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NOTE

A new synthesis of 5-substituted-3-phenyl-2*H*-pyrano[2,3-*b*]quinolin-2-ones

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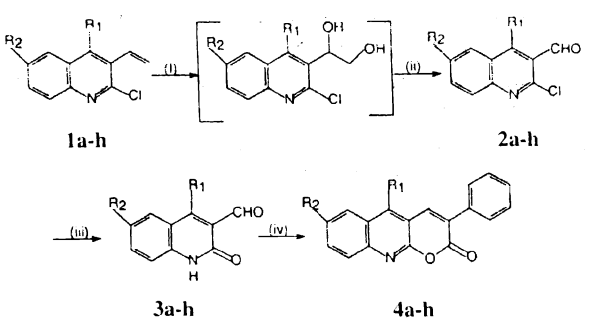
Synthesis of title compounds and derivatives is reported by the Perkin reaction of 3-formyl-4-phenyl/methyl-2-quinolones (3) with sodium salt of phenylacetic acid. The 3-formyl-2-quinolones 3 were obtained from 2-chloro-3-formyl-4-phenyl/methylquinolines (2) which inturn were prepared from 2-chloro-4-phenyl/methyl-3-vinylquinolines (1).

The synthesis of pyranoquinolines has gained momentum in recent years as they constitute parent ring structure of pyranoquinoline alkaloids which have been reported to be associated with interesting pharmacological properties[1], biological and chemical properties[2]. Herein we report a convenient and new methodology for the synthesis of 2-chloro-3-formyl-4-phenyl/methylquinolines from 2-chloro-4-phenyl/methyl-3-vinylquinolines as precursors and to utilise them for the construction of 5-phenyl/methyl-3-phenyl-2*H*-pyrano[2,3-*b*]quinolin-2-ones which are expected to be pharmacologically active (Scheme 1).



a $R_1 = C_6H_5$; $R_2 = H$ **b** $R_1 = C_6H_4$-CH_3; $R_2 = H$
c $R_1 = C_6H_4$-OCH_3; $R_2 = H$ **d** $R_1 = C_6H_5$; $R_2 = Cl$
e $R_1 = C_6H_5$; $R_2 = CH_3$ **f** $R_1 = C_6H_4$-Cl; $R_2 = H$
g $R_1 = C_6H_4$-Br; $R_2 = H$ **h** $R_1 = CH_3$; $R_2 = H$

Scheme 1. *Reagents* : (i) $KMnO_4$/t-butanol, (ii) $CH_3OH/NaIO_4$, (iii) 4 *M* HCl, (iv) $C_6H_5CH_2COONa/Ac_2O$.

Results and Discussion

2-Amino benzophenone was treated with 3-butenoyl chloride to get 4-phenyl-3-vinyl-2-quinolone[3,4]. This on heating with $POCl_3$ produces 2-chloro-3-vinyl-4-phenylquinoline (**1a**). The chloroquinoline (**1a**) so obtained was treated with $KMnO_4$ and NaOH at 0° with constant stirring for 3–5 min in t-butanol medium and after passing SO_2 gas, the resultant mass was continuously extracted with methylene chloride using Soxhlet apparatus to give a pasty mass. The pasty mass was then dissolved in methanol and treated with $NaIO_4$ at 3° with stirring for 15 min and after adding NaCl the contents were extracted with chloroform gave 2-chloro-3-formyl-4-phenylquinoline (**2a**) in 40% yield, m.p. 135–137°. Its IR spectrum showed peaks at 1705 cm^{-1} (CHO) and 1080 cm^{-1} (C–Cl). The chloroaldehyde (**2a**) so obtained was then converted to oxo compound (**3a**) by refluxing with aqueous 4 *M* HCl followed by usual work up gave a product in 80% yield, which melts at 302–304°. Its IR spectrum showed peaks at 1705 cm^{-1} (CHO) and 1620 cm^{-1} (-NHC=O). The 3-formyl-4-phenyl-2-quinolone (**3a**) so obtained was subjected to Perkin reaction with sodium phenyl acetate and acetic anhydride gave a compound in 69% yield, which melts at 287–288°. From IR, ^1H NMR and mass spectrum data (Table 2), the compound was identified as 3,5-diphenyl-2*H*-pyrano[2,3-*b*]quinoline-2-one (**4a**). The reaction sequence leading to **4a** was then extended to synthesise (**4b-h**). The compound (**4h**) was synthesised by following a similar procedure starting from 2-amino acetophenone through the intermediate 2-chloro-4-methyl-3-vinyl quinoline[5] (**1h**).

Experimental

Melting points were determined using Raaga Melting Point apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 597 Infrared spectrometer as KBr pellets. ^1H NMR spectra were recorded on a AMX 400 spectrometer in $CDCl_3$. Mass spectra were recorded on a Jeol-D 300 Mass spectrometer. Elemental analysis were performed by Perkin-Elmer model 240B CHN analyser. For all the compounds satisfactory microanalysis values were obtained (C, H, N ±0.4%)

Typical procedures : *2-chloro-3-formyl-4-phenyl/methylquinolines*[6,7] (**2a-h**) : A solution of $KMnO_4$ (0.00148 mol) and NaOH (0.00125 mol) in 8 ml of water cooled to 0°, was added quickly with vigorous stirring to a freezing mixture of t-butanol (10 ml), 2 ml of water and 2-chloro-4-phenyl/methyl-3-vinylquinoline[3-5] (0.001 mol). After 3–5

min, most of the permanganate colour has been discharged and SO_2 gas was passed immediately to ensure complete reduction of permanganate. The precipitate of MnO_2 was filtered and most of the t-butanol was removed by distillation at atmospheric pressure and the resultant mass was continuously extracted with methylene chloride using Soxhlet apparatus for 48 h. The compound obtained as a pasty mass while removing the solvent, was taken to subsequent experiment without purification. The pasty mass so obtained was dissolved in minimum amount of methanol and $NaIO_4$ (0.5 mmol) in 3 ml of water at 3° was added dropwise with stirring. After 15 min a saturated solution of NaCl was added and the contents were extracted with chloroform. After evaporation the compound was separated as a yellow solid which was chromatographed over silica gel using petroleum ether-ethyl acetate mixture (90 : 10, v/v). The product was then recrystallized from chloroform (Table 1).

3-Formyl-4-phenyl/methyl-2-quinolones[8] (**3a-h**) : A mixture of **2** (0.0104 mol) and aqueous hydrochloric acid (35 ml : 4 *M*) was heated under reflux for 8 h in an oil bath at 120–130° and then allowed to cool at room temperature. After 1 h the reaction mixture was poured into crushed ice, when the product was separated as a yellow solid. It was filtered, washed with water, dried and recrystallized from aqueous acetic acid (Table 1).

5-Phenyl/methyl-3-phenyl-2H-pyrano[2,3-b]quinolin-2-ones[9] (**4a-h**) : A mixture of **3** (0.001 mol), freshly fused sodium phenyl acetate (0.0016 mol), acetic anhydride (0.05 mol) was heated under reflux for 8 h at 170–180° in an oil

Table 1. Physical and spectroscopic data of **2a-h**[a] and **3a-h**[b]

Compd.	M.p. °C	Yield %	IR[c] cm^{-1}	MS *m/z* (M^+)
2a	135–137[10]	40	1705, 2860, 1080	267
				269
2b	161–162[10]	41	1705, 2870, 1085	281
				283
2c	122–124[10]	40	1700, 2864, 1086	297
				299
2d	168–170	42	1695, 2875, 1080	302
				304
2e	129–131[10]	41	1710, 2865, 1090	281
				283
2f	143–145	42	1705, 2875, 1076	302
				304
2g	138–140	40	1705, 2862, 1081	347
				349
2h	119–120	40	1705, 2950, 1080	205
				207
3a	302–304	80	1705, 1620	249
3b	308–310	80	1705, 1630	263
3c	284–286	79	1710, 1625	299
3d	320–321	80	1710, 1630	284
				286
3e	277–278	80	1705, 1620	263
3f	315–317	79	1690, 1610	284
				286
3g	311–313	78	1710, 1615	329
				331
3h	299–300	80	1705, 1640	187

[a]Recrystallised form chloroform, [b]recrystallised from aq.acetic acid, [c]as KBr pellet.

Table 2. Physical and spectroscopic data of **4a-h**[a]

Compd.	M.p.[a] (Yield %)	IR[b] cm^{-1}	^1H NMR[c] (δ) ppm	MS *m/z* (M^+)
4a	287–288	1749	δ 7.27–7.69 (14H, m, C_3 and C_5-Ar-H, C_4-H,	349
	(69)	1650	C_6-H, C_7-H and C_8-H); δ 8.16 (1H, d, C_9-H)	
4b	295–296	1750	δ 2.51 (3H, s, C_5-C'_4-CH_3); δ 7.02–7.51	363
	(70)	1648	(13H, m, C_3 and C_5-Ar-H, C_4-H, C_6-H, C_7-H	
			and C_8-H); δ 8.19 (1H, d, C_9-H)	
4c	271–272	1762	δ 3.64 (3H, s, C_5-C'_4-OCH_3); δ 7.01–7.64	379
	(70)	1660	(13H, m, C_3 and C_5-Ar-H, C_4-H, C_6-H,	
			C_7-H and C_8-H); δ 8.19 (1H, d, C_9-H)	
4d	297–298	1735	δ 7.39–7.73 (13H, m, C_3 and C_5-Ar-H, C_4-H,	384
	(70)	1650	C_6-H and C_8-H); δ 8.16 1H, d, C_9-H)	386
4e	282–284	1748	δ 2.62 (3H, s, C_7-CH_3); δ 7.12–7.71 (13H, m,	363
	(70)	1647	C_3 and C_5-Ar-H, C_4-H, C_6-H and C_8-H);	
			δ 8.29 (1H, d, C_9-H)	
4f	298–299	1760	δ 7.21–7.831 (13H, m, C_3 and C_5-Ar-H, C_4-H,	384
	(65)	1655	C_6-H, C_7-H and C_8-H); δ 8.14 (1H, d, C_9-H)	386
4g	292(d)	1755	δ 7.36–7.86 (13H, m, C_3 and C_5-Ar-H, C_4-H,	429
	(65)	1650	C_6-H, C_7-H and C_8-H); δ 8.29 (1H, d, C_9-H)	431
4h	285(d)	1720		287
	(70)	1625		

[a]Recrystallised from acetic acid, [b]as KBr pellet, [c]in $CDCl_3$, [d]decomposed.

bath. The reaction mixture was then poured into crushed ice (≈100 g) with stirring and kept aside for 4–5 h. The resulting solid was filtered, dried and recrystallized from acetic acid to yield **4a-h** (Table 2).

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