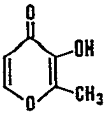
Note

Synthesis of acetoxydihydromaltol acetate and dihydromaltol

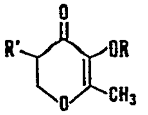
FRANK D. MILLS
Northern Regional Research Laboratory, Agricultural Research Service,
U.S. Department of Agriculture, Peoria, Illinois 61604 (U. S. A.)

(Received December 21st, 1971; accepted with revisions, February 15th, 1972)

A straightforward synthesis was undertaken to establish the structure of a compound (**2a**) isolated in our laboratory from pyrolysis of an amine–hexose system[1], and to decide among other structural proposals that had been suggested in earlier studies[2–7]. Also, as a result of the synthetic scheme, a new compound **2c** having a caramel odor was prepared. The synthesis selected depends on the different reactivities towards hydrogenation of the two C=C bonds in the α,β-substituted γ-pyrone (**1**). Other reduced γ-pyrone systems have been reported[8,9], but none have been derived from 2-methyl-3-hydroxy-4(*H*)-pyran-4-one. It is apparent from previous work that an approach starting from maltol (**1**) would probably generate a new, easily prepared source for a caramel aroma and, perhaps, a new flavoring agent[10,11].

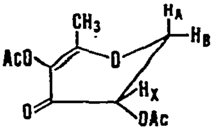


1



2

a R = H, R' = OH
b. R = Ac, R' = H
c. R = H, R' = H



3

Maltol was acetylated in 82% yield by using acetic anhydride, with sodium acetate as a catalyst. It was important to acylate **1** before hydrogenation, because reduction of the parent compound led to only a small proportion of dihydromaltol (**2c**) and a much greater production of more-volatile components. No effort was made to identify these further-reduced products. In the reduction (palladium on carbon) of acetylated maltol, evidence from g.l.c. monitoring indicated that a reaction time greater than 4 h gave a poorer ratio of the dihydro derivative to further-reduced material. The proportions (peak areas) of reaction products at 4 h were 50:40:10 of dihydro derivative–maltol acetate–miscellaneous products. Pure **2b** was obtained after column chromatography on silica gel; the product was sharply resolved from the starting material and byproducts. Compound **2c** was obtained in excellent yield from **2b** by deacetylation with sodium methoxide in methanol. Distillation of the crude product produced a viscous oil that solidified at −15°; the oil possessed a strong caramel aroma with fruity overtones and, dissolved in water (150 mg in 100 ml), evoked an oily taste with a detectable burnt-coconut and -strawberry flavor.

Several attempts to hydrolyze the dihydromaltol acetate with acid (M, 2M HCl, and 4M acetic acid at 80° for up to 1 h) failed to remove a significant amount of the acetate; however, the methoxide-catalyzed hydrolysis was complete in 20 min. The established acid-stable character of **2b** allowed α-acetoxylation to be effected with lead tetraacetate in glacial acetic acid[12]; the α,α'-diacetate was obtained in 16% yield after column chromatography. The acetoxylation can be explained by the enolization mechanism suggested by Henbest *et al.*[13] and Cocker *et al.*[14], but the fact that a large quantity of **2b** remained, even after reaction periods of 48 h and the use of boron trifluoride as catalyst, indicates the need for further study on why the reaction ceases.

N.m.r.-spectral analysis indicated structure **3** for the diacetoxy product. Because of the equivalency of the *pseudo*-axial and -equatorial A and X protons in **2b** and **2c**, the simplified A_2X_2 pattern (triplet, $J_{AX} = J_{A'X'} = 6.2$ Hz) indicated the presence of a conformational mixture and, very likely, again a distorted-chair form in the dihydro-γ-pyrone system[15,16]. Products **2b**, **2c** and **3** were stable under refrigeration, but the deacetylated product **2a** was very susceptible to acid hydrolysis and yielded further, important, nonenzymic-browning products: maltol and isomaltol (a furan derivative)[6]. Attempts to convert the diacetate **3** into **2a** by hydrolysis with acid or base were not successful. In aqueous acid (2M HCl) under extended reflux, **3** decomposed into several compounds; one was tentatively identified as diacetylformoin, but no measurable amount of deacetylated **3** was formed. The increased ease of decomposition of deacetylated **3** probably arose by way of beta elimination and condensation reactions, which would be promoted in the underivatized product.

EXPERIMENTAL

General. — All melting points were recorded on a Thomas–Hoover Unimelt* apparatus and are uncorrected. I.r. spectra were obtained with a Perkin–Elmer Model 612 spectrophotometer and from solutions in chloroform. The mass spectra were determined with a Nuclide 90G double-focusing spectrometer, and a direct or heated inlet (150°) was employed. The n.m.r. data were obtained with a Varian Model HA-100 instrument from chloroform-*d* solutions with Me_4Si as an internal standard. Analytical and preparative g.l.c. were performed on a Varian Aerograph 1800 instrument equipped with effluent splitters and flame-ionization detectors. The columns were 15% SE-30 on 80–100 Chromosorb W (UPH) in 6 ft × 1/4 in. copper or stainless-steel tubing; an on-column injection technique was used. Baker (chromatographic grade) silica gel containing 10% of water by weight was used.

---

*Mention of firm names or trade products does not imply that they are endorsed or recommended by the Department of Agriculture over other firms or similar products not mentioned.

3-Acetoxy-2-methyl-4(H)*-pyran-4-one*. — Maltol (30 g) was acetylated with acetic anhydride (35 ml) and sodium acetate (1.5 g) in 150 ml of refluxing chloroform for 4 h. Treatment of the cooled organic phase with ice–water (1 h, with stirring) followed by extraction with chloroform provided 35 g (86%) of maltol acetate; m.p. 56–58°, $b_{0.2}$ 85–89°. G.l.c. on a 6 ft × 1/4 in. 15% SE-30 stainless-steel column at 140° showed a single peak, retention time 17.5 min; mass spectrum, *m/e* 268 (M^+); n.m.r. ($CDCl_3$) δ (H): 7.80 (1, H_A), 6.40 (1, H_X) (J_{AX} 5.9 Hz), 2.27 (3) (vinyl methyl), 2.32 (3) (acetyl methyl), $\lambda_{max}^{CHCl_3}$ 3000, 1767, 1640, 1419, 1365, 1245, 1185, and 1160 cm^{-1}.

5-Acetoxy-2,3-dihydro-6-methyl-4(H)*-pyran-4-one* (**2b**). — Maltol acetate (15 g), 1 g of 10% palladium-on-carbon, and abs. ethanol (75 ml) contained in a glass bottle was hydrogenated for 4 h at 26° and 50 lb.in.^{2}. After filtration of the mixture, the filtrate was concentrated to a thick oil. The residue (16.4 g) was introduced onto a column of neutral silica gel previously fabricated in benzene. Elution was conducted with benzene at 1 ml/min, and 15-ml fractions were collected; fractions 160–200 (product by g.l.c. analysis, retention time on the 15% SE-30 column at 7 min) were combined and the solvent was removed *in vacuo*; yield 10.2 g (67%) of a syrup that failed to crystallize (hydrogenation for 1, 2, and 5 h gave no improvement in yield); *m/e* (rel. %): 172 (0.2), 171 (1), 170 (6), 130 (1), 129 (6) 128 (84), 100 (3) 86 (1), 85 (12), 72 (28), 58 (2), 57 (19), 56 (1), 55 (3), 43 (100); n.m.r. ($CDCl_3$) δ (H): 4.43 ($2H_A$), 2.61 ($2H_X$) (J_{AX} 6.2 Hz, triplet), 2.20 (3) (vinyl acetyl Me), 1.92 (3) (vinyl Me); $\lambda_{max}^{CHCl_3}$ 2940, 2880, 1759s, 1670s, 1627s, 1458, 1398, 1380, 1365, 1352, 1178, and 1170 cm^{-1}.

2,3-Dihydro-5-hydroxy-6-methyl-4(H)*-pyran-4-one* (**2c**). — Dihydromaltol acetate (5.0 g) was treated with 10mM sodium methoxide (20 ml). The solution was stirred for 20 min and then made acidic with excess Dowex-50W-8X (H^+) ion-exchange resin. The resin was removed by filtration and the washings were combined with the filtrate. Concentration produced an oily product that solidified upon cooling at −15°; yield 3.10 g (83%), $b_{0.1}$ 87–90°; *m/e* (rel. %): 130 (0.5), 129 (2), 128 (27), 100 (2), 98 (2), 86 (6), 85 (6), 67 (16), 58 (7), 57 (18), 56 (5), 55 (11), 43 (100); n.m.r. ($CDCl_3$) δ (H): 4.31 ($2H_A$), 2.61 ($2H_X$) (J_{AX} 6.2 Hz, triplet), 2.04 (3) (vinyl Me); $\lambda_{max}^{CHCl_3}$ 3480, 3030, 1742 w, 1626 vs, 1460, 1252, 1185, and 1178 cm^{-1}. G.l.c. on the SE-30 column showed this material to be homogeneous (retention time at 140°, 5 min).

3,5-Diacetoxy-2,3-dihydro-6-methyl-4(H)*-pyran-4-one* (**3**). — Dihydromaltol acetate (1.0 g) was dissolved in 16 ml of glacial acetic acid containing acetic anhydride (2 ml). Lead tetraacetate (2.84 g) was added and the resulting solution kept[12] under nitrogen for 30 h with stirring at 80°. The excess solvent was removed *in vacuo* and the residue dissolved in water (50 ml). The aqueous phase was extracted with benzene (four 50-ml portions) and the combined organic phases were dried over sodium sulfate. Filtration and concentration produced a residue that was applied to a dry-packed column[17] of silica gel (35 g). The column was developed with benzene and 8-ml fractions were collected. Fractions 200–240 contain a single component that, upon removal of solvent and recrystallization from ethyl acetate–hexane, yielded 152 mg (16%) of product; m.p. 57–59°. The yield was not improved when the same reaction was repeated in benzene (140 ml) and 10 ml boron trifluoride etherate under reflux. Mass spectrum, *m/e* (rel. %): 144 (20), 115 (15), 101 (20), 85 (2), 73 (8), 72 (15), 55 (20), 43 (100); n.m.r. ($CDCl_3$) δ (H): 1.99 (3) (vinyl Me), 2.11 (3) (aliphatic acetyl Me), 2.22 (3) (vinyl acetyl Me), 4.53 ($1H_A$, quartet), 4.39 ($1H_B$, quartet), 5.41 ($1H_X$, quartet), (J_{AB} −12 Hz, J_{AX} 6 Hz, and J_{BX} 8 Hz); $\lambda_{max}^{CHCl_3}$ 2920, 1765, 1750, 1691, 1618, 1460, 1442, 1425, 1398, 1378, 1188, 1159, 1058, and 1042 cm^{-1}.

ACKNOWLEDGMENT

Mr. Larry Tjarks recorded the n.m.r. spectra and Dr. William Rohwedder the mass spectral data for this work. Mr. John E. Hodge was supervisor.

REFERENCES

1 F. D. Mills, D. Weisleder, and J. E. Hodge, *Tetrahedron Lett.*, 15 (1970) 1243.
2 Th. Severin and W. Seilmeier, *Z. Lebensm. Unters. Forsch.*, 137 (1968) 4.
3 P. E. Shaw, J. H. Tatum, and R. E. Berry, *Carbohyd. Res.*, 5 (1967) 266.
4 P. E. Shaw. J. H. Tatum, and R. E. Berry, *J. Agr. Food. Chem.*, 16 (1968) 979.
5 J. H. Tatum, P. E. Shaw, and R. E. Berry, *J. Agr. Food Chem.*, 15 (1967) 733.
6 P. E. Shaw, J. H. Tatum, and R. E. Berry, *Carbohyd. Res.*, 16 (1971) 207.
7 G. A. M. Van Den Ouweland and H. G. Peer, *Rec. Trav. Chim.* 89 (1970) 750.
8 J. J. De Vrieze, *Rec. Trav. Chim.*, 78 (1959) 91.
9 S. Gelin and R. Gelin, *Compt. Rend.* 263 (1966) 1029.
10 J. E. Hodge, *Chemistry and Physiology of Flavors*, Avi Publishing Co., Westport, Conn., 1967, p. 465.
11 A. O. Pittet, P. Rittersbacher, and R. Muralidhara, *J. Agr. Food Chem.*, 18 (1970) 929.
12 E. Seebeck and T. Reichstein, *Helv. Chim. Acta*, 27 (1944) 948.
13 H. B. Henbest, D. N. Jones, and G. P. Slater, *J. Chem. Soc.*, (1961) 4472.
14 J. D. Cocker, H. B. Henbest, G. H. Phillipps, C. P. Slater, and D. A. Thomas, *J. Chem. Soc.*, (1965) 6.
15 L. M. Jackman, *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*, MacMillan Co., New York, 1964, p. 92.
16 E. L. Eliel, *Stereochemistry of Carbon Compounds*, McGraw–Hill Co., Inc., New York, 1962, p. 239.
17 B. Loev and M. M. Goodman, *Chem. Ind.* (London), (1967) 2026.