ion-exchange resin and the water removed under vacuum to give 0.8 g of a syrup identical on a Waters carbohydrate column to that obtained from the sulfuric acid catalyzed hydrolysis of **6**.

This syrup (0.36 g) was dissolved in acetic anhydride (7 mL) with sodium acetate (0.6 g) and boiled for 10 min. Workup and crystallization (petroleum ether 60–80 °C) gave 0.2 g of 1,2,4,6-tetra-*O*-acetyl-3-deoxy-3-fluoro-α-D-glucose: mp 116–120 °C (lit. mp 119–120 °C).[5]

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Registry No.—**1**, 582-52-5; **3**, 2774-28-9; **4**, 2595-05-3; **5**, 64872-56-6; **6**, 14049-05-9; **7**, 14049-03-7; **8**, 55951-90-1; DAST, 38078-09-0; trifluoromethanesulfonic anhydride, 358-23-6; acetic anhydride, 108-24-7.

References and Notes

(1) This work was supported by U.S. Public Health Service Grants 5 P01 HL13851 and P50 NSO 6833.
(2) P. W. Kent, pp 169–214, and N. F. Taylor, pp 215–238, in "Carbon–Fluorine Compounds", A CIBA Symposium, Associated Scientific Publishers, Amsterdam, 1972.
(3) N. F. Taylor, A. Romaschin, and D. Smith, *ACS Symp. Ser.* **28**, 99–116 (1976).
(4) A. Romaschin, N. F. Taylor, D. A. Smith, and D. Lopes, *Can. J. Biochem.*, **55**, 369 (1977).
(5) A. B. Foster, R. Hems, and J. M. Webber, *Carbohydr. Res.*, **5**, 292 (1967).
(6) ^{18}F decays by positron emission and is of interest for positron emission tomography. M. G. Straatmann and M. J. Welch, *J. Nucl. Med.* **18**, 151 (1977).
(7) W. Middleton, *J. Org. Chem.*, **40**, 574 (1975).
(8) M. Sharma and W. Korytnyk, *Tetrahedron Lett.*, 573 (1977).
(9) J. D. Stevens, *Methods Carbohydr. Chem.*, **6**, 123–128 (1972).
(10) H. Zinner, G. Wulf, and R. Heinatz, *Chem. Ber.*, **97**, 3536 (1964).
(11) D. G. Ibbott and A. F. Janzen, *Can. J. Chem.*, **50**, 2428 (1972).
(12) R. N. Haszeldine, A. E. Tipping, and T. J. Tewson, *J. Chem. Soc., Perkin Trans. 1*, in press.
(13) D. C. C. Smith, *J. Chem. Soc.*, 1244 (1956).
(14) M. L. Wolfrom, J. Bernsmann, and D. Horton, *J. Org. Chem.*, **27**, 4505 (1962).
(15) V. G. Nayak and R. L. Whistler, *J. Org. Chem.*, **34**, 3819 (1969).
(16) R. L. Whistler and L. W. Doner, *J. Org. Chem.*, **35**, 3562 (1970).
(17) Produced on the Washington University Medical School cyclotron by bombardment of neon/15% H_2 with 7 MeV deuterons. Procedure is similar to that in ref 5. Exact details to be published elsewhere.
(18) L. D. Hall and D. C. Miller, *Carbohydr. Res.*, **47**, 299 (1976).
(19) T. G. Bonner and N. M. Saville, *J. Chem. Soc.*, 2851 (1960).
(20) A. B. Forster, R. Hems, and L. D. Hall, *Can. J. Chem.*, **48**, 3937 (1970).

Antineoplastic Agents. 55. Isolation and Structure of Multigilin and Multistatin[1]

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Two new cytotoxic and antineoplastic pseudoguaianolides designated multigilin (**2b**) and multistatin (**2d**) have been isolated from *Baileya multiradiata* Harv. and Gray. The related sesquiterpene lactone fastigilin A (**1c**) was also found to be a constituent of this plant. With the x-ray crystal structure of radiatin (**1a**) serving as a valuable reference, complete structural and stereochemical assignments were made for fastigilin A (**1c**), multigilin (**2b**), and multistatin (**2d**). Interpretation of the ^{13}C nuclear magnetic resonance spectra provided a firm basis for these assignments and allowed further confirmation of structures previously proposed for fastigilin B (**1b**), fastigilin C (**2a**), and multiradiatin (**2c**).

A detailed investigation of *Baileya multiradiata* Harv. and Gray (Compositae) cytotoxic and antineoplastic constituents begun in 1966 led to the isolation of six sesquiterpene lactones displaying such physiological activity.[2] Of these growth inhibitory substances radiatin (**1a**), fastigilin B (**1b**), fastigilin C (**2a**), and multiradiatin (**2c**) appeared most promising. Until 1973, requirements for these compounds were met through re-collections of the plant made in June within a 40-mile radius in Mohave County, Arizona. In April 1975 when it became necessary to increase supplies of radiatin and fastigilin C for further biological evaluation, re-collection of the plant was made at lower elevations some 100–150 miles south of previous collections. Sesquiterpene fractions from these specimens of *Baileya multiradiata* expected to contain primarily radiatin were found instead to be largely fastigilin B (**1b**) and fastigilin A[3,4] (**1c**), and those fractions presumed to contain fastigilin C and multiradiatin were found to also contain two new pseudoguaianolides that we have designated multigilin (**2b**) and multistatin (**2d**). The terpene assumed to be fastigilin A (**1c**) was confirmed by comparison with authentic fastigilin A provided by Professor W. Herz. A summary of the compelling spectral evidence supporting structural assignments for sesquiterpene lactones **1c**, **2b**, and **2d** and further confirmation for the structures previously assigned to fastigilin B[2,4] (**1b**), fastigilin C[3,4] (**2a**), and multiradiatin[2] (**2c**) now follow.

On casual inspection fastigilin A, multigilin, and multistatin could readily be mistaken for the isomeric and known constituents of *Baileya multiradiata* lactones **1b**, **2a**, and **2c**. The mass spectra by electron impact and thin-layer chromatographic behavior were indistinguishable from the known constituents. However, inspection of the ^1H NMR spectra revealed that the ester side chain methyl group resonances were shifted from the expected δ 1.80 and 2.12 (typical of a senecioate ester[4]) to δ 1.72 and 1.82, respectively (typical of an angelate). Eventually this observation served as a useful qualitative method for distinguishing between mixtures of multigilin with fastigilin C and fastigilin A with fastigilin B and the pure substances. Indeed certain compositions of multigilin with fastigilin C behaved in other respects as a pure substance and resisted all attempts at complete separation. A further challenge was presented by the quantities available, with fastigilin A and multigilin obtainable in approximately 0.002% yield while multistatin was isolated in only trace amounts. Both the ^1H NMR and infrared spectra of multigilin and multistatin suggested that they bore the same relationship

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Table I. ^{13}C NMR Spectra of *Baileya multiradiata* Components

	Radiatin (1a)	Fastigilin A (1c)	Fastigilin B (1b)	Fastigilin C (2a)	Multigilin[c] (2b)	Multiradiatin (2c)	Multistatin (2d)
C-1[a]	49.48	49.71	49.32	49.71	50.10	51.56	51.40
C-2	161.67	161.51	161.51	161.60	161.86	159.07	158.91
C-3	130.01	129.97	130.01	129.88	129.81	132.38	132.41
C-4	209.00	209.17	209.17	208.65	208.87	207.61	207.54
C-5	54.52	54.49	54.36	55.33	55.43	55.43	55.56
C-6	72.17	71.55	70.61	77.00[b]	79.19	70.06	71.07
C-7[a]	47.04	47.17	47.24	45.71	45.68	46.52	46.85
C-8	84.72	84.78	84.82	83.45	83.39	78.32	78.22
C-9	78.06	77.96	77.93	77.83	77.70	205.59	205.43
C-10	32.83	32.74	32.80	33.06	33.00	44.67	44.63
C-11	40.54	40.47	40.51	137.71	137.55	132.61	132.41
C-12	177.96	178.15	178.09	169.02	169.31	167.94	167.81
C-13	10.79	10.79	10.83	126.27	126.23	121.68	121.88
C-14	15.80	15.70	15.73	15.86	15.90	16.35	16.42
C-15	17.30	17.30	17.36	18.21	18.11	17.88	17.85
C-1′	166.03	166.32	165.02	165.15	166.51	164.66	165.90
C-2′	136.02	127.27	115.34	115.31	127.14	114.69	126.72
C-3′	126.20	139.34	158.48	159.13	139.95	160.17	140.77
C-2′-Me	18.14	20.38[a]			20.45[a]		20.25[a]
C-3′-Me		15.70[a]	20.35	30.45	15.90[a]	20.48	15.83[a]
C-3′-Me			27.34	27.47		27.54	

[a] Assignments for C-2′ methyl groups and C-3′ methyl groups may be reversed. In addition C-1 and C-7 values may be reversed in each example except for fastigilin C (see text). [b] This value is approximate, since the resonance is obscured by a $CDCl_3$ resonance. [c] This spectrum was obtained from a solution of **2b** contaminated with **2a**. Some resonances of these two substances overlapped.

as fastigilin C and multiradiatin. Confirmation of this assumption was obtained by chromium trioxide oxidation of alcohol **2b** to ketone **2d** and this interconversion was employed to obtain larger quantities of multistatin.

After uncovering the preceding relationships a ^{13}C NMR study was undertaken to confirm the skeletal assignments and where feasible the stereochemical relationships among this group of pseudoguaianolides. Completion[5] of an x-ray crystal structure analysis of radiatin (**1a**) provided a valuable benchmark structure for comparison purposes. Most probable ^{13}C NMR assignments for radiatin (**1a**) and the six related sesquiterpene lactones are given in Table I. Carbon atoms C-2, C-3, C-4, C-5, C-12, C-1′, and C-2′ of radiatin were assigned on the basis of shifts observed with model compounds[6,7] and off-resonance decoupling experiments. The same means and the downfield shift seen upon introduction of a double bond were used to assign C-11. In addition to chemical shift and off-resonance decoupling experiments, single-frequency proton decoupling was used to assign C-6, C-8, C-9, C-10, C-13, C-14, C-15, C-3′, and the C-2′ methyl group. The ^1H NMR frequencies corresponding to the hydrogens attached to each of these carbons were obtained from assignments recorded by Yoshitake and Geissman.[8] The only uncertainty resides with the assignments for C-1 and C-7, since these notations are based on single-frequency proton-decoupling experiments carried out with fastigilin C (see below) and may be reversed for radiatin.

With the ^{13}C NMR resonance assignments for radiatin in hand, interpretation of the corresponding spectra of fastigilin A (**1c**) and fastigilin B (**1b**) was readily achieved and this allowed the first complete structural proposal for fastigilin A[4] and removed any uncertainties in the fastigilin B stereochemistry.[2] With fastigilin A the only resonances which differed appreciably from those of radiatin were those at C-6 bearing the ester linkage and the ester side chain. The side-chain resonances were characteristic of a substituted acrylic acid ester bearing methyl groups on both the α and β carbons, rather than the methacrylic ester system of radiatin. Since the C-2′ and C-3′ methyl resonances were further downfield than expected for a tiglate ester[9] the angelate ester was confirmed. In view of the relatively high degree of steric crowding in fastigilin A, changes in relative configuration at any of the eight chiral centers would be expected to result in large chemical-shift changes. Therefore, radiatin and fastigilin A differ only in the ester side chain and bear the same relative configuration at each asymmetric carbon. Accordingly, the skeletal system and relative positioning of substituents proposed by Herz[4] for fastigilin A were quite correct.

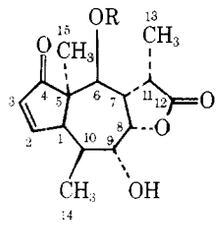
Analogous off-resonance decoupling experiments and model compound shifts were employed in the assignment of structure **1b** to fastigilin B. The chemical shifts for fastigilin B were found nearly identical with those of radiatin and fastigilin A with the exception of those for C-6 and the ester side chain. The latter shifts were characteristic of a senecioate ester[9] and this confirms the structural features proposed by Herz and co-workers.[4] In addition, we were able to complete the configurational notation as shown for the C-11 methyl group.

In conjunction with determining the structures of multigilin and multistatin, it became necessary to study fastigilin C and multiradiatin. Application of the ^{13}C NMR techniques applied to pseudoguaianolides **1a–c** led to the carbon shift assignments in Table I for fastigilin C. The spectrum of α,β-unsaturated lactone **2a** when compared with that of saturated lactone **1a** shows the expected upfield shift of C-12 and the downfield shifts of C-11 and C-13. The chemical shifts for C-1, C-7, C-8, C-9, C-14, and C-15 were assigned on the basis of proton single-frequency decoupling experiments using the proton values reported by Herz.[4] The resonance for C-6 was found shifted downfield to approximately 77 ppm and under conditions of broadband decoupling this resonance was obscured by deuteriochloroform. The ^{13}C NMR resonance assignments for fastigilin C coupled with the fact that lactones **2a** and **1b** have been hydrogenated to a common intermediate[4] leave no doubt that fastigilin C (**2a**) has the structure originally proposed by Herz and co-workers.[4,10]

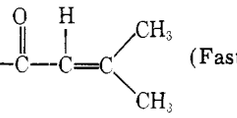
We have interrelated fastigilin C and multiradiatin by a chromium trioxide oxidation step[2] (**2a** → **2c**) and the ^{13}C NMR spectrum of multiradiatin was easily interpreted. The resonances at C-6, C-8, C-10, C-14, and C-15 were verified using proton single-frequency decoupling techniques. The proton values were consistent with those made by Herz and co-workers[10] for the oxidation product of linearifolin A, a

closely related terpene. The major changes observed in the spectrum after oxidation of alcohol **2a** to multiradiatin were the downfield shift of C-9 and C-10 and the upfield shift of C-8. All were consistent with oxidation of C-9 to a carbonyl group. Evidently the carbonyl group of multiradiatin results in a significant conformational change as compared to fastigilin C. This was indicated by shift changes observed for C-2, C-3, C-6, C-8, C-11, and C-13, and to a lesser extent with other resonances relatively remote from the carbonyl group. On the assumption that oxidation of fastigilin C with Jones reagent does not change any configuration except that of C-9, multiradiatin must have the same relative configuration as fastigilin C and structure **2c** was substantiated.

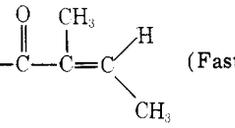
A comparison of the ^{13}C NMR spectrum of multistatin (**2d**) with that of multiradiatin (**2c**) shows clearly that the only resonance positions that differ significantly are those for C-6 and the ester side chain. The ester side chain of multistatin corresponded to an angelate and this completed structure **2b** for multistatin. Since multistatin was obtained from multigilin by oxidation, structure **2b** was proposed for multigilin. This structure was confirmed by the ^{13}C NMR spectrum, which differed significantly from that of alcohol **2a** only in the resonances of C-6 and the angelate side chain.



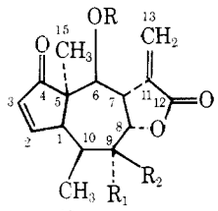
1a, R = —C(=O)—C(CH$_3$)=CH$_2$ (Radiatin)



b, R = —C(=O)—CH(CH$_3$)—C(CH$_3$)=CH$_2$ (Fastigilin B)

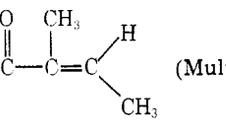


c, R = —C(=O)—CH(CH$_3$)—C(H)=CH$_2$ (Fastigilin A)



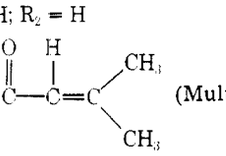
2a, R = —C(=O)—CH(CH$_3$)—C(CH$_3$)=CH$_2$ (Fastigilin C)

R_1 = OH; R_2 = H



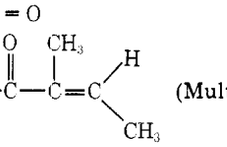
b, R = —C(=O)—CH(CH$_3$)—C(H)=CH$_2$ (Multigilin)

R_1 = OH; R_2 = H



c, R = —C(=O)—CH(CH$_3$)—C(CH$_3$)=CH$_2$ (Multiradiatin)

R_1 = R_2 = O



d, R = —C(=O)—CH(CH$_3$)—C(H)=CH$_2$ (Multistatin)

R_1 = R_2 = O

Preliminary biological evaluation of fastigilin A (P388 ED_{50} 2.1 and KB ED_{50} 3.9), multigilin (P388 T/C 164 at 12.5 mg/kg), and multistatin (P388 ED_{50} = 0.37 and T/C 131 at 32 mg/kg) in the National Cancer Institute's lymphocytic leukemia P388 cell line and in vivo screen indicates that all three of the pseudoguaianolides are capable of inhibiting neoplastic cell growth. Apparently, *Baileya multiradiata* has a very versatile mechanism for synthesizing cytotoxic and antineoplastic agents of the pseudoguaianolide type. The present study also indicates that minor changes in the plant's environment or growth period can markedly affect biosynthesis of the ester side chains. Alternatively the latter observation might reflect a hitherto unknown species variation of *Baileya multiradiata* and be of further interest from a taxonomic standpoint.

Experimental Section

All solvents were redistilled. Column chromatography unless otherwise noted was performed with silica gel (70–230 mesh and 30–70 mesh) or with prepacked silica gel 60 columns sizes B and C, both from E. Merck, Darmstadt. The material to be chromatographed was first adsorbed[11] on silica gel and when the prepacked column technique was employed the preadsorbed material was placed in a precolumn.[12] Thin-layer chromatography was performed with silica gel GF Uniplates supplied by Analtech Inc. and with precoated TLC plates (5 × 20 cm) of silica gel F254 supplied by E. Merck. The very careful fractionation performed with the precolumn/prepacked silica gel columns was partially automated using a Gilson microfractionator. Visualization of the plates was conducted as previously described.[2]

The mutual identity of authentic and isolated specimens was confirmed by thin-layer chromatographic and infrared spectral (KBr) comparisons. All melting points are uncorrected and were observed utilizing a Koefler-type melting point apparatus. The circular dichroism data (methanol solution) was obtained by Mr. J. Holler using a JASCO ORD/UV-5 instrument. The infrared (KBr) and ^1H NMR spectra (deuteriochloroform solution, tetramethylsilane internal standard) were nicely provided by Dr. J. Witschel, Jr., using a Beckman Model 12 infrared equipment and the Varian A-60 or XL-100 NMR instruments. The ^{13}C NMR spectra were measured at 22.6 MHz using a Bruker WH-90 NMR spectrometer and are reported in parts per million downfield from tetramethylsilane. Tetramethylsilane was used as an internal standard in 10-mm sample tubes containing approximately 0.08 M solutions of sesquiterpene in deuteriochloroform. Mass spectra were obtained by Messrs. E. Kelley and R. Scott employing the Atlas CH-4B and SM-1B (equipped for field ionization or electron impact) instruments. Elemental analyses were determined at the Spang Microanalytical Laboratory, Ann Arbor, Mich.

Collection and Extraction of *Baileya multiradiata*. In April 1975, a large scale re-collection of *Baileya multiradiata* Harv. and Gray aerial portion was made (G.R.P. assisted by Dr. Richard H. Ode, Messrs. Lawrence D. Vanell, Gregory C. Bryan, Russell Myers, and Miss Robin K. Pettit) near Wickenberg on the Yavapai/Maricopa County border, Arizona. The plant was in the flowering stage and upon air drying a 48.6-kg amount was extracted with chloroform as previously described.[2] The 800 g of crude green gummy extract was dissolved in ethanol (7.5 L) and hot water (22.5 L) was added. The solution was filtered through Celite and extracted with chloroform. Removal of solvent from the chloroform extract led to 212 g of amber-colored oil. Two 106-g portions of this oily fraction were each chromatographed on 2.85 kg of silica gel. The column was packed dry and the fractions eluted by 9:1 benzene–ethyl acetate led to 27-g amounts each of mixtures containing fastigilin A (**1c**), multistatin (**2d**), and multigilin (**2b**).[15]

Multigilin (2b). A 7.0-g aliquot of the benzene–ethyl acetate fractions noted in the preceding experiment was chromatographed on a column of silica gel (200 g). Careful elution with 9:1 benzene–ethyl acetate led to a fraction (1.65 g) containing primarily multigilin. Final purification was achieved employing chromatography on a size C prepacked silica-gel column with the enriched fraction preadsorbed on 4 g of silica gel. Elution (6-mL fractions) with 95:5 benzene–ethyl

acetate allowed multigilin to be concentrated in fractions 330–355. Removal of solvent gave 0.53 g of oily solid which crystallized from ethyl acetate–hexane as oily crystals (0.15 g): NMR ($CDCl_3$) δ 1.01 (3 H, s), 1.43 (3 H, d, J = 7 Hz), 1.78 (3 H, m, J = 2 Hz), 1.96 (3 H, dq, J = 7, 2 Hz), 2.2 (2 H, m), 3.10 (1 H, m), 3.68 (2 H, m), 5.07 (1 H, dd, J = 7, 3 Hz), 5.38 (1 H, s), 6.15 (2 H, dd, J = 6, 4 Hz), 6.38 (1 H, d, J = 2 Hz), 6.57 (1 H, d, J = 2 Hz), 7.80 (1 H, dd, J = 6, 3 Hz); MS m/e 360 (M^+), 342 (M − 18), 277 (M − 83), 261 (M − 99), 260 (M − 100), and 83 base peak.

Multistatin (2d). Method A. From *Baileya multiradiata*. Column chromatography on silica gel (200 g) of a fraction (7 g) containing multigilin provided a multigilin-rich fraction (4 g) which eluted with 9:1 benzene–ethyl acetate. Attempted crystallization of this fraction from acetone–hexane afforded approximately 10 mg of multistatin. Characterization was completed as summarized in Method B.

Method B. By Oxidation of Multigilin (2b). To a cold (ice-bath) solution of multigilin (**2b**, 0.467 g) in dry acetone (20 mL redistilled from potassium permanganate) was added (dropwise) excess 8 N Jones reagent.[13] Approximately 5 min later isopropyl alcohol (10 mL) was added followed by dilution with water (100 mL). The mixture was extracted with methylene chloride (3 × 10 mL) and the combined extracts were washed successively with 5% potassium carbonate (10 mL), saturated sodium chloride solution (10 mL), and water. Removal of solvent gave a pale yellow solid residue (0.39 g). Examination by thin-layer chromatography with benzene–ethyl acetate (3:1) as mobile phase indicated the presence of ketone **2d** (R_f 0.33) as the major product accompanied by some unreacted multigilin (R_f 0.18). The total product was chromatographed on a column of CC-4 SilicAR silica gel (20 g, supplied by Mallinckrodt). Elution with methylene chloride–ethyl acetate (9:1) provided in the first 65 mL a minor quantity of oily products and in the next 70 mL a 0.16-g (34%) yield of multistatin. The next 300 mL of solvent eluted 0.15 g of unreacted multigilin. The multistatin was pure as evidenced by thin-layer chromatography and recrystallized from heptane–acetone as colorless crystals melting at 257–260 °C: NMR ($CDCl_3$) δ 0.89 (s, 3, C_5-CH_3), 1.50 (d, J = 7 Hz, 3, C_{10}-CH_3), 1.77 (d, J = 2 Hz, 3, 2′-angelate Me), 1.94 (d of d, J = 2 and 6 Hz, 3, 4′-CH_3), 2.72 (m, J = 7 and 14 Hz, 1, C_{10}-H), 3.40 (m, 1, C_1-H), 3.72 (m, 1, C_7-H), 5.60 (d, J = 8 Hz, 1, C_{10}-H), 5.73 (s, 1, C_6-H), 5.93 (d, J = 3 Hz, 1, *exo*-C_{13}-H), 6.16 (d of d, J = 2 and 7 Hz, 1, 3′-H), 6.32 (d of d, J = 2 and 6 Hz, 1, C_3-H), 6.42 (d, J = 3 Hz, 1, *exo*-C_{13}-H), 7.70 (d of d, J = 2 and 6 Hz, 1, C_2-H); IR (KBr) 1773 (C=O), 1720–1705 (br band, C=O) cm^{-1}; MS m/e 358 (M^+), 340 (M − 18), 330 (M − 28), 275 (M − 83), 259 (M − 99), 258 (M − 100), 83 (M − 275) base peak. The isolated multistatin and the multigilin oxidation product were identical by IR, MS, TLC, and NMR.

Anal. Calcd for $C_{20}H_{22}O_6$: C, 67.02; H, 6.18; O, 26.78. Found: C, 67.03; H, 6.21; O, 26.88.

Fastigilin A (1c). Method A. From *Baileya multiradiata*. The careful chromatographic separation of multigilin described above gave fractions containing fastigilin A and this substance was isolated in pure form by rechromatography on a size C prepacked silica gel column (2.03 g). Elution with 9:1 to 4:1 hexane–acetone afforded 0.35 g of fastigilin A, identical by NMR, TLC, and MS comparisons with fastigilin A described in method B.

Method B. From *Baileya pleniradiata*. Chromatographic fractions from *Baileya pleniradiata* kindly provided by Professor Geissman[3] were found to contain as principal components radiatin (**1a**) and fastigilin A (**1c**). A mixture (0.68 g) of this approximate composition was carefully chromatographed employing a size B prepacked silica gel column. Fractions (6 mL each) 184–193 eluted by 9:1 to 4:1 heptane–acetone afforded 0.06 g of fastigilin A. Recrystallization from acetone–hexane yielded colorless needles: mp 179–183 °C; CD λ_{max} 326 nm ($[\theta]$ −4022); NMR ($CDCl_3$) δ 1.02 (3 H, s), 1.40 (3 H, d, J = 7 Hz), 1.57 (3 H, d, J = 6 Hz), 1.71 (3 H, m, J = 2 Hz), 1.90 (3 H, dq, J = 7, 2 Hz), 2.2 (2 H, m), 3.06 (3 H, m), 3.52 (1 H, m), 4.92 (1 H, dd, J = 6, 3 Hz), 5.46 (1 H, s), 6.09 (2 H, dd, J = 6, 4 Hz), and 7.72 (1 H, dd, J = 6, 3 Hz); IR (KBr) 3460, 1760, 1715–1730 cm^{-1}; MS m/e 362 (M^+), 344 (M − 18), 334 (M − 28), 279 (M − 83), 263 (M − 99) base peak, and 262 (M − 100).

The compound was identical with an authentic sample of fastigilin A[4] by infrared and NMR comparisons.

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References and Notes

(1) For part 54 see G. R. Pettit, C. L. Herald, R. H. Ode, and L. D. Vanell *Eur. J. Cancer*, submitted.
(2) G. R. Pettit, C. L. Herald, G. F. Judd, G. Bolliger, L. D. Vanell, E. Lehto, and C. P. Pase, *Lloydia*, in press; G. R. Pettit, C. L. Herald, G. F. Judd, G. Bolliger, and P. S. Thayer, *J. Pharm. Sci.*, **64**, 2023 (1975).
(3) T. G. Waddell and T. A. Geissman, *Phytochemistry*, **8**, 2371 (1969).
(4) W. Herz, S. Rajappa, S. K. Roy, J. J. Schmid, and R. N. Mirrington, *Tetrahedron*, **22**, 1907 (1966).
(5) G. R. Pettit, C. L. Herald, J. J. Einck, and R. B. Von Dreele, *J. Org. Chem.*, manuscript in preparation.
(6) J. B. Stothers, "Carbon-13 NMR Spectroscopy", Academic Press, New York, N.Y., 1972.
(7) G. C. Levy and G. L. Nelson, "Carbon-13 Nuclear Magnetic Resonance for Organic Chemists", Wiley-Interscience, New York, N.Y., 1972.
(8) A. Yoshitake and T. A. Geissman, *Phytochemistry*, **8**, 1753 (1969).
(9) H. Brouwer and J. B. Stothers, *Can. J. Chem.*, **50**, 601 (1972).
(10) W. Herz, K. Aota, and A. L. Hall, *J. Org. Chem.*, **35**, 4117 (1970).
(11) G. R. Pettit, C. L. Herald, and J. P. Yardley, *J. Org. Chem.*, **35**, 1389 (1970).
(12) D. L. Herald, R. H. Ode, and G. R. Pettit, *J. Chromatogr. Sci.*, **14**, 356 (1976).
(13) K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, 39 (1946); C. Djerassi, R. R. Engle, and A. Bowers, *J. Org. Chem.*, **21**, 1547 (1956).
(14) R. I. Geran, N. H. Greenberg, M. M. Macdonald, A. M. Schumacher, and B. J. Abbott, *Cancer Chemother. Rep., Part 3*, **3**, No. 2 (Sept 1972). Consult also G. R. Pettit and G. M. Cragg, "Biosynthetic Products for Cancer Chemotherapy", Vol. 2, Plenum Publishing Corp., New York, N.Y., in press.
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