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Synthesis and Characterization of Some New Quinoline Derivatives Derived from 2-Amino Benzonitrile

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ABSTRACT A series of new quinoline derivatives was synthesized involving two main steps. In the first step, imine derivatives were obtained through the condensation reaction of 2-aminobenzonitrile with different substituted aliphatic aldehyde and ketone substrates in the presence of sodium hydroxide as a catalyst. The intramolecular-cyclization of the imine derivatives in the presence of a base like ^{t}BuOK afforded new 4-aminpquinoline derivatives. The structures of all the new products were confirmed by spectral and analytical data.

KEYWORDS Imines, Quinolines, 2-Aminobenzonitrile, Cyclization processes.

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INTRODUCTION

Quinoline, the first of the most important heterocyclic compounds,[1-6] was discovered by the chemist GermanFriedlieb Ferdinand Runge in 1834, as a hygroscopic colorless liquid acquired through the distillation of coal tar.[7] Quinolones are key sources within a distribution of natural products,[8] having a biological effect on compounds,[9] and are the most worthy intermediates in organic synthesis.[10-13] Classic routes to quinolines include the famed Doebnere Miller and Friedlander,[14] Skraup,[15] and Combessynthesis.[16,17] One of the easiest ways to obtain highly functionalized poly-substituted quinolines in organic synthesis continues to be the Friedländer annulation which prepared quinoline by the condensation of *o*-aminobenzaldehyde with acetaldehyde in the presence of sodium hydroxide. Typically, this transformation is carried out by condensing 2-amino aryl aldehydes or ketones that contain active methylene in the presence of an acid or base.[18,19] However, nitrogen-inclusive heterocycles like quinolones,[20-23] which have different biological activity coordination, offer particular benefits. For instance, quinoline compounds have been shown to control a wide range of advantageous biological processes, including globally anti- anthelmintic,[24] antiviral,[25] antimicrobial,[26] antibacterial,[27] antimalarial,[28] anti-neoplastic[29] inhibitors of oncogenic Ras,[30] antioxidant activities,[31] antiproliferative,[32] antitumor,[28] anti-oxidant,[33] and tuberculosis.[34] Because of these aspects, quinoline derivatives are garnering plenty of interest regarding their synthesis and biological relevance. Our existing research plan is an extension of our great efforts through a versatile design and protocol toward the synthesis of some new quinoline derivatives using two basic steps: Intermediate imine synthesis[35] and the cyclic process [**Scheme 1**].

RESULTS AND DISCUSSION

Some new quinoline derivatives products were obtained by a two-step route staring from 2-aminobenzonitrile **[Scheme 1]**. The reaction started with imine formation (**9-15**) by condensation between 2-aminobenzonitrile **1** with different substitutes of aliphatic aldehydes and ketones (**2-8)** in basic conditions using NaOH as a catalyst **[Scheme 2 and Table 1]**. The FT-IR spectra of **2-15** showed a strong band for C=N imine group at ν_{max} (1682–1558) cm^{-1}. According to the aromatic structure in these compounds, the ^{1}H NMR spectra of the compounds **9-15** was found with a new imine signal at δ (8.34–7.99) ppm

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142.95(Car), 130.64 (Car), 129.29 (2Car), 128.99 (2Car), 128.92 (Car), 126.88 (Car), 126.44 (Car), 124.15 (Car), 120.25 (Car), 116.92 (Car), 32.29 (C).

*3-(1-Phenylethyl)quinolin-4-amine***19**

Orange solid, 85%, m.p.=82–83°C, IRν_{max}(cm^{-1}): 3335, 3245, 3060, 3028, 2963, 2927, 1601,1451.^{1}HNMR ($CDCl_3$, 500 MHz) δ (ppm): 8.30 (s, 1H, CH=N), 7.91 (dd, 1H, *J*=1.5 and 7.5Hz, CH), 7.66 (dd, 1H, *J*=1.5 and 7.5Hz, CH), 7.47 (td, 1H, *J*=1.5 and 7.5Hz, CH), 7.30–7.16 (m, 6H, CH), 4.16 (q, 1H, *J*=6.5 Hz, CH), 3.93 (s, 2H, NH_2), 1.69 (d, 3H, *J*=6.5Hz, CH_3). ^{13}CNMR ($CDCl_3$, 125.8 MHz) δ (ppm):155.99 (C=N), 147.65 (Car), 146.99 (Car), 142.72 (Car), 130.70 (Car), 129.40 (2Car), 128.79 (2Car), 128.53 (Car), 127.18 (Car), 126.33 (Car), 123.89 (Car), 123.13 (Car), 116.68 (Car), 41.71 (C), 24.11 (C).

*1,2,3,4-Tetrahydroacridin-9-amine***20**

Pale-Yellow solid, 85%, m.p.=183–184°C, IRν_{max}(cm^{-1}): 3278, 3158, 2923,2853, 1643, 1609,1484.^{1}HNMR ($CDCl_3$,500 MHz) δ (ppm):7.84 (dd, 1H, *J*=1.5 and 7.5 Hz, CH), 7.55 (dd, 1H, *J*=1.5 and 7.5Hz, CH), 7.44 (td, 1H, *J*=1.5 and 7.5Hz, CH), 7.25 (td, 1H, *J*=7 and 8 Hz, CH), 5.79 (s, 2H, NH_2), 3.17 (t, 2H, *J*=6 Hz, CH_2), 2.32 (t, 2H, *J*=6 Hz, CH_2),1.76–1.73 (m, 4H, CH_2). ^{13}CNMR ($CDCl_3$, 125.8 MHz) δ (ppm): 163.04 (C=N), 151.25 (Car), 139.55 (Car), 131.32 (Car), 130.33 (Car), 125.65 (Car), 123.44 (Car), 116.29 (Car), 116.27 (Car), 32.12 (C), 29.09 (C), 24.47 (C), 23.49 (C).

*2-(Thiophen-2-yl)quinolin-4-amine***21**

Deep-Green solid, 82%, m.p.=163-165°C, IRν_{max}(cm^{-1}): 3318,3100, 2923,2854, 1610,1572, 1513, 1484.^{1}HNMR ($CDCl_3$, 500 MHz) δ (ppm):7.95 (dd, 1H, *J*=1 and 7.5Hz, CH), 7.74 (dd, 1H, *J*=1.5 and 7.5Hz, CH), 7.64 (dd, 1H, *J*=1.5 and 7.5Hz, CH), 7.53 (td, 1H, *J*=1.5 and 7.5Hz, CH), 7.38 (dd, 1H, *J*=1 and 7.5Hz, CH),7.33 (dd, 1H, *J*=1.5 and 7.5Hz, CH),7.30–7.26 (m, 1H, CH), 6.79 (s, 1H, CH), 3.40 (s, 2H, NH_2).^{13}CNMR ($CDCl_3$,125.8 MHz) δ (ppm):159.98 (C=N), 157.53 (Car), 146.53 (Car), 136.57 (Car), 132.07 (Car), 132.02 (Car), 130.01 (Car), 128.79 (Car), 127.52 (Car), 123.63 (Car), 121.64 (Car), 112.48 (Car), 97.37 (Car).

*3-Methyl-2-(thiophen-2-yl) quinolin-4-amine***22**

Brown solid, 75%, m.p. =130–132°C, IRν_{max}(cm^{-1}): 3310, 3244,3090, 2922,2863, 1630,1563, 1529, 1492.^{1}HNMR ($CDCl_3$, 500 MHz) δ (ppm): 7.89 (dd, 1H, *J*=1.5 and 7.5Hz, CH), 7.67 (dd, 1H, *J*=1.5 and 7.5Hz, CH), 7.55 (dd, 1H, *J*=1.5 and 7.5Hz, CH), 7.48 (td, 1H, *J*=1 and 7.5 Hz, CH), 7.35 (dd, 2H, *J*=1.5 and 7.5Hz, CH), 7.28–7.25 (m, 1H, CH), 3.58 (s, 2H, NH_2), 2.12 (s, 3H, CH_3).^{13}CNMR ($CDCl_3$, 125.8 MHz) δ (ppm): 159.78 (C=N), 157.17 (Car), 143.21 (Car), 140.51 (Car), 132.51 (Car), 132.02 (Car), 130.46 (Car), 128.79 (Car), 127.21 (Car), 127.05 (Car), 124.46 (Car), 116.62 (Car), 112.66 (Car), 13.25 (C).

CONCLUSION

In a summary, suitable and useful forming of quinoline derivatives have been described. The modality was inception with imine synthesis by the condensation between aliphatic aldehydes and ketones with 2-Aminobenzonitril under basic and soft conditions, and followed by the functional intramolecular cyclization process from imines synthesis, finished the conforming quinoline derivatives products in higher yields. Completely obtained imines, good yields of the products, flexible reaction conditions, and stubby reaction times are the fundamental utility of this process.

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