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A Facile synthesis of substituted quinolines by NaH mediated benzylic C-H functionalization of methyl aza-arenes and nucleophilic addition to aromatic aldehydes

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ABSTRACT

A method for synthesizing condensed quinolines by using NaH catalyzed A mixture of substituted methyl quinolines and Various aromatic aldehydes in the presence of THF solvents were successfully synthesized in excellent yields via C-C single bond formation. The quinoline ring derivatives widely used as has been found to possess antimalarial, anti-bacterial, antifungal, anthelmintic, cardiotonic, anticonvulsant, anti-inflammatory, and analgesic activity.

Keywords: Quinoline, nucleophilic addition, biological activity, THF

INTRODUCTION

A quinoline ring containing compounds exhibit potent biological activities and has been proved by number of recent reports. [1-12]

The quinoline ring system is present as an essential structural fragment in a large number of natural and unnatural compounds exhibiting a broad variety of applications in biology and pharmacology. Indeed, thanks to their presence in a broad variety of drugs, quinolines represent a paradigm of privileged structures. The direct C-H functionalization by forming a C-C bond provides input for building of more complex molecules from simple precursors. Csp^2-H functionalization using transition metal catalysts proved a valuable tool in C–C bond formation. In contrast; Csp^3–H functionalization of alkyl group directly attached to aromatic ring is less explored. A few known methods involve the use of Pd and Cu based catalysts for the C–H activation of substituted azines and azarenes. Recent investigations demonstrated the role of Lewis acid catalysts in Csp^3–H functionalization of 2 methylazaarenes with α,β-unsaturated carbonyls, aldimines, carbonyls, and azodicarboxylates. [13-22]

In addition, different protocols have been reported that Lewis acid catalyzed reaction of methyl aza-arenes with aldehydes at elevated temperatures produced dehydrated products. To the best of our knowledge only one method is known for the benzylic C–H bond functionalization of aza-arenes promoted by Bronsted acid. Indeed, this protocol is limited only to aromatic aldehydes bearing electron withdrawing groups. Though the reported methods are satisfactory, they suffer from certain drawbacks like the use of expensive catalysts, toxic metals, extended reaction

times, and environmentally hazardous organic solvents. In view of this, the development of a mild and highly efficient method for the direct sp^3 C–H functionalization of alkyl aza-arenes is still desirable [23-24].

RESULTS AND DISCUSSION

A mixture of substituted methyl quinolines **13a-e** and NaH in dry THF was stirred for 30min below room temperature. Various aromatic aldehydes **14a-j** were added drop wise and the reaction mixture was stirred for 12.0-13.0 hours to afforded the corresponding products in excellent yields (**15k-o**). In a similar manner, the reaction of 2-methylquinoxaline **13f** with *p*-nitrobenzaldehyde **14k** to produce **15p** in 91% yield. The reaction of 2,6-dimethylpyridine **13g** and 2-methyl pyridine **13h** with *p*-nitrobenzaldehyde (**14k**) to afford **15p** and **15q** in 90 and 87% yields, respectively. All the reactions proceeded in good to excellent yields (86–92%). The results are summarized in **Table 1**.

In a typical experimental procedure, a mixture of methyl quinolines **13a** and NaH in dry THF was stirred for 30 min below room temperature. To this 1,3-benzodioxole-5-carbaldehyde **14a** was added drop wise and the reaction mixture was stirred for 2.0 h. The reaction proceeded in 92% yield and no by-product formation was observed. The most probable mechanism for the transformation of **13** to **15** is depicted in **Scheme 2.**

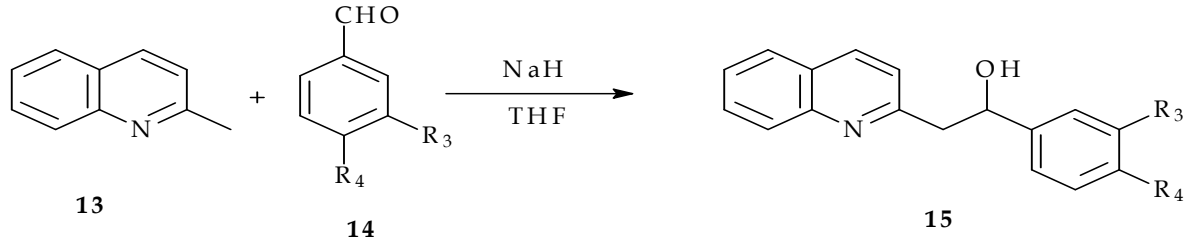
The advantages of the present protocol are mild reaction condition, easy work-up procedure, low toxicity, the yields are very good, the purity is excellent and inexpensive of the reagents that make the procedure an attractive alternative to the existing methods for the nucleophilic additions to aromatic aldehydes.

The compounds **15a-r** obtained were characterized by spectroscopic IR, ^{1}HNMR and MS) data, elemental analyses and finally by comparison with authentic samples.

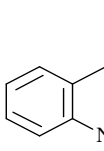
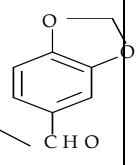
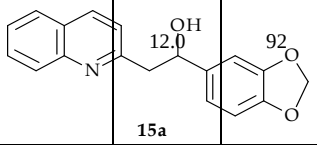
General procedure for the synthesis of substituted quinolines

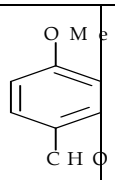
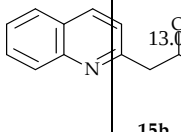
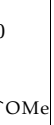
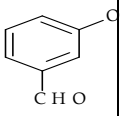
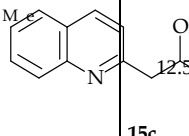
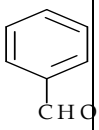
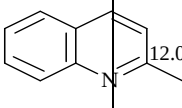
A mixture of substituted methyl quinolines (**13**, 1mmol) and NaH (1mmol) in dry THF (10 mL) was stirred for 30 min below room temperature. Various aromatic aldehydes (**14a-k,** 1mmol) were added drop wise and the reaction mixture was stirred for specified time 12.0-13.0 hours. The progress of the reaction was monitored by TLC. After completion of the reaction, the reaction mixture was treated with cold water and extracted with ethyl acetate. The combined ethyl acetate extracts were then dried over Na_2SO_4 and after removal of the solvent the mixture was purified by (silica gel) column chromatography (hexane/AcOEt, 70:30 as eluent) to give pure products **15a-r**. The obtained results were summarized in **Table 1** and **Table 2**.

Table 1: Sp^3 C-H activation of methyl quinolines and nucleophilic addition to various aromatic aldehydes

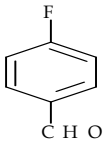
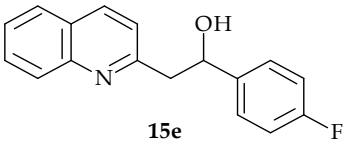
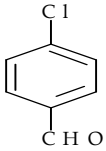
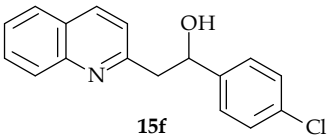
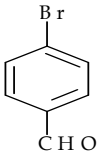
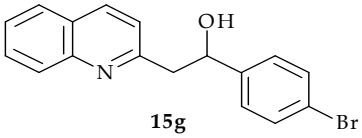
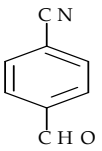
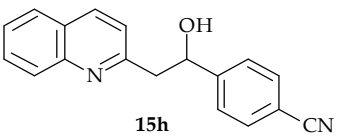


13 **14** **15**

Entry	Methyl quinoline	Aldehyde(**14**)	Product(**15**)	Time (hr)	Yield (%)
1	 **13a**	 **14a**	 **15a**	12.0	92

2	**13a**	 **14b**		13.0	90  **15b**
3	**13a**	 **14c**		12.5	88  **15c**
4	**13a**	 **14d**		12.0	87 **15d**

Contd..

Entry	Methyl quinoline	Aldehyde(**14**)	Product(**15**)	Time (hr)	Yield (%)
5	**13a**	 **14e**	 **15e**	12.0	92
6	**13a**	 **14f**	 **15f**	12.5	90
7	**13a**	 **14g**	 **15g**	13.0	88
8	**13a**	 **14h**	 **15h**	12.0	87

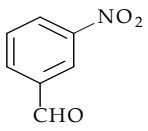
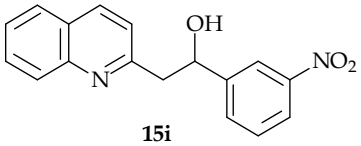
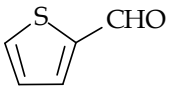
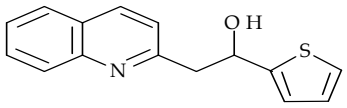
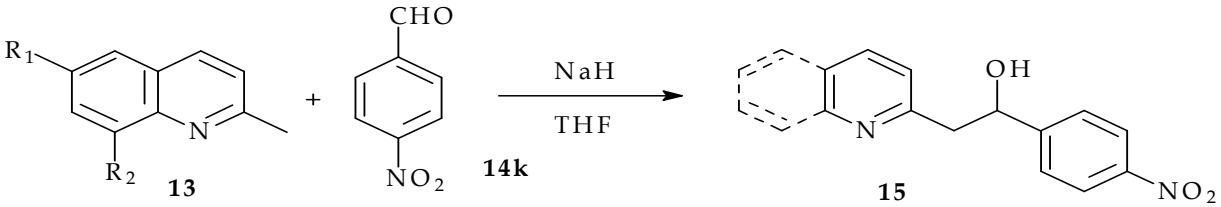
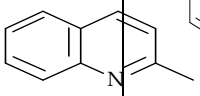
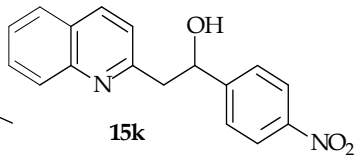
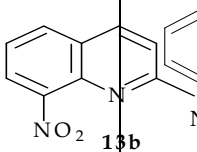
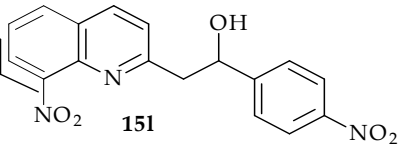
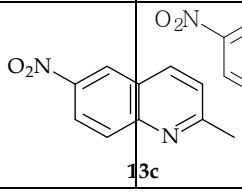
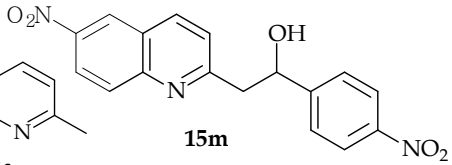
9	**13a**	 **14i**	 **15i**	12.5	91
10	**13a**	 **14j**	 **15j**	12.5	86

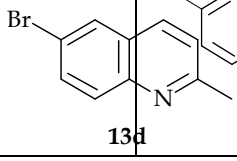
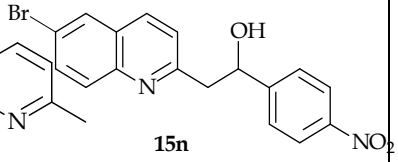
Table 2: Sp^3 C-H activation of methyl aza-arenes and nucleophilic addition to 4-nitrobenzaldehyde

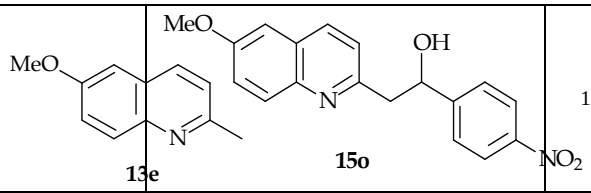
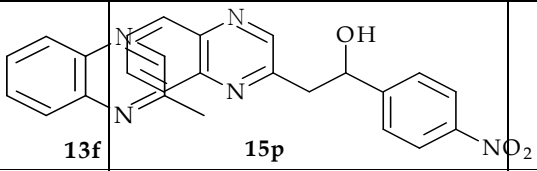
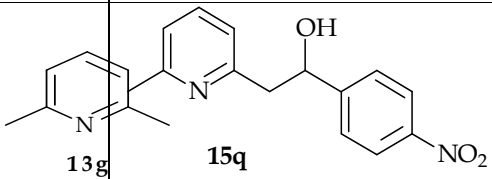
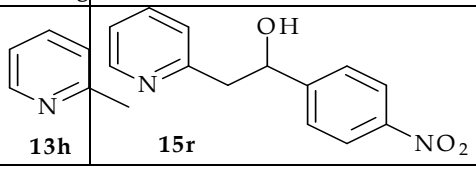


Scheme 2

Entry	Methyl quinoline (**13**)	Product (**15**)	Time (hr)	Yield (%)
1	 **13a**	 **15k**	12.5	88
2	 **13b**	 **15l**	12.0	92
3	 **13c**	 **15m**	12.5	91

Contd..

Entry	Methyl quinoline (**13**)	Product (**15**)	Time (hr)	Yield (%)
4	 **13d**	 **15n**	12.5	89

5	 **13e** **15o**		13.0	90
6	 **13f** **15p**		12.0	87
7	 **13g** **15q**		12.5	91
8	 **13h** **15r**		12.5	88

Physical and Spectral data for products 15a-15r (Table 2; Entry1)

1-(1,3-Benzodioxol-5-yl)-2-(quinolin-2-yl)ethanol (**15a)**

Yield 40%; m.p. 125-126 ^{0}C; **IR (KBr)** ν 3425, 3197, 3065, 2854, 1668, 1562, 1291, 1025, 820 cm^{-1}; **^{1}H NMR (300 MHz, CDCl$_3$):**δ 8.09 (t, *J* = 9.2 Hz, 2H), 7.81 (d, *J* = 7.9 Hz, 1H), 7.73 (t, *J* = 7.3 Hz, 1H), 7.54 (t, *J* = 7.5 Hz, 1H), 7.23 (d, *J* = 8.4 Hz, 1H), 7.02 (s, 1H), 6.92 (d, *J* = 7.7 Hz, 1H), 6.79 (d, *J* = 7.8 Hz, 1H), 6.18 (br, 1H), 5.95 (s, 2H), 5.24 (dd, *J* = 3.5 Hz, *J* = 8.1 Hz, 1H), 3.21-3.36 (m, 2H); **^{13}C NMR (75 MHz, CDCl$_3$)**: δ 160.3, 147.6, 146.8, 146.7, 138.1, 136.9, 129.8, 128.5, 127.5, 126.8, 126.2, 122.0, 119.1, 108.0, 106.6, 100.8, 72.8, 46.1; **MS (ESI):***m/z* 296 $[M+H]^+$; Anal. Calcd for $C_{18}H_{15}NO_3$: C, 73.71; H, 5.15; N, 4.78. Found: C, 73.84; H, 5.17; N, 4.82%.

1-(4-Methoxyphenyl)-2-(quinolin-2-yl)ethanol(15b)

Yield, 55%; m.p. 135-137 ^{0}C; **IR (KBr):** υ 3434, 1614, 1582, 1291, 1096, 1017, 833 cm^{-1}; **^{1}H NMR (600 MHz, CDCl$_3$):**δ 8.12 (t, *J* = 8.2 Hz, 2H), 7.82 (d, *J* = 7.9 Hz, 1H), 7.75 (t, *J* = 7.5 Hz, 1H), 7.55 (t, *J* = 7.5 Hz, 1H), 7.40 (d, *J* = 8.2 Hz, 2H), 7.24 (d, *J* = 8.2 Hz, 1H), 6.90 (d, *J* = 8.6 Hz, 2H), 6.05 (br, 1H), 5.28 (dd, *J* = 2.6 Hz, *J* = 9.0 Hz, 1H), 3.81 (s, 3H), 3.29-3.39 (m, 2H); **^{13}C NMR (75 MHz, CDCl$_3$):**δ 160.3, 158.8, 137.3, 136.0, 130.1, 128.1, 127.5, 127.0, 126.8, 126.4, 122.1, 113.7, 72.5, 55.2, 45.9; **MS (ESI):***m/z* 280 $[M+H]^+$; Anal. Calcd for $C_{18}H_{17}NO_2$: C, 77.40; H, 6.13; N, 5.01. Found: C, 77.51; H, 6.15; N, 5.07%.

1-(3-Methoxyphenyl)-2-(quinolin-2-yl)ethanol (**15c**)

Yield, 65%; m.p. 92-93 ^{0}C; **IR(KBr)**: υ 3421, 2928, 1598, 1495, 1461, 1255, 1040, 744 cm^{-1}; **^{1}H NMR (600 MHz, CDCl$_3$):**δ 8.11 (t, *J* = 9.4 Hz, 2H), 7.81 (d, *J* = 8.2 Hz, 1H), 7.74 (t, *J* = 7.1 Hz, 1H), 7.75 (t, *J* = 7.5 Hz, 1H), 7.28 (d, *J* = 7.9 Hz, 1H), 7.23 (d, *J* = 8.2 Hz, 1H), 7.07 (s, 1H), 7.04 (d, *J* = 7.9 Hz, 1H), 6.82 (dd, *J* = 2.6 Hz, *J* =7.9 Hz, 1H), 6.16 (br, 1H), 5.31 (t, *J* = 5.6 Hz, 1H), 3.81 (s, 3H), 3.34 (d, *J* = 5.6 Hz, 2H); **^{13}C NMR (75 MHz, CDCl$_3$):**δ 160.3, 159.6, 146.6, 145.5, 137.0, 129.9, 129.3, 128.3, 127.5, 126.8, 126.3, 122.1, 118.1, 113.0, 111.1, 72.8, 55.1, 45.9; **MS (ESI):***m/z* 280 $[M+H]^+$; Anal. Calcd for $C_{18}H_{17}NO_2$: C, 77.40; H, 6.13; N, 5.01. Found: C, 77.50; H, 6.16; N, 5.05%.

1-Phenyl-2-(quinolin-2-yl)ethanol(**15d**)

Yield, 65%; m.p. 124-125 ^{0}C; **IR (KBr)**: υ 3216, 3057, 2865, 1599, 1501, 1078, 810, 773 cm^{-1}; **^{1}H NMR (300 MHz, CDCl$_3$):**δ 8.08 (t, *J* = 8.1 Hz, 2H), 7.80 (d, *J* = 7.9 Hz, 1H), 7.72 (t, *J* = 8.1 Hz, 1H), 7.54 (d, *J* = 7.7 Hz, 1H), 7.48 (d, *J* = 8.4 Hz, 2H), 7.36(t, *J* = 7.1Hz, 2H), 7.29 (d, *J* = 7.1 Hz, 1H), 7.22 (d, *J* = 8.3 Hz, 1H), 6.20 (br, 1H), 5.33 (dd, *J* = 4.5 Hz, *J* = 7.5 Hz, 1H), 3.26-3.39 (m, 2H); **^{13}C NMR (75 MHz, CDCl$_3$):** δ 160.4, 146.8, 143.8,

136.8, 129.8, 128.6, 128.3, 127.5, 127.2, 126.8, 126.2, 125.8, 122.0, 72.9, 46.0;**MS (ESI):***m/z* 250 $[M+H]^+$; Anal. Calcd for $C_{17}H_{15}NO$: C, 81.90; H, 6.06; N, 5.62. Found: C, 81.99; H, 6.07; N, 5.67%.

1-(4-Fluorophenyl)-2-(quinolin-2-yl)ethanol(15e)
Yield, 70%; m.p. 133-135 ^{0}C; **IR(KBr)**: υ 3213, 2930, 1600, 1505, 1220, 1081, 835 cm^{-1}; **^{1}H NMR (300 MHz, $CDCl_3$):**δ 8.09 (dd, *J* = 8.4 Hz, *J* = 12.4 Hz, 2H), 7.81 (d, *J* = 8.1 Hz, 1H), 7.73 (t, *J* = 8.3 Hz, 1H), 7.54 (t, *J* = 7.1 Hz, 1H), 7.41-7.47 (m, 2H), 7.22 (d, *J* = 8.3 Hz, 1H), 7.04 (t, *J* = 8.6 Hz, 2H), 6.31 (br, 1H), 5.31 (dd, *J* = 4.5 Hz, *J* = 7.1 Hz, 1H), 3.23-3.36 (m, 2H); **^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6):**δ 160.0, 146.4, 139.5, 137.3, 130.1, 128.7, 127.6, 127.5, 127.4, 126.4, 122.0, 115.2, 114.9, 72.3, 45.8; **MS (ESI):***m/z* 268 $[M+H]^+$; Anal. Calcd for $C_{17}H_{14}FNO$: C, 76.39; H, 5.28; N, 5.24. Found: C, 76.50; H, 5.30; N, 5.28%.

1-(4-Chlorophenyl)-2-(quinolin-2-yl)ethanol(15f)
Yield, 70%; m.p. 142-143 ^{0}C; **IR (KBr)**: υ 3417, 2924, 1603, 1492, 1061, 827 cm^{-1}; **^{1}H NMR (600 MHz, $CDCl_3$):**δ 8.11 (d, *J* = 8.2 Hz, 1H), 8.07 (d, *J* = 8.2 Hz, 1H), 7.81 (d, *J* = 8.2 Hz, 1H), 7.73 (t, *J* = 7.1 Hz, 1H), 7.54 (t, *J* = 7.1 Hz, 1H), 7.40 (d, *J* = 8.2 Hz, 2H), 7.31 (d, *J* = 8.2 Hz, 2H), 7.21 (d, *J* = 8.2 Hz, 1H), 6.34 (br, 1H), 5.30 (t, *J* = 6.0 Hz, 1H), 3.29 (d, *J* = 6.0 Hz, 2H); **^{13}C NMR (75 MHz, $CDCl_3$):**δ 160.0, 157.9, 146.6, 142.3, 137.1, 132.8, 130.0, 128.4, 127.5, 126.8, 126.3, 122.0, 72.2, 45.7;**MS (ESI):***m/z* 284 $[M+H]^+$; Anal. Calcd for $C_{17}H_{14}ClNO$: C, 71.96; H, 4.97; N, 4.94. Found: C, 72.08; H, 4.98; N, 4.98%.

1-(4-Bromophenyl)-2-(quinolin-2-yl)ethanol (15g)
Yield, 70%; m.p. 152-154 ^{0}C; **IR(KBr)**: υ 3248, 2927, 1598, 1480, 1063, 824, 748 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.09 (dd, *J* = 8.3 Hz, *J* = 17.5 Hz, 2H), 7.82 (d, *J* = 7.5 Hz, 1H), 7.74 (t, *J* = 7.5 Hz, 1H), 7.55 (t, *J* = 7.5 Hz, 1H), 7.48 (d, *J* = 7.5 Hz, 2H), 7.35 (d, *J* = 8.3 Hz, 2H), 7.21 (d, *J* = 8.3 Hz, 1H), 6.38 (br, 1H), 5.29 (t, *J* = 5.8 Hz, 1H), 3.29 (d, *J* = 5.8 Hz, 2H); **^{13}C NMR (75 MHz, $CDCl_3$):** δ 160.0, 146.6, 142.9, 137.1, 131.4, 130.0, 128.4, 127.6, 126.9, 126.8, 126.4, 122.0, 121.0, 72.3, 45.7; **MS (ESI):** *m/z* 328 $[M+H]^+$; Anal. Calcd for $C_{17}H_{14}BrNO$: C, 62.21; H, 4.30; N, 4.27. Found: C, 62.34; H, 4.32; N, 4.31%.

4-(1-Hydroxy-2-(quinolin-2-yl)ethyl)benzonitrile (15h)
Yield, 75%; m.p. 169-170 ^{0}C; **IR(KBr):** υ 3160, 2956, 2228, 1601, 1503, 1072, 829, 754 cm^{-1}; **^{1}H NMR (600 MHz, $CDCl_3$+DMSO-d_6):**δ 8.21 (d, *J* = 7.9 Hz, 1H), 7.99 (d, *J* = 8.2 Hz, 1H), 7.89 (d, *J* = 8.2 Hz, 1H), 7.72 (t, *J* = 7.1 Hz, 1H), 7.69 (d, *J* = 7.9 Hz, 2H), 7.59 (d, *J* = 7.9 Hz, 2H), 7.54 (t, *J* = 7.1 Hz, 1H), 7.40 (d, *J* = 8.2 Hz, 1H), 5.79 (br, 1H), 5.27 (t, *J* = 6.3 Hz, 1H), 3.27 (d, *J* = 6.3 Hz, 2H); **^{13}C NMR (75 MHz, $CDCl_3$+DMSO-d_6):**δ 157.5, 149.1, 145.1, 134.5, 130.0, 127.6, 126.3, 125.9, 125.0, 124.9, 124.1, 120.8, 116.9, 108.2, 70.2, 45.8; **MS (ESI):** *m/z* 275 $[M+H]^+$; Anal. Calcd for $C_{18}H_{14}N_2O$: C, 78.81; H, 5.14; N, 10.21. Found: C, 78.93; H, 5.16; N, 10.26%.

1-(3-Nitrophenyl)-2-(quinolin-2-yl)ethanol (15i)
Yield, 85%; m.p. 154-155 ^{0}C; **IR(KBr)**: υ 3257, 2939, 1603, 1528, 1350, 1051, 822 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$):** δ 8.36 (s, 1H), 8.12-8.23 (m, 3H), 7.87 (dd, *J* = 4.0 Hz, *J* = 8.0 Hz, 2H), 7.79 (t, *J* = 8.0 Hz, 1H), 7.60 (t, *J* = 8.0 Hz, 1H), 7.54 (t, *J* = 8.0 Hz, 1H), 7.27 (d, *J* = 2.4 Hz, 1H), 6.59 (br, 1H), 5.45 (dd, *J* = 2.4 Hz, *J* = 8.8 Hz, 1H), 3.34-3.49 (m, 2H);**^{13}C NMR (75 MHz, $CDCl_3$):**δ 159.4, 148.3, 146.0, 137.6, 137.1, 132.0, 130.3, 129.3, 128.1, 127.6, 126.9, 126.7, 122.3, 121.9, 120.9, 71.9, 45.1; **MS (ESI):** *m/z* 295 $[M+H]^+$; Anal. Calcd for $C_{17}H_{14}N_2O_3$: C, 69.38; H, 4.79; N, 9.52. Found: C, 69.48; H, 4.81; N, 9.58%.

2-(Quinolin-2-yl)-1-(thiophen-2-yl)ethanol (15j)
Yield, 70%; m.p. 98-100 ^{0}C; **IR(KBr):** υ 3126, 2925, 1598, 1503, 1425, 1309, 1044, 822, 748 cm^{-1};**^{1}H NMR (600 MHz, $CDCl_3$):** δ 8.12 (d, *J* = 8.2 Hz, 1H), 8.06 (d, *J* = 8.2 Hz, 1H), 7.81 (d, *J* = 8.2 Hz, 1H), 7.73 (t, *J* = 7.1 Hz, 1H), 7.54 (t, *J* = 7.5 Hz, 1H), 7.26 (d, *J* = 8.6 Hz, 1H), 7.23 (d, *J* = 6.0 Hz, 1H), 7.03 (d, *J* = 3.3 Hz, 1H), 6.97 (dd, *J* = 3.3 Hz, *J* = 4.8 Hz, 1H), 6.50 (br, 1H), 5.60 (t, *J* = 5.6 Hz, 1H), 3.46 (d, *J* = 5.6 Hz, 2H); **^{13}C NMR (75 MHz, $CDCl_3$):** δ 159.8, 147. 9, 146.5, 137.1, 130.0, 128.3, 127.5, 126.8, 126.5, 126.4, 124.2, 123.1, 122.1, 69.2, 45.6;**MS (ESI):***m/z* 256 $[M+H]^+$; Anal. Calcd for $C_{15}H_{13}NOS$: C, 70.56; H, 5.13; N, 5.49. Found: C, 70.68; H, 5.14; N, 5.54%.

1-(4-Nitrophenyl)-2-(quinolin-2-yl)ethanol(15k)
Yield, 85%; m.p. 151-153 ^{0}C;**IR(KBr)**: υ 3526, 2923, 1601, 1512, 1345, 847, 758 cm^{-1}; **^{1}H NMR (600 MHz, $CDCl_3$):**δ 8.22 (d, *J* = 8.6 Hz, 2H), 8.13 (d, *J* = 8.2 Hz, 1H), 8.06 (d, *J* = 8.2 Hz, 1H), 7.83 (d, *J* = 8.2 Hz, 1H), 7.76 (t, *J* = 8.2 Hz, 1H), 7.65 (d, *J* = 8.6 Hz, 2H), 7.56 (t, *J* = 7.5 Hz, 1H), 7.22 (d, *J* = 8.2 Hz, 1H), 6.82 (br, 1H), 5.45

(dd, *J* = 2.2 Hz, *J* = 9.0 Hz, 1H), 3.26-3.37 (m, 2H); **^{13}C NMR (75 MHz, $CDCl_3$):**δ 159.4, 151.3, 147.1, 146.6, 137.4, 130.2, 128.3, 127.6, 126.9, 126.6, 123.6, 121.9, 72.1, 45.1; **MS (ESI):***m/z* 295 $[M+H]^+$; Anal. Calcd for $C_{17}H_{14}N_2O_3$: C, 69.38; H, 4.79; N, 9.52. Found: C, 69.46; H, 4.82; N, 9.59%.

1-(4-Nitrophenyl)-2-(8-nitroquinolin-2-yl)ethanol(15l)
Yield, 75%; m.p. 163-165 ^{0}C; **IR(KBr):** υ 3384, 2927, 1598, 1518, 1423, 1339, 851 cm^{-1}; **^{1}H NMR (600 MHz, DMSO-d_6):**δ 8.30-8.40 (m, 1H), 8.07- 8.19 (m, 4H), 7.58-7.67 (m, 3H), 7.49-7.57 (m, 1H), 5.78 (br, 1H), 5.29 (t, *J* = 6.4 Hz, 1H), 3.31 (d, *J* = 6.4 Hz, 2H);**^{13}C NMR (75 MHz, $CDCl_3$):** δ 160.0, 150.8, 145.5, 144.6, 134.4, 129.9, 125.5, 125.1, 123.0, 122.5, 122.0, 121.4, 121.2, 69.5, 45.7; **MS (ESI):** *m/z* 340 $[M+H]^+$; Anal. Calcd for $C_{17}H_{13}N_3O_5$: C, 60.18; H, 3.86; N, 12.38. Found: C, 60.29; H, 3.88; N, 12.43%.

1-(4-Nitrophenyl)-2-(6-nitroquinolin-2-yl)ethanol (15m)
Yield 65%; m.p. 176-177 ^{0}C; **IR (KBr):** υ 3364, 2925, 1604, 1513, 1343, 850 cm^{-1}; **^{1}H NMR (600 MHz, DMSO-d_6):**δ 9.01 (s, 1H), 8.59 (d, *J* = 8.6 Hz, 1H)), 8.42 (d, *J* = 8.6 Hz, 1H), 8.18 (d, *J* = 8.2 Hz, 2H), 8.13 (d, *J* = 9.4 Hz, 1H), 7.68 (t, *J* = 7.9 Hz, 3H), 5.81 (d, *J* = 4.5 Hz, 1H), 5.32-5.36 (m, 1H), 3.29-3.37 (m, 2H); **^{13}C NMR (75 MHz, DMSO-d_6):**δ 163.3, 153.1, 149.1, 146.4, 144.4, 137.9, 130.1, 127.0, 125.4, 124.8, 124.4, 123.6, 122.6, 71.4, 47.9; **MS (ESI):** *m/z* 340 $[M+H]^+$; Anal. Calcd for $C_{17}H_{13}N_3O_5$: C, 60.18; H, 3.86; N, 12.38. Found: C, 60.26; H, 3.87; N, 12.42%.

2-(6-Bromoquinolin-2-yl)-1-(4-nitrophenyl)ethanol(15n)
Yield 65%; m.p. 152-153 ^{0}C; **IR (KBr)**: υ 3323, 2925, 1593, 1515, 1342, 1061, 827 cm^{-1}; **^{1}H NMR (600 MHz, $CDCl_3$+DMSO-d_6):**δ 8.15 (t, *J* = 9.0 Hz, 3H), 8.10 (s, 1H), 7.89 (d, *J* = 9.0Hz, 1H), 7.76 (d, *J* = 9.0 Hz, 1H), 7.65 (d, *J* = 7.5 Hz, 2H), 7.42 (d, *J* = 8.6 Hz, 1H), 5.83 (br, 1H), 5.33 (dd, *J* = 3.3 Hz, *J* = 5.2 Hz, 1H), 3.28 (d, *J* = 6.4 Hz, 2H); **^{13}C NMR (75 MHz, $CDCl_3$+ DMSO-d_6):**δ 158.1, 151.3, 144.8, 144.1, 133.3, 130.6, 128.7, 127.8, 126.1, 125.1, 121.8, 121.3, 117.2, 70.0, 46.1; **MS(ESI):***m/z* 373 $[M+H]^+$; Anal. Calcd for $C_{17}H_{13}BrN_2O_3$: C, 54.71; H, 3.51; N, 7.51. Found: C, 54.82; H, 3.53; N, 7.55%.

2-(6-Methoxyquinolin-2-yl)-1-(4-nitrophenyl)ethanol(15o)
Yield 65%; m.p. 170-171 ^{0}C; **^{1}H NMR (300 MHz, $CDCl_3$):**δ8.19 (d, *J* = 7.5 Hz, 2H), 8.02 (d, *J* = 8.3 Hz, 1H), 7.96 (d, *J* = 8.3 Hz, 1H), 7.63 (d, *J* = 8.3 Hz, 2H), 7.39 (dd, *J* = 2.2 Hz, *J* = 9.0 Hz, 1H), 7.17 (d, *J* = 8.3 Hz, 1H), 7.07 (s, 1H), 5.41 (dd, *J* = 3.0 Hz, *J* = 9.0 Hz, 1H), 3.94 (s, 3H), 3.17-3.37 (m, 2H); **^{13}C NMR (75 MHz, $CDCl_3$):**δ 157.7, 156.7, 151.4, 147.0, 142.6, 136.0, 129.7, 127.9, 126.5, 123.5, 122.8, 122.1, 105.0, 72.2, 55.5, 44.8; **MS (ESI):***m/z* 325 $[M+H]^+$; Anal. Calcd for $C_{18}H_{16}N_2O_4$: C, 66.66; H, 4.97; N, 8.64. Found: C, 66.77; H, 4.99; N, 8.68%.

1-(4-Nitrophenyl)-2-(quinoxalin-2-yl)ethanol(15p)
Yield 60%; m.p. 142-143 ^{0}C; **IR(KBr)**: υ 3256, 2926, 1601, 1516, 1341, 1066, 772 cm^{-1}; **^{1}H NMR (600 MHz, $CDCl_3$)**: δ 8.71 (s, 1H), 8.23 (d, *J* = 8.6 Hz, 2H), 8.11 (d, *J* = 8.2 Hz, 1H), 8.07 (d, *J* = 8.2 Hz, 1H), 7.76-7.83 (m, 2H), 7.66 (d, *J* = 8.6 Hz, 2H), 5.48 (dd, *J* = 2.6 Hz, *J* = 9.0 Hz, 1H), 3.33-3.45 (m, 2H); **^{13}C NMR (75 MHz, $CDCl_3$):**δ 154.0, 150.5, 147.3, 145.8, 141.6, 141.0, 130.6, 129.8, 129.3, 128.5, 126.5, 123.7, 71.8, 43.3; **MS (ESI):***m/z* 296 $(M+H)^+$; Anal. Calcd for $C_{16}H_{13}N_3O_3$: C, 65.08; H, 4.44; N, 14.23. Found: C, 65.18; H, 4.45; N, 14.28%.

2-(6-Methylpyridin-2-yl)-1-(4-nitrophenyl)ethanol(15q)
Yield 55%; m.p. 114-116 ^{0}C; **IR(KBr)**: υ 3414, 3113, 2923, 1596, 1521, 1456, 1344, 1057, 849, 773cm^{-1};**^{1}H NMR (300 MHz, $CDCl_3$):**δ 8.20 (d, *J* = 8.6 Hz, 2H), 7.60 (d, *J* = 8.6 Hz, 2H), 7.53 (d, *J* = 7.7 Hz, 1H), 7.08 (d, *J* = 7.7 Hz, 1H), 6.91 (d, *J* = 7.5 Hz, 1H), 5.26 (dd, *J* = 3.2 Hz, *J* = 8.4 Hz, 1H), 3.00-3.18 (m, 2H), 2.58 (s, 3H);**^{13}C NMR (75 MHz, $CDCl_3$):** δ 158.0, 157.3, 151.5, 147.0, 137.5, 126.5, 123.4, 121.6, 120.7, 72.4, 44.4, 24.1; **MS (ESI):***m/z* 259 $[M+H]^+$;Anal. Calcd for $C_{14}H_{14}N_2O_3$: C, 65.11; H, 5.46; N, 10.85. Found: C, 65.22; H, 5.47; N, 10.89%.

1-(4-Nitrophenyl)-2-(pyridin-2-yl)ethanol (15r)
Yield, 50%; m.p. 162-164 ^{0}C; **IR(KBr)**: υ 3138, 2851, 1598, 1511, 1348, 1068, 760 cm^{-1}; **^{1}H NMR (600 MHz, $CDCl_3$):** δ 8.54 (d, *J* = 4.5 Hz, 1H), 8.19 (d, *J* = 8.6 Hz, 2H), 7.66 (t, *J* = 7.5 Hz, 1H), 7.60 (d, *J* = 8.6 Hz, 2H), 7.24 (t, *J* = 6.0 Hz, 1H), 7.11 (d, *J* = 7.5 Hz, 1H), 5.29 (dd, *J* = 2.2 Hz, *J* = 9.0 Hz, 1H), 3.09-3.21 (m, 2H); **^{13}C NMR (75 MHz, $CDCl_3$):**δ 158.6, 151.3, 148.2, 147.1, 137.4, 126.5, 123.9, 123.5, 122.1, 72.4, 44.6; MS (ESI): *m/z* 245 $[M+H]^+$;Anal. Calcd for $C_{13}H_{12}N_2O_3$: C, 63.93; H, 4.95; N, 11.47. Found: C, 63.99; H, 4.97; N, 11.52%.

CONCLUSION

In the present work we synthesized a condensed series of substituted quinoline with various aldehydes **(15a -15r).** They widely potent for further biological studies.

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REFERENCES

[1] Praveen Kumar Darsi S S, Rama Devi B & Naidu A, *Indian J Chem*, 54B, **2015**, 142.
[2] Desai N C, Joshi V V, Rajpara K M, Uaghani H V &Satodiya, *Indian J Chem*, 52B, **2013**, 1191.
[3] Gisela C M, Stephanie H, Graciela Y B, Silvia E A & Michael G, *Bioorg& Med Chem Lett*, 24, **2014**, 1545.
[4] Shiva Kumar K, Kiran Kumar S, Yogi Sreenivas B, Dhilli Rao G, RavikumarKapavarapu, Rambabu D, Rama Krishna G, Malla Reddy C, Basaveswara Rao M V, Parsa K V L &Manojit Pal, *Bioorg& Med Chem Lett*, 20, **2012**, 2199.
[5] Pandey S, Agarwal P, Srivastava K, Rajakumar S, Puri S K, Verma P, Saxena J K, Sharma A, Lal J & Chauhan P M S, *Eur J Med Chem*, 66, **2013**, 69.
[6] Nageswara Rao N, Rambhau Mali P, Meshram H M, *Indian J Chem*, 53B, **2014**, 1153.
[7] Haiyang Liu, Xiaoshuang Li, Feng Liu, Ying Tan &Yuyang Jiang, *J Organometallic Chem*, 794, **2015**, 27.
[8] Lei Wang, XubenHou, Huansheng Fu, Xiaole Pan, Wenfang Xu, Weiping Tang, Hao Fang, *Bioorg& Med Chem*, 23, **2015**, 4364.
[9] Carlos Coa J, Castrillon W, Cardona W, Miguel C, Victoria O, Munoz J A, Velez I D, Robledo S M, *Eur J Med Chem*, 101, **2015**, 746.
[10] Ashraf Kareem El-Damasy, SeonHeeSeo, Nam-Chul Cho, Soon Bang Kang, Ae NimPae, Key-Sun Kim, GyochangKeum, , *Eur J Med Chem*, 101, **2015**, 754.
[11] El-Feky S A H, El-Samii Z K A, Osman N A, Lashine J, Kamel M A &Thabet H K, *BioorgChem*, 58, **2015**, 104.
[12] Abouelhassan Y, Garrison A T, Burch G M, Wong W, Norwood V M, Huigens R W, *Bioorg& Med Chem Lett*, 24, **2014**, 5076.
[13] Michael J P, *Nat Prod Rep*, 25,**2008**, 166.
[14] Kouznetsov V V, Vargas Mendez L Y & Melendez Gomez C M, *Curr Org Chem*, 9, **2005**, 141.
[15] Bongarzone S, Bolognesi M L, *CurrOpinDrugDiscovery Dev*, 6, **2011**, 251.
[16] Chen D Y K &Youn S W, *Eur J Chem*, 18, **2012**, 9452.
[17] (a) Ye M, Gao G L & Yu J Q, Am J ChemSoc, 133, **2011**, 6964;
(b) Seregin I V &Gevorgyan V, *ChemSoc Rev*, 36, **2007**, 1173.
[18] (a) Qian B, Guo S, Shao J, Zhu Q, Yang L, Xia C & Huang H, *Am J ChemSoc*, 132, **2010**, 3650; (b) Jiang H, Chen H, Wang A & Liu X, *ChemCommun*,**2010**, 7259.
[19] (a) Komai, H.; Yoshino, T.; Matsunaga, S.; Kanai, M. Org. Lett. 2011, 13, 1706;
(b) Yang Y, Xie C, Xie Y & Zhang Y, *Org Lett*, 14, **2012**, 957.
[20] (a) Yan Y, Xu K, Fang Y & Wang Z, *J Org Chem*, 76, **2011**, 6849;
(b) Qian B, Xie P, Xie Y & Huang H, *Org Lett*, 13, **2011**, 2580;
(c) Rueping A, Tolstoluzhsky N, Org Lett, 13, **2011**, 1095.
[21] Niu R, Xiao J, Liang T& Li X, *Org Lett*, 14, **2012**, 676.
[22] Yu W Y, Sit W N, Lai K M, Zhou Z & Chan A S C, *Am J ChemSoc*, 130, **2008**, 3304.
[23] (a) Staderini M, Cabezas N, Bolognesi M L, Menendez J C, *Synlett*, **2011**, 2577;
(b) Chang S, Chen W, Wang C, Tzeng C C& Chen Y, *Bioorg Med Chem*, 18, **2010**, 124.
[24] Wang F F, Luo C P, Wang Y, Deng G & Yang L, *Org BiomolChem*, 10, **2012**, 8605.