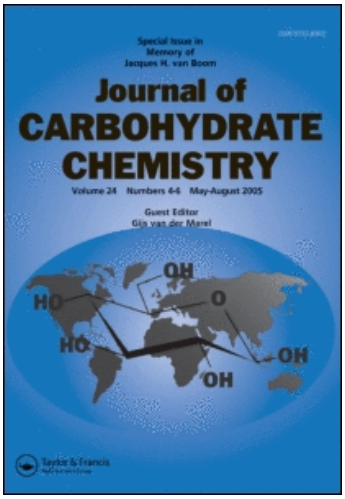


Journal of Carbohydrate Chemistry
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713617200

Studies of Hexuronic Acid Ester Glycals and the Synthesis of 2-Deoxy-β-glycoside Precursors

Joachim Thiem[ab]; Petra Ossowski[a]
[a] Institut für Organische Chemie und Biochemie der Universität Hamburg, Hamburg, Federal Republic of Germany [b] Organisch-Chemisches Institut der Universität Münster, Münster, Federal Republic of Germany

To cite this Article Thiem, Joachim and Ossowski, Petra(1984) 'Studies of Hexuronic Acid Ester Glycals and the Synthesis of 2-Deoxy-β-glycoside Precursors', Journal of Carbohydrate Chemistry, 3: 2, 287 — 313
To link to this Article: DOI: 10.1080/07328308408058822
URL: http://dx.doi.org/10.1080/07328308408058822

J. CARBOHYDRATE CHEMISTRY, 3(2), 287-313 (1984)

STUDIES OF HEXURONIC ACID ESTER GLYCALS AND THE SYNTHESIS OF 2-DEOXY-β-GLYCOSIDE PRECURSORS

Joachim Thiem[≠)*] and Petra Ossowski

Institut für Organische Chemie und Biochemie
der Universität Hamburg
Martin-Luther-King-Platz 6
D-2000 Hamburg 13
Federal Republic of Germany

Received November 23, 1983

ABSTRACT

The hexuronic acid methyl ester glycals with L-ribo (7), D-lyxo (9), and D-xylo configuration (11a) were synthesized and their conformations and that of the D-arabino derivative 2a were studied. Using the N-iodosuccinimide glycosylation procedure these glycals were transformed into cyclohexyl 2-deoxy-2-iodoglycosides 13 - 28 and their α/β-anomer ratios determined by ^{1}H NMR spectrocopy. The mechanism of the N-iodosuccinimide glycosylation and the correlation between glycal conformation and glycoside configuration are discussed.

≠) New address: Organisch-Chemisches Institut der Universität Münster, Orléans-Ring 23, D-4400 Münster, Federal Republic of Germany

 0732-8303/84/0302-0287$3.50/0

INTRODUCTION

Recently we observed that methyl 3,4-diacetyl-D-glucuronal (2a, methyl 3,4-di-O-acetyl-1,5-anhydro-2-deoxy-D-arabino-hex-1-enitol-pyranuronate), in contrast to triacetyl-D-glucal (1), unexpectedly prefers a $^5H_4$ (D) conformation and shows reduced reactivity in N-iodosuccinimide glycosylations in leading to 2-deoxy-2-iodo-β-disaccharide derivatives predominantly.[1] The present study addresses the questions whether glycals of other uronic acid esters show analogous conformational effects and how these effects might be utilized for a directed synthetic application in glycosylations following the N-iodosuccinimide procedure.

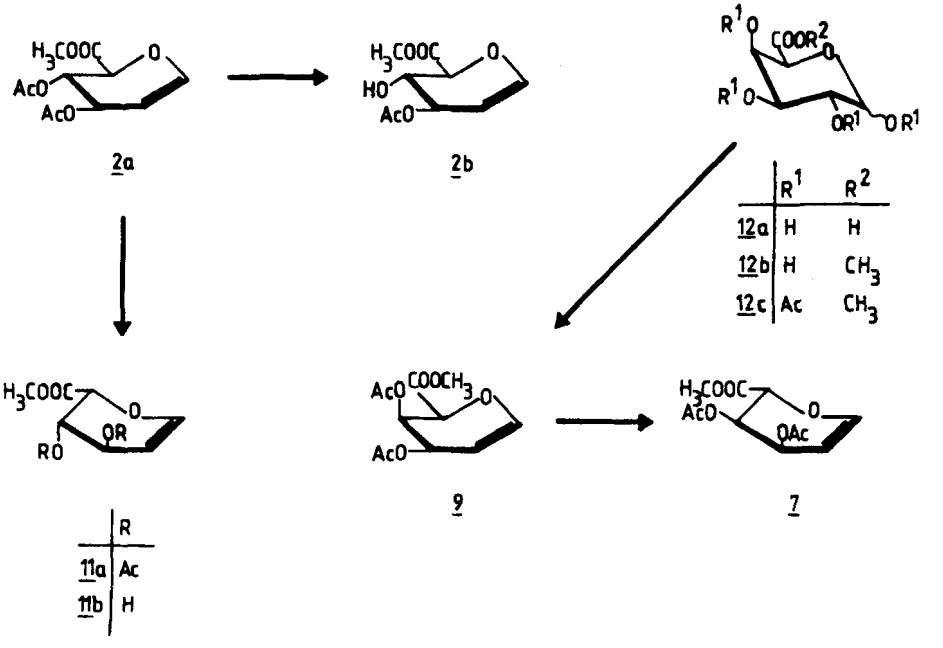
RESULTS AND DISCUSSION

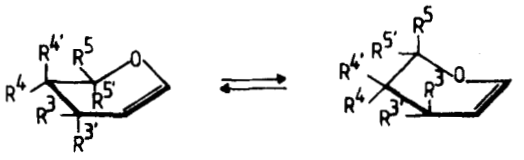
Syntheses and Conformations of Uronic Acid Ester Glycals

By mild partial deacetylation using sodium carbonate in absolute methanol the easily accessible methyl 3,4-diacetyl-D-glucuronal (2a)[2,3] regioselectively afforded a crystalline 3-monoacetate 2b, isolated in 22% yield after chromatographic separation from the starting material and unblocked methyl D-glucuronal 2c. Inversion of uronic acid ester derivatives at C-5 using aqueous sodium hydroxide[4] or sodium methylate in methanol[5] favourably leads to the epimeric compounds. Thus treatment of 2a with 1% sodium methylate in absolute methanol for 12 h at room temperature gave an isomer mixture of the wanted methyl L-guluronal (11b) and the transesterification product 2c in a ratio of 80 : 20 (^{1}H NMR). The glycal 11b, obtained following chromatography, was further characterized as its diacetate 11a.[6]

D-Galacturonic acid (12a) was converted to the methyl ester 12b[7] and further to its tetraacetate 12c.[8] The usual treatment with hydrogen bromide/acetic acid (cf. lit.[3] for uronic acid derivatives) gave the glycosyl bromide and a subsequent reductive elimination (Zn/HOAc) led to methyl 3,4-diacetyl-D-galacturonal (9).[9] Contrary to the smooth inversion of 2a to 11b the reaction of 9 with sodium methylate was not a clean process, and, in addition to epimerization, considerable decomposition of both starting material and product was observed. Following reacetylation of the reaction mixture and chromatography the syrupy methyl 3,4-diacetyl-L-alluronal (7) was isolated in 20% yield.

The syntheses described gave the isomeric hexuronic acid methyl ester glycals with D-arabino (2a), L-ribo





$^4H_5$ $^5H_4$

		R^3	$R^{3'}$	R^4	$R^{4'}$	R^5	$R^{5'}$
D-arabino	1	OAc	H	OAc	H	CH_2OAc	H
	2a	OAc	H	OAc	H	COOMe	H
	2b	OAc	H	OH	H	COOMe	H
	2c	OH	H	OH	H	COOMe	H
	3	OAc	H	OAc	H	CH_2I	H
L-arabino	4a	H	OAc	H	OAc	H	Me
	4b	H	OAc	H	OH	H	Me
	4c	H	OH	H	OAc	H	Me
	4d	H	OH	H	OH	H	Me
D-ribo	5	H	OAc	OAc	H	CH_2OAc	H
	6a	H	OAc	OAc	H	Me	H
	6b	H	OH	OH	H	Me	H
L-ribo	7	OAc	H	H	OAc	H	COOMe
D-lyxo	8	OAc	H	H	OAc	CH_2OAc	H
	9	OAc	H	H	OAc	COOMe	H
D-xylo	10	H	OAc	H	OAc	CH_2OAc	H
L-xylo	11a	OAc	H	OAc	H	H	COOMe
	11b	OH	H	OH	H	H	COOMe

(7), D-lyxo (9) and L-xylo (11a) configuration for conformational and preparative studies.

Previous ^{1}H NMR spectroscopic studies[10,11] on the conformations of simple glycals and derivatives in solution showed a preference in the D-series for $^4H_5$ over the inverted $^5H_4$ half chair (or half boat) conformation, and the $^5H_4$ over the $^4H_5$ form in the L-series.[12] It seemed advantageous to evaluate "normal" and variably substituted glycals of the same configuration together with the uronic acid ester glycals in order to get a better conformational understanding of the latter.

^{1}H NMR spectra of the four hexuronic acid methyl ester glycals (2a, 7, 9, 11a) and three derivatives (2b, 2c, 4b) as well as seven configurationally comparable glycals were taken, and compiled with literature data of the glycals 1, 5, 8, and 10 (Table 1). The molar fraction for arabino and ribo derivatives $[^4H_5] = (J_{obs} - J_{ee})/(J_{aa} - J_{ee})$ or for lyxo and xylo derivatives $[^4H_5] = (J_{obs} - J_{ae})/(J_{ae} - J_{ea})$ (Table 1, second column) is determined from the observed J(4,5) coupling constants (Table 1, first column).[12] Values obtained from fitting calculations (J_{aa} = 11.63, J_{ee} = 2.00, J_{ae} = 4.24, and J_{ea} = 1.40 Hz)[11] were used here as limits for the equilibrium determination which lead to reliable results for the arabino and ribo configurations. More critical should be the J_{ae} and J_{ea} limiting values for the gauche protons 4- and 5-H in lyxo and xylo derivates. Finally, the free enthalpy differences of the conformers in the equilibrium mixture are listed $\Delta G = -R \cdot T \cdot \ln {}^4H_5/[{}^5H_4]$ (T = 300 K, probe temperature)[12] (Table 1, third column).

The equilibrium of glycals should be considerably influenced by the allylic effect,[13] which in acetylated glycals favours a quasi axial orientation of the allylic acetoxy groups at C-3 by approximately 0.8 kcal/mol.[10]

TABLE 1

Conformation of Glycals and Anomeric Ratio of Cyclohexyl 2-Deoxy-2-Iodo-Glycosides

Compound	J(4,5)[Hz]	$[^4H_5(\underline{D})]$ or $[^5H_4(\underline{L})]$	ΔG[kcal/mol]	Glycosides α	Glycosides β	Ratio % α	Ratio % β	isolated yields % α	isolated yields % β
D-arabino 1	7.75[a,b]	0.59[b]	-0.22[b]	13	14	83	17	46	6
2a	2.7[a]	0.07	1.55	15	16	63.5	36.5	39	20
2b	3.9[a]	0.19	0.87	15	16	78	22		
2c	5.4[a]	0.35	0.37						
3	6.5[c]	0.46	0.11						
L-arabino 4a	8.0[d]	0.62	-0.29	17	18	85.5	14.5	65	11
4b	9.6[d]	0.79	-0.79						
4c	8.9[d]	0.72	-0.57						
4d	9.8[a]	0.81	-0.87						

D-ribo	5	11.01[a,b]	0.94[b]	-1.70[b]	19	20	91	9		51	
	6a	10.4[c]	0.87	-1.14	21	22	89	11		43	
	6b	9.6[c]	0.79	-0.79							
L-ribo	7	12.2[c]			23	-	100	-	32		-
D-lyxo	8	1.76[a,b]	0.88[b]	-1.20[b]	24	25	94	6		36	
	9	1.9[d]	0.82	-0.91	26	-	100	-	43		-
D-xylo	10	1.51[a,b]	0.95[b]	-1.80[b]							
L-xylo	11a	1.6[c]	0.93	-1.55	27	28	90	10		46	
	11b	1.7[a]	0.89	-1.25							

a. in $[D_6]$-acetone; b. according to lit.[11], calculated; c. in $CDCl_3$;

d. in C_6D_6; e. according to ^1H NMR; f. not optimized.

This is observed for tri-O-acetyl-D-glucal (1) and di-O-acetyl-L-rhamnal[14] (4a) both of which adopt the expected $^4H_5$ (D) and $^5H_4$ (L) conformation, respectively, to only 60% because obviously the corresponding inverted half chair forms are energetically less disfavoured with the quasi axial 3-acetoxy group. With unblocked D-rhamnal[14] (4d) as well as the monoacetylated 3- (4b) and 4-O-acetyl-D-rhamnals (4c), both obtained from 4a in minor yields by partial ester cleavage, 70-80% of the $^5H_4$ (L) conformation is observed. This is expected for 4c and 4d, but for 4b there should have been a deviation because of the allylic effect. These findings do not exclude the operation of an allylic effect but question its dominant influence on the equilibria of acylated glycals.

In the D-ribo series tri-O-acetyl-D-allal[15,16] (5), di-O-acetyl-D-digitoxal[17] (6a), and D-digitoxal[18] (6b) clearly favour the $^4H_5$ (D) conformation (80-90%), and the same is observed with the D-lyxo derivative tri-O-acetyl-D-galactal[19] (8) as well as the D-xylo compound tri-O-acetyl-D-gulal[20] (10) (90-95%). In addition to an allylic effect in 5 and 10 these compounds show 1,2-quasi equatorial-equatorial interaction between the substituents at C-3 and C-4, 1,2-diequatorial interaction between the substituents at C-4 and C-5, and also 1,3-quasi axial-axial interaction between substituents at C-3 and C-5.[10,13] All these interactions favour the $^4H_5$ (D) conformation.

The glucuronic acid methyl ester glycals 2a - 2c, however, largely adapt the inverted $^5H_4$ (D) half chair conformations (65-100%) whereas the isomeric uronic acid ester glycals with L-ribo (methyl 3,4-diacetyl-L-alluronal, 7), D-lyxo [methyl 3,4-diacetyl-D-galacturonal, 9, 82% $^4H_5$ (D)], and L-xylo configuration [the L-guluronals 11a and 11b, approximately 90% $^5H_4$ (L)]

prefer the expected conformations. Thus, the inverted half chair conformations in the arabino hexuronic acid ester glycals require one quasi axial (at C-3) and two axial substituents (at C-4 and C-5). This result is in marked contrast to the isomeric derivatives 7, 9, and 11a which also uniformly exhibit equatorially disposed methoxycarbonyl groups.

According to conformational studies in cyclohexane systems the methoxycarbonyl group is attributed an A-value of 1.1 kcal/mol.[21] For tetrahydro-2-pyrancarbonic acid methyl ester the conformer with an equatorial ester group is favoured by 1.62 kcal/mol,[5] which indicates that this group exerts no anomeric effect but rather an inverse anomeric effect[22] of 0.5 kcal/mol. Even for the parent compound of these hexuronic acid methyl ester glycals, that is 2,3-dihydro-2-pyrancarbonic acid methyl ester, an estimation gave approximately 60-70% of the conformer with an equatorially disposed ester group in the equilibrium mixture.[23] By and large the results of the conformational analysis in hexuronic acid ester glycals are in accord with the expectation and previous findings of the glucoronic acid ester derivatives. However, the conformational anomaly in the arabino case does not conform with the given arguments.

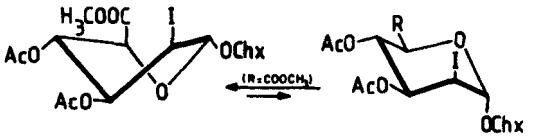
Preparation and Properties of Cyclohexyl 2-Deoxy-2-Iodo-Glycosides

For an elucidation of the preparative scope all the hexuronic acid ester glycals as well as some representatives of the other glycals were glycosylated using cyclohexanol as a model aglycon in the N-iodosuccinimide procedure. Subsequent to the uniformly performed reactions the α/β anomer ratio was monitored by ^{1}H NMR spectrocopy. Generally the mixtures were separated by prep-

arative thin layer chromatography and the pure anomers analytically characterized. The product ratios and the unoptimized yields are given in Table 1.

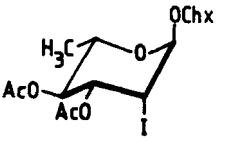
Within three hours at room temperature a quantitative conversion of tri-O-acetyl-D-glucal (1) gave product mixture of predominantly the cyclohexyl α- (13) and some β-glycoside (14). Under similar conditions diacetyl-L-rhamnal (4a) afforded the glycosides 17 and 18 with about the same α/β ratio. The α-glycosides 13 and 17 are easily assigned by their small J(1,2) trans diequatorial coupling constants and the β-anomers 14 and 18 by their larger J(1,2) coupling constants. A considerable slower glycosylation (24 h at room temperature) of the glucuronic acid methyl ester glycal 2a lead to the cyclohexyl β- (16) and α-glycoside (15) in approximately 40 and 60%, respectively. The β-compound 16 shows a large J(1,2) coupling and altogether seems to be conformationally uniform, but surprisingly in its α-anomer 15 also a larger J(1,2) = 5.5 Hz is observed. Further couplings J(2,3) = 3.6, J(3,4) = 6.5, and J(4,5) = 5.7 Hz suggest a considerable portion of a flattened $^{1,4}B$ (D) boat conformation in the equilibrium. In this unusual conformation the two acetoxy and the cyclohexyloxy groups occupy exo positions, and the ester group and the 2-iodo function are in endo positions and rather close. Obiously, even the anomeric effect[22] of the cyclohexyloxy residue is surpassed by this conformational anomaly. A steric reasoning owing to the size of the substituents at C-1 and C-2 cannot be considered, because both the isomeric α-derivatives 23 and 26 adopt a normal chair conformation.

Following glycosylation of the monoacetylated glucuronal 2b the primary products were peracetylated and gave the derivatives 15 and 16 with an α/β-ratio of 4:1.

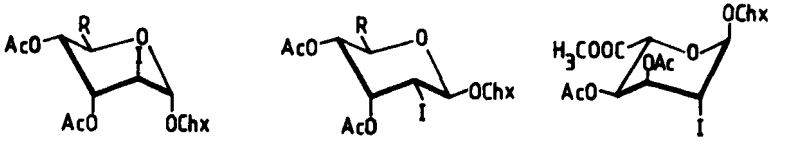


	R	
13	CH_2OAc	14
15	$COOCH_3$	16

Chx = Cyclohexyl

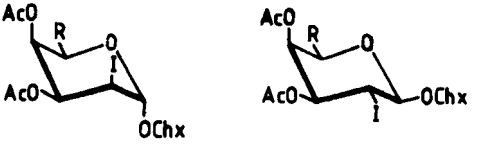


17 18

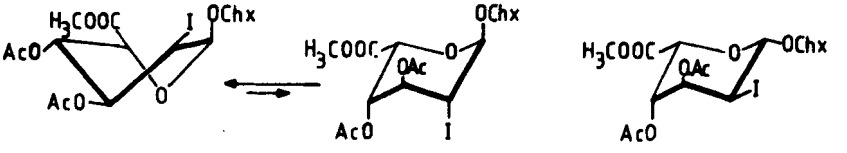


	R	
19	CH_2OAc	20
21	CH_3	22

23



	R	
24	CH_2OAc	25
26	$COOCH_3$	



27 28

Tri-acetyl-D-allal (5) and diacetyl-D-digitoxal (6a) led to α/β-anomer ratios of approximately 9:1, with all the cyclohexyl glycosides adopting a $^4C_1$ (D) chair conformation as expected. Similarly, the alluronal derivative 7 gave exclusively the α-glycoside 23, as $^1C_4$ (L) chair form. In the lyxo series the N-iodosuccinimide glycosylation of 8 gave the α/β-glycosides 24 and 25 (ratio 94:6) with only 24 isolated, and the galacturonal 9 yielded only crystalline α-glycoside 26. Finally, the L-guluronal 11a afforded a 9:1 mixture of α- (27) and β-glycoside (28), the latter isomer in a $^1C_4$ (L) chair conformation. Like was observed for the anomer pair 15/16, the α-glycoside 27 shows unusually large coupling constants [J(1,2) = 6.6, J(2,3) = 8.8, J(3,4) = 7.3, J(4,5) = 5.3 Hz] pointing to an increased population of a flattened $^{1,4}B$ (L) boat conformer. This case deviates from the former with respect to the exo positions of all the substituents except the cyclohexyloxy group which is in a quasi endo arrangement and additionally enjoys an anomeric effect.[22]

Mechanism of the N-Iodosuccinimide Glycosylation and Glycal Conformation versus Glycoside Configuration

Presently the glycosylation of glycals following the N-iodousccinimide procedure[24] may be summarized as illustrated for a glycal I of the D-series. In the conformational equilibrium mixture of I, both the $^4H_5$ (a) and the inverted $^5H_4$ half chair/half boat species (b) are present. Each of the conformers are expected to interact with the iodo cation to form a 1,2-iodonium intermediate II. The conformer a should, in principle, lead to the intermediates c and/or d, the former being favoured considerably because of the inverse anomeric effect[22] due to the cationic anomeric substituent. Correspondingly, the conformer b should lead to e and/or

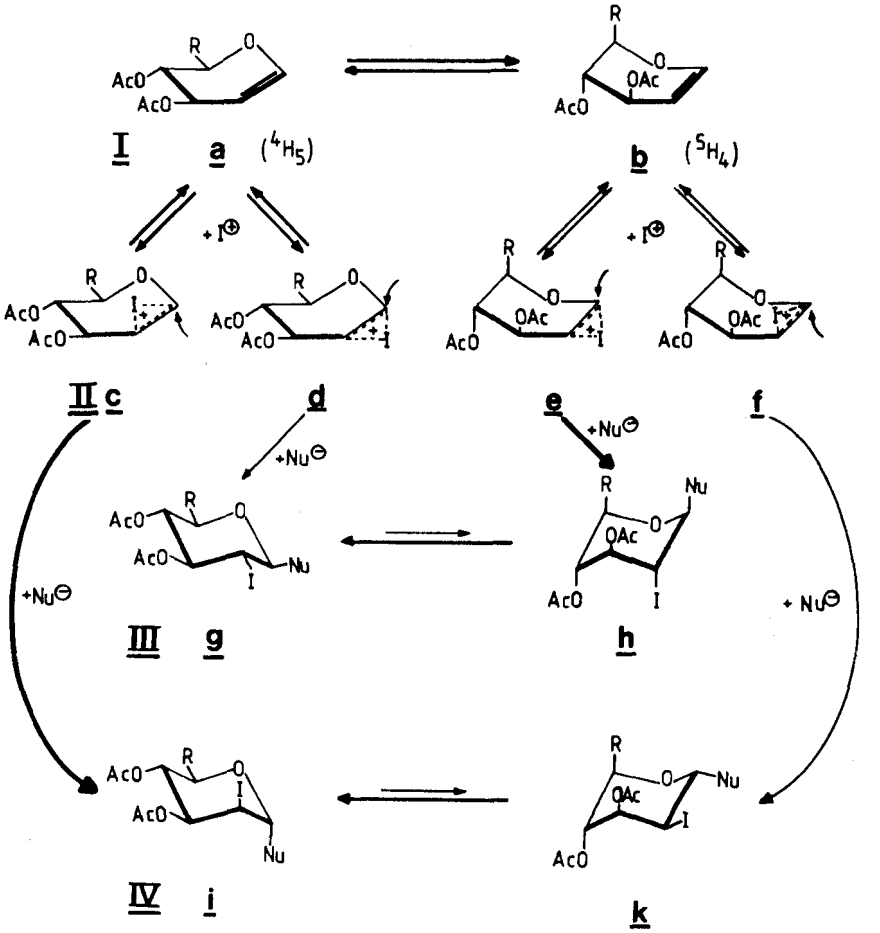
f, with e expected to be more stable than f for the same reason. When the 1,2-iodonium intermediates c to f react with the available nucleophile (Nu^-) the 1,2-trans-diequatorial and the 1,2-trans-diaxial products III and IV are formed. The $^4C_1$ chair forms in the conformer equilibrium g ⇄ h (in III) and i ⇄ k (in IV) would probably be favoured given the configurations at C-3, C-4, and C-5. The Curtin-Hammett principle can be applied to these equilibria assuming a lower energy barrier for the conformer equilibration a ⇄ b in comparison to the subsequent reactions a ⇄ c and a ⇄ d or b ⇄ e and b ⇄ f ($\Delta G_i^{\neq} >> \Delta G$).[25] Based upon this assumption the product ratio is not governed by the actual concentration of the conformers (expressed by the free enthalpy ΔG) but rather by the difference in free activiation enthalpies $\Delta G^{\neq}$. Thus no prediction can be made as to which iodonium intermediate would result from which conformer, and by which course the final products III and IV would be obtained. If, however,, additional factors increase the interconversion energy between conformers a and b to the same order of magnitude as the free activation enthalpy for the subsequent electrophilic addition to the enol ether, the Curtin-Hammett principle is no longer applied. In such a case individual reaction courses starting with conformers a or b should be observed.

In an earlier N-iodosuccinimide mediated disaccharide synthesis employing 3,4-O-isopropylidene-D-fucal, we observed the exclusive formation of a β-glycoside with the galacto configuration in the non reducing ring.[26] There is no doubt that in this reaction the voluminous 3,4-cis blocking group favours a transfer to iodonium intermediates like d and e, both of which are precursors to the β-compound III.

Practically all the glycals discussed here show a normal conformation except the glucuronic acid

methyl ester derivatives which predominantly adopt a $^5H_4$ (D) half chair form. In the glycals with arabino configuration the ΔG values (Table 1) are comparatively small, giving rise to a facile half chair inversion. Evidently, electron attracting groups at C-5 favour the alternate half chair conformation wich is expressed in the ΔG-values of the series L-rhamnal (4a, -0.29), D-glucal (1, -0.22), 6-deoxy-6-iodo-D-glucal[27,28] (3, 0.11), and methyl glucuronal (2a, 1.55).

A closer inspection reveals a dependance of configuration of the glycoside formed on the conformation of



the starting glycals: an increased ratio of inverted half chair conformation in the glycal always shifts the α/β anomer ratio towards increased β-glycoside yields, the minimum being 5%, the maximum 40%. This considerable transfer to a β-species is presently restricted to glucuronic acid ester glycals and we consider this a "conformational effect" which renders a useful synthesis of 2-deoxy-β-glycosides with arabino configuration.

Cyclohexene derivatives carrying an electronegative substituent at position 4 were shown to exhibit reduced reactivity in electrophilic additions, and kinetic studies proved this to be an electrostatic influence of the substituent on the double bond ("field effect").[29] Another interpretation for the deactivation of the double bond assumed it to be of a conformational origin; interaction of the π-electrons of the double bond and the electronegative substituent at position 3 giving a predominant conformer population with an axial substituent ("supra-annular effect").[30,31] However, critical NMR studies on such systems rejected a specific conformational effect based on the fact that in none of the compounds evaluated (including 2,3-dihydro-2-pyrancarbonic acid methyl ester) was the axial conformer observed in appreciable amount under equilibrium conditions.[23]. A possible homoconjugation of the double bond with an electronegative group (CHO, COOR, NO_2 and others) however could not be excluded in principle.

We assume that glucuronic acid ester glycals are governed by a "supra-annular effect". In case of the $^5H_4$ conformation b a homoconjugative interaction between the methoxycarbonyl group and the electron rich enol ether double bond occurs. Then the enthalpy of conformer interconversion approaches the order of magnitude of the free activation enthalpy of the subsequent reaction rendering inapplicable the Curtin-Hammett

principle. Electrophilic attack on the predominantly fixed conformation b favours the iodonium intermedate e leading to formation of III as conformation h which then flips over to the normal chair form g.

A comparable conformational preference in the other normal or uronic acid ester glycals was not observed, and no increase in the β-glycoside formation occurred. Presently, there is no satifsfactory explanation available for this marked divergence in conformational behavior between 2a and its L-ribo (7), D-lyxo (9), and L-xylo configurational enol ether isomers. In accord with our previous findings all these cases show a predominant or virtually exclusive formation of 1,2-trans-diaxial derivatives in N-iodosuccinimide glycosylations.

EXPERIMENTAL

For general remarks and procedures (acetylation = GP 1; workup of N-iodosuccinimide reactions = GP 2) see lit.[1].

Methyl 3-O-acetyl-1,5-anhydro-2-deoxy-D-arabino hex-1-enitol-pyranuronate (2b). A solution of compound 2a (5.5 g, 21.3 mmol) in abs methanol (50 mL) was stirred with dry sodium carbonate (2.0 g) for 2 h at room temperature. Following filtration, treatment with an ion exchange resin (Amberlite IR 120 H^+), and concentration, the mixture was chromatographed (ethyl acetate/n-hexane, 1:1) to give 1.0 g (22%): mp 86°C, $[a]_D^{20}$ -128.7 (c 0.61, acetone).
Anal. Calcd for $C_9H_{12}O_6$ (216.2): C, 50.00; H, 5.60. Found: C, 49.47; H, 5.35.

3-O-Acetyl- (4b) and 4-O-Acetyl-1,5-anhydro-2,6-dideoxy-L-arabino-hex-1-enitol (4c). A solution of compound 4a (100 mg, 0.47 mmol) in abs methanol (10 mL)

was stirred with dry sodium carbonate (10 mg) for 2 h at room temperature. Over 15 min the mixture was warmed to 40°C, then cooled, neutralized (Amberlite IR 120 H^+), filtered, concentrated and separated by preparative thin layer chromatography (ethyl acetate/n-hexane, 1:1). In addition to 4d (50 mg, 82%) 4b was obtained (1.5 mg, 2%) as a colourless syrup; for 4b: $[a]_D^{20}$ + 59.3 (c 0.15, ethyl acetate). In a similar experiment both 4b and 4c were obtained as a mixture and characterized by ^1H NMR (Table 2).

Methyl 1,5-anhydro-2-deoxy-L-xylo-hex-1-enitol-pyranuronate (11b). Compound 2a (258 mg, 1.0 mmol) was dissolved in 1% sodium methylate in methanol (10 mL), the solution left for 12 h at room temperature, neutralized (Amberlite IR 120 H^+), filtered and concentrated. ^1H NMR reveals 80% 11b and 20% 2c. Separation (preparative TLC, ethyl acetate) gave 94 mg (54%), colourless syrup, $[a]_D^{20}$ -74.5 (c 0.93, methanol).
Anal. Calcd for $C_7H_{10}O_5$ (174.2): C, 48.28; H, 5.79.
Found: C, 48.79; H, 5.35.

Methyl 3,4-di-O-acetyl-1,5-anhydro-2-deoxy-L-xylo-hex-1-enitol-pyranuronate (9). 12c (300 mg, 0.80 mmol) was dissolved in 38% HBr in acetic acid (3 ml) and left at 5°C for 2 d. This solution was added dropwise to a mixture of sodium acetate (3.5 g), copper sulfate (300 mg), and zinc dust (3 g) in 50% aqueous acetic acid (10 mL) at -10°C with vigorous stirring. Following the addition stirring was continued for another 3 h at -10°C, then filtered and the residue washed with 50% aqueous acetic acid (5 mL). The combined filtrates were treated with ice water (30 mL) and extracted four times with chloroform. The chloroform solution was washed with water, saturated sodium hydrogen carbonate solution, again with water, dried $MgSO_4$) and then concentrated. The light yellow syrup was purified by column chromato-

TABLE 2

Chemical Shifts [δ] and Coupling Constants [Hz] of Glycals

	2a[a]	2b[a,b]	2c[a,c]	3[e]	4a[g]	4b[g,i]	4c[c,g]
1-H	6.69 ddd[dt]	6.57 ddd	6.42 dd	6.50 dd	6.16 ddd	6.15 dd	6.09 dd
2-H	4.95 dddd	4.83 ddd	4.83 ddd	4.87 ddd	4.69 dd	4.53 dd	4.57 dd
3-H	4.89 dddd	4.93 dddd	3.98 dddd[ddt]	5.31 dddd[ddt]	5.47 dddd	5.18 ddd	4.12 ddd
4-H	5.39 dddd	4.24 ddddd	4.03 ddd	5.25 ddd	5.15 dd	3.49 dd	4.82 dd
5-H	4.91 ddd	4.67 dd	4.47 dd	4.12 dddd	3.86 dddq[dtq]	3.67 dq	3.71 dq
$COOCH_3$	3.76 s	3.73 s	3.70 s	f	1.11 d[h]	1.30 d[h]	1.13 d[h]
OAc	1.95, 2.07 s	1.93 s	-	2.07, 2.10 s	1.64, 1.65 s	1.57 s	1.58 s
J(1,2)	6.1	6.2	6.1	6.2	6.1	6.0	6.0
J(1,3)	0.5	0.8	1.0	1.2	1.5	1.5	1.6
J(1,4)	0.4	0.4	d	d	d	d	d
J(1,5)	d	d	d	d	0.3	d	d
J(2,3)	5.1	4.7	4.0	3.5	3.0	2.4	2.6
J(2,4)	1.6	1.4	1.0	0.7	d	d	d
J(2,5)	0.5	d	d	d	d	d	d
J(3,4)	2.5	3.4	4.2	5.0	6.0	6.7	6.5
J(3,5)	1.5	1.2	1.0	1.1	0.7	d	d
J(4,5)	2.7	3.9	5.4	6.5	8.0	9.6	8.9
J(5,6)	-	-	-	f	6.5	6.2	6.4

	4d[a,k]	6a[e]	6b[e,l]	7[e]	9[g]	11a[e]	11b[a,m]
1-H	6.23 dd	6.51 d	6.44 d	6.14 dd	6.20 dddd	6.68 ddd[dq]	6.50 dddd[dq]
2-H	4.63 dd	4.87 dd[t]	4.95 dd[t]	5.13 dddd	4.51 ddd	5.08 ddd	4.96 ddd
3-H	4.09 dddd[ddt]	5.41 dd	4.11 ddd[dq]	4.95 mc	5.50 dddd	4.94 dddd	3.87 dddd
4-H	3.27 ddd	4.87 dd	3.49 ddd	4.41 ddd	5.75 dddd	5.33 dddd	4.11 dddd
5-H	3.72 dq	4.17 dq	3.81 dq	4.03 ddd	4.19 ddd	4.54 ddd	4.47 ddd
$COOCH_3$	1.27 d[h]	1.31 d[h]	1.40 d[h]	3.83 s	3.31 s	3.81 s	3.78 s
OAc	-	2.06; 2.08 s	-	2.07;2.08 s	1.68;1.69 s	2.05;2.08 s	-
J(1,2)	6.1	5.8	6.0	5.1	6.3	6.2	6.2
J(1,3)	1.7	d	d	1.4	1.9	0.7	0.6
J(1,4)	d	d	d	d	0.5	0.5	0.6
J(1,5)	q	d	d	d	0.5	0.7	0.6
J(2,3)	2.1	5.8	5.4	2.7	2.4	5.3	5.2
J(2,4)	d	d	d	1.8	1.7	1.7	1.8
J(2,5)	d	d	d	0.6	d	d	d
J(3,4)	7.2	3.9	4.4	2.9	4.4	2.4	2.4
J(3,5)	d	d	d	1.7	1.0	0.7	0.9
J(4,5)	9.8	10.4	9.6	12.2	1.9	1.6	1.7
J(5,6)	6.3	6.4	6.3	-	-	-	-

TABLE 3

Chemical Shifts [δ-values in C_6D_6] and Couplings Constants [Hz] of Cyclohexyl Glycosides

	13	14	15	16	17[c]	18	19	20
1-H	5.15 d	4.31 d	5.51 d	4.27 d	5.18 ddd[dt]	4.36 d	5.15 d	4.83 d
2-H	4.50 dd	3.84 dd	4.58 dd	3.81 dd	4.62 ddd	3.89 dd	4.35 dd	3.75 dd
3-H	4.83 dd	5.40 dd	5.27 dd	5.46 dd	4.91 ddd	5.42 dd	5.59 dd	5.69 dd[t]
4-H	5.61 dd[t]	5.06 dd	5.75 dd	5.30 dd	5.57 ddd[dt]	4.78 dd	5.74 dd	
5-H	4.13 ddd	3.15 ddd	4.71 d	3.77 d	4.12 ddq	3.13 dq	4.39 ddd	
$COOCH_3$	a	b	3.23 s	3.26 s	1.22 d[d]	1.05 d[d]	e	
Cyclo-hexyl-1H	3.26 mc	3.56 mc	3.67 mc	3.55 mc	3.27 mc	3.58 mc	3.38 mc	
OAc	1.70, 1.70, 1.76 s	1.68, 1.69, 1.74 s	1.53, 1.65 s	1.70, 1.71 s	1.66, 1.68 s	1.67, 1.75 s	1.60, 1.71, 1.74 s	1.67, 1.69, 1.82 s
J(1,2)	1.3	8.9	5.5	8.9	1.5	9.0	3.1	9.0
J(2,3)	4.3	11.2	3.6	11.0	4.3	11.2	5.9	3.0
J(3,4)	9.5	9.0	6.5	9.1	9.5	9.1	3.3	2.9
J(4,5)	9.7	10.1	5.7	9.8	9.7	9.6	7.9	
J(5,6)	d	b	-	-	6.3	6.2	e	

	21[f]	22[f]	23	24[g]	25	26[f,i]	27	28
1-H	5.05 d	4.79 d	5.09 d	5.38 dd	4.41 d	5.59 dd	5.79 d	4.28 d
2-H	4.21 dd	4.10 dd	3.88 dd	4.19 ddd		4.21 ddd	3.99 dd	
3-H	5.22 dd	5.56 dd[t]	4.95 dd	4.95 ddd	5.17 dd	5.02 ddd	5.83 dd	
4-H	5.16 dd	4.61 dd	5.97 dd	5.43 ddd	5.27 dd	5.66 ddd	5.27 dd	
5-H	4.24 dq	3.93 dq	4.31 d	4.27 ddd[dt]		4.77 d	4.91 d	
$COOCH_3$	1.26 d[d]	1.16 d[d]	3.31 s	[h]		3.76 s	3.18 s	3.33 s
Cyclo-hexyl-1H	3.56 mc		3.66 mc	3.29 mc	3.43 mc	3.66 mc	3.64 mc	
OAc	2.04, 2.04 s	1.94, 2.15 s	1.63, 1.73 s	1.66, 1.74, 1.86 s		2.07, 2.12 s	1.64, 1.67 s	
J(1,2)	4.3	9.0	3.2	1.6	9.0	1.9	6.6	9.4
J(2,3)	6.7	2.8	4.5	4.7	11.1	4.7	8.8	
J(3,4)	3.2	2.9	6.2	3.6	3.9	3.6	7.3	
J(4,5)	6.5	9.9	8.0	1.5	1.5	2.5	5.3	
J(5,6)	6.7	6.3	-	[h]		-	-	-

Footnotes to Table 2:

a. in [D_6]-acetone; b. 4.86 [d, J(4,4-OH) = 5.0, 4-OH]; c. exchanged with CD_3OD; d. < 0.4 Hz; e. in $CDCl_3$; f. 3.44 (dd, 6a-H), 3.36 (dd, 6b-H); J(5,6a) = 5.3, J(5,6b) = 7.1, J(6a,6b) = -11.0; g. in C_6D_6; h. 6-CH_3; i. 2.94 (mc, 4-OH); k. 4.26 (d, 3-OH), 4.58 (d, 4-OH); J(3,3-OH) = 4.9, J(4,4-OH) = 4.6; l. 1.76 (d, 3-OH), 2.52 (d, 4-OH); J(3,3-OH) = 6.4, J(4,4-OH) = 9.4; m. exchanged with D_2O.

Footnotes to Table 3:

Generally cyclohexyl-H between δ 0.8 -2.0. a. 4.20 (mc, 6a-, 6b-H); J(5,6a)≈4.3, J(5,6b) = 3.1; b. 4.28 (dd, 6a-H), 3.98 (dd, 6b-H), J(5,6a) = 4.4, J(5,6b) = 2.3, J(6a,6b) ◻ -12.4; c. J(1,3) = 0.7, J(1,5) = 0.6, J(2,4) = 0.6; d. 6-CH_3; e. 4.27 (dd, 6a-H), 4.11 (dd, 6b-H); J(5,6a) = 5.8, J(5,6b) = 3.1, J(6a,6b) = -12.0; f. in $CDCl_3$; g. J(1,3) = 0.6, J(2,4) = 0.9; h. 4.21 (mc, 6a-, 6b-H), J(5,6a) = 5.8, J(5,6b) = 5.8; i. J(1,3) = 0.5, J(2,4) = 0.9.

graphy (ethyl acetate/n-hexane, 2:3) to give 9 105 mg (51%), as a low viscous syrup, $[a]_D^{20}$ +9.0 (c 2.94, chloroform).

Methyl 3,4-di-O-acetyl-1,5-anhydro-2-deoxy-L-ribo-hex-1-enitol-pyranuronate (7). Compound 9 (50 mg, 0.19 mmol) was dissolved in 1% sodium methylate in methanol (3 mL) and left for 5 h at room temperature. Following neutralization (Amberlite IR 120 H^+) and concentration the resulting crude material was acetylated according to GP 1 and separated by preparative TLC (ethyl acetate/n-hexane, 2:3) to give 7 10 mg (20%), colourless syrup, $[a]_D^{20}$ +106.9 (c 0.61, chloroform).

Anal. Calcd for $C_{11}H_{14}O_7$ (258.2): C, 51.16; H, 5.46.
Found for 7 : C, 51.68; H, 5.21.
Found for 9 : C, 50.79; H, 5.54.
Found for 11a: C, 51.10; H, 5.54.

General procedure for the preparation of Cyclohexyl 2-deoxy-2-iodo-glycosides 13 to 27. The glycal (1 mmol) and cyclohexanol (1.5 mmol) were stirred with molecular sieves 3 Å (100 mg) in abs acetone (10 mL) for 1 h. After addition of N-iodosuccinimide (2 mmol) the reaction was left at room temperature for 2 d. The workup followed GP 2, the purification and separation was done by preparative TLC. The yields are listed in Table 1, the ^1H NMR data in Table 3.

Anal. Calcd for $C_{16}H_{25}IO_6$ (440.3): C, 43.65; H, 5.72
Found for 17: C, 43.85; H, 5.81.
Found for 18: C, 43.96; H, 5.36.
Found for 21: C, 43.16; H, 5.51.

Anal. Calcd for $C_{17}H_{25}IO_8$ (484.3): C, 42.16; H, 5.20.
Found for 15: C, 42.73; H, 5.73.
Found for 16: C, 42.41; H, 5.55.

Compound	$[a]_D^{20}$	c (chloroform)
Cyclohexyl 3,4,6-tri-O-acetyl-2-deoxy-2-iodo-α-D-mannopyranoside (13), colourless syrup	+20.8	1.20
Cyclohexyl 3,4,6-tri-O-acetyl-2-deoxy-2-iodo β-D-glucopyranoside (14), colourless syrup	+ 7.7	2.51
Methyl(cyclohexyl 3,4-di-O-acetyl-2-deoxy-2-iodo-α-D-mannopyranoside)-uronate (15), colourless syrup	+30.0	1.05
Methyl(cyclohexyl 3,4-di-O-acetyl-2-deoxy-2-iodo-β-D-glucopyranoside)-uronate (16), colourless syrup	+20.7	0.42
Cyclohexyl 3,4-di-O-acetyl-2,6-dideoxy-2-iodo-α-L-mannopyranoside (17), mp 80°C	-31.7	2.08
Cyclohexyl 3,4-di-O-acetyl-2,6-dideoxy-2-iodo-β-L-glucopyranoside (18),mp 90 - 92°C	-58.6	0.73
Cyclohexyl 3,4,6-tri-O-acetyl-2-deoxy-2-iodo α-D-altropyranoside (19), colourless syrup	+41.4	0.64
Cyclohexyl 3,4-di-O-acetyl-2,6-dideoxy-2-iodo-α-D-altropyranoside (21), colourless syrup	+43.5	5.32
Methyl(cyclohexyl 3,4-di-O-acetyl-2-deoxy-2-iodo-α-L-altropyranoside)-uronate (23), colourless syrup	+ 8.0	0.30
Cyclohexyl 3,4,6-tri-O-acetyl-2-deoxy-2-iodo-α-D-talopyranoside (24), colourless syrup	+38.0	2.16
Methyl(cyclohexyl 3,4-di-O-acetyl-2-deoxy-2-iodo-α-D-talopyranoside)-uronate (26), mp 106-107°C	+67.6	0.88
Methyl(cyclohexyl 3,4-di-O-acetyl-2-deoxy-2-iodo-α-D-iodopyranoside)-uronate (27) colourless syrup	-38.6	0.76

Found for 23: C, 42.27; H, 5.06.
Found for 26: C, 42.57; H, 5.50.
Found for 27: C, 42.04; H, 5.39.

Anal. Calcd for $C_{18}H_{27}IO_8$ (498.3): C, 43.39; H, 5.46.
Found for 13: C, 43.04; H, 5.33.
Found for 14: C, 42.83; H, 5.17.
Found for 19: C, 43.81; H, 5.66.
Found for 24: C, 42.98; H, 5.25.

ACKNOWLEDGEMENT

Support of this work by the Fonds der Chemischen Industrie is gratefully acknowledged.

REFERENCES AND FOOTNOTES

1. J. Thiem, P. Ossowski, and U. Ellermann, Liebigs Ann. Chem., 2228 (1981).

2. Y. Nitta and H. Morita, Yakugaku Zasshi, 81, 1214 (1961); [Chem. Abstr., 56, 4851 b (1962)].

3. P. C. Wyss, J. Kiss, and W. Arnold, Helv. Chim. Acta, 58, 1847 (1975).

4. F. G. Fischer and H. Schmidt, Chem. Ber., 92, 2184 (1959).

5. C. B. Anderson and T. D. Sepp, J. Org. Chem., 33, 3272 (1968).

6. R. R. Schmidt and R. Angerbauer, Carbohydr. Res., 89, 159 (1981); D/L-mixture, no physical data.

7. H. B. Wood Jr., Meth. Carbohydr. Chem., 2, 57 (1963).

8. S. Morell and K. P. Link, J. Biolog. Chem., 108, 763 (1935).

9. T. Kondo and T. Goto, Agr. Biol. Chem., 35, 912 (1971); [Chem. Abstr., 75, 77187 x (1971)].

10. A. A. Chalmers and R. H. Hall, J. Chem. Soc., Perkin Trans. 2, 728 (1974).

11. M. Rico and J. Santoro, Org. Magn. Reson., 8, 49 (1976).

12. The given equations correspond to compounds of the D-series and analogously refer to derivatives of the L-series.

13. R. J. Ferrier and G. H. Sankey, J. Chem. Soc. (C), 2345 (1966).

14. W. Roth and W. Pigman, Meth. Carbohydr. Chem., 2, 405 (1963).

15. H. Paulsen und J. Thiem, Chem. Ber., 106, 3850 (1973).

16. R. D. Guthrie and R. W. Irvine, Carbohydr. Res., 72, 285 (1979).

17. J. Thiem, P. Ossowski, and J. Schwentner, Chem. Ber., 113, 955 (1980).

18. F. Micheel, Ber. Dtsch. Chem. Ges., 63, 347 (1930).

19. F. Shafizadeh, Meth. Carbohydr.Chem., 2, 409 (1963).

20. D. M. Ciment and R. J. Ferrier, J. Chem. Soc. (C), 441 (1966).

21. E. L. Eliel, N. J. Allinger, S. J. Angyal and G. A. Morrison, "Conformational analysis", J. Wiley and Sons, Inc., New York, N.Y., 1964, p. 44.

22. A. J. Kirby, "The Anomeric Effect and Related Stereoelectronic Effects at Oxygen", Springer, Berlin, 1983.

23. N. S. Zefirov, V. N. Chekulaeva and A. I. Belozerov, Tetrahedron, 25, 1997 (1969).

24. J. Thiem, H. Karl and J. Schwentner, Synthesis, 696 (1978).

25. R. W. Hoffmann, "Aufklärung von Reaktionsmechanismen", G. Thieme, Stuttgart, 1976, p. 150; E. L. Eliel, "Stereochemistry of Carbon Compounds", McGraw-Hill, New York, N.Y., 1962, p. 149.

26. J. Thiem and B. Meyer, Chem. Ber., 113, 3067 (1980).

27. J. Kiss, Carbohydr. Res., 11, 579 (1969).

28. G. Descotes, J. C. Martin, and Tachi-Dung, Carbohydr. Res., 62, 61 (1978).

29. H. Kwart and L. J. Miller, J. Am. Chem. Soc., 83, 4552 (1961).

30. G. P. Kugatova-Shemyakina and G. N. Nikolaev, Tetrahedron, 23, 2987 (1967).

31. G. P. Kugatova-Shemyakina, G. N. Nikolaev, and V. M. Andreev, Tetrahedron, 23, 2721 (1967).