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Preliminary communication

A STANNYL MODIFICATION OF THE HILBERT—JOHNSON METHOD FOR THE SYNTHESIS OF PYRIMIDINE NUCLEOSIDES

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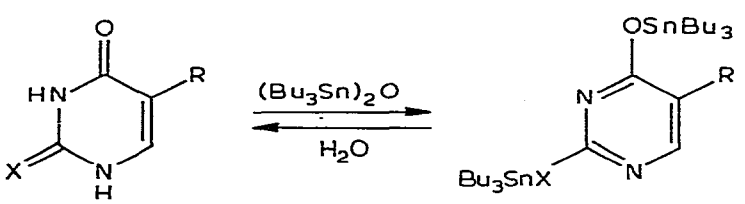
Summary

Reaction of tri-n-butylstannylated pyrimidines with peracylated β-D-ribofuranose in the presence of tin tetrachloride afforded high yields of protected pyrimidine nucleosides.

Among the available synthetic procedures for pyrimidine nucleosides, the silyl modification of the Hilbert—Johnson method with halogenoses [1] and with peracylated sugars in the presence of a Friedel—Crafts catalyst [2] has become the most frequently employed procedure.

As an alternative method, we report here a modified procedure for the synthesis of pyrimidine nucleosides which is based on the reactivity of stannylated pyrimidines (IIa—IId). These were prepared simply by refluxing the corresponding pyrimidines (Ia—Id) with bis(tri-n-butylstannyl) oxide in toluene with continuous azeotropic removal of water*. Neither attempted distillation nor column chromatography on silica gel was successful for the purification of stannylated pyrimidines. ^{1}H NMR data (δ, ppm in $CDCl_3$) of the crude IIa—IId, however,



(Ia) X = O, R = H
(Ib) X = O, R = Me
(Ic) X = O, R = Br
(Id) X = S, R = H

(IIa–IId)

*For the general preparative methods for trialkylstannyl alkoxides, see ref. 3.

TABLE 1

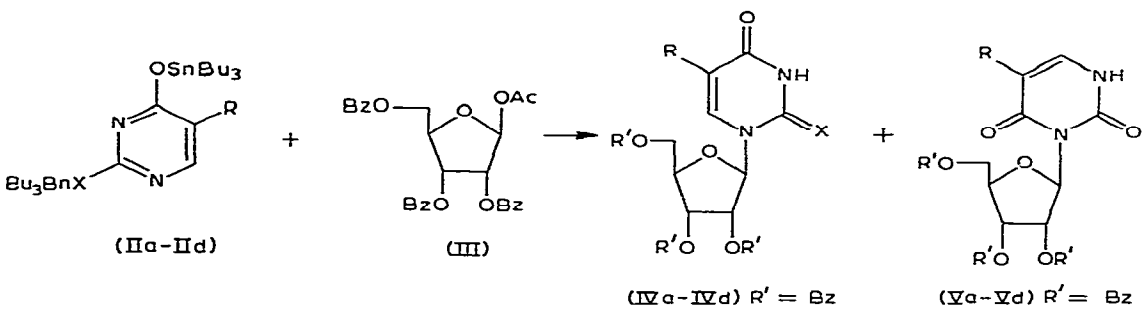
REACTION CONDITIONS AND PRODUCTS OF COMPOUNDS II WITH B-D-RIBOFURANOSYL ACETATE (III)

Starting compound	X	R	Reaction time	Reaction temperature (°C)	Solvent	Product	Yield (%)	M.p.[a] (°C)	$[\alpha]_D(c)$ in $CHCl_3$	Reference
IIa	O	H	6 days	10	CH_2Cl_2	IVa (40%)	70	145—148	−40.2° (0.58)	7[b]
						Va (60%)		118—121	+25.1° (1.1)	6
IIb	O	Me	2 days	20	$ClCH_2CH_2Cl$	IVb	63	167—169	−81.9° (1.0)	7[b]
IIc	O	Br	19 h	20	$ClCH_2CH_2Cl$	IVc	97	180—183	−99.2° (0.64)	8
IId	S	H	19 h	20	$ClCH_2CH_2Cl$	IVd	90	147—149	−33.9° (0.79)	5

[a]M.P. are not corrected. Yields are not optimized. All reactions were carried out under nitrogen atmosphere. [b]Identified by comparison with the authentic samples prepared by the published method [7].

supported each structure: IIa, 5.60, 1H,d, J 7 Hz for C(5)—H; 7.05, 1H,d, J 7 Hz for C(6)—H; IIb, 6.87, 1H,s, hhw 3 Hz for C(6)—H; 1.88, 3H,s, for C(5)—CH_3; IIc, 7.30, 1H,s, for C(6)—H; IId, 6.17, 1H,d, J 6 Hz for C(5)—H, 7.80, 1H,d, J 6 Hz for C(6)—H. Since stannylated pyrimidines are easily hydrolysed back to the starting pyrimidines on exposure to atmospheric moisture, they were used directly, without isolation, for the next step after evaporation of toluene under reduced pressure.

The reactions of the stannylated pyrimidines with peracylated β-D-ribofuranose were examined. In the presence of a Lewis acid such as tin tetrachloride the corresponding nucleosides were formed in high yields. The reaction can proceed under reasonably mild conditions and is stereochemically controlled. The experimental operation is simple, as seen from the following example. A solution of 2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl acetate (III) [4], 2m M in 10 ml dry dichloroethane containing an equivalent amount of tin tetrachloride, was kept at 20° C for 3 h. To this solution was added the stannylated pyrimidine (IId, one equivalent in 2 ml of dichloroethane) at 20° C. After it had been stirred for 19 h at 20° C, the mixture was poured into an ice cold aqueous sodium bicarbonate solution and then was extracted by dichloromethane. The organic layer was washed with water, dried over anhydrous magnesium sulfate and evaporated. The residual oil was purified by silica gel column chromatography (toluene/ether/cyclohexane 10/10/1), affording the benzoylated nucleoside (IV) [5] in 90% yield. Bis(tri-n-butylstannyl) oxide could be recovered in better than 80% yield by refluxing the less polar fraction from the silica gel column in methanolic sodium hydroxide and subsequent distillation.



It is to be noted that in the case of stannylated uracile the major product (42% yield) was isouridine (Va) [6] while the normal ribosidation product (IVa) was obtained in only 28% yield. The efficient recovery of organotin compounds from the reaction mixture makes this procedure of some advantage over the silyl method where the recovery of trimethylsilyl derivatives is not efficient.

Table 1 lists the reaction conditions and products for the reaction of compounds II with β-D-ribofuranosyl acetate (III).

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Book review

"Polymer Syntheses", Vol. II, by S.R. Sandler and W. Karo, Academic Press, New York/San Francisco/London, 1977, $39.50, £28.05.

This volume complements very nicely the first volume by the same authors which was concerned primarily with linear polymers from both condensation and addition polymerization reactions. This book provides an equally well-detailed and extensive treatment of the cross-linked or thermoset polymers.

As in the first volume, the organization in each chapter includes an introductory description of the polymerization reactions involved, including valuable tabular information on reaction conditions and product descriptions, followed by detailed discussions of preparative methods. The authors claim that the "procedures are chosen on the basis of safety considerations and of being carried out with standard laboratory equipment," and a survey of the procedures included certainly seems to justify this claim.

All chapters are referenced through 1974 with at least 100, and generally more, literature citations per chapter. The specific types of polymerization reactions included are the following: amino resins (urea-and melamine-formaldehyde resins and others): phenol-aldehyde resins; epoxides; silicones; alkyds; polyacetals and poly(vinyl acetals); poly(vinyl ethers); poly(*N*-vinylpyrrolidone); acrylic acid and related monomers; and poly(vinyl chloride). The last two chapters are particularly valuable additions to the first volume on the polymerization of important vinyl monomers, but the greatest value of this book is in its extensive coverage of thermoset resins, a subject which is minimized in other books on laboratory procedures in polymer chemistry.

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