

α,α -Bis(2-hydroxy-6-isopropyltropon-3-yl)toluenes (**13g-i**) were prepared in the same manner.

α,α -Bis(7-hydroxy-5-isopropyltropon-2-yl)-2-methoxytoluene (**13g**): mp 148–151 °C (from MeOH-CH₂Cl₂); yield 8%; NMR (CDCl₃) δ 3.76 (s, 3 H, OCH₃); MS, *m/e* 446 (M⁺). Anal. (C₂₈H₃₀O₅) C, H.

α,α -Bis(7-hydroxy-5-isopropyltropon-2-yl)-3-methoxytoluene (**13h**): mp 192–194 °C (from MeOH-CH₂Cl₂); yield 27%; NMR (CDCl₃) δ 3.76 (s, 3 H, OCH₃); MS, *m/e* 446 (M⁺). Anal. (C₂₈H₃₀O₅) C, H.

α,α -Bis(7-hydroxy-5-isopropyltropon-2-yl)-3,4-dimethoxytoluene (**13i**): mp 177–178 °C (from MeOH-CH₂Cl₂); yield 36%; NMR (CDCl₃) δ 3.80 (s, 3 H, OCH₃), 3.90 (s, 3 H, OCH₃); MS, *m/e* 476 (M⁺). Anal. (C₂₉H₃₂O₆) C, H.

α,α -Bis(7-hydroxy-4-isopropyltropon-2-yl)-4-methoxytoluene (**14**). A mixture of *p*-anisaldehyde diethyl acetal (3.5 g, 17 mmol) and 5-isopropyltropolone (γ -thujaplicin)⁴ (4.9 g, 30 mmol) was heated at 180 °C for 2 h under an argon atmosphere. The reaction mixture was column chromatographed on silica gel with petroleum ether-AcOEt (10:1) to give **14** (0.7 g, 13% based on γ -thujaplicin): mp 186–188 °C (from MeOH-CH₂Cl₂); NMR (CDCl₃) δ 1.25 (d, 12 H, CHMe₂ \times 2, *J* = 7 Hz), 2.58–3.18 (m, 2 H, CHMe₂ \times 2), 3.76 (s, 3 H, OCH₃), 6.65 (s, 1 H, CH), 6.68–7.58 (m, 10 H, tropolone H and aromatic H); MS, *m/e* 446 (M⁺). Anal. (C₂₈H₃₀O₅) C, H.

Culture of KB Cells and Determination of ED₅₀ of the Drugs. A clonal KB cell line, established by Dr. M. Green, St. Louis University, and kindly supplied by Dr. K. Fujinaga, Sapporo Medical College, was grown in Eagle's minimal essential medium containing 10% calf serum (Grand Island Biological).⁹ Cells were grown in plastic dishes (Lux Scientific) at 37 °C in 5% CO₂-95%

air. The cells grew exponentially for at least 72 h under these cell densities, and the doubling time of the KB cell populations was about 20 h.

The cytotoxic activity of the drugs on cultured KB cells was measured by determining the IC₅₀.⁹ KB cells were seeded in plastic dishes (diameter, 60 mm; Lux Scientific) at a density of 2100 cells/cm² growth surface. At 24 h after inoculation, the medium was changed and the cells were treated with graded concentration (0.3–100 μ g/mL) of the drugs. Two dishes were used for each drug concentration. The cells were cultivated for 48 h in the presence of drugs. The medium was removed and the cell layer was washed with phosphate buffered saline (PBS) and trypsinized with an aliquot of 0.25% trypsin-EDTA (Grand Island Biological). PBS containing 2% fetal calf serum was added to neutralize the trypsin. The cells were suspended by pipeting and enumerated with a Coulter counter. The IC₅₀ of each drug was obtained by plotting the logarithm of the drug concentration vs. the growth rate (percentage of control) of the treated cells.

Antitumor Assays in Vivo. Groups of six CDF₁ mice were inoculated ip with 10⁶ P388 leukemia cells. Drug treatment was (ip) initiated 24 h after inoculation of leukemia cells. Compounds tested were dissolved in dimethyl sulfoxide.

Acknowledgment. We express appreciation to the late Professor Ryuzo Hirohata and Kanto Ishi Seiyaku Co., Ltd., for supplying hinokitiol and γ -thujaplicin.

Registry No. **2**, 499-44-5; **10**, 92397-04-1; **11**, 92397-05-2; **13f**, 92397-06-3; **13g**, 92397-07-4; **13h**, 92397-08-5; **13i**, 92397-09-6; **14**, 92397-10-9; CH₃CH=CHCH(OEt)₂, 10602-34-3; PhCH=CHCH(OEt)₂, 7148-78-9; (EtO)₂CH-*o*-C₆H₄Me, 5469-00-1; (EtO)₂CH-*o*-C₆H₄OMe, 6314-98-3; (EtO)₂CH-*m*-C₆H₄OMe, 2403-47-6; 3,4-(MeO)₂C₆H₃CH(OEt)₂, 40527-43-3; (EtO)₂CH-*p*-C₆H₄OMe, 2403-58-9; γ -thujaplicin, 672-76-4.

(9) T. Tsuruo, H. Iida, S. Tsukagoshi, and Y. Sakurai, *Cancer Res.*, **39**, 1063 (1979).

Additions and Corrections

1983, Volume 26

Kam-Sing Cheung, Steven A. Wasserman, Edward Dudek, Stephen A. Lerner, and Michael Johnston*: Chloroalanyl and Propargylglycyl Dipeptides. Suicide Substrate Containing Antibacterials.

Page 1740. In the acknowledgment, Merrell Dow Pharmaceuticals should read Dow Chemical Co.

1984, Volume 27

J. B. Hynes,* Y. C. S. Yang, J. E. McGill, S. J. Harmon, and W. L. Washtien: Improved Synthesis and Antitumor Evaluation of 5,8-Dideazaisofolic Acid and Closely Related Analogues.

Page 233. In Table I, the following footnote should be added for IAHQ: "The sample of IAHQ tested was derived by the route described in ref 13; the 9-CHO-IAHQ and 9-CH₃-IAHQ tested were prepared from this sample of IAHQ."

Book Review: The Peptides: Analysis, Synthesis, Biology. Volume 5. Special Methods in Peptide Synthesis, Part B.

Page 553. The correct price for Volume 5 is \$79.50.

Herbert T. Nagasawa,* David J. W. Goon, William P. Muldoon, and Richard T. Zera: 2-Substituted Thiazolidine-4(*R*)-carboxylic Acids as Prodrugs of L-Cysteine.

Protection of Mice against Acetaminophen Hepatotoxicity.

Page 592. In Table I, the data for compound **10** should read as follows (column heading/correction): survival/17/18, 4+/1, 3+/1, 1+/3, 0/13.

R. M. DeMarinis,* A. J. Krog, D. H. Shah, J. Lafferty, K. G. Holden, J. P. Hieble, W. D. Matthews, J. W. Regan, R. J. Lefkowitz, and M. G. Caron: Development of an Affinity Ligand for Purification of α_2 -Adrenoceptors from Human Platelet Membranes.

Page 918. The correct author list should read: R. M. DeMarinis,* H. Oh, A. J. Krog, D. H. Shah, J. Lafferty, K. G. Holden, J. P. Hieble, W. D. Matthews, J. W. Regan, R. J. Lefkowitz, and M. G. Caron. In the paper as published H. Oh had been inadvertently omitted.

Charles D. Jones,* Mary G. Jevnikar, Andrew J. Pike, Mary K. Peters, Larry J. Black, Allen R. Thompson, Julie F. Falcone, and James A. Clemens: Anti-estrogens. 2. Structure-Activity Studies in a Series of 3-Aroyl-2-arylbenzo[*b*]thiophene Derivatives Leading to [6-Hydroxy-2-(4-hydroxyphenyl)benzo[*b*]thien-3-yl][4-[2-(1-piperidinyl)ethoxy]phenyl]methanone Hydrochloride (LY156758), a Remarkably Effective Estrogen Antagonist with Only Minimal Intrinsic Estrogenicity.

Page 1061. In Table III, footnote *c* should read "Every rat received 0.1 μ g of estradiol/day sc in corn oil".