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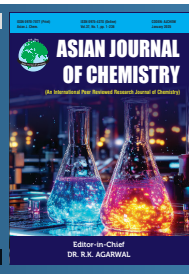


# An Efficient Synthesis of Quinoline Derivatives using Polymer-Supported Sulphonic Acid *via* Friendlier Pathway: A Green Protocol

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An efficient method for synthesizing quinoline derivatives (**3a-l**) was reported using polyethylene glycol-based sulphonic acid (PEG-SA) and polystyrene-supported polyethylene glycol-based sulphonic acid (PS-PEG-SA) as recyclable catalysts *via* a friendlier reaction pathway. This strategy is more environmentally sustainable than traditional methods for synthesizing quinoline derivatives, yielding favorable yields and facilitating ease of operation under mild reaction conditions. In presence of PEG-SA/PS-PEG-SA catalyst, carbonyl compounds with an active α-methylene group were added to 2-aminophenyl ketones/aldehydes to produce substituted quinoline compounds. Adhering to green chemistry principles, this strategy provides a productive way to synthesize functionally useful quinoline derivatives, raising the hope for the breakthrough in the pharmaceutical and material sciences.

**Keywords: PEG, Polystyrene, Sulphonic acid, Quinolines, Multicomponent reactions.**

## INTRODUCTION

The compounds containing quinoline scaffold are the most important nitrogen-based heterocyclic aromatic compounds and have reached scientists' attention because of their diverse range of biological applications and wide utility in organic synthesis [1,2]. The quinoline derivatives occur in several natural products, particularly alkaloids [3]. Chloroquine, mefloquine, lenvatinib, cabozantinib, ciprofloxacin and moxifloxacin are the well-known drugs containing quinoline moiety in their structure [4-7]. Several compounds having quinoline pharmacophore showed a broad spectrum of biological activities such as anticancer [8-12], antifungal [13-15], antibacterial [16-18], antituberculosis [19], antiviral [20,21], antimalarial [22] antimicrobial [23], *etc*. Several quinoline compounds are identified as having applications in agrochemicals [24], pharmaceuticals, N-donor ligands [25], pharmacologically active [26] and also useful in bioorganic and bio-organometallic chemistry [27]. Additionally, they have also been employed as ligands for the synthesis of conjugated polymers, which are utilized as important chemosensors for metal ions and fluorides [28, 29]. Some substituted quinoline derivatives like quinaldic acid and quinalidine display their activity as anticorrosion agents for mild steel in hydrochloric acid [30]. Some compounds containing quinolines have been investigated in recent years for the structural modification of the anticancer drug sorafenib [31].

The literature revealed that several synthetic approaches were reported for the friendlier synthesis of quinoline derivatives. The use of various catalysts such as $Zr(NO_3)_4$ and $Zr(HSO_4)_4$ [32], microwave irradiation [33], malic acid [34], trifluoro acetic acid [35], calcium triflate [36], $In(OTf)_3$ [37], KOH/air [38], zeolite, montmorrilonite K-10, sulfated zirconia [39] and $CuSO_4$-D-glucose [40] with good to moderate yields was reported. Despite having good isolation yields, the majority of these reactions have certain disadvantages. All of these factors prompted a search for a better catalyst to synthesize quinoline derivatives. Over the last few years, the application of solid acids as heterogeneous catalysts has procured usefulness in various parts of synthetic organic chemistry [41]. The heterogeneous solid acid catalysts are useful over conventional homogeneous acid catalysts, as they can be easily recovered and recycled, accordingly, making them more eco-friendly from an economic standpoint [42-44].

Presently, polyethylene glycol-sulphonic acid (PEG-SA) and polystyrene supported polyethylene glycol-sulphonic acid (PS-PEG-SA) were used for several organic transformations including condensation reactions [45,46]. In PS-PEG-SA, a polystyrene linker is attached to polyethylene glycol-sulphonic acid and shows excellent catalytic activity towards the organic synthesis. The addition of a polystyrene linker in PS-PEG-SA enhances the heterogeneous characteristics and stability of catalyst, also improving the mass transfer ratio of product from the reactants [47]. Therefore, the synthesis and characterization of the quin-oline derivatives using PEG-SA and PS-PEG-SA catalysts were achieved in this work.

## EXPERIMENTAL

All chemicals and solvents were acquired from a different commercial suppliers and purified using procedures reported in the literature. To check the progress of the reactions, thin layer chromatography (TLC) was used on aluminum plates coated in silica gel $F_{254}$ plates (Merck). The melting points were recorded using a Universal melting point apparatus (capillary tubes in a paraffin oil bath) and the Equiptronics digital melting point apparatus and are uncorrected. Bruker spectrometer equipment was used to record $^1$H (400 or 500 MHz) NMR and $^{13}$C (101 or 126 MHz) NMR spectra, with $CDCl_3$ as a solvent. FTIR spectra were recorded using Bruker Vector-22 infrared spectrometer to identify the functional groups. Silica gel (100-200 mesh) was used for column chromatography. Polyethylene glycol-based sulphonic acid (PEG-SA) and polystyrene-supported polyethylene glycol-based sulphonic acid (PS-PEG-SA) were prepared as per literature [48,49].

### General procedure for the synthesis of quinoline derivatives

**Method 1:** A round bottom flask (25 mL) containing ethanol (5 mL), PEG-SA (20 mg) and methyl ketone/aldehyde (1 mmol) was poured and stirred for 10 min. Then 2-aminophenyl ketone /aldehyde (1 mmol) was added and the resultant solution was stirred at 80 ºC. The reaction progress was monitored after every 10 min by using TLC. The reaction was completed within 60 min. The crude product was extracted in ethyl acetate (15 mL × 3), dried over anhydrous $Na_2SO_4$ and then under a vacuum. The product was purified by using column chromatography in ethyl acetate/hexane (2:8) as eluent gave quinoline derivatives **3a-l** with good yields of 82-90% (**Scheme-I**).

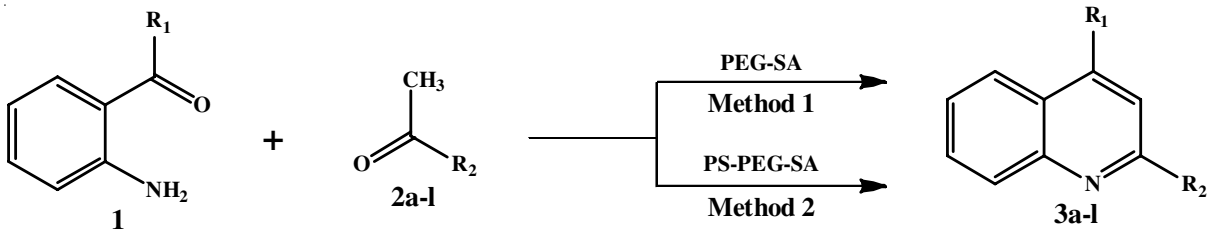
**Method-2:** A similar procedure was performed for the quinoline derivatives (**3a-l**) using PS-PEG-SA catalyst with an improved yield of 83-92% (**Scheme-I**).

**Quinoline (3a):** Yellowish liquid; b.p.: 238-242 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ ppm: 8.60 (dd, *J* = 7.5, 1.5 Hz, 1H, Ar-H), 8.07-8.02 (m, 2H, Ar-H), 7.73 (dt, *J* = 7.5, 1.5 Hz, 1H, Ar-H), 7.60 (td, *J* = 7.6, 1.5 Hz, 1H, Ar-H), 7.46 (td, *J* = 7.5, 1.5 Hz, 1H, Ar-H), 7.31 (t, *J* = 7.5 Hz, 1H, Ar-H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ ppm: 150.06 (CH, quinoline C2), 145.90 (C, quinoline C8a), 135.45 (CH, quinoline C4), 129.37 (C, quinoline C4a), 129.17 (CH, quinoline C7), 129.03 (CH, quinoline C8), 126.82 (CH, quinoline C5), 126.76 (CH, quinoline C6), 121.99 (CH, quinoline C3); HRMS (ESI, *m/z*): calculated for $C_9H_7N$: 130.0651 $(M + H)^+$; found: 130.0649.

**2-Phenylquinoline (3b):** White solid; m.p.: 84-86 ºC; $^1$H NMR (500 MHz, $CDCl_3$) δ ppm: 8.12-8.07 (m, 4H, Ar-H), 7.77 (d, *J* = 8.5 Hz, 1H, Ar-H), 7.75-7.69 (m, 1H, Ar-H), 7.65-7.62 (m, 1H, Ar-H), 7.45-7.41 (m, 3H, Ar-H), 7.37 (t, *J* = 7.3 Hz, 1H, Ar-H); $^{13}$C NMR (126 MHz, $CDCl_3$) δ ppm: 157.41 (C, quinoline C2), 148.30 (C, quinoline C8a), 139.71 (C, Ar-C1), 136.82 (CH, quinoline C4), 129.75 (CH, Ar-C4), 129.70 (CH, quinoline C8), 129.35 (CH, quinoline C7), 128.88 (2CH, Ar-C3, C5), 127.62 (2CH, Ar-C2, C6), 127.49 (CH, quinoline C5), 127.21 (C, quinoline C4a), 126.32 (CH, quinoline C6), 119.06 (CH, quinoline C3); HRMS (ESI, *m/z*): calculated for $C_{15}H_{11}N$: 206.0964 $(M + H)^+$; found: 206.0962.

**2,4-Dimethylquinoline (3c):** Brown liquid; b.p.: 262-264 ºC; $^1$H NMR (500 MHz, $CDCl_3$) δ ppm: 7.94 (dd, *J* = 8.3, 1.0 Hz, 1H, Ar-H), 7.86 (dd, *J* = 8.3, 1.0 Hz, 1H, Ar-H), 7.60-7.57 (m, 1H, Ar-H), 7.43-7.40 (m, 1H, Ar-H), 7.05 (d, *J* = 0.7 Hz, 1H, Ar-H), 2.61 (d, 3H, *J* = 0.9 Hz, Ar-$CH_3$), 2.58 (d, *J* = 0.9 Hz, 3H, Ar- $CH_3$); $^{13}$C NMR (126 MHz, $CDCl_3$) δ ppm: 158.66 (C, quinoline C2), 147.65 (C, quinoline C8a), 144.26 (C, quinoline C4), 129.14 (CH, quinoline C7), 129.08 (CH, quinoline C8), 126.57 (C, quinoline C4a), 125.44 (CH, quinoline C6), 123.59 (CH, quinoline C5), 122.73 (CH, quinoline C3), 25.18 ($CH_3$, quinoline C2-$CH_3$), 18.59 ($CH_3$, quinoline C4-$CH_3$); HRMS (ESI, *m/z*): calculated for $C_{11}H_{11}N$: 158.0964 $(M + H)^+$; found: 158.0959.

**2-(Trifluoromethyl)quinoline (3d):** Off-white solid; m.p.: 60-62 ºC; $^1$H NMR (500 MHz, $CDCl_3$) δ 8.27 (d, *J* = 8.5 Hz, 1H, Ar-H), 8.15 (d, *J* = 8.5 Hz, 1H, Ar-H), 7.82 (d, *J* = 8.2 Hz, 1H, Ar-H), 7.76-7.73 (m, 1H, Ar-H), 7.66 (d, *J* = 8.5 Hz, 1H, Ar-H), 7.61-7.53 (m, 1H, Ar-H); $^{13}$C NMR (126 MHz, $CDCl_3$) δ 148.35, 148.07, 147.80 and 147.52 (C, quinoline C2, $^2J_{C\text{-}F}$ = 35.2 Hz), 147.18 (C, quinoline C8a), 138.13 (CH, quinoline C4), 130.82 (CH, quinoline C8), 130.12 (CH, quinoline C7), 128.86 (C, quinoline C4a), 128.61 (CH, quinoline C5), 127.69 (CH, quinoline C6), 124.86, 122.67, 120.49 and 118.30 ($CF_3$, Ar-$CF_3$, $^1J_{C\text{-}F}$ = 275.5 Hz), 116.81, 116.79, 116.77 and 116.76 (CH, quinoline C3, $^3J_{C\text{-}F}$ = 2.5 Hz); $^{19}$F NMR (377 MHz, $CDCl_3$) δ ppm: -68.90 (s, F, Ar-$CF_3$); HRMS (ESI, *m/z*): calculated for $C_{10}H_6F_3N$: 198.0525 $(M + H)^+$; found: 198.0525.




**Scheme-I:** Synthesis of quinoline derivatives (**3a-l**) (for $R_1$ and $R_2$ kindly refer Table-3)

**4-Phenylquinoline (3e):** Yellowish solid; m.p.: 58-60 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ ppm: 8.76 (d, *J* = 7.7 Hz, 1H, Ar-H), 8.12 (dd, *J* = 7.5, 1.5 Hz, 1H, Ar-H), 7.76 (dd, *J* = 7.5, 1.5 Hz, 1H, Ar-H), 7.65 (dd, *J* = 7.4, 1.3 Hz, 2H, Ar-H), 7.53 (td, *J* = 7.5, 1.5 Hz, 1H, Ar-H), 7.49-7.37 (m, 5H, Ar-H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ ppm: 149.40 (CH, quinoline C2), 147.08 (C, quinoline C8a), 145.62 (C, quinoline C4), 140.15 (C, Ar-C1), 129.95 (C, quinoline C4a), 129.17 (CH, quinoline C8), 128.87 (2CH, Ar-C2, C6), 128.63 (CH, quinoline C7), 128.55 (2CH, Ar-C3, C5), 127.53 (CH, Ar-C4), 125.92 (CH, quinoline C6), 123.99 (CH, quinoline C5), 117.76 (CH, quinoline C3); HRMS (ESI, *m/z*): calculated for $C_{15}H_{11}N$: 206.0964 $(M + H)^+$; found: 206.0960.

**2,4-Diphenylquinoline (3f):** White solid; m.p.: 106-108 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ ppm: 8.10 (dd, *J* = 7.5, 1.5 Hz, 1H, Ar-H), 7.98 (dd, *J* = 7.4, 1.3 Hz, 2H, Ar-H), 7.77 (dd, *J* = 7.5, 1.5 Hz, 1H, Ar-H), 7.71 (s, 1H, Ar-H), 7.64 (dd, *J* = 7.4, 1.3 Hz, 2H, Ar-H), 7.52 (td, *J* = 7.5, 1.5 Hz, 1H, Ar-H), 7.47-7.34 (m, 7H, Ar-H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ ppm: 154.65 (C, quinoline C2), 153.60 (C, quinoline C4), 144.51 (C, quinoline C8a), 139.49 (C, Ar-C1′), 138.06 (C, Ar-C1), 130.45 (CH, Ar-C4), 130.37 (CH, quinoline C8), 129.14 (2CH, Ar-C2′, C6′), 129.02 (2CH, Ar-C3, C5 and CH, quinoline C7), 128.46 (2CH, Ar-C3′, C5′), 128.10 (2CH, Ar-C2, C6), 127.81 (CH, Ar-C4′), 126.44 (CH, quinoline C6), 125.23 (C, quinoline C4a), 124.15 (CH, quinoline C5), 115.97 (CH, quinoline C3); HRMS (ESI, *m/z*): calculated for $C_{21}H_{15}N$: 282.1277 $(M + H)^+$; found: 282.1274.

**4-Methyl-2-phenylquinoline (3g):** White solid; m.p.: 62-64 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ ppm: 8.02 (ddd, *J* = 23.8, 7.4, 1.4 Hz, 3H, Ar-H), 7.89 (dd, *J* = 7.5, 1.5 Hz, 1H, Ar-H), 7.61 (td, *J* = 7.5, 1.5 Hz, 1H, Ar-H), 7.53-7.32 (m, 5H, Ar-H), 2.67 (s, 3H, Ar-$CH_3$); $^{13}$C NMR (101 MHz, $CDCl_3$) δ ppm: 157.76 (C, quinoline C2), 144.14 (C, quinoline C8a), 144.11 (C, quinoline C4), 138.06 (C, Ar-C1), 130.45 (CH, Ar-C4), 130.15 (CH, quinoline C7, C8), 129.02 (2CH, Ar-C3, C5), 128.10 (2CH, Ar-C2, C6), 127.86 (CH, quinoline C6), 124.84 (CH, quinoline C5), 124.30 (C, quinoline C4a), 119.10 (CH, quinoline C3), 21.50 ($CH_3$, Ar-$CH_3$); HRMS (ESI, *m/z*): calculated for $C_{16}H_{13}N$: 220.1120 $(M + H)^+$; found: 220.1120.

**2-Methyl-4-phenylquinoline (3h):** Yellowish solid; m.p.: 124-126 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ ppm: 8.07 (dd, *J* = 7.5, 1.5 Hz, 1H, Ar-H), 7.66 (ddd, *J* = 10.4, 7.3, 1.4 Hz, 3H, Ar-H), 7.53-7.33 (m, 6H, Ar-H), 2.74 (s, 3H, Ar-$CH_3$); $^{13}$C NMR (101 MHz, $CDCl_3$) δ ppm: 159.64 (C, quinoline C2), 147.17 (C, quinoline C8a), 145.40 (C, quinoline C4), 139.49 (C, Ar-C1), 129.93 (CH, quinoline C7), 129.14 (2CH, Ar-C2, C6), 129.00 (CH, quinoline C8), 128.46 (2CH, Ar-C3, C5), 127.81 (CH, Ar-C4), 126.63 (C, quinoline C4a), 124.10 (CH, quinoline C6), 123.82 (CH, quinoline C5), 117.27 (CH, quinoline C3), 24.38 ($CH_3$, Ar-$CH_3$); HRMS (ESI, *m/z*): calculated for $C_{16}H_{13}N$: 220.1120 $(M + H)^+$; found: 220.1118.

**4-(Trifluoromethyl)quinoline (3i):** Yellow solid; b.p.: 82-84 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ ppm: 8.73 (d, *J* = 7.5 Hz, 1H, Ar-H), 8.10 (dd, *J* = 7.4, 1.5 Hz, 1H, Ar-H), 8.02 (dd, *J* = 7.5, 1.5 Hz, 1H, Ar-H), 7.83 (d, *J* = 7.5 Hz, 1H, Ar-H), 7.63-7.52 (m, 2H, Ar-H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ ppm: 149.81 (C, quinoline C8a), 148.43 (CH, quinoline C2), 141.00, 140.73, 140.46 and 140.19 (C, quinoline C4, $^2J_{C\text{-}F}$ = 27 Hz), 131.45 (CH, quinoline C8), 129.97 (CH, quinoline C7), 128.16, 125.54, 122.92, 120.30 ($CF_3$, Ar-$CF_3$, $^1J_{C\text{-}F}$ = 264.5 Hz), 126.40, 126.32, 126.25 and 126.18 (C, quinoline C4a, $^3J_{C\text{-}F}$ = 7 Hz), 125.19 (CH, quinoline C6), 123.73 (CH, quinoline C5), 118.00, 117.94, 117.87, 117.79 (CH, quinoline C3, $^3J_{C\text{-}F}$ = 7 Hz); $^{19}$F NMR (377 MHz, $CDCl_3$) δ ppm: -59.60 (s, F, Ar-$CF_3$); HRMS (ESI, *m/z*): calculated for $C_{10}H_6F_3N$: 198.0525 $(M + H)^+$; found: 198.0520.

**2-(4-Fluorophenyl)quinoline (3j):** White solid; m.p.: 92-94 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ ppm: 8.34 (dd, *J* = 7.5, 1.5 Hz, 1H, Ar-H), 8.07 (dd, *J* = 7.5, 1.5 Hz, 1H, Ar-H), 8.00-7.97 (m, 2H, Ar-H), 7.81 (dt, *J* = 7.5, 1.4 Hz, 1H, Ar-H), 7.64 (td, *J* = 7.5, 1.5 Hz, 1H, Ar-H), 7.54-7.47 (m, 2H, Ar-H), 7.20 (t, *J* = 7.8 Hz, 2H, Ar-H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ ppm: 165.37 and 162.74 (C, Ar-C4, $^1J_{C\text{-}F}$ = 265.5 Hz), 157.20 (C, quinoline C2), 144.78 (C, quinoline C8a), 137.93 (CH, quinoline C4), 132.10 (C, Ar-C1), 130.69 and 130.62 (2CH, Ar-C2, C6, $^3J_{C\text{-}F}$ = 7 Hz), 130.10 (CH, quinoline C8), 129.77 (CH, quinoline C7), 127.21 (CH, quinoline C5), 127.13 (CH, quinoline C6), 126.08 (C, quinoline C4a), 119.26 (CH, quinoline C3), 116.41 and 116.14 (2CH, Ar-C3, C5, $^2J_{C\text{-}F}$ = 27.2 Hz); $^{19}$F NMR (377 MHz, $CDCl_3$) δ ppm: -110.70 (s, F, Ar-F); HRMS (ESI, *m/z*): calculated for $C_{15}H_{10}FN$: 224.0870 $(M + H)^+$; found: 224.0870.

**2-(4-Chlorophenyl)quinoline (3k):** Off-white solid; m.p.: 118-120 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ ppm: 8.33 (dd, *J* = 7.5, 1.5 Hz, 1H, Ar-H), 8.08 (dd, *J* = 7.5, 1.5 Hz, 1H, Ar-H), 7.93 (d, *J* = 7.4 Hz, 2H, Ar-H), 7.81 (dt, *J* = 7.5, 1.5 Hz, 1H, Ar-H), 7.64 (td, *J* = 7.5, 1.5 Hz, 1H, Ar-H), 7.53-7.47 (m, 4H, Ar-H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ ppm: 157.20 (C, quinoline C2), 144.78 (C, quinoline C8a), 137.93 (CH, quinoline C4), 135.39 (C, Ar-C1), 134.83 (C, Ar-C4), 130.10 (CH, quinoline C8), 129.77 (CH, quinoline C7), 129.71 (2CH, Ar-C2, C6), 129.43 (2CH, Ar-C3, C5), 127.21 (CH, quinoline C5), 127.13 (CH, quinoline C6), 126.08 (C, quinoline C4a), 119.26 (CH, quinoline C3); HRMS (ESI, *m/z*): calculated for $C_{15}H_{10}ClN$: 240.0574 $(M + H)^+$; 240.0572.

**2-(4-Bromophenyl)quinoline (3l):** Yellowish solid; m.p.: 128-130 ºC; $^1$H NMR (400 MHz, $CDCl_3$) δ ppm: 8.33 (dd, *J* = 7.5, 1.5 Hz, 1H, Ar-H), 8.07 (dd, *J* = 7.5, 1.5 Hz, 1H, Ar-H), 7.89 (d, *J* = 7.4 Hz, 2H, Ar-H), 7.81 (dt, *J* = 7.5, 1.5 Hz, 1H, Ar-H), 7.66-7.62 (m, 3H, Ar-H), 7.53-7.47 (m, 2H, Ar-H); $^{13}$C NMR (101 MHz, $CDCl_3$) δ ppm: 157.20 (C, quinoline C2), 144.78 (C, quinoline C8a), 137.93 (CH, quinoline C4), 135.77 (C, Ar-C1), 131.83 (2CH, Ar-C3, C5), 130.17 (2CH, Ar-C2, C6), 130.10 (CH, quinoline C8), 129.77 (CH, quinoline C7), 127.21 (CH, quinoline C5), 127.13 (CH, quinoline C6), 126.08 (C, quinoline C4a), 125.33 (C, Ar-C4), 119.26 (CH, quinoline C3); HRMS (ESI, *m/z*): calculated for $C_{15}H_{10}BrN$: 284.0069 $(M + H)^+$; 248.0066.

## RESULTS AND DISCUSSION

The synthetic approach utilized for the synthesis of quinoline derivatives (**3a-l**) is outlined in **Scheme-I**. The cyclization of 2-aminophenyl ketones/aldehydes and methyl ketones/

aldehydes offered the quinoline derivatives. The polymer supported sulphonic acid were employed as a catalyst for various cyclocondensation reactions. From this perspective, the PEG-SA catalyst was studied to investigate the progress of the reaction, it was also compared with the PS-PEG-SA catalyst. The substrates 1,1,1-trifluoropropan-2-one and 2-aminobenzaldehyde were chosen to optimize reaction conditions for the synthesis of quinoline derivatives. The reaction conditions were initially studied by using PEG-SA (20 mg) and then changing the amount of the catalyst, solvent, reaction temperature and time were studied. The outcomes of the course of the reaction is shown in Table-1. The reactions were carried out in different solvents and the reaction was monitored at room temperature and the reflux temperature of the solvent. At ambient temperature, only a small amount of product was formed in water and solvent-free conditions after 120 min of reaction time. Also, at the same reaction temperature and time, the reaction in ethanol, acetonitrile, toluene and THF gave 30%, 25%, trace % and 28% yields, respectively (Table-1, entries 3-6). Therefore, further reaction was performed in ethanol, acetonitrile and THF at reflux temperature and after every 10 min, the progress of reaction was monitored. It was observed that all these solvents offered a good yield of the products at 60 min of reaction time (Table-1, entries 7-9). The reaction was again maintained for 120 min and no change in the yield was noticed. Consequently, by using ethanol as a solvent, the reaction progress was further monitored for the screening of PEG-SA catalyst (10 mg to 25 mg) (Table-2). It was found that 20 mg of PEG-SA catalyst facilitated the complete conversion of the reactant to product **3d** with a yield of 90% (Table-2, entry 4). Based on this improved reaction procedure, it was found that 20 mg of PEG-SA catalyst, ethanol as a solvent and 80 ºC reaction temperature were considered to be a more suitable experimental protocol for the synthesis of the quinoline derivatives. To validate the findings of these modified reaction conditions, 12 quinoline derivatives were synthesized with good yields. In comparison, equal amount of PS-PEG-SA catalyst resulted in improved yield of products (Table-3), which demonstrated that in the optimized experimental conditions, PEG-SA and PS-PEG-SA are efficient catalysts for the preparation of a variety of quinoline derivatives. It was noted that carbonyl compounds with electron-donating groups (–$CH_3$, –Ph) on the phenyl ring gave moderate yields (65-73%, Table-3, method 1). While, carbonyl compounds with electron withdrawing substituents like trifluoromethyl, 4-fluorophenyl, 4-chlorophenyl and 4-bromophenyl gave the desired products in better to good yields (80-90%, Table-3, method 1). In comparison, PS-PEG-SA presented the results with a little improvement in the yield (66-92%, Table-3, method 2).

As a representative spectral characterization of the structure of 2-(trifluoromethyl)quinoline (**3d**) is illustrated. In $^1$H NMR spectrum, two doublets occurred in the aromatic region at δ 8.27 and 7.66 ($J$ = 8.5 Hz) integrated for a single proton, each assigned to the C-4 and C-3 protons of quinoline, respectively. The C-5 proton of the quinoline exhibited doublet at δ 7.82 ($J$ = 8.2 Hz) assigned to the single aromatic proton. The C-6 and C-7 aromatic protons of the quinoline showed two multiplets at δ 7.61-7.53 and 7.76-7.73 ppm, respectively, each assigned to the single proton. The de-shielded C-8 carbon of the quinoline showed doublet at δ 8.15 ($J$ = 8.5 Hz) in the aromatic region integrated for the single proton. The $^{13}$C NMR spectrum of compound **3d** displayed singlet in the aromatic region at δ 138.13, 128.61, 127.69, 130.12 and 130.82 assigned to the C-4, C-5, C-6, C-7 and C-8 carbons of quinoline, respectively. The carbons of quinoline exhibited characteristic C–F couplings as two quartets at δ 148.35, 148.07, 147.80, 147.52 ($^2J_{C\text{-}F}$ = 35.20 Hz) assigned to the C-2 and 116.81, 116.79, 116.77,

TABLE-1
OPTIMIZATION OF REACTION CONDITIONS FOR THE SYNTHESIS OF 2-(TRIFLUOROMETHYL)QUINOLINE (**3d**) FROM 2-AMINOBENZALDEHYDE AND 1,1,1-TRIFLUOROPROPAN-2-ONE

| Entry | Solvent | Temp. (ºC) | Time (min) | Yield (%)[a] |
|---|---|---|---|---|
| 1 | [b]– | RT | 120 | Trace |
| 2 | Water | RT | 120 | Trace |
| 3 | Ethanol | RT | 120 | 30 |
| 4 | Acetonitrile | RT | 120 | 25 |
| 5 | Toluene | RT | 120 | Trace |
| 6 | THF | RT | 120 | 28 |
| 7 | Ethanol | Reflux | 60 | 90 |
| 8 | Acetonitrile | Reflux | 60 | 80 |
| 9 | THF | Reflux | 60 | 86 |

[#]General reaction conditions: 2-Aminobenzaldehyde (1 mmol) and 1,1,1-trifluoropropan-2-one (1 mmol), PEG-SA catalyst (20 mg), ethanol (5 mL). [a]Yields refer to pure isolated products, [b]Solvent free.

TABLE-2
SCREENING OF CATALYST FOR THE SYNTHESIS OF 2-(TRIFLUOROMETHYL)QUINOLINE (**3d**) FROM 2-AMINOBENZALDEHYDE AND 1,1,1-TRIFLUOROPROPAN-2-ONE

| Entry | Catalyst | Amount of catalyst (mg) | Yield (%)[a] |
|---|---|---|---|
| 1 | [b]– | – | Trace |
| 2 | PEG-SA | 10 | 60 |
| 3 | PEG-SA | 15 | 68 |
| 4 | PEG-SA | 20 | 90 |
| 5 | PEG-SA | 25 | 90 |

[#]General reaction conditions: 2-Aminobenzaldehyde (1 mmol) and 1,1,1-trifluoropropan-2-one (1 mmol), ethanol (5 mL), 80 ºC, 60 min. [a]Yields refer to pure isolated products, [b]Absence of catalyst.

TABLE-3
POLYSTYRENE-SUPPORTED POLYETHYLENE GLYCOL-BASED SULPHONIC ACID (PS-PEG-SA) CATALYZED ONE-POT SYNTHESIS OF QUINOLINE **3a-l** DERIVATIVES

| Entry | Compd. | $R_1$ | $R_2$ | Yield (%)[a] | |
|---|---|---|---|---|---|
| | | | | Method 1 | Method 2 |
| 1 | **3a** | H | H | 86 | 88 |
| 2 | **3b** | H | Ph | 73 | 74 |
| 3 | **3c** | Me | Me | 65 | 66 |
| 4 | **3d** | H | $CF_3$ | 90 | 92 |
| 5 | **3e** | Ph | H | 70 | 73 |
| 6 | **3f** | Ph | Ph | 65 | 68 |
| 7 | **3g** | Me | Ph | 68 | 70 |
| 8 | **3h** | Ph | Me | 66 | 68 |
| 9 | **3i** | $CF_3$ | H | 89 | 90 |
| 10 | **3j** | H | 4-Fluorophenyl | 81 | 84 |
| 11 | **3k** | H | 4-Chlorophenyl | 80 | 82 |
| 12 | **3l** | H | 4-Bromophenyl | 80 | 80 |

[a]Yields refer to pure isolated products.

116.76 ($^3J_{C\text{-}F}$ = 2.5 Hz) assigned to the C-3 carbon. The fused C-4a and C-8a carbons of the quinoline resonated at δ 128.86 and 147.18, respectively. The highly deshielded aliphatic carbon of -$CF_3$ substituent showed a quartet at δ 124.86, 122.67, 120.49 and 118.30 ($^1J_{C\text{-}F}$ = 275.5 Hz). The $^{19}$F NMR spectrum compound **3d** showed singlet at δ -68.90 ppm assigned to the -$CF_3$ substituent of quinoline. The structure of compound **3d** was further confirmed by molecular ion peak at *m/z* 198.0525 $(M + H)^+$ and 199.0563 $(M+1+H)^+$. The structure of all the synthesized quinoline derivatives was thus characterized accordingly.

## Conclusion

This work emphasizes the synthetic applications of polymer supported sulphonic acid catalysts as an efficient and green protocol for the synthesis of quinoline derivatives *via* a friendlier reaction pathway. The quinoline derivatives (**3a-l**) were synthesized by using PEG-SA and PS-PEG-SA catalysts in ethanol solvent. The synthesized quinolone **3a-l** derivatives were characterized by spectroscopic methods specifically IR, NMR and mass spectrometry, ensuring their purity and structural integrity. The use of PEG-SA and PS-PEG-SA catalysts for the cyclocondensation reaction offered a good yield of the product (65% to 90% and 66% to 92%, respectively).

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## CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

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