Pergamon

Tetrahedron: Asymmetry, Vol. 7, No. 2, pp. 407-408, 1996

0957-4166/96 $15.00 + 0.00

S0957-4166(96)00019-5

Highly Enantioselective Rearrangement of Quaternary Carbon-Containing *meso*-Epoxides to Allylic Alcohols

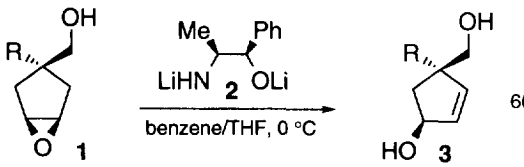
David M. Hodgson* and Andrew R. Gibbs

The Dyson Perrins Laboratory, University of Oxford, South Parks Road, Oxford OX1 3QY, UK[1]

and Department of Chemistry, The University of Reading, Whiteknights, Reading RG6 2AD, UK

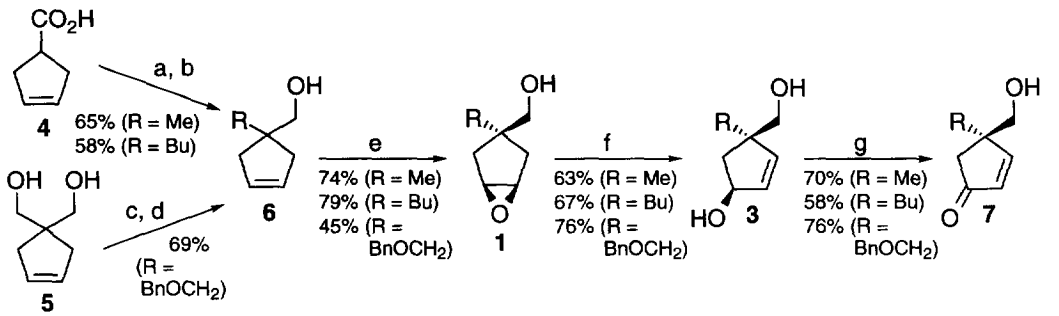
Abstract: The asymmetric synthesis of 4-substituted cis-4-(hydroxymethyl)cyclopent-2-en-1-ols **3** (R = alkyl, benzyloxymethyl) via highly enantioselective rearrangement of 3-substituted cis-6-oxabicyclo[3.1.0]hexane-3-methanols **1** (R = alkyl, benzyloxymethyl) is described.

The enantioselective rearrangement of *meso*-epoxides to allylic alcohols using homochiral bases has been the focus of much research.[2] However, this strategy has not been investigated with *meso*-epoxides containing quaternary (tetra-carbon substituted) carbon centres.[3] This could be due to perceived difficulties in establishing the relative stereochemistry between the epoxide and the quaternary centre in the *meso*-starting material. We recently reported an enantioselective rearrangement of a *meso*-epoxy alcohol for carbocyclic nucleoside synthesis (Eq. 1, R = H).[4] In that work the hydroxyl group served to initially direct epoxidation with excellent stereocontrol (*cis*:*trans* ≥ 97:3) and subsequently to promote the rearrangement and an excellent level of asymmetric induction - the highest *ee* recorded to date for a transformation of this type. It was therefore considered important to determine the scope of this chemistry. Here we communicate our preliminary results concerning the effect of additional *trans*-substituents (Eq. 1, R ≠ H) on the rearrangement as methodology for the asymmetric synthesis of quaternary carbon-containing materials, itself an area of considerable research interest.[5] This chemistry was examined in the knowledge that epoxide → allylic alcohol transformations are considered to occur *via* proton removal *syn* to the epoxide.[6] Therefore in our work *trans*-substituents were predicted not to disrupt substantially the transition state aggregate for rearrangement, and hence the *ee*, from that which operated with the original *meso*-epoxy alcohol (Eq. 1, R = H).



66%, ≥ 95% *ee* for R = H (1)

In order to examine this chemistry readily available 3-cyclopentenecarboxylic acid **4**[7] and 3-cyclopentene-1,1-dimethanol **5**[7] were first converted into the alcohols **6** using standard procedures (Scheme 1), followed by hydroxyl-directed epoxidation under our previously reported conditions[4] to give the representative *meso*-epoxy alcohols **1** (R = Me, Bu, $BnOCH_2$). Analysis of the ^1H nmr spectra of the crude *meso*-epoxy alcohols **1** (R = Me, Bu, $BnOCH_2$) indicated that, in each case, only a single isomer was produced. *cis*-Relative stereochemistry between the hydroxymethyl and epoxide groups were assigned by analogy with our earlier work.[4]



(a) LDA (2 equiv.), RI, THF, 0 °C, 15 h; (b) $LiAlH_4$, Et_2O, 25 °C, 3 h; (c) PhCHO, cat. *p*-TSA, benzene, reflux, 24 h; (d) DIBAL-H, CH_2Cl_2, 25 °C, 4 h; (e) Bu^tOOH, cat. $VO(acac)_2$, CH_2Cl_2, 25 °C, 24 h; (f) (1*R*,2*S*)-norephedrine (3 equiv.), BuLi (6 equiv.), 3:2 benzene/THF, 0 °C to 25 °C, 12 h; (g) PDC, 2% AcOH in EtOAc, 25 °C, 1.5 h.

Scheme 1[8]

In accord with our prediction the *meso*-epoxy alcohols smoothly rearranged using dilithiated (1*R*,2*S*)-norephedrine **2** to give the *cis*-diols **3** in reproducibly good *ee*s [R = Me (99%), Bu (96%), $BnOCH_2$ (89%)], as determined by HPLC analyses [Daicel Chiralpak AD column (4.6 mm x 250 mm), 75:25 EtOH/Hexane as eluent] of the 2,4-dinitrobenzoate derivatives of the corresponding hydroxy enones **7**. The absolute stereochemistry of the major enantiomer of the diol **3** (R = Bu) is as shown in Scheme 1, and was determined *via* the corresponding hydroxy enone **7** (R = Bu) after 3,5-dinitrobenzoate derivatisation, ketalisation [(–)-(2*R*,3*R*)-2,3-bis(TMSO)butane, cat. TMSOTf, CH_2Cl_2, –78 °C to 25 °C, 12 h, 63% yield][9] and subsequent X-ray crystallographic analysis.[10] The sense of asymmetric induction parallels that observed in our earlier study (Eq. 1, R = H).[4] The absolute stereochemistry induced in the diols **3** (R = Me, $BnOCH_2$) was assigned by analogy with diol **3** (R = Bu).

In summary, this work establishes that *meso*-epoxide desymmetrisation using a chiral base can be used to prepare, in good *ee*s, potentially useful functionalised cyclopentenols containing quaternary (tetra-carbon substituted) stereocentres. In addition, the present results combine with those obtained in our earlier work[4] to suggest that the reactions we have examined proceed by a *syn* elimination mechanism.

Acknowledgements: We thank the Paul Beswick Memorial Trust for financial support of this work, The Royal Society for a Research Grant towards a HPLC system and the EPSRC Mass Spectrometry Service Centre for mass spectra. We also thank Zeneca (Strategic Research Fund) for a generous unrestricted grant.

REFERENCES AND NOTES

1. Address for correspondence.
2. Cox, P. J.; Simpkins, N. S. *Tetrahedron: Asymmetry* **1991**, *2*, 1-26.
3. For a tertiary alcohol prepared using this strategy see: Asami, M.; Ishizaki, T.; Inoue, S. *Tetrahedron Lett.* **1995**, *36*, 1893-1894.
4. Hodgson, D. M.; Witherington, J.; Moloney, B. A. *J. Chem. Soc., Perkin Trans. 1* **1994**, 3373-3378.
5. Fuji, K. *Chem. Rev.* **1993**, *93*, 2037-2066.
6. Crandall, J. K.; Apparu, M. *Org. React. (N. Y.)* **1983**, *29*, 345-443.
7. Deprés, J.-P.; Greene, A. E. *J. Org. Chem.* 1984, **49**, 928-931. Paulsen, H.; Maaß, U. *Chem. Ber.* **1981**, *114*, 346-358.
8. Isolated total yields of chromatographically homogeneous, spectroscopically pure products are reported.
9. Mash, E. A.; Fryling, J. A. *J. Org. Chem.* **1987**, *52*, 3000-3003.
10. Full details will be reported at a later date.

(*Received in UK* 1 *December* 1995)