HL ISSN: 2231 – 3087(print) / 2230 – 9632 (Online)
http://heteroletters.org Vol. 3: (1), 2013, 37-40

SYNTHESIS OF CHALCONES BY A CLAISEN – SCHMIDT REACTION USING MAGNESIUM HYDROGEN SULPHATE AS A CATALYST UNDER SOLVENT – FREE CONDITION

Jayapal .Maleraju, and N.Y. Sreedhar

Department of Chemistry, S.V. University, Tirupati - 517 502
Email; mrjayapal007@gmail.com

Abstract:-

Cross aldol condensations of ketones with aromatic aldehydes are carried out efficiently in the presence of magnesium hydrogen sulfate under solvent – free conditions in good to excellent yield without the occurrence of any self – condensation.

Key Words:-

Aldehydes, Crossaldol reaction, Ketones, Magnesium hydrogen sulfate.

Introduction:-

α, β – Unsaturated ketones, especially 1,3 – diarylprop –2-en- 1 – ones, commonly known as chalcones, have received considerable attention in Medicinal Chemistry. Chalcones of natural or synthetic compounds belonging to the flavonoid family,[II] and they are important compounds not only because of their biological properties but also because they serve as important intermediates for the synthesis of a large number of hetero cyclic systems,[I] They are also very important as a Michael acceptor in organic syntheses. [III]

Moreover, Chalcones have been extensively studied [IV] for their broad spectrum of biological activities, including bacteriostatic, fungistatic, antiparasitic, cardiovascular, antitumor, [V] anticancer,[VI,VII] anti-inflammatory,[VIII,IX] antileishmanial, [X] antitubercular, [XI] and antifung[XII]activities. In fact, the pharmocological properties of chalcones are due to the presence of both α,β – un saturation [XIII] and an aromatic ring. Constant in chalconeshas resulted in syntheses of new derivatives using both classical [XIV], [XV] and combinatorial techniques. [XVI]

Experimental

Products were characterized by ^{1}H NMR, IR, and mass spectra ^{1}H NMR spectra were run on a Bruker Avance 500 spectrometer at 500 MHz. IR spectra were obtained using a JASCO FT/IR-5300 spectrophotometer. Mass spectra were recorded on a Shimadzu LCMS-2010 spectrometer. Melting points were determined in open capillaries with a Galenkamp melting point apparatus and are corrected. Reaction monitoring was accomplished by thin layer chromatography on silica gel PolyGram S1L G/UV 254 sheets. Yields refer to isolated products.

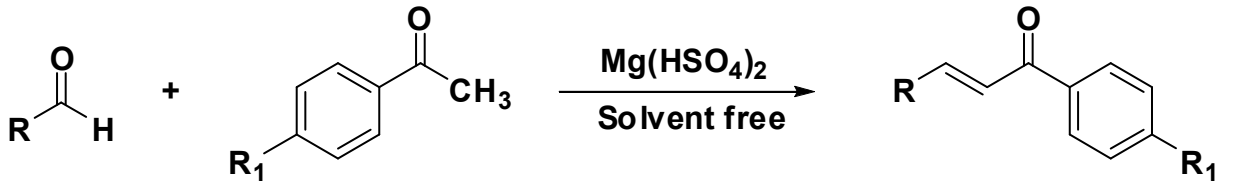
Preparation of magnesium hydrogen sulfate

A 500 cm^3 suction flask was equipped with a constant-pressure dropping funnel. The gas outlet

was conducted to a vacuum system through an adsorbing solution (H_20) and an alkali trap. Anhydrous $MgC1_2$ (47.6 g, 0.5 mol) was charged in the flask, and concentrated H_2SO_4 (98.07 g, 1 mol) was added drop wise over a period of 30 min at room temperature. HCl gas was evolved immediately. After completion of the addition, the mixture was shaken for 30 min; meanwhile, the residual HCl was removed by suction. $Mg\ (HS0_4)_2$ was obtained as a white solid material (107 g).

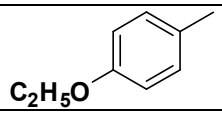
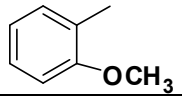
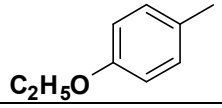
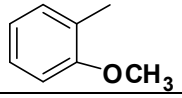
General procedure

Ketone (1.20g), aromatic aldehyde (1.O6g), and $Mg(HSO_4)_2$ (4 mmol) were placed in a mortar and mixed. The mixture was heated in an oven at 60°C for 2-8 h. For monitoring of the reaction progress, a sample of the reaction mixture was added to a few drops of CH_2Cl_2, and the solution was subjected to TLC after insoluble $Mg(HSO_4)_2$ had settled down. After completion of the reaction, 40 em^3 CH_2C1_2 were added, the mixture was filtered over a sintered glass funnel, and the residue was washed with 2x 10 em^3 CH_2C1_2. The solvent was evaporated, and the remaining solid was purified on a short silica gel column (eluent: $CC1_4$:CH_2C1_2= 3:2) or by recrystallization from EtOH.



synthesis of chalcones. **T**

TABLE-1

Product	*R*	*R1*	Time (mins)	Yield (%)	MP(^{0}C)
1a		**H**	**30**	**88**	**51**
1b		**H**	**26**	**86**	**52**
1c		**Cl**	**24**	**86**	**125**
1d		**Cl**	**27**	**86**	**75**

Results and Discussion

the results are summarized in Table 1. Different types of Aromatic ketones and Aldehydes were condensed in the presence of the reagent under neat conditions at 60'C. The results are summarized in Table 1.The reactions were completed within 2-8 h with good to excellent yields;. The reaction of aldehydes with ketones did not proceed satisfactorily. When similar reactions were conducted in different solvents such as dichloromethane, toluene, or acetonitrile, product mixtures were obtained in poor yields. In conclusion, the presented method is a very

efficient and selective protocol for crossed aldol condensations of ketones with aromatic aldehydes with a very cheap and stable reagent. In addition, it has the chemical and environmental advantages of solvent-free reactions.

Physical and spectral data

3-(4-Ethoxypheny1)-1-phenylpropenone

MP 50°C. (52-53)[3D]; IR (KB,'): 3024, 2931, 1665, 1592, 1212, and 762 cm^{-1}; ^{1}HNMR (300 MHz, $CDCl_3$): δ=8,01 (d, *J=7.2* Hz, 2H), 7.79 (d, *J=15.9* Hz, 1H), 7.57-7.38 (m, 6H), 6.89 (d, *.J=7.9* Hz, 2H), 4.01 (q, *J =7.5,* 6.8 Hz, 2H), and 1.40 (t, *J=6.7* Hz, 3H); C^{13} N.M.R. (75 MHz): δ= 190.48, 161.20, 144.74, 138.52, 132.66, 132.30, 128.49, 127.3 119.50, 114.93, 63.52, and 14.54; ESI *(m/z)* 252 $[M+H]^+$ (Table 1, product 1a).

3-(2-Methoxypheny1)-1-phenylpropenone

MP 52-53°C (53-54)[30]; IR (KBr): 3064, 2954, 2834, 1657, 1594, 1342, 1246, 1207, 1016, and 754 cm^{-1}; 1H NMR ($CDC1_3$, 300 MHz): δ= 8.17 (d, *J=15.4* Hz, 1H), 8.04 (d, *J=7.7* Hz, 2H), 7.67-7.45 (m, 5H), 7.34 (t, *J=7.7* Hz, 1H), 6.99-6.94 (t, *J=7.7* Hz, 1H), 6.89 (d, J=9.0 Hz, 1H), and3.8(s,3H); ^{13}CNMR(75MHz):191.01,158.96.138.55,132.79,132.01,129.26,128.5 123.90 122.72,120.89, 111.34, and 55.62; ESI *(m/z)* 239 [M +H] (Table 1. product 1b).

1-(4-Chloropheny1)-3-(4-ethoxyphenyl)-propenone

MP 125°C (125-126)[3°]; **IR** (KBr): 3017, 1654, 1604, 1218, 1026, and 759 cm^{-1};NMR (CDC_3,300 MHz): δ=7.95 (d, J=9.0 Hz, 2H), 7.77 (d, J =15.7 Hz, 1H), 7.56 (d, J=7.9 Hz, 2H), 7.44 (d, *J*=7.8 Hz, 2H), 7.35 (d, *J =15.8* Hz, 1H), 7.31 (d, *J =8.9* Hz, 2H), 4.05 (q, *J =7.5,* 6.8 Hz, 2H), and 1.42 (t, J=6.7 **Hz,** 3H); ^{13}C NMR (50 MHz): the results are summarized in Table 1 = 189.79, 162.06 146.03 139.32, 137.26, 130.28 129.3 127.65 119.31 115.35, 64.15, 15.17. *ESI (m/z) 287 [M +H]* (Table 1, product 1c)

1-(4-Chloropheny1)-3-(2-methoxyphenyl)-propenone

MP 75-76°C (75-76)[30]; IR (KBr): 3015, 2932, 1652, 1594, 1502, 1215, 1164, 1025, and 756 cm^{-1}; NMR($CDC1_3$, 300 MHz): δ= 8.13 (d, *J=14.8* Hz, IH), 7.94 (d, *J=9.2* Hz, 2H), 7.61 (d, *J =8.3* Hz, 1H), 7.54(s, 1H), 7.42 (d, J ---- 7.3 Hz, 2H), 7.36 (t, J 7.4 Hz, 1H), 6.99-6.89 (m, 2H), and 3.88 (s, 3H); ^{13} CNMR (5O MHz): δ =190.06, 159.44, 141.23, 139.29, 137.18, 132.47, 130.4, 129.69. 129.25, 124.06, 122.56, 121.24, 111.68, and 55.93; ESI *(m/z)* 273 $[M+H]^+$. (Table 1, product 1d)

Conclusion

In Summary with continuation of our studies on the application of magnesium hydrogen sulfate as a cheap and versatile reagent in organic synthesis we report a simple, efficient, and selective method for the crossed aldol condensation of ketones with aromatic aldehydes under solvent – free conditions.

REFERENCE

I. Ansari, F. L.; Nazir, S.; Noureen, H.; Mirza, B. Combinatorial synthesis and evaluation of an indexed chalcone library. *Chem. Biodivers.* 2005, *2,* 1656-1664.

II. Lunardi, F.; Guzela, M.; Rodrigues, A. T.; Correa, R.; Eger-Mangrich, I.; steindel, M.; Grisard, E. C.; Assreuy, J.; Calixto, J. B.; Santos, R. S. Trypanocidal and leishmanicidal properties of substitution-containing chalcones. *Antimicro. Agents Chemother.* 2003, 47(4), 1449-1451.

III. Ceylan, M.; Gezegen, H. Preparation of 1,5-diketones by addition of

cyclohexanone to chalcones under solvent-free phase transfer catalyst condition. *Turk Chem,* 2008, *32,* 55-61.

IV. Dhar, D. N. *The Chemistry of (Chalcones and Related Compounds.* Wiley: New York, 1981.

V. Konieczny, M. T.: Horowska, B.; Kunikowski, A.; Konopa, J.; Wierzba, K.; Yamada, Y.; Asao, T. Synthesis of polyhydroxylated derivatives of phenyl vinyl sulfone as structural analogs of chalcones. *Synthsis* 2001, *9,* 1363-1367.

VI. Park, E. J.; Park, H. R.; Lee, J. S.; Kim, J. Licochalcone A: An inducer of cell differentiation and cytotoxic agent from pogostemon cablin. *Planta Med.* 1998, *64(5),* 464-466.

VII. Anto, R. J.; Sukumaran, K.; Kuttan, G.; Rao, M. N. A.; Subbaraju, V.; Kuttan R. Anticancer and antioxidant activity of synthetic chalcones and related compounds. *Cancer Lett.* **1995,** 97(1), 33-37,

VIII. Ko, H. H.; Tsao, L. T.; Yu, K. L.; Liu, C. T.; Wang, J. P.; Lin, C. N. Structure—activity relationship studies on chalcone derivatives: The potent inhibition of chemical mediator release. *Bioorg. Med. Chem.* 2003, *11,* 105-111,

IX . Hesieh, H. K.; isao, L. T.; Wang, J. P.; Lin, C. N. Synthesis and anti- inflammatory effect of chalcones. *J. Pharm. Pharmacol.* **2000,** *52,* 163-171.

X. Nielsen, S. F.; Christensen, S. B.; Cruciani, G.; Kharazmi, A.; Liljefors, T. Antileishmanial chalcones: Statistical design, synthesis, and three-dimensional quantitative structure—activity relationship analysis. *J. Med. Chem.* **1998,** *41,* 4819-4832.

XI. Lin, Y. M.; Zhou, Y.; Flavin, M. T.; Zhou, L. M.; Nie, W.; Chen, F. C. Chalcones and flavonoids as anti-tuberculosis agents. *Bioorg. Med. Chem.* 2002, *10,* 2795-2802.

XII. Lopez, S. N.; Castelii, M. V.; Zacchino, S. A.; Dominguez, J. N.; Lobo, G.; Charris-Charris, J.; Cortes, J. C. G.: Ribas, J. C.; Devia, C.; Rodriguez, A. M.; Enriz, R. D. In vitro antifungal evaluation and structure—activity relationships of a new series of chalcone derivatives and synthetic analogues, with inhibitory Properties against polymers of the fungal cell wall. *Bidorg. Med. Chem.* **2001, 9(8),**1999-2013.

XIII. Furusawa, M.; Tanaka, T.; Ito, T.; Nishiwaka, A.; Yamazaki, N.; Nakaya, K. I.; Matsuura, N.; Tsuchiya, H.; Nagayama, M.; Iinuma, M. Antioxidant activity of hydroxyflavonoids. *J. Health Sci.* 2005, *51,* 376-378.

XIV. Hsieh, H. K.; Lee, T. H.; Wang, J. P.; Wang, J. J.; Lin, C. N. Synthesis and anti-inflammatory effect of chalcones and related compounds. *Pharm. Res.* **1998,** *15,* 39-46.

XV. Lin, C. N.; Lee, T. H.; Hsu, M. F.; Wang, J. P.; Ko, F. N.; Teng, C. M. 2',5'- Dihydroxychalcone as a potent chemical mediator and cyclooxygenase inhibitor. *J. Pharm. Pharmacol* 1997, *49,* 530-536.

XVI. Powers, D. G.; Casebier, D. S.; Fokas, D.; Ryan, W. J.; Troth, J. R.; Coffen, D. L. Automated parallel synthesis of chalcone-based screening libraries. *Tetrahedron.* **1998,** *54,* 4085-4096.

. Received on November 11,2012