Efficient Reaction Between Substituted 2-Acetyl-1-Naphthol/2-Acetyl-1-Naphthol And Different Substituted Benz aldehydes

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ABSTRACT: ***we have developed a simple, efficient and more eco-friendly method for synthesis of chalcones by grinding technique. The notable advantages of present method are no organic solvent required (except for the product recrystallization), waste minimization, simple operation, clean reaction profile, easy work-up, shorter reaction time (4-8 min.), high yields (84-95 %) and eco- friendly as compared to conventional method.***

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1. INTRODUCTION

The utility of chalcones due to their usefulness as in synthesis of various heterocyclic compounds, as plant origin [1] and exhibit antimalarial [2], antibacterial [3], antifibrogenic [4], anticancer [5], antitrichomonal [6], antinflammatory [7], antileishmanial[8], cytotoxic and anti-*Trypanosoma cruzi* [9] activities.

A classical method for synthesis of chalcones is claisen-schmidt condensation in which aldehyde reacted with acetophenone in the presence of aqueous alkaline bases [10], $Ba(OH)_2$ / LiOH [11]. Chalcones also synthesized by using microwave irradiation, ultrasound irradiation [12] and by Suzuki reaction [13]. Recently various modified methods for synthesis of chalcones has been reported using different catalyst such as $SOCl_2$ [14], natural phosphate lithium nitrate [15], KF / natural phosphate [16], acyclic acidic ionic liquid [17], Na_2CO_3 [18], high temperature water [19], silica-sulphuric acid [20], $ZrCl_4$ and ionic liquid [21], silica-sulphuric acid [22], NaOH-Al_2O_3 [23] and silica chloride [24].

A classical synthesis of these compounds involves the condensation of acetophenones and aldehydes to give chalcones. The combination of solvents and long reaction time, costly chemicals / catalyst makes this method environmentally hazardous. This provided the stimulus to synthesize some new chalcones using grindstone technique [25]. In grindstone technique, reaction occurs through generation of local heat by grinding of crystals of substrate and reagent by mortar and pestle. Reactions are initiated by grinding, with the small amount of energy through friction. In some cases, a mixture and reagents turns to a glassy material. Such reaction are simple to handle, reduce pollution, comparatively cheaper to operate and may be regarded as more economical and ecologically favorable procedure in chemistry [26]. Solid-state reaction occurs more efficiently and more selectively than does the solution reaction, since molecules in the crystal are arranged tightly and regularly [27].

In present work, grindstone technique was used for the synthesis of titled compounds. This method is superior to conventional method; since it is eco-friendly, high yielding, requires no special apparatus, non-hazardous, operationally simple and convenient.

Newly synthesized chalcones were prepared by grinding together equivalent amounts of the appropriate 2-acetyl-1-naphthol / substituted 2-acetyl-1-naphthol and different substituted benzaldehydes in presence of solid KOH in a porcelain mortar under solvent-free conditions for 4-8 min. On completion of reaction (TLC), the reaction mixture was diluted with cold water, neutralized by dilute HCl and recrystalised from acetic acid.

2. METHODS

2.1 Chemistry

Melting points were determined in an open capillary tube and are uncorrected. IR spectra were recorded in KBr on a Perkin-Elmer spectrometer. ^1H NMR spectra were recorded on a Gemini 300-MHz instrument in DMSO as solvent and TMS as an internal standard. The mass spectra were recorded on EISHIMADZU-GC-MS

spectrometer. Elemental analysis was carried out on a Carlo Erba1108 analyzer. The purity of products was checked by Thin Layer Chromatography (TLC) on silica gel.

2.2 General procedure for synthesis of chalcones

2-acetyl-1-naphthol / substituted 2-acetyl-1-naphthol (0.01mmol), different substituted benzaldehydes (0.01mmol) and solid pallete of KOH (0.02mmol) were taken in morter and grind for several minute (Table-1). On completion of grinding as monitored by TLC, the obtained solid mixture was diluted with cold water, neutralized by dil HCl and recrystlized from acetic acid to give the corresponding chalcone derivatives.

3-(3,4-Dimethoxy-phenyl)-1-(1-hydroxy-naphthalen-2-yl)-propenone (3a): IR (v max) cm^{-1} 3255 (OH), 1629 (C=O), 1569, 1495 (ring C=C), ^{1}H NMR (300 MHZ, DMSO) δ 3.73 (s, 6H, two- OCH_3), δ 6.90 (d, J=16 HZ 1H, H), δ 7.56 (d, J=16 HZ 1H, Hβ), δ 7.35-8.08 (m, 9H, Ar-H), δ 12.8 (s, 1H,OH). MS m/z: 334 (M^+). Anal.Calc for C H O : C, 75.44; H, 5.38. Found: C, 75.64; H, 5.54.

1-(1-Hydroxy-naphthalen-2-yl)-3-(4-methoxy-phenyl)-propenone (3b): IR (v max) cm^{-1}: 3252 (OH), 1626 (C=O), 1567, 1490 (ring C=C), ^{1}H NMR (300 MHZ, DMSO) δ 3.75 (s, 3H, - OCH_3), δ 6.82 (d, J= 15.5 HZ 1H, H), δ 7.52 (d, J= 15.5 HZ 1H, Hβ), δ 7.30-8.10 (m, 10H, Ar-H), δ 13.1 (s, 1H, OH). MS m/z: 304 (M^+). Anal. Cacl for C H O : C, 78.94; H, 5.26. found: C, 79.10; H, 5.45.

1-(1-Hydroxy-4-iodo-naphthalen-2-yl)-3-(4-methoxy-phenyl)-propenone (3c): IR (v max) cm^{-1}: 3250 (OH), 1625 (C=O), 1560, 1480 (ring C=C), ^{1}H NMR (300 MHZ, DMSO) δ 3.70 (s, 3H, - OCH_3), δ 6.80 (d, J= 17 HZ 1H, H), δ 7.60 (d, J= 17 H 1H, H), δ 7.30-8.12 (m, 8H, αZβ Ar-H), δ 7.70 (s, 1H, Ar-H), δ 13.2 (s, 1H, OH). MS m/z: 430 (M^+). Anal. Cacl for $C_{20}H_{15}O_3I$: C, 55.81; H, 3.48; I, 29.53. found: C, 56.00; H, 3.60; I, 29.65.

1-(4-Bromo-1-hydroxy-naphthalen-2-yl)-3-(3,4-dimethoxy-phenyl)-propenone (3d): IR (v max) cm^{-1}: 3258 (OH), 1629 (C=O), 1557, 1485 (ring C=C), ^{1}H NMR (300 MHZ, DMSO) δ 3.70 (s, 6H, two - OCH_3), δ 6.92 (d, J= 16 HZ 1H, H), δ 7.54 (d, J= 16 HZ 1H, Hβ), δ 7.35-8.10 (m, 7H, Ar-H), δ 7.73 (s, 1H, Ar-H), δ 13.0 (s, 1H, OH). MS m/z: 413 (M^+). Anal. Cacl for $C_{21}H_{17}O_4Br$: C, 61.01; H, 4.11; Br, 19.37. found: C, 61.10; H, 4.24; I, 19.51.

1-(4-Bromo-1-hydroxy-naphthalen - 2 - yl) - 3 - (3, 4, 5-trimethoxy-phenyl)-propenone (3e): IR (v max) cm^{-1}: 3260 (OH), 1626 (C=O), 1557,1490 (ring C=C), **^{1}H NMR** (300 MH , DMSO): δ 3.71 (s, 9H, 3 X -OCH), δ 6.86 (d, J= 15.5 H 1H, H), δ 7.56 (d, J= 15.5 H 1H, H), δ 7.36-8.13 (m, 7H, Ar-H), δ 13.0 (s, 1H, OH). **MS** m/z: 443 (M^+). Anal. Cacl for $C_{22}H_{19}O_5Br$: C, 55.59; H, 4.28; Br, 18.0. found: C, 55.70; H, 4.45; Br, 18.08.

3-(4-Chloro-phenyl)-1-(1-hydroxy-naphthalen-2-yl)-propenone (3f): IR (v max) cm^{-1}: 3257 (OH), 1625 (C=O), 1572, 1490 (C=C). **^{1}H NMR** (300 MHZ, DMSO): δ 6.84 (d, J= 17 HZ 1H, Hα), δ 7.52 (d, J= 17 HZ 1H, Hβ), δ 7.36-8.10 (m, 10H, Ar-H), δ 12.9 (s, 1H, OH). **MS** m/z: 308 (M^+). Anal. Cacl for $C_{19}H_{13}O_2Cl$: C, 74.02; H, 4.22; Cl, 11.36. found: C, 74.10; H, 4.45; Cl, 11.48.

3-(4-Chloro-phenyl)-1-(1-hydroxy-4-iodo-naphthalen-2-yl)-propenone (3g): IR (v max) cm^{-1}: 3250 (OH), 1628 (C=O), 1574, 1488 (C=C). **^{1}H NMR** (300 MHZ, DMSO): δ 6.88 (d, J= 16 HZ 1H, H), δ 7.58 (d, J= 16 HZ 1H, Hβ), δ 7.38-8.10 (m, 8H , Ar-H), δ 7.78 (s, 1H, Ar-H), δ 13.1 (s, 1H, OH). **MS** m/z: 434 (M^+). Anal. Cacl for C H O ICl: C, 52.53; H, 2.76; X (I+Cl), 37.32. found: C, 52.70; H, 2.88; X (I+Cl), 37.47. 19 12 2

1-(4-Bromo-1-hydroxy-naphthalen-2-yl)-3-(4-fluoro-phenyl)-propenone (3h): IR (v max) cm^{-1}: 3255 (OH), 1629 (C=O), 1570, 1492 (C=C). **^{1}H NMR** (300 MH , DMSO): δ 6.86 (d, J= 15.5 H 1H, Hα), δ 7.54 (d, 15.5 HZ 1H, Hβ), δ 7.37-8.12 (m, 9H , Ar-H), δ 13.2 (s, 1H, OH). **MS** m/z: 371 (M^+). Anal. Cacl for $C_{19}H_{12}O_2BrF$: C, 61.45; H, 3.23; X (Br+F), 26.68. found: C, 61.54; H, 3.38; X, (Br+F), 26.78.

3-(4-Fluoro-phenyl)-1-(1-hydroxy-naphthalen-2-yl)-propenone (3i): IR (v max) cm^{-1}: 3260 (OH), 1628 (C=O), 1574, 1486 (C=C). **^{1}H NMR** (300 MHZ, DMSO): δ 6.82 (d, J= 17 HZ 1H, Hα), δ 7.52 (d, J= 17 HZ 1H, Hβ), δ 7.35-8.09 (m, 10H , Ar-H), δ 13.2 (s, 1H, OH). **MS**

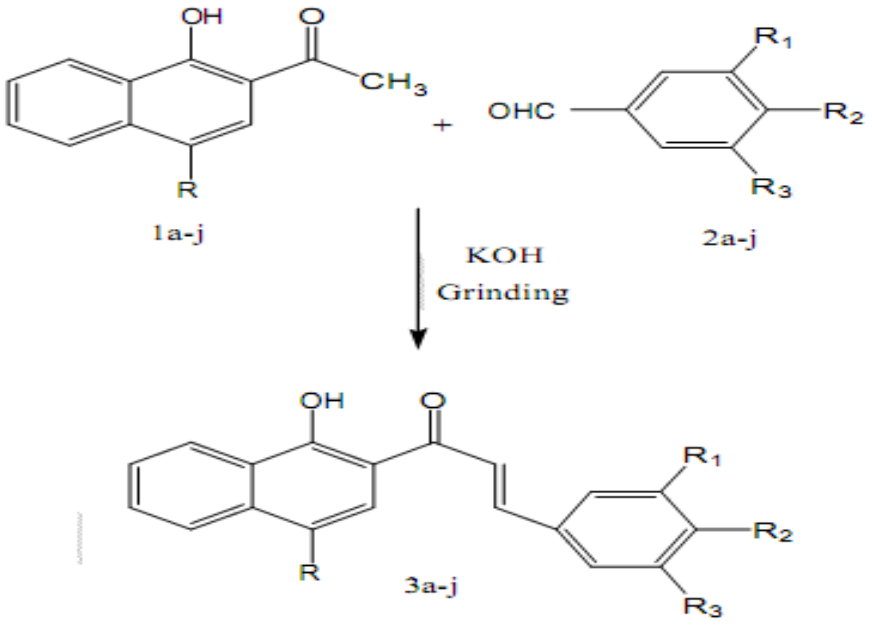
m/z: 292 (M^+). Anal. Cacl for $C_{19}H_{13}O_2F$: C, 78.08; H, 4.45; F, 6.16. found: C, 78.19; H, 4.56; F, 6.28.

1-(1-Hydroxy-4-iodo-naphthalen-2-yl)-3-(3,4,5-trimethoxy-phenyl)-propenone (3j): IR (v max) cm^{-1}: 3260 (OH), 1626 (C=O), 1557, 1490 (ring C=C), **^{1}H NMR** (300 MHZ, DMSO): δ 3.74 (s, 9H, three - OCH_3), δ 6.86 (d, J= 16 HZ 1H, H), δ 7.56 (d, J= 16 HZ 1H, Hβ), δ 7.36- 8.13 (m, 6H, Ar-H), δ 7.78 (s, 1H, Ar-H), δ 13.2 (s, 1H, OH). **MS** m/z: 490 (M^+). Anal. Cacl for $C_{22}H_{19}O_5I$: C, 53.87; H, 3.87; I, 25.91. found: C, 54.02; H, 4.01; I, 26.04.

3. RESULTS AND DISCUSSION

In continuation of our earlier research works on solvent-free organic synthesis [28, 29] herein, we would like to report a simple, efficient and solvent-free synthesis of some new chalcones by grinding method (Scheme-I). Claisen-Schmidt condensation of 2- acetyl-1-naphthol / substituted 2-acetyl-1-naphthol (**1a-j**) with various substituted benzaldehydes (**2a-j**) in the presence of solid KOH in combination with grinding at room temperature in the absence of solvent afforded chalcones (**3a-j**). The yields of the products are excellent and purity is high as compared to conventional method. The process is simple, efficient, and economical. It is also consistent with the green chemistry approach because it does not need heating or microwave irradiation. The structures of the newly synthesized chalcones (**3a-j**) were established by their elemental analysis and spectral data (IR, ^{1}HNMR and MS).

Scheme



3_a: R, R_1= H, R_2, R_3= OCH_3
3_b: R,R_1,R_3= H, R_2= OCH_3
3_c: R=I, R_1,R_3=H,R_2=OCH_3
3_d: R=Br, R_1=H, R_2,R_3= OCH_3
3_e: R=Br, R_1,R_2,R_3= OCH_3
3_f : R,R_1,R_3= H, R_2= Cl
3_g: R= I, R_1,R_3= H, R_2= Cl
3_h: R= Br, R_1,R_3= H, R_2= F
3_i: R,R_1,R_3= H, R_2= F
3j: R=H, R_1,R_2,R_3= OCH_3

Table-1: Physical data of Synthesized Chalcones.

Entry	M.P. °C	Yield (%)	Time (min.)
3a	154	88	4.5
3b	188	92	6.5
3c	259	85	7.0
3d	128	90	5.5
3e	142	87	5.0
3f	178	91	4.0
3g	227	94	5.0
3h	247	87	6.5
3i	196	93	8.0
3j	278	94	5.0

4. CONCLUSION

In summary, we have developed a simple, efficient and more eco-friendly method for synthesis of chalcones by grinding technique. The notable advantages of present method are no organic solvent required (except for the product recrystallisation), waste minimization, simple operation, clean reaction profile, easy work-up, shorter reaction time (4-8 min.), high yields (84-95 %) and eco-friendly as compared to conventional method.

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