ment of 1,3-dihydro-1-phenylfuro[3,4-*b*]quinolin-3-one[7] (**10**) with phenylmagnesium bromide according to the procedure of Cava and Van Meter[6] gave the title compound in 48% yield: mp 210–211° (from ethanol); ir 1625, 1600, 1025, 770, 750, and 700 cm^{-1}; nmr τ 2.5 (m, 20 H), 3.8 (s, 1 H).

Anal. Calcd for $C_{29}H_{21}NO$: C, 87.19; H, 5.30; N, 3.51. Found: 87.39; H, 5.24; N, 3.48.

Acknowledgment. We thank Professors C. H. Issidorides and M. Nazer for stimulating discussions.

Registry No.—**3c,** 52260-31-8; **3d,** 52260-32-9; **3e,** 52260-33-0; **3f,** 52260-34-1; **4,** 480-96-6; **5a,** 52260-35-2; **5b,** 52260-36-3; **6,** 52260-37-4; **7a,** 19029-35-7; **7b,** 52260-38-5; **8b,** 52260-39-6; **9c,** 52260-40-9; **9d,** 52260-41-0; **9e,** 52341-46-5; **9f,** 52260-42-1; **10,** 52260-43-2; **11,** 52260-44-3; phenylacetylacetophenone, 3442-15-7; *o*-aminobenzaldehyde, 529-23-7; hydrazine, 302-01-2; *N*-phenylmaleimide, 941-69-5.

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A New Synthesis of Maltol[1]

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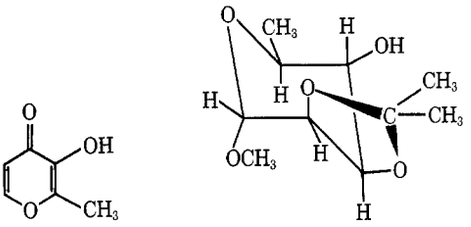
Maltol (2-methyl-3-hydroxy-4*H*-pyran-4-one), **1,** is known to exist in several plants, *e.g.*, fern leaves and larch bark, and in food materials, *e.g.*, roasted chicory, coffee, caramel, and corn.[3] Streptomycin on alkaline hydrolysis also yields up to 30% maltol.[4,5] It was isolated in 1894 by Brand and its structure was established by Peratoner and Tamburello in 1905.[3]

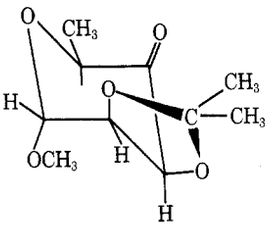
Although maltol is of great value as a flavoring agent in food industry, its reported laboratory syntheses proceed in poor yields and under severe experimental conditions.[6,7]

The purpose of this work was to provide a facile synthesis of **1** from readily available materials in reasonable yields under mild experimental conditions.

Oxidation of methyl 2,3-*O*-isopropylidene-α-L-rhamnopyranoside (**2**)[8,9] with chromium trioxide–pyridine complex, prepared at room temperature, according to the procedure of Poos and coworkers,[10] gave a syrupy material, identified as methyl 2,3-*O*-isopropylidene-6-deoxy-α-L-*lyxo*-hexopyranos-4-ulose (**3**) in 55% yield. Its ir and nmr spectra and the elemental analysis of its crystalline oxime confirmed its structure.



1 **2**



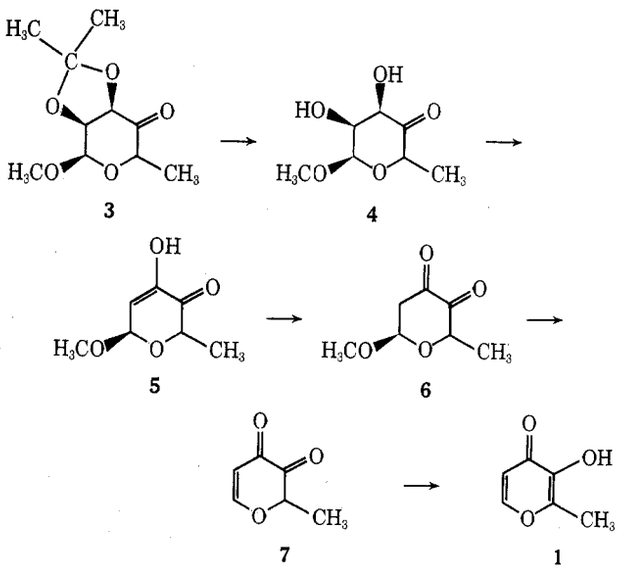
3

Compound **3** was heated on a steam bath with Dowex 50 (H^+) and Dowex 1 (OH^-) ion exchange resins, in water and in benzene, and the appearance of maltol was determined colorimetrically at 540 nm at given intervals.[11] Maximum yields were obtained by hydrolysis of **3** in aqueous medium by means of Dowex 50 (H^+) ion exchange resin: 72% in 60 hr. The final product was characterized as maltol (**1**) by its nmr and ir spectra, its elemental analysis, and by comparison of its tlc behavior with a commercial sample of maltol.

The yield of maltol by reaction of **3** with Dowex 1 (OH^-) ion exchange resin in aqueous medium was poor (15% yield). In benzene, the hydrolysis did not proceed to any significant extent (<1% yield) in the presence of acidic or basic ion exchange resins.

The following pathway is suggested for the degradation of **3** to maltol under the conditions of hydrolysis (Scheme I). The pathway involves elimination of acetone under the

Scheme I



influence of Dowex 50 (H^+) ion exchange resin (known lability of the isopropylidene group to mild acid conditions),[12] followed by β elimination of water in which H atom α to the carbonyl function is lost (**4** and **5**). After tau-

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

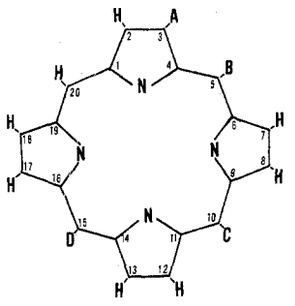

Figure 1. (A) A = B = C = D = H; (B) A = C = D = H and B = NO_2; (C) A = D = H; B = C = NO_2.