Synthesis of 1,4-Dihydro-N-[1' : 3' : 4' : 6'-tetraacetylglucosyl-(2')]-3,5-diacetylpyridine Derivatives

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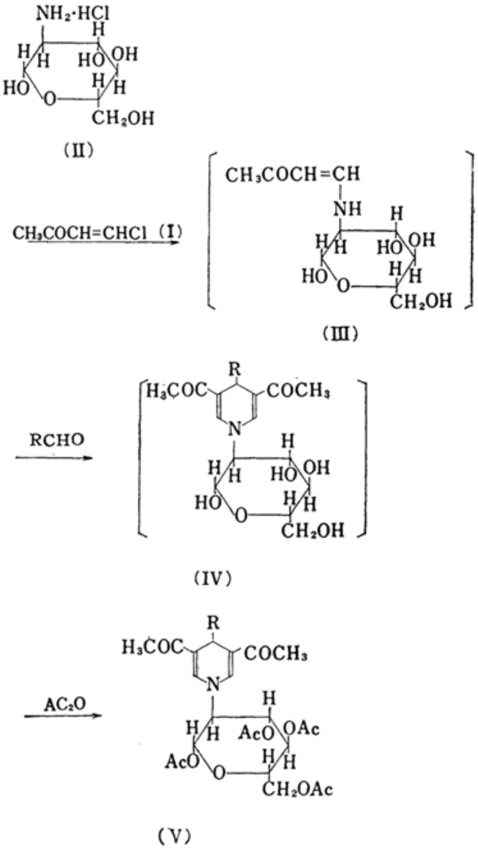
Fischer et al.[1] had reported the synthesis of N-[tetraacetylglucosyl-(1')]-pyridinium salts by the condensation of pyridine and tetraacetylglucosyl bromide. As a model compound of DPN[*1], Karrer[2] and Todd[3] synthesized various sugar derivatives of nicotinamide by this method. We could not find any other N-sugar derivatives of pyridine or pyridine derivatives in the literature.

In his previous papers[4], Inouye has reported that 1,4-dihydro-3,5-diacetylpyridine derivatives are obtained in a good yield by the condensation of aldehydes with methyl β-(N-monosubstituted amino)-vinylketone. According to this method, 1,4-dihydro-N-[glucosyl-(2')]-3,5-diacetylpyridine derivatives (IV) will be obtained by the condensation of aldehydes with methyl β-[N-glucosyl-(2')-amino]-vinylketone (III), which, in trun, is prepared from methyl β-chlorovinylketone (I) and glucosamine (II). In fact, we could obtain the expected compound, V. Although the yield of V was not good, similar derivatives with other sugar or substituents can be synthesized by this method. We will report on the results of this experiment.

In the presence of potassium carbonate, aldehyde was added to the condensation products of methyl β-chlorovinylketone (I) with glucosamine hydrochloride (II) in water or ethanol. From the reaction mixture, the expected compounds IV could not be obtained in a crystalline state. However, by acetylation, pure 1,4-dihydro-N-[1' : 3' : 4' : 6'-tetraacetylglucosyl-(2')]-3,5-diacetylpyridine derivatives Va, Vb were obtained. Formaldehyde did not give the corresponding compound, Vc.



(II)

(III)

(IV)

(V)

a: R, CH_3
b: R, C_6H_5
c: R, H

The structure of Va and Vb were confirmed by a comparison of their spectral data with those of the corresponding 1,4-dihydropyridine derivatives, VI, VII, VIII and IX (Table I). The infrared spectra of 3,5-diacetyldihydropyridine derivatives show a band at 1640 and 1642 cm^{-1} respectively. The absorption maxima of the ultraviolet spectra of Va and Vb (377, 375 mμ) are nearly the same. The same relationships exist between the spectra of VI and VIII or VIII and IX. The shift of λ_{max} on the nitrogen atom by changing substituents seems to be due to the difference in the

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* This paper constitutes Part V of a series entitled "The Synthetic Reaction with Methyl β-Chlorovinylketone". Part IV: G. Inouye, N. Sugiyama and T. Ozawa, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zasshi*), **82**, 1272 (1961).

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[1] E. Fischer and K. Raske, *Ber.*, **43**, 1750 (1910).

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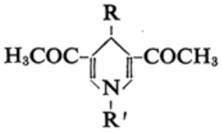
[3] A. R. Todd and L. J. Haynes, *J. Chem. Soc.*, **1950**, 303.

[4] G. Inouye, *J. Chem. Soc. Japan, Pure Chem. Sec.* (*Nippon Kagaku Zasshi*), **79**, 1243 (1958); **80**, 1061 (1959).

[*1] Diphosphopyridine nucleotide

TABLE I. ULTRAVIOLET ABSORPTION SPECTRA AND INFRARED ABSORPTION SPECTRA OF 1,4-DIHYDRO-3,5-DIACETYLPYRIDINE DERIVATIVES



	R	R'	λ_{max}, mμ (log ε)	$\nu_{C=O}$, cm^{-1} [c]	Fluorescence
Va	CH_3	TAGL[a]	377[b] (3.92)	1640	Blue
Vb	C_6H_5	TAGL	375[b] (3.89)	1642	Blue
VI	CH_3	C_6H_5	386 (3.94)	1640	Blue
VII	C_6H_5	C_6H_5	385 (3.91)	1645	Blue
VIII	CH_3	CH_3	396 (4.00)	1637	Blue
IX	C_6H_5	CH_3	394 (3.98)	1632	Blue

a) Tetraacetylglucosyl-(2')
b) In methanol; all others in ethanol
c) KBr

effects of the methyl, phenyl and tetraacetylglucosyl groups on the nitrogen atom[*2].

Experimental

1,4-Dihydro-*N*-[1' : 3' : 4' : 6'-tetraacetylglucosyl-(2')]-4-phenyl-3, 5-diacetylpyridine (Va). — I(10 g.) was stirred drop by drop into an ice-cooled solution of glucosamine hydrochloride (21 g.) and potassium carbonate (30 g.) in water (70 ml.), and the stirring was then continued for 6 hr. Acetaldehyde (5.5 g., 80% aqueous solution) was added to the reaction mixture, and the mixture was left overnight at room temperature. After filtering off the precipitates, concentrated hydrochloric acid (20 ml.) was added to the filtrate. The solution was evaporated to dryness under reduced pressure in an atmosphere of nitrogen. The residue was acetylated by refluxing in acetic anhydride (50 ml.) for an hour. The acetic anhydride was removed under reduced pressure in an atmosphere of nitrogen. After dissolving in ethyl acetate and chromatographing on an alumina column, the residue gave 1,4-dihydro-*N*-[1' : 3' : 4' : 6'-tetraacetylglucosyl-(2')-4-methyl-3, 5-diacetylpyridine (Va) in the form of pale yellow needles (from benzene), m. p. 180°C (decomp.).

Found: N, 2.43. Calcd. for $C_{24}H_{31}O_{11}N$: N, 2.74%.

1, 4-Dihydro-*N*-[1' : 3' : 4' : 6'-tetraacetylglucosyl-(2')]-4-phenyl-3, 5-diacetylpyridine (Vb).—I(10 g.) was stirred drop by drop into an ice cooled mixture of glucosamine hydrochloride (21 g.), ethanol (50 ml.) and a saturated aqueous solution (50 g.) of potassium carbonate, and the stirring was continued for 6 hr. Benzaldehyde (10 g.) was added to the reaction mixture, and the mixture was left overnight at room temperature. After acidification with concentrated hydrochloric acid, the excess benzaldehyde was removed by steam distillation. The solution was evaporated to dryness under reduced pressure in an atmosphere of nitrogen. The residue was acetylated by refluxing in acetic anhydride (50 ml.) for an hour. After cooling, saturated aqueous solution (50 ml.) of sodium acetate was added to the mixture. 1,4-Dihydro-*N*-[1' : 3' : 4' : 6'-tetraacetylglucosyl(2')]-4-phenyl-3,5-diacetylpyridine (Vb) was separated and crystallized from acetic acid-water in the form of pale yellow needles, m. p. 265°C (decomp.).

Found: C, 60.41; H, 5.74; N, 2.28. Calcd. for $C_{29}H_{33}O_{11}N$: C, 60.94; H, 5.77; N, 2.45%.

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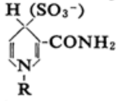
[*2] The ultraviolet absorption spectra of similar compounds have been reported as:



R=Methyl, λ_{max} 339 mμ
R=Tetraacetylglucosyl(β) λ_{max} 313 mμ

G. Pfleiderer, E. Soun and A. Stock, *Chem. Ber.*, 93, 3091 (1960).