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SONOCHEMICAL SYNTHESIS OF 2, 4-DISUBSTITUTED QUINOLINES CATALYSED BY PHOSPHOSULFONIC ACID (PSA) UNDER SOLVENT-FREE CONDITIONS

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Abstract: A simple, efficient and environment-friendly one-pot multicomponent method has been developed for synthesizing 2, 4-disubstituted quinolones. It uses ultrasound-mediated condensation of aldehydes, alkynes and amines in the presence of various catalysts under solvent-free conditions. Phosphosulfonic acid (PSA) was found to be superior to other catalysts for the reaction of 2-methoxybenzaldehyde and ethynylbenzene with 4-methoxyaniline. A series of 2,4-disubstituted quinolines were synthesized in good to excellent yields after short reaction times when compared to the conventional thermal method. This new procedure provides several advantages over current methods, including: simple work-up, cost effectiveness, a wide range of functional group tolerance and use of an inexpensive reusable heterogeneous catalyst. All new compounds were identified and characterized by ^1H, ^{13}C NMR and HRMS spectra.

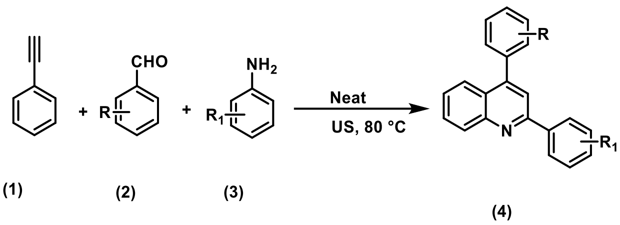
Key words: Quinolones, Phosphosulfonic acid, ^1H NMR, ^{13}C NMR, HRMS.

INTRODUCTION

Quinoline analogues are an important class of natural and synthetic bicyclic nitrogen-containing heterocyclic compounds which have a wide range of applications. These include biological roles as antagonists for the N-methyl-D-aspartate (NMDA) receptor glycine site [1-4] and the Follicle-stimulating hormone (FSH) receptor.[5,6] Some quinolones also have important roles as antimalarial[7], anti-bacterial, antifungal, anti-inflammatory, antitumor[8], anthelmintic, cardiotonic, analgesic activity, anticonvulsant, and antioxidant drugs.[9,10] Quinolines and other heterocyclic molecules were also useful ligands for transition-metal complexes[11] and are important building blocks in organic chemistry.[12-16] The inherent fluorescent properties of quinolones make them useful as emitting chromophores.[17,18] There is therefore considerable ongoing interest in improved syntheses of useful quinoline derivatives -particularly environmentally-friendly syntheses.[19-25] Most of the present routes to substituted quinolones have environmental drawbacks like using organic solvents, or traditional Lewis and Bronsted acids.[26-28] Most of these synthetic routes also produce a large amount of waste and require long reaction times.[29]

We therefore set out to devise improved synthetic routes to quinolone derivatives. We decided to react various alkynes and aldehydes with amines using ultra sound irradiation under solvent-free conditions. Additionally, we decided to use solid-supported catalysts because they are cost-effective due to the fact that they are reusable and they also have ecological benefits. Solid acid catalysts are easily handled and have high catalytic activities. Phosphosulfonic acid (PSA) is one of these and it provides easy accessibility of active sites, stability, hygroscopic properties, handling, reusability, and good product yields. Ultrasound-promoted synthesis is known to shorten many reaction times and important heterocycles have been synthesized under solvent-free conditions using this technique.[30-38]

To the best of our knowledge, there are no reports on the synthesis of 2, 4-disubstituted quinolines under solvent-free ultrasound irradiation at 80 °C catalyzed by PSA which should provide a more environmentally friendly route to these compounds. This would be quite desirable if current yields and reaction times were at least maintained. Herein, we report a facile one-pot synthesis of 2,4-disubstituted quinolines via three-component coupling of alkynes, aldehydes and amines under solvent-free conditions using solid-supported PSA catalyst and ultrasound irradiation at 80°C (**Scheme 1**).



Scheme 1: Synthesis of 2, 4-disubstituted quinolines.

RESULT AND DISCUSSION

The conventional and ultrasonic synthesis of 4-(2-methoxyphenyl)-2-(4-methoxyphenyl) quinolone (**4a**) from ethynylbenzene (**1**), 4-methoxybenzaldehyde (**2**) and 4-methoxyaniline (**3**) was used as a model (Table 1) to determine the best experimental conditions. We initially carried out the reactions without any catalyst (**Table 1, entry 1**). The reaction was then examined utilizing different catalysts under both conventional and ultrasound irradiation without solvent (**Table 2, entries 2-10**). In every case except one (**Table 2, entry 5**), ultrasonic conditions produced shorter reaction times and larger yields than conventional conditions.

The reaction produced very low (<40% conventional and < 52% ultrasonic) yields when InF_3, CAN-SiO_2, and $ZnCl_2$-SiO_2were used as catalysts (**Table 1, entries 2–4**). Catalysts such as $MnCl_2{\cdot}4H_2O$, Yb $(OAc)_3$, $NbCl_5$ and $FePO_4$ gave larger (45-55% conventional and 55-70% ultrasonic) yields (**Table 1, entries 5–8**) but these were

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all lower than solid-supported catalysts such as PS/PTSA, MSA, and PSA (**Table 1, entries 9–11**). Among these solid-supported catalysts, PSA showed the best results under ultrasound irradiation conditions. (**Table 1, entry 11**).The data in Table 1 reveal that yields increased slightly with mol % PSA up to 5%. Yields at 10% PSA (**Table 1, entry 14**) were identical to those at 5%. The best results were obtained in the presence of PSA (5mol %) at 80 °C (**Table 1, entry 11**) affording 4-(2-methoxyphenyl)-2-(4-methoxyphenyl) quinolone (**4a**) in 85% yield after 15 min at 80°C. Therefore, 5mol% of PSA was found necessary and sufficient for the total completion of the reaction under both conventional and ultrasonic conditions.

The superiority of the present methodology over some of the recently reported procedures was established by comparison of the result obtained with the PSA-catalyzed reaction with that of other reported catalysts/systems (Table 1 & 2). Comparison of the Catalytic Efficiency of PSA with Various Catalysts for the Synthesis of 4a.

Table 1: Influence of the catalyst for the synthesis of **4a**[a]

Entry	Catalyst (mol%)	Conventional		Ultrasonic	
		Time (min)	Yield[b] (%)	Time (min)	Yield[b] (%)
1	-	160	20	90	45
2	InF_3 (5)	90	35	50	45
3	CAN-SiO_2 (5)	100	30	60	52
4	$ZnCl_2$-SiO_2 (5)	120	40	70	48
5	$MnCl_2 \cdot 4H_2O$ (5)	100	50	60	70
6	$Yb(OAc)_3$ (5)	110	45	80	55
7	$NbCl_5$ (5)	80	55	45	65
8	$FePO_4$ (5)	95	45	60	70
9	PS/PTSA (5 mol %)	65	70	30	80
10	MSA(5 mol %)	60	72	30	85
11 [c]	PSA (5 mol %)	50	81	15	94, 91, 90, 87
12	PSA (1 mol %)	70	60	30	80
13	PSA (2 mol %)	60	75	25	85
14	PSA (10 mol %)	50	81	15	94

[a]Reaction of ethynylbenzene, (**1,** 1 mmol), 2-methoxybenzaldehyde (**2,** 1 mmol) and 4-methoxyaniline (**3,** 1 mmol) under solvent free condition at 80 °C. [b]Isolated yields. [c]Catalyst was reused three times.

Table 2: Screening of various solvent for the synthesis of compound **4a**[a]

Entry	Solvent (5mL)	Conventional		Ultrasonic	
		Time (min)	Yield[b] (%)	Time (min)	Yield[b] (%)
1	CH_3OH	72	69	38	73
2	CH_3CH_2OH	62	72	42	76
3	*i*-PrOH	80	58	50	70
4	CH_2Cl_2	78	46	48	68
5	CH_3CN	63	71	40	79
6	Neat	48	85	16	94

[a]Reaction of ethynylbenzene (1, 1 mmol), 3-methoxybenzaldehyde (2, 1 mmol), 4-methoxyaniline (3, 1 mmol), PSA catalyst (5 mol %) at 80 °C. [b]Isolated yields.

We next studied the effect of solvent on the conventional and ultrasonic reaction conducted under the "ideal" conditions at 80 °C using 5 mol %PSA with solvent-free (neat) conditions and in the presence of different solvents. The yield of products was lower (**Table 2, entries 1–5**) with all solvents relative to solvent-free (neat) conditions (**Table 2, entry 6**). Poor product yields in solvent may be due to solvation of the substrates in the reaction medium.

The ability to recycle the PSA catalyst was also checked by running the same model reaction in three additional cycles using recovered PS/PTSA. Use of the same PSA catalyst for an initial and three subsequent runs gave **4a** yields of 94%, 91%, 90% and 87% (**Table1, entry 11**). Thus it appears the catalyst can be used multiple times without much loss of efficiency.

To establish the generality, various aldehydes, amines, and alkynes were subjected to a one-pot reaction catalyzed by PSA (Table 3). Under these optimized set of experimental reaction conditions, the condensation of aldehydes (**2**) with different alkynes and various amines (**3a**) was carried out and obtained a variety of 2,4-disubstituted quinolines(**4a**), and the results were described in **Table 3**. As shown in **Table 3**, in all cases, with either electron-donating or electron-withdrawing groups on aldehydes reacted smoothly with alkyne and amines in the presence of 5% PSA at 80 °C to form the corresponding 2,4-disubstituted quinolines in good to excellent yields without formation of any side products.

We have described herein PSA as a new and extremely efficient catalyst for synthesis of 2,4-disubstituted quinolones by a three-component, one-pot reaction. With the increasing concern for need of green synthetic procedures, the advantages such as the (i) solvent-free reaction, 22 (ii) high yields, (iii) eco-friendly, and (iv) ease of product isolation/purification fulfill the triple bottom line philosophy of green chemistry23 and make the present methodology environmentally benign. The chemical structures of all the synthesized compounds were characterized by IR, ^{1}H, ^{13}CNMR, and HRMS studies and their data are presented in the experimental section. In the

^{1}H NMR spectra of compounds **4a-4s**, the chemical shifts of aromatic hydrogens of the phenyl ring appeared as multiplets in the region d 6.22–6.87.[39-43] In ^{13}C NMR chemical shifts for compounds 6i were observed in their expected regions.[44-47]

Conclusion

In conclusion, we have found an efficient and practical procedure for the preparation of 2,4-disubstituted quinolines from alkynes and different aromatic aldehydes with various aromatic amines in the presence of PSA under ultrasound irradiation at room temperature using solvent-free conditions. Ultrasound irradiation speeds up the reaction compared to traditional (reflux) methods and provides better yields. This protocol provides the advantages of increased yields, shorter reaction times, ecofriendly catalyst and easy workup.

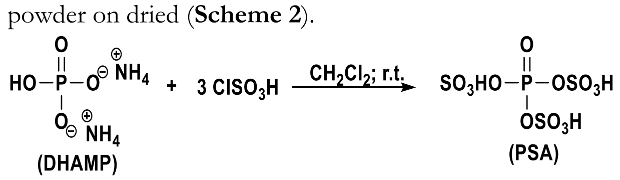
Materials and Methods

4-(2-methoxyphenyl)-2-(4-methoxyphenyl) quinoline (4a).

A mixture of ethynylbenzene (1, 1 mmol), 3-methoxybenzaldehyde (2, 1 mmol), 4-methoxyaniline (3, 1 mmol) in the presence of PSA (5 mol %) were placed on a 25 mL beaker and exposed to ultrasonic irradiation at room temperature for appropriate time (**Table 3**) in solvent-free condition. The progress of the reaction was monitored by TLC. After completion of the reaction, the mixture was washed with chloroform and filtered to recover the catalyst. The filtrate was evaporated, and the crude product was recrystallized from ethanol to afford pure **4a** in excellent yields.

Synthesis of Phosphosulfonic acid (PSA)

25mL reaction flask was equipped with a constant-pressure dropping funnel and the gas outlet which was connected to a vacuum system through an alkali solution trap. DHAMP (1 g, 7.5 mmol) was charged into the flask and chlorosulfonic acid (2.62 g, ca. 1.5 mL, 22.5 mmol) in CH_2Cl_2 (10 mL) was added drop wise over a period of 15 min at room temperature. After completion of the addition, the reaction mixture was shaken for 2 h, while the residual HCl was eliminated by suction. Then the mixture was washed with excess of CH_2Cl_2 and obtained the white powder on dried (**Scheme 2**).



Scheme 2: Preparation of PSA

4-(2-Methoxyphenyl)-2-(4-methoxyphenyl)quinoline (4a): Yellow solid; ^{1}H NMR(500 MHz, $CDCl_3$): δ = 3.79 (s, 3H), 3.83 (s, 3H), 7.02 (d, 3*J* = 10.0 Hz, 2H), 7.10-7.14 (m, 1H), 7.21-7.24 (m, 1H), 7.35-7.39 (m, 2H), 7.49-7.59 (m, 5H), 7.84-7.86 (m, 1H), 8.13-8.15 (m, 2H), ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ =55.6, 55.8, 108.8, 111.7, 121.4, 124.3, 128.3, 128.7, 129.6, 130.2, 131.5, 131.7, 139.2, 145.0, 15.6, 154.4, 157.1, 157.9 ppm. HRMS: calcd. For $C_{23}H_{19}NO_2$[M+H] 342.1416; found 342.1426.

2-(4-Methoxyphenyl)-4-(o-tolyl)quinoline(4b): Yellow solid; ^{1}H NMR(500 MHz, $CDCl_3$): δ = 2.45 (s, 3H), 3.80 (s, 3H), 7.24 (d, *J* = 10.0 Hz, 2H), 7.29-7.32 (m, 3H), 7.39-7.42 (m, 1H), 7.48-7.58 (m, 6H), 8.13 (d, *J* = 10.0 Hz, 1H), ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 20.6, 55.64, 103.77, 122.9, 122.9, 126.1, 128.5, 128.8, 129.5, 129.9, 131.0, 131.6, 136.4, 138.7, 140.6, 144.7, 147.4, 154.7, 157.5 ppm. HRMS: calcd. for$C_{23}H_{19}NO$[M+H] 326.1467; found 326.1476.

4-(4-Isopropylphenyl)-2-(4-methoxyphenyl) quinoline (4c): Yellow solid; ^{1}H NMR(500 MHz, $CDCl_3$): δ = 1.29 (d, *J* = 10.0 Hz, 6H), 2.96-2.99 (m, 1H), 3.78 (s, 3H), 7.17 (d, *J* = 3.2 Hz, 1H), 7.35-7.38 (m, 3H), 7.49-7.57 (m, 5H), 8.06 (d, *J* = 10.0 Hz, 2H), 8.13 (d, *J* = 10.0 Hz, 1H), ppm. 13C NMR (75 MHz, $CDCl_3$): δ = 24.1, 33.9, 55.8, 103.9, 120.0, 121.7, 127.1, 127.5, 128.8, 129.5, 131.6, 137.6, 145.4, 150.0, 158.3 ppm. HRMS: calcd. for$C_{25}H_{23}NO$[M+H] 354.1780; found 354.1786.

2-(3,4-Dimethoxyphenyl)-4-(2-fluorophenyl) quinoline (4d): Yellow solid; ^{1}H NMR(500 MHz, $CDCl_3$): δ = 3.86 (s, 3H), 4.06 (s, 3H), 7.15-7.18 (m,1H), 7.20 (s, 1H), 7.25-7.32 (m, 1H), 7.36-7.40 (m, 1H), 7.48-7.58 (m, 6H), 7.68 (d, *J* = 3.65 Hz, 1H), 8.04-8.09 (m, 1H), ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 56.5, 56.3, 103.3, 108.8, 116.5, 121.2, 124.5, 128.4, 128.8, 129.5, 130.6, 131.4, 138.9, 146.1, 146.8, 150.2, 152.4 ppm. HRMS: calcd. for$C_{23}H_{18}FNO_2$[M+H] 360.1322; found 360.1331.

2-(3,4-Dimethoxyphenyl)-4-(4-nitrophenyl) quinoline (4e): Yellow solid; ^{1}H NMR(500 MHz, $CDCl_3$): δ = 3.84 (s, 3H), 4.06 (s, 3H), 7.15 (s,1H), 7.51-7.55 (m, 6H), 7.67 (m, 1H), 8.28 (m, 4H), 7.68 (d, *J* = 3.65 Hz, 1H), 8.04-8.09 (m, 1H), ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 56.7, 56.9, 103.5, 109.4, 118.9, 122.5, 124.7, 128.5, 129.5, 129.9, 138.8, 146.4, 148.6, 152.3, 154.5 ppm. HRMS: calcd. for$C_{23}H_{18}N_2O_4$[M+H] 387.1267; found 387.1273.

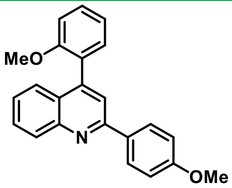
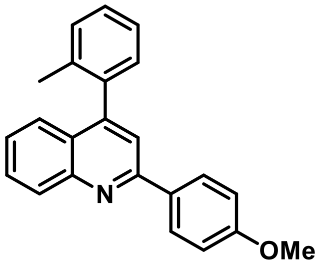
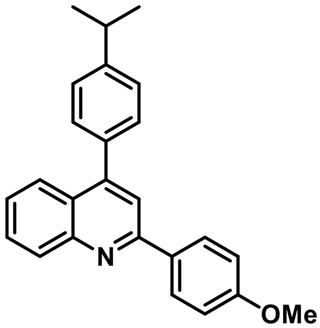
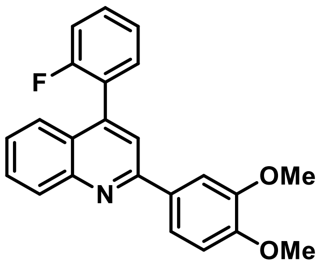
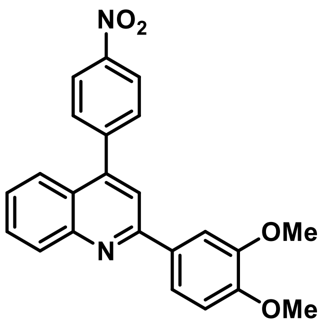
4-(4-Isopropylphenyl)-2-(4-methoxyphenyl)quinoline (4l): Yellow solid; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.28 (d, *J* = 10.0 Hz, 6H), 2.94-2.98 (m, 1H), 3.84 (s, 3H), 7.05 (d, *J* = 8.5 Hz, 2H), 7.48 (m, 1H), 7.53 (d, *J* =8.1 Hz, 2H), 7.62-7.66 (m, 2H), 7.71-7.73 (m, 1 H), 7.82 (s, 1H), 7.96(d, *J* = 8.5 Hz, 1H), 8.21-8.26 (m, 2H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 24.1, 33.9, 55.8, 115.2, 118.9, 126.5, 127.6, 128.1 128.9, 129.7, 131.1, 131.6, 132.4, 133.6, 135.3, 149.2, 151.2, 152.7, 157.2, 158.0 ppm. HRMS: calcd. for $C_{25}H_{23}NO$ [M+H] 354.1780; found 354.1789.

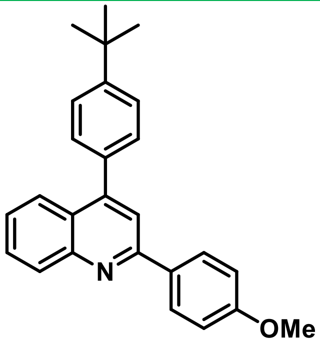
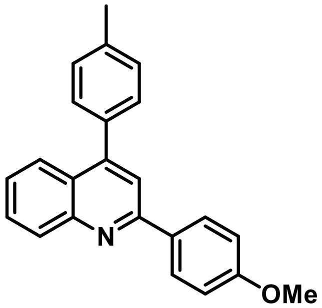
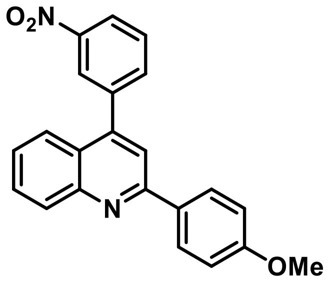
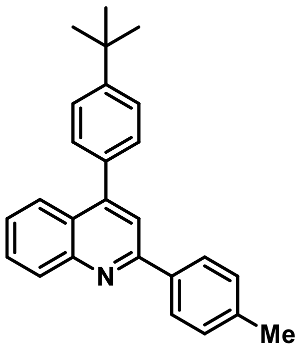
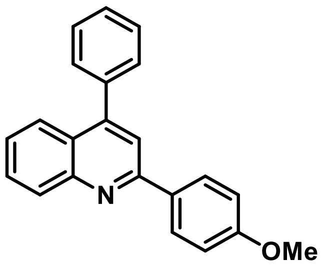
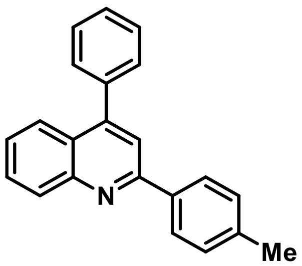
4-(4-chlorophenyl)-2-(3,4-dimethoxyphenyl) quinoline (4m): Yellow solid; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.86 (s, 3H), 4.02 (s, 3H), 7.16 (s, 1H), 7.53-7.57 (m, 6H), 7.64-7.66 (m, 1H), 8.23-8.26 (m, 4H), 7.72 (d, *J* = 3.65 Hz, 1H), 8.01-8.05 (m, 1H), ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.6, 56.2, 104.2, 108.3, 119.6, 123.4, 126.8, 127.4, 129.3, 129.8, 132.6, 145.6, 147.5, 153.2, 153.4 ppm. HRMS: calcd. for $C_{23}H_{18}ClNO_2$ [M+H] 376.1026; found 376.1031.

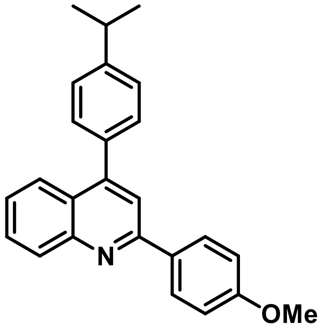
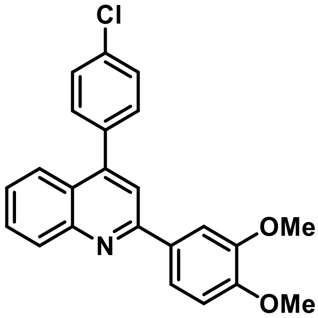
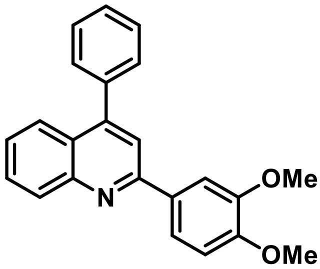
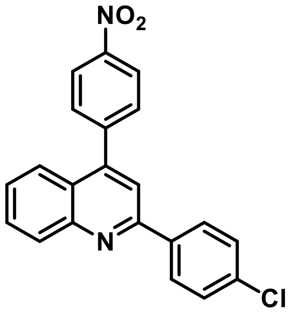
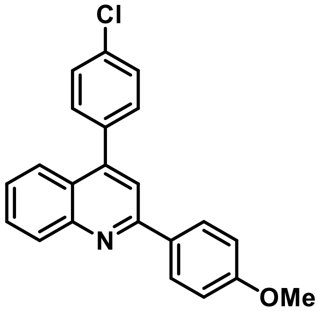
4-(4-chlorophenyl)-2-(4-methoxyphenyl) quinolone (4p): Yellow solid; ^{1}H NMR(500 MHz, $CDCl_3$): δ =3.86 (s, 3H),7.04 (d, *J* = 8.5 Hz, 2H),7.23-7.26 (m, 1H),7.36-7.38 (m, 2H),7.64-7.69 (m, 2H),7.93 (d, *J* = 8.5 Hz, 1H),8.02 (d, *J* = 7.8 Hz, 1H),8.08-8.14 (m 3H),8.21-8.24 (m, 2H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ =55.1, 113.2, 118.1, 120.3, 121.2, 123.6, 124.5, 125.9, 127.4, 128.2, 128.8, 129.3, 131.2, 134.4, 139.3, 145.1, 147.3, 148.4, 150.2, 160.4 ppm; HRMS: calcd. for$C_{22}H_{16}ClNO$346.0920 [M+H], Found: 346.0928.

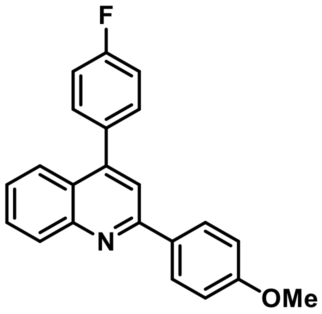
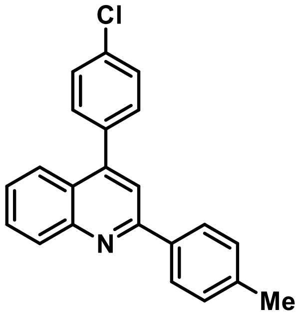
4-(4-Fluorophenyl)-2-(4-methoxyphenyl) quinoline (4q): Yellow solid; ^1H NMR(500 MHz, $CDCl_3$): δ =3.86 (s, 3H),7.02-7.04 (m, 2H),7.22-7.26 (m, 2H),7.43-7.46 (m, 3H),7.68-7.70 (m, 1H),7.78 (s, 1H),7.84 (d, *J* = 8.5 Hz, 1H),8.22 (d, *J* = 10.0 Hz, 2H),8.28 (d, *J* = 8.7 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ =55.6, 113.2, 116.4, 116.3, 118.9, 124.3, 127.3, 128.6, 129.5, 130.4, 131.2, 132.1, 132.9, 133.0, 133.7, 149.2, 150.5, 161.5, 164.5 ppm. HRMS: calcd. for$C_{22}H_{16}FNO$329.1216 [M+H], Found: 329.1223.

Table 3: One-pot three-component synthesis of 2,4-disubstituted quinolone analogues (**4a-4s**).

Entry	Product	R¹	R²	Time (min)	Yield (%)	Mp (°C) observed (Literature)
4a		2-Methoxy	4- Methoxy	25	85	152–153
4b		2-Methyl	4- Methoxy	28	90	138–140
4c		4-Isopropyl	4- Methoxy	33	81	165–167
4d		2-fluoro	3,4-dimethoxy	17	88	148–149
4e		4-nitro	3,4-dimethoxy	31	81	162–163

4f		4-tert-butyl	4-methoxy	38	92	132–134 (133)[48]
4g		4-methyl	4-methoxy	26	85	116-118 (115–117)[48]
4h		4-nitro	4-methoxy	35	90	138–140
4i		4-tert-butyl	4-methyl	33	81	120–121 (120)[48]
4j		--	4-methoxy	28	88	76–77(75-76)[49]
4k		--	4-methyl	25	85	116-117 (116-117)[50]

4l		4-isopropyl	4-methoxy	34	90	138–140
4m		4-chloro	3,4-dimethoxy	30	81	125–127
4n		--	3,4-dimethoxy	28	88	143-144 (142–144)[51]
4o		4-nitro	4-chloro	24	85	144-145 (145)[48]
4p		4-chloro	4-methoxy	22	90	138–140

4q		4-fluoro	4-methoxy	37	81	125–127
4r		4-chloro	4-methyl	20	85	101-102(102–103) [52]

REFERENCES

1. Cai SX, Zhou ZL, Huang JC, Whittemore ER, Egbuwoku ZO. Synthesis and structure-activity relationships of 1,2,3,4-tetrahydroquinoline-2,3,4-trione 3-oximes: Novel and highly potent antagonists for NMDA receptor glycine site. Journal of Medicinal Chemistry 39(1996): 3248-3255.

2. Keana JFW, Kher SM, Cai SX, Dinsmore CM, Glenn AG. Synthesis and Structure-Activity-Relationships of Substituted 1,4-Dihydroquinoxaline-2,3-Diones - Antagonists of N-Methyl-D-Aspartate (Nmda) Receptor Glycine Sites and Non-Nmda Glutamate Receptors. Journal of Medicinal Chemistry 38(1995): 4367-4379.

3. Leeson PD, Carling RW, Moore KW, Moseley AM, Smith JD. 4-Amido-2-Carboxytetrahydroquinolines - Structure-Activity-Relationships for Antagonism at the Glycine Site of the Nmda Receptor. Journal of Medicinal Chemistry 35(1992): 1954-1968.

4. Carling RW, Leeson PD, Moseley AM, Baker R, Foster AC. 2-Carboxytetrahydroquinolines - Conformational and Stereochemical Requirements for Antagonism of the Glycine Site on the Nmda Receptor. Journal of Medicinal Chemistry 35(1992): 1942-1953.

5. Manivannan E, Prasanna S. First QSAR report on FSH receptor antagonistic activity: Quantitative investigations on physico-chemical and structural features among 6-amino-4-phenyltetrahydroquinoline derivatives. Bioorganic & Medicinal Chemistry Letters 15(2005): 4496-4501.

6. Van Straten NCR, van Berkel THJ, Demont DR, Karstens WJF, Merkx R. Identification of substituted 6-amino-4-phenyltetrahydroquinoline derivatives: Potent antagonists for the follicle-stimulating hormone receptor. Journal of Medicinal Chemistry 48(2005): 1697-1700.

7. Joshi AA, Viswanathan CL. Docking studies and development of novel 5-heteroarylamino-2,4-diamino-8-chloropyrimido-[4,5-b]quinolines as potential antimalarials. Bioorganic & Medicinal Chemistry Letters 16(2006): 2613-2617.

8. Wallace OB, Lauwers KS, Jones SA, Dodge JA. Tetrahydroquinoline-based selective estrogen receptor modulators (SERMs). Bioorganic & Medicinal Chemistry Letters 13(2003): 1907-1910.

9. Marella A, Tanwar OP, Saha R, Ali MR, Srivastava S. Quinoline: A versatile heterocyclic. Saudi Pharmaceutical Journal 21(2013): 1-12.

10. Dorey G, Lockhart B, Lestage P, Casara P. New quinolinic derivatives as centrally active antioxidants. Bioorganic & Medicinal Chemistry Letters 10(2000): 935-939.

11. Mamo A, Nicoletti S, Tat NC. Synthesis of substituted 2-pyridyl-4-phenylquinolines. Molecules 7(2002): 618-627.

12. Ramage R. Comprehensive Heterocyclic Chemistry - the Structure, Reactions, Synthesis and Uses of Heterocyclic-Compounds - Katritzky,Ar, Rees,Cw. Nature 315(1985): 354-354.

13. Rani VJ, Vani KV, Rao CV. Peg-So3h as a Catalyst for the Preparation of Bis-Indolyl and Tris-Indolyl Methanes in Aqueous Media. Synthetic Communications 42(2012): 2048-2057.

14. Rao VK, Reddy SS, Krishna BS, Naidu KRM, Raju CN. Synthesis of Schiff's bases in aqueous medium: a green alternative approach with effective mass yield and high reaction rates. Green Chemistry Letters and Reviews 3(2010): 217-223.

15. Kilaru RB, Valasani KR, Yellapu NK, Osuru HP, Kuruva CS. Design, synthesis, in silico and in vitro studies of novel 4-methylthiazole-5-carboxylic acid derivatives as potent anti-cancer agents. Bioorganic & Medicinal Chemistry Letters 24(2014): 4580-4585.

16. Babu KR, Rao VK, Kumar YN, Polireddy K, Subbaiah KV. Identification of substituted [3, 2-a] pyrimidines as selective antiviral agents: Molecular modeling study. Antiviral Research 95(2012): 118-127.

17. Tan SS, Kim SJ, Kool ET. Differentiating between Fluorescence-Quenching Metal Ions with Polyfluorophore Sensors Built on a DNA Backbone. Journal of the American Chemical Society 133(2011): 2664-2671.

18. Tumarnbac GE, Rosencrance CM, Wolf C. Selective metal ion recognition using a fluorescent 1,8-diquinolylnaphthalene-derived sensor in aqueous solution. Tetrahedron 60(2004): 11293-11297.

19. Rehan M, Hazra G, Ghorai P. Synthesis of Polysubstituted Quinolines via Transition-Metal-Free Oxidative Cycloisomerization of o-Cinnamylanilines. Organic Letters 17(2015): 1668-1671.

20. Tajik H, Niknam K, Sarrafan M. 1-Butyl-3-methylimidazolium Hydrogen Sulfate ([bmim]-HSO4)-Mediated Synthesis of Polysubstituted Quinolines. Synthetic Communications 41(2011): 2103-2114.

21. Ebraheem MA, Rai KML, Kudva NU, Bahjat AS. Synthesis of new polysubstituted (pyrazoles, pyrimidines and quinolines) five and six-membered heterocycles: reaction of alpha,alpha-dioxoketene dithioacetals with nucleophiles. Tetrahedron Letters 51(2010): 3486-3492.

22. Dinh NH, Hoang TTL, Tran TTT, Dat ND. A novel and simple route for the synthesis of polysubstituted quinolines and furoxans starting from eugenoxyacetic acid. Abstracts of Papers of the American Chemical Society 238(2009).

23. Dabiri M, Bashiribod S. Phosphotungstic Acid: An Efficient, Cost-effective and Recyclable Catalyst for the Synthesis of Polysubstituted Quinolines. Molecules 14(2009): 1126-1133.

24. Bandgar BP, More PE, Kamble VT. Synthesis of Polysubstituted Quinolines Using Cyanuric Chloride as a Catalyst under Aqueous Conditions. Journal of the Chinese Chemical Society 55(2008): 947-951.

25. Kim SC, Gowrisankar S, Kim JN. Synthesis of polysubstituted quinolines from the acetates of Baylis-Hillman adducts: Aza-claisen rearrangement as the key step. Bulletin of the Korean Chemical Society 26(2005): 1001-1004.

26. Ferry A, Stemper J, Marinetti A, Voituriez A, Guinchard X. Thiophostone-Derived Bronsted Acids in the Organocatalyzed Transfer Hydrogenation of Quinolines: Influence of the P-Stereogenicity. European Journal of Organic Chemistry 2014(2014): 188-193.

27. Wang DS, Zhou YG. Asymmetric hydrogenation of quinolines activated by Bronsted acids. Tetrahedron Letters 51(2010): 3014-3017.

28. Andreev VP. Molecular complexes of the pyridines and quinolines N-oxides styryl derivatives with the Bronsted-Lowry acids. Russian Journal of General Chemistry 79(2009): 820-825.

29. Reddy SS, Ravi Sankar AU, Naga Raju C, Koteswara Rao V. Synthesis and antimicrobial activity of new α-aminophosphonic acid esters. South African Journal of Chemistry 61(2008): 97-101.

30. Mahmoodi NO, Shoja S, Tabatabaeian K, Sharifzadeh B. Ultrasound-promoted one-pot five-components synthesis of biologically active novel bis((6-alkyl or phenyl-2-phenylpyrimidine-4-yl) oxy) alkane or methyl benzene derivatives. Ultrasonics Sonochemistry 23(2015): 31-36.

31. Raju BR, Sampaio DMF, Silva MM, Coutinho PJG. Goncalves MST Ultrasound promoted synthesis of Nile Blue derivatives. Ultrasonics Sonochemistry 21(2014): 360-366.

32. Nasrollahzadeh M, Ehsani A, Rostami-Vartouni A. Ultrasound-promoted green approach for the synthesis of sulfonamides using natural, stable and reusable Natrolite nanozeolite catalyst at room temperature. Ultrasonics Sonochemistry 21(2014): 275-282.

33. Chen BH, Li JT, Lan RJ, Chen GF. Ultrasound-promoted One-pot Synthesis of 2-Thioxo-dihydropyrimidine Derivatives Bearing Piperidinylamide Moiety. Letters in Organic Chemistry 11(2014): 643-650.

34. Hussein EM. Ultrasound-promoted efficient domino reaction for the one-pot synthesis of spiro-5-cyanopyrimidines: a rapid procedure. Monatshefte Fur Chemie 144(2013): 1691-1697.

35. Dar BA, Ahmad SN, Wagay MA, Hussain A, Ahmad N. Ultrasound promoted expeditious, catalyst-free and solvent-free approach for the synthesis of N,N '-diarylsubstituted formamidines at room temperature. Tetrahedron Letters 54(2013): 4880-4884.

36. Balaji GL, Rajesh K, Priya R, Iniyavan P, Siva R. Ultrasound-promoted synthesis, biological evaluation and molecular docking of novel 7-(2-chloroquinolin-4-yloxy)-4-methyl-2H-chromen-2-one derivatives. Medicinal Chemistry Research 22(2013): 3185-3192.

37. Rao VK, Babu BH, Babu KR, Srinivasulu D, Raju CN. Ecofriendly Synthesis of Tetrahydropyrimidine Derivatives in Aqueous Medium under Ultrasonic Irradiation. Synthetic Communications 42 (2012): 3368-3376.

38. Rao AJ, Rao PV, Rao VK, Mohan C, Raju CN. Microwave assisted one-pot synthesis of novel α-aminophosphonates and their biological activity. Bull Korean Chem Soc 31(2010): 1863.

39. Vangavaragu JR, Valasani KR, Gan X, Yan SS. Identification of human presequence protease (hPreP) agonists for the treatment of Alzheimer's disease. Eur J Med Chem 76(2014): 506-516.

40. Koteswara Rao V, Janardhan Rao A, Subba Reddy S, Naga Raju C, Visweswara Rao P. Synthesis, spectral characterization and biological evaluation of phosphorylated derivatives of galanthamine. Eur J Med Chem 45(2010): 203-209.

41. Valasani KR, Hu G, Chaney MO, Yan SS. Structure-based design and synthesis of benzothiazole phosphonate analogues with inhibitors of human ABAD-Abeta for treatment of Alzheimer's disease. Chem Biol Drug Des 81(2013): 238-249.

42. Rao VK, Reddy SS, Krishna BS, Reddy CS, Reddy NP. Design, Synthesis and Anti Colon Cancer Activity Evaluation of Phosphorylated Derivatives of Lamivudine (3TC). Letters in Drug Design & Discovery 8 (2011): 59-64.

43. Rani VJ, Raghavendra A, Kishore P, Kumar YN, Kumar KH. Synthesis and biological activity evaluation of cytidine-5 '-deoxy-5-fluoro-N-[(alkoxy/aryloxy)] carbonyl-cyclic 2 ',3 '-

carbonates. European Journal of Medicinal Chemistry 54(2012): 690-696.

44. Valasani KR, Chaney MO, Day VW, Yan SS. Acetylcholinesterase Inhibitors: Structure Based Design, Synthesis, Pharmacophore Modeling, and Virtual Screening. Journal of Chemical Information and Modeling 53(2013): 2033-2046.

45. Valasani KR, Vangavaragu JR, Day VW, Yan SS. Structure Based Design, Synthesis, Pharmacophore Modeling, Virtual Screening, and Molecular Docking Studies for Identification of Novel Cyclophilin D Inhibitors. Journal of Chemical Information and Modeling 54(2014): 902-912.

46. Rao VK, Reddy SS, Peer ED, Rao AJ, Raju CN. Synthesis and Antimicrobial Activity of Novel Iminophosphocin Derivatives. Chinese Journal of Chemistry 27(2009): 2379-2384.

47. Babu KR, Rao VK, Sudhakar Y, Raju CN. First stereoselective total synthesis of (3R, 3aS, 6aR)-hexahydrofuro [2,3-b]furan-3-yl (2R,3S)-4-(4-amino-N-isobutyl phenylsulfonamido)-3-hydroxy-1-phenylbutan-2-yl-carbamate (diastereomer of Darunavir). Indian Journal of Chemistry Section B-Organic Chemistry Including Medicinal Chemistry 51(2012): 849-854.

48. Rotzoll S, Willy B, Schonhaber J, Rominger F, Muller TJJ. Regiospecific Three-Component Access to Fluorescent 2, 4-Disubstituted Quinolines via One-Pot Coupling-Addition-Cyclocondensation-Sulfur Extrusion Sequence. European Journal of Organic Chemistry: 18(2010): 3516-3524.

49. Venkatesham R, Manjula A, Rao BV. (Bromodimethyl) sulfonium Bromide Catalyzed Solvent-Free Friedlander Synthesis of Substituted Quinolines. Journal of Heterocyclic Chemistry 49(2012): 833-838.

50. Wu FW, Hou RS, Wang HM, Kang IJ, Chen LC. Catalyst Free Indirect Friedlander Synthesis of Substituted Quinolines from Alcohols in PEG-400. Journal of the Chinese Chemical Society 59(2012): 535-539.

51. Kumar A, Rao VK. Microwave-Assisted and Yb(OTf)(3)-Promoted One-Pot Multicomponent Synthesis of Substituted Quinolines in Ionic Liquid. Synlett (2011): 2157-2162.

52. Park DJ, Fulmer TD, Beam CF. Preparation of 2,4-Diarylquinolines and Substituted Dihydrobenz-[C]Acridines by the Condensation of Certain C-Alpha, O-Dilithiooximes with 2-Aminobenzophenones. Journal of Heterocyclic Chemistry 18(1981): 649-651.

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