A New Facile Synthesis of Benzo[*c*]acridines

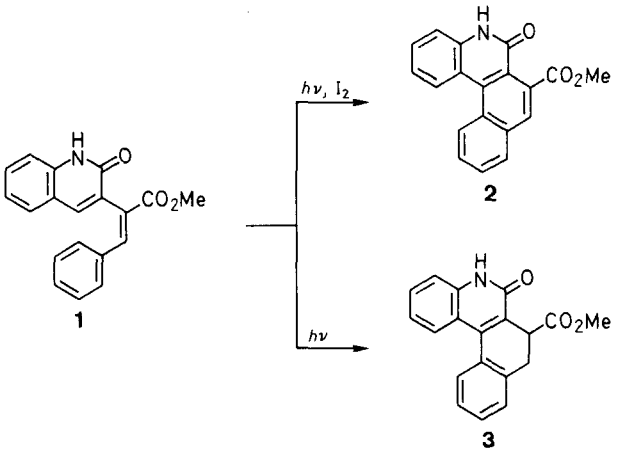
L. Jayabalan, P. Shanmugam*
Department of Chemistry, Bharathiar University, Coimbatore-641 046, India

A photochemical synthesis of benzo[c]acridines using 2-chloro-3-(1-carboxy-2-phenylethenyl)-4-quinolinones as precursors is reported. The precursors quinolinones are obtained from 4-hydroxy-2-quinolinone-3-acetic acid.

The pharmacological properties such as antimalarial,[1] carcinogenic,[2-5] anticarcinogenic,[2-5] and antiamebic[6] activities of benzo[c]acridine derivatives have stimulated investigation of the synthesis of these compounds.[7-10] The known syntheses involve the annulation of a quinoline moiety to a naphthalene ring, the new ring formed in this process being the pyridine ring. These methods are applicable only to a few derivatives and the yields obtained are generally poor.

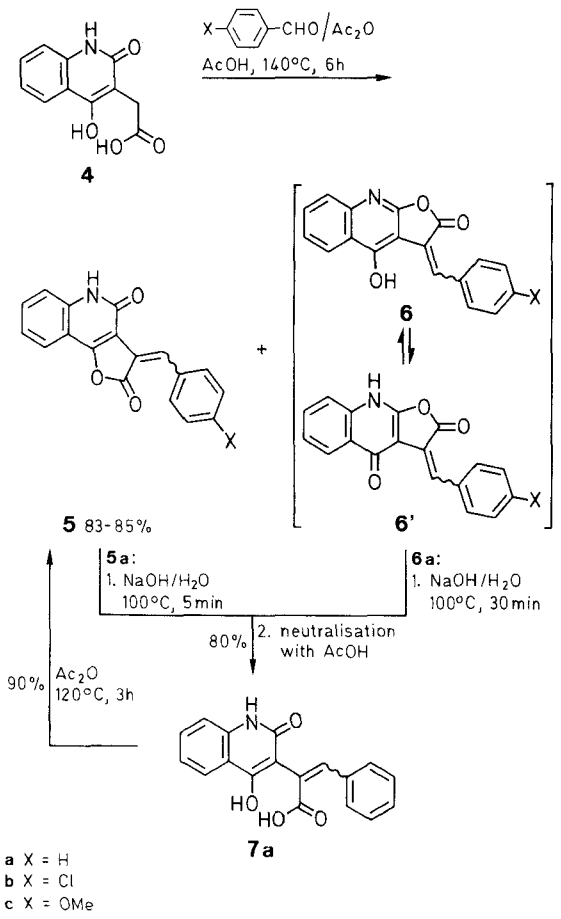
We now present a different synthesis of the benzo-[*c*]acridine system. The key precursor chosen for our strategy is a 3-styryl-4-quinolinone such as **11'a** which may be expected to undergo photolytical peri-ring closure at C-2 to give the benzo[*c*]acridine system, unlike the 3-styryl-2-quinolinones **1** which, due to fixation of the 3,4-double bond, undergo photocyclization only at C-4 to give the benzo[*k*]phenanthridine system[11,12] (eg., **2** and **3**).

Heating a mixture of benzaldehyde, 4-hydroxy-2-quinolinone-3-acetic acid **(4)**,[13] acetic anhydride, and acetic acid gave a yellow crystalline solid in 85% yield. Its

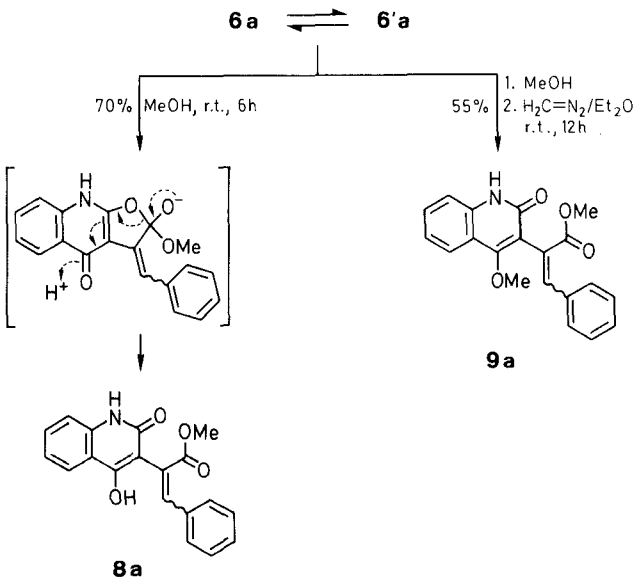


IR spectrum exhibited two bands in the carbonyl region at $\nu = 1775$ and 1650 cm^{-1}, ascribable to a lactone and a 2-quinolinone[14] moiety, respectively. The failure of this product to react with diazomethane and its ^{1}H-NMR spectrum fully attested the assigned angular benzylidene-lactone structure **5a**. The filtrate obtained upon isolation of **5a** from the reaction mixture was evaporated to give a gummy mass to which was assigned the structure of the linear lactone **6a** (⇌**6'a**) on the basis of its IR spectrum which exhibited, in addition to the lactone carbonyl band

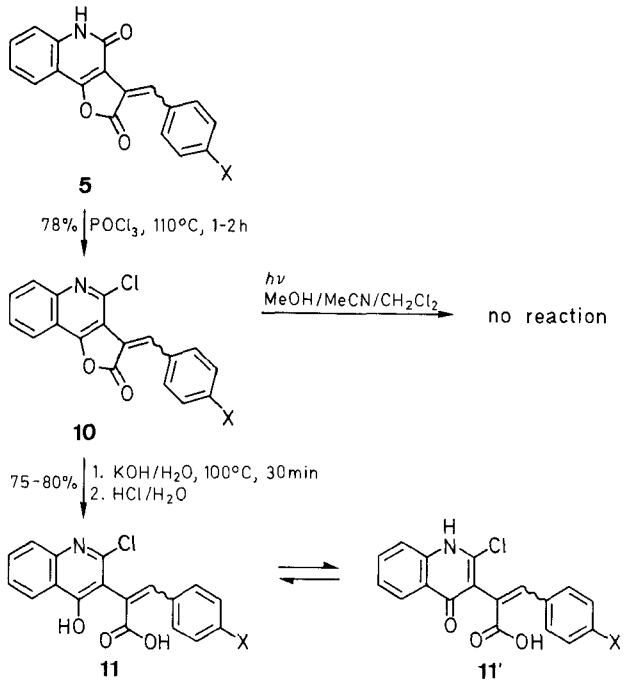
at $\nu = 1750\,cm^{-1}$, a band at $\nu = 1638\,cm^{-1}$ ascribable[14] to the 4-quinolinone moiety in **6'a**. As expected, both lactones **5a** and **6a** were cleaved to the acid **7** on digestion with alkali followed by neutralization with acetic acid. Compound **7** was readily reconverted into lactone **5a** when heated with acetic anhydride.



A characteristic difference between **5a** and **6a** is that **5a** remains unchanged even on prolonged boiling with methanol whereas **6a** readily dissolves in methanol with lactone-ring cleavage and esterification to give product **8a**. Upon treatment with methanol/ethereal diazomethane, compound **6a** is converted into the ring-cleaved methoxy ester **9a**.

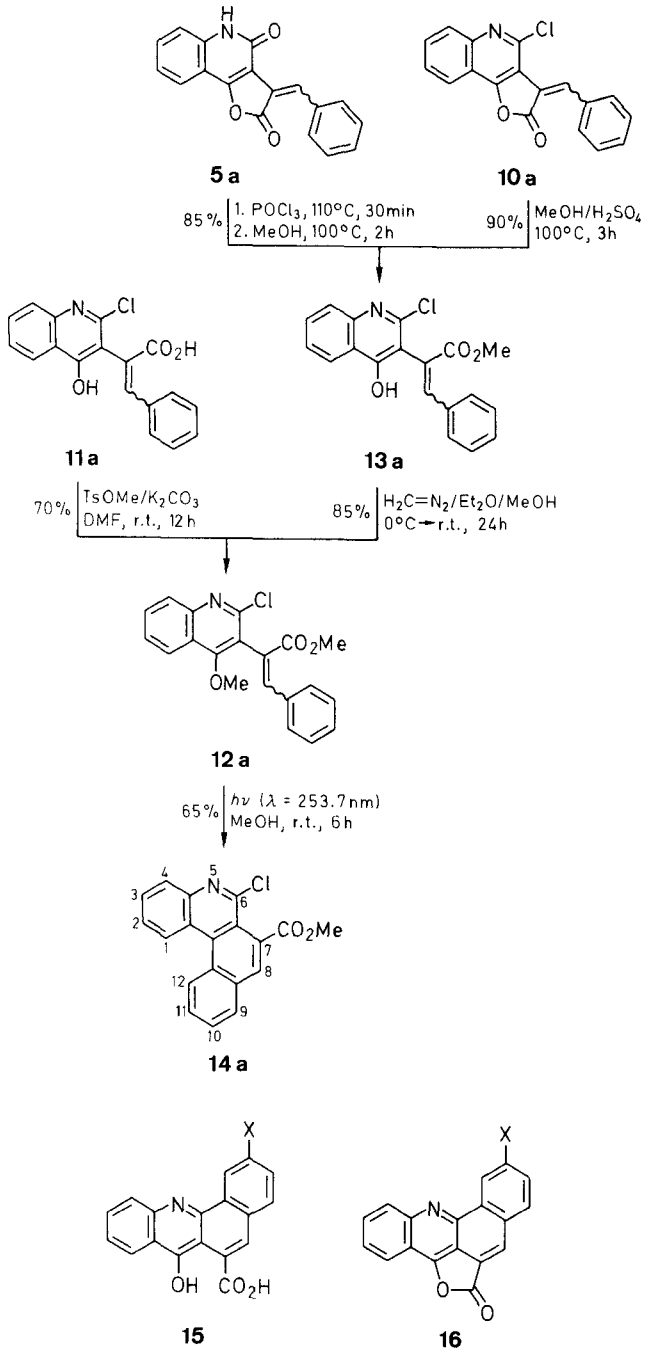


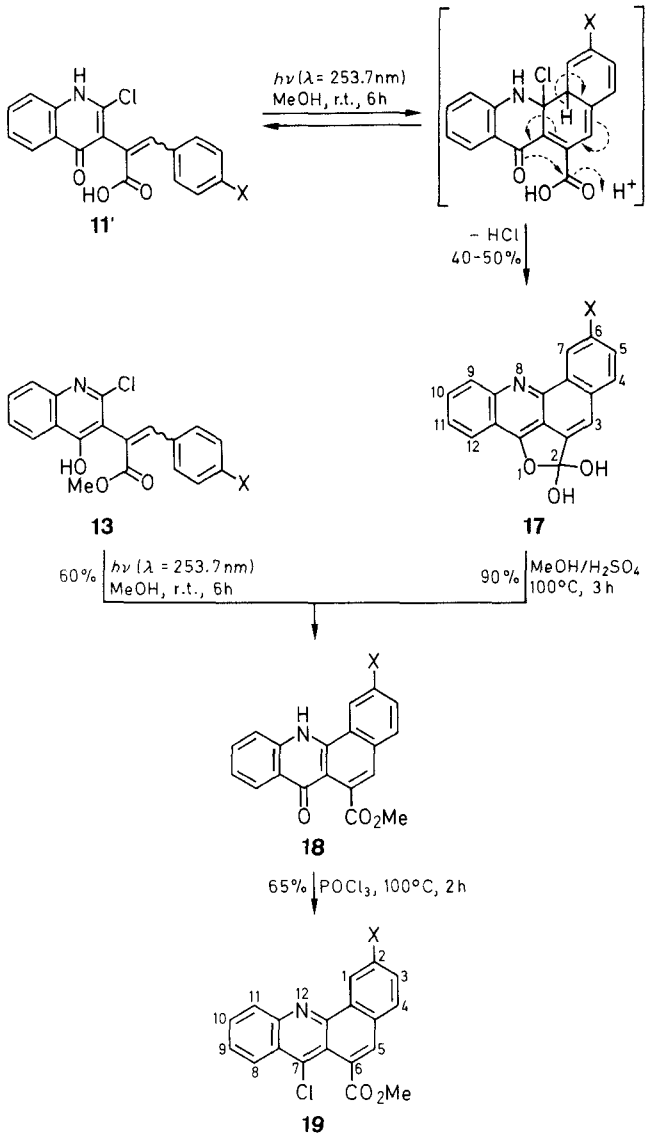
The envisaged synthon **11'a** was obtained from the 2-quinolinone **5a** by brief treatment with phosphoryl chloride, heating of the resultant lactone **10a** with 15% aqueous potassium hydroxide, and acidification.



Before proceeding with the photocyclization of **11a** (⇌**11'a**), we investigated the photobehaviour of **10a**. This compound was recovered unchanged even on prolonged irradiation in methanol or other solvents (MeCN, CH_2Cl_2) at $\nu = 253.7$ nm using a Rayonet Photochemical Reactor (RPR model-208). However, the 4-methoxy compound **12a**, obtained from **5a** or **10a** via **13a** or from **11'a**, readily underwent photocyclization in methanol under the same conditions. The product obtained was identified as the known benzo[*k*]phenanthridine **14a**,[11] resulting from an eliminative photocyclization[15] involving the 4-methoxy group.

We then tried to obtain the title system by irradiating a methanol solution of **11a**⇌**11'a** under the same conditions. While the irradiation proceeded, a crystalline product separated out and its formation was complete during after six hours. This product which was expected to be the free hydroxy acid **15a** or its lactone **16a**, was not soluble in aqueous sodium hydrogen carbonate even on heating. Its IR spectrum did not show any band in the carbonyl region; there was only a compact group of peaks in the OH region. The mass spectrum showed the base peak at $m/z = 271$ (100%), which corresponds to lactone **16a**, and a very low peak (1%) at $m/z = 289$, which probably corresponds to the lactone hydrate **17a**. The element analysis of this product (dried at 100°C) corresponded only fairly to **17a** (C + 0.81, H − 0.48). Product





17a is only little soluble in the usual spectral solvents. Its ^{1}H-NMR spectrum in hot DMSO-d_6 showed the individual singlets of the two hydroxy protons at $\delta = 11.87$ (sharp) and at $\delta = 12.82$ (fairly broad), respectively. These facts led us to surmise the mechanistic pathway outlined in the last Scheme.

However, on boiling in dry methanol containing a catalytic amount of concentrated sulfuric acid, product **17a** was readily converted into benzo[*c*]acridanone **18a**, the structure of which was confirmed by its spectral characteristics and analytical data. Product **18a** was identical with the product obtained by photolysis of **13a**. Further proof of the structure **18a** was obtained by analysing the crystalline colorless compound **19a** which was formed on treatment of **18a** with phosphoryl chloride.

Performance of the reaction sequence with 4-chloro- and 4-methoxybenzaldehyde gave the corresponding benzo[*c*]acridines **19b,c**. The characteristic low-field absorption[16,17] of the proton at C-1 of the benzo[*c*]acridines system is discernable in the ^{1}H-NMR spectra of **17a–c**, **18a–c**, and **19a–c**.

The fact that the photocyclization product formed from **11a–c** is isolated as the *gem*-diol **17a–c** and not as the dehydrated product **16** may be rationalized on the basis of the I-strain concept.[18] The formation of the hydrate ($sp^2 \rightarrow sp^3$) relieves some of the I-strain of the lactone carbonyl group in **16** which has to assume an angle of $\sim 90°$ to be in consonance with the ring angle on the adjacent oxygen atom.

3-Benzylidene-2,4-dioxo-2,3,4,5-tetrahydrofuro[3,2-*c*]quinolines 5a–c; General Procedure:

A mixture of 4-hydroxy-2-quinolinone-3-acetic acid[13] (**4**; 8.76 g, 0.04 mol), AcOH (20 mL), Ac_2O (25 mL), and a benzaldehyde (0.45 mol) is heated at 140 °C (oil bath) for 6 h. After cooling, the precipitated angular lactone **5** is isolated, washed with $CHCl_3$ (100 mL), dried, and recrystallized from EtOH as a yellow crystalline powder (see Table).

Table. Compounds **5–19** Prepared

Product	Yield (%)	mp[a] (°C) (solvent)	Molecular Formula[b] or Lit. mp	MS[c] m/z (M^+)	IR[d] (KBr) ν (cm^{-1})	^{1}H-NMR[e] (solvent/TMS) δ, J(Hz)
5a	85	> 300 (EtOH)	$C_{18}H_{11}NO_3$ (289.3)	289	2800, 1775, 1650	(DMSO-d_6): 7.20–7.82 (m, 8H$_{arom}$), 8.14 (d, 1H, 5-H), 8.46 (s, 1H$_{olefin}$), 12.16 (s, 1H, NH)
5b	85	> 300 (EtOH)	$C_{18}H_{10}ClNO_3$ (323.7)	323	2810, 1780, 1655	(DMSO-d_6): 7.36–7.84 (m, 7H$_{arom}$), 8.2 (d, 1H, 5-H), 8.4 (s, 1H$_{olefin}$), 12.16 (s, 1H, NH)
5c	83	> 300 (EtOH)	$C_{19}H_{13}NO_4$ (319.3)	319	2810, 1770, 1655	(DMSO-d_6): 3.9 (s, 3H, OCH_3), 7.06–7.82 (m, 7H$_{arom}$), 8.27 (d, 1H, 5-H), 8.46 (s, 1H$_{olefin}$), 12.1 (s, 1H, NH)
6a (⇌ **6'a**)	5		gummy mass		($CHCl_3$): 1750, 1638	($CDCl_3$): 7.3–8.2 (m, 7H$_{arom}$), 8.20 (m, 2H, 5-H, 8-H), 8.7 (s, 1H$_{olefin}$), 10 (s, 1H, OH)
7a	80	> 300 (EtOH)	$C_{18}H_{13}NO_4$ (307.2)	307	3310–2720 (br), 1670, 1640	(DMSO-d_6): 6.93 (s, 1H$_{olefin}$), 7.01–7.85 (m, 7H$_{arom}$), 7.98 (d, 1H, 8-H), 8.15 (d, 1H, 5-H), 8.47 (s, 1H, OH), 11.43 (s, 1H, CO_2H), 12.47 (s, 1H, NH)
8a	70	182 (dec) (MeOH)	$C_{19}H_{15}NO_4$ (321.3)	321	3350–3150 (br), 2950, 1710, 1650	(DMSO-d_6): 3.85 (s, 3H, CO_2CH_3), 7.52 (s, 1H$_{olefin}$), 7.32–8.15 (m, 8H$_{arom}$), 8.2 (d, 1H, 5-H), 8.75 (br s, 1H, OH), 12.1 (br s, 1H, NH)
9a	55	234 (MeOH)	$C_{20}H_{17}NO_4$ (335.3)	335	3510–3400 (br), 1705, 1660	(DMSO-d_6): 3.75 (s, 3H, OCH_3), 4.0 (s, 3H, CO_2CH_3), 7.1 (s, 1H$_{olefin}$), 7.3–8.4 (m, 9H$_{arom}$), 9.7 (br s, 1H, NH)
10a	75	220 (C_6H_6)	$C_{18}H_{10}ClNO_2$ (307.7)	307	1775, 1625	($CDCl_3$): 8.7 (s, 1H$_{olefin}$), 7.3–8.3 (m, 9H$_{arom}$)
10b	78	230–232 (C_6H_6)	$C_{18}H_9Cl_2NO_2$ (342.2)	341	1780, 1630	(DMSO-d_6): 8.55 (s, 1H$_{olefin}$), 7.4–8.2 (m, 8H$_{arom}$)
10c	80	223–225 (C_6H_6)	$C_{19}H_{12}ClNO_3$ (337.75)	337	1770, 1630	(DMSO-d_6): 3.8 (s, 3H, OCH_3), 8.55 (s, 1H$_{olefin}$), 7.2–8.3 (m, 8H$_{arom}$)
11a (⇌ **11'a**)	76	272 (dec) (C_6H_6/MeOH, 3 : 1)	$C_{18}H_{12}ClNO_3$ (325.7)	325	3280–3220 (br), 1700, 1630	(DMSO-d_6): 7.0–7.8 (m, 10H$_{arom}$, OH), 8.1 (d, 1H, 5-H), 12.85 [br s, 1H, CO_2H (D_2O-exchangeable)]
11b (⇌ **11'b**)	80	> 300 (C_6H_6/MeOH, 3 : 1)	$C_{18}H_{11}Cl_2NO_3$ (360.2)	359	3280–3220 (br), 1700, 1630	(DMSO-d_6): 6.99–7.73 (m, 9H$_{arom}$, OH), 8.09 (d, 1H, 5-H), 12.85 [br s, 1H, CO_2H (D_2O-exchangeable)]
11c (⇌ **11'c**)	82	> 300 (C_6H_6/MeOH, 3 : 1)	$C_{19}H_{14}ClNO_4$ (355.8)	355	3280–3220 (br), 1695, 1625	(DMSO-d_6): 3.81 (s, 3H, OCH_3), 6.88–7.33 (m, 9H$_{arom}$, OH), 8.09 (d, 1H, 5-H), 12.85 [br s, 1H, CO_2H (D_2O-exchangeable)]
12a	70	115 (PE)[f]	$C_{20}H_{16}ClNO_3$ (353.8)	353	1705, 1610	($CDCl_3$): 3.8 (s, 3H, OCH_3), 4.2 (s, 3H, CO_2CH_3), 7.2 (s, 1H$_{olefin}$), 7.3–8.1 (m, 8H$_{arom}$), 8.3 (d, 1H, J = 9, 5-H)
13a	85	157 (C_6H_6)	$C_{19}H_{14}ClNO_3$ (339.8)	339	3490–3110 (br), 1710, 1625	(DMSO-d_6): 3.6 (s, 3H, CO_2CH_3), 7.13 (s, 1H$_{olefin}$), 7.25–8.0 (m, 9H$_{arom}$, OH), 8.08 (d, 1H, 5-H)
14a	65	152 (PE)[f]	150–152[11]	321	1730	($CDCl_3$): 4.0 (s, 3H, CO_2CH_3), 7.4–8.4 (m, 7H$_{arom}$), 8.7–9.0 (m, 2H, 1-H, 4-H)
17a	40	> 300	$C_{18}H_{11}NO_3$ (289.3)	289 (1%) [271 (100%)]	3320–2920 (series of peaks), 1665 (shoulder), 1630 (s)	(DMSO-d_6): 7.4 (m, 1H, 11-H), 7.65 (s, 1H, 3-H), 7.83 (m, 3H, 6-, 5-, 10-H), 8.05 (d, 1H, 4-H), 8.12 (dd, 1H, 12-H), 8.26 (d, 1H, 9-H), 9.02 (dd, 1H, 7-H), 11.87 (s, 1H, OH), 12.82 (br s, 1H, OH)
17b	42	> 300	$C_{18}H_{10}ClNO_3$ (323.7)	323 (2.5%) [305 (100%)]	3300–2900 (series of peaks), 1660 (shoulder), 1630 (s)	(DMSO-d_6): 7.33 (d, 1H, 11-H), 7.43 (d, 1H, 10-H), 7.70 (s, 1H, 3-H), 7.83 (dd, 1H, 5-H), 8.03 (d, 1H, 4-H), 8.2 (d, 1H, 12-H), 8.25 (d, 1H, 9-H), 9.15 (s, 1H, 7-H), 11.87 (s, 1H, OH), 12.88 (br s, 1H, OH)
17c	44	> 300	$C_{19}H_{13}NO_4$ (319.2)	319 (3%) [301 (100%)]	3300–2940 (series of peaks), 1665 (shoulder), 1635 (s)	(DMSO-d_6): 4.08 (s, 3H, OCH_3), 7.4 (m, 1H, 11-H), 7.5 (dd, 1H, 10-H), 7.65 (s, 1H, 3-H), 7.85 (dd, 1H, 5-H), 8.03 (d, 1H, 4-H), 8.10 (d, 1H, 12-H), 8.25 (d, 1H, 9-H), 8.4 (s, 1H, 7-H), 11.98 (s, 1H, OH), 12.8 (br s, 1H, OH)
18a	90	218 (MeOH)	$C_{19}H_{13}NO_3$ (303.2)	303	3560–3290 (br), 1720, 1625	(DMSO-d_6): 4.0 (s, 3H, CO_2CH_3), 7.25–8.07 (m, 7H$_{arom}$), 8.25 (d, 1H, 8-H), 9.0 (m, 1H, 1-H), 11.6 (br s, 1H, NH)
18b	85	> 300 (MeOH)	$C_{19}H_{12}ClNO_3$ (337.75)	337	3475–3250 (br), 1700, 1623	(DMSO-d_6): 3.75 (s, 3H, CO_2CH_3), 7.0–7.9 (m, 6H$_{arom}$), 8.20 (d, 1H, 8-H), 8.75 (m, 1H, 1-H), 11.5 (br s, 1H, NH)

Table. (continued)

Product	Yield (%)	mp[a] (°C) (solvent)	Molecular Formula[b] or Lit. mp	MS[c] m/z (M^+)	IR[d] (KBr) ν(cm^{-1})	^{1}H-NMR[e] (solvent/TMS) δ, J(Hz)
18c	88	> 300 (MeOH)	$C_{20}H_{15}NO_4$ (333.3)	333	3550–3250 (br), 1700, 1625	(DMSO-d_6): 3.75 (s, 3H, OCH_3), 3.95 (s, 3H, CO_2CH_3), 7–7.8 (m, 6H_{arom}), 8.20 (d, 1H, 8-H), 8.40 (d, 1H, 1-H), 11.5 (br s, 1H, NH)
19a	62	154 (PE)[f]	$C_{19}H_{12}ClNO_2$ (321.75)	321	1720	($CDCl_3$): 4.09 (s, 3H, CO_2CH_3), 7.69–7.80 (m, 5H_{arom}), 7.85 (s, 1H, 5-H), 8.36 (d, 1H, J = 10, 8-H), 8.49 (d, 1H, J = 10, 11-H), 9.48 (dd, 1H, J = 10, 2, 1-H)
19b	60	175 (PE/C_6H_6, 3:1)	$C_{19}H_{11}Cl_2NO_2$ (356.2)	355	1700	($CDCl_3$ + DMSO-d_6): 3.98 (s, 3H, CO_2CH_3), 7.7–8.04 (m, 4H_{arom}), 8.09 (s, 1H, 5-H), 8.28 (d, 1H, J = 10, 8-H), 8.39 (d, 1H, J = 10, 11-H), 9.18 (d, 1H, J = 2, 1-H)
19c	65	212 (C_6H_6)	$C_{20}H_{14}ClNO_3$ (351.8)	351	1700	($CDCl_3$ + DMSO-d_6): 3.95 (s, 3H, OCH_3), 4.05 (s, 3H, CO_2CH_3), 7.40–8.01 (m, 4H_{arom}), 8.12 (s, 1H, 5-H), 8.32 (d, 1H, J = 10, 8-H), 8.44 (d, 1H, J = 10, 11-H), 8.79 (d, 1H, J = 2, 1-H)

[a] Uncorrected, measured using a Mettler-FP5 apparatus and a Boetius Microheating Table.
[b] Satisfactory microanalyses obtained: C ±0.23, H ±0.11; except for **17a–c** (see Text).
[c] Recorded on a Jeol JMS-D 300 Mass Spectrometer.
[d] Recorded on a Perkin-Elmer-597 Infrared Spectrophotometer.
[e] Obtained on Varian-T60, Bruker (90 MHz), Varian-Em 390 (90 MHz) and Bruker WH-270 MHz NMR Instruments.
[f] PE = petroleum ether (bp 60–80 °C).

3-(1-Carboxy-2-phenylethenyl)-2,4-dioxo-1,2,3,4-tetrahydroquinoline (7a):

From **6a**: The combined filtrate and $CHCl_3$ washings from the above reaction are washed with 5% aq $NaHCO_3$ (50 mL), 5% aq $NaHSO_3$ (25 mL), and H_2O (2 × 100 mL). The dried (Na_2SO_4) extract is evaporated to give **6a** as a gummy mass. This material is mixed with 2 N aq NaOH (50 mL), the mixture warmed for 5 min, and filtered. The clear filtrate is carefully neutralized with AcOH and the precipitated solid is isolated by suction, dried, and recrystallized from EtOH to give **7a** as a crystalline powder; yield: 0.88 g (8%) (Table).

From **5a**: A mixture of compound **5a** (1.45 g, 0.005 mol) and 2 N aqueous NaOH (100 mL) is heated on a steam bath for 30 min, then filtered. The clear filtrate is carefully neutralized with AcOH. The precipitated solid is isolated by suction, dried, and recrystallized from EtOH; yield: 1.2 g (80%) (Table).

3-Benzylidene-2,4-dioxo-2,3,4,5-tetrahydrofuro[3,2-*c*]quinoline (5a) from 7a:

A mixture of acid **7a** (0.614 g, 0.002 mol) and freshly distilled Ac_2O (15 mL) is heated at 120 °C (oil bath) for 3 h. It is then cooled and the precipitated solid is isolated by suction and washed with 5% aq $NaHCO_3$ (50 mL) and with H_2O (100 mL), dried, and recrystallized from EtOH to give **5a** as a crystalline yellow solid; yield: 0.530 g (85%); mp > 300 °C.

3-(1-Methoxycarbonyl-2-phenylethenyl)-2,4-dioxo-1,2,3,4-tetrahydroquinoline (8a):

The weighed amount of the gummy mass **6a** (0.5 g) is mixed with absolute MeOH (10 mL) and this mixture is stirred at room temperature for 6 h. It is then filtered and MeOH is allowed to evaporate from the filtrate to half of the total volume of the mixture, which is then mixed with ice water (20 mL). The precipitated solid was isolated by suction, collected, dried, and recrystallized from MeOH to give **8a** as a pale yellow solid; yield: 0.4 g (20%) (Table).

4-Methoxy-3-(1-methoxycarbonyl-2-phenylethenyl)-2-oxo-1,2-dihydroquinoline (9a):

A clear solution of the gummy mass **6a** (0.5 g) in MeOH (20 mL) is of nitrosomethylurea) at 0 °C and this mixture is stirred for 24 h at room temperature. Excess diazomethane is then destroyed by the addition of AcOH (3 drops) and the mixture is evaporated. The residue is placed on a column of silica gel (20 cm × 1 cm, 60–120 mesh) and eluted with benzene/EtOAc (2:1) to afford **9a** as dirty white crystalline powder; yield: 0.32 g (55%) (Table).

In the condensation reactions of 4-chloro- and 4-methoxybenzaldehydes with **4**, the yield of the linear lactones (**6b** and **6c**, respectively) is low, and hence further experimentation was not done to recover the quinolinone acids.

3-Benzylidene-4-chloro-2-oxo-2,3-dihydrofuro[3,2-*c*]quinolines 10a–c; General Procedure:

A mixture of the lactone **5a–c** (0.01 mol) with $POCl_3$ (30 mL) is refluxed in an oil bath until a homogeneous solution is obtained, and then for another 20 min. The mixture is cooled and poured onto crushed ice. The solid formed is isolated by suction, washed with H_2O (200 mL), dried, and recrystallized from benzene to give **10a–c** as a yellow crystalline solid.

An analytically pure sample of **10a–c** is obtained by column chromatography over neutral alumina (10 cm × 1 cm, ~ 150 mesh) using petroleum ether (bp 60–80 °C)/benzene (3:1) as eluent (Table).

3-(1-Carboxy-2-phenylethenyl)-2-chloro-4-quinolones 11′a–c (⇌11a–c); General Procedure:

The chloro compound **10a–c** (0.01 mol) is heated with 15% aq KOH (50 mL) on a steam bath for 30 min, and then filtered. The filtrate is cooled and acidified with dilute (1:1) aq HCl. The precipitated acid is isolated by suction and further purified by dissolution in 5% aq $NaHCO_3$ (50 mL) and subsequent acidification with dilute (1:1) aq HCl, isolation, and recrystallization from benzene/MeOH (3:1) to give a pale yellow crystalline powder (Table).

2-Chloro-4-methoxy-3-(1-methoxycarbonyl-2-phenylethenyl)-quinoline (12a):

From **11a⇌11′a**: To a stirred mixture of **11a⇌11′a** (0.877 g, 0.0025 mol) and anhydrous K_2CO_3 (0.690 g, 0.005 mol) in DMF (5 mL) is added methyl *p*-toluenesulfonate (1 mL, 0.0055 mol). The

into H_2O (50 mL) and left aside for 5 h. This mixture is extracted with $CHCl_3$ (2 × 25 mL). The $CHCl_3$ extract is dried (Na_2SO_4) and concentrated, and the residue is column chromatographed on neutral alumina (15 cm × 1 cm, ~ 150 mesh) using petroleum ether (bp 60–80 °C)/benzene (3:1) as eluent to give **12a** as white cubic crystals; yield: 0.66 g (70%) (Table).

From **13a:** A solution of **13a** (0.678 g, 0.002 mol) in MeOH (10 mL) is treated dropwise with ethereal diazomethane (prepared from 3 g of nitrosomethylurea) at 0 °C and stirred at r.t. for 24 h. Excess diazomethane is destroyed by the addition of AcOH (3 drops), the solution is concentrated, and the residue is column chromatographed on neutral alumina (10 cm × 1 cm, ~ 150 mesh) using petroleum ether (bp 60–80 °C)/benzene (3:1) as eluent; yield: 0.60 g (85%); mp 115 °C (petroleum ether). This product is identical with that obtained from **11a**⇌**11'a**.

2-Chloro-4-hydroxy-3-(1-methoxycarbonyl-2-phenylethenyl)-quinoline (13a):

From **5a**: A mixture of compound **5a** (2.89 g, 0.01 mol) and $POCl_3$ (25 mL) is refluxed until **5a** has completely dissolved. Excess $POCl_3$ is then stripped off, the residue is cooled in an ice bath, and MeOH (50 mL) is added dropwise (reflux condenser). The mixture is then refluxed on a steam bath for 2 h. Excess MeOH is removed and the remaining solution is poured into ice water. The precipitated ester **15** is isolated by suction, dried, and recrystallized from benzene/MeOH (3:1) to give a pale yellow crystalline powder; yield: 2.85 g (85%) (Table).

From **10a**: A mixture of compound **10a** (0.307 g, 0.001 mol), absolute MeOH (20 mL), and concentrated H_2SO_4 (0.2 mL) is refluxed on a steam bath for 3 h, then concentrated to 1/3 of its volume, cooled, and poured into ice water (50 mL). The precipitated ester is isolated by suction, dried, and recrystallised from benzene/MeOH (3:1) to give a pale yellow crystalline powder; yield: 0.350 g (90%); mp 157 °C.

6-Chloro-7-methoxycarbonylbenzo[*k*]phenanthridine (14a), 2,2-Dihydroxy-2*H*-benzo[*c*]furo[2,3,4-*mn*]acridines 17a,b,c, and 6-Methoxycarbonyl-7-oxo-7,12-dihydrobenzo[*c*]acridines 18a,b,c; General Photocyclization Procedure:

A solution of the substrate **12a, 11'a,b,c** (⇌**11a,b,c**), or **13a,b,c**, respectively, (1 mmol) in dry MeOH (250 mL) is placed in a quartz tube which is purged with O_2-free dry N_2 for 30 min. It is then irradiated at $\lambda = 253.7$ nm using UV lamps in a Rayonet Preparative Photoreactor (RPR Model-208) for 6 h. In the case of substrates **11'a–c** the products **17a–c** are obtained as crystalline mass which precipitates from the solution. The mixture is cooled and the solid product isolated by suction, washed with MeOH, and dried. In the case of substrates **12a** and **13a–c**, the products **14a** and **18a–c**, respectively, are isolated by evaporation of the mixture and column chromatography of the residue on silica gel (column 15 cm × 1 cm; 60–120 mesh) using petroleum ether (bp 60–80 °C)/benzene (3:1; for **12a**) or benzene/EtOAc (2:1; for **18a,b,c**) as eluents (Table).

6-Methoxycarbonyl-7-oxo-7,12-dihydrobenzo[*c*]acridines 18a,b,c from 17a,b,c; General Procedure:

The *gem*-diol **17a,b,c** (2 mmol) is heated in a large excess of boiling MeOH (20 mL) containing traces of conc. H_2SO_4 (2–3 drops) for 3 h. Then, the excess MeOH is distilled off and the residue is poured into ice water (25 mL). The precipitated ester **18a,b,c** is isolated by suction, washed with H_2O (100 mL), and recrystallized from MeOH (Table).

7-Chloro-6-methoxycarbonylbenzo[*c*]acridines 19a,b,c; General Procedure:

A mixture of compound **18a,b,c** (0.2 mmol) and $POCl_3$ (2 mL) is heated on a steam bath for 3 h, then cooled, and poured into ice water. The resultant mixture is extracted with $CHCl_3$ (2 × 10 mL), dried (Na_2SO_4), and evaporated. The residue is column chromatographed on neutral alumina (5 cm × 1 cm; ~ 150 mesh) using petroleum ether (bp 60–80 °C)/benzene (3:1) as eluent to afford products **19a,b,c** as needles (Table).

We acknowledge the UGC (New Delhi) for the award of a research fellowship to one of us (LJ). We thank Dr. N. P. Damodaran and Mr. A. K. Vimalan, International Institute for Ayurveda, Mr. M. Palanisamy, Technician, Department of Chemistry, Bharathiar University, Coimbatore for their help in recording IR spectra. Thanks are due to RSIC, Lucknow, and sophisticated Instruments Facility, I.I.Sc., Bangalore, for providing mass and NMR spectra of some of the samples.

Received: 31 August 1989; revised: 12 April 1990

(1) Rosowsky, A.; Chaykovsky, M.; Yeager, S.A.; Amand, R.A.; Lin, M.; Modest, E.J. *J. Med. Chem.* **1971**, *8*, 809.
(2) Lacassagne, A.; Buu-Hoi, N.P.; Daudel, R.; Zajdela, F. *Adv. Cancer Res.* **1956**, *4*, 315.
(3) Lacassagne, A.; Zajdela, F.; Buu-Hoi, N.P. *C.R. Soc. Biol.* **1958**, *152*, 1312.
(4) Buu-Hoi, N.P.; Lacassagne, A.; Lecocq, J.; Fudali, G. *C.R. Soc. Biol.* **1945**, *139*, 485.
(5) Lewis, M.R.; Goland, P.P. *Amer. J. Med. Sci.* **1948**, *215*, 282.
(6) Radke, R.A. *Gastroenterology* **1959**, *36*, 590.
(7) Robinson, D.A., in: *The Chemistry of Heterocyclic Compounds – Acridines*, Vol. 9, Acheson, R.M., (ed.), Interscience Publishers, New York, 1973, p. 530–538, and references cited therein.
(8) Campbell, N., in: *Rodds Chemistry of Carbon Compounds*, Vol. *IVG*, Coffey, S. (ed.), Elsevier, New York, 1978, p. 75–78. Hepworth, J.D., in: *Rodds Chemistry of Carbon Compounds*, supplement to Vol. *IVG*, Ansell, M.F., (ed.), Elsevier, New York 1987, p. 80–92, and references cited therein.
(9) Ramesh, D.; Kar Gandhi, K.; Chatterjee, B.G.; Ray, J.K. *J. Org. Chem.* **1988**, *53*, 212.
(10) Cortés, E.; Martínez, R.; Avila, J.G., Toscano, R.A. *J. Heterocycl. Chem.* **1988**, *25*, 895.
(11) Arisvaran, V.; Ramesh, M.; Rajendran, S.P.; Shanmugam, P. *Synthesis* **1981**, 821.
(12) Arisvaran, V.; Rajan, R.D.; Shanmugam, P. *Indian J. Chem. Sec. B* **1984**, *23*, 855.
(13) Geissman, T.A.; Cho, A.K. *J. Org. Chem.* **1959**, *24*, 41.
(14) McCorkindale, N.J. *Tetrahedron* **1961**, *14*, 223.
(15) Veeramani, K.; Shanmugam, P. *Indian J. Chem. Sec. B.* **1987**, *26*, 116, and references cited therein.
(16) Van der Donckt, E.; Martin, R.H.; Geerts-Evrard, F. *Tetrahedron* **1964**, *20*, 1495.
(17) Martin, R.H.; Defay, N.; Geerts-Evrard, F.; Bogaert-Verhoogen, D. *Tetrahedron Suppl. 8*, Part-I, **1967**, 181.
(18) March, J. *Advanced Organic Chemistry*, 3rd ed., Wiley Interscience, New York, 1985, p. 783–784.