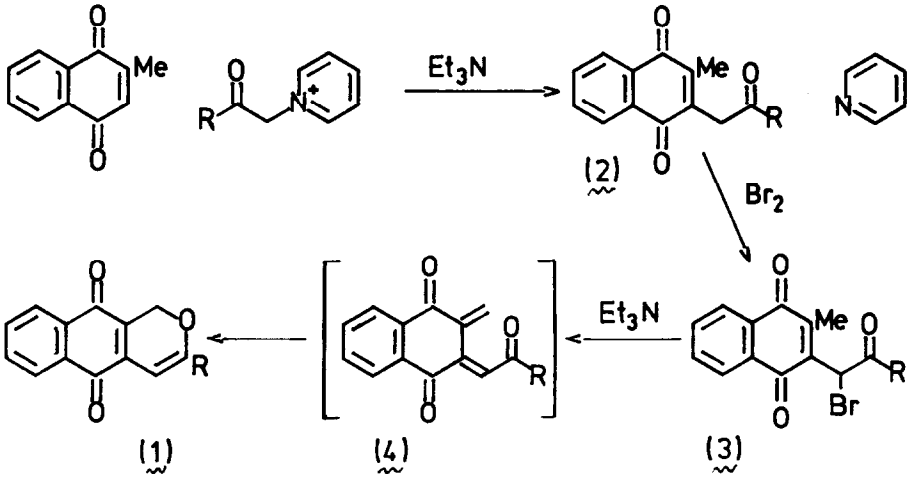
Tetrahedron Letters, Vol.27, No.2, pp 255-258, 1986 0040-4039/86 $3.00 + .00
Printed in Great Britain

DERIVATIVES OF NAPHTHO[2,3-c]PYRAN-5,10-DIONE ; A SIMPLE SYNTHESIS AND A NOTE OF THEIR CHROMOGENIC PROPERTIES.

Michael F.Aldersley, Francis M.Dean, and Ahad S.Hamzah
The Robert Robinson Laboratories, The Unversity of Liverpool, Liverpool, L69 3BX.

Summary: Appropriate N-ylides convert 2-methyl-1,4-naphthoquinone into 3-(acylmethyl) derivatives which can be cyclised to naphtho[2,3-c]pyran-5,10-diones by treatment with bromine and dehydrobromination with triethylamine; these diones give a variety of striking colours in acid media.

The nucleus in (1) is basic to a number of fungal pigments such as fusarubin[1] and eleutherin[2] and to some aphid pigments.[3] Certain members of the series have significant antibiotic and other biological activities[4] so that several syntheses have been reported e.g., in connection with kalafungin, the nanomycins, and other compounds.[5] We have already shown that quinones, including menaphthone, accept acylmethyl groups from pyridinium ylides[6] (Scheme) and we now demonstrate that the products (2) are easily and efficiently converted into derivatives (1) of naphtho[2,3-c]pyran-5,10-dione.



Scheme

Chloroketones or bromoketones (either purchased or prepared from commercial ketones by bromination with copper(II) bromide[7]) reacted with pyridine to give pyridinium salts in the usual way; the salts with menaphthone in acetonitrile containing triethylamine furnish the requisite substituted quinones (2) as described previously,[6] new examples being listed in the Table. Several of these compounds appear to exist in two forms, one consisting of small bright yellow prisms, the other of large brownish prisms, but both forms have i.r. absorption bands for the side chain carbonyl group as well as the quinone bands, and the ^{1}H n.m.r. spectra both show methylenic and methyl resonances and so both correspond to the non-enolic structure (2).

For the cyclisation, the substituted quinone (0.01 mol; either form) is dissolved in tetrachloromethane (or dichloromethane if necessary) (50 ml) and slowly treated in the dark with bromine (0.01 mol) in tetrachloromethane (10 ml). After 40 min. the solvent and HBr are removed under vacuum leaving a bromoketone which may not be very stable and is normally used at once in the next step; however (3; R=Ph) was examined in detail and had m.p. 155 - 158°; $\nu_{max.}$ (KBr) 1 708 (PhCO), 1 665, 1 650, 1 610 and 1 595 cm^{-1} (naphthoquinone), and δ ($CDCl_3$) 2.19 (CH_3), 7.01 (CHBr) and 7.3 - 8.3 (m, ArH), but changed when kept into a substance m.p. 223 - 227° devoid of quinonoid characteristics. For preparative purposes, the crude bromoketone is dissolved in dichloromethane (20 ml) and treated under nitrogen and in the dark with triethylamine (0.015 mol); the solution becomes green immediately but this colour changes to dark red. The green species is probably a salt (or a related radical) corresponding to the bromoketone, whereas the red species is the desired naphthopyrandione (1). The colour change is fast unless electron-withdrawing substituents (halogen, nitro) are present that could stabilise the anion, when it may take 40 min. A slow colour change does not appear to impair the efficiency of the reaction, and we assume that it is the loss of bromine (i.e., removal of a proton from the methyl group) that is slow and that the quinone methide (4) always cyclises rapidly. The pigment is isolated simply by passing the reaction solution down a column of silica when it comprises the only mobile band.

The naphthopyrandiones (1) (Table) are characterised by methylenic resonances near δ 5.3, vinylic resonance near 6.8 (when R is aromatic), and the absence of vinylic methyl resonances. In the i.r. spectrum the strongest band in the double bond stretching region is no longer a carbonyl band, but a vinylic ether band at 1555 $\pm$ 5 cm^{-1}. The naphthopyrandione (1; R = Ph) was further characterised by reduction under nitrogen with sodium borohydride and acetylation by acetic anhydride to give a quinol acetate which formed colourless prisms, m.p. 237 - 238°C (from ethanol-trichloromethane); $\nu_{max.}$ (KBr) 1 745, 1 750 (both vs, br) (OAc), 1 620 and 1 595(Ar) cm^{-1}; δ ($CDCl_3$) 2.48 (OAc), 2.54 (OAc), 5.26 (CH_2O), 6.44 (C:CH), and ca. 7.37 - 7.74 (ArH).

TABLE 2-Acylmethyl-3-methyl-1,4-naphthoquinones (2) and Derivatives (1) of 1H-Naphtho[2,3-c]-pyran-5,10-dione.

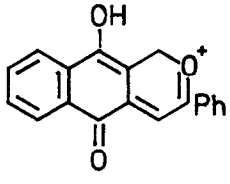
FORMULA NUMBER AND SUBSTITUENT R		m.p.[a] (°C)	IR (C:O str.; cm^{-1})		ArH (o-C:O)	^{1}H NMR (δ) ArH (other)		CH_2	CH:C-O	Me
(2)	CMe_3	79-81	1 705	1 670	8.20[b]	7.24		3.88		2.16(3H), 1.28(9H)
(2)	4-BrC_6H_4	150-151	1 683	1 670	8.08[b]	7.91	7.68	4.33		2.15
(2)	2,4-$Cl_2C_6H_3$	76- 79	1 680	1 632	8.04[b]	7.66	7.46 7.35	4.35		2.25
(2)	2-naphthyl	168-170	1 686	1 635	8.00[b]	8.60	7.70 7.60	4.50		2.18
(1)	CMe_3	81- 83	1 680	1 650	8.07[b]	7.70		5.04	6.01	1.20
(1)	Ph	188-191	1 670	1 650	8.09[b]	7.81	7.71 7.42	5.30	6.71	
(1)	4-BrC_6H_4	210-212	1 678	1 650	8.09[b]	7.70	7.64 7.54	5.27	6.67	
(1)	2,4-$Cl_2C_6H_3$	170-172	1 670	1 650	8.12[b]	7.74 7.52	7.49 7.30	5.34	6.62	
(1)	4-$NO_2C_6H_4$	240-242	1 680	1 655	8.08[c]	8.26	8.12 7.87	5.35	6.92	
(1)	2-naphthyl	232-234	1 670	1 650	8.05[c]	8.43	7.58	5.37	6.88	
(1)	Ph				8.11[d]	7.78	7.43	5.34	6.78	

a All compounds crystallised from mixtures of ethanol and trichloromethane, and gave satisfactory analytical and/or mass spectroscopic results.

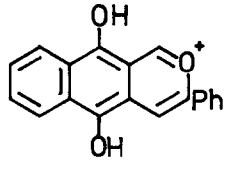
b In $CDCl_3$. The aromatic protons appeared as multiplets generally not analyzed. All bands had the appropriate relative intensities. TMS internal reference.

c In d_6-DMSO; TMS internal reference.

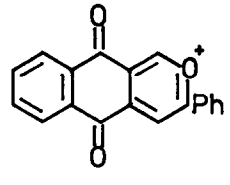
d In $F_3C\ CO_2H$; acetone external reference.



(5)



(6)



(7)

In non-acidic solvents or in acetic acid the naphthopyrandione (1; R = Ph) gives orange-red solutions, e.g. in CH_3CN it has $\lambda_{max.}$ 264 and 487 nm (log ε 4.57, 3.93), but in trifluoroacetic acid it is instantly protonated giving a brilliant purple solution slowl changing to inky blue-black. The purple cation is stable for days in a mixture of dichloro methane and trifluoroacetic acid (2:1, V/V) in which it has $\lambda_{max.}$ 310 and 529 nm (log ε 4.31, 3.92). The absence of bands characteristic of the parent compound shows that protonation is complete, and since the PMR spectrum is little changed (Table), we conclude that the purple cation is that shown in (5). In sulphuric acid the naphthopyrandione (1; R = Ph) gives a bright green solution having $\lambda_{max.}$ 310, 352, 390 and 660 nm (log ε 3.94, 3.83, 3.74 and 3.73). This colour is not extractable into dichloromethane, and contact with oxidising agents including air or dilution with air-saturated solvents alters it to a deep yellow, $\lambda_{max.}$ 234 and 408 nm (log ε 4.14, 3.78), very like that of 2,3-dimethyl-1,4-naphthoquinone in sulphuric acid which has $\lambda_{max.}$ 257, 307 and 414 nm (log ε 4.01, 3.85 and 3.39). The PMR spectra were too diffuse to be useful, but the colour changes are consistent with isomerisation to a fully aromatic cation (6) and then oxidation to a quinonoid cation (7). The other diones give similar colours except the naphthyl naphthopyran (1; R = $C_{10}H_7$) which is blue in trifluoroacetic acid and the t-butyl naphthopy (1; R = ^tBu) which is blue in sulphuric acid.

REFERENCES

1. H.W.Ruelius and A.Gauhe, *Liebigs Ann.*, 1950, 569, 38; 1951, 570, 121.
2. W.Eisenmuth and H.Schmid, *Helv.Chim.Acta*, 1958, 41, 2021.
3. T.A.Chorn, R.G.F.Giles, I.R.Green and P.P.K.Mitchell, *J.Chem.Soc., Perkin Trans. 1*, 1983, 1249.
4. L.E.Johnson and A.Dietz, *Appl.Microbiol.*, 1968, 16, 1815; M.E.Bergy, *J.Antibiot.*, 1968, 21, 24; O.Vaartaja, *Forestry Technical Report, Canadian Forestry Services*, 1976, 14,
5. G.Kraus, H.Cho, S.Crowley, B.Roth and H.Sugimoto, *J.Org.Chem.*, 1984, 48, 3439; T.Li and R.Ellison, *J.Am.Chem.Soc.*, 1978, 100, 6263; T.Kometani, Y.Tabeuchi and E.Yoshii, *J.Chem.Soc., Perkin Trans. 1*, 1981, 1197; R.G.F.Giles, I.R.Green, V.I.Hugo and P.R.K.Mitchell, *J.Chem.Soc., Perkin Trans. 1*, 1984, 2383; Y.Naruto, H.Unto and K.Maruyama, *J.Chem.Soc., Chem.Commun.*, 1981, 1277; J.N.Freskos and J.S.Swenton, *J.Chem.Soc., Chem.Commun.*, 1985, 658.
6. M.F.Aldersley, F.M.Dean and R.Nayyir-Mashir, *J.Chem.Soc., Perkin Trans. 1*, 1983, 1753.
7. L.C.King and G.K.Ostrum, *J.Org.Chem.*, 1964, 29, 3459.

(Received in UK 14 November 1985)