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# AN UNUSUAL SYNTHESIS OF BENZOPENTALENE DERIVATIVES

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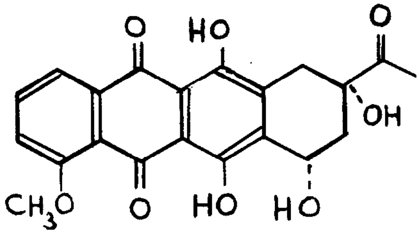
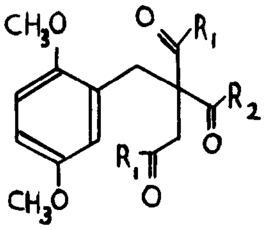
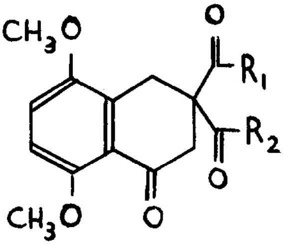
In connection with studies directed toward the total synthesis of anthracyclinones[1] related to daunomycinone (**1**)[2] we have prepared a series of dimethoxytetralones of general structure **3**[3]. For example, the triester **2a**, formed in 76% yield by alkylation of trimethyl 1,1,2-ethanetricarboxylate with 2,5-dimethoxybenzyl chloride, cyclizes cleanly in polyphosphoric acid (1 hr, 105°) to give 60% of the expected tetralone diester **3a**, mp 121-122°; $\nu_{CO}$ 1727, 1681 $cm^{-1}$; $\lambda_{max}$ 348 nm ($\varepsilon$ = 3900), 255 nm ($\varepsilon$ = 6000) and 231 nm ($\varepsilon$ = 15,400).[4]



**1**



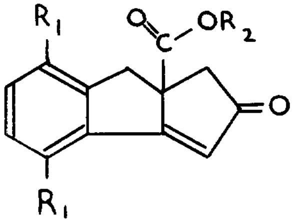
**2a** $R_1 = R_2 = OCH_3$
**2b** $R_1 = OCH_3$, $R_2 = CH_3$
**2c** $R_1 = OC_2H_5$, $R_2 = CH_3$



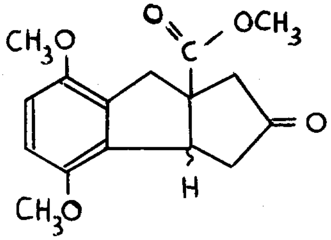
**3a** $R_1 = R_2 = OCH_3$
**3b** $R_1 = OCH_3$, $R_2 = CH_3$

When, however, the ketodiester **2b** is treated with polyphosphoric acid (20 min, 105°) none of the expected tetralone **3b** is observed. There is obtained instead as the major neutral product 25-30% of a colorless compound, mp 174-175°, which has the molecular formula $C_{16}H_{16}O_5$ and spectroscopic properties profoundly different from either **2b** or **3b**. The unknown exhibited ir maxima at 1730, 1709 and 1621 $cm^{-1}$, a new uv chromophore with $\lambda_{max}$ 352 nm

($\varepsilon$ = 5370), 296 nm ($\varepsilon$ = 18,300), 253 nm ($\varepsilon$ = 8740), and pmr signals (100 MHz) at $\delta$ 2.52 and 2.92 (2H, AB quartet, J = 16.5 Hz), 2.71 and 3.80 (2H, AB quartet, J = 16.5 Hz), 3.56 (3H,s), 3.76 (3H,s), 3.80 (3H,s), 6.28 (1H,s), 6.66 and 6.86 (2H, AB quartet, J = 9.5 Hz). These data are uniquely accommodated by structure 4b.



4a $R_1 = H$, $R_2 = C_2H_5$
4b $R_1 = OCH_3$, $R_2 = CH_3$
4c $R_1 = OCH_3$, $R_2 = C_2H_5$



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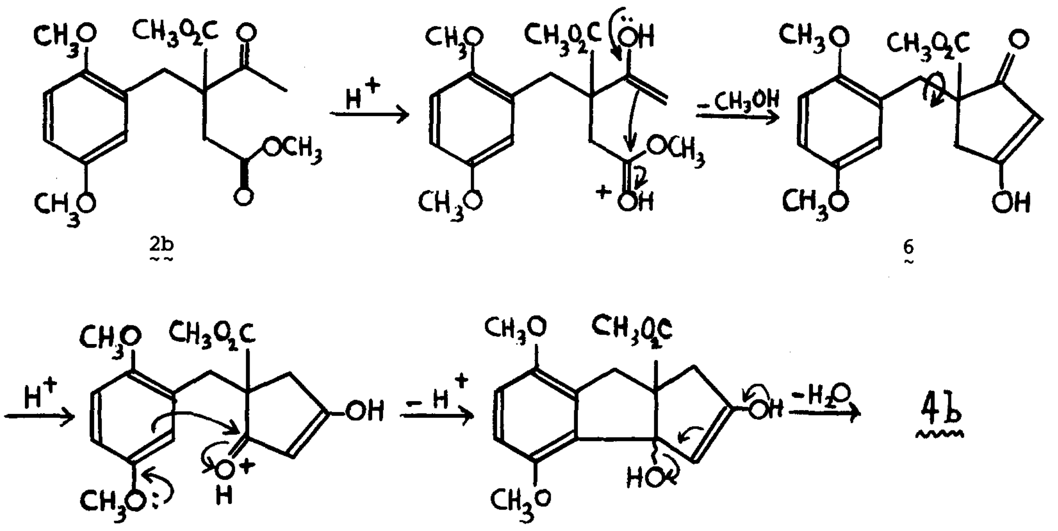
Cmr spectroscopy revealed a signal at $\delta$ 208.2 for the cyclopentenone carbonyl, peaks at $\delta$ 177.8 and 173.3 for the $\beta$-carbon of an enone and an ester carbonyl, plus three signals at $\delta$ 53.6, 47.5 and 36.4 corresponding to the saturated ring carbons of structure 4b. The structure was further confirmed by catalytic hydrogenation (10% Pd/C) to the oily dihydro derivative 5 ($\nu_{CO}$ 1740 cm$^{-1}$; $\lambda_{max}$ 286 nm, $\varepsilon$ = 3460), characterized as the crystalline 2,4-dinitrophenylhydrazone, mp 95-96°, $\nu_{CO}$ 1729 cm$^{-1}$.

This unexpected generation of the benzopentalene system 4 may well be general. The ethyl ester 4c is formed in 33% yield from ketodiester 2c, and the reaction does not require an activated benzene ring. Thus the compound 4a, mp 126-127°, is formed in 40% yield from the desmethoxy counterpart of 2c under the usual conditions.

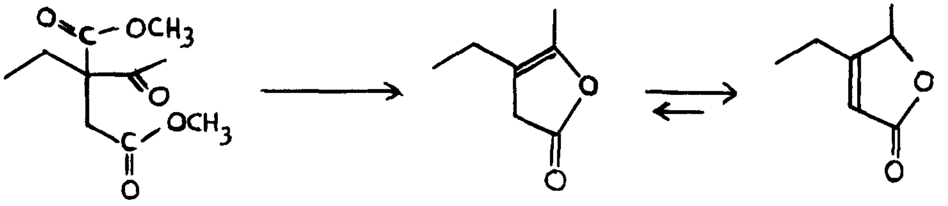
We have considered two mechanisms to account for the formation of system 4 instead of a tetralone in these cyclizations. Mechanism A postulates initial conversion of the side chain by enol acylation to a cyclopentenolone (6) followed by acylation of the aromatic ring.

## Mechanism A



2b 6

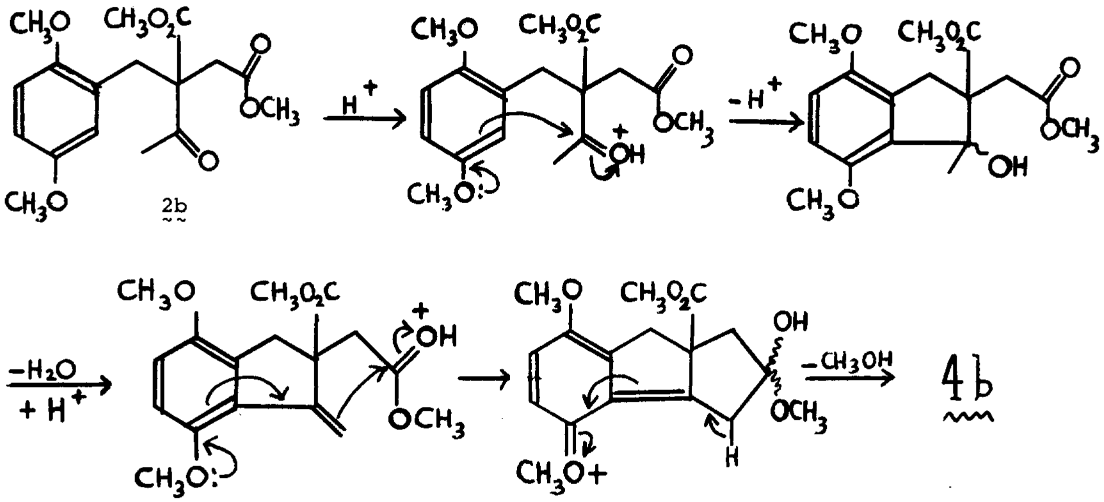
An independent experiment reveals, however, that the model ketodiester 7 is smoothly converted by polyphosphoric acid predominantly to the butenolide 8 (54%; $\nu_{CO}$ 1757 $cm^{-1}$; nmr $\delta$ 1.24, 3H, t; 1.42, 3H, d; 2.32, 2H, m; 4.98, 1H, q; 5.82, 1H, m).



7 8

Since no cyclopentenolone could be detected from 7 we conclude that system 4 arises from the alternative sequence shown as Mechanism B.

## Mechanism B



We are continuing our study of the scope and utility of these vinylogous acylations.

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## References

1. For an excellent review see R. H. Thompson, "Naturally Occurring Quinones," Academic Press, London, 1971, pp. 537-575.

2. F. Arcamone et al, J. Amer. Chem. Soc., 86, 5334, 5335 (1964); Tetra-Lett., 3349, 3353 (1968); C. M. Wong, R. Schwenk, D. Popien and T.-L. Ho, Can. J. Chem., 51, 466 (1973).

3. Cf. C. M. Wong, D. Popien, R. Schwenk and J. Te Raa, Can. J. Chem., 49, 2712 (1971); E. C. Horning and G. N. Walker, J. Amer. Chem. Soc., 74, 5147 (1952).

4. All new compounds gave combustion analyses, mass spectra, uv, ir and nmr data in accord with the proposed structures. The uv, ir and nmr data refer to methanol, chloroform and CDCl$_3$ solvents, respectively. Both pmr and cmr values are given in ppm downfield from TMS.