lene,** mp 172–174° [*Anal.* ($C_{12}H_{11}NO$) C, H], in 85–90% yields by refluxing for 2.5 hr in 95% HCOOH (4 ml/g). A soln of 16 ml of Br_2 in 50 ml of $CHCl_3$ was added during 45 min to a stirred slurry of 0.6 g of Fe filings, 1.2 g of I_2, and 150 g of 1-formylamino-2-methylnaphthalene in 500 ml of $CHCl_3$. After adding 200 ml of H_2O and stirring well there was obtd 4-bromo-1-formylamino-2-methylnaphthalene,** mp 212–215°, in 76–84% yields. A pure sample,** mp 224–225° [*Anal.* ($C_{12}H_{10}BrNO$) C, H], was obtd by recrystn from Me_2CO. By hydrolysis with KOH in ethylene glycol at 100° for 2.5 hr fairly pure 1-amino-4-bromo-2-methylnaphthalene,[7] mp 78–80°, was obtd in over 90% yield. To a vigorously stirred slurry of 100 g of 1-amino-4-bromo-2-methylnaphthalene in 108 ml of concd HCl and 286 ml of H_2O cooled by a MeOH–ice bath, was added dropwise during 2 hr a soln of 15 g of $NaNO_2$ in 30 ml of H_2O.[5] After adding 60 ml of 48% HF the suspension was stirred for an addl 30 min. The solid was collected, washed with ice water, and air-dried, to yield 131.5 g (92%) of crude fluoroborate salt, mp 130.0–132.0°. The dry salt was then heated until gas evoln ceased and the residue was taken up in PhH. Evapn of the solvent followed by distn and recrystn from 2-PrOH gave 62.1 g (66%) of **6**,** mp 34.5–36.5°, bp 86–90° (0.07 mm). The analytical sample was recrystd from 2-PrOH to give colorless needles, mp 38.0–38.5° [*Anal.* ($C_{11}H_8BrF$) C, H].

2-(4-Fluoro-3-methyl-1-naphthoyl)-6-methylbenzoic Acid (8). The Grignard reagent prepd in 92% yield from 55.0 g of **6** using a small amt of $BrCH_2CH_2Br$[8] in 210 ml of dry Et_2O and 30 ml of PhH was added rapidly to a hot stirred soln of 40 g of 3-methylphthalic anhydride[5] in 300 ml of PhH and 60 ml of dry Et_2O. After overnight stirring at reflux, the reaction mixt was cooled and poured onto iced HCl. The entire acid portion (52 g), isolated in the usual way, was dissolved in 600 ml of MeOH satd with HCl and refluxed overnight. The resulting ester mixt (53 g), isolated in the usual way, was treated with 700 ml of concd H_2SO_4 held at room temp. After standing 2 hr, this soln was poured on ice and sepd into acid and neutral fractions in the usual way. The crude acid **8**, mp 193–203°, amounted to 33 g (44%). This material was pure enough for use in the next reaction. Pure **8**,** mp 210.0–212.0° [*Anal.* ($C_{20}H_{15}FO_3$) C, H], was obtd by crystn from CH_2Cl_2–Skellysolve B with little loss. The neutral fraction obtd as described above yielded 11.3 g (15%) of the Me ester of **7**.** Recrystn from MeOH gave with little loss the analytical sample, mp 169–170° [*Anal.* ($C_{21}H_{17}FO_3$) C, H].

The structure of **8** was established by decarboxylation[9] to be 4-fluoro-3-methyl-1-naphthoyl *m*-tolyl ketone (**8a**) which was identical with an authentic sample prepared by reaction of 4-fluoro-3-methyl-1-naphthylmagnesium bromide with *m*-tolunitrile. As the ketone is a liquid, the 2,4-dinitrophenylhydrazones (C, H, N), mp 228.0–230.0° dec** [*Anal.* ($C_{25}H_{19}FN_4O_4$) C, H, N] (alone and mixed), were prepd and compared. The ir spectra were identical.

7-Methyl-3-(4-fluoro-3-methyl-1-naphthyl)phthalide (9). Attempted Zn reductions of **8** under alk and acid conditions resulted in loss of F. Accordingly **8** was reduced to **9** in 86% yield (based on **8** consumed) essentially as described for the prepn of 3-phenylphthalide.[10] Recrystn from Skellysolve B gave the analytical sample of **9**,** mp 162.0–162.5° [*Anal.* ($C_{20}H_{15}FO_2$) C, H, F].

2-(4-Fluoro-3-methyl-1-naphthylmethyl)-6-methylbenzoic Acid (10). To a hot soln of 9.8 g of **9** in 10% KOH–ethylene glycol was added 30 g of Zn activated by a trace of $CuSO_4$. The suspension was refluxed overnight, cooled, and filtered. The filtrate was worked up in the usual way to yield 1.4 g of recovered lactone and 7.2 g (85%) of **10**, mp 171–174°. Recrystn from 60–110 petr ether–PhH gave the analytical sample of **10**,** mp 173.0–174.0° [*Anal.* ($C_{20}H_{17}FO_2$) C, H, F].

5-Fluoro-6,8-dimethylbenz[*a*]anthracene (4). Attempts to cyclize **10** and to reduce the resulting benzanthrone failed to yield **4**. The redn of **10** with LAH in Et_2O and in THF gave mixts of aldehyde **12** and alcohol **11** in about 70% yield. When these mixts were oxidized wtih CrO_3 in pyridine at room temp for 2 hr, crude oily **12** was obtained. This material was then heated with PPA on a steam bath for 15 min. The product isolated in the usual way was treated with picric acid in EtOH. Recrystn from EtOH afforded dark red elongated prisms of the picrate** of **4**, mp 147.5–148.0° [*Anal.* ($C_{26}H_{18}FN_3O_7$) C, H, N]. By chromatog on alumina, followed by recrystn from PhH–EtOH, **4**** was obtd (in 62% overall yield from the crude mixt of **11** and **12**) as pale yellow prisms, mp 125–126° [*Anal.* ($C_{20}H_{15}F$) C, H, F].

**All compounds designated by a double asterisk had analyses by Galbraith Labs, Knoxville, Tenn., within ±0.02% of theory for the elements listed in parentheses.

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New Compounds

2-Pyrazinecarboxanilides

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A number of pyrazinamides have been prepared and evaluated for their tuberculostatic[1,2] and local anesthetic activity.[3] Pyrazinecarboxanilides, however, have not been reported, and it was desired to obtain the anilide, 2-toluidide, 2,6-xylidide, and 2,4,6-mesidide both as intermediates for the preparation of the corresponding piperazinecarboxanilides[4] and for evaluation as local anesthetics. The pyrazinecarboxanilides were obtained and subjected to primary screening for biological activity.[5] Neither local anesthetic nor any significant biological effect was found with these compounds.

Experimental Section

Two methods were utilized in their synthesis. Method I, a modification of that of Solomons and Spoerri,[3] involved the prepn of 2-pyrazinoyl chloride using $SOCl_2$ in the absence of the arom amine. In method II, a modification of that of Lemaire *et al.*,[6] the acid chloride was prepd in the presence of the amine using PCl_3. Equiv yields were obtd from the 2 procedures, but method II was less time consuming.

All melting points were detd with a Mel-Temp apparatus and are uncor. Ir spectra were obtd with a Perkin-Elmer 137B spectrometer. Microanalyses were done by Schwarzkopf Microanalytical Laboratory, Woodside, N. Y. Where analyses are indicated by symbols of the elements, analytical results were within ±0.4% of theoretical values.

Method I. $SOCl_2$ (100 ml, 166 g, 1.40 moles) was added to 24.8 g (0.20 mole) of 2-pyrazinecarboxylic acid (Aldrich Organic Chemicals) suspended in 150 ml of dry C_6H_6, and the reaction mixt was refluxed 90 min. The solvent and excess $SOCl_2$ were removed *in vacuo* yielding a dark red residue which decompd readily on standing. To the freshly prepared 2-pyrazinoyl chloride was added 0.48 mole of the appropriate arom amine dissolved in 300 ml of dry C_6H_6. After being refluxed for 5 hr, the hot reaction mixt was filtered, and the filtrate was concd to 200 ml. Addn of 400 ml of petr ether and cooling gave solid 2-pyrazinecarboxanilide. Recrystn was achieved in aqueous MeOH (3:1) (charcoal) and repeated.

Method II. A mixt of 49.6 g (0.40 mole) of 2-pyrazinecarboxylic acid, 20 ml (30.4 g, 0.24 mole) of PCl_3, and 0.84 mole of the arom amine in 1000 ml of dry C_6H_6 was refluxed 5 hr. The hot reaction mixt was filtered, and the filtrate was evapd to dryness. The crude 2-pyrazinecarboxanilide was recrystd as above. All the anilides were soluble in 6 *M* HCl but insoluble in 3 *M* HCl, and they were greater than 2% soluble in propylene glycol at room temp.

2-Pyrazinecarboxanilide. A yield of 57.2 g (72%) of beige crystals was obtained: mp 123–125°; ν_{max}^{KBr} 3400, 1675, 1600, 1535, 1470, 755 cm^{-1}. *Anal.* ($C_{11}H_9N_3O$) C, H, N.

2-Pyrazinecarbox-2′-toluidide. A yield of 74.0 g (87%) of beige crystals was obtained: mp 113–114°; ν_{max}^{KBr} 3400, 1680, 1580, 1535, 1460, 750 cm^{-1}. *Anal.* ($C_{12}H_{11}N_3O$) C, H, N.

2-Pyrazinecarbox-2′,6′-ylidide. A yield of 69.6 g (77%) of beige crystals was obtained: mp 110–112°; ν_{max}^{KBr} 3400, 1680, 1525, 1470, 1400, 765 cm^{-1}. *Anal.* ($C_{13}H_{13}N_3O$) C, H, N.

2-Pyrazinecarbox-2′,4′,6′-mesidide. A yield of 79.0 g (82%) of beige crystals was obtained: mp 124–125°; ν_{max}^{KBr} 3400, 1680, 1525, 1400, 840 cm^{-1}. *Anal.* ($C_{14}H_{15}N_3O$) C, H, N.

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2,5-Anhydro-1-deoxy-1-[(6-methylthio)purin-9-yl]-D-allitol†

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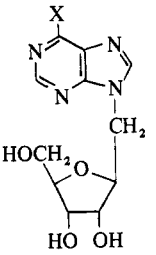
The reasons for our interest in the purin-9-yl-D-allitols and the preparation of 2,5-anhydro-1-(6-chloropurin-9-yl)-1-deoxy-3,4-*O*-isopropylidene-D-allitol (**1**) have been outlined.[1] Compound **1**, prepared by the method described in the Experimental Section, was converted to 2,5-anhydro-1-deoxy-1-(6-mercaptopurin-9-yl)-D-allitol (**2**), which was methylated to give 2,5-anhydro-1-deoxy-1-[(6-methylthio)-purin-9-yl]-D-allitol (**3**), a homolog of the potent anticancer agent 6-(methylthio)purine ribonucleoside.[2]

These purin-9-yl allitols (**2** and **3**) and 1-adenin-9-yl-2,5-anhydro-1-deoxy-D-allitol were evaluated for their toxicity



2, X = SH
3, X = SCH_3

to human epidermoid carcinoma cells No. 2 in culture,[3] but they did not significantly inhibit the growth of these cells at 100 μg/ml, the highest level tested.

Experimental Section‡

2,5-Anhydro-1-deoxy-1-(6-mercaptopurin-9-yl)-D-allitol (2). Anhydro-1-deoxy-1-(5-amino-6-chloropyrimidin-4-yl)amino-3,4-*O*-2,5-isopropylidene-D-allitol (1 g, 3 mmoles) in ethyl orthoformate (8 ml) contg 0.35 ml of concd HCl was allowed to stand overnight (tlc, 9:1 $CHCl_3$–MeOH) before the addn of thiourea (304 mg, 4 mmoles) in alcohol (12 ml). This soln was then heated at 70–80° for 2 hr, cooled, and filtered. A soln of the ppt in 0.1 *N* NaOH was filtered and acidified with glacial HOAc. The ppt [tlc, 9:1 $CHCl_3$–MeOH, mp 260–264°] was collected by filtration and suspended in 65% EtOH contg 6.7 ml of 0.6 *N* HCl, and the suspension was heated at 100° for 30 min. The soln was filtered before neutralization with 1 *N* NaOH and concd *in vacuo*. The solids obtained were recrystd from H_2O: yield 290 mg; tlc, 9:1 $CHCl_3$–MeOH; mp 248–250°; $[\alpha]^{24}D$ −38.5° ±1.6° (*c* 0.92, 0.1 *N* NaOH); λ_{max} in nm (pH 1) 226 (8.85), 324 (22.4); (pH 7) 227 (9.76), 320 (25.2); (pH 13) 233 (113.9), 310 (23.2). *Anal.* ($C_{11}H_{14}N_4O_4S$) C, H, N.

2,5-Anhydro-1-deoxy-1-[(6-methylthio)purin-9-yl]-D-allitol (3). To a soln of 2,5-anhydro-1-deoxy-1-(6-mercaptopurin-9-yl)-D-allitol (175 mg, 0.58 mmole) in H_2O contg 1 equiv of NaOH was added dropwise MeI (0.29 ml) with vigorous stirring, and the mixt was stirred for 3 hr before it was evapd to dryness. The residue, dissolved in EtOH (20 ml), was treated with Amberlite MB1 resin suspended in H_2O (20 ml). The resin was removed by filtration and the filtrate evapd to dryness. The residue was recrystd twice from EtOH: yield 100 mg (92%); tlc, 1:1 $CHCl_3$–EtOAc, 9:1 PhH–MeOH; 1:1 PhH–Et_2O; mp 115°, $[\alpha]^{25.5}D$ −41.3° ± 0.6° (*c* 1.06, EtOH); λ_{max} in nm (pH 1) 287 (sh), 294 (17.7); (pH 7, 13) 286 (19.7), 292 (19.5). *Anal.* ($C_{12}H_{16}N_4O_4S \cdot 0.5EtOH$) C, H, N. The presence of EtOH in the sample was confirmed by mass spectrometry, *m/e* 312 (calcd 312).

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‡Silica gel H (Brinkmann) was used for thin-layer analyses (tlc). Chromatographic homogeneity was established for all reported compds in the solvents indicated. The uv spectra were detd with a Cary Model 14 spectrophotometer, the mass spectrum with a Hitachi Perkin-Elmer RMU-7, and the optical rotations with a Rudolph Model 80 polarimeter. Melting points were detd with a Mel-Temp apparatus.