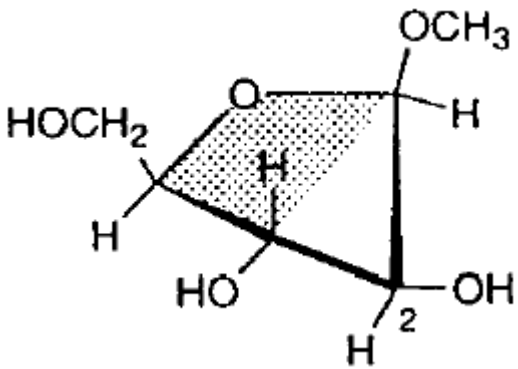
Conformation of carbohydrates

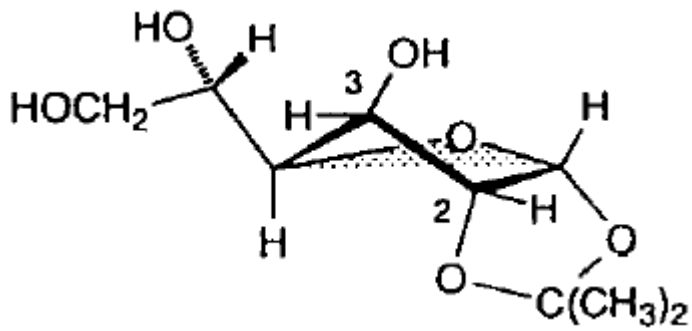
five and six membered-rings,
the *gauche*-effect,
the *anomeric*-effect

Conformation of rings

Envelope, E_2



Twist, $^3T_2$



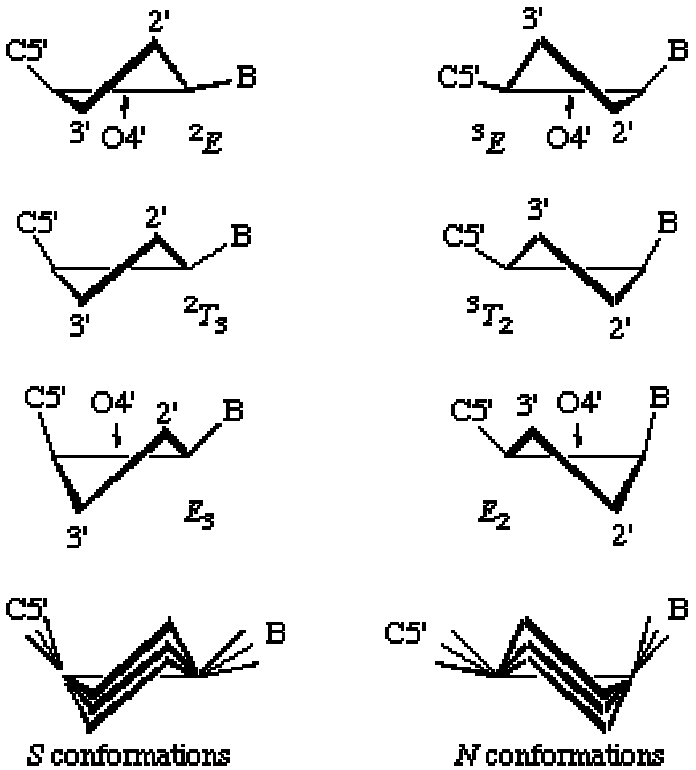
Endocyclic torsions are not independent!

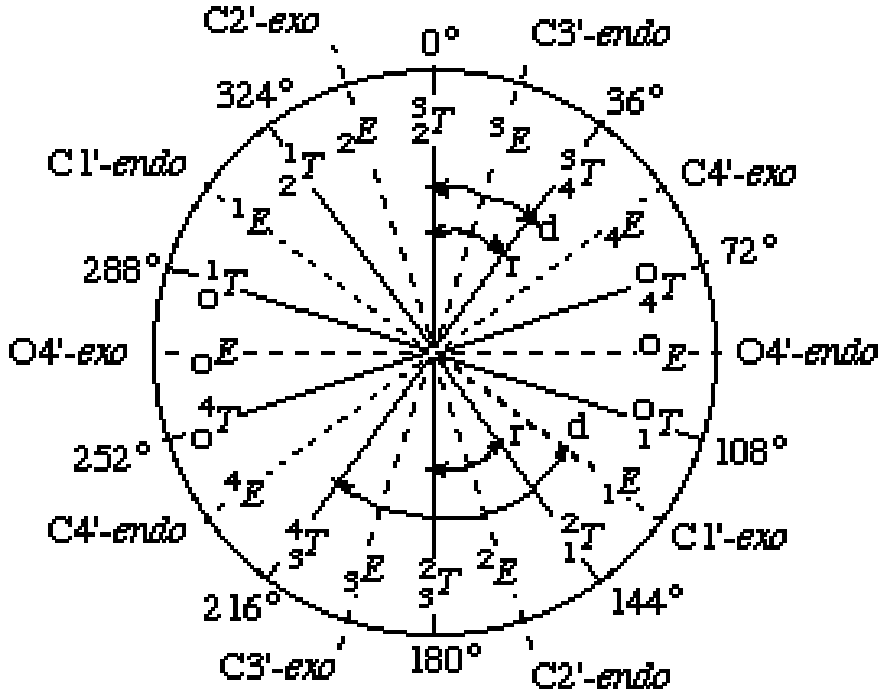
$$\nu_n = \phi \times \cos(P + n \times 144°)$$

ϕ – puckering
P – phase

Altona and Sundaralingam
J. Am. Chem. Soc. **94** (1972) 8205-8212

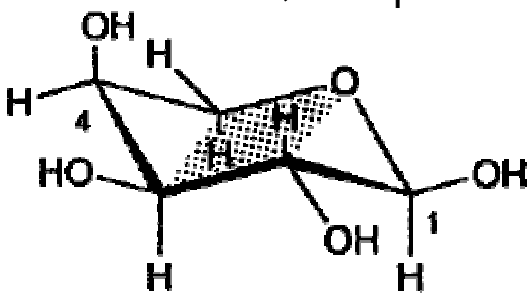
Phase (P) and puckering (Φ)



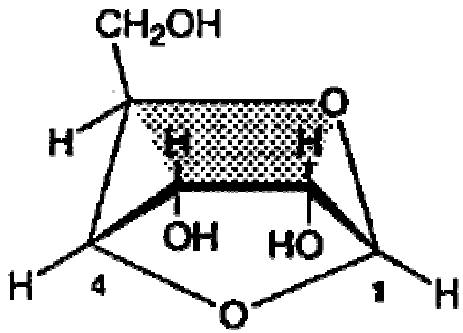


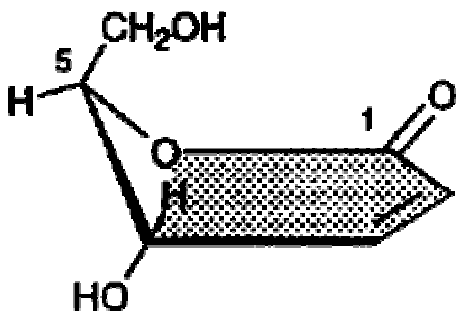
Rings cont.

Chair, $^4C_1$

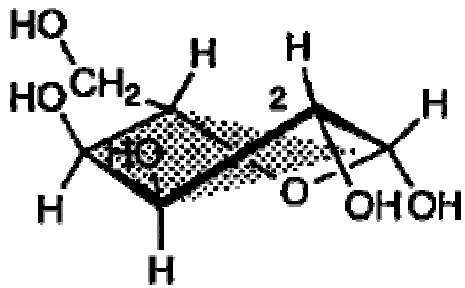


Boat, $B_{1,4}$



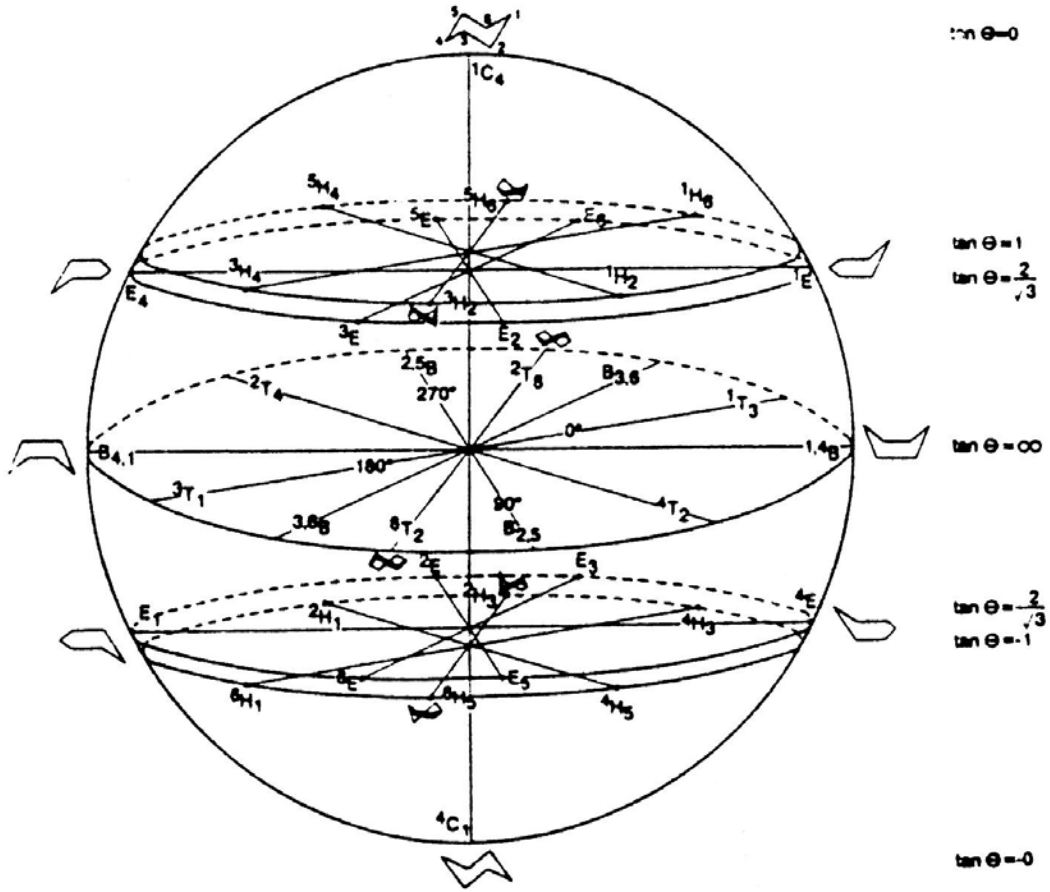


Envelope, ^5E



Skew, $^2S_0$

Pseudorotation of 6- membered rings



Ring conformation

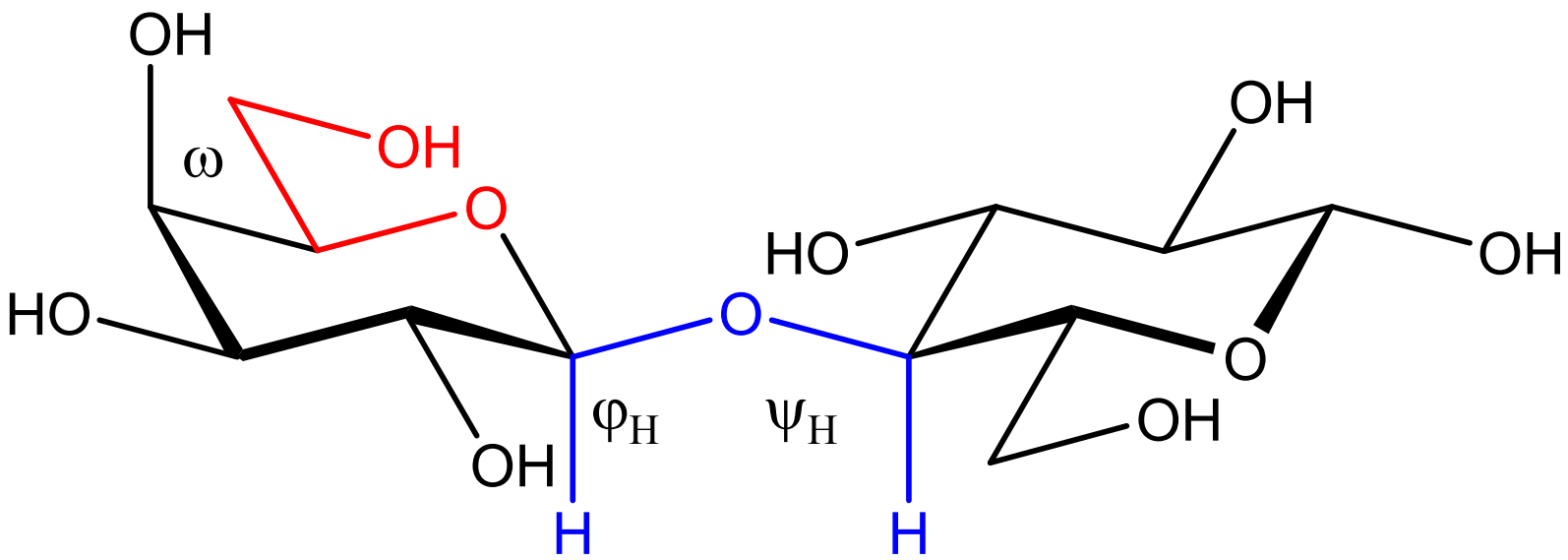
5-membered rings are flexible – mostly with anomeric substituent axial

6-membered rings are rigid except some pentoses and idose

6-membered rings prefer chain conformations – boats have high energy

$^{3}J_{HH}$-values can be used to determine conformation

Degrees of freedom

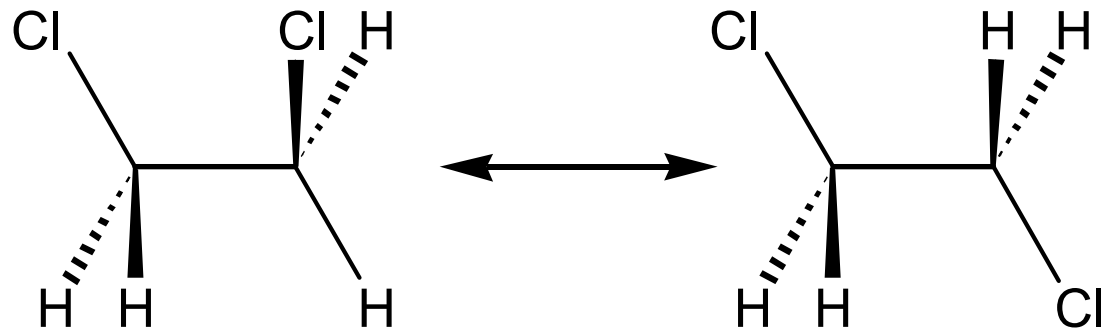


ω – O5-C5-C6-O6

φ_H – H1’-C1’-O4-C4

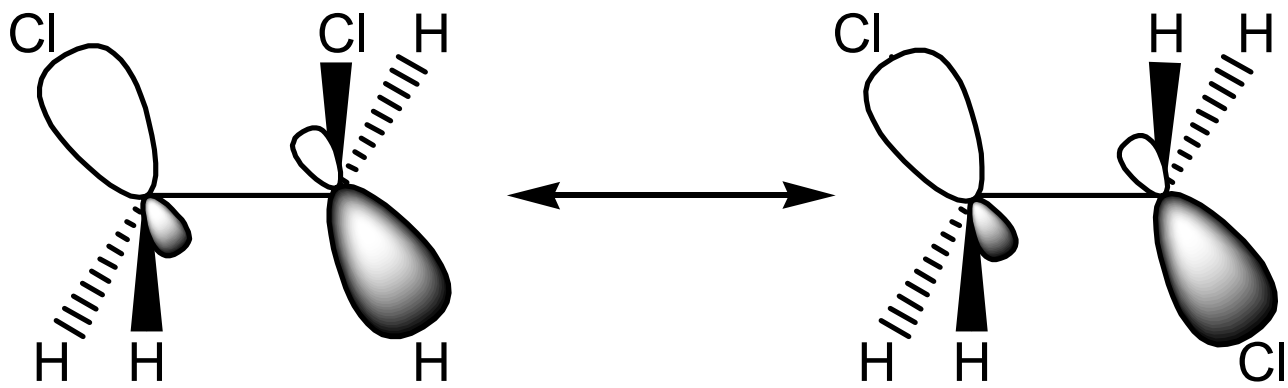
ψ_H – C1’-O4-C4-H4

Gauche effect



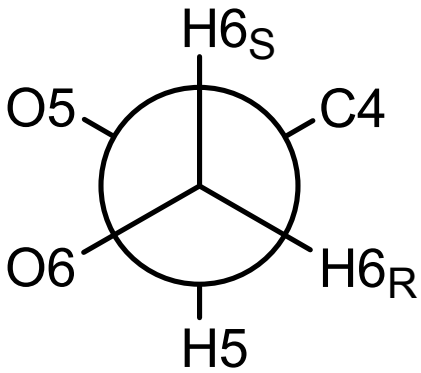
Solvent	ε	ΔH^0(kcal/mol)
gas	1	0.9-1.3
c-hexane	2.0	0.91
Et_2O	4.3	0.69
EtOAc	6.0	0.42
CH_3COCH_3	20.7	0.18
CH_3CN	36.2	0.15

Gauche effect



Overlap of C-Cl and C-H bond orbitals is more favourable than overlap of the orbitals of two C-Cl bonds

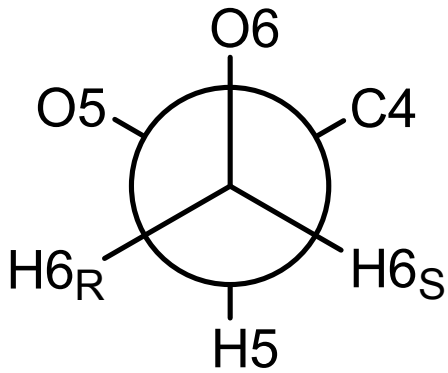
C5-C6 torsion



ω≈+65°

gt

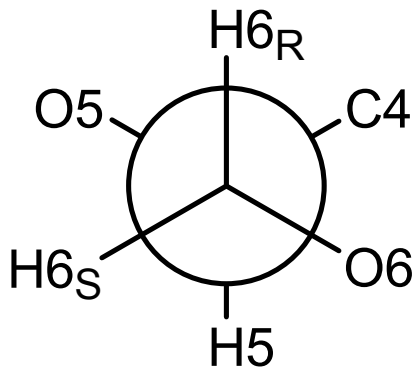
gauche effect



ω≈-65°

gg

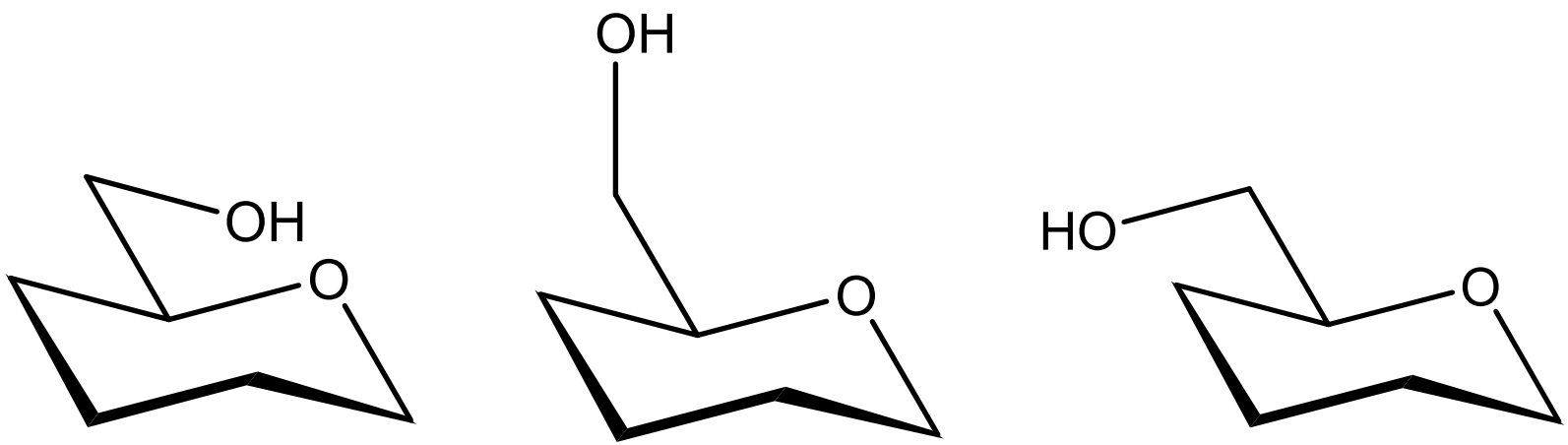
gauche effect



ω≈180°

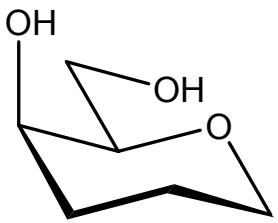
tg

C5-C6 torsion

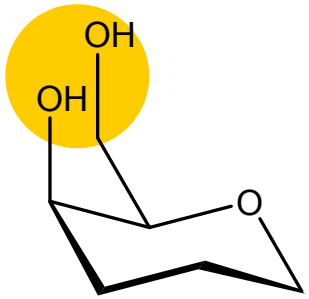


54% 45% 1%

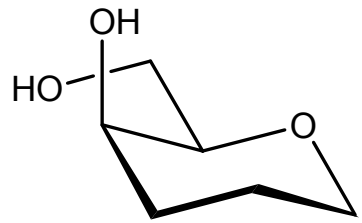
Hassel-Ottar effect



75%



16%



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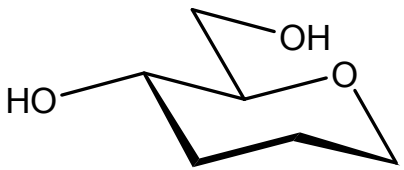
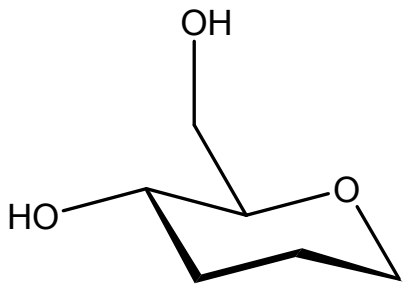
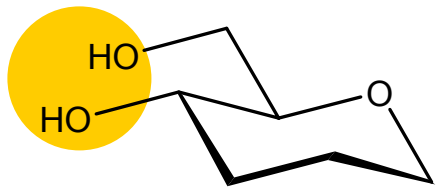


47%



53%



0%

Analyses using $^3J_{H5,H6}$

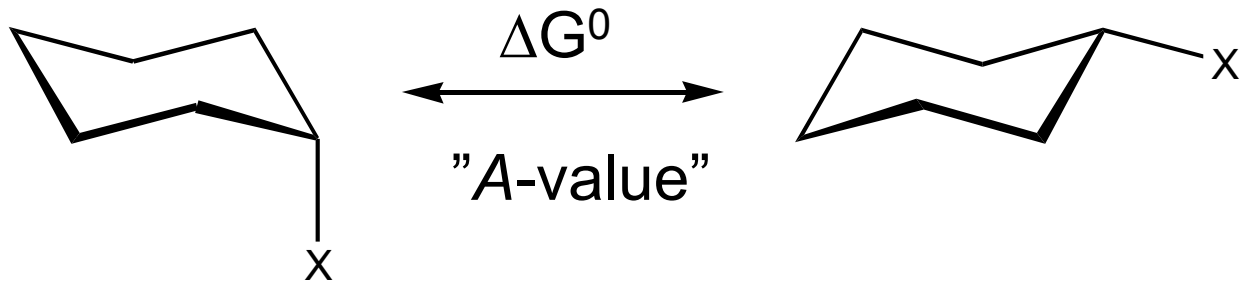
$$^3J_{H5,H6R} = P_{gt} \times {}^3J_{H5H6R}(gt) + P_{gg} \times {}^3J_{H5H6R}(gg) + P_{tg} \times {}^3J_{H5H6R}(tg)$$
$$^3J_{H5,H6S} = P_{gt} \times {}^3J_{H5H6S}(gt) + P_{gg} \times {}^3J_{H5H6S}(gg) + P_{tg} \times {}^3J_{H5H6S}(tg)$$
$$1 = P_{gt} + P_{gg} + P_{tg}$$

three equations – three unknowns

assignment of $H6_R$ and $H6_S$ is required

values of coupling constants in the three rotamers have to be estimated

Cyclohexanes

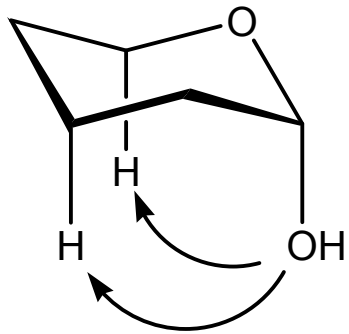


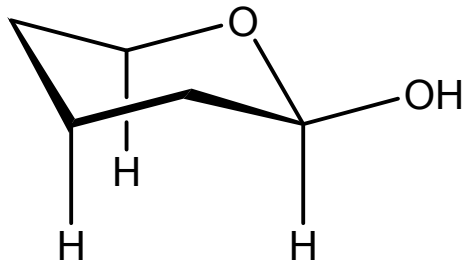
X	A (kcal/mol)	X	A (kcal/mol)
H	0	NH_2	1.5
F	0.3	CH_3	1.7
Cl, Br, I	0.6	$CH(CH_3)_2$	2.2
OH	0.8	$C(CH_3)_3$	4.8
SH	1.2	Ph	2.8

Anomeric effect

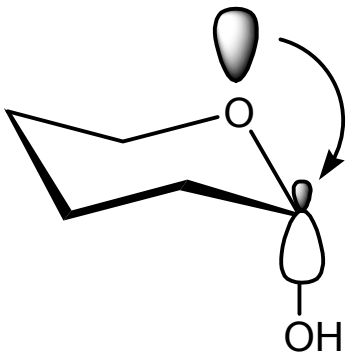
In an equilibrium between anomers there is a significantly larger amount of axial isomer than would be expected on steric grounds alone…

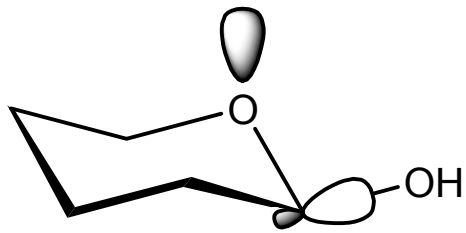
Steric- and stereo-electronic effects





unfavourable steric interactions





favourable stereoelectronic effect

2-methoxy-tetrahydropyran

ax→eq $\Delta H^0 \approx 0$, $\Delta S^0 \approx -2{,}7$ cal/Kmol

($CFCl_3$-$CDCl_3$ 85:15 v/v)

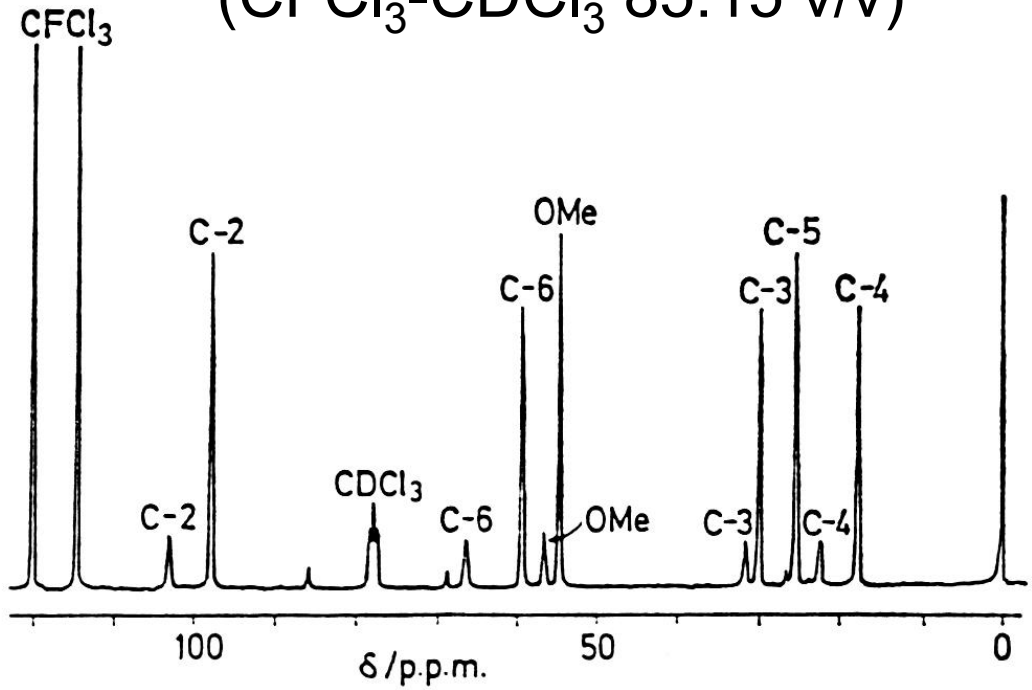
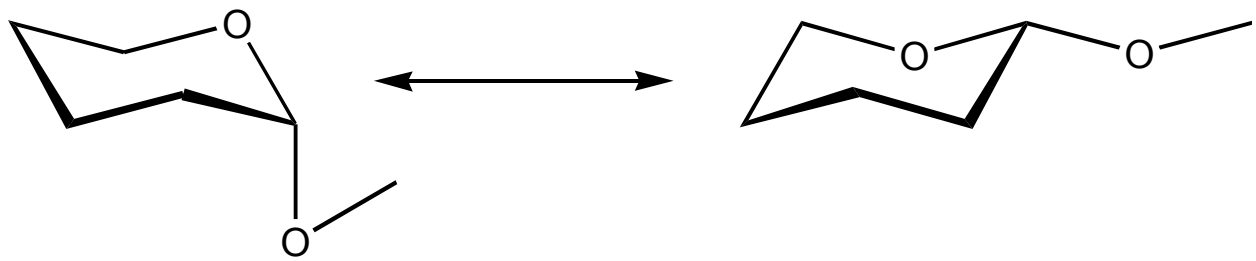


Figure 1. ^{13}C Fourier transform n.m.r. spectrum at 62.901 MHz of [(**1**) ⇌ (**2**)] in $CFCl_3$–$CDCl_3$ at 150 K.

H. Booth *et al.*, *J.C.S., Chem. Commun.* (1982) 1047-1048

2-methoxy-tetrahydropyran



axial *O*-methyl
μ=0 D

equatorial *O*-methyl
μ=1.84 D

Solvent	ε	%axial	K=[ax]/[eq]
C_6H_6	2.3	82	4.56
$CHCl_3$	4.8	71	2.45
CH_3OH	32	69	2.23
H_2O	78	52	1.08

R.U. Lemieux *et al*., *Can. J. Chem.* **47** (1969) 4427-4439

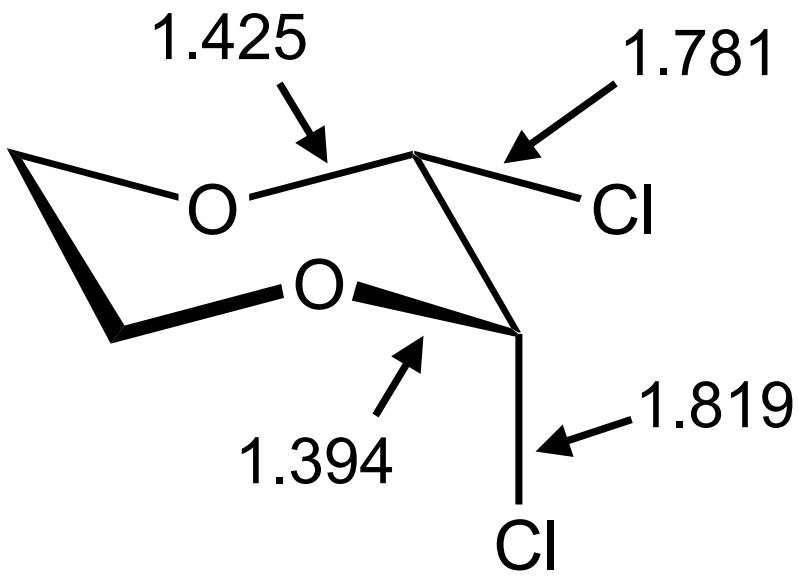
Anomeric effect

$$AE = \Delta G_{oxane} - \Delta G_{cyclohexane}$$

X	ΔG_{oxane}	$\Delta G_{cyklohexane}$	AE (kcal/mol)
Cl	1.8	-0.6	2.4
Br	1.8	-0.5	2.3
OCH_3	0.9	-0.8	1.7
SCH_3	0.5	-1.0	1.5
$NHCH_3$	-0.9	-1.3	0.4
$COOCH_3$	-1.4	-1.3	-0.1

E. Juaristi, G. Cuevas, *Tetrahedron* **48** (1992) 5019-5087

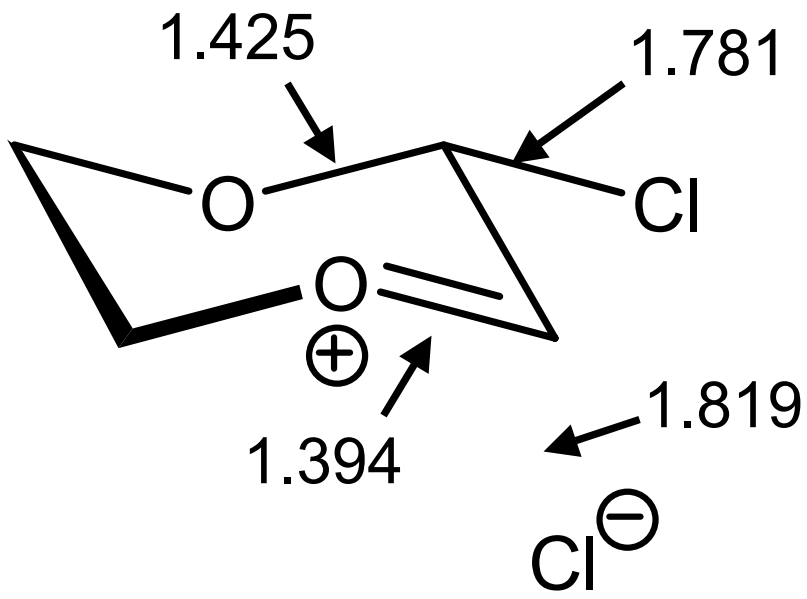
Bond lengths



	Ax. Cl	Equ. Cl	Ax-Equ
O-C	1.394	1.425	-0.031
C-Cl	1.819	1.781	0.038

E. Juaristi, G. Cuevas, *Tetrahedron* **48** (1992) 5019-5087

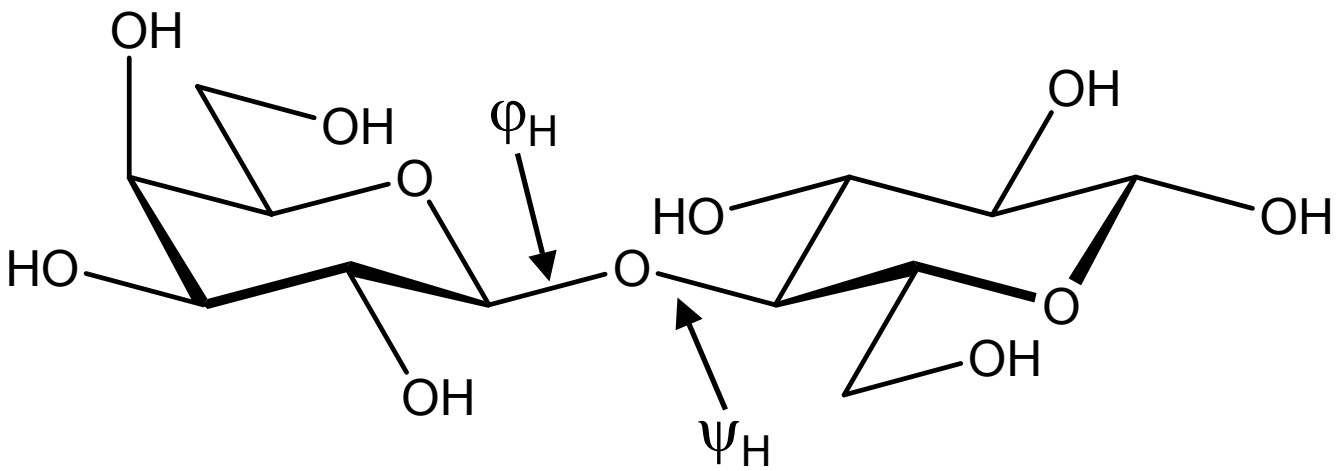
”Hyperconjugation”



	Ax. Cl	Equ. Cl	Ax-Equ
O-C	1.394	1.425	-0.031
C-Cl	1.819	1.781	0.038

E. Juaristi, G. Cuevas, *Tetrahedron* **48** (1992) 5019-5087

Conformation of oligosaccharides

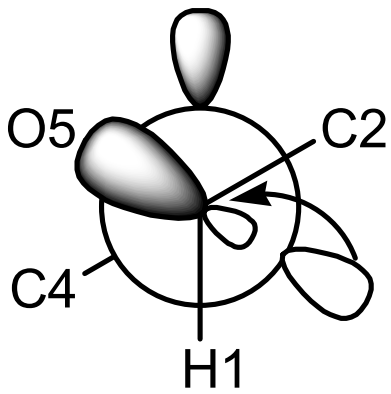


φ_H – exo-anomeric effect & steric effects

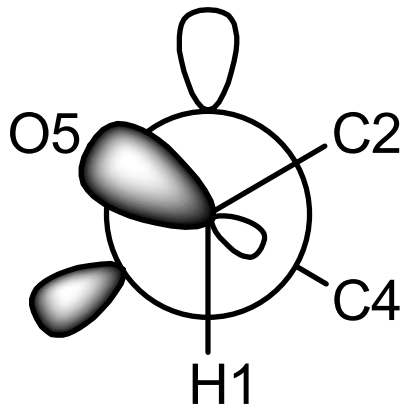
ψ_H – only steric effects

Exo-anomeric effect

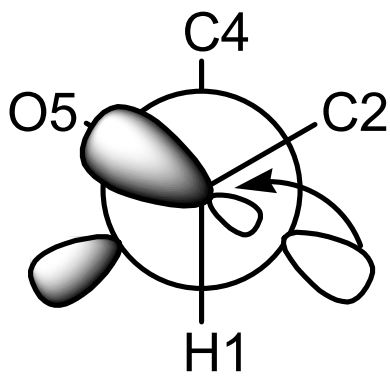
$\varphi_H \approx +60°$



$\varphi_H \approx -60°$



$\varphi_H \approx 180°$



Conformation of glycosides

Determined by the exo-anomeric effect and steric interactions

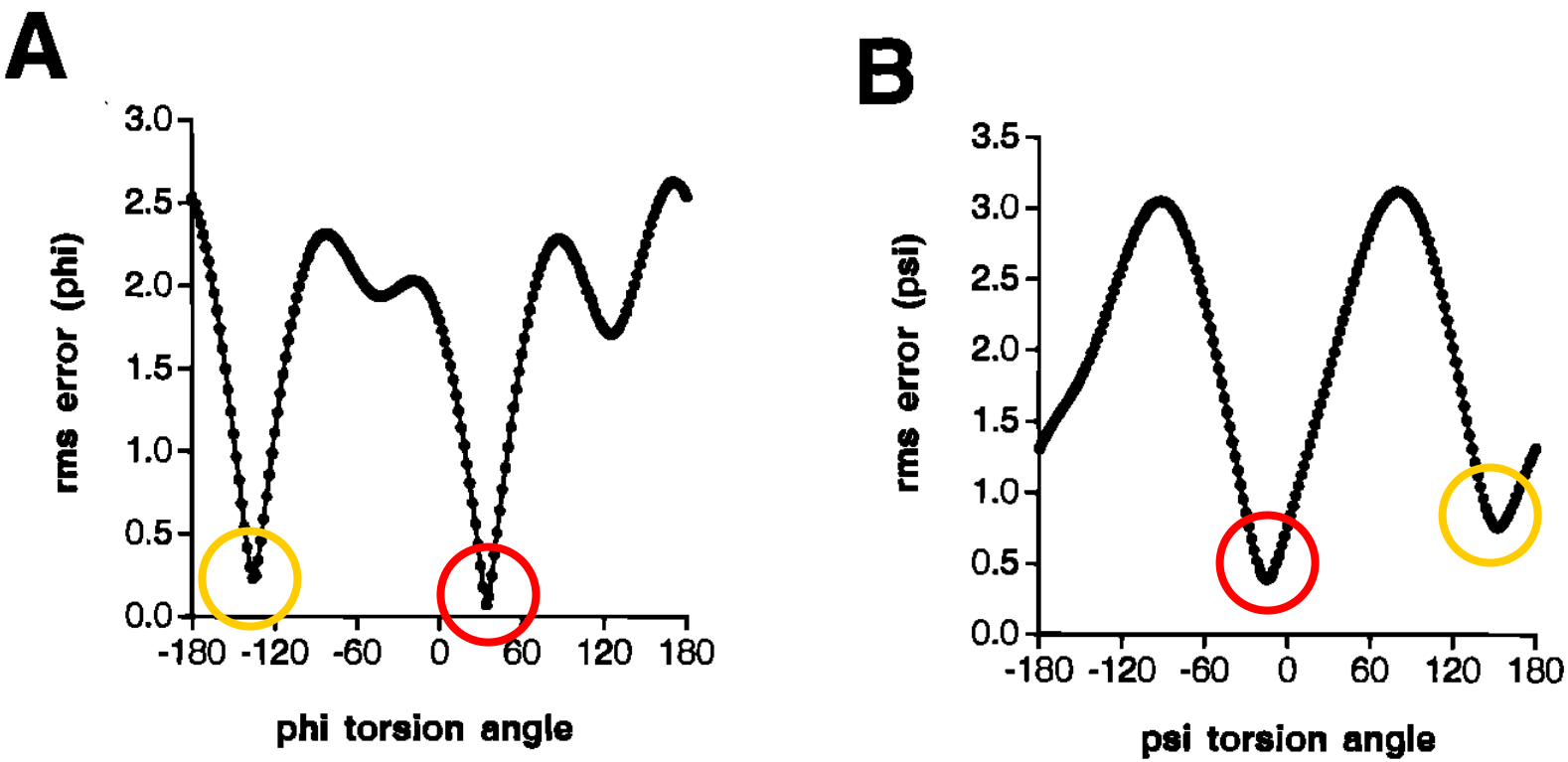
α-D/β-L $\varphi_H \approx -40°$

β-D/α-L $\varphi_H \approx +40°$

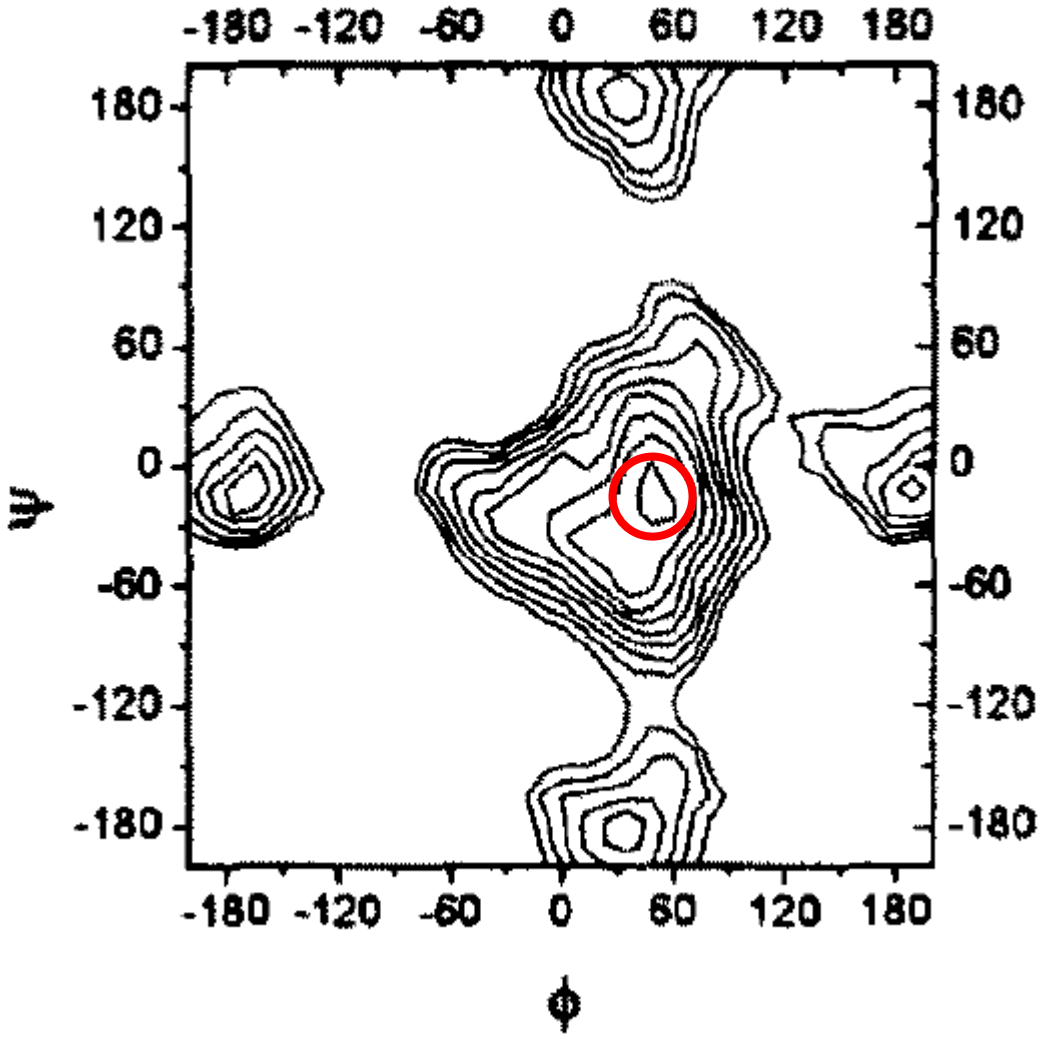
$\psi_H \approx -50° - +50°$ more flexible

Fit to experimental ^3J values

φ_H=+40°, ψ_H=-15°



Lactose PES



J. Mol. Struct. **395-396** (1997) 245-270

Methyl β-lactoside

φ_H=+32°, ψ_H=-40°

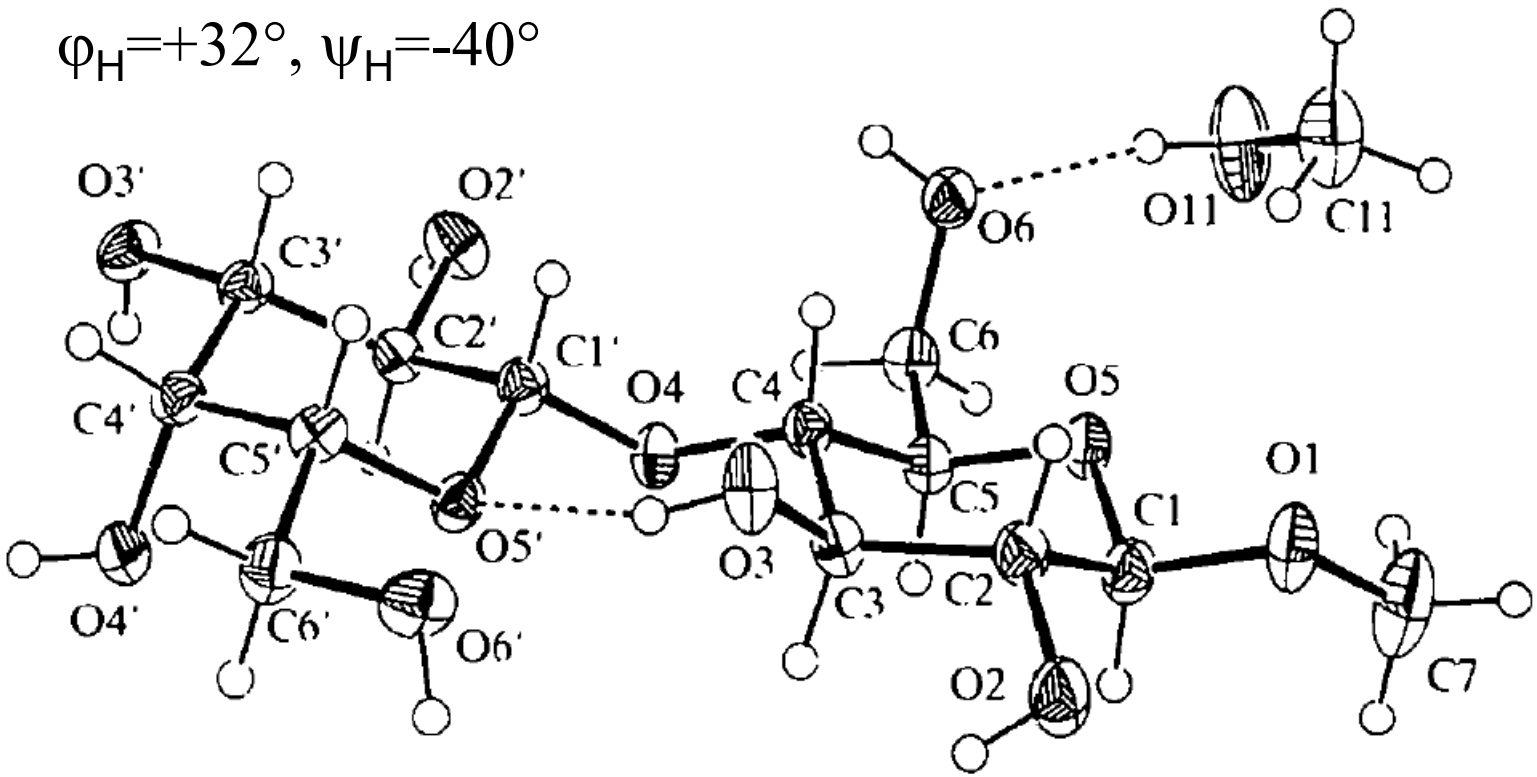


Fig. 1. The structure and atomic numbering in (I). 40% probability displacement ellipsoids are shown for the C and O atoms, and H atoms are shown as spheres of an arbitrary radius.