New Compounds

Some Aminoacyl Derivatives of Amino Sugar Nucleosides

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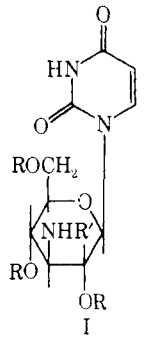
It was recently reported[1] that amino acids could be condensed with amino sugar nucleosides to give the corresponding aminoacyl derivatives. In the quest for new potential nucleoside antibiotics the L-Lys and the L-Glu-γ-Me ester derivatives of 1-(3-amino-3-deoxy-β-D-glucopyranosyl)uracil were prepared. Their syntheses are given below.



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a, R = Ac; R′ = H
b, R = Ac; R′ = Cbo-L-Glu-γ-Me ester
c, R = OH; R′ = Cbo-L-Glu-γ-Me ester
d, R = OH; R′ = L-Glu-γ-Me ester
e, R = OH, Ac, Ac; R′ = di-Cbo-L-Lys
f, R = OH, Ac, Ac; R′ = L-Lys

Cbo = $C_6H_5CH_2OCO$

Experimental Section[2]

1-(3-*N*-Carbobenzoxy-L-glutamylamido-γ-methyl Ester 3-Deoxy-2′,4′,6′-tri-*O*-acetyl-β-D-glucopyranosyl)uracil (Ib).—1-(3-Amino-3-deoxytri-*O*-acetyl-β-D-glucopyranosyl)uracil·HCl[3] (Ia·HCl) (1.2 g, 2.9 mmoles) was added to 7 ml of dry $CHCl_3$. Soln took place upon the addition of 0.81 ml (5.8 mmoles) of Et_3N. A second soln was prepd containing *N*-Cbo-L-Glu-γ-Me ester[4] (856 mg, 2.9 mmoles), Et_3N (0.41 ml, 2.9 mmoles), and $CHCl_3$ (8 ml). Both solns were cooled to 0° in an ice bath. Methyl chloroformate (0.22 ml, 2.9 mmoles) was added to the second soln, and the mixture was stirred for 20 min at 0°. The soln contg the nucleoside was added to the mixed anhydride, and the mixture was stirred for an additional 15 min at 0° followed by overnight stirring at room temp. The soln was extd with 0.2 *N* HCl, followed by a satd soln of $NaHCO_3$ and finally with H_2O contg a few crystals of NaCl (to discourage emulsion formation). The $CHCl_3$ layer was dried ($MgSO_4$) and evapd *in vacuo*. Trituration of the residue with cyclohexane–$CHCl_3$ (10:1) yielded partially cryst material (450 mg, 23%). It had an indefinite melting point beginning at 105°. Silica gel tlc ($CHCl_3$–MeOH, 5:1) indicated one spot with a slight trace of impurity. *Anal.* ($C_{30}H_{36}N_4O_{14}$) C, H, N.

1-(3-*N*-Carbobenzoxy-L-glutamylamido-γ-methyl Ester 3-Deoxy-β-D-glucopyranosyl)uracil (Ic).—Compound Ib (450 mg) was added to 15 ml of anhyd MeOH. Following the addition of 7 mg of anhyd LiOH the soln, protected from moisture, was allowed to stir for 26 hr at room temp. Li ion was removed by the addition of a small amt of Dowex 50 (H^+) resin and stirring the slurry for 1 hr. Silica gel tlc ($CHCl_3$–MeOH, 5:1) indicated one major component along with a trace of impurity. The compd had an indefinite melting point, yield 320 mg (85% based on Ib). *Anal.* ($C_{24}H_{30}N_4O_{11}\cdot H_2O$) C, H, N. The H_2O presumably came from the resin.

1-(3-*N*-L-Glutamylamido-γ-methyl Ester 3-Deoxy-β-D-glucopyranosyl)uracil (Id).—Compd Ic was prepd without the isolation of Ib and was dissolved in 80% aq MeOH. The soln pH was maintained at *ca.* 1 by adding HCl during hydrogenolysis (10% Pd–C). The product, a tan-colored compd, was isolated by filtration of the catalyst and evapn of the supernatant soln. Recrystn from *n*-PrOH gave a compd in a yield of 280 mg (19% based on Ia). The melting point was of no value as shrinking began at *ca.* 60° and continued slowly with rising temp. Silica gel tlc (*t*-BuOH–MEK–H_2O–NH_4OH 4:3:2:1) indicated minor impurities similar to those found prior to purification. *Anal.* ($C_{15}H_{22}N_4O_9\cdot HCl\cdot C_3H_7OH\cdot H_2O$) C, N; H: calcd, 6.43; found, 5.63.

1-(3-*N*,*N*′-Dicarbobenzoxy-L-lysylamido-3-deoxydi-*O*-acetyl-β-D-glucopyranosyl)uracil (Ie).—The prodedure followed was similar to that for Ib and Ic except that *N*,*N*′-di-Cbo-L-Lys[5] was used. During the deacetylation reaction with LiOH a ppt developed which was filtered and washed well with Et_2O; yield 18% (based on Ia), mp 110–125°. Silica gel tlc ($CHCl_3$–MeOH, 5:1) indicated a pure compd. *Anal.* ($C_{36}H_{43}N_5O_{13}\cdot CH_3OH$) C, H; N: calcd, 8.92; found 8.43. The results indicate that only one acetate group was removed during the deacetylation reaction, the resultant diacetoxy compd being insol. Prolonged reaction times with increased amts of LiOH did not change the results according to tlc. The position of deacetylation remains uncertain.

1-(3-L-Lysylamido-3-deoxydi-*O*-acetyl-β-D-glucopyranosyl)uracil Dihydrochloride (If).—The procedure followed was similar to that for Id except that EtOH was used for trituration; white solid, yield 67% (based on Ie); mp 196–203°. *Anal.* ($C_{18}H_{31}N_5O_9\cdot 2HCl\cdot 0.5H_2O$) C, H; N: calcd, 12.89; found, 12.30.

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(5) National Biochemicals Corp., Cleveland, Ohio

Heterocyclic *N*-Carboxamides as Anticonvulsants

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In view of the potent anticonvulsant activity of carbamazepine,[1] three new heterocyclic *N*-carboxamides were synthesized. Anticonvulsant tests have shown that only 1-carbamyl-2,3-diphenylaziridine (**4**) is active, even though its potency was found to be distinctly inferior to that of carbamazepine.

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(1) H. A. Friedman, K. A. Watanabe, and J. J. Fox, *J. Org. Chem.*, **32**, 3775 (1967).

(2) Melting points were taken on a Thomas-Hoover capillary melting point apparatus and are uncorr. Microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, Tenn. Where analyses are indicated only by symbols of the elements, analytical results obtained for those elements were within ±0.4% of the theoretical values.

(3) K. A. Watanabe, and J. J. Fox, *Chem. Pharm. Bull.*, **12**, 975 (1964); K. A. Watanabe, J. Beranek, H. A. Friedman, and J. J. Fox, *J. Org. Chem.*, **30**, 2735 (1965).

(4) Mann Research Laboratories, New York, N.Y.