INTRODUCTION

Flavonoids are an important class of natural products with wide range activities. Flavonoids includes flavone, flavanone, flavane & flavanol. The synthetic route involves synthesis of chalcone followed by ring closing to give flavanone. So many catalysts were mentioned in past literature. But most efficient catalyst is methane sulphonlic acid. It is easy to handle, less reaction time & easily available. Flavanones were synthesized from chalcone using methane sulphonic acid under thermal condition, microwave and ultrasound condition. Flavanones are synthesized in very less time compared to other conditions.

Key words: Flavanone, Methanesulphonic acid, Thermal, Microwave, Ultrasound.

ABSTRACT

Flavonoids are an important class of natural products with wide range activities. Flavonoids includes flavone, flavanone, flavane & flavanol. The synthetic route involves synthesis of chalcone followed by ring closing to give flavanone. So many catalysts were mentioned in past literature. But most efficient catalyst is methane sulphonlic acid. It is easy to handle, less reaction time & easily available. Flavanones were synthesized from chalcone using methane sulphonic acid under thermal condition, microwave and ultrasound condition. Flavanones are synthesized in very less time compared to other conditions.

Key words: Flavanone, Methanesulphonic acid, Thermal, Microwave, Ultrasound.
Flavonoids are synthesized by various methods like Clause-Schmidt, Baker-Venkatraman, Ganguly’s method and Robinson’s method etc.13 Armoatic aldehydes and ketones gives chalcone which on cyclization gives flavanone. In past methods chalcone are cyclized to flavanone by I2/ DMSO15, AcOH/H2SO416, silicagel17, poly phosphonic acid18, TFA19, N-methyl imidazole20, alkali metal carbonates21, KOH/MeOH22, pyridine23, DBU/MW24, HBr/AcOH25, potassium ferricyanide26 etc. We synthesized flavanone by using methane sulphonic acid under different conditions.

EXPERIMENTAL

All material purchased from Sigma-Aldrich and solvents from Merck Chemical India. Melting points determined in parafin bath. IR & 1HNMR spectra gives structure of compound.

Representative procedure

Thermal condition

A mixture of substituted 2- hydroxy chalcone (1mole) was added in RBF. Then arrange the apparatus with thermometer in oil bath. Place apparatus on digital hot plate. Add through neck of RBF acetic acid and then add dropwise MSA (15 mole %). Maintain temperature 105-115°C till completion of reaction. Reaction was monitored by TLC. Pour the reaction mass in water, filter to get solid. Recrystalise with suitable solvent. Calculate yield, M.P. After checking solubility in suitable solvent it was given for spectral analysis.

Ultra sound condition

A mixture of substituted 2- hydroxy chalcone (1mole) and methane sulphonic acid was added (15 mole %) in RBF. Add acetic acid minimum to dissolve the reaction mass. Then keep RBF in a water bath with ultrasound. Maintain temp. 95°C. Carry out reaction for 30 minute under ultrasound. Check TLC. Carry out work up as above.

Under micro-wave condition

A mixture of substituted 2- hydroxy chalcone (1mole) and methane sulphonic acid was added (15 mole %) in RBF. Add acetic acid minimum to dissolve the reaction mass. Then RM subjected to micro-wave. Check TLC. Carry out work up as above.

Spectral Data

2-phenylchroman-4-one (2a)

Colour

Light yellow/white powder, M.P. -76°C, TLC system- Hex+E.A.(7:3), Soluble – CHCl3

IR (KBr) \( \nu_{\text{max}}/\text{cm}^{-1} \)

1720, 1675, 1616-1500, 1300, 750, 690.

1H NMR (CDCl3) \( \delta \)

5.51(d, 1H, J = 7 Hz), 3.20(d, 2H, J = 7 Hz), 7.40(dd, 1H, J = 7.5, 1.5 Hz), 7.0(1H, m, J = 7.5, 1.5 Hz), 7.50(dd, 1H, J = 7.5, 1.5 Hz), 7.15(dd, 1H, J = 7.5, 1.5 Hz), 7.32(dd, 2H, J = 7.5, 1.5 Hz), 7.25(dd, 1H, J = 7.5, 1.5 Hz), 7.22(m, 1H, J = 7.5, 1.5 Hz)

2-(4-hydroxyphenyl)chroman-4-one (2b)

Colour

Light yellow powder, M.P. -180°C, TLC system-Hex+E.A.(7:3), Soluble – DMSO

IR (KBr) \( \nu_{\text{max}}/\text{cm}^{-1} \)

3480, 1700, 1692, 1608, 754, 697.

1H NMR (DMSO) \( \delta \)

5.53(d, 1H, J = 7 Hz), 3.28(d, 2H, J = 7 Hz), 9.79(s, 1H, -OH), 6.78(d, 2H, J = 7.5, 1.5 Hz), 7.33(dd, 2H, J = 7.5, 1.5 Hz), 7.34(dd, 1H, J = 7.5, 1.5 Hz), 7.046(m, 1H, J = 7.5, 1.5, 1.4 Hz), 7.09(m, 1H, J = 7.6, 1.5, 1.5), 7.21 (m, 1H, J = 7.5, 1.5, 1.5 Hz), 7.57(dd, 1H, J = 7.5, 1.5 Hz), 7.60(dd, 1H, J = 7.5, 1.5 Hz), 7.76(dd, 1H, J = 7.5, 1.5 Hz), 7.78(m, 1H, J = 7.5, 1.5, 1.5 Hz)

2-(3-hydroxyphenyl)chroman-4-one (2c)

Colour

White powder, M.P. -134°C, TLC system-Hex+CHCl3+Acetone.(6:3:1), Soluble – DMSO

IR (KBr) \( \nu_{\text{max}}/\text{cm}^{-1} \)

3400, 1711, 1656, 1610, 1515, 750, 690.

1H NMR (DMSO) \( \delta \)

5.42(d, 1H, J = 7 Hz), 3.14(d, 2H, J = 7 Hz), 6.75(dd, 1H, J = 7.5, 1.5 Hz), 6.92(m, 1H, J = 7.5, 1.5 Hz), 7.09(m, 1H, J = 7.6, 1.5, 1.5), 7.21(m, 1H, J = 7.5, 1.5, 1.5 Hz), 7.57(dd, 1H, J = 7.5, 1.5 Hz), 7.60(dd, 1H, J = 7.5, 1.5 Hz), 7.76(dd, 1H, J = 7.5, 1.5 Hz), 7.78(m, 1H, J = 7.5, 1.5, 1.5 Hz)

2-(3,4-dimethoxyphenyl)chroman-4-one (2d)

Colour

Light yellow powder, M.P. -134°C, TLC system-Hex+CHCl3+Acetone.(6:3:1), Soluble – DMSO

IR (KBr) \( \nu_{\text{max}}/\text{cm}^{-1} \)

3400, 1711, 1656, 1610, 1515, 750, 690.

1H NMR (DMSO) \( \delta \)

5.70(d, 1H, J = 7 Hz), 3.17(d, 1H, J = 7 Hz), 6.75(dd, 1H, J = 1.5, 1.5 Hz), 6.92(m, 1H, J = 7.5, 1.5 Hz), 7.09(m, 1H, J = 7.6, 1.5, 1.5), 7.21(m, 1H, J = 7.5, 1.5, 1.5 Hz), 7.57(dd, 1H, J = 7.5, 1.5 Hz), 7.60(dd, 1H, J = 7.5, 1.5 Hz), 7.76(dd, 1H, J = 7.5, 1.5 Hz), 7.78(m, 1H, J = 7.5, 1.5, 1.5 Hz)

2-(3,4-dimethoxyphenyl)chroman-4-one (2d)

Colour

Light yellow powder, M.P. -134°C, TLC system-Hex+CHCl3+Acetone.(6:3:1), Soluble – DMSO

IR (KBr) \( \nu_{\text{max}}/\text{cm}^{-1} \)

1700, 1656, 1600, 1512, 740.

1H NMR (DMSO) \( \delta \)

5.42(d, 1H, J = 7 Hz), 3.14(d, 2H, J = 7 Hz), 3.17(d, 1H, J = 7 Hz), 6.75(dd, 1H, J = 1.5, 1.5 Hz), 6.92(m, 1H, J = 7.5, 1.5 Hz), 7.09(m, 1H, J = 7.6, 1.5, 1.5), 7.21(m, 1H, J = 7.5, 1.5, 1.5 Hz), 7.57(dd, 1H, J = 7.5, 1.5 Hz), 7.60(dd, 1H, J = 7.5, 1.5 Hz), 7.76(dd, 1H, J = 7.5, 1.5 Hz), 7.78(m, 1H, J = 7.5, 1.5, 1.5 Hz)
Scheme 1: Synthesis of flavanone from chalcone

Fig. 1: Molecules with biological activity

Pancreatic cancer  Antibacterial  Dimethylachrysins  Anticancer

Antifungal  Breast Cancer

Solophenol D  Anti-microbial  Antifungal
5-methoxy-2-phenylchroman-4-one (2e)

Colour: Yellow powder, M.P. -141°C, TLC system: Benzene+E.A.(9.5+0.5), Soluble—CHCl₃.

IR (KBr) \( \nu_{\text{max}}/\text{cm}^{-1} \) 1720, 1654, 1600, 1500, 1300, 980.

\( ^1\text{H NMR (CDCl}_3\) \( \delta \)

\begin{align*}
5.50 (d,1H,J = 7 Hz), & 3.19 (d,2H,J = 7 Hz), 2.80 (s,3H), 6.72 (2H,d,J = 7.5 Hz), 7.50 (d,1H,J = 7.5 Hz), 7.35 (s,5 H) \\
& 3.92 (s,3H,-OMe), 3.90 (s,3H,-OMe), 6.90 (d,1H,J = 7 Hz), 7.008 (d,1H,J = 7 Hz), 7.15 (dd,1H,J = 7.5,1.5 Hz), 7.52 (dd,1H,J = 7.5,1.5 Hz), 7.94 (m,1H,J = 7.5,1.5,1.5,1.5 Hz)
\end{align*}

7-hydroxy-2-phenylchroman-4-one (2f)


IR (KBr) \( \nu_{\text{max}}/\text{cm}^{-1} \) 3500, 1717, 1660, 1500, 1300, 980.

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<th>Entry</th>
<th>Molecule</th>
<th>Time at different condition</th>
<th>Thermal</th>
<th>MW</th>
<th>Ultrasound</th>
<th>% Yield</th>
<th>Melting point</th>
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<td>45 min.</td>
<td>80</td>
<td>140⁰C</td>
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1H NMR (CDCl₃) δ
5.51 (d, 1H, J = 7 Hz), 3.40 (d, 2H, J = 7 Hz), 6.46 (dd, 1H, J = 7.5 Hz), 6.50 (d, 1H, J = 1.5 Hz), 7.50 (d, 1H, J = 7.5 Hz), 7.40 (dd, 2H, J = 7.5, 1.5 Hz), 7.35 (m, 3H, J = 7.5, 1.5 Hz).

5,7-dimethoxy-2-phenylchroman-4-one (2g)

Colour
White powder, M.P. -14°C

IR (KBr) νmax/cm⁻¹
1702, 1674, 1608, 1489, 1300, 943.

RESULTS AND DISCUSSION
Methane sulphonic acid is used as an acid catalyst in organic reactions because it is a non-volatile, strong acid that is soluble in organic solvents. Methanesulfonic acid is convenient for industrial applications because it is liquid at ambient temperature, while the closely related to para toluene sulphonic acid which solid at room temperature. MSA is considered as an intermediate between sulphuric acid and methyl sulphonyl methane. It maintains Pn which is necessary to go reaction smoothly. So many acids like acetic acid, sulphuric acid, pTSA, poly H₃PO₄, hydrochloric acid were used in previous method. Sometimes mixture of acids, mixed solvents are used in previous methods. So as per our opinion Pn is important for the acidic synthesis of flavanone from 2-hydroxy chalcones. We also compared reaction under various conditions like ultrasound, thermal and microwave conditions.

CONCLUSION
We found cheap, environmental friendly process for the synthesis of flavanones. Methane sulphonic acid is green catalyst compared to other catalysts. We compare different conditions for the reaction. We concluded that reaction under MW will complete in minimum time.

ACKNOWLEDGMENT
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