Attempted Conversion of (III) and (IV) to (VII) and (VIII)——Refluxing of (Ⅲ) with 10% MeOH-KOH solution for 5 hr. or heating in a sealed tube for 3 hr. in boiling water resulted in recovery of the original material. The same treatment of (Ⅳ) failed to produce (Ⅷ).

The authors are indebted to Mrs. Baba and Miss Okabe for the microanalyses.

Summary

The ethoxyl analogs of 2,3-dihydrodictamnine (Ⅲ) and 2,3-dihydroevolitrine (Ⅳ) were prepared from the corresponding 4-chloro-3-(2-chloroethyl)carbostyrils (I and Ⅱ) by heating with ethanolic alkali. Dehydrogenation of (Ⅲ) gave the ethoxyl analog of dictamnine (V), whose alkoxyl interchange with methanolic potassium hydroxide furnished dictamnine (VI). 2,3-Dihydrodictamnine (Ⅶ), 2,3-dihydroevolitrine (Ⅷ), and 2,3-dihydroskimmianine (Ⅸ) did not undergo conversion, except (Ⅶ), to the corresponding ethoxyl analogs with ethanolic alkali. An attempted conversion of (Ⅲ) and (Ⅳ) to the respective (Ⅶ) and (Ⅷ) failed.

(Received July 4, 1960)

UDC 591.133.2:547.592.1'314.2

Toshiro Murata: Metabolic Fate of 1-Ethynylcyclohexyl Carbamate. IV.[*1] Supplementary Studies on the Glucuronide excreted from the Urine of Man receiving 1-Ethynylcyclohexyl Carbamate.

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In the previous paper[2)] of this series, isolation of a glucuronide from the urine of man who received 1-ethynylcyclohexyl carbamate (ECC) orally was reported. The glucuronide thus obtained was paper chromatographically proved to be a glucuronide of 1-ethynyl-4-hydroxycyclohexyl carbamate (OH-ECC) which has been isolated as a metabolite of ECC by the present author[2)] and by McMahon,[3)] and whose chemical structure was established by McMahon.[4)]

In the present work, attempt was made to obtain crystalline derivative of the glucuronide. The purified glucuronide was successively methylated and acetylated with diazomethane and acetic anhydride. The derivative obtained was identified as methyl [(4-ethynyl-4-carbamyloxycyclohexyl) tri-O-acetyl-β-D-glucopyranosid]uronate from its elemental analysis and infrared absorption spectrum.

Experimental

Isolation of Urinary Glucuronide of OH-ECC——Isolation of the glucuronide was carried out by the method described in a previous paper.[2)]

Preparation of Derivative of the Glucuronide——An Et$_2$O solution of CH_2N_2, freshly prepared

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[*1] Part Ⅲ. This Bulletin, **9**, 167 (1961).
[*2] Kuhonji, Ōe-machi, Kumamoto (村田敏郎).
1) Part Ⅱ. T. Murata: This Bulletin, **9**, 146 (1961).
2) T. Murata: *Ibid.*, 8, 629 (1960).
3) R.E. McMahon: J. Am. Chem. Soc., **80**, 411 (1958).
4) *Idem*: J. Org. Chem., **24**, 1834 (1959).

from 5 g. of nitrosomethylurea, was added to a solution of 18 mg. of purified glucuronide dissolved in 2 cc. of MeOH, the mixture was allowed to stand overnight in a refrigerator, and a small amount of precipitate formed was removed by filtration. The filtrate was evaporated to dryness in a reduced pressure to yield a pale brown material, which was dissolved in 5 g. of pyridine and 4 g. of Ac_2O was added to the solution. After the mixture was allowed to stand at room temperature for 5 days, it was poured into ice-water with stirring and extracted 3 times with Et_2O. The combined Et_2O extract was washed successively with dil. HCl and H_2O, dried over anhyd. Na_2SO_4, and evaporated to dryness. The residue was dissolved in MeOH and the solution was passed through alumina column. The column was eluted with CCl_4 and with MeOH. The MeOH solution was evaporated to dryness and the residue was dried over P_2O_5 *in vacuo* for 3 days. The solidified derivative of the glucuronide was recrystallized twice from iso-PrOH, m.p. 75~78°. Yield, 11.0 mg. *Anal.* Calcd. for $C_{22}H_{29}O_{12}N$: C, 52.90; H, 5.86; N, 2.81. Found: C, 52.13; H, 6.02; N, 2.44.

Infrared absorption spectrum of the derivative is shown in Fig. 1 and the absorptions indicate the loss of a free OH band at 3650~3590 cm^{-1} and appearances of bands characteristic to C-O in acetate at 1250 cm^{-1}, C=O in normal saturated ester at 1752 cm^{-1}, and C-O-C in a six-membered ring at 1035 cm^{-1}.

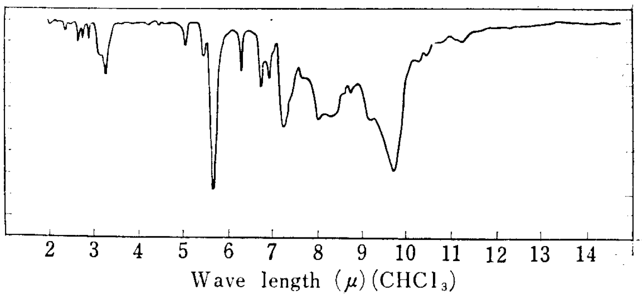

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Fig. 1. Infrared Absorption Spectrum of Methyl [(4-Ethynyl-4-carbamyloxycyclohexyl) tri-O-acetyl-β-D-glucopyranosid]uronate

The author expresses his deep gratitude to Prof. H. Tsukamoto, Kyushu University, for his kind encouragement in this work. He is indebted to the members of the Analysis Room of the Institute of Pharmaceutical Sciences, Kyushu University, for infrared spectral measurement, and to Miss S. Fujishima in this Faculty for microanalysis.

Summary

Methyl [(4-ethynyl-4-carbamyloxycyclohexyl) tri-O-acetyl-β-D-glucopyranosid]uronate was prepared from glucuronide which had been obtained from the urine of man receiving 1-ethynylcyclohexyl carbamate.

(Received January 20, 1961)

UDC 591.133.2:547.592.1'314.2

Toshiro Murata: Metabolic Fate of 1-Ethynylcyclohexyl Carbamate. V.[*1] Studies on 1-Ethynyl-1,2-cyclohexanediol in the Urine of Man receiving 1-Ethynylcyclohexyl Carbamate.

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In the previous paper of this series,[1] excretion of 1-ethynyl-1,2-cyclohexanediol in the urine of man who received 1-ethynylcyclohexyl carbamate (ECC) was suggested and synthesis of cyclohexanediols was attempted.

[*1] Part IV. This Bulletin, 9, 334 (1961).

[*2] Kuhonji, Ōe-machi, Kumamoto (村田敏郎).

[1] Part III. T. Murata: This Bulletin, **9**, 167 (1961).