measured at those constant field strengths. They are shown at the bottom of Figure 1, together with field-free isotropic spectrum A. The $A_{\parallel}^{E}$ and $A_{\perp}^{E}$ spectra of helical $(Glu)_n$ cross each other at 199 nm and near 223–222 nm. For coiled $(Glu)_n$, the $A_{\parallel}^{E}$ spectrum is larger than the $A_{\perp}^{E}$ spectrum throughout the 230–187-nm region, while the peak of $A_{\parallel}^{E}$ is shifted toward the red side by 2 nm and that of $A_{\perp}^{E}$ slightly toward the blue relative to the peak of the isotropic spectrum. Since the relation $3A = A_{\parallel}^{E} + 2A_{\perp}^{E}$ holds for the helical and coiled states within experimental errors, the electrochromism does not seem to occur.[8]

The dependence of $\Delta A/A$ on wavelength was determined, for the first time, for the peptide chromophore in the 230–187-nm region (middle figures). It is the dependence of reduced dichroism $\Delta A/A$,[6] but not dichroism ΔA,[9] on wavelength and on field strength that quantitatively reveals spectral features, such as angles, θ, numbers of transition moments, and weak absorption bands hidden in a solution[10] or film spectrum.[11] Changes in $\Delta A/A$ with wavelength indicate that at least three overlapping absorption bands, each with a different angle, exist in the peptide spectra of $(Glu)_n$ above 187 nm regardless of its overall conformations. For helical $(Glu)_n$, those bands may be separated into three regions: 230–215, 215–200, and 200–187 nm. For coiled $(Glu)_n$, $\Delta A/A$ values unexpectedly show a three-step change: a constant 230–210-nm region, a maximum in 205–203 nm, and a minimum near 190 nm. Therefore, the broad 190-nm peptide band of coiled $(Glu)_n$ must be a composite of at least two intense component bands and a weak one. The nonsplit broad peak in the isotropic spectrum has been considered to be characteristic of the random-coiled conformation,[12,13] but we now propose that the spectral feature of the coiled form is closely related to that of the helical form in the 210–187-nm region.

The 230–210-nm band has been assigned to an n–π^* transition for helical and coiled $(Glu)_n$ because of its weak intensity.[13] The value of $(\Delta A/A)_s$ should be +3.0 or −1.5, if an isolated transition moment is either parallel ($\theta = 0°$) or perpendicular ($\theta = 90°$) to the orientation axis ($\Phi = 1$).[4,6,8] By using observed values of $(\Delta A/A)_s$, the angles were calculated to be ±51.0° at the 208-nm shoulder and ±57.3° at the 190-nm peak for completely oriented $(Glu)_n$ helices. This unexpected result is partly due to a strong overlap of the two closely located bands. It is, however, difficult to simulate the observed wavelength dependence of $\Delta A/A$ on the basis of a Moffitt-type band split,[2,9,13] unless the intensity ratio of the 208-nm band (the parallel band[2]) to the 190-nm band (the perpendicular band[2]) is assumed to be ca. 1.0:1.5 even at the center of the 208-nm band and also the 190-nm band is overlapped by another strongly positive ($\Delta A/A > 0$) band below 190 nm. It is difficult at present to evaluate the exact angle of the two transition moments inside the broad 190-nm peptide band of coiled $(Glu)_n$, because (i) the axis of orientation may not coincide with the axis of molecular symmetry[14] and (ii) the 205–203-nm and 190-nm transitions overlap each other. A rough estimate, however, indicates that these transitions appear to be inclined neither at 0° nor at 90° relative to the $(Glu)_n$ chain.

This ELD study revealed that, if the predicted band split of a peptide chromophore occurs,[2] it should be seen in the isotropic spectra of $(Glu)_n$ not only in helical but also in coiled conformations. Careful reinvestigations are needed on the polarization spectra of low-molecular-weight amide compounds for better understanding the optical transition and the solution conformation of polypeptides.

Registry No. Poly(2-L-glutamic acid) (homopolymer), 25513-46-6; poly(2-L-glutamic acid) (SRU), 24991-23-9.

(9) Mandel, R.; Holzwarth, G. *J. Chem. Phys.* **1972**, *57*, 3469–3477.
(10) Charney, E.; Milstien, J. B.; Yamaoka, K. *J. Am. Chem. Soc.* **1970**, *92*, 2657–2664.
(11) Gratzer, W. B.; Holzwarth, G. M.; Doty, P. *Proc. Natl. Acad. Sci. U.S.A.* **1961**, *47*, 1785–1791.
(12) Imahori, K.; Tanaka, J. *J. Mol. Biol.* **1959**, *1*, 359–364.
(13) Woody, R. W. *J. Polym. Sci. Macromol. Rev. Ed.* **1977**, *12*, 181–320. Extensive references are cited in this comprehensive review.
(14) Yamaoka, K.; Ichibakase, T.; Ueda, K.; Matsuda, K. *J. Am. Chem. Soc.* **1980**, *102*, 5109–5110.

Rhodium(I)-Catalyzed Hydrogenation of Olefins. The Documentation of Hydroxyl-Directed Stereochemical Control in Cyclic and Acyclic Systems

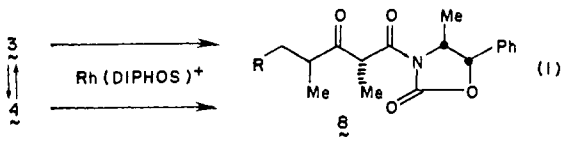
David A. Evans* and Michael M. Morrissey

Department of Chemistry, Harvard University
Cambridge, Massachusetts 02138

Received March 12, 1984

Several studies have recently appeared that document the important observation that proximal hydroxyl groups can be employed to "direct" the stereochemical course of selected transition-metal-catalyzed olefin hydrogenations. Stork[1] and Crabtree[2] have convincingly demonstrated that the cationic iridium catalyst $Ir(COD)(py)(PCy_3)PF_6$ (**1**)[3] is effective in the directed reduction of *cyclic* allylic and homoallylic alcohols. In a complimentary study, Brown and Naik[4] have provided two cases where the cationic rhodium catalyst $[Rh(NBD)(DIPHOS\text{-}4)]BF_4$ (**2**)[5] is also responsive to the same stereochemical control elements as demonstrated in the reduction of an *acyclic* allylic and homoallylic alcohol. In ongoing studies in our laboratory we have had the opportunity to critically evaluate each of these catalysts in both cyclic and acyclic systems, and our *unanticipated* observations should prove to significantly extend the utility of these hydrogenation catalysts.

On the basis of the principles of acyclic conformational analysis in allylic systems,[6] the hydroxyl-directed reduction of the allylic alcohols **3** and **4**,[7] via their preferred C_3–C_4 conformers might be expected to lead stereoselectively to the complementary diastereomeric aldol adducts **5** and **6**, respectively (Scheme I).[8] Surprisingly, the iridium catalyst **1**, which exhibits excellent levels of directed hydrogenation when the hydroxyl function is rigidly disposed on one olefin diastereoface,[1] proved ineffective in the stereoselective reductions of acyclic allylic alcohols **3** and **4** either at atmospheric (Table I) or elevated hydrogen pressures.[9] Even more surprising was the observation that the cationic rhodium complex **2** appeared to afford low levels of reaction diastereoselection under the reported hydrogenation conditions (CH_2Cl_2, 25 °C, 15 psi H_2).[4] In addition, the presence of ketonic byproducts such as **8** (eq 1) suggested that competitive olefin isomerization



(1)

might be a major problem. Fortunately, these reductions were found to respond dramatically to an increase in hydrogen pressure. For example, when the analogous reactions were carried out at elevated hydrogen pressures (640 psi), this catalyst exhibited

(1) Stork, G.; Kahne, D. E. *J. Am. Chem. Soc.* **1983**, *105*, 1072.
(2) Crabtree, R. H.; Davis, M. W. *Organometallics* **1983**, *2*, 681.
(3) Crabtree, R. H.; Felkin, H.; Fellebeen-Khan, T.; Morris, G. E. *J. Organomet. Chem.* **1979**, *168*, 183. COD = 1,5-cyclooctadiene, Cy = cyclohexyl, py = pyridine.
(4) Brown, J. M.; Naik, R. *J. Chem. Soc., Chem. Commun.* **1982**, 348.
(5) Prepared in direct analogy to the general procedure described by Stille: Stille, J. K.; Amma, J. P. *J. Org. Chem.* **1982**, *47*, 468. NBD = norbornadiene, DIPHOS-4 = 1,4-bis(diphenylphosphino)butane. The detailed procedure for the preparation of **2** is provided in the supplementary material. The complex $[Rh(COD)(DIPHOS\text{-}4)]BF_4$, has also been reported: Brown, J. M.; Chaloner, P. A.; Kent, A. G.; Murrer, B. A.; Nicholson, P. N.; Parker, D.; Sidebottom, P. J. *J. Organomet. Chem.* **1981**, *216*, 263.
(6) Johnson, F. *Chem. Rev.* **1968**, *68*, 375.
(7) The allylic alcohols **3** and **4** were synthesized via our recently reported aldol process: Evans, D. A.; Bartroli, J.; Shih, T. *J. Am. Chem. Soc.* **1981**, *103*, 2127.
(8) Unequivocal stereochemical assignments for **5** and **6** were made by independent asymmetric synthesis: Evans, D. A.; Ennis, M. D.; Mathre, D. J. *J. Am. Chem. Soc.* **1982**, *104*, 1737 and ref 7.
(9) The high-pressure hydrogenation data for catalyst **1** were not included due to the fact that little pressure-dependent diastereoselection was observed. For example, in the hydrogenation of **3** (R = Me) the **5**:**6** ratio was 51:49 at 15 psi and 64:36 at 640 psi of hydrogen.

0002-7863/84/1506-3866$01.50/0

Scheme I

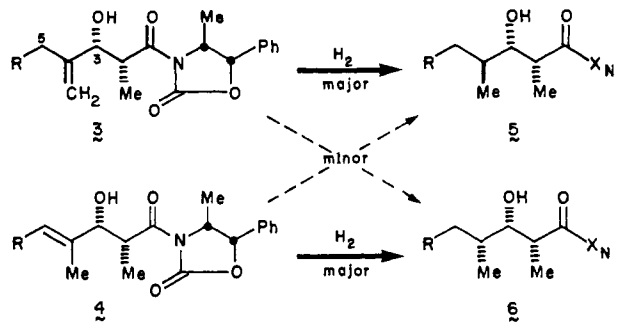


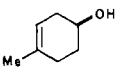
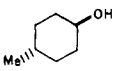
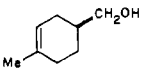
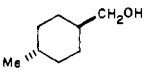
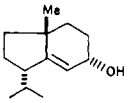
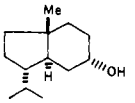
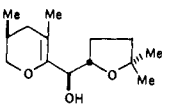
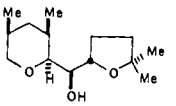
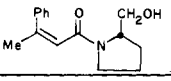
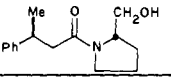
Table I. Stereoselective Hydrogenation of **3** and **4** Catalyzed by Iridium and Rhodium Catalysts **1** and **2** (Scheme I)[10]

substrate	ratio, **5**:**6**[a] (15 psi H_2) Ir (**1**)[b,c]	Rh (**2**)[d,e]	**5**:**6** (640 psi H_2) Rh (**2**)[c,d]
3, R = Me	51:49	25:75	93:7
4, R = Me	56:44	13:87	9:91
3, R = Ph	54:46	71:29	93:7
4, R = Ph	60:40	21:79	6:94
3, R = *i*-C_3H_7	47:53	52:48	94:6
4, R = *i*-C_3H_7	54:46	12:88	8:92

[a] All product ratios determined by capillary gas chromatography. [b] Carried out in anhydrous CH_2Cl_2 with 17.5 mol % **1** according to the general procedure provided in ref 1. [c] Less than 1% β-keto imide **8** was observed in these reductions. [d] Carried out in anhydrous CH_2Cl_2 with 17.5 mol % **2** as described in ref 11. [e] From 8–40% **8** observed under these conditions.

excellent levels of reaction diastereoselection with all six substrates.[11] In all instances, the isolated yields of reduction products exceeded 90% with no greater than 1% ketonic byproduct contamination.[10] Although we have no addressed the mechanistic implications of the observed pressure-dependent reaction diastereoselectivity in detail, the issue of competing olefin isomerization was investigated. In this study catalyst **2** was reduced to Rh(DIPHOS-4)$^+$ (**7**) and its ability to effect olefin isomerization (CH_2Cl_2, 25 °C) was examined (eq 1). For olefin pair **3** and **4** (R = Me), extensive equilibration had occurred after 2 h. In addition, each substrate afforded substantial amounts of the β-keto imide **8** (from **3**, R = Me, at 25 °C, 1 h; **3**:**4**:**8** = 3:37:58). Since significant quantities of **8** were present in the low-pressure rhodium hydrogenations, it appears that the rates of hydrogenation and olefin isomerization under these conditions are roughly comparable. This is clearly evident in the reduction of **3** (R = Ph) where hydrogenation and isomerization occur competitively. In direct analogy with the mechanistic details revealed in the reduction of dehydroamino acids by closely related rhodium catalysts,[12] it is quite plausible that a hydrogen pressure-dependent change in the rate-determining step has been observed. Accordingly, we have adopted the working hypothesis that, at low pressures (15 psi H_2), oxidative addition of hydrogen to the catalyst–substrate complex is rate determining while substrate–catalyst complexation becomes rate determining at elevated hydrogen pressures. Fortunately, competing olefin isomerization (eq 1), which was also evident in the earlier study,[4] could be completely suppressed by this simple change in protocol. It is most interesting that the reaction diastereoselection noted for the reduction of **3** and **4** with the iridium catalyst **1** showed an insignificant response to changes in hydrogen pressure.[9]

Table II. Representative Hydroxyl-Directed Olefin Hydrogenations with Cationic Rhodium(I) and Iridium(I) Catalysts **1** and **2**[10]

entry	substrate	product[a,b]	catalyst, ratio	yield
A			Rh(I), 290:1; Ir(I), 74:1	95%; 49%[c]
B			Rh(I), 64:1; Ir(I), 33:1	95%; 85%[c]
C			Rh(I), 19:1; Ir(I), 25:1	88%; 93%
D			Rh(I), 70:1	95%[d]
E			Rh(I), 12:1	65%
F			Rh(I), 4:1	97%

[a] Reductions were carried out in CH_2Cl_2 (25 °C). Experimental conditions employing catalysts **1** and **2** are described in ref 1 and 11, respectively. [b] Product diastereomer ratios determined by capillary gas chromatography. [c] Data obtained from ref 1. [d] This experiment carried out in THF with 5% catalyst at 800 psi H_2 by Dr. T. A. Engler.

A diverse selection of hydrogenations in both cyclic and acyclic systems is provided in Table II. It is quite significant that good directivity is noted for either **1** or **2** with cyclic allylic, homoallylic, and bishomoallylic alcohols (entries A–C). The substrate illustrated in entry D constitutes a case where an exceptional level of steric conjestion is disposed to override hydroxyl directivity. Due to the lability of this particular allylic alcohol toward the Lewis acidic catalyst **2**, successful reduction was only achieved when the reaction was carried out in tetrahydrofuran rather than the normally employed dichloromethane solvent. In addition, elevated hydrogen pressures were again instrumental in the successful execution of this reduction. It is a true testament to the potential utility of these rhodium catalysts that such hindered double bonds can be selectively reduced. To date, this reduction has not been successfully executed under any conditions with the iridium catalyst **1**.[13] The utility of Rh(DIPHOS-4)$^+$ in the directed reduction of sterically hindered olefins is further illustrated in entry E. The stereochemical outcome of this reaction is readily predicted by A(1,3)-strain conformational considerations.[6] It is noteworthy that this dihydropyran could not be cleanly reduced with either Pd or Pt catalysts. Finally, the stereoselective reduction of the illustrated carboxamide (Table II, entry F) provides an

(10) Satisfactory spectral data and elemental analyses were obtained on all compounds reported herein.

(11) Experimental conditions for the high-pressure hydrogenations of the illustrated substrates and rhodium catalyst **2**: To a small 22-mL autoclave fitted with a glass liner, which is dried and flushed with argon, are added the unsaturated alcohol and catalyst **2** (2–20 mol%). Anhydrous CH_2Cl_2, distilled from CaH_2 under nitrogen, is added via syringe to achieve a substrate concentration of 0.06 M. The autoclave is pressure-flushed with hydrogen (3 times) and pressurized to the desired level. At 640 psi of hydrogen, substrated **3** and **4** are reduced in 1 h (exceptions: **3**, R = Ph requires 7 h; **3**, R = *i*-C_3H_7 requires 2.5 h). Catalyst removal is conveniently achieved by filtration of the reaction mixture through a short column of silica gel (1:1 ethyl acetate:hexane). As a cautionary note, these reductions are quite sensitive to both oxygen and moisture contamination. A more detailed experimental procedure is provided in the supplementary material.

(12) (a) Chan, A. S. C.; Pluth, J. J.; Halpern, J. *J. Am. Chem. Soc.* **1980**, *102*, 5952 and earlier references cited therein. (b) Chua, P. S.; Roberts, K.; Bosnich, B.; Okrasinski, S. J.; Halpern, J. *J. Chem. Soc., Chem. Commun.* **1981**, 1278. (c) Brown, J. M.; Chaloner, P. A. *J. Am. Chem. Soc.* **1980**, *102*, 3040. (d) Brown, J. M.; Chaloner, P. A.; Morris, G. A. *J. Chem. Soc., Chem. Commun.* **1983**, 644. (e) Landis, C. R.; Halpern, J. *J. Organomet. Chem.* **1983**, *250*, 485. (f) Ojima, I.; Kogure, T.; Yoda, N. *J. Org. Chem.* **1980**, *45*, 4728.

(13) Corey, E. J.; Engler, T. A. *Tetrahedron Lett.* **1984**, *26*, 149.

impressive example of 1,5-asymmetric induction. Additional studies employing both cationic iridium and rhodium catalysts are continuing in this laboratory.[14]

Acknowledgment. The National Science Foundation (CHE-8342576) and The National Institutes of Health (GM-33327) are gratefully acknowledged. We thank Dr. Thomas Engler for his collaboration on aspects of this research.

Supplementary Material Available: Detailed procedure for the synthesis of rhodium catalyst **2** along with precise experimental conditions for the hydrogenation process (2 pages). Ordering information is given on any current masthead page.

(14) After completion of this study we made the observation that the reaction diastereoselectivity in the iridium-catalyzed reductions is dependent upon the *amount* of catalyst employed. At lower catalyst/substrate ratios (2.5%) improved levels of directivity may be achieved; however, under even optimal conditions the rhodium catalysts appear to be superior in the reduction of acyclic systems. This data will be reported elsewhere.

Hexanoate as a Starter Unit in Polyketide Biosynthesis

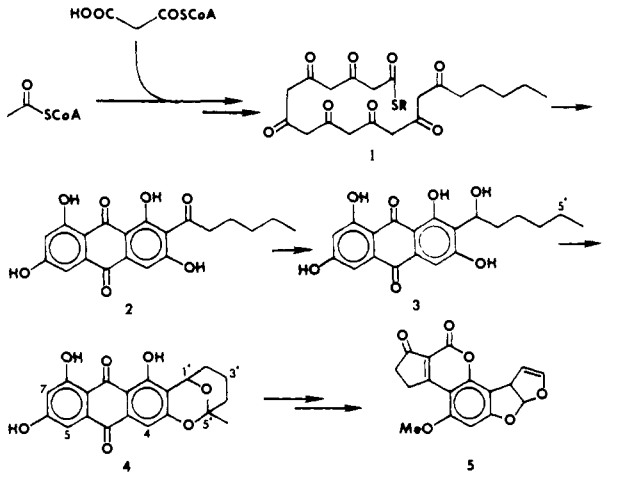
Craig A. Townsend,*† Siegfried B. Christensen, and Katrin Trautwein

Department of Chemistry
The Johns Hopkins University
Baltimore, Maryland 21218

Received November 3, 1983

Almost without exception polyketide-derived aromatic natural products utilize acetate as the primer in their biosynthesis.[1,2] In plants benzenoid starters having their origins in shikimate are observed, most notably *p*-coumaric acid in flavone/isoflavone formation. Low molecular weight acids as propionic[3] and branched acids as isobutyric[4,5] and 2-methylbutyric[5] from catabolism of valine and isoleucine, respectively, have been demonstrated to serve as initiators in a few instances.[6] Prior to the early 1970s, when ^{13}C NMR rapidly became the predominant tool of polyketide biosynthetic investigation, observations had been made that the levels of specific radioactivity from incorporation of [^{14}C]acetate in polyketide-derived metabolites occasionally differed in saturated hydrocarbon side chains (usually lower by 5-10%) with respect to aromatic nuclei to which they were bound.[11] Attempts to test intact incorporation of the corresponding C_4 or greater acid, however, fell victim to rapid catabolism by β-oxidation, and only incorporation of radiolabel as acetate/malonate was experimentally observed.[12] In the absence of experimental proof, therefore, the important fundamental point that linear primers C_4 or larger may function in polyketide biosynthesis has remained moot. We provide in this paper the first demonstration for the case of hexanoate in averufin (**4**) biosynthesis (Scheme I).

Scheme I



The development of *Aspergillus parasiticus* mutants blocked in the anthraquinone portion of the aflatoxin B_1 (**5**) biosynthetic pathway was key to progress in this field[13] beyond the now classic [^{14}C]acetate incorporation experiments of Büchi.[14] It emerged from studies using these mutants[15] (Scheme I) that norsolorinic acid (**2**) is the first-formed anthraquinone precursor of the potent mycotoxin **5** followed linearly by averantin (**3**) and averufin (**4**).[16] The latter is apparently generated by oxidation at C-5′—the center derived from the carboxyl of the acetate starter. This realization was surprising in view of a generalization, which may be formulated from an admittedly limited number of [1-^{13}C,$^{18}O_2$]acetate incorporation studies reported recently,[17] that oxygen bound to a carboxyl-derived carbon typically has its origins in the progenitor polyketide.

[1-^{13}C]Hexanoic acid, therefore, was examined for its intact incorporation into averufin under two distinct feeding protocols.

† Research Fellow of the Alfred P. Sloan Foundation 1982-1986; Camille and Henry Dreyfus Teacher-Scholar 1983-1988.

(1) For reviews of polyketide biosynthesis, see: Bu'Lock, J. C. In "Comprehensive Organic Chemistry"; Barton D., Ollis, W. D., Eds.; Pergamon: Oxford, 1979; Vol. 5, pp 927-987. Weiss, U.; Edwards, J. M. "The Biosynthesis of Aromatic Compounds"; Wiley-Interscience: New York, 1980; pp 326-459. Turner, W. B. "Fungal Metabolites"; Academic Press: London, 1971; pp 26-61.

(2) Tetracyclines appear to be unique in the use of a malonate starter unit: Thomas, R.; Williams, D. J. *J. Chem. Soc., Chem. Commun.* **1983**, 677-679.

(3) See, for example: Ollis, W. D.; Sutherland, I. O.; Codner, R. C.; Gordon, J. J.; Miller, G. A. *Proc. Chem. Soc.* **1960**, 347-349. Mosbach, K. *Acta Chem. Scand.* **1964**, *18*, 1591-1595. Paulick, R. C.; Casey, M. L.; Whitlock, H. W. *J. Am. Chem. Soc.* **1976**, *98*, 3370-3371.

(4) Zylber, J.; Zissman, E.; Polonsky, J.; Lederer, E.; Merrien, A. M. *Eur. J. Biochem.* **1969**, *10*, 278-283.

(5) Drawert, F.; Beier, J. *Phytochemistry* **1976**, *15*, 1695-1696.

(6) In fatty acid biosynthesis the analogous roles for valine, isoleucine, and leucine have been established.[7] Similarly, aleprolic acid [(2-cyclopentenyl)-carboxylic acid], derived from (2-cyclopentenyl)glycine,[8] and cyclohexane-carboxylic acid, derived from shikimate,[9,10] have been shown to serve as starters in specialized instances of fatty acid biosynthesis.

(7) For an early review, see: Lennarz, W. J. *Adv. Lipid Res.* **1966**, *4*, 175-225.

(8) Mangold, H. K.; Spener, F. In "The Biochemistry of Plants"; Stumpf, P. K., Conn, E. E., Eds.; Academic Press: New York, 1980; Vol. 4, pp 647-663.

(9) DeRosa, M.; Gambacorta, A.; Minale, L.; Bu'Lock, J. D. *Biochem. J.* **1972**, *128*, 751-754. Oshima, M.; Ariga, T. *J. Biol. Chem.* **1975**, *250*, 6963-6968.

(10) DeRosa, M.; Gambacorta, A.; Bu'Lock, J. D. *Phytochemistry* **1974**, *13*, 905-910.

(11) See, for example: Hadfield, J. R.; Holker, J. S. E.; Stanway, D. N. *J. Chem. Soc. C* **1967**, 751-755. Tannenbaum, S. W.; Nakajima, S. *Biochemistry* **1969**, *8*, 4626-4631. Gellerman, J. L.; Anderson, W. H.; Schlenk, H. *Lipids* **1974**, *9*, 722-725.

(12) Birch, A. J. *Proc. Chem. Soc.* **1962**, 3-13. Birkenshaw, J. M.; Gowland, A. *Biochem. J.* **1962**, *84*, 342-347. Tannenbaum, S. W.; Nakajima, S. *Biochemistry* **1969**, *8*, 4626-4631. Grove, J. F. *J. Chem. Soc. C* **1970**, 1860-1863. Cross, B. E.; Hendley, P. *J. Chem. Soc., Chem. Commun.* **1975**, 124-125. Vederas, J. C.; Graf, W.; David, L.; Tamm, Ch. *Helv. Chim. Acta* **1975**, *58*, 1886-1898.

(13) Bennett, J. W.; Christensen, S. B. *Adv. Appl. Microbiol.* **1983**, *29*, 53-92.

(14) Biollaz, M.; Büchi, G.; Milne, G. *J. Am. Chem. Soc.* **1968**, *90*, 5017-5019, 5019-5020; **1976**, *92*, 1035-1043.

(15) Bennett, J. W.; Lee, L. S.; Shoss, S. M.; Boudreaux, G. H. *Appl. Environ. Microbiol.* **1980**, *39*, 835-839. Hsieh, D. P. H.; Lin, M. T.; Yao, R. C.; Singh, R. *J. Agric. Food Chem.* **1976**, *24*, 1170-1174.

(16) The central role of averufin in aflatoxin biosynthesis has been the focus of recent efforts: Townsend, C. A.; Christensen, S. B.; Davis, S. G. *J. Am. Chem. Soc.* **1982**, *104*, 6152-6153, 6154-6155. Simpson, T. J.; deJesus, A. E.; Steyn, P. S.; Vleggaar, R. *J. Chem. Soc., Chem. Commun.* **1982**, 631-632. Townsend, C. A.; Davis, S. G. *Ibid.* **1983**, 1420-1422.

(17) Lane, M. P.; Nakashima, T. T.; Vederas, J. C. *J. Am. Chem. Soc.* **1982**, *104*, 913-915 and references compiled therein. In reduced polyketides the possibility exists for reduction/dehydration to occur to afford olefin/polyene intermediates that could be rehydrated or epoxidized to lead on to final products. The latter appears to play a significant role in polyether biosynthesis: Hutchinson, C. R. *Acc. Chem. Res.* **1983**, *16*, 7-14. Cane, D. E.; Celmer, W. D.; Westley, J. W. *J. Am. Chem. Soc.* **1983**, *105*, 3594-3600.

0002-7863/84/1506-3868$01.50/0