Hz); ^{13}C NMR (CDCl_3) δ 124.8, 128.8, 129.3, 130.5, 134.2, 143.7, 153.4, 189.4; HRMS (m/z): 234.10

1,5-bis(4-methoxyphenyl)-1,4-pentadien-3-one (3b): IR (KBr) in cm^{-1} 3042, 2911, 2903, 1689, 1616, 1590, 1582, 1223, 1175, 980; ^1H NMR (CDCl_3) δ 3.83(s, 6H), 6.87(d, 4H, $J=8.5$ Hz), 6.96(d, 2H, $J=15.8$ Hz), 7.58 (d, 4H, $J=8.5$ Hz), 7.66(d, 2H, $J=15.8$ Hz); ^{13}C NMR (CDCl_3) δ 55.3, 113.9, 123.8, 127.4, 130.6, 142.7, 162.2, 188.4; HRMS (m/z): 294.13

1,5-bis(4-hydroxyphenyl)-1,4-pentadien-3-one (3c): IR (KBr) in cm^{-1} 3350, 3045, 1657, 1622, 1606, 1524, 1328; ^1H NMR (CDCl_3) δ 6.72(d, 4H, $J=8.3$ Hz), 6.96(d, 2H, $J=15.7$ Hz), 7.15(d, 2H, $J=8.3$ Hz), 7.57(d, 2H, $J=15.7$ Hz), 11.3(s, 1H, OH); ^{13}C NMR (CDCl_3) δ 115.4, 122.9, 127.3, 127.6, 153.5, 157.9, 189.3; HRMS (m/z): 266.09

1,5-bis(4-chlorophenyl)-1,4-pentadien-3-one (3d): IR (KBr) in cm^{-1} 3056, 3008, 1660, 1620, 1584, 806, 710; ^1H NMR (CDCl_3) δ 7.05(d, 2H, $J=15.4$ Hz), 7.36(d, 2H, $J=9.1$ Hz), 7.59(d, 2H, $J=9.1$ Hz), 7.71(d, 2H, $J=15.4$ Hz); ^{13}C NMR (CDCl_3) δ 125.8, 129.2, 129.9, 133.4, 136.9, 142.5, 189.1; HRMS (m/z): 302.03

1,5-bis(4-nitrophenyl)-1,4-pentadien-3-one (3e): IR (KBr) in cm^{-1} 3075, 1673, 1631, 1590, 1529, 1348; ^1H NMR (CDCl_3) δ 7.20(2H, d, $J=15.2$

Hz), 7.89 (d, 2H, $J=15.2$ Hz), 7.96 (d, 4H, $J=9.1$ Hz), 8.24(d, 4H, $J=9.1$ Hz); ^{13}C NMR (CDCl_3) δ 122.2, 123.9, 128.5, 141.8, 148.6, 154.2, 189.9; HRMS (m/z): 324.07

1,5-bis-(2-nitrophenyl)-1,4-pentadien-3-one (3f): IR (KBr) in cm^{-1} 3065, 1684, 1628, 1603, 1520, 1342, 832, 738, 697; ^1H NMR (CDCl_3) δ 7.24(d, 2H, $J=15.6$ Hz), 7.42(m, 2H), 7.59(m, 2H), 7.75 (m, 2H), 8.24 (m, 2H), 8.34(d, 2H, $J=15.6$ Hz); ^{13}C NMR (CDCl_3) δ 121.2, 123.6, 127.8, 129.4, 131.2, 135.6, 147.2, 153.4, 189.7; HRMS (m/z): 325.15

1,5-p-tolyl-1,4-pentadien-3-one (3g): IR (KBr) in cm^{-1} 3038, 2913, 1656, 1611, 1578, 1543; ^1H NMR (CDCl_3) δ 2.32(s, 3H); 6.91(d, 4H, $J=8.3$ Hz), 6.96(d, 2H, $J=15.3$ Hz), 7.46(d, 2H, $J=8.3$ Hz), 7.65 (d, 2H, $J=15.6$ Hz); ^{13}C NMR (CDCl_3) δ 25.3, 123.7, 126.4, 129.1, 132.4, 137.9, 152.9, 188.6; HRMS (m/z): 262.14

1,5-bis(2-chlorophenyl)-1,4-pentadien-3-one (3h): IR (KBr) in cm^{-1} 3060, 3022, 1659, 1621, 1583, 1558, 760, 734; ^1H NMR (CDCl_3) δ 7.10(d, 2H, $J=15.6$ Hz), 7.65-7.23 (m, 8H), 8.04(d, 2H, $J=15.6$ Hz); ^{13}C NMR (CDCl_3) δ 127.2, 127.6, 127.9, 130.1, 131.4, 133.2, 135.8, 139.7, 188.9; HRMS (m/z): 302.04

1,5-bis(3-nitrophenyl)-1,4-pentadien-3-one (3i): IR (KBr) in cm^{-1} 3070, 1680, 1626, 1523, 1344, 840, 731; ^1H NMR (CDCl_3) δ 7.17(d, 2H, $J=15.9$ Hz), 7.68(t, 2H, $J=7.4$ Hz, 8.2Hz), 7.83(d, 2H, $J=15.9$ Hz), 7.98 (d, 2H, $J=8.2$ Hz), 8.26 (d, 2H, $J=7.4$ Hz), 8.45(s, 2H); ^{13}C NMR (CDCl_3) δ 120.7, 121.9, 123.5, 129.8, 132.7, 136.3, 148.9, 152.7, 189.2; HRMS (m/z): 324.12

1,5-bis(4-bromophenyl)-1,4-pentadien-3-one (3j): IR (KBr) in cm^{-1} 3045, 1659, 1616, 1520, 826, 794, ; ^1H NMR (CDCl_3) δ 7.06(d, 2H, $J=15.6$ Hz), 7.45(d, 4H, $J=8.8$ Hz), 7.56(d, 4H, $J=8.8$ Hz), 7.64(d, 2H, $J=15.6$ Hz); ^{13}C NMR (CDCl_3) δ 125.4, 129.9, 132.1, 133.7, 139.8, 142.6, 189.9; HRMS (m/z): 391.89.

4. Conclusions

We studied the aldol condensation between diacetone alcohol and aromatic aldehydes using calcium hydroxide as base and observed that diacetone underwent retro-aldol condensation to

form the acetone. The generated acetone reacted with aldehydes to give the corresponding dibenzylidene acetones. This is an alternative method for the synthesis of dibenzylidene acetone. The merits of this method include the use of inexpensive and naturally abundant calcium hydroxide as catalyst; circumvention the extraction process during isolation of products, high yield, easy work-up, and no toxic reagents.

References and Notes

- [1] Wangn, S.; Yu, G.; Lu, j.; Xiao, K.; Hu, Y.; Hu, H. *Synthesis* **2003**, 487. [\[Crossref\]](#)
- [2] Sarada, S. R.; Puri, V. A.; Rode, A. B.; Dalawe, T. N.; Jadhav, W. N.; Pawar, R. P. *Arkivoc*, **2007**, xvi, 246. [\[Crossref\]](#)
- [3] Ballesteros, J. F.; Sanz, M. J.; Ubeda, A.; Miranda, M. A.; Iborra, S.; Paya, M.; Alcaraz, M. *J. Med. Chem.* **1995**, 38, 2794. [\[Crossref\]](#)
- [4] Go, M. L.; Wu, X.; Liu, X. L. *Curr. Med. Chem.* **2005**, 12, 483. [\[Crossref\]](#)
- [5] Mukerjee, V. K.; Prased, A. K.; Raj, A. G.; Brakhe, M. E.; Olsen, C. E.; Jain, S. C.; Parmer, V. P. *Bioorg. Med. Chem.* **2001**, 9, 337. [\[Crossref\]](#)
- [6] Liu, U. M.; Wilairat, P.; Croft, S. L.; Tan, A. L.; Go, M. *Bioorg. Med. Chem.* **2003**, 11, 2729. [\[Crossref\]](#)
- [7] Sivakumar, P. M.; Geetha Babu, S. K.; Mukesh, D. *Chem. Pharm. Bull.* **2007**, 55, 44. [\[Crossref\]](#)
- [8] Viana, G. S.; Bandeira, M. A.; Mantos, F. J. *Phytomedicine* **2003**, 10, 189. [\[Crossref\]](#)
- [9] Nakamura, C.; Kawasaki, N.; Miyataka, H.; Jayachandran, E.; Kim, I. H.; Kirk, K. L.; Taguchi, T.; Takeuchi, Y.; Hori, H.; Satoh, T. *Bioorg. Med. Chem.* **2002**, 10, 699. [\[Crossref\]](#)
- [10] Ducki, S.; Forrest, R.; Hadfield, J. A.; Kendall, A.; Lawrence, N. J.; Mc-Gown, A. T.; Rennison, D. *Bioorg. Med. Chem.* **1998**, 8, 1051. [\[Crossref\]](#)
- [11] Kumar, S.; Lamba, M. S.; Makrandi, J. K. *Green Chem. Lett. Rev.* **2008**, 1, 123. [\[Crossref\]](#)
- [12] Srinivasa Rao, M.; Kotes, J.; Narukulla, R.; Duddeck, H. *Arkivoc*, **2004**, xiv, 96. [\[Crossref\]](#)
- [13] Calvino, V.; Picallo, M.; Lopez-peinado, A. J.; Martin-Aranda, R. M.; Duran-Valle, C. *Appl. Surf. Sci.* **2006**, 252, 6071. [\[Crossref\]](#)
- [14] Eddarir, S.; Catelle, N.; Bakkour, Y.; Ronlando, C. *Tetrahedron Lett.* **2003**, 44, 5359. [\[Crossref\]](#)
- [15] Konieczny, M. T.; Konieczny, W.; Sabisz, M.; Skladanowski, A.; Wakiec, R.; Augustynowicz, K. E.; Zwolska, Z. *European J. Medicinal Chem.* **2007**, 42, 729. [\[Crossref\]](#)
- [16] Sebti, S.; Solhy, A.; Smahi, A.; Kossir, A.; Oumimoun, H. *Catalysis Commun.* **2002**, 3, 335. [\[Crossref\]](#)
- [17] Bora, U.; Saikia, A.; Boruah, R. C. *Indian J. Chem.* **2005**, 44B, 2523.
- [18] Jhala, Y.S.; Dulawat, S. S.; Verma, B. L. *Indian J. Chem.* **2006**, 45B, 466.
- [19] Perozo-Rondon, E.; Martin-Aranda, R. M.; Casal, B.; Duran-Valle, C. J.; Lau W. N.; Zhang, X. F.; Yeung, K. L. *Catal. Today* **2006**, 114, 183. [\[Crossref\]](#)
- [20] Greenwood, N. N.; Earnshaw, A. *Chemistry of the Elements*; Pergamon Press, New York, 1984.
- [21] Hari, S. G.; Lee, Y. R. *Bull. Korean Chem. Soc.* **2011**, 32, 2949. [\[Crossref\]](#)
- [22] Jensen, B. S. *Acta. Chem. Scand.* **1959**, 13, 1668. [\[Crossref\]](#)
- [23] Saimoto, H.; Yoshida, K.; Murakami, T.; Morimoto, M.; Sashiwa, H.; Shigemasa, Y. *J. Org. Chem.*, **1996**, 61, 6768. [\[Crossref\]](#)
- [24] Yu, L.; Han, M.; Luan, J.; Xu, L.; Ding, Y.; Xu, Q. *Sci. Rep.* **2016**, 6, 30432. [\[Crossref\]](#)
- [25] Kulkarni, P. S.; Swami, P. M.; Zubaidha, P. K. *Synth. React. Inorg., Met.-Org., Nano-Met. Chem.* **2013**, 43, 617. [\[Crossref\]](#)
- [26] Kulkarni, P. S.; Kondhare, D. D.; Varala, R.; Zubaidha, P. K. *Acta Chimica Slovaca* **2013**, 6, 150. [\[Crossref\]](#)
- [27] Reddy, N. S.; Badam, R.; Sattibabu, R.; Molli, M.; Muthukumar, V. S.; Sai, S. S. S.; Rao, G. N. *Chem. Phys. Lett.*, **2014**, 616-617, 142. [\[Crossref\]](#)
- [28] Liang, G.; Li, X.; Chen, L.; Yang, S.; Wu, X.; Studer, E.; Gurley, E.; Hylemon, P. B.; Ye, F.; Li, Y.; Zhou, H. *Bioorg. Med. Chem. Lett.* **2008**, 18, 1525. [\[Crossref\]](#)
- [29] Weber, W. M.; Hunsaker, L. A.; Abcouper, S. F.; Deck, L. M.; Jagt, D. L. V. *Bioorg. Med. Chem.* **2005**, 13, 3811. [\[Crossref\]](#)
- [30] Ding, L.; Wang, W.; Zhang, A. *Ultrason. Sonochem.*, **2007**, 14, 563. [\[Crossref\]](#)