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A NOVEL 2,3-DIOXO-NORCAR-4-ENE-7-CARBOXYLIC ACID VIA REARRANGEMENT OF AN α-DIKETONE

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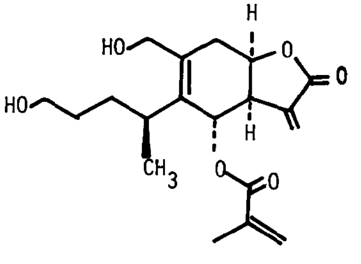
Summary: The structural rearrangement product of an α-diketone from a singlet oxygen reaction has been identified. The proposed intermediate has been trapped by diazomethane esterification.

Wasserman and Ives[2] have developed a useful method for transforming methylene ketones into α-diketones by singlet oxygen cleavage of the derived α-dimethylaminomethylene ketone. We have had occasion to employ this reaction sequence on enamino ketone 6 in an effort to prepare α-diketone 7, a key intermediate in a synthetic route toward eriolanin (1) via the cyclopropylcarbinyl mesylate solvolysis developed earlier in this laboratory.[3]



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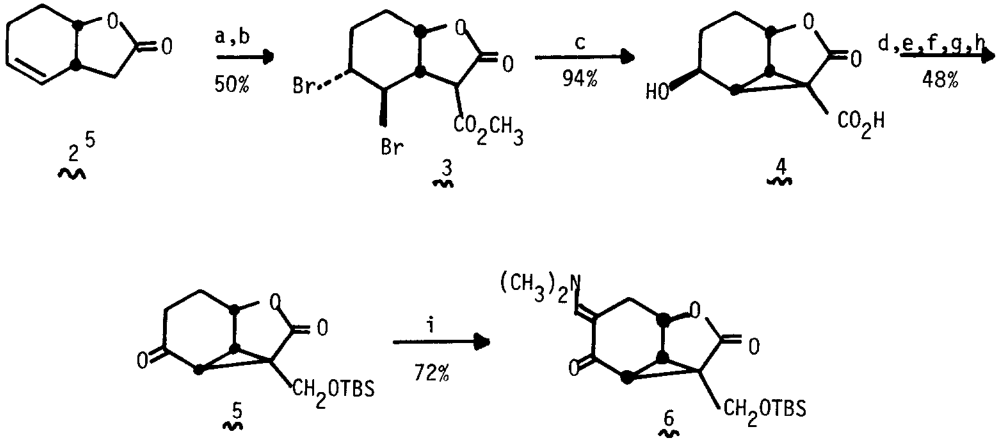
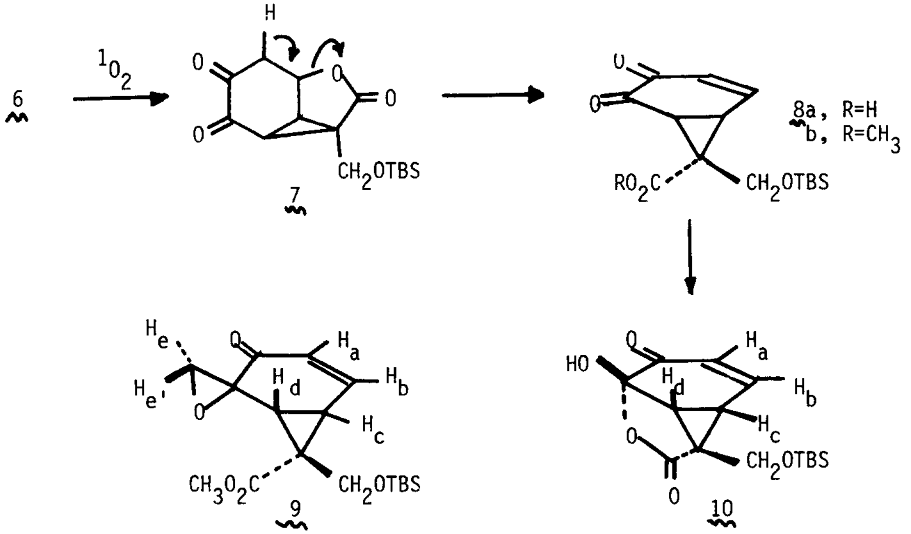
The synthesis of enaminoketone 6 is outlined in Scheme I. The trans-dibromide 3 can be fractionally crystallized from its other trans diastereomer and the mother liquors from the crystallization recycled (Zn-HOAc) through the olefinic lactone ester. Particularly noteworthy is the transformation 3 → 4 which at 0°C initially effects ring closure[4] and subsequently at 25°C saponifies the ester function and displaces (S_N2) the cyclopropylcarbinyl bromide in a highly efficient sequence.

Singlet oxygen cleavage of the vinylgous amide 6 (-78°C, 40 min, 1.2 equiv O_2, bis-acenaphthalenethiophene (BANT)) gave rise to a single product (mp 145-147°C; IR ($CHCl_3$) 3600-3000, 1786, and 1707 cm^{-1}; NMR ($CDCl_3$, 90MHz) δ 7.05 ($1H_b$, dd, $J_{a,b}$=10Hz, $J_{b,c}$=5Hz); 6.28 ($1H_a$, d, $J_{a,b}$=10Hz), 4.24 (1H, d, J=11Hz, -C$\underline{H}$H-), 3.99 (1H, d, J=11Hz, -CH$\underline{H}$-), 2.93 ($1H_d$, d, $J_{c,d}$=5Hz), 2.68 ($1H_c$,m), 0.90 (9H, s, t-C_4H_9), and 0.10 (6H, s, CH_3). Although the 5-membered lactone ring (1786 cm^{-1}) had been retained, clearly the appearance of two coupled vinylic hydrogens precluded α-diketone 7 or its enol tautomer from consideration as the singlet oxygen product. The spectroscopic data were more readily accommodated by the structure 10[9].

Scheme I



a) NaH, $(CH_3O)_2CO$, toluene, reflux, b) Br_2, CH_2Cl_2, c) KOH, CH_2Cl_2/H_2O, d) Ac_2O, pyr., e) $BH_3\cdot DMS$, f) t-butyldimethylchlorosilane (TBSCl), imidazole, DMF[6], g) K_2CO_3, aq. CH_3OH, h) $C_5H_5NHCl\cdot CrO_3$, NaOAc, CH_2Cl_2[7], i) $((CH_3)_2N)_2CHOCH_3$, 60°C[8].



The intermediate acid **8a** could neither be detected spectroscopically nor isolated. However, evidence for a finite equilibrium **8a**⇄**10** was obtained by treatment of **10** with an excess of diazomethane (Et_2O-CH_2Cl_2, 0°C, 0.3h) which produced the yellow[10],crystalline norcarenedione ester **8b** (mp 104-105.5°C; IR (CCl_4) 1732 and 1696 cm^{1}; NMR ($CDCl_3$, 270MHz) δ 7.00 (1H, dd, J=4 and 10Hz), 6.41 (1H, d, J=10Hz), 4.10 (1H, d, J=11Hz), 3.98 (1H, d, J=11Hz), 3.66 (3H,s), 2.96 (1H, d, J=6Hz), 2.82 (1H,m), 0.89 (9H,s), 0.10 (3H,s), and 0.08 (3H,s); UV (CH_3CN) λ_{max}=271 (ε=4060), 424nm (ε=16) in 69% yield from **6**. We believe this compound to be the first norcarane of this substitution pattern.[11]

A minor component **9** (IR (CCl_4) 1728 and 1684 cm^{-1}; NMR ($CDCl_3$, 270 MHz) δ6.90 (1H$_b$, dd, J$_{a,b}$=10Hz, J$_{b,c}$=5Hz), 6.20 (1H$_a$, d, J$_{a,b}$=10Hz), 4.22 (1H$_f$, d, J$_{f,f'}$=10Hz), 3.62 (3H,s), 3.61 (2H, m, H$_e$, H$_f$), 2.97 (1H$_e$, d, J$_{e,e'}$=6Hz), 2.31 (1H$_c$, dd, J$_{b,c}$=5Hz, J$_{c,d}$=8Hz), 2.98 (1H, d, J$_{c,d}$ = 8Hz), 0.87 (9H,s), and 0.05 (6H,s) could be isolated from the diazomethane reaction. Its NMR spectrum differed from that of **8b** by the presence of an AB pattern at δ3.61 and 2.98. Irradiation of the obscured 2-proton signal at δ3.61 caused the collapse of both the signal at δ2.98 and 4.22 substantiating the presence of two geminal methylene groups in the molecule. Individual irradiation of the protons H$_a$, H$_b$, H$_c$, and H$_d$ confirmed their contiguous arrangement about the 6-membered ring.

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9. While our initial data indicated that the enol of 7 had been formed, a more detailed analysis of a higher field NMR spectrum revealed that rearrangement had occurred.
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