Stereochemistry of Osmylation of Chiral Dienes: Diastereoselective Synthesis of Octitols

Kesavaram Narkunan and Madhavarao Nagarajan*

School of Chemistry, University of Hyderabad, Hyderabad-500 134, India

The synthesis of higher sugars by hydroxylation of sugar derived dienes **2** and **4** using OsO_4–NMO is described.

In the context of the synthesis of higher sugars,[1] we were interested in *bis*-osmylation of chiral sugar dienes. It is surprising that inspite recent advances in catalytic asymmetric dihydroxylation and the vast knowledge about the diastereoselective nature of osmylation,[2] *bis*-osmylation of chiral dienes is not known in the literature. This motivated us to explore its potential for use in higher sugar synthesis, as it would simultaneously generate several contiguous chiral centres.

Kishi showed that the relative stereochemistry between the existing hydroxy or alkoxy group and the adjacent newly introduced hydroxy group of the major product is *erythro* in all cases.[3] Recently, Sharpless observed that on osmylation of achiral dienes and trienes, the major product has an *erythro* relationship between the hydroxy groups formed between two double bonds[4] and selective asymmetric dihydroxylation of unsymmetrical dienes occurs at the more substituted double bond.[5] At this stage we were interested in making a model in which both Kishi's and Sharpless's observations would be operative (*i.e.* a diene attached to a chiral centre). We thus chose dienes **2** and **4** and the structures of all the possible hydroxylated conversion products, **7**–**10** and **11**–**14**, respectively were analysed (Fig. 1). Both dienes **2** and **4** on hydroxylation will provide one *meso* and one C_2 symmetric diastereoisomer each, one of the diastereoisomers obtainable from both **2** and **4** form an enantiomeric pair and one of the diastereoisomers obtainable from **2** is identical to one of those derivable from **4**. These features allow for easy and unambiguous product identification.

Dienes **2** and **4** were synthesised by the Wittig reaction of the known enals **1**[6] and **3**,[7] respectively (Scheme 1). Dienes **2** and **4** were osmylated using OsO_4–NMO, and the resulting hydroxylated products were converted to their peracetylated octitol mixtures **5** and **6**, respectively, using conventional protection and deprotection methods as shown in Scheme 2. Separation of the diastereoisomeric peracetylated octitol mixture **5** from **2** by partial crystallisation revealed that **7**-OAc, **8**-OAc and **9**-OAc were formed in a ratio of 1.15 : 6.6 : 1. The diastereoisomeric peracetylated octitol mixture **6** obtained from **4** by partial crystallisation and HPLC separation showed that **11**-OAc, **12**-OAc and **14**-OAc were present in a 1.33 : 1 : 1 ratio, respectively.† The structure of **7**-OAc (mp 184–185 °C) was confirmed by converting it into the known (*meso*)-*threo*-gluco-octitol **7**.[8] Further evidence for its structure comes from its ^1H and ^{13}C NMR spectra and it showed no optical rotation. The structure **8**-OAc was assigned to a syrupy material obtained from **2**, since its enantiomer **12**-OAc (identical ^1H and ^{13}C NMR spectra but equal and opposite optical rotation) was obtained from **4**. Subsequently, the structure of the crystalline product obtained from **2** (one of the three diastereoisomers) is **9**-OAc, as evidenced from its

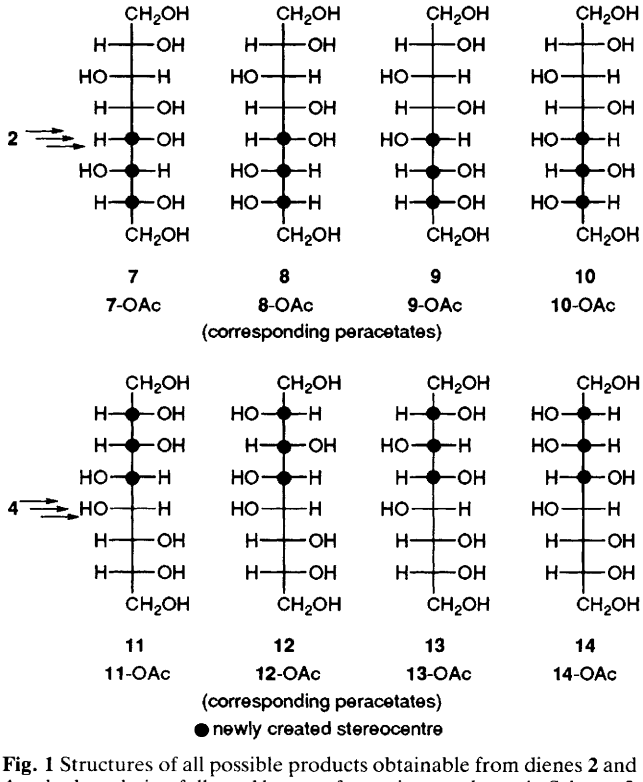
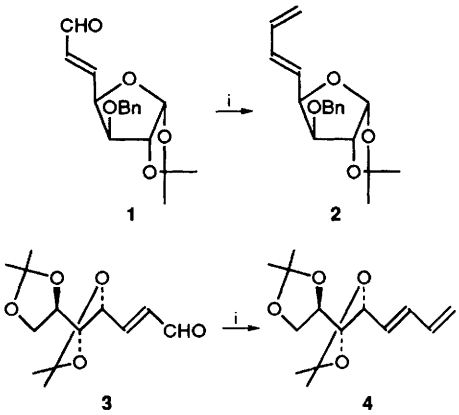
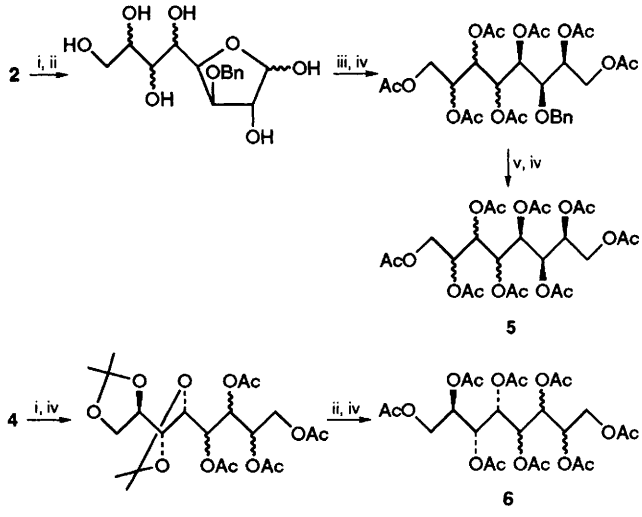


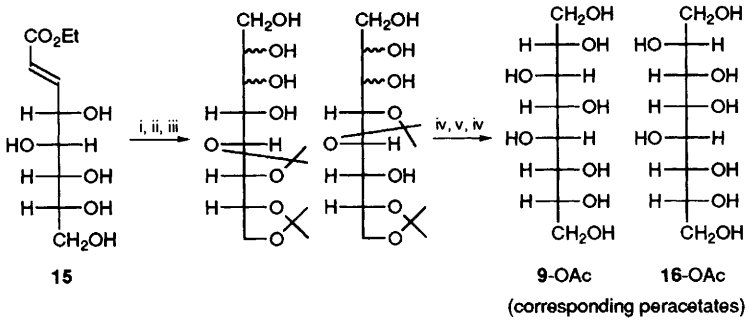
Fig. 1 Structures of all possible products obtainable from dienes **2** and **4** on hydroxylation followed by transformations as shown in Scheme 2



Scheme 1 *Reagents and conditions*: i, $Ph_3P{=}CH_2$, THF, 0 °C, 2 h



Scheme 2 *Reagents and conditions*: i, OsO_4, NMO, acetone, 8 h; ii, TFA : H_2O (9 : 1); iii, $NaBH_4$, H_2O; iv, Ac_2O, Py, 100 °C, 3 h; v, Pd/C, H_2, ethanol, 50 psi, 6 h



Scheme 3 *Reagents and conditions*: i, acetone, H_2SO_4, $CuSO_4$, 25 h; ii, OsO_4, NMO; iii, LAH, THF, reflux, 1 h; iv, Ac_2O, Py, 100 °C, 3 h; v, TFA : H_2O (9 : 1)

NMR spectrum (non-symmetric). Incidentally, as **10**-OAc has C_2 symmetry, it would show only half the number of signals in the ^1H and ^{13}C NMR spectra when compared to **9**-OAc. In order to provide further evidence for the structure of **9**-OAc, the known ethyl-2,3-di-deoxy-D-gluco-oct-2(*E*)-enonate **15**[9] was osmylated and further transformed to a mixture of **9**-OAc and **16**-OAc (Scheme 3). **9**-OAc was separated from **16**-OAc by partial crystallisation and its spectra (^1H and ^{13}C NMR) and rotation were identical to those of **9**-OAc obtained from **2**. The identities of **11**-OAc and **14**-OAc were established by comparing their physical data with that reported.[10,11]

Results of the diastereoselective hydroxylation of dienes **2** and **4** indicate that the major isomer formed is the one in which both the relations between the existing hydroxy group and the adjacent newly introduced hydroxy group as well as the hydroxy groups formed between two double bonds are *erythro*. It is also interesting to note that stereoisomers **10**-OAc and **13**-OAc were not formed at all, since in both of them the relations are *threo*. We are now applying this methodology incorporating asymmetric dihydroxylation for the synthesis of higher sugars.[12]

We thank the DST and the UGC(JRF as well as COSIST programme) for their financial support.

Received, 12th April 1994; Com. 4/02150I

Footnote

† Partial crystallization of **5** gave **7**-OAc, **8**-OAc and **9**-OAc in a ratio of 1.15 : 6.6 : 1 with a recovery of 90%, based on **5**. Similarly, **6** on partial crystallization gave a 2 : 3 mixture of pure **11**-OAc and unseparated **12**-OAc and **14**-OAc in 95% yield based on **6**. The mixture of **12**-OAc and **14**-OAc was converted to their corresponding benzoates in 72% yield by saponification of the acetates followed by benzoylation. The perbenzoylated diastereoisomeric mixture was separated by HPLC in to two components in a 1 : 1 ratio with 92% recovery and were further hydrolysed and acetylated to obtain **12**-OAc (75%) and **14**-OAc (87%). All the new compounds were satisfactorily characterised.

References

1 J. S. Brimacombe, in *Studies in Natural Products Chemistry*, ed. Atta-ur-Rahman, Elsevier, Amsterdam, 1989, **4**, 157–193; A. Zamojski and S. Jarosz, *Pol. Acad. Sci.*, 1992, **66**, 525.
2 K. B. Sharpless, W. Amberg, Y. L. Bennani, G. A. Crispino, J. Hartung, K. S. Jeong, H. L. Kwong, K. Morikawa, Z. M. Wang, D. Xu and X. L. Zhang, *J. Org. Chem.*, 1992, **57**, 2768.
3 J. K. Cha, W. J. Christ and Y. Kishi, *Tetrahedron*, 1984, **40**, 2247.
4 C. Y. Park, B. M. Kim and K. B. Sharpless, *Tetrahedron Lett.*, 1991, **32**, 1003.
5 D. Xu, G. A. Crispino and K. B. Sharpless, *J. Am. Chem. Soc.*, 1992, **114**, 7570.
6 D. Horton and J. H. Tsai, *Carbohydr. Res.*, 1979, **75**, 151.
7 D. Horton, A. Liav and S. E. Walker, *Carbohydr. Res.*, 1973, **28**, 201.
8 J. C. Barnes, J. S. Brimacombe and G. McDonald, *J. Chem. Soc., Perkin Trans I.*, 1989, 1483.
9 N. K. Kochetkov and B. A. Dmitriev, *Tetrahedron.*, 1965, **21**, 803.
10 R. M. Hann, W. D. Maclay, A. E. Knauf and C. S. Hudson, *J. Am. Chem. Soc.*, 1939, **61**, 1268.
11 R. Schaffer and A. Cohen, *J. Org. Chem.*, 1963, **28**, 1929.
12 G. A. Crispino, A. Makita, Z. M. Wang and K. B. Sharpless, *Tetrahedron Lett.*, 1994, **35**, 543.