Tetrahedron Letters,Vol.26,No.34,pp 4133-4136,1985 0040-4039/85 $3.00 + .00
Printed in Great Britain

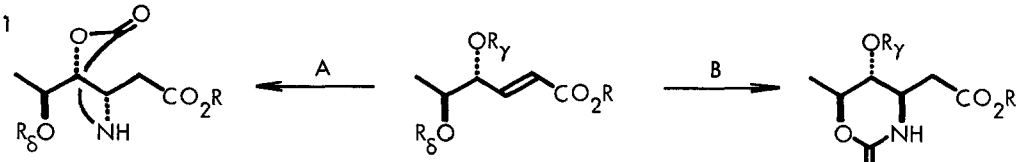
DIASTEREOSELECTIVE SYNTHESIS OF N-ACETYL-D,L-ACOSAMINE AND N-BENZOYL-D,L-RISTOSAMINE

Masahiro Hirama*, Takeo Shigemoto, Yutaka Yamazaki and Shô Itô*
Department of Chemistry, Tohoku University
Sendai 980, Japan

Abstract: N-Acyl derivatives of D,L-acosamine and D,L-ristosamine were synthesized with high stereoselectivity utilizing intramolecular Michael addition of γ- and δ-carbamoyloxy-α,β-unsaturated esters.

Recently we have found prominent 1,2- and 1,3-asymmetric induction in the intramolecular Michael additions of γ- and δ-carbamoyloxy-α,β-unsaturated esters[1]. Since the attack of nitrogen nucleophile to the diastereotopic face of β-carbon is controlled by both the position and the configuration of carbamoyloxy group in these reactions, they provide excellent ways to achieve diastereoselective amination of acyclic systems by choosing the site of carbamoyloxy group, as are exemplified in eq. 1 by the sinthesis of epimeric 3-amino-4,5-erythro-dihydroxy acid derivatives[1]. In this communication, we demonstrate the synthetic utility of this method by the stereoselective synthesis of N-acetyl-D,L-acosamine (1)[2] and N-benzoyl-D,L-ristosamine (2)[3], N-acyl derivatives of two important 3-amino-2,3,6-trideoxyhexoses.

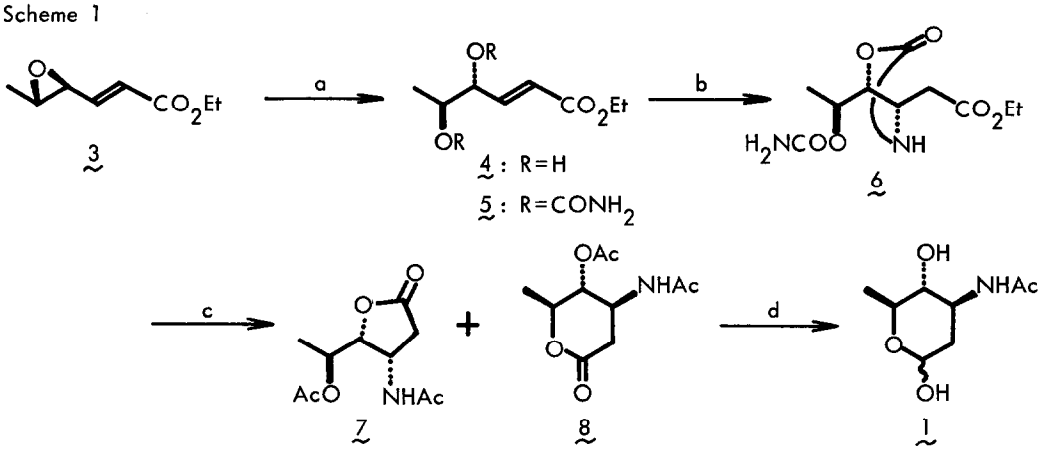
eq. 1



A : R_γ=$CONH_2$, R_δ= protecting group
B : R_γ= protecting group, R_δ=$CONH_2$

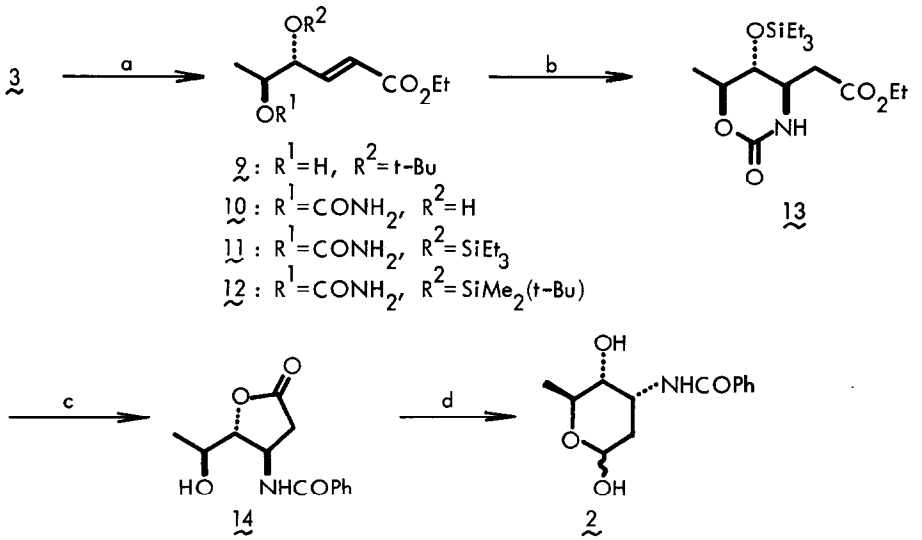
Both sugars can be synthesized from the common starting material, ethyl sorbate. The synthesis of N-acetyl-D,L-acosamine 1 is outlined in Scheme 1. The epoxide 3[2b] obtained by the epoxidation of ethyl sorbate with MCPBA (84% yield) was hydrolyzed to the erythro-diol 4[4] exclusively. Treatment of 4 with $ClSO_2NCO$ followed by partial hydrolysis of the resulting chlorosulfonyl carbamate yielded the crystalline bis-carbamate 5[4]. Base-catalyzed intramolecular Michael addition[1] of 5 afforded the trans-oxazolidinone 6[4] with D,L-arabino configuration nearly exclusively (>20: 1)[5]. The conversion of 6

Scheme 1



(a) i) 0.14 M aq. $HClO_4$, r.t., overnight (92%); ii) $ClSO_2NCO$ (3 mol. eq.), CH_2Cl_2, -20°C, 25 min; H_2O, 70°C, 45 min (73%). (b) t-BuOK (1.1 eq.), THF, 0°C, 30 min (79%). (c) 1N aq. NaOH (4.5 mol. eq.), EtOH, 60°C, overnight; evaporation; Ac_2O, r.t., overnight → 60°C, 3 h (79% overall). (d) i) 1M DIBAL/hexane (2.0 mol. eq.), THF, -78°C, 30 min → -50°C, 30 min; ii) 1N aq. NaOH, MeOH, r.t., 1 h (44% overall).

Scheme 2



(a) i) t-BuOH (11.5 eq.), $BF_3 \cdot OEt_2$ (1.2 eq.), Et_2O, r.t., 1 day (58%); ii) $ClSO_2NCO$ (1.5 eq.), CH_2Cl_2, -78°C, 30 min; H_2O, 70°C, overnight (86%); iii) $ClSiEt_3$ (1.1 eq.), imidazole, DMF, r.t., (92%). (b) t-BuOK (1.0 eq.), THF, 0°C (74%). (c) 1N aq. NaOH (10 mol. eq.), EtOH, 60°C, overnight; CO_2; PhCOCl (4.3 mol. eq.), $NaHCO_3$ (5.5 mol. eq.), aq. acetone (1:1), r.t., overnight (77%). (d) 1M DIBAL/hexane (3.0 mol. eq.), THF, -78°C, 1 h.

to the D,L-acosamine derivative 1 was accomplished virtually in three steps: Alkaline hydrolysis of both the carbamate and ester groups, evaporation of the volatiles and acetylation of the residue gave a 1:1 mixture of the γ-lactone 7[4] and the δ-lactone 8[4]. Though the mixture can be separated by SiO_2-chromatography, it was reduced without separation by 2 molar eq. of DIBAL, and subsequent hydrolysis of O-acetyl group afforded N-acetyl-D,L-acosamine 1[6] [m.p. 174-178°C, lit[2b]: m.p. 170-174°C] after purification by known procedure[2b]. The ^{1}H NMR (200 MHz) and IR spectral data of 1 were in good agreement with those reported by Dyong, and the ratio of α- and β-anomers in D_2O was 1:1.6 after 1 day as determined by ^{1}H NMR spectra.

In order to achieve ribo configuration by the intramolecular Michael addition leading to the synthesis of the D,L-ristosamine derivative 2, the homoallylic carbamate of the type B (eq. 1), hence regioselective protection of the γ-hydroxyl group in the diol 4 is necessary. Thus, as shown in Scheme 2, the threo-epoxide 3 was regioselectively cleaved by the known procedure[2b,7] to ethyl (±)-erythro-4-t-butoxy-5-hydroxy-trans-hex-2-enoate (9) in 58% yield[8]. Treatment of 9 with $ClSO_2NCO$ followed by partial hydrolysis with water afforded the mono-carbamate 10[4], thus achieving the carbamation of δ-hydroxyl group and deprotection of γ-t-butoxyl in one pot. Triethylsilylation of γ-hydroxyl of 10 gave the crystalline 11[4]. Cyclization of 11 proceeded smoothly with base to 13[4] exclusively (>50:1)[9]. Alkaline hydrolysis of 13 and subsequent benzoylation of the reaction mixture under Schotten-Baumann condition resulted in the formation of the D,L-ribo-γ-lactone 14[4]. The final reduction of 14 with DIBAL gave N-benzoyl-D,L-ristosamine 2[4] in 43% yield. The ^{1}H NMR spectral data of 14 and 2 are identical with those reported for optically active compounds[3b].

The steric and stereoelectronic factors controlling the diastereofacial selectivity in the present functionalization of acyclic olefins and its application to the synthesis of D,L-daunosamine derivative are discussed in the following paper.

References and Notes

1) M. Hirama, T. Shigemoto, Y. Yamazaki and S. Itô, J. Am. Chem. Soc., 107, 1797 (1985).

2) (a) For recent acosamine syntheses, see: T. Hiyama, K. Nishide and K. Kobayashi, Tetrahedron Letters, 25, 569 (1984) and references cited therein. (b) I. Dyong and H. Bendlin, Chem. Ber., 111, 1677 (1978).

3) (a) For recent ristosamine syntheses, see: C.H. Heathcock and S.H. Montgomery, Tetrahedron Letters, 24, 4637 (1983) and references therein. (b) G. Fronza, C. Fuganti and P. Grasselli, J.C.S. Perkin I, 885 (1982).

4) (a) Satisfactory spectral data (IR, ^{1}H NMR) and elemental analyses were obtained for all compounds reported herein.
(b) Characteristic physical data: 2: m.p. 114-118°C.
5: m.p. 157-158°C; ν (KBr) 1720, 1696 cm^{-1}; δ (90 MHz, $CDCl_3$) 1.25 (3H, d, J=6.4 Hz), 1.30 (3H, t, J=7.0 Hz), 4.21 (2H, q, J=7.0 Hz), 4.68 (2H, m), 4.78 (2H, m), 5.00 (1H, dq, J=3.6, 6.4 Hz), 5.44 (1H, ddd, J=1.6, 3.6, 5.3 Hz), 6.08 (1H, dd, J=1.6, 15.8 Hz), 6.88 (1H, dd, J=5.3, 15.8 Hz).
6: m.p. 134-136°C; ν (KBr) 1756, 1710, 1688 cm^{-1}; δ (200 MHz, DMSO-d_6) 1.15 (3H, d, J=6.8

Hz), 1.22 (3H, t, J=7.2 Hz), 2.57 (1H, dd, J=7.0, 16.4 Hz), 2.68 (1H, dd, J=6.4, 16.4 Hz), 3.89 (1H, ddd, J=4.8, 6.4, 7.0 Hz), 4.0-4.3 (2H, m), 4.34 (1H, dd, J=4.2, 4.8 Hz), 4.80 (1H, dq, J=4.6, 6.8 Hz), 6.63 (2H, m), 7.89 (1H, m).

7: ν ($CHCl_3$) 1782, 1734, 1674 cm^{-1}; δ (90 MHz, $CDCl_3$) 1.39 (3H, d, J=6.5 Hz), 1.97 (3H, s), 2.07 (3H, s), 2.48 (1H, dd, J=2.2, 18.5 Hz), 2.95 (1H, dd, J=7.4, 18.5 Hz), 4.43 (1H, dd, J=5.0, 8.6 Hz), 5.04 (1H, ddd, J=2.2, 5.0, 7.4 Hz), 5.17 (1H, dq, J=8.6, 6.5 Hz), 6.1-6.4 (1H, m).

8: ν ($CHCl_3$) 1736, 1674 cm^{-1}; δ (90 MHz, $CDCl_3$) 1.40 (3H, d, J=6.5 Hz), 1.97 (3H, s), 2.13 (3H, s), 2.57 (1H, dd, J=7.6, 18.0 Hz), 3.15 (1H, dd, J=7.0, 18.0 Hz), 4.40 (1H, dq, J=9.4, 6.5 Hz), 4.1-4.6 (1H, m), 4.80 (1H, dd, J=8.1, 9.4 Hz), 5.9-6.2 (1H, m).

11: m.p. 67-68°C; ν (KBr) 1724, 1700 cm^{-1}; δ (90 MHz, $CDCl_3$) 0.44-1.08 (15H, m), 1.17 (3H, d, J=6.6 Hz), 1.30 (3H, t, J=7.0 Hz), 4.20 (2H, q, J=7.0 Hz), 4.47 (1H, ddd, J=1.8, 3.3, 4.6 Hz), 4.74 (2H, m), 4.80 (1H, dq, J=3.3, 6.6 Hz), 6.08 (1H, dd, J=1.8, 15.6 Hz), 6.88 (1H, dd, J=4.6, 15.6 Hz).

13: m.p. 109-111.5°C; ν (KBr) 1715 (sh), 1703 cm^{-1}; δ (200 MHz, $CDCl_3$) 0.57-0.80 (6H, m), 0.90-1.08 (9H, m), 1.01 (3H, t, J=7.2 Hz), 1.20 (3H, d, J=6.3 Hz), 2.36 (1H, dd, J=10.5, 16.6 Hz), 2.84 (1H, dd, J=2.2, 16.6 Hz), 3.40 (1H, dd, J=8.3, 9.0 Hz), 3.60 (1H, ddd, J=2.2, 8.3, 10.5 Hz), 4.18 (1H, dq, J=9.0, 6.3 Hz), 4.23 (2H, m), 5.85 (1H, m).

14: m.p. 137.0-138.5°C; ν (KBr) 1758, 1639 cm^{-1}; δ (200 MHz, $CDCl_3$) 1.39 (3H, d, J=6.5 Hz), 2.65 (1H, dd, J=4.7, 18.5 Hz), 3.16 (1H, dd, J=9.3, 18.5 Hz), 4.09 (1H, ddq, J=4.4, 4.8, 6.5 Hz), 4.34 (1H, dd, J=3.7, 4.8 Hz), 4.88 (1H, dddd, J=3.7, 4.7, 7.3, 9.3 Hz), 6.93 (1H, br.d, J=7.3 Hz), 7.52 (3H, m), 7.83 (2H, m).

5) The structure of the minor product detected by ^1H NMR was not rigorously assigned. It could be either the diastereomer of 6 or a regioisomer resulted from the cyclization of the homoallylic carbamoyloxy group. It can easily be removed by recrystallization, although the subsequent transformations were usually conducted without separation at this stage.

6) Attempts to deprotect O-acetyl group concurrently with reduction of lactone using excess (≥3 molar eq.) DIBAL were unsuccessful because hemiacetal is also reduced.

7) M.S. Malinovskii, L.P. Glushko and N.J. Pokhodenko, Khim Geterotsiki. Soedin., 164 (1974): Chem. Abstract, 81, 3312m (1974).

8) Stoichiometric amount of $BF_3 \cdot OEt_2$ was necessary to achieve the satisfactory yield. Under the reported conditions (0.2 eq. of $BF_3 \cdot OEt_2$) the yield remained ~30%. The regioisomer formed (10%) can be separated by SiO_2 chromatography.

9) The triethylsilyl group is generally considered to be much smaller than t-butyldimethylsilyl from the reactions on silicon atom such as formation and hydrolysis of silyl ethers. The former group situated adjacent to the site of reaction, however, appears to have somewhat larger effective size than the latter since 12 exhibited the lower selectivity of 36:1 [1]. We have observed the similar tendency in several other reactions, one of which is reported in the following paper.

(Received in UK 14 June 1985)