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SYNTHESIS OF THE NAPHTHACENEQUINONE SS-228R

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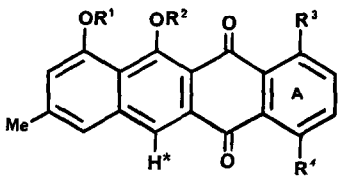
Abstract. The two structures (1) and (2) proposed for the naphthacenequinone SS-228R have both been synthesised, thereby establishing the correctness of structure (2).

The naphthacenequinone SS-228R, derived from a photolabile, antibiotic precursor SS-228Y, was originally assigned the novel structure (1)[1]. More recently this has been questioned in favour of the isomeric structure (2)[2]. Both assignments were based on spectroscopic data and, in part, biosynthetic considerations.

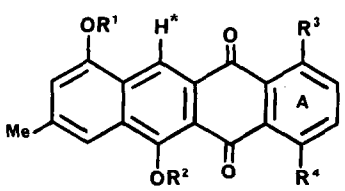
This paper reports syntheses of both (1) and (2) thereby establishing the correctness of the latter. This envisaged forming the respective A-rings by cycloaddition of an appropriate diene to the new 1,4-anthraquinones (3) and (4). In both cases a methoxy group peri to carbonyl was expected to assist the desired regioselectivity[3]. Compounds (3) and (4) were respectively derived by selective reduction of helminthosporin (5)[4] and its methyl ether (6)[5].

Thus addition of 1-methoxy-3-methyl-1-trimethylsilyloxy-1,3-butadiene[6] to naphthazarin and subsequent oxidative aromatisation (DDQ) gave both (5) (11%) and (6) (80%), m.p. 286-287° together. Catalytic reduction[7] of (5) (H_2, PtO_2, EtOH) followed by reoxidation (o-chloranil) yielded the 1,4-anthraquinone (7) (51%), m.p. 189-191° [δ_{OH} ($CDCl_3$) 10.02, 15.87, δ_{H^*} 7.86]. Similar treatment of (6) proceeded with the opposite regioselectivity, as expected[8], to give (8), dec. 265° [δ_{OH} 13.76, δ_{H^*} 8.52] (20%). A better yield of (8) (65%) resulted from reduction of (6) with zinc borohydride in dimethoxyethane[9] at 0°. The isomeric quinone (9), dec. >350° [δ_{OH} 14.93, δ_{H^*} 7.86] was obtained (60%) by selective methylation of (7) (MeI, Me_2SO, NaOH)[8].

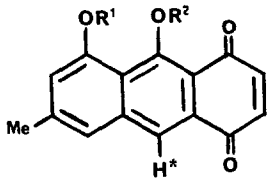
Complete methylation of (9) and (8) (MeI, $CHCl_3$, Ag_2O) respectively gave the required ethers (3) (83%), m.p. 280-281.5° [δ_{H^*} 8.26] and (4) (95%), m.p. 204.5-206° [δ_{H^*} 8.83.]. The regiochemical series (3), (9) was differentiated from the isomeric series (4), (8) by the observed deshielding of H* in the latter pair and of the OH group in (9) relative to (8).



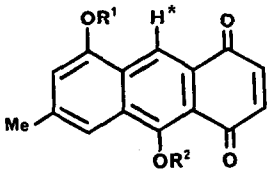
	R^1	R^2	R^3	R^4
1	H	H	H	OH
10	Me	Me	H	OH
11	Me	Me	OH	H



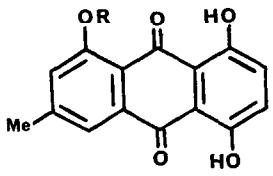
	R^1	R^2	R^3	R^4
2	H	H	OH	H
12	Me	Me	OH	H
13	Me	Me	H	OH
14	H	H	H	OH



	R^1	R^2
3	Me	Me
7	H	H
9	Me	H



	R^1	R^2
4	Me	Me
8	Me	H



5 R = H
6 R = Me

Boiling (3) with 1-trimethylsilyloxy-1,3-butadiene[10] in CH_2Cl_2 gave, after oxidative aromatisation (Jones reagent, 0°), the isomeric naphthacenediones (10) (53%), m.p. 209.5-210.5° [δ_{OH} 12.72, δ_{H*} 8.50] and (11) (13%), m.p. 242-243.5° [δ_{OH} 13.41, δ_{H*} 8.49]. This expected regioselectivity[3] was confirmed by the relative deshielding of the OH resonance in (11)[11] [cf. also the model compounds 1-hydroxy-5(8)-methoxy-9,10-anthraquinone, δ_{OH} 12.46 (12.95)]. Demethylation of (10) (BBr_3, CH_2Cl_2) gave (1) (96%), m.p. 314-315° [δ_{H*} (C_5D_5N) 8.17].

Cycloaddition to (4) was less selective, giving an inseparable mixture of diones (12) (29%) [δ_{OH} 12.91, δ_{H*} 9.05] and (13) (17%) [δ_{OH} 13.25, δ_{H*} 9.05]. But chromatographic separation occurred following demethylation of the mixture to give (2) (52%), dec. >268° [δ_{H*} (C_5D_5N) 9.28] and (14) (38%), dec. >315° [δ_{H*} (C_5D_5N) 9.33]. A non-chelated carbonyl band [ν_{max} (KBr) 1655 cm^{-1}] in the i.r. spectrum of (14), but not of (2) or (1), confirmed the orientation.

The electronic, i.r. and ^1H n.m.r. spectra of (2) agreed with actual spectra of SS-228R[12]. Since (1) and (2) are readily differentiated by these criteria as well as chromatographically this establishes (2) as the correct structure for this compound and supports the conclusions of Imamura et al.,[2] in regard to the structure of its photolabile precursor SS-228Y.

Satisfactory elemental analyses and spectra were obtained for all new compounds herein, except for (9) and (14) (exact mass). We are grateful to Dr Y. Okami for spectra of SS-228R and to Dr P. G. Griffiths for discussion.

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