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ORIGINAL PAPER

# An efficient synthesis of novel functionalized benzo[*h*]pyrano[2,3-*b*] quinolines and pyrano[2,3-*b*]quinoline derivatives via one-pot multicomponent reactions

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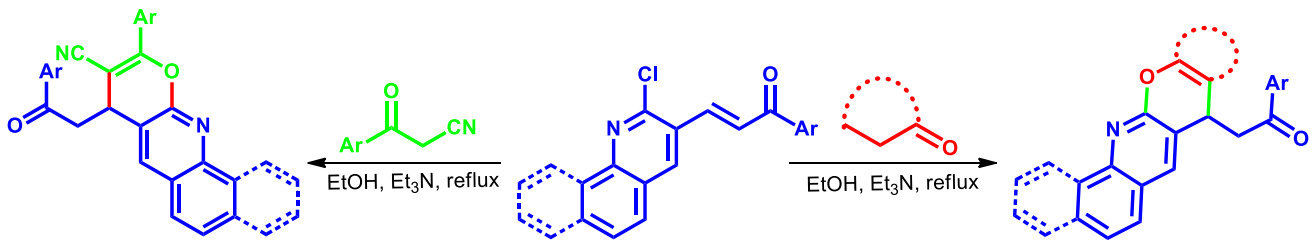
## Abstract

In this paper, a convenient, one-pot, for the straightforward synthesis of pyrano[2,3-*b*]quinoline and benzo[*h*]pyrano[2,3-*b*]quinoline derivatives is presented, which includes a three-component reaction of (2-chloroquinoline-3-carbaldehyde, 2-chlorobenzo[*h*]quinoline-3-carbaldehyde), and 1-phenyl-2-(1,1,1-triphenyl-$\lambda^5$- phosphanylidene)ethan-1-one (Wittig reagent) with the active methylene compounds such as (benzoylacetonitrile, dimedone, 1,3-dimethylbarbituric acid, 4-hydroxycoumarin and 3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one), during the two processes of C–C bond formation (Michael addition) and intramolecular cyclization (by the attack of the oxygen atom of active methylene compounds). Advantages of this protocol include easily accessible starting materials, excellent yields (65–98%), absence of a metal catalyst and simple workup procedure (the pure products were obtained simply by washing the products with EtOH).

## Graphic abstract

A series of pyrano[2,3-*b*]quinoline and benzo[*h*]pyrano[2,3-*b*]quinoline derivatives have been synthesized in excellent yields (65–98%) via a one-pot three-component reaction of (2-chloroquinoline-3-carbaldehyde, 2-chlorobenzo[*h*]quinoline-3-carbaldehyde) and 1-phenyl-2-(1,1,1-triphenyl-$\lambda^5$-phosphanylidene)ethan-1-one (Wittig reagent) with the active methylene compounds such as (benzoylacetonitrile, dimedone, 1,3-dimethylbarbituric acid, 4-hydroxycoumarin and 3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one), during the two processes of C–C bond formation (Michael addition) and intramolecular cyclization (by the attack of the oxygen atom of active methylene compounds). Advantages of this protocol include easily accessible starting materials, excellent yields (65–98%), absence of a metal catalyst and simple workup procedure (the pure products were obtained simply by washing the products with EtOH).




**6 examples, yield 86-96%** **7 examples, yield 65-98%**

**Keywords** 2-Chlorobenzo[*h*]quinoline-3-carbaldehyde · 2-Chloroquinoline-3-carbaldehyde · Multicomponent reaction · 1-Phenyl-2-(1,1,1-triphenyl-$\lambda^5$-phosphanylidene)ethan-1-one (Wittig reagent) · Pyrano[2,3-*b*]quinoline · Benzo[*h*]pyrano[2,3-*b*]quinoline

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## Introduction

Multicomponent reactions (MCRs) are one of the useful pathways in chemical synthesis as well as industrially, which has attracted a lot of attention in recent years. It can successfully combine complex structures from simple substrates in a one-pot reaction that does not need the isolation of intermediate compounds, which is the highest contributor toward the environment. Moreover, it provides several advantages, such as short reaction periods, greater efficiency, high chemical efficiency, high complexity, and diversity of molecular [1–8]. MCRs are often selective and also often increase the number of substrates that lead to inefficiency reactions and the production of by-products [9].

One of the primary goals of organic and medicinal chemistry is the design and synthesis of scaffolds possessing biological features. Heterocycles including nitrogen rings are targeted molecules in synthetic and medicinal chemistry since the nitrogen ring is a key scaffold in different biologically active compounds. Quinoline and its derivatives as one of the most important heterocyclic compounds with nitrogen ring recognized, which are widespread in medicinal agents and natural products [10, 11]. Among them, 2-chloroquinoline-3-carbaldehydes are one of the easiest available starting materials and very interesting compounds due to their high reactivity activity, they have an active aldehyde group in position **3**, and the substitution of chlorine in position **2**, these features provide increased reactivity, using materials containing these structures, in a variety of multi-component reactions including nucleophilic substitution reactions, electrophilic substitution reactions, Diels–Alder [12], 1,3-dipolar reactions [13], Knoevenagel condensation [14, 15], Ugi reaction [16] and …, new heterocycles with active biological properties have been synthesized. Many of those heterocyclic compounds are known as antibacterial [17, 18], anti-inflammatory [19, 20], anticancer [21], antimalarial [22], antifungal [23], antitumor [24] and anti-parasitic activity [25]. Recently, several reviews of multicomponent reactions of these aldehydes have been reported [26, 27].

Considering the advantages mentioned, quinolines are one of the important classes of heterocycles and have been used as templates for the synthesis of many drugs prescribed for a lot of pathologies; especially those with a pyranoquinoline ring system are of considerable interest. This nucleus is also frequently recognized in the structure of numerous naturally occurring alkaloids [28] such as flindersine, oricine, and vesprisine, simulenoline, huajiaosimuline [29–34] and synthetic compounds with interesting biological and pharmacological properties. These derivatives are important class of quinolones in which

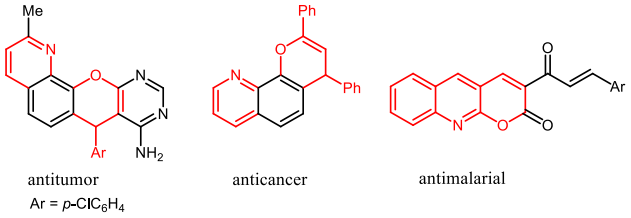



**Fig. 1** Examples of bioactive pyranoquinolines

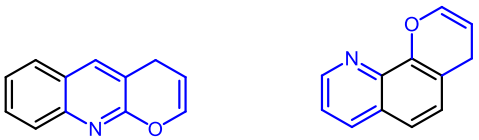


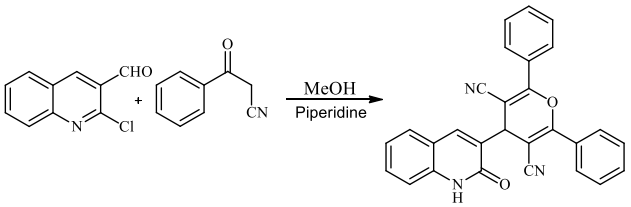

**Fig. 2** Pyranoquinoline derivatives

pyran ring is fused of quinolone ring. They have wide applications, for example, as drugs, pharmaceuticals, and agrochemicals, and possess a significant range of biological activities, such as antileishmanial [35], antimalarial [36], antitumor [37], antioxidant [38], anti-inflammatory, and anticancer [39] and antiallergic, psychotropic, and estrogenic [40–42] activities. Additionally, promising biological activities of structurally diverse pyranoquinolines (Fig. 1) were described in a number of recent articles [43–45].

Recently, considerable efforts have been accomplished to the preparation and synthetic of novel heterocyclic compounds including pyranoquinolines of one-pot reactions 2-chloroquinoline-3-carbaldehydes with the methylene active compounds, for example, synthesis 2-amino-3-cyano-4-*H*-chromenes [46], 2-amino-4*H*-benzo[*b*]pyran [47], and, synthesis 4*H*-pyrans and pyrano tacrines, of one-pot reactions 2-chloroquinoline-3-carbaldehydes with (malononitrile, ethyl acetoacetate, and dimedone) [48]. Among the pyranoquinolines, pyrano[2,3-*b*]quinoline systems are of interest because they are linear benzaza analogs of coumarins, in which the pyran ring is fused to the **b** bond of the quinolone ring (Fig. 2).

So far, only a few methods have been reported for the construction of pyrano[2,3-*b*]quinolines, for example, 1,4-dihydropyrazolo-pyrano-[2,3-*b*]quinolines [49], copper-catalyzed cycloaddition reactions of 2-chloroquinoline-3-carboxaldehydes with phenylacetylene gave pyrano[4,3-*b*]quinolines [50]. Recently, Zhang and coworkers reported the synthesis of pyrano[2,3-*b*]quinolines from cyclopentanecarboxamides mediated by concentrated $H_2SO_4$ [51] and Bhuyan et al. have reported a one-pot synthesis of tetracyclic pyrano[2,3-*b*]quinolines via intramolecular 1,3-dipolar

cycloaddition reactions using 1,3-dipoles such as nitrones, nitrile oxides and nitrile imines [52]. Also, domino cyclization reaction for the synthesis of 2,2a,10,11 tetrahydrofuro[20,40:4,6]pyrano[2,3-*b*]quinolines and intramolecular electrophilic cyclization of 3-homoallyl-2-quinolones with iodine and sodium bicarbonate by B. Singh et al. has been reported [53, 54]. Recently, Farid Abdel-Rehem Badria, and co-workers reported the one-pot reaction of 2-chloroquinoline-3-carbaldehyde with benzoylacetonitrile in metal-free conditions (Scheme 1) [55].

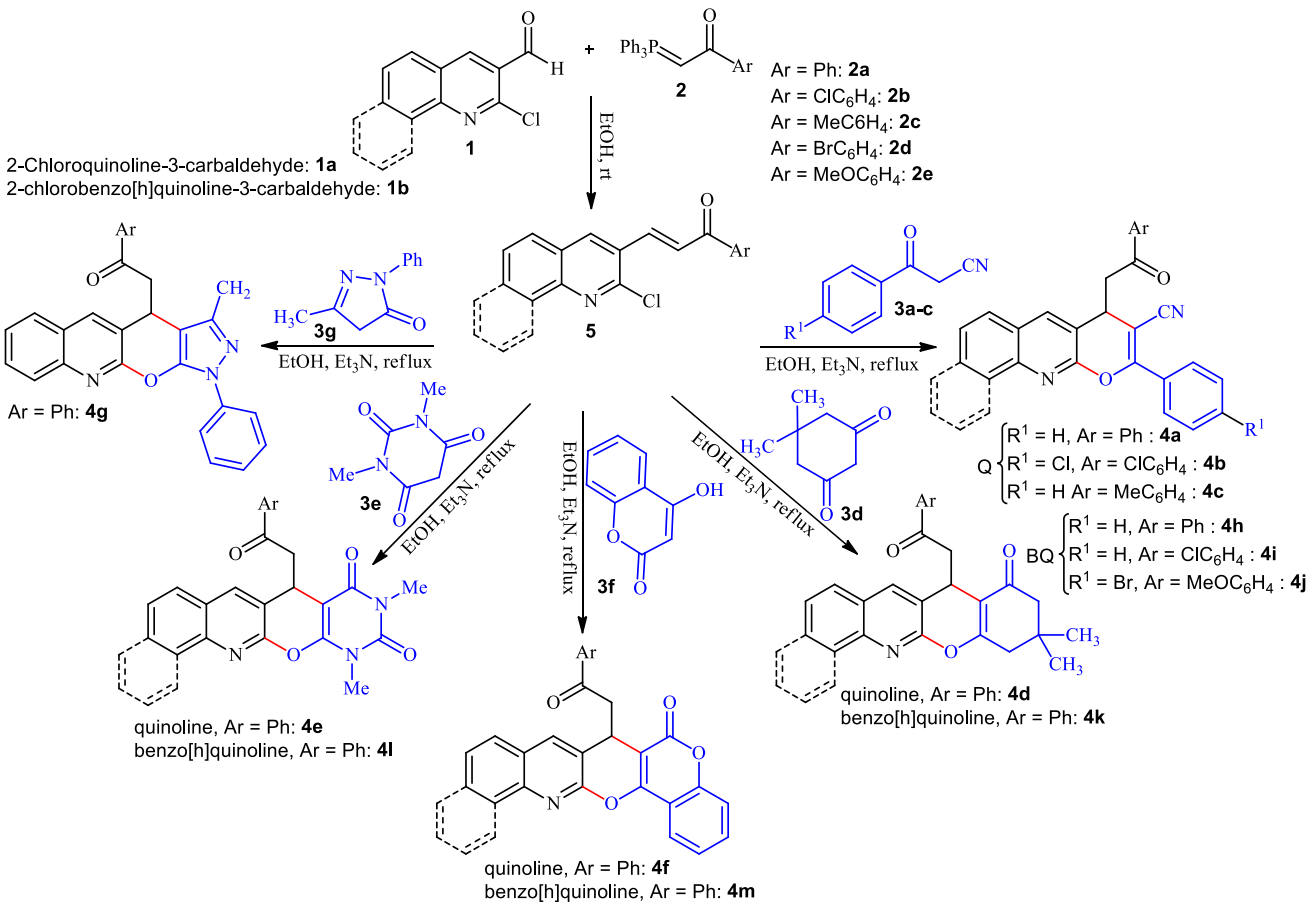



**Scheme 1** Reaction of 2-chloroquinoline-3-carbaldehyde with benzoylacetonitrile in metal-free conditions

Hereine, we report an efficient synthesis of functionalized pyrano[2,3-*b*]quinoline and benzo[*h*]pyrano[2,3-*b*]quinoline derivatives by using 2-chloroquinoline-3-carbaldehyde **1a**, 2-chlorobenzo[*h*]quinoline-3-carbaldehyde **1b**, 1-aryl-2-(1,1,1-triphenyl-$\lambda^5$-phosphanylidene)ethan-1-one (Wittig reagent) **2** and the active methylene compounds **3** under mild conditions in good to excellent yields (Scheme 2).

## Experimental section

Melting points measured on an Electrothermal 9100 apparatus. IR spectra were recorded as KBr pellets on a NICOLET FT-IR 100 spectrometer. $^1$H NMR (500 and 300 MHz) and $^{13}$C NMR (125 and 75 MHz) spectra were obtained using Bruker DRX-500 AVANCE and Bruker DRX-300 AVANCE spectrometers. NMR spectra at room temperature were recorded in DMSO-$d_6$. Chemical shifts are reported in parts per million ($\delta$) downfield from an internal tetramethylsilane reference. Coupling constants ($J$ values) are reported in Hertz (Hz), and spin multiplicities are indicated by the following symbols: bs (broad singlet), s (singlet), d (doublet),




**Scheme 2** Synthesis of pyrano[2,3-*b*]quinoline and benzo[*h*]pyrano[2,3-*b*]quinoline derivatives by a three-component reaction

t (triplet), m (multiplet). Elemental analyses for C, H, and N performed using a Heraeus CHN–O–Rapid analyzer. All the products recrystallized from $CH_3CN$ for CHN analysis. Mass spectra were recorded on a FINNIGAN-MATT 8430 mass spectrometer operating at an ionization potential of 20 or 70 eV. All the reagents and solvents purchased from Merck or Aldrich without any purification.

### General procedure for the one-pot synthesis of pyrano[2,3-*b*]quinoline and benzo[*h*]pyrano[2,3-*b*]quinolines derivatives (4a-m)

A mixture of quinolines (2-chloro quinoline-3-carbaldehyde or 2-chloro benzo[*h*]quinoline-3-carbaldehyde) **1** (0.5 mmol) and 1-aryl-2-(1,1,1-triphenyl-$\lambda^5$-phosphanylidene)ethan-1-one **2** (0.5 mmol) in **5** mL EtOH stirred for 30 min; then active methylene compounds **3** (0.5 mmol) and triethylamine (100 mmol%) were added and further stirred for 2–3 h at reflux temperature. After the completion of the reaction (monitored by TLC), the resulting precipitate was filtered and washed with EtOH, and recrystallized from EtOH to afford the pure product as solid in good yields (**4a-m**).

### 4-(2-Oxo-2-phenylethyl)-2-phenyl-4*H*-pyrano[2,3-*b*]quinoline-3-carbonitrile (4a)

White powder, m.p = 233–234 °C (dec.), 0.38 g, yield: 95%. IR (KBr)($\nu_{max}$, $cm^{-1}$): 2205 (CN), 1680 (C=O), 1629, 1577, 1499 (Ar), 1256, 1207, (C-O). $^1$H NMR (500.13 MHz, DMSO-$d_6$): 3.95 (2H, ABqd, $^2J_{HH}$ = 18.4 Hz, $^3J_{HH}$ = 4.5 Hz, $CH_2$), 4.69 (1H, t, $^3J_{HH}$ = 4.5 Hz, $CH^4$), 7.51 (2H, t, $^3J_{HH}$ = 7.6 Hz, $2CH_{meta}$ of Ph), 7.55 (1H, t, $^3J_{HH}$ = 7.5 Hz, $CH_{para}$ of Ph), 7.60 (1H, t, $^3J_{HH}$ = 7.5 Hz, $CH^7$ of quinoline), 7.62 (2H, $^3J_{HH}$ = 9.5 Hz, t, $2CH_{meta}$ of PhCO), 7.64 (1H, t, $^3J_{HH}$ = 7.4 Hz, $CH_{para}$ of PhCO), 7.75 (1H, t, $^3J_{HH}$ = 7.5 Hz, $CH^8$ of quinoline), 7.86 (2H, d, $^3J_{HH}$ = 6.4 Hz, $2CH_{ortho}$ of Ph), 7.90 (1H, d, $^3J_{HH}$ = 8.3 Hz, $CH^9$ of quinoline), 7.92 (1H, d, $^3J_{HH}$ = 7.9 Hz, $CH^6$ of quinoline), 7.98 (2H, d, $^3J_{HH}$ = 7.4 Hz, $2CH_{ortho}$ of PhCO), 8.48 (1H, s, $CH^5$ of quinoline). $^{13}$C NMR (125.75 MHz, DMSO-$d_6$): 33.21 ($CH^4$), 45.08 ($CH_2$), 88.50 ($C^3$), 118.65 (CN), 118.84 ($C^{4a}$), 126.45 ($CH^7$ of quinoline), 127.67 ($C^{5a}$ of quinoline), 127.79 ($CH^6$ of quinoline), 128.06 ($CH^8$ of quinoline), 128.42 ($2CH_{meta}$ of PhCO), 128.53 ($2CH_{meta}$ of Ph), 129.19 ($2CH_{ortho}$ of Ph), 129.21 ($2CH_{ortho}$ of PhCO), 130.86 ($CH^9$ of quinoline), 131.75 ($C_{ipso}$ of Ph), 131.96 ($CH_{para}$ of Ph), 134.05 ($CH_{para}$ of PhCO), 136.67 ($C_{ipso}$ of PhCO), 138.21 ($CH^5$ of quinoline), 145.43 ($C^{9a}$ of quinoline), 155.07 ($C^{10a}$ of quinoline), 161.71 ($C^2$), 197.54 (C=O). MS (EI, 70 eV) *m/z* (%): 403 ($M^+$ + 1, 12), 402 ($M^+$, 33), 297 (21), 285 (8), 284 (61), 283 (100), 255 (8), 254 (11), 253 (12), 228 (6), 227 (9), 217 (23), 216 (64), 106 (7) 105 (60), 77 (21). Anal. calcd. for $C_{27}H_{18}N_2O_2$ (402.44): C, 80.58; H, 4.51; N, 6.96. Found: C, 80.54; H, 4.53; N, 6.98%.

### 2-(4-Chlorophenyl)-4-[2-(4-chlorophenyl)-2-oxoethyl]-4*H*-pyrano[2,3-*b*]quinoline-3-carbonitrile (4b)

White powder, m.p = 224–225 °C (dec), 0.42 g, yield: 90%. IR (KBr) ($\nu_{max}$, $cm^{-1}$): 2206 (CN), 1680 (C=O), 1632, 1587, 1490 (Ar), 1255, 1212 (C-O) .$^1$H NMR (500.13 MHz, DMSO-$d_6$): 3.92 (2H, ABqd, $^2J_{HH}$ = 14.6 Hz, $CH_2$), 4.66 (1H, bs, $CH^4$), 7.55 (3H, $^3J_{HH}$ = 7.2 Hz, 2CH of Ar and $CH^7$ of quinoline). 7.67 (2H, d, $^3J_{HH}$ = 7.3 Hz, 2CH of Ar), 7.73 (1H, t, $^3J_{HH}$ = 6.5 Hz, $CH^8$ of quinoline), 7.88 (2H, d, $^3J_{HH}$ = 6.5 Hz, 2CH of Ar), 7.85–7.88 (2H, m, $CH^6$ and $CH^9$ of quinoline), 7.97 (2H, d, $^3J_{HH}$ = 7.3 Hz, 2CH of Ar), 8.45 (1H, s, $CH^5$ of quinoline). $^{13}$C NMR (125.75 MHz, DMSO-$d_6$): 32.68 ($CH^4$), 44.70 ($CH_2$), 88.52 ($C^3$), 117.89 (CN), 118.13 ($C^{4a}$), 126.03 ($CH^7$ of quinoline), 127.20 ($C^{5a}$ of quinoline), 127.31 ($CH^6$ of quinoline), 127.59 ($CH^8$ of quinoline), 128.78 ($2CH_{meta}$ of Ar), 128.92 ($2CH_{meta}$ of Ar), 129.81 ($2CH_{ortho}$ of Ar), 129.97 ($2CH_{ortho}$ of Ar), 130.02 ($C_{ipso}$ –$C^2$), 130.44 ($CH^9$ of quinoline), 134.85 ($C_{ipso}$-CO), 136.18 ($C_{ipso}$-Cl), 137.85 ($CH^5$ of quinoline), 138.50 ($C_{ipso}$-Cl), 144.92 ($C^{9a}$ of quinoline), 154.45 ($C^{10a}$ of quinoline), 160.12 ($C^2$), 196.12 (C=O). MS (EI, 70 eV) *m/z* (%): 472 ($M^+$ + 2, 4), 471 ($M^+$ + 1, 2), 470 ($M^+$, 5), 331 (5), 320 (8), 319 (39), 318 (25), 317 (100), 267 (3), 254 (6), 253 (11), 252 (10), 251 (6), 250 (21), 216 (4), 140 (9), 139 (28), 111 (9). Anal. calcd. for $C_{27}H_{16}Cl_2N_2O_2$ (471.33): C, 68.80; H, 3.42; N, 5.94. Found: C, 68.76; H, 3.44; N, 5.96%.

### 4-[2-(4-Methylphenyl)-2-oxoethyl]-2-phenyl-4*H*-pyrano[2,3-*b*]quinoline-3-carbonitrile (4c)

White powder, m.p = 205–207 °C (dec.), 0.39 g, yield: 93%. IR (KBr)($\nu_{max}$, $cm^{-1}$): 2205 (CN), 1678 (C=O), 1632, 1602, 15,574, 1498 (Ar), 1249, 1205 (C-O). $^1$H NMR (500.13 MHz, DMSO-$d_6$): 2.10 (3H, S, Me), 3.89 ( 2H, $AB_q$d, $^2J_{HH}$ = 18.3 Hz, $^3J_{HH}$ = 4.3 Hz, $CH_2$), 4.67 (1H, bs, $CH^4$), 7.30 (2H, d, $^3J_{HH}$ = 7.7 Hz, 2CH of Ar), 7.54 (1H, t, $^3J_{HH}$ = 7.2 Hz, $CH_{para}$ of Ph), 7.60 (2H, d, $^3J_{HH}$ = 7.3 Hz, $2CH_{meta}$ of Ph and $CH^7$ of quinoline), 7.74 (1H, t, $^3J_{HH}$ = 7.5 Hz, $CH^8$ of quinoline), 7.86 (2H, d, $^3J_{HH}$ = 7.1 Hz, $2CH_{ortho}$ of Ph), 7.88 (2H, d, $^3J_{HH}$ = 7.7 Hz, 2CH of Ar), 7.89 (1H, d, $^3J_{HH}$ = 8.3 Hz, $CH^9$ of quinoline), 7.91(1H, d, $^3J_{HH}$ = 8.0 Hz, $CH^6$ of quinoline), 8.46 (1H, s, $CH^5$ of quinoline). $^{13}$C NMR (125.75 MHz, DMSO-$d_6$): 21.60 (Me), 33.29 ($CH^4$), 44.97 ($CH_2$), 88.52 ($C^3$), 118.65 (CN), 118.87 ($C^{4a}$), 126.44 ($CH^7$ of quinoline), 127.67 ($C^{5a}$ of quinoline), 127.79 ($CH^6$ of quinoline), 128.05 ($CH^8$ of quinoline), 128.40 ($2CH_{meta}$ of Ph), 128.64 ($2CH_{meta}$ of Ar), 129.20 ($2CH_{ortho}$ of Ph), 129.70 ($2CH_{ortho}$ of Ar), 130.84 ($CH^9$ of quinoline), 131.74 ($C_{ipso}$ of Ph), 131.95 ($CH_{para}$ of

Ph), 134.28 ($C_{ipso}$-CO), 138.17 ($CH^5$ of quinoline), 144.50 ($C_{ipso}$-Me), 145.42 ($C^{9a}$ of quinoline), 155.06 ($C^{10a}$ of quinoline), 161.67 ($C^2$), 197.02 (C=O). MS (EI, 70 eV) *m/z* (%): 417 ($M^+ + 1$, 6), 416 ($M^+$, 10), 297 (8), 284 (43), 283 (100), 255 (4), 254 (5), 253 (5), 230 (3), 217 (12), 216 (39), 120 (8), 119 (70), 105 (6), 91 (15), 77 (3). Anal. calcd. for $C_{28}H_{20}N_2O_2$ (416.47): C, 80.75; H, 4.84; N, 6.73. Found: C, 80.71; H, 4.86; N, 6.75%.

### 3-Dimethyl-12-(2-oxo-2-phenylethyl)-2,3,4,12-tetrahydro-1*H*-chromeno[2,3-*b*]quinolin-1-one (4d)

White powder, m.p = 186–187 °C (dec.), 0.39 g, yield: 98%. IR (KBr) ($\nu_{max}$, $cm^{-1}$): 1680 (C=O), 1638, 1499 (Ar), 1240, 1221 (C-O). $^1$H NMR (500.13 MHz, DMSO-$d_6$): 0.99 (3H, s, Me) and 1.06 (3H, s, Me), 2.25 (2H, ABq, $^3J_{HH} = 16.0$ Hz, $CH_2^2$), 3.82 (2H, ABq, $^3J_{HH} = 17.7$ Hz, $CH_2^4$), 3.62 (2H, ABqd, $^2J_{HH} = 17.2$ Hz, $^3J_{HH} = 5.6$ Hz, $CH_2^1$), 4.49 (1H, bs, $CH^{12}$), 7.42 (1H, t, $^3J_{HH} = 7.2$ Hz, 2$CH_{meta}$ of PhCO), 7.47 (1H, t, $^3J_{HH} = 7.3$ Hz, $CH_{para}$ of PhCO), 7.55 (1H, t, $^3J_{HH} = 7.2$ Hz, $CH^8$ of quinoline), 7.67 (1H, t, $^3J_{HH} = 7.2$ Hz, $CH^9$ of quinoline), 7.79 (1H, d, $^3J_{HH} = 8.3$ Hz, $CH^7$ of quinoline), 7.83 (2H, d, $^3J_{HH} = 7.9$ Hz, $CH^{10}$ of quinoline), 7.83 (2H, d, $^3J_{HH} = 7.2$ Hz, 2$CH_{ortho}$ of PhCO), 8.33(1H, s, $CH^{11}$ of quinoline). $^{13}$C NMR (125.75 MHz, DMSO-$d_6$): 26.95 ($CH^{12}$), 29.06 (Me), 29.21 (Me), 32.27 ($C^3$), 40.98 ($CH_2^4$), 45.36 ($CH_2^1$), 50.58 ($CH_2^2$), 111.83 ($C^{12a}$), 121.57 ($C^{11a}$), 126.11 ($CH^9$ of quinoline), 127.45 ($C^{10a}$), 127.67 ($CH^{10}$ of quinoline), 127.88 ($CH^8$ of quinoline), 128.66 (2CH of PhCO), 129.10 (2CH of PhCO), 130.46 ($CH^7$ of quinoline), 133.72 ($CH_{para}$ of PhCO), 136.91 ($C_{ipso}$-C=O), 138.48 ($CH^{10}$ of quinoline), 145.17 ($C^{6a}$ of quinoline), 155.64 ($C^{5a}$ of quinoline), 166.53 ($C^{4a}$), 196.95 (C=O), 198.54 (C=O). MS (EI, 70 eV) *m/z* (%): 397 ($M^+$, 35), 314 (3), 313 (23), 293 (8), 292 (59), 279 (22), 278 (100), 259 (7), 258 (32), 237 (4), 236 (23), 223 (9), 222 (54), 194 (7), 180 (12), 167 (9), 166 (43), 153 (7), 152 (34), 151 (5), 140 (12), 139 (8), 125 (6), 106 (6), 105 (59), 91 (10), 77 (41), 57 (21), 56(10), 55(19). Anal. calcd. for $C_{26}H_{23}NO_3$ (397.47): C, 78.57; H, 5.83; N, 3.52. Found: C, 78.52; H, 5.86; N, 3.54%.

### 1,3-Dimethyl-5-(2-oxo-2-phenylethyl)-1,5-dihydro-2*H*-pyrimido[5',4':5,6]pyrano[2,3-*b*]quinoline-2,4(3*H*)-dione (4e)

White powder, m.p = 256–257 °C (dec.), 0.38 g, yield: 92%. IR (KBr)($\nu_{max}$, $cm^{-1}$): 1707. 1668 (C=O), 1635, 1576, 1495 (Ar), 1243, 1218, 1184 (C-O). $^1$H NMR (300.13 MHz, DMSO-$d_6$): 3.15 (3H, s, Me), 3.43 (3H, s, Me), 3.75 (2H, ABqd, $^2J_{HH} = 17.3$ Hz, $CH_2$), 4.53 (1H, bs, $CH^5$), 7.41 (2H, d, $^3J_{HH} = 7.2$ Hz, 2$CH_{meta}$ of PhCO), 7.51 (2H, m, $CH_{para}$ Of PhCO and $CH^8$ of quinoline), 7.69 (1H, t, $^3J_{HH} = 7.3$ Hz, $CH^9$ of quinoline), 7.79 (1H, d, $^3J_{HH} = 8.5$ Hz, $CH^{10}$ of quinoline), 7.80 (2H, d, $^3J_{HH} = 7.8$ Hz, 2 $CH_{ortho}$ of PhCO), 7.83 (1H, d, $^3J_{HH} = 7.9$ Hz, $CH^7$ of quinoline), 8.41 (1H, s, $CH^6$ of quinoline). $^{13}$C NMR (75.46 MHz, DMSO-$d_6$): 27.66 ($CH^{12}$), 28.96 (Me), 29.11 (Me), 44.19 ($CH_2$), 87.38 ($C^{4a}$), 120.03 ($C^{5a}$), 126.12 ($CH^8$ of quinoline), 127.16 ($CH^7$ and $C^{6a}$ of quinoline), 127.44 ($CH^9$ of quinoline), 127.74 (2CH of PhCO), 128.56 (2CH of PhCO), 130.27 ($CH^{10}$ of quinoline), 133.29 ($CH_{para}$ of PhCO), 136.27 ($C_{ipso}$ C=O), 138.17 ($CH^6$ of quinoline), 144.38 ($C^{10a}$ of quinoline), 149.93 ($C^{11a}$), 153.09 and 154.09 ($C{=}O_{amide}$), 161.05 ($C^{12a}$), 198.09 (C=O). MS (EI, 70 eV) *m/z* (%): 414 ($M^+ + 1$, 4), 413 ($M^+$, 10), 309 (5), 308 (25), 295 (25), 294 (100), 251 (11), 238 (5), 237 (29), 209 (2), 194 (4), 166 (8), 152 (11), 140 (3), 128 (1), 105 (6), 77 (4). Anal. calcd. for $C_{24}H_{19}NO_3$ (413.43): C, 69.72; H, 4.63; N, 10.16. Found: C, 69.77; H, 4.60; N, 10.14%.

### 7-(2-Oxo-2-phenylethyl)-6*H*,7*H*-chromeno[3',4':5,6]pyrano[2,3-*b*]quinolin-6-one (4f)

White powder, m.p = 255–256 °C (dec.), 0.33 g, yield: 80%. IR (KBr) ($\nu_{max}$, $cm^{-1}$): 1717 (C=O of ester), 1674 (C=O), 1649, 1627, 1609, 1579 (Ar), 1245, 1206, 1041 (C-O). $^1$H NMR (300.13 MHz, DMSO-$d_6$): 3.90 (2H, ABqd, $^2J_{HH} = 14.3$ Hz, $CH_2$), 4.64 (1H, bs, $CH^7$), 7.38–7.52 (6H, m, $CH^2$, $CH^4$, $CH^{10}$ of quinoline, 2$CH_{meta}$ of Ph and $CH_{para}$ Of Ph), 7.67 (1H, t, $^3J_{HH} = 6.6$ Hz, $CH^{11}$ of quinoline), 7.67 (1H, t, $^3J_{HH} = 6.6$ Hz, $CH^3$), 7.82 (1H, d, $^3J_{HH} = 7.3$ Hz, $CH^{12}$ of quinoline), 7.82 (2H, d, $^3J_{HH} = 7.3$ Hz, 2$CH_{meta}$ of Ph), 8.01 (1H, d, $^3J_{HH} = 7.0$ Hz, $CH^1$), 8.41 (1H, s, $CH^8$ of quinoline). $^{13}$C NMR (75.46 MHz, DMSO-$d_6$): 29.81 ($CH^7$), 44.00 ($CH_2^1$), 102.83 ($C^{6a}$), 113.60 ($C^{14b}$), 116.47 ($CH^4$), 119.93 ($C^{7a}$), 122.38 ($CH^2$), 124.68 ($CH^1$), 125.95 ($CH^{10}$ of quinoline), 127.15 ($C^{8a}$ of quinoline), 127.21 ($CH^9$ of quinoline), 127.45 ($CH^{11}$ of quinoline), 127.80 (2CH of Ph), 128.56 (2CH of Ph), 130.22 ($CH^{12}$ of quinoline), 132.61 ($CH^3$), 133.35 ($CH_{para}$ of Ph),136.09 ($C_{ipso}$-CO), 138.17 ($CH^8$ of quinoline), 144.67 ($C^{12a}$), 152.05 ($C^{13a}$), 154.13 ($C^{4a}$), 156.24 (COO), 160.45 ($C^{14a}$), 197.71 (C=O). MS (EI, 70 eV) *m/z* (%): 420 ($M^+ + 1$, 6), 419 ($M^+$, 19), 316 (2), 315 (11). 314 (48), 301 (25), 300 (100), 272 (5), 216 (4), 215 (4), 189 (3), 152 (3), 121 (2), 105 (13), 77 (10), 28 (4). Anal. calcd. for $C_{27}H_{17}NO_4$ (419.43): C, 77.32; H, 4.09; N, 3.34. Found: C, 77.38; H, 4.05; N, 3.32%.

### 2-(3-Methyl-1-phenyl-1,4-dihydropyrazolo[4',3':5,6]pyrano[2,3-*b*]quinolin-4-yl)-1-phenylethanone (4g)

White powder, m.p = 188–189 °C (dec.), 0.41 g, yield: 95%. IR (KBr) ($\nu_{max}$, $cm^{-1}$): 1685 (C=O), 1627, 1597, 1516, 1494 (Ar), 1238, 1209, 1150 (C-O). $^1$H NMR (300.13 MHz, DMSO-$d_6$): 2.22 (3H, s, Me), 3.80—3.84 (2H, m, $CH_2$), 4.81 (1H, bs, $CH^4$), 7.33 (1H, t, $^3J_{HH} = 6.7$ Hz, 2$CH_{meta}$ of Ph),

7.42 (2H, t, $^3J_{HH}$ = 7.4 Hz, $CH_{meta}$ of PhCO), 7.47 (1H, t, $^3J_{HH}$ = 7.7 Hz, $CH_{para}$ of PhCO), 7.55 (1H, t, $^3J_{HH}$ = 6.9 Hz), 7.55 (2H, t, $^3J_{HH}$ = 6.9 Hz, $2CH_{meta}$ of Ph), 7.68 (1H, t, $^3J_{HH}$ = 6.8 Hz, $CH^8$ of quinoline), 7.82 (2H, d, $^3J_{HH}$ = 8.3 Hz, $CH^9$ and $CH^6$ of quinoline), 7.86 (4H, m, 2 $CH_{ortho}$ of PhCO and $2CH_{ortho}$ Of Ph). 8.47 (1H, s, $CH^5$ of quinoline). $^{13}$C NMR (75.46 MHz, DMSO-$d_6$): 13.00 (Me), 29.13 ($CH^4$), 45.98 ($CH_2$), 97.87 ($C^{3a}$), 120.15 (2CH of Ph), 121.09 ($C^{4a}$), 125.74 ($C^{5a}$ of quinoline), 126.10 ($CH_{para}$ Of Ph), 126.70 ($CH^7$ Of quinoline), 127.03 ($CH^6$ of quinoline), 127.43 ($CH^8$ of quinoline), 127.95 (2CH of Ph), 128.62 (2CH of PhCO), 129.41 (2CH of PhCO), 130.19 ($CH^9$ of quinoline), 133.33 ($CH_{para}$ of PhCO), 136.33 ($C_{ipso}$-C=O), 137.74 ($CH^5$ of quinoline), 139.03 ($C_{ipso}$ Ph), 144.47 ($C^{9a}$ of quinoline), 145.20 ($C^3$), 146.36 ($^{10a}$), 155.49 ($C^{11a}$), 197.65 (C=O). MS (EI, 70 eV) *m/z* (%): 433 ($M^+$ + 2, 12), 432 ($M^+$ + 1, 34), 431 ($M^+$, 1) 327 (12), 315 (25), 314 (100), 313 (100), 312 (100), 278 (100), 298 (7), 297 (3), 273 (6), 272 (26), 271 (8), 270 (7), 269 (10), 256 (5), 255 (3), 244 (14), 243 (16), 242 (6), 217 (11), 216 (3), 196 (6), 195 (6), 193 (7), 192 (6), 191 (4), 190 (3), 168 (10), 167 (8), 166 (6), 164 (12), 141 (27), 140 (8), 118 (2), 119 (9), 106 (33), 105 (3). 92 (17), 91 (4), 79 (10), 78 (95), 77 (4), 66 (8), 52 (27). Anal. calcd. for $C_{28}H_{21}N_3O_2$ (431.49): C, 77.94; H, 4.91; N, 9.74. Found: C, 77.91; H, 4.92; N, 9.76%.

### 8-(2-Oxo-2-phenylethyl)-10-phenyl-8*H*-benzo[*h*]pyrano[2,3-*b*]quinoline-9-carbonitrile (4h)

White powder, 0.39 g, yield: 86%. IR (KBr) ($\nu_{max}$, $cm^{-1}$): 2204 (CN), 1679 (C=O), 1642, 1619, 1598 (Ar), 1267, 1217, (C-O). $^1$H NMR (500.13 MHz, DMSO-$d_6$): 3.94 (2H, ABqd, $^2J_{HH}$ = 16.7 Hz, $CH_2$), 4.71 (1H, bs, $CH^8$), 7.49 (2H, t, $^3J_{HH}$ = 7.6 Hz, $2CH_{meta}$ of Ph), 7.60–7.63 (4H, m, $CH_{para}$ of Ph, $CH_{para}$ of PhCO and $2CH_{meta}$ of PhCO), 7.73–7.75 ( 2H, m, $CH^2$ and $CH^3$ of quinoline), 7.79 ( 1H, d, $^3J_{HH}$ = 8.2 Hz, $CH^5$ of quinoline), 7.86–7.89 (3H, m, $CH^6$ of quinoline and $2CH_{ortho}$ of Ph), 7.98 (2H, d, $^3J_{HH}$ = 7.4 Hz, $2CH_{ortho}$ of PhCO), 8.01( 1H, d, $^3J_{HH}$ = 8.0 Hz, $CH^4$ of quinoline), 8.50 (1H, s, $CH^7$ of quinoline), 8.97 (1H, bs, $CH^1$ of quinoline). $^{13}$C NMR (125.75 MHz, DMSO-$d_6$): 32.70 ($CH^8$), 44.63 ($CH^2$), 88.07 ($C^9$), 117.85 (CN), 118.15 ($C^{7a}$), 123.77 ($CH^1$ of quinoline), 124.77 ($CH^6$ of quinoline), 125.09 ($C^{6a}$), 126.74 ($CH^2$ of quinoline), 127.11 ($CH^3$ of quinoline), 128.01 ($2CH_{meta}$ of PhCO), 128.05 ($CH^3$ of quinoline and $2CH_{meta}$ of Ph), 128.56 ($CH^4$ of quinoline), 128.70 ($2CH_{ortho}$ of Ph), 128.75 ($2CH_{ortho}$ of PhCO), 129.66 ($C^{12b}$), 131.36 ($C_{ipso}$ of Ph), 131.46 ($CH_{para}$ of Ph), 133.48 ($C^{4a}$), 133.54 ($CH_{para}$ of PhCO), 136.19 ($C_{ipso}$-CO), 137.92 ($CH^7$ of quinoline), 143.04 ($C^{12a}$ of quinoline), 154.36 ($C^{11a}$ of quinoline), 161.43 ($C^{10}$), 197.16 (C=O). MS (EI, 70 eV) *m/z* (%): 453 ($M^+$ + 1, 4), 452 ($M^+$, 10), 347 (5), 335 (5), 334 (36), 333 (100), 305 (3), 304 (6), 303 (5), 267 (4), 266 (17), 216 (6), 105 (15), 77 (3). Anal. calcd. for $C_{31}H_{20}N_2O_2$ (452.50): C, 82.28; H, 4.45; N, 6.19. Found: C, 82.24; H, 4.47; N, 6.21%.

### 8-[2-(4-Chlorophenyl)-2-oxoethyl]-10-phenyl-8*H*-benzo[*h*]pyrano[2,3-*b*]quinoline-9-carbonitrile (4i)

White powder, m.p. = 255–257 °C (dec.), 0.43 g, yield: 88%. IR (KBr) ($\nu_{max}$, $cm^{-1}$): 2207 (CN), 1683 (C=O), 1663, 1619, 1601, 1586 (Ar), 1263, 1220 (C-O). $^1$H NMR (500.13 MHz, DMSO-$d_6$): 3.93 (2H, ABqd, $^2J_{HH}$ = 18.2 Hz, $CH_2$), 4.71 (1H, bs, $CH^8$), 7.49 (2H, t, $^3J_{HH}$ = 7.6 Hz, $2CH_{meta}$ of Ph), 7.62 (1H, t, $^3J_{HH}$ = 7.5 Hz, $CH_{para}$ of Ph), 7.70 (2H, d, $^3J_{HH}$ = 7.15 Hz, 2CH of Ar), 7.74 (2H, t, $^3J_{HH}$ = 7.5 Hz, $CH^2$ and $CH^3$ of quinoline), 7.79 (1H, d, $^3J_{HH}$ = 8.2 Hz, $CH^5$ of quinoline), 7.89 (1H, d, $^3J_{HH}$ = 8.2 Hz, $CH^6$ of quinoline), 7.91 (2H, d, $^3J_{HH}$ = 7.5, $2CH_{ortho}$ of Ph), 7.97 (2H, d, $^3J_{HH}$ = 6.7 Hz, 2CH of Ar), 8.01 (1H, d, $^3J_{HH}$ = 8.3 Hz, $CH^4$ of quinoline), 8.50 (1H, s, $CH^7$ of quinoline), 8.98 (1H, bs, $CH^1$ of quinoline. $^{13}$C NMR (125.75 MHz, DMSO-$d_6$): 32.71 ($CH^8$), 44.66 ($CH_2$), 88.61 ($C^9$), 117.75 (CN), 117.93 ($C^{7a}$), 123.77 ($CH^1$ of quinoline), 124.76 ($CH^6$ of quinoline), 125.13 ($C^{6a}$ of quinoline), 126.79 ($CH^2$ of quinoline), 127.13 ($CH^3$ of quinoline), 128.05 ($CH^5$ of quinoline and 2CH of Ph), 128.57 ($CH^4$ of quinoline), 128.69 (2CH of Ph), 128.95 (2CH of Ar), 129.69 ($C_{ipso}$ of Ph), 129.89 (2CH of Ar), 130.13 ($C^{12b}$), 133.49 ($C^{4a}$ of quinoline), 133.54 ($CH_{para}$ of Ph), 136.15 ($C_{ips}$-CO), 136.25 ($C_{ipso}$-Cl), 137.95 ($CH^7$ of quinoline), 143 ($C^{12a}$ of quinoline), 154.24 ($C^{11a}$ of quinoline), 160.25 ($C^{10}$), 197.12 (C=O). MS (EI, 70 eV) *m/z* (%): 488 ($M^+$ + 2, 7), 487 ($M^+$ + 1, 26), 486 ($M^+$, 71), 379 (5), 377 (10), 345 (12), 344 (47), 343 (37), 342 (100), 314 (3), 279 (14), 278 (7), 203 (5), 202 (16), 201 (7), 175 (5), 141 (28), 140 (8), 139 (84), 111 (14). Anal. calcd. for $C_{31}H_{19}ClN_2O_2$ (486.95): C, 76.46; H, 3.93; N, 5.75. Found: C, 76.42; H, 3.95; N, 5.77%.

### 10-(4-Bromophenyl)-8-[2-(4-methoxyphenyl)-2-oxoethyl]-8*H*-benzo[*h*]pyrano[2,3-*b*]quinoline-9-carbonitrile (4j)

White powder, m.p. = 245–246 °C (dec.), 0.53 g, yield: 96%. IR (KBr) ($\nu_{max}$, $cm^{-1}$): 2211 (CN), 1671 (C=O), 1642, 1619, 1598 (Ar), 1267, 1218 (C-O).$^1$H NMR (300.13 MHz, DMSO-$d_6$): 3.78 (3H, s, OMe), 3.90 (2H, ABqd, $^2J_{HH}$ = 18.10 Hz, $CH_2$), 4.65 (1H, bs, $CH^8$), 6.98 (2H, d, $^3J_{HH}$ = 7.9 Hz, 2CH of Ar), 7.74 (2H, d, $^3J_{HH}$ = 7.5 Hz, $CH^2$ and $CH^3$ of quinoline), 7.78–7.88 (6H, m, 4CH of Ar and 2CH of $CH^4$ and $CH^5$ quinoline), 7.93 (2H, d, $^3J_{HH}$ = 7.9 Hz, 2CH of Ar), 7.99 (1H, d, $^3J_{HH}$ = 8.2 Hz, $CH^6$ of quinoline), 8.45 (1H, s, $CH^7$ of quinoline), 8.95 (1H, bs, $CH^1$ of quinoline). $^{13}$C NMR (75.46 MHz, DMSO-$d_6$): 32.78 ($CH^8$), 44.24 ($CH_2$), 55.52

(OMe), 88.65 ($C^9$), 113.87 (2CH of Ar), 117.86 (CN), 117.99 ($C^{7a}$), 123.76 ($CH^1$ of quinoline), 124.76 ($CH^6$ of quinoline), 125.00 ($C_{ipso}$-Br), 125.10 ($C^{6a}$ of quinoline), 126.76 ($CH^2$ of quinoline), 127.14 ($CH^3$ of quinoline), 128.05 ($CH^5$ of quinoline), 128.56 ($CH^4$ of quinoline), 129.21 ($C_{ipso}$–$C^{10}$), 129.66 ($C_{ipso}$-CO), 130.01 (2CH of Ar and $C^{12b}$), 130.43 (2CH of Ar), 131.87 ( 2CH of Ar), 131.89 (2CH of Ar), 133.45 ($C^{4a}$ of quinoline), 137.86 ($CH^7$ of quinoline), 142.92 ($C^{12a}$ of quinoline), 154.20 ($C^{11a}$ of quinoline), 160.22 ($C^{10}$), 163.39 ($C_{ipso}$-OMe), 195.36 (C=O). MS (EI, 70 eV) *m/z* (%): 562 ($M^+$, 2), 561 ($M^+$-1, 2),, 427 (2), 426 (3), 425 (3), 412 (30), 411 (7), 410 (30), 334 (4), 333 (16), 266 (15), 136 (10), 135 (100), 121 (7), 109 (8), 108 (8), 107 (4), 105 (4), 77 (8). Anal. calcd. for $C_{32}H_{21}BrN_2O_3$ (561.42): C, 68.46; H, 3.77; N, 4.99. Found: C, 69; H, 3.79; N, 4.93%.

### 11,11-Dimethyl-8-(2-oxo-2-phenylethyl)-8,10,11,12-tetrahydro-9*H*-benzo[*h*]chromeno[2,3-*b*]quinolin-9-one (4k)

White powder, m.p = 170–171 °C (dec.), 0.38 g, yield: 85%. IR (KBr) ($\nu_{max}$, $cm^{-1}$): 1681(C=O), 1642, 1596, 1597 (Ar), 1211, 1259 (C-O). $^1$H NMR (500.13 MHz, DMSO-$d_6$): 0.99 (3H, s, Me), 1.06 (3H, s, Me), 2.24 (2H, ABq, $^2J_{HH}$ = 15.9 Hz, $2CH_2$), 2.57 (2H, ABq, $^2J_{HH}$ = 17.5 Hz, $CH_2$), 3.61 (2H, ABqd, $^2J_{HH}$ = 17.5 Hz, $^3J_{HH}$ = 5.4 Hz, $CH_2$), 4.49 (1H, bs, $CH^8$), 7.41 (2H, t, $^3J_{HH}$ = 7.3 Hz, $2CH_{meta}$ of Ph), 7.53 (1H, t, $^3J_{HH}$ = 6.7 Hz, $CH_{para}$ of Ph), 7.67–7.72 (3H, m, $CH^2$, $CH^3$ and $CH^5$ of quinoline), 7.80 (1H, d, $^3J_{HH}$ = 8.2 Hz, $CH^6$ of quinoline), 7.82 (2H, $^3J_{HH}$ = 7.8 Hz, $2CH_{ortho}$ of Ph), 7.96 (1H, d, $^3J_{HH}$ = 8.3 Hz, $CH^4$ of quinoline), 8.34 (1H, s, $CH^7$ of quinoline), 8.93 (1H, d, $^3J_{HH}$ = 8.3 Hz, $CH^1$ of quinoline). $^{13}$C NMR (125.75 MHz, DMSO-$d_6$): 26.95 ($CH^8$), 29.05 (Me), 29.24 (Me), 32.25 ($C^{11}$), 40.98 ($CH_2$), 45.26 ($CH_2$), 50.58 ($CH_2$), 111.17 ($C^{8a}$), 121.08 ($C^{7a}$), 124.11 ($CH^1$ of quinoline), 125.18 ($CH^6$ of quinoline), 125.24 ($CH^{6a}$ of quinoline), 126.81 ($CH^2$ of quinoline), 127.43 ($CH^3$ of quinoline), 128.25 (2CH of Ph), 128.44 ($CH^5$ of quinoline), 128.77 ($CH^4$ of quinoline), 129.08 (2CH of Ph), 130.25 ($CH^{14b}$ of quinoline), 133.69 ($CH_{para}$ Of Ph), 133.81 ($CH^{4a}$ of quinoline), 136.95 ($C_{ipso}$-C=O), 138.68 ($CH^7$ of quinoline), 143.03 ($C^{14a}$ of quinoline), 155.34 ($C^{13a}$), 166.58 ($C^{12a}$), 196.97 (C=O), 198.60 (C=O). MS (EI, 70 eV) *m/z* (%): 449 ($M^+$ + 2, 3), 448 ($M^+$ + 1, 12), 447 ($M^+$,23), 364 (4), 363 (14), 343(10), 342 (23), 330 (4), 329 (29), 328 (100), 309 (9), 308 (36), 286 (11), 273 (6), 272 (30), 244 (11), 230 (7), 217 (6), 216 (30), 215 (8), 202 (9), 189 (3), 105 (19), 77 (10). Anal. calcd. for $C_{30}H_{25}NO_3$ (447.52): C, 80.51; H, 5.63; N, 3.13. Found: C, 80.53; H, 5.65; N, 3.07%.

### 10,12-Dimethyl-8-(2-oxo-2-phenylethyl)-8*H*-benzo[*h*]pyrimido[5',4':5,6]pyrano[2,3-*b*]quinoline-9,11(10*H*,12*H*)-dione (4l)

White powder, m.p = 260–262 °C (dec.), 0.32 g, yield: 70%. IR (KBr) ($\nu_{max}$, $cm^{-1}$): 1709, 1684, 1668 (C=O), 1645, 1597, 1579 (Ar), 1222, 1259 (C-O). $^1$H NMR (300.13 MHz, $CDCl_3$): 3.38 (3H, s, Me), 3.70 (3H, s, Me), 3.71 (2H, ABqd, $^2J_{HH}$ = 17.7 Hz, $^3J_{HH}$ = 5.9 Hz, $CH_2$), 4.76 (1H, bs, $CH^8$), 7.39 (2H, t, $^3J_{HH}$ = 7.3 Hz, $2CH_{meta}$ of PhCO), 7.51 (1H, t, $^3J_{HH}$ = 7.1 Hz, $CH_{para}$ Of Ph), 7.60 (1H, d, $^3J_{HH}$ = 8.7 Hz, $CH^5$ of quinoline), 7.65–7.75 (3H, m, $CH^2$, $CH^3$, $CH^6$ of quinoline), 7.86–7.89 (3H, m, $2CH_{ortho}$ of PhCO and $CH^4$ of quinoline), 8.14 (1H, s, $CH^7$ of quinoline), 9.13 (1H, d, $^3J_{HH}$ = 7.3 Hz $CH^1$ of quinoline).$^{13}$C NMR (75.46 MHz, $CDCl_3$): 28.13 ($CH^{12}$), 29.59 (Me), 29.65 (Me), 45.09 ($CH_2$), 88.30 ($C^{8a}$), 119.16 ($C^{7a}$), 124.31 ($CH^1$ of quinoline), 124.52 ($CH^6$ of quinoline), 125.57 ($C^{6a}$ of quinoline), 127.08 ($CH^2$ of quinoline), 127.47 ($CH^3$ of quinoline), 127.82 ($CH^5$ of quinoline), 127.99 (2CH of PhCO), 128.58 (2CH of PhCO and $CH^4$ of quinoline), 130.34 ($C^{14b}$ of quinoline), 133.34 ($CH_{para}$ of PhCO), 133.80 ($C^{4a}$ of quinoline), 136.49 ($C_{ipso}$ C=O), 138.07 ($CH^7$ of quinoline), 143.76 ($C^{14a}$ of quinoline), 150.66 ($C^{13a}$), 153.84 and 153.98 ($C=O_{amide}$), 161.95 ($C^{12a}$), 197.66 (C=O). MS (EI, 70 eV) *m/z* (%): 465 ($M^+$ + 2, 2), 464 ($M^+$ + 1, 4), 463 ($M^+$,12), 359 (4), 358 (15), 346 (5), 345 (33), 344 (100), 301 (6), 288 (6), 287 (30), 272 (6), 260 (3), 244 (7), 216 (6), 202 (2), 179 (1), 150 (2), 105 (5), 91 (2), 77 (3). Anal. calcd. for $C_{28}H_{21}N_3O_4$ (463.48): C, 72.56; H, 4.57; N, 9.07. Found: C, 72.50; H, 4.59; N, 9.11%.

### 7-(2-Oxo-2-phenylethyl)-6*H*,7*H*-benzo[*h*]chromeno[3',4':5,6]pyrano[2,3-*b*]quinolin-6-one (4m)

White powder, m.p = 281–282 °C (dec.), 0.30 g, yield: 65%. IR (KBr) ($\nu_{max}$, $cm^{-1}$): 1705 (COO), 1684 (C=O), 1646, 1608, 1578 (Ar), 1258, 1205, 1151 (C-O). $^1$H NMR (300.13 MHz, DMSO-$d_6$): 3.84 (2H, ABqd, $^2J_{HH}$ = 17.8 Hz, $^3J_{HH}$ = 6.7 Hz, $CH_2$), 4.92 (1H, ABq, $^3J_{HH}$ = 3.1 Hz, $CH^7$), 7.41 (1H, t, $^3J_{HH}$ = 7.4 Hz, $CH^2$), 7.42 (1H, t, $^3J_{HH}$ = 7.6 Hz, $CH^4$), 7.51 (2H, t, $^3J_{HH}$ = 8.7 Hz, $2CH_{meta}$ of Ph),7.54 (1H, t, $^3J_{HH}$ = 8.0 Hz, $CH_{para}$ of Ph),7.75 (2H, d, $^3J_{HH}$ = 6.8 Hz, $2CH_{ortho}$ of Ph), 7.76–7.88 (m, 5H), 8.00 (1H, d, $^3J_{HH}$ = 8.0 Hz, $CH^4$ of quinoline), 8.15 (1H, d, $^3J_{HH}$ = 7.6 Hz, $CH^1$), 8.51 (1H, s, $CH^8$ of quinoline), 9.03 (1H, d, $^3J_{HH}$ = 6.7 Hz, $CH^1$ of quinoline). $^{13}$C NMR (75.46 MHz, $CDCl_3$): 30.27 ($CH^7$), 45.10 ($CH_2{}^1$), 102.92 ($C^{6a}$), 114.23 ($C^{16b}$), 116.62 ($CH^4$), 118.86 ($C^{7a}$), 123.53 ($CH^2$), 124.42 ($CH^9$, and $CH^{14}$ of quinoline), 124.63 ($CH^1$), 125.49 ($C^{8a}$ of quinoline), 127.01 ($CH^{13}$ of quinoline), 127.25 ($CH^{12}$ of quinoline), 127.79 ($CH^{10}$ of quinoline), 128.02 (2CH of Ph), 128.50 ($CH^{11}$ of quinoline), 128.60 (2CH of Ph), 130.43

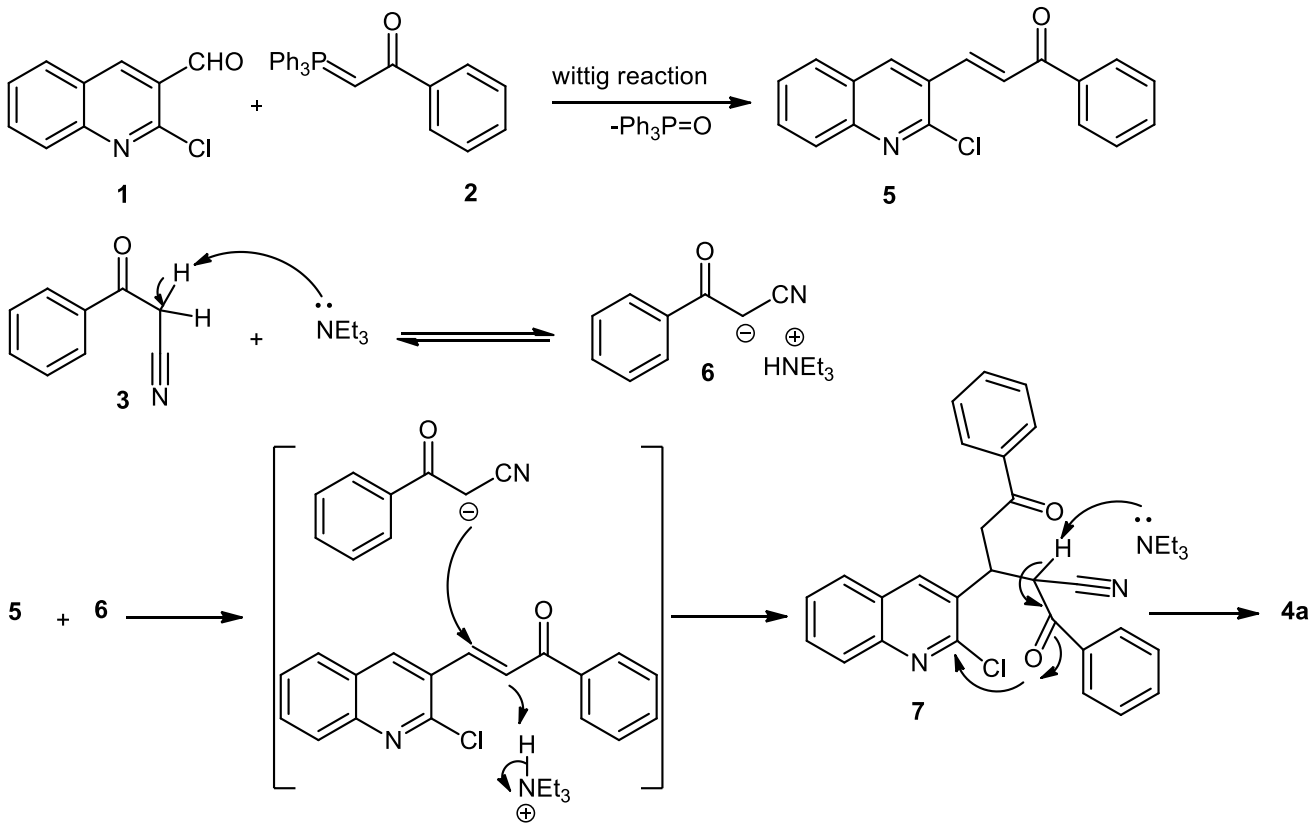
($C^{14a}$ of quinoline), 132.43 ($CH^{3}$), 133.35 ($CH_{para}$ of Ph), 133.84 ($C^{10a}$ of quinoline), 136.43 ($C_{ipso}$-CO), 138.38 ($CH^{8}$ of quinoline), 144.07 ($C^{14b}$), 152.78 ($C^{15a}$), 154.13 ($C^{4a}$), 157.87 (COO), 161.64 ($C^{16a}$), 197.15 (C=O). MS (EI, 70 eV) *m/z* (%): 470 ($M^+ + 1$, 4), 469 ($M^+$, 11), 365 (7), 364 (26), 352 (5), 351 (32), 350 (100), 322 (4), 265 (6), 182(6), 105 (7), 77 (3). Anal. calcd. for $C_{31}H_{19}NO_4$ (469.49): C, 79.31; H, 4.08; N, 2.98. Found: C, 79.34; H, 4.10; N, 2.93%.

## Results and Discussion

Initially, we started our investigations with the reaction of aldehyde **1** and Wittig reagent **2**, in ethanol solvent at room temperature. The reaction was monitored by TLC, within for 30 min starting materials were consumed completely and *α*,*β*-unsaturated compound **5** was formed.

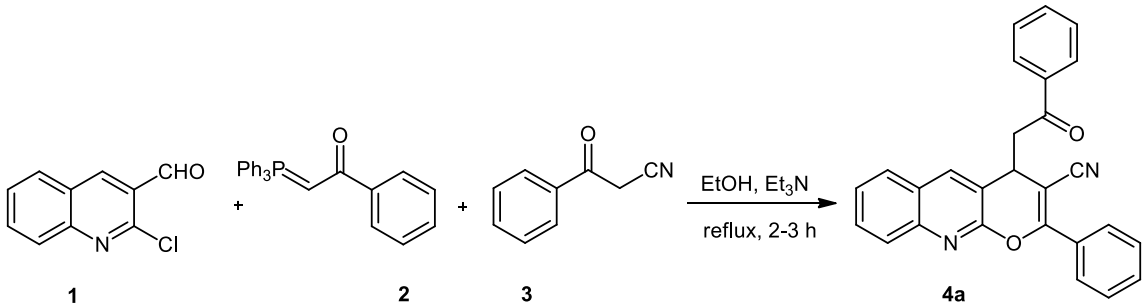
As seen in Scheme 3, there are three potential electrophilic sites in the structure of *α*,*β*-unsaturated compound **5** and according to literature [48] chlorine atom usually replaces by oxygen atom of active methylene compounds. In the next step, via a one-pot reaction, the reaction mixture was refluxed by adding active methylene compounds and $Et_3N$ as base. Gratifyingly during 2–3 h a white precipitates with high efficiency was observed. To find the optimal reaction conditions, different solvents such as DMF, MeCN, $CH_2Cl_2$ and catalysts, were examined to optimize the reaction conditions. Among them, EtOH was chosen as the best solvent for high productivity. In order to evaluate the catalytic efficiency of triethylamine, we performed the reaction with several equivalents of triethylamine from 15 to 100%. An excessive amount of catalyst (100 mol %) in the reflux condition increased the yield remarkably as shown in Table 1. This showed that the catalyst concentration has an important role in optimizing product performance.

Therefore, we chose the best conditions for the synthesis of **4a-m** compounds, which are as follows: use of $Et_3N$ (100 mol %) as the base and dry EtOH as the solvent to perform two processes Michael addition and intramolecular cyclization under reflux conditions during 2–3 h. We probed the scope of the annulation with different active methylene compounds such as (benzoylacetonitrile, dimedone, 1,3-dimethylbarbituric acid, 4-hydroxycoumarin and 3-methyl-1-phenyl-1*H*-pyrazol-5(4*H*)-one). All four active methylene compounds led the reaction to pyrano[2,3-*b*]quinolines with excellent yields. Unfortunately, when acetylacetone and ethyl acetylacetate were applied the reaction did not proceed to yield pyrano[2,3-*b*]quinolines.




**Scheme 3** Mechanistic rationale for the synthesis of **4a**

**Table 1** Optimization of the reaction conditions[a]




| Entry | Catalyst | Solvent (5 mL) | Temperature (°C) | Yield (%)[b] |
|---|---|---|---|---|
| 1 | none | EtOH | Reflux | N.R |
| 2 | $Et_3N$ (15%) | EtOH | Reflux | 65 |
| 3 | $Et_3N$ (50%) | EtOH | Reflux | 80 |
| 4 | $Et_3N$ (100%) | EtOH | Reflux | 95 |
| 5 | Piperidine | EtOH | Reflux | 85 |
| 6 | $Et_3N$ | $CH_3CN$ | Reflux | 85 |
| 7 | $Et_3N$ | DMF | Reflux | 70 |
| 8 | $Et_3N$ | $CH_2Cl_2$ | no temperature[c] | 50 |
| 9 | $K_2CO_3$ | EtOH | Reflux | 50 |
| 10 | $CH_3COONa$ | EtOH | Reflux | 40 |
| 11 | Piperidine | $CH_3CN$ | Reflux | 80 |

[a]Reaction conditions: 2-Chloroquinoline-3-carbaldehyde (0.5 mmol), 1-phenyl-2-(1,1,1-triphenyl-$\lambda^5$-phosphanylidene)ethan-1-one (0.5 mmol), benzoylacetonitrile (0.5 mmol), solvent (5 mL) and $Et_3N$ (100 mol%) in EtOH under reflux condition

[b]Isolated yields

[c]Reaction performed at rt

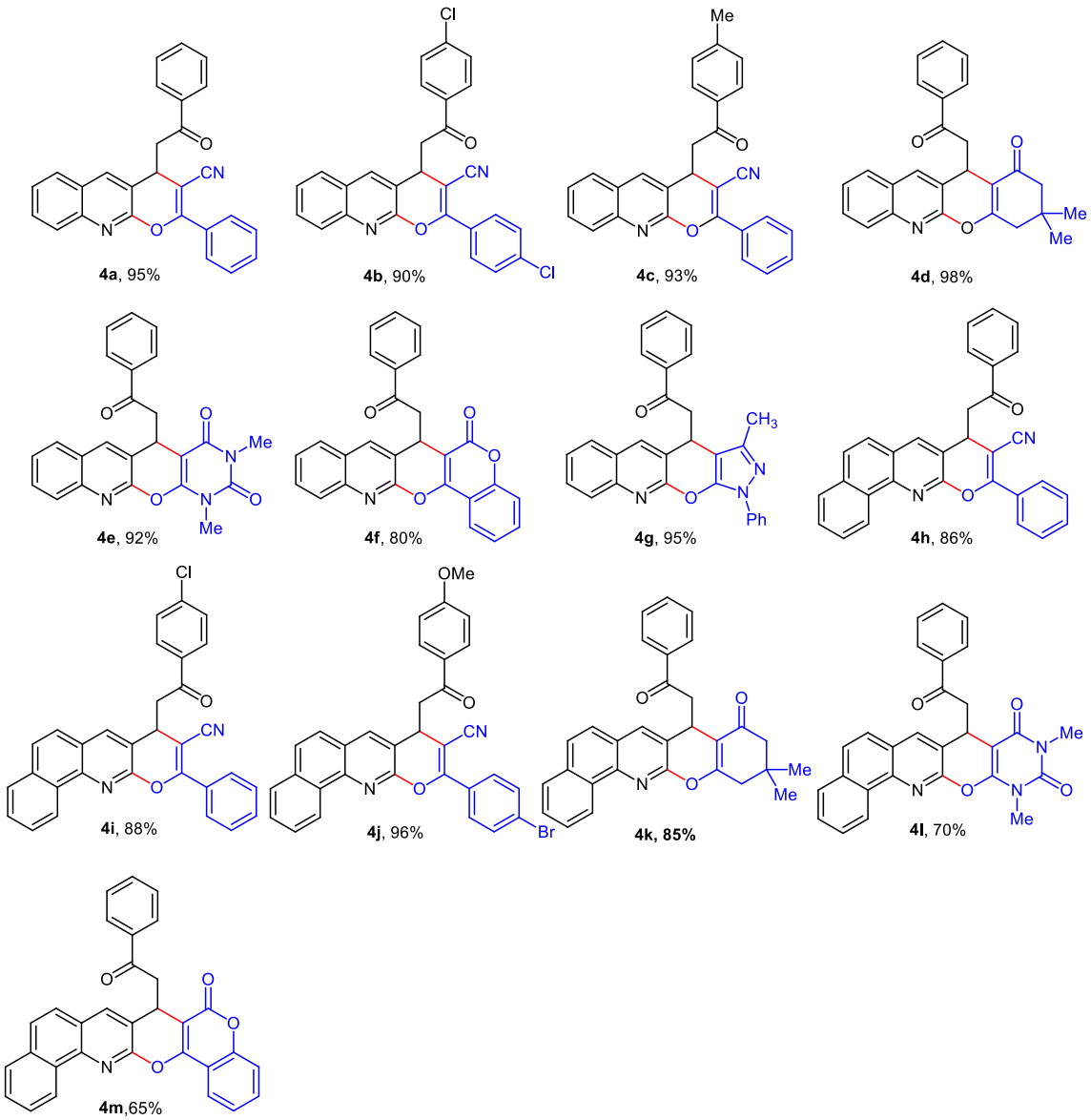
The electronic nature of the substituent on the aromatic rings affected the reaction and excellent yields. Therefore, the generality and efficiency of this reaction were deliberated using differently substituted benzoylacetonitriles and substitutions on phenyl Wittig. Eventually, products **4a-m** were obtained in excellent yields. It was clear that the reaction yield in the presence of electron-withdrawing substituents such as Br and Cl on phenyl of benzoylacetonitriles was better than electron-donating (Me and OMe) substituents on phenyl it. For this purpose, we selected electron-withdrawing substituents such as Br and Cl on phenyl nucleophiles (benzoylacetonitriles, $R^2 = Ph$, $p$-$ClC_6H_4$, $p$-$BrC_6H_4$). But, the product was not observed when a strong electron-withdrawing group such as $NO_2$ was present on the aromatic ring of it. It was also clear that by selecting the electron donor substitution on the aromatic ring of Wittig reagent, the reaction is more efficient. Therefore, product **4j** was selected as the most efficient reaction product. The results are illustrated in Table 2.

Should be mentioned the steric effect was also examined in this scope the steric effect on the aromatic ring did influence the reaction efficiency with a great reduction in the isolated yield. So that by selecting substituents Cl on ortho of the aromatic rings, no product was observed.

The structures of all the products **4a-m** were deduced from their IR, mass, $^1$H NMR, and $^{13}$C NMR spectra. The mass spectrum of **4a** displayed the molecular ion peak at $m/z = 402$, which is in agreement with the proposed structure. In the IR spectrum of **4a**, absorption band at 2205 $cm^{-1}$ attributed to the CN. Also, absorption band C=O in stretching frequencies 1680 $cm^{-1}$. The $^1$H NMR spectrum of **4a** exhibited AB quartet of doublet (ABqd) at $\delta = 3.95$ ppm related to $CH_2$ and $\delta = 4.69$ ppm a triplet with $J = 4.5$ Hz related to CH of the pyran ring respectively. Also, the singlet peak at $\delta = 8.48$ ppm attributed to $CH^5$ of quinoline. Observation of 23 distinct signals in the $^1$H-decoupled $^{13}$C NMR spectrum of **4a** is in agreement with the proposed structure. The $^{13}$C-NMR data showed two peaks in the aliphatic region at 32.21 ppm and 45.08 ppm for $CH^2$ and CH of the pyran ring, respectively, and a peak in 197.54 ppm for carbonyl group.

A plausible mechanism for the synthesis of **4a** is outlined in Scheme 3. Initially, the Wittig reagent and the aldehyde moiety form the $\alpha,\beta$-unsaturated compound **5**. Then, by activating

**Table 2** Synthesis of pyrano[2,3-*b*]quinoline and benzo[*h*]pyrano[2,3-*b*]quinolines derivatives **4a-m**[a]




[a]Reaction conditions: 2-Chloroquinoline-3-carbaldehyde **1a** or 2-chlorobenzo[*h*]quinoline-3-carbaldehyde **1b**, (0.5 mmol), 1-aryl-2-(1,1,1-triphenyl-$\lambda^5$-phosphanylidene)ethan-1-one **2** (0.5 mmol), active methylene compounds **3** (0.5 mmol), solvent (5 mL) and $Et_3N$ (100 mol %) in EtOH under reflux condition

methylene of benzoylacetonitrile by triethylamine, a C–C bond is formed (Michael addition, intermediate **7**). Eventually, the oxygen atom of benzoylacetonitrile undergoes intramolecular cyclization, leading to the formation of pyranoquinolines **4a**.

## Conclusions

In summary, we developed a convenient method for the synthesis of pyrano[2,3-*b*]quinoline and benzo[*h*]pyrano[2,3-*b*]quinoline derivatives from the available starting materials such as (2-chloroquinoline-3-carbaldehyde or 2-chlorobenzo[*h*]quinoline-3-carbaldehyde), 1-aryl-2-(1,1,1-triphenyl-$\lambda^5$-phosphanylidene)ethan-1-one (Wittig reagents) and the active methylene compounds, during the two processes of C–C bond formation (Michael addition) and intramolecular cyclization. Absence of a metal catalyst, simple workup procedure and excellent yields of the products make it an efficient route for synthesizing pyranoquinoline heterocycles. Considering the biological properties of pyrano-quinolines that have been studied and mentioned in

the introduction, the products obtained may represent interesting pharmacological properties.

**Supplementary Information** The online version contains supplementary material available at https://doi.org/10.1007/s13738-021-02376-9.

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## References


1. C. Simon, T. Constantieux, J. Rodriguez, Eur. J. Org. Chem. **24**, 4957 (2004)
2. M. Murakami, Angew. Chem. Int. Ed. **42**, 718 (2003)
3. G. Balme, E. Bossharth, N. Monteiro, Eur. J. Org. Chem. **21**, 4091 (2003)
4. V. Nair, C. Rajesh, A.U. Vinod, S. Bindu, A.R. Sreekanth, J.S. Mathen, L. Balagopal, Acc. Chem. Res. **36**, 899 (2004)
5. J. Zhu, Eur. J. Org. Chem. **34**, 1133 (2003)
6. S.V.N. Vuppalapati, Y.R. Lee, Tetrahedron **68**, 8286 (2012)
7. Y. Li, H. Chen, C. Shi, D. Shi, S. Ji, J. Comb. Chem. **12**, 231 (2010)
8. M. Ghandi, T. Momani, M.T. Nazari, N. Serenade, M. Dubicki, Tetrahedron Lett. **54**, 2983 (2013)
9. M. Seydimemet, K. Ablajan, M. Hamdulla, W. Li, A. Omar, M. Obul, Tetrahedron **72**, 7599 (2016)
10. J.K. Kato, Y. Ito, R. Ijuin, H. Aoyama, T. Yokomatsu, Org. Lett. **15**, 3794 (2013)
11. M.E. Jason, W.C. Robert, C. Mark, G.C. Gary, H.H. Peter, A.J. Brian, A. MacLeod, M. Rose, M.L. Georgina, M. Elena, M. Fraser, R. Michael, R. Inmaculada, G.N.R. Michael, S. Bindi, L.T. Kwei, W. Brian, Bioorg. Med. Chem. Lett. **16**, 5748 (2006)
12. N.J. Parmar, B.M. Labana, H.A. Barad, R. Kant, V.K. Gupta, Monatsh. Chem. **145**, 1179 (2014)
13. A. Alizadeh, A. Roosta, R. Rezaiyehrad, M.R. Halvagar, Tetrahedron **73**, 6706 (2017)
14. M. Ghandi, N. Zarezadeh, S. Rahimi, J. Iran. Chem. Soc. **12**, 1577 (2015)
15. M. Ghandi, N. Zarezadeh, J. Iran. Chem. Soc. **12**, 1313 (2015)
16. M. Ghandi, N. Zarezadeh, A. Abbasi, Mol. Divers. **20**, 483 (2016)
17. C.D. Wells, J.P. Cegielski, L.J. Nelson, K.F. Laserson, T.H. Holtz, A. Finlay, K.G. Castro, K. Weyer, J. Infect. Dis. **196**, S68 (2007)
18. M.W. Khan, M.J. Alam, M.A. Rashid, R. Chowdhury, Bioorg. Med. Chem. **13**, 4796 (2005)
19. G. Roma, M.D. Braccio, G. Grossi, F. Mattioli, M. Ghia, Eur. J. Med. Chem. **35**, 1021 (2000)
20. A. Marella, O.P. Tanwar, R. Saha, M.R. Ali, S. Srivastava, M. Akhter, M. Shaquiquzzaman, M.M. Alam, Saudi Pharm. J. **21**, 1 (2013)
21. S.I. Alqasoumi, A.M. Al-Taweel, A.M. Alafeefy, E. Noaman, M.M. Ghorab, Eur. J. Med. Chem. **45**, 738 (2010)
22. I. Radini, T. Elsheikh, E. El-Telbani, R. Khidre, Molecules **21**, 909 (2016)
23. R. Musiol, J. Jampilek, V. Buchta, L. Silva, H. Niedbala, B. Podeszwa, A. Palka, K. Majerz-Maniecka, B. Oleksyn, J. Polanski, Bioorg. Med. Chem. **14**, 3592 (2006)
24. R.E. Khidre, A.A. Abu-Hashem, M. El-Shazly, Eur. J. Med. Chem. **46**, 5057 (2011)
25. K. Kaur, M. Jain, R.P. Reddy, R. Jain, Eur. J. Med. Chem. **45**, 3245–3264 (2010)
26. B.F. Abdel-Wahab, R.E. Khidre, J. Chem. **2013**, 13 (2013)
27. M.A.M. Massoud, W.A. Bayoumi, A.A. Farahat, M.A. El-Sayed, B. Mansour, Archive **I**, 244 (2018)
28. M. Ramesh, P.A. Mohan, P. Shanmuganm, Tetrahedron **40**, 4041 (1984)
29. S. Chen, I.W. Tsai, C.M. Teng, J.J. Chem, Y.L. Chang, F.N. Ko, M.C. Lu, J.M. Pezzuto, Phytochemistry **46**, 525 (1997)
30. A. Dandia, S. Gautam, J. Flour. Chem. **128**, 1454 (2007)
31. R.A. Corral, O.O. Orazi, Tetrahedron Lett. **7**, 583 (1967)
32. M. Sekar, K.J.R. Prasad, J. Nat. Prod. **61**, 294 (1998)
33. L. Puricelli, G. Innocenti, G.D. Monache, R. Caniato, R. Filippini, E.M. Cappelletti, Nat. Prod. Lett. **16**, 95 (2002)
34. J.L. Marco, M.C. Carreiras, J. Med. Chem. **6**, 518 (2003)
35. L.G. Rocha, J.R.G.S. Almeida, R.O. Macedo, J.M. Barbosa-Filho, Phytomedicine **12**, 514 (2005)
36. K. Kaur, M. Jain, T. Kaur, R. Jain, Synthesis **3**, 43 (2019)
37. M. Behforouz, W. Cai, F. Mohammadi, M.G. Stocksdale, Z. Gu, M. Ahmadian, N.C. Behforouz, Bioorg. Med. Chem. **15**, 495 (2007)
38. F. Abas, N.H. Lajis, D.A. Israf, S. Khozirah, Y.U. Kalsom, Food Chem. **95**, 566 (2006)
39. K. Upadhyay, N. Dodia, C. Khunt, C.R.S. Rupesh, A.K. Shah, A.C.S. Med, Chem. Lett. (2018). https://doi.org/10.1021/acsmedchemlett.7b00545
40. N. Yamada, S. Kadowaki, K. Takahashi, K. Umezu, Biochem. Pharmacol. **44**, 1211 (1992)
41. K. Faber, H. Stueckler, T. Kappe, J. Heterocycl. Chem. **21**, 1177 (1984)
42. J.V. Johnson, B.S. Rauckmann, D.P. Baccanari, B. Roth, J. Med. Chem. **32**, 1942 (1989)
43. A.M. El-Agrody, H.S. Abd-Rabboh, A.M. Al-Ghamdi, Med. Chem. Res. **22**, 1339 (2013)
44. A.M. El-Agrody, A.M. Fouda, A.A.M. Al-Dies, Med. Chem. Res. **23**, 3187 (2014)
45. N. Pramod, N. S. Vaishnavi, M. N. Babu, S. A. Begum, C. Gopinath, Y. P. Kumar, Synthesis of Pyranoquinoline Derivatives and In-Silico Anti-Malarial Activity Using Docking Studies (2015).
46. M.M. Heravi, T. Hosseinnejad, Z. Faghihi, M. Shiri, M. Vazinfard, J. Iran. Chem. Soc. **14**, 823 (2017)
47. B. Aplal, S. Nagaraju, P. Veerabhadraiah, K. Sujatha, S. Kanvah, B.V.D. Kashinath, RSC Adv. **4**, 54168 (2014)
48. N. Garcia-Font, H. Hayour, A. Belfaitah, J. Pedraz, I. Moraleda, I. Iriepa, A. Bouraiou, M. Chioua, J. Marco-Contelles, M.J. Oset-Gasque, Eur. J. Med. Chem. **118**, 178 (2016)
49. M. Shiri, M. Heydari, V. Zadsirjan, Tetrahedron **73**, 2116 (2017)
50. A. Chandra, B. Singh, R.S. Khanna, R. Singh, J. Org. Chem. **74**, 5664 (2009)
51. Q. Zhang, Z. Zhang, Z. Yan, Q. Liu, T. Wang, Org. Lett. **9**, 3651 (2007)
52. P.J. Bhuyan, B. Baruah, P.K. Kalita, Tetrahedron Lett. **47**, 7779 (2006)
53. M.K. Singh, A. Chandra, B. Singh, R.M. Singh, Tetrahedron Lett. **48**, 5987 (2007)
54. B. Singh, A. Chandra, S. Upadhyay, R.M. Singh, M.C. Puerta, P. Valerga, Tetrahedron Lett. **49**, 6423 (2008)
55. R.E. Khidre, B.F. Abdel-Wahab, F.A.-R. Badria, Lett. Drug Des. Discov. **8**, 640 (2011)