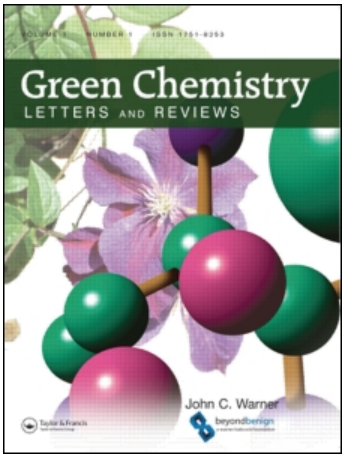

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An efficient green procedure for the synthesis of chalcones using C-200 as solid support under grinding conditions

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ORIGINAL ARTICLE

An efficient green procedure for the synthesis of chalcones using C-200 as solid support under grinding conditions

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A simple, rapid, efficient and environmentally benign procedure for the synthesis of chalcones has been achieved by grinding aryl aldehydes and acetophenones with anhydrous barium hydroxide (C-200) in the absence of any solvent. The use of organic solvent for extraction of compound is also avoided. This present method is highly useful for the synthesis of 2′-hydroxy chalcones, required intermediates for the synthesis of flavanoids.

Keywords: aryl aldehyde; chalcones; solid base; solvent-free conditions

Introduction

In recent years chemistry of chalcones has attracted attention as these compounds have been found to exhibit anticancer (*1*), antimalarial (*2*), antimicrobial (*3*) and antiinflammatory (*4*) activities. 2′-Hydroxy chalcones are a group of naturally occurring compounds and are used as the intermediates for the synthesis of various other flavanoids (*5,6*). Generally, chalcones are obtained by Claisen Schmidt condensation between aryl aldehydes and acetophenones in the presence of alkali metal hydroxide or sodium ethoxide (*7*). The use of several other catalysts such as basic alumina (*8*), zinc chloride (*9*), Lewis acid such as BF_3, $AlCl_3$ (*10*), Mg–Al–OBu hydrotalcite (*11*), has also been reported. Other reagents and conditions have also been used, including the use of strong alkali catalysts under phase transfer conditions (*12*), barium hydroxide in ethanol (*13*), calcine $NaNO_3$/natural phosphate (*14*), potassium phosphate (*15*), the use of M.W. conditions (*16*), and ultrasonic conditions (*17*).

All these reported methods make use of organic solvents either during condensation reactions or during isolation of the products by way of extraction. These organic solvents have been considered to be hazardous to human health and the environment due to their volatile nature. Thus developments of procedures under solvent-free conditions have attained much importance as being eco-friendly alternatives. Most of these methods when used for the synthesis of 2′-hydroxy chalcones generally are accompanied by the formation of flavanones, aurones via cyclization (13). Very poor yield, long reaction time and complexity of the procedures are also *major limitations* of the reported methods (Table 1).

Results and discussion

We wish to report herein a simple and rapid procedure for the synthesis of chalcones (Scheme 1) which involves the grinding of a mixture of aryl aldehydes, acetophenones and anhydrous barium hydroxide in a mortar and pestle for 2–5 minutes in the absence of any solvent. The product is also easily obtained by acidifying the mixture without extraction. Poor yields were obtained when barium hydroxide was replaced by other solid bases such as magnesium oxide, calcium oxide, basic alumina and calcium hydroxide and also the reaction was not found to be completed after a long period. The efficiency of the anhydrous barium hydroxide (C-200) as catalyst in the present case appears due to the appropriate crystalline structure of barium hydroxide and the nature of adsorbed carbanion and aldehyde on it (*13*). To fine-tune the amount of C-200 required for the reaction to occur, different amounts of C-200 were used. The best results were obtained when 3–4 molar equivalents of C-200 were used.

To check the validity of the results, various substituted aryl aldehydes and acetophenones were condensed to obtain chalcones in high yield (83–92%). The present method was found to be highly useful as condensation between 2′-hydroxy acetophenones and aryl aldehydes which gave 2′-hydroxy chalcones selectively. No cyclization was found to take place under these conditions to give side

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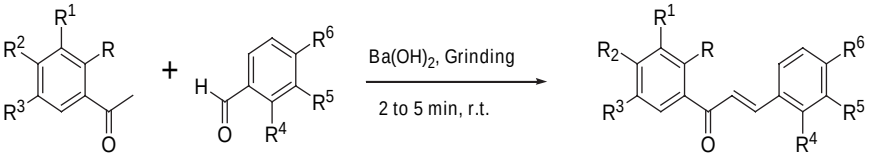
Table 1. Comparison of the results of the present method used for the synthesis of chalcones with the reported ones.

Entry	Catalyst	Time	Temperature	Yield (%)	Ref.
1	KOH	24–47 hours	Room temperature	41–50	*7*
2	Basic Al_2O_3	2.5 hours	Room temperature	72–83	*8*
3	$ZnCl_2$	Five minutes	M.W.	75–90	*9*
4	$ZnCl_2$	Six hours	100°C	45–50	*9*
5	$AlCl_3/CS_2$	Six hours	Room temperature	91	*10b*
6	BF_3	Three hours	Room temperature	61	*10a*
7	$KOH/TEBA/C_2H_5OH/H_2O$	24 hours	30°C	71–92	*12*
8	Mg–Al–O^{t}Bu hydrotalcite/Toluene	1–8 hours	Reflux	77–93	*11*
9	$NaNO_3/NP/CH_3OH$	16–48 hours	Room temperature	40–98	*14*
10	KOH/C_2H_5OH	4–300 minutes	Ultrasound irradiation	52–97	*17b*
11	KF/Al_2O_3	4–960 minutes	Ultrasound irradiation	83–98	*17b*
12	$NaOH/C_2H_5OH/$	Two minutes	M.W.	85–96	*16*
13	$Ba(OH)_2/C_2H_5OH$	Four hours	Reflux	24–89	*13*
14	$Ba(OH)_2/C_2H_5OH$	10 minutes + 24 hours	Ultrasound irradiation	5–80	*17a*
15	$Ba(OH)_2$ grinding*	2–5 minutes	Room temperature	83–92	–

*Present method.



Scheme 1. General procedure for the synthesis of chalcones.

products. The reaction time reduces from hours to few minutes and the yields are much better (Table 2). To our knowledge it is the first time when C-200 catalyst has been used for condensation reactions for the synthesis of chalcones at room temperature in the absence of any solvent.

Conclusion

In conclusion, we have described a simple, highly efficient and economical protocol for the synthesis of chalcones by grinding technique under solvent-free conditions in high yields.

Table 2. Synthesis of chalcones[a] under solvent-free conditions by grinding.

Entry	R	R^1	R^2	R^3	R^4	R^5	R^6	Melting point (°C)	Low melting point (°C)	Yield (%)[b]
1	H	H	H	H	H	H	H	55–56	55(*9*)	90
2	H	H	H	H	H	H	CH_3	94–95	96(*17b*)	88
3	H	H	Br	H	H	H	OCH_3	145–147	145–146(*18*)	92
4	H	NO_2	H	H	H	H	OCH_3	167–169	167–168(*19*)	85
5	H	H	H	H	H	H	NO_2	160–161	160(*17b*)	87
6	H	H	H	H	H	H	OCH_3	74–75	76(*9*)	91
7	H	H	H	H	H	H	Cl	112–113	112(*9*)	85
8	OH	H	H	H	H	H	H	89–90	88(*13*)	87
9	OH	H	H	H	H	H	Cl	148–150	150(*13*)	84
10	OH	H	H	H	H	H	OCH_3	90–92	92(*13*)	83
11	OH	H	H	H	H	H	CH_3	105–106	108(*13*)	86
12	OH	H	H	H	H	H	NO_2	205–206	209(*13*)	88
13	OH	H	H	H	OCH_3	H	OCH_3	113–115	114–115(*20*)	88
14	OH	H	OCH_3	H	H	H	OCH_3	110–112	113–114(*21*)	90
15	OH	H	OCH_3	H	OCH_3	H	OCH_3	154–156	156(*21*)	84

[a]All the compounds were characterized by ^{1}H NMR, IR and compared with their reported melting points.
[b]Yield after recrystallization.

Experimental section

The reaction by grinding was carried out in a mortar and pestle at room temperature. During the grinding, sudden change in color took place, indicating the progress of reaction. The full conversion of the reaction mixture to a solid mass indicates the completion of reaction. The ^{1}H NMR spectra were recorded on Bruker Avance II 400 spectrometer at 400 MHz in $CDCl_3$ using TMS as internal standard. The IR spectra were recorded using Perkin Elmer spectrometer (KBr plates).

General procedure

A mixture of acetophenone (4 mmol), aryl aldehyde (4.1 mmol) and anhydrous barium hydroxide (C-200, 2 g) is ground at room temperature for 2–5 minutes in a mortar and pestle. The reaction mixture is allowed to stand for 10 minutes. Ice-cold water (30 ml) was added to the reaction mixture and acidified with conc. HCl. The product was collected by vacuum filtration and then recrystallized from ethanol.

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References

(1) (a) Wattenberg, L.W.; Coccia, J.B.; Galbraith, A.R. *Cancer Lett*. **1994**, *83* (1), 165; (b) Dinkova-Kostova, A.T.; Abeygunawardana, C.; Talalay, P. *J. Med. Chem*. **1998**, *41* (26), 5287.
(2) Ram, V.J.; Saxena, A.S.; Srivastava, S.; Chandra, S. *Med. Chem. Lett*. **2000**, *10* (19), 2159.
(3) Kidwai, M.; Sapra, P.; Misra, P.; Saxena, R.K.; Singh, M. *Bioorg. Med. Chem*. **2001**, *9* (2), 217.
(4) Ballesteros, J.F.; Sanz, M.J.; Ubeda, A.; Miranda, M.A.; Iborra, S.; Paya, M.; Alcaraz, M.J. *J. Med. Chem*. **1995**, *38* (14), 2794.
(5) Harborne, J.B.; Mabry, T.J.; Mabry, H. *The Flavonoids*; Chapmann & Hall: London, 1975; pp 127–213.
(6) Dhar, D.N. *The Chemistry of Chalcones and Related Compounds*; Wiley: New York, 1981.
(7) Dhar, D.N.; Lal, J.B. *J. Org. Chem*. **1958**, *23*, 1159.
(8) Rajender, S.V.; George, N.K.; Lau, T.; Richard, M. *Synth. Commun*. **1985**, *15*, 279.
(9) Reddy, G.V.; Maitraie, D.; Narsaiah, B.; Rambabu, Y.; Rao, P.S. *Synth. Commun*. **2001**, *31* (18), 2881.
(10) (a) Breslow, D.S.; Hauser, C.R. *J. Am. Chem. Soc*. **1940**, *62*, 2385; (b) Calloway, N.O.; Green, L.D. *J. Am. Chem. Soc*. **1937**, *59*, 809.
(11) Kantam, M.L.; Prakash, V.B.; Reddy, C.V. *Synth. Commun*. **2005**, *35*, 1971.
(12) Jain, P.K.; Pinkey; Grover, S.K. *Curr. Sci* **1983**, *52*, 1185.
(13) Alcantara, D.R.; Marinas, J.M.; Sinisterra, J.V. *Tetrahedron Lett*. **1987**, *28* (14), 1515.
(14) Sebti, S.; Solhy, A.; Tahir, R.; Boulaajaj, S.; Mayoral, J.A.; Fraile, J.M.; Kossir, A.; Oumimoun, H. *Tetrahedron Lett*. **2001**, *42*, 7953.
(15) Pore, D.; Desai; Uday; Thopte, T.; Wadgaonkar, P. *Russ. J. Org. Chem*. **2007**, *43* (7), 1088.
(16) Gupta, R.; Gupta, A.K.; Paul, S.; Kachroo, P.L. *Indian J. Chem*. **1995**, *34 B*, 61.
(17) (a) Fuentes, A.; Marinas, J.M.; Sinisterra, J.V. *Tetrahedron Lett*. **1987**, *28* (39) 4541; (b) Li, J.T.; Yang, W.Z.; Wang, S.X.; Li, S.H.; Li, T.S. *Ultrason. Sonochem*. **2002**, *9*, 237; (c) Calvino, V.; Picallo, M.; Lopez-Peinado, A.J.; Martin-Aranda, R.M.; Duran-Valle, C. *J. Appl. Surf. Sci*. **2006**, *252*, 6071.
(18) Barnes, R.P.; Godwin, T.G. J. *Am. Chem. Soc*. **1947**, *69*, 3135.
(19) Barnes, R.P.; Sneed, J.L. *J. Am. Chem. Soc*. **1945**, *67*, 138.
(20) Ozawa, H; Okuda, T; Kawanishi, M.; Fujii, K. *J. Pharm. Soc. Jpn*. **1951**, *71*, 1178.
(21) Singh, O.V.; Muthukrishnan, M. *Indian J. Chem*. **2005**, *44B*, 2575.