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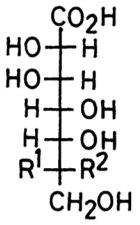
SYNTHESIS OF DESTOMIC ACID AND ITS 6-EPIMER

Hironobu HASHIMOTO, Katsuji ASANO, Fumiko FUJII,
and Juji YOSHIMURA
Laboratory of Chemistry for Natural Products, Faculty of Science,
Tokyo Institute of Technology, Nagatsuta, Midoriku, Yokohama 227

The structure of 6-aminoheptonic acid component contained in destomycin A and C was confirmed first by chemical synthesis.

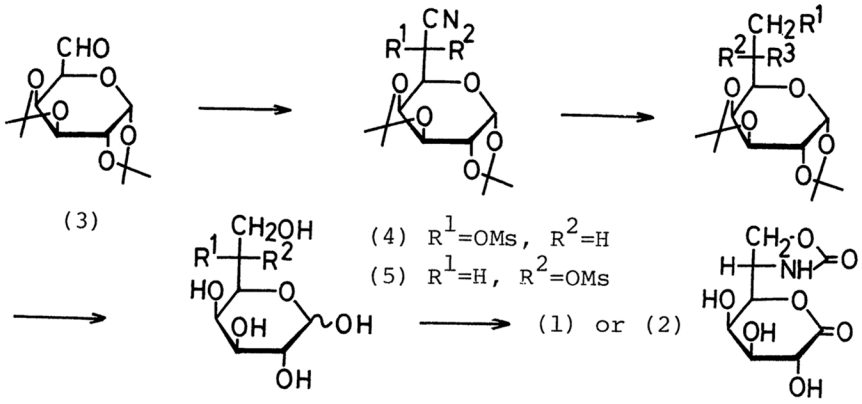
Destomycins isolated from *Streptomyces rimofaciens*[1] have anthelmintic activity and also unique glycosylidene linkage between 6-aminoheptonic acids, named destomic acid (1) in destomycin A and C or 4-epi-destomic acid in destomycin B, and the remaining pseudo-disaccharide moiety.[2] In this paper, destomic acid and its 6-epimer were synthesized from D-galactose, confirming the previously elucidated structure.[2]



(1) $R^1=NH_2$, $R^2=H$
(2) $R^1=H$, $R^2=NH_2$

Among the several methods to prepare 6-amino higher sugar derivatives such as lincosamine[3] and purpurosamine B[4], the cyanosulfonylation of dialdose derivative followed by epimino ring formation was considered to be most convenient for the synthesis of the title compounds. At first, the cyanomesylation of 1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-hexodialdo-1,5-pyranose (3) was examined in two methods. In the first method a syrupy mixture of corresponding cyanohydrins obtained by treatment of (3) with potassium cyanide in methanol-water (2:1) was mesylated in pyridine to afford a mixture of the D-*glycero*-D-*galacto*-(4) and L-*glycero*-D-*galacto*-(5) heptononitrile derivatives in the ratio of 2.8:1 in 82% yield, while the cyanotosylation of (3) under the almost same conditions gave the corresponding products in about 25% yield.[4] In the second method (3) was treated with hydrogen cyanide followed by mesylation in pyridine gave also a mixture of (4) and (5) in the ratio of 1.7:1.0 in a quantitative yield. In the latter, fractional crystallization of the product mixture from ethanol gave crystalline (5) [mp 157-159.5°C, $[\alpha]_D$ -46.8° (*c* 1.6, $CHCl_3$)] in 27% yield. Then the syrup obtained from the mother liquor was subjected to a silica gel column using ether-hexane (11:9) as an eluant to give pure (4) [mp 124-125°C, $[\alpha]_D$ -98.6° (*c* 1.0, $CHCl_3$)] in 52% yield.

Lithium alminium hydride reduction of (4) and successive benzyloxycarbonylation in water-dioxane gave 6,7-epimino-L-*glycero*-D-*galacto*-heptose derivative [(6): syrup, $[\alpha]_D$ -75.8° (*c* 2.0, $CHCl_3$)] and its N-benzyloxycarbonyl derivative [(7): mp 127-129°C, $[\alpha]_D$ -120.7° (*c* 2.0, $CHCl_3$)] in 94 and 57% yields, respectively. The configuration of C-6 was determined by chemical conversion of (6) *via* its reduction product (8) into *N*-dinitrophenyl-L-alanine by sequential reactions of dinitrophenylation, de-*O*-isopropylidenation, periodate and then permanganate oxidations.



(3) (4) R^1=OMs, R^2=H; (5) R^1=H, R^2=OMs; (1) or (2); (6) R^1,R^3=NH, R^2=H; (7) R^1,R^3=NZ, R^2=H; (8) R^1=R^2=H, R^3=NH_2; (9) R^1=OH, R^2=H, R^3=NHZ; (12) R^1,R^2=NH, R^3=H; (13) R^1,R^2=NZ, R^3=H; (14) R^1=OH, R^2=NHZ, R^3=H

(10) R^1=H, R^2=NHZ; (15) R^1=NHZ, R^2=H; (11)

Ms=methylsulfonyl
Z =benzyloxycarbonyl

Acetolysis of (7) with acetic acid followed by deacetylation afforded 6-benzyloxycarbonylamino-L-*glycero*-D-*galacto*-heptopyranose derivative [(9): syrup, $[\alpha]_D$ -47.8° (*c* 2.0, $CHCl_3$)] in 86% yield. Oxidation of de-*O*-isopropylidenated compound [(10): mp 170-173°C (dec.), $[\alpha]_D$ +52.9° (*c* 1.0, H_2O)] with bromine in the presence of barium carbonate followed by catalytic reduction in the presence of palladium-charcoal gave destomic acid [(1): mp 200-202°C (dec.), $[\alpha]_D$ +1.5° (*c* 1.1, H_2O); lit.[2] mp 207-209°C (dec.), $[\alpha]_D$ +1.9° (*c* 2, H_2O)] in 63% yield. It is noteworthy that potassium hypoiodate oxidation[5] of (10) gave 6,7-*N*,*O*-carbonate derivative [(11): mp 189-191°C (dec.), $[\alpha]_D$ -124°, (*c* 1.0, H_2O)] in 89% yield instead of expected 6-(benzyloxycarbonyl)amino-L-*glycero*-D-*galacto*-heptonolactone.

On the other hand, 6-epimer (2) of destomic acid was derived from (5) in the same reaction sequence as described for (1) as shown in the scheme. [(12): syrup, $[\alpha]_D$ -84.8° (*c* 2.0, $CHCl_3$); (13): mp 77-78°C, $[\alpha]_D$ -26.9° (*c* 2.0, $CHCl_3$); (14): mp 96-97°C, $[\alpha]_D$ -44.6° (*c* 2.0, $CHCl_3$); (15): mp 198-201°C, $[\alpha]_D$ +32.8° (*c* 1.0, H_2O); (2) mp 193-195°C (dec.), $[\alpha]_D$ +17.4° (*c* 1.0, H_2O)].

Comparison of some physical properties including chromatographic behaviour proved the identity of synthesized and natural destomic acid.

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References

1) a) S. Kondo, M. Sezaki, M. Koike, M. Shimura, E. Akita, K. Satoh, and T. Hara, J. Antibiotics, A18, 38(1965). b) M. Shimura, Y. Sekizawa, K. Iinuma, H. Naganawa, and S. Kondo, J. Antibiotics, 28, 83(1975).

2) a) M. Shimura, Y. Sekizawa, K. Iinuma, H. Naganawa, and S. Kondo, Agr. Biol. Chem., 40, 611(1976). b) S. Kondo, K. Iinuma, H. Naganawa, M. Shimura, and Y. Sekizawa, J. Antibiotics, 28, 79 (1975).

3) a) G. B. Howarth, W. A. Szarek, and J. K. N. Jones, J. Chem. Soc. (C), 1970, 2218. b) B. J. Margerlein, Tetrahedron Lett., 1970, 33. c) H. Saeki, and E. Ohki, Chem. Pharm. Bull. Japan, 18, 789 (1970).

4) T. Suami, Y. Honda, T. Kato, Chem. Lett., 1978, 1125.

5) P. Andrews, L. Hough, and J. M. Ricken, Biochem. J., 94, 75 (1965).

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