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PREPARATION OF (2E)-t-BUTYL 4,5,7-TRIHYDROXY-2-OCTENOATES CONTAINING THREE NON-RACEMIC CHIRAL CENTERS[1]

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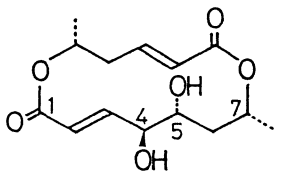
The hydrophilic part of 14-membered-ring macrolide, colletodiol, containing three chiral centers has been prepared from L-rhamnose and D-glucose, suitable for further synthesis.

Colletodiol (1) was isolated from Colletricum capsici in 1966 and subsequently shown to be 14-membered cyclic dilactone.[2] We wish to report herein a convenient synthesis of the hydrophilic part (C-1~O-8) of 1 as well as its isomer from carbohydrates.[3]



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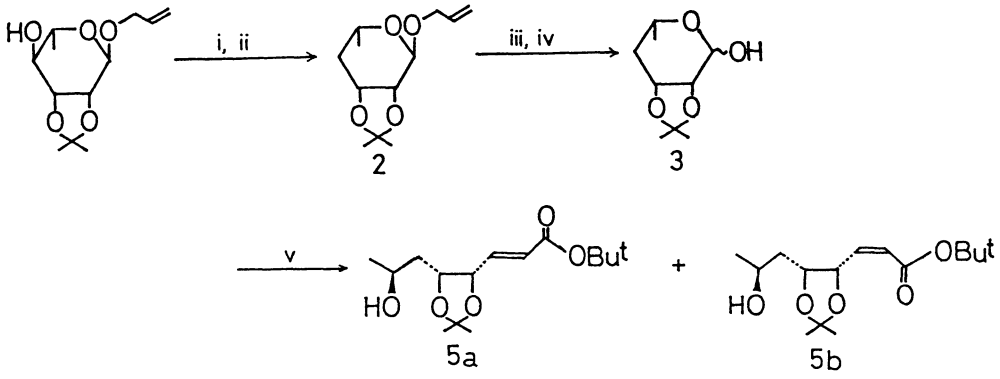
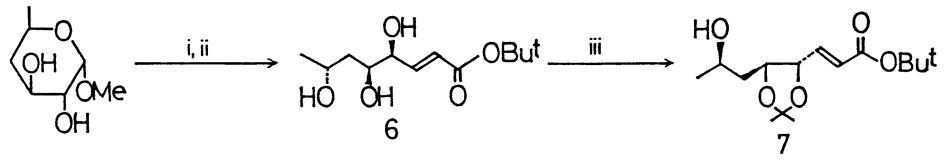
(2E,4S,5R,7S)-t-Butyl 4,5-O-isopropylidene-4,5,7-trihydroxy-2-octenoate. Allyl 2,3-O-isopropylidene-α-L-rhamnopyranoside was converted into the corresponding 4-deoxyrhamnopyranoside (2) by Barton procedure.[4] Allyl group was then removed by successive treatment of 2 with $RhCl(Ph_3P)_3$-DABCO and acetone-H_2O-$HgCl_2$[5] giving 3 in 37% overall yield.[6] The reaction of 3 with t-butoxycarbonylmethylenetriphenylphosphorane (4) resulted in the formation of the title compound (5a) and Z-isomer (5b) in 21 and 52% yields, respectively.



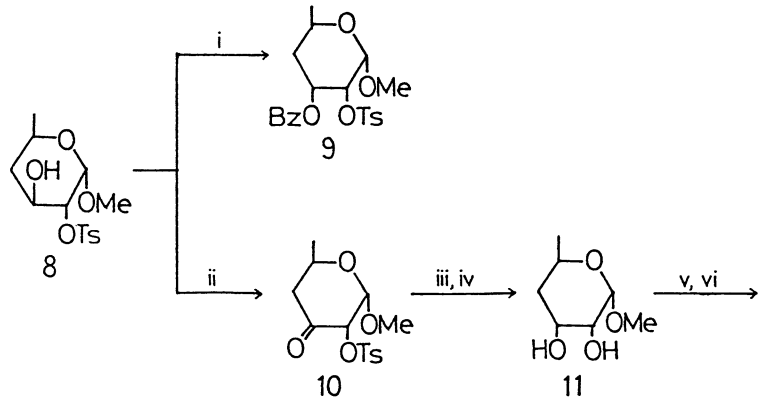
i) NaH, CS_2, imidazole, then MeI (87%). ii) Bu_3SnH, toluene, reflux, 10 h (74%). iii) $RhCl(Ph_3P)_3$-DABCO, EtOH-H_2O (9:1), reflux, 2 h (74%). iv) acetone-H_2O (10:1), $HgCl_2$, r.t., 25 min (78%). v) t-$BuO_2CCH{=}PPh_3$ (4), benzene, reflux, 2 h.

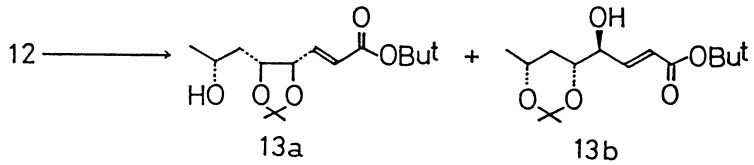
(2E,4S,5S,7R)-t-Butyl 4,5,7-trihydroxy-2-octenoate. Methyl 4,6-dideoxy-α-D-glucopyranoside was hydrolyzed, followed by treatment with 4 to give the title compound (6) in 65% overall yield. When the triol (6) was treated with acetone-2,2-dimethoxypropane in the presence of p-TsOH at room temperature, 4,5-O-isopropylidene derivative (7) was exclusively obtained in 97% yield.[7]



i) H_2O, Dowex-50(H^+), reflux, 2 h. ii) 4, benzene, reflux, 4 h. iii) acetone-$Me_2C(OMe)_2$, p-TsOH, r.t., 26 h (97%)

(2E,4S,5R,7R)-t-Butyl 4,5,7-trihydroxy-2-octenoate. When methyl 2-O-p-tosyl-4,6-dideoxy-α-D-glucopyranoside (8) was allowed to react with benzoic acid in the presence of diethyl azodicarboxylate and triphenylphosphine,[8] the desired methyl 2-O-p-tosyl-3-O-benzoyl-4,6-dideoxy-α-D-allopyranoside (9) was obtained in 24% yield with 65% recovery of the starting pyranoside.[9] Since several attempts to increase the yield of 9 were unsuccessful, an oxidation-reduction sequence was utilized for the inversion of 3-hydroxyl group.[10] Thus 8 was oxidized to ulose 10





i) $PhCO_2H$ + $EtO_2CN{=}NCO_2Et$ + Ph_3P,(24%). ii) DMSO-DCC, H_3PO_4, r.t., 2 days (84%). iii) $NaBH_4$ (79%). iv) $LiAlH_4$ (76%). v) H_2O, Dowex-50(H^+), reflux, 3 h (93%). vi) 4, benzene, reflux, 5.5 h (77%). vii) acetone-$Me_2C(OMe)_2$, p-TsOH, r.t., 15 h.

by Pfitzner-Moffatt reaction, followed by treatment with $NaBH_4$ to afford crystalline methyl 2-O-tosyl-4,6-dideoxyallopyranoside which was readily purified by recrystallization.[11] The $LiAlH_4$ reduction of the allopyranoside gave methyl 4,6-dideoxy-α-D-allopyranoside (11). Compound 11 was converted into the title compound (12) in 72% yield by the procedure described above. When 12 was treated with acetone and 2,2-dimethoxypropane in the presence of p-TsOH at room temperature for 15 h, 4,5-O-isopropylidene derivative (13a) and 5,7-O-isopropylidene derivative (13b) were obtained in 26 and 49% yields, respectively.[7] The predominant formation of six-membered acetonide would be attributed to non-bonded interaction between t-butoxycarbonylvinyl and 2-hydroxypropyl groups which destabilizes the 13a.[12]

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Table 1. 60-MHz NMR Chemical Shifts (ppm) in CCl_4

Compound	C_8H	C_7H	C_6H	C_4H, C_5H	C_3H*	C_2H*
5a**	1.2(d)	3.5-4.4(m)	1.4-1.8(m)	4.3-4.8(m)	6.72(dd)	5.95(dd)
7	1.15(d)	3.5-4.4(m)	1.5-2.0(m)	3.5-4.4(m)	6.75(dd)	5.9(dd)
13a	1.15(d)	3.87 (sextet)	1.2-1.9(m)	4.15-4.5 (3 lines) 4.5-4.8 (3 lines)	6.67(dd)	5.9(dd)
13b	1.15(d)	3.6-4.2(m)	1.3-1.8(m)	3.6-4.2(m) 4.1-4.5(m)	6.75(dd)	6.02(dd)

* First order coupling constants (Hz); $J_{2,3}$=15, $J_{3,4}$=4~6, $J_{2,4}$=1~1.5.

** Solution in $CDCl_3$.

References

1) Part VI of Stereospecific and Stereoselective Reactions. For Part V, see T. Kurihara, M. Sugizaki, I. Kime, M. Wada, and O. Mitsunobu, Bull. Chem. Soc. Jpn., 54, 2107 (1981).

2) J. MacMillan and T. J. Simpson, J. Chem. Soc., Perkin Trans, 1, 1973, 1487, and refs. therein.

3) The use of carbohydrates as starting materials for the construction of chiral natural products has been reviewed. See for example; S. Hanessian, Acc. Chem. Res., 12, 159 (1979). Y. Nakahara and T. Ogawa, in "Kosentakuteki Hanno", H. Nozaki, T. Mukaiyama, and R. Noyori, Ed., Kagakudozin, Kyoto (1981), pp 101-116. H. Ohrui, Yuki Gosei Kagaku Kyokai Shi (J. Synthetic Org. Chem. Jpn.), 39, 275 (1981).

4) D. H. R. Barton and S. W. McCombie, J. Chem. Soc., Perkin Trans. 1, 1975, 1574.

5) P. A. Gent and R. Gigg, J. Chem. Soc., Chem. Commun., 1974, 277, and refs. therein.

6) It has been reported that the reaction of methyl 2,3-O-isopropylidene-α-L-rhamnopyranoside with triphenylphosphite methiodide affords methyl 4,6-dideoxy-4-iodo-2,3-O-isopropylidene-α-L-mannopyranoside, methyl 5,6-dideoxy-5-iodo-2,3-O-isopropylidene-β-D-allofuranoside, and methyl 5,6-dideoxy-5-iodo-2,3-O-iso-

propylidene-α-L-talofuranoside. On hydrogenolysis over Raney nickel, the mannopyranoside gives methyl 4-deoxy-2,3-O-isopropylidene-α-L-rhamnopyranoside. N. K. Kochetkov, A. I. Usov, and K. S. Adamyants, Tetrahedron, 27, 549 (1971). K. Kefurt, J. Jary, and Z. Samek, J. Chem. Soc., Chem. Commun., 1969, 213.

7) Determination of structures of 7, 13a, and 13b was not possible via direct spectroscopic method. Therefore, they were respectively oxidized to ketones by pyridinium chlorochromate in the presence of sodium acetate.[13] The ^{1}H-NMR (60 MHz) spectra of ketones derived from 7 and 13a show three-proton singlet at δ 2.1~2.15, assigned to C_8 protons. On the other hand, signals for C_8 protons and olefinic protons of the ketone derived from 13b appear as doublet at δ 1.15 and AB-quartet at δ 6.64 and 7.35 with J=16 Hz.

8) O. Mitsunobu, Synthesis, 1981, 1.

9) No attempt was made to confirm the configuration at C_3. Based on related reactions, however, it would be reasonable to assume that inversion took place during the reaction.[8]

10) B. R. Baker and D. H. Buss, J. Org. Chem., 30, 2304 (1965). D. C. Baker, J. Defaye, A. Gadelle, and D. Horton, ibid., 41, 3834 (1976). Y. Kondo, Carbohydr. Res., 30, 386 (1973). H. Honig and H. Weidmann, ibid., 39, 374 (1975), and refs. therein.

11) Thin layer chromatography of the crude reaction mixture indicated the presence of trace of 8, which could be removed by recrystallization from ethanol-hexane.

12) The ratio of 13a to 13b did not practically change when the reaction was carried out over a period of 44 h.

13) E. J. Corey and W. Suggs, Tetrahedron Lett., 1975, 2647.

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