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

J. M. SINGH

Defence Science Laboratory, Delhi-6, India

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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-aminothiazole[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.

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

J. WILLIAM HANIFIN, ROSEMARY CAPUZZI, AND ELLIOTT COHEN

Organic Chemical Research Section, Lederle Laboratories, A Division of American Cyanamid Company, Pearl River, New York 10965

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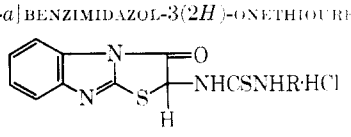
We have reinvestigated the reaction of monosodium urea with methyl 3,5-diamino-6-chloropyrazinecarboxylate[1] as well as the 5-methylamino analog and found that a small amount of the desired *N*-carbamoylpyrazinecarboxamide is produced in each case. The products were isolated by liquid–liquid partition 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	$C_6H_{13}ClN_4S_2$	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	61	++++	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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