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New examples of synthetic applications of 2-chloro-3-formylquinoline, as evident from the novel and facile syntheses of 3-aminoisooxazolo[5,4-*b*]quinoline (4), 3-hydroxyfuro[2,3-*d*]thieno[2,3-*b*]quinoline-2-carboxamide (7) and 3-hydroxymethyl-2-(3-formyl)phenylquinoline (13), have been furnished.

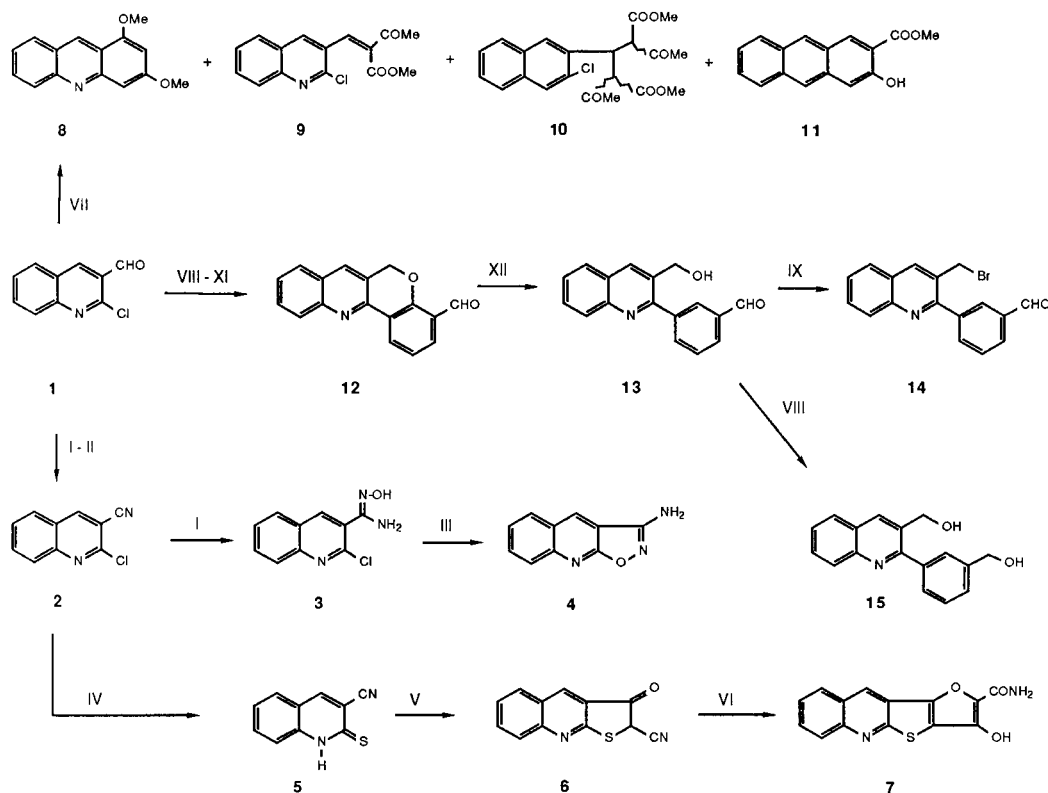
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In continuation of our programme [2-11] for exploring the synthetic applications of 2-chloro-3-formylquinoline, a number of tri- and tetracyclic heterocycles have been synthesised and during the course of this investigation, a novel synthesis of 2-substituted phenylquinoline derivative has been developed. These are reported here.

Reaction of 2-chloro-3-cyanoquinoline (2), prepared from 2-chloro-3-formylquinoline (1) by the method reported earlier [4], with hydroxylamine gave 3 which on ring closure in the presence of anhydrous potassium carbonate yielded 4. The spectroscopic data of 4 supported the assigned structure. Reaction of 2 with thiourea [5] furnished 5 which was subjected to ring closure by reacting it

with chloroacetonitrile in the presence of anhydrous potassium carbonate. The spectroscopic data of this reaction product 6 were in agreement with the assigned structure. However, in solution it exhibited keto-enol tautomerism. This tricyclic heterocycle 6 could be elaborated to a tetracyclic compound 7 by reacting the former with chloroacetonitrile in presence of polyphosphoric acid.

Reaction of 1 with methyl acetoacetate in the presence of dry pyridine gave a number of products which were separated by column chromatography over silica gel. The structural assignment of the reaction products 8-11 have been made on the basis of their spectroscopic data. However, the pmr spectrum of 8 deserves special atten-



I: NH₂OH · HCl, CH₃COONa, CH₃OH; II: SOCl₂, benzene; III: anhydrous K₂CO₃, CH₃OH; IV: thiourea, aqueous NaOH,

CH₃OH; V: ClCH₂CN, anhydrous K₂CO₃, DMF; VI: ClCH₂CN, PPA; VII: methylacetoacetate, pyridine, CH₃OH; VIII: NaBH₄,

CH₃OH; IX: PBr₃, benzene; X: salicylaldehyde, anhydrous K₂CO₃, DMF; XI: NaH, THF; XII: palladium-carbon, CH₃OH.

Table

Physical, Analytical and Spectral Data of the Previously Unknown Compounds

Compound	MP °C	Yield %	Molecular formula	Analysis % Calcd./Found			Spectra Data	
				C	H	N		
3 [b]	192	44	C ₁₀ H ₈ ClN ₃ O	52.1	3.9	18.2	ir:	3400 (OH), 3200 (NH ₂)
				52.3	3.6	18.2	nmr	(deuteriochloroform + deuterio-dimethylsulphoxide): 7.30-8.00 (m, ArH, 4H), 8.30 (s, 4-ArH, 1H), 8.55 (s, OH, 1H), 11.65 (s, NH ₂ , 2H)
4	188	32	C ₁₀ H ₇ N ₃ O	64.9	3.8	22.7	ir:	3190 (NH ₂)
				64.7	3.8	22.7	nmr	(deuteriochloroform + deuterio-dimethylsulphoxide): 6.80-7.65 (m, ArH, 4H), 7.80 (s, NH ₂ , 2H), 8.35 (s, 4-ArH, 1H)
6	250	85	C ₁₂ H ₆ N ₂ OS	63.7	2.7	12.4	ms:	185 (M ⁺)
				63.7	2.6	12.1	nmr	ir: 2250 (C≡N), 1670 (C=O) (deuteriodimethylsulphoxide): 7.20-8.20 (m, ArH, 5H), 9.12 (s, OH, 1H)
7	250-253	67	C ₁₄ H ₈ N ₂ O ₃ S	59.2	2.8	9.9	ms:	226 (M ⁺)
				59.2	3.0	10.1	nmr	ir: 3400 (OH, 3200 (NH ₂) (deuteriochloroform + deuterio-dimethylsulphoxide): 6.50-8.20 (m, ArH and NH ₂ , 7H), 8.895 (s, OH, 1H)
8	118	32	C ₁₅ H ₁₃ NO ₂	75.3	5.4	5.8	ms:	284 (M ⁺)
				75.2	5.4	5.6	nmr	ir: 1610 (C=N) (Carbon tetrachloride): 3.29 (s, 2OCH ₃ , 6H), 5.52 (s, 3-ArH, 1H), 7.30-7.90 (m, ArH, 5H), 8.20 (s, 5-ArH, 1H)
9	132-134	4	C ₁₅ H ₁₂ ClNO ₃	62.2	4.1	4.8	ms:	239 (M ⁺)
				62.2	4.0	4.8	nmr	ir: 1740 and 1720 (2 X C=O) (deuteriochloroform): 2.20 and 2.45 (2s, COCH ₃ , 3H), 3.65 and 3.85 (2s, COOCH ₃ , 3H), 7.20-8.20 (m, CH and ArH, 6H)
10 [c]	Oil	10	C ₂₀ H ₂₀ ClNO ₆	59.2	4.9	3.5	ms:	289 (M ⁺), 291 (M + 2)
				59.3	4.8	3.6	nmr	ir: 1750 and 1740 (C=O) (deuteriochloroform): 1.95-2.55 (m, 2XCOCH ₃ , 6H), 3.00-3.80 (m, 2XCOOCH ₃ , 6H), 3.90-5.10 (m, CH, 3H), 640-8.20 (m, ArH, 5H)
11	140	2	C ₁₅ H ₁₁ NO ₃	71.1	4.3	5.5	ms:	405 (M ⁺), 407 (M + 2)
				71.2	4.6	5.3	nmr	ir: 1680 (C=O) (deuteriodimethylsulphoxide): 3.30 (s, COOCH ₃ , 3H), 7.20-8.60 (m, ArH, 7H), 11.35 (s, OH, 1H)
13 [b]	130	40	C ₁₇ H ₁₃ NO ₂	75.0	5.1	5.1	ms:	253 (M ⁺)
				74.8	4.8	5.1	nmr	ir: 3400 (OH), 1690 (C=O) (deuteriochloroform): 5.30 (s, CH ₂ , 2H), 6.90-8.30 (m, ArH, 9H), 8.95 (s, OH, 1H), 10.5 (s, CHO, 1H)
14 [a]	260	50	C ₁₇ H ₁₂ BrNO	59.3	4.1	4.1	ms:	263 (M ⁺)
				59.3	3.9	4.1	nmr	ir: 1680 (C=O) (deuteriochloroform): 5.49 (s, CH ₂ , 2H), 7.24-8.08 (m, ArH, 9H), 10.10 (s, CHO, 1H)
							ms:	325 (M ⁺), 327 (M + 2)

Table (continued)

Compound	MP °C	Yield %	Molecular formula	Analysis %			Spectra Data	
				Calcd./Found	C	H		
15	134	50	C ₁₇ H ₁₅ NO ₂	76.9	5.7	5.3	ir:	3400 (OH)
				76.9	5.7	5.3	nmr	(deuteriochloroform): 4.65 (s, CH ₂ , 2H), 5.20 (s, CH ₂ , 2H), 6.75-8.20 (m, ArH, 9H), 8.70-9.00 (bs, 2XOH, 2H)
							ms:	265 (M ⁺)

[a] Crystallized as the hydrate. [b] Crystallized as the hemihydrate. [c] Mixture of diastereomers.

tion. The aromatic proton at C-3 in this compound appeared at δ 5.52 ppm. Although this appears to be unusual, it is not unexpected since C-3 of acridine is extremely electron rich [12] and the proton attached to this carbon experiences shielding of the two adjacent methoxyl groups. The nuclear overhauser effect on this proton, observed after irradiation at δ 3.29 ppm, is significant (26%) and the chemical shift of C-3 at 100.58 ppm in ¹³C-nmr spectrum explains the upfield shift of the proton at C-3. Literature precedence for a significant upfield shift of aromatic protons in 3,5-dimethoxyaniline exists [13]. Hydrogenolysis of 6*H*-[1]benzopyrano[4,3-*b*]quinoline (**12**), prepared by the method reported earlier [9], in the presence of palladium-carbon led to an unusual ring opening and yielded **13**. The structural assignment of **13** has been supported by its conversion to the bromo derivative **14** and diol **15**.

EXPERIMENTAL

Melting points were determined on an electrically heated block. The ir spectra were recorded on a Perkin-Elmer 157 grating instrument. The ¹H nmr spectra were recorded on a Perkin-Elmer R-32 spectrometer using tetramethylsilane as internal reference.

2-Chloroquinoline-3-amidoxime (**3**).

A mixture of 2-chloro-3-cyanoquinoline (**2**, 0.005 mole), hydroxylamine hydrochloride (0.012 mole) and sodium acetate (0.010 mole) in methanol (30 ml) was refluxed under constant stirring for 2.5 hours. The reaction mixture was cooled, the solvent removed by distillation and the addition of water (35 ml) furnished the crude solid which was crystallized from chloroform-hexane (20:80) to yield **3** as a crystalline solid.

3-Aminoisooxazolo[5,4-*b*]quinoline (**4**).

A mixture of oxime **3** (0.002 mole) and anhydrous potassium carbonate (0.004 mole) in methanol (20 ml) was refluxed under constant stirring for 8 hours. The usual work up of the reaction mixture gave a solid which was recrystallized from a mixture of methanol-water (10:90) to give **4** as a colourless solid.

2,3-Dihydro-2-cyano-3-oxothieno[2,3-*b*]quinoline (**6**).

A mixture of thione **5** (0.013 mole), anhydrous potassium carbonate (0.013 mole) and chloroacetonitrile (0.019 mole) in dimethylformamide (20 ml) was stirred at room temperature (30°) for 12 hours. The reaction mixture was diluted with water and the separated solid was filtered and

dried. This was crystallized from a mixture of chloroform-hexane (20:80) to give **6** as a yellow crystalline solid.

3-Hydroxyfuro[2,3-*d*]thieno[2,3-*b*]quinoline-2-carboxamide (**7**).

A mixture of theinoquinoline **6** (0.002 mole), chloroacetonitrile (0.006 mole) and polyphosphoric acid (6.0 g) was heated on the steam bath for 2.5 hours and then left at room temperature (30°) for 12 hours. Addition of ice cold water furnished a solid which was crystallized from a mixture of dimethylsulphoxide-water (5:95) to yield **7** as a pale yellow crystalline solid.

Reaction of 2-Chloro-3-formylquinoline (**1**) with Methyl Acetoacetate: Formation of Compounds **8-11**.

A mixture of **1** (0.02 mole), methyl acetoacetate (0.02 mole) and dry pyridine (0.3 ml) in methanol (50 ml) was refluxed with stirring for 4 hours. The reaction mixture was cooled, diluted with water and extracted with ethyl acetate. The usual work up of the organic layer gave an oil which was purified by column chromatography over silica gel. Elution of the column with hexane furnished unreacted aldehyde (20%). Further elution of the column with chloroform, hexane (20:80) yielded **8** which was crystallized from a mixture of chloroform-hexane (20:80). Next elution of the column with chloroform:hexane (50:50) gave **9**, recrystallized from a mixture of chloroform-hexane (20:80). Further elution of the column with chloroform gave **10** as an oil. Finally elution of the column with chloroform:methanol (90:10) gave **11** as a solid which was crystallized from a mixture of chloroform:hexane (20:80).

3-Hydroxymethyl-2-(3-formyl)phenylquinoline (**13**).

A solution of pyranoquinoline **12** (2.7 g, 0.010 mole) in methanol (30 ml) was hydrogenated over palladium-carbon (0.36 g) for 55 minutes. The usual work up of the reaction mixture gave the crude product which was purified by column chromatography over silica gel using benzene as the eluant to give **13** as a greenish-white solid. It was recrystallized from a mixture of chloroform:hexane (20:80).

3-Bromomethyl-2-(3-formyl)phenylquinoline (**14**).

To a solution of hydroxymethyl compound **13** (0.002 mole) in dry benzene (5 ml) was added phosphorus tribromide (0.002 mole) and the mixture refluxed under stirring for 4.5 hours. Evaporation of the solvent followed by addition of chilled water (15 ml) gave the required compound **14** which was crystallized from a mixture of dimethylsulphoxide:water (5:95).

3-Hydroxymethyl-2-(3-hydroxymethyl)phenylquinoline (**15**).

To a well stirred solution of **13** (0.002 mole) in methanol (20 ml) was added sodium borohydride (0.003 mole) and the mixture was further stirred at room temperature (30°) for 5 minutes. The solvent was removed *in vacuo* and the residue was neutralized with glacial acetic acid (0.4 ml). Addition of water gave **15** as a colourless solid which was recrystallized from a mixture of chloroform:hexane (20:80).

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