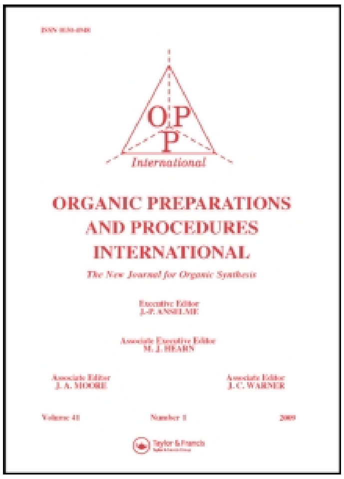


Organic Preparations and Procedures International
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t902189982

α,α-*bis*(BENZYLIDENE)CYCLOALKANONES BY CONDENSATION IN WATER UNDER PTC CATALYSIS AND MICROWAVE IRRADIATION

Jianfeng Zhou[a]
[a] Department of Chemistry, Huaiyin Normal College, Huaian, PR CHINA

To cite this Article Zhou, Jianfeng(2005) 'α,α-*bis*(BENZYLIDENE)CYCLOALKANONES BY CONDENSATION IN WATER UNDER PTC CATALYSIS AND MICROWAVE IRRADIATION', Organic Preparations and Procedures International, 37: 1, 75 — 79

To link to this Article: DOI: 10.1080/00304940509355403

URL: http://dx.doi.org/10.1080/00304940509355403

ORGANIC PREPARATIONS AND PROCEDURES INT., 37 (1), 75-102 (2005)

OPPI BRIEFS

α,α'-*bis*(BENZYLIDENE)CYCLOALKANONES BY CONDENSATION IN WATER UNDER PTC CATALYSIS AND MICROWAVE IRRADIATION

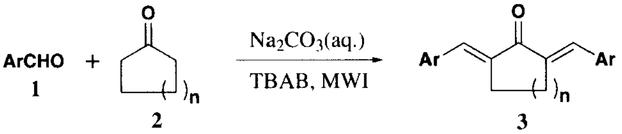
Submitted by Jianfeng Zhou
(08/13/04)

Department of Chemistry, Huaiyin Normal College
Huaian 223300, P. R. CHINA

As useful precursors to potentially bioactive pyrimidine derivatives, α,α'-*bis*(benzylidene) cycloalkanones have attracted considerable attention for many years.[1] Usually, the preparation of α,α'-*bis*(benzylidene)cycloalkanones can be realized through cross aldol-type reaction of the ketones and aromatic aldehydes, but traditional acid- or base-catalyzed reaction suffers from reverse reaction and thus gives the corresponding products in low yields.[2] Aoyama and co-workers[3] obtained α,α'-*bis*(benzylidene)cyclohexanones through Rh(III)-porphyrin complex-catalyzed condensation in only 30% yields, while Nakano and co-workers[4] found that the use of Cp_2TiPh_2 as the catalyst gave good yields which was only obtained at high temperatures in sealed ampoules. Cross-aldol condensation of cycloalkanones and aromatic aldehydes catalyzed by *bis*(*p*-methoxyphenyl)tellurium oxide under microwave irradiation,[5] $FeCl_3$-$6H_2O$, $SmCl_3$ in ionic liquids,[6-7] KF-Al_2O_3 under ultrasound irradiation,[8] $RuCl_3$,[9] $InCl_3$,[10-11] have also been reported in the literature.

Since Toda *et al.*[12] reported the first example of aldol condensation in the absence of solvent, organic chemists have sought to develop clean, economical, and environmental safer methodologies. Recently, there has been increasing recognition that water is an attractive medium for many organic reactions.[13] The use of microwave irradiation for organic reactions has become a well-established procedure since reactions are clean, rapid and economical. Application of Phase-transfer catalysis (PTC) instead of traditional technologies for industrial processes provides substantial benefits for the environment. The combination of the these techniques has been a field which has shown excellent results.[14]

As a continuation of our interest,[15] we now report an efficient and clean synthesis of α,α'-*bis*(benzylidene)cycloalkanones performed by condensation of aromatic aldehydes with cyclopentanone and cyclohexanone in aqueous sodium carbonate solution and in the presence of teterabutylammonium bromide (TBAB) using microwave irradiation. This reaction requires only 0.5-7 minutes and proceeds in 80~99% yields, low energy consumption, environmentally benign and easier work-up.



First of all, the influence of TBAB in the aldol condensations was explored. The results showed that the presence of TBAB has a remarkable influence on the yields. For example, the title compound **3b** was not obtained by the reaction of a 4-chlorobenzaldehyde with cyclopentanone in the absence of the TBAB after microwave irradiation 14 minutes (*Table 1, Entry 1*). This is due to the fact that the reactants exist as a non-miscible mixture of oil and water in the absence of TBAB. The rate of the reactions do not increase on increasing the amounts of TBAB. The results show the optimized yields obtained (*Table 1, Entry 2*) when the mole ratio of TBAB, aromatic aldehyde and cyclopentanone were 0.15:2:1. It is also obvious that the rate of the reactions were accelerated by microwave irradiation. For instance, in the case of **3b**, the yield is only 80% after refluxing 4 hrs (*Table 1, Entry 5*).

Table 1. Influence of Amount of the TBAB and Concentration of Na_2CO_3[a]

Entry	Yield (%)	Time (min)	TBAB (g)	Na_2CO_3 (%)
1	0	14	0	saturated
2	91	5	0.1	saturated
3	76	5	0.2	saturated
4	70	5	0.3	saturated
5	80	240[b]	0.1	saturated
6	0	10	0.1	0
7	59	5	0.1	5
8	64	5	0.1	10
9	84	5	0.1	15

a) 4-Chlorobenzaldehyde (4mmol), cyclopentanone (2mmol), 5mL of Na_2CO_3 solution and TBAB; microwave power 195W, pulsed irradiation. b) Carried out under conventional reflux heating instead of microwave irradiation.

The influence of the concentration of Na_2CO_3 to the aldol condensation was shown to be important as yields increased as the concentration of $NaCO_3$ in the presence of TBAB and under microwave irradiation (*Table 1*).

Table 2 shows the experimental results of the aldol condensations of aromatic aldehydes with cyclopentanone and cyclohextanone in saturated sodium carbonate solution and in the presence of TBAB under microwave irradiation. This reaction requires only 0.5~7minutes and in yields as high as 80~99%.

Table 2. The Reaction Time and Yields of the Compound **3a~3s**[a]

Cmpd	Ar	n	Time (min)	Yield (%)	mp°C (*lit.* mp°C)
3a	C_6H_5	1	7	96	188-189 (*lit.*[5] 188-189)
3b	$4\text{-}ClC_6H_4$	1	5	91	222.5-224 (*lit.*[7] 224-225)
3c	$4\text{-}O_2NC_6H_4$	1	0.5	85	229.5-231.5 (*lit.*[5] 230-231)
3d	$3\text{-}O_2NC_6H_4$	1	0.5	93	226.8-226.9
3e	$4\text{-}CH_3OC_6H_4$	1	7	82	209.5-210 (*lit.*[5] 210-211)
3f	$4\text{-}(CH_3)_2NC_6H_4$	1	7	90	>260 (*lit.*[11] >250°C
3g	$2\text{-}ClC_6H_4$	1	5	99	152-153 (*lit.*[4] 152.3-152.6)
3h	$3,4\text{-}(OCH_2O)C_6H_3$	1	7	81	261-262.5
3i	$3,4\text{-}(CH_3O)_2C_6H_3$	1	7	80	172-173
3j	$4\text{-}CH_3C_6H_4$	1	7	98	245-246 (*lit.*[16] 245-246)
3k	C_6H_5	2	5	87	114.5-115 (*lit.*[7] 115-116)
3l	$4\text{-}ClC_6H_4$	2	3	94	144-145 (*lit.*[15] 146-147)
3m	$4\text{-}O_2NC_6H_4$	2	0.5	93	162-164 (*lit.*[10] 159)
3n	$3\text{-}O_2NC_6H_4$	2	0.5	97	181.5-182 (*lit.*[11] 179-181)
3o	$4\text{-}CH_3OC_6H_4$	2	5	86	161-162 (*lit.*[11] 160-162)
3p	$4\text{-}(CH_3)_2NC_6H_4$	2	5	98	>250 (*lit.*[11] >250)
3q	$3,4\text{-}(OCH_2O)C_6H_3$	2	5	82	157-158
3r	$3,4\text{-}(CH_3O)_2C_6H_3$	2	5	81	159-160
3s	$4\text{-}CH_3C_6H_4$	2	5	90	174.5-175 (*lit.*[7] 172-173)

[a] aromatic aldehyde (4mmol), cycloalkanone (2mmol), 5mL of Na_2CO_3 solution, 0.1 g TBAB; Microwave power 195W, pulsed irradiation.

In conclusion, an efficient, simple and environmentally friendly procedure for the synthesis of α,α'-*bis*(benzylidene)cycloalkanones from the corresponding aromatic aldehydes with cyclopenlanone and cyclohexanone has been developed.

EXPERIMENTAL SECTION

Mps were determined in WRS-1B digital melting point apparatus and uncorrected. IR spectra were recorded on a Nicolet Avatar360FT-IR instrument. ^{1}HNMR were measured on a Burke 300 MHz spectrometer in $CDCl_3$ with TMS as internal standard. MS spectra were recorded on a LCQ Advanbage instrument. Elemental analyzer were determined using Perkin-Elmer 240C elemental analyzer. The reactions were carried out with a modified commercial microwave oven (Sanle WP650D 650w) under atmospheric pressure. All the reagents are commercially available.

α,α'-*bis*(Benzylidene)cycloalkanones (3a-s). General Procedure.- A mixture of the aromatic aldehyde (4 mmol), cyclopentanone or cyclohexanone (2 mmol), saturated sodium carbonate aqueous 5 mL and TBAB (0.1 g) into an Erlenmeyer flask (25 mL) equipped with reflux condenser were irradiated in a microwave oven for 0.5~7 minutes (as indicated by TLC). The reaction mixture was allowed to stand at room temperature to solidify. The crude product was collected, washed with water and recystallized from 95% ethanol.

Compound **3d**, mp. 226.8-226.9°C; ^{1}H NMR (DMSO-d_6, 300 MHz,): δ 8.32 (2H, s, CH=), 8.11-7.61 (8H, m, arom H), 3.33 (4H, s, $2CH_2$); IR(KBr): 3063, 2917, 1688, 1604, 1527, 1348, 1188, 739cm^{-1}; MS$(M+H)^+$ 351.

Anal. Calcd for $C_{19}H_{14}N_2O_5$: C 65.14; H 4.00; N 8.00. Found: C 64.92; H 3.86; N 7.88

Compound **3h**, mp. 261-262.5°C; ^{1}H NMR (CDCl$_3$, 300 MHz,): δ 7.52 (s, 2H, CH=), 7.13-6.89 (m, 6H, arom H), 6.05(s,4H, $2OCH_2O$), 3.09(s,4H, $2CH_2$); IR(KBr): 3083, 2909, 1680, 1596, 1490, 1444, 1219, 1034, 808cm^{-1}; MS$(M+H)^+$ 349.

Anal. Calcd for $C_{21}H_{16}O_5$: C 72.41; H 4.60. Found: C 72.26; H 4.54

Compound **3i**, mp. 172.1~172.9°C; ^{1}H NMR (CDCl$_3$, 300 MHz,): δ 7.55 (s, 2H, CH=), 7.25-6.93 (m, 6H, arom H), 3.95 (s, 12H, $4OCH_3$), 3.17-3.06 (s, 4H, $2CH_2$); IR(KBr): 3088, 2909, 2847, 1686, 1622, 1589, 1255, 1174, 815cm^{-1}; MS$(M+H)^+$ 381.

Anal. Calcd for $C_{23}H_{24}O_5$: C 72.63; H 6.32. Found: C 72.44; H 6.18

Compound **3q**, mp. 157-158°C; ^{1}H NMR (CDCl$_3$, 300 MHz,): δ 7.72 (2H, s, CH=), 6.86-7.05 (m, 6H, arom H), 6.02 (s, 4H, $2OCH_2O$), 2.90-2.93(t, 4H, $2CH_2$), 1.80-1.84, (m, 2H, CH_2); IR(KBr): 3073, 2955, 2894, 1649, 1586, 1545, 1499, 1233, 1163, 1039, 809 cm^{-1}; MS$(M+H)^+$ 363.

Anal. Calcd for $C_{22}H_{18}O_5$: C 72.93; H 4.97. Found: C 72.78; H 4.90

Compound **3r**, mp. 159-160°C; ^{1}H NMR (CDCl$_3$, 300 MHz,): δ 7.77 (s, 2H, CH=), 6.91-7.14 (m, 6H, arom H), 3.93 (s, 12H, $4OCH_3$), 2.95-2.98 (t, 4H, $2CH_2$), 1.80-1.86 (m, 2H, CH_2); IR(KBr): 3073, 2930, 2832, 1659, 1595, 1513, 1449, 1249, 1138, 1021, 843cm^{-1}; MS$(M+H)^+$ 395.

Anal. Calcd for $C_{24}H_{26}O_5$: C 73.10; H 6.60. Found: C 72.92; H 6.45

Acknowledgments.- We would like to thank the Nature Science Foundation of Jiangsu Province Education Department of China (No. 02KJD 150006).

REFERENCES

1. J. Deli, T. Lorand, D. Szabo and A. Foldesi, *Pharmazie*, **39**, 539 (1984).
2. B. A. Hathaway, *J. Chem. Educ.*, **64**, 367 (1987).
3. Y. Aoyama, Y. Tanaka, T. Yoshida, H. Toi and H. Ogoshi, *J. Organometal Chem.*, **329**, 251 (1987).
4. T. Nakano and T. Migita, *Chemistry Lett.*, **12**, 2157 (1993).

5. M. Zheng, L. Wang, J. Shao and Q. Zhong, *Synth. Commun.*, **27**, 351 (1997).

6. X. Zhang, X. Fan, H. Niu and J. Wang, *Green Chem.*, **5**, 267 (2003).

7. X. Zheng and Y. Zhang, *Synth. Commun.*, **33**, 161 (2003).

8. J. T. Li, W. Z. Yang, G. F. Chen and T. S. Li, *Synth. Commun.*, **33**, 2619 (2003).

9. N. Iranpoor and F. Kazemi, *Tetrahedron*, **54**, 9475 (1998).

10. G. Deng and T. Ren, *Synth. Commun.*, **33**, 2995 (2003).

11. L. Ying, J. Lu and Y. J. Bai, *Chin. J. Org. Chem.*, **23**, 659 (2003); *Chem. Abs.*, **139**, 364653 (2003).

12. F. Toda, K. Tanaka and K. hamai, *J. Chem. Soc., Perkin Trans, 1*, 3207 (1990).

13. C. J. Li, *Chem. Rev.*, **93**, 2023 (1993).

14. S. Deshayes, M. Liagre, A. Loupy, J. L. Luche and A. Petit, *Tetrahedron Lett.*, **55**, 10851 (1999).

15. J. F. Zhou, J. M. Xu, H. Wei and L. L. Zhang, *Chin. J. Org. Chem.*, **21**, 322 (2001); *Chem. Abst.* **135**, 33344z(2002).

16. H. Frey, G. Behmann and G. Kaupp, *Chem. Ber.*, **120**, 387 (1987).

****