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SYNTHESIS OF HIGHER-CARBON SUGARS BY TRIBUTYLTIN HYDRIDE - AZOBISISOBUTYRONITRILE INDUCED RADICAL ADDITIONS

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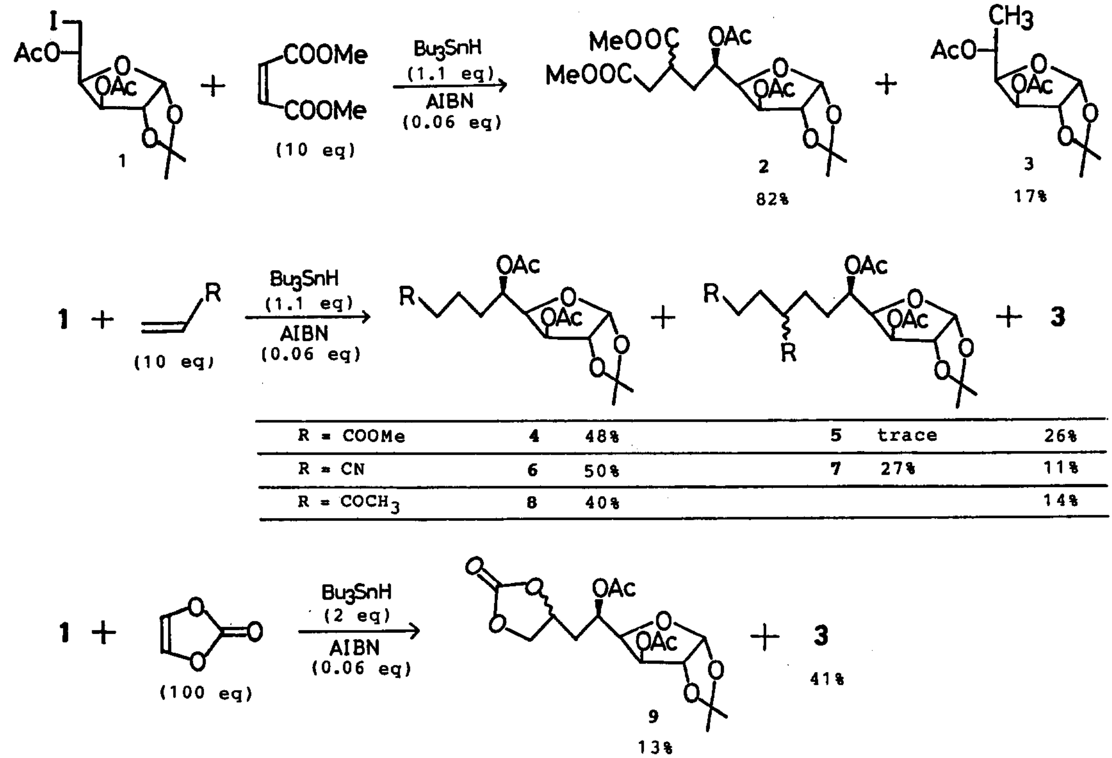
Abstract : The Bu_3SnH - AIBN induced radical additions of 3,5-di-O-acetyl-6-deoxy-6-iodo-1,2-O-isopropylidene-α-D-gluco- and -allofuranose (**1** and **10**), and methyl 5-deoxy-5-iodo-2,3-O-isopropylidene-β-D-ribofuranoside (**19**) to dimethyl maleate, methyl acrylate, acrylonitrile, methyl vinyl ketone, and vinylene carbonate gave various types of higher-carbon sugars.

Higher-carbon sugars were found in nature as important substructural units of various types of antibiotics such as hikizimycin,[2] apramycin,[3] tunicamycin,[4] and mildiomycin.[5] Valuable and interesting biological properties of these antibiotics as well as the unique and complex structures of the sugar constituents caused many research groups to investigate total sytheses of these antibiotics; the central problems of these investigations were the syntheses of higher-carbon sugars.[6] However, there are only two communications utilizing radical process; radical addition - eliminations of 6-bromo-6-deoxy-D-glucopyranosides with allyltin[7] or vinyltin[8] derivatives.

Successful results of tributyltin hydride (Bu_3SnH) - azobisisobutyronitrile (AIBN) induced radical additions of glycosyl halides[9] or xanthate[10] to electron deficient olefins for the synthesis of C-glycosyl compounds prompted us to investigate similar radical additions of terminal halogenosugars to olefins. Although total syntheses of octosyl acid A were recently communicated by two groups,[11,12] our synthetic interests are still focussed on octosyl acids,[13] ezomycins,[14] and griseolic acids,[15] because of their nucleoside-like structures with bicyclic higher-carbon sugars. Thus we examined the carbon-chain elongation at terminal positions of furanose derivatives of D-glucose, D-allose, and D-ribose using radical addition reactions.

Separate and simultaneous addition over 2 h of two solutions of Bu_3SnH (1.1 eq) in benzene and of AIBN (0.06 eq) in benzene to a refluxing solution of 3,5-di-O-acetyl-6-deoxy-6-iodo-1,2-O-isopropylidene-α-D-glucofuranose (**1**)[16] (1.0 eq) and dimethyl maleate (10 eq) in benzene under argon, and further refluxing of the resulting solution for 30 min gave a diasteremeric mixture (ca. 1 : 1) of methyl 3,5-di-O-acetyl-6,7,8-trideoxy-1,2-O-isopropylidene-7-C-methoxycarbonylnonofuranuronate (**2**)[17] (82% yield) along with the reduced product, 3,5-di-O-acetyl-6-deoxy-1,2-O-isopropylidene-α-D-glucofuranose (**3**)[18] (17% yield). Similar treatments of **1** with methyl acrylate,

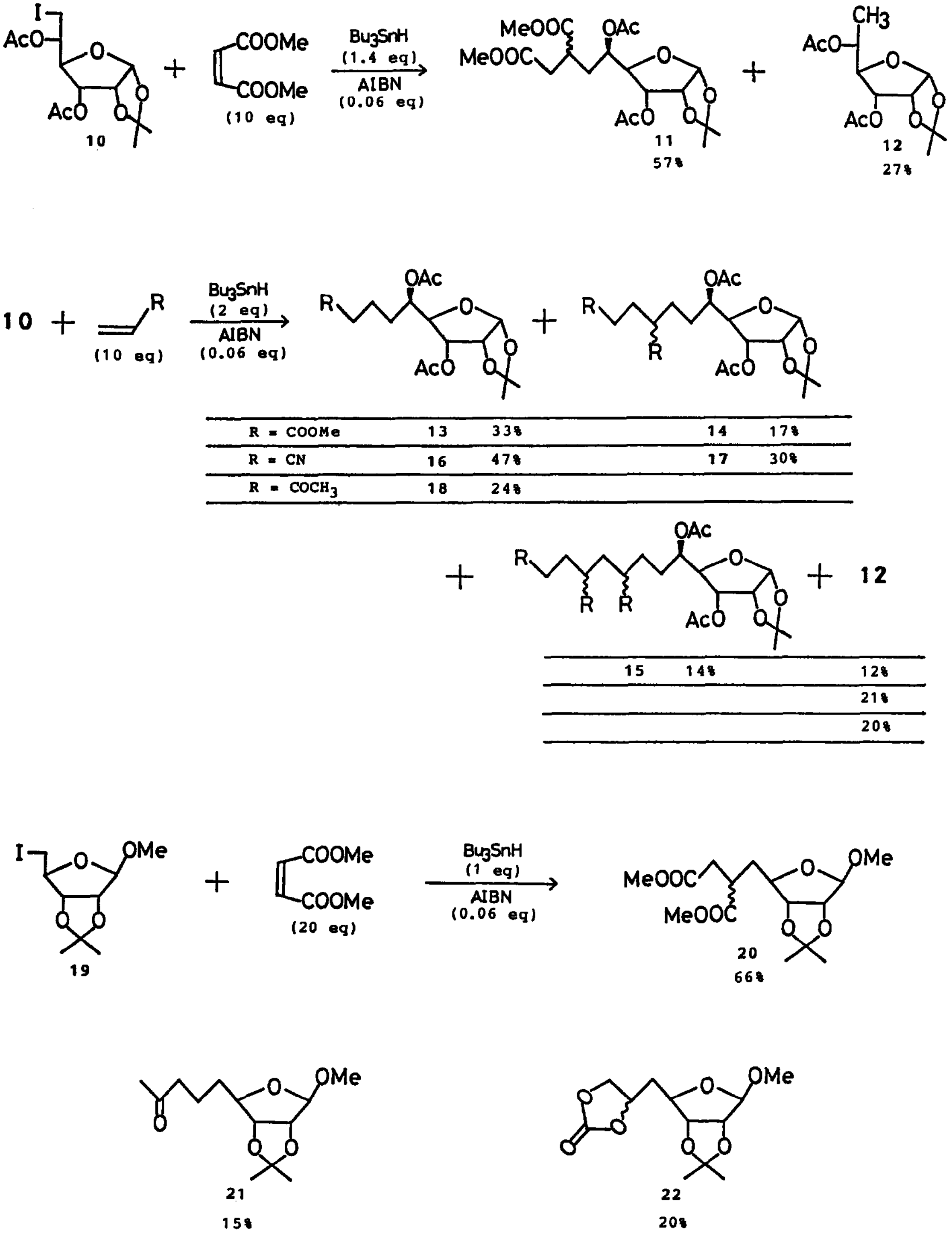


R = COOMe	4	48%	5	trace	26%
R = CN	6	50%	7	27%	11%
R = $COCH_3$	8	40%			14%

Scheme 1

acrylonitrile, and methyl vinyl ketone gave the corresponding adducts **4**[18] (48% yield), **6**[18] (50% yield), and **8**[18] (40% yield), respectively. In these three reactions, 1 : 2, 1 : 3, and higher addition products were also formed (t.l.c. examinations); among these higher adducts, 1 : 2 adducts with methyl acrylate (**5**)[19] (trace) and 1 : 2 adducts with acrylonitrile (**7**)[19] (27% yield) were isolated. The formations of these higher adducts are due to the high reactivities of these olefins. Several attempts to reduce the formation of these higher adducts resulted in increasing the formation of the reduced products.[20] In the reaction with less reactive vinylene carbonate[10] (100 eq), desired addition product **9**[19] was obtained in a 13% yield along with the reduced product **3** (41% yield).

Similar reactions of 3,5-di-O-acetyl-6-deoxy-6-iodo-1,2-O-isopropylidene-α-D-allofuranose (**10**)[16] with dimethyl maleate, methyl acrylate, acrylonitrile, and methyl vinyl ketone , and of methyl 5-deoxy-5-iodo-2,3-O-isopropylidene-β-D-ribofuranoside (**19**)[16] with dimethyl maleate, methyl vinyl ketone, and vinylene carbonate gave the desired adducts as illustrated in Scheme 2, **11**[19] (57% yield), **13**[18] (33% yield) , **16**[18] (47% yield), **18**[18] (24% yield), **20**[19] (66% yield), **21**[18] (15% yield), and **22**[19] (20% yield), respectively. Higher addition products **14**[19] (17% yield), **15**[19] (14% yield), and **17**[19] (30% yild) were also isolated.



R = COOMe	13	33%	14	17%	15	14%	12%
R = CN	16	47%	17	30%			21%
R = $COCH_3$	18	24%					20%

Scheme 2

From the above results it was concluded that Bu_3SnH - AIBN induced radical addition reactions are also applicable to terminal halogeno sugars for syntheses of various types of higher-carbon sugars.

NOTES AND REFERENCES

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17 One diastereomer (**2a**) of the two of **2** was obtained as crystalls from hexane (33% yield); the other (**2b**) was as a syrup containing a small amount of **2a** (28% yield). The configurations at position 7 of **2a** and **2b** were not determined.

18 The structures of these compounds were confirmed by their ir and nmr spectra, and by their micro-elemental analyses.

19 These compounds were obtained as mixtures of the corresponding diastereomers.

20 Using a reduced amount (3.0 eq) of methyl acrylate, **1** gave the reduced product **3** in a 45% yield and the desired adduct **2** in a 34% yield. Further examinations are now in progress.

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