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Alkenyl Oxazolidinones by Stereoselective Epoxidation of δ-Hydroxy Allylic Phosphine Oxides: Synthesis of Any Isomer (*RR*, *RS*, *SR* or *SS*; *E* or *Z*) Bearing 1,4-Related Chiral Centres Across a Double Bond

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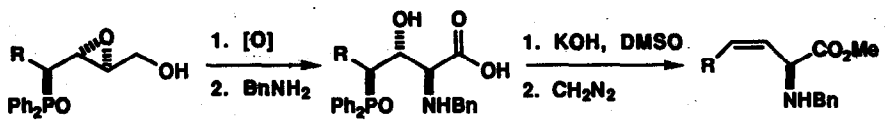
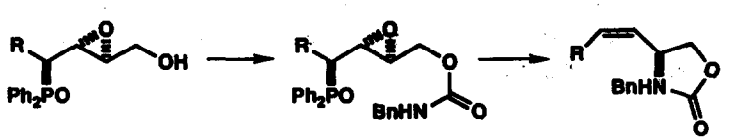
***Abstract:** Alkenyl oxazolidinones 5 have been made from the urethane derivatives 4 of diphenylphosphinoyl epoxy alcohols 1 by a tandem intramolecular ring closure – Horner-Wittig elimination sequence. The stereoisomers of diphenylphosphinoyl epoxy alcohols containing further chiral centres have been made by enantio- and diastereoselective epoxidation, and converted stereospecifically to alkenyl oxazolidinones with 1,4-related chiral centres across a controlled geometry double bond.*

Recently,[1] we showed that regioselective nucleophilic attack on the epoxy acids derived from epoxy alcohols **1**, followed by Horner-Wittig elimination of the product β-hydroxy phosphine oxides **2**, can be used to make the unsaturated amino acids **3**. By combining enantioselective and *anti* diastereoselective Sharpless kinetic resolution[2] with *syn* diastereoselective peracid epoxidation,[1] we were able to make four stereoisomers of the epoxy alcohols **1** and therefore all four (*R* or *S*, *E* or *Z*) possible stereoisomers of the amino acids **3**.

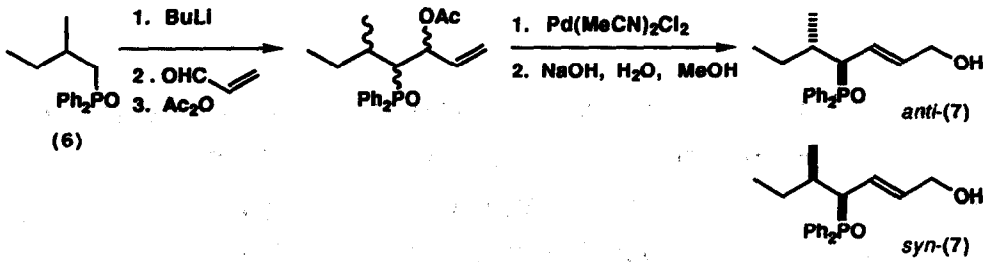


(1) (2) (3)

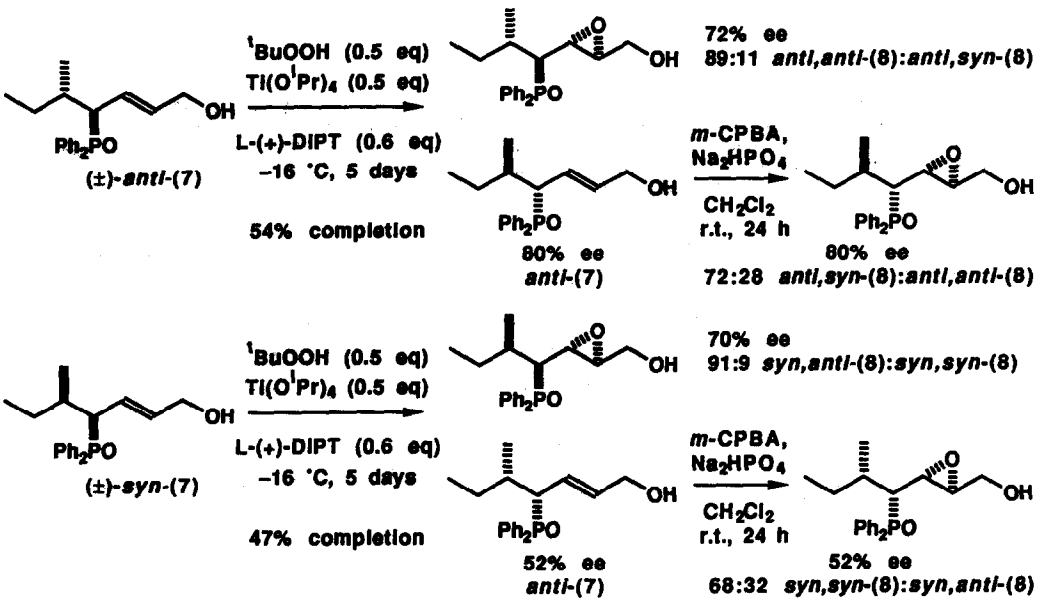
In this paper we report an alternative synthetic route from epoxy alcohols **1**, making use of a regioselective intramolecular epoxide opening.[3] Ring-closure of urethane **4** under basic conditions reveals an oxyanion which, in the same step, takes part in a stereospecific Horner-Wittig elimination, forming the alkenyl oxazolidinones **5** in good yield directly from the urethanes **4**. By introducing further chiral centres into epoxy alcohols **1** (R = CHMeEt), it is possible to control 1,4-related chiral centres across a double bond of controlled geometry.



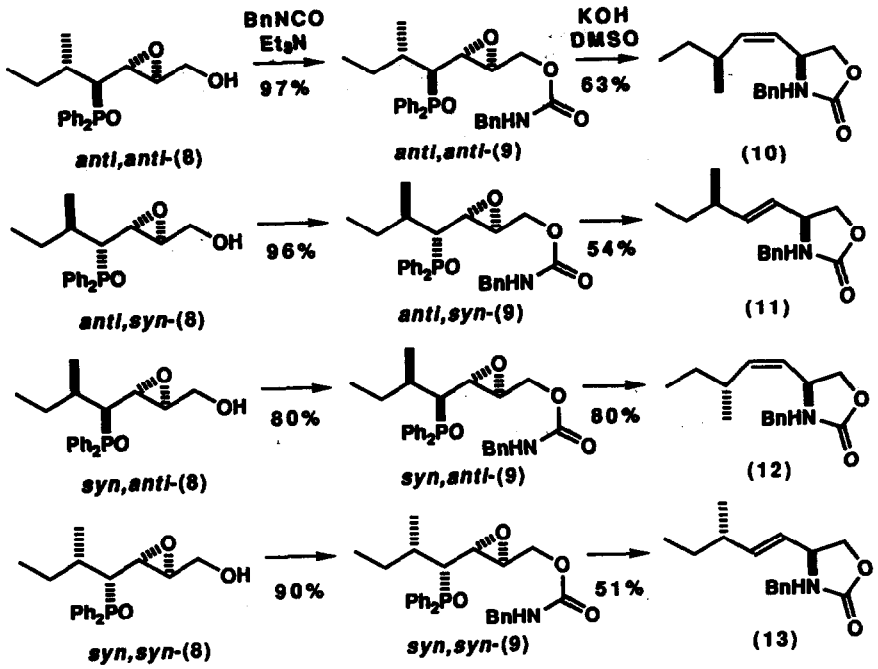
(1) (4) (5)



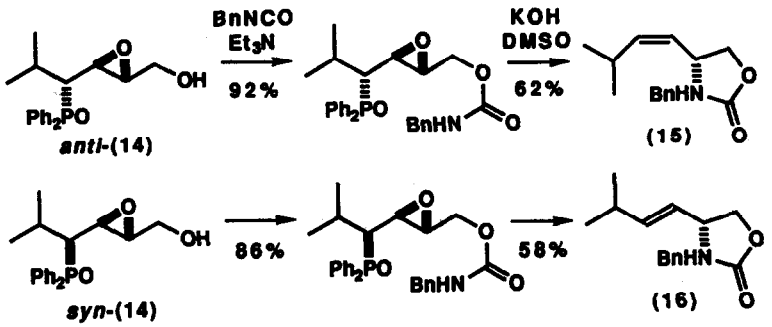
Stereorandom addition of phosphine oxide **6** to acrolein, followed by acetylation, palladium(II)-catalysed allylic transposition[4] and hydrolysis of the transposed acetates gave a mixture of the allylic alcohols *anti*-**7** and *syn*-**7**, which were separated by HPLC. Sharpless kinetic resolution[2] [^{t}BuOOH (0.5 eq), Ti(O^{i}Pr)$_4$ (0.5 eq), L-(+)-DIPT] of both *anti*-**7** and *syn*-**7** was highly *anti*-selective, giving *anti,anti*-**8** and *syn,anti*-**8** in high enantiomeric excess.[5] *Syn* selective *m*-CPBA epoxidation[1] of the enantiomerically enriched starting material from the kinetic resolution enabled us to make four stereoisomers of epoxy alcohol **8**.

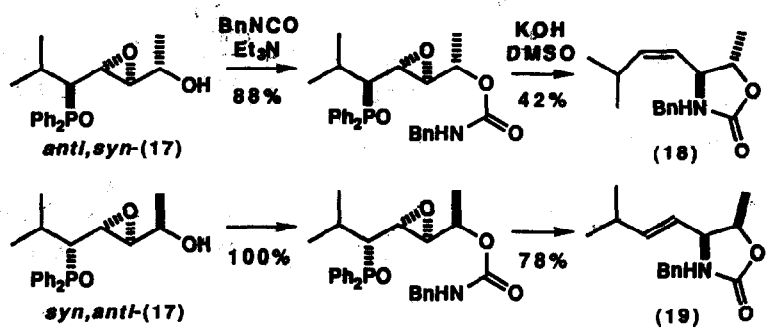


The urethanes **9** were easily made in excellent yield by stirring the epoxy alcohols **8** overnight with benzyl isocyanate and triethylamine. Treatment of **9** with potassium hydroxide in DMSO at 60 °C for 1-2 h led to ring-opening of the epoxide by the urethane anion,[3] followed by stereospecific Horner-Wittig elimination,[6] giving a single isomer (by ^{1}H NMR) of the alkenyl oxazolidinones **10-13** from each stereoisomer of the epoxy alcohol **8**. In **10-13**, we have all four possible stereoisomers in one enantiomeric series. The enantiomers of **10-13** are clearly available simply by using D-(−)-dialkyl tartrate in the kinetic resolution. The ^{1}H NMR spectra of **10-13** were all discernibly different, though those of the *E* compounds **11** and **13** were more alike than those of the *Z* compounds **10** and **12**.



Compounds like **10-13**, bearing 1,4-related chiral centres separated by a double bond, have been the subject of considerable interest, because of their value as synthetic intermediates[7] and as precursors to dipeptide isosteres.[8] Of the several methods available for controlling 1,4-related chiral centres, few allow formation of a *Z* double bond,[9] and, to our knowledge, none allows the general synthesis of any isomer of the product. The strategy employed here, namely stereospecific removal of the middle two of a string of four chiral centres, is similar to (but more general than) those that we[9] and others[7] have used before, and quite different from methods involving stereospecific rearrangements,[8,10] which invariably give *E* double bonds. The stereospecificity of the Horner-Wittig elimination giving hindered *Z* alkenes **10** and **12** in high yield is also remarkable. We are currently also investigating other routes to hindered *Z* alkenes.





Treatment of a range of other diphenylphosphinoyl epoxy alcohols such as **14** and **17** with benzyl isocyanate and then potassium hydroxide allowed us to make several more alkenyl isoxazolidinones **15**, **16**, **18** and **19** in a stereocontrolled manner. These compounds are conveniently protected unsaturated α-amino alcohols, which have found applications[11] in amino acid and carbohydrate chemistry.

Acknowledgements

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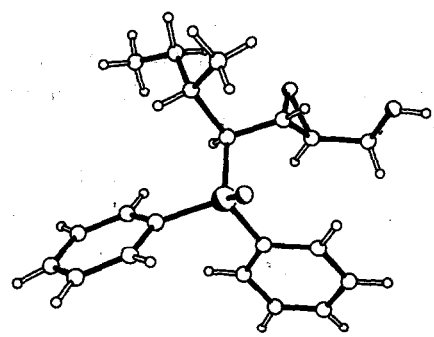
References and Footnotes

1. Clayden, J.; Collington, E.; Warren, S. *Tetrahedron Lett.*, 1993, **34**, 1327-1330.
2. Clayden, J.; Collington, E.; Warren, S. *Tetrahedron Lett.*, 1992, **33**, 7043-7046; Gao, Y.; Hanson, R. M.; Klunder, J. M.; Ko, S. Y.; Masamune, H.; Sharpless, K. B. *J. Am. Chem. Soc.*, 1987, **109**, 5765-5780.
3. Roush, W. R.; Adam, M. A. *J. Org. Chem.*, 1985, **50**, 3752-3757.
4. Clayden, J.; Collington, E.; Warren, S. *Tetrahedron Lett.*, 1992, **33**, 7039-7042.
5. Relative configurations were assigned by correlation of ^{1}H and ^{13}C NMR spectra with those of *anti,anti*-**8**, whose relative and absolute stereochemistry was determined by X-ray crystallography (see figure). Enantiomeric excesses were determined by 400 MHz ^{1}H NMR spectroscopy in the presence of Pirkle's chiral solvating agent, 2,2,2-trifluoro-1-(9-anthryl)ethanol: Pirkle, W. H.; Sikkenga, D. L.; Parkin, M. J. *J. Org. Chem.*, 1977, **42**, 384-387.



6. Buss, A. D.; Warren, S. *J. Chem. Soc., Perkin Trans. 1*, 1985, 2307-2325.
7. Murphy, P. J.; Procter, G. *Tetrahedron Lett.*, 1990, **31**, 1059-1062.
8. Ibuka, T.; Habashita, H.; Funakoshi, S.; Fujii, N.; Oguchi, Y.; Uyehara, T.; Yamamoto, Y. *Angew. Chem., Int. Ed. Eng.*, 1990, **29**, 801-803.
9. Hall, D.; Sévin, A.-F.; Warren, S. *Tetrahedron Lett.*, 1991, **32**, 7123-7126.
10. Aggarwal, V. K.; Coldham, I.; McIntyre, S.; Warren, S. *J. Chem. Soc., Perkin Trans. 1*, 1991, 451-460; Hartley, R. C.; Richards, I. C.; Warren, S.; *Tetrahedron Lett.*, in the press.
11. Sibi, M. P.; Renhowe, P. A. *Tetrahedron Lett.*, 1990, **31**, 7407-7410; Beaulieu, P. L.; Duceppe, J.-L.; Johnson, C. *J. Org. Chem.*, 1991, **56**, 4196-4204; Sibi, M. P.; Li, B. *Tetrahedron Lett.*, 1992, **33**, 4115-4118.

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