

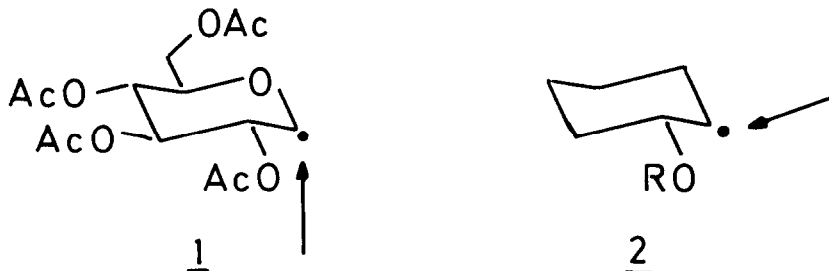
ANOMERIC EFFECT OF RADICALS

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Summary: The glucosyl radical 1 is attacked predominately at the axial position. This can be explained by an anomeric effect that stabilizes o-radical 5.

Recently we have shown that glucosyl radicals 1 react with acrylonitrile in a cis addition to give an axial substituted product¹⁾. Baldwin²⁾, Praly³⁾ and Vasella⁴⁾ observed similar stereoselectivities with acrylic ester and But_3SnD . These results are surprising because in cyclohexyl radicals 2 trans additions predominate⁵⁾. To prove whether the axial attack at 1 is caused by an anomeric effect rel. rates and activation enthalpies for the formation of axial and equatorial deuterated products 7 and 8 have been measured.



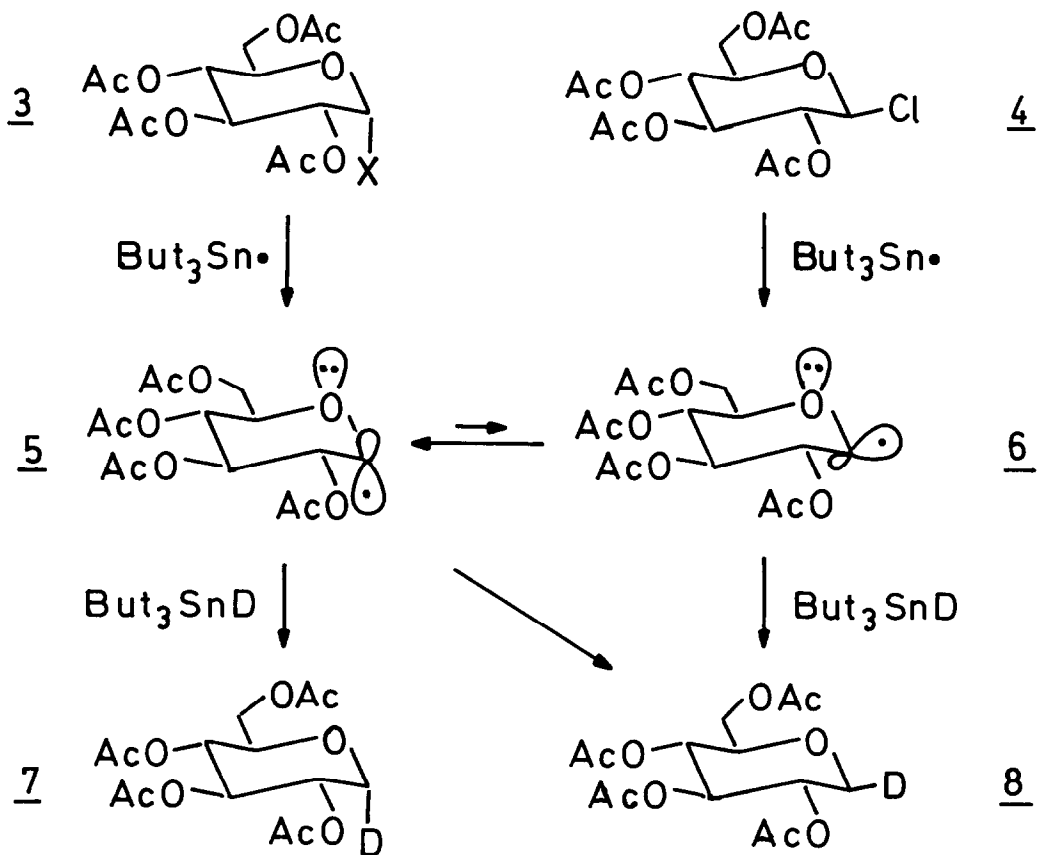
In reductions of α -glucosyl halides 3 and β -glucosyl chloride 4 with But_3SnD identical mixtures of products 7 and 8 are formed. The ratio of 7:8 varies from 98:2 at -20°C to 82:18 at 90°C (Table I). This means that the axial attack occurs with 3.9 kcal/mol lower activation enthalpy than the equatorial attack.

Ingold⁶⁾ has shown that the activation enthalpy of H-abstraction from But_3SnH with alkyl radicals is between 3 and 4 kcal/mol and that the substituent effect on the rate is very small. Therefore, a 3.9 kcal/mol difference in the transition states can not be explained by the selectivity of one π -radical.

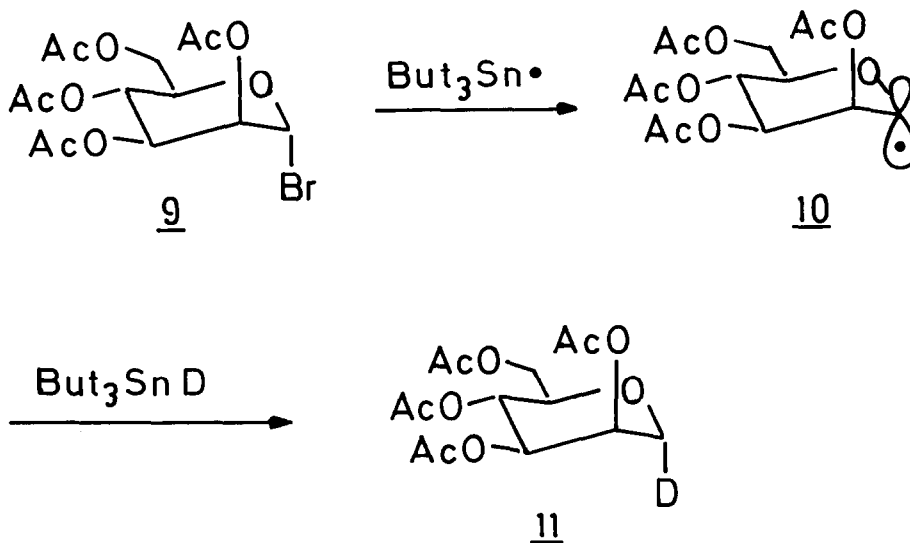
Table I

Reduction of glucosyl halides 3 and 4 with But_3SnD

Glucosyl halide	Solvent/ Initiation	Temperature (°C)	Product ratio	Yield (%)
			<u>7</u> : <u>10</u>	
<u>3</u> (X=Br)	THF/hv	-20	98:2	80
<u>3</u> (X=Br)	THF/hv	10	96:4	81
<u>3</u> (X=Br)	THF/hv	30	95:5	75
<u>3</u> (X=Br)	THF/hv	60	90:10	90
<u>3</u> (X=Br)	Toluene/AIBN	90	82:18	86
<u>4</u>	Toluene/AIBN	90	83:17	65



It is more likely that two interconverting σ -radicals 5 and 6 are formed. The back lobe of the σ -orbital in 5 interacts with non-bonded electrons of the adjacent oxygen. Radom and Schaefer⁷⁾ have calculated that such an interaction considerably increases the stability of the hydroxymethyl radical. This stabilizing effect is further supported by the rate of the formation of radicals 5 and 6. Halogen abstraction experiments with tributyltin radicals show that the more stable α -glucosyl-chloride 3 (X=Cl) cleaves the carbon-chlorine bond with about the same rate as the less stable β -glucosyl chloride 4. Therefore, the stabilizing anomeric effect⁸⁾ in radical 5 should be of the same order as the anomeric effect of glucosyl chlorides^{8,9)}. This increases the ratio of 5:6 in the equilibrium of the radicals. Because the rates of different alkyl radicals in reactions with But_3SnH are very similar⁶⁾ the higher concentration of 5 leads to the predominate formation of 7.



The minor isomer 8 is either the product of radical 6 or, as Clark¹⁰⁾ has pointed out, the product of attack at the back lobe of radical 5. In the mannosyl radical 10 this back lobe is shielded by an axial substituent at C-2. Reactions of α -mannosyl bromide 9 with But_3SnD at 90°C show that the axial deuterated product 11 is formed with more than 95 % rel. yield. This increase of the stereoselectivity at 90°C from 4.5 to at least 20 is in accord with an attack at the back lobe of 5 although it does not exclude the direct reaction from radical 6 to product 8.

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Notes and References

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