

The Total Synthesis of Destomic Acid

Adam Golebiowski and Janusz Jurczak*

Institute of Organic Chemistry, Polish Academy of Sciences, 01-224 Warszawa, Poland

1-Benzoyloxy-2-*t*-butyldimethylsilyloxy-4-ethoxybuta-1,3-diene (**3**) reacts with *N*-benzyloxycarbonyl-*O*-*t*-butyldiphenylsilyl-L-serinal (**4**) to give, with high selectivity, compound (**5a**) which was subsequently transformed into derivatives of destomic acid (**7**) and (**8**).

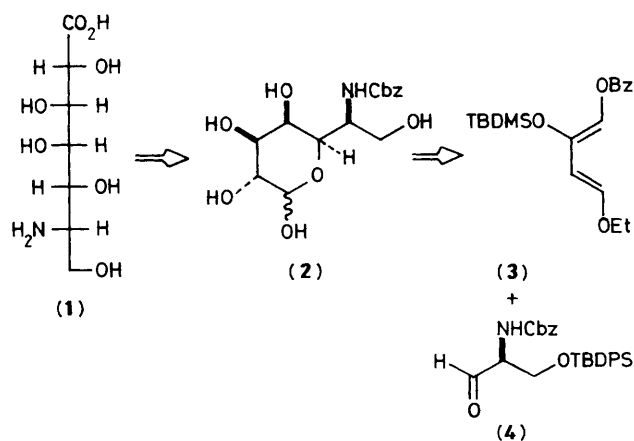
6-Amino-6-deoxy-L-glycero-D-galacto-heptonic acid (**1**), commonly named destomic acid, is one of the three components of a new type of aminocyclitol antibiotic: destomycin A,^{1,2} B,^{2,3} and hygromycin B.⁴ The syntheses of destomic acid and its 4-epimer, starting from D-galactose and D-glucose, respectively, have recently been published.⁵

During our studies on applications of chiral *N*-protected α -amino aldehydes in organic synthesis⁶ we found that they are very convenient and versatile heterodienophiles. High-pressure⁷⁻⁹ or Lewis acid-mediated¹⁰⁻¹² (4 + 2)cycloaddition of 1,3-dienes to *N*-protected α -amino aldehydes offers easy access to the respective optically pure adducts which were readily transformed into several natural products.⁶

Now we report on a new application of this methodology to the total synthesis of destomic acid (**1**). Retrosynthetic analysis shown in Scheme 1 suggested that 1-benzoyloxy-2-*t*-butyldimethylsilyloxy-4-ethoxybuta-1,3-diene (**3**)¹³ and *N*-benzyloxycarbonyl-*O*-*t*-butyldiphenylsilyl-L-serinal (**4**)[†] could serve as starting materials.

The cyclocondensation reaction of diene (**3**) with aldehyde (**4**) in the presence of ZnBr₂, followed by treatment with trifluoroacetic acid, led to a mixture of four possible diastereoisomeric adducts (**5**); as can be expected^{10,12,14} (4*S*,5*R*)-diastereoisomer (**5a**) was formed as a major product‡ (Scheme 2).

The Luche-type reduction¹⁵ of the chromatographically pure adduct (**5a**),§ followed by basic debenzoylation, afforded diol (**6**) which was subjected to the *cis*-hydroxylation reaction¹⁶ to yield tetraol (**7**). Compound (**7**) can be easily transformed into destomic acid (**1**), but for direct comparison we converted it into the previously described⁵ compound (**8**) and its 7-*O*-acetyl derivative. The latter compound has, after chromatographic purification, $[\alpha]_D^{25} -43.3^\circ$ (*c* 0.9, chloroform); lit.⁵ $[\alpha]_D^{RT} -47.8^\circ$ (*c* 2.0, chloroform). The ¹H n.m.r. and i.r. spectra of compound (**8**) and of its 7-*O*-acetyl

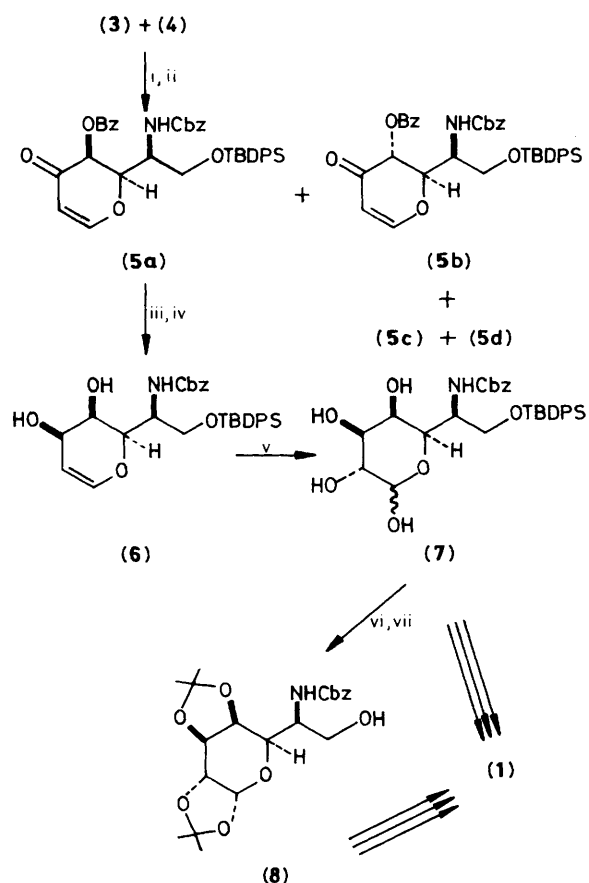


Scheme 1

† Compound (**4**) was prepared in the following reaction sequence starting from L-serine: i, SOCl₂, MeOH; ii, CbzCl, NaHCO₃, AcOEt; iii, TBDPSCl, imidazole, DMF; iv, DIBAL, Et₂O, -78°C.

‡ The diastereoisomeric proportion was (**5a**):(**5b**):(**5c**):(**5d**) = 87:8:4:1. The direction of asymmetric induction on the C-5 carbon atom can be rationalized on the ground of α -chelation-controlled cycloaddition.

§ Satisfactory analyses and spectral data were obtained for all new compounds.



Scheme 2. Reagents and conditions: i, ZnBr_2 , THF, rt; ii, TFA, CH_2Cl_2 , rt; iii, NaBH_4 , $\text{CeCl}_3 \cdot 7\text{H}_2\text{O}$, MeOH, -78°C ; iv, K_2CO_3 , MeOH, rt; v, OsO_4 , NMO, Bu^tOH , H_2O , rt; vi, DMP, p -TsOH, Me_2CO , rt; vii, Bu_4NF , THF, rt.

derivative obtained by us were identical with those measured by Hashimoto *et al.*⁵ Compound (8) can be transformed into destomic acid (1) according to the known procedure.⁵

The presented total synthesis of destomic acid proves to be a practical alternative to the known approach of Hashimoto *et al.*⁵ Moreover, it exemplifies the usefulness of *N*-protected α -amino aldehydes in the synthesis of natural products.

Financial support from the Polish Academy of Sciences (Grant CPBP 01.13) is gratefully acknowledged.

Received, 30th August 1988; Com. 8/03484B

References

- 1 S. Kondo, E. Akita, and M. Koike, *J. Antibiot., Ser. A.*, 1966, **19**, 139.
- 2 S. Kondo, K. Iinuma, H. Naganawa, M. Shimura, and Y. Sekizawa, *J. Antibiot.*, 1975, **28**, 79.
- 3 M. Shimura, Y. Sekizawa, K. Iinuma, H. Naganawa, and S. Kondo, *Agric. Biol. Chem.*, 1976, **40**, 611.
- 4 N. Neuss, K. F. Koch, B. B. Molloy, W. Day, L. L. Hickstep, D. E. Dorman, and J. D. Roberts, *Helv. Chim. Acta*, 1970, **53**, 2314.
- 5 H. Hashimoto, K. Asano, F. Fujii, and J. Yoshimura, *Carbohydr. Res.*, 1982, **104**, 87.
- 6 J. Jurczak and A. Golebiowski, *Chem. Rev.*, in the press.
- 7 A. Golebiowski, J. Izdebski, U. Jacobsson, and J. Jurczak, *Heterocycles*, 1986, **24**, 1205.
- 8 A. Golebiowski, U. Jacobsson, M. Chmielewski, and J. Jurczak, *Tetrahedron*, 1987, **43**, 599.
- 9 A. Golebiowski, U. Jacobsson, and J. Jurczak, *Tetrahedron*, 1987, **43**, 3063.
- 10 S. Danishefsky, S. Kobayashi, and J. F. Kerwin, Jr., *J. Org. Chem.*, 1982, **47**, 1983.
- 11 P. Garner, *Tetrahedron Lett.*, 1984, **25**, 5855.
- 12 P. Garner and S. Ramakanth, *J. Org. Chem.*, 1986, **51**, 2609.
- 13 S. Danishefsky and C. J. Maring, *J. Am. Chem. Soc.*, 1985, **107**, 1269.
- 14 J. Jurczak, A. Golebiowski, and J. Raczko, *Tetrahedron Lett.*, 1988, **29**, 5975.
- 15 J.-L. Luche and A. L. Gemal, *J. Am. Chem. Soc.*, 1979, **101**, 5842.
- 16 S. Danishefsky, E. Larson, and J. P. Springer, *J. Am. Chem. Soc.*, 1985, **107**, 1274.