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OXIDATION OF 4,5-DIHYDROXYHOMOCUBANE: OXIDATIVE CLEAVAGE OF THE CENTRAL BOND TO GENERATE TETRACYCLO $[4.3.0.0^{3,9}.0^{4,7}]$ NONANE-2,5-DIONE

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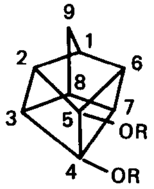
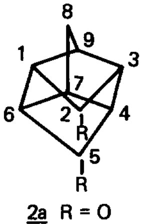
Until now, no derivatives containing the highly strained (65-75 Kcal/mole) tetracyclo $[4.3.0.0^{3,9}.0^{4,7}]$ nonane skeleton have been described. Models indicate that sp^2 hydridization at positions 2 and 5 (e.g. 2a and 2b) creates additional strain, complete rigidity and an interaction distance of only 2.6A between carbon atoms 2 and 5.[1] These factors combined make derivatives such as 2a and 2b excellent candidates for a study of transannular spectral[3] and chemical interactions. We describe here the generation of 2a by oxidative cleavage of the 4,5 bond of an appropriately disubstituted homocubane derivative.

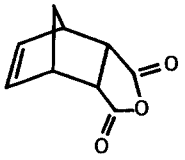
Previous attempts to cleave the 4,5-bond of substituted homocubanes have failed due to the increased lability of the peripheral cyclobutane bonds relative to the central bond.[4] This tendency has been rationalized energetically on grounds of maximal skeletal strain relief attending chemical transformation. For this reason, activation of the central bond by reactive functionalization at both C_4 and C_5 was considered essential to successful cleavage. In this respect, the recently synthesized 4,5-dihydroxyhomocubane, 1a,[5] provides an excellent starting material.



1a R = H
1b R = Et



2a R = O
2b R = CH_2



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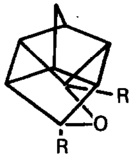
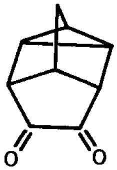
Addition of the diol 1a to a suspension of $Pb(OAc)_4$ in acetone at room temperature resulted in the rapid disappearance of starting material and the isolation of the diketone 2a in 50-60% yield: mp 106-108°dec., $^1H_{nmr}$ $\tau(CDCl_3)$ 6.71 (distorted t, J=1.5Hz, 4H), 6.95 (2H) and 7.75 (unresolved multiplet, 1/2 wd 4Hz, 2H); ir($CDCl_3$) 3000, 2950, 2860, 1782, 1760, 1245, 1115, 1050, 855 and 780 cm^{-1}; mass spectroscopic molecular weight 148. Irradiation of the multiplet at τ 6.95 caused the corresponding absorptions at τ 6.71 and 7.75 to collapse to singlets. The ultraviolet spectrum of 2a in acetonitrile showed only a single broad featureless n-π* maximum at λ 282nm (ε=59). No additional short wavelength maxima were observed at λ> 210nm. The UV data thus provides no direct evidence of transannular interaction between the carbonyl groups in spite of their proximity. A final decision on the extent of ground state interaction must await analysis of the photoelectron spectrum of 2a which is in progress.

The diketone 2a was stable at room temperature when pure but decomposed thermally in solution at temperatures as low as 90°.[6] The strain and proximity of the carbonyl groups in 2a was manifested in a pronounced tendency toward transannular reactions in protic solvents containing catalytic amounts of acid. For example, when 1.1 equivalents of water was added to a solution of 2a in THF which contained a catalytic amount of p-toluenesulfonic acid, the transannular hemiketal 4a was produced in quantitative yield: $^1H_{nmr}$ (acetone d_6) τ 6.21 (br s, 2H), 7.28 (s, 6H) and 8.41 (s, 2H); ir(KBr) 3350 (br), 2980, 2960, 2930, 2850, 1350, 1316, 1260, 1170, 1130, 1100, 1010, 935 and 890 cm^{-1}; mass spectroscopic molecular weight 166. Since the insolubility of 4a and its tendency to retain water precluded further purification, the corresponding diacetate derivative 4b was prepared by stirring with acetic anhydride-pyridine for seven days; mp 112-114°; $^1H_{nmr}$ τ ($CDCl_3$) 6.81 (t, J=2Hz, 4H), 7.22m, 2H) 7.92 (s, 6H) and 8.38 (unresolved multiplet, 1/2wd 4.5Hz, 2H); ir(KBr) 3000, 2970, 2940, 2920, 2825, 1770, 1750(sh), 1320, 1310, 1220, 1200, 1160, 1130, 1040, 1010 and 985 cm^{-1}. As previously described[5] the preparation of diacetate derivatives destroys the accidental chemical equivalence of the bridgehead methine protons in these cage coupounds. Similarly, when 2a was dissolved in acetic acid d_4, the nmr signals of the starting material were rapidly replaced by those of the transannular hydrate 4a which is apparently formed by addition of water present in the solvent. When this solution was treated with $Pb(OAc)_4$, the hydrate was rapidly transformed into the anhydride 3 in quantitative yield.[7]

Interestingly, the $Pb(OAc)_4$ products of the oxidation of 1a show a curious solvent dependence. In benzene, the dione 2a is a minor product and two additional compounds could be isolated by glpc. The material with the shorter retention time, which was intensely yellow, was identified by its spectral data as the α-diketone 5: $^1H_{nmr}$ τ ($CDCl_3$) 7.32 (m, 2H), 7.67 (m, 1H), 8.11 (t, J=4.5 Hz complicated by additional splitting, 1H), 8.25 (t, J=2Hz, 2H) and 8.61 (d, J=4.5Hz with additional splitting, 1H); ir(neat) 3080, 2980, 2940, 2870, 1760(sh), 1755, 1210, 1163, 815 and 795 cm^{-1}; visible spectrum λ_{max} CH_2Cl_2 440(ε=25), 450(ε=28), 458(ε=28), 467(ε=25) and 480nm (ε=17); mass spectroscopic molecular weight 148. A sample of 5 was prepared independently in low yield by the oxidation of the known ketone 6[8] with SeO_2 in refluxing xylene. The material of longer retention time was similarly identified as the corresponding anhydride 7; mp 86-88°; $^1H_{nmr}$ τ ($CDCl_3$) 7.21 (unresolved m, 2H), 7.48 (m, 1H), and 8.28 (m, 5H); ir($CDCl_3$) 3080, 2960, 2880, 1810, 1755, 1285, 1260, 1259, 1180, 1145, 1115, 990, 960 and 810cm^{-1}; mass spectroscopic molecular weight 164. The relative ratio of 5/7 in the crude mixture varied from one run to the next. The anhydride 7 is apparently produced from 5 by subsequent oxidation by Pb(IV). In fact, if two moles of $Pb(OAc)_4$ per mole of diol are employed, 7 is isolated in 60% yield. This reaction has synthetic potential for the preparation of a number of difficulty accessible substituted nortricyclene derivatives.



4a R = OH
4b R = OAc
4c R = OEt



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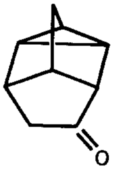

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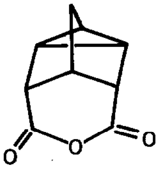

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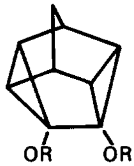

8a R = H
8b R = Et

While the mechanism of the transformation of 1 into 5 and ultimately to 7 is not known with certainty, it is suspected that the oxidation is preceded by rearrangement to the diol 8 or lead ester thereof and subsequent oxidative rearrangement.[9] Consistently, 8a[10] is rapidly transformed into a mixture of 5 and 7 upon treatment with lead tetraacetate in benzene. The suggested conversion of the homocubyl skeleton of 1a to the postulated intermediate 8a is reminiscent of similar transformations induced by the transition metals.[11] However, this type of interconversion has never been reported using Pb(IV).

In hopes of observing this transformation without subsequent oxidation, the diether 1b was treated with $Pb(OAc)_4$ in benzene at 25° (4 hr). The starting material was recovered (50-60%) from the reaction mixture, and no rearranged isomer 8b could be detected by nmr. The only volatile product isolated from this reaction was the transannular ketal 4c (15%) resulting formally from the unusual insertion of oxygen into the strained 4,5-bond. While 1b does not undergo the desired transformation in the presence of $Pb(OAc)_4$, that is no assurance that the rearrangement prone diol 1a, which is probably present in solution as a lead ester, will not.

Further investigation of the mechanism of this transformation is proceeding.

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