Novel Syntheses of 3-Cyano-3,4-dihydroquinolin-2(1*H*)-one and Derivatives of 2,3-Dicarbomethoxy-2-hydroxycyclopenta[*b*]quinoline [1]

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A facile solid phase conversion of 2-chloro-3-cyano-4-substituted-1,4-dihydroquinolines to 3-cyano-4-substituted-3,4-dihydroquinolin-2(1*H*)-ones in almost quantitative yields and a novel synthesis of 2,3-dicarbomethoxy-2-hydroxycyclopenta[*b*]quinoline are described.

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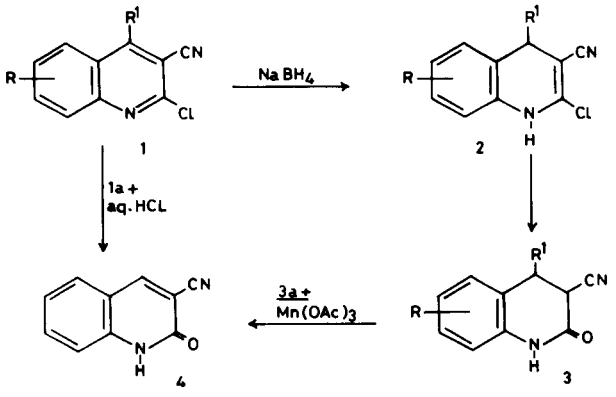
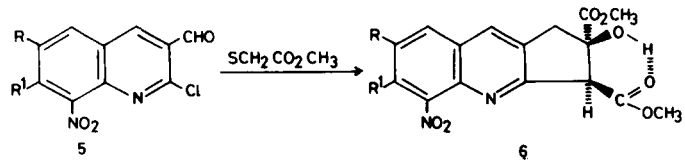
Novel syntheses of 3-cyano-3,4-dihydroquinolin-2(1*H*)-one and 4-alkyl derivatives as well as 2,3-dicarbomethoxy-2-hydroxycyclopenta[*b*]quinolines, developed during the course of our investigations for exploring the synthetic utility of 2-chloro-3-formylquinolines, are reported here.

A facile synthesis of 3-cyano-3,4-dihydroquinolin-2(1*H*)-one (**3a**) has been observed during the sodium borohydride reduction of 2-chloro-3-cyanoquinoline (**1a**) [2], which in turn, was prepared from 2-chloro-3-formylquinoline [3]. The 1,4-dihydroquinoline **2a**, obtained as the borohydride reduction product of **1a**, on storage under laboratory conditions (30-35°) quantitatively converted to 3-cyano-3,4-dihydroquinolin-2(1*H*)-one (**3a**). The spectroscopic data of this compound (Table 1) agreed well with the assigned structure and additional support for the assigned structure was obtained by oxidising **3a** with manganic acetate. The carbostyril derivative **4**, so obtained, was found to be identical in all respects with the one prepared by refluxing **1a** with aqueous hydrochloric acid (30%, v/v) in methanol for 4 hours. Like **2a**, other 1,4-dihydroquunolines **2b-2f** [2] in the solid phase were converted to **3b-3f** (Figure 1) in excellent yields. The conversion is complete within 24-48 hours and the method appears to have preparative value.



a: R=R¹=H ; b: R=H, R¹=CH₃; c: R=H, R¹=C₂H₅;
d: R=6-OCH₃, R¹=H ; e: R=6-OCH₃, R¹=CH₃;
f: R=6-OCH₃, R¹=C₂H₅

Fig. 1



a: R=R¹=OCH₃ ; b: R=R¹=OC₂H₅

Fig. 2

Reaction of 2-chloro-6,7-dimethoxy-3-formyl-8-nitroquinoline (**5a**) [4], with methyl thioglycolate in the presence of potassium carbonate has been reported earlier [5] to yield 2-carbomethoxy-6,7-dimethoxy-8-nitrothieno[2,3-*b*]quinoline and 2-carbomethoxy-6,7-dimethoxy-3-hydroxy-8-nitrothieno[2,3-*b*]quinoline. However, when the same reaction of **5a** was carried out with two moles of methyl thioglycolate, besides the thieno[2,3-*b*]quinoline, a good yield of 2,3-dicarbomethoxy-6,7-dimethoxy-2-hydroxy-5-nitrocyclopenta[*b*]quinoline (**6a**, Figure 2) was obtained. Like **5a**, the reaction of **5b** with methyl thioglycolate gave **6b**. The assigned structures of **6a-6b** agreed well with the spectroscopic data and elemental analyses.

EXPERIMENTAL

Melting points were determined on an electrically heated block and are uncorrected. The ir spectra were recorded on a Perkin-Elmer 157 grating instrument. The ^{1}H nmr spectra were recorded on Perkin-Elmer R-32 spectrometer using tetramethylsilane as internal reference. Mass spectra were recorded on Jeol-JMS-D 300.

2-Chloro-3-cyanoquinoline (**1a**), 2-Chloro-3-cyano-4-methylquinoline (**1b**), 2-Chloro-3-cyano-4-ethylquinoline (**1c**) and the Corresponding 6-Methoxy-derivatives **1d**, **1e** and **1f**.

These were prepared by the method reported in the literature [2].

2-Chloro-3-cyano-1,4-dihydroquinoline (**2a**), 2-Chloro-3-cyano-4-methyl-1,4-dihydroquinoline (**2b**), 2-Chloro-3-cyano-4-ethyl-1,4-dihydroquinoline (**2c**) and the Corresponding 6-Methoxy-derivatives **2d**, **2e** and **2f**.

General Procedure.

To a solution of the appropriately substituted 3-cyanoquinoline (**1**, 0.01 mole), in methanol (30 ml) was added under stirring sodium borohydride (0.015 mole). The reaction was allowed to continue at room temperature (30-35°) for 0.5 hour. It was then diluted with water (50 ml) and the separated solid (**2a-2f**) was filtered and recrystallized from a mixture of methanol:water (1:2).

Table 1

Physical, Analytical and Spectral Data of Compounds Synthesized

Compound	Mp °C	Molecular formula	Analysis % Calcd./Found C	H	N	Spectral Data
2a	201-202	$C_{10}H_7ClN_2$	62.99 63.00	3.67 3.58	14.69 14.50	ms: 190 (M^+), 192 (M + 2); ir: 3300 (NH), 2250 (-C≡N); nmr (deuteriochloroform + deuteriodimethyl sulfoxide): 3.69 (s, 2H, CH_2), 6.60-7.20 (m, 5H, Ar-H and -NH)
2d	156-157	$C_{11}H_9ClN_2O$	59.86 59.70	4.08 4.00	12.69 12.50	ms: 220 (M^+), 222 (M + 2); ir: 3280 (NH), 2250 (-C≡N); nmr (deuteriodimethyl sulfoxide): 3.68 (s, 3H, OCH_3), 3.80 (s, 2H, CH_2), 6.65-7.00 (m, 4H, Ar-H and NH)
3a	220-221	$C_{10}H_8N_2O$	69.76 69.80	4.65 4.80	16.27 16.40	ms: 172 (M^+); ir: 3200 (NH), 2250 (-C≡N), 1680 (-C=O); nmr (deuteriodimethyl sulfoxide): 3.25 (d, 2H, CH_2), 4.10-4.50 (t, 1H, 3-H), 6.80-7.30 (m, 4H, Ar-H), 10.60 (bs, 1H, NH).
3b	184-187	$C_{11}H_{10}N_2O$	70.96 70.80	5.37 5.40	15.05 15.00	ms: 186 (M^+); ir: 3250 (NH), 2200 (-C≡N), 1690 (-C=O); nmr (deuteriodimethyl sulfoxide): 1.40 (s, 3H, CH_3), 3.15-3.55 (m, 1H, 4-H), 3.88 (2d, 1H, 3-H), 6.80-7.30 (m, 5H, Ar-H and NH)
3c	123-124	$C_{12}H_{12}N_2O$	72.00 72.30	6.00 6.12	14.00 14.30	ms: 200 (M^+); ir: 3200 (NH), 2220 (-C≡N), 1680 (-C=O); nmr (deuteriochloroform + deuteriodimethyl sulfoxide): 0.75-1.20 (m, 3H, $-CH_2CH_3$), 1.50-2.00 (m, 2H, $-CH_2CH_3$), 2.98-3.25 (m, 1H, 4-H), 3.77 (2d, 1H, 3-H), 6.80-7.80 (m, 5H, Ar-H and -NH)
3d	161	$C_{11}H_{10}N_2O_2$	65.34 65.40	4.95 4.80	13.86 14.00	ms: 202 (M^+); ir: 3200 (NH), 2250 (-C≡N), 1685 (-C=O); nmr (deuteriodimethyl sulfoxide): 3.20 (bs, 3H, 4-H and 3-H), 3.68 (s, 3H, OCH_3), 6.10-6.80 (m, 4H, Ar-H and NH)
3e	130-132	$C_{12}H_{12}N_2O_2$	66.66 66.50	5.55 5.70	12.96 12.83	ms: 216 (M^+); ir: 3300 (NH), 2200 (-C≡N), 1690 (-C=O); nmr (deuteriodimethyl sulfoxide): 1.30 (2d, 3H, CH_3), 3.00-3.30 (m, 1H, 4-H), 3.63 (2d, 1H, 3-H), 3.72 (s, 3H, OCH_3), 6.10-6.80 (m, 4H, Ar-H and -NH)
3f	159-160	$C_{13}H_{14}N_2O_2$	67.82 67.90	6.08 6.00	12.17 12.38	ms: 230 (M^+); ir: 3250 (NH), 2250 (-C≡N), 1685 (-C=O); nmr (deuteriodimethyl sulfoxide): 0.80-1.00 (m, 3H, CH_2CH_3), 1.50-1.80 (m, 2H, CH_2CH_3), 3.00-3.25 (m, 1H, 4-H), 3.70 (s, 3H, OCH_3), 4.20 (2d, 1H, 3-H), 6.20-6.90 (m, 4H, Ar-H and NH)
4	>300	$C_{10}H_6N_2O$	70.58 70.40	3.52 3.70	16.47 16.60	ms: 170 (M^+); ir: 3200 (NH), 2250 (-C≡N), 1670 (-C=O); nmr (deuteriodimethyl sulfoxide): 6.70 (bs, 1H, NH), 7.10-7.70 (m, 4H, Ar-H), 8.60 (s, 1H, 4-H)
6a	155-157	$C_{18}H_{18}N_2O_9$	53.20 53.45	4.43 4.62	6.89 6.57	ms: 406 (M^+); ir: 3400 (OH), 1720 (-C(OH)CO_2CH_3), 1715 (CO_2CH_3), 1340 (NO_2); nmr (deuteriochloroform): 3.40 (s, 3H, CO_2CH_3), 3.60 (s, 2H, $CH_2CO_2CH_3$), 3.88 (s, 3H, CO_2CH_3), 3.93 (s, 6H, 2 × OCH_3), 7.33 (s, 1H, 8-H), 7.92 (s, 1H, 9-H), 9.10 (s, 1H, OH)
6b	202-204	$C_{20}H_{22}N_2O_9$	55.17 55.40	5.05 5.00	6.43 6.25	ms: 435 (M^+); ir: 3400 (OH, 1740 (-C(OH)CO_2CH_3), 1725 (CO_2CH_3), 1340 (NO_2); nmr (deuteriochloroform): 1.20-1.80 (m, 6H, 2 × OCH_2CH_3), 3.40 (s, 3H, CO_2CH_3), 3.70 (s, 2H, $-CH_2CO_2CH_3$), 3.90 (s, 3H, CO_2CH_3), 4.25 (q, 4H, 2 × OCH_2CH_3), 7.48 (s, 1H, C-8H), 8.12 (s, 1H, C-9H), 8.82 (s, 1H, OH)

3-Cyano-3,4-dihydroquinolin-2(1*H*)-one (**3a**), 3-Cyano-4-methyl-3,4-dihydroquinolin-2(1*H*)-one (**3b**), 3-Cyano-4-ethyl-3,4-dihydroquinolin-2(1*H*)-one (**3c**) and the Corresponding 6-Methoxy-derivatives **3d**, **3e** and **3f**.

General Procedure.

The 1,4-dihydroquinoline derivatives **2a-2f** were allowed to stand at room temperature (30-35°) for 24-48 hours and the complete conversion was monitored by tlc. The 3,4-dihydrocarbostyril derivatives **3a-3f** so obtained were recrystallized from methanol.

3-Cyanoquinolin-2(1*H*)-one (**4**).

A mixture of **1a** (0.001 mole) and aqueous hydrochloric acid (20 ml of 30%, v/v) in methanol (10 ml) was refluxed under constant stirring for 4 hours. The reaction mixture was cooled and the separated solid so obtained was filtered and recrystallized from acetone to yield **4** as a colourless solid.

Alternatively, **4** was prepared from **3a**. To a well stirred solution of **3a** (0.001 mole) in xylene (15 ml) was added in three equal portions manganic acetate (0.002 mole) and the suspension was refluxed under stirring for 4 hours. The separated manganous salt was filtered off and the filtrate concentrated to furnish **4** as solid.

2-Chloro-6,7-dialkoxy-3-formyl-8-nitroquinolines **5a-5b**.

These were prepared by the method reported in the literature [4].

6,7-Dialkoxy-2,3-dicarbomethoxy-2-hydroxy-5-nitrocyclopenta[*b*]quinolines **6a-6b**.

A mixture of the appropriately substituted nitroaldehyde (**5**, 0.01 mole), methylthioglycolate (0.02 mole) and anhydrous potassium carbonate (0.02 mole) in dimethyl formamide (20 ml) was stirred for 8 hours at room temperature (30-35°). Dilution of the reaction mixture with water (50 ml) furnished a solid which was filtered and washed with water. Column chromatography of the crude solid over silica gel and elution with

chloroform:ethyl acetate mixture (60:40) yielded **6a-6b** as crystalline solids.

REFERENCES AND NOTES

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