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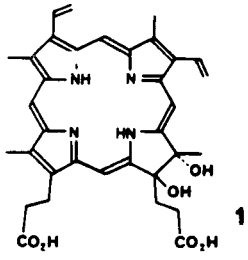
When *vic*-dihydroxychlorins undergo a pinacol-pinacolone rearrangement, the migratory aptitudes of common porphyrin substituents follow the order: alkyl groups, propionate side chain, H > methyl group > acetate side chain. *C*-Alkylchlorins can be made by extremely short syntheses utilizing such rearrangement.

J. Heterocyclic Chem., **22**, 1739 (1985).

Apart from the iron porphyrin-containing cytochromes found in animals and plants, d-type cytochromes present in many microbial nitrite reductases/cytochrome oxidases contain a green heme prosthetic group whose structure has been assumed since the late 1950's to be a chlorin. The dihydroporphyrin structure originally proposed by Barrett [1] for heme *d* isolated from *Aerobacter aerogenes* has recently been reinvestigated [2] to show that it is in fact a derivative of 5,6-dihydroxyprotochlorin IX (**1**). The vicinal dihydroxy structure is stable under oxidizing conditions but labile in acids as it would undergo a pinacol-pinacolone rearrangement to produce oxochlorins. The oxo derivatives of chlorin and isobacteriochlorin are known compounds [3,4] but their biological significance has not been recognized. We [5] have recently suggested that heme d_1 obtained from *Pseudomonas aeruginosa* and *Parracocus denitrificans* is not a chlorin but a dioxoisobacteriochlorin (**2**). This novel dioxo structure has now been



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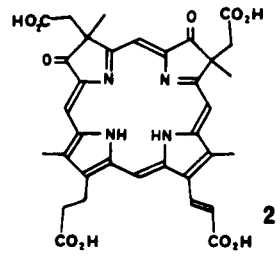

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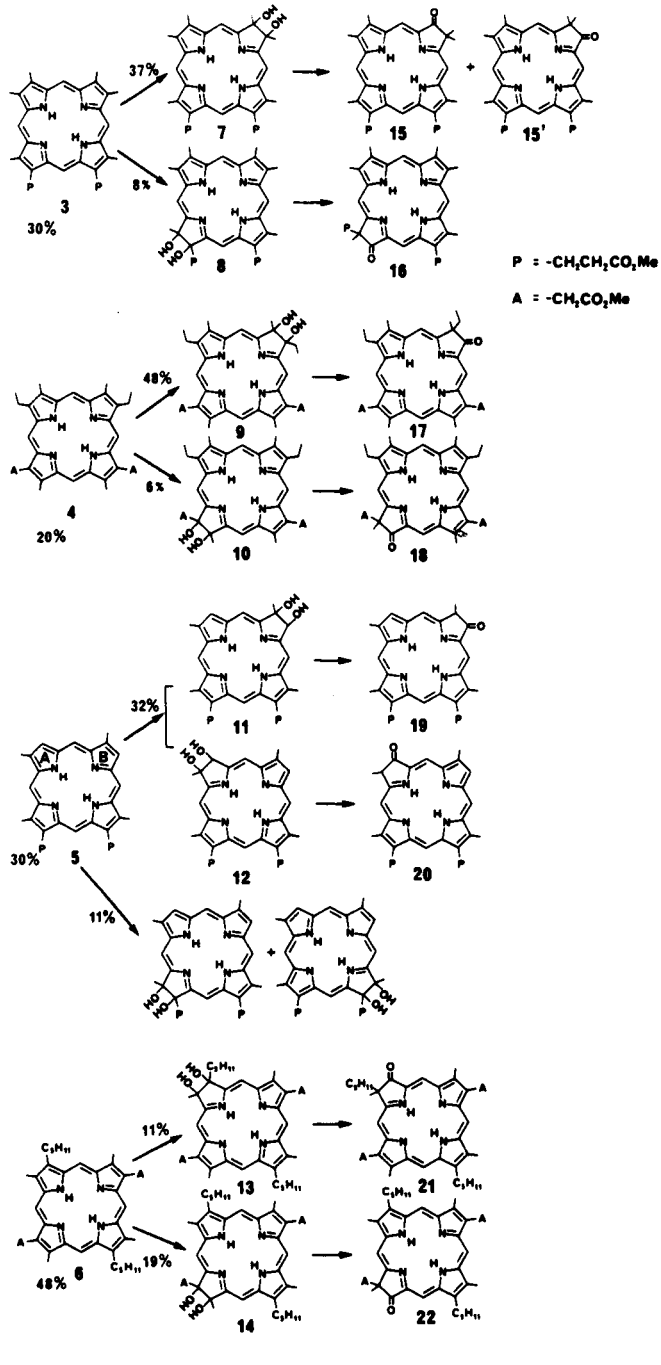
verified by comparative studies of the purified heme d_1 ligand and model compounds [6]. This realization has brought unprecedented attention to the oxo family of porphyrin derivatives. Of special interest is the biosynthetic pathways by which the oxo compounds come into being. The passage from a *vic*-dihydroxy or epoxy precursor to the keto macrocycle *via* pinacolic rearrangements is a viable possibility. A central question in the pinacolic rearrangement is the migratory aptitude of the side chains. While this question has been addressed amply in alicyclic systems [7], the outcome when applied to porphyrin rings is not readily predictable. We here report the migratory aptitudes of several common and biologically important porphyrin side chains.

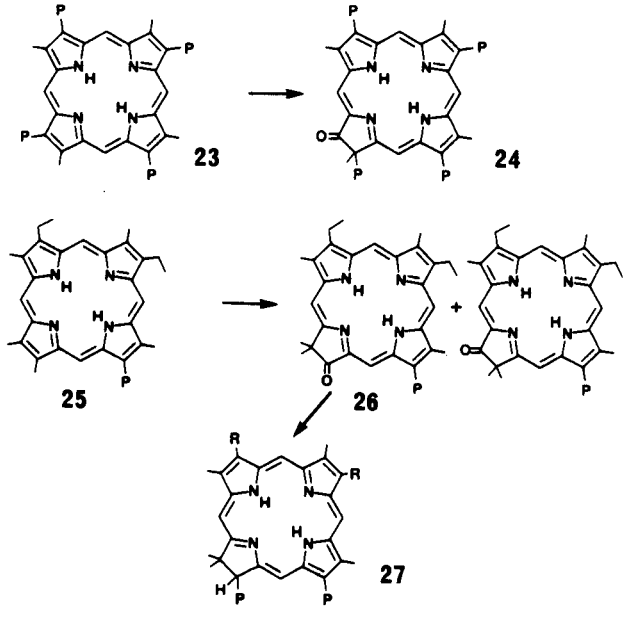


SCHEME I

Four porphyrins **3-6** were chosen for investigation [8]. These phorphyrins were converted into the dihydroxychlorins using osmium tetroxide as reported [9]. The porphyrins were allowed to react with 1.2 equivalents of osmium tetroxide in methylene chloride and the reaction was quenched after 20 hours with the osmium esters being decomposed by hydrogen sulfide. Analyses (tlc, silica gel, methylene chloride-methanol) indicated that the reaction mixtures contained variable amounts of chlorins plus the unreacted porphyrin. Isolation of individual components by chromatography and crystallization afforded the chlorin isomers as well as the starting porphyrin with yields shown in Scheme I. The formation of the osmium esters is highly dependent on the porphyrin substituents. The relative yields of the chlorins thus produced a crude reactivity scale for the osmium tetroxide addition to porphyrin β-β' double bonds: as would be expected, barring electronic effects, the larger the side chain, the slower the rate. The chlorin structures were determined by ^{1}H nmr and by mass spectra. In the case of deuteroporphyrin dimethyl ester **5**, the separation of A-ring and B-ring chlorins was difficult; the mixture was employed for the subsequent rearrangement study.

The acid-catalyzed pinacol-pinacolone rearrangement required different acid strength depending on whether the substituents are electron releasing or withdrawing. For example, while diol **7** was converted smoothly into equal amounts of the two ketones by one drop of 70% perchloric acid in methylene chloride, the rearrangement of **10** required dissolution in 98% sulfuric acid for 2 hours. Except for **7**, each diol gave only one oxochlorin with a yield generally greater than 75%. The structure of the oxochlorins was established by nuclear Overhauser enhancements (NOE). Selective irradiation of methyl or methylene protons resulted in enhancement (>5%) at the nearest meso protons. Since the meso proton adjacent to the reduced ring, but not next to the keto group, invariably appears as a singlet near 9.0-9.1 ppm and the other three meso protons are around 9.5-9.9 ppm, it is possible to assign the structures unambiguously. In the case of the mixture of **19** and **20**, irradiation of the 2- and 4-pyrrole protons resulted in a strong enhancement of both the 9.12 and 9.50 ppm meso protons; had the rearrangement gone the other direction, NOE should occur only at the two downfield meso protons, not at the 9.12 ppm peak. These experiments thus established the migratory aptitudes of the substituents: hydrogen, ethyl, alkyl groups including propionate side chains will migrate over methyl group. The only group that has a lower mobility than methyl is acetate; this is confirmed in two compounds **18** and **22**. Again, the electron-withdrawing nature of the acetate seems to play a determinant role.

The knowledge of the migratory aptitudes, besides being useful in discerning possible biosynthetic precursors, is immediately applicable in planning new chlorin syntheses. For example, starting with coproporphyrin I, the above hydroxylation-rearrangement sequence gave a type III coprochlorin **24**. Alkylation of the keto group by Wittig reagents as described before [9] would afford all-alkyl chlorins. Similarly, 7-methyl pyrroporphyrin IX (**25**) [10] produced two easily separable gem-dimethyl oxochlorins, one of which, **26**, after coupling with the appropriate Wittig reagent and hydrogenation, would provide an easy entry into the family of the exotic echurian pigment bonellin **27** [11]. Previously, (±) bonellin has been made by a rather long synthesis [12].



EXPERIMENTAL

General Procedure of Oxidation and Rearrangement.

Osmium tetroxide (1.2 mmoles) in ether (3 ml) was added to a dichloromethane solution (200 ml) of porphyrin (1 mmole) containing pyridine (0.2 ml). The mixture was allowed to stir at room temperature under nitrogen for 20 hours. The solvent was evaporated and the residue was dissolved in a mixture of methanol (100 ml) and dichloromethane (30 ml). Hydrogen sulfide was passed through the solution to decompose the osmium ester. The mixture was filtered and the filtrate was concentrated and chromatographed on silica gel using dichloromethane/1-3% methanol as eluent.

The pinacolic rearrangement of the dihydroxychlorins were brought about by 3 different acid treatments: (1) dichloromethane with a couple drops of 70% perchloric acid (**7, 9, 13**); (2) chlorin in dichloromethane, shaking with concentrated sulfuric acid (**8, 11, 12**); (3) neat concentrated sulfuric acid for several hours, followed by esterification (**10,14**).

Representative ^{1}H NMR (Deuteriochloroform) and UV-VIS (Dichloromethane):

Compound **9** had: 2.61 (2H, br s), 0.67 (3H, t), 1.75 (3H, t), 2.12 (3H, s), 2.20 (2H, q), 3.22, 3.33, 3.37 (3H each, s), 3.66, 3.68 (3H each s, OMe), 3.89 (2H, q), 4.60 (2H, dd), 4.72 (2H, s), 8.88, 8.89, 9.50, 9.66 (1H each, s); λ max (ϵ_M) 642 nm (41,000), 612 (3,150), 588 (3,890), 526 (2,950), 498

(12,600), 494 (12,500), 394 (173,000).

Compound **17** had: 2.88-2.73 (1H each, br s), 0.44 (3H, t), 1.82 (3H, t), 2.06 (3H, s), 2.75 (2H, q), 3.40, 3.47, 3.51 (3H each, s), 3.71, 3.80 (3H each s, OMe), 4.00 (2H, q), 4.78, 4.94 (2H each, s), 9.08, 9.74, 9.80, 9.79 (1H each s); λ max (ϵ_M) 638 nm (26,400), 582 (5,050), 546 (10,600), 508 (8,150), 490 (5,500), 406 (151,000).

Acknowledgement.

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