Synthesis of optical and electrochemical studies on 3-cyano-2-indolyl quinoline derivatives

A Hariharan*[1], K Subramanian[2], K Dinakaran[3], K Balaji[1], M Alagar[1], T Lakshmikandhan[4]

[1]Polymer Engineering Laboratory, PSG Institute of Technology and Applied Research, Neelambur, Coimbatore - 641062, Tamil Nadu, India.

[2]Department of Chemistry, Anna University, Chennai - 600025, Tamil Nadu, India.

[3]Department of Chemistry, Thiruvalluvar University, Vellore-632115, Tamil Nadu, India.

[4]Department of Chemistry, Bharath Institute of Higher Education and Research, Selaiyur - 600073, Chennai, India.

Corresponding author: A Hariharan✉:hariharannalan@gmail.com

Abstract:

The highly efficient and simple approach for the preparation of poly-substituted quinolines derivatives through Friedlander hetero-annulation reaction and Pfitzinger condensation reaction between 2-aminoaryl ketones or isatin and active methylene carbonyl compound of cyanoacetyl indole in the presence of p-toluenesulphonic acid (p-TSA) catalyst was reported. The molecular structure of 3-cyano-2-indolyl quinoline derivatives synthesized in the present work, namely 6-chloro-2-(1H-indol-3-yl)-4-phenyl-quinoline-3-carbonitrile (Q-1), 2-(1H-Indol-3-yl)-6-nitro-4-phenyl-quinoline-3-carbonitrile(Q-2) and 3-cyano-2-(1H-indol-3-yl)-quinoline-4-carboxylic acid (Q-3) were confirmed by ^{1}H-NMR, Mass and FTIR spectroscopic analyses. Further, the title compounds electrochemical band gap value was found to be 2.4, 2.22 and 2.7 eV for the compounds Q-1, Q-2 and Q-3 respectively and their corresponding emissive quantum yield were 0.66, 0.65 and 0.34 respectively.

Keywords: Friedlander annulation, Pfitzinger condensation, cyanoacetyl indole, electrochemical band gap.

INTRODUCTION

The development of compounds with new functionality is one of the most important and scope full approaches in modern organic, synthetic chemistry to meet the demands of pharmaceutical and electronics industries. Due to inherent strong requirement in the pharmaceutical industries, major research on heterocyclic compound is a sustaining region for organic chemists. Hydrocarbon skeleton having nitrogen substituted ring structures play their crucial role in the fields of modern technologies. In the mid of heterocycle compounds, quinoline, indole and their derivatives were considered as an important class of compounds. Since, they have potential activities against malarial [1-2], tuberculosis [3], inflammatory [4-5], iasthmatic [6], cancer [7], oxidative [8-9], mutagenic [10] and anti HIV agent [11-12]. In addition, quinoline derivatives and quinoline based polymers are also employed as potential candidate towards the fabrication of optoelectronic devices [13-15].

In case of conjugated polymers and oligomers, quinoline core acts as an acceptor in the intramolecular charge transfer (ICT) system [16]. This electron acceptor-donor (A-D) system can influence molecular HOMO–LUMO energy levels in their intra systems. In this view considerable interest has been developed to obtain diverged range of quinoline derivatives with enhanced optoelectronic properties. The poly substituted quinoline scaffold serves as electron-acceptor unit in systems such as fluorene-quinoline, carbazole-quinoline, aryl vinylene - quinoline copolymers and oligomers with intramolecular charge transfer (ICT) behavior [15-17]. In particular, poly substituted quinoline based compounds constitute an important component in optoelectronic materials as pi-conjugated bridging unit in nonlinear optical polymers. In this regard, much interest and scope have also been found towards the development of organic light emiting diodes (OLEDs) [18] using quinolines derivatives [19].

Synthetic reports of the quinoline and their derivatives reveal that there is a need for simple approach. The existing methodologies such as Doebner reaction, Gould-Jacobs reaction, Skraup synthesis, and Camps quinoline synthesis possess harsh reaction condition, low quanta and consume expensive reagents. However, Friedlander and pfitzinger route afford quinoline from precursor like ketone with the active methylene center through different approach. This approach also affords poly substituted quinolines in high yield through one pot mechanism [20-26].

Recently, the development of heterocompounds with significant properties requires moiety with fused multi-functional ring skeleton. Previous reports on the synthesis of heterocyclic substituted quinoline units offers better products with optoelectronic applications [27-28]. In this view, the present work focuses on the synthesis of new 3-cyano-2-indolyl

quinoline derivatives through the prominent Friedlander and Pfitzingerquinoline annulation reactions. The synthesized 3-cyano-2-indolyl quinoline compounds may expect to possess better optoelectronics behaviour. Therefore, we report herein the synthesis of novel 6-chloro-2-(1H-indol-3-yl)-4-phenyl-quinoline-3-carbonitrile(Q-1),2-(1H-indol-3-yl)-6-nitro-4-phenyl quinoline-3-carbonitrile (Q-2) and 3-cyano-2-(1H-indol-3-yl)-quinoline-4-carboxylic acid (Q-3). In addition to synthetic approach, their optical properties were studied by using UV-Vis absorption and PL emission spectra, whose results deliver the band gaps and quantum yields respectively. Further their electrochemical studies were also performed to determine electrochemical band gap of indolylquinoline derivatives.

MATERIALS

Potassium hydroxide was procured from SRL (Mumbai, Maharashtra, India), iodine, indole and cyanoacetic acid were purchased from Spectrochem Private Limited (Mumbai, India). p-toluenesulphonic acid (99%) from Merck, India. 2-amino-5-chlorobenzophenone from Alfa Aesar, (UK). Isatin from Sigma Aldrich were received and used. 2-amino-5-nitrobenzophenone from TCI Limited (Mumbai, India). Ethanol (99.8%) and acetic anhydride (98%) were received from Fisher Scientific (Mumbai, India).

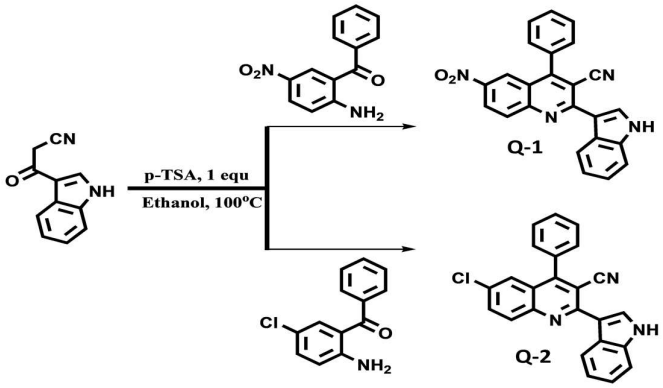
EXPERIMENTAL

Synthesis of 3-(1H-Indol-3-yl)-3-oxo-propionitrile (or) 3-cyanoacetyl indole

Indole dissolved in acetic anhydride was refluxed at 60°C for 15 minutes and the solution of cyanoacetic acid present in 10 ml of acetic anhydride was slowly added. The solution was allowed to heat at 80°C for another 3 h. During that course of reaction period, material crystallization was seen. Then reaction mixture was allowed to cool for 2 h at room temperature. The resulted solid product was filtered and washed with ethanol. White solid 3-(1H-Indol-3-yl)-3-oxo-propionitrile was dried and used as a starting material for further reaction.

Synthesis of 6-Chloro-2-(1H-indol-3-yl)-4-phenyl-quinoline-3-carbonitrile (Q-1)

A mixture of 2-amino-5-chlorobenzophenone (5 mmol), 3-cyanoacetyl indole (α-ethylene ketone) and p-TSA (1 equ) in ethanol (5.0 mL) was allowed to stir at 100˚C for 8 h. After completion of the reaction as monitored by TLC, the reaction mixture was quenched with cold water (25 mL). The yellow solid was filtered and washed with ethanol and dried to get pure quinolone of yield 82%. FTIR (KBr): 3394, 3130, 2924, 2242, 1623, 1594, 1499, 1211, 768cm^{-1}. ^{1}H-NMR in $CDCl_3$ (ppm):7.01 (t,1H), 7.15 (t,1H), 7.22 (t,1H), 7.29 (d,1H) 7.5-7.7 (m,5H), 7.91 (d,1H), 8.19 (d,1H), 8.42(s,1H), 8.61 (d,1H), 11.96 (d,1H). LC Mass m/z =379.



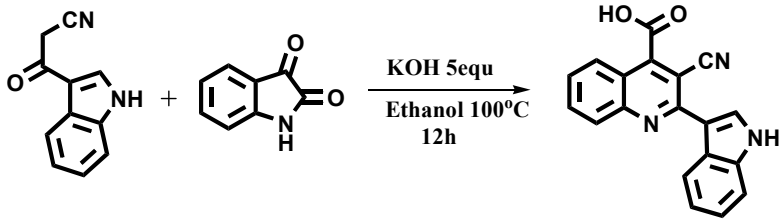
Scheme 1. Synthesis of poly substitute quinoline through Friedlander quinoline annulations reaction

Synthesis of 2-(1H-indol-3-yl)-6-nitro-4-phenylquinoline-3-carbonitrile (Q-2)

A mixture of the 2-amino-5-nitrobenzophenone (5 mmol), 3-cyanoacetyl indole (α-ethylene ketone) and p-TSA (1 equ) in ethanol (5.0 mL) was allowed to stir at 100°C for 8 h. After completion of the reaction as monitored by TLC, the reaction mixture was quenched with cold water (25 mL). The obtained solid yellow color precipitate was filtered and washed with ethanol to get pure quinoline. The product was dried and 68% yield was noticed. FTIR (KBr): 3440, 3182, 2257, 1645, 1600, 1429, 1250, 747cm^{-1}. ^{1}H-NMR in $CDCl_3$ (ppm): 6.9 (t,1H), 7.3 (t,1H), 7.4 – 7.8 (m,7H), 8.0 (d,1H), 8.4 (d,1H), 8.8 (s,1H), 11.6 (d 1H). LC Mass m/z =391.1.

Synthesis of 3-cyano-2-(1H-indol-3-yl)-quinoline-4-carboxylic acid (Q-3)

Isatin and potassium hydroxide in ethanol was refluxed for 1 h. 3-cyanoaceyl indole was added and reaction was monitored by TLC. After the completion of the reaction, the reaction mixture was poured into water and the aqueous layer was acidified with acetic acid until neutralization. The brown colored precipitate of compound Q-3 was collected and washed with ethanol, which results 65% of pure Q-3. FTIR (KBr): 3492, 3362, 3093,2985, 2217, 1702, 1617, 1517, 1424, 1242, 751cm^{-1}. ^{1}H-NMR in $CDCl_3$ (ppm): 6.7-7.6 (m,6H), 8.2 (t,1H) 9.6 (d,1H), 11.0 (s,1H), 11.9 (d,1H). LC Mass m/z = 312.



Scheme 2. Synthesis of poly substitute quinolinethrough Pfitzinger reaction (Q-3)

Measurements

^{1}H-NMR (400 MHz) spectra were recorded on a Bruker instrument (Billerica, Massachusetts, USA). Liquid chromatography–mass spectroscopy (LCMS) analysis was carried out on an Agilent (Santa Clara, California, USA) instrument. Fourier transform infrared (FTIR) spectra were measured using Perkin Elmer (Waltham, Massachusetts, USA) FTIR Spectrum RX1. UV–Visible absorption spectra and photoluminescence (PL) spectroscopy were obtained from Shimadzu (Kyoto, Japan). The cyclic voltammograms of the polymers were carried out using CHI-660D instrument (CH Instruments, Inc. Electrochemical Instrumentation; Austin, USA).

RESULTS AND DISCUSSION

The synthesis of 3-cyano-2-indolyl quinoline derivatives were carried out through Friedlander quinoline annulation and pfitzingerquinoline synthesis. The formation of 6-chloro-2-(1H-indol-3-yl)-4-phenyl-quinoline-3-carbonitrile (Q-1) and 2-(1H-indol-3-yl)-6-nitro-4-phenyl quinoline-3-carbonitrile (Q-2) were performed by Friedlander synthesis (Scheme 1). To optimize the reaction with different catalyst such as iodine, KOH and p-TSA, 2-amino-5-chloro benzophenone was treated with 3-cyanoacetyl indole using ethanol as solvent. It is noteworthy that when using p-TSA, Q-1 was isolated with 82% yield, whereas, iodine and KOH affords only less than 25% of Q-1 (Table 1).

Table 1.Optimization of the Synthesis of indolylquinoline Q-1

Catalyst	Solvent	Temperature	Time/h	Yield of indolylquinolone(%)
KOH	Ethanol	100°C	24	<25
I_2	Ethanol	40°C	24	<25
I_2	Ethanol	100°C	18	45%
p-TSA	Ethanol	100°C	8	82%

4-quinolinecarboxylic (cinchoninic) acid derivative namely 3-cyano-2-(1H-indol-3-yl)-quinoline-4-carboxylic acid (Q-3) was synthesized through pfitzingerquinoline approach (Scheme 2). The Q-3 product was obtained as a result of reaction of isatin with same equivalent of 3-cyanoacetyl indole in the presence of KOH. The product Q-3 was obtained about 65% in yield. The molecular structures of the synthesized Q-1, Q-2 and Q-3

compounds were confirmed through FTIR, Mass and 1H-NMR spectroscopy analysis (Figure1).

From the FTIR spectra structural, functional groups of Q-1, Q-2 and Q-3 compounds were confirmed. The appeared peaks in the range of 1600–1650 cm-1 attributed to an aromatic C=N group of quinoline ring, peaks at 2230 and 3400 cm-1 corresponds to the CN and NH stretching vibrations of Q-1, Q-2 and Q-3 moieties respectively. 1H-NMR spectral signals around 7.0 -9.0 ppm corresponding to quinoline aryl groups, whereas a signal around 11.5 to 12.0 ppm corresponds to the indolyl NH proton. Moreover, all mass spectra were also consistent with their assigned structures.

Optical properties

Quinoline electron-acceptor linked with indole electron-donor systems were expected to possess potential photoelectronic properties. The optical properties of quinolinederivatives Q-1, Q-2 and Q-3 were examined using UV-Visible and photoluminescence spectroscopic techniques. The absorption spectra of quinoline derivatives are shown in Figure 1a. From the absorption onset value, the corresponding band gaps (Eg^{opt}) of the quinoline derivatives were calculated [29-30] and are presented in Table 2.

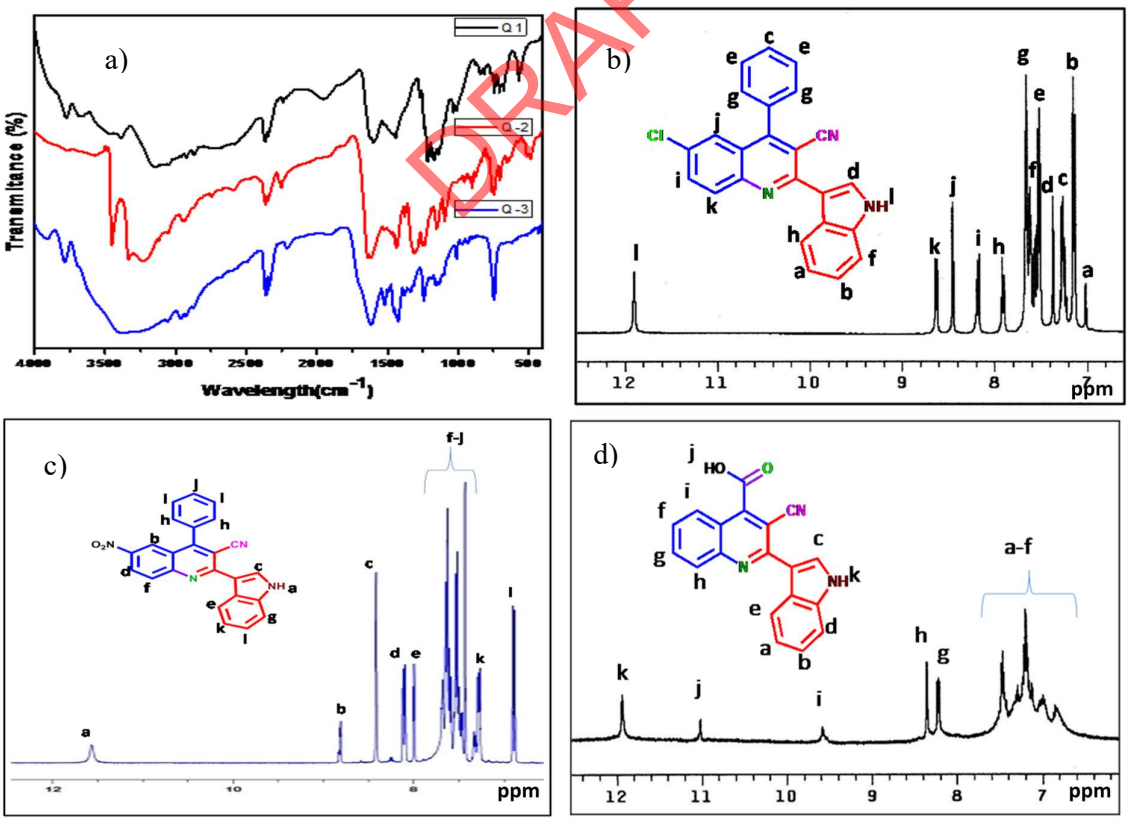


Figure 1.(a) FTIR spectra of Q-1, Q-2 and Q-3 (b) ^{1}H-NMR spectrum of Q-1 (c) ^{1}H-NMR spectrum of Q-2 (d) ^{1}H-NMR spectrum of Q-3.

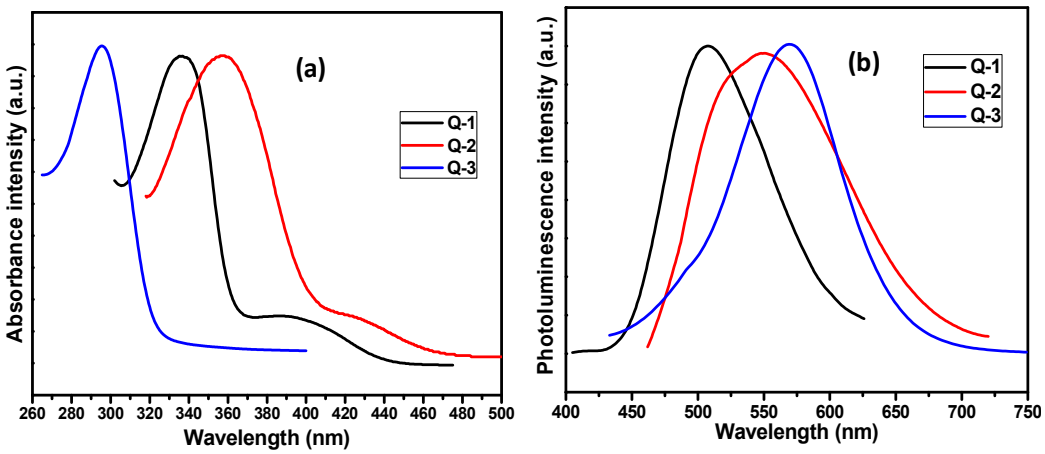


Figure 2. (a) UV-Vis spectra of poly substituted quinoline in THF (b) Photoluminescence of poly substituted quinoline in THF.

The absorption maxima of the Q-1, Q-2 and Q-3 quinolines in THF solution exhibit peaks at 337 (394), 357 (427) and 298 nm respectively (Figure 2a). The longer absorption bands of the quinoline systems may be explained due to the reflection of intramolecular charge transfer (ICT) between donors and acceptor moieties. Comparing Q-2 with Q-1 and Q-3, the absorption wavelengths λ-max are red-shifted by 20 and 59 nm respectively, which may be attributed to the presence of the more extended conjugated skeleton of Q-2.

The photoluminescence spectra of various indolyl substituted quinoline derivatives (Q-1, Q-2 and Q-3) in THF solution are shown in Figure 2b. The emission maxima of Q-1, Q-2 and Q-3 were obtained at 507nm (Φ_{PL}=0.66), 549nm (Φ_{PL}=0.65) and 569nm (Φ_{PL}=0.38) respectively, with a blue-yellow emitting. Emission maxima observed in the spectra of compounds Q-1, Q-2 and Q-3 are due to the presence of increased pi-electron delocalization that occurred in the quinoline ring through the moderate and strong indolyl donor groups. These results suggest that electron acceptor moieties such as quinoline core could increase the effective conjugation. The quantum yields (Φ_{PL}) of both 3-cyano-2-indolyl quinoline were examined using Rhodamine 6G as a reference standard [31-32] and the results are presented in Table 2.

It is known that energy level is an important parameters for optoelectronic devices. Hence in order to tune the energy level of molecular network in agreement with molecule design concept, the introduction of cyano and indole groups on the quinoline moiety has remarkable impact on its HOMO-LUMO energy level. Thus energy levels of 3-cyano-2-indolyl quinoline derivatives can be altered, by incorporating different substituents on their skeleton. In present research, indolylquinoline molecules Q-1, Q-2 and Q-3 have the band gap values of 2.7 eV, 2.5 eV and 3.4 eV respectively, which demonstrate that low band gap

Q-1 and Q-2 can be utilized as fabric materials in optoelectronic devices. Thus the donor-acceptor moiety of 3-cyano-2-indolyl quinoline has a stronger influence in tuning the energy levels.

Electrochemical properties

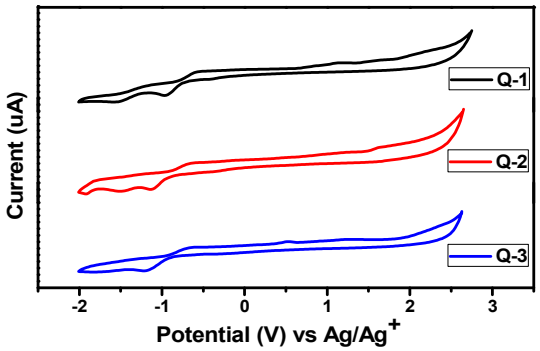


Figure3.Cyclic voltammograms of compounds of Q-1, Q-2 and Q-3

The CV cell consisted of a glassy carbon electrode, a Pt wire counter electrode, and a Ag/AgCl reference electrode. All measurements were performed using acetonitrile solutions of 0.1M Bu_4NBF_4 as a supporting electrolyte with a scan rate of $50mVs^{-1}$. All the potentials were calibrated with ferrocene as an external standard. HOMO (Highest occupied molecular orbital) and LUMO (Lowest unoccupied molecular orbital) levels were calculated with the following equation [33-34]

$$E_{HOMO} = - E_{ox/onset} - 4.8 \text{ eV}$$

$$E_{LUMO} = - E_{red/onset} - 4.8 \text{ eV}$$

The results of the CV measurements of 3-cyano-2-indolyl quinoline derivatives are in shown in Figures 3 and 4 and summarized in Table 2. The HOMO and LUMO energy levels estimated from the CV data are presented in Table 2. In addition, the band gaps of Q-1, Q-2 and Q-3 estimated from CV results are 2.4, 2.2 and 2.7 eV, respectively.

Table 2.Optical and electrochemical band gap of poly substituted quinoline derivatives

S.No.	Sample name	Optical property				Electrochemical studies		
		UV-Vis absorbtion$\lambda_{max}/\lambda_{onset}$[nm]	PL λ_{max} [nm]	Eg^{Opt} [eV][a]	Φ_{PL}[b] [%]	HOMO [eV]	LUMO [eV]	Eg^{elect} [eV][c]
1	Q-1	337,394/456	507	2.72	0.66	-6.30	-3.90	2.40
2	Q-2	357,394/481	549	2.51	0.65	-6.29	-4.07	2.22
3	Q-3	298/363	569	3.41	0.38	-6.62	-3.92	2.70

[a]Calculated from the onset wavelength of corresponding UV−Vis absorption spectra. E_g^{Opt}=1240/λ(nm) eV. [b]Quantum yield estimated from photoluminescence emission spectra in THF and Rhodamine 6G in ethanol was taken as the standard (Φ_{PL} = 0.94). [c]Electro chemical band gap from cyclic voltammetry

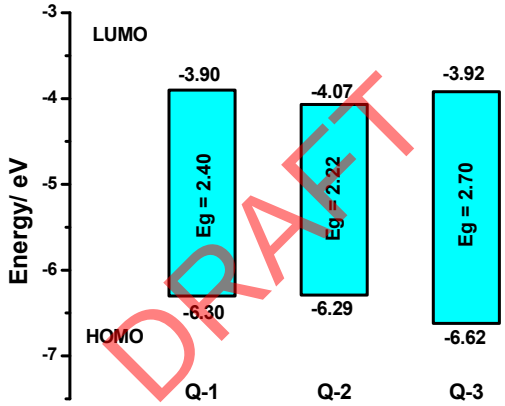


Figure 4.The HOMO-LUMO energy level of Q-1,Q-2 and Q-3

CONCLUSION

In summary, we report the synthesis and characterization of three new poly substituted quinolines (Q-1, Q-2 and Q-3) through Friedlander and pfitzingerquinoline synthesis. The synthesized indolylquinoline Q-1, Q-2 and Q-3 have a band gap value of 2.7 eV, 2.5 eV and 3.4 eV respectively, which demonstrates a low band gap value compared to the other quinoline derivatives reported in the literature. Thus the donor-acceptor moiety of 3-cyano-2-indolyl quinoline has a stronger influence in tuning the energy levels.

DECLARATIONS

FUNDING

No funds, grants, or other support was received.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

ACKNOWLEDGMENT

The authors thank the PSG Management and Secretary and Principal, PSG Institute ofTechnology and Applied Research, Neelambur - 641 062, Coimbatore, India for their moral and financial support.

REFERENCES

1. H. Raj Bhat,U. Pratap Singh,P. Gahtori,S. Kumar Ghosh,K. Gogoi, A. Prakash,and R. K. Singhm,New J Chem, **37**, 2654 (2013).
2. M. G. Uchuskin,A. S. Pilipenko,O. V. Serdyuk,I. V. Trushkovc,A. V. Butin, Org Biomol Chem, **10**,7262 (2012).
3. S. Eswaran, A. V.Adhikari,I. H. Chowdhury,N. K. Pal,and K. D. Thomas, Euro J Med. Chem, **45**, 3374 (2010)
4. Y.L.Chen,Y.L. Zhao,C.M. Lu,C.C. Tzeng,and J.P.Wang, Bio Med Chem,**14**, 4373 (2006).
5. O. Mazzoni,G. Esposito,M. V. Diurno,D. Brancaccio,A. Carotenuto,P. Grieco,E. Novellino,and W. Filippelli,Arch Pharm Chem Life Sci, **10**, 561(2010).
6. A.R. Chabukswar,B.S. Kuchekar,S.C. Jagdale,P.D.Lokhande,V.V. Chabukswar,S.U. Shisodia,R. Mahabal,A.M. Londhe,and N.S.Ojha,Euro J Med Chem, **45**, 3374. (2016).
7. F.A. Bassyouni,S.M. Abu-Baker,K.Mahmoud, M. Moharam,S.S. El-Nakkady,and M.A. Rehim, RSC Adv,**14**, 24131 (2014).
8. M.G. Malakyan,S.A. Badzhinyan,L.A. Vardevanyan,D.S. Grigoryan,D.É.Egiazaryan, A.A.Avetisyan,I.L.Aleksanyan,.Ambartsumyan, L.P.and Sargsyan, K.S.Pharm Chem J,**43**, 1 (2009).
9. M. Sankaran,C. Kumarasamy,U. Chokkalingam, andP. S. Mohan, Bio Med Chem Lett, **20**,7147(2010).
10. T. A. Kato,A. Hakura,T. Mizutani,K.I. Saeki, Mutation Res,**465**, 173(2000).
11. N. Ahmed,G. Brahmbhatt,S. Sabde,D. Mitra,I. Pal Singh,and K.K.Bhutani, Bio Med Chem,**18**, 2872(2010).
12. L.M. Bedoyaa,M.J. Abad,E. Calonge,L.A. Saavedra,M.C. Gutierrez,V.V. Kouznetsov, J. Alcami,and P. Bermejo, Antiviral res, **87**,338(2010).
13. S.P. Economopoulos,A.K. Andreopoulou,V.G. Gregotiou,and J.K.Kallitsis, J MacromolSc, Part A: Pure Appl Chem, **43**, 977(2006).

14. J.L. Kim,J.K. Kim,H.N. Cho,D.Y. Kim,C.Y. Kim,and S.I. Hong, Macromolecules,**33**, 5880(2000).
15. A.Hariharan,K. Subramanian,M. Alagar,and K. Dinakaran, High Perform Polym, **27**, 724 (2015).
16. J. A.Mikroyannidis,M. Fakis,and I. K. Spiliopoulos,J. Polym. Sci. Polym. Chem,**47**, 3370 (2009).
17. S. A. Jenekhe, L. Lu,and M. M. Alam,Macromol,**34**, 7315 (2001).
18. K. Dinakaran, S. M. Hsiao,and C. H. Chou,Macromol,**38**, 10429 (2005).
19. H. Tong, L. Wang, X. Jing,and F. Wang,Macromol. Rapid.Commun, **23**, 877 (2002).
20. C. S. Jia, Z. Zhang, S. J. Tu,and G. W. Wang,Org.Biomol. Chem, **4**, 104 (2006).
21. Q. Lv, L. Fang, P. Wang, C. Lu,and F. Yan,Monatsh.Chem,**144**, 391 (2013).
22. M. A. Zolfigol, P. Salehi, A. Ghaderi,and M. Shiri,J. Chinese. Chem.Soc, **54**, 267 (2007).
23. L. Xia, A. Idhayadhulla, Y. R. Lee,S. H. Kim,and Y. J. Wee,ACS. Comb. Sci, **16**, 333 (2014).
24. J. Wu, H. G. Xia,and K. Gao, Org.Biomol. Chem, **4**, 126 (2006).
25. B. M. Bahirwar, R. G. Atramb, R. B. Pode,and S. V. Moharil,Mater. Chem. Phys, **106**, 364 (2007).
26. H. K. Dahule, N. Thejokalyani, and S. J. Dhoble,Luminescence,**30**, 405 (2015).
27. Z. Rahmani, M. Pordel,and A. Davoodnia, Bull.Korean.Chem.Soc, **35**, 551 (2014).
28. M. Malathi,P. S. Mohan, R. J. Butcher,and C. KulandaisamyVenil,Can. J. Chem, **87**, 692 (2009).
29. H. J. Lee, H. Xin, S. M. Park, S. I. Park, T. Ahn, D. K. Park,S. A. Jenekhe,and T. W. Kwon, Bull.Korean.Chem.Soc, **33**, 1627 (2012).
30. A. Slodek,M. Filapek, G.Szafraniec, I. Grudzka, W. A. Pisarski, J. G. Malecki, L. Zur, Grela, W. Danikiewicz,and S. Krompiec, Eur.J.Org.Chem, **24**, 5256 (2014).
31. A. M. Brouwer, Pure.Appl.Chem, **83**, 2213 (2011).
32. C. Wurth, G. Martin, and Gonzalez, Talanta, **90**, 30 (2012).
33. Y. Wu, Z. Li,Q. Liu,S. Gong,X. Wang,H. Yan, Z. Liu, and W. He, Org.Biomol.Chem,**13**, 5775 (2015).
34. J. Zhang, Z. Li, H. Xing, W. Zhang, L. Guo, Y. Liu, M. Shing Wong, and G. Yu, Org Chem Front, **1**, 333 (2014).