tomerization to a dione (6), which loses methanol by a β elimination, compound 7 is obtained. In the last step, a keto–enol tautomerization gives maltol (1). Fried,[12] in his mechanism for degradation of streptomycin to maltol, has proposed analogous intermediates, as arising from rearrangement of streptose moiety of streptomycin.

The low yield of maltol from hydrolysis of **3**, when aqueous Dowex 1 (OH^-) ion exchange resin is employed, can be explained in part by the relative stability of ketals under conditions of alkaline hydrolysis. An additional likely factor is instability of maltol to basic conditions of hydrolysis. When a known amount of maltol was heated with aqueous Dowex 1 (OH^-) ion exchange resin (conditions of hydrolysis of **3**), more than 50% maltol was lost within 72 hr.

Experimental Section

Melting points were observed on Köfler hot stage and are corrected. The nmr spectra were recorded on Varian A-60 spectrophotometer; the ir spectra were taken on Perkin-Elmer Model 137 recording infracord spectrophotometer. Spectronic 20 Bausch and Lomb colorimeter was used for colorimetric analyses. All solvents and reagents were of reagent grade. Anhydrous pyridine was prepared by distilling analytical grade pyridine over KOH pellets and was stored over KOH pellets.

Methyl, 2,3-*O*-Isopropylidene-6-deoxy-α-L-*lyxo*-hexopyranos-4-ulose (3). Chromium trioxide (97 g, 970 mmol) was gradually added to 1 l. of anhydrous pyridine at room temperature and under constant stirring. A solution of 21.4 g (98.1 mmol) of methyl 2,3-*O*-isopropylidene-α-L-rhamnopyranoside (**2**)[8,9] in 200 ml of anhydrous pyridine was added to the above mixture and the stirring was continued for 16 hr at room temperature. Pyridine was then evaporated *in vacuo* and the residue was extracted with chloroform. The chloroform extract was washed with 2 *N* HCl (3 × 400 ml), dried over anhydrous $MgSO_4$, and evaporated to give 15 g of dark syrupy residue. It was immediately chromatographed on a column packed with silicic acid that had previously been kept in a water-saturated desiccator for 24 hr. The column (25 cm × 4 cm) was eluted with $CHCl_3$ (volume of each fraction, 50 ml). The first 600 ml of effluent was discarded; the next 1500 ml contained 11.362 g (52.6 mmol; 55% yield) of **3**. This compound was chromatographically homogeneous. Its ir spectrum (liquid film) showed ν_{max} 3.40, 5.74, 6.91, 7.25, 8.15, 9.20, 10.21, and 11.66 μ among other absorptions. The elemental analysis of its crystalline oxime was consistent with its composition.

Anal. Calcd for $C_{10}H_{17}NO_5$: C, 51.94; H, 7.41; N, 6.06. Found: C, 51.73; H, 7.28; N, 6.11.

Maltol (1). A. Exploratory. To a solution of **3** (21.710 mg, 0.1 mmol) in 7–8 ml of water (or benzene) was added about 100 mg of dry ion exchange resin. The mixture was heated on a steam bath under reflux, the reflux condenser for benzene being fitted with a drying tube. At specified intervals, 1–2 ml of reaction mixture was withdrawn and treated with ferric ammonium sulfate reagent.[11] The blue color, fully developed at 10 min, was monitored at 540 nm; maltol content in the reaction mixture was determined from a standard curve.

B. Preparative. A mixture containing 4.610 g (21.34 mmol) of **3** in 60 ml of water and 1 g of dry Dowex 50 (H^+) ion exchange resin was heated on a steam bath for 60 hr. Resin was removed by filtration and the aqueous solution was extracted with $CHCl_3$ for 6 hr. Solvent was evaporated *in vacuo* and the residue was crystallized from cyclohexane. Resulting tan-colored crystals were further purified by sublimation at 100° under reduced pressure (40 μ). The product weighed 1.916 g (72% yield) and showed a corrected mp 159.5° (lit.[3] 159°). Melting point of a mixture of synthetic and commercial samples of maltol remained unchanged. Tlc analysis and ir spectra of the synthetic material were identical with those for the commercial sample. The nmr spectrum (saturated $CDCl_3$ solution) of the compound showed absorptions at τ 7.63 (3 H, s), 3.55 (1 H, d, J = 5.8 Hz), 2.84 (1 H, broad, s), and 2.33 (1 H, d, J = 5.8 Hz). The ir spectrum (8% solution in $CHCl_3$, 0.1-mm cell path), showed ν_{max} 3.04, 3.31, 6.17, 6.40, 7.93, 8.42, 10.82, and 11.78 μ among others.

Anal. Calcd for $C_6H_6O_3$: C, 57.14; H, 4.79. Found: C, 57.27; H, 4.81.

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Registry No.—1, 118-71-8; 2, 14133-63-2; 3, 2592-53-2; 3 oxime, 35010-57-2.

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Electrophilic Substitution on Porphin. I. Nitration

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Previous studies of electrophilic substitution on the porphyrin periphery have used porphyrins which were substituted on most or all of the β positions (*viz.*, positions 2, 3, 7, 8, 12, 13, 17, 18, Figure 1A).[1-12] Therefore, the results of such efforts could not be used to determine the difference, if any, between the β and meso positions during electrophilic attack. To examine any reactivity differences on the porphyrin periphery, we have studied the nitration of porphin, the parent porphyrin. We have also studied the nitration of nitroporphin to find any directive effects which may be operating. It was found that porphin gave a mono-nitro derivative upon nitration with a stoichiometric amount of nitric acid at 0°. The nitrated product, shown to be a single compound by tlc, exhibited an etio-type visible spectrum. Its nmr spectrum showed that it was meso substituted

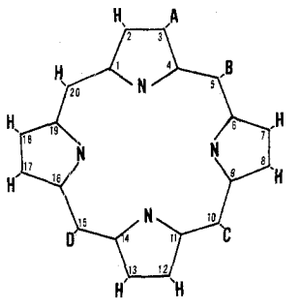

Figure 1. (A) A = B = C = D = H; (B) A = C = D = H and B = NO_2; (C) A = D = H; B = C = NO_2.

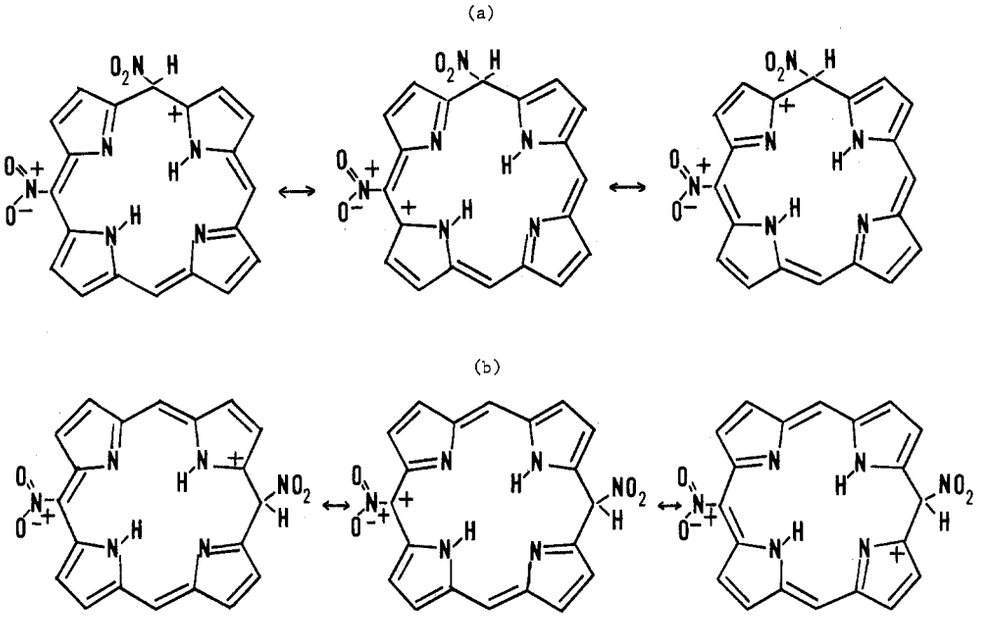

Figure 2. Important resonance forms for attack at (a) the β-meso position and (b) the γ-meso position of nitroporphin

(Figure 1B) since the β/meso proton ratio was equal to 2.60 and the meso protons appeared as two separate peaks with a relative area of 2:1. The same ratio for a β-substituted porphin would be 1.75. Chemical degradation afforded additional structural verification. No β-nitromaleimide was found among the degradation products of the nitrated porphin, The main degradation product was maleimide. If the nitro group were on the β position up to 25% β-nitromaleimide would be formed.

To determine the existence of a directive effect which may be operating in the porphyrin ring system, dinitroporphin was prepared by nitrating nitroporphin. Tlc analysis affirmed that it was a single compound. Its visible spectrum was also of the etio type but shifted bathochromically relative to nitroporphin. Analysis of its nmr spectrum showed that it was di-meso substituted since the meso proton absorption had collapsed to a singlet and the β/meso proton ratio was equal to 4. In addition since the β proton absorption pattern was unsymmetrical we concluded that the isomer obtained was the 5,10-dinitroporphin (Figure 1C). The 5,15-dinitroporphin would be expected to be quite symmetric. Chemical degradation again furnished evidence for the di-meso substitution assignment.

Discussion

Fleischer[13,14] has proposed on the basis of X-ray data that the electronic structure of porphin exhibits an inner π ring of 12 carbon and four nitrogen atoms; each carbon and two of the nitrogen atoms contribute one electron to the π system of this ring while the imine nitrogens (–C=N–) each contribute two electrons, making a total of 18-π electrons, a number consistent with Hückel's rule for aromaticity. The conclusion is that the main path of conjugation is the inner 16-membered ring with the outer pyrrole bonds being olefinic.

Caughey[15] has reported a ^{13}C Fourier transform nmr study of deuterioporphyrin IX dimethyl ester which lends supporting evidence to Fleischer's theory of porphin electronic structure. It was found that the ^{13}C chemical shifts were in the same range for all the protonated carbons except the meso carbons. Caughey concludes that the meso positions experience strong resonance effects owing to delocalization *via* the inner 16-membered ring with the β–β carbon bonds left as pure double bonds. It is interesting to note that the X-ray data show no single-bond character in the β-carbon–β-carbon bonds.

A mechanism for the meso substitution of porphin can be advanced by considering that the free base prophin (although initially present in very small concentrations in the highly acidic nitration medium) is attacked by the nitronium ion at the aromatic portion of the porphin periphery, the inner 16-membered ring. A true electrophilic substitution occurs involving an initial π-complex formation, collapse to a σ complex and rearomatization *via* proton loss. The apparent directive effect of the nitro group on the position of nitration of nitroporphin can be rationalized by considering the relative stabilities of the σ complexes leading to the respective nitration products.

An examination of Figure 2a and 2b reveals that the 5,10-disubstituted product should be favored because no resonance structures can be written that will place a positive charge on the carbon atom bearing the nitro group; such a transition state possesses a lower relative energy than that of the 5,15-disubstituted product whose transition state has one resonance form with a positive charge on the nitro-substituted carbon atom. The results show, under the conditions described herein, that the meso position of porphin is preferentially nitrated. It has also been demonstrated that the nitro group directs the course of subsequent nitration to the 10 position.

Experimental Section

General. Porphin was synthesized by the method of Adler and Beitchman.[16] Melting points were taken on a Mel-Temp melting point apparatus and are uncorrected. Visible spectra were taken on a Cary 14 recording spectrophotometer. Nmr spectra were obtained with a Varian 220-MHz spectrometer with TMS as an internal standard. The porphyrins were dissolved in a solvent consisting of 33% $CDCl_3$ and 66% CF_3CO_2D at a concentration $\simeq$0.7 *M*.

Nitroporphin. To a stirred, ice-cooled solution containing 200 mg of porphin (6.4×10^{-4} mol) and 6 ml of concentrated H_2SO_4 was added over a 3-min period a 1.33% HNO_3 in H_2SO_4 solution which had been pre-cooled to 0°. During the addition of the HNO_3 solution the reaction mixture turned from red to blue-green, the porphin dication color. After all the HNO_3 solution had been added, the reaction mixture was allowed to stir at 0° for 5 min, whereupon it was poured into 600 ml of ice water containing 10 g of sodium acetate. The brown-black precipitate which formed im-

mediately was filtered and dried in a 100° oven for 2 hr. After drying, the solid was dissolved in $CHCl_3$ and chromatographed on alumina. The nitroporphin was eluted with a chloroform–benzene (50:50, v/v) mixture yielding 151 mg of product: 70% yield; extinction coefficients at maxima ϵ_{628} 6000, ϵ_{572} 6860, ϵ_{540} 8770, ϵ_{499} 13,120, ϵ_{406} 200,000.

Anal. Calcd for $C_{20}H_{13}N_5O_2$: C, 67.6; H, 3.68; N, 19.nd C, 67.44; H, 3.67; N, 19.64.

Dinitroporphin. Dinitroporphin was prepared in the same manner as mononitroporphin except that it was eluted with chloroform after a small amount of unreacted mononitroporphin was eluted with the chloroform–benzene mixture. A 56% yield of dinitroporphin was obtained (20% of the unreacted mono-nitroporphin was recovered): extinction coefficients at maxima ϵ_{632} 4820, ϵ_{578} 5400, ϵ_{543} 7000, ϵ_{504} 10,800, ϵ_{407} 145,000.

Anal. Calcd for $C_{20}H_{12}N_6O_4$: C, 60.02; H, 3.02; N, 20.99. Found: C, 59.98; H, 3.00; N, 20.89.

Oxidative Degradation of Nitro- and Dinitroporphin. The degradations were accomplished according to the method of Neuberger and Muir[17] for the degradation of mesoporphyrin. The porphin in question was dissolved in a 50% aqueous H_2SO_4 solution at 0°. To this solution was added dropwise an ice-cold 10% aqueous CrO_3 solution. The mixture was then stirred at 0° for 2 hr and an additional 2 hr at room temperature. The solution was then diluted with 50 ml of distilled water and extracted four times with anhydrous ether. The ether extracts were washed once with 50 ml of water and dried over anhydrous $CaSO_4$. The ether was evaporated leaving a white solid. In all cases, the solid melted at 90–92° and was shown to be identical with an authentic sample of maleimide. The maleimide degradation product was analyzed *via* tlc for the presence of nitromaleimide. The tlc analysis was accomplished using a developing solvent consisting of ethyl acetate–carbon tetrachloride–cyclohexane (10:5:1) with a development distance of 10 cm. The plate was removed from the chromatography chamber, dried, and exposed to Cl_2 for 5 min. It was then heated to 100° for 5 min. The locating reagent is a 0.5% benzidene solution in ethanol containing a 10% aqueous KI solution per 100 ml of the benzidene solution.[18] No evidence of the presence of nitromaleimide was ever observed.

4-Nitro-2-pyrrolecarboxaldehyde. The preparation of 4-nitro-2-pyrrolecarboxaldehyde followed the procedure of Fournari and Tirouflet[19] except that the 4-nitro isomer was extracted from a saturated aqueous $NaHCO_3$ solution containing the 4- and 5-nitro isomers with ether. Typically, 10 g of the isomer mixture is dissolved in 500 ml of a saturated aqueous $NaHCO_3$ solution. This solution is extracted six times with 100-ml portions of anhydrous ether. The extracts are dried over $CaSO_4$ and decolorized. The ether was evaporated leaving 3.5 g of a yellow solid, 4-nitro-2-pyrrolecarboxaldehyde, which was recrystallized from alcohol–water, mp 135–136° (lit.[20] 142°).

Nitromaleimide. To an ice-cooled solution containing 5 g of 4-nitro-2-pyrrolecarboxaldehyde in 20 ml of acetone was added with stirring 150 ml of a 50% aqueous H_2SO_4 solution. After the acid addition was completed, a solution containing 40 g (0.136 mol) of $K_2Cr_2O_7$ in 100 ml of H_2O was added slowly so that the reaction temperature did not exceed 10°. After the dichromate addition was finished, the reaction mixture was heated to 60° for 30 min; then it was poured into 200 ml of ice water. The aqueous solution was extracted four times with 100-ml portions of anhydrous ether. The ether extracts were dried, decolorized, and stripped leaving a white yellow solid which was recrystallized from water, mp 205° dec.

Anal. Calcd for $C_4H_2N_2O_4$; C, 42.86; H, 2.87; N, 19.99. Found: C, 42.50; H, 2.80; N, 19.85.

Registry No.—Porphin, 101-60-0; nitroporphin, 52358-25-5; dinitroporphin, 52358-26-6; maleimide, 541-59-3; 4-nitro-2-pyrrolecarboxaldehyde, 19611-63-3; nitromaleimide, 52358-27-7.

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μ-Truxinic Acid

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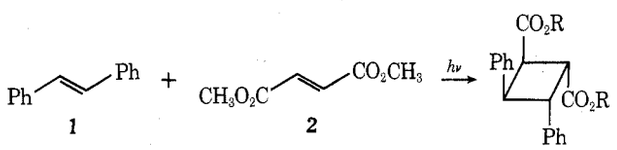
The photoaddition of *trans*-stilbene to fumaric acid would seem to be a straightforward approach to the synthesis of μ-truxinic acid since both stilbene[1] and fumaric acid derivatives[2] undergo photodimerization to cis-anti-cis configurated dimers. However, a previous approach along these lines was reported to be unsuccessful.[3]

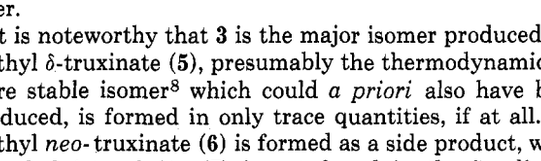
We have repeated this method, irradiating *trans*-stilbene with an excess of dimethyl fumarate in benzene solution, and find that dimethyl μ-truxinate (**3**) is formed



smoothly in acceptable yields. The nmr spectrum uniquely fits that anticipated for **3**: a single carbomethoxyl signal is present at δ 3.33, shifted upfield as a result of the shielding *cis*-β-phenyl groups.[4]

Although the diphenylcyclobutanedicarboxylic (truxillic and truxinic) acids are often presented as classical examples of configurational isomerism where all 11 possible isomers are known,[5] the melting point of μ-truxinic acid, **4**, obtained by acid hydrolysis of **3**, differs from that reported by Shemiakin for this material.[6] Ettlinger had earlier questioned the structure assignment to Shemiakin's μ-truxinic acid and suggested that this material was a lactonic acid.[7] Reesterification of **4** with methanol affords **3**; we thus report the first synthesis of μ-truxinic acid and its dimethyl ester.

It is noteworthy that **3** is the major isomer produced; dimethyl δ-truxinate (**5**), presumably the thermodynamically more stable isomer[8] which could *a priori* also have been produced, is formed in only trace quantities, if at all. Dimethyl *neo*-truxinate (**6**) is formed as a side product, while dimethyl ζ-truxinate (**7**) is not found in the irradiation



products. These results are accommodated by a mechanism involving the addition of excited singlet state *trans*-stilbene to dimethyl fumarate *via* a nonconcerted pathway.[9]