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Synthesis of Flavanones using Methane Sulphonic Acid as a Greencatalystand Comparision under Different Conditions

R.B. KSHATRIYA[1], J.K. Machhi and G.M. NAZERUDDIN[1]*

[1]Department of Organic Chemistry & Research Centre, Poona College of Arts, Science and Commerce, (Affiliated to University of Pune). Camp, Maharashtra, India.
*Corresponding author E-mail: rbkshatriya123@gmail.com

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ABSTRACT

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

Key words: Flavanone, Methanesulphonic acid, Thermal, Micro wave, Ultrasound.

INTRODUCTION

Natural products includes alkaloids, terpenoids, coumarins, amino acid derivatives and flavonoids.Flavonoids are found in plant as a secondary metabolite acts as defence from bacteria and viruses.They also acts as coluring agent in flowers to attract insect,honeybees and butterfy toward flower.Due to which pollination occurs easily in plants.Flavonoids are also important for human health as it present in fruits,vegetables and flowers.Initially it isnamed as Vitamin P.But due to its yellow colour it is named as flavonoids.

Flavonoids are mainly classified as flavone,flavanone and flavane etc[1].Human interest is to isolate and synthesize flavone skeleton having pharmacological activity.From past literature we found that flavonoid skeleton (C6-C3-C6 & two oxygen atoms) have wide range of activities. Synthetic and naturallly occuring flavonoids i.e.flavanone have interesting pharmaceutical activity like anticancer[1],anti-estrogen[2], antimycobacterial[3], antimicrobial[4], anti-lungcancer[5], anti-bacterial[6], anti-viral[7], anti-tuberculosis[8], antifungal[9], anti-oxidant[10], anti-arrhythmic[11], antihypertensive[12], anti-proliferative[13] etc.

Flavonoids aresynthesized by various methods like Clause-Schmidt,Baker-Venkatraman, Ganguly's method and Robinson'smethod etc.[13] Armoatic aldehydes and ketones gives chalcone which on cyclization gives flavanone.In past methods chalcone are cyclized to flavanone by I_2/ DMSO[15], AcOH/H_2SO_4[16], silicagel[17], poly phosporic acid[18], TFA[19],N-methyl imidazole[20],alkali metal carbonates[21], KOH/MeOH[22], pyridine[23], DBU/MW[24], HBr/AcOH[25], pottasium ferricynide[26]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 &^{1}HNMR 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 %).Maitain 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 yeild, 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^{0}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^{0}C,**TLC system**- Hex+E.A.(7:3),**Soluble** – $CHCl_3$

IR (KBr) ν_{max}**/cm^{-1}**1720,1675,1616-1500,1300, 750, 690.

^{1}H NMR ($CDCl_3$) δ

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^{0}C,TLC system-Hex+E.A.(7:3),Soluble – DMSO

IR (KBr) ν_{max}/cm^{-1}: 3480,1700,1692, 1608, 1514,754,697.

^{1}H NMR (DMSO) δ

5.53(d,1H,J=7Hz),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(d,1H,J = 7.5,1.5 Hz), 7.046 (m,1H, J=7.5,7.2,1.5 Hz),7.55(dd,1H,J = 7.5,1.5 Hz),7.76(m,1H,J=7.2,7.2,1.5 Hz),7.76(m,1H J = 7.6,7.2,1.5 Hz).

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

Colour

White powder,M.P.-134^{0}C,TLC system-Hex+$CHCl_3$+Acetone.(6:3:1),Soluble– DMSO

IR (KBr) ν_{max}/cm^{-1}3400, 1711, 1656, 1610, 1515, 750, 690.

^{1}H NMR (DMSO) δ 5.70(d,1H,J=7Hz),3.17(d,1H,J = 7Hz),6.75(dd,1H,J = 1.5,1.5 Hz),6.92(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)

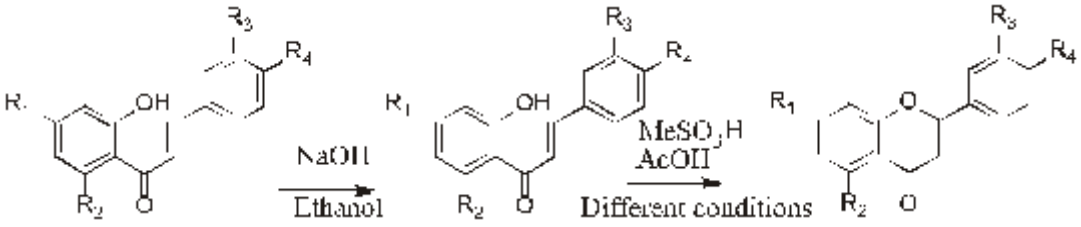
2-(3,4-dimethoxyphenyl)chroman-4-one (2d)

Colour

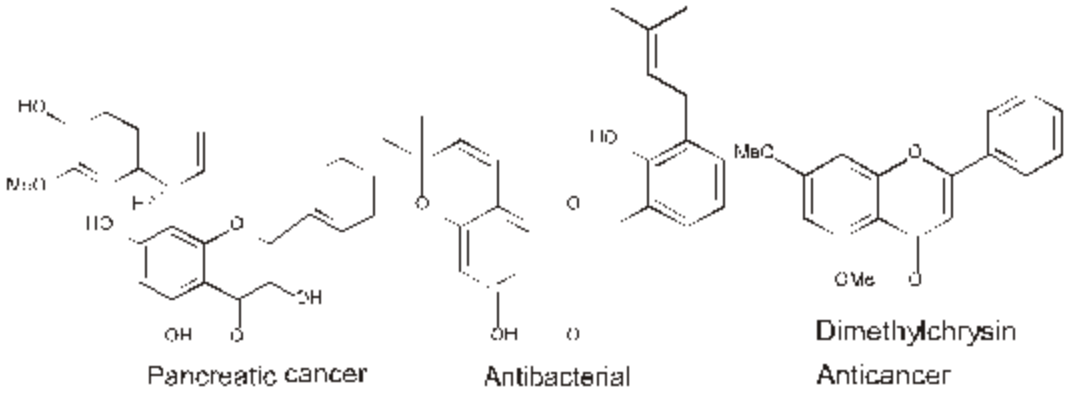
light yellow powder,M.P.-134^{0}C,TLC system-Hex+E.A.(7:3),Soluble– DMSO.

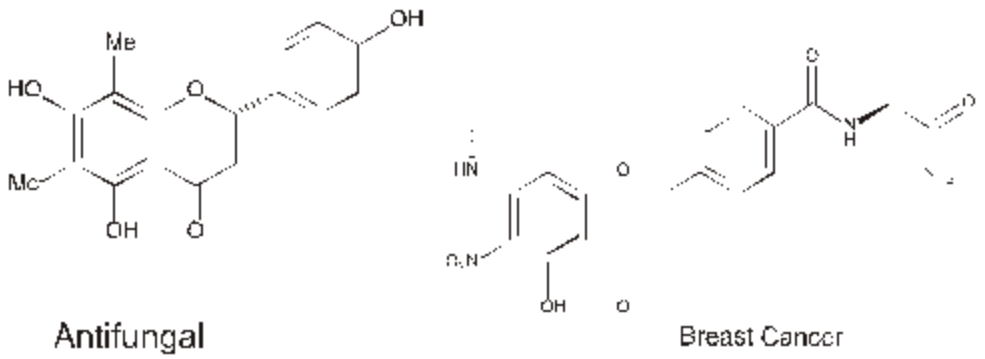
IR (KBr) ν_{max}/cm^{-1}1700,1656,1600,1512,740.

^{1}H NMR (DMSO) d 5.42(d,1H,J = 7 Hz),3.14(d,2H,J



Scheme 1: Synthesis of flavanone from chalcone





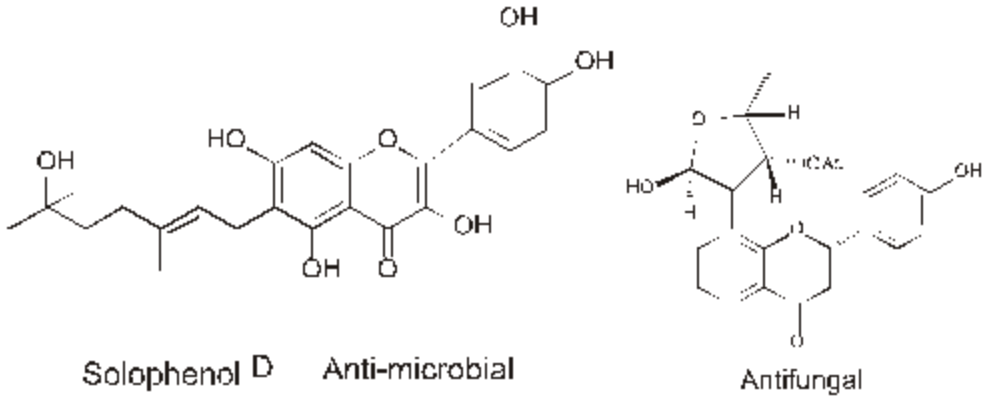


Fig. 1: Molecules with biological activity

= 7 Hz),3.92(s,3H,-OMe) 3.90(s,3H,-OMe), 6.90 (d,1H,J =7 Hz),7.008(d,1H,J=7Hz),7.027(d,1H,J = 1.5 Hz), 7.15(dd,1HJ = 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)

5-methoxy-2-phenylchroman-4-one (2e)
Colour

Yellow powder,M.P.-141^{0}C,TLC system-Benzene+E.A.(9.5+0.5),Soluble–$CHCl_3$.

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

^{1}H NMR ($CDCl_3$) δ

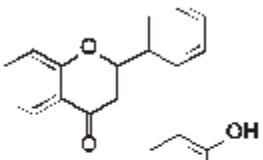
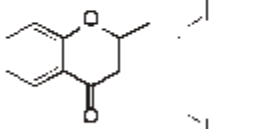
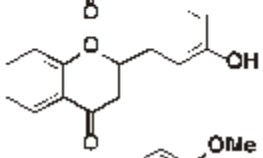
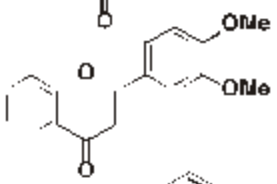
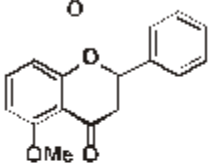
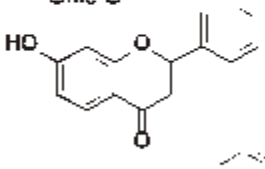
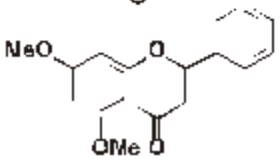
5.50 (d,1H,J = 7 Hz),3.19(d,2H,J = 7 Hz),2.80(s,3H), 6.72(2H,d,J = 7.5 Hz),7.50(d,1H,J = 7.5 Hz),7.35(s,5 H)

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

Yellow powder,**M.P**.-188^{0}C,**TLC system**-Hex+E.A.(7:3),**Soluble**–$CHCl_3$.

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

Table 1.Synthesis of flavanones under thermal microwave and ultrasound conditions

Entry	Molecule	Time at diffrent condition			% Yield	Melting point
		Thermal	MW	U.sound		
2a		2 Hrs	30 min	45 min.	80	73^{0}C
2b		2 Hrs	30 min	45 min.	80	220^{0}C
2c		2 Hrs	30 min	45 min.	80	129^{0}C
2d		2 Hrs	30 min	45 min.	80	118^{0}C
2e		2 Hrs	30 min	45 min.	80	138^{0}C
2f		2 Hrs	30 min	45 min.	80	184^{0}C
2g		2 Hrs	30 min	45 min.	80	140^{0}C

^{1}H NMR ($CDCl_3$) δ

5.51(d,1H,J = 7 Hz),3.40(d,2H,J = 7 Hz),6.46(dd,1H,J=7.5,
1.5 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**.-144^{0}C,**TLC system**-$CHCl_3$+ MeOH.(9:1),**Soluble** – $CHCl_3$

IR (KBr) V_{max}/cm^{-1}

17021674, 1608, 1489,1300,943.

^{1}H NMR ($CDCl_3$) δ

5.51(d,1H,J = 7 Hz),3.029(d,2H,J= 7Hz), 2.79 (s,3H),2.62 (s,3H),6.16(d,1H,J= 1.5 Hz), 6.10(d,1H,J = 1.5 Hz),7.38(m,1H,J = 1.5,1.5 Hz), 7.41 (m,1H,J = 7.5,1.5,1.5 Hz),7.45(m,1H,J=7.5, 1.5, 1.5, 1.5 Hz)

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 isconsidered asintermediate between sulphuric acid and methyl sulphonyl methane.It maintains P^H which is necessary to go reaction smoothly. So many acids like acetic acid, sulphuric acid, pTSA,poly H_3PO_4,Hydrochloric acid were used in previous method.Sometimes mixture of acids,mixed solvents are used in previous methods.So as per our opinion P^H isimportant for the acidic synthesis of flavanone from 2-hydroxy chalcones. We also comparedreaction 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.

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