liquid, which was further dissolved in Et_2O and filtered to remove an insoluble material. Removal of Et_2O from the filtrate afforded 0.65 g of liquid [ν max (neat) 1700 (broad), 1565, and 1355 cm^{-1}].

5-Nitro-2-thiadiazole Derivatives.—Standard techniques or methods[2] were used for the preparation of the compounds described below and the yields are based on the amount of **5** used.

3-{[(5-Nitro-1,3,4-thiadiazol-2-yl)methylene]amino}-2-oxazolidinone (6) was obtained in 6–15% yield and recrystallized from Me_2CO–EtOH as yellow crystals, mp 250–255°. *Anal.* ($C_6H_5N_5O_4S$) C, H, N, S.

1-{[(5-Nitro-1,3,4-thiadiazol-2-yl)methylene]amino}-2-imidazolidinone (7) was obtained in 13–23% yield and recrystallized from 50% aq EtOH as yellow crystals, mp 230–233°; nmr (DMSO-d_6): τ 2.1 (s, 1 H, CH=N), 2.3 (s, 1 H, NH), 5.8–6.7 (m, 4 H, CH_2CH_2). *Anal.* ($C_6H_6N_6O_3S$) C, H, N, S.

5-Nitro-1,3,4-thiadiazole-2-carboxaldehyde thiosemicarbazone (8) was obtained in 22% yield as a red solid; no suitable solvent for recrystallization was found, mp > 290°. *Anal.* ($C_4H_4N_6O_2S_2$) C, N, S, H: calcd 1.73; found 2.70.

2-Amino-5-(5-nitro-1,3,4-thiadiazol-2-yl)-1,3,4-thiadiazole (9).—The method reported previously[2] was used; 46% yield from **8**, recrystallized from EtOH–DMF, yellow crystals, mp 240° dec. *Anal.* ($C_4H_2N_6O_2S_2$) C, H, N, S.

Acknowledgment.—We wish to thank Dr. T. L. Chang (Stamford Laboratories, American Cyanamid Co.) for the mass spectral data and interpretation, Dr. G. A. Kemp and staff for *in vitro* and *in vivo* antibacterial assays, Mr. A. C. Dornbush and staff (Lederle Laboratories) for the *in vitro* antifungal assays, and Mr. G. S. Redin and staff (Lederle Laboratories) for their *in vivo* antibacterial assays.

New Compounds

Some Indole Derivatives[1]

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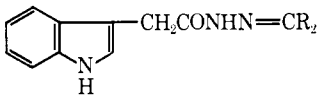
In connection with other work in progress in this laboratory it was necessary to prepare the compounds described in Tables I and II for screening purposes,

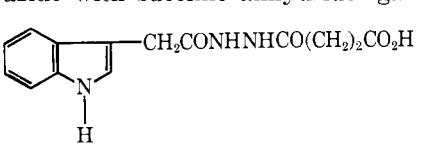
TABLE I



R_2CO	Mp, °C[a]	Yield, %	Formula	Analyses[b,c]
Androstanolone benzoate	161–162	90	$C_{36}H_{48}N_2O_3$	H, N[d]
Estrone 3-methyl ether	225–227	10[e]	$C_{29}H_{33}N_3O_2$	H, N[f]
Pregnenolone	252–254[g]	66[h]	$C_{31}H_{41}N_3O_2$	C, H
Testosterone benzoate	165–167	67[i]	$C_{36}H_{41}N_3O_3$	N
2-Nitrobenzaldehyde	174–175[j]	85	$C_{17}H_{14}N_4O_3$	C, H, N
4-Chloro-2-nitrobenzaldehyde	203–204	83	$C_{17}H_{13}ClN_4O_3$	C, H
Indole-3-carboxaldehyde	228–230[k]	77	$C_{19}H_{16}N_4O$	C, H, N

[a] Recrystallized from EtOH unless otherwise noted. [b] Analyses indicated within 0.3%. [c] All compounds exhibited expected spectra. [d] Calcd: C, 76.43. Found: C, 75.72. [e] Yield (93%) based on recovered steroid. [f] Calcd: C, 76.45. Found: C, 75.70. [g] Not recrystallized. [h] Yield (94%) based on recovered steroid. [i] Reaction time increased to 5 hr. [j] Reaction product is $C_{17}H_{14}N_4O_3 \cdot C_2H_5OH$, (mp 111–112°, analyses: C, H); the product was heated to 130° to give the product in the Table. [k] A. Alemany, M. Bernabe, C. Elorriaga, E. F. Alvarez, M. Lora-Tamayo, and O. Nieto [*Bull. Soc. Chim. Fr.*, 2486 (1966)] report mp 193°.

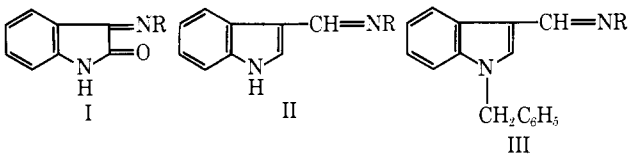
by condensing indole-3-acetic acid hydrazide with carbonyl compounds and by condensing isatin, indole-3-carboxaldehyde, and 1-benzylindole-3-carboxaldehyde with various amines. Reaction of indole-3-acetic acid hydrazide with succinic anhydride[2] gave I while



I

reaction of 3-aminocarbazole with 4-[bis(2-chloroethyl)-amino]-*o*-tolualdehyde gave the expected imine.[3]

TABLE II



Type	RNH_2	Mp, °C[a]	Yield, %	Formula	Analyses[b,c]
I	Sulfanilamide[l]	276–278	83	$C_{14}H_{11}N_3O_3S$	C, H
I	Sulfisoxazole[l]	237–239[d]	60	$C_{19}H_{16}N_4O_4S$	C, H
I	Sulfathiazole[l]	335–336	93	$C_{17}H_{12}N_4O_3S_2$	C, H
I	Sulfaguanidine[l]	296–297	44	$C_{15}H_{13}N_5O_3S$	H, N[e]
I	*p*-Sulfobenzoic acid *p*-hydrazide[l]	254–256	74	$C_{15}H_{11}N_3O_5S$	C, H
I	*p*-Toluenesulfon-*p*-hydrazide	207–209[f]	90	$C_{15}H_{13}N_3O_3S$	C, H
I	3-(2-Aminoethyl)-indole	174–176	66	$C_{18}H_{15}N_3O$	H[g]
II	*p*-Sulfobenzoic acid hydrazide	240–241	88	$C_{16}H_{13}N_3O_4S$	C, H
II	2-Nitrophenyl-hydrazine	224–226[d]	93	$C_{15}H_{12}NO_2$	H[h]
II	D-Cycloserine	223–224[j]	56	$C_{12}H_{11}N_3O_2$	H, N[i]
III	Sulfathiazole	192–193[k]	51	$C_{25}H_{20}N_4O_3S_2$	C, H
III	Sulfanilamide	156–158	53	$C_{22}H_{19}N_3O_2S$	C, H

[a] Recrystallized from EtOH unless otherwise noted. [b] Analyses indicated within 0.3%. [c] All compounds exhibited expected spectra. [d] Not recrystallized. [e] Calcd: C, 52.47. Found: C, 51.99. [f] M. P. Cava, R. O. Little, and D. R. Napier [*J. Amer. Chem. Soc.*, **80**, 2257 (1958)] report mp 190–200°. [g] Calcd: C, 74.72. Found: C, 74.11. [h] Calcd: C, 64.28. Found: C, 63.78. [i] Calcd: C, 62.87. Found: C, 62.18. [j] Triturated with hot EtOH–EtOAc. [k] From EtOAc. [l] Inactive (T/C = 83 – 102%) at 400 mg/kg against L-1210 lymphoid leukemia.

(1) This work was supported by a research grant (CA 10345) from the National Cancer Institute, U. S. Public Health Service.

(2) F. W. Short and L. M. Long, *J. Heterocycl. Chem.*, **6**, 707 (1969).

(3) F. D. Popp, *J. Med. Chem.*, **7**, 210 (1964).

Experimental Section[4]

Condensations with Indole-3-acetic Acid Hydrazide.—Equimolar quantities of indole-3-acetic acid hydrazide and the appropriate carbonyl compounds were dissolved in a minimum of EtOH and heated on a steam bath for 30 min. After cooling, and in some cases standing for several days the products described in Table I were obtained by filtration.

Condensations with Amines.—In a similar manner equimolar quantities of isatin, indole-3-carboxaldehyde, or 1-benzylindole-3-carboxaldehyde were allowed to react in EtOH with the appropriate amines to give the compounds in Table II.

Indole-3-acetic Acid Hydrazide and Succinic Anhydride.—A mixture of 1.89 g (0.01 mole) of indole-3-acetic acid hydrazide and 1.00 g (0.01 mole) of succinic anhydride in Me_2CO (5 ml) was refluxed for 15 min and allowed to stand overnight at room temperature. Filtration gave 2.30 g (80%) of I, mp 203–204° from EtOH; ir(KBr): 3400, 3240, 2945, 1700 (broad), 1610 cm^{-1}. *Anal.* ($C_{14}H_{15}N_3O_4$): C, H.

Tolualdehyde Mustard and 3-Aminocarbazole.—A mixture of 1.82 g (0.01 mole) of 3-aminocarbazole and 2.60 g (0.01 mole) of 4-[bis-(2-chloroethyl)amino]-*o*-tolualdehyde was refluxed in EtOH to give 3.22 g (76%) of imine, mp 188° from EtOH. *Anal.* ($C_{24}H_{23}Cl_2N_3$): N.

(4) Analyses by Spang Microanalytical Laboratory, Ann Arbor, Mich. All melting points were taken in capillaries and are corrected.

Studies of the Chemistry of Azole Derivatives. XII. Possible Anticonvulsant Thiazolo[3,2-*a*]benzimidazoles

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In view of the potent pharmacological activity of a large number of heterocyclic thioureas[1-3] additional thioureidothiazolo[3,2-*a*]benzimidazoles were synthesized. These compounds have been tested for anticonvulsant activity (Table I).

Experimental Section

2-Aminothiazolo[3,2-*a*]benzimidazol-3-(2*H*)-one.—A solution of thiazolo[3,2-*a*]benzimidazol-3(2*H*)-one[4] (5 g) in AcOH (20 ml) was slowly added at 0° to a solution of PhN_2Cl with stirring. The mixture was kept for 1 hr at (0–5°) and the product obtained was crystallized from EtOH. The azo compound (5 g) was dissolved in hot EtOH (25 ml). A solution of $Na_2S_2O_4$ (25 g) in H_2O (50 ml) was added and the mixture was refluxed for 30 min and then cooled. The amino compound obtained was recrystallized from EtOH, yield 57%, mp 185°. *Anal.* ($C_9H_7N_3S$): N, S.

Synthesis of Thioureas.—Equimolecular quantities of 2-aminothiazolo[3,2-*a*]benzimidazol-3(2*H*)-one and an aryl isothiocyanate were refluxed in abs EtOH for 5 hr and cooled. The precipitated thioureas were crystalized (C_6H_6). The hydrochlorides were prepared in Et_2O solution.

Acknowledgment. The author is thankful to Dr. Kartar Singh, Director, Defence Science Laboratory for encouragement and Dr. H. K. Acharya for providing facilities.

(4) Part XI: J. M. Singh, *J. Med. Chem.*, **12**, 962 (1969).

A Reinvestigation of the Reaction of Monosodium Urea with Various Substituted Pyrazinecarboxylate Esters

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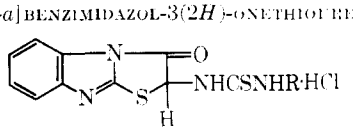
We have reinvestigated the reaction of monosodium urea with methyl 3,5-diamino-6-chloropyrazinecarboxylate[1] as well as the 5-methylamino analog and found that a small amount of the desired *N*-carbamoylpyrazinecarboxamide is produced in each case. The products were isolated by liquid–liquid partition chromatography (llpc) and shown to be the desired compounds by comparison of ir, mass spectrum, tlc,

TABLE I

2-AMINOTHIAZOLO[3,2-*a*]BENZIMIDAZOL-3(2*H*)-ONETHIOUREA HYDROCHLORIDES



No.	R	Formula	Mp, °C	Yield, %	Activity	LD_{50} (toxicity)
1	Ph	$C_{16}H_{13}ClN_4S_2$	220–221	60	++	200
2	*o*-MePh	$C_{17}H_{15}ClN_4S_2$	195–197	65	++	260
3	*p*-MePh	$C_{17}H_{15}ClN_4S_2$	175–177	59	++	240
4	*m*-MePh	$C_{17}H_{15}ClN_4S_2$	198–200	58	++	280
5	*o*-BrPh	$C_{16}H_{12}ClBrN_4S_2$	210	60	+++	300
6	*p*-BrPh	$C_{16}H_2ClBrN_4S_2$	165–166	65	+++	280
7	*m*-BrPh	$C_{16}H_{12}ClBrN_4S_2$	189	58	+++	290
8	*o*-ClPh	$C_{16}H_2Cl_2N_4S_2$	202–204	62	++++	300
9	*p*-ClPh	$C_{16}H_{12}Cl_2N_4S_2$	211	59	++++	350
10	*m*-ClPh	$C_{16}H_{12}Cl_2N_4S_2$	215	64	+++++	330

[a] All new compounds were analyzed for N, S and the analytical values were within ±0.4% of the calculated values. [b] Mice were used for the experiments for anticonvulsant activity following the method in Putnam and H. H. Merritt, *Science*, **85**, 525 (1937). A +++++ rating was given if the convulsive threshold is elevated more than 60 ma, ++++ is raised to 60 ma, +++ is raised by 40 ma, ++ is raised by 15–20 ma and + is raised by 10–15 ma, 3.5 hr after treatment.

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(2) T. N. Ghosh and A. R. Chaudhuri, *J. Indian Chem. Soc.*, **28**, 268 (1951).
(3) H. F. Kantmann and P. Schultz, *Arch. Pharm.*, **273**, 22 (1935).

(1) J. William Hanifin, Rosemary Capuzzi, and Elliott Cohen, *J. Med. Chem.*, **12**, 1102 (1969).