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RESEARCH ARTTICLE

SYNTHESIS, CHARACTERIZATION AND ANTI-MICROBIAL ACTIVITY OF A PYRIMIDINE DERIVATIVES DERIVED FROM QUINOLINYL CHALCONE

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ABSTRACT

Various pyrimidine derivatives have been synthesized by reacting chalcones with urea in presence of concentrated hydrochloric acid in methanol. The structure of newly synthesized heterocycles were confirmed by their elemental analysis, IR spectra and ^{1}H NMR spectra. They were evaluated for their antimicrobial activity.

INTRODUCTION

The pyrimidine entity is one of the most prominent structures found in nucleic acid chemistry. Pyrimidine have been isolated from the nucleic acid hydrolyses. The presence of a pyrimidine base in thymine, cytosine and uracil which are the essential building blocks of nucleic acids in DNA and RNA is one of the possible reasons for their activities. Pyrimidine derivatives form a component in a number of useful drugs and are associated with many pharmaceutical and therapeutical activities. Furthermore, many condensed heterocyclic systems, especially when linked to a chalcone as pyrimidine ring play an important role as antibacterial, anti-inflammatory, anticancer, antimicrobial, antidiabetic, antituberculosis and anti malarial activities.

One of the method for the synthesis of pyrimidine is from α, β-unsaturated carbonyls by the cyclisation with urea and thiourea. The synthesis of sulphur and oxygen containing heterocycles has been explored for their therapeutic activity. Pyrimidine heterocycles possessing hydroxyl group has a unique place in medicinal chemistry and also plays a vital role in biological processes as well as synthetic drugs. Pyrimidine and quinoline moieties clubbed into one molecule, the resultant molecule may enhance the pharmaceutical activity up to some extent. Hence, it was thought interesting to explore the study of such molecules. Thus the present paper describes the synthesis of 4-(2-chloro-5,7-diflouro quinolin-3-yl) -6- (substituted phenyl) pyrimidine-2-ol [5(a-j)] derived from (E)-3-(2-chloro-5,7-difluoro quinoline-3-yl)-1-(substituted phenyl) prop-2-en-1-one [4(a-j)].

MATERIALS AND METHODS

All the melting points were measured in open capillary tube in scientific melting point apparatus and were uncorrected. Thin layer chromatography (TLC) was performed on silica gel plate (Merck, 60, F254) was used for purity checking and reaction monitoring. IR spectra of synthesized compound have been scanned in KBr pellets by using Shimashu 1801 FTIR. ^{1}H NMR spectra were measured in DMSO on a BRUKER AVANCE II 400 spectrometer and tetramethylsilane (TMS) as an internal standard.

Synthesis of 2-Chloro-5,7-difluoro quinoline-3-carbaldehyde [Compound 3]

To a solution of 3,5-difluoro acetanilide (8.56 gm, 0.05 mol) in dry DMF (10.9gm, 0.15 mol) at 0-5 ^{0}C temperature,

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phosphoryl chloride (53.58gm, 0.35mol) was added drop wise with stirring and mixture was refluxed at 85-90 ^{0} C for time ranging between 4-16 hours. The mixture was poured on to crushed ice, stirred for 1h and kept overnight. The resulting solid was filtered, washed well with water and dried. The compound was recrystallised from ethyl acetate. Yield: 72 %, m.p.170-180 ^{o}C.

Synthesis of (E)-3-(2-Chloro-5,7-difluoro quinoline-3-yl)-1-(substituted phenyl) prop-2-en-1-one [4(a-j)]

Equimolar quantities of 2-chloro-5,7-difluoroquinoline-3-carbaldehyde (0.01mol) and substituted acetophenone (0.01 mol) in methanol was stirred at 0-5 ^{0}C for 2h, while drop wise addition of aqueous sodium hydroxide (NaOH 25%, 4ml) to the solution and stirring was continuous for 24 h at room temperature. The reaction mixture was poured into crushed ice and acidified if necessary with dilute hydrochloric acid (10% HCl). The solid mass separated out was filtered, washed with water and crystallized from ethanol to yellow product. The residue was purified by column chromatography using ethanol.

(E)-3-(2-Chloro-5,7-difluoroquinoline-3-yl)-1-(4-chlorophenyl) prop-2-en-1-one [4a]

m.p.: 153 ^{0}C, Yield: 70%, IR (KBr in cm^{-1}): 3085 (Ar-H C-H str.), 1681(C=O str., chalcone gr.), 1639 (CH=CH str.),1581(C=N str.)., 1445 (Ar C=C str.), 1213 (C-N str.), 1125 (Ar C-F str.), 736 (C-Cl str.). ^{1}H NMR (400MHz, DMSO-d6, δ ppm): 7.73(1H, d, H_α), 8.03 (1H, d, H_β), 6.59 (1H, s, Ar-$H_{f'}$), 7.09 (1H, s, Ar-$H_{h'}$), 7.61 (2H, d, Ar-$H_{C,E}$), 7.92 (2H, d, Ar-H $_{B,F}$), 8.58 (1H, s, Ar-$H_{d'}$). Anal. Calcd for : $C_{18}H_9Cl_2F_2NO$: (364.17) : C, 59.37; H, 2.49; N, 3.85. Found: C,59.32; H, 2.44; N, 3.80.

(E)-3-(2-Chloro-5,7-difluoroquinoline-3-yl)-1-(2,4-difluorophenyl)prop-2-en-1-one [4g]

m.p.: 112 ^{0}C, Yield: 79%, IR (KBr in cm^{-1}): 3070 (Ar C-H str.), 1676(C=O str., chalcone gr.), 1641 (CH=CH str.), 1596 (C=N str.)., 1488 (Ar C=C str.), 1122 (C-F str.), 761(C-Cl str.) ^{1}H NMR (400MHz, DMSO-d6, δ ppm) : 7.67 (1H, d, H_α), 8.01 (1H, d, H_β), 6.61 (1H, s, Ar-$H_{f'}$), 6.73 (1H, s, Ar-H_C), 7.28 (1H, d, Ar-H_E), 7.35 (1H, s, Ar-$H_{h'}$), 7.92 (1H, d, Ar-H_F), 8.53 (1H, s, Ar-$H_{d'}$). Anal. Calcd for: $C_{18}H_8ClF_4NO$: (365.71) : C,59.12; H, 2.20; N, 3.83. Found: C, 59.17; H, 2.12; N, 3.77.

Synthesis of 4-(2-chloro-5,7-diflouro quinolin-3-yl)-6-(substituted phenyl) pyrimidine-2-ol [5(a-j)]

(E)-3-(2-Chloro-5,7-difluoro quinoline-3-yl) -1-(substituted phenyl) prop-2-en-1-one (0.01 mol) was reacted with urea (0.015 mol) using methanol as solvent in round bottom flask. Few drop of HCl were added and the reaction mixture was refluxed on water bath at 80 °C for 10-14h. The process of the reaction was monitored by TLC (toluene:ethyl acetate, 8:2). After completion of reaction, mixture was cooled and poured into crushed ice with constant stirring for an hour. Then the precipitate was collected by filtration and washed with water. The crude product was dried and crystallized from ethanol (99.9 %).

4-(2-Chloro-5,7-diflouroquinolin-3-yl)-6-(4-chlorophenyl) pyrimidin-2-ol [5a]: m.p.: 225 ^{0}C, Yield: 65 %, IR (KBr in cm^{-1})

3340 (O-H str., hydroxy gr.), 3082 (Ar C-H str.), 1577 (C=N str., tertiary amine), 1429 (Ar C=C str.), 1357 (O-H bend.), 1095 (C-F str.), 732 (C-Cl str.) ^{1}H NMR (400MHz, DMSO-d6, δ ppm) : 10.20 (1H, s, pyrimidine OH), 7.90 (1H, s, pyrimidine ring), 6.90 (1H, s, Ar-$H_{f'}$), 7.20 (1H, s, Ar-$H_{h'}$), 7.55 (2H, d, Ar-H_{CE}), 8.20 (2H, d, Ar-H_{BF}), 8.58 (1H, s, Ar-$H_{d'}$). Anal. Calcd for: $C_{19}H_9Cl_2F_2N_3O$: C-56.46, H-2.24, N-10.40; Found: C-56.42; H-2.19; N-10.33.

4-(4-Bromophenyl)-6-(2-chloro-5,7-diflouroquinolin-3-yl)pyrimidin -2-ol [5b]: m.p.: 190 ^{0}C, Yield

75 %, IR (KBr in cm^{-1}): 3342 (O-H str., hydroxy gr.), 3079 (Ar C-H str.), 1575 (C=N str., tertiary amine), 1430 (Ar C=C str.), 1355 (O-H bend.), 1095 (C-F str.), 581 (C-Br str.) 732 (C-Cl str.), Anal. Calcd for: $C_{19}H_9BrClF_2N_3O$: C-50.86, H-2.02, N-9.37, Found: C-50.88, H-1.97, N-9.39.

4-(2-Chloro-5,7-diflouroquinolin-3-yl)-6-(4-methoxyphenyl) pyrimidin-2-ol [5c]: m.p.: 110 ^{0}C, Yield: 58 %, IR (KBr in cm^{-1})

3364 (O-H str., hydroxy gr.)3050 (Ar. C-H str.), 2975,2890 (C-H str., methoxy gr.) 1589 (C=N str., tertiary amine), 1415 (Ar. C=C str.), 1330 (O-H bend.), 1218, 1081 (C-O-C str.) 1178 (C-F str.), 761 (C-Cl str.), ^{1}H NMR (400MHz, DMSO-d6, δ ppm) : 10.28 (1H, s, pyrimidine OH), 7.96 (1H, s, pyrimidine ring), 3.82 (3H, s, Ar-H_D), 6.99 (1H, s, Ar-$H_{f'}$), 7.40 (1H, s, Ar-$H_{h'}$), 7.70 (2H, d, Ar-H_{CE}), 8.27 (2H, d, Ar-H_{BF}), 8.60 (1H, s, Ar-$H_{d'}$), Anal. Calcd for: $C_{20}H_{12}ClF_2N_3O_2$: C-60.09, H-3.03, N-10.51, Found: C-60.04, H-2.97, N-10.46.

4-(4-Aminophenyl)-6-(2-chloro-5,7-diflouroquinolin-3-yl)pyrimidin -2-ol [5d]: m.p.: 156 ^{0}C, Yield: 61%, IR (KBr in cm^{-1})

3342 (O-H str., hydroxy gr.), 3280, 3219 (N-H str., amino gr.) 3079 (Ar C-H str.), 1568 (C=N str., tertiary amine), 1412 (Ar. C=C str.), 1635 (N-H bend.), 1128 (C-F str.), 752 (C-Cl str.), Anal. Calcd for: $C_{19}H_{11}ClF_2N_4O$: $C_{19}H_{11}ClF_2N_4O$: C-59.31, H-2.88, N-14.56, Found: C-59.90, H-2.81, N-14.51.

4-(2-Chloro-5,7-diflouroquinolin-3-yl)-6-(3-flourophenyl) pyrimidin-2-ol [5e]: m.p.: 228 ^{0}C, Yield: 84 %, IR (KBr in cm^{-1})

3362 (O-H str., hydroxy gr.), 3058 (Ar C-H str.), 1554 (C=N str., tertiary amine), 1417 (Ar. C=C str.), 1128 (C-F str.), 752 (C-Cl str.), Anal. Calcd for: $C_{19}H_9ClF_3N_3O$: C-58.85, H-2.34; N-10.84, Found: C-58.79, H-2.29, N-10.79.

4-(2-Chloro-5,7-diflouroquinolin-3-yl)-6-(3-methoxyphenyl) pyrimidine-2-ol[5f]:m.p.: 280 ^{0}C, Yield

70 %, IR (KBr in cm^{-1}): 3381 (O-H str., hydroxy gr.), 3056 (Ar. C-H str.), 2968, 2871 (C-H str., methoxy gr.) 1580 (C=N str.,

tertiary amine), 1411 (Ar. C=C str.), 1324 (O-H bend.), 1209, 1072 (C-O-C str.) 1178 (C-F str.), 761 (C-Cl str.), Anal. Calcd for: $C_{20}H_{12}ClF_2N_3O_2$: C- 60.09, H-3.03, N-10.51, Found: C-60.03, H-2.99, N-10.46.

4-(2-Chloro-5,7-diflouroquinolin-3-yl)-6-(2,4-diflourophenyl) pyrimidine-2-ol[5g]*: *m.p.*:*204 ^{0}C, Yield

86%, IR (KBr in cm^{-1}): 3375 (O-H str., hydroxy gr.), 3061 Ar. C-H str.), 1565 (C=N str., tertiary amine), 1421 (Ar. C=C str.), 1329 (O-H bend.), 1116 (C-F str.), 732 (C-Cl str.), Anal. Calcd for: $C_{19}H_8ClF_4N_3O$: C- 56.24, H-1.99, N-10.36, Found: C-56.19, H-2.01, N-10.31.

4-(2-Chloro-5,7-diflouroquinolin-3-yl)-6-(2,4-dichloro-5-flourophenyl)pyrimidine-2-ol [5h]: m.p.: 198 ^{0}C, Yield

76%, IR (KBr in cm^{-1}): 3336 (O-H str., hydroxy gr.), 3057 (Ar. C-H str.), 1570 (C=N str., tertiary amine), 1479 (Ar. C=C str.), 1356 (O-H bend.), 1141 (C-F str.), 754 (C-Cl str.), Anal. Calcd for: $C_{19}H_7Cl_3F_3N_3O$: C- 49.98, H-1.55, N-9.20, Found: C-49.91, H-1.51, N-9.21.

4-(5-Chloro-2,4-diflourophenyl)-6-(2-chloro-5,7-diflouroquinolin-3-yl) pyrimidine -2-ol [5i]: m.p.: 118 ^{0}C, Yield

66%, IR (KBr in cm^{-1}): 3341 (O-H str., hydroxy gr.), 3051 (Ar. C-H str.), 1566 (C=N str., tertiary amine), 1452 (Ar. C=C str.), 1381 (O-H bend.), 1131 (C-F str.), 766 (C-Cl str.), Anal. Calcd for: $C_{19}H_7Cl_2F_4N_3O$: C-51.84, H-1.60, N-9.55, Found: C-51.87, H-1.62, N-9.55.

4-(2-Chloro-5,7-diflouroquinolin-3-yl)-6-(2,4,5-trichlorophenyl)pyrimidine-2-ol [5j]: m.p.: 170 ^{0}C, Yield: 89%, IR (KBr in cm^{-1})

3355 (O-H str., hydroxy gr.), 3048 (Ar. C-H str.), 1545 (C=N str., tertiary amine), 1461 (Ar. C=C str.), 1364 (O-H bend.), 1095 (C-F str.), 760 (C-Cl str.), Anal. Calcd for: $_{19}H_7Cl_4F_2N_3O$: C-48.24, H-1.49, N-8.88, Found: C-48.19, H-1.44, N-8.84.

Antimicrobial Activity

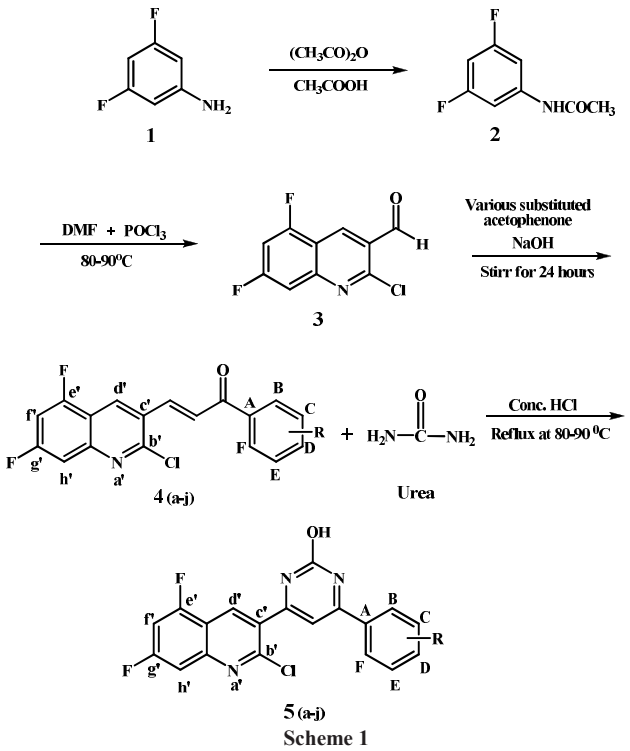
The antimicrobial activity was carried out using 'Broth Dilution Method. The antimicrobial activity of the all synthesized pyrimidine derivatives were evaluated against four bacterial strains viz. *E. coli, P.aeruginosa*, *S. aureus, S. pyogenes* and two fungus strain viz.*C. albicans*, S. mycescervecieaceae. Each of the test compound and standards were dissolved in DMSO obtaining 2000 µg/ml concentration, as a stock solution. Serial dilutions were prepared in primary and secondary screening. In primary screening 1000, 500, 250, 125 and 62.5 µg/ml concentrations of the synthesized drugs were taken. In secondary screening the drugs found active in primary screening were similarly diluted to obtain 100, 50, 25, 12.5, 6.50, 3.250 and 1.5650 µg/ml concentrations. Ciprofloxacin, Gentamicin and Flucanazole were used as standard drugs for antibacterial and antifungal activities.

Table 1

Compounds	M B C in µg/ml Gram negative organisms		Gram positive organisms		M F C in µg/ml	
	E. coli	*P. aeruginosa*	*S.aureus*	*B. subtilis*	*C. albicans*	S. cerveceaceae
5a	250	250	250	500	500	1000
5b	125	250	250	250	1000	500
5c	125	250	250	250	500	500
5d	250	250	125	250	500	1000
5e	500	500	250	500	1000	1000
5f	125	500	500	500	500	1000
5g	125	100	250	250	500	500
5h	1000	500	1000	1000	500	1000
5i	500	1000	250	250	500	1000
5j	500	500	250	250	250	250
Ciprofloxacin	50	50	50	50	---	---
Gentamicin	50	50	50	50	---	---
Flucanazole	---	---	---	---	100	100

MBC- Minimal Bactericidal Concentration
MFC- Minimal Fungicidal Concentration

Reaction scheme



Scheme 1

Where,
R = 4-Cl, 4-Br, 4-OCH_3, 4-NH_2, 3-F, 3-OCH_3, 2,4-di F, 2,4-di Cl 5-F, 2,4- di F 5-Cl, 2,4,5- tri Cl.

RESULTS AND DISCUSSION

The synthetic route for the formation of target compounds [5(a-j)] is depicted in Scheme I. Synthesized compounds [5 (a-j)] were synthesized in good yield and purity. 3,5-Difluoro acetanilide (2) and 2-chloro-5,7-difluoro quinoline-3-carbaldehyde (3) were refluxed for 4-16 hours in presence of Vilsmeier-Haack reagent to form a chalcone derivatives [4(a-j)]. Further, chalcone derivatives [4(a-j)] along with urea was refluxed for 10-14 hours in presence of conc. HCl in methanol. After completion of reaction, reaction mixture was pour on crushed ice to form final compound [5(a-j)]. The synthesized

compounds were characterized on the basis of the spectral and analytical studies.

The IR spectra of chalcone C=O group is observed as a strong and sharp band at 1685-1665 cm^{-1}. Compound [5(a-j)] showed a band in the region 3400-3200 cm^{-1} due to the hydroxy groups. The C-H (aliphatic and aromatic), C=C stretching vibrations are observed at their usual positions. Further, ^{1}H NMR spectra exhibited multiples in the region at 6.95-8.60 δ ppm for aromatic protons of compound [5(a-j)]. One proton of hydroxyl in pyrimidine ring showed ranging between 10.05-10.65 δ ppm.

All compounds were purified by column chromatography and characterized on the basis of spectral studies. The spectral details of all the synthesized compounds are given in appropriate place and are at agreement with the assigned structures.

From the antibacterial results of **[5(a-j)]** in table-1, compounds 5b, 5c, 5f and 5g exhibited excellent activity of 125 μg/ml against *E. coli.* Compound 5g showed excellent activity of 100 μg/ml against *P. aeruginosa* and B_4 shows very good activity of 125 μg/ml against *S. aureus*. Rest of compounds showed good to moderate activity. The antifungal results of this series compound 5j showed better activity of 250 μg/ml against two fungal species and other derivatives showed moderate and good activity against remaining fungal species.

CONCLUSION

In summary, we have synthesized a various type of quinoline containing pyrimidine derivatives from chalcone as starting materials. The compounds **[5(a-j)]** in a good yield. Elemental analysis was found to be in good agreement. IR and NMR spectra also agreed with the proposed structures. Synthesized substituted quinolinyl pyrimidine derivatives **[5(a-j)]** showed moderate to high antimicrobial activity against *E.coli, P. aeruginosa*, *S. aureus, S. pyogenes*, *C. albicans and* S. mycescervecieaceae.

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References

1. Amir M., Javed S.A. and Kumar H,(2007) *Indian Journal of Pharmaceutical Science*, 69(3): 337-343.
2. Andrews B. and Mansur A., (2015) *Indian journal of Chemistry*, 54(B): 406-411.
3. Belluti F., Fontana G., Dal Bo L., Carenini N., Giommarelli C. and Zunino F., (2010) *Bioorganic Medicinal Chemistry*, 18: 3543–3550.
4. Baddiley J., Lythgoe B. and Todd A.R., (1944) *Journal of Chemical Society*, 4: 318–322.
5. Desenko S.M., Lipsum V.V. and Gorbenko N.I., (1995) *Journal of Pharmaceutical Chemistry*, 29 : 265.
6. Dinakaran V.S., Jacob D. and Mathew J.E., (2012) *Medicinal Chemistry Research*, 21:3598-3606.
7. Fathalla O.A., Awad S.M., and Mohamed M. S., *Archives Pharmacal Research*, (2005) 28(11), :1205-1212.
8. Goudgaon N.M., and Reddy R.Y., (2014) *International Journal of Pharmaceutical Chemical and Biological Sciences*, 4(1): 64-68.
9. Joshi A.A. and Viswanathan C.L., (2005) *Bioorganic Medicinal Chemistry. Letters,* 15: 73.
10. Jadhav D.H. and Rama C.S., (2007) *Indian journal of Chemistry.*, 46B: 2064-2067.
11. Kundapura U., Bhanuprakash V., Khan M.T.H., Balladka K.S., Yogisharadhya R., Chenna G., Darshan R. and Raghavendra R., (2014) *Medicinal Chemistry Research*., 23: 168-180.
12. Kumar B.P., Venkantraman S., Mehta R. and Devi P., (2011) *International Journal of Chemical Science*, 9(1): 69-79.
13. Lahsasni S. A., (2014) *Pharmaceutical Chemistry Journal,* 48(3): 171-174.
14. Lilienkampf A., Mao J., Wan B., Wang Y., Franzblau S. and Kozikowski A. P., (2009) *Journal of Medcinal Chemistry.,* 52: 2109.
15. Meth-Cohn O., Narine B., Tamowski B., (1981) *Jounal of Chemical Society, Perkin Trans.,*1: 1520-1530.
16. Monks A., Scudiero D., Paull K., Vistica D., C. Hose, (1991) *J. Natl. Cancer Inst*, 83, 757.
17. Mohan J., *Organic Spectroscopy*, *Principles and Applications*, (2000), 188, Narosa Publishing House.
18. National Committee for Clinical Laboratory Standard. (1997) Reference Method for broth dilution antifungal susceptibility testing of yeasts Approved standard M27A., NCCLS, Wayne, PA.
19. Patel R., Desai K. and Chikhalia K., (2003) *Journal of Indian Chemical Society*, 80: 138.
20. Panda S.S. and Chowdary P.V.R., (2008) *Indian Journal of Pharmaceutical Science*., 70: 208.
21. Rizvi S.U.F., Siddiqui H.L, Parvez M., Ahmad M., Siddiqui W.H. and Yasinz M., (2010) *Chem. Pharm. Bull.,* 58(3): 301-306.
22. Sondhi S.M., Singh J. and Agrawal S.K., (2012) *Medicinal Chemistry Research*, 12: 91-99.
23. Seekarajapuram D.V., Keloth K.S. and Peralam Y.P., (2012) *Medicinal Chemistry Research*, 21: 2998–3005.
24. Srivastava A. and Singh R.M., (2005) *Indian journal of Chemistry*, 44B: 1868-1875.
25. Silverstein R.M. & Webster F.X., (1998) *Spectrometric Identification of Organic Compounds*, 4thEd. John wiely & Sons, Ind.
26. Vachala S.D., Srinivasan K.K. and Prakash P.Y., (2014) *Medicinal Chemistry Research*, 23: 168-180.

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