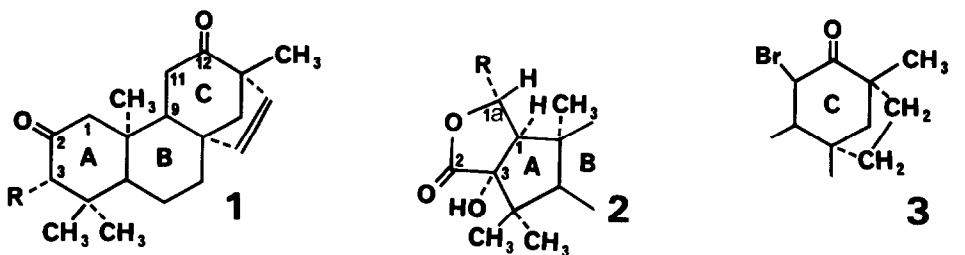


THE X-RAY CRYSTAL AND MOLECULAR STRUCTURE OF A TETRACYCLIC DITERPENOID -  
 BENZALDEHYDE REACTION PRODUCT AND THE LONG RANGE PROTECTIVE INFLUENCE OF ITS  
 BENZENE RING

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Base induced oxidation converts the ketol (1a) in the presence of oxygen to the 2-hydroxy-1-en-3-one diosphenol which in turn undergoes a base catalysed aldol condensation with benzaldehyde at C(1) from the  $\beta$ -face of the molecule. This is followed by a benzilic acid type ring A contraction and final esterification to give the lactone (2a), m.p. 267-268 $^{\circ}$ ,  $\nu_{\max}$  1750  $\text{cm}^{-1}$  and  $\tau$  4.83 and 7.31 (each 1H, d, J 9.0 Hz, 1a-H and 1-H respectively).



(1) a, R = OH  
 b, R = OAc

(2) B/C/D ring system as  
 in (1)  
 a, R = C<sub>6</sub>H<sub>5</sub>  
 b, R = H

(3) a, lactone/A/B ring  
 system as in (2a)  
 b, A/B ring system  
 as in (1b)

This lactone is obtained in good yield when a mixture of the ketol (1a) and benzaldehyde in aq. ethanol is treated with dilute sodium hydroxide in the presence of oxygen (over 50% crystalline yield from the reaction mixture); the use of formaldehyde produces an analogous product (2b), m.p. 219-220 $^{\circ}$ ,  $\nu_{\max}$  1770  $\text{cm}^{-1}$  and  $\tau$  5.76 and 6.01 (each 1H, t, J<sub>1a $\alpha$ ,1a $\beta$</sub>  10.0 Hz)

and 7.43 (1H, d, J 10 Hz, 1-H). A similar stereospecific reaction has been reported<sup>1</sup> for formaldehyde and a steroidal ring D-Homo diosphenol. Since geminal and vicinal electronegative substituents extend the range of proton coupling constants,<sup>2</sup> these values ( $J_{1,1a}$  9.0 Hz in (2a) and 7.2 Hz in (3a)) could not be used to determine the configuration of the nor-ring A/lactone system. However, stereochemical arguments indicated structure (2a).

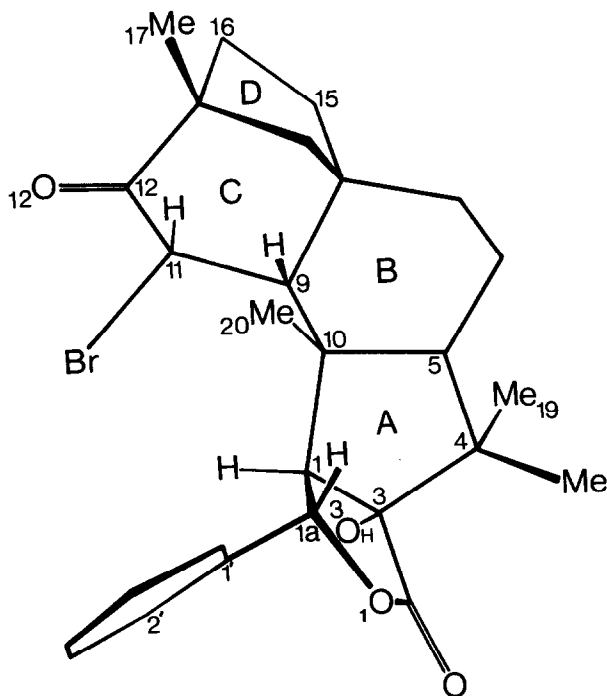
The two related 11 $\beta$ -bromo compounds (3a), m.p. 270-272<sup>o</sup> dec.,  $J_{1,1a}$  7.2 Hz and  $J_{9,11}$  12.4 Hz, and (3b),<sup>3</sup>  $J_{9,11}$  6.6 Hz, form stable crystals but each readily exchanges its bromine for hydrogen under mild conditions in the presence of proton donating solvents (e.g. acetolysis, base hydrolysis and, for (3a), after a few minutes treatment with boiling methanol) and it has not been possible to effect dehydrobromination.

The decrease in  $J_{9,11}$  from 12.4 Hz in (3a) to 6.6 Hz in (3b) reflects the steric interaction between the benzene ring and the 11 $\beta$ -equatorial bromine in (3a) which forces the 9 $\beta$  and the 11 $\alpha$  hydrogens into a more perfect transdiaxial conformation. In product (2a), the benzene ring protects the 12-keto group from  $\beta$ -attack. Thus, while NaBH<sub>4</sub> reduction of (1a) resulted in high conversion of the 12-keto group to a 12 $\alpha$ -equatorial alcohol,<sup>3</sup> similar reduction of (2a) gave an easily separable mixture of the 12 $\alpha$ - and the otherwise not readily accessible 12 $\beta$ -axial alcohol in a 3:2 ratio respectively. This reversal of steric hindrance at C(12) was even more pronounced when the bulkier LiAl(t-BuO)<sub>3</sub>H was used; the main reduction product from (2a) was the 12 $\beta$ -axial alcohol (70% crystalline yield). Thus the long range shielding effect of the benzene ring is more effective over the  $\beta$ -face of the molecule than the short range protection afforded by the  $\alpha$ -diaxially oriented D-ring towards the  $\alpha$ -side of the molecule.

Crystals of the 11 $\beta$ -bromo compound (3a) C<sub>27</sub>H<sub>33</sub>BrO<sub>4</sub>, were orthorhombic, space group P2<sub>1</sub>2<sub>1</sub>2<sub>1</sub>.  $\underline{a}$  = 21.20,  $\underline{b}$  = 11.42,  $\underline{c}$  = 9.84 ( $\pm 0.01$ Å), U = 2382 Å<sup>3</sup>,  $D_m$  = 1.31 gcm<sup>-3</sup>, Z = 4.

Intensity data were collected on a Philips four circle diffractometer with Zr-filtered Mo-K $\alpha$  radiation. The structure was solved by the usual heavy atom and Fourier methods, and refined isotropically (Br anisotropic) by block-diagonal least squares to R = 0.08 for 1230 observed data. (All calculations were done with the local set of programs;<sup>4</sup> further refinement is continuing.)

The stereochemistry of the molecular skeleton confirms that the rearrangements took place as suggested (Figure: a projection down  $\underline{a}$ ). The bond lengths and angles are generally normal; Br-C(11) = 1.99 Å.



Angle C(4)-C(5)-C(10) = 105°, while angle C(1)-C(10)-C(5) = 99°. Similar distortions at analogous carbon atoms carrying an axial substituent have been observed previously in related compounds.<sup>5</sup> Methyl group C(20) is in close contact with three groups: methyl C(19)-3.33 Å; hydroxyl O(3)-3.25 Å and C(15) of the bridge in the D ring -3.42 Å. The latter separation is distinctly larger than that found for the analogous pair of atoms in a closely related molecule,<sup>5</sup> in which the rings C and D are 5- and 6-membered respectively.

The nor-ring A/lactone system is twisted up and clockwise relative to the average plane of ring C. This results in the torsion angle between the hydrogen atoms on C(11) and C(9) being  $173^\circ$ , (consistent with the observed coupling constant of 12.4 Hz). The torsion angle between the hydrogen atoms on C(1) and C(1a) is  $124^\circ$ , again consistent<sup>6</sup> with the observed coupling constant of 7.2 Hz.

The distortions in the skeleton are caused by the short non-bonded distance between the bromine atom and the benzene ring: Br--C(2') = 3.52, Br--C(1') = 3.46 Å. The strain is relieved also by angular distortion at C(11) and C(1a) where the internal angles are opened up considerably: C(9)-C(11)-Br =  $113^\circ$ , C(12)-C(11)-Br =  $107^\circ$ , C(1)-C(1a)-C(1') =  $120^\circ$ , O(1)-C(1a)-C(1') =  $106^\circ$ .

It is evident that when the only substituents on C(11) are H atoms, the benzene ring can approach C(11) more closely and hence shield C(12) and O(12) more effectively from above.

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#### REFERENCES:

1. N.L. Wendler, D. Taub and R.P. Graber, *Tetrahedron*, 1959, 7, 173.
2. D.H. Williams and I. Fleming, *Spectroscopic Methods in Organic Chemistry*, McGraw-Hill, London, 1966, pp. 109-110.
3. K.H. Pegel, L.P.L. Piacenza, L. Phillips, E.S. Waight, *Chem. Comm.* 1971, 1346.
4. M. Laing, *Acta Cryst.*, 1972, B28, 986.
5. M. Laing, D. Hanouskova, P. Sommerville, K.H. Pegel, L.P.L. Piacenza, L. Phillips and E.S. Waight, *Chem. Comm.* 1972, 196.
6. J.R. Hanson, G.M. McLaughlin, G.A. Sim, *J. Chem. Soc., Perkin II*, 1972, 1124.