natural pesticides. Plants from tropical regions of the world offer particularly intriguing possibilities in this regard since they are subjected to severe disease and insect pressures. This is especially true for mangrove plants because of their proximity to water. Heritol (1) is interesting since it possesses toxic properties and is a novel structure of the cadinane sesquiterpene class with an unusual oxygenation pattern and aromatic ring. The toxicity of heritol (1) to fish and related organisms is currently under examination for the purpose of evaluating the potential for agrochemical utilization.

Experimental Section

Isolation of Heritol (1). The dried, chopped roots of *H. littoralis* (21 kg) were extracted for 16 h in a Soxhlet extractor with *n*-hexane. The plant material was then extracted with 95% ethanol for 16 h. Evaporation of the ethanol in vacuo yielded 254 g of crude extract, which was then partitioned between chloroform and water (1:1). The chloroform solution was evaporated in vacuo to give 38.4 g of crude material. Methylene chloride was added to this material. The soluble portion (23.9 g after evaporation of the methylene chloride in vacuo) showed toxicity to fish (100% mortality in 5 h at 100 ppm) during the "quick screening test"[3] while the insoluble portion showed no activity. The methylene chloride soluble portion was chromatographed on an open column with silica gel as an absorbent. The column was eluted with hexane–benzene–chloroform–methanol solvent systems. The 20% benzene–chloroform fractions were combined. This concentrated fraction was dissolved in a minimum amount of hot methanol and heritol (1) crystallized after 24 h at room temperature in the form of white needles: mp 271–272 °C dec; $[\alpha]^{25}{}_{\mathrm{D}}$ +261.3; IR (KBr) 3350, 3000, 1750, 1660, 1620, 1370, 1070, 890 cm^{-1}; UV (cyclohexane) $\lambda_{\max}$ 217 nm (ϵ 12600), 228 (ϵ 11950), 285 (ϵ 14215), 305 (ϵ 8076). Anal. Calcd for $C_{15}H_{16}O_3$: C, 73.77; H, 6.65; mol wt, 244.1100. Found: C, 74.14; H, 6.81; mol wt (mass spectroscopy), 244.1110.

Other significant peaks: high-resolution mass spectrum, m/e (composition, %) 229 (36), 215 (19), 201 (23), 185 (20), 173 (24), 161 (17), 128 (15), 115 (13), 77 (10), 51 (7); ^{1}H NMR ($CDCl_3$) δ 1.42 (d, 3 H, J = 10 Hz), 2.18 (s, 3 H), 2.30 (s, 3 H), 2.62 (m, 1 H), 3.10 (m, 1 H), 4.90 (dd, J = 10 and 3 Hz), 5.22 (s, 1 H), 6.85 (s, 1 H), 7.42 (s, H).

Crystals of heritol (1) were grown by slow evaporation of methanol. Preliminary X-ray photographs revealed the orthorhombic symmetry with unit cell parameters a = 8.028 (3) Å, b = 10.286 (6) Å, c = 15.46 (9) Å, and β = 90.0°. The space group was $P2_12_12_1$ with ρ_{calcd} = 1.29 g cm^{-3} for Z = 4. Intensities were collected in the usual manner[8] with standard fluctuations of ±2%. One independent octant of data was measured to $2\theta_{\max}$ = 44°, with 845 of 966 reflections considered observed ($I > 3\sigma(I)$) with no absorption correction (μ = 0.83 cm^{-1}). The structure was solved by MULTAN[9] and refined for carbon and oxygen atoms with anisotropic and thermal parameters to give R = 0.053 and R_w = 0.052. Figure 1 shows the molecular structure and numbering scheme.

Acknowledgment. This study was supported by the Divison for International Programs, National Science Foundation (INT Grant 8202732). We are indebted to Drs. Catherine Costello and Thomas Dorsey of the MIT Mass Spectrometry Facility for their invaluable assistance in obtaining the mass spectrum of heritol. We thank Dr. Jim Dechter and Vicki Farr of the University of Alabama NMR facility for their help in obtaining ^{1}H NMR data.

Supplementary Material Available: Listings of distances and angles, atomic positional parameters with their anisotropic thermal factors, isotropic thermal factors, and crystal data for the natural product (9 pages); observed and calculated structure factors (5 pages). Ordering information is given on any current masthead page.

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A Convenient Synthesis of Haloethyl Alkyl Sulfides

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Received March 16, 1987

The synthesis of 2-bromoethyl benzyl sulfide (**1a**) was required for the preparation of a series of compounds to be evaluated as radioprotective agents. The preparations of 2-haloethyl alkyl sulfides were reported by the routes shown in Scheme I.

Scheme I

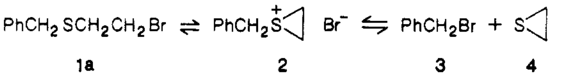
$$PhCH_2SCH_2CH_2OH + HCl \rightarrow \underset{\mathbf{1b}}{PhCH_2SCH_2CH_2Cl} \qquad \text{(ref 1)}$$

$$(EtO_2)PSCH_2Ph + Cl_2 + CH_2{=}CH_2 \rightarrow \mathbf{1b} \qquad \text{(ref 2)}$$

$$PhCH_2SSCH_2Ph + Cl_2 + CH_2{=}CH_2 \rightarrow \mathbf{1b} \qquad \text{(ref 3)}$$

$$PhCH_2SH + Br_2 + CH_2{=}CH_2 \rightarrow \mathbf{1a} \qquad \text{(ref 4)}$$

We chose the last route in Scheme I[4] for the preparation of **1a**; however, from each reaction the product seemed to be contaminated with about 7% of benzyl bromide (CH_2, 4.45 ppm) as determined by proton NMR analysis of the product mixture. The formation of this impurity was not expected, and the benzyl bromide proved to be difficult to remove by distillation. One rationalization for the formation of benzyl bromide was the equilibrium formation of the cyclic sulfonium salt **2** as shown in eq 1. The first step of this equilibrium has been proposed by Bartlett and Swain[5] for the mechanism of the S_N1 hydrolysis of β-halo sulfides such as mustard, and thus the cyclization and salt formation are not unexpected. Ogston,[6] whose studies were the basis of most of the mechanisms of reaction of mustard derivatives, conducted the displacement reaction in an aqueous solution. Thus the sulfonium salt would be expected to give primarily hydrolysis in excess water while in our reaction, the decomposition to benzyl bromide (**3**) and ethylene sulfide (**4**) was facilitated by the nonpolar solvent and the absence of any nucleophile except halide ion.



(1)

In order to test this hypothesis the synthesis of **1a** was attempted by starting with benzyl bromide (**3**) and excess ethylene sulfide. The reaction proceeded to give a quantitative yield of **1a**. A similar reaction with trityl chloride gave the novel, solid 2-chloroethyl trityl sulfide (**1c**) in 81% yield. The reaction failed with benzyl chloride. This indicates a failure of the halide to form a salt on reaction with ethylene sulfide, which is obviously a requirement for the synthesis.

$$\underset{\mathbf{1c}}{Ph_3CSCH_2CH_2Cl}$$

The success of this synthesis to give pure samples of **1a** and **1c** is interesting in view of the problem of obtaining **1a** free of benzyl bromide when it was prepared by the ref

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4 reaction in Scheme I. Excess ethylene sulfide was used in our reaction to shift the equilibrium to **1a**; however, distillation of the product (**1a**) did not give **3** as an impurity as was observed with the ref 4 reaction in Scheme I. This may result from an impurity such as bromine or a bromo compound in the product from the ref 4 reaction in Scheme I acting as a catalyst for the reaction of **1a**.

These results clearly demonstrate the validity of the potential equilibrium given in eq 1.

Experimental Section

All reagents were used as obtained from Aldrich without further purification. ^{1}H and ^{13}C nuclear magnetic resonance (NMR) data were obtained on a JEOL FX90Q Fourier transform nuclear magnetic resonance (FTNMR) spectrometer and were referenced vs. tetramethylsilane. Elemental analyses were performed by Midwest Microlabs, Indianapolis, IN.

Bromoethyl Benzyl Sulfide (1a). To 75 g of ethylene sulfide was added 171 g of benzyl bromide. The neat mixture was heated to 50 °C and monitored by ^{1}H NMR for the disappearance of the benzyl bromide methylene proton signal. This occurred after 24 h, at which time the solution was flushed with dry nitrogen gas to remove excess ethylene sulfide. The crude reaction mixture afforded a quantitative yield of the bromoethyl benzyl sulfide (**1a**), and the ^{1}H NMR spectrum was comparable to that from the product obtained by Schneider's procedure.[4] An aliquot of our product was distilled to give **1a**: bp 120–123 °C (0.55 torr), [lit.[4] bp 111 °C (0.2 torr)]; ^{1}H NMR ($CDCl_3$) δ 2.78 (t, 2, CH_2S), 3.31 (t, 2, $BrCH_2$), 3.68 (s, 2, SCH_2Ph), 7.25 (s, 5, Ph).

Chloroethyl Trityl Sulfide (1c). To a flask was added 5.58 g (0.02 mol) of trityl chloride and 2.4 g (0.04 mol) of ethylene sulfide in 25 mL of dichloromethane and stirred for 48 h at room temperature. The solvent was evaporated, and the residue was recrystallized once from benzene/petroleum ether (50:50) to afford **1c** in an 81% yield.

The ^{1}H NMR spectra of this solid and the analytical sample were identical: ^{1}H NMR ($CDCl_3$) δ 2.63 (t, 2, CH_2S), 3.08 (t, 2, $ClCH_2$), 7.15–7.52 (m, 15, Ph_3C). A sample was twice recrystallized as above to give **1c**, mp 119.5–121 °C.

Anal. Calcd for $C_{21}H_{19}ClS$: C, 74.43; H, 5.65; Cl, 10.46; S, 9.46. Found: C, 74.36; H, 5.85; Cl, 10.41; S, 9.71.

Acknowledgment. We thank the U.S. Army Medical Research and Development Command for financial support of this research by Contract DAMD17-82-C-2075.

Registry No. **1a**, 60671-59-2; **1c**, 108418-96-8; **3**, 100-39-0; **4**, 420-12-2; trityl chloride, 76-83-5.

A Convenient Synthesis of *lin*-Benzopurines through a Common Intermediate

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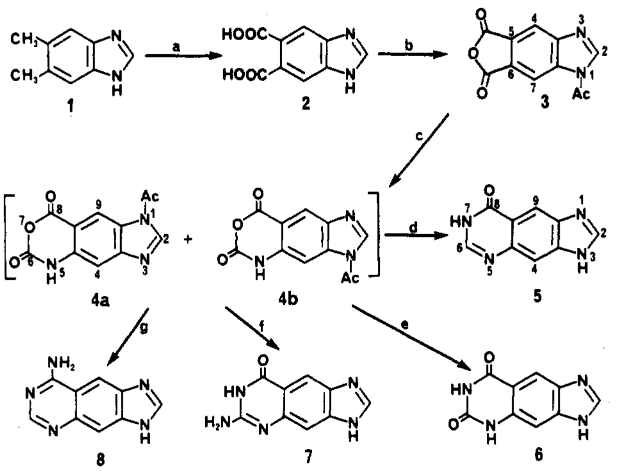
Received January 22, 1987

Continuing interest in *lin*-benzopurine derivatives as dimensional probes of binding and activity[1] has prompted us to seek improvement in the synthesis of the tricyclic heteroaromatic nuclei so as to make the entire series more readily available. For example, the initial synthesis of *lin*-benzoadenine required the separation of isomeric substituted quinazolones at an intermediate stage.[2] Now, by recourse to symmetrical substitution on benzimidazole, it is possible to avoid isomeric diversion away from precursors that lead to the linear tricyclic ring system. 5,6-Dimethylbenzimidazole (**1**), which is readily available, was oxidized by potassium permanganate to benzimidazole-5,6-dicarboxylic acid (**2**) in 48% yield. Conversion to 1-acetylbenzimidazole-5,6-dicarboxylic anhydride (**3**) in 93% yield was effected by heating **2** with acetic anhydride. The five-membered cyclic anhydride was enlarged to a six-membered oxazinedione ring by treatment with azidotrimethylsilane, Me_3SiN_3 (Scheme I).[3-5]

Scheme I[a]



[a] (a) $KMnO_4$, H_2O/*tert*-butyl alcohol; (b) $(CH_3CO)_2O$; (c) Me_3SiN_3; (d) $HC(=NH)NH_2 \cdot CH_3COOH$; (e) H_2NCONH_2; (f) NH_2CN, $(CH_3)_3COK$; (g) NH_3/DMF, $POCl_3$, NH_4OH.

The mixture of 1- and 3-acetylimidazo[4,5-*g*]-7,5-benzoxazine-6,8(5*H*)-dione (**4a**, **4b**) was then used directly in the crude form as the pivotal intermediate for the synthesis of *lin*-benzohypoxanthine (**5**),[2] *lin*-benzoxanthine (**6**),[6] *lin*-benzoguanine (**7**),[7,8] and *lin*-benzoadenine (**8**).[2] In short, the intermediate **4a,b** serves as the common branch point for all the stretched-out purines related to the naturally occurring purines. Some of our observations that led to the development of more efficient synthetic methodology for the tricyclic series are worthy of comment. It is important to use freshly distilled azidotrimethylsilane in anhydrous acetonitrile with the rigorous exclusion of moisture to effect an efficient conversion of anhydride **3** to the complex isatoic anhydride intermediate **4a,b**. Extension of the reaction time beyond that described in the Experimental Section led to increased formation of an unwanted side product.[9] Formamidine acetate[4,5] in DMF or Cellosolve was used to convert **4a,b** to *lin*-benzohypoxanthine, imidazo[4,5-*g*]quinazolin-8(7*H*)-one (**5**),[2] in 86% overall yield from **3**. Fusion with urea[5] produced *lin*-benzoxanthine, imidazo[4,5-*g*]quinazoline-6,8(5*H*,7*H*)-dione (**6**),[6] in an overall yield of 55% or greater. The NMR

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