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PROPELLANES. LXXXVIII.[*] HYDROXYLATION OF 11,13-DIOXO-12-METHYL-12-AZA[4.3.3]PROPELLA-3,8-DIENE WITH OSMIUM TETROXIDE[†]

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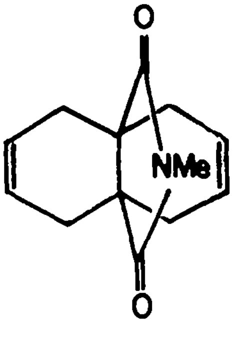
Abstract - The all-anti-tetrol *2* is the major product of OsO_4-hydroxylation of the title compound *1*.

We hoped that the cage diether *3* might be prepared *via* the intermediate *2* which may be prepared, at least as one component of a tetrol mixture by *cis*-hydroxylation of *1*.



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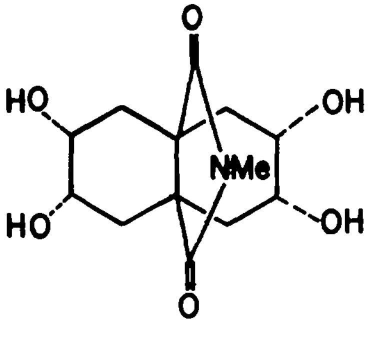

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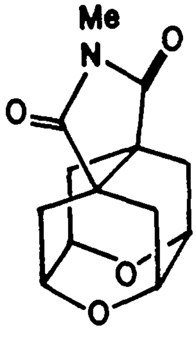

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Since *1* has C_{2v} symmetry one may expect *a priori* that (catalytic) hydroxylation using osmium tetroxide of only one of its two double bonds could afford two configurationally-related ene-diols, one with the set of *cis*-hydroxyls *syn* with respect to the imide ring, the other *anti* to it. If both double bonds were hydroxylated one could obtain three isomeric tetrols (all-*syn*, all-anti *2* and syn-syn-anti-anti). The reaction mixture might contain six components including starting material *1*. Since in our experience[1] we were able to separate components of product mixtures we braved this new experiment, for if *2a* could be isolated it might be cyclized into the cage diether *3* which contains the dioxa-iceane skeleton.

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[*] Dedicated to PROFESSOR RALPH A. RAPHAEL, F.R.S., dear friend and great scientist, on the occasion of his 65th birthday, and, of course, to PRUDENCE, however young she may be.

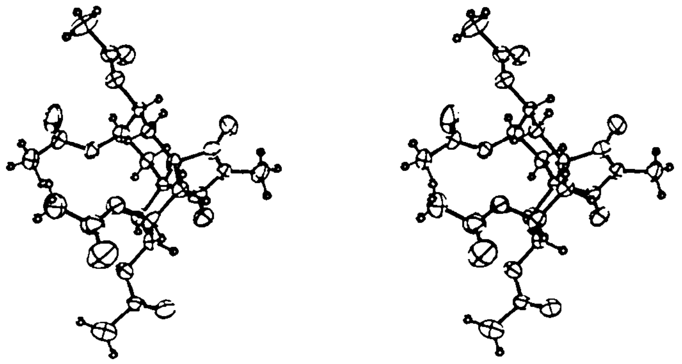
[†] Part LXXXVII. D. Ginsburg, L. Stehling, G. Wilke, R. Benn, and R. Goddard, *Helv.Chim.Acta*, in press.

In eating the pudding, catalytic osmium tetroxide hydroxylation of *1* in the presence of N-methylmorpholine oxide (NMMO) indeed gave a mixture of products as was immediately obvious from observation of the NMR spectrum of the crude product-mixture (vinylic protons : in part only one double bond hydroxylated, many N-CH_3 signals). The pudding was intractably inedible. Attempted chromatographic separation of the polyol mixture was unsuccessful. Since we have an example[1a] of separation of an even more complex reaction mixture (albeit by a Swiss chemist) we decided not to join Sisyphus even if it meant eventual success. We were pragmatically satisfied with the isolation in 40% yield of the major component (all-*anti*) particularly since this is the very intermediate we require.

However, isolation was indirect. We acetylated the polyol mixture with acetic anhydride in pyridine, separated a pure fraction of *2b* from the silica column, and did not deal with the other, oily, fractions. Saponification of *2b* afforded the desired tetrol *2a*.

Nevertheless we were unsuccessful in obtaining *3* by variegated reaction conditions. Perhaps by Ralph Raphael's 70th birthday we may succeed in preparing *3* by employing certain epoxides which we have prepared long ago.[1b]

The structure of *2b* was proved unequivocally as the all-*anti* tetraacetate. The structure of *2a* follows.



ORTEP *2b*

The formation of *2a* as the major (but by no means exclusive) product may point to the intermediacy of a complex[2] in which osmium is simultaneously bound to both double bonds of *1* in a di-boat conformation. Such an intermediate would explain the relative high yield of *2a*.

EXPERIMENTAL

Hydroxylation of *1*.- To a mixture of *1* (2.21g), NMMO·H_2O[3] (2.93g) in t-BuOH (40 ml), water (13 ml) and pyridine (1.5 ml) was added 0_8O_4 (104 mg) in t-BuOH (5 ml) and the whole was heated under reflux (N_2) for 20 h. An aqueous (20 ml) solution of $NaHSO_3$ (4.39g) was added, mixing was continued for 1 h and the solution was evaporated to dryness (water pump). Unreacted *1* (71 mg) was recovered after extraction with benzene and evaporation of solvent. The aqueous phase was evaporated to dryness (5.48g; quantitative hydroxylation would have afforded only 2.85g) and the residue was extracted with MeOH. The ^1H-NMR spectrum of the crude mixture showed a peak at 5.8 (vinylic protons. The conditions employed are a modification of the published one[3].

Tetraacetate *2b*.- To the above crude product (5.1g) in pyridine (60 ml) was added acetic anhydride (15 ml) dropwise with ice-bath cooling under N_2. After 70 h (to assume acetylation of OH groups of every configuration), ice was added and the whole was evaporated to dryness. Extraction with benzene afforded a mixture of diacetates (vinylic protons) and tetraacetates. Chromatography on silica (Woelm, aktiv, 70-150 mesh) using AcOEt(1)/hexane(1) gave many impure fractions and a major fraction of pure *2b* (40%), m.p. 230°C. The analytical sample had m.p. 234° (MeOH). IR($CHCl_3$): 1780, 1741, 1710. ^1H-NMR($CDCl_3$): 4.95 (t, 4 CHO); 2.98 (s, 3 NCH_3); 2.25-1.95 (m, s, 12 CH_3CO + 8 CH_2). MS: 393 (41, M^+-AcOH); 351(15); 333(9); 273(7); 231(100). Calc. C, 55.62; H, 5.98; N, 3.09, found C, 55.67; H, 6.24; N, 3.41.

Hydrolysis to *2a*. - *2b* (227 mg) was dissolved in the minimal amount of AcOH (0.65 ml) with heating. HCl (2N, 13 ml) was added and the whole heated under reflux for 5 h and evaporated to dryness (oil pump). Treatment with benzene gave crude *2a* (140 mg), m.p. 218-228°. The analytical sample had m.p. 232-234°C (i-PrOH). IR (KBr): 3400 (br), 1779, 1700. ^{1}H-NMR (TFA): 3.75 (br s, 4 CHO); 2.7 (s, 3 NCH_3); 2.1-1.7 (m, 8 CH_2). MS: 285 (2.4, M^+); 242 (9); 241 (100); 223 (13); 198 (42); 180 (39); 167 (13).

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