SHORT PAPER

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Synthesis of α,α′-bis(substitutedbenzylidene) cycloalkanones by a grinding method†

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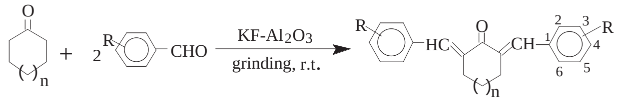
$KF-Al_2O_3$ catalyses the crossed aldol condensation of various aromatic aldehydes with cycloalkanones, giving corresponding α,α′-bis(substitutedbenzylidene)cycloalkanones under solvent free conditions by a grinding method at room temperature.

Keywords: bis(substitutedbenzylidene)cycloalkanones synthesis grinding method

Due to the importance of the methylene structural unit which is found in many naturally occurring compounds and antibiotics and the use of α,α′–bis(substitutedbenzylidene)cycloalkanones as precursors for the synthesis of bioactive pyrimidine derivatives,[1] condensations of cycloalkanones with aromatic aldehydes are of special interest. Several methods are available for the preparation of these compounds, but they usually have some disadvantages: traditional acid- or basic-catalyzed reaction[2] suffers from the reverse reaction and the catalyst cannot be recycled easily, some metal ions or organometallic compounds used as catalysts or reagents[3-9] are not prepared easily, and so on. Recently, the application of inorganic supported catalysts in organic synthesis has rapidly increased[10] because such reactions often involve easier work-up procedures than homogenous methods. $KF-Al_2O_3$ is an efficient supported catalyst for Knoevenagel condensation under ultrasound irradiation.[11]



1 **2a~2f** **3a~3l**

n= 0		*n*= 0	*n*= 1
n= 1	**2a:** R= H	**3a:** R= H	**3g:** R= H
	2b: R= 4-CH_3O	**3b:** R= 4-CH_3O	**3h:** R= 4-CH_3O
	2c: R= 4-Cl	**3c:** R= 4-Cl	**3i:** R= 4-Cl
	2d: R= 4-NO_2	**3d:** R= 4-NO_2	**3j:** R= 4-NO_2
	2e: R= 3-NO_2	**3e:** R= 3-NO_2	**3k:** R= 3-NO_2
	2f: R= 4-CH_3	**3f:** R= 4-CH_3	**3l:** R= 4-CH_3

The grinding method has increasingly been used in organic synthesis in recent years. Compared with traditional methods, this method is more efficient and selective. A large numbers of organic reactions can be carried out in high yield, under mild conditions and simply by the grinding method.[12-16]

All of the results stated above spur us to study the possibility of crossed aldol condensation of aromatic aldehydes with cycloalkanones catalysed by an other catalyst without solvent. Herein, we wish to report the condensation using $KF-Al_2O_3$ as catalyst under solvent free conditions by the grinding method at room temperature.

Some products described herein were previously prepared by classical methods. As shown in Table 1, the crossed aldol condensation of cycloalkanones with aromatic aldehydes affords α,α′–bis(substitutedbenzylidene)cycloalkanones in good yields. The solvent-free grinding method represented a better procedure in terms of the higher yield, milder reaction and easier work-up. For example, compounds (**3b**, **3d**, **3h**, **3j** and **3i**) were previously prepared in moderate yields (53.5%[8], 81%[8], 69.5%[8], 71.4%[8], 40–60%[2]) by the heating method in solution, whereas under solvent-free condition by the grinding method they were obtained in higher yields (90%, 92%, 89%, 90% and 91%). In order to compare the efficiency of the grinding method, the reaction of benzaldehyde with cycloalkanones by stirring using ethanol as solvent was studied; the yield is not good (Table 1, **3a**[c] and **3g**[c]). This is because that the reaction in the absence of solvent has a high concentration of reactants and the surface area of the catalyst increases greatly on being ground. Similar results are given in the reaction of benzaldehyde with cycloalkanones on 20 mmol scale (Table 1, **3a**[d] and **3g**[d]).

$KF-Al_2O_3$ is able to be reused after simple heating at 120 °C for 4h. We have successfully used the recycled $KF-Al_2O_3$ to catalyse the crossed aldol condensation of cycloalkanones with aromatic aldehydes, the yield of which is excellent (Table 2).

In the reaction, whether the mole ratio of the benzaldehyde to cyclopentanone is 2:1, 1:1 or 1:2, α, α′ –bis(substitutedbenzylidene)cyclopentanone (**3a, 3a**[a]**, 3a**[b]) is the only product and the yields are 86%, 87% and 86%, respectively.

In conclusion, We have found a practical crossed aldol condensation for the preparation of α,α′ –bis(substitutedbenzylidene)cycloalkanones catalysed by $KF-Al_2O_3$ in absence of solvent by using the grinding method at room temperature.

Experimental

Liquid aldehydes and cycloalkanones were purified by distillation before use. IR spectra were recorded on a Bio-Rad FIS-40 spectrometer (KBr). MS were determined on a VG-7070E spectrometer (EI, 70eV). ^1H NMR spectra were measured on an AVANCE-400 spectrometer using TMS as internal standard and $CDCl_3$ as solvent.

Preparation and activation of $KF-Al_2O_3$: The $KF–Al_2O_3$ was prepared by dissolving 20g of KF in 80 ml of water and 30g of basic Al_2O_3.The mixture was stirred at 65 °C ~75 °C for 1h. The water was removed under reduced pressure. The resulting free flowing powder was dried at 120 °C for 4h. The content of KF is about 30%.

General procedure: Aromatic aldehyde (2 mmol), cycloalkanone (1 mmol) and $KF-Al_2O_3$ (200mg) were added to a mortar. The mixture was ground by mortar and pestle at room temperature for 5 min, and was kept at room temperature for a period. The completion of the reaction was monitored with TLC. The product was extracted with dichloromethane and filtered; the solvent was evaporated under reduced pressure. The solid obtained was recrystallised from 95% EtOH, affording **3a**–**3l**. The authenticity of the products was established by comparing their melting points, IR, MS, and ^1H NMR spectra with the data in the literature.

3d: ν_{max}/cm^{-1} (KBr) 3 080, 1 680, 1 610, 1 520, 1 350, 1 260, 1 190, 870, 820, 770; δ_H 3.22 (m, 4H $–CH_2\text{-}CH_2\text{-}$), 7.67 (s, 2 H, 2 $–HC=$),

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† This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*

Table 1 Condensation of cycloalkanones with aromatic aldehydes catalysed by KF-Al_2O_3

Product	n	R	Reacn. Time/min	Room temp. /°C	M.p. (lit. m.p.)/°C	Yield*, (%)(lit)
3a	0	H	25	17	188–190 (188–189)[8]	86 (84.5)[8]
3a[a]	0	H	20	23	188–190	87
3a[b]	0	H	20	23	188–190	86
3a[c]	0	H	25	25	188–190	43
3a[d]	0	H	25	22	188–190	91
3b	0	4-CH_3O	20	17	209–210 (210–211)[8]	90 (53.5)[8]
3c	0	4-Cl	15	18	221–222 (221–223)[17]	93 (95)[17]
3d	0	4-NO_2	15	19	251–253 (259–260)[18,E]	92 (81)[8]
3e	0	3-NO_2	15	18	224–226 (222)[19]	85
3f	0	4-CH_3	30	16	234–236 (235–236)[2]	89 (60-90)[2]
3g	1	H	40	19	114–116 (114–115)[17]	89 (87)[17]
3g[c]	1	H	40	23	114–116	47
3g[d]	1	H	46	22	114–116	90
3h	1	4-CH_3O	40	20	158–160 (157–162)[20,E]	89 (69.5)[8]
3i	1	4-Cl	35	18	144–146 (146–147)[17]	90 (91)[17]
3j	1	4-NO_2	30	17	207–208 (206)[21,E]	90 (71.4)[8]
3k	1	3-NO_2	30	16	189–190 (189–191)[20]	87
3l	1	4-CH_3	50	19	168–169 (170)[2]	91 (40-60)[2]

* Isolated yield, based on the aldehydes.
[a] The mole ratio of benzaldehyde to cyclopentanone is 1:1. [b] The mole ratio of benzaldehyde to cyclopentanone is 1:2. [c] Ethanol as solvent, stirring method. [d] The reaction was carried out on 20 mmol scale. [e] The melting points of **3d, 3h**, and **3j** given in ref. 8 must be incorrect.

Table 2 The condensation of cycloalkanones with aromatic aldehydes catalysed by recycled KF–Al_2O_3

Product	n	R	Reacn. time/min	Room temp. /°C	M.p./°C	Yield*, (%)
3e	0	3-NO_2	25	24	224-226	86
3f	0	4-CH_3	45	24	235-237	88
3g	1	H	50	23	114-116	89
3h	1	4-CH_3O	50	23	160-161	90
3i	1	4-Cl	35	23	144-146	90

* Isolated yield, based on the aldehydes.

7.76 (d, *J* 8.0 Hz, 4 H, $H_{2,6}$), 8.33 (d, *J*8.0Hz, 4 H, J 8.0 Hz, $H_{3,5}$); *m/z*: 350 (M^+, 15), 304 (15), 303 (46), 228 (13), 126 (43), 115 (100), 77 (32).

3e: ν_{max}/cm^{-1} (KBr) 2 922, 1 691, 1 613, 1 528, 1 350, 1 246, 1 184, 899, 810, 736; δ_H 3.26 (s, 4 H –CH_2–CH_2–), 7.67 (m, 4 H, $H_{5,6}$), 7.91 (d, 2 H, *J* 7.5 Hz, H_4), 8.28 (d, *J* 6.3 Hz, 2 H, H_2), 8.49 (s, 2 H, 2 -C*H*=); *m/z* 350 (M^+, 15), 303 (20), 228 (10), 128 (23), 115 (60), 101 (15), 89 (18), 75 (18).

3h: ν_{max}/cm^{-1} (KBr) 2 850, 1 670, 1 590, 1 240,1 150–1 101, 1 018, 930, 828; δ_H 1.76 (m, 2H, –CH_2–CH_2 –CH_2–), 2.94 (m, 4 H, –CH_2–CH_2–CH_2-), 3.86 (s, 6 H, 2 –OCH_3), 6.95 (t, J_1 8.7 Hz, J_2 2.4 Hz, 4 H, $H_{3,5}$) 7.47 (d, *J* 8.7 Hz, 4 H, $H_{2,6}$), 7.78 (s, 2 H, 2 –*H*C=); *m/z* 334 (M^+,19), 306 (15), 270 (11), 172 (11), 160 (15), 147 (62), 131 (47), 121 (55), 115 (40), 103 (100), 91 (38), 77 (38).

3j: ν_{max}/cm^{-1} (KBr) 3 100, 1 680, 1 590, 1 520, 1 490, 1 350, 860, 810; δ_H 1.86 (m, 2 H –$CH_2CH_2CH_2$-), 2.95 (m, 4 H, –CH_2–CH_2–CH_2), 7.60 (t, *J* 8 .9 Hz, 4 H, $H_{2,6}$), 7.80 (s,2 H, 2 -*H*C=), 8.28 (d, *J* 8.7 Hz, 4 H, $H_{3,5}$); *m/z* 364 (M^+,6), 348 (30), 318 (15), 290 (19), 245 (11), 216 (28), 168 (19), 153 (20), 128 (50), 115 (71), 103 (42), 91 (29), 77 (45), 65(80).

3k: ν_{max}/cm^{-1} (KBr) 2 952, 1 662, 1 609, 1 527, 1 347, 1 168, 896, 807, 719; δ_H 1.89 (m, 2 H –CH_2–CH_2–CH_2–), 2.99 (m, 4 H, –CH_2–CH_2-CH_2–), 7.63 (t, *J* 7.3 Hz, 2 H, H_5), 7.78 (d, *J* 7.3 Hz, 2 H, H_6), 7.83 (s, 2 H, H_2), 8.23 (d, *J* 5.9 Hz, 2 H, H_4), 8.34 (s,2 H, -*H*C=); *m/z* 364(M^+, 30), 347 (53), 317 (20), 289 (20), 215 (15), 165 (15), 152 (15), 128 (48), 115 (48), 101 (18), 89 (20), 77 (35), 63 (20).

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References

1 J. Deli, T. Lorand, D. Szabo and A. Foldesi, *Pharmazi*, 1984, **39**, 539.
2 B.A. Hathaway, *J. Chem. Educ*., 1987, **64**, 367.
3 N. Tatsuya, I. Shinji, U. Shigetoshi, I. Akihiro, I. Yasutaka and O. Masaya, *J. Org. Chem.*, 1987, **52**, 2239.
4 T. Nakano and T. Migita, *Chem. Lett.*, 1993, **21**, 57.
5 W. L. Bao and Y. M. Zhang, *Chin. J. Org. Chem.*, 1998, **18**, 272.
6 N. Iranpoor and F. Kazemi, *Tetrahedron*, 1998**, 54**, 9475.
7 N. Iranpoor, B. Zeynizadeh and A. Aghapour, *J. Chem. Research* (S), 1999, 554.
8 M. Zheng, L.C. Wang, J.G. Shao and Q. Zhong, *Synth. Comm.*, 1997, **27**, 351.
9 N.J. Leonard, L.A. Miller and J.W. Berry, *J. Am. Chem. Soc.*, 1957, **79**, 1482.
10 E. Obrador, M. Castro, J. Tamariz, G. Zepeda, R. Miranda and F. Delgado, *Synth. Comm.*, 1998, **28** (24), 4649.
11 S.X. Wang, J.T. Li, W.Z. Yang and T.S. Li, *Ultrason. Sonochem.*, 2002, **9**, 159.
12 J. Morey and A. Frontera, *Chem. Ed.*, 1995, **72,** 63.
13 F. Toda, K. Tanaka and A. Sekikawa, *JCS, Chem. Commun.*, 1987, 279.
14 K. Tanaka and F. Toda, *Chem. Rev.*, 2000, **100**, 1025.
15 X.L. Li, H. Ma, Y.M. Wang and J.B. Meng, *Chem. J. Chin.Univer.*, 1995, **16**, 1903.
16 L.J. Geng, S.X. Wang, J.T. Li and C.H. Liu, *Chin. J. Org. Chem.*, 2002, **22**, 1047.
17 J.F. Zhou, J.M. Xu, H. Wei and L.L. Zhang, *Chin. J. Org. Chem.*, 2001, **21**, 322.
18 H. Heinrich and D. Dieter, *Ann.*1962, **656**, 89 (CA **57**:14951h, 1962)
19 R.W. Kierstead, R.P. Linstead and B.C.L. Weedon, *J. Chem. Soc.*, 1952, 3616 (Chem. Abs. **47**:4847i, 1953)
20 E.P. Dibella, U.S. 3389986, 1968 (Chem. Abs. **69**:5182y, 1968)
21 M. Ionescu and C. Makkay, Studia Univ. Babes-Bolyai, Ser. Chem. 1966, **11**, 115 (Chem. Abs **65**:20115b, 1966)