Available online at www.sciencedirect.com
ScienceDirect
Mendeleev Commun., 1992, **2(2)**, 65–67
Mendeleev Communications

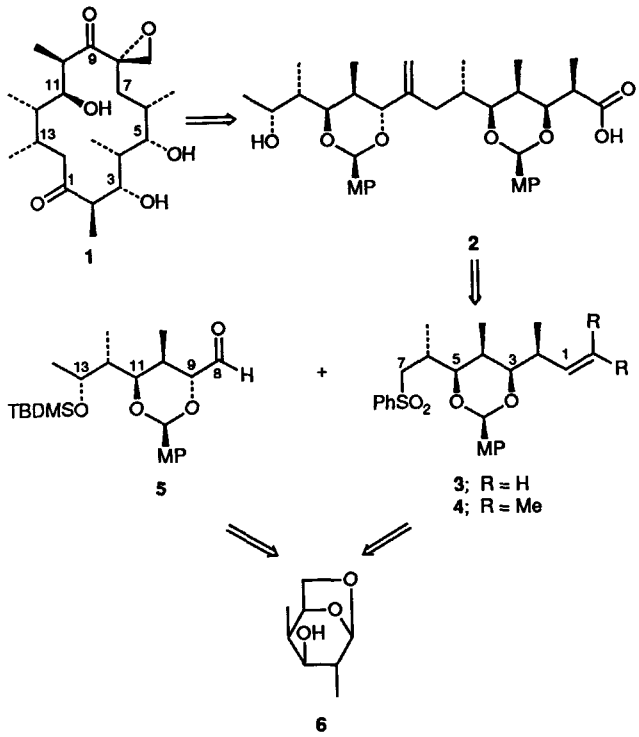
Novel Stereoselective Synthesis of the C-1–C-7 Segment of Oleandonolide and Lankanolide

Alexander F. Sviridov,* Alexander S. Kuz'min, Dmitrii V. Yashunskii and Nikolai K. Kochetkov

N. D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences, 117913 Moscow, Russian Federation. Fax: + 7 095 135 5328

The stereoselective synthesis of the C-1–C-7 segment of oleandonolide and lankanolide from a D-galactose derivative has been accomplished.

Recently, we have reported our initial studies directed toward the total synthesis of lankanolide and oleandonolide **1**, starting from carbohydrate precursors.[1,2] The above macrolides contain an identical C-1–C-7 segment (**3** or **4**) (the synthesis of **3** from 1,6-anhydro-2,4-dideoxy-2,4-di-*C*-methyl-β-D-glucose has been reported[1]) and the closely related C-8–C-15[1] and C-8–C-13 **5** segments, respectively. The latter was synthesized from galacto-derivative **6**.[2] Here we report a new efficient synthesis of the C-1–C-7 segment of oleandonolide and lankanolide (in the form of sulfone **4**) from the same derivative **6**. This approach allowed us to realize a convergent synthesis of oleandonolide **1** (through **2**) from a single precursor,



Scheme 1

1,6-anhydro-2,4-dideoxy-2,4-di-*C*-methyl-β-D-galactose **6**[3] (Scheme 1).

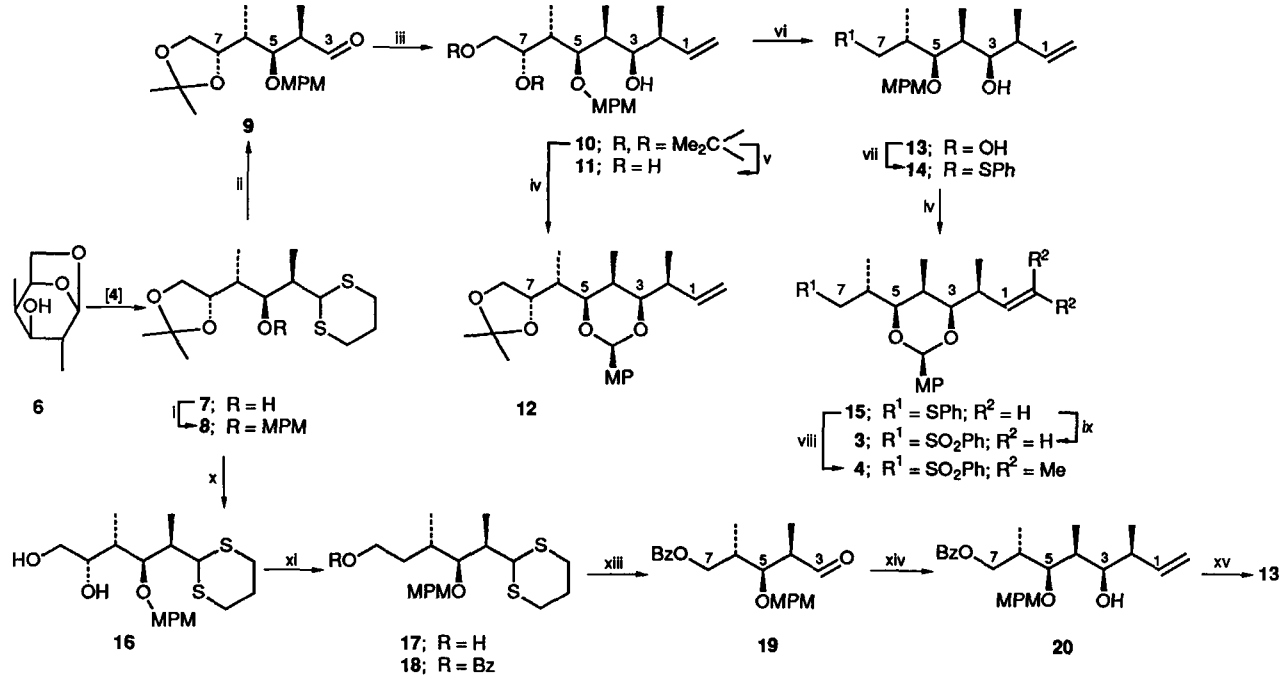
The addition of tri-n-butylcrotyltin to aldehyde **9** or **19** was chosen as the key step of this new synthesis of the C-1–C-7 segment **4**. The above reagent is known to exhibit high *syn*-selectivity for Lewis acid-promoted addition to aldehydes,[5,6] irrespective of the double bond geometry that makes it very attractive from a preparative point of view. Recent studies revealed that the diastereoselectivity of addition of tri-n-butylcrotyltin to chiral α- and β-alkoxyaldehydes can be controlled by the nature of the Lewis acid and the structure of the substrate.[6,7]

It was found that BF_3-promoted addition of tri-n-butylcrotyltin to aldehyde **9** (derived from the known **8**[4]) afforded the 2,3:3,4-*syn* product **10** (Scheme 2). The configuration of adduct **10** at C-3 was confirmed by ^{1}H NMR analysis of the cyclic acetal **12**.† Final confirmation of the stereochemistry was

† All compounds were obtained as chromatographically pure syrups and gave satisfactory ^{1}H NMR spectra. All ^{1}H NMR spectra were measured on a Bruker WM-250 spectrometer in $CDCl_3$. All optical rotations were measured on a DIP-360 instrument (JASCO, Japan) in $CHCl_3$ (*c* 1.0).

Characterisation data for **12**: $[\alpha]_D^{27}$ −23.8; δ_H 0.92 (d, 3H, $J_{Me,4}$ 7.0 Hz, 4-Me), 0.96 (d, 3H, $J_{Me,6}$ 7.0 Hz, 6-Me), 1.14 (d, 3H, $J_{Me,2}$ 7.0 Hz, 2-Me), 1.36 and 1.43 (s, 6H, acetal Me), 1.69 (m, 1H, 4-H), 1.84 (m, 1H, 6-H), 2.47 (m, 1H, 2-H), 3.42 (dd, 1H, $J_{3,4}$ 2.0 Hz, $J_{3,2}$ 10 Hz, 3-H), 3.56 (dd, 1H, $J_{5,4}$ 2.0 Hz, $J_{5,6}$ 8.0 Hz, 5-H), 3.68 (dd, 1H, $J_{8,8'}$ 8.0 Hz, $J_{8,7}$ 7.0 Hz, 8-H), 3.81 (s, 3H, 3,5-C*H*$_3$OC$_6$H$_4$CH), 4.05 (dd, 1H, $J_{8',7}$ 7.0 Hz, 8'-H), 4.23 (ddd, 1H, $J_{7,6}$ 2.0 Hz, 7-H), 5.08 (dd, 1H, $J_{1'cis,1}$ 10.0, $J_{1'cis,1'trans}$ 2.0 Hz, 1'*cis*-H), 5.15 (ddd, 1H, $J_{1'trans,1}$ 17.0 Hz, $J_{1'trans,2}$ 1.0 Hz, 1'*trans*-H), 5.48 (s, 1H, 3,5-MeOC$_6$H$_4$C*H*), 5.65 (ddd, 1H, $J_{1,2}$ 8.5 Hz, 1-H), 6.90 and 7.43 (m, 4H, 3,5-MeOC$_6$*H*$_4$CH); NOE: (H acetal) 3-H 10%; (H acetal) 5-H 10%.

4: $[\alpha]_D^{27}$ −26.3; δ_H 0.76 (d, 3H, $J_{Me,4}$ 7.0 Hz, 4-Me), 1.00 (d, 3H, $J_{Me,2}$ 7.0 Hz, 2-Me), 1.16 (d, 3H, $J_{Me,6}$ 7.0 Hz, 6-Me), 1.69 (m, 1H, 4-H), 1.65 and 1.71 (d, 6H, $J_{Me,1}$ 1.7 Hz, 1'-Me), 2.30 (m, 1H, 6-H), 2.56 (m, 1H, 2-H), 2.92 (dd, 1H, $J_{7,7'}$ 13.0 Hz, $J_{7,6}$ 8.0 Hz, 7-H), 3.35 (m, 2H, 3-H and 7'-H), 3.67 (dd, 1H, $J_{5,4}$ 2.0 Hz, $J_{5,6}$ 10.0 Hz, 5-H), 3.82 (s, 3H, 3,5-C*H*$_3$OC$_6$H$_4$CH), 4.81 (dt, 1H, $J_{1,2}$ 10.0 Hz, 1-H), 5.31 (s, 1H, 3,5-MeOC$_6$H$_4$C*H*), 6.86 and 7.36 (m, 4H, 3,5-MeOC$_6$*H*$_4$CH), 7.44–7.68 and 7.89 (m, 5H, C$_6$H$_5$SO$_2$).



Scheme 2 *Reagents and conditions*: i, *p*-methoxybenzyl chloride, NaH–dimethylformamide (DMF) (100%); ii, Hg(OAc)$_2$–CdCO$_3$, Me$_2$CO–H$_2$O (8:1) (50%); iii, tri-n-butylcrotyltin, $BF_3 \cdot Et_2O$, CH_2Cl_2, −78 °C (56%); iv, 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ), 3 Å molecular sieves, CH_2Cl_2 (86%); v, AcOH–tetrahydrofuran (THF)–H$_2$O (4:1:1), 60 °C (37%); vi, $NaIO_4$, Me$_2$CO–H$_2$O (4:1); $NaBH_4$, EtOH (92%); vii, Ph_2S_2, Bu$^n_3$P, pyridine (Py) (91%); viii, OsO_4, $NaIO_4$, Me$_2$CO–H$_2$O (6:1); Bu^{n}Li, Pr^{i}PPh$_3$I, THF, −65→20 °C (43%); ix, *m*-chloroperbenzoic acid (MCPBA), CH_2Cl_2 (100%); x, 1 mol dm^{-3} HCl, THF (87%); xi, Pb(OAc)$_4$, KOAc, MeCN; $NaBH_4$, Pr^{i}OH–$CHCl_3$ (4:1) (76%); xii, BzCl, Py (100%); xiii, Hg(OAc)$_2$–CdCO$_3$, Me$_2$CO–H$_2$O (6:1) (78%); xiv, tri-n-butylcrotyltin, $BF_3 \cdot Et_2O$, CH_2Cl_2, −78 °C (75%); xv, 15% NaOH, MeOH (95%)

secured by transformation of **10** into the known[1] derivatives **15** and **3**.

The modified sequence for the synthesis of the intermediate **13** was more efficient. Thus, the addition of tri-n-butylcrotyltin to aldehyde **19** (derived from the known **8**) in the presence of $BF_3 \cdot Et_2O$ afforded the adduct **20** in 75% yield. The latter was transformed into the known diol **13**. The routine four-step transformation of diol **13** (*cf.* refs. 1,2) led to the desired sulfone **4**,† the C-1–C-7 segment of oleandonolide and lankanolide.

Received: Moscow, 6th December 1991
Cambridge, 27th January 1992; Com. 2/00204C

References

1 N. K. Kochetkov, D. V. Yashunskii, A. F. Sviridov and M. S. Ermolenko, *Carbohydr. Res.*, 1990, **200**, 209.
2 A. F. Sviridov, D. V. Yashunsky, A. S. Kuz'min and N. K. Kochetkov, *Mendeleev Commun.*, 1991, 4.
3 N. K. Kochetkov, A. F. Sviridov, D. V. Yashunskii, M. S. Ermolenko and V. S. Borodkin, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1986, 441 (*Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1986, 408).
4 N. K. Kochetkov, A. F. Sviridov, M. S. Ermolenko, D. V. Yashunskii and V. S. Borodkin, *Tetrahedron*, 1989, **45**, 5109.
5 Y. Yamamoto, H. Yatagai, Y. Ishihara, N. Maeda and K. Maruyama, *Tetrahedron*, 1984, **40**, 2239.
6 G. E. Keck and E. P. Boden, *Tetrahedron Lett.*, 1984, **25**, 1879.
7 G. E. Keck and E. P. Boden, *Tetrahedron Lett.*, 1984, **25**, 1883.