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Preliminary communication

A possibility for sequential analysis of oligosaccharides by stepwise degradation*. The selective cleavage of 2,3,4,6,2′,3′,6′,2″,3″,6″-deca-*O*-methylmaltotriitol into 2,3,4,6,2′,3′,6′-hepta-*O*-methylmaltose and 2,3,6-tri-*O*-methyl-D-glucitol

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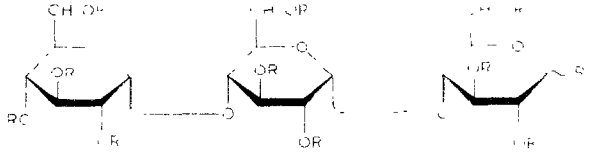
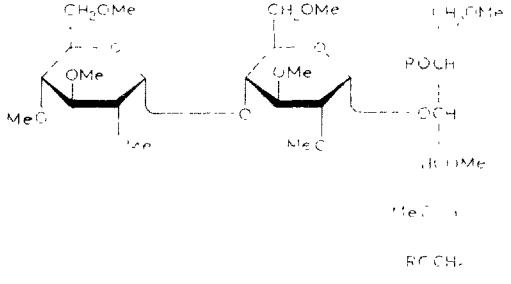
For peptide-sequencing analyses, stepwise degradation is a well established procedure, but in the carbohydrate field, no comparable method is so far known. We now demonstrate, with maltotriose as a model compound, the possibility of stepwise degradation of an oligosaccharide chain from the reducing end, which is generally the only position susceptible to exclusive reactions.



1 R = H, R′ = $NHC_2H_4NO_2$

2 R = Me, R′ = OH



3 R = H

4 R = SO Me

*See ref. 1.

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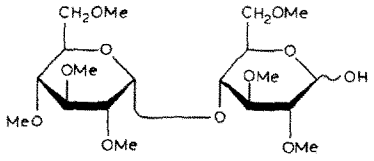
Maltotriose is converted into its *N*-*p*-nitrophenylglycosylamine[2] (**1**), which, after permethylation[3] and subsequent hydrolysis under mild conditions[4], yields 2,3,4,6,2′,3′,6′,2″,3″,6″-deca-*O*-methylmaltotriose (**2**). Compound **2** is reduced with sodium borohydride[5], to give 2,3,4,6,2′,3′,6′,2″,3″,6″-deca-*O*-methylmaltotriitol (**3**), characterized[6], after mesylation[7], as 2,3,4,6,2′,3′,6′,2″,3″,6″-deca-*O*-methyl-1,5-di-*O*-(methylsulfonyl)maltotriitol (**4**); m.p. 94–95° (from diethyl ether), $[\alpha]_{578}^{20}$ +116.4° (*c* 1.0, $CHCl_3$); ν_{max}^{KBr} 1345 (SO_2) and 1170 cm^{-1} (O-SO_2); ^{1}H-n.m.r. data ($CDCl_3$, 250 MHz): δ 3.07, 3.1 (2 s, 3 H, $MeSO_2$), 3.32–3.65 (10 s, 3 H, MeO), and 5.25 and 5.68 (2 d, 1 H, $J'_{1,2a} = J''_{1,2a} = 3.5$ Hz, H-1′, 1″).



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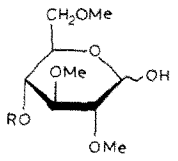
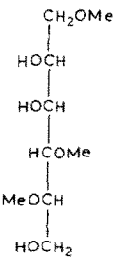


6 R = Me
7 R = H



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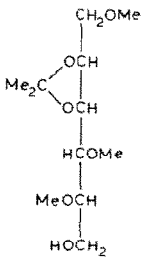

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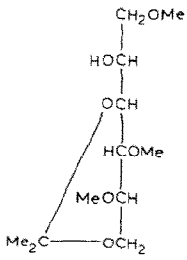

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When **3** (0.1 mmol) in diisopropyl ether (6 mL) containing acetone (5 mL, 68 mmol) and boron trifluoride etherate (0.4 mmol) was boiled under reflux, the starting material had disappeared after ~15 h. The reaction was monitored by gas–liquid chromatography (see Fig. 1 and Table I), and the compounds could be separated on a column of Chromosorb–SE-52 as their trimethylsilyl derivatives[8]. The reaction products, namely, 2,3,4,6,2′,3′,6′-hepta-*O*-methylmaltose (**5**), 2,3,4,6-tetra-*O*-methylglucose (**6**), 2,3,6-tri-*O*-methylglucose (**7**), 2,3,6-tri-*O*-methylglucitol (**8**), 4,5-*O*-isopropylidene-2,3,6-tri-*O*-methylglucitol (**9**) and 1,4-*O*-isopropylidene-2,3,6-tri-*O*-methylglucitol (**10**), were identified, and quantitatively determined, using authentic standards, as follows. Compounds **5** and **6** were synthesized in the same way as **2**. Compounds **6** and **7** were prepared by permethylation[3] of maltose, subsequent hydrolysis of the glycosidic bonds with a cation-exchange resin (H^+), and separation by continuous extraction with chloroform (**6** after

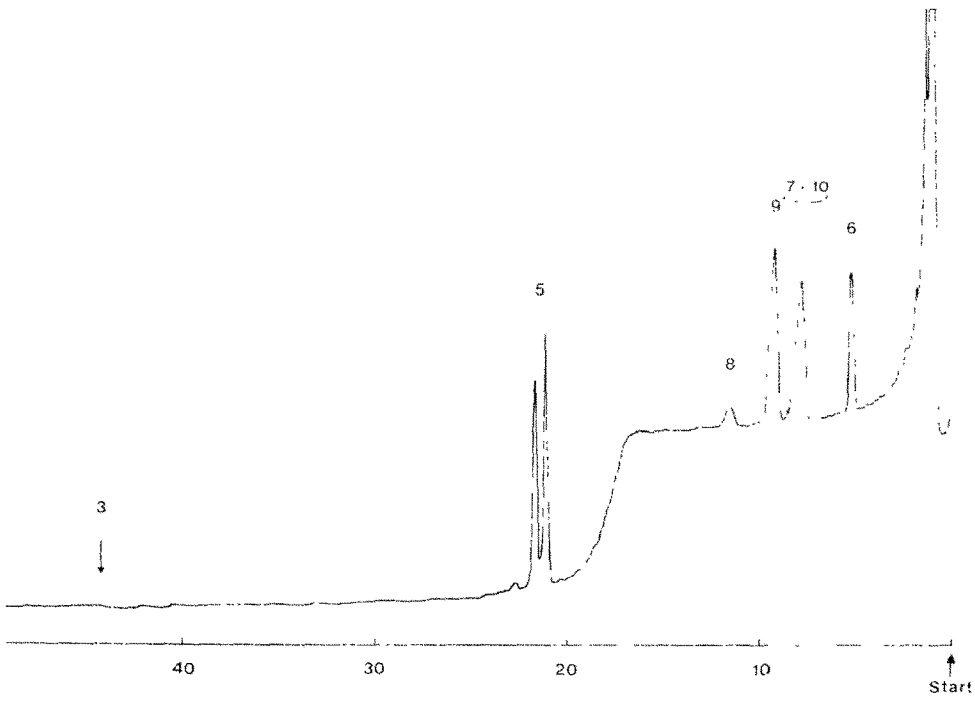

Fig. 1. Gas–liquid chromatogram of the trimethylsilylated reaction-products, reaction time, 15 h. [Pye Unicam GCD, column: Chromosorb, 3% of SE-52; f.i.d.; temperature program, 175° for 15 min, → 275° (fast), and 275° for 35 min.]

TABLE I

MOLAR CONCENTRATIONS OF SUBSTRATE 3 AND THE REACTION PRODUCTS 5 AND 6, AS THE TRIMETHYLSILYLATED DERIVATIVES, DETERMINED BY G.L.C., USING AUTHENTIC STANDARDS

Reaction time (h)	*Compound (mol %)*		
	3	5	6
0	100	0	0
1.5	59	38	3
3	35	60	5
6	17	74	9
9	6	81	13
12	2	82	16
15 [a]	0	82	18

[a] See gas–liquid chromatogram (Fig. 1).

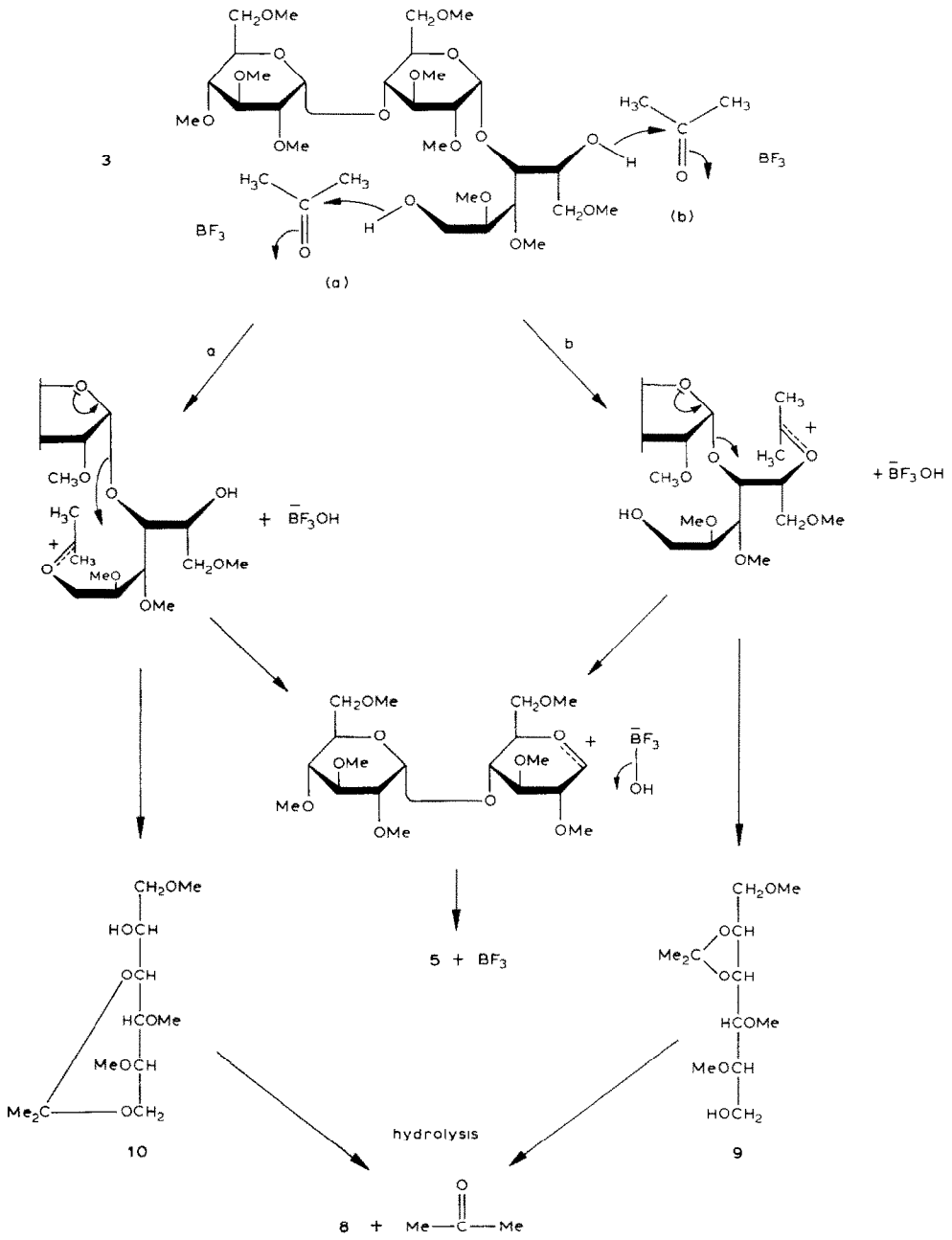

Fig. 2. Selective cleavage of compound **3** by neighboring-group participation.

15 h; 7 after 3 d). Following reduction of **7** with sodium borohydride[c] to **8**, the latter was converted by acetonation[9] into (mainly) **9** and a little **10**.

The calculated yield (g.l.c.) of >80% (see Table 1) of compound **5** clearly indicates the selective cleavage of the glycosidic bond nearer to the reducing end of maltotriose. For the selective cleavage by neighboring-group participation, the mechanism in Fig. 2 is suggested: the cleavage must include the formation of a carboxonium ion, because no selective reaction occurs in the absence of acetone, under conditions otherwise the same.

Cleavage of the reaction product **5** into compounds **6** and **7** could occur by a similar, electrophilic attack of the acetone–boron trifluoride complex on the glycosidic bond, and subsequent hydrolysis by traces of water in the reaction mixture. Acid-catalyzed hydrolysis, by hydrogen fluoride as a product of decomposition of boron trifluoride, can be excluded, because cleavage of **5** is not inhibited by addition of pyridine. Hydrolysis of the isopropylidene groups in **9** and **10** yields the small proportion of **8** found in the original reaction-mixture.

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