Reduction of the α-bromoketones with an ethereal slurry of lithium aluminum hydride yielded the corresponding bromoalcohols as the main product. Although no products from side reactions were isolated, the aqueous layer, from hydrolysis of the reaction mixture, showed the presence of bromide ion indicating some replacement of the bromine did occur.

The epoxides were obtained in good yields by treating the bromoalcohols with hot 50 percent aqueous sodium hydroxide. The substituted 1-heptafluoropropyl-1,2-epoxides were converted to the *vicinal* diols as was evidenced by a positive periodic acid test. It was thus assumed that the substituted trifluoromethyl epoxides were also 1,2-epoxides.

The physical properties, analysis, and yields of the new compounds prepared are reported in Table I.

The infrared spectra of the epoxides were compared with that of the corresponding bromoalcohols and bromoketones. In the trifluoromethyl epoxide series new bands appeared at 7.95 mμ, 11.2–11.4 mμ, and 12.6 mμ. The latter band was displaced to 12.1–12.25 mμ in the heptafluoropropyl epoxide series but no new band appeared in the 11.2 region. A new band was present as a shoulder in C_3F_7-$\overset{\frown}{CHCO}(CH_3)_2$, the carbon-fluorine absorption masked out this region in the other two epoxides. Spectra were determined in the liquid state.

EXPERIMENTAL

Alkyl perfluoroalkyl ketones. A. From perfluorocarboxylic acids. The ketones were prepared by the general procedure described by Dishart and Levine.[3] To three moles of alkyl Grignard reagent in one liter of ether cooled in an ice-bath was added dropwise with stirring one mole of perfluorocarboxylic acid in an equal volume of ether. After stirring overnight, the reaction mixture was hydrolyzed by pouring into ice-concentrated hydrochloric acid. The ether layer was separated and the water layer was extracted with three-100 ml. portions of ether. The combined ether layers were dried over Drierite and distilled to remove the ether; the residual liquid then was dried over phosphoric anhydride and fractionally distilled at atmospheric pressure through an efficient column.

B. Lithium salt of perfluorocarboxylic acid method. The lithium salt of perfluorobutyric acid was prepared by slowly adding one mole of the acid to one-half mole of lithium carbonate in 20 ml. of water. After evaporation of the water, the salt was dried thoroughly in a vacuum oven at 80–100°.

One mole of lithium perfluorobutyrate was dissolved in one liter of dry ether and cooled in an ice-bath. To this vigorously stirred solution was added dropwise 1.10 moles of previously prepared ethylmagnesium bromide in 400 ml. of ether over a period of two hours. The reaction mixture was stirred for an additional two hours at room temperature, then cooled in an ice-bath, and finally was hydrolyzed by the dropwise addition of 200 ml. of 20% sulfuric acid. The ether layer was separated and the water layer was extracted with three-100 ml. portions of ether. The combined ether layers were dried over Drierite and the ether was removed by distillation. The residual liquid was dried with phosphorus pentoxide and rectified to give 105 g. (44% yield) of ethyl heptafluoropropyl ketone, b.p. 82–83°, n_D^{20} 1.3030 and 70 g. of 2 $C_3F_7CO_2H.Et_2O$, b.p. 129°.

1,2-Epoxides. The perfluoroalkyl alkyl ketones were converted to the 1,2-epoxides using the procedure of McBee and Burton.[1,2] Bromination of the ketones in concentrated sulfuric acid yielded the α-bromo derivatives which upon reduction with an ethereal slurry of lithium aluminum hydride gave the α-bromoalcohols. Epoxidation of the bromoalcohols was accomplished with 50% aqueous sodium hydroxide. The yields of these reactions are reported in Table I.

Hydrolysis of 1,2-epoxides. 1,1,1,2,2,3,3-Heptafluoro-4,5-epoxyheptane (2 g.) was heated in a sealed tube with 6 ml. of 20% sulfuric acid at 105° for 60 hours. Upon cooling, a white solid was obtained which was recrystallized from benzene to yield 1,1,1,2,2,3,3,-heptafluoro-4,5-heptanediol, m.p. 88°. The diol gave a positive periodic acid test.[6]

Similar treatment of 1,1,1,2,2,3,3-heptafluoro-4,5-epoxyhexane and 1,1,1,2,2,3,3-heptafluoro-5-methyl-4,5-epoxyhexane gave oils which were the corresponding glycols; each of which gave a positive periodic acid test.

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Synthesis and Biological Activity of Some 6-(Substituted)thiopurines

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The effect of 6-(2-furfuryl)aminopurine (Kinetin) on cell division in tobacco wound callus tissue[2–4] as well as the effects of a series of 6-(substituted)aminopurines upon development in mosses[5,6] and more recently, the use of 6-(substituted)amino- and -thio-purines upon the inhibition of tentacle regeneration in hydra[7,8] have been reported. These results suggest a widespread importance of 6-(sub-

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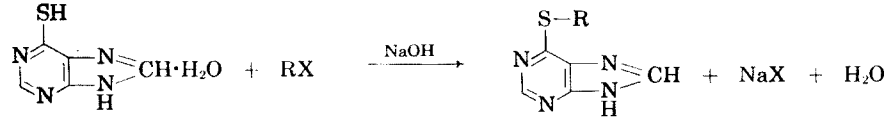
TABLE I

6-(SUBSTITUTED)THIOPURINES



Alkyl Halide Used	Reaction Conditions: Time, hrs.	Reaction Conditions: Temp., °C.	Yield, %	M.p., °C.	Empirical Formula	Analysis[a]: Calculated: Carbon	Analysis[a]: Calculated: Hydrogen	Analysis[a]: Found: Carbon	Analysis[a]: Found: Hydrogen	Biological Activity: Minimum conc'n for full inhibition, μ-mole/ml.	Biological Activity: Activity in terms of adenine
1-Iodohexane[d]	15	27	81	77	$C_{11}H_{16}N_4S$	55.90	6.82	55.40	7.22	0.01	500
1-Iodoheptane[d]	15	27	79	79–81	$C_{12}H_{18}N_4S$	57.56	7.25	57.93	7.62	0.004	1250
1-Iodooctane[d]	68	27	80	78–80	$C_{13}H_{20}N_4S$	59.05	7.62	58.99	7.18	0.004	1250
1-Bromodecane[d]	9	90	72	84–85	$C_{15}H_{24}N_4S$	61.60	8.27	61.23	8.82	0.01	500
1-Bromohexadecane[d]	12	90	76	101	$C_{21}H_{36}N_4S$	66.97	9.63	66.27	9.49	[f]	
1-Iodo-2-methylpropane[c,e]	(17 (12	27) 90)	49	199	$C_9H_{12}N_4S$	51.89	5.81	52.17	6.21	0.07	70
1-Iodo-3-methylbutane[e]	5[b]	27	50	126–127	$C_{10}H_{14}N_4S$	54.02	6.35	53.97	6.47	0.04	125
2-Iodoethylbenzene[d]	8	27	82	159–160	$C_{13}H_{12}N_4S$	60.91	4.72	60.32	4.72	0.01	500
3-Bromopropylbenzene[d]	12	27	68	142–143	$C_{14}H_{14}N_4S$	62.19	5.22	61.74	5.02	0.005	1000
5-Bromopentylbenzene[d]	17	90	57	98–100	$C_{16}H_{18}N_4S$	64.40	6.08	64.65	6.03	0.002	2500

[a] These compounds burned with difficulty in the carbon and hydrogen analysis. [b] Reacted an additional hour over steam-heat. [c] This alkyl halide was washed with mercury and redistilled immediately before use. [d] Reaction solvent: 50% alcohol. [e] Reaction solvent: water. [f] No inhibition at saturated solution (*ca.* 10 γ/ml.).

stituted)purines to processes of cell division and development.

6-(Alkyl)thiopurines were reported[8] to produce inhibitions roughly comparable to the corresponding 6-(alkyl)aminopurines in tentacle regeneration studies on hydra. In an effort to examine more completely this relationship between the sulfur and nitrogen analogs, a series of 6-(substituted)-thiopurines have been prepared and tested.

These 6-(substituted)thiopurines were synthesized through the usual procedure by preparing an alcohol or alcohol-water solution of 6-mercaptopurine, containing one equivalent of sodium hydroxide, and adding over a short period of time one equivalent of the appropriate alkyl halide or ω-phenylalkyl halide. In some cases, as indicated in Table I, heat was required to complete the reaction. The reaction products normally were recovered by removing a part of the alcohol solvent at room temperature using a jet of air. After one recrystallization from alcohol-water the products were analytically pure.

The biological activity presented in Table I is expressed as the minimum concentration of these compounds required to completely inhibit tentacle regeneration in hydra. The levels of inhibition obtained with these new 6-(substituted)thiopurines are equivalent to, or slightly greater than, the previously reported activities of the corresponding 6-(substituted)aminopurines.[8] The experimental techniques have been described elsewhere[9] and adenine has been adopted as a standard unit for evaluating these activities. Under the conditions used, adenine is given a value of 1 and 6-(2-furfuryl)aminopurine (kinetin) has a value of 18.

EXPERIMENTAL[10,11]

Starting materials. The alkyl halides, with the indicated exception, were obtained through normal commercial sources and were used without further purification.

5-Phenyl-1-pentyl bromide. This compound was prepared through the interaction of the corresponding alcohol and phosphorus tribromide, b.p. 117–120° (5 mm.); n_D^{25} 1.5325.[12]

6-(Substituted)thiopurines. The preparation of each of these compounds was effected in approximately the same manner, and the experimental conditions for each compound are presented in Table I. The general procedure was patterned after that of Elion, Burgi, and Hitchings[13] whereby a sample of 6-mercaptopurine was allowed to react with slightly more than one equivalent of sodium hydroxide until complete solution was effected (*e.g.* 250 mg. of 6-methylmercaptopurine in 31 ml. of 0.049 *N* NaOH). In the case of the less soluble alkyl halides, the aqueous solution was diluted to form a 50% ethanol-water mixture before adding an equivalent amount of the halogen compound. Shaking at room temperature was sufficient to cause reaction in some cases, wherein complete reaction was evidenced by the disappearance of the organic phase. With the higher members of the series, however, heating was required to effect the reaction within a reasonable time. This was done by placing the reaction mixture in a stainless steel bomb and heating for the appropriate time in an oven.

The reaction mixtures were usually water-white at the end of the reaction period. A portion of the alcohol then was removed, using an air jet, and the corresponding 6-(substituted)thiopurine crystallized in a colorless form. A yellow tint usually indicated some unreacted 6-mercaptopurine had co-precipitated with the reaction product, and this was further evidenced by the ultraviolet spectrum of the sample. The 6-(substituted)thiopurines have characteristic absorption maxima at about 281 mμ and 292 mμ in 95% ethyl alcohol solution whereas the unreacted 6-mercaptopurine has a strong absorption at 328 mμ.

Where necessary, the samples were recrystallized from an alcohol-water solution at alkaline *p*H to remove the unreacted 6-mercaptopurine.

Biological testing. The testing procedure was the same as that previously reported.[9]

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(9) Ham, Fitzgerald and Eakin, *J. Exp. Zool., in press.*

(10) All melting points were determined on a Fisher-Johns melting point block.

(11) Analyses were done by Mr. J. R. Claybrook of the Biochemical Institute, The University of Texas, and Drs. G. Weiler and F. B. Strauss, Microanalytical Laboratory, 164 Banbury Road, Oxford, England.

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