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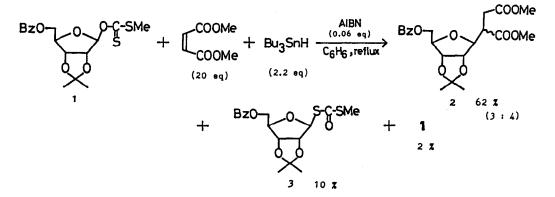
ADDITIONS OF A RIBOFURANOSYL RADICAL TO OLEFINS. A FORMAL SYNTHESIS OF SHOWDOMYCIN

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<u>Abstract</u>: The Bu₃SnH - AIBN induced radical additions of $5-\underline{0}$ -benzoyl-2,3- $\underline{0}$ -isopropylidene-1- $\underline{0}$ -methylthiothiocarbonyl- β -D-ribofuranose (1) to olefins such as dimethyl maleate, methyl vinyl ketone, methyl acrylate <u>etc</u>. gave corresponding \underline{C} -ribofuranosyl compounds. And one of the adducts was converted to the key intermediate of a showdomycin synthesis.

Organotin compound mediated additions of glycosyl radicals to olefins have been recently shown to give <u>C</u>-glycosyl compounds in good yields²⁻⁷. There is, however, no application of this methodology to the synthesis of naturally occurring <u>C</u>-glycosyl compounds or their analogues. In a previous communication, we have described the α, α' -azobisisobutyronitrile (AIBN) tributyltin hydride (Bu₃SnH) induced additions of glucopyranosyl radicals to olefins and suggested the utility of these addition reactions for the synthesis of <u>C</u>-glycosyl heterocycles such as showdomycin analogues⁸. As a part of this approach, addition reactions of a ribofuranosyl radical⁹ to olefins and a formal synthesis of showdomycin will be described in this communication.

Since $2,3-\underline{0}$ -isopropylidene-5- $\underline{0}$ -trityl- $\boldsymbol{\beta}$ -D-ribofuranosyl chloride¹⁰ and 2,3,5-tri- $\underline{0}$ -acetyl-D-ribofuranosyl bromide¹¹ were both proved to be unsuitable¹² as precursors of ribofuranosyl radicals, 5- $\underline{0}$ -benzoyl-2,3- $\underline{0}$ -isopropylidene-1- $\underline{0}$ -methylthiothiocarbonyl- $\boldsymbol{\beta}$ -D-ribofuranose (1)¹³ was used as a ribofuranosyl radical precursor¹⁴. Dropwise addition of a solution of Bu₃SnH (2.2 eq) in benzene to a refluxing solution of 1 (1.0 eq), dimethyl maleate (20 eq), and AIBN (0.06 eq) in benzene gave a diastereomeric mixture of dimethyl



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 $2-(5-\underline{0}-\text{benzoyl}-2,3-\underline{0}-\text{isopropylidene}-\beta-D-\text{ribofuranosyl})$ succinates (2)¹⁵ (62% yield), the rearranged product, $5-\underline{0}-\text{benzoyl}-2,3-\underline{0}-\text{isopropylidene}-1-\underline{S}-(\text{methyl-thio})$ carbonyl-1-thio- β -D-ribofuranose (3)¹⁶ (10% yield), and 1 (2% recovery yield). In this reaction, 2.2 equivalents of Bu₃SnH was needed for the disappearance of 1 (t.l.c. examination): addition of Bu₃Sn• to dimethyl maleate occurs competitively. Thus the reactivity of 1 with Bu₃Sn• was decided to be rather low and comparable to that of dimethyl maleate.

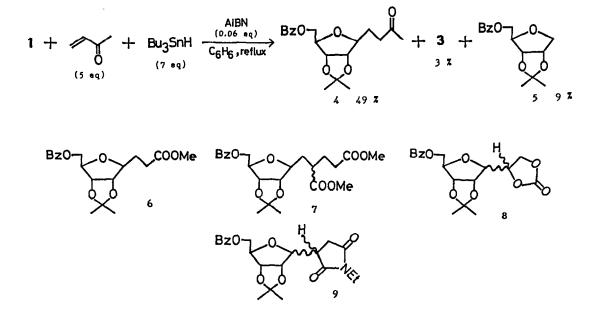
In the similar reactions of 1 with methyl vinyl ketone and methyl acrylate, more reactive than dimethyl maleate^{4,8}, it is necessary to reduce the amount of olefin and/or to increase the amount of Bu₃SnH in order to minimize the competitive addition of Bu₃Sn• to olefin. Thus, by the use of 5 equivalents of methyl vinyl ketone and 7 equivalents of Bu₃SnH, the corresponding <u>C</u>-glycosyl compound, $4-(5-\underline{0}-\text{benzoyl}-2,3-\underline{0}-\text{isopropylidene}-\mathbf{\beta}-D-\text{ribofuranosyl})-2-butanone (4)¹⁶ (49% yield), 3 (3% yield), and the reduced product, 1,4-anhydro-5-\underline{0}-benzoyl-2,3-\underline{0}-\text{isopropylidene}-D-\text{ribitol} (5)¹⁶ (9% yield) were obtained; and by the use of 4 equivalents of methyl acrylate and 2 equivalents of Bu₃SnH, methyl <math>3-(5-\underline{0}-\text{benzoyl}-2,3-\underline{0}-\text{isopropylidene}-\mathbf{\beta}-D-\text{ribofuranosyl})$ propionate (6)¹⁶ (34% yield), a diastereomeric mixture of methyl 5-(5-\underline{0}-benzoyl-2,3-\underline{0}-\text{isopropylidene}-\mathbf{\beta}-D-\text{ribofuranosyl})propionate (6)¹⁶ (34% yield), a diastereomeric mixture of methyl 5-(5-\underline{0}-benzoyl-2,3-\underline{0}-\text{isopropylidene}-\mathbf{\beta}-D-\text{ribofuranosyl})propionate (6)¹⁶ (34% yield), a diastereomeric mixture of methyl 5-(5-\underline{0}-benzoyl-2,3-\underline{0}-\text{isopropylidene}-\mathbf{\beta}-D-\text{ribofuranosyl})-4-methoxycarbonylpentano-ate (7) (14% yield), and 3 (5% yield) were obtained.

Treatment of 1 with 5 equivalents of dimethyl acetylenedicarboxylate and 2.7 equivalents of Bu_3SnH gave no <u>C</u>-glycosyl compounds (almost all of 1 remained unchanged : t.l.c. examination), whereas treatment of 1 with 1 equivalent of dimethyl acetylenedicarboxylate and 2.7 equivalents of Bu_3SnH gave a diastereomeric mixture of 2 (34% yield), 3 (5% yield), and 5 (23% yield). It is clear that dimethyl acetylenedicarboxylate reacted first with Bu_3Sn and then with ribofuranosyl radical to give 2 after the normal working up.

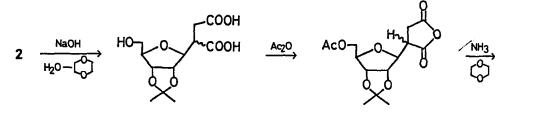
Vinylene carbonate, maleimide, maleic anhydride, <u>N</u>-ethylmaleimide, and furan were also applied as olefin derivatives to the reaction under several conditions. Among these olefins vinylene carbonate and <u>N</u>-ethylmaleimide gave the corresponding <u>C</u>-ribofuranosyl compounds, $4-(5-\underline{O}-\text{benzoyl}-2,3-\underline{O}-\text{isopropyli-}$ dene-D-ribofuranosyl)-1,3-dioxolan-2-one (**8**)¹⁷ (20% yield) and 2-(5-\underline{O}-\text{benzoyl}-2,3-\underline{O}-\text{isopropylidene-D-ribofuranosyl})-<u>N</u>-ethylmaleimide (9)¹⁷ (28% yield), respectively. It was thus concluded that ribofuranosyl radical additions to olefins has potential utilities for the construction of various types of <u>C</u>ribofuranosyl compounds.

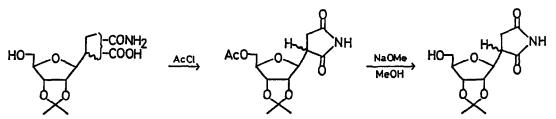
Then, the diastereomeric mixture of 2 was converted to $2-(5-\underline{0-t}-buty)di-phenylsilyl-2,3-\underline{0}-isopropylidene-$ **<math>\beta**-D-ribofuranosyl)succinimide (12 and 13) straightforword by 6 steps in a 25.4 % overall yield as shown in Scheme 1. The **\beta**-configurations at 1'-positions of 12 and 13 were confirmed at the stage of the corresponding 5'-OH derivatives (10 and 11), which were partly isolated and proved to be identical with authentic specimen¹⁸, respectively. The mixture of DL-12 and -13 had been converted to DL-showdomycin (DL-14) by the

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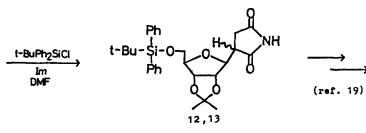


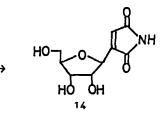
Scheme 1





10,11





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sequential treatments with LICA, PhSeCl, NaIO,, and TFA¹⁹. Therefore the synthesis of showdomycin (14) was achieved formally. This synthesis is the third example of showdomycin synthesis via C - C bond formation between ribofuranosyl moiety and C_{L} -aglycone moiety^{20,21}.

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- About $\tilde{3}$: 4 mixture of the corresponding diastereomers. 15 The nmr spectrum and the micro-elemental analysis data of this mixture agree well with its structure.
- 16 The structures of these compounds were confirmed by their ir and nmr spectra, and by their micro-elemental analyses.
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