TABLE I

Isoflavthione (yield, %)	Ratio (g) isoflavone/P_2S_5	Mp, °C	Color[a]	Infrared data (cm^{-1})	λ_{max}^{Nujol}, mμ (ε)	Formula	Calcd, % C	Calcd, % H	Calcd, % S	Found, % C	Found, % H	Found, % S
2a (51)	0.50	189–191	Magenta prisms	1610, 1510, 1440	385 (17,200),[b] 282 (11,200),[b] 355 (10,700)[b,c]	$C_{14}H_{13}OS$	73.79	1.85	8.56	73.32	1.51	8.51
2b (184)	0.38	163–164	Magenta prisms	1770, 1615, 1600, 1510	381 (14,100), 276 (11,500)	$C_{15}H_{12}OS$	66.25	1.32	9.81	66.23	1.35	9.61
2c (85)	0.71	181–185	Purple rods	1760, 1600, 1546, 1505	373 (16,800), 278 (11,900)	$C_{16}H_{14}OS$	67.05	1.75	9.10	67.30	1.81	9.31
2d (38.4)	0.50	93 and 110–112 (dimorphous)	Purple-black rods	1770, 1620, 1602, 1550, 1520	377 (16,300), 285 (12,600)	$C_{16}H_{14}OS$	68.17	5.47	8.69	68.63	5.86	8.58

[a] The color is undoubtedly due to solid-state and association phenomena, for it was imparted only to very concentrated solutions and was unmeasurable in the region 400–600 mμ employing 10^{-3} to 10^{-5} *M* solutions of the isoflavthiones **2** in methanol, benzene, and hexane. [b] Benzene, not methanol, was the solvent. [c] Shoulder.

Synthesis of Potential Antineoplastic Agents. XVIII. Synthesis of New Alkylating Agents[1]

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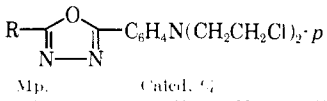
The preparation of a number of potential biological alkylating agents and related compounds is reported.

Experimental Section[3]

2-{*p*-[Bis(2-chloroethyl)amino]phenyl}-5-alkyl-1,3,4-oxadiazole.—Following the procedure of Ainsworth,[4] 2.0 g of *p*-[bis(2-chloroethyl)amino]benzhydrazide[5] was heated to reflux in 15 ml of the appropriate, freshly distilled, triethylorthoalkyl ester. The mixture was refluxed overnight and the excess orthoester was removed *in vacuo*. The oxadiazoles were recrystallized from ethanol–water and are shown in Table I.

TABLE I



R	Yield, %	Mp, °C	Calcd, % C	Calcd, % H	Calcd, % N	Found, % C	Found, % H	Found, % N
H[a]	55	68–70	50.36	4.58	14.69	50.56	4.60	14.62
CH_3	79	122–125	52.01	5.04	14.00	52.11	5.13	13.92
C_2H_5	84	109–113	53.14	5.45	13.37	53.35	5.58	13.12

[a] We should like to thank Dr. D. W. Alwani for assistance with this compound. This compound was inactive[7] against Walker carcinosarcoma.

1,4-Bis[(2-chloroethyl)thio]-2,3,5,6-tetrafluorobenzene. A mixture of 1 g of 1,4-bis[(2-hydroxyethyl)thio]-2,3,5,6-tetrafluorobenzene[6] and 5 ml of $SOCl_2$ was refluxed for 3 hr and the excess $SOCl_2$ was removed *in vacuo* to give 1.3 g of solid, mp 110–116°. Recrystallization from ethanol gave white needles, mp 114–116°.

Anal. Calcd for $C_{10}H_8F_4Cl_2S_2$: C, 35.40; H, 2.37; F, 22.40; Cl, 20.90; S, 18.90. Found: C, 35.30; H, 2.75; F, 22.06; Cl, 20.85; S, 18.90.

This compound was inactive[7] against Walker carcinosarcoma 256.

Diethyl [Bis(2-hydroxyethyl)amino]methylenemalonate.—A mixture of 5.07 g (0.048 mole) of bis(2-hydroxyethyl)amine and 10.5 g (0.048 mole) of diethyl ethoxymethylenemalonate in 60 ml of absolute ethanol was refluxed for 1 hr and the solvent was removed *in vacuo* to give an oil. Distillation gave 9.9 g (74%) of liquid, bp 58–61° (0.8 mm).

Anal. Calcd for $C_{12}H_{19}NO_6$: C, 52.35; H, 7.69; N, 5.09. Found: C, 52.09; H, 7.66; N, 4.89.

This compound was inactive[7] against Sarcoma 180 and L1210 lymphoid leukemia.

[Bis(2-hydroxyethyl)amino]methylenemalononitrile.—Using a similar procedure 8.6 g (98%) of solid, mp 86–87° (from ethanol), was obtained.

Anal. Calcd for $C_9H_{11}N_3O_2$: C, 53.03; H, 6.12; N, 23.19. Found: C, 52.86; H, 5.93; N, 23.32.

This compound was inactive[7] against L1210 lymphoid leukemia and S91 Cloudman melanoma and only very slightly (T/C = 61% at 500 mg/kg) active against Sarcoma 180.

Ethyl [Bis(2-chloroethyl)amino]methylenecyanoacetate.—A solution of 0.05 mole of ethyl ethoxymethylenecyanoacetate and bis(2-chloroethyl)amine (from 0.05 mole of its hydrochloride) in benzene was refluxed for 6 hr. Removal of the solvent *in vacuo* gave an oil which was chromatographed on acid-washed alumina and the solid eluted was recrystallized from ethanol to give 4.7 g (36%) of solid, mp 56–59°.

Anal. Calcd for $C_{11}H_{15}Cl_2N_3O_2$: C, 45.30; H, 5.32; N, 10.57; Cl, 26.74. Found: C, 45.31; H, 5.42; N, 10.52; Cl, 26.78.

This compound was inactive[7] against Walker carcinosarcoma 256. The hydroxyethyl analog of this compound[8] was inactive[7] against L1210 lymphoid leukemia and Friend virus leukemia and only slightly active (T/C = 65% at 62 mg/kg) against Heptoma 129. Preliminary attempts to convert this hydroxyethyl compound directly to the chloroethyl compound with $SOCl_2$ failed.

(8) A. A. Sandilli, W. F. Bruce, and T. S. Osdene, *J. Med. Chem.*, **7**, 68 (1964).

Synthesis of Potential Antineoplastic Agents. XIX. Some 5-(ω-Chloroacylamino)quinolines and 4- and 5-(ω-Chloroacylamino)isoquinolines[1]

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A number of 5-(ω-chloroacylamino)quinolines and 4- and 5-(ω-chloroacylamino)isoquinolines were prepared by reaction of

(1) (a) Part XVII: F. D. Popp, F. P. Silver, and D. W. Alwani, *J. Med. Chem.*, **10**, 481 (1967). (b) Supported in part by research grants from the American Cancer Society and from the National Cancer Institute.

(2) Abstracted in part from the M.S. Thesis of F. P. S.

(3) Analyses by Spang Microanalytical Laboratory, Ann Arbor, Mich. Melting points are taken in capillaries and are corrected.

(4) C. Ainsworth, *J. Am. Chem. Soc.*, **77**, 1148 (1955).

(5) R. C. Elderfield and T. K. Liao, *J. Org. Chem.*, **26**, 4996 (1961).

(6) J. Burdon, V. Damodaran, and J. Tatlow, *J. Chem. Soc.*, 763 (1964).

(7) Screening results were supplied by the CCNSC of the National Institutes of Health.

(1) (a) Part XVIII: F. D. Popp, F. P. Silver, and A. C. Noble, *J. Med. Chem.*, **10**, 986 (1967). (b) Supported in part by research grants from the American Cancer Society and from the National Cancer Institute. (c) A portion of this material is abstracted from the M.S. Thesis of F. P. S., Clarkson College of Technology, 1967.