Available online at www.sciencedirect.com

SCIENCE DIRECT®

Journal of Molecular Catalysis A: Chemical 247 (2006) 182–185

JOURNAL OF MOLECULAR CATALYSIS A: CHEMICAL

www.elsevier.com/locate/molcata

Short communication

Convenient and facile cross-Aldol condensation catalyzed by molecular iodine: An efficient synthesis of α,α′-bis(substituted-benzylidene) cycloalkanones[☆]

Biswanath Das*, Ponnaboina Thirupathi, Ibram Mahender, Kongara Ravinder Reddy

Organic Chemistry Division—I, Indian Institute of Chemical Technology, Hyderabad 500007, India

Received 28 October 2005; received in revised form 22 November 2005; accepted 23 November 2005
Available online 18 January 2006

Abstract

Cross-Aldol condensation of aromatic aldehydes with cyclic ketones in the presence of catalytic amount of iodine at room temperature afforded α,α′-bis(substituted-benzylidene) cycloalkanones in high yields.

© 2005 Elsevier B.V. All rights reserved.

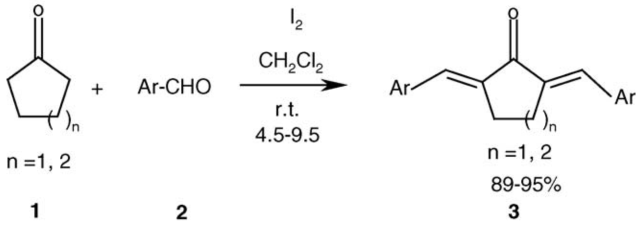
Keywords: Cross-Aldol condensation; Aromatic aldehyde; Cyclic ketone; Iodine; α,α′-Bis(substituted-benzylidene) cycloalkanones

Cross-Aldol condensation of aromatic aldehydes with cyclic ketones is an important synthetic reaction for the preparation of α,α′-bis(substituted-benzylidene) cycloalkanones. These benzylidene derivatives are intermediates of various pharmaceuticals, agrochemicals and perfumes [1]. They are frequently used for the synthesis of bioactive pyrimidene compounds [2]. They also find applications in the preparation of non-linear optical materials [3] and liquid-crystalline polymers [4].

Cross-Aldol condensation is classically carried out using strong acid or base [5]. However, this process suffers from reverse and side reactions resulting in low yields of the products. Different complexes of metal(II) ions have also been used as catalysts but the yields (<38%) were not satisfactory [6]. Various other reagents such as $Cp_2Ti\,Ph_2$ [7a], BMPTO [7b], $RuCl_3$ [7c], SmI_3 [7d], Cp2ZrH$_2$ [7e], $TiCl_3\,(SO_3\,CF_3)$ [7f], KF–Al_2O_3 [7g], $FeCl_3$ [7h], $BF_3{\bullet}OEt_2$ [7i], $InCl_3$ [7j], TMSCl/NaI [7k] and Yb $(OTf)_3$ [7l] are known to catalyze the reaction. However, in most cases the yields are good at high temperatures and some of the reagents require longer reaction times and tedious purification procedures. Cross-Aldol reaction has also been carried out in an ionic liquid using $FeCl_3{\cdot}6H_2O$ as a catlyst but the reaction was conducted at 80 °C [8].

In recent years molecular iodine has been considered as an efficient, inexpensive and readily available catalyst for several organic transformations [9]. In continuation of our work on the application of this catalyst for development of useful synthetic methodologies we have observed that this is very suitable to catalyze the cross-Aldol condensation of aromatic aldehydes with cyclic ketones at room temperature (Scheme 1).

Various aromatic aldehydes (**1**) and cyclopentanone/cyclohexanone (**2**) were reacted following the above method to prepare a series of α,α′-bis(substituted-benzylidene) cycloalkanones (**3**) (Table 1) [10]. The products were formed in excellent yields. Aromatic aldehydes containing both electron donating and withdrawing groups underwent the conversion smoothly. Cinnamaldehyde and furfural also afforded the desired products in high yields. Both cyclopentanone and



Scheme 1.

[☆] Part 68 in the series, “Studies on Novel Synthetic Methodologies”. IICT Communication No. 051113.

* Corresponding author. Tel.: +91 40 7160512; fax: +91 40 7160512.
E-mail address: biswanathdas@yahoo.com (B. Das).

1381-1169/$ – see front matter © 2005 Elsevier B.V. All rights reserved.
doi:10.1016/j.molcata.2005.11.044

Table 1
Preparation of α,α′-bis(substituted-benzylidene) cycloalkanones catalyzed by molecular iodine[a]

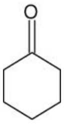
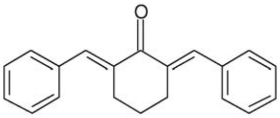
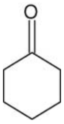
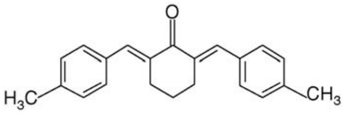
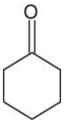
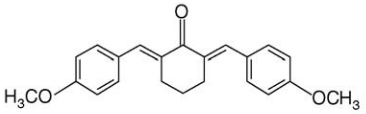
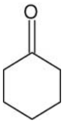
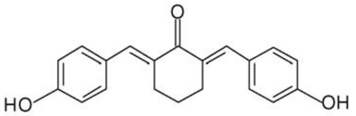
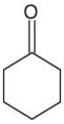
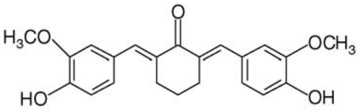
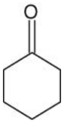
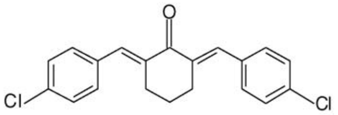
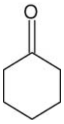
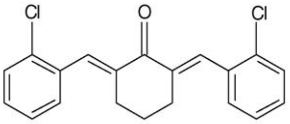
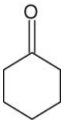
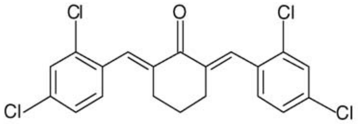
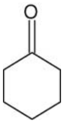
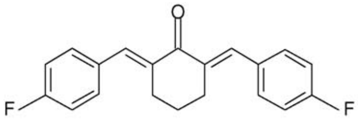
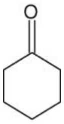
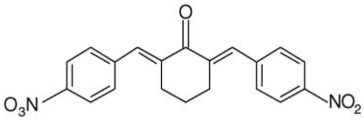
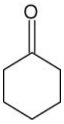
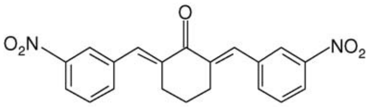
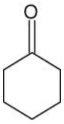
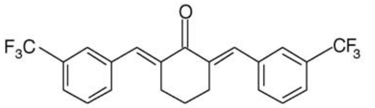
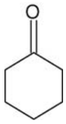
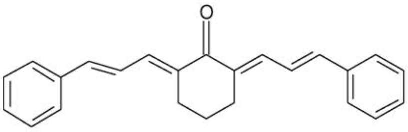
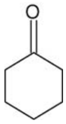
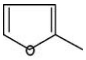
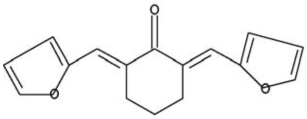
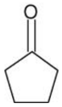
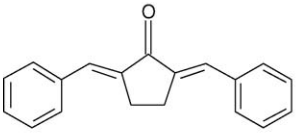
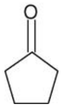
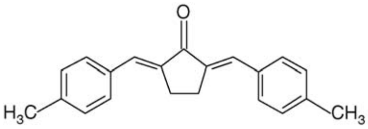
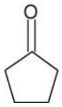
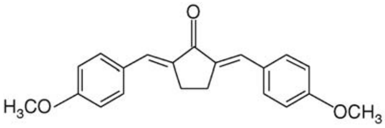
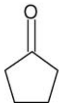
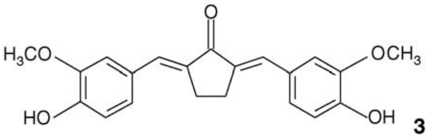
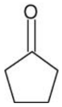
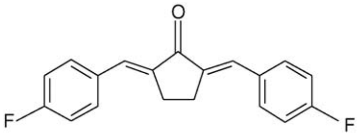
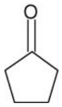
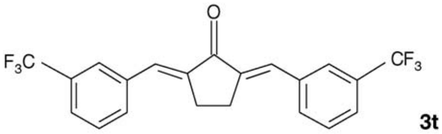
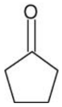
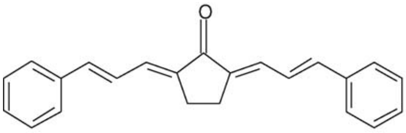
Entry	Ketone **1**	ArCHO **2**	Product **3**	Time (h)	Isolated yield (%)
a		Ph	 **3a**	4.5	92
b		4-$CH_3C_6H_4$	 **3b**	4.5	94
c		4-$CH_3OC_6H_4$	 **3c**	4.5	95
d		4-HOC_6H_4	 **3d**	4.5	95
e		4-HO-3-$OCH_3C_6H_3$	 **3e**	4.5	92
f		4-ClC_6H_4	 **3f**	4.5	94
g		2-ClC_6H_4	 **3g**	5.5	90
h		2,4-$Cl_2C_6H_3$	 **3h**	5.5	90
i		4-FC_6H_4	 **3i**	5.0	91
j		4-$NO_2C_6H_4$	 **3j**	9.5	89
k		3-$NO_2C_6H_4$	 **3k**	9.5	89
l		3-$CF_3C_6H_4$	 **3l**	5.5	92

Table 1 (*Continued*)

Entry	Ketone **1**	ArCHO **2**	Product **3**	Time (h)	Isolated yield (%)
m		$C_6H_5CH{=}CH$	 **3m**	5.5	90
n			 **3n**	7.5	87
o		Ph	 **3o**	4.5	89
p		4-$CH_3C_6H_4$	 **3p**	4.5	92
q		4-$CH_3OC_6H_4$	 **3q**	4.5	92
r		4-HO-3-OCH_3	 **3r**	5.0	90
s		4-FC_6H_4	 **3s**	5.0	92
t		3-$CF_3C_6H_4$	 **3t**	5.5	90
u		$C_6H_5CH{=}CH$	 **3u**	5.5	90

[a] The structures of the products were determined from their spectroscopic (^1H NMR and MS) data.

cyclohexanone showed the similar activity towards the condesation with aromatic aldehydes. All the reactions were free from by-products, which are generally found in classical reactions conditions [5]. The structures of the products were established here from their spectroscopic (^1H NMR and MS) data. In absence of iodine no product could be detected within 6 h of reaction indicating the catalytic role of iodine.

In the present conversion iodine has been found to be more efficient than the conventional Lewis acids such as $ZnCl_2$, $SnCl_2$, $FeCl_3$ and $AlCl_3$ in terms of yields and times of reaction [7l]. These metal chlorides induced the self-condensation of aldehydes and ketones rather than the cross-Aldol condensation. Iodine showed remarkable efficiency at room temperature. There are a limited number of methods where the catalyst is active at room temperature to afford high yields of the target products [7k].

In conclusion, we have developed an easy and efficient method for cross-Aldol condensation of aromatic aldehydes with cyclic ketones to form α,α′-bis(substituted-benzylidene) cycloalkanones using iodine at ambient temperature. The mild reaction conditions, shorter reaction times, high yields and application of an inexpensive and readily available catalyst are the great advantages of the method.

1. Experimental section

1.1. General procedure for the preparation of α,α′-bis(substituted-benzylidene) cycloalkanones

To a solution of an aromatic aldehyde (2.2 mmol) and a cyclic ketone (1 mmol) in CH_2Cl_2 (5 mL) iodine (0.076 g, 0.3 mmol) was added. The mixture was stirred at room temperature and the reaction was monitored by TLC. After completion the mixture was treated with aqueous $Na_2S_2O_3$ solution and extracted with EtOAc (3 × 10 mL). The extract was concentrated and residue was subjected to column chromatography over silica gel using 30% EtOAc in hexane as eluent to obtain pure α,α′-bis(substituted-benzylidene) cycloalkanone.

The spectral (^{1}H NMR and MS) and analytical data of the unknown compounds are given below.

1.1.1. Compound ***3e***

Light yellow solid; mp 178–180 °C; ^{1}H NMR ($CDCl_3$ 200 MHz): δ 7.75 (2H, brs), 7.10 (2H, dd, *J* = 8.0, 2.0 Hz), 7.01 (2H, d, *J* = 2.0 Hz), 6.96 (2H, d, *J* = 8.0 Hz), 5.82 (2H, brs), 3.90 (6H, s), 2.94 (4H, dt *J* = 7.0, 2.0 Hz), 1.90–1.73 (2H, m). EIMS: *m/z* 366 ($M^{+\bullet}$). Anal. calcd. for $C_{22}H_{22}O_5$: C, 73.10; H, 6.00; Found: C, 73.18; H, 6.09.

1.1.2. Compound ***3k***

Yellow needles; mp 200–202 °C; ^{1}H NMR ($CDCl_3$ 200 MHz): δ 8.33 (2H, brs), 8.21 (2H, dd, *J* = 8.0, 2.0 Hz), 7.78 (2H, d, *J* = 2.0 Hz), 7.74 (2H, dd, *J* = 8.0, 2.0), 7.60 (2H, t, *J* = 8.0 Hz), 2.99 (4H, dt, *J* = 7.0, 2.0 Hz), 1.95–1.82 (2H, m). EIMS: *m/z* 364 ($M^{+\bullet}$). Anal. calcd. for $C_{20}H_{16}N_2O_5$: C, 65.93; H, 4.39; N, 7.69; Found: C, 65.99; H, 4.44; N, 7.73.

1.1.3. Compound ***3l***

Yellow solid; mp 102–104 °C; ^{1}H NMR ($CDCl_3$ 200 MHz): δ 7.827.46 (10H, m), 2.93 (4H, dt, *J* = 7.0, 2.0 Hz), 1.98–1.77 (2H, m). EIMS: *m/z* 410 ($M^{+\bullet}$). Anal. calcd. for $C_{22}H_{16}OF_6$: C, 64.39; H, 3.90; F, 27.80; Found: C, 64.46; H, 3.98; F, 27.87.

1.1.4. Compound ***3r***

Light yellow solid; mp 172–174 °C; ^{1}H NMR ($CDCl_3$ 200 MHz): δ 7.54 (2H, brs), 7.22 (2H, dd, *J* = 8.0, 2.0 Hz), 7.12 (2H, d, *J* = 2.0 Hz), 6.99 (2H, d, *J* = 8.0 Hz), 3.95 (6H, s), 3.10 (4H, brs). EIMS: *m/z* 352 ($M^{+\bullet}$). Anal. calcd. for $C_{21}H_{20}O_5$: C, 71.59; H, 6.68; Found: C, 71.63; H, 6.69.

1.1.5. Compound ***3t***

Yellow solid; mp 206–208 °C; ^{1}H NMR ($CDCl_3$ 200 MHz): δ 7.85–7.52 (10H, m), 3.15 (4H, m). EIMS: *m/z* 396 ($M^{+\bullet}$). Anal. calcd. for $C_{21}H_{14}OF_6$: C, 63.63; H, 3.53; F, 28.78; Found: C, 63.69; H, 3.59; F, 28.80.

Acknowledgements

The authors thank CSIR and UGC, New Delhi for financial assistance.

References

[1] M. Ogawa, Y. Ishii, T. Nakano, S. Irifune, Jpn. Kohai Tokkyo JP 63192446 A2 (1988) (Chem. Abstr. 1988, 63, 238034).

[2] J. Deli, T. Lorand, D. Szabo, A. Foldesi, Pharmazie 39 (1984) 539–540.

[3] J. Kawamata, K. Inoue, T. Inabe, M. Kiguchi, M. Kato, Y. Taniguchi, Chem. Phys. Lett. 249 (1996) 29–34.

[4] Gangadhara, K. Kaushal, Polymer 36 (1995) 1903–1910.

[5] A.T. Nielsen, W. Houlihan, J. Org. React. 16 (1968) 1–438.

[6] K. Irie, K. Watanabe, Bull. Chem. Soc. Jpn. 53 (1980) 1366–1371.

[7] (a) T. Nakano, T. Migita, Chem. Lett. (1993) 2157–2158;
(b) M. Zheng, L. Wang, J. Shao, Q. Zhong, Synth. Commun. 27 (1997) 351–354;
(c) N. Iranpoor, F. Kazemi, Tetrahedron 54 (1998) 9475–9480;
(d) W.L. Bao, Y.M. Zhang, You Ji Hua Xue 18 (1998) 272–274;
(e) T. Nakano, S. Irfune, S. Umano, A. Inada, Y. Ishii, M. Ogawa, J. Org. Chem. 52 (1987) 2239–2244;
(f) N. Iranpoor, B. Zeynizadeh, A. Aghaapour, J. Chem. Res (S) (1999) 554;
(g) J.S. Yadav, B.V.S. Reddy, A. Nagaraju, J.A.R.P. Sarma, Synth. Commun. 32 (2002) 893–896;
(h) X.Y. Zhang, X.S. Fan, H.Y. Niu, J.J. Wang, Green Chem. 5 (2003) 267–269;
(i) D.F. Huang, J.X. Wang, Y.L. Hu, Chin. Chem. Lett. 14 (2003) 333;
(j) G. Deng, T. Ren, Synth. Commun. 33 (2003) 2995–3001;
(k) G. Sabitha, G.S.K. Reddy, K.B. Reddy, J.S. Yadav, Synthesis (2004) 263–266;
(l) L. Wang, J. Sheng, H. Tian, J. Han, Z. Fan, C. Qian, Synthesis (2004) 3060–3064.

[8] P. Saleshi, M.M. Khodaei, M.A. Zolfigol, A. Keyvan, Monatsch. Chem. 133 (2002) 1291–1295.

[9] (a) H. Firouzabadi, N. Iranpoor, H. Hazarkhani, J. Org. Chem. 66 (2001) 7527–7529;
(b) K. Ramalinga, P. Vijayalakshmi, T.N.B. Kaimal, Tetraheron Lett. 43 (2002) 879–882;
(c) J.S. Yadav, B.V.S. Reddy, M.S. Reddy, A.R. Prasad, Tetrahedron Lett. 43 (2002) 9703–9706;
(d) B. Das, J. Banerjee, R. Ramu, R. Pal, N. Ravindranath, C. Ramesh, Tetrahedron Lett. 44 (2003) 5465–5468;
(e) K.V.N.S. Srinivas, B. Das, Synthesis (2004) 2091–2093;
(f) B.K. Banik, M. Fernandez, C. Alvarez, Tetrahedron Lett. 46 (2005) 2479–2482.