Tetrahedron Letters,Vol.25,No.26,pp 2743-2746,1984 0040-4039/84 $3.00 + .00
Printed in Great Britain

DIASTEREOSELECTIVE SYNTHESIS OF BRANCHED 2-DEOXY SUGARS VIA RADICAL C-C BOND FORMATION REACTIONS

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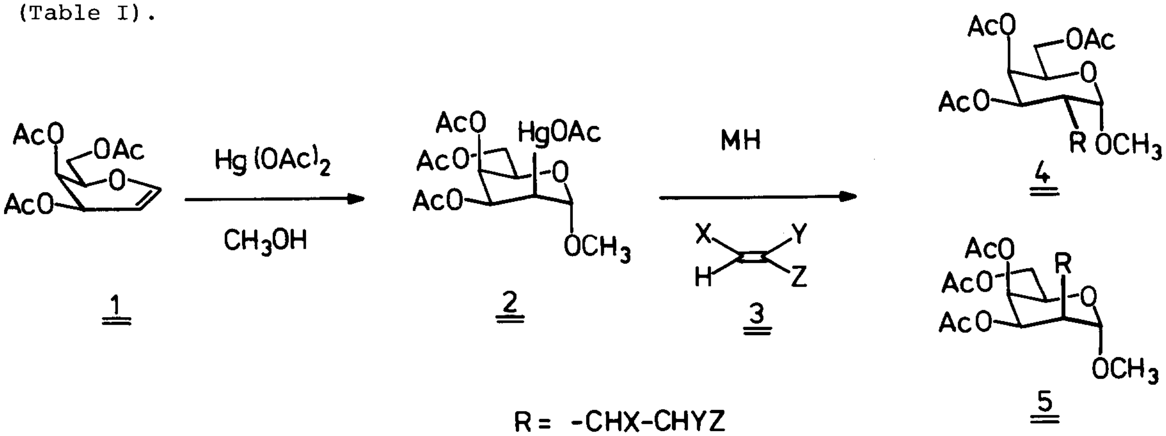
Summary: From glycals 1 and 6, 2-deoxy sugars can be synthesized in 40-72% yields. With 1,2-disubstituted alkenes 3 this radical C-C bond formation reaction leads with high stereoselectivity to the isomers 4 and 8.

The formation of C-C bonds via solvomercuration of electron-rich alkenes and reduction with hydrides in the presence of electron-poor alkenes is a new versatile method$^{1)}$ for the synthesis of target molecules$^{2)}$. We have now shown that this method can also be applied to carbohydrate chemistry. Solvomercuration of the galactal 1 leads, in a stereospecific reaction, to the organomercuric salt 2$^{3)}$. In situ reduction of 2 with boro or tin hydrides (HM) in the presence of a tenfold excess of alkenes 3 gives branched deoxy sugars 4 and 5$^{4)}$. The yields of the overall reactions are 40 to 67% (Table I). The major deoxy sugar products are formed with the new C-C bond in the equatorial position. The selectivity depends on the alkene substituents: With acrylonitrile, a 2:1 mixture of 4 and 5 is formed, whereas with fumaric ester only isomer 4 can be detected (Table I).



R= -CHX-CHYZ

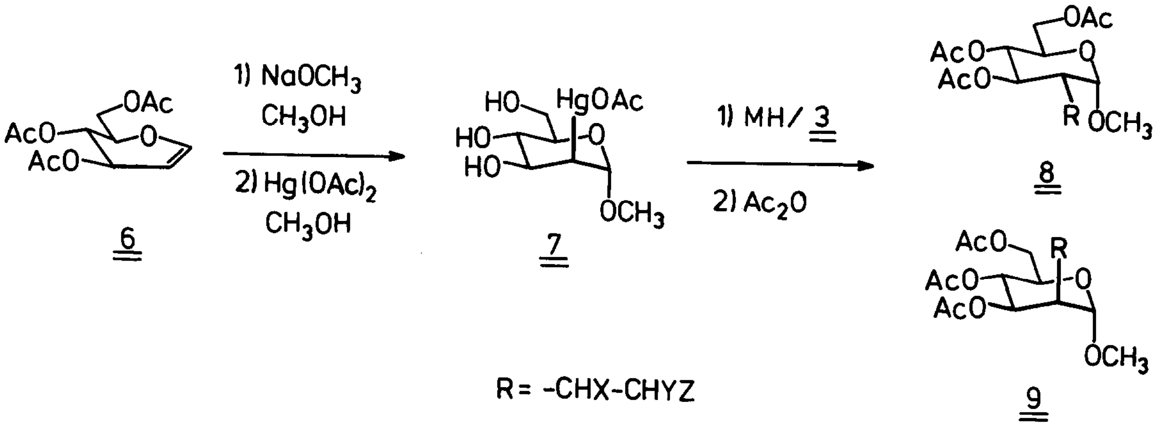


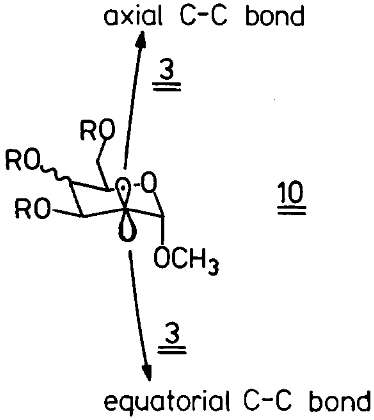
Table I

Yields and stereoselectivity of the formation of 2-deoxy sugars via solvomercuration and radical C-C bond formation of glycals 1 and 6.

Glycal	Alkene 3 X	 Y	 Z	MH	Yield (%) 4+5 or 8+9	Stereoselectivity 4:5 or 8:9
1	H	H	CN	Bu_4NBH_4	60	67/33
1	H	H	CN	Bu_3SnH	67	67/33
1	H	H	CO_2CH_3	Bu_3SnH	55	71/29
1	CN	H	CN	Bu_3SnH	55	90/10
1	CO_2CH_3	H	CO_2CH_3	Bu_4NBH_4	50	>97/<3
1	CH_3	CN	CN	Bu_3SnH	40	>95/<5
6	H	H	CN	Bu_3SnH	72	67/33
6	CN	H	CN	Bu_3SnH	40	>95/<5

Since glucals with an equatorial substituent at C-4 react stereospecifically with mercuric acetate only if the OH groups are not acetylated[5], the mercuration of triacetyl glucal 6 was carried out after in situ solvolysis. Reduction of 7 in the presence of alkene 3 and acetylation gives 8 and 9[4] in 40 and 72% yield (Table I). Again, the equatorial C-C bond formation predominates with acrylonitrile giving a 2:1 mixture of products 8 and 9 and fumarodinitrile yielding 8 as the only detectable isomer.

The conformation of the carbohydrate radical is not known. But the predominant formation of an equatorial C-C bond can be explained by π-radical 10 in which one lobe of the half-occupied orbital tends away from the ring and is more easily accessible than the other lobe. This leads to differences in steric effects and 1,2-disubstituted alkenes react with high stereoselectivity because substituents at the attacked C-atom of alkene 3 always increase these differences$^{6)}$.



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Acknowledgement. This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

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4) Assigment of the structures followed unequivocally from the ^{1}H-NMR spectra (300 MHz). With 1,2-di- or trisubstituted alkenes 3 two diastereomers, denoted as I and II, are formed:
4a ($R=CH_2CH_2CN$): $\delta=4.81$ (d, 1H, H-1); 5.06 (dd, 1H, H-3); 5.32 (d, 1H, H-4); $J_{1,2}=3.4$ Hz; $J_{2,3}=11.7$; $J_{3,4}=3.1$ Hz; $J_{4,5}<1$ Hz.
5a ($R=CH_2CH_2CN$): $\delta=4.72$ (s, 1H, H-1); 5.23-5.30 (m, 1H, H-4); 5.38 (dd, 1H,

H-3); $J_{1,2}$<1Hz; $J_{2,3}$=5.1 Hz; $J_{3,4}$=3.5 Hz.

4b ($R=CH_2CH_2CO_2CH_3$):δ=4,77 (d, 1H, H-1); 5.06 (dd, 1H, H-3); 5.26-5.36 (m, 1H, H-4); $J_{1,2}$=3.4 Hz; $J_{2,3}$=11.8 Hz; $J_{3,4}$=3.1 Hz.

5b ($R=CH_2CH_2CO_2CH_2$):δ=4.70 (s, 1H, H-1); 5.26-5.36 (m, 2H, H-3, H-4); $J_{1,2}$<1Hz.

4c ($R=CHCNCH_2CN$): I: δ=2.65 (ddd, 1H, H-2); 4.98 (d, 1H, H-1); 5.26 (dd, 1H, H-3); 5.40 (d, 1H, H-4); $J_{1,2}$=3.4 Hz; $J_{2,3}$=11.7 Hz; $J_{3,4}$=3.1 Hz; $J_{4,5}$<1 Hz. II: δ=2.53-2.71 (m, 1H, H-2); 4.95 (d, 1H, H-1); 5.28 (dd, 1H, H-3); 5.40 (d, 1H, H-4); $J_{1,2}$=3.3 Hz; $J_{2,3}$=11.8 Hz; $J_{3,4}$=3.1 Hz; $J_{4,5}$=<1 Hz.

5c ($R=CHCNCH_2CN$):δ=4.78 (d, 1H, H-1); 5.53, 5.58 (dd, 1H, H-3); $J_{1,2}$=1.0 Hz; $J_{2,3}$=4.5 Hz; $J_{3,4}$=3.6 Hz.

4d ($R=CH(CO_2CH_3)CH_2CO_2CH_3$): I: δ=2.70-2.83 (m, 1H, H-2); 4.82 (d, 1H, H-1); 5.33 (dd, 1H, H-3); 5.33-5.39 (m, 1H, H-4); $J_{1,2}$=3.1 Hz; $J_{2,3}$=12.0 Hz, $J_{3,4}$=3.5 Hz. II: δ=2.70-2.83 (m, 1H, H-2); 4.72 (d, 1H, H-1); 5.23 (dd, 1H, H-3); 5.33-5.39 (m, 1H, H-4); $J_{1,2}$=3.0 Hz; $J_{2,3}$=12.2 Hz; $J_{3,4}$=3.2 Hz.

4e ($R=CH(CH_3)CH(CN)_2$): I: δ=2.50 (dt, 1H, H-2); 4.87 (d, 1H, H-1); 5.28 (dd, 1H, H-3); 5.38 (d, 1H, H-4); $J_{1,2}$=3.0 Hz; $J_{2,3}$=12,0 Hz; $J_{3,4}$=3.1 Hz; $J_{4,5}$<1 Hz. II: δ=4.88 (d, 1H, H-1); 5.21 (dd, 1H, H-3); 5.40 (d, 1H, H-4); $J_{1,2}$=3.0 Hz; $J_{2,3}$=11.5 Hz; $J_{3,4}$=2.9 Hz; $J_{4,5}$<1 Hz.

8a ($R=CH_2CH_2CN$):δ=3.86-3.96 (m, 1H, H-5); 4.08 (dd, 1H, H-6); 4.29 (dd, 1H, H-6); 4.78 (d, 1H, H-1), 4.98 (dd, 1H, H-4); 5.21 (dd, 1H, H-3); $J_{1,2}$=3.4 Hz; $J_{2,3}$=11.1 Hz; $J_{3,4}$=9.2 Hz; $J_{4,5}$=10.1 Hz; $J_{5,6}$=2.3 Hz; $J_{5,6'}$=4.7 Hz; $J_{6,6'}$=12.3 Hz.

9a ($R=CH_2CH_2CN$):δ=3.86-3.94 (m, 1H, H-5); 4.11 (dd, 1H, H-6); 4.22 (dd, 1H, H-6); 4.65 (d, 1H, H-1): 5.05 (t, 1H, H-4); 5.42 (dd, 1H, H-3); $J_{1,2}$=1.7 Hz; $J_{2,3}$=5.2 Hz; $J_{3,4}$=9.7 Hz; $J_{4,5}$=9.7 Hz; $J_{5,6}$=2,5 Hz; $J_{5,6'}$=5.0 Hz; $J_{6,6'}$=12.2 Hz.

8c ($R=CHCNCH_2CN$): I: δ=3.96 (ddd, 1H, H-5); 4.10 (dd, 1H, H-6); 4.29 (dd, 1H, H-6'), 4.94 (d, 1H, H-1); 5.03 (dd, 1H, H-4); 5.36 (dd, 1H, H-3); $J_{1,2}$=3.4 Hz; $J_{2,3}$=11.4 Hz; $J_{3,4}$=9.1 Hz; $J_{4,5}$=10.2 Hz; $J_{5,6}$=2.3 Hz; $J_{5,6'}$=4.6 Hz; $J_{6,6'}$=12,3 Hz. II: δ=2.49 (ddd, 1H, H-2); 3.98 (ddd, 1H, H-5); 4.10 (dd, 1H, H-6); 4.29 (dd, 1H, H-6'); 4.93 (d, 1H, H-1), 5.02 (dd, 1H, H-4); 5.40 (dd, 1H, H-3); $J_{1,2}$=3.5 Hz; $J_{2,3}$=11.3 Hz; $J_{3,4}$=9.0Hz; $J_{4,5}$=10.3 Hz; $J_{5,6}$=2.3 Hz; $J_{5,6}$=4.4 Hz; $J_{6,6'}$=12.3 Hz.

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(Received in Germany 15 March 1984)