POLISH JOURNAL OF CHEMISTRY
(FORMERLY ROCZNIKI CHEMII
65, 2283 (1991)

ANALYSIS OF THE PRODUCTS PARTIAL O-ACETYLATION OF 1,2-ISOPROPYLIDENE-D-GLUCOFURANOSE

by Andrzej WIŚNIEWSKI, Eugenia SKORUPOWA, Janusz SOKOŁOWSKI, and Juergen METZGER

Institute of Chemistry, University, Sobieskiego 18, 80952 Gdańsk (A.W., E.S., and J.S.)
University of Oldenburg, Fachbereich Chemie, D-2900 Oldenburg, Germany (J.M.)

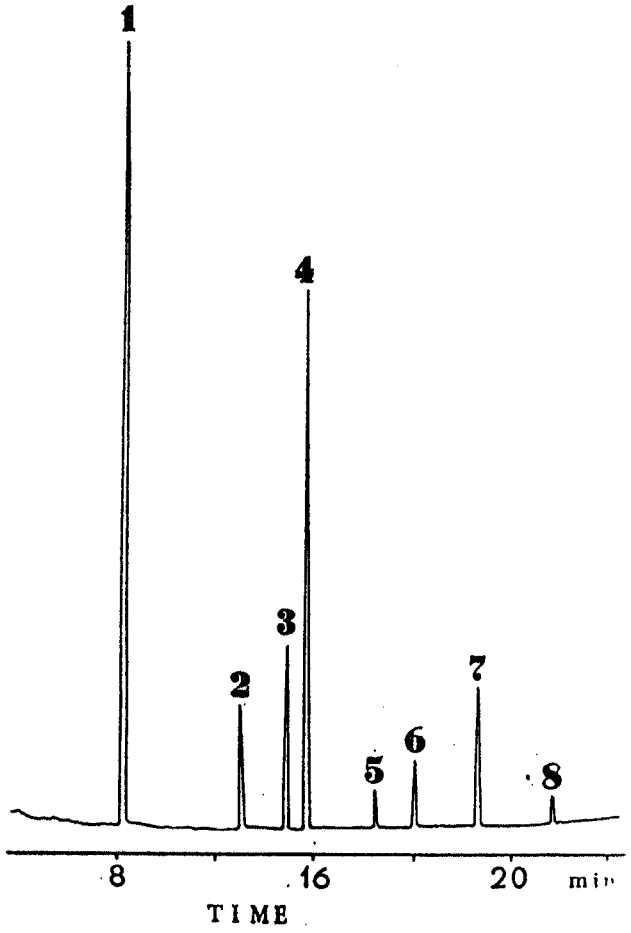
Recognition of the relative reactivity of individual hydroxyl groups is an important and permanently actual problem in the chemistry of sugars and their derivatives [1]. The reactivity depends on the steric and electronic interactions within the molecule and on the nature of the reagent used [2]. These mutual influences can be estimated by quantifying the concentrations of the products of a particular reaction by preparative chromatographic methods. The structure of the isolated products are usually elucidated by NMR spectroscopy [3–12]. Recently, the analytical CGC–MS method [13–20] has gained importance in solving those problems.

An illustative example of a gas chromatogram (the Figure) of a mixture of products resulting from O-acetylation of 1,2-isopropylidene-D-glucofuranose (IPGF) (reaction (i)), following its exhaustive O-trimethylsilylation, consists of eight well resolved peaks.

Peaks 1 and 8, assigned respectively to the tri-O-trimethylsilyl and tri-O-acetyl derivatives of IPGF, were identified by the standard co-injection method. Compounds eluted between these peaks are successively the isomers of the mono-O-acetyl-di-O-trimethylsilyl derivative (peaks 2, 3 and 4) and of the di-O-acetyl-mono-O-trimethylsilyl derivative of IPGF (peaks 5, 6 and 7). This sequence of eluation is due to the well-known difference between the O-trimethylsilyl and O-acetyl derivatives in volatility [21]. The suggested structure are shown below in Table 1.

Analysis of the mass spectra of compounds **2**—**7**, consisting in a search for diagnostic ions arising from simple fragmentation, enables elucidation of their structure. For instance, the compound being eluted as peak 4 is 6-O-acetyl-3,5-di-O-TMS-1,2-ispropylidene-D-glucofuranose (Scheme, Table 1 and 2).

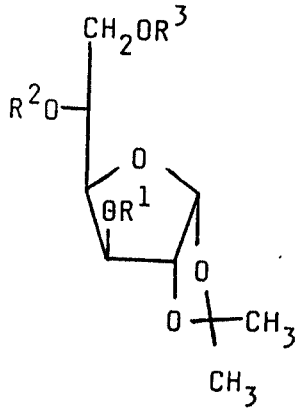
In this way the structure of compounds **2**, **3**, **4**, **5** and **7** were established. The mass spectrum of compound **6** is poorly legible and the structure of this



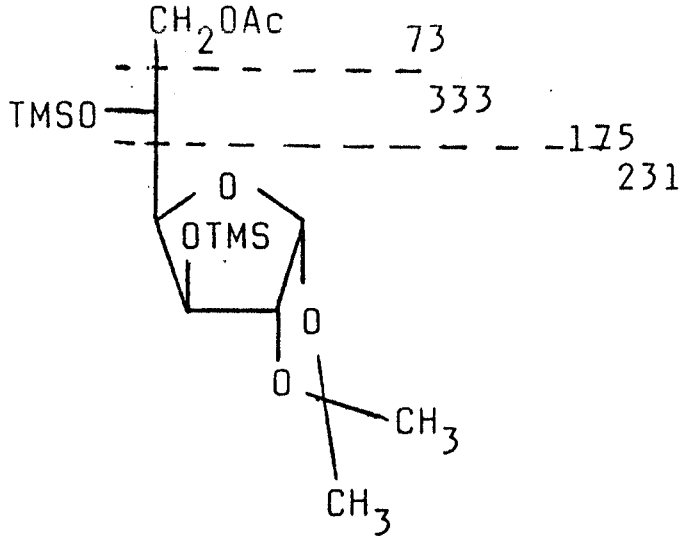
A cappillary gas chromatogram of the exhaustively O-trimethylsilylated products of partial O-acetylation of 1,2-isopropylidene-D-glucofuranose (reaction (i))

Table 1

Compound No.	R^1	R^2	R^3
1	TMS	TMS	TMS
2	TMS	Ac	TMS
3	Ac	TMS	TMS
4	TMS	TMS	Ac
5	TMS	Ac	Ac
6	Ac	Ac	TMS
7	Ac	TMS	Ac
8	Ac	Ac	Ac



TMS = $Si(CH_3)_3$; Ac = CH_3CO.



4, M=406

Table 2

Partial mass spectra of per-O-trimethysilylated derivatives of mono- and di-O-acetyl-1,2-isopropylidene-D-glucofuranose (compounds **2, 3, 4, 5, 6, 7**; Scheme)

Compound 2		Compound 3		Compound 4	
m/e	rel. int.	*m/e*	rel. int.	*m/e*	rel. int.
73	100	73	100	73	89
75	59	75	25	75	23
93	93	93	46	93	8
95	33	95	20	103	10
103	20	103	19	117	27
117	32	117	31	131	28
129	46	129	8	133	17
131	29	131	18	175	100
187	14	185	12	217	24
191	9	201	2	231	14
231	11	205	35	277	2
273	7	243	6	333	2
277	4	303	22	391	1
303	5				

Compound 5		Compound 6		Compound 7	
m/e	rel. int.	*m/e*	rel. int.	*m/e*	rel. int.
73	94	73	88	73	61
75	43	75	35	75	32
84	21	85	22	89	18
103	58	89	28	93	13
117	100	93	39	117	58

Continued Table 2

131	39	100	24	133	23
143	63	103	12	143	23
145	30	116	38	175	100
183	18	117	42	199	5
199	32	129	66	201	8
231	11	145	10	203	10
256	8	175	10	303	10
303	7	201	6	361	4
361	19	216	7		
		361	4		

Diagnostic ions are underlined.

compound, established on the basis of the exclusion principle, is that of the 3,5-di-O-Ac-6-O-TMS-1,2-isopropylidene derivative of D-glucofuranose.

The yields of the reaction products are summarized in Table 3. Table 3

Table 3

Compound No.	Percentage of the components in reaction mixtures following acetylation*			
	a	b	c	Position of OAc group
1	45.4	9.5	1.1	
2	5.7	3.7	1.4	C–5
3	8.8	6.3	2.3	C–3
4	28.9	36.6	23.4	C–6
5	1.6	5.1	2.6	C–5 and C–6
6	2.8	7.4	8.6	C–3 and C–5
7	5.6	19.4	27.4	C–3 and C–6
8	1.2	12.0	33.2	

*Calculated from peak areas in CGC.

shows that the contents of individual isomers of the mono-O-acetyl derivative (compounds **2, 3** and **4**) and of the di-O-acetyl derivative of IPGF (compounds **5, 6** and **7**) in the products assume similar patterns in all experiments ((i), (ii) and (iii)), regardless of the extent of consumption of the reactant (the loss of compound **1** as a consequence of the quantity of acetic anhydride used).

The highest reactivity was exhibited by the hydroxyl group occurring in the primary alcoholic system at C–6, which is quite vulnerable to electrophilic attack by the molecule of the acetylating reagent. Consequently, compound **4** (C–6–O–Ac–IPGF) preponderates in the mixture of the mono-O-acetyl derivatives of IPGF.

In experiment (i), where the molar Ac_2O/IPGF ratio based on a single hydroxyl group was 1:3, the least amounts of the di-O-acetyl derivatives were

formed owing to the greatest deficiency of the acetylating reagent. In consequence, the relative concentration of mono–O–Ac–IPGF could be arranged in the following sequence: compound **2** (C–5–O–Ac–IPGF) 5.7% < compound **3** (C–3–O–Ac–IPGF) 8.8% ≪ compound **4** (C–6–O–Ac–IPGF) 28.9%.

The markedly lower concentration in the reation product of the isomers of the mono–O–acetyl derivative with the O–acetyl at C–3 (compound **3**) and at C–6 (compound **2**) testifies to the conderably lower reactivity of these hydroxyl groups owing to their restricted steric accessibility. The relative difference in reactivity between the hydroxyl groups at C–3 and C–5 is not too large, but undoubtedly noticeable.

The higher reactivity of C–3–OH as compared to C–5–OH can be attributed to considerable shielding of the latter by the C–6–OH group, both in the steric and electronic (inductive effect) aspect.

A comparison of the relative concentrations of the di–O–acetyl derivatives of IPGF reveals the highest contribution of compound 7 (C–3 and C–6 di–O–Ac–IPGF), namely 5.6%, and the lowest contribution of compound **5** (C–5 and C–6 di–O–Ac–IPGF), i.e. 1.6%, in experiment (i). The result seems quite meaningful, as the yield of compound 7 is high owing to high concentration of the transient compound **4** (C–6–O–Ac–IPGF) and to the easier accessibility of C–3–OH than of C–5–OH.

Again, compound **5** (C–5 and C–6 di–O–Ac–IPGF) arises with difficulty from compound **4** (C–6–O–Ac–IPGF), because of the shielding effect of the C–6–O–Ac group relative to the C–5–OH group. At the same time, compound **5** is formed slowly from compound **2** (C–5–O–Ac–IPGF) both owing to shielding of the C–6–OH group by C–5–O–Ac and to the very lowe concentration of compound **2**.

The observed sequence of the quantities of the products in selected sets **5, 6** and **6, 7**; **7>6** and **6>5**, appears also to be well substantiated.

Compound **7** arises more readily than compound **6**, because of the extremely reactive, not sterically hindered, primary alcohol group C–6–OH,

Again, compound **6** arises more readily than **5**, because in compound **2** (C–5–O–Ac–IPGF) the C–5–OH group shield s,the C–6–OH group, and does not hinder the access to the C–3–OH groups.

EXPERIMENTAL

O–Acetylation of 1,2-isopropylidene-D-glucofuranose (IPGF) was performed on a micro scale.

The **reaction**. To screw-capped ampoules, each containig 4.4 mg (2×10^{-5} mole) of IPGF and 200 mm^3 of anhydrous pyridine, was added respctively: (i) 1.9 mm^3 (2×10^{-5} mole), (ii) 3.8 mm^3 (4×10^{-5} mole), (iii) 5.7 mm^3 (6×10^{-5} mole) of acetic anhydride. The ampoules were tightly closed and left for 24 hrs at ambient temperature. Volatile constituents were then removed in a nitrogen stream and the residues were exhaustively O-trimethylsilylated with 200 mm^3 of BSTFA for 10 min at 100°C. The products were then analyzed by the CGC and CGC–MS methods.

Capillary gas chromatography (CGC)

The reaction products were separated by means of a CHROMATRON Model GCHF 18.3 gas chromatograph equipped with a glass capillary column (30 m × 0.3 mm) coated with Carbowax 20M TPA on barium carbonate (film thickness 0.07 μm) [22] and with a flame-ionization detector (FID). Hydrogen was used as carried gas, with a linear flow rate of 58 cm · s^{-1}. The injector port and detector temperature was programmed from 140 to 220°C, 4 deg · min^{-1}.

Capillary gas chromatography - mass spectrometry (CGC—MS)

The reaction products were analysed by the CGC—MS method. The mixture was separated in a gas chromatograph equipped with a capillary column (20 m × 0.2 mm) coated with Carbowax 20M, which was coupled with a Finnigan—MAT 212 mass spectrometer. The injector port temperature was 240°C. An electron beam of 70 eV was used for ionization.

Acknowledgment

This work was partly supported by Polish Academy of Sciences under grant CPBP-01.13.2.13.

Received November 19th, 1990.

REFERENCES

1. HAINES A.H., *Adv. Carb. Chem. Biochem.*, **33**, 11 (1976).
2. HORTON D., PRIEBE W., VERELA O., *Carbohydrate Res.*, **144**, 317 (1985).
3. KONDO Y., YABUUCHI K., HIRANO S., *Carbohydrate Res.*, **82**, 398 (1980).
4. RANA S.S., PISKORZ C.F., BARLOW J.J., MATTA K.L., *Carohydrate Res.*, **83**, 170 (1980).
5. CHITTENDEN G.J.F., *Carbohydrate Res.*, **91**, 85 (1981).
6. FLOWERS H.M., *Carbohydrate Res.*, **99**, 170 (1981); *ibid.*, **100**, 418 (1982).
7. KONDO Y., *Carbohydrate Res.*, **103**, 154 (1982); *ibid.*, **107**, 303 (1982); *ibid.*, **111**, 325 (1983); *ibid.*, **114**, 335 (1983); *ibid.*, **121**, 324 (1983), *ibid.*, **128**, 175 (1984).
8. CLODE D.M., LAURIE W.A., SHERIDAN J.B., *Carobohydrate Res.*, **139**, 147 (1985).
9. KONG F., DU J., WU H., *Carbohydrate Res.*, **147**, 337 (1986).
10. KONDO Y., *Carbohydrate Res.*, **154**, 305 (1986); *ibid.*, **162**, 159 (1987).
11. WU H., KONG F., *Carbohydrate Res.*, **162**, 166 (1987).
12. KONDO Y., *Carbohydrate Res.*, **193**, 279 (1989).
13. FUNAKOSHI I., YAMASHINA I., *Koenshu-Iyo Masu Kenkyukai*, **3**, 117 (1978).
14. BARRETTO-BERGTER E., HOGGE L., GORIN P.A.J., *Carbohydrate Res.*, **97**, 147 (1981).
15. STORTZ C., MATULEWICZ M., CEREZO A., *Carbohydrate Res.*, **111**, 31 (1982).
16. BACIC A., HARRIS P.J., HAK E.W., CLARK A.E., *J. Chromatogr.*, **315**, 373 (1984).
17. HARRIS P.J., BACIC A., CLARK A.E., *J. Chromatogr.*, **350**, 304 (1985).
18. TACKEN A., BRADE H., FRANK F.M., CHARON D., *Carbohydrate Res.*, **149**, 263 (1986).
19. SHEA E., CARPITA N., *J. Chromatogr.*, **445**, 424 (1988).
20. RIVIERE M., FOURNIE J-J., MONSARAT B., PUZO G., *J. Chromatogr.*, **445**, 87 (1988).
21. DUTTON G., *Advances in Carbohydrate Chem.*, **28**, 11 (1973).
22. GROB K., GROB G., *J. Chromatogr.*, **125**, 471 (1976).