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THE CHLORINATION OF PURPURIN, PURPURIN-2-METHYL ETHER, AND QUINIZARIN.

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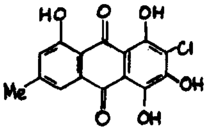
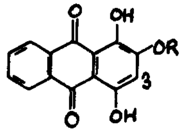
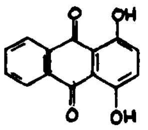
In connection with studies on the synthesis of papulosin(I)[2] we have investigated the chlorination of purpurin(II), purpurin-2-methyl ether(III) and quinizarin(IV).



(I)

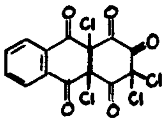


(II) R=H
(III) R=Me

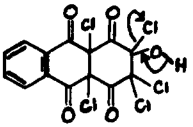


(IV)

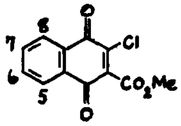
Purpurin(II) on treatment with an excess of chlorine in glacial acetic acid at room temperature afforded the tetrachlorocompound (V)[3,4] in 56.6% yield. Compound (V) formed pale yellow needles, m.p. 178-180° dec. (from $CHCl_3/CCl_4$); mass spectrum, molecular ion at m/e 391.88173 ($^{12}C_{14}\,^{1}H_4\,^{35}Cl_4\,^{16}O_5$ requires 391.88128) and breakdown pattern consistent with the assigned structure; λ_{max}^{MeOH} 232, 270, 308 nm (ε 21,200, 6600 and 2400);[5] $\nu_{max}^{CHCl_3}$ 1760 and 1722 cm^{-1}; n.m.r. ($CDCl_3$, 60MHz) τ1.80 (m, aromatic H). The formation of (V) probably involves substitution of chlorine at the 3-position, oxidation to the diquinone, and addition of two moles of chlorine to produce (VI). (V) would be produced from (VI) by elimination (arrows) of HCl.



(V)



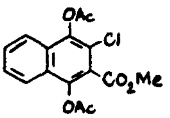
(VI)



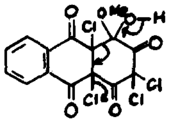
(VII)

Compound (V) on refluxing with methanol containing a trace of sulphuric acid yielded the naphthoquinone (VII; 89%). Compound (VII) formed pale yellow plates, m.p. 129-130°

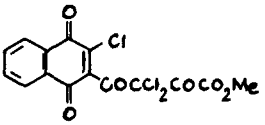
(from MeOH); mass spectrum, molecular ion at m/e 250.0033 ($^{16}C_{12}{}^{1}H_{7}{}^{35}Cl^{16}O_{4}$ requires 250.0033); λ_{max}^{MeOH} 248, 253, 272, and 338 nm (ε 14, 100, 14, 700, 13, 100 and 300); $\nu_{max}^{CHCl_3}$ 1740 and 1680 cm^{-1}; n.m.r. ($CDCl_3$, 60 MHz) τ 1.71 (m, 2H, 5- and 8-H), 2.08 (m, 2H, 6- and 7-H), and 5.94 (s, 3H, $C\underline{H}_3$). Reductive acetylation of (VII) gave the leuco-acetate (VIII) as rosettes of needles m.p. 180-181.5° (from MeOH); mass spectrum, molecular ion at m/e 336.0404 ($^{12}C_{16}{}^{1}H_{13}{}^{35}Cl^{16}O_{6}$ requires 336.0401); λ_{max}^{MeOH} 229, 277 (sh), 285, 295 (sh), and 327 nm (ε 62, 600, 5200, 5900, 4600, and 1100); $\nu_{max}^{CHCl_3}$ 1775 and 1735 cm^{-1}; n.m.r. ($CDCl_3$, 60 MHz) τ 2.22 (m, aromatic H), 5.98 (s, 3H, $CO_2C\underline{H}_3$), 7.48 and 7.56 (each s, 3H, $OCOC\underline{H}_3$). The formation of (VII) probably involves (IX), which undergoes (arrows) elimination of HCl to produce (X). Conventional acidic methanolysis of the β-diketone function of (X) would afford (VII).



(VIII)



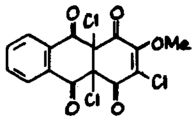
(IX)



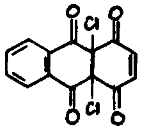
(X)

Under similar conditions to those employed above, purpurin-2-methyl ether (III) yielded the trichlorocompound (XI, 67.5%),[4] involving substitution of chlorine at the 3-position, oxidation to the diquinone and addition of one mole of chlorine. Compound (XI) formed pale yellow prisms, m.p. 153-155° (from MeOH); mass spectrum, molecular ion at m/e 371.9362 ($^{12}C_{15}{}^{1}H_{7}{}^{35}Cl_{3}{}^{16}O_{5}$ requires 371.9359); λ_{max}^{EtOH} 237.5, 272, and 308 nm (ε 21, 200, 13, 100, and 7700); $\nu_{max}^{CHCl_3}$ 1735 cm^{-1}; n.m.r. ($CDCl_3$, 60 MHz) τ 1.82 (m, 4H aromatic H), and 5.65 (s, 3H, $OC\underline{H}_3$).

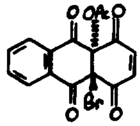
Prolonged reaction of quinizarin (IV) with an excess of chlorine in glacial acetic acid at room temperature gave the dichlorocompound (XII)[4] in 55.1% yield, presumably via oxidation of (IV) to the diquinone followed by addition of one mole of chlorine. This addition parallels that encountered in the formation of (XIII) on reaction of quinizarin quinone with bromine in acetic acid in presence of $Pb(OAc)_2$.[8] Compound (XII) formed pale yellow plates, m.p. 218-220° (from CCl_4); mass spectrum, molecular ion at m/e 307.9650 ($^{16}C_{14}{}^{1}H_{6}{}^{35}Cl_{2}{}^{16}O_{4}$ requires 307.9643); $\lambda_{max}^{CHCl_3}$ 239, 274, and 300 (sh) nm (ε 20, 200, 13, 500, and 8100); ν_{max}^{KCl} 1735 cm^{-1}; n.m.r. ($CDCl_3$, 60MHz) τ 1.71 (m, aromatic H).



(XI)

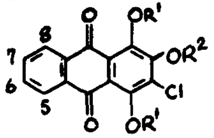


(XII)

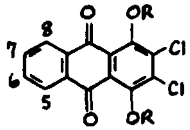


(XIII)

Purpurin-2-methyl ether (III) on reaction with an excess of chlorine in acetic acid in a sealed tube at 130° underwent substitution only and gave (XIV) in 70% yield. Compound (XIV) formed orange-red needles, m.p. 215-216° (from benzene); n.m.r. ($CDCl_3$, 60MHz) τ-3.91 and -3.57 (each s, 1H, O$\underline{H}$), 1.55 (m, 2H, 5- and 8-H), 2.05 (m, 2H, 6- and 7-H) and 5.78 (s, 3H, OC$\underline{H}_3$). The dimethyl ether (XV) of (XIV) was obtained as pale yellow needles, m.p. 141-142°. Demethylation (pyridine hydrochloride) of (XIV) gave (XVI), which sublimed under reduced pressure as red needles, m.p. 281-283°[9].



(XIV) R^1=H, R^2=Me
(XV) R^1=R^2=Me
(XVI) R^1=R^2=H



(XVII) R=H
(XVIII) R=Ac

Chlorination of quinizarin (IV) under similar conditions gave (XVII) in 66.8% yield as orange platelets, m.p. 249.5-251° (from acetone). The diacetate (XVIII) of (XVII) formed pale yellow needles, m.p. 249-251° (from EtOH); n.m.r. ($CDCl_3$, 60MHz) τ 1.33 (m, 2H, 5- and 8-H), 1.73 (m, 2H, 6- and 7-H) and 7.44 (s, 6H, C$\underline{H}_3$).

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REFERENCES

1. Author to whom inquiries should be addressed: Department of Organic Chemistry, University of Western Australia, Nedlands, W.A. 6009, Australia.

2. C. H. Fox, W. S. G. Maass, and T. P. Forrest, *Tetrahedron Letters*, 919 (1969).

3. All new compounds were homogeneous on T.L.C. in a number of solvent systems and gave satisfactory C and H analyses.

4. The stereochemistry about the ring junction is not defined.

5. This spectrum is markedly similar to that of 2,3-dichloro-2,3-dihydro-1,4-naphthoquinone[6] [λ_{max} 232, 270, and 308 nm (ε 16, 500, 5100, and 1900)], but different from that of 2,3-dibromo-2,3-dihydro-1,4:9,10-anthradiquinone[7] [n.m.r. ($CDCl_3$/acetone-d_6/DMSO-d_6, 60MHz) 2.01 (br. s., 4H, aromatic H) and 5.20-5.65 (m, 2H, methine H)] which is typically naphthoquinonoid [$\lambda_{max}^{CHCl_3}$ 263 (sh.) and 360 nm (ε 19, 400 and 2100)].

6. R. H. Thomson, *J. Chem. Soc.*, 1737 (1950).

7. O. Dimroth, E. Schultze, and F. Heinze, *Ber.*, **54**, 3035 (1921).

8. H. H. Inhoffen, H. Muxfeldt, V. Koppe, and J. Heimann-Trosien, *Chem. Ber.* **90**, 1448 (1957).

9. This structure has been ascribed previously to two different products: (i) m.p. 242-243°;[10] (ii) m.p. 270-273°.[11]

10. G. Heller, *Ber.*, **46**, 2703 (1913).

11. C. Mettler, *Ber.*, **45**, 800 (1912).