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Synthesis of three of the four diastereomers of 2-(1′,2′-isopropylidenedioxyethyl)-3-methyloxetane from D-mannitol

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The synthesis of three highly oxygenated, diastereomeric and optically active oxetanes from D-mannitol is described.

Keywords: asymmetric synthesis, chiral pool, oxetanes

The synthesis of oxetanes remains an important challenge. Oxetane rings have been found in a wide range of biologically active compounds.[2–7] Oxetanes are potentially useful synthetic equivalents for the a^3-synthon.[9–13]

We based our syntheses on the availability of protected glyceraldehyde **4**.[19] Aldehyde **4** underwent aldol reactions with enolates **5**,[20] **12**,[23] and **15**[25] to give β-hydroxy carboxylic acid derivatives **6** (as a mixture of diastereoisomers), **13** and **16** which may be reduced with lithium aluminium hydride (**6** and **13**) or lithium borohydride/water (**16**) to give three diastereomeric 1,3-diols, **9, 10** and **17**. Transformation of diol **17** into the corresponding Mosher's ester was not successful. Diols **9** and **10** had $[\alpha]_D^{22} = +19.0$ (lit. +31.7)[21] and $[\alpha]_D^{22} = +14.4$ (lit. +15.8)[21] suggesting enantiomeric excesses of the order of 60 and 91% respectively. The isolation of **17** as a single diastereoisomer (as shown by ^{1}H NMR) suggests an enantiomeric excess of >95%.

Treatment of the 1,3-diols with methane sulfonyl chloride/triethylamine followed by potassium *tert*butoxide gave the corresponding optically active oxetanes, **11**, **14** and **18**, as single diastereomers.

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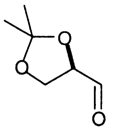
Techniques used: TLC, m.p., optical rotation, FTIR, ^{1}H and ^{13}C NMR, LRMS and HRMS.

References: 26

Schemes: 6



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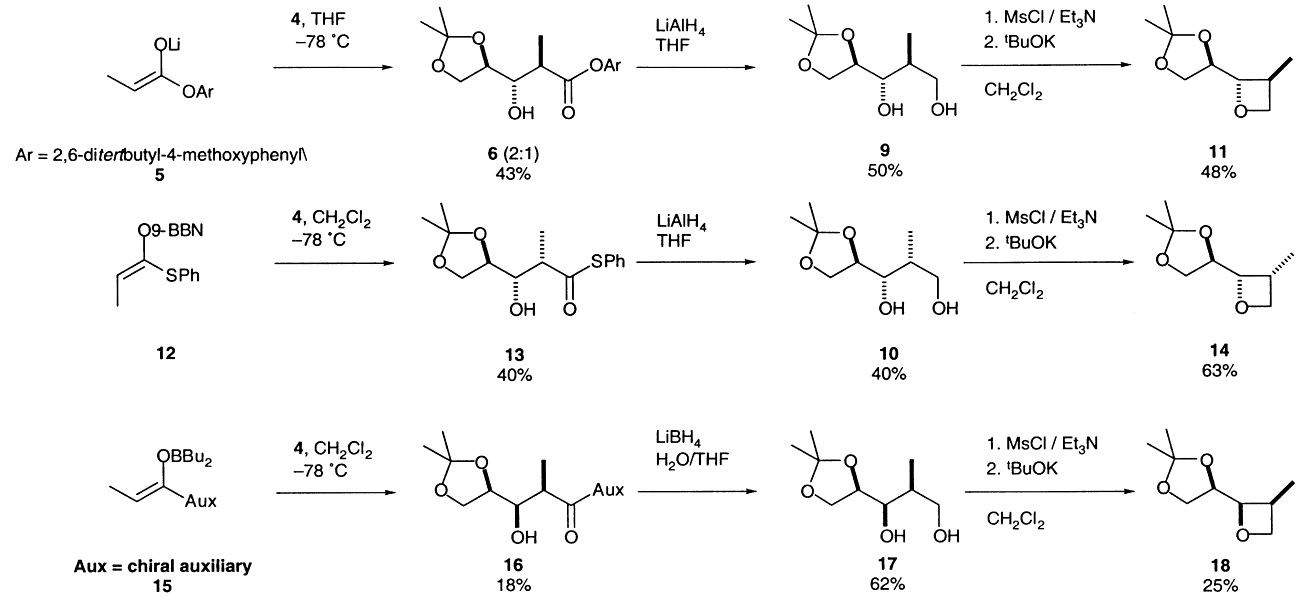
References cited in this synopsis

2 K.C. Nicolaou and R.K. Guy, *Angew. Chem., Int. Ed. Eng.*, 1995, **34**, 2079.
3 S.S. Bhagwat, P.R. Hamann and W.C. Still, *J. Am. Chem. Soc.*, 1985, **107**, 6372.
4 F.A. Macías, J.M. G. Molinillo and G.M. Massanet, *Tetrahedron*, 1993, **49**, 2499.
5 T. Suzuki and E. Kurosawa, *Chem. Lett.*, 1979, 301.
6 D.W. Norbeck and J.B. Kramer, *J. Am. Chem. Soc.*, 1988, **110**, 7217.



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7 Y. Kawahata, S. Takatsuto, N. Ikekawa, M. Murata and S. Omura, *Chem. Pharm. Bull.*, 1986, **34**, 3102.

9 T. Bach, F. Eilers and K. Kather, *Liebigs Ann./ Recueil*, 1997, 1529.

10 H. Xianming and R. M. Kellogg, *Tetrahedron: Asymmetry*, 1995, **6**, 1399.

11 P. Crotti, L. Favero, F. Macchia and M. Pineschi, *Tetrahedron Lett.*, 1994, **35**, 7089.

12 D.R. Morton and R.A. Morge, *J. Org. Chem.*, 1978, **43**, 2093.

13 A. Bochki, L.R. Falvello, F. Foubelo and M. Yus, *Tetrahedron: Asymmetry*, 1997, **8**, 2633.

19 C.R. Schmid and J.D. Bryant, *Org. Synth.*, 1995, **72**, 6.

20 C. H. Heathcock, C. T. Buse, W. A. Kleschick, M. C. Pirrung, J.E. Sohn and T. Lampe, *J. Org. Chem.*, 1980, **45**, 1066.

21 C.H. Heathcock, S.D. Young, J.P. Hagen, M.C. Pirrung, C.T. White and D. VanDerveer, *J. Org. Chem.*,1980, **45**, 3846.

23 S. Masamune, W. Choy, J. S. Peterson and L. R. Sita, *Angew. Chem., Int. Ed. Engl.*, 1985, **24**, 1.

25 D.A. Evans, J. Bartroli and T.L. Shih, *J. Am. Chem. Soc.*, 1981, **103**, 2127.