cis-3- and *trans*-3-Dodecen-1-yne (X).—A solution of 32 g (0.095 mol) of *p*-toluenesulfonic esters of 1-dodecyn-4-ol and 1,2-dodecadien-4-ol (prepared from nonanal and propargyl bromide by the method of Butenandt, *et al.*[4]), 7 g of potassium hydroxide, 30 ml of water, and 150 ml of ethanol was refluxed under nitrogen for 75 min, cooled, and extracted twice with 200-ml portions of pentane. The pentane solution was washed with water, dried over sodium sulfate, and concentrated to give 14 g (90%) of yellow oil. This product was flash-distilled at 5 mm and fractionated by glc [Carbowax 20M, 20% on Chromosorb P, 10–60 mesh, 2.4 m × 12.7 mm (i.d.) stainless steel tubing, 115°, 350 cm³ helium per min] to give 6.2 g of *cis*-3-dodecen-1-yne (Xa) at 46 to 66 min (99.8% pure) which had ir (λ^{film}, μ) 3.1 (C≡CH), 3.32 (C=CH), 13.5 (*cis* -CH=CH-). The yield of *trans*-3-dodecen-1-yne (Xb) was (2.4 g) (98% pure) at 67–87 min and had ir (λ^{film}, μ) 3.1 (C≡CH), 3.32 (C=CH), 10.4 (*trans* -CH=CH-).

Anal. Calcd for $C_{12}H_{20}$, Xa: C, 87.7; H, 12.3. Found: C, 88.0; H, 12.4. Xb: C, 87.7; H, 12.3. Found: C, 87.6; H, 12.4.

cis-5-Tetradecen-3-yn-1-ol (XIa).—A mixture of 1.25 g (0.0076 mol) of *cis*-3-dodecen-1-yne (Xa), 2 ml of anhydrous ethyl ether, and 2.8 ml (0.0084 mol) of methylmagnesium bromide (3 *M* in ethyl ether) was refluxed under N_2 with stirring for 1.5 hr with ethyl ether added at intervals to compensate for evaporation. The reaction mixture was cooled with an ice bath and a solution of 0.9 ml (0.02 mol) of ethylene oxide in 4 ml of ethyl ether was added. After 5 min, 15 ml of benzene was added to the gel that had formed, the ethyl ether was boiled off, and the mixture was refluxed for 2 hr under nitrogen, during which time the gel disappeared and a dark red solution resulted. The solution was cooled and poured into ice water containing 2 g of ammonium chloride. The mixture was extracted twice with ethyl ether. The organic solution was washed with water, dried over magnesium sulfate, and concentrated. The residue was distilled evaporatively at 105° (0.05 mm), and 0.8 g of distillate was collected. A portion of this was fractionated (Carbowax 20 M, 5% on Chromosorb G, 60–80 mesh, 0.9 m × 9.4 mm aluminum tubing, 177°, 100 cm³ He/min) and the major peak (90%) was collected at 10 to 18 min. Ir (λ^{film}, μ) 3.05, 3.32, 9.55, 13.5.

Anal. Calcd for $C_{14}H_{24}O$: C, 80.7; H, 11.6. Found: C, 80.4; H, 11.7.

trans-5-Tetradecen-3-yn-1-ol (XIb).—This was prepared from Xb with the same procedure used to prepare XIa. The distillate had ir (λ^{film}, μ) 3.05, 3.32, 9.55, and 10.4 (*trans* -CH=CH-).

Methyl *cis*-5-Tetradecen-3-ynoate (XIIIa).—Chromic acid solution[5] (1.1 ml) was added dropwise (2 min) to a stirred solution of 0.40 (2.0 mmol) of *cis*-5-tetradec-3-yn-1-ol (XIa) in 10 ml of acetone at 15°. Stirring was continued under nitrogen for 10 min, and 25 ml of pentane was added. The pentane solution was decanted, washed twice with water, and extracted twice with sodium carbonate solution. The sodium carbonate solution was acidified with 1 *N* hydrochloric acid and extracted with ethyl ether. The ether solution was washed twice with water, dried over magnesium sulfate, and concentrated to give 0.30 g of *cis*-5-tetradecen-3-yn-oic acid (XIIa). Ir (λ^{film}, μ) 2.9 to 4.1 (characteristic COOH pattern), 4.5 and 4.6 (weak doublet, C≡C), 5.8 (C=O), 6.15 (weak, C=C), 10.7 (COOH dimer), and 13.6 (*cis* -CH=CH-).

A solution of diazomethane (4 mmol) in 10 ml of ethyl ether was added to a cold solution of 0.3 g (1.5 mmol) of XIIa in 5 ml of ethyl ether. After 5 min at 0°, the solution was concentrated to give 0.3 g of product. A portion of this was fractionated (Carbowax 20 M, 10% on Gas Chrom Q, 60–80 mesh, 0.6 m × 8 mm i.d. Pyrex, 170°, 100 cm³ He/min), and the major peak (30 to 40 min) was collected. Ir (λ^{film}, μ) 3.33 (C=CH), 4.5 (very weak, C≡C), 5.83 (C=O), 9.85, 13.5 (broad, *cis* -CH=CH-).

Anal. Calcd for $C_{15}H_{24}O_2$: C, 76.2; H, 10.2. Found: C, 76.3; H, 10.7.

Methyl *trans*-5-Tetradecen-3-ynoate (XIIIb).—This was prepared from XIb using the same procedure used to prepare XIIIa. Compound XIIIb had ir (λ^{film} μ) 2.9–4.1 (characteristic COOH pattern), 4.5 and 4.6 (weak doublet, C≡C), 5.81 (C=O), 6.15 (weak, C=C), 10.45 (*trans*-CH=CH-), 10.7 (shoulder, COOH dimer). XIIIb: ir (λ^{film}, μ) 3.33 (C=CH), 4.5 (very weak, C≡C), 5.83 (C=O), 9.85, 10.4 (*trans* -CH=CH-).

Methyl *cis*-3,*cis*- and -*trans*-5-Tetradecadienoate (IXa and XIV).—These dienoic esters were prepared from their corresponding enyne compounds (XIIIa and XIIIb) using the procedure for the preparation of IXa and IXb. Spectra for IXa synthesized by both sequences were congruent.

The data obtained on the *cis*-3,*trans*-5 isomer (XIV) were very similar to those obtained on the *trans*-3,*cis*-5 isomer (IXb). Subtle differences in the nmr and ir spectra were observed. The main distinguishing feature was the 9.8 μ ir band, which was very weak in IXb and moderate in XIV where it is as strong as the 10.5 μ band. The uv spectra were indistinguishable as were the retention times on 3 m × 3 mm columns with the following substrates: Carbowax 20 M, Versamid 900, STAP, EGSS-X, CHDMS, PDEAS, HI-EFF-IBP, ECNSS-S.

Methyl *trans*-3,*trans*-5-Tetradecadienoate (XV).—A solution of 10 mg of methyl *cis*-3,*trans*-5-tetradecadienoate in 0.3 ml of carbon tetrachloride containing ~1 μmol of iodine in a sealed Pyrex tube was irradiated with a 250-W lamp for 16 hr. The solvent and iodine were removed under reduced pressure, and the residue was tube-distilled at 100° and 0.02 mm pressure to give 7 mg of distillate. Ir (λ^{film}, μ) 3.32, 5.73, 8.0, 8.35, 8.60, 10.1 (*trans*, *trans* -CH=CHCH=CH-); uv (λ_{max}^{hexane}, mμ) 229 (ϵ 28,000).

Glc data on the 4 isomeric esters (Carbowax 20 M, 4% on Chromosorb G 60–80 mesh, 3 m × 3 mm aluminum tubing, 160°, 20 cm³ He min), IXb, XIV, IXa, XV, showed retention times of 28.5, 28.5, 30.2, and 34 min, respectively.

Synthesis of Megatomoic Acid Isomers (II, III, and IV).—In each case, 1-mg samples of the ester (a glc fraction, 98 to 99% pure) was hydrolysed as described for megatomoic acid. The products showed the following uv data (λ_{max}^{hexane}, mμ): II, 235; III, 233; IV, 229. A portion of each acid solution was reesterified and analyzed by glc (conditions described above).

Registry No.—I, 23400-52-4; II, 25091-12-7; III, 17022-64-9; IV, 25091-14-9; V, 25091-15-0; *cis*-VI, 25091-16-1; *trans*-VI, 25091-17-2; *cis*-VII, 25091-18-3; *trans*-VII, 25091-19-4; *cis*-VIII, 25091-20-7; *trans*-VIII, 25091-21-8; IXa, 25091-22-9; IXb, 25091-23-0; Xa, 25091-24-1; Xb, 25091-25-2; XIa, 25091-26-3; XIb, 25091-27-4; XIIIa, 25091-28-5; XIIIb, 25091-29-6; XV, 25091-30-9.

(5) L. F. Fieser and M. Fieser," Reagents for Organic Synthesis," Wiley, New York, N. Y., p 142.

Studies on Resin Acids. VI. Synthesis of (+)-4-Epidehydroabietic Acid[1]

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(+)-4-Epidehydroabietic acid (callitrisic acid, abieta-8,11,13-trien-19-oic acid) (1) has recently been isolated as a natural product by several workers[2] and its synthesis from agathic acid has been reported.[3] In addition, the total synthesis of racemic 1 has been reported by several groups.[3a,4]

An obvious synthetic approach to 4-epidehydroabietic is its preparation from podocarpic acid (2) *via* methyl 12-methoxy abieta-8,11,13-trien-19-oate (3).[5] This general approach was attempted by Chuah and

(1) Part V: J. W. Huffman, *J. Org. Chem.*, **35**, 478 (1970). This work was supported in part by Career Development Award GM-5433 from the National Institutes of Health.

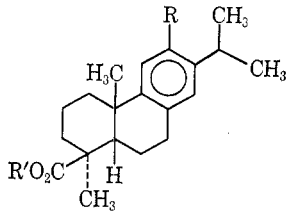
(2) (a) R. M. Carman and H. C. Deeth, *Aust. J. Chem.*, **20**, 2789 (1967); (b) L. J. Gough, *Tetrahedron Lett.*, 295 (1968); (c) Y. S. Chuah and A. D. Wood, *Aust. J. Chem.*, **22**, 1333 (1969).

(3) (a) R. M. Carman, H. C. Deeth, R. A. Marty, K. Mori, and M. Matsui, *Tetrahedron Lett.*, 3359 (1968); (b) R. C. Carman and R. A. Marty, *Aust. J. Chem.*, **22**, 2696 (1969).

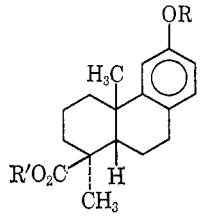
(4) (a) R. D. Haworth and R. L. Barker, *J. Chem. Soc.*, 1299 (1939); (b) M. Sharma, U. R. Ghatak, and P. C. Dutta, *Tetrahedron*, **19**, 985 (1963).

(5) W. P. Campbell and D. Todd, *J. Amer. Chem. Soc.*, **62**, 1287 (1940).

Wood;[2c] however the hydrogenolysis of the benzoxazolyl ether derived from **3** (**4**) failed even under extreme conditions.[6] In our hands, however, a modification of this procedure affords a convenient synthesis of 4-epidehydroabietic acid.



1, R, R′ = H
3, R = OCH_3; R′ = CH_3
4, R = OC_7H_4NO; R′ = CH_3
6, R = OH; R′ = CH_3
7, R = $OC_7H_5N_4$; R′ = CH_3
8, R = H; R′ = CH_3



2, R, R′ = H
5, R, R′ = CH_3

The conversion of methyl 12-methoxypodocarpa-8,11,13-trien-19-oate (**5**) to **3** was carried out essentially as described by Campbell and Todd.[5] However, the reaction of podocarpic acid (**2**) with dimethyl sulfate and base gave **5** as the major product, rather than the corresponding acid as described previously.[7] Demethylation of **3** with boron tribromide[8] gave methyl 12-hydroxy-abieta-8,11,13-trien-19-oate (**6**) in 85% yield.[9] The attempted conversion of **6** to the phenyltetrazolyl ether (**7**) by the published method[10] gave only recovered starting materials; however, the interaction of the preformed anion of **6** with 2 equiv of 1-phenyl-5-chlorotetrazole in dimethyl formamide gave **7** in 68% yield. The hydrogenolysis of **7** proceeded smoothly under mild conditions to afford methyl abieta-8,11,13-trien-19-oate (methyl 4-epidehydroabietate, **8**) which was identical with the methyl ester of the natural product.[11] The hydrolysis of **8** to give **1** has been described previously.[2a,c] Since the total synthesis of (+)-podocarpic acid has been described,[12] this work constitutes a formal total synthesis of (+)-4-epidehydroabietic acid.

Experimental Section[13]

12-Methoxypodocarpa-8,11,13-trien-19-oic Acid and Methyl 12-Methoxypodocarpa-8,11,13-trien-19-oate.—The methylation of podocarpic acid was carried out essentially as described by Bennett and Cambie;[7] however, in contrast to the results reported by these authors, the principal product was methyl 12-methoxypodocarpa-8,11,13-trien-19-oate, rather than the corresponding acid. From 55.74 g of podocarpic acid, 78 ml of dimethyl sulfate, and 33.4 g of sodium hydroxide in 100 ml of water, there was obtained 43.50 g of hexane soluble material, mp 105–108°, and only a trace of hexane insoluble brown gum. The hexane soluble material was suspended in 400 ml of 10% aqueous potassium hydroxide and the insoluble material was collected and recrystallized from hexane to give 27.81 g (43%) of methyl ester (**5**), mp 125–126° (lit. mp 127–128°). Acidification of the basic solution gave 10.97 g (18%) of 12-methoxypodocarpa-8,11,13-trien-19-oic acid, mp 154–156° (lit. mp 157–158°), as off-white needles from aqueous ethanol.[14]

Methyl 12-Methoxyabieta-8,11,13-trien-19-oate (3).—This material, mp 105–107° (lit.[5] mp 109°), was prepared from methyl 12-methoxypodocarpa-8,11,13-trien-19-oate (**5**) by the method of Campbell and Todd.[5] The infrared spectrum of this compound showed $\lambda_{C=O}$ 5.81 μ and nmr signals at 1.03 (s, C-10 methyl), 1.19 (d, J = 7 Hz, isopropyl), 1.27 (s, H-18), 3.62 (s, CO_2CH_3), 3.78 (s, CH_3O), and 6.72, 6.86 (br s, Ar H).

Methyl 12-Hydroxyabieta-8,11,13-trien-19-oate (6).—To a solution of 5.50 g of methyl 12-methoxyabieta-8,11,13-trien-19-oate (**3**) in 200 ml of methylene chloride was added 2.0 ml of boron tribromide. The reaction mixture was stirred at room temperature overnight and concentrated to dryness on the steam bath, and the dark brown residue was taken up in 250 ml of methanol and 20 ml of water. This mixture was heated at reflux for 4 hr, concentrated to a small volume, taken up in ether, and washed with saturated aqueous sodium bicarbonate and water. After drying, the solvent was removed leaving a brown crystalline mass. Recrystallization from aqueous methanol gave 4.47 g (85%) of off-white needles, mp 178–179° (lit.[9] mp 178–180°), λ_{OH} 2.93 μ, $\lambda_{C=O}$ 5.86 μ, and nmr signals at 1.00 (s, C-10 methyl), 1.21 (d, J = 6 Hz, isopropyl), 1.27 (s, H-18), 3.62 (s, CO_2CH_3), and 6.58, 6.75 (br s, Ar H). An analytical sample, mp 180–181°, was prepared by recrystallization from aqueous methanol.

Anal. Calcd for $C_{21}H_{30}O_3$: C, 76.33; H, 9.15. Found: C, 76.15; H, 9.12.

Phenyltetrazolyl Ether of Methyl 12-Hydroxyabieta-8,11,13-trien-10-oate (7).—To a suspension of 0.60 g of sodium hydride (50% suspension in mineral oil, washed with four portions of hexane and dried at 1 mm and room temperature) in 80 ml of anhydrous dimethyl formamide was added 2.00 g of methyl 12-hydroxyabieta-8,11,13-trien-19-oate (**6**). The reaction mixture was stirred at ambient temperature under a nitrogen atmosphere until the evolution of hydrogen ceased (approximately 30 min), and 1.47 g of 1-phenyl-4-chlorotetrazole was added. The temperature was gradually raised to 50° and the mixture stirred under nitrogen at this temperature for 4 hr. The mixture was cooled, an additional 1.47 g of tetrazole added, and heating with stirring under nitrogen continued for 20 hr. The reaction mixture was cooled, water was added cautiously to destroy any excess hydride, and the solution was poured into water. After acidification with 10% hydrochloric acid, the aqueous mixture was extracted with two portions of ether. The ethereal extracts were washed with water and dried, and the solvent was removed to give a pale brown semisolid mass. Two recrystallizations from methanol gave 1.94 g (68%) of **7** as white crystals, mp 157–159°. The analytical sample, mp 161–162°, was crystallized from methanol and showed nmr signals at 1.04 (s, C-10 methyl), 1.20 (d, J = 7 Hz, isopropyl), 1.28 (s, H-18), 3.65 (s, CO_2CH_3), 7.03, 7.22 (Ar H), and 7.67 (m, C_6H_5).

Anal. Calcd for $C_{28}H_{34}N_4O_3$: C, 70.86; H, 7.22; N, 11.80. Found: C, 71.16; H, 7.41; N, 11.96.

The attempted preparation of this compound by using Musliner and Gates procedure (potassium carbonate in acetone) gave only recovered phenol and tetrazole. The above method using 1 equiv of chlorotetrazole gave the ether in only 16% yield, and the product could be isolated only after chromatography on Merck alumina and elution with benzene.

Methyl Abieta-8,11,13-trien-19-oate (8).—A solution of 2.28 g of tetrazolyl ether (**2**) in 275 ml of ethanol was hydrogenated at 40 psig and 40° using 2.20 g of 5% palladium on carbon for 20 hr. The catalyst was filtered off, the ethanol removed at reduced pressure, and the residue taken up in ether. The ethereal extracts were washed with two portions of 5% aqueous sodium hydroxide to remove the 1-phenyltetrazolone and dried, and the solvent was removed to give a colorless oil which slowly crystal-

(6) W. L. Meyer and C. W. Sigel, *Tetrahedron Lett.*, 2485 (1967), reported, without comment, the hydrogenolysis of a 7-oxo 4-epimer of **4**.

(7) C. R. Bennett and R. C. Cambie, *Tetrahedron*, **23**, 927 (1967).

(8) J. F. McOmie, M. L. Watts, and D. E. West, *ibid.*, **24**, 2289 (1968), and references therein.

(9) S. M. Bocks, R. C. Cambie, and T. Takahashi, *ibid.*, **19**, 1109 (1963), have carried out this conversion in two steps from **3**.

(10) W. J. Musliner and J. W. Gates, *J. Amer. Chem. Soc.*, **88**, 4271 (1966).

(11) We would like to thank Dr. R. M. Carman of the University of Queensland for a sample of this material.

(12) (a) E. Wenkert and A. Tahara, *J. Amer. Chem. Soc.*, **82**, 3229 (1960); (b) E. Wenkert, A. Afonso, J. B. Bredenberg, C. Kaneko, and A. Tahara, *ibid.*, **86**, 2038 (1964).

(13) Melting points were determined on a Kofler hot stage and are uncorrected. Infrared spectra were taken as potassium bromide pellets on a Perkin-Elmer Model 137 spectrophotometer, and nuclear magnetic resonance spectra were recorded on a Varian Associates A-60 nuclear magnetic resonance spectrometer using deuteriochloroform as solvent and tetramethylsilane as an internal standard. Signals are given in parts per million relative to this standard. Rotations were determined using a Rudolph Model 70 polarimeter and analyses were performed by Galbraith Laboratories, Knoxville, Tenn.

(14) Bennett and Cambie (ref 7) reported that this procedure gives a 5% yield of methyl ester and 64% of the acid.

lized. Recrystallization from aqueous methanol gave 1.01 g (59%) of material: mp 79–80° (lit. mp 79,[2b] 80–81°[2a]); $[\alpha]^{28}D$ +140° (C=O, 557, ethanol) (reported +137°,[2b] +140°[2a]). An additional 0.01 g (0.6%) of material, mp 73–76°, could be obtained by concentration of the mother liquors. The infrared spectrum of this material, mp 79–80°, was identical with that of an authentic sample: lit.[11] mp 78.5–79.5°; mmp 79–80°. The nmr spectrum of the ester showed signals at 1.03 (s, C-10 methyl), 1.22 (d, J = 7 Hz, isopropyl), 1.27 (s, H-18), 3.67 (s, CO_2CH_3), 6.91 (br s, H-14), 7.00 (q, J_{ortho} = 7.5 Hz, J_{meta} = 2 Hz, H-12), and 7.24 (d, J = 7.5 Hz, H-11).

Registry No.—**1**, 18045-62-0; **6**, 25356-78-9; **7**, 25454-68-6; **8**, 18045-63-1.

Griseofulvin Analogs. VII.[1] 5′-Formyl-, 5′-Alkoxalyl-, and 5′-Halogriseofulvins

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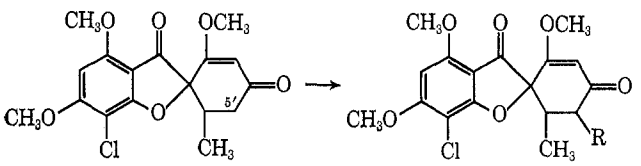
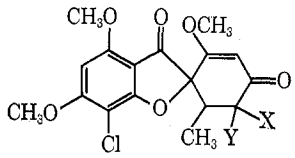
Although a large number of griseofulvin analogs have been prepared involving a variety of positions,[2,3] the 5′ position has not heretofore been manipulated except for the preparation of 5′-hydroxygriseofulvin by microbiological oxidation[4a] and 5,5′-dichlorogriseofulvin.[4b] We have now succeeded in activating the 5′ position of griseofulvin (**1**) by formylation in very high yield (and in much inferior yield by alkoxalylation) thus making it amenable to extensive manipulation. We describe here the preparation of the bromo, chloro, iodo, and fluoro derivatives and present some interesting aspects of their chemistry.

Formylation of griseofulvin (**1**) to form the 5′-formyl derivative **2** was accomplished in 94% yield by simply stirring griseofulvin in a large excess of neat methyl formate in the presence of a molar excess of sodium methoxide for 40 hr. Although methoxalylation and ethoxalylation of the 5′ position were also effected to give **3** and **4**, respectively, the poor yields in which they were obtained precluded their suitability for further transformations.



1 → **2**, R = CHO; **3**, R = $COCO_2CH_3$; **4**, R = $COCO_2Et$

The formyl derivative **2** underwent facile bromination with N-bromosuccinimide in chloroform at room temperature to give 5′-bromo-5′-formyl griseofulvin (**5**) as a mixture of isomers A and B separable by fractional crystallization.[5] The bromo–formyl mixture **5** underwent rapid deformylation to the 5′-bromo derivative **6**



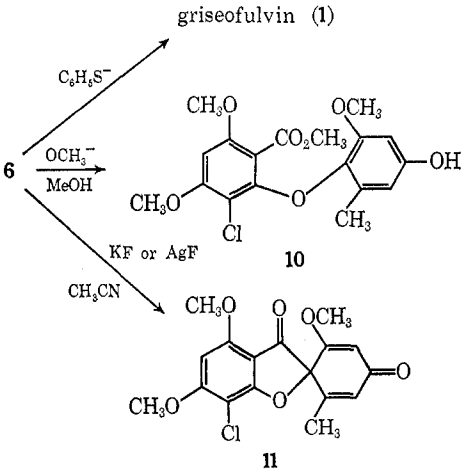
5a, X = Br; Y = CHO
5b, X = CHO; Y = Br
6, X = Br; Y = H
7, X = Cl; Y = H
8, X = I; Y = H
9, X = F; Y = H

with methanolic methoxide. In fact, the two steps could be conveniently combined and **6** isolated directly. In a similar manner, using N-chlorosuccinimide and N-iodosuccinimide, the corresponding 5′-chloro analog **7** and 5′-iodo analog **8** were prepared.

The 5′-fluoro derivative **9** was obtained by treating the sodium salt of **2** in methanol with perchloryl fluoride. Formation of **9** was accompanied by hydrolysis of the enol ether moiety to give 5′-fluorogriseofulvic acid (**9a**) (OH in place of OCH_3 on ring C in **9**) in *ca.* equivalent yield.[6,7]

It has been anticipated that 5′-bromogriseofulvin (**6**) would be a most suitable substrate for introducing a variety of substituents *via* simple displacement. It, however, quickly became apparent that this was not to be the case.

Thus, with even as ideal a nucleophile as thiophenolate ion, **6** underwent preferential reduction to griseofulvin (**1**) rather than displacement. With methoxide in methanol, **6** was converted to the diphenyl ether **10**[8] and with potassium fluoride or silver fluoride in acetonitrile to dehydrogriseofulvin **11**.[9]



(1) See ref 3 for previous papers in this series.

(2) J. F. Grove, *Progr. Chem. Org. Natur. Prod.*, **22**, 203 (1964).

(3) H. Newman and R. B. Angier, *J. Org. Chem.*, **34**, 3484 (1969), and previous publications cited there.

(4) (a) W. Andres, W. McGahren, and M. Kunstmann, *Tetrahedron Lett.*, 3777 (1969). See also the patent application filed July 1, 1968 (Serial No. 741,328), by H. Newman, P. Shu, and W. Andres in which the microbiological reduction of the ring B sulfur analog of dehydrogriseofulvin[4c] is described. The products obtained there were the ring B sulfur analog of griseofulvin and the ring B sulfur analog of 5′-hydroxygriseofulvin, the latter presumably arising by the microbiological oxidation of the former. (b) D. Taub, C. H. Kuo, and N. L. Wendler, *J. Org. Chem.*, **28**, 3344 (1963). (c) H. Newman and R. B. Angier, *ibid.*, **34**, 1463 (1969); see ref 11 cited there.

(5) The very much lower optical rotation exhibited by isomer A compared with isomer B and the other 5′-halogriseofulvins (see Experimental Section) would appear to suggest that the configuration of the halogen in A is different than it is in the others. Nmr spectroscopy indicates a *trans* diequatorial relationship between the 6′-CH_3 and the 5′-halogen in the 5′-halogriseofulvins (*cf. ca.* 13 Hz coupling constant between the 6′ and 5′ protons). In isomer A, therefore, these substituents would appear to be *cis* oriented.

(6) It is extremely unlikely that fluorination followed hydrolysis, since the expected product would then be the 3′-fluoro derivative.

(7) See, W. A. Sheppard, *Tetrahedron Lett.*, 83 (1969), for a discussion of the mechanism of fluorination with perchloryl fluoride.

(8) E. Kyburz, J. Wursch, and A. Brossi, *Helv. Chem. Acta*, **45**, 813 (1962).

(9) D. Taub, C. H. Kuo, H. L. Slates, and N. C. Wendler, *Tetrahedron*, **19**, 1 (1963).