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THE TOTAL SYNTHESIS OF L-TALONIC LACTONE

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Abstract: The total synthesis of L-talonic lactone from L-ascorbic acid is reported.

As part of our investigation of the chemistry of vitamin C, we have recently described the preparation of D-mycinose from isoascorbic acid *via* a hydroxyl directed hydrogenation.[1] Herein, we report the synthesis of L-talonic lactone, **1**, from ascorbic acid utilizing the aforementioned reduction technology. In addition, we introduce an *o*-xylyl group as a bridged protecting device.

In order to employ the hydroxyl directed beta-face reduction of the C-2,3 olefin of vitamin C, it was necessary to prepare compound **2**. Treatment of a DMF solution of O-5,6-isopropylidene ascorbic acid, **3** (0.5 M), and K_2CO_3 (1.1 equ, 60°C, 30 min) with α,α'-dichloro-*o*-xylene (1 equ 0.5 M in DMF, 2.5 h) gave *o*-xylyl-bridged **4** in 62% yield.[2-4] The ethylidene diol sidechain was exposed by acetonide removal with acidic methanol (0.25 M, 1.1 equ of 1 M HCl, overnight, room temp, 99% yield) to **5**.[4] The O-6 benzyloxy methyl ether was next introduced using standard reaction conditions (0.1 M in CH_2Cl_2; 2 equ of i-Pr_2NEt and 1.2 equ of BOMCl; overnight, room temp; then, 2 equ of i-Pr_2NEt and 1.2 equ of BOMCl, 2 days, room temp; 57% yield) to afford **2**.[4,5]

The α-hydroxy tetronic acid double bond was reduced by treatment of an admix of **3** and Rh(Diphos-4)(NBD)BF_4 (0.2 equ) in CH_2Cl_2 (0.06 M) with 1950 psi hydrogen pressure (room temp, 20 h)providing **6** in 90% yield.[1] It is important that only the C-5 hydroxyl be available for complexation to the catalyst; otherwise, no reaction occurs. Finally, simultaneous hydrogenolysis of the *o*-xylyl protecting group and the benzyloxy methyl ether over Pearlman's catalyst (20 % wt, 0.1 M in EtOH, 1 atm H_2, room temp, 4 h) afforded a quantitative yield of L-talonic lactone, **1**.[4,6,7]

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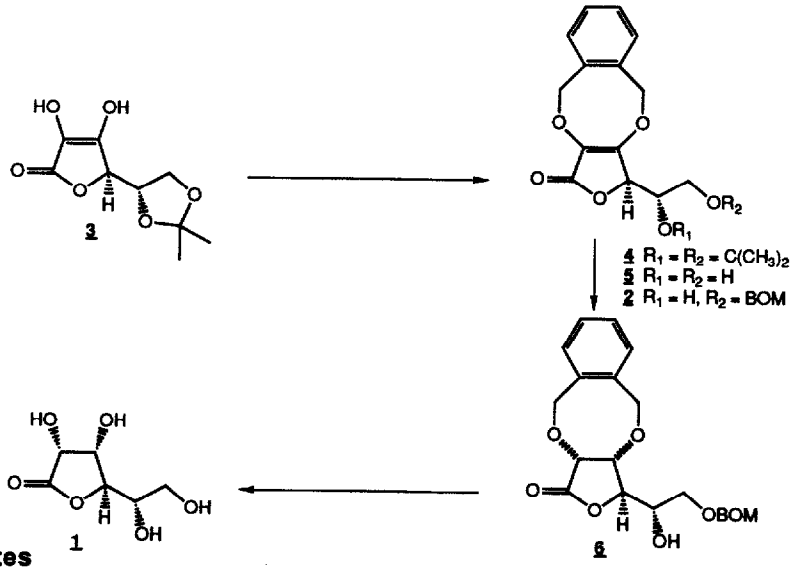

References and Notes

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4. Compound **4**: mp 160-1°C (hexanes/acetone); $[\alpha]_D$ = -3.6 (c = 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ = 1.21 (s, 3 H), 1.25 (s, 3 H), 3.89 (t, J = 6.7, 8.5 Hz, 1 H), 4.00 (t, J = 6.7, 8.3 Hz, 1 H), 5.45 (d, J = 11.5 Hz, 1 H), 5.65 (d, J = 11.5 Hz, 1 H), 7.2 (m, 1 H), 7.35 (m, 3 H); ^{13}C NMR: δ = 25.4, 25.8, 65.2, 72.2, 74.2, 74.7, 75.2, 100.4, 122.0, 128.8, 129.3, 130.5, 132.2, 133.5, 137.0, 158.0, 169.2. Compound **5**: mp 81-3°C (EtOAc); $[\alpha]_D$ = -1.3 (c = 1.0, MeOH); ^1H NMR (d_6-DMSO): δ = 3.35 (s, 2 H), 3.61 (qt, J = 6.04, 6.25, 6.48 Hz, 1 H), 4.66 (s, 1 H), 4.84 (s, 1 H), 4.96 (d, J = 6.04 Hz, 1 H), 5.16 (d, J = 11.5 Hz, 1 H), 7.43 (m, 4 H); ^{13}C NMR (d_6-DMSO): δ = 61.7, 68.9, 71.3, 73.8, 74.6, 120.8, 129.0, 129.1, 130.3, 132.9, 133.2, 137.2, 157.1, 169.3. Compound **2**: mp 96-7°C (hexanes/acetone); $[\alpha]_D$ = +10.1 (c = 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ = 3.63 (m, 2 H), 3.89 (bs, 1 H), 4.54 (s, 2 H), 4.59 (s, 1 H), 4.69 (s, 2 H), 5.28 (s, 2 H), 5.47 (d, J = 11.5 Hz, 1 H), 5.6 (d, J = 11.5 Hz, 1 H), 7.32 (m, 9 H); ^{13}C ($CDCl_3$): δ = 68.6, 68.7, 69.9, 72.1, 75.2, 75.3, 95.4, 121.8, 128.2, 128.3, 128.8, 129.3, 130.7, 132.2, 133.3, 137.1, 137.9, 158.3, 169.6. Compound **6**: $[\alpha]_D$ = +36.0 (c = 1.0, $CHCl_3$); ^1H NMR ($CDCl_3$): δ = 2.96 (s, 1 H), 3.56 (dd, J = 8.5, 11.1 Hz, 1 H), 3.75 (dd, J = 3.8, 10.8 Hz, 1 H), 3.82 (s, 1 H), 4.04 (d, J = 5.3 Hz, 1 H), 4.42 (s, 1 H), 4.56 (s, 2 H), 4.57 (d, J = 5.3 Hz, 1 H), 4.75 (m, 4 H), 5.24 (d, J = 13.9 Hz, 1 H), 5.37 (d, J = 11.8 Hz, 1 H), 7.23 (m, 9 H). Compound **1**: $[\alpha]_D$ = +33.3 (c = 1.17, H_2O), lit.[7] $[\alpha]_D$ = +34.4 (c = 1.17, H_2O); ^1H NMR (d_6-DMSO): δ = 3.43 (s, 2 H), 3.73 (t, J = 6.4 Hz, 1 H), 4.24 (d, J = 5.4 Hz, 1 H), 4.44 (s, 1 H), 4.53 (d, J = 5.4 Hz, 1 H), 4.94 (bs, 1 H), 5.34 (bs, 1 H), 5.46 (bs, 1 H), 5.83 (bs, 1 H); ^{13}C NMR (d_6-DMSO): δ = 61.7, 68.7, 70.5, 70.9, 84.6, 177.3.
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