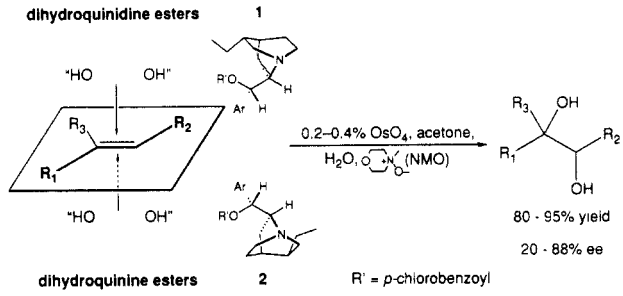
Scheme I



At least in the case of styrene, the rate acceleration in the presence of the alkaloid is completely accounted for by facilitation of the initial osmylation step.[13] The strikingly opposite effects of quinuclidine and **1** on the catalysis can be related to the fact that although quinuclidine also accelerates the addition of osmium tetroxide to olefins,[10] it binds too strongly to the resulting osmium(VI) ester intermediate and inhibits catalyst turnover by retarding the hydrolysis/reoxidation steps of the cycle. In contrast, the alkaloid appears to achieve a balancing act which renders it near perfect for its role as an accelerator of the dihydroxylation catalysis. It binds strongly enough to OsO_4 to accelerate addition to olefins, but not so tightly to the osmate esters that it interferes (as does quinuclidine) with subsequent stages of the catalytic cycle. As expected from their known affinity for forming stable octahedral osmium(VI) glycolate ester complexes,[14] we find that chelating tertiary amines [e.g., 2,2'-bipyridine and (−)-(*R*,*R*)-*N*,*N*,*N*',*N*'-tetramethyl-1,2-cyclohexanediamine][5b] at 0.2 M completely inhibit the catalysis. Perhaps more surprising is the observation that pyridine at 0.2 M has the same effect; pyridine is also an excellent ligand for osmate esters, which probably accounts for its deleterious effect here.[15]

This catalytic asymmetric oxidation has noteworthy features: (1) unlike asymmetric epoxidation and asymmetric hydrogenations, it requires no directing functional group (though so far aromatic olefins give better results); (2) thanks to the ligand-acceleration phenomenon, very little osmium catalyst is needed (as little as one part in 50000 to date), thus making it, asymmetric induction aside, the most active known catalytic osmylation; (3) the two readily available cinchona alkaloid diastereomers (quinine and quinidine) essentially fulfill the function of enantiomers and are easily recovered; (4) being insensitive to air and water and seeming actually to work better under conditions of high concentration (indicating little or no product inhibition), the process is simple to perform on any scale.

In summary, what this transformation lacks in uniformly high asymmetric inductions it makes up for in broad applicability and ease of execution. Among existing catalytic asymmetric reductions and oxidations involving olefins, this process seems to have the largest pool of potential substrates.

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Supplementary Material Available: Details for the preparation and recovery of the alkaloid ligands **1** and **2** (4 pages). Ordering information is given on any current masthead page.

(13) For more highly substituted olefins, steps involving the osmate ester may become turnover limiting. The presence of the alkaloid also seems to affect such cases, but its mode(s) of action remain to be established.

(14) Resch, J. F.; Meinwald, J. *Tetrahedron Lett.* **1981**, *22*, 3159, and references therein.

(15) However pyridine has also been reported[2d] to facilitate, albeit at higher temperatures, a catalytic osmylation process.

Probing Ergot Alkaloid Biosynthesis: Identification of Advanced Intermediates along the Biosynthetic Pathway

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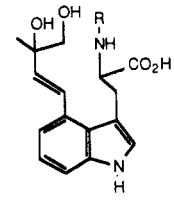
The biosynthesis of ergot alkaloids, e.g., chanoclavine-I (I) and elymoclavine (II) from L-tryptophan, methionine, and dimethylallyl pyrophosphate via *N*-methyl-4-(γ,γ-dimethylallyl)-tryptophan (III) is well established.[1-3] While the conversion of I to II is well understood,[1,4] the detailed mode of closure of ring C, i.e., the conversion III → I, is still obscure. In an effort to shed light on this matter we recently prepared a labeled version (IVc)



IVa, R=H
IVb, R=CH_3
IVc, R=CD_3

of a proposed[1,2] intermediate, the diol IVb.[5] However, feeding of both diastereomers of IVc to replacement cultures of *Claviceps sp.* strain SD58 failed to reveal any incorporation into II.[6] In view of this negative result it was decided to synthesize the monohydroxylated dimethylallyltryptophan derivative Vb (Scheme II) to examine its possible incorporation into II.

As shown in Scheme I, the required indole was prepared in labeled form from *N*-tosylindole-4-carboxaldehyde (**1**) by the addition of isobutenylmagnesium bromide, protection of the resulting alcohol **2** as its SEM ether, cleavage of the tosyl group, and then gramine formation with use of *N*,*N*-dimethyl(methylene)ammonium chloride. Next, the gramine intermediate was condensed with dimethyl [*N*-trideuteriomethyl-*N*-(2,2,2-trichloroethoxycarbonyl)amino]malonate[6] in the presence of tri-*n*-butylphosphine to produce the amidomalonate **5**. Intermediate **5** was treated in turn with pyridinium *p*-toluenesulfonate to afford the tertiary alcohol **6**. This acid-catalyzed process thus served to remove the SEM ether group with concomitant allylic rearrangement. The nitrogen-protecting group was now cleaved under reductive conditions, and the diester decarbomethoxylated by using 5% aqueous potassium hydroxide followed by acid treatment. Lastly, the monoester **7** was saponified with use of 2 N KOH in a mixture of methanol and tetrahydrofuran to provide the racemic amino acid Vb.

(1) Floss, H. G. *Tetrahedron* **1976**, *32*, 873.

(2) Floss, H. G.; Anderson, J. A. In *The Biosynthesis of Mycotoxins*; Steyn, P. S., Ed.; Academic Press: New York, NY, 1980; pp 17-67.

(3) Otsuka, H.; Quigley, F. R.; Gröger, D.; Anderson, J. A.; Floss, H. G. *Planta Med.* **1980**, *40*, 109.

(4) Floss, H. G.; Tcheng-Lin, M.; Chang, C.-j.; Naidoo, B.; Blair, G. E.; Abou-Chaar, C.; Cassady, J. M. *J. Am. Chem. Soc.* **1974**, *96*, 1898.

(5) The original proposal[1] suggested the intermediacy of IVa; this had to be modified to IVb when it was discovered[3] that N-methylation precedes C-ring closure.

(6) Kozikowski, A. P.; Okita, M.; Kobayashi, M.; Floss, H. G. *J. Org. Chem.*, in press.

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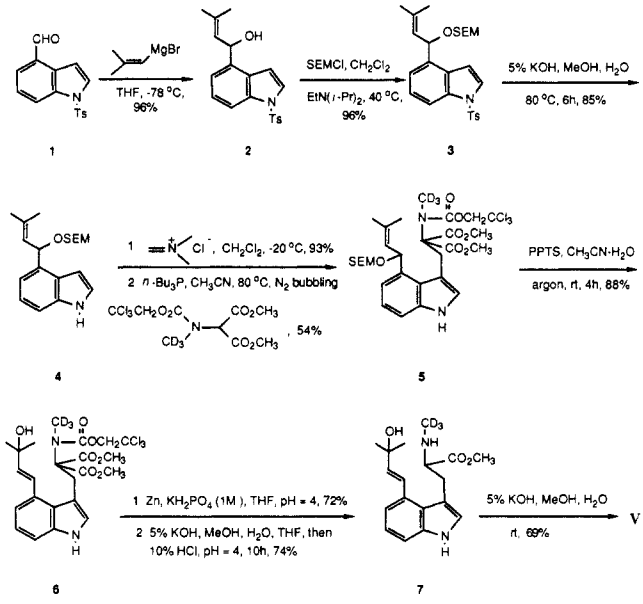
Scheme I. Synthesis of the Amino Acid V



A sample of Vb (9 mg) was fed to a 50-mL replacement culture of *Claviceps sp.* strain SD58 as described earlier.[6,7] After incubation at 25 °C with shaking for 2 days, II was isolated and subjected to GC–MS analysis.[6] The mass spectrum showed the presence of only M and M + 3 species in the molecular ion of II, and their ratio corresponded to 33% specific incorporation of Vb into II. A repetition of the experiment with a separately synthesized sample (5 mg) gave 9% specific incorporation. The high and specific (no enhanced M + 1 or M + 2 species) incorporation of Vb into II leaves no doubt in the specific precursor role of this compound.

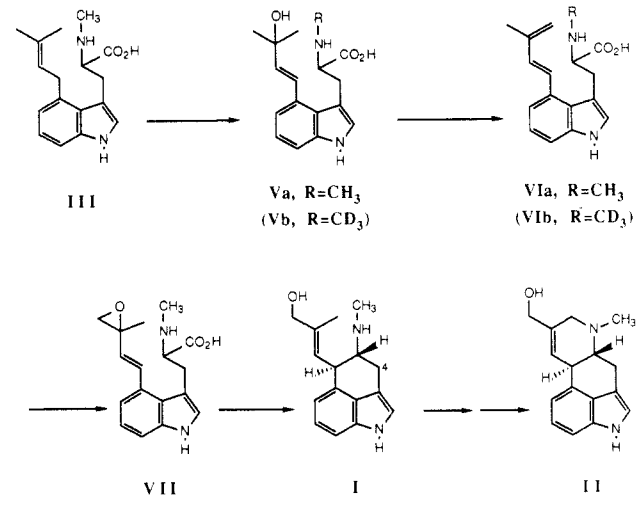
The present result would suggest that biosynthetically the tertiary alcohol is converted by dehydration to the diene VIa. This intermediate may then be epoxidized by cytochrome P-450 to the vinyl oxirane VII, which has been proposed[8] to undergo decarboxylative ring closure via an S_N2' process to provide chanoclavine. Further support of this notion comes from trapping experiments with Vb. To a replacement culture containing unlabeled L-tryptophan (1 mg), D,L-mevalonic acid (2 mg), and L-methionine (1 mg) was added Vb (10 μg). After 1 h incubation with shaking, V was reisolated by filtration and 1-butanol extraction of the filtrate, methylated with CH_2N_2, and analyzed by GC–MS. An authentic sample of Vb methylated in the same way showed two peaks of t_{ret} 22.1 min and t_{ret} 21.7 min, identified by their mass spectra as the methyl esters of *N*-methyl Vb and VIb, respectively. The GC–MS of the reisolated V showed the same two peaks; the spectrum of the methyl ester of *N*-methyl Vb showed no dilution with Va, but the spectrum of the t_{ret} 21.7 min peak indicated dilution of the VIb with 19% VIa. Hence, while there is no evidence for the presence of Va in the culture, the presence of VIa is clearly indicated. This was confirmed by working up replacement cultures (2 × 100 mL, 3 h) in the same way without any addition of V and demonstrating, by GC–MS with selective ion monitoring, the presence of VIa, as the methyl ester of its *N*-methyl derivative, in the methylated extract.

On the basis of these results we propose the reaction sequence shown in Scheme II for the closure of ring C in ergot alkaloid biosynthesis. Whether Va is a true intermediate in this sequence or whether the diene can be formed more directly from III must in light of the negative outcome of the trapping experiment remain open. Further efforts to examine the laboratory synthesis and

(7) The original procedure[6] was modified to shake the resuspended mycelia for 2 h before the final filtration and suspension in the incubation buffer. This reduced considerably the amount of preformed II remaining in the cells.

(8) Pachlatko, P.; Tabacik, C.; Acklin, W.; Arigoni, D. *Chimia* **1975**, *29*, 526.

Scheme II. Proposed Reaction Sequence for C-Ring Formation in Ergot Alkaloid Biosynthesis



biosynthetic incorporation of the proposed diene and epoxide intermediates are underway.

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Supplementary Material Available: A listing of spectroscopic and analytical data for compounds **2**–**7** and Va (3 pages). Ordering information is given on any current masthead page.

Convenient Preparation and Structures of Selenometalates $MoSe_4^{2-}$, WSe_4^{2-}, and $MoSe_9^{2-}$ from Polyselenide Anions and Metal Carbonyls

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The tetrathiometalates, MoS_4^{2-} and WS_4^{2-}, and their tetrahedral analogues such as VS_4^{3-} have been well known for many years.[1,2] They serve as building blocks for metalloenzyme models and can act as precursors and models for hydrodesulfurization catalysts.[2-7] In contrast, the selenium analogues, though known, have received very little study.[8,9] Recently, however, workers have begun exploring the chemistry of binary metal selenides with promising results.[10,11]

We have been investigating the reactions of soluble polychalcogenides extracted from Zintl phases, with metal salts[12] and metal carbonyls.[13] It was found that polytellurides react cleanly

(1) Müller, A.; Diemann, E.; Jostes, R.; Bogge, H. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 934.
(2) Müller, A. *Polyhedron* **1986**, *5*, 323 and references therein.
(3) Coucouvanis, D. *Acc. Chem. Res.* **1981**, *14*, 201.
(4) Holm, R. H. *Chem. Soc. Rev.* **1981**, *10*, 455.
(5) Averill, B. A. *Struct. Bonding (Berlin)* **1983**, *53*, 59.
(6) *Nitrogen Fixation, The Chemical, Biochemical and Genetic Interface*; Müller, A.; Newton, W. E., Eds.; Plenum Press: New York, 1983.
(7) Chianelli, R. R. *Cat. Rev.-Sci. Eng.* **1984**, *26*, 361.
(8) Müller, A. Diemann, E. *Chem. Ber.* **1969**, *102*, 945.
(9) Lenher, V. Fruehan, A. C. *J. Am. Chem. Soc.* **1927**, *49*, 3076.
(10) (a) Wardle, R. W. M.; Chau, C.-N.; Ibers, J. A. *J. Am. Chem. Soc.* **1987**, *109*, 1859. (b) Chau, C.-N.; Wardle, R. W. M.; Ibers, J. A. *Inorg. Chem.* **1987**, *26*, 2740.
(11) Strasdeit, H.; Krebs, B.; Henkel, G. *Inorg. Chim. Acta* **1984**, *89*, L11.
(12) Flomer, W. A.; O'Neal, S. C.; Cordes, W.; Kolis, J. W., to be published.
(13) Flomer, W. A.; O'Neal, S. C.; Cordes, W.; Jeter, D.; Kolis, J. W., submitted to *Inorg. Chem.*

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