Pergamon

*Tetrahedron*, Vol. 53, No. 12, pp. 4511-4520, 1997

0040-4020/97 $17.00 + 0.00

PII: S0040-4020(97)00125-7

# Conversion of a 4-Quinolone into a 1,6-Diazaphenalene

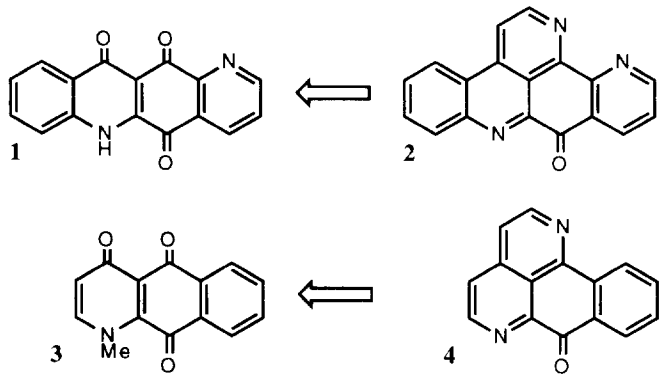
**Lidia Feliu[a], Wadi Ajana[a], Mercedes Alvarez,[a]* and John A. Joule[b]***

a Laboratori de Química Orgànica, Facultat de Farmàcia, Universitat de Barcelona, E 08028 Barcelona, malvarez@far.ub.es

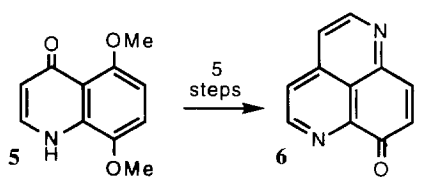
b Chemistry Department, The University of Manchester, Manchester M13 9PL, U.K., j.a.joule@man.ac.uk

***Abstract***: 5,8-Dimethoxyquinolin-4-one has been transformed in five steps into a 7-oxo-1,6-diazaphenalene and in 4 steps into 6-aza-1-oxaphenalene. © 1997 Elsevier Science Ltd.

Our strategy[1] for the construction of alkaloids such as dercitine[2] and related substances,[3] kuanoniamine A, and related substances,[4] shermilamine A[5] and related products,[6,7] and ascididemine[8] and related alkaloids,[9] in all of which one can discern a pyrido[2,3,4-*kl*]acridine unit, culminates in the requirement that the 'top' pyridine ring be added to a quinolin-4-one-quinone unit. For example **1**[1] needs the addition of two carbons and a nitrogen to arrive at ascididemine, **2**. An exactly analogous pyridine ring anellation, together with an *N*-demethylation, would be required for the conversion of **3**[10] into sampangine,[11] **4**.



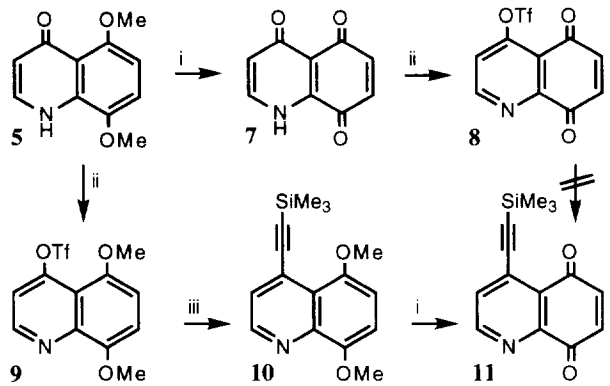
We describe here the achievement of this type of transformation exemplified by the conversion of 5,8-dimethoxyquinolin-4-one **5** *via* a quinone into 7-oxo-1,6-diazaphenalene, **6**.[12]



Knowing that intermediates such as **1** and **3** are available to us from previous work,[1,10] we firstly examined the possibility of utilising the quinolin-4-one-quinone **7** as a model for the addition of an additional pyridine ring. It was the plan to introduce a two-carbon $CH_2CH{=}O$ synthon at the quinoline 4-position by coupling to a suitable derivative of the quinolin-4-one, and then to bring about pyridine ring formation by interaction of ammonia with the aldehyde-equivalent carbon and the C-5 quinone carbonyl group.

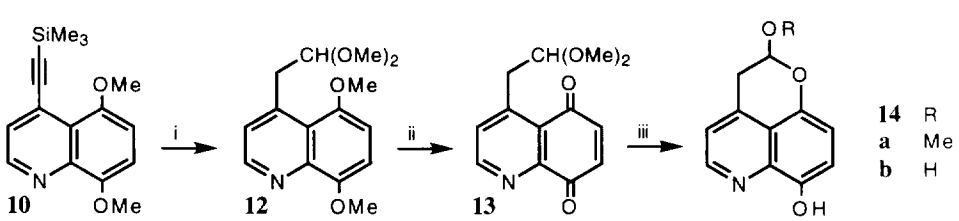
Oxidation of 5,8-dimethoxyquinolin-4-one[13] **5** with ceric ammonium nitrate (CAN) produced **7**[14] in modest yield. Reaction of the quinolin-4-one-quinone with trifluoromethanesulfonic anhydride ($Tf_2O$) converted it into the quinone-triflate **8**, but again in only modest yield. We were finally forced to abandon this route however, when conditions could not be found to bring about palladium(0)-catalysed coupling of this quinone-triflate with either of the $CH_2CH{=}O$ synthons, trimethylsilylacetylene or $Bu_3SnCH{=}CHOEt$.[15]

Aware of examples of the coupling of 5,8-dimethoxyquinolin-4-ol triflate[16] and of 6-bromo-5,8-dimethoxyquinolin-4-ol triflate[17] with aryltin reagents we turned to the possibility of using 6,7-dimethoxyquinolin-4-ol triflate **9**. Formation of the triflate from **5** proceeded efficiently, and now we found that highly effective coupling could be achieved with trimethylsilylacetylene producing alkyne **10**, oxidation with CAN then giving the quinone **11** (Scheme 1).



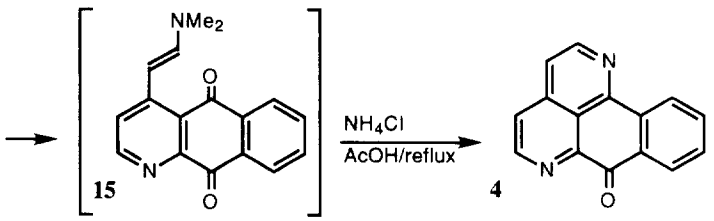
**Scheme 1**
**Reagents**: i, CAN, MeCN, $H_2O$, 20 °C (58% **7**; 87% **11**); ii, $Tf_2O$, DMAP, 2,6-lutidine, $CH_2Cl_2$ 2h at 0 °C → 20 °C (35% **8**; 90% **9**); iii, $HC{\equiv}CSiMe_3$, $Pd(dba)_3.CHCl_3$, $Ph_3P$, *i*$Pr_2NEt$, DMF, 20 °C (90%).

The silyl-alkyne **10** was smoothly converted into the aldehyde acetal **12** by reaction with NaOMe and this too could be converted into a quinone, **13**, with CAN. Unfortunately, on exposure to hydroxylamine hydrochloride only the dihydro-6-aza-1-oxaphenalene **14a** was obtained and in an attempt to deprotect the aldehyde, as well as a trace of **14a**, the cyclic hemiacetal **14b** was obtained on reaction with aq HCl.



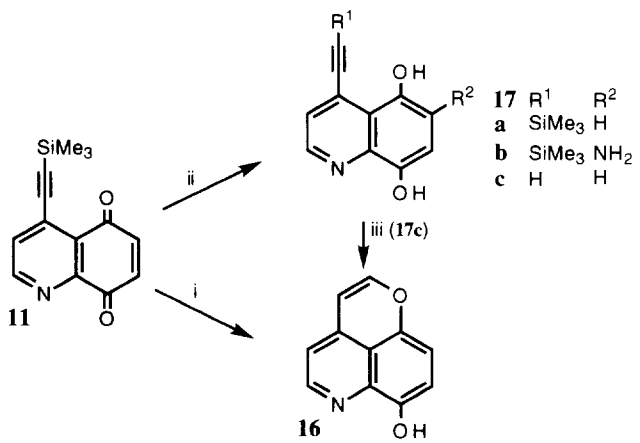
**Scheme 2**
**Reagents**: i, NaOMe, MeOH, DMF, 60 °C (77%); ii, CAN, MeCN, $H_2O$, 20 °C (60%); iii, $H_2NOH.HCl$, MeOH, reflux (**14a**, 21%); aq 2N HCl, $CH_2Cl_2$, reflux (**14a**, 2%, **14b**, 25%).

We next turned to the possibility that the alkynyl-quinone would react with ammonia, by addition to the triple bond as observed for methoxide, the resulting primary enamine then to undergo a cyclisation producing the target system. We were encouraged in this aspiration by reports[18] of four examples of the cyclisation of enamines such as **15**, in which pyridine ring formation took place with ammonium chloride in hot acetic acid (Scheme 3: **15** gave **4**).




**Scheme 3**

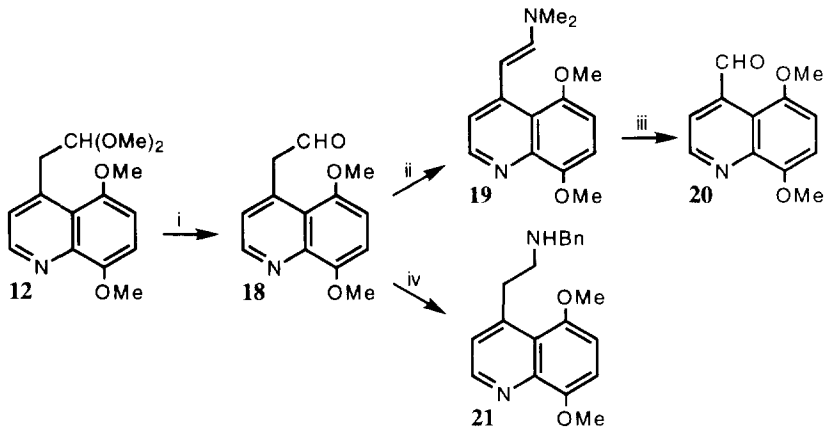
When the alkyne **11** was treated with $NH_4Cl$ in AcOH, conversion to the pyrano[4,3,2-*de*]quinoline **16** took place; no trace of the desired 1,6-diazaphenalene could be found. This stands in distinct contrast to the reported[18] conversions of quinones with $NH_4Cl$/AcOH, into *pyridine*-containing products, as illustrated in Scheme 3. The reaction of **11** with $NH_3$ was more complex: from the product mixture, three compounds could be isolated and characterised, **17a-c**, all of which were quinoline-5,8-diols. Once again, no trace of a 1,6-diazaphenalene could be found. Acid converted **17c** quantitatively into **16**. These transformations of **11** are summarised in Scheme 4.




**Scheme 4**
**Reagents**: i, $NH_4Cl$, AcOH, reflux (43%); ii, $NH_3$, THF, -78 → 20 °C (18% **17a**; 22% **17b**; 23% **17c**); iii. TsOH, *o*-$Cl_2C_6H_4$, reflux (100%).

The location of the amino group in **17b** was established by long distance H-C correlation (HMBC): the correlation of the signal at δ 8.86, for H-2 and the signal at δ 6.14, for H-7 with the carbon signal at 149.7 for C-8a places the amino group at C-6. The formation of **17b** simply represents conjugate addition of ammonia to the quinone, then tautomerisation. Comparable regiochemistry has been reported[18b,c] in the addition of

arylamines to quinoline-5,8-quinone in the presence of cerium(3) chloride, though it was attributed[18b] to complexation of metal ion to ring nitrogen and adjacent carbonyl oxygen. The formation of the two reduced derivatives, **17a** and **17c** probably represents reduction by the particularly easily oxidised amino-quinol **17b**. thus forming an amino-quinone which was not isolated.

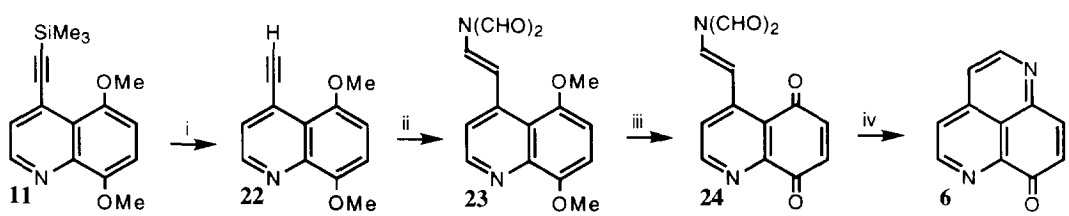



**Scheme 5**
**Reagents**: i, aq 2N HCl, $CH_2Cl_2$, reflux (87%); ii, $Me_2NH.HCl$, MeOH, reflux (94%); iii, CAN, MeCN, $H_2O$, 20 °C (24%); iv, $BnNH_2.HCl$, *i*PrOH, reflux then $NaB(CN)H_3$, rt (49%).

In an attempt to move even closer to the literature precedent (Scheme 3) we converted acetal **12** into the corresponding aldehyde **18** and this then into the enamine **19**. However, this route was cut short when we found that CAN treatment of **19** led not to quinone formation, but to oxidative cleavage of the enamine double bond, simply giving the quinoline aldehyde **20** (Scheme 5).

To avoid the formation of products with an oxygen-containing heterocyclic ring (Schemes 2 and 5), it seemed that it would be necessary for the two-carbon chain, introduced *via* the coupling, to have the future pyridine ring nitrogen covalently attached to it before attempting the final ring closure. Accordingly, the aldehyde **18** was condensed with benzylamine, then the imine reduced without isolation giving **21**. The formation of a complex mixture on treatment of **12** with CAN led us to pursue this no further (Scheme 5).

The difficulties were finally overcome by removing the silicon protection from **11**, giving alkyne **22** which was then reacted with $NaN(CHO)_2$[19] generating ene-*bis*-formamide **23** in good yield. CAN oxidation then producing the corresponding quinone **24**, without destroying the ene-*bis*-formamide unit. Finally,




**Scheme 6**
**Reagents**: i, $Bu_4NF.3H_2O$, MeOH, reflux (96%); ii, $2NaN(CHO)_2$, DMF, reflux (75%); iii, CAN, MeCN, $H_2O$ (35%); iv, TFA, MeOH, reflux (31%).

exposure of **24** to trifluoroacetic acid (TFA) in methanol produced the target tricycle **6** (Scheme 6), with identical IR and $^1$H-NMR spectroscopic properties to those reported for this compound prepared[12] by singlet oxygen oxidation of the parent heterocycle.[20]

## EXPERIMENTAL SECTION

Melting points were determined in a capillary tube and are uncorrected. TLC was carried out on $SiO_2$ (silica Gel 60 $F_{254}$, Merck 0.063-0.200 mm) and spots were located with iodoplatinate reagent or UV light. Column chromatography was carried out on $SiO_2$ (silica Gel 60 SDS 0.060-0.2 mm). Flash chromatography was carried out on $SiO_2$ (silica Gel 60 A CC (Merck). Organic extracts were dried over anhydrous $Na_2SO_4$, and solutions were evaporated under reduced pressure with a rotatory evaporator. IR spectra were performed on a Nicolet 205 FT-IR and peaks are given in cm$^{-1}$. NMR spectra were measured with Varian Gemini-200 (200 MHz), Varian Gemini-300 (300 MHz) and Varian VXR-500 (500 MHz) spectrometers; data are given in $\delta$ referred to TMS with $^1$H-NMR coupling constants ($J$) in Hz. Mass spectra were measured in the electron impact (EI) and chemical ionisation (CI) modes with a Hewlett-Packard model 5989A; ions are recorded as *m/z* with percentage abundances relative to the molecular ion given in parentheses. Elemental analyses were performed on a Carlo Erba Fisons EA-1108 in the Serveis Científico-Tècnics de la Universitat de Barcelona.

**4,5,8(1*H*)-Quinolinetrione (7).** A solution of CAN (5.7 g, 9.7 mmol) in $H_2O$ (25 ml) was added to a solution of **5** (1 g, 4.9 mmol) in MeCN (50 ml). The reaction mixture became dark and was stirred for 10 min at rt, $H_2O$ (25 ml) was added and the solution was extracted with $CH_2Cl_2$. The organic solution was dried and evaporated affording **7** as a solid (lit[14] mp >300 °C) (0.5 g, 58%): IR (KBr): 3550, 1667, 1625, 1567. $^1$H-NMR ($CDCl_3$, 300 MHz): 7.03 (d, $J$ = 10.4, 1H); 7.11 (d, $J$ = 10.4, 1H); 7.14 (d, $J$ = 5.8, 1H); 7.75 (d, $J$ = 5.8, 1H). $^{13}$C-NMR ($CDCl_3$, 70.4 MHz): 114.9 (s); 117.2 (d); 137.6 (2d); 139.6 (d); 148.2 (s); 166.7 (s); 182.6 (s); 190.9 (s). MS (EI): 176 ($MH^+$, 21), 175 ($M^+$, 100), 147 (20), 119 (41).

**4-Hydroxy-5,8-quinolinedione triflate (8).** To a solution of **7** (0.5 g, 2.8 mmol) in dry $CH_2Cl_2$ (25 ml) under $N_2$ was added successively DMAP (70 mg, 0.6 mmol), 2,6-lutidine (0.5 ml, 4 mmol) and $Tf_2O$ (0.5 ml, 3.4 mmol). The reaction mixture was stirred at 0 °C for 2 h and for 1 h at rt. The organic solution was washed with $H_2O$, dried and evaporated. The residue was purified by column chromatography. Elution with hexane/$CH_2Cl_2$ (3:7) gave **8** (300 mg, 35%) as a gum: $^1$H-NMR ($CDCl_3$, 300 MHz): 7.08 (d, $J$ = 10.5, 1H); 7.21 (d, $J$ = 10.5, 1H); 7.56 (d, $J$ = 5.3, 1H); 9.16 (d, $J$ = 5.3, 1H). $^{13}$CNMR ($CDCl_3$, 70.4 MHz): 121.7 (d); 138.0 (d); 139.0 (d); 156.4 (d).

**5,8-Dimethoxyquinolin-4-ol triflate (9).** To a solution of **5** (400 mg, 1.9 mmol) in $CH_2Cl_2$ (20 ml) under $N_2$ were successively added DMAP (48 mg, 0.4 mmol), 2,6-lutidine (0.3 ml, 2.7 mmol) and $Tf_2O$ (0.4 ml, 2.3 mmol). The reaction mixture was stirred at 0 °C for 2 h and for 1 h at rt. The organic solution was washed with $H_2O$, dried and evaporated. The residue was purified by column chromatography. Elution with hexane/$CH_2Cl_2$ (3:7) gave **9** (593 mg, 90%) as a yellow oil: IR (KBr): 1610, 1430, 1220, 1137. $^1$H-NMR ($CDCl_3$, 300 MHz): 3.98 (s, 3H); 4.07 (s, 3H); 6.93 (d, $J$ = 8.7, 1H); 7.08 (d, $J$ = 8.7, 1H); 7.26 (d, $J$ = 4.6, 1H); 8.95 (d, $J$ = 4.6, 1H). $^{13}$C-NMR ($CDCl_3$, 70.4 MHz): 55.5 (q); 56.2 (q); 106.8 (d); 108.7 (d); 114.2 (d); 115.1 (s); 118.7 (q); 143.2 (s); 147.5 (s); 149.3 (s); 149.8 (d); 152.8 (s). HRMS calcd for $C_{12}H_{10}F_3NO_5S$ 337.0232, found 337.0238.

**5,8-Dimethoxy-4-(trimethylsilylethynyl)quinoline (10).** To a solution of **9** (2.6 g, 7.7 mmol) in dry DMF (20 ml) under $N_2$ were successively added $Pd(dba)_3.CHCl_3$ (0.8 g, 0.8 mmol), $Ph_3P$ (0.7 g, 2.6 mmol), $iPr_2NEt$ (4 ml, 23.1 mmol) and trimethylsilylacetylene (1.6 ml, 11.8 mmol). The mixture was stirred at rt for 4 h. After this time $Et_2O$ (50 ml) was added and the organic solution was washed with $H_2O$, dried and evaporated *in vacuo* to give a residue which was purified by column chromatography. Elution with hexane/$CH_2Cl_2$ (2:3) gave **10** (2 g, 90%) as a yellow solid, mp 118-119 °C ($Et_2O$): IR (KBr): 2240, 1613, 1506, 1471, 1270. $^1$H-NMR ($CDCl_3$, 200 MHz): 0.32 (s, 9H); 3.61 (s, 3H); 3.72 (s, 3H); 6.81 (d, $J$ = 8.8, 1H); 6.94 (d, $J$ = 8.8, 1H); 7.56 (d, $J$ = 4.4, 1H); 8.82 (d, $J$ = 4.4, 1H). $^{13}$C-NMR ($CDCl_3$, 50.3 MHz): -0.2 (q); 55.9 (q); 103.1 (s); 103.7 (s); 106.3 (d); 107.2 (d); 126.8 (s); 127.2 (d); 148.3 (d); 149.3 (s); 149.7 (s). MS (EI): 286 ($MH^+$, 8), 285 ($M^+$, 34), 270 (100). Anal. Calcd for $C_{16}H_{19}NO_2Si$: C, 67.33; H, 6.71; N, 4.91%. Found: C, 66.83; H, 6.81; N, 4.86%.

**4-(Trimethylsilylethynyl)-5,8-quinolinedione (11).** A solution of CAN (5.8 g, 10.6 mmol) in $H_2O$ (25 ml) was added to a solution of **10** (1.5 g, 5.3 mmol) in MeCN (50 ml). The reaction mixture became dark and was stirred for 10 min at rt, $H_2O$ (25 ml) was added and the product extracted with $CH_2Cl_2$ . The organic solution was dried and evaporated to afford **11** (1.2 g, 87%) as a black solid, mp 101-103 °C ($Et_2O$): IR (KBr): 1688, 1667, 1564, 1308. $^1$H-NMR ($CDCl_3$, 300 MHz): 0.28 (s, 9H); 6.97 (d, $J$ = 10.4, 1H); 7.04 (d, $J$ = 10.4, 1H); 7.65 (d, $J$ = 4.7, 1H); 8.87 (d, $J$ = 4.7, 1H). $^{13}$C-NMR ($CDCl_3$, 70.4 MHz): 0.7 (q); 100.1 (s); 109.3 (s); 128.2 (s); 128.7 (s); 132.4 (d); 137.3 (d); 138.8 (d); 147.7 (s); 152.8 (d); 182.4 (s); 182.9 (s). MS (EI): 256 ($MH^+$, 4), 255 ($M^+$, 13), 240 (100). HRMS calcd for $C_{14}H_{13}NO_2Si$ 255.0715, found 255.0713.

**5,8-Dimethoxy-4-(2,2-dimethoxyethyl)quinoline (12).** A solution of **10** (500 mg, 1.7 mmol) in dry DMF (2.5 ml) was added to a solution of NaOMe (378 mg, 7 mmol) in dry MeOH (2.5 ml). The black mixture was stirred at 60 °C for 1.5 h, $H_2O$ (4 ml) was added and the solution was extracted with ether. The organic layer was washed with $H_2O$, dried and evaporated to give **12** (417 mg, 86%) as a yellow oil: IR (Film): 1614, 1465, 1267. $^1$H-NMR ($CDCl_3$, 300 MHz): 3.33 (s, 6H); 3.58 (d, $J$ = 5.2, 2H); 3.94 (s, 3H); 4.05 (s, 3H); 4.70 (t, $J$ = 5.2, 1H); 6.81 (d, $J$ = 8.7, 1H); 6.94 (d, $J$ = 8.7, 1H); 7.25 (d, $J$ = 4.4, 1H); 8.80 (d, $J$ = 4.4, 1H). $^{13}$C-NMR ($CDCl_3$, 70.4 MHz): 40.9 (t); 56.7 (q); 55.3 (q); 55.9 (q); 104.7 (d); 105.1 (d); 106.3 (d); 120.9 (s); 125.3 (d); 141.4 (s); 143.5 (s); 148.8 (d); 149.8 (s); 150.1 (s). MS (EI): 278 ($MH^+$, 3), 277 ($M^+$, 13), 262 (7), 75 (100). Picrate mp 150-152 °C (MeOH). Anal. Calcd for $C_{15}H_{20}NO_4.C_6H_2N_3O_7$: C, 49.80; H, 4.38; N, 11.06%. Found: C, 49.90; H, 4.31; N, 10.87%.

**4-(2,2-Dimethoxyethyl)quinoline-5,8-dione (13).** To a solution of **12** (409 mg, 1.5 mmol) in MeCN (15 ml) was added a solution of CAN (1.6 g, 2.9 mmol) in $H_2O$ (7.5 ml). The mixture was stirred for 10 min at rt, $H_2O$ (7.5 ml) was added and the solution was extracted with $CH_2Cl_2$. The organic solution was dried and evaporated to give **13** (241 mg, 65%) mp 165-167 °C ($Et_2O$-$Me_2CO$): IR (Film): 1681, 1664. $^1$H-NMR ($CDCl_3$, 300 MHz): 3.30 (s, 6H); 3.43 (d, $J$ = 5.5, 2H); 4.49 (t, $J$ = 5.5, 1H); 6.92 (d, $J$ = 10.4, 1H); 7.02 (d, $J$ = 10.4, 1H); 7.47 (d, $J$ = 4.9, 1H); 8.79 (d, $J$ = 4.9, 1H). $^{13}$C-NMR ($CDCl_3$, 70.4 MHz): 37.8 (t); 54.1 (q); 103.6 (d); 127.1 (s); 132.0 (d); 137.1 (d); 139.5 (d); 148.3 (s); 148.7 (s); 152.9 (d); 183.0 (s); 186.6 (s). MS (CI): 250 (100), 248 ($MH^+$, 3), 247 ($M^+$, 3). HRMS calcd for $C_{13}H_{13}NO_4$ 247.0844, found 247.0832.

**2,3-Dihydro-7-hydroxy-2-methoxypyrano[4,3,2-*de*]quinoline (14a).** A solution of **13** (70 mg, 0.3 mmol) and hydroxylamine hydrochloride (79 mg, 1.1 mmol) in MeOH (3 ml) was stirred and refluxed for 1.5 h. The cold solution was made basic with saturated aq $NaHCO_3$ and extracted with $CH_2Cl_2$. The organic layer was dried and evaporated to yield a residue which was purified by column chromatography. Elution with $CH_2Cl_2$

afforded **14a** (13 mg, 21%) as an oil: IR (Film): 1474, 1010. $^1$H-NMR ($CDCl_3$, 200 MHz): 3.20 (dd, $J$ = 2.2 and 19.4, 1H); 3.42 (dd, $J$ = 2.2 and 19.4, 1H); 3.49 (s, 3H); 5.41 (t, $J$ = 2.2, 1H); 6.95 (d, $J$ = 8.0, 1H); 7.11 (d, $J$ = 8.0, 1H); 7.18 (d, $J$ = 4.4, 1H); 8.70 (d, $J$ = 4.4, 1H). $^{13}$C-NMR ($CDCl_3$, 50.3 MHz): 33.6 (t); 55.8 (c); 98.2 (d); 110.6 (d); 109.7 (s); 111.4 (d); 117.0 (s); 119.1 (d); 135.1 (s); 138.9 (s); 148.2 (d); 146.4 (s). MS (EI): 218 ($MH^+$, 47), 217 ($M^+$, 100). HRMS calcd for $C_{12}H_{11}NO_3$ 217.0738, found 217.00732.

**2,3-Dihydro-2,7-dihydroxypyrano[4,3,2-*de*]quinoline (14b) and (14a).** A mixture of **13** (100 mg, 0.4 mmol), $CH_2Cl_2$ (5 ml) and 2N HCl (3 ml) was stirred and refluxed for 10 min. The cold solution was made basic with saturated aq $NaHCO_3$ and extracted with $CH_2Cl_2$. The organic layer was dried and evaporated yielding a residue which was purified by column chromatography. Elution with $CH_2Cl_2$ afforded **14b** (20 mg, 25%) as an oil: IR (Film): 3400, 1610, 1472. $^1$H-NMR ($CDCl_3$, 200 MHz): 3.23 (dd, $J$ = 16.8 and 3.6, 1H); 3.41 (dd, $J$ =16.8 and 1.8, 1H); 5.83 (dd, $J$ = 3.6 and 1.8, 1H); 6.92 (d, $J$ = 8.3, 1H); 6.98 (s, 1H); 7.10 (d, $J$ = 8.3, 1H); 7.20 (d, $J$ = 4.4, 1H); 8.70 (d, $J$ = 4.4, 1H). $^{13}$C-NMR ($CDCl_3$, 50.3 MHz): 29.6 (t); 92.2 (d); 98.0 (s); 110.7 (d); 111.2 (d); 112.3 (s); 119.2 (d); 138.2 (s); 141.9 (s); 148.3 (d); 149.3 (s). MS (EI): 204 ($MH^+$, 12), 203 ($M^+$, 90), 174 (100). HRMS calcd for $C_{11}H_9NO_3$ 203.0582, found 203.0589, and **14a** (2 mg, 2%).

**7-Hydroxy-6-aza-1-oxaphenalene (16).** $NH_4Cl$ (932 mg, 17.4 mmol) was added to a solution of **11** (250 mg, 0.98 mmol) in glacial AcOH (9.3 ml) under $N_2$. The reaction mixture was stirred at reflux for 45 min then cooled, $H_2O$ (100 ml) was added, the solution made basic with $NaHCO_3$ and extracted with $CH_2Cl_2$. The organic solution was dried and evaporated to give a black residue which was purified by flash chromatography. Elution with $CH_2Cl_2$ afforded **16** (79 mg, 43%) as an orange solid, mp 110-113 °C ($Et_2O$): IR (Film): 3200, 1641, 1518, 1417. $^1$H-NMR ($CDCl_3$, 300 MHz): 5.94 (d, $J$ = 5.9, 1H); 6.57 (d, $J$ = 4.6, 1H); 6.84 (d, $J$ = 8.4, 1H); 6.98 (d, $J$ = 5.9, 1H); 7.09 (d, $J$ = 8.4, 1H); 8.41 (d, $J$ = 4.6, 1H). $^{13}$C-NMR ($CDCl_3$, 70.4 MHz): 104.2 (d); 107.2 (d); 109.9 (d); 110.9 (d); 149.7 (d); 151.0 (d). MS (CI): 186 ($MH^+$, 100), 185 ($M^+$, 55). MS (EI): 185 ($M^+$, 100). Anal. Calcd for $C_{11}H_{17}NO_2$: C, 71.37; H, 3.81; N, 7.56%. Found: C, 71.58; H, 3.49; N, 7.35%. HRMS calcd for $C_{11}H_7NO_2$ 185.0477, found 185.0473.

**5,8-Dihydroxy-4-(trimethylsilylethynyl)quinoline (17a), 6-amino-5,8-dihydroxy-4-(trimethylsilylethynyl)quinoline (17b) and 4-ethynyl-5,8-dihydroxyquinoline (17c).** $NH_3$ gas was bubbled during 10 min through a cooled (-78 °C) solution of **11** (228 mg, 0.9 mmol) in dry THF (15 ml); the solution colour changed from brown to dark red. The cooling bath was removed and the stirring was continued for 2 h. The solvent was evaporated and the residue dissolved in EtOAc. The solution was washed with brine, dried and evaporated. The residue was purified by column chromatography. Elution with hexane/$CH_2Cl_2$ (1:1) gave **17c** (38 mg, 23%) as a yellow solid: IR (KBr): 3453, 3201, 2100. $^1$H-NMR ($CDCl_3$, 200 MHz): 3.95 (s, 1H); 7.01 (d, $J$ = 8.4, 1H); 7.14 (d, $J$ = 8.4, 1H); 7.54 (d, $J$ = 4.6, 1H); 7.81 (brs, 2H); 8.71 (d, $J$ = 4.6, 1H). $^{13}$C-NMR ($CDCl_3$, 50.3 MHz): 89.4(d); 111.7 (d); 113.6 (d); 126.9 (d); 147.3 (d). MS (CI): 186 ($MH^+$, 100), 185 ($M^+$, 29). MS (EI): 185 ($M^+$, 100). HRMS calcd for $C_{11}H_7NO_2$ 185.0477, found 185.0484. The following fractions afforded **17a** (41 mg, 18%): IR (Film): 3456, 2250. $^1$H-NMR ($CDCl_3$, 200 MHz): 0.35 (s, 9H); 6.97 (d, $J$ = 8.6, 1H); 7.13 (d, $J$ = 8.6, 1H); 7.46 (d, $J$ = 4.4, 1H); 7.78 (s, 1H); 8.09 (s, 1 H); 8.68 (d, $J$ = 4.4, 1H). $^{13}$C-NMR ($CDCl_3$, 50.3 MHz): 0.0 (q); 111.6 (d); 113.1 (d); 126.0 (d); 147.3 (d). MS (EI): 258 ($MH^+$, 21), 257 ($M^+$, 100), 242 (51). HRMS calcd for $C_{14}H_{15}NO_2Si$ 257.0872, found 257.0860. Elution with $CH_2Cl_2$/MeOH (99:1) gave **17b** (53 mg, 22%) as a red solid: IR (KBr): 3421, 3225, 2100. $^1$H-NMR ($CDCl_3$, 200 MHz): 0.33 (s, 9H); 5.48 (brs, 2H); 6.16 (s, 1H); 7.57 (d, $J$ = 4.7, 1H);

8.86 (d, $J$ = 4.7, 1H). $^{13}$C-NMR ($CDCl_3$, 70.4 MHz): 0.4 (q); 100.8 (s); 104.9 (d); 108.9 (s); 126.6 (s); 130.7 (s); 131.1 (d); 148.4 (s); 149.7 (s); 153.2 (d); 179.8 (s); 181.1 (s). MS (EI): 272 ($M^+$, 33), 255 (100). HRMS calcd for $C_{14}H_{16}N_2O_2Si$ 272.0981, found 272.0989.

**5,8-Dimethoxyquinolin-4-ylethanal (18).** A mixture of **12** (600 mg, 2.2 mmol), $CH_2Cl_2$ (17 ml) and 2N HCl (17 ml) was stirred and refluxed for 10 min. The cold solution was made basic with aq $NaHCO_3$ and extracted with $CH_2Cl_2$. The organic layer was dried and evaporated giving **18** (433 mg, 87%) as an oil: IR (KBr): 1719. $^1$H-NMR ($CDCl_3$, 200 MHz): 3.86 (s, 3H); 4.06 (s, 3H); 4.21 (s, 2H); 6.81 (d, $J$ = 8.7, 1H); 6.99 (d, $J$ = 8.7, 1H); 7.21 (d, $J$ = 4.4, 1H); 8.86 (d, $J$ = 4.4, 1H); 9.77 (s, 1H). $^{13}$C-NMR ($CDCl_3$, 50.3 MHz): 51.1 (t); 55.3 (q); 56.0 (q); 104.9 (d); 106.4 (s); 107.0 (d); 120.7 (s); 125.1 (d); 139.3 (s); 148.8 (s); 149.2 (d); 149.9 (s); 198.2 (d). MS (EI): 232 ($MH^+$, 10), 231 ($M^+$, 50), 216 (100). HRMS calcd for $C_{13}H_{13}NO_3$ 231.0895, found 231.0890.

**5,8-Dimethoxy-4-(2-dimethylaminoethenyl)quinoline (19).** A solution of **18** (150 mg, 0.65 mmol) and $Me_2NH.HCl$ (58 mg, 0.7 mmol) in MeOH (7 ml) was refluxed for 2 h. The solvent was evaporated, the residue triturated with aq $NaHCO_3$ and the product extracted with $CH_2Cl_2$ then the organic layer was dried and evaporated affording **19** (157 mg, 94%) as an oil: IR (KBr): 1618, 1581, 1290. $^1$H-NMR ($CDCl_3$, 200 MHz): 2.95 (s, 6H); 3.89 (s, 3H); 3.98 (s, 3H); 6.63 (d, $J$ = 13.4, 1H); 6.71 (d, $J$ = 8.4, 1H); 6.86 (d, $J$ = 8.4, 1H); 6.99 (d, $J$ = 13.4, 1H); 7.24 (d, $J$ = 5.0, 1H); 8.57 (d, $J$ = 5.0, 1H). $^{13}$C-NMR ($CDCl_3$, 70.4 MHz): 40.5 (2q); 55.7 (q); 55.8 (q); 97.3 (d); 104.6 (d); 106.1 (d); 114.2 (d); 128.6 (s); 141.7 (s); 143.9 (d); 146.6 (s); 147.7 (d); 149.4 (s); 151.4 (s). MS (EI): 258 ($M^+$, 49), 243 (100). HRMS calcd for $C_{15}H_{18}N_2O_2$ 258.1368, found 258.1371.

**5,8-Dimethoxyquinolin-4-ylcarboxaldehyde (20).** To a solution of **19** (65 mg, 0.2 mmol) in MeCN (3 ml) was added a solution of CAN (276 mg, 0.5 mmol) in $H_2O$ (1 ml). The mixture was stirred for 5 min at rt. $H_2O$ (2 ml) was added and the solution was extracted with $CH_2Cl_2$. The organic solution was dried and evaporated to give a residue which was purified by column chromatography. Elution with $CH_2Cl_2$ afforded **20** (13 mg, 24%) mp 187-189 °C ($Et_2O$-$Me_2CO$): IR (KBr): 1686. $^1$H-NMR ($CDCl_3$, 300 MHz): 4.00 (s, 3H); 4.09 (s, 3H); 6.94 (d, $J$ = 8.6, 1H); 7.04 (d, $J$ = 8.6, 1H); 7.66 (d, $J$ = 4.1, 1H); 9.07 (d, $J$ = 4.1, 1H); 11.04 (s, 1H). $^{13}$C-NMR ($CDCl_3$, 70.4 MHz): 56.1 (q); 56.2 (q); 106.2 (d); 107.4 (d); 119.6 (d); 149.7 (d); 194.5 (d). MS (EI): 217 ($M^+$, 15), 202 (33), 83 (100). MS (CI): 218 ($MH^+$, 100), 217 ($M^+$, 15).

**4-(2-Benzylaminoethyl)-5,8-dimethoxyquinoline (21).** A solution of **18** (696 mg, 3 mmol) and benzylamine hydrochloride (964 mg, 9 mmol) in *i*PrOH (35 ml) was stirred at reflux for 5 h. To the ice-cold solution, $NaB(CN)H_3$ was added until the solution was basic. The solution was stirred at rt for 16 h then the solvent was evaporated, the residue dissolved in $CH_2Cl_2$ and the solution washed with $H_2O$. The organic solution was dried and evaporated affording a residue which was purified by column chromatography. Elution with $CH_2Cl_2$/MeOH (9:1) gave **21** (473 mg, 49%) as an oil: IR (Film): 1616, 1465, 1269. $^1$H-NMR ($CDCl_3$, 300 MHz): 3.14 (t, $J$ = 6.9, 2H); 3.56 (t, $J$ = 6.9, 2H); 3.88 (s, 3H); 3.94 (s, 5H); 6.75 (d, $J$ = 8.6, 1H); 6.84 (d, $J$ = 8.6, 1H); 7.21-7.36 (m, 6H); 8.46 (d, $J$ = 4.4, 1H). $^{13}$C-NMR ($CDCl_3$, 50.3 MHz): 34.6 (t); 48.8 (t); 52.8 (t); 55.4 (q); 55.9 (q); 105.4 (d); 107.7 (d); 119.8 (s); 124.7 (d); 128.7 (d); 129.0 (d); 130.0 (d); 131.6 (s); 139.5 (s); 144.4 (s); 147.6 (s); 148.1 (d); 149.7 (s). MS (CI): 323 ($MH^+$, 4), 322 ($M^+$, 1), 91 (100). HRMS calcd for $C_{20}H_{22}N_2O_2$ 322.1681, found 322.1680.

**4-Ethynyl-5,8-dimethoxyquinoline (22).** $Bu_4NF$ (1.7 g, 5.2 mmol) was added to a solution of **11** (500 mg, 1.7 mmol) in MeOH (30 ml) and the mixture was stirred at reflux for 2 h. The solvent was evaporated and

the residue was dissolved in EtOAc. The organic solution was washed with $H_2O$, dried and evaporated to give **22** (373 mg, 96%): IR (Film): 3200, 2100, 1615, 1556, 1339. $^1$H-NMR ($CDCl_3$, 200 MHz): 3.62 (s, 1H); 3.93 (s, 3H); 4.04 (s, 3H); 6.84 (d, $J$ = 8.8, 1H); 6.97 (d, $J$ = 8.8, 1H); 7.60 (d, $J$ = 4.6, 1H); 8.85 (d, $J$ = 4.6, 1H). $^{13}$C-NMR ($CDCl_3$, 50.3 MHz): 56.0 (q); 56.2 (q); 82.6 (s); 84.8 (d); 106.6 (d); 107.4 (d); 120.8 (s); 126.1 (s); 127.7 (d); 141.1 (s); 148.3 (d); 149.2 (s); 149.8 (s). MS (EI): 213 ($M^+$, 28), 198 (100).

**4-(2-Diformylaminoethenyl)-5,8-dimethoxyquinoline (23).** Sodium diformylamide (90 mg, 0.9 mmol) was added to a solution of **22** (100 mg, 0.5 mmol) in dry DMF (5 ml) and the mixture was stirred at reflux for 15 min. The solvent was removed and the residue was dissolved in $CH_2Cl_2$ and washed with $H_2O$. The organic solution was dried and evaporated affording a residue which was purified by column chromatography. Elution with $CH_2Cl_2$/MeOH (99:1) gave **23** (100 mg, 75%) as a solid, mp 185-187 °C ($CH_2Cl_2$-$Et_2O$): IR (film): 1688, 1636. $^1$H-NMR ($CDCl_3$, 500 MHz): 3.81 and 3.83 (2xs, 3H); 3.96 and 3.97 (2xs, 3H); 6.73 and 6.75 (2xd, $J$ = 8.5, 1H); 6.86 and 6.88 (2xd, $J$ = 8.5, 1H); 7.24 and 7.44 (2xd, $J$ = 4.5, 1H); 7.20-7.50 (m, 2H); 7.55 and 7.65 (2xbrs, 1H); 8.20 (brs, 1H); 8.71 and 8.73 (2xd, $J$ = 4.5, 1H). $^{13}$C-NMR ($CDCl_3$, 50.3 MHz): 55.9 (q); 105.7 (d); 106.7 (d); 114.7 (d); 118.8 (d); 119.5 (s); 123.6 (d); 141.3 (s); 142.8 (s); 148.5 (d); 149.6 (s); 150.5 (s); 158.8 (d). MS (EI): 287 ($MH^+$, 0.01), 286 ($M^+$, 0.03), 243 (100). Anal. Calcd for $C_{15}H_{14}N_2O_4$: C, 62.93; H, 4.93; N, 9.78%. Found: C, 62.73; H, 5.08; N, 9.21%.

**4-(2-Diformylaminoethenyl)-5,8-quinolinedione (24).** A solution of CAN (438 mg, 0.8 mmol) in $H_2O$ (1 ml) was added to a solution of **23** (100 mg, 0.4 mmol) in MeCN (3 ml) and the mixture was stirred during 5 min at rt, $H_2O$ (5 ml) was added and the solution was extracted whith $CH_2Cl_2$. The organic layer was dried and evaporated giving **24** (40 mg, 35%) as a solid, mp 176-178 °C ($Et_2O$): IR (film): 1684, 1673, 1634. $^1$H-NMR ($CDCl_3$, 300 MHz): 6.95 and 6.99 (2xd, $J$ = 10.4, 1H); 7.08 and 7.19 (2xd, $J$ = 10.4, 1H); 7.65 and 7.75 (2xd, $J$ = 4.8 and 5.4, 1H); 7.56-7.68 and 7.86-7.97 (2xm, 1H); 8.37 and 8.64 (2xbrs, 1H); 8.58-8.65 (m, 2H); 8.85 and 9.12 (2xd, $J$ = 5.4 and 4.8, 1H). MS (EI): 257 ($MH^+$, 4), 256 ($M^+$, 2), 185 (41).

**7-Oxo-1,6-diazaphenalene (6).** Ar was passed through a solution of **24** (100 mg, 0.4 mmol) in MeOH (5 ml) for 3 min then TFA (40 ml, 0.4 mmol) was added and the resulting mixture was refluxed for 30 min. Aqueous $NaHCO_3$ was added and the solution was extracted with $CH_2Cl_2$. The organic layer was dried and the residue was purified by column chromatography, elution with $CH_2Cl_2$ giving **6** (25 mg, 31%) as a solid mp 224-226 °C ($Et_2O$): IR (film): 1662, 1618, 1585. $^1$H-NMR ($CDCl_3$, 300 MHz): 6.99 (d, $J$ = 10.2, 1H); 7.75 (d, $J$ = 5.8, 1H); 7.84 (d, $J$ = 10.2, 1H); 7.95 (d, $J$ = 5.5, 1H); 8.86 (d, $J$ = 5.8, 1H); 9.16 (d, $J$ = 5.5, 1H). $^{13}$C-NMR ($CDCl_3$, 70.4 MHz): 100.4 (s); 109.2 (s); 120.2 (d); 123.7 (d); 133.5 (d); 142.1 (d); 147.9 (d); 149.0 (d); 152.5 (s); 184.0 (s); 186.0 (s). MS (EI): 183 ($MH^+$, 25), 182 ($M^+$, 63), 154 (54), 83 (100). HRMS calcd for $C_{11}H_6N_2O$ 182.0480, found 182.0480.

## ACKNOWLEDGEMENTS

We thank for generous support CIRIT (Generalitat de Catalunya) for Grant QFN 96-4701 and Comissionat per a Universitats i Recerca (Generalitat de Catalunya) for Grant GRQ94-1009. We also thank the CIRIT for a fellowship (LF).

## REFERENCES

1 Ajana, W.; López-Calahorra, F.; Joule, J. A.; Alvarez, M. *Tetrahedron*, **1997**, *53*, 341.

2 Gunawardana, G. P.; Kohmoto, S.; Gunasekera, S. P.; McConnell, O. J.; Koehn, F. E. *J. Am. Chem. Soc.*, **1988**, *110*, 4856; Gunawardana, G. P.; Koehn, F. E.; Lee, A. Y.; Clardy, J.; He, H.; Faulkner, D. J. *J. Org. Chem.*, **1992**, *57*, 1523.

3 Gunawardana G. P.; Kohmoto, S.; Burres, N. S. *Tetrahedron Lett.*, **1989**, *30*, 4359.

4 Carrol A. R.; Scheuer, P. J. *J. Org. Chem.*, **1990**, *55*, 4426.

5 Cooray, N. M.; Scheuer, P. J.; Parkanyi, L.; Clardy, J. *J. Org. Chem.*, **1988**, *53*, 4619.

6 Carroll, A. R.; Cooray, N. M.; Pointer, A.; Scheuer, P. J. *J. Org. Chem.*, **1989**, *54*, 4231.

7 Rudi, A.; Kashman, Y. *J. Org. Chem.*, **1989**, *54*, 5331.

8 Kobayashi, J.; Cheng, J.; Nakamura, H.; Ohizumi, Y.; Hirata, Y.; Sasaki, T.; Ohta, T.; Nozoe, S. *Tetrahedron Lett.*, **1988**, *29*, 1177.

9 Bloor, S. J.; Schmitz, F. J. *J. Am. Chem. Soc.*, **1987**, *109*, 6134; de Guzman, F. S.; Schmitz, F. J. *Tetrahedron Lett.*, **1989**, *30*, 1069.

10 Meghani, P.; Mills, O. S.; Joule, J. A. *Heterocycles*, **1990**, *30*, 1121.

11 Rao, J. U. M.; Giri, G. S.; Hanumaiah, T.; Rao, K. V. J. *J. Nat. Prod.*, **1986**, *49*, 346.

12 Avasthi, K.; Lee, S-J.; Cook, J. M.; Pickett, J. E.; Wasserman, H. H. *Heterocycles*, **1981**, *16*, 1453.

13 Cassis, R.; Tapia, R.; Valderrama, J. A. *Synth. Commun.* **1985**, *15*, 125.

14 Withopf, P.; Lackner, H. *Tetrahedron* **1987**, *43*, 4549.

15 Leusink, A. J.; Budding, H. A.; Drenth, W. *J. Organometal. Chem.* **1968**, *11*, 541; Wollenberg, R. H.; Albizati, K. F.; Peries, R. *J. Am. Chem. Soc*, **1977**, *99*, 7363.

16 Echavarren, A. M.; Stille, J. K. *J. Am. Chem. Soc.*, **1988**, *110*, 4051.

17 Gómez-Bengoa, E.; Echavarren, A. M. *J. Org. Chem.*, **1991**, *56*, 3497.

18 (a) Bracher, F. *Justus Liebigs Ann. Chem.*, **1989**, 87; (b) *idem Heterocycles*, **1989**, *29*, 2093; (c) *idem Justus Liebigs Ann. Chem.*, **1990**, 205; *ibid.*, **1993**, 1205.

19 Yinglin, H.; Hongwen, H. *Synthesis*, **1990**, 122.

20 Chang, J.-C.; El-Sheikh, M. I.; Cook, J. M. *Heterocycles*, **1979**, *12*, 903.

(*Received in UK* 31 *December* 1996; *revised* 28 *January* 1997; *accepted* 30 *January* 1997)