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MONOMERIC HEXOFURANOSES HAVING AN ACETYLIMINO GROUP IN THE HEMIACETAL RING*

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ABSTRACT

Acetolysis of methyl 4-acetamido-4-deoxyhexopyranosides of *gluco* and *galacto* configuration yields not only the corresponding 4-acetamido-4-deoxypyranoses, but also ring contraction products, *i.e.*, 4-acetamido-1,2,3,5,6-penta-*O*-acetyl-4-deoxy-D-gluco- and -D-galactofuranose, respectively, with the ease of acetolysis and product distribution depending on the configuration at C-4. Mechanistic implications with respect to the formation of acylic and cyclic intermediates are discussed.

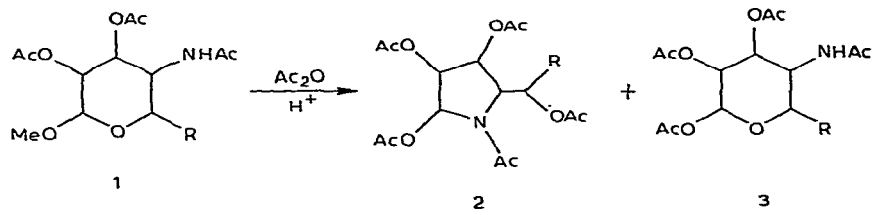
INTRODUCTION

Sulfuric acid-catalyzed acetolysis[1] of methyl 4-acetamido-4-deoxypentopyranosides (**1**, R = H) exclusively yields 4-acetamido-4-deoxyfuranoses[2–4] of type **2**. By contrast, hexoses of type **1**, *i.e.*, the methyl 4-amino-4-deoxyhexopyranosides of D-glucose[5], 6-deoxy-D-glucose[6] and 6-deoxy-D-galactose[7], appear preferentially, if not exclusively, to maintain the pyranose ring on acetolysis, affording products of structure **3** in yields of 78, 71, and 31%, respectively. Although the comparatively low yield in the last example may imply** the formation of products other than **3**, no hexoses of type **2** have as yet been uncovered. Herein we describe the first monomeric*** hexofuranoses having an acetylimino group in the hemiacetal ring (**2**), that in fact are readily formed alongside their pyranose isomers (**3**) on acetolysis of the 4-acetamido-4-deoxyhexosides **1**, the ease of acetolysis and the ratio of **2** to **3** formed depending on the configuration at C-4.

*Dedicated to Professor Kurt Heyns, on the occasion of his 70th birthday.

The isolation from the complex mixture resulting from the acetolysis of methyl 4-acetamido-2,3-di-*O*-benzyl-4,6-dideoxy-α-D-galactopyranoside of, *inter alia*, two partially deacetylated monobenzyl compounds for which pyrrolidine type structures have tentatively been considered[7] is another indication for the possible formation of hexofuranoses of type **2.

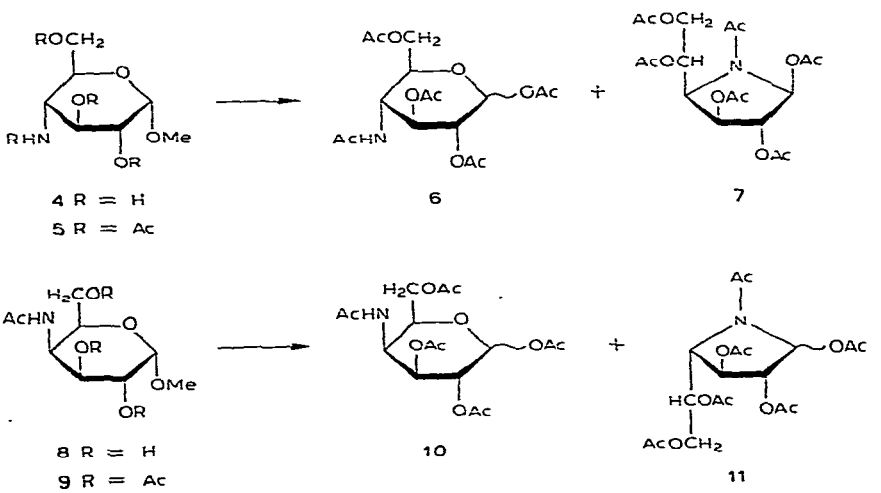
***Only the octaacetates of two *dimeric* 4-amino-4-deoxyhexoses having one ring acetylimino group within the tricyclic structure have been described[8].



1 2 3

RESULTS AND DISCUSSION

When methyl 4-amino-4-deoxy-α-D-glucopyranoside (**4**) or its tetra-*O*-acetyl derivative **5** was acetolyzed in 17:17:1 acetic anhydride–acetic acid–sulfuric acid at ambient temperature, not only the acetamidodeoxypyranose **6** was formed, as claimed previously[5], but two products accumulate in an approximate 3:2 ratio. The major component obtained in 41% yield after separation on silica gel was indeed 4-acetamido-1,2,3,6-tetra-*O*-acetyl-4-deoxy-D-glucopyranose (**6**) as a 5:1 mixture of α and β anomers; the other product, isolable in crystalline form in 21% yield, proved to be 4-acetamido-1,2,3,5,6-penta-*O*-acetyl-4-deoxy-D-glucofuranose (**7**) on the basis



of i.r., p.m.r., and m.s. data (*cf.* below). Whilst the acetolysis of the 4-amino-4-deoxy-glucosides **4** or **5** took several days at room temperature for completion, the 4-epimeric *galacto* analogs[9] **8** or **9** reacted considerably faster, acetolysis being essentially complete after 24 h. More salient, however, than the greater ease of acetolysis (D-galactose derivatives in general hydrolyze and anomerize 2–5-times faster than their D-glucose epimers[10]) was the higher tendency of the D-galactosides **8** or **9** to undergo ring contraction. In the approximate 5:2 mixture of products obtained, furanose derivative **11** was the major component, isolable in 51% yield upon silica

gel chromatography, and readily characterizable by spectroscopic means (*cf.* below), whereas 4-acetamido-1,2,3,6-tetra-*O*-acetyl-4-deoxy-D-galactopyranose (**10**), in the form of an approximate 4:1 mixture of α and β anomers, was the minor product obtained in 20% yield and identified by comparison with authentic[9] material.

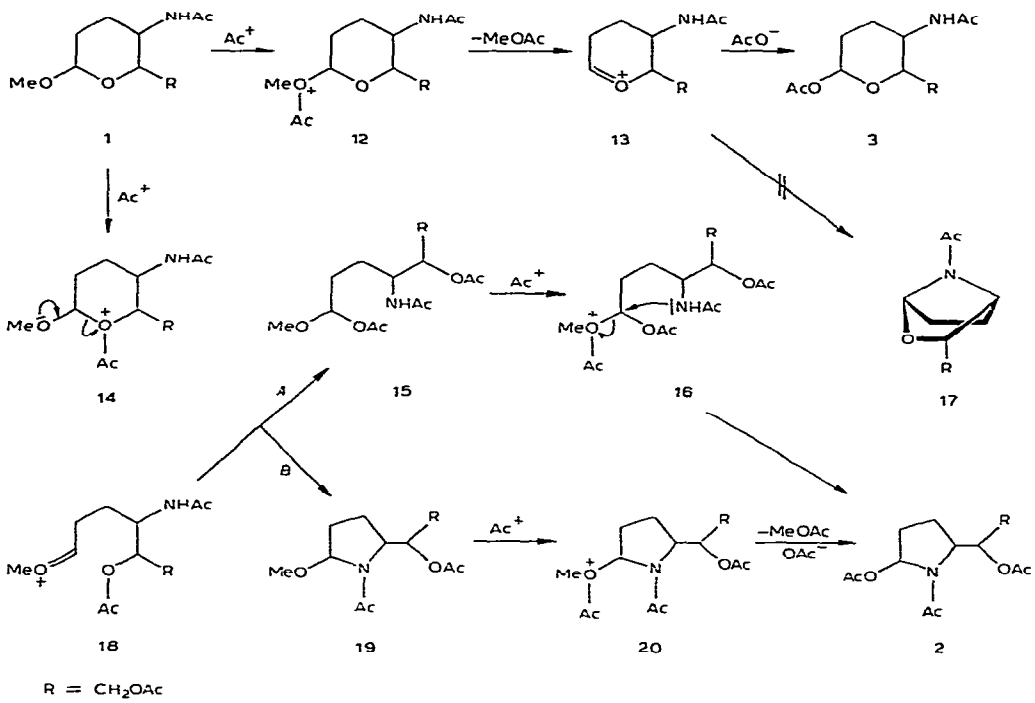
Structural and configurational assignments for the pyrrolidine derivatives **7** and **11** rest on the following evidence: (a) **7** and **11** show strong i.r. bands at 1740 (OAc) and 1675 cm^{-1} (Amide I), yet absorption attributable to a secondary acetamido group, *i.e.*, around 3300 (NH) and 1560 cm^{-1} (Amide II) as in the acetamidodeoxy-pyranoses **6** and **10**, is distinctly absent; (b) the p.m.r. spectra of **7** and **11** convincingly correspond to the furanose structures, *e.g.*, they exhibit 6 acetyl-group signals in the $\delta 2$ region as compared to only 5 shown by the penta-*O*-acetylpyranoses **6** and **10**, and all of the acetyl resonances observed on the solution in chloroform-*d* lie below δ 2.20 (*i.e.*, within δ 2.14–2.02 in **7** and δ 2.20–2.01 in **11**), thus excluding the possibility of the isomeric *N,N*-diacetylpyranose structure, the acetamido resonances of which should appear in the δ 2.33–2.42 range[11]; and (c) distinct differences between acetamidodeoxy-pyranoses and -furanoses are observed in the mass-spectral fragmentation patterns, the former being characterized by excision of the anomeric substituent (M − AcO · at *m/e* 330), and the latter ($M^+ + 1$ at *m/e* 432) by removal of · OAc as well as of the side chain $AcOCH_2 - \dot{C}HOAc$ to yield pyrroline fragments of *m/e* 372 and 286, respectively*. Evidence for the β-D configuration of the acetamidodeoxy-D-glucofuranose **7** is provided by its low optical rotation and by the small coupling constant exhibited by the anomeric proton ($J_{1,2} < 1.5$ Hz), which is similarly observed for configurationally related β-D-xylofuranose derivatives[13]. The syrupy galacto-furanose derivative **11**, by contrast, shows $J_{1,2}$ 5.5 Hz, and, hence, may be primarily the α-D anomer.

That each of the products obtained is directly arising from glycoside acetolysis rather than from a pyranose $\rightleftarrows$ furanose interconversion was readily established: **7**, when exposed to the acetolysis mixture used for **5**, slowly gave rise to a new, as yet uncharacterized product, clearly different from the acetamidodeoxy-D-glucopyranose derivative **6** (t.l.c.), whereas **6** is unaffected by these conditions over days. Similarly, when the acetamidodeoxy-D-galactopyranose derivative **10** was subjected to acetic anhydride–acetic acid–sulfuric acid, no furanose derivative **11** was detectable by t.l.c., the latter compound being continuously converted into products other than **10** (presumably pyrroline derivatives) under acetolysis conditions. This stability of both acetamidodeoxypyranoses (**6** and **10**, respectively) is remarkable in so far as an isomerization corresponding to the conversion of **6** → **7** has been reported for 1,2,3-tri-*O*-acetyl-4-benzamido-4-deoxy-D-xylopyranose in acetic anhydride–sulfuric acid[14]. Apparently, a substituent at C-5 in pyranose peracetates, as in **6**, considerably impedes ring contraction during acetolysis.

In attempting to rationalize these results, in particular the observation that a pyranose $\rightleftarrows$ furanose isomerization is not observed under the acetolysis conditions

*A detailed discussion of fragmentation routes is contained in ref. 12.

applied, a mechanism is suggested by the product distribution (see Scheme 1). For the formation of the acetamidodeoxypyranoses **6** and **10**, a mechanism[1] involving a cycle is expected, which comprises attack of the acetyl cation at the glycosidic oxygen atom (**1** → **12**), followed by expulsion of methyl acetate and stabilization of the cyclic carboxonium ion intermediate **13** by recombination with an acetate ion (**13** → **3**)*.



Scheme 1

In view of the ease with which 1,4-anhydropyranoses are formed on displacement of 4-sulfonyloxy groups[15], not only an acyclic intermediate mechanism[1,16] is to be considered for the formation of ring-contraction products **7** and **11**, but also one *via* bicyclic intermediates of type **17**, originating from carboxonium ion **13** by direct participation of the acetamido nitrogen atom (**13** → **17**). This course, however, can be excluded on the basis of the fact that under acetolysis conditions, *i.e.*, a reaction medium that is certain to generate carboxonium ion intermediates (**3** → **13**), neither of the acetamidodeoxypyranoses can be induced to form acetamidodeoxyfuranose peracetates. Hence, formation of ring-contraction products necessitates the operation

*The formation of the acetamidodeoxypyranoses **6** and **10** *via* acyclic intermediates can, of course, not be excluded, but it appears less likely, as it would involve cyclization of intermediate **16** with participation of AcO-5 that is less nucleophilic than an amide nitrogen atom.

of an acyclic-intermediate mechanism[1], *i.e.*, coordination of the acetyl cation with the ring oxygen atom (**1** → **14**), subsequent ring opening to a carboxonium ion of type **18**, and recyclization with participation of the amide nitrogen atom, the methoxyl group being expelled either before, during (route *A*), or after cyclization (route *B*). Of these possibilities, the intermediate formation of a methyl 4-acetamido-4-deoxyfuranoside (**18** → **19**), followed by acetolysis of the glycosidic substituent (route *B*), appears to be as plausible as route *A*, which involves formation of an open-chain hemiacetal **15** and subsequent cyclization with elimination of methyl acetate (**16** → **2**). The latter course, hereby, receives some support from the observation that hemiacetals of type **16** have been encountered in acetolysis reactions of a series of methyl pentosides[17,18] and of methyl α-D-mannopyranoside[18]. The third possibility, however, involving the formation of *aldehydo* peracetates of type **16** (Ac instead of Me) prior to cyclization appears to be less likely.

In conclusion, all of these considerations strongly indicate that the 4-acetamido-4-deoxyfuranose compound was formed *via* an acyclic mechanism, the 4-acetamido-4-deoxypyranose compound, however, *via* cyclic intermediates. Consequently, the extent to which each of these mechanisms was operating is directly indicated by the ratio in which deoxyfuranose and deoxypyranose compounds are present in the acetolysis mixture, *i.e.*, preference of the cyclic mechanism for the D-glucose compound *vs.* predominance of the acyclic course for the 4-epimeric D-galactose compound.

EXPERIMENTAL

General methods. — Melting points were determined on a Bock–Monoskop and are uncorrected. I.r. spectra were recorded with a Perkin–Elmer 125 spectrophotometer, optical rotations with a Perkin–Elmer 141 polarimeter, p.m.r. spectra with a Varian XL-100 spectrometer, and m.s. with a Varian CH4B instrument. T.l.c. was performed on Kieselgel F_{254} plastic sheets (Merck, Darmstadt, Germany) and was used to monitor the reactions and to ascertain the purity of the reaction products. Developers employed: (*A*) 60:2:1 (v/v) ethyl acetate–ethanol–water and (*B*) 3:2 (v/v) ethyl acetate–benzene. The spots were detected by u.v. light or by spraying the plates with 80% aqueous sulfuric acid and charring at 120° for 5 min. Column chromatography was carried out on Kieselgel 60 (70–230 mesh, Merck).

*Acetolysis of methyl 4-acetamido-2,3,6-tri-*O*-acetyl-4-deoxy-α-*D*-glucopyranoside* (**5**). — To a cold solution (0 to −5°) of **5** (5.00 g, 13.8 mmol, ref. 3) in 1:1 (v/v) acetic anhydride–acetic acid (100 ml) was added conc. sulfuric acid (2.8 ml) dropwise with vigorous stirring. The mixture was then kept for 5 days* at ambient temperature, and was subsequently decomposed by being gradually stirred into 1.4 L of saturated aqueous sodium hydrogencarbonate solution. Extraction with chloroform (3 × 100 ml)

*On processing after 3 days (the reaction time specified by Reist *et al.*[5]), the pyranose (**6**) fraction contained about 20% of educt **5** (methoxyl signal at δ 3.40 in chloroform-*d*).

followed by washing of the combined extracts with water, drying (sodium sulfate), and evaporation to dryness *in vacuo* afforded 4.7 g of a yellowish syrup*, consisting of an approximate 3:2 mixture of **6** and **7** (R_F 0.44 and 0.77, respectively, *A*) together with some minor components of R_F 0.56, 0.22 and 0. The syrup was dissolved in a small amount of ethyl acetate, placed on a silica gel column (5 × 60 cm), and eluted with ethyl acetate.

*4-Acetamido-1,2,3,5,6-penta-*O*-acetyl-4-deoxy-*D*-glucofuranose* (**7**). — The appropriate fractions containing **7**, eluted first, were evaporated to dryness. Dissolution of the residue in chloroform, charcoal treatment, and re-evaporation gave a colorless and chromatographically homogeneous syrup (1.62 g, 28%) that crystallized on trituration with ethanol, giving, after recrystallization from ethanol, 1.20 g (21%) of **7** as colorless crystals, m.p. 95–96°, $[\alpha]_D^{23}$ +18° (*c* 1, chloroform); ν_{max}^{KBr} 1740 (ester CO) and 1675 (Amide I), no absorption around 3300 (NH) and 1560 cm^{-1} (Amide II); p.m.r. ($CDCl_3$): δ 6.35 (broadened s, 1 H, half-width 3 Hz, H-1), 5.4 (complex m, 3 H, H-2, H-3, and H-5), 4.85 (m, 1 H, H-4), 4.20 (m, 2 H, AB-system for CH_2), and acetyl resonances at 2.14, 2.12, 2.08 (2), and 2.02; p.m.r. [$(CD_3)_2SO$]: 6.33 (broad s, 1 H, H-1), 5.47 (m, 3 H, H-2, H-3, H-5), 4.67 (q, 1 H, $J_{3,4}$ 4 and $J_{4,5}$ 8 Hz, H-4), 5.82 (m, 2 H, CH_2), and acetyl resonances at 2.09, 2.05 (2), 2.03, and 1.97; m.s. (70 eV, major peaks above 250): *m/e* 432 ($M^+ + 1$), 372 (M − OAc), 371 (M − HOAc), 329 (M − HOAc and CH_2CO), 311 (M − 2 HOAc), 286 (M − $AcOCH_2$ − $\dot{C}$HOAc), 269 (M − 2 HOAc and CH_2CO), and 251 (M − 3 HOAc).

Anal. Calc. for $C_{18}H_{25}NO_{11}$: C, 50.11; H, 5.84; N, 3.25. Found: C, 50.03; H, 5.81; N, 3.19.

When methyl 4-amino-4-deoxy-α-D-glucopyranoside[5] (**4**) was subjected to the acetolysis conditions just described, it was assumed that acetylation (**4** → **5**) preceded acetolysis, as the reaction course and distribution of products **6**/**7** were identical.

*4-Acetamido-1,2,3,6-tetra-*O*-acetyl-4-deoxy-*D*-glucopyranose* (**6**). — The later fractions, eluted from the column separation just described, were processed in a manner identical to that described for **7**, to afford 2.18 g (41%) of a colorless syrup not amenable to crystallization from the usual solvents, $[\alpha]_D^{23}$ +93° (*c* 1, chloroform); based on n.m.r. data (intensity of H-1 and OAc-1) the α:β ratio was 5:1; ν_{max}^{KBr} 3280 (NH), 1740 (ester CO), 1660 (Amide I), and 1560 cm^{-1} (Amide II); p.m.r. ($CDCl_3$): δ 6.37 (d, 1, $J_{1,2}$ 3.5 Hz, H-1), 5.74 (d, 1, $J_{4,NH}$ 9 Hz, NH), 2.16 (axial OAc-1), 2.09, 2.05, and 2.01 (3 s, 3 H each, 3 OAc), and 1.93 (s, 3, NHAc); p.m.r. [$(CD_3)_2SO$]: δ 8.01 (d, 1, $J_{4,NH}$ 9 Hz, NH), 6.19 (d, 1, $J_{1,2}$ 3.5 Hz, H-1), Ac resonances at 2.15 (OAc-1), 1.99, 1.96 (2), and 1.76 (NHAc); m.s. (70 eV, major peaks above 250): *m/e* 330 (M − ·OAc) and 269 (M − HOAc and ·OAc). For a product obtained by acetylation of 4-acetamido-4-deoxy-D-glucopyranose, an α:β ratio of 4:1 and $[\alpha]_D^{20}$ +83° (*c* 0.5, chloroform) were reported[8].

*Reist *et al.*[5], by treatment of an analogously prepared syrup with ethyl acetate–cyclohexane, obtained a "gummy solid" of m.p. 55–57.5° in 78% yield, which allegedly was the pure pyranose **6** in the form of its half-hydrate.

Anal. Calc. for $C_{16}H_{23}NO_{10}$: C, 49.35; H, 5.95; N, 3.60. Found: C, 49.29; H, 5.79; N, 3.54.

*Acetolysis of methyl 4-acetamido-2,3,6-tri-*O*-acetyl-4-deoxy-α-*D*-galacto-pyranoside* (**9**). — To an ice-cold solution of **9** (900 mg, 2.5 mmol, ref. 9) in acetic anhydride (17 ml) was added a cold mixture of acetic acid (17 ml) and conc. sulfuric acid (1 ml)* dropwise with stirring. After the addition was complete, the mixture was left at ambient temperature for 2 days**, and then stirred into ice–water (300 ml). The aqueous mixture was extracted with chloroform (3 × 100 ml), and the extracts were washed with saturated sodium hydrogencarbonate solution. Drying (Na_2SO_4) and evaporation left a syrup consisting of **11** (R_F 0.63, *A*) and **10** (R_F 0.5, *A*) in the ratio of ~5:2, together with other, as yet unidentified components having R_F 0 (possibly decomposition products) and 0.19. Separation was readily effected on a silica gel column (2.5 × 40 cm) by elution with ethyl acetate.

*4-Acetamido-1,2,3,5,6-penta-*O*-acetyl-4-deoxy-*D*-galactofuranose* (**11**). — Evaporation of the first fraction and drying *in vacuo* afforded 550 mg (51%) of **11**, syrup, $[\alpha]_D^{25}$ +58° (*c* 1, chloroform); $\nu_{max}^{CHCl_3}$ 1750 (ester CO), 1680 (Amide I), and no absorption around 3300 (NH) and 1560 cm^{-1} (Amide II); p.m.r. ($CDCl_3$): δ 6.65 (d, 1, $J_{1,2}$ 5 Hz, H-1), 5.70 (m, 2, H-2, H-3), 5.28 (m, 1, H-4), ~4.4 (broad m, 3, H-5 and CH_2-6), and Ac resonances at 2.20, 2.14 (broadened, NAc), 2.08 (3), and 2.02; m.s. (70 ev): *m/e* 432 ($M^+ + 1$), 372 (M − ·OAc), 371 (M − HOAc), 312 (M − HOAc and OAc), and 286 (M − $AcOCH_2$ − ĊHOAc, intensity 50% of base peak at 142).

Anal. Calc. for $C_{18}H_{25}NO_{11}$: C, 50.11; H, 5.84; N, 3.25. Found: C, 50.20; H, 5.79; N, 3.29.

*4-Acetamido-1,2,3,6-tetra-*O*-acetyl-4-deoxy-α,β-*D*-galactopyranose* (**10**). — The more slowly moving fraction, on evaporation to dryness *in vacuo*, yielded 210 mg (20%) of **10**, syrup, $[\alpha]_D^{23}$ +76° (*c* 0.5, chloroform), consisting mainly (80%) of the α anomer (intensities of the anomeric H, 3 Hz at δ 6.35 for H-1_{eq} *vs.* 9 Hz at δ 5.66 for H-1_{ax}; and Ac resonances, OAc_{ax}-1 at δ 2.16 in $CDCl_3$, well separated from the others). For a 9:1 anomeric mixture of α,β anomers of **10**, prepared by a different route[9], $[\alpha]_D^{25}$ was +82° (*c* 1, chloroform).

Anal. Calc. for $C_{16}H_{23}NO_{10}$: C, 49.35; H, 5.95; N, 3.60. Found: C, 49.27; H, 6.03; N, 3.53.

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*By use of a more vigorous acetolysis mixture, *i.e.*, 20:1 (v/v) acetic anhydride–sulfuric acid, the reaction rate was considerably enhanced, the educt **9** being consumed after 5 h with formation of a higher proportion of by-products that remain at the start of the t.l.c. plate (*A*).

For a longer duration (*e.g.*, >4 days), the amount of **11 present in the mixture decreased with the formation of products remaining at the start of the t.l.c. plate (*A* or *B*), whilst **10** appeared to be unchanged.

REFERENCES

1 R. D. GUTHRIE AND J. F. MCCARTHY, *Adv. Carbohydr. Chem.*, 22 (1967) 11–23.
2 A. J. DICK AND J. K. N. JONES, *Can. J. Chem.*, 43 (1965) 977–982.
3 E. J. REIST, D. E. GUEFFROY, R. W. BLACKFORD, AND L. GOODMAN, *J. Org. Chem.*, 31 (1966) 4025–4030.
4 E. J. REIST, L. V. FISHER, AND L. GOODMAN, *J. Org. Chem.*, 32 (1967) 2541–2544.
5 E. J. REIST, R. R. SPENCER, D. F. CALKINS, B. R. BAKER, AND L. GOODMAN, *J. Org. Chem.*, 30 (1965) 2312–2317.
6 C. L. STEVENS, P. BLUMBERGS, AND D. H. OTTERBACH, *J. Org. Chem.*, 31 (1966) 2817–2822.
7 C. L. STEVENS, P. BLUMBERGS, F. A. DANIHER, D. H. OTTERBACH, AND K. G. TAYLOR, *J. Org. Chem.*, 31 (1966) 2822–2829.
8 H. PAULSEN, K. STEINERT, AND K. HEYNS, *Chem. Ber.*, 103 (1970) 1599–1620.
9 F. W. LICHTENTHALER AND P. HEIDEL, *J. Org. Chem.*, 39 (1974) 1457–1462.
10 W. A. BONNER, *J. Am. Chem. Soc.*, 81 (1959) 1448–1452; B. CAPON AND W. G. OVEREND, *Adv. Carbohydr. Chem.*, 15 (1960) 11–51; W. G. OVEREND, C. W. REES, AND J. S. SEQUEIRA, *J. Chem. Soc.*, (1962) 3429–3440; M. S. FEATHER AND J. F. HARRIS, *J. Org. Chem.*, 30 (1965) 153–157; J. N. BEMILLER, *Adv. Carbohydr. Chem.*, 22 (1967) 25–108.
11 F. A. L. ANET, R. A. B. BANNARD, AND L. D. HALL, *Can. J. Chem.*, 41 (1963) 2331–2338; T. D. INCH AND H. G. FLETCHER, JR., *J. Org. Chem.*, 31 (1966) 1815–1820; T. D. INCH. J. R. PLIMMER, AND H. G. FLETCHER, JR., *ibid.*, 31 (1966) 1825–1829; N. PRAVDIĆ AND H. G. FLETCHER, JR., *ibid.*, 32 (1967) 1806–1810.
12 G. BAMBACH, Dissertation, Technische Hochschule Darmstadt, 1971.
13 J. D. STEVENS AND H. G. FLETCHER, JR., *J. Org. Chem.*, 33 (1968) 1799–1805.
14 H. WEIDMANN, E. FAULAND, R. HELBIG, AND H. K. ZIMMERMANN, *Justus Liebigs Ann. Chem.*, 694 (1966) 183–189.
15 J. S. BRIMACOMBE, J. MINSHALL, AND L. C. N. TUCKER, *J. Chem. Soc. Chem. Commun.*, (1973) 142; J. S. BRIMACOMBE AND L. C. N. TUCKER, *Carbohydr. Res.*, 5 (1967) 36–44.
16 J. JANSON AND B. LINDBERG, *Acta Chem. Scand.*, 14 (1960) 877–881; B. LINDBERG, J. LÖNNGREN, AND S. SVENSSON, *Adv. Carbohydr. Chem. Biochem.*, 31 (1975) 185–240.
17 E. M. MONTGOMERY, R. M. HANN, AND C. S. HUDSON, *J. Am. Chem. Soc.*, 59 (1937) 1124–1129.
18 F. W. LICHTENTHALER, J. BREUNIG, AND W. FISCHER, *Tetrahedron Lett.*, (1971) 2825–2828; J. BREUNIG, Dissertation, Technische Hochschule Darmstadt, 1975.