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Solvent Free Synthesis Of Substituted Quinolines Catalyzed By Cellulose Sulphuric Acid

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Abstract:

In this paper, we developed a simple route to synthesize substituted quinoline catalyzed by cellulose sulphuric acid. The method has wide advantages over existing methodologies such as, simple, efficient and easy workup procedure, small reaction time, high yields of product. Moreover, the procedure consists of solvent free synthesis, which all contributes to green chemistry.

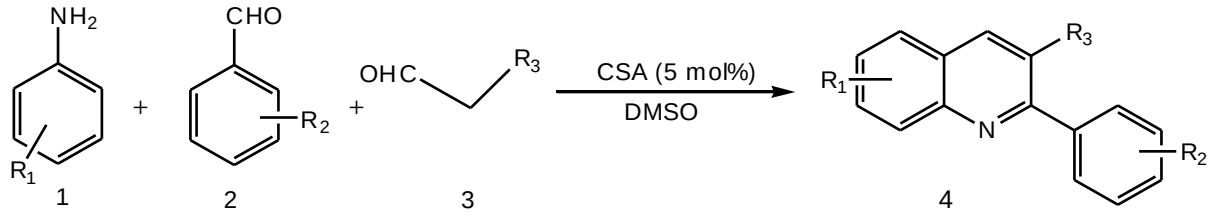
Keywords: Quinoline, Solvent free, Cellulose sulphuric acid.

Introduction:

Quinoline compounds are the naturally occurring alkaloids, which contain a hetero atom (Nitrogen) in their skeleton structure. Friedlander annulation is the well known named reaction for the preparation of quinolines and their derivative compounds from the past 100 years [1]. Quinolines are pharmaceutically important compound because it shows antibacterial, antifungal activities [2]. Natural quninoline are basic important for the synthesis of novel pharmaceutical important compounds. For the condensation of quinolines so much acid catalysts were applied in friedlander reactions, which were most effective in such conditions like sulfamic acid, phosphoric acid [3], HCl and other more catalysts like triflates, ionic liquids. Somehow, these all above mentioned catalysts undergo from poor yields, relatively expensive, lengthy times, difficulties to work-up, and tedious procedures [4].

Due to the importance of quinoline and its derivatives, there are many methods are available to synthesize it. Which includes, solvent free and catalyst free protocol [5], BHS [6], TMSCl [7], Chloramines T [8], Acetic medium [9], SiO_2-Zn-MgO [10], NbCl5 [11], MCM-41 on sulphonic caid [12]. Among these many methods show some drawback such as harsh reaction condition, longer time. So, there is need to develop new methods to synthesize this compounds.

Cellulose is one of the most abundant natural materials in the world and it has been widely studied during the past decades in organic transformations. Cellulose is biodegradable material, can be obtained from renewable resources and has potential as a catalyst to yield clean, efficient and fast reactions. Cellulose sulphuric acid, a non-hygroscopic solid state catalyst for the synthesis of substituted quinolines.



Materials and Methods:

All chemicals were purchased from Merck, Aldrich and Rankem chemical companies and used without further purification. The uncorrected melting points of compounds were taken in an open capillary in a paraffin bath. The progress of the reactions was monitored by TLC. ^{1}H NMR spectra were recorded on an 400 MHz FT-NMR spectrometer in $CDCl_3$ /DMSO-d_6 as a solvent and chemical shift values are recorded in units δ (ppm) relative to tetramethylsilane (Me_4Si) as an internal standard. Mass spectra MS (ESI) were recorded on a Water-Micro mass Quattro-II spectrophotometer. And IR spectra are measured on Jasco FTIR spectrophotometer.

Preparation of cellulose sulphuric acid

To a magnetically stirred mixture of 5 g of cellulose (DEAE for column chromatography, Merck) in 20 mL of n-hexane, 1.0 g of chlorosulfonic acid (9 mmol) was added dropwise at 0 ºC over 2 hrs HCl gas was removed from the reaction vessel immediately. After the addition was

complete, the mixture was stirred for 2 hrs at room temperature, the mixture was then filtered and washed with 30 mL of acetonitrile and dried at room temperature to obtain 5.47 g cellulose sulphuric acid as a white powder.

General Procedure for the synthesis of substituted quinolines.

To a mixture of arylamine (1 mmol), arylaldehyde (1 mmol) and aliphatic aldehyde (1 mmol), Cellulose sulphuric acid (0.1 mmol) was added and the medium was DMSO. The reaction mixture was stirred at 90 ^{o}C for 40 min. The progress of the reaction was monitored by TLC (eluent: *n*-hexane and ethyl acetate, 9:1). After completion of the reaction, the mixture was diluted with 5 mL water and 5 mL EtOAc, and shaken vigorously. The organic layer was separated and was dried at 60-70 ^{o}C under vacuum to remove water. The organic layer was dried over Na_2SO_4 and evaporated. The crude product was purified by recrystallization from EtOH to obtain the pure product in 85-94% yields.

Spectral data of some compounds

3-Ethyl-6-nitro-2-(3-nitrophenyl)quinoline

IR (KBr): νmax = 2973, 2869,1611, 1524, 1478, 1350, 1081, 927, 833, 731, 684 cm^{-1}.

^{1}H NMR (500M Hz, $CDCl_3$): δ = 1.30 (t, *J* = 7.2 Hz, 3H), 2.90 (q, *J* = 7.2 Hz, 2H), 7.74-7.78 (m, 1H), 7.97-7.99 (m, 1H), 8.27-8.41 (m, 3H), 8.49-8.52 (m, 2H), 8.87 (s, 1H).

MS: *m*/*z* = 323.05 [M]+

6-Chloro-2-(2,4-dichlorophenyl)quindine

IR (KBr): νmax = 2923, 2854,1593, 1546, 1476, 1383, 1072, 876, 821, 777, 686 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.36 (s, 1H), 7.48 (s, 1H), 7.64 (d, *J* = 7.0 Hz, 2H), 7.72 (d, *J* =7.2 Hz, 1H), 7.82 (s, 1H), 8.12 (d, *J* = 7.0 Hz, 2H).

MS: *m*/*z* = 310.95 [M]+

Results and discussion:

In a typical experiment, a mixture of an 4-chloroaniline **1** and a 3-bromobenzaldehyde **2** in a 1:1 ratio in DMSO was stirred in the presence of Cellulose sulphuric acid (0.1 mmol) at room temperature for 1 h. Butanal **3** was added and the resulting mixture was heated at 90 ℃ for 4 h. The usual work up and TLC gave 86% yields (Table 2, Entry 4a).

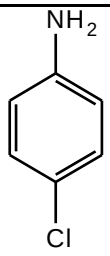
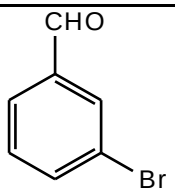
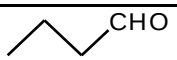
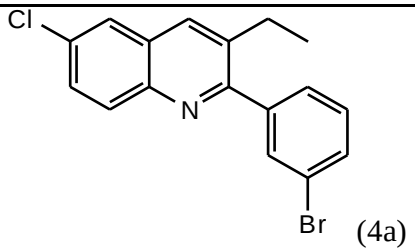
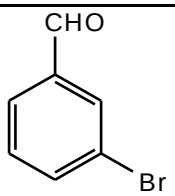
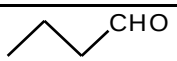
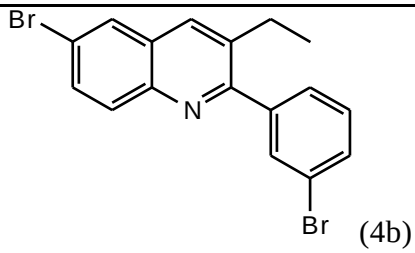
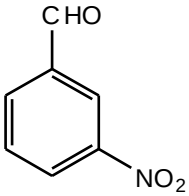
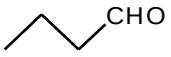
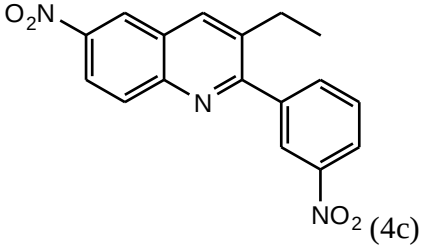
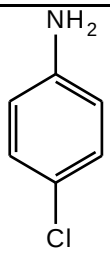
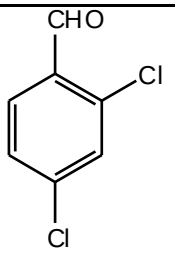
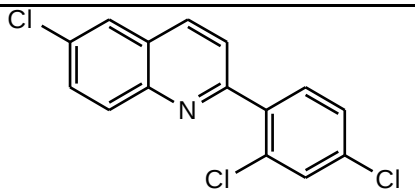
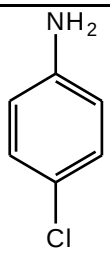
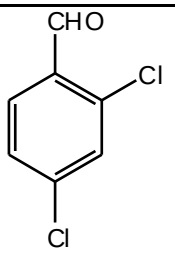
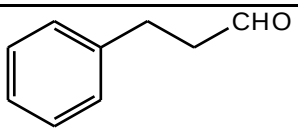
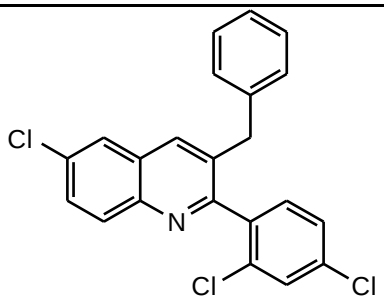
However, mostly imines are hygroscopic and difficult to purify by distillation. Therefore three-component coupling reaction using an aromatic amine, and two aldehydes directly without isolation of imines is desirable for practical synthesis.

To find out the role of catalyst the same reaction was carried out without catalyst but we do not found any product after 6 hrs also, then we increase the catalyst amount as 0.1, 0.2, 0.3, 0.4, 0.5, 0.6 mmol but the product found was 41, 53, 66, 78, 86, 86 respectively, hence, we kept 5 mmol catalyst constant for further reaction.

Various substituted quinolines were obtained using cellulose sulphuric acid catalyzed three-component coupling reaction in a one pot. A wide range of substituted anilines, aromatic aldehydes, and ali-phatic aldehydes were subjected to this procedure to synthesize the corresponding quinolines as shown in Table 1. Functional groups such as Chloro, Bromo Methoxy, Nitro, are incorporated in this synthesis. The yields are shown in Table 2.

Table 1. Table shows the product formed and amine and aldehyde used for the synthesis of 2,3-disubstituted quinolines by using cellulose sulphuric acid as a catalyst.

Sr. No.	Arylamine (1)	Aldehyde (2)	Aldehyde (3)	Product (4)

1				 (4a)
2				 (4b)
3				 (4c)
4			CH_3CHO	 (4d)
5				 (4e)

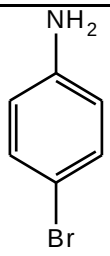
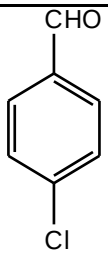
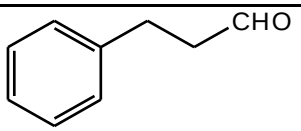
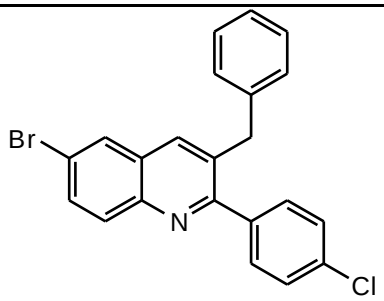
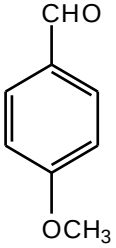
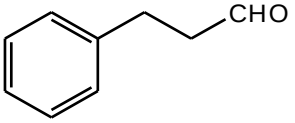
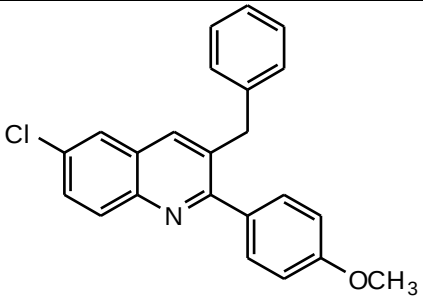
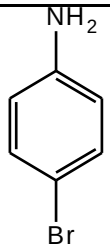
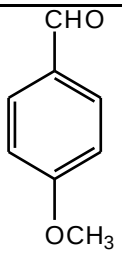
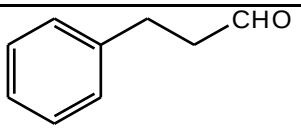
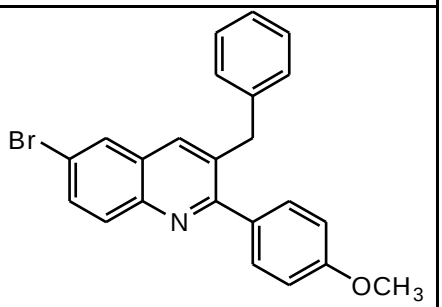
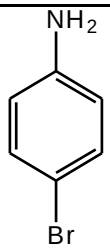
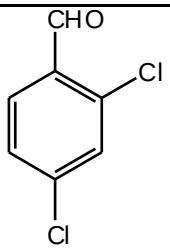
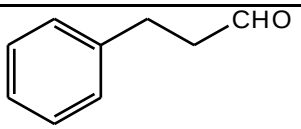
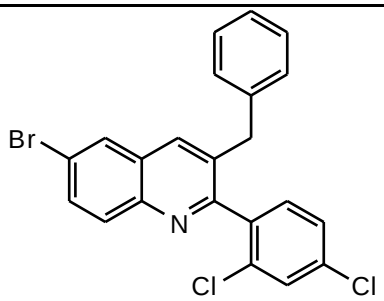
6				 (4f)
7				 (4g)
8				 (4h)
9				 (4i)

Table 2. Synthesis of 2,3-disubstituted quinolines by using cellulose sulphuric acid as a catalyst.

Entry	Time (hrs)	Yield (%)[a,b]	Melting Points (℃)
4a	4.0	86	126-127
4b	3.5	87	156-158
4c	4.0	90	170-172
4d	4.5	85	219-220
4e	4.0	91	137-138
4f	4.0	86	146-147
4g	3.5	93	120-122
4h	3.5	94	130-132
4i	4.0	88	142-143

[a]- All products are known compound and NMR, IR and Mass spectral data matched with authentic sample. [b]- Yields refer to pure compound.

Conclusion:

In summary, we have developed an efficient and general route to substituted quinolines in a one-pot synthesis from an arylamine, an aromatic aldehyde and an aliphatic aldehyde in the presence of catalytic amount of cellulose sulphuric acid. The method is very simple, high yielding, and easy workup procedure.

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