thiolate addition to 9 is reversible. The success of our synthesis depends on forming just enough 9 to form 3 without getting a lot of 7 or trimer 8 while at the same time avoiding (*E,Z*)-isomerization of 5 or MeCH=CHSH.

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Supplementary Material Available: Experimental procedures for preparation of stereoisomers of 1-4, 6 and 7 (6 pages). This material is contained in many libraries on microfiche, immediately following this article in the microfilm version of the journal and can be ordered from the ACS; see any current masthead page for ordering information.

Sch 47918: A Novel PAF Antagonist from the Fungus *Phoma* sp.

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Summary: A novel platelet activating factor (PAF) antagonist, Sch 47918, was isolated from the fermentation broth of the fungus, *Phoma* sp. The structure of this compound was elucidated by spectroscopic methods. The proposed structure and stereochemistry of Sch 47918 were confirmed by single-crystal X-ray diffraction analysis. Sch 47918 was found to be active at IC_{50} = 6.96 μM in the in vitro PAF-induced human platelet aggregation assay.

Platelet activating factor (PAF, 1-*O*-alkyl-*sn*-glycerol-3-phosphocholine) is a potential mediator of allergic[1,2] and nonallergic inflammatory[3] diseases. This substance is a very attractive target for developing a new type of antiallergic and antiinflammatory drug. In the course of our screening program for new PAF antagonists, a novel macrocyclic compound, Sch 47918, has been discovered from the fermentation of a fungal culture, SCF-0592, *Phoma* sp.[4] (ATCC 74077). The microorganism, *Phoma* sp., was isolated from a leaf litter sample of mixed *Quercus* species, which was collected in a second growth mixed hardwood lot in Baton Rouge, Louisiana. In this paper, we describe the structure elucidation and biological properties of Sch 47918.

The purification of Sch 47918 was accomplished by EtOAc extraction and gel permeation chromatography followed by precipitation and recrystallization.[5] Its molecular formula, $C_{20}H_{28}O_3$, was determined by HREIMS (*m/z* calcd 316.2038, found 316.2034) in combination with carbon and proton NMR data.[6] IR absorptions at 1705 and 1689 cm^{-1} indicated the presence of aldehyde and conjugated ketone functional groups, and their existence was supported by signals at δ 193.7 and 203.0, respectively, in the ^{13}C NMR spectrum. APT and DEPT experiments revealed that two vinyl carbon signals overlapped at δ 137.9, and thus a total of four olefinic carbons were involved in two C=CH bonds. Two oxygenated carbon resonances at δ 63.3 and 64.2 were ascribed to a trisubstituted epoxide. ^1H NMR spectral data were consistent with the analysis of the ^{13}C NMR spectrum. A doublet of an aldehyde proton at δ 9.90 (*J* = 1.2 Hz) was split by an adjacent methine proton at δ 3.80. Two vinyl protons at δ 5.23 and 6.96 displayed two trisubstituted double bonds. A singlet of oxygenated proton at δ 3.47 suggested an epoxide which is conjugated with a carbonyl group. One doublet and three singlets at δ 0.88, 1.11, 1.32, and 1.60 were assigned as four methyl groups in connection with a methine, an oxygenated carbon, a quarternary carbon, and a double bond, respectively. Analysis of the results of 2D-COSY, HETCOR, and SINEPT experiments (Figure 1) suggested a partial structure (1) containing an aldehyde-attached cyclohexene ring conjugated with a carbonyl group, as well as a subunit (2) that possessed a seven-carbon chain with a trisubstituted double bond and an epoxide ring. As shown in Figure 1, SINEPT long-range ^1H–^{13}C correlation experiments further suggested that the

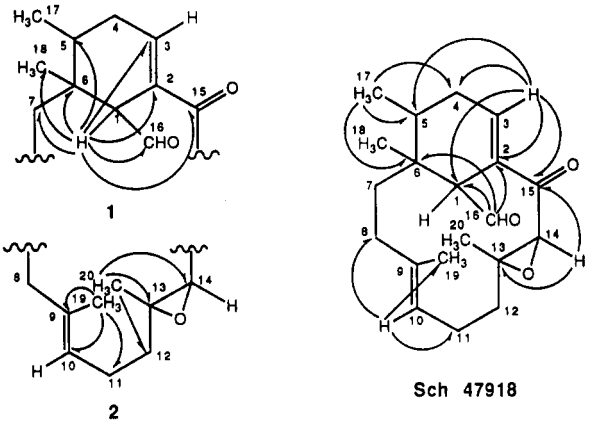

Figure 1. Structure of Sch 47918 as revealed by SINEPT experiments. Arrows indicate ^1H–^{13}C long-range couplings.

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(5) A paper describing details of the taxonomy, fermentation, and isolation will be submitted to *J. Antibiot.*
(6) Sch 47918: mp 204–205 °C, $[\alpha]_D^{22}$ +22.4° (*c* 0.3, $CHCl_3$); CI-MS *m/z* 317 $(M + H)^+$; λ_{max} (MeOH) end, 244 (6, 352); ^1H NMR (300 MHz, $CDCl_3$) δ 0.88 (d, *J* = 7.1 Hz, 3H-17), 1.11 (s, 3H-20, 1.12–2.10 (m, 2H-12), 1.32 (s, 3H-18), 1.50–1.65 (m, 1H-5), 1.60 (s, 3H-19), 1.75 (dd, *J* = 7.8, 14.3 Hz, 2H-7), 1.86–2.68 (m, 2H-4), 1.88–2.35 (m, 2H-8), 1.90–2.44 (m, 2H-11), 3.47 (s, 1H-14), 3.80 (br. s, 1H-1), 5.23 (br. d, *J* = 12.1 Hz, 1H-10), 6.96 (br. s, 1H-3) 9.90 (d, *J* = 1.2 Hz, 1H-16); ^{13}C NMR (75 MHz, $CDCl_3$) δ 53.0 (C_1) 133.3 (C_2), 137.9 (C_3), 31.0 (C_4), 36.0 (C_5), 40.2 (C_6), 34.4 (C_7), 24.7 (C_8) 137.9 (C_9), 125.0 (C_{10}), 35.0 (C_{11}), 38.1 (C_{12}), 63.3 (C_{13}), 64.2 (C_{14}), 203.0 (C_{15}), 193.7 (C_{16}), 17.4 (C_{17}), 21.8 (C_{18}), 16.0 (C_{19}), 14.4 (C_{20}).

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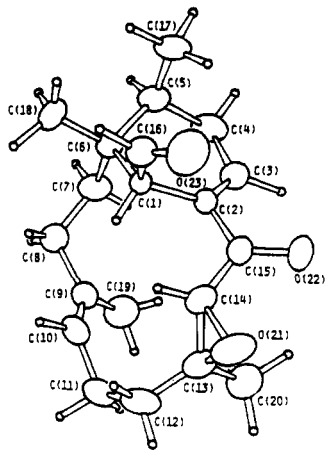

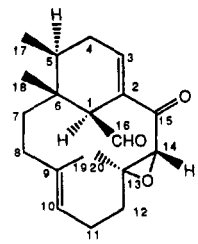

Sch 47918

Figure 2. ORTEP diagram showing the structure (relative stereochemistry) and solid-state conformation of Sch 47918; small circles represent hydrogen atoms.

fragments (1) and (2) should be connected through a two-site linkage to form a macrocyclic ring.

In order to verify the proposed structure and establish the overall stereochemistry of Sch 47918, X-ray diffraction analysis[7] was performed on a crystal obtained from a MeOH–$CHCl_3$ (1:2) solution. An ORTEP diagram showing the relative stereochemistry and solid-state conformation is provided in Figure 2. Sch 47918 is a new member of the rare cleomane class of diterpene, the only previous example being cleomeolide.[8]

Sch 47918 was tested in PAF-induced platelet aggregation assay[9] which was performed using freshly prepared human platelet rich plasma. The IC_{50} of this antagonist was found to be 6.96 μM in vitro. Sch 47918 was inactive against Gram-positive and Gram-negative bacteria and various fungi (*Candida* sp.) in agar diffusion assays (at 30 μg/disc). Additional details of the chemical and biological properties of Sch 47918 and related minor components will be reported elsewhere.[5]

Acknowledgment. We thank Dr. R. Bishop for biological data and Dr. P. Das for mass spectral data.

Supplementary Material Available: ^1H and ^{13}C NMR spectra and X-ray data for Sch 47918. The author has deposited atomic coordinates for this structure with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK (11 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

(7) Crystallographic data for Sch 47918: $C_{20}H_{28}O_3$, M = 316.44, monoclinic, space group $P2_1$ (C^2_2) No. 4, a = 10.101 (1) Å, b = 11.538 (1) Å, c = 8.237 (1) Å, β = 112.93 (1)°, V = 884.1 (3) Å^3, Z = 2, D_{calcd} = 1.189 g cm^{-3}, μ (Cu Kα) = 5.8 cm^{-1}. Crystal dimensions 0.05 × 0.20 × 0.40 mm. Intensity data ($\pm h$,$-k$,$+l$, 1911 nonequivalent reflections, $\omega - 2\theta$ scans, θ_{max} = 75°) were recorded on an Enraf-Nonius CAD-4 diffractometer (Cu Kα radiation, λ = 1.5418 Å graphite monochromator). The crystal structure was solved by direct methods (RANTAN). Full-matrix least-squares refinement of atomic positional and thermal parameters (anisotropic C, O; fixed H contributions) converted (maximum shift:esd = 0.02σ) at R = 0.045 (R_w = 0.060, GOF = 1.24) over 1360 reflections with $I > 3.0\sigma(I)$. Crystallographic calculations were performed on PDP 11/44 and Micro VAX computers by use of the Enraf-Nonius Structure Determination Package (SDP).

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Articles

Synthesis of the Bis-spiroacetal Moiety of 17-Epi-20-deoxysalinomycin

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The synthesis of the bis-spiroacetal moiety of 17-epi-20-deoxysalinomycin (4) is reported in which the key step involves oxidative cyclization of the hydroxy spiroacetals 14 and 15 to the bis-spiroacetals 16 and 17 using (diacetoxyiodo)benzene and iodine under photolytic conditions.

The polyether antibiotic salinomycin (1),[1] isolated from the fermentation medium of *Streptomyces albus*, was found to exhibit marked activity against mycobacteria and fungi in addition to antibacterial and anticoccidial properties. Growth of *S. albus* in a different culture medium led to the isolation of both 17-epi-20-deoxysalinomycin (4) and 20-deoxysalinomycin (2) with the former antibiotic being present at much greater levels than the latter[2] while 4-methylsalinomycin or narasin A (3) was isolated from a culture of *S. aureofaciens*.[3] The interesting 1,6,8-tri-

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