Communications to the Editor

Total Synthesis of Ionophores. 6.[1] Asymmetric Induction in the Permanganate-Promoted Oxidative Cyclization of 1,5-Dienes

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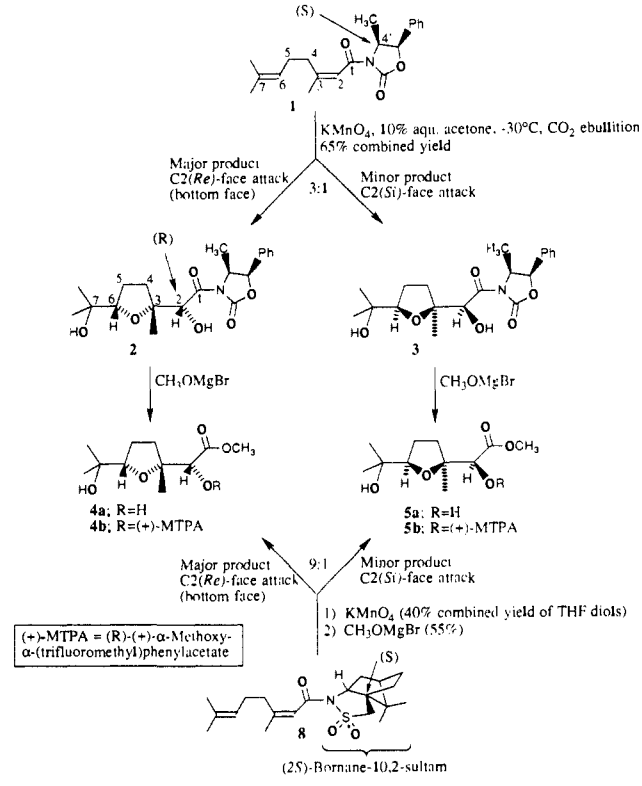
We and others have demonstrated the utility of the permanganate-promoted oxidative cyclization of 1,5-dienes for synthesis of structural fragments found in oxygenated natural products[1a,b,2] and materials of medicinal importance.[3] In the standard implementation of this reaction, a structurally complex product possessing four new tetrahedral stereocenters is created stereospecifically from a simple achiral diene precursor in a single transformation. Of course under these circumstances racemic product is produced. On the basis of mechanistic considerations, we felt that it would be possible to achieve enantioselectivity in the overall process by oxidation of a diene possessing a regio- and diastereoface-differentiating substituent at one of the terminal alkenyl carbons. Herein we report realization of this concept by demonstration of relative asymmetric induction in the oxidative cyclization of functionalized 2,6-dienoates.

As shown at the top of Scheme I, initial experiments were performed using the neroate diene system functionalized with the norephedrine-derived oxazolidone chiral auxiliary of Evans.[4] Oxidation of enantiomerically enriched dienoate **1**($4'S,5'R$)[5,6a,b] affords nonracemic THF diol products **2** and **3**[6a] in a 3:1 ratio[7] and 65% total isolated yield, with the major diastereomer **2** resulting from attack of permanganate on the *Re* face of the conjugated double bond. The structure of the major diastereomer was established unequivocally by single-crystal X-ray analysis of the major diastereomeric THF diol resulting from oxidation of racemic dienoate **1**.[8] This material may be considered to arise from initial attack of permanganate on the sterically least hindered face of the *conjugated* double bond if the auxiliary takes the conformation shown in the diagrams (carbonyl groupings anti).

Scheme I. Oxidative Cyclization of Chiral Neroic Acid Imides



The relatively low diastereoselectivity observed is consistent with the observations of Evans in Diels-Alder reactions of oxazolidone-functionalized dieneophiles that Lewis acid catalysis, and presumably chelation, is required to obtain high face selectivity.[9] In the permanganate oxidation, cyclization of **1** using zinc permanganate on silica gel[10] in THF solvent afforded the same product ratio as the standard conditions indicated in Scheme I, and there is no evidence that such oxidations can be Lewis acid catalyzed.

Removal of the chiral auxiliary from diastereomers **2** and **3** with methoxymagnesium bromide gave enantiomerically enriched THF diol esters **4a** and **5a**, respectively.[11] While this process is complicated by formation of considerable amounts of rearranged products upon removal of the auxiliary,[12] clean samples of the nonracemic THF diols could be obtained in this way after chromatography (55% isolated yield).

(1) Previous papers in this series: (a) Walba, D. M.; Wand, M. D.; Wilkes, M. C. *J. Am. Chem. Soc.* **1979**, *101*, 4396-4397. (b) Walba, D. M.; Edwards, P. D. *Tetrahedron Lett.* **1980**, *21*, 3531-3534. (c) Walba, D. M.; Stoudt, G. S. *Tetrahedron Lett.* **1982**, *23*, 727-730. (d) Walba, D. M.; Wand, M. D. *Tetrahedron Lett.* **1982**, *23*, 4995-4998. (e) Walba, D. M.; Thurmes, W. N.; Haltiwanger, R. C. *J. Org. Chem.* **1988**, *53*, 1046-1056.

(2) Weiler, L.; Spino, C. *Tetrahedron Lett.* **1987**, *28*, 731-734.

(3) Walba, D. M.; Stoudt, G. S. *J. Org. Chem.* **1983**, *48*, 5404-5406.

(4) Evans, D. A.; Bartroli, J.; Shih, T. L. *J. Am. Chem. Soc.* **1981**, *103*, 2127-2129.

(5) The oxizolidone-functionalized dienoates were prepared by addition of a THF solution of the lithium salt of the oxazolidone to a THF solution of the corresponding acid chloride at -78 °C. The sultam-functionalized dienoates were prepared by addition of a toluene solution of the corresponding acid chloride to a toluene solution of the sodium salt of the bornane-10,2-sultam at room temperature.

(6) (a) This compound showed spectral properties consistent with the given structure and (b) either an appropriate combustion analysis or an appropriate exact mass spectrum.

(7) The ratios of diastereomeric THF diol products produced in the cyclizations were determined by ^{1}H NMR and/or HPLC analysis of the crude reaction mixtures.

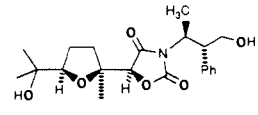
(8) Racemic compound **2**, prepared from racemic **1**, exhibited ^{1}H and ^{13}C NMR and IR spectra identical with those of enantiomerically enriched **2**. Racemic **2** was further characterized by single-crystal X-ray diffraction (it was not possible in our hands to obtain suitable crystals of enantiomerically enriched **2** for X-ray analysis) and shown to possess the relative stereochemistry indicated in Scheme I. Racemic and nonracemic **3** were characterized by ^{1}H NMR and IR spectroscopy.

(9) Evans, D. A.; Chapman, K. T.; Bisaha, J. *J. Am. Chem. Soc.* **1984**, *106*, 4261-4263.

(10) Wolfe, S.; Ingold, C. F. *J. Am. Chem. Soc.* **1983**, *105*, 1155.

(11) Compounds **4a** and **5a** showed spectral properties identical with those exhibited by the fully characterized racemic THF diol ester formed upon oxidative cyclization of methyl neroate (Buswell, R. L. Ph.D. Thesis, University of Colorado at Boulder, 1987).

(12) The rearranged product from the minor diastereomer in the racemic series (**3** racemic) was proven to possess the expected structure shown below by single-crystal X-ray analysis.



Evans has observed similar rearrangements of α-hydroxy carboximides: Evans, D. A.; Morrissey, M. M.; Dorow, R. L. *J. Am. Chem. Soc.* **1985**, *107*, 4346-4348.

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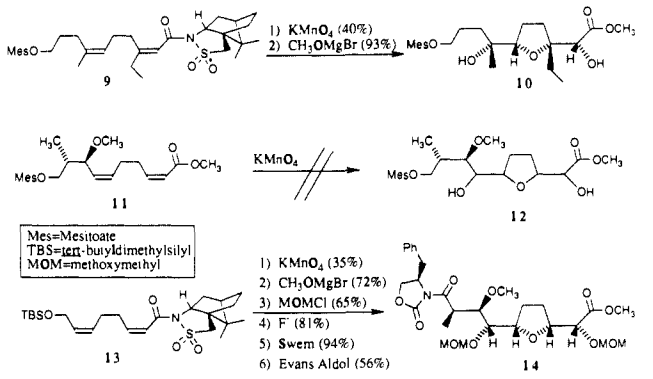
Scheme II. Oxidative Cyclization of Unsymmetrical Dienoates and Enantioselective Synthesis of an Ionophore Fragment



The problems of low face selectivity and difficulty in removal of the chiral auxiliary are solved with Oppolzer's bornane-10,2-sultam system.[13] Thus, oxidation of dienoate **8**,[5,6a,b] functionalized with (2*S*)-bornane-10,2-sultam, gave a >9:1 mixture of diastereomers,[7] from which the major diastereomer[6a,b] could be readily isolated by flash chromatography in 38% yield. Treatment of this THF diol with CH_3OMgBr then gave a sample of nonracemic THF diol **4a** (55%), shown to possess the 2*R* absolute configuration by correlation with the Mosher ester (**4b**) from authentic diol **4a** prepared from enantiomerically enriched dienoate **1**.[14]

Thus, the major diastereomer in oxidation of the bornane-10,2-sultam derived dienoate **8** results from attack on the *Re* face of the conjugated double bond. As expected, this is the same facial bias observed by Oppolzer in the osmylation of sultam-functionalized enoates.[15] It must be pointed out, however, that the mechanism of the oxidative cyclization reaction is not known, the mass balance is never quantitative, and α-ketol byproducts are always produced, most likely from the same intermediate that leads to THF diol. Thus, the ratio of THF diol diastereomers is not necessarily a reflection of the face selectivity in the attack of permanganate on thee unsaturated system. Nevertheless, diastereofacial bias in initial attack of permanganate on the conjugated double bond to give a Mn(V) diester, followed by oxidative cyclization by the Sharpless-type mechanism previously suggested by us in the literature.[1c,16] is certainly an attractive explanation of the observed results.

In order to further explore the scope of the asymmetric oxidative cyclization, we have studied the cyclization of dienoates **9**,[6a,b17] **11**[6a,18] and **13**,[6a,18] as shown in Scheme II. Cyclization of the dienoate **9** proceeded similarly to that of dienoate **8**, to give the expected 9:1 ratio of diastereomeric THF diols.[7] The major diastereomer, assigned the structure resulting from *Re*-face attack by analogy with the results presented above, was easily purified by flash chromatography and isolated in 40% yield.[6a,b] Treatment of this material with CH_3OMgBr then gave enantiomerically pure THF diol **10** in good yield.[6a,b] Compound **10** has the substitution pattern of the C ring of monensin, but of opposite absolute configuration.

Interestingly, oxidation of dienoate **11** with permanganate under our standard conditions gave no trace of THF diol **12**. Apparently, the substitution at the allylic carbon remote from the dienoate carbonyl effectively shuts down oxidative cyclization in favor of other pathways (the only products isolated from this reaction, in 79% combined yield, were identified as diastereomeric mixtures of the two regioisomeric α-ketols resulting from attack of permanganate at the conjugated double bond). A product possessing the substitution pattern present in THF diol **12**, however, could easily be obtained by diastereoselective oxidative cyclization of dienoate **13**, followed by straightforward elaboration as shown in Scheme II to give THF diol derivative **14**.[6a,19]

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(13) Oppolzer, W.; Chapuis, C.; Bernardinelli, G. *Helv. Chim. Acta* **1984**, *67*, 1397-1401.

(14) The esters **4b** and **5b** were easily prepared regioselectively from diols **4a** and **5a**, respectively, by treatment of the diols with (*R*)-(+)-α-methoxy-α-(trifluoromethyl)phenylacetic acid in the presence of 1,3-dicyclohexylcarbodiimide and (dimethylamino)pyridine. The ^1H NMR spectra of these esters proved nicely diagnostic of their structure. Thus, for example, the proton at C2 of ester **4b** appears as a sharp singlet at δ 4.81, while the C2 proton of ester **5b** appears as a sharp singlet at δ 4.85. In mixtures of these esters, the resonances for the C2 protons are completely resolved.

(15) Oppolzer, W.; Barras, J.-P. *Helv. Chim. Acta* **1987**, *70*, 1666-1675.

(16) Walba, D. M.; DePuy, C. H.; Grabowski, J. J.; Bierbaum, V. M. *Organometallics* **1984**, *3*, 498-499.

(17) Dienoate **9** was prepared by coupling of the acid chloride of the corresponding dienoic acid with the bornane-10,2-sultam auxiliary as described in footnote 5. The acid was prepared by hydrolysis (KOH/MeOH) of the methyl dienoate, which was prepared by simple modification of the route given in ref 1b. All intermediates leading to dienoate **9** have been fully characterized.

(18) Dienoates **11** and **13** were prepared from hexadiyne. The tetrahedral stereocenters of dienoate **11** were introduced enantioselectively by means of standard Evans aldol chemistry (ref 4, for detailed experimental procedures used in our group see ref 1e), and the trigonal stereocenters of both **11** and **13** were introduced diastereoselectively by hydrogenation of triple bonds with 5% $Pd/BaSO_4$ poisoned with quinoline. All intermediates in the routes to dienoates **11** and **13**, and materials in the route leading from **13** to **14**, were characterized spectroscopically.

(19) The face selectivity in the oxidative cyclization of dienoate **13** was assigned by analogy to that for the neroate system, and the relative stereochemistry of the aldol process was assigned by analogy with similar Evans aldol processes.

Photoluminescence of $[Pt^{II}(4,7\text{-diphenyl-}1,10\text{-phenanthroline})(CN)_2]$ in Solution

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Aromatic molecules are well-known to undergo excited-state dimerization in solution.[1,2] Under suitable conditions the formation of excited dimers (excimers) can be monitored by the simultaneous appearance of the monomer and excimer luminescence. With regard to coordination compounds, Pt^{II} complexes are promising candidates for the observation of emissive monomers and excimers.[3,4] Unfortunately, the majority of mononuclear Pt^{II} complexes are not luminescent in fluid solution. This seems to be associated with the presence of low-energy dd states. The few mononuclear Pt^{II} complexes that are indeed luminescent in solution[5-9] emit from intraligand (IL) $\pi\pi^*$ or metal to ligand charge transfer (MLCT) states. In addition to these mononuclear com-

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(3) An excimer of $[Pt(o\text{-phen})_2]^{2+}$ in the solid state has been reported recently.[4]

(4) Miskowski, V. M.; Houlding, V. H. *Inorg. Chem.* **1989**, *28*, 1529.

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