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Sugar Enolones, VII [1]

Synthesis and γ-Pyrone Formation of α,β-Unsaturated Hexopyranosid-4-uloses

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Dimethyl sulfoxide/acetic anhydride oxidation of methyl 2,3,6-tri-*O*-benzoyl-α-D-galactopyranoside (**1**) is accompanied by β-elimination of benzoic acid to yield the 3,4-enolone **4**. The intermediate 4-uloside **2**, comprising about 65% of an 8 h oxidation mixture, could therefrom not be isolated in pure form because of its propensity towards enolone formation. In basic and acidic medium, the 3,4-enolone structure in **4** is readily converted into the γ-pyrone system by loss of the anomeric substituent to yield hydroxymaltol derivatives (**13**, **14**). Some intermediates in this reaction, e. g. dihydropyranone **10**, can be isolated under mild conditions. The mechanistic implications of the 3,4-enolone → γ-pyrone conversion are discussed in relation to the formation of a pyrylium salt from the 3,4-enaminone analogue of **4** (**6** → **12**) and to the γ-pyrone formation from hexose-3,2-enolones.

Zucker-enolone, VII [1]

Synthese und γ-Pyron-Bildung α,β-ungesättigter Hexopyranosid-4-ulosen

Die Dimethylsulfoxid/Acetanhydrid-Oxidation von Methyl-2,3,6-tri-*O*-benzoyl-α-D-galactopyranosid (**1**) führt infolge sich anschließender β-Eliminierung von Benzoesäure zum 3,4-Enolon **4**. Das intermediäre 4-Ulosid **2** ist zwar in einem 8 h-Oxidationsgemisch zu 65% vorhanden, läßt sich jedoch aufgrund seiner Neigung zur Enolon-Bildung nicht in reiner Form isolieren. – Basische und saure Bedingungen überführen die 3,4-Enolon-Struktur **4** unter Verlust des anomeren Substituenten glatt in das γ-Pyron-System, wobei Hydroxymaltol-Derivate (**13**, **14**) gebildet werden, unter milden Bedingungen jedoch Zwischenprodukte, so das Dihydropyranon **10**, isolierbar sind. Die mechanistischen Grundlagen dieser 3,4-Enolon → γ-Pyron-Umwandlung werden diskutiert, insbesondere im Hinblick auf die Bildung eines Pyryliumsalzes aus dem 3,4-Enaminon-Analogen von **4** (**6** → **12**), und der γ-Pyron-Bildung aus Hexose-3,2-enolonen.

Glycopyranosides containing a 3,4-enolone structure (e. g., **4**) have long been postulated [2] as intermediates in the ready formation of maltol from the streptose portion of streptomycin [3] and of methyl streptobiosaminide dimethyl acetal [4] on treatment with alkali.

[1] [1a] Part VI: *F. W. Lichtenthaler, T. Sakakibara,* and *E. Oeser,* Carbohydr. Res. **58** (1977), in press. – [1b] Portions of this work have been subject of a preliminary report: *F. W. Lichtenthaler* and *P. Heidel,* Angew. Chem. **81**, 998 (1969); Angew. Chem., Int. Ed. Engl. **8**, 978 (1969).

[2] *R. U. Lemieux* and *M. L. Wolfrom,* Adv. Carbohydr. Chem. **3**, 374 (1948); *R. U. Lemieux* in *P. de Mayo:* Molecular Rearrangements, Vol. 2, p. 753, Interscience, New York 1964.

[3] *J. R. Schenk* and *M. A. Spielmann,* J. Am. Chem. Soc. **67**, 2276 (1945).

[4] *N. G. Brink, F. A. Kuehl, jr., E. H. Flynn,* and *K. Folkers,* J. Am. Chem. Soc. **68**, 2557 (1946).

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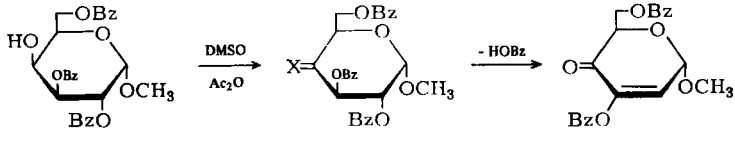
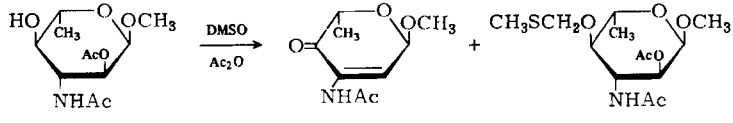
Similarly, the hydroxymaltol formation from the 3-*C*-formyllyxose portion of hydroxystreptomycin[5] can be interpreted to proceed *via* a 3,4-enolone intermediate with subsequent enolization and elimination of the anomeric substituent. Analogous intermediates have recently been proposed to account for the partial conversion of a 4,6-*O*-benzylidene-2-*O*-tosylhexopyranosid-3-ulose into a derivative of hydroxymaltol in basic medium[6], and for the formation of maltol from a 2,3-*O*-isopropylidene-6-deoxy-hex-4-uloside upon acid treatment[7]. We here report on the simple preparation of a 3,4-enolone (**4**) and an enaminone analogue thereof (**6**) from readily accessible, partially acylated hexosides as well as on the pronounced tendency of **4** and **6** to elaborate respectively γ-pyrone and pyrylium salt structures with a maltol type substitution pattern, thus providing the first direct evidence for the formation of 3,4-enolone intermediates in the above-mentioned conversions.

Formation of Hexenopyranosid-4-uloses

As has been evidenced in a variety of examples[8-13], dimethyl sulfoxide oxidation of a free hydroxyl group in an otherwise acylated aldopyranoside is followed by β-elimination of an acyloxy function to form α,β-unsaturated carbonyl derivatives. For methyl 2,3,6-tri-*O*-benzoyl-α-D-galactopyranoside (**1**) and methyl 3-acetamido-2-*O*-acetyl-3,6-dideoxy-α-L-glucopyranoside (**5**), consequently, a similar oxidation-elimination sequence was to be anticipated and, indeed, could be experimentally verified.



1 **2:** X = O **3:** X = NNHAr **4**



5 **6** **7**

[5] *W. E. Grundy, J. R. Schenk, R. K. Clark, jr., M. P. Hargie, R. K. Richards,* and *J. C. Sylvester,* Arch. Biochem. **28**, 150 (1950); *F. H. Stodola, O. L. Shotwell, A. M. Borud, R. G. Benedict,* and *A. C. Riley, jr.,* Science **112**, 77 (1950); J. Am. Chem. Soc. **73**, 2290 (1951).

[6] *W. A. Szarek, A. Dmytraczenko,* and *J. K. N. Jones,* Carbohydr. Res. **35**, 203 (1974); J. Chem. Soc. D **1971**, 1220.

[7] *R. J. Chawla* and *W. E. McGonigal,* J. Org. Chem. **39**, 3281 (1974).

[8] *H. Shibata, I. Takeshita, N. Kurihara,* and *M. Nakajima,* Agric. Biol. Chem. **32**, 1006 (1968).

[9] *G. M. Cree, D. M. Mackie,* and *A. S. Perlin,* Can. J. Chem. **47**, 511 (1969); *A. S. Perlin, D. M. Mackie,* and *C. P. Dietrich,* Carbohydr. Res. **18**, 185 (1971).

[10] *T. Tsuchiya, K. Suo,* and *S. Umezawa,* Bull. Chem. Soc. Jpn. **43**, 531 (1970).

[11] *F. W. Lichtenthaler,* Methods Carbohydr. Chem. **6**, 348 (1972).

[12] *D. M. Mackie* and *A. S. Perlin,* Carbohydr. Res. **24**, 67 (1972).

[13] *F. W. Lichtenthaler, K. Strobel,* and *G. Reidel,* Carbohydr. Res. **49**, 57 (1976).

When **1** or **5** was subjected to treatment with 2 : 1 or 3 : 2 mixtures of dimethyl sulfoxide/acetic anhydride for 48 h at room temperature, the respective hexenopyranosid-4-uloses, i.e. enolone **4** and enaminone **6**, were obtained in crystalline form and in yields of 61 and 53%. The latter conversion (**5** → **6**) appeared to be much more encumbered by substantial formation of the methylthiomethyl ether – **7** could be isolated in 33% yield – than the former (**1** → **4**), where the corresponding 4-*O*-thioether was detectable in the reaction mixture by TLC and an SCH_3-signal at $\delta = 2.14$. Structural proof for **4** and **6** could readily be educed from analytical, mass spectral and, most convincingly, from ^1H NMR spectra, which exhibit 3.5 Hz doublets each for an olefinic hydrogen (2-H at $\delta = 6.70$ for **4** and 7.58 for **6**) and the anomeric proton ($\delta = 5.42$ and 5.24, resp.).

Although the first step in the oxidation-elimination sequence **1** → **4** appears to be the faster one, the isolation of the intermediate methyl 2,3,6-tri-*O*-benzoyl-α-D-galacto-pyranosid-4-ulose (**2**) proved to be difficult. Monitoring the course of the reaction by ^1H NMR spectroscopy – TLC in a variety of solvent systems was found inadequate owing to the near identity of ulose and enolone mobilities – revealed that after 8 h at room temperature 90% of **1** had been converted into a 3 : 1 mixture of uloside **2** and enolone **4**. After 14 h, the starting material had reacted completely to give a 1 : 1 mixture of **2** and **4**. Thereafter the ratio changed to 1 : 2 (19 h), 1 : 4 (40 h) and about 1 : 5 (2 days) in favor of the enolone **4**. On addition of 2,4-dinitrophenylhydrazine to an 8 h oxidation mixture and fractional crystallization of the mixture of hydrazones formed, a uniform (TLC) product was obtained in 10% yield, which on the basis of its ^1H NMR data clearly was the uloside-2,4-dinitrophenylhydrazone **3**. However, attempts to isolate the ulose **2** itself in crystalline form from 3–10 h oxidation mixtures were consistently unsuccessful. This result is in clear contrast to a previous report on the dimethyl sulfoxide oxidation of **1** describing the high yield (72%) isolation of crystalline **2** on workup after 8 h[14].

In view of these results, the previous observations of *Gabriel*[15] on the dimethyl sulfoxide oxidation of **1** may be reinterpreted as follows: after 19 h the fast moving product (R_F 0.70 in **B**) corresponded to the 4-*O*-methylthiomethyl derivative of **1** (rather than the presumed 4-*O*-acetate), whilst the second component (R_F 0.62) in fact constituted an approximately 1 : 2 mixture of ulose **2** and enolone **4**. Ensuing reduction with sodium borotritiide then led not only to the methyl hexosides of *gluco*- and *galacto*-configuration in a 2 : 1 ratio, but also to other components that undoubtedly were enolone reduction products.

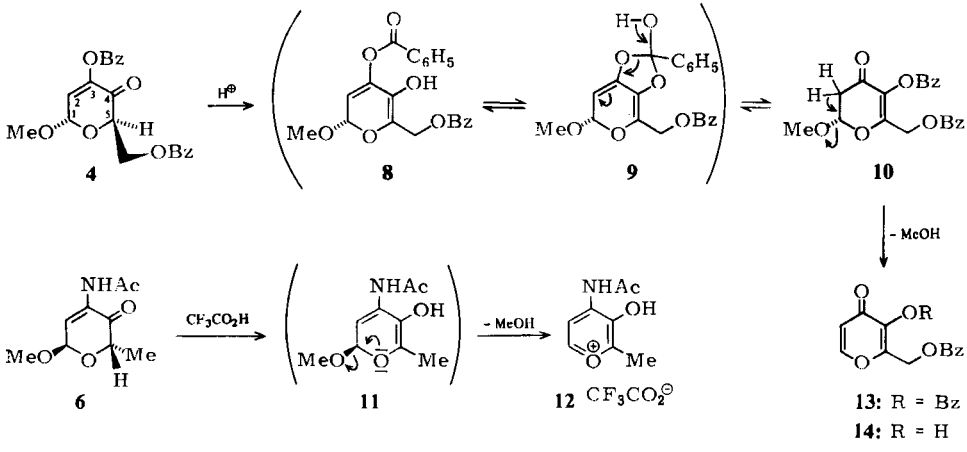
γ-Pyrone Formation

Not unexpectedly, in view of similar conversions in the 3,2-enolone series[13,16], the 3,4-enolone **4** showed a marked tendency to elaborate the γ-pyrone system. When treated with acetic acid/sodium acetate (2 h, 90°C), i.e. a system capable of accepting as well as releasing protons, **4** yielded benzoylbenzoyloxymaltol (**13**) in 65% yield. The structure for **13** unambiguously followed from ^1H NMR data (5 Hz doublet at $\delta = 6.45$ for 5-H

[14] *P. M. Collins, P. T. Doganges, A. Kolarikol,* and *W. G. Overend,* Carbohydr. Res. **11**, 199 (1969).
[15] *O. Gabriel,* Carbohydr. Res. **6**, 319 (1968).
[16] *F. W. Lichtenthaler* and *U. Kraska,* Carbohydr. Res. **57** (1977), in press.

and 8.16 for 6-H) and from the fact that **13** was converted into maltol by treatment with zinc and hydrochloric acid.

The enolone **4** is similarly sensitive towards purely acidic conditions. No reaction occurs in acetic acid or acetic acid/chloroform at room temperature, but when **4** is dissolved in trifluoroacetic acid, complete loss of optical activity is observed within 5 min owing to formation of benzoyloxymaltol **14**, which can be isolated in 89% yield. Under somewhat less forcing acidic conditions the conversion **4** → **14** is traceable in more detail. Thus, trichloroacetic acid (1 molar equiv.) in chloroform or even silica gel/chloroform slowly convert enolone **4** into a mixture of three products, "compound A", "compound B", and benzoylbenzoyloxymaltol **13**, as is readily demonstrable on TLC plates. For preparative purposes it was found advantageous to absorb enolone **4** on silica gel and to subject the dry mixture to brief heating (30 min, 70°C). After removal of unreacted **4** by crystallization (36%) a mixture of "A", "B", and **13** in an approximately 4:2:1 ratio was obtained. Of these products, since "A" proved to be particularly acid labile – its conversion into "B" already took place during TLC –, only "B" was isolated upon chromatography on a silica gel column (beside **13**) and characterized as an amorphous substance of $[\alpha]_D = +24°$. Microanalytical data indicated B to be isomeric with enolone **4**, the ^1H NMR spectrum revealed the presence of a $CH-CH_2$-coupling system (1H-t at $\delta = 5.37$ and 2H-q at 2.92 with $J = 4$ Hz) together with a sharp singlet of the benzoyloxy-substituted methylene group ($\delta = 5.10$). Treatment of **B** with trichloroacetic acid/chloroform resulted in the formation of **13** and **14**. On the basis of this evidence, compound **B** has been assigned the dihydropyranone structure **10**, whereas its more acid-labile precursor, i.e. compound A, has been tentatively assigned the dienol structure **8**.

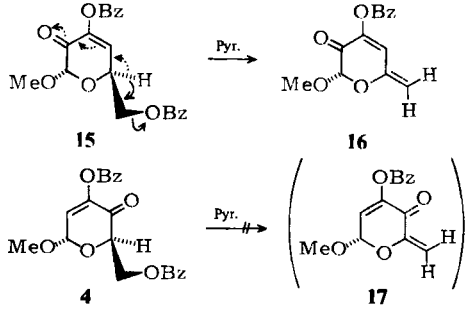


Under mild basic conditions, e.g. piperidine (1 molar equivalent) in chloroform or in ethanol at room temperature, enolone **4** is converted into benzoyloxymaltol **14** within 3 h. On standing in absolute pyridine, i.e. under conditions that result in elimination of the terminal benzoyloxy group in the 3,2-enolone series[13,16], **4** yields no detectable products other than **4** and dihydropyranone **10** after 24 h at ambient temperature and **10** can be isolated from the mixture in yields of up to 50% by chromatography.

On the basis of these results, the mechanistic course of the acid-induced conversion of enolone **4** into hydroxymaltol derivatives is reasonably explained by an initial 4,5-enolization (**4** → **8**) followed by an intramolecular $O^3 \rightarrow O^4$-benzoyl migration *via* orthoacid intermediate **9** to give dihydropyranone **10**, from which methanol is eliminated to give benzoylbenzoyloxymaltol (**10** → **13**). Under the more forcing acidic conditions, however, the γ-pyrone system, i.e. benzoyloxymaltol **14**, may be formed by direct elimination of the elements of methyl benzoate from **8** rather than *via* *O*-debenzoylation of **13**.

The base-evoked 3,4-enolone → γ-pyrone conversion may be understood to proceed in a similar manner, the initial formation of the enolate of **8** being followed by elimination of methyl benzoate, which may proceed directly (**8**-enolate → **14**), or stepwise *via* the enolate of **10**, elimination of methoxide to **13** and mono-debenzoylation (**13** → **14**). The exclusive formation of **10** from **4** in pyridine solution appears to sustain the stepwise pathway.

This mechanistic rationalization receives further support from the reaction of enaminone **6** in trifluoroacetic acid. Like **4**, **6** gives a solution devoid of optical activity within 10 min, yet seemingly due to the inability of the initially formed enol **11** to split off an *N*-acyl group *via* an intermediate of type **9**, a pyrylium salt structure is elaborated by direct elimination of methanol. Although attempts to isolate **12** as a perchlorate or hexachloroantimonate have not been successful so far, its presence in trifluoroacetic acid solution clearly followed from the ^{1}H NMR spectrum, which exhibits a 3H-singlet for the $C-CH_3$ group at $\delta = 2.84$ and 5.5 Hz-doublets for 5-H and 6-H at $\delta = 8.49$ and 8.77, respectively, beside 3H-signals for the acetamido group (2.37) and for the methanol or methyl trifluoroacetate formed (3.98). Although directly comparable data of analogously substituted pyrylium salts are not available, the chemical shifts for the α- and β-protons in pyrylium perchlorate ($\delta = 9.6$ and 8.5 in liquid SO_2) and for the methyl protons in 2,6-dimethylpyrylium hexachloroantimonate ($\delta = 3.04$)[17] appear to support structure **12**.



15 **16**

4 **17**

In conclusion, it appears to be of relevance to elaborate the distinct reactivity differences between 3,4-enolones, such as **4**, and systems with the reverse arrangement of the enolone structural unit, i.e. 3,2-enolones. The latter, e.g. **15** or its β-anomer, are remarkably stable towards acidic conditions, readily afford 2,4-dinitrophenylhydrazones, are exclusively converted into kojic acid derivatives in mildly basic, protic medium, yet on standing in pyridine yield exclusively a dienone (**15** → **16**) *via* elimination of benzoic

[17] *A. T. Balaban, G. R. Bedford,* and *A. R. Katritzky,* J. Chem. Soc. **1964**, 1646.

acid from the 5,6-position[13,16]. In contrast, the 3,4-enolone **4** is very sensitive towards acidic conditions, on treatment with 2,4-dinitrophenylhydrazine gives at least four products containing the DNP-residue, and on standing in pyridine does not forms a dienone corresponding to **16** by 5,6-elimination of benzoic acid (**4** ⇏ **17**) but a dihydropyranone (**10**).

The underlying reasons for these distinct reactivity differences can be rationalized on the basis that enolization is much more readily effected in a 3,4-enolone, in which a proton vicinal to the carbonyl function is removed (e.g. **4** → **8**), than in a 3,2-enolone, in which the initial enolization step is provoked by removal of a vinylogous and hence less acidic proton (e.g. **15**, dotted arrows). A second factor contributing to these differences is the ease of removal of the anomeric substituent, i.e. the final step of these γ-pyrone conversions: in the 3,4-enolone intermediate (enol or enolate of **10**) the expulsion of methoxide would be expected to proceed more readily than in the corresponding 3,2-enolone intermediate carrying the benzoyloxy function at C-3 instead of at C-4 as in **10**.

The decisively different behaviour of **4** and **15** towards pyridine, i.e. a very weak, aprotic base, may be rationalized on similar grounds. In **4**, the electron pair generated at C-5 on abstraction of the proton will, owing to the vicinal carbonyl group, immediately be delocalized to form the enolate of **8**, which is a practically irreversible first step towards formation of **10**. In the 3,2-enolone **15** or its β-anomer, however, the corresponding C-5 carbanion initially formed on abstraction of its proton by pyridine will delocalize its electron pair towards the vinylogous carbonyl function less readily and to a lesser extent than its 3,4-enolone counterpart, this process (cf. dotted arrows in **15**) being additionally impeded by the benzoyloxy substituent at the CC double bond. This provides the basis for an alternate pathway, i.e. 5,6-elimination of benzoic acid (**15**, solid arrows), which undoubtedly receives considerable momentum from the elaboration of a thermodynamically favorable, linear-conjugated dienone (**16**), in contrast to the 3,4-enolone case where the same process would generate the less favorable, cross-conjugated dienone **17**.

We express our appreciation with thanks to Dr. *K. Čapek*, Laboratory of Monosaccharides, Technical University, Prague, for kindly providing a generous sample of methyl 3-acetamido-2-*O*-acetyl-3,6-dideoxy-α-L-glucopyranoside, to the *Humboldt-Foundation* for granting a research fellowship (to S. O.) and to the *Deutsche Forschungsgemeinschaft* for continuous support of these investigations.

Experimental Part

Melting points are determined on a Bock-Monoskop and are uncorrected. Spectral measurements were effected with Perkin-Elmer 125 (IR), Perkin-Elmer 141 (rotations), Jasco J-20 (CD), Varian A-60A and XL 100 (NMR), and Varian CH4B (MS) instruments. TLC was performed on Kieselgel F_{254} plastic sheets (Merck, Darmstadt) and was used to monitor the reactions and to ascertain the purity of the reaction products. Developers employed: A dichloromethane/ethyl acetate (20:1), B benzene/methanol (99:1), C benzene/2-propanol (50:1), D ethyl acetate/ethanol/water (15:2:1), E water saturated with 2-butanone. The spots were visualized by UV light or by spraying with 80% aqueous sulfuric acid and charring at 110°C for 5 min. Column chromatography was carried out on Kieselgel 60 (70–230 mesh, Merck).

Methyl 3,6-di-O-benzoyl-2-deoxy-α-D-glycero-hex-2-enopyranosid-4-ulose (**4**): A solution of 5.2 g (10 mmol) of methyl 2,3,6-tri-*O*-benzoyl-α-D-galactopyranoside (**1**)[18] in dimethyl sulfoxide

[18] *E. J. Reist, R. R. Spencer, D. F. Calkins, B. R. Baker*, and *L. Goodman*, J. Org. Chem. **30**, 2312 (1965).

(35 ml) and acetic anhydride (20 ml) was kept at ambient temperature for 48 h and then poured into ice-water; the syrup that separated was dissolved in chloroform, washed with water and dried (Na_2SO_4). Removal of the solvent *in vacuo* left a residue, which crystallized on addition of methanol. Filtration (mother liquor cf. below) and recrystallization from ethanol afforded 2.35 g (61%) of **4** as colorless needles, homogeneous on TLC (A, B, and C), m.p. 127–128 °C, $[\alpha]_D^{25} = +70°$ (c = 1, chloroform).

NMR ($CDCl_3$): δ = 8.13 and 7.50 (two m, 4H and 6H, 2Ph), 6.70 (d, 1H, $J_{1,2}$ = 3.5 Hz, 2-H), 5.42 (d, 1H, 1-H), 4.80 (m, 3H, ABC-system for 5-H and 6-, 6'-H), 3.55 (s, 3, OCH_3). – UV (dioxane): λ_{max} at 339 (lg ε = 1.67) with shoulders at 330 (1.61), 354 (1.51) and 375 nm (1.00); CD (dioxane): 208 ($\Delta\varepsilon = -10.12$), 237 (+13.83), 327 (−1.52), 342 (−2.15), 355 (−1.99), 377 nm (−0.80). – MS above m/e = 260 (base peak = M − $C_6H_5CO_2H$): 382 (16%, $M^{\oplus}$), 351 (31, M − OCH_3) 350 (66, M − CH_3OH), 277 (5, M − C_6H_5CO).

$C_{21}H_{18}O_7$ (382.3) Calc. C 65.96 H 4.74 Found C 65.89 H 4.76

The methanolic mother liquor remaining after isolation of **4** showed spots (TLC in A) at R_F 0.40 (dihydropyranone **10**), 0.54 (enolone **4**), and 0.62 (the 4-*O*-methylthiomethyl derivative of **1** identified by its indifference to 2,4-dinitrophenylhydrazine spray and a signal attributable to an SCH_3 group at δ = 2.14 in the ^1H NMR spectrum in $CDCl_3$ of the mixture). The benzoic acid formed (0.57 g, 78%) of m. p. and mixed m. p. 122 °C was isolated on evaporation to dryness and sublimation of the residue at 70 °C/0.02 Torr.

Using dimethyl sulfoxide/acetic anhydride ratios of 3 : 2, 3 : 1,7 (as above) or 2 : 1 [1b] does not significantly affect the conversion **1** → **4**.

Interim course of the dimethyl sulfoxide/acetic anhydride oxidation of methyl 2,3,6-tri-O-benzoyl-α-D-galactoside (**1**): A set of four solutions, each containing 500 mg of **1** in a mixture of dimethyl sulfoxide (3 ml) and acetic anhydride (2 ml), was agitated at room temperature, the reactions being interrupted at 8, 14, 19 and 40 h, respectively, by stirring into aqueous saturated sodium hydrogen carbonate (30 ml each). Decantation from the gummy product formed was followed by washing a chloroform solution (20 ml) with water several times and drying (Na_2SO_4). Evaporation to dryness *in vacuo* (finally 0.2 Torr) gave 400–450 mg of a syrup that was examined by ^1H NMR spectroscopy and TLC. Determination of the respective ratios of uloside **2** and enolone **4** was based on the intensities of the 10.5 Hz doublet at δ = 6.20 for 3-H of **2** as compared to that of the 3.5 Hz doublet at δ = 6.70 for the olefinic proton (2-H) in **4**. The differentation of **2** and **4** by TLC in solvent systems A–D (or others) is impeded by the near-identity of R_F values, **4** giving a narrow distinct spot on top of the extended spot invariably observed for ulose **2**.

Results: a) After 8 h, more than 90% of educt **1** had been converted into a 3 : 1 mixture of uloside **2** and enolone **4**; b) after 14 h, educt **1** had disappeared completely at expense of the formation of a 1 : 1 mixture of **2** and **4**; c) after 19 h, a 1 : 2 mixture of **2** and **4** was detected, and d) after 41 h, a syrup (400 mg) containing **2** and **4** in a 1 : 3 ratio, was obtained, from which on trituration with ethanol, 190 mg (51%) of enolone **4**, m. p. 126–128 °C, could be crystallized.

Analogous experiments revealed that variation of the dimethyl sulfoxide/acetic anhydride ratio from 3 : 2 (as above) to 2 : 1 or reaction of **1** in the double amount of 3 : 2 oxidant solution gave no significant changes in reaction rate or in product distribution.

Methyl 2,3,6-tri-O-benzoyl-α-D-xylo-hexopyranosid-4-ulose 2,4-dinitrophenylhydrazone (**3**): On workup of an 8 h dimethyl sulfoxide/acetic anhydride oxidation of **1** (1.0 g) as described for **4** and subsequent treatment of the syrupy residue with 2,4-dinitrophenylhydrazine solution [19], a mixture of hydrazones (5 yellow spots on TLC in A) separated containing **3** as the major com-

[19] *L. F. Fieser* and *M. Fieser,* Reagents for Organic Synthesis, p. 330, J. Wiley & Sons, Inc. New York 1967.

ponent. Repeated fractional crystallization from ethyl acetate/ethanol afforded 130 mg (9.6%) of **3** as yellow needles of m.p. 145.5–147.5°C, $[\alpha]_D^{25} = +0.5°$ ($c = 0.7$, dichloromethane), $[\alpha]_D^{25} = +23.0°$C ($c = 0.3$, dioxane).

NMR ($CDCl_3$): $\delta = 11.90$ (s, 1H, NH), 9.00 (2.5 Hz-d, 1H, 3'-H), 6.36 (d, 1H, $J_{2,3} = 8.0$ Hz, 3-H), 5.77 (dd, 1H, $J_{1,2} = 3.5$ Hz, 2-H), 5.31 (d, 1H, 1-H), 4.98 (m, 3H, ABC-system for 5-H and 6-, 6'-H), 3.56 (s, 3H, OCH_3). – NMR ([D_6]DMSO): $\delta = 11.47$ (s), 8.77 (d), 6.49 (d, $J_{2,3} = 7.5$ Hz), 5.80 (dd, $J_{1,2} = 3.5$ Hz), 5.40 (d), 4.97 (m), 3.51 (s, OCH_3).

$C_{34}H_{28}N_4O_{12}$ (684.6) Calc. C 59.65 H 4.12 N 8.18 Found C 59.58 H 4.06 N 8.20

For a similarly prepared product of the same analytical composition, a m.p. of 131–132°C and $[\alpha]_D = +100°$C (chloroform) were reported[14] together with NMR data in [D_6]DMSO that, curiously, correspond perfectly with ours in $CDCl_3$.

Methyl 3-acetamido-2,3,6-trideoxy-α-L-glycero-hex-2-enopyranosid-4-ulose (**6**): A solution of 500 mg (1.9 mmol) of methyl 3-acetamido-2-*O*-acetyl-3,6-dideoxy-α-L-glucopyranoside (**5**)[20] in dimethyl sulfoxide (8 ml) and acetic anhydride (5 ml) was kept at ambient temperature for 2 days. The reaction mixture was then diluted with chloroform (30 ml) and thoroughly washed with water (5 × 15 ml), dried (Na_2SO_4) and evaporated *in vacuo* to dryness. The residue, comprising an approximately 2:1 mixture (TLC in D) of enaminone **6** and the thiomethyl ether **7** (R_F 0.7 and 0.45, resp.), was reevaporated several times from benzene and methanol, and then applied to a silica gel column (2.5 × 35 cm). Elution with ethyl acetate readily separated the enaminone (detectable by UV) from the thiomethyl ether (detected on TLC by charring with sulfuric acid). The fraction containing **6** was evaporated to dryness, affording 210 mg (53%), m.p. 115–116°C, $[\alpha]_D^{20} = -103°$ ($c = 1$, chloroform).

UV (methanol): λ_{max} at 266 with shoulder at 330 nm. – IR (KBr): 1670, 1530 (NHAc), 1710 (C=O, conj.), 1650 cm^{-1} (C=C, conj.). – NMR ($CDCl_3$): $\delta = 7.70$ (br s, 1H, NH), 7.58 (d, 1H, $J_{1,2} = 3.5$ Hz, 2-H), 5.24 (d, 1H, 1-H), 4.68 (q, 1H, $J_{5,6} = 7$ Hz, 5-H), 3.51 (s, 3, OCH_3), 2.12 (s, 3H, NAc), 1.42 (7 Hz-d, 3H, 6-, 6'-, 6''-H).

$C_9H_{13}NO_4$ (199.2) Calc. C 54.26 H 6.58 N 7.03 Found C 54.01 H 6.45 N 6.88

Methyl 3-acetamido-2-O-acetyl-3,6-dideoxy-4-O-methylthiomethyl-α-L-glucopyranoside (**7**): Evaporation of the UV-inactive fraction from the column separation (cf. above) gave 190 mg (33%) of **7** as colorless crystals; m.p. 173–174°C; $[\alpha]_D^{20} = -74°$ ($c = 1$, chloroform). – NMR ($CDCl_3$): $\delta = 1.29$ (d, 3, $J_{5,6} = 6$ Hz, 6-, 6'-, 6''-H), 1.94, 2.07 and 2.14 (three 3H-s, OAc, NHAc, SCH_3), 3.38 (s, 3, OCH_3), 3.30 (m, 1H, 2-H), 4.73 (s, 2H, OCH_2S), 5.65 (m, 1H, NH), 5.0–3.5 (complex m, 4H, 1-H, 3-H–5-H).

$C_{13}H_{23}NO_6S$ (321.4) Calc. N 4.36 S 9.98 Found N 4.31 S 9.80

3-Benzoyloxy-2-benzoyloxymethyl-4H-pyran-4-one (Benzoylbenzoyloxymaltol) (**13**): A mixture of freshly fused sodium acetate (500 mg) and glacial acetic acid (10 ml) was heated to 90°C for 2 h, diluted with water and extracted with chloroform (2 × 30 ml). The combined extracts were washed with sodium hydrogencarbonate solution and water (3 ×) and dried over sodium sulfate. Evaporation to dryness left a yellowish, chromatographically homogeneous (TLC in A) syrup (300 mg, 65%) that was purified by elution from a silica gel column with chloroform/ethyl acetate (5:1) to give 195 mg (43%) of sirupy analytically pure product. – NMR ([D_6]DMSO): $\delta = 8.16$ (d, 1H, $J_{5,6} = 5.5$ Hz, 6-H), 8.1–7.3 (m, 10H, 2Ph), 6.44 (5.5 Hz-d, 1H, 5-H), 5.37 (s, 2H, CH_2).

$C_{20}H_{14}O_6$ (350.3) Calc. C 68.57 H 4.03 Found C 68.45 H 4.10

2-Benzoyloxymethyl-3-hydroxy-4H-pyran-4-one (Benzoyloxymaltol) (**14**): Enolone **4** (600 mg, 1.5 mmol) was dissolved in trifluoroacetic acid (6 ml) to give after an initially yellow coloration a colorless solution which within 5 min was devoid of any optical activity. Concentration to

[20] *K. Čapek, J. Steffkova,* and *J. Järv,* Collect. Czech. Chem. Commun. **31**, 1854 (1966).

dryness *in vacuo* after 2 h standing followed by repeated reevaporations from methanol afforded a crystalline residue, which was recrystallized from isopropyl alcohol: 340 mg (89%) of **14** as colorless prisms, m.p. 136–139°C. – NMR ([D_6]DMSO): δ = 9.51 (s, 1H, OH), 8.16 (d, 1H, $J_{5,6}$ = 5 Hz, 6-H), 7.95 and 7.60 (two m, 2 and 3H, Ph), 6.45 (d, 1H, 5-H) 5.37 (s, 2H, CH_2).

$C_{13}H_{10}O_5$ (246.2) Calc. C 63.41 H 4.09 Found C 63.31 H 4.04

Conversion of Benzoyloxymaltol (**14**) *into Maltol*[21]: A mixture of **14** (200 mg, 0.8 mmol), zinc dust (100 mg), and 40 ml of 1:1 ethanol/water was heated to 70°C, and then 6 ml of N HCl was gradualy added (within ca. 2 h). After a total of 5 h at 70°C the reaction mixture was neutralized by the addition of 2 N NaOH and the inorganic materials were filtered off. Concentration *in vacuo* to dryness and extraction of the residue with chloroform followed by evaporation gave a solid product, that was subjected to fractional sublimation at 40 and 60°C/10^{-3} Torr, to give aside from some benzoic acid (first fraction) 68 mg (67%) of prisms of m.p. 160–161°C (lit.[23] 160–161°C), identical in m.p., mixed m.p., and IR data with a commercially available specimen that had also been sublimated. – NMR ([D_6]DMSO): δ = 8.70 (s, 1H, OH), 8.02 (d, 1H, $J_{5,6}$ = 5 Hz, 6-H), 6.45 (d, 1H, 5-H), 2.25 (s, 3, CH_3).

3-Benzoyloxy-2-benzoyloxymethyl-6(S)-methoxy-5,6-dihydro-4H-pyran-4-one (**10**)

a) *By treatment of* **4** *with silica gel:* To a slurry of silica gel in chloroform (50 mg in 100 ml) was added a chloroform solution of enolone **4** (2.0 g in 30 ml). The solvent was evaporated and the residual white powder was heated at ≈70°C for 30 min in a water bath. Extraction of the now yellow powder with hot ethyl acetate (3 × 60 ml) and evaporation of the combined extracts gave a syrup, from which educt **4** (720 mg, 36%) crystallized on trituration with ethanol (20 ml) and standing in a refrigerator overnight.

The mother liquor was evaporated to dryness, yielding a brownish syrup that consisted (TLC in A) of four components: R_F 0.60 (tentatively **8**), 0.54 (enolone 4), 0.40 (dihydropyranone **10**), 0.20 (benzoylbenzoyloxymaltol **13**) and its monobenzoate **14** together with benzoic acid as an extended spot close to the start. On fractionation of this mixture (0.83 g) on a silica gel column (25 g, 2 × 15 cm) by elution with 20:1 dichloromethane/ethyl acetate only fractions containing **10** together with **14** and benzoic acid were eluted, seemingly due to conversion of residual **4** and **8** into **13**/**14** on the column. The combined eluates were washed twice with aqueous sodium hydrogencarbonate solution for removal of **14** and benzoic acid, dried (Na_2SO_4) and evaporated to dryness. Yield 240 mg (12%) of a chromatographically uniform syrup, $[\alpha]_D^{25}$ = +24° (*c* = 0.5, chloroform). – NMR ($CDCl_3$): δ = 5.37 (3 Hz-t, 1, 6-H), 5.10 (s, 2, CH_2OBz), 3.53 (s, 3, OCH_3), 2.92 (q with $J_{5,6} \approx J_{5',6} \approx 4$ Hz, 1, 5-H).

$C_{21}H_{18}O_7$ (382.3) Calc. C 65.96 H 4.75 Found C 65.73 H 4.90

b) *By treatment of enolone* **4** *with pyridine:* A solution of **4** (1.0 g, 2.6 mmol) in absol. pyridine (40 ml) was left for 24 h at room temperature. Evaporation to dryness by codestillation with toluene followed by several reevaporations of the residue from toluene left a brownish syrup that contained enolone **4** and dihydropyranone **10** as major components (TLC in A). The mixture was fractionated on a silica gel column (2.5 × 30 cm) by elution with 20:1 dichloromethane/ethyl acetate. Eluates containing **10** were pooled and evaporated to dryness: 220 mg (22%) of a chromatographically uniform syrup, identical with respect to rotation and ^{1}H NMR data with the one described above, were obtained.

[21] In adaptation of a procedure used previously[22] for the conversion of hydroxymaltol (**14**, H instead of Bz) into maltol, yet with omission of copper sulfate.

[22] *Chas. Pfizer and Co.* (by *R. L. Miller, B. E. Tate, R. P. Allingham,* and *H. Rutner*), Belg. Pat. 625, 114 (May 21, 1963) [C. A. **60**, 10651g (1964)].

[23] *I. Ichimoto, K. Fujii,* and *C. Tatsumi,* Agric. Biol. Chem. (Tokyo), **29**, 325 (1965).