Pure & Appl. Chem., Vol. 60, No. 11, pp. 1655–1658, 1988.
Printed in Great Britain.

Stereoselective syntheses with carbohydrate radicals

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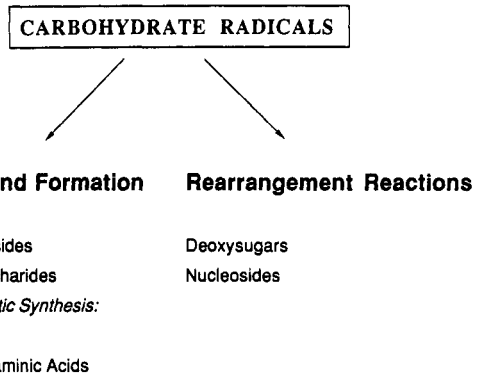
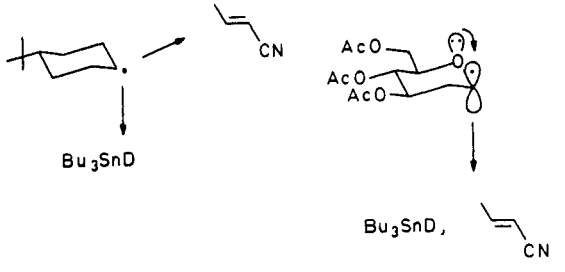
Abstract - Carbohydrate radicals are used for stereoselective syntheses of C-glycosides, C-disaccharides, and deoxysugars.

Carbohydrate radicals, in particular glycosyl radicals, can be easily generated from halides, selenides, and nitro compounds with trialkylstannanes (ref. 1). Utilization of these radicals leads (a) in CC-bond formation reactions to C-glycosides, and (b) in rearrangement reactions to 2-deoxysugars (Scheme 1).

Scheme 1

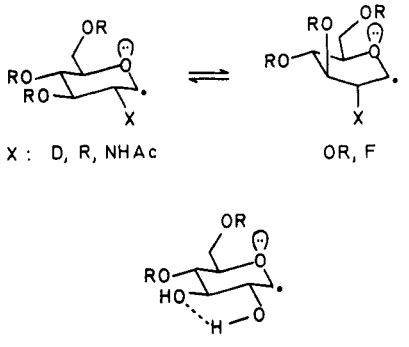


Scheme 2

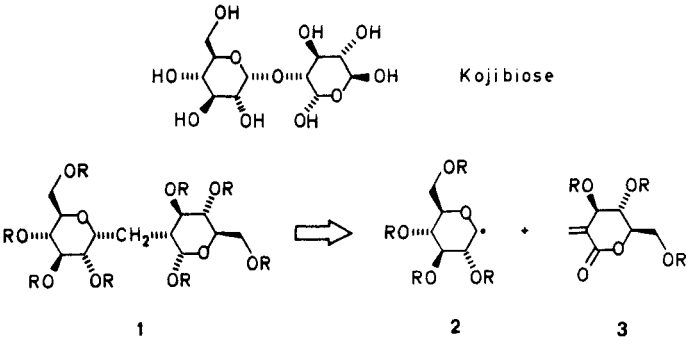


Because of the ring oxygen, the stereochemistry of glycosyl radicals often differs from that of cyclohexyl radicals. Thus cyclohexyl radicals are attacked by 1,2-disubstituted alkenes preferentially from the less crowded equatorial position, whereas stereoelectronic effects give rise to trans attack with respect to the non-bonding electron pair of the ring oxygen of the glycosyl radical (Scheme 2). This leads to α-C-glycosides, if the radicals adopt $^4C_1$ or $B_{2,5}$ conformations (Scheme 3). But if small atoms or groups like H, Cl (ref. 2) or OH (ref. 3) are transferred to the radical centers, cyclohexyl radicals are also axially attacked. The synthesis of C-disaccharide 1 from glucosyl radical 2 and alkene 3 is a good example for this stereoselectivity in which both CC- and the CH-bonds are formed via axial attack (Scheme 4).

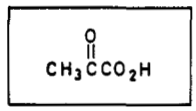
Scheme 3

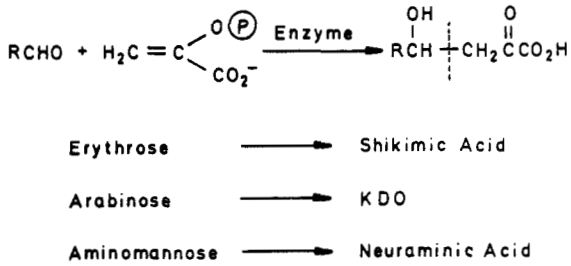


Scheme 4

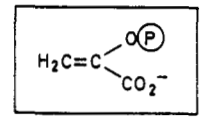


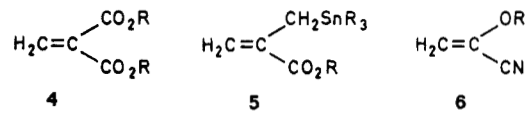
Scheme 5





Scheme 6

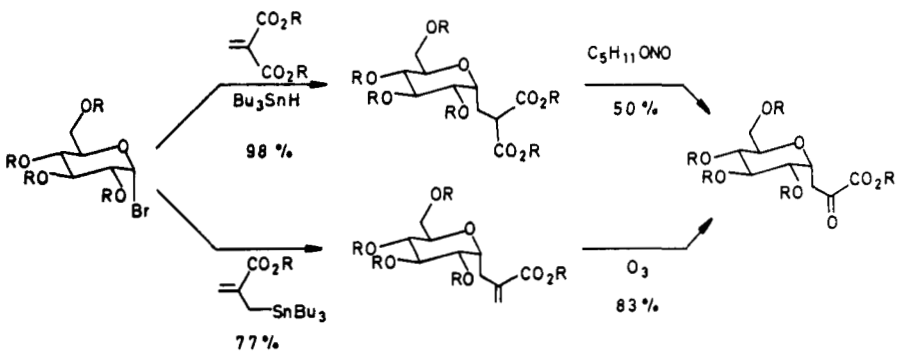




Glycosyl radicals can also be used in syntheses that mimic enzymatic aldol reactions between phosphoenol pyruvate and carbohydrates (Scheme 5).

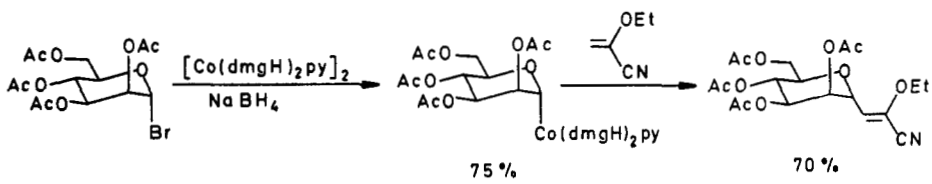
Whereas respective ionic in vitro reactions fail in the absence of enzymes, alkenes 4 - 6 are suitable synthons for pyruvate in radical CC-bond forming reactions (Scheme 6). Alkenes 4 and 5 lead via trialkyltin radicals and subsequent oxidation to aldol products. But these alkenes differ from phosphoenol pyruvate being C-4 instead of C-3 units (Scheme 7).

Scheme 7



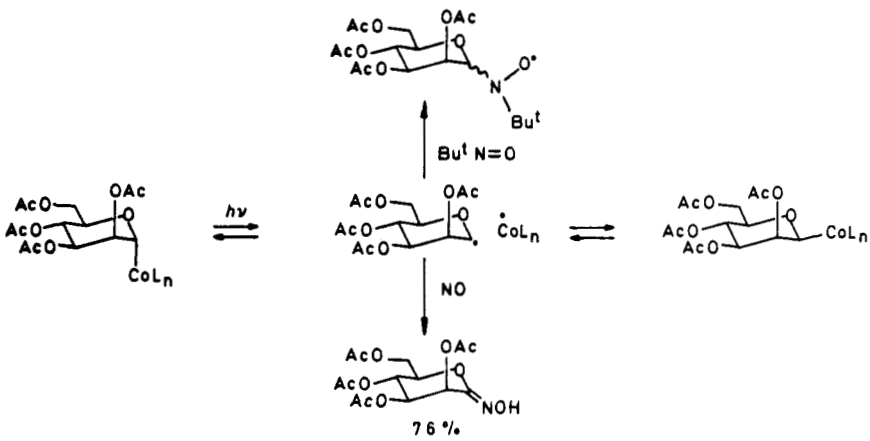
A more suitable synthon of phosphoenol pyruvate is ethoxyacrylonitrile, which reacts as C-3 unit with glycosyl-Co complexes and gives substitution products (Scheme 8).

Scheme 8

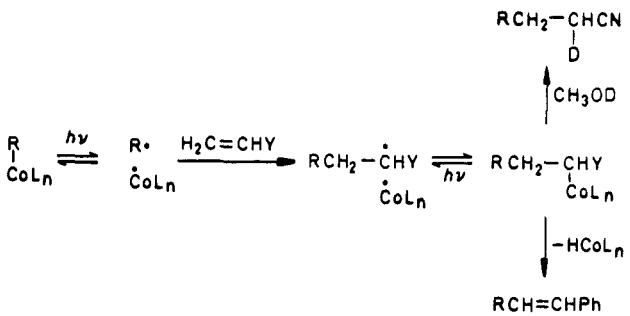


The glycosyl-Co complexes can be synthesized from glycosylbromides and Co(I) complexes. Photolysis gives glycosyl radicals that react with radical traps (Scheme 9).

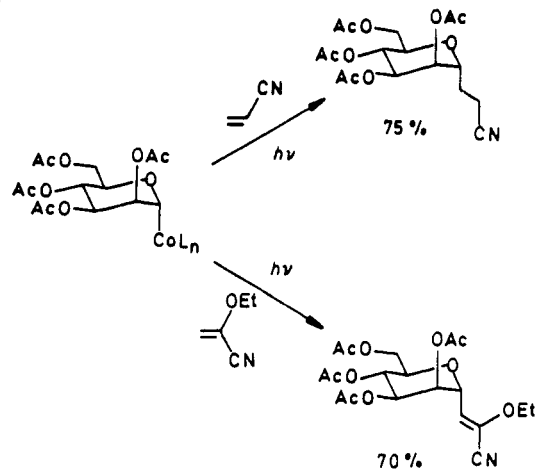
Scheme 9



Scheme 10



Scheme 11

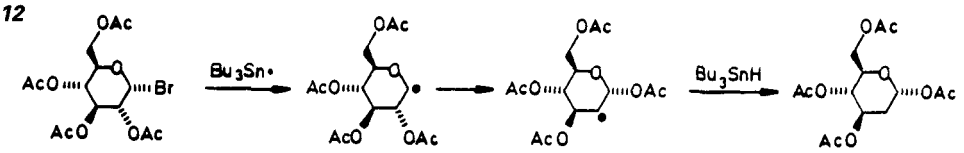


With alkenes these radicals lead after combination with the Co(II) complex to new organo-Co compounds. Depending upon the substituent Y either solvolysis or elimination reactions lead to products (ref. 4) (Scheme 10).

Glycosyl-Co complexes react with acrylonitrile to addition products whereas ethoxyacrylonitrile undergoes substitution reactions, which give aldol reaction products after hydrolysis (Scheme 11).

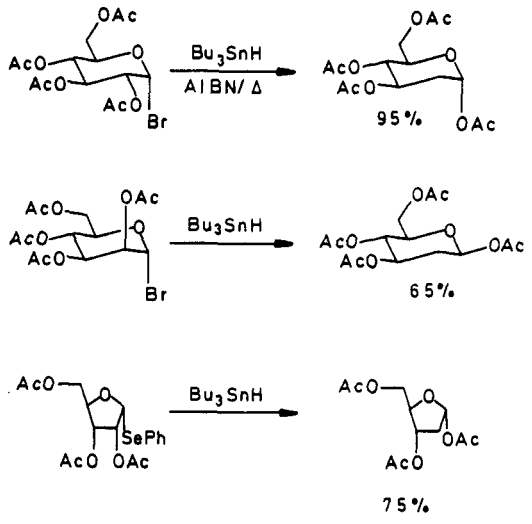
In the absence of radical traps acylated glycosyl radicals isomerize. Thus, in the presence of only tiny concentrations of tributylstannane, these glycosyl radicals undergo an ester migration. Hydrogen atom abstraction then leads to an 2-deoxysugars (ref. 5) (Scheme 12).

Scheme 12

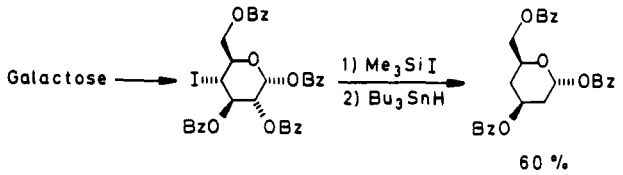


This is a general synthesis of 2-deoxysugars, that can be applied to α- or β-glycosides, to pyranoses and furanoses (Scheme 13). Rearrangement only occurs if the anomeric carbon atom is the radical center. Therefore halogen atoms at other positions of the carbohydrates lead to reduction products without migration (Scheme 14). The driving force for the rearrangement is the formation of an acetal-like center (ref. 6) (Scheme 15).

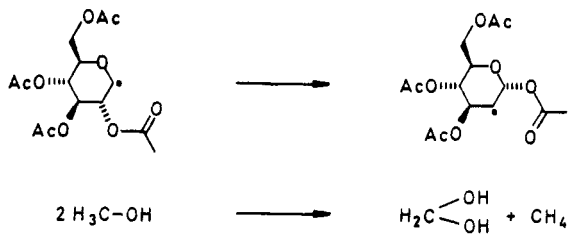
Scheme 13



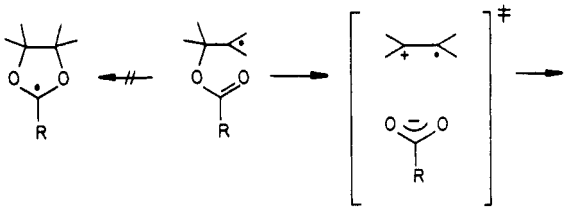
Scheme 14



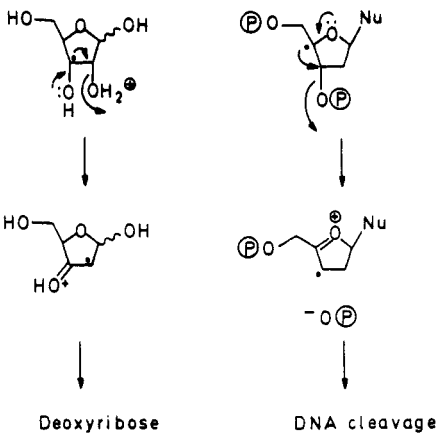
Scheme 15



Scheme 16



Scheme 17



Solvent and substituent effects have shown that the ester migration proceeds via a dipolar transition state, intermediates are presumably not formed (ref. 7) (Scheme 16).

Similar to these isomerization reactions are fragmentation reactions of carbohydrate radicals that are postulated to occur in the biosynthesis of deoxyribose (ref. 8) and the radical induced DNA cleavage (ref. 9) (Scheme 17).

Acknowledgements This work was supported by the VW-Stiftung and the Deutsche Forschungsgemeinschaft.

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