Research Article

Silica Sulphuric Acid: An Efficient Reusable, Heterogeneous Acidic Media for Synthesis of Flavones (2-aryl-4H-chromen-4-one) by Cyclocondensation of o-hydroxyphenyl aryl-1, 3-propanediones

M. M. V. Ramana*, Amey P. Nimkar, Rahul R. Betkar, Prasanna B. Ranade
Department of Chemistry, University of Mumbai, Vidyanagari, Santacruz (East), Mumbai, India.
***Corresponding author's E-mail:** mmvramana@yahoo.co.in

Accepted on: 04-02-2014; **Finalized on:** 31-03-2014.

ABSTRACT

Cyclocondensation of o-hydroxyphenyl aryl-1, 3-propanediones is a key step for the synthesis of flavones. In this work we report a very simple procedure for this conversion by using reusable, heterogeneous acidic media silica sulphuric acid with high efficiency.

Keywords: Cyclocondensation, Flavones, Heterogeneous, o-Hydroxyphenyl aryl-1, 3-propanediones, Silica sulphuric acid.

INTRODUCTION

Flavones are widely spread in nature and are having various biological activities. Flavonoid derivatives exhibit antihepatitic[1], anticancer[2], antioxidant[3], antifungal[4], antiallergic[5], anticoagulative[6], and vasorelaxant[7] activities. Therefore synthesis of flavones has enormous importance in pharmaceutical field. Flavones are abundant in fruits, vegetables, nuts, seeds, and flowers and are regular part of our diet.[8]

Flavones are synthesized by methods like Allan-Robinson method[9], Algar-Flynn-Oymanda method[10], Baker-Venkataraman Rearrangement[11] etc. Cyclocondensation of o-hydroxyphenyl aryl-1, 3-propanediones gives flavone. Generally this transformation is carried out in acidic media. Some of the reported methods for this cyclocondensation include use of sulphuric acid in glacial acetic acid[12], $CuCl_2$ in ethanol[13] , ionic liquid under microwave irradiation[14], $FeCl_3$ catalyzed synthesis of flavones at room temperature.[15] Flavones have been synthesized from o-hydroxyphenyl aryl-1, 3-propanediones using many solid phase catalysts like silica supported $NaHSO_4$[16] and silica supported Well-Dowson acid catalysts.[17] To the best of our knowledge silica sulphuric acid has not been utilized for the conversion of o-hydroxyphenyl aryl-1, 3-propanediones to flavones.

The use of traditional acid catalysts like sulphuric, phosphoric acid etc. causes pollution and corrosion in the environment.[18] The use of heterogeneous acid media overcomes these hazards. Silica sulphuric acid has been used as solid acid catalyst for many chemical transformations like synthesis of oxazolines and imidazolines[19], acetylation of aldehydes and sugars[20], synthesis of substituted pyrroles[21], Fischer's esterification[22], synthesis of benzimidazoles[23], thionitrites and disulfides.[24] The wide use of this catalyst in chemical reactions is due to the ease of handling, enhanced reaction rate and simple work up in most cases. Silica sulphuric acid is synthesized at room temperature easily by treatment of silica gel with chlorosulphonic acid.[19]

Preparation of this acidic media is an easy process and without any work up as HCl gas escapes on addition of chlorosulphonic acid.

Here in we report the use of heterogeneous and reusable acidic media silica sulphuric acid for the synthesis of flavones from cyclocondensation of 1-(2-Hydroxy phenyl)-3-arylpropane-1, 3-dione as delineated in Scheme.

MATERIALS AND METHODS

All ^1H NMR (300 MHz) spectra were recorded on Bruker AVANCE spectrometer (Bruker BioSpin AG, Fällanden, Switzerland; 300 MHz). FT-Infrared spectra were recorded on a Perkin Elmer (Model-Frontier) spectrometer (Waltham, MA, USA). Silica gel of commercial source (60–120 mesh) was used for preparation of catalyst. All melting points are uncorrected. A mortar and pestle of porcelain was used for all reactions.

General procedure for synthesis of acidic media

Silica gel (60-120mesh) (30.0 g) was taken in two necked round bottom flask. Chlorosulfonic acid (6.0 ml) is added dropwise in 30 minutes time interval. Rapidly generated HCl gas was neutralized by NaOH solution. Once the addition is over, the reaction mixture is shaken for another 30 minutes.

Reaction

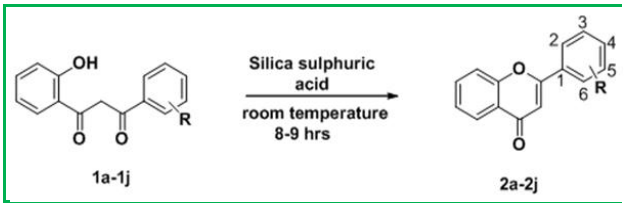
Synthesis of compounds 1a to 1j

Compounds **1a-1j** have been synthesized as per literature procedure.[12]

Synthesis of compounds 2a to 2j

1-(2-Hydroxy phenyl)-3-arylpropane-1, 3-dione **1a-1j** (0.002M) were ground with 5.0 g silica sulphuric acid in a mortar with pestle. Reaction mixture was shaken for some time and kept for 9 hours at room temperature.

Completion of reaction was monitored by TLC. After the completion of reaction, 25.0 ml of ethyl acetate was added to reaction mixture and filtered the mixture to remove the silica sulphuric acid. Ethyl acetate was recovered under reduced pressure to obtain compounds **2a-2j** as delineated in Table 1. ^{1}H NMR spectra of **2a-2j** were consistent with the data reported in literature.[12, 25, 26]



Scheme: Synthesis of flavones (2-aryl-4*H*-chromen-4-one) **2a-2j**

Table 1: Synthesis of flavones (2-aryl-4*H*-chromen-4-one) **2a-2j**

Compound	Substituent R	M.P.°C (observed)	M.P.°C (literature)	Yield %	Time (in hours)
2a	H	95	93-95 [25]	80	9.0
2b	2'-Cl	116	118 [14]	74	8.5
2c	3'-Cl	110	109-110 [29]	75	9.0
2d	4'-Cl	185	185-187 [14]	71	8.5
2e	4'-F	145	145-148 [27]	70	8.5
2f	4'-OMe	155	155-156 [14]	72	8.5
2g	2'-Br	135	134-135 [28]	70	9.0
2h	3'-OMe	128	128-129 [14]	70	8.0
2i	4'-CH_3	108	106-109 [25]	68	9.0
2j	3'-F	98	96-98 [25]	68	9.0

Table 2: Synthesis of flavones **2a** and **2d** with recycled silica sulphuric acid

Entry	compound	Product	Time (hrs)	Yield %	Recycle yield (%)				
					1	2	3	4	5
1	1a	2a	9.0	80	78	78	78	76	76
2	1d	2d	8.5	71	68	68	66	66	66

RESULTS AND DISCUSSION

An efficient procedure for the cyclocondensation of 1-(2-Hydroxy phenyl)-3-arylpropane-1, 3-dione under solvent free conditions at room temperature has been described which involves grinding of 1-(2-Hydroxy phenyl)-3-arylpropane-1, 3-dione with silica sulphuric acid media previously prepared by literature procedure.[24] The product is separated just by adding appropriate organic solvent and silica sulphuric acid is recovered by simple filtration of the reaction mixture.

Silica sulphuric acid reuse and recovery

Reusability is one of the important aspects of using heterogeneous media, therefore we tried some experiments for reusability of the silica sulphuric acid. After the completion of the reaction, the product was dissolved in organic solvent and silica sulphuric acid was filtered. Repeated washings with the organic solvent were given to remove the trace amount of product. Silica sulphuric acid was dried at 60°C and again used for the conversion (**1a** & **1d**) to (**2a** & **2d**) respectively, successively five times without significantly affecting its activity as delineated in **Table 2**.

CONCLUSION

In conclusion, the present method for the synthesis of flavones (2-aryl-4*H*-chromen-4-one) from corresponding 1-(2-Hydroxy phenyl)-3-arylpropane-1, 3-dione is simple, highly efficient and green method. Being mild and ecofriendly method, we can use it as an alternative method to the known literature methods.

Acknowledgement: The authors are thankful to Department of chemistry, University of Mumbai for the facilities and for the award of Departmental Research Fellowship to Amey P. Nimkar and Rahul R. Betkar. Prasanna B. Ranade is thankful to UGC for the award of BSR fellowship.

REFERENCES

1. Shie PH, Huang RL, Lay HL, The Flavonoids in *Citrus madurensis Lour* and their Anti Hepatitis B Virus Activity, Pharm. Anal. Acta, 4, 2013, 1000239/1-1000239/5.
2. Juvale K, Stefan K, Wiese M, Synthesis and biological evaluation of flavones and benzoflavones as inhibitors of BCRP/ABCG2, Eur. J. Med. Chem, 67, 2013, 115-126.
3. Venkatachalam H, Nayak Y, Jayashree BS, Evaluation of the Antioxidant Activity of Novel Synthetic Chalcones and Flavonols, Int. J. Chem. Eng. Appli, 3, 2012, 216-219.

4. Prakash O, Kumar R, Prakash V, Synthesis and antifungal activity of some new 3-hydroxy-2-(1-phenyl-3-aryl-4-pyrazolyl) chromones, Eur. J. Med. Chem, 43, 2008, 435-440.

5. Makino T, Kanemaru M, Okuyama S, Shimizu R, Tanaka H, Mizukami H, Anti-allergic effects of enzymatically modified isoquercitrin (α-oligoglucosyl quercetin 3-*O*-glucoside), quercetin 3-*O*-glucoside, α-oligoglucosyl rutin, and quercetin, when administered orally to mice, J. Nat. Med., 67, 2013, 881-886.

6. Liao XL, Luo JG, Kong LY, Flavonoids from *Millettia nitida* var. *hirsutissima* with their anticoagulative activities and inhibitory effects on NO production, J. Nat. Med., 67, 2013, 856-861.

7. Chen Z, Hu Y, Wu H, Jiang H, Synthesis and biological evaluation of flavonoids as vasorelaxant agents, Bio. Med. Chem. Lett., 14, 2004, 3949-3952.

8. Peterson J, Dwyer J, Flavonoids: Dietary Occurrence and Biochemical Activity, Nutr. Res., 18, 1998, 1995-2018.

9. Dyke SF, Ollis WD, Sainsbury M, Synthesis of Isoflavones. Part III. Caviunin, J.Org. Chem., 26, 1961, 2453-2455.

10. Bennett M, Burke AJ, O'Sullivan WI, Aspects of the Algar-Flynn-Oyamada (AFO) Reaction, Tetrahedron, 52, 1996, 7163-7178.

11. A) Baker W, Molecular Rearrangement of Some O-Acyloxyacetophenones and the Mechanism of the Production of 3-Acylchromones, J. Chem. Soc., 1933, 1381-1389.

    B) Mahal HS, Venkataraman K, Synthetical Experiments in the Chromone group.Part XIV.The action of Sodamide on 1-acyloxy-2-acetonaphthones, J. Chem. Soc., 1934, 1767-1769.

12. Joshi AJ, Gadhwal MK, Joshi UJ, D'Mello P, Sinha R, Govil G, Synthesis of B-ring substituted flavones and evaluation of their antitumor and antioxidant activities, Med. Chem. Res., 22, 2013, 4293-4299.

13. Kabalka GW, Mereddy AR, Microwave-assisted synthesis of functionalized flavones and chromones, Tetrahedron Lett., 46, 2005, 6315-6317.

14. Bhosale RS, Sarda SR, Giram RP, Parwe SP, Ardhapure SS, Pawar RP, Ionic liquid promoted expeditious synthesis of flavones, J. Iran. Chem. Soc., 6, 2009, 519-522.

15. Zubaidha PK, Hashmi AM, Bhosale RS, $FeCl_3$ catalyzed dehydrative cyclisation of 1, 3-(diaryl diketones) to flavones, Heterocyclic Communication., 11, 2005, 97-100.

16. Kucukislamoglu M, Neioglu M, Zengin M, Arslan M, Yayli N, An environmentally benign synthesis of flavones from 1, 3-diketones using silica gel supported $NaHSO_4$ catalyst, J. Chem. Res., 2005, 2005, 556-557.

17. Bennardi DO, Romanelli GP, Jios JL, Autino JC, Baronetti GT, Thomas HJ, Synthesis of substituted flavones and chromones using a Wells-Dawson heteropolyacid as catalyst, ARKIVOC, 2008, (xi), 123-130.

18. Vazquez P, Pizzio L, Romanelli G, Autino J, Caceres C, Blanco M, Mo and W heteropolyacid based catalyst applied to the preparation of flavones and substituted chromones by cyclocondensation of O-hydroxyphenyl aryl 1, 3-propanediones, Appl. Catal. A: Gen., 235, 2002, 233-240.

19. Baltork IM, Mirkhani V, Moghadam M, Tangestaninejad S, Zolfigol MA, Alibeik MA, Khosropour AR, Kargar H, Hojati SF, Silica sulfuric acid: A versatile and reusable heterogeneous catalyst for the synthesis of oxazolines and imidazolines under various reaction conditions, Catalysis Communication., 9, 2008, 894-901.

20. Wu H, Shen Y, Fan L, Wan Y, Shi D, Solid silica sulfuric acid (SSA) as a novel and efficient catalyst for acetylation of aldehydes and sugars, Tetrahedron, 62, 2006, 7995-7998.

21. Veisi H, Silica sulfuric acid (SSA) as a solid acid heterogeneous catalyst for one-pot synthesis of substituted pyrroles under solvent-free conditions, Tetrahedron Lett., 51, 2010, 2109-2114.

22. Rajendran A, Karthikeyan C, Silica suphuric acid catalyzed Fischer esterification reaction under solventless condition: A novel green chemical reaction, Am. Chem. Sci. J., 1, 2011, 28-36.

23. Sadeghi B, Nejad MG, Silica sulfuric acid: an ecofriendly and reusable catalyst for synthesis of Benzimidazole Derivatives, J. Chem., 2013, 2012, 1-5

24. Zolfigol MA, Silica-sulfuric acid/$NaNO_2$ as a novel heterogeneous system for production of thionitrites and disulfides under mild conditions, Tetrahedron, 57, 2001, 9509-9511.

25. Min M, Choe H, Hong S, Regioselective cross-dehydrogenative coupling of chromones and non-activated arenes, Asian J. Org. Chem., 1, 2012, 47-50.

26. Du Z, Ng H, Zhang K, Zeng H, Wang J, Ionic liquid mediated Cu-catalyzed cascade oxa-Michael-oxidation: efficient synthesis of flavones under mild reaction conditions, Org. Biomol. Chem., 9, 2011, 6930-6933.

27. Bapna M, Nema RK, Synthesis of some novel Non-Nucleoside Reverse Transcriptase Inhibitor, Asian J. Chem., 21, 2009, 1244-1248.

28. Zhao J, Zhao Y, Fu H, Transition-metal free intramolecular Ullmann type O-arylation: Synthesis of chromone derivative, Angew. Chem.Int. Ed., 50, 2011, 3769-3773.

29. Zhou Z, Zhao P, Huang W, Yang G, A selective transformation of flavanones to 3-bromoflavones and flavones under microwave irradiation, Adv. Synth. Catal., 348, 2006, 63-67.

Source of Support: Nil, **Conflict of Interest:** None.